THE UNIVERSITY OF HULL

Parallel Kinetic Resolutions
using Active Esters

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by

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Abstract

Obtaining enantiomerically pure compounds is of major importance in modern organic chemistry; the resolution of racemic compounds is a very useful and practical method of achieving this. Parallel kinetic resolutions are an interesting variation on the more classical resolution methods; this method has been recently introduced to the scientific community by Vedeejs and there are currently very few examples of successful parallel kinetic resolutions in the literature.

The aim of the project, outlined in this report, was to investigate the use of parallel kinetic resolution methodology to resolve racemic carboxylic acids and secondary alcohols. This aim was achieved and in total four distinct parallel kinetic resolution methods were developed; one for the resolution of carboxylic acids, one for the resolution of secondary alcohols, and two that can be used to resolve either carboxylic acids or secondary alcohols. The development process is described for each of these distinct resolutions and their relative scope and limitations are discussed. This report also details the possible reasons for the levels of selectivity found in these reactions, and discusses what effect the reaction conditions have on the level of stereocontrol. Similarities between all four of the resolutions are described, and the possibility of a generic stereoselective pathway is discussed.

This report however is not limited only to findings directly related to parallel kinetic resolutions; it also encompasses all findings from the above mentioned studies. As such, it also describes an unusual observation; the fact that the sign of optical rotation for the common resolving agent 4-isopropyl oxazolidinone is solvent dependant. The discovery and further exploration of a method for synthesising a range of optical pure secondary alcohols from the commercial available (S)-enantiomer of 1-(2-bromo-phenyl)-ethanol is also described. An interesting method for the determination of enantiomeric excess of carboxylic acids is also discussed.
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# Abbreviations

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<tr>
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<td>Ac</td>
<td>Acetyl</td>
</tr>
<tr>
<td>Ar</td>
<td>Aryl</td>
</tr>
<tr>
<td>BINAP</td>
<td>2,2’-Bis(diphenylphosphino)-1,1’-binaphthyl</td>
</tr>
<tr>
<td>Bn</td>
<td>Benzyl</td>
</tr>
<tr>
<td>Bu</td>
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<td>CDI</td>
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</tr>
<tr>
<td>DCC</td>
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<td>DMAP</td>
<td>4-Dimethylaminopyridine</td>
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<td>Dimethyl sulfoxide</td>
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<tr>
<td>KR</td>
<td>Kinetic resolution</td>
</tr>
<tr>
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</tr>
<tr>
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<td>Methyl</td>
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<td>Parallel kinetic resolution</td>
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</tr>
<tr>
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<td>tert-Butyldimethylsilyl</td>
</tr>
<tr>
<td>THF</td>
<td>Tetrahydrofuran</td>
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Chapter 1

Literature Review

Chirality was first introduced to the scientific community in 1848 by Pasteur when he carried out his influential work with the sodium ammonium salts of tartaric acid 1.\(^1\) He showed that the tartrate salts had two hemihedral\(^2\) crystal forms and that upon separating and dissolving them, two optically active solutions were obtained.\(^3\) From these observations, Pasteur speculated that the structure of tartaric acid 1 was asymmetric and hence two different (enantiomeric) variations of tartaric acid 1 must exist that are non super-imposable mirror images of each other.\(^4\)

![Figure 1.1: Both enantiomers of Tartaric acid 1.](image)

The work of both Le Bel and van’t Hoff in 1874 helped to explain Pasteur’s earlier observations when they separately concluded that the carbon atom must exist in a three dimensional tetrahedron arrangement when bound to four other atoms.\(^5,6\) These early ideas and observation still form the foundation of modern day chirality and stereochemistry.

Pasteur was also the first to notice the biological implication of these different enantiomers, during his study of tartaric acid 1. He found that (2\(R\),3\(R\))-tartaric acid 1 (Figure 1.1) was digested by the mould *Penicillium glaucum*, whilst its corresponding enantiomer (2\(S\),3\(S\))-1 was not.\(^1\) We now know that this phenomenon is due to the fact that biological systems are themselves chiral, as a result of this they will interact differently with each enantiomer of a chiral compound. This abundance of chirality in nature is due in part to the incorporation of amino acids in almost all biological systems, as all amino acids (with the exception of glycine) are chiral. For all of these amino acids the (\(S\))-enantiomer is the only one found in natural biological systems.\(^7\)
Tartaric acid 1 is not the only compound whose different enantiomers interact differently with biological systems; for example both enantiomers of the compound limonene 3 exist in nature. The (R)-enantiomer of limonene 3 is from oranges and gives them their characteristic smell, whereas the (S)-enantiomer interacts with the receptors in the human nose differently and we detect the odour of lemons.\(^8\) This of course means that chirality has to be taken into account whenever synthesising perfumes and other odorants as well as flavourings.

Medicinal chemistry however is the area where it is the most important to use the correct enantiomer. Due to the chiral nature of proteins (as they are made of the (S)-enantiomers of amino acids 2) the compounds that interact with them in the most desirable ways are often also chiral themselves, hence many drugs are chiral. The other enantiomer of these drugs however will often interact with the human body in a completely different fashion. The drug (S)-dopa 4 for example is used to help treat people with Parkinson’s disease,\(^9\) this drug is a chiral amino acid that helps to restore nerve function; its other enantiomer (R)-dopa 4 however is toxic.\(^7,10\) As a result dopa 4 has to be used as the single (S)-enantiomer.
The importance of chirality however is not just limited to human biochemistry; all aspects of nature are chiral even seemingly simple creatures such as bacteria. Because of this chirality, it is important in any man made chemical that will interact with biological systems; therefore the agricultural industry also uses enantiomerically pure compounds, as pesticides and herbicides.\(^1\) The importance of using enantiomerically pure compounds is not just limited to biochemistry, as our understanding of chirality increases more uses for it are being discovered; for example in the area of materials chemistry liquid crystal, display devices are being designed that use enantiomerically pure compounds.\(^1\)

The need to obtain single enantiomers of chiral compounds is of great importance to modern day organic chemistry. There is however two fundamental problems with trying to do this, firstly any reaction that starts with achiral materials to give a chiral product will always yield a racemic mixture (exact equal mixture of both enantiomers). Secondly, a pair of enantiomers possess identical physical properties (apart from how they interact with polarised light), this means that their separation is impossible using conventional organic chemical methods.

Numerous methods have been developed all with the aim of obtaining single enantiomers of chiral compounds, by finding ways around the two fundamental problems mentioned above. Although this work has been carried out by multiple research groups across the world for many years all of the different methods approximately fit into one of the following three categories: chiral pool; asymmetric synthesis; and resolution. It is these three different categories that this review shall look at in turn.

The first area we shall look at is the “chiral pool”; as mentioned earlier everything in nature is chiral, so simple harvesting of these compounds gives a large array of enantiomerically pure reagents; this group is collectively called the chiral pool. The two most common groups of enantiomerically pure compounds that can be obtained from nature are sugars and amino acids. An example of this is \((S)\)-alanine \(^5\), this is a simple amino acid and it can be obtained from vegetable proteins by hydrolysing them.\(^7\)
This method is by far the most convenient way of obtaining single enantiomers of a compound; however the “chiral pool” is limited, not all compounds that modern day chemistry requires exist in nature. The other common problem is that often only one enantiomer will exist in nature, leading to the term natural and unnatural enantiomers of a compound. One way in which the “chiral pool” can be used is to obtain enantiomerically pure compounds that can undergo chemical modification to give the required product. For example the natural occurring amino acid (R,S)-threonine 6 can be converted through multiple steps into the bacteriocide thienamycin 7 (Scheme 1.1).  

![Scheme 1.1: (R,S)-Threonine 6 to thienamycin 7.](image)

There are a range of interesting reactions that can be carried out on chiral compounds, for example the chiral centre can be inverted using the Appel reaction,\(^1\)\(^2\)\(^3\) the Mitsunobu reaction\(^4\)\(^5\) or by simple nucleophilic substitution.\(^6\) Alternatively the configuration can be retained while converting the functional group directly bound to the chiral centre using a Fleming-Kumada oxidation.\(^7\)\(^8\) However, great care must be taken not too accidentally racemize the chiral centre during any modifications to the molecule, this can be especially problematic if there is an acid proton bound to the chiral centre.

It is even possible to obtain more complex compounds from nature, an example of this is the very complex compound taxol 8 (Figure 1.6) that contains multiple chiral centres. This possible cancer chemotherapeutic drug (taxol 8) can be extracted from the bark of the Pacific Yew (Taxus berifolia);\(^9\) however, this is not done frequently due to problems with the harvesting and extraction process. As a result of this taxol 8 has been the target compound of some research groups;\(^10\)\(^11\) this is an area of chemistry known as natural product synthesis, where research groups try to make naturally occurring
compounds that are too problematic to regularly extract from the organism that they are found in.

![Taxol 8](image)

**Figure 1.6**: Taxol 8.

Although a large array of homochiral pure compounds can be obtained from the “chiral pool”, and further modification to these compounds can yield an even larger array, these compounds cannot satisfy all the requirements of the modern day chemistry. As such other more complex ways of obtaining enantiomerically pure compounds are constantly being explored by numerous research groups across the world.

The second method of obtaining enantiomerically pure compounds that this report shall describe is the category known as asymmetric synthesis, the basis of this method is to take an achiral (prochiral) compound and carry out a reaction on it to produce one enantiomer of a chiral compound. Not any achiral chemical can be used for this method, only a prochiral compound can be. A molecule is prochiral if it is firstly achiral, and secondly contains a carbon atom that is attached to two different groups and two groups that are identical. Meaning that a carbon atom is a prochiral centre if its substituent fits the pattern $C_{abc}$, this can be seen easily in the prochiral compound phenylmethanol 9 (Figure 1.7). In this example the carbon atom is bound to two different groups, a phenyl ring and a hydroxyl group as well as two identical groups the hydrogen atoms, meaning that it is prochiral.

![Prochiral compounds](image)

**Figure 1.7**: Prochiral compounds.

Benzaldehyde 10 (Figure 1.7) is also prochiral, the two different groups being the phenyl ring and the hydrogen atom, while the two identical groups are the faces of
the carbonyl group. Although the carbonyl group is clearly only one group the carbon atom is bound to it twice (through a double bond) and hence benzaldehyde 10 still fits the criteria of being a prochiral molecule. Perhaps an easier way to think of a prochiral molecule, is one that can become chiral in one simple step, by replacing one of the two identical carbon bonds with a new bond. So phenylmethanol 9 can become chiral by replacing one of the hydrogen atoms with a methyl group to form 1-phenylethanol (S)-11, while benzaldehyde 10 can become chiral by adding a methyl group and breaking one of the bounds of the carbonyl group to form 1-phenylethanol (S)-11 (Scheme 1.2).

![Scheme 1.2: Prochiral to chiral.](image)

As stated earlier, any reaction that starts with achiral materials to give a chiral product will always yield a racemic mixture; therefore at least one reagent used in the reaction must be enantiomerically pure. The standard method of asymmetric synthesis is to take a prochiral compound such as phenyl-acetic acid 12 and react this with an enantiomerically pure compound (a chiral auxiliary) to form an optical pure compound such as 13 (Scheme 1.3). Normal achiral reagents can then be used to replace one of the two identical groups at the prochiral centre, in this example one of the hydrogen atoms is replaced with a methyl group. This will generate an unequal ratio of two different products 14a and 14b, each made by replacing a different hydrogen atom, as each product is formed through a different energy pathway, and the nature of these two pathways is governed by the chiral auxiliary used.

![Scheme 1.3: Generic method for asymmetric synthesis.](image)

Compounds 14a and 14b will always be diastereoisomers of each other and hence will have different physical properties and can be separated using classical methodology. The final step in this process is to remove the chiral auxiliary from 14a
and 14b to yield the required enantiomerically pure products (S)-15 and (R)-15 in this example. There are numerous difficulties in this method; firstly a chiral auxiliary (an enantiomerically pure compound) is required, and this is usually obtained directly or with subsequent modification from the “chiral pool,” for the reaction to become viable however this source of chirality must be readily available. The chiral centre (or centres) of the chiral auxiliary must be chemically robust enough not to be racemized during any of the steps of the synthesis. For a high yield of the required enantiomer of the product to be formed the chiral auxiliary also needs to be highly stereo-directing when the new chiral centre is formed (in the step where 14a and 14b are formed from 13 in Scheme 1.3). Finally the removal of the chiral auxiliary has to be achievable using reaction conditions that are mild enough not to racemize the newly formed chiral centre(s).

One very well known name in the area of asymmetric synthesis is Evans; he has studied the formation of chiral carboxylic acids from enolates. To achieve this goal, Evans attached a prochiral carboxylic acid such as 16 to an amine (or amide) based chiral auxiliary to form an amide (or imide) with the general structure of 17. Deprotonation of this compound yielded one of two enolates, the E or the Z isomer of 18 (Scheme 1.4), it is obviously very important to have a very high level of selectivity at this stage so that only one isomer is being dealt with. Evans has shown that this high level of enolate selectivity is relatively easy to obtain, if the simple (achiral) amine pyrrolidine is used to form 19 and LDA is used as the base the Z-enol 20 is almost exclusively formed (ratio >97 : 3 Z- to E-enolate, Scheme 1.4). The Z-enol is presumably preferentially formed as its transition state is less strained as the methyl group is furthest away from any groups bound to the nitrogen atom.

![Scheme 1.4: Enol formation.](image-url)
With the Z-enol in hand, Evans next had to consider how to orient the R group with the chiral information on with respect to the rest of the molecule. There are two distinct configurations of this, the W-form with the chiral group pointing towards the oxygen of the carbonyl group, or the U-form with the chiral group pointing away from the oxygen of the carbonyl group (Figure 1.8). Again it was very important that only one of these forms is created in the reaction, Evans’ tailor made his chiral auxiliaries so that they would contain a group able to coordinate with the metal bound to the oxygen of the enolate. By varying where this coordinating group was on the chiral auxiliary he could lock his compounds in either the W- or U-conformation. To lock the compound in the W-conformation Evans used the chiral auxiliaries based around \((S)-22\), a hydroxyl group has been included on the chiral ligand in this case. This enables both oxygen atoms to coordinate once deprotonation has occurred, it should be noted that two equivalents of a base is needed in this case to form the enolate.

The chiral auxiliary \((S)-24\) could be used to ensure that the U-conformation was always formed, as this auxiliary included a coordinating group on the opposite side to the chiral centre. The lone pair of the oxygen of the carbonyl group in this case presumably coordinates with the metal ion bound to the enolates oxygen atom. With the Z-enolate in hand and in a constant conformation the stereo-directing step could finally be carried out; here an electrophile (normally an alkyl halide) was added to the enolate. When this reaction was carried out using butyl iodide as the electrophile with the enolate \((S)-26\) (in the W-conformation) addition occurred primarily on the sterically less hindered face of the carbon-carbon double bond (the opposite side to the chiral group) to yield \((R,S)-27\) (Scheme 1.5). The overall selectivity of this reaction was
very high (diastereoisomeric ratio 94 : 6), this implies highly selective enolate formation and good conformational control as well as a final highly stereo-selective addition step.

![Scheme 1.5: Addition of butyl iodide to enolate W-(S)-26.]

Evans has tested a variety of different alkyl halides and has found that increasing their steric bulk makes the reaction more selective (diastereoisomeric ratio of 97 : 3 for isobutyl iodide);\textsuperscript{26} this is presumable due to the extra steric bulk making the disfavoured approach even higher in energy. When the electrophile 3-bromo-1-propene was used comparable levels of selectivity were obtained (diastereoisomeric ratio of 96 : 4), clearly indicating that the reaction has a robust nature. The required carboxylic acid (\(R\))-\textsuperscript{29} is obtainable by removal of the chiral auxiliary (Scheme 1.6). Evans has shown that this two step process occurs without any noticeable levels of racemization.\textsuperscript{24}

![Scheme 1.6: Hydrolysis of amide (R,S)-27.]

Evans is better known however for his work with the U-conformation of enolates using chiral auxiliaries such as (\(S\))-\textsuperscript{24,28,29,30} the work he carried out with these auxiliaries has had such an impact that they are often referred to as “Evans Oxazolidin-2-ones.”\textsuperscript{31,32,33,34} These oxazolidin-2-ones can be prepared from their appropriate amino acids (\(S\))-\textsuperscript{30} by reduction to an amino alcohol (\(S\))-\textsuperscript{31} and the ring closed using diethyl carbonate (Scheme 1.7).\textsuperscript{23} The main advantage of this synthetic strategy is that the starting material is an amino acid, which is readily available from nature in an optical pure form. This oxazolidin-2-one was easily attached to the prochiral carboxylic acid in very high yields (86-99\%, Scheme 1.7), by first converting the carboxylic acid into an acid chloride using thionyl chloride and then reacting this with the deprotonated oxazolidin-2-one (formed from (\(S\))-\textsuperscript{24} and \(n\)-BuLi).
Scheme 1.7: Synthesis of oxazolidin-2-one (S)-24.

Evans showed that the enolate of (S)-33 could be formed by simply reacting it with an appropriate base (often LDA), as mentioned earlier the Z-enol was formed in the U-conformation. In a similar fashion to the W-conformations mentioned above addition of an alkyl halide primarily occurred on the opposite face to the chiral group, remarkably however higher levels of selectivity were obtained. When the sterically less demanding ethyl iodide was used, a diastereoisomeric ratio of 96 : 4 was obtained, while the large 3-bromo-2-methylpropene gave a diastereoisomeric mixture of 98 : 2, this could be increased to an amazing high diastereoisomeric ratio of 120 : 1 when benzyl bromide is used as the electrophile (Scheme 1.8). Evans theorised that these improved levels of selectivity were due to the different nature of the W- and U-conformations, the chiral group of the auxiliary is closer to the carbon-carbon double bond in the U-conformation and hence logical it should work better.

Scheme 1.8: Addition of benzyl bromide to the enolate of (S)-33.

Further investigation by Evans of alternative oxazolidin-2-ones showed that the size of the 4-substituent of the oxazolidin-2-one appeared to be rather unimportant, with methyl, isopropyl and phenyl substituent giving similar levels of diastereoselectivity. This observation is rather counter intuitive, as one would
expect larger groups to provide more steric hindrance and hence give better results, presumable however any steric bulk at this position is sufficient. This did however imply other benefits as the chiral auxiliary could therefore be chosen for alternative reasons, such as cost or its crystalline properties. Due to the success of these chiral auxiliaries, variations of the generic oxazolidin-2-ones structure have been widely investigated, for example the oxazolidine-2-thiones derivatives.\textsuperscript{37,38,39}

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{figure19.png}
\caption{4- Substituted oxazolidin-2-ones and oxazolidine-2-thiones.}
\end{figure}

One flaw with the use of oxazolidin-2-ones as chiral auxiliaries however is that their removal after the asymmetric synthetic step has been carried out is slightly problematic. This is due to a competitive side reaction were the carbonyl group of the oxazolidin-2-one is cleaved to give the so called \textit{endo}- product \textbf{38} (Scheme 1.9).\textsuperscript{40}

Although this occurrence is a problem in the asymmetric synthesis being carried out by Evans it does lead to an interesting product \textbf{38}, which can easily contain two defined chiral centres with a variety of different \textit{R}$_1$ and \textit{R}$_2$ groups. This reaction pathway has been explored\textsuperscript{41} and exploited in the synthesis of numerous natural products.\textsuperscript{42,43,44}

\begin{scheme}
\centering
\includegraphics[width=0.5\textwidth]{scheme19.png}
\caption{Endo- and exo- cleavage of oxazolidin-2-one adducts.}
\end{scheme}

Kanomata has shown a simplistic way of reducing and in some cases completely eliminating this side reaction by the addition of an excess of dimethyl carbonate along with sodium methoxide.\textsuperscript{45} This presumably works by simply moving the equilibrium of the reaction over to the required \textit{exo}-product, as the dimethyl carbonate would be formed as a by-product in the \textit{endo}-pathway. Therefore including a large excess of this product in the starting mixture will make this \textit{endo}-pathway less favoured. Kanomata has shown this process to work with a variety of different groups bound to the carbonyl group and with no loss of chirality throughout the process (Scheme 1.10).
Scheme 1.10: Kanomatas endo-cleavage of oxazolidin-2-one adducts.

Davies has also investigated the problems associated with endo-cleavage of oxazolidin-2-one adducts; however, he has taken a very different approach at attempting to solve this problem. Instead of investigating the reaction conditions used to remove the oxazolidin-2-one, he has developed different auxiliaries closely resembling Evans’ oxazolidin-2-ones which are resistance to endo-cleavage. His first generation of such auxiliaries were of the general structure \((R)-41\) (Figure 1.10), the increased steric hindrance around the ring in these auxiliaries was successful in stopping the endo-reaction pathway.\(^{46}\) As their structure was so similar to the traditional oxazolidin-2-one they continued to give approximately the same results as Evans’ had obtained when used in an asymmetric synthetic reaction. The main drawback of adducts like \((R)-41\) is their somewhat long winded synthesis.\(^ {47}\)

Figure 1.10: Davies auxiliaries.

Davies next generation of sterically hindered oxazolidin-2-ones had the general structure of \((S)-42\) (Figure 1.10); the advantage of these compounds is that they are readily synthesised from amino acids.\(^ {48}\) This synthesis is almost identical to that of the original Evans oxazolidin-2-ones apart from the initial reduction reaction of the amino acid is replaced with an addition of methyl groups using MeMgI (Scheme 1.7). These adducts were found to mimic Evans traditions oxazolidin-2-ones, apart from they did not readily undergo endo-cleavage presumably due to their increased steric hindrance around the ring system.\(^ {49,50,51}\)

One interesting difference between the C(5)-substituted adducts and Evans original oxazolidin-2-one is that they gave slightly higher levels of selectivity, for example in the simple addition of MeI to Davies’ adduct \((R)-45\) higher levels of
selectivity were obtained than when the same reaction was carried out on Evans adduct \((R)-43\) (Table 1.1). Further investigation showed that the selectivity Davies had obtained using adduct \((R)-45\) was more in line with the adduct \((R)-47\) which had the much larger \(t\)-Bu group. Davies has theorised that this is due to the methyl groups on his adduct \((R)-45\) forcing the \(i\)-Pr to point away from their position, hence mimicking the size of the \(t\)-Bu group.\(^{53}\) Other groups have also looked at similar sterically hindered oxazolidin-2-ones for the same reasons and with similar levels of success as Davies. These including Einhorn who has investigated Grignard addition to amino acids to generate substituted oxazolidin-2-ones,\(^{54}\) and Seebach who has studied oxazolidin-2-ones with phenyl groups in place of Davies’ methyl groups.\(^{55,56,57,58}\)

![Scheme 1.11](image)

**Scheme 1.11:** Comparison between Evans and Davies oxazolidin-2-ones.

An interesting variation on asymmetric synthesis is the use of a chiral reagent instead of having a chiral auxiliary that needs to be first bound and later removed. The chiral nature of this reagent means that it will prefer to react with one section of the prochiral molecule over the other, for example it will prefer to remove one of the two identical hydrogen atoms or react on one face of a prochiral compound. The advantage of this method is that the reagent does not need to first be attached to the prochiral molecule or removed at the end of the reaction process. The disadvantage of this approach is that it will always give a mixture of enantiomers, which will have identical physical properties and therefore the enantiomeric excess of the final product will be directly related to the selectivity of the reaction. While for the above mentioned asymmetric reactions a pair of diastereo-isomers were always the product, which have different physical properties and hence a completely enantiomerically pure reagent is always accessible using this process.
One compound that has been used frequently as a reagent in asymmetric synthesis is (-)-sparteine 49,59 this diamine can been found in the plants belonging to the Leguminosae family.60 The lone pairs on the nitrogen atoms of (-)-sparteine 49 allow it to coordinate with metal atoms, and as such it is normally used in conjunction with a metal derived base, such as s-BuLi.61,62,63 These two reagents react together to form the active reagent, a chiral base, this can then be used to selectively remove one proton from a prochiral molecule.64,65 For example, if this chiral base [s-BuLi and (-)-sparteine 49] is used to deprotonate the amide 50 it will preferably remove the (S)-hydrogen atom to form (S)-51 (Scheme 1.12) with very high levels of selectivity.66 This selectivity has been shown to be a kinetic element of the reaction by Wiberg, who has used molecular modelling to show that the transition state that leads to (S)-51 is more stable than its counter part [which would lead to (R)-51] by 3.1 kcal/mol.67 This is presumed to simply be due to less steric hindrance in the more stable transition state, that leads to (S)-51.

Scheme 1.12: Using (-)-sparteine 49 as a chiral reagent.

A logical extension of chiral reagent based asymmetric synthesis is enantioselective catalysis, with this method the chiral compound is only used in a catalytic amount instead of a full molar equivalent. This method has the obvious advantage of needing less of the chiral compound for the amount of the final product generated and is therefore more commercially viable.68,69 Perhaps a general way of carrying out a enantioselective catalysis reaction is to use a transition metal with at least one chiral ligand bound to it, this complex can then act as a template that allows a classical organic reaction to occur in an enantioselective fashion.70 Numerous
transitions metals have been used\textsuperscript{71} with a large variety of different chiral ligands,\textsuperscript{72} achieving some excellent levels of selectivity even on a large industrial scale.\textsuperscript{73}

One ligand that has shown particular promise is BINAP \textsuperscript{52} (Figure 1.12),\textsuperscript{74,75} this diphosphine does not contain a stereogenic carbon atom but possesses axial chirality,\textsuperscript{76} simple steric hindrance inhibits free rotation around the bond binding the two naphthyl rings together, so the compound is configurationally stable.\textsuperscript{76} One of the first reported synthesis of a single enantiomer of BINAP \textsuperscript{52} was in 1980,\textsuperscript{77} however since that time methods have been improved,\textsuperscript{78} and can now also be used to synthesis various analogues of BINAP \textsuperscript{52}.

\begin{figure}
\centering
\includegraphics[width=0.7\textwidth]{figure1.12}
\caption{BINAP 52.}
\end{figure}

\((R_{ax})\)-BINAP \textsuperscript{52} has been used by Vinogradov as a chiral ligand for the ruthenium mediated reduction of ketone \textsuperscript{53} to its corresponding alcohol \((R)\)-\textsuperscript{54} with exceptionally high levels of stereoselectivity (Scheme 1.13).\textsuperscript{79} Low catalytic loading levels could be used and gave very reasonable yields, this combined with the fact that the ruthenium was supplied in the relatively cheap form RuCl\textsubscript{3} made the reaction economically attractive. The reactive catalyst in this reaction was \((R_{ax})\)-BINAP-RuCl\textsubscript{2} which was formed in situated from the RuCl\textsubscript{3} and \((R_{ax})\)-BINAP \textsuperscript{52}, while the hydrochloric acid present in the system was simply included to speed up the reaction process.

\begin{scheme}
\centering
\includegraphics[width=0.7\textwidth]{scheme1.13}
\caption{Using \((R_{ax})\)-BINAP \textsuperscript{52} as an asymmetric catalyst.}
\end{scheme}

Perhaps the most remarkable and certainly the most sophisticated catalysts are naturally occurring enzymes, as stated earlier all life forms contain chirality and enzymes are how nature regulates which enantiomer is produced. The use and manipulation of enzymes to generate chiral centres through asymmetric catalysis is an
area of growing importance. Very high levels of selectivity can be achieved using this method (>99\% e.e.), the problems associated with this method however are normally biochemical in nature, and as such will not be discussed in this review.

It may seem that the use of chiral reagents or catalysis is a far more effective method of asymmetric synthesis than using chiral auxiliaries, as fewer steps are needed in the reaction procedure and it removes the difficulties associated with attaching or removing the chiral auxiliary. Although this is true, asymmetric synthesis using a chiral auxiliary can always obtain completely optical pure compounds, because during this route a pair of physically different diastereoisomers are formed. While in the chiral reagents or catalysis route the enantiomeric excess of the product is always directly related to the selectivity of the reaction.

The final overall method that this report shall discuss is resolution; this is the separation of a racemic mixture into its two corresponding enantiomers. It is possible to achieve this by making either one or both enantiomers of the racemic mixture interact or react with an enantiomerically pure reagent, normally called a resolving agent. The main advantage of this generic method over the asymmetric synthesis approach discussed above is that the stereogenic chiral centre can be introduced into the compound in an unselective fashion, and hence it is easier to synthesis a much larger variety of chiral compounds. Of course the separation of the enantiomer of a racemic mixture is often far from trivial, however a large number of research groups across the world have developed numerous methods in an attempt to achieve this goal.

The method of separating a pair of enantiomers from a racemic mixture, that is closest to traditional separation techniques, is chiral chromatography, and is also one of the most elegant ways of resolving a racemic mixture. Like traditional chromatography, a stationary and mobile phase are used in conjunction, the resolving agent in this method is the stationary phase which is homochiral pure. One enantiomer will interact more favourably with the chiral stationary phase over the other, this interaction is normal due to hydrogen bonding, and simple steric hindrance governs how one enantiomer will interact more than the other with the stationary phase.

The natural occurring polymer cellulose (made up of multiple D-glucose units) and its derivatives are often used as the chiral element of the stationary phase. This polymer is often supported on silica for ease of use, the chiral columns made using this stationary phase can then be used in traditional HPLC machines. The main advantage of this method is that separation is almost always possible, as even if the
difference in the interactions between the enantiomers and the chiral stationary phase is small simply extending the length of the column or reducing the flow rate of the mobile phase will eventually result in complete separation. The main drawback of this method is its expense and low output, which make this method unsuitable when large quantities of racemic mixture need to be separated. This method however can be used in an analytical fashion to give very accurate measurement on the relative ratios of enantiomer present in a scalemic mixture (a non equal mixture of enantiomers).  

An alternative method that is favoured by industry is the formation of diastereoisomeric salts and their subsequent separation based on their differences in solubility. In this method the racemic mixture being resolved is added to a single enantiomer with which it can bind, this method is often carried out using a carboxylic acid and an amine (one being the racemic mixture the other the resolving agent), which results in two diastereoisomeric salts being formed. As the salts are diastereoisomers of each other they will have different physical properties which mean they can be separated using traditional methods. The very first example of this type of resolution was carried out by Pasteur, when he formed the ammonium salts of tartaric acid and physically separated them on their appearance.

An example of this type of resolution is the separation of a racemic mixture of the carboxylic acid 56; this was achieved by using the natural occurring (S)-enantiomer of the amino acid 57 (Scheme 1.14). The amino acid (S)-57 was added to an excess of carboxylic acid (rac)-56 (six molar equivalents) in water and the mixture was heated to ensure that both compounds were completely dissolved. Subsequent cooling and filtration of the crystal yielded a one to one mixture of (S)-57 and 56, the carboxylic acid part of this salt was primarily the (S)-enantiomer with an enantiomeric excess of 85%. The main advantages of this method that makes it so industrially applicable is its practical ease, simply mixing at an elevated temperature followed by cooling and filtration. It should also be noted that scalemic mixtures obtained from this resolution can undergo the same process a second time to further increase its enantiomeric excess.

![Image of Scheme 1.14: Acid (S)-56 and amino acid (S)-57.](image-url)
There are two main drawbacks to this type of resolution; firstly it works best for acids and bases,\textsuperscript{91} meaning that there is a limited number of different racemic compounds that can be resolved using this process. The second problem is the non-robust nature of the method, a very small change to any group on the compound being resolved is likely to completely stop the system from working. This means that a new set of conditions need to be developed each and every time a new substrate is used, this is primarily due to the fact that the resolution is carried out though the formation of crystals, obviously any slight change of the compound being resolved would greatly affect its crystal structure hence effecting the resolution.

Due to the industrial importance of this generic method it has been explored and extended often with the aim of reducing the quantity of the chiral component required for an affective resolution. It is possible to substitute half of the resolving agent with an achiral compound; in this case the more thermodynamically stable salt of the racemate and resolving agent will form while the other enantiomer of the racemate will be soaked up with the achiral compound.\textsuperscript{92,93,94} This slightly alternative method is more industrial applicable simply because less of the expensive enantiomerically pure resolving agent has to be used, further methods to reduce cost can be used including carrying at the reaction without any solvents.\textsuperscript{95}

An alternative method to salts formation is known as kinetic resolution; in this procedure the racemate is chemically reacted with a single enantiomerically pure resolving agent. Each enantiomer of the racemic mixture will react with this resolving agent at a different speed; this is because the amount of steric hindrance and electronic stability in the transition states will be different for each enantiomer. The enantiomer that reacts through a pathway with the lowest transition state will require less energy to react and hence will react faster. In a perfect kinetic resolution the difference in the reactivity of both enantiomers with the chosen resolving agent will be large and hence only one enantiomer will react under the reaction conditions. Simple classical chemical methodology can then be employed to separate the enantiomers as one is now bound to the resolving agent making it physically different.\textsuperscript{96}

Kinetic resolutions have been used extensively with the aim of resolving racemic secondary alcohols; this has often been achieved through an enantioselective acylation reaction. Perhaps one of the simplest examples\textsuperscript{97} of this process was reported by Evans, he used oxazolidin-2-ones adducts, such as (S)-\textsuperscript{58}, as his resolving agents, which could be readily synthesised from the enantiomerically pure oxazolidin-2-ones.
that he had used previously (see Scheme 1.7). The oxazolidin-2-one was the key to this reaction as it acted as a leaving group, when the racemic alcohol attached at the exo-carbonyl group, and as the stereo-directing group. The enantioselective of this reaction was found to be directly related to the size of the four substituent on the oxazolidin-2-one ring, with smaller groups giving reduced levels of selectivity (e.g. 72% e.e. when i-Pr group was used). This clearly indicates that the (R)-enantiomer of alcohol 11 reacted preferentially, as the pathway it proceeds through was less sterically demanding than of its counter enantiomer.

\[
\text{Scheme 1.15: Kinetic resolution of alcohol (rac)-11 using (S)-58.}
\]

It should be noted that Evans used the divalent metal ion, magnesium, in this reaction, presumably this acted as a linkage between the alcohol and one or both of the carbonyl groups of the resolving agent (S)-58. This effectively ensures that the reagents can only approach in one distinct fashion and therefore limiting the possible pathways that the reaction can proceed through, and is probably the reason that high levels of selectivity have been achieved for this reaction. Other research groups have further extended this work by using variations on the oxazolidin-2-one resolving agents; including using oxazolidin-2-thiones and related adducts that transfer a phosphorus rather than carbon motif.

A common alternative to the resolving agent used by Evans is the use of modified variations of dimethylaminopyridine (DMAP) as an acyl transfer agent. Vedejs has used the DMAP derived salt (R)-60 as his resolving agent, in a similar fashion to Davies work the leaving group (in this case the pyridine) also contained the stereodirecting group. The presence of the sterically bulky groups at the two position on of the pyridine ring and on the carbonyl group that was being transferred during the reaction would appear to indicate that the selectivity in this reaction is primarily due to the steric hindrance. This theory is backed-up by the fact that if the phenyl ring of the alcohol has a large substituent in the two position the selectivity of the reaction increases (for Me 85% e.e. and for Cl 89% e.e.). It should also be noted that Vedejs had also used a magnesium salt in his reaction, presumably for the same reasons that Davies has.
Very similar methods have been employed that use a simple unsubstituted DMAP with the chiral information being attached to the carbonyl group that is being transferred during the reaction. This method can be used to not only resolve racemic alcohols but can be reversed so that racemic carboxylic acids can be resolved using enantiomerically pure alcohols. However, this method can be adapted so that a sub-stoichiometric amount of chiral DMAP equivalent is required; this enantiomerically pure compound is used in conjunction with an achiral anhydride. The DMAP equivalent 63 reacts with the anhydride 62 to form the resolving agent 64, which reacts in a selective fashion with the racemic alcohol 11 to generate an enantiomeric enriched ester 65 and return the chiral DMAP equivalent 63 so that it can continue to act as an enantioselective catalyst.

The DMAP equivalent catalyst (S)-66 has been used in conjunction with the sterically demanding isobutric anhydride to resolve racemic 1-(2-naphthyl)-ethanol, obtaining the (S)-ester product (of the same general structure as 65) with an enantiomeric excess of 63%. As little as 1 molar equivalent of this resolving agent could be used to drive the reaction to 43% completion. It should be noted that 50% completion is the maximum required as this allows one enantiomer of the racemic mixture to react, if 50% completion is exceeded the enantiomeric excess of the ester product would be diminished. Fu and co-workers have used the more complex DMAP equivalent catalyst (R)-67 with great success, obtaining (S)-1-phenylethanol 11 in 95.2% enantiomeric excess, by forming an ester with the other enantiomer.
achieve this only 2 molar percentage of the resolving agent was required; this was used in conjunction with the acetic anhydride. The robust nature of this catalyst has been shown as it has been used to resolve a range of different secondary alcohols.\textsuperscript{108,109} Modifications to this DMAP equivalent have also been carried out in attempts to further understand and improve the levels of enantioselectivity that can be achieved with this type of catalyst.\textsuperscript{110,111}

![Figure 1.13: DMAP equivalent catalysts.](image)

The obvious main advantage to using catalytic kinetic resolution as opposed to normal kinetic resolutions is that less of the expensive homochiral resolving agent is required. The catalyst themselves can sometimes be complex to synthesise, and as such the use of natural occurring enzymes as chiral catalyst could be beneficial. Lipase enzymes can be used in a similar fashion to the DMAP equivalent catalyst discussed above, when used in conjunction with an acyl donor (like acetic anhydride, but more often vinyl acetate when using enzymes) they can resolve racemic alcohols, by forming an ester primarily with one enantiomer of the alcohol.\textsuperscript{112} For example it has been shown that Lipase AK can be used to resolve the racemic alcohol 68, with exceptionally high levels of selectivity (Scheme 1.18).\textsuperscript{113} Lipase enzymes can also be used in a reverse fashion, hence starting with a racemic ester which is selectivity hydrolysed to give an enantiomeric enriched alcohol.\textsuperscript{114,115} It may seem from this report that the use of enzymes as chiral catalyst is by far the best approach as such enzymes are available from nature and give exceptional levels of selectivity. Although this is true it should be noted that the reactions that such enzymes can carry out are very limited, as are the substrate that such reaction are affective with,\textsuperscript{116} and as such the exploration of chemical catalytic kinetic resolutions is still very much worthwhile.
Scheme 1.18: Enzymatic kinetic resolution.

One of the main advantages already mentioned with catalytic kinetic resolutions is that they are rather economic, as only a very small quantity of the expensive enantiomerically pure resolving agent (this can be a chemical or an enzyme) is required. However the separation of the resolved compounds (for example the remaining alcohol \text{11} and the ester \text{65, Scheme 1.17}) can sometimes be problematic and expensive, especially when this is carried out on a large scale. As such, research has been carried out with solid supported enzymes,\textsuperscript{117} so that they can be removed more easily from the reaction mixture, solid supported reagents have also been used in enzymatic kinetic resolution to allow for simple separation of the resolved components.\textsuperscript{118}

All of the above methods of kinetic resolution suffer from one common drawback however, and this is often referred to as the concentration affect.\textsuperscript{119} As mentioned earlier in any kinetic resolution one enantiomer of a racemic mixture reacts with the resolving agent faster than the other enantiomer, and this is simply due to differences in the activation energy that the two pathways require to proceed. However, this is only strictly true when the two enantiomer of the racemic mixture are in exactly equal proportions, for example at the very beginning of any kinetic resolution. As the reaction proceeds the two enantiomers of the compound being resolved will no longer be in an equal ratio, the less reactive enantiomers’ relative concentration will increase. This change in the relative ratio of the enantiomers will promote the normally unfavoured enantiomer to react; this will obviously decrease the overall selectivity of the resolution and the enantiomeric excess of the final products.

Perhaps the simplest practical way to limit the concentration affect is to have a large excess of the racemate being resolved, as then the two enantiomers will stay in approximately the same ratio throughout the resolution. A similar alternative is stopping the reaction after a small level of completeness; again here the relative ratios of the two enantiomers would still be approximately even. Both of these methods however are not economical, as a large amount of starting materials is required in comparison to the amount of the resolved product obtained. Theoretically the simplest way to stop the concentration effect from harming the enantiomeric excess of the product is for the
reaction to have such a high level of selectivity that it will effectively not react with one of the enantiomers.\(^{119}\) It is however practically extremely difficult to find a reaction that is this selective, that said the levels of selectivity shown by some enzymes are very high, but are very limited in what substrates they can resolve.

Therefore an obvious research aim is to find a process that will ignore the concentration effect but without having to use the racemic substrate in a non-economical fashion. One such technique is dynamic kinetic resolution, in such a resolution there is an additional reaction, the racemization of the compound being resolved. If this racemization occurs faster than the resolution reaction then there will never be a change in the relative ratio of the two enantiomers, they will always stay as a racemic mixture, hence completely eliminating the concentration effect.\(^{120}\) The main difficulty with this type of resolution is that both the resolution reaction and racemization reaction have to take place at the same time under the same conditions without having a detrimental effect on each other.\(^{121}\)

Enzyme catalysed kinetic resolutions have often be modified by the addition of a racemization agent so that they become dynamic kinetic resolutions; the type of agent added is obviously dependant on type of racemate being resolved. If an ester is used as the starting material in a selective hydrolysis reaction a base can be added as the racemization agent. As the alcohol is being resolved the addition of a transition metal catalyst such as 71 can be used to reversibly interconvert the alcohol to a ketone. This method has been shown to be very successful, giving very high levels of selectivity (Scheme 1.19)\(^{122}\) when a lipase enzyme is used in conjunction with this ruthenium derived catalyst, it should be noted that a wide variety of ruthenium derived racemization catalyst have been used with success\(^{123,124,125,126}\) and a few example of palladium catalysts also exist.\(^{127}\)

\[\text{Scheme 1.19: Dynamic kinetic resolution.}\]

It should be noted that in the example shown in scheme 1.19 the yield of the product is 89%, in all the previous kinetic resolutions mentioned so far the maximum
yield has been 50%, as only one enantiomer (50% of the starting racemic mixture) can react to give the required product. Obviously if the starting material is continually being racemized then all of the starting material can be converted over the course of the reaction to the required enantiomer and then react, giving a maximum yield of 100%. This also means that there is none of the other enantiomer left at the end of the reaction, greatly simplifying purification of the final product. This racemization process has also been used in salt formation reactions, so that greater yields and easier purification can be achieved, rather than the removal of the concentration effect.

An alternative way to remove the concentration effect from a resolution is known as a parallel kinetic resolution (PKR), in such a resolution two resolving regents are used together. One of the resolving agents selectively reacts with one enantiomer while the other resolving agent should react with the other enantiomer. For example resolving agent A primarily reacts with the (S)-enantiomer of the racemic mixture to give (S)-A, while the other resolving agent B reacts in an equal and opposite fashion to primarily give (R)-B (Scheme 1.20). If these two resolving agents react with similar speeds and similar levels of selectivity then the enantiomers should remain in a one to one ratio through the resolution. This will of course eliminate the concentration effect, meaning that the levels of selectivity displayed by the reaction will now be independent of how far the reaction has progressed. As such a PKR can be allowed to go to completion and still have the same levels of selectivity as the same traditional KR would if it had only gone to 1% completion. Hence it should be possible to obtain high yields and high levels of enantiomeric excess with this process.

\[ \text{(S)} \xrightarrow{A} \text{(S)-A} \quad \text{(S)} \xrightarrow{B} \text{(S)-B} \]
\[ \text{(R)} \xrightarrow{B} \text{(R)-B} \quad \text{(R)} \xrightarrow{A} \text{(R)-A} \]

**Scheme 1.20: Parallel kinetic resolution.**

However the two resolving agents that are being used have to fill certain criteria, they must react at approximately the same speed, with similar levels of selectivity; the products obtained also need to be easily separable from each other. It is also important that both of these resolving agents can work under the same reaction conditions and without mutual interference. Although the combination of all these criteria would seem hard to accommodate it can be achieve more easily if a pair of quasienantiomers are used as the resolving agents. *Quasi-*enantiomers are compounds that have opposite
configurations, just like a pair of normal enantiomers, however they also differ by having at least one different group on, therefore compounds (S)-74 and (R)-75 are quasienantiomers of each other.\textsuperscript{134} As quasienantiomers are almost easy to distinguish and separate enantiomer of each other they have proven to be very useful,\textsuperscript{135,136} and can be used effectively in PKRs as they fulfil many of the criteria listed above.\textsuperscript{96,137}

![Figure 1.14: A pair of quasienantiomers.](image)

The first example of a PKR was reported by Vedejs, who adapted his kinetic resolution\textsuperscript{102} (shown in Scheme 1.16) by using an additional resolving agent (S)-76 which was a quasi-enantiomer of his original resolving agent (R)-60.\textsuperscript{138} Both resolving agents worked well giving the required products in high enantiomeric excess and in near quantitative yields. The resolving agent (S)-76 worked almost perfectly, giving a level of selectivity that was almost identical to that of its normal KR after 1\% completion, this clearly showed that the concentration effect had been cancelled out in this reaction. The other resolving agent (R)-60 did not quite perform as well, although still better than its kinetic resolution (Scheme 1.21 vs. 1.16), Vedejs theorised that this could be attributed to a degree of interference from (S)-76. So although not a perfect example of a PKR it does certainly show that the method can be used successfully.

![Scheme 1.21: Vedejs PKR.](image)

Since Vedejs initial report of a successful PKR numerous other examples have been reported,\textsuperscript{132,139,140} one of practical interest has been carried out by Fox, who has
successfully resolved the racemic mixed anhydride 82. Unlike Vedejes example this technique has the resolving agent as the nucleophile rather than a leaving group; however overall it is still a selective addition to a carbonyl group followed by an elimination step. It is however Fox’s pair of quasi-enantiomer resolving agents that makes this reaction so interesting, firstly they are a pair of oxazolidin-2-ones, which are readily synthesisable from their corresponding amino acids. One of the resolving agents contains a simple phenyl group in (S)-80 whilst its quasi-enantiomeric partner has a 4-hydroxyphenyl group in (R)-81, this groups is protected by a TBDMS group during the resolution process (Scheme 1.22). As this group is so far away from the active site of the resolving agent (the nitrogen atom) and has been protected so it does not interfere with the reaction the two resolving agent (S)-80 and (R)-81 will react at very similar speeds and with similar levels of selectivity. However, after the resolution step the protecting group is removed, leaving a simple hydroxyl group, this now means that the two compounds produced during the reaction (S,S)-83 and (R,R)-84 are significantly different allowing for easy separation. This “switching” process from compounds of similar reactivity to ones with very different physical properties is an interesting alterative way to fulfil the numerous criteria mentioned above.

Scheme 1.22: Fox’s PKR.

Both of the examples of PKR mentioned above and in fact the majority of cases found within the literature all use molar equivalents of the resolving agents, of course if sub-stoichiometric amounts of these reagents could be used in a catalytic PKR the process would become far more economically viable. However achieving this is far from easy, as not only do two catalyst need to be found that will react at approximately the same rate and with similar but reversed levels of selectivity, they also have to transfer a different group onto each enantiomer. Hence each catalyst must only be able
to activate one of the two derivatizing agents in the reaction mixture, e.g. catalyst A must only activate the derivatizing agents X to give A-X which must then preferentially react with the (S)-enantiomer of the racemic mixture to give (S)-X, while the other catalyst reacts in an equal and yet opposite fashion (Scheme 1.23). If any cross derivatization were to occur, say catalyst A activating the derivatizing agents Y, then this would dramatically reduce the enantiomeric excess of the final products as it would lead to the enantiomers being bound to the incorrect derivatizing agents, for example (S)-Y would be synthesised.

**Scheme 1.23:** Catalytic PKR.

Vedejs however has managed to overcome the multiple problems associated with a catalytic PKR to successfully resolve the racemic alcohol 77. Vedejs used a solid supported lipase (ChiroCLEC-PC) as one catalytic resolving agent and the phosphine 87 as the other catalytic resolving agent. The two derivatizing agents employed were chosen with great care, vinyl pivalate 85 was chosen as one such agent as it was found to be activated by the lipase but not the phosphine 87. A solid supported anhydride 86 was used as the other derivatizing agent, the fact that this compound was on a polymer support stopped it from interacting with the solid supported lipase. Hence the two resolving agents would only activate a single derivatizing agent each, this was indeed found to be the case, and Vedejs managed to successfully resolve the racemic alcohol 77 (Scheme 1.24). Although this is a rather complex example of a catalytic PKR it does show that such a reaction is indeed possible.

**Scheme 1.24:** Vedejs catalytic PKR.
An interesting and very elegant variation to a PKR is a divergent kinetic resolution, in this type of reaction there is only one resolving agent but it reacts with each enantiomer in a different fashion. Hence leading to two different products, these can of course be separated using traditional chemical methods. Also if the resolving agent reacts at a similar speed with each enantiomer then their relative ratios will remain unchanged throughout the reaction and the concentration effect will be ignored. The role of the resolving agent in such a reaction is much more complex, as it needs to be able to react with each enantiomer in a stereo selective fashion at the same time with the same speed and similar levels of selectivity, and to give different products from each enantiomer of the resolving agent.

Despite the fact that the resolving agent in a divergent kinetic resolution needs to fulfil a number of complex roles successful examples of this type of resolution do exist. For example, the racemic epoxide 90 can be resolved through a copper-mediated nucleophilic addition and ring opening reaction (Scheme 1.25). The ligand 91 binds in situ with the copper metal ion to form the active chiral catalyst, this catalyst allows the direct ring opening of the (S)-enantiomer of the epoxide to give (S,S)-92. The (R) enantiomer of the epoxide however will not readily undergo direct ring opening in the presence of this chiral catalyst, and as such the addition step occurs at the carbon carbon double bond (away from the chiral site of the epoxide) which is followed by rearrangement and ring opening to give (R,R)-93.

Scheme 1.25: Divergent kinetic resolution.

To conclude, the principals behind chirality and resolutions have been discussed, the nature of enantiomers has been described and the need for effective ways of obtaining enantiomers has been explained. Three generic methods for obtaining enantiomerically pure compounds have been described, the simplest and yet most limiting being from the “chiral pool,” the advantages and disadvantages of direct asymmetric synthesis of enantiomerically pure compounds has also been discussed.
The final method for obtaining enantiomeric pure compounds was resolution, this broad area has been split up into distinct sections of salt formation, kinetic resolution using both stoichiometric and sub-stoichiometric equivalents of resolving agent, dynamic kinetic resolution, parallel kinetic resolution and divergent kinetic resolutions, and the unique benefits and difficulties of each of these types of resolutions has been described.
Chapter 2

Resolution of Active Esters using Oxazolidin-2-ones

Before I joined the Eames group in 2006 they had discovered and begun to further develop a method for the parallel kinetic resolution of active esters, such as (rac)-95, using a pair of quasi-enantiomeric oxazolidin-2-ones like (R)-94 and (S)-24 (Scheme 2.1). As part of my PhD, I would attempt to improve and extend this resolution method, and try to develop a better understanding of how it works. However, before I could begin to carry out any resolutions of my own, I needed to synthesise the different active esters and oxazolidin-2-ones that I would require during my studies.

\[
\text{(R)-94} \quad \text{(S)-24} \quad \text{(rac)-95} \quad \text{(S,R)-syn-96} \quad \text{(R,R)-anti-96} \quad \text{(R,S)-syn-97} \quad \text{(S,S)-anti-97}
\]

Scheme 2.1: PKR of active ester (rac)-95.

The oxazolidin-2-ones that I needed for my project were synthesised directly from commercially available amino acids. Amino acids are a set of chemicals from the “chiral pool” meaning that they are available from nature in an optical pure form; this makes them ideal for using as resolving agents. The first step in the synthesis of the oxazolidin-2-one was to simply reduce the carboxylic acid group of the amino acid to a primary alcohol using LiAlH₄; this process worked efficiently and could be used on differently substituted amino acids. The reduction of the carboxylic acid group proceeded with retention of the chiral centre (Schemes 2.2 and 2.3); this is obviously very important when attempting to synthesise an optical pure resolving agent.
Scheme 2.2: Reduction of amino acid 98.

Scheme 2.3: Reduction of amino acid (S)-57.

The oxazolidin-2-one (rac)-syn-104 was not derived from an amino acid; instead the commercial available salt (rac)-syn-101 was used as the starting material. The simple addition of a strong base to this salt, gave the required amino alcohol (rac)-syn-102 (Scheme 2.4). With the amino alcohols in hand, we chose to react them with ethyl chloroformate in a two step process; firstly the amine attacks the carbonyl group eliminating the chloride forming the intermediate (rac)-syn-103 or (rac)-105. The second step of the reaction allowed the alcohol group to internally attack the carbonyl group, thus eliminating ethanol to give the required oxazolidin-2-one in high yield (Schemes 2.4 and 2.5).

Scheme 2.4: Synthesis of oxazolidin-2-one (rac)-syn-104.

Scheme 2.5: Synthesis of oxazolidin-2-one (rac)-94.
The synthesis of the oxazolidin-2-one \((rac)-94\) from the appropriate amino alcohol \((rac)-99\) could be reduced to a single step by replacing the ethyl chloroformate with diethyl carbonate under harsher reaction conditions (Scheme 2.6). Although this alternative reaction worked, it gave the product \((rac)-94\) in a lower yield, mainly due to purification difficulties arising from this method. Although, the initial method using ethyl chloroformate involved a two step procedure, we chose to use it as the yields were higher and the purification was easier (Schemes 2.4 and 2.5 vs. Scheme 2.6).

![Scheme 2.6: One step synthesis of oxazolidin-2-one \((rac)-94\).](image)

We were also interested in changing the oxygen atom of the carbonyl group in the oxazolidin-2-one for a sulphur atom, hence creating an oxazolidin-2-thione, so that it could be tested in the resolution work described below. We found that simply refluxing the appropriate amino alcohol in carbon disulphide in the presence of a base, \(\text{NaCO}_3\), gave the required oxazolidin-2-thiones in acceptable yields (Schemes 2.7 to 2.10).

![Scheme 2.7: Synthesis of oxazolidin-2-thione \((R,S)-\text{syn-106}\).](image)

![Scheme 2.8: Synthesis of oxazolidin-2-thione \((S)-107\).](image)
Scheme 2.9: Synthesis of oxazolidin-2-thione (R)-109.

Scheme 2.10: Synthesis of oxazolidin-2-thione 110.

With the required oxazolidin-2-ones and oxazolidin-2-thiones in hand, we next turned our attention towards synthesising a range of active esters. We used a simple DCC mediated coupling reaction between the appropriate carboxylic acid and pentafluorophenol, this gave the required esters in high yields for a range of carboxylic acids with different aryl ring structures (Table 2.1).

Table 2.1: Synthesis of racemic active esters.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Acid</th>
<th>Ar</th>
<th>R</th>
<th>Ester</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>111</td>
<td>Ph</td>
<td>Me</td>
<td>95</td>
<td>92%</td>
</tr>
<tr>
<td>2</td>
<td>112</td>
<td>para-C₆H₄CH₃</td>
<td>Me</td>
<td>113</td>
<td>85%</td>
</tr>
<tr>
<td>3</td>
<td>114</td>
<td>para-C₆H₄CH₂CHMe₂</td>
<td>Me</td>
<td>115</td>
<td>90%</td>
</tr>
<tr>
<td>4</td>
<td>116</td>
<td>para-C₆H₄Cl</td>
<td>Me</td>
<td>117</td>
<td>89%</td>
</tr>
</tbody>
</table>

The same coupling procedure could also be used to synthesise a range of optically pure esters from the appropriate enantiomerically pure carboxylic acids (Tables 2.2 and 2.3). It was found that small changes to the aliphatic group of the
carboxylic acid (from methyl, ethyl and methoxy) had no detrimental affect on the reaction, and hence still yielded the appropriate ester products.

![Chemical structure](image)

**Table 2.2**: Synthesis of optical pure active esters.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Acid</th>
<th>Ar</th>
<th>R</th>
<th>Ester</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>111</td>
<td>Ph</td>
<td>Me</td>
<td>95</td>
<td>62%</td>
</tr>
<tr>
<td>2</td>
<td>118</td>
<td>Ph</td>
<td>Et</td>
<td>119</td>
<td>75%</td>
</tr>
<tr>
<td>3</td>
<td>116</td>
<td>para-C₆H₄Cl</td>
<td>Me</td>
<td>117</td>
<td>63%</td>
</tr>
<tr>
<td>4</td>
<td>114</td>
<td>para-C₆H₄CH₂CHMe₂</td>
<td>Me</td>
<td>115</td>
<td>84%</td>
</tr>
<tr>
<td>5</td>
<td>120</td>
<td>Ph</td>
<td>OMe</td>
<td>121</td>
<td>78%</td>
</tr>
<tr>
<td>6</td>
<td>122</td>
<td>6-Methoxynaphthalen-2-yl</td>
<td>Me</td>
<td>123</td>
<td>69%</td>
</tr>
</tbody>
</table>

**Table 2.3**: Synthesis of optical pure active esters.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Acid</th>
<th>Ar</th>
<th>R</th>
<th>Ester</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>111</td>
<td>Ph</td>
<td>Me</td>
<td>95</td>
<td>68%</td>
</tr>
<tr>
<td>2</td>
<td>118</td>
<td>Ph</td>
<td>Et</td>
<td>119</td>
<td>91%</td>
</tr>
</tbody>
</table>

Although the DCC coupling procedure worked for a small range of carboxylic acids with different aliphatic groups it was found that if this aliphatic group was increased in size to an isopropyl group the reaction did not give the required ester *(rac)-126*. Instead this reaction gave the corresponding anhydride *(rac)-125* (Scheme 2.11), which presumably was formed through self-coupling. This result is somewhat strange, as anhydride formation has not previously been observed when synthesising these active esters. From this result it would seem to suggest that increasing the steric hindrance of the carboxylic acid in this reaction makes the formation of the active ester unfavourable and therefore an alternative reaction pathway is favoured. It seems strange how that this alternative reaction pathway would result in a more sterically crowded anhydride *(rac)-125*.

An alternative explanation is that the anhydride is always formed in these coupling procedures and it is this intermediate anhydride that then reacts with the pentafluorophenol to give the appropriate ester product. The use of the isopropyl carboxylic acid *(rac)-124* results in an anhydride that is too sterically crowded for the addition of pentafluorophenol to occur, so the intermediate anhydride *(rac)-125* is
instead isolated. Although this explanation does sound plausible it does go against the classically text-book mechanism for a DCC coupling reaction.

In order to better understand the mechanism of this reaction and to hopefully isolate the required active ester (rac)-126, we modified how we carried out this reaction. Instead of adding all the carboxylic acid (rac)-124 at the beginning of this reaction, we added it slowly to the reaction mixture after all the other reagents, hence reducing the likelihood of anhydride forming. This alternative approach did indeed give the required ester (rac)-126 with no anhydride being formed (Scheme 2.11); this method was also successful in synthesising the optical pure ester (S)-126 (Scheme 2.12).

\[
\begin{align*}
\text{Ph} & \quad \text{O} \\
(rac)-124 \quad & \quad i) \quad \text{DCC, DCM} \\
& \quad \text{ii) } \text{C}_6\text{F}_5\text{OH} \\
\text{Ph} & \quad \text{O} \\
(meso)-\text{syn and (rac)-anti-125} & \quad \text{in 50 : 50 mixture} \\
& \quad 49\% \\
\text{C}_6\text{F}_5\text{OH} \quad & \quad i) \quad \text{DCC, DCM} \\
& \quad \text{ii) } \text{Ph} \quad \text{O} \\
\quad \quad \quad \text{ added slowly over 1 hour } \\
124-(rac) \quad & \quad \text{O} \\
\text{Ph} \quad & \quad \text{OH} \\
126-(rac) & \quad 82\% \\
\end{align*}
\]

**Scheme 2.11:** Reactions with carboxylic acid (rac)-126.

\[
\begin{align*}
\text{Ph} & \quad \text{O} \\
(S)-124 \quad & \quad i) \quad \text{DCC, DCM} \\
& \quad \text{ii) } \text{C}_6\text{F}_5\text{OH} \\
\text{Ph} & \quad \text{O} \\
& \quad \text{OC}_6\text{F}_5 \\
(S)-126 & \quad 72\% \\
\text{added slowly over 1 hour } \\
\end{align*}
\]

**Scheme 2.12:** Synthesis of ester (S)-126.

From these reactions it is my belief that we were indeed always forming an anhydride due to the order that we added the reagents. It just so happened that the steric nature of the anhydride (meso)- and (rac)-125 was such that it did not allow the second step of the reaction procedure to occur, the formation of the ester. However, by changing the order of which the reagents were added the reaction followed the classical text-book mechanism for a DCC coupling reaction, and therefore anhydride formation was disfavoured.
We also chose to synthesise a range of both racemic and optically pure active esters with different phenol pro-leaving groups so that we could later investigate their effect on the proposed resolution reactions. This simple DCC coupling reaction worked well in almost all cases giving the required esters in good yields, and without racemization of the optical pure carboxylic acids (Tables 2.4 and 2.5). However when the very sterically bulky 2,6-dimethyl-4-nitro-phenol was used, none of the required active ester \((rac)-129\) was formed. However, this active ester \((rac)-129\) could however be formed when a sub-stoichiometric amount of the acyl transfer reagent DMAP was used.

![Diagram of DCC coupling reaction]

**Table 2.4:** Synthesis of racemic active esters with different phenol groups.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Phenol</th>
<th>Ester</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>para-NO₂C₈H₄OH</td>
<td>127</td>
<td>95%</td>
</tr>
<tr>
<td>2</td>
<td>C₆H₅OH</td>
<td>128</td>
<td>60%</td>
</tr>
<tr>
<td>3</td>
<td>4-NO₂-2-Me-6-Me-C₆H₄OH</td>
<td>129</td>
<td>0% *</td>
</tr>
<tr>
<td>4</td>
<td>C₆F₅SH</td>
<td>130</td>
<td>76%</td>
</tr>
</tbody>
</table>

* Note this yield was increased to 50% by adding 0.2 equiv.'s of DMAP to the reaction mixture.

**Table 2.5:** Synthesis of optical pure active esters with different phenol groups.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Phenol</th>
<th>Ester</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>para-NO₂C₈H₄OH</td>
<td>127</td>
<td>54%</td>
</tr>
<tr>
<td>2</td>
<td>C₆H₅OH</td>
<td>128</td>
<td>52%</td>
</tr>
</tbody>
</table>

We also needed to synthesise some acid chlorides for the resolution work; in order to achieve this we simply refluxed the appropriate carboxylic acid in thionyl chloride. This method was successful in synthesising a range of acid chlorides, these compounds were purified by distillation due to their reactivity. Unfortunately some of these acid chlorides were not volatile enough and so could only be obtained as the crude product. When the carboxylic acid \((rac)-120\) was used in this reaction, a by-product, benzaldehyde, was also formed, which could not be separated from the required acid chloride.
Table 2.6: Synthesis of acid chlorides.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Acid</th>
<th>Ar</th>
<th>R</th>
<th>Acid Chloride</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>118</td>
<td>Ph</td>
<td>Et</td>
<td>131</td>
<td>93%</td>
</tr>
<tr>
<td>2</td>
<td>124</td>
<td>Ph</td>
<td>i-Pr</td>
<td>132</td>
<td>13%</td>
</tr>
<tr>
<td>3</td>
<td>116</td>
<td>para-C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;Cl</td>
<td>Me</td>
<td>133</td>
<td>~100%</td>
</tr>
<tr>
<td>4</td>
<td>120</td>
<td>Ph</td>
<td>OMe</td>
<td>134</td>
<td>~66%*</td>
</tr>
<tr>
<td>5</td>
<td>135</td>
<td>Ph</td>
<td>OAc</td>
<td>136</td>
<td>~100%</td>
</tr>
</tbody>
</table>

* Also gave Benzaldehyde ~33%

The carboxylic acid (S)-122 used to synthesise the active ester (S)-123 (in Table 2.2) is only commercially available in an optical pure form, which is very useful, as it means this active ester can potentially be used as a resolving agent. However, most of the screening studies were performed using mutually kinetic resolutions, in such reactions all of the reagents used must be racemic. Therefore in order to test the active ester 123 we had to synthesise it in a racemic form. We chose to do this by first converting the acid (S)-122 into an ester (S)-137 using a simple DCC mediate coupling process. Sodium ethoxide (formed from sodium hydride and ethanol) was then used in a transesterification reaction that also racemized this compound to form the ethyl ester (rac)-138.

This racemization occurs as the acidic proton alpha to the carbonyl group is removed by the strong base, sodium ethoxide, to form the achiral ketene after elimination of the phenol. This highly reactive ketene then reacts in a stereo random fashion with the ethanol to form the ester (rac)-138. Simple hydrolysis gives the required racemic carboxylic acid (rac)-122, which can be readily converted to the required active ester (rac)-123 using our standard DCC coupling procedure (Scheme 2.13).
Scheme 2.13: Racemization of carboxylic acid (S)-122.

With the required starting materials now in hand, we set out to investigate the resolution outlined in Scheme 2.1. Although we wished to develop a parallel kinetic resolution, we chose to study the reaction by mainly carrying out mutual kinetic resolutions (MKRs), where both the reagents are racemic; hence this is not an actual optical resolution. However, as a method of screening reaction conditions and different reagents, MKRs are extremely useful, as they are inexpensive, as all the materials are racemic. More importantly the pair of enantiomers of the resolving agent in a MKR (that would be exchanged for a pair of quasi-enantiomers in a PKR) are the same compound, and as such, will react at exactly the same rate. This means that the level of selectivity obtained from a MKR is the natural selectivity of the reaction, and has not been altered by the changing relative reagent quantities as the reaction progresses.

We first chose to explore the resolution method that had been developed previously in the group by doing two mutual kinetic resolutions each with a different base. To see if the base only deprotonated the oxazolidin-2-one, or if it also somehow played a role in the stereoselective step of the reaction, perhaps by acting as a coordinating species. This reaction clearly showed that base was indeed somehow linked to the stereoselective step of the reaction; n-BuLi gave very high levels of selectivity and a good yield (Table 2.7) and hence we chose to use this base for the rest of the study outlined in this chapter.
We next decided to probe the temperature that the reaction was carried out at, this should let us identify if the stereoselectivity of the reaction is kinetic in nature. If the stereoselectivity of the reaction is indeed kinetic, the selectivity of the reaction should decrease as the temperature rises. This was found to be the case, although the loss of selectivity was relatively small, however it still indicated that the selectivity of this reaction was kinetically driven. Surprisingly the yield of the product decreased as the temperature rose; this suggested that the product or a key intermediate was perhaps unstable under these conditions.

Now that ideal reaction conditions had been found, we investigated how the leaving ability and steric bulk of the leaving group on the active ester affected the reaction. When the steric bulk of this leaving group was dramatically increased (Table 2.9; entries 2 and 3) the reaction simply stopped working altogether, even when the reaction time was extended, no product was formed. However, if the leaving groups leaving ability was reduced (Table 2.9; entries 4 and 5), the reaction slowed down and would only give a small amount of the product (rac)-96, even after an extended reaction time. Interestingly, the small amount of the product (rac)-96 obtained had greatly

![Chemical structure](image)

**Table 2.7:** MKRs using different bases.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>Ratio syn : anti</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>n-BuLi</td>
<td>97 : 3</td>
<td>66%</td>
</tr>
<tr>
<td>2</td>
<td>MeMgBr</td>
<td>83 : 17</td>
<td>41%</td>
</tr>
</tbody>
</table>

**Table 2.8:** MKRs at different temperatures.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Temp. °C</th>
<th>Ratio syn : anti</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-78</td>
<td>97 : 3</td>
<td>66%</td>
</tr>
<tr>
<td>2</td>
<td>-41</td>
<td>98 : 2</td>
<td>33%</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>90 : 10</td>
<td>34%</td>
</tr>
<tr>
<td>4</td>
<td>25</td>
<td>91 : 9</td>
<td>28%</td>
</tr>
<tr>
<td>5</td>
<td>50</td>
<td>90 : 10</td>
<td>29%</td>
</tr>
</tbody>
</table>
reduced levels of diastereoselectivity. The selectivity of the reaction changed again when a 2-methoxyphenol was used as the leaving group, and even more surprisingly the selectivity is almost completely reversed when an acid chloride \((\text{rac})-140\) rather than when the active ester was used. These results clearly show that the leaving group plays an important part in the diastereoselective step of this reaction.

![Scheme 2.14: KR of active ester (rac)-95.](image)

Table 2.9: MKRs with different leaving groups.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Active ester</th>
<th>(R)</th>
<th>Ratio syn : anti</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>95</td>
<td>(\text{C}_9\text{H}_13\text{O})</td>
<td>97 : 3</td>
<td>66%</td>
</tr>
<tr>
<td>2</td>
<td>129</td>
<td>2.6-\text{dMe}-4-\text{NO}_2\text{C}_6\text{H}_2\text{O}</td>
<td>-</td>
<td>0%</td>
</tr>
<tr>
<td>3</td>
<td>129</td>
<td>2.6-\text{dMe}-4-\text{NO}_2\text{C}_6\text{H}_2\text{O}</td>
<td>-</td>
<td>0%</td>
</tr>
<tr>
<td>4</td>
<td>128</td>
<td>(\text{C}_9\text{H}_15\text{O})</td>
<td>-</td>
<td>0%</td>
</tr>
<tr>
<td>5</td>
<td>128</td>
<td>(\text{C}_9\text{H}_13\text{O})</td>
<td>40 : 60</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>6</td>
<td>139</td>
<td>\text{ortho-MeOC}_6\text{H}_2\text{O}</td>
<td>63 : 37</td>
<td>27%</td>
</tr>
<tr>
<td>7</td>
<td>140</td>
<td>CI</td>
<td>12 : 88</td>
<td>39%</td>
</tr>
</tbody>
</table>

* Reaction time extended to over night.

We next decided to see how the above method would work in a kinetic resolution (KR) instead of a MKR; we decided to use two equivalents of the active ester \((\text{rac})-95\) in order to limit the problems caused by the concentration affect. This reaction worked surprisingly well with levels of diastereoselectivity only slightly lower than that of the corresponding MKR. This showed that the diastereoselective step of this reaction is rather robust, and not overly affected by slight changes in relative concentration of the substrate being resolved.

![Scheme 2.14: KR of active ester (rac)-95.](image)

With an optimised MKR method in place, we next chose to start modifying the aryl and aliphatic groups of the active ester, and four substituent of the oxazolidin-2-one. The oxazolidin-2-one \((\text{rac})\text{-syn}\text{-104}\) was tested as the four substituent on the ring was a small methyl group, which would tell us if the steric nature of this substituent
played an important role in the diastereoselectivity step of this reaction. All of the active esters tested against this oxazolidin-2-one gave approximately the same low levels of selectivity (Table 2.10). These results suggested that in all of these reactions, the small size of the four substituent of the oxazolidin-2-one is the limiting factor; hence the different active esters gave the same results.

Table 2.10: MKRs with oxazolidin-2-one (rac)-syn-104.

We decided to slightly increase the size of the four substituent on the oxazolidin-2-one from a methyl group in (rac)-syn-104 to a benzyl group (rac)-145, hoping that this would increase the overall selectivity of the reaction. For the simplest active ester (rac)-95 used, the size increase from methyl to benzyl had no effect on the selectivity of the reaction, it only slight reduced the yield of the product. Interestingly, however, there became a greater difference in the results obtained from the different active esters, most notable is that the selectively dropped when the chlorine atom was in the para-position of the phenyl ring of the active ester (rac)-117. As such a far away group could clearly not influence this reaction sterically; the electronic nature of this aryl ring must have played an important role on the stereoselective outcome of this reaction.

Table 2.11: MKRs with oxazolidin-2-one (rac)-145.
The next logical step was to increase the size of the oxazolidin-2-ones four substituent even further to an isopropyl group (rac)-24. For the simplest active ester (rac)-95, this gave a massive increase in the selectivity of the reaction, clearly showing that the diastereoselective step in the reaction was highly dependant on the size of this group. Again, the para-chloro active ester (rac)-117 gave dramatically lower levels of stereoselectivity, whilst the naphthyl active ester (rac)-123, gave levels of selectivity which were comparable to the phenyl active ester (rac)-95 (Table 2.12 entries 1, 3 and 4). This information confirms that the electronic nature of the aryl ring of the active ester plays a vital role in the stereoselectivity of the reaction. The more sterically demanding active ester (rac)-126 not only gave a reduced yield, which could be expect, but also reduced levels of selectivity, perhaps indicating that the reaction is too sterically crowded in this particular case.

\[
\begin{align*}
\text{(rac)-24} & \quad \text{i) } n\text{-BuLi, THF, } -78^\circ\text{C} \\
& \quad \text{ii) } \text{Ester} \\
\text{(rac)-syn} & \quad \text{(rac)-anti}
\end{align*}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>R</th>
<th>Ester</th>
<th>Ratio syn : anti</th>
<th>Product</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph</td>
<td>Me</td>
<td>95</td>
<td>95 : 5</td>
<td>97</td>
<td>80%</td>
</tr>
<tr>
<td>2</td>
<td>Ph</td>
<td>iPr</td>
<td>126</td>
<td>68 : 32</td>
<td>150</td>
<td>34%</td>
</tr>
<tr>
<td>3</td>
<td>para-C6H4Cl</td>
<td>Me</td>
<td>117</td>
<td>74 : 26</td>
<td>151</td>
<td>52%</td>
</tr>
<tr>
<td>4</td>
<td>6-Methoxynaphthalen-2-yl</td>
<td>Me</td>
<td>123</td>
<td>98 : 2</td>
<td>152</td>
<td>58%</td>
</tr>
</tbody>
</table>

Table 2.12: MKRs with oxazolidin-2-one (rac)-24.

From the results shown in tables 2.10 to 2.12, it is clear that the size of the four substituent on the oxazolidin-2-one ring is crucial to this reaction. We next wished to probe the electronic character of this substituent, so we chose to test the 4-phenyl-oxazolidin-2-one (rac)-94. The use of this oxazolidin-2-one gave exceptionally good levels of selectivity for all the active esters tested (Table 2.13), clearly showing that it is not just the size of this substituent that is important, but also its electronic character. As all the levels of diastereoselectivity have increased, it is difficult to tell if the effect from the aryl ring of the active ester is still in play or not. The sterically bulky active ester (rac)-126, again gave reduced levels of selectivity and a reduced yield, this matches what was seen when using the oxazolidin-2-one (rac)-24.
As the MKRs using 4-phenyl-oxazolidin-2-one (rac)-94 had worked so well, we were interested in seeing if other groups with a \(sp^2\)-hybridised carbon atom bound directly to the oxazolidin-2-one ring at its four position would give similar results; hence we next tested the oxazolidin-2-one (rac)-157. Having a sterically bulky substituent at the four position of this oxazolidin-2-one ring with a \(sp^2\) hybridised carbon atom seems to be what is required for good levels of diastereoselectivity, as these levels of selectivity shown in table 2.14 were very similar to those obtained with oxazolidin-2-one (rac)-94.

### Table 2.13: MKRs with oxazolidin-2-one (rac)-94.

<table>
<thead>
<tr>
<th>Entry</th>
<th>(Ar)</th>
<th>(R)</th>
<th>Ester</th>
<th>Ratio syn : anti</th>
<th>Product</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph</td>
<td>Me</td>
<td>95</td>
<td>97 : 3</td>
<td>96</td>
<td>66%</td>
</tr>
<tr>
<td>2</td>
<td>Ph</td>
<td>i-Pr</td>
<td>126</td>
<td>87 : 13</td>
<td>154</td>
<td>25%</td>
</tr>
<tr>
<td>3</td>
<td>(p)-C(_6)(_2)Cl</td>
<td>Me</td>
<td>117</td>
<td>&gt;95 : 5</td>
<td>155</td>
<td>49%</td>
</tr>
<tr>
<td>4</td>
<td>6-Methoxynaphthalen-2-yl</td>
<td>Me</td>
<td>123</td>
<td>&gt;95 : 5</td>
<td>156</td>
<td>49%</td>
</tr>
</tbody>
</table>

### Table 2.14: MKRs with oxazolidin-2-one (rac)-157.

<table>
<thead>
<tr>
<th>Entry</th>
<th>(Ar)</th>
<th>(R)</th>
<th>Ester</th>
<th>Ratio syn : anti</th>
<th>Product</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph</td>
<td>Me</td>
<td>95</td>
<td>95 : 5</td>
<td>158</td>
<td>33%</td>
</tr>
<tr>
<td>2</td>
<td>Ph</td>
<td>i-Pr</td>
<td>126</td>
<td>57 : 43</td>
<td>159</td>
<td>52%</td>
</tr>
<tr>
<td>3</td>
<td>(p)-C(_6)(_2)Cl</td>
<td>Me</td>
<td>117</td>
<td>95 : 5</td>
<td>160</td>
<td>23%</td>
</tr>
<tr>
<td>4</td>
<td>6-Methoxynaphthalen-2-yl</td>
<td>Me</td>
<td>123</td>
<td>97 : 3</td>
<td>161</td>
<td>45%</td>
</tr>
</tbody>
</table>

Whilst investigating how the structural nature of the leaving group affected this reaction (Table 2.9), we found that although pentafluorophenol gave the highest levels of diastereoselectivity, the use of an acid chloride gave reversed selectivity. As a result, we next chose to test a range of acid chlorides with a variety of different oxazolidin-2-ones used above. However when we tested oxazolidin-2-one (rac)-145 we found that the reaction gave almost no stereoselectivity.
Table 2.15: MKRs with oxazolidin-2-one (rac)-145.

Increasing the size of the four substituent of the oxazolidin-2-one from benzyl in (rac)-145 to isopropyl in (rac)-24, again improved the levels of selectivity (Table 2.16). All the acid chlorides tested with this oxazolidin-2-one (rac)-24, however, did give the opposite selectivity than had been obtained previously. It would appear that the use of the much smaller leaving group, chloride, rather than pentafluorophenolate gave the same trends simply reversed, perhaps indicating that the key intermediate in the stereoselective process had been inverted.

Table 2.16: MKRs with oxazolidin-2-one (rac)-24.

With this information in hand, we presumed that the use of the 4-phenyl-oxazolidin-2-one (rac)-94 would give the highest levels of diastereoselectivity with the anti-diastereoisomer being the dominant species formed. This was indeed the case with the simplest acid chloride (rac)-140; but this is where all similarities ended. The other active ester tested gave what appears to be a random collection of results, with the levels of selectivity changing and even inverting in some cases (Table 2.17). This seemingly random collection of results would suggest that there are at least two different mechanistic pathways that the reaction can go through, each of which lead to different levels of diastereoselectivity. Altering the acid chloride appears to change which of these pathways is preferred, hence giving an apparent random collection of results.
Table 2.17: MKRs with oxazolidin-2-one (rac)-94.

The results from the MKRs using the oxazolidin-2-one (rac)-157 gave very similar results to those obtained when the oxazolidin-2-one (rac)-94 was used; hence eliminating the possibility that the results obtained in table 2.17 could be down to simple experimental error. Unfortunately no useful conclusions could be drawn as to why these levels of diastereocntrol were obtained.

Table 2.18: MKRs with oxazolidin-2-one (rac)-157.

After carrying out all of the MKRs described above we felt that it would be appropriate to test out a PKR in order to see if indeed the results from MKRs could be used to develop PKRs. The PKR of active ester (rac)-126 (Scheme 2.15) showed an interesting effect when compared to its corresponding MKRs. The half of the PKR that should give the lowest levels of selectivity [the half forming the oxazolidin-2-one adduct (R,S)-syn-150] gave higher levels of selectivity than its corresponding MKR. While the other half of the PKR [the half forming the oxazolidin-2-one adduct (R,S)-syn-154] gave lower levels of selectivity than its corresponding MKR. Hence the halves of the PKR evened out to give levels of diastereoselectivity that were similar to each other. This is presumably down to which enantiomer of the substrate being resolved is in excess as the reaction progresses; in the example below there will be more...
(R)-126 available to react as the reaction progresses. Hence, increasing the selectivity of the half of the PKR that wishes to react with this enantiomer, and at the same time reducing the selectivity of the other half of the PKR.

**Scheme 2.15:** PKR of active ester (rac)-126.

In order to accurately determine which diastereoisomer is the syn-diastereoisomer and which is the anti-diastereoisomer it is normal to simply synthesise one from optically pure reagents, hence forming only one of the two diastereoisomers. This had already been done by previous members of the group for most of the oxazolidin-2-ones adducts formed above, however I was the first member of the group to use the carboxylic acid 124 to synthesis the oxazolidin-2-one adduct 154. Unfortunately, the carboxylic acid 124 which is used to form the active ester 126 and then the oxazolidin-2-one adduct 154 is only commercially available as a racemate, so in order to carry out a stereospecific synthesis of oxazolidin-2-one adduct 154 we first needed to resolve the carboxylic acid (rac)-124.

The MKRs above showed that the diastereoisomers of the benzyl oxazolidin-2-one adducts syn- and anti-148 was separable, so we carried out a KR of the active ester (rac)-126 using oxazolidin-2-one (R)-145 (Scheme 2.16). Although the selectivity of this reaction was very poor as only one equivalent of the active ester (rac)-126 was used this was not important as the two diastereoisomers were indeed separable. With the two diastereoisomers in hand, we next hydrolysed these adducts to return the oxazolidin-2-one and yield the required optical pure carboxylic acids (R)- and (S)-124. The sign of these adducts were obtained by comparing their optical rotations with literature values [lit: (R)-124: [α]D -34, c 1.6 in CHCl₃]. As we now knew the sign of these carboxylic acids 124, we could work out the actual configuration of the oxazolidin-2-one adducts syn- and anti-148.


With the optically pure carboxylic acids (S)- and (R)-124 in hand, we could synthesise the required enantiomERICALLY pure active esters (S)- and (R)-126, and then in turn use these in stereospecific reactions with the oxazolidin-2-ones (R,S)-syn-104, (S)-24 and (R)-94. These reactions all gave the required single diastereoisomers (Scheme 2.18), and hence allowed us to confirm the configuration of the product that we had obtained from the previous MKRs.

As seen in Scheme 2.17, lithium hydroxide and hydrogen peroxide can be used to hydrolyse the oxazolidin-2-one adducts to give the corresponding carboxylic acid and oxazolidin-2-one. We decided to test this hydrolysis method on a range of substituted oxazolidin-2-one adducts to see if any of the groups would hinder this process. The reaction seemed rather robust and gave good yields of both the oxazolidin-2-ones and carboxylic acids for a variety of different oxazolidin-2-one adducts (Schemes 2.19 to 2.24).

We carried out a hydrolysis reaction of the labelled oxazolidin-2-one adduct (R,S)-syn-161, the most acidic proton of this oxazolidin-2-one adduct had been replaced with a deuterium atom. If the percentage deuterium content of the carboxylic acid (R)-162 obtained was the same as that of the starting material then it would confirm that this method does not interfere with the chiral centres of this reaction in any way. This reaction did indeed give an optically pure carboxylic acid (R)-162 with identical levels of deuterium content as the starting material (Scheme 2.22 entry 3), combined with the fact that all previous hydrolysis reactions gave products with the expected optical purity, it can be concluded that this hydrolysis reaction did not interfere with the chiral centre of the products.

Scheme 2.23: Hydrolysis of oxazolidin-2-one adducts (S,R)-syn-155.

Scheme 2.24: Hydrolysis of oxazolidin-2-one adducts (S,R)-syn-163.

In conclusion, a reliable and robust resolution method for racemic carboxylic acids has been developed, by first converting them into their corresponding active esters and then reacting them with a lithiated oxazolidin-2-one in either kinetic or parallel kinetic resolution. The resulting adducts can be easily hydrolysed without loss of optical purity to give the required carboxylic acids. The highest levels of diastereoselectivity were obtained when the four substituent of the oxazolidin-2-one ring was a relatively bulky group with an sp2 hybridised connecting carbon atom (e.g. a phenyl ring). The pentafluorophenyl leaving group of the active ester gave the highest levels of diastereoselectivity in favour of the syn-diastereoisomer, whilst the use of a related acid chloride gave slightly lower levels of diastereoselectivity in favour of the complementary anti-diastereoisomer.
With this methodology in place, we wished to explore the resolution of active esters with different overall structures, such as the acetoxy based active ester (rac)-165. Interestingly, when we carried out a MKR of this pentafluorophenyl active ester (rac)-165 with the oxazolidin-2-one (rac)-94 that had given the highest levels of stereoselectivity previously, we obtained an almost equal mixture of the two diastereoisomers (Table 2.19 entry 1). Clearly the acetoxy group must behave in a very different fashion than the methyl group in the active ester (rac)-95 screened previously. We know that the electronic nature of the substituent on the oxazolidin-2-one and the phenyl ring of the active ester play a curial role in the stereoselective step of the reaction, so it is quite feasible that having an additional coordinating group on the active ester has adversely affected this stereoselective step.

![Chemical structure](image)

**Table 2.19**: MKRs of acetoxy based active esters.

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Ester</th>
<th>Ratio syn:anti</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>OCF₃</td>
<td>165</td>
<td>44:56</td>
<td>60%</td>
</tr>
<tr>
<td>2</td>
<td>ortho-OC₆H₄OMe</td>
<td>166</td>
<td>-</td>
<td>0%</td>
</tr>
<tr>
<td>3</td>
<td>para-OC₆H₄OMe</td>
<td>167</td>
<td>-</td>
<td>0%</td>
</tr>
<tr>
<td>4</td>
<td>para-OC₆H₄Cl</td>
<td>168</td>
<td>88:12</td>
<td>37%</td>
</tr>
<tr>
<td>5</td>
<td>para-OC₆H₄Me</td>
<td>169</td>
<td>74:26</td>
<td>&lt;10%</td>
</tr>
</tbody>
</table>

To see if we could increase the selectivity of this reaction, we decided to change the leaving group of this active ester, as we knew from previous work (Table 2.9) that this has a dramatic effect on the selectivity of the reaction. When an electron donating methoxy group was put on the phenol leaving group [e.g. active ester (rac)-166 and (rac)-167] the reaction completely stopped regardless of the position of this substituent. Presumably, the methoxy group reduces the leaving ability of the phenol to such a degree that no product is formed. However, addition of an electron withdrawing group to the para position of this ring did indeed improve the selectivity of this reaction; however as they were not as good a leaving group, as pentafluorophenol, the yield of these reactions decreased (Table 2.19).

In order to get a better understanding of how much the different leaving groups would affect the rate of the reaction, we carried out two competitive reactions (Schemes 2.25 and 2.26). In both examples, one of the active esters has a pentafluorophenyl
leaving group, whereas the other has a para-chlorophenyl leaving group. One of the acetoxy groups is slightly altered just so that the products can be distinguished from one another. These reactions clearly show that pentafluorophenyl is a far better leaving group and hence is dominant in both reactions.

Scheme 2.25: Competitive chemoselective reaction.

Interestingly, when we attempted our normal hydrolysis method on the acetoxy based oxazolidin-2-one adduct (rac)-syn-164, we could not reisolate the carboxylic acid (rac)-135 (Scheme 2.27). The oxazolidin-2-one (rac)-94 was obtained in good yield, indicating that cleavage had taken place. We speculated that the excess base (as two equivalents of lithium hydroxide were used) may have also hydrolysed the acetoxy group. As a result we chose to only use one equivalent of base in the hope that this would chemoselectively hydrolyse the more electrophilic C=O bond between the carbonyl group and the nitrogen atom of the oxazolidin-2-one ring. This approach was successful for both diastereoisomers of the oxazolidin-2-one 164, giving the corresponding oxazolidin-2-ones and carboxylic acids in good yield with no loss of optical purity (Scheme 2.28).
ad developed a reliable resolution method that could be adapted to resolve a range of different carboxylic acids there was still one main problem we had to overcome. We had only found two different oxazolidin-2-ones 94 and 157 that gave

Scheme 2.27: Attempted hydrolysis of oxazolidin-2-one adduct (rac)-syn-164.

Scheme 2.28: Hydrolysis of oxazolidin-2-one adducts (R,R)-anti and (S,R)-syn-164.

From the results obtained in Schemes 2.27 and 2.28, we speculated that if a large excess of base was used in the hydrolysis of an oxazolidin-2-one adduct (rac)-164 then both acetoxy group and oxazolidin-2-one would be cleaved, giving the carboxylic acid (rac)-56. However when this reaction was attempted, we could only isolate the oxazolidin-2-one (rac)-94 (Scheme 2.29), again in a high yield which indicated that the reaction should have worked. So we wondered if the carboxylic acid (rac)-56 was simply not being extracted from the aqueous layer. Through dissolving a sample of this carboxylic acid (rac)-56 in water, and trying to extract it we found that it was simply too water soluble to extract from the aqueous solution and this had been the only reason why we could never isolate it.

Scheme 2.29: Attempted hydrolysis of oxazolidin-2-one adduct (rac)-syn-164.

Although we had developed a reliable resolution method that could be adapted to resolve a range of different carboxylic acids there was still one main problem we had to overcome. We had only found two different oxazolidin-2-ones 94 and 157 that gave
the high levels of selectivity that were required, however, as it was the four substituent that differed on these two oxazolidin-2-ones, their relative rates also differed (Scheme 2.13 entry 1 and Scheme 2.14 entry 1). For a good PKR these reaction rates as well as the levels of diastereoselectivity need to be perfectly matched, we speculated that this could be obtained by keeping the four substituent of the oxazolidin-2-one the same in both cases but changing the five substituents on one of the two oxazolidin-2-one rings.

The simplest way to test this method was to replace both the hydrogen atoms at the five position with deuterium atoms, as this would give two products with identical yields and levels of diastereoselectivity (Scheme 2.30). However, the draw back of this reaction, was that the products could only be distinguished from each other and not separated.

Scheme 2.30: PKR of active ester (rac)-113.

We decided to investigate the use of phenyl substituents in the five position of the oxazolidin-2-one ring, as they would hopefully work in a similar fashion to the deuterium atoms in Scheme 2.30, but also allow for the separation of products. However before attempting to use the oxazolidin-2-one 175 in a PKR, we chose to carry out a number of MKRs with different active esters, so that their results could be compared to those obtained when using the traditional oxazolidin-2-one (rac)-94 (Scheme 2.13). Interestingly the levels of selectivity were slightly lower while using this oxazolidin-2-one 175, and perhaps stranger still the levels of selectivity increased when the aryl ring of the active ester was modified (Table 2.20).
Table 2.20: MKRs using oxazolidin-2-one (rac)-175.

We were initially unsure how changing the substituent at the five position could alter the diastereoselectivity of this reaction, with it being so far away from where the active ester would approach. We wondered if the additional two phenyl groups had made the oxazolidin-2-one more basic, and as a result, it was starting to racemize the active esters. To test this theory we carried out a stereospecific reaction (Scheme 2.31), however this only gave one diastereoisomer, clearly showing that no racemization had taken place.

Scheme 2.31: Stereospecific synthesis of oxazolidin-2-one adduct (S,R)-syn-182.

An alternative way we could explain why the levels of selectivity had been lower whilst using oxazolidin-2-one (rac)-175 was that the oxazolidin-2-ones did not react as a single species in solution but as a collection of at least two. If this was the case, then substituents at the five position would change the shape of this aggregate which in turn would also alter the diastereoselectivity of the reaction. We also considered that the addition of an achiral oxazolidin-2-one, such as 183, would therefore also change the shape and reactivity of this aggregate, and hence change the diastereoselectivity of this reaction. The addition of this achiral oxazolidin-2-one did indeed change the selectivity of this reaction; it improved it to a similar level of selectivity as the original MKR obtained when using the oxazolidin-2-one (rac)-94.
This suggested that the additional two phenyl rings of oxazolidin-2-one \textit{(rac)}-175 made the aggregate too sterically crowded.

![Scheme 2.32](image)

\textbf{Scheme 2.32:} MKR with additional achiral oxazolidin-2-one 183.

We also carried out this reaction under kinetic resolution conditions; however there was almost no change in the levels of selectivity with or without the achiral oxazolidin-2-one 183. From these results this suggests that the aggregates for these MKRs and PKRs contain at least one of each isomer of the oxazolidin-2-one.

![Scheme 2.33](image)

\textbf{Scheme 2.33:} KR of active ester \textit{(rac)}-95.

![Scheme 2.34](image)

\textbf{Scheme 2.34:} KR of active ester \textit{(rac)}-95 with additional achiral oxazolidin-2-one 183.

If the stereodirecting step in this reaction is indeed based around an aggregate, we wondered what effect the use of a \textit{quasi}-enantiomeric mixture rather than a racemic mixture of active esters would have on the selectivity of this reaction. In order to test this, we next carried out a PKR of oxazolidin-2-one \textit{(rac)}-174 using the pair of active esters \textit{(S)}-123 and \textit{(R)}-119. The levels of diastereoselectivity for this reaction was much higher than for the corresponding MKRs (Scheme 2.35 vs. Table 2.20); this indicated that either the active esters are also part of this aggregate or both active esters react at the same time with one aggregate.
Scheme 2.35: PKR of oxazolidin-2-one (rac)-175.

As these reactions seemed to be based around the formation of an aggregate the only way we could really analyse them was by carrying out the actual PKRs that we were interested in. The levels of selectivity were exceptionally high for all of these PKRs (Table 2.21); clearly indicating that the aggregate formed between the two oxazolidin-2-ones (S)-175 and (R)-94 were perfectly matched for this resolution. The only active ester that gave lower levels of selectivity was the highly sterically demanding active ester (rac)-126, which had also given poor levels of selectivity irrespective of the oxazolidin-2-one used to resolve it.

Table 2.21: PKRs using oxazolidin-2-ones (S)-175 and (R)-94.
As the levels of selectivity were exceptional for most of the PKRs (Table 2.21), it became very difficult to accurately determine which of the two oxazolidin-2-ones used was dominate in the reactions. In order to try and figure this out we carried out two reactions with none equal ratios of the quasi-enantiomers oxazolidin-2-ones (R)-94 and (S)-175. The enantiomer in the lowest ratio should give the highest levels of selectivity, whilst the enantiomer in the higher ratio should give the lowest levels of selectivity. When oxazolidin-2-one (S)-175 was used in the higher ratio it gave better levels of selectivity than when oxazolidin-2-one (R)-94 was in the higher ratio. This would indicate that the oxazolidin-2-one (S)-175 was the most selective resolving agent out of the two.

![Scheme 2.36: Competitive reactions.](image)

The yields obtained from the PKRs (Table 2.21) were always very similar, suggesting that the oxazolidin-2-one (R)-94 and (S)-175 have similar overall reaction rates. We wished to further investigate this, so we chose to deprotonate an equimolar mixture of (R)-94 and (S)-175 with n-BuLi, followed by the addition an acidic deuterium source. The results obtained suggest that the oxazolidin-2-one (R)-94 is more acidic than the triphenyl oxazolidin-2-one (S)-175.

![Scheme 2.37: Competitive deprotonation.](image)

Although deprotonation is obviously a vital part in determining the rate of the reaction so is the addition process. Therefore, we next decided to carry out competitive
reactions with a variety of different sized electrophiles with different leaving groups. We hoped that this would give us more information about the rates of this reaction; we decided to only use achiral electrophiles, as this would not complicate this reaction by formation of diastereoisomers. We first synthesised a range of achiral active esters, by hydrolysing the appropriate acid chloride and then using a DCC coupling reaction on the resulting carboxylic acid to give the required achiral active esters (Scheme 2.38).

![Scheme 2.38: Synthesis of an achiral active esters.](attachment:image)

With the range of achiral electrophiles synthesised, we started carrying out competitive reactions between oxazolidin-2-ones (R)-94 and (S)-175. When relatively small electrophiles were used there did not appear to be much difference in their relative rates of reaction (Table 2.22 entries 1 to 6). However, when a more sterically demanding electrophile was used the smaller oxazolidin-2-one (R)-94 reacted considerably quicker (Table 2.22 entry 7 to 10).
Table 2.22: Competitive reactions with achiral electrophiles.

The last reaction that we chose to carry out with this pair of oxazolidin-2-ones was a cross over reaction; this is similar to a PKR apart from two pairs of quasi-enantiomers were used rather than one pair and a racemic substrate. This reaction is not an actual resolution; each oxazolidin-2-one should simply react with its preferred active ester. However, there should only be four products made during the reaction, if any additional product were to form it would show that racemization, and or epimerisation has occurred. When this reaction was carried out it only gave the expected four products (Scheme 2.39), showing that none of the chiral centres were changed during this reaction and the levels of selectivity were also very high as expected from their relative PKRs.

Scheme 2.39: Cross over reaction of oxazolidin-2-one (S)-175 and (R)-94.
With a very selective PKR in place, using the pair of oxazolidin-2-ones 94 and 175, we only needed to show that the required carboxylic acid could be cleaved off the oxazolidin-2-one after the resolution. Using our standard hydrolysis procedure, we were able to easily cleave the carboxylic acid 111 from the oxazolidin-2-one, and by deuterium labelling the oxazolidin-2-one adduct we were able to confirm that no racemization occurred during this reaction.

While I was investigating the use of the 4,5,5-triphenyl oxazolidin-2-one 175 as a partner for the 4-phenyl oxazolidin-2-one 94, other members of the group were testing other oxazolidin-2-ones for this role. They had also managed to find several oxazolidin-2-ones that could be used as a partner in a PKR with the 4-phenyl oxazolidin-2-one 94, all of which had proved to be highly selective in MKRs. We wished to see which pair of these oxazolidin-2-ones would be the best partner. We decided to evaluate this by looking at their relative rates of reaction; if we could find a pair with almost identical rates of reaction they should give the highest levels of diastereoselectivity.

We decided that the best way to do this would be to carry out competitive stereospecific reactions, as the results should therefore not be affected by the selective nature of the compounds being screened. By carrying out this competitive reaction with each possible combination of oxazolidin-2-ones, we were able to discover their relative rates of reaction. The oxazolidin-2-one (R)-218 was by far the slowest, and in fact did not react in any of our competitive reactions; presumably the hydroxyl group on the aryl ring slows the reaction rate down by adding additional competitive coordinating in the intermediates.

The 4,5,5-triphenyl oxazolidin-2-one (R)-175 reacted slightly slower than the two oxazolidin-2-ones (R)-94 and (R)-219, increased steric hindrance presumably

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**Scheme 2.40:** Hydrolysis of oxazolidin-2-one (R,S)-syn-176 and (R,S)-syn-217.
slowing down the rate at which this compound reacts. The remaining two oxazolidin-2-ones \((R)-94\) and \((R)-219\) reacted faster than all other compounds and actually reacted at almost identical rates. We therefore believe that this combination of oxazolidin-2-ones would give the highest levels of selectivity in PKRs.

![Scheme 2.41](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ox A</th>
<th>R₁</th>
<th>R₂</th>
<th>Ox B</th>
<th>R₃</th>
<th>R₄</th>
<th>Product X</th>
<th>Ratio X : Y</th>
<th>Product Y</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>94</td>
<td>Ph</td>
<td>H</td>
<td>175</td>
<td>Ph</td>
<td>Ph</td>
<td>163</td>
<td>70 : 30</td>
<td>180</td>
</tr>
<tr>
<td>2</td>
<td>94</td>
<td>Ph</td>
<td>H</td>
<td>218</td>
<td>para-C₆H₄OH*</td>
<td>H</td>
<td>163</td>
<td>100 : 0</td>
<td>220</td>
</tr>
<tr>
<td>3</td>
<td>94</td>
<td>Ph</td>
<td>H</td>
<td>219</td>
<td>para-C₆H₄OTBDMS</td>
<td>H</td>
<td>163</td>
<td>52 : 48</td>
<td>221</td>
</tr>
<tr>
<td>4</td>
<td>175</td>
<td>Ph</td>
<td>Ph</td>
<td>218</td>
<td>para-C₆H₄OH*</td>
<td>H</td>
<td>180</td>
<td>100 : 0</td>
<td>220</td>
</tr>
<tr>
<td>5</td>
<td>175</td>
<td>Ph</td>
<td>Ph</td>
<td>219</td>
<td>para-C₆H₄OTBDMS</td>
<td>H</td>
<td>180</td>
<td>30 : 70</td>
<td>221</td>
</tr>
<tr>
<td>6</td>
<td>218</td>
<td>para-C₆H₄OH*</td>
<td>H</td>
<td>219</td>
<td>para-C₆H₄OTBDMS</td>
<td>H</td>
<td>220</td>
<td>0 : 100</td>
<td>221</td>
</tr>
</tbody>
</table>

* 3.3 equiv.’s of nBuLi used

Table 2.23: Rates of reaction of different oxazolidin-2-ones.

We were next interested in seeing if we could get the very slow oxazolidin-2-one \((R)-218\) to react when used in conjunction with a second oxazolidin-2-one. So we carried out two PKR with this oxazolidin-2-one \((R)-218\) and simply increased the reaction time from two hours to overnight, so that this slower oxazolidin-2-one would have time to react. This approach proved reasonably successful, however even with the extended reaction time, the yields of the required product \((S,R)-syn-222\) was below 50% in both cases (Schemes 2.41 and 2.42).

![Scheme 2.41](image)

**Scheme 2.41:** PKR of active ester \((rac)-95\).
Scheme 2.42: PKR of active ester (rac)-95.

We wished to try one final oxazolidin-2-one 223 that could possibly be used as a partner for our original 4-phenyl oxazolidin-2-one 94 in a PKR, to investigate this, we simply carried out a KR with the new oxazolidin-2-one 223. The levels of selectivity of for this reaction however were slightly reduced in comparison to the original MKR using 4-phenyl oxazolidin-2-one (rac)-94. Clearly, the non-aromatic ring on the four position of this oxazolidin-2-one (rac)-223 interferes with the stereo-determining step within this reaction.

