ASYMMETRIC INDUCTION IN REACTIONS OF CHIRAL CARBOXYLIC ESTERS AND SILYL ENOL ETHERS

THESIS

Submitted in fulfilment of the
requirements for
the degree of
DOCTOR OF PHILOSOPHY
of Rhodes University

by

MELANIE DARYL EVANS

December 1997

Department of Chemistry
Rhodes University
Grahamstown

CONTENTS

ACKNOWLEDGEMENTS

First and foremost, I would like to thank Prof. Kaye for all that I have learnt from his extensive chemical knowledge which has constantly encouraged me while under his supervision, as well as for his seemingly endless assistance and patience. It was all much appreciated.

For all the technical assistance I obtained, I would like to thank Prof. J. A. Boeyens and Leanne Cooke (from the University of the Witwatersrand) for the X-ray crystallographic analysis they carried out and secondly, Prof. P. Boshoff (of the Cape Technikon Mass Spectrometry Unit) for all the high resolution mass spectrometry he carried out. Thanks must also go to the technical staff at the Chemistry Department, such as Aubrey Sonemann who ran all my low resolution mass spectra and solved many a technical problem, Johan Buys the storeman, Andy Soper for NMR support and Andre Adriaan the glass blower. The academic staff and the secretaries were also always there in times of need.

I would like to thank all my friends and colleagues, both at University and at work, for their support, encouragement and camaraderie, with special thanks to Warner, Ross, Ruth, Cathy, Jannie and Chris. I have especially appreciated the assistance of my lab partner, Justin Hagemann, both in and out the laboratory and for proof-reading my thesis.

Finally, I would like to thank my family and Cliff for all their support throughout my studies.

ABSTRACT

Several camphor and pinane derivatives have been synthesised and evaluated for use as chiral auxiliaries in asymmetric synthesis. Various blocking groups have been attached to the camphor skeleton in attempts to improve stereofacial selectivity; these include α-methoxybenzyl and xylyl groups, and novel stereoisomeric ketal moieties derived from *meso*- and (*R,R*)-(-)-2,3-butanediol.

Benzylation reactions carried out on the lithium enolates of ester derivatives of the camphor-derived chiral auxiliaries afforded α-benzylated products in 5-60% diastereomeric excess. Stereochemical aspects have been explored using high resolution NMR, X-ray crystallographic and computer modelling techniques, and hydrolysis of selected α-benzylated products has permitted the diastereoselective bias to be confirmed. Opposite configurations at the new stereogenic centre are clearly favoured by the xylyl and ketal blocking groups - an observation rationalised in terms of the presence or absence of chelating potential in the blocking group. Baylis-Hillman reactions carried out on a series of specially prepared camphor-derived acrylic esters containing the ketal blocking group exhibited both low diastereoselectivities (0-30% d.e.) and very long reaction times.

Chiral silyl enol ethers, synthesised using both pinane and camphor derivatives as chiral auxiliaries, showed up to 20% diastereomeric excess in MCPBA oxidation, alkylation and Mukaiyama reactions. Attempts to bring the prochiral centre in the silyl enol ether substrates closer to the chiral auxiliary, and thus improve the stereofacial selectivity, proved unsuccessful. The silyl enol ether derivatives, however, display interesting fragmentation patterns in their electron impact mass spectra, which were investigated using a combination of high resolution MS, comparative low resolution MS and metastable peak analysis.

INTRODUCTION

1.1 Asymmetric Synthesis

1.1.1 Definition of asymmetric synthesis

Asymmetric synthesis has been defined as :-

"a reaction in which an achiral unit in an ensemble of substrate molecules is converted by a chiral unit in such a manner that the stereoisomeric products are produced in unequal amounts".[1]

There are five main methods of carrying out these types of reactions,[2, 3] *viz.*,

a) first-generation - substrate-controlled methods;

b) second-generation - auxiliary-controlled methods;

c) third-generation - reagent-controlled methods;

d) fourth-generation - catalyst-controlled methods;

e) beyond the fourth generation - asymmetric amplification;

a) *First-generation - substrate-controlled methods*

These methods involve reactions on homochiral compounds. Such compounds are obtained from the chiral pool, which consists of compounds synthesised by living organisms, and include sugars, amino acids, terpenes and steroids. A new chiral centre is typically formed under the influence of an adjacent stereogenic centre in the substrate.

For example, starting from (-)-camphor (**1**) (see Figure 1), a number of new products containing new chiral centres have been synthesised. These include (-)-β-santalene (**2**), (+)-ylangocamphor (**3**), (+)-copacamphor (**4**), (-)-sativene (**5**) and (-)-copacamphene (**6**).[4]

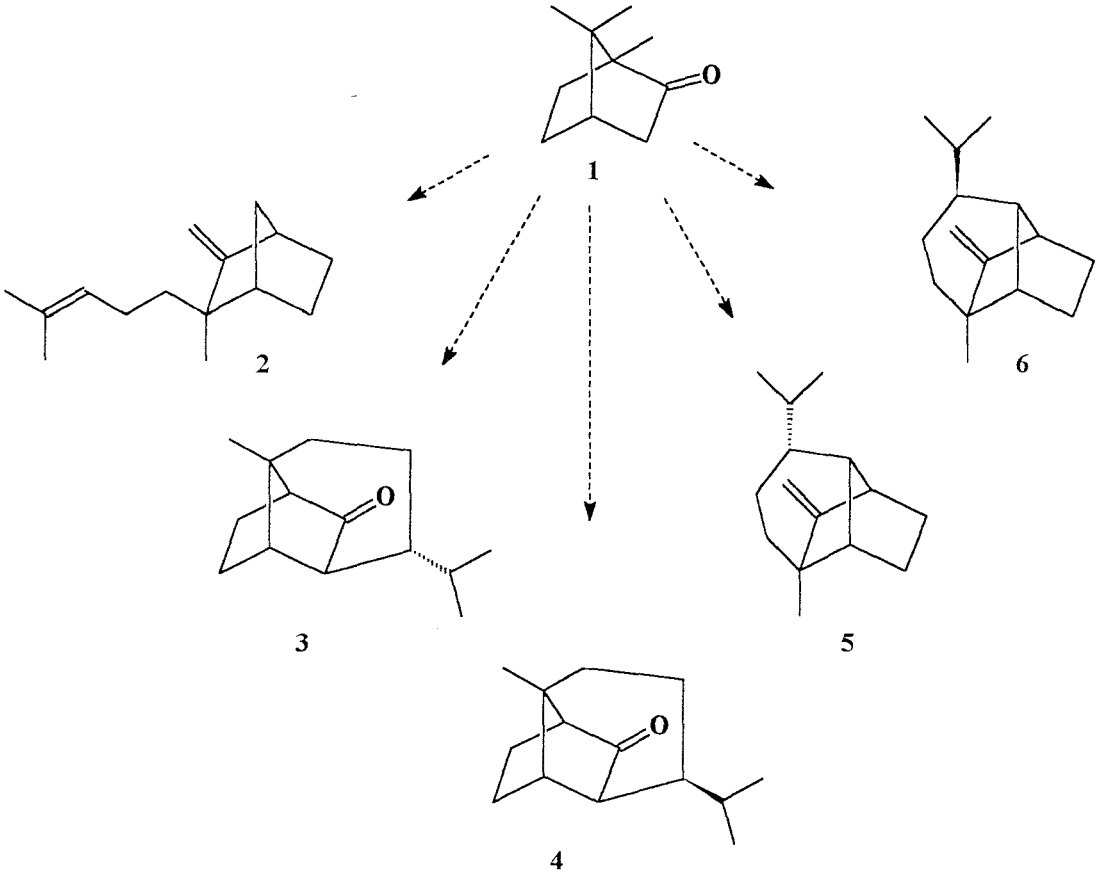


FIGURE 1. Compounds synthesised stereospecifically from (-)-camphor (**1**).

b) *Second-generation - auxiliary-controlled methods*

These methods involve three steps (see Figure 2):-

i) attachment of the prochiral substrate to a chiral auxiliary;

ii) reaction of the modified substrate to form a new chiral centre; and

iii) removal of the chiral auxiliary without racemisation of the chiral product.

This approach has the advantage that the chiral auxiliary can be recovered and re-cycled. In principle, diastereomers formed in the second step can be separated because, unlike enantiomers, they may be expected to have different chemical and physical properties. However, this method does suffer from the disadvantage that two extra steps are required.

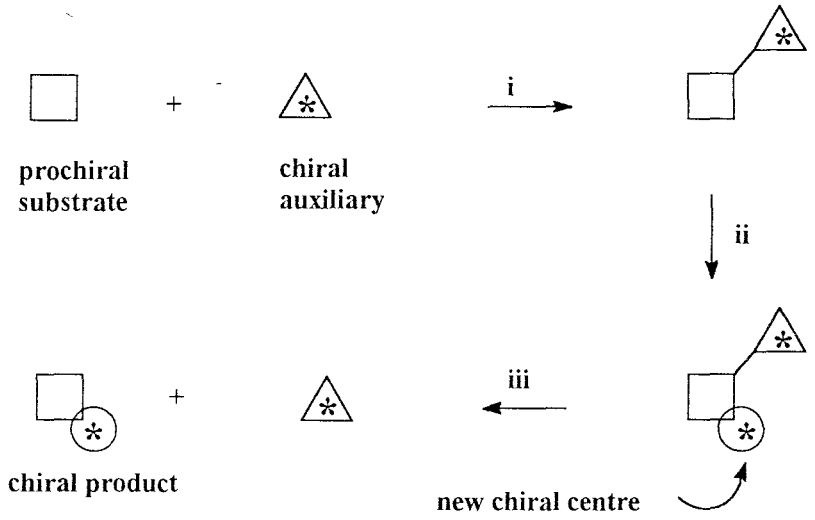
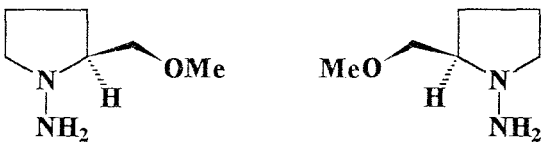


FIGURE 2. A schematic representation of asymmetric synthesis using chiral auxiliaries.

There are a number of requirements for a good chiral auxiliary.[5]

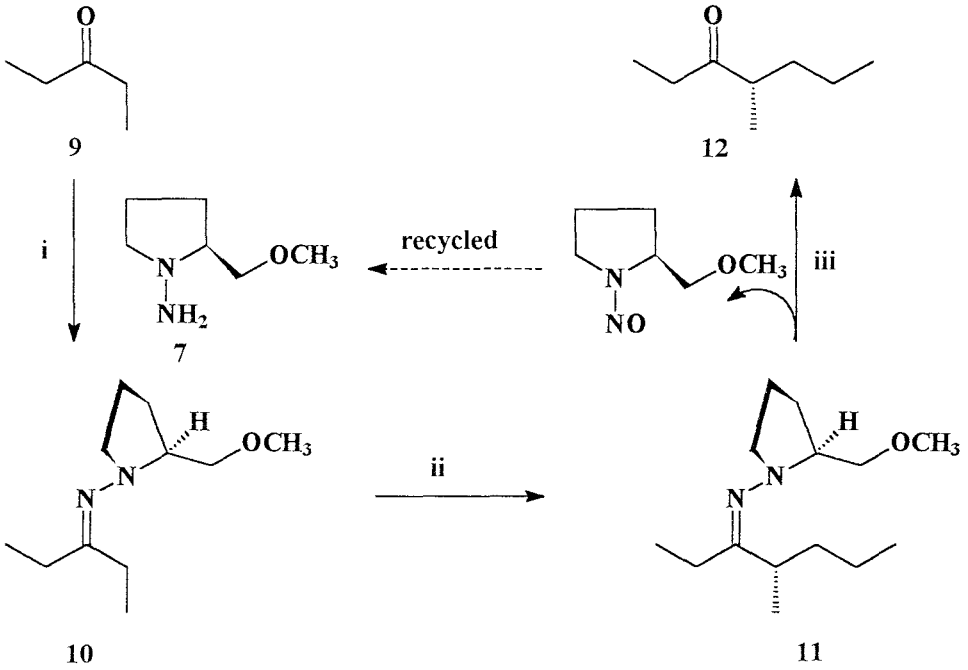
1) It should be available in both enantiomeric forms, to permit selective synthesis of either enantiomeric product.
2) It must induce high stereoselectivity.
3) Its derivatives should preferably be crystalline to facilitate purification of the diastereomeric products.
4) Cleavage of the chiral auxiliary should afford the required enantiomer in high yield, without racemization.
5) The chiral auxiliary should be recovered in high yields.

(*S*)-(-)-1-Amino-2-methoxymethylpyrrolidine (*S*AMP) (**7**) and (*R*)-(+)-1-amino-2-methoxymethylpyrrolidine (*R*AMP) (**8**) are chiral auxiliaries which have been developed by Enders *et al.*[6]



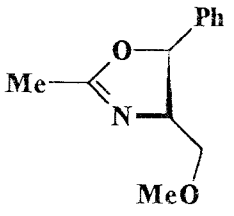
***S*AMP** **7** ***R*AMP** **8**

They have been used in C-C bond-forming reactions which proceed *via* metallated hydrazone enolate equivalents. Scheme 1 depicts the asymmetric synthesis of an α-alkylated ketone (**12**).[7] Firstly the hydrazone derivative (**10**) of the ketone (**9**) is formed, and its lithium enolate equivalent is then alkylated to form the intermediate (**11**). Finally, removal of the chiral auxiliary, which can be recycled, affords the required ketone, in this case, in greater than 97% e.e. These auxiliaries have also been used in the synthesis of chiral aldehydes, β-ketols and β-keto esters.[8]

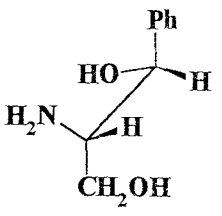


SCHEME 1. Reagents: i) 60 °C;
ii) LDA, Et_2O, 0 °C; *n*-C_3H_7I, -110 °C;
iii) O_3, CH_2Cl_2, -78 °C.

Another example of auxiliary-mediated asymmetric synthesis is the approach developed by Meyers *et al.*,[9] which involves the use of chiral oxazolines, such as the oxazoline (**13**), [prepared from (1*S*, 2*S*)-(+)-1-phenyl-2-amino-1,3-propanediol (**14**)]. These oxazolines are used in the synthesis of chiral acids, esters, lactones, alcohols, thiiranes, dihydropyridines and biaryls.[10]



13



14

c) *Third-generation - reagent-controlled methods*

In this approach, an achiral substrate is converted into a chiral product using chiral reagents. A very efficient example, which has been applied in asymmetric epoxidation reactions, was developed by Sharpless *et al.*[11] This reaction involves the use of optically pure diethyl tartrate (or its derivatives), titanium tetraisopropoxide and *t*-butyl hydroperoxide, and requires the substrate (**15**) to have an allylic hydroxyl group available for coordination. For a given tartrate enantiomer, the stereochemistry of the products (**16**) or (**17**) can be predicted, as delivery of oxygen can only occur from one face (Figure 3). Reactions with other substrate-types have been carried out successfully using the Sharpless methodology,[12] Applications include the kinetic resolution of racemic allylic alcohols [13] and β-hydroxy amines.[14]

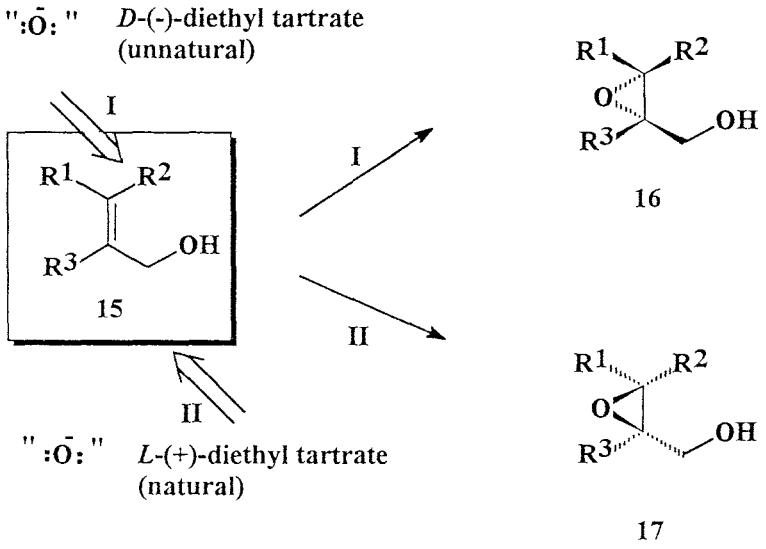
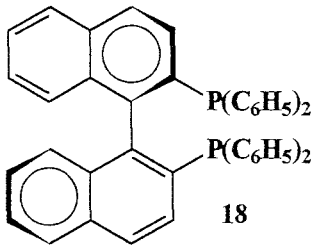


FIGURE 3.

d) *Fourth-generation - catalyst-controlled methods*

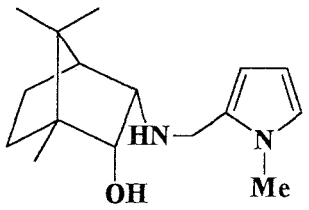
These methods involve the reaction of a prochiral substrate in the presence of a chiral catalyst, to produce a chiral product. Enzymes, of course, are naturally occurring chiral catalysts - Nature's method of carrying out asymmetric synthesis. (+)-Bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) (**18**) is an axially chiral ligand, which is also available as the (-)-enantiomer.[15, 16] Complexes of BINAP with metals, such as rhodium and ruthenium, are very good catalysts in asymmetric hydrogenation reactions.[17, 18]



18

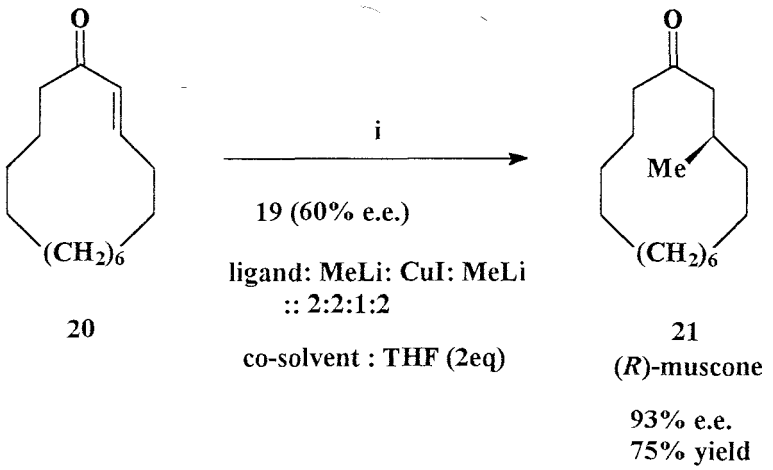
e) *Beyond the fourth generation - asymmetric amplification*

Asymmetric amplification is the term used to define a process in which the product is formed in greater optical purity than the chiral auxiliary used. One such case is the synthesis of (*R*)-(-)-muscone (**21**) (Scheme 2).[19] This product is formed by the methylation of (*E*)-cyclopentadec-2-ene (**20**) *via* an alkoxydimethyl cuprate derived from (-)-3-[(1-methylpyrrol-2-yl)methylamino]-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (**19**). Investigations of these effects are still in their infancy.



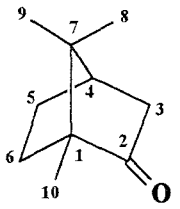
19

In the synthesis, various factors had to be optimised to obtain the best yields and the best stereocontrol. These factors included the choice of co-solvent,[20] the nature of the camphor derivative,[21] the ratios of the reagents and the enantiomeric purity of the camphor derivative.[22] This is a good example of asymmetric amplification, as the product was obtained in 93% e.e. using a ligand with an optical purity of only 60%. Alkylation is proposed to occur *via* a dimeric copper complex. The amplification obtained has been attributed to the difference in chemical properties between the intermediate diastereomeric, dinuclear complexes or between the homochiral and heterochiral dimeric copper complexes.



SCHEME 2. Reagents: i) Chiral ligand (19), MeLi, CuI, toluene, -78°C.

1.2 The Use of Camphor in Asymmetric Synthesis



22

Camphor presents many advantages in the synthesis of chiral auxiliaries. These include its availability in both (+)-and (-)- enantiomeric forms [(**1**) and (**22**) respectively], and the fact that it has a very rigid bicyclic skeleton, with steric bulk being provided by the 8-, 9- and 10- methyl groups. Moreover, functionalities can be introduced directly or indirectly at C-2, C-3, C-5, C-8, C-9 and C-10, while the C(1)-C(2) bond and the C(2)-C(3) bond of the camphor skeleton can be cleaved.[23] In fact, it has been said that "No substance known to us suffers rearrangement of its parts and undergoes a complete change of type more readily than does camphor..."[24]

Mackenzie *et al.*[25, 26] carried out some of the first reactions in which the camphor skeleton was used as a chiral auxiliary, by reacting bornyl α-keto esters with Grignard reagents to form optically active α-hydroxyacids. However, it was Prelog *et al.*[27] who first suggested that the asymmetric induction was due to steric hindrance in the transition state and who carried out Grignard reactions on α-keto esters of borneol and its derivatives.

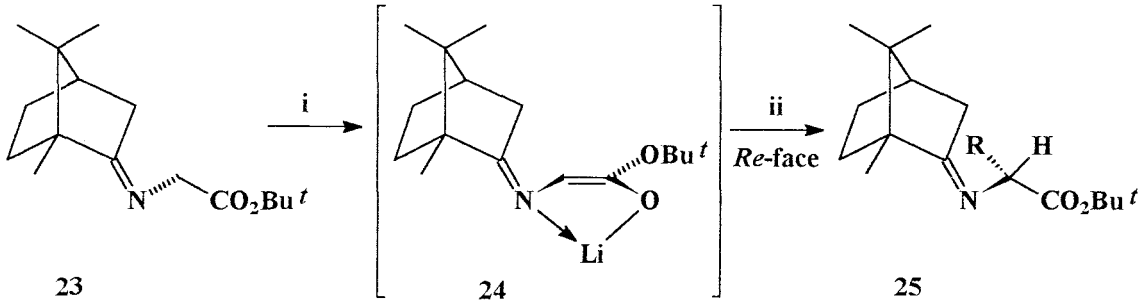
Since these earlier studies, many reactions have been carried out using camphor-derived chiral auxiliaries. These include:- the reduction of deuterated aldehydes using isobornyloxymagnesium bromide;[28] aldol condensations on bornyl esters;[29] Reformatsky reactions on bornyl bromo esters;[30] Baylis-Hillman reactions on bornyl acrylates;[31] and various reactions on bornyl silicon derivatives, including Mukiyama and alkylations[32] and MCPBA oxidations,[33] to name a few.

1.2.1 Chiral auxiliaries obtained from camphor and its derivatives

In a number of cases, camphor itself has been used as a chiral auxiliary. To improve the asymmetric induction obtained, various blocking groups have been added to the camphor skeleton. In other words, conformationally rigid derivatives have been developed, in which one diastereotopic face of the prochiral centre is sterically shielded.

1.2.1.1 Camphor as a chiral auxiliary

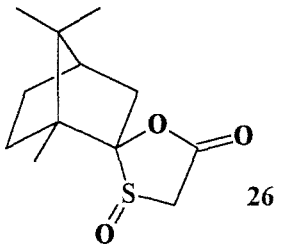
Camphor-derived imines were first used as intermediates in asymmetric alkylation reactions by McIntosh *et al.*[34] The condensation of amines and camphor yielded exclusively (*E*)-imines. Asymmetric alkylation of the *t*-butyl glycinate imine derivative (**23**) (Scheme 3) was proposed to occur *via* the enolate intermediate (**24**) in which attack occurs from the *Re*-face yielding the (*R*)-alkylated product (**25**) with high stereoselectivity.[35] Alkylation reactions have also been carried out on benzylamine-derived imines (36 - 90% d.e.)[36] and 1-(aminomethyl)naphthalene-derived imines (20 - 64% d.e.).[37] Other transformations involving imines derived from camphor include asymmetric allylation reactions (3 - 90% d.e.)[38] and asymmetric aldol reactions.[39]



23 24 25

SCHEME 3. Reagents: i) LDA, THF, -78 °C;
ii) RX, HMPA.

Camphor has also been used as a chiral auxiliary in the synthesis of α-aryl thioglycolic acid derivatives *via* Pummerer reactions of oxathiolanone derivatives, such as (**26**), with reasonable diastereoselectivity.[40]

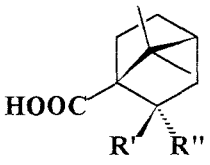


26

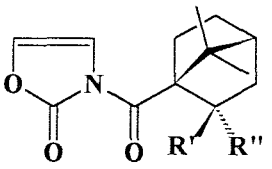
1.2.1.2 Ketopinic acid as a chiral auxiliary

Kunieda *et al.* have used (+)-ketopinic acid (**27a**) and (-)-ketopinic acid[41] as chiral auxiliaries in reactions of oxazolone derivatives.[42] Thus, the oxazolone (**28a**) underwent methoxybromination addition reactions with excellent regioselectivity and up to 90% d.e. This reaction has been used in the synthesis of *vic*-amino alcohols, such as (2*S*, 3*R*)-3-hydroxyglutamic acid and (+)-statine. Ether derivatives of ketopinic acid, such as (**27b**), have also been synthesised for use in methoxybromination and methoxyselenylation addition reactions.[43] Interestingly, the addition products of methoxybromination and methoxyselenylation reactions formed with the opposite π-facial selectivity. The best stereocontrol was obtained using the chiral auxiliary (**27b**), the addition products being obtained in up to 96% d.e.

a) R', R'' = O
b) R' = $O(CH_2)_2OCH_3$
R'' = H



27

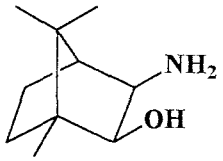


28

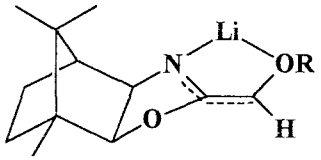
1.2.1.3 A camphor-derived *exo,exo*-amino alcohol as a chiral auxiliary

3-*Exo*-amino-2-*exo*-hydroxy camphor[44] (**29**) has been used as a chiral auxiliary to prepare oxazoline intermediates,[45] which have been alkylated in up to 88% d.e. The structure of the intermediate (**30**) of the oxazoline was based on models and supported by the stereochemistry of the products. Because the stereoselectivities of the reaction with different substrates were so similar, it was suggested that the stereocontrol is due to the stereochemistry of the anion intermediate (**30**).

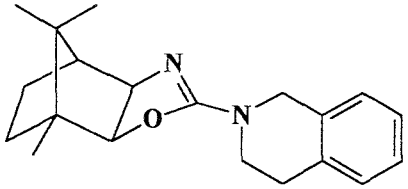
The amino alcohol (**29**) has also been used to prepare oxazolines, such as (**31**).[46] Asymmetric alkylation of these oxazolines using Grignard reagents, has been achieved with moderate stereoselectivity, and the reaction has been extended to the synthesis of (+)-corlumine, (+)-bicuculline, (+)-egenine and (+)-corytensine.[47] The chiral auxiliary (**29**) has also been used in the synthesis of optically active heterohelicines.[48]



29



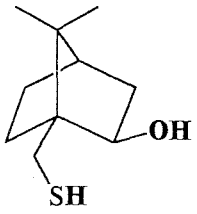
30



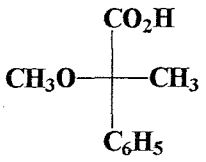
31

1.2.1.4 10-Mercaptoisoborneol and 10-mercaptoborneol derivatives as chiral auxiliaries

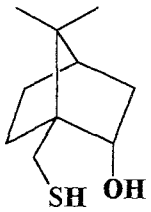
The chiral auxiliary, 10-mercaptoisoborneol (**32**) was first used as a chiral auxiliary by Eliel *et al.* to prepare a hemithioacetal intermediate,[49] which underwent a Grignard reaction to afford atrolactic acid methyl ether (**33**) in 97% e.e.



32

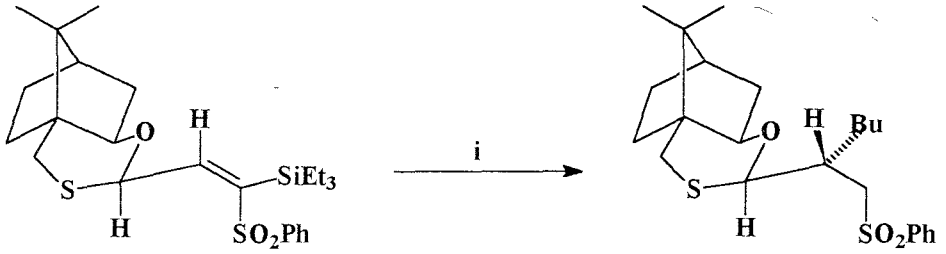


33



34

The chiral auxiliary (**32**) was also used to achieve stereocontrol in "heteroconjugate addition" reactions of a hemithioacetal derivative.[50] These reactions were found to be dependent on the solvent and the presence of salts, the best stereocontrol being obtained when the triethylsilyl hemithioacetal (**35**) was treated with BuLi in the presence of LiBr in Et_2O, to yield the alkylated product (**36**) in 98% d.e. (Scheme 4). Chelation of the Li cation with the hemithioacetal oxygen atom is presumed to direct attack by the nucleophile from the "back" of the double bond. This was confirmed by the synthesis of (+)-citronellal in 98% e.e.



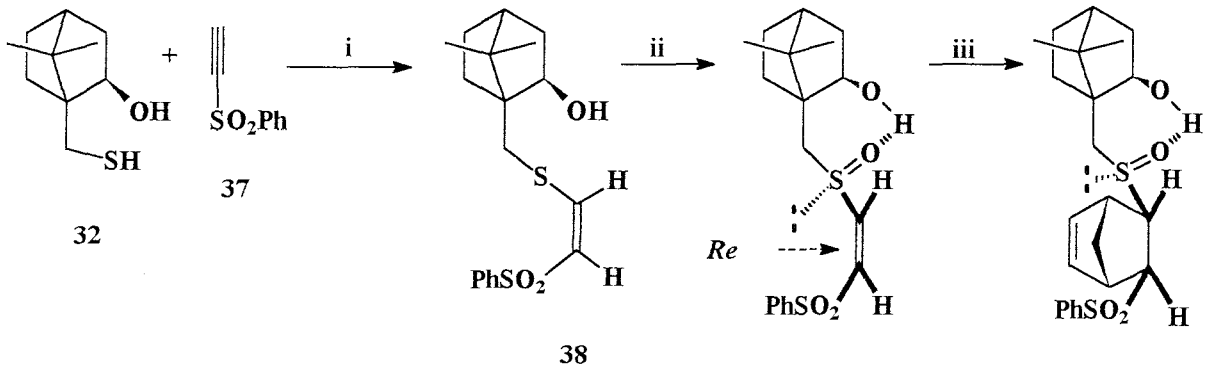
35 36

SCHEME 4. Reagents: i) BuLi, LiBr-Et_2O; *n*-Bu_4NF.

The mercapto chiral auxiliaries (**32**) and (**34**) have both been used in asymmetric Diels-Alder reactions by De Lucchi *et al.* (Scheme 5).[51, 52] Addition of the chiral auxiliaries to alkynyl sulfones, such as (**37**) yielded the required (*Z*)-adducts, *e.g.* (**38**) (Scheme 5), which were then oxidised to the corresponding sulfoxide using MCPBA. The high stereoselectivity obtained in the oxidation was attributed to be due to hydrogen bonding between the hydroxyl group on the chiral auxiliary and the oxidant. The new, chiral, sulfoxide sulfur was assigned the (*R*)-configuration , as shown for the sulfoxide (**39**), since such hydrogen bonding should direct oxidation to the same face as the hydroxyl group. When the oxidation was carried out in polar solvents, such as MeOH, poorer stereoselectivities were observed due to decreased hydrogen bonding. When the borneol-derived auxiliary (**34**) was used instead of the isoborneol-derived auxiliary (**32**), lower stereoselectivities were obtained in the oxidation step, which was suggested to be because of the less favourable geometry of the hydroxyl group for hydrogen bonding with the oxidant.

The Diels-Alder reactions were carried out using cyclopentadiene and the (*Z*)-alkenes (**38**) and (**39**), but low stereoselectivities were obtained with the former. When diastereomeric mixtures of sulfoxides, such as (**39**), were reacted, the products, *e.g.* (**40**), were obtained in the same ratios as the substrate sulfoxides; for example, when the substrate was an 80% d.e. mixture, the Diels-Alder products were also obtained as an 80% d.e. mixture. However, when the diastereomerically pure sulfoxide (**39**) was used, only the diastereomeric product (**40**) was obtained in 98% d.e.

From this, it was deduced that chirality was directed by the asymmetric sulfoxide group. The chiral auxiliary was removed relatively easily from the Diels-Alder adducts, using DBU (1,8-diazabicyclo[5.4.0]undec-7-ene).

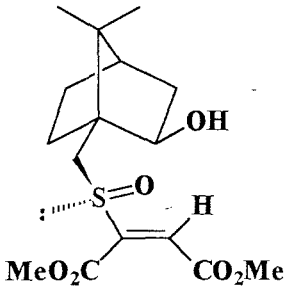


32 37 38 39 40

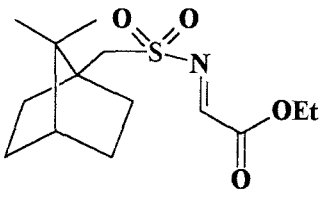
SCHEME 5. Reagents: i) MeCN, morpholine, 0 °C;
ii) MCPBA, CH_2Cl_2, 0 °C;
iii) cyclopentadiene,$CDCl_3$, 5 °C.

When the conformational rigidity provided by hydrogen bonding was relaxed by the use of polar solvents, no change in the ratios of products was observed, indicating that hydrogen bonding is not a requirement for stereocontrol in this Diels-Alder reaction. The orientation of the hydroxy group on the camphor skeleton was also shown to play no role in the stereoselectivity of the reaction, as there was no change in the stereoselectivity when either chiral auxiliary (**32**) or (**34**) was used. The stereochemistry of the double bond, however, was shown to play a role in the control of the reaction, as (*E*)-alkene derivatives of the sulfoxide (**39**) produced a complex mixture of products.

Diels-Alder reactions were also carried out by Koizume *et al.* on the isoborneol-derived maleate (**41**) to prepare chiral precursors for the synthesis of (-)-aristeromycin, (-)-neplanocin A[53] and bicyclo[2.2.1]heptane lactones.[54] Once again, it was found that MCPBA oxidation of the sulfide to the (R_S)-sulfoxide occurred with high diastereoselectivity, reflecting the influence of the hydroxyl group.[55] The Diels-Alder reactions were carried out using $ZnCl_2$ as a promoter, and gave diastereoselectivities of up to 88%, while removal of the auxiliary was achieved using $Sm(II)I_2$.[56]



41

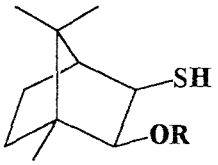


42

Conjugate addition reactions to vinyl sulfoxide derivatives of the chiral auxiliary (**32**) revealed that (*Z*)-isomers showed much better stereofacial selectivity than the corresponding (*E*)-isomer.[57] The chiral auxiliary (**32**) has also been used in the synthesis of (+)-(*S*)-(*E*)-γ-hydroxy-α,β-enolates,[58] chiral secondary alcohols from α,β-unsaturated ketones,[59] and in the resolution of (*R*)-(+)-4-*t*-butoxycyclopent-2-enone,[60] while its sulfonyl imine derivative (**42**) has been used in diastereoselective aza-Diels-Alder reactions with stereoselectivities of 0 - 40%.[61]

1.2.1.5 3-*Exo*-Mercaptoisoborneol derivatives as chiral auxiliaries

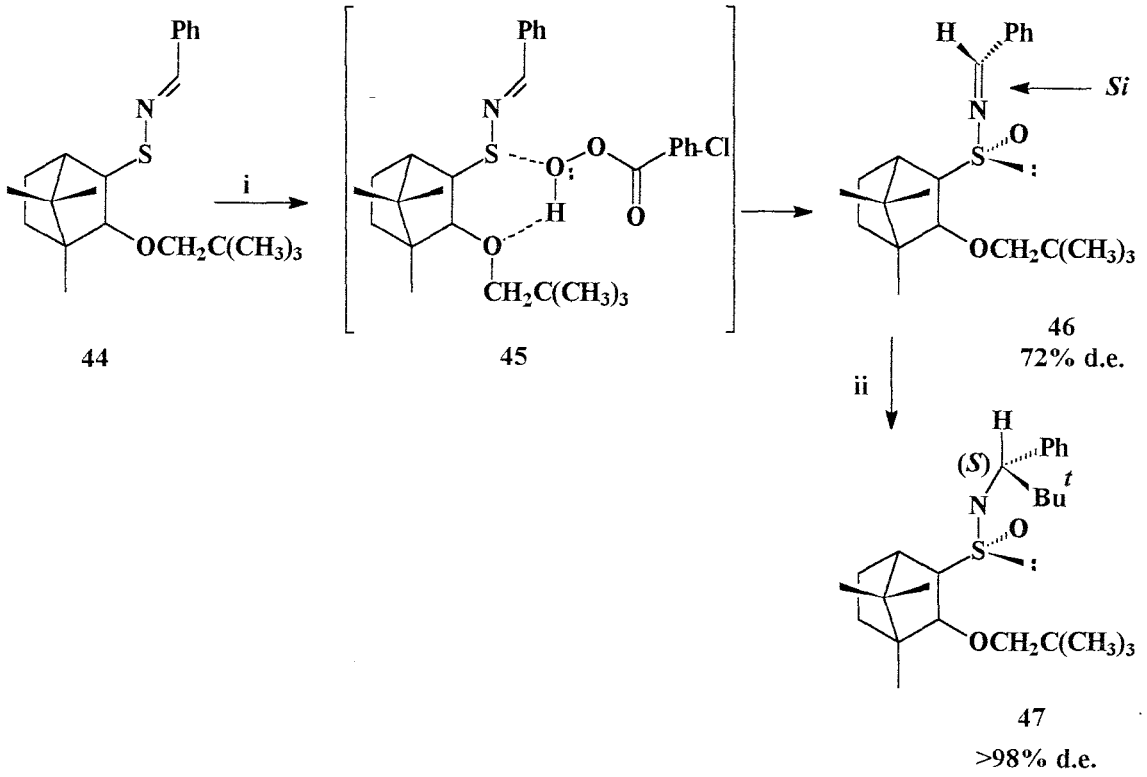
The camphor-derived thiol (**43a**) has been used as a chiral auxiliary in Solladie-type reductions[62] of sulfide or sulfoxide intermediates. These reactions showed high stereoselectivities, and the sense of induction could be altered by changing the catalyst used.



	R
a	H
b	Me
c	$(CH_3)_3CCH_2$
d	$PhCH_2$

43(a - d)

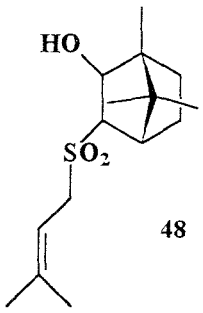
Sulfenimines have been prepared from the chiral auxiliary (**43b**) by Yang *et al.*,[63] with the intention of using them to synthesise of chiral amino acids (Scheme 6). For this purpose, the chiral auxiliaries (**43a**), (**43c**) and (**43d**) were synthesised.[64] Sulfenimines, such as (**44**), obtained from the thiol (**43c**), were oxidised by MCPBA at low temperatures to sulfinimines, such as (**46**) in 40 - 98% d.e., the diastereoselectivities being attributed to the chelation shown for the intermediate (**45**). The sulfenimine derived from auxiliary (**43a**) produced only one diastereomeric sulfinimine when oxidised.



SCHEME 6. Reagents: i) MCPBA, CH_2Cl_2, -78 °C;
ii) *t*-BuMgBr/ THF/ 30min.

Asymmetric alkylations have been effected on the sulfenimines, such as (**44**), and sulfinimines, such as (**46**), using Grignard reagents at -10 °C. While size increments in the nucleophiles resulted in higher diastereoselectivities, the sulfenimines, such as (**44**) showed poor stereoselectivity, demonstrating the importance of chelation of the metal to the sulfinimine oxygen. When the Grignard reagent was replaced with an alkyl lithium reagent, lower stereoselectivities were obtained. Attack was proposed to occur from the *Si*-face, either due to chelation or due to shielding of the *Re*-face by the bicyclic skeleton. This facial selectivity was confirmed by X-ray crystallographic analysis of product (**47**).

Aldol and alkylation reactions of the sulfone derivative (**48**) have been shown to proceed with good stereoselectivity, and have been used to synthesise (1*S*, 3*S*)-*trans* chrysanthemic methyl ester in 25% overall yield.[65]

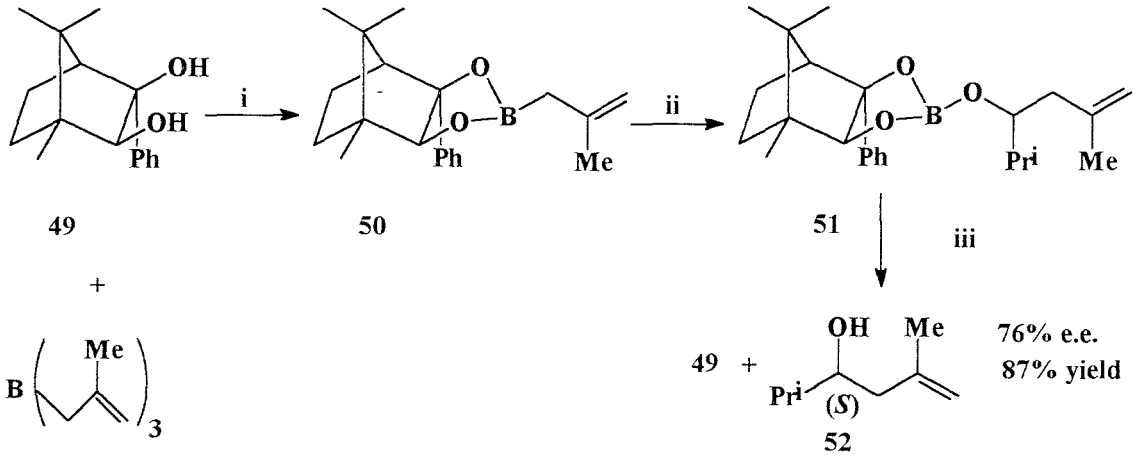


48

1.2.1.6 Dihydroxybornane derivatives as chiral auxiliaries

(+)-2-*Exo*-3-*exo*-dihydroxy-3-*endo*-phenylbornane (**49**) was used as a chiral auxiliary by Hoffmann *et al.*[66] Chiral homoallylic alcohols, such as compound (**52**) were synthesised by reacting allylboronic esters (**50**) with aldehydes to yield (**51**), followed by cleavage and recovery of the chiral auxiliary (Scheme 7). The stereoselectivity of the reaction was explored by varying the configuration of suitably substituted allylbornanes,[67] by using a chiral aldehyde to achieve double stereodifferentiation, [68] and by varying the blocking group at C-3.[69]

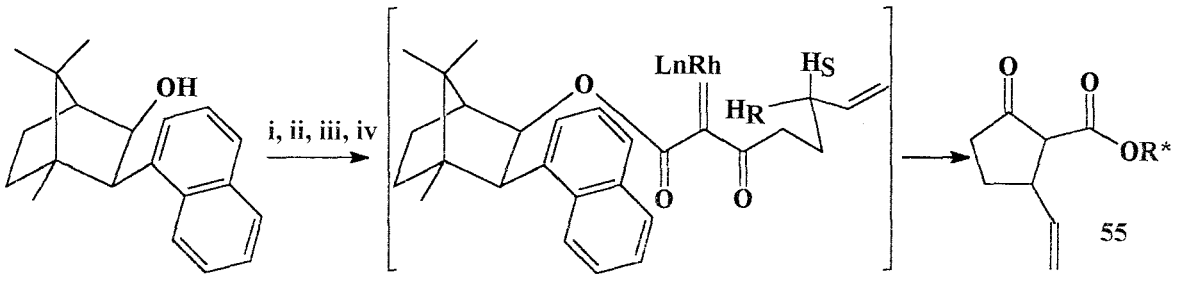
More recently, acetals derived from 2-*exo*-3-*exo*-dihydroxybornane and various aldehydes, have been used in the synthesis of chiral lactams[70] and in alkylation reactions.[71] In both cases, however, low stereoselectivity was observed. In our research group, cyclopropanation reactions carried out on acetals synthesised from α,β-unsaturated aldehydes and 2-*exo*-3-*exo*-dihydroxybornane, have shown good stereoselectivity. The stereocontrol has been improved by the introduction of a phenyl sulphonate blocking group at C-10, resulting in the synthesis of cyclopropanation products in >99% d.e.[72]



SCHEME 7. Reagents: i) 50 °C, 30 min;
ii) i-PrCHO, -40 °C, 1 h; 25 °C, 12 h;
iii) 1.2 eq. $N(CH_2CH_2OH)_3$, 25 °C, 2 h.

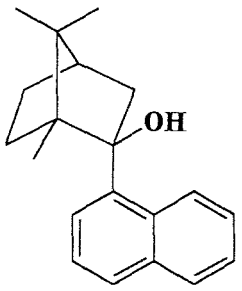
1.2.1.7 Camphor-derived chiral auxiliaries with aromatic blocking groups

A number of aromatic groups have been used as blocking groups on camphor. Taber *et al.*[73] synthesised the auxiliary (**53**) in which a naphthyl blocking group is attached to the bicyclic skeleton. Ester derivatives of this compound were used in enantioselective carbocyclisations to afford chiral cyclopentanones (**55**) (Scheme 8). In the proposed intermediate (**54**), the napthyl group directs attack towards H_R. This methodology has been used in the synthesis of (+)-estrone methyl ether,[74] 1,25-dihydroxy-vitamin D_3,[75] and in Robinson Annulation reactions used in the synthesis of (+)-methyljoubertiamine.[76]

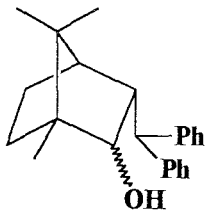


SCHEME 8. Reagents: i) dikenene, Et_3N;
ii) NaH, THF; *n*-BuLi; RBr;
iii) TsN_3, CH_3CN;
iv) Rh_2OAc_4, CH_2Cl_2, rt.

The naphthyl group has also been attached to the bicyclic skeleton at C-2, as in compound (**56**). When acrylates derived from this auxiliary were used in Diels-Alder reactions, stereoselectivities of up to 95% d.e. were observed.[77] Camphor-derived auxiliaries with benzyl blocking groups, such as (**57**) have also been synthesised,[78] and acrylate derivatives have been reported to undergo Diels-Alder reactions with up to 82% d.e., and hetero Diels-Alder reactions with up to 88% d.e.[79]



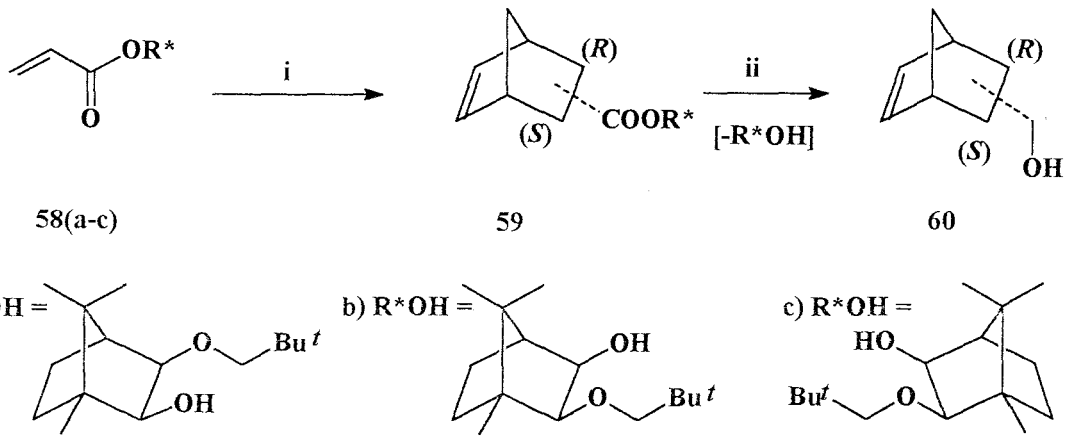
56



57

1.2.1.8 Camphor-derived chiral auxiliaries with ether blocking groups

Chiral auxiliaries with a neopentyloxy blocking group, developed by Oppolzer *et al.*,[80] have been synthesised in 60% overall yield from (+)- and (-)-camphor. When the acrylate esters of these auxiliaries (**58a-c**) were reacted with cyclopentadiene in the presence of a Lewis acid (Scheme 9; Table 1), the Diels-Alder products (**59**) were obtained in good yield and with good stereoselectivity. Reduction of the Diels-Alder products furnished the alcohol chiral auxiliaries and the alcohol product (**60**). This approach has also been used to synthesise (-)-norbornenone and (-)-β-santalene.[81, 82]



58(a-c) 59 60

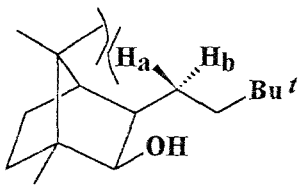
SCHEME 9. Reagents: i) Cyclopentadiene, $TiCl_2(OPr^i)_2$, -20 °C; ii) LAH.

TABLE 1. Data from Diels-Alder reactions using ether derivatives of camphor (Scheme 9).[80]

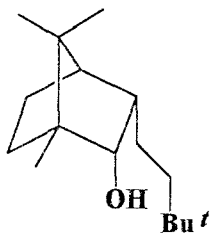
Chiral auxiliary	Yield of (60)/ %	endo : exo ratio	Endo-Adduct Configuration	Endo-Adduct/ % d.e.
58a	95	96/4	*S*	97
58b	96	96/4	*R*	>99
58c	96	95/5	*S*	>99

From models, Oppolzer was able to show that the C(α)-*Re* face of the acrylate (**58b**) was blocked by the neopentyloxy group, thus only allowing attack from the C(α)-*Si* face. He also proposed that the marginal increase in stereoselectivity obtained in the reaction using (**58b**) over (**58a**) was due to the fact that the 10-methyl group on the auxiliary pushed the neopentyloxy group closer to the acryloyl group, thus making it a more effective blocking group, *i.e.* the 10-methyl group exerts a buttressing effect.

Oppolzer *et al.* also attached the neopentyl group to the bicyclic skeleton *via* a methylene spacer to obtain the chiral auxiliaries (**61**) and (**62**).[83] However, lower stereoselectivities were obtained in Diels-Alder reactions on acrylate esters of these auxiliaries. One explanation given for this was H_a/8-Me repulsion in the substrate derived from the compound (**61**) causing the neopentyl group to shift out of alignment and, hence reducing its blocking effect. It was also proposed that in the reactions of the substrates (**58a-c**), the titanium chelates to the ether and carbonyl oxygens, thus improving stereoselectivity.



61

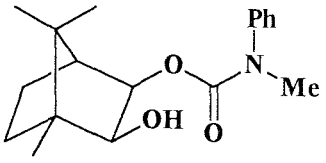


62

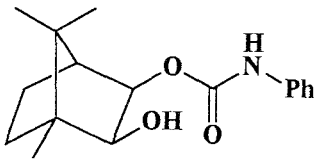
Diels-Alder reactions have also been carried out on *N*-sulfinyl carbamates derived from Oppolzer's neopentyloxy chiral auxiliaries,[84] while 1,4-addition reactions using these derivatives have been used in the synthesis of (*S*)-(-)-citronellic acid,[85] (-)-khusimone[86] and California red scale pheromone.[87] These camphor derivatives have also been used in the Pauson-Khand bicyclisation reaction,[88] and tandem inter [4+2]/[3+2] cycloaddition reactions.[89]

1.2.1.9 Camphor-derived chiral auxiliaries with amine or amide blocking groups

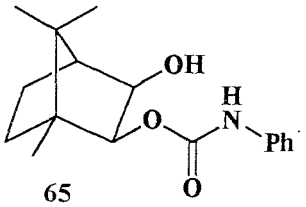
The chiral auxiliary (**63**), developed by Helmchen *et al.*,[90] was used to synthesise (*R*)- and (*S*)-17,21-dimethylheptatriacontane in up to 86% d.e.[91] Asymmetric hydroxylations have also been achieved using this auxiliary with 4 - 72% d.e.[92]



63

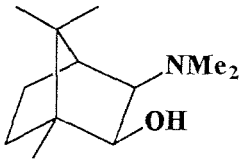


64

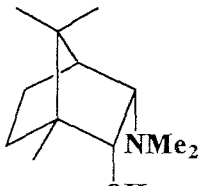


65

The auxiliaries (**64**) and (**65**) were also developed by Helmchen *et al.*[93] and their acrylates were used in Diels-Alder reactions to anthracene and cyclopentadiene.[94] These reactions exhibited high stereoselectivities in both catalysed and uncatalysed reactions. Inversion of configuration was obtained by interchanging the chiral auxiliary used [*i.e.* between (**64**) and (**65**)], but auxiliary (**64**) gave poorer yields and lower stereoselectivities. Auxiliary (**65**) has also been used in the asymmetric addition of the phenylsulfenyl group to it's acrylate derivative, with stereoselectivities of up to 87% d.e.[95]



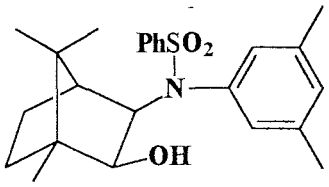
66



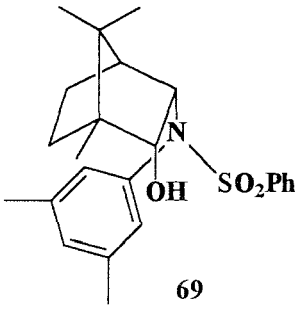
67

The asymmetric synthesis of β-lactams has been achieved using camphor-derived amines, the best stereoselectivities being obtained with auxiliaries (**66**) and (**67**).[96] Inversion of the configuration of the products was obtained by interchanging the chiral auxiliary, and the products were obtained with stereoselectivities of up to 99% e.e.

1.2.1.10 Camphor-derived chiral auxiliaries with sulfonamide blocking groups

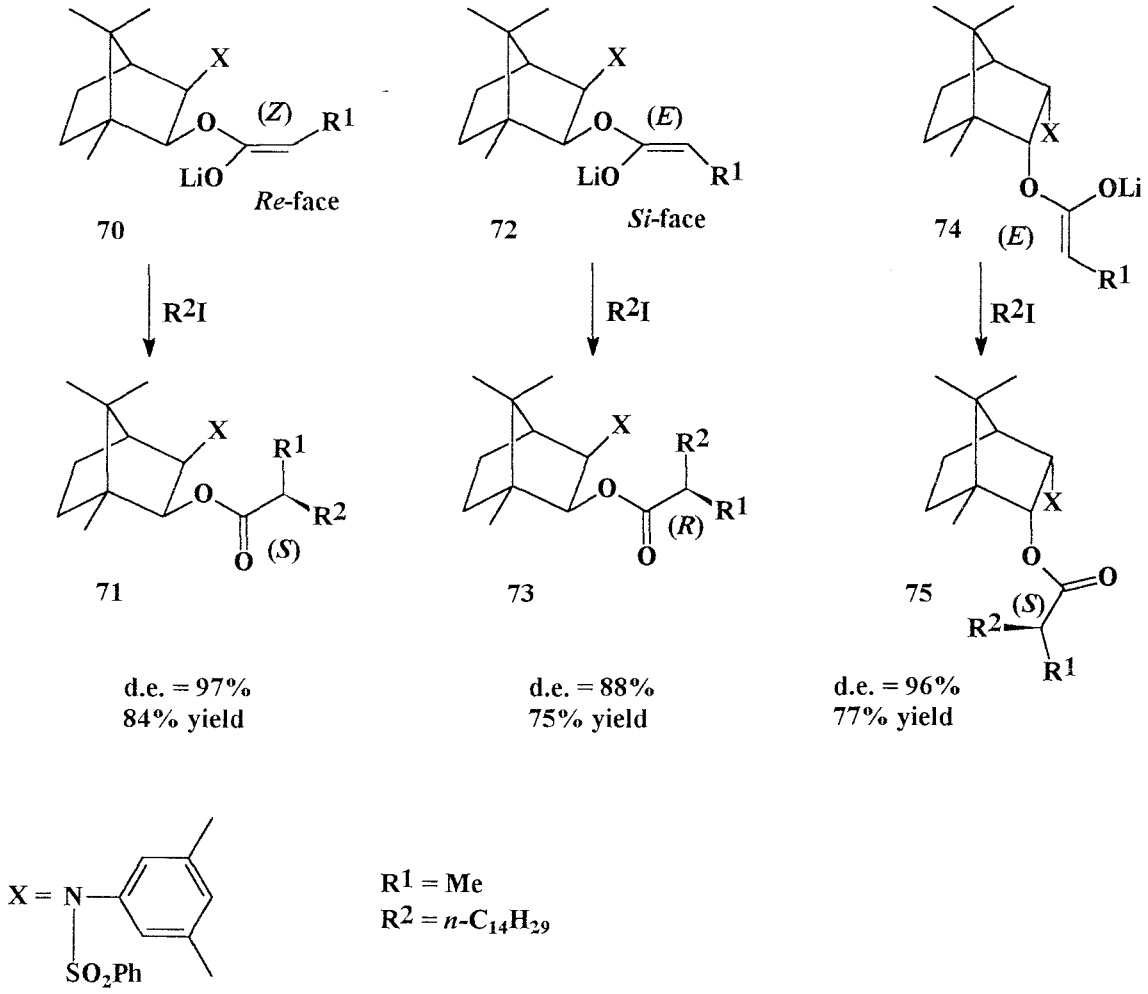


68



69

The camphor-derived sulfonamides (**68**) and (**69**) were developed by Helmchen *et al.*[91] When the propanoic esters of the chiral auxiliaries were alkylated, it was found that the configuration of the alkylated product could be inverted by altering the solvent used in the reaction (Scheme 10). The (*Z*)-enolates, such as (**70**), were formed using LICA (lithium isopropylcyclohexylamine) in THF, with the alkyl halide attacking the enolate from the front *Re*-face, resulting in the formation of product (**71**) with an (*S*)-configuration at the new chiral centre. However, the opposite configuration could be obtained when the lithium enolates were formed using a mixture of THF and HMPT (hexamethylphosphoric triamide) as the solvent, the alkyl halide reacting with the (*E*)-enolate (**72**) to form the (*R*)-ester (**73**). Alkylation of the (*E*)-enolate (**74**), generated in THF-HMPT, resulted in the formation of th product (**75**) with an (*S*)-chiral centre, the opposite configuration to that obtained using the (*E*)-enolate (**72**). The configuration of the new chiral centres could also be inverted by interchanging the R^1 and R^2 groups. When alkylations were carried out on *O*-benzylglycolate derivatives of either chiral auxiliary, (**68**) or (**69**), the same stereoisomers were formed with stereoselectivities of 87.5 - 94.5% d.e., irrespective of the solvent system used.[97] The proposal that these reactions occur *via* (*E*)-enolates, was confirmed by the synthesis of the corresponding silyl enol ethers from the lithium enolates. The methodology developed by Helmchen *et al.* has been used in the synthesis of enantiomerically pure vitamin E,[98] and (4*R*)-4-[(*E*)-2-butenyl]-4,*N*-dimethyl-*L*-threonine (MeBMT).[99]



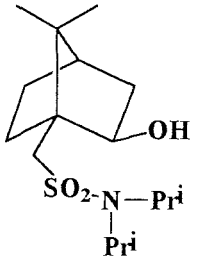
SCHEME 10.

Conjugate addition of Cl_3CMgCl to the crotonyl ester of the chiral auxiliary (**68**) has been shown to proceed with 98% diastereoselectivity,[100] while reaction of organocopper reagents with enolate derivatives of chiral auxiliaries (**68**) and (**69**) afford products with >99% e.e and in >90% yield.[101] Inversion of configuration in conjugate additions was accomplished by interchanging either the auxiliaries or the metals used, the sense of induction being found to be a function of the metal used, *i.e.* Li or Cu.

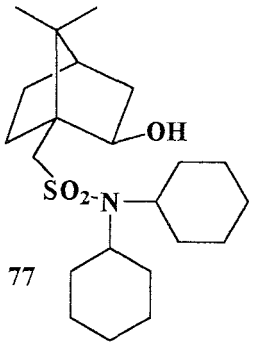
Aldol reactions were carried out on acetate esters of chiral auxiliaries (**68**) and (**69**).[102] Addition of aldehydes to the lithium acetate enolates proceeded with poor stereoselectivity, whereas the addition of aldehyde-$TiCl_4$ complexes to silyl enol ethers of the acetate ester (the Mukaiyama

reaction), showed much improved stereoselectivity (>86% d.e.). Addition of aldehydes to Li-propanoic enolates also gave poor stereocontrol, but again, much greater diastereoselectivity (*c.a.* 84% d.e.) was achieved using the Mukaiyama methodology. The chiral auxiliaries were removed, without racemisation, either by saponification with KOH to yield the carboxylic acids, or by reduction with $LiAlH_4$ to yield the alcohols.

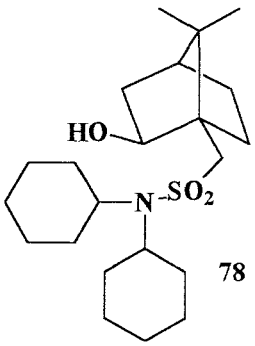
The auxiliaries (**68**) and (**69**) have also been used in the asymmetric synthesis of α-hydroxy esters,[103] dictyoterene B,[104] (-)-verrucarinolactone[105] and in oxidative coupling reactions.[106]



76



77

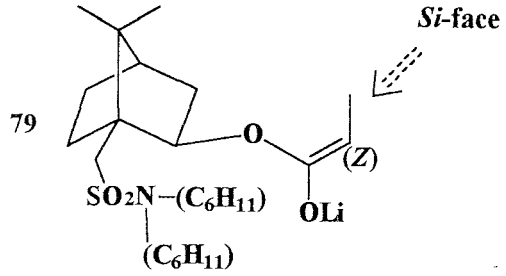


78

Auxiliaries (**76**), (**77**) and (**78**) were synthesised from 10-camphorsulfonic acid by Oppolzer *et al.*[107, 108] Diels-Alder reactions of the acrylate ester of auxiliary (**76**) gave good stereoselectivity (up to 94% *endo*, 77% d.e.). These results were improved when acrylate derivatives of auxiliary (**77**) were used (up to 100% *endo*, 99% d.e.), the antipode (**78**) providing the opposite diastereofacial selectivity. X-ray analysis of the acrylate ester of auxiliary (**77**) revealed that one cyclohexane ring projected on top of the olefinic C(α)-*Re* face, thus shielding it from attack; in the case of its antipode (**78**), of course, the C(α)-*Si* face would be shielded.

Aldol reactions on the lithium enolate of the acetate ester of alcohol (**77**), showed poor stereoselection,[109] but in Ti-promoted Mukaiyama-type reactions of silyl enol ethers of the acetate ester, the stereoselectivities were increased dramatically (92-99% e.e.). The (*E*)-silyl enol ethers of the propanoic ester, obtained by kinetically controlled deprotonation, reacted with aldehydes in the presence of the Lewis acid, $TiCl_4$, to give, predominantly, the *anti*-products. The use of boron as a Lewis acid, resulted in a decrease in the *syn*/*anti* ratio. The (*Z*)-enolate, formed under thermodynamic control, exhibited increased *anti* selection, but afforded the opposite enantiomeric *anti*-product.

Boron-mediated organocopper 1,4-addition reactions on α,β-unstaurated carboxylic esters of auxiliaries (77) and (78) resulted in the formation of β-alkylated products in 94%-98% e.e.[110] The configuration at C(β) can be reversed either by using the antipodal auxiliary, or by interchanging the β-substituent on the α,β-unsaturated ester and the alkyl group of the organocopper species. This reaction has been used in the synthesis of southern corn rootworm pheromone.



Alkylation has been achieved by kinetically controlled deprotonation of propanoic esters to form the (*Z*)-enolate (79) followed by the addition of 1° alkyl bromides with 78% - 98% diastereoselectivity, while asymmetric α-acetoxylation reactions have been carried out on ester derivatives of chiral auxiliaries (76), (77) and (78)[111] In the latter reaction, the lithium enolates were formed under kinetic control and then silylated; silyl enol ethers were then reacted with $Pb(OAc)_4$ to form the acetoxy esters (83) in 95 - 100% d.e. (Figure 4). These reactions are proposed to occur *via* attack at the electrophilic metal from the C(α)-*Si* face of the silyl enol ether (80). Acetate then opens the transient leadonium ion (81 → 82) with the ultimate formation of the α-acetoxy ester (83). By using the antipodal chiral auxiliary, the configuration of the product can be predictably controlled. The consecutive organocopper addition and acetoxylation reactions on α,β-unsaturated esters of these auxiliaries results in the formation of two adjacent asymmetric centres with up to 99.6% d.e. and 100% e.e.

Asymmetric halogenation of esters derived from chiral auxiliaries (77) and (78)[112] have afforded chiral halohydrins and terminal epoxides. In these reactions, the (*E*)-silyl enol ethers (80) were again synthesised *via* kinetically controlled deprotonation, and addition of the halogen occurred from the C(α)-*Si* face (84) yielding the halogenated esters (85), in 97 - 99% d.e. This reaction has been used for the synthesis of (*R*)- and (*S*)-2-bromohexadecanoic acids.[113] Once again, two contiguous chiral centres can be synthesised by initial 1,4-addition reactions using organocopper reagents followed by halogenation.

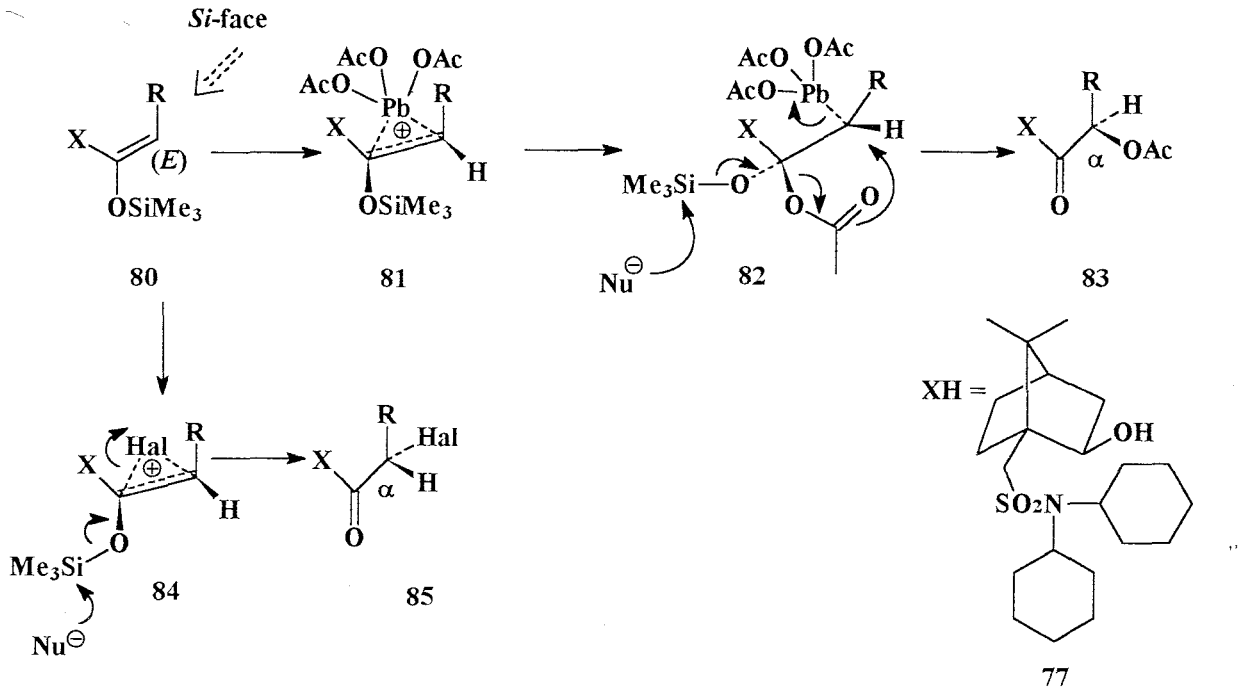
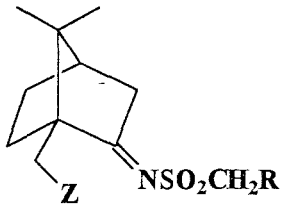


FIGURE 4. Mechanism for halogenation and $Pb(OAc)_4$-mediated α-acetoxylation.

This approach has also been used in the synthesis of α-amino acids.[114] Substitution of the halogen by an azide group, followed by transesterification and hydrogenolysis, yielded the amino acids, including L-alloisoleucine in 93.8 - 98% e.e. Once again, two contiguous chiral centres could be synthesised, by carrying out an initial organocopper addition reaction.

In all the above-mentioned reactions, using auxiliaries (**76**), (**77**) and (**78**), facile purification of the diastereomers by recrystallisation was often possible, and the chiral auxiliaries could often be removed, without racemisation, by reduction with $LiAlH_4$, or by saponification using NaOH. These chiral auxiliaries have also been used in Baylis-Hillman reactions,[115, 116] as well as in the preparation of chiral propanediols,[117] intermediates for the synthesis of insect growth regulators,[118] and the aromatase inhibitor 3-ethyl-3-(4-pyridyl)piperidine-2,6-dione.[119]

Camphorsulfonimines, such as (**86a**) have also been used in the synthesis of α-functionalised sulfonamides,[120] and the relative efficiency of analogues (**86b**) and (**86c**) derived from auxiliaries (**76**) and (**77**), have been examined.[121]

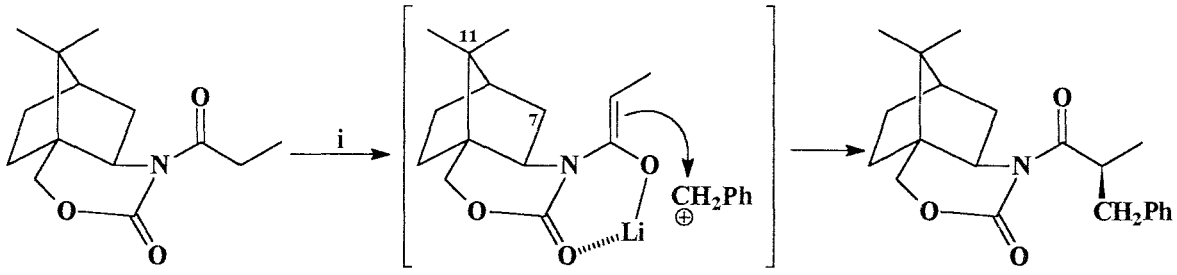


	Z
a	H
b	$SO_2N(Pr^i)_2$
c	$SO_2N(C_6H_{11})$

86

1.2.1.11 Camphor-derived chiral auxiliaries with oxazinone blocking groups

Camphor-derived oxazinone chiral auxiliaries such as (**87**), synthesised from ketopinic acid, were developed by Ahn *et al.*[122] Aldol reactions *via* a titanium enolate, showed stereoselectivities of >99%, while stereoselectivities of 99.8% were obtained in the formation of products such as (**89**) *via* asymmetric alkylation reactions (Scheme 11).[123] The latter reactions were proposed to proceed *via* the (*Z*)-enolate (**88**), in which the C(α)-*Si* face is blocked from attack by the 11-methyl group and by the methylene bridge, thus allowing attack from the C(α)-*Re* face only.



87 88 89

60% yield
98.8% d.e.

SCHEME 11. Reagents: i) LDA, -78 °C; $PhCH_2Br$, -78 °C to 24 °C.

1.2.1.12 Camphor-derived chiral auxiliaries with oxazolidinone and oxazolidinethione blocking groups

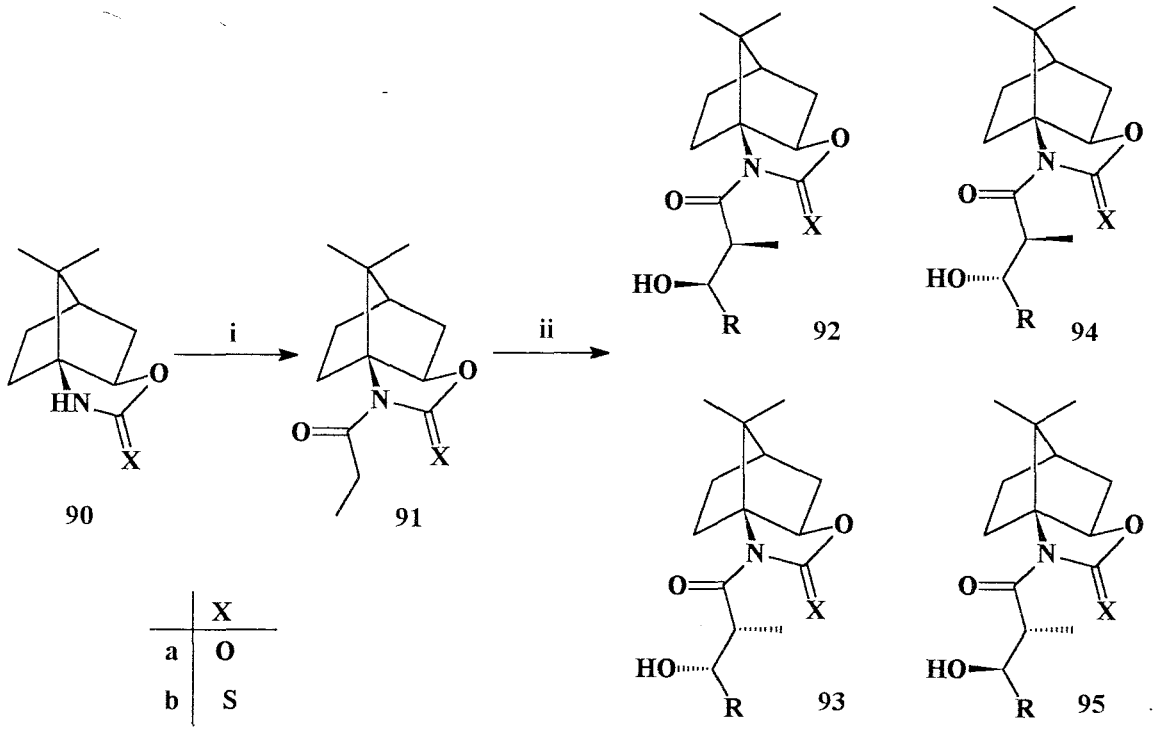
A camphor-derived oxazolidinone (**90a**), synthesised from ketopinic acid, has been developed by Yan *et al.*,[124] and has shown good stereoselectivity in asymmetric alkylation,[125] and aldol reactions (Scheme 12).[124] Aldol reactions carried out on (*Z*)-boron enolates (non-chelation

control) of the propanoyl oxazolidinone (**91a**), showed good stereoselectivity and resulted predominantly in the "Evans" *syn* product (**92a**) (entry 1; Table 2), as was formed in the titanium-mediated reaction (entry 2; Table 2). In the case of the (*Z*)-lithium enolate, when the reaction mixture was allowed to equilibrate thermodynamically, the "non-Evans" product (**93a**) was formed predominantly with moderate diastereoselectivities (entry 3; Table 2). The lower stereoselectivity obtained in this case, was attributed to the longer Li-O bond (compared to the B-O bond), and the differences in coordination number of Li and B.

The oxazolidinethione (**90b**) was also developed by Yan *et al.*[126] "Non-Evans" *syn* aldols (**93b**) were formed with good stereoselectivity in chelation controlled aldol reactions of titanium enolates, rather than the aldol products (**92b**) formed in boron-mediated aldol reactions (entries 4 and 5; Table 2). The differences in stereoselectivities exhibited by the chiral auxiliaries (**90a**) and (**90b**) in the titanium-mediated reactions, was attributed to the fact that the thioketone in the oxazolidinethione (**91b**) has a greater potential to coordinate with Ti, unlike the carbonyl in the oxazolidinone (**91a**). Moreover, the thioketone is considered to have a smaller dipole moment, thus minimising dipole repulsion in the transition state.

Aldol reactions of titanium enolates, in which the aldehyde was added as a titanium complex, exhibited lower stereoselectivity (entry 6; Table 2).[127] *Anti*-aldols were obtained *via* an open transition state by reacting boron enolates with Sn(IV) or Ti(IV) as co-catalysts. The best stereoselectivity was observed when 9-BBN (9-borabicyclo[3.3.1]nonane) enolates were reacted using the co-catalyst $SnCl_4$ (entry 7; Table 2).[128] The stereochemistry of the aldol products was confirmed by forming methyl esters following removal of the chiral auxiliary, and comparing them to the known, optically pure compounds.

Aldol-type reactions have also been carried out on acetate derivatives of the chiral auxiliaries (**90a**) and (**90b**) with up to 99% stereoselectivity.[129, 130] These auxiliaries have the advantage of allowing non-destructive removal from the product, and being available as both antipodes.

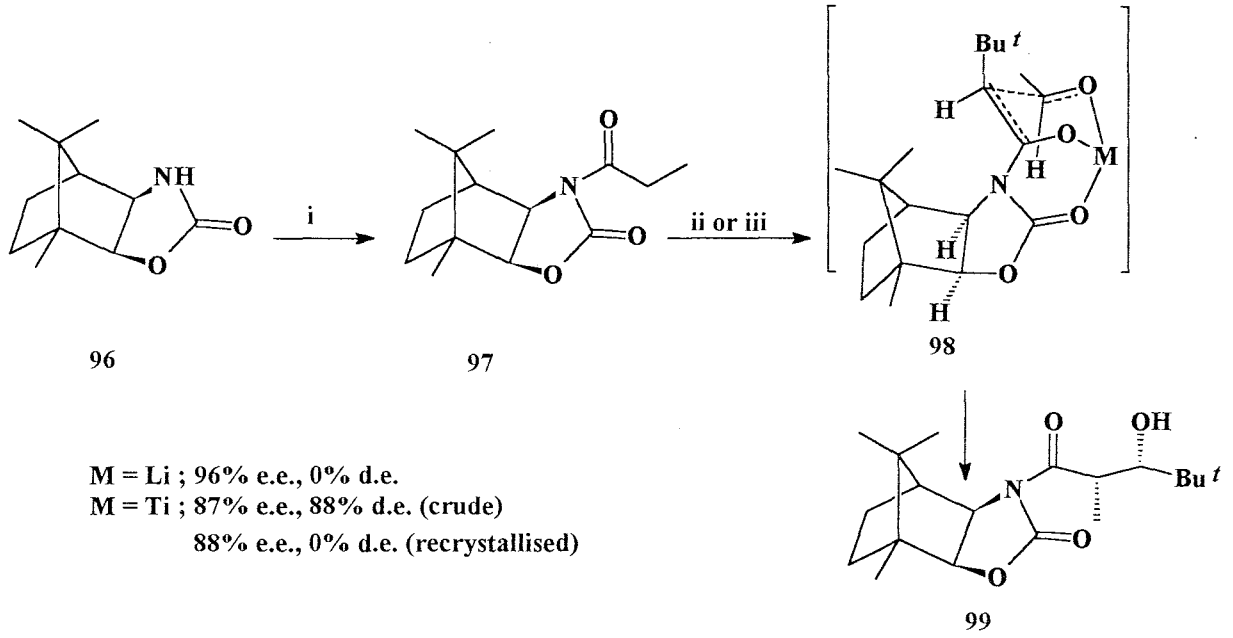


SCHEME 12. Reagents: i) NaH, THF, EtCOCl;
ii) A) $(n\text{-Bu})_2BOTf$, $EtN(i\text{-Pr})_2$, CH_2Cl_2; RCHO, -78 °C;
B) $TiCl_4$, $EtN(i\text{-Pr})_2$, CH_2Cl_2; RCHO, -78 °C ;
C) $LiN(i\text{-Pr})_2$, THF; RCHO, -78 °C;
D) $TiCl_4$, $EtN(i\text{-Pr})_2$, CH_2Cl_2; $TiCl_4$-RCHO, -78 °C ;
E) 9-BBN, $EtN(i\text{-Pr})_2$, CH_2Cl_2; $SnCl_4$, RCHO, -90 °C.

TABLE 2. Data for aldol reactions using chiral auxiliary (90) (Scheme 12).

Entry	R	X	Reagent	*syn* : *anti*	92 :93	% yield
1	*n*-Pr	O	A	>99:1	>99:1	85
2	*n-Pr*	O	B	>99:1	95:5	87
3	*n*-Pr	O	C	>99:1	1:6	92
4	*n*-Pr	S	A	>99:1	>99:1	78
5	*n*-Pr	S	B	>99:1	<1:99	88
6	*n*-Pr	O	D	75:25	10:65	64
7	Ph	O	E	4:96	-	86

Thornton *et al.*[131] have developed an oxazolidinone auxiliary (**96**) synthesised from camphorquinone, and used the *N*-propionyl derivative (**97**) successfully in aldol reactions *via* lithium and titanium enolates, obtaining high facial stereoselectivity (Scheme 13). Of the 4 possible aldol products, the *syn* aldol (**99**) was formed in up to 98% d.e. A further increase in stereoselectivity (up to 100% d.e.) was obtained in double asymmetric reactions using chiral aldehydes. The intermediacy of a (*Z*)-enolate was confirmed by trapping the enolate as a silyl enol ether. In the proposed chelated transition state (**98**), the distal diastereotopic face was favoured, the other face being hindered by the *syn*-7-Me group. Advantages of this oxazolidinone chiral auxiliary are that its derivatives are crystalline and the auxiliary can be removed without isomerisation.

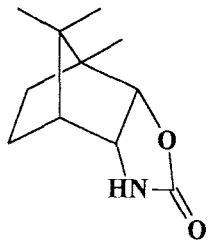


SCHEME 13. Reagents: i) BuLi, THF, EtCOCl;
ii) LDA, Et_2O, -78 °C; *t*-BuCHO;
iii) LDA, Et_2O, -78 °C; $Ti[OCH(CH_3)_2]_3Cl$, -40 °C; -78 °C, *t*-BuCHO, -40 °C.

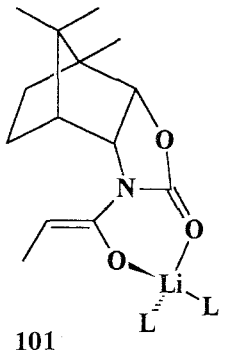
Subsequently, the *endo* oxazolidinone (**100**) was obtained serendipitously from *endo*-borneol, while attempting aziridination reactions.[132] Alkylation reactions carried out on the *N*-propionyl oxazolidinone were proposed to involve the (*Z*)-enolate (**101**) and gave stereoselectivities of up to 99% d.e. Reactions using smaller alkyl halides, such as acetyl chloride and propionyl chloride, however, were marred by the formation of small amounts of (*O*)-alkylated oxazolidinones. The stereoselectivity of aldol reactions involving lithium enolates, was poor, but was much improved

by the use of boron enolates. The boron-mediated aldol reactions were proposed to occur *via* the transition state (**102**), yielding single, diastereomerically pure *erythro*-aldols.

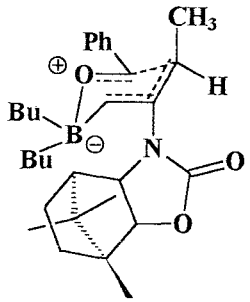
Diels-Alder reactions on acrylate derivatives of the chiral auxiliary (**100**), however, proved to be disappointing.[132] Tanaka *et al.*[133] carried out further Diels-Alder reactions on *N*-crotonyl and *N*-cinnamoyl derivatives of the chiral auxiliary (**100**) and its *exo* derivative (**96**), with improved stereoselectivity. They also managed to obtain diastereofacial differentiation by altering the Lewis acid used; in other words, different Lewis acids result in the formation of different stereoisomeric Diels-Alder products.



100



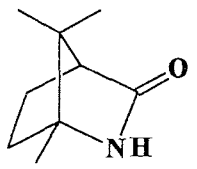
101



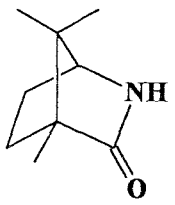
102

1.2.2 Camphor lactams as chiral auxiliaries

The camphor lactams (**103**) and (**104**)[134] and their antipodes, have been utilised as chiral auxiliaries by Boeckman *et al.*[135]



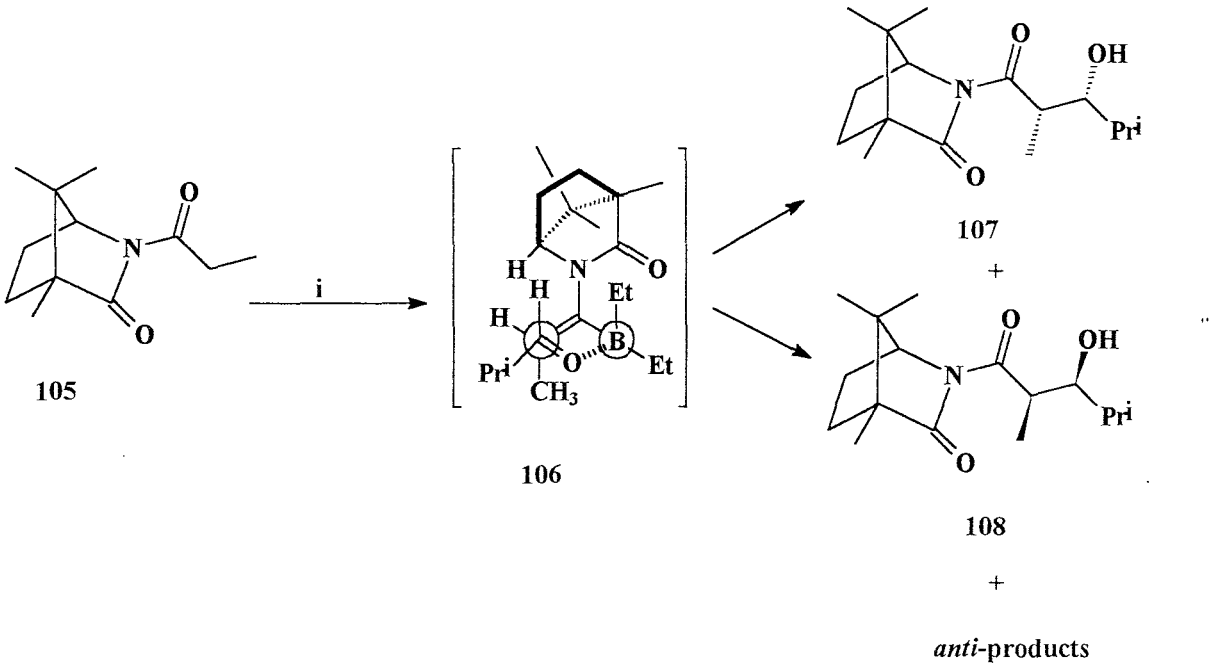
103



104

Aldol reactions carried out on the amide derivative (**105**) showed better stereoselectivity than those using the isomeric auxiliary (**103**). Improved stereoselectivity was obtained in the reaction shown in Scheme 14, when the aldehyde was added in a 2-3 fold excess. Optimal *syn*:*anti* and facial selectivity was obtained at low temperatures (-78 °C), but this required longer reaction times. Molecular modelling indicated the favoured (*Z*,*Z*)-chair transition state (**106**) to be that

leading to the formation of the major product (**107**) and avoiding the steric interaction between the boron ligand and the camphor methylene bridge.[136] These lactam auxiliaries have been used in Diels-Alder reactions[135] as well as in the synthesis of (+)-tetronolide[137, 138] and (-)-cassioside.[139]



SCHEME 14. Reagents: i) Et_2BOTf, i-PrNEt / CH_2Cl_2; i-PrCHO; CH_3OH/ H_2O_2.

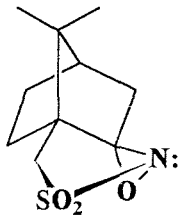
1.2.3 Industrial Applications of Asymmetric Synthesis

Different stereoisomers can have very different properties. For example, one enantiomer of limonene smells of lemon, while the other of orange and, although both enantiomers of sucrose are sweet, only one enantiomer is metabolised in the body. The differences in properties can have disastrous effects when chiral drugs are involved. One such case is penicillamine, where one enantiomer has antiarthritic properties, while the other is toxic.[140] Another example is the antipsychotic drug, zacopride, where one enantiomer is a $5HT_3$-blocker, while the other is an agonist. In some cases, one stereoisomer is pharmacologically active while the other, inactive, as exemplified by ibuprofen, where the (*S*)-isomer relieves pain, while the (*R*)-isomer is inactive.[141]

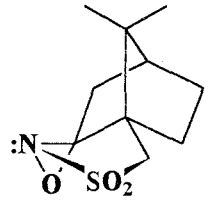
Hence, there is an ever expanding need for isomerically pure compounds in the pharmaceutical and agrochemical industries. The worldwide market for single enantiomeric forms of chiral drugs surged in 1994, the market for dosage forms of these drugs reaching $45.2 billion, according to the consulting firm, Technology Catalysts International. This represents a 27% increase from 1993 levels. Thus, research in asymmetric synthesis has been stimulated, both in the academic and industrial fields.[142]

Industrially, optically pure compounds can be obtained using either of two general approaches. A racemic modification can be synthesised and the enantiomers resolved using techniques such as chromatography or enzymatic resolution. The second approach is to synthesise the required enantiomer selectively using asymmetric synthesis. However, in some cases, the latter option can be more costly and time-consuming as more steps are typically involved.

A number of camphor derivatives, which have been used in asymmetric synthesis are now available in multi kilogram quantities and, thus, are leading candidates for industrial scale asymmetric synthesis.[143] Examples of such compounds are (+)-(2*R*, 8a*S*)-(camphorylsulfonyl)oxaziridine (**109**) and the enantiomer (**110**) which have both been developed by Davis *et al.*,[144, 145] and have been used as chiral oxidising agents,[146, 147] for example in the synthesis of α-hydroxyesters, -ketones and -amides.[148]

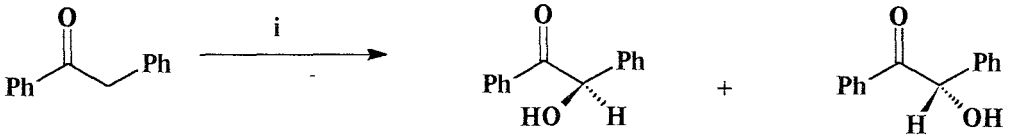


109



110

In the example shown in Scheme 15, the ketone (**111**) was oxidised to the α-hydroxyketone (**112**) with good stereoselectivity. Oxaziridines (**109**) and (**110**) have also been used in the asymmetric oxidation of sulfides to sulfoxides.[149]



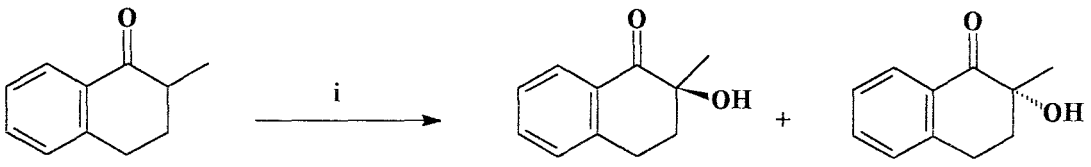
111 (*R*)-112 (*S*)-112

(+)-109 4 : 95 (84% yield)
(-)-110 95 : 0 (88% yield)

SCHEME 15. Reagents: i) NHMDS [sodium bis(trimethylsilyl)amide], oxaziridine (109) or (110).

113 114

The dichloro derivatives (**113**) and (**114**)[150] have been found to offer better stereocontrol in some cases, than the parent system, for example, use of oxaziridine (**109**) as the chiral oxidising agent yields 2-hydroxy-2-methyl-1-tetralone (**116**) from 2-methyl-1-tetralone (**115**) in 16% e.e., where as the oxaziridine (**113**) gave the same product (**116**) with vastly improved stereoselectivity (>95% ee) (Scheme 16).

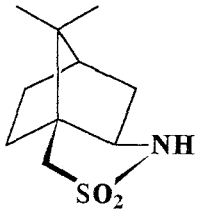


115 (*S*)-116 (*R*)-116

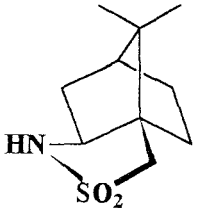
109, (*R*) 16% e.e., 90% yield
113, (*R*) >95% e.e., 66% yield

SCHEME 16: Reagents: i) NHMDS , oxaziridine (109) or (113).

The most versatile camphor-derived chiral auxiliaries have been the sultams developed by Oppolzer *et al.* [151] (-)-Bornane-10,2-sultam (**117**) and its enantiomer (**118**) are readily prepared from the corresponding and relatively inexpensive camphorsulfonyl chlorides in 76% overall yield.



117



118

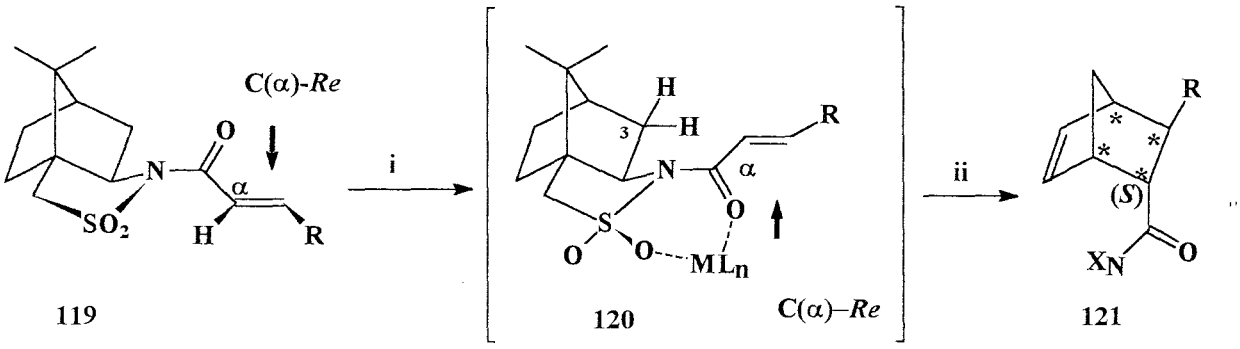
The versatility of these sultam auxiliaries has been demonstrated by their use in asymmetric Diels-Alder additions, dihydroxylations, 1,4-additions, aldolisations, alkylations, brominations and "aminations".[152, 153, 154, 155] Their use also presents a number of advantages.

1) Almost all the *N*-acyl derivatives are crystalline, allowing easy purification.
2) The diastereomeric products can be analysed using ^{1}H-NMR and GLC techniques, thus facilitating the determination of asymmetric induction.
3) The auxiliary can be easily cleaved off the substrate and recovered without racemization, using mild reagents such as LiOH, LiOOH and $LiAlH_4$.

Oppolzer's sultam was originally synthesised as a dienophile auxiliary for asymmetric Diels-Alder reactions.[156] X-Ray diffraction analysis was carried out on both the uncoordinated *N*-crotonyl sultam (**119b**)[151] and the Lewis acid-coordinated *N*-crotonyl sultam (**120b**) (Scheme 17).[157] Both structures revealed an s-*cis* conformation about the C(O) and C(α) bonds. The uncoordinated sultam, however, was shown to have an s-*trans* arrangement of the carbonyl and sulfonyl groups about the N-C(O) bond, as well as a pyramidal nitrogen atom. Because of the unexpected stereoselectivity obtained in uncatalysed Diels-Alder reactions, it was suggested that the chiral information from the bornane skeleton was transmitted to the distant C(α)=C(β) bond *via* the pyramidal nitrogen, with attack at the C(α)-*Re* face (entries 1 and 2; Table 3).[153]

When Lewis acids were used, the Diels Alder reactions were found to be less sluggish and exhibited much improved π-face stereoselectivity (entries 3 and 4; Table 3). Even when the less

reactive *N*-crotonyl sultam was used, the reaction could be carried out at low temperatures. X-Ray diffraction analysis of the chelated *N*-crotonyl derivative of auxiliary **(117)** showed coordination to titanium through the carbonyl and upper sulfoxide oxygens, resulting in an s-*cis* arrangement of the carbonyl and sulfonyl groups about the N-C(O) bond. This results in *endo* and C(α)-*Re* attack by the diene [the C(α)-*Si* face being blocked by the *exo* hydrogen on C-3] (Scheme 17).



	R
a	H
b	Me

SCHEME 17. Reagents : i) Lewis acid, CH_2Cl_2;
ii) cyclopentadiene.
X_N = **(117)**

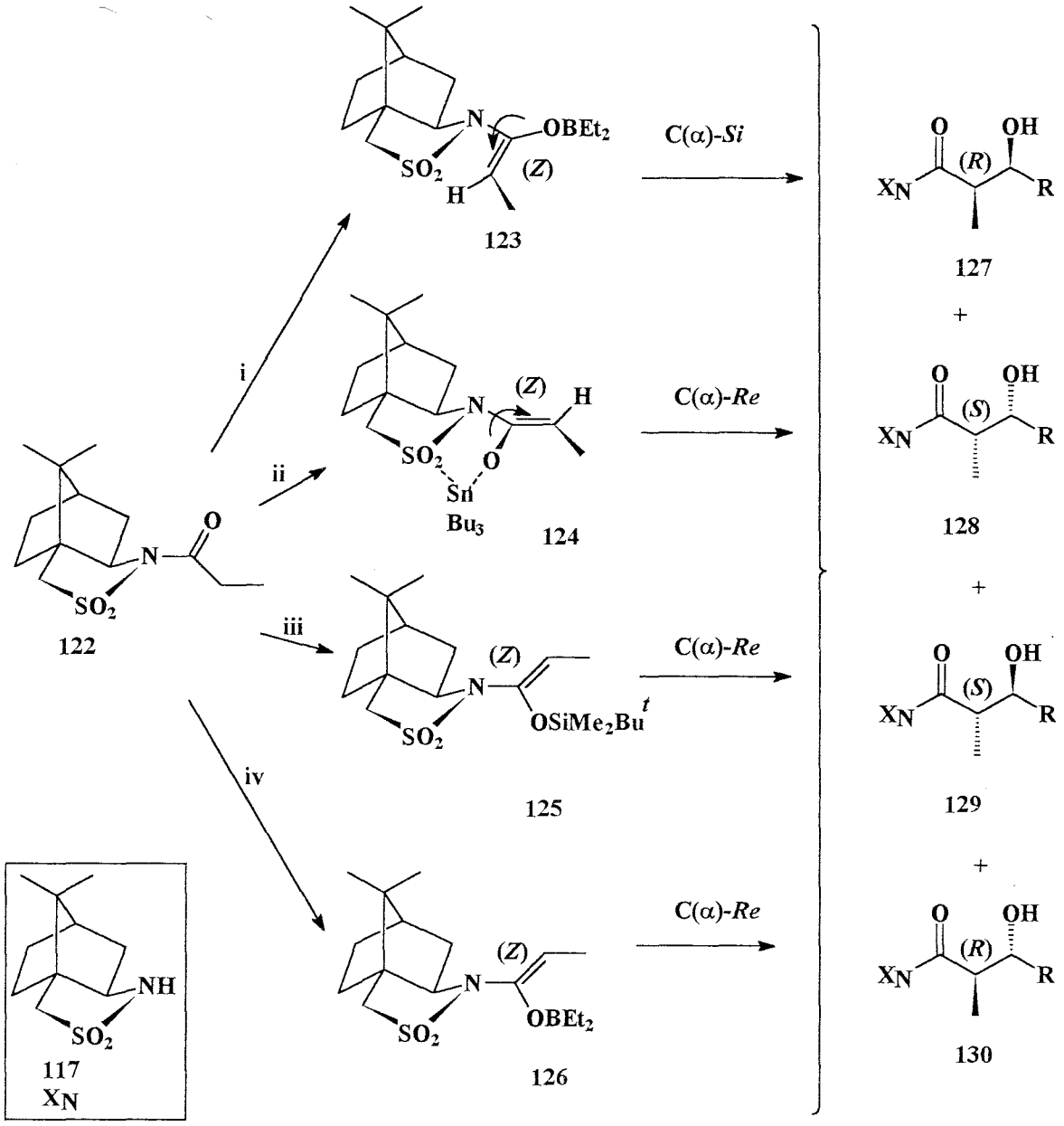
TABLE 3. Data for Diels-Alder reactions using Oppolzer's sultam as a chiral auxiliary (Scheme 17)

Entry	R	Lewis Acid	T/ °C	time/ h	*endo*/ %	d.e./ % 121	Yield/ % 121
1	H	none	21	72	89	66	80
2	Me	none	21	79	96	52	51
3	H	$TiCl_4$	-130	6	97	94	89
4	Me	$TiCl_4$	-78	18	99	93	98

Oppolzer's general approach has also been applied to intramolecular Diels-Alder reactions of *N*-acyl-camphor-sultam trienes.[158] Reversal of the asymmetric induction can be achieved by using the enantiomeric sultam (**118**), as illustrated in the synthesis of (-)-1-*O*-methyl loganin aglucone.[159] Uncoordinated *N*-enoyl sultams have also exhibited good stereoselectivity and C(α)-*Re* attack in addition reactions, such as the dihydroxylations carried out using OsO_4 and *N*-methylmorpholine *N*-oxide.[160] The α,β-unsaturated carbonyl system has also been shown to undergo stereoselective 1,4-addition reactions with Grignard[161] and Gilman[162] reagents - a reaction which has been successfully employed in the synthesis of (1*R*, 4*R*)-β-necrodol.[163]

Aldol reactions involving *N*-acylsultams, such as (**122**), also proceeded with good stereoselectivity (Scheme 18; Table 4). When synthesising the *syn*-aldols (**127**) and (**128**),[164] it was found that the absolute configuration of the aldol products could be inverted by changing the enolate counterion (entries 1 and 2; Table 4). The enolate formed with the B(III) counterion (**123**) and those formed with Li(I) or Sn(IV) counterions (**124**) are proposed to have (*Z*)-configurations. The Li(I) and Sn(IV) counterions, however, are able to coordinate with the sultam oxygens, leading to an s-*cis* arrangement of the carbonyl and sulfonyl groups about the enolate N-C(O) bond, and consequently, to attack by the aldehyde from the C(α)-*Re* face, *i.e.* from the bottom *endo* face, away from the nitrogen lone pair to afford aldol (**128**) (entry 2; Table 4). In the case of the boron enolate (**123**), boron cannot coordinate any further and, thus, an s-*trans* arrangement of the carbonyl and sulfonyl groups about the C(O)-N bond of the enolate is favoured, allowing *endo* attack at the C(α)-*Si* face to afford aldol (**127**) (entry 1; Table 4).

Anti-aldols, on the other hand, can be synthesised *via* an *O*-*t*-butyldimethylsilylketene aminal (**125**) of the *N*-acylsultam (**122**). Lewis acid-promoted addition of aromatic and aliphatic aldehydes occurs at the C(α)-*Re* face of this system to afford (**129**) (entry 3; Table 4).[165] The bornyl enolates can be used in the synthesis of either *syn*- or *anti*- aldols, the stereochemistry of the products being determined by the presence or absence of a Lewis acids (entries 1 and 4; Table 4).[166] When the Lewis acid is present, an s-*cis* arrangement of the (*Z*)-enolate about the C(O)-N-bond is favoured, allowing attack from the C(α)-*Re* face to afford the aldol (**129**).



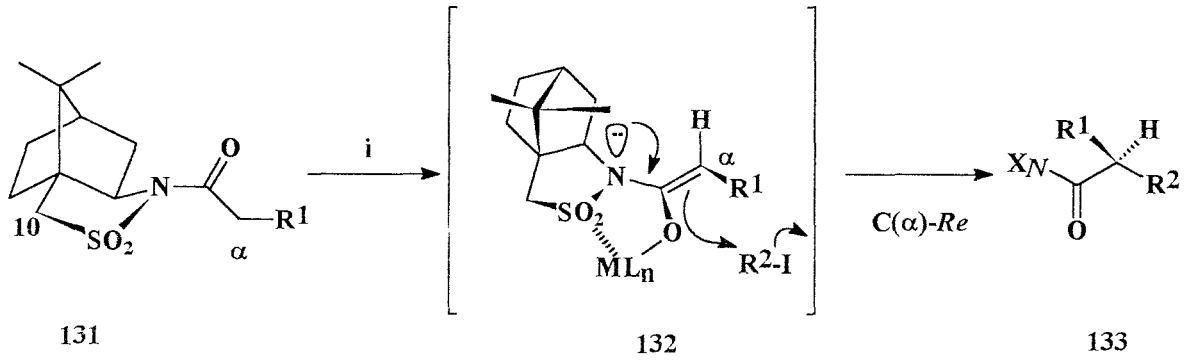
SCHEME 18. Reagents: i) Et_2BOTf, $Et(i\text{-}Pr)_2N$, CH_2Cl_2, -5 °C; RCHO, -78 °C;
ii) BuLi, Bu_3SnCl; RCHO, -78 °C;
iii) TBDMSOTf, Et_3N; $TiCl_4$, RCHO, -78 °C;
iv) Et_2BOTf, $Et(i\text{-}Pr)_2N$, -10 °C; RCHO, $TiCl_4$, -78 °C.

TABLE 4. Data for the aldol reaction using Oppolzer's sultam as a chiral auxiliary (Scheme 18)

Entry	R	Counter -ion	Lewis acid	*syn : anti*	Major product	yield/ % (cryst.)	d.e./ % (cryst.)
1	i-Pr	B(III)	-	100 : 0	**127**	76	>99
2	i-Pr	Sn(IV)	-	97.5 : 2.5	**128**	44	>99
3	i-Pr	Si[a]	$TiCl_4$	0.8 : 99.2	**129**	76	>99
4	i-Pr	B(III)	$TiCl_4$	0.6 : 99.4	**129**	75	>99

[a] as silyl enol ether

Alkylation of *N*-acylsultams, such as compound (**131**), permits the synthesis of C(α,α)-disubstituted carboxylic acid derivatives (**133**) *via* a (*Z*)-enolate intermediate (**132**) (Scheme 19).[167] To prevent competitive alkylation at C-10, NHMDS (sodium hexamethyldisilazide) or BuLi was used (entries 1 and 2; Table 5). Another advantage of using the sultam is that non-activated alkyl halides can be used. Attack occurs at the *endo*-face opposite the nitrogen lone pair [the C(α)-*Re* face]. By interchanging R^1 and R^2 (entry 3; Table 5) or by using the sultam antipode (**118**), the opposite configuration at C(α) can be obtained. This method can also be used in the synthesis of α,β-dialkylated carboxylic acid derivatives of enoylsultams *via* an initial 1,4 addition reaction.



131 132 133

SCHEME 19. Reagents: i) Base, -78 °C; HMPA.
X_N = (**117**)

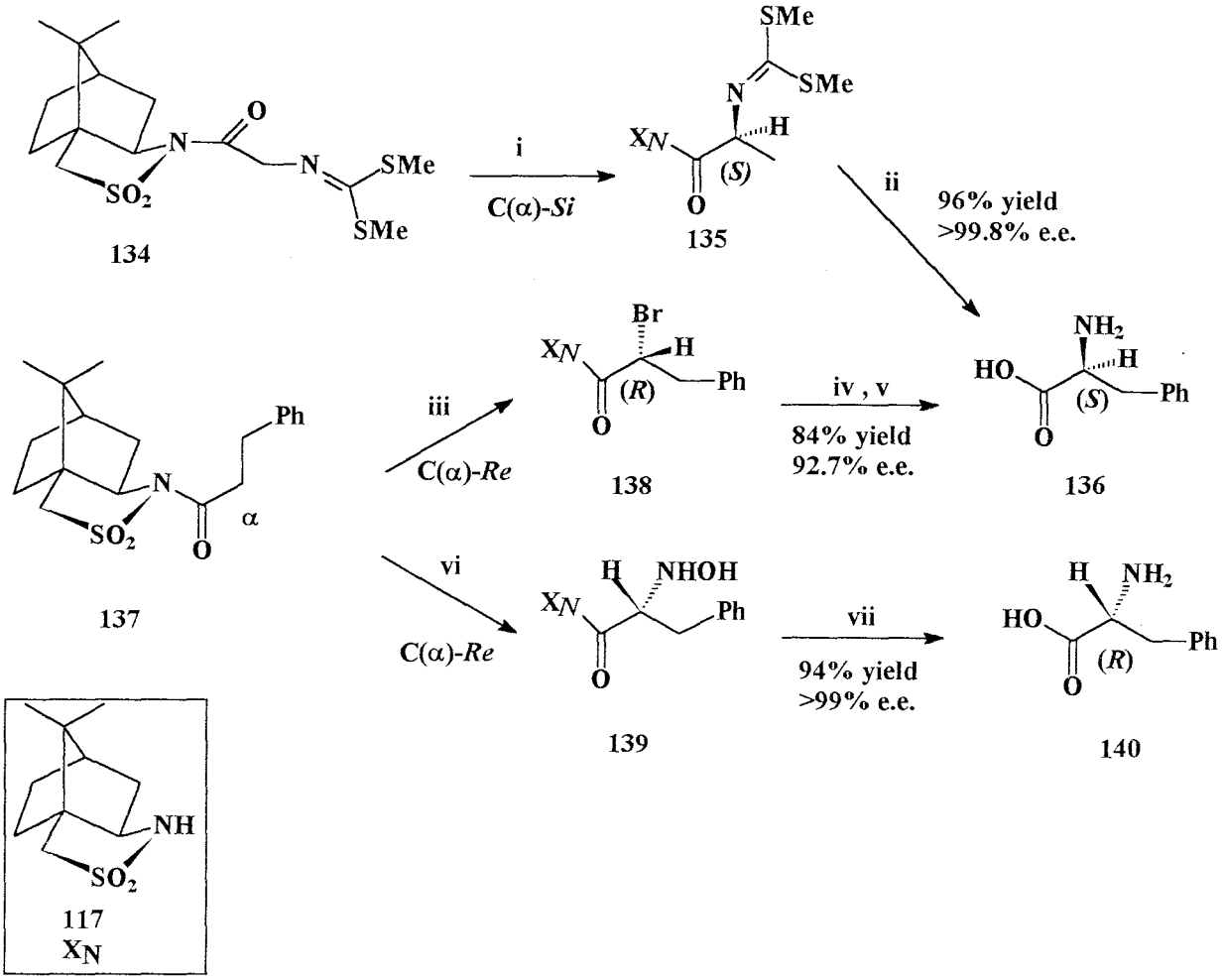
TABLE 5. Data for asymmetric alkylations using Oppolzer's sultam as a chiral auxiliary (Scheme 19)

Entry	R^1	R^2	Base	% yield (cryst.)	% d.e. (cryst.)	Config. (α)
1	Me	$PhCH_2$	NHMDS	89	98.4	*S*
2	Me	$PhCH_2$	BuLi	89	98.5	*S*
3	$PhCH_2$	Me	BuLi	88	>99	*R*

There are a number of ways of synthesising α-amino acids using Oppolzer's sultam (Scheme 20). One method involves alkylation of the sultam-derived *N*-[bis(methylthio)methylene]glycinate (**134**) to afford the intermediate (**135**). The alkylation step is followed by *N*-deprotection and cleavage of the chiral auxiliary to afford (*S*)-amino acids (**136**).[168] Attack on the enolate intermediate occurs on the face remote from the nitrogen lone pair, *i.e.* from the C(α)-*Si* face. Alkylation of the glycinate derivative (**134**) has also been effected with 'activated' organo halides using ultrasound-assisted phase-transfer catalysis,[169] - an approach which has been applied to the synthesis of α-deuterated amino acids.[170] α-Amino acids can also be synthesised by attaching a heteroatom at the α-position of an *N*-acylsultam. For example, reaction of the enolate derived from the *N*-acylsultam (**137**) with NBS affords the brominated product (**138**), which undergoes substitution by azidation in an S_N2 reaction. Subsequent hydrogenolysis and removal of the chiral auxiliary then yields the (*S*)-amino acid (**136**) in good enantiomeric excess.[153]

α-Amino acids, α-hydroxyamino acids and *N*-protected amino acids may be synthesised *via* electrophilic 'amination'.[171] Thus, treatment of enolates derived from *N*-acylsultams, such as (**137**) with 1-chloro-1-nitrosocyclohexane affords hydroxylamine products such as (**139**). The corresponding (*R*)-amino acid (**140**) may then be obtained by hydrogenolysis of the hydroxylamine (**139**) followed by hydrolysis to remove the sultam. Electrophilic attack again occurs from the C(α)-*Re* face, *i.e.* opposite to the sultam nitrogen lone pair.

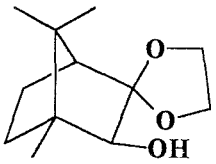
This method can also be used in the synthesis of C(β)-branched amino acids *via* addition to an *N*-enoylsultam,[172] as well as *N*-alkylated α-amino acids.[173] One example of this approach is in the synthesis of (-)-pinidine in 9 steps in 18.5% overall yield.[174] The diversity of the reactions carried out using chiral sultams even extends to the polymerisation and teleomerisation of chiral acrylamides[175] and, more recently, to the synthesis of chiral aziridines *via* the aza-Darzen reaction.[176]



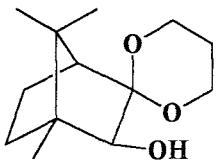
SCHEME 20. Reagents: i) BuLi, THF, -78 °C; $PhCH_2I$, HMPA;
ii) 0.5 **M**-HCl, THF, r.t.; LiOH, THF; ion exchange;
iii) Bu_2BOTf, $Et(i\text{-}Pr)_2N$, CH_2Cl_2, -5 °C; NBS, THF,-78°C;
iv) $(Me_2N)_2C{=}NH_2^+N_3^-$;
v) H_2, Pd-C; LiOH, THF;
vi) NHMDS; $ON(Cl)C_6H_{10}$; 1**M**-HCl, r.t.;
vii) Zn, aq. HCl, AcOH, 0 °C; LiOH, THF; ion exchange.

1.3 Previous Work in the Research Group and Aims of the Present Investigation

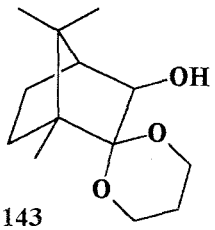
Chiral silyl enol ethers, synthesised by our research group using borneol, menthol and cholesterol as chiral auxiliaries,[177] showed poor stereoselectivities (up to 14% d.e.) in MCPBA oxidation reactions[33] and reactions with electrophiles under Lewis acid catalysed conditions.[32] In an attempt to try and improve on these results, a number of chiral auxiliaries (**141 - 144**) were synthesised. However, silyl enol ethers derived from auxiliaries (**141**) showed stereoselectivities of up to 12% in Lewis acid-mediated reactions with electrophiles.[178] α-Benzylation reactions were also carried out on esters derived from the auxiliaries (**141 - 144**),[179, 180] the best stereoselectivity (58% d.e.) being obtained using the auxiliary (**143**).



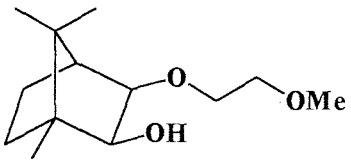
141



142



143



144

The present study is part of an ongoing program and the main objectives have been the following:-

i) The synthesis and investigation of the stereofacial selectivity of camphor- and pinane-derived chiral auxiliaries, in:-
   a) MCPBA oxidation, Mukaiyama, alkylation and cyclopropanation reactions of silyl enol ether derivatives.
   b) α-Alkylations of ester derivatives.
   c) Baylis-Hillman reactions of ester derivatives.

ii) The use of molecular modelling techniques to explore conformational properties and to design novel camphor-derived chiral auxiliaries.

iii) The attachment of silicon directly to the camphor skeleton to improve diastereoselectivity of silyl enol ether derivatives.

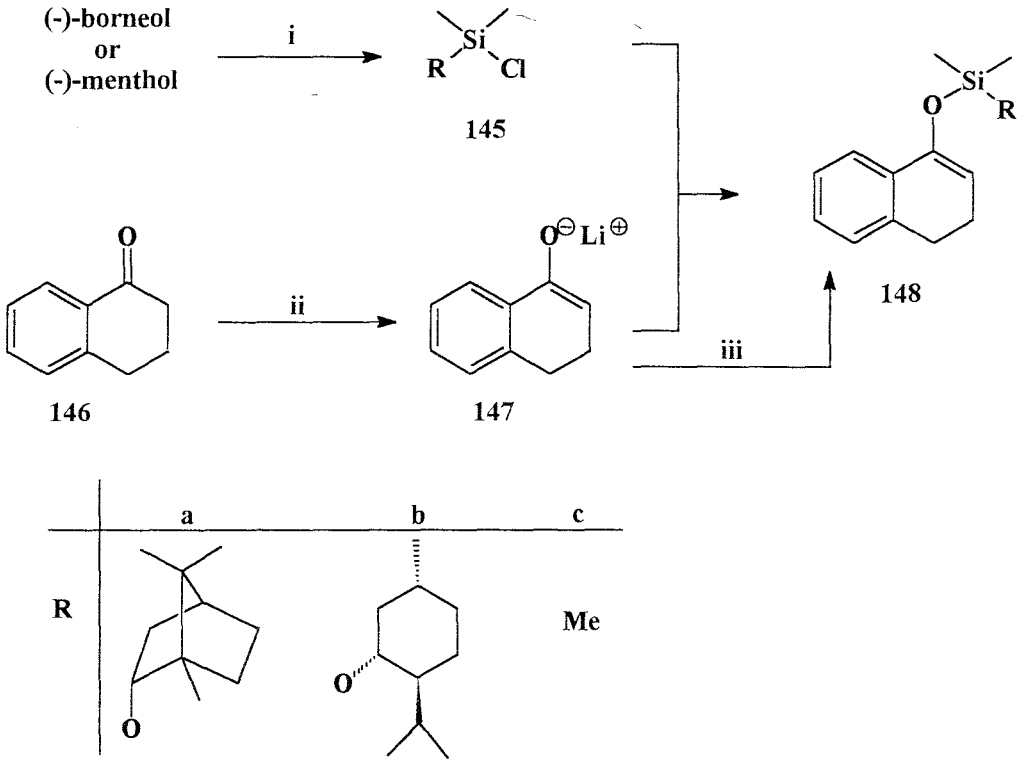
iv) The analysis of the fragmentation pattern in the electron impact mass spectra of chiral silyl enol ethers.[181]

DISCUSSION

This project has been concerned with the development and synthesis of a number of chiral auxiliaries, and an investigation of their stereofacial selectivity. Initially, as a continuation of previous work by our research group, the cyclopropanation of menthol- and borneol-derived silyl enol ethers was studied (Section 2.1). The chiral auxiliary, pinane, has also been investigated (Section 2.2) but attention has been concentrated mainly on the development of camphor-derived chiral auxiliaries. These auxiliaries include:- a camphor derivative with an α-methoxybenzyl blocking group (Section 2.3); a camphor-derived auxiliary developed by Helmchen *et al.*,[182] containing a xylyl blocking group (Section 2.4); and two camphor derivatives with ketal blocking groups (Section 2.6 and Section 2.7). Finally, mass spectrometry studies carried out on the silyl enol ethers synthesised throughout this project will be discussed (Section 2.8).

2.1 Borneol and Menthol-derived Silyl Enol Ethers

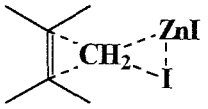
Various methods have been used for the synthesis of silyl enol ethers.[183] A convergent approach (Scheme 1) was used by Learmonth[177] to avoid the formation of bis-substituted silanes - a problem detected when using the synthetic procedure developed by Walkup *et al.*[184] In the present study, the tetralone silyl enol ethers (**148a**) and (**148b**) were prepared following the convergent approach (Scheme 1). The first step, involving the reaction of the chiral alcohols [(-)-menthol or (-)-borneol)] with dichlorodimethylsilane (Me_2SiCl_2) and triethylamine (Et_3N), gave disappointing yields of the corresponding chlorosilanes (**145a**) and (**145b**). Deprotonation of α-tetralone (**146**) to form the enolate (**147**) was carried out using lithium diisopropylamide (LDA) at -78 °C, and addition of the respective chlorosilanes resulted in the formation of the chiral silyl enol ethers (**148a**), (**148b**) and the trimethylsilyl enol ether (**148c**) in reasonable yields.



SCHEME 1. Reagents: i) Me_2SiCl_2, Et_3N, Et_2O;
ii) LDA, Et_2O, -78 °C;
iii) LDA, Et_2O, -78 °C, then Me_3SiCl (**145c**).

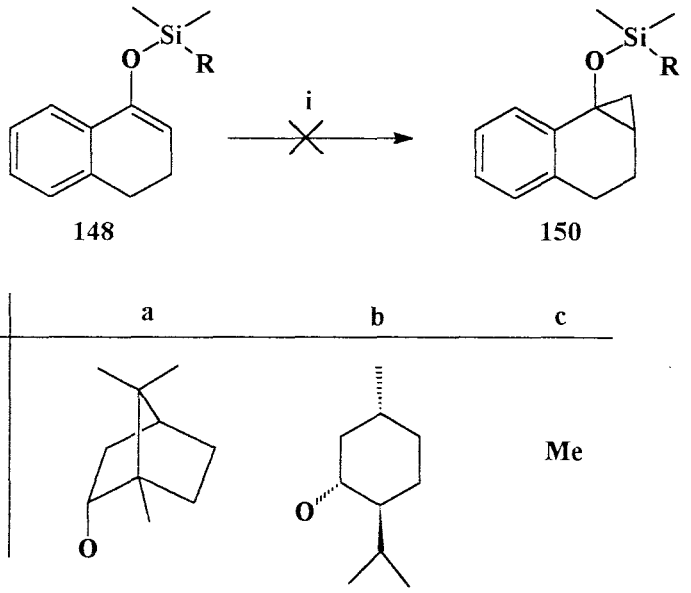
2.1.1 Cyclopropanation of the silyl enol ethers (148a), (148b) and (148c)

In a cognate study,[72] Simmons-Smith cyclopropanation of chiral α,β-unsaturated acetals has been shown to proceed with high diastereofacial selectivity, and such reactions were carried out on the α-tetralone silyl enol ethers (**148a**), (**148b**) and (**148c**). The Simmons-Smith reagent, CH_2I_2-Zn(Cu), has been used in the cyclopropanation of the trimethyl silyl enol ether of α-naphthalone with moderate success,[185, 186] but better results were reported when the cyclopropanation was carried out using diethylzinc.[187] The Simmons-Smith reaction involves a carbenoid intermediate (**149**) which reacts similarly to a carbene but is not actually a carbene. The proposed organozinc attacking species, bis(iodomethyl)zinc.zinc iodide $[(ICH_2)_2Zn.ZnI_2]$, formed by the reaction of diiodomethane with the zinc couple, is reported to react stereoselectively *via* the intermediate (**149**) to produce the *syn* product by a concerted mechanism.[188]



149

In our work, however, the cyclopropanations were carried out using an 'improved' Simmons-Smith reagent, *viz.* a Zn/Ag couple.[189] These reactions proved to be disappointing as complex mixtures of products were obtained in the reaction of all three silyl enol ethers (**148a-c**) (Scheme 2), and various attempts to separate these mixtures proved unsuccessful. Given these difficulties and the fact that menthol- and borneol-derived silyl enol ethers have previously exhibited low stereoselectivity in MCPBA oxidations,[33] Mukaiyama reactions and alkylations using *t*-BuCl,[32] it was decided to explore alternative and, hopefully, more efficient chiral auxiliaries. Consequently, the use of pinane as a chiral auxiliary was investigated.



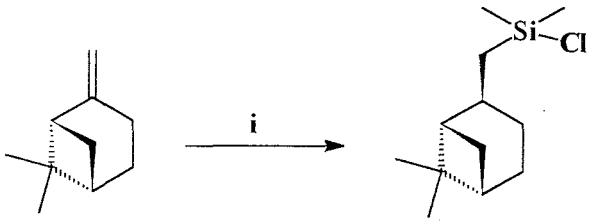
SCHEME 2. Reagents: i) Zn(Ag), then CH_2I_2, Et_2O, reflux.

2.2 Pinane as a Chiral Auxiliary

Work was carried out using α- and β-pinene in an attempt to synthesise chiral silyl enol ethers in which the silicon was attached directly to a chiral bicyclic skeleton instead of through the silyl ether bond, as was the case in the silyl enol ethers discussed in the previous section.

2.2.1 The hydrosilation of β-(-)-pinene

The (1*S*)-(-)-*trans*-pinane-derived hydrosilane, prepared *via* the chlorosilane (**152**) by Wang and Chan,[190] has been used as a chiral auxiliary in the asymmetric reduction of ketones. The silyl chloride (**152**) has also been used to prepare a solid membrane employed in the resolution of chiral molecules,[191] as well as in the synthesis of chiral allyl silanes, which have been employed in asymmetric addition reactions with aldehydes.[192] In the present study, (1*S*)-(-)-β-pinene (**151**) was hydrosilylated with very high stereoselectivity using Me_2ClSiH and chloroplatinic acid as the catalyst (Scheme 3).[193] Only the one diastereomer of the expected terminal silyl chloride was detected by ^1H and ^{13}C NMR spectroscopy.



151 **152**

SCHEME 3. Reagents: i) Me_2ClSiH, $H_2PtCl_6.xH_2O$, reflux, 6h.

2.2.1.1 Chiral silyl enol ethers prepared from the pinane auxiliary

The silyl enol ethers (**153**) and (**156**) were prepared from α-tetralone (**146**) and pinacolone (**154**) respectively as depicted in Scheme 4. Abstraction of an α-hydrogen from each of the ketones was carried out using LDA; once formed, the corresponding enolates (**147**) and (**155**) were silylated using the chlorosilane (**152**). The structures of both silyl enol ethers were unambiguously characterised using 1- and 2-D NMR techniques. The ^1H and ^{13}C NMR spectra of the silyl enol ether (**156**) are shown in Figure 1.

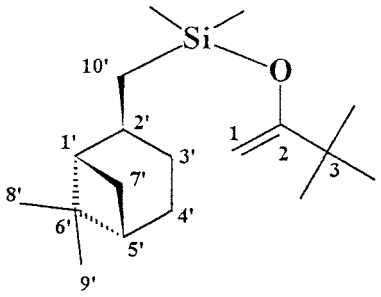
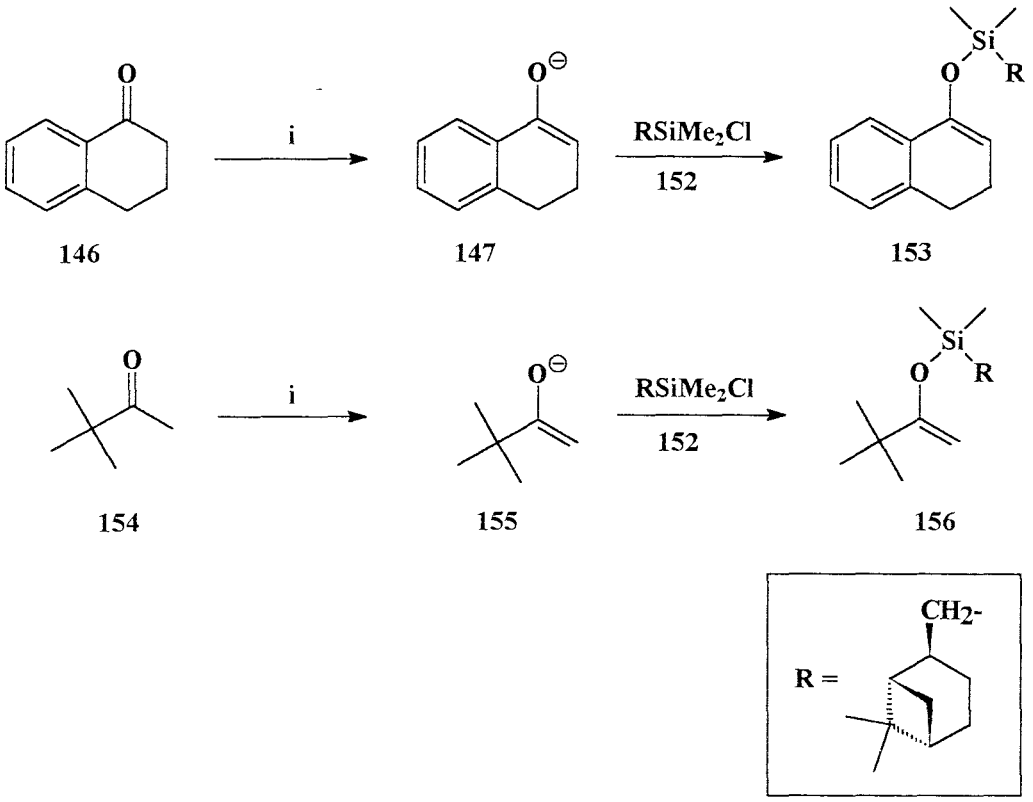
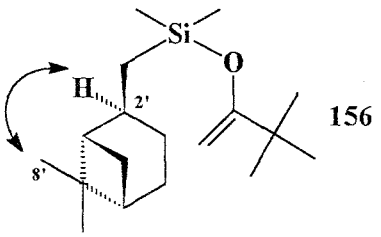


FIGURE 1. a) 400 MHz ^1H; and b) 100 MHz ^{13}C NMR spectra of silyl enol ether (156) in $CDCl_3$.



SCHEME 4. Reagents: i) LDA , Et_2O, -78 °C.

The stereochemistry of the new stereocentre C-2 of the pinane moiety in the chlorosilane (**152**) was determined by analysis of the pinacolone derived silyl enol ether (**156**). Examination of the derivative was necessitated by the highly reactive nature of the chlorosilane and, thus, by its rapid decomposition. Nuclear Overhauser effects (NOE) in the silyl enol ether (**156**) were detected using the 2-D NMR technique, NOESY (nuclear **O**verhauser and exchange spectroscopy)[194] (see Figure 2). This experiment revealed an NOE interaction between H-2' and the 8'-Me group, and as the 8'-Me group is *endo*, it may be inferred that H-2' is also *endo* and that the silicon is therefore attached to the *exo*-face. Consequently, the new stereocentre C-2' is assigned an (*S*)-configuration.



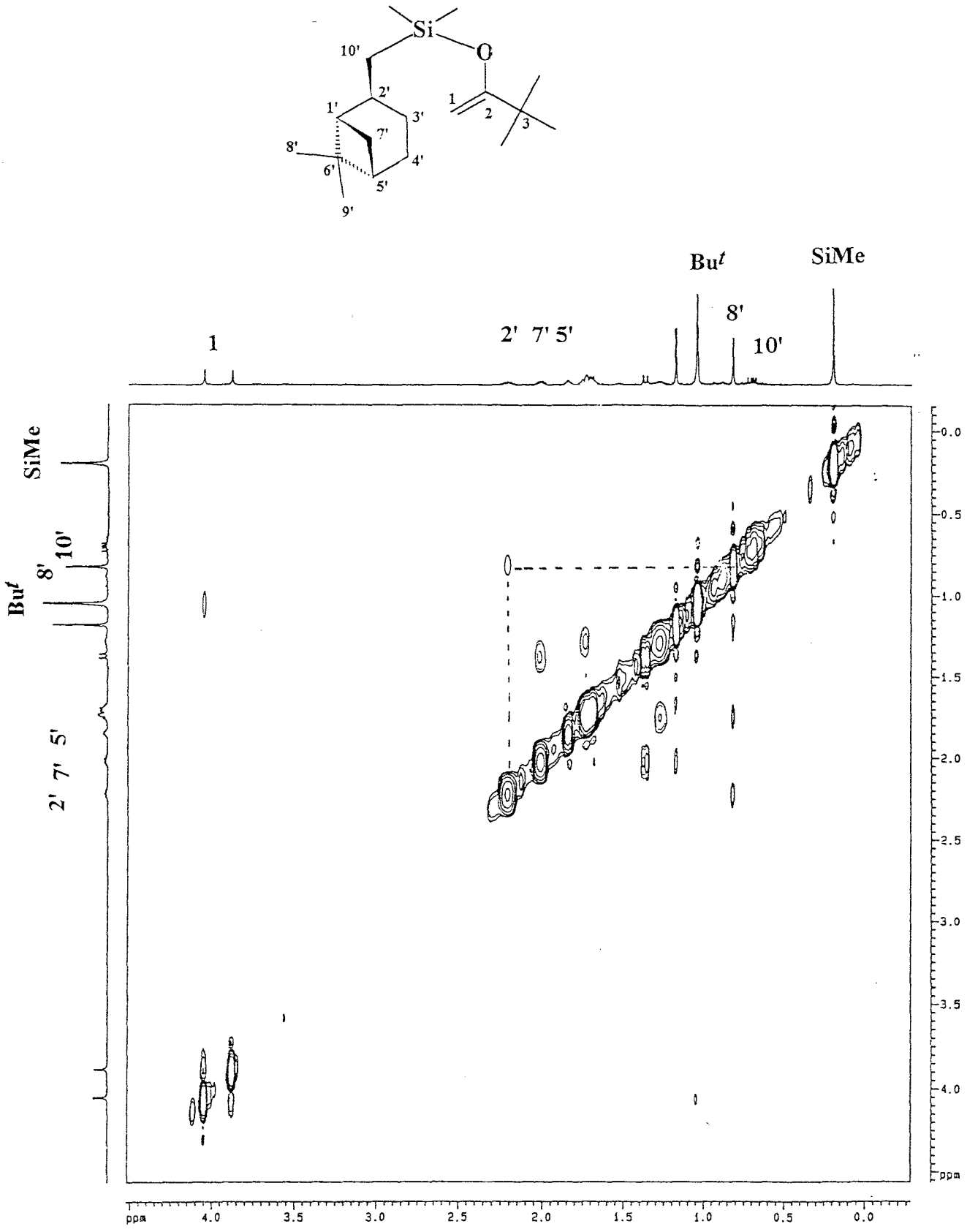


FIGURE 2. 400 MHz NOESY spectrum of silyl enol ether (156) in $CDCl_3$.

To determine the stereocontrol afforded by the pinane chiral auxiliary, a number of reactions were carried out on its silyl enol ether derivatives, *viz.*, i) MCPBA oxidation;[195]

ii) alkylation with *t*-BuCl-$TiCl_4$;[196]

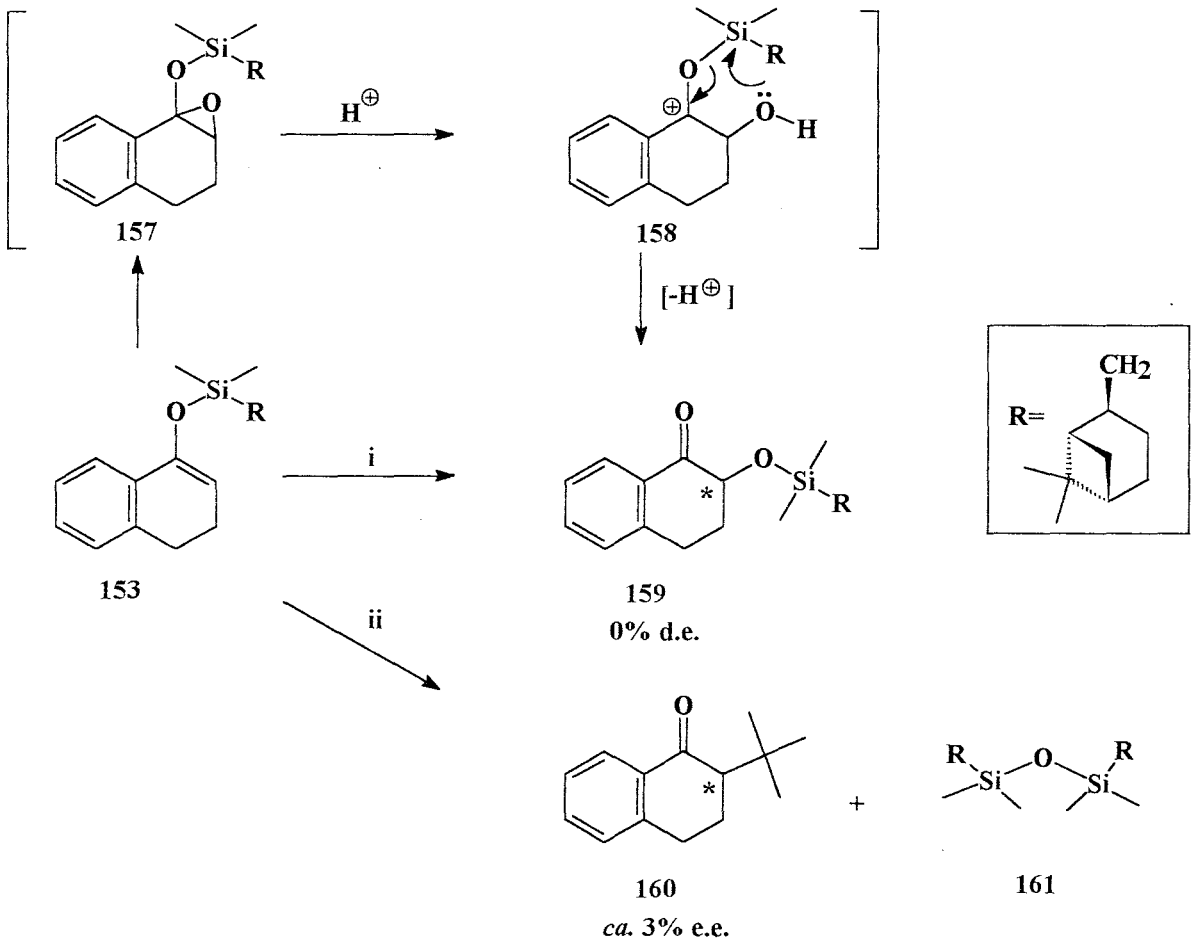
iii) the Mukaiyama reaction with PhCHO-$TiCl_4$.[197, 109]

When diastereomeric products are formed, as in the case of MCPBA oxidation, the diastereomeric excess can be determined directly by integration of suitably resolved ^{1}H NMR signals corresponding to the diastereomers present. In order to obviate errors arising from possible changes in the diastereomer distribution during purification, the diastereomeric excess was determined from the crude reaction mixtures. ^{1}H NMR Spectroscopic analysis of enantiomeric mixtures was achieved using the chiral shift reagents, tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III) [Eu(hfc)$_3$] and tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]praseodymium(III) [Pr(hfc)$_3$].[198] Addition of these shift reagents permitted resolution of selected signals in the enantiomeric species, thus providing % e.e. data for the alkylation and Mukaiyama reactions.

i) MCPBA oxidation of the α-tetralone-derived silyl enol ether (**153**) is outlined in Scheme 5. The reaction is proposed to occur *via* the intermediate silyloxyepoxide (**157**) which, on protonation, opens up to form an oxycarbocation (**158**) resulting in the formation of the α-silyloxyketone (**159**).[195] In our case, however, the diastereomeric product (**159**) was formed without any apparent stereoselectivity.‡ This was determined by the integration of the diastereomeric 2-H signals in the ^{1}H NMR spectrum of the diastereomeric product (**159**) shown in Figure 3.

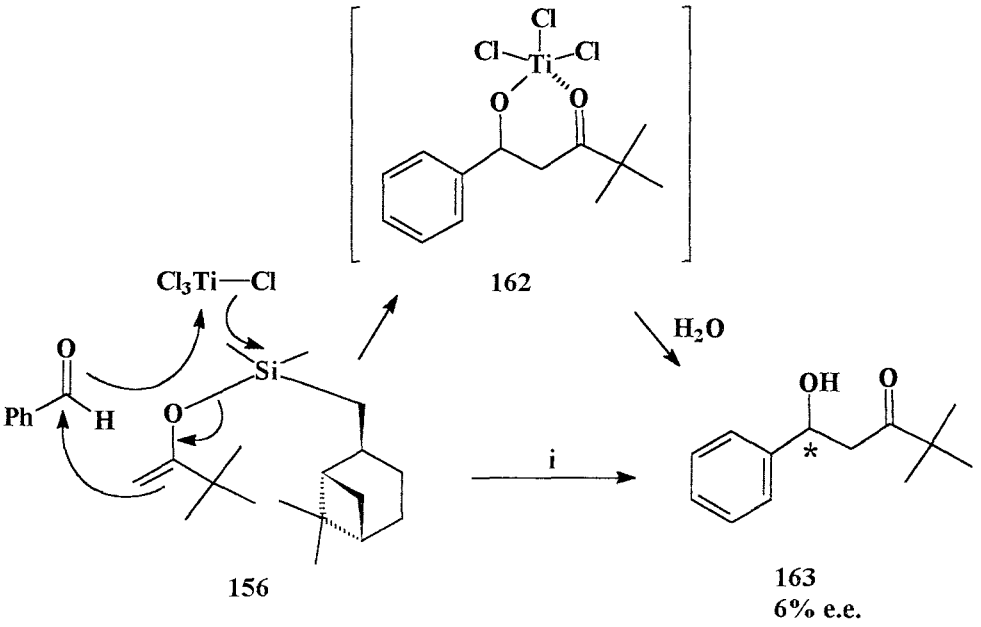
‡ New stereocentres are denoted by an asterisk.

ii) The α-tetralone-derived silyl enol ether (**153**) was also subjected to Lewis acid ($TiCl_4$)-catalysed alkylation with *t*-BuCl, as depicted in Scheme 5. The α-alkyl ketone (**160**) was obtained in 2% and 4% e.e., as determined by integration of the resolved *t*-butyl peaks in the ^1H NMR spectrum of (**160**) after addition of the chiral shift reagents, [Eu(hfc)$_3$] and [Pr(hfc)$_3$] respectively. A corresponding spectrum is shown in Figure 3. In this reaction, the pinane-derived disiloxane (**161**) was also isolated in low yield (*ca.* 11%).



SCHEME 5. Reagents: i) MCPBA, $NaHCO_3$, CH_2Cl_2, 0 °C, 2h;
ii) *t*-BuCl, CH_2Cl_2, -23 °C, then $TiCl_4$, 3h.

iii) Finally, the pinacolone-derived silyl enol ether (**156**) underwent a $TiCl_4$-catalysed Mukaiyama reaction with benzaldehyde (Scheme 6). This reaction is proposed to occur *via* the aldolate intermediate (**162**) affording the enantiomeric α-hydroxyketone (**163**).[199] The low enantiomeric excess (6% e.e.) observed in this reaction was determined by integration of the ^1H NMR *t*-butyl peaks, which were resolved by the use of the chiral shift reagent [Eu(hfc)$_3$] (displayed in Figure 3). From a less reliable means, a 3% e.e. of the (*R*)-isomer was determined using optical rotation.



SCHEME 6. Reagents: i) PhCHO, $TiCl_4$, CH_2Cl_2, -78 °C, 4.5h.

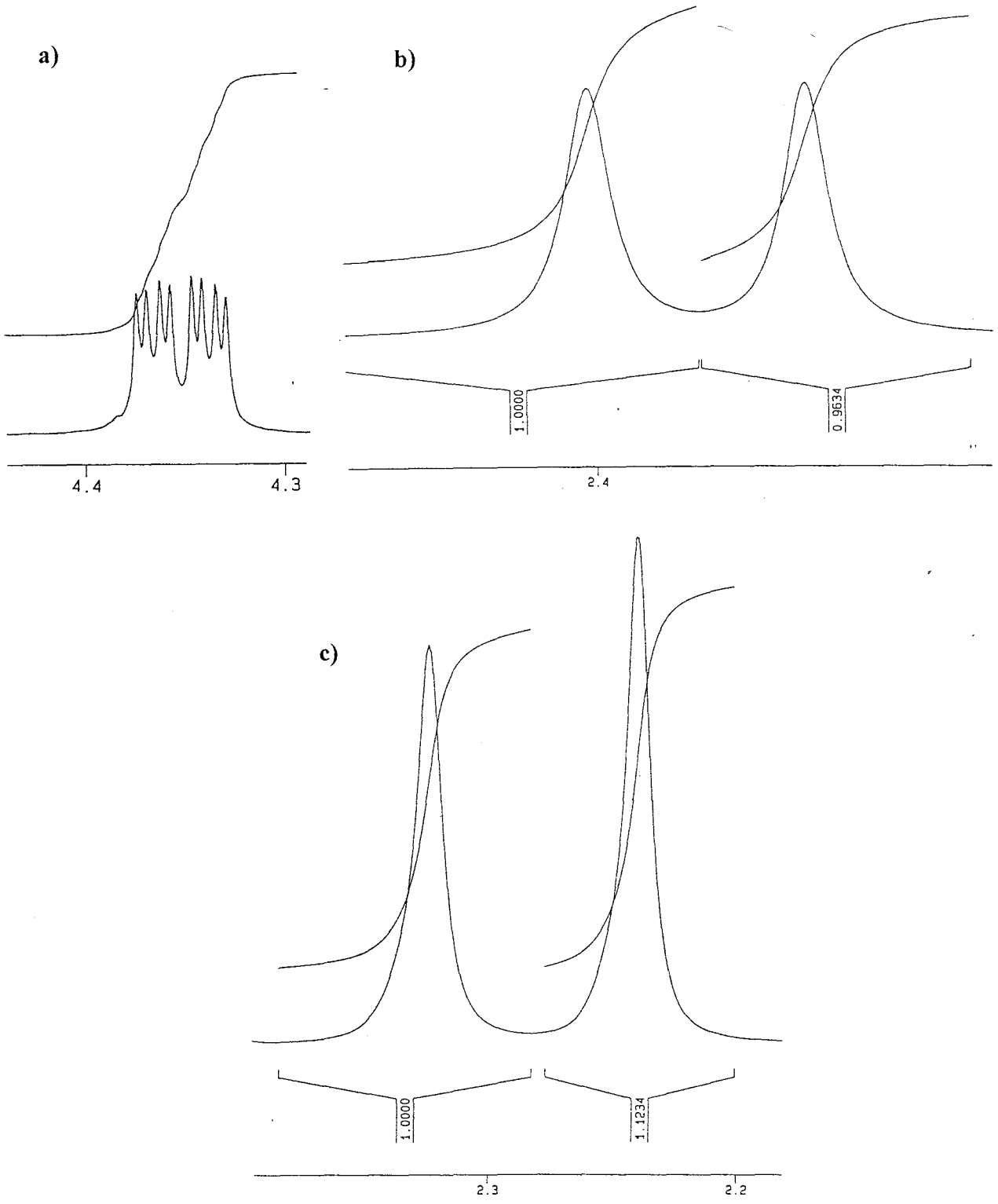


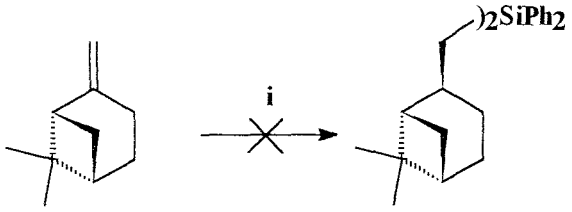
FIGURE 3.

a) An integrated 400 MHz ^{1}H NMR spectrum of (**159**) in $CDCl_3$ showing the diastereomeric 2-H signals.

b) An integrated 400 MHz ^{1}H NMR spectrum of (**160**) in $CDCl_3$ showing the *t*-butyl peaks resolved using [Eu(hfc)$_3$].

c) An integrated 400 MHz ^{1}H NMR spectrum of (**163**) in $CDCl_3$ showing the *t*-butyl peaks resolved using [Eu(hfc)$_3$].

The disappointing stereocontrol observed in the reactions of the silyl enol ethers (**153**) and (**156**) prompted an attempt to synthesise a silyl derivative containing two pinane moieties (**164**). However, in a metal-catalysed reaction using Ph_2SiH_2 and 2 equivalents of β-pinene (Scheme 7), a complex mixture of products was obtained. An alternative, peroxide-catalysed hydrosilation could not be used in this case as the method results in cleavage of the bicyclic pinane ring system.[200]

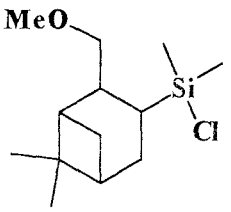


151 **164**

SCHEME 7. Reagents: i) Ph_2SiH_2, $H_2PtCl_6.xH_2O$, reflux, 3h.