Scheme 2.43: KR using oxazolidin-2-one (rac)-223.

The adducts synthesised above using these new oxazolidin-2-ones could be readily hydrolysed by slightly modifying our standard procedure, we only used one equivalent of base to ensure that other groups were not cleaved during this reaction. This strategy proved successful, and again was shown to proceed without altering the optical purity of the compounds (Schemes 2.44 and 2.45).
We next turned our attention to the resolution of the more sterically demanding active ester 228, which could be readily synthesised from the corresponding carboxylic acid 227 (Scheme 2.46). We wanted to try and resolve this active ester 228 as it was structurally different from the active esters we had resolved previously, as it does not have an acidic hydrogen atom alpha to the carbonyl group.

Scheme 2.46: Synthesis of active ester (R)-228.

However, when we carried out what we believed to be a simple stereospecific reaction, we did not obtain the expected product (Scheme 2.47). The oxazolidin-2-one (S)-94 appears to reacted with the active ester (R)-228 to give the expected oxazolidin-2-one but this has then fragmented to give the two products (R,S)-syn-229 and (R,S)-syn-230. We believe that this fragmentation was caused by the product reacting with
lithium butoxide which is present in some bottles of \( n \)-BuLi. To check this we simply deprotonated butanol and then reacted it with this oxazolidin-2-one adduct \((R,S)\)-syn-231, to give one of the fragmented products obtained before, suggesting, that our argument was correct.

**Scheme 2.47:** Attempted stereospecific synthesis.

![Scheme 2.47](image)

**Scheme 2.48:** Synthesis of \((R,S)\)-syn-229.

We were able to synthesise the required oxazolidin-2-one adduct \((R,S)\)-syn-231 by using a base, \([\text{KNSiMe}_3]_2\), which did not have the ability to form alkoxides, however the sterically demanding nature of this active ester \((R)\)-228 did mean that the product was only obtained in a low yield (Scheme 2.49). However, we did not attempt to perform a resolution using this base, \([\text{KNSiMe}_3]_2\), as all previous resolutions had used \( n \)-BuLi; instead we considered using the alternative oxazolidin-2-one 175. We hoped that the addition phenyl substituents on the oxazolidin-2-one ring would prevent this endo-cleavage seen in Scheme 2.47.

**Scheme 2.49:** Stereospecific synthesis of oxazolidin-2-one adduct \((R,S)\)-syn-231.

We realised that if this method was successful, it would be very difficult to find an additional oxazolidin-2-one that we could use as a partner in a PKR, so we decide
that we should simply study the KRs of the active ester \((\text{rac})-228\). This new approach proved very successful giving the required oxazolidin-2-one adduct 232 with high levels of diastereoselectivity, and without any other by-products being formed (Scheme 2.50). The stereospecific variation of this reaction also proceeded efficiently allowing us to actually determine that the \((\text{S},\text{R})\)-\(\text{syn}\)-232 diastereoisomer had been the major diastereoisomer.

![Scheme 2.50: KR of active ester \((\text{rac})-228\).](image-url)

Just for curiosity, we decided to see if the more sterically demanding oxazolidin-2-one adduct \((\text{R},\text{S})\)-\(\text{syn}\)-232 would ring open in the presence of a large excess of lithium butoxide. Surprisingly, it did indeed ring open, to give the products \((\text{R},\text{S})\)-\(\text{syn}\)-234 and \((\text{R},\text{S})\)-\(\text{syn}\)-235, however the more dominant reaction was the cleaving of the acid motif from the oxazolidin-2-one to give the butyl ester \((\text{R})\)-233 and the oxazolidin-2-one \((\text{S})\)-175 (Scheme 2.52). The butyl ester \((\text{R})\)-233 was also synthesized by a DCC coupling reaction just to check that this was indeed the product that we had obtained (Scheme 2.53).
Scheme 2.52: Reaction of LiOBu with oxazolidin-2-one adduct (R,S)-syn-232.

Scheme 2.53: Synthesis of ester (R)-233.

With a highly selective KR in place all we had left to do was to carry out a hydrolysis reaction so that we could obtain the required carboxylic acid (R)-227. Surprisingly the sterically demanding nature of the carboxylic motif in 232 meant that the rate of hydrolysis was reduced and a degree of endo-ring opening had also occurred (Scheme 2.54).


All the oxazolidin-2-ones that we have so far screened have the same ring structure but with different substituents. We were next interested in studying the resolution of oxazolidin-2-thiones, to see what role, the sulphur atom might play. We decided to test the resolving agent 4-phenyl oxazolidin-2-thione (rac)-236, with a range of different active esters; the results obtained were very promising giving levels of selectivity at least as high as those obtained for the original oxygen counter part (rac)-94 (Table 2.24 vs. 2.13).
Again to determine the actual stereochemistry we carried out a stereospecific reaction (Table 2.25); the yields of these reactions were very low, which could have been due to experimental error as these reactions were carried out on a small scale and the base used could have degraded. Although, the yield for the synthesis of (S,R)-syn-237 was low (20%), the (R,R)-anti-237 adduct was not formed, which we found initially surprising.

Table 2.24: MKRs with oxazolidin-2-thione (rac)-236.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>R</th>
<th>Ester</th>
<th>Ratio syn : anti</th>
<th>Product</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph</td>
<td>Me</td>
<td>95</td>
<td>97 : 3</td>
<td>237</td>
<td>63%</td>
</tr>
<tr>
<td>2</td>
<td>Ph</td>
<td>Et</td>
<td>119</td>
<td>&gt;98 : 2</td>
<td>238</td>
<td>34%</td>
</tr>
<tr>
<td>3</td>
<td>Ph</td>
<td>i-Pr</td>
<td>126</td>
<td>-</td>
<td>239</td>
<td>0%</td>
</tr>
<tr>
<td>4</td>
<td>6-Methoxynaphthalen-2-yl</td>
<td>Me</td>
<td>123</td>
<td>93 : 7</td>
<td>240</td>
<td>57%</td>
</tr>
</tbody>
</table>

Table 2.25: Stereospecific of oxazolidin-2-thione adduct 237.

Due to the results obtained from these stereospecific reactions, we decided to further evaluate the resolving agent 236 by looking at how it preformed in KR. We therefore carried out two KR, one with an equal ratio of oxazolidin-2-thione (R)-236 and active ester (rac)-95, and one with twice as much active ester (rac)-95. The reaction using two equivalents of active ester (rac)-95 gave very high levels of selectivity which were only slightly less than those for the MKR (Scheme 2.55 entry 2 vs. Table 2.24 entry 1). However, more surprisingly the level of selectivity for the reaction using only one equivalent of active ester (rac)-95 was also very high (Scheme 2.55 entry 1), such a high level of selectivity for a one to one kinetic reaction is most unusual.
Scheme 2.55: KRs using oxazolidin-2-thione (R)-236.

The main difference between a KR and a MKR, is that a MKR is independent of the concentration effect, whilst a one to one KR is the most susceptible to the concentration effect. If very high levels of selectivity were observed in a one to one KR then a MKR should lead to exceptional selectivity; however, in this particular case there is not a vast difference between the two resolutions. The only way to explain this is that the concentration affect is not a major factor in this reaction, indicating that this reaction is not completely kinetic in nature. We believe that the selectivity of the reaction is largely thermodynamically driven, and hence part of the reaction process must be reversible.

This would suggest that the initial addition of the oxazolidin-2-thione (R)-236 to the active ester (rac)-95 creates an intermediate that can fragment in two ways. Either by loss of the oxazolidin-2-thione (R)-236 to regenerate the starting materials, or the by loss of pentafluorophenol to generate the product; the second pathway is presumably dominate when the syn-diastereoisomer is formed. This work is currently being further investigated by Najla Al Shaye as part of her PhD studies in the Eames group.

To conclude, a method that had been discovered prior to my PhD studies has been optimised both by testing different reaction conditions and by exploring a wide range of oxazolidin-2-ones that could be used as partners for the initial resolving agent 4-phenyl oxazolidin-2-one 94. The method has also been greatly extended so that a much larger range of active esters can be resolved, including active ester that significantly differ from the original pentafluorophenyl-2-phenyl-propionate (rac)-95. The diastereoselective mechanism of the reaction has also started to be explained, we now know that the four substituent of the oxazolidin-2-one has to be aryl, the structural nature of the aryl ring of the active ester is also incredibly important. We also believe
that the reactive intermediate is in fact an aggregate including at least one of each enantiomer, and that for the highest levels of diastereoselectivity in a PKR resolution, reagents with almost identical reaction rates should be used. With the results obtained from the oxazolidin-2-thione 236 work it would appear that selectivity of all the above reactions have a degree thermodynamic character to them.
Chapter 3

The Optical Rotation of 4-Isopropyl-oxazolidin-2-one

During the development of the resolution method outlined in Chapter 2, we carried out a kinetic resolution of the racemic oxazolidin-2-one \((\text{rac})-24\) using the enantiomerically pure active ester \((S)-115\). The levels of diastereoselectivity were found to be somewhat modest (Scheme 3.1). During the purification of this reaction we re-isolated the remaining oxazolidin-2-one \(24\) and measure its optical rotation then compared this to the literature in order to measure its enantiomeric excess. However, the initial value was found to have the opposite sign than to what we had obtained.\(^{149}\) A more in-depth search into the literature revealed that a variety of values had been obtained for the optical rotation of oxazolidin-2-one \((S)-24\) from +16.8 to -20.0.\(^{150,151,152,153,154}\) The same levels of discrepancy was also true for oxazolidin-2-one \((R)-24\).\(^{155,152,156,157}\)

![Scheme 3.1: KR of oxazolidin-2-one (rac)-24.](image)

Although it is common to see changes in optical rotation from one research group to another, I personally had never seen two publications giving opposite signs of rotation for the same enantiomer. What seemed especially strange is that this oxazolidin-2-one \((S)-24\) is a rather common substrate, and is readily commercially available, we decided that this was worthy of further investigation. The first thing we did was to synthesise both enantiomers of 24 from their appropriate amino acids 30, by LiAlH\(_4\) reduction followed with ring closer using diethyl carbonate (Scheme 3.2). With these compounds in hand, we chose to react them with an enantiomerically pure active ester \((S)-115\), to check that they had in fact been synthesised in an optically pure form, both of these reactions indeed only gave one diastereoisomer (Scheme 3.3).
Scheme 3.2: Synthesis of oxazolidin-2-one (S)-24 and (R)-24.

Scheme 3.3: Stereospecific reactions.

With both enantiomers of oxazolidin-2-one 24 in hand, and with the knowledge that they were enantiomerically pure, we decided to start investigating their physical properties. Their melting points were found to be identical which suggested that both had been synthesised with the same degree of purity (Table 3.1), we then recorded the optical rotations in chloroform which gave very similar values of opposite sign that agreed with the previous measurements we had taken in Scheme 3.1. However, we then carried out the optical rotations in a second solvent, ethanol, remarkably the sign of the rotation swapped for both enantiomers. At first we believed that the result was simply an error caused by mixing the samples up, however multiple repeats of the optical rotation for both enantiomers in both solvents kept on giving the same results.
<table>
<thead>
<tr>
<th>Sign</th>
<th>Enantiomeric excess</th>
<th>Mp</th>
<th>$[\alpha]_d^{25}$ in CHCl$_3$</th>
<th>$[\alpha]_d^{25}$ in Ethanol</th>
</tr>
</thead>
<tbody>
<tr>
<td>$S$</td>
<td>100%</td>
<td>67-70$^\circ$C</td>
<td>+14.9 (C = 4.2)</td>
<td>-15.8 (C = 5.0)</td>
</tr>
<tr>
<td>$S$</td>
<td>50%</td>
<td>64-68$^\circ$C</td>
<td>+8.1 (C = 3.8)</td>
<td>-7.5 (C = 4.2)</td>
</tr>
<tr>
<td>rac</td>
<td>0%</td>
<td>73-76$^\circ$C</td>
<td>0 (C = 3.8)</td>
<td>0 (C = 4.8)</td>
</tr>
<tr>
<td>$R$</td>
<td>50%</td>
<td>64-68$^\circ$C</td>
<td>-7.6 (C = 3.6)</td>
<td>+8.1 (C = 4.6)</td>
</tr>
<tr>
<td>$R$</td>
<td>100%</td>
<td>67-70$^\circ$C</td>
<td>-13.1 (C = 4.2)</td>
<td>+16.1 (C = 4.6)</td>
</tr>
</tbody>
</table>

Table 3.1: Physical properties of oxazolidin-2-one 24.

At this point, we also chose to measure the same physical properties for a racemic and two scalemic mixtures, the racemic mixture gave zero for optical rotation as had been expected; while both scalemic mixtures followed the same results obtained previously but with reduced values as expected. Interestingly when we looked back in the literature we noticed that values reported were in agreement with what we observed, for example almost all the optical rotations of ($S$)-24 that gave positive values had been carried out in chloroform, whilst all the negative values had been carried out in ethanol. This would suggest that in fact almost all the data in the literature was correct, even though it was rather confusing and misleading.

It appeared however that no other research group had noticed this strange phenomenon, so we wanted to see if we could try to understand why this was observed. So we decide to take optical rotations of oxazolidin-2-one ($S$)-24 in mixtures of ethanol and chloroform (Table 3.2). Starting in pure chloroform a positive value was obtained, however, this quickly diminished as ethanol was added until an optical rotation of zero was observed at a 85 : 15 mixture of chloroform to ethanol. Further increases in the amount of ethanol used gave negative values of rotation that steadily increased with the amount of ethanol.
<table>
<thead>
<tr>
<th>Ratio CHCl₃ : Ethanol</th>
<th>$[\alpha]^{25}_d$</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 : 0</td>
<td>+15.5</td>
<td>5.2</td>
</tr>
<tr>
<td>99 : 1</td>
<td>+14.3</td>
<td>6.2</td>
</tr>
<tr>
<td>90 : 10</td>
<td>+2.8</td>
<td>5.2</td>
</tr>
<tr>
<td>85 : 15</td>
<td>0.0</td>
<td>6.2</td>
</tr>
<tr>
<td>80 : 20</td>
<td>-1.8</td>
<td>6.4</td>
</tr>
<tr>
<td>70 : 30</td>
<td>-5.1</td>
<td>6.2</td>
</tr>
<tr>
<td>60 : 40</td>
<td>-7.2</td>
<td>7.0</td>
</tr>
<tr>
<td>50 : 50</td>
<td>-9.8</td>
<td>6.8</td>
</tr>
<tr>
<td>40 : 60</td>
<td>-12.7</td>
<td>5.8</td>
</tr>
<tr>
<td>30 : 70</td>
<td>-13.6</td>
<td>7.0</td>
</tr>
<tr>
<td>20 : 80</td>
<td>-14.3</td>
<td>6.0</td>
</tr>
<tr>
<td>15 : 85</td>
<td>-14.4</td>
<td>6.0</td>
</tr>
<tr>
<td>10 : 90</td>
<td>-16.1</td>
<td>5.8</td>
</tr>
<tr>
<td>1 : 99</td>
<td>-16.1</td>
<td>6.2</td>
</tr>
<tr>
<td>0 : 100</td>
<td>-16.1</td>
<td>5.2</td>
</tr>
</tbody>
</table>

Table 3.2: Specific rotations of oxazolidin-2-one (S)-24.

We next wished to explore how concentration might affect the optical rotations, so we carried out three measurements of oxazolidin-2-one (S)-24 in each solvent, one with a very low, one a normal, and one with a very high concentration. For the specific rotations taken in chloroform the medium and high levels of concentration gave very similar results, whilst the low concentration sample gave a much lower value. However when ethanol was used the value steadily decreased as the concentration rose, and in a much less dramatic fashion than for the samples in chloroform (Table 3.3).
Table 3.3: Specific rotations of oxazolidin-2-one (S)\textsuperscript{-24}.  

<table>
<thead>
<tr>
<th>([\alpha])\textsubscript{D}</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>+10.0</td>
<td>0.6 in CHCl\textsubscript{3}</td>
</tr>
<tr>
<td>+15.6</td>
<td>3.0 in CHCl\textsubscript{3}</td>
</tr>
<tr>
<td>+16.5</td>
<td>10.4 in CHCl\textsubscript{3}</td>
</tr>
<tr>
<td>-16.0</td>
<td>0.7 in Ethanol</td>
</tr>
<tr>
<td>-15.7</td>
<td>4.4 in Ethanol</td>
</tr>
<tr>
<td>-14.6</td>
<td>11.0 in Ethanol</td>
</tr>
</tbody>
</table>

The next logical step was to see how other solvents would affect the rotations, so we simple carried out a range of optical rotations with approximately the same concentration each time but different solvents (Table 3.4). The results were quite astonishing, with optical rotations varying from -21.9 with methanol to +25.2 in diethyl ether and approximately zero when using 1,4-Dioxane and THF. When the results were tabulated in order of the optical rotation obtained (Table 3.4), the solvents lined up in order of hydrogen bonding, with the best hydrogen bonders giving lowest optical rotations (\textit{i.e.}, -21.9 with MeOH).
<table>
<thead>
<tr>
<th>$[\alpha]_D^2$</th>
<th>C</th>
<th>Solvent</th>
</tr>
</thead>
<tbody>
<tr>
<td>-21.9</td>
<td>2.8</td>
<td>MeOH</td>
</tr>
<tr>
<td>-20.2</td>
<td>4.2</td>
<td>DMSO</td>
</tr>
<tr>
<td>-17.4</td>
<td>2.6</td>
<td>EtOH</td>
</tr>
<tr>
<td>-13.2</td>
<td>5.0</td>
<td>DMF</td>
</tr>
<tr>
<td>-11.7</td>
<td>4.6</td>
<td>MeCN</td>
</tr>
<tr>
<td>-9.2</td>
<td>2.8</td>
<td>i-PrOH</td>
</tr>
<tr>
<td>-4.6</td>
<td>6.2</td>
<td>Acetone</td>
</tr>
<tr>
<td>+0.25</td>
<td>3.2</td>
<td>1,4-Dioxane</td>
</tr>
<tr>
<td>+0.3</td>
<td>5.2</td>
<td>THF</td>
</tr>
<tr>
<td>+2.8</td>
<td>3.4</td>
<td>EtOAc</td>
</tr>
<tr>
<td>+5.1</td>
<td>2.8</td>
<td>CCl₄</td>
</tr>
<tr>
<td>+6.8</td>
<td>4.4</td>
<td>EtOCO₂Et</td>
</tr>
<tr>
<td>+9.7</td>
<td>2.6</td>
<td>CH₂Cl₂</td>
</tr>
<tr>
<td>+15.6</td>
<td>3.0</td>
<td>CHCl₃</td>
</tr>
<tr>
<td>+25.2</td>
<td>2.4</td>
<td>Et₂O</td>
</tr>
</tbody>
</table>

Table 3.4: Specific rotations of oxazolidin-2-one (S)-24.

All of these results seem to point to one thing, the oxazolidin-2-one (S)-24 appeared to form an aggregate, presumably of two hydrogen bond molecules, this aggregate had an optical rotation of around +15, the results obtained when the poor hydrogen bonding solvent CHCl₃ was used. If this aggregate was broken up, either by the concentration being low that aggregation is disfavoured, or by using a good hydrogen bonding solvent, such as ethanol, the optical rotation is lowered until it reaches the natural rotation for the monomer around -20.

With a possible explanation in hand for this unusual observation, we were interested in seeing if this was limited only to the oxazolidin-2-one 24 or if it was a common occurrence among all oxazolidin-2-ones (Table 3.5). The four benzyl oxazolidin-2-one (R)-145 was also showed to have the same solvent dependence for optical rotations; however, this is clearly not a common feature amongst all oxazolidin-2-ones.
To conclude, an unusual inversion in optical rotation was observed both in our own studies and the literature; this was found to be due to the solvent the optical rotation was carried out in. This solvent dependency was explained through aggregate formation and was also found to occur for a related oxazolidin-2-one \((R)-145\).

Table 3.5: Optical rotations of oxazolidin-2-ones in CHCl₃ and Ethanol.
Chapter 4

The Resolution of 1-Phenylethanol using Oxazolidin-2-one Adducts

The studies carried out in Chapter 2 gave a reliable method for obtaining enantiomerically pure and enriched carboxylic acids and optically pure oxazolidin-2-one adducts. In 1993, Evans published a method for the kinetic resolution of 1-phenylethanol (rac)-11 using the oxazolidin-2-one adduct (S)-242 (Scheme 4.1). We believed that our oxazolidin-2-one adducts which were synthesised in Chapter 2, may be more suited for this resolution as they contain two stereocentres, and using a PKR we might also be able to improve the levels of diastereoselectivity for this reaction.

![Scheme 4.1: KR of 1-phenylethanol by Evans.](image)

We chose to start investigating this area by deprotonating 1-phenylethanol (rac)-11 with MeMgBr, so that a magnesium salt would be present in this reaction as in line with Evans’ example, followed by the addition of our oxazolidin-2-one adduct (rac)-syn-96 (Scheme 4.2). This initial MKR did indeed give the required ester (rac)-anti-245 and with relatively high levels of diastereoselectivity, the oxazolidin-2-one (rac)-94 was also reisolated. The yield of this reaction was far from desired, however, some of the starting material (rac)-syn-96 was reisolated, which partially accounted for this low conversation. Most problematic however was the formation of a second product, the carbonate (meso)-syn-243, this was found to be inseparable from the required ester product (rac)-anti-245. The compound (rac)-syn-244 was also isolated and in a similar yield to the carbonate (meso)-syn-243, clearly indicating that the carbonate was formed by a double addition of 1-phenylethanol (rac)-11 to the exo-carbonyl group of the oxazolidin-2-one (rac)-syn-96.
Scheme 4.2: MKR of 1-phenylethanol (rac)-11.

The carbonate 243 was synthesised separately for characterisation purposes, simply by adding deprotonated 1-phenylethanol 11 to CDI. This reaction was carried out with racemic and homochiral 1-phenylethanol (rac)- and (R)-11 so that the two different diastereoisomers of the carbonate 243 could be identified (Scheme 4.3).

Scheme 4.3: Synthesis of carbonate 243.

At first it seemed strange why in our reaction the carbonate had formed whilst Evans had never reported the presence of this compound in his related resolution work. However, closer examination of the two reactions gave some possible explanation; firstly the oxazolidin-2-one adduct (S)-242 used by Evans is much more likely to exo-cleave at the required nitrogen carbonyl bond, whereas our oxazolidin-2-one adduct (rac)-syn-96 was less likely to exo-cleave, as it is more sterically crowded at this location. Secondly, Evans had used much milder conditions compared to ours, presumably as a direct result of potential exo-cleavage.

As we had formed the unwanted carbonate 243, we now wished to try and understand a little more about how it was formed during this reaction. So we repeated the same reaction as above, but with a substoichiometric amount of base, to see if this would increase or decrease the amount of carbonate 243 formed in comparison to the ester 245. These reactions unfortunately did not further our understanding of the
carbonate 243 formation; however they did show a very interesting result (Table 4.1). As the relative amount of 1-phenylethanol (rac)-11 present increased, because the amount of base used reduced, the yield of the ester (rac)-anti-245 product increased to a very reasonable 77%.

![Scheme 4.4](image)

**Table 4.1**: MKR with substoichiometric amount of base.

<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>Ester d.e.</th>
<th>Ester yield</th>
<th>Carbonate d.e.</th>
<th>Carbonate yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.25</td>
<td>78%</td>
<td>77%</td>
<td>~20%</td>
<td>10%</td>
</tr>
<tr>
<td>2</td>
<td>0.5</td>
<td>74%</td>
<td>68%</td>
<td>~20%</td>
<td>4%</td>
</tr>
</tbody>
</table>

All yields based on MeMgBr.

As these reactions had not given us any further information about the carbonate formation we decided to see if the carbonate could be formed if the reaction was carried out using the oxazolidin-2-one (rac)-94 rather than an oxazolidin-2-one adduct (rac)-syn-96. However this reaction (Scheme 4.4) showed that the carbonate 243 can only be formed when the nitrogen atom of the oxazolidin-2-one ring had an exo-carbonyl group attached to it.

![Scheme 4.4](image)

**Scheme 4.4**: Reaction of 1-phenylethanol (rac)-11 with oxazolidin-2-one (rac)-94.

With this information in hand we next turned our attention towards improving the diastereoselectivity of this reaction; we first chose to change the four substituent of the oxazolidin-2-one ring for a variety of groups of differing in size and electronic configurations. We chose to increase the amount of 1-phenylethanol (rac)-11 used in these reactions, hoping that it would increase the yield as we had observed in Table 4.1. The yield of the required ester (rac)-anti-245 when using the original oxazolidi-2-one adduct (rac)-syn-96 was increased form 29% to 55% (Scheme 4.2 vs. Table 4.2 entry
4). When less sterically demanding four subsistent were used the diastereoselectivity of this reaction greatly diminished (Table 4.2 entries 1, 2 and 4), whilst the use of a large isopropyl group (Table 4.2 entry 3) gave the highest levels of diastereoselectivity but also the lowest yield. The ester group of (rac)-syn-158 could not be used as it was cleaved under these reaction conditions and an unassignable organic residue was obtained.

![Chemical structure](image)

**Table 4.2**: MKR with different syn oxazolidi-2-one adducts.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Oxazolidinone adduct</th>
<th>R</th>
<th>R₁</th>
<th>Ester d.e.</th>
<th>Ester yield</th>
<th>Carbonate d.e.</th>
<th>Carbonate yield*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>141</td>
<td>Me</td>
<td>Ph</td>
<td>32%</td>
<td>79%</td>
<td>-</td>
<td>0%</td>
</tr>
<tr>
<td>2</td>
<td>146</td>
<td>CH₂Ph</td>
<td>H</td>
<td>30%</td>
<td>52%</td>
<td>6%</td>
<td>12%</td>
</tr>
<tr>
<td>3</td>
<td>97</td>
<td>i-Pr</td>
<td>H</td>
<td>76%</td>
<td>37%</td>
<td>0%</td>
<td>8%</td>
</tr>
<tr>
<td>4</td>
<td>96</td>
<td>Ph</td>
<td>H</td>
<td>68%</td>
<td>55%</td>
<td>30%</td>
<td>14%</td>
</tr>
<tr>
<td>5</td>
<td>158</td>
<td>CO₂Et</td>
<td>H</td>
<td>-</td>
<td>0%</td>
<td>-</td>
<td>0%</td>
</tr>
</tbody>
</table>

* yield based on MeMgBr

These results clearly showed that the reaction is highly dependent on the structural nature of the four substituent; with the larger groups giving higher levels of selectivity, but also the lowest yields. We next chose to screen the same oxazolidin-2-one adducts, but this time using the anti-diastereoisomers, to see how altering the combination of chiral centres would affect this reaction. The levels of diastereoselectivity were found to be lower for the anti-diastereoisomeric adducts, however, the same diastereoisomer of the ester (rac)-anti-245 was formed. From this study it suggested that the chiral centre on the propionate fragment of the oxazolidin-2-one adduct is in fact the more dominant directing group for this reaction, and the four substituent of oxazolidin-2-one ring plays a minor role.
Enracilar rate; and the ester (\(\text{C}_2\)) and how the \(\text{C}_0\) \(\text{ER}\) array out a competitive reaction to \(\text{C}_4\) (\(\text{C}_3\)) studies this stereocontrol oxazolidinidn.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Oxazolidinone adduct</th>
<th>R</th>
<th>(\text{R}_1)</th>
<th>Ester d.e.</th>
<th>Ester yield</th>
<th>Carbonate d.e.</th>
<th>Carbonate yield*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>141</td>
<td>Me</td>
<td>Ph</td>
<td>24%</td>
<td>47%</td>
<td>-</td>
<td>0%</td>
</tr>
<tr>
<td>2</td>
<td>146</td>
<td>(\text{CH}_3)Ph</td>
<td>H</td>
<td>48%</td>
<td>62%</td>
<td>0%</td>
<td>14%</td>
</tr>
<tr>
<td>3</td>
<td>97</td>
<td>(\text{i-Pr})</td>
<td>H</td>
<td>22%</td>
<td>34%</td>
<td>-</td>
<td>0%</td>
</tr>
<tr>
<td>4</td>
<td>96</td>
<td>Ph</td>
<td>H</td>
<td>24%</td>
<td>41%</td>
<td>4%</td>
<td>14%</td>
</tr>
<tr>
<td>5</td>
<td>158</td>
<td>(\text{CO}_2\text{Et})</td>
<td>H</td>
<td>-</td>
<td>0%</td>
<td>-</td>
<td>0%</td>
</tr>
</tbody>
</table>

* yield based on \(\text{MeMgBr}\)

Table 4.3: MKR with different anti oxazolidi-2-one adducts.

In an attempt to understand how these different diastereoisomeric oxazolidin-2-one adducts affect this reaction, we chose to carry out a competitive reaction to see which diastereoisomers reacted preferentially. Interestingly both diastereoisomers appeared to react at a very similar rate; and the ester (\(\text{rac}\)-anti-245) obtained had the appropriate levels of diastereoisomeric excess.

Scheme 4.5: Competitive MKR.

With this information in hand, we believed that the four substituent of this oxazolidin-2-one ring only assisted this reaction and was not crucial for high levels of stereocontrol. To test this theory, we wished to use an oxazolidin-2-one adduct without a four substituent. This adduct was easily synthesised from the simple oxazolidin-2-one 183 and the active ester (\(\text{rac}\)-95) (Scheme 4.6). When the MKR of 1-phenylethanol (\(\text{rac}\)-11) was carried out using this new oxazolidin-2-one adduct (\(\text{rac}\)-184), surprisingly this reaction was completely stereounselective. This seemed to contradicts our previous studies in Tables 4.2 and 4.3; it perhaps suggests that for there to be any level of
selectivity a four substituent is required, however which diastereoisomer is formed is
governed by the propionate group.

Scheme 4.6: Synthesis of oxazolidin-2-one adduct (rac)-184.

Scheme 4.7: MKR using oxazolidin-2-one adduct (rac)-11.

From all of the above results the best oxazolidin-2-one adduct appears to be the
one with a phenyl substituent (rac)-syn-96, although the isopropyl oxazolidin-2-one
adduct (rac)-syn-97 had given higher levels of selectivity the yields obtained were
unacceptable (Table 4.2). We next chose to use the four substituent on the oxazolidin-
2-one ring but test it with a variety of different groups on the propionate substituent.
Changes to the aryl ring of the propionate group were found to have minimal affect on
the reaction rate and the selectivity of this reaction (Table 4.4), whilst exchanging the
propionate group for a more sterically bulky butanoate group significantly increased
selectivity of the reaction, whilst reducing the yield.
Table 4.4: MKR with different oxazolidi-2-one adducts.

With these results in hand, we next decided to carry out three PKRs of 1-phenylethanol (rac)-11. In all of these reactions one of the quasi-enantiomers used was the oxazolidin-2-one adduct (S,R)-syn-156, as this would lead to the ester (S,S)-anti-249, which would be more polar than any of the other esters formed due to the methoxy group on the naphthyl ring; this would allow the two esters products to be separated from each other. The other quasi-enantiomer was changed each time, so that we could get a better understanding of this PKR process, for each resolution the levels of diastereoselectivity and yields were similar to those obtained for their appropriate MKRs.

Scheme 4.8: PKR of 1-phenylethanol (rac)-11.
Scheme 4.9: PKR of 1-phenylethanol (rac)-11.

Scheme 4.10: PKR of 1-phenylethanol (rac)-11.

With a successful set of PKRs carried out, we next re-evaluated the reaction conditions to try and improve this reaction; one drawback with the resolution was that ten equivalents of 1-phenylethanol (rac)-11 had to be used. This could be seen as somewhat wasteful and undesirable in a PKR, we did know from earlier work (Table 4.1) that an excess of alcohol was required to obtain a reasonable yield, so we tried carrying out a simple MKR using two equivalents of 1-phenylethanol (rac)-11. This reaction was found to give almost identical results to that obtained previously (Scheme 4.11 vs. Table 4.2 entry 4), clearly indicating that only a slight excess of 1-phenylethanol (rac)-11 was required for these reactions.
Scheme 4.11: MKR only using two equivalents of 1-phenylethanol (rac)-11.

We next chose to investigate how the solvent might affect the reaction, primarily so we could get a better understanding of this reaction process. We chose to carry out this reaction with a non-coordinating solvent, DCM, with our normal ten equivalents of 1-phenylethanol (rac)-11 and only one equivalent to see how this might affect the levels of diastereoselectivity. When only one equivalent of 1-phenylethanol (rac)-11 was used, the reaction did not proceed, presumably as the resulting magnesium alkoxide was less solvated. However, when ten equivalents of this alcohol (rac)-11 was used, this reaction gave slightly higher levels of diastereoselectivity than when the co-ordinating solvent THF had been used (Table 4.5 entry 2 vs. Table 4.2 entry 4).

Table 4.5: MKRs in DCM.

<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>Ester d.e.</th>
<th>Ester yield</th>
<th>Carbonate d.e.</th>
<th>Carbonate yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>-</td>
<td>0%</td>
<td>-%</td>
<td>0%</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>78%</td>
<td>69%</td>
<td>24%</td>
<td>14%*</td>
</tr>
</tbody>
</table>

* Yield based on MeMgBr

It was believed that additional co-ordination from the solvent must make the diastereoselective intermediate more relaxed, hence increasing the chance of the less favoured diastereoisomer being formed. In order to check that this was indeed the case, these reaction conditions were repeated using a more sterically demanding oxazolidin-2-one adduct (rac)-syn-153 (Scheme 4.12). Again higher levels of diastereoselectivity were obtained while using DCM rather than THF. However, again the more sterically demanding group on this oxazolidin-2-one adduct (rac)-syn-153 caused the yield of this reaction to be lower.

To conclude, a method for the PKR of 1-phenylethanol (rac)-11 using a pair of quasi-enantiomeric oxazolidin-2-one adducts has been designed, which gave the required esters in reasonably yields, with high levels of diastereoselectivity. The main drawback to this method is the competitive formation of the carbonate 243 which was found to be inseparable from the required ester products.
Chapter 5

The Resolution of Alcohols using Active Esters

The method of resolving oxazolidinones by deprotonation followed by the addition of an active ester (outlined in Chapter 2), was seen as being very successful, as high levels of diastereoccontrol could be obtained in reasonable yields (e.g. 94% d.e., 66% yield, Table 2.7 entry 1). We were therefore interested in extending this methodology towards the resolution of racemic secondary alcohols. 1-Phenylethanol (rac)-11 was chosen as our model substrate, due to its similarities to 4-phenyl-oxazolidin-2-one (rac)-94 which was shown to give high levels of diastereoccontrol in our original work. Both of these substrates include a phenyl ring directly bound to their chiral centre, as well as a hydrogen atom and a $sp^3$-hybridised carbon atom. They both also contain an acidic proton bound to their hetero atom which is in turn bound to this chiral centre. The most important difference is that the oxazolidinone framework is rigid due to its ring structure, which contains a carbonyl group that gives internal resonance stabilisation and additional coordination site, whereas 1-phenylethanol 11 is acyclic (Scheme 5.1).

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{HN} & \quad \text{HQ} \\
\text{Ph} & \quad \text{Me} \\
(R)-94 & \quad (S)-11
\end{align*}
\]

Scheme 5.1: 4-Phenyl-oxazolidin-2-one (R)-94 and 1-phenylethanol (S)-11.

In our first attempt to probe this methodology we chose to carry out a mutual kinetic resolution of our chosen alcohol, 1-phenylethanol (rac)-11 using the active ester (rac)-95. This active ester was used as it had been most thoroughly investigated in our previous project (see Chapter 2); the reaction condition were also kept similar to this previous project; by deprotonating with $n$-BuLi at -78°C in THF.
Scheme 5.2: MKR of 1-phenylethanol (rac)-11 with active ester (rac)-95.

This preliminary reaction gave the required ester (rac)-245, in a reasonable yield of 64%, however a second ester (rac)-250 was also formed and was found to be inseparable from the required product. This unwanted ester (rac)-250 was derived from the addition of n-BuOLi to the active ester (rac)-95, which can be formed in bottles of n-BuLi, when this base reacts with molecular oxygen in the air. The butyl ester (rac)-250 had also occasionally been formed in the original oxazolidinone project (Chapter 2), however, this was not a major concern as its polarity differed greatly from the oxazolidin-2-one adducts, and hence was easily removed during purification of these oxazolidin-2-one products. The initial MKR also proved to be non-diastereoselective ($anti : syn$ 57 : 43). The low levels of diastereoselectivity suggested that the configuration of the chiral centres were being changed in a random fashion during the reaction. In order to check this, we carried out a stereospecific reaction (Scheme 5.3), using the enantiomerically pure reagents and the same reaction conditions as for the MKR in Scheme 5.2.

Scheme 5.3: Stereospecific synthesis of 1-phenylethyl-2-phenyl-propionate ($S,R$)-syn-245.

The stereospecific reaction showed that a degree of epimerisation was indeed occurring during this reaction as both the syn- and anti-diastereoisomers of the ester 245 were formed. This epimerisation occurs by removal of the acidic proton at the carbon atom alpha to the carbonyl group, and its subsequent stereorandom re-protonation. Epimerisation never occurred during the oxazolidin-2-one project; we therefore believe that this is due to the more basic nature of the lithium alkoxide (due to lack of resonance stabilisation) that allows this process to occur. We next attempted to prevent this
epimerisation by varying the relative ratios of reagents used. During this stage, we also chose to change the base being used from \( n \)-BuLi to LDA in order to stop the formation of the unwanted butyl ester product (\( rac \) \( \mathbf{250} \)). The active ester was also changed to (\( S \)-\( \mathbf{115} \)), as this active ester is easily derived from the carboxylic acid ibuprofen \( \mathbf{114} \), whose \( (S) \)-enantiomer is readily available commercially.

![Chemical structure](image)

Table 5.1: Stereospecific synthesis of 1-phenylethyl-2-(4-isopropyl-phenyl)-propionate 248.

The stereospecific reactions (Table 5.1) showed that if equivalent amounts of alcohol and base were used epimerisation occurred; the degree of epimerisation was found to increase with an increase of base. By simply using an excess of the starting alcohol this epimerisation process was stopped completely, this is presumably because the base prefers to deprotonate the more acidic proton of the excess alcohol, than the relatively less acidic alpha-proton of the ester. With this stereospecific process in place, we next chose to synthesise a range of enantiomerically pure esters so that we could reliably confirm the configuration of the ester products.

![Chemical structure](image)

Table 5.2: Stereospecific synthesis of (\( R,R \))-\( \text{anti} \) esters.
Table 5.3: Stereospecific synthesis of (R,S)-syn esters.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>R</th>
<th>Ester</th>
<th>d.e.</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><em>para</em>-C\textsubscript{6}H\textsubscript{4}Me</td>
<td>Me</td>
<td>113</td>
<td>247</td>
<td>100%</td>
</tr>
<tr>
<td>2</td>
<td>6-Methoxynaphthalen-2-yl</td>
<td>Me</td>
<td>123</td>
<td>249</td>
<td>100%</td>
</tr>
<tr>
<td>3</td>
<td>Ph</td>
<td>Et</td>
<td>119</td>
<td>246</td>
<td>100%</td>
</tr>
</tbody>
</table>

Table 5.4: Stereospecific synthesis of (S,S)-anti esters.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>R</th>
<th>Ester</th>
<th>d.e.</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6-Methoxynaphthalen-2-yl</td>
<td>Me</td>
<td>123</td>
<td>249</td>
<td>100%</td>
</tr>
<tr>
<td>2</td>
<td>Ph</td>
<td>Et</td>
<td>119</td>
<td>246</td>
<td>100%</td>
</tr>
</tbody>
</table>

Changes to the aryl and aliphatic groups of these active esters had no overall noticeable effect on the outcome of this reaction. We next attempted the stereospecific process using a 2-phenoxy-propionate based active ester (S)-251, to determine if a slight increase in the acidity of the proton alpha to the carbonyl group allowed epimerisation to occur. The esters (S,S)- and (S,R)-252 were obtained enantiomerically pure, showing that this slight increase in the acidity of the proton alpha to the carbonyl group did not interfere with this reaction.

Scheme 5.4: Stereospecific synthesis of 1-phenylethyl-2-phenoxy-propionate 252.
Further increasing the acidity of this proton when using the 2-phenyl-2-methoxy-ethanoate based active esters \((S)-121\) resulted in complete epimerisation, hence giving an equal mixture of both anti- and syn-esters \(253\). Presumably, this is because the proton alpha to the carbonyl group is of similar acidity to the alcohol \(11\).

\[
\begin{align*}
\text{OH} & \quad \text{Ph} \\
\text{(S)-11} & \quad \text{3 equiv.} \quad \text{i) LDA 1.5 equiv., THF} \quad \text{ii) Ph} \\
& \quad \text{O} \quad \text{C} \quad \text{OcF}_5 \quad \text{OMe} \quad \text{(S)-121} \\
& \quad \text{Ph} \quad \text{OMe} \\
\text{(R)-11} & \quad \text{3 equiv.} \quad \text{i) LDA 1.5 equiv., THF} \quad \text{ii) Ph} \\
& \quad \text{O} \quad \text{C} \quad \text{OcF}_5 \quad \text{OMe} \quad \text{(S)-121} \\
\end{align*}
\]

**Scheme 5.5:** Stereospecific synthesis of 2-phenyl-2-methoxy-ethionate esters \(253\).

In an attempt to better understand this epimerisation process, we reacted an ester of known configuration, \((S,S)-anti-249\), with an alkoxide formed from a different alcohol, \((rac)-254\). The ester present at the end of the reaction had no incorporation of the alternative alcohol, however a large degree of epimerisation had taken place, clearly indicating that trans-esterification does not occur during the epimerisation process.

\[
\begin{align*}
\text{OH} & \quad \text{Ar} \\
\text{(rac)-254} & \quad \text{1 equiv.} \quad \text{i) LDA 1 equiv., THF} \quad \text{ii) Ar} \quad \text{O} \quad \text{Ph} \\
& \quad \text{Ar}_1 \quad \text{O} \quad \text{Ar} \quad \text{Ph} \\
\text{(S,S)-anti-249} & \quad \text{34\% d.e.} \quad \text{100 : 0} \quad \text{(rac)-255} \\
\end{align*}
\]

**Scheme 5.6:** Determining if transesterification occurs.

With this information in hand, we chose to re-investigate the original mutual kinetic resolution of 1-phenylethanol \((rac)-11\) with the active ester \((rac)-95\), in this process an excess of the alcohol was used to stop unwanted epimerisation. In order to try an improve levels of diastereoselectivity, a range of different bases were screened at this stage (Table 5.5).
The stereodirecting step of this reaction, possibly indicating that the anion plays some part in the stereodirecting step of this reaction. Interestingly, lithium hydride gave no product, this however can be attributed to lack of solubility of the reagent in THF, rather than its ability to act as a base for this system.

The use of bases with different cations: lithium, sodium, potassium and magnesium (Table 5.5, entries 1 and 5-7), surprisingly gave very similar levels of diastereoselectivity, approximate ratio anti : syn 75 : 25. This information would suggest that the stereodirecting step in the formation of ester 245 is either one where the cation is not present, or the cation is in such an arrangement that its relative size, coordinating ability and nucleophilicity have no effect on the stereooutcome of this reaction. Entries 8 to 9 and 11 to 14 of Table 5.5 clearly show that a relatively strong base must be used to fully form the alkoxide in order for the ester 245 to be formed under these reaction conditions.

The highest levels of diastereoselectivity obtained from these MKRs were much lower than those obtained during the oxazolidinone project, there are a few possible explanations for this. It is possible that the mechanistic pathways that the reactions
proceed through are completely different, and hence different levels of
diastereoselectivity will be obtained. Alternatively both reactions could follow a similar
mechanistic pathway, in which case it is likely that either the increased basicity of the
alkoxide or its lack of coordination have reduced the stereoselective nature of one of the
key steps during this reaction. It was believed that the addition of a co-ordinating salt
may solve this problem, as the salt could lower the basicity of this lithium alkoxide as
well as increasing the possibility of co-ordination.

![Chemical Reaction Diagram]

Table 5.6: MKR of 1-phenylethanol (rac)-11 using different bases with MgBr₂.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>Ratio anti : syn</th>
<th>Product yield</th>
<th>Butyl yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>n-BuLi</td>
<td>76 : 24</td>
<td>6%</td>
<td>0%</td>
</tr>
<tr>
<td>2</td>
<td>LDA</td>
<td>78 : 22</td>
<td>62%</td>
<td>0%</td>
</tr>
<tr>
<td>3</td>
<td>LiH</td>
<td>-</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>4</td>
<td>NaH</td>
<td>-</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>5</td>
<td>MeMgBr</td>
<td>73 : 27</td>
<td>50%</td>
<td>0%</td>
</tr>
<tr>
<td>6</td>
<td>NE₃</td>
<td>73 : 27</td>
<td>56%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Table 5.7: MKR of 1-phenylethanol (rac)-11 using different bases with ZnCl₂.
Zinc chloride proved to be a very useful coordinating salt, when used in conjunction with a lithium derived base as excellent levels of diastereoselectivity were observed (ratio anti : syn 92 : 8). However, the reaction did appear to require a base with a non-coordinating counter-ion for a reasonable yield of the required ester (rac)-245 to be obtained (Table 5.7, entries 1 and 2). As this reaction was highly diastereoselective, we chose at this stage to focus our attention on trying to optimise these conditions rather than continue to search for alternative reagents.

![Chemical Reaction](image)

**Table 5.8:** MKR of 1-phenylethanol (rac)-11 in different solvents.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Ratio anti : syn</th>
<th>Product yield (%)</th>
<th>Butyl yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>THF</td>
<td>92 : 8</td>
<td>56%</td>
<td>5%</td>
</tr>
<tr>
<td>2</td>
<td>DCM</td>
<td>-</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

We next decided to investigate the affect of the co-ordinating ability of the solvent on this reaction to aid a better understanding of the reaction mechanism. This study indicated that the solvent used was important; replacing THF with a non-coordinating solvent (such as dichloromethane) prevented ester formation. This could be because the reagents were more soluble in THF than dichloromethane, or it could indicate that part of the reaction proceeds through an intermediate that required additional stabilisation though external co-ordination.

![Chemical Reaction](image)

**Table 5.9:** MKR of 1-phenylethanol (rac)-11 using different equivalents of ZnCl₂.

<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>Ratio anti : syn</th>
<th>Product yield (%)</th>
<th>Butyl yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>78 : 22</td>
<td>63%</td>
<td>2%</td>
</tr>
<tr>
<td>2</td>
<td>1.5</td>
<td>92 : 8</td>
<td>56%</td>
<td>4%</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>94 : 6</td>
<td>47%</td>
<td>2%</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>96 : 4</td>
<td>2%</td>
<td>0%</td>
</tr>
</tbody>
</table>
In an attempt to further understand how the above reaction proceeded a number of reactions were carried out using varying equivalents of zinc chloride. Changing this variable had a dramatic effect on the diastereoselectivity of this reaction and its overall yield. If less zinc chloride than base was used, this reaction appeared to prefer to occur through the original pathway, as the levels of diastereoselectivity were similar to those obtained when no zinc chloride was used (Table 5.7: entry 1 and Table 5.9: entry 1). Whereas using more zinc chloride than base increased the diastereoselectivity of this reaction, however, this lowered the overall yield. Equimolar amounts of zinc chloride and base gave the highest levels of selectivity without reducing the yield by an unacceptable amount.

We found that simply increasing the amount of base and zinc chloride used to three equivalents increased the yield from 56% to 65% without harming the diastereoselective nature of this reaction (Table 5.9: entry 2 and Table 5.10: entry 1). With these optimised reaction conditions in hand, we next chose to study the structural nature of the active ester.

![Chemical reaction image]

Table 5.10: MKR of 1-phenylethanol (rac)-11 using different active esters.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>Ester</th>
<th>Product</th>
<th>Ratio anti : syn</th>
<th>Yield</th>
<th>Butyl ester</th>
<th>Butyl yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph</td>
<td>95</td>
<td>245</td>
<td>95 : 5</td>
<td>65%</td>
<td>250</td>
<td>4%</td>
</tr>
<tr>
<td>2</td>
<td>para-C6H4CH3</td>
<td>113</td>
<td>247</td>
<td>94 : 6</td>
<td>58%</td>
<td>257</td>
<td>4%</td>
</tr>
<tr>
<td>3</td>
<td>para-C6H4CH2CHMe2</td>
<td>115</td>
<td>248</td>
<td>91 : 9</td>
<td>58%</td>
<td>258</td>
<td>4%</td>
</tr>
<tr>
<td>4</td>
<td>para-C6H4Cl</td>
<td>117</td>
<td>256</td>
<td>95 : 5</td>
<td>67%</td>
<td>259</td>
<td>6%</td>
</tr>
<tr>
<td>5</td>
<td>6-Methoxynaphthalene-2-yl</td>
<td>123</td>
<td>249</td>
<td>90 : 10</td>
<td>67%</td>
<td>260</td>
<td>4%</td>
</tr>
</tbody>
</table>

Changes to the aryl ring of the active ester had no real effect on the overall yield of these reactions; surprisingly however, the levels of diastereoselectivity of these reactions were slightly dependent on the structural nature of this aryl ring, although there is no obvious pattern to this dependency. In all cases, the unwanted butyl ester was formed, and was found to be inseparable from the required ester. We therefore chose to synthesise all of these butyl esters independently for characterisation and assignment purposes (Table 5.11 and Scheme 5.7).
Although surprisingly still formed trace amounts of the butyl esters, LDA seem a logical choice it gave reduced yields in comparison to other alkyl esters; this is presumably because of a side reaction between one of the many solvents and stabilisers that LDA is sold as a mixture in, with the active ester. An alternative idea, was to use LiNH₂, however no product could be formed when using this base; this could be down to simple solubility of this base in THF.

Scheme 5.7: Synthesis of butyl 2-(6-methoxy-2-naphthyl)-propionate (S)-260.

From the above results it is evident that an alternative to n-BuLi had to be found that did not allow the formation of these butyl esters such as (rac)-250; however we knew that an alternative base would still have to contain a lithium cation. Although LDA seem a logical choice it gave reduced yields in comparison to n-BuLi, and surprisingly still formed trace amounts of the butyl and other alkyl esters; this is presumably because of a side reaction between one of the many solvents and stabilisers that LDA is sold as a mixture in, with the active ester. An alternative idea, was to use LiNH₂, however no product could be formed when using this base; this could be down to simple solubility of this base in THF.

Table 5.11: Synthesis of butyl esters.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>R</th>
<th>Acid</th>
<th>Ester product</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph</td>
<td>Me</td>
<td>111</td>
<td>250</td>
<td>73 %</td>
</tr>
<tr>
<td>2</td>
<td>Ph</td>
<td>Et</td>
<td>118</td>
<td>261</td>
<td>52 %</td>
</tr>
<tr>
<td>3</td>
<td>para-C₆H₄Me</td>
<td>Me</td>
<td>112</td>
<td>257</td>
<td>74 %</td>
</tr>
<tr>
<td>4</td>
<td>para-C₆H₄CH₂CH₃Me</td>
<td>Me</td>
<td>114</td>
<td>258</td>
<td>85 %</td>
</tr>
<tr>
<td>5</td>
<td>para-C₆H₄Cl</td>
<td>Me</td>
<td>116</td>
<td>259</td>
<td>68 %</td>
</tr>
</tbody>
</table>

Ar : 6-Methoxynaphthalen-2-yl

Table 5.12: MKR of 1-phenylethanol (rac)-11 using different bases.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>Ratio anti : syn</th>
<th>Yield of product</th>
<th>Yield of butyl ester</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>n-BuLi</td>
<td>95 : 5</td>
<td>65%</td>
<td>4%</td>
</tr>
<tr>
<td>2</td>
<td>LDA</td>
<td>93 : 7</td>
<td>53%</td>
<td>1%</td>
</tr>
<tr>
<td>3</td>
<td>LiNH₂</td>
<td>-</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>4</td>
<td>tert-BuLi</td>
<td>94 : 6</td>
<td>71%</td>
<td>0%</td>
</tr>
</tbody>
</table>
The final idea was to use tert-BuLi, if this base reacted with molecular oxygen, it would form lithium tert-butoxide, which should react with the active ester more slowly than the secondary lithium alkoxide of 1-phenylethanol 11. When carrying out this reaction, using tert-BuLi, no other esters byproducts were formed, and the diastereoselectivity of this reaction remained unchanged. The yield of the required ester did increase slightly; this is presumably due to the removal of this competitive side reaction.

![Chemical structure of reaction](image)

**Table 5.13**: MKR of 1-phenylethanol (rac)-11 using different equivalents of ZnCl₂.

<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>Ratio anti : syn</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>62 : 38</td>
<td>72%</td>
</tr>
<tr>
<td>2</td>
<td>1.5</td>
<td>72 : 28</td>
<td>71%</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>94 : 6</td>
<td>71%</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>97 : 3</td>
<td>32%</td>
</tr>
</tbody>
</table>

We felt that it would be prudent to re-evaluate the link between the equivalents of zinc chloride and base being used before we further investigated the use of tert-BuLi. Again, it was found that less equivalents of zinc chloride gave reduced selectivity, whereas excess equivalents of zinc chloride reduced the yield; equimolar equivalents of base and zinc chloride again, gave the best levels of diastereoselectivity and yield.

![Chemical structure of reaction](image)

**Table 5.14**: MKR of 1-phenylethanol (rac)-11 using different active esters.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>Ester</th>
<th>Ratio anti : syn</th>
<th>Product</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph</td>
<td>95</td>
<td>94 : 6</td>
<td>245</td>
<td>71%</td>
</tr>
<tr>
<td>2</td>
<td>para-C₆H₄CH₃</td>
<td>113</td>
<td>94 : 6</td>
<td>247</td>
<td>61%</td>
</tr>
<tr>
<td>3</td>
<td>para-C₆H₄CH₂CHMe₂</td>
<td>115</td>
<td>94 : 6</td>
<td>248</td>
<td>66%</td>
</tr>
<tr>
<td>4</td>
<td>para-C₆H₄Cl</td>
<td>117</td>
<td>93 : 7</td>
<td>256</td>
<td>56%</td>
</tr>
<tr>
<td>5</td>
<td>6-Methoxynaphthalene-2-yl</td>
<td>123</td>
<td>94 : 6</td>
<td>249</td>
<td>68%</td>
</tr>
</tbody>
</table>
With this information in hand, we chose to re-evaluate the use of other active esters; surprisingly the use of tert-BuLi as the base appeared to make this reaction more robust. The use of different aryl groups on the active ester, gave no change in the level of diastereoselectivity; also the products were all obtained in a similar yield. The fact that the structural nature of the aryl group of these active esters had little or no effect on the diastereoselectivity of this reaction was excellent, as it meant that the aryl group could be used as a handle to allow the quasi-enantiomeric products to be separated in a PKR.

Scheme 5.8: PKR of 1-phenylethanol (rac)-11 using active esters (R)-95 and (S)-123.

With an optimised method now developed, we chose to carry out a PKR of 1-phenylethanol (rac)-11 (Scheme 5.8), the active esters used were chosen because we knew that their products had different polarities and hence could be easily separated by flash column chromatography. The reaction proceeded as planned, giving both products esters 245 and 249 in almost identical yield, indicating that they must be formed at an almost identical rate; the levels selectivity were within experimental error of those obtained when carrying out their relative MKRs (Table 14: entries 1 and 5 and Scheme 5.8).

Scheme 5.9: MKR of 2-naphthylethanol (rac)-261.
As a way of confirming that no racemization or epimerisation had occurred during this PKR (Scheme 5.8); we wished to carry out a reaction known as a cross-over reaction. Here the racemic component of a PKR would be substituted with a quasi-enantiomeric mixture; however in order for us to carry out this reaction, we first had to test an alternative alcohol so that is could be used as part of this quasi-enantiomeric mixture. 2-Naphthylethanol \textbf{261} was chosen as it closely resembled 1-phenylethanol \textbf{11}, and is commercially available in an optical pure form. The MKR of this alcohol gave similar level of diastereoselectivity to that of its parent alcohol 1-phenylethanol \textbf{(rac)-11} (Table 5.14 entry 1 and Scheme 5.9).

Scheme 5.10: Cross over reaction.

With a quasi-enantiomeric mixture of alcohols \textbf{(R)-11} and \textbf{(S)-261} in hand, we carried out this cross-over reaction, which clearly showed that no racemization or epimerisation had occurred during this reaction, as only the four esters shown in Scheme 5.10 were obtained. Interestingly the levels of diastereoselectivity were reduced during this cross-over reaction, presumable this is caused by the quasi-enantiomeric mixture of alcohols reacting at a different rate to each other.

The above mentioned PKR (Scheme 5.8) works very well, giving high levels of diastereoselectivity and good yields, however, there were two problems with this reaction. Firstly, the relative amounts of zinc chloride and \textit{tert}-BuLi used in this reaction were extremely important; should these two reagents not be of exact equimolar amounts the yields or diastereoselectivity of the reaction was reduced. Secondly, \textit{tert}-BuLi is spontaneously flammable in air, not only does this make the reaction rather
hazardous, and therefore unlikely to be commercially applicable, it also means that accurately measuring the molarity of the tert-BuLi solution is almost impossible, and hence making it very difficult to use the same amounts of base as the zinc chloride.

In order to overcome this problem, we speculated that lithium tert-butoxide 266 could be used in place of tert-BuLi, as the lithium cation could interchange between the lithium tert-butoxide and secondary alcohol being resolved. The secondary lithium alkoxide formed should react with the active ester in preference to the starting material, hence giving the required ester product. Also lithium tert-butoxide 266 is a solid powder, so it should be much easier to accurately measure than tert-BuLi, and is also far less hazardous.

![Scheme 5.11: Synthesis of alkoxide.](image)

Lithium tert-butoxide 266 was found to be easily synthesised from tert-butanol 264 and lithium; an excess of the alcohol was used and this was removed by simple vacuum distillation at the end of the reaction. Interestingly if the reaction was not carried out under a flow of nitrogen gas, or if the alcohol was not freshly distilled before use, lithium hydroxide was also formed; presumably this is due to the more reactive nature of water in comparison to tert-butanol 264. The same reaction conditions could also be used to synthesise sodium tert-butoxide 265.
Table 5.15: Using tert-BuOLi with various reaction conditions.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Hours</th>
<th>Equiv's of ZnCl₂</th>
<th>Ratio anti : syn</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>0</td>
<td>61 : 39</td>
<td>52%</td>
</tr>
<tr>
<td>2</td>
<td>12</td>
<td>1.5</td>
<td>72 : 28</td>
<td>61%</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>3</td>
<td>92 : 8</td>
<td>27%</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
<td>6</td>
<td>&gt;93 : 7</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>5</td>
<td>36</td>
<td>0</td>
<td>60 : 40</td>
<td>94%</td>
</tr>
<tr>
<td>6</td>
<td>36</td>
<td>1.5</td>
<td>74 : 26</td>
<td>50%</td>
</tr>
<tr>
<td>7</td>
<td>36</td>
<td>3</td>
<td>92 : 8</td>
<td>34%</td>
</tr>
<tr>
<td>8</td>
<td>36</td>
<td>6</td>
<td>-</td>
<td>0%</td>
</tr>
<tr>
<td>9</td>
<td>60</td>
<td>0</td>
<td>52 : 48</td>
<td>73%</td>
</tr>
<tr>
<td>10</td>
<td>60</td>
<td>1.5</td>
<td>77 : 23</td>
<td>65%</td>
</tr>
<tr>
<td>11</td>
<td>60</td>
<td>3</td>
<td>93 : 7</td>
<td>27%</td>
</tr>
<tr>
<td>12</td>
<td>60</td>
<td>6</td>
<td>&gt;93 : 7</td>
<td>&lt;5%</td>
</tr>
</tbody>
</table>

Our first investigation into using tert-BuOLi as the base simply involved mixing this base with all the other reagents overnight; however this approach resulted in an unacceptably low yield. Although it was found that the yield can be increased by using less equivalents of zinc chloride, this again reduced the levels of diastereoselectivity (Table 5.15 entry 1 to 5). Interestingly, increasing the reaction time did not increase the overall yield, in fact the reaction appeared to be independent of time, after an initial 12 hours.

Table 5.16: Using tert-BuOLi under reflux conditions.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Equiv's of ZnCl₂</th>
<th>Ratio anti : syn</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>52 : 48</td>
<td>58%</td>
</tr>
<tr>
<td>2</td>
<td>1.5</td>
<td>62 : 38</td>
<td>62%</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>84 : 16</td>
<td>68%</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>85 : 15</td>
<td>53%</td>
</tr>
<tr>
<td>5</td>
<td>8</td>
<td>82 : 18</td>
<td>51%</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>82 : 18</td>
<td>35%</td>
</tr>
<tr>
<td>7</td>
<td>12</td>
<td>79 : 21</td>
<td>29%</td>
</tr>
</tbody>
</table>

We next attempted to increase the yield of the reaction by simply refluxing the reaction mixture; this method was successful in increasing the yield, however, it came at the expense of reducing the selective nature of this reaction (Table 5.15 entry 3 vs.
Table 5.16: entry 3). This is unsurprising as the diastereoselectivity of this reaction is believed to be of a kinetic nature, so increasing the kinetic energy present in this reaction should of course lower diastereoselectivity of this reaction. We had hoped that increasing the relative equivalents of zinc chloride used would increase the diastereoselectivity of this reaction to compensate for the increased kinetic energy. However in these experiments, an excess of zinc chloride only seemed to reduce the overall yield of this reaction.

Table 5.17: Alternative relative reagent ratio’s.

<table>
<thead>
<tr>
<th>Entry</th>
<th>ratio X : Y</th>
<th>Ratio ant : syn</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 : 9</td>
<td>92 : 8</td>
<td>16 %</td>
</tr>
<tr>
<td>2</td>
<td>1 : 99</td>
<td>-</td>
<td>0 %</td>
</tr>
<tr>
<td>3</td>
<td>1 : 0</td>
<td>94 : 6</td>
<td>19 %</td>
</tr>
<tr>
<td>4</td>
<td>100 : 0</td>
<td>92 : 8</td>
<td>62 %</td>
</tr>
</tbody>
</table>

From our previous study we know that high yields of the required ester product could be obtained when using tert-BuOLi as the base, by simply increasing the amount of kinetic energy in the reaction. We next chose to investigate what effect varying the relative equivalents of the reagents may have on the outcome of this reaction. The use of a second alcohol 264 to aid in the transfer of the lithium cation proved to be unsuccessful especially when a large excess of it was used. Whereas reducing the relative equivalents of 1-phenylethanol (rac)-11 proved equally unsuccessful. However, the use of 100 equivalents of the racemic alcohol 11 did give the required product in high yields with good levels of diastereoselectivity. Although this approach was successful, it was deemed to be unsatisfactory due to the large amount of 1-phenylethanol (rac)-11 that was required. Not only was this wasteful, it also made purification difficult as a theoretical 100% yield would give a relative ratio of 1 equivalent of ester product 245 to 99 equivalents of starting alcohol 11.
From the previous discussed reactions it was evident that the reaction gave acceptable yields when the base was allowed to fully react with the alcohol in the presences of the zinc chloride; presumably forming the zinc alkoxide. This could be achieved by either using a strong base (Table 5.12: entry 4), performing the reaction at elevated temperatures (Table 5.16 entry 3), and when the relative amounts of the reagents were in an optimal ratio (Table 5.17 entry 4). We were therefore interested to see if this reactive intermediate could be synthesised using reflux conditions, followed by cooling the reaction (so that the temperature was more suitable to carrying out a kinetic-based resolution) before adding the active ester. This approach was indeed successful, it was however, found that a slight excess of 1-phenylethanol (rac)-11 had to be employed, and that this excess alcohol could not be substituted with an achiral tertiary alcohol (Table 5.19 entry 2 and 3).

Table 5.18: Two step process.

<table>
<thead>
<tr>
<th>Entry</th>
<th>ratio X : Y</th>
<th>Ratio anti : syn</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 : 0</td>
<td>-</td>
<td>0 %</td>
</tr>
<tr>
<td>2</td>
<td>10 : 0</td>
<td>93 : 7</td>
<td>68 % *</td>
</tr>
<tr>
<td>3</td>
<td>1 : 9</td>
<td>88 : 12</td>
<td>24 %</td>
</tr>
</tbody>
</table>

* Note product obtained in 92 : 8 ratio with 73% yield when refluxed for 1 night rather than 2 hours.

Table 5.19: Using different alkoxides.

<table>
<thead>
<tr>
<th>Entry</th>
<th>M</th>
<th>Ratio anti : syn</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Li</td>
<td>93 : 7</td>
<td>68 %</td>
</tr>
<tr>
<td>2</td>
<td>Na</td>
<td>-</td>
<td>0 %</td>
</tr>
<tr>
<td>3</td>
<td>K</td>
<td>-</td>
<td>0 %</td>
</tr>
</tbody>
</table>

With this newly designed reaction, we next attempted to investigate the cation effect on this process. Unfortunately, using sodium or potassium based alkoxide gave
no products (Table 5.19). It was believed that this was due to their low solubility in THF, in comparison to lithium tert-butoxide 266 rather than an indication that the reaction requires a certain cation.

![Diagram](image)

**Table 5.20: Different zinc salts.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Salt</th>
<th>Ratio anti : syn</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ZnF₂</td>
<td>51 : 49</td>
<td>72 %</td>
</tr>
<tr>
<td>2</td>
<td>ZnCl₂</td>
<td>93 : 7</td>
<td>68 %</td>
</tr>
<tr>
<td>3</td>
<td>ZnBr₂</td>
<td>88 : 12</td>
<td>52 %</td>
</tr>
<tr>
<td>4</td>
<td>ZnI₂</td>
<td>90 : 10</td>
<td>52 %</td>
</tr>
<tr>
<td>5</td>
<td>ZnO</td>
<td>65 : 35</td>
<td>20 %</td>
</tr>
</tbody>
</table>

We also chose to investigate what effect of different zinc salts would have on this reaction in an attempt to understand what role if any the zinc counter ions played in this reaction. The type of zinc salt used did indeed appear to have an interesting effect on this reaction; zinc chloride, bromide and iodide all gave similar levels of selectivity and yields, whereas zinc fluoride gave no levels of diastereoselectivity. The use of zinc oxide in this reaction not only reduced the selectivity of the reaction but also dramatically reduced the yield of the required ester product 245. These results did not appear to make sense, as some suggested that the anion of the salt played a very dramatic role in the key steps of the reaction (Table 5.20: entries 1, 2 and 5). Whereas other results suggested that the main step in the reaction pathway was independent of the anion (Table 5.2: entries 2 to 4).

![Scheme](image)

**Scheme 5.12: Using ZnEt₂ as base.**

In an attempt to try and understand the role that the zinc plays in this reaction mechanism, we next carried out a MKR of 1-phenylethanol (*rac*)-11 using ZnEt₂ as the
base. This reaction proved to be less diastereoselective than our previous reactions and gave the required ester 245 in lower yield; seemingly indicating that zinc had to be used in conjunction with a lithium derived base.

Scheme 5.13: Stereospecific synthesis of ester (S,S)-anti-245 using ZnF₂.

The attempted stereospecific synthesis of ester (S,S)-anti-245 using ZnF₂ gave an explanation to the previous seemingly illogical results; racemization and/or epimerisation occurred during this reaction as a mixture of both the syn- and anti-esters 245 were obtained (Scheme 5.13). Clearly, zinc fluoride somehow increased the racemization and/or epimerisation pathways within this reaction, this was perhaps due to its more electronegative character in comparison to the larger halide anions.

Scheme 5.14: Stereospecific synthesis of ester (S,S)-anti-245 using ZnO.

This information was backed up when a stereospecific syntheses of ester (S,S)-
anti-245 using ZnO was carried out, again racemization and/or epimerisation occurred during this reaction. This combined evidence (Table 5.20 and Schemes 5.13 and 5.14) would indicate that the stereoselective step in this reaction was indeed independent of the counter ion to the zinc, and it is only when this anion facilitates an alternative reaction pathway that different results are obtained. Interestingly, using zinc oxide as the salt also gave reduced yield of the ester product 245, and also generated the carboxylic acid 111, suggesting that this reagent promoted hydrolysis of the active ester 95 rather than synthesis of the ester product 245.
Interestingly, when carrying out the MKR of 1-phenylethanol (rac)-11 using the lithium alkoxide 266 that had been synthesised without a blanket of nitrogen gas (Table 5.11 entry 3), the selectivity and yield of the reaction diminished (Scheme 5.15). To further explore this process, we carried out a MKR with an equal mixture of tert-BuOLi and lithium hydroxide (the believed impurity in the “wet” lithium alkoxide). The results from this reaction clearly indicated that lithium hydroxide prevented the normal reaction pathway as no product 245 was formed.

Scheme 5.16: MKR using tert-BuOLi and LiOH.

It should be noted that zinc oxide can be easily synthesised from zinc chloride in the presence of aqueous sodium hydroxide (Scheme 5.17). This shows that zinc oxide and lithium hydroxide affected the reaction in the same manner. The presence of water in this reaction, of course, would also lead to the same result, as tert-BuOLi in water will yield lithium hydroxide.

Scheme 5.17: Synthesis of ZnO.

With this information in hand we attempted to improve the selectivity of this reaction, by simply trying to further remove any traces of water that these reagents might contain. The use of very high purity ZnCl₂ (99.999% pure), however, did not have an effect upon the reaction, it should be noted that the other reagents were of the

Scheme 5.15: MKR using “wet” tert-BuOLi.
standard grade we had previously used. So theoretically the selectivity and yield of the reaction may increase if all of the reagents and solvents could be supplied completely free of trace amounts of water.

\[ \text{Scheme 5.18: MKR using “pure” zinc chloride.} \]

We next turned our attention to trying to improve this reaction by changing the leaving group of the active ester. This area had previously been investigated by a project student (Anna Andreou)\(^ {158} \); however this study was carried out using the first generation reaction conditions with tert-BuLi as the base. The overall findings from this work showed that pentafluorophenol was the best leaving group for both the yield and diastereoselectivity for this reaction. As a result of this, only a small study of different leaving groups was carried out in order to see if the overall conclusions appeared to be the same as this previous study.

\[ \text{Table 5.21: MKRs using different leaving groups.} \]

This study into the leaving group effect shows that a relatively good leaving group has to be used in order to obtain acceptable yields. Either the electronic or steric nature of pentafluorophenol seems to be very important to the diastereoselective nature of this reaction. As the different leaving groups gave much reduced levels of diastereoselectivity, it seemed prudent to carry out these reactions with enantiomerically pure reagents so that the possibility of racemization and/or epimerisation could be ruled
out. When all of the above reactions were carried out in a stereospecific fashion, no significant levels of racemization nor epimerisation were detected (Table 5.22).

![Chemical reaction diagram]

Table 5.22: Stereospecific synthesis using different leaving groups.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Lg</th>
<th>Active ester</th>
<th>d.e.</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>OC₅H₅</td>
<td>128</td>
<td>98.2%</td>
<td>16%</td>
</tr>
<tr>
<td>2</td>
<td>OC₆F₅</td>
<td>95</td>
<td>99.4%</td>
<td>82%</td>
</tr>
<tr>
<td>3</td>
<td>para-OC₆H₄NO₂</td>
<td>127</td>
<td>96.8%</td>
<td>92%</td>
</tr>
</tbody>
</table>

We next investigated the role that the solvent plays in this reaction, interestingly the diastereoselectivity remained approximately unchanged regardless of the solvent used, which presumably indicates that the key stereochemical determining step in this reaction does not involve a solvent molecule co-ordinating to the rest of the reagents. However, the yield of the ester product 245 was found to be extremely dependent upon the solvent used; only THF gave an acceptable yield (Table 5.23). This can be accounted for by the solubility of the reaction mixture in different solvents, when the reaction was carried out in THF a clear liquid was obtained; whereas if an alternative solvent was used the reaction mixture formed a white suspension.

![Chemical reaction diagram]

Table 5.23: MKRs using different solvents.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Ratio anti : syn</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CH₂Cl₂</td>
<td>~ 90 : 10</td>
<td>~1%</td>
</tr>
<tr>
<td>2</td>
<td>EtOEt</td>
<td>93 : 7</td>
<td>42%</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>93 : 7</td>
<td>68%</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>~</td>
<td>0%</td>
</tr>
<tr>
<td>5</td>
<td>MeO</td>
<td>91 : 9</td>
<td>14%</td>
</tr>
</tbody>
</table>
With this information in hand, we studied what affect the structural nature of the aliphatic group of the active ester, had on this reaction. Increasing the size of this group, from methyl to an ethyl, gave increased levels of diastereoselectivity, without having too much of a detrimental effect on the yield (Table 5.24: entries 1 vs. 2). Further increasing the size of this aliphatic group to an isopropyl group (Table 5.24: entry 3) almost prevented this reaction from occurring, clearly indicating that in the key transition state there is a very limited volume of space that the aliphatic group can fill, and that this is one of the most important aspects of the stereo selective nature of this reaction.

The next logical step was to change the aryl group of this active ester; this had surprisingly little effect on this reaction (Table 5.25). Although, the differences between the results obtained were small they indicated that the less aromatic in character the aryl ring was, the lower the overall selectivity of this reaction.

Table 5.24: MKRs using active ester with different aliphatic groups.

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Active Ester</th>
<th>Ester Product</th>
<th>Ratio anti : syn</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me</td>
<td>95</td>
<td>245</td>
<td>93 : 7</td>
<td>68 %</td>
</tr>
<tr>
<td>2</td>
<td>Et</td>
<td>119</td>
<td>246</td>
<td>96 : 4</td>
<td>60 %</td>
</tr>
<tr>
<td>3</td>
<td>i-Pr</td>
<td>126</td>
<td>267</td>
<td>~ 90 : 10</td>
<td>~1 %</td>
</tr>
</tbody>
</table>
Table 5.25: MKRs using active ester with different aromatic groups.

With an optimised method in place and with multiple resolving agents screened by MKRs, we now had all the information we required to carry out a PKR using this improved method. We again chose to use the active ester (S)-123 as one of the resolving agents due to its polar nature, which would allow the corresponding products to be easily separated. However, this time we chose to use the more sterically demanding active ester (R)-119, as it had given the highest levels of diastereoselectivity in our screening process. The PKR proceeded as planned with each active ester reacting with identical levels of selectivity as to their corresponding MKRs (Tables 5.24 and 5.25). The active ester (S)-123 reacted slightly faster than its quasi-enantiomeric partner, presumably the difference in the size of the aliphatic group governed the rate of this reaction; however, this slight difference in reaction rates did not appear to overly hinder the outcome of this PKR.
Scheme 5.19: PKR of 1-phenylethanol (rac)-11.

With a working resolution method in hand we next turned our attention towards expanding the method towards the resolution of other racemic secondary alcohols. The first alcohol we chose to use was 2-naphthylethanol (rac)-261, due to its similarities to 1-phenylethanol (rac)-11. Unfortunately this alcohol 261 was not (readily) commercially available as a racemate, so we synthesised it from the corresponding aldehyde 268 and methyl magnesium bromide (Scheme 5.20). Although this reaction proceeded effectively there was also a trace of the primary alcohol 269 formed during this reaction.

Scheme 5.20: Synthesis of 2-naphthylethanol (rac)-261 from the aldehyde 268.

When this mixture of alcohols was subsequently screened in a MKR with active ester (rac)-95 a mixture of esters 262 and 270 was obtained (Scheme 5.21), one derived from the secondary alcohol (rac)-261 and the other derived from the primary alcohol 269. Interestingly, the relative ratio of the products did not match that of the starting materials; the primary alcohol 269 appeared to react at a significantly faster rate. This was also seen to be the case when this mixture of alcohols was resolved in a kinetic fashion using the active ester (S)-119 as the resolving agent (Scheme 5.22).
**Scheme 5.21:** MKR of impure 2-naphthylethanol (rac)-261.

![Scheme 5.21](image)

**Scheme 5.22:** KR of impure 2-naphthylethanol (rac)-261.

In order to determine if the unwanted ester was indeed a product of the trace primary alcohol 269, the primary alcohol 269 was synthesised by reduction of the corresponding aldehyde 268. The resulting alcohol 269 was then used to synthesise both of the unwanted esters (rac)-270 and (S)-272, they were found to be identical to the esters previously obtained in the MKR and KR (Schemes 5.21 and 5.22).

![Scheme 5.22](image)

**Scheme 5.23:** Synthesis of 2-naphthylmethanol 269.

![Scheme 5.23](image)

**Scheme 5.24:** Synthesis of ester (rac)-270.

![Scheme 5.24](image)

**Scheme 5.25:** Synthesis of (S)-272.

To more actually gauge the relative rates of reaction of these primary and secondary alcohols under our standard reaction conditions, we chose to conduct a competitive reaction with equimolar amounts of both types of alcohol. This reaction showed that the primary alcohol 207 must have a considerably higher rate of reaction, as the only ester formed was that derived from the primary alcohol 270.
Scheme 5.26: Competitive reaction of primary and secondary alcohol.

Therefore further synthesis of secondary alcohols had to be carried out using an alternative reaction pathway that did not lead to any traces amounts of primary alcohols being formed. It was found that sodium borohydride reduction of the appropriate ketones gave the required pure secondary alcohols, and it is this method that was used to synthesise all the other secondary alcohols that were required for screening.

Table 5.26: Synthesis of secondary alcohols.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>R</th>
<th>Ketone</th>
<th>Product</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph</td>
<td>-Pr</td>
<td>273</td>
<td>274</td>
<td>95 %</td>
</tr>
<tr>
<td>2</td>
<td>Ortho-CH\textsubscript{2}C\textsubscript{6}H\textsubscript{4}</td>
<td>Me</td>
<td>275</td>
<td>276</td>
<td>86 %</td>
</tr>
<tr>
<td>3</td>
<td>Ortho-BrC\textsubscript{6}H\textsubscript{4}</td>
<td>Me</td>
<td>277</td>
<td>278</td>
<td>89 %</td>
</tr>
<tr>
<td>4</td>
<td>Ortho-CH\textsubscript{2}OC\textsubscript{6}H\textsubscript{4}</td>
<td>Me</td>
<td>279</td>
<td>280</td>
<td>71 %</td>
</tr>
<tr>
<td>5</td>
<td>Para-CH\textsubscript{2}OC\textsubscript{6}H\textsubscript{4}</td>
<td>Me</td>
<td>281</td>
<td>254</td>
<td>34 %</td>
</tr>
<tr>
<td>6</td>
<td>Naphthalen-2-yl</td>
<td>Me</td>
<td>268</td>
<td>261</td>
<td>99 %</td>
</tr>
<tr>
<td>7</td>
<td>Ph</td>
<td>C\textsubscript{6}H\textsubscript{11}</td>
<td>281</td>
<td>282</td>
<td>75 %</td>
</tr>
</tbody>
</table>

Increasing the bulk of the aliphatic group of the secondary alcohol from methyl to an ethyl revealed a side-reaction, that is the reduction of the alcohol to a ketone (Table 5.27: entry 2). Increasing the size of this group further to an isopropyl group (Table 5.27: entry 3) made this side-reaction the dominant reaction; none of the required ester product 285 was formed. Interestingly, further size increases to this aliphatic group effectively stopped this reaction from occurring, presumably due to the increased energy barrier for this reaction because of increased steric hindrance.
Changes to the aryl ring on the alcohol also proved to be interesting, increasing the size of this group from a phenyl ring to an o-tolyl ring greatly reduced the yield of the reaction (Table 5.28). However, it should be noted that no side reactions were observed. A 2-bromo-phenyl ring, which is slightly smaller than the o-tolyl ring, gave almost identical result to that obtained for the initial phenyl ring, seeming to indicate that there is a critical size, that once exceeded greatly reduces the rate of this reaction. Putting a co-ordinating species in the two position of the phenyl ring reduced both yield and selectivity of the reaction. Whereas having the same methoxy group in the para-position gave almost no product. Interestingly changing the electronic character of this aryl ring, from a phenyl to a naphthyl ring, also reduced the selectivity of the reaction; this would appear to show that it is the electronic nature of this aryl ring that helps to control the stereoselective process rather than its size. This was confirmed when the phenyl ring was replaced with a nonacyl cyclohexyl ring, as the selectivity of the reaction completely diminished.

Table 5.27: MKRs of alcohols with different aliphatic chains.

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Alcohol</th>
<th>Ester Product</th>
<th>Ratio anti : syn</th>
<th>Yield</th>
<th>Ketone</th>
<th>Ketone Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me</td>
<td>11</td>
<td>245</td>
<td>93 : 7</td>
<td>68 %</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>Et</td>
<td>283</td>
<td>284</td>
<td>93 : 7</td>
<td>49 %</td>
<td>289</td>
<td>12 %</td>
</tr>
<tr>
<td>3</td>
<td>i-Pr</td>
<td>274</td>
<td>285</td>
<td>–</td>
<td>0 %</td>
<td>273</td>
<td>45 %</td>
</tr>
<tr>
<td>4</td>
<td>t-Bu</td>
<td>286</td>
<td>287</td>
<td>~80 : 20</td>
<td>~1 %</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>5</td>
<td>C_6H_{11}</td>
<td>282</td>
<td>288</td>
<td>–</td>
<td>0 %</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>
Table 5.28: MKRs of alcohols with different aromatic rings.

As we had discovered three different alcohols (11, 278 and 261) that worked well in our MKRs, we were interested in seeing if combinations of these alcohols could be used to resolve the active ester 95 in a PKR. Two different combinations of alcohols were chosen, 1-phenylethanol (R)-11 was used in both cases with the (S) enantiomer of alcohols 261 and 278. These parallel kinetic resolutions proved effective, giving the required esters with similar levels of diastereocontrol as their corresponding MKRs. It should however be noted that the all of the ester obtained were very similar in structure, and hence they could not be separated using tradition purification techniques.

Scheme 5.27: PKR of active ester (rac)-95 using alcohols (S)-216 and (R)-11.
Scheme 5.28: PKR of active ester \((rac)-95\) using alcohols \((S)-278\) and \((R)-11\).

As this reaction was different from our initial method we decided that it would be prudent to carry out another cross-over reaction (like that carried out in Scheme 5.10) to check that none of the chiral centres were changing during the reaction. This again clearly showed that no racemization and or epimerisation were occurring during the reaction, as only the four different esters shown in Scheme 5.29 were obtained.

Scheme 5.29: Cross over reaction.

Now that we had successfully developed a method for the PKR of 1-phenylethnaol \((rac)-11\) and some structurally related alcohols, we turned our attention to trying to simplify this methodology. We considered using the same reaction conditions as for the previous MKRs and PKRs but only using one resolving agent, hence carrying out a traditional kinetic resolution. There are two main advantages to using a KR over a PKR, these are, firstly, one less resolving agent is required, and secondly, as only one product is formed purification of the crude product becomes much easier. The disadvantage of this strategy is that the concentration effect now starts to play a role in the diastereoselectivity of the reaction. However, as our standard
method uses ten equivalents of the racemic substrate being resolved, we hoped that the concentration effect would have a minimal impact on this reaction.

![Chemical structure](image)

Table 5.29: KRs of alcohols with different aliphatic chains.

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Alcohol</th>
<th>Ester Product</th>
<th>Ratio anti : syn</th>
<th>Yield</th>
<th>Ketone</th>
<th>Ketone Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me</td>
<td>11</td>
<td>246</td>
<td>95.5 : 4.5</td>
<td>52 %</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>Et</td>
<td>283</td>
<td>295</td>
<td>95 : 5</td>
<td>57 %</td>
<td>289</td>
<td>20 %</td>
</tr>
<tr>
<td>3</td>
<td>i-Pr</td>
<td>274</td>
<td>296</td>
<td>–</td>
<td>0 %</td>
<td>273</td>
<td>40 %</td>
</tr>
<tr>
<td>4</td>
<td>C₂H₁₁</td>
<td>282</td>
<td>297</td>
<td>–</td>
<td>0 %</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

Active ester (S)-119 was used for the KRs as it had proven to be the most selective resolving agent in our previous MKRs (Tables 5.24 and 5.25), and it was also commercially available optical pure. The KR of 1-phenylethanol (rac)-11 was almost as selective as its corresponding MKR (Table 5.24: entry 2 vs. Table 5.30: entry 1), indicating that the use of ten equivalents of the racemic alcohol 11 was enough to counter the concentration effect. Changes to the aliphatic chain of the alcohol had the same affects for the KRs as they had for the MKRs carried out earlier (Table 5.27 vs. Table 5.29).
The effect of altering the aromatic group of the alcohol in the KRs was almost identical to the original work carried in the MKRs (Table 5.28 vs. Table 5.30), the only notable differences being the slightly lower yields for the KRs. This difference is presumably due to the fact that the active ester (S)-119 being used in the KRs is more sterically hindered than the active ester (rac)-95 that was used in our MKRs.

Now that successful PKR and KR methodology had been developed, we decided to turn our attention towards the separation of labelled racemic alcohols. Not only would this be useful as a separation method, but would also definitively confirm the stability of the chiral centre of the alcohol. The labelled variant of 1-phenylethanol (rac)-11 was easily synthesised by reducing the relevant ketone 303 with LiAlD₄ (Scheme 5.30). With this labelled alcohol in hand, we screened it using our standard MKR and KR methods, the results obtained were almost identical to those obtained when using the non-deuterium labelled alcohol.

Table 5.30: KRs of alcohols with different aromatic rings.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>Alcohol</th>
<th>Ester Product</th>
<th>Ratio anti : syn</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>11</td>
<td>246</td>
<td>95.5 : 4.5</td>
<td>52 %</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>276</td>
<td>298</td>
<td>94 : 6</td>
<td>11 %</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>278</td>
<td>299</td>
<td>95.5 : 4.5</td>
<td>40 %</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>280</td>
<td>300</td>
<td>95 : 5</td>
<td>10 %</td>
</tr>
<tr>
<td>5</td>
<td>MeO</td>
<td>254</td>
<td>301</td>
<td>~ 95 : 5</td>
<td>~ 1 %</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>261</td>
<td>271</td>
<td>92 : 8</td>
<td>42 %</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>293</td>
<td>302</td>
<td>71 : 29</td>
<td>9 %</td>
</tr>
</tbody>
</table>
Scheme 5.30: Synthesis of 1-deuterio-1-phenylethanol (rac)-304.

Scheme 5.31: MKR and KR of 1-deuterio-1-phenylethanol (rac)-304.

Simple comparison of resolutions carried out using the labelled and unlabelled alcohols showed that the presence of the deuterium did not have a dramatic affect upon the reaction. In order to identify if deuterium incorporation had any subtle effects on the reaction rate a competitive MKR was carried out. Using an equimolar amount of labelled and unlabelled alcohols showed that both reacted at identical rates with the same levels of diastereoselectivity (Scheme 5.32).

Scheme 5.32: Competitive reaction of labelled and non-labelled alcohols.

In all of the above reactions involving the lithium alkoxide the reactive mixture, made from refluxing the alcohol, lithium alkoxide and zinc salt in THF, had been used shortly after synthesising it. If this reaction mixture was stable at this stage we could simply make a stock solution, and then react this with any active esters at our leisure. However, it was found that leaving this reaction mixture to stand for any length of time
dramatically reduced the yield, a small amount of white precipitate formed after allowing the reaction to stand for a few days, seemingly indicating that some of the reagents were precipitating from solution. Interestingly, a butyl ester (rac)-250 was also formed when this method was used, presumably the reactive mixture ring opened the THF to form a butoxide which could in turn react with the active ester (rac)-95 to give the observed butyl ester (rac)-250.

![Chemical reaction diagram]

**Scheme 5.33:** Hydrolysis of ester (S,S)-anti-249.

As hydrolysis of this esters 249 had not worked we next attempted to reduce this ester using a number of weak reducing agents, although a degree of reduction took place whilst using all of the weaker reducing agents some of the starting ester remained in all cases (Table 5.32). We finally used the much stronger reducing agent, LiAlH₄, which was successful in completely reducing the ester 249 to give two alcohols, the separation

<table>
<thead>
<tr>
<th>Entry</th>
<th>Left to stand for X days</th>
<th>Ratio anti : syn</th>
<th>Yield</th>
<th>Ratio 245 : 250</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>92 : 8</td>
<td>34 %</td>
<td>92 : 8</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>91 : 9</td>
<td>35 %</td>
<td>94 : 6</td>
</tr>
<tr>
<td>3</td>
<td>102</td>
<td>90 : 10</td>
<td>17 %</td>
<td>91 : 9</td>
</tr>
</tbody>
</table>

Table 5.31: MKRs using a reactive mixture that had been allowed to stand.
of these alcohols (R)-307 and (R)-11 proved to be very difficult due to their similar polarities (Scheme 5.34). The reduction of ester (S,S)-anti-249 was more successful as the resulting alcohols (S)-308 and (S)-11 could be separated by flash column chromatography (Scheme 5.35).

![Diagram]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reducing agent</th>
<th>Ratio 245 : 307 : 11</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Li-iBuAlH</td>
<td>29 : 51 : 20</td>
</tr>
<tr>
<td>2</td>
<td>LiBH₄</td>
<td>49 : 34 : 17</td>
</tr>
<tr>
<td>3</td>
<td>LiBHET₃</td>
<td>21 : 53 : 26</td>
</tr>
</tbody>
</table>

**Table 5.32: Attempted reduction of ester (rac)-245.**

(R,R)-anti-245 86% d.e.

![Diagram]

**Scheme 5.34: Reduction of ester (R,R)-anti-245.**

Scheme 5.35: Reduction of ester (S,S)-anti-249.

As the reduced products of the ester 245 were problematic to separate we attempted a transesterification followed by hydrolysis method in order to obtain the pure 1-phenylethanol 11. We first used potassium tert-butoxide as a transesterification agent, this method was successful, giving the required 1-phenylethanol in 69% yield, however a side reaction also took place, which seemingly reduced the alcohol to form the ketone 303. Fortunately this side reaction could be prevented by using a less sterically demanding alkoxide, sodium ethoxide (easily synthesised from ethanol and sodium, Scheme 5.36). When using sodium ethoxide however, a second step had to be incorporated to hydrolyse the ethyl ester 309 formed in this reaction, however this reaction could all be carried out as a one pot procedure.
Scheme 5.36: Synthesis of sodium ethoxide.

\[
\begin{align*}
\text{EtOH} & \xrightarrow{\text{Na, 0°C, N}_2} \text{NaOEt} \\
\end{align*}
\]

Scheme 5.37: Transesterification of ester \textit{(rac)}-245.

When the above mentioned procedure was carried out on the ester \textit{(S,S-anti)-246} (88% \textit{d.e.}) obtained from a KR, the required 1-phenylethanol \textit{(S)-11} was obtained in good yield (78%) with equivalent enantiomeric excess as the diastereoisomeric excess of the starting ester \textit{(S,S-anti)-246} (Scheme 5.38). However the carboxylic acid 118 obtained was racemic, indicating that the ester was opened by the base removing the acidic proton alpha to the carbonyl group, and forming a ketene by elimination of the alcohol component of this ester.

Scheme 5.38: Transesterification of ester \textit{(S,S-anti)-246}.
To conclude, we have successfully resolved 1-phenylethanol (rac)-11 using a PKR process and it was found during this study that an excess of alcohol must be used to stop epimerisation from occurring. To obtain the highest levels of diastereoselectivity with a reasonable yield, equimolar amounts of a lithium derived base and a zinc salt had to be used. In order to obtain a pure product there could be no contamination of the reagents with a primary alcohol, meaning that the type of base used and the way that the racemic secondary alcohol was synthesised was extremely important. Although the solvent of the reaction seemed to play no role in the diastereo-determining step, a powerful solvating solvent had to be used in order to keep the reaction intermediates (mainly the lithium and zinc alkoxides) in solution.

From all of the above information we believe that the method we have developed follows the reaction pathway shown in Scheme 5.39. It should be noted that the zinc alkoxide is the reactive species, we believe this because if a sub-stoichiometric amount of zinc to lithium is used the selectivity of the reaction diminishes, suggesting that the lithium alkoxide reacts in a less stereo selective fashion.

![Scheme 5.39: Reaction pathway.](image)

The intermediate (S,S)-311 is presumably formed, we believe that this intermediate is much more stable than its counter part (S,R)-311. The metal ion in (S,S)-311 can be sandwiched between the aromatic ring of the alcohol and active ester component, while there is too much steric hindrance in (S,R)-311 for this to occur so increasing the energy of the system as the metal ion can not internally coordinate. This would explain why the use of a non aryl alcohol gives such poor levels of diastereoselectivity (Table 5.28 entry 7).

We also speculate that the formation of the intermediate 311 is in fact reversible, so either the pentafluorophenyl group can leave to give the ester 245 or the alkoxide 310 can leave to return the starting materials. We believe this because of the work carried out in the project described in Chapter 2, especially the work done with the oxazolidin-2-thiones. This may explain why the combination of zinc and lithium must be used together, as the reversible step may involve the competitive leaving ability of the pentafluorophenyl bound to lithium against the zinc alkoxide 310. It may also explain
why the type of leaving group is so important in the reaction, to poor a leaving group is used and the equilibrium is pushed over to the left, resulting in a low yield. If too good a leaving group, the equilibrium is pushed over to the right, this means that when $\text{(S,S)}$ and $\text{(S,R)-311}$ are formed they will both go on to form the respective product $\text{245}$, rather than $\text{(S,R)-311}$ return the starting materials, hence lowering the overall diastereoselectivity of the reaction (Table 5.21).
Chapter 6

The Modification of 2-Bromo-phenylethanol

During the project outline in Chapter 5 we attempted to resolve 1-(2-bromo-phenyl)-ethanol (rac)-278 using tert-BuLi and ZnCl₂ using active ester (rac)-95 (Scheme 6.1). Although this reaction proved to be somewhat unsuccessful as the yield of the required ester (rac)-290 was very low, and interesting effect was noticed, the returned alcohol was not all 1-(2-bromo-phenyl)-ethanol (rac)-11, 1-phenylethanol (rac)-11 was also present. After eliminating the possibilities of contamination or simple mixing up of samples we were led to the assumption that the bromine must have be removed during the reaction, presumably by the strong base (tert-BuLi) being used in the reaction.

Scheme 6.1: MKR of 1-(2-bromo-phenyl)-ethanol (rac)-278 using tert-BuLi and ZnCl₂.

In order to validate if it was indeed some combination of the tert-BuLi and ZnCl₂ that was removing the bromine during the reaction we used the same reaction conditions but simply did not add any active ester and instead quenched with water. This gave a mixture of alcohols, clearly indicating that the active ester played no part in this de-bromination reaction.

Scheme 6.2: De-bromination of 1-(2-bromo-phenyl)-ethanol (rac)-278 using tert-BuLi and ZnCl₂.
At this stage we could not tell if the tert-BuLi or ZnCl₂ or indeed a combination of these two reagents were de-brominating the alcohol, so we carried out the original MKR without any ZnCl₂ in order to see if de-bromination would still occur. A mixture of the two alcohols (rac)-278 and (rac)-11 was again obtained and in almost an identical ratio to the original reaction (Scheme 6.1 vs. Scheme 6.3), clearly indicating that the zinc salt played no part in this de-bromination reaction. This reaction also gave a mixture of esters (rac)-290 and (rac)-245, one derived from each alcohol, showing that either the 1-phenylethanol (rac)-11 formed in this reaction was reacting with the active ester, or the bromo ester (rac)-290 was also being de-brominated.

**Scheme 6.3**: MKR of 1-(2-bromo-phenyl)-ethanol (rac)-278 using tert-BuLi

We next chose to evaluate the relative equivalents of base that would be needed to cause a degree of de-bromination and if complete de-bromination could occur. To do this we simply used tert-BuLi and quenched this reaction with water. These results showed that complete de-bromination was achieved using five equivalents (or more) of tert-BuLi. More interestingly, we found that a degree of de-bromination occurred even when using sub-stoichiometric amounts of base. This seems somewhat strange as one would imagine that the first equivalent of any base added to 1-(2-bromo-phenyl)-ethanol (rac)-278 would deprotonate the alcohol group, and it would require an additional equivalent of base to then remove the bromine atom. These results obtained clearly contradict this; it would seem to suggest that the initial equivalent of base de-brominates the alcohol. Should deprotonation occur initially it would seem logical that a six-membered ring would be formed, with the lithium cation from the base, bridging the oxygen and bromine atoms of the alcohol. It is therefore my belief that this is how de-bromination occurs, with the base first deprotonating the alcohol and then de-brominating it.
Table 6.1: De-bromination of 1-(2-bromo-phenyl)-ethanol (rac)-278 using varying equivalents of tert-BuLi.

Although de-bromination occurred readily, five equivalents of tert-BuLi had to be used to obtain only 1-phenylethanol (rac)-11, we theorised that simply increasing the temperature that the reaction was carried out at may increase de-bromination and hence mean that less equivalents of tert-BuLi would be needed. Increasing the temperature of this reaction while using two equivalents of base did indeed increase the amount of de-bromination occurring, but complete conversion to 1-phenylethanol (rac)-11 was never obtained, so we chose to continue the work using five equivalents of base.

Table 6.2: De-bromination of 1-(2-bromo-phenyl)-ethanol (rac)-278 at different temperatures.

At this stage, we were next interested in seeing how varying the strength of the base may affect this reaction; we also hope that a less hazardous base than tert-BuLi could be used for this process. Weaker bases resulted in only partial, or in the case of LDA, no de-bromination, however a reasonably strong base (n-BuLi) did result in the complete formation of 1-phenylethanol (rac)-11.
Table 6.3: De-bromination of 1-(2-bromo-phenyl)-ethanol (rac)-278 using different bases.

We had previously surmised that 1-phenylethanol (rac)-11 was formed when the de-brominated alcohol reacted with the water used to quench the reaction. As a way of testing this and to determine where the hydrogen atom present in 1-phenylethanol (rac)-11 was from, we chose to simply quench the reaction with D$_2$O instead of water. The reaction showed that we were correct, as only 1-(2-deutério-phenyl)-ethanol (rac)-312 was obtained from this reaction. We also chose to carry out our normal de-bromination reaction using an optical pure sample of 1-(2-bromo-phenyl)-ethanol (S)-278; if the product was also optically pure it would indicate that the reaction mechanism did not involve the chiral centre. This reaction gave 1-phenylethanol (S)-11, showing that our speculations were indeed correct and the chiral centre is left unaffected during the reaction.

Scheme 6.4: Investigations of the de-bromination reaction.

As water and D$_2$O could be used to quench the reaction and give different products it stood to reason that other electrophiles could also be used to give a range of alternatively two substituted alcohols. We chose to use the simple electrophile methyl iodide to test this theory, we also decided to use a range of equivalents of this
electrophile to find out how many would be needed for complete substitution. These reactions did indeed give the required two methyl substituted alcohol \(( rac \)-276\), and it appeared that an excess of the electrophile was needed. Unfortunately in all of these cases 1-phenylethanol 11 was also formed, perhaps because the methyl iodide had failed to quench all of the reactive intermediate or because some water was getting into the reaction mixture and reacting at the same time as the methyl iodide.

The mixture of alcohols \(( rac \)-276\) and \(( rac \)-11\) proved to be imposable to separate using conventionally organic purification techniques, meaning that this was a poor way to synthesise two substituted alcohols. Therefore when we chose the next electrophile we made sure that it would give the alcohol product different physical properties to 1-phenylethanol \(( rac \)-11\) to help separation of the mixture formed. Using silye based electrophiles worked well and gave alcohols that could be easily separated using flash column chromatography from any other alcohols formed during the reaction.

When dimethyl tert-butyl silye chloride was used (Scheme 6.7) a good yield was obtain, we therefore decided to carry out this reaction on an optical pure alcohol \(( S \)-278\), this also gave a good yield and the chiral centre was left unaffected.

**Table 6.4:** Quenching with methyl iodide.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Equiv.'s of Mel</th>
<th>Ratio 278 : 276 : 11</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>12 : 62 : 26</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>6 : 83 : 11</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>8 : 79 : 13</td>
</tr>
</tbody>
</table>

**Scheme 6.5:** Reacting \(( rac \)-278\) with methyl iodide.

**Scheme 6.6:** Reacting \(( rac \)-278\) with trimethyl silye chloride.
Scheme 6.7: Reacting 278 with dimethyl tert-butyl silye chloride.

The next electrophile we chose to study was PhSSPh, and although this reacted and gave the required alcohol (rac)-315 it was found to be inseparable from 1-phenylethanol (rac)-11. A third alcohol (rac)-316 was also formed, although we were somewhat unsure of how it was synthesised. We did speculate that it could have been from the direct addition of oxygen to the reactive alcohol, so we tested this reaction and found that it could indeed be formed in this fashion. The presence of 1-phenylethanol (rac)-11 in this reaction (Scheme 6.9) is presumably due to the presence of water in the reaction. As a way of confirming our assignment of this alcohol (rac)-316 we synthesised it traditionally from the appropriate aldehyde 317 (Scheme 6.10).

Scheme 6.8: Reacting (rac)-278 with PhSSPh.

Scheme 6.9: Reacting (rac)-278 with O₂.
Scheme 6.10: Synthesis of 1-(2-hydroxy-phenyl)-ethanol (rac)-316.