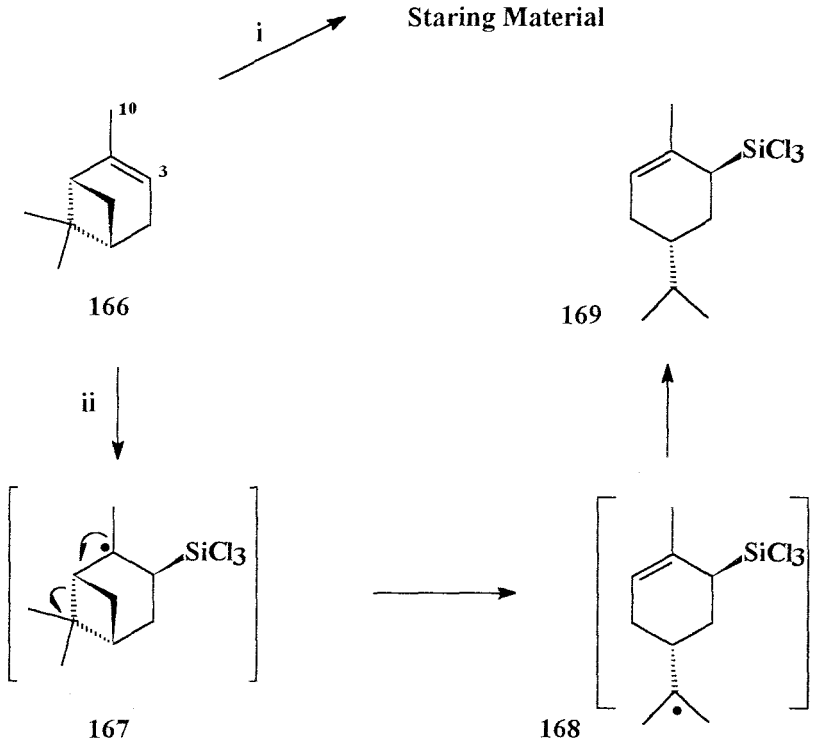
2.2.2 The hydrosilation of α-(-)-pinene

The low stereoselectivities obtained in the above reactions were attributed to the distance between the chiral auxiliary and the prochiral centre, as well as the lack of a chelating group on the auxiliary when $TiCl_4$ was used. It was anticipated that a direct Si-C bond to the pinane bicyclic skeleton might alleviate the first problem. Such a bond has been formed by Taddei *et al.*[201] *via* the addition of phenyldimethylsilylcuprate to the α,β-unsaturated aldehyde, (1R)-(-)-myrtenal; replacement of the phenyl group by chlorine afforded the chlorosilane derivative (**165**) which also contains a chelating group. The chlorosilane (**165**) was then used in the synthesis of chiral allyl silanes, reactions with carbonyl compounds gave addition products in up to 59% e.e.[202]



165

In an attempt to synthesise a similar chlorosilane, hydrosilation reactions were carried out on (1*S*)-(-)-α-pinene (**166**). In the first, metal-catalysed approach (method 1), the terpene substrate was treated with chloroplatinic acid and Me_2ClSiH (Scheme 8) but only the starting materials were detected in the reaction mixture. In the second approach (method 2), a free radical induced hydrosilation reaction[203] was carried out using benzoyl peroxide and Cl_3SiH; however, this resulted in rearrangement of the bicyclic ring system instead of the expected addition of silicon to C-3.



SCHEME 8. Reagents: Method 1 i) Me_2ClSiH, $H_2PtCl_6.xH_2O$, reflux, 5h;
Method 2 ii) Cl_3SiH, $(C_6H_5CO)_2O_2$, reflux, 6h, 25mmHg.

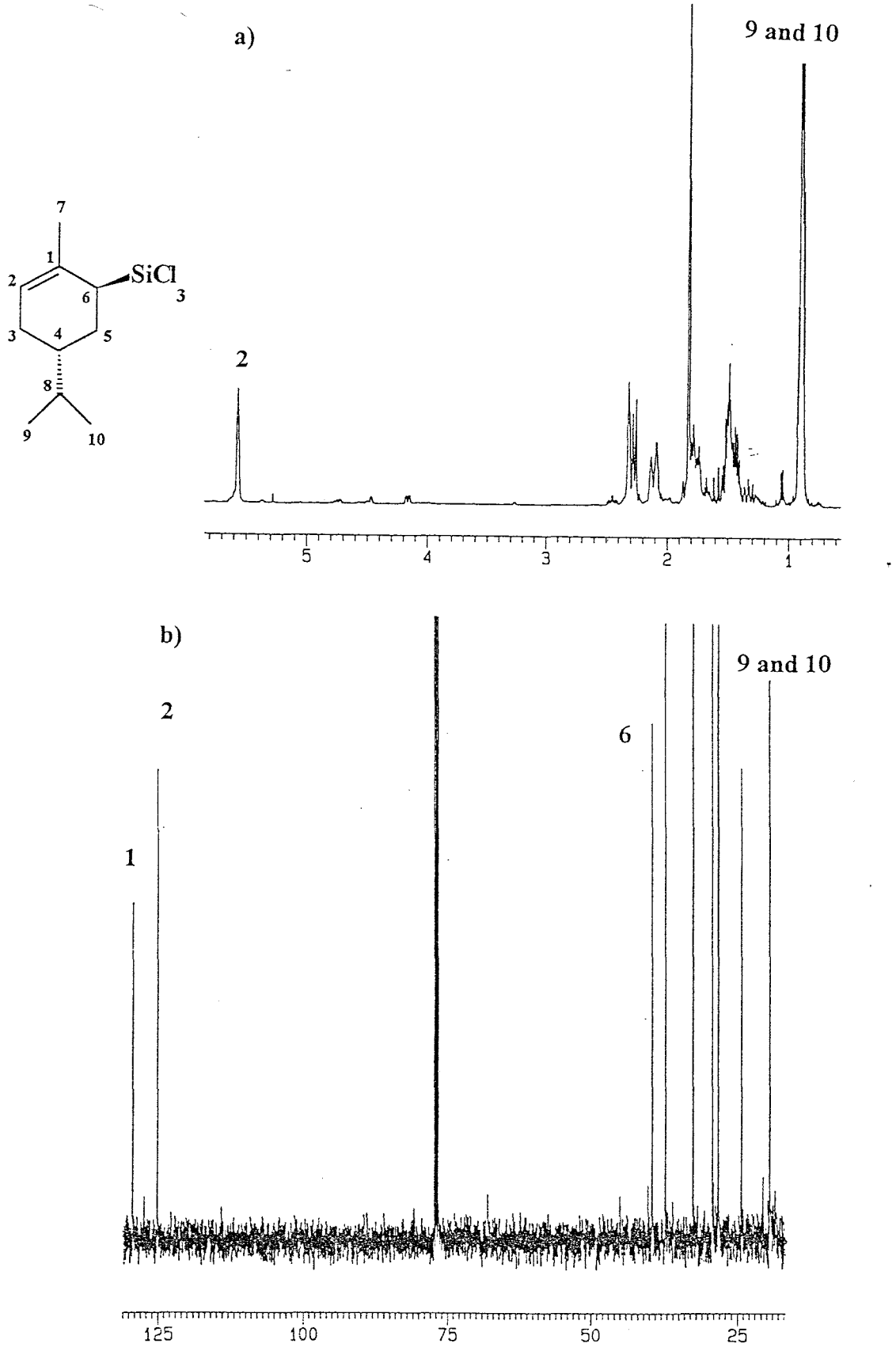


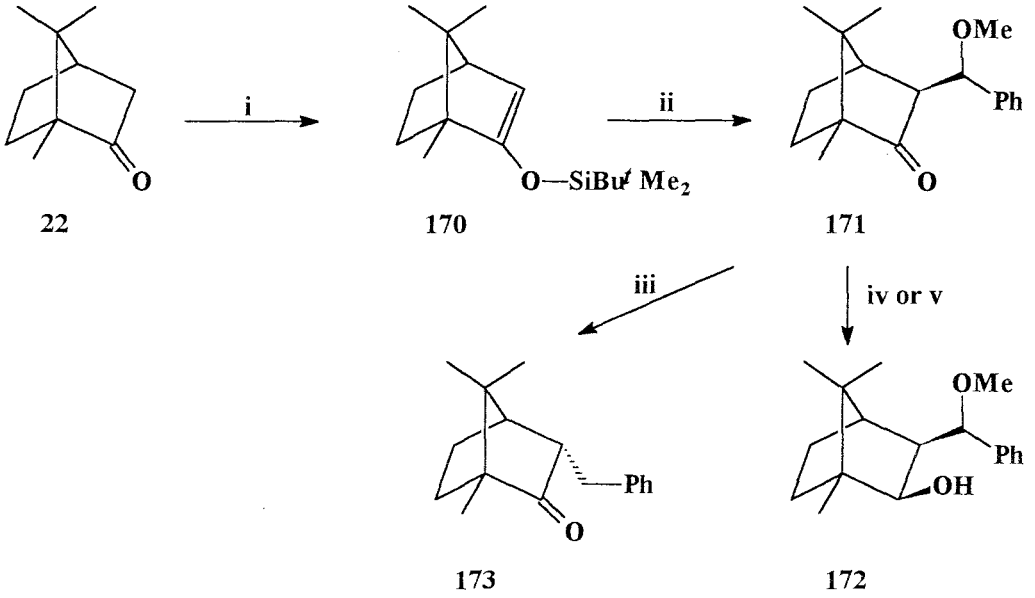
FIGURE 4. a) 400 MHz ^{1}H; and b) 100 MHz ^{13}C NMR spectra of the chlorosilane (169) in $CDCl_3$.

The trichlorosilane product (**169**), once purified, was found to comprise a single diastereomer. This is clearly evident from the absence of signal-splitting in both the ^{1}H and ^{13}C NMR spectra (Figure 4). The coincidence and congestion of signals in the ^{1}H NMR spectrum complicated interpretation of the NOE spectrum and conclusions about the stereochemistry of the trichlorosilane (**169**) could not be reached. However, from observed trends in the hydrosilation of β-pinene and in the hydroboration of α-pinene,[204] it was expected that the trichlorosilyl radical would attach at the face opposite to the bridge containing the two methyl groups. This presumes the formation of the intermediate (**167**), followed by rearrangement of the bicyclic ring system to form the tertiary radical (**168**) and, hence, product (**169**).

Since the investigation into the use of pinane as a chiral auxiliary appeared to hold little promise, attention was given to the use of various camphor derivatives. Reasonable stereofacial selectivities (up to 58% d.e.) had been obtained previously in our research group using camphor derivatives.[180] A chiral auxiliary, developed from camphor and containing an α- methoxybenzyl blocking group, was the first to be studied.

2.3 The Camphor-derived Chiral Auxiliary (172)

Camphor has many advantages when used as a chiral auxiliary, some of which were discussed in the introduction. Yamamoto *et al.*[205] synthesised the ketone (**171**) *via* the Mukaiyama reaction in very good yields and with high stereoselectivity. It was anticipated that the hydroxy derivative (**172**) might be an effective chiral auxiliary due to the presence of both a phenyl group, blocking attack of the reactive site from one face, as well as a methoxy group which could complex with the metal counter-ion in alkylation reactions, further improving diastereofacial selectivity.



SCHEME 9. Reagents: i) LDA,Et_2O, -78 °C, then *t*-$BuMe_2SiCl$;
ii) $PhCH(OMe)_2$ (**174**), CH_2Cl_2, -78 °C, then $TiCl_4$, 15 min;
iii) L-Selectride, THF, -78 °C;
iv) $NaBH_4$, MeOH, 0 °C;
v) $LiAlH_4$, Et_2O, 0 °C.

In order to synthesise the auxiliary (**172**), (+)-camphor was treated with LDA and *t*-$BuMe_2SiCl$ to yield the silyl enol ether (**170**). This was followed by a Mukaiyama reaction using $TiCl_4$ and benzaldehyde dimethyl acetal (**174**), which had been prepared from benzaldehyde and trimethyl orthoformate.[206] It has been suggested that this reaction proceeds *via* an S_N2 mechanism,[207] to yield a single stereoisomer, the *exo-threo* product (**171**).[205] Reduction of this product using L-selectride[208] gave a benzylated camphor derivative (**173**) together with small quantities of the expected product (**172**). Use of alternative reducing agents were then explored, *viz.*, sodium borohydride ($NaBH_4$)[209] and lithium aluminium hydride ($LiAlH_4$).[210, 211] Both reagents afforded the

required chiral auxiliary (**172**), the latter reagent giving a marginally higher yield. *Endo* hydride delivery during the reduction of camphor systems is well established,[211] and the observed coupling constant between H-2 and H-3 ($J_{2,3}$ 7.5 Hz) in the ^{1}H NMR spectrum of the product (**172**) (Figure 5) is consistent with a *syn* arrangement of these protons, thus confirming the initial *exo*-addition of the α-methoxybenzyl blocking group.[205] This is also confirmed in the NOESY spectrum of product (**172**), NOE interactions being detected between the 2-H_{endo} and the 3-H_{endo}; the 2-H_{endo} and the 6-H_{endo}; and the 3-H_{endo} and the 5-H_{endo} nuclei.

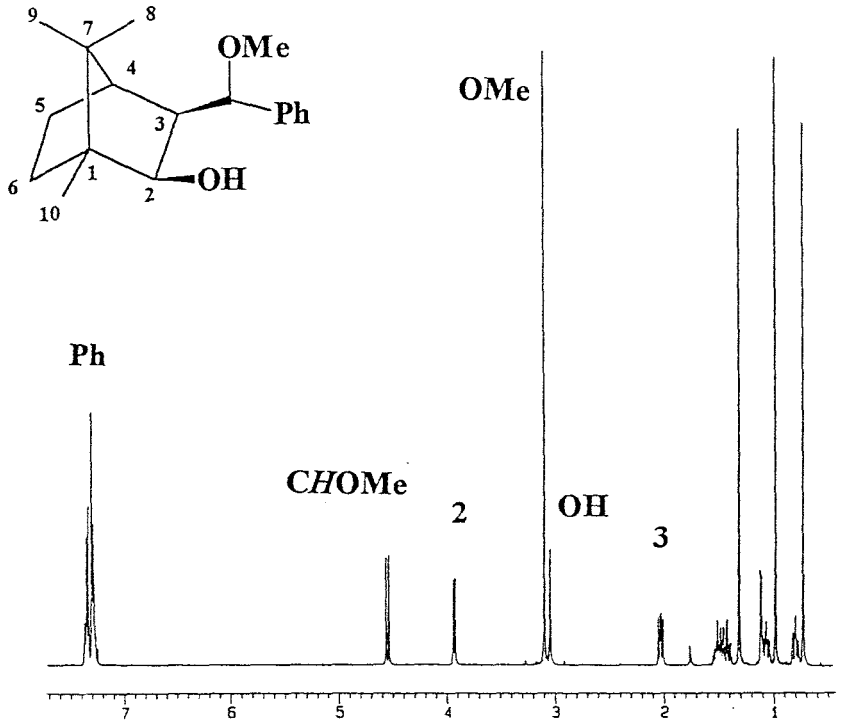


FIGURE 5. A 400 MHz ^{1}H NMR spectrum of the chiral auxiliary (**172**) in $CDCl_3$.

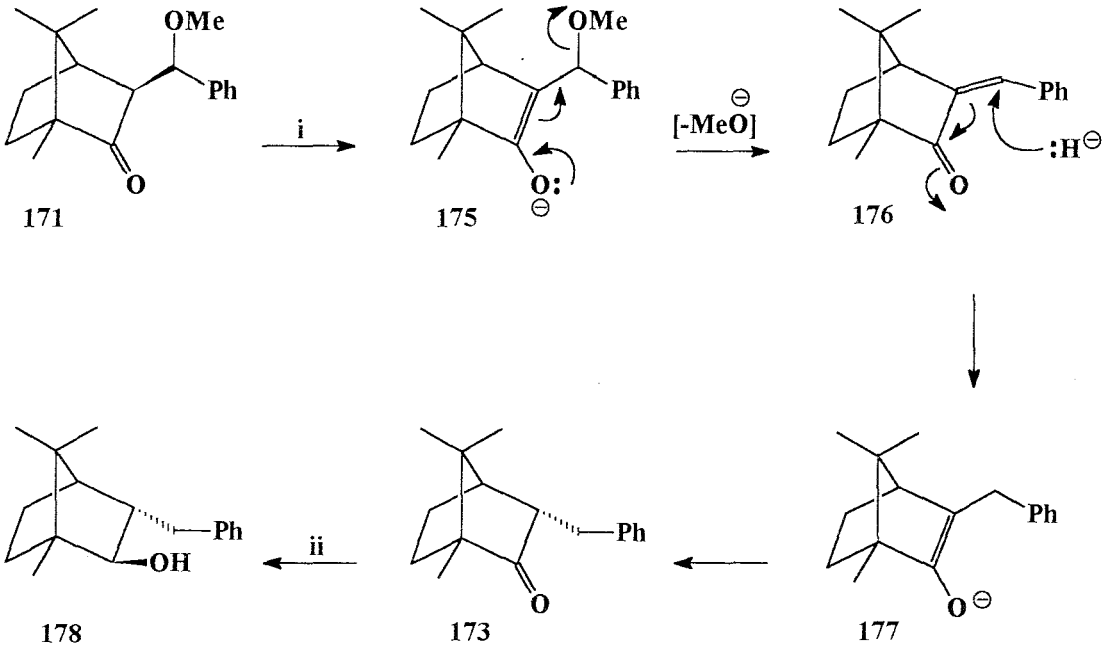
The *endo*-orientation of the 3-benzyl group in compound (**173**) is supported by:-

i) the exact correspondence of its NMR spectra with those of a sample of 3-*endo*-benzyl camphor prepared by an alternative route (see Section 2.5.2, p. 91);

ii) comparison of the ^{1}H and ^{13}C NMR data for the reduction product (**178**) (Scheme 10) of the latter sample with literature values;[212, 213] and

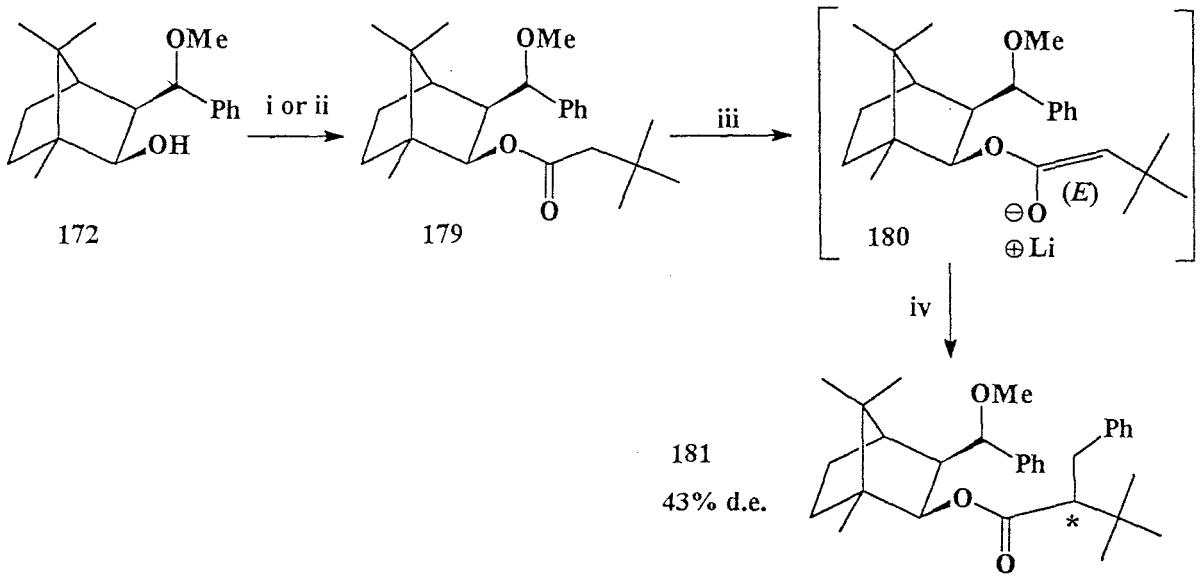
iii) the apparent absence of NOE interactions between the 3-H nucleus and either the 2-H_{endo} or the 5-H_{endo} nuclei in the NOESY spectrum of the reduction product (**178**).

Although there is a precedent for the cleavage of ethers using $LiAlH_4$ in the presence of the Lewis acid, aluminium trichloride ($AlCl_3$),[214, 215] we suggest that the formation of enolate intermediates (**175**) and (**177**) facilitate both cleavage of the methoxy group and final formation of the more stable *endo*-product (see Scheme 10).



SCHEME 10. Reagents: i) L-Selectride, THF, -78 °C;
ii) $LiAlH_4$, Et_2O, 0 °C.

In order to determine the efficiency of the auxiliary (**172**), the alkylation of the *t*-butyl ester derivative (**179**) was investigated. The initial step was the esterification of the chiral auxiliary (**172**) (Scheme 11), in which deprotonation of the alcohol, using NaH or BuLi, was followed by acylation with 3,3-dimethylbutanoyl chloride. When the deprotonation step was carried out using BuLi, the ester (**179**) was obtained cleanly and in high yields. Alkylation of the ester enolate (**180**) with benzyl bromide yielded the benzylated derivative (**181**) as a diastereomeric mixture, integration of the 2'-H_{endo} peaks in the crude reaction mixture (Figure 6) indicating a diastereomeric excess of 43%. From a consideration of likely transition state effects, it is proposed that preferential attack occurs from the *Si*-face of the (*E*)-enolate affording, as the major product, the diastereomer having an (*S*)-configuration at the new chiral centre. (See Section 2.4.1., p. 65 for further discussion on enolate geometry).



172 179 180

181
43% d.e.

SCHEME 11. Reagents: i) NaH, *t*-$BuCH_2COCl$, THF, reflux;
ii) BuLi, *t*-$BuCH_2COCl$, Et_2O, 0 °C;
iii) LDA, THF, -78 °C;
iv) $PhCH_2Br$, -78 °C.

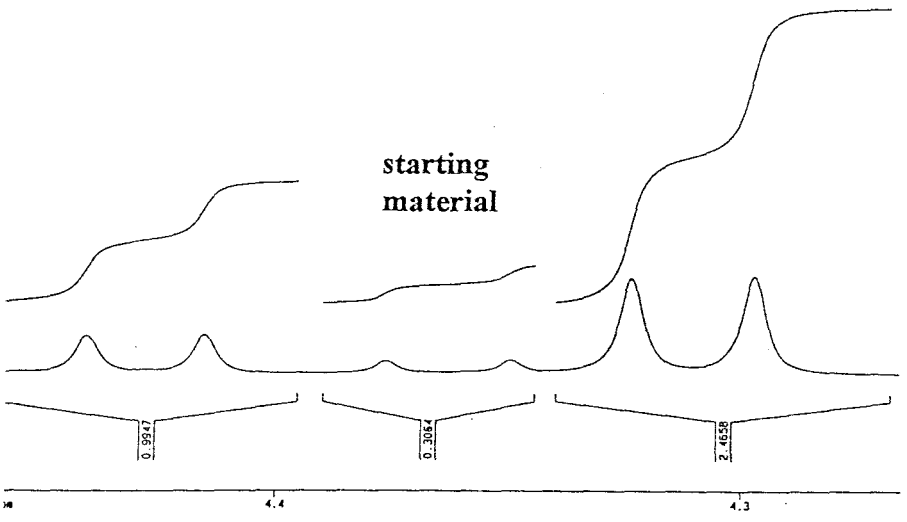


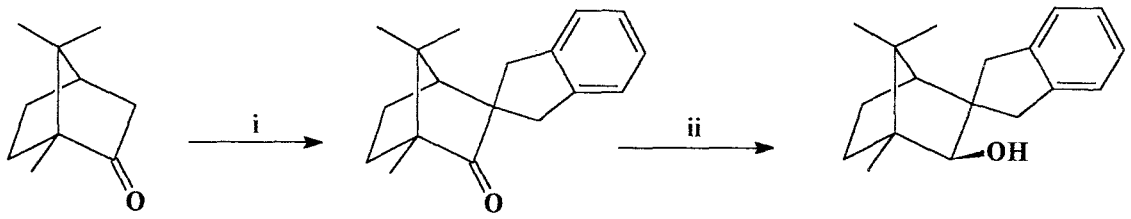
FIGURE 6. An integrated 400 MHz ^1H NMR spectrum of (181) in $CDCl_3$ showing the diastereomeric C*H*(OMe) signals.

Since low yields were obtained in the synthesis of the chiral auxiliary (172) (24% overall), and the alkylation reaction failed to show any significant improvement on the stereofacial selectivity achieved with other chiral auxiliaries previously synthesised in the research group, no further work was carried out using this particular auxiliary.

2.4 The Camphor-derived Chiral Auxiliary (183)

The camphor-derived chiral auxiliary (**183**) was first developed by Helmchen *et al.*,[182] and was used in asymmetric alkylation of its propanoic ester with stereoselectivities of up to 62% d.e. However, intermolecular Pauson-Khand reactions carried out using this chiral auxiliary showed no stereoselectivity,[216] and palladium catalysed oxidative cyclisation showed little stereofacial selectivity (12% d.e.).[217] This compound (**183**) has also been used in the preparation of chiral 1-aminoalkylphosphonic acids,[218] and as an ingredient in topical preparations used in the treatment of skin diseases.[219]

The initial step in the synthesis of the auxiliary is the addition of the xylyl blocking group. Deprotonation of (+)-camphor (**22**) was achieved using NaH and was followed by alkylation of the enolate anion intermediate with α,α'-dichloro-*o*-xylene (Scheme 12). Reduction of the ketone (**182**) using $LiAlH_4$ afforded the chiral auxiliary (**183**) in an overall yield of 41%.



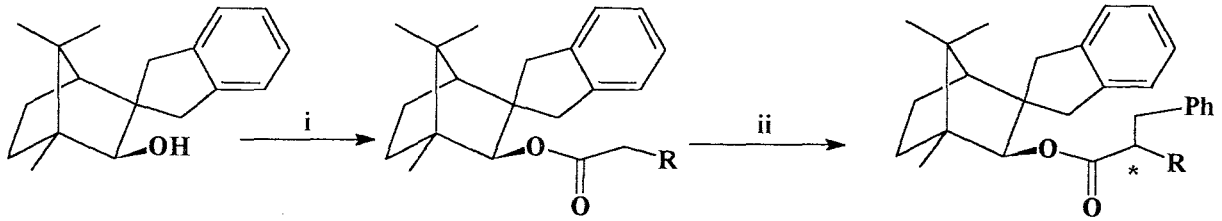
22 182 183

SCHEME 12. Reagents: i) 2 eq. NaH, toluene, then α,α'-dichloro-*o*-xylene, reflux;
ii) $LiAlH_4$, Et_2O, 0 °C.

2.4.1 Ester derivatives of the chiral auxiliary (183)

Helmchen *et al.*[182] in exploring alkylation of the propanoic ester of the chiral auxiliary (**183**), used lithium cyclohexylisopropylamide (LICA) to generate the enolate intermediate [both in the presence and absence of hexamethylphosphoric triamide (HMPT)]. In our research we examined the stereofacial selectivity afforded by this chiral auxiliary in the alkylation of a range of alkanoate esters, including the propanoic ester. Preparation of the ester substrates (**184**) is

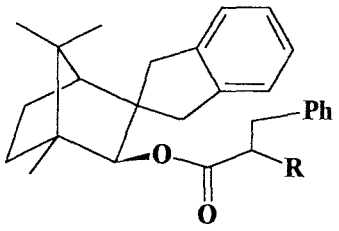
outlined in Scheme 13. In each case, initial deprotonation of the alcohol (**183**) with BuLi, to form the alkoxy anion, was followed by acylation using the appropriate acid chloride. Propanoyl chloride (**186a**), butanoyl chloride (**186b**) and phenoxyacetyl chloride (**186f**) were prepared by treating the corresponding carboxylic acids with $SOCl_2$, the other acid chlorides being obtained commercially. The enolate intermediates of these esters were then formed using LDA, and alkylation was effected by the addition of benzyl bromide.



183 184 185

SCHEME 13. Reagents: i) BuLi, Et_2O, 0 °C, then RCH_2COCl (**186**);
ii) LDA, THF, -78 °C, then $PhCH_2Br$.

TABLE 1. Stereoselectivity data for the α-benzylation of ester derivatives of the chiral auxiliary (**183**) (Scheme 13).



185

Entry	Substrate	R	% Yield (185)	% d.e. (185)
1	**184a**	Me	82	53
2	**184b**	Et	67	58
3	**184c**	Pr^i	63	60
4	**184d**	Bu^t	41	57
5	**184e**	Ph	68	9
6	**184f**	PhO	50[a]	21

[a] The yield was determined by integration of the ^1H NMR spectrum of the isolated mixture.

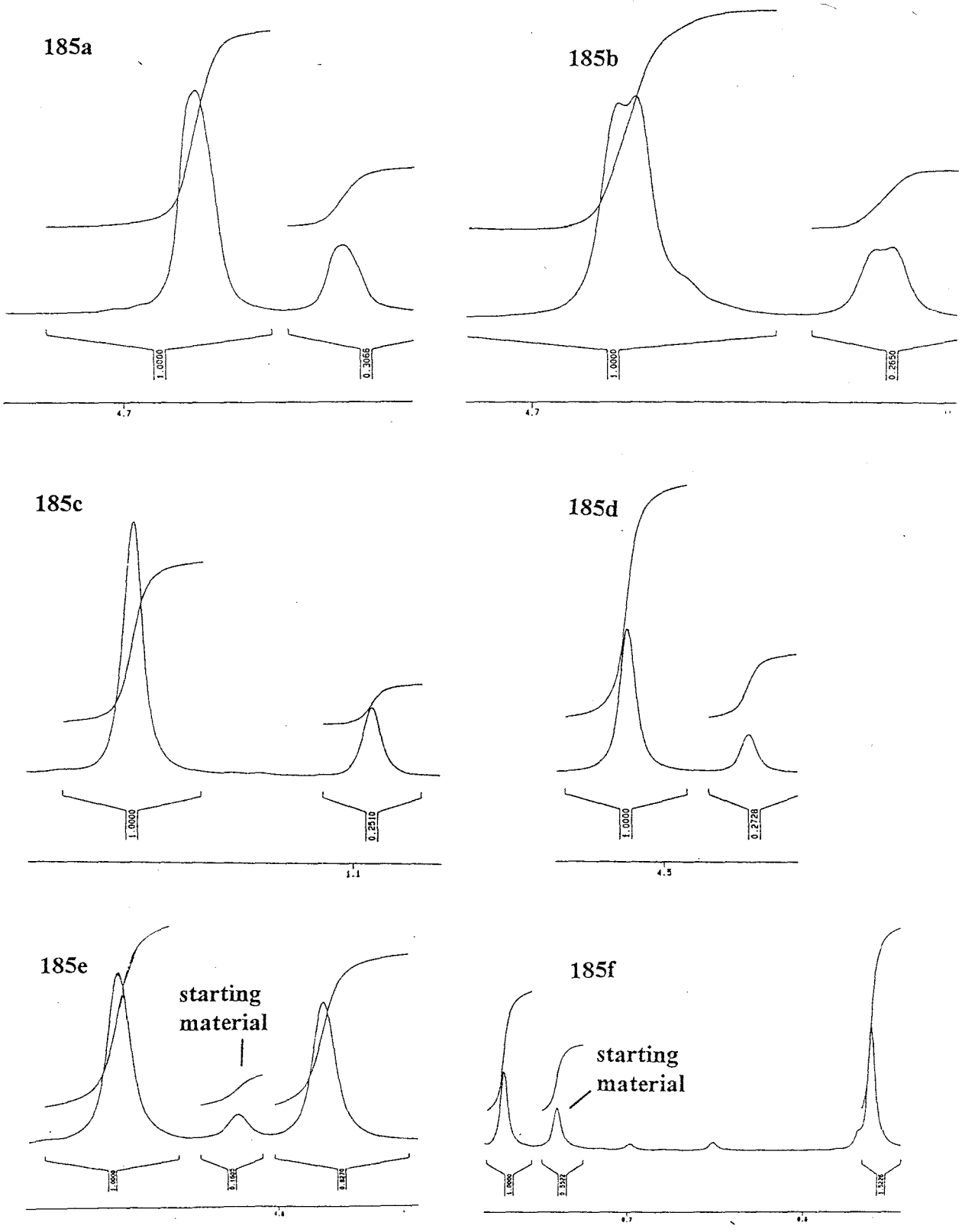
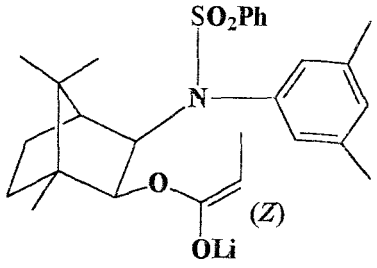


FIGURE 7. Integrated 400 MHz ^{1}H NMR spectra of mixtures of the diastereomeric esters (185a-f) in $CDCl_3$, showing the signals of the diastereomeric components.

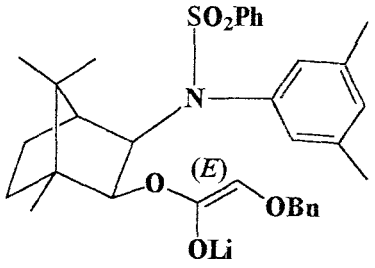
The stereoselectivities of the alkylation reactions were determined by integration of the 2'-H_{endo} signals of the diastereomeric components in the ^{1}H NMR spectra of the crude reaction mixtures as illustrated in Figure 7. In the two cases, (**185c**) and (**185d**), the ^{1}H NMR spectra were too congested and so the stereoselectivities were determined after purification of the diastereomeric products. The results are shown in Table 1. In most cases, the 2'-H_{endo} singlets are well separated from the rest of the spectrum, the only exception being the phenoxyacetate ester (**185f**) where the benzylic proton signals overlapped with the 2'-H_{endo} signals. In this case, the 10'-Me signals were integrated to determine the diastereoselectivity of the reaction.

Another difficulty encountered with the phenoxyacetate system (**185f**) was that hydrolysis of the ester occurred either during the reaction or on work-up, resulting in low yields and complicating isolation of the product. While the stereoselectivities observed for α-benzylations of the phenylacetate (**185e**) and phenoxyacetate (**185f**) systems are surprisingly low, the remaining products examined gave diastereoselectivities which are comparable with Helmchen's results (62% d.e.) for the propanoate ester (**185a**),[182] and certainly better than the 43% d.e. obtained using the chiral auxiliary (**172**) (see Section 2.3, p. 61).

Helmchen *et al.*[91] have suggested that the (*Z*)-enolate (**70**) is formed from the corresponding propanoate ester when LICA is used as a base. However, the (*E*)-enolate intermediate (**187**) has been proposed for the *O*-benzylglycolate derivative of this chiral auxiliary when LICA is used as a base with or without the co-solvent HMPT[97] - a proposal which was confirmed by the synthesis of a silyl enol ether derivative of the enolate and its subsequent analysis by ^{1}H NMR spectroscopy. Evans *et al.*[220] also proposed a (*Z*)-configuration for amide enolates which is equivalent to the (*E*)-geometry of these ester enolates.



70



187

Ireland *et al.*[221] have proposed two possible transition states in the formation of enolates. Application of their proposals of the enolates formed from esters of chiral auxiliary (**183**) are depicted in Figure 8. If, following Ireland's argument, the steric repulsion between the xylyl blocking group and the R-group of the ester in TSC$^{\#}$I is sufficiently greater than that between the R-group and diisopropylamine in TSC$^{\#}$II, then formation of the (*Z*)-enolate (**188**) would be inhibited and formation of the (*E*)-enolate (**189**) *via* TSC$^{\#}$II would be favoured. In any event, subsequent equilibration would favour the more stable enolate species. In order to explore the steric effects more fully, the (*Z*)- and (*E*)-enolates (**188**) and (**189**) were modelled using the HYPERCHEM® computer modelling program.

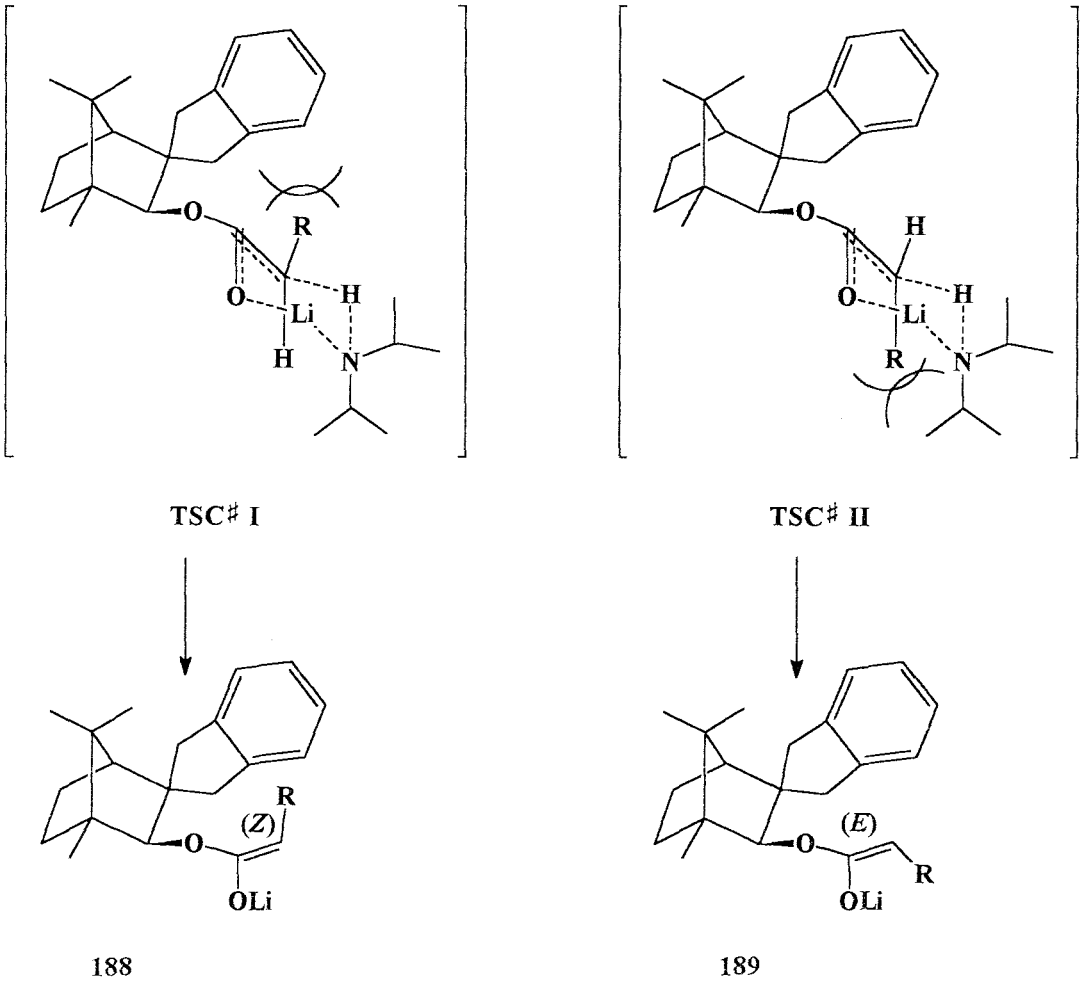


FIGURE 8. The two possible transition states in the formation of the enolate intermediates (**188**) and (**189**).

Although Helmchen *et al.*[182] have proposed the intermediacy of a (*Z*)-enolate intermediate (**188**), we are suggesting preferential formation of an (*E*)-enolate intermediate (**189**). The structures and the computer-generated models of two possible conformations (**189a**) and (**189b**) of this enolate intermediate (**189**), are illustrated in Figure 9 and Figure 10 respectively.

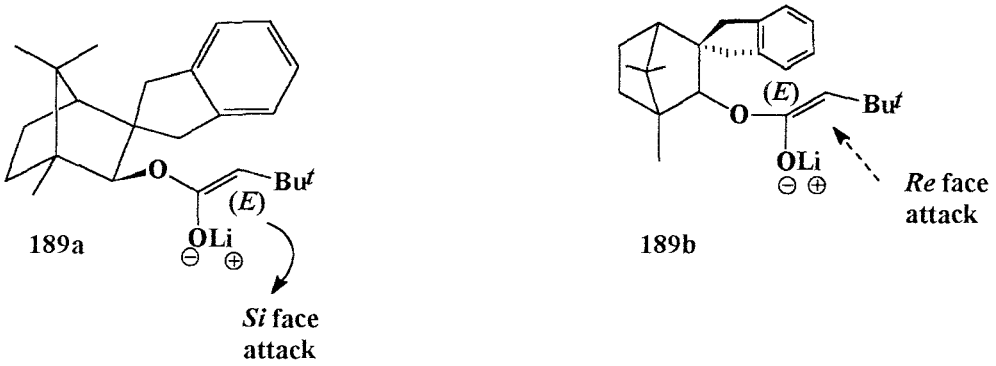


FIGURE 9. The two proposed conformations of the enolate intermediates (**189a**) and (**189b**).

In structure (**189a**):- i) the enolate moiety adopts an (*E*)-configuration with the 8-Me group being sufficiently distant from the R-substituent to minimise steric interactions; ii) the O-CO system adopts an *s-trans* arrangement with the OLi moiety *endo* oriented; and iii) the planar enolate moiety is quasi-parallel to the aromatic blocking group. In structure (**189b**), the enolate moiety is proposed to be much the same as (**189a**) except that it is twisted away from and quasi-perpendicular to the aromatic blocking group due to repulsion between the polar OLi moiety and the aromatic group.

The data summarised in Table 1 may, in fact, be rationalised in terms of the proposed model (**189b**). Thus, we suggest that in all cases (entries 1-6), electrophilic attack occurs predominantly at the *endo-Re*-face[¶] of the favoured (*E*)-enolate conformation (**189b**). In this conformation the 8-Me group would inhibit attack from the *exo*-face. In the case of the phenylacetyl (**185e**) and phenoxyacetyl (**185f**) systems (entries 5 and 6), however, the stereoselectivity of the alkylation is much lower, due to a greater contribution to the conformational equilibrium by the quasi-parallel arrangement (**189a**), in which favourable π-stacking of the aromatic blocking group and the aromatic ester group is possible.

[¶] The *Re* face at the α-carbon (*Si* for R = PhO).

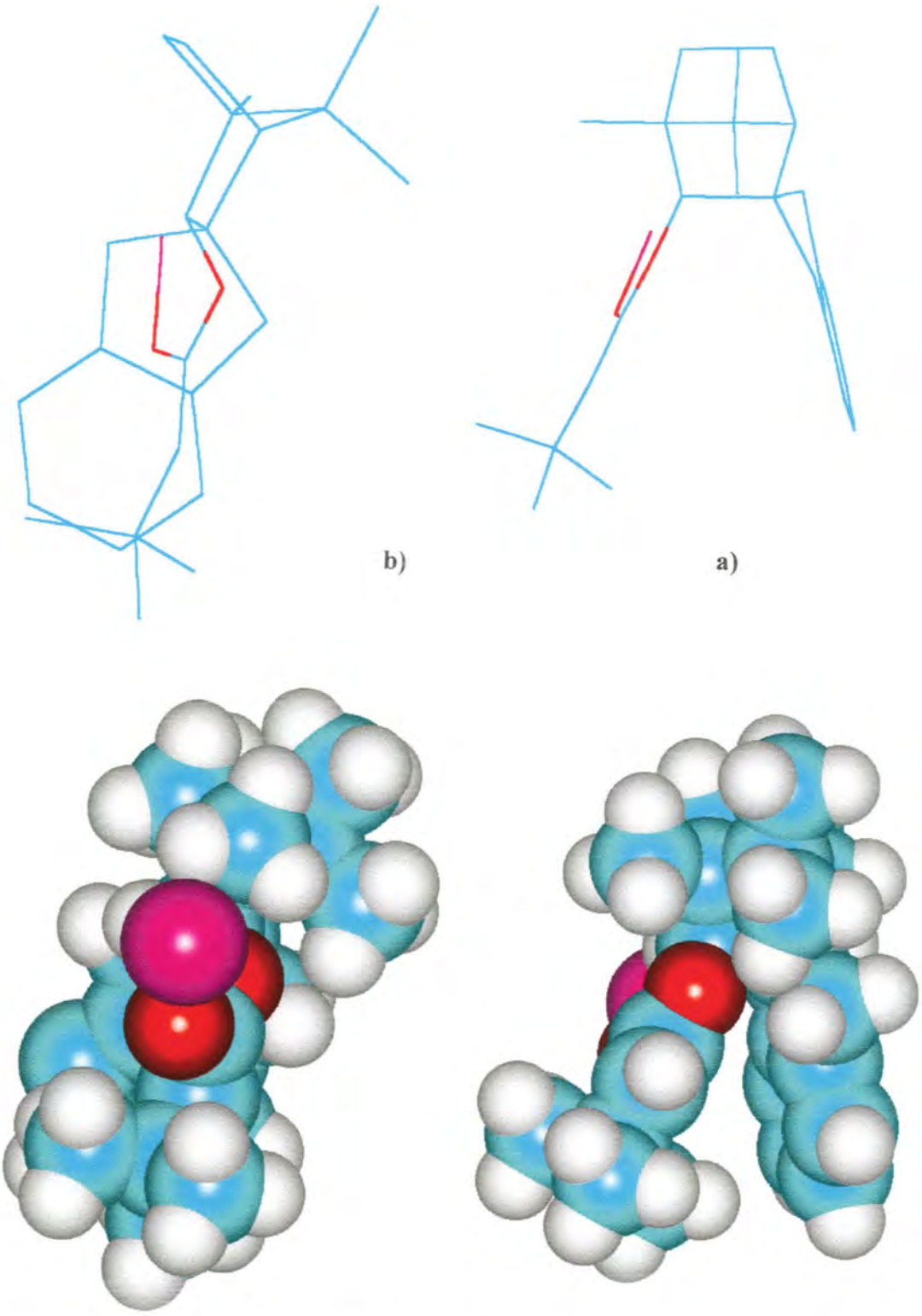
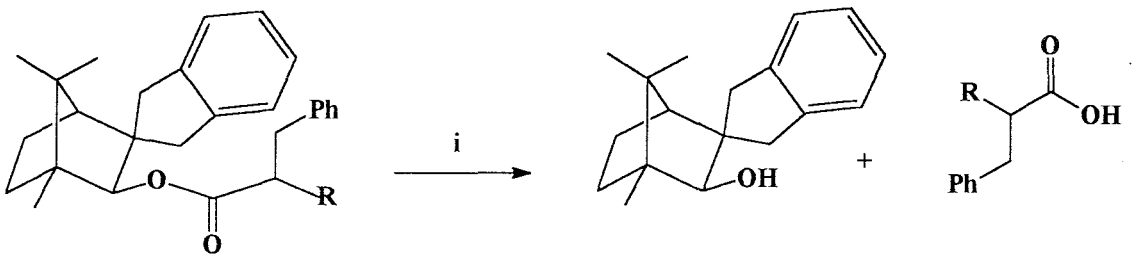


FIGURE 10. Stick and space-filling representation of computer-modelled conformations of the lithium (*E*)-enolate intermediates of the ester (**184d**), namely :
a) the quasi-parallel conformation (**189a**); and
b) the quasi-perpendicular conformation (**189b**).

In order to confirm these hypotheses it was decided to hydrolyse selected systems and subject the resulting acids to polarimetric analysis. Four different methods were used for this hydrolysis, all of which are shown in Scheme 14. Attempts to hydrolyse the alkylated ester (**185a**) using lithium hydroxide were unsuccessful due, possibly, to the relative insolubility of the lithium hydroxide in the THF-H_2O solvent used. To alleviate this problem, a crown ether (12-crown-4) was added, but without success. However, a 2**M** solution of KOH in MeOH effected hydrolysis of the ester (**185a**), permitting isolation of the chiral auxiliary (**183**) and the acid (**190a**).

Concentrated sulfuric acid has been used to hydrolyse sterically hindered esters.[222] When this was used to effect hydrolysis of the esters (**185a**) and (**185b**), the respective organic acids were isolated; the chiral auxiliary, however, decomposed to form a complex mixture of products.



185 183 190

	R
a	Me
b	Et

SCHEME 14. Reagents: Method 1: i) $LiOH.H_2O$, H_2O_2, THF-H_2O (1:1), r.t., 5 days;
Method 2: i) $LiOH.H_2O$, H_2O_2, THF-H_2O (1:1), 12-crown-4, r.t., 5 days;
Method 3: i) 2**M** KOH in MeOH, reflux, 3 days;
Method 4: i) conc. H_2SO_4, then ice.

When the chiral esters are hydrolysed using base, there is a significant possibility of isomerisation of the new stereocentre due to deprotonation at the α-carbon. Although there is some precedent for acid-catalysed enolisation,[223] isomerisation under acidic conditions has been shown not to occur (see Section 2.6.2, p. 104). The optical rotation of the acid (**190a**) obtained from base- and acid-catalysed hydrolysis of the ester (**185a**) corresponded to 42% and 45% e.e. respectively - in both cases, somewhat lower than the 53% d.e. observed by integration of diastereomeric peaks in

the ^{1}H NMR spectrum of the ester. The optical rotation obtained for the acid (**190b**) resulting from acid-catalysed hydrolysis of the ester (**185b**) corresponds to 46% e.e., which is again lower than the 58% d.e. obtained from integration of diastereomeric peaks in the ^{1}H NMR spectrum of the ester. Attempts were made to confirm the % enantiomeric excess for the isolated acids using the chiral shift reagents, [Eu(hfc)$_3$] and [Pr(hfc)$_3$], but no resolution of signals was observed.

The main purpose of hydrolysing the esters (**185a**) and (**185b**) was to determine the stereochemistry of the new stereocentres. In both cases, a positive optical rotation was observed indicating preferential formation of the (*S*)-isomers. These results are consistent with either electrophilic attack at the "front-face" of the (*Z*)-enolates of esters of the chiral auxiliary (**183**) as proposed by Helmchen *et al.*[182] or, as we are suggesting, electrophilic attack from the *endo*-face of the quasi-perpendicular (*E*)-enolate (**189b**).

2.4.2 Silyl enol ether derivatives of the chiral auxiliary (183)

Given the moderate success obtained with the asymmetric α-benzylation of alkanoate esters of the chiral auxiliary (**183**), it was decided to explore the influence of this auxiliary on reactions of its silyl enol ether derivatives. Synthetic approaches to silyl enol ethers of the ketones, α-tetralone (**146**) and pinacolone (**154**) are outlined in Scheme 15. A number of methods were investigated, *viz.*,

method 1: a two-step process involving isolation and purification of the chlorosiloxy intermediates prior to reaction with the alkoxide (**192**), which was generated using NaH;

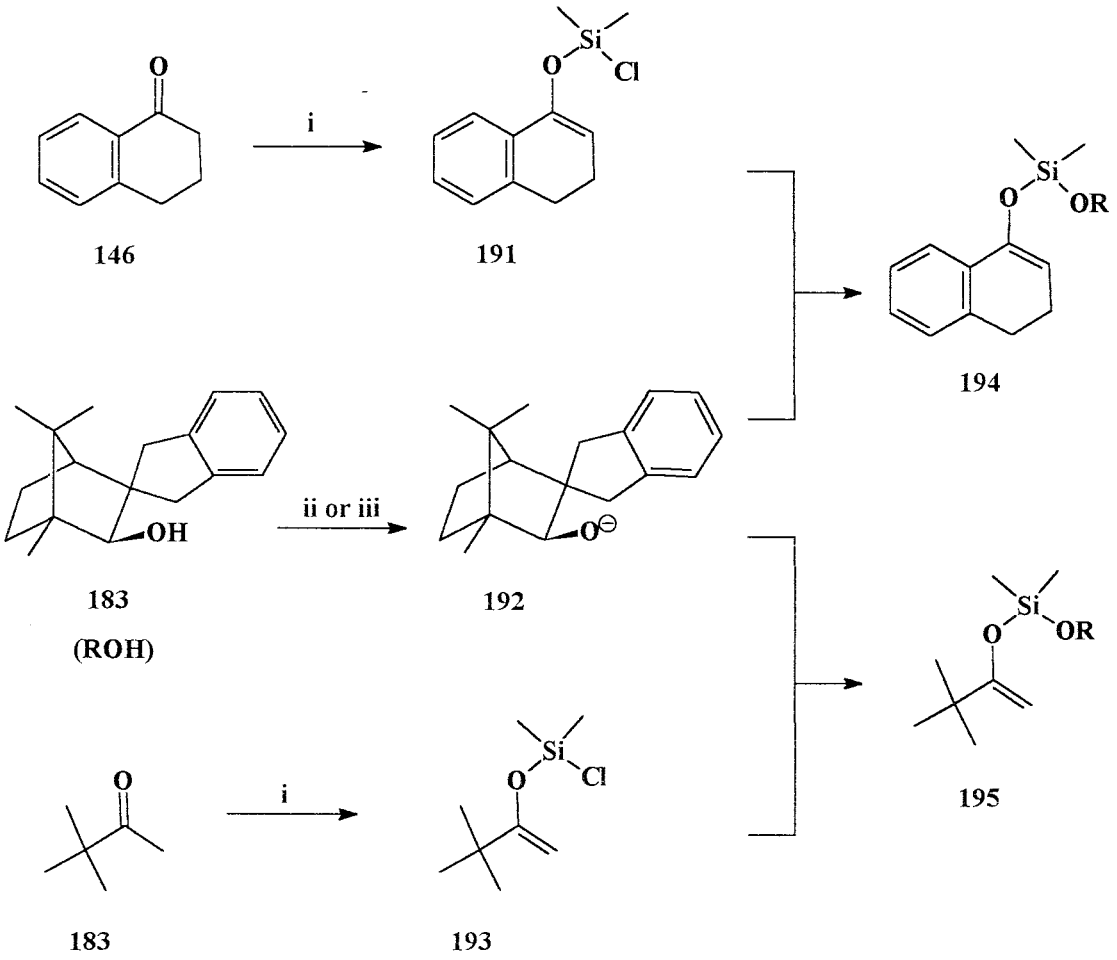
method 2: a one-pot variation of method 1, without isolation of the chlorosiloxy intermediate, and using BuLi to generate the alkoxide (**192**); and

method 3: a one-pot variation of method 2 in which the alkoxide (**192**) was generated with NaH.

In the case of the α-tetralone-derived silyl enol ether (**194**), the two-step protocol (method 1) was initially applied. The chlorosiloxy intermediate (**191**) was formed from α-tetralone using LDA and Me_2SiCl_2, purified, and then reacted with the alkoxy anion (**192**) [formed by treating the chiral alcohol (**183**) with NaH] to yield the chiral silyl enol ether (**194**) in 30% overall yield. This yield was improved when the reaction was carried out as a one-pot procedure using method 2. The chlorosiloxy intermediate (**191**) was formed as in method 1 and reacted directly, without isolation, with the alkoxy anion (**192**) (generated using BuLi) to afford the chiral silyl enol ether (**194**) in 72% yield.

The pinacolone-derived silyl enol ether (**195**) was prepared using the two one-pot procedures (method 2 and 3), varying only in the base used to form the alkoxy anion (**192**). Thus, the alkoxide (**192**), generated using NaH (method 3), was reacted with the chlorosiloxy intermediate (**193**) to produce the silyl enol ether (**195**) in 63% yield. However, application of method 2, which involved the use of BuLi, gave the silyl enol ether (**195**) in 94% yield. The preferred synthesis for both silyl enol ethers thus appears to be method 2 - the one-pot approach involving generation of the nucleophilic alkoxide (**192**) using BuLi.

The silyl enol ethers (**194**) and (**195**) were unambiguously identified using 1- and 2-D NMR techniques; the HETCOR spectrum is illustrated for compound (**194**) in Figure 11.



SCHEME 15. Reagents: i) LDA, Et_2O or THF, -78 °C, then Me_2SiCl_2;
ii) NaH, THF, reflux;
iii) BuLi, THF, 0° C.

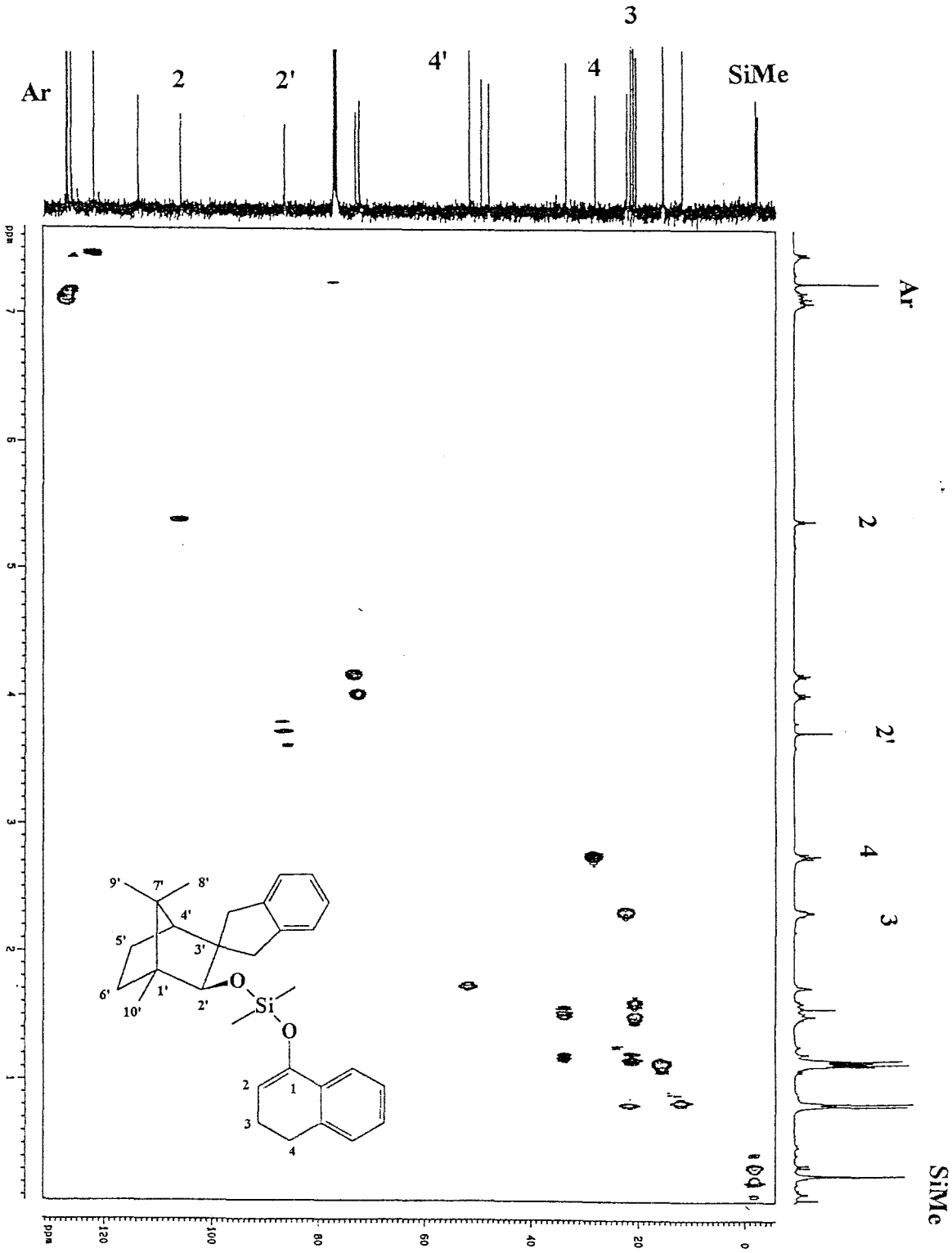


FIGURE 11. The 400 MHz HETCOR spectrum of the silyl enol ether (194) in $CDCl_3$.

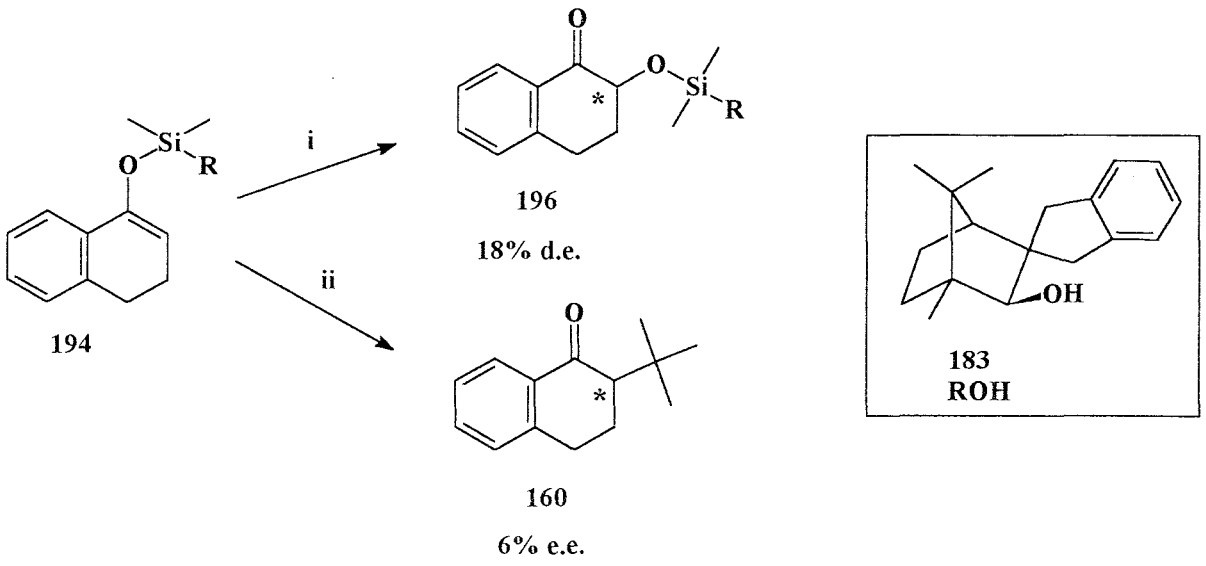
Once again, as in the reaction of the silyl enol ethers (**153**) and (**156**) (Section 2.2.1.1, p. 46), the silyl enol ethers (**194**) and (**195**) were each reacted to permit the formation of a single, new stereocentre. Three transformations were investigated to deterermine the stereocontrol afforded by the chiral auxiliary, *viz.*, i) MCPBA oxidation;

ii) alkylation with *t*-BuCl-$TiCl_4$; and

iii) the Mukaiyama reaction with PhCHO-$TiCl_4$

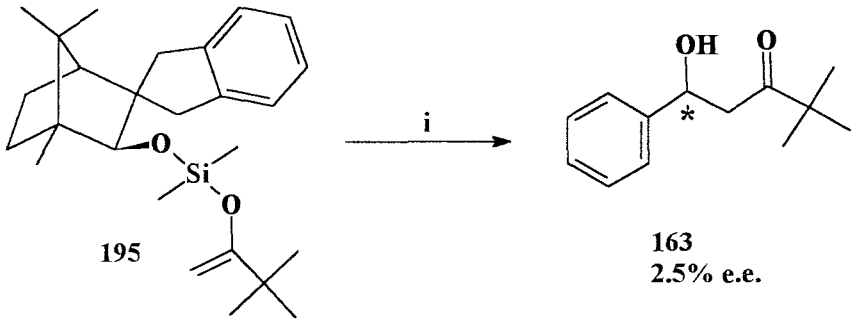
i) MCPBA oxidation of the α-tetralone-derived silyl enol ether (**194**) afforded the α-silyloxyketone (**196**) in 18% d.e. (Scheme 16). The stereoselectivity was determined from the integrals of the SiMe peaks (seen in Figure 12) of the diastereomeric components in the ^{1}H NMR spectrum of the crude reaction mixture.

ii) Alkylation of the α-tetralone-derived silyl enol ether (**194**) afforded the α-alkylated ketone (**160**) in 6% e.e. (Scheme 16). The stereoselectivity was determined, in this case, by integration of the *t*-butyl ^{1}H NMR signals of the enantiomeric components, the signals being resolved with the aid of the chiral shift reagent [Eu(hfc)$_3$] (see Figure 12).



SCHEME 16. Reagents: i) MCPBA, $NaHCO_3$, CH_2Cl_2, 0 °C, 2h;
ii) *t*-BuCl, CH_2Cl_2, -23 °C, then $TiCl_4$, 3h.

iii) The Mukaiyama reaction between the pinacolone-derived silyl enol ether (**195**) and benzaldehyde (Scheme 17) yielded the chiral β-hydroxyketone (**163**). The stereoselectivity for this transformation was once again determined by integration of the *t*-butyl ^{1}H NMR signals of the enantiomeric components in the product mixture, the peaks being resolved with the aid of the chiral shift reagents, [Eu(hfc)$_3$] (0% e.e.) and [Pr(hfc)$_3$] (5% e.e.) (see Figure 12).‡ An enantiomeric excess of 2% of the (*R*)-stereoisomer was determined by optical rotation.



195 **163**
2.5% e.e.

SCHEME 17. Reagents: i) PhCHO, $TiCl_4$, CH_2Cl_2, -78 °C, 4.5h.

While significant stereofacial selectivities were obtained in certain reactions using the chiral auxiliary (**183**), there was clearly room for improvement, especially in the case of the silyl enol ether derivatives. The next section is concerned with alternative approaches to the development of chiral auxiliaries, with the aim of improving stereocontrol.

‡ The % e.e. was determined to be 2.5% by averaging the results obtained from the ^{1}H NMR spectra using both chiral shift reagents.

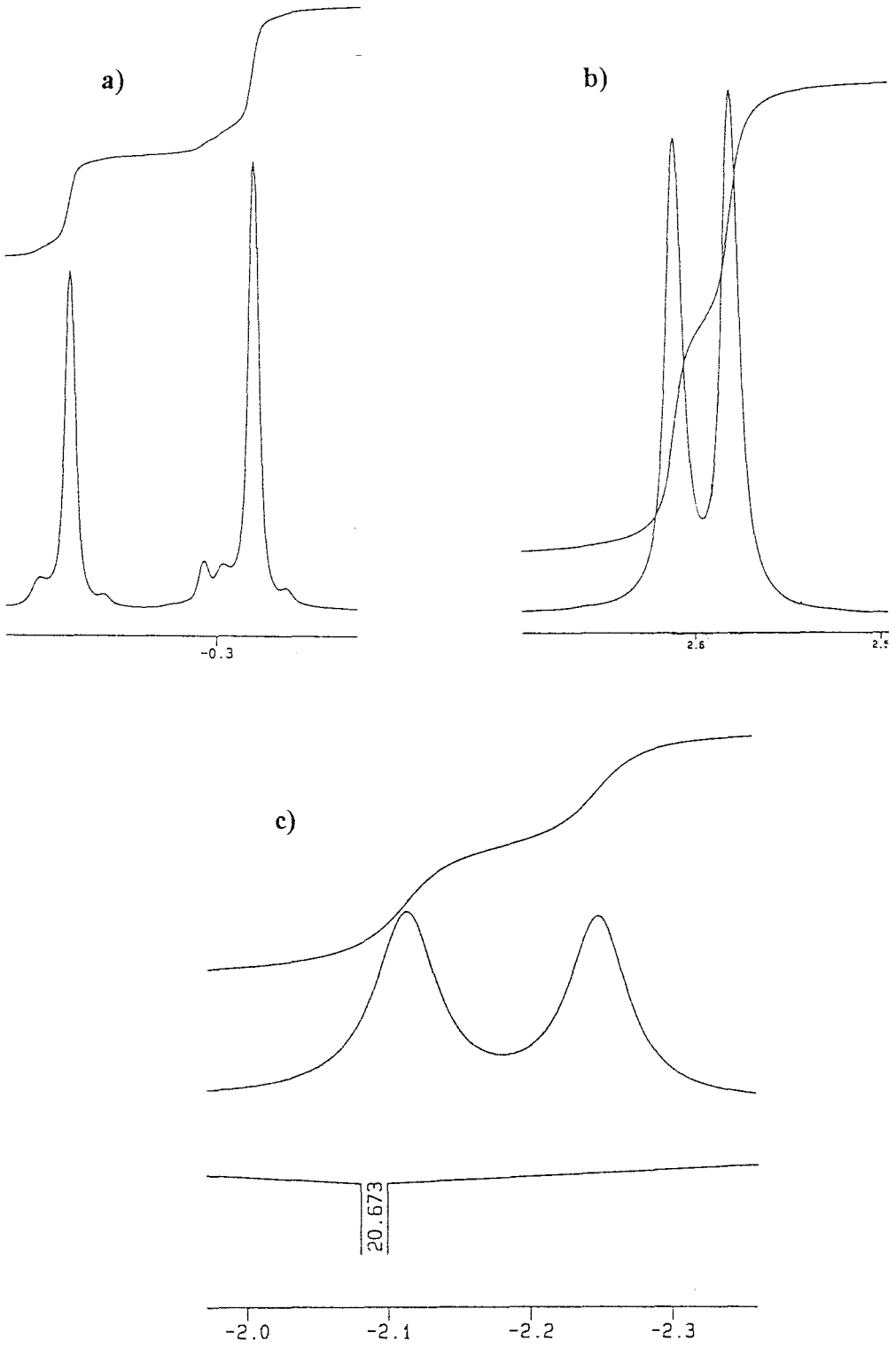


FIGURE 12.

a) An integrated 400 MHz ^{1}H NMR spectrum of (196) in $CDCl_3$ showing the diastereomeric SiMe signals.

b) An integrated 400 MHz ^{1}H NMR spectrum of (160) in $CDCl_3$ showing the *t*-butyl peaks resolved using [Eu(hfc)$_3$].

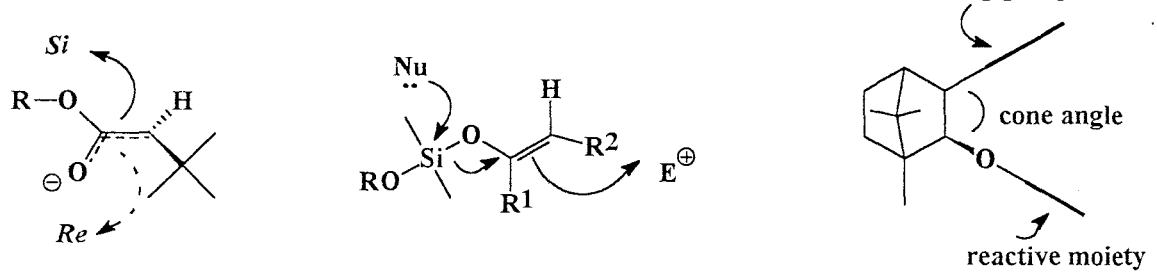
c) An integrated 400 MHz ^{1}H NMR spectrum of (163) in $CDCl_3$ showing the *t*-butyl peaks resolved using [Pr(hfc)$_3$].

2.5 Strategies to Improve Stereofacial Selectivity

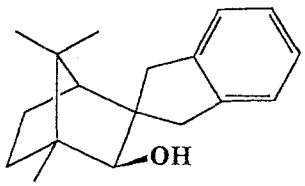
Examination of the structure of the enolate (197) [which is based on computer modelling data (Figure 10)] and the generalised representation (198) of the silyl enol ethers (194) and (195) (Figure 13) reveals that :-

i) in the enolate (197) the prochiral centre is 3 atoms away from the chiral bornyl bicyclic moiety, while for the silyl enol ethers the reactive α-carbon is 5 atoms away;[¥] and

ii) as a result of the inherent bonding angles in the bornyl system [if it is aligned quasi-parallel to the aromatic blocking group of the chiral auxiliary (183)], shown diagrammatically as (199), mere extension of the blocking group is unlikely to alter the cone of access significantly.[224]



a) 197 b) 198 c) 199



183
(ROH)

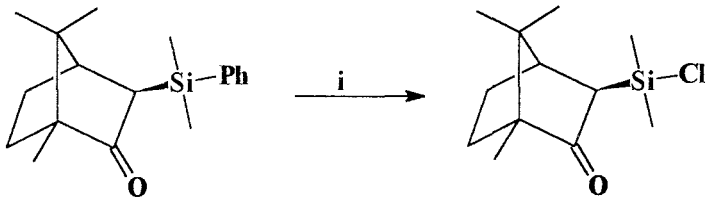
FIGURE 13. a) The structure of the bornyl ester enolate (197) indicating *Re*- and *Si*-facial attack; b) a generalised representation (198) of the silyl enol ethers (194) and (195); and c) representation of derivatives of the chiral auxiliary (183) illustrating the cone angle.

[¥] For silyl enol ether (194) the α-carbon is prochiral; for Mukaiyama reactions of the pinacolone-derived analogue (195), the prochiral centre is provided by the aldehyde.

The first strategy was to attempt to bring the prochiral centre in the silyl enol ethers closer to the chiral auxiliary by forming a direct Si-C bond to the bicyclic skeleton instead of the Si-O-C bond used previously. The second strategy was to increase the effective steric bulk of the blocking group on the chiral auxiliary. If the enolate reacts *via* a quasi-parallel enolate intermediate, this increase in the bulk of the blocking group should increase the stereoselectivity of camphor-derived chiral auxiliaries.

2.5.1 The attempted formation of a direct Si-C bond to the bicyclic skeleton

The formation of a direct Si-C bond to the camphor skeleton has been carried out previously by Taddei *et al.*,[225] but their approach requires up to three steps and the separation of a diasteroemeric mixture and, moreover, does not allow for the easy attachment of an effective blocking group to the chiral auxiliary. Our initial intention was to generate the chlorosilane (**201**) *via* an intermediate silyl enol ether of camphor (**200**) as outlined in Scheme 18; the carbonyl functionality could then be modified to provide a blocking group.

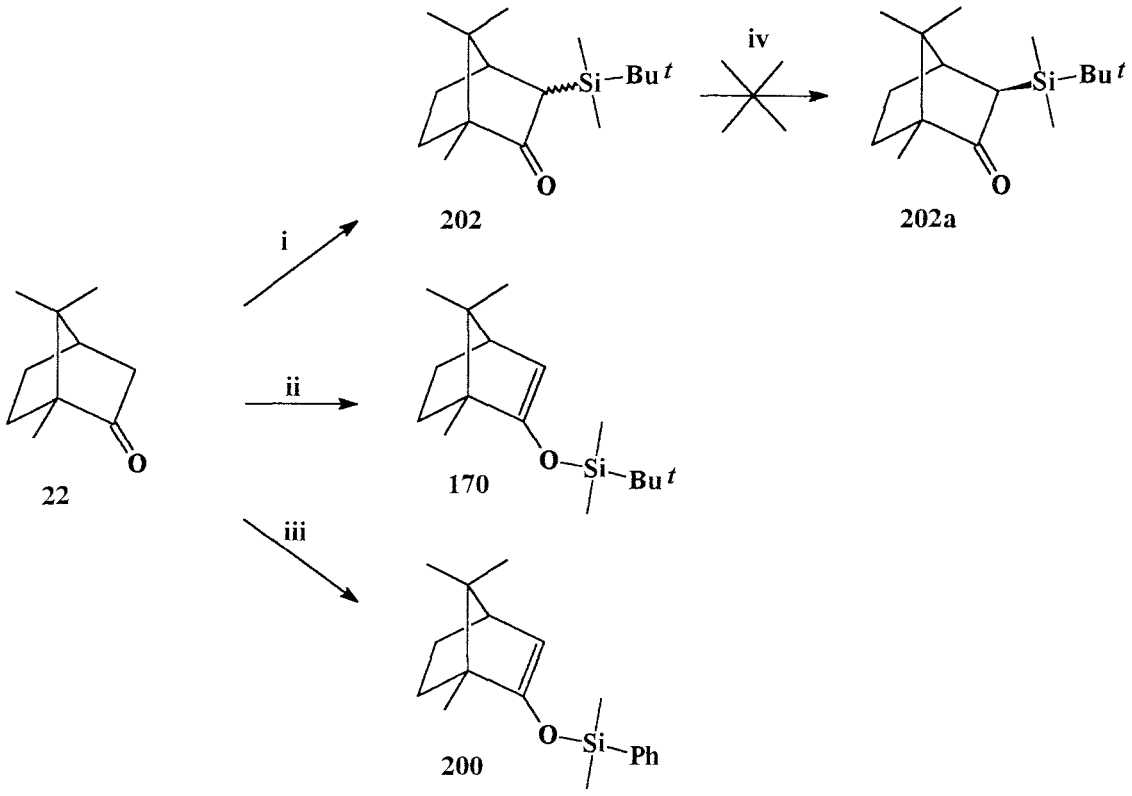


200 **201**

SCHEME 18. Reagents: i) HCl.

In an attempt to synthesise the camphor-derived silyl enol ether (**170**), using LDA and *t*-$BuMe_2SiCl$, the reaction mixture was stirred overnight at room temperature to yield the α-silylketone (**202**) as a diastereomeric mixture (0% d.e.) in low yield (Scheme 19). Longer reaction times (up to 5 days at room temperature) failed to increase the yield of the α-silylketone (**202**). Heating the reaction mixture resulted in the formation of the silyl enol ether (**170**). A similar reaction was carried out at room temperature using camphor (**22**) and $PhMe_2SiCl$ to afford the silyl enol ether (**200**) directly but in low yield; the yield increased, however, when the reaction mixture was boiled under reflux. In an attempt to improve the diastereomeric ratio of the α-silylketone (**202**), the diastereomeric mixture was treated with LDA to form an enolate intermediate, the expectation being that on quenching the reaction mixture at low temperature

with a solution of $NaHCO_3$, preferential *endo*-protonation would favour the formation of the *exo*-α-silylketone (**202a**). This, however, did not occur and the reaction led to the formation of a complex mixture of products.

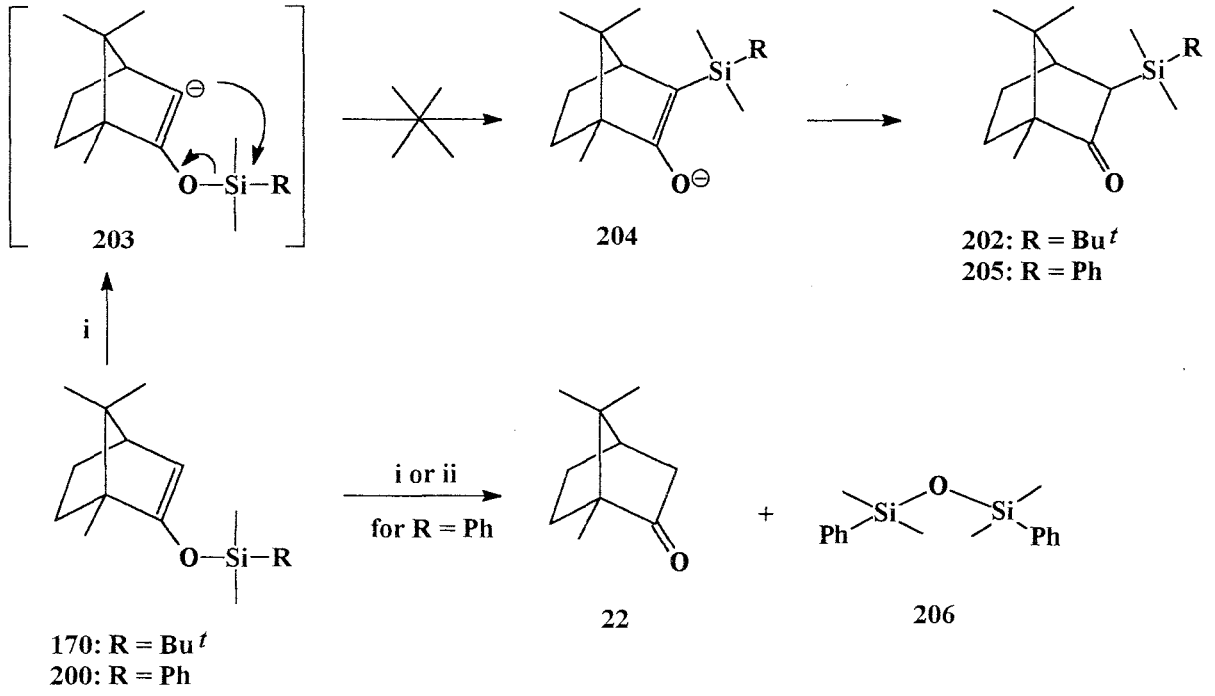


SCHEME 19. Reagents: i) LDA, *t*-$BuMe_2SiCl$, Et_2O, -78 °C, then r.t., 24 h; ii) LDA, *t*-$BuMe_2SiCl$, Et_2O, -78 °C, then reflux, 10 h; iii) LDA, $PhMe_2SiCl$, Et_2O, -78 °C, then reflux, 5 h; iv) LDA, THF, then satd. aq. $NaHCO_3$, -78 °C.

2.5.1.1 The attempted rearrangement of the silyl enol ethers (170) and (200)

Research has previously been carried out on the base-catalysed rearrangement of silyl enol ethers to α-silyl ketones.[226] This rearrangement appears to occur *via* the removal of an α-allylic proton. Although the camphor-derived silyl enol ethers (**170**) and (**200**) do not have a proton at this allylic position (C-1), loss of a vinylic proton might be expected to induce rearrangement *via* the intermediate (**203**) and the enolate (**204**) (see Scheme 20). However, no rearrangement to the α-

silyl ketones (**202**) and (**205**) took place when silyl enol ethers (**170**) and (**200**) were reacted with *t*-BuOK and BuLi. In the case of compound (**170**), a complex mixture of products was obtained, while in the case of the phenyl analogue (**200**), the silyl enol ether was cleaved to form camphor (**22**) and the disiloxane (**206**). A titanium tetrachloride-catalysed rearrangement of the silyl enol ether (**200**) was also attempted, with and without $PhMe_2SiCl$. Once again, camphor (**22**) and the disiloxane (**206**) were formed in the reaction.

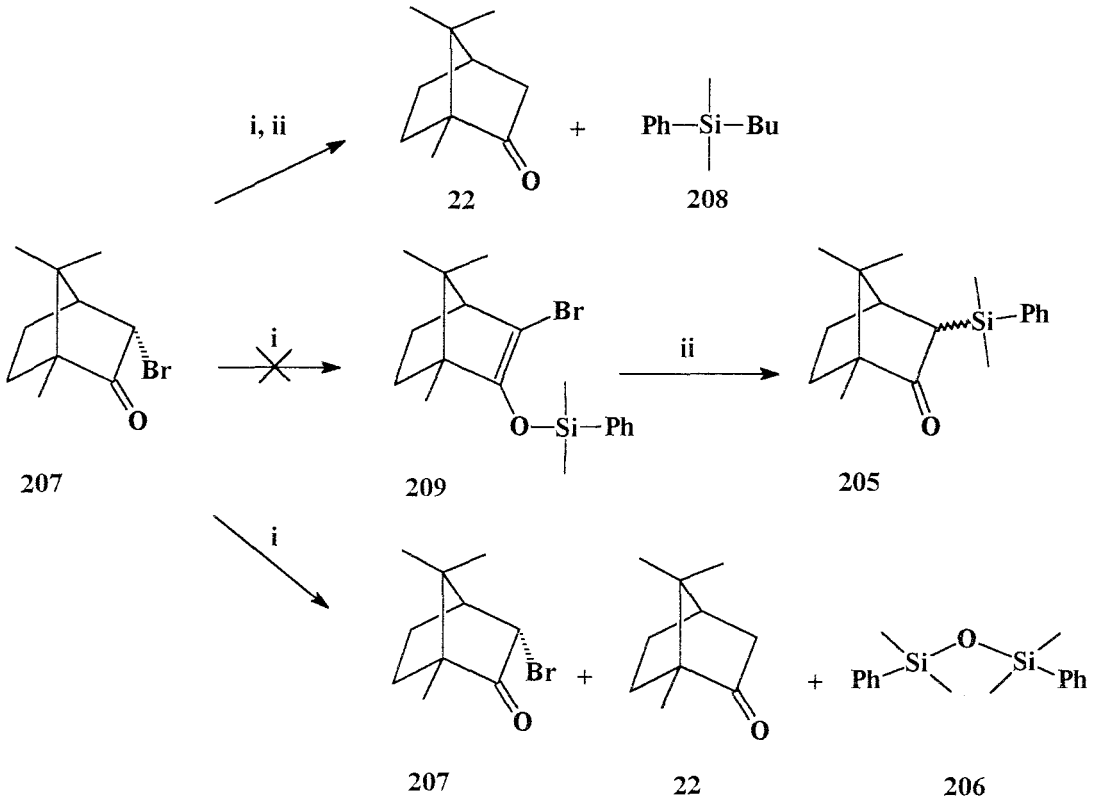


SCHEME 20. Reagents: i) *t*-BuOK, BuLi, hexane, r.t., 24h;
ii) $PhMe_2SiCl$, CH_2Cl_2, -23 °C, then $TiCl_4$.

2.5.1.2 The attempted synthesis of α-silylketones from α-bromoketones

Wiemer *et al.* have reported the synthesis of α-trimethylsilylketones from α-bromoketones, including 3-bromocamphor.[227] This reaction was investigated using 3-*endo*-bromocamphor and $PhMe_2SiCl$ instead of Me_3SiCl (Scheme 21). The bromocamphor (**207**) was treated with LDA and $PhMe_2SiCl$ at -78 °C, followed by the addition of BuLi, but this failed to yield the expected α-silylketone, giving instead, camphor (**22**) and the silane $BuMe_2PhSi$ (**208**), the latter compound presumably arising from the reaction of BuLi with $PhMe_2SiCl$. The isolation of camphor (**22**) confirmed that metal-halogen exchange was indeed taking place, and the reaction was repeated as a two step process, with the intention of isolating the intermediate silyl enol ether (**209**).

However, reaction of 3-*endo*-bromocamphor (**207**) with LDA and $PhMe_2SiCl$ did not afford the silyl enol ether (**209**); instead, unreacted bromocamphor (**207**), camphor (**22**) and the disiloxane (**206**) were detected in the reaction mixture.

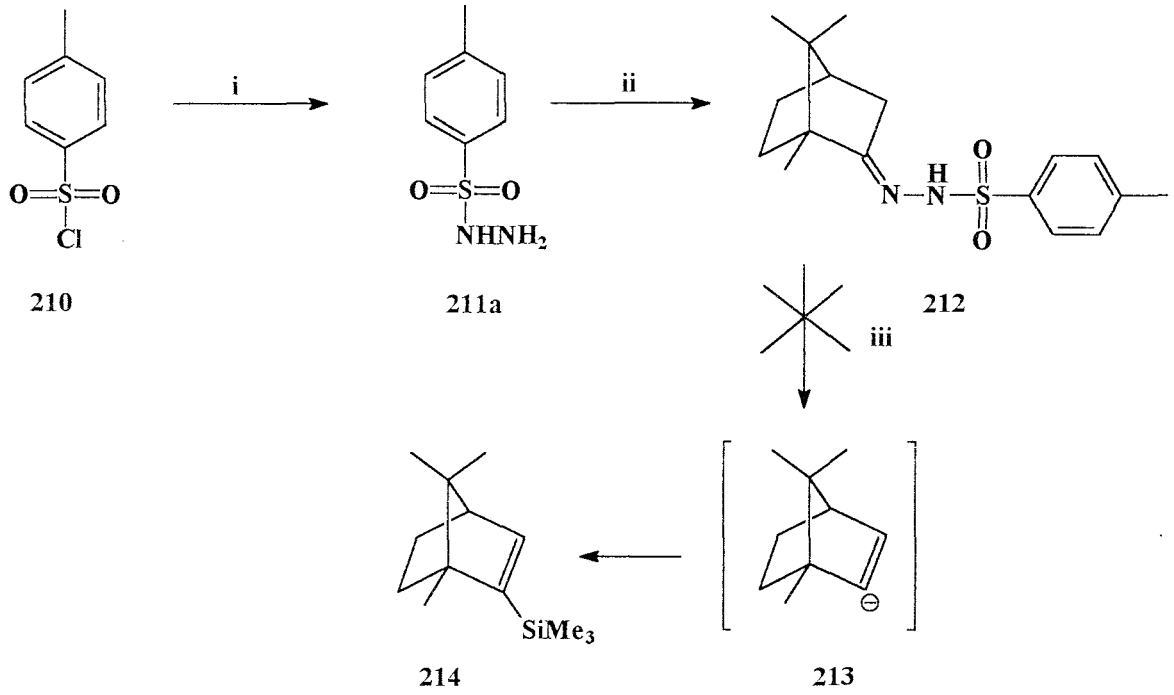


SCHEME 21. Reagents: i) LDA, THF, -78 °C, then $PhMe_2SiCl$;
ii) 2 eq. BuLi, -78 °C.

2.5.1.3 The attempted synthesis of vinylsilanes from the camphor-derived hydrazone (212)

Chan *et al.*[228] have reported the synthesis of vinylsilanes from benzenesulfonylhydrazones. This reaction has been used in the synthesis of the vinylsilane of camphor,[229] in the 1,2-transposition of ketones[230] and in regiospecific cyclopentanone annulations.[231] Consequently, the camphor hydrazone (**212**) was synthesised as shown in Scheme 22 . The formation of *p*-toluenesulfonylhydrazine (**211a**) involved the reaction of *p*-toluenesulfonyl chloride (**210**) and aqueous hydrazine hydrate; the resulting hydrazine (**211a**) was then reacted with camphor (**22**) to form the hydrazone (**212**). The formation of the vinylsilane (**214**) has been proposed to occur *via*

the intermediate vinylic anion (**213**), generated by the addition of 4 equivalents of BuLi . However, instead of the expected vinylsilane (**214**), a complex mixture of products was obtained and this approach was abandoned.

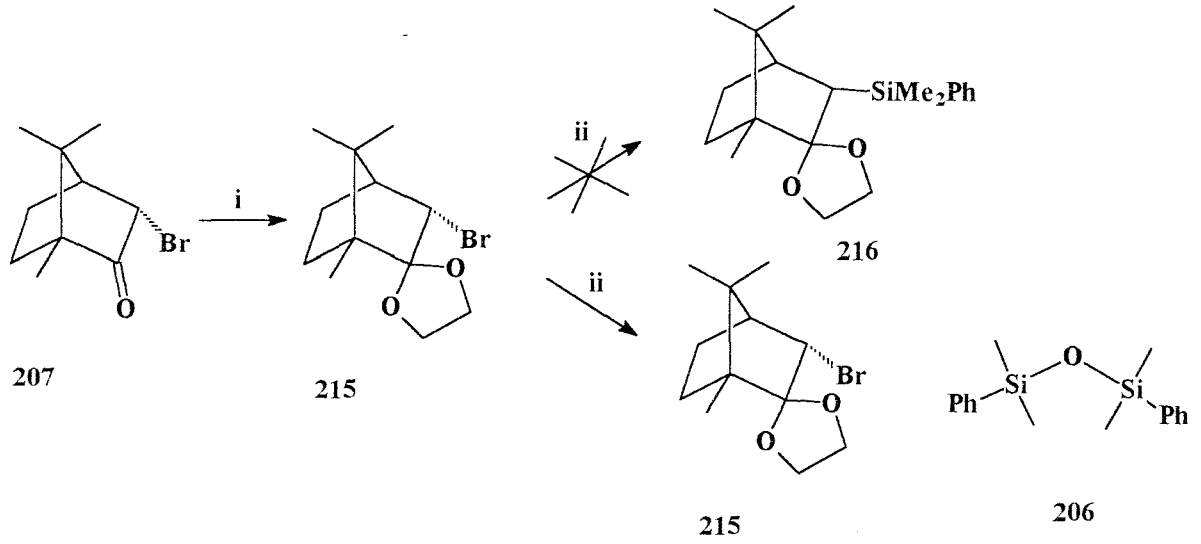


210 **211a** **212** **214** **213**

SCHEME 22. Reagents: i) $NH_2NH_2.xH_2O$ (50%), THF, 10-15 °C, 15 min;
ii) camphor (**22**), EtOH, reflux, 4h;
iii) TMEDA, 4 eq. BuLi, -45 °C, then 4 eq. Me_3SiCl, 0 °C.

2.5.1.4 The attempted synthesis of the camphor-derived silane (216) *via* zinc-mediated coupling

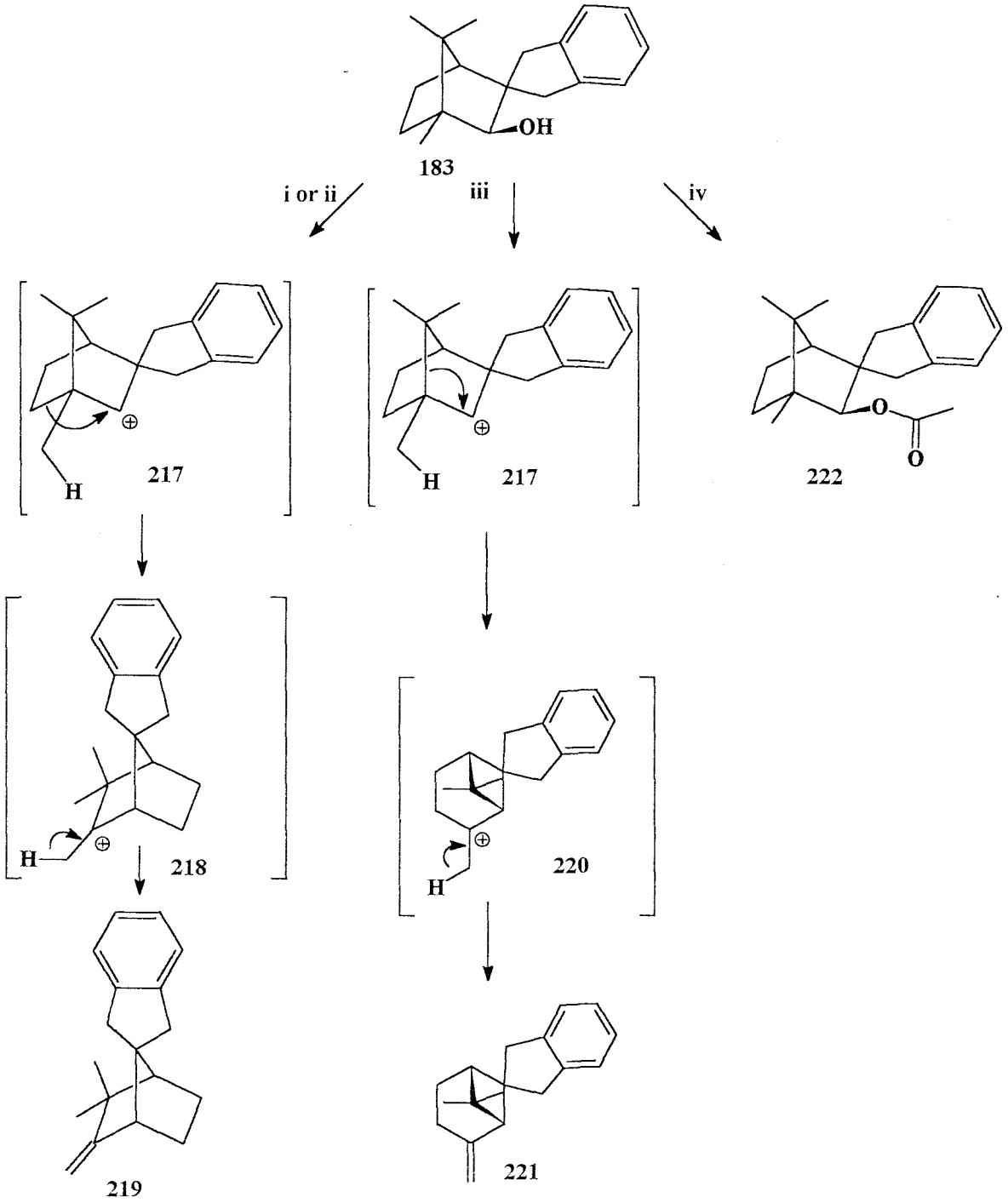
The next approach that was attempted involved the use of zinc[232] to couple $PhMe_2SiCl$ with the bromocamphor derivative (**215**) (Scheme 23). This required prior introduction of the ketal protecting group to 3-*endo*-bromocamphor (**207**) by reacting the ketone with ethylene glycol and *p*-toluenesulfonic acid. In an attempt to couple the alkyl halide (**215**) and $PhMe_2SiCl$ to form the silyl derivative (**216**), the two compounds were treated with activated zinc dust in dimethylsulfoxide (DMSO). This reaction, however, yielded the disiloxane (**206**) together with the starting material.



SCHEME 23. Reagents: i) $HOCH_2CH_2OH$, TsOH, reflux, 4 days;
ii) Zn dust, DMSO, then $PhMe_2SiCl$.

2.5.1.5 The attempted synthesis of camphor-derived silanes *via* substitution reactions using silyl lithium and silyl copper lithium reagents

One final attempt was made to form a Si-C bond to the bicyclic skeleton using organometallic reagents. Initially, the idea was to use the camphor-derived chiral auxiliary (**183**) (Scheme 24) to form a Grignard reagent, which could then be reacted with a silyl chloride, thus forming the Si-C bond.



SCHEME 24. Reagents: i) $SOCl_2$, pyridine, r.t., 4h;
ii) BuLi, THF, 0 °C, then TsCl, reflux;
iii) BuLi, THF, 0 °C, then TsCl, r.t.;
iv) BuLi, THF, 0°C, then acetyl chloride.

This required replacement of the hydroxyl group by chlorine using thionyl chloride ($SOCl_2$), but the reaction resulted in the formation of the camphene derivative (**219**). This derivative is presumably obtained *via* rearrangement of the secondary carbocation intermediate (**217**) to the more stable tertiary carbocation (**218**) followed by deprotonation - a process for which there is some precedent.[23] The structure of the camphene derivative (**219**) was established unambiguously by MS and NMR spectroscopic methods, and is depicted in the NOESY spectrum (Figure 14).

The next approach was to generate a better leaving group without displacing the oxygen in the chiral auxiliary (**183**). With that in mind, tosylation of the chiral auxiliary (**183**) was attempted using BuLi and *p*-toluenesulfonyl chloride. Once again, however, rearrangement took place yielding the camphene derivative (**219**). Interestingly, when the same reaction was carried out without any heating, the β-pinene derivative (**221**) was isolated instead (Scheme 24). The secondary carbocation intermediate (**217**) is presumed to rearrange to form the tertiary carbocation (**220**) - a rearrangement for which there is once again a precedent.[23] The rearrangement product (**221**) was fully characterised using spectroscopic methods; the NOESY spectrum of which is displayed in Figure 15.

As a final attempt to make the hydroxyl group on the chiral auxiliary (**183**) a better leaving group, it was acetylated by treating its lithium alkoxide with acetyl chloride to yield the acetate (**222**), which could then be used in coupling reactions.

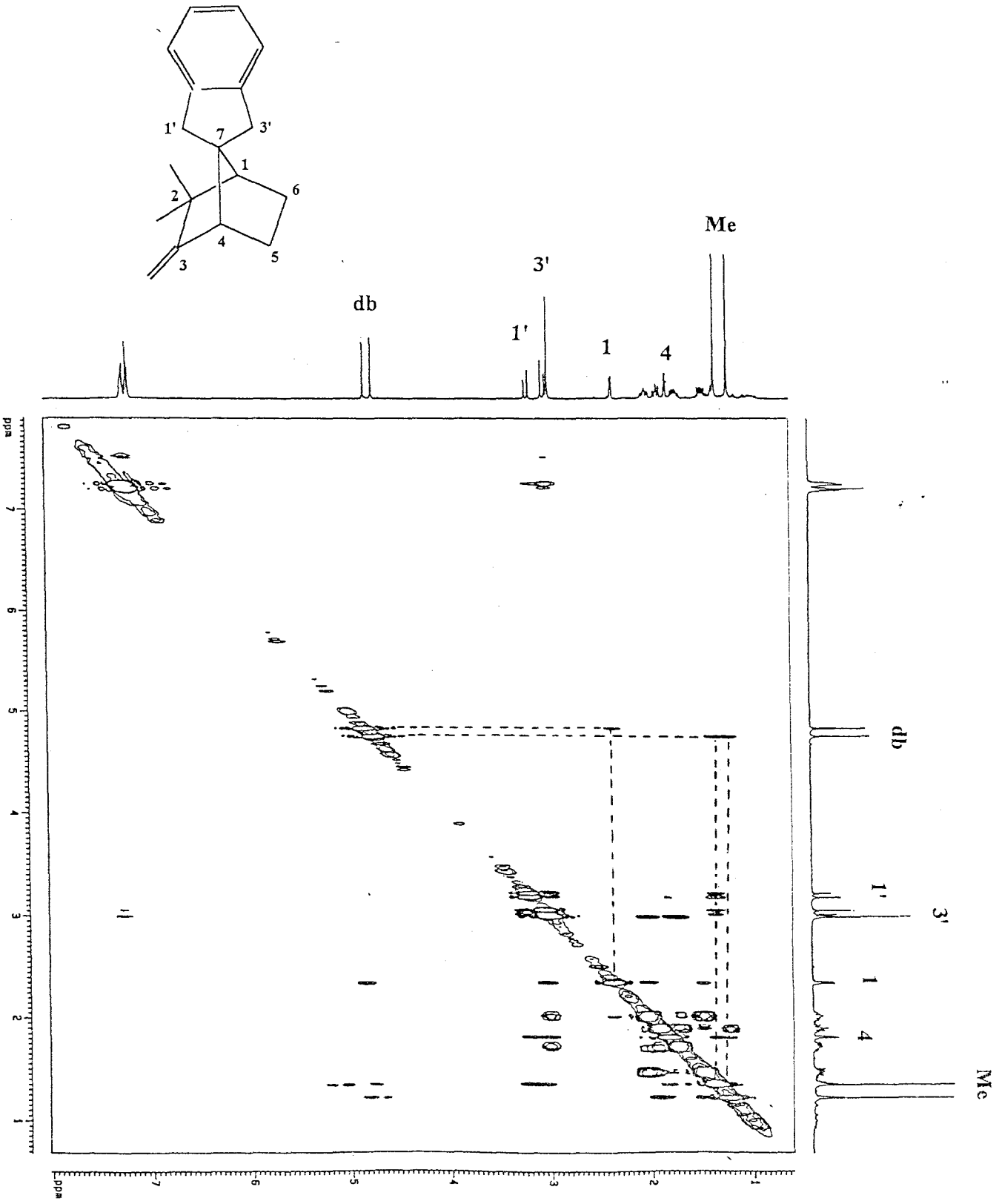


FIGURE 14. The 400MHz NOESY spectrum of the camphene-derivative (219) in $CDCl_3$.

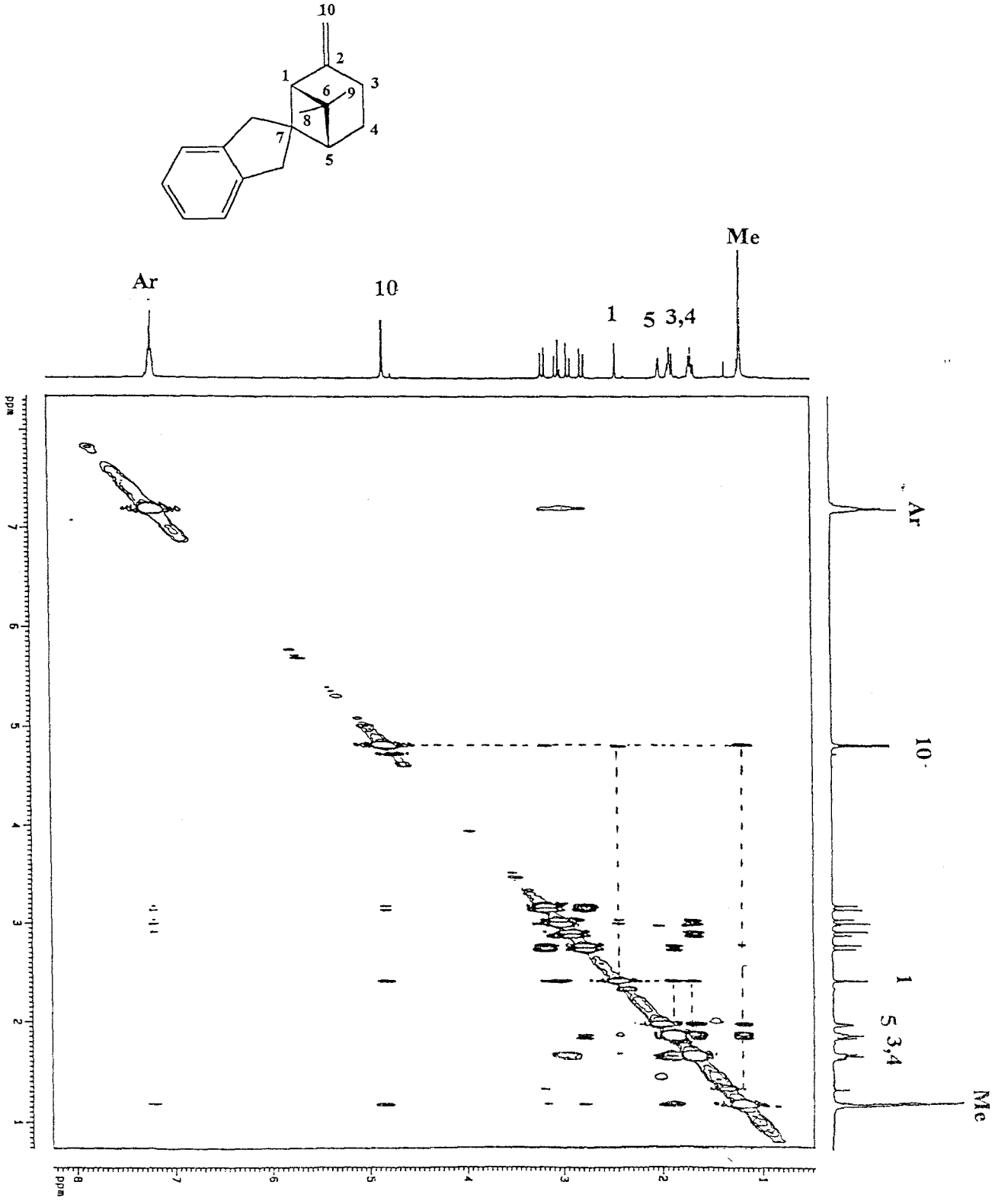
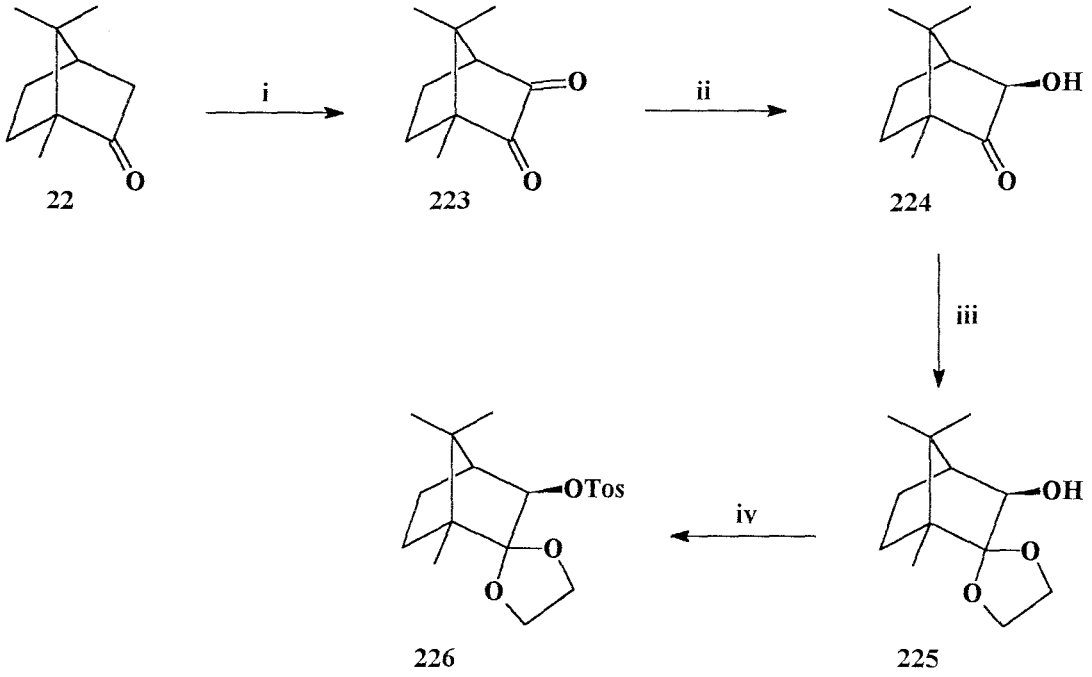


FIGURE 15. The 400MHz NOESY spectrum of the pinene-derivative (221) in $CDCl_3$.

A variation on the chiral auxiliary (**215**) (see Section 2.5.1.4, p. 82) is the camphor derivative (**225**), previously synthesised in our group,[233] the synthesis of which is depicted in Scheme 25. Initially, camphor was oxidised to camphorquinone (**223**) using selenium dioxide. Selective reduction of the C-3 carbonyl group using Raney nickel yielded the α-ketol (**224**). Ethylene glycol was then reacted with the C-2 carbonyl group in the presence of a catalytic amount of *p*-toluenesulfonic acid to yield the ketal (**225**), tosylation of which, using *p*-toluenesulfonyl chloride and BuLi (to form the alkoxy anion), gave the ester (**226**). Both camphor derivatives, (**215**) and (**226**), possess ketal blocking groups at C-2 thus allowing comparison of the *endo*-bromo and *exo*-toluenesulfonyl moieties as leaving groups in substitution reaction.



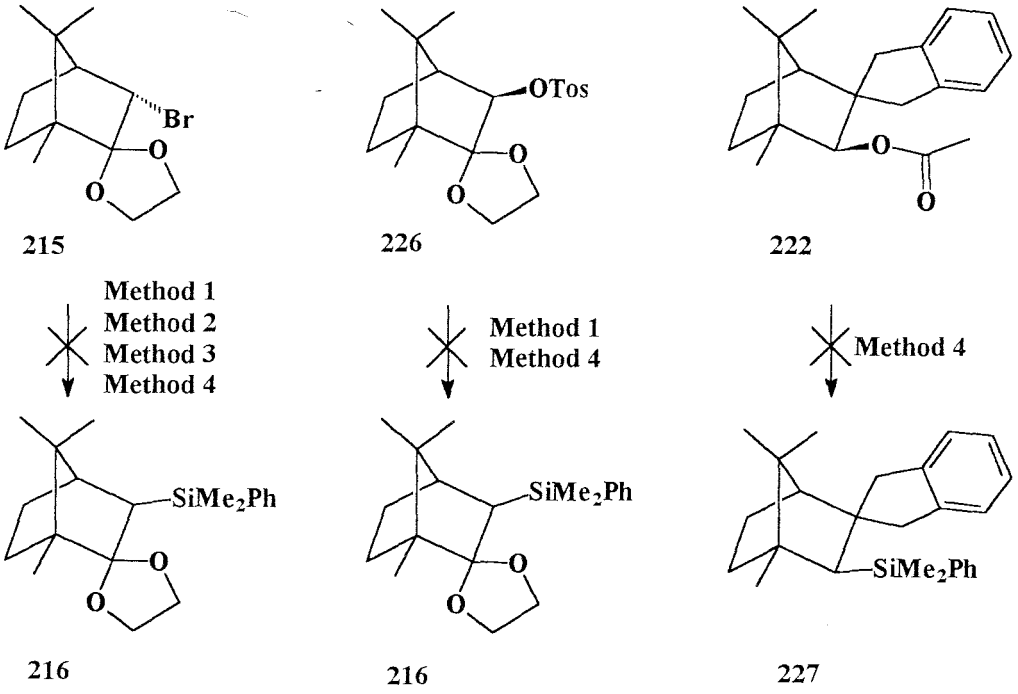
SCHEME 25. Reagents: i) SeO_2, acetic anhydride, reflux, 5h;
ii) Raney nickel, H_2, EtOH, r.t;
iii) ethylene glycol, TsOH, benzene, reflux, 24h;
iv) BuLi, THF, 0°C, then TsCl.

Organolithium reagents have been used as nucleophiles in substitution reactions; one particularly interesting case involves the substitution of an *endo*-bromine on the camphor skeleton.[234] The silyl lithium reagent, phenyldimethylsilyllithium,[235] was synthesised from lithium shot and phenyldimethylsilyl chloride and reacted with the chiral auxiliaries (**215**) and (**226**) (Scheme 26; method 1). It was hoped that the silyllithium would displace the bromo or toluenesulfonyl group to yield the silyl-derivative (**216**). Unfortunately, only the chiral auxiliaries and the silyl ether (**206**) were detected by ^{1}H NMR analysis of the reaction mixtures after work-up.

In a second attempt to introduce a silyl group, silver acetate was added to a solution of the bromo compound (**215**) prior to addition of phenyldimethylsilyllithium (Scheme 26; method 2). It was hoped that formation of the silver bromide salt might facilitate displacement of the bromide. However, when the reaction was carried out, once again only the starting material (**215**) and the silyl ether (**206**) were detected by ^{1}H NMR analysis of the reaction mixture after work-up.

The third method to be attempted involved the use of an organocopper reagent formed from phenyldimethylsilyllithium and CuI. Allylsilanes have been synthesised from allylic acetates, allylic urethanes,[236] allylic halides and allylic sulfonates[237] using this reagent, while silyl copper lithium reagents have found frequent use in substitution reactions.[238] When the silyl copper lithium reagent was reacted with the auxiliary (**215**), however, no reaction took place, the unreacted chiral auxiliary (**215**) and the silyl ether (**206**) again being detected by ^{1}H NMR analysis of the reaction mixture after work-up (Scheme 26; method 3).

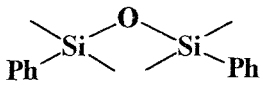
Finally, a silyl copper lithium reagent, synthesised from 1 equivalent of CuCN and 2 equivalents of phenyldimethylsilyllithium, was reacted with each of the three chiral auxiliaries (**215**), (**226**) and (**222**) (Scheme 26; method 4). This silyl copper lithium reagent has been use in many applications,[239] including the formation of allylsilanes from allylic acetates[240, 241] - a precedent which encouraged us to explore the use of the acetate (**222**). Organocopper reagents formed from CuCN instead of CuI have shown to be preferable for substitution reactions with secondary halides and sulfonates.[242]



215 226 222

216 216 227

SCHEME 26. Reagents: Method 1: i) $PhMe_2SiCl$. Li shot, THF, 0 °C; ii)THF, -5 °C;
Method 2: i) $PhMe_2SiCl$. Li shot, THF, 0 °C; ii) AgAc, THF, 0 °C;
Method 3: i) $PhMe_2SiCl$. Li shot, THF, 0 °C; ii) CuI, THF, 0 °C;
Method 4: i) $PhMe_2SiCl$. Li shot, THF, 0 °C; ii) CuCN, THF, 0 °C.



206

However, when the reactions were carried out using the silyl copper lithium reagent formed from phenyldimethylsilyllithium and CuCN, only the starting materials and the silyl ether (206) were detected by ^1H NMR analysis of reaction mixtures, even when the reaction times were varied [the data for which is shown in the experimental section 3.2.5, p. 179, Table 1)].

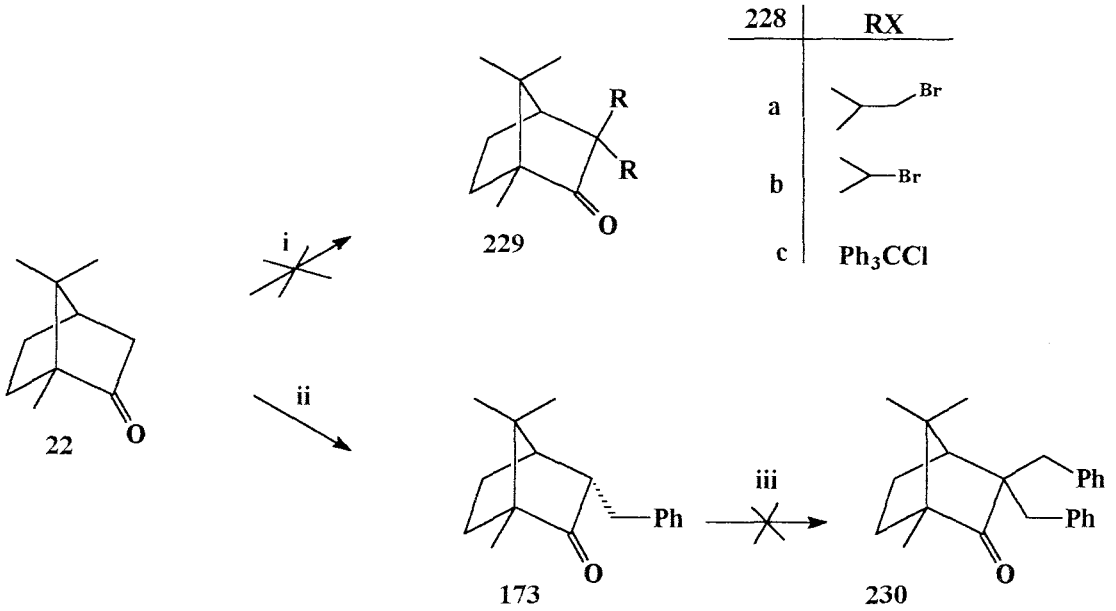
In summary, the substitution of secondary bromide, acetate and *p*-toluenesulfonate groups at C-2 or C-3 of the camphor skeleton was attempted, using four different methods, without success. The chiral auxiliaries were still intact after work-up, indicating that either the silyl group was not sufficiently nucleophilic or, assuming and S_N2 pathway, the electrophilic centre was too sterically hindered. Due to time constraints, no further work was carried out on the direct linkage of silicon to the camphor skeleton.

2.5.2 Methods attempted to increase the bulk of the blocking group

As attempts to bring the chiral centre closer to the camphor skeleton by forming a direct Si-C bond were unsuccessful, attention was turned to increasing the bulk of the blocking group attached to the chiral auxiliary. To this end, alkylation reactions (Scheme 27) were carried out on camphor using various alkyl halides in an attempt to form alkylated camphor derivatives equivalent to the xylyl derivatives (**183**). Two equivalents of NaH were used to deprotonate camphor, and the resulting enolate intermediate was reacted with two equivalents of the alkyl halides, 1-bromo-2-methylpropane (**228a**), 2-bromopropane (**228b**) and triphenylchloromethane (**228c**). In all three cases, only unreacted camphor was isolated after work-up.

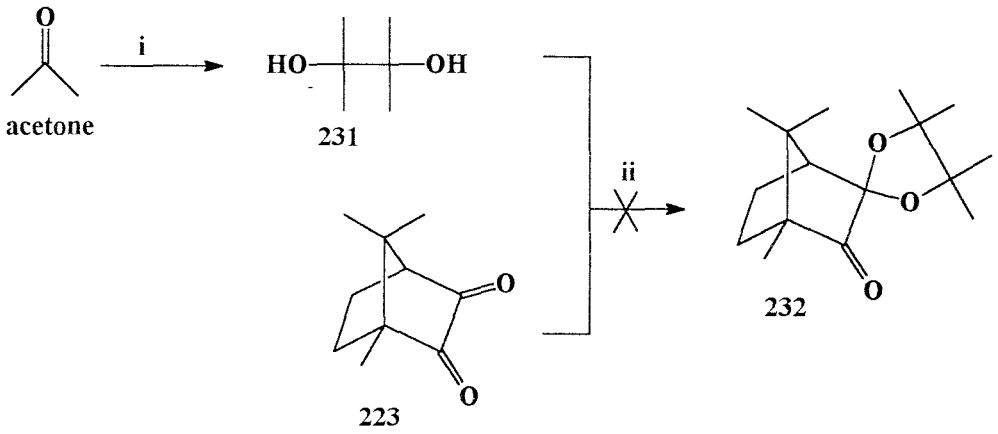
However, when camphor was reacted with 2 equivalents of NaH and 2 equivalents of benzyl bromide, the mono-benzylated product (**173**) was isolated instead of the expected dibenzylated derivative (**230**). An attempt was made to form the dibenzylated derivative (**230**) using either NaH or BuLi and reacting the resulting enolate with benzyl bromide. Once again, however, only the starting materials were detected in the ^{1}H NMR spectrum of the reaction mixture after work-up. The benzyl group on (**173**) was shown to be *endo*-orientated (see Section 2.3, p 58),- not surprisingly, since benzylation is expected at the less hindered *endo*-face of the enolate intermediate.

It seems that the alkylation of camphor requires an "activated" alkyl halide, such as benzyl bromide; however, steric hindrance in the monobenzylated derivative (**173**) presumably prevents the addition of a further benzyl group. As this method of increasing the bulk of the blocking group on camphor proved uncooperative, attempts were made to prepare bulky ketal derivatives of camphor.



SCHEME 27. Reagents: i) NaH (2 eq.), toluene, reflux, then (**228**) (2 eq.), reflux;
ii) NaH (2 eq.), toluene, reflux, then $PhCH_2Br$ (2 eq.), reflux;
Method 1: iii) NaH (1 eq.), toluene, reflux, then $PhCH_2Br$ (2 eq.), reflux;
Method 2: iii) BuLi (1 eq.), Et_2O, 0°C, then $PhCH_2Br$ (1 eq.).

In the first attempt, pinacol (**231**) (synthesised from magnesium and acetone)[243] was reacted with camphorquinone (**223**) in the presence of *p*-toluenesulfonic acid, in the expectation of obtaining the 3,3-ketal (**232**) (Scheme 28). However, the camphorquinone (**223**) was recovered, leading us to conclude that pinacol (**231**) was too sterically hindered to be attached to the camphor skeleton.

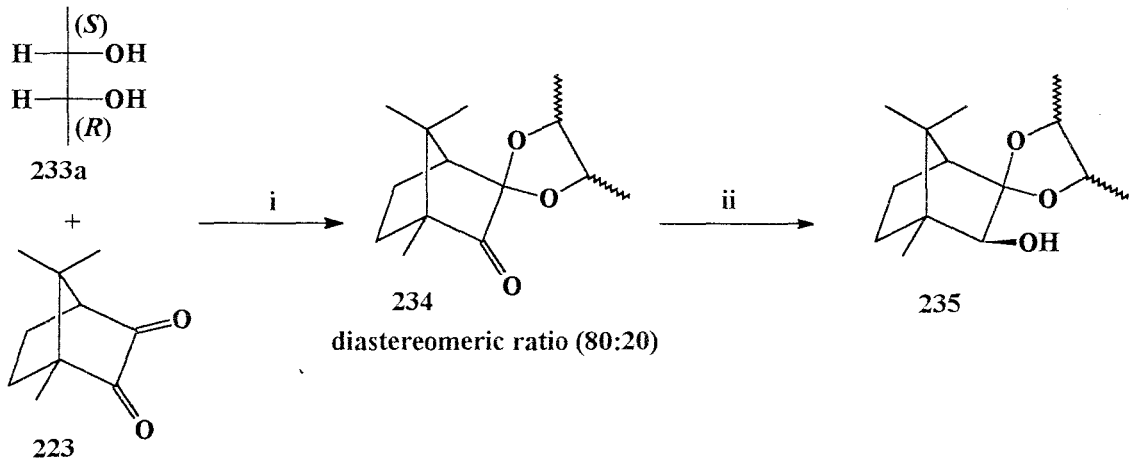


SCHEME 28. Reagents: i) Mg, $Hg(II)Cl_2$, benzene, reflux;
ii) TsOH, benzene, reflux.

A final attempt at increasing the bulk of the blocking group afforded the chiral auxiliary (**235a**), which was used in a number of stereoselective reactions, all of which are discussed in the following section.

2.6 The Camphor-derived Chiral Auxiliary (235a)

The camphor-derived chiral auxiliary (**235a**), which contains a bulky ketal group, was synthesised from camphorquinone (**223**) and *meso*-2,3-butanediol (**233a**) (Scheme 29). *D*-2,3-Butanediol has been used in the resolution of the two stereoisomers of camphor *via* the corresponding ketal derivatives,[244] and it was expected that the stereoisomeric 2,3-butanediols could be used to form ketal blocking groups on camphor. As the 2,3-butanediol enantiomers are expensive, it was decided to explore the ketalisation of camphorquinone (**223**) using the less expensive *meso*-2,3-butanediol (**233a**). Of course, the enantiomeric stereoisomers of 2,3-butanediol exhibit C_2-symmetry and, consequently, would each form a single monoketal at C-3; there are, however, two diastereomeric possibilities when *meso*-2,3-butanediol is used. The two diastereomeric products were, in fact, obtained in a ratio of approximately 80:20. Even more interesting, was the fact that when the 2-carbonyl group was reduced using $LiAlH_4$, a single, essentially pure,[§] stereoisomer of the chiral auxiliary (**235a**) was isolated in good yield, the ^1H and ^{13}C NMR spectra of which are displayed in Figure 16.



SCHEME 29. Reagents: i) TsOH, toluene, reflux;
ii) $LiAlH_4$, Et_2O.

[§] Later observations (see Section 2.6.1, p. 96) were to indicate concomitant formation of small quantities of the 2-*endo*-hydroxy diastereomers.

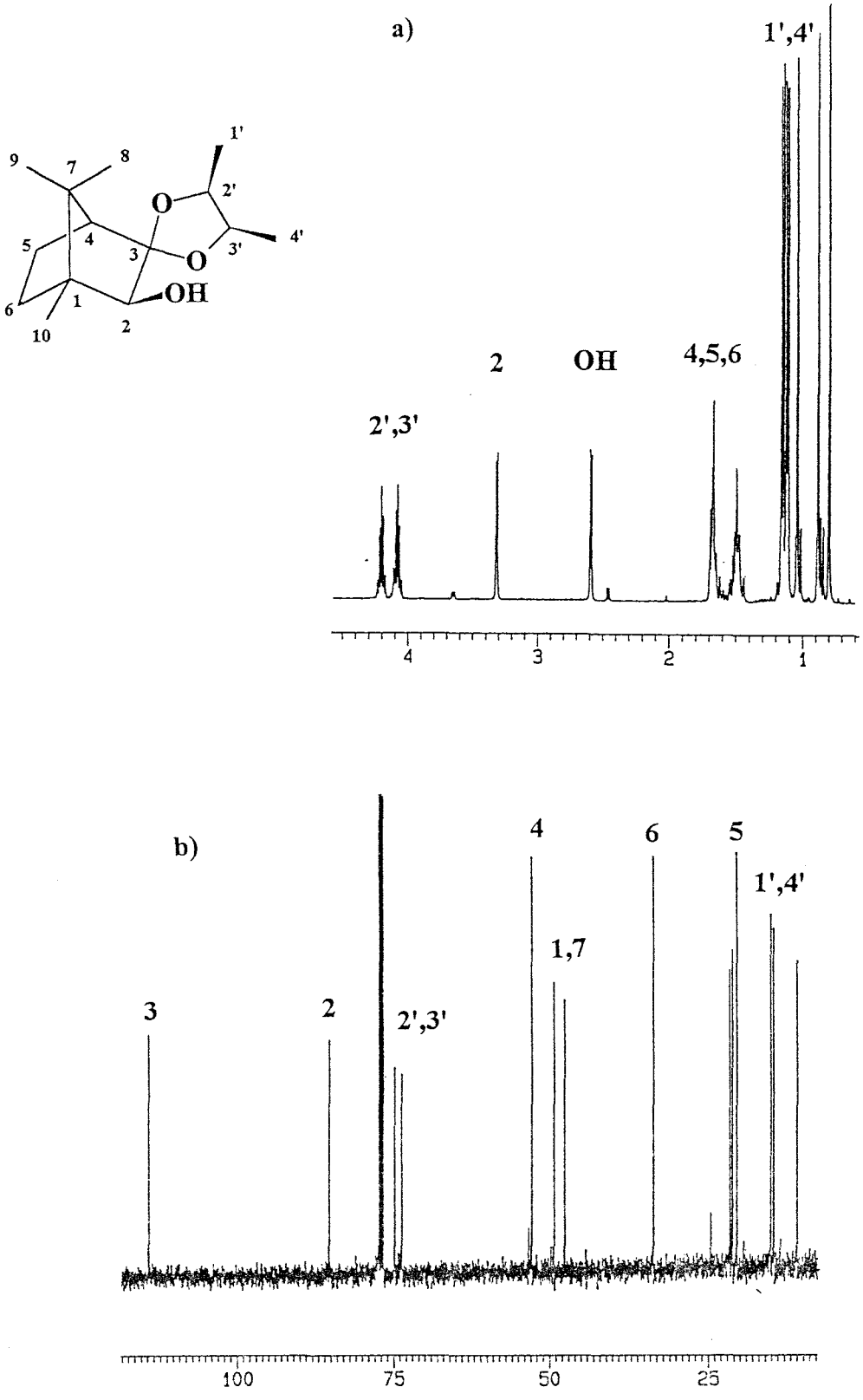
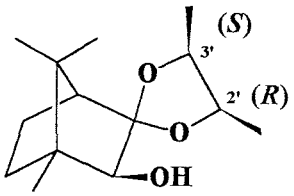


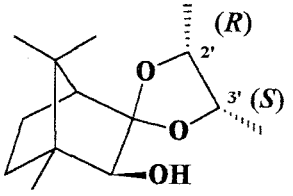
FIGURE 16. a) 400 MHz ^{1}H; and b) 100 MHz ^{13}C NMR Spectra of the chiral auxiliary (235a) in $CDCl_3$.

2.6.1 Determination of the stereochemistry of the chiral auxiliary (235a)

Although efficient isolation of one of the two diatereomeric hydroxyketals had been achieved, the structure of this stereoisomer still had to be established. The two diastereomers differ in the orientation of the *cis*-methyl groups, which may project towards the 2-hydroxy group, as in (**235a**), or away from the 2-hydroxy group as in (**235b**).



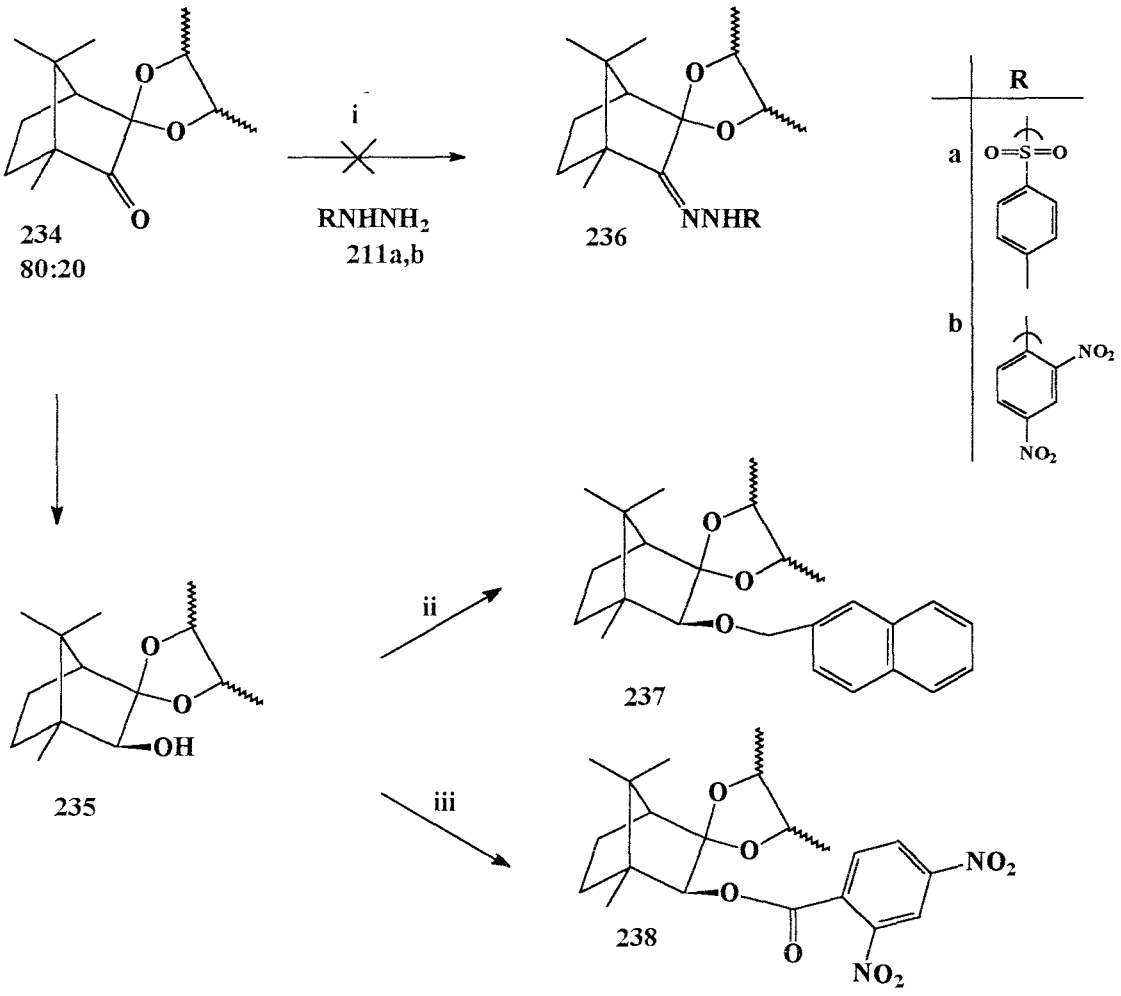
235a



235b

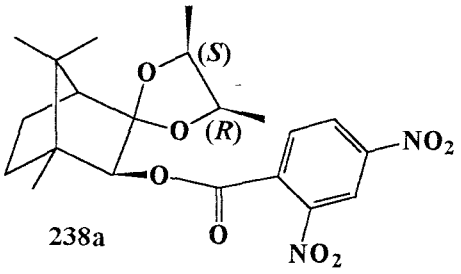
The first method used to establish the stereochemistry of the isolated hydroxy ketal (**235**) was the 2-D NOE difference experiment NOESY. Such spectra were obtained for the chiral auxiliary (**235a**), as well as for some of its ester derivatives, the synthesis of which is discussed in the next section (section 2.6.2, p. 101). This method, however, proved disappointing as no distinctive NOE interactions were detected.

It was also decided to synthesise a crystalline derivative that could be analysed by X-ray crystallography. Treatment of a mixture of the diastereomeric ketones (**234**) with *p*-toluenesulfonylhydrazine (**211a**) and 2,4-dinitrophenylhydrazine (**211b**) in EtOH (Scheme 30) failed to afford the corresponding hydrazones (**236**), and attention was given to the preparation of the crystalline derivatives of the hydroxy compound (**235**). Butyllithium was used to generate the alkoxide of (**235**) which was then treated with 2-bromomethylnaphthalene, but none of the expected ether (**237**) was isolated. Finally, the 2,4-dinitrobenzoic ester (**238**) was obtained by reacting the alkoxide with 2,4-dinitrobenzoyl chloride (Scheme 30).

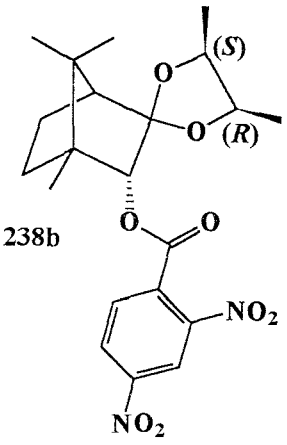


SCHEME 30. Reagents: i) EtOH, reflux, 4h;
ii) BuLi, Et_2O, 0 °C, then 2-(bromomethyl)naphthalene;
iii) BuLi, Et_2O, 0 °C, then 2,4-dinitrobenzoyl chloride.

Great difficulty was experienced in obtaining crystals of the ester (**238**) which were suitable for single crystal X-ray analysis. Twinning of the crystals proved to be a major problem, especially when the solvent used was ethanol. This phenomenon is attributed to slipping during crystal growth, resulting in the formation of twinned crystals.[245] When hexane was used as a recrystallisation solvent, twinning appeared less marked and a crystal, which appeared to be suitable for X-ray analysis, was finally obtained. Remarkably, the X-ray crystallographic analysis revealed a unit cell containing a pair of diastereomeric esters, *viz.*, the 2-*exo* ester (**238a**) and, quite unexpectedly, the 2-*endo* ester (**238b**).



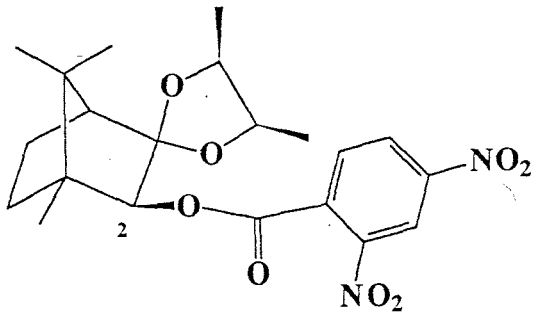
238a



238b

The formation of such crystals suggests fortuitous co-crystallisation of trace quantities of the 2-*endo* isomer, which is not readily apparent in the NMR spectra of the initially isolated ester (**236**). However, on further examination, each consecutive recrystallisation resulted in an increase in concentration of the 2-*endo* ester, clearly determined using ^{1}H NMR analysis by integration of the diastereomeric 2-H signals (see Figure 17).

Although the final R-factor is rather high (11%), it is clear from Figure 18 that the *cis*-methyl groups in the ketal moiety of both diastereomers, project towards the 2-ester group. The preferred stereochemistry of the ketal moiety, is thus, as indicated in the structure (**235a**).



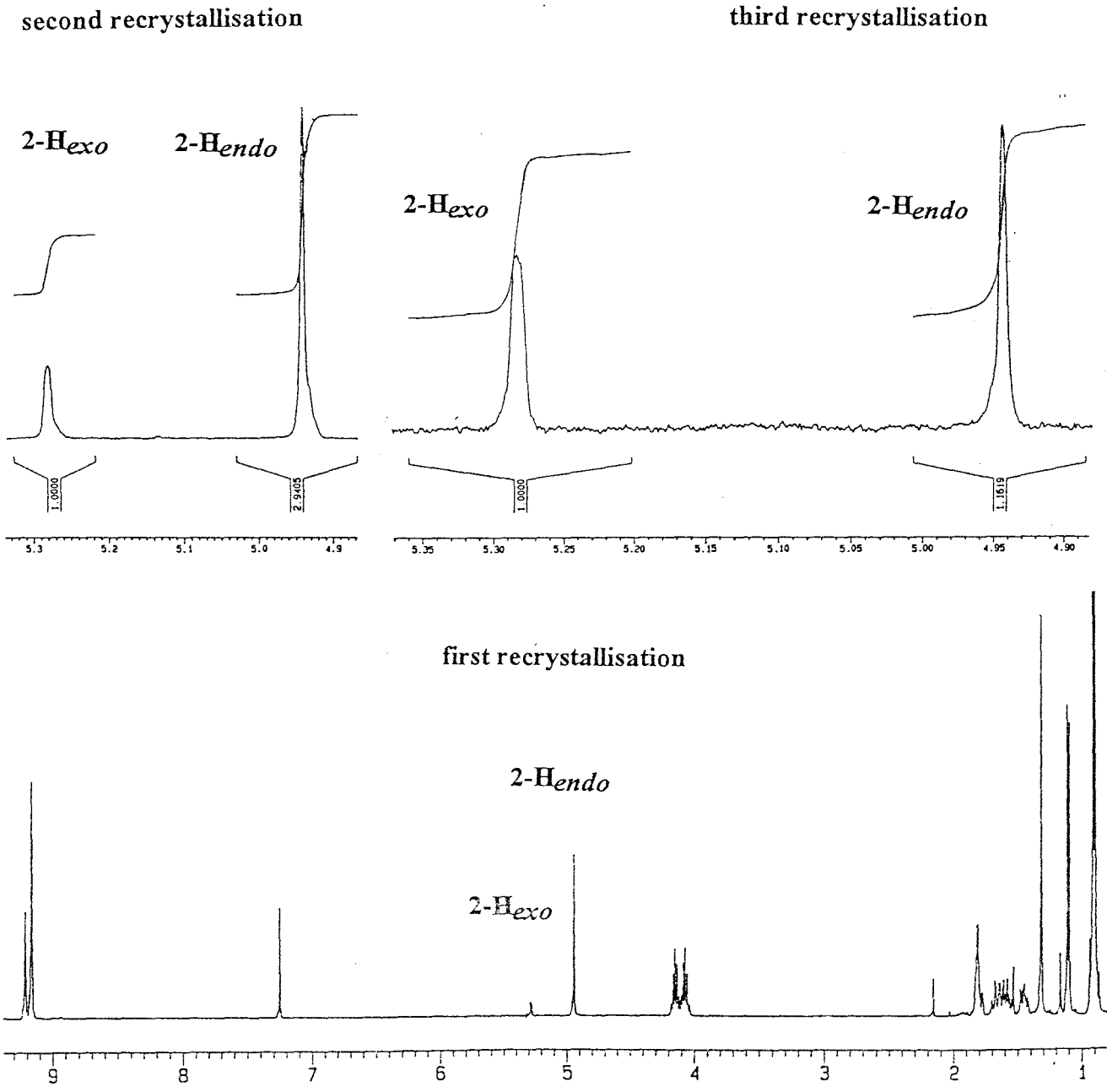
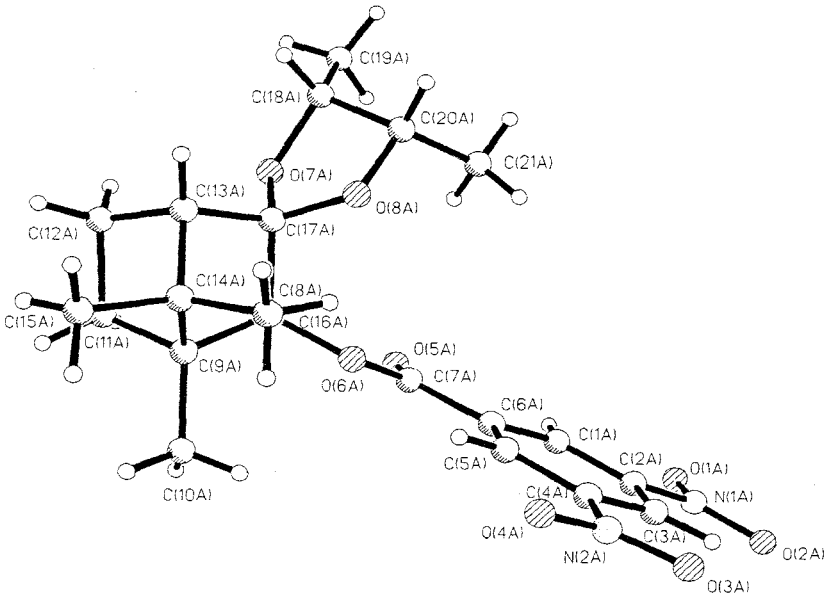


FIGURE 17. ^{1}H NMR Spectra of the ester (238) in $CDCl_3$ showing the concentration of the 2-*endo* ester after consecutive recrystallisations.

a)



b)

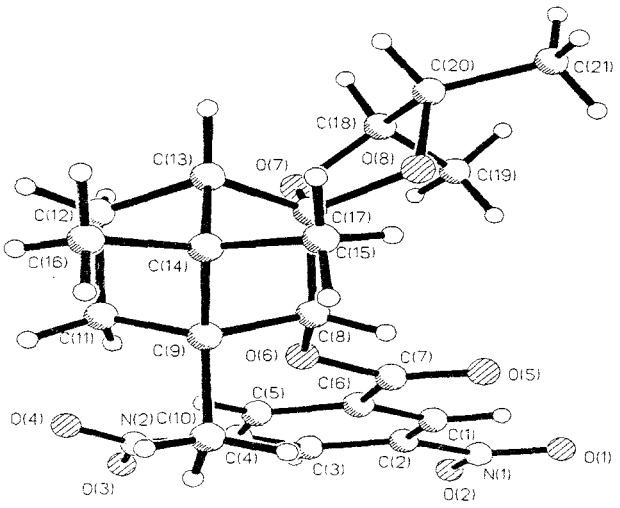
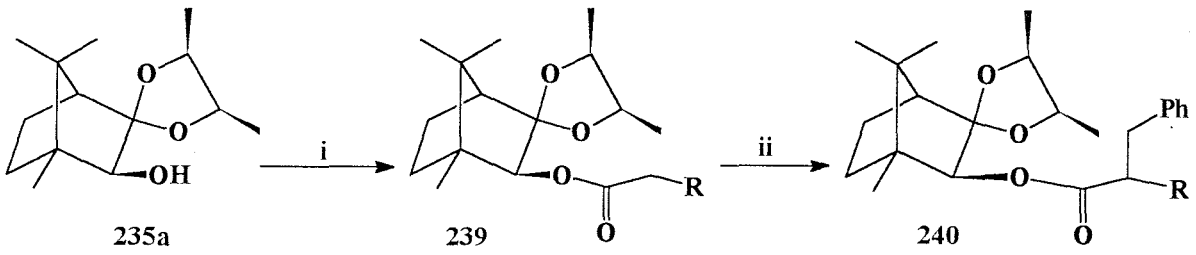


FIGURE 18. Pluto diagrams showing crystallographic numbering for the X-ray structure of: a) the 2-*exo*-ester (**238a**), (C-2 obscured by the 8-Me group); and
b) the 2-*endo*-ester (**238b**).

2.6.2 Ester derivatives of the chiral auxiliary (235a)

A number of ester derivatives were synthesised from the chiral auxiliary (**235a**). Deprotonation of the hydroxy group was effected using BuLi and the resulting alkoxide was treated with a series of acid chlorides (Scheme 31). These esters (**239**) were obtained in good yield (≥ 70 %) and were fully characterised. In order to evaluate the stereocontrol afforded by the camphor ketal auxiliary, each of the esters (**239**) were α-benzylated to afford (**240**), using benzyl bromide as the alkylating agent and LDA to generate the intermediate enolates.



235a 239 240

SCHEME 31. Reagents: i) BuLi, RCH_2COCl, Et_2O (**186**), 0 °C;
ii) LDA, $PhCH_2Br$, THF, -78 °C.

The yields of the α-benzylated products (**240a-f**) varied from 14-89 % (Table 2), and the stereoselectivities of the benzylation reaction were typically determined from the integrals of the 2'-H_{endo} ^1H NMR signals of the diastereomeric components in each of the crude reaction mixtures. In the case of the benzylated products (**240c**) and (**240f**), however, the 2'-H_{endo} signals in the ^1H NMR spectra of the crude reaction mixtures could not be integrated due to congestion in this area of the spectrum. Consequently, the stereoselectivity of the reactions were determined from the ^1H NMR spectra of the purified diastereomeric mixtures. These integrated spectra are shown in Figure 19.

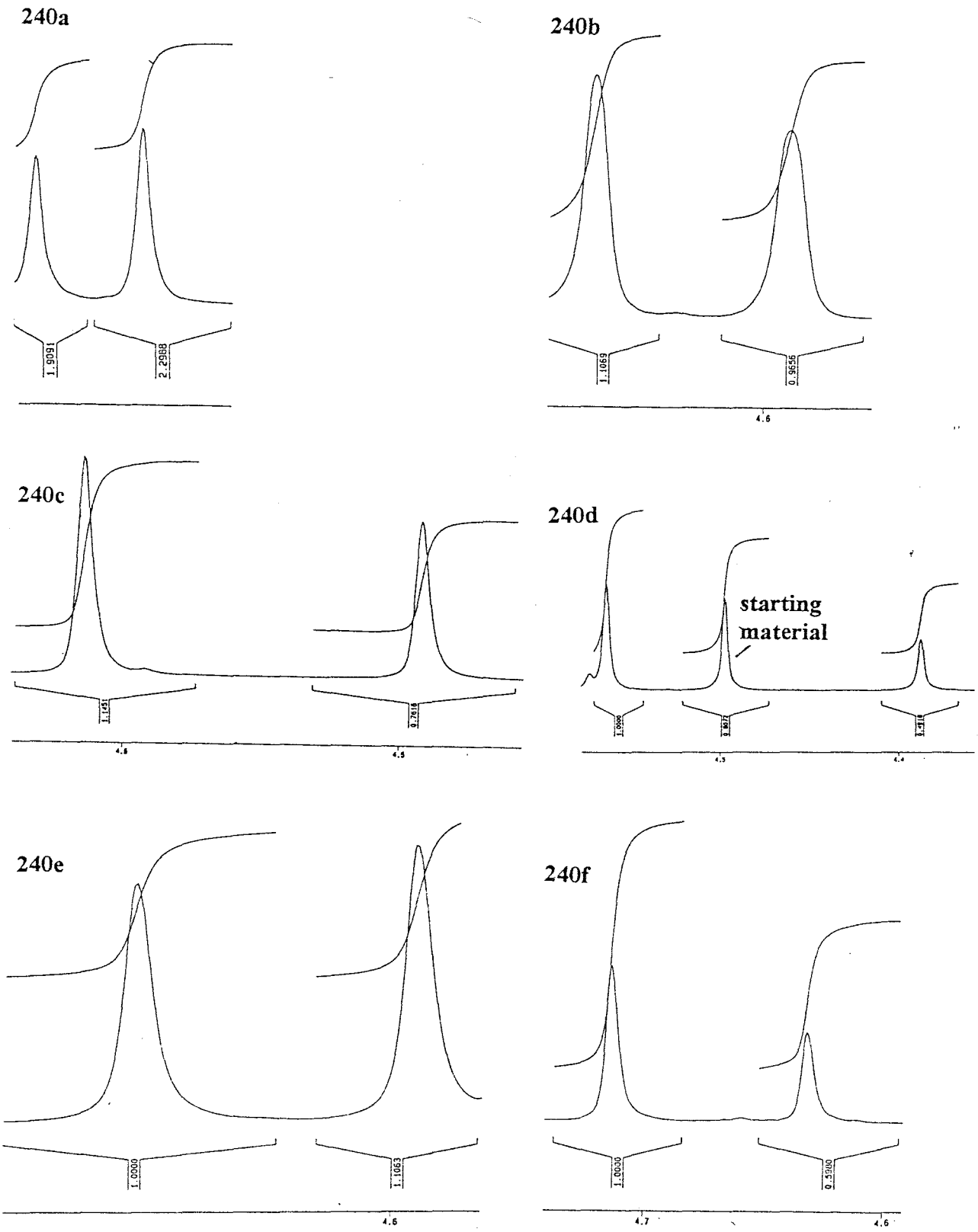
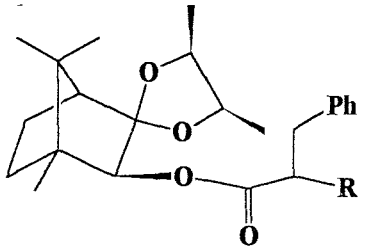


FIGURE 19. Integrated 400 MHz ^{1}H NMR spectra of alkylated esters (**240a-f**) of the chiral auxiliary (**235a**) in $CDCl_3$ showing the 2-H_{endo} signals of the diastereomeric components.