By addition of a silye group to the alcohol we had managed to synthesis a two substituted alcohol which was separable from any other alcohols due to its less polar nature, we theorised that adding a motif that made the product more polar should therefore also work. The reaction shown in Scheme 6.9 used a gas as a reagent and this appeared to work, if only to a small degree, we therefore thought that using CO2 as the electrophile might work. Should it react it would give a carboxylic acid group on the alcohol, this should make it very easy to purify. When we carried out this reaction however we obtained the lactone (rac)-318 in good yield (Scheme 6.11), this reaction could also be done using optically pure starting alcohol (S)-278 and again gave good yield with no loss of optical purity.

Scheme 6.11: Synthesis of the lactone.

At first glance the lactone (rac)-318 appears to be a very strange product to obtain from this reaction. However if you assume that the first step of the reaction goes as previously believed with the de-bromination followed by addition of the now nucleophilic carbon of the ring to CO2, this should give a carbonyl group in the two position of the ring with some form of hydroxyl motif bound to it (rac)-320. Presumably the oxygen of the alcohol is deprotonated at this time and will therefore attack the carbon of the carbonyl group which in turn will eliminate the hydroxyl group, forming the five membered lactone ring (rac)-318 (Scheme 6.12).
**Scheme 6.12:** The formation of the lactone 318.

With a reliable synthesis for the lactone 318 in both its racemic and optically pure forms in hand, we were very interested in the possibility of ring opening reactions, hence giving access to a wide range of interesting optical pure compounds. However, using a variety of different nucleophiles and reaction conditions we could only reisolate the lactone 318. These results suggest that the lactone is thermodynamically very stable, so that if anything adds to the carbonyl group it is simple eliminated rather than breaking the five membered ring system.

**Table 6.5:** Attempted ring opening of the lactone (rac)-318.

We next turned our attention to trying to open this lactone ring by direct addition of MeMgBr, however when only one equivalent was used it again only returned the starting materials. When an excess of MeMgBr was used the reaction was pushed to completion and formed the alcohol (rac)-322 in a reasonable yield (Scheme 6.13).
Scheme 6.13: Reacting the lactone (rac)-11 with MeMgBr.

As we had now seen that the lactone ring was very stable but could be open using harsh reaction condition we suspected that it could be reduced using LiAlH₄, this indeed was the case and gave the required product (rac)-323. It is also worth noting that this process can be carried out on the optical pure lactone (S)-318, to give an optical pure diol (S)-323.

Scheme 6.14: Reduction of lactone 318.

To conclude a mutual kinetic resolution that gave an unexpected result has been examined, understood and used to synthesise a small range of two substituted alcohols. The limiting factors in this methodology were that a large excess (five equivalents) or base had to be used and a number of very similar alcohols were often made in the reaction due to side reactions, hence creating problems in purification and limiting the variety of pure alcohols that could be obtained. Interestingly, a lactone 318 could also be formed using this method and could itself be further modified. All of these products can be obtained enantiomerically pure as the starting material, 1-(2-bromo-phenyl)-ethanol (S)-278, is commercially available.
Chapter 7

The Resolution of 1-Phenylethanol using Carboxylic Acids and DCC

During the resolution of 1-phenylethanol (rac)-11 by the formation of esters, such as (rac)-245, described in Chapters 4 and 5, there was a common problem, we needed too stereospecific enantiomerically pure samples of these ester. It was very important that we obtain these as they were the only way that we could accurately identify which of the diastereoisomers was which. Using the methods outlined in Chapters 4 and 5 were problematic, as all esters obtained from Chapter 4 were contaminated with the carbonate 243. Whereas initial reactions from Chapter 5 had a degree of epimerisation or contained the unwanted butyl ester 250. Although a method based on the studies in Chapter 5 was eventually found, we had already explored other ways to achieve this goal.

One idea we had to obtain pure esters was to carry out a simple DCC mediated coupling reaction of the corresponding carboxylic acid and alcohol, surprisingly when we carried out this reaction only a very small amount of the ester (rac)-245 was actually formed (Scheme 7.1). The carboxylic acid (rac)-111 instead reacted with itself to form the anhydride (meso)- and (rac)-324, it is interesting to note that neither the ester (rac)-245 or anhydride (meso)- and (rac)-324 showed any level of diastereoisomeric excess.

\[
\text{Scheme 7.1: DCC coupling of carboxylic acid (rac)-111 and alcohol (rac)-11.}
\]

Although this result was somewhat of a surprise, we believed that the simple addition of a sub-stoichiometric amount the acyl transfer reagent DMAP would increase the formation of the required ester product (rac)-245. This was indeed shown to be the case, the required ester (rac)-245 was obtained in high yield and its purification was very simple as all other by-products of the reaction or remaining starting material were much more polar than the required ester (rac)-245.
With a simple method for the formation of ester \((rac)-245\) in place we chose to see if this method could be used with optically pure starting materials to yield only one diastereoisomer. We found that the appropriate ester were indeed formed and that neither chiral centre was adversely affected during the reaction. This method worked well for the synthesis of both the syn- and anti-diastereoisomers. A small range of different aliphatic and aryl groups on both the carboxylic acids and alcohols showed that these groups had no real affect on the reaction (Scheme 7.3 to 7.5).

**Scheme 7.3:** Synthesis of ester \((R,R)\)-anti and \((S,S)\)-anti-248.

**Scheme 7.4:** Synthesis of ester \((S,S)\)-anti and \((S,R)\)-syn-249.
As this reaction seemed rather robust, we became interested in seeing if the acidity of the proton alpha to the carbonyl group was important. We tested this by carrying out the reaction with the carboxylic acid (S)-120, the above mentioned alpha hydrogen for this acid is very acid as it is in between a carbonyl group, phenyl group and a methoxy group. The product from this reaction, ester 253, was the only ester that we had previously been unable synthesis in a stereospecific fashion using other methods. This new method however was successful in the stereospecific synthesis of ester (S,S)-anti and (S,R)-syn-253.

This method for synthesising the pure esters we needed for characterisation purposes had many advantages, firstly it never epimerised any of the esters, it was also very simple to carry out practically and purification of the products was trivial. Perhaps more importantly than all of the above, no strong bases or air sensitive reagents were used, this meant that the reaction worked every time, there was no chance that base had degraded. As a result, this became our method of choice, as such we used it to synthesis the pure esters that had proven problematic to obtain in other projects (Scheme 7.7 and 7.8).
The enantiomeric excess of alcohols.

Scheme 7.7: Synthesis of ester (rac)-anti and syn-294, and ester (rac)-anti and syn-302.

Scheme 7.8: Synthesis of ester (rac)-anti and syn-325.

As neither of the chiral centres are affected in the reaction we surmised that this method could be used as a way of determining the enantiomeric excess of alcohols. By reacting an alcohol of unknown enantiomeric excess with an enantiomerically pure carboxylic acid a diastereoisomeric mixture of syn- and anti- esters should be obtained. The enantiomeric excess of this alcohol can be directly related to the relative ratio of these diastereoisomeric esters. This methodology did indeed work, however, the accuracy of this reaction was not perfect, as the reaction itself is somewhat stereoselective, meaning that this reaction gave an approximate enantiomeric excess of the alcohol rather than a definitive result (Scheme 7.9).

Scheme 7.9: Determining the enantiomeric excess of an alcohol.

The initial reaction involving DMAP (Scheme 7.2) showed a degree of diastereoselectivity (ratio anti : syn 76 : 24), although a relatively poor level of selectivity the reaction was selective. Presumably this selectivity must arise from the selective addition of the alcohol to the intermediate (rac)-326 (Scheme 7.10).
Interestingly there are a number of research groups that have used a related approach to resolve racemic alcohols, however in all of these cases they use a chiral DMAP equivalent, where the acyl group being transferred is achiral. However, this requires the synthesis of these chiral DMAP equivalents; we believed that our simpler approach of using a commercially available chiral carboxylic acid and achiral DMAP may be an alternative way of resolving 1-phenylethanol (rac)-11.

We started to develop this methodology by using other simple achiral DMAP equivalents; one of the first we chose to screen was pentafluoropyridine. This was chosen as its intermediate would closely resemble the active ester (rac)-95 which had given excellent results in Chapter 5. However, this particular acyl transfer reagent was not nucleophilic enough, and almost none of the required ester (rac)-245 was formed. Further studies into the most diastereoselective DMAP equivalent was carried out by Najla Al Shaye during her MSc project, she found that 3,5-lutidine was the reagent of choice.

We also screened a range of different carboxylic acids, we changed both the aliphatic and aryl groups of the carboxylic acid so that we could observe what effect this had on the reaction, (Table 7.1, note that additional carboxylic acids were also screened by Najla Al Shaye). Increasing the steric bulk of the aliphatic group on the carboxylic acid increased the levels of diastereoselectivity, while slightly reducing the yield. Interestingly the addition of an electron-withdrawing atom at the four position of the aryl ring reduced the diastereoselectivity of this reaction. These results seemed to
indicate that the diastereoselectivity of this reaction is driven by both the electronic and steric nature of the reagents.

![Chemical structure](image)

**Table 7.1**: MKR of 1-phenylethanol (rac)-11 using different carboxylic acids.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>R</th>
<th>Ester</th>
<th>Product</th>
<th>Ratio : syn</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph</td>
<td>Me</td>
<td>111</td>
<td>245</td>
<td>82 : 18</td>
<td>57%</td>
</tr>
<tr>
<td>2</td>
<td>Ph</td>
<td>Et</td>
<td>118</td>
<td>246</td>
<td>85 : 15</td>
<td>51%</td>
</tr>
<tr>
<td>3</td>
<td>para-C6H4Cl</td>
<td>Me</td>
<td>116</td>
<td>256</td>
<td>76 : 24</td>
<td>57%</td>
</tr>
</tbody>
</table>

With a range of different carboxylic acids screened using our standard MKR methodology we chose to turn our attention to the PKR of 1-phenylethanol (rac)-11. Three different sets of quasi-enantiomers were chosen for these resolutions, the carboxylic acid (R)-111 was used in all of these combinations as it had given the highest levels of diastereoselectivity in the MKR screening studies. The other quasi-enantiomer was changed in each of the three PKRs (Schemes 7.12 to 7.14). All of the reactions proceeded as expected and gave results that corresponded with their associated MKRs, it should be noted that only the PKR shown in Scheme 7.12 gave esters that could be easily separated, while all others were obtained as inseparable mixtures.

![Chemical structures](image)

**Scheme 7.12**: PKR using carboxylic acid (R)-118 and (S)-122.
For completeness we also carried out a cross-over reaction (like those carried out in the previous chapters) just to ensure that no racemization and/or epimerisation was occurring. This reaction proceeded effectively and only gave products that could be obtained without altering any of the chiral centres in any of the reagents (Scheme 7.15).

To conclude a coupling reaction between carboxylic acids and alcohols, mediated by DCC and DMAP, was used to easily synthesise a range of enantiomerically pure esters in a stereospecific fashion, that were need for characterisation for the studies outlined in Chapter 4 and 5. This methodology was then modified so that it could be used to resolve 1-phenylethanol (rac)-11 in a PKR fashion.
Chapter 8

Determining the Enantiomeric Excess of Carboxylic Acids

During the project described in Chapter 7 an anhydride was formed in a DCC mediate reaction. Interestingly both possible diastereoisomers (syn- and anti-) were formed in exactly the same relative proportions (Scheme 7.1). From this study described in Chapter 7 we were confident that no racemization or epimerisation occurred during this DCC mediated reaction, this would indicate that this reaction had absolutely no stereo control. If this was the case, this could be a very useful reaction, as the diastereoisomeric ratio of products can be related to the enantiomeric excess of the starting material (Figure 8.1), and as such a table can be constructed which relates the enantiomeric excess of the starting materials to the expected diastereoisomeric excess of the products (Table 8.1).

![Figure 8.1: Relating e.e. to d.e. in a stereorandom self coupling reaction.](image)

<table>
<thead>
<tr>
<th>e.e.</th>
<th>0</th>
<th>10</th>
<th>50</th>
<th>90</th>
<th>100</th>
</tr>
</thead>
<tbody>
<tr>
<td>d.e.</td>
<td>0</td>
<td>1</td>
<td>25</td>
<td>81</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 8.1: Theoretical values of diastereoisomeric excess.

In order to test this theory we carried out a number of reactions using a carboxylic acids 114 with different enantiomeric excesses and measured the diastereoisomeric excesses of the product 327 formed. The results did indeed show that the reaction was completely stereorandom; the results obtained comparing almost
perfectly with the theoretical values (Table 8.2 vs. Table 8.1). The accuracy of this process, however, was seen to reduce when the starting material had low enantiomeric excess. We did not feel that this was overly problematic as normally the need for an accurate measurement of the enantiomeric excess is only required for substrates with moderate to high levels of enantiomeric excesses.

![Chemical structure](image)

**Table 8.2**: Self coupling of carboxylic acid 114.

<table>
<thead>
<tr>
<th>Entry</th>
<th>e.e. of acid</th>
<th>d.e. of anhydride</th>
<th>Yield of anhydride</th>
<th>d.e. of ester</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>100%</td>
<td>100%</td>
<td>88%</td>
<td>100%</td>
</tr>
<tr>
<td>2</td>
<td>90%</td>
<td>80%</td>
<td>89%</td>
<td>~100%</td>
</tr>
<tr>
<td>3</td>
<td>50%</td>
<td>26%</td>
<td>89%</td>
<td>70%</td>
</tr>
<tr>
<td>4</td>
<td>10%</td>
<td>4%</td>
<td>85%</td>
<td>36%</td>
</tr>
<tr>
<td>5</td>
<td>0%</td>
<td>0%</td>
<td>78%</td>
<td>22%</td>
</tr>
</tbody>
</table>

Entry 2 was repeated in an NMR tube and gave anhydride 327 with 78% d.e.
Entry 2 was repeated on 10 mg scale and gave anhydride 327 in 84% yield with 82% d.e.

As a way of checking that these selectivities were accurate, we hydrolysed each of the anhydrides 327 and re-isolated the starting material 114. The level of optical purity of this carboxylic acid was then confirmed by optical rotation and coupling onto an enantiomerically pure alcohol (S)-11. The results from this re-coupling procedure do not come out quite as expected; this is due to the inaccuracy of this method (as it is stereoselective) rather than any indication of problems in the anhydride formation.

With a method in hand that almost perfectly matched the theoretical values, we decided it was time to test the robustness of this reaction. The first study had all been carried out using the carboxylic acid 114, simply because it is inexpensive and available in both enantiomerically pure and in racemic forms. We wished to probe if increasing the possibility of sterically demanding nature of the carboxylic acid, by increasing the size of the aliphatic group on the carboxylic acid would affect the reaction. The size of this group appeared to have no effect on this reaction with all the carboxylic acids 111, 118 and 124 giving the appropriate anhydrides in the expected ratio (Table 8.3 entry 1 to 9).
Table 8.3: Self coupling of a range of carboxylic acids.

We also chose to study how altering the aryl group may affect the reaction, again the reaction showed no levels of stereoselectivity and simply gave values approximately equal to those obtained statistically (Table 8.3: entries 1 to 3 and 10 to 15). We also decided to screen the carboxylic acid 328, as its phenoxy group would increase the acidity of the proton alpha to the carbonyl group as well as changing the overall structure of the carboxylic acid backbone; this had no effect on this reaction (Table 8.3 entry 16 to 18). We also tested the deuterated carboxylic acid (R)-333 to further check the robustness of this reaction; this gave the value expected from the theoretical calculations (Scheme 8.1).

Scheme 8.1: Self coupling of carboxylic acid 333.

Although this method for determining the enantiomeric excess of numerous carboxylic acids worked very well, we hoped that we could make it easier to carry out by using the water soluble DCC equivalent, EDAC, and thus making purification of the products easier. When this new coupling agent was used on a racemic sample of carboxylic acid (rac)-114, an equal mixture of the anti- and syn-diastereoisomers were obtained, and purification was indeed much easier than the original method. However,
when an enantiomerically pure sample of this carboxylic acid (S)-114 was screened a mixture of diastereoisomers was obtained; obviously the EDAC is more basic than DCC and as such is causing racemization and/or epimerisation during the reaction. This meant that EDAC was unusable as a coupling reagent in such reactions, and we would have to be satisfied with the DCC method previously developed.

Scheme 8.2: Using EDAC as the coupling agent.

To conclude, we have developed an accurate and robust method for determining the enantiomeric excess of a carboxylic acid with related structures to that of 114. The main advantage of this method is that it is a stereorandom coupling process and therefore the reaction does not need to be driven to completion and it is hence independent of time. As the reaction is a self-coupling process no expensive additional enantiomerically pure reagents are needed. This reaction is presumably completely stereorandom as the two chiral centres of the anhydride are separated by four bonds; this distance clearly means they are too far apart to put any preference on which diastereoisomer is formed. However, it should be noted that if the chiral centre were even further apart there would be even less chance of diastereoselectivity, however, it would also become harder to distinguish between the different diastereoisomers.
Chapter 9

Conclusion

This thesis has detailed four distinct resolutions; the resolution of active esters such as 95 using oxazolidin-2-ones such as 94 as outlined in Chapter 2. The resolution of alcohols, such as 11, using oxazolidin-2-one adducts like 96 as described in Chapter 4, or using active esters based on 95 as seen in Chapter 5, or using carboxylic acids of the generic structure 111 as shown in Chapter 7. Although these four resolutions appear at first glance to be very different, as they all use different reagents and conditions, they all in fact contain the same key element. This is the addition of a chiral nucleophile to the carbonyl group of the propionate 335, followed by elimination of a leaving group. Almost all of the products obtained from these resolutions have the same overall stereochemistry, for example the anti-245 ester was the favoured diastereoisomer in all three chapters that it was synthesised in. If this ester anti-245 is drawn in the same format as the major oxazolidinone adduct, syn-96, then the fact that these are of the same overall relative stereochemistry is evident (Figure 9.1).

Scheme 9.1: Generic resolution process.

Figure 9.1: Ester anti-245 and oxazolidinone adduct syn-96.

This leads us to speculate that the four different resolution methods must contain the same (or very similar) stereo-directing step or steps. This idea was reinforced when more of the results are compared, for example if the methyl group, in 335, is increased in size to an ethyl group the levels of selectivity increased for every type of resolution, although the yields were lower. If this same group is increased further to an isopropyl...
group the selectivity dramatically decreased for all the resolutions, similarly when the phenyl ring of 335 was replaced with para-chloro-substituted phenyl ring, the levels of selectivity decreased for all the different types of resolutions. These results confirmed our suspicions that all the resolutions contain very similar elements to their stereoselective nature, this also drove us to try and understand how this generic stereoselective step or steps functioned.

If we organise the resolutions in order of the leaving ability of L (on 335 in Scheme 9.1) then we notice that the nucleophiles are ordered in relative strength, but in a reverse fashion to the leaving groups (Scheme 9.2). So the best leaving group is being attacked by the weakest nucleophile (337 and 11), while the worst leaving group is being attacked by the strongest nucleophile (96 and 338). Interestingly the active ester 95 was used in two separate resolutions and the two nucleophiles used in these resolutions are of very similar strength. This seems far too coincidental to be a random occurrence; it implies the leaving ability and nucleophilicity have to be closely linked. It is also interesting to note that changes to the leaving ability greatly affected these individual reactions, for example 3,5-lutidine showed the best results in Chapter 7, whereas pentafluorophenol was required as the active ester in both Chapters 2 and 5. The strength of the nucleophile was also very important in individual resolutions, for example the stronger lithium alkoxide variation of 310 was greatly less effective than the weaker zinc alkoxide 310 in Chapter 5.

![Scheme 9.2: Resolutions in order of leaving ability of L (on 335).](image)
The results obtained from the kinetic resolutions using the oxazolidin-2-thione 236 (Scheme 2.55) gave a lot of insight into why the leaving group ability and the strength of the nucleophile have to be so closely matched. As mentioned in Chapter 2 the results obtained with the oxazolidin-2-thione 236 would indicate that the stereoselective step in this reaction is thermodynamic in nature not kinetic. As such there is a degree of thermodynamic character in all of the above mentioned resolutions. The overall stereoselective pathway in all the resolutions appears to be as follows. The nucleophile (Nu*) will add in a selective fashion to 335, this selectivity will be kinetically driven as the different isomers of 339 will be obtained through different energy pathways, this kinetic energy difference will primarily be sterically driven. Once the reactive intermediate 339 is formed it can fragment in two different ways, by the loss of Nu* to return the starting martial, or by loss of the leaving group to give the required product 336. This step is also selective and is thermodynamic in nature, implying that the final compound 336 or an intermediate between 339 and 336 is of lower energy for the major diastereoisomer. This is why the leaving ability and nucleophilicity in the reaction have to be so closely balanced.

Scheme 9.3: Generic stereoselective pathway.

To conclude, the selectivity in all four of the above mentioned resolutions are connected and proceed through the generic pathway outlined in Scheme 9.3. The selectivity in all cases are derived from a kinetically driven addition step followed by a thermodynamically driven elimination step. It is the combination of these two stereoselective steps that makes this process highly stereoselective and robust enough so that it works for a multiple of different reagents, under an array of different reaction conditions.
Chapter 10

Experimental

General

All reactions were carried out under nitrogen using dry glass ware, THF was dried over sodium wire, and dichloromethane was dried over magnesium sulphate. Flash column chromatography was carried out using Silica-Gel 35-70u 60A with freshly distilled solvents. Thin layer chromatography (TLC) was carried out on commercially available pre-coated aluminium sheets (silica gel 60 with fluorescent indicator UV 254). Proton, fluorine and carbon NMR were carried out on a Jeol Lambda 400 Fourier transform spectrometer using an internal deuterium reference. Chemical shifts are quoted in parts per million downfield from tetramethylsilane. Infrared spectra were recorded on a PerkinElmer RX1 FT-IR instrument, optical rotations were recorded on a polar® 3001 automated polarimeter and mass spectrometry was performed by the EPSRC in Swansea. Experiments labelled [S/TX.X; EX] S/TX.X corresponds to scheme or table number, EX corresponds to entry number if applicable.

Section 1: Experiments from Chapter 2

Synthesis of 2-phenyl-2-amino-ethan-1-ol (rac)-99 [S2.2; E1].

Phenylglycine (rac)-98 (13.29 g, 0.087 mol) was slowly added to LiAlH₄ (5 g, 0.13 mol) in THF (120 ml) at 0°C. The resulting solution was stirred for half an hour at room temperature and then refluxed over night. The reaction was diluted with diethyl ether (100 ml) then quenched over 2 hours with water (4.7 ml), potassium hydroxide (15%, 4.7ml) and water (14.1 ml). The solid precipitate was removed by filtration; the organic layer was extracted with diethyl ether (3 × 100 ml), dried over MgSO₄ and evaporated under reduced pressure. To give 2-phenyl-2-amino-ethan-1-ol (rac)-99 (7.78 g, 66%) as a white powder mp 69-71°C; νmax (CHCl₃)/cm⁻¹ 3325 (OH), 2968 and 2968 (NH₂); δH (400 MHz; CDCl₃) 7.37-7.24 (5H, m, 5 × CH; Ph), 4.03 (1H, dd, J 8.3 and 4.4, CHNH), 3.72 (1H, dd, J 10.8 and 4.4, CH₃OH), 3.55 (1H, dd, J 10.8 and 8.3, CH₃H₂OH), and 2.40 (3H, br s, OH and NH₂); δC (100 MHz; CDCl₃) 142.4 (i-C; Ph), 128.5; 127.4 and 126.4 (5 × CH; Ph), 68.1 (CHNH), and 57.4 (CH₂O); (Found MH⁺, 138.0910; C₈H₁₂NO requires 138.0919).
Synthesis of 2-phenyl-2-amino-ethan-1-ol (S)-99 [S2.2; E2].

In the same way as S2.2; E1, phenylglycine (S)-98 (13.29 g, 0.087 mol) and LiAlH₄ (5 g, 0.13 mol) in THF (120 ml). Gave 2-phenyl-2-amino-ethan-1-ol (S)-99 (10.52 g, 87%); which was spectroscopically identical to that obtained elsewhere.

Synthesis of 2-phenyl-2-amino-ethan-1-ol (R)-99 [S2.2; E3].

In the same way as S2.2; E1, phenylglycine (R)-98 (7.73 g, 0.051 mol) and LiAlH₄ (2.91 g, 0.077 mol) in THF (70 ml). Gave 2-phenyl-2-amino-ethan-1-ol (R)-99 (4.2 g, 60%); which was spectroscopically identical to that obtained elsewhere.

Synthesis of 3-phenyl-2-amino-propan-1-ol (S)-100 [S2.3].

In the same way as S2.2; E1, phenylalanine (S)-57 (14.52 g, 0.087 mol) and LiAlH₄ (5 g, 0.13 mol) in THF (120 ml). Gave 3-phenyl-2-amino-propan-1-ol (S)-100 (9.51 g, 72%); δH (400 MHz; CDCl₃) 7.30 (2H, tt, J 7.0 and 1.8, 2 × CH; Ph), 7.25-7.16 (3H, m, 3 × CH; Ph), 3.63 (1H, dd, J 10.8 and 3.9, CH₃H₅OH), 3.39 (1H, dd, J 10.8 and 7.2, CH₃H₅OH), 3.15-3.08 (1H, m, CHNH₂), 2.79 (1H, dd, J 13.5 and 5.2, CH₃H₅Ph), 2.52 (1H, dd, J 13.5 and 8.7, CH₃H₅Ph) and 2.07 (3H, br s, OH and NH₂); δC (100 MHz; CDCl₃) 138.6 (i-C; Ph), 129.2, 128.6 and 126.4 (5 × CH; Ph), 66.2 (CH₂OH), 54.2 (CHNH₂) and 40.8 (CH₂Ph).

Synthesis of 1-phenyl-2-amino-propan-1-ol (rac)-syn-102 [S2.4; E1].

n-BuLi (58.60 ml, 2.5M in hexanes, 0.147 mol) was slowly added to 1-phenyl-2-amino-propan-1-ol HCl salt (rac)-syn-101 (25 g, 0.133 mol) in THF (250 ml) at -78°C. The resulting mixture was stirred half an hour. The reaction was quenched with water (100 ml), the organic layer was extracted with dichloromethane (3 × 250 ml), washed with water (100 ml), dried over MgSO₄ and evaporated under reduced pressure. To give the crude product 1-phenyl-2-amino-propan-1-ol (rac)-syn-102 (15.3 g, 76%); δH (400 MHz; CDCl₃) 7.29-7.25 (5H, m, 5 × CH; Ph), 4.54 (1H, d, J 4.8, CHO), 3.21 (1H, qd, J 6.4 and 4.8, CHNH₂), 1.74 (3H, br s, NH₂ and OH) and 0.98 (3H, d, J 6.4, CH₃); δC (100 MHz; CDCl₃) 141.3 (i-C; Ph), 128.2, 127.5 and 126.5 (5 × CH; Ph), 51.9 (CHO) and 18.2 (CH₃).
Synthesis of 1-phenyl-2-amino-N-ethylcarbonate-propan-1-ol (rac)-syn-103 [S2.4; E2].

Ethyl chloroformate (4.35 ml, 45.56 mmol) was added to a mixture of 1-phenyl-2-amino-propan-1-ol (rac)-syn-102 (6.88 g, 45.56 mmol) and NEt₃ (6.20 ml, 45.56 mmol) in dichloromethane (60 ml) at 0°C. The resulting mixture was stirred over night. The reaction was quenched with water (50 ml), the organic layer was extracted with dichloromethane (3 × 50 ml), washed with water (50 ml), dried over MgSO₄ and evaporated under reduced pressure. To give crude product 1-phenyl-2-amino-propan-1-ol (rac)-syn-103 (9.81 g, 97%); δ_H (400 MHz; CDCl₃) 7.41-7.26 (5H, m, 5 × CH; Ph), 4.93-4.81 (2H, m, CHO and CHNH), 4.14 (2H, q, J 7.2, CH₂CH₃), 4.04 (1H, br s, NH or OH), 2.95 (1H, br s, NH or OH), 1.26 (3H, t, J 7.2, CH₂CH₃) and 1.00 (3H, d, J 7.0, CH₃); δ_C (100 MHz; CDCl₃) 156.8 (C=O), 140.7 (i-C; Ph), 128.2, 127.5 and 126.2 (5 × CH; Ph), 61.0 (CHNH), 52.3 (CHNH), 52.2 (CH₂) 14.6 and 14.5 (2 × CH₃).

Synthesis of 4-methyl-5-phenyl-oxazolidin-2-one (rac)-syn-104 [S2.4; E3].

A mixture of 1-phenyl-2-aminoacetate-propan-1-ol (rac)-syn-103 (9.81 g, 43.99 mmol) and potassium tert-butoxide (5.43 g, 48.39 mmol) in THF (100 ml) was stirred at 0°C for 15 minutes. The reaction was quenched with water (25 ml), the organic layer was extracted with dichloromethane (3 × 50 ml), washed with water (50 ml), dried over MgSO₄ and evaporated under reduced pressure. To give 4-methyl-5-phenyl-oxazolidin-2-one (rac)-syn-104 (7.17 g, 96%) as an white solid mp 137-140 °C; ν_max (CHCl₃)/cm⁻¹ 1760 (C=O); δ_H (400 MHz; CDCl₃) 7.41-7.26 (5H, m, 5 × CH; Ph), 5.70 (1H, d, J 7.9, CHO), 5.28 (1H, br s, NH), 4.18 (1H, dq, J 7.9 and 6.6, CHNH) and 0.79 (3H, d, J 6.6, CH₃); δ_C (100 MHz; CDCl₃) 159.5 (C=S), 134.9 (i-C; Ph), 128.5, 128.4 and 125.9 (5 × CH; Ph), 81.0 (CHO), 52.4 (CHNH) and 17.5 (CH₃).

Synthesis of 2-phenyl-2-amino-N-ethylcarbonate-ethan-1-ol (rac)-105 [S2.5; E1].

In the same way as S2.4; E2, ethyl chloroformate (1.57 ml, 16.4 mmol), 2-phenyl-2-amino-ethan-1-ol (rac)-99 (2.25 g, 16.4 mmol) and NEt₃ (2.24 ml, 16.4 mmol) in dichloromethane (20 ml). Gave the crude product 2-phenyl-2-aminoacetate-ethan-1-ol (3.38 g, 98%), which was used in S2.5; E2.

Synthesis of 4-phenyl-oxazolidin-2-one (rac)-94 [S2.5; E2].

In the same way as S2.4; E3, 2-phenyl-2-aminoacetate-ethan-1-ol (rac)-105 (3.38 g, 16.17 mmol) and potassium tert-butoxide (2.00 g, 17.79 mmol) in THF (10 ml).
Gave 4-phenyl-oxazolidin-2-one \((rac)\text{-syn-94}\) (2.51 g, 95%) as a white solid mp 135-137°C; \(\nu_{\text{max}}\) (CHCl\(_3\))/cm\(^{-1}\) 3276 (NH) and 1775 (C=O); \(\delta_H\) (400 MHz; CDCl\(_3\)) 7.44-7.18 (5H, m, 5 \times CH; Ph), 6.53 (1H, br s, NH), 4.94 (1H, dd, \(J\ 8.6\) and 7.0, CHPh), 4.70 (1H, d, \(J\ 8.6\), \(CH_A\)H\(_B\)O) and 4.14 (1H, dd, \(J\ 8.6\) and 7.0, \(CH_A\)H\(_B\)O); \(\delta_C\) (100 MHz; CDCl\(_3\)) 160.1 (C=O), 139.6 (\(\text{i-C}\); Ph), 129.2,\(^2\) 128.8\(^1\) and 127.2\(^2\) (5 \times CH; Ph), 72.5 (CHPh) and 56.4 (CH\(_2\)O); (Found MH\(^+\), 164.0720; C\(_9\)H\(_{10}\)NO\(_2\) requires 164.0712).

**Synthesis of 4-phenyl-oxazolidin-2-one \((rac)\text{-94}\) using diethyl carbonate [S2.6; E3].**

A mixture of 2-phenyl-2-amino-ethanol-1-ol \((rac)\text{-syn-99}\) (6.87 g, 50.15 mmol), K\(_2\)CO\(_3\) (0.69 g, 5.01 mmol) and diethyl carbonate (13.02 g, 110.32 mmol) in toluene (100 ml) was refluxed over night. The toluene, excess diethyl carbonate and ethanol were removed by distillation. The organic layer was extracted with dichloromethane (3 \times 50 ml), washed brine (50 ml), dried over MgSO\(_4\) and evaporated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (1:1 → 0:1) to give 4-phenyl-oxazolidin-2-one \((rac)\text{-94}\) (4.38 g, 54%), which was spectroscopically identical to that obtained elsewhere.

**Synthesis of 4-methyl-5-phenyl-oxazolidin-2-thione \((R,S)\text{-syn-106}\) [S2.7].**

A mixture of 1-phenyl-2-amino-propan-1-ol \((R,S)\text{-syn-102}\) (2.051 g, 13.56 mmol) and carbon disulphide (1.22 ml, 20.34 mmol) in Na\(_2\)CO\(_3\)(aq) (1M, 100 ml) was refluxed for 15 minutes, allowed to cool to room temperature. The organic layer was extracted with dichloromethane (3 \times 50 ml), washed with water (50 ml), dried over MgSO\(_4\) and evaporated under reduced pressure. Gave 4-methyl-5-phenyl-oxazolidin-2-thione \((R,S)\text{-syn-106}\) (1.572 g, 60%) as an oil; \([\alpha]_D^{20}\) = +177.4 (c 5.4, CHCl\(_3\)); \(\nu_{\text{max}}\) (CHCl\(_3\))/cm\(^{-1}\) 1217 (C=S); \(\delta_H\) (400 MHz; CDCl\(_3\)) 7.70 (1H, br s, NH), 7.34-7.25 (3H, m, 3 \times CH; Ph), 7.20-7.16 (2H, m, 2 \times CH; Ph), 5.84 (1H, d, \(J\ 8.8\), CHO), 4.32 (1H, dq, \(J\ 8.8\) and 6.6, CHNH) and 0.77 (3H, d, J 6.6, CH\(_3\)); \(\delta_C\) (100 MHz; CDCl\(_3\)) 189.2 (C=S), 133.5 (\(\text{i-C}\); Ph), 128.9\(^1\) 128.6\(^2\) and 126.1\(^2\) (5 \times CH; Ph), 86.6 (CHO), 55.9 (CHNH) and 16.6 (CH\(_3\)); (Found MH\(^+\), 194.0634; C\(_{10}\)H\(_{12}\)ONS requires 194.0634).

**Synthesis of 4-benzyloxazolidin-2-thione \((S)\text{-107}\) [S2.8].**

In the same way as S2.7, 3-phenyl-2-amino-propan-1-ol \((S)\text{-100}\) (9.41 g, 0.062 mol) and carbon disulphide (5.62 ml, 0.093 mol) in Na\(_2\)CO\(_3\)(aq) (1M, 120 ml). Gave 4-benzyloxazolidin-2-thione \((S)\text{-107}\) (6.19 g, 51%) as an oil; \([\alpha]_D^{20}\) = -85.7 (c 2.8, CHCl\(_3\));
\[ R = C - C - \text{phenyloxazolidin} \]

\[ S \]

\[ \delta \text{C (100 MHz; CDCl}_3) 189.6 (\text{C=S}), 135.1 (\text{i-C; Ph}), 129.2, 128.9^2 \text{ and } 127.5^1 (5 \times \text{CH; Ph}), 74.8 (\text{CH}_2O), 57.8 (\text{CHNH}) \text{ and } 40.5 (\text{CH}_2\text{Ph}); \text{(Found M}^+, 193.0553; C_{10}H_{11}ONS \text{ requires 193.0556).}

**Synthesis of 4-isopropylxazolidin-2-thione (R)-109 [S2.9].**

In the same way as S2.7, 3-methyl-2-amino-butanol-1-ol (R)-108 (3.89 g, 0.038 mol) and carbon disulphide (3.40 ml, 0.057 mol) in Na$_2$CO$_3$(aq) (1M, 100 ml). Gave 4-isopropylxazolidin-2-thione (R)-109 (1.492 g, 27%) as an oil; [\( \alpha \)]$_D^{20}$ = +34.1 (c 3.8, CHCl$_3$); \( \nu_{\text{max}} \text{(CHCl}_3) \text{cm}^{-1} 1216 (\text{C=S}); \delta_H \text{(400 MHz; CDCl}_3) 3.63 (1H, br s, NH), 4.66 (1H, t, J 9.1, CH$_{3}H_{2}O$), 4.35 (1H, dd, J 9.1 and 6.7, CH$_{3}H_{2}O$), 3.81 (1H, dt, J 9.1 and 6.7, CHNH), 1.85-1.74 (1H, m, CH$_{3}$CHCH$_3$), 0.95 (3H, d, J 6.9 CH$_{3}$CHCH$_3$) and 0.90 (3H, d, J 6.9 CH$_{3}$CHCH$_3$); \( \delta \text{C (100 MHz; CDCl}_3) 189.7 (\text{C=S}), 73.5 (\text{CH}_2O), 62.4 (\text{CHNH}), 32.1 (\text{CH}_3\text{CHCH}_3), 18.0 (\text{CH}_3\text{CHCH}_3) \text{ and } 17.8 (\text{CH}_3\text{CHCH}_3); \text{(Found M}^+, 146.0634; C_{9}H_{12}ONS \text{ requires 146.0634).}

**Synthesis of 4-phenylxazolidin-2-thione (rac)-110 [S2.10; E2].**

In the same way as S2.7, 2-phenyl-2-amino-ethanol-1-ol (rac)-99 (6.66 g, 0.049 mol) and carbon disulphide (4.39 ml, 0.073 mol) in Na$_2$CO$_3$(aq) (1M, 150 ml). Gave 4-phenylxazolidin-2-thione (rac)-110 (5.719 g, 66%) as an white powder mp 158-162°C; \( \nu_{\text{max}} \text{(CHCl}_3) \text{cm}^{-1} 1219 (\text{C=S}); \delta_H \text{(400 MHz; CDCl}_3) 8.17 (1H, s, NH), 7.44-7.36 (3H, m, 3 \times \text{CH; Ph}), 7.30 (2H, dd, J 7.6 and 1.5, 2 \times \text{CH; Ph}), 5.08 (1H, dd, J 9.2 and 6.8, CHNH), 4.99 (1H, t, J 9.2, CH$_{3}H_{2}O$) \text{ and } 4.48 (1H, dd, J 9.2 and 6.8, CH$_{3}H_{2}O$); \( \delta \text{C (100 MHz; CDCl}_3) 189.7 (\text{C=S}), 137.7 (\text{i-C; Ph}), 129.3, 129.1^2 \text{ and } 126.1^1 (5 \times \text{CH; Ph}), 77.5 (\text{CH}_2O) \text{ and } 60.1 (\text{CHNH}); \text{(Found M}^+, 180.0481; C_{9}H_{10}NOS \text{ requires 180.0478).}

**Synthesis of 4-phenylxazolidin-2-thione (S)-110 [S2.10; E2].**

In the same way as S2.7, 2-phenyl-2-amino-ethanol-1-ol (S)-99 (10.52 g, 0.077 mol) and carbon disulphide (6.93 ml, 0.12 mol) in Na$_2$CO$_3$(aq) (1M, 150 ml). Gave 4-phenylxazolidin-2-thione (S)-110 (7.3 g, 53%) as an yellow solid mp 96-98 °C; [\( \alpha \)]$_D^{20}$ = +56.0 (c 4.2, CHCl$_3$), which was spectroscopically identical to that obtained elsewhere.
Synthesis of 4-phenyloxazolidin-2-thione (R)-110 [S2.10; E3].

In the same way as S2.7, 2-phenyl-2-amino-ethan-1-ol (R)-99 (4.25 g, 0.031 mol) and carbon disulphide (2.80 ml, 0.047 mol) in Na₂CO₃ (aq) (1M, 30 ml). Gave 4-phenyloxazolidin-2-thione (R)-110 (2.31 g, 42%) as an yellow solid mp 188-190°C; [α]ᵦ = -19.0 (c 0.1, ethanol, note poor solubility), which was spectroscopically identical to that obtained elsewhere.

Synthesis of pentafluorophenyl-2-phenylpropionate (rac)-95 [T2.1; E1]

DCC (6.05 g, 0.029 mol) was added to 2-phenylpropionic acid (rac)-111 (4 g, 0.027 mol) in dichloromethane (50 ml) followed by pentafluorophenol (4.90 g, 0.027 mol) in dichloromethane (50 ml). The resulting mixture was stirred over night. Then filtered to remove DCU, the organic layer was extracted with dichloromethane (3 × 50 ml), washed with water (50 ml), dried over MgSO₄ and evaporated under reduced pressure. The crude mixture was purified by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / dichloromethane (1:1) to give pentafluorophenyl-2-phenylpropionate (rac)-95 (7.743 g, 92%) as a white solid mp 27-28°C; Rᵢ [light petroleum spirit (bp 40-60°C) / dichloromethane (1:1)] 0.79; νmax (CHCl₃)/cm⁻¹ 1784 (C=O); δH (400 MHz; CDCl₃) 7.41-7.28 (5H, m, 5 × CH; Ph), 4.07 (1H, q, 7.2, CH) and 1.64 (3H, d, J 7.2, CH₃CH); δC (100 MHz; CDCl₃) 170.6 (C=O), 141.1 (142.40 and 139.90, 2C, ddt, ¹J_C,F 251.3 Hz, ²J_C,F 12.2 Hz and ³J_C,F 3.8 Hz, 2 × CF; Ar), 139.4 (140.70 and 138.18, 1C, dtt, ¹J_C,F 253.2 Hz, ²J_C,F 13.4 Hz and ³J_C,F 4.2 Hz, CF; Ar), 138.7 (i-C; Ph), 137.8 (139.05 and 136.58, 2C, dtdd, ¹J_C,F 249.1 Hz, ²J_C,F 14.5 Hz, ³J_C,F 5.7 Hz, ⁴J_C,F 3.1 Hz, 2 × CF; Ar), 128.9, ²127.8¹ and 127.5² (5 × CH; Ph), 125.2 (1C, tdt, ²J_C,F 14.2 Hz, ³J_C,F 4.2 Hz, ⁴J_C,F 2.0 Hz, i-CO; Ar), 45.1 (CH) and 18.5 (CH₃); δF (378 MHz; CDCl₃) -152.6 (2F, d, ³J_F,F 20.9, F_ortho), -157.9 (1F, t, ³J_F,F 20.9, F_para) and -162.3 (2F, t, ³J_F,F 20.9, F_meta); (Found M⁺, 316.0514; C₁₅H₁₀F₅O₂ requires 316.0517).

Synthesis of pentafluorophenyl-2-(4-methyl-phenyl)-propionate (rac)-113 [T2.1; E2]

In the same way as T2.1; E1, DCC (1.757 g, 8.51 mmol), 2-(4-methyl-phenyl)propionic acid (rac)-112 (1.271 g, 7.74 mmol) and pentafluorophenol (1.425 g, 7.74 mmol) in dichloromethane (25 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) pentafluorophenyl-2-(4-methyl-phenyl)-propionate (rac)-113 (2.165 g, 85%)
as an oil; $R_F$ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.78; $\nu_{\text{max}}$ (CHCl$_3$)/cm$^{-1}$ 1785 (C=O); $\delta_H$ (400 MHz; CDCl$_3$) 7.24 (2H, d, $J$ 8.2, 2 × CH; Ar), 7.18 (2H, d, J 8.2, 2 × CH; Ar), 4.03 (1H, q, 7.2, CH), 2.34 (3H, s, CH$_3$Ar) and 1.62 (3H, d, J 7.2, CH$_2$CH); $\delta_C$ (100 MHz; CDCl$_3$) 170.6 (C=O), 141.1 (142.51 and 139.89, 2C, ddt, $^1J_{C,F}$ 251.6 Hz, $^2J_{C,F}$ 11.9 Hz and $^3J_{C,F}$ 4.6 Hz, 2 × CF; Ar), 139.4 (140.63 and 138.12, 1C, dtt, $^1J_{C,F}$ 252.8 Hz, $^2J_{C,F}$ 13.4 Hz and $^3J_{C,F}$ 3.8 Hz, CF; Ar), 137.8 (139.07 and 136.56, 2C, dttdd, $^1J_{C,F}$ 252.8 Hz, $^2J_{C,F}$ 12.1 Hz, $^3J_{C,F}$ 5.3 Hz and $^4J_{C,F}$ 3.1 Hz, 2 × CF; Ar), 137.4 and 135.8 (2 × i-C; Ar), 129.5 and 127.2 (4 × CH; Ar), 125.2 (1C, tdt, $^2J_{C,F}$ 14.3 Hz, $^4J_{C,F}$ 4.6 Hz and $^3J_{C,F}$ 2.3 Hz, i-CO; Ar), 44.6 (CH), 20.8 (CH$_3$Ar) and 18.4 (CH$_3$); $\delta_F$ (378 MHz; CDCl$_3$) -152.6 (2F, d, $^3J_{F,F}$ 18.5, F$_{ortho}$), -158.0 (1F, t, $^3J_{F,F}$ 20.8, F$_{para}$) and -162.4 (2F, dd, $^3J_{F,F}$ 20.8 and 18.5, F$_{meta}$); (Found M$^+$, 330.0671; C$_{16}$H$_{11}$F$_5$O$_2$ requires 330.0674).

**Synthesis of pentafluorophenyl-2-(4-isobutyl-phenyl)-propionate (rac)-115 [T2.1; E3]**

In the same way as T2.1; E1, DCC (2.86 g, 13.87 mmol), 2-(4-isobutyl-phenyl)-propionic acid (rac)-114 (2.60 g, 12.60 mmol) and pentafluorophenol (2.32 g, 12.60 mmol) in dichloromethane (30 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) pentafluorophenyl-2-(4-isobutyl-phenyl)-propionate (rac)-115 (4.23 g, 90%) as a white solid mp 48-49°C; $R_F$ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.85; $\nu_{\text{max}}$ (CHCl$_3$)/cm$^{-1}$ 1782 (C=O); $\delta_H$ (400 MHz; CDCl$_3$) 7.26 (2H, dt, $J$ 8.2 and 2.2, 2 × CH; Ar), 7.14 (2H, dt, J 8.2 and 2.2, 2 × CH; Ar), 4.04 (1H, q, 7.2, CHCO), 2.46 (2H, d, J 7.2, CH$_2$Ar), 1.92-1.80 (1H, m CH$_2$CHCH$_3$), 1.62 (3H, d, J 7.2 CH$_3$CHCO), 0.99 (3H, d, J 6.7, CH$_3$CHCH$_3$) and 0.88 (3H, d, J 6.7, CH$_3$CHCH$_3$); $\delta_C$ (100 MHz; CDCl$_3$) 170.3 (C=O), 140.8 (i-C; Ar), 141.2 (142.92 and 139.42, 2C, dtt, $^1J_{C,F}$ 251.3 Hz, $^2J_{C,F}$ 11.9 Hz and $^3J_{C,F}$ 4.2 Hz, 2 × CF; Ar), 138.9 (140.18 and 137.66, 1C, dtt, $^1J_{C,F}$ 253.2 Hz, $^2J_{C,F}$ 13.8 Hz and $^3J_{C,F}$ 3.8 Hz, CF; Ar), 137.3 (138.61 and 136.08, 2C, dttdd, $^1J_{C,F}$ 254.7 Hz, $^2J_{C,F}$ 14.5 Hz, $^3J_{C,F}$ 5.3 Hz and $^4J_{C,F}$ 3.0 Hz, 2 × CF; Ar), 135.5 (i-C; Ar), 129.1 and 126.7 (4 × CH; Ar), 124.7 (1C, tdt, $^2J_{C,F}$ 14.2 Hz, $^4J_{C,F}$ 4.6 Hz and $^3J_{C,F}$ 2.3 Hz, i-CO; Ar), 44.5 (CH$_2$Ar), 44.4 (CHCO), 29.7 (CH$_3$CHCH$_3$), 21.9 (CH$_3$CHCH$_3$) and 18.0 (CH$_3$CHCO); $\delta_F$ (378 MHz; CDCl$_3$) -152.6 (2F, d, $^3J_{F,F}$ 18.5, F$_{ortho}$), -158.2 (1F, t, $^3J_{F,F}$ 20.8, F$_{para}$) and -162.5 (2F, dd, $^3J_{F,F}$ 20.8 and 18.5, F$_{meta}$); (Found M$^+$, 372.1144; C$_{19}$H$_{17}$F$_3$O$_2$ requires 372.1143).
Synthesis of pentafluorophenyl-2-(4-chloro-phenyl)-propionate (rac)-117 [T2.1; E4]

In the same way as T2.1; E1, DCC (1.625 g, 7.88 mmol), 2-(4-chloro-phenyl)-propionic acid (rac)-116 (1.322 g, 7.16 mmol) and pentafluorophenol (1.318 g, 7.16 mmol) in dichloromethane (50 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) pentafluorophenyl-2-(4-chloro-phenyl)-propionate (rac)-117 (2.242 g, 89%) as an white solid mp 37-40 °C; Rf [light petroleum spirit (bp 40-60°C) / dichloromethane (1:1)] 0.87; ν_{max} (CHCl₃)/cm⁻¹ 1782 (C=O); δ_H (400 MHz; CDCl₃) 7.36 (2H, dt, J 8.8 and 2.2, 2 × CH; Ar), 7.30 (2H, dt, J 8.8 and 2.2, 2 × CH; Ar), 4.06 (1H, q, 7.2, CH) and 1.64 (3H, d, J 7.2, CH₂CH); δ_C (100 MHz; CDCl₃) 170.2 (C=O), 141.1 (142.30 and 139.82, 2C, ddt, ¹JC,F 251.3 Hz, ²JC,F 12.7 Hz and ³JC,F 4.6 Hz, 2 × CF; Ar), 139.5 (140.74 and 138.22, 1C, dtt, ¹JC,F 253.7 Hz, ²JC,F 13.8 Hz and ³JC,F 3.8 Hz, CF; Ar), 137.8 (139.08 and 136.55, 2C, dttdd, ¹JC,F 255.2 Hz, ²JC,F 12.3 Hz, ³JC,F 5.4 Hz and ⁴JC,F 2.3 Hz, 2 × CF; Ar), 137.1 and 133.8 (2 × i-C; Ar), 129.1² and 128.9² (4 × CH; Ar), 125.0 (1C, tdd, ²JC,F 15.3 Hz, ⁴JC,F 6.9 Hz and ³JC,F 3.1 Hz, i-CO; Ar), 44.4 (CH) and 18.5 (CH₃); δ_F (378 MHz; CDCl₃) -152.7 (2F, d, ¹J_F,F 16.2, F_{ortho}), -157.7 (1F, t, ²J_F,F 20.8, F_{para}) and -162.1 (2F, dd, ³J_F,F 20.8 and 16.2, F_{meta}); (Found M^{35}Cl⁺, 350.0124; C₁₅H₈ClF₃O₂ requires 350.0127).

Synthesis of pentafluorophenyl-2-phenylpropionate (S)-95 [T2.2; E1]

In the same way as T2.1; E1, DCC (0.261 g, 1.27 mmol), 2-phenylpropionic acid (S)-111 (0.173 g, 1.15 mmol) and pentafluorophenol (0.212 g, 1.15 mmol) in dichloromethane (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / dichloromethane (1:1) pentafluorophenyl-2-phenylpropionate (S)-95 (0.247 g, 68%) as an oil; [α]_D^{20} = +74.5 (c 4.9, CHCl₃), which was spectroscopically identical to that obtained elsewhere.

Synthesis of pentafluorophenyl-2-phenylbutanoate (S)-119 [T2.2; E2]

In the same way as T2.1; E1, DCC (0.464 g, 2.23 mmol), 2-phenylbutyric acid (S)-118 (0.307 g, 2.04 mmol) and pentafluorophenol (0.376 g, 2.04 mmol) in dichloromethane (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) pentafluorophenyl-2-phenylbutinate (S)-119 (0.506 g, 75%) as a oil; R_f [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.88; [α]_D^{20} = -77.4 (c 34.8, CHCl₃); ν_{max}
(CHCl₃)/cm⁻¹ 1700 (C=O); δH (400 MHz; CDCl₃) 7.41-7.27 (5H, m, 5 × CH; Ph), 3.83 (1H, t, 7.7, CH), 2.31-2.18 (1H, m, CH₂H₈CH), 2.01-1.98 (1H, m, CH₂H₈CH), and 1.01 (3H, t, J 7.5, CH₃CH₂CH); δC (100 MHz; CDCl₃) 170.1 (C=O), 141.2 (142.43 and 139.93, 2C, ddt, 1J_C,F 251.3 Hz, 2J_C,F 11.9 Hz, 3J_C,F 3.4 Hz and 4J_C,F 3.4 Hz, 2 × CF; Ar), 139.5 (140.72 and 138.24, 1C, dtt, 1J_C,F 252.8 Hz, 2J_C,F 13.9 Hz and 3J_C,F 3.8 Hz, CF; Ar), 137.9 (139.14 and 136.60, 2C, dttdd, 1J_C,F 254.3 Hz, 2J_C,F 14.2 Hz, 3J_C,F 4.9 Hz and 4J_C,F 2.6 Hz, 2 × CF; Ar), 137.3 (i-C; Ph), 128.9, 127.9 and 127.8 (5 × CH; Ph), 125.2 (1C, tdt, 2J_C,F 14.2 Hz, 4J_C,F 4.4 Hz, 3J_C,F 2.2 Hz, i-CO; Ar), 52.8 (CH), 26.7 (CH₂) and 11.9 (CH₃); δF (378 MHz; CDCl₃) -152.4 (2F, d, J_F,F 17.1, Fortho, -157.9 (1F, t, J_F,F 21.9, Fpara) and -162.3 (2F, dd, J_F,F 21.9 and 17.1, Fmeta); (Found M⁺, 330.0677; C₁₆H₁₁F₃O₂ requires 330.0674).

**Synthesis of pentafluorophenyl-2-(4-chloro-phenyl)-propionate (S)-117 [T2.2; E3]**

In the same way as T2.1; E1, DCC (0.25 g, 1.19 mmol), 2-(4-chloro-phenyl)-propionic acid (S)-116 (0.20 g, 1.08 mmol) and pentafluorophenol (0.20 g, 1.08 mmol) in dichloromethane (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) pentafluorophenyl-2-(4-chloro-phenyl)-propionate (S)-117 (0.24 g, 63%) as a white solid mp 27-28 °C; [α]D20 = -93.6 (c 5.6, CHCl₃), which was spectroscopically identical to that obtained elsewhere.

**Synthesis of pentafluorophenyl-2-(4-isobutyl-phenyl)-propionate (S)-115 [T2.2; E4]**

In the same way as T2.1; E1, DCC (0.762 g, 3.70 mmol), 2-(4-isobutyl-phenyl)-propionic acid (S)-114 (0.693 g, 3.36 mmol) and pentafluorophenol (0.618 g, 3.36 mmol) in dichloromethane (20 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) pentafluorophenyl-2-(4-isobutyl-phenyl)-propionate (S)-115 (1.056 g, 84%) as an oil; [α]D20 = +80.0 (c 1.2, CHCl₃), which was spectroscopically identical to that obtained elsewhere.

**Synthesis of pentafluorophenyl-2-phenyl-2-methoxy-acetate (S)-121 [T2.2; E5].**

In the same way as T2.1; E1, DCC (0.56 g, 2.71 mmol), 2-phenyl-2-methoxy-acetic acid (S)-120 (0.41 g, 2.46 mmol) and pentafluorophenol (0.45 g, 2.46 mmol) in dichloromethane (15 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1)
pentafluorophenyl-2-phenyl-2-methoxy-acetate (S)-121 (0.64 g, 78%) as a oil; \( R_F \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.64; \( [\alpha]_D^20 = +67.8 \) (c 12.8, CHCl₃); \( \nu_{\max} \) (CHCl₃)/cm⁻¹ 1772 (C=O); \( \delta_H \) (400 MHz; CDCl₃) 7.55-7.50 (2H, m, 2 × CH; Ph), 7.46-7.39 (3H, m, 2 × CH; Ph), 5.12 (1H, s, CH) and 3.53 (3H, s, CH₃); \( \delta_C \) (100 MHz; CDCl₃) 170.5 (C=O), 133.3 (134.54 and 132.12, 2C, dm, \( ^1J_{\text{CF}} \) 243.7 Hz, 2 × CF; Ar), 133.2 (134.46 and 131.99, 2C, dm, \( ^1J_{\text{CF}} \) 248.3 Hz, 2 × CF; Ar), 130.4 (i-C; Ph), 130.2 (131.45 and 129.00, 2C, dtt, \( ^1J_{\text{CF}} \) 246.0 Hz, \( ^2J_{\text{CF}} \) 13.8 Hz and \( ^3J_{\text{CF}} \) 3.8 Hz, 2 × CF; Ar), 126.8 (1C, tdt, \( ^2J_{\text{CF}} \) 12.3 Hz, \( ^4J_{\text{CF}} \) 3.8 Hz, \( ^3J_{\text{CF}} \) 2.3 Hz, i-CO; Ar), 124.4,\(^124.1\)² and 122.6² (5 × CH; Ph), 77.3 (CH) and 52.5 (CH₃); \( \delta_F \) (378 MHz; CDCl₃) -162.9 (2F, dd, \( ^3J_{\text{FF}} \) 20.8 and 4.6, F\(_{\text{ortho}}\)), -164.3 (1F, t, \( ^3J_{\text{FF}} \) 20.8, F\(_{\text{para}}\)) and -169.3 (2F, tt, \( ^3J_{\text{FF}} \) 20.8 and 4.6, F\(_{\text{meta}}\)).

**Synthesis of pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propionate (S)-123 [T2.2; E6].**

In the same way as T2.2; E1, DCC (0.48 g, 2.34 mmol), 2-phenyl-2-(6-methoxy-2-naphthyl)-propanic acid (S)-122 (0.49 g, 2.12 mmol) and pentafluorophenol (0.39 g, 2.12 mmol) in dichloromethane (15 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propionate (S)-123 (0.58 g, 69%) as a white powder mp 78-80°C; \( R_F \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.62; \( [\alpha]_D^20 = +93.6 \) (c 5.6, CHCl₃); \( \nu_{\max} \) (CHCl₃)/cm⁻¹ 1781 (C=O); \( \delta_H \) (400 MHz; CDCl₃) 7.76-7.13 (6H, m, 6 × CH; Ar), 4.38 (1H, q, \( ^J_{\text{FH}} \) 7.2, CH), 3.91 (3H, s, CH₃O) and 1.71 (3H, d, \( ^J_{\text{FH}} \) 7.2 CHCH\(_3\)); \( \delta_C \) (100 MHz; CDCl₃) 170.7 (C=O), 157.9 (i-C; Ar), 141.0 (142.32 and 139.82, 2C, dtt, \( ^1J_{\text{CF}} \) 249.8 Hz, \( ^2J_{\text{CF}} \) 12.2 Hz and \( ^3J_{\text{CF}} \) 4.6 Hz, 2 × CF; Ar), 139.3 (140.63 and 138.11, 1C, dtt, \( ^1J_{\text{CF}} \) 252.1 Hz, \( ^2J_{\text{CF}} \) 13.0 Hz and \( ^3J_{\text{CF}} \) 4.5 Hz, CF; Ar), 137.8 (139.04 and 136.54, 2C, dtt, \( ^1J_{\text{CF}} \) 250.6 Hz, \( ^2J_{\text{CF}} \) 13.8 Hz, \( ^3J_{\text{CF}} \) 5.3 Hz and \( ^4J_{\text{CF}} \) 3.0 Hz, 2 × CF; Ar), 133.9, 133.7 and 128.9 (i-C; Ph); 129.3, 127.5, 126.2, 125.7, 119.3 and 105.6 (6 × CH; Ar), 125.2 (1C, m, i-CO; Ar), 55.3 (CH₃O), 45.9 (CH) and 18.5 (CHCH\(_3\)); \( \delta_F \) (378 MHz; CDCl₃) -152.5 (2F, d, \( ^3J_{\text{FF}} \) 17.0, F\(_{\text{ortho}}\)), -157.9 (1F, t, \( ^3J_{\text{FF}} \) 21.6, F\(_{\text{para}}\)) and -162.3 (2F, dd, \( ^3J_{\text{FF}} \) 21.6 and 17.0, F\(_{\text{meta}}\)). (Found M⁺, 396.0783; C\(_{20}\)H\(_{13}\)F\(_3\)O\(_3\) requires 396.0779).

**Synthesis of pentafluorophenyl-2-phenylproionate (R)-95 [T2.3; E1].**

In the same way as T2.1; E1, DCC (0.290 g, 1.41 mmol), 2-phenylpropionic acid (R)-111 (0.192 g, 1.28 mmol) and pentafluorophenol (0.235 g, 1.28 mmol) in
dichloromethane (20 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / dichloromethane (1:1) pentafluorophenyl-2-phenylpropionate \( (S) \)-95 \( (0.247 \text{ g, 68%}) \) as an oil; \( [\alpha]_{D}^{20} = -75.0 \) \( (c \ 3.3, \text{CHCl}_3) \), which was spectroscopically identical to that obtained elsewhere.

**Synthesis of pentafluorophenyl-2-phenylbutanoate \( (R) \)-119 [T2.3; E2]**

In the same way as T2.1; E1, DCC \( (2.892 \text{ g, 0.014 mol}) \), 2-phenylbutyric acid \( (R) \)-118 \( (1.914 \text{ g, 0.012 mol}) \) and pentafluorophenol \( (2.346 \text{ g, 0.013 mol}) \) in dichloromethane (20 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) pentafluorophenyl-2-phenylbutionate \( (R) \)-119 \( (3.499 \text{ g, 91%}) \) as a oil; \( [\alpha]_{D}^{20} = -59.6 \) \( (c \ 5.6, \text{CHCl}_3) \), which was spectroscopically identical to that obtained elsewhere.

**Attempted synthesis of pentafluorophenyl-2-phenyl-3-methyl-butanoate \( \text{(rac)} \)-126 [S2.11; E1]**

In the same way as T2.1; E1, DCC \( (1.12 \text{ g, 5.43 mmol}) \), 2-phenyl-3-methylbutyric acid \( \text{(rac)} \)-124 \( (0.88 \text{ g, 4.94 mmol}) \) and pentafluorophenol \( (0.91 \text{ g, 4.94 mmol}) \) in dichloromethane (20 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) di-(2-phenyl-3-methyl-butyl)-anhydride \( \text{(meso)} \)-syn and \( \text{(rac)} \)-(anti) \)-125 \( (0.41 \text{ g, 49%}) \), which were spectroscopically identical to that obtained elsewhere.

**Synthesis of pentafluorophenyl-2-phenyl-3-methyl-butanoate \( \text{(rac)} \)-126 [S2.11; E2]**

DCC \( (1.652 \text{ g, 8.01 mmol}) \) was added to pentafluorophenol \( (1.340 \text{ g, 7.28 mol}) \) in dichloromethane (10 ml) followed by slow addition over 2 hours of 2-phenyl-3-methyl-butyric acid \( \text{(rac)} \)-124 \( (1.3 \text{ g, 7.28 mol}) \) in dichloromethane (10 ml). The resulting mixture was stirred over night. Then filtered to remove DCU, the organic layer was extracted with dichloromethane \((3 \times 50 \text{ ml})\), washed with water \((50 \text{ ml})\), dried over MgSO\(_4\) and evaporated under reduced pressure. The crude mixture was purified by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) to give pentafluorophenyl-2-phenyl-3-methyl-butionate \( \text{(rac)} \)-126 \( (2.06 \text{ g, 82%}) \) as a white solid mp 45-48 °C; \( R_f \) [light petroleum spirit (bp 40-60°C) / diethyl ether (9:1)] \( 0.83; \nu_{\text{max}} \) (CHCl\(_3\))/cm\(^{-1}\) 1776 (C=O); \( \delta_{H} \) (400 MHz; CDCl\(_3\)) 7.39-7.30 (5H, m, 5 × CH; Ph), 3.53 (1H, d, \( J \ 10.5, \text{CHO} \)), 2.54-2.40 (1H, m, CHCHO), 1.78 (3H, d, \( J \ 6.4, \text{CH}_2\text{CHCH}_3 \)) and 0.81 (3H, d, \( J \ 6.8, \text{CH}_3\text{CHCH}_3 \)); \( \delta_{C} \) (100 MHz;
CDCl₃) 169.9 (C=O), 141.1 (142.37 and 139.88, 2C, ddt, ¹JC,F 251.4 Hz, ²JC,F 12.3 Hz and ³JC,F 3.8 Hz, 2 × CF; Ar), 139.4 (140.65 and 138.14, 1C, dtt, ¹JC,F 252.9 Hz, ²JC,F 13.8 Hz and ³JC,F 4.6 Hz, CF; Ar), 137.8 (139.05 and 136.58, 2C, dtd, ¹JC,F 249.1 Hz, ²JC,F 13.1 Hz, ³JC,F 5.4 Hz, ⁴JC,F 3.1 Hz, 2 × CF; Ar), 136.4 (i-C; Ph), 128.8, ² 128.5 and 127.9 (5 × CH; Ph), 125.1 (1C, dt, ²JC,F 14.6 Hz, ⁴JC,F 4.6 Hz, ³JC,F 2.3 Hz, i-CO; Ar), 121.9, F,F and 17.3, F,F and 145.3 (2 × CH; Ph), 129.0, ² 124.1, 1C, dtdd, ³JC,F 7.2, CO; Ar), 128.8, ² 127.5, 1C, ddt, ³JC,F 9.0, 1C; Ph); δF (378 MHz; CDCl₃) -152.3 (2F, d, ³J,F,F 17.3, F,ortho), -158.0 (1F, t, ³J,F,F 21.9, F,para) and -162.4 (2F, dd, ³J,F,F 21.9 and 17.3, F,meta); (Found M⁺, 344.0829; C₁₇H₁₃F₃O₂ requires 344.0830).

**Synthesis of pentafluorophenyl-2-phenyl-3-methyl-butanoate (S)-126 [S2.12]**

In the same way as S2.11; E2, DCC (90 mg, 0.43 mmol), pentafluorophenol (70 mg, 0.39 mmol) phenyl-3-methyl-butrylic acid (S)-124 (69 mg, 0.39 mmol) in dichloromethane (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) pentafluorophenyl-2-phenyl-3-methyl-butanoate (S)-126 (94 mg, 72%) as a yellow solid mp 50-52°C; [α]D = +47.0 (c 2.8, CHCl₃), which was spectroscopically identical to that obtained elsewhere.

**Synthesis of para-nitro-phenyl-2-phenylpropionate (rac)-127 [T2.4; E1]**

In the same way as T2.1; E1, DCC (0.378 g, 1.83 mmol), 2-phenylpropionic acid (rac)-111 (0.250 g, 1.66 mmol) and para-nitro-phenol (0.232 g, 1.66 mmol) in dichloromethane (20 ml). Gave after purification by filtration with hexane extraction para-nitro-phenyl-2-phenylpropionate (rac)-127 (0.429 g, 95%) as a yellow solid mp 46-50 °C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.54; νmax (CHCl₃)/cm⁻¹ 1761 (C=O); δH (400 MHz; CDCl₃) 8.22 (2H, dt, J 9.0 and 3.1, 2 × CH; Ar), 7.42-7.29 (5H, m, 5 × CH; Ph), 7.18 (2H, dt, J 9.0 and 3.1, 2 × CH; Ar), 3.99 (1H, d, J 7.2, CHO) and 1.63 (3H, d, J 7.2, CHCH₃); δC (100 MHz; CDCl₃) 172.1 (C=O, 155.5 and 145.3 (2 × i-C; Ar), 139.3 (i-C; Ph), 129.0, ² 127.8 and 127.5 (5 × CH; Ph), 125.4 and 122.3 (4 × CH; Ar), 45.7 (CHO) and 18.4 (CHCH₃); (Found M⁺, 271.0836; C₁₃H₁₁O₄N requires 271.0839).

**Synthesis of phenyl-2-phenylpropionate (rac)-128 [T2.4; E2]**

In the same way as T2.1; E1, DCC (0.378 g, 1.83 mmol), 2-phenylpropionic acid (rac)-111 (0.250 g, 1.66 mmol) and phenol (0.157 g, 1.66 mmol) in dichloromethane (20 ml). Gave after purification by flash column chromatography on
silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) phenyl-2-phenylpropionate (rac)-128 (0.228 g, 60%) as a clear oil; \( R_F \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.78; \( \nu_{\text{max}} \) (CHCl\(_3\))/cm\(^{-1}\) 1750 (C=O); \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.44-7.28 (7H, m, 7 × CH; Ph\(_A\) and Ph\(_B\)), 7.20 (1H, tt, J 7.5 and 1.7, CH; Ph\(_A\) or Ph\(_B\)), 7.00 (2H, tt, J 7.5 and 1.7, CH; Ph\(_A\) or Ph\(_B\)), 3.98 (1H, d, J 7.2, CHO) and 1.63 (3H, d, J 7.2, CHCH\(_3\)\)); \( \delta_C \) (100 MHz; CDCl\(_3\)) 173.0 (C=O), 150.8 and 140.1 (2 × i-C; Ph\(_A\) and Ph\(_B\)), 129.3, 128.8, 127.5, 127.3, 125.7 and 121.3 (10 × CH; Ph\(_A\) and Ph\(_B\)), 45.6 (CHO) and 18.5 (CHCH\(_3\)) (Found MNH\(_2^+\), 244.1333; C\(_{15}\)H\(_{18}\)O\(_2\)N requires 244.1322).

Synthesis of (4-nitro-2,6-di-methyl-phenyl)-2-phenylpropionate (rac)-129 [T2.4; E3]

In the same way as T2.1; E1, DCC (1.358 g, 6.58 mmol), 2-phenylpropionic acid (rac)-111 (0.898 g, 5.98 mmol) and 4-nitro-2,6-di-methyl-phenol (1.0 g, 5.98 mmol) in dichloromethane (25 ml). Gave back starting materials.

Synthesis of (4-nitro-2,6-di-methyl-phenyl)-2-phenylpropionate (rac)-129 using DMAP [T2.4; E3*]

In the same way as T2.1; E1, DCC (1.358 g, 6.58 mmol), 2-phenylpropionic acid (rac)-111 (0.896 g, 5.98 mmol), DMAP (0.152 g, 1.20 mmol) and 4-nitro-2,6-di-methyl-phenol (1.0 g, 5.98 mmol) in dichloromethane (25 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) (4-nitro-2,6-di-methyl-phenyl)-2-phenylpropionate (rac)-129 (0.892 g, 50%) as a white solid mp 68-71 °C; \( R_F \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.63; \( \nu_{\text{max}} \) (CHCl\(_3\))/cm\(^{-1}\) 1755 (C=O); \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.91 (2H, br s, 2 × CH; Ar), 7.46-7.31 (5H, m, 5 × CH; Ph), 4.06 (1H, q, J 7.2, CH), 2.00 (6H, br s, 2 × CH\(_3\)Ar) and 1.69 (3H, d, J 7.2, CHCH\(_3\)\)); \( \delta_C \) (100 MHz; CDCl\(_3\)) 171.4 (C=O), 152.9, 145.2, 139.1 and 132.3 (5 × i-C; Ph and Ar), 128.9, 127.8, 127.7 and 123.7 (7 × CH; Ph and Ar), 45.4 (CHO), 17.8 (CHCH\(_3\)) and 16.2 (2 × CH\(_3\)Ar); (Found MNH\(_2^+\), 317.1489; C\(_{17}\)H\(_{21}\)O\(_2\)N requires 317.1496).

Synthesis of pentafluorothiophenyl-2-phenylpropionate (rac)-130 [T2.4; E4]

In the same way as T2.1; E1, DCC (0.937 g, 4.54 mmol), 2-phenylpropionic acid (rac)-111 (0.620 g, 4.13 mmol) and pentafluorothiophenol (0.826 g, 4.13 mmol) in dichloromethane (50 ml). Gave after purification by flash column chromatography on
silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) pentafluorothiophenyl-2-phenylpropionate (rac)-130 (1.044 g, 76%) as a yellow oil; \( R_F \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.73; \( \nu_{\text{max}} \) (CHCl\(_3\))/cm\(^{-1} \) 1727 (C=O) and 1217 (CS); \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.42-7.31 (5H, m, 5 × CH; Ph), 4.03 (1H, q, J 7.2, CH) and 1.60 (3H, d, J 7.2, CHCH\(_3\)); \( \delta_C \) (100 MHz; CDCl\(_3\)) 194.5 (C=O), 146.9 (148.11 and 145.63, 2C, ddd, \( J_{C_F} \) 8 Hz, 2 × CF; Ar), 142.6 (143.91 and 141.34, 1C, dtt, \( J_{C_F} \) 262.9 Hz, \( J_{C_F} \) 13.8 Hz and \( J_{C_F} \) 5.4 Hz, CF; Ar), 138.2 (i-C; Ph), 137.7 (139.00 and 136.46, 2C, dttt, \( J_{C_F} \) 260.6 Hz, \( J_{C_F} \) 13.1 Hz, \( J_{C_F} \) 5.3 Hz and \( J_{C_F} \) 2.3 Hz, 2 × CF; Ar), 129.0\(^1\) and 128.2\(^2\) (5 × CH; Ph), 128.4 (1C, ttt, \( J_{C_F} \) 9.2 Hz, \( J_{C_F} \) 4.6 Hz, \( J_{C_F} \) 1.5 Hz, i-CO; Ar), 54.3 (CH) and 18.3 (CH\(_3\)); \( \delta_F \) (378 MHz; CDCl\(_3\)) -130.7 (2F, d, \( J_{F_F} \) 16.2, F\(_{ortho}\), -149.3 (1F, t, \( J_{F_F} \) 20.8, F\(_para\)) and -160.4 (2F, ddd, \( J_{F_F} \) 20.8 and 16.2, F\(_{meta}\)).

**Synthesis of para-nitro-phenyl-2-phenylpropionate (S)-127 [T2.5; E1]**

In the same way as T2.1; E1, DCC (0.227 g, 1.10 mmol), 2-phenylpropionic acid (S)-111 (0.150 g, 1.00 mmol) and para-nitro-phenol (0.140 g, 1.00 mmol) in dichloromethane (10 ml). Gave after purification by filtration with hexane extraction para-nitro-phenyl-2-phenylpropionate (S)-127 (0.145 g, 54%) as a yellow solid mp 62-64 °C; \([\alpha]_{D}^{20} = +98.12 \ (c \ 3.0, \ CHCl_3)\), which was spectroscopically identical to that obtained elsewhere.

**Synthesis of phenyl-2-phenylpropionate (S)-128 [T2.5; E2]**

In the same way as T2.1; E1, DCC (0.213 g, 1.03 mmol), 2-phenylpropionic acid (S)-111 (0.141 g, 0.94 mmol) and phenol (88 mg, 1.00 mmol) in dichloromethane (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) phenyl-2-phenylpropionate (S)-128 (0.111 g, 52%) as a clear oil; \([\alpha]_{D}^{20} = +76.5 \ (c \ 3.0, \ CHCl_3)\), which was spectroscopically identical to that obtained elsewhere.

**Synthesis of 2-phenylbutanyl chloride (rac)-131 [T2.6; E1]**

SOCl\(_2\) (10.87 ml, 91.36 mmol) was added to 2-phenylbutyric acid (rac)-118 (10 g, 60.91 mmol). The resulting mixture was refluxed for 1.5 hours. Gave after purification by distillation 2-phenylbutanyl chloride (rac)-131 (10.38 g, 93%) \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.40-7.23 (5H, m, 5 × CH; Ph), 3.88 (1H, t, J 7.5, CH), 2.27-2.15 (1H, m, CHCH\(_2\)CH\(_3\)), 1.92-1.80 (1H, m, CHCH\(_2\)CH\(_3\)) and 0.92 (3H, t, J 7.3, CH\(_3\)); \( \delta_C \)
(100 MHz; CDCl₃) 175.0 (C=O), 136.0 (i-C; Ph), 129.2, 128.4 and 128.3 (5 × CH; Ph), 65.2 (CH), 26.6 (CH₂) and 11.7 (CH₃).

**Synthesis of 2-phenyl-3-methyl-butanyl chloride (rac)-132 [T2.6; E2]**

In the same way as T2.6; E1, SOCl₂ (2.32 g, 19.53 mmol) and 2-phenyl-3-methyl-butyric acid (rac)-124 (2.32 g, 13.02 mmol). Gave after purification by distillation 2-phenyl-3-methyl-butanyl chloride (rac)-132 (0.58 g, 13%) δₗ (400 MHz; CDCl₃) 7.50-7.37 (5H, m, 5 × CH; Ph), 3.76 (1H, d, J 10.3, CHCO), 2.61-2.47 (1H, m, CH₃CH/CH₃), 1.24 (3H, d, J 6.6, CH₃CHCH₃) and 0.83 (3H, d, J 6.8, CH₃CHCH₃); δc (100 MHz; CDCl₃) 174.7 (C=O), 134.9 (i-C; Ph), 128.9, 128.8, 128.3 (5 × CH; Ph), 71.7 (CHCO), 32.0 (CH₂CHCH₃), 21.2 (CH₂CHCH₃) and 19.8 (CH₃CHCH₃).

**Synthesis of 2-(4-chloro-phenyl)-propionyl chloride (rac)-133 [T2.6; E3]**

In the same way as T2.6; E1, SOCl₂ (0.84 ml, 11.54 mmol) and 2-(4-chloro-phenyl)-propionic acid (rac)-116 (1.42 g, 7.69 mmol). Gave after removal of SOCl₂ by distillation 2-(4-chloro-phenyl)-propionyl chloride (rac)-133 (~1.56 g, ~100%) δₗ (400 MHz; CDCl₃) 7.36 (2H, dt, J 8.6 and 2.0, 2 × CH; Ar), 7.23 (2H, dt, J 8.6 and 2.0, 2 × CH; Ar), 4.10 (1H, q, J 7.0, CH) and 1.59 (3H, d, J 7.0, CH₃); δc (100 MHz; CDCl₃) 175.2 (C=O), 135.9 and 134.2 (2 × i-C; Ar), 129.3 (4 × CH; Ar), 56.7 (CH) and 18.9 (CH₃).

**Synthesis of 2-phenyl-2-methoxy-acetyl chloride (rac)-134 [T2.6; E4]**

In the same way as T2.6; E1, SOCl₂ (0.69 ml, 9.56 mmol) and 2-phenyl-2-methoxy-acetic acid (rac)-120 (1.059 g, 6.37 mmol). Gave after removal of SOCl₂ by distillation a mixture of 2-phenyl-2-methox acetyl chloride (rac)-134 (~0.77 g, ~66%) δₗ (400 MHz; CDCl₃) 7.58-7.32 (5H, m, 5 × CH; Ph), 5.00 (1H, s, CH) and 3.52 (3H, s, CH₃); δc (100 MHz; CDCl₃) 173.4 (C=O), 134.4 (i-C; Ph), 129.7, 129.0 and 127.8 (5 × CH; Ph), 89.9 (CH) and 58.0 (CH₃) and benzaldehyde (~0.22 g, ~33%) δₗ (400 MHz; CDCl₃) 9.96 (1H, s, CHO), 7.82 (5H, ddd, J 8.0, 2.2 and 1.4, 2 × CH; Ph), 7.57 (1H, tt, J 7.3 and 2.2, CH; Ph) and 7.46 (2H, ddd, J 8.0, 7.3 and 1.4, 2 × CH; Ph); δc (100 MHz; CDCl₃) 192.2 (C=O), 136.2 (i-C; Ph), 134.3, 129.5 and 128.8 (5 × CH; Ph).

**Synthesis of 2-phenyl-2-acetoxy-acetyl chloride (rac)-136 [T2.6; E5]**

In the same way as T2.6; E1, SOCl₂ (0.59 ml, 8.12 mmol) and 2-phenyl-2-acetoxy-acetic acid (rac)-135 (1.051 g, 5.41 mmol). Gave after removal of SOCl₂ by
distillation of 2-phenyl-2-acetoxy-acetyl chloride (rac)-136 (~1.15 g, ~100%) δ_H (400 MHz; CDCl_3) 7.52-7.29 (5H, m, 5 × CH; Ph), 6.09 (1H, s, CH) and 2.22 (3H, s, CH_3); δ_C (100 MHz; CDCl_3) 170.7 and 169.9 (2 × C=O), 133.1 (i-C; Ph), 130.2, 129.2 and 128.3 (5 × CH; Ph), 80.8 (CH) and 20.4 (CH_3).

**Synthesis of 2,4-di-chlorophenyl-2-(6-methoxy-2-naphthyl)-propionate (S)-137 [S2.13; E1].**

DCC (0.56 g, 2.69 mmol) was added to a solution of 2-(6-methoxy-2-naphthyl)-propionic acid (S)-122 (0.62 g, 2.69 mmol) in dichloromethane (10 ml) followed by 2,4-di-chlorophenol (0.44 g, 2.69 mmol) in dichloromethane (5 ml). The resulting mixture was stirred over night. The reaction was quenched with water (50 ml), the organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO_4 and evaporated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) to give 2,4-di-chlorophenyl-2-(6-methoxy-2-naphthyl)-propionate (S)-137 (0.67 g, 66%), as a white solid mp = 52-54°C; R_F [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.67; [α]_D^20 = +76.2 (c 6.8, CHCl_3); ν_max (CHCl_3)/cm⁻¹ 1780 (C=O); δ_H (400 MHz; CDCl_3) 7.78 (1H, d, J 1.8, CH; Ar), 7.74 (2H, t, J 8.1, 2 × CH; Ar), 7.50 (1 H, dd, J 8.6 and 1.8, CH; Ar), 7.40 (1 H, d, J 2.6, CH; Ar), 7.22-7.13 (3H, m, 3 × CH; Ar), 6.95 (1 H, d, J 8.6, CH; Ar), 4.15 (1H, q, J 7.2, CH), 3.93 (3H, s, CH_3O) and 1.73 (3H, d, J 7.2, CH_3CH); δ_C (100 MHz; CDCl_3) 172.0 (C=O), 157.7, 145.7, 134.7, 133.4, 131.8, 128.9 and 127.8 (7 × i-C; Ar_A and Ar_B), 130.0, 129.3, 127.8, 127.3, 126.3, 126.2, 124.4, 119.2 and 105.6 (9 × CH; Ar_A and Ar_B), 55.3 (CH_3O), 45.3 (CH) and 18.5 (CHCH_3); (Found MNH⁺ for 2 × Cl⁻, 392.0821 C_{20}H_{20}Cl_4O_3 requires 392.0820).

**Synthesis of ethyl-2-(6-methoxy-2-naphthyl)-propionate (rac)-138 [S2.13; E2].**

Sodium hydride (0.81 g, 60% dispersed on mineral oil, 20.39 mmol), was added to ethanol (40 ml) at 0°C, after 5 minuets 2,4-di-chlorophenyl-2-(6-methoxy-2-naphthyl)-propionate (S)-137 (5.1 g, 13.59 mmol) in THF (15 ml) was added. The resulting mixture was stirred over night. The reaction was quenched with water (50 ml), the organic layer was extracted with dichloromethane (3 × 50 ml), dried over MgSO_4 and evaporated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) to give ethyl-2-(6-methoxy-2-naphthyl)-propionate (rac)-138 (2.44 g, 70%),
as a white solid mp = 51-53°C; $R_f$ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.64; $v_{\text{max}}$ (CHCl$_3$)cm$^{-1}$ 1729 (C=O); $\delta_H$ (400 MHz; CDCl$_3$) 7.71 (2H, d, $J$ 8.5, CH; Ar), 7.68 (1 H, d, $J$ 1.7, CH; Ar), 7.42 (1 H, dd, $J$ 8.5 and 1.7, CH; Ar), 7.17-7.10 (2 H, m, 2 × CH; Ar), 4.21-4.07 (2H, m, CH), 3.91 (3H, s, CH$_3$O), 3.85 (1H, q, $J$ 7.2, CH), 1.58 (3H, d, $J$ 7.2, CH$_2$CH) and 1.21 (3H, t, $J$ 7.2, CH$_2$CH$_3$); $\delta_C$ (100 MHz; CDCl$_3$) 174.7 (C=O), 157.6, 135.8, 133.6 and 128.9 (4 × i-C; Ar), 129.2, 127.1 126.2 125.9, 118.9 and 105.5 (6 × CH; Ar), 60.7 (CH$_3$O), 55.2 (CH$_3$O), 45.4 (CH), 18.6 (CHCH$_3$) and 14.1 (CH$_3$CH$_2$); (Found MNH$_x$, 276.1595 C$_{16}$H$_{22}$O$_3$N requires 276.1594).

**Synthesis of 2-(6-methoxy-2-naphthyl)-propionic acid (rac)-122 [S2.13; E3].**

Sodium hydride (0.45 g, 60% dispersed on mineral oil, 11.15 mmol), was added to ethyl-2-(6-methoxy-2-naphthyl)-propionate (rac)-138 (2.4 g, 9.29 mmol) in THF/water (3:1, 40 ml). The resulting mixture was refluxed over night. The reaction was quenched with water (50 ml), the organic layer was extracted with dichloromethane (3 × 50 ml), dried over MgSO$_4$ and evaporated under reduced pressure. To return ethyl-2-(6-methoxy-2-naphthyl)-propionate (rac)-138 (0.12 g, 5%). The aqueous layer was acidified with HCl (3M, 20 ml), the organic layer was extracted with dichloromethane (3 × 50 ml), washed with water (50 ml), dried over MgSO$_4$ and evaporated under reduced pressure. Gave 2-(6-methoxy-2-naphthyl)-propionic acid (rac)-122 (1.98 g, 92%), as a white solid mp = 150-152°C; $R_f$ [diethyl ether] 0.44; $v_{\text{max}}$ (CHCl$_3$)cm$^{-1}$ 1710 (C=O); $\delta_H$ (400 MHz; CDCl$_3$) 7.73-7.68 (3H, m, 3 × CH; Ar), 7.41 (1 H, dd, $J$ 8.4 and 1.8, CH; Ar), 7.16-7.10 (2 H, m, 2 × CH; Ar), 3.91 (3H, s, CH$_3$O), 3.88 (1H, q, $J$ 7.0, CH) and 1.59 (3H, d, $J$ 7.0, CH$_2$CH); $\delta_C$ (100 MHz; CDCl$_3$) 180.2 (C=O), 157.9, 134.8, 133.8 and 128.9 (4 × i-C; Ar), 129.3, 127.2, 126.2, 126.1, 119.0 and 105.6 (6 × CH; Ar), 55.3 (CH$_3$O), 45.2 (CH) and 18.1 (CHCH$_3$).

**Synthesis of pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propionate (rac)-123 [S2.13; E4].**

In the same way as T2.1 E1, DCC (2.10 g, 10.18 mmol), 2-(6-methoxy-2-naphthalenyl)-propionic acid (rac)-122 (2.13 g, 9.25 mmol) and pentafluorophenol (1.70 g, 9.25 mmol) in dichloromethane (30 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propionate (rac)-123 (2.35 g, 65%), as a white solid mp = 51-53°C; which was spectroscopically identical to that obtained elsewhere.
MKR of active ester (rac)-95 using 4-phenyl-oxazolidin-2-one (rac)-94 with n-BuLi [T2; E1].

n-BuLi (5.40 ml, 2.5M in hexanes, 0.013 mol) was added to mixture of 4-phenyl-oxazolidin-2-one (rac)-94 (2 g, 0.012 mol) in THF (25 ml) at -78°C. After stirring for 1 hour pentafluorophenyl-2-phenyl-propionate (rac)-95 (3.88 g, 0.012 mol) in THF (5 ml) was added and the reaction stirred for a further 2 hours. The reaction mixture was quenched with water (50 ml), extracted with dichloromethane (3 × 50 ml) and dried over MgSO₄. To give a mixture of 3-(2-phenyl-propionyl)-4-phenyl-oxazolidin-2-one (rac)-syn and anti-96 (ratio 97 : 3), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) gave 3-(2-phenyl-propionyl)-4-phenyl-oxazolidin-2-one (rac)-anti-96 (70 mg, 2%), as a white solid mp 92-100°C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.40; ν max (CHCl₃)/cm⁻¹ 1780 and 1700 (2 × C=O); δH (400 MHz; CDCl₃) 7.39-7.26 (10H, m, 10 × CH; 2 × Ph), 5.32 (1H, dd, J 8.8 and 3.2, CHN), 5.11 (1H, q, J 7.2, CHCH₃), 4.55 (1H, t, J 8.8, CH₃H₄O), 4.21 (1H, dd, J 8.8 and 3.2, CH₃H₄O) and 1.40 (3H, d, J 7.2, CHCH₃); δC (100 MHz; CDCl₃) 174.1 and 152.9 (2 × C=O), 140.2 and 139.4 (2 × i-C; 2 × Ph), 129.3, 128.7, 128.6, 128.5, 128.3, 128.2, 127.3, 125.8 (10 × CH; Ph), 69.7 (CH₂O), 58.1 (CHN), 43.2 (PhCH), 19.4 (CH₃); (Found MH⁺, 296.1282; C₁₈H₁₈NO₃ requires 296.1287), and 3-(2-phenyl-propionyl)-4-phenyl-oxazolidin-2-one (rac)-syn-96 (2.32 g, 64%), as a white solid mp 132-134°C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.30; ν max (CHCl₃)/cm⁻¹ 1780 and 1705 (2 × C=O); δH (400 MHz; CDCl₃) 7.29-7.21 (10H, m, 10 × CH; 2 × Ph), 5.45 (1H, dd, J 9.0 and 5.1, CHN), 5.09 (1H, q, J 6.9, CHCH₃), 4.63 (1H, t, J 9.0, CH₃H₄O), 4.08 (1H, dd, J 9.0 and 5.1, CH₃H₄O) and 1.39 (3H, d, J 6.9, CHCH₃); δC (100 MHz; CDCl₃) 173.7 and 153.2 (2 × C=O), 139.9 and 138.3 (2 × i-C; 2 × Ph), 128.9, 128.7, 128.5, 128.2, 127.1 and 125.9 (10 × CH; Ph), 69.6 (CH₂O), 57.9 (CHN), 43.9 (PhCH) and 18.6 (CH₃); (Found MH⁺, 296.1286; C₁₈H₁₈NO₃ requires 296.1287).

MKR of active ester (rac)-95 using 4-phenyl-oxazolidin-2-one (rac)-94 with MeMgBr [T2; E2].

In the same way as T2; E, MeMgBr (0.41 ml, 3M in diethyl ether, 1.23 mmol), 4-phenyl-oxazolidin-2-one (rac)-94 (0.2 g, 1.23 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.39 g, 1.23 mmol) in THF (10 ml). Gave a mixture of 3-(2-phenylpropionly)-4-phenyl-oxazolidin-2-one (rac)-syn and anti-96 (ratio syn : anti 83
: 17), after purification gave 3-(2-phenylpropionyl)-4-phenyl-oxaolidin-2-one (rac)-anti-96 (20 mg, 5%) and 3-(2-phenylpropionyl)-4-phenyl-oxaolidin-2-one (rac)-syn-96 (0.13 g, 36%), which were spectroscopically identical to that obtained elsewhere.

MKR of 4-phenyl-oxaolidin-2-one (rac)-94 using active ester (rac)-95 at -78°C [T2.8; E1].
See T2.7; E1.

MKR of 4-phenyl-oxaolidin-2-one (rac)-94 using active ester (rac)-95 at -41°C [T2.8; E2].

In the same way as T2.7; E1 but at -41°C, n-BuLi (0.28 ml, 2.5M in hexanes, 0.70 mmol), 4-phenyl-oxaolidin-2-one (rac)-94 (0.103 g, 0.63 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave a mixture of 3-(2-phenylpropionyl)-4-phenyl-oxaolidin-2-one (rac)-syn and anti-96 (ratio syn : anti 98 : 2), after purification gave 3-(2-phenylpropionyl)-4-phenyl-oxaolidin-2-one (rac)-anti-96 (2 mg, 1%) and 3-(2-phenylpropionyl)-4-phenyl-oxaolidin-2-one (rac)-syn-96 (59 mg, 32%), which were spectroscopically identical to that obtained elsewhere.

MKR of 4-phenyl-oxaolidin-2-one (rac)-94 using active ester (rac)-95 at 0°C [T2.8; E3].

In the same way as T2.7; E1 but at 0°C, n-BuLi (0.28 ml, 2.5M in hexanes, 0.70 mmol), 4-phenyl-oxaolidin-2-one (rac)-94 (0.103 g, 0.63 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave a mixture of 3-(2-phenylpropionyl)-4-phenyl-oxaolidin-2-one (rac)-syn and anti-96 (ratio syn : anti 90 : 10), after purification gave 3-(2-phenylpropionyl)-4-phenyl-oxaolidin-2-one (rac)-anti-96 (5 mg, 3%) and 3-(2-phenylpropionyl)-4-phenyl-oxaolidin-2-one (rac)-syn-96 (44 mg, 24%), which were spectroscopically identical to that obtained elsewhere.

MKR of 4-phenyl-oxaolidin-2-one (rac)-94 using active ester (rac)-95 at 25°C [T2.8; E4].

In the same way as T2.7; E1 but at 25°C, n-BuLi (0.28 ml, 2.5M in hexanes, 0.70 mmol), 4-phenyl-oxaolidin-2-one (rac)-94 (0.103 g, 0.63 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml).
Gave a mixture of 3-(2-phenylpropionyl)-4-phenyl-oxazolidin-2-one (\textit{rac}-\textit{syn}) and \textit{anti-96} (ratio \textit{syn} : \textit{anti} 91 : 9), after purification gave 3-(2-phenylpropionyl)-4-phenyl-oxazolidin-2-one (\textit{rac}-\textit{syn}-96) (53 mg, 28%), which was spectroscopically identical to that obtained elsewhere.

**MKR of 4-phenyl-oxazolidin-2-one (\textit{rac})-94 using active ester (\textit{rac})-95 at 50°C [T2.8; E5].**

In the same way as T2.7; E1 but at 50°C, \textit{n}-BuLi (0.28 ml, 2.5M in hexanes, 0.70 mmol), 4-phenyl-oxazolidin-2-one (\textit{rac})-94 (0.103 g, 0.63 mmol) and pentafluorophenyl-2-phenylpropionate (\textit{rac})-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave a mixture of 3-(2-phenylpropionly)-4-phenyl-oxazolidin-2-one (\textit{rac}-\textit{syn} and \textit{anti-96} (ratio \textit{syn} : \textit{anti} 91 : 9), after purification gave 3-(2-phenylpropionly)-4-phenyl-oxazolidin-2-one (\textit{rac}-\textit{syn}-96) (54 mg, 29%), which was spectroscopically identical to that obtained elsewhere.

**MKR of 4-phenyl-oxazolidin-2-one (\textit{rac})-94 using active ester (\textit{rac})-95 [T2.9; E1].**

See T2.7; E1.

**MKR of 4-phenyl-oxazolidin-2-one (\textit{rac})-94 using active ester (\textit{rac})-129 [T2.9; E2].**

In the same way as T2.7; E1, \textit{n}-BuLi (0.27 ml, 2.5M in hexanes, 0.67 mmol), 4-phenyl-oxazolidin-2-one (\textit{rac})-94 (0.100 g, 0.61 mmol) and 2,6-dimethyl-4-nitrophenyl-2-phenylpropionate (\textit{rac})-129 (0.183 g, 0.61 mmol) in THF (10 ml). Returned starting materials.

**MKR of 4-phenyl-oxazolidin-2-one (\textit{rac})-94 using active ester (\textit{rac})-129 [T2.9; E3].**

In the same way as T2.7; E1 but with the reaction mixture being left to stir over night, \textit{n}-BuLi (0.27 ml, 2.5M in hexanes, 0.67 mmol), 4-phenyl-oxazolidin-2-one (\textit{rac})-94 (0.100 g, 0.61 mmol) and 2,6-dimethyl-4-nitrophenyl-2-phenylpropionate (\textit{rac})-129 (0.183 g, 0.61 mmol) in THF (10 ml). Returned starting materials.

**MKR of 4-phenyl-oxazolidin-2-one (\textit{rac})-94 using active ester (\textit{rac})-128 [T2.9; E4].**

In the same way as T2.7; E1, \textit{n}-BuLi (0.13 ml, 2.5M in hexanes, 0.36 mmol), 4-phenyl-oxazolidin-2-one (\textit{rac})-94 (50 mg, 0.31 mmol) and phenyl-2-phenylpropionate (\textit{rac})-128 (69 mg, 0.31 mmol) in THF (10 ml). Returned starting materials.
MKR of 4-phenyl-oxazolidin-2-one (rac)-94 using active ester (rac)-128 [T2.9; E5].

In the same way as T2.7; E1 but with the reaction mixture being left to stir over night, n-BuLi (0.13 ml, 2.5M in hexanes, 0.36 mmol), 4-phenyl-oxazolidin-2-one (rac)-94 (50 mg, 0.31 mmol) and phenyl-2-phenylpropiante (rac)-128 (69 mg, 0.31mmol) in THF (10 ml). Gave by crude ¹H NMR 3-(2-phenylpropionly)-4-phenyl-oxazolidin-2-one (rac)-syn and anti-96 (<5%, ratio syn : anti 40 : 60), which were spectroscopically identical to that obtained elsewhere.

MKR of 4-phenyl-oxazolidin-2-one (rac)-94 using active ester (rac)-139 [T2.9; E6].

In the same way as T2.7; E1, n-BuLi (0.29 ml, 2.5M in hexanes, 0.71 mmol), 4-phenyl-oxazolidin-2-one (rac)-94 (0.129 g, 0.65 mmol) and 2-methoxyphenyl-2-phenylpropiionate (rac)-139 (0.166 g, 0.65 mmol) in THF (10 ml). Gave a mixture of 3-(2-phenyl-propionyl)-4-phenyl-oxaolidin-2-one (rac)-syn and (rac)-anti-96 (ratio syn : anti 63 : 37), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) gave 3-(2-phenylpropionly)-4-phenyl-oxaolidin-2-one (rac)-anti-96 (13 mg, 7%) and (rac)-syn-96 (39 mg, 20%), which were spectroscopically identical to that obtained elsewhere.

MKR of 4-phenyl-oxazolidin-2-one (rac)-94 using acid chloride (rac)-140 [T2.9; E7].

In the same way as T2.7; E1, n-BuLi (3.97 ml, 2.5M in hexanes, 9.99 mmol), 4-phenyl-oxazolidin-2-one (rac)-94 (1.47 g, 9.01 mmol) and 2-phenylpropionyl chloride (rac)-140 (1.52 g, 9.01 mmol) in THF (13 ml). Gave a mixture of 3-(2-phenyl-propionyl)-4-phenyl-oxaolidin-2-one (rac)-syn and (rac)-anti-96 (ratio syn : anti 12 : 88), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) gave 3-(2-phenyl-propionyl)-4-phenyl-oxaolidin-2-one (rac)-anti-96 (0.27 g, 10%) and 3-(2-phenyl-propionyl)-4-phenyl-oxaolidin-2-one (rac)-syn-96 (0.77 g, 29%), which were spectroscopically identical to that obtained elsewhere.

KR of active ester (rac)-95 using 4-phenyl-oxazolidin-2-one (R)-94 [S2.14].

In the same way as T2.7; E1, n-BuLi (0.32 ml, 2.5M in hexanes, 0.79 mmol), 4-phenyl-oxazolidin-2-one (R)-94 (0.129 g, 0.79 mmol) and pentafluorophenyl-2-phenylpropiionate (rac)-95 (0.500 g, 1.60 mmol) in THF (10 ml). Gave a mixture of 3-(2-phenyl-propionyl)-4-phenyl-oxaolidin-2-one (rac)-syn and (rac)-anti-96 (ratio syn :
anti 95 : 5), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) gave 3-(2-phenylpropinyl)-4-phenyl-oxazolidin-2-one (rac)-anti-96 (18 mg, 7%) and (rac)-syn-96 (0.152 g, 65%), which were spectroscopically identical to that obtained elsewhere.

MKR of active ester (rac)-95 using 4-methyl-5-phenyl-oxazolidin-2-one (rac)-syn-104 [T2.10; E1].

In the same way as T2.7; E1, n-BuLi (1.21 ml, 2.5M in hexanes, 3.04 mmol), 4-methyl-5-phenyl-oxazolidin-2-one (rac)-syn-104 (0.49 g, 2.77 mmol) and pentafluorophenyl-2-phenyl-propionate (rac)-95 (0.87 g, 2.77 mmol) in THF (15 ml). Gave a mixture of 3-(2-phenyl-propionyl)-4-methyl-5-phenyl-oxazolidin-2-one (rac)-anti-syn and (rac)-syn-syn-141 (87 : 13), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) gave 3-(2-phenyl-propionyl)-4-methyl-5-phenyl-oxazolidin-2-one (rac)-anti-syn-141 (0.19 g, 22%), as a solid mp 89-92°C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.76; νmax (CHCl3)/cm⁻¹ 1778 and 1697 (2 × C=O); δH (400 MHz; CDCl3) 7.44-7.24 (10H, m, 10 × CH; 2 × Ph), 5.49 (1H, d, J 7.1, PhCHO), 5.14 (1H, q, J 7.1, PhCHO), 4.66-4.70 (1H, m, CHN), 1.51 (3H, d, J 7.1, CH3CHPh), and 0.94 (3H, d, J 6.6, CH3CHN); δC (100 MHz; CDCl3) 174.5 and 152.6 (2 × C=O), 140.5 and 133.3 (2 × i-C; 2 × Ph), 129.2, 129.1, 128.7, 128.2, 127.3 and 125.6 (10 × CH; 2 × Ph), 78.7 (PhCHO), 55.5 (CHN), 43.4 (PhCH), 19.3 and 14.6 (2 × CH3); (Found MH⁺, 310.1430; C19H20NO3 requires 310.1443), and 3-(2-phenyl-propionyl)-4-methyl-5-phenyl-oxazolidin-2-one (rac)-syn-syn-141 (0.60 g, 70%), as a solid mp 92-95°C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.63; νmax (CHCl3)/cm⁻¹ 1774 and 1701 (2 × C=O); δH (400 MHz; CDCl3) 7.40-7.17 (10H, m, 10 × CH; 2 × Ph), 5.64 (1H, d, J 7.2, PhCHO), 5.08 (1H, q, J 7.1, PhCH(CH3)), 4.80-4.84 (1H, m, CHN), 1.51 (3H, d, J 7.1, CH3CHPh), and 0.74 (3H, d, J 6.6, CH3CHN); δC (100 MHz; CDCl3) 174.3 and 152.5 (2 × C=O), 140.3 and 133.5 (2 × i-C; 2 × Ph), 128.9, 128.8, 128.6, 128.1, 127.1 and 125.7 (10 × CH; 2 × Ph), 78.8 (PhCHO), 54.7 (CHN), 43.6 (PhCH), 19.4 and 14.1 (2 × CH3); (Found MH⁺, 310.1460; C19H20NO3 requires 310.1443).

MKR of active ester (rac)-126 using 4-methyl-5-phenyl-oxazolidin-2-one (rac)-syn-104 [T2.10; E2].

In the same way as T2.7; E1, n-BuLi (0.19 ml, 2.5M in hexanes, 0.48 mmol), 4-methyl-5-phenyl-oxazolidin-2-one (rac)-syn-104 (69 mg, 0.39 mmol) and
pentafluorophenyl-2-phenyl-3-methyl-butanoate (rac)-126 (0.200 g, 0.58 mmol) in THF (10 ml). Gave a mixture of 3-(2-phenyl-3-methyl-butanyl)-4-phenyl-oxaolidin-2-one (rac)-anti-syn and (rac)-syn-syn-142 (73 : 27), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) gave 3-(2-phenyl-3-methyl-butanyl)-4-phenyl-oxaolidin-2-one (rac)-anti-syn-142 (12 mg, 9%), as a solid mp 98-100°C; R_f [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.71; \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 1778 and 1697 (2 × C=O); \( \delta_{\text{H}} \) (400 MHz; CDCl_3) 7.38-7.18 (10H, m, 10 × CH; Ph), 5.42 (1H, d, J 7.2, CHO), 4.75 (1H, d, J 10.6, PhCHCH), 4.67-4.59 (1H, m, CH_3CHCH_3), 0.98 (3H, d, J 6.6, CH_3), 0.87 (3H, d, J 6.6, CH_3) and 0.65 (3H, d, J 6.8, CH_3); \( \delta_{\text{C}} \) (100 MHz; CDCl_3) 174.1 and 152.8 (2 × C=O), 138.2 and 133.3 (2 × i-C; Ph), 129.1, 128.7, 128.7, 128.5, 124.7 and 125.6 (10 × CH; Ph), 78.4 (CH_2O), 56.0 (CHCHPh), 55.2 (CHN), 32.5 (CHCHPh), 21.4, 20.2 and 14.6 (3 × CH_3), and 3-(2-phenyl-3-methyl-butanyl)-4-methyl-5-phenyl-oxaolidin-2-one (rac)-syn-syn-142 (60 mg, 46%) as a solid mp 101-103°C; R_f [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.66; \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 1778 and 1702 (2 × C=O); \( \delta_{\text{H}} \) (400 MHz; CDCl_3) 7.44-7.19 (10H, m, 10 × CH; Ph), 5.64 (1H, d, J 7.3, CHO), 4.81 (1H, dq, J 7.3 and 6.6, CHN), 4.66 (1H, d, J 10.6, PhCHCH), 2.50-2.40 (1H, m, CH_3CHCH_3), 1.07 (3H, d, J 6.4, CH_3CHCH_3), 0.71 (3H, d, J 6.8, CH_3CHCH_3) and 0.66 (3H, d, J 6.6, CH_3CHN); \( \delta_{\text{C}} \) (100 MHz; CDCl_3) 173.7 and 152.6 (2 × C=O), 137.7 and 133.4 (2 × i-C; Ph), 129.2, 128.7, 128.6, 128.4, 124.2 and 125.6 (10 × CH; Ph), 78.7 (CH_2O), 56.7 (CHCHPh), 54.8 (CHN), 31.9 (CHCHPh), 21.7, 20.1 and 14.0 (3 × CH_3).

**MKR of active ester (rac)-117 using 4-methyl-5-phenyl-oxaolidin-2-one (rac)-syn-104 [T2.10; E3].**

In the same way as T2.7; E1, n-BuLi (0.26 ml, 2.5M in hexanes, 0.66 mmol), 4-methyl-5-phenyl-oxaolidin-2-one (rac)-syn-104 (0.107 g, 0.60 mmol) and pentafluorophenyl-2-(4-chloro-phenyl)-propionate (rac)-117 (0.211 g, 0.60 mmol) in THF (10 ml). Gave a mixture of 3-[2-(4-chloro-phenyl)-propionyl]-4-methyl-5-phenyl-oxaolidin-2-one (rac)-anti-syn and (rac)-syn-syn-143 (70 : 30), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) gave 3-[2-(4-chloro-phenyl)-propionyl]-4-methyl-5-phenyl-oxaolidin-2-one (rac)-anti-syn-143 (38 mg, 18%), as a white solid mp 84-86 °C; R_f [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.67; \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 1779 and 1698 (2 × C=O); \( \delta_{\text{H}} \) (400 MHz; CDCl_3) 7.37-7.17 (9H, m, 9 × CH; Ph and Ar), 5.45
(1H, d, J 7.2, CHO), 5.05 (1H, q, J 7.0, CHAr), 4.61 (1H, appears as septet J 6.4, CHN), 3.91 (3H, s, CH₃O), 1.42 (3H, d, J 7.0, CH₃CHAr) and 0.87 (3H, d, J 6.6, CH₃CHN); δc (100 MHz; CDCl₃) 174.0 and 152.5 (2 × C=O), 138.8, 131.1 and 133.0 (3 × i-C; Ph and Ar), 129.5, 128.8, 128.8, 128.7 and 125.6 (9 × CH; Ph and Ar), 78.7 (CHO), 55.3 (CHN), 42.7 (CHAr), 19.2 and 14.5 (2 × CH₃), and 3-[2-(4-chloro-phenyl)-propionyl]-4-methyl-5-phenyl-oxaolidin-2-one (rac)-syn-syn-143 (85 mg, 41%) as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.50; νmax (CHCl₃)/cm⁻¹ 1781 and 1698 (2 × C=O); δH (400 MHz; CDCl₃) 7.33-7.20 (7H, m, 7 × CH; Ph and Ar), 7.15-7.11 (2H, m, 2 × CH; Ph), 5.59 (1H, d, J 7.3, CHO), 4.97 (1H, q, J 7.0, CHAr), 4.74 (1H, appears as septet J 6.6, CHN), 3.91 (3H, s, CH₃O), 1.41 (3H, d, J 7.0, CH₃CHAr) and 0.67 (3H, d, J 6.6, CH₃CHN); δc (100 MHz; CDCl₃) 173.8 and 152.4 (2 × C=O), 138.7, 133.2 and 132.9 (3 × i-C; Ph and Ar), 129.4, 128.7, 128.6 and 125.6 (9 × CH; Ph and Ar), 78.8 (CHO), 54.7 (CHN), 43.0 (CHAr), 19.3 and 14.1 (2 × CH₃).

**MKR of active ester (rac)-123 using 4-methyl-5-phenyl-oxaolidin-2-one (rac)-syn-syn-104 [T2.10; E4].**

In the same way as T2.7; E1, n-BuLi (0.20 ml, 2.5M in hexanes, 0.49 mmol), 4-methyl-5-phenyl-oxaolidin-2-one (rac)-syn-syn-104 (79 mg, 0.45 mmol) and pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propionate (rac)-123 (0.177 g, 0.45 mmol) in THF (10 ml). Gave a mixture of 3-[2-(6-enthyoxy-2-naphthyl)-propionyl]-4-methyl-5-phenyl-oxaolidin-2-one (rac)-anti-syn and (rac)-syn-syn-144 (73 : 27), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) gave 3-[2-(6-enthyoxy-2-naphthyl)-propionyl]-4-methyl-5-phenyl-oxaolidin-2-one (rac)-anti-syn-144 (24 mg, 14%), as a solid mp 106-108 °C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.60; νmax (CHCl₃)/cm⁻¹ 1778 and 1698 (2 × C=O); δH (400 MHz; CDCl₃) 7.76 (1H, d, J 1.7, CH; Ar), 7.72 (2H, dd, J 8.7 and 4.5, 2 × CH; Ar), 7.49 (1H, dd, J 8.7 and 1.7, CH; Ar), 7.42-7.32 (3H, m, 3 × CH; Ph), 7.27-7.23 (2H, m, 2 × CH; Ar), 7.16-7.10 (2H, m, 2 × CH; Ph), 5.46 (1H, d, J 7.2, CHO), 5.27 (1H, q, J 7.0, CHAr), 4.67 (1H, appears as septet J 6.8, CHN), 3.91 (3H, s, CH₃O), 1.58 (3H, d, J 7.0, CH₃CHAr) and 0.95 (3H, d, J 6.6, CH₃CHN); δc (100 MHz; CDCl₃) 174.5 and 157.6 (2 × C=O), 152.6, 135.6, 133.7, 133.1 and 128.9 (5 × i-C; Ph and Ar), 129.4, 128.7, 128.6, 127.2, 126.7, 126.6, 125.6, 118.9 and 105.5 (11 × CH; Ph and Ar), 78.6 (CHO), 55.4 (CHN), 55.3 (CHAr), 43.2 (CH₃O), 19.2 and 14.5 (2 × CH₃), and 3-[2-(6-enthyoxy-2-naphthyl)-propionyl]-4-methyl-5-phenyl-oxaolidin-2-one (rac)-syn-syn-144 (61 mg, 35%) as an
oil; \( R_f \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.42; \( \nu_{\text{max}} \) (CHCl\(_3\))/cm\(^{-1}\) 1779 and 1697 (2 × C=O); \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.72 (1H, d, \( J \) 1.5, CH; Ar), 7.68 (2H, d, \( J \) 8.6, 2 × CH; Ar), 7.45 (1H, dd, \( J \) 8.6 and 1.8, CH; Ar), 7.31-7.27 (3H, m, 3 × CH; Ph), 7.16-7.07 (4H, m, 4 × CH; Ar and Ph), 5.63 (1H, d, \( J \) 7.5, CHO), 5.19 (1H, q, \( J \) 7.0, CHAr), 4.86-4.78 (1H, m, CHN), 3.89 (3H, s, CH\(_3\)O), 1.55 (3H, d, \( J \) 7.0, CH\(_2\)CHAr) and 0.70 (3H, d, \( J \) 6.6, CH\(_3\)CHN); \( \delta_C \) (100 MHz; CDCl\(_3\)) 174.4 and 157.6 (2 × C=O), 152.5, 135.4, 133.6, 133.4 and 128.9 (5 × \( i \)-C; Ph and Ar), 129.4, \(^1\) 128.7, \(^2\) 128.5, \(^2\) 127.1, \(^1\) 126.7, \(^1\) 125.6, \(^2\) 118.8 \(^1\) and 105.5 \(^1\) (11 × CH; Ph and Ar), 78.7 (CHO), 55.3 (CHN), 54.7 (CHAr), 43.5 (CH\(_3\)O), 19.3 and 14.2 (2 × CH\(_3\)).

**MKR of active ester** (rac)-95 using 4-benzyl-oxazolidin-2-one (rac)-145 [T2.11; E1].

In the same way as T2.7; E1, n-BuLi (2.43 ml, 2.5M in hexanes, 6.68 mmol), 4-benzyl-oxazolidin-2-one (rac)-145 (0.98 g, 5.53 mmol) and pentafluorophenyl-2-phenyl-propionate (rac)-95 (1.75 g, 5.53 mmol) in THF (15 ml). Gave a mixture of 3-(2-phenyl-propionyl)-4-benzyl-oxazolidin-2-one (rac)-syn and anti-146 (ratio 71 : 29), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) gave 3-(2-phenyl-propionyl)-4-benzyl-oxazolidin-2-one (rac)-anti-146 (0.32 g, 19%), as a white solid mp 64-67°C; \( R_f \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.66; \( \nu_{\text{max}} \) (CHCl\(_3\))/cm\(^{-1}\) 1780 and 1699 (2 × C=O); \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.39-7.21 (10H, m, 10 × CH; 2 × Ph), 5.12 (1H, q, \( J \) 7.0, PhCH), 4.61-4.54 (1H, m, CHN), 4.12-4.10 (2H, m, CH\(_2\)O), 3.35 (1H, dd, \( J \) 13.1 and 3.2, CH\(_A\)HbPh), 2.80 (1H, dd, \( J \) 13.1 and 9.8, CH\(_A\)HbPh) and 1.55 (3H, d, \( J \) 7.0, CHCH\(_3\)); \( \delta_C \) (100 MHz; CDCl\(_3\)) 174.7 and 152.9 (2 × C=O), 140.3 and 135.4 (2 × \( i \)-C; 2 × Ph), 129.5, \(^2\) 129.0, \(^2\) 128.7, \(^2\) 128.1, \(^2\) 127.4 \(^1\) and 127.3 \(^1\) (10 × CH; 2 × Ph), 65.9 (CH\(_2\)O), 55.8 (CHN), 43.2 (PhCH), 38.0 (CH\(_2\)Ph) and 19.5 (CH\(_3\)); (Found MH\(^+\), 310.1442; C\(_{19}\)H\(_{20}\)NO\(_3\) requires 310.1443), and 3-(2-phenyl-propionyl)-4-benzyl-oxazolidin-2-one (rac)-syn-146 (0.68 g, 40%), as an oil; \( R_f \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.43; \( \nu_{\text{max}} \) (CHCl\(_3\))/cm\(^{-1}\) 1775 and 1700 (2 × C=O); \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.45-6.94 (10H, m, 10 × CH; 2 × Ph), 5.11 (1H, q, \( J \) 6.9, PhCH), 4.79-4.70 (1H, m, CHN), 4.18 (1H, t, \( J \) 8.5, CH\(_A\)HbO), 4.07 (1H, dd, \( J \) 8.5 and 3.2, CH\(_A\)HbO), 3.08 (1H, dd, \( J \) 13.5 and 3.2, CH\(_A\)HbPh), 2.58 (1H, dd, \( J \) 13.5 and 8.8, CH\(_A\)HbPh) and 1.52 (3H, d, \( J \) 6.9, CHCH\(_3\)); \( \delta_C \) (100 MHz; CDCl\(_3\)) 174.5 and 153.0 (2 × C=O), 140.2 and 135.0 (2 × \( i \)-C; 2 × Ph), 129.4, \(^2\) 128.8, \(^2\) 128.6, \(^2\) 128.3, \(^2\) 127.3 \(^1\) and 127.2 \(^1\) (10 × CH; 2 × Ph), 65.8 (CH\(_2\)O), 54.9 (CHN), 43.2 (PhCH), 37.4 (CH\(_2\)Ph) and 19.2 (CH\(_3\)); (Found MH\(^+\), 310.1438; C\(_{19}\)H\(_{20}\)NO\(_3\) requires 310.1443).
MKR of active ester (rac)-126 using 4-benzyl-oxazolidin-2-one (rac)-145 [T2.11; E2].

In the same way as T2.7; E1, n-BuLi (0.22 ml, 2.5M in hexanes, 0.55 mmol), 4-benzyl-oxazolidin-2-one (rac)-145 (79 mg, 0.44 mmol) and pentafluorophenyl-2-phenyl-3-methyl-butanoate (rac)-126 (0.229 g, 0.67 mmol) in THF (10 ml). Gave a mixture of 3-(2-phenyl-3-methyl-butanyl)-4-phenyl-oxazolidin-2-one (rac)-anti and syn-147 (66 : 34), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) gave 3-(2-phenyl-3-methyl-butanyl)-4-phenyl-oxazolidin-2-one (rac)-anti-147 (21 mg, 14%), as a white solid mp 86-89 °C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.61; νmax (CHCl3)/cm⁻¹ 1779 and 1693 (2 × C=O); δH (400 MHz; CDCl3) 7.43 (2H, dt, J 6.8 and 1.7, 2 × CH; Ph), 7.37-7.23 (8H, m, 8 × CH; Ph), 4.81 (1H, d, J 10.6, PhCHCH), 4.61 (1H, dddd, J 10.0, 9.0, 3.3 and 2.4, CHN), 4.09 (1H, dd, J 9.0 and 2.4, CHAHB), 4.02 (1H, t, J 9.0, CHAHB), 3.42 (1H, dd, J 13.4 and 3.3, CHAHB), 2.75 (1H, dd, J 13.4 and 10.0, CHAHB), 2.59-2.49 (1H, m, CH3CHCH3), 1.11 (3H, d, J 6.6, CH3CHCH3) and 0.74 (3H, d, J 6.6, CH3CHCH3); δC (100 MHz; CDCl3) 174.2 and 153.0 (2 × C=O), 138.0 and 135.3 (2 × i-C; Ph), 129.4,129.1,128.9,128.4,127.3 and 127.3 (10 × CH; 2 × Ph), 65.6 (CH2O), 55.8 (CHN), 55.7 (CHPh), 38.0 (CH3Ph) 32.5 (CH3CHCH3), 21.5 and 20.1 (2 × CH3), and 3-(2-phenyl-3-methyl-butonyl)-4-phenyl-oxazolidin-2-one (rac)-syn-147 (37 mg, 25%) as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.43; νmax (CHCl3)/cm⁻¹ 1774 and 1691 (C=O); δH (400 MHz; CDCl3) 7.48 (2H, dt, J 7.0 and 1.5, 2 × CH; Ph), 7.37 (2H, tt, J 7.5 and 1.7, 2 × CH; Ph), 7.31 (1H, dt, J 7.3 and 1.5, 2 × CH; Ph), 7.22-7.15 (3H, m, 3 × CH; Ph), 6.89 (2H, dd, J 7.9 and 1.7, 3 × CH; Ph), 4.82-4.76 (1H, m, CHN), 4.74 (1H, d, J 10.6, PhCHCH), 4.23 (1H, t, J 7.9, CHAHB), 4.11 (1H, dd, J 7.9 and 2.8, CHAHB), 2.98 (1H, dd, J 13.6 and 3.3, CHAHB), 2.62 (1H, dd, J 13.6 and 8.3, CHAHB), 2.58-2.50 (1H, m, CH3CHCH3), 1.08 (3H, d, J 6.4, CH3CHCH3) and 0.75 (3H, d, J 6.8, CH3CHCH3); δC (100 MHz; CDCl3) 173.9 and 153.0 (2 × C=O), 137.8 and 134.7 (2 × i-C; Ph), 129.4,129.3,128.7,128.5,127.3 and 127.1 (10 × CH; 2 × Ph), 65.5 (CH2O), 56.4 (CHN), 54.8 (CHPh), 37.1 (CH2Ph) 31.7 (CH3CHCH3), 21.7 and 20.1 (2 × CH3).
MKR of active ester (rac)-117 using 4-benzyl-oxazolidin-2-one (rac)-145 [T2.11; E3].

In the same way as T2.7; E1, n-BuLi (0.23 ml, 2.5M in hexanes, 0.59 mmol), 4-benzyl-oxazolidin-2-one (rac)-145 (94 mg, 0.53 mmol) and pentafluorophenyl-2-(4-chloro-phenyl)-propionate (rac)-117 (0.184 g, 0.53 mmol) in THF (12 ml). Gave a mixture of 3-[2-(4-chloro-phenyl)-propionyl]-4-benzyl-oxazolidin-2-one (rac)-syn and (rac)-anti-148 (59 : 41), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) gave 3-[2-(4-chloro-phenyl)-propionyl]-4-benzyl-oxazolidin-2-one (rac)-anti-148 (30 mg, 16%) as a white solid mp 72-74 °C; \( R_F \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.46; \( \nu \text{max} \) (CHCl\(_3\))/cm\(^{-1}\) 1780 and 1697 (C=O); \( \delta \text{H} \) (400 MHz; CDCl\(_3\)) 7.29-7.12 (9H, m, 9× CH; Ph and Ar), 5.02 (1H, q, J 7.0, CHAr), 4.55-4.48 (1H, m, CHN), 4.07-3.98 (2H, m, CH\(_3\)O), 3.26 (1H, dd, J 13.3 and 3.3, CH\(_2\)H\(_3\)Ph), 2.73 (1H, dd, J 13.3 and 9.7, CH\(_2\)H\(_3\)Ph) and 1.45 (3H, d, J 7.0, CH\(_3\)H); \( \delta \text{C} \) (100 MHz; CDCl\(_3\)) 174.2 and 152.9 (2× C=O), 138.6, 135.2 and 133.2 (3 × i-C; Ph and Ar), 129.5, 129.4, 129.0, 128.8\(^2\) and 127.4\(^1\) (9 × CH; Ph and Ar), 66.0 (ArCH), 55.7 (CHN), 42.5 (CH\(_2\)O), 37.9 (PhCH\(_2\)) and 19.4 (CHCH\(_3\)), and 3-[2-(4-chloro-phenyl)-propionyl]-4-benzyl-oxazolidin-2-one (rac)-syn-148 (40 mg, 22%) as an oil; \( R_F \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.31; \( \nu \text{max} \) (CHCl\(_3\))/cm\(^{-1}\) 1779 and 1698 (C=O); \( \delta \text{H} \) (400 MHz; CDCl\(_3\)) 7.30 (2H, dt, J 8.8 and 2.4, 2× CH; Ar), 7.25 (2H, dt, J 8.8 and 2.4, 2× CH; Ar), 7.21-7.11 (3H, m, 3× CH; Ph), 6.90 (2H, dd, J 6.4 and 3.0, 2× CH; Ph), 5.01 (1H, q, J 7.0, CHAr), 4.66 (1H, tt, J 8.4 and 3.3, CHN), 4.12 (1H, t, J 8.4, CH\(_2\)H\(_3\)O), 4.02 (1H, dd, J 8.4 and 3.3, CH\(_2\)H\(_3\)O), 3.01 (1H, dd, J 13.5 and 3.3, CH\(_2\)H\(_3\)Ph), 2.52 (1H, dd, J 13.3 and 8.4, CH\(_2\)H\(_3\)Ph) and 1.43 (3H, d, J 7.0, CH\(_3\)H); \( \delta \text{C} \) (100 MHz; CDCl\(_3\)) 174.0 and 152.9 (2× C=O), 138.6, 134.7 and 133.1 (3 × i-C; Ph and Ar), 129.7, 129.3, 128.8\(^2\) and 127.3\(^1\) (9 × CH; Ph and Ar), 65.9 (ArCH), 54.9 (CHN), 42.5 (CH\(_2\)O), 37.4 (PhCH\(_2\)) and 19.0 (CHCH\(_3\)).

MKR of active ester (rac)-123 using 4-benzyl-oxazolidin-2-one (rac)-149 [T2.11; E4].

In the same way as T2.11; E1, n-BuLi (0.32 ml, 2.5M in hexanes, 0.81 mmol), 4-benzyl-oxazolidin-2-one (rac)-145 (0.13 g, 0.73 mmol) and pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propionate (rac)-123 (0.29 g, 0.73 mmol) in THF (12.5 ml). Gave a mixture of 3-[2-(6-methoxy-2-naphthyl)-propionyl]-4-benzyl-oxazolidin-2-one (rac)-syn and (rac)-anti-149 (67 : 33), purification by flash column chromatography on
MKR of active ester (rac)-95 using 4-isopropyl-oxazolidin-2-one (rac)-24 [T2.12; E1].

In the same way as T2.7; E1, n-BuLi (1.67 ml, 2.5M in hexanes, 4.17 mmol), 4-isopropyl-oxazolidin-2-one (rac)-24 (0.49 g, 3.79 mmol) and pentfluorophenyl-2-phenyl-propionate (rac)-95 (1.20 g, 3.79 mmol) in THF (15 ml). Gave a mixture of 3-(2-phenyl-propionyl)-4-isopropyl-oxazolidin-2-one (rac)-syn and anti-97 (ratio 95 : 5), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) gave 3-(2-phenyl-propionyl)-4-isopropyl-oxazolidin-2-one (rac)-97 (40 mg, 4%), as an oil; $R_F$ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.64; $\nu_{max}$ (CHCl$_3$)/cm$^{-1}$ 1774 and 1701 (2 × C=O); $\delta_H$ (400 MHz; CDCl$_3$) 7.50-7.67 (3H, m, 3 × CH; Ar), 7.41 (1H, d, $J_{Ar}$ 1.1, CHAr), 7.31 (1H, d, $J_{Ar}$ 1.1, CHAr), 7.18-7.28 (3H, m, 3 × CH; Ph), 7.00 (2H, m, 2 × CH; Ph), 5.17 (1H, q, $J_{CH}$ 7.0, CHAr), 4.78 (1H, dq, $J_{CH}$ 7.0, CHAr), 4.58 (1H, dq, $J_{CH}$ 7.0, CHAr), 4.51 (1H, q, $J_{CH}$ 7.0, CHAr), 4.40 (1H, dq, $J_{CH}$ 7.0, CHAr), 4.11 (1H, dd, $J_{CH}$ 7.0, CHAr), 4.00 (1H, dd, $J_{CH}$ 7.0, CHAr), 3.92 (1H, dd, $J_{CH}$ 7.0, CHAr), 3.90 (1H, dd, $J_{CH}$ 7.0, CHAr), 3.60 (1H, dd, $J_{CH}$ 7.0, CHAr), 3.55 (1H, dd, $J_{CH}$ 7.0, CHAr), 3.40 (1H, dd, $J_{CH}$ 7.0, CHAr), 2.81 (1H, dt, $J_{CH}$ 7.0, CHAr), 2.16 (3H, s, CH$_3$).
MKR of active ester (rac)-126 using 4-isopropyl-oxazolidin-2-one (rac)-24 [T2.12; E2].

In the same way as T2.7; E1, n-BuLi (0.18 ml, 2.5M in hexanes, 0.45 mmol), 4-isopropyl-oxazolidin-2-one (rac)-24 (46 mg, 0.36 mmol) and pentafluorophenyl-2-phenyl-3-methyl-butanoate (rac)-126 (0.184 g, 0.57 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) an inseparable mixture of 3-(2-phenyl-3-methyl-butanyl)-4-isopropyl-oxazolidin-2-one (rac)-syn (rac)-anti-150 (35 mg, 34%, ratio syn : anti 68 : 32), as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.57; v_max (CHCl3)/cm⁻¹ 1778 and 1694 (C=O); δ_H (400 MHz; CDCl3) 7.30 (2H, dt, J 7.0 and 1.5, 2 × CH; Ph), 7.24-7.13 (3 H, m, 3 × CH; Ph), 4.70 (1H, d, J 10.6, PhCH), 4.42 (1H, dt, J 9.0 and 3.3, CHN), 4.17 (1H, t, J 9.0, CH₂B(O)), 4.02 (1H, dd, J 9.0 and 3.3, CH₂B(O)), 2.47-2.33 (1H, m, CH₃CHCH₃), 2.11-1.98 (1H, m, CH₃CHCH₃), 0.72 (3H, d, J 6.4, CH₃), 0.69 (3H, d, J 7.0, CH₃), 0.63 (3H, d, J 6.8, CH₃) and 0.28 (3H, d, J 6.8, CH₃); δ_C (100 MHz; CDCl3) 174.0 and 153.6 (2 × C=O), 138.1 (i-C; Ph), 129.1, 128.4 and 127.2 (5 × CH; Ph), 62.7 (PhCH), 58.0 (CH₃), 56.5 (CH₂O), 31.0 and 27.8 (2 × CH₃CHCH₃) and 21.7, 20.1, 17.7 and 13.8 (4 × CH₃), for (rac)-anti-150 δ_H (400 MHz; CDCl3) 7.40-7.33 (2H, m, 2 × CH; Ph), 7.30-7.17 (3 H, m,
3 × CH; Ph), 4.79 (1H, d, J 10.6, PhCHCH), 4.36 (1H, dt, J 7.8 and 3.6, CHN), 4.12-4.05 (2H, m, CH₂O), 2.50-2.39 (2H, m, 2 × CH₃CHCH₃), 1.03 (3H, d, J 6.6, CH₃), 0.90 (3H, d, J 6.9, CH₃), 0.89 (3H, d, J 7.2, CH₃) and 0.68 (3H, d, J 6.6, CH₃).

**MKR of active ester (rac)-117 using 4-isopropyl-oxazolidin-2-one (rac)-24 [T2.12; E3].**

In the same way as T2.7; E1, n-BuLi (0.26 ml, 2.5M in hexanes, 0.64 mmol), ethyl 4-isopropyl-oxazolidin-2-one (rac)-24 (75 mg, 0.56 mmol) and pentafluorophenyl-2-(4-chloro-phenyl)-propionate (rac)-117 (0.204 g, 0.58 mmol) in THF (12 ml). Gave a mixture of ethyl 3-[2-(4-chloro-phenyl)-propionyl]-4-isopropyl-oxazolidin-2-one (rac)-syn and (rac)-anti-151 (ratio syn : anti 74 : 26), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) gave 3-[2-(4-chloro-phenyl)-propionyl]-4-isopropyl-oxazolidin-2-one (rac)-anti-151 (30 mg, 17%) as a white solid mp 64-66 °C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.54; νmax (CHCl₃)/cm⁻¹ 1779 and 1698 (2 × C=O); δH (400 MHz; CDCl₃) 7.29-7.27 (4H, m, 4 × CH; Ar), 5.12 (1H, q, J 7.0, CHAr), 4.38-4.33 (1H, m, CHN), 4.18-4.12 (2H, m, CH₂O), 2.47-2.37 (1H, m, CH₃CHCH₃), 1.50 (3H, d, J 7.0, CH₃CH) 0.92 (3H, d, J 6.8, CH₃CHCH₃) and 0.91 (3H, d, J 7.0, CH₃CHCH₃); δC (100 MHz; CDCl₃) 174.3 and 153.6 (2 × C=O), 138.7 and 133.1 (2 × i-C; Ar), 129.6² and 128.7² (4 × CH; Ar), 63.1 (ArCH), 58.9 (CHN), 42.3 (CH₂CHN), 29.4 (CH₃CHCH₃), 19.6 (CH₂CHCH₃), 18.0 (CH₂CHCH₃) and 14.7 (CH₃CHCH₃), and 3-[2-(4-chloro-phenyl)-propionyl]-4-isopropyl-oxazolidin-2-one (rac)-syn-151 (60 mg, 35%) as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.35; νmax (CHCl₃)/cm⁻¹ 1778 and 1698 (2 × C=O); δH (400 MHz; CDCl₃) 7.25-7.18 (4H, m, 4 × CH; Ar), 5.03 (1H, q, J 7.0, CHAr), 4.41 (1H, dt, J 8.9 and 3.7, CHN), 4.18 (1H, t, J 8.9, CH₃H₂O), 4.05 (1H, dd, J 8.9 and 3.7, CH₃H₂O), 2.17-2.05 (1H, m, CH₂CHCH₃), 1.38 (3H, d, J 7.0, CH₃CH), 0.74 (3H, d, J 7.2, CH₃CHCH₃) and 0.43 (3H, d, J 7.0, CH₃CHCH₃); δC (100 MHz; CDCl₃) 174.0 and 153.4 (2 × C=O), 138.9 and 133.0 (2 × i-C; Ar), 129.4² and 128.7² (4 × CH; Ar), 63.0 (ArCH), 58.1 (CHN), 42.6 (CH₂CHN), 27.8 (CH₃CHCH₃), 18.7 (CH₂CHCH₃), 17.7 (CH₃CHCH₃) and 14.1 (CH₃CHCH₃).
MKR of active ester (rac)-123 using 4-isopropyl-oxazolidin-2-one (rac)-24 [T2.12; E4].

In the same way as T2.7; E1, n-BuLi (0.72 ml, 2.5M in hexanes, 1.79 mmol), 4-isopropyl-oxazolidin-2-one (rac)-24 (0.21 g, 1.63 mmol) and pentafluorophenyl-2-[(6-methoxy-2-naphthyl)-propionate (rac)-123 (0.64 g, 1.63 mmol) in THF (12.5 ml). Gave a mixture of 3-[2-(6-methoxy-2-naphthyl)-propionyl]-4-isopropyl-oxazolidin-2-one (rac)-syn and (rac)-anti-152 (ratio syn : anti 92 : 8), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) gave 3-[2-(6-methoxy-2-naphthyl)-propionyl]-4-isopropyl-oxazolidin-2-one (rac)-anti-153 (60 mg, 10%) as a white solid mp 124-126 °C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.35; ν<sub>max</sub> (CHCl<sub>3</sub>)cm<sup>-1</sup> 1779 and 1694 (2 × C=O); δ<sub>H</sub> (400 MHz; CDCl<sub>3</sub>) 7.65 (1H, d, J 1.7, CH; Ar), 7.62 (2H, dd, J 8.7 and 4.0, 2 × CH; Ar), 7.39 (1H, dd, J 8.7 and 1.7, CH; Ar), 7.08-7.01 (2H, m, 2 × CH; Ar), 5.21 (1H, q, J 7.0, CHAr), 4.31-4.236 (1H, m, CH; Ar), 4.09-4.00 (2H, m, CH₂O), 3.83 (3H, s, CH₃O), 2.45-2.35 (1H, m, CH₃CHCH₃), 1.51 (3H, d, J 7.0, CH₃CH), 0.86 (3H, d, J 7.2, CH₃CHCH₃) and 0.85 (3H, d, J 6.8, CH₃CHCH₃); δ<sub>C</sub> (100 MHz; CDCl<sub>3</sub>) 174.8 and 157.6 (2 × C=O), 153.6, 135.5, 133.7 and 128.9 (4 × i-C; Ar), 129.4, 127.1, 126.9, 126.6, 118.9 and 105.5 (6 × CH; Ar), 63.0 (ArCH), 59.0 (CH₂O), 55.3 (CHN), 42.9 (CH₃O), 28.5 (CH₃CHCH₃), 19.6, 18.0 and 14.7 (3 × CH₃), and 3-[2-(6-methoxy-2-naphthyl)-propionyl]-4-isopropyl-oxazolidin-2-one (rac)-syn-152 (0.29 g, 48%) as a white solid mp 90-92 °C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.24; ν<sub>max</sub> (CHCl<sub>3</sub>)cm<sup>-1</sup> 1778 and 1697 (2 × C=O); δ<sub>H</sub> (400 MHz; CDCl<sub>3</sub>) 7.66 (1H, d, J 1.7, CH; Ar), 7.62 (2H, dd, J 8.6 and 2.5, 2 × CH; Ar), 7.39 (1H, dd, J 8.6 and 1.8, CH; Ar), 7.07-7.02 (2H, m, 2 × CH; Ar), 5.20 (1H, q, J 7.0, CHAr), 4.44 (1H, dt, J 8.8 and 3.5, CHN), 4.12 (1H, t, J 8.8, CH₃H₈O), 4.02 (1H, dd, J 8.8 and 3.5, CH₃H₈O), 3.84 (3H, s, CH₃O), 2.18-2.08 (1H, m, CH₃CHCH₃), 1.47 (3H, d, J 7.0, CH₃CH), 0.71 (3H, d, J 7.2, CH₃CHCH₃) and 0.33 (3H, d, J 7.0, CH₃CHCH₃); δ<sub>C</sub> (100 MHz; CDCl<sub>3</sub>) 174.0 and 153.4 (2 × C=O), 138.9 and 133.0 (2 × i-C; Ar), 129.4<sup>2</sup> and 128.7<sup>2</sup> (4 × CH; Ar), 63.0 (ArCH), 58.1 (CHN), 42.6 (CH₂O), 27.9 (CH₃CHCH₃), 18.7, 17.7 and 14.1 (3 × CH₃).

MKR of active ester (rac)-95 using 4-phenyl-oxazolidin-2-one (rac)-94 [T2.13; E1].
See T2.7; E1.
MKR of active ester (rac)-126 using 4-phenyl-oxazolidin-2-one (rac)-94 [T2.13; E2].

In the same way as T2.7; E1, n-BuLi (0.18 ml, 2.5M in hexanes, 0.46 mmol), 4-phenyl-oxazolidin-2-one (rac)-94 (60 mg, 0.37 mmol) and pentafluorophenyl-2-phenyl-3-methyl-butinoate (rac)-126 (0.191 g, 0.55 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) an inseparable mixture of 3-[(2-phenyl-3-methyl-butonyl)-4-phenyl-oxaolidin-2-one (rac)-syn and (rac)-anti-154 (30 mg, 25%, ratio syn : anti 87 : 13), as a white solid mp 60-62 °C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.43; νmax (CHCl3/cm⁻¹) 1781 and 1780 (2 × C=O); δH (400 MHz; CDCl3) 7.17-7.02 (8H, m, 8 × CH; Ph), 6.72 (2H, dt, J 6.9 and 1.6, 2 × CH; Ph), 5.40 (1H, dd, J 9.1 and 4.7, CHN), 4.68 (1H, d, J 10.6, PhCHCH), 4.57 (1H, t, J 9.1, CHA2H3O), 3.98 (1H, dd, J 9.1 and 4.7, CH2H2O), 2.35-2.21 (1H, m, CH3CHCH3), 0.97 (3H, d, J 6.6, CH3CHCH3) and 0.61 (3H, d, J 6.6, CH3CHCH3); δC (100 MHz; CDCl3) 172.9 and 153.2 (2 × C=O), 138.2 and 137.1 (2 × i-C; Ph), 129.2, 128.8, 128.3, 127.2, 125.3 (10 × CH; 2 × Ph), 69.4 (CH2O), 57.6 (CHN), 56.9 (PhCHCH), 30.7 (CH3CHCH3), 21.6 and 20.0 (2 × CH3), for (rac)-anti-154 δH (400 MHz; CDCl3) 7.36-7.02 (10H, m, 10 × CH; Ph), 5.27 (1H, dd, J 8.9 and 3.6, CHN), 4.70 (1H, d, J 10.6, PhCHCH), 4.48 (1H, t, J 8.9, CHA2H3O), 4.13 (1H, dd, J 8.9 and 3.6, CHA2H3O), 2.35-2.21 (1H, m, CH3CHCH3), 0.71 (3H, d, J 6.6, CH3CHCH3) and 0.58 (3H, d, J 6.9, CH3CHCH3).

MKR of active ester (rac)-117 using 4-phenyl-oxazolidin-2-one (rac)-94 [T2.13; E3].

In the same way as T2.7; E1, n-BuLi (0.70 ml, 2.5M in hexanes, 1.75 mmol), 4-phenyl-oxazolidin-2-one (rac)-94 (0.26 g, 1.59 mmol) and pentafluorophenyl-2-(4-chloro-phenyl)-propionate (rac)-117 (0.56 g, 1.59 mmol) in THF (10 ml). Gave a mixture of 3-[2-(4-chloro-phenyl)-propionyl]-4-phenyl-oxaolidin-2-one (rac)-syn and (rac)-anti-155 (ratio syn : anti >95 : 5), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) gave 3-[2-(4-chloro-phenyl)-propionyl]-4-phenyl-oxaolidin-2-one (rac)-syn-155 (0.26 g, 49%) as an white solid mp 124-130°C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.18; νmax (CHCl3/cm⁻¹) 1773 and 1700 (2 × C=O); δH (400 MHz; CDCl3) 7.33-7.23 (3H, m, 3 × CH; Ph), 7.19 (2H, dt, J 8.4 and 2.0, 2 × CH; Ar), 7.02 (2H, dt, J 8.4 and 2.0, 2 × CH; Ar), 6.96 (2H, dd, J 6.8 and 1.7, 2 × CH; Ph), 5.45 (1H,
MKR of active ester (rac)-123 using 4-phenyl-oxazolidin-2-one (rac)-94 [T2.13; E4].

In the same way as T2.7; E1, n-BuLi (0.30 ml, 2.5M in hexanes, 0.75 mmol), 4-phenyl-oxazolidin-2-one (rac)-94 (97 mg, 0.60 mmol) and pentfluorophenyl-2-(6-methoxy-2-naphthyl)-propionate (rac)-123 (0.355 g, 0.90 mmol) in THF (10 ml). Gave a mixture of 3-[2-(6-methoxy-2-naphthyl)-propionyl]-4-phenyl-oxazolidin-2-one (rac)-syn and (rac)-anti-156 (ratio syn : anti >95 : 5), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 3:7) gave 3-[2-(6-methoxy-2-naphthyl)-propionyl]-4-phenyl-oxazolidin-2-one (rac)-syn-156 (0.109 g, 49%), as a white solid mp 137-139 °C; \( R_f \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.17; \( \nu_{max} (\text{CHCl}_3)/\text{cm}^{-1} \) 1780 and 1699 (C=O); \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.63 (1H, d, J 8.4, CH; Ar), 7.52 (1H, d, J 8.4, CH; Ar), 7.33 (1H, br s, CH; Ar), 7.28-7.23 (3H, m, 3 × CH; Ar and/or Ph), 7.15-7.10 (4H, m, 4 × CH; Ar and or/Ph), 6.91 (2H, br d, J 7.0, CH; Ar), 5.78 (1H, dd, J 9.0 and 5.3, CHN), 5.21 (1H, q, J 6.8, CHAr), 4.64 (1H, t, J 9.0, CH\(_2\text{H}_3\)O), 4.06 (1H, dd, J 9.0 and 5.3, CH\(_2\text{H}_3\)O), 3.92 (3H, s, CH\(_3\)) and 1.46 (3H, d, J 6.8, CH\(_3\)); \( \delta_C \) (100 MHz; CDCl\(_3\)) 173.6 and 153.0 (2 × C=O), 157.6, 138.2, 135.1, 133.6 and 128.8 (5 × i-C; Ar and Ph), 129.4, 127.0, 126.4, 126.3, 118.7 and 105.5 (6 × CH; Ar), 128.8, 127.2, 125.9 (5 × CH; Ph), 69.5 (CH\(_2\)O), 57.8 (CHN), 55.3 (CH\(_3\)O), 43.8 (CHAr) and 18.7 (CH\(_3\)CH); (Found MH\(^+\), 376.1553; C\(_{23}\)H\(_{22}\)F\(_5\)NO\(_4\) requires 376.1543).

MKR of active ester (rac)-95 using ethyl 2-oxa-oxazolidin-4-carboxylate (rac)-157 [T2.14; E1].

In the same way as T2.7; E1, n-BuLi (2.76 ml, 2.5M in hexanes, 6.91 mmol), ethyl 2-oxa-oxazolidin-4-carboxylate (rac)-157 (1 g, 6.28 mmol) and pentfluorophenyl-2-phenyl-propionate (rac)-95 (1.99 g, 6.28 mmol) in THF (15 ml). Gave a mixture of ethyl 2-oxa-3-(2-phenyl-propionyl)-oxazolidin-carboxylate (rac)-syn and (rac)-anti-157 (ratio syn : anti 95 : 5), purification by flash column chromatography.
on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3 → 1:1) gave 2-oxa-3-(2-phenyl-propionyl)-oxaolidin-carboxylate (rac)-anti-158 (50 mg, 3%) as an oil; $R_F$ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.39; $\nu_{\text{max}}$ (CHCl$_3$)/cm$^{-1}$ 1794, 1747 and 1705 (3 × C=O); $\delta_H$ (400 MHz; CDCl$_3$) 7.33-7.20 (5H, m 5 × CH; Ph), 5.10 (1H, q, $J$ 7.0, CHCH$_3$), 4.77 (1H, dd, $J$ 9.4 and 3.7, CHN), 4.38 (1H, t, $J$ 9.4, CH$_2$H$_3$), 4.31-4.21 (3H, m, CH$_3$H$_2$O and CH$_2$CH$_3$), 1.50 (3H, d, $J$ 7.0, CH$_3$CH) and 1.30 (3H, t, $J$ 7.2, CH$_3$CH$_2$); $\delta_C$ (100 MHz; CDCl$_3$) 174.5, 168.7 and 152.1 (3 × C=O), 140.0 (i-C; Ph), 128.7, 128.3 and 127.4 (5 × CH; Ph), 64.3 (CH$_2$O), 62.6 (CH$_2$O), 55.9 (CHN), 43.0 (CHCH$_3$), 19.3 (CH$_2$CH$_3$) and 14.1 (CH$_2$CH$_3$); (Found MH$^+$, 292.1195; C$_{15}$H$_{18}$NO$_3$ requires 292.1185), and 2-oxa-3-(2-phenyl-propionyl)-oxaolidin-carboxylate (rac)-syn-158 (0.54 g, 30%) as an oil; $R_F$ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.30; $\nu_{\text{max}}$ (CHCl$_3$)/cm$^{-1}$ 1793, 1747 and 1705 (3 × C=O); $\delta_H$ (400 MHz; CDCl$_3$) 7.40-7.20 (5H, m 5 × CH; Ph), 5.03 (1H, q, $J$ 7.0, CHCH$_3$), 4.94 (1H, dd, $J$ 9.3 and 4.9, CHN), 4.52 (1H, t, $J$ 9.3, CH$_2$H$_3$), 4.23 (1H, dd, $J$ 9.3 and 4.9, CH$_2$H$_3$), 4.11 (2H, q, $J$ 7.1, CH$_2$CH$_3$), 1.48 (3H, d, $J$ 7.0, CH$_2$CH) and 1.11 (3H, t, $J$ 7.2, CH$_3$CH$_2$); $\delta_C$ (100 MHz; CDCl$_3$) 174.3, 168.1 and 152.0 (3 × C=O), 139.8 (i-C; Ph), 128.5, 128.2 and 127.2 (5 × CH; Ph), 64.3 (CH$_2$O), 62.4 (CH$_2$O), 55.7 (CHN), 43.2 (CHCH$_3$), 19.4 (CH$_2$CH$_3$) and 13.9 (CH$_2$CH$_3$); (Found MH$^+$, 292.1195; C$_{15}$H$_{18}$NO$_3$ requires 292.1185).

MKR of active ester (rac)-126 using ethyl 2-oxa-oxazolidin-4-carboxylate (rac)-157 [T2.14; E2].

In the same way as T2.7; E1, n-BuLi (0.18 ml, 2.5M in hexanes, 0.45 mmol), ethyl 2-oxa-oxazolidin-4-carboxylate (rac)-157 (66 mg, 0.41 mmol) and pentafluorophenyl 2-phenyl-3-methyl-butanoate (rac)-126 (0.142 g, 0.41 mmol) in THF (5 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of ethyl 2-oxa-3-(2-phenyl-3-methyl-butanyl)-oxaolidin-carboxylate (rac)-syn and (rac)-anti-159 (70 mg, 52%, ratio syn : anti 57 : 43), a clear solid mp 70-74 °C; $R_F$ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.41; $\nu_{\text{max}}$ (CHCl$_3$)/cm$^{-1}$ 1791, 1749 and 1702 (3 × C=O); $\delta_H$ (400 MHz; CDCl$_3$) 7.33-7.29 (2H, m, 2 × CH; Ph), 7.26-7.14 (3H, m, 3 × CH; Ph), 4.88 (2H, dd, $J$ 9.6 and 4.4, CHN), 4.61 (1H, d, $J$ 10.6, PhCH), 4.45 (1H, t, $J$ 9.6, CH$_2$H$_3$), 4.16 (1H, dd, $J$ 9.6 and 4.4, CH$_2$H$_3$), 3.99-3.90 (2H, m, CH$_2$CH$_3$), 2.43-2.32 (1H, m, CH$_3$CHCH$_3$), 0.96 (3H, d, $J$ 6.4, CH$_3$CHCH$_3$), 0.91 (3H, t, $J$ 7.2, CH$_3$CH$_2$) and 0.64 (3H, d, $J$ 6.6, CH$_3$CHCH$_3$); $\delta_C$ (100 MHz; CDCl$_3$) 173.7,
MKR of active ester (rac)-117 using ethyl 2-oxa-oxazolidin-4-carboxylate (rac)-157 [T2.14; E3].

In the same way as T2.7; E1, n-BuLi (0.30 ml, 2.5M in hexanes, 0.75 mmol), ethyl 2-oxa-oxazolidin-4-carboxylate (rac)-157 (0.108 g, 0.68 mmol) and pentafluorophenyl-2-(4-chloro-phenyl)-propionate (rac)-117 (0.238 g, 0.68 mmol) in THF (12 ml). Gave a mixture of ethyl 2-oxa-3-[2-(4-chloro-phenyl)-propionyl]-oxaolidin-carboxylate (rac)-syn and (rac)-anti-160 (ratio syn : anti 95 : 5), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) gave 2-oxa-3-[2-(4-chloro-phenyl)-propionyl]-oxaolidin-carboxylate (rac)-syn-160 (50 mg, 23%) as an oil; $R_f$ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.17; $\nu_{max}$ (CHCl$_3$)/cm$^{-1}$ 1790, 1748 and 1705 (3 × C=O); $\delta_{HI}$ (400 MHz; CDCl$_3$) 7.50 (4H, s, 4 × CH; Ar), 5.01 (1H, q, J 7.0, CHAr), 4.95 (1H, dd, J 9.6 and 4.6, CHN), 4.55 (1H, t, J 9.6, $CH_AH_B$CHN), 4.26 (1H, dd, J 9.6 and 4.6, $CH_AH_B$CHN), 4.16 (2H, qd, J 7.2 and 1.1, $CH_B$CH$_3$), 1.47 (3H, d, J 7.0, $CH_B$CH) and 1.17 (3H, t, J 7.2, $CH_B$CH$_2$); $\delta_C$ (100 MHz; CDCl$_3$) 173.8, 167.9 and 151.9 (3 × C=O), 138.1 and 133.0 (2 × i-C; Ar), 129.6$^2$ and 128.6$^2$ (4 × CH; Ar), 64.2 (ArCH), 62.4 (CHN), 55.5 ($CH_2$CHN), 42.6 ($CH_2$CH$_3$), 19.2 ($CH_B$CH$_3$) and 13.8 ($CH_2$CH$_3$).

MKR of active ester (rac)-123 using ethyl 2-oxa-oxazolidin-4-carboxylate (rac)-157 [T2.14; E4].

In the same way as T2.7; E1, n-BuLi (0.58 ml, 2.5M in hexanes, 1.45 mmol), ethyl 2-oxa-oxazolidin-4-carboxylate (rac)-157 (0.210 g, 1.32 mmol) and pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propionate (rac)-123 (0.52 g, 1.32 mmol) in THF (12.5 ml). Gave a mixture of ethyl 2-oxa-3-[2-(6-methoxy-2-naphthyl)-propionyl]-oxaolidin-carboxylate (rac)-syn and (rac)-anti-161 (ratio syn : anti 97 : 3), purification by flash column chromatography on silica gel eluting with light petroleum
spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) gave 2-oxa-3-[2-(6-methoxy-2-naphthyl)-propionyl]-oxazolidin-carboxylate \((rac)-\text{syn-161}\) (0.22 g, 45%) as a white solid mp 106-108 °C; \(R_F\) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.12; \(\nu_{\max} \) (CHCl\(_3\))/cm\(^{-1}\) 1791, 1748 and 1704 (3 × C=O); \(\delta_H\) (400 MHz; CDCl\(_3\)) 7.76 (1H, br s, CH; Ar), 7.71 (2H, dd, \(J\) 8.6 and 4.0, 2 × CH; Ar), 7.46 (1H, dd, \(J\) 8.4 and 1.8, CH; Ar), 7.16-7.09 (2H, m, 2 × CH; Ar), 5.18 (1H, q, \(J\) 7.0, ArCH), 4.97 (1H, dd, \(J\) 9.7 and 4.8, CHN), 4.53 (1H, t, \(J\) 9.7, \(CH_A\)\(_3\)H\(_8\)CHN), 4.24 (1H, dd, \(J\) 9.7 and 4.8, CH\(_A\)H\(_8\)CHN), 4.14-4.05 (2H, m, CH\(_2\)CH\(_3\)), 3.91 (3H, s, CH\(_3\)O), 1.57 (3H, d, \(J\) 7.0, CH\(_3\)CH) and 1.05 (3H, t, \(J\) 7.2, CH\(_3\)CH\(_2\)); \(\delta_C\) (100 MHz; CDCl\(_3\)) 174.3, 167.9 and 157.6 (3 × C=O), 151.9, 134.8, 133.7 and 128.9 (4 × i-C; Ar), 129.4, 126.9, 126.9, 126.8, 118.7 and 105.5 (6 × CH; Ar), 64.2 (ArCH), 62.3 (CHN), 55.6 (CH\(_2\)CHN), 55.3 (CH\(_2\)CH\(_3\)), 43.0 (CH\(_3\)O), 19.2 (CHCH\(_3\)) and 13.7 (CH\(_2\)CH\(_3\)).

**MKR of acid chloride (rac)-132 using 4-benzyl-oxazolidin-2-one (rac)-145 [T2.15; E1].**

In the same way as T2.7; E1, n-BuLi (0.40 ml, 2.5M in hexanes, 0.99 mmol), 4-benzyl-oxazolidin-2-one (rac)-145 (0.16 g, 0.90 mmol) and 2-phenyl-3-methyl-butanyl chloride (rac)-132 (0.182 g, 0.90 mmol) in THF (10 ml). Gave a mixture of 3-(2-phenyl-3-methyl-butanyl)-4-benzyl-oxazolidin-2-one (rac)-syn and (rac)-anti-147 (ratio syn : anti 46 : 54), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) gave 3-(2-phenyl-3-methyl-butanyl)-4-benzyl-oxazolidin-2-one (rac)-anti-147 (80 mg, 26%) and 3-(2-phenyl-3-methyl-butanyl]-4-benzyl-oxazolidin-2-one (rac)-syn-147 (30 mg, 10%), which were spectroscopically identical to that obtained elsewhere.

**MKR of acid chloride (rac)-133 using 4-benzyl-oxazolidin-2-one (rac)-145 [T2.15; E2].**

In the same way as T2.7; E1, n-BuLi (0.37 ml, 2.5M in hexanes, 0.93 mmol), 4-benzyl-oxazolidin-2-one (rac)-145 (0.15 g, 0.85 mmol) and 2-(4-chloro-phenyl)-propionyl chloride (rac)-133 (0.172 g, 0.85 mmol) in THF (10 ml). Gave a mixture of ethyl 3-[2-(4-chloro-phenyl)-propionyl]-4-benzyl-oxazolidin-2-one (rac)-syn and (rac)-anti-148 (ratio syn : anti 47 : 53), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) gave 3-[2-(4-chloro-phenyl)-propionyl]-4-benzyl-oxazolidin-2-one (rac)-anti-148 (70 mg, 24%) and
3-[2-(4-chloro-phenyl)-propionyl]-4-benzyl-oxaolidin-2-one \textit{(rac)-syn-148} (50 mg, 17%), which were spectroscopically identical to that obtained elsewhere.

**MKR of acid chloride \textit{(rac)-140} using 4-isopropyl-oxaolidin-2-one \textit{(rac)-24} \textbf{[T2.16; E1]}.**

In the same way as T2.7; E1, n-BuLi (0.83 ml, 2.5M in hexanes, 2.13 mmol), 4-isopropyl-oxaolidin-2-one \textit{(rac)-24} (0.25 g, 1.94 mmol) and 2-phenyl-propionyl chloride \textit{(rac)-140} (0.33 g, 1.94 mmol) in THF (5 ml). Gave a mixture of 3-(2-phenyl-propionyl)-4-isopropyl-oxaolidin-2-one \textit{(rac)-syn} and \textit{(rac)-anti-97} (ratio syn : anti 45 : 55), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) gave 3-(2-phenyl-propionyl)-4-isopropyl-oxaolidin-2-one \textit{(rac)-anti-97} (0.14 g, 27%) and 3-(2-phenyl-propionyl)-4-isopropyl-oxaolidin-2-one \textit{(rac)-syn-97} (0.15 g, 29%), which were spectroscopically identical to that obtained elsewhere.

**MKR of acid chloride \textit{(rac)-132} using 4-isopropyl-oxaolidin-2-one \textit{(rac)-24} \textbf{[T2.16; E2]}.**

In the same way as T2.7; E1, n-BuLi (0.41 ml, 2.5M in hexanes, 1.02 mmol), 4-isopropyl-oxaolidin-2-one \textit{(rac)-24} (0.12 g, 0.93 mmol) and 2-phenyl-3-methyl-butanyl chloride \textit{(rac)-132} (0.188 g, 0.93 mmol) in THF (12.5 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) an inseparable mixture of 3-[2-(4-chloro-phenyl)-propionyl]-4-isopropyl-oxaolidin-2-one \textit{(rac)-syn} and \textit{(rac)-anti-150} (0.13 g, 47%, ratio syn : anti 40 : 60), which were spectroscopically identical to that obtained elsewhere.

**MKR of acid chloride \textit{(rac)-133} using 4-isopropyl-oxaolidin-2-one \textit{(rac)-24} \textbf{[T2.16; E3]}.**

In the same way as T2.7; E1, n-BuLi (0.35 ml, 2.5M in hexanes, 0.88 mmol), 4-isopropyl-oxaolidin-2-one \textit{(rac)-24} (0.10 g, 0.80 mmol) and 2-(4-chloro-phenyl)-propionyl chloride \textit{(rac)-133} (0.163 g, 0.80 mmol) in THF (10 ml). Gave a mixture of ethyl 3-[2-(4-chloro-phenyl)-propionyl]-4-isopropyl-oxaolidin-2-one \textit{(rac)-syn} and \textit{(rac)-anti-151} (ratio syn : anti 36 : 64), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) gave 3-[2-(4-chloro-phenyl)-propionyl]-4-isopropyl-oxaolidin-2-one \textit{(rac)-anti-151} (80 mg, 34%)
and 3-[2-(4-chloro-phenyl)-propionyl]-4-isopropyl-oxaolidin-2-one \( (\text{rac}-\text{syn})-151 \) (30 mg, 15%), which were spectroscopically identical to that obtained elsewhere.

**MKR of acid chloride \( (\text{rac})-140 \) using 4-phenyl-oxaolidin-2-one \( (\text{rac})-94 \) [T2.17; E1].**

See T2.9; E7.

**MKR of acid chloride \( (\text{rac})-131 \) using 4-phenyl-oxaolidin-2-one \( (\text{rac})-94 \) [T2.17; E2].**

In the same way as T2.7; E1, \( n \)-BuLi (1.75 ml, 2.5M in hexanes, 4.38 mmol), 4-phenyl-oxaolidin-2-one \( (\text{rac})-94 \) (0.65 g, 3.99 mmol) and 2-phenyl-butanyl chloride \( (\text{rac})-131 \) (0.73 g, 3.99 mmol) in THF (10 ml). Gave a mixture of 3-(2-phenyl-butanyl)-4-phenyl-oxaolidin-2-one \( (\text{rac})-\text{syn} \) and \( (\text{rac})-\text{anti} \) \( 153 \) (ratio \( \text{syn} : \text{anti} \) 88: 12), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) gave of 3-(2-phenyl-butanyl)-4-phenyl-oxaolidin-2-one \( (\text{rac})-\text{anti} \) \( 153 \) (40 mg, 3%) as an oil; \( R_f \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.41; \( \nu_{\max} (\text{CHCl}_3)/\text{cm}^{-1} \) 1780 and 1703 (2 × C=O); \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.44-7.21 (10H, m, \( 10 \times \text{CH} \); Ph), 5.34 (1H, dd, \( J 8.7 \) and 3.4, CHN), 4.96 (1H, t, \( J 7.7 \), CH\(_2\)CH\(_2\)), 4.54 (1H, br t, \( J 8.7 \), CH\(_2\)CH\(_2\)B\(_8\)O), 4.20 (1H, dd, \( J 8.7 \) and 3.4, CH\(_2\)H\(_8\)O), 2.18-1.97 (1H, m, CH\(_2\)H\(_8\)CH\(_3\)), 1.86-1.68 (1H, m, CH\(_2\)H\(_8\)CH\(_3\)) and 0.76 (3H, t, \( J 7.4 \), CH\(_2\)CH\(_2\)) \( \delta_C \) (100 MHz; CDCl\(_3\)) 173.7 and 153.4 (2 × C=O), 139.5 and 138.6 (2 × i-C; Ar), 129.1 \(^2\) 128.8 \(^2\) 128.7 \(^1\) 128.5 \(^2\) 127.3 \(^1\) and 125.8 \(^2\) (10 × CH; 2 × Ph), 69.4 (CH\(_2\)O), 58.1 (CHN), 50.4 (PhCH), 27.7 (CH\(_2\)CH\(_3\)) and 12.0 (CH\(_2\)CH\(_3\)); (Found MH\(^+\), 310.1430; C\(_{19}\)H\(_{28}\)NO\(_3\) requires 310.1443), and 3-(2-phenyl-butoxynyl)-4-phenyl-oxaolidin-2-one \( (\text{rac})-\text{syn} \) \( 153 \) (0.49 g, 40%), as a yellow solid mp 58-62 °C; \( R_f \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.33; \( \nu_{\max} (\text{CHCl}_3)/\text{cm}^{-1} \) 1772 and 1700 (2 × C=O); \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.17-7.09 (6H, m, \( 6 \times \text{CH} \); Ph), 7.04-7.02 (2H, m, \( 2 \times \text{CH} \); Ph), 6.81-6.79 (2H, m, \( 2 \times \text{CH} \); Ph), 5.38 (1H, dd, \( J 8.8 \) and 5.0, CHN), 4.82 (1H, t, \( J 7.5 \), CHCH\(_2\)), 4.55 (1H, t, \( J 8.8 \), CH\(_2\)H\(_8\)O), 3.98 (1H, dd, \( J 8.8 \) and 5.0, CH\(_2\)H\(_8\)O), 2.01-1.90 (1H, m, CH\(_2\)H\(_8\)CH\(_3\)), 1.68-1.57 (1H, m, CH\(_2\)H\(_8\)CH\(_3\)) and 0.84 (3H, t, \( J 7.5 \), CH\(_2\)CH\(_3\)) \( \delta_C \) (100 MHz; CDCl\(_3\)) 173.0 and 153.1 (2 × C=O), 138.2 and 138.0 (2 × i-C; 2 × Ph), 128.8 \(^2\) 128.7 \(^2\) 128.4 \(^1\) 128.3 \(^2\) 127.1 \(^1\) and 125.6 \(^2\) (10 × CH; 2 × Ph), 69.4 (CH\(_2\)O), 57.7 (CHN), 51.1 (PhCH), 26.2 (CH\(_2\)CH\(_3\)) and 11.9 (CH\(_2\)CH\(_3\)); (Found MH\(^+\), 310.1437; C\(_{19}\)H\(_{28}\)NO\(_3\) requires 310.1443).
MKR of acid chloride \((rac)-132\) using 4-phenyl-oxazolidin-2-one \((rac)-94\) [T2.17; E3].

In the same way as T2.7; E1, \(n\)-BuLi (0.43 ml, 2.5M in hexanes, 1.08 mmol), 4-phenyl-oxazolidin-2-one \((rac)-94\) (0.16 g, 0.98 mmol) and 2-phenyl-3-methyl-butyl chloride \((rac)-132\) (0.190 g, 0.98 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) gave of 3-[2-(phenyl-3-methyl-butyl)oxazolidin-2-one \((rac)-syn\) and \((rac)-anti-154\) (0.21 g, 66%, ratio \(syn : anti\) 71 : 29) as an oil, which were spectroscopically identical to that obtained elsewhere.

MKR of acid chloride \((rac)-133\) using 4-phenyl-oxazolidin-2-one \((rac)-94\) [T2.17; E4].

In the same way as T2.7; E1, \(n\)-BuLi (0.53 ml, 2.5M in hexanes, 1.33 mmol), 4-phenyl-oxazolidin-2-one \((rac)-94\) (0.20 g, 1.21 mmol) and 2-(4-chloro-phenyl)propionyl chloride \((rac)-133\) (0.245 g, 1.12 mmol) in THF (10 ml). Gave a mixture of ethyl 3-[2-(4-chloro-phenyl)-propionyl]-4-phenyl-oxaolidin-2-one \((rac)-syn\) and \((rac)-anti-155\) (ratio \(syn : anti\) 51 : 49), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) gave of 3-[2-(4-chloro-phenyl)-propionyl]-4-phenyl-oxaolidin-2-one \((rac)-anti-155\) (90 mg, 23%) and 3-[2-(4-chloro-phenyl)-propionyl]-4-phenyl-oxaolidin-2-one \((rac)-syn-155\) (0.11 g, 28%), which were spectroscopically identical to that obtained elsewhere.

MKR of acid chloride \((rac)-132\) using ethyl 2-oxa-oxazolidin-4-carboxylate \((rac)-157\) [T2.18; E1].

In the same way as T2.7; E1, \(n\)-BuLi (0.39 ml, 2.5M in hexanes, 0.92 mmol), ethyl 2-oxa-oxazolidin-4-carboxylate \((rac)-157\) (0.14 g, 0.88 mmol) and 2-phenyl-3-methyl-butyl chloride \((rac)-132\) (0.178 g, 0.88 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) an inseparable mixture of ethyl 2-oxa-3-(2-phenyl-3-methyl-butyl)-oxaolidin-carboxylate \((rac)-syn\) and \((rac)-anti-159\) (0.16 g, 56%, ratio \(syn : anti\) 35 : 65), which were spectroscopically identical to that obtained elsewhere.
MKR of acid chloride (rac)-133 using ethyl 2-oxa-oxazolidin-4-carboxylate (rac)-157 [T2.18; E2].

In the same way as T2.7; E1, n-BuLi (0.48 ml, 2.5M in hexanes, 1.19 mmol), ethyl 2-oxa-oxazolidin-4-carboxylate (rac)-157 (0.17 g, 1.08 mmol) and 2-(4-chlorophenyl)-propionyl chloride (rac)-133 (0.220 g, 1.08 mmol) in THF (10 ml). Gave a mixture of ethyl 2-oxa-3-[2-(4-chloro-phenyl)-propionyl]-oxazolidin-carboxylate (rac)-syn (rac)-anti-160 (ratio syn : anti 50 : 50), purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3 → 1:1) gave 2-oxa-3-[2-(4-chloro-phenyl)-propionyl]-oxazolidin-carboxylate (rac)-anti-160 (90 mg, 26%) as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.40; vmax (CHCl3)/cm⁻¹ 1790, 1748 and 1713 (3 × C=O); δH (400 MHz; CDCl3) 7.32-7.24 (4H, m, 4 × CH; Ar), 5.09 (1H, q, J 7.0, CHAr), 4.79 (1H, dd, J 9.4 and 3.7, CHN), 4.45 (1H, t, J 9.4, CH₂H₂CHN), 4.33-4.24 (3H, m, CH₂H₂CHN and CH₂CH₃), 1.50 (3H, d, J 7.0, CH₃CH) and 1.31 (3H, t, J 7.2, CH₃CH₂); δC (100 MHz; CDCl3) 174.1, 168.4 and 152.0 (3 × C=O), 138.2 and 133.3 (2 × i-C; Ar), 129.6² and 128.8² (4 × CH; Ar), 64.3 (ArCH), 62.6 (CHN), 55.7 (CH₂CHN), 42.3 (CH₂CH₃), 19.1 (CHCH₃) and 14.0 (CH₂CH₃), and 2-oxa-3-[2-(4-chloro-phenyl)-propionyl]-oxazolidin-carboxylate (rac)-syn-160 (60 mg, 17%), which was spectroscopically identical to that obtained elsewhere.

PKR of active ester (rac)-126 using 4-phenyl-oxazolidin-2-one (R)-94 and 4-isopropyl-oxazolidin-2-one (S)-24 [S2.15].

In the same way as T2.7; E1, n-BuLi (0.57 ml, 2.5M in hexanes, 1.43 mmol), 4-phenyl-oxazolidin-2-one (R)-94 (0.106 g, 0.65 mmol), 4-isopropyl-oxazolidin-2-one (S)-24 (84 mg, 0.65 mmol) and pentafluorophenyl-2-phenyl-3-methyl-butanoate (rac)-126 (0.449 g, 1.30 mmol) in THF (12 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) a mixture of 3-(2-phenyl-3-methyl-butanyl)-4-phenyl-oxazolidin-2-one (S,R)-syn and (R,R)-anti-154 (0.178 g, 85%, ratio syn : anti 84 : 16) and a mixture of 3-(2-phenyl-3-methyl-butanyl)-4-isopropyl-oxazolidin-2-one (R,S)-syn and (S,S)-anti-150 (0.145 g, 78%, ratio syn : anti 79 : 21), which were spectroscopically identical to that obtained elsewhere.
KR of active ester (rac)-126 using 4-benzyl-oxazolidin-2-one (R)-145 [S2.16].

In the same way as T2.7; E1, n-BuLi (3.36 ml, 2.5M in hexanes, 8.40 mmol), 4-benzyl-oxazolidin-2-one (R)-145 (0.106 g, 0.65 mmol) and pentafluorophenyl-2-phenyl-3-methyl-butanoate (rac)-126 (2.63 g, 7.64 mmol) in THF (30 ml). Gave a mixture of 3-(2-phenyl-3-methyl-butanyl)-4-benzyl-oxaolidin-2-one (S,R-syn and (R,R)-anti-148 (ratio syn : anti 57 : 43), after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) obtained 3-(2-phenyl-3-methyl-butanyl)-4-benzyl-oxaolidin-2-one (R,R)-anti-148 (0.76 g, 29%) as a white solid mp 114-116°C; [α]D = -78.0 (c 5.4, CHCl₃), and 3-(2-phenyl-3-methyl-butanyl)-4-benzyl-oxaolidin-2-one (S,R-syn-148 (1.02 g, 40%) as an oil; [α]D = -40.3 (c 2.8, CHCl₃), which were spectroscopically identical to that obtained elsewhere.

Hydrolysis of 3-(2-phenyl-3-methyl-butanyl)-4-benzyl-oxaolidin-2-one (S,R)-syn-148 [S2.17; E1].

LiOH.H₂O (0.24 g, 5.81 mmol) and H₂O₂ (1.65 ml, 3.53M in water, 5.81 mmol) were added to a mixture of 3-(2-phenyl-3-methyl-butanyl)-4-benzyl-oxaolidin-2-one (S,R)-syn-148 (0.98 g, 2.91 mmol) in THF/water (3:1, 40 ml). The resulting mixture was stirred over night, diluted with water (20 ml), extracted with dichloromethane (3 × 20 ml), dried over MgSO₄, and evaporated under reduced pressure to give 4-benzyl-oxaolidin-2-one (R)-145 (0.489 g, 95%) as an yellow solid mp 64-70 °C; Rf [dichloromethane] 0.11; [α]D = +35.6 (c 5.0, CHCl₃); νmax (CHCl₃)/cm⁻¹ 1758 (C=O); δH (400 MHz; CDCl₃) 7.36-7.23 (3H, m, 3 × CH; Ph), 7.17 (2H, br d, J 6.9, 2× CH; Ph), 6.08 (1H, s, NH), 4.41 (1H, t, J 8.13, CH₃CH₅O), 4.13 (1H, dd, J 8.13 and 5.63, CH₃HHO), 4.14-4.04 (1H, m, CHN) and 2.87 (2H, qd, J 11.6 and 6.6, CH₂Ph); δC (100 MHz; CDCl₃) 159.5 (C=O), 135.9 (i-C; Ph), 129.0 2 128.9 2 and 127.1 5 (× CH; Ph), 69.5 (CH₂O), 53.7 (CHN) and 41.3 (CH₂Ph). The aqueous layer was acidified (3M HCl) extracted with dichloromethane (3 × 20 ml), dried over MgSO₄, and evaporated under reduced pressure to give 2-phenyl-3-methyl-butionic acid (S)-124 (0.35 g, 68%), as an oil; Rf [dichloromethane] 0.19; [α]D = +57.8 (c 3.6, CHCl₃); νmax (CHCl₃)/cm⁻¹ 1705 (C=O); δH (400 MHz; CDCl₃) 7.35-7.23 (5H, m, 5 × CH; Ph), 3.14 (1H, d, J 10.6, PhCH), 2.39-2.28 (1H, m, CH₂CH₃H₂), 1.08 (3H, d, J 6.6, CH₃CH₃H₂) and 0.71 (3H, d, J 6.8, CH₃CH₃H₃); δC (100 MHz; CDCl₃) 179.8 (C=O), 137.7 (i-C; Ph), 128.6 2 128.5 2 and 127.4 5 (× CH; Ph), 59.9 (PhCH), 31.5 (CH₃CH₃H₂), 21.4 and 20.1 (2 × CH₃).
Hydrolysis of 3-(2-phenyl-3-methyl-butanyl)-4-benzyl-oxazolidin-2-one \((R,R)-anti-148\) [S2.17; E2].

In the same way as S2.17; E1, 3-(2-phenyl-3-methyl-butanyl)-4-benzyl-oxazolidin-2-one \((R,R)-anti-148\) (0.70 g, 2.08 mmol), LiOH.H₂O (0.17 g, 4.15 mmol) and H₂O₂ (1.65 ml, 3.53M in water, 4.15 mmol) in THF/water (3:1, 40 ml). Gave 4-benzyl-oxazolidin-2-one \((R)-145\) (0.249 g, 95%), and 2-phenyl-3-methyl-butionic acid \((R)-124\) (0.35 g, 95%), as an oil; \([\alpha]_D^{20} = -57.6\) (c 3.2, CHCl₃), which were spectroscopically identical to that obtained elsewhere.

**Stereo-specific synthesis 3-(2-phenyl-3-methyl-butionyl)-4-methyl-5-phenyl-oxazolidin-2-one \((S,R,S)-syn-syn-142\) [S2.18; E1].**

In the same way as T2.7; E1, n-BuLi (0.06 ml, 2.5M in hexanes, 0.16 mmol), 4-methyl-5-phenyl-oxazolidin-2-one \((R,S)-syn-104\) (26 mg, 0.145 mmol) and pentafluorophenyl-2-phenyl-3-methyl-butanionate \((S)-126\) (50 mg, 0.145 mmol) in THF (7.5 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 3-(2-phenyl-3-methyl-butionyl)-4-methyl-5-phenyl-oxaolidin-2-one \((S,R,S)-syn-syn-142\) (11 mg, 22%) as a white solid mp 69-73 °C; \([\alpha]_D^{20} = +61.1\) (c 2.2, CHCl₃), which was spectroscopically identical to that obtained elsewhere.

**Stereo-specific synthesis 3-(2-phenyl-3-methyl-butanyl)-4-isopropyl-oxazolidin-2-one \((R,S)-syn-150\) [S2.18; E2].**

In the same way as T2.7; E2, n-BuLi (0.05 ml, 2.5M in hexanes, 0.134 mmol), 4-isopropyl-oxazolidin-2-one \((S)-24\) (16 mg, 0.122 mmol) and pentafluorophenyl-2-phenyl-3-methyl-butanoate \((R)-126\) (42 mg, 0.122 mmol) in THF (7.5 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 3-(2-phenyl-3-methyl-butionyl)-4-isopropyl-oxaolidin-2-one \((R,S)-syn-150\) (13 mg, 36%) as an oil; \(R_f\) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.57; \([\alpha]_D^{20} = +0.46\) (c 2.6, CHCl₃), which was spectroscopically identical to that obtained elsewhere.
Stereo-specific synthesis 3-(2-phenyl-3-methyl-butanyl)-4-phenyl-oxazolidin-2-one (R,S)-syn-154 [S2.18; E3].

In the same way as T2.7; E2, n-BuLi (0.10 ml, 2.5M in hexanes, 0.262 mmol), 4-phenyl-oxazolidin-2-one (R)-94 (39 mg, 0.238 mmol) and pentafluorophenyl-2-phenyl-3-methyl-butanoate (S)-126 (82 mg, 0.238 mmol) in THF (7.5 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 3-(2-phenyl-3-methyl-butyonil)-4-phenyl-oxazolidin-2-one (R,S)-syn-154 (4 mg, 5%) as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.46; [α]D0 = +45.5 (c 0.8, CHCl3), which was spectroscopically identical to that obtained elsewhere.

Hydrolysis of 3-(2-phenylpropionyl)-4-methyl-3-phenyl-oxazolidin-2-one (R,R,S)-anti-syn-141 [S2.19].

In the same way as S2.17; E1, 3-(2-phenylpropionyl)-4-methyl-3-phenyl-oxazolidin-2-one (R,R,S)-anti-syn-141 (1.378 g, 4.45 mmol), LiOH.H2O (0.374 g, 8.91 mmol) and H2O2 (2.52 ml, 3.53M in water, 8.91mmol) in THF/water (3:1, 10 ml). Gave 4-phenyl-3-phenyl-oxazolidin-2-one (R,S)-syn-104 (0.755 g, 96%), and 2-phenyl-propionic acid (R)-111 (0.598 g, 89%), as an oil; [α]D0 = -60.5 (c 8.2, CHCl3); Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:9)] 0.5; vmax (CHCl3)/cm⁻¹ 1706 (C=O); δH (400 MHz; CDCl3) 7.45-6.98 (5H, m, 5 × CH; Ph), 3.75 (1H, q, J 7.2, PhCHCH3) and 1.50 (3H, d, J 7.2, PhCHCH3); δC (100 MHz; CDCl3) 180.4 (C=O), 139.7 (i-C; Ph), 128.7, 127.6² and 127.4² (5 × CH; Ph), 45.3 (PhCHCH3) and 18.1 (PhCHCH3); (Found MH⁺, 151.0753; C₉H₁₁NO₂ requires 151.0759).

Hydrolysis of 3-[2-(4-chloro-phenyl)-propionyl]-4-isopropyl-oxazolidin-2-one (R,S)-syn-151 [S2.20; E1].

In the same way as S2.17; E1, 3-[2-(4-chloro-phenyl)-propionyl]-4-isopropyl-oxazolidin-2-one (R,S)-syn-151 (0.51 g, 1.49 mmol), LiOH.H₂O (0.13 g, 2.99 mmol) and H₂O₂ (0.85 ml, 3.53M in water, 2.99 mmol) in THF/water (3:1, 8 ml). Gave 4-isopropyl-oxazolidin-2-one (S)-24 (0.17 g, 88%), and 2-(4-chloro-phenyl)-propionic acid (R)-116 (0.27 g, 98%), as an solid mp 59-61°C; Rf [dichloromethane] 0.06; [α]D0 = -23.0 (c 0.4, CHCl₃); vmax (CHCl₃)/cm⁻¹ 1710 (C=O); δH (400 MHz; CDCl₃) 7.30 (2H, dt, J 8.8 and 2.2, 2 × CH; Ar), 7.25 (2H, dt, J 8.8 and 2.2, 2 × CH; Ar), 3.72 (1H, q, J 7.2, CH) and 1.50 (3H, d, J 7.2, CH₃); δC (100 MHz; CDCl₃) 178.9 (C=O), 138.2 and 133.3 (2 × i-C; Ar), 129.0² and 128.8² (4 × CH; Ar), 44.5 (CH) and 18.1 (CH₃).
Hydrolysis of 3-[2-(4-chloro-phenyl)-propionyl]-4-isopropyl-oxazolidin-2-one (S,S)-anti-151 [S2.20; E2].

In the same way as S2.17; E1, 3-[2-(4-chloro-phenyl)-propionyl]-4-isopropyl-oxazolidin-2-one (S,S)-anti-151 (0.378 g, 1.28 mmol), LiOH.H₂O (0.11 g, 2.55 mmol) and H₂O₂ (0.72 ml, 3.53M in water, 2.55 mmol) in THF/water (3:1, 4 ml). Gave 4-isopropyl-oxazolidin-2-one (S)-24 (0.15 g, 91%), and 2-(4-chloro-phenyl)-propionic acid (S)-116 (0.20 g, 85%), as an solid mp 49-53°C; [α]D = +48.5 (c 4.0, CHCl₃), which was spectroscopically identical to that obtained elsewhere.

Hydrolysis of 3-[2-(6-methoxy-2-naphthyl)-propionyl]-4-isopropyl-oxazolidin-2-one (S,R)-syn-152 [S2.21].

In the same way as S2.17; E1, 3-[2-(6-methoxy-2-naphthyl)-propionyl]-4-isopropyl-oxazolidin-2-one (S,R)-syn-152 (0.12 g, 0.35 mmol), LiOH.H₂O (29 mg, 0.70 mmol) and H₂O₂ (0.20 ml, 3.53M in water, 0.70 mmol) in THF/water (3:1, 4 ml). Gave 4-isopropyl-oxazolidin-2-one (R)-24 (21 mg, 46%), and 2-(6-methoxy-2-naphthyl)-propionic acid (S)-122 (40 mg, 49%), which were spectroscopically identical to that obtained elsewhere.

Hydrolysis of 3-(2-phenyl-propionly)-4-phenyl-oxazolidin-2-one (S,R)-syn-96 [S2.22; E1].

In the same way as S2.17; E1, 3-(2-phenyl-propionly)-4-phenyl-oxazolidin-2-one (S,R)-syn-96 (2.333 g, 7.90 mmol), LiOH.H₂O (0.663 g, 15.80 mmol) and H₂O₂ (4.48 ml, 3.53M in water, 15.80 mmol) in THF/water (3:1, 40 ml). Gave 4-phenyl-oxazolidin-2-one (R)-94 (0.889 mg, 69%), and 2-phenyl-propionic acid (S)-111 (0.918 g, 77%), which were spectroscopically identical to that obtained elsewhere.

Hydrolysis of 3-(2-phenyl-propionly)-4-phenyl-oxazolidin-2-one (R,R)-anti-96 [S2.22; E2].

In the same way as S2.17; E1, 3-(2-phenyl-propionly)-4-phenyl-oxazolidin-2-one (R,R)-anti-96 (1.72 g, 5.15 mmol), LiOH.H₂O (0.43 g, 10.29 mmol) and H₂O₂ (2.92 ml, 3.53M in water, 10.29 mmol) in THF/water (3:1, 40 ml). Gave 4-phenyl-oxazolidin-2-one (R)-94 (0.60 g, 71%), and 2-phenyl-propionic acid (R)-111 (0.60 g, 78%), which were spectroscopically identical to that obtained elsewhere.
Hydrolysis of 3-(2-deuterio-2-phenyl-propionly)-4-phenyl-oxazolidin-2-one (R,S)-syn-161 [S2.22; E3].

In the same way as S2.17; E1, 3-(2-deuterio-2-phenyl-propionly)-4-phenyl-oxazolidin-2-one (R,S)-syn-161 (44 mg, 0.15 mmol), LiOH.H₂O (12 mg, 0.30 mmol) and H₂O₂ (0.08 ml, 3.53M in water, 0.30 mmol) in THF/water (3:1, 4 ml). Gave 4-phenyl-oxazolidin-2-one (S)-94 (23 mg, 95%), which was spectroscopically identical to that obtained elsewhere, and 2-deuterio-2-phenyl-propionic acid (R)-162 (15 mg, 67%), as a white solid mp 45-50 °C; R_F [dichloromethane] 0.10; [α]_D^20 = -63.6 (c 3.0, CHCl₃); νmax (CHCl₃)/cm⁻¹ 2400 (CD) and 1732 (C=O); δ_H (CDCl₃) 7.29-7.17 (5H, m, 5 × CH; Ph) and 1.44 (3H, CH₃); δ_C (CDCl₃) 180.7 (C=O), 140.1 (i-C; Ph), 129.1, 128.0, and 127.8 (5 × CH; Ph), 45.4 (1C, t [1:1:1], J_C,D 20.1 CD) and 18.4 (CH₃); (Found MNH₂⁺, 169.1081; C₉H₁₃DNO₂ requires 169.1082).

Hydrolysis of 3-[2-(4-chloro-phenyl)-propionly]-4-phenyl-oxazolidin-2-one (S,R)-syn-155 [S2.23].

In the same way as S2.17; E1, 3-[2-(4-chloro-phenyl)-propionly]-4-phenyl-oxazolidin-2-one (S,R)-syn-155 (92 mg, 0.28 mmol), LiOH.H₂O (23 mg, 0.56 mmol) and H₂O₂ (0.16 ml, 3.53M in water, 0.56 mmol) in THF/water (3:1, 8 ml). Gave 4-phenyl-oxazolidin-2-one (R)-94 (43 mg, 95%), and 2-(4-chloro-phenyl)-propionic acid (S)-116 (46 mg, 89%), which were spectroscopically identical to that obtained elsewhere.

Hydrolysis of 3-[2-(4-isobutyl-phenyl)-propionly]-4-phenyl-oxazolidin-2-one (S,S)-anti-163 [S2.24].

In the same way as S2.17; E1, 3-[2-(4-isobutyl-phenyl)-propionly]-4-phenyl-oxazolidin-2-one (S,S)-anti-163 (75 mg, 0.21 mmol), LiOH.H₂O (18 mg, 0.43 mmol) and H₂O₂ (0.12 ml, 3.53M in water, 0.43 mmol) in THF/water (3:1, 4 ml). Gave 4-phenyl-oxazolidin-2-one (S)-94 (34 mg, 95%), and 2-(4-isobutylly-phenyl)-propionic acid (S)-114 (44 mg, 95%), which were spectroscopically identical to that obtained elsewhere.

MKR of 4-phenyl-oxazolidin-2-one (rac)-94 using active ester (rac)-165 [T2.19; E1].

In the same way as T2.7; E1, n-BuLi (0.90 ml, 2.5M in hexanes, 2.25 mmol), 4-phenyl-oxazolidin-2-one (rac)-94 (0.334 mg, 2.05 mmol) and pentafluorophenyl-2-
acetoxy-2-phenyl-acetate (rac)-165 (0.773 g, 2.05 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3 → 3:7) 3-(2-acetoxy-2-phenyl-acetate)-4-phenyl-oxaolidin-2-one (rac)-syn-164 (0.189 g, 27%) and (rac)-anti-164 (0.227 g, 33%) (ratio syn : anti 44 : 56), which were spectroscopically identical to that obtained elsewhere.

MKR of 4-phenyl-oxazolidin-2-one (rac)-94 using active ester (rac)-166 [T2.19; E2].

In the same way as T2.7; E1, n-BuLi (0.29 ml, 2.5M in hexanes, 0.72 mmol), 4-phenyl-oxazolidin-2-one (rac)-94 (0.107 g, 0.66 mmol) and 2-methoxy-phenyl-2-acetoxy-2-phenyl-acetate (rac)-166 (0.168 g, 0.66 mmol) in THF (10 ml). Returned starting materials.

MKR of 4-phenyl-oxazolidin-2-one (rac)-94 using active ester (rac)-167 [T2.19; E3].

In the same way as T2.7; E1, n-BuLi (0.25 ml, 2.5M in hexanes, 0.62 mmol), 4-phenyl-oxazolidin-2-one (rac)-94 (92 mg, 0.56 mmol) and 4-methoxy-phenyl-2-acetoxy-2-phenyl-acetate (rac)-167 (0.144 g, 0.56 mmol) in THF (10 ml). Returned starting materials.

MKR of 4-phenyl-oxazolidin-2-one (rac)-94 using active ester (rac)-168 [T2.19; E4].

In the same way as T2.7; E1, n-BuLi (0.35 ml, 2.5M in hexanes, 0.89 mmol), 4-phenyl-oxazolidin-2-one (rac)-94 (0.131 mg, 0.81 mmol) and 4-chloro-phenyl-2-acetoxy-2-phenyl-acetate (rac)-168 (0.210 g, 0.81 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3 → 3:7) 3-(2-acetoxy-2-phenyl-acetate)-4-phenyl-oxaolidin-2-one (rac)-syn-164 (91 mg, 33%) and (rac)-anti-164 (9 mg, 4%) (ratio syn : anti 88 : 12), which were spectroscopically identical to that obtained elsewhere.

MKR of 4-phenyl-oxazolidin-2-one (rac)-94 using active ester (rac)-169 [T2.19; E5].

In the same way as T2.7; E1, n-BuLi (0.34 ml, 2.5M in hexanes, 0.84 mmol), 4-phenyl-oxazolidin-2-one (rac)-94 (0.121 mg, 0.76 mmol) and 4-methyl-phenyl-2-acetoxy-2-phenyl-acetate (rac)-169 (0.217 g, 0.76 mmol) in THF (10 ml). Gave by
crude $^1$H NMR 3-(2-acetoxy-2-phenyl-acetate)-4-phenyl-oxazolidin-2-one ($rac$)-syn and anti-$^{164}$ (<10%, ratio syn : anti 74 : 26), which were spectroscopically identical to that obtained elsewhere.

**Competitive MKR of active ester ($rac$)-168 and active ester ($rac$)-170 with 4-phenyl-oxazolidin-2-one ($rac$)-94 [S2.25].**

In the same way as T2.7; E1, $n$-BuLi (0.28 ml, 2.5M in hexanes, 0.70 mmol), 4-phenyl-oxazolidin-2-one ($rac$)-$^{94}$ (0.104 g, 0.64 mmol), pentafluorophenyl-2-(benzyl-acetoxy)-2-phenyl-acetate ($rac$)-$^{170}$ (0.278 g, 0.64 mmol) and 4-chlorophenyl-2-acetoxy-2-phenyl-acetate ($rac$)-$^{168}$ (0.166 g, 0.64 mmol) in THF (10 ml). Gave by crude 1H NMR 3-[2-(benzyl-acetoxy)-2-phenyl-acetate]-4-phenyl-oxazolidin-2-one ($rac$)-syn and ($rac$)-anti-$^{164A}$ (ratio syn : anti 47 : 53), and 3-(2-acetoxy-2-phenyl-acetate)-4-phenyl-oxazolidin-2-one ($rac$)-syn and ($rac$)-anti-$^{164}$ (ratio syn : anti 91 : 9) (ratio benzyl : acetoxy 8 : 92), which were spectroscopically identical to that obtained elsewhere.

**Competitive reaction of active ester (S)-123 and active ester (S)-171 with 4-phenyl-oxazolidin-2-one ($R$)-94 [S2.26].**

In the same way as T2.7; E1, $n$-BuLi (0.33 ml, 2.5M in hexanes, 0.82 mmol), 4-phenyl-oxazolidin-2-one ($R$)-$^{94}$ (0.121 g, 0.74 mmol), pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propionate (S)-$^{123}$ (0.294 g, 0.74 mmol) and 4-chlorophenyl-2-(1,1,1-trideuterio-acetoxy)-2-phenyl-acetate (S)-$^{171}$ (0.196 g, 0.74 mmol) in THF (10 ml). Gave by crude 1H NMR 3-[2-(6-methoxy-2-naphthyl)-propionate]-4-phenyl-oxazolidin-2-one ($S,R$)-syn-$^{156}$ and 3-[2-(1,1,1-trideuterio-acetoxy)-2-phenyl-acetate]-4-phenyl-oxazolidin-2-one ($S,R$)-syn-$^{164B}$ (ratio naphthyl : acetoxy 94 : 6), which were spectroscopically identical to that obtained elsewhere.

**Hydrolysis of 3-(2-acetoxy-2-phenyl-acetate)-4-phenyl-oxazolidin-2-one ($rac$)-syn-$^{164}$ [S2.27].**

In the same way as S2.17; E1, 3-(2-acetoxy-2-phenyl-acetate)-4-phenyl-oxazolidin-2-one ($rac$)-syn-$^{164}$ (50 mg, 0.15 mmol), LiOH.H$_2$O (12 mg, 0.29 mmol) and H$_2$O$_2$ (0.08 ml, 3.53M in water, 0.29 mmol) in THF/water (3:1, 4 ml). Gave 4-phenyl-oxazolidin-2-one ($rac$)-$^{94}$ (21 mg, 87%), which was spectroscopically identical to that obtained elsewhere.
Hydrolysis of 3-(2-acetoxy-2-phenyl-acetate)-4-phenyl-oxazolidin-2-one (R,R)-anti-164 [S2.28; E1].

In the same way as S2.17; E1, 3-(2-acetoxy-2-phenyl-acetate)-4-phenyl-oxazolidin-2-one (R,R)-anti-164 (0.120 g, 0.35 mmol), LiOH.H₂O (15 mg, 0.35 mmol) and H₂O₂ (0.10 ml, 3.53M in water, 0.35 mmol) in THF/water (3:1, 4 ml). Gave 4-phenyl-oxazolidin-2-one (R)-94 (45 mg, 78%) which was spectroscopically identical to that obtained elsewhere, and 2-acetoxy-2-phenyl-acetic acid (R)-135 (38 mg, 55%), as a brown solid mp 75-81 °C; [α]ᵢ₀ = -146.5 (c 3.8, CHCl₃), Rᵢ [dichloromethane] 0.08; νₘₙₙ (CHCl₃)/cm⁻¹ 1728 (C=O); δₓ (400 MHz; CDCl₃) 7.49-7.44 (2H, m, 2 × CH; Ph), 7.41-7.36 (3H, m, 3 × CH; Ph), 5.92 (1H, s, CH) and 2.18 (3H, CH₃); δₓ (100 MHz; CDCl₃) 174.3 and 170.6 (2 × C=O), 133.0 (i-C; Ph), 129.4,¹ 128.8² and 127.6² (5 × CH; Ph), 74.1 (CHPh) and 20.5 (CH₃); (Found MNH⁺, 212.0914; C₁₀H₁₄O₄N requires 212.0917).

Hydrolysis of 3-(2-acetoxy-2-phenyl-acetate)-4-phenyl-oxazolidin-2-one (S,R)-syn-164 [S2.28; E2].

In the same way as S2.17; E1, 3-(2-acetoxy-2-phenyl-acetate)-4-phenyl-oxazolidin-2-one (S,R)-syn-164 (0.100 g, 0.29 mmol), LiOH.H₂O (12 mg, 0.29 mmol) and H₂O₂ (0.08 ml, 3.53M in water, 0.29 mmol) in THF/water (3:1, 4 ml). Gave 4-phenyl-oxazolidin-2-one (R)-94 (46 mg, 96%), and 2-acetoxy-2-phenyl-acetic acid (S)-135 (49 mg, 86%), as a brown solid mp 75-81 °C; [α]ᵢ₀ = +132.2 (c 4.1, CHCl₃), which were spectroscopically identical to that obtained elsewhere.

Hydrolysis of 3-(2-acetoxy-2-phenyl-acetate)-4-phenyl-oxazolidin-2-one (rac)-syn-164 [S2.29].

In the same way as S2.17; E1, 3-(2-acetoxy-2-phenyl-acetate)-4-phenyl-oxazolidin-2-one (rac)-syn-164 (62 mg, 0.18 mmol), LiOH.H₂O (31 mg, 0.73 mmol) and H₂O₂ (0.21 ml, 3.53M in water, 0.73 mmol) in THF/water (3:1, 4 ml). Gave 4-phenyl-oxazolidin-2-one (rac)-94 (25 mg, 84%), which was spectroscopically identical to that obtained elsewhere.

PKR of active ester (rac)-113 using 4-phenyl-oxazolidin-2-one (R)-94 and 4-phenyl-5,5-diduetrio-oxazolidin-2-one (S)-172 [S2.30].

In the same way as T2.7; E1, n-BuLi (0.63 ml, 2.5M in hexanes, 1.57 mmol), 4-phenyl-oxazolidin-2-one (R)-94 (0.101 g, 0.62 mmol), 4-phenyl-5,5-diduetrio-oxazolidin-2-one (S)-172 (97 mg, 0.59 mmol) and pentafluorophenyl-2-(4-methyl-
phenyl)-propionate (rac)-113 (0.400 g, 1.21 mmol) in THF (13 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 3-[2-(4-methyl-phenyl)-propionyl]-4-phenyl-oxazolidin-2-one (S,R)-syn and (R,R)-anti-173 and 3-[2-(4-methyl-phenyl)-propionyl]-4-phenyl-5,5-dideutiro-oxazolidin-2-one (R,S)-syn and (S,S)-anti-174 (0.18 g, 48%, ratio syn:anti 95:5, ratio H₂ to D₂ 50:50) which were spectroscopically identical to that obtained elsewhere.

MKR of active ester (rac)-95 using 4,5,5,-triphenyl-oxazolidin-2-one (rac)-175 [T2.20; E1].

In the same way as T2.7; E1, n-BuLi (0.28 ml, 2.5M in hexanes, 0.70 mmol), 4,5,5-triphenyl-oxazolidin-2-one (rac)-175 (0.200 g, 0.63 mmol) and pentafluorophenyl-2-phenyl-propionate (rac)-95 (0.201 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 3-(2-phenyl-propionyl)-4,5,5-triphenyl-oxazolidin-2-one (rac)-syn and (rac)-anti-176 (0.15 g, 53%, ratio syn:anti 88:12) as a white solid mp 160-165°C; Rᵋ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.58; ν_max (CHCl₃)/cm⁻¹ 1780 and 1704 (2 × C=O); δ_H (400 MHz; CDCl₃) 7.63 (2H, br d, J 7.7, 2 × CH; Ph), 7.46-7.36 (4H, m, 4 × CH; Ph), 7.19 (2H, dd, J 5.0 and 2.0, 2 × CH; Ph), 7.11-7.07 (2H, m, 2 × CH; Ph), 7.01-6.86 (8H, m, 8 × CH; Ph), 6.65 (2H, br d, J 7.7, 2 × CH; Ph), 6.25 (1H, s, CHN), 4.98 (1H, q, J 7.0, CHCH₃) and 1.35 (3H, d, J 7.0, CH₃); δ_C (100 MHz; CDCl₃) 173.2 (NC=O), 152.0 (OC=O), 141.8, 139.5, 138.0 and 135.0 (4 × i-C; 4 × Ph), 128.9,² 128.8,¹ 128.4,² 128.3,² 127.9,³ 127.6,² 127.5,³ 127.4,² 127.0,¹ 126.2 and 126.1² (20 × CH; 4 × Ph), 88.5 (CPh₂O), 66.0 (CHN), 44.0 (CHCH₃) and 19.0 (CH₃); (Found M⁺, 447.1835; C₃₀H₂₅NO₃ requires 447.1829), for (rac)-anti-176 characteristic data δ_H (400 MHz; CDCl₃) 6.07 (1H, s, CHN) and 5.05 (1H, q, J 7.0, CHCH₃).

MKR of active ester (rac)-119 using 4,5,5,-triphenyl-oxazolidin-2-one (rac)-175 [T2.20; E2].

In the same way as T2.7; E1, n-BuLi (0.14 ml, 2.5M in hexanes, 0.35 mmol), 4,5,5-triphenyl-oxazolidin-2-one (rac)-175 (0.100 g, 0.32 mmol) and pentafluorophenyl-2-phenyl-butanoate (rac)-119 (0.105 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 3-(2-
phenyl-butionate)-4,5,5-triphenyl-oxazolidin-2-one (rac)-syn and (rac)-anti-177 (0.121 g, 83%, ratio syn : anti 95 : 5) as a white solid mp 158-160°C; \( R_f \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.61; \( \nu_{\text{max}} \) (CHCl\(_3\))/cm\(^{-1}\) 1780 and 1707 (2 × C=O); \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.57 (2H, br d, \( J \) 7.5, 2 × CH; Ph), 7.41-7.30 (3H, m, 3 × CH; Ph), 7.16-7.05 (5H, m, 5 × CH; Ph), 6.94-6.79 (8H, m, 8 × CH; Ph), 6.57 (2H, br d, \( J \) 7.5, 2 × CH; Ph), 6.20 (1H, s, CHN), 4.72 (1H, t, \( J \) 7.3, PhCH) 1.97-1.85 (1H, m, \( CH_3 \)H\(_R\)), 1.69-1.57 (1H, m, \( CH_3 \)H\(_B\)) and 0.70 (3H, t, \( J \) 7.3, CH\(_3\)); \( \delta_C \) (100 MHz; CDCl\(_3\)) 172.8 (NC=O), 152.1 (OC=O), 141.7, 138.0, 137.7 and 135.0 (4 × i-C; 4 × Ph), 128.9, 128.8, 128.3, 127.9, 127.8, 127.5, 127.4, 127.3, 127.1, 126.3, 126.2 and 126.2 (20 × CH; 4 × Ph), 88.6 (CPh\(_2\)O), 65.9 (CHN), 51.1 (PhCHCH\(_2\)), 26.7 (CH\(_2\)) and 11.8 (CH\(_2\)CH\(_3\)); (Found \( M^+ \), 462.2067; C\(_{31}\)H\(_{28}\)ClNO\(_3\) requires 462.2064), for (rac)-anti-177 characteristic data \( \delta_H \) (400 MHz; CDCl\(_3\)) 6.05 (1H, s, CHN) and 4.88 (1H, t, \( J \) 7.7, CHCH\(_2\)).

MKR of active ester (rac)-126 using 4,5,5,triphenyl-oxazolidin-2-one (rac)-175 [T2.20; E3].