TABLE 2. Stereoselectivity data for the α-benzylation of ester derivatives of the chiral auxiliary (**235a**) (Scheme 31).

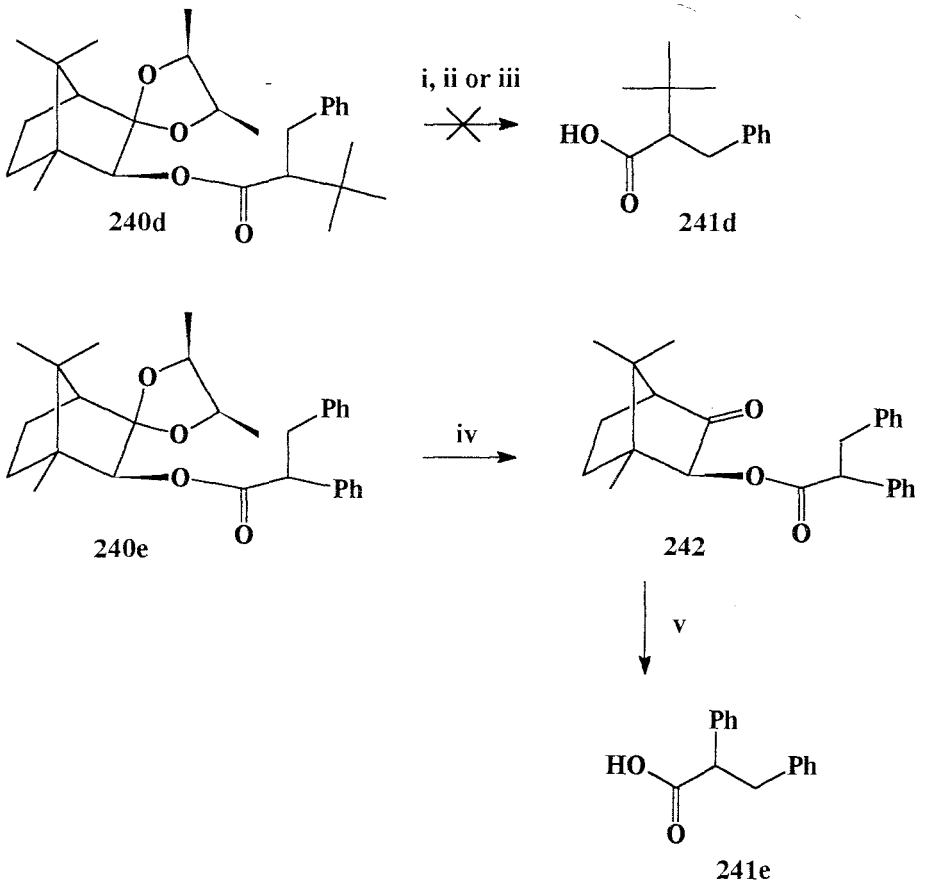


240

Entry	Substrate	R	% Yield (240)	% d.e. (240)
1	**239a**	Me	29[a]	9
2	**239b**	Et	40[a]	7
3	**239c**	Pr^i	89	20
4	**239d**	Bu^t	57	34
5	**239e**	Ph	80	5
6	**239f**	PhO	14	25

[a] The yields were determined by integration of the ^{1}H NMR spectrum of the isolated mixture.

The diastereoselectivities obtained in these benzylation reactions were lower than those obtained using the chiral auxiliary (**183**) (see Section 2.4.1; p. 62). It had been expected that increasing the bulk of the blocking group would increase the stereoselectivity of the reaction, if the enolate moiety lay quasi-parallel to the blocking group. However, this is clearly not the case. In order to rationalise these observations, attempts were made to hydrolyse a representative ester and establish the configuration at the new chiral centre from the optical rotation of the resulting acid.

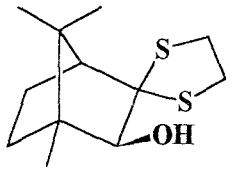


SCHEME 32. Reagents: i) $LiOH.H_2O$, H_2O_2, THF-H_2O (1:1), r.t.;
ii) $LiOH.H_2O$, H_2O_2, THF-H_2O (1:1), 12-crown-4-ether, r.t.;
iii) 2**M** KOH in MeOH, reflux;
iv) conc. H_2SO_4, ice;
v) $LiOH.H_2O$, THF, r.t.

Initial attempts to hydrolyse the ester (**240d**) to yield the corresponding acid (**241d**) using a solution of lithium hydroxide in aqueous THF with or without 12-crown-4, or a solution of 2**M** KOH in methanol, were unsuccessful (Scheme 32). This suggested that the bulky ketal and 10'-methyl groups presented too much steric hindrance to allow for ready hydrolysis of the ester. When the ester derivative (**240e**) was treated with concentrated sulfuric acid and the resulting mixture poured on ice, the ketal, but not the ester group was hydrolysed and the crude camphor ester (**242**) was isolated. Interestingly, ^{1}H NMR analysis of the ester (**242**) revealed a

diastereomeric excess (9% d.e.) comparable to that observed for the substrate (**240e**) (7% d.e.).[¥] This suggests that enolisation of the ester functionality is negligible on treatment with sulfuric acid. The ester (**242**) was then hydrolysed using lithium hydroxide in aqueous THF to yield the acid (**241e**). The relative ease of this final hydrolysis supports the proposal that steric hindrance by the ketal group prevents hydrolysis of the ester under mild conditions. Polarimetric analysis revealed the major enantiomer to be the (+)-(*S*)-2,3-diphenylpropanoic acid (**241e**).

Helmchen *et al.*[182] have proposed that cation chelation of enolate intermediates of ester derivatives of the borneol dithioketal (**243**) influences the stereoselectivity of alkylation reactions. In addition, an (*E*)-enolate intermediate was proposed in the alkylation of glycolate esters of chiral auxiliaries derived from the camphor sulfonamides (**68**) and (**69**) (see Section 1.2.1.10, p. 21).[97]



243

There are two obvious conformations of the (*E*)-enolate intermediate which would account for the preferential formation of the (*S*)-stereoisomer in the alkylation of the ester derivative (**240e**) (and the equivalent stereoisomers in the case of the other five ester derivatives). The first conformation depicted as the structure (**244a**) (see Figure 20), corresponds to the conformation described in Section 2.4.1, p. 67 for the enolate intermediates (**189a**). In this conformation, the enolate (**244a**) lies quasi-parallel to the ketal blocking group, where attack from the front at the less hindered *Si*-face would favour the formation of the (*S*)-stereoisomer. However, if the enolate adopted this conformation, one would have expected greater stereoselectivity in the alkylation reaction due to the presence of the larger blocking group.

[¥] The diastereomeric excess of the ester derivative (**240e**) is higher than that quoted for the stereoselectivity of the alkylation reaction (see Table 2) as an increase in the diastereomeric excess occurred during purification.

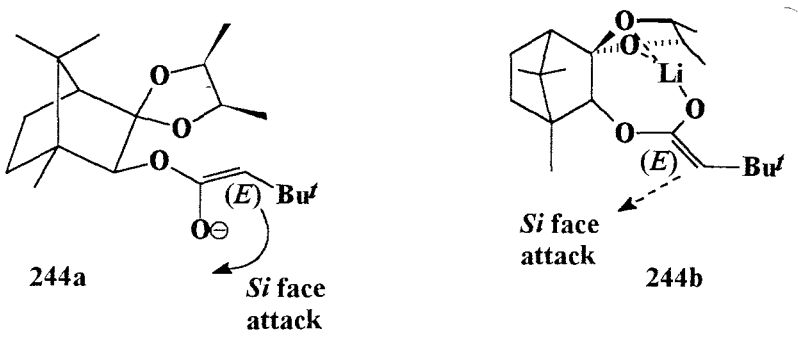


FIGURE 20. The two proposed conformations of the (*E*)-enolate intermediate, (**244a**) and (**244b**).

If, on the other hand, the enolate intermediate adopts conformation (**244b**), in which the enolate moiety is twisted to permit coordination of the lithium cation with the ketal oxygens, the benzyl bromide electrophile would preferentially approach from the *endo*-face due to the presence of the 8-Me group on the camphor skeleton. It is noted, however, from the computer-generated models of the enolate intermediates (**244a**) and (**244b**), depicted in Figure 21, that the enolate moiety swings away from the ketal blocking group. This raises the possibility that the 10-Me group might sterically inhibit attack by the electrophilic benzyl bromide, which would account for both the low yields and the low stereoselectivities observed in this reaction.

While either conformation of the (*E*)-enolate [(**244a**) and (**244b**)] would favour *Si*-face attack and, hence, formation of the (*S*)-2,3-diphenylpropanoic acid (**241e**), the coordination factor would seem to be significant, since, in the analogous xylyl derivatives (**189**), chelation is not possible and *Re*-face attack is favoured. The observed switch in diastereofacial selectivity may, thus be rationalised by assuming a preference for *endo*-*Si*-face attack in the chelated ketal system (**244b**), but *endo*-*Re*-face attack in the non-chelated, quasi-perpendicular xylyl system (**189b**).

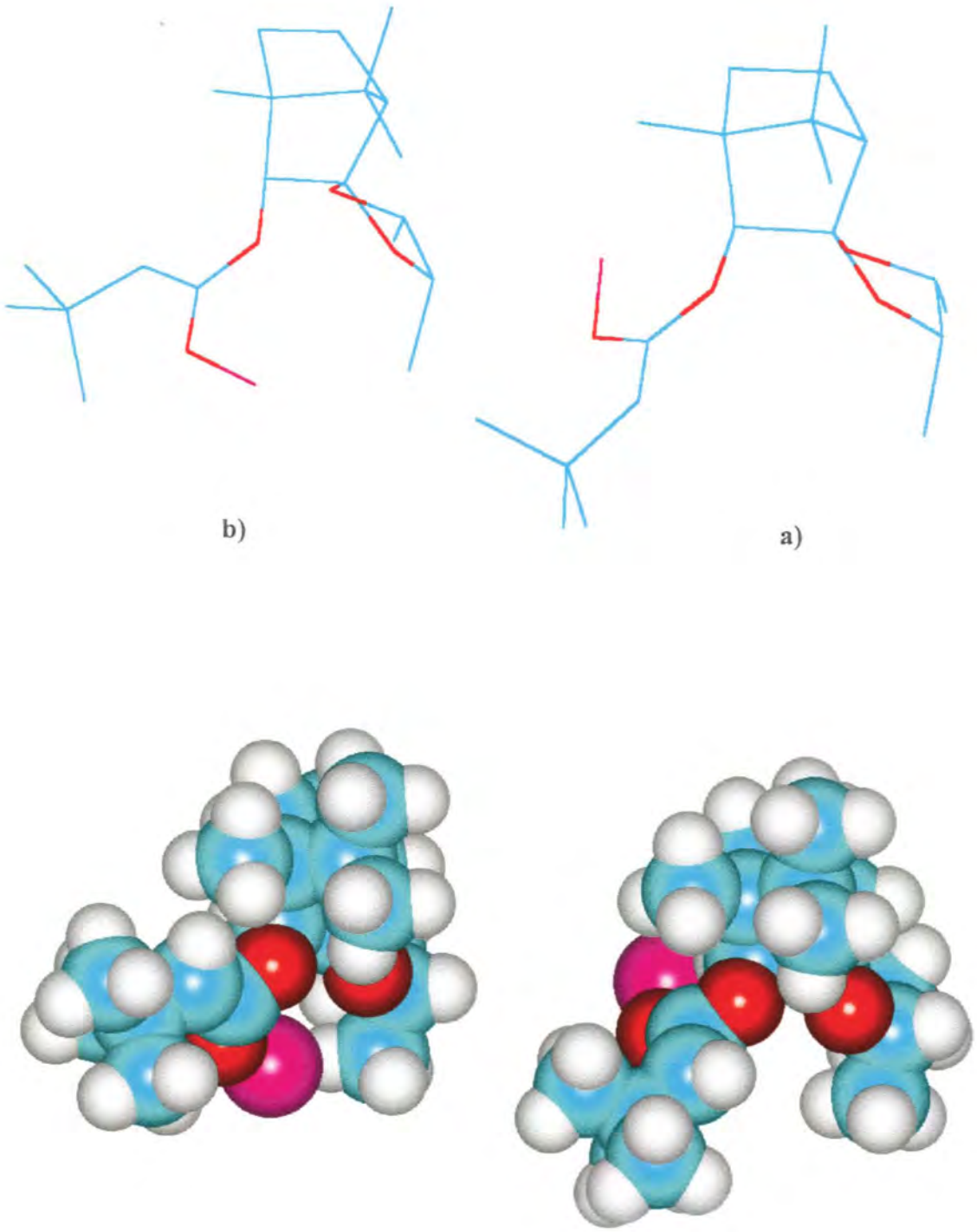
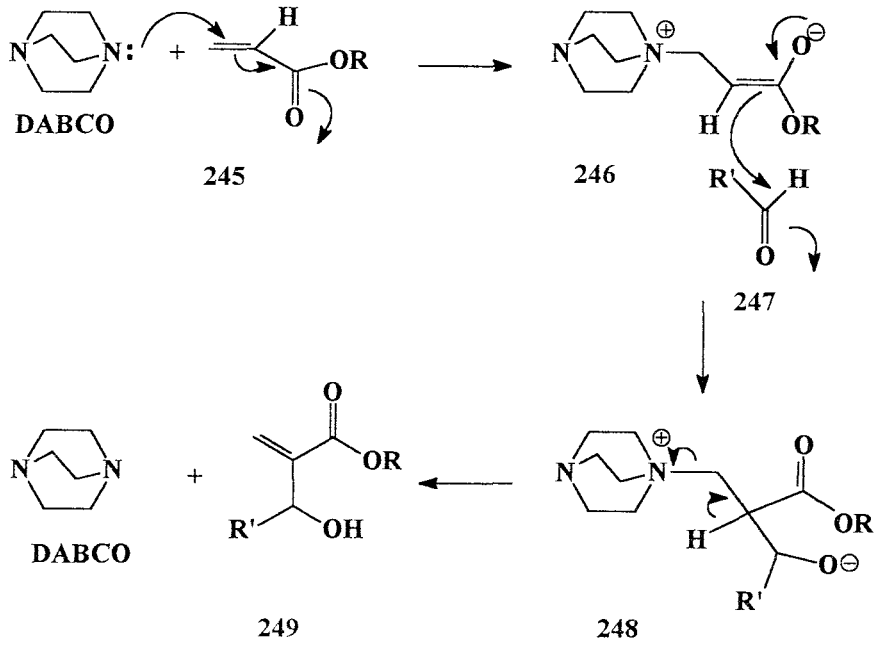


FIGURE 21. The stick and space-filling representations of the computer-modelled conformations of the lithium (*E*)-enolate intermediates, namely :-
a) the quasi-parallel conformation (**244a**), and
b) the quasi-perpendicular conformation (**244b**).

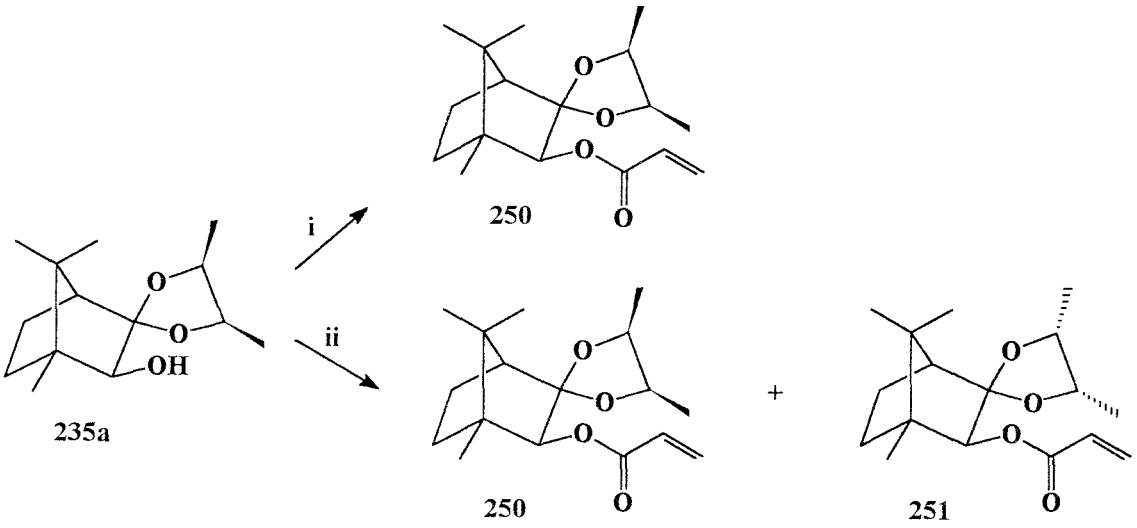
2.6.3 Acrylate derivatives of the chiral auxiliary (235a)

Acrylate derivatives of the chiral auxiliary (**235a**) were synthesised in order to determine the stereofacial selectivity provided by the chiral auxiliary in asymmetric Baylis-Hillman reactions.[246] The Baylis-Hillman reaction is considered to involve 3 steps (Scheme 33).[247] Initially, the acrylate (**245**) and the 3° amine (DABCO) react to form the zwitterion intermediate (**246**), which then attacks the aldehyde (**247**). Elimination of the 3° amine from the intermediate (**248**) results in the formation of the Baylis-Hillman product (**249**).



SCHEME 33.

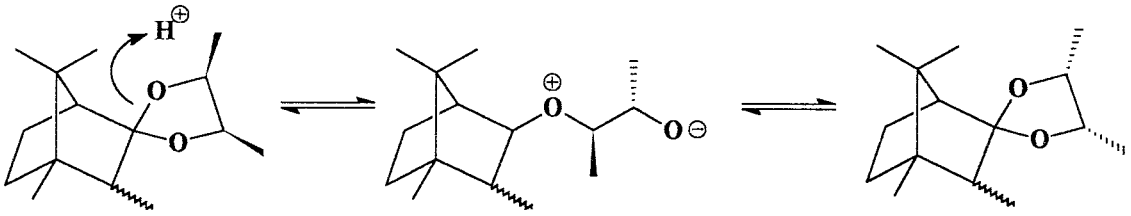
Baylis-Hillman reactions have been carried out using chiral acrylate systems - a general approach that has been used on a number of occasions with limited success.[115, 116] In our investigation, the first method used to synthesise a chiral acrylate system involved the reaction of acryloyl chloride with the lithium alkoxide of the chiral alcohol (**235a**), the required product (**250**) being obtained in 85% yield (Scheme 34). However, in an alternative approach, the alcohol (**235a**) was reacted directly with acryloyl chloride in the presence of 3Å molecular seives,[248] to give two stereoisomeric products. One of these products was the expected ester (**250**), while the second was shown to be the stereoisomer (**251**). NMR Data clearly indicated the formation of two different acrylic esters of bornyl alcohols, each containing a ketal blocking group at C-3. Furthermore, it was apparent that the only difference between the stereoisomers (**250**) and (**251**) was the orientation of the methyl groups in the ketal moiety.



235a 250 250 251

SCHEME 34. Reagents: i) BuLi, Et_2O, 0 °C, then acryloyl chloride;
ii) Acryloyl chloride, 3Å molecular sieves, CCl_4, reflux.

Since the substrate comprised a single stereoisomer (**235a**), it was apparent that some inversion of configuration had occurred at the pseudoasymmetric centre, C-3, during the esterification. This inversion of the ketal blocking group is proposed to occur *via* acid catalysed opening of the ketal (**252**) due to the presence of the HCl formed in the reaction, to give the hemiketal intermediate (**253**) (Scheme 35). Subsequent ring closure could then occur at either face of the C-3 carbocation to give a mixture of stereoisomeric systems (**252**) and (**254**).



252 **253** **254**

SCHEME 35.

The unexpected formation of the two esters (**250**) and (**251**) with opposite orientation of the ketal moiety, allowed us to confirm the stereochemistry of the ketal blocking groups by comparing their NOESY spectra (these spectra are displayed in Figures 21 and 22 respectively) as well as their ^{13}C NMR spectra (see Figure 23). In the case of the ester (**250**), NOE interactions are evident between the 4'-H and the 2" and 3" methine protons; in the case of the ester (**251**), however, NOE interactions between the 4'-H and the 1" and 4" methyl groups are apparent. These observations clearly confirm the stereochemistry of the ketal blocking group in the two stereoisomers and are consistent with the configurational assignments discussed earlier (see Section 2.6.1, p. 96.

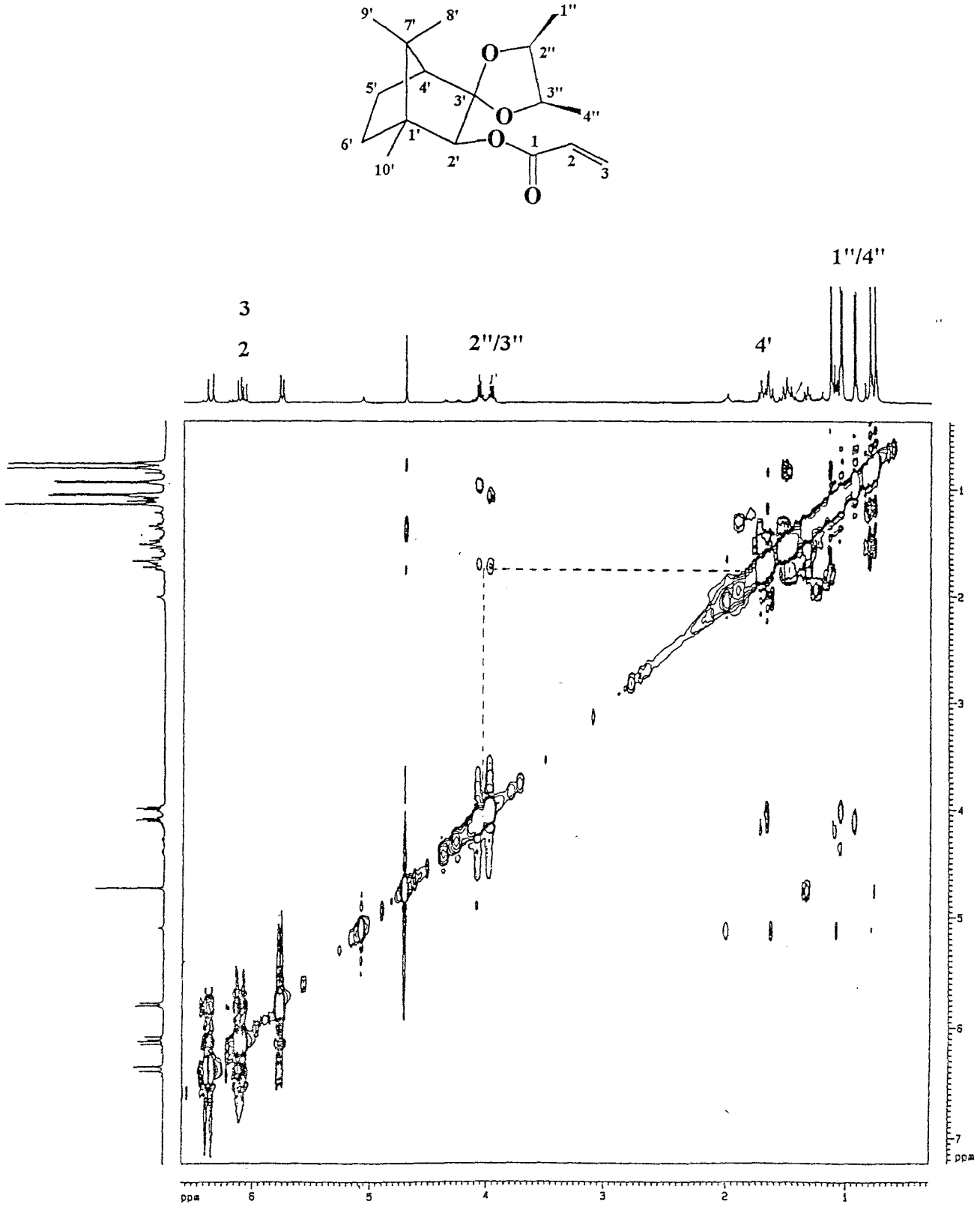


FIGURE 21. The 400 MHz NOESY spectrum of the chiral acrylate (250) in $CDCl_3$.

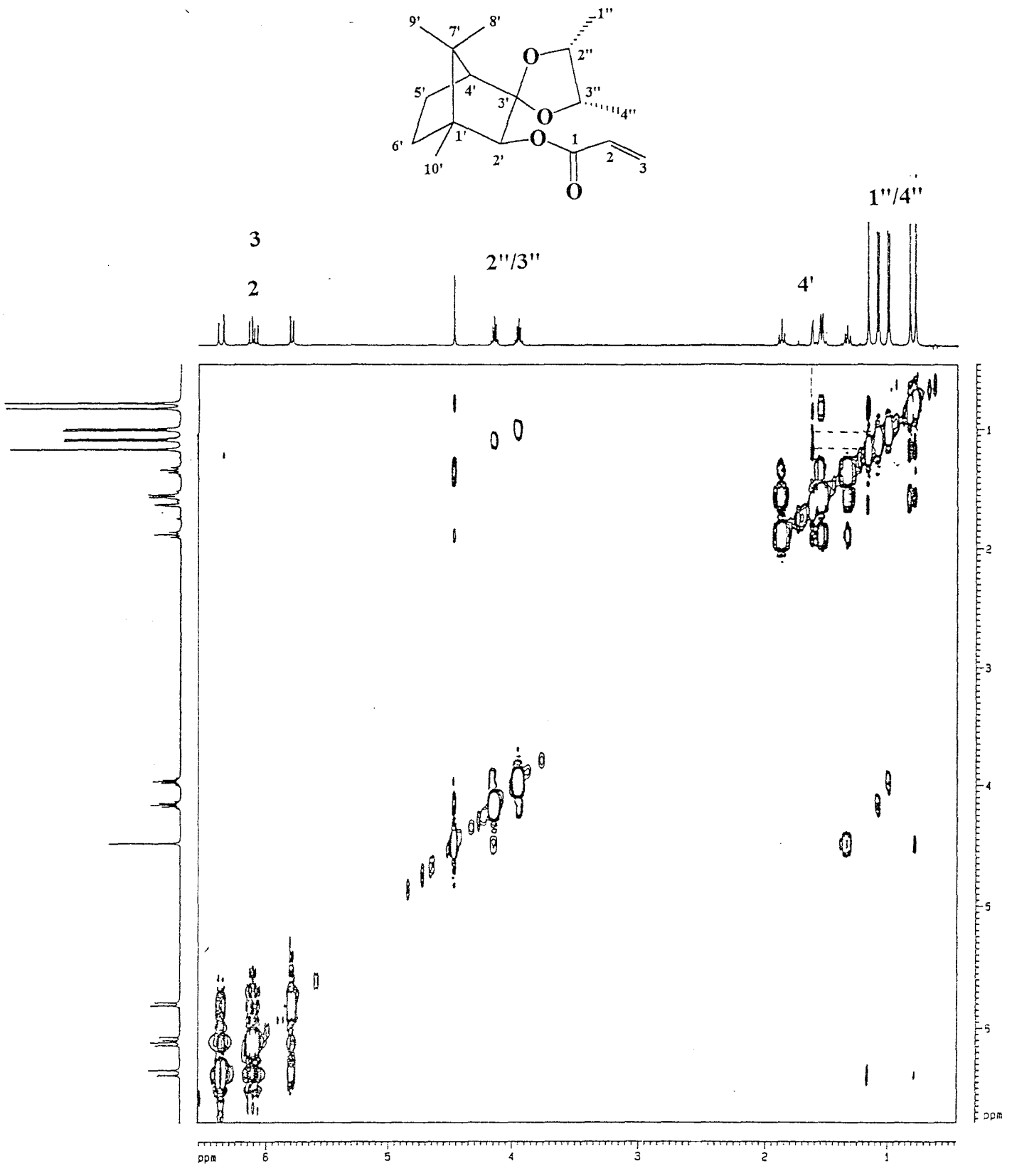


FIGURE 22. The 400 MHz NMR spectrum of the chiral acrylate (**251**) in $CDCl_3$.

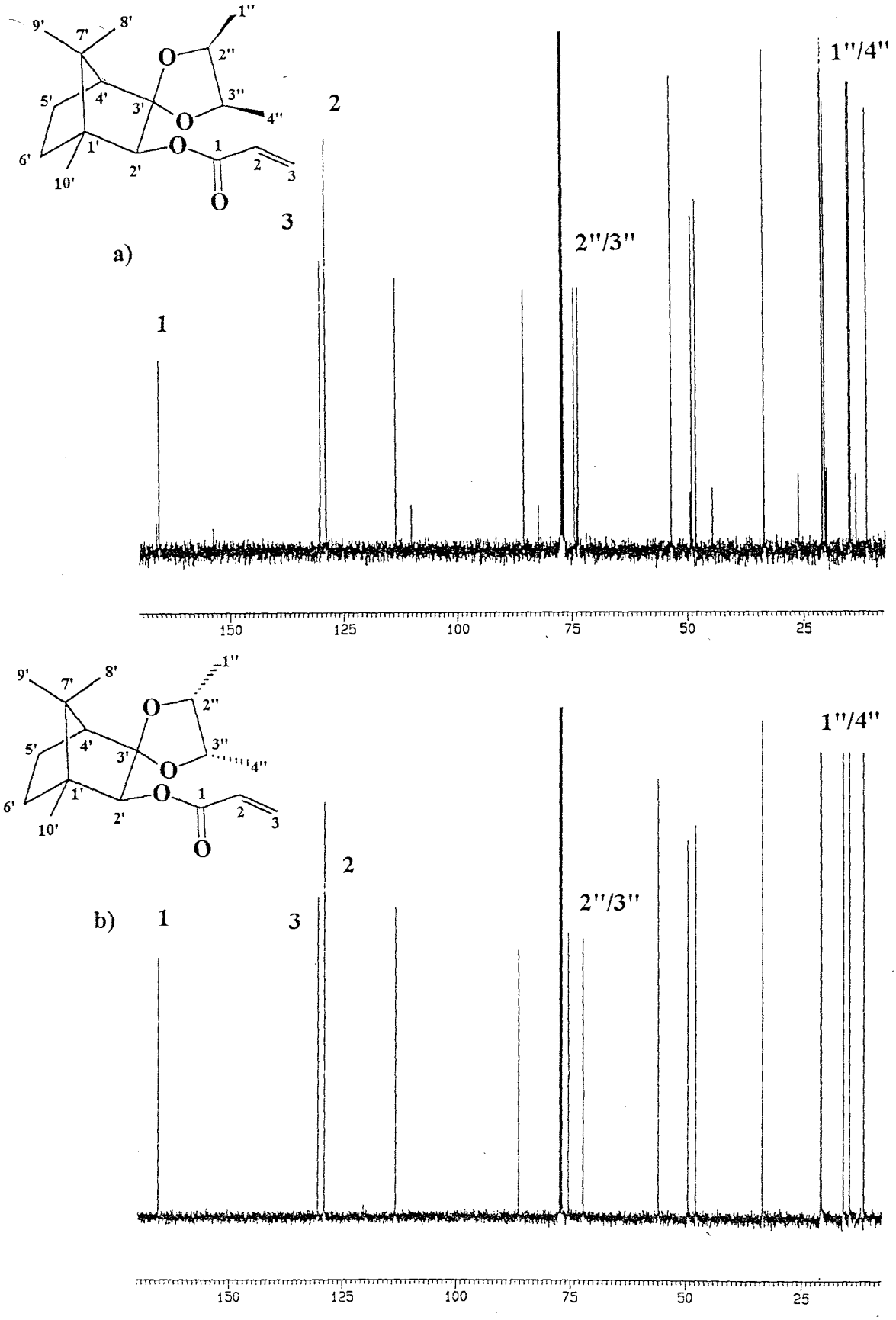
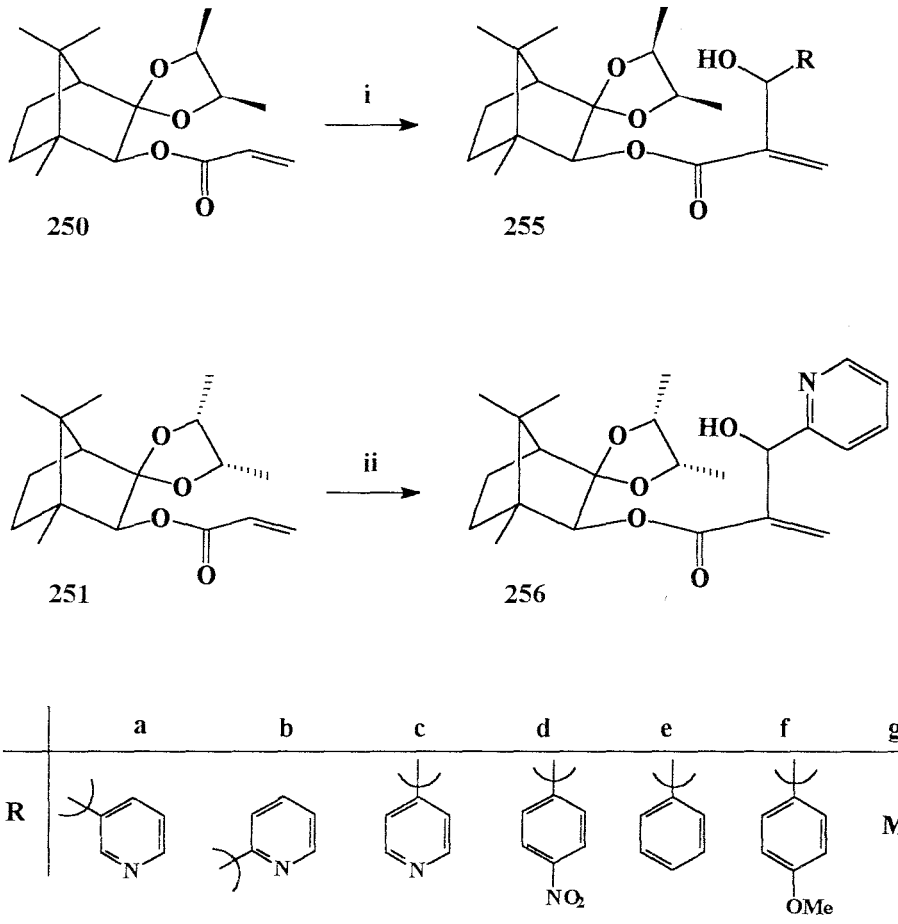


FIGURE 23. The 100 MHz ^{13}C NMR spectra in $CDCl_3$ for: a) (250), and b) (251).

A number of Baylis-Hillman reactions were carried out (Scheme 36), using the two chiral esters (**250**) and (**251**) and nine different aldehydes. Two different 3° amines, DABCO and 3-quinuclidinol were used to compare the stereoselectivity and reaction rates, since 3-quinuclidinol has been shown to increase the rate of the reaction by stabilising the zwitterion intermediate.[247] In order to determine the effect of complexation on the stereoselectivity, the use of $ZnBr_2$ was also explored. The results of the various Baylis-Hillman reactions are summarised in Table 3.



SCHEME 36. Reagents: i) Method 1: RCHO, 3-quinuclidinol, $CDCl_3$; i) Method 2: RCHO, DABCO, $CDCl_3$; i) Method 3: RCHO, DABCO, $ZnBr_2$, $CDCl_3$; ii) RCHO, DABCO, $CDCl_3$.

The stereoselectivity exhibited in these reactions was determined by comparing the 2'-H_{endo} signal integrals in the ^1H NMR spectrum of the purified diastereomeric mixture. In most cases, the presence of broad and overlapping signals precluded the use of the ^1H NMR spectra of the crude reaction mixtures.

TABLE 3. Stereoselectivity data for Baylis-Hillman reaction of the chiral acrylates (**250**) and (**251**) (Scheme 36).

Entry	Substrate	RCHO	3° amine	Time	Product	% d.e.
1	**250**	pyridine-3-carboxaldehyde	3-quinuclidinol	2 weeks	**255a**	0
2	**250**	pyridine-3-carboxaldehyde	DABCO	2 weeks	**255a**	5
3	**250**	pyridine-3-carboxaldehyde	DABCO/ $ZnBr_2$	2 weeks	**255a**	4 (0)[a]
4	**250**	pyridine-2-carboxaldehyde	3-quinuclidinol	1 week	**255b**	19 (20)[a]
5	**250**	pyridine-2-carboxaldehyde	DABCO	1 week	**255b**	27
6	**251**	pyridine-2-carboxaldehyde	DABCO	1 week	**256b**	18 (21)[a]
7	**250**	pyridine-4-carboxaldehyde	DABCO	1 week	**255c**	9 (9)[a]
8	**250**	4-nitrobenzaldehyde	DABCO	1 week	**255d**	12
9	**250**	benzaldehyde	DABCO	3 months	**255e**	6
10	**250**	4-methoxy-benzaldehyde	DABCO	4 months	**255f**	8
11	**250**	acetaldehyde	DABCO	3 months	**255g**	30 (18)[a]
12	**250**	propanaldehyde	DABCO	3 months	**255h**	35
13	**250**	butyraldehyde	DABCO	3 months	**255i**	34 (29)[a]

[a] Diastereomeric excess determined from the crude reaction mixture

Based on the tabulated data, several observations are possible.

i) The stereoselectivity is disappointing (0 - 34% d.e.).

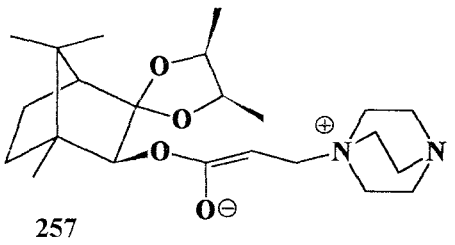
ii) Variation of the catalyst, or addition of $ZnBr_2$ appears to have little effect on the stereoselectivity (entries 1 - 3).

iii) There is a marked difference in the reaction times, ranging from one or two weeks for electrophilic aldehydes (entries 1 - 8) to months for the less electrophilic substrates (entries 9 - 13).

iv) Although very slow, the reactions with aliphatic aldehydes (entries 11- 13) appear to offer the best stereocontrol (30 - 34% d.e.).

v) Use of the chiral acrylate (**250**) provides marginally higher stereocontrol (27% d.e.; entry 5) than the substrate (**251**) (18% d.e., entry 6).

The unusually long reaction times[¥] observed for these Baylis-Hillman reactions suggests that access to the chiral acrylates (**250**) and (**251**) is sterically impeded. This is displayed in the computer generated model of the zwitterion enolate intermediate (**257**) of the chiral acrylate (**250**) (see Figure 24). Unfortunately, however, the steric constraints do not appear to provide meaningful diastereofacial selectivity.



257

[¥] Baylis-Hillman reactions typically take several days or weeks to reach completion.[247]

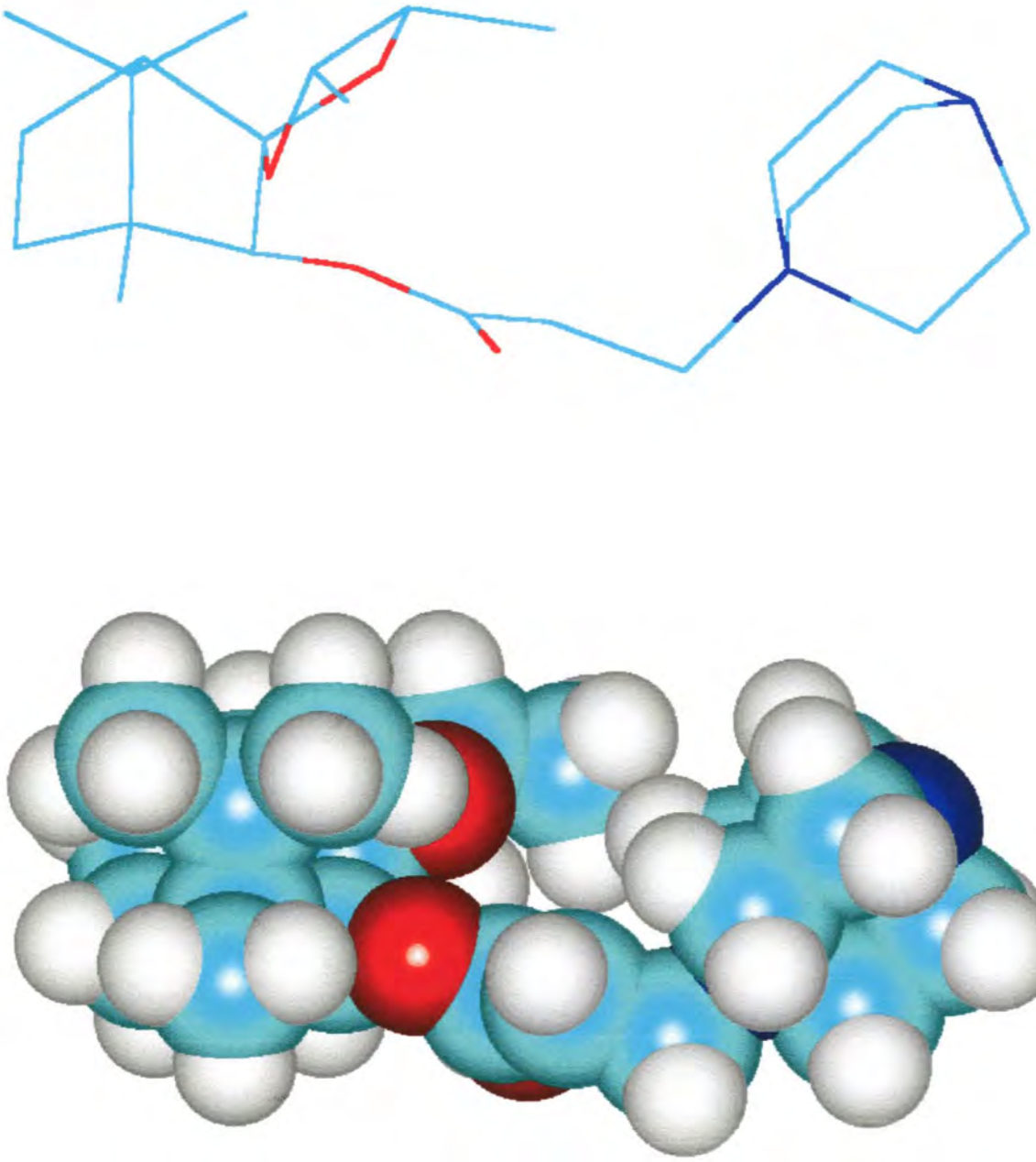
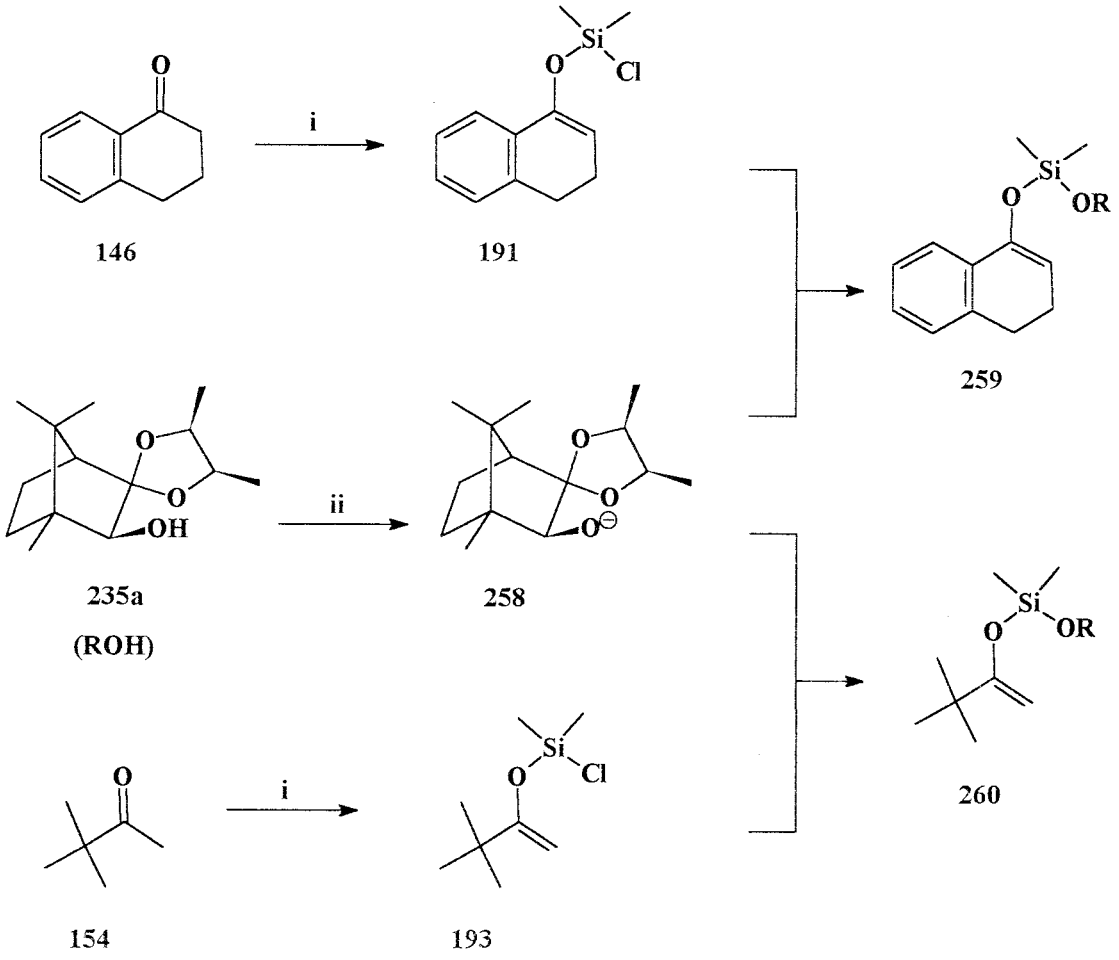


FIGURE 24. Stick and space-filling representations of the computer-modelled conformation of the zwitterion intermediate (**257**), generated in the Baylis-Hillman reaction.

2.6.4 Silyl enol ether derivatives of the chiral auxiliary (235a)

Although limited stereofacial selectivity had been obtained with the chiral auxiliary (**235a**), the α-tetralone- and pinacolone-derived silyl enol ethers (**259**) and (**260**) of this chiral auxiliary were synthesised to complete the study. Using the convergent approach discussed previously (Section 2.4.2, p. 70), α-tetralone- and pinacolone chlorosiloxy derivatives (**191**) and (**193**) were reacted with the alkoxy anion (**258**) of the chiral auxiliary (**235a**) to yield the respective silyl enol ethers (**259**) and (**260**), which were fully characterised (Scheme 37).



SCHEME 37. Reagents: i) LDA, THF, -78 °C, then Me_2SiCl_2;
ii) BuLi, THF, 0 °C.

To determine the stereocontrol afforded by the chiral auxiliary (**235a**), the three reactions used to evaluate the pinane-derived analogues (see Section 2.2.1.1, p. 46) were carried out, *viz.*,

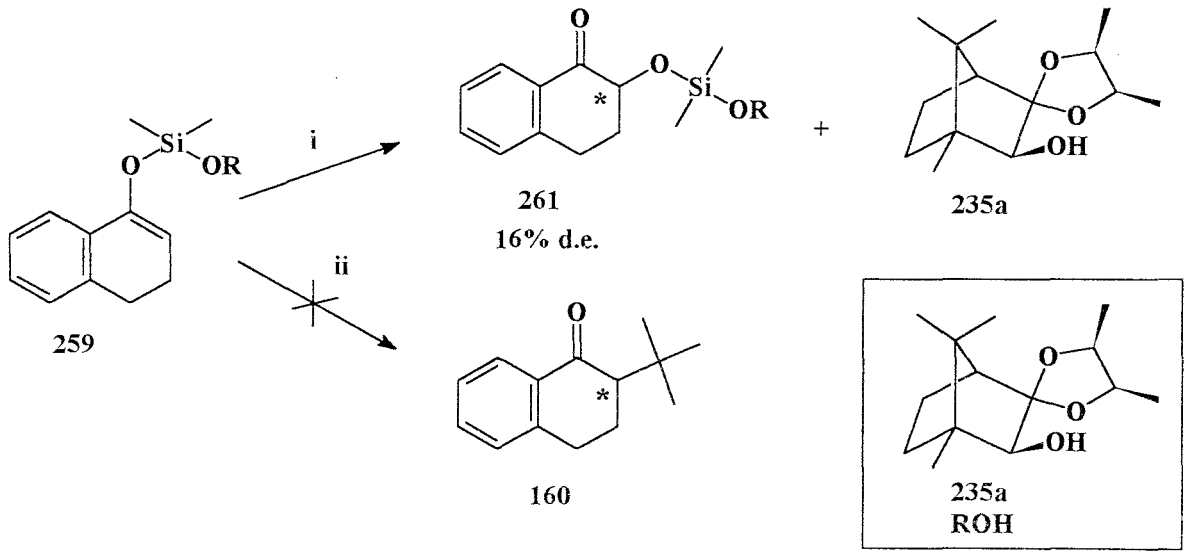
i) MCPBA oxidation;

ii) alkylation with *t*-BuCl-$TiCl_4$; and

iii) the Mukaiyama reaction with PhCHO-$TiCl_4$.

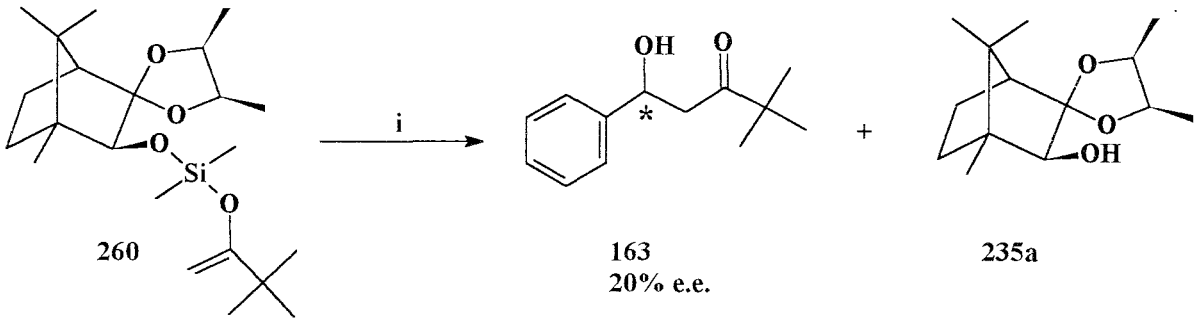
i) The α-tetralone-derived silyl enol ether (**259**) was oxidised using MCPBA to yield the α-silyloxyketone (**261**) in 16% d.e. (Scheme 38). The stereoselectivity was determined by integration of the SiMe ^1H NMR signals of the diastereomeric components in the crude reaction mixture (see Figure 25). The material yield, however, was very low, and the α-silyloxyketone (**261**) was isolated together with the cleaved chiral auxiliary (**235a**), indicating the instability of the α-silyloxy system (**261**).

ii) Attempted alkylation of the α-tetralone-derived silyl enol ether (**259**) with *t*-BuCl in the presence of $TiCl_4$ (Scheme 38) resulted in the formation of a complex mixture of products and the reaction was not investigated further.



SCHEME 38. Reagents: i) MCPBA, $NaHCO_3$, CH_2Cl_2, 0 °C, 2h;
ii) *t*-BuCl, CH_2Cl_2, -23 °C, then $TiCl_4$, 3h.

iii) The final reaction involved a Mukaiyama reaction between the pinacolone-derived silyl enol ether (**260**) and benzaldehyde. The reaction was found to yield the chiral β-hydroxyketone (**163**) in 24% yield (Scheme 39). The isolation of the intact chiral auxiliary (**235a**) also confirms that the ketal is not cleaved by $TiCl_4$. The enantiomeric excess was determined by integration of the *t*-butyl ^1H NMR signals of the enantiomeric components in the product mixture, the signals being resolved with the aid of the chiral shift reagents, [Eu(hfc)$_3$] and [Pr(hfc)$_3$] (see Figure 25). An enantiomeric excess of 20% was measured using both shift reagents. This is the highest stereoselectivity obtained for reactions of the pinacolone-derived silyl enol ethers of the various chiral auxiliaries discussed previously. Polarimetric analysis indicated an 8% enantiomeric excess of the known (*R*)-enantiomer, the lower value being attributed to the presence of an optically active impurity.



260 **163** **235a**
20% e.e.

SCHEME 39. Reagents: i) PhCHO, $TiCl_4$, CH_2Cl_2, -78 °C, 4.5h.

It was observed that the silyl enol ethers (**259**) and (**260**) underwent rapid decomposition on storage, and this instability could account for the low material yields in these reactions. Given the poor diastereoselectivities obtained, it was concluded that the hydroxy ketal (**235a**) is not a viable chiral auxiliary for asymmetric reactions of silyl enol ether derivatives.

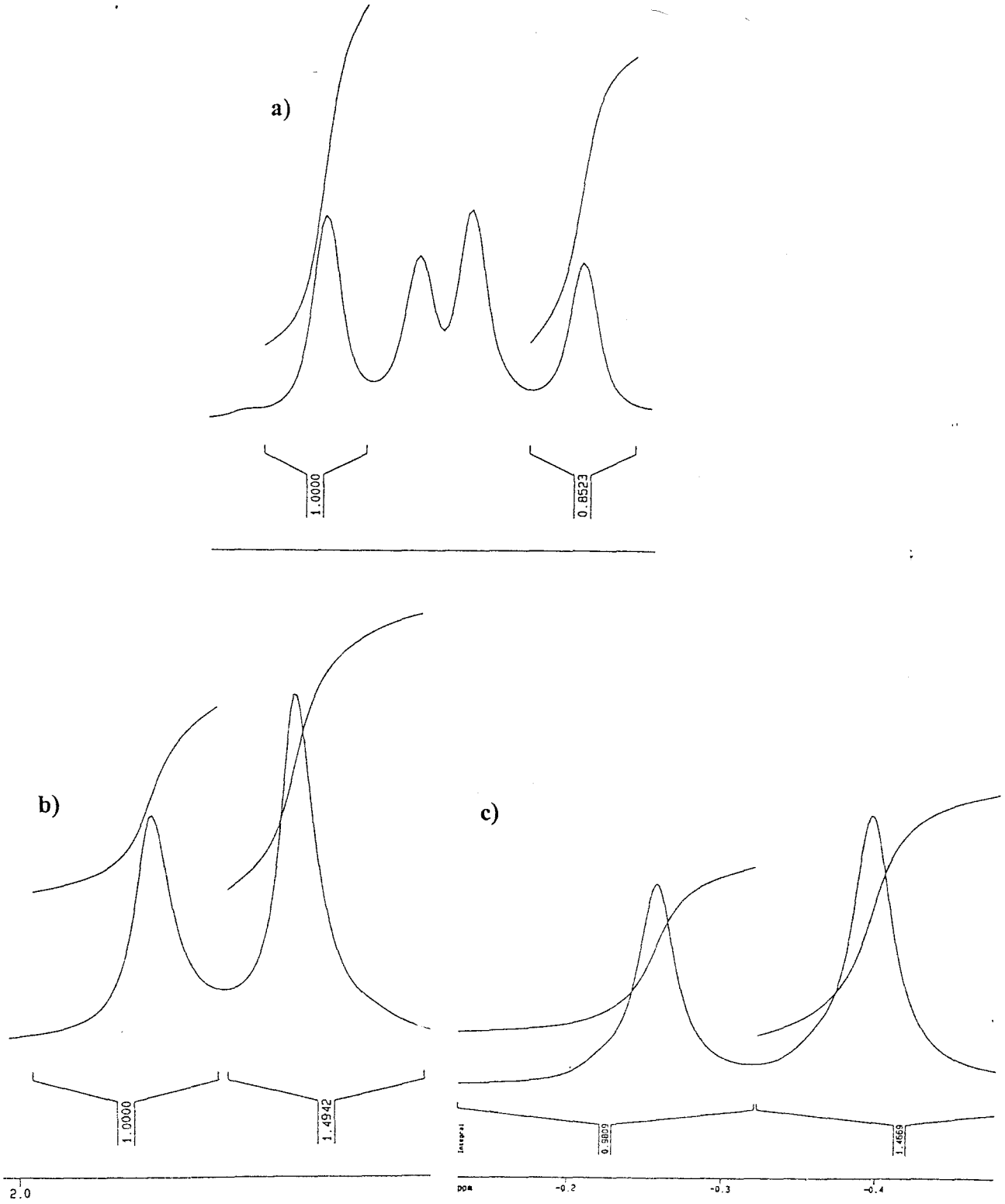


FIGURE 25.

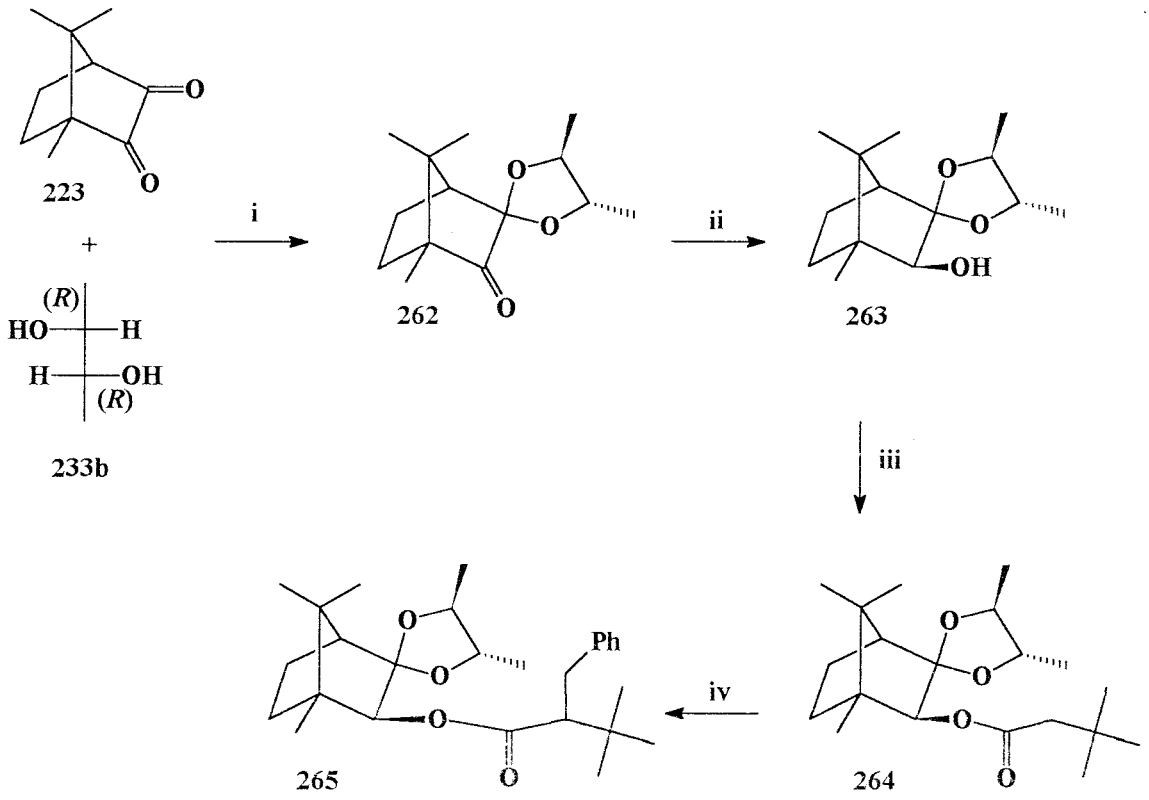
a) An integrated 400 MHz ^{1}H NMR spectrum of (**261**) in $CDCl_3$ showing the diastereomeric SiMe signals.

b) An integrated 400 MHz ^{1}H NMR spectrum of (**163**) in $CDCl_3$ showing the *t*-butyl peaks resolved using [Eu(hfc)$_3$].

c) An integrated 400 MHz ^{1}H NMR spectrum of (**163**) in $CDCl_3$ showing the *t*-butyl peaks resolved using [Pr(hfc)$_3$].

2.7 The Camphor-derived Chiral Auxiliary (263)

To complete our investigation of 2,3-butanediol-derived ketals as chiral auxiliaries, (*R*, *R*)-(-)-2,3-butanediol (**233b**) was reacted with camphorquinone (**223**) to yield the camphor derivative (**262**) (Scheme 40). Reduction using $LiAlH_4$ afforded the chiral auxiliary (**263**). The diol (**233b**) exhibits C_2 symmetry and only one isomeric product is possible. In order to compare the stereofacial selectivity provided by the isomeric chiral auxiliaries (**235a**) and (**263**), the ester derivative (**264**) was synthesised as a model substrate. Following the method used for the α-benzylation of the diastereomeric chiral ester (**239d**) (see Section 2.6.2, p. 101), the ester (**264**) was treated with LDA and benzyl bromide to yield the alkylated product (**265**) in 25% d.e. Further purification by preparative layer chromatography afforded a single diastereomer of (**265**).



SCHEME 40. Reagents: i) TsOH, reflux;
ii) $LiAlH_4$, Et_2O;
iii) BuLi, THF, 0 °C, then 3,3-dimethylbutanoyl chloride;
iv) LDA, THF, -78 °C, then $PhCH_2Br$.

The diastereomeric excess of 25% obtained using the ester (**264**) of the chiral auxiliary (**263**) is slightly lower than that obtained using the diastereomeric ester derivative (**239d**) of the chiral auxiliary (**235a**) (34% d.e.) (see Section 2.6.2, p. 101). The difference in stereoselectivity, in a single reaction, is not significant enough, however, to draw any conclusions as to which chiral auxiliary is the more effective.

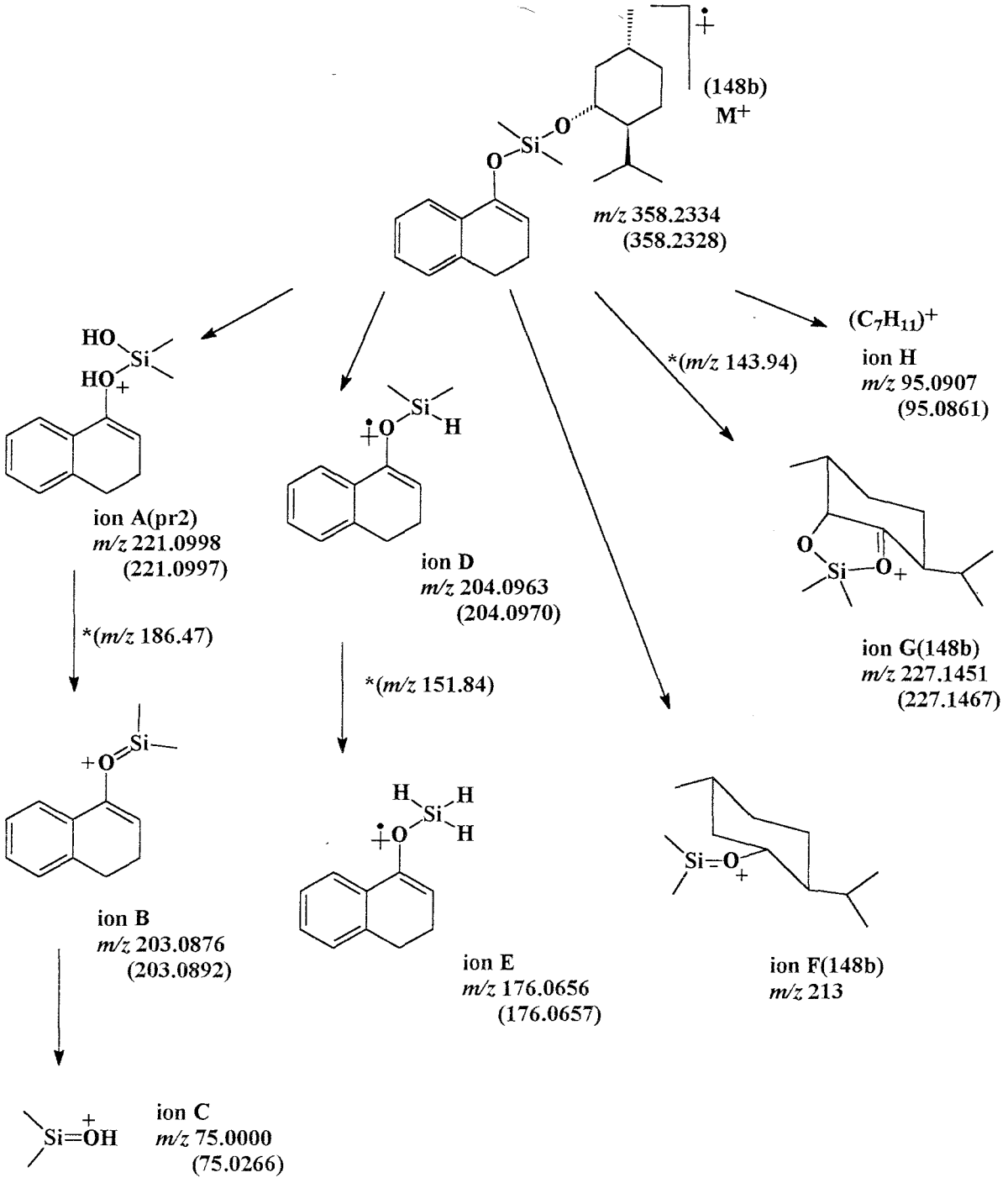
2.8 Mass Spectrometric Analysis of Chiral Silyl Enol Ethers

A previous investigation[249] had revealed some interesting fragmentation patterns in the electron impact (EI) mass spectra of the silyl enol ethers (**148a**) and (**148b**). Since the present investigation has been concerned with the synthesis and reactions of these and other silyl enol ethers, it was decided to undertake a detailed mass spectrometric study[181] of these systems using a combination of high-resolution, comparative low-resolution and metastable peak analysis. The EI mass spectra of compounds (**148a**) and (**148b**) are shown in Figure 26, high resolution data are summarised in Table 4 and the proposed major fragments are illustrated for the menthol-derived silyl enol ether (**148b**) in Scheme 41. The fragmentation patterns and, in many cases, the fragmentations themselves are common to the various silyl enol ethers examined. For the sake of clarity, the following discussion will focus largely on the fragmentation of the menthol-derived system (**148b**).

Of the eight ion types (**A** - **H**) illustrated for the menthol-derived silyl enol ether (**148b**) in Scheme 41, ions **F** and **G** are clearly menthol-specific; the remaining ions (**A** - **E**, **H**) are characteristic of the dimethylsilyloxy moiety present in both silyl enol ethers, (**148a**) and (**148b**).

TABLE 4. Data obtained from high resolution mass spectroscopy analysis of the fragments obtained from the silyl enol ethers (**148a**) and (**148b**).

Compound	ion Type	Mol. Formula	Mass Found	Mass Required
148a	M^+	$C_{22}H_{32}O_2Si$	356.2183	356.2172
	ion A	$C_{12}H_{17}O_2Si$	221.0988	221.0997
	ion B	$C_{12}H_{15}OSi$	203.0939	203.0892
	ion C	C_2H_7OSi	--	--
	ion D	$C_{12}H_{16}OSi$	204.0983	204.0970
	ion E	$C_{10}H_{12}OSi$	176.0657	176.0657
	ion F(148a)	$C_{12}H_{23}OSi$	--	--
	ion G(148a)	$C_{12}H_{21}O_2Si$	225.1281	225.1310
	ion H	C_7H_{11}	95.0872	95.0861
148b	M^+	$C_{22}H_{34}O_2Si$	358.2334	358.2328
	ion A	$C_{12}H_{17}O_2Si$	221.0988	221.0998
	ion B	$C_{12}H_{15}OSi$	203.0876	203.0892
	ion C	C_2H_7OSi	--	--
	ion D	$C_{12}H_{16}OSi$	204.0963	204.0970
	ion E	$C_{10}H_{12}OSi$	176.0656	176.0657
	ion F(148b)	$C_{12}H_{25}OSi$	--	--
	ion G(148b)	$C_{12}H_{23}O_2Si$	227.1451	227.1467
	ion H	C_7H_{11}	95.0907	95.0861



SCHEME 41. MS Fragmentation patterns for the menthol-derived silyl enol ether (148b) Accurate masses (*m/z*) are followed, in parentheses, by the calculated masses. An asterisk indicates a pathway supported by a metastable peak, which is given in parentheses.

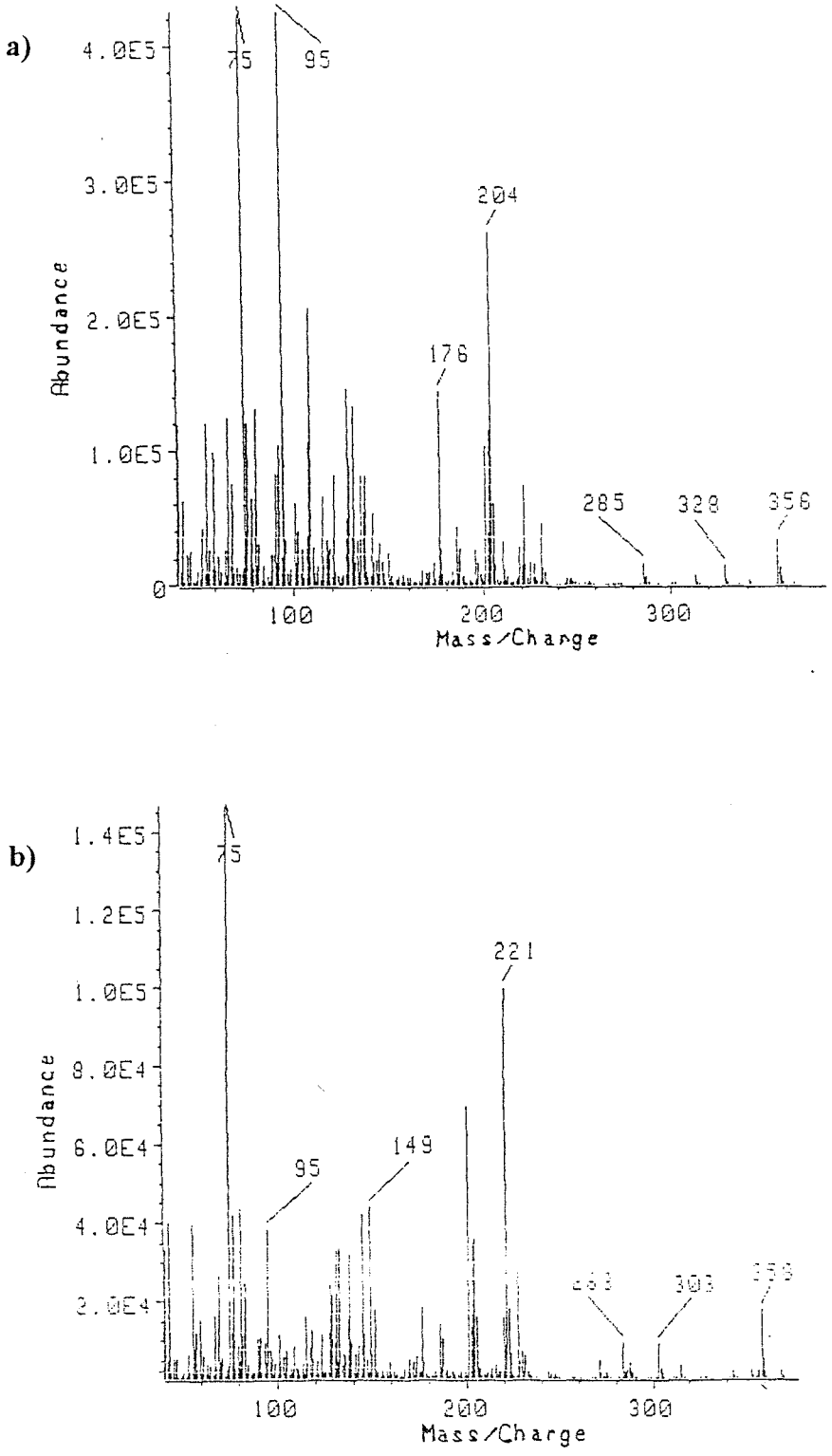
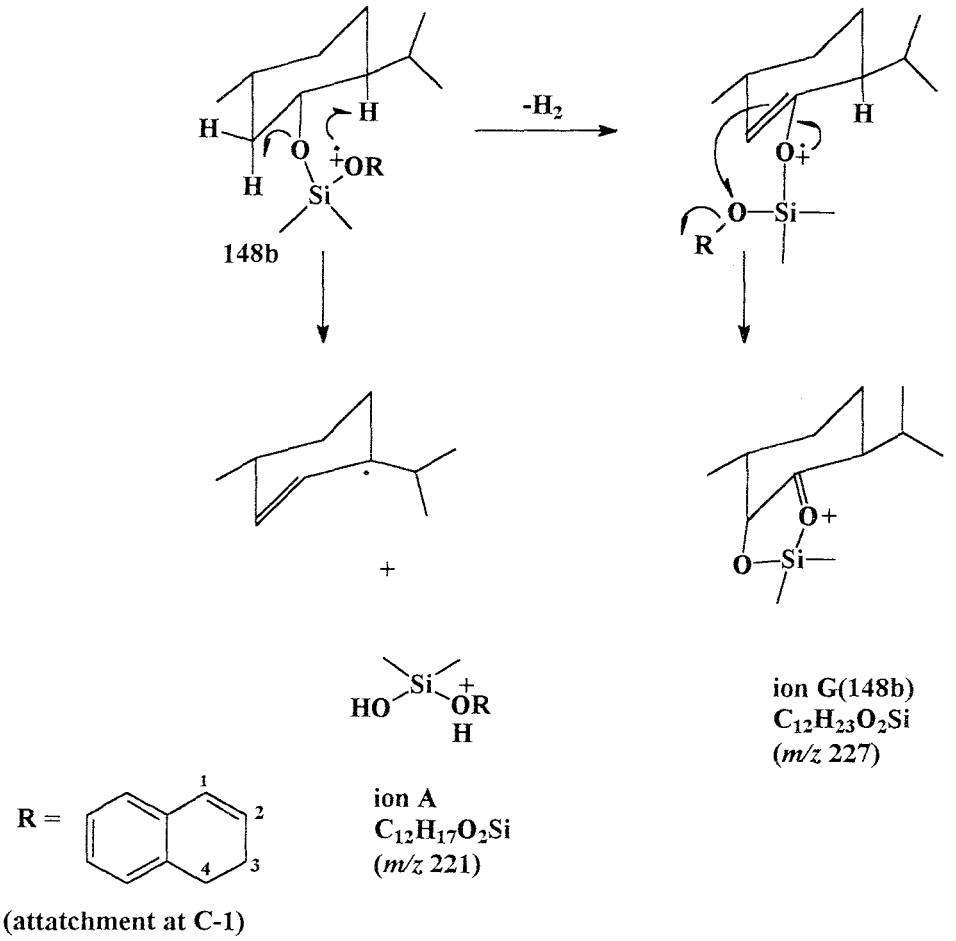


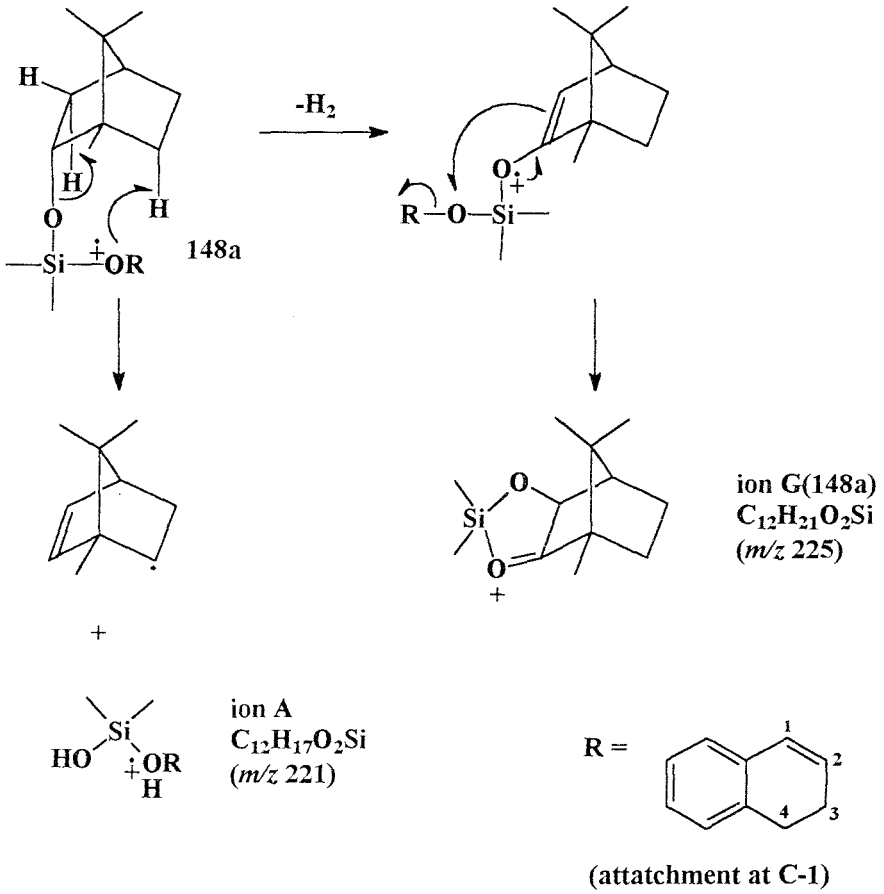
FIGURE 26. EI Mass spectra of: a) the borneol-derived silyl enol ether (148a); and b) the menthol-derived silyl enol ether (148b).