In the same way as T2.7; E1, n-BuLi (0.14 ml, 2.5M in hexanes, 0.35 mmol), 4,5,5-triphenyl-oxazolidin-2-one (rac)-175 (0.100 g, 0.32 mmol) and pentafluorophenyl-2-phenyl-3-methyl-butan-2-0ate (rac)-126 (0.109 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) an inseparable mixture of 3-[2-(4-chloro-phenyl)-propionate]-4,5,5-triphenyl-oxazolidin-2-one (rac)-syn and (rac)-anti-178 (0.88 mg, 58%, ratio syn : anti 92 : 8) as a white solid mp 135-138°C; \( R_f \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.68; \( \nu_{\text{max}} \) (CHCl\(_3\))/cm\(^{-1}\) 1781 and 1708 (2 × C=O); \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.58 (2H, br d, \( J \) 7.7, 2 × CH; Ph), 7.40-7.30 (3H, m, 3 × CH; Ph), 7.10 (2H, dt, \( J \) 8.2 and 1.9, 2 × CH; Ar), 6.94 (2H, dt, \( J \) 8.2 and 1.9, 2 × CH; Ar), 6.99-6.82 (8H, m, 8 × CH; Ph), 6.60 (2H, br d, \( J \) 7.2, 2 × CH; Ph), 6.19 (1H, s, CHN), 4.90 (1H, q, \( J \) 7.0, ArCHCH\(_3\)) and 1.28 (3H, d, \( J \) 7.0, ArCHCH\(_3\)); \( \delta_C \) (100 MHz; CDCl\(_3\)) 172.8 (NC=O), 151.9 (OC=O), 141.8, 139.0, 137.9, 134.9 and 132.8 (5 × i-C; 3 × Ph and 2 × Ph), 129.6, 128.9, 128.1, 128.0, 127.9, 127.6, 127.4, 127.4, 126.1 and 126.0 (17 × CH; 3 × Ph and Ar), 88.6 (CPh\(_2\)O), 65.9 (CHN), 43.3 (ArCHCH\(_3\)) and 18.9 (ArCHCH\(_3\)); (Found M\(^{+}\)(\(^{35}\)Cl)NH\(_3\), 499.1786; C\(_{30}\)H\(_{26}\)ClN\(_2\)O\(_3\) requires 499.1783).
MKR of active ester (rac)-113 using 4,5,5,-triphenyl-oxazolidin-2-one (rac)-175 [T2.20; E4].

In the same way as T2.7; E1, n-BuLi (0.14 ml, 2.5M in hexanes, 0.35 mmol), 4,5,5-triphenyl-oxazolidin-2-one (rac)-175 (0.100 g, 0.32 mmol) and pentafluorophenyl-2-(4-methyl-phenyl)-propionate (rac)-113 (0.105 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 3-[2-(4-methyl-phenyl)-propionate]-4,5,5-triphenyl-oxazolidin-2-one (rac)-syn and (rac)-anti-179 (88 mg, 60%, ratio syn : anti 94 : 6) as a white solid mp 153-158°C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.57; νmax (CHCl3)/cm⁻¹ 1780 and 1703 (2 × C=O); δH (400 MHz; CDCl3) 7.64 (2H, br d, J 7.7, 2 × CH; Ar), 7.48-7.38 (3H, m, 3 × CH; Ph), 7.04-6.89 (12H, m, 12 × CH; Ph), 6.69 (2H, br d, J 7.7, 2 × CH; Ar), 6.23 (1H, s, CHN), 4.95 (1H, q, J 7.0, ArCH), 2.32 (3H, s, CH3Ar) and 1.35 (3H, d, J 7.0, CHCH3); δC (100 MHz; CDCl3) 173.4 (NC=O), 152.0 (OC=O), 141.8, 138.0, 136.6, 136.5 and 135.1 (5 × i-C; 3 × Ph and Ar), 129.1, 128.9, 128.1, 127.9, 127.5, 127.4, 127.3, 126.2 and 126.1 (19 × CH; 3 × Ph and Ar), 88.5 (CPh2O), 66.0 (CHN), 44.6 (ArCHCH3), 21.1 (CH3Ar) and 19.1 (ArCHCH3); (Found MNH₂, 462.2062; C31H32NO3 requires 462.2064), for (rac)-anti-179 characteristic data δH (400 MHz; CDCl3) 6.02 (1H, s, CHN) and 4.98 (1H, q, J 7.0, ArCH).

MKR of active ester (rac)-115 using 4,5,5,-triphenyl-oxazolidin-2-one (rac)-175 [T2.20; E5].

In the same way as T2.7; E1, n-BuLi (0.14 ml, 2.5M in hexanes, 0.35 mmol), 4,5,5-triphenyl-oxazolidin-2-one (rac)-175 (0.100 g, 0.32 mmol) and pentafluorophenyl-2-(4-isobutyl-phenyl)-propionate (rac)-115 (0.118 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 3-[2-(4-isobutyl-phenyl)-propionate]-4,5,5-triphenyl-oxazolidin-2-one (rac)-syn and (rac)-anti-180 (0.152 g, 95%, ratio syn : anti 93 : 7) as a white solid mp 158-162°C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.72; νmax (CHCl3)/cm⁻¹ 1778 and 1704 (2 × C=O); δH (400 MHz; CDCl3) 7.66 (2H, br d, J 7.3, 2 × CH; Ar), 7.49-7.38 (3H, m, 3 × CH; Ph), 7.06-6.87 (12H, m, 12 × CH; 3 × Ph), 6.66 (2H, br d, J 7.3, 2 × CH; Ar), 6.28 (1H, s, CHN), 5.00 (1H, q, J 7.0, ArCH) 2.44 (2H,
dd, $J$ 7.2 and 1.6, CH$_2$Ar), 1.91-1.79 (1H, m, CH$_3$CH$_3$H), 1.37 (3H, d, $J$ 7.0, ArCHCH$_3$), 0.92 (3H, d, $J$ 6.6, CH$_3$CHCH$_3$) and 0.91 (3H, d, $J$ 6.6, CH$_3$CHCH$_3$); $\delta$C (100 MHz; CDCl$_3$) 173.5 (NC=O), 152.0 (OC=O), 141.8, 140.5, 138.1, 136.6 and 135.0 (5 × i-C; 3 × Ph and Ar), 129.1, $^2$ 128.9, $^2$ 128.9, $^1$ 128.0, $^2$ 127.9, $^1$ 127.8, $^2$ 127.5, $^2$ 127.4, $^3$ 126.3$^2$ and 126.2$^2$ (19 × CH; 3 × Ph and Ar), 88.5 (CPh$_2$O), 66.0 (CHN), 45.0 (CH$_3$CHCH$_3$), 43.4 (ArCHCH$_3$), 30.2 (CH$_2$Ar), 22.4 (CH$_3$CHCH$_3$), 22.3 (CH$_3$CHCH$_3$) and 18.9 (ArCHCH$_3$); (Found MNH$_3^+$, 521.2796; C$_{34}$H$_{37}$N$_2$O$_3$ requires 521.2799), for (rac)-anti-180 characteristic data $\delta$H (400 MHz; CDCl$_3$) 6.06 (1H, s, CHN) and 5.01 (1H, q, $J$ 7.0, ArCH).

MKR of active ester (rac)-117 using 4,5,5-triphenyl-oxazolidin-2-one (rac)-175 [T2.20; E6].

In the same way as T2.7; E1, n-BuLi (0.14 ml, 2.5M in hexanes, 0.35 mmol), 4,5,5-triphenyl-oxazolidin-2-one (rac)-175 (0.100 g, 0.32 mmol) and pentafluorophenyl-2-(4-chloro-phenyl)-propionate (rac)-117 (0.111 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 3:7) an inseparable mixture of 3-(2-phenyl-3-methyl-butanoyl)-4,5,5-triphenyl-oxazolidin-2-one (rac)-syn and (rac)-anti-181 (27 mg, 18%, ratio syn : anti 78 : 22) as a white solid mp 166-172°C; $R_F$ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.71; $\nu$$_{max}$ (CHCl$_3$)/cm$^{-1}$ 1780 and 1702 (2 × C=O); $\delta$H (400 MHz; CDCl$_3$) 7.57 (2H, br d, $J$ 7.7, 2 × CH; Ph), 7.40-7.30 (3H, m, 3 × CH; Ph), 7.19-7.00 (5H, m, 5 × CH; Ph), 6.95-6.70 (8H, m, 8 × CH; Ph), 6.52 (2H, br d, $J$ 7.7, 2 × CH; Ph), 6.19 (1H, s, CHN), 4.55 (1H, br d, $J$ 10.1, PhCHCH), 2.35-2.19 (1H, m, CH$_3$CHCH$_3$), 0.77 (3H, d, $J$ 6.9, CH$_3$CHCH$_3$) and 0.55 (3H, d, $J$ 6.9, CH$_3$CHCH$_3$); $\delta$C (100 MHz; CDCl$_3$) 172.8 (NC=O), 152.3 (OC=O), 141.6, 137.8, 136.9 and 134.9 (4 × i-C; 4 × Ph), 129.3, $^2$ 128.9, $^1$ 128.8, $^2$ 128.2, $^2$ 127.9, $^2$ 127.7, $^1$ 127.5, $^2$ 127.4, $^1$ 127.1, $^1$ 127.0, $^2$ 126.3$^2$ and 126.4$^2$ (20 × CH; 4 × Ph), 88.6 (CPh$_2$O), 65.8 (CHN), 56.7 (PhCHCH), 31.5 (CH$_3$CHCH$_3$), 21.3 (CH$_3$CHCH$_3$) and 20.0 (CH$_3$CHCH$_3$); (Found MNH$_3^+$, 493.2488; C$_{32}$H$_{35}$N$_2$O$_3$ requires 493.2486), for minor 3-(2-phenyl-3-methyl-butanoyl)-4,5,5-triphenyl-oxazolidin-2-one (rac)-anti-181 $\delta$H (400 MHz; CDCl$_3$) 7.40-7.30 (5H, m, 5 × CH; Ph), 7.19-7.00 (5H, m, 5 × CH; Ph), 6.95-6.70 (10H, m, 10 × CH; Ph), 5.98 (1H, s, CHN), 4.70 (1H, br d, $J$ 10.3, PhCHCH), 2.35-2.19 (1H, m, CH$_3$CHCH$_3$), 0.77 (3H, d, $J$ 6.9, CH$_3$CHCH$_3$) and 0.58 (3H, d, $J$ 6.9, CH$_3$CHCH$_3$).
Stereo-specific synthesis of 3-[2-(6-methoxy-2-naphthyl)-propionyl]-4,5,5-triphenyl-oxazolidin-2-one (S,R)-syn-182 [S2.31].

In the same way as T2.7; E1, n-BuLi (0.11 ml, 2.5M in hexanes, 0.28 mmol), 4,5,5-triphenyl-oxazolidin-2-one (R)-175 (79 mg, 0.25 mmol) and pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propionate (S)-123 (99 mg, 0.25 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) 3-[2-(6-methoxy-2-naphthyl)propionyl]-4,5,5-triphenyl-oxazolidin-2-one (S,R)-syn-182 (60 mg, 45%) as a white solid mp 194-196°C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.48; [α]D20 = +416.3 (c 4.0, CHCl₃), νmax (CHCl₃)/cm⁻¹ 1781 and 1711 (2 × C=O); δH (400 MHz; CDCl₃) 7.60-7.51 (3H, m, 3 × CH; Ar and Ph), 7.41-7.33 (4H, m, 4 × CH; Ph and/or Ar), 7.23 (1H, br s, 2 × CH; Ar), 7.20 (1H, dd, J 8.4, and 1.8, CH; Ph and/or Ph), 7.05-7.01 (2H, m, 2 × CH; Ph and/or Ar), 6.90 (1H, d, J 7.9, CH; Ph or Ar), 6.88-6.81 (5H, m, 5 × CH; Ph and Ar), 6.70 (2H, t, J 7.9, 2 × CH; Ar), 6.58 (2H, d, J 7.3, 2 × H; Ar), 6.22 (1H, s, PhCH), 5.05 (1H, br q, J 7.0, ArCH), 3.85 (3H, s, CH₃O) and 1.36 (3H, d, J 7.0, CHCH₃); δC (100 MHz; CDCl₃) 173.2 (NC=O), 151.8 (OC=O), 157.6, 141.8, 138.0, 135.0, 134.9, 133.6 and 128.7 (7 × i-C; 3 × Ph and Ar), 129.4, 127.0, 126.3, 126.2, 118.6 and 105.5 (6 × CH; Ar), 128.9, 128.8, 127.9, 127.5, 127.4, 127.3, 126.2 and 126.1 (15 × CH; 3 × Ph), 88.5 (CPh₂O), 66.0 (CHN), 55.3 (CH₃O), 44.0 (CHCH₃) and 19.1 (CHCH₃); (Found M⁺, 527.2085; C₃₅H₃₀NO₄ requires 527.2091).

MKR of active ester (rac)-95 using 4,5,5-triphenyl-oxazolidin-2-one (rac)-175 in the presence of oxazolidin-2-one 183 [S2.23].

In the same way as T2.7; E1, n-BuLi (0.51 ml, 2.5M in hexanes, 1.26 mmol), 4,5,5-triphenyl-oxazolidin-2-one (S)-175 (0.181 g, 0.57 mmol), oxazolidin-2-one 183 (50 mg, 0.57 mmol) and pentafluorophenyl-2-phenyl-propionate (rac)-95 (0.363 g, 1.15 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3 → 0:1) an inseparable mixture of 3-(2-phenyl-propionyl)-4,5,5-triphenyl-oxazolidin-2-one (rac)-syn and (rac)-anti-176 (95 mg, 37%, ratio syn : anti 95 : 5) and 3-(2-phenyl-propionyl)-oxazolidin-2-one (rac)-184 (79 mg, 63%), which were spectroscopically identical to that obtained elsewhere.
KR of active ester (rac)-95 using 4,5,5-triphenyl-oxazolidin-2-one (S)-175 [S2.23].

In the same way as T2.7; E1, n-BuLi (0.32 ml, 2.5M in hexanes, 0.79 mmol), 4,5,5-triphenyl-oxazolidin-2-one (S)-175 (0.249 g, 0.79 mmol) and pentafluorophenyl-2-phenyl-propionate (rac)-95 (0.500 g, 1.60 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) an inseparable mixture of 3-(2-phenyl-propionyl)-4,5,5-triphenyl-oxazolidin-2-one (R,S)-syn and (S,S)-anti-176 (0.265 g, 75%, ratio syn : anti 85 : 15), which were spectroscopically identical to that obtained elsewhere.

KR of active ester (rac)-95 using 4,5,5-triphenyl-oxazolidin-2-one (S)-175 in the presence of oxazolidin-2-one 183 [S2.34].

In the same way as T2.7; E1, n-BuLi (0.51 ml, 2.5M in hexanes, 1.26 mmol), 4,5,5-triphenyl-oxazolidin-2-one (S)-175 (0.181 g, 0.57 mmol), oxazolidin-2-one 183 (50 mg, 0.57 mmol) and pentafluorophenyl-2-phenyl-propionate (rac)-95 (0.363 g, 1.15 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3 → 0:1) an inseparable mixture of 3-(2-phenyl-propionyl)-4,5,5-triphenyl-oxazolidin-2-one (R,S)-syn and (S,S)-anti-176 (0.159 g, 62%, ratio syn : anti 86 : 14) and 3-(2-phenyl-propionyl)-oxazolidin-2-one (scalemic)-184 (62 mg, 49%), which were spectroscopically identical to that obtained elsewhere.

PKR of 4,5,5-triphenyl-oxazolidin-2-one (rac)-175 using active esters (R)-119 and (S)-123 [S2.35].

In the same way as T2.7; E1, n-BuLi (0.06 ml, 2.5M in hexanes, 0.15 mmol), 4,5,5-triphenyl-oxazolidin-2-one (rac)-175 (42 mg, 0.13 mmol), pentafluorophenyl-2-phenyl-butanoate (R)-119 (22 mg, 0.067 mmol) and pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propionate (S)-123 (26 mg, 0.067 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) an inseparable mixture of 3-(2-phenyl-butinoyl)-4,5,5-triphenyl-oxazolidin-2-one (R,S)-syn and (R,R)-anti-177 (15 mg, 50%, ratio syn : anti 96 : 4) and an inseparable mixture of 3-[2-(6-methoxy-2-naphthyl)-propionyl]-4,5,5-triphenyl-oxazolidin-2-one (S,R)-syn and (S,S)-anti-182 (15 mg, 43%, ratio syn : anti 96 : 4), which were spectroscopically identical to that obtained elsewhere.
PKR of active ester (rac)-95 using 4-phenyl-oxazolidin-2-one (R)-94 and 4,5,5-triphenyl-oxazolidin-2-one (S)-175 [T2.21; E1].

In the same way as T2.7; E1, n-BuLi (0.28 ml, 2.5M in hexanes, 0.70 mmol), 4-phenyl-oxazolidin-2-one (R)-94 (50 mg, 0.32 mmol), 4,5,5-triphenyl-oxazolidin-2-one (S)-175 (0.100 g, 0.32 mmol) and pentafluorophenyl-2-phenyl-propionate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave a crude mixture of two sets of diastereoisomeric oxazolidin-2-ones; (S,R)-syn and (R,R)-anti-96 (ratio syn : anti 97 : 3), and oxazolidin-2-ones; (R,S)-syn and (S,S)-anti-176 (ratio syn : anti 98 : 2). The crude residue gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) an inseparable mixture of 3-(2-phenyl-propionyl)-4,5,5-triphenyl-oxazolidin-2-one (R,S)-syn and (S,S)-anti-176 (85 mg, 60%, ratio syn : anti 98 : 2) as a white solid mp 154-156°C; \([\alpha]_D^{20} = -255.1 (c 3.4, \text{CHCl}_3)\), and 3-(2-phenyl-propionyl)-4-phenyl-oxazolidin-2-one (S,R)-syn-96 (54 mg, 58%) as a white solid mp 140-142°C; \([\alpha]_D^{20} = +88.5 (c 4.0, \text{CHCl}_3)\), which were spectroscopically identical to that obtained elsewhere.

PKR of active ester (rac)-119 using 4-phenyl-oxazolidin-2-one (R)-94 and 4,5,5-triphenyl-oxazolidin-2-one (S)-175 [T2.21; E2].

In the same way as T2.7; E1, n-BuLi (0.28 ml, 2.5M in hexanes, 0.70 mmol), 4-phenyl-oxazolidin-2-one (R)-94 (50 mg, 0.32 mmol), 4,5,5-triphenyl-oxazolidin-2-one (S)-175 (0.100 g, 0.32 mmol) and pentafluorophenyl-2-phenyl-butanoate (rac)-119 (0.209 g, 0.63 mmol) in THF (10 ml). Gave a crude mixture of two sets of diastereoisomeric oxazolidin-2-ones; (S,R)-syn and (R,R)-anti-153 (ratio syn : anti 99 : 1), and oxazolidin-2-ones; (R,S)-syn and (S,S)-anti-177 (ratio syn : anti 97 : 3). The crude residue gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) an inseparable mixture of 3-(2-phenyl-butanoyl)-4,5,5-triphenyl-oxazolidin-2-one (R,S)-syn and (S,S)-anti-177 (86 mg, 59%, ratio syn : anti 97 : 3) as a white solid mp 150-153°C; \([\alpha]_D^{20} = -195.2 (c 3.4, \text{CHCl}_3)\), and 3-(2-phenyl-butanoyl)-4-phenyl-oxazolidin-2-one (S,R)-syn-153 (62 mg, 63%) as a white solid mp 82-84°C; \([\alpha]_D^{20} = +77.4 (c 4.0, \text{CHCl}_3)\), which were spectroscopically identical to that obtained elsewhere.
PKR of active ester (rac)-126 using 4-phenyl-oxazolidin-2-one (R)-94 and 4,5,5-
tri phenyl-oxazolidin-2-one (S)-175 [T2.21; E3].

In the same way as T2.7; E1, n-BuLi (0.28 ml, 2.5M in hexanes, 0.70 mmol), 4-
phenyl-oxazolidin-2-one (R)-94 (50 mg, 0.32 mmol), 4,5,5-triphenyl-oxazolidin-2-one
(S)-175 (0.100 g, 0.32 mmol) and pentafluorophenyl-2-phenyl-3-methyl-butanoate
(rac)-126 (0.218 g, 0.63 mmol) in THF (10 ml). Gave a crude mixture of two sets of
diastereoisomeric oxazolidin-2-ones; (S,R)-syn and (R,R)-anti-154 (ratio syn : anti 79 : 21), and oxazolidin-2-ones; (R,S)-syn and (S,S)-anti-178 (ratio syn : anti 90 : 10). The crude residue gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 3:7) an inseparable mixture of 3-(2-phenyl-3-methyl-butanoyl)-4,5,5-triphenyl-oxazolidin-2-one (R,S)-syn and (S,S)-anti-178 (0.65 mg, 43%, ratio syn : anti 88 : 12) as a white solid mp 170-178°C; [α]D = -270.9 (c 2.6, CHCl3), and 3-(2-phenyl-3-methyl-butanoyl)-4-
phenyl-oxazolidin-2-one (S,R)-syn and (R,R)-anti-154 (80 g, 79%, ratio syn : anti 77 : 23) as a white solid mp 80-92°C; [α]D = +1.3 (c 3.0, CHCl3), which were spectroscopically identical to that obtained elsewhere.

PKR of active ester (rac)-113 using 4-phenyl-oxazolidin-2-one (R)-94 and 4,5,5-
triphenyl-oxazolidin-2-one (S)-175 [T2.21; E4].

In the same way as T2.7; E1, n-BuLi (0.28 ml, 2.5M in hexanes, 0.70 mmol), 4-
phenyl-oxazolidin-2-one (R)-94 (50 mg, 0.32 mmol), 4,5,5-triphenyl-oxazolidin-2-one
(S)-175 (0.100 g, 0.32 mmol) and pentafluorophenyl-2-(4-methyl-phenyl)-propionate (rac)-113 (0.209 g, 0.63 mmol) in THF (10 ml). Gave a crude mixture of two sets of diastereoisomeric oxazolidin-2-ones; (S,R)-syn and (R,R)-anti-185 (ratio syn : anti 99 : 1), and oxazolidin-2-ones; (R,S)-syn and (S,S)-anti-179 (ratio syn : anti 98 : 2). The crude residue gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) an inseparable mixture of 3-[2-(4-methyl-phenyl)-propionate]-4,5,5-triphenyl-oxazolidin-2-one (R,S)-syn and (S,S)-anti-179 (75 mg, 51%, ratio syn : anti 98 : 2) as a white solid mp 119-121°C; [α]D = -258.6 (c 2.4, CHCl3), and 3-[2-(4-isopropyl-phenyl)-propionate]-4-phenyl-oxazolidin-2-one (S,R)-syn-185 (44 mg, 45%) as a white solid mp 105-110°C; [α]D = +121.6 (c 0.6, CHCl3), which were spectroscopically identical to that obtained elsewhere.
PKR of active ester (rac)-115 using 4-phenyl-oxazolidin-2-one (R)-94 and 4,5,5-, triphenyl-oxazolidin-2-one (S)-175 [T2.21; E5].

In the same way as T2.7; E1, n-BuLi (0.28 ml, 2.5M in hexanes, 0.70 mmol), 4-phenyl-oxazolidin-2-one (R)-94 (50 mg, 0.32 mmol), 4,5,5-triphenyl-oxazolidin-2-one (S)-175 (0.100 g, 0.32 mmol) and pentafluorophenyl-2-(4-isobutyl-phenyl)-propionate (rac)-115 (0.235 g, 0.63 mmol) in THF (10 ml). Gave a crude mixture of two sets of diastereoisomeric oxazolidin-2-ones; (S,R)-syn and (R,R)-anti-163 (ratio syn : anti 97 : 3), and oxazolidin-2-ones; (R,S)-syn and (S,S)-anti-180 (ratio syn : anti 98 : 2). The crude residue gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 3:7) an inseparable mixture of 3-[2-(4-isobutyl-phenyl)-propionate]-4,5,5-triphenyl-oxazolidin-2-one (R,S)-syn and (S,S)-anti-180 (88 mg, 55%, ratio syn : anti 98 : 2) as a white solid mp 62-64°C; [α]_D^20 = -306.7 (c 4.4, CHCl₃), and 3-[2-(4-isobutyl-phenyl)-propionate]-4-phenyl-oxazolidin-2-one (S,R)-syn-163 (67 mg, 60%) as a white solid mp 86-88°C; [α]_D^20 = +118.7 (c 6.0, CHCl₃), which were spectroscopically identical to that obtained elsewhere.

PKR of active ester (rac)-117 using 4-phenyl-oxazolidin-2-one (R)-94 and 4,5,5-, triphenyl-oxazolidin-2-one (S)-175 [T2.21; E6].

In the same way as T2.7; E1, n-BuLi (0.28 ml, 2.5M in hexanes, 0.70 mmol), 4-phenyl-oxazolidin-2-one (R)-94 (50 mg, 0.32 mmol), 4,5,5-triphenyl-oxazolidin-2-one (S)-175 (0.100 g, 0.32 mmol) and pentafluorophenyl-2-(4-chloro-phenyl)-propionate (rac)-117 (0.222 g, 0.63 mmol) in THF (10 ml). Gave a crude mixture of two sets of diastereoisomeric oxazolidin-2-ones; (S,R)-syn and (R,R)-anti-155 (ratio syn : anti 93 : 7), and oxazolidin-2-ones; (R,S)-syn and (S,S)-anti-181 (ratio syn : anti 96 : 4). The crude residue gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 3:7) an inseparable mixture of 3-[2-(4-chloro-phenyl)-propionate]-4,5,5-triphenyl-oxazolidin-2-one (R,S)-syn and (S,S)-anti-181 (0.91 mg, 60%, ratio syn : anti 96 : 4) as a white solid mp 100-102°C; [α]_D^20 = -296.2 (c 3.4, CHCl₃), and 3-[2-(4-chloro-phenyl)-propionate]-4-phenyl-oxazolidin-2-one (S,R)-syn-155 (74 g, 71%) as a white solid mp 142-145°C; [α]_D^20 = +144.4 (c 1.6, CHCl₃), which were spectroscopically identical to that obtained elsewhere.

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Unbalance PKR of active ester \((rac)-95\) using 4-phenyl-oxazolidin-2-one \((R)-94\) and 4-phenyl-5,5,5-diphenyl-oxazolidin-2-one \((S)-175\) [S2.36; E1].

In the same way as T2.7; E1, \(n\)-BuLi (0.54 ml, 2.5M in hexanes, 1.35 mmol), 4-phenyl-oxazolidin-2-one \((R)-94\) (0.150 g, 0.92 mmol), 4-phenyl-5,5,5-diphenyl-oxazolidin-2-one \((S)-175\) (97 mg, 0.31 mmol) and pentafluorophenyl-2-phenylpropiante \((rac)-95\) (0.388 g, 1.23 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) 3-(2-phenylpropiante)-4-phenyl-oxazolidin-2-one \((S,R)-syn-96\) (0.129 g, 48%), \((R,R)-anti-96\) (47 mg, 17%) (ratio \(syn : anti \ 76 : 24\) and an inseparable mixture of 3-(2-phenylpropiante)-4-phenyl-5,5,5-diphenyl-oxazolidin-2-one \((R,S)-syn\) and \((S,S)-anti-176\) (0.102 g, 74%, ratio \(syn : anti \ 98 : 2\), which were spectroscopically identical to that obtained elsewhere.

Unbalance PKR of active ester \((rac)-95\) using 4-phenyl-oxazolidin-2-one \((R)-94\) and 4-phenyl-5,5,5-diphenyl-oxazolidin-2-one \((S)-175\) [S2.36; E2].

In the same way as T2.7; E1, \(n\)-BuLi (0.54 ml, 2.5M in hexanes, 1.35 mmol), 4-phenyl-oxazolidin-2-one \((R)-94\) (50 mg, 0.31 mmol), 4-phenyl-5,5,5-diphenyl-oxazolidin-2-one \((S)-175\) (0.290 g, 0.92 mmol) and pentafluorophenyl-2-phenylpropiante \((rac)-95\) (0.388 g, 1.23 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) 3-(2-phenylpropiante)-4-phenyl-oxazolidin-2-one \((S,R)-syn-96\) (48 mg, 53%, ratio \(syn : anti >98 : 2\) and an inseparable mixture of 3-(2-phenylpropiante)-4-phenyl-5,5,5-diphenyl-oxazolidin-2-one \((R,S)-syn\) and \((S,S)-anti-176\) (0.185 g, 45%, ratio \(syn : anti \ 93 : 7\), which were spectroscopically identical to that obtained elsewhere.

Competitive reaction of 4-phenyl-oxazolidin-2-one \((R)-94\) and 4,5,5,5-triphenyl-oxazolidin-2-one \((S)-175\) with D\(^1\) acetic acid 186 [S2.37].

\(n\)-BuLi (0.14 ml, 2.5M in hexanes, 0.35 mmol) was added to a mixture of 4-phenyl-oxazolidin-2-one \((R)-94\) (50 mg, 0.32 mmol) and 4,5,5,5-triphenyl-oxazolidin-2-one \((S)-175\) (0.100 g, 0.32 mmol) in THF (10 ml). The resulting solution was stirred for 1 hour, D\(^1\) acetic acid (55 mg, 0.94 mmol) was added, after 15 minutes of stirring the reaction mixture was evacuated under reduced pressure. Gave by crude \(^1\)H NMR, 4-phenyl-oxazolidin-2-one \((R)-187\) (75% deuterated) and 4,5,5,5-triphenyl-oxazolidin-2-one \((S)-188\) (66% deuterated).
Synthesis of phenyl-acetic acid 12 [S2.38; E1].

LiOH.H₂O (1.47 g, 0.035 mol) was added to 2-phenyl-acetyl chloride 189 (3.60 g, 0.023 mmol) in THF/water (3:1, 50 ml). The resulting solution was stirred for 5 hours, the organic layer was extracted with dichloromethane (3 × 50 ml) washed with HCl (0.5M, 25 ml), dried over MgSO₄, evaporated under reduced pressure. Gave 2-phenyl-acetic acid 12 (2.948 g, 93%) as a brown solid mp 70-73 °C, R_F [dichloromethane] 0.23; ν_max (CHCl₃)/cm⁻¹ 1713 (C=O); δ_H (400 MHz; CDCl₃) 7.37-7.26 (5H, m, 5 × CH; Ph) and 3.66 (2H, s, CH₂); δ_C (100 MHz; CDCl₃) 178.1 (C=O), 133.2 (i-C; Ph), 129.3, 128.6 and 127.3 (5 × CH; Ph) and 41.0 (CH₂).

Synthesis of pentafluorophenyl-2-phenyl-acetate 190 [S2.38; E2].

DCC (0.709 g, 3.44 mmol) was added to 2-phenyl-acetic acid 12 (0.425 g, 3.13 mmol) in dichloromethane (10 ml), followed be pentafluorophenyl (0.575 g, 3.13 mmol) in dichloromethane (10 ml). The resulting solution was stirred over night, the mixture was filtered to remove DCU, the organic layer was extracted with dichloromethane (3 × 20 ml) washed with water (20 ml), dried over MgSO₄, evaporated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) to give pentafluorophenyl-2-phenyl-acetate 190 (0.785 g, 83%) as an oil, R_F [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.82; ν_max (CHCl₃)/cm⁻¹ 1790 (C=O); δ_H (400 MHz; CDCl₃) 7.42-7.31 (5H, m, 5 × CH; Ph) and 3.97 (2H, s, CH₂); δ_C (100 MHz; CDCl₃) 167.5 (C=O), 141.1 (142.36 and 139.85, 2C, dtt, ¹J_{C,F} = 251.4 Hz, ²J_{C,F} = 12.3 Hz and ³J_{C,F} = 3.8 Hz, 2 × CF; Ar), 139.5 (140.76 and 138.24, 1C, dtt, ¹J_{C,F} = 253.7 Hz, ²J_{C,F} = 13.8 Hz and ³J_{C,F} = 3.8 Hz, CF; Ar), 137.8 (139.10 and 136.57, 2C, dtdd, ¹J_{C,F} = 254.4 Hz, ²J_{C,F} = 13.8 Hz, ³J_{C,F} = 3.8 Hz and ⁴J_{C,F} = 3.0 Hz, 2 × CF; Ar), 132.0 (i-C; Ph), 129.2, 128.9 and 127.8 (5 × CH; Ph), 125.1 (1C, tdt, ²J_{C,F} = 14.6 Hz, ⁴J_{C,F} = 6.1 Hz and ³J_{C,F} = 1.5 Hz, i-C; Ar) and 40.1 (CH₂); δ_F (378 MHz; CDCl₃) -152.5 (2C, d, ³J_{C,F} = 18.5, o-CF; Ar), -157.7 (1C, d, ³J_{C,F} = 20.8, p-CF; Ar) and -162.2 (2C, dd, ³J_{C,F} = 20.8 and 18.5, m-CF; Ar).

Synthesis of 2,2-dimethyl-propionic acid 192 [S2.38; E3].

In the same way as S2.38; E1, LiOH.H₂O (5.23 g, 0.12 mol) and 2,2-dimethyl-propionyl chloride 191 (10 g, 0.083 mmol) in THF/water (3:1, 100 ml). Gave 2,2-dimethyl-propionic acid 192 (3.564 g, 42%) as an oil, R_F [dichloromethane] 0.10; ν_max
(CHCl₃)/cm⁻¹ 1603 (C=O); δ_H (400 MHz; CDCl₃) 1.21 (9H, s, 3 × CH₃); δ_C (100 MHz; CDCl₃) 158.6 (C=O), 38.6 (CMe₃) and 26.9₃ (3 × CH₃).

**Synthesis of pentafluorophenyl-2,2-dimethyl-propionate 193 [S2.38; E4].**

In the same way as S2.38; E2, DCC (3.85 g, 0.019 mol) was added to 2,2-dimethyl-propionic acid 192 (1.730 g, 0.017 mol) and pentafluorophenol (3.12 g, 0.017 mol) in dichloromethane (100 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) to give pentafluorophenyl-2,2-dimethyl-propionate 193 (1.872 g, 41%) as clear liquid, R_F [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.78; ν_max (CHCl₃)/cm⁻¹ 1774 (C=O); δ_H (400 MHz; CDCl₃) 1.32 (9H, s, 3 × CH₃); δ_C (100 MHz; CDCl₃) 174.6 (C=O), 141.2 (142.46 and 139.93, 2C, ddt, J_C,F = 255.2 Hz, J_C,F = 11.5 Hz and J_C,F = 4.6 Hz, 2 × CF; Ar), 139.3 (140.54 and 138.03, 1C, dtt, J_C,F = 252.9 Hz, J_C,F = 13.8 Hz and J_C,F = 3.8 Hz, CF; Ar), 137.9 (139.12 and 136.59, 2C, dttdd, J_C,F = 254.4 Hz, J_C,F = 13.1 Hz, J_C,F = 5.0 Hz and J_C,F = 3.2 Hz, 2 × CF; Ar), 125.6 (1C, dt, J_C,F = 14.6 Hz, J_C,F = 4.6 Hz and J_C,F = 2.3 Hz, i-C; Ar), 39.5 (CMe₃) and 26.9₃ (3 × CH₃); δ_F (378 MHz; CDCl₃) -153.6 (2C, d, J_C,F = 16.2, o-CF; Ar), -158.5 (1C, t, J_C,F = 20.8, p-CF; Ar) and -162.6 (2C, dd, J_C,F = 20.8 and J_C,F = 16.2, m-CF; Ar).

**Synthesis of benzoic acid 195 [S2.38; E5].**

In the same way as S2.38; E1, LiOH.H₂O (4.48 g, 0.11 mol) and benzoyl chloride 194 (10 g, 0.071 mmol) in THF/water (3:1, 100 ml). Gave benzoic acid 195 (4.064 g, 47%) as a white solid mp 118-120 °C, R_F [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.11; ν_max (CHCl₃)/cm⁻¹ 1694 (C=O); δ_H (400 MHz; CDCl₃) 8.13 (2H, dd, J 8.5 and 1.3, 2 × CH; Ph), 7.62 (1H, tt, J 7.5 and 1.3, CH; Ph) and 7.48 (2H, dd, J 8.5 and 7.5, 2 × CH; Ph); δ_C (100 MHz; CDCl₃) 172.1 (C=O), 133.8, J_C,F = 130.2² and 128.5² (5 × CH; Ph) and 129.3 (i-C; Ph).

**Synthesis of pentafluorophenyl-benzyl acetate 196 [S2.38; E6].**

In the same way as S2.38; E2, DCC (3.17 g, 0.015 mol) was added to benzoic acid 195 (1.730 g, 0.014 mol) and pentafluorophenol (2.56 g, 0.014 mol) in dichloromethane (100 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) to give pentafluorophenyl-benzyl acetate 196 (3.001 g, 73%) as a white solid mp 70-71 °C, R_F [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.74; ν_max (CHCl₃)/cm⁻¹ 1760
(C=O); δ_H (400 MHz; CDCl_3) 8.20 (2H, dd, J 8.4 and 1.3, 2 × CH; Ph), 7.70 (1H, tt, J 7.5 and 1.3, CH; Ph) and 7.55 (2H, dd, J 8.4 and 7.5, 2 × CH; Ph); δ_C (100 MHz; CDCl_3) 162.6 (C=O), 141.4 (142.61 and 140.12, 2C, ddt, J_C,F = 251.4 Hz, J_C,F = 12.3 Hz and J_C,F = 4.6 Hz, 2 × CF; Ar), 139.5 (140.80 and 138.27, 1C, dtt, J_C,F = 253.7 Hz, J_C,F = 13.1 Hz and J_C,F = 3.8 Hz, CF; Ar), 137.9 (139.18 and 136.69, 2C, dtd, J_C,F = 250.6 Hz, J_C,F = 13.1 Hz, J_C,F = 5.2 Hz and J_C,F = 3.3 Hz, 2 × CF; Ar), 134.7, J_C,F = 130.7^2 and 128.9^2 (5 × CH; Ph), 126.9 (i-C; Ph) and 125.6-125.2 (1C, m, i-C; Ar); δ_F (378 MHz; CDCl_3) -152.3 (2C, d, J_C,F = 18.5, o-CF; Ar), -157.8 (1C, t, J_C,F = 20.8, p-CF; Ar) and -162.2 (2C, dd, J_C,F = 20.8 and J_C,F = 18.5, m-CF; Ar).

**Competitive reaction of 4-phenyl-oxazolidin-2-one (R)-94 and 4,5,5-triphenyl-oxazolidin-2-one (S)-175 with methyl iodide [T2.22; E1].**

In the same way as T2.7; E1, n-BuLi (0.14 ml, 2.5M in hexanes, 0.35 mmol), 4-phenyl-oxazolidin-2-one (R)-94 (50 mg, 0.32 mmol), 4,5,5-triphenyl-oxazolidin-2-one (S)-175 (0.100 g, 0.32 mmol) and methyl iodide (0.04 ml, 0.63 mmol) in THF (5 ml). Gave by crude ^1_H NMR 3-methyl-4-phenyl-oxazolidin-2-one (R)-197 characteristic data δ_H (400 MHz; CDCl_3) 4.62-4.52 (2H, m, CHN and CHA_H)O), 4.01 (1H, dd, J 7.2 and 6.4, CHA_H)O) and 2.65 (3H, s, CH_3O), and 3-methyl-4,5,5-triphenyl-oxazolidin-2-one (S)-198 data δ_H (400 MHz; CDCl_3) 5.31 (1H, s, CHN) and 2.67 (3H, s, CH_3O), (ratio evans 197 : seeback 198 48 : 52).

**Competitive reaction of 4-phenyl-oxazolidin-2-one (R)-94 and 4,5,5-triphenyl-oxazolidin-2-one (S)-175 with methyl iodide [T2.22; E2].**

In the same way as T2.7; E1, n-BuLi (0.28 ml, 2.5M in hexanes, 0.70 mmol), 4-phenyl-oxazolidin-2-one (R)-94 (50 mg, 0.32 mmol), 4,5,5-triphenyl-oxazolidin-2-one (S)-175 (0.100 g, 0.32 mmol) and methyl iodide (0.04 ml, 0.63 mmol) in THF (5 ml). Gave by crude ^1_H NMR 3-methyl-4-phenyl-oxazolidin-2-one (R)-197, and 3-methyl-4,5,5-triphenyl-oxazolidin-2-one (S)-198, (ratio evans 197 : seeback 198 47 : 53).

**Competitive reaction of 4-phenyl-oxazolidin-2-one (R)-94 and 4,5,5-triphenyl-oxazolidin-2-one (S)-175 with benzyl bromide [T2.22; E3].**

In the same way as T2.7; E1, n-BuLi (0.14 ml, 2.5M in hexanes, 0.35 mmol), 4-phenyl-oxazolidin-2-one (R)-94 (50 mg, 0.32 mmol), 4,5,5-triphenyl-oxazolidin-2-one (S)-175 (0.100 g, 0.32 mmol) and benzyl bromide (0.07 ml, 0.63 mmol) in THF (5 ml). Gave by crude ^1_H NMR 3-benzyl-4-phenyl-oxazolidin-2-one (R)-199, characteristic
data $\delta_H$ (400 MHz; CDCl$_3$) 4.92-4.76 (2H, m, CHN and CH$_A$H$_B$O), 4.47-4.43 (1H, m, CH$_A$H$_B$O) and 4.40 (2H, s, CH$_2$Ph), and 3-benzyl-4,5,5-triphenyl-oxazolidin-2-one (S)-

**200,** characteristic data $\delta_H$ (400 MHz; CDCl$_3$) 5.08 (1H, s, CHN) and 4.40 (2H, s, CH$_2$Ph), (ratio evans 199 : seeback 200 50 : 50).

**Competitive reaction of 4-phenyl-oxazolidin-2-one (R)-94 and 4,5,5,-triphenyl-oxazolidin-2-one (S)-175 with benzyl bromide [T2.22; E4].**

In the same way as T2.7; E1, n-BuLi (0.28 ml, 2.5M in hexanes, 0.70 mmol), 4-phenyl-oxazolidin-2-one (R)-94 (50 mg, 0.32 mmol), 4,5,5-triphenyl-oxazolidin-2-one (S)-175 (0.100 g, 0.32 mmol) and benzyl bromide (0.07 ml, 0.63 mmol) in THF (5 ml). Gave by crude $^1$H NMR 3-benzyl-4-phenyl-oxazolidin-2-one (R)-199, and 3-benzyl-4,5,5-triphenyl-oxazolidin-2-one (S)-200, (ratio evans 199 : seeback 200 50 : 50).

**Competitive reaction of 4-phenyl-oxazolidin-2-one (R)-94 and 4,5,5,-triphenyl-oxazolidin-2-one (S)-175 with active ester 190 [T2.22; E5].**

In the same way as T2.7; E1, n-BuLi (0.14 ml, 2.5M in hexanes, 0.35 mmol), 4-phenyl-oxazolidin-2-one (R)-94 (50 mg, 0.32 mmol), 4,5,5-triphenyl-oxazolidin-2-one (S)-175 (0.100 g, 0.32 mmol) and pentafluorophenyl-2-phenylacetate 190 (0.192 g, 0.63 mmol) in THF (10 ml). Gave by crude $^1$H NMR 3-(2-phenylactetyl)-4-phenyl-oxazolidin-2-one (R)-201, characteristic data $\delta_H$ (400 MHz; CDCl$_3$) 5.42 (1H, dd, $J$ 8.8 and 3.9, CHN), 4.69 (1H, t, $J$ 8.8, CH$_A$H$_B$O) and 4.30-4.24 (3H, m, CH$_2$Ph and CH$_A$H$_B$O), and 3-(2-phenylactetyl)-4,5,5-triphenyl-oxazolidin-2-one (S)-202, characteristic data $\delta_H$ (400 MHz; CDCl$_3$) 6.20 (1H, s, CHN) and 4.28 (2H, br s, CH$_2$Ph); (ratio evans 201 : seeback 202 49 : 51).

**Competitive reaction of 4-phenyl-oxazolidin-2-one (R)-94 and 4,5,5,-triphenyl-oxazolidin-2-one (S)-175 with active ester 190 [T2.22; E6].**

In the same way as T2.7; E1, n-BuLi (0.28 ml, 2.5M in hexanes, 0.70 mmol), 4-phenyl-oxazolidin-2-one (R)-94 (50 mg, 0.32 mmol), 4,5,5-triphenyl-oxazolidin-2-one (S)-175 (0.100 g, 0.32 mmol) and pentafluorophenyl-2-phenylacetate 190 (0.192 g, 0.63 mmol) in THF (10 ml). Gave by crude $^1$H NMR 3-(2-phenylactetyl)-4-phenyl-oxazolidin-2-one (R)-201, and 3-(2-phenylactetyl)-4,5,5-triphenyl-oxazolidin-2-one (S)-202, (ratio evans 201 : seeback 202 59 : 41).
Competitive reaction of 4-phenyl-oxazolidin-2-one (R)-94 and 4,5,5,-triphenyl-oxazolidin-2-one (S)-175 with active ester 193 [T2.22; E7].

In the same way as T2.7; E1, n-BuLi (0.14 ml, 2.5M in hexanes, 0.35 mmol), 4-phenyl-oxazolidin-2-one (R)-94 (50 mg, 0.32 mmol), 4,5,5-triphenyl-oxazolidin-2-one (S)-175 (0.100 g, 0.32 mmol) and pentafluorophenyl-2,2-dimethyl-propionate 193 (0.164 g, 0.63 mmol) in THF (10 ml). Gave by crude $^1$H NMR 3-(2,2-dimethyl-propionate)-4-phenyl-oxazolidin-2-one (R)-203 characteristic data $\delta_H$ (400 MHz; CDCl$_3$) 5.41 (1H, dd, $J_{2.7}$ and $J_{4.6}$, CHN), 6.14 (1H, s, CHN), 4.61 (1H, t, $J_{8.6}$, CH$_3$H$_8$O) and 4.13 (1H, dd, $J_{8.6}$ and 4.6, CH$_3$H$_8$O), and 3-(2,2-dimethyl-propionate)-4,5,5-triphenyl-oxazolidin-2-one (S)-204 characteristic data $\delta_H$ (400 MHz; CDCl$_3$) 6.14 (1H, s, CHN), (ratio evans 203 : seeback 204 94 : 6).

Competitive reaction of 4-phenyl-oxazolidin-2-one (R)-94 and 4,5,5,-triphenyl-oxazolidin-2-one (S)-175 with active ester 193 [T2.22; E8].

In the same way as T2.7; E1, n-BuLi (0.28 ml, 2.5M in hexanes, 0.70 mmol), 4-phenyl-oxazolidin-2-one (R)-94 (50 mg, 0.32 mmol), 4,5,5-triphenyl-oxazolidin-2-one (S)-175 (0.100 g, 0.32 mmol) and pentafluorophenyl-2,2-dimethyl-propionate 193 (0.164 g, 0.63 mmol) in THF (10 ml). Gave by crude $^1$H NMR 3-(2,2-dimethyl-propionate)-4-phenyl-oxazolidin-2-one (R)-203, and 3-(2,2-dimethyl-propionate)-4,5,5-triphenyl-oxazolidin-2-one (S)-204, (ratio evans 203 : seeback 204 100 : 0).

Competitive reaction of 4-phenyl-oxazolidin-2-one (R)-94 and 4,5,5,-triphenyl-oxazolidin-2-one (S)-175 with active ester 196 [T2.22; E9].

In the same way as T2.7; E1, n-BuLi (0.14 ml, 2.5M in hexanes, 0.35 mmol), 4-phenyl-oxazolidin-2-one (R)-94 (50 mg, 0.32 mmol), 4,5,5-triphenyl-oxazolidin-2-one (S)-175 (0.100 g, 0.32 mmol) and pentafluorophenyl benzyl acetate 196 (0.182 g, 0.63 mmol) in THF (10 ml). Gave by crude $^1$H NMR 3-(benzyl acetyl)-4-phenyl-oxazolidin-2-one (R)-205 characteristic data $\delta_H$ (400 MHz; CDCl$_3$) 5.57 (1H, dd, $J_{8.9}$ and 7.3, CHN), 4.71 (1H, t, $J_{8.9}$, CH$_3$H$_8$O) and 4.26 (1H, dd, $J_{8.9}$ and 7.3, CH$_3$H$_8$O), and 3-(benzyl acetyl)-4,5,5-triphenyl-oxazolidin-2-one (S)-206 characteristic data $\delta_H$ (400 MHz; CDCl$_3$) 6.25 (1H, s, CHN), (ratio evans 205 : seeback 206 79 : 21).
Competitive reaction of 4-phenyl-oxazolidin-2-one \((R)-94\) and 4,5,5,-triphenyl-oxazolidin-2-one \((S)-175\) with active ester 196 [T2.22; E10].

In the same way as T2.7; E1, \(n\)-BuLi (0.28 ml, 2.5M in hexanes, 0.70 mmol), 4-phenyl-oxazolidin-2-one \((R)-94\) (50 mg, 0.32 mmol), 4,5,5-triphenyl-oxazolidin-2-one \((S)-175\) (0.100 g, 0.32 mmol) and pentafluorophenyl benzyl acetate 196 (0.182 g, 0.63 mmol) in THF (10 ml). Gave by crude \(^1\)H NMR 3-(benzyl acetyl)-4-phenyl-oxazolidin-2-one \((R)-205\), and 3-( benzyl acetyl)-4,5,5-triphenyl-oxazolidin-2-one \((S)-206\), (ratio evans 205 : seeback 206 65 : 35).

Cross over reaction 4-phenyl-oxazolidin-2-one \((R)-94\) and 4-phenyl-5,5,-diphenyl-oxazolidin-2-one \((S)-175\) and active esters \((R)-119\) and \((S)-123\) [S2.39].

In the same way as T2.7; E1, \(n\)-BuLi (0.24 ml, 2.5M in hexanes, 0.60 mmol), 4-phenyl-oxazolidin-2-one \((R)-94\) (43 mg, 0.27 mmol), 4,5,5-triphenyl-oxazolidin-2-one \((S)-175\) (86 mg, 0.27 mmol), pentafluorophenyl-2-phenylbutanoate \((R)-119\) (90 mg, 0.27 mmol) and pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propionate \((S)-123\) (0.108 g, 0.27 mmol) in THF (10 ml). Gave a mixture of two sets of oxazolidin-2-ones, from 4,5,5-triphenyl-oxazolidin-2-one \((S)-175\): \((R)_2\)-syn-177 and \((S)_2\)-anti-182 (ratio syn : anti >95 : 5) and from 4-phenyl-oxazolidin-2-one \((R)-94\): \((S)_2\)-syn-156 and \((R)_2\)-anti-153 (ratio syn : anti >95 : 5). The crude residue gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 3:7) 3-(2-phenyl-butanoyl)-4,5,5-triphenyl-oxazolidin-2-one \((R,S)-\)syn-177 (84 mg, 67%) and 3-[(6-methoxy-2-naphthyl)-propionyl]-4-phenyl-oxazolidin-2-one \((S,R)-\)syn-156 (49 mg, 48%), which were spectroscopically identical to that obtained elsewhere.

Hydrolysis of 3-(2-phenyl-propionly)-4,5,5-triphenyl-oxazolidin-2-one \((R,S)-\)syn-176 [S2.40; E1].

In the same way as S2.17; E1, 3-(2-phenyl-propionly)-4,5,5-triphenyl-oxazolidin-2-one \((R,S)-\)syn-176 (66 mg, 0.15 mmol, 96% d.e.), LiOH.H2O (12 mg, 0.29 mmol) and H2O2 (0.08 ml, 3.53M in water, 0.29 mmol) in THF/water (3:1, 4 ml). Gave 4,5,5-triphenyl-oxazolidin-2-one \((S)-175\) (44 mg, 95%), as a white solid mp above 200 °C, \([\alpha]_D^{20} = -213.9\) (c 2.1, CHCl3), and 2-phenyl-propionic acid \((R)-111\) (21 mg, 95%) as an oil, \([\alpha]_D^{20} = -55.9\) (c 3.8, CHCl3),which were spectroscopically identical to that obtained elsewhere.
Hydrolysis of 3-(2-deuterio-2-phenyl-propionly)-4-phenyl-5,5-diphenyl-oxazolidin-2-one \((R,S)\)-syn-217 [S2.40; E2].

In the same way as S2.17; E1, 3-(2-deuterio-2-phenyl-propionly)-4-phenyl-5,5-phenyl-oxazolidin-2-one \((R,S)\)-syn-217 \((61 \text{ mg}, 0.14 \text{ mmol})\), LiOH.H\(_2\)O \((11 \text{ mg}, 0.27 \text{ mmol})\) and H\(_2\)O\(_2\) \((0.08 \text{ ml}, 3.53\text{M in water}, 0.27 \text{ mmol})\) in THF/water \((3:1, 4 \text{ ml})\). Gave 4-phenyl-5,5-phenyl-oxazolidin-2-one \((S)\)-175 \((41 \text{ mg}, 95\%)\), which was spectroscopically identical to that obtained elsewhere, and 2-deuterio-2-phenyl-propionic acid \((R)\)-162 \((19 \text{ mg}, 92\%)\), which were spectroscopically identical to that obtained elsewhere.

Competitive reaction of 4-phenyl-oxazolidin-2-one \((R)\)-94 and 4,5,5-triphenyl-oxazolidin-2-one \((R)\)-175 with active ester \((S)\)-115 [T2.23; E1].

In the same way as T2.7; E1, n-BuLi \((0.28 \text{ ml}, 2.5\text{M in hexanes}, 0.69 \text{ mmol})\), 4-phenyl-oxazolidin-2-one \((R)\)-94 \((51 \text{ mg}, 0.31 \text{ mmol})\), 4,5,5-triphenyl-oxazolidin-2-one \((R)\)-175 \((99 \text{ mg}, 0.31 \text{ mmol})\) and pentafluorophenyl-2-(4-isobutyl-phenyl)-propionate \((S)\)-115 \((0.117 \text{ g}, 0.31 \text{ mmol})\) in THF \((10 \text{ ml})\). Gave by crude \(^1\text{H NMR}\) a mixture of 3-[2-(4-isobutyl-phenyl)-propionyl]-4-phenyl-oxazolidin-2-one \((S,R)\)-syn-163 and 3-[2-(4-isobutyl-phenyl)-propionyl]-4,5,5-triphenyl-oxazolidin-2-one \((S,R)\)-syn-180 (ratio \((S,R)\)-syn-163 : \((S,R)\)-syn-180 \(70 : 30\)).

Competitive reaction of 4-phenyl-oxazolidin-2-one \((R)\)-94 and 4-(4-hydroxy-phenyl)-oxazolidin-2-one \((R)\)-218 with active ester \((S)\)-115 [T2.23; E2].

In the same way as T2.7; E1, n-BuLi \((0.27 \text{ ml}, 2.5\text{M in hexanes}, 0.66 \text{ mmol})\), 4-phenyl-oxazolidin-2-one \((R)\)-94 \((33 \text{ mg}, 0.20 \text{ mmol})\), 4-(4-hydroxy-phenyl)-oxazolidin-2-one \((R)\)-218 \((36 \text{ mg}, 0.20 \text{ mmol})\) and pentafluorophenyl-2-(4-isobutyl-phenyl)-propionate \((S)\)-115 \((75 \text{ mg}, 0.20 \text{ mmol})\) in THF \((10 \text{ ml})\). Gave by crude \(^1\text{H NMR}\) 3-[2-(4-isobutyl-phenyl)-propionyl]-4-phenyl-oxazolidin-2-one \((S,R)\)-syn-163 (no 3-[2-(4-isopropyl-phenyl)-propionyl]-4-(4-hydroxy-phenyl)-oxazolidin-2-one \((S,R)\)-syn-220 was obtained).

Competitive reaction of 4-phenyl-oxazolidin-2-one \((R)\)-94 and 4-(4-tert-butyldimethylsilyoxy-phenyl)-oxazolidin-2-one \((R)\)-219 with active ester \((S)\)-115 [T2.23; E3].

In the same way as T2.7; E1, n-BuLi \((0.26 \text{ ml}, 2.5\text{M in hexanes}, 0.65 \text{ mmol})\), 4-phenyl-oxazolidin-2-one \((R)\)-94 \((48 \text{ mg}, 0.29 \text{ mmol})\), 4-(4-tert-butyldimethylsilyoxy-
phenyl)-oxazolidin-2-one \((R)-219\) (86 mg, 0.29 mmol) and pentafluorophenyl-2-(4-isobutyl-phenyl)-propionate \((S)-115\) (0.109 g, 0.29 mmol) in THF (10 ml). Gave by crude \(^1\)H NMR a mixture of 3-[2-(4-isobutyl-phenyl)-propionyl]-4-phenyl-oxazolidin-2-one \((S,R)\)-syn-163 and 3-[2-(4-isobutyl-phenyl)-propionyl]-4-(4-tert-butyldimethylsilyloxy-phenyl)-oxazolidin-2-one \((S,R)\)-syn-221 (ratio \((S,R)\)-syn-163 : \((S,R)\)-syn-221 52 : 48). Characteristic data for 3-[2-(4-isobutyl-phenyl)-propionyl]-4-(4-tert-butyldimethylsilyloxy-phenyl)-oxazolidin-2-one \((S,R)\)-syn-221 \(\delta_H\) (400 MHz; CDCl\(_3\)) 5.10 (1H, dd, \(J\) 9.2 and 5.2, CHN), 4.7t (1H, q, \(J\) 7.0, CHCH\(_3\)), 4.31 (1H, t, \(J\) 9.2, \(CH_AH_B\)O) and 3.77 (1H, dd, \(J\) 9.2 and 5.2, \(CH_AH_B\)O).

**Competitive reaction of 4,5,5-triphenyl-oxazolidin-2-one \((R)\)-175 and 4-(4-hydroxy-phenyl)-oxazolidin-2-one \((R)\)-218 with active ester \((S)\)-115 \([T2.23; E4]\).**

In the same way as T2.7; E1, \(n\)-BuLi (0.41 ml, 2.5M in hexanes, 1.01 mmol), 4,5,5-triphenyl-oxazolidin-2-one \((R)\)-175 (97 mg, 0.31 mmol), 4-(4-hydroxy-phenyl)-oxazolidin-2-one \((R)\)-218 (55 mg, 0.31 mmol) and pentafluorophenyl-2-(4-isobutyl-phenyl)-propionate \((S)\)-115 (0.114 g, 0.31 mmol) in THF (10 ml). Gave by crude \(^1\)H NMR 3-[2-(4-isobutyl-phenyl)-propionyl]-4,5,5-triphenyl-oxazolidin-2-one \((S,R)\)-syn-180 (no 3-[2-(4-isopropyl-phenyl)-propionyl]-4-(4-hydroxy-phenyl)-oxazolidin-2-one \((S,R)\)-syn-220 was obtained).

**Competitive reaction of 4,5,5-triphenyl-oxazolidin-2-one \((R)\)-175 and 4-(4-tert-butyldimethylsilyloxy-phenyl)-oxazolidin-2-one \((R)\)-219 with active ester \((S)\)-115 \([T2.23; E5]\).**

In the same way as T2.7; E1, \(n\)-BuLi (0.21 ml, 2.5M in hexanes, 0.53 mmol), 4,5,5-triphenyl-oxazolidin-2-one \((R)\)-175 (76 mg, 0.24 mmol), 4-(4-tert-butyldimethylsilyloxy-phenyl)-oxazolidin-2-one \((R)\)-218 (71 mg, 0.24 mmol) and pentafluorophenyl-2-(4-isobutyl-phenyl)-propionate \((S)\)-115 (90 mg, 0.24 mmol) in THF (10 ml). Gave by crude \(^1\)H NMR a mixture of 3-[2-(4-isobutyl-phenyl)-propionyl]-4,5,5-triphenyl-oxazolidin-2-one \((S,R)\)-syn-180 and 3-[2-(4-isobutyl-phenyl)-propionyl]-4-(4-tert-butyldimethylsilyloxy-phenyl)-oxazolidin-2-one \((S,R)\)-syn-221 (ratio \((S,R)\)-syn-180 : \((S,R)\)-syn-221 30 : 70).
Competitive reaction of 4-(4-hydroxy-phenyl)-oxazolidin-2-one (R)-218 and 4-(4-tert-butyldimethylsilyloxy-phenyl)-oxazolidin-2-one (R)-219 with active ester (S)-115 [T2.23; E6].

In the same way as T2.7; E1, n-BuLi (0.42 ml, 2.5M in hexanes, 1.05 mmol), 4-(4-hydroxy-phenyl)-oxazolidin-2-one (R)-218 (57 mg, 0.32 mmol), 4-(4-tert-butyldimethylsilyloxy-phenyl)-oxazolidin-2-one (R)-219 (93 mg, 0.32 mmol) and pentafluorophenyl-2-(4-isopropyl-phenyl)-propionate (S)-115 (0.118 g, 0.32 mmol) in THF (10 ml). Gave by crude ¹H NMR 3-[2-(4-isobutyl-phenyl)-propionyl]-4-(4-tert-butyldimethylsilyloxy-phenyl)-oxazolidin-2-one (S,R)-syn-220 (no 3-[2-(4-isopropyl-phenyl)-propionyl]-4-(4-hydroxy-phenyl)-oxazolidin-2-one (S,R)-syn-221 was obtained).

PKR of active ester (rac)-95 using 4-(4-hydroxy-phenyl)-oxazolidin-2-one (R)-218 and 4-phenyl-oxazolidin-2-one (S)-94 [S2.41].

In the same way as T2.7; E1 but leaving the reaction to stir over night, n-BuLi (0.81 ml, 2.5M in hexanes, 2.02 mmol), 4-(4-hydroxy-phenyl)-oxazolidin-2-one (R)-218 (0.110 g, 0.61 mmol), 4-phenyl-oxazolidin-2-one (S)-94 (0.100 g, 0.61 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.446 g, 1.41 mmol) in THF (10 ml). Gave a mixture of 3-(2-phenyl-propionyl)-4-(4-hydroxy-phenyl)-oxazolidin-2-one (S,R)-syn and (R,R)-anti-222 (ratio syn : anti >95 : 5) and 3-(2-phenyl-propionyl)-4-phenyl-oxazolidin-2-one (R,S)-syn and (S,S)-anti-96 (ratio syn : anti >95 : 5). After purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 0:1) obtained 3-(2-phenyl-propionyl)-4-phenyl-oxazolidin-2-one (R,S)-syn-96 (0.148 g, 82%) which was spectroscopically identical to that obtained elsewhere, and 3-(2-phenyl-propionyl)-4-(4-hydroxy-phenyl)-oxazolidin-2-one (S,R)-syn-222 (58 mg, 30%) as a white solid mp 135-137°C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.07; [α]D 0 = +81.2 (c 1.3, CHCl₃), v_max (ethanol)/cm⁻¹ 1783 and 1756 (2 × C=O); δ_H (400 MHz; CDCl₃) 7.16-7.11 (3H, m, 3 × CH; Ph), 7.05-6.99 (2H, m, 2 × CH; Ph), 6.73 (2H, dt, J 8.6 and 2.4, 2 × CH; Ar), 6.55 (2H, dt, J 8.6 and 2.4, 2 × CH; Ar), 5.95 (1H, s, OH), 5.32 (1H, dd, J 9.0 and 5.0, CHN), 5.01 (1H, q, J 7.0, CHPh), 4.54 (1H, t, J 9.0, CH₃H₂O), 4.00 (1H, dd, J 9.0 and 5.0, CH₃H₂O) and 1.33 (3H, d, J 7.0, PhCHCH₃); δ_C (100 MHz; CDCl₃) 173.8 (NC=O), 155.7, 139.8 and 130.4 (3 × i-C; Ph and Ar), 153.1 (OC=O), 128.5² 128.1² and 127.1¹ (5 × CH; Ph), 127.5² and 115.6² (4 × CH; Ar), 69.7 (CH₂O), 57.4 (CHN),
PKR of active ester (rac)-95 using 4-(4-hydroxy-phenyl)-oxazolidin-2-one (R)-218 and 4,5,5-triphenyl-oxazolidin-2-one (S)-175 [S2.42].

In the same way as T2.7; E1 but leaving the reaction to stir over night, n-BuLi (0.74 ml, 2.5M in hexanes, 1.84 mmol), 4-(4-hydroxy-phenyl)-oxazolidin-2-one (R)-218 (0.1 g, 0.55 mmol), 4,5,5-triphenyl-oxazolidin-2-one (S)-175 (0.175 g, 0.55 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.41 g, 1.28 mmol) in THF (10 ml). Gave a mixture of 3-(2-phenyl-propionyl)-4-(4-hydroxy-phenyl)-oxazolidin-2-one (S,R)-syn and (R,R)-anti-222 (ratio syn : anti >95 : 5) and 3-(2-phenyl-propionyl)-4,5,5-triphenyl-oxazolidin-2-one (R,S)-syn and (S,S)-anti-176 (ratio syn : anti 92 : 8). After purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3 → 0:1) obtained 3-(2-phenyl-propionyl)-4,5,5-triphenyl-oxazolidin-2-one (S,S)-anti and (R,S)-syn-176 (0.142 g, 57%, ratio syn : anti 92 : 8), and 3-(2-phenyl-propionyl)-4-(4-hydroxy-phenyl)-oxazolidin-2-one (S,R)-syn-222 (78 mg, 45%), which were spectroscopically identical to that obtained elsewhere.

KR of active ester (rac)-95 using 4-(2,5-dihydrophenyl)-oxazolidin-2-one (R)-223 [S2.43].

In the same way as T2.7; E1, n-BuLi (0.46 ml, 2.5M in hexanes, 1.11 mmol), 4-(2,5-dihydrophenyl)-oxazolidin-2-one (rac)-223 (0.1 g, 0.56 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.65 g, 2.07 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) 3-(2-phenyl-propionyl)-4-(2,5-dihydrophenyl)-oxazolidin-2-one (R,R)-anti-224 (21 mg, 7%) as yellow solid mp 94-96 °C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.45; \( \nu_{\text{max}} \) (CHCl₃)/cm⁻¹ 1779 and 1704 (2 × C=O); \( \delta_H \) (400 MHz; CDCl₃) 7.40-7.20 (5H, m, 5 × CH; Ph), 5.76-5.68 (3H, m, 3 × CH=), 5.12 (1H, q, J 7.0, CHAr), 4.78 (1H, dd, J 8.6 and 2.9, CHN), 4.32 (1H, t, J 8.6, CH₃H₈O), 4.04 (1H, dd, J 9.0 and 3.1, CH₃H₈O), 2.88-2.47 (4H, m, 2 × CH₂) and 1.50 (3H, d, J 7.0, ArCHCH₃); \( \delta_C \) (100 MHz; CDCl₃) 174.2 and 153.3 (2 × C=O), 140.2 (i-C; Ph), 131.3 and 129.2 (2 × C=), 128.6,² 128.2 and 127.2 (5 × CH; Ph), 124.2 and 122.8 (2 × CH=), 67.1 (CH₂O), 59.5 (CHN), 43.1 (PhCHCH₃), 26.4 and 24.1 (2 × CH₂) and 19.5 (PhCHCH₃), and 3-(2-phenyl-propionyl)-4-(2,5-dihydrophenyl)-oxazolidin-2-one (S,R)-syn-224 (0.112 g, 36%) (ratio syn : anti 91 : 9),
as an oil; $R_f$ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.44; $\nu_{\max}$ (CHCl$_3$)/cm$^{-1}$ 1775 and 1705 (2 × C=O); $\delta_H$ (400 MHz; CDCl$_3$) 7.41-7.17 (5H, m, 5 × CH; Ph), 5.63-5.57 (1H, m, CH=), 5.53-5.47 (1H, m, CH=), 5.44-5.39 (1H, m, CH=), 5.10 (1H, q, J 7.0, CHAr), 4.89 (1H, dd, J 8.8 and 3.8, CHN), 4.39 (1H, t, J 8.8, CH$_4$H$_8$O), 3.96 (1H, dd, J 8.8 and 3.8, CH$_3$H$_6$O), 2.66-2.50 (2H, m, CH$_2$), 2.45-2.31 (1H, m, CH$_3$H$_8$B), 2.02-1.91 (1H, m, CH$_3$H$_8$B) and 1.43 (3H, d, J 7.0, ArCHCH$_3$); $\delta_C$ (100 MHz; CDCl$_3$) 173.8 (NC=O), 153.1 (OC=O), 140.0 (C=), 128.5. $^2$ 128.1. $^2$ and 127.0 (5 × CH; Ph), 123.6, 122.9 and 122.8 (3 × CH=), 66.6 (CH), 58.7 (CHN), 43.4 (PhCHCH$_3$), 26.1 and 23.6 (2 × CH$_2$) and 18.6 (PhCHCH$_3$); (Found MH$^+$, 315.1702; C$_{18}$H$_{25}$N$_2$O$_3$ requires 315.1703).

**Hydrolysis of 3-(2-phenyl-propionly)-4-[4-(tert-butyl-dimethylsilyloxy)-phenyl]-oxazolidin-2-one (rac)-syn-225 [S2.44; E1].**

In the same way as S2.17; E1, 3-(2-phenyl-propionly)-4-[4-(tert-butyl-dimethylsilyloxy)-phenyl]-oxazolidin-2-one (rac)-syn-225 (48 mg, 0.11 mmol), LiOH.H$_2$O (5 mg, 0.11 mmol) and H$_2$O$_2$ (0.03 ml, 3.53M in water, 0.11 mmol) in THF/water (3:1, 4 ml). Gave 4-[4-(tert-butyl-dimethylsilyloxy)-phenyl]-oxazolidin-2-one (rac)-219 (22 mg, 66%) as white solid mp 104-106 °C; $R_f$ [dichloromethane] 0.13; $\nu_{\max}$ (CHCl$_3$)/cm$^{-1}$ 1761 (C=O); $\delta_H$ (400 MHz; CDCl$_3$) 8.13 (1 H, s, NH), 7.27 (2 H, d, J 8.4, 2 × CH; Ar), 6.91 (2 H, d, J 8.4, 2 × CH; Ar), 4.91 (1 H, dd, J 8.4 and 6.7, CHN), 4.67 (1 H, t, J 8.4, CH$_4$H$_8$O), 4.01 (1 H, dd, J 8.4 and 6.7, CH$_3$H$_6$O), 0.99 (9 H, s, 3 × CH$_3$C; t-Bu) and 0.22 (6 H, s, 2 × CH$_3$Si); $\delta_C$ (100 MHz; CDCl$_3$) 158.9 (C=O), 154.9 (i-CO; Ar), 133.8 (i-C; Ar), 127.5 and 120.1 (4 × CH; Ar), 71.5 (CH$_2$O), 54.7 (CHN), 25.6 (3 × CH$_3$C; t-Bu), 17.9 (CH$_3$C; t-Bu) and -4.5 (2 × CH$_3$Si), and 2-phenyl-propionic acid (rac)-111 (16 mg, 95%), which was spectroscopically identical to that obtained elsewhere.

**Hydrolysis of 3-(2-deutério-2-phenyl-propionly)-4-[4-(tert-butyl-dimethylsilyloxy)-phenyl]-oxazolidin-2-one (S,R)-syn-226 [S2.44; E2].**

In the same way as S2.17; E1, 3-(2-phenyl-propionly)-4-[4-(tert-butyl-dimethylsilyloxy)-phenyl]-oxazolidin-2-one (S,R)-syn-226 (73 mg, 0.17 mmol), LiOH.H$_2$O (7 mg, 0.17 mmol) and H$_2$O$_2$ (0.05 ml, 3.53M in water, 0.17 mmol) in THF/water (3:1, 4 ml). Gave 4-[4-(tert-butyl-dimethylsilyloxy)-phenyl]-oxazolidin-2-one (R)-219 (44 mg, 88%) as yellow solid mp 130-133 °C; $[\alpha]_{D}^{20} = +68.0$ (c 1.7, CHCl$_3$),
and 2-deuterio-2-phenyl-propionic acid (S)-162 (20 mg, 77%), as an oil; \([\alpha]_D^{20} = +68.0\) (c 1.7, CHCl$_3$), which were spectroscopically identical to that obtained elsewhere.

**Hydrolysis of 3-(2-phenyl-propionly)-4-(4-hydroxy-phenyl)-oxazolidin-2-one (R,S)-syn-222 [S2.45].**

In the same way as S2.17; E1, 3-(2-phenyl-propionly)-4-(4-hydroxy-phenyl)-oxazolidin-2-one (R,S)-syn-222 (0.111 g, 0.36 mmol), LiOH.H$_2$O (60 mg, 1.43 mmol) and H$_2$O$_2$ (0.40 ml, 3.53M in water, 1.43 mmol) in THF/water (3:1, 4 ml). Gave 4-(4-hydroxy-phenyl)-oxazolidin-2-one (S)-218 (18 mg, 28%) as a white solid mp 141-143°C, \(R_F\) [diethyl ether] 0.05; \([\alpha]_D^{20} = +41.4\) (c 1.7, ethanol); \(\nu_{max}\) (CHCl$_3$)/cm$^{-1}$ 2974 (NH) and 1751 (C=O); \(\delta_H\) (400 MHz; CDCl$_3$) 9.47 (1H, s, OH), 8.03 (1H, s, NH), 7.12 (2H, dt, J 8.5 and 2.4, 2 × CH; Ar), 6.75 (2H, dt, J 8.5 and 2.4, 2 × CH; Ar), 4.80 *1H, dd, J 8.4 and 6.8, CHN), 4.58 (1H, t, J 8.4, CH$_3$H$_2$O) and 3.93 (1H, dd, J 8.4 and 6.8, CH$_3$H$_2$O); \(\delta_C\) (100 MHz; CDCl$_3$) 158.9 (C=O), 157.2 and 131.0 (2 × i-C; Ar), 127.4$^2$ and 115.4$^2$ (4 × CH; Ar), 71.6 (CH$_2$O) and 54.8 (CHN); (Found MNH$_2^+\cdot$197.0923; C$_9$H$_{13}$N$_2$O$_3$ requires 197.0921), and 2-phenyl-propionic acid (R)-111 (48 mg, 90%), which were spectroscopically identical to that obtained elsewhere.

**Synthesis of pentafluorophenyl-2-methoxy-2-phenyl-2-trifluoromethyl-acetate (R)-228 [S2.46].**

DCC (2.469 g, 0.012 mol) was added to 2-methoxy-2-phenyl-2-trifluoromethyl-acetic acid (R)-227 (2.547 g, 0.011 mol) in dichloromethane (50 ml), followed be pentafluorophenyl (2.00 g, 0.011 mol) in dichloromethane (50 ml). The resulting solution was stirred over night, the mixture was filtered to remove DCU, the organic layer was extracted with dichloromethane (3 × 100 ml) washed with water (100 ml), dried over MgSO$_4$, evaporated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) to give pentafluorophenyl-2-methoxy-2-phenyl-2-trifluoromethyl-acetate (R)-228 (3.645 g, 84%) as solid mp 43-44°C, \(R_F\) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.88; \([\alpha]_D^{20} = +42.4\) (c 1.0, CHCl$_3$); \(\nu_{max}\) (CHCl$_3$)/cm$^{-1}$ 1790 (C=O); \(\delta_H\) (400 MHz; CDCl$_3$) 7.62-7.60 (2H, m, 2 × CH; Ph), 7.49-7.45 (3H, m, 3 × CH; Ph) and 3.69 (3H, s, CH$_3$); \(\delta_C\) (100 MHz; CDCl$_3$) 163.2 (C=O), 140.9 (142.25 and 139.73, 2C, ddt, $^1$J$_{C,F}$ = 253.1 Hz, $^2$J$_{C,F}$ = 12.0 Hz and $^3$J$_{C,F}$ = 4.6 Hz, 2 × CF; Ar), 140.1 (141.37 and 138.83, 1C, ddt, $^1$J$_{C,F}$ = 254.0 Hz, $^2$J$_{C,F}$ = 13.8 Hz and $^3$J$_{C,F}$ = 3.8 Hz, CF; Ar), 138.0 (139.24 and 136.89, 2C, dtdd, $^1$J$_{C,F}$ = 249.0 Hz, $^2$J$_{C,F}$

In the same way as T2.7; E1, n-BuLi (0.25 ml, 2.5M in hexanes, 0.63 mmol), 4-phenyl-oxazolidin-2-one \((S)\)-94 (94 mg, 0.58 mmol) and pentafluorophenyl-2-methoxy-2-phenyl-2-trifluoromethyl-acetate \((R)\)-228 (0.231 g, 0.58 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) \(N\)-(2-hydroxy-1-phenylethyl)-2-phenyl-2-methoxy-2-trifluoromethylacetamide \((R,S)\)-syn-229 (57 mg, 28%) which was spectroscopically identical to that obtained elsewhere, and \((2\text{-phenyl-2methyl-2trifluoroethanoyl})[2-[(butoxycarbonyl)oxy]-1-phenyl-ethyl] carbonate \((R,S)\)-syn-230 (82 mg, 31%) as an oil, \(R_F\) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.50; \([\alpha]_{D}^{20} = -24.75\) (c 3.2, CHCl₃); \(\nu_{\text{max}}\) (CHCl₃)/\(\text{cm}^{-1}\) 1742 and 1702 (2 × C=O); \(\delta_{\text{H}}\) (400 MHz; CDCl₃) 7.55-7.51 (2H, m, 2 × CH; Ph), 7.39-7.36 (4H, m, 4 × CH; Ph), 7.35-7.33 (2H, m, 2 × CH; Ph), 7.32-7.29 (2H, m, 2 × CH; Ph), 5.27 (1H, dt, \(J 8.4\) and 6.0, PhCHN), 4.38 (2H, d, \(J 6.0\), CH₂O), 4.08 (2H, td, \(J 6.8\) and 3.8, CH₂O; OBu), 3.36 (3H, s, CH₃O), 1.59 (2H, appears as a quintet, \(J 6.7\), CH₂), 1.35 (2H, appears as a sextet, \(J 7.3\), CH₂) and 0.85 (3H, t, \(J 7.3\), CH₃CH₂); \(\delta_{C}\) (100 MHz; CDCl₃) 166.2 (NC=O), 155.3 (OC=O), 137.2 and 132.3 (2 × i-C; Ph), 129.5,¹ 128.9,² 128.5,² 128.2,¹ 127.8² and 126.6² (10 × CH; Ph), 123.7 (1C, q, \(J_{C,F} = 288.3\), CF₃), 84.1 (1C, q, \(J_{C,F} = 26.8\), PhCCF₃), 68.7 (CH₂O), 68.3 (CH₂O), 54.9 (PhCHN), 52.5 (OCH₃), 30.6 (CH₂), 18.8 (CH₂) and 13.6 (CH₃); \(\delta_{F}\) (378 MHz; CDCl₃) -68.7 (1C, s, CF₃); (Found MH⁺, 454.1835; C₂₃H₂₇F₃NO₅ requires 454.1836).

Reaction of butanol with oxazolidinone adduct \((R,S)\)-syn-231 [S2.48].

\(n\)-BuLi (0.07 ml, 2.5M in hexanes, 0.18 mmol) was added to butanol (22 mg, 0.30 mmol) in THF (2.5 ml) at -78°C, followed by 3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-4-phenyl-oxazolidin-2-one \((R,S)\)-syn-231 (23 mg, 0.06 mmol) in THF (2.5 ml). The resulting mixture was stirred over night, quenched with water (5
ml), the organic layer was extracted with dichloromethane (3 × 10 ml), washed with brine (10 ml), dried over MgSO₄, and evaporated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3 → 3:7) to give N-(2-hydroxy-1-phenylethyl)-2-phenyl-2-methoxy-2-trifluoromethylacetamide (R,S)-syn-229 (9 mg, 42%) as a white solid mp 160-163°C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.04; [α]D⁰ = +42.8 (c 1.1, CHCl₃); νmax (CHCl₃)/cm⁻¹ 3020 (OH and NH) and 1782 (C=O); δH (400 MHz; CDCl₃) 7.51-7.48 (3H, m, 3 × CH; Ph), 7.40-7.19 (9H, m, 7 × CH; Ph, OH and NH), 5.06 (1H, dt, J 7.7 and 4.9, PhCHN), 3.86-3.78 (2H, m, CH₂O) and 3.31 (3H, s, CH₃O); δC (100 MHz; CDCl₃) 166.7 (C=O), 138.1 and 132.2 (2 × i-C; Ph), 129.6, 128.9, 128.8, 128.0, 127.8 and 126.6 (10 × CH; Ph), 123.8 (1C, q, 1JCF = 24.7, CF₃), 66.1 (CH₂O), 55.5 (CH₃O) and 54.9 (PhCHN); δF (378 MHz; CDCl₃) -70.1 (1C, s, CF₃); (Found MH⁺, 354.1310; C₁₉H₁₉F₃NO₃ requires 354.1312).

**Stereo-specific synthesis of 3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-4-phenyl-oxazolidin-2-one (R,S)-syn-231 [S2.49].**

In the same way as T2.7: E1, KN(SiMe₃)₂ (0.110 g, 0.55 mmol), 4-phenyl-oxazolidin-2-thione (S)-94 (82 mg, 0.50 mmol) and pentafluorophenyl-2-methoxy-phenyl-2-trifluoromethyl-acetate (R)-228 (0.200 g, 0.50mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 3:7) 3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-4-phenyl-oxazolidin-2-one (R,S)-syn-231 (65 mg, 34%) as white solid mp 173-175°C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.13; [α]D⁰ = +17.4 (c 1.4, CHCl₃); νmax (CHCl₃)/cm⁻¹ 1796 (C=O) and 1702 (C=O); δH (400 MHz; CDCl₃) 7.45-7.42 (2H, m, 2 × CH; Ph), 7.35-7.26 (8H, m, 8 × CH; Ph), 5.50 (1H, dd, J 6.0 and 2.5, PhCHN), 4.55 (1H, t, J 6.0, CH₃H₈O), 4.22 (1H, dd, J 6.0 and 2.5, CH₃H₈O) and 3.45 (3H, s, CH₃O); δC (100 MHz; CDCl₃) 166.3 (NC=O), 149.7 (OC=O), 138.1 and 131.8 (2 × i-C; Ph), 129.3, 129.2, 129.0, 127.6, 126.6 and 126.5 (10 × CH; Ph), 123.3 (1C, q, 1JCF = 291.3 CF₃), 85.6 (1C, q, 2JCF = 26.2 CCF₃), 69.9 (CH₂O), 58.7 (PhCHN) and 56.6 (1C, d, 4JCF = 2.3 CH₃O); δF (378 MHz; CDCl₃) -71.0 (3F, s, CF₃); (Found MH⁺, 397.1372; C₁₉H₂₀N₂O₄ requires 379.1370).

**KR of active ester (rac)-228 using 4,5,5-triphenyl-oxazolidin-2-one (S)-175 [S2.50].**

In the same way as T2.7: E1, n-BuLi (0.10 ml, 2.5M in hexanes, 0.24 mmol), 4,5,5-triphenyl-oxazolidin-2-one (S)-175 (68 mg, 0.22 mmol) and pentafluorophenyl-2-
methoxy-2-phenyl-2-trifluoromethyl-acetate \((rac)-228\) (0.173 g, 0.43 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) 3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-4,5,5-triphenyl-oxazolidin-2-one \((R,S)-\text{syn}\) and \((S,S)-\text{anti}-232\) (42 mg, 51%, ratio syn : anti 95 : 5), which were spectroscopically identical to that obtained elsewhere.

**Stereo-specific synthesis of 3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-4,5,5-triphenyl-oxazolidin-2-one \((R,S)-\text{syn}-232\)** [S2.51].

In the same way as T2.7; E1, \(n\)-BuLi (0.56 ml, 2.5M in hexanes, 1.40 mmol), 4,5,5-triphenyl-oxazolidin-2-one \((S)-175\) (0.401 g, 1.27 mmol) and pentafluorophenyl-2-methoxy-2-phenyl-2-trifluoromethyl-acetate \((R)-282\) (0.509 g, 1.27 mmol) in THF (20 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) 3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-4,5,5-triphenyl-oxazolidin-2-one \((R,S)-\text{syn}-232\) (0.330 g, 69%) as an oil, \(R_F\) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.75; [\(\alpha\)]\(_D\) = -2.7 (c 0.9, CHCl\(_3\)); \(\nu_{max}\) (CHCl\(_3\))/cm\(^{-1}\) 1792 and 1715 (2 × C=O); \(\delta_H\) (400 MHz; CDCl\(_3\)) 7.53-747 (2H, m, 2 × CH; Ph), 7.40-7.30 (4H, m, 4 × CH; Ph), 7.10 (1H, t, J 7.3, CH; Ph), 7.05-6.85 (13H, m, 13 × CH; Ph), 6.23 (1H, s, PhCH) and 3.35 (3H, s, CH\(_3\)O); \(\delta_C\) (100 MHz; CDCl\(_3\)) 165.6 (NC=O), 149.0 (OC=O), 141.7, 137.2, 135.1 and 131.4 (4 × i-C; Ph), 129.0,\(^2\) 128.9,\(^1\) 128.8,\(^1\) 128.4,\(^1\) 128.3,\(^2\) 127.8,\(^2\) 127.7,\(^2\) 127.6,\(^2\) 127.5,\(^2\) 126.4,\(^1\) 125.9\(^2\) and 125.5\(^2\) (20 × CH; Ph), 123.3 (1C, q, \(^1\)J\(_{CF}\) = 290.4, CF\(_3\)), 89.2 (CPh\(_2\)), 85.4 (1C, q, \(^2\)J\(_{CF}\) = 25.4, PhCCF\(_3\)), 67.6 (PhCN) and 56.0 (1C, d, \(^4\)J\(_{CF}\) = 2.3, CH\(_3\)O); \(\delta_F\) (378 MHz; CDCl\(_3\)) -71.7 (1C, s, CF\(_3\)); (Found MNa\(^+\), 554.1548; C\(_{31}\)H\(_{24}\)F\(_3\)NO\(_4\)Na requires 554.1550).

**Reaction of butanol with oxazolidinone adduct \((R,S)-\text{syn}-232\)** [S2.52].

In the same way as T2.7; E1 \(n\)-BuLi (0.41 ml, 2.5M in hexanes, 1.03 mmol) was added to butanol (0.127 g, 1.71 mmol) and 3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-4,5,5-triphenyl-oxazolidin-2-one \((R,S)-\text{syn}-232\) (0.130 g, 0.34 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 3:7) butyl-2-methoxy-2-phenyl-2-trifluoromethyl-acetate \((R)-233\) (20 mg, 20%) which was spectroscopically identical to that obtained elsewhere, (2-phenyl-2methyl-2 trifluoroethanoyl){2-[(butoxycarbonyl)oxy]-2-diphenyl-1-phenyl-ethyl} carbonate \((R,S)-\text{syn}-234\) (37 mg,
24%) as a oil, \( R_F \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.54; \([\alpha]_D^{20} = -48.3 \) (c 6.2, CHCl₃, for a mix of \((R,S)\)-syn-234 and \((R,S)\)-syn-232 ratio 89 : 11); \( \nu_{\text{max}} \) (CHCl₃/cm\(^{-1}\)) 1740 and 1709 (2 × C=O); \( \delta_H \) (400 MHz; CDCl₃) 8.90 (1H, br s, NH), 7.55 (2H, br d, J 7.1, 2 × CH; Ph), 7.45-7.35 (3H, m, 3 × CH; Ph), 7.28-7.14 (11H, m, 11 × CH; Ph), 7.05 (2H, br d, J 7.1, 2 × CH; Ph), 6.76 (2H, br d, J 7.1, 2 × CH; Ph), 6.28 (1H, d, J 9.1., PhCH), 4.41 (2H, td, J 6.6 and 1.8, CH₂O; OBu), 3.28 (3H, s, CH₃O), 1.64 (2H, appears as a quintet J 6.6, CH₂), 1.39 (2H, appears as a sextet, J 7.3, CH₂) and 0.94 (3H, t, J 7.3 CH₃CH₂); \( \delta_C \) (100 MHz; CDCl₃) 165.2 (NC=O), 154.1 (OC=O), 141.5, 139.6, 136.5 and 132.4 (4 × i-C; Ph), 129.3, 128.5, 2128.4, 128.1, 127.9, 127.8, 127.7, 127.5, 127.3 and 127.2 (20 × CH; Ph), 123.6 (1C, q, \( J_{C,F} = 288 \), CF₃), 89.1 (CPh₂), 83.4 (1C, q, \( J_{C,F} = 25.2 \), PhCCF₃), 68.3 (CH₂O) 57.9 (PhCHN), 55.1 (CH₃O), 30.6 (CH₂), 18.7 (CH₃) and 13.6 (CH₃); \( \Delta F \) (378 MHz; CDCl₃) -69.0 (1C, s, CF₃); (Found MH⁺, 606.2465; C₃₅H₃₁F₃N₅O₃ requires 606.2462), returned 3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-4,5,5-triphenyl-oxazolidin-2-one (\( R,S \))-syn-232 (5 mg, 4%), which was spectroscopically identical to that obtained elsewhere, also gave (2-phenyl-2-methyl-2-trifluoroethanoyl)-2,2-diphenyl-1-phenyl-ethylamide (\( R,S \))-syn-235 (4 mg, 3%) as a white solid mp 156-160 °C, \( R_F \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.50; \([\alpha]_D^{20} = -132.0 \) (c 1.6, CHCl₃); \( \nu_{\text{max}} \) (CHCl₃/cm\(^{-1}\)) 1781 (C=O); \( \delta_H \) (400 MHz; CDCl₃) 7.86 (1H, br d, J 9.1, NH), 7.50 (2H, dt, J 6.7 and 1.6, 2 × CH; Ph), 7.28-7.20 (3H, m, 3 × CH; Ph), 7.20-7.14 (4H, m, 4 × CH; Ph), 7.14-7.05 (6H, m, 6 × CH; Ph), 7.05-6.99 (5H, m, 5 × CH; Ph), 6.01 (1H, d, J 9.1, PhCH), 3.05 (3H, s, CH₃O) and 2.58 (1H, s, OH); \( \delta_C \) (100 MHz; CDCl₃) 165.1 (C=O), 143.9, 143.7, 136.8 and 131.7 (4 × i-C; Ph), 129.1, 128.5, 128.4, 128.1, 127.9, 127.8, 127.7, 127.2, 127.1, 125.8 and 125.4 (20 × CH; Ph), 123.7 (1C, q, \( J_{C,F} = 289 \), CF₃), 83.9 (1C, q, \( J_{C,F} = 26.1 \), PhCCF₃), 80.8 (CPh₂), 58.8 (CH₂O) and 54.7 (PhCHN); \( \Delta F \) (378 MHz; CDCl₃) -69.1 (1C, s, CF₃); (Found MNH⁺, 523.2208; C₃₀H₃₀F₃N₅O₃ requires 523.2203), and 4,5,5-triphenyl-oxazolidin-2-one (\( S \))-175 (21 mg, 19%), which was spectroscopically identical to that obtained elsewhere.

**Synthesis of butyl-2-methoxy-2-phenyl-2-trifluoromethyl-acetate (\( R \))-233 [S2.53].**

DCC (0.181 g, 0.88 mmol) was added to 2-methoxy-2-phenyl-2-trifluoromethyl-acid (\( R \))-227 (0.187 g, 0.80 mmol) in dichloromethane (5 ml), followed by DMAP (20 mg, 0.16 mmol) and butanol (59 mg, 0.80 mmol) in dichloromethane (5 ml). The resulting solution was stirred over night, the mixture was filtered to remove DCU, the organic layer was extracted with dichloromethane (3 × 20 ml) washed with water

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(20 ml), dried over MgSO₄ and evaporated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) to give butyl-2-methoxy-2-phenyl-2-trifluoromethyl-acetate (R)-233 (0.105 g, 45%) as an oil. Rₐ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.76; [α]D²⁰ = +48.0 (c 5.8, CHCl₃); ν max (CHCl₃)/cm⁻¹ 1747 (C=O); δH (400 MHz; CDCl₃) 7.53-7.48 (2H, m, 2 × CH; Ph), 7.41-7.36 (3H, m, 3 × CH; Ph), 4.36-4.25 (2H, m, CH₂O) 3.53 (3H, q, 3J CF 1.1, OCH₃), 1.70-1.62 (2H, m, CH₂), 1.39-1.30 (2H, appears as a br sextet 7.3, CH₂) and 0.89 (3H, t, J 7.5 CH₃CH₂); δC (100 MHz; CDCl₃) 166.5 (C=O), 132.3 (i-C; Ph), 129.5, 128.3 and 127.2 (5 × CH; Ph), 124.1 (1C, q, 1J CF = 286.5, CF₃), 84.5 (1C, q, 2J CF = 26.7, PhCF₃), 66.2 (CH₂O), 55.3 (OCH₃), 30.3 (CH₂), 18.9 (CH₂) and 13.4 (CH₃); δF (378 MHz; CDCl₃) -71.5 (1C, s, CF₃); (Found MNH⁺, 308.1467; C₁₄H₂₁F₃NO₃ requires 308.1468).

Hydrolysis of 3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-4,5,5-triphenyloxazolidin-2-one (R,S)-syn-232 [S2.54].

In the same way as S2.54; E1, 3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-4,5,5-triphenyloxazolidin-2-one (R,S)-syn-232 (49 mg, 0.092 mmol), LiOH.H₂O (8 mg, 0.18 mmol) and H₂O₂ (0.05 ml, 3.53M in water, 0.18 mmol) in THF/water (3:1, 4 ml). Gave (2-phenyl-2-methyl-2-trifluoromethanoyl)-2,2-diphenyl-1-phenyl-ethylamide (R,S)-syn-235 (11 mg, 24%), 4,5,5-triphenyloxazolidin-2-one (S)-175 (5 mg, 17 %) and 2-methoxy-2-phenyl-2-trifluoromethyl-acetic acid (S)-227 (10 mg, 46%), which were spectroscopically identical to that obtained elsewhere.

MKR of active ester (rac)-95 using 4-phenyl-oxazolidin-2-thione (rac)-236 [T2.24; E1].

In the same way as T2.7; E1, n-BuLi (0.77 ml, 2.5M in hexanes, 1.91 mmol), 4-phenyl-oxazolidin-2-thione (rac)-236 (0.31 g, 1.74 mmol) and pentfluorophenyl-2-phenyl-propionate (rac)-95 (0.55 g, 1.74 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) an inseparable mixture of 3-(2-phenyl-propionyl)-4-phenyl-oxazolidin-2-thione (rac)-anti and (rac)-syn-237, (0.34 g, 63%, ratio syn : anti 97 : 3), as white solid mp 95-97°C; Rₐ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.50; ν max (CHCl₃)/cm⁻¹ 1708 (C=O) and 1216 (C=S); δH (400 MHz; CDCl₃) 7.30-7.14 (6H, m, 6 × CH; Ph), 7.04-7.00 (2H, m, 2 × CH; Ph), 6.99-6.95 (2H, m, 2 × CH; Ph), 6.05 (1H, q, J 7.0, PhCHCH₃), 5.70 (1H, dd, J 9.2 and
MKR of active ester (rac)-119 using 4-phenyl-oxazolidin-2-thione (rac)-236 [T2.24; E2].

In the same way as T2.7; E1, n-BuLi (0.36 ml, 2.5M in hexanes, 0.90 mmol), 4-phenyl-oxazolidin-2-thione (rac)-236 (0.15 g, 0.82 mmol) and pentafluorophenyl-2-phenyl-butationate (rac)-119 (0.27 g, 0.82 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) an inseparable mixture of 3-(2-phenyl-butionyl)-4-phenyl-oxazolidin-2-thione (rac)-anti and (rac)-syn-238, (90 mg, 34%, ratio syn : anti >98 : 2), as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.57; νmax (CHCl₃)/cm⁻¹ 1706 (C=O) and 1219 (C=S); δH (400 MHz; CDCl₃) 7.28-7.14 (6H, m, 6 × CH; Ph), 7.05 (2H, br d, J 7.0, 2 × CH; Ph), 6.93 (2H, br d, J 7.0, 2 × CH; Ph), 5.92 (1H, t, J 7.3, PhCHCH₂), 5.70 (1H, dd, J 9.2 and 6.2, CHN), 4.78 (1H, t, J 9.2, CH₃H₂O), 4.27 (1H, dd, J 9.2 and 6.2, CH₃H₂O), 2.13-2.01 (1H, m, CH₃H₂CH₃), 1.79-1.67 (1H, m, CH₃H₂CH₃) and 0.87 (3H, d, J 7.2, CH₃); δC (100 MHz; CDCl₃) 185.4 (C=S), 174.4 (C=O), 137.3 and 137.0 (2 × i-C; 2 × Ph), 128.9, 128.9, 128.6, 128.4, 127.2 and 126.3 (10 × CH; 2 × Ph), 73.6 (ArCH), 62.6 (CHN), 51.1 (CH₂O), 26.8 (CH₂CH₃) and 12.0 (CH₃); (Found MH⁺, 326.1209; C₁₉H₂₀NO₂S requires 326.1209).

MKR of active ester (rac)-126 using 4-phenyl-oxazolidin-2-thione (rac)-239 [T2.24; E3].

In the same way as T2.7; E1, n-BuLi (0.43 ml, 2.5M in hexanes, 1.09 mmol), 4-phenyl-oxazolidin-2-thione (rac)-236 (0.18 g, 0.90 mmol) and pentafluorophenyl-2-phenyl-3-methyl-butationate (rac)-126 (0.34 g, 0.99 mmol) in THF (10 ml). Returned starting materials.
MKR of active ester (rac)-123 using 4-phenyl-oxazolidin-2-thione (rac)-240 [T2.24; E4].

In the same way as T2.7; E1, n-BuLi (0.18 ml, 2.5M in hexanes, 0.44 mmol), 4-phenyl-oxazolidin-2-thione (rac)-236 (7 mg, 0.40 mmol) and pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propionate (rac)-123 (16 mg, 0.40mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3 → 1:1) an inseparable mixture of 3-[2-(6-methoxy-2-naphthyl)-propionyl]-4-phenyl-oxazolidin-2-thione (rac)-anti and (rac)-syn-240, (9 mg, 57%, ratio syn : anti 93 : 7), as white solid mp 134-136°C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.30; υ \text{max} (CHCl_3)/cm^{-1} 1704 (C=O) and 1218 (C=S); δ_H (400 MHz; CDCl_3) 7.59 (1H, d, J 8.4, CH; Ar), 7.44 (1H, d, J 8.4, CH; Ar), 7.25-7.2 (2H, m, 2 × CH; Ph), 7.19 (1H, br s, CH; Ar), 7.13-7.03 (4H, m, 3 × CH; Ph and CH; Ar), 6.93 (2H, d, J 7.3, 2 × CH; Ar), 6.15 (1H, q, J 6.8, ArCH), 5.73 (1H, dd, J 9.2 and 6.2, CHN), 4.78 (1H, t, J 9.2, CH_AH_B), 4.26 (1H, dd, J 9.2 and 6.2, CH_AH_B), 3.93 (3H, s, CH_3O) and 1.49 (3H, d, J 6.8, CHCH_3); δ_C (100 MHz; CDCl_3) 188.6 (C=S), 178.3 (C=O), 161.1, 140.3, 137.8, 137.1 and 132.7 (5 × i-C; Ph and Ar), 132.9, 132.3, 132.1, 130.5, 129.9, 129.9, 122.1 and 108.9 (11 × CH; Ph and Ar), 77.0 (ArCH), 66.1 (CHN), 58.7 (CH_2O), 47.5 (CH_3O) and 22.4 (CHCH_3); (Found M^+, 391.1231; C_{23}H_{21}NO_3S requires 391.1237), for (rac)-anti-240 δ_H (400 MHz; CDCl_3) 6.25 (1H, q, J 6.8, ArCH), 5.60 (1H, dd, J 9.2 and 6.2, CHN), 4.61 (1H, t, J 9.2, CH_AH_B), 4.38 (1H, dd, J 9.2 and 6.2, CH_AH_B) and 3.92 (3H, s, CH_3O).

Stereo-specific synthesis of 3-(2-phenylpropionyl)-4-phenyl-oxazolidin-2-thione (S,R)-syn-237 [T2.25; E1].

In the same way as T2.7; E1, n-BuLi (0.10 ml, 2.5M in hexanes, 0.25 mmol), 4-phenyl-oxazolidin-2-thione (R)-236 (40 mg, 0.22 mmol) and pentafluorophenyl-2-phenylpropionate (S)-95 (78 mg, 0.25mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 0:1) 3-(2-phenylpropyl)-4-phenyl-oxazolidin-2-thione (S,R)-syn-237 (14 mg, 20%) as yellow solid mp 96-100 °C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.43; [α]_D^{20} = -125.0 (c 0.4, CHCl_3); also returned pentafluoro-2-phenylpropionate (S)-95 (20 mg, 26%) and 4-phenyl-oxazolidin-2-thione (R)-236 (9 mg, 23%), which were spectroscopically identical to that obtained elsewhere.
Stereo-specific synthesis of 3-(2-phenylpropyl)-4-phenyl-oxazolidin-2-thione \((R,R)\)-anti-237 [T2.25; E2].

In the same way as T2.7; E1, \(n\)-BuLi (0.09 ml, 2.5M in hexanes, 0.23 mmol), 4-phenyl-oxazolidin-2-thione \((R)\)-236 (37 mg, 0.21 mmol) and pentafluoro-2-phenylpropionate \((R)\)-95 (72 mg, 0.23 mmol) in THF (10 ml). Gave by crude \(^1\)H NMR no product, after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 0:1) returned pentafluoro-2-phenylpropionate \((R)\)-95 (29 mg, 40%) and 4-phenyl-oxazolidin-2-thione \((R)\)-236 (21 mg, 57%), which were spectroscopically identical to that obtained elsewhere.

KR of active ester \((rac)\)-95 using 4-phenyl-oxazolidin-2-thione \((S)\)-236 [S2.55; E1].

In the same way as T2.7; E1, \(n\)-BuLi (0.38 ml, 2.5M in hexanes, 0.95 mmol), 4-phenyl-oxazolidin-2-thione \((S)\)-236 (0.1 g, 0.56 mmol) and pentafluoro-2-phenylpropionate \((rac)\)-95 (0.35 g, 1.12 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) an inseparable mixture of 3-(2-phenylpropyl)-4-phenyl-oxazolidin-2-thione \((S,R)\)-syn and \((R,R)\)-anti-237 (81 mg, 47%, ratio \(syn : anti\) 94 : 6), which were spectroscopically identical to that obtained elsewhere.

KR of active ester \((rac)\)-95 using 4-phenyl-oxazolidin-2-thione \((R)\)-236 [S2.55; E2].

In the same way as T2.7; E1, \(n\)-BuLi (0.25 ml, 2.5M in hexanes, 0.61 mmol), 4-phenyl-oxazolidin-2-thione \((R)\)-236 (0.155 g, 0.86 mmol) and pentafluoro-2-phenylpropionate \((rac)\)-95 (0.273 g, 0.86 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) an inseparable mixture of 3-(2-phenylpropyl)-4-phenyl-oxazolidin-2-thione \((R,S)\)-syn and \((S,S)\)-anti-237 (88 mg, 33%, ratio \(syn : anti\) 92 : 8), which were spectroscopically identical to that obtained elsewhere.
Section 2: Experiments from Chapter 3

KR of 4-isopropyl-oxazolidin-2-one (rac)-24 using active ester (S)-115 [S3.1].

\( n\)-BuLi (0.54 ml, 2.5M in hexanes, 1.34 mmol) was added to 4-isopropyl-oxazolidin-2-one (rac)-24 (0.170 g, 1.34 mmol) in THF (5 ml) at -78°C, the resulting mixture was stirred for 1 hour, pentafluorophenyl-2-(4-isopropyl-phenyl)-propionate (S)-115 (0.100 g, 0.27 mmol) in THF (5 ml) was then added, the resulting mixture was stirred for 2 hours. The reaction was quenched with water (20 ml), the organic layer was extracted with dichloromethane (3 × 25 ml), dried over MgSO\(_4\) and evaporated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 0:1) to give 3-[2-(4isopropyl[phenyl))-propionate]-4-isopropyl-oxazolidin-2-one (S,R)-anti and (S,S)-syn-241 (60 mg, 70%, ratio syn : anti) and 4-isopropyl-oxazolidin-2-one (S)-24 (0.11 g, 64%, 16% e.e.), which were spectroscopically identical to that obtained elsewhere.

Synthesis of 2-amino-3-methyl-butan-1-ol (R)-108 [S3.2; E1].

2-Amino-3-methyl-butyric acid (R)-30 (10.30 g, 0.088 mol) was slowly added to LiAlH\(_4\) (5 g, 0.13 mol) in THF (120 ml) at 0°C. The resulting mixture was refluxed over night. The reaction was diluted with diethyl ether (100 ml), quenched over 1.5 hours with water (4.7 ml), KOH\(_{\text{aq}}\) (15%, 4.7 ml) and water (14.1 ml), the resulting mixture was stirred for half an hour. The solid precipitate was filtered off and the organic layer was extracted with diethyl ether (200 ml), dried over MgSO\(_4\) and evaporated under reduced pressure. To give 2-amino-3-methyl-butan-1-ol (R)-108 (7.13 g, 79%) as a yellow oil; \( R_f \) ethyl acetate 0.0; \([\alpha]_D^{20} = -23.2 \) (c 3.7, CHCl\(_3\)) and \([\alpha]_D^{20} = -15.0 \) (c 4.2, ethanol); \( \nu_{\text{max}} \) (CHCl\(_3\))/cm\(^{-1}\): 3019 and 2965 (NH and OH); \( \delta_H \) (400 MHz; CDCl\(_3\)) 3.58 (1H, dd, \( J \) 10.7 and 3.9, \( CHA\)H\(_B\)OH), 3.25 (1H, dd, \( J \) 10.7 and 8.6, \( CHA\)H\(_B\)OH), 2.51 (1H, ddd, \( J \) 8.6, 6.4 and 3.9, \( CHNH2\)), 2.13 (3H, br s, OH and NH\(_2\)), 1.53 (1H, appears as an octet, \( J \) 6.8, \( CH3\)CHCH\(_3\)), 0.87 (3H, d, \( J \) 7.0, \( CH3\)CHCH\(_3\)) and 0.86 (3H, d, \( J \) 6.8, \( CH3\)CHCH\(_3\)).

Synthesis of 4-isopropyl-oxazolidin-2-one (R)-24 [S3.2; E2].

A mixture of 2-amino-3-methyl-butan-1-ol (R)-108 (2.00 g, 0.02 mol), K\(_2\)CO\(_3\) (0.28 g, 2.0 mmol) and diethyl carbonate (4.76 g, 0.04 mol) was refluxed for 3 hours with a distillation arm setup to catch ethanol formed during the reaction. The reaction
was allowed to cool to room temperature the organic layer was extracted with dichloromethane (50 ml), dried over MgSO₄ and evaporated under reduced pressure. To give 4-isopropyl-oxazolidin-2-one (R)-24 (2.345 g, 90%) as a white solid mp 67-70°C; Rf diethyl ether 0.30; [α]D° = -13.1 (c 4.2, CHCl₃) and [α]D° = +15.0 (c 2.8, ethanol); \( \nu_{\text{max}} \) (CHCl₃)/cm\(^{-1} \) 3263 (N-H) and 1751 (C=O); δH (400 MHz; CDCl₃) 6.78 (1H, br s, NH), 4.37 (1H, t, J 8.6, CH₃H₂O), 4.04 (1H, dd, J 8.6 and 6.4, CH₃H₂O), 3.55 (1H, br dt, J 8.6 and 6.4, CH₂NH), 1.65 (1H, appears as an octet, J 6.8, CH₂CH₂CH₃), 0.90 (3H, d, J 6.6, CH₃CH₂CH₃) and 0.83 (3H, d, J 6.8, CH₃CH₂CH₃); δC (100 MHz; CDCl₃) 160.2 (C=O), 68.6 (CH₂O), 58.4 (CH₂NH), 32.7 (CH₃CH₂CH₃), 18.0 (CH₂CH₂CH₃) and 17.7 (CH₃CH₂CH₃); (Found MH⁺, 130.0880 C₆H₁₂NO₂ requires 130.0868).

**Synthesis of 2-amino-3-methyl-butan-1-ol (S)-108 [S3.2; E3].**

In the same way as S3.2; E1, 2-amino-3-methyl-butryic acid (S)-30 (10.30 g, 0.088 mol) and LiAlH₄ (5 g, 0.13 mol) in THF (120 ml). Gave 2-amino-3-methyl-butan-1-ol (S)-108 (7.08 g, 78%) as a yellow oil; [α]D = +20.8 (c 5.8, CHCl₃) and [α]D = +15.6 (c 3.8, ethanol), which was spectroscopically identical to that obtained elsewhere.

**Synthesis of 4-isopropyl-oxazolidin-2-one (S)-24 [S3.2; E4].**

In the same way as S3.2; E2, 2-amino-3-methyl-butan-1-ol (S)-108 (2.00 g, 0.02 mol), K₂CO₃ (0.28 g, 2.0 mmol) and diethyl carbonate (4.76 g, 0.04 mol). Gave after purification by re-crystallisation in ethyl acetate 4-isopropyl-oxazolidin-2-one (S)-24 (0.576 g, 22%) as a white solid mp 67-70°C; [α]D = +15.6 (c 3.0, CHCl₃) and [α]D = -17.4 (c 2.4, ethanol), which was spectroscopically identical to that obtained elsewhere.

**Synthesis of 3-[2-(4-isobutyl-phenyl)-propionate]-4-isopropyl-oxazolidin-2-one (S,R)-syn-241 [S3.3; E1].**

In the same way as S3.1, n-BuLi (0.40 ml, 2.5M in hexanes, 1.00 mmol), 4-isopropyl-oxazolidin-2-one (R)-24 (0.117 g, 0.91 mmol), pentafluorophenyl-2-(4-isobutyl-phenyl)-propionate (S)-115 (0.337 g, 0.91 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) 3-[2-(4-isobutyl-[phenyl]-propionate]-4-isopropyl-oxazolidin-2-one (S,R)-syn-241 (0.171 g, 59%) as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.33; [α]D = +31.5 (c 8.4, CHCl₃); \( \nu_{\text{max}} \) (CHCl₃)/cm\(^{-1} \) 1778 and 1699 (2 × C=O); δH (400 MHz; CDCl₃) 7.23 (2H, d, J 8.2, 2×
CH; Ar), 7.03 (2H, d, J 8.2, 2× CH; Ar), 5.11 (1H, q, J 6.9, CHAr), 4.47 (1H, dt, J 8.8 and 3.5, CHN=H), 4.21 (1H, t, J 8.6, CH₂ArH₂O), 4.07 (1H, dd, J 8.6 and 3.5, CH₂ArH₂O), 2.40 (2H, d, J 7.2, CH₂Ar), 2.19-2.07 (1H, m, CH₃CHCH₃; oxazolidin-2-one), 1.87-1.75 (1H, m, CH₃CHCH₃; CH₂Ar), 1.44 (3H, d, J 6.9, ArCH₃), 0.85 (3H, d, J 6.7, CH₃CHCH₃; CH₂Ar), 0.84 (3H, d, J 6.7, CH₃CHCH₃; CH₂Ar), 0.76 (3H, d, J 6.9, CH₃CHCH₃; oxazolidin-2-one) and 0.38 (3H, d, J 6.9, CH₃CHCH₃; oxazolidin-2-one); δC (100 MHz; CDCl₃) 174.8 (NC≡O), 153.5 (OC≡O), 140.6 and 137.6 (i-C; Ar), 129.3² and 127.8² (4 × CH; Ar), 62.8 (CH₂O), 58.0 (CHNH), 45.0 (CH₃CHCH₃; CH₂Ar), 42.9 (ArCH₃), 30.2 (CH₂Ar), 27.8 (CH₃CHCH₃; CH₂Ar), 22.7 (CH₃CHCH₃; CH₂Ar), 22.3 (CH₃CHCH₃; CH₂Ar), 18.5 (CH₃CHCH₃; oxazolidin-2-one), 17.7 (CH₃CHCH₃; oxazolidin-2-one) and 14.0 (ArCH₃); (Found M⁺, 317.1979 C₁₉H₂₇NO₃ requires 317.1985).

**Synthesis of 3-[2-(4-isobutyl-phenyl)-propionate]-4-isopropyl-oxazolidin-2-one (S,S)-anti-241 [S3.3; E2].**

In the same way as S3.1, n-BuLi (0.41 ml, 2.5M in hexanes, 1.02 mmol), 4-isopropyl-oxazolidin-2-one (S)-24 (0.120 g, 0.93 mmol), pentafluorophenyl-2-(4-isopropyl-phenyl)-propionate (S)-115 (0.345 g, 0.93 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) 3-[2-(4isobutyl][phenyl)-propionate]-4-isopropyl-oxazolidin-2-one (S,R)-anti-241 (0.188 g, 64%) as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.64; [α]D²⁰ = +108.9 (c 9.7, CHCl₃); νmax (CHCl₃)/cm⁻¹ 1776 and 1692 (2 × C=O); δH (400 MHz; CDCl₃) 7.23 (2H, d, J 8.2, 2× CH; Ar), 7.07 (2H, d, J 8.2, 2× CH; Ar), 5.11 (1H, q, J 7.2, CHAr), 4.35 (1H, dt, J 7.2 and 3.8, CHN=H), 4.15-4.07 (2H, m, CH₂O), 2.49-2.37 (1H, m, CH₃CHCH₃; oxazolidin-2-one), 2.46-2.39 (2H, m, CH₂Ar), 1.87-1.77 (1H, m, CH₃CHCH₃; CH₂Ar), 1.49 (3H, d, J 7.2, ArCH₃) and 0.92-0.86 (12H, m, 4 × CH₃); δC (100 MHz; CDCl₃) 174.9 (NC≡O), 153.6 (OC≡O), 140.6 and 137.5 (i-C; Ar), 129.3² and 127.8² (4 × CH; Ar), 63.1 (CH₂O), 59.0 (CHNH), 45.1 (CH₃CHCH₃; CH₂Ar), 42.6 (ArCH₃), 30.2 (CH₂Ar), 28.6 (CH₃CHCH₃; CH₂Ar), 22.7 (CH₃CHCH₃; CH₂Ar), 22.4 (CH₃CHCH₃; CH₂Ar), 19.7 (CH₃CHCH₃; oxazolidin-2-one), 18.0 (CH₃CHCH₃; oxazolidin-2-one) and 14.7 (ArCH₃); (Found MH⁺, 318.2062 C₁₉H₂₈NO₃ requires 318.2064).
Section 3: Experiments from Chapter 4

MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-syn-96 [S4.2].

MeMgBr (0.26 ml, 3M in diethyl ether, 0.78 mmol) was added to 1-phenylethanol (rac)-11 (0.10 g, 0.78 mmol) in THF (5 ml) at 0°C. The resulting mixture was stirred for 10 minutes, 3-(2-phenylpropinyl)-4-phenyl-oxazolidin-2-one (rac)-syn-96 (0.23 g, 0.78 mmol) in THF (5 ml) was added. The resulting mixture was stirred for over night. The reaction quenched with NH₄Cl (aq) (10 ml), the organic layer was extracted with dichloromethane (3 × 25 ml), washed water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 0:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (57 mg, 29%, ratio anti : syn 85 : 15) and di-(1-phenylethyl)-carbonate (meso)-syn and (rac)-anti-243 (3 mg, 2.6%, ratio syn : anti ~74 : 26), returned 3-(2-phenylpropinyl)-4-phenyl-oxazolidin-2-one (rac)-syn-96 (50 mg, 22%), 4-phenyl-oxazolidin-2-one (rac)-syn-94 (60 mg, 26%), which was spectroscopically identical to that obtained elsewhere. And N-(hydroxyl-1-phenyl-ethyl)-2-phenyl-propionamide (rac)-syn-244 (10 mg, 4.8%) as a white solid m.p. 132-134°C; Rₐ diethyl ether 0.17; νₘₐₓ (CHCl₃)/cm⁻¹: 3019 (NH and OH) and 1653 (C=O); δₜ (400 MHz; CDCl₃) 7.32-7.15 (8H, m, 8 × CH; Phₐ and Phₜ), 7.00-6.95 (2 H, m, 2 × CH; Phₐ and/or Phₜ), 5.94 (1H, d, J 7.2, NH), 4.96 (1H, dt, J 7.2 and 4.8, CHN), 3.76 (2H, dd, J 6.2 and 4.8, CHO), 3.58 (1H, q, J 7.2, CH₂CH₃), 2.22 (1H, t, J 6.2, OH) and 1.47 (3H, d, J 7.2, CH₃CH); δ C (100 MHz; CDCl₃) 174.5 (C=O), 141.2 and 138.8 (2 × i-C; Phₐ and Phₜ), 129.0, 128.8, 127.7, 127.6, 127.4 and 126.3 (10 × CH; Phₐ and Phₜ), 66.7 (CHN), 55.8 (CH₂O), 47.1 (CH₂CH₃) and 18.4 (CHCH₃); (Found MH⁺, 270.1485 C₁₇H₂₀O₄N requires 270.1489).

Synthesis of di-(1-phenylethyl)-carbonate (meso)-syn and (rac)-anti-243 [S4.3; E1].

NaH (0.16 g, 60% on mineral oil, 4.09 mmol) was added to 1-phenylethanol (rac)-11 (0.50 g, 4.09 mmol) in THF (10 ml) at 0°C. The resulting mixture was stirred for 10 minutes, CDI (0.33 g, 2.05 mmol) in THF (5 ml) was added. The resulting mixture was stirred over night. The reaction quenched with NH₄Cl (aq) (10 ml), the organic layer was extracted with dichloromethane (3 × 25 ml), washed water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-
60°C) / diethyl ether (9:1) an inseparable mixture di-(1-phenylethyl)-carbonate (meso)-
syn and (rac)-anti-243 (0.30 g, 61%, ratio syn : anti ~50 : 50). Characterisation data for
di-(1-phenylethyl)-carbonate (meso)-syn-243: an oil; $R_F$ [light petroleum spirit (bp 40-
60°C) / diethyl ether (1:1)] 0.63; $\nu_{\text{max}}$ (CHCl$_3$)/cm$^{-1}$ 1751 (C=O); $\delta_H$ (400 MHz; CDCl$_3$)
7.39-7.23 (10H, m, 10 × CH; Ph$_A$ and Ph$_B$), 5.69 (2H, q, $J$ 6.8, 2 × PhCH) and 1.59 (6H,
d, $J$ 6.8, 2 × CH$_2$CH); $\delta_C$ (100 MHz; CDCl$_3$) 153.9 (C=O), 141.2$^2$ (2 × i-C; Ph$_A$ and
Ph$_B$), 128.5,$^4$ 128.1$^2$ and 126.1$^4$ (10 × CH; Ph$_A$ and Ph$_B$), 76.4$^2$ (2 × PhCH) and 22.4$^2$ (2
× CHCH$_3$); (Found MNH$_2^\circ$, 288.1593; C$_{17}$H$_{22}$NO$_4$ requires 288.1594).

**Synthesis of di-(1-phenylethyl)-carbonate (R,R)-anti-243 [S4.3; E2].**

MeMgBr (0.55 ml, 3M in diethyl ether, 1.64 mmol) was added to 1-
phenylethanol ($R$)-11 (0.20 g, 1.64 mmol) in THF (5 ml) at 0°C. The resulting mixture
was stirred for 10 minutes, CDI (0.11 g, 0.68 mmol) in THF (5 ml) was added. The
resulting mixture was stirred over night. The reaction quenched with NH$_4$Cl$_{aq}$ (10 ml),
the organic layer was extracted with dichloromethane (3 × 25 ml), washed water (25
ml), dried over MgSO$_4$ and evaporated under reduced pressure. Gave after purification
by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-
60°C) / diethyl ether (9:1) di-(1-phenylethyl)-carbonate (R,R)-anti-243 (40 mg, 22%) as
an oil; $R_F$ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.79; $\left[\alpha\right]_D^{20} = +116.6$
(c 0.8, CHCl$_3$); $\nu_{\text{max}}$ (CHCl$_3$)/cm$^{-1}$ 1742 (C=O); $\delta_H$ (400 MHz; CDCl$_3$) 7.38-7.26 (10H,
m, 10 × CH; Ph$_A$ and Ph$_B$), 5.66 (2H, q, $J$ 6.8, 2 × PhCH) and 1.53 (6H, d, $J$ 6.8, 2 ×
CH$_2$CH); $\delta_C$ (100 MHz; CDCl$_3$) 153.8 (C=O), 141.1$^2$ (2 × i-C; Ph$_A$ and Ph$_B$), 128.5,$^4$
128.0$^2$ and 126.0$^4$ (10 × CH; Ph$_A$ and Ph$_B$), 76.3$^2$ (2 × PhCH) and 22.2$^2$ (2 × CHCH$_3$);
(Found MNH$_2^\circ$, 288.1593; C$_{17}$H$_{22}$NO$_4$ requires 288.1594).

**MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-96 [T4.1; E1].**

In the same way as S4.2, MeMgBr (0.06 ml, 3M in diethyl ether, 0.17 mmol), 1-
phenylethanol (rac)-11 (80 mg, 0.68 mmol) and 3-(2-phenylpropinyl)-4-
phenyloxazolidin-2-one (rac)-syn-96 (0.20 g, 0.68 mmol) in THF (10 ml). Gave after
purification by flash column chromatography on silica gel eluting with light petroleum
spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-
phenylpropinate (rac)-anti and (rac)-syn-245 (33 mg, 77%, ratio anti : syn 89 : 11) and
di-(1-phenylethyl)-carbonate (meso)-syn and (rac)-anti-243 (7 mg, 10%, ratio syn : anti
~60 : 40), which was spectroscopically identical to that obtained elsewhere.
MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-96 [T4.1; E2].

In the same way as S4.2, MeMgBr (0.11 ml, 3M in diethyl ether, 0.34 mmol), 1-phenylethanol (rac)-11 (80 mg, 0.68 mmol) and 3-(2-phenylpropinyl)-4-phenyloxazolidin-2-one (rac)-syn-96 (0.20 g, 0.68 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (58 mg, 68%, ratio anti : syn 87 : 13) and di-(1-phenylethyl)-carbonate (meso)-syn and (rac)-anti-243 (2 mg, 4%, ratio syn : anti ~60 : 40), which was spectroscopically identical to that obtained elsewhere.

Reaction of 1-phenylethanol (rac)-11 with 4-phenyl-oxazolidin-2-one (rac)-94 [S4.4].

In the same way as S4.2, MeMgBr (0.29 ml, 3M in diethyl ether, 0.86 mmol), 1-phenylethanol (rac)-11 (1.05 g, 8.58 mmol) and 4-phenyl-oxazolidin-2-one (rac)-94 (0.14 g, 0.86 mmol) in THF (10 ml). Returned stating materials.

MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-syn-syn-141 [T4.2; E1].

In the same way as S4.2, MeMgBr (0.22 ml, 3M in diethyl ether, 0.65 mmol), 1-phenylethanol (rac)-11 (0.79 g, 6.4 mmol) and 3-(2-phenylpropinyl)-4-methyl-5-phenyl-oxazolidin-2-one (rac)-syn-syn-141 (0.20 g, 0.65 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (0.13 g, 79%, ratio anti : syn 66 : 34), which was spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-syn-146 [T4.2; E2].

In the same way as S4.2, MeMgBr (0.22 ml, 3M in diethyl ether, 0.65 mmol), 1-phenylethanol (rac)-11 (0.79 g, 6.47 mmol) and 3-(2-phenylpropinyl)-4-benzyl-oxazolidin-2-one (rac)-syn-146 (0.20 g, 0.65 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (85 mg, 52%, ratio anti : syn 65 : 35)
and di-(1-phenylethyl)-carbonate (meso)-syn and (rac)-anti-243 (21 mg, 14%, ratio syn : anti 53 : 47), which was spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-syn-97 [T4.2; E3].

In the same way as S4.2, MeMgBr (0.26 ml, 3M in diethyl ether, 0.65 mmol), 1-phenylethanol (rac)-11 (0.94 g, 7.65 mmol) and 3-(2-phenylpropinyl)-4-isopropyl-oxazolidin-2-one (rac)-syn-97 (0.20 g, 0.77 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (71 mg, 37%, ratio anti : syn 88 : 12) and di-(1-phenylethyl)-carbonate (meso)-syn and (rac)-anti-243 (17 mg, 8%, ratio syn : anti 50 : 50), which was spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-syn-96 [T4.2; E4].

In the same way as S4.2, MeMgBr (0.23 ml, 3M in diethyl ether, 0.68 mmol), 1-phenylethanol (rac)-11 (0.83 g, 6.77 mmol) and 3-(2-phenylpropinyl)-4-phenyl-oxazolidin-2-one (rac)-syn-96 (0.20 g, 0.68 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (95 mg, 55%, ratio anti : syn 84 : 16) and di-(1-phenylethyl)-carbonate (meso)-syn and (rac)-anti-243 (25 mg, 14%, ratio syn : anti 65 : 35), which was spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-syn-158 [T4.2; E5].

In the same way as S4.2, MeMgBr (0.65 ml, 3M in diethyl ether, 1.96 mmol), 1-phenylethanol (rac)-11 (2.39 g, 19.56 mmol) and ethyl 2-oxa-3-(2-phenylpropinyl)-oxazolidin-4-carboxylate (rac)-syn-158 (0.57 g, 1.96 mmol) in THF (15 ml). Gave an unassailable organic residue.
MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-anti-syn-141 [T4.3; E1].

In the same way as S4.2, MeMgBr (0.19 ml, 3M in diethyl ether, 0.58 mmol), 1-phenylethanol (rac)-11 (0.71 g, 5.82 mmol) and 3-(2-phenylpropinyl)-4-methyl-5-phenyl-oxazolidin-2-one (rac)-anti-syn-141 (0.18 g, 0.58 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (70 mg, 47%, ratio anti : syn 62 : 38), which was spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-anti-146 [T4.3; E2].

In the same way as S4.2, MeMgBr (0.14 ml, 3M in diethyl ether, 0.42 mmol), 1-phenylethanol (rac)-11 (0.51 g, 4.20 mmol) and 3-(2-phenylpropinyl)-4-benzyl-oxazolidin-2-one (rac)-anti-146 (0.13 g, 0.42 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (66 mg, 62%, ratio anti : syn 74 : 26) and di-(1-phenylethyl)-carbonate (meso)-syn and (rac)-anti-243 (16 mg, 14%, ratio syn : anti 50 : 50), which was spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-anti-97 [T4.3; E3].

In the same way as S4.2, MeMgBr (0.15 ml, 3M in diethyl ether, 0.46 mmol), 1-phenylethanol (rac)-11 (0.56 g, 4.58 mmol) and 3-(2-phenylpropinyl)-4-isopropyl-oxazolidin-2-one (rac)-anti-97 (0.12 g, 0.46 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (40 mg, 34%, ratio anti : syn 61 : 39), which was spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-anti-96 [T4.3; E4].

In the same way as S4.2, MeMgBr (0.26 ml, 3M in diethyl ether, 0.78 mmol), 1-phenylethanol (rac)-11 (0.95 g, 7.79 mmol) and 3-(2-phenylpropinyl)-4-phenyl-
oxazolidin-2-one (rac)-anti-96 (0.23 g, 0.78 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (81 mg, 41%, ratio anti : syn 62 : 38) and di-(1-phenylethyl)-carbonate (meso)-syn and (rac)-anti-243 (9 mg, 14%, ratio syn : anti 52 : 48), which was spectroscopically identical to that obtained elsewhere.

**MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-anti-158 [T4.3; E5].**

In the same way as S4.2, MeMgBr (0.05 ml, 3M in diethyl ether, 0.17 mmol), 1-phenylethanol (rac)-11 (0.21 g, 1.72 mmol) and ethyl 2-oxa-3-(2-phenylpropinyl)-oxazolidin-4-carboxylate (rac)-anti-158 (50 mg, 0.17 mmol) in THF (10 ml). Gave an unassailable organic residue.

**Competitive MKR of 1-phenylethanol (rac)-11 using oxazolidinone adducts (rac)-syn- and anti-96 [S4.5].**

In the same way as S4.2, MeMgBr (0.15 ml, 3M in diethyl ether, 0.37 mmol), 1-phenylethanol (rac)-11 (45 mg, 0.37 mmol) and 3-(2-phenylpropinyl)-4-phenyl-oxazolidin-2-one (rac)-96 (0.22 g, 0.74 mmol, ratio syn : anti 63 : 37) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (57 mg, 61%, ratio anti : syn 78 : 22) and di-(1-phenylethyl)-carbonate (meso)-syn and (rac)-anti-243 (3 mg, 6.4%, ratio syn : anti 61 : 39), which was spectroscopically identical to that obtained elsewhere. Crude 1H NMR revealed that the ratio of 3-(2-phenylpropinyl)-4-phenyl-oxazolidin-2-one (rac)-syn and (rac)-anti-96 was syn : anti 64 : 36.

**Synthesis of 3-(2-phenylpropinyl)-oxazolidin-2-one (rac)-184 [S4.6].**

n-BuLi (0.96 ml, 2.5 M in hexanes, 2.40 mmol) was added to oxazolidin-2-one 183 (0.19 g, 2.18 mmol) in THF (5 ml) at -78°C. The resulting mixture was stirred for 1 hour, pentafluorophenyl-2-phenylpropinate (rac) 95 (0.69 g, 2.18 mmol) in THF (15 ml) was added. The resulting mixture was stirred for 2 hours. The reaction quenched with water (25 ml), the organic layer was extracted with dichloromethane (3 × 25 ml), dried over MgSO4 and evaporated under reduced pressure. Gave after purification by flash column chromatography on silica gel eluting with diethyl ether 3-(2-
phenylpropinyl)-oxazolidin-2-one (rac)-184 (0.29 g, 61%) as an oil; \( R_f \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.14; \( \nu_{\text{max}} \) (CHCl\textsubscript{3})/cm\textsuperscript{-1} 1772 (NC=O) and 1700 (C=O); \( \delta_H \) (400 MHz; CDCl\textsubscript{3}) 7.37 (2H, dt, \( J \) 7.1 and 1.5, 2 \( \times \) CH; Ph), 7.31 (2H, br ddd, \( J \) 7.1, 1.5 and 1.0, CH; Ph), 7.27-7.22 (1H, m, CH; Ph), 5.11 (1H, q, \( J \) 7.0, CHCH\textsubscript{3}), 4.42-4.25 (2H, m, CH\textsubscript{2}O), 4.11-4.02 (1H, ABq, CH\textsubscript{3}H\textsubscript{3}N), 3.97-3.89 (1H, m, CH\textsubscript{3}H\textsubscript{3}N) and 1.50 (3H, d, \( J \) 7.0, CH\textsubscript{3}CH); \( \delta_C \) (100 MHz; CDCl\textsubscript{3}) 174.4 (NC=O), 152.9 (OC=O), 140.2 (i-C; Ph), 128.6, 128.1, 127.2 (5 \( \times \) CH; Ph), 61.6 (CH\textsubscript{2}O), 42.7 (CH\textsubscript{2}N), 42.6 (CHCH\textsubscript{3}) and 19.2 (CHCH\textsubscript{3}); (Found M\textsuperscript{+}, 219.0888 C\textsubscript{12}H\textsubscript{13}NO\textsubscript{3} requires 219.0890).

**MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-184 [S4.7].**

In the same way as S4.2, MeMgBr (0.37 ml, 3M in diethyl ether, 1.0 mmol), 1-phenylethanol (rac)-11 (1.23 g, 10.0 mmol) and 3-(2-phenylpropinyl)-oxazolidin-2-one (rac)-184 (0.22 g, 1.0 mmol) in THF (12.5 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (0.15 g, 59%, ratio anti : syn 50 : 50) and di-(1-phenylethyl)-carbonate (meso)-syn and (rac)-anti-243 (<1 mg, <1%, ratio syn : anti ~50 : 50), which was spectroscopically identical to that obtained elsewhere.

**MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-syn-96 [T4.4; E1].**

See T4.2; E4.

**MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-syn-153 [T4.4; E2].**

In the same way as S4.2, MeMgBr (0.34 ml, 3M in diethyl ether, 1.03 mmol), 1-phenylethanol (rac)-11 (1.26 g, 10.31 mmol) and 3-(2-phenylbutinyl)-4-phenyloxazolidin-2-one (rac)-syn-153 (0.32 g, 1.03 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylbutinate (rac)-anti and (rac)-syn-246 (98 mg, 35%, ratio anti : syn 88 : 12) and di-(1-phenylethyl)-carbonate (meso)-syn and (rac)-anti-243 (53 mg, 19%, ratio syn : anti 62 : 38), which was spectroscopically identical to that obtained elsewhere.
MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-syn-185 [T4.4; E3].

In the same way as S4.2, MeMgBr (0.52 ml, 3M in diethyl ether, 1.55 mmol), 1-phenylethanol (rac)-11 (1.90 g, 15.52 mmol) and 3-[2-(4-methylphenyl)-propinyl]-4-phenyl-oxazolidin-2-one (rac)-syn-185 (0.48 g, 1.55 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-(4-methylphenyl)-propionate (rac)-anti and (rac)-syn-247 (0.21 g, 53%, ratio anti : syn 83 : 17) and di-(1-phenylethyl)-carbonate (meso)-syn and (rac)-anti-243 (50 mg, 12%, ratio syn : anti 62 : 38), which was spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-syn-163 [T4.4; E4].

In the same way as S4.2, MeMgBr (0.52 ml, 3M in diethyl ether, 1.56 mmol), 1-phenylethanol (rac)-11 (1.91 g, 15.65 mmol) and 3-[2-(4-isobutylphenyl)-propinyl]-4-phenyl-oxazolidin-2-one (rac)-syn-163 (0.55 g, 1.56 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-(4-isopropylphenyl)-propionate (rac)-anti and (rac)-syn-248 (0.26 g, 54%, ratio anti : syn 85 : 15) and di-(1-phenylethyl)-carbonate (meso)-syn and (rac)-anti-243 (88 mg, 21%, ratio syn : anti 63 : 37), which was spectroscopically identical to that obtained elsewhere.

PKR of 1-phenylethanol (rac)-11 using oxazolidinone adducts (S,R)-syn-156 and (R,S)-syn-96 [S4.8].

In the same way as S4.2, MeMgBr (1.65 ml, 3M in diethyl ether, 4.94 mmol), 1-phenylethanol (rac)-11 (6.04 g, 49.35 mmol), 3-[2-(6-methoxy-2-naphthyl)-propinyl]-4-phenyl-oxazolidin-2-one (S,R)-syn-156 (0.93 g, 2.47 mmol) and 3-(2-phenylpropinyl)-4-phenyl-oxazolidin-2-one (R,S)-syn-96 (0.73 g, 2.47 mmol) in THF (60 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (R,R)-anti and (R,S)-syn-245 (0.39 g, 62%, ratio anti : syn 87 : 13) and di-(1-phenylethyl)-carbonate (meso)-syn and (rac)-anti-243 (0.24 g, 18%, ratio syn : anti 57 : 43) and an inseparable mixture of 1-phenylethyl-2-(6-
methoxy-2-naphthyl)-propinate \((S,S)-anti\) and \((S,R)-syn-249\) (0.55 g, 66\%, ratio \(anti : syn\) 84 : 16), which was spectroscopically identical to that obtained elsewhere.

**PKR of 1-phenylethanol \((rac)\)-11 using oxazolidinone adducts \((S,R)-syn-156\) and \((R,S)-syn-163\) [S4.9].**

In the same way as S4.2, MeMgBr (0.59 ml, 3M in diethyl ether, 1.76 mmol), 1-phenylethanol \((rac)\)-11 (2.15 g, 17.59 mmol), 3-[2-(6-methoxy-2-naphthyl)-propinyl]-4-phenyl-oxazolidin-2-one \((S,R)-syn-156\) (0.331 g, 0.88 mmol) and 3-[2-(4-isobutylphenyl)-propinyl]-4-phenyl-oxazolidin-2-one \((R,S)-syn-153\) (0.309 g, 0.88 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) an inseparable mixture of 1-phenylethyl-2-(4-isobutylphenyl)-propionate \((R,R)-anti\) and \((R,S)-syn-248\) (0.154 g, 56\%, ratio \(anti : syn\) 88 : 12) and di-(1-phenylethyl)-carbonate \((meso)\)-syn and \((rac)-anti-243\) (60 mg, 25\%, ratio \(syn : anti\) 54 : 46) and an inseparable mixture of 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propionate \((S,S)-anti\) and \((S,R)-syn-249\) (0.137 g, 46\%, ratio \(anti : syn\) 81 : 19), which was spectroscopically identical to that obtained elsewhere.


In the same way as S4.2, MeMgBr (0.23 ml, 3M in diethyl ether, 0.69 mmol), 1-phenylethanol \((rac)\)-11 (0.84 g, 17.59 mmol), 3-[2-(6-methoxy-2-naphthyl)-propinyl]-4-phenyl-oxazolidin-2-one \((S,R)-syn-156\) (0.13 g, 0.35 mmol) and 3-2-phenylbutinyl-4-phenyl-oxazolidin-2-one \((R,S)-syn-153\) (0.11 g, 0.35 mmol) in THF (11 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) an inseparable mixture of 1-phenylethyl-2-phenylbutinate \((R,R)-anti\) and \((R,S)-syn-246\) (44 mg, 47\%, ratio \(anti : syn\) 89 : 11) and di-(1-phenylethyl)-carbonate \((meso)\)-syn and \((rac)-anti-243\) (36 mg, 20\%, ratio \(syn : anti\) 61 : 39) and an inseparable mixture of 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propinate \((S,S)-anti\) and \((S,R)-syn-249\) (60 mg, 52\%, ratio \(anti : syn\) 81 : 19), which was spectroscopically identical to that obtained elsewhere.

**MKR of 1-phenylethanol \((rac)\)-11 using oxazolidinone adduct \((rac)\)-96 [S4.11].**

In the same way as S4.2, MeMgBr (0.23 ml, 3M in diethyl ether, 0.68 mmol), 1-phenylethanol \((rac)\)-11 (0.17 g, 1.35 mmol) and 3-(2-phenylpropinyl)-4-phenyl-
oxazolidin-2-one (rac)-syn-96 (0.20 g, 0.68 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (88 mg, 51%, ratio anti: syn 85 : 15) and di-(1-phenylethyl)-carbonate (meso)-syn and (rac)-anti-243 (12 mg, 14%, ratio syn : anti 52 : 48), which was spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-96 [T4.5; E1].

In the same way as S4.2, MeMgBr (0.23 ml, 3M in diethyl ether, 0.68 mmol), 1-phenylethanol (rac)-11 (80 mg, 0.68 mmol) and 3-(2-phenylpropinyl)-4-phenyloxazolidin-2-one (rac)-syn-96 (0.20 g, 0.68 mmol) in dichloromethane (10 ml). Returned starting materials.

MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-96 [T4.5; E2].

In the same way as S4.2, MeMgBr (0.23 ml, 3M in diethyl ether, 0.68 mmol), 1-phenylethanol (rac)-11 (0.83 g, 6.77 mmol) and 3-(2-phenylpropinyl)-4-phenyloxazolidin-2-one (rac)-syn-96 (0.20 g, 0.68 mmol) in dichloromethane (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (0.119 g, 69%, ratio anti: syn 91 : 9) and di-(1-phenylethyl)-carbonate (meso)-syn and (rac)-anti-243 (26 mg, 14%, ratio syn : anti 62 : 38), which was spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using oxazolidinone adduct (rac)-153 [S4.12].

In the same way as S4.2, MeMgBr (0.24 ml, 3M in diethyl ether, 0.71 mmol), 1-phenylethanol (rac)-11 (0.87 g, 7.11 mmol) and 3-(2-phenylbutinyl)-4-phenyloxazolidin-2-one (rac)-syn-153 (0.22 g, 0.71 mmol) in dichloromethane (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylbutinate (rac)-anti and (rac)-syn-246 (38 mg, 20%, ratio anti: syn 91 : 9) and di-(1-phenylethyl)-carbonate (meso)-syn and (rac)-anti-243 (2 mg, 2%, ratio syn : anti 50 : 50), which was spectroscopically identical to that obtained elsewhere.
Section 4: Experiments from Chapter 5

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [S5.2].

$n$-BuLi (3.6 ml, 2.5M in hexanes, 9.0 mmol) was added to 1-phenylethanol (rac)-11 (1 g, 8.19 mmol) in THF (10 ml) followed by pentafluorophenyl-2-phenylpropinate (rac)-95 (2.59 g, 8.19 mmol) in THF (10 ml). The resulting mixture was stirred overnight. The reaction was quenched with NH₄Cl(aq) (20 ml). The organic layer was extracted with dichloromethane (3 × 50 ml), washed with water (50 ml), dried over MgSO₄ and evaporated under reduced pressure. The crude mixture was purified by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) to give an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (1.331 g, 64%, ratio anti : syn 57 : 43) and butyl-2-phenylpropinate (rac)-250 (0.219 g, 13%) which were spectroscopically identical to that obtained elsewhere.

Stereospecific synthesis of 1-phenylethyl-2-phenylpropinate (S,R)-syn-245 using n-BuLi [S5.3].

In the same way as S5.2, n-BuLi (0.22 ml, 2.5M in hexanes, 0.56 mmol), 1-phenylethanol (R)-11 (60 mg, 0.51 mmol) and pentafluorophenyl-2-phenylpropinate (S)-95 (0.16 g, 0.51 mmol) in THF (5 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (1:1) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (R,R)-anti and (S,R)-syn-245 (76 mg, 59%, ratio anti : syn 8 : 92) as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.80; [α]D = +55.3 (c 4.0, CHCl₃); νmax (CHCl₃)/cm⁻¹ 1730 (C=O); δH (400 MHz; CDCl₃) 7.30-7.14 (8H, m, 8 × CH; PhA and PhB), 7.05-7.00 (2H, m, 2 × CH; PhA and/or PhB), 5.78 (1H, q, 6.6, CHO), 3.68 (1H, q, 7.2, CHCO), 1.43 (3H, d, J 7.2, CH₃CHCO) and 1.42 (3H, d, J 6.6, CH₃CHO); δC (100 MHz; CDCl₃) 173.5 (C=O), 141.6 and 140.4 (2 × i-C; PhA and PhB), 128.5, 128.3, 127.6, 127.5, 127.0 and 125.6 (10 × CH; PhA and PhB), 72.4 (CHO), 45.7 (CHCO), 22.3 (CH₃CHO) and 18.3 (CH₃CHCO); (Found MNH⁺, 272.1647; C₁₇H₂₂N₂O₂ requires 272.1645), and butyl-2-phenylpropinate (S)-250 (17 mg, 16%), which was spectroscopically identical to that obtained elsewhere.
Stereospecific synthesis of 1-phenylethyl-2-(4-isobutylphenyl)-propinate (S,S)-anti-248 using LDA [T5.1; E1].

In the same way as S5.2, LDA (0.20 ml, 1.8M in THF/heptane/ethylbenzene, 0.36 mmol), 1-phenylethanol (S)-11 (44 mg, 0.36 mmol) and pentafluorophenyl-2-(4-isobutylphenyl)-propinate (S)-115 (0.135 g, 0.36 mmol) in THF (5 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-(4-isobutylphenyl)-propinate (S,S)-anti and (R,S)-syn-248 (70 mg, 62%, ratio anti : syn 98 : 2) as an oil; RF [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.85; [α]$_D^{20}$ = +15.5 (c 2.6, CHCl$_3$); ν$_{max}$ (CHCl$_3$)/cm$^{-1}$ 1723 (C=O); δ$_H$ (400 MHz; CDCl$_3$) 7.21-7.17 (3H, m, 3 × CH; Ph), 7.11 (2H, br d, J 8.1, 2 × CH; Ar), 7.08-7.05 (2H, m, 2 × CH; Ph), 7.05 (2H, br d, J 8.1, 2 × CH; Ar), 5.78 (1H, q, 6.6, CHO), 3.65 (1H, q, 7.2, CHCO), 2.37 (2H, d, 7.1, CH$_2$Ar), 1.77 (1H, tripe septet, J 7.1 and 6.6, CH$_3$CH$_2$Ar), 1.42 (3H, d, J 6.6, CH$_3$CHCO), 1.41 (3H, d, J 7.1, CH$_3$CHAr), and 0.82 (6H, d, J 6.6, CH(CH$_3$)$_2$); δ$_C$ (100 MHz; CDCl$_3$) 173.7 (C=O), 141.7 (i-C; Ph), 140.4 (i-CCHCO; Ar), 137.6 (i-CCH$_2$; Ar), 129.2$^2$ and 125.6$^2$ (4 × CH; Ar), 128.2$^2$ 127.5$^1$ and 127.3$^2$ (5 × CH; Ph), 72.3 (CHO), 45.3 (CHCO), 45.0 (CH$_2$Ar), 30.2 (CHCH$_2$), 22.3$^3$ (CH(CH$_3$)$_2$ and CH$_3$CHO) and 18.2 (CH$_3$CHCO); (Found MNH$_4^+$, 328.2273; C$_{21}$H$_{30}$N$_1$O$_2$ requires 328.2271).

Stereospecific synthesis of 1-phenylethyl-2-(4-isobutylphenyl)-propinate (S,S)-anti-248 using LDA [T5.1; E2].

In the same way as S5.2, LDA (0.39 ml, 1.8M in THF/heptane/ethylbenzene, 0.71 mmol), 1-phenylethanol (S)-11 (0.87 g, 0.71 mmol) and pentafluorophenyl-2-(4-isobutylphenyl)-propinate (S)-115 (0.176 g, 0.47 mmol) in THF (5 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-(4-isobutylphenyl)-propinate (S,S)-anti and (R,S)-syn-248 (93 mg, 63%, ratio anti : syn 72 : 28), which were spectroscopically identical to that obtained previously.

Stereospecific synthesis of 1-phenylethyl-2-(4-isobutylphenyl)-propinate (S,S)-anti-248 using LDA [T5.1; E3].

In the same way as S5.2, LDA (0.50 ml, 1.8M in THF/heptane/ethylbenzene, 0.91 mmol), 1-phenylethanol (S)-11 (0.11 g, 0.91 mmol) and pentafluorophenyl-2-(4-isobutylphenyl)-propinate (S)-115 (0.169 g, 0.45 mmol) in THF (5 ml). Gave after
purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-(4-isobutylphenyl)-propionate (S,S)-anti and (R,S)-syn-248 (96 mg, 68%, ratio anti : syn 63 : 37), which were spectroscopically identical to that obtained previously.

**Stereospecific synthesis of 1-phenylethyl-2-(4-isobutylphenyl)-propionate (S,R)-syn-248 using LDA [T5.1; E4].**

In the same way as S5.2, LDA (0.11 ml, 1.8M in THF/heptane/ethylbenzene, 0.20 mmol), 1-phenylethanol (R)-11 (49 mg, 0.40 mmol) and pentafluorophenyl-2-(4-isobutylphenyl)-propionate (S)-115 (50 mg, 0.13 mmol) in THF (6 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-(4-isobutylphenyl)-propionate (S,R)-syn-248 (26 mg, 62%, 100% d.e.), as an oil; R_F [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.84; [α]_D^20 = +29.4 (c 0.65, CHCl_3); ν_max (CHCl_3)/cm\(^{-1}\) 1723 (C=O); δ_H (400 MHz; CDCl_3) 7.27-7.19 (5H, m, 5 × Ph; Ar), 7.14 (2H, dt, J 8.1 and 1.8, 2 × CH; Ar), 7.02 (2H, dt, J 8.1 and 1.8, 2 × CH; Ar), 5.78 (1H, q, 6.6, CHO), 5.78 (1H, q, 6.6, CHCO); (Found MNH\(_+\) requires 328.2271).

**Stereospecific synthesis of 1-phenylethyl-2-phenylpropionate (R,R)-anti-245 using LDA [T5.2; E2].**

In the same way as S5.2, LDA (0.10 ml, 1.8M in THF/heptane/ethylbenzene, 0.18 mmol), 1-phenylethanol (R)-11 (44 mg, 0.36 mmol) and pentafluorophenyl-2-phenylpropionate (R)-95 (38 mg, 0.12 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-phenylethyl-2-phenylpropionate (R,R)-anti-245 (29 mg, 95%, 100% d.e.), as a transparent solid; mp 81-83°C; R_F [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.80; [α]_D^20 = +10.5 (c 3.0, CHCl_3); ν_max (CHCl_3)/cm\(^{-1}\) 1730 (C=O); δ_H (400 MHz; CDCl_3) 7.30-7.14 (8H, m, 8 × CH; Ph\(_A\) and Ph\(_B\)), 7.05-7.00 (2H, m, 2 × CH; Ph\(_A\) and/or Ph\(_B\)), 5.78 (1H, q, J 6.6, CHO), 3.68 (1H, q, J 7.2, CHCO), 1.43
(3H, d, J 7.2, CH₃CHCO) and 1.42 (3H, d, J 6.6, CH₃CHO); δC (100 MHz; CDCl₃) 173.5 (C=O), 141.6 (i-C; PhCHO), 140.4 (i-C; PhCHCO), 128.5, 128.3, 127.6, 127.5, 127.0 and 125.6 (10 × CH; Ph₂ and Ph₃), 72.4 (CHO), 45.7 (CHCO), 22.3 (CH₃CHO) and 18.3 (CH₃CHCO); (Found MNH⁺, 272.1648; C₁₇H₂₂NO₂ requires 272.1645).

**Stereospecific synthesis of 1-phenylethyl-2-(4-methylphenyl)-propinate (R,R)-anti-247 using LDA [T5.2; E2].**

In the same way as S5.2, LDA (0.17 ml, 1.8M in THF/heptane/ethylbenzene, 0.30 mmol), 1-phenylethanol (R)-11 (74 mg, 0.61 mmol) and pentafluorophenyl-2-(4-methylphenyl)-propinate (R)-113 (67 mg, 0.20 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-phenylethyl-2-(4-methylphenyl)-propinate (R,R)-anti-247 (26 mg, 48%, 100% d.e.) as a yellow solid; mp 40-42°C; Rₚ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.79; [α]⁺[o] = +9.3 (c 11.2, CHCl₃); νₚ (CHCl₃)/cm⁻¹ 1730 (C=O); δₚ (400 MHz; CDCl₃) 7.20-7.12 (3H, m, 3 × CH; Ph), 7.08-7.00 (6H, m, 6 × CH; Ph and Ar), 5.78 (1H, q, J 6.6, CHO), 3.64 (1H, q, J 7.2, CHCO), 2.25 (3H, s, CH₃Ar), 1.41 (3H, d, J 6.6, CH₃CHO) and 1.40 (3H, d, J 7.2, CH₃CHCO); δC (100 MHz; CDCl₃) 173.7 (C=O), 141.7 (i-C; Ar), 137.4 (i-C; Ph), 136.6 (i-CCH₃; Ar), 129.2 and 125.7 (4 × CH; Ar), 128.3, 127.5 and 127.4 (5 × CH; Ph), 72.4 (CHO), 45.3 (CHCO), 22.3 (CH₃CHO), 21.0 (CH₃Ar) and 18.4 (CH₃CHCO); (Found MNH⁺, 286.1804; C₁₈H₂₄NO₂ requires 286.1802).

**Stereospecific synthesis of 1-phenylethyl-2-(4-methylphenyl)-propinate (S,R)-syn-247 using LDA [T5.3; E1].**

In the same way as S5.2, LDA (0.23 ml, 1.8M in THF/heptane/ethylbenzene, 0.42 mmol), 1-phenylethanol (R)-11 (0.102 g, 0.84 mmol) and pentafluorophenyl-2-(4-methylphenyl)-propinate (S)-113 (92 mg, 0.28 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-phenylethyl-2-(4-methylphenyl)-propinate (S,R)-syn-247 (43 mg, 58%, 100% d.e.) as a oil; Rₚ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.79; [α]⁺[o] = +47.9 (c 5.8, CHCl₃); νₚ (CHCl₃)/cm⁻¹ 1723 (C=O); δₚ (400 MHz; CDCl₃) 7.38-7.27 (5H, m, 5 × CH; Ph), 7.22 (2H, br d, J 8.2, 2 × CH; Ar), 7.15 (2H, br d, J 8.2, 2 × CH; Ar), 5.87 (1H, q, J 6.6, CHO), 3.72 (1H, q, J 7.1, CHCO), 2.34 (3H, s, CH₃Ar), 1.48 (3H, d, J 7.1, CH₃CHCO) and 1.44 (3H, d, J 6.6,
CH₃CHO); δc (100 MHz; CDCl₃) 173.9 (C=O), 141.7 (i-C; Ar), 137.5 (i-C; Ph), 136.6 (i-CCH₃; Ar), 129.2 and 126.0 (4 × CH; Ar), 128.4, 2 127.8 and 127.3 (5 × CH; Ph), 72.4 (CHO), 45.2 (CHCO), 22.0 (CH₃CHO), 21.0 (CH₃Ar) and 18.5 (CH₃CHCO); (Found MNH₄, 286.1801; C₁₈H₂₄NO₂ requires 286.1802).

Stereospecific synthesis of 1-phenylethyl-2-(6-methoxy-2-naphthly)-propionate (S,R)-syn-249 using LDA [T5.3; E3].

In the same way as S5.2, LDA (0.13 ml, 1.8M in THF/heptane/ethylbenzene, 0.23 mmol), 1-phenylethanol (R)-11 (56 mg, 0.46 mmol) and pentafluorophenyl-2-(6-methoxynaphthly)-propionate (S)-123 (61 mg, 0.15 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propionate (S,R)-syn-249 (32 mg, 62%, 100% d.e.) as a white solid; mp 73-75°C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.61; [α]D sup20 = +8.8 (c 1.6, CHCl₃); \( \nu_{max} \) (CHCl₃)/cm⁻¹ 1730 (C=O); δH (400 MHz; CDCl₃) 7.68 (2H, dd, J 8.4 and 2.0, 2 × CH; Ar), 7.66 (1H, br s, CH; Ar), 7.40 (1H, dd, J 8.4 and 1.8, CH; Ar), 7.33-7.25 (5H, m, 5 × CH; Ph), 7.12 (1H, dd, J 8.4 and 1.8, CH; Ar), 7.10 (1H, br s, CH; Ar), 5.85 (1H, q, J 6.6, CHO), 3.90 (3H, s, OCH₃; Ar), 3.85 (1H, q, J 7.2, CHCO), 1.54 (3H, d, J 7.2, CH₃CHCO) and 1.40 (3H, d, J 6.6, CH₃CHO); δc (100 MHz; CDCl₃) 173.9 (C=O), 157.6 (i-CO; Ar), 141.6 (i-C; Ph), 135.7, 133.6 and 128.9 (3 × i-C; Ar), 129.3, 127.0, 126.3, 125.9, 118.9 and 105.5 (6 × CH; Ar), 128.4, 2 127.8 and 126.0 (5 × CH; Ph), 72.6 (CHO), 55.3 (OCH₃), 45.6 (CHCO), 22.0 (CH₃CHO) and 18.5 (CH₃CHCO); (Found MNH₄, 352.1905; C₂₂H₂₆NO₃ requires 352.1907).

Stereospecific synthesis of 1-phenylethyl-2-phenylbutinate (S,R)-syn-246 using LDA [T5.3; E3].

In the same way as S5.2, LDA (0.36 ml, 1.8M in THF/heptane/ethylbenzene, 0.64 mmol), 1-phenylethanol (R)-11 (0.16 g, 1.28 mmol) and pentafluorophenyl-2-phenylbutinate (S)-119 (0.141 g, 0.43 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-phenylethyl-2-phenylbutinate (S,R)-syn-246 (80 mg, 70%, 100% d.e.) as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.75; [α]D sup20 = +56.4 (c 2.0, CHCl₃); \( \nu_{max} \) (CHCl₃)/cm⁻¹ 1723 (C=O); δH (400 MHz; CDCl₃) 7.38-7.23 (10H, m, 10 × CH; PhA and PhB), 5.88 (1H, q, J 6.6, CHO), 3.51 (1H, t, J 7.5, CHCO), 2.17-2.05 (1H, m, CH₃CH₃(CH₂CH₂CH), 1.87-1.75 (1H, m, CH₃CH₃H₂CH), 1.44
(3H, d, J 6.6, CH₃CHO) and 0.87 (3H, t, J 7.5, CH₃CH₂CH); δC (100 MHz; CDCl₃) 173.3 (C=O), 141.7 and 139.1 (2 × i-C; Phₐ and Phₐ), 128.5, 128.4, 127.9, 127.7, 127.1, and 126.0 (10 × CH; Phₐ and Phₐ), 72.5 (CHO), 53.6 (CHCO), 26.6 (CH₃CH₂CH), 21.9 (CH₃CHO) and 12.1 (CH₂CH₂CH); (Found MNH₃, 286.1805; C₁₈H₂₄O₂N requires 286.1802).

**Stereospecific synthesis of 1-phenylethyl-2-(6-methoxy-2-naphthly)-propionate (S,S)-anti-249 using LDA [T5.4; E1].**

In the same way as S5.2, LDA (0.18 ml, 1.8M in THF/heptane/ethylbenzene, 0.33 mmol), 1-phenylethanol (S)-11 (80 mg, 0.66 mmol) and pentafluorophenyl-2-(6-methoxynaphthly)-propionate (S)-123 (87 mg, 0.22 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propionate (S,S)-anti-249 (63 mg, 86%, 100% d.e.), as a white solid; mp 94-96°C; Rₑ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.62; [α]ᵢ° = +26.6 (c 3.2, CHCl₃); νmax (CHCl₃)/cm⁻¹ 1723 (C=O); δH (400 MHz; CDCl₃) 7.66 (1H, d, J 8.4, CH; Ar), 7.63 (1H, d, J 8.4, CH; Ar), 7.55 (1H, br s, CH; Ar), 7.33 (1H, dd, J 8.3 and 1.8, CH; Ar), 7.19-7.08 (7H, m, 7 × CH; Ph and Ar), 5.86 (1H, q, J 6.6, CHO), 3.90 (3H, s, OCH₃; Ar), 3.88 (1H, q, J 7.2, CHCO), 1.56 (3H, d, J 7.2, CH₃CHCO) and 1.50 (3H, d, J 6.6, CH₃CHO); δC (100 MHz; CDCl₃) 173.7 (C=O), 147.5 (i-CO; Ar), 141.6 (i-C; Ph), 135.6, 133.6 and 128.9 (3 × i-C; Ar), 129.3, 127.0, 126.4, 126.0, 118.8 and 105.5 (6 × CH; Ar), 128.2, 127.5, 125.7 (5 × CH; Ph), 72.5 (CHO), 55.3 (OCH₃), 45.6 (CHCO), 22.3 (CH₃CHO) and 18.4 (CH₂CHCO); (Found MNH₃, 352.1907; C₂₂H₂₆NO₃ requires 352.1907).

**Stereospecific synthesis of 1-phenylethyl-2-phenylbutinate (S,S)-anti-246 using LDA [T5.4; E2].**

In the same way as S5.2; E1, LDA (0.77 ml, 1.8M in THF/heptane/ethylbenzene, 1.39 mmol), 1-phenylethanol (S)-11 (0.339 g, 2.77 mmol) and pentafluorophenyl-2-phenylbutinate (S)-119 (0.305 g, 0.92 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-phenylethyl-2-phenylbutinate (S,S)-anti-246 (0.18 g, 73%, 100% d.e.), as an oil; Rₑ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.79; [α]ᵢ° = -12.9 (c 6.2, CHCl₃); νmax (CHCl₃)/cm⁻¹ 1723 (C=O); δH (400 MHz; CDCl₃) 7.30-7.14 (8H, m, 8 × CH; Phₐ and Phₐ), 7.05-7.00 (2H, m, 2 × CH;
PhA and/or PhB), 5.88 (1H, q, J 6.6, CHO), 3.51 (1H, t, J 7.6, CHCO), 2.22-2.10 (1H, m, CH₂CH₂A₂B₂CH₃), 1.91-1.79 (1H, m, CH₂CH₂A₂B₂CH₃), 1.51 (3H, d, J 6.6, CH₃CHO) and 0.90 (3H, t, J 7.5, CH₂CH₂CH₃); δC (100 MHz; CDCl₃) 172.8 (C=O), 141.5 and 138.8 (2 × i-C; PhA and PhB), 128.3, 128.1, 127.9, 127.4, 126.9 and 125.9 (10 × CH; PhA and PhB), 72.2 (CHO), 53.5 (CHCO), 26.4 (CH₃CH₂CH₃), 22.2 (CH₃CHO) and 12.0 (CH₃CH₂CH₃); (Found MNH⁺, 286.1802; C₁₈H₂₆NO₂ requires 286.1805).

Stereospecific synthesis of 1-phenylethyl-2-phenoxypropinate (S,S)-syn-252 using LDA [S5.4; E1].

In the same way as S5.2, LDA (0.02 ml, 1.8M in THF/heptane/ethylbenzene, 0.041 mmol), 1-phenylethanol (S)-11 (10 mg, 0.081 mmol) and pentafluorophenyl-2-phenoxypropinate (S)-251 (9 mg, 0.027 mmol) in THF (5 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-phenylethyl-2-phenoxypropinate (S,S)-syn-252 (5 mg, 68%, 100% d.e.), as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.75; [α]D⁰ = -84.4 (c 0.09, CHCl₃); νmax (CHCl₃)/cm⁻¹ 1744 (C=O); δH (400 MHz; CDCl₃) 7.27-7.10 (5H, m, 5 × CH; PhA and/or PhB), 7.17-7.15 (2H, m, 2 × CH; PhA and/or PhB), 6.95 (1H, tt, J 7.4 and 0.9, CH; PhO), 6.85-6.83 (2H, m, 2 × CH; PhO), 5.86 (1H, q, J 6.6, PhCHO), 4.71 (1H, q, J 6.8, PhOCHCO), 1.52 (3H, d, J 6.8, CH₃CHOPh) and 1.49 (3H, d, J 6.6, CH₃CHPh); δC (100 MHz; CDCl₃) 171.5 (C=O), 157.6 (i-CO; PhO), 140.9 (i-C; Ph), 129.5, 128.4, 127.9, 126.0, 121.5 and 115.1 (10 × CH; PhA and PhB), 73.3 (PhOCH), 72.5 (PhCH), 22.1 (CH₃CHPh) and 18.5 (CH₃CHOPh); (Found M⁺, 270.1250; C₁₇H₁₈O₃ requires 270.1250).

Stereospecific synthesis of 1-phenylethyl-2-phenoxypropinate (S,R)-anti-252 using LDA [S5.4; E2].

In the same way as S5.2, LDA (0.05 ml, 1.8M in THF/heptane/ethylbenzene, 0.081 mmol), 1-phenylethanol (R)-11 (12 mg, 0.16 mmol) and pentafluorophenyl-2-phenoxypropinate (S)-251 (18 mg, 0.054 mmol) in THF (5 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-phenylethyl-2-phenoxypropinate (S,R)-anti-252 (8 mg, 55%, 100% d.e.), as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.69; [α]D⁰ = +22.4 (c 0.32, CHCl₃); νmax (CHCl₃)/cm⁻¹ 1744 (C=O); δH (400 MHz; CDCl₃) 7.31-7.12 (7H, m, 7 × CH; PhA and/or PhB), 6.87 (1H, tt, J 7.5 and 1.1, CH; PhO), 6.76-6.73 (2H, m, 2 × CH; PhO), 5.86 (1H, q, J 6.6, PhCHO), 4.68 (1H, q, J 6.8, 246
PhOCHCO), 1.55 (3H, d, J 6.8, CH₃CHOPh) and 1.40 (3H, d, J 6.6, CH₃CHPh); δC (100 MHz; CDCl₃) 171.5 (C=O), 157.5 (i-CO; PhO), 140.9 (i-C; Ph), 129.4, 128.5, 128.1, 126.1, 121.4, 115.0 (10 × CH; Phₓ and Phᵧ), 73.2 (PhOCH), 72.6 (PhCH), 21.8 (CH₃CHPh) and 18.5 (CH₃CHOPh); (Found M⁺, 270.1249; C₁₇H₁₈O₃ requires 270.1250).

Stereospecific synthesis of 1-phenylethyl-2-methoxy-2-phenylacetate (S,S)-anti-253 using LDA [S5.5; E1].

In the same way as S5.2; E1, LDA (0.27 ml, 1.8M in THF/heptane/ethylbenzene, 0.48 mmol), 1-phenylethanol (S)-11 (0.12 g, 0.98 mmol) and pentafluorophenyl-2-metoxy-2-phenylacetate (S)-121 (0.108 g, 0.33 mmol) in THF (10 ml). Gave by crude 1H NMR a 50:50 mix of 1-phenylethyl-2-methoxy-2-phenylacetate (S,S)-anti and (R,S)-syn-253, which were spectroscopically identical to that obtained elsewhere.

Stereospecific synthesis of 1-phenylethyl-2-methoxy-2-phenylacetate (S,R)-syn-253 using LDA [S5.5; E2].

In the same way as S5.2; E1, LDA (0.27 ml, 1.8M in THF/heptane/ethylbenzene, 0.48 mmol), 1-phenylethanol (R)-11 (0.118 g, 0.97 mmol) and pentafluorophenyl-2-metoxy-2-phenylacetate (S)-121 (0.107 g, 0.32 mmol) in THF (10 ml). Gave by crude 1H NMR a 50:50 mix of 1-phenylethyl-2-methoxy-2-phenylacetate (S,R)-syn and (R,R)-anti-253, which were spectroscopically identical to that obtained elsewhere.

Epimerisation of ester (S,S)-anti-249 using alcohol (rac)-254 [S5.6].

Added LDA (0.05 ml, 1.8M in THF/heptane/ethylbenzene, 0.09 mmol) to 1-(4-methoxyphenyl)-ethanol (rac)-254 (14 mg, 0.09 mmol) in THF (5 ml), followed by 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propinate (S,S)-anti-249 (30 mg, 0.09 mmol) in THF (5 ml). The resulting mixture was stirred over night. The reaction was quenched with NH₄Cl(aq) (10 ml). The organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. The crude mixture was purified by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) to give an inseparable mixture of 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propinate (S,S)-anti
and (R,S)-syn-249 (21 mg, 70%, anti : syn 67 : 33), which were spectroscopically identical to that obtained previously.

MKR of 1-phenylethanol (rac)-11 using n-BuLi [T5.5; E1].
In the same way as S5.2, n-BuLi (0.38 ml, 2.5M in hexanes, 0.95 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (80 mg, 50%, ratio anti : syn 73 : 27) and butyl-2-phenylpropionate (rac)-250 (17 mg, 13%), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using LDA [T5.5; E2].
In the same way as S5.2, LDA (0.53 ml, 1.8M in THF/heptane/ethylbenzene, 0.95 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (80 mg, 50%, ratio anti : syn 80 : 20), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using PhLi [T5.5; E3].
In the same way as S5.2, PhLi (1.90 ml, 1M in dibutylether, 1.90 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.32 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (0.147 g, 91%, ratio anti : syn 62 : 38) and butyl-2-phenylpropionate (rac)-250 (5 mg, 4%), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using LiH [T5.5; E4].
In the same way as S5.2, LiH (8 mg, 0.95 mmol), 1-phenylethanol (rac)-11 (0.773 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave back starting materials.
MKR of 1-phenylethanol \textit{(rac)}-11 using NaH [T5.5; E5].

In the same way as S5.2, NaH (38 mg, 60% on mineral oil, 0.95 mmol), 1-phenylethanol \textit{(rac)}-11 (0.77 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropionate \textit{(rac)}-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate \textit{(rac)}-anti and \textit{(rac)}-syn-245 (70 mg, 43%, ratio \textit{anti} : \textit{syn} 75 : 25) which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol \textit{(rac)}-11 using KN(SiMe$_3$)$_2$ [T5.5; E6].

In the same way as S5.2, KN(SiMe$_3$)$_2$ (0.190 g, 0.95 mmol), 1-phenylethanol \textit{(rac)}-11 (0.773 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropionate \textit{(rac)}-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate \textit{(rac)}-anti and \textit{(rac)}-syn-245 (32 mg, 16%, ratio \textit{anti} : \textit{syn} 79 : 21), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol \textit{(rac)}-11 using MeMgBr [T5.5; E7].

In the same way as S5.2, MeMgBr (0.32 ml, 3M in diethylether, 0.95 mmol), 1-phenylethanol \textit{(rac)}-11 (0.77 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropionate \textit{(rac)}-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate \textit{(rac)}-anti and \textit{(rac)}-syn-245 (0.133 g, 83%, ratio \textit{anti} : \textit{syn} 73 : 27), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol \textit{(rac)}-11 using NEt$_3$ [T5.5; E8].

In the same way as S5.2, NEt$_3$ (0.13 ml, 0.95 mmol), 1-phenylethanol \textit{(rac)}-11 (0.773 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropionate \textit{(rac)}-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave back starting materials.

MKR of 1-phenylethanol \textit{(rac)}-11 using LiNH$_2$ [T5.5; E9].

Added LiNH$_2$ (33 mg, 1.42 mmol) to 1-phenylethanol \textit{(rac)}-11 (0.579 g, 4.74 mmol) in THF (5 ml) after 15 mins cooled to -78°C and added pentafluorophenyl-2-
phenylpropinate (rac)-95 (0.150 g, 0.47 mmol) in THF (5 ml). The resulting mixture was stirred overnight. The reaction was quenched with NH₄Cl (aq) (10 ml). The organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. Gave back starting materials.

MKR of 1-phenylethanol (rac)-11 using NaNH₂ [T5.5; E10].

In the same way as S5.2; E10, NaNH₂ (37 mg, 0.95 mmol), 1-phenylethanol (rac)-11 (0.773 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropinate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (8 mg, 5%, ratio anti : syn 64 : 36), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using LiBr [T5.5; E11].

In the same way as S5.2, LiBr (82 mg, 0.95 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropinate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave back starting materials.

MKR of 1-phenylethanol (rac)-11 using Li₂CO₃ [T5.5; E12].

In the same way as S5.2, Li₂CO₃ (35 mg, 0.47 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropinate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave back starting materials.

MKR of 1-phenylethanol (rac)-11 using Na₂CO₃ [T5.5; E13].

In the same way as S5.2, Na₂CO₃ (50 mg, 0.47 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropinate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave back starting materials.

MKR of 1-phenylethanol (rac)-11 using K₂CO₃ [T5.5; E14].

In the same way as S5.2, K₂CO₃ (66 mg, 0.47 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropinate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave back starting materials.
MKR of 1-phenylethanol (rac)-11 using n-BuLi and MgBr₂.OEt₂ [T5.6; E1].

In the same way as S5.2, n-BuLi (0.38 ml, 2.5M in hexanes, 0.95 mmol), MgBr₂.OEt₂ (0.25 g, 0.95 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (10 mg, 6%, ratio anti : syn 76 : 24), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using LDA and MgBr₂.OEt₂ [T5.6; E2].

In the same way as S5.2, LDA (0.53 ml, 1.8M in THF/heptane/ethylbenzene, 0.95 mmol), MgBr₂.OEt₂ (0.25 g, 0.95 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (0.100 g, 62%, ratio anti : syn 78 : 22), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using LiH and MgBr₂.OEt₂ [T5.6; E3].

In the same way as S5.2, LiH (8 mg, 0.95 mmol), MgBr₂.OEt₂ (0.25 g, 0.95 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.32 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave back starting materials.

MKR of 1-phenylethanol (rac)-11 using NaH and MgBr₂.OEt₂ [T5.6; E4].

In the same way as S5.2, NaH (38 mg, 60% on mineral oil, 0.95 mmol), MgBr₂.OEt₂ (0.25 g, 0.95 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.32 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave back starting materials.

MKR of 1-phenylethanol (rac)-11 using MeMgBr and MgBr₂.OEt₂ [T5.6; E5].

In the same way as S5.2, MeMgBr (0.32 ml, 3M in diethylether, 0.95 mmol), MgBr₂.OEt₂ (0.25 g, 0.95 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light
petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-
phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (80 mg, 50%, ratio anti : syn 73 : 27), which were spectroscopically identical to that obtained elsewhere.

**MKR of 1-phenylethanol (rac)-11 using NEt₃ and MgBr₂·OEt₂ [T5.5; E6].**

In the same way as S5.2, NEt₃ (13 ml, 0.95 mmol), MgBr₂·OEt₂ (0.25 g, 0.95 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.33 mmol) and pentafluorophenyl-2-
phenylpropionate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-
60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (90 mg, 56%, ratio anti : syn 73 : 27), which were spectroscopically identical to that obtained elsewhere.

**MKR of 1-phenylethanol (rac)-11 using n-BuLi and ZnCl₂ [T5.7; E1].**

In the same way as S5.2, n-BuLi (0.38 ml, 2.5M in hexanes, 0.95 mmol), ZnCl₂ (0.95 ml, 1M in diethylether, 0.95 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.32 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-
phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (90 mg, 56%, ratio anti : syn 92 : 8) and butyl-2-phenylpropionate (rac)-250 (5 mg, 5%), which were spectroscopically identical to that obtained previously.

**MKR of 1-phenylethanol (rac)-11 using LDA and ZnCl₂ [T5.7; E2].**

In the same way as S5.2, LDA (0.53 ml, 1.8M in THF/heptane/ethylbenzene, 0.95 mmol), ZnCl₂ (0.95 ml, 1M in diethylether, 0.95 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.32 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (50 mg, 31%, ratio anti : syn 93 : 7), which were spectroscopically identical to that obtained elsewhere.
MKR of 1-phenylethanol (rac)-11 using LiH and ZnCl₂ [T5.7; E3].

In the same way as S5.2, LiH (8 mg, 0.95 mmol), ZnCl₂ (0.95 ml, 1M in diethylether, 0.95 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.32 mmol) and pentafluorophenyl-2-phenylpropinate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave back starting materials.

MKR of 1-phenylethanol (rac)-11 using NaH and ZnCl₂ [T5.7; E4].

In the same way as S5.2, NaH (38 ml, 60% on mineral oil, 0.95 mmol), ZnCl₂ (0.95 ml, 1M in diethylether, 0.95 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.32 mmol) and pentafluorophenyl-2-phenylpropinate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave back starting materials.

MKR of 1-phenylethanol (rac)-11 using MeMgBr and ZnCl₂ [T5.7; E5].

In the same way as S5.2, MeMgBr (0.32 ml, 3M in diethylether, 0.95 mmol), ZnCl₂ (0.95 ml, 1M in diethylether, 0.95 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.32 mmol) and pentafluorophenyl-2-phenylpropinate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (0.1 g, 62%, ratio anti : syn 74 : 26), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using NEt₃ and ZnCl₂ [T5.7; E6].

In the same way as S5.2, NEt₃ (13 ml, 0.95 mmol), ZnCl₂ (0.95 ml, 1M in diethylether, 0.95 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.32 mmol) and pentafluorophenyl-2-phenylpropinate (rac)-95 (0.200 g, 0.63 mmol) in THF (10 ml). Gave back starting materials.

MKR of 1-phenylethanol (rac)-11 in THF [T5.8; E1].

See T5.7; E1.

MKR of 1-phenylethanol (rac)-11 in dichloromethane [T5.8; E2].

In the same way as S5.2, n-BuLi (0.38 ml, 2.5M in hexanes, 0.95 mmol), ZnCl₂ (0.95 ml, 1M in diethylether, 0.95 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.32 mmol) and pentafluorophenyl-2-phenylpropinate (rac)-95 (0.200 g, 0.63 mmol) in dichloromethane (10 ml). Gave back starting materials.
MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.9; E1].

In the same way as S5.2, n-BuLi (0.38 ml, 2.5M in hexanes, 0.95 mmol), ZnCl₂ (0.63 ml, 1M in diethylether, 0.63 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.2 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethylether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (78 mg, 63%, ratio anti : syn 78 : 22) and butyl-2-phenylpropionate (rac)-250 (2 mg, 2%), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.9; E2].

See T5.7; E1.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.9; E3].

In the same way as S5.2, n-BuLi (0.38 ml, 2.5M in hexanes, 0.95 mmol), ZnCl₂ (1.27 ml, 1M in diethylether, 1.27 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.2 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethylether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (75 mg, 47%, ratio anti : syn 94 : 6) and butyl-2-phenylpropionate (rac)-250 (2 mg, 2%), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.9; E4].

In the same way as S5.2, n-BuLi (0.38 ml, 2.5M in hexanes, 0.95 mmol), ZnCl₂ (1.90 ml, 1M in diethylether, 1.90 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.2 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethylether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (4 mg, 2%, ratio anti : syn 96 : 4), which were spectroscopically identical to that obtained elsewhere.
MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.10; E1].

In the same way as S5.2, n-BuLi (0.76 ml, 2.5M in hexanes, 1.90 mmol), ZnCl₂ (1.90 ml, 1M in diethylether, 1.90 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.2 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (0.104 mg, 65%, ratio anti : syn 95 : 5) and butyl-2-phenylpropionate (rac)-250 (5 mg, 4%), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-113 [T5.10; E2].

In the same way as S5.2, n-BuLi (0.70 ml, 2.5M in hexanes, 1.76 mmol), ZnCl₂ (1.76 ml, 1M in diethylether, 1.76 mmol), 1-phenylethanol (rac)-11 (0.72 g, 5.87 mmol) and pentafluorophenyl-2-(4-methylphenyl)-propionate (rac)-113 (0.194 g, 0.59 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-(4-methylphenyl)-propionate (rac)-anti and (rac)-syn-247 (91 mg, 58%, ratio anti : syn 94 : 6) and butyl-2-(4-methylphenyl)-propionate (rac)-257 (5 mg, 4%), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-115 [T5.10; E3].

In the same way as S5.2, n-BuLi (0.70 ml, 2.5M in hexanes, 1.76 mmol), ZnCl₂ (1.76 ml, 1M in diethylether, 1.76 mmol), 1-phenylethanol (rac)-11 (0.72 g, 5.86 mmol) and pentafluorophenyl-2-(4-isobutylphenyl)-propionate (rac)-115 (0.218 g, 0.59 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-(4-isobutylphenyl)-propionate (rac)-anti and (rac)-syn-248 (0.105 g, 58%, ratio anti : syn 91 : 9) and butyl-2-(4-isobutylphenyl)-propionate (rac)-258 (6 mg, 4%), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-117 [T5.10; E4].

In the same way as S5.2, n-BuLi (0.67 ml, 2.5M in hexanes, 1.67 mmol), ZnCl₂ (1.67 ml, 1M in diethylether, 1.67 mmol), 1-phenylethanol (rac)-11 (0.68 g, 5.56 mmol) and pentafluorophenyl-2-(4-chlorophenyl)-propinate (rac)-117 (0.195 g, 0.56 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel
eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-(4-chlorophenyl)-propinate \((\text{rac})\text{-anti}\) and \((\text{rac})\text{-syn}\) \(256\) (0.107 g, 67%, ratio \(\text{anti} : \text{syn} 95 : 5\)) and butyl-2-(4-chlorophenyl)-propinate \((\text{rac})-259\) (8 mg, 6%), which were spectroscopically identical to that obtained elsewhere.

**MKR of 1-phenylethanol \((\text{rac})\)-11 using active ester \((\text{rac})\)-123 [T5.10; E5].**

In the same way as S5.2, \(n\)-BuLi (0.58 ml, 2.5M in hexanes, 1.45 mmol), \(\text{ZnCl}_2\) (1.45 ml, 1M in diethyl ether, 1.45 mmol), 1-phenylethanol \((\text{rac})\)-11 (0.59 g, 4.84 mmol) and pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propionate \((\text{rac})\)-123 (0.192 g, 0.48 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propinate \((\text{rac})\text{-anti}\) and \((\text{rac})\text{-syn}\) \(249\) (0.109 g, 67%, ratio \(\text{anti} : \text{syn} 90 : 10\)) and butyl-2-(6-methoxy-2-naphthyl)-propionate \((\text{rac})\)-260 (6 mg, 4%), which were spectroscopically identical to that obtained elsewhere.

**Synthesis of butyl-2-phenylpropionate \((\text{rac})\)-250 [T5.11; E1].**

\(\text{DCC} (0.42 g, 2.05 \text{ mmol})\) was added to 2-phenylpropanoic acid \((\text{rac})\)-111 (0.28 g, 1.86 mmol) in dichloromethane (10 ml), followed by DMAP (45 mg, 0.37 mmol) and butanol (0.14 g, 1.86 mmol) in dichloromethane (5 ml). The resulting mixture was stirred over night. The reaction was filtered to remove DCU. The organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over \(\text{MgSO}_4\) and evaporated under reduced pressure. To give after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) butyl-2-phenylpropionate \((\text{rac})\)-250 (0.28 g, 73%) as an oil; \(R_F\) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.76; \(\nu_{\text{max}} \text{(CHCl}_3) / \text{cm}^{-1} 1737 \text{ (C=O)}; \delta\text{H} (400 \text{ MHz}; \text{CDCl}_3) 7.35-7.22 (5\text{H}, \text{ m, } 5 \times \text{CH; Ph}), 4.12-4.02 (2\text{H}, \text{ m, CH}_2\text{O}), 3.72 (1\text{H}, \text{ q, J 7.2, CHCO}), 1.61-1.46 (2\text{H}, \text{ m, CH}_2\text{CH}_2\text{O}), 1.50 (3\text{H}, \text{ d, J 7.2, CH}_3\text{CHCO}), 1.35-1.24 (2\text{H}, \text{ m, CH}_2\text{CH}_2\text{CH}_2\text{O}) \text{ and 0.88 (3H, t, J 7.5, CH}_3\text{CH}_2\text{CHCO); } \delta_{\text{C}}\text{ (100 MHz; CDCl}_3) 174.6 \text{ (C=O) , 140.6 (i-C; Ph) , 128.5, }^2 127.4^2 \text{ and 127.0}^1 (5 \times \text{CH; Ph) , 64.5 (CH}_2\text{O), 45.5 (CHCO), 30.5 (CH}_2\text{CH}_2\text{O), 19.0 (CH}_3\text{CH}_2\text{CH}_2\text{O), 18.5 (CH}_3\text{CHCO) and 13.6 (CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{O); } \text{(Found M}^+ , 206.1299 \text{C}_{13}\text{H}_{18}\text{O}_2\text{ requires 206.1301).} \)
Synthesis of butyl-2-phenylbutinate \((rac)-261\) [T5.11; E2].

In the same way as T5.11; E1, DCC (0.280 g, 1.34 mmol), 2-phenylbutonic acid \((rac)-118\) (0.200 g, 1.22 mmol), DMAP (30 mg, 0.24 mmol) and butanol (90 mg, 1.22 mmol) in dichloromethane (15 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) butyl-2-phenylbutinate \((rac)-261\) (0.14 g, 52%) as an oil; \(R_f\) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.81; \(\nu_{\text{max}}\) (CHCl\(_3\))/cm\(^{-1}\) 1725 (C=O); \(\delta_H\) (400 MHz; CDCl\(_3\)) 7.35-7.22 (5H, m, 5 \(\times\) CH; Ph), 4.13-4.01 (2H, m, CH\(_2\)O), 3.45 (1H, t, \(J\) 7.7, CHCO), 2.17-2.05 (1H, m, CH\(_3\)CH\(_2\)H\(_8\)CHCO), 1.86-1.74 (1H, m, CH\(_3\)CH\(_2\)H\(_8\)CHCO), 1.63-1.53 (2H, m, CH\(_2\)CH\(_2\)O), 1.35-1.25 (2H, m, CH\(_2\)CH\(_2\)CH\(_2\)O), 0.90 (3H, t, \(J\) 7.5, CH\(_2\)CH\(_2\)CH\(_2\)O) and 0.88 (3H, t, 7.5, CH\(_2\)CH\(_2\)CH\(_2\)CH\(_2\)O); \(\delta_C\) (100 MHz; CDCl\(_3\)) 174.1 (C=O), 139.2 (i-C; Ph), 128.5, 2, 127.9 and 127.0 (5 \(\times\) CH; Ph), 64.4 (CH\(_2\)O), 53.6 (CHCO), 30.6 (CH\(_2\)CH\(_2\)Ph), 26.7 (CH\(_2\)CH\(_2\)O), 19.0 (CH\(_2\)CH\(_2\)CH\(_2\)O), 13.6 (CH\(_3\)CH\(_2\)CH\(_2\)CH\(_2\)O) and 12.1 (CH\(_3\)CH\(_2\)CHCO); (Found MH\(^+\), 221.1535 C\(_{14}\)H\(_{21}\)O\(_2\) requires 221.1536).

Synthesis of butyl-2-(4-methylphenyl)-propionate \((rac)-257\) [T5.11; E3].

In the same way as T5.11; E1, DCC (0.1 g, 0.48 mmol), 2-(4-methylphenyl)-proponic acid \((rac)-112\) (72 mg, 0.44 mmol), DMAP (11 mg, 0.09 mmol) and butanol (33 mg, 0.44 mmol) in dichloromethane (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) butyl-2-(4-methylphenyl)-propionate \((rac)-257\) (71 mg, 74%) as a clear oil; \(R_f\) [light petroleum spirit (bp 40-60°C) / dichloromethane (1:1)] 0.36; \(\nu_{\text{max}}\) (CHCl\(_3\))/cm\(^{-1}\) 1726 (C=O); \(\delta_H\) (400 MHz; CDCl\(_3\)) 7.19 (2H, d, 7.2, 2 \(\times\) CH; Ar), 7.12 (2H, d, 8.1, 2 \(\times\) CH; Ar), 4.06 (1H, t, 6.8, CH\(_3\)Ar), 4.05 (1H, t, 6.6, CH\(_3\)Ar), 3.67 (1H, q, 7.2, CHCO), 2.33 (3H, s, CH\(_3\)Ar), 1.61-1.50 (2H, m, CH\(_2\)CH\(_2\)O), 1.48 (3H, d, 7.2, CH\(_2\)CHCO), 1.35-1.24 (2H, m, CH\(_2\)CH\(_2\)O) and 0.88 (3H, t, 7.5, CH\(_2\)CH\(_2\)O); \(\delta_C\) (100 MHz; CDCl\(_3\)) 174.8 (C=O), 137.7 and 136.6 (2 \(\times\) i-C; Ar), 129.2, 2 and 127.3 (4 \(\times\) CH; Ar), 64.5 (CH\(_2\)O), 45.2 (CHCO), 30.6 (CH\(_3\)Ar), 21.0 (CH\(_2\)CH\(_2\)O), 19.0 (CH\(_2\)CH\(_2\)O), 18.5 (CH\(_3\)CHCO) and 13.6 (CH\(_3\)CH\(_2\)O).

Synthesis of butyl-2-(4-isobutlyphenyl)-propionate \((rac)-258\) [T5.11; E4].

In the same way as T5.11; E1, DCC (0.260 g, 1.28 mmol), 2-(4-isobutlyphenyl)-proponic acid \((rac)-114\) (0.240 g, 1.16 mmol), DMAP (30 mg, 0.23 mmol) and butanol (90 mg, 1.16 mmol) in dichloromethane (15 ml). Gave after
purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) butyl-2-(4-isobutylphenyl)-propinate (rac)-258 (0.26 g, 85%) as an oil; \( R_F \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.83; \( \nu_{\text{max}} \) (CHCl$_3$)/cm$^{-1}$ 1718 (C=O); \( \delta_H \) (400 MHz; CDCl$_3$) 7.12 (2H, br d, J 8.0, 2 × CH; Ar), 7.01 (2H, br d, J 8.0, 2 × CH; Ar), 3.98 (2H, t, J 6.6, CH$_2$O), 3.60 (1H, q, J 7.2, CHCO), 2.37 (2H, d, J 7.3, CH$_2$Ar), 1.77 (1H, m, appears as a septet J 6.6, CH$_3$CH$_2$Ar), 1.51-1.43 (2H, m, CH$_2$CH$_2$O), 1.40 (3H, d, J 7.2, CH$_3$CHCO), 1.26-1.15 (2H, m, CH$_2$CH$_2$CH$_2$O), 0.82 (6H, d, J 6.6, CH$_3$CHCH$_3$) and 0.79 (3H, t, J 7.3, CH$_3$CH$_2$CH$_2$O); \( \delta_C \) (100 MHz; CDCl$_3$) 174.8 (C=O), 140.4 and 137.9 (2 × i-C; Ar), 129.2 and 127.1 (4 × CH; Ar), 64.5 (CH$_2$O), 45.1 (CHCO), 45.0 (CH$_2$Ar), 30.6 (CHCH$_2$Ar), 30.2 (CH$_2$CH$_2$O), 22.3 (CH$_3$CHCH$_3$), 19.0 (CH$_2$CH$_2$CH$_2$O), 18.4 (CH$_3$CHCO) and 13.6 (CH$_3$CH$_2$CH$_2$CH$_2$O); (Found M$^+$, 262.1927 C$_{17}$H$_{26}$O$_2$ requires 262.1927).

**Synthesis of butyl-2-(4-chlorophenyl)-propinate (rac)-259 [T5.11; E5].**

In the same way as T5.11; E1, DCC (0.1 g, 0.48 mmol), 2-(4-chlorophenyl)-propanic acid (rac)-116 (81 mg, 0.44 mmol), DMAP (11 mg, 0.09 mmol) and butanol (32 mg, 0.44 mmol) in dichloromethane (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) butyl-2-(4-chlorophenyl)-propinate (rac)-259 (72 mg, 68%) as clear oil; \( R_F \) [light petroleum spirit (bp 40-60°C) / dichloromethane (1:1)] 0.39; \( \nu_{\text{max}} \) (CHCl$_3$)/cm$^{-1}$ 1728 (C=O); \( \delta_H \) (400 MHz; CDCl$_3$) 7.23-7.14 (4H, m, 4 × CH; Ar), 3.98 (2H, t, J 6.6, CH$_2$O), 3.61 (1H, q, J 7.3, CHCO), 1.51-1.43 (2H, m, CH$_2$CH$_2$O), 1.40 (3H, d, J 7.2, CH$_3$CHCO), 1.27-1.17 (2H, m, CH$_2$CH$_3$) and 0.81 (3H, t, J 7.3, CH$_2$CH$_3$); \( \delta_C \) (100 MHz; CDCl$_3$) 174.1 (C=O), 139.1 and 132.9 (2 × i-C; Ar), 128.8$^2$ and 128.6$^2$ (4 × CH; Ar), 64.7 (CH$_2$O), 45.0 (CHCO), 30.4 (CH$_2$CH$_2$O), 19.0 (CH$_2$CH$_3$), 18.4 (CH$_3$CHCO) and 13.6 (CH$_3$CH$_2$).

**Synthesis of butyl-2-(6-methoxy-2-naphthyl)-propinate (rac)-260 [S5.7].**

In the same way as T5.11; E1, DCC (0.12 g, 0.58 mmol), 2-(6-methoxy-2-naphthyl)-propanic acid (S)-122 (0.210 g, 0.53 mmol), DMAP (13 mg, 0.11 mmol) and butanol (40 mg, 0.53 mmol) in dichloromethane (15 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) butyl-2-(6-methoxy-2-naphthyl)-propinate (rac)-260 (0.10 g, 42%) as a white solid mp 56-58°C; \( R_F \) [light petroleum spirit (bp 40-60°C) / diethyl
ether (1:1] 0.71; $\nu_{\text{max}}$ (CHCl$_3$)/cm$^{-1}$ 1725 (C=O); $\delta$$_H$ (400 MHz; CDCl$_3$) 7.64-7.57 (3H, m, 3 $\times$ CH; Ar), 7.33 (1H, dd, $J$ 8.4 and 1.8, CH; Ar), 7.08-7.02 (2H, m, 2 $\times$ CH; Ar), 4.04-3.93 (2H, m, CH$_2$O), 3.83 (3H, s, CH$_3$O), 3.76 (1H, q, $J$ 7.2, CHCO), 1.53-1.43 (2H, m, CH$_2$CH$_2$O), 1.49 (3H, d, $J$ 7.2, $CH_3$CHCO), 1.26-1.15 (2H, m, CH$_2$CH$_2$CH$_2$O) and 0.78 (3H, t, $J$ 7.5, $CH_2$CH$_2$CH$_2$CH$_2$O); $\delta$$_C$ (100 MHz; CDCl$_3$) 174.7 (C=O), 157.6, 135.8, 133.6 and 128.9 (4 $\times$ i-C; Ar), 129.2, 127.0, 126.3, 125.9, 118.9 and 105.5 (6 $\times$ CH; Ar), 64.6 (CH$_2$O), 55.3 (CH$_3$O), 45.5 (CHCO), 30.6 (CH$_2$CH$_2$O), 19.0 (CH$_2$CH$_2$CH$_2$O), 18.5 (CH$_3$CHCO) and 13.6 (CH$_3$CH$_2$CH$_2$O).

**MKR of 1-phenylethanol (rac)-11 using n-BuLi [T5.12; E1].**

See T5.7; E1.

**MKR of 1-phenylethanol (rac)-11 using LDA [T5.12; E2].**

In the same way as S5.2, LDA (1.05 ml, 1.8M in THF/heptane/ethylbenzene, 1.90 mmol), ZnCl$_2$ (1.90 ml, 1M in diethylether, 1.90 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.2 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (86 mg, 53%, ratio anti : syn 93 : 7) and butyl-2-phenylpropionate (rac)-250 (1 mg, 1%), which were spectroscopically identical to that obtained elsewhere.

**MKR of 1-phenylethanol (rac)-11 using LiNH$_2$ [T5.12; E3].**

Added LiNH$_2$ (33 mg, 1.42 mmol) to 1-phenylethanol (rac)-11 (0.579 g, 4.74 mmol) in THF (5 ml) after 15 mins cooled to -78°C and added ZnCl$_2$ (1.42 ml, 1M in diethylether, 1.42 mmol) followed by pentafluorophenyl-2-phenylpropionate (rac)-95 (0.150 g, 0.47 mmol) in THF (5 ml). The resulting mixture was stirred over night. The reaction was quenched with NH$_2$Cl$_{\text{(aq)}}$ (10 ml). The organic layer was extracted with dichloromethane (3 $\times$ 25 ml), washed with water (25 ml), dried over MgSO$_4$ and evaporated under reduced pressure. Gave back starting materials.

**MKR of 1-phenylethanol (rac)-11 using tert-BuLi [T5.12; E4].**

In the same way as S5.2, tert-BuLi (1.12 ml, 1.7M in pentane, 1.90 mmol), ZnCl$_2$ (1.90 ml, 1M in diethylether, 1.90 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.33 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.2 g, 0.63 mmol) in THF
(10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (0.115 g, 71%, ratio anti : syn 94 : 6), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.13; E1].

In the same way as S5.2, tert-BuLi (1.12 ml, 1.7M in pentane, 1.90 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.32 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.2 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (0.116 g, 72%, ratio anti : syn 62 : 38), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.13; E2].

In the same way as S5.2, tert-BuLi (1.12 ml, 1.7M in pentane, 1.90 mmol), ZnCl₂ (0.95 ml, 1M in diethylether, 0.95 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.32 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.2 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (0.115 g, 71%, ratio anti : syn 72 : 28), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.13; E3].

See T5.12; E4.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.13; E4].

In the same way as S5.2, tert-BuLi (1.12 ml, 1.7M in pentane, 1.90 mmol), ZnCl₂ (3.79 ml, 1M in diethylether, 3.79 mmol), 1-phenylethanol (rac)-11 (0.77 g, 6.32 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.2 g, 0.63 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (52 mg, 32%, ratio anti : syn 97 : 3), which were spectroscopically identical to that obtained elsewhere.
MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.14; E1].
See T5.12; E4.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-113 [T5.14; E2].
In the same way as S5.2, tert-BuLi (1.22 ml, 1.7M in pentane, 2.08 mmol),
ZnCl₂ (2.08 ml, 1M in diethylether, 2.08 mmol), 1-phenylethanol (rac)-11 (0.847 g,
6.93 mmol) and 1-phenylethyl-2-(4-methylphenyl)-propionate (rac)-113 (0.229 g, 0.69
mmol) in THF (10 ml). Gave after purification by flash column chromatography
on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an
inseparable mixture of 1-phenylethyl-2-(4-methylphenyl)-propionate (rac)-anti and
(rac)-syn-247 (0.113 g, 61%, ratio anti : syn 94 : 6), which were spectroscopically
identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-115 [T5.14; E3].
In the same way as S5.2, tert-BuLi (0.93 ml, 1.7M in pentane, 1.59 mmol),
ZnCl₂ (1.59 ml, 1M in diethylether, 1.59 mmol), 1-phenylethanol (rac)-11 (0.65 g, 5.29
mmol) and 1-phenylethyl-2-(4-isobutylphenyl)-propionate (rac)-115 (0.197 g, 0.53
mmol) in THF (10 ml). Gave after purification by flash column chromatography
on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an
inseparable mixture of 1-phenylethyl-2-(4-isobutylphenyl)-propionate (rac)-anti and
(rac)-syn-248 (0.109 g, 66%, ratio anti : syn 94 : 6), which were spectroscopically
identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-117 [T5.14; E4].
In the same way as S5.2, tert-BuLi (0.62 ml, 1.7M in pentane, 1.06 mmol),
ZnCl₂ (1.06 ml, 1M in diethylether, 1.06 mmol), 1-phenylethanol (rac)-11 (0.432 g,
3.54 mmol) and pentafluorophenyl-2-(4-chlorophenyl)-propionate (rac)-117 (0.124 g,
0.35 mmol) in THF (10 ml). Gave after purification by flash column chromatography
on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an
inseparable mixture of 1-phenylethyl-2-(4-chlorophenyl)-propionate (rac)-anti and (rac)-
syn-256 (57 mg, 56%, ratio anti : syn 93 : 7) as an oil; Rf [light petroleum spirit (bp 40-
60°C) / diethyl ether (1:1)] 0.76; νmax (CHCl₃)/cm⁻¹ 1731 (C=O); δH (400 MHz; CDCl₃)
7.34-7.22 (5H, m, 5 × CH; Ph and Ar), 7.16 (2H, dd, J 8.8 and 2.4, 2 × CH; Ar), 7.14-
7.09 (2H, m, 2 × CH; Ph), 5.84 (1H, q, 6.6, CHO), 3.73 (1H, q, 7.2, CHCO), 1.50 (3H,
d, J 6.6, CH₃CHO) and 1.48 (3H, d, J 7.2, CH₃CHCO); δC (100 MHz; CDCl₃) 173.0
MKR of 1-phenylethanol (rac)-11 using active ester (rac)-123 [T5.14; E5].

In the same way as S5.2, tert-BuLi (0.88 ml, 1.7M in pentane, 1.49 mmol), ZnCl₂ (1.49 ml, 1M in diethyl ether, 1.49 mmol), 1-phenylethanol (rac)-11 (0.61 g, 4.97 mmol) and pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propinate (rac)-123 (0.197 g, 0.50 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propinate (rac)-anti and (rac)-syn-249 (0.113 g, 68%, ratio anti : syn 94 : 6), [note this fraction contained pentafluorophenol which was removed by washing with NaOH (3M) and extraction with dichloromethane], which were spectroscopically identical to that obtained previously.

PKR of 1-phenylethanol (rac)-11 using active ester (S)-123 and (R)-95 [S5.8].

In the same way as S5.2, tert-BuLi (1.81 ml, 1.7M in pentane, 3.07 mmol), ZnCl₂ (3.07 ml, 1M in diethyl ether, 3.07 mmol), 1-phenylethanol (rac)-11 (1.25 g, 10.25 mmol), pentafluorophenyl-2-phenylpropionate (R)-95 (0.162 g, 0.51 mmol) and pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propinate (S)-123 (0.203 g, 0.51 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (R,R)-anti and (R,S)-syn-245 (0.100 g, 77%, ratio anti : syn 93 : 7). Also gave an inseparable mixture of 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propinate (S,S)-anti (S,R)-syn-249 (0.13 g, 76%, ratio anti : syn 94 : 6), [note this fraction contained pentafluorophenol which was removed by washing with NaOH (3M) and extraction with dichloromethane], which were spectroscopically identical to that obtained elsewhere.

MKR of 1-(2-naphthyl)-ethanol (rac)-261 using active ester (rac)-95 [S5.9].

In the same way as S5.2, tert-BuLi (0.56 ml, 1.7M in pentane, 0.95 mmol), ZnCl₂ (0.95 ml, 1M in diethyl ether, 0.95 mmol), 1-(2-naphthyl)-ethanol (rac)-261 (C=O), 141.4, 138.8 and 132.8 (3 × i-C; Ph and Ar), 128.9, 128.6, 128.3, 127.7 and 125.7 (9 × CH; Ph and Ar), 72.7 (CHO), 45.0 (CHCO), 22.2 and 18.3 (2 × CH₃). For minor diastereoisomer (rac)-syn-256: δH (400 MHz; CDCl₃) 7.34-7.22 (5H, m, 5 × CH; Ph and Ar), 7.18-7.09 (4H, m, 4 × CH; Ph and Ar), 5.85 (1H, q, 6.6, CHO), 3.71 (1H, q, 7.2, CHCO), 1.47 (3H, d, J 7.2, CH₃CHCO) and 1.43 (3H, d, J 6.6, CH₃CHO).

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(0.544 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate \((rac)-95\) (0.1 mg, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-(2-naphthyl)-ethyl-2-phenylpropionate \((rac)-anti\) and \((rac)-syn-262\) (65 mg, 68%, ratio anti : syn 93 : 7).

**Cross over reaction of 1-(2-naphthyl)-ethanol \((S)-261\) and 1-phenylethanol \((R)-11\) using active ester \((S)-123\) and \((R)-95\) [S5.10].**

In the same way as S5.2, tert-BuLi (0.33 ml, 1.7M in pentane, 0.57 mmol), ZnCl₂ (0.57 ml, 1M in diethylether, 0.57 mmol), 1-(2-naphthyl)-ethanol \((S)-261\) (0.163 g, 0.95 mmol), 1-phenylethanol \((R)-11\) (0.116 g, 0.95 mmol), pentafluorophenyl-2-phenylpropionate \((R)-95\) (30 mg, 0.095 mmol) and pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propionate \((S)-123\) (38 mg, 0.095 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate \((R,R)-anti-245\) (12 mg, 50%) and 1-(2-naphthyl)-ethyl-2-phenylpropionate \((R,S)-syn-262\) (2 mg, 8%) (ratio anti : syn 87 : 13), which were spectroscopically identical to that obtained elsewhere. Also gave an inseparable mixture of 1-(2-naphthyl)-ethyl-2-(6-methoxy-2-naphthyl)-propionate \((S,S)-anti-263\) (13 mg, 34%) as a white solid mp 114-118 °C; \(R_F\) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.62; \([\alpha]_D^{20} = +53.3\) (c 1.2, CHCl₃, note: of mixture of \((S,S)-anti-263\) and \((S,R)-syn-249\)); \(v_{max}\) (CHCl₃) cm⁻¹ 1728 (C=O); \(\delta_H\) (400 MHz; CDCl₃) 7.66 (1H, br d, J 8.3, CH; Arₐ or Arₐ), 7.61-7.47 (4H, m, 4 × CH; Arₐ and/or Arₐ), 7.35-7.23 (4H, m, 4 × CH; Arₐ and/or Arₐ), 7.14-7.00 (4H, m, 4 × CH; Arₐ and/or Arₐ), 5.95 (1H, q, 6.6, CHO), 3.86 (3H, s, CH₂O), 3.82 (1H, q, 7.2, CHCO), 1.50 (3H, d, J 7.2, CH₃CHO) and 1.49 (3H, d, J 6.6, CH₃CHO); \(\delta_C\) (100 MHz; CDCl₃) 173.7 (C=O), 157.6, 141.6, 139.1, 135.7, 133.7, 133.0 and 132.7 (7 × i-C; 2 × Ar), 129.3, 128.3, 127.5, 127.1, 126.4, 126.0, 125.9, 125.8, 125.7, 124.2, 123.8, 118.9 and 105.5 (13 × CH; 2 × Ar), 72.5 (CHO), 55.3 (CHCO), 45.6 (CH₃O), 22.3 and 18.4 (2 × CH₃), and 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propionate \((S,R)-syn-249\) (7 mg, 20%) (ratio anti : syn 63 : 37), which was spectroscopically identical to that obtained elsewhere.