The formation of ion A(**148b**) is proposed to occur by the transfer of two hydrogen atoms and the loss of the menthyl group as a tertiary allylic radical as shown in Scheme 42. A metastable peak at *m/z* 143.94 supports the formation of ion G(**148b**) from the molecular ion, which requires the consecutive or concerted loss of H_2 from the molecular ion before cyclisation to form the siladioxolane, ion G(**148b**).



SCHEME 42. Proposed fragmentation pathways for the menthol-derived silyl enol ether (148b) showing the formation of ion A and ion G(148b).

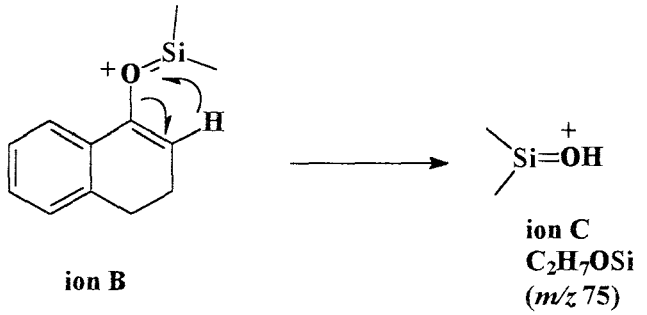
In the mass spectrum of the borneol-derived silyl enol ether (**148a**), the presence of ion A is supported by high resolution data and its formation, in this case, is attributed to concomitant transfer of the two *endo* hydrogens (from C-3 and C-6) and the loss of a secondary radical, as shown in Scheme 43. This radical could, of course, rearrange to a more stable species. The formation of ion G(**148a**) [corresponding to ion G(**148b**) in the mass spectrum of the menthol analogue (**148b**)] was confirmed by high resolution analysis.



SCHEME 43. The fragmentation pathways for the borneol-derived silyl enol ether (**148a**) showing the formation of ion A and ion G(**148a**).

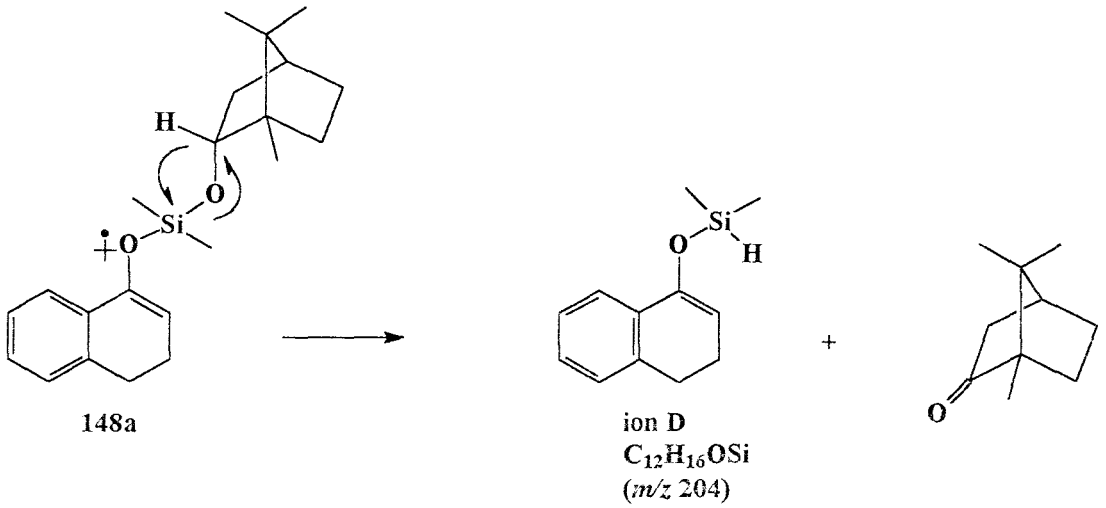
The dehydration of ion A (Scheme 41) would account for the formation of ion B [observed as a peak at *m/z* 203 in the mass spectra of both silyl enol ethers (**148a**) and (**148b**)] and is supported by a metastable peak in the case of the menthol-derived silyl enol ether (**148b**). Further fragmentation of ion B is proposed to afford ion C (Scheme 44), parallelling a fragmentation

pattern previously reported for trimethylsilyl enol ethers.[183] The peak at *m/z* 75 (corresponding to ion C) is very intense in the mass spectra of both silyl enol ethers and is, in fact, the base peak in the case of the menthol-derived silyl enol ether (**148b**).



SCHEME 44. The proposed fragmentation pattern for the formation of ion C from ion B.

The formation of ion D (Scheme 41) is proposed to occur *via* hydrogen transfer and homolysis of the Si-O bond of the molecular ion in a fragmentation supported, in the case of the borneol-derived silyl enol ether (**148a**), by a metastable peak at *m/z* 116.90 (Scheme 45). The fragmentation of ion D to form ion E is also supported by metastable peaks in the mass spectra of (**148a**) and (**148b**); such fragmentation, involving Si-C bond cleavage and hydrogen transfer, has also been observed in the mass spectra of the trimethylsilyl enol ethers studied by House *et al.*[183]



SCHEME 45. The proposed fragmentation pattern for the formation of ion D from silyl enol ether (**148a**).

Fission of the C-O(Si) bond *via* fragmentations corresponding to fission of the terpene C-O(Si) ($M^+ \rightarrow$ ION A $\rightarrow$ ION B) does not appear to be significant. Thus, the terpenoid equivalents to ion A were only detected as very weak peaks in the mass spectra of both (**148a**) and (**148b**) (0.7% and 2.6% respectively), while the ions of type F (the terpenoid equivalent to ion B) also appeared as weak peaks (2.5% and 1.1% respectively). Finally, ion H [$(C_7H_{11})^+$] appears to be responsible for major peaks in the spectra of both silyl enol ethers and is, in fact, the base peak in the EI mass spectrum of the menthol-derived silyl enol ether (**148b**). The $(C_7H_{11})^+$ fragment is commonly found in the mass spectra of terpenes,[250, 251] and its presence in the fragmentation of both silyl enol ethers was confirmed by high resolution data.

The relative abundance of the major fragments formed in the mass spectra of both silyl enol ethers (**148a**) and (**148b**) can be found in Table 5. The EI mass spectra of the chiral silyl enol ethers (**153**), (**156**), (**194**), (**259**) and (**260**) were also examined, and the corresponding data are included in Table 5. Inspection of this data reveals that, with few exceptions, the same fragments or fragment types occur in the mass spectra of the systems examined.

In the mass spectra of the pinene-derived silyl enol ethers (**153**) and (**156**), the fragment equivalent to ion F and ion G (Scheme 41) would not be formed due to the lack of an oxygen atom on the chiral auxiliary. The mass spectra of the silyl enol ether (**195**) derived from the chiral auxiliary (**183**) could not be obtained. However, the mass spectrum of the silyl enol ether of the same chiral auxiliary (**194**) did not contain the fragment equivalent to ion H (Scheme 41). Interestingly, fragments equivalent to ion F and ion G (Scheme 41) were detected in the mass spectrum of (**194**), even though there is no H atom at C-1 or C-3 adjacent to the oxygen atom of the chiral auxiliary; presumably, the formation of these ions involves elimination of the adjacent 5'-H_{endo} and 6'-H_{endo} atoms on the chiral auxiliary. Finally, all fragments, except the fragment equivalent to ion G were detected in the mass spectra of silyl enol ether derivatives (**259**) and (**260**) of the chiral auxiliary (**235a**). They were, however, low intensity peaks, indicative of the inherent instability of these silyl enol ethers which, while stored, showed rapid decomposition.

TABLE 5. Selected peaks (*m/z*; followed, in parenthesis, by % relative abundance) from EI mass spectra of chiral silyl enol ethers classified according to ion types A-H.

	ION Types								
Compd.	**M^+**	**ion A**	**ion B**	**ion C**	**ion D**	**ion E**	**ion F**	**ion G**	**ion H**
148a	356 (8.0)	221 (17.3)	203 (26.9)	75 (99.5)	204 (61.5)	176 (33.8)	211 (2.5)	225 (3.8)	95 (100)
148b	358 (10.7)	221 (46.8)	203 (17.0)	75 (100)	204 (19.5)	176 (10.9)	213 (1.1)	227 (20.5)	95 (16.4)
153	340 (14.7)	221 (0.4)	203 (76.3)	75 (100)	204 (25.9)	176 (36.1)	--	--	--
156	294 (1.9)	175 (0.5)	157 (12.3)	75 (100)	158 (2.7)	130 (0.3)	--	--	--
194	458 (13.9)	221 (100)	203 (43.2)	75 (63.4)	204 (44.6)	176 (16.8)	313 (13.5)	327 (10.7)	--
259	442 (1.1)	221 (9.6)	203 (7.3)	75 (97.8)	204 (1.7)	176 (0.6)	297 (5.8)	---	95 (17.5)
260	430 (0.07)	175 (0.9)	157 (1.7)	75 (1.0)	158 (0.3)	130 (1.8)	297 (0.08)	---	95 (7.0)

2.9 Conclusion

In the course of this research, attention has been focused on the development and use of camphor- and pinane-derived chiral auxiliaries in asymmetric synthesis. Various blocking groups have been attached to the camphor system in attempts to improve the stereofacial selectivity offered by the chiral moiety; these include an α-methoxybenzyl group, a xylyl group and ketal groups derived from *meso*-2,3-butanediol and (*R*,*R*)-(-)-2,3-butanediol.

The 3,3-(2,3-butanedioxy)camphor ketals were obtained by regioselective mono-ketalisation of camphorquinone. While (*R*,*R*)-(-)-2,3-butanediol exhibits C_2-symmetry and affords a single 3,3-ketal derivative, ketalisation with the *meso*-diol generates a pseudo-asymmetric centre at C-3 of the camphor skeleton and an 80:20 mixture of diastereomeric 3,3-ketals was obtained. Reduction of this mixture using $LiAlH_4$ afforded an essentially pure 2-*exo*-hydroxy 3,3-ketal, permitting the configuration at the pseudo-asymmetric centre (C-3) to be investigated using NMR techniques; final confirmation was obtained by X-ray crystallographic analysis of the 2,4-dinitrobenzoic ester, which unexpectedly indicated co-crystallisation of a minor contaminant, *viz.*, the 2-*endo*-analogue.

Series of carboxylic esters of various chiral auxiliaries were synthesised and alkylation of the lithium enolates with benzyl bromide has been used to evaluate their asymmetric induction potential. The corresponding α-benzylated products were obtained in 9-60% d.e. and high resolution NMR and computer modelling techniques have been used to examine the diastereofacial preferences. Configurational bias was confirmed by polarimetric analysis of known, chiral carboxylic acids, obtained by hydrolysis of selected benzylated products. Interestingly, alkylation reactions carried out using the chiral auxiliaries with the xylyl and ketal blocking groups attached to the camphor skeleton gave products with opposite stereochemistry - an observation attributed to the orientation of the enolate moiety in the presence or absence of chelation.

Asymmetric Baylis-Hillman reactions between a series of aldehydes and acrylic esters of camphor derivatives containing a ketal blocking group, proceeded in yields of 41-86% and exhibited diastereoselectivities of 0-34% d.e., with reaction times ranging from 1 week to 4 months.

In a continuation of earlier work,[32, 33] attention has also been given to asymmetric reactions of silyl enol ethers. Silyl enol ether derivatives of pinane and the camphor-derived chiral auxiliaries containing the xylyl and ketal blocking groups were successfully prepared, but a maximum of 20% d.e. was obtained in the three reactions examined, *viz.*, MCPBA oxidation, alkylation and the Mukaiyama reaction. Silyl enol ethers, however, show interesting fragmentation patterns in their electron impact mass spectra and these were investigated,[181] using a combination of high resolution MS, comparative low resolution MS and metastable peak analysis.

Attempts to bring the prochiral centre closer to the chiral auxiliary and thus, improve the stereofacial selectivity of these asymmetric reactions, were unsuccessful. However, during these attempts, a β-pinene- and a camphene-derivative of the chiral auxiliary containing the xylyl blocking group were isolated and fully characterised using NMR techniques. Their formation is proposed to occur *via* a carbocation intermediate at C-2 of the camphor skeleton.

Diastereoselectivities observed in various reactions of the wide range of chiral substrates investigated, have ranged from disappointing to moderate and it is apparent that many challenges remain. Future research is expected to address the following issues.

1) The role of coordinating solvents and chelating cations in increasing transition state rigidity and diastereofacial selectivity.
2) An investigation of the configurational and conformational preferences of the enolate intermediates using, for example, low temperature NMR techniques.
3) The development of efficient chiral auxiliaries for controlling stereoselectivity in reactions of silyl enol ethers.

EXPERIMENTAL

3.1 General

Melting points were measured on a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded on a Perkin Elmer 180 spectrometer, as thin films or KBr disks. Although some ^{1}H NMR spectra were run on a Perkin-Elmer R12 A instrument, ^{1}H NMR and ^{13}C NMR spectra were typically obtained in $CDCl_3$ on a Bruker AMX400 spectrometer, and were referenced using the solvent signals (7.25 ppm for ^{1}H spectra and 77.0 ppm for the central line of the $CDCl_3$ triplet for ^{13}C spectra); coupling constants (*J*) are given in Hz. Low resolution mass spectra were recorded on a Hewlett Packard 5988A mass spectrometer, while high resolution mass spectra were obtained on a double-focusing Kratos MS 80RF mass spectrometer (Cape Technikon Mass Spectrometry Unit). Optical rotations were measured on a Perkin Elmer 141 polarimeter using a 1dm cell, and concentrations are given in g/100 ml. The optical rotations measured should be used more as an indicator of positive or negative rotation rather than as absolute rotations as the polarimeter was found not to be accurate, especially on dilute solutions.

The atom numbering used in quoting the NMR data follows the systematic nomenclature. Chiral auxiliaries and other optically pure compounds were ultimately derived from one of the following, commercially available, homochiral compounds (the common name of each compound is used throughout to facilitate quick recognition):

i) (1*R*)-(+)- camphor

ii) (1*S*)-(-)- borneol

iii) (1*R*, 2*S*, 5*R*)-(-)- menthol

iv) (1*S*)-(-)-α-pinene

v) (1*S*)-(-)-β-pinene

All aldehydes used in the Baylis-Hillman reactions were distilled prior to use. When reactions were carried out using air- or moisture-sensitive reagents, such as $LiAlH_4$, BuLi, chlorosilanes, NaH and $TiCl_4$, the glassware was flame dried prior to use. Anhydrous solvents were obtained as follows:

i) Benzene, Et_2O (diethyl ether) and THF (tetrahydrofuran) were dried by boiling under reflux over sodium wire, in the presence of benzophenone, distilled and collected over 4Å molecular sieves.

ii) Hexane was dried by boiling under reflux over sodium wire, distilled and collected over 4Å molecular sieves.

iii) Toluene and dichloromethane (CH_2Cl_2) were boiled under reflux over CaH_2, distilled and collected over 3Å molecular sieves.

iv) Dimethylformamide (DMF) and triethylamine (Et_3N) were boiled under reflux over 4Å molecular sieves, distilled and collected over 4Å molecular sieves.

v) Carbon tetrachloride (CCl_4) was boiled under reflux over $CaCl_2$ and distilled.

vi) Diisopropylamine was boiled under reflux over NaH, distilled and collected over 4Å molecular sieves.

vii) Pinacolone and α-tetralone were stored over 4Å molecular sieves.

viii) N,N,N',N'-Tetramethylethylenediamine (TMEDA) and dimethylsulfoxide (DMSO) were boiled under reflux over CaH_2, distilled and collected over 4Å molecular sieves.

NaH was washed free of oil, prior to use, by stirring in dry solvent (that used in the subsequent reaction). After allowing the NaH to settle, the solvent was decanted; this process was repeated 3 times. Lithium tri-*sec*-butylborohydride (L-selectride) was supplied as a 1.0 **M** solution in THF by Aldrich. $TiCl_4$ was used, either freshly distilled from CaH_2, or as the 1.0 **M** solution in CH_2Cl_2 supplied by Aldrich.

Flash chromatography[252] was achieved using Merck silica gel 60 [particle size 0.046-0.063 mm (230 - 400 mesh)]. Preparative layer chromatography (PLC) was performed on Merck silica gel PF_{254} plates and thin layer chromatography on Merck silica gel 60 F_{254} pre-coated plates. TLC plates were analysed by inspection under UV light or using iodine vapour.

Computer modelling was conducted using the "HYPERCHEM" molecular modelling software package supplied by Autodesk Inc..

3.2 Synthetic Procedures

3.2.1 Borneol- and menthol-derived silyl enol ethers

Preparation of *(2*-endo-*bornyloxy)chlorodimethylsilane* (145a)[177]

(-)-Borneol (6.65 g, 43.1 mmol) in dry Et_2O (20 ml) was added dropwise to a solution of Me_2SiCl_2 (5.59 g, 43.4 mmol) and Et_3N (8.9 ml, 64 mmol) in dry Et_2O (100 ml) under dry nitrogen. The slurry resulting from the exothermic reaction was stirred overnight and then filtered under nitrogen. The solvent was removed by distillation and vacuum distillation yielded, as an oil, (2-*endo*-bornyloxy)chlorodimethylsilane (**145a**) (2.88 g, 27%), b.p.118 °C/7 mmHg (lit.,[249] 63 °C/0.7 mmHg); δ_H(60 MHz; $CDCl_3$) 0.48 (6H, s, SiMe), 0.84 and 0.89 (9H, 2xs, 8-, 9- and 10-Me), 1.08-2.57 (7H, complex of multiplets, 3-, 5- and 6-CH_2 and 4-H) and 4.20 (1H, br d, 2-H).

Preparation of *chloro(1*-endo-*menthyloxy)dimethylsilane* (145b)

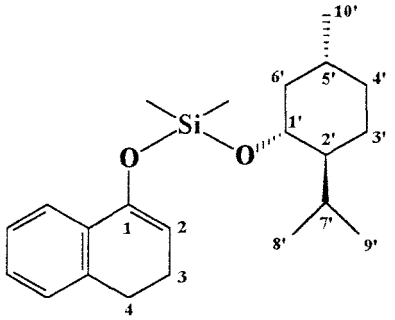
(-)-Menthol (9.37 g, 60.0 mmol) in dry Et_2O (20 ml), and Et_3N (9.0 ml, 65 mmol) and Me_2SiCl_2 (8.00 g, 61.9 mmol) in dry Et_2O (75 ml) were reacted as described for the synthesis of (2-*endo*-bornyloxy)chlorodimethylsilane (**145a**). Work-up and vacuum distillation yielded, as an oil, chloro(1-*endo*-menthyloxy)dimethylsilane (**145b**) (4.0 g, 27%), b.p. 130 °C/5 mmHg (lit.,[253] 95.5-96.0 °C/4 mmHg); δ_H(60 MHz; $CDCl_3$) 0.45 (6H, s, SiMe), 0.61-1.05 (9H, complex of multiplets, 8-, 9- and 10-Me), 1.05-2.40 (9H, complex of multiplets, 3-, 4- and 6-CH_2 and 2-, 5- and 8-H) and 3.18 (1H, br m, 3-H).

Preparation of *1-[(2*-endo-*bornyloxy)dimethylsilyloxy]-3,4-dihydronaphthalene* (148a)[177]

A stirred solution of diisopropylamine (1.12 g, 11.1 mmol) in dry Et_2O (40 ml) under nitrogen was cooled to -78 °C and BuLi (15% in hexane; 7.9 ml, 11 mmol) was then added dropwise. After 1h, α-tetralone (1.47 g, 10.1 mmol) in dry Et_2O (10 ml) was added, and a further hour later, (2-*endo*-bornyloxy)chlorodimethylsilane (**145a**) (2.9 g, 8.1 mmol) in dry Et_20 (15 ml). The resulting mixture was allowed to warm to r.t. overnight, then quenched with satd. aq. $NaHCO_3$ (100 ml) and extracted with Et_2O (2x100 ml). The organic fraction was dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. Flash chromatography [elution with hexane-EtOAc (49:1)] yielded, as

an oil, 1-[(2-*endo*-bornyloxy)dimethylsilyloxy]-3,4-dihydronaphthalene (**148a**)[249] (3.44 g, 84%) (Found: $\mathbf{M}^+$ 356.2183. Calc. for $C_{22}H_{32}O_2Si$: *M*, 356.2171); δ_H(400 MHz; $CDCl_3$) 0.24 (6H, s, SiMe), 0.80 (3H, s, 10'-Me), 0.83 (3H, s, 9'-Me), 0.86 (3H, s, 8'-Me), 1.03 (1H, dd, 3'-H_{endo}), 1.11-1.29 (2H, complex of multiplets, 5'-H_{endo} and 6'-H_{exo}), 1.59 (1H, m, 4'-H), 1.63-1.75 (1H, m, 5'-H_{exo}), 2.00-2.21 (2H, complex of multiplets, 3'-H_{exo} and 6'-H_{endo}), 2.33 (2H, dt, $J_{2,3}$ 4.6 and $J_{3,4}$ 8.0, 3-CH_2), 2.77 (2H, t, $J_{3,4}$ 8.0, 4-CH_2), 4.14 (1H, m, 2'-H), 5.32 (1H, t, $J_{2,3}$ 4.6, 2-H), 7.05-7.23 (3H, complex of multiplets, Ar-H) and 7.42-7.48 (1H, m, Ar-H); δ_C(100 MHz; $CDCl_3$) -2.3 and -2.0 (SiMe), 13.5 (C-10'), 18.8 (C-8'), 20.2 (C-9'), 22.2 (C-3), 26.2 (C-6'), 28.1 (C-4), 28.3 (C-5'), 39.1 (C-3'), 45.2 (C-4'), 47.3 (C-7'), 49.7 (C-1'), 77.7 (C-2'), 105.5 (C-2), 121.8, 126.1, 126.9, 127.2, 133.4 and 137.0 (Ar-C) and 147. 5 (C-1); *m/z* 356 ($\mathbf{M}^+$, 8.0%), 75 (99.5), 176 (33.8), 203 (26.9), 204 (61.5), 211(2.5), 221 (17.3), 225 (3.8) and 95 (100).

Preparation of *1-[(1-*endo*-menthyloxy)dimethylsilyloxy]-3,4-dihydronaphthalene* (148b)



α-Tetralone (1.60 g, 11.0 mmol) in dry Et_2O (10 ml) was treated with LDA [generated from diisopropylamine (1.14 g, 11.2 mmol) in dry Et_2O (10 ml) and butyllithium (15% in hexane; 7.9 ml, 11 mmol)] and chloro(1-*endo*-menthyloxy)dimethylsilane (**145b**) (3.02 g, 12.1 mmol) in dry Et_2O (15 ml) as described for the synthesis of 1-[(2-*endo*-bornyloxy)dimethylsilyloxy]-3,4-dihydronaphthalene (**148a**). Work-up and flash chromatography [elution with hexane-EtOAc (49:1)] yielded, as an oil, 1-[(1-*endo*-menthyloxy)dimethylsilyloxy]-3,4-dihydronaphthalene (**148b**) (2.47 g, 63%), b.p. 120 °C/0.2 mmHg (lit.,[249] 132-138 °C/0.04 mmHg) (Found: $\mathbf{M}^+$ 358.2334. Calc. for $C_{22}H_{34}O_2Si$: *M*, 358.2328); δ_H(400 MHz; $CDCl_3$) 0.25 and 0.27 (6H, 2xs, SiMe), 0.74 (3H, d, *J* 6.9, 9'-Me), 0.82 (1H, m, 4'-H_{ax}), 0.86 (3H, d, *J* 7.1, 10'-Me), 0.90 (3H, d, *J* 6.5, 8'-Me), 0.95 (1H, m, 3'-H_{ax}), 1.07 (1H, m, 6'-H_{ax}), 1.20 (1H, m, 2'-H), 1.29-1.43 (1H, m, 5'-H), 1.55-1.67 (2H, complex of multiplets, 3'-H_{eq} and 4'-H_{eq}), 2.01 (1H, m, 6'-H_{eq}), 2.20 (1H, m, 7'-H), 2.32 (2H, dt, $J_{2,3}$ 4.7 and $J_{3,4}$ 8.2, 3-CH_2), 2.77 (2H, t, $J_{3,4}$ 8.2, 4-CH_2), 3.64 (1H, m, 1'-H), 5.30 (1H, t, $J_{2,3}$ 4.7, 2-H), 7.07-7.34 (3H, complex of multiplets, Ar-H) and 7.45 (1H, m, Ar-

H); δ_C(100 MHz; $CDCl_3$) -1.9 and -1.6 (SiMe), 15.9 (C-9'), 21.2 (C-8'), 22.2 (C-10'), 23.9 and 23.0 (C-3 and C-3'), 25.4 (C-7'), 28.1 (C-4), 31.7 (C-5'), 34.5 (C-4'), 45.2 (C-6'), 49.9 (C-2'), 73.1 (C-1'), 105.6 (C-2), 121.8, 126.1, 126.9, 127.2, 133.4 and 137.0 (Ar-C) and 147.5 (C-1); *m/z* 358 (M^+, 10.7%), 95 (16.4), 176 (10.9), 203 (17.0), 204 (19.5), 213 (1.1), 221 (46.8), 227 (20.5) and 75 (100).

Preparation of *1-(trimethylsilyloxy)-3,4-dihydronaphthalene* (148c)

α-Tetralone (4.33 g, 29.6 mmol) in dry Et_2O (10 ml) was treated with LDA [generated from diisopropylamine (3.25 g, 32.1 mmol) in dry Et_2O (35 ml) and butyllithium (15% in hexane; 20.0 ml, 32.5 mmol)] and chlorotrimethylsilane (3.37 g, 31.0 mmol) as described for the synthesis of 1-[(2-*endo*-bornyloxy)dimethylsilyloxy]-3,4-dihydronaphthalene (**148a**). Work-up and flash chromatography [elution with hexane-EtOAc (49:1)] yielded, as an oil, 1-(trimethylsilyloxy)-3,4-dihydronaphthalene (**148c**)[185] (5.11 g, 79%), δ_H(60 MHz; $CDCl_3$) 0.17 (9H, s, SiMe), 1.90-2.88 (4H, complex of multiplets, 3- and 4-CH_2), 5.05 (1H, t, 2-H) and 6.85-7.44 (4H, complex of multiplets, Ar-H).

Cyclopropanation of silyl enol ethers (148a), (148b) and (148c)

Part A. Preparation of the Zn-Ag couple[254]

Silver acetate (25 mg, 0.10 mmol) was added to boiling acetic acid (25 ml) in a 100 ml round-bottomed flask fitted with a reflux condenser. Zinc powder (4.9 g, 75 mmol) was added and after *ca.* 30s, the acetic acid decanted and the resultant Zn-Ag couple washed with Et_2O (4x25 ml).

Part B. Cyclopropanation of silyl enol ethers[255]

The Zn-Ag couple (2 mol eq.) was placed in the reaction vessel, and then the apparatus was flame-dried under nitrogen. A solution of CH_2I_2 (1 mol eq.) in dry Et_2O (0.5 mol.dm^{-3}) was added to the cooled reaction vessel (the mixture warmed to reflux without external heating), followed by the silyl enol ether (1 mol eq.) in dry Et_2O (0.25 mol.dm^{-3}). After boiling under reflux until the silyl enol ether was consumed (confirmed by thin layer chromatography), the reaction mixture was cooled to 0 °C and the reaction quenched with an Et_2O-pyridine (1:1) solution. The resulting mixture was filtered, the Et_2O removed from the filtrate *in vacuo* and the residue dispersed in pentane and refiltered. The filtrate was dried (anhydr. $MgSO_4$), concentrated *in vacuo* and the residue purified by either flash chromatography or preparative layer chromatography (PLC). All

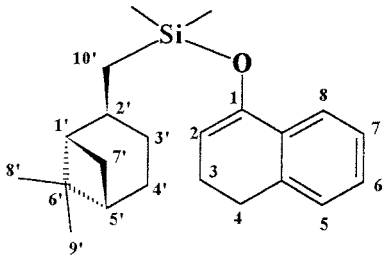
three silyl enol ethers gave complex mixtures which resisted separation, even when $AgNO_3$-impregnated PLC plates where used.

3.2.2 Pinane as a chiral auxiliary

Preparation of *chlorodimethyl(10-pinanyl)silane* (152)[193]

A mixture of (-)-β-pinene (10.2 g, 75.0 mmol), $ClMe_2SiH$ (14.7 g, 135 mmol) and $H_2PtCl_6.xH_2O$ (0.2 g) was boiled under reflux for 6 h and then stirred at r.t. overnight. The excess $ClMe_2SiH$ was removed by distillation and the residue was distilled *in vacuo* to yield chlorodimethyl(10-pinanyl)silane (**152**) (8.4 g, 48%), b.p. 66 °C/0.1 mmHg (lit.,[256] 93-4 °C/2 mmHg); δ_H(60 MHz; $CDCl_3$) 0.50 (6H, s, SiMe), 0.93 and 1.28 (6H, 2xs, 8- and 9-Me) and 0.97-2.20 (11H, complex of multiplets, 3-, 4-, 7- and 10-CH_2 and 1-, 2- and 5-H).

Preparation of *1-[dimethyl(10-pinanyl)silyloxy]-3,4-dihydronaphthalene* (153)



α-Tetralone (2.92 g, 20.0 mmol) was treated with LDA [generated from diisopropylamine (2.16 g, 21.3 mmol) and butyllithium (15% solution in hexane; 13.3 ml, 21.7 mmol)] and chlorodimethyl(10-pinanyl)silane (**152**) (4.70 g, 20.4 mmol) in dry Et_2O (50 ml) as described for the synthesis of 1-[(2-*endo*-bornyloxy)dimethylsilyloxy]-3,4-dihydronaphthalene (**148a**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded, as an oil, *1-[dimethyl(10-pinanyl)silyloxy]-3,4-dihydronaphthalene* (**153**) (5.3 g, 77%) (Found: M^+ 340.2202. $C_{22}H_{32}OSi$ requires *M*, 340.2222); $[\alpha]_D^{21}$ -4.3 (*c* 1.6 in $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1590 (C=C) and 1250 (SiMe); δ_H(400 MHz; $CDCl_3$) 0.26 (6H, s, SiMe), 0.83 and 1.18 (6H, 2xs, 8'- and 9'-Me), 0.77-0.88 (2H, m, 10'-CH_2), 1.25-1.38 (1H, m, 3'-CH_2), 1.40 (1H, d, *J* 9.9, 7'-CH_2), 1.67-1.83 (4H, complex of multiplets, 3'- and 4'-CH_2 and 1'-H), 1.86 (1H, m, 5'-H), 2.04 (1H, m, 7'-CH_2), 2.26 (1H, m, 2'-H), 2.34 (2H, m, 3-CH_2), 2.78 (2H, t, *J* 7.9, 4-CH_2), 5.18 (1H, t, *J* 4.6, 2-H), 7.09-7.24 (3H, complex of multiplets, Ar-H) and 7.43-7.46 (1H, m, Ar-H); δ_C(100 MHz;

$CDCl_3$) -0.4 and 0.0 (SiMe), 20.0 and 26.9 (C-8' and C-9'), 22.2 (C-3), 23.0 (C-7'), 24.8 (C-10'), 24.9 (C-4'), 25.5 (C-3'), 28.2 (C-4), 30.5 (C-2'), 39.5 (C-6'), 40.7 (C-5'), 49.0 (C-1'), 105.0 (C-2), 121.9, 126.1, 126.9, 127.2, 133.6 and 137.0 (Ar-C) and 148.2 (C-1); *m/z* 340 (**M**$^+$, 14.7%), 176 (36.1), 203 (76.3), 204 (25.9), 221 (0.4) and 75 (100).

Preparation of *3,3-dimethyl-2-[dimethyl(10-pinanyl)silyloxy]-1-butene* (156)

Pinacolone (2.17 g, 21.8 mmol) was treated with LDA [generated from diisopropylamine (2.16 g, 21.3 mmol) and butyllithium (15% solution in hexane; 13.3 ml, 21.7 mmol)] and chlorodimethyl(10-pinanyl)silane (**152**) (4.70 g, 20.4 mmol) in dry Et_2O (50 ml) as described for the synthesis of 1-[(2-*endo*-bornyloxy)dimethylsilyloxy)-3,4-dihydronaphthalene (**148a**). Work-up and filtration of the residue through a silica plug [elution with hexane-EtOAc (49:1)] yielded, as an oil, *3,3-dimethyl-2-[dimethyl(10-pinanyl)silyloxy]-1-butene* (**156**) (6.02 g, 100%) (Found: **M**$^+$ 294.2387. $C_{18}H_{34}OSi$ requires *M*, 294.2380); $[\alpha]_D^{21}$ -4.2 (*c* 2.1 in $CHCl_3$); ν_{max}(liquid film)/cm^{-1} 1630 (C=C) and 1255 (SiMe); δ_H(400 MHz; $CDCl_3$) 0.19 (6H, s, SiMe), 0.70 (2H, m, 10'-CH_2), 0.83 and 1.18 (6H, 2xs, 8'- and 9'-Me), 1.05 [9H, s, $C(CH_3)_3$], 1.23-1.34 (1H, m, 3'-CH_2), 1.38 (1H, d, *J* 9.9, 7'-CH_2), 1.65-1.79 (4H, complex of multiplets, 3'- and 4'-CH_2 and 1'-H), 1.84 (1H, m, 5'-H), 2.03 (1H, m, 7'-CH_2), 2.21 (1H, m, 2'-H) and 3.97 (2H, 2xd, *J* 1.2, 1-CH_2); δ_C(100 MHz; $CDCl_3$) -0.5 and -0.3 (SiMe), 20.3 and 26.9 (C-8' and C-9'), 23.0 (C-7'), 24.8 (C-10'), 25.1 (C-4'), 25.5. (C-3'), 28.2 [$C(CH_3)_3$], 30.4 (C-2'), 36.5 (C-3), 39.5 (C-6'), 40.7 (C-5'), 49.0 (C-1'), 85.3 (C-1) and 167.2 (C-2); *m/z* 294 (**M**$^+$, 1.9%), 130 (0.3), 157 (12.3), 158 (2.7), 175 (0.5) and 75 (100).

Preparation of *2-[dimethyl(10-pinanyl)silyloxy]-1,2,3,4-tetrahydro-1-naphthalone* (159)[195]

1-[Dimethyl(10-pinanyl)silyloxy]-3,4-dihydronaphthalene (**153**) (1.0 g, 3.0 mmol) was added to a cooled mixture of $NaHCO_3$ (0.70 g, 8.7 mmol) and MCPBA (55%; 1.1 g, 3.7 mmol) in CH_2Cl_2 (50 ml) and the reaction mixture stirred at 0 °C for 2 h. The mixture was allowed to warm to r.t. and then quenched with 5% aq. Na_2CO_3 (50 ml). The resulting mixture was extracted with Et_2O (3x50 ml) and the combined organic extracts were dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded, as an oil, a diastereomeric mixture of *2-[dimethyl(10-pinanyl)silyloxy]-1,2,3,4-tetrahydro-1-naphthalone* (**159**) (0.75 g, 70%) (0% d.e.; as determined by ^{1}H NMR spectroscopy) (Found: **M**$^+$ 356.2148. $C_{22}H_{32}O_2Si$ requires *M*, 356.2171); ν_{max}(liquid film)/cm^{-1} 1705 (CO) and 1250 (SiMe);

δ_H(400 MHz; $CDCl_3$) 0.18/0.20† (6H, s, SiMe), 0.60-0.95 (2H, complex of multiplets, 10'-CH_2), 0.81 and 1.18/1.19 (6H, 2xs, 8'- and 9'-Me), 0.21-1.32 (1H, m, 3'-CH_2), 1.36/1.37 (1H, d, 7'-CH_2), 1.63-1.77 (4H, complex of multiplets, 3'- and 4'-CH_2 and 1'-H), 1.80-1.87 (1H, m, 5'-H), 1.94-2.03 (1H, m, 7'-CH_2), 2.12-2.31 (3H, complex of multiplets, 4-CH_2 and 2'-H), 2.98-3.13 (2H, m, 3-CH_2), 4.33-4.37 (1H, m, 2-H), 7.19-7.49 (3H, complex of multiplets, Ar-H) and 7.98-8.05 (1H, m, Ar-H); δ_C(100 MHz; $CDCl_3$) -0.6/-0.4 and -0.2/0.2 (SiMe), 20.0 and 26.9 (C-8' and C-9'), 23.0 (C-7'), 24.8 (C-10'), 25.05/25.13 (C-4'), 25.3/25.4 (C-3'), 27.7 (C-4), 30.45/30.51 (C-2'), 33.0 (C-3), 39.5 (C-6'), 40.7 (C-5'), 49.1 (C-1'), 74.7 (C-2'), 126.7, 127.7, 128.5, 131.9, 133.3 and 143.5 (Ar-C) and 197.2 (C-1); *m/z* 356 ($\mathbf{M}^+$, 0.4%) and 219 (100).

Preparation of *2-t-butyl-1,2,3,4-tetrahydro-1-naphthalone* (160)[32]

A stirred solution of 1-[dimethyl(10-pinanyl)silyloxy]-3,4-dihydronaphthalene (**153**) (0.51 g, 1.5 mmol) and *t*-BuCl (0.18 g, 2.0 mmol) in dry CH_2Cl_2 (5 ml) was cooled to -23 °C, and $TiCl_4$ (1.0 **M** in CH_2Cl_2; 1.5 ml, 1.5 mmol) was added. The mixture was stirred at -23 °C for 3 h and the reaction quenched with ice-cold H_2O (20 ml). The aqueous layer was extracted with CH_2Cl_2 (2x30 ml) and the combined organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue [elution with hexane-EtOAc (24:1)] yielded, as oils, two fractions.

Fraction 1.

2-*t*-Butyl-1,2,3,4-tetrahydro-1-naphthalone (**160**)[257] (0.22 g, 73%) (Found: $\mathbf{M}^+$ 202.1351. Calc. for $C_{14}H_{18}O$: *M*, 202.1358); ν_{max}(thin film)/cm^{-1} 1685 (CO); δ_H(400 MHz; $CDCl_3$) 1.00 [9H, s, $C(CH_3)_3$], 2.81 (1H, m, 2-H), 2.12-2.20 and 2.79-2.92 (4H, 2xm, 3- and 4-CH_2), 7.07 (1H, m, 5-H), 7.14 and 7.29 (2H, 2xm, 6- and 7-H) and 7.84 (1H, m, 8-H); δ_C(100 MHz; $CDCl_3$) 25.2 and 29.4 (C-3 and C-4), 28.2 [$C(CH_3)_3$], 33.0 [$C(CH_3)_3$], 56.6 (C-2), 126.3, 127.0, 128.2, 132.5, 134.5 and 143.3 (Ar-C) and 199.8 (C-1); *m/z* 202 ($\mathbf{M}^+$, 16.6%) and 91 (100).

†The two chemical shift values quoted in this format, here and below, refer to corresponding signals for the diastereomeric products, the combinations, in some cases, being necessarily tentative. Reference to single peaks in the ^{13}C NMR spectra indicate coincidence of two diastereomeric peaks.

The enantiomeric excess was determined by two methods:

i) Addition of $Eu(hfc)_3$ (28 mg) to the enantiomeric mixture of 2-*t*-butyl-1,2,3,4-tetrahydro-1-naphthalone (**160**) (12 mg) in $CHCl_3$ resulted in a downfield shift and resolution of the respective *t*-Bu signals in the ^1H NMR spectrum. Two enantiomeric signals, tentatively assigned to the 8-H nuclei, were also resolved. The enantiomeric excess was determined to be 2% by integration of both sets of signals.

ii) Addition of $Pr(hfc)_3$ (19 mg) to the enantiomeric mixture of 2-t-butyl-1,2,3,4-tetrahydro-1-naphthalone (**160**) (10 mg) in $CHCl_3$ resulted in an upfield shift and resolution of the respective *t*-Bu signals in the ^1H NMR spectrum. The enantiomeric excess was determined to be 4% by integration of the signals.

Fraction 2.

Bis[dimethyl(10-pinanyl)silyl]ether (**161**) (0.07 g, 11%), (Found: $\mathbf{M}^+$ 406.3076. Calc. for $C_{24}H_{46}OSi_2$: *M*, 406.3076); ν_{max}(thin film)/cm^{-1} 1250 (SiMe) and 1060 (SiO); δ_H(400 MHz; $CDCl_3$) 0.04 and 0.05 (12H, 2xs, SiMe), 0.52 (4H, m, 10-CH_2), 0.82 and 1.18 (12H, 2xs, 8- and 9-Me), 1.21-1.29 (2H, m, 3-CH_2), 1.35 (2H, m, 7-CH_2), 1.62-1.77 (8H, complex of multiplets, 3- and 4-CH_2 and 1-H), 1.83 (2H, m, 5-H), 2.00 (2H, m, 7-CH_2) and 2.13 (2H, m, 2-H); δ_C(100 MHz; $CDCl_3$) 1.5 and 1.7 (SiMe), 20.1 and 27.0 (C-8 and C-9), 23.0 (C-7), 24.8 (C-4), 25.5 (C-3), 26.6 (C-10), 30.6 (C-2), 39.5 (C-6), 40.7 (C-5) and 49.1 (C-1); *m/z* 406 ($\mathbf{M}^+$, 0.1%) and 131 (100).

Preparation of *1-hydroxy-4,4-dimethyl-1-phenyl-3-pentanone* (163)[32]

3,3-Dimethyl-2-[dimethyl(10-pinanyl)silyloxy]-1-butene (**156**) (0.51 g, 1.7 mmol) was added to a cooled solution (-78 °C) of benzaldehyde (0.17 g, 1.6 mmol) and $TiCl_4$ (0.19 ml, 1.7 mmol) in dry CH_2Cl_2 (15 ml). After the solution had been allowed to stir for 4.5 h at -78 °C, the reaction was quenched by the addition of satd. aq. $NaHCO_3$ (20 ml). The reaction mixture was extracted with EtOAc (2x30 ml), and the organic fractions were combined, dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue yielded, as an oil, an enantiomeric mixture of 1-hydroxy-4,4-dimethyl-1-phenyl-3-pentanone (**163**)[258] (6% e.e.) (0.26 g, 81%) (Found: $\mathbf{M}^+$ 206.1313. Calc. for $C_{13}H_{18}O_2$: *M*, 206.1307); ν_{max}(thin film)/cm^{-1} 3455 (OH) and 1700 (CO); δ_H(400 MHz; $CDCl_3$) 1.13 [(9H, s, $C(CH_3)_3$], 2.88 (2H, d, *J* 6.0, 2-CH_2), 3.53 (1H, d, *J* 2.9, OH), 5.12 (1H, m, 1-H) and 7.26-7.38 (5H, complex of multiplets, Ar-H); δ_C(100 MHz;

$CDCl_3$) 26.2 [$C(CH_3)_3$], 44.4 (C-4), 45.5 (C-2), 70.1 (C-1), 125.7, 127.6, 128.5 and 143.1 (Ar-C) and 216.8 (C-3); *m/z* 206 (M^+, 20.6%) and 107 (100).

The enantiomeric excess was determined by two methods:

i) Addition of Eu(hfc)$_3$ (25 mg) to the enantiomeric mixture of 1-hydroxy-4,4-dimethyl-1-phenyl-3-pentanone (**163**) (12 mg) in $CDCl_3$ resulted in a downfield shift and resolution of the respective *t*-Bu signals in the ^{1}H NMR spectrum. Two enantiomeric signals, tentatively assigned to the 1-H nuclei, were also resolved. The enantiomeric excess was determined to be 6% by integration of both sets of signals.

ii) From the optical rotation of the enantiomeric mixture of 1-hydroxy-4,4-dimethyl-1-phenyl-3-pentanone (**163**) $[\alpha]_D^{21} = -1.9$ (*c* 2.2 in $CHCl_3$) {[lit.,[259, 260] $[\alpha]_D^{25} = +45.9$ ($CHCl_3$), for 75% e.e. (*R*)}, the enantiomeric excess was determined to be 3%.

Attempted preparation of *diphenylbis(10-pinanyl)silane* (164)

β-(-)-Pinene (2 eq.; 7.39 g, 54.3 mmol) was reacted with Ph_2SiH_2 (10.0 ml, 54.3 mmol) and $H_2PtCl_6.xH_20$ (0.2 g) as described for the synthesis of chlorodimethyl(10-pinanyl)silane (**152**). Distillation of the reaction mixture *in vacuo* yielded a complex mixture of products.

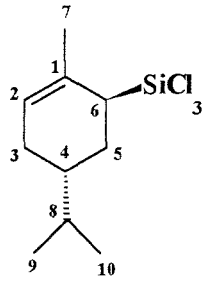
Attempted hydrosilation of α-(-)-pinene

Method 1.

α-(-)-Pinene (2.00 g, 14.7 mmol) was reacted with $ClMe_2SiH$ (2.9 ml, 27 mmol) and $H_2PtCl_6.xH_2O$ (0.4 g) as described for the synthesis of chlorodimethyl(10-pinanyl)silane (**152**). ^{1}H NMR Spectroscopy of the crude reaction mixture revealed the presence of the starting materials only. The same result was obtained when the reaction was carried out in sealed vials, which were heated in a water bath for 3 h.

Method 2.[203]

Preparation of *6-(trichlorosilyl)-1-menthene* (169)



A mixture of (-)-α-pinene (4.0 g, 2.9 mmol), Cl_3SiH (5.9 ml, 5.8 mmol) and benzoyl peroxide (0.70 g, 2.9 mmol) was boiled under reflux for 6 h in an atmosphere of dry nitrogen at a pressure of 785 mmHg. Distillation of the crude reaction mixture *in vacuo* yielded, as an oil, *6-(trichlorosilyl)-1-menthene* (**169**) (0.51 g, 66%), b.p.55 °C/0.02 mmHg (Found: $\mathbf{M}^+$ 270.0161. $C_{10}H_{17}SiCl_3$ requires *M*, 270.0165); δ_H(400 MHz; $CDCl_3$) 0.91 (6H, m, 9- and 10-Me), 1.38-1.59 (3H, complex of multiplets, 5-CH_2 and 4- and 8-H), 1.72-1.86 (1H, m, 3-CH_2), 1.83 (3H, s, 7-CH_3), 2.05-2.16 (1H, m, 3-CH_2), 2.27 (1H, m, 5-CH_2), 2.30-2.34 (1H, m, 6-H) and 5.57 (1H, m, 2-H); δ_C(100 MHz; $CDCl_3$) 19.5 and 19.6 (C-9 and C-10), 24.3 (C-7), 28.2 (C-5), 29.2 (C-3), 32.5 and 37.3 (C-4 and C-8), 39.5 (C-6), 125.1 (C-2) and 129.3 (C-1); *m/z* 272 ($\mathbf{M}^+$, 4.2%) and 81 (100).

3.2.3 The camphor-derived chiral auxiliary (172)

Preparation of *benzaldehyde dimethyl acetal* (174)[206]

A mixture of benzaldehyde (4.25 g, 40.1 mmol), trimethyl orthoformate (5.10 g, 48.1 mmol) and a catalytic quantity of NH_4NO_3 (0.43 g, 5.3 mmol) in MeOH (20 ml) was stirred at r.t. overnight. The reaction was then quenched with satd. aq. Na_2CO_3 (40 ml) and the resulting mixture extracted with Et_2O (3x20 ml). The combined organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo* to yield, as an oil, benzaldehyde dimethyl acetal (**174**) (5.51 g, 90%); δ_H(400 MHz; $CDCl_3$) 3.32 (6H, s, OMe), 5.38 (1H, s, PhC*H*) and 7.28-7.65 (5H, complex of multiplets, Ar-H).

Preparation of *2-(t-butyldimethylsilyloxy)-2-bornene* (170)[183]

To a solution of diisopropylamine (3.47 g, 34.3 mmol) in dry Et_2O (100 ml) at -78 °C, was added BuLi (15% in hexane; 23 ml, 27 mmol). The mixture was stirred for 1 h before the addition of a solution of (+)-camphor (5.12 g, 34.0 mmol) in dry Et_2O (10 ml) (pre-dried over 4Å molecular sieves), followed, 1 h later, by *t*-$BuMe_2SiCl$ (5.40 g, 35.8 mmol). The mixture was allowed to warm to r.t. overnight and then boiled under reflux for 10 h. The Et_2O was removed by distillation, and the residue distilled *in vacuo* to yield, as an oil, 2-(*t*-butyldimethylsilyloxy)-2-bornene (**170**)[261] (7.19 g, 79%), b.p. 88 °C/0.2 mmHg (Found: $\mathbf{M}^+$ 266.2049. Calc. for $C_{16}H_{30}OSi$: *M*, 266.2066); ν_{max}(thin film)/cm^{-1} 1615 (C=C); δ_H(400 MHz; $CDCl_3$) 0.12 and 0.15 (6H, 2xs, SiMe), 0.73 (3H, s, 10-Me), 0.86 and 0.87 (6H, 2xs, 8- and 9-Me), 0.93 [9H, s, $C(CH_3)_3$], 1.01-1.15, 1.44-1.52 and 1.78-1.87 (4H, complex of multiplets, 5- and 6-CH_2), 2.17 (1H, m, 4-H) and 4.56 (1H, d, *J* 4.0, 3-H); δ_C(100 MHz; $CDCl_3$) -4.9 and -4.6 (SiMe), 10.1 (C-10), 18.1 [$C(CH_3)_3$], 19.8 and 20.1 (C-8 and C-9), 25.7 [$C(CH_3)_3$], 27.4 (C-5), 31.3 (C-6), 49.6 (C-4), 53.5 and 54.6 (C-1 and C-7), 102.5 (C-3) and 160.6 (C-2); *m/z* 266 ($\mathbf{M}^+$, 12.1%) and 73 (100).

Preparation of *3-exo-(α-methoxybenzyl)-2-bornanone* (171)[205]

A solution of benzaldehyde dimethyl acetal (**174**) (1.0 g, 6.6 mmol) in CH_2Cl_2 (40 ml) was cooled to -78 °C, and $TiCl_4$ (1.6 g, 8.4 mmol) was then added dropwise, followed by the addition of 2-(*t*-butyldimethylsilyloxy)-2-bornene (**170**) (2.0 g, 7.5 mmol). The mixture was stirred for 15 min, and then quenched by the addition of ice-cold H_2O (100 ml). The resulting mixture was extracted with CH_2Cl_2 (2x50 ml), and the combined organic extracts were washed with satd. aq. $NaHCO_3$ (100 ml), dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue [elution with hexane-EtOAc (19:1)] yielded, as white crystals, 3-*exo*-(α-methoxybenzyl)-2-bornanone (**171**) (0.98 g, 54%), m.p. 68-69 °C[ɬ] (Found: $\mathbf{M}^+$ 272.1771. Calc. for $C_{18}H_{24}O_2$: *M*, 272.1776); ν_{max}(thin film)/cm^{-1} 1745 (CO); δ_H(400 MHz; $CDCl_3$) 0.71, 0.82 and 0.84 (9H, 3xs, 8-, 9- and 10-Me), 1.16, 1.41, 1.48 and 1.73 (4H, 4xm, 5- and 6-CH_2), 1.36 (1H, m, 4-H), 2.31 (1H, d, *J* 9.2, 3-H), 3.08 (3H, s, OMe), 4.12 (1H, d, *J* 9.2, C*H*OMe) and 7.13-7.30 (5H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 9.3, 20.0 and 21.9 (C-8, C-9 and C-10), 29.1 and 29.4 (C-5 and C-6), 46.0 and 58.2 (C-1 and C-7), 46.5 (C-4), 56.2 (OMe), 60.1 (C-3), 84.9

ɬ No physical data given in reference.[205]

(*C*HOMe), 127.6, 127.9, 128.4 and 140.5 (Ar-C) and 217.9 (C-2); *m/z* 272 ($\mathbf{M}^+$, 0.3%) and 121 (100).

Preparation of *3*-exo-*(α-methoxybenzyl)-2*-exo-*bornanol* (172)

Method 1.[108]

A solution of L-selectride (1.0 **M** in THF; 3.0 ml, 3.0 mmol) was added dropwise to a solution of 3-*exo*-(α-methoxybenzyl)-2-bornanone (**171**) (0.73 g, 2.7 mmol) in dry THF (4 ml) cooled to -78 °C. The reaction mixture was allowed to warm to r.t. overnight, quenched by the consecutive addition of H_2O (0.60 ml), EtOH (2.3 ml), 3 **M** NaOH (3.1 ml) and 30% H_2O_2 (2.3 ml) at 0 °C and the resulting mixture saturated with solid K_2CO_3. After stirring for 1 h, the mixture was extracted with EtOAc (3x20 ml) and the organic fraction was dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. The residue was shown by ^{1}H NMR spectroscopy to contain two components which could be separated by flash column chromatography [elution with hexane-EtOAc (9:1)] to afford two fractions.

Fraction 1.

White crystals of *3*-exo-*(α-methoxybenzyl)-2*-exo-*bornanol* (**172**) (0.16 g, 23%), m.p. 43-45 °C (Found: $\mathbf{M}^+$ 274.1928. $C_{18}H_{26}O_2$ requires *M*, 274.1933); $[\alpha]_D^{27}$ +78.1(*c* 2.1); ν_{max}(thin film)/cm^{-1} 3510 (OH); δ_H(400 MHz; $CDCl_3$) 0.74 and 1.32 (6H, 2xs, 8- and 9-Me), 0.80 (1H, m, 5-CH_2), 0.98 (3H, s, 10-Me), 1.07 (1H, m, 6-CH_2), 1.12 (1H, m, 4-H), 1.43 (1H, m, 6-CH_2), 1.52 (1H, m, 5-CH_2), 2.04 (1H, dd, $J_{2,3}$ 7.5 and $J_{3,CHOMe}$ 11.3, 3-H), 3.05 (1H, br s, OH), 3.10 (3H, s, OMe), 3.94 (1H, d, $J_{2,3}$ 7.5, 2-H), 4.55 (1H, d, $J_{3,CHOMe}$ 11.3, C*H*OMe) and 7.26-7.38 (5H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.6 (C-10), 21.97 and 22.02 (C-8 and C-9), 29.9 (C-5), 33.7 (C-6), 47.0 and 49.6 (C-1 and C-7), 47.4 (C-4), 55.5 (OMe), 57.4 (C-3), 81.5 (C-2), 84.8 (*C*HOMe) and 127.8, 128.4 and 141.0 (Ar-C)[¥]; *m/z* 242 ($\mathbf{M}^+$- CH_4O, 4.5%) and 121 (100).

[¥] There is coalescence of two of the aromatic peaks in the ^{13}C NMR spectrum.

Fraction 2.

As an oil, 3-*endo*-benzyl-2-bornanone[h] (**173**) (61%)[212] (Found: $\mathbf{M}^+$ 242.1673. Calc. for $C_{17}H_{22}O$: *M*, 242.1671); ν_{max}(thin film)/cm^{-1} 1740 (CO); δ_H(400 MHz; $CDCl_3$) 0.85, 0.93 and 0.97 (9H, 3xs, 8-, 9- and 10-Me), 1.32-1.42 and 1.65-1.83 (4H, complex of multiplets, 5- and 6-CH_2), 1.93 (1H, m, 4-H), 2.52 (1H, dd, $J_{a,b}$ 14.3 and $J_{a,3}$ 11.2, $PhCH_a$), 2.67-2.74 (1H, m, 3-H), 3.17 (1H, dd, $J_{b,a}$ 14.3 and $J_{b,3}$ 4.3, $PhCH_b$) and 7.16-7.33 (5H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 9.5, 19.2 and 19.5 (C-8, C-9 and C-10), 20.2 (C-5), 31.0 (C-6), 32.7 ($PhCH_2$), 45.7 and 58.7 (C-1 and C-7), 45.8 (C-3), 51.8 (C-4), 126.0, 128.4, 128.5 and 140.3 (Ar-C) and 220.2 (C-2).; *m/z* 242 ($\mathbf{M}^+$, 38.7%) and 91 (100).

Method 2.[209]

A solution of 3-*exo*-(α-methoxybenzyl)-2-bornanone (**171**) (1.2 g, 4.3 mmol) in MeOH (20 ml) was cooled to 0 °C before adding $NaBH_4$ (0.20 g, 5.3 mmol). The reaction mixture was stirred at 0 °C for 2 h and then allowed to warm to r.t. overnight. The resulting solution was diluted with H_2O (20 ml) and extracted with EtOAc (3x20 ml). The organic layer was dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue [elution with hexane-EtOAc (9:1)] afforded, as white crystals, 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornanol (**172**) (0.60 g, 50%).

Method 3.[211]

A solution of 3-*exo*-(α-methoxybenzyl)-2-bornanone (**171**) (1.6 g, 5.8 mmol) in dry Et_2O (2 ml) was added dropwise under nitrogen to a stirred suspension of $LiAlH_4$ (0.10 g, 2.6 mmol) in dry Et_2O (20 ml) at 0 °C. The stirred mixture was allowed to warm to r.t. overnight, before quenching the reaction by the successive addition of H_2O (0.1 ml), 10% NaOH (0.1 ml) and H_2O (0.3 ml) under nitrogen. The resulting precipitate was collected and extracted by boiling with Et_2O (2x20 ml) under reflux. The filtrate and organic extracts were combined, washed with satd. aq. $NaHCO_3$, dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue [elution with hexane-EtOAc (19:1)] afforded, as white crystals, 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornanol (**172**) (0.90 g, 56%).

---

[h]Although the product (**173**) was isolated from another reaction mixture of the same reaction, its presence was detected in the ^{1}H NMR spectrum of the above crude reaction mixture.

Preparation of *3*-endo-*benzyl-2*-exo-*bornanol* (178)[212, 213]

3-*Endo*-benzyl-2-bornanone (**173**) (5.19 g, 21.4 mmol) and $LiAlH_4$ (0.34 g, 9.0 mmol) in dry Et_2O (50 ml) were reacted as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornanol (**172**) (Method 3). Work-up and flash chromatography yielded, as an oil, 3-*endo*-benzyl-2-*exo*-bornanol (**178**) (1.92 g, 37%), (Found: $\mathbf{M}^+$ 244.1821. Calc. for $C_{17}H_{24}O$: *M*, 244.1827); ν_{max}(thin film)/cm^{-1} 3450 (OH); δ_H(400 MHz; $CDCl_3$) 0.84, 0.86 and 1.04 (9H, 3xs, 8-, 9- and 10-Me), 0.90-1.11 and 1.48-1.77 (6H, complex of multiplets, 5- and 6-CH_2, 4-H and OH), 2.37 (1H, m, 3-H), 2.63 (1H, dd, J_{gem} 13.6 and J_{vic} 8.7, $ArCH_2$), 2.85 (1H, dd, J_{gem} 13.6 and J_{vic} 6.1, $ArCH_2$), 3.22 (1H, d, *J* 4.0, 2-H) and 7.15-7.33 (5H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.4, 19.6 and 20.8 (C-8, C-9 and C-10), 20.2 (C-5), 34.5 (C-6), 37.1 ($PhCH_2$), 47.4 and 49.7 (C-1 and C-7), 48.1 (C-3), 50.9 (C-4), 85.8 (C-2) and 125.7, 128.3, 128.7 and 141.6 (Ar-C); *m/z* 244 ($\mathbf{M}^+$, 5.3%) and 95 (100).

Preparation of *3*-exo-*(α-methoxybenzyl)-2*-exo-*bornyl 3,3-dimethylbutanoate* (179)

Method 1.

3-*Exo*-(α-methoxybenzyl)-2-*exo*-bornanol (**172**) (1.0 g, 3.6 mmol) in dry THF (5 ml) was added to pre-washed NaH (50% suspension in oil; 0.21 g, 4.4 mmol) in dry THF (25 ml) under nitrogen. The resulting mixture was stirred at r.t. for 1 h and then boiled under reflux for a further 1 h. Once cooled to r.t., 3,3-dimethylbutanoyl chloride (0.59 g, 4.4 mmol) was added dropwise, and the resulting mixture stirred overnight before being boiled under reflux for 1.5 h. The mixture was cooled to r.t. and quenched with satd. aq. $NaHCO_3$ (40 ml). The resultant mixture was extracted with EtOAc (2x40 ml) and the combined organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue [elution with hexane-EtOAc (9:1)] yielded a complex reaction mixture in which only 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornanol (**172**) (0.58 g) could be clearly identified.

Method 2.

Butyllithium (15% solution in hexane; 1.6 ml, 2.5 mmol) was added dropwise under nitrogen to a stirred solution of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornanol (**172**) (0.70 g, 2.6 mmol) in dry Et_2O (20 ml) at 0 °C. After 1 h, 3,3-dimethylbutanoyl chloride (0.43 ml, 3.1 mmol) was added and the stirred mixture allowed to warm to r.t. overnight. The reaction was quenched with satd. aq. $NaHCO_3$ (50 ml) and the resulting mixture extracted with EtOAc (3x50 ml). The combined

organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue [elution with hexane-EtOAc (19:1)] afforded, as white crystals, *3*-exo-*(α-methoxybenzyl)-2*-exo-*bornyl 3,3-dimethylbutanoate* (**179**) (0.52 g, 55%), m.p. 59-60 °C (Found: $\mathbf{M}^+$ 372.2650. $C_{24}H_{36}O_3$ requires *M*, 372.2664); $[\alpha]_D^{27}$ +4.0 (*c* 0.1); ν_{max}(thin film)/cm^{-1} 1740 (CO); δ_H(400 MHz; $CDCl_3$) 0.70 and 1.20 (6H, 2xs, 8'- and 9'-Me), 0.85 (3H, s, 10'-Me), 0.86-0.94 (1H, m, 5'-CH_2), 1.09 [9H, s, $C(CH_3)_3$], 1.22-1.30 (1H, m, 6'-CH_2), 1.42-1.56 (2H, complex of multiplets, 5'- and 6'-CH_2), 1.58 (1H, m, 4'-H), 2.19 (1H, dd, $J_{2',3'}$ 10.8 and $J_{3',CHOMe}$ 8.3, 3'-H), 2.28 (2H, d, *J* 2.1, 2-CH_2), 3.00 (3H, s, OMe), 4.34 (1H, d, $J_{2',3'}$ 10.8, 2'-H), 5.24 (1H, d, $J_{3',CHOMe}$ 8.3, C*H*OMe) and 7.23-7.40 (5H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.9 (C-10'), 21.5 and 21.8 (C-8' and C-9'), 29.75 (C-5'), 29.83 [C(*C*H_3)$_3$], 30.5 (C-3), 33.1 (C-6'), 47.2 and 49.8 (C-1' and C-7'), 47.7 (C-4'), 48.3 (C-2), 55.9 (MeO), 56.4 (C-3'), 80.0 (C-2'), 83.7 (*C*HOMe), 127.6, 127.7, 128.4 and 141.5 (Ar-C) and 171.3 (C-1); *m/z* 256 ($\mathbf{M}^+$- $C_6H_{11}O_2$, 4.7%) and 121 (100).

Preparation of *3*-exo-*(α-methoxybenzyl)-2*-exo-*bornyl 2-benzyl-3,3-dimethylbutanoate* (181)[179]

Butyllithium (15% in hexane; 0.85 ml, 1.4 mmol) was added to a stirred solution of diisopropylamine (0.15 g, 1.5 mmol) in dry THF (5 ml) under nitrogen at -78 °C. After 30 min., 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**) (0.42 g, 1.1 mmol) was added dropwise, followed, 1h later, by benzyl bromide (0.22 g, 1.3 mmol). The mixture was maintained at -78 °C for a further 1 h and then allowed to warm to r.t. overnight. The reaction was then quenched with satd. aq. $NaHCO_3$ (20 ml) and the resulting mixture extracted with EtOAc (3x20 ml). The organic fractions were combined, dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded an oil (0.36 g) comprising a 2:1 mixture of the starting material 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**) and a diastereomeric mixture of *3*-exo-*(α-methoxybenzyl)-2*-exo-*bornyl 2-benzyl-3,3-dimethylbutanoate* (**181**) (24%) (43% d.e.; as determined by ^{1}H NMR spectroscopy).[ξ]

[ξ] The ratios were determined by integration of the ^{1}H NMR spectrum of the reaction mixture.

Further purification by PLC [elution with hexane-EtOAc (49:1)] resulted in the isolation of two fractions.

Fraction 1.

White crystals of the major diastereomer of *3*-exo-*(α-methoxybenzyl)-2*-exo-*bornyl 2-benzyl-3,3-dimethylbutanoate* (**181**), m.p. 74-76 °C (Found: $\mathbf{M}^+$-CH_4O 430.2870 . $C_{30}H_{38}O_2$ requires *M-CH₄O*, 430.2872); $[\alpha]_D^{20}$ +4.0 (*c* 0.4); ν_{max}(thin film)/cm^{-1} 1715 (CO); δ_H(400 MHz; $CDCl_3$) 0.64 and 1.12 (6H, 2xs, 8'- and 9'-Me), 0.87 (3H, s, 10'-Me), 0.88-0.93 (1H, m, 5'-CH_2), 1.00 (1H, m, 4'-H), 1.09 [9H, s, $C(CH_3)_3$], 1.24-1.49 (3H, complex of multiplets, 5'- and 6'-CH_2), 2.18 (1H, m, 3'-H), 2.48 (3H, s, OMe), 2.62 (1H, dd, $J_{2,a}$ 4.2 and $J_{2,b}$ 8.7, 2-H), 2.92 (1H, dd, $J_{2,a}$ 4.2 and $J_{a,b}$ 14.4, $PhCH_2$), 3.16 (1H, dd, $J_{2,b}$ 8.7 and $J_{a,b}$ 14.4, $PhCH_2$), 4.29 (1H, d, *J* 10.4, C*H*OMe), 5.19 (1H, d, *J* 8.3, 2'-H) and 7.10-7.35 (10H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 12.9 (C-10'), 21.2 and 22.0 (C-8' and C-9'), 28.7 [C(*C*H_3)$_3$], 29.8 (C-5'), 33.5 (C-6'), 33.8 (C-3), 34.3 ($PhCH_2$), 47.0 and 50.8 (C-1' and C-7'), 48.0 (C-4'), 55.4 (MeO), 56.2 (C-3'), 57.6 (C-2), 81.8 (C-2'), 83.2 (*C*HOMe), 126.0, 127.5, 127.8, 128.3, 128.4, 129.0, 141.2 and 141.7 (Ar-C) and 174.4 (C-1); *m/z* 430 ($\mathbf{M}^+$- CH_4O, 0.7%) and 121 (100).

Fraction 2.

As an oil, the minor diastereomer of *3*-exo-*(α-methoxybenzyl)-2*-exo-*bornyl 2-benzyl-3,3-dimethylbutanoate* (**181**), ν_{max}(thin film)/cm^{-1} 1710 (CO); δ_H(400 MHz; $CDCl_3$) 0.12 and 0.82 (6H, 2xs, 8'- and 9'-Me), 0.48 (3H, s, 10'-Me), 0.82-0.88 (1H, m, 5'-CH_2), 0.91 (1H, m, 4'-H), 1.12 [9H, s, $C(CH_3)_3$], 1.14-1.48 (3H, complex of multiplets, 5'- and 6'-CH_2), 2.23 (1H, m, 3'-H), 2.61 (1H, t, *J* 7.1, 2-H), 2.89 (3H, s, MeO), 2.95 (2H, d, *J* 7.1, $PhCH_2$), 4.41 (1H, d, *J* 10.1, C*H*OMe), 5.07 (1H, d, *J* 8.3, 2'-H) and 7.13-7.36 (10H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.5 (C-10'), 21.0 and 21.4 (C-8' and C-9'), 28.2 [C(*C*H_3)$_3$], 29.8 (C-5'), 32.9 (C-6'), 33.3 (C-3), 24.8 ($PhCH_2$), 46.7 and 50.6 (C-1' and C-7'), 48.5 (C-4'), 55.8 (MeO), 56.3 (C-3'), 58.5 (C-2), 81.5 (C-2'), 83.1 (*C*HOMe), 126.1, 127.6, 127.9, 128.3, 128.4, 129.3, 140.5 and 141.6 (Ar-C) and 174.2 (C-1).

3.2.4 The camphor-derived chiral auxiliary (183)

Preparation of *spiro[bornane-3,2'-indan]-2-one* (182)[182]

(+)-Camphor (10.1 g, 66.6 mmol) was added to pre-washed NaH (50% suspension in oil; 7.0 g, 0.15 mol) in dry toluene (150 ml) under nitrogen and the resulting mixture was stirred for 1 h. α,α'-Dichloroxylene (11.5 g, 65.7 mmol) was then added and the reaction mixture was boiled under reflux for 18 h. Satd. aq. $NaHCO_3$ (200 ml) was added and the resulting mixture extracted with EtOAc (2x100 ml). The combined organic layers were dried (anhyd. $MgSO_4$) and concentrated *in vacuo*. The residue was recrystallised from Et_2O and the crystalline product was washed with MeOH to afford white crystals of spiro[bornane-3,2'-indan]-2-one (**182**) (9.5 g, 57%), m.p. 90-92 °C (from Et_2O)[♮] (Found: $\mathbf{M}^+$ 254.1686. Calc. for $C_{18}H_{22}O$: *M*, 254.1671); ν_{max}(thin film)/cm^{-1} 1740 (CO); δ_H(400 MHz; $CDCl_3$) 0.93 (3H, s, 10-Me), 0.99 and 1.03 (6H, 2xs, 8- and 9-Me), 1.41-1.50 and 1.62-1.91 (4H, complex of multiplets, 5- and 6-CH_2), 1.98-2.00 (1H, m, 4-H), 2.97 and 3.30 (2H, 2xd, *J* 16.3, $ArCH_2$), 3.09 and 3.21 (2H, 2xd, *J* 16.1, $ArCH_2$) and 7.09-7.14 (4H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 9.9 (C-10), 20.9 and 22.7 (C-8 and C-9), 23.3 (C-5), 30.1 (C-6), 42.4 and 46.1 (2x$ArCH_2$), 46.7, 57.8 and 58.9 (C-1, C-3 and C-7), 53.4 (C-4), 123.7, 123.9, 126.45, 126.48, 141.1 and 141.9 (Ar-C) and 223.8 (C-2); *m/z* 254 ($\mathbf{M}^+$, 3.2%) and 115 (100).

Preparation of *spiro[bornane-3,2'-indan]-2*-exo-*ol* (183)[182]

Spiro[bornane-3,2'-indan]-2-one (**182**) (11 g, 43 mmol) in dry Et_2O (5 ml) was treated with $LiAlH_4$ (1.0 g, 26 mmol) in dry Et_20 (50 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornanol (**172**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (19:1)] afforded, as an oil, spiro[bornane-3,2'-indan]-2-*exo*-ol (**183**) (7.88 g, 72%) (Found: $\mathbf{M}^+$ 256.1843. Calc. for $C_{18}H_{24}O$: *M*, 256.1827); ν_{max}(thin film)/cm^{-1} 3450 (OH); δ_H(400 MHz; $CDCl_3$) 0.87 (3H, s, 10-Me), 0.89 and 1.24 (6H, 2xs, 8-and 9-Me), 1.11-1.17 and 1.50-1.69 (4H, complex of multiplets, 5- and 6-CH_2), 1.45 (1H, br s, OH), 1.72-1.74 (1H, m, 4-H), 2.74 and 3.17 (2H, 2xd, *J* 15.3, $ArCH_2$), 2.78 and 3.63 (2H, 2xd, *J* 15.8, $ArCH_2$), 3.32 (1H, br s, 2-H) and 7.08-7.17 (4H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 12.0 (C-10), 21.8 and 22.2 (C-8 and C-9), 24.3 (C-5), 34.5 (C-6), 40.9 and 47.4 (2x$ArCH_2$), 49.0 and 51.1

[♮] No melting point given in reference.[182]

(C-1 and C-7), 57.4 (C-3), 56.2 (C-4), 89.8 (C-2) and 123.7, 123.9, 125.9, 126.3, 141.8 and 144.8 (Ar-C); *m/z* 256 (M^+, 6.4%) and 115 (100).