**Synthesis of tert-BuONa 265 [S5.11; E1].**

Added Na (0.986 g, 0.043 mol) to tert-BuOH 264 (9.53 g, freshly distilled, 0.129 mol) under nitrogen and stirred the resulting solution at 50°C over night. The
resulting mixture was evaporated under reduced pressure to give \textit{tert}-BuONa 265 as a white solid.

**Synthesis of \textit{tert}-BuOLi 266 [S5.11; E2].**

Added Li (0.582 g, 0.084 mol) to \textit{tert}-BuOH 264 (18.647 g, freshly distilled, 0.25 mol) under nitrogen and stirred the resulting solution at 50°C over night. The resulting mixture was evaporated under reduced pressure to give \textit{tert}-BuOLi 266 (4.847 g, 72%) as a white solid.

**Synthesis of “wet” \textit{tert}-BuOLi 266 [S5.11; E3].**

Added Li (1.250 g, 0.18 mol) to \textit{tert}-BuOH 264 (40.05 g, 0.54 mol) and stirred the resulting solution at 50°C over night. The resulting mixture was evaporated under reduced pressure to give wet \textit{tert}-BuOLi 266 as a white solid, which also contained LiOH.

**MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.15; E1].**

Added \textit{tert}-BuOLi 266 (76 mg, 0.95 mmol) to 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) in THF (5 ml) after 1 hour added pentafluorophenyl-2-phenylpropinate (rac)-95 (0.1 g, 0.32 mmol) in THF (5 ml). The resulting mixture was stirred over night. The reaction was quenched with NH\textsubscript{4}Cl\textsubscript{aq} (10 ml). The organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO\textsubscript{4} and evaporated under reduced pressure. Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (42 mg, 52%, \textit{anti} : syn 61 : 39), which were spectroscopically identical to that obtained elsewhere.

**MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.15; E2].**

In the same way as T5.15; E1, \textit{tert}-BuOLi 266 (76 mg, 0.95 mmol), ZnCl\textsubscript{2} (65 mg, 0.47 mmol), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (49 mg, 61%, \textit{anti} : syn 72 : 28), which were spectroscopically identical to that obtained elsewhere.
MKR of 1-phenylethanol \((\text{rac})-11\) using active ester \((\text{rac})-95\) [T5.15; E3].

In the same way as T5.15; E1, \textit{tert}-BuOLi 266 (76 mg, 0.95 mmol), ZnCl\textsubscript{2} (0.129 g, 0.95 mmol), 1-phenylethanol \((\text{rac})-11\) (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropinate \((\text{rac})-95\) (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropinate \((\text{rac})-\text{anti}\) and \((\text{rac})-\text{syn}\)-245 (22 mg, 27%, \textit{anti} : \textit{syn} 92 : 8), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol \((\text{rac})-11\) using active ester \((\text{rac})-95\) [T5.15; E4].

In the same way as T5.15; E1, \textit{tert}-BuOLi 266 (76 mg, 0.95 mmol), ZnCl\textsubscript{2} (0.259 g, 1.90 mmol), 1-phenylethanol \((\text{rac})-11\) (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropinate \((\text{rac})-95\) (0.1 g, 0.32 mmol) in THF (10 ml). Gave by crude \textsuperscript{1}H NMR 1-phenylethyl-2-phenylpropinate \((\text{rac})-\text{anti}\) and \((\text{rac})-\text{syn}\)-245 (<5 mg, <5%, \textit{anti} : \textit{syn} >93 : <7), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol \((\text{rac})-11\) using active ester \((\text{rac})-95\) [T5.15; E5].

Added \textit{tert}-BuOLi 266 (76 mg, 0.95 mmol) to 1-phenylethanol \((\text{rac})-11\) (0.386 g, 3.16 mmol) in THF (5 ml) after 1 hour added pentafluorophenyl-2-phenylpropinate \((\text{rac})-95\) (0.1 g, 0.32 mmol) in THF (5 ml). The resulting mixture was stirred for 36 hours. The reaction was quenched with \(\text{NH}_{4}\text{Cl(aq)}\) (10 ml). The organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO\textsubscript{4} and evaporated under reduced pressure. Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropinate \((\text{rac})-\text{anti}\) and \((\text{rac})-\text{syn}\)-245 (76 mg, 94%, \textit{anti} : \textit{syn} 60 : 40), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol \((\text{rac})-11\) using active ester \((\text{rac})-95\) [T5.15; E6].

In the same way as T5.15; E5, \textit{tert}-BuOLi 266 (76 mg, 0.95 mmol), ZnCl\textsubscript{2} (65 mg, 0.47 mmol), 1-phenylethanol \((\text{rac})-11\) (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropinate \((\text{rac})-95\) (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-
60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (40 mg, 50%, anti : syn 74 : 26), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.15; E7].

In the same way as T5.15; E5, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 g, 0.95 mmol), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropinate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti (rac)-syn-245 (27 mg, 34%, anti : syn 92 : 8), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.15; E8].

In the same way as T5.15; E5, tert-BuOLi (76 mg, 0.95 mmol), ZnCl₂ (0.259 g, 1.90 mmol), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropinate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave back starting materials.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.15; E9].

Added tert-BuOLi 266 (76 mg, 0.95 mmol) to 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) in THF (5 ml) after 1 hour added pentafluorophenyl-2-phenylpropinate (rac)-95 (0.1 g, 0.32 mmol) in THF (5 ml). The resulting mixture was stirred for 60 hours. The reaction was quenched with NH₄Cl(aq) (10 ml). The organic layer was extracted with dichloromethane (3 x 25 ml), washed with water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (59 mg, 73%, anti : syn 52 : 48), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.15; E10].

In the same way as T5.15; E9, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (65 mg, 0.47 mmol), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropinate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification
by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (52 mg, 65%, anti : syn 77 : 23), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.15; E11].

In the same way as T5.15; E9, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 g, 0.95 mmol), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (22 mg, 27%, anti : syn 93 : 7), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.15; E12].

In the same way as T5.15; E9, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.259 g, 1.90 mmol), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave by crude ¹H NMR 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (<5 mg, <5%, anti : syn >93 : <7), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester ( rac)-95 [T5.16; E1].

Added tert-BuOLi 266 (76 mg, 0.95 mmol) to 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) in THF (5 ml) followed by pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (5 ml). The resulting mixture was refluxed over night. The reaction was quenched with NH₄Clₐq (10 ml). The organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (47 mg, 58%, anti : syn 52 : 48), which were spectroscopically identical to that obtained elsewhere.
MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.16; E2].

In the same way as T5.16; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (65 mg, 0.47 mmol), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (50 mg, 62%, anti : syn 62 : 38), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.16; E3].

In the same way as T5.16; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 g, 0.95 mmol), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (55 mg, 68%, anti : syn 84 : 16), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.16; E4].

In the same way as T5.16; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.295 g, 1.90 mmol), 1-phenylethanol (rac)-95 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (43 mg, 53%, anti : syn 85 : 15), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.16; E5].

In the same way as T5.16; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.345 g, 2.53 mmol), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (41 mg, 51%, anti : syn 82 : 18), which were spectroscopically identical to that obtained elsewhere.
MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.16; E6].

In the same way as T5.16; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.431 g, 3.16 mmol), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (28 mg, 35%, anti : syn 82 : 18), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.16; E7].

In the same way as T5.16; E1, tert-BuOLi (76 mg, 0.95 mmol), ZnCl₂ (0.517 g, 3.79 mmol), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (23 mg, 29%, anti : syn 79 : 21), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.17; E1].

Added tert-BuOLi 266 (76 mg, 0.95 mmol) and ZnCl₂ (0.129 mg, 0.95 mmol) to 1-phenylethanol (rac)-11 (39 mg, 0.32 mmol) and tert-BuOH 264 (0.211 g, 2.85 mmol) in THF (5 ml), after ~5 mins added pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (5 ml). The resulting mixture was stirred over night. The reaction was quenched with NH₄Cl aq (10 ml). The organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (13 mg, 16%, anti : syn 92 : 8), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.17; E2].

In the same way as T5.17; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 mg, 0.95 mmol), 1-phenylethanol (rac)-11 (39 mg, 0.32 mmol), tert-BuOH 264
(2.32 g, 31.31 mmol) and pentafluorophenyl-2-phenylpropinate \((rac)-95\) (0.1 g, 0.32 mmol) in THF (10 ml). Gave back starting materials.

**MKR of 1-phenylethanol \((rac)-11\) using active ester \((rac)-95\) [T5.17; E3].**

In the same way as T5.17; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 mg, 0.95 mmol), 1-phenylethanol \((rac)-11\) (39 mg, 0.32 mmol) and pentafluorophenyl-2-phenylpropinate \((rac)-95\) (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate \((rac)-anti\) and \((rac)-syn-245\) (15 mg, 19%, \(anti: syn\ 94:6\), which were spectroscopically identical to that obtained elsewhere.

**MKR of 1-phenylethanol \((rac)-11\) using active ester \((rac)-95\) [T5.17; E4].**

In the same way as T5.17; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 mg, 0.95 mmol), 1-phenylethanol \((rac)-11\) (3.86 g, 31.62 mmol) and pentafluorophenyl-2-phenylpropinate \((rac)-95\) (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate \((rac)-anti\) and \((rac)-syn-245\) (50 mg, 62%, \(anti: syn\ 92:8\), which were spectroscopically identical to that obtained elsewhere.

**MKR of 1-phenylethanol \((rac)-11\) using active ester \((rac)-95\) [T5.18; E1].**

Added tert-BuOLi 266 (76 mg, 0.95 mmol) and ZnCl₂ (0.129 mg, 0.95 mmol) to 1-phenylethanol \((rac)-11\) (39 mg, 0.32 mmol) followed by THF (5 ml). The resulting mixture was refluxed for 2 hours, then cooled to R.T. over 1 hour and pentafluorophenyl-2-phenylpropinate \((rac)-95\) (0.1 g, 0.32 mmol) in THF (5 ml) was added. The resulting mixture was stirred over night. The reaction was quenched with \(\text{NH}_4\text{Cl} (aq)\) (10 ml). The organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. To give back starting materials.

**MKR of 1-phenylethanol \((rac)-11\) using active ester \((rac)-95\) [T5.18; E2].**

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 g, 0.95 mmol), 1-phenylethanol \((rac)-11\) (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropinate \((rac)-95\) (0.1 g, 0.32 mmol) in THF (10 ml).
Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (55 mg, 68%, anti : syn 93 : 7), which were spectroscopically identical to that obtained elsewhere.

**MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.18; E2*].**

In the same way as T5.18; E1, however refluxed over night rather than 2 hours, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl$_2$ (0.129 g, 0.95 mmol), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (59 mg, 73%, anti : syn 92 : 8), which were spectroscopically identical to that obtained elsewhere.

**MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.18; E3].**

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl$_2$ (0.129 g, 0.95 mmol), 1-phenylethanol (rac)-11 (39 mg, 0.32 mmol), tert-BuOH 264 (0.211 g, 2.85 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (19 mg, 24%, anti : syn 88 : 12), which were spectroscopically identical to that obtained elsewhere.

**MKR of 1-phenylethanol (rac)-11 using tert-BuOLi [T5.19; E1].**

See T5.18; E2.

**MKR of 1-phenylethanol (rac)-11 using tert-BuONa [T5.19; E2].**

In the same way as T5.18; E1, tert-BuONa (91 mg, 0.95 mmol), ZnCl$_2$ (0.129 g, 0.95 mmol), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave back starting materials.
MKR of 1-phenylethanol \((\text{rac})-11\) using \(\text{tert-BuOK}\) [T5.19; E3].

In the same way as T5.18; E1, \(\text{tert-BuOK}\) (0.182 g, 0.95 mmol), ZnCl\(_2\) (0.129 g, 0.95 mmol), 1-phenylethanol \((\text{rac})-11\) (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate \((\text{rac})-95\) (0.1 g, 0.32 mmol) in THF (10 ml). Gave back starting materials.

MKR of 1-phenylethanol \((\text{rac})-11\) using ZnF\(_2\) [T5.20; E1].

In the same way as T5.20; E1, \(\text{tert-BuOLi}\) (76 mg, 0.95 mmol), ZnF\(_2\) (98 mg, 0.95 mmol), 1-phenylethanol \((\text{rac})-11\) (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate \((\text{rac})-95\) (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate \((\text{rac})\)-anti and \((\text{rac})\)-syn-245 (58 mg, 72%, \(\text{anti} : \text{syn} 51 : 49\)), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol \((\text{rac})-11\) using ZnCl\(_2\) [T5.20; E2].

See T5.18, E2.

MKR of 1-phenylethanol \((\text{rac})-11\) using ZnBr\(_2\) [T5.20; E3].

In the same way as T5.18; E1, \(\text{tert-BuOLi}\) (266 mg, 0.95 mmol), ZnBr\(_2\) (0.213 g, 0.95 mmol), 1-phenylethanol \((\text{rac})-11\) (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate \((\text{rac})-95\) (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate \((\text{rac})\)-anti and \((\text{rac})\)-syn-245 (42 mg, 52%, \(\text{anti} : \text{syn} 88 : 12\)), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol \((\text{rac})-11\) using ZnI\(_2\) [T5.20; E4].

In the same way as T5.18; E1, \(\text{tert-BuOLi}\) (266 mg, 0.95 mmol), ZnI\(_2\) (0.303 g, 0.95 mmol), 1-phenylethanol \((\text{rac})-11\) (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate \((\text{rac})-95\) (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate \((\text{rac})\)-anti and \((\text{rac})\)-syn-245 (42 mg, 52%, \(\text{anti} : \text{syn} 90 : 10\)), which were spectroscopically identical to that obtained elsewhere.
MKR of 1-phenylethanol (rac)-11 using ZnO [T5.20; E5].

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnO (78 mg, 0.95 mmol), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropinate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (16 mg, 20%, anti : syn 65 : 35), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using ZnEt₂ [S5.12].

Added ZnEt₂ (0.86 ml, 1.1M in toluene, 0.95 mmol) to 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) in THF (5 ml) and stirred for 3 hours, added pentafluorophenyl-2-phenylpropinate (rac)-95 (0.1 g, 0.32 mmol) in THF (5 ml). The resulting mixture was stirred over night. The reaction was quenched with NH₄Cl (aq) (10 ml). The organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. The crude mixture was purified by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) to give an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (6 mg, 7%, anti : syn 75 : 25), which were spectroscopically identical to that obtained elsewhere.

Stereospecific synthesis of 1-phenylethyl-2-phenylpropinate (S,S)-anti-245 using ZnF₂ [S5.13].

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnF₂ (98 mg, 0.95 mmol), 1-phenylethanol (S)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropinate (S)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropinate (S,S)-anti and (R,S)-syn-245 (59 mg, 73%, anti : syn 54 : 46), which were spectroscopically identical to that obtained previously.
Stereospecific synthesis of 1-phenylethyl-2-phenylpropinate \((S,S)\)-anti-245 using ZnO [S5.14].

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnO (78 mg, 0.95 mmol), 1-phenylethanol \((S)\)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate \((S)\)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropinate \((S,S)\)-anti and \((R,S)\)-syn-245 (15 mg, 19%, anti : syn 96 : 4). The aqueous layer was acidified HCl (20 ml, 3M), the organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO\(_4\) and evaporated under reduced pressure to give 2-phenylpropanoic acid \((S)\)-111 (28 mg, 59%, 84% e.e.) which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol \((rac)\)-11 using “wet” tert-BuOLi [S5.15].

In the same way as T5.18; E1, “wet” tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl\(_2\) (0.129 g, 0.95 mmol), 1-phenylethanol \((rac)\)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate \((rac)\)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate \((rac)\)-anti and \((rac)\)-syn-245 (36 mg, 45%, anti : syn 88 : 12), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol \((rac)\)-11 using ZnCl\(_2\) and LiOH [S5.16].

In the same way as T5.18; E1, tert-BuOLi 266 (38 mg, 0.47 mmol), LiOH.H\(_2\)O (20 mg, 0.47 mmol), ZnCl\(_2\) (0.129 g, 0.95 mmol), 1-phenylethanol \((rac)\)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate \((rac)\)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave back alcohol and ~ 50% active ester \((rac)\)-95, no product.

Synthesis of ZnO [S5.17].

Added NaOH (3M) drop wise to a solution of ZnCl\(_2\) in water, a white precipitate was formed, ZnO which was subsequently filtered off and dried by heating under vacuum.

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MKR of 1-phenylethanol (rac)-11 using dry ZnCl₂ [S5.18].

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 g, 0.95 mmol, 99.999% pure; H₂O < 100 ppm), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentfluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (44 mg, 55%, anti : syn 92 : 8), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-128 [T5.21; E1].

In the same way as T18; E1, tert-BuOLi 266 (0.106 g, 1.33 mmol), ZnCl₂ (0.180 g, 1.33 mmol), 1-phenylethanol (rac)-11 (0.540 g, 4.42 mmol) and phenyl-2-phenylpropionate (rac)-128 (0.100 g, 0.44 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (31 mg, 28%, anti : syn 67 : 33), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.21; E2].

See T5.18; E2.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-127 [T5.21; E3].

In the same way as T5.18; E1, tert-BuOLi 266 (89 mg, 1.11 mmol), ZnCl₂ (0.151 g, 1.11 mmol), 1-phenylethanol (rac)-11 (0.450 g, 3.69 mmol) and 4-nitrophenyl-2-phenylpropionate (rac)-127 (0.100 g, 0.37 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (65 mg, 69%, anti : syn 72 : 28), which were spectroscopically identical to that obtained elsewhere.

Stereospecific synthesis of 1-phenylethyl-2-phenylpropionate (S,S)-anti-245 using active ester (S)-128 [T5.22; E1].

In the same way as T5.18; E1, tert-BuOLi 266 (61 mg, 0.76 mmol), ZnCl₂ (103 mg, 0.76 mmol), 1-phenylethanol (S)-11 (0.308 g, 2.51 mmol) and phenyl-2-phenylpropionate (S)-128 (57 mg, 0.25 mmol) in THF (10 ml). Gave after purification
by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-phenylethyl-2-phenylpropionate (S,S)-anti-245 (10 mg, 16%, 98.2% d.e.), which was spectroscopically identical to that obtained elsewhere.

**Stereospecific synthesis of 1-phenylethyl-2-phenylpropionate (S,S)-anti-245 using active ester (S)-95 [T5.22; E2].**

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 g, 0.95 mmol), 1-phenylethanol (S)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate (S)-95 (0.100 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-phenylethyl-2-phenylpropionate (S,S)-anti-245 (66 mg, 82%, 99.4% d.e.), which was spectroscopically identical to that obtained elsewhere.

**Stereospecific synthesis of 1-phenylethyl-2-phenylpropionate (S,S)-anti-245 using active ester (S)-127 [T5.22; E3].**

In the same way as T5.18; E1, tert-BuOLi 266 (75 mg, 0.94 mmol), ZnCl₂ (0.128 g, 0.94 mmol), 1-phenylethanol (S)-11 (0.383 g, 3.14 mmol), 4-nitrophenyl-2-phenylpropionate (S)-127 (85 mg, 0.31 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-phenylethyl-2-phenylpropionate (S,S)-anti-245 (73 mg, 92%, 96.8% d.e.), which was spectroscopically identical to that obtained elsewhere.

**MKR of 1-phenylethanol (rac)-11 in dichloromethane [T5.23; E1].**

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 g, 0.95 mmol), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in dichloromethane (10 ml). Gave by crude ¹H NMR 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (<5 mg, ~1%, anti : syn ~ 90 : 10), which where spectroscopically identical to that obtained elsewhere.

**MKR of 1-phenylethanol (rac)-11 in diethylether [T5.23; E2].**

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 g, 0.95 mmol), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in diethylether (10
ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (34 mg, 42%, anti : syn 93 : 7), which where spectroscopically identical to that obtained elsewhere.

**MKR of 1-phenylethanol (rac)-11 in THF [T5.23; E3].**
See T5.18; E2.

**MKR of 1-phenylethanol (rac)-11 in 1,4-dioxane [T5.23; E4].**
In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 g, 0.95 mmol), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in 1,4-dioxane (10 ml). Gave back starting materials.

**MKR of 1-phenylethanol (rac)-11 in 1,2-dimethoxyethane [T5.23; E5].**
In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 g, 0.95 mmol), 1-phenylethanol (rac)-11 (0.386 g, 3.16 mmol) and pentafluorophenyl-2-phenylbutinate (rac)-119 (0.1 g, 0.30 mmol) in 1,2-dimethoxyethane (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylbutinate (rac)-anti and (rac)-syn-245 (11 mg, 14%, anti : syn 91 : 9), which where spectroscopically identical to that obtained elsewhere.

**MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.24; E1].**
See T5.18; E2.

**MKR of 1-phenylethanol (rac)-11 using active ester (rac)-119 [T5.24; E2].**
In the same way as T5.18; E1, tert-BuOLi 266 (73 mg, 0.91 mmol), ZnCl₂ (0.124 g, 0.91 mmol), 1-phenylethanol (rac)-11 (0.370 g, 3.03 mmol) and pentafluorophenyl-2-phenylbutinate (rac)-119 (0.1 g, 0.30 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylbutinate (rac)-anti and (rac)-syn-246 (49 mg, 60%, anti : syn 96 : 4), which where spectroscopically identical to that obtained elsewhere.
MKR of 1-phenylethanol (rac)-11 using active ester (rac)-126 [T5.24; E3].

In the same way as T5.18; E1, tert-BuOLi 266 (70 mg, 0.87 mmol), ZnCl₂ (0.119 g, 0.87 mmol), 1-phenylethanol (rac)-11 (0.355 g, 2.90 mmol) and pentafluorophenyl-2-phenyl-3-methylbutinate (rac)-126 (0.1 g, 0.29 mmol) in THF (10 ml). Gave by crude ¹H NMR 1-phenylethyl-2-phenyl-3-methylbutinate (rac)-anti and (rac)-syn-267 (<5 mg, ~ 1%, anti : syn ~ 90 : 10); characteristic feature of 1-phenylethyl-2-phenyl-3-methylbutinate (rac)-anti-267 δH (400 MHz; CDCl₃) 5.77 (1H, q, J 6.6, CHO).

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.25; E1].

See T5.18; E2.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-113 [T5.25; E2].

In the same way as T5.18; E1, tert-BuOLi 266 (72 mg, 0.91 mmol), ZnCl₂ (0.124 g, 0.91 mmol), 1-phenylethanol (rac)-11 (0.370 g, 3.03 mmol) and pentafluorophenyl-2-(4-methylphenyl)-propinate (rac)-113 (0.1 g, 0.30 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-(4-methylphenyl)-propinate (rac)-anti and (rac)-syn-247 (60 mg, 74%, anti : syn 93 : 7), which where spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-115 [T5.25; E3].

In the same way as T5.18; E1, tert-BuOLi 266 (65 mg, 0.81 mmol), ZnCl₂ (0.110 g, 0.81 mmol), 1-phenylethanol (rac)-11 (0.328 g, 2.69 mmol) and pentafluorophenyl-2-(4-isobutylphenyl)-propinate (rac)-115 (0.1 g, 0.27 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) and inseparable mixture of 1-phenylethyl-2-(4-isobutylphenyl)-propinate (rac)-anti and (rac)-syn-248 (46 mg, 55%, anti : syn 93 : 7), which where spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-117 [T5.25; E4].

In the same way as T5.18; E1, tert-BuOLi 266 (68 mg, 0.86 mmol), ZnCl₂ (0.117 g, 0.86 mmol), 1-phenylethanol (rac)-11 (0.348 g, 2.85 mmol) and
pentafluorophenyl-2-(4-chlorophenyl)-propionate (rac)-117 (0.1 g, 0.29 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-(4-chlorophenyl)-propionate (rac)-anti and (rac)-syn-256 (62 mg, 75%, anti : syn 89 : 11), which where spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-123 [T5.25; E5].

In the same way as T5.18; E1, tert-BuOLi 266 (61 mg, 0.76 mmol), ZnCl₂ (0.103 g, 0.76 mmol), 1-phenylethanol (rac)-11 (0.308 g, 2.52 mmol) and pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propionate (rac)-123 (0.1 g, 0.25 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) and extraction with DCM, washing with 2M NaOH (to remove pentafluorophenol) an inseparable mixture of 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propionate (rac)-anti and (rac)-syn-249 (56 mg, 66%, anti : syn 91 : 9), which where spectroscopically identical to that obtained elsewhere.

PKR of 1-phenylethanol (rac)-11 using active ester (S)-123 and (R)-119 [S5.19].

In the same way as T5.18; E1, tert-BuOLi 266 (68 mg, 0.85 mmol), ZnCl₂ (0.116 g, 0.85 mmol), 1-phenylethanol (rac)-11 (0.348 g, 2.85 mmol), pentafluorophenyl-2-phenylbutinate (R)-119 (47 mg, 0.14 mmol) and pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propionate (S)-123 (56 mg, 0.14 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 8:2) and inseparable mixture of 1-phenylethyl-2-phenylbutinate (R,R)-anti and (R,S)-syn-246 (19 mg, 50%, anti : syn 96 : 4) [α]₂⁰D = +7.5 (c 5.0, CHCl₃), and 1-phenylethyl-2-(6-methoxy-2-naphtyl)-propinate (S,S)-anti and (S,R)-syn-249 (30 mg, 63%, anti : syn 91 : 9) which where spectroscopically identical to that obtained elsewhere.

Synthesis of 1-(2-naphthyl)-ethanol (rac)-261 using MeMgBr [S5.20.]

Added MeMgBr (17.23 ml, 3M in diethylether, 0.052 mol) to naphthaldehyde 268 (6.762 g, 0.043 mol) at -78°C, the resulting mixture was stirred while warming to R.T. for 3 hours. The reaction was quenched with NH₄Cl(aq) (10 ml). The organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. To give an inseparable mixture of 1-(2-
naphthyl)-ethanol (rac)-261 (6.81 g, 92%) and 2-naphthylmethanol 269 (0.100 g, 1%) which was spectroscopically identical to that obtained elsewhere.

MKR of 1-(2-naphthyl)-ethanol (rac)-261 using active ester (rac)-266 [S5.21].

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 g, 0.95 mmol), 1-(2-naphthyl)-ethanol (rac)-261 (0.544 g, 3.16 mmol) with a trace of 2-naphthylmethanol 269 and pentafluorophenyl-2-phenylpropinate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-(2-naphthyl)-ethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (53 mg, 55%, anti : syn 89 : 11) and (2-naphthyl)-methyl-2-phenylbutinate (rac)-270 (10 mg, 10%), which were spectroscopically identical to that obtained elsewhere.

KR of 1-(2-naphthyl)-ethanol (rac)-261 using active ester (S)-119 [S5.22].

In the same way as T5.18; E1, tert-BuOLi 266 (73 mg, 0.91 mmol), ZnCl₂ (0.124 g, 0.91 mmol), 1-(2-naphthyl)-phenylethanol (rac)-261 (0.521 g, 3.03 mmol) with a trace of 2-naphthylmethanol 269 and pentafluorophenyl-2-phenylbutinate (S)-119 (0.1 g, 0.30 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-(2-naphthyl)-ethyl-2-phenylbutinate (S,S)-anti and (S,R)-syn-271 (37 mg, 38%, anti : syn 85 : 15) and (2-naphthyl)-methyl-2-phenylbutinate (S)-272 (6 mg, 7%) which were spectroscopically identical to that obtained elsewhere.

Synthesis of 2-naphthylmethanol 269 [S5.23].

NaBH₄ (0.320 g, 8.45 mmol) was added to a solution of 2-naphthaldehyde 268 (0.440 g, 2.82 mmol) in ethanol 50 ml and stirred over night. The mixture was quenched with NaOH (20 ml, 3 M) then acidified with HCl (20 ml, 3 M). The organic layer was extracted with dichloromethane (3 × 50 ml), washed with water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. The crude mixture was purified by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) to give 2-naphthylmethanol 269 (0.862 g, 85%) as a white solid mp 64-66 °C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.29; νmax (CHCl₃)/cm⁻¹ 3019 (C=O); δH (400 MHz; CDCl₃) 7.87-7.81 (4H, m, 4 × CH; Ar), 7.52-7.46 (3H, m, 3 × CH; Ar), 4.88 (2H, d, J 5.9, CH₂Ar) and 1.74 (1H, t, J 5.9, OH);
δC (100 MHz; CDCl₃) 138.2, 133.3 and 132.9 (3 × i-C; Ar), 128.2, 127.8, 127.6, 126.1, 125.8, 125.3 and 125.1 (7 × CH; Ar) and 65.3 (CH₂Ar); (Found M⁺, 158.0729 C₁₁H₁₀O requires 158.0726).

Synthesis of (2-naphthyl)-methyl-2-phenylpropionate (rac)-270 [S5.24].

In the same way as T5.11; E1 DCC (0.141 mg, 0.68 mmol), 2-phenylproponic acid (rac)-111 (93 mg, 0.62 mmol), DMAP (15 mg, 0.12 mmol) and (2-naphthyl)-methanol 269 (97 mg, 0.62 mmol) in dichloromethane (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1): (2-naphthyl)-methyl-2-phenylpropionate (rac)-270 (0.123 g, 69%) as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.76; νmax (CHCl₃)/cm⁻¹ 1732 (C=O); δH (400 MHz; CDCl₃) 7.85-7.74 (3H, m, 3 × CH; Ar), 7.66 (1 H, brs, CH; Ar), 7.51-7.46 (2H, m, 2 × CH; Ar), 7.36-7.26 (5H, m, 5 × CH; ph), 5.29 (2H, s, CH₂Ar), 3.83 (1H, q, J 7.2, CHPH) and 1.56 (3H, d, J 7.2, CH₃CHPH); δC (100 MHz; CDCl₃) 174.3 (C=O), 140.4, 133.4, 133.1 and 133.0 (4 × i-C; Ar and Ph), 128.6, 128.2, 127.9, 127.6, 127.2, 126.8, 126.2, 126.1, and 125.5 (12 × CH; Ph and Ar), 66.4 (CH₂Ar), 45.6 (CHPH) and 18.4 (CH₃CHPH); (Found MNH⁺, 308.1649 C₂₀H₂₂O₂N requires 308.1645).

Synthesis of (2-naphthyl)-methyl-2-phenylbutinate (S)-272 [S5.25]

In the same way as T5.11; E1 DCC (80 mg, 0.39 mmol), 2-phenylbutric acid (S)-118 (58 mg, 0.35 mmol), DMAP (9 mg, 0.07 mmol) and (2-naphthyl)-methanol 269 (55 mg, 0.35 mmol) in dichloromethane (5 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1): (2-naphthyl)-methyl-2-phenylbutinate (S)-272 (66 mg, 62%) as a white solid mp 48-52 °C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.79; [α]Dᵐ = +7.0 (c 2.4, CHCl₃); νmax (CHCl₃)/cm⁻¹ 1732 (C=O); δH (400 MHz; CDCl₃) 7.84-7.74 (3H, m, 3 × CH; Ar), 7.66 (1 H, brs, CH; Ar), 7.51-7.46 (2H, m, 2 × CH; Ar), 7.36-7.26 (6H, m, 6 × CH; Ph and Ar), 5.31 (1H, d, ABq, J 12.7, CH₃H₈Ar), 5.26 (1H, d, ABq, J 12.7, CH₃H₈Ar), 3.56 (1H, t, J 7.7, CHPH), 2.22-2.10 (1H, m, CH₃CH₃H₈CHPH), 1.91-1.79 (1H, m, CH₃CH₃H₈CHPH) and 0.91 (3H, t, J 7.3, CH₃CH₂CHPH); δC (100 MHz; CDCl₃) 173.9 (C=O), 139.0, 133.5, 133.1 and 133.0 (4 × i-C; Ar and Ph), 128.6, 128.2, 128.1, 127.9, 127.6, 127.2, 126.8, 126.2, 126.1, and 125.5 (12 × CH; Ph and Ar), 66.3 (CH₂Ar), 53.5 (CHPH), 26.6 (CH₂CHPH) and 12.2 (CH₃CH₂CHPH); (Found MNH⁺, 322.1805 C₂₁H₂₄O₂N requires 322.1802).
Competitive reaction of primary and secondary alcohol [S5.26].

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 g, 0.95 mmol), 1-phenylethanol (rac)-11 (0.193 g, 1.58 mmol) and phenylmethanol 207 (0.171 g, 1.58 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / dichloromethane (1:1) phenylmethyl-2-phenylpropionate (rac)-208 (47 mg, 62%) as an oil; R_f [light petroleum spirit (bp 40-60°C) / dichloromethane (1:1)] 0.39; ν_max (CHCl₃)/cm⁻¹ 1731 (C=O); δ_H (400 MHz; CDCl₃) 7.35-7.21 (10H, m, 10 × CH; 2 × Ph), 5.11 (2H, ABq, appears as a q, J 12.8, CH₂Ph), 3.79 (1H, q, J 7.2, CHPh) and 1.53 (3H, d, J 7.2, CH₃); δ_C (100 MHz; CDCl₃) 174.3 (C=O), 140.4 and 136.0 (2 × i-C; Ph), 128.6,² 128.4,² 128.0,¹ 127.8,² 127.5² and 127.1² (10 × CH; 2 × Ph), 66.4 (CH₂), 45.5 (CHPh) and 18.4 (CH₃).

Synthesis of 1-phenyl-2-methyl-propan-1-one (rac)-274 using NaBH₄ [T5.26; E1].

In the same way as S5.23, NaBH₄ (0.75 g, 19.8 mmol) and 1-phenyl-2-methylpropan-1-one 273 (2.93 g, 19.8 mol) in ethanol (25 ml). Gave 1-phenyl-2-methylpropan-1-one (rac)-274 (2.81 g, 95%) as an oil; R_f [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.48; ν_max (CHCl₃)/cm⁻¹ 3019 (C=O); δ_H (400 MHz; CDCl₃) 7.30-7.18 (5H, m, 5 × CH; Ph), 4.28 (1H, dd, J 6.8 and 2.8, CHOH), 1.96 (1H, d, J 2.8, OH), 1.89 (1H, octet, J 6.8, CHCHOH), 0.94 (3H, d, J 6.8, CH₂CHCH₃) and 0.74 (3H, d, J 6.8, CH₃CHCH₃); δ_C (100 MHz; CDCl₃) 143.6 (i-C; Ph), 128.1,² 127.3¹ and 126.5² (5 × CH; Ph), 80.0 (CHOH), 35.2 (CHCHOH), 18.9 (CH₂CHCH₃) and 18.2 (CH₃CHCH₃); (Found M+, 150.1037; C₁₀H₁₄O requires 150.1039).

Synthesis of 1-(2-methylphenyl)-ethanol (rac)-276 using NaBH₄ [T5.26; E2].

In the same way as S5.23, NaBH₄ (4.166 g, 0.11 mol) and (2-methylphenyl)-ethanone 275 (4.919 g, 0.037 mol) in ethanol (25 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (3:7) 1-(2-methylphenyl)-ethanol (rac)-276 (4.309 g, 86%) as an oil; R_f [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.45; ν_max (CHCl₃)/cm⁻¹ 3019 (C=O); δ_H (400 MHz; CDCl₃) 7.51 (1H, brd, J 7.3, CH; Ar), 7.24 (1H, brt, J 7.7, CH; Ar), 7.18 (1H, td, J 7.3 and 1.3, CH; Ar), 7.14 (1H, brd, J 7.7, CH; Ar), 5.12 (1H, q, J 6.4, CHOH), 2.35 (3H, s, ArCH₃), 1.88 (1H, s, OH) and 1.47 (3H, d, J 6.4, CH₃CH); δ_C
(100 MHz; CDCl₃) 143.8 and 134.2 (2 × i-C; Ar), 130.3, 127.1, 126.3 and 124.4 (4 × CH; Ar), 66.8 (CHOH), 23.9 (ArCH₃) and 18.9 (CHCH₃); (Found M⁺, 136.0884 C₉H₁₂O requires 136.0883).

**Synthesis of 1-(2-bromophenyl)-ethanol (rac)-278 using NaBH₄ [T5.26; E3].**

In the same way as S5.23, NaBH₄ (5.70 g, 0.15 mol) and 1-(2-bromophenyl)-ethanone 277 (10 g, 0.05 mol) in ethanol (200 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3 → 3:7) 1-(2-bromophenyl)-ethanol (rac)-278 (9.02 g, 89%) as a yellow oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.52; νmax (CHCl₃)/cm⁻¹ 3020 (OH); δ_H (400 MHz; CDCl₃) 7.60 (1H, dd, J 7.8 and 1.7, CH; Ar), 7.52 (1H, dd, J 7.8 and 1.3, CH; Ar), 7.35 (1H, td, J 7.8 and 1.3, CH; Ar), 7.14 (1H, td, J 7.8 and 1.7, CH; Ar), 5.25 (1H, q, J 6.4, CHOH), 2.09 (1H, s, OH) and 1.49 (3H, d, J 6.4, CH₃); δ_C (100 MHz; CDCl₃) 144.6 and 121.7 (2 × C; Ph), 132.6, 128.7 127.8 and 126.6 (4 × CH; Ph), 69.2 (CHOH) and 23.5 (CH₃); (Found M⁺, 199.9832; C₈H₆OBr requires 199.9831).

**Synthesis of 1-(2-methoxyphenyl)-ethanol (rac)-280 using NaBH₄ [T5.26; E4].**

In the same way as S5.23, NaBH₄ (2.548 g, 0.067 mol) and 2-methoxyphenyl-ethanone 279 (3.372 g, 0.022 mol) in ethanol (20 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3 → 3:7) 1-(2-methoxyphenyl)-ethanol (rac)-280 (2.411 g, 71%), as a white solid mp 30-34 °C; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.38; νmax (CHCl₃)/cm⁻¹ 3019 (OH); δ_H (400 MHz; CDCl₃) 7.35 (1H, dd, J 7.5 and 1.7, CH; Ar), 7.26 (1H, dt, J 7.5 and 1.7, CH; Ar), 6.97 (1H, br t, J 7.5, CH; Ar), 6.89 (1H, br d, J 7.5, CH; Ar), 5.10 (1H, q, J 6.6, CHOH), 3.87 (3H, s, OCH₃), 2.59 (1H, s, OH) and 1.52 (3H, d, J 6.6, CH₃CH); δ_C (100 MHz; CDCl₃) 156.5 and 133.4 (2 × i-C; Ar), 128.3, 126.1, 120.8 and 110.4 (4 × CH; Ar), 66.5 (CHOH), 55.2 (OCH₃) and 22.8 (CHCH₃); (Found M⁺, 152.0830 C₉H₁₀O₂ requires 152.0832).

**Synthesis of 1-(4-methoxyphenyl)-ethanol (rac)-254 using NaBH₄ [T5.26; E5].**

In the same way as S5.23, NaBH₄ (3.281 g, 0.087 mol) and 4-methoxyphenyl-ethanone 281 (4.342 g, 0.029 mol) in ethanol (25 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (1:1 → 3:7) 1-(4-methoxyphenyl)-ethanol (rac)-254 (1.494 g, 34%), as an
oil; \( R_f \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.30; \( \nu_{\text{max}} \) (CHCl\(_3\))/cm\(^{-1}\) 3019 (OH); \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.29 (2H, dt, \( J \) 8.8 and 2.2, 2 × CH; Ar), 6.88 (2H, dt, \( J \) 8.8 and 2.2, 2 × CH; Ar), 4.84 (1H, br q, \( J \) 6.6, CHO\(_2\)), 3.80 (3H, s, OCH\(_3\)), 1.83 (1H, br s, OH) and 1.47 (3H, d, \( J \) 6.4, \( CH_3\)CH); \( \delta_C \) (100 MHz; CDCl\(_3\)) 159.0 and 138.0 (2 × i-C; Ar), 126.6\(^2\) and 113.8\(^2\) (4 × CH; Ar), 69.9 (CHO\(_2\)), 55.3 (OCH\(_3\)) and 25.0 (CH\(_3\)CH\(_3\)); (Found M\(^+\), 152.0834 C\(_5\)H\(_7\)O\(_2\) requires 152.0832).

**Synthesis of 1-(2-naphthyl)-ethanol (rac)-261 using NaBH\(_4\) [T5.26; E6].**

In the same way as S5.23; E1, NaBH\(_4\) (5.527 g, 0.146 mol) and 2-naphthyl-ethanone 268 (8.290 g, 0.049 mol) in ethanol (50 ml). Gave 1-(2-naphthyl)-ethanol (rac)-261 (8.31 g, 99%), as a white solid mp 65-66°C; \( R_f \) [light petroleum spirit (bp 40-60°C) / dichloromethane (1:1)] 0.11; \( \nu_{\text{max}} \) (CHCl\(_3\))/cm\(^{-1}\) 3019 (OH); \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.78-7.72 (4H, m, 4 × CH; Ar), 7.45-7.36 (3H, m, 3 × CH; Ar), 4.99 (1H, q, \( J \) 6.5, CHO\(_2\)), 1.78 (1H, s, OH) and 1.51 (3H, d, \( J \) 6.5, \( CH_3\)CH); \( \delta_C \) (100 MHz; CDCl\(_3\)) 143.2, 133.3 and 132.9 (3 × i-C; Ar), 128.3, 127.9, 127.7, 126.1, 125.8 and 123.8\(^2\) (7 × CH; Ar), 70.5 (CHO\(_2\)) and 25.1 (CH\(_3\)CH\(_3\)); (Found M\(^+\), 172.0884 C\(_{12}\)H\(_{12}\)O requires 172.0883).

**Synthesis of 1-phenyl-1-chyclohexyl-methanol (rac)-282 using NaBH\(_4\) [T5.26; E7].**

In the same way as S5.23; E1, NaBH\(_4\) (0.502 g, 13.27 mmol) and 1-phenyl-1-cyclohexyl-ketone 281 (0.833 g, 4.42 mmol) in ethanol (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (1:1) 1-phenyl-1-chyclohexyl-methanol (rac)-282 (0.631 g, 75%) as a oil; \( R_f \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.56; \( \nu_{\text{max}} \) (CHCl\(_3\))/cm\(^{-1}\) 3019 (C=O); \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.36-7.24 (5H, m, 5 × CH; Ph), 4.35 (1H, dd, \( J \) 7.2 and 2.0, CHO\(_2\)), 2.02-1.94 (1H, m, CHCHO\(_2\)), 1.85 (1H, d, \( J \) 2.0, OH), 1.80-1.73 (1H, m, CH: C\(_6\)H\(_{11}\)), 1.69-1.56 (3H, m, 3 × CH: C\(_6\)H\(_{11}\)), 1.40-1.33 (1H, m, CH: C\(_6\)H\(_{11}\)) and 1.29-0.85 (5H, m, 5 × CH: C\(_6\)H\(_{11}\)); \( \delta_C \) (100 MHz; CDCl\(_3\)) 143.6 (i-C; Ph), 128.2\(^2\) 127.4\(^1\) and 126.6\(^2\) (5 × CH; Ph), 79.4 (CHO\(_2\)), 44.9 (CHCHO\(_2\)), 29.3 (CH\(_2\); C\(_6\)H\(_{11}\)), 28.8 (CH\(_2\); C\(_6\)H\(_{11}\)), 26.4 (CH\(_2\); C\(_6\)H\(_{11}\)), 26.1 (CH\(_2\); C\(_6\)H\(_{11}\)) and 26.0 (CH\(_2\); C\(_6\)H\(_{11}\)); (Found M\(^+\), 190.1348 C\(_{13}\)H\(_{18}\)O requires 190.1352).

MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.27; E1].

See T5.18; E2.
MKR of 1-phenyl-propanol (rac)-283 using active ester (rac)-95 [T5.27; E2].

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 g, 0.95 mmol), 1-phenyl-propanol (rac)-283 (0.430 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylpropyl-2-phenylpropionate (rac)-anti and (rac)-syn-284 (42 mg, 49%, anti : syn 93 : 7) as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.83; ν_{max} (CHCl₃)/cm⁻¹ 1781 (C=O); δ_{H} (400 MHz; CDCl₃) 7.42-7.19 (8H, m, 8 × CH; Phₐ and Ph₈), 7.09-7.05 (2H, m, 2 × CH; Ph₋ₐ or Ph₋₈), 5.64 (1H, dd, J 7.3 and 6.3, CHO), 3.78 (1H, q, J 7.2, CHCH₃), 1.92-1.71 (2H, m, CH₂CH₃), 1.51 (3H, d, J 7.2, CHCH₃) and 0.85 (3H, t, J 7.5, CH₂CH₃); δ_{C} (100 MHz; CDCl₃) 173.6 (C=O), 140.5 and 140.4 (2 × i-C; 2 × Ph), 128.9, 95; 128.5, 7.9 and 14.2 (10 × CH; 2 × Ph), 77.5 (CHO), 45.7 (CHCO), 29.5 (CH₂), 18.3 (CH₃CH₂) and 9.8 (CH₂CH₃); (Found MNH₂, 286.1804; C₁₈H₂₄O₂N requires 286.1802). For minor diastereoisomer (rac)-syn-284: δ_{H} (400 MHz; CDCl₃) 7.42-7.19 (10H, m, 10 × CH; Ph₋ₐ and Ph₋₈), 5.64 (1H, dd, J 7.3 and 6.3, CHO), 3.75 (1H, q, J 7.2, CHCH₃), 1.92-1.71 (2H, m, CH₂CH₃) 1.49 (3H, d, J 7.2, CHCH₃) and 0.70 (3H, f, J 7.4, CH₂CH₃), and 1-phenyl-propan-1-one 289 (5 mg, 12%) as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.78; ν_{max} (CHCl₃)/cm⁻¹ 1729 (C=O); δ_{H} (400 MHz; CDCl₃) 7.90 (2H, dd, J 7.2 and 1.8, 2 × CH; Ph), 7.48 (1H, tt, J 7.2 and 1.8, CH; Ph), 7.39 (2H, t, J 7.2, 2 × CH; Ph), 2.94 (2H, q, J 7.3, CH₂CH₃) and 1.16 (3H, t, J 7.3, CH₂CH₃); δ_{C} (100 MHz; CDCl₃) 170.6 (C=O), 138.7 (i-C; Ph), 127.8, 127.5 and 127.4 (5 × CH; Ph), 45.0 (CH₂CO) and 18.5 (CH₃CH₂).

MKR of 1-phenyl-2-methylpropanol (rac)-274 using active ester (rac)-95 [T5.27; E3].

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 g, 0.95 mmol), 1-phenyl-2-methyl-propanol (rac)-274 (0.474 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave 2-methyl-1-phenyl-propan-1-one 273 (21 mg, 45%) as an oil; Rf [dichloromethane] 0.64; ν_{max} (CHCl₃)/cm⁻¹ 1682 (C=O); δ_{H} (400 MHz; CDCl₃) 7.80 (2H, dd, J 7.9 and 1.6, 2 × CH; Ph), 7.55 (1H, tt, J 7.2 and 1.6, CH; Ph), 7.46 (2H, dd, J 7.9 and 7.2, 2 × CH; Ph), 3.56 (1H, septet, J 6.8, CH₂CH₃CH₃) and 1.22 (6H, d, J 6.8, CH₃CHCH₃); δ_{C} (100 MHz; CDCl₃) 204.5 (CO), 136.2 (i-C; Ph), 132.8, 128.6 and
128.3^2 (5 × CH; Ph), 35.3 (CH) and 19.1 (2 × CH₃); (Found MH⁺, 149.0958 C₁₀H₁₃O requires 149.0961).

**MKR of 1-phenyl-2,2-dimethyl-propanol (rac)-286 using active ester (rac)-95 [T5.27; E4].**

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 g, 0.95 mmol), 1-phenyl-2,2-dimethylpropanol (rac)-286 (0.519 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropinate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave by crude ^1H NMR 1-phenyl-2,2-dimethylpropyl-2-phenylpropinate (rac)-anti and (rac)-syn-287 (<1 mg, ~1%, anti : syn ~ 80 : 20); characteristic feature of 1-phenyl-2,2-di-methylpropyl-2-phenylpropinate (rac)-anti-287 δ_H (400 MHz; CDCl₃) 5.32 (1H, S, CHO) and 3.72 (1H, q, J 7.3, CH₂CH₃); characteristic feature of 1-phenyl-2,2-dimethylpropyl-2-phenylpropinate (rac)-syn-287 δ_H (400 MHz; CDCl₃) 5.34 (1H, S, CHO).

**MKR of 1-phenyl-1-cyclohexyl-methanol (rac)-282 using active ester (rac)-95 [T5.27; E5].**

In the same way as T5.18; E1, tert-BuOLi 266 (34 mg, 0.43 mmol), ZnCl₂ (59 mg, 0.43 mmol), 1-phenyl-1-cyclohexyl-methanol (rac)-282 (0.272 g, 1.43 mmol), pentafluorophenyl-2-phenylpropinate (rac)-95 (45 mg, 0.14 mmol) in THF (10 ml). Gave back the starting materials.

**MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.28; E1].**

See T5.18; E2.

**MKR of 1-(2-methylphenyl)-ethanol (rac)-276 using active ester (rac)-95 [T5.28; E2].**

In the same way as T5.18; E1, tert-BuOLi 266 (73 mg, 0.91 mmol), ZnCl₂ (0.124 g, 0.91 mmol), 1-(2-methylphenyl)-ethanol (rac)-276 (0.412 g, 3.03 mmol) and pentafluorophenyl-2-phenylpropinate (rac)-95 (91 mg, 0.30 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-(2-methylphenyl)-ethyl-2-phenylpropionate (rac)-anti and (rac)-syn-289 (5 mg, 6%, anti : syn ~ 90 : 10) as an oil; R_f [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.79; ν_max (CHCl₃)/cm⁻¹ 1727 (C=O); δ_H (400 MHz; CDCl₃) 7.26-7.14 (5H, m, 5 × CH;
Ph), 7.06-6.90 (4 H, m, 4 × CH; Ar), 5.94 (1H, q, J 6.6, CHAr), 3.68 (1H, q, J 7.2, CHPh), 2.20 (3H, s, CH3Ph), 1.42 (3H, d, J 7.2, CH2CHPh) and 1.39 (3H, d, J 6.6, CH3CHAr); \( \delta_C \) (100 MHz; CDCl3) 173.5 (C=O), 140.3, 140.0 and 134.5 (3 × i-C; Ar and Ph), 130.1, 128.5, 127.6, 127.4, 127.0, and 124.9 (9 × CH; Ph and Ar), 69.6 (CHAr), 45.7 (CHPh), 21.3, 18.8 and 18.3 (3 × CH3); (Found MNH+3, 286.1805 C14H24O2N requires 286.1802). For minor diastereoisomer (S,R)-syn-289: \( \delta_H \) (400 MHz; CDCl3) 7.26-7.14 (5H, m, 5 × CH; Ph), 7.06-6.90 (4 H, m, 4 × CH; Ar), 5.97 (1H, q, J 6.6, CHAr), 3.63 (1H, q, J 7.2, CHPh), 2.27 (3H, s, CH3Ph), 1.41 (3H, d, J 7.2, CH2CHPh) and 1.32 (3H, d, J 6.6, CH3CHAr).

**MKR of 1-(2-bromophenyl)-ethanol (rac)-278 using active ester (rac)-95 [T5.28; E3].**

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl2 (0.129 g, 0.95 mmol), 1-(2-bromophenyl)-ethanol (rac)-278 (0.636 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropinate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-(2-bromophenyl)-ethyl-2-phenylpropionate (rac)-anti and (rac)-syn-290 (69 mg, 66%, anti : syn 91 : 9) as an oil; \( R_f \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.77; \( \nu_\text{max} \) (CHCl3)/cm\(^{-1}\) 1733 (C=O); \( \delta_H \) (400 MHz; CDCl3) 7.40-7.36 (1H, m, CH; Ar), 7.27-7.15 (5 H, m, 5 × CH; Ph), 7.00-6.94 (2H, m, 2 × CH; Ar), 6.80-6.76 (1H, m, CH; Ar), 6.03 (1H, q, J 6.5, CHAr), 3.71 (1H, q, J 7.2, CHPh), 1.43 (3H, d, J 7.2, CH2CHPh) and 1.38 (3H, d, J 6.5, CH3CHAr); \( \delta_C \) (100 MHz; CDCl3) 173.5 (C=O), 140.3, 140.0 and 134.5 (3 × i-C; Ar and Ph), 130.1, 128.5, 127.6, 127.4, 127.0, and 124.9 (9 × CH; Ph and Ar), 69.6 (CHAr), 45.7 (CHPh), 21.3 and 18.8 (CH3); (Found MNH+3, 350.0753; C17H21ONBr requires 350.0750). For minor diastereoisomer (S,R)-syn-290: \( \delta_H \) (400 MHz; CDCl3) 7.46-7.42 (1H, m, CH; Ar), 7.27-7.15 (5 H, m, 5 × CH; Ph), 7.09-7.00 (2H, m, 2 × CH; Ar), 6.80-6.76 (1H, m, CH; Ar), 6.06 (1H, q, J 6.5, CHAr), 3.70 (1H, q, J 7.2, CHPh), 1.44 (3H, d, J 7.2, CH2CHPh) and 1.33 (3H, d, J 6.5, CH3CHAr).

**MKR of 1-(2-methoxyphenyl)-ethanol (rac)-280 using active ester (rac)-95 [T5.28; E4].**

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl2 (0.129 g, 0.95 mmol), 1-(2-methoxyphenyl)-ethanol (rac)-280 (0.481 g, 3.16 mmol) and
pentafluorophenyl-2-phenylpropinate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / dichloromethane (1:1 → 0:1) an inseparable mixture of 1-(2-methoxyphenyl)-ethyl-2-phenylpropinate (rac)-anti and (rac)-syn-291 (22 mg, 24%, anti : syn 87 : 13) as an oil; \( R_F \) [light petroleum spirit (bp 40-60°C) / dichloromethane (1:1)] 0.44; \( \nu_{\text{max}} \) (CHCl\(_3\))/cm\(^{-1}\) 1729 (C=O); \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.27-7.15 (5H, m, 5 × CH; Ph), 7.10 (1 H, td, \( J \) 7.7 and 1.6, CH; Ar), 6.85 (1 H, dd, \( J \) 7.7 and 1.6, CH; Ar), 6.72 (1 H, dd, \( J \) 7.7 and 1.2, CH; Ar), 6.68 (1 H, td, \( J \) 7.7 and 1.2, CH; Ar), 6.12 (1H, q, \( J \) 6.5, CHAr), 3.69 (1H, q, \( J \) 7.2, CHCH\(_2\)), 3.67 (1H, s, CH\(_3\)O), 1.44 (3H, d, \( J \) 7.2, CH\(_3\)CHPh) and 1.37 (3H, d, \( J \) 6.5, CH\(_3\)CHAr); \( \delta_C \) (100 MHz; CDCl\(_3\)) \( \delta \)C (100 MHz; CDCl\(_3\)) 173.4 (C=O), 155.9, 140.6 and 130.3 (3 × i-C; Ar and Ph), 128.5, \(^{2}\) 128.3, \(^{1}\) 127.7, \(^{2}\) 127.0, \(^{1}\) 125.4, \(^{1}\) 120.3 and \(^{1}\) 110.2 (9 × CH; Ph and Ar), 67.5 (CHAr), 55.2 (CHPh), 45.7 (CH\(_3\)O), 21.0 (CH\(_3\)CHAr) and 18.3 (CH\(_3\)CHPh); (Found MNH\(_3\), 302.1753 C\(_{18}\)H\(_{21}\)O\(_3\)N requires 302.1751). For minor diastereoisomer (rac)-syn-291: \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.27-7.15 (5H, m, 5 × CH; Ph), 7.10 (1 H, td, \( J \) 7.7 and 1.6, CH; Ar), 6.78 (1 H, dd, \( J \) 7.7 and 1.6, CH; Ar), 6.72 (1 H, dd, \( J \) 7.7 and 1.2, CH; Ar), 6.68 (1 H, td, \( J \) 7.7 and 1.2, CH; Ar), 6.14 (1H, q, \( J \) 6.5, CHAr), 3.73 (1H, s, CH\(_3\)O), 3.70 (1H, q, \( J \) 7.2, CHCH\(_2\)), 1.43 (3H, d, \( J \) 7.2, CH\(_3\)CHPh) and 1.30 (3H, d, \( J \) 6.5, CH\(_3\)CHAr).

MKR of 1-(4-methoxyphenyl)-ethanol (rac)-254 using active ester (rac)-95 [T5.28; E5].

In the same way as T5.18; E1, tert-BuOLi 266 (73 mg, 0.91 mmol), ZnCl\(_2\) (0.124 g, 0.91 mmol), 1-(4-methoxyphenyl)-ethanol (rac)-254 (0.460 g, 3.03 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (91 mg, 0.30 mmol) in THF (10 ml). Gave by crude \(^1\)H NMR a mixture of 1-(4-methoxyphenyl)-ethyl-2-phenylpropionate (rac)-anti and (rac)-syn-292 (<1% yield by \(^1\)H NMR, anti : syn ~ 95 : 5) characteristic \(^1\)H NMR (400 MHz; CDCl\(_3\)) data for 1-(4-methoxyphenyl)-ethyl-2-phenylpropionate (rac)-anti-292: 5.81 (1H, q, \( J \) 6.4, CHO); characteristic \(^1\)H NMR (400 MHz; CDCl\(_3\)) data for 1-(4-methoxyphenyl)-ethyl-2-phenylpropionate (rac)-syn-292: 5.82 (1H, q, \( J \) 6.4, CHO).

MKR of 1-(2-naphthyl)-ethanol (rac)-261 using active ester (rac)-95 [T5.28; E6].

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl\(_2\) (0.129 g, 0.95 mmol), 1-(2-naphthyl)-ethanol (rac)-261 (0.544 g, 3.16 mmol) and
pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / dichloromethane (1:1) an inseparable mixture of 1-(2-naphthyl)-ethyl-2-phenylpropionate (rac)-anti and (rac)-syn-262 (52 mg, 54%, anti : syn 89 : 11) as an oil; \(R_F\) [light petroleum spirit (bp 40-60°C) / dichloromethane (1:1)] 0.40; \(\nu_{\text{max}}\) (CHCl\(_3\)/cm\(^{-1}\) 1728 (C=O); \(\delta_H\) (400 MHz; CDCl\(_3\)) 7.80-7.76 (1H, m, CH; Ar), 7.72 (1 H, d, J 8.4, CH; Ar), 7.66-7.63 (1 H, m, CH; Ar), 7.48-7.42 (3 H, m, 3 × CH; Ar), 7.33-7.24 (5H, m, 5 × CH; Ph), 7.23 (1H, dd, J 8.4 and 1.8, CH; Ar), 6.02 (1H, q, J 6.6, CHAr), 3.81 (1H, q, J 7.2, CHPh), 1.58 (3H, d, J 6.6, CH\(_2\)CHAr) and 1.52 (3H, d, J 7.2, CH\(_3\)CHPh); \(\delta_C\) (100 MHz; CDCl\(_3\)) 173.5 (C=O), 140.5, 139.1, 133.1 and 132.8 (4 × i-C; Ar and Ph), 128.6, 128.0, 127.6, 127.5, 127.1, 126.0, 125.8, 124.2, 123.8, 12 × CH; Ph and Ar), 72.4 (CHAr), 45.7 (CHPh), 22.4 (CHAr) and 18.2 (CHPh); (Found MNH\(_2\), 322.1806 C\(_{21}\)H\(_9\)O\(_2\)N requires 322.1802). For minor diastereoisomer (S,R)-syn-262: \(\delta_H\) (400 MHz; CDCl\(_3\)) 7.80-7.76 (1H, m, CH; Ar), 7.72 (1 H, d, J 8.4, CH; Ar), 7.66-7.63 (1 H, m, CH; Ar), 7.48-7.42 (3 H, m, 3 × CH; Ar), 7.33-7.22 (6H, m, CH; Ar and 5 × CH; Ph), . 6.03 (1H, q, J 6.6, CHAr), 3.79 (1H, q, J 7.2, CHPh), 1.56 (3H, d, J 6.6, CH\(_3\)CHAr) and 1.52 (3H, d, J 7.2, CH\(_3\)CHPh).

**MKR of 1-cyclohexylethanol (rac)-293 using active ester (rac)-95 [T5.28; E7].**

In the same way as T5.28; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl\(_2\) (0.129 g, 0.95 mmol), 1-cyclohexylethanol (rac)-293 (0.405 g, 3.16 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of returned pentafluorophenyl-2-phenylpropionate (rac)-95 (36 mg, 36%) which was spectroscopically identical to that obtained previously and 1-cyclohexylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-294 (14 mg, anti : syn 63 : 37, 17%) as an oil; \(R_F\) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.89; \(\nu_{\text{max}}\) (CHCl\(_3\)/cm\(^{-1}\) 1720 (C=O); \(\delta_H\) (400 MHz; CDCl\(_3\)) 7.33-7.28 (3H, m, 3 × CH; Ph), 7.26-7.20 (2 H, m, 2 × CH; Ph), 4.70 (1H, septet, J 6.4, CH\(_2\)CH\(_3\)), 3.68 (1H, q, J 7.3, CHPh), 1.74-1.28 (6H, m, 6 × CH; C\(_6\)H\(_5\)), 1.49 (3H, d, J 7.3, CH\(_3\)CHPh), 1.16-0.75 (5H, m, 5 × CH; C\(_6\)H\(_5\)) and 1.13 (3H, d, J 6.2, CH\(_2\)CH\(_2\)C\(_6\)H\(_5\)); \(\delta_C\) (100 MHz; CDCl\(_3\)) 174.1 (C=O), 140.9 (i-C; Ph), 128.4, 127.5 and 127.0 (5 × CH; Ph), 74.7 (CH\(_2\)C\(_6\)H\(_5\)), 53.9 (CHPh), 45.9, 28.4, 27.9, 26.3, 26.0 and 25.9 (6 × CH, C\(_6\)H\(_5\)), 18.2 (CH\(_3\)CH\(_2\)C\(_6\)H\(_5\)) and 17.0 (CH\(_3\)CHPh); (Found MNH\(_2\), 278.2120 C\(_{17}\)H\(_{28}\)O\(_2\)N; C\(_{21}\)H\(_9\)O\(_2\)N requires 278.2115). For minor
diastereoisomer \textit{(rac)-syn-294}: \(\delta_H\) (400 MHz; CDCl\textsubscript{3}) 7.33-7.28 (3H, m, 3 \times CH; Ph), 7.26-7.20 (2 H, m, 2 \times CH; Ph), 4.71 (1H, septet, \(J\) 6.4, CH\textsubscript{3}C\textsubscript{6}H\textsubscript{11}), 3.70 (1H, q, \(J\) 7.3, CHPh), 1.74-1.28 (6H, m, 6 \times CH; C\textsubscript{6}H\textsubscript{11}), 1.50 (3H, d, \(J\) 7.3, CH\textsubscript{3}CHPh), 1.16-0.75 (5H, m, 5 \times CH; C\textsubscript{6}H\textsubscript{11}) and 1.04 (3H, d, \(J\) 6.2, CH\textsubscript{3}CH\textsubscript{3}CH\textsubscript{3}H\textsubscript{11}) and 2-cyclohexylmethyl-2-phenylpropionate \textit{(rac)} (3 mg, 4%) (formed from 3% of 2-cyclohexylmethanol present in the 1-cyclohexylethanol) characteristic peaks \(\delta_H\) (400 MHz; CDCl\textsubscript{3}) 4.92 (2H, septet, \(J\) 6.1, CH\textsubscript{2}O) and 3.60 (1H, q, \(J\) 7.3, CHPh).

**PKR of pentafluorophenyl-2-phenylpropionate \textit{(rac)-95} using 1-phenylethanol \(R\)-11 and 1-(2-naphthyl)-ethanol \(S\)-261 [S5.27].**

In the same way as T5.18; E1, \textit{tert-BuOLi} 266 (76 mg, 0.95 mmol), ZnCl\textsubscript{2} (0.129 g, 0.95 mmol), 1-phenylethanol \((R)-11\) (0.193 g, 1.58 mmol), 1-(2-naphthyl)-ethanol \((S)-261\) (0.272 g, 1.58 mmol) and pentafluorophenyl-2-phenylpropionate \textit{(rac)-95} (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60\degree C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate \((R,R)\)-\textit{anti} and \((S,R)\)-\textit{syn-245} (18 mg, \textit{anti}: \(\delta\) 95 : 5, 45%) and of 1-(2-naphthyl)-ethyl-2-phenylpropionate \((S,S)\)-\textit{anti} and \((R,S)\)-\textit{syn-262} (23 mg, \textit{anti}: \(\delta\) 91 : 9, 48%) \([\alpha]_D^{20} = -3.4\) (c 4.2, CHCl\textsubscript{3}, note this is of entire mixture); which were spectroscopically identical to that obtained elsewhere.

**PKR of pentafluorophenyl-2-phenylpropionate \textit{(rac)-595} using 1-phenylethanol \(R\)-11 and 1-(2-bromophenyl)-ethanol \(S\)-278 [S5.28].**

In the same way as T5.18; E1, \textit{tert-BuOLi} 266 (76 mg, 0.95 mmol), ZnCl\textsubscript{2} (0.129 g, 0.95 mmol), 1-phenylethanol \((R)-11\) (0.193 g, 1.58 mmol), 1-(2-bromophenyl)-ethanol \((S)-278\) (0.318 g, 1.58 mmol) and pentafluorophenyl-2-phenylpropionate \textit{(rac)-95} (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60\degree C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate \((R,R)\)-\textit{anti} and \((S,R)\)-\textit{syn-245} (19 mg, \textit{anti}: \(\delta\) 95 : 5, 47%) and 1-(2-bromo)-phenylethyl-2-phenylpropionate \((S,S)\)-\textit{anti} and \((R,S)\)-\textit{syn-290} (38 mg, \textit{anti}: \(\delta\) 91 : 9, 72%) \([\alpha]_D^{20} = +34.1\) (c 3.8, CHCl\textsubscript{3}, note this is of entire mixture); which were spectroscopically identical to that obtained elsewhere.
Cross over reaction of 1-(2-naphthyl)-ethanol (S)-261 and 1-phenylethanol (R)-11 using active ester (S)-123 and (R)-119 [S5.29].

In the same way as T5.18; E1, tert-BuOLi 266 (73 mg, 0.91 mmol), ZnCl₂ (0.124 g, 0.91 mmol), 1-(2-naphthyl)-ethanol (S)-261 (0.260 g, 1.51 mmol), 1-phenylethanol (R)-11 (0.185 g, 1.51 mmol), pentafluorophenyl-2-phenylbutinate (R)-119 (50 mg, 0.15 mmol) and pentafluorophenyl-2-(6-methoxy-2-naphthyl)-propinate (S)-123 (60 mg, 0.15 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylbutinate (R,R)-anti-246 (25 mg, 61%) and 1-(2-naphthyl)-ethyl-2-phenylbutinate (R,S)-syn-271 (1 mg, 3%) (ratio anti : syn 95 : 5) which were spectroscopically identical to that obtained elsewhere. Also gave an inseparable mixture of 1-(2-naphthyl)-ethyl-2-(6-methoxy-2-naphthyl)-propinate (S,S)-anti-263 (32 mg, 55%) and 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propinate (S,R)-syn-249 (5 mg, 9%) (ratio anti : syn 88 : 12) which were spectroscopically identical to that obtained elsewhere.

KR of 1-phenylethanol (rac)-11 using active ester (S)-119 [T5.29; E1].

In the same way as T5.18; E1, tert-BuOLi 266 (73 mg, 0.91 mmol), ZnCl₂ (0.124 g, 0.91 mmol), 1-phenylethanol (rac)-11 (0.370 g, 3.03 mmol) and pentafluorophenyl-2-phenylbutinate (S)-119 (0.1 g, 0.30 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-phenylethyl-2-phenylbutinate (S,S)-anti and (S,R)-syn-246 (42 mg, 52%, anti : syn 95.5 : 4.5) which was spectroscopically identical to that obtained elsewhere.

KR of 1-phenylpropanol (rac)-283 using active ester (S)-119 [T5.29; E2].

In the same way as T5.18; E1, tert-BuOLi 266 (73 mg, 0.91 mmol), ZnCl₂ (0.124 g, 0.91 mmol), 1-phenylpropanol (rac)-283 (0.412 g, 3.03 mmol) and pentafluorophenyl-2-phenylbutinate (S)-119 (0.1 g, 0.30 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-phenylproply-2-phenylpropinate (S,S)-anti and (S,R)-syn-295 (45 mg, 57%, anti : syn 95 : 5) as an oil; Rₐ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.84; [α]₂₀° = -9.64 (c 4.4, CHCl₃); νₙₐₓ (CHCl₃)/cm⁻¹ 1728 (C=O); δₜ (400 MHz; CDCl₃) 7.33-7.18 (8H, m, 8 × CH; Phₐ and Phₜ), 7.11-7.06 (2 H, m, 2 × CH; Phₐ and/or Phₜ), 6.64 (1H, dd, J 7.1 and 6.3, 291
CHO), 3.51 (1H, t, J 7.7, CHCO), 2.17-2.05 (1H, m, CH$_3$CH$_2$H$_2$CHCO), 1.92-1.71 (3H, m, CH$_3$CH$_2$H$_2$CHCO and CH$_3$CH$_2$CHO), 0.89 (3H, t, J 7.3, CH$_3$) and 0.85 (3H, t, J 7.5, CH$_3$); $\delta$C (100 MHz; CDCl$_3$) 173.1 (C=O), 140.5 and 138.9 (2 × i-C; Ph$_A$ and Ph$_B$), 128.4, 128.1, 128.0, 127.5, 127.0 and 126.1 (10 × CH; Ph$_A$ and Ph$_B$), 77.4 (CHO), 53.7 (CHCO), 29.5 (CH$_2$), 26.3 (CH$_2$) 12.1 (CH$_3$) and 9.8 (CH$_3$); (Found MNH$_4^+$, 300.1960 C$_{10}$H$_2$O$_2$N requires 300.1958). For minor diastereoisomer (S,R)-syn-295: $\delta$H (400 MHz; CDCl$_3$) 7.33-7.18 (8H, m, 8 × CH; Ph$_A$ and Ph$_B$), 7.11-7.06 (2 H, m, 2 × CH; Ph$_A$ and/or Ph$_B$), 6.64 (1H, dd, J 7.1 and 6.3, CHO), 3.50 (1H, t, J 7.7, CHCO), 2.17-2.05 (1H, m, CH$_3$CH$_2$H$_2$CHCO), 1.92-1.71 (3H, m, CH$_3$CH$_2$H$_2$CHCO and CH$_3$CH$_2$CHO), 0.84 (3H, t, J 7.3, CH$_3$) and 0.71 (3H, t, J 7.5, CH$_3$) and 1-phenylpropan-1-one 289 (8 mg, 20%) which was spectroscopically identical to that obtained elsewhere.

KR of 1-phenyl-2-methylpropanol (rac)-274 using active ester (S)-119 [T5.29; E3].

In the same way as T5.18; E1, tert-BuOLi 266 (73 mg, 0.91 mmol), ZnCl$_2$ (0.124 g, 0.91 mmol), 1-phenyl-2-methylpropanol (rac)-274 (0.454 g, 3.03 mmol) and pentafluorophenyl-2-phenylbutinate (S)-119 (0.1 g, 0.30 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-phenyl-2-methylpropan-1-one 273 (18 mg, 40%) which was spectroscopically identical to that obtained elsewhere.

KR of 1-phenyl-1-cyclohexyl-methanol (rac)-282 using active ester (S)-119 [T5.29; E4].

In the same way as T5.18; E1, tert-BuOLi 266 (26 mg, 0.33 mmol), ZnCl$_2$ (45 mg, 0.33 mmol), 1-phenyl-1-cyclohexyl-methanol (rac)-282 (0.209 g, 1.10 mmol) and pentafluorophenyl-2-phenylbutinate (S)-119 (36 mg, 0.11 mmol) in THF (10 ml). Gave back the starting materials.

KR of 1-phenylethanol (rac)-11 using active ester (S)-119 [T5.30; E1].

See T5.29; E1.

KR of 1-(2-methylphenyl)-ethanol (rac)-276 using active ester (S)-119 [T5.30; E2].

In the same way as T5.18; E1, tert-BuOLi 266 (73 mg, 0.91 mmol), ZnCl$_2$ (0.124 g, 0.91 mmol), 1-(2-methylphenyl)-ethanol (rac)-276 (0.412 g, 3.03 mmol) and pentafluorophenyl-2-phenylbutinate (S)-119 (0.1 g, 0.30 mmol) in THF (10 ml). Gave
after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-(2-methyphenyl)-ethyl-2-phenylpropionate (rac)-anti and (rac)-syn-298 (9 mg, 11%, anti : syn 94 : 6) as an oil; \( R_f \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.81; [\( \alpha \)]\( _D^{20} \) = +12.0 (c 0.6, CHCl_3); \( \nu_{\text{max}} \) (CHCl_3)/cm\(^{-1}\) 1727 (C=O); \( \delta_H \) (400 MHz; CDCl_3) 7.32-7.21 (5H, m, 5 × CH; Ph), 7.13-7.0 (4 H, m, 4 × CH; Ar), 6.02 (1H, q, J 6.6, CHAr), 3.48 (1H, t, J 7.7, CHPh), 2.26 (3H, s, CH_3Ph), 2.15-2.04 (1H, m, CH_3CH_AH_B CH), 1.86-1.74 (1H, m, CH_3CH_AH_B CH), 1.46 (3H, d, J 6.6, CH_3CH_AH_B CH) and 0.89 (3H, t, J 7.3, CH_3CH_2CH_Ph); \( \delta_C \) (100 MHz; CDCl_3) 173.0 (C=O), 139.9, 138.9 and 134.6 (3 × i-C; Ar and Ph), 132.6, 128.8, 127.6, and 121.6 (3 × CH; Ar and Ph), 6.83-6.79 (1H, m, CH), 6.03 (1H, q, J 6.6, CHAr), 3.43 (1H, t, J 7.7, CHPH), 2.34 (3H, s, CH_3Ph), 2.15-2.04 (1H, m, CH_3CH_AH_B CH), 1.86-1.74 (1H, m, CH_3CH_AH_B CH), 1.39 (3H, d, J 6.6, CH_3CH_AH_B CH) and 0.85 (3H, t, J 7.3, CH_3CH_2CH_Ph).

**KR of 1-(2-bromophenyl)-ethanol (rac)-278 using active ester (S)-119 [T5.30; E3].**

In the same way as T5.18; E1, tert-BuOLi 266 (73 mg, 0.91 mmol), ZnCl_2 (0.124 g, 0.91 mmol), 1-(2-bromophenyl)-ethanol (rac)-278 (0.609 g, 3.03 mmol) and pentafluorophenyl-2-phenylbutinate (S)-119 (0.1 g, 0.30 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-(2-bromophenyl)-ethyl-2-phenylbutinate (S,S)-anti and (S,R)-syn-299 (42 mg, 40%, anti : syn 95.5 : 4.5) as an oil; \( R_f \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.77; [\( \alpha \)]\( _D^{20} \) = +50.0 (c 2.0, CHCl_3); \( \nu_{\text{max}} \) (CHCl_3)/cm\(^{-1}\) 1732 (C=O); \( \delta_H \) (400 MHz; CDCl_3) 7.40-7.36 (1H, m, CH; Ar), 7.26-7.15 (5H, m, 5 × CH; Ph), 6.99-6.94 (2H, m, 2 × CH; Ar), 6.83-6.79 (1H, m, CH; Ar), 6.03 (1H, q, J 6.6, CHAr), 3.44 (1H, t, J 7.7, CHPH), 2.10-1.98 (1H, m, CH_3CH_AH_B CHPH), 1.79-1.67 (1H, m, CH_3CH_AH_B CHPH), 1.39 (3H, d, J 6.6, CH_3CH_AH_B CH) and 0.83 (3H, t, J 7.3, CH_3CH_2CH); \( \delta_C \) (100 MHz; CDCl_3) 172.6 (C=O), 141.2, 138.8 and 121.6 (3 × i-C; Ar and Ph), 132.6, 128.8, 128.5, 128.1, 127.5, 127.1 and 126.2 (9 × CH; Ph and Ar), 71.6 (CHAr), 53.5 (CHPH), 26.3 (CH_3CHPH), 21.2 (CH_3CHAr) and 12.1 (CH_3CH_2CHPH); (Found MNH_4^+; 364.0913 C_{18}H_{23}O_2NBr requires 364.0907). For minor diastereoisomer (S,R)-syn-299: \( \delta_H \) (400 MHz; CDCl_3) 7.40-7.36 (1H, m, CH; Ar), 7.26-7.15 (5H, m, 5 × CH; Ph),
6.99-6.94 (2 H, m, 2 × CH; Ar), 6.83-6.79 (1 H, m, CH; Ar), 6.04 (1H, q, J 6.6, CHAr), 3.44 (1H, t, J 7.7, CHP), 2.10-1.98 (1 H, m, CH_3CH_2H_8CHPh), 1.79-1.67 (1 H, m, CH_3CH_AH_8CHPh), 1.33 (3H, d, J 6.6, CH_3CHAr) and 0.80 (3H, t, J 7.3, CH_3CH_2CH).

**KR of 1-(2-methoxyphenyl)-ethanol (rac)-280 using active ester (S)-119 [T5.30; E4].**

In the same way as T5.18; E1, tert-BuOLi 266 (73 mg, 0.91 mmol), ZnCl_2 (0.124 g, 0.91 mmol), 1-(2-methoxyphenyl)-ethanol (rac)-280 (0.481 g, 3.16 mmol) and pentafluorophenyl-2-phenylbutinate (S)-119 (0.1 g, 0.30 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / dichloromethane (1:1) an inseparable mixture of 1-(2-methoxyphenyl)-ethyl-2-phenylbutinate (S,S)-anti and (S,R)-syn-300 (9 mg, 10%, anti : syn 95 : 5) as an oil; Rf [light petroleum spirit (bp 40-60°C) / dichloromethane (1:1)] 0.64; [α]_D^20 = +17.2 (c 2.0, CHCl_3); νmax (CHCl_3)/cm⁻¹ 1728 (C=O); δ_H (400 MHz; CDCl_3) 7.24-7.17 (5H, m, 5 × CH; Ph), 7.10 (1 H, td, J 7.3 and 1.8, CH; Ar), 6.90 (1 H, dd, J 7.3 and 1.8, CH; Ar), 6.72 (1 H, dd, J 7.3 and 1.2, CH; Ar), 6.69 (1 H, td, J 7.3 and 1.2, CH; Ar), 6.13 (1H, q, J 6.6, CHAr), 3.65 (1H, s, CH_3O), 3.42 (1H, t, J 7.7, CH_2CH), 2.11-1.99 (1H, m, CH_3CH_AH_8CH), 1.79-1.67 (1H, m, CH_3CH_AH_8CH), 1.38 (3H, d, J 6.6, CH_3CHAr) and 0.83 (3H, t, J 7.3, CH_3CH_2CH); δ_C (100 MHz; CDCl_3) 172.9 (C=O), 155.9, 139.2 and 130.2 (3 × i-C; Ar and Ph), 128.4, 128.3, 128.9, 127.0, 125.4, 120.3 and 110.2 (9 × CH; Ph and Ar), 67.4 (CHAr), 55.3 (CHPh), 53.7 (CH_3O), 26.7 (CH_2), 21.0 and 12.2 (2 × CH_3); (Found MNH_4⁺, 316.1911 C_{19}H_{26}O_{10}N requires 316.1907). For minor diastereoisomer (S,R)-syn-300: δ_H (400 MHz; CDCl_3) 7.24-7.17 (5H, m, 5 × CH; Ph), 7.10 (1 H, td, J 7.3 and 1.8, CH; Ar), 6.90 (1 H, dd, J 7.3 and 1.8, CH; Ar), 6.72 (1 H, dd, J 7.3 and 1.2, CH; Ar), 6.69 (1 H, td, J 7.3 and 1.2, CH; Ar), 6.14 (1H, q, J 6.6, CHAr), 3.73 (1H, s, CH_3O), 3.42 (1H, t, J 7.7, CH_2CH), 2.11-1.99 (1H, m, CH_3CH_AH_8CH), 1.79-1.67 (1H, m, CH_3CH_AH_8CH), 1.34 (3H, d, J 6.6, CH_3CHAr) and 0.81 (3H, t, J 7.3, CH_3CH_2CH).

**KR of 1-(4-methoxyphenyl)-ethanol (rac)-254 using active ester (S)-119 [T5.30; E5].**

In the same way as T5.18; E1, tert-BuOLi 266 (73 mg, 0.91 mmol), ZnCl_2 (0.129 g, 0.91 mmol), 1-(4-methoxyphenyl)-ethanol (rac)-254 (0.460 g, 3.03 mmol) and pentafluorophenyl-2-phenylbutinate (S)-119 (0.1 g, 0.30 mmol) in THF (10 ml). Gave and inseparable mixture of 1-(4-methoxy)-phenylethyl-2-phenylpropinate (rac)-anti and
(rac)-syn-301 (<1% yield by 1H NMR, anti : syn ~ 95 : 5), characteristic data δH (400 MHz; CDCl3) 5.81 (1H, q, J 6.6, CHAr).

**KR of 1-(2-naphthyl)-ethanol (rac)-261 using active ester (S)-119 [T5.30; E6].**

In the same way as T5.18; E1, tert-BuO Li 266 (73 mg, 0.91 mmol), ZnCl2 (0.124 g, 0.91 mmol), 1-(2-naphthyl)-ethanol (rac)-261 (0.520 g, 3.03 mmol) and pentafluorophenyl-2-phenylbutinate (S)-119 (0.1 g, 0.30 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / dichloromethane (1:1) an inseparable mixture of 1-(2-naphthyl)-ethyl-2-phenylbutinate (S,S)-anti and (S,R)-syn-271 (40 mg, 42%, anti : syn 92 : 8), which were spectroscopically identical to that obtained elsewhere.

**KR of 1-cyclohexylethanol (rac)-293 using active ester (S)-119 [T5.30; E7].**

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl2 (0.129 g, 0.95 mmol), 1-cyclohexylethanol (rac)-293 (0.405 g, 3.16 mmol) and pentafluorophenyl-2-phenylbutinate (S)-119 (0.106 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of returned pentafluorophenyl-2-phenylbutinate (S)-302 (64 mg, 60%) which was spectroscopically identical to that obtained previously and 1-cyclohexylethyl-2-phenylbutinate (S,S)-anti and (S,R)-syn-302 (8 mg, anti: syn 71 : 29, 9%) as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.92; [α]D20 = -1.2 (c 1.0, CHCl3); νmax (CHCl3)/cm−1 1721 (C=O); δH (400 MHz; CDCl3) 7.32-7.28 (3H, m, 3 × CH; Ph), 7.26-7.20 (2 H, m, 2 × CH; Ph), 4.70 (1H, septet, J 6.2, CHAr), 3.41 (1H, t, J 7.7, CHPh), 2.17-2.04 (1H, m, CH3CH2H8CH), 1.86-1.74 (1H, m, CH3CH3H8CH), 1.74-1.28 (6H, m, 6 × CH; C6H11), 1.16-0.75 (5H, m, 5 × CH; C6H11), 1.13 (3H, d, J 6.2, CH3CHAr) and 0.90 (3H, t, J 7.3, CH3CHPh); δC (100 MHz; CDCl3) 173.6 (C=O), 139.5 (t-C; Ph), 128.4, 128.0 and 127.0 (5 × CH; Ph), 74.7 (CH3CH2H8CH), 53.9 (CH3CHPh), 42.5 (CH3CH2CH3CH2H11) 28.4, 28.0, 26.4, 26.3 26.0 and 25.9 (6 × CH; C6H11), 17.0 (CH3CH3CH2H11) and 12.2 (CH3CH2CHPh); (Found MNH+1, 292.2273 C18H30O2N requires 292.2271). For minor diastereoisomer (S,R)-syn-302: δH (400 MHz; CDCl3) 7.32-7.28 (3H, m, 3 × CH; Ph), 7.26-7.20 (2 H, m, 2 × CH; Ph), 4.72 (1H, septet, J 6.2, CHAr), 3.42 (1H, t, J 7.7, CHPh), 2.17-2.04 (1H, m, CH3CH2H8CH), 1.86-1.74 (1H, m, CH3CH3H8CH), 1.74-1.28 (6H, m, 6 × CH; C6H11), 1.16-0.75 (5H, m, 5 × CH; C6H11), 1.04 (3H, d, J 6.2, CH3CHAr) and 0.91 (3H, t, J 7.3, CH3CHPh) and 2-cyclohexylmethyl-2-phenylbutinate
(S) (1 mg, 1%) (formed from 3% of 2-cyclohexylmethanol present in the 1-cyclohexylethanol) characteristic peaks δ_H (400 MHz; CDCl\textsubscript{3}) 4.99 (2H, septet, J 6.2, CH\textsubscript{2}O) and 3.41 (1H, t, J 7.7, CHPh).

**Synthesis of 1-phenyl-1-deuterio-ethanol 304 [S5.30].**

LiAlD\textsubscript{4} (1.046 g, 0.025 mol) was added to a solution of 1-phenylethanone 303 (4.84 g, 0.040 mol) in THF 25 ml and stirred over 36 hours. The mixture was quenched with NaOH (20 ml, 3 M) then acidified with HCl (20 ml, 3 M). The organic layer was extracted with dichloromethane (3 × 50 ml), washed with water (25 ml), dried over MgSO\textsubscript{4} and evaporated under reduced pressure. The crude mixture was purified by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3 → 1:1) to give 1-phenyl-1-deuterio-ethanol 304 (2.64 g, 53%) as an oil; R\textsubscript{f} [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.35; \nu\textsubscript{max} (CHCl\textsubscript{3})/cm\textsuperscript{-1} 3019 (OH) and 2400 (CD); δ_H (400 MHz; CDCl\textsubscript{3}) 7.39-7.33 (4H, m, 4 × CH; Ph), 7.30-7.25 (1H, m, CH; Ph), 1.96 (1H, s, OH) and 1.49 (3H, t, J\textsubscript{H-D} 0.9, CH\textsubscript{3}); δ_C (100 MHz; CDCl\textsubscript{3}) 145.7 (i-C; Ph), 128.3,\textsuperscript{2} 127.3\textsuperscript{1} and 125.3\textsuperscript{2} (5 × CH; Ph) 69.8 (1C, t, \textsuperscript{1}J\textsubscript{CD} 21.4, CD) and 24.9 (CH\textsubscript{3}); (Found MNH\textsuperscript{1+}, 141.1132; C\textsubscript{8}H\textsubscript{13}DON requires 141.1133).

**MKR of 1-phenyl-1-deuterio-ethanol (rac)-304 using active ester (rac)-95 [S5.31; E1].**

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl\textsubscript{2} (0.129 g, 0.95 mmol), 1-phenyl-1-deuterio-ethanol (rac)-304 (0.389 g, 3.16 mmol), pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.30 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenyl-1-deuterio-ethyl-2-phenylpropionate (rac)-anti and (rac)-syn-305 (46 mg, 57%, anti : syn 93 : 7) as an oil; R\textsubscript{f} [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.81; \nu\textsubscript{max} (CHCl\textsubscript{3})/cm\textsuperscript{-1} 2400 (CD) and 1781 (C=O); δ_H (400 MHz; CDCl\textsubscript{3}) 7.34-7.20 (8H, m, 8 × CH; Ph\textsubscript{A} and Ph\textsubscript{B}), 7.13-7.09 (2H, m, 2 × CH; Ph\textsubscript{A} and/or Ph\textsubscript{B}), 3.76 (1H, q, J 7.2, CHPh), 1.50 (3H, d, J 7.2, CH\textsubscript{2}CHPh) and 1.49 (3H, s, CH\textsubscript{3}CD); δ_C (100 MHz; CDCl\textsubscript{3}) 173.5 (C=O), 141.6 and 140.4 (2 × i-C; Ph\textsubscript{A} and Ph\textsubscript{B}), 128.5,\textsuperscript{2} 128.3,\textsuperscript{2} 127.6,\textsuperscript{2} 127.5,\textsuperscript{1} 127.0\textsuperscript{1} and 125.6\textsuperscript{2} (10 × CH; Ph\textsubscript{A} and Ph\textsubscript{B}), 72.1 (1C, t, \textsuperscript{1}J\textsubscript{C,D} = 22.3 Hz, CD), 45.7 (CHPh), 22.1 and 18.3 (2 × CH\textsubscript{3}); (Found MNH\textsuperscript{1+}, 273.170 C\textsubscript{17}H\textsubscript{21}DO\textsubscript{2}N requires 273.1708). For minor diastereoisomer (rac)-syn-304: δ_H (400 MHz; CDCl\textsubscript{3}) 7.34-7.20
KR of 1-phenyl-1-deutero-ethanol (rac)-304 using active ester (S)-119 [S5.31; E2].

In the same way as T5.18; E1, tert-BuOLi 266 (73 mg, 0.91 mmol), ZnCl₂ (0.124 g, 0.91 mmol), 1-phenyl-1-deutero-ethanol (rac)-304 (0.372 g, 3.03 mmol) and pentafluorophenyl-2-phenylbutinate (S)-119 (0.1 g, 0.30 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-pentyl-1-deutero-ethyl-2-phenylbutinate (S,S)-anti- (S,R)-syn-306 (37 mg, 46%, anti : syn 95 : 5) as an oil; Rₚ [light petroleum spirit (bp 40-60°C) / diethyl ether (9:1)] 0.64; [α]°D = -7.3 (c 2.4, CHCl₃); νmax (CHCl₃)/cm⁻¹ 2401 (CD) and 1728 (C=O); δH (400 MHz; CDCls) 7.33-7.21 (8H, m, 8 × CH; Phₐ and Ph₈), 7.15-7.11 (2H, m, 2 × CH; Phₐ and/or Ph₈), 3.49 (1H, t, J 7.7, CHCH), 2.18-2.06 (1H, m, CH₃CH₂H₈CH), 1.86-1.74 (1H, m, CH₃CH₂H₈CH), 1.50 (3H, s, CH₃CD) and 0.90 (3H, t, J 7.3, CH₃CH₂CH); δC (100 MHz; CDCls) 177.9 (C=O), 146.4 and 143.8 (2 × i-C; Phₐ and Ph₈), 133.3,² 133.1,² 132.9,³ 132.4,¹ 131.9¹ and 130.6² (10 × CH; Phₐ and Ph₈), 76.9 (1C, t, JCD = 23.1 Hz, CD), 58.5 (CH₂Ph), 31.4 (CHCH₂CH₃), 27.1 (CDCH₃) and 17.0 (CHCH₂CH₃); (Found MNH⁺, 287.1868 C₁₈H₂₃D₈O₇N requires 287.1864). For minor diastereoisomer (S,R)-syn-306: δH (400 MHz; CDCls) 7.33-7.21 (8H, m, 8 × CH; Phₐ and Ph₈), 7.15-7.11 (2H, m, 2 × CH; Phₐ and/or Ph₈), 3.49 (1H, t, J 7.7, CHCH₂), 2.18-2.06 (1H, m, CH₃CH₂H₈CH₂), 1.86-1.74 (1H, m, CH₃CH₂H₈CH₂), 1.42 (3H, s, CH₃CD) and 0.85 (3H, t, J 7.3, CH₃CH₂CH).

Competitive MKR of 1-phenyl-1-deutero-ethanol (rac)-304 and 1-phenylethanol (rac)-11 using active ester (rac)-95 [S5.32].

In the same way as T5.18; E1, tert-BuOLi 266 (76 mg, 0.95 mmol), ZnCl₂ (0.129 g, 0.95 mmol), 1-phenyl-1-deutero-ethanol (rac)-304 (0.195 g, 1.58 mmol), 1-phenylethanol (rac)-11 (0.193 g, 1.58 mmol) and pentafluorophenyl-2-phenylpropionate (rac)-95 (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenyl-1-deutero-ethyl-2-phenylpropionate (rac)-anti and (rac)-syn-305 and 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (43 mg, 53%, anti : syn 92 : 8, deuterium : hydrogen 50 : 50), which were spectroscopically identical to that obtained elsewhere.
Synthesis of Alcohol, alkoxide, zinc reagent in THF [T5.31].

A mixture of 1-phenylethanol \((rac)-\text{11}\) (3.86 g, 31.6 mmol), tert-BuOLi \(266\) (0.760 g, 9.49 mmol) and ZnCl\(_2\) (1.292 g, 9.49 mmol) in THF (50 ml) was refluxed for 2 hours. The resulting solution was allowed to cool, and 5 ml allocates (3.20 mmol of 1-phenylethanol \(\text{11}\)) where used in the subsequent reactions T5.31; E2-3.

MKR of 1-phenyethanol \((rac)-\text{11}\) using active ester \((rac)-\text{95}\) [T5.31; E1].

Mixture of 1-phenylethanol \((rac)-\text{11}\) (0.386 g, 3.16 mmol), tert-BuOLi \(266\) (0.076 g, 0.95 mmol) and ZnCl\(_2\) (0.129 g, 0.95 mmol) in THF (5 ml) was refluxed for 2 hours. The resulting solution was allowed to cool to R.T. over 2 days and a solution of pentafluorophenyl-2-phenylpropinate \((rac)-\text{95}\) (0.1 g, 0.32 mmol) in THF (5 ml) was added. The resulting mixture was stirred over night. The reaction was quenched with NH\(_4\)Cl\(\text{aq}\) (10 ml). The organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO\(_4\) and evaporated under reduced pressure. The crude mixture was purified by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) to give an inseparable mixture of 1-phenylethyl-2-phenylpropinate \((rac)-\text{anti}\) and \((rac)-\text{syn-245}\) (27 mg, 34%, \text{anti} : \text{syn} 92 : 8) and \(n\)-butyl-2-phenylpropinate \((rac)-\text{250}\) (2 mg, 3%), which were spectroscopically identical to that obtained previously.

MKR of 1-phenyethanol \((rac)-\text{11}\) using active ester \((rac)-\text{95}\) [T5.31; E2].

10 day old alcohol, alkoxide, zinc reagent from above (5 ml, 3.20 mmol based on 1-phenylethanol) was added to a solution pentafluorophenyl-2-phenylpropinate \((rac)-\text{95}\) (0.1 g, 0.32 mmol) in THF (5 ml). The resulting mixture was stirred over night. The reaction was quenched with NH\(_4\)Cl\(\text{aq}\) (10 ml). The organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO\(_4\) and evaporated under reduced pressure. The crude mixture was purified by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / dichloromethane (1:1) to give an inseparable mixture of 1-phenylethyl-2-phenylpropinate \((rac)-\text{anti}\) and \((rac)-\text{syn-245}\) (26 mg, 32%, \text{anti} : \text{syn} 91 : 9) and \(n\)-butyl-2-phenylpropinate \((rac)-\text{250}\) (2 mg, 3%), which were spectroscopically identical to that obtained elsewhere.
MKR of 1-phenylethanol (rac)-11 using active ester (rac)-95 [T5.31; E2].

102 day old alcohol, alkoxide, zinc reagent from above (5 ml, 3.20 mmol based on 1-phenylethanol) was added to a solution pentafluorophenyl-2-phenylpropinate (rac)-95 (0.1 g, 0.32 mmol) in THF (5 ml). The resulting mixture was stirred over night. The reaction was quenched with NH₄Cl(aq) (10 ml). The organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. The crude mixture was purified by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / dichloromethane (1:1) to give an inseparable mixture of 1-phenylethyl-2-phenylpropinate (rac)-anti and (rac)-syn-245 (14 mg, 17%, anti : syn 90 : 10) and n-butyl-2-phenylpropinate (rac)-250 (~1 mg, 2%), which were spectroscopically identical to that obtained elsewhere.

Hydrolysis of 1-phenylehtyl-2-(6-methoxy-2-naphthyl)propinate (S,S)-anti-249 [S5.33].

Added LiOH.H₂O (0.130g 2.99 mmol) and H₂O₂ (0.85 ml, 3.53M in water, 2.99 mmol) to 1-phenylehtyl-2-(6-methoxy-2-naphthyl)-propinate (S,S)-anti-249 (0.5 g, 1.49 mmol) in THF/water (3:1, 16ml). The resulting mixture was stirred over night. The reaction was diluted with water (10 ml). The organic layer was extracted with dichloromethane (3 × 25 ml), dried over MgSO₄ and evaporated under reduced pressure. To give a mixture of returned 1-phenylehtyl-2-(6-methoxy-2-naphthyl)propinate (S,S)-anti-249 and 1-phenylethanol (S)-11 (ratio ester : alcohol 75:25), which were spectroscopically identical to that obtained elsewhere.

Reduction of 1-phenylehtyl-2-phenylpropionate (rac)-245 using Di-i-BuAlH [T5.32; E1].

Di-i-BuAlH (0.28 ml, 1 M in hexanes, 0.28 mmol) was added to a solution of 1-phenylethyl-2-phenylpropionate (rac)-anti-245 (35 mg, 80% d.e., 0.14 mmol) in THF (4 ml). The resulting mixture was stirred over 2 days, quenched with NaOH (4 ml, 3 M), acidified with HCl (4 ml, 3M). The organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. To give a crude mixture of 1-phenylethyl-2-phenylpropionate (rac)-245 (80% d.e.), 2-phenylpropanol (rac)-307 and 1-phenylethanol (rac)-11 in a (ratio 20 : 51 : 29), which were spectroscopically identical to that obtained previously.
Reduction of 1-phenylethyl-2-phenylpropionate (rac)-245 using LiBH₄ [T5.32; E2].

In the same way as T5.32; E1 LiBH₄ (7 mg, 0.31 mmol), 1-phenylethyl-2-phenylpropionate (rac)-anti-245 (39 mg, 80% d.e., 0.15 mmol) in THF (4 ml). Gave a crude mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti-245 (80% d.e.), 2-phenylpropanol (rac)-307 and 1-phenylethanol (rac)-11 in a ratio 49 : 34 : 17, which were spectroscopically identical to that obtained previously.

Reduction of 1-phenylethyl-2-phenylpropionate (rac)-245 using LiBHEt₃ [T5.32; E3].

In the same way as T5.32; E1 LiBHEt₃ (44 ml, 1 M in THF, 0.44 mmol), 1-phenylethyl-2-phenylpropionate (rac)-anti-245 (56 mg, 80% d.e., 0.22 mmol) in THF (4 ml). Gave a crude mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti-245 (~0% d.e.), 2-phenylpropanol (rac)-307 and 1-phenylethanol (rac)-11 in a ratio 21 : 53 : 26, which were spectroscopically identical to that obtained previously.

Reduction of 1-phenylethyl-2-phenylpropionate (R,R)-anti-245 [S5.34].

In the same way as T5.32; E1 LiAlH₄ (26 mg, 0.68 mmol), 1-phenylethyl-2-phenylpropionate (R,R)-anti-245 (87 mg, 86% d.e., 0.34 mmol) in THF (5 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) a partially separable mixture of 1-phenylethanol (R)-11 (19 mg, 46%, ~86% e.e.) as an oil; Rₐ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.35; [α]D₀ = +24.4 (c 1.8, CHCl₃); νmax (CHCl₃)/cm⁻¹ 3019 (OH); δH (400 MHz; CDCl₃) 7.38-7.24 (5H, m, 5 × CH; Ph), 4.88 (1H, dq, J 6.4 and 1.9, CH₃CH), 2.04 (1H, d, J 1.9, OH) and 1.49 (3H, d, J 6.4, CH₃CH); δC (100 MHz; CDCl₃) 145.8 (i-C; Ph), 128.5,² 127.4¹ and 125.3² (5 × CH; Ph), 70.3 (CH₃CH) and 25.1 (CH₃CH); (Found M⁺, 122.0725 C₈H₁₆O requires 122.0726) and 2-phenylpropanol (R)-307 (23 mg, 49%, ~86% e.e.) as an oil; Rₐ [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.33; [α]D₀ = +16.9 (c 4.8, CHCl₃, with 23% of 1-phenylethanol impurity in); νmax (CHCl₃)/cm⁻¹ 3019 (OH); δH (400 MHz; CDCl₃) 7.30-7.12 (5H, m, 5 × CH; Ph), 3.61 (2H, dd, J 6.5 and 5.9, CH₂OH), 2.91-2.81 (1H, m, CH₃(CH₂) 1.41 (1H, s, OH) and 1.20 (3H, d, J 7.0, CH₃CHCH₂); δC (100 MHz; CDCl₃) 143.6 (i-C; Ph), 128.6,² 127.4² and 126.6² (5 × CH; Ph), 68.6 (CH₂), 43.4 (CH) and 17.5 (CH₃).
Reduction of 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propinate \((S,S)-anti-249\) [S5.35].

In the same way as T5.32; E1, LiAlH\(_4\) (52 mg, 1.37 mmol), 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propionate \((S,S)-anti-249\) (0.229 g, 0.69 mmol) in THF (5 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3 → 1:1) 1-phenylethanol \((S)-11\) (60 mg, 72%) as an oil; \([\alpha]_D^{20} = -43.0\) (c 11.4, CHCl\(_3\)); which was spectroscopically identical to that obtained elsewhere and 2-(6-methoxy-2-naphthyl)-propanol \((S)-308\) (0.11 g, 74%) as an oil; \(R_F\) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.20; \([\alpha]_D^{20} = -17.7\) (c 22.0, CHCl\(_3\)); \(\nu_{max}\) (CHCl\(_3\))/cm\(^{-1}\) 3019 (OH); \(\delta_H\) (400 MHz; CDCl\(_3\)) 7.64 (1H, d, J 8.4, CH; Ar), 7.62 (1H, d, J 8.4, CH; Ar), 7.53 (1H, br s, CH; Ar), 7.27 (1H, dd, J 8.6 and 1.8, CH; Ar), 7.09-7.03 (2H, m 2 × CH; Ar), 3.83 (3H, s, CH\(_2\)O), 3.70 (2H, ABq, CH\(_2\)OH), 3.01 (1H, ddq (appears as a sextet with J 6.9) CH\(_3\)CH), 1.29 (1H, br s, OH) and 1.28 (3H, d, J 7.2, CH\(_3\)CH); \(\delta_C\) (100 MHz; CDCl\(_3\)) 157.4 (i-CO; Ar), 138.6, 133.5 and 129.0 (3 × i-C; Ar), 129.1, 127.2, 126.2, 125.9, 118.9 and 105.6 (6 × CH; Ar), 68.6 (CH\(_3\)O), 55.3 (CH\(_2\)OH), 42.3 (CH\(_3\)CH) and 17.6 (CH\(_3\)CH); (Found M\(^+\), 216.1142 C\(_{14}\)H\(_{16}\)O\(_2\) requires 216.1145).

Synthesis of Sodium ethoxide [S5.36].

Added Na\(_{\omega}\) to an excess of ethanol at 0°C, stirred the resulting solution overnight. The resulting mixture was evaporated under reduced pressure to give sodium ethoxide as a white solid.

Hydrolysis of 1-phenethyl-2-phenylpropionate \((rac)-anti-245\) using tert-BuOK [S5.37; E1].

\textit{tert-}BuOK (0.554 g, 4.94 mmol) was added to a solution of 1-phenethyl-2-phenylpropionate \((rac)-anti-245\) (0.251 g, 0.99 mmol) in THF (5 ml). The resulting mixture was stirred overnight. The reaction was quenched with water (20 ml), the organic layer was extracted with dichloromethane (3 × 25 ml), dried over MgSO\(_4\) and evaporated under reduced pressure. To give a mixture of 1-phenylethanol \((rac)-11\) (83 mg, 69%), which was spectroscopically identical to that obtained elsewhere and acetophenone \(303\) (20 mg, 17%) as an oil; \(R_F\) [dichloromethane] 0.60; \(\nu_{max}\) (CHCl\(_3\))/cm\(^{-1}\) 1686 (C=O); \(\delta_H\) (400 MHz; CDCl\(_3\)) 7.88 (2H, dd, J 7.8 and 1.3, 2 × CH; Ph), 7.49 (1H, td, J 7.8 and 1.3, CH; Ph), 7.39 (1H, td, J 7.8 and 1.3, 2 × CH; Ph) and 2.53 (3H, s, CH\(_3\)); \(\delta_C\) (100 MHz; CDCl\(_3\)) 198.1 (C=O), 137.0 (i-C; Ph), 133.0,\(^1\) 128.5\(^2\) and 128.2\(^2\) (5
× CH; Ph) 26.5 (CH₃). The aqueous layer was acidified with HCl (10 ml, 3M), the organic layer was extracted with dichloromethane (3 × 25 ml), dried over MgSO₄ and evaporated under reduced pressure. To give 2-phenylpropic acid (rac)-111 (81 mg, 55%) which was spectroscopically identical to that obtained elsewhere.

**Hydrolysis of 1-phenyethyl-2-phenylpropionate (rac)-anti-245 using NaOEt [S5.37; E2].**

In the same way as S5.37; E1 NaOEt (0.268 g, 3.94 mmol), 1-phenyethyl-2-phenylpropionate (rac)-anti-245 (0.2 g, 0.79 mmol) in THF (5 ml). Gave after organic extraction a mixture of 1-phenylethanol (rac)-1 (75 mg, 78%) which was spectroscopically identical to that obtained elsewhere and ethyl-2-phenylproipinate (rac)-309 (78 mg, 56%) as an oil; δH (400 MHz; CDCl₃) 7.32-7.17 (5H, m, 5 × CH; Ph), 4.11-3.97 (2H, m, CH₂CH₃), 3.62 (1H, q, J 7.2, CHPh) 1.42 (3H, d, J 7.2, CHCH₃) and 1.13 (3H, t, J 7.2, CH₂CH₃). The aqueous layer was acidified with HCl (10 ml, 3M), the organic layer was extracted with dichloromethane (3 × 25 ml), dried over MgSO₄ and evaporated under reduced pressure. To give 2-phenylpropic acid (rac)-111 (37 mg, 31%), which was spectroscopically identical to that obtained elsewhere.

**Hydrolysis of 1-phenylethanol (rac)-11 and 1-ethyl-2-phenylpropionate (rac)-309 mixture [S5.37; E3].**

LiOH·H₂O (37 mg, 0.88 mmol) and H₂O₂ (0.25 ml, 0.88 mmol) were added to a mixture of 1-phenylethanol (rac)-11 and 1-ethyl-2-phenylpropionate (rac)-309 (0.153 g, obtained from S5.37; E2) in THF/water 3:1 mix (4ml). The resulting mixture was stirred over night. The reaction was diluted with water (20 ml), the organic layer was extracted with dichloromethane (3 × 25 ml), dried over MgSO₄ and evaporated under reduced pressure. To give 1-phenylethanol (rac)-11 (56 mg, 58%), which was spectroscopically identical to that obtained elsewhere. The aqueous layer was acidified with HCl (10 ml, 3M), the organic layer was extracted with dichloromethane (3 × 25 ml), dried over MgSO₄ and evaporated under reduced pressure. To give 2-phenylpropic acid (rac)-111 (56 g, 47%), which was spectroscopically identical to that obtained elsewhere.
Hydrolysis of 1-phenyethyl-2-phenylpropionate (rac)-anti-245 using NaOEt and LiOH [S5.37; E4].

NaOEt (0.268 g, 3.94 mmol) was added to a solution of 1-phenyethyl-2-phenylpropionate (rac)-anti-245 (0.2 g, 0.79 mmol) in THF (5 ml). The resulting mixture was stirred overnight. Water (1.67 ml) was added to the reaction mixture followed by LiOH.H$_2$O (66 mg, 1.57 mmol) and H$_2$O$_2$ (0.45 ml, 1.57 mmol). The resulting mixture was stirred overnight. Reaction was diluted with water (20 ml), the organic layer was extracted with dichloromethane (3 x 25 ml), dried over MgSO$_4$ and evaporated under reduced pressure. To give 1-phenylethanol (rac)-11 (69 mg, 72%), which was spectroscopically identical to that obtained elsewhere. The aqueous layer was acidified with HCl (10 ml, 3M), the organic layer was extracted with dichloromethane (3 x 25 ml), dried over MgSO$_4$ and evaporated under reduced pressure. To give 2-phenylpropionic acid (rac)-111 (0.104 g, 88%), which was spectroscopically identical to that obtained elsewhere.

Hydrolysis of 1-phenyethyl-2-phenylbutinate (S, S)-anti-246 [S5.38].

In the same way as S5.37; E4, NaOEt (0.1 g, 1.47 mmol), 1-phenyethyl-2-phenylbutinate (S, S)-anti-246 (79 mg, 88% d.e., 0.29 mmol) in THF (5 ml). LiOH.H$_2$O (25 mg, 0.59 mmol), H$_2$O$_2$ (0.17 ml, 0.59 mmol) in THF/water 3:1 (7 ml). Gave after organic extraction and purification by flash column chromatography on silica gel eluting with dichloromethane 1-phenylethanol (S)-11 (28 mg, 84% e.e., 78%), [α]$_D^{20}$ = -14.5 (c 2.2, CHCl$_3$), after acid extraction 2-phenylbutiric acid (rac)-118 (34 mg, 0% e.e., 70%), [α]$_D^{20}$ = -4.6 (c 2.0, CHCl$_3$), which was spectroscopically identical to that obtained elsewhere.
Section 5: Experiments from Chapter 6

MKR of 1-(2-bromo-phenyl)-ethanol \((rac)-278\) using active ester \((rac)-95\) and ZnCl\(_2\) [S6.1].

\(\text{tert-BuLi} (0.56 \text{ ml, } 1.7\text{M in pentane, } 0.95 \text{ mmol})\) was added to 1-(2-bromo-phenyl)-ethanol \((rac)-278\) (0.636 g, 3.16 mmol) in THF (5 ml) at -78°C, followed by ZnCl\(_2\) (0.95 ml, 1M in diethyl ether, 0.95 mmol) and pentafluorophenyl-2-phenyl-propionate \((rac)-95\) (0.1 g, 0.32 mmol) in THF (5 ml). The resulting mixture was stirred overnight. The reaction was quenched with water (10 ml), the organic layer was extracted with dichloromethane (3 × 25 ml), washed water (25 ml), dried over MgSO\(_4\) and evaporated under reduced pressure. Gave by crude \(^1\)H NMR 1-(2-bromo-phenyl)-ethyl-2-phenylpropionate \((rac)-\text{anti} and \text{syn-290}\) (<5%, ratio \text{anti} : \text{syn} ~95 : 5), and 1-(2-bromo-phenyl)-ethanol \((rac)-278\) and 1-phenylethanol \((rac)-11\) (ratio \(278 : 11 = 88 : 12\)), which were spectroscopically identical to that obtained elsewhere.

**Reaction of 1-(2-bromo-phenyl)-ethanol \((rac)-278\) with \(\text{tert-BuLi}\) and ZnCl\(_2\) [S6.2].**

\(\text{tert-BuLi} (0.20 \text{ ml, } 1.7\text{M in pentane, } 0.34 \text{ mmol})\) was added to 1-(2-bromo-phenyl)-ethanol \((rac)-278\) (68 mg, 0.34 mmol) in THF (5 ml) at -78°C, followed by ZnCl\(_2\) (0.34 ml, 1M in diethyl ether, 0.34 mmol). The resulting mixture was stirred for 1 hour. The reaction was quenched with water (10 ml), the organic layer was extracted with dichloromethane (3 × 25 ml), washed water (25 ml), dried over MgSO\(_4\) and evaporated under reduced pressure. Gave by crude \(^1\)H NMR 1-(2-bromo-phenyl)-ethanol \((rac)-278\) and 1-phenylethanol \((rac)-11\) (ratio of \(278 : 11 = 68 : 32\)), which were spectroscopically identical to that obtained elsewhere.

MKR of 1-(2-bromo-phenyl)-ethanol \((rac)-278\) using active ester \((rac)-95\) [S6.3].

In the same way as S6.1, \(\text{tert-BuLi} (0.56 \text{ ml, } 1.7\text{M in pentane, } 0.95 \text{ mmol})\), 1-(2-bromo-phenyl)-ethanol \((rac)-278\) (0.636 g, 3.16 mmol) and pentafluorophenyl-2-phenyl-propionate \((rac)-95\) (0.1 g, 0.32 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-(2-bromo-phenyl)-ethyl-2-phenylpropionate \((rac)-\text{anti} and \text{syn-290}\) (ratio \text{anti} : \text{syn} 71 : 29) and 1-phenylethyl-2-phenylpropionate \((rac)-\text{anti} and \text{syn-245}\) (ratio \text{anti} : \text{syn} ~70 : 30) (combined 72 mg, 68% ratio of \(290 : 245 = 97 : 3\)). From crude \(^1\)H NMR 1-(2-bromo-phenyl)-ethanol
(rac)-278 and 1-phenylethanol (rac)-11 (ratio 278 : 11 = 87 : 13), which were spectroscopically identical to that obtained elsewhere.

**Reaction of 1-(2-bromo-phenyl)-ethanol (rac)-278 with tert-BuLi 0.25 equiv. [T6.1; E1].**

tert-BuLi (0.14 ml, 1.7M in pentane, 0.24 mmol) was added to 1-(2-bromo-phenyl)-ethanol (rac)-278 (0.191 g, 0.95 mmol) in THF (5 ml) at -78°C. The resulting mixture was stirred for 2 hour. The reaction was quenched with water (10 ml), the organic layer was extracted with dichloromethane (3 × 25 ml), washed water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. Gave by crude ¹H NMR 1-(2-bromo-phenyl)-ethanol (rac)-278 and 1-phenylethanol (rac)-11 (ratio of 278 : 11 = 89 : 11), which were spectroscopically identical to that obtained elsewhere.

**Reaction of 1-(2-bromo-phenyl)-ethanol (rac)-278 with tert-BuLi 0.5 equiv. [T6.1; E2].**

In the same way as T6.1; E1, tert-BuLi (0.10 ml, 1.7M in pentane, 0.17 mmol) and 1-(2-bromo-phenyl)-ethanol (rac)-278 (68 mg, 0.34 mmol) in THF (5 ml). Gave by crude ¹H NMR 1-(2-bromo-phenyl)-ethanol (rac)-278 and 1-phenylethanol (rac)-11 (ratio of 278 : 11 = 76 : 24), which were spectroscopically identical to that obtained elsewhere.

**Reaction of 1-(2-bromo-phenyl)-ethanol (rac)-278 with tert-BuLi 1 equiv. [T6.1; E3].**

In the same way as T6.1; E1, tert-BuLi (0.20 ml, 1.7M in pentane, 0.34 mmol) and 1-(2-bromo-phenyl)-ethanol (rac)-278 (68 mg, 0.34 mmol) in THF (5 ml). Gave by crude ¹H NMR 1-(2-bromo-phenyl)-ethanol (rac)-278 and 1-phenylethanol (rac)-11 (ratio of 278 : 11 = 73 : 27), which were spectroscopically identical to that obtained elsewhere.

**Reaction of 1-(2-bromo-phenyl)-ethanol (rac)-278 with tert-BuLi 1 equiv. [T6.1; E3*].**

In the same way as T6.1; E1, but stirred over night, tert-BuLi (0.20 ml, 1.7M in pentane, 0.34 mmol) and 1-(2-bromo-phenyl)-ethanol (rac)-278 (68 mg, 0.34 mmol) in THF (5 ml). Gave by crude ¹H NMR 1-(2-bromo-phenyl)-ethanol (rac)-278 and 1-
phenylethanol (rac)-11 (ratio of 278 : 11 = 78 : 22), which were spectroscopically identical to that obtained elsewhere.

**Reaction of 1-(2-bromo-phenyl)-ethanol (rac)-278 with tert-BuLi 2 equiv. [T6.1; E4].**

In the same way as T6.1; E1, tert-BuLi (0.40 ml, 1.7M in pentane, 0.68 mmol) and 1-(2-bromo-phenyl)-ethanol (rac)-278 (68 mg, 0.34 mmol) in THF (5 ml). Gave by crude $^1$H NMR 1-(2-bromo-phenyl)-ethanol (rac)-278 and 1-phenylethanol (rac)-11 (ratio of 278 : 11 = 53 : 47), which were spectroscopically identical to that obtained elsewhere.

**Reaction of 1-(2-bromo-phenyl)-ethanol (rac)-278 with tert-BuLi 3 equiv. [T6.1; E5].**

In the same way as T6.1; E1, tert-BuLi (0.60 ml, 1.7M in pentane, 1.01 mmol) and 1-(2-bromo-phenyl)-ethanol (rac)-278 (68 mg, 0.34 mmol) in THF (5 ml). Gave by crude $^1$H NMR 1-(2-bromo-phenyl)-ethanol (rac)-278 and 1-phenylethanol (rac)-11 (ratio of 278 : 11 = 55 : 45), which were spectroscopically identical to that obtained elsewhere.

**Reaction of 1-(2-bromo-phenyl)-ethanol (rac)-278 with tert-BuLi 5 equiv. [T6.1; E5].**

In the same way as T6.1; E1, tert-BuLi (0.99 ml, 1.7M in pentane, 1.69 mmol) and 1-(2-bromo-phenyl)-ethanol (rac)-278 (68 mg, 0.34 mmol) in THF (5 ml). Gave by crude $^1$H NMR only 1-phenylethanol (rac)-11, which was spectroscopically identical to that obtained elsewhere.

**Reaction of 1-(2-bromo-phenyl)-ethanol (rac)-278 with tert-BuLi 10 equiv. [T6.1; E6].**

In the same way as T6.1; E1, tert-BuLi (1.99 ml, 1.7M in pentane, 3.38 mmol) and 1-(2-bromo-phenyl)-ethanol (rac)-278 (68 mg, 0.34 mmol) in THF (5 ml). Gave by crude $^1$H NMR only 1-phenylethanol (rac)-11, which was spectroscopically identical to that obtained elsewhere.
Reaction of 1-(2-bromo-phenyl)-ethanol (rac)-278 with tert-BuLi at -78°C [T6.2; E1].
See T6.1; E4.

Reaction of 1-(2-bromo-phenyl)-ethanol (rac)-278 with tert-BuLi at -42°C [T6.2; E2].

In the same way as T6.1; E1, tert-BuLi (0.40 ml, 1.7M in pentane, 0.68 mmol) and 1-(2-bromo-phenyl)-ethanol (rac)-278 (68 mg, 0.34 mmol) in THF (5 ml). Gave by crude $^1$H NMR 1-(2-bromo-phenyl)-ethanol (rac)-278 and 1-phenylethanol (rac)-11 (ratio of 278 : 11 = 27 : 73), which were spectroscopically identical to that obtained elsewhere.

Reaction of 1-(2-bromo-phenyl)-ethanol (rac)-278 with tert-BuLi at 0°C [T6.2; E3].

In the same way as T6.1; E1, tert-BuLi (0.40 ml, 1.7M in pentane, 0.68 mmol) and 1-(2-bromo-phenyl)-ethanol (rac)-278 (68 mg, 0.34 mmol) in THF (5 ml). Gave by crude $^1$H NMR 1-(2-bromo-phenyl)-ethanol (rac)-278 and 1-phenylethanol (rac)-11 (ratio of 278 : 11 = 16 : 84), which were spectroscopically identical to that obtained elsewhere.

Reaction of 1-(2-bromo-phenyl)-ethanol (rac)-278 with tert-BuLi at 20°C [T6.2; E4].

In the same way as T6.1; E1, tert-BuLi (0.40 ml, 1.7M in pentane, 0.68 mmol) and 1-(2-bromo-phenyl)-ethanol (rac)-278 (68 mg, 0.34 mmol) in THF (5 ml) (Note the reaction was a little violent, should not be repeated on a larger scale). Gave by crude $^1$H NMR 1-(2-bromo-phenyl)-ethanol (rac)-278 and 1-phenylethanol (rac)-11 (ratio of 278 : 11 = 19 : 81), which were spectroscopically identical to that obtained elsewhere.

Reaction of 1-(2-bromo-phenyl)-ethanol (rac)-278 with PhLi [T6.3; E1].

In the same way as T6.1; E1, PhLi (1.69 ml, 1M in di-butylether, 1.69 mmol) and 1-(2-bromo-phenyl)-ethanol (rac)-278 (68 mg, 0.34 mmol) in THF (5 ml). Gave by crude $^1$H NMR 1-(2-bromo-phenyl)-ethanol (rac)-278 and 1-phenylethanol (rac)-11 (ratio of 278 : 11 = 39 : 61), which were spectroscopically identical to that obtained elsewhere.
Reaction of 1-(2-bromo-phenyl)-ethanol (rac)-278 with LDA [T6.3; E2].

In the same way as T6.1; E1, LDA (0.94 ml, 1.8M in THF/heptane/ethylbenzene, 1.69 mmol) and 1-(2-bromo-phenyl)-ethanol (rac)-278 (68 mg, 0.34 mmol) in THF (5 ml). Gave by crude $^1$H NMR only 1-(2-bromo-phenyl)-ethanol (rac)-278, which was spectroscopically identical to that obtained elsewhere.

Reaction of 1-(2-bromo-phenyl)-ethanol (rac)-278 with n-BuLi [T6.3; E3].

In the same way as T6.1; E1, n-BuLi (0.68 ml, 2.5M in hexanes, 1.69 mmol) and 1-(2-bromo-phenyl)-ethanol (rac)-278 (68 mg, 0.34 mmol) in THF (5 ml). Gave by crude $^1$H NMR only 1-phenylethanol (rac)-11, which was spectroscopically identical to that obtained elsewhere.

Reaction of 1-(2-bromo-phenyl)-ethanol (rac)-278 with n-BuLi [S6.4; E1].

In the same way as T6.1; E1, n-BuLi (2.49 ml, 2.5M in hexanes, 6.21 mmol) and 1-(2-bromo-phenyl)-ethanol (rac)-278 (0.250 g, 1.24 mmol) in THF (5 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 3:7) 1-phenylethanol (rac)-11 (81 mg, 53%), which was spectroscopically identical to that obtained elsewhere.

Synthesis of 1-(2-deutrio-phenyl)-ethanol (rac)-312 [S6.4; E2].

n-BuLi (2.49 ml, 2.5M in hexanes, 6.21 mmol) was added to 1-(2-bromo-phenyl)-ethanol (rac)-278 (0.250 g, 1.24 mmol) in THF (5 ml) at -78°C. The resulting mixture was stirred for 2 hours. D$_2$O (1 ml, an excess) was then added and the resulting mixture stirred over night. The reaction was quenched with water (10 ml), the organic layer was extracted with dichloromethane (3 × 25 ml), washed water (25 ml), dried over MgSO$_4$ and evaporated under reduced pressure. Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) 1-(2-deutrio-phenyl)-ethanol (rac)-312 (78 mg, 51%), as an oil $R_f$ [light petroleum spirit (b.p. 40-60 °C) / diethyl ether (1:1)] 0.54; $\nu_{\text{max}}$ (CHCl$_3$)/cm$^{-1}$ 3019 (OH), 2400 (CD); $\delta_{\text{H}}$ (400 MHz, CDCl$_3$): 7.40-7.33 (3 H, m, 3 × CH; Ar), 7.30-7.25 (1 H, m, CH; Ar), 4.90 (1 H, q, $J$ 6.4, CHCH$_3$), 1.81 (1 H, Br s, OH) and 1.50 (3 H, d, $J$ 6.4, CHCH$_3$). $\delta_{\text{C}}$ (100 MHz, CDCl$_3$): 145.7 (i-C, Ar), 128.4, 128.3, 127.4 and 125.3 (4 × CH; Ar), 125.0 (1 C, t [1:1:1], $^{1}J_{\text{CD}}$ = 24.5, CD; Ar), 70.3 (CHCH$_3$) and 25.1 (CHCH$_3$).
Reaction of 1-(2-bromo-phenyl)-ethanol (S)-278 with n-BuLi [S6.4; E1].

In the same way as T6.1; E1, n-BuLi (4.98 ml, 2.5M in hexanes, 12.45 mmol) and 1-(2-bromo-phenyl)-ethanol (S)-278 (0.501 g, 2.49 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) 1-phenylethanol (S)-11 (0.200 g, 66%), which was spectroscopically identical to that obtained elsewhere.

Synthesis of 1-(2-methyl-phenyl)-ethanol (rac)-276 using 1 equiv. of MeI [T6.4; E1].

n-BuLi (2.49 ml, 2.5M in hexanes, 6.21 mmol) was added to 1-(2-bromo-phenyl)-ethanol (rac)-278 (0.250 g, 1.24 mmol) in THF (10 ml) at -78°C. The resulting mixture was stirred for 2 hours. MeI (0.08 ml, 1.24 mmol) was then added and the resulting mixture stirred over night. The reaction was quenched with water (10 ml), the organic layer was extracted with dichloromethane (3 × 25 ml), washed water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) an inseparable mixture of 1-(2-bromo-phenyl)-ethanol (rac)-278, 1-(2-methyl-phenyl)-ethanol (rac)-276 and 1-phenylethanol (rac)-11 (ratio of 278 : 276 : 11 = 12 : 62 : 26), which were spectroscopically identical to that obtained elsewhere.

Synthesis of 1-(2-methyl-phenyl)-ethanol (rac)-276 using 3 equiv. of MeI [T6.4; E2].

In the same way as T6.4; E1, n-BuLi (2.49 ml, 2.5M in hexanes, 6.21 mmol), 1-(2-bromo-phenyl)-ethanol (rac)-278 (0.250 g, 1.24 mmol) and MeI (0.23 ml, 3.73 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) an inseparable mixture of 1-(2-bromo-phenyl)-ethanol (rac)-278, 1-(2-methyl-phenyl)-ethanol (rac)-276 and 1-phenylethanol (rac)-11 (ratio of 278 : 276 : 11 = 6 : 83 : 11), which were spectroscopically identical to that obtained elsewhere.

Synthesis of 1-(2-methyl-phenyl)-ethanol (rac)-276 using 3 equiv. of MeI [T6.4; E3].

In the same way as T6.4; E1, n-BuLi (2.49 ml, 2.5M in hexanes, 6.21 mmol), 1-(2-bromo-phenyl)-ethanol (rac)-278 (0.250 g, 1.24 mmol) and MeI (0.46 ml, 7.46
mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) an inseparable mixture of 1-(2-bromo-phenyl)-ethanol (rac)-278, 1-(2-methyl-phenyl)-ethanol (rac)-276 and 1-phenylethanol (rac)-11 (ratio of 278 : 276 : 11 = 8 : 79 : 13), which was spectroscopically identical to that obtained elsewhere.

**Synthesis of 1-(2-methyl-phenyl)-ethanol (rac)-276 using 3 equiv. of MeI [S6.5].**

In the same way as T6.4; E1, n-BuLi (2.49 ml, 2.5M in hexanes, 6.21 mmol), 1-(2-bromo-phenyl)-ethanol (rac)-278 (0.250 g, 1.24 mmol) and MeI (0.46 ml, 7.46 mmol) in THF (5 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3) an inseparable mixture of 1-(2-bromo-phenyl)-ethanol (rac)-278 (84 mg, 50%) and 1-phenylethanol (rac)-11 (12 mg, 8%), which were spectroscopically identical to that obtained elsewhere.

**Synthesis of 1-(2-trimethyl-silyl-phenyl)-ethanol (rac)-313 [S6.6; E2].**

In the same way as T6.4; E1, n-BuLi (2.19 ml, 2.5M in hexanes, 5.47 mmol), 1-(2-bromo-phenyl)-ethanol (rac)-278 (0.220 g, 1.09 mmol) and chloro-trimethyl-silane (0.713 g, 6.57 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) 1-(2-tri-methyl-silyl-phenyl)-ethanol (rac)-313 (93 mg, 44%), as a white solid mp 53-57°C Rf [light petroleum spirit (b.p. 40-60 °C) / diethyl ether (1:1)] 0.52; ν<sub>max</sub> (CHCl<sub>3</sub>)/cm<sup>-1</sup> 3019 (OH); δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>): 7.60 (1 H, br d, J 7.8, CH; Ar), 7.47 (1 H, dd, J 7.6 and 1.0, CH; Ar), 7.42 (1 H, td, J 7.8 and 1.0, CH; Ar), 7.26 (1 H, td, J 7.6 and 1.3, CH; Ar), 5.15 (1 H, q, J 6.3, CHCH<sub>3</sub>), 1.70 (1 H, br s, OH), 1.49 (3 H, d, J 6.3, CHCH<sub>3</sub>) and 0.34 (9 H, s, (CH<sub>3</sub>)<sub>3</sub>Si). δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>): 151.5 and 136.9 (2 × i-C, Ar), 134.2, 129.9, 127.0 and 125.1 (4 × CH; Ar), 69.6 (CHCH<sub>3</sub>), 25.2 (CHCH<sub>3</sub>) and 0.64 ((CH<sub>3</sub>)<sub>3</sub>Si). Found MNH<sub>4</sub>^+·H<sub>2</sub>O, 194.1361; C<sub>11</sub>H<sub>20</sub>NSi requires 194.1360.

**Synthesis of 1-(2-tert-butyl-dimethyl-silyl-phenyl)-ethanol (rac)-314 [S6.7; E2].**

In the same way as T6.4; E1, n-BuLi (16.55 ml, 2.5M in hexanes, 41.38 mmol), 1-(2-bromo-phenyl)-ethanol (rac)-278 (1.664 g, 8.28 mmol) and tert-butyl-chloro-dimethyl-silane (7.486 g, 49.66 mmol) in THF (20 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) /
diethyl ether (9:1 → 7:3) 1-(2-tert-butyl-dimethyl-silyl-phenyl)-ethanol (rac)-314 (1.498 g, 77%), as a white solid mp 80-85°C, $R_t$ [light petroleum spirit (b.p. 40-60°C) / diethyl ether (1:1)] 0.58; $\nu_{\text{max}}$ (CHCl$_3$/cm$^{-1}$) 3019 (OH); $\delta_{\text{H}}$ (400 MHz, CDCl$_3$): 7.53 (1 H, br d, J 7.7, CH; Ar), 7.36 (1 H, ddd, J 7.5, 1.5 and 0.6, CH; Ar), 7.32 (1 H, tdd, J 7.7, 1.5 and 0.6, CH; Ar), 7.16 (1 H, td, J 7.5 and 1.3, CH; Ar), 5.01 (1 H, q, J 6.2, CHCH$_3$), 1.52 (1 H, br s, OH), 1.39 (3 H, d, J 6.2, CHCH$_3$), 0.81 (9 H, s, (CH$_3$)$_3$C), 0.27 (3 H, s, CH$_3$SiCH$_3$) and 0.26 (3 H, s, CH$_3$SiCH$_3$). $\delta_C$ (100 MHz, CDCl$_3$): 152.0 and 134.3 (2 × i-C; Ar), 135.9, 129.7, 126.6 and 125.3 (4 × CH; Ar), 70.2 (CHCH$_3$), 2.69 ((CH$_3$)$_3$C), 25.3 (CHCH$_3$), 17.6 ((CH$_3$)$_3$C), -2.3 (CH$_3$SiCH$_3$) and -3.2 (CH$_3$SiCH$_3$). (Found MNH$^+$, 254.1937; C$_{14}$H$_{30}$ONSi requires 254.1935).

**Synthesis of 1-(2-tert-butyl-dimethyl-silyl-phenyl)-ethanol (S)-314 [S6.7; E2].**

In the same way as T6.4; E1, n-BuLi (2.49 ml, 2.5M in hexanes, 6.21 mmol), 1-(2-bromo-phenyl)-ethanol (rac)-278 (0.250 g, 1.24 mmol) and tert-butyl-chloro-dimethyl-silane (1.12 g, 7.46 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) 1-(2-tert-butyl-dimethyl-silyl-phenyl)-ethanol (S)-314 (0.206 g, 70%), as a white solid mp 44-46°C; $[\alpha]_D^{23}$ -46.2 ($c$ = 3.4 in CHCl$_3$), which was spectroscopically identical to that obtained elsewhere.

**Synthesis of 1-(2-phenylsulfanyl-phenyl)-ethanol (rac)-315 [S6.8].**

In the same way as T6.4; E1, n-BuLi (2.49 ml, 2.5M in hexanes, 6.21 mmol), 1-(2-bromo-phenyl)-ethanol (rac)-278 (0.250 g, 1.24 mmol) and phenyl disulfide (1.629 g, 7.46 mmol) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 1:1) an inseparable mixture of 1-(2-phenylsulfanyl-phenyl)-ethanol (rac)-315 (0.201 g, 74%), as an oil; $R_t$ [light petroleum spirit (b.p. 40-60°C) / diethyl ether (1:1)] 0.44; $\nu_{\text{max}}$ (CHCl$_3$/cm$^{-1}$) 3063 (OH); $\delta_{\text{H}}$ (400 MHz, CDCl$_3$): 7.34 (1 H, dd, J 7.9 and 1.1, CH; Ar or Ph), 7.37 (1 H, td, J 8.0 and 1.3, CH; Ar or Ph), 7.35-7.17 (7 H, m, 7 × CH; Ar and Ph), 5.41 (1 H, q, J 6.4, CHCH$_3$) 2.02 (1H, s, OH) and 1.45 (3 H, d, J 6.4, CHCH$_3$); $\delta_C$ (100 MHz, CDCl$_3$): 147.2, 136.5 and 131.4 (3 × i-C; Ar and Ph), 133.9,$^1$ 129.5,$^2$ 129.2,$^2$ 128.6,$^1$ 128.1,$^1$ 126.5$^1$ and 126.0$^1$ (9 × CH; Ar and Ph), 67.4 (CHCH$_3$) and 24.2 (CHCH$_3$). Found MNH$^+$, 253.0659; C$_{14}$H$_{14}$ONaS requires 253.0658, 1-phenylethanol (21 mg, 14%) and 1-(2-hydroxy-phenyl)-ethanol (9 mg, 5%), which were spectroscopically identical to that obtained elsewhere.
Synthesis of 1-(2-hydroxy-phenyl)-ethanol (rac)-316 [S6.9].

In the same way as T6.4; E1, n-BuLi (2.49 ml, 2.5M in hexanes, 6.21 mmol), 1-(2-bromo-phenyl)-ethanol (rac)-278 (0.250 g, 1.24 mmol) and O2(g) (an excess) in THF (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (1:1 → 3:7) an inseparable mixture of 1-phenylethanol (33 mg, 22%) and 1-(2-hydroxy-phenyl)-ethanol (23 mg, 13%), which were spectroscopically identical to that obtained elsewhere.

Synthesis of 1-(2-hydroxy-phenyl)-ethanol (rac)-316 [S6.10].

MeMgBr (6.8 ml, 3M in diethyl ether, 6.2 mmol) was added to 2-hydroxy-benzaldehyde 317 (1.135 g, 9.29 mmol) in THF (5 ml) at -78°C. The resulting mixture was stirred over night. The reaction was quenched with NHCl4(aq) (5 ml), the organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO4 and evaporated under reduced pressure. Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (7:3 → 3:7) 1-(2-hydroxy-phenyl)-ethanol (rac)-316 (0.728 g, 57%), as a yellow oil; Rf [light petroleum spirit (b.p. 40-60 °C) – diethyl ether (1:1)] 0.38; νmax (CHCl3)/cm\(^{-1}\) br 3371 and 3019 (2 × OH) cm\(^{-1}\); δ\(_H\) (400 MHz, CDCl3): 7.94 (1 H, br s, OH), 7.18 (1 H, td, J 7.3 and 1.6, CH; Ar), 6.99 (1 H, dd, J 7.9 and 1.6, CH; Ar), 6.88 (1 H, dd, J 7.9, and 1.0, CH; Ar), 6.84 (1 H, td, J 7.3 and 1.0, CH; Ar), 5.09 (1 H, q, J 6.6, CHCH3), and 1.60 (3 H, d, J 6.6, CHCH3). δ\(_C\) (100 MHz, CDCl3): 155.5 and 128.2 (2 × i-C; Ar), 129.0, 126.4, 119.8 and 117.2 (4 × CH; Ar), 71.8 (CHCH3) and 23.4 (CHCH3). (Found M\(^+\), 138.0675; C9H10O2 requires 138.0675).

Synthesis of 3-methylphthalide (rac)-318 [S6.11; E1].

n-BuLi (2.49 ml, 2.5M in hexanes, 6.2 mmol) was added to 1-(2-bromo-phenyl)-ethanol (rac)-278 (0.250 g, 1.24 mmol) in THF (10 ml) at -78°C. The resulting mixture was stirred for 1 hour. CO2(g) (an excess) was then bubble through the reaction mixture, the resulting mixture was stirred over night. The reaction was quenched with water (10 ml), the organic layer was extracted with dichloromethane (3 × 25 ml). The aqueous layer was acidified with HCl (3M, 5 ml), the organic layer was extracted with dichloromethane (3 × 25 ml), washed water (25 ml), dried over MgSO4 and evaporated under reduced pressure. Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (1:1) 3-
methylphthalide (rac)-318 (0.108 g, 59%), as an oil, R$_t$ [light petroleum spirit (b.p. 40-60 °C) – diethyl ether (1:1)] 0.33; $\nu$$_{max}$ (CHCl$_3$)/cm$^{-1}$ 1755 (C=O) cm$^{-1}$; $\delta$$_H$ (400 MHz, CDCl$_3$): 7.87 (1 H, d, J 7.5, CH; Ar), 7.67 (1 H, td, J 7.5 and 0.9, CH; Ar), 7.50 (1 H, br t, J 7.5, CH; Ar), 7.43 (1 H, br d, J 7.5 CH; Ar), 5.55 (1 H, q, J 6.8, CHCH$_3$) and 1.62 (3 H, d, J 6.8, CHCH$_3$). $\delta$$_C$ (100 MHz, CDCl$_3$): 170.6 (C=O), 151.2 and 125.8 (2 × i-C; Ar), 134.0, 129.0, 125.7 and 121.5 (4 × CH; Ar), 77.7 (CHCH$_3$) and 20.4 (CHCH$_3$). (Found M$^+$, 148.0518; C$_9$H$_8$O$_2$ requires 148.0519).

**Synthesis of 3-methylphthalide (S)-318 [S6.11; E2].**

In the same way as S6.11; E1, n-BuLi (0.99 ml, 2.5M in hexanes, 2.49 mmol), 1-(2-bromo-phenyl)-ethanol (rac)-278 (0.100 g, 0.50 mmol) and CO$_2$(g) (an excess) in THF (5 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (1:1) 3-methylphthalide (rac)-318 (45 g, 61%), as a white solid mp 35-37°C; $[\alpha]_D^{25}$ -28.6 (c = 2.9 in CHCl$_3$), which was spectroscopically identical to that obtained elsewhere.

**Reaction of 3-methylphthalide (rac)-318 with PhCHMeNH$_2$ and DAMP [T6.5; E1].**

A mixture of 1-phenyl-ethyl-amine (rac) (0.328 g, 2.70 mmol), DMAP (34 mg, 0.27 mmol) and 3-methylphthalide (rac)-318 (0.200 g, 1.35 mmol) was stirred over night. The reaction was quenched with NH$_4$Cl$_{aq}$ (10 ml), the organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO$_4$ and evaporated under reduced pressure. To return the starting materials.

**Reaction of 3-methylphthalide (rac)-318 with PhCHMeNH$_2$ and DAMP in ethanol [T6.5; E2].**

In the same way as T6.5; E1, 1-phenyl-ethyl-amine (rac) (0.328 g, 2.70 mmol), DMAP (34 mg, 0.27 mmol) and 3-methylphthalide (rac)-318 (0.200 g, 1.35 mmol) in ethanol (10 ml). Returned the starting materials.

**Reaction of 3-methylphthalide (rac)-318 with DAMP [T6.5; E3].**

In the same way as T6.5; E1, DMAP (34 mg, 0.27 mmol) and 3-methylphthalide (rac)-318 (0.200 g, 1.35 mmol) in ethanol (5 ml). Returned the starting materials.
Reaction of 3-methylphthalide (rac)-318 with PhCH₂NLiCHMePh [T6.5; E4].

n-BuLi (0.60 ml, 2.5M in hexanes, 1.50 mmol) was added to benzyl-(1-phenyl-ethyl)-amine (rac) (0.291 g, 1.37 mmol) in THF (5 ml) at 0°C, the resulting mixture was stirred for 2 hours. 3-methylphthalide (rac)-318 (0.202 g, 1.37 mmol) in THF (5 ml) was then added at -78°C. The resulting mixture was stirred for 2 hours. The reaction was quenched with NH₄Cl (aq) (10 ml), the organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. To return the starting materials.

Reaction of 3-methylphthalide (rac)-318 with MeMgBr [S6.13; E1].

MeMgBr (0.53 ml, 3M in diethyl ether, 1.58 mmol) was added to 3-methylphthalide (rac)-318 (0.213 g, 1.44 mmol) in THF (5 ml) at -78°C. The resulting mixture was stirred for 4 hours. The reaction was quenched with NH₄Cl (aq) (10 ml), the organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. To return the starting material.

Synthesis of 1-[2-(propan-2-ol)-phenyl]-ethanol (rac)-322 [S6.13; E2].

In the same way as S6.13; E1, MeMgBr (1.32 ml, 3M in diethyl ether, 3.95 mmol) and 3-methylphthalide (rac)-318 (0.195 g, 1.32 mmol) in THF (5 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (1:1 → 3:7) 1-[2-(propan-2-ol)-phenyl]-ethanol (rac)-322 (0.145 g, 61%), as a white solid mp 64-68°C; Rf [diethyl ether] 0.52; νmax (CHCl₃)/cm⁻¹ 3020 (OH); δH (400 MHz, CDCl₃): 7.60 (1 H, dd, J 7.8 and 1.6, CH; Ar), 7.34-7.27 (2 H, m, 2 × CH; Ar), 7.22 (1 H, td, J 7.7 and 1.6, CH; Ar), 5.76 (1 H, q, J 6.7, CHCH₃), 2.21 (2 H, br s, 2 × OH), 1.71 (3 H, s, CH₃CCH₃), 1.67 (3 H, s, CH₃CCH₃) and 1.56 (3 H, d, J 6.7, CHCH₃). δC (100 MHz, CDCl₃): 144.5 and 143.7 (i-C; Ar), 127.6, 127.5, 127.2 and 125.5 (4 × CH; Ar), 74.1 (CH₃CCH₃), 66.4 (CHCH₃), 32.7 (CH₃CCH₃), 32.6 (CH₃CCH₃) and 23.7 (CHCH₃). (Found MNH⁺, 198.1487; C₁₁H₂₀O₂N requires 198.1489).

Synthesis of 1-(2-methanol-phenyl)-ethanol (rac)-323 [S6.14; E1].

3-Methylphthalide (rac)-318 (0.421 g, 2.84 mmol) in THF (10 ml) was to LiAlH₄ (0.162 g, 4.36 mmol) in THF (10 ml) at 0°C. The resulting mixture was stirred for 3 hours. The reaction was quenched with KOH (aq) (10 ml), acidified with HCl (aq)
(3M, 10 ml), the organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. To give 1-(2-methanol-phenyl)-ethanol (rac)-323 (0.358 g, 83%), as a white solid mp 56-58°C; Rᵋ [diethyl ether] 0.20; ν_max (CHCl₃)/cm⁻¹ 3020 (OH); δ_H (400 MHz, CDCl₃): 7.45 (1 H, br d, J 7.7, CH; Ar), 7.36-7.23 (3 H, m, 3 × CH; Ar), 5.12 (1 H, q, J 6.5, CHCH₃), 4.76 (1 H, ABq, J 12.1, CH₃OH), 4.60 (1 H, ABq, J 12.1, CH₃OH), 3.09 (2 H, br s, 2 × OH) and 1.55 (3 H, d, J 6.5, CHCH₃). δ_C (100 MHz, CDCl₃): 143.2 and 138.0 (i-C; Ar), 129.8, 128.6, 127.9 and 125.8 (4 × CH; Ar), 67.0 (CHCH₃), 63.7 (CH₂OH) and 22.8 (CHCH₃). (Found MNa⁺, 175.0730; C₉H₁₂O₂Na requires 175.0730).

**Synthesis of 1-(2-methanol-phenyl)-ethanol (S)-323 [S6.14; E2].**

In the same way as S6.14; E1, 3-methylphthalide (S)-318 (25 mg, 0.17 mmol) and LiAlH₄ (10 mg, 0.25 mmol) in THF (5 ml). Gave 1-(2-methanol-phenyl)-ethanol (S)-323 (22 mg, 86%), as a yellow oil; [α]D²⁵ -26.5 (c = 2.2 in CHCl₃), which was spectroscopically identical to that obtained elsewhere.
Section 6: Experiments from Chapter 7

MKR of 1-phenylethanol (rac)-11 using DCC [S7.1].

DCC (0.319 g, 1.55 mmol) was added to a solution of 2-phenylpropanic acid (rac)-111 (0.211 g, 1.40 mmol) in dichloromethane (10 ml) followed by 1-phenylethanol (rac)-11 (0.172 g, 1.40 mmol) in dichloromethane (10 ml). The resulting mixture was stirred over night. The reaction mixture was filtered to remove DCU, the organic layer was extracted with dichloromethane (3 × 25 ml), washed with water (25 ml), dried over MgSO₄ and evaporated under reduced pressure. Gave by crude 1H NMR a mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (ratio anit : syn ~50 : 50) and 2-phenylpropanic anhydride (rac)-anti and (meso)-syn-324 (ratio anit : syn ~50 : 50), (ratio ester : anhydride 7 : 93), which was spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylethanol (rac)-11 using DCC with DMAP [S7.2].

In the same way as S7.1, DCC (3.02 g, 0.015 mol), 2-phenylpropanic acid (rac)-111 (2 g, 0.013 mol), DMAP (0.325 g, 0.0027 mol) and 1-phenylethanol (rac)-11 (1.63 g, 0.013 mol) in dichloromethane (100 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / dichloromethane (1:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (2.834 g, 84%, ratio anit : syn 76 : 24), which was spectroscopically identical to that obtained elsewhere.

Stereospecific synthesis of 1-phenylethyl-2-(4-isobutylphenyl)-propinate (R,R)-anti-248 [S7.3; E1].

In the same way as S7.1, DCC (0.28 g, 1.34 mmol), 2-(4-isobutylphenyl)-propanic acid (R)-114 (0.252 g, 1.22 mmol), DMAP (30 mg, 0.24 mmol) and 1-phenylethanol (R)-11 (0.15 g, 1.22 mmol) in dichloromethane (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-phenylethyl-2-(4-isopropylphenyl)-propinate (R,R)-anti-248 (0.22 g, 58%) [α]D₂⁰ = -14.2 (c 9.8, CHCl₃), which was spectroscopically identical to that obtained elsewhere.
Stereospecific synthesis of 1-phenylethyl-2-(4-isobutylphenyl)-propionate (S,S)-anti-248 [S7.3; E2].

In the same way as S7.1, DCC (0.11 g, 0.53 mmol), 2-(4-isobutylphenyl)-proionic acid (S)-114 (0.1 g, 0.48 mmol), DMAP (18 mg, 0.14 mmol) and 1-phenylethanol (S)-11 (59 mg, 0.48 mmol) in dichloromethane (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / dichloromethane (1:1) 1-phenylethyl-2-(4-isopropylphenyl)-propionate (S,S)-anti-248 (0.112 g, 74%) which was spectroscopically identical to that obtained elsewhere.

Stereospecific synthesis of 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propionate (S,S)-anti-249 [S7.4; E2].

In the same way as S7.1, DCC (0.46 g, 2.25 mmol), 2-(6-methoxy-2-naphthyl)-proionic acid (S)-122 (0.46 g, 2.05 mmol), DMAP (50 mg, 0.41 mmol) and 1-phenylethanol (S)-111 (0.25 g, 2.05 mmol) in dichloromethane (20 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propionate (S,S)-anti-249 (0.49 g, 72%), which was spectroscopically identical to that obtained elsewhere.

Stereospecific synthesis of 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propionate (S,R)-syn-249 [S7.4; E2].

In the same way as S7.1, DCC (0.34 g, 1.67 mmol), 2-(6-methoxy-2-naphthyl)-proionic acid (S)-122 (0.35 g, 1.52 mmol), DMAP (40 mg, 0.30 mmol) and 1-phenylethanol (R)-11 (0.19 g, 1.52 mmol) in dichloromethane (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1 → 7:3) 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propionate (S,R)-syn-249 (0.36 g, 71%), which was spectroscopically identical to that obtained elsewhere.

Stereospecific synthesis of 1-(2-naphthyl)-ethyl-2-phenylbutinate (S,S)-anti-271 [S7.5; E1].

In the same way as S7.1, DCC (0.178 g, 0.86 mmol), 2-phenylbutyric acid (S)-118 (0.129 g, 0.79 mmol), DMAP (20 mg, 0.16 mmol) and 1-(2-naphthyl)-ethanol (S)-261 (0.135 g, 0.79 mmol) in dichloromethane (20 ml). Gave after purification by flash
column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-(2-naphthyl)-ethyl-2-phenylbutinate (S,S)-anti-271 (0.189 g, 76%, >95% d.e.) as a white solid mp 52-55°C; \( R_f \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.73; \([\alpha]_D^{20} = -16.6 \) (c 5.0, CHCl\(_3\)); \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 1728 (C=O); \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.71-7.67 (1H, m, CH; Ar), 7.63 (1H, d, J 8.4, CH; Ar), 7.57-7.53 (1H, m, CH; Ar), 7.39 (1H, brs, CH; Ar), 7.37-7.33 (2H, m, 2 × CH; Ar), 7.21-7.13 (6H, m, CH; Ar and 5 × CH; Ph), 5.94 (1H, q, J 6.6, CHAr), 3.46 (1H, t, J 7.7, CH\(_2\)CH), 2.11-1.98 (1H, m, CH\(_3\)CH\(_2\)H\(_8\)CH), 1.79-1.67 (1H, m, CH\(_3\)CH\(_3\)H\(_8\)CH), 1.50 (3H, d, J 6.6, CH\(_3\)CHAr) and 0.83 (3H, t, J 7.5, CH\(_2\)CH\(_2\)CH); \( \delta_C \) (100 MHz; CDCl\(_3\)) 173.0 (C=O), 139.1, 139.0, 133.1 and 132.8 (4 × i-C; Ar and Ph), 128.5, \(^2\) 128.1, \(^2\) 128.0, \(^1\) 128.0, \(^1\) 127.5, \(^1\) 127.1, \(^1\) 126.0, \(^1\) 125.8, \(^1\) 124.2, \(^1\) 123.8, \(^1\) (12 × CH; Ph and Ar), 72.4 (CHAr), 56.6 (CHPh), 26.4 (CH\(_2\)CH\(_3\)), 22.3 (CH\(_3\)CH\(_3\)) and 12.1 (CH\(_2\)CH\(_3\)); (Found M\(^+\), 318.1618; C\(_{22}\)H\(_{22}\)O\(_2\) requires 318.1614).

**Stereospecific synthesis of 1-(2-naphthyl)-ethyl-2-phenylbutate (R,S)-syn-271 [S7.5; E2].**

In the same way as S7.1, DCC (0.267 g, 1.29 mmol), 2-phenylbutyric acid (R)-118 (0.193 g, 1.18 mmol), DMAP (30 mg, 0.24 mmol) and 1-(2-naphthyl)-ethanol (S)-261 (0.202 g, 1.18 mmol) in dichloromethane (20 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-(2-naphthyl)-ethyl-2-phenylbutinate (R,S)-syn-271 (0.278 g, 74%, >95% d.e.) as a white solid mp 89-90°C; \( R_f \) [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.78; \([\alpha]_D^{20} = -53.9 \) (c 5.0, CHCl\(_3\)); \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 1726 (C=O); \( \delta_H \) (400 MHz; CDCl\(_3\)) 7.83-7.76 (3H, m, 3 × CH; Ar), 7.72 (1H, br s, CH; Ar), 7.49-7.45 (2H, m, 2 × CH; Ar), 7.41 (1H, dd, J 8.5 and 1.7, CH; Ar), 7.35-7.24 (5H, m, 5 × CH; Ph), 6.02 (1H, q, J 6.6, CHAr), 3.52 (1H, t, J 7.9, CH\(_2\)CH), 2.17-2.04 (1H, m, CH\(_3\)CH\(_2\)H\(_8\)CH), 1.86-1.74 (1H, m, CH\(_3\)CH\(_2\)H\(_8\)CH), 1.51 (3H, d, J 6.6, CH\(_3\)CHAr) and 0.86 (3H, t, J 7.5, CH\(_3\)CH\(_2\)CH); \( \delta_C \) (100 MHz; CDCl\(_3\)) 173.3 (C=O), 139.1, 139.0, 133.1 and 132.9 (4 × i-C; Ar and Ph), 128.5, \(^2\) 128.3, \(^1\) 128.0, \(^3\) 127.6, \(^1\) 127.1, \(^1\) 126.2, \(^1\) 126.0, \(^1\) 124.8 and 124.0 (12 × CH; Ph and Ar), 72.6 (CHAr), 53.7 (CHPh), 26.6 (CH\(_2\)CH\(_3\)), 21.9 (CH\(_3\)CH\(_3\)) and 12.2 (CH\(_2\)CH\(_3\)); (Found M\(^+\), 318.1615 C\(_{22}\)H\(_{22}\)O\(_2\) requires 318.1614).
Stereospecific synthesis of 1-phenylethyl-2-methoxy-2-phenylacetate (S,S)-anti-253 [S7.6; E1].

In the same way as S7.1, DCC (38 mg, 0.19 mmol), 2-methoxy-2-phenylacetic acid (S)-120 (28 mg, 0.17 mmol), DMAP (4 mg, 0.03 mmol) and 1-phenylethanol (S)-11 (21 mg, 0.17 mmol) in dichloromethane (15 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-phenylethyl-2-methoxy-2-phenylacetate (S,S)-anti-253 (20 mg, 44%) as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.62; [α]D = +14.0 (c 3.0, CHCl₃); νmax (CHCl₃)/cm⁻¹ 1746 (C=O); δH (400 MHz; CDCl₃) 7.41-7.37 (2H, m, 2 × CH; PhA and/or PhB), 7.35-7.31 (3H, m, 3 × CH; PhA and/or PhB), 7.22-7.18 (3H, m, 2 × CH; PhA and/or PhB), 7.08-7.03 (2H, m, 2 × CH; PhA and/or PhB), 5.92 (1H, q, J 6.6, CHCH₃), 4.80 (1H, s, CHCOO), 3.41 (3H, s, CH₃O) and 1.53 (3H, d, J 6.6, CH₂CH); δC (100 MHz; CDCl₃) 169.8 (C=O), 141.0 and 136.1 (2 × i-C; PhA and PhB), 128.6, 128.5, 128.3, 127.6, 127.3, 125.6 (10 × CH; PhA and PhB), 82.7 (CHCH₃), 73.0 (CHCOO), 57.3 (CH₃O) and 22.2 (CH₃CH); (Found MNH⁺, 288.1593 C₁₇H₂₂O₃N requires 288.1594).

Stereospecific synthesis of 1-phenylethyl-2-methoxy-2-phenylacetate (S,R)-syn-253 [S7.6; E2].

In the same way as S7.1, DCC (34 mg, 0.17 mmol), 2-methoxy-2-phenylacetic acid (S)-170 (25 mg, 0.15 mmol), DMAP (4 mg, 0.03 mmol) and 1-phenylethanol (R)-11 (18 mg, 0.15 mmol) in dichloromethane (15 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) 1-phenylethyl-2-methoxy-2-phenylacetate (S,R)-syn-253 (40 mg, 98%) as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.67; [α]D = +52.8 (c 5.8, CHCl₃); νmax (CHCl₃)/cm⁻¹ 1744 (C=O); δH (400 MHz; CDCl₃) 7.50-7.45 (2H, m, 2 × CH; PhA and/or PhB), 7.41-7.27 (8H, m, 8 × CH; PhA and PhB), 5.95 (1H, q, J 6.6, CHCH₃), 4.80 (1H, s, CHCOO), 3.42 (3H, s, CH₃O) and 1.42 (3H, d, J 6.6, CH₃CH); δC (100 MHz; CDCl₃) 169.9 (C=O), 141.0 and 136.2 (2 × i-C; PhA and PhB), 128.6, 128.5, 128.4, 128.0, 127.1, 126.0 (10 × CH; PhA and PhB), 82.6 (CHCH₃), 73.1 (CHCOO), 57.3 (CH₃O) and 21.7 (CH₃CH); (Found MNH⁺, 288.1597 C₁₇H₂₂O₃N requires 288.1594).
MKR of 1-cyclohexylethanol (rac)-293 using carboxylic acid (rac)-111 [S7.7; E2].

In the same way as S7.1, DCC (0.177 g, 0.86 mmol), 2-phenylpropionic acid (rac)-111 (0.1 g, 0.78 mmol), DMAP (19 mg, 0.16 mmol) and 1-cyclohexylethanol (rac)-293 (0.17 mg, 0.78 mmol) in dichloromethane (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-cyclohexylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-294 (0.138 g, 68%, ratio anti : syn 64 : 36) as an oil, which was spectroscopically identical to that obtained elsewhere.

MKR of 1-cyclohexylethanol (rac)-293 using carboxylic acid (rac)-118 [S7.7; E2].

In the same way as S7.1, DCC (0.151 g, 0.73 mmol), 2-phenylbutyric acid (rac)-118 (0.1 g, 0.67 mmol), DMAP (16 mg, 0.13 mmol) and 1-cyclohexylethanol (rac)-293 (85 mg, 0.67 mmol) in dichloromethane (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-cyclohexylethyl-2-phenylbutinate (rac)-anti and (rac)-syn-302 (0.119 g, 69%, ratio anti : syn 65 : 35) as an oil, which was spectroscopically identical to that obtained elsewhere.

MKR of 1-phenylpropanol (rac)-283 using carboxylic acid (rac)-114 [S7.8].

In the same way as S7.1, DCC (0.167 g, 0.81 mmol), 2-(4-isobutylphenyl)-proponic acid (rac)-114 (0.151 g, 0.73 mmol), DMAP (19 mg, 0.15 mmol) and 1-phenylpropanol (rac)-283 (0.100 g, 0.73 mmol) in dichloromethane (30 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylpropyl-2-(4-isobutylphenyl)-propionate (rac)-anti and syn-325 (0.174 g, 73%, ratio anti : syn 67 : 33) as an oil; Rf [light petroleum spirit (bp 40-60°C) / diethyl ether (1:1)] 0.81; ν_{max} (CHCl3)/cm^{-1} 1728 (C=O); δ_H (400 MHz; CDCl3) 7.34-7.17 (4H, m, 4 × CH; Ph and/or Ar), 7.16-7.03 (5H, m, 5 × CH; Ph and/or Ar), 5.64 (1H, q, J 5.9, CHO), 3.75 (1H, q, J 7.2, CHAr), 2.46 (2H, d, J 7.2 CH2Ar), 1.91-1.65 (3H, m, CHCH2Ar and CH3CH2CHO), 1.50 (3H, d, J 7.2, CH3CHAr), 0.91 (6H, d, J 6.6, CH3CHCH3) and 0.85 (3H, t, J 7.3, CH3CH2CHO); δ_C (100 MHz; CDCl3) 173.8 (C=O), 140.6, 140.4 and 137.6 (3 × i-C; Ph and Ar), 129.2^2 128.1^2 127.4^1 127.3^2 and 126.0^2 (9 × CH; Ph and Ar), 77.3 (CHO), 45.3 (CHAr), 45.0 (CH2Ar), 30.2 (CH2CHO), 29.5 (CHCH2Ar), 22.3^3 (CH3CHCH3), 18.2 (CH3CHAr) and 9.8 (CH3CH2CHO). For minor diastereoisomer (rac)-syn-325: δ_H (400 MHz; CDCl3) 7.34-7.17 (4H, m, 4 × CH; Ph and/or Ar), 7.16-
7.03 (5H, m, 5 × CH; Ph and/or Ar), 5.63 (1H, q, J 5.9, CHO), 3.73 (1H, q, J 7.2, CHAr), 2.46 (2H, d, J 7.2 CH₂Ar), 1.91-1.65 (3H, m, CHCH₂Ar and CH₃CH₂CHO), 1.48 (3H, d, J 7.2, CH₃CHAr), 0.90 (6H, d, J 6.6, CH₃CHCH₃) and 0.69 (3H, t, J 7.5, CH₃CH₂CHO).

### Determining the enantiomeric excess of 1-phenylethanol (S)-11 [S7.9].

In the same way as S7.1, DCC (52 mg, 0.25 mmol), 2-(4-isobutylphenyl)-proionic acid (S)-114 (47 mg, 0.23 mmol), DMAP (6 mg, 0.046 mmol) and 1-phenylethanol (S)-11 (28 mg, ~88% e.e., 0.23 mmol) in dichloromethane (5 ml). Gave 1-phenylethyl-2-(4-isobutylphenyl)-propionate (S,S)-anti-248 (84 % d.e.), which was spectroscopically identical to that obtained elsewhere. Note by crude ¹H NMR all the 1-phenylethanol (S)-11 had reacted.

### MKR of 1-phenylethanol (rac)-11 using pentafluoropyridine [S7.11].

In the same way as S7.1, DCC (0.302 g, 1.47 mmol), 2-phenylpropionic acid (rac)-11 (0.2 g, 1.33 mmol), pentafluoropyridine (0.225 g, 1.33 mmol) and 1-phenylethanol (rac)-11 (0.163 g, 1.33 mmol) in dichloromethane (20 ml). Gave by crude ¹H NMR a mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and (rac)-syn-245 (<5%, ratio anti : syn ~50 : 50), which were spectroscopically identical to that obtained elsewhere.

### MKR of 1-phenylethanol (rac)-11 using carboxylic acid (rac)-111 [T7.1; E1].

In the same way as S7.1, DCC (0.302 g, 1.47 mmol), 2-phenylpropionic acid (rac)-111 (0.2 g, 1.33 mmol), 3,5-luitidine (29 mg, 0.27 mmol) and 1-phenylethanol (rac)-11 (0.163 g, 1.33 mmol) in dichloromethane (20 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylpropionate (rac)-anti and syn-245 (0.192 g, 57%, ratio anti : syn 82 : 18), which were spectroscopically identical to that obtained elsewhere.

### MKR of 1-phenylethanol (rac)-11 using carboxylic acid (rac)-118 [T7.1; E2].

In the same way as S7.1, DCC (0.341 g, 1.65 mmol), 2-phenylbutyric acid (rac)-118 (0.247 g, 1.50 mmol), 3,5-luitidine (0.161 g, 1.50 mmol) and 1-phenylethanol (rac)-11 (0.184 g, 1.50 mmol) in dichloromethane (20 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-
60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylbutinate (rac)-anti and syn-246 (0.206 g, 51%, ratio anti : syn 85 : 15), which were spectroscopically identical to that obtained elsewhere.

**MKR of 1-phenylethanol (rac)-11 using carboxylic acid (rac)-116 [T7.1; E3].**

In the same way as S7.1, DCC (0.334 g, 1.62 mmol), 2-(4-chlorophenyl)propionic acid (rac)-116 (0.272 g, 1.47 mmol), 3,5-luitidine (0.158 g, 1.47 mmol) and 1-phenylethanol (rac)-11 (0.180 g, 1.47 mmol) in dichloromethane (20 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-(4-chlorophenyl)-propionate (rac)-anti and syn-256 (0.243 g, 57%, ratio anti : syn 76 : 24), which were spectroscopically identical to that obtained elsewhere.

**PKR of 1-phenylethanol (rac)-11 using carboxylic acid (S)-122 and (R)-118 [S7.12].**

In the same way as S7.1, DCC (0.918 g, 4.45 mmol), 2-phenylbutyric acid (R)-118 (0.332 g, 2.02 mmol), 2-(6-methoxy-2-naphthyl)-propionic acid (S)-122 (0.466 g, 2.02 mmol), 3,5-luitidine (0.433 g, 4.04 mmol) and 1-phenylethanol (rac)-11 (0.494 g, 4.04 mmol) in dichloromethane (20 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-(4-chlorophenyl)-propionate (rac)-anti and syn-246 (0.255 g, 47%, ratio anti : syn 86 : 14) and an inseparable mixture of 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propionate (S,S)-anti and (S,R)-syn-249 (0.394 g, 58%, ratio anti : syn 82 : 18), which were spectroscopically identical to that obtained elsewhere.

**PKR of 1-phenylethanol (rac)-11 using carboxylic acid (S)-114 and (R)-118 [S7.13].**

In the same way as S7.1, DCC (0.207 g, 1.00 mmol), 2-phenylbutyric acid (R)-118 (75 mg, 0.46 mmol), 2-(4-isobutylphenyl)-propionic acid (S)-114 (94 mg, 0.46 mmol), 3,5-luitidine (98 mg, 0.91 mmol) and 1-phenylethanol (rac)-11 (0.112 g, 0.91 mmol) in dichloromethane (20 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylbutinate (R,R)-anti and (R,S)-syn-246 (68 mg, 55%, ratio anti : syn 83 : 17), 1-phenylethyl-2-(4-isobutylphenyl)-propionate (S,S)-anti and (S,R)-syn-248 (95 mg, 67%, ratio anti : syn 84 : 16), which were spectroscopically identical to that obtained elsewhere.
PKR of 1-phenylethanol (rac)-11 using carboxylic acid (S)-111 and (R)-118 [S7.14].

In the same way as S7.1, DCC (83 mg, 0.40 mmol), 2-phenylbutyric acid (R)-118 (30 mg, 0.18 mmol), 2-phenylproionic acid (S)-111 (27 mg, 0.18 mmol), 3,5-luitidine (39 mg, 0.37 mmol) and 1-phenylethanol (rac)-11 (45 mg, 0.37 mmol) in dichloromethane (10 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylbutinate (R,R)-anti and (R,S)-syn-246 (35 mg, 71%, ratio anti : syn 84 : 16), 1-phenylethyl-2-phenylpropinate (S,S)-anti and (S,R)-syn-245 (33 mg, 72%, ratio anti : syn 83 : 17), which were spectroscopically identical to that obtained elsewhere.

Cross over reaction of 1-(2-naphthyl)-ethanol (S)-261 and 1-phenylethanol (R)-11 using carboxylic acid (S)-122 and (R)-118 [S7.15].

In the same way as S7.1, DCC (0.581 g, 2.81 mmol), 2-phenylbutyric acid (R)-118 (0.210 g, 1.28 mmol), 2-(6-methoxy-2-naphthyl)-proionic acid (S)-122 (0.294 g, 1.28 mmol), 3,5-luitidine (0.274 g, 2.56 mmol), 1-phenylethanol (R)-11 (0.156 g, 1.28 mmol) and 1-(2-naphthyl)-ethanol (S)-261 (0.220 g, 1.28 mmol) in dichloromethane (20 ml). Gave after purification by flash column chromatography on silica gel eluting with light petroleum spirit (bp 40-60°C) / diethyl ether (9:1) an inseparable mixture of 1-phenylethyl-2-phenylbutinate (R,R)-anti-246 (0.123 g, 36%) and 1-(2-naphthly)-ethyl-2-phenylbutinate (R,S)-syn-271 (33 mg, 8%) (total yield from acid (R)-118 44%, ratio anti : syn 82 : 18), and an inseparable mixture of 1-(2-naphthyl)-ethyl-2-(6-methoxy-2-naphthyl)-propionate (S,S)-anti-263 (0.232 g, 54%) and 1-phenylethyl-2-(6-methoxy-2-naphthyl)-propionate (S,R)-syn-249 (54 mg, 11%) (total yield from acid (S)-122 65%, ratio anti : syn 83 : 17), which were spectroscopically identical to that obtained elsewhere.
Section 7: Experiments from Chapter 8

**Synthesis of 2-(4-isobutyl-phenyl)-propionic anhydride (S,S)-anti-327 [T8.2; E1].**

DCC (60 mg, 0.29 mmol) was added to 2-(4-isobutyl-phenyl)-proponic acid (S)-114 (0.100 g, 0.48 mmol) in dichloromethane (5 ml). The resulting mixture was stirred over 2 hours. The reaction mixture was filtered to remove DCU, the organic layer was extracted with dichloromethane (3 × 5 ml), washed with water (5 ml), dried over MgSO₄ and evaporated under reduced pressure. The resulting residue was purified by filtration extracting with pentane to give 2-(4-isobutyl-phenyl)-propionic anhydride (S,S)-anti-327 (85 mg, 89%), as an oil; [α]₀²⁰ = +60.8 (c 3.6, CHCl₃); ν_{max} (CHCl₃)/cm⁻¹ 1811 (C=O, asymm) and 1742 (C=O, symm); δ_H (400 MHz; CDCl₃) 7.08-7.02 (8H, m, 8 × CH; Arₐ and Arₐ), 3.66 (2H, q, J 7.2, 2 × CH), 2.45 (2H, d, J 7.3, 2 × CH₂Ar), 1.91-1.80 (2H, m, 2 × CHCH₂Ar), 1.41 (6H, d, J 7.2, 2 × ArCHCH₃) and 0.89 (12H, d, J 6.7, 2 × CH₃CHCH₃); δ_C (100 MHz; CDCl₃) 170.0² (2 × C=O), 141.0² and 135.8² (4 × i-C; Arₐ and Arₐ), 129.5² and 127.3² (8 × CH; Arₐ and Arₐ), 46.0² (2 × CHAr), 45.0² (2 × CH₂Ar), 30.22 (2× CHCH₂Ar), 22.4² (2 × CH₃CHCH₃) and 17.7² (ArCHCH₃); (Found MNH₄⁺, 412.2851; C₂₆H₃₈NO₂ requires 412.2846).

**Checking the enantiomeric excess of anhydride (S,S)-anti-327 [T8.2; E1 check].**

A mixture of 2-(4-isobutyl-phenyl)-proponic anhydride (S,S)-anti-327 (96 mg, 0.24 mmol, from T8.2; E1), LiOH.H₂O (10 mg, 0.24 mmol) and H₂O₂ (0.07 ml, 3.53 mmol) in THF/water (3:1, 5 ml) was stirred over night. Acidified (3M, 2.5 ml), the organic layer was extracted with dichloromethane (3 × 5 ml), washed with water (5 ml), dried over MgSO₄ and evaporated under reduced pressure. DCC (0.110 g, 0.53 mmol), DMAP (12 mg, 0.10 mmol) and 1-phenylethanol (S)-11 (59 mg, 0.48 mmol) were added to the crude residue in dichloromethane (5 ml). The resulting mixture was stirred over night. The reaction mixture was filtered to remove DCU, the organic layer was extracted with dichloromethane (3 × 5 ml), washed with water (5 ml), dried over MgSO₄ and evaporated under reduced pressure. By crude 1H NMR gave 1-phenylethyl-2-(4-isobutyl-phenyl)-propionate (S,S)-anti-248, which was spectroscopically identical to that obtained elsewhere.
Synthesis of 2-(4-isobutyl-phenyl)-propionic anhydride (scalemic)-anti and (meso)-syn-327 [T8.2; E2].

In the same way as T8.2; E1, DCC (60 mg, 0.29 mmol) and 2-(4-isobutyl-phenyl)-proponic acid (S)-114 (0.100 g, 90% e.e., 0.48 mmol) in dichloromethane (5 ml). Gave 2-(4-isobutyl-phenyl)-proponic anhydride (scalemic)-anti and (meso)-syn-327 (85 mg, 89%, ratio anti : syn 90 : 10), which were spectroscopically identical to that obtained elsewhere.

Checking the enantiomeric excess of anhydride 327 [T8.2; E2 check].

In the same way as T8.2; E1 check, 2-(4-isobutyl-phenyl)-proponic anhydride-327 (96 mg, 0.24 mmol, from T8.2; E2), LiOH.H2O (10 mg, 0.24 mmol) and H2O2 (0.07 ml, 3.53 mmol) in THF/water (3:1, 5 ml). Followed by DCC (0.110 g, 0.53 mmol), DMAP (12 mg, 0.10 mmol) and 1-phenylethanol (S)-11 (59 mg, 0.48 mmol) in dichloromethane (5 ml). Gave by crude 1H NMR 1-phenylethyl-2-(4-isobutyl-phenyl)-propionate (S,S)-anti-248, which was spectroscopically identical to that obtained elsewhere.

Synthesis of 2-(4-isobutyl-phenyl)-propionic anhydride (scalemic)-anti and (meso)-syn-327 [T8.2; E3].

In the same way as T8.2; E1, DCC (60 mg, 0.29 mmol) and 2-(4-isobutyl-phenyl)-proponic acid (S)-114 (0.100 g, 50% e.e., 0.48 mmol) in dichloromethane (5 ml). Gave 2-(4-isopropyl-phenyl)-proponic anhydride (scalemic)-anti and (meso)-syn-327 (85 mg, 89%, ratio anti : syn 63 : 37), which were spectroscopically identical to that obtained elsewhere.

Checking the enantiomeric excess of anhydride 327 [T8.2; E3 check].

In the same way as T8.2; E1 check, 2-(4-isobutyl-phenyl)-proponic anhydride-327 (96 mg, 0.24 mmol, from T8.2; E3), LiOH.H2O (10 mg, 0.24 mmol) and H2O2 (0.07 ml, 3.53 mmol) in THF/water (3:1, 5 ml). Followed by DCC (0.110 g, 0.53 mmol), DMAP (12 mg, 0.10 mmol) and 1-phenylethanol (S)-11 (59 mg, 0.48 mmol) in dichloromethane (5 ml). Gave by crude 1H NMR 1-phenylethyl-2-(4-isopropyl-phenyl)-propionate (S,S)-anti and (R,S)-syn-248 (ratio anti : syn 85 : 15), which were spectroscopically identical to that obtained elsewhere.
Synthesis of 2-(4-isobutyl-phenyl)-propionic anhydride (scalemic)-anti and (meso)-syn-327 [T8.2; E4].

In the same way as T8.2; E1, DCC (60 mg, 0.29 mmol) and 2-(4-isobutyl-phenyl)-proionic acid (S)-114 (0.100 g, 10% e.e., 0.48 mmol) in dichloromethane (5 ml). Gave 2-(4-isobutyl-phenyl)-proionic anhydride (scalemic)-anti and (meso)-syn-327 (81 mg, 85%, ratio anti : syn 52 : 48), which were spectroscopically identical to that obtained elsewhere.

Checking the enantiomeric excess of anhydride 327 [T8.2; E4 check].

In the same way as T8.2; E1 check, 2-(4-isobutyl-phenyl)-proonic anhydride-327 (96 mg, 0.24 mmol, from T8.2; E4), LiOH.H2O (10 mg, 0.24 mmol) and H2O2 (0.07 ml, 3.53 mmol) in THF/water (3:1, 5 ml). Followed by DCC (0.110 g, 0.53 mmol), DMAP (12 mg, 0.10 mmol) and 1-phenylethanol (S)-11 (59 mg, 0.48 mmol) in dichloromethane (5 ml). Gave by crude 1H NMR 1-phenylethyl-2-(4-isobutyl-phenyl)-propionate (S,S)-anti and (R,S)-syn-248 (ratio anti : syn 69 : 31), which were spectroscopically identical to that obtained elsewhere.

Synthesis of 2-(4-isobutyl-phenyl)-propionic anhydride (rac)-anti and (meso)-syn-327 [T8.2; E5].

In the same way as T8.2; E1, DCC (60 mg, 0.29 mmol) and 2-(4-isobutyl-phenyl)-proionic acid (rac)-114 (0.100 g, 0.48 mmol) in dichloromethane (5 ml). Gave 2-(4-isopropyl-phenyl)-proionic anhydride (scalemic)-anti and (meso)-syn-327 (75 mg, 78%, ratio anti : syn 50 : 50), which were spectroscopically identical to that obtained elsewhere.

Checking the enantiomeric excess of anhydride 327 [T8.2; E5 check].

In the same way as T8.2; E1 check, 2-(4-isobutyl-phenyl)-proionic anhydride-327 (96 mg, 0.24 mmol, from T8.2; E5), LiOH.H2O (10 mg, 0.24 mmol) and H2O2 (0.07 ml, 3.53 mmol) in THF/water (3:1, 5 ml). Followed by DCC (0.110 g, 0.53 mmol), DMAP (12 mg, 0.10 mmol) and 1-phenylethanol (S)-11 (59 mg, 0.48 mmol) in dichloromethane (5 ml). Gave by crude 1H NMR 1-phenylethyl-2-(4-isobutyl-phenyl)-propionate (S,S)-anti and (R,S)-syn-248 (ratio anti : syn 61 : 39), which were spectroscopically identical to that obtained elsewhere.
Synthesis of 2-(4-isobutyl-phenyl)-propionic anhydride (scalemic)-anti and (meso)-syn-327 in a NMR tube [T8.2; E2 NMR tube].

In the same way as T8.2; E1, DCC (~2 mg, ~0.01 mmol) and 2-(4-isobutyl-phenyl)-propanic acid (S)-114 (20 mg, 90% e.e., 0.10 mmol) in CDCl₃ (NMR sample). Gave a mixture of 2-(4-isobutyl-phenyl)-propanic anhydride (scalemic)-anti and (meso)-syn-327 (ratio anti : syn 89 : 11) and returned 2-(4-isobutyl-phenyl)-propanic anhydride 114 (ratio anhydride : acid 18 : 82) which were spectroscopically identical to that obtained elsewhere.

Synthesis of 2-(4-isobutyl-phenyl)-propionic anhydride (scalemic)-anti and (meso)-syn-327 on a 10 mg scale [T8.2; E2 10 mg].

In the same way as T8.2; E1, DCC (6 mg, 0.03 mmol) and 2-(4-isobutyl-phenyl)-propanic acid (S)-114 (10 mg, 90% e.e., 0.05 mmol) in dichloromethane (1 ml). Gave 2-(4-isobutyl-phenyl)-propanic anhydride (scalemic)-anti and (meso)-syn-327 (8 mg, 84%, ratio anti : syn 91 : 9), which were spectroscopically identical to that obtained elsewhere.

Synthesis of 2-phenylpropionic anhydride (R,R)-anti-324 [T8.3; E1].

In the same way as T8.2; E1, DCC (82 mg, 0.40 mmol) and 2-phenylpropanic acid (R)-111 (0.100 g, 0.67 mmol) in dichloromethane (5 ml). Gave 2-phenylpropionic anhydride (R,R)-anti-324 (81 mg, 86%), as an oil; [α]D = -101.0 (c 3.2, CHCl₃); νmax(CHCl₃)/cm⁻¹ 1812 (C=O, asymm) and 1742 (C=O, symm); δH (400 MHz; CDCl₃) 7.30-7.24 (6H, m, 6 × CH; Phₐ and Ph₈); 7.15-7.11 (4H, m, 4 × CH; Phₐ and Ph₈), 3.66 (2H, q, J 7.2, 2 × CH) and 1.43 (6H, d, J 7.2, 2 × CH₃); δC (100 MHz; CDCl₃) 169.7 (2 × C=O), 138.6² (2 × i-C; Phₐ and Ph₈), 128.8, 127.6 and 127.5 (10 × CH; Phₐ and Ph₈), 46.4² (2 × CH) and 17.8² (CH₃); (Found MH⁺, 283.2498; C₁₅H₁₉O₃⁺ requires 283.1328).

Synthesis of 2-phenylpropionic anhydride (scalemic)-anti and (meso)-syn-324 [T8.3; E2].

In the same way as T8.2; E1, DCC (82 mg, 0.40 mmol) and 2-phenylpropanic acid (R)-111 (0.100 g, 50% e.e., 0.67 mmol) in dichloromethane (5 ml). Gave 2-phenylpropionic anhydride (scalemic)-anti and (meso)-syn-324 (93 mg, 99%, ratio anti : syn 63 : 37), which were spectroscopically identical to that obtained elsewhere.
Synthesis of 2-phenylpropionic anhydride (rac)-anti and (meso)-syn-324 [T8.3; E3].

In the same way as T8.2; E1, DCC (82 mg, 0.40 mmol) and 2-phenylproponic acid (rac)-111 (0.100 g, 0.67 mmol) in dichloromethane (5 ml). Gave 2-phenylpropionic anhydride (rac)-anti which was spectroscopically identical to that obtained elsewhere and (meso)-syn-324 (74 mg, 79%, ratio anti : syn 50 : 50), \( \Delta H \) (400 MHz; CDCl\(_3\)) 7.37-7.25 (6H, m, \( 6 \times CH \); Ph\(_A\) and Ph\(_B\)), 7.15-7.09 (4H, m, \( 4 \times CH \); Ph\(_A\) and Ph\(_B\)), 3.69 (1H, q, \( J 7.2, CH \)) and 1.43 (6H, d, \( J 7.2, 2 \times CH_3 \)); \( \Delta C \) (100 MHz; CDCl\(_3\)) 169.6\(^2\) (2 \( \times C=O \)), 138.5\(^2\) (2 \( \times i-C; Ph\(_A\) and Ph\(_B\)), 128.7\(^4\) 127.5\(^4\) and 127.4\(^2\) (10 \( \times CH \); Ph\(_A\) and Ph\(_B\)), 46.3\(^2\) (2 \( \times CH \) and 17.7\(^2\) (CH\(_3\)).

Synthesis of 2-phenylbutyric anhydride (S,S)-anti-329 [T8.3; E4].

In the same way as T8.2; E1, DCC (0.113 g, 0.55 mmol) and 2-phenylbutyric acid (S)-118 (0.150 g, 0.91 mmol) in dichloromethane (5 ml). Gave 2-phenylbutyric anhydride (S,S)-anti-329 (0.124 g, 87%), as an oil; [\( \alpha \)]\(^D\) = +92.0 (c 2.8, CHCl\(_3\)); \( \nu_{\max} \) (CHCl\(_3\))/cm\(^{-1}\) 1812 (C=O, asymm) and 1742 (C=O, symm); \( \Delta H \) (400 MHz; CDCl\(_3\)) 7.23-7.17 (6H, m, \( 6 \times CH \); Ph\(_A\) and Ph\(_B\)), 7.07-7.02 (4H, m, \( 4 \times CH \); Ph\(_A\) and Ph\(_B\)), 3.34 (2H, t, \( J 7.5, 2 \times CH \)), 2.01-1.91 (2H, m, \( 2 \times CHCH_2H_2CH_3 \)), 1.72-1.61 (2H, m, \( 2 \times CHCH_2H_2CH_3 \)) and 0.76 (6H, t, \( J 7.5, 2 \times CH_3 \)); \( \Delta C \) (100 MHz; CDCl\(_3\)) 169.2\(^2\) (2 \( \times C=O \)), 137.1\(^2\) (2 \( \times i-C; Ph\(_A\) and Ph\(_B\)), 128.7\(^4\) 128.1\(^4\) and 127.5\(^2\) (10 \( \times CH \); Ph\(_A\) and Ph\(_B\)), 54.0\(^2\) (2 \( \times CH \)), 25.8\(^2\) (2 \( \times CHCH_2 \)) and 11.7\(^2\) (CH\(_3\)). (Found isoureaH\(^+\), 371.2691; C\(_{23}\)H\(_{33}\)N\(_2\)O\(_2\)\(^+\) requires 371.2693).

Synthesis of 2-phenylbutyric anhydride (scalemic)-anti and (meso)-syn-329 [T8.3; E5].

In the same way as T8.2; E1, DCC (75 mg, 0.37 mmol) and 2-phenylbutyric acid (S)-118 (0.100 g, 50% e.e., 0.61 mmol) in dichloromethane (5 ml). Gave 2-phenylbutyric anhydride (scalemic)-anti and (meso)-syn-329 (69 mg, 73%, ratio anti : syn 63 : 37), which were spectroscopically identical to that obtained elsewhere.

Synthesis of 2-phenylbutyric anhydride (rac)-anti and (meso)-syn-329 [T8.3; E6].

In the same way as T8.2; E1, DCC (75 mg, 0.37 mmol) and 2-phenylbutyric acid (rac)-118 (0.100 g, 0.61 mmol) in dichloromethane (5 ml). Gave 2-phenylbutyric anhydride (rac)-anti which was spectroscopically identical to that obtained elsewhere and (meso)-syn-329 (63 mg, 67%, ratio anti : syn 50 : 50), \( \Delta H \) (400 MHz; CDCl\(_3\)) 7.30-7.22 (6H, m, \( 6 \times CH \); Ph\(_A\) and Ph\(_B\)), 7.12-7.08 (4H, m, \( 4 \times CH \); Ph\(_A\) and Ph\(_B\)), 3.41 (2H,
t, J 7.5, 2 × CH), 2.09-1.96 (2H, m, 2× CHCH_2H_2CH_3), 1.80-1.66 (2H, m, 2× CHCH_2H_2CH_3) and 0.82 (6H, t, J 7.5, 2 × CH); δ_ΔC (100 MHz; CDCl_3) 169.0^2 (2 × C=O), 137.1^2 (2 × i-C; Phₐ and Ph₈), 128.7^2, 128.0^4 and 127.5^2 (10 × CH; Phₐ and Ph₈), 54.0^2 (2 × CH), 25.7^2 (2 × CHCH_2) and 11.7^2 (CH₃).

**Synthesis of 2-phenyl-3-methyl-butyric anhydride (R,R)-anti-125 [T8.3; E7].**

In the same way as T8.2; E1, DCC (19 mg, 0.09 mmol) and 2-phenyl-3-methyl-butyric acid (R)-124 (28 mg, 0.16 mmol) in dichloromethane (5 ml). Gave 2-phenylbutyric anhydride (R,R)-anti-125 (14 mg, 53%), as an oil; [α]_D = -31.1 (c 4.6, CHCl₃); ν_max (CHCl₃)/cm⁻¹ 1812 (C=O, asymm) and 1739 (C=O, symm); δ₂H (400 MHz; CDCl₃) 7.26-7.21 (6H, m, 6 × CH; Phₐ and Ph₈), 7.15-7.11 (4H, m, 4 × CH; Phₐ and Ph₈), 3.10 (2H, d, J 10.2, 2 × PhCH), 2.28 (2H, double sepet, J 10.2 and 6.5, 2× PhCHCH), 0.94 (6H, d, J 6.5, 2× CH₃CHCH₃) and 0.60 (6H, d, J 6.5, 2× CH₃CHCH₃); δ₇ (100 MHz; CDCl₃) 168.9^2 (2 × C=O), 136.4^2 (2 × i-C; Phₐ and Ph₈), 128.7, 128.6^4 and 127.6^2 (10 × CH; Phₐ and Ph₈), 60.5^2 (2 × CH), 31.2^2 (2 × CHCH₂), 21.3^2 and 19.4^2 (4 × CH₃); (Found isoureah⁺, 385.2857; C₂₄H₃₇N₂O₂⁺ requires 385.2849).

**Synthesis of 2-phenyl-3-methyl-butyric anhydride (scalemic)-anti and (meso)-syn-125 [T8.3; E8].**

In the same way as T8.2; E1, DCC (35 mg, 0.17 mmol) and 2-phenyl-3-methyl-butyric acid (S)-124 (50 mg, 50% e.e., 0.28 mmol) in dichloromethane (5 ml). Gave 2-phenyl-3-methyl-butyric anhydride (scalemic)-anti and (meso)-syn-125 (30 mg, 63%, ratio anti : syn 66 : 34), which where spectroscopically identical to that obtained elsewhere.

**Synthesis of 2-phenyl-3-methyl-butyric anhydride (rac)-anti and (meso)-syn-125 [T8.3; E9].**

In the same way as T8.2; E1, DCC (69 mg, 0.34 mmol) and 2-phenyl-3-methyl-butyric acid (rac)-124 (0.100 g, 0.56 mmol) in dichloromethane (5 ml). Gave 2-phenyl-3-methyl-butyric anhydride (rac)-anti which was spectroscopically identical to that obtained elsewhere and (meso)-syn-125 (43 mg, 45%, ratio anti : syn 50 : 50), δ₂H (400 MHz; CDCl₃) 7.23-7.16 (6H, m, 6 × CH; Phₐ and Ph₈), 7.11-7.05 (4H, m, 4 × CH; Phₐ and Ph₈), 3.09 (2H, d, J 10.2, 2 × PhCH), 2.22 (2H, double sepet, J 10.2 and 6.5, 2× PhCHCH), 0.95 (6H, d, J 6.5, 2× CH₃CHCH₃) and 0.61 (6H, d, J 6.5, 2× CH₃CHCH₃); δ₇ (100 MHz; CDCl₃) 168.8^2 (2 × C=O), 136.3^2 (2 × i-C; Phₐ and Ph₈), 128.7, 128.6. 
and 127.6^2 (10 × CH; Ph_A and Ph_B), 60.7^2 (2 × CH), 31.1^2 (2 × CHCH_2), 21.2^2 and 19.6^2 (4 × CH_3).

Synthesis of 2-(4-methyl-phenyl)-propionic anhydride (S,S)-anti-330 [T8.3; E10].

In the same way as T8.2; E1, DCC (7 mg, 0.033 mmol) and 2-(4-methyl-phenyl)-propionic acid (S)-112 (9 mg, 0.055 mmol) in dichloromethane (2 ml). Gave 2-(4-methyl-phenyl)-propionic anhydride (S,S)-anti-330 (8 mg, 94%), as an oil; [α]_D^20 = +83.8 (c 1.6, CHCl_3); ν_max (CHCl_3)/cm\(^{-1}\) 1812 (C=O, asymm) and 1743 (C=O, symm); δ_H (400 MHz; CDCl_3) 7.06 (4H, dABq, J 7.9, 4 × CH; Ar_A and Ar_B), 7.01 (4H, dABq, J 7.9, 4 × CH; Ar_A and Ar_B), 3.63 (2H, d, J 7.2, 2 × CH), 2.32 (6H, s, 2× ArCH_3) and 1.41 (6H, d, J 7.2, 2× CH_2CH); δ_C (100 MHz; CDCl_3) 169.9^2 (2 × C=O), 137.1^2 and 135.6^2 (2 × C; Ar_A and Ar_B), 129.4^4 and 127.5^4 (8 × CH; Ar_A and Ar_B), 45.9^4 (2 × CH and 2 × ArCH_3) and 17.8^2 (2 × CHCH_3); (Found MNH_3^+, 327.0083; C_{20}H_{23}NO_3^+ requires 327.1829).

Synthesis of 2-(4-methyl-phenyl)-propionic anhydride (scalemic)-anti and (meso)-syn-330 [T8.3; E11].

In the same way as T8.2; E1, DCC (24 mg, 0.12 mmol) and 2-(4-methyl-phenyl)-propionic acid (S)-112 (32 mg, 50% e.e., 0.19 mmol) in dichloromethane (3 ml). Gave 2-(4-methyl-phenyl)-propionic anhydride (scalemic)-anti and (meso)-syn-330 (29 mg, 95%, ratio anti : syn 66 : 34), which where spectroscopically identical to that obtained elsewhere.

Synthesis of 2-(4-methyl-phenyl)-propionic anhydride (rac)-anti and (meso)-syn-330 [T8.3; E12].

In the same way as T8.2; E1, DCC (64 mg, 0.31 mmol) and 2-(4-methyl-phenyl)-propionic acid (rac)-112 (85 mg, 0.52 mmol) in dichloromethane (5 ml). Gave 2-(4-methyl-phenyl)-propionic anhydride (rac)-anti which was spectroscopically identical to that obtained elsewhere and (meso)-syn-330 (76 mg, 95%, ratio anti : syn 50 : 50), δ_H (400 MHz; CDCl_3) 7.08 (4H, dABq, J 7.9, 4 × CH; Ar_A and Ar_B), 7.01 (4H, dABq, J 7.9, 4 × CH; Ar_A and Ar_B), 3.65 (2H, d, J 7.2, 2 × CH), 2.32 (6H, s, 2× ArCH_3) and 1.41 (6H, d, J 7.2, 2× CH_2CH); δ_C (100 MHz; CDCl_3) 169.8^2 (2 × C=O), 137.0^2 and 135.5^2 (2 × C; Ar_A and Ar_B), 129.3^4 and 127.4^4 (8 × CH; Ar_A and Ar_B), 45.9^4 (2 × CH and 2 × ArCH_3) and 17.7^2 (2 × CHCH_3).
Synthesis of 2-(6-methoxy-2-naphthyl)-propionic anhydride (S,S)-anti-331 [T8.3; E13].

In the same way as T8.2; E1, DCC (54 mg, 0.26 mmol) and 2-(6-methoxy-2-naphthyl)-propionic acid (S)-122 (0.100 g, 0.43 mmol) in dichloromethane (5 ml). Gave 2-(6-methoxy-2-naphthyl)-propionic anhydride (S,S)-anti-331 (45 mg, 47%), as an oil; [α] D 30 = +18.1 (c 3.5, CHCl3); νmax (CHCl3)/cm⁻¹ 1812 (C=O, asymm) and 1743 (C=O, symm); δH (400 MHz; CDCl3) 7.42 (2H, d, J 8.5, 2 × CH; ArA and ArB), 7.41 (2H, d, J 8.8, 2 × CH; ArA and ArB), 7.32 (2H, br s, 2 × CH; ArA and ArB), 7.06 (2H, dd, J 8.5 and 1.8, 2 × CH; ArA and ArB), 7.02 (2H, dd, J 8.8 and 2.5, 2 × CH; ArA and ArB), 6.95 (2H, d, J 2.5, 2 × CH; ArA and ArB), 3.85 (6H, s, 2 × OCH3), 3.71 (2H, q, J 7.2, 2 × CH) and 1.41 (6H, d, J 7.2, 2 × CH2CH); δC (100 MHz; CDCl3) 170.02 (2 × C=O), 157.7, 133.7, 133.6 and 128.8 (8 × i-C; ArA and ArB), 129.2, 127.3, 126.3, 125.8, 119.0 and 105.5 (12 × CH; ArA and ArB), 55.3 (2 × OCH3), 46.3 (CH) and 17.8 (2 × CHCH3); (Found isoureaH⁺, 437.2803; C27H37N2O3⁺ requires 437.2798).

Synthesis of 2-(6-methoxy-2-naphthyl)-propionic anhydride (scalemic)-anti and (meso)-syn-331 [T8.3; E14].

In the same way as T8.2; E1, DCC (54 mg, 0.26 mmol) and 2-(6-methoxy-2-naphthyl)-propionic acid (S)-122 (0.100 g, 50% e.e., 0.43 mmol) in dichloromethane (5 ml). Gave 2-(6-methoxy-2-naphthyl)-propionic anhydride (scalemic)-anti and (meso)-syn-331 (49 mg, 51%, ratio anti : syn 63 : 37), which were spectroscopically identical to that obtained elsewhere.

Synthesis of 2-(6-methoxy-2-naphthyl)-propionic anhydride (rac)-anti and (meso)-syn-331 [T8.3; E15].

In the same way as T8.2; E1, DCC (54 mg, 0.26 mmol) and 2-(6-methoxy-2-naphthyl)-propionic acid (rac)-331 (0.100 g, 0.43 mmol) in dichloromethane (5 ml). Gave 2-(6-methoxy-2-naphthyl)-propionic anhydride (rac)-anti which was spectroscopically identical to that obtained elsewhere and (meso)-syn-122 (39 mg, 41%, ratio anti : syn 50 : 50), δH (400 MHz; CDCl3) 7.43 (2H, d, J 8.5, 2 × CH; ArA and ArB), 7.41 (2H, d, J 8.8, 2 × CH; ArA and ArB), 7.30 (2H, br s, 2 × CH; ArA and ArB), 7.06 (2H, dd, J 8.5 and 1.8, 2 × CH; ArA and ArB), 7.02 (2H, dd, J 8.8 and 2.5, 2 × CH; ArA and ArB), 6.93 (2H, d, J 2.5, 2 × CH; ArA and ArB), 3.85 (6H, s, 2 × OCH3), 3.71 (2H, q, J 7.2, 2 × CH) and 1.40 (6H, d, J 7.2, 2 × CH2CH); δC (100 MHz; CDCl3) 170.02 (2 × C=O), 157.6, 133.7, 133.6 and 128.8 (8 × i-C; ArA and ArB), 129.1, 127.2, 126.2, 331
125.8, 2 119.0 and 105.5 (12 × CH; Ar_A and Ar_B), 55.3 (2 × OCH_3), 46.3 (CH) and 17.7 (2 × CHCH_3).

**Synthesis of 2-phenoxypropionic anhydride (S,S)-anti-332 [T8.3; E16].**

In the same way as T8.2; E1, DCC (25 mg, 0.12 mmol) and 2-phenoxypropionic acid (S)-328 (34 mg, 0.20 mmol) in dichloromethane (3 ml). Gave 2-phenoxypropionic anhydride (S,S)-anti-332 (30 mg, 93%), as an oil; [α]_D^20 = -50.0 (c 6.0, CHCl_3); ν_max (CHCl_3)/cm^-1 1833 (C=O, asymm) and 1758 (C=O, symm); δ_H (400 MHz; CDCl_3) 7.18 (4H, t, J 7.6, 4 × CH; Ph_A and Ph_B), 6.93 (2H, t, J 7.6, 2 × CH; Ph_A and Ph_B), 6.75 (4H, d, J 7.6, 4 × CH; Ph_A and Ph_B), 4.71 (2H, q, J 7.0, 2 × CH) and 1.55 (6H, d, J 7.0, 2 × CH_3CH); δ_C (100 MHz; CDCl_3) 167.6 (2 × C=O), 157.0 (2 × i-C; Ar_A and Ar_B), 129.6, 2 122.1 and 115.1 (10 × CH; Ph_A and Ph_B), 72.6 (2 × CH) and 17.9 (2 × CH_3); (Found isoureaH^+, 373.2491; C_{22}H_{33}N_2O_3^+ requires 373.2485).

**Synthesis of 2-phenoxypropionic anhydride (scalemic)-anti and (meso)-syn-332 [T8.3; E17].**

In the same way as T8.2; E1, DCC (25 mg, 0.12 mmol) and 2-phenoxypropionic acid (S)-328 (34 mg, 50% e.e., 0.20 mmol) in dichloromethane (3 ml). Gave 2-phenoxypropionic anhydride (scalemic)-anti and (meso)-syn-332 (27 mg, 84%, ratio anti : syn 63 : 37), which where spectroscopically identical to that obtained elsewhere.

**Synthesis of 2-phenoxypropionic anhydride (rac)-anti and (meso)-syn-332 [T8.3; E18].**

In the same way as T8.2; E1, DCC (54 mg, 0.26 mmol) and 2-phenoxypropionic acid (rac)-328 (72 mg, 0.43 mmol) in dichloromethane (5 ml). Gave 2-phenoxypropionic anhydride (rac)-anti which was spectroscopically identical to that obtained elsewhere and (meso)-syn-332 (66 mg, 97%, ratio anti : syn 50 : 50), δ_H (400 MHz; CDCl_3) 7.19 (4H, t, J 7.6, 4 × CH; Ph_A and Ph_B), 6.94 (2H, t, J 7.6, 2 × CH; Ph_A and Ph_B), 6.80 (4H, d, J 7.6, 4 × CH; Ph_A and Ph_B), 4.75 (2H, q, J 7.0, 2 × CH) and 1.52 (6H, d, J 7.0, 2 × CH_3CH); δ_C (100 MHz; CDCl_3) 167.4 (2 × C=O), 157.0 (2 × i-C; Ar_A and Ar_B), 129.7, 2 122.2 and 115.0 (10 × CH; Ph_A and Ph_B), 72.6 (2 × CH) and 17.8 (2 × CH_3).

In the same way as T8.2; E2 NMR tube, DCC (~2 mg, ~0.01 mmol) and 2-phenyl-3,3,3-trideuterio-propionic anhydride ($R$)-333 (~5 g, ~0.03 mmol) in CDCl$_3$. Gave 2-phenyl-3,3,3-trideuterio-propionic anhydride ($R,R$)-anti-334 characteristic feature $\delta_H$ (400 MHz; CDCl$_3$): 3.66 (2H, s, 2 $\times$ CH).

Synthesis of 2-(4-isobutyl-phenyl)-propionic anhydride (rac)-anti and (meso)-syn-327 using EDAC [S8.2; E1].

1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDAC) (46 mg, 0.24 mmol) was added to a solution of 2-(4-isobutyl-phenyl)-proponic acid (rac)-114 (0.100 g, 0.48 mmol) in dichloromethane (5 ml). The resulting mixture was stirred over night. The reaction was quenched with water (10 ml), the organic layer was extracted with dichloromethane (3 $\times$ 10 ml), dried over MgSO$_4$ and evaporated under reduced pressure. Gave 2-(4-isobutyl-phenyl)-propionic anhydride (rac)-anti and (meso)-syn-327 (ratio ant : syn 50 : 50), which where spectroscopically identical to that obtained elsewhere.

Synthesis of 2-(4-isobutyl-phenyl)-propionic anhydride ($S,S$)-anti-114 using EDAC [S8.2; E2].

In the same way as S8.2; E1, EDAC (56 mg, 0.29 mmol) and 2-(4-isobutyl-phenyl)-proponic acid (rac)-114 (0.100 g, 0.48 mmol) in dichloromethane (5 ml). Gave 2-(4-isopropyl-phenyl)-propionic anhydride (scalemic)-anti and (meso)-syn-327 (ratio ant : syn 75 : 25), which where spectroscopically identical to that obtained elsewhere.
Publications

From Chapter 2:


From Chapter 3:

From Chapter 4:


From Chapter 5:


From Chapter 7:


From Chapter 8:

References

Anna Andreou, BSc Project Report, The University of Hull, 2008.