Preparation of *propanoyl chloride* (186a)[262]

Propanoic acid (23 g, 0.31 mol) was added dropwise to a stirred solution of $SOCl_2$ (22.0 ml, 0.30 mol) at 60 °C and the resulting mixture was boiled under reflux for 1 h. Distillation yielded, as a colourless liquid, propanoyl chloride (**186a**) (18.0 g, 64%), b.p. 82 °C (lit.,[263] 80 °C); δ_H(60 MHz; $CDCl_3$) 1.30 (3H, t, 3-CH_3) and 3.00 (2H, q, 2-CH_2).

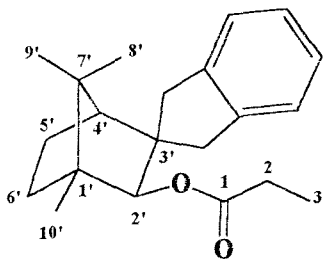
Preparation of *butanoyl chloride* (186b)

Butanoic acid (12 ml, 0.12 mol) and $SOCl_2$ (9.1 ml, 0.13 mol) were reacted as described for the synthesis of propanoyl chloride (**186a**). Distillation yielded, as a colourless liquid, butanoyl chloride (**186b**) (6.81 g, 53%), b.p. 96-99 °C (lit.,[263] 102 °C); ν_{max}(thin film)/cm^{-1} 1800 (CO); δ_H(400 MHz; $CDCl_3$) 9.98 (3H, t, *J* 7.3, 4-Me), 1.72 (2H, m, 3-CH_2) and 2.85 (2H, t, *J* 6.2, 2-CH_2).

Preparation of *phenoxyacetyl chloride* (186f)

Phenoxyacetic acid (8.15 g, 53.6 mmol) and $SOCl_2$ (9.30 g, 78.2 mmol) were reacted as described for the synthesis of propanoyl chloride (**186a**). Vacuum distillation yielded, as a colourless oil, phenoxyacetyl chloride (**186f**) (6.68 g, 74%), b.p. 90 °C/2 mmHg (lit.,[264] 109 °C/9 mmHg); ν_{max}(thin film)/cm^{-1} 1805 (CO); δ_H(60 MHz; $CDCl_3$) 5.02 (2H, s, 2-CH_2) and 6.80-7.68 (5H, complex of multiplets, Ar-H).

Preparation of *spiro[bornane-3,2'-indan]-2*-exo-*yl propanoate* (184a)



Spiro[bornane-3,2'-indan]-2-*exo*-ol (**183**) (1.0 g, 3.9 mmol) was treated with butyllithium (15% solution in hexane; 2.4 ml, 3.9 mmol) and propanoyl chloride (**186a**) (0.49 g, 4.9 mmol) in dry Et_2O (20 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (19:1)] afforded, as an oil, spiro[bornane-3,2'-indan]-2-*exo*-yl propanoate (**184a**) (0.81 g, 65%) (Found: $\mathbf{M}^+$ 312.2080. Calc. for $C_{21}H_{28}O_2$: *M*, 312.2089); ν_{max}(thin film)/cm^{-1} 1735(CO); δ_H(400 MHz; $CDCl_3$) 0.80 (3H, s, 10'-Me), 0.93 and 1.26 (6H, 2xs, 8'- and 9'-Me), 1.03 (3H, t, *J* 7.6, 3-CH_3), 1.31-1.40 and 1.59-1.75 (4H, complex of multiplets, 5'- and 6'-CH_2), 1.77-179 (1H, m, 4'-H), 2.17 (2H, m, 2-CH_2), 2.86 and 3.17 (2H, 2xd, *J* 15.3, $ArCH_2$), 2.41 and 2.95 (2H, 2xd, *J* 15.7, $ArCH_2$), 4.66 (1H, s, 2'-H) and 7.04-7.18 (4H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 9.2 (C-10'), 11.6, 21.8 and 22.0 (C-8', C-9' and C-3), 24.0 (C-5'), 27.7 (C-2), 33.9 (C-6'), 41.7 and 46.6 (2x$ArCH_2$), 49.3 and 50.9 (C-1' and C-7'), 55.8 (C-4'), 57.1 (C-3'), 88.3 (C-2'), 123.1, 123.9, 126.0, 126.1, 141.4 and 143.5 (Ar-C) and 172.9 (C-1); *m/z* 312 ($\mathbf{M}^+$, 0.9%) and 57 (100).

Preparation of *spiro[bornane-3,2'-indan]-2*-exo-*yl butanoate* (184b)

Spiro[bornane-3,2'-indan]-2-*exo*-ol (**183**) (0.99 g, 3.9 mmol) was treated with butyllithium (15% solution in hexane; 2.4 ml, 3.9 mmol) and butanoyl chloride (**186b**) (0.52 g, 4.9 mmol) in dry Et_2O (20 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (19:1)] yielded, as an oil, *spiro[bornane-3,2'-indan]-2*-exo-*yl butanoate* (**184b**) (0.85 g, 68%) (Found: $\mathbf{M}^+$ 326.2238. $C_{22}H_{30}O_2$ requires *M*, 326.2246); $[\alpha]_D^{28}$ +2.5 (*c* 4.0); ν_{max}(thin film)/cm^{-1} 1740 (CO); δ_H(400 MHz; $CDCl_3$) 0.76 (3H, s, 10'-Me), 0.82 (3H, t, *J* 7.4, 4-Me), 0.89 and 1.22 (6H, 2xs, 8'- and 9'-Me), 1.28-1.37 and 1.56-1.71 (4H, complex of multiplets, 5'- and 6'-CH_2), 1.49 (2H, m, 3-CH_2), 1.74-1.77 (1H, m, 4'-H), 2.10 (2H, m, 2-CH_2), 2.85 and 3.37 (2H, 2xd, *J* 15.7, $ArCH_2$), 2.93 and 3.16 (2H, 2xd, *J* 15.3, $ArCH_2$), 4.64 (1H, s, 2'-H) and 7.02-7.14 (4H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.7 (C-10'), 13.7, 21.8 and 22.0 (C-8', C-9' and C-4), 18.3 (C-3), 24.0 (C-5'), 33.9 (C-6'), 36.3 (C-2), 41.8 and 46.7 (2x$ArCH_2$), 49.1 and 50.9 (C-1' and C-7'), 55.9 (C-4'), 57.1 (C-3'), 88.4 (C-2'), 123.2, 123.9, 126.0, 126.1, 141.4 and 143.6 (Ar-C) and 172.2 (C-1); *m/z* 326 ($\mathbf{M}^+$, 0.3%) and 43 (100).

Preparation of *spiro[bornane-3,2'-indan]-2*-exo-*yl 3-methylbutanoate* (184c)

Spiro[bornane-3,2'-indan]-2-*exo*-ol (**183**) (1.1 g, 4.2 mmol) was treated with butyllithium (15% solution in hexane; 2.4 ml, 3.9 mmol) and 3-methylbutanoyl chloride (0.56 g, 4.9 mmol) in dry Et_2O (20 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (19:1)] yielded, as an oil, *spiro[bornane-3,2'-indan]-2*-exo-*yl 3-methylbutanoate* (**184c**) (0.99 g, 70%) (Found: $\mathbf{M}^+$ 340.2410. $C_{23}H_{32}O_2$ requires *M*, 340.2410); $[\alpha]_D^{22}$ +7.6 (*c* 2.0); ν_{max}(thin film)/cm^{-1} 1735 (CO); δ_H(400 MHz; $CDCl_3$) 0.75 (3H, s, 10'-Me), 0.77 and 0.80 [6H, dd, *J* 6.5, $CH(CH_3)_2$], 0.88 and 1.20 (6H, 2xs, 8'- and 9'-Me), 1.27-1.38 and 1.58-1.70 (4H, complex of multiplets, 5'- and 6'-CH_2), 1.74-1.77 (1H, m, 4'-H), 1.86-2.07 (3H, complex of multiplets, 2-CH_2 and 3-H), 2.83 and 3.38 (2H, 2xd, *J* 15.8, $ArCH_2$), 2.92 and 3.16 (2H, 2xd, *J* 15.4, $ArCH_2$), 4.65 (1H, s, 2'-H) and 7.01-7.15 (4H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.8 (C-10'), 21.8 and 22.0 (C-8' and C-9'), 22.39 and 22.43 [$CH(CH_3)_2$], 24.1 (C-5'), 25.4 (C-3), 33.9 (C-6'), 41.8 and 46.7 (2x$ArCH_2$), 43.5 (C-2), 49.3 and 51.0 (C-1' and C-7'), 56.0 (C-4'), 57.0 (C-3'), 85.5 (C-2'), 123.3, 123.9, 126.1, 141.4 and 143.5 (Ar-C) and 171.8 (C-1); *m/z* 340 ($\mathbf{M}^+$, 0.6%) and 57 (100).

Preparation of *spiro[bornane-3,2'-indan]-2*-exo-*yl 3,3-dimethylbutanoate* (184d)

Spiro[bornane-3,2'-indan]-2-*exo*-ol (**183**) (2.0 g, 7.9 mmol) was treated with butyllithium (15% solution in hexane; 6.2 ml, 9.4 mmol) and 3,3-dimethylbutanoyl chloride (1.3 g, 9.4 mmol) in dry Et_2O (40 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**) . Work-up and flash chromatography of the residue [elution with hexane-EtOAc (19:1)] yielded, as an oil, *spiro[bornane-3,2'-indan]-2*-exo-*yl 3,3-dimethylbutanoate* (**184d**) (0.87 g, 74%) (Found: $\mathbf{M}^+$ 354.2544. $C_{24}H_{34}O_2$ requires *M*, 354.2559); $[\alpha]_D^{27}$ +0.7 (*c* 2.0); ν_{max}(thin film)/cm^{-1} 1720 (CO); δ_H(400 MHz; $CDCl_3$) 0.79 (3H, s, 10'-Me), 0.90 and 1.22 (6H, 2xs, 8'- and 9'-Me), 0.90 [9H, s, $C(CH_3)_3$], 1.27-1.37 and 1.56-1.62 (4H, complex of multiplets, 5'- and 6'-CH_2), 1.74-1.76 (1H, m, 4'-H), 1.97 and 2.08 (2H, d, *J* 2.1, 2-CH_2), 2.85 and 3.48 (2H, 2xd, *J* 15.8, $ArCH_2$), 2.94 and 3.16 (2H, 2xd, *J* 15.3, $ArCH_2$), 4.67 (1H, s, 2-H) and 7.02-7.15 (4H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 12.1 (C-10'), 21.8 and 22.0 (C-8' and C-9'), 24.0 (C-5'), 29.6 ($C(CH_3)_3$), 30.3 (C-3), 34.0 (C-6'), 41.9 and 46.7 (2x$ArCH_2$), 47.8 (C-2), 49.3 and 50.9 (C-1' and C-7'), 56.0 (C-3'), 56.9 (C-4'), 88.7 (C-2'), 123.4, 123.8, 126.0, 126.1, 141.4 and 143.5 (Ar-C) and 171.1 (C-1); *m/z* 354 ($\mathbf{M}^+$, 1.5%)

and 57 (100).

Preparation of *spiro[bornane-3,2'-indan]-2*-exo-*yl phenylacetate* (184e)

Spiro[bornane-3,2'-indan]-2-*exo*-ol (**183**) (1.0 g, 3.9 mmol) was treated with butyllithium (15% solution in hexane; 2.4 ml, 3.9 mmol) and phenylacetyl chloride (0.72 g, 4.9 mmol) in dry Et_2O (20 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (19:1)] yielded, as an oil, *spiro[bornane-3,2'-indan]-2*-exo-*yl phenylacetate* (**184e**) (0.40 g, 36%) (Found: $\mathbf{M}^+$ 374.2231. $C_{26}H_{30}O_2$ requires *M*, 374.2246); $[\alpha]_D^{22}$ +18.6 (*c* 1.3); ν_{max}(thin film)/cm^{-1} 1735 (CO); δ_H(400 MHz; $CDCl_3$) 0.67 (3H, s, 10'-Me), 0.87 and 1.03 (6H, 2xs, 8'- and 9'-Me), 1.23-1.76 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 2.74 and 3.15 (2H, 2xd, $ArCH_2$), 2.91 and 3.15 (2H, 2xd, $ArCH_2$), 3.44 (2H, m, 2-CH_2), 4.64 (1H, s, 2'-H) and 6.89-7.33 (9H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.6 (C-10'), 21.5 and 21.9 (C-8' and C-9'), 24.0 (C-5'), 33.8 (C-6'), 41.55 and 41.63 (2x$ArCH_2$), 46.1 (C-2), 49.3 and 51.1 (C-1' and C-7'), 55.9 (C-4'), 57.0 (C-3'), 89.1 (C-2'), 123.1, 123.9, 126.0, 126.1, 126.9, 128.4, 129.4, 134.2, 141.2 and 143.5 (Ar-C) and 170.0 (C-1); *m/z* 374 ($\mathbf{M}^+$, 0.5%) and 91 (100).

Preparation of *spiro[bornane-3,2'-indan]-2*-exo-*yl phenoxyacetate* (184f)

Spiro[bornane-3,2'-indan]-2-*exo*-ol (**183**) (0.98 g, 3.8 mmol) was treated with butyllithium (15% solution in hexane; 2.4 ml, 3.9 mmol) and phenoxyacetyl chloride (**186f**) (0.80 g, 4.9 mmol) in dry Et_2O (20 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (19:1)] yielded, as an oil, *spiro[bornane-3,2'-indan]-2*-exo-*yl phenoxyacetate* (**184f**) (1.13 g, 75%), m.p. 71-73 °C (Found: $\mathbf{M}^+$ 390.2196. $C_{26}H_{30}O_3$ requires *M*, 390.2195); $[\alpha]_D^{20}$ +25.8 (*c* 4.9); ν_{max}(thin film)/cm^{-1} 1760 (CO); δ_H(400 MHz; $CDCl_3$) 0.80 (3H, s, 10'-Me), 0.95 and 1.19 (6H, 2xs, 8'- and 9'-Me), 1.33-1.80 (4H, complex of multiplets, 5'- and 6'-CH_2), 1.82-1.85 (1H, m, 4'-H), 2.90 and 3.48 (2H, 2xd, *J* 15.8, $ArCH_2$), 2.96 and 3.20 (2H, 2xd, *J* 15.3, $ArCH_2$), 4.42 and 4.50 (2H, 2xd, *J* 16.3, 2-CH_2), 4.82 (1H, s, 2'-H) and 6.73-7.31 (9H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.6 (C-10'), 21.6 and 21.9 (C-8' and C-9'), 24.1 (C-5'), 33.8 (C-6'), 41.7 and 46.7 (2x$ArCH_2$), 49.3 and 51.2 (C-1' and C-7'), 55.8 (C-4'), 57.4 (C-3'), 64.7 (C-2), 89.7 (C-2'), 114.3, 121.4, 123.1, 124.2, 126.26, 126.34, 129.4, 141.2, 143.6 and 157.8 (Ar-C) and 168.0 (C-1); *m/z* 390 ($\mathbf{M}^+$, 0.7%) and 77 (100).

Preparation of *spiro[bornane-3,2'-indan]-2*-exo-*yl 2-methyl-3-phenylpropanoate* (185a)

Spiro[bornane-3,2'-indan]-2-*exo*-yl propanoate (**184a**) (0.48 g, 1.5 mmol) was reacted with LDA [generated from diisopropylamine (0.18 g, 1.8 mmol) and butyllithium (15% in hexane; 1.2 ml, 1.9 mmol)] and benzyl bromide (0,31 g, 1.8 mmol) in dry THF (5 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate (**181**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded, as an oil, a diastereomeric mixture of spiro[bornane-3,2'-indan]-2-*exo*-yl 2-methyl-3-phenylpropanoate (**185a**) (0.50 g, 82%) (53% d.e.; as determined by ^{1}H NMR spectroscopy) (Found: $\mathbf{M}^+$ 402.2563. Calc. for $C_{28}H_{34}O_2$: *M*, 402.2559); ν_{max}(thin film)/cm^{-1} 1735 (CO); δ_H(400 MHz; $CDCl_3$) 0.60/0.76 (3H, s, 10'-Me), 0.89/0.91 and 1.21/1.24 (6H, 2xs, 8'- and 9'-Me), 0.97/1.03 (3H, d, *J* 6.9/6.9, CH_3CHCO), 1.27-1.78 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 2.41-3.46 (7H, complex of multiplets, $PhCH_2$, $ArCH_2$ and 2-H), 4.63/4.67 (1H, s, 2'-H) and 7.02-7.27 (9H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.5/11.7 (C-10'), 16.3/16.7 (CH_3CHCO), 21.7/21.8 and 21.9/22.0 (C-8' and C-9'), 23.99/24.04 (C-5'), 33.86/33.91 (C-6'), 39.2/39.7 (C-3), 41.3/41.9 and 46.6/46.8 ($ArCH_2$), 41.7 (C-2), 49.29/49.33 and 51.1 (C-1' and C-7'), 55.9/56.1 (C-4'), 56.9/57.0 (C-3'), 88.7 (C-2'), 123.3/123.4, 123.90/123.93, 126.01/126.06, 126.13, 126.16, 128.3, 128.9, 139.3/139.5, 141.37/141.40 and 143.41/143.5 (Ar-C) and 174.56/174.60 (C-1); *m/z* 402 ($\mathbf{M}^+$, 0.1%) and 91 (100).

Preparation of *spiro[bornane-3,2'-indan]-2*-exo-*yl 2-benzylbutanoate* (185b)

Spiro[bornane-3,2'-indan]-2-*exo*-yl butanoate (**184b**) (0.50 g, 1.5 mmol) was reacted with LDA [generated from diisopropylamine (0.18 g, 1.8 mmol) and butyllithium (15% in hexane; 1.2 ml, 1.9 mmol)] and benzyl bromide (0,31 g, 1.8 mmol) in dry THF (5 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate (**181**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded, as an oil, a diastereomeric mixture of *spiro[bornane-3,2'-indan]-2*-exo-*yl 2-benzylbutanoate* (**185b**) (0.42 g, 67%) (58% d.e.; as determined by ^{1}H NMR spectroscopy) (Found: $\mathbf{M}^+$ 416.2710. $C_{29}H_{36}O_2$ requires *M*, 416.2715); ν_{max}(thin film)/cm^{-1} 1735 (CO); δ_H(400 MHz; $CDCl_3$) 0.56/0.75 (3H, s, 10'-Me), 0.66/0.71 (3H, t, *J* 7.4/7.4, 4-Me), 0.87/0.90 and 1.17/1.22 (6H, 2xs, 8'- and 9'-Me), 1.27-1.78 (7H, complex of multiplets, 4'-H and 3-, 5'- and 6'-CH_2), 2.41-3.45 (7H, complex of multiplets, $PhCH_2$, $ArCH_2$ and 2-H), 4.63/4.68 (1H, s, 2'-H) and 7.00-7.26 (9H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.5 (C-4), 11.6/12.0 (C-10'), 21.74/21.88

and 21.90/22.00 (C-8'- and C-9'), 23.9/24.0 and 24.1/21.5 (C-3 and C-5'), 33.9 (C-6'), 37.5/37.8 ($PhCH_2$), 41.7/41.8 and 46.5/46.9 ($ArCH_2$), 48.8 (C-2), 49.3 and 51.1/51.3 (C-1' and C-7'), 55.9/46.4 (C-4'), 56.5/56.7 (C-3'), 88.0/89.1 (C-2'), 123.5/123.6, 123.8/123.9, 126.06, 126.07/126.11, 126.14, 128.25/128.27, 128.87/128.93, 139.4/139.6, 141.4 and 143.4/143.5 (Ar-C) and 174.2/174.3 (C-1); *m/z* 416 ($\mathbf{M}^+$, 1.0%) and 91 (100).

Preparation of *spiro[bornane-3,2'-indan]-2*-exo-*yl 2-benzyl-3-methylbutanoate* (185c)

Spiro[bornane-3,2'-indan]-2-*exo*-yl 3-methylbutanoate (**184c**) (0.51 g, 1.0 mmol) was reacted with LDA [generated from diisopropylamine (0.19 g, 1.9 mmol) and butyllithium (15% in hexane; 1.2 ml, 1.9 mmol)] and benzyl bromide (0,31 g, 1.8 mmol) in dry THF (5 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate (**181**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded, as an oil, a diastereomeric mixture of *spiro[bornane-3,2'-indan]-2*-exo-*yl 2-benzyl-3-methylbutanoate* (**185c**) (0.40 g, 63%) (60% d.e.; as determined by ^{1}H NMR spectroscopy) (Found: $\mathbf{M}^+$ 430.2860. $C_{30}H_{38}O_2$ requires *M*, 430.2872); ν_{max}(thin film)/cm^{-1} 1720 (CO); δ_H(400 MHz; $CDCl_3$) 0.32/0.75 (3H, s, 10'-CH_3), 0.75/0.85 and 0.82/0.66 [6H, dd, $CH(CH_3)_2$], 0.83/0.88 and 1.09/1.17 (6H, 2xs, 8'- and 9'-Me), 1.22-1.71 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 1.73-1.88 (1H, m, 3-H), 2.44-3.43 (1H, m, 2-H), 2.66-3.43 (6H, complex of multiplets, $PhCH_2$ and $ArCH_2$), 4.58-4.63 (1H, s, 2'-H) and 6.96-7.41 (9H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.4/12.3 (C-10'), 19.5/19.8 and 20.3/20.5 [$CH(CH_3)_2$], 21.7/22.0 and 21.8/22.1 (8'-C and 9'-C), 23.6/23.9 (C-5'), 29.8/30.1 (C-3), 33.9/34.0 (C-6'), 34.4/35.0 ($PhCH_2$), 41.5/41.8 and 45.7/46.9 ($ArCH_2$), 49.2/49.3 and 50.9/51.2 (C-1' and C-7'), 53.7/54.2 (C-2), 55.3/56.5 (C-4'), 56.1/56.5[¥] (C-3'), 89.3/89.5 (C-2'), 123.6/123.7, 123.6/123.8, 125.9, 125.97/125.99, 126.03, 128.2/128.4, 128.7/128.9, 139.7/140.1, 141.4 and 143.3/143.4 (Ar-C) and 173.7/174.0 (C-1); *m/z* 430 ($\mathbf{M}^+$, 0.1%) and 91 (100).

[¥] There is coincidence with the C-4' signal.

Preparation of *spiro[bornane-3,2'-indan]-2*-exo-*yl 2-benzyl-3,3-dimethylbutanoate* (185d)

Spiro[bornane-3,2'-indan]-2-*exo*-yl 3,3-dimethylbutanoate (**184d**) (0.53 g, 1.0 mmol) was reacted with LDA [generated from diisopropylamine (0.18 g, 1.8 mmol) and butyllithium (15% in hexane; 1.2 ml, 1.9 mmol)] and benzyl bromide (0,31 g, 1.8 mmol) in dry THF (5 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate (**181**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded, as an oil, a diastereomeric mixture of *spiro[bornane-3,2'-indan]-2*-exo-*yl 2-benzyl-3,3-dimethylbutanoate* (**185d**) (0.27 g, 41%) (57% d.e.; as determined by ^{1}H NMR spectroscopy), m.p. 98-101 °C (Found: $\mathbf{M}^+$ 444.3033. $C_{31}H_{40}O_2$ requires *M*, 444.3028); ν_{max}(thin film)/cm^{-1} 1730 (CO); δ_H(400 MHz; $CDCl_3$) 0.77/0.79 (3H, s, 10'-Me), 0.81/0.87 and 0.96/1.04 (6H, 2xs, 8'- and 9'-Me), 0.83/1.05 [9H, s, $C(CH_3)_3$], 1.15-1.57 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 1.90-3.43 (7H, complex of multiplets, $PhCH_2$, $ArCH_2$ and 2-H), 4.48/4.51 (1H, s, 2'-H) and 6.79-7.24 (9H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 12.8/15.2 (C-10'), 21.7/22.1 and 21.8/22.4 (C-8' and C-9'), 22.8/23.7 (C-5'), 27.9/28.1 [$C(CH_3)_3$], 33.0/33.2 (C-3), 33.9/34.1(C-6'), 34.35/34.38 ($PhCH_2$), 40.9/42.2 and 43.5/46.9 ($ArCH_2$), 49.16/49.23 and 50.1/51.3 (C-1' and C-7'), 53.5/56.8 (C-4'), 55.6/56.1 (C-3'), 58.4/58.5 (C-2), 89.4/90.4 (C-2'), 123.1/123.6, 124.2, 125.51/125.87, 125.63/125.94, 126.1/126.2, 128.2/128.3, 128.8/129.1, 139.8/140.2, 141.5/141.6 and 143.2/143.3 (Ar-C) and 173.9/174.5 (C-1); *m/z* 444 ($\mathbf{M}^+$, 0.3%) and 91 (100).

Further purification by PLC [elution with hexane-EtOAc (49:1)] yielded a single diastereomer of *spiro[bornane-3,2'-indan]-2*-exo-*yl 2-benzyl-3,3-dimethylbutanoate* (**185d**) m.p. 98-101 °C; $[\alpha]_D^{27}$ -3.8 (*c* 0.6).

Preparation of *spiro[bornane-3,2'-indan]-2*-exo-*yl 2,3-diphenylpropanoate* (185e)

Spiro[bornane-3,2'-indan]-2-*exo*-yl phenylacetate (**184e**) (0.36 g, 1.0 mmol) was reacted with LDA [generated from diisopropylamine (0.12 g, 1.2 mmol) and butyllithium (15% in hexane; 0.79 ml, 1.3 mmol)] and benzyl bromide (0,21 g, 1.2 mmol) in dry THF (4 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate (**181**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded, as an oil, a diastereomeric mixture of *spiro[bornane-3,2'-indan]-2*-exo-*yl 2,3-diphenylpropanoate* (**185e**) (0.30 g, 68%) (9% d.e.; as determined by ^{1}H NMR spectroscopy), m.p. 56-60 °C (Found:

M^+ 464.2704. $C_{33}H_{36}O_2$ requires *M*, 464.2715); ν_{max}(thin film)/cm^{-1} 1735 (CO); δ_H(400 MHz; $CDCl_3$) 0.42/0.46 (3H, s, 10'-Me), 0.80/0.82 and 0.99/1.04 (6H, 2xs, 8'- and 9'-Me), 0.84-1.70 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 2.22-3.28 (6H, complex of multiplets, $ArCH_2$), 3.62/3.73 and 3.64/3.75 (1H, 2xd, *J* 6.7/6.7, 2-H), 4.53/4.58 (1H, s, 4'-H) and 6.44-7.28 (14H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.3/11.4 (C-10'), 21.6 and 21.88/21.92 (C-8' and C-9'), 23.90/23.94 (C-5'), 33.8/33.9 (C-6'), 38.5/39.3 ($PhCH_2$), 41.4/41.7 and 46.4/46.8 ($ArCH_2$), 49.2 and 51.1/51.2 (C-1' and C-7'), 53.5/54.1 (C-2), 55.7/56.3 (C-4'), 56.6/57.0 (C-3'), 89.2/89.4 (C-2'), 123.2/123.4, 123.5/123.9, 125.8/126.0, 126.07, 126.10/126.21, 127.1, 128.08/128.15, 128.21/128.32, 128.34/128.54, 128.7/128.9, 138.58/138.62, 139.07/139.14, 141.0/141.3 and 143.0/143.5 (Ar-C) and 171.9/172.2 (C-1); *m/z* 464 (M^+, 0.7%) and 181 (100).

Preparation of *spiro[bornane-3,2'-indan]-2*-exo-*yl 2-phenoxy-3-phenylpropanoate* (185f)

Spiro[bornane-3,2'-indan]-2-*exo*-yl phenoxyacetate (**184f**) (0.60 g, 1.5 mmol) was reacted with LDA [generated from diisopropylamine (0.18 g, 1.8 mmol) and butyllithium (15% in hexane; 1.2 ml, 1.9 mmol)] and benzyl bromide (0,31 g, 1.8 mmol) in dry THF (5 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate (**181**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded an oil (0.48 g) comprising a (1:4) mixture of the starting material spiro[bornane-3,2'-indan]-2-*exo*-ol (**183**) and a diastereomeric mixture of *spiro[bornane-3,2'-indan]-2*-exo-*yl 2-phenoxy-3-phenylpropanoate* (**185f**) (50%) (21% d.e.; as determined by ^{1}H NMR spectroscopy). Further purification by PLC [elution with hexane-EtOAc (49:1)] yielded two fractions.

Fraction 1.

A diastereomeric mixture of *spiro[bornane-3,2'-indan]-2*-exo-*yl 2-phenoxy-3-phenylpropanoate* (**185f**) (49% d.e.; as determined by ^{1}H NMR spectroscopy) (Found: M^+ 480.2655. $C_{33}H_{36}O_3$ requires *M*, 480.2664); ν_{max}(thin film)/cm^{-1} 1730 (CO); δ_H(400 MHz; $CDCl_3$) 0.54/0.76 (3H, s, 10'-Me), 0.83/0.89 and 1.03/1.17 (6H, 2xs, 8'- and 9'-Me), 1.21-1.78 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 2.73-3.58 (6H, complex of multiplets, $PhCH_2$ and $ArCH_2$), 4.57-4.62 and 4.66-4.71 (2H, complex of multiplets, 2'- and 2-H) and 6.52-7.28 (14H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.7/11.9 (C-10'), 21.5/21.7 and 21.8/21.9 (C-8' and C-9'), 23.9/24.1 (C-5'), 33.8 (C-6'), 39.0/39.1 (C-3), 41.7/41.8 and 46.7/47.0 ($ArCH_2$), 49.3/49.4

and 51.4/51.6 (C-1' and C-7'), 56.2 (C-4'), 56.7/57.0 (C-3'), 77.2/77.3 (C-2), 90.3/90.5 (C-2'), 114.7/115.3, 121.2/121.5, 123.5, 123.8/124.1, 126.2/126.3, 126.4/126.7, 128.32/128.35, 129.2, 129.3, 129.4, 136.9/137.0, 141.18/141.24, 143.2/143.7 and 157.7/157.8 (Ar-C) and 170.2 (C-1); *m/z* 480 ($\mathbf{M}^+$, 1.0%) and 91 (100).

Fraction 2.

Spiro[bornane-3,2'-indan]-2-*exo*-ol (**183**).

Hydrolysis of *spiro[bornane-3,2'-indan]-2*-exo-*yl 2-methyl-3-phenylpropanoate* (185a)

Method 1.[265]

Spiro[bornane-3,2'-indan]-2-*exo*-yl 2-methyl-3-phenylpropanoate (**185a**) (0.21 g, 0.52 mmol) was added to a solution of lithium hydroxide monohydrate (0.03g, 0.7 mmol) and hydrogen peroxide (0.14 ml, 1.1 mmol) in THF-H_2O (1:1; 4 ml), and the resulting mixture stirred at r.t. for 5 days. The reaction mixture was then diluted with H_2O (20 ml), basified to pH 10 with 33% NH_4OH and extracted with $CHCl_3$ (3x20 ml). The combined organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo* to afford spiro[bornane-3,2'-indan]-2-*exo*-yl 2-methyl-3-phenylpropanoate (**185a**) without any racemisation.[¥] The aqueous fraction was acidified with dil. HCl to pH 1 and extracted with Et_2O (3x20 ml). The combined organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo*, without yielding any significant amount of organic material.

Method 2.

Spiro[bornane-3,2'-indan]-2-*exo*-yl 2-methyl-3-phenylpropanoate (**185a**) (0.18 g, 0.45 mmol) was added to a solution of lithium hydroxide monohydrate (0.060 g, 1.5 mmol), hydrogen peroxide (0.14 ml, 1.1 mmol) and 12-crown-4 (0.13 g, 0.81 mmol) in THF (3 ml), and the mixture was stirred at r.t. for 5 days. The reaction mixture was then diluted with H_2O (20 ml), basified to pH 10 with 33% NH_4OH and extracted with $CHCl_3$ (3x20 ml). The combined organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo* to afford a mixture of spiro[bornane-3,2'-indan]-2-*exo*-yl 2-methyl-3-phenylpropanoate (**185a**) (without any racemisation) and12-crown-4. The aqueous fraction was acidified with dil. HCl to pH 1 and

---

[¥] This was confirmed by integration of the ^1H NMR spectrum of the diastereomeric mixture.

extracted with Et_2O (3x20 ml). The combined organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo*, without yielding any significant amount of organic material.

Method 3.[101]

A solution of spiro[bornane-3,2'-indan]-2-*exo*-yl 2-methyl-3-phenylpropanoate (**185a**) (0.20 g, 0.50 mmol) in a 2**M** solution of KOH in MeOH (3 ml) was boiled under reflux for 3 days. Once cooled to r.t., the reaction mixture was diluted with H_2O (20 ml), basified to pH 10 with 33% NH_4OH and extracted with $CHCl_3$ (3x20 ml). The combined organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo* to yield spiro[bornane-3,2'-indan]-2-*exo*-ol (**183**) (0.14 g, 95%). The aqueous phase was acidified using dil. HCl to pH 1and extracted with Et_2O (3x20 ml). The combined organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo* to yield an enantiomeric mixture of 2-methyl-3-phenylpropanoic acid (**190a**) (0.077 g, 100%) (42% e.e. of the *S*-enantiomer; as determined by optical rotation); $[\alpha]_D^{25}$ +11.3 (*c* 4.3 in benzene) {lit.,[266, 267] $[\alpha]_D^{25}$ +27.06 (*c* 3.7 in benzene, for the *S*-enantiomer)}; ν_{max}(thin film)/cm^{-1} 1710 (CO) and 1450 (OH); δ_H(400 MHz; $CDCl_3$) 1.18 (3H, d, $J_{3,2}$ 6.9, 3-CH_3), 2.67 (1H, dd, $J_{A,B}$ 13.4 and *J* 8.0, CH_2), 2.76 (1H, m, 2-H), 3.08 (1H, dd, $J_{A,B}$ 13.4 and *J* 6.3, CH_2), 7.15-7.33 (5H, complex of multiplets, Ar-H) and 9.67 (1H, br s, OH); δ_C(100 MHz; $CDCl_3$) 16.4 (C-3), 39.3 (Ph*C*H_2), 41.2 (C-2), 126.4, 128.4, 129.0 and 139.0 (Ar-C) and 182.3 (C-1); *m/z* 164 (M^+, 91.8%) and 91 (100).

Method 4.[222]

Spiro[bornane-3,2'-indan]-2-*exo*-yl 2-methyl-3-phenylpropanoate (**185a**) (0.20 g, 0.50 mmol) was added dropwise to conc. H_2SO_4 (0.5 ml). The reaction mixture was then poured onto ice (20 ml), basified to pH 10 with 33% NH_4OH and extracted with Et_2O (3x20 ml). The combined organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo* to yield a complex mixture of products that could not be identified. The aqueous phase was then acidified with dil. HCl to pH 1 and extracted with Et_2O (3x20 ml). The combined organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo* to yield 2-methyl-3-phenylpropanoic acid (**190a**) (0.030 g, 37%) (45% e.e. of the *S*-enantiomer; as determined by optical rotation); $[\alpha]_D^{25}$ +12.3 (*c* 1.5 in benzene).

Hydrolysis of spiro[bornane-3,2'-indan]-2-*exo*-yl 2-benzylbutanoate (185b)

Spiro[bornane-3,2'-indan]-2-*exo*-yl 2-benzylbutanoate (**185b**) (0.083 g, 0.20 mmol) was reacted with conc H_2SO_4 (0.5 ml) as described for the synthesis of the hydrolysis of spiro[bornane-3,2'-indan]-2-*exo*-yl 2-methyl-3-phenylpropanoate (**185a**) (Method 4) to yield 2-benzylbutanoic acid (**190b**) (0.021 g, 58%) (46% e.e. of the *S*-enantiomer; as determined by optical rotation); $[\alpha]_D^{25}$ +18.8 (*c* 1.0 in benzene) {lit.,[266, 268] $[\alpha]_D^{25}$ +40.99 (*c* 2.5 in benzene, for the *S*-enantiomer)}; ν_{max}(thin film)/cm^{-1} 1705 (CO) and 3450 (OH); δ_H(400 MHz; $CDCl_3$) 0.96 (3H, t, *J* 7.4, 4-CH_3), 1.63 (2H, m, 3-CH_2), 2.62 (1H, m, 2-H), 2.76 (1H, dd, $J_{A,B}$ 13.7 and *J* 7.0, PhCH_2), 2.98 (1H, dd, $J_{A,B}$ 13.7 and *J* 7.9, PhCH_2), 7.12-7.31 (5H, m, Ar-H) and 7.85 (1H, br s, OH); δ_C(100 MHz; $CDCl_3$) 11.6 (C-4), 24.8 (C-3), 37.7 (PhCH_2), 48.8 (C-2), 126.4, 128.4, 128.9 and 139.2 (Ar-C) and 139.2 (C-1); *m/z* 178 (**M**$^+$, 79.7%) and 91 (100).

Preparation of *1-{dimethyl(spiro[bornane-3,2'-indan]-2-*exo*-oxy)silyloxy}-3,4-dihydronaphthalene* (194)

Method 1.

Part A.

Preparation of *chloro(3,4-dihydro-1-naphthyloxy)dimethylsilane* (191)

A solution of diisopropylamine (3.24 g, 32.1 mmol) in dry Et_2O (100 ml) was cooled to -78 °C under nitrogen, after which BuLi (15% in hexane; 21.5 ml, 35.2 mmol) was added, and the resulting mixture stirred for 30 min. α-Tetralone (4.53 g, 31.0 mmol) was then added, followed, 1 h later, by Me_2SiCl_2 (4.15 g, 32.1 mmol). The reaction mixture was allowed to warm to r.t. overnight, left to settle and the supernatant solution decanted using a canula. The solvent was removed from the solution by distillation and the residue was distilled to yield *chloro(3,4-dihydro-1-naphthyloxy)dimethylsilane* (**191**) (3.17 g, 43%), b.p. 102-104 °C/0.4 mmHg;[ɬ] δ_H(400 MHz; $CDCl_3$) 0.62 (6H, s, SiMe), 2.37 (2H, dt, 3-CH_2), 2.80 (2H, t, 4-CH_2), 5.46 (1H, t, 2-H), 7.10-7.24 (3H, complex of multiplets, Ar-H) and 7.40 (1H, m, Ar-H); δ_C(100 MHz; $CDCl_3$) 2.3 (SiMe), 22.0 (C-3), 27.9 (C-4), 107.1 (C-2), 121.6, 126.2, 127.1, 127.6, 132.4 and 136.9 (Ar-C) and 146.8 (C-1).

[ɬ] IR and MS data could not be obtained due to the ready decomposition of the chlorosilane.

Part B.

Spiro[bornane-3,2'-indan]-2-*exo*-ol (**183**) (1.6 g, 6.3 mmol) was added to a washed suspension of NaH (50% suspension in oil; 5.00 g, 10.4 mmol) in dry THF (10 ml) under nitrogen and the resulting mixture was boiled under reflux for 2 h. The mixture was allowed to cool before the addition of chloro(3,4-dihydro-1-naphthyloxy)dimethylsilane (**191**) (1.9 g, 8.1 mmol). The resulting suspension was stirred at r.t. overnight, boiled under reflux for 1h, cooled and then quenched with satd. aq. $NaHCO_3$ (20 ml). The mixture was extracted with EtOAc (3x20 ml) and the organic fractions were dried and concentrated *in vacuo*. Flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded, as an oil, *1-{dimethyl(spiro[bornane-3,2'-indan]-2-exo-oxy)silyloxy}-3,4-dihydronaphthalene* (**194**) (2.01 g, 70%) (Found: $\mathbf{M}^+$ 458.2627. $C_{30}H_{38}O_2Si$ requires *M*, 458.2640); $[\alpha]_D^{20}$ +0.14 (*c* 2.2 in $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1635 (C=C), 1245 (SiMe) and 1080 (SiO); δ_H(400 MHz; $CDCl_3$) -0.30 and -0.12 (6H, 2xs, SiMe), 0.90 and 1.26 (6H, 2xs, 8'- and 9'-Me), 0.92 (3H, s, 10'-Me), 1.08-1.22, 1.28-1.30 and 1.51-1.72 (4H, complex of multiplets, 5'- and 6'-CH_2), 1.74 (1H, m, 4'-H), 2.31 (2H, dt, $J_{2,3}$ 4.7 and $J_{3,4}$ 8.0, 3-CH_2), 2.76 (2H, t, $J_{3,4}$ 8.0, 4-CH_2), 2.80 and 2.85 (2H, 2xd, *J* 5.1, $ArCH_2$), 3.25 and 3.67 (2H, 2xd, *J* 15.7, $ArCH_2$), 3.59 (1H, s, 2'-H), 5.25 (1H, t, $J_{2,3}$ 4.7, 2-H), 7.07-7.22 (7H, complex of multiplets, Ar-H) and 7.38 (1H, m, Ar-H); δ_C(100 MHz; $CDCl_3$) -3.5 and -2.7 (SiMe), 12.8 (C-10'), 21.7 and 22.3 (C-8' and C-9'), 22.2 (C-5'), 24.3 (C-3), 28.1 (C-4), 34.1 (C-6'), 41.7 and 47.6 (2x$ArCH_2$), 49.2 and 51.6 (C-1' and C-7'), 56.7 (C-4'), 57.2 (C-3'), 91.3 (C-2'), 105.2 (C-2), 121.9, 123.7, 124.2, 125.8, 126.07, 126.10, 126.8, 127.2, 133.4, 137.0, 141.9 and 144.8 (Ar-C) and 147.4 (C-1); *m/z* 458 ($\mathbf{M}^+$, 13.9%), 327 (10.7), 313 (13.5), 204 (44.6), 203 (43.2), 176 (16.8), 75 (73.4) and 221 (100).

Method 2.

Part A.

A solution of diisopropylamine (1.07 g, 10.5 mmol) in dry THF (30 ml) was cooled to -78 °C under nitrogen, after which BuLi (15% in hexane; 6.7 ml, 11 mmol) was added. The resulting mixture was stirred for 30 min. α-Tetralone (1.39 g, 9.54 mmol) was then added, followed, 1 h later, by Me_2SiCl_2 (1.41 g, 10.9 mmol). The stirred mixture was then warmed to r.t. overnight.

Part B.

In a separate reaction vessel, BuLi (15% in hexane; 4.8 ml, 7.8 mmol) was added dropwise to a stirred solution of spiro[bornane-3,2'-indan]-2-*exo*-ol (**183**) (2.0 g, 7.9 mmol) in dry THF (30 ml) at 0 °C under nitrogen. The stirred mixture was allowed to warm to r.t. overnight. The chlorosilane solution prepared in Part A was then added and the resulting mixture was once again stirred overnight. The reaction was then quenched with satd. aq. $NaHCO_3$ (60 ml) and the resulting mixture was extracted with EtOAc (3x60 ml). The organic fractions were combined, dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded, as an oil, 1-{dimethyl(spiro[bornane-3,2'-indan]-2-*exo*-oxy)silyloxy}-3,4-dihydronaphthalene (**194**) (3.3 g, 72%).

Preparation of *3,3-dimethyl-2-{dimethyl(spiro[bornane-3,2'-indan]-2-*exo*-oxy)silyloxy}but-1-ene* (195)

Method 1.

Part A.

To a solution of diisopropylamine (0.94 g, 9.3 mmol) in dry Et_2O (20 ml), cooled to -78 °C under nitrogen, was added BuLi (15% in hexane; 5.3 ml, 8.7 mmol), and the resulting mixture stirred for 30 min. Pinacolone (0.84 g, 8.5 mmol) was then added, followed, 1 h later, by Me_2SiCl_2 (1.1 g, 8.8 mmol). The stirred reaction mixture was then warmed to r.t. and stirred overnight.

Part B.

In a separate reaction vessel, spiro[bornane-3,2'-indan]-2-*exo*-ol (**183**) (1.1 g, 4.3 mmol) was added to a washed suspension of NaH (50% suspension in oil; 4.0 g, 8.3 mmol) in dry THF (20 ml) under nitrogen and the resulting mixture was boiled under reflux for 2 h. The mixture was allowed to cool before the addition of the chlorosilane solution prepared in Part A. The resulting suspension was stirred at r.t. overnight, boiled under reflux for 1h, and then cooled. The reaction was quenched with satd. aq. $NaHCO_3$ (20 ml). The resulting mixture was extracted with EtOAc (3x20 ml) and the organic fractions were combined, dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded, as an oil, *3,3-dimethyl-2-{dimethyl(spiro[bornane-3,2'-indan]-2-*exo*-oxy)silyloxy}but-1-ene* (**195**) (1.11 g, 63%) (Found: $\mathbf{M}^+$ 412.2779. $C_{26}H_{40}O_2Si$ requires *M*, 412.2798); $[\alpha]_D^{21}$ +6.8 (*c* 2.0 in $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1620 (C=C), 1255 (SiMe) and 1035 (SiO); δ_H(400 MHz; $CDCl_3$) -

0.46 and -0.17 (6H, 2xs, SiMe), 0.85, 0.86 and 1.22 (9H, 3xs, 8'-, 9'- and 10'-Me), 0.99 [9H, s, $C(CH_3)_3$], 1.10-1.17, 1.25-1.29, and 1.50-1.67 (4H, complex of multiplets, 4'- and 5'-CH_2), 1.70 (1H, m, 4'-H), 2.75 and 2.79 (2H, 2xd, *J* 9.3, $ArCH_2$), 3.21 and 3.60 (2H, 2xd, *J* 15.7, $ArCH_2$), 3.50 (1H, s, 2'-H), 3.89 and 4.03 (2H, 2xd, *J* 1.2, 1-CH_2) and 7.03-7.14 (4H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) -4.2 and -2.9 (SiMe), 12.7 (C-10'), 21.7 and 22.3 (C-8' and C-9'), 24.3 (C-5'), 27.9 [$C(CH_3)_3$], 34.1 (C-6'), 36.3 (C-3), 41.6 and 47.6 ($ArCH_2$), 49.2 and 51.6 (C-1' and C-7'), 56.6 (C-4'), 57.3 (C-3'), 86.4 (C-1), 91.2 (C-2'), 123.6, 124.1, 125.7, 126.0, 141.9 and 144.8 (Ar-C) and 166.1 (C-2).[§]

Method 2.

Part A.

Diisopropylamine (1.06 g, 10.6 mmol), BuLi (15% in hexane; 6.7 ml, 11 mmol) pinacolone (0.93 g, 9.4 mmol) and Me_2SiCl_2 (1.42 g, 11.0 mmol) in dry THF (30 ml) were reacted as described for the synthesis of 1-{dimethyl(spiro[bornane-3,2'-indan]-2-*exo*-oxy)silyloxy}-3,4-dihydronaphthalene (**194**) using (Method 2; Part A).

Part B.

Spiro[bornane-3,2'-indan]-2-*exo*-ol (**183**) (1.8 g, 6.9 mmol), BuLi (15% in hexane; 4.8 ml, 7.8 mmol) in dry THF (30 ml) and the chlorosilane formed in part A, were reacted as described for the synthesis of 1-{dimethyl(spiro[bornane-3,2'-indan]-2-*exo*-oxy)silyloxy}-3,4-dihydronaphthalene (**194**) (Method 2; Part B). Work-up and flash chromatography [elution with hexane-EtOAc (49:1)] yielded, as an oil, 3,3-dimethyl-2-{dimethyl(spiro[bornane-3,2'-indan]-2-*exo*-oxy)silyloxy}but-1-ene (**195**) (2.66 g, 94%).

Preparation of *2-{dimethyl(spiro[bornane-3,2'-indan]-2-*exo*-oxy)silyloxy}-1,2,3,4-tetrahydro-1-naphthalone* (196)

1-{Dimethyl(spiro[bornane-3,2'-indan]-2-*exo*-oxy)silyloxy}-3,4-dihydronaphthalene (**194**) (0.51 g, 1.1 mmol) was reacted with MCPBA (55%; 0.40 g, 1.3 mmol) and $NaHCO_3$ (0.28 g, 3.3 mmol) in CH_2Cl_2 (30 ml) at 0 °C as described for the synthesis of 2-[dimethyl(10-pinanyl)silyloxy]-1,2,3,4-tetrahydro-1-naphthalone (**159**). Work-up and flash chromatography of

[§] The molecular ion could not be detected in the mass spectrum of the silyl enol ether (**195**).

the residue [elution with hexane-EtOAc (49:1)] yielded, as an oil, a diastereomeric mixture of *2-{dimethyl(spiro[bornane-3,2'-indan]-2*-exo-*oxy)silyloxy}-1,2,3,4-tetrahydro-1-naphthalone* (**196**) (0.40 g, 75%) (18% d.e.; as determined by ^{1}H NMR spectroscopy);[¥] ν_{max}(thin film)/cm^{-1} 1705 (CO), 1255 (SiMe) and 1065 (SiO); δ_H(400 MHz; $CDCl_3$) -0.38/-0.27 and -0.14/-0.07 (6H, 2xs, SiMe), 0.84/0.86 (3H, s, 10'-Me), 0.86[‡] and 1.19 (6H, 2xs, 8'- and 9'-Me), 1.08-1.24 and 1.48-1.70 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 2.01-2.20 (2H, complex of multiplets, 3-CH_2), 2.71-2.84, 3.15-3.27 and 3.58-3.70 (4H, complex of multiplets, ArCH_2), 2.90-3.03 (2H, m, 4-CH_2), 3.55/3.66 (1H, s, 2'-H), 4.03/4.12 (1H, dd, *J* 4.9 and 12.0, 2-H), 6.83-7.35 (6H, complex of multiplets, Ar-H), 7.40-7.49 (1H, m, Ar-H) and 7.93-8.04 (1H, m, Ar-H); δ_C(100 MHz; $CDCl_3$) -3.4/-2.8 and -2.3/-1.5 (SiMe), 13.00/13.04 (C-10'), 21.74/21.76 and 22.3 (C-8' amd C-9'), 24.18/24.21 (C-5'), 27.87/27.91 (C-4), 32.7/32.8 (C-3), 34.0/34.1 (C-6'), 41.7 and 47.6/47.7 (ArCH_2), 49.1/49.2 and 51.52/51.54 (C-1' and C-7'), 56.86/56.91 (C-3'), 56.95/57.01 (C-4'), 74.5/74.8 (C-2), 90.5/90.7 (C-2'), 123.6/123.8, 123.9/124.1, 125.70/125.72, 126.0/126.1, 126.6, 127.6, 128.45/128.47, 131.8/132.0, 133.2/133.3, 142.0/142.1, 143.4/143.5 and 144.8/144.9 (Ar-C) and 196.9/197.1 (C-1).

Preparation of *2-t-butyl-1,2,3,4-tetrahydro-1-naphthalone* (160)

A solution of 1-{dimethyl(spiro[bornane-3,2'-indan]-2-*exo*-oxy)silyloxy}-3,4-dihydronaphthalene (**194**) (0.51 g, 1.1 mmol) and *t*-BuCl (0.11 g, 1.2 mmol) in dry CH_2Cl_2 (10 ml) was reacted with $TiCl_4$ (0.12 ml, 1.1 mmol) as described in section 3.2.2, p. 142. Work-up and flash chromatography yielded, as an oil, 2-*t*-butyl-1,2,3,4-tetrahydro-1-naphthalone (**160**) (0.13 g, 58%).

[¥] The molecular ion could not be detected in the mass spectrum of the silyl enol ether (**195**) and no high resolution ms data could be obtained for this compound, presumably due to its tendancy to decompose.

[‡] Coincidence with a 10'-Me signal.

The enantiomeric excess was determined as follows:
Addition of $Eu(hfc)_3$ (50 mg) to the enantiomeric mixture of 2-t-butyl-1,2,3,4-tetrahydro-1-naphthalone (**160**) (25 mg) in CCl_4 resulted in a downfield shift and resolution of the respective *t*-Bu signals in the ^1H NMR spectrum. Two other signals, tentatively assigned to the 8-H nuclei, were also resolved. The enantiomeric excess was determined to be 6% by integration of both sets of signals.

Preparation of *1-hydroxy-4,4-dimethyl-1-phenyl-3-pentanone* (163)
3,3-Dimethyl-2-{dimethyl(spiro[bornane-3,2'-indan]-2-*exo*-oxy)silyloxy}but-1-ene (**195**) (0.51 g, 1.2 mmol), $TiCl_4$ (0.14 ml, 1.3 mmol) and PhCHO (0.14 g, 1.3 mmol) in dry CH_2Cl_2 (10 ml) were reacted as described in Section 3.2.2, p. 143. Work-up and flash chromatography yielded, as an oil, 1-hydroxy-4,4-dimethyl-1-phenyl-3-pentanone (**163**) (0.07 g, 26%).

The enantiomeric excess was determined as follows:
i) The addition of $Eu(hfc)_3$ (40 mg) to the enantiomeric mixture of 1-hydroxy-4,4-dimethyl-1-phenyl-3-pentanone (**163**) (11 mg) in $CDCl_3$ resulted in a downfield shift and resolution of the *t*-Bu signals in the ^1H NMR spectrum. The enantiomeric excess was determined to be 0% by integration of the signals.
ii) The addition of $Pr(hfc)_3$ (21 mg) to the enantiomeric mixture of 1-hydroxy-4,4-dimethyl-1-phenyl-3-pentanone (**163**) (11 mg) in $CDCl_3$ resulted in an upfield shift and resolution of the *t*-Bu signals in the ^1H NMR spectrum. The enantiomeric excess was determined to be 5% by integration of the signals.
iii) The optical rotation of the enantiomeric mixture of 1-hydroxy-4,4-dimethyl-1-phenyl-3-pentanone (**163**) was determined as $[\alpha]_D^{21}$ +1.4 (*c* 0.7 in $CHCl_3$) [lit.,[259, 260] $[\alpha]_D^{25}$ + 45.9 ($CHCl_3$), for 75% e.e. of the *R*-enantiomer]. From this data, the enantiomeric excess was determined to be 2%.

3.2.5 Strategies to improve stereofacial selectivity

Preparation of *3-(t-butyldimethylsilyl)-2-bornanone* (202)[183]
To a solution of diisopropylamine (1.82 g, 18.0 mmol) in dry Et_2O (50 ml), cooled to -78 °C under dry nitrogen, was added BuLi (15% in hexane; 11.5 ml, 18.9 mmol). After stirring for 1 h,

(+)-camphor (2.54 g, 16.7 mmol) in dry Et_2O (pre-dried over 4Å molecular sieves; 5 ml) was added, followed, 1 h later, by *t*-$BuMe_2SiCl$ (2.64 g, 17.5 mmol). The reaction mixture was allowed to warm to r.t. overnight and then stirred at r.t. for a further 12 h. The reaction was quenched with satd. aq. $NaHCO_3$ (30 ml) and the resulting mixture extracted with EtOAc (3x30 ml). The combined organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue yielded, as an oil, a diastereomeric mixture of *3-(t-butyldimethylsilyl)-2-bornanone* (**202**) (0.36 g, 8%) (0% d.e.; as determined by ^1H NMR spectroscopy); ν_{max}(thin film)/cm^{-1} 1705 (CO) and 1230 (SiMe); δ_H(400 MHz; $CDCl_3$) -0.09/-0.07 and -0.024/-0.022 (6H, 2xs, SiMe), 0.68/0.75, 0.77/0.78 and 0.82/0.86 (9H, 3xs, 8-, 9- and 10-Me), 0.80/0.84 [9H, s, $C(CH_3)_3$] and 1.16-2.10 (6H, complex of multiplets, 3-H, 4-H and 5- and 6-CH_2); δ_C(100 MHz; $CDCl_3$) -6.9/-6.0 and -5.4/-5.2 (SiMe), 9.3/9.6, 19.1/19.5 and 20.0/21.0 (C-8, C-9 and C-10), 16.94/16.98 [$C(CH_3)_3$], 25.2/29.2 (C-5), 26.1/26.7 [$C(CH_3)_3$], 30.4/30.8 (C-6), 41.6/44.0 and 46.4/46.9 (C-3 and C-4), 46.3/48.8 and 57.3/58.1 (C-1 and C-7) and 219.4/219.6 (C-2); *m/z* 209 (M^+ - C_4H_9, 90.2%) and 75 (100).

Attempted preparation of one diastereoisomer of *3-(t-butyldimethylsilyl)-2-bornanone* (202)

To a solution of diisopropylamine (1.1 mol eq. in dry THF (1 $mol.dm^{-3}$), cooled to -78 °C under dry nitrogen, was added BuLi (15% in hexane; 1.2 mol eq.). After 1h, 3-(*t*-butyldimethylsilyl)-2-bornanone (**202**) (1 mol eq.) was added and the mixture was stirred at -78 °C for 2h before quenching the reaction at -78 °C with excess satd. aq. $NaHCO_3$. The resulting mixture was extracted with Et_2O and the combined organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. ^1H NMR Spectroscopy of the crude reaction mixture indicated a complex mixture of products.

Preparation of *2-(dimethylphenylsilyloxy)-2-bornene* (200)

Camphor (2.30 g, 15.1 mmol) was reacted with LDA [generated from diisopropylamine (1.62 g, 16.2 mmol) and BuLi (15% in hexane; 10 ml, 17 mmol)] and $PhMe_2SiCl$ (2.58 g, 15.1 mmol) in dry Et_2O (60 ml) as described for the synthesis of 2-(*t*-butyldimethylsilyloxy)-2-bornene (**170**) (Section 3.2.3; p. 146). Work-up and vacuum distillation yielded, as an oil, *2-(dimethylphenylsilyloxy)-2-bornene* (**200**) (1.80 g, 42%), b.p. 114 °C/0.5 mmHg; ν_{max}(thin film)/cm^{-1} 1590 (C=C) and 1255 (SiMe); δ_H(400 MHz; $CDCl_3$) 0.48 (6H, s, SiMe), 0.74, 0.87 and 0.95 (9H, 3xs, 8-, 9- and 10-Me), 1.01, 1.13, 1.50 and 1.83 (4H, 4xm, 5- and 6-CH_2), 2.16

(1H, m, 4-H), 4.54 (1H, d, *J* 3.2, 3-H), 7.36-7.45(3H, complex of multiplets, Ar-H) and 7.60-7.65 (2H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) -1.3 (SiMe), 10.0, 19.7 and 20.1 (C-8, C-9 and C-10), 27.2 (C-5), 31.2 (C-6), 49.5 (C-4), 53.4 and 54.8 (C-1 and C-7), 104.0 (C-3), 127.7, 129.6, 133.4 and 137.6 (Ar-H) and 160.1 (C-2); *m/z* 286 (M^+, 10.0%) and 135 (100).

Attempted isomerisation of *2-(t-butyldimethylsilyloxy)-2-bornene* (170)[226]

2-(*t*-Butyldimethylsilyloxy)-2-bornene (**170**) (1 mol eq.) in dry hexane (1 mol.dm^{-3}) was added to a mixture of Bu^{t}OK (2.5 mol eq.) in dry hexane (1 mol.dm^{-3}) and BuLi (15% in hexane; 2 mol eq.) under nitrogen. The mixture was stirred at r.t. for 24h and the reaction was quenched with satd. aq. $NaHCO_3$. The mixture was extracted with EtOAc and the organic fraction dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. ^{1}H NMR analysis of the residue revealed unreacted 2-(*t*-butyldimethylsilyloxy)-2-bornene (**170**).

Attempted isomerisation of *2-(dimethylphenylsilyloxy)-2-bornene* (200)

Method 1.

2-(Dimethylphenylsilyloxy)-2-bornene (**200**) was treated with Bu^{t}OK and BuLi as described for the isomerisation of 2-(*t*-butyldimethylsilyloxy)-2-bornene (**170**). Work-up and ^{1}H NMR spectroscopy revealed the presence of camphor (**22**) together with bis(dimethylphenylsilyl)ether (**206**),[263] which was isolated by flash chromatography [elution with hexane-EtOAc (19:1)]; ν_{max}(thin film)/cm^{-1} 1250 (SiMe) and 1040 (SiO); δ_H(400 MHz; $CDCl_3$) 0.35 (12H, s, SiMe), 7.33-7.42 (6H, complex of multiplets, Ar-H) and 7.54-7.64 (4H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 0.8 (SiMe) and 127.7, 129.2, 133.0 and 139.8 (Ar-C); *m/z* 286 (M^+, 8.5%) and 193 (100)}.

Method 2.

To a solution of 2-(dimethylphenylsilyloxy)-2-bornene (**200**) (1 mol eq.) and $PhMe_2SiCl$ (0.3 mol eq.) in dry CH_2Cl_2 (0.2 mol.dm^{-3}), cooled to -23 °C, was added $TiCl_4$ (0.3 mol eq.). After stirring the reaction mixture at -23 °C for 3h, the reaction was quenched with ice cold water. The aq. layer was then extracted with CH_2Cl_2, and the combined organic fractions were washed with satd. aq. $NaHCO_3$, dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. ^{1}H NMR analysis of the residue showed the presence of camphor (**22**) and bis(dimethylphenylsilyl)ether (**206**). The reaction was also carried out without $PhMe_2SiCl$, but with the same result.

Attempted synthesis of *3-(dimethylphenylsilyl)-2-bornanone* (205)[227] from 3-*endo*-bromocamphor (207)

Part A.

To a solution of diisopropylamine (1.1 mol eq.) in dry THF (1.5 mol.dm^{-3}) cooled to -78 °C under nitrogen was added BuLi (15% in hexane; 1.2 mol eq.) dropwise. After 1 h, 3-*endo*-bromocamphor (1 mol eq.) was added, followed, 1 hour later, by $PhMe_2SiCl$ (1.1 mol eq.). The reaction mixture was allowed to warm to r.t. and stirred for a further 2 hours.

Part B.

The reaction mixture from Part A was cooled to -78 °C before adding BuLi (15% in hexane; 2 mol eq.). The mixture was allowed to warm to r.t. and was then quenched with satd. aq. NH_4Cl. The resulting mixture was extracted with EtOAc and the combined organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. ^{1}H NMR Analysis of the crude reaction mixture indicated the presence of camphor (**22**) and butyldimethylphenylsilane (**208**) [isolated by distillation *in vacuo*, b.p. 45 °C/0.2 mmHg (lit.,[269] 106 °C/19 mmHg); ν_{max}(thin film)/cm^{-1} 1250 (SiMe) and 1110 (SiO); δ_H(400 MHz; $CDCl_3$) 0.28 (6H, s, SiMe), 0.75-0.96 (5H, complex of multiplets, $SiCH_2$ and Me), 1.28-1.43 (4H, complex of multiplets, 2xCH_2), 7.34-7.43 (3H, complex of multiplets, Ar-H) and 7.51-7.57 (2H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) -3.0 (SiMe), 13.7 (Me), 15.4 ($SiCH_2$), 26.1 and 26.5 (CH_2) and 127.7, 128.7, 133.6 and 139.8 (Ar-C)].

Variations of the reaction procedure were investigated. These included boiling the mixture under reflux at the end of Part A. The reaction was also stopped after Part A , and ^{1}H NMR spectroscopy of the residue after work-up revealed the presence of camphor (**22**), bromocamphor (**207**) and the silyl ether (**206**).

Preparation of p-*toluenesulfonylhydrazine* (211a)[270]

A solution of *p*-toluenesulfonyl chloride (20 g, 0.10 mol) in THF (40 ml) was cooled to 10-15 °C. Aq. hydrazine (50%; 0.23 mol) was then added, maintaining the temperature of the mixture ≤15 °C and the resulting mixture was stirred for 15 min. The THF layer was then washed with satd. aq. NaCl (40 ml), dried (anhydr. $MgSO_4$) and concentrated *in vacuo* to yield, as white crystals, *p*-toluenesulfonylhydrazine (**211a**) (13.9 g, 74%), m.p. 108-110 °C (lit.,[270] 104-107 °C) (Found: M^+

186.0457. Calc. for $C_7H_{10}N_2O_2S$: *M*, 186.0463); ν_{max}(thin film)/cm^{-1} 3430, 3260 and 1650 (NH) and 1305 and 1155 (SO_2); δ_H(400 MHz; $CDCl_3$) 2.40 (3H, s, Me), 3.15 (2H, br s, NH_2), 5.62 (1H, s, NH), 7.35 (2H, m, Ar-H) and 7.78 (2H, m, Ar-H); δ_C(100 MHz; $CDCl_3$) 21.6 (Me) and 128.3, 129.9, 133.2 and 144.6 (Ar-C); *m/z* 186 ($\mathbf{M}^+$, 0.5%) and 71 (100).

Preparation of *camphor* p-*toluenesulfonylhydrazone* (212)[271]

A mixture of (+)-camphor (9.81 g, 64.4 mmol) and *p*-toluenesulfonylhydrazine (**211a**) (13.9 g, 74.4 mmol) in EtOH (15 ml) was boiled under reflux for 4 h. The mixture was cooled and filtered, and the EtOH was removed from the filtrate *in vacuo*. The residual crystals were recrystallised from EtOH-$CHCl_3$ to yield, as white crystals, camphor *p*-toluenesulfonylhydrazone (**212**) (15.60 g, 76%), m.p. 163-165 °C (from EtOH-$CHCl_3$) (lit.,[272] 161-162 °C) (Found: $\mathbf{M}^+$ 320.1557. Calc. for $C_{17}H_{24}N_2O_2S$: *M*, 320.1558); ν_{max}(thin film)/cm^{-1} 3450, 3240 and 1640 (NH) and 1355 and 1165 (SO_2); δ_H(400 MHz; $CDCl_3$) 0.47, 0.82 and 0.86 (9H, 3xs, 8-, 9- and 10-Me), 1.03-1.26 (2H, complex of multiplets, 6-CH_2), 1.55-1.79 and 2.18-2.24 (4H, complex of multiplets, 3- and 5-CH_2), 1.86 (1H, m, 4-H), 2.37 (3H, s, Ar-Me), 7.25 (2H, m, Ar-H), 7.57 (1H, br s, NH) and 7.80 (2H, m, Ar-H); δ_C(100 MHz; $CDCl_3$) 10.8, 18.4 and 19.0 (C-8, C-9 and C-10), 21.4 (Ar-CH_3), 27.0 (C-5), 32.0 and 33.6 (C-3 and C-6), 43.8 (C-4), 47.8 (C-7), 52.9 (C-1), 127.9, 129.2, 135.4 and 143.6 (Ar-C) and 171.4 (C-2); *m/z* 320 ($\mathbf{M}^+$, 1.8%) and 165 (100).

Attempted preparation of *2-trimethylsilyl-2-bornene* (214)

To a solution of dry TMEDA (20 ml) and camphor *p*-toluenesulfonylhydrazone (**212**) (1.0 g, 3.1 mmol), cooled to -45 °C, was added BuLi (15% in hexane; 8.8 ml, 14 mmol). The resulting mixture was stirred for 30 min, warmed to r.t and then stirred for a further 2 h. After cooling to 0 °C, Me_3SiCl (1.36 g, 12.5 mmol) was added to the deep red solution and the mixture was stirred at r.t overnight. The reaction was quenched by the addition of pentane (50 ml) and H_2O (50 ml) to the dark solution. The organic fraction was washed sequentially with H_2O (2x50 ml), satd. aq. $CuSO_4$ (50 ml) and brine (50 ml), dried (anhydr. $MgSO_4$) and then concentrated *in vacuo*. ^1H NMR Analysis of the crude reaction mixture indicated a complex mixture of products that could not be separated.

Preparation of *3*-endo-*bromo-2,2-(ethylenedioxy)bornane* (215)[273]

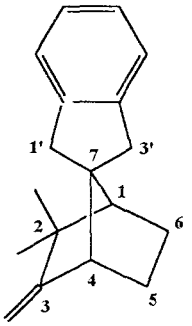
A mixture of (+)-3-*endo*-bromocamphor (**207**) (7.11 g, 30.8 mmol), ethylene glycol (6.7 ml, 0.12 mol) and *p*-toluenesulfonic acid (0.4 g) in toluene (30 ml) was placed in a reaction flask fitted with a Dean-Stark trap and boiled under reflux for 4 days. (During this period approximately 1.0 ml of H_2O was collected.) 1**M** NaOH (50 ml) was then added and the organic phase was washed with H_2O (2x50 ml) and dried (anhydr. $MgSO_4$). The solvent was removed *in vacuo* and flash chromatography of the residual oil [elution with hexane-EtOAc (19:1)] yielded, as an oil, *3*-endo-*bromo-2,2-(ethylenedioxy)bornane* (**215**) (4.86 g, 57%) (Found: $\mathbf{M}^+$ 274.0557. $C_{12}H_{19}O_2Br$ requires *M*, 274.0568); $[\alpha]_D^{20}$ +51.9 (*c* 4.3 in $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1660 (CO); δ_H(400 MHz; $CDCl_3$) 0.78, 0.92 and 1.07 (9H, 3xs, 8-, 9- and 10-Me), 1.29-1.36, 1.54-1.62 and 1.83-1.92 (5H, complex of multiplets, 4-H and 5- and 6-CH_2), 3.71-4.04 (4H, complex of multiplets, OCH_2CH_2O) and 4.50 (1H, dd, *J* 2.1 and 4.2, 3-H); δ_C(100 MHz; $CDCl_3$) 9.7, 20.0 and 20.9 (C-8, C-9 and C-10), 21.5 (C-5), 28.9 (C-6), 46.6 and 52.4 (C-1 and C-7), 52.1 (C-4), 64.4 (C-3), 64.6 and 65.1 (OCH_2CH_2O) and 113.1 (C-2).

Attempted preparation of *2,2-(ethylenedioxy)-3-(dimethylphenylsilyl)bornane* (216)

Zinc dust was activated by washing the zinc powder with 3% HCl (3x8 ml), H_2O and acetone and drying *in vacuo* at 100 °C for 2h. To a slurry of the activated zinc powder (0.10 g, 1.5 mmol) in dry DMSO (2 ml) was added 3-*endo*-bromo-2,2-(ethylenedioxy)bornane (**215**) (1.1 g, 4.0 mmol) over a period of 30 min, followed by $PhMe_2SiCl$ (0.41 ml, 3.6 mmol) and the resulting mixture was stirred at r.t. overnight. The reaction was quenched by the addition of satd. aq. $NaHCO_3$ (20 ml) and the mixture was extracted with EtOAc (3x20 ml). The combined organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue yielded 3-*endo*-bromo-2,2-(ethylenedioxy)bornane (**215**) (0.66 g, 67%) and bis(dimethylphenylsilyl)ether (**206**) (0.45 g, 44%).

Preparation of *spiro[camphene-7,2'-indan]* (219)

Method 1.[274]

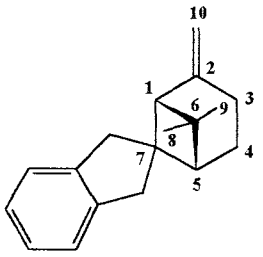


A mixture of spiro[bornane-3,2'-indan]-2-*exo*-ol (**183**) (2.0 g, 7.8 mmol), $SOCl_2$ (1.1 ml, 16 mmol) and pyridine (0.62 g, 7.8 mmol) was stirred at r.t for 4 h. The reaction was quenched by the addition of 5% NaOH (25 ml) and the resulting mixture was extracted with EtOAc (3x25 ml). The combined organic fractions were washed with water (2x30 ml), dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue [elution with hexane-EtOAc (19:1)] yielded, as an oil, *spiro[camphene-7,2'-indan]* (**219**) (0.95 g, 51%) (Found: $\mathbf{M}^+$ 238.1731. $C_{18}H_{22}$ requires *M*, 238.1721); $[\alpha]_D^{27}$ +13.2 (*c* 2.1 in $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1660 (C=C); δ_H(400 MHz; $CDCl_3$) 1.13 and 1.26 (6H, 2xs, Me), 1.37 (1H, m, 6_{endo}-H), 1.64 (1H, m, 5_{exo}-H), 1.73 (1H, m, 4-H), 1.82 (1H, m, 5_{endo}-H), 1.94 (1H, m, 6_{exo}-H), 2.26 (1H, m, 1-H), 2.92 (2H, s, 3'-CH_2), 2.95 and 3.12 (2H, 2xd, 1'-CH_2), 4.69 (2H, d, C=CH_2) and 7.09-7.20 (4H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 24.4 (C-5), 26.7 (C-6), 29.3 and 29.6 (Me), 39.2 (C-3'), 40.4 (C-1'), 41.7 (C-2), 52.4 (C-1), 54.9 (C-4), 59.3 (C-7), 101.5 (C=CH_2), 124.1, 124.3, 125.88, 125.93, 142.1 and 143.7 (Ar-C) and 166.4 (C-3); *m/z* 238 ($\mathbf{M}^+$, 24.4%) and 155 (100).

Method 2.

Butyllithium (15% solution in hexane; 5.7 ml, 9.4 mmol) was added dropwise to a stirred solution of spiro[bornane-3,2'-indan]-2-*exo*-ol (**183**) (2.1 g, 8.4 mmol) in dry THF (50 ml) under nitrogen, at 0 °C. After 1 h, *p*-toluenesulfonyl chloride (1.8 ml, 9.6 mmol) was added and the stirred mixture allowed to warm to r.t. overnight and then boiled under reflux for 1h. After cooling to r.t., the reaction was quenched with satd. aq. $NaHCO_3$ (50 ml) and the resulting mixture extracted with EtOAc (3x50 ml). The combined organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue [elution with hexane-EtOAc (19:1)] afforded, as an oil spiro[camphene-7,2'-indan] (**219**) (1.26 g, 64%).

Preparation of *spiro[β-pinene-7,2'-indan]* (221)



Butyllithium (15% solution in hexane; 5.2 ml, 8.4 mmol) was added dropwise to a stirred solution of spiro[bornane-3,2'-indan]-2-*exo*-ol (**183**) (2.2 g, 8.4 mmol) in dry THF (50 ml) under nitrogen, at 0 °C. After 1 h, *p*-toluenesulfonyl chloride (1.8 ml, 9.6 mmol) was added and the stirred mixture allowed to warm to r.t. overnight. The reaction was then quenched with satd. aq. $NaHCO_3$ (50 ml) and the resulting mixture extracted with EtOAc (3x50 ml). The combined organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue [elution with hexane-EtOAc (19:1)] afforded, as an oil, *spiro[β-pinen-7,2'-indan]* (**221**) (1.32 g, 65.8%), m.p. 60-63 °C; (Found: $\mathbf{M}^+$ 238.1723. $C_{18}H_{22}$ requires *M*, 238.1723); $[\alpha]_D^{26}$ +34.1 (*c* 2.0 in $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1655 (C=C); δ_H(400 MHz; $CDCl_3$) 1.09 and 1.10 (6H, 2xs, 8- and 9-Me), 1.54-1.63 (2H, complex of multiplets, 3- and 4-CH_2), 1.74-1.82 (2H, complex of multiplets, 3- and 4-CH_2), 1.90 (1H, m, 5-H), 2.34 (1H, br s, 1-H), 2.68 and 3.08 (2H, 2xd, *J* 15.9, Ar-CH_2), 2.82 and 2.95 (2H, 2xs, *J* 15.6, Ar-CH_2), 4.73 (2H, d, *J* 7.0, 10-CH_2), 7.08-7.17 (4H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 25.1 and 30.1 (C-8 and C-9), 37.1 and 39.8 (C-3 and C-4), 41.6 (C-6), 43.4 and 49.2 (ArCH_2), 48.6 (C-1), 49.3 (C-7), 56.7 (C-5), 103.4 (C-10), 124.15, 124.18, 125.9, 126.0, 142.9 and 143.6 (Ar-C) and 161.8 (C-2); *m/z* 238 ($\mathbf{M}^+$, 44.5%) and 129 (100).

Preparation of *spiro[bornane-3,2'-indan]-2-*exo*-yl acetate* (222)

Spiro[bornane-3,2'-indan]-2-*exo*-ol (**183**) (1.4 g, 5.5 mmol) was treated with butyllithium (15% solution in hexane; 3.6 ml, 5.9 mmol) and acetyl chloride (0.57 ml, 7.9 mmol) in dry THF (20 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (19:1)] yielded, as an oil, *spiro[bornane-3,2'-indan]-2-*exo*-yl acetate* (**222**) (1.00 g, 61%) (Found: $\mathbf{M}^+$ 298.1922. $C_{20}H_{26}O_2$ requires *M*, 298.1933); $[\alpha]_D^{27}$ +3.4 (*c* 2.0 in $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1745 (C=O); δ_H(400 MHz; $CDCl_3$) 0.78 (3H, s, 10'-Me), 0.90 and 1.22 (6H, 2xs, 8'- and 9'-Me), 1.27-1.38 and 1.49-1.72 (4H, complex of multiplets, 5'- and 6'-CH_2), 1.76 (1H, m, 4'-H), 1.82 (3H, s,

2-Me), 2.85 and 3.38 (2H, 2xd, *J* 15.6, $ArCH_2$), 2.93 and 3.15 (2H, 2xd, *J* 15.3, $ArCH_2$), 4.63 (1H, s, 2'-H) and 7.04-7.18 (4H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.6 (C-10'), 20.6 (C-2), 21.8 and 22.0 (C-8' and C-9'), 24.0 (C-5'), 33.9 (C-6'), 41.7 and 46.6 (Ar-CH_2), 49.3 and 50.8 (C-1' and C-7'), 55.8 (C-4'), 57.2 (C-3'), 88.6 (C-2'), 123.0, 124.0, 126.10, 126.13, 141.3 and 141.6 (Ar-C) and 169.7 (C-1); *m/z* 298 ($\mathbf{M}^+$, 4.1%) and 4.3 (100).

Preparation of *camphorquinone* (223)

A mixture of (+)-camphor (40 g, 0.24 mol) and SeO_2 (50 g, 0.45 mol) in acetic anhydride (40 ml) was boiled under reflux for 5 h and then left stirring overnight at r.t. The suspended black selenium powder was removed by filtration, and the filtrate neutralised with 10% aq. NaOH. The resulting yellow precipitate was filtered off, washed with H_2O and suction dried. The semi-dry material was recrystallised from petroleum ether (80-100 °C) affording, as bright yellow needles, camphorquinone (**223**) (28.8 g, 63%), m.p. 179-181 °C [from petroleum ether (80-100 °C)] (lit.,[275] 183-186 °C); ν_{max}(KBr)/cm^{-1} 1770 and 1750 (CO); δ_H(400 MHz; $CDCl_3$) 0.90, 1.04 and 1.09 (9H, 3xs, 8-, 9- and 10-Me), 1.57-2.19 (4H, complex of multiplets, 5- and 6-CH_2) and 2.59-2.61 (1H, m, 4-H).

Preparation of *3*-exo-*hydroxy-2-bornanone* (224)[275]

Camphorquinone (**223**) (6.14 g, 36.9 mmol) and Raney nickel (3.50 g) in EtOH (200 ml) were stirred under an atmosphere of nitrogen at r.t. overnight. The resultant suspension was filtered through celite and the filtrate concentrated *in vacuo* to yield, as white chrystals, 3-*exo*-hydroxy-2-bornanone (**224**) (6.10 g, 98%), m.p. 196-198 °C (lit.,[275] 209-211 °C) (Found: $\mathbf{M}^+$ 168.1161. Calc. for $C_{10}H_{16}O_2$: *M*, 168.1150); ν_{max}(thin film)/cm^{-1} 3400 (OH) and 1745 (C=O); δ_H(400 MHz; $CDCl_3$) 0.92, 0.94 and 0.97 (9H, 3xs, 8-, 9- and 10-Me), 1.31-1.49, 1.60-1.71 and 1.94-2.04 (4H, complex of multiplets, 3- and 4-CH_2), 2.08 (1H, m, 4-H), 2.29 (1H, br s, OH) and 3.75 (1H, s, 3-H); *m/z* 168 ($\mathbf{M}^+$, 5.2%) and 43 (100).

Preparation of *2,2-(ethylenedioxy)-3*-exo-*bornanol* (225)

3-*exo*-Hydroxy-2-bornanone (**224**) (5.96 g, 35.4 mmol), ethylene glycol (4.1 ml, 74 mmol) and *p*-toluenesulfonic acid (0.4 g) in benzene (30 ml) were reacted as described for the synthesis of 3-*endo*-bromo-2,2-(ethylenedioxy)bornane (**215**), boiling under reflux for 24h. Work-up and flash chromatography [elution with hexane-EtOAc (4:1)] yielded, as white crystals, 2,2-(ethylenedioxy)-3-*exo*-bornanol (**225**)[233] (4.43 g, 59%), m.p. 150-152 °C (Found: $\mathbf{M}^+$ 212.1424. Calc. for $C_{12}H_{20}O_3$: *M*, 212.1412); ν_{max}(thin film)/cm^{-1} 3450 (OH); δ_H(400 MHz; $CDCl_3$) 0.80, 0.82 and 1.06 (9H, 3xs, 8-, 9- and 10-Me), 1.08-1.17, 1.27-1.37 and 1.63-1.84 (5H, complex of multiplets, 5- and 6-CH_2 and 4-H), 2.51 (1H, d, OH), 3.43 (1H, d, 3-H) and 3.70-4.06 (4H, complex of multiplets, OCH_2); δ_C(100 MHz; $CDCl_3$) 9.3, 21.2 and 21.6 (C-8, C-9 and C-10), 24.6 (C-5), 29.1 (C-6), 47.7 and 51.8 (C-1 and C-7), 51.6 (C-4), 63.9 and 66.6 (OCH_2), 83.1 (C-3) and 117.0 (C-2); *m/z* 212 ($\mathbf{M}^+$, 7.9%) and 73 (100).

Preparation of *2,2-(ethylenedioxy)-3*-exo-*bornyl* p-*toluenesulfonate* (226)

2,2-(Ethylenedioxy)-3-*exo*-bornanol (**225**) (2.48 g, 11.7 mmol) was treated with butyllithium (15% solution in hexane; 8.6 ml, 14 mmol) and *p*-toluenesulfonyl chloride (2.59 g, 13.6 mmol) in dry THF (50 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (19:1)] yielded, as an oil, *2,2-(ethylenedioxy)-3*-exo-*bornyl* p-*toluenesulfonate* (**226**) (3.82 g, 89%), m.p. 89-91 °C (Found: $\mathbf{M}^+$ 366.1478. $C_{19}H_{26}O_5S$ requires *M*, 366.1495); $[\alpha]_D^{26}$ -4.4 (*c* 3.5 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 0.75, 0.76 and 1.07 (9H, 3xs, 8-, 9- and 10-Me), 1.07-1.14, 1.24-1.35 and 1.62-1.83 (5H, complex of multiplets, 5- and 6-CH_2 and 4-H), 2.42 (3H, s, Ar-C*H*$_3$), 3.58-3.67, 3.76-3.88 and 3.90-3.96 (4H, complex of multiplets, OCH_2), 4.18 (1H, s, 3-H) and 7.32 and 7.76 (4H, 2xd, *J* 8.1, Ar-H); δ_C(100 MHz; $CDCl_3$) 9.2 (C-10), 20.7 and 21.6 (C-8, C-9 and Ar-Me[¥]), 24.4 (C-5), 28.6 (C-6), 48.0 and 52.1 (C-1 and C-7), 50.1 (C-4), 63.6 and 66.4 (OCH_2), 89.7 (C-3), 115.8 (C-2) and 127.6, 129.7, 134.5 and 144.5 (Ar-C).

[¥] Two of the methyl signals coalesce in the ^{13}C NMR spectrum.

Attempted silylation of the camphor derivatives *3*-endo-*bromo-2,2-(ethylenedioxy)bornane* (215), *2,2-(ethylenedioxy)-3*-exo-*bornyl* p-*toleunesulfonate* (226) and *spiro[bornane-3,2'-indan]-2*-exo-*yl acetate* (222)

Method 1.

Part A.[235]

Lithium shot (3 mol eq.) was added to a solution of $PhMe_2SiCl$ (1 mol eq.) in dry THF (0.4 $mol.dm^{-3}$) at 0 °C. The resulting solution was allowed to warm to r.t. overnight to yield a deep red solution of phenyldimethylsilyllithium.

Part B.[235]

To a solution of the chiral auxiliary 3-*endo*-bromo-2,2-(ethylenedioxy)bornane (**215**) or 2,2-(ethylenedioxy)-3-*exo*-bornyl *p*-toluenesulfonate (**226**) (1 mol eq.) in THF (0.3 $mol.dm^{-3}$) was added the deep red solution of phenyldimethylsilyllithium (formed in Part A; 1.1 eq.) at -5 °C. The reaction mixture was stirred for 30 min before quenching with satd. aq. NH_4Cl. The resulting solution was extracted with EtOAc and the organic fraction dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. In each case, ^1H NMR analysis of the residue showed the presence of the unreacted chiral auxiliary and bis(dimethylphenylsilyl)ether (**206**).

Method 2.

The deep red solution of phenyldimethylsilyllithium (formed as described in Method 1, Part A; 1 mol eq.) was added to a mixture of 3-*endo*-bromo-2,2-(ethylenedioxy)bornane (**215**) (1 mol eq.) and silver acetate (1 mol eq.) in dry THF (5 $mol.dm^{-3}$) at 0 °C and the resulting mixture was stirred for 30 min before quenching with satd. aq. $NaHCO_3$. The mixture was extracted with EtOAc and the organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. ^1H NMR Analysis of the residue showed the presence of unreacted 3-*endo*-bromo-2,2-(ethylenedioxy)bornane (**215**) and bis(dimethylphenylsilyl)ether (**206**).

Method 3.[236]

To a solution of phenyldimethylsilyllithium (formed as described in Method 1, Part A; 2.5 mol eq.) was added CuI (purified by boiling under reflux overnight in CH_2Cl_2 using a Soxhlet apparatus; 1.2 mol eq.) at 0 °C and stirred for 20 min. This was followed by the addition of 3-*endo*-bromo-2,2-(ethylenedioxy)bornane (**215**) (1 mol eq.) at 0 °C. The reaction mixture was

stirred for a further 20 min before quenching with satd. aq. NH_4Cl. The resulting mixture was extracted (EtOAc), and the organic fraction dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. ^1H NMR Analysis of the residue showed the presence of unreacted 3-*endo*-bromo-2,2-(ethylenedioxy)bornane (**215**) and bis(dimethylphenylsilyl)ether (**206**).

Method 4.[276]

To a solution of phenyldimethylsilyllithium (formed as described in Method 1, Part A; 4 mol eq.) cooled to 0 °C, was added CuCN (2 mol eq.) and the reaction mixture was then stirred for 20 min. This was followed by adding, in separate reactions at 0 °C, one of the chiral auxiliaries 3-*endo*-bromo-2,2-(ethylenedioxy)bornane (**215**), 2,2-(ethylenedioxy)-3-*exo*-bornyl *p*-toluenesulfonate (**226**) or spiro[bornane-3,2'-indan]-2-*exo*-yl acetate (**222**). (The various reaction times used are summarised in Table 1). The reaction mixture was then quenched by the addition of satd. aq. NH_4Cl and extracted with EtOAc. The organic fraction was dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. ^1H NMR Analysis of the residue, in each case, showed the presence of the unreacted chiral auxiliary and bis(dimethylphenylsilyl)ether (**206**).

TABLE 1. The reaction conditions used in the attempted silylation of the chiral auxiliaries (**215**), (**226**) and (**222**).

Entry	Chiral auxiliary	Reaction Time
1	215	0 °C, 4h; r.t., overnight
2	215	0 °C, 4h; r.t., 4 days
3	226	0 °C, 5h
4	226	0 °C, 4h; r.t., overnight
5	222	0 °C, 4h; r.t., overnight

Attempted α,α-dialkylations of camphor (22)

Method 1.

Camphor (2.11 g, 13.8 mmol) was added to a pre-washed suspension of NaH (1.40 g, 29.2 mmol) in toluene (50 ml) and the resulting mixture boiled under reflux for 1h. After cooling to r.t., benzyl bromide (3.6 ml, 30 mmol) was added and the mixture boiled under reflux for a further 4h. After stirring at r.t. overnight, the resulting suspension was quenched by the addition

of satd. aq. $NaHCO_3$ (50 ml) and extracted with EtOAc (3x50 ml). The organic fraction was dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. Vacuum distillation of the residue yielded, as an oil, 3-*endo*-benzyl-2-bornanone (**173**) (1.01 g, 30%), b.p. 180-182 °C/0.1 mmHg.

Method 2.

The procedure described in Method 1 was repeated, replacing benzyl bromide, in turn, with 2 eq. of 1-bromo-2-methylpropane (**228a**), 2 eq. of 2-bromopropane (**228b**) and triphenylchloromethane (**228c**). In all three cases, camphor was isolated after work-up.

Attempted α-alkylation of 3-*endo*-benzyl-2-bornanone (173)

Method 1.

To a pre-washed suspension of NaH (0.95 g, 20 mmol) in toluene (50 ml), was added 3-*endo*-benzyl-2-bornanone (**173**) (4.05 g, 16.7 mmol) and benzyl bromide (2.4 ml, 20 mmol) as described for the synthesis of 3-*endo*-benzyl-2-bornanone (**173**). Work-up and ^1H NMR analysis of the residue showed the presence of benzyl bromide and 3-*endo*-benzyl-2-bornanone (**173**).

Method 2.

3-*endo*-Benzyl-2-bornanone (**173**) (2.0 g, 8.3 mmol) in dry Et_2O (30 ml) was reacted with BuLi (15% solution in hexane; 5.0 ml, 8.3 mmol) and benzyl bromide (1.2 ml, 9.9 mmol) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**). Work-up and ^1H NMR analysis of the residue showed the presence of benzyl bromide and 3-*endo*-benzyl-2-bornanone (**173**).

Preparation of *pinacol* (231)[243]

A solution of $Hg(II)Cl_2$ (11.3 g, 41.4 mmol) in acetone (25 g, 0.43 mol) was added dropwise to a suspension of Mg turnings (10 g, 0.41 mol) in dry benzene (500 ml) to maintain gentle reflux. This was followed by the addition of a solution of acetone (25 g, 0.43 mol) in dry benzene (25 ml). The reaction mixture was then boiled under reflux, on a water bath, until all the magnesium had disappeared (3h). Water (25 ml) was added *via* the dropping funnel and the mixture was boiled under reflux for a further 1h. The mixture was then cooled and filtered and the isolated precipitate was boiled under reflux for a further 10 min in fresh benzene (60 ml), cooled and filtered. The filtrate fractions were combined and concentrated to half the volume *in vacuo*.

Water (40 ml) was added to the concentrated residue and the solution cooled on an ice bath. The resulting suspension was then filtered, and the water removed from the isolated crystals by an azeotropic distillation in benzene. Finally, distillation yielded, as white crystals, pinacol (**231**) (17 g, 37%), b.p. 175-177 °C (lit.,[243] 169-173 °C); δ_H(400 MHz; $CDCl_3$) 1.20 (12H, s, Me) and 2.18 (2H, s, OH); δ_C(100 MHz; $CDCl_3$) 24.8 (CH_3) and 75.0 (COH).

Attempted ketalisation of camphorquinone (223) using pinacol (231)

Camphorquinone (**223**) (1.0 g, 6.2 mmol), pinacol (**231**) (1.53 g, 12.9 mmol) and *p*-toluenesulfonic acid (0.05 g) in benzene (10 ml) were reacted as described for the synthesis of 3-*endo*-bromo-2,2-(ethylenedioxy)bornane (**215**). Work-up and ^{1}H NMR analysis of the residue showed the presence of unreacted camphorquinone (**223**).

3.2.6 The Camphor-derived chiral auxiliary (235a)[§]

Preparation of *3,3-[(2R,3S)-2-*endo*,3-*exo*-butanedioxy]-2-bornanone* (234)

A mixture of camphorquinone (**223**) (9.39 g, 56.5 mmol), *meso*-2,3-butanediol (10.0 g, 113 mmol) and *p*-toluenesulfonic acid (0.5 g) in benzene (60 ml) was placed in a reaction vessel fitted with a Dean-Stark trap and boiled under reflux for 4 days. During this period, approximately 1.5 ml of H_2O was collected. The reaction mixture was then treated with 1**M** NaOH (50 ml) and the organic layer was washed with H_2O (2x50 ml) and dried (anhyd. $MgSO_4$). The solvent was removed *in vacuo* and flash chromatography of the residual oil [elution with hexane-EtOAc (19:1)] yielded *3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-bornanone* (**234**) (8.37 g, 62%)[¥] (Found: $\mathbf{M}^+$ 238.1584. $C_{14}H_{22}O_3$ requires *M*, 238.1569); ν_{max}(thin film)/cm^{-1} 1750 (CO); δ_H(400 MHz; $CDCl_3$) 0.89, 0.94 and 0.96 (9H, 3xs, 8-, 9- and 10-Me), 1.18 and 1.19 (6H, 2xd, 1'- and 4'-Me), 1.46-1.94 (5H, complex of multiplets, 4-H and 5- and 6-CH_2) and 4.14 (2H, m, 2'-and 3'-H); δ_C(100 MHz; $CDCl_3$) 9.4, 19.4 and 21.5 (C-8, C-9 and C-10), 14.8 and 14.9 (C-1' and C-4'), 20.8 (C-5), 30.6 (C-6), 43.4 and 57.6 (C-1 and C-7), 52.3 (C-4), 75.3 and 75.6 (C-2' and C-3'), 106.7 (C-3) and 215.9 (C-2); *m/z* 238 ($\mathbf{M}^+$, 1.9%) and 127 (100).

[§] The *exo*- and *endo*- nomenclature is used to distinguish between the two possible configurations at the pseudo-asymmetric centre (C-3) of the camphor skeleton.

[¥] Obtained as a mixture, shown by NMR spectroscopy, to contain predominantly compound (**234**) (80%).

Preparation of *3,3-[(2R,3S)-2-*endo,*3-*exo-*butanedioxy]-2-*exo-*bornanol* (235a)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-bornanone (**234**) (80%; 7.51 g, 31.5 mmol) was treated with $LiAlH_4$ (0,77 g, 20 mmol) in dry Et_2O (30 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornanol (**172**). Work-up and flash chromatography of the residual oil [elution with hexane-EtOAc (19:1)] yielded, as an oil, *3,3-[(2*R,*3*S*)-2-*endo,*3-*exo-*butanedioxy]-2-*exo-*bornanol* (**235a**) (5.49 g, 73%) (Found: $\mathbf{M}^+$ 240.1714. $C_{14}H_{24}O_3$ requires *M*, 240.1720); $[\alpha]_D^{19}$ +2.7 (*c* 2.1 in $CHCl_3$); ν_{max}(thin film)/cm^{-1} 3650-3450 (OH); δ_H(400 MHz; $CDCl_3$) 0.89 (3H, s, 10-Me), 0.98 and 1.04 (6H, 2xs, 8- and 9-Me), 1.12 and 1.13 (6H, 2xd, *J* 6.4 and 6.4, 1'- and 4'-Me), 1.47-1.69 (5H, complex of multiplets, 4-H and 5- and 6-CH_2), 2.59 (1H, d, *J* 4.7, OH), 3.31 (1H, d, *J* 4.7, 2-H), and 4.07 and 4.20 (2H, 2xm, 2'- and 3'-H); δ_C(100 MHz; $CDCl_3$) 10.9 (C-10), 14.6 and 15.1 (C-1' and C-4'), 20.4 (C-5), 21.1 and 21.6 (C-8 and C-9), 33.5 (C-6), 47.6 and 49.3 (C-1 and C-7), 52.8 (C-4), 73.7 and 74.8 (C-2' and C-3'), 85.2 (C-2) and 113.7 (C-3); *m/z* 240 ($\mathbf{M}^+$, 50.8%) and 155 (100).

Attempted preparation of the hydrazone of *3,3-[(2*R,*3*S*)-2-*endo,*3-*exo-*butanedioxy]-2-bornanone* (234)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-bornanone (**234**) and *p*-toluenesulfonylhydrazine (**211a**) or, in a separate reaction, 2,4-dinitrophenylhydrazine (**211b**) were reacted as described for the synthesis of camphor *p*-toluenesulfonylhydrazone (**212**). Removal of the EtOH *in vacuo* without prior workup, and ^1H NMR analysis of the residues showed the presence of the unreacted starting materials.

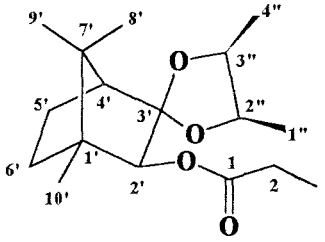
Attempted preparation of *2-{3,3-[(2*R,*3*S*)-2-*endo,*3-*exo-*butanedioxy]-2-*exo-*bornyloxymethyl}naphthalene* (237)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornanol (**235a**) (1.1 g, 4.5 mmol) was treated with butyllithium (15% solution in hexane; 2.5 ml, 4.2 mmol) and 2-(bromomethyl)naphthalene (1.1 g, 5.0 mmol) in dry Et_2O (40 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**). Work-up and ^1H NMR spectroscopy of the residue showed the presence of unreacted 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornanol (**235a**) and 2-(bromomethyl)naphthalene.

Preparation of *3,3-[(2R,3S)-2-*endo,*3-*exo-*butanedioxy]-2-*exo-*bornyl 2,4-dinitrobenzoate* (238)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornanol (**235a**) (0.59 g, 2.4 mmol) was treated with butyllithium (15% solution in hexane; 1.3 ml, 2.1 mmol) and 2,4-dinitrobenzoyl chloride (0.64 g, 2.8 mmol) in dry Et_2O (20 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (9:1)] yielded, as white crystals, *3,3-[(2*R,*3*S*)-2-*endo,*3*-exo-*butanedioxy]-2*-exo-*bornyl 2,4-dinitrobenzoate* (**238**) (0.76 g, 72%), m.p. 132-133 °C (from hexane) (Found: $\mathbf{M}^+$ 434.1684. $C_{21}H_{26}O_8N_2$ requires *M*, 434.1689); $[\alpha]_D^{20}$ -18.0 (*c* 1.1 in $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1725 (C=O) and 1540 and 1340 (NO_2); δ_H(400 MHz; $CDCl_3$) 0.89, 0.90 and 1.31 (9H, 3xs, 8-, 9-, and 10-Me), 0.90 and 1.09 (6H, 2xd, *J* 6.3 and 6.3, 1'- and 4'-Me), 1.40-1.47, 1.53-1.70 and 1.78-1.83 (5H, complex of multiplets, 5- and 6-CH_2 and 4-H), 4.07-4.14 (2H, 2xm, 2'- and 3'-H), 4.93 (1H, s, 2-H), 9.14 (2H, m, Ar-H) and 9.19 (1H, m, Ar-H) ; δ_C(100 MHz; $CDCl_3$) 11.4 (C-10), 14.8 and 15.2 (C-1' and C-4'), 20.3 (C-5), 20.8 and 21.1 (C-8 and C-9), 33.5 (C-6), 48.3 and 49.1 (C-1 and C-7), 53.1 (C-4), 73.7 and 74.3 (C-2' amd C-3'), 87.9 (C-2), 113.0 (C-3), 122.2, 129.4, 134.5 and 148.8 (Ar-C) and 161.9 (C=O); *m/z* 434 ($\mathbf{M}^+$, 17.1%) and 155 (100%).

Preparation of *3,3-[(2R,3S)-2-*endo,*3-*exo-*butanedioxy]-2-*exo-*bornyl propanoate* (239a)



3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornanol (**235a**) (1.1 g, 4.5 mmol) was treated with butyllithium (15% solution in hexane; 2.5 ml, 4.2 mmol) and propanoyl chloride (**186a**) (0.46 g, 4.9 mmol) in dry Et_2O (20 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (19:1)] yielded, as an oil, *3,3-[(2*R,*3*S*)-2-*endo,*3*-exo-*butanedioxy]-2*-exo-*bornyl propanoate* (**239a**) (0.99 g, 75%) (Found: $\mathbf{M}^+$ 296.1979. $C_{17}H_{28}O_4$ requires *M*, 296.1988); $[\alpha]_D^{22}$ -29.5 (*c* 2.1 in $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1740 (CO); δ_H(400 MHz; $CDCl_3$) 0.77 (3H, s, 10'-Me). 0.82 and 1.13 (6H, 2xs, 8'- and 9'-Me), 0.99 and 1.07 (6H,

2xd, *J* 6.3 and 6.3, 1"- and 4"-Me), 1.16 (3H, t, *J* 7.6, 3-Me), 1.31-1.77 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 2.35 (2H, q, *J* 7.6, 2-CH_2), 3.99 and 4.10 (2H, 2xm, 2"- and 3"-H) and 4.66 (1H, s, 2'-H); δ_C(100 MHz; $CDCl_3$) 9.4 (C-10'), 11.1 (C-3), 14.8 and 15.1 (C-1" and C-4"), 20.3 (C-5'), 20.8 and 21.1 (C-8' and C-9'), 28.0 (C-2), 33.5 (C-6'), 48.0 and 48.7 (C-1' and C-7'), 53.3 (C-4'), 73.4 and 74.2 (C-2" and C-3"), 85.0 (C-2'), 113.3 (C-3') and 173.5 (C-1); *m/z* 296 ($\mathbf{M}^+$, 5.5%) and 155 (100).

Preparation of *3,3-[(2R,3S)-2-*endo,*3-*exo-*butanedioxy]-2-*exo-*bornyl butanoate* (239b)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornanol (**235a**) (1.1 g, 4.4 mmol) was treated with butyllithium (15% solution in hexane; 2.5 ml, 4.2 mmol) and butanoyl chloride (**186b**) (0.53 g, 4.9 mmol) in dry Et_2O (20 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (19:1)] yielded, as an oil, *3,3-[(2*R,*3*S*)-2-*endo,*3-*exo-*butanedioxy]-2-*exo-*bornyl butanoate* (**239b**) (0.96 g, 71%) (Found: $\mathbf{M}^+$ 310.2143. $C_{18}H_{30}O_4$ requires *M*, 310.2144); $[\alpha]_D^{22}$ -26.7 (*c* 1.8 in $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1740 (CO); δ_H(400 MHz; $CDCl_3$) 0.77 (3H, s, 10'-Me), 0.82 and 1.13 (6H, 2xs, 8'- and 9'-Me) 0.95 (3H, t, *J* 7.4, 4-Me), 1.01 and 1.07 (6H, 2xd, *J* 6.3 and 6.4, 1"- and 4"-Me), 1.30-1.79 (7H, complex of multiplets, 4'-H and 5'-, 6'- and 3-CH_2), 2.30 (2H, t, *J* 7.5, 2-CH_2), 4.00 and 4.11 (2H, 2xm, 2"- and 3"-H) and 4.66 (1H, s, 2'-H); δ_C(100 MHz; $CDCl_3$) 11.2 (C-10'), 13.8 (C-4), 14.8 and 15.2 (C-1" and C-4"), 18.5 (C-3), 20.3 (C-5'), 20.8 and 21.1 (C-8' and C-9'), 33. 5 (C-6'), 36.6 (C-2), 48.0 and 48.8 (C-1' and C-7'), 53.3 (C-4'), 73.4 and 74.2 (C-2" and C-3"), 85.0 (C-2') , 113.3 (C-3') and 172.7 (C-1); *m/z* 310 ($\mathbf{M}^+$, 3.1%) and 155 (100).

Preparation of *3,3-[(2R,3S)-2-*endo,*3-*exo-*butanedioxy]-2-*exo-*bornyl 3-methylbutanoate* (239c)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornanol (**235a**) (1.0 g, 4.3 mmol) was treated with butyllithium (15% solution in hexane; 2.5 ml, 4.2 mmol) and 3-methylbutanoyl chloride (0.60 g, 4.9 mmol) in dry Et_2O (20 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (19:1)] yielded, as an oil, *3,3-[(2*R,*3*S*)-2-*endo,*3-*exo-*butanedioxy]-2-*exo-*bornyl 3-methylbutanoate* (**239c**) (1.05 g, 75%) (Found: $\mathbf{M}^+$ 324.2302. $C_{19}H_{32}O_4$ requires *M*, 324.2301); $[\alpha]_D^{20}$ -16.4 (*c* 1.3 in $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1728 (CO);

δ_H(400 MHz; $CDCl_3$) 0.76 (3H, s, 10'-Me), 0.79 and 1.10 (6H, 2xs, 8'- and 9'-Me), 0.94 [6H, d, *J* 6.5, $CH(CH_3)_2$], 0.99 and 1.05 (6H, 2xd, *J* 6.3 and 6.3, 1"- and 4"-Me), 1.27-1.76 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 2.08 (1H, m, 3-H), 2.18 (2H, d, 2-CH_2), 3.97 and 4.08 (2H, 2xm, 2"- and 3"-H) and 4.64 (1H, s, 2'-H); δ_C(100 MHz; $CDCl_3$) 11.2 (C-10'), 14.8 and 15.1 (C-1" and C-4"), 20.3 (C-5'), 20.7 and 21.0 (C-8' and C-9'), 22.51 and 22.53 [$CH(CH_3)_2$], 25.4 (C-3), 33.5 (C-6'), 43.7 (C-2), 48.0 and 48.7 (C-1' and C-7), 53.2 (C-4'), 73.3 and 74.1 (C-2" and C-3"), 85.0 (C-2'), 113.2 (C-3') and 172.1 (C-1); *m/z* 324 ($\mathbf{M}^+$, 9.4%) and 57 (100).

Preparation of *3,3-[(2R,3S)-2-*endo,*3-*exo-*butanedioxy]-2-*exo-*bornyl 3,3-dimethylbutanoate* (239d)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornanol (**235a**) (1.0 g, 4.3 mmol) was treated with butyllithium (15% solution in hexane, 2.5 ml; 4.2 mmol) and 3,3-dimethylbutanoyl chloride (0.67 g, 4.9 mmol) in dry Et_2O (20 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (19:1)] yielded, as an oil, *3,3-[(2*R,*3*S*)-2-*endo,*3*-exo-*butanedioxy]-2-*exo-*bornyl 3,3-dimethylbutanoate* (**239d**) (1.01 g, 70%) (Found: $\mathbf{M}^+$ 338.2444. $C_{20}H_{34}O_4$ requires *M*, 338.2457); $[\alpha]_D^{20}$ -22.5 (*c* 2.2 in $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1730 (CO); δ_H(400 MHz; $CDCl_3$) 0.79 (3H, s, 10'-Me). 0.81 and 1.12 (6H, 2xs, 8'- and 9'-Me), 1.03 and 1.07 (6H, 2xd, 1"- and 4"-Me), 1.04 [9H, s, $C(CH_3)_3$], 1.31-1.79 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 2.22 (2H, s, 2-CH_2), 3.99 and 4.11 (2H, 2xm, 2"- and 3"-H) and 4.66 (1H, s, 2'-H); δ_C(100 MHz; $CDCl_3$) 11.5 (C-10'), 15.0 and 15.2 (C-1" and C-4"), 20.3 (C-5'), 20.8 and 21.1 (C-8' and C-9'), 29.7 [$C(CH_3)_3$], 30.6 (C-3), 33.6 (C-6'), 48.1 and 48.7 (C-1' and C-7'), 48.3 (C-2), 53.1 (C-4'), 73.3 and 74.1 (C-2" and C-3"), 85.1 (C-2'), 113.2 (C-3') and 171.4 (C-1); *m/z* 338 ($\mathbf{M}^+$, 13.4%) and 155 (100).

Preparation of *3,3-[(2R,3S)-2-*endo,*3-*exo-*butanedioxy]-2-*exo-*bornyl phenylacetate* (239e)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornanol (**235a**) (0.95 g, 4.0 mmol) was treated with butyllithium (15% solution in hexane; 2.5 ml, 4.2 mmol) and phenylacetyl chloride (0.77 g, 4.9 mmol) in dry Et_2O (20 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (19:1)] yielded, as an oil, *3,3-[(2*R,*3*S*)-2-*endo,*3*-exo-*butanedioxy]-2-*exo-

bornyl phenylacetate (**239e**) (1.13 g, 79%) (Found: $\mathbf{M}^+$ 358.2135. $C_{22}H_{30}O_4$ requires *M*, 358.2144); $[\alpha]_D^{20}$ -21.9 (*c* 2.1 in $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1735 (CO); δ_H(400 MHz; $CDCl_3$) 0.66 (3H, s, 10'-Me), 0.79 and 1.04 (6H, 2xs, 8'- and 9'-Me), 0.91 and 1.03 (6H, 2xd, 1"- and 4"-Me), 1.28-1.74 (5H, complex of multiplets, 4'-H and 5' - and 6'-CH_2), 3.63 (2H, s, 2-CH_2), 3.97 and 4.07 (2H, 2xm, 2"- and 3"-H), 4.65 (1H, s, 2'-H) and 7.19-7.32 (5H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.0 (C-10'), 14.8 and 15.0 (C-1" and C-4"), 20.3 (C-5'), 20.7 and 21.0 (C-8' and C-9'), 33.5 (C-6'), 41.8 (C-2), 48.0 and 48.8 (C-1' and C-7'), 53.2 (C-4'), 73.5 and 74.2 (C-2" and C-3"), 85.6 (C-2'), 113.2 (C-3'), 126.9, 128.3, 129.6 and 134.3 (Ar-C) and 170.6 (C-1); *m/z* 358 ($\mathbf{M}^+$, 11.7%) and 155 (100).

Preparation of *3,3-[(2R,3S)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl phenoxyacetate* (239f)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornanol (**235a**) (1.1 g, 4.7 mmol) was treated with butyllithium (15% solution in hexane; 2.5 ml, 4.2 mmol) and phenoxyacetyl chloride (**186f**) (0.85 g, 4.9 mmol) in dry Et_2O (20 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (19:1)] yielded, as an oil, *3,3-[(2*R*,3*S*)-2-*endo*,3-exo-butanedioxy]-2-*exo*-bornyl phenoxyacetate* (**239f**) (1.37 g, 78%) (Found: $\mathbf{M}^+$ 374.2098. $C_{22}H_{30}O_5$ requires *M*, 374.2093); $[\alpha]_D^{20}$ -17.8 (*c* 2.0 in $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1760 (CO); δ_H(400 MHz; $CDCl_3$) 0.75 (3H, s, 10'-Me), 0.81 and 1.07 (6H, 2xs, 8'- and 9'-Me), 1.04 and 1.08 (6H, 2xd, *J* 6.3 and 6.4, 1"- and 4"-Me), 1.31-1.77 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 4.02 and 4.13 (2H, 2xm, 2"- and 3"-H), 4.64 (2H, s, 2-CH_2), 4.75 (1H, s, 2'-H), 6.89-7.00 (3H, complex of multiplets, Ar-H) and 7.23- 7.29 (2H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.1 (C-10'), 14.9 and 15.2 (C-1" and C-4"), 20.3 (C-5'), 20.7 and 21.0 (C-8' and C-9'), 33.4 (C-6'), 48.1 and 48.8 (C-1' and C-7'), 53.1 (C-4'), 65.2 (C-2), 73.5 and 74.2 (C-2" and C-3"), 86.1 (C-2'), 113.0 (C-3'), 114.7, 121.5, 129.4 and 158.0 (Ar-C) and 168.2 (C-1); *m/z* 374 ($\mathbf{M}^+$, 13.5%) and 155 (100).

Preparation of *3,3-[(2R,3S)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 2-methyl-3-phenylpropanoate* (240a)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl propanoate (**239a**) (0.35 g, 1.2 mmol) was reacted with LDA [generated from diisopropylamine (0.15 g, 1.5 mmol) and butyllithium (15% in hexane; 0.77 ml, 1.3 mmol)] and benzyl bromide (0.14 ml, 1.2 mmol) in dry THF (5 ml)

as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate (**181**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded an oil (0.17 g) comprising a 1:4 mixture of the starting material, 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl propanoate (**239a**) and a diastereomeric mixture of *3,3-[(2*R,3S*)-2*-endo,*3*-exo-*butanedioxy]-2*-exo-*bornyl 2-methyl-3-phenylpropanoate* (**240a**) (29%)[¥] (9% d.e.; as determined by ^{1}H NMR spectroscopy) (Found: $\mathbf{M}^+$ 386.2467. $C_{24}H_{34}O_4$ requires *M*, 386.2457); ν_{max}(thin film)/cm^{-1} 1740 (C=O); δ_H(400 MHz; $CDCl_3$) 0.63/0.77 (3H, s, 10'-Me), 0.81/0.83 and 0.94-1.19 (15H, complex of multiplets, CHC*H*$_3$, 8'-, 9'-, 1"- and 4"-Me), 1.29-1.76 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 2.55-2.66 and 3.06-3.20 (2H, 2xm, 3-CH_2), 2.70-2.82 (1H, m, 2-H), 3.95-4.16 (2H, complex of multiplets, 2"- and 3"-H), 4.63/4.65 (1H, s, 2-H) and 7.13-7.28 (5H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.0/11.2 (C-10'), 14.91/14.95 and 15.1/15.2 (C-1" and C-4"), 16.6/16.8 (CH*C*H$_3$), 20.3 (C-5'), 20.8 and 21.1 (C-8' and C-9'), 33.48/33.54 (C-6'), 39.5/39.7 (C-3), 41.67/42.70 (C-2), 48.0 and 48.7/48.9 (C-1' and C-7'), 53.1/53.2 (C-4'), 73.42/73.45 and 74.0/74.1 (C-2" and C-3"), 84.9/85.0 (C-2'), 113.1/113.2 (C-3'), 126.2, 128.3, 129.02/129.05 and 139.65/139.68 (Ar-C) and 174.9/175.1; *m/z* 386 ($\mathbf{M}^+$, 11.4%) and 91 (100). Attempts were made to separate the diastereomeric products from the starting material by PLC [elution with hexane-EtOAc (49:1)], but even when the plates were run in solvent up to eight times, the components could not be resolved.

Preparation of *3,3-[(2*R,3S*)-2*-endo,*3*-exo-*butanedioxy]-2*-exo-*bornyl 2-benzylbutanoate* (240b)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl butanoate (**239b**) (0.47 g, 1.5 mmol) was reacted with LDA [generated from diisopropylamine (0.19 g, 1.9 mmol) and butyllithium (15% in hexane; 1.2 ml, 1.9 mmol)] and benzyl bromide (0.21 ml, 1.8 mmol) in dry THF (5 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate (**181**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded an oil (0.37 g) comprising a 1:2 mixture of the starting material, 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl butanoate (**239b**) and a diastereomeric

[¥] The ratios were determined by integration of the ^{1}H NMR spectrum of the isolated mixture.

mixture of *3,3-[(2*R,*3*S*)-2*-endo,*3*-exo-*butanedioxy]-2*-exo-*bornyl 2-benzylbutanoate* (**240b**) (40%)† (7% d.e.; as determined by ^{1}H NMR spectroscopy)ϟ (Found: $\mathbf{M}^+$ 400.2602. $C_{25}H_{36}O_4$ requires *M*, 400.2613); ν_{max}(thin film)/cm^{-1} 1745 (C=O); δ_H(400 MHz; $CDCl_3$) 0.57/0.77 (3H, s, 10'-Me), 0.79/0.83 and 1.12/1.16 (6H, 2xs, 8'- and 9'-Me), 0.92-1.12 (9H, complex of multiplets, 4-, 1"- and 4"-Me), 1.27-1.78 (7H, complex of multiplets, 4'-H and 3-, 5'- and 6'-CH_2), 2.70-2.76 and 2.98-3.12 (3H, complex of multiplets, 2-H and $ArCH_2$), 3.95-4.15 (2H, complex of multiplets, 2"- and 3"-H), 4.59/4.65 (1H, s, 2'-H) and 7.12-7.28 (5H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.0/11.4 (C-10'), 11.6/11.9 (C-4), 15.0/15.2 and 15.1 (C-1" and C-4"), 20.28/20.30 (C-5'), 20.7/20.8 and 21.1 (C-8' and C-9'), 24.1/24.7 (C-3), 33.5/33.6 (C-6'), 37.7/38.0 ($PhCH_2$), 48.0/48.1 and 48.7/48.9 (C-1' and C-7'), 49.0/49.4 (C-2), 53.0/53.1 (C-4'), 73.3/73.4 and 74.96/74.04 (C-2" and C-3"), 85.09/85.12 (C-2'), 113.0/113.1 (C-3'), 126.1, 128.3, 128.98/129.02 and 139.79/139.81 (Ar-C) and 174.32/174.34 (C-1); *m/z* 400 ($\mathbf{M}^+$, 9.1%) and 91 (100). Attempts were made to separate the diastereomeric products from the starting material by PLC [elution with hexane-EtOAc (49:1)], but even when the plates were run in solvent up to eight times, the components could not be resolved.

Preparation of *3,3-[(2*R,*3*S*)-2*-endo,*3*-exo-*butanedioxy]-2*-exo-*bornyl 2-benzyl-3-methylpropanoate* (240c)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-methylbutanoate (**239c**) (0.42 g, 1.3 mmol) was reacted with LDA [generated from diisopropylamine (0.17 g, 1.7 mmol) and butyllithium (15% in hexane; 1.2 ml, 1.9 mmol)] and benzyl bromide (0,31 g, 1.8 mmol) in dry THF (5 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate (**181**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded, as an oil, a diastereomeric mixture of *3,3-[(2*R,*3*S*)-2*-endo,*3*-exo-*butanedioxy]-2*-exo-*bornyl 2-benzyl-3-methylbutanoate* (**240c**) (0.48 g, 89%) (20% d.e.; as determined by ^{1}H NMR spectroscopy) (Found: $\mathbf{M}^+$ 414.2766. $C_{26}H_{38}O_4$ requires *M*, 414.2770);

† The ratios were determined by integration of the ^{1}H NMR spectrum of the isolated mixture.

ϟ The diastereomeric excess was determined from the ^{1}H NMR spectrum of the reaction mixture after purification by preparative layer chromatograpgy as the diastereomeric peaks in the crude reaction mixture could not be integrated due to overlapping signals

ν_{max}(thin film)/cm^{-1} 1735; δ_H(400 MHz; $CDCl_3$) 0.34-1.16 [21H, complex of multiplets, 8'-, 9'-, 10'-, 1"- and 4"-Me and $CH(CH_3)_2$], 1.20-1.75 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 1.93-2.08 (1H, m, 3-H), 2.51-2.69 (1H, complex of multiplets, 2-H), 2.72-3.03 (2H, complex of multiplets, $PhCH_2$), 3.90-4.14 (2H, m, 2"- and 3"-H), 4.49/4.61 (1H, s, 2'-H) and 7.09-7.26 (5H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 10.7/11.6 (C-10'), 14.8/14.9 and 15.0/15.3 (C-1" and C-4"), 19.9 [$CH(CH_3)_2$], 20.2/20.3 (C-5'), 20.4/20.6 and 20.8/21.0 (C-8' and C-9'), 29.7/30.4 (C-3), 33.4/33.7 (C-6'), 34.0/35.4 ($PhCH_2$), 47.9/48.0 and 48.6/49.0 (C-1' and C-7'), 52.8 /53.1 (C-4'), 53.6/54.5 (C-2), 73.2/73.3 and 73.8/74.1 (C-2" and C-3"), 85.3 (C-2'), 112.9/113.1 (C-3'), 125.9/126.0, 128.2, 128.9 and 140.3/140.4 (Ar-C) and 173.6/173.9 (C-1); *m/z* 414 ($\mathbf{M}^+$, 4.9%) and 91 (100).

Preparation of *3,3-[(2R,3S)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate* (240d)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3,3-dimethylbutanoate (**239d**) (0.50 g, 1.5 mmol) was reacted with LDA [generated from diisopropylamine (0.22 g, 2.2 mmol) and butyllithium (15% in hexane; 1.2 ml, 1.9 mmol)] and benzyl bromide (0,31 g, 1.8 mmol) in dry THF (5 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate (**181**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded, as an oil, a diastereomeric mixture of *3,3-[(2*R*,3*S*)-2-*endo*,3-exo-butanedioxy]-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate* (**240d**) (0.36 g, 57%) (34% d.e.; as determined by ^{1}H NMR spectroscopy) (Found: $\mathbf{M}^+$ 428.2919. $C_{27}H_{40}O_4$ requires *M*, 428.2927); ν_{max}(thin film)/cm^{-1} 1735 and 1740 (CO); δ_H(400 MHz; $CDCl_3$) 0.10/0.73 (3H, s, 10'-Me), 0.71/0.81 and 0.98/1.14 (6H, 2xs, 8'- and 9'-Me), 0.84/0.88 and 0.97/1.08 (6H, 2xd, *J* 6.4 and 6.4, 1"- and 4"-Me), 1.06/1.10 [9H, s, $C(CH_3)_3$], 1.28-1.73 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 2.49/2.63 and 2.53/2.66 (1H, 2xd, *J* 3.5 and 3.4, 2-H), 2.77-3.08 (2H, complex of multiplets, $PhCH_2$), 3.86-4.17 (2H, m, 2"- and 3"-H), 4.36/4.53 (1H, s, 2'-H) and 7.07-7.24 (5H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 10.5/12.0 (C-10'), 14.8/15.0 and 15.3/15.5 (C-1" and C-4"), 20.2/20.3 (C-5'), 20.5/20.9 and 21.0/21.1 (C-8' and C-9'), 28.1/28.2 [$C(CH_3)_3$], 33.1/33.4 (C-3), 33.4/33.9 (C-6'), 33.9/34.2 ($PhCH_2$)[¥], 47.9/48.0 and 48.4/49.0 (C-1' and C-7'), 52.6/52.7 (C-4'), 57.4/59.0 (C-2), 73.1 and 73.7/73.8 (C-2" and C-3"), 85.5/85.9 (C-

[¥] There is coincidence of the C-3, C-6' and $PhCH_2$ signals.

2'), 112.7/112.9 (C-3'), 125.85/125.91, 128.16/128.24, 128.6/129.0 and 140.5/140.7 (Ar-C) and 173.5/173.8 (C-1); *m/z* 428 ($\mathbf{M}^+$, 7.7%) and 91 (100).

Preparation of *3,3-[(2*R*,3*S*)-2*-endo,*3*-exo-*butanedioxy]-2*-exo-*bornyl 2,3-diphenylpropanoate* (240e)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl phenylacetate (**239e**) (0.53 g, 1.5 mmol) was reacted with LDA [generated from diisopropylamine (0.19 g, 1.9 mmol) and butyllithium (15% in hexane; 1.2 ml, 1.9 mmol)] and benzyl bromide (0,31 g, 1.8 mmol) in dry THF (5 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate (**181**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded, as an oil, a diastereomeric mixture of *3,3-[(2*R*,3*S*)-2*-endo,*3*-exo-*butanedioxy]-2*-exo-*bornyl 2,3-diphenylpropanoate* (**240e**) (0.53 g, 80%) (5% d.e. as determined by ^{1}H NMR spectroscopy) (Found: $\mathbf{M}^+$ 448.2603. $C_{29}H_{36}O_4$ requires *M*, 448.2614); ν_{max}(thin film)/cm^{-1} 1730 (CO); δ_H(400 MHz; $CDCl_3$) 0.34/0.43 (3H, s, 10'-Me), 0.59/0.78 and 0.87/0.93 (6H, 2xd, *J* 6.2 and 6.4, 1"- and 4"-Me), 0.74/0.78 and 1.06/1.07 (6H, 2xs, 8'- and 9'-Me), 1.24-1.74 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 3.00-3.12 and 3.43-3.54 (2H, 2xm, 3-CH_2), 3.85-4.09 (3H, complex of multiplets, 2"-, 3"- and 2-H), 4.57-4.62 (1H, s, 2'-H) and 7.10-7.41 (10H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 10.5/10.7 (C-10'), 14.3 and 14.7 (C-1" and C-4"), 20.19/20.24 (C-5'), 20.7 and 20.87/20.93 (C-8' and C-9'), 33.39/33.44 (C-6'), 38.9/39.4 (C-3), 47.96/47.98 and 48.8/49.3 (C-1' and C-7'), 53.2/53.4 (C-2), 53.9/54.1 (C-4'), 73.4/73.5 and 74.1/74.3 (C-2" and C-3"), 85.5 (C-2'), 113.0/113.2 (C-3'), 126.1/126.2, 127.11/127.13, 128.16/128.22, 128.29/128.31, 128.35/128.37, 129.0/129.1, 138.7/139.0 and 139.2/139.4 (Ar-C) and 172.3/172.4 (C-1); *m/z* 448 ($\mathbf{M}^+$, 9.3%) and 155 (100).

Preparation of *3,3-[butane-2*-endo-*(*R*),*3*-exo-*(*S*)-dioxy]-2*-exo-*bornyl 2-phenoxy-3-phenylpropanoate* (240f)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl phenoxyacetate (**239f**) (0.56 g, 1.5 mmol) was reacted with LDA [generated from diisopropylamine (0.25 g, 2.5 mmol) and butyllithium (15% in hexane; 1.2 ml, 1.9 mmol)] and benzyl bromide (0,31 g, 1.8 mmol) in dry THF (5 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate (**181**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (49:1)] and PLC [elution with hexane-EtOAc (49:1)] yielded, as an oil, a

diastereomeric mixture of *3,3-[(2*R*,3*S*)-2*-endo,*3*-exo-*butanedioxy]-2*-exo-*bornyl 2-phenoxy-3-phenylpropanoate* (**240f**) (0.10 g, 14%) (25% d.e. as determined by ^{1}H NMR spectroscopy)[‡] (Found: $\mathbf{M}^+$ 464.2550. $C_{29}H_{36}O_5$ requires *M*, 464.2562); ν_{max}(thin film)/cm^{-1} 1755 (CO); δ_H(400 MHz; $CDCl_3$) 0.49-1.18 (15H, complex of multiplets, 8'-, 9'-, 10'-, 1"- and 4"-Me), 1.10-1.78 (5H, 4'-H and 5'- and 6'-CH_2), 3.17-3.39 (2H, complex of multiplets, 3-CH_2), 3.97-4.16 (2H, complex of multiplets, 2"- and 3"-H), 4.63/4.71 (1H, s, 2'-H), 4.74-4.83 (1H, m, 2-H), 6.77-6.93 (3H, m, Ar-H) and 7.14-7.37 (7H, m, Ar-H); δ_C(100 MHz; $CDCl_3$) 10.9/11.3 (C-10'), 15.0 and 15.1/15.3 (C-1" and C-4"), 20.3 (C-5'), 20.6/20.7 and 21.06/21.11 (C-8' and C-9'), 33.5 (C-6'), 39.3/39.5 (C-3), 48.1/48.2 and 48.7/48.8 (C-1' and C-7'), 53.0 (C-4'), 73.46/73.53 and 74.0 (C-2" and C-3"), 77.9/78.0 (C-2), 86.1/86.2 (C-2'), 112.7/112.8 (C-3'), 115.39/115.39, 121.4/121.5, 126.72/126.76, 128.37/128.39, 129.27/129.29, 129.38/129.41, 137.1/137.5 and 158.0 (Ar-C) and 170.3/170.5 (C-1); *m/z* 464 ($\mathbf{M}^+$, 14.0%) and 155 (100%).

Hydrolysis of *3,3-[(2*R*,3*S*)-2*-endo,*3*-exo-*butanedioxy]*-2-exo-*bornyl 2-benzyl-3,3-dimethylbutanoate* (240d)

Attempts were made to hydrolyse 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate (**240d**) applying Methods 1, 2 and 3 used in the hydrolysis of spiro[bornane-3,2'-indan]-2-*exo*-yl 2-methyl-3-phenyl propanoate (**185a**). In all the cases, however, work-up afforded unreacted 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate (**240d**).

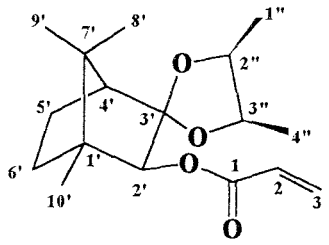
Hydrolysis of *3,3-[(2*R*,3*S*)-2*-endo,*3*-exo-*butanedioxy]-2*-exo-*bornyl 2,3-diphenylpropanoate* (240e)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 2,3-diphenylpropanoate (**240e**) (0.21 g, 0.48 mmol) (7% d.e. as determined by ^{1}H NMR spectroscopy) and conc. H_2SO_4 (0.5 ml) were reacted as described for the synthesis of 2-methyl-3-phenylpropanoic acid (**190a**) (Method 4). Acidic workup yielded what was proposed to be crude bornan-3-on-2-*exo*-yl 2,3-diphenylpropanoate (**242**) (0.10 g, 58%) (9% d.e. as determined by ^{1}H NMR spectroscopy).

[‡]The diastereomeric excess was determined from the ^{1}H NMR spectrum of the reaction mixture after purification by preparative layer chromatography as the diastereomeric peaks in the crude reaction mixture could not be integrated due to overlapping signals.

A mixture of the crude bornan-3-on-2-*exo*-yl 2,3-diphenylpropanoate (**242**) (0.19 g, 0.50 mmol) and $LiOH.H_2O$ (0.40 g, 0.96 mmol) in THF (4 ml) was stirred at r.t for 3 days. The reaction mixture was then diluted with water (20 ml), basified to pH 10 with 33% NH_4OH and extracted with $CHCl_3$ (3x20 ml). The combined organic fractions were dried (anhydr. $MgSO_4$) and concentrated *in vacuo*. ^1H NMR analysis of the residue showed the presence of a complex mixture of products that could not be separated. The aqueous phase was then acidified using dil. HCl to pH 1 and extracted with Et_2O (3x20 ml), the combined organic fractions dried (anhydr. $MgSO_4$) and concentrated *in vacuo* to yield an enantiomeric mixture of 2,3-diphenylpropanoic acid (**241e**) (0.09 g, 79%) (4% e.e.; as determined from optical rotation); $[\alpha]_D^{27}$ +5.3 (*c* 1.0 in benzene) {lit.,[277] $[\alpha]_D^{25}$ +140.8 (*c* 4.5 in benzene, for the *S*-enantiomer)}; ν_{max}(thin film)/cm^{-1} 1700 (C=O) and 3400 (OH); δ_H(400 MHz; $CDCl_3$) 3.05 (1H, dd, $J_{A,2}$ 6.9 and $J_{A,B}$ 13.7, 3-CH_2), 3.02 (1H, dd, $J_{B,2}$ 8.4 and $J_{A,B}$ 13.7, 3-CH_2), 3.86 (1H, t, *J* 7.6, *2*-H), 7.05-7.35 (10H, complex of multiplets, Ar-H) and 9.85 (1H, br s, OH); δ_C(100 MHz; $CDCl_3$) 39.3 (C-3), 53.4 (C-2), 126.5, 127.6, 128.1, 128.4, 128.7, 128.9, 137.9 and 138.7 (Ar-C) and 179.1 (C-1); *m/z* 226 (M^+, 31.7%) and 91 (100).

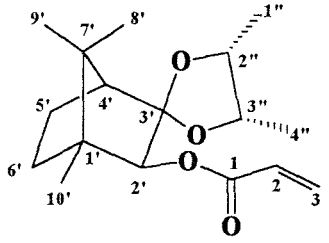
Preparation of *3,3-[(2R,3S)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl acrylate* (250)



3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornanol (**235a**) (2.0 g, 8.4 mmol) was treated with butyllithium (15% solution in hexane; 5.0 ml, 8.3 mmol) and acryloyl chloride (0.91 g, 10 mmol) in dry Et_2O (40 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (19:1)] yielded, as an oil, *3,3-[(2R,3S)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl acrylate* (**250**) (2.1 g, 85%) (Found: M^+ 294.1828. $C_{17}H_{26}O_4$ requires *M*, 294.1831); $[\alpha]_D^{21}$ -19.8 (*c* 1.4 in $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1725 (CO); δ_H(400 MHz; $CDCl_3$) 0.77 (3H, s, 10'-Me), 0.83 and 1.17 (6H, 2xs, 8'- and 9'-Me), 0.96 and 1.07 (6H, 2xd, *J* 6.3 and 6.4, 1"- and 4"-Me), 1.33-1.78 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 4.00 and 4.11 (2H, 2xm, 2"- and 3"-H), 4.74 (1H, s, 2'-H), 5.78 and 5.81 (1H, dd, $J_{A,B}$ 1.4 and $J_{A,2}$ 10.4, 3-CH_2), 6.37 and

6.40 (1H, dd, $J_{A,B}$ 1.4 and $J_{B,2}$ 17.3, 3-CH_2) and 6.10 and 6.15 (1H, dd, $J_{A,2}$ 10.4 and $J_{B,2}$ 17.3, 2-H); δ_C(100 MHz; $CDCl_3$) 11.1 (C-10'), 14.6 and 15.1 (C-1" and C-4"), 20.3 (C-5'), 20.8 and 21.0 (C-8' and C-9'), 33.5 (C-6'), 48.1 and 49.0 (C-1' and C-7'), 53.3 (C-4'), 73.5 and 74.4 (C-2" and C-3"), 85.4 (C-2'), 113.4 (C-3'), 128.9 (C-2), 130.1 (C-3) and 165.4 (C-1); *m/z* 194 ($\mathbf{M}^+$, 11.9%) and 155 (100).

Preparation of *3,3-[(2R,3S)-2-*exo*,3-*endo*-butanedioxy]-2-*exo*-bornyl acrylate* (251)[248]



A stirred mixture of 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornanol (**235a**) (2.1 g, 8.7 mmol), acryloyl chloride (0.91 g, 10 mmol) and pulverised 3Å molecular sieves (2 g) in dry CCl_4 (20 ml) was boiled under reflux overnight. The molecular sieves were removed by filtration and the filtrate concentrated *in vacuo*. Flash column chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded two fractions.

Fraction 1.

As an oil, *3,3-[(2*R*,3*S*)-2-*exo*,3-*endo*-butanedioxy]-2-*exo*-bornyl acrylate* (**251**) (0.72 g, 28%) (Found: $\mathbf{M}^+$ 294.1823. $C_{17}H_{26}O_4$ requires *M*, 294.1831); $[\alpha]_D^{28}$ -34.2 (*c* 2.1 in $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1725 (CO); δ_H(400 MHz; $CDCl_3$) 0.77 (3H, s, 10'-Me), 0.82 and 1.16 (6H, 2xs, 8'- and 9'-Me), 1.00 and 1.08 (6H, 2xd, *J* 6.4 and 6.4,1"- and 4"-Me), 1.29-1.90 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 3.96 and 4.15 (2H, 2xm, 2"- and 3"-H), 4.47 (1H, s, 2'-H), 5.78 and 5.81 (1H, dd, $J_{A,B}$ 1.5 and $J_{A,2}$ 10.4, 3-CH_2), 6.34 and 6.38 (1H, dd, $J_{A,B}$ 1.5 and $J_{B,2}$ 17.3, 3-CH_2) and 6.08 and 6.13 (1H, dd, $J_{A,2}$ 10.4 and $J_{B,2}$ 17.4, 2-H); δ_C(100 MHz; $CDCl_3$) 11.3 (C-10'), 14.4 and 15.8 (C-1" and C-4"), 20.6 and 20.9 (C-8' and C-9'), 20.7 (C-5'), 33.4 (C-6'), 47.8 and 49.4 (C-1' and C-7'), 56.0 (C-4'), 72.2 and 75.4 (C-2" and C-3"), 86.2 (C-2'), 113.2 (C-3'), 128.9 (C-2), 130.3 (C-3) and 165.3 (C-1); *m/z* 294 ($\mathbf{M}^+$, 2.3%) and 55 (100).

Fraction 2.

The stereoisomer 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl acrylate (**250**) (0,59 g, 23%).

Preparation of *3,3-[(2R,3S)-2-endo,3-exo-butanedioxy]-2-exo-bornyl 3-hydroxy-2-methylene-3-(3-pyridyl)propanoate* (255a)

Method 1.

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl acrylate (**250**) (0.29 g, 0.97 mmol), pyridine-3-carboxaldehyde (0.12 g, 1.1 mmol) and 3-quinuclidinol (0.33 g, 1.1 mmol) in $CDCl_3$ (0.4 ml) were placed in an NMR tube and ^1H NMR spectra were run at regular intervals until the reaction was seen to be complete. After 7 days, the solvent was removed *in vacuo* and the residue purified by flash chromatography [elution with EtOAc-hexane (3:2)] yielding, as a diastereomeric mixture, *3,3-[(2R,3S)-2-*endo,*3-*exo-*butanedioxy]-*2-exo-*bornyl 3-hydroxy-2-methylene-3-(3-pyridyl)propanoate* (**255a**) (0.18 g, 48%) (0% d.e. as determined by ^1H NMR spectroscopy) (Found: $\mathbf{M}^+$ 401.2201. $C_{23}H_{31}O_5N$ requires *M*, 401.2202); ν_{max}(thin film)/cm^{-1} 3350 (OH), 1715 (C=O) and 1630 (C=C); ν_{max}(2 mmol.dm^{-3} in $CHCl_3$)/cm^{-1} 3700 and 3630 (OH); δ_H(400 MHz; $CDCl_3$)[♮] 0.53/0.68 (3H, s, 10'-Me), 0.69/0.73 and 0.78/1.11 (6H, 2xs, 8'- and 9'-Me), 0.85/0.940 and 0.942/0.95 (6H, 2xd, 1''- and 4''-Me), 1 .23-1.74 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 3.89-4.08 (2H, complex of multiplets, 2''- and 3''-H), 4.55 (1H, br s, OH), 4.70/4.75 (1H, s, 2'-H), 5.46/5.54 (1H, s, 3-H), 5.56/5.86 and 6.35/6.49 (2H, 2xs, C=CH_2), 7.15-7.13, 7.64-7.72, 8.35-8.41 and 8.48-8.53 (4H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 10.9/11.0 (C-10'), 14.55/14.59 and 14.7/14.9 (C-1'' and C-4''), 20.06/20.13 (C-5'), 20.5/20.7 and 20.8/20.9 (C-8' and C-9'), 33.3/33.4 (C-6'), 47.8/48.0 and 48.9/49.1 (C-1' and C-7'), 52.8/53.0 (C-4'), 70.3/71.9 (3-H), 73.4/73.5 and 74.3 (C-2'' and C-3''), 85.5/85.8 (C-2'), 113.2/113.3 (C-3'), 126.5/127.9 (C=CH_2), 123.0/123.2, 134.0/134.8, 136.7/137.6, 140.7/142.5, 147.9/148.4 (Ar-C), 148.65/148.70 (C-2) and 164.8/164.9 (C-1); *m/z* 401 ($\mathbf{M}^+$, 3.4%) and 55 (100).

[♮] The ^1H and ^{13}C NMR chemicl shifts of the Baylis-Hillman products were found to be slightly concentration dependant, presumably reflecting intermolecular hydrogen-bonding effects. The effect is particularly apparent in the signal corresponding to the acrylate moiety.

Method 2.

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl acrylate (**250**) (0.30 g, 1.0 mmol), pyridine-3-carboxaldehyde (0.11 g, 1.1 mmol) and 1,4-diazabicyclo[2.2.2]octane (DABCO) (0.12 g, 1.1 mmol) in $CDCl_3$ (0.4 ml) were reacted as described in Method 1. After 18 days, work-up and flash chromatography [elution with hexane-EtOAc (3:2)] yielded , as a diastereomeric mixture, 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(3-pyridyl)propanoate (**255a**) (0.31 g, 76%) (5% d.e. as determined by ^{1}H NMR spectroscopy).

Method 3.

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl acrylate (**250**) (0.30 g, 1.0 mmol), pyridine-3-carboxaldehyde (0.13 g, 1.2 mmol), (DABCO) (0.15 g, 1.4 mmol) and $ZnBr_2$ (0.02 g, 0.1 mmol) in $CDCl_3$ (0.4 ml) were reacted as described in Method 1. After 18 days, work-up and flash chromatography [elution with hexane-EtOAc (3:2)] yielded, as a diastereomeric mixture, 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(3-pyridyl)propanoate (**255a**) (0.30 g, 73%) [3% d.e. (0 % d.e.)[§] as determined by ^{1}H NMR spectroscopy].

Preparation of *3,3-[(2R,3S)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(2-pyridyl)propanoate* (255b)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl acrylate (**250**) (0.30 g, 1.0 mmol), pyridine-2-carboxaldehyde (0.12 g, 1.2 mmol) and 3-quinuclidinol (0.14 g, 1.1 mmol) in $CDCl_3$ (0.4 ml) were reacted as described for the synthesis of 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(3-pyridyl)propanoate (**255a**) (Method 1). After 7 days, work-up and flash chromatography of the residue [elution with hexane-EtOAc (4:1)] yielded, as a diastereomeric mixture, *3,3-[(2R,3S)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(2-pyridyl)propanoate* (**255b**) (0.27 g, 65%) [20% d.e. (19 % d.e.) as determined by ^{1}H NMR spectroscopy] (Found: M^+ 401.2193. $C_{23}H_{31}O_5N$ requires *M*, 401.2202); ν_{max}(thin film)/cm^{-1} 3450 (OH), 1715 (C=O) and 1630 (C=C); δ_H(400 MHz; $CDCl_3$) 0.57/0.72 (3H, s, 10'-

[§] The diastereomeric excess cited in brackets here and elsewhere, refers to that determined from the crude reaction mixture.

), 0.72/0.77‡ and 0.87/1.08 (6H, 2xs, 8'- and 9'-Me), 0.86/0.94 and 0.96/0.97 (6H, 2xd, *J* 6.35/6.37, 1"- and 4"-Me), 1.15-1.73 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 3.90-4.08 (2H, complex of multiplets, 2"- and 3"-H), 4.70/4.75 (1H, s, 2'-H), 4.73-4.90 (1H, complex of multiplets, OH), 5.54/5.62 (1H, m, 3-H), 5.59/5.87 and 6.32/6.39 (2H, 2xs, C=CH_2) and 7.08-7.15, 7.43-7.49, 7.54-7.64 and 8.43-8.49 (4H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) .10.9/11.0 (C-10'), 14.65 and 14.71 (C-1" and C-4"), 20.09/20.13 (C-5'), 20.57/20.62 and 20.8/20.9 (C-8' and C-9'), 33.3/33.4 (C-6'), 47.8/47.9 and 49.0 (C-1' and C-7'), 53.0/53.1 (C-4'), 72.0/72.2, 73.4 and 74.3 (C-3, C-2" and C-3"), 85.4/85.6 (C-2'), 113.27/113.34 (C-3'), 121.2/121.5, 122.3/122.4, 136.46/136.51, 141.5/142.2 and 148.1/148.2 (Ar-C), 126.5/127.1 (C=*C*H_2), 159.8/160.1 (C-2) and 165.18/165.23 (C-1); *m/z* 401 (M^+, 0.7%) and 155 (100).

Preparation of *3,3-[(2R,3S)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(2-pyridyl)propanoate* (255b)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl acrylate (**250**) (0.30 g, 1.0 mmol), pyridine-2-carboxaldehyde (0.12 g, 1.1 mmol) and DABCO (0.11 g, 0.98 mmol) in $CDCl_3$ (0.4 ml) were reacted as described for the synthesis of 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(3-pyridyl)propanoate (**255a**) (Method 2). After 7 days, work-up and flash chromatography [elution with hexane-EtOAc (4:1)] yielded, as a diastereomeric mixture, 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-exo-bornyl 3-hydroxy-2-methylene-3-(2-pyridyl)propanoate (**255b**) (0.19 g, 47%) (27% d.e. as determined by ^{1}H NMR spectroscopy).

Preparation of *3,3-[(2R,3S)-2-*exo*,3-*endo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(2-pyridyl)propanoate* (256b)

3,3-[(2*R*,3*S*)-2-*Exo*,3-*endo*-Butanedioxy]-2-*exo*-bornyl acrylate (**251**) (0.31 g, 1.1 mmol), pyridine-2-carboxaldehyde (0.13 g, 1.2 mmol) and DABCO (0.12 g, 1.1 mmol) in $CDCl_3$ (0.4 ml) were reacted as described for the synthesis of 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(3-pyridyl)propanoate (**255a**) (Method 2). After 7 days, work-up and elution of the residue through a silica plug (with hexane as the eluant) yielded, as a diastereomeric mixture, *3,3-[(2*R*,3*S*)-2-*exo,*3-*endo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-*

‡ There is coincidence with the 10'-Me signal.

methylene-3-(2-pyridyl)propanoate (**256b**) (0.34 g, 80%) [18% d.e. (21 % d.e.) as determined by ^{1}H NMR spectroscopy] (Found: $\mathbf{M}^+$ 401.2199. $C_{23}H_{31}O_5N$ requires *M*, 401.2202); ν_{max}(thin film)/cm^{-1} 3450 (OH), 1710 (C=O) and 1620 (C=C); δ_H(400 MHz; $CDCl_3$) 0.66/0.75 (3H, s, 10'-Me), 0.78/0.82 and 1.03/1.14 (6H, 2xs, 8'- and 9'-Me), 0.95/0.99 and 1.06/1.07 (6H, 2xd, *J* 6.41/6.34, 1"- and 4"-Me), 1.27-1.95 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 3.78-4.08 (2H, complex of multiplets, 2"- and 3"-H), 4.51/4.52 (1H, s, 2'-H), 4.71/4.84 (1H, br s, OH), 5.62/5.64 (1H, br s, 3-H), 5.71/5.92 and 6.33/6.38 (2H, 2xs, C=CH_2) and 7.13-7.22, 7.42-7.50, 7.60-7.69 and 8.48-8.56 (4H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 11.2/11.3 (C-10'), 14.4/14.5 and 15.7/15.8 (C-1" and C-4"), 20.5/20.6 and 20.89/20.91 (C-8' and C-9'), 20.7 (C-5'), 33.44/33.46 (C-6'), 47.7/47.8 and 49.49/49.52 (C-1' and C-7'), 55.85/55.88 (C-4'), 72.3, 72.41/72.45 and 75.3 (C-3, C-2" and C-3"), 86.4/86.5 (C-2'), 113.35/113.42 (C-3'), 121.2/121.3, 122.51/122.55, 136.61/136.64, 141.8/142.2 and 148.2/148.4 (Ar-C), 126.6/126.9 (C=*C*H_2), 159.8/159.9 (C-2) and 165.3/165.4 (C-1); *m/z* 401 ($\mathbf{M}^+$, 0.1%) and 155 (100).

Preparation of *3,3-[(2R,3S)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(4-pyridyl)propanoate* (255c)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl acrylate (**250**) (0.31 g, 1.1 mmol), pyridine-2-carboxaldehyde (0.11 g, 1.1 mmol) and DABCO (0.12 g, 1.1 mmol) in $CDCl_3$ (0.4 ml) were reacted as described for the synthesis of 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(3-pyridyl)propanoate (**255a**) (Method 2). After 7 days, work-up and flash chromatography [elution with hexane-EtOAc (1:1)] yielded, as a diastereomeric mixture, *3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(4-pyridyl)propanoate* (**255c**) (0.36 g, 86%) [9% d.e. (9% d.e.) as determined by ^{1}H NMR spectroscopy] (Found: $\mathbf{M}^+$ 401.2202. $C_{23}H_{31}O_5N$ requires *M*, 401.2202); ν_{max}(thin film)/cm^{-1} 3450 (OH), 1730 (C=O) and 1650 (C=C); δ_H(400 MHz; $CDCl_3$) 0.51/0.69 (3H, s, 10'-Me), 0.73/0.82 and 0.96/1.13 (6H, 2xs, 8'- and 9'-Me), 0.87-1.15 (6H, complex of multiplets, 1"- and 4"-Me), 1.16-1.77 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 3.91-4.12 (2H, complex of multiplets, 2"- and 3"-H), 5.51 (1H, br s , OH), 4.73/4.77 (1H, s, 2'-H), 5.40/5.85 and 6.37/6.51 (2H, 2xs, C=CH_2), 5.52 (1H, br s, 3-H) and 7.27-7.36 and 8.42-8.54 (4H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 10.8/11.0 (C-10'), 14.5/14.6 and 14.8/14.9 (C-1" and C-4"), 20.1/20.2 (C-5'), 20.7 and 20.8/21.0 (C-8' and C-9'), 33.3/33.4 (C-6'), 47.8/48.0 and 49.0/49.1 (C-1' and C-7'), 52.8/53.0 (C-4'), 71.3/73.2, 73.4/73.5 and 74.4 (C-3, C-2" and C-3"), 85.7/85.9

(C-2'), 113.25/113.34 (C-3'), 121.1/121.9, 140.1/142.0 and 149.46/149.52 (Ar-C), 127.0/128.9 (C=CH_2), 150.1/151.2 (C-2) and 164.7/165.0 (C-1); *m/z* 401 (M^+, 8.2%) and 155 (100).

Preparation of *3,3-[(2R,3S)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(4-nitrophenyl)propanoate* (255d)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl acrylate (**250**) (0.29 g, 1.0 mmol), 4-nitrobenzaldehyde (0.15 g, 0.99 mmol) and DABCO (0.12 g, 1.0 mmol) in $CDCl_3$ (0.4 ml) were reacted as described for the synthesis of 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(3-pyridyl)propanoate (**255a**) (Method 2). After 7 days, work-up and elution of the residue through a silica plug (with hexane as the eluant) yielded, as a diastereomeric mixture, *3,3-[(2R,3S)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(4-nitrophenyl)propanoate* (**255d**) (0.29 g, 65%) (12% d.e. as determined by ^{1}H NMR spectroscopy) (Found: M^+ 445.2110. $C_{24}H_{31}O_7N$ requires *M*, 445.2100); ν_{max}(thin film)/cm^{-1} 3460 (OH), 1710 (C=O) and 1620 (C=C); δ_H(400 MHz; $CDCl_3$) 0.53/0.67 (3H, s, 10'-Me), 0.70/0.77 and 0.84/1.15 (6H, 2xs, 8'- and 9'-Me), 0.94-1.04 (6H, complex of multiplets, 1"- and 4"-Me), 1.27-1.79 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 3.95-4.16 (3H, complex of multiplets, OH and 2"- and 3"-H), 4.75/4.82 (1H, s, 2'-H), 5.37/5.51 (1H, s, 3-H), 5.64/5.86 and 6.37/6.54 (2H, 2xs, C=CH_2) and 7.54-7.62 and 8.13-8.23 (4H, 2xm, Ar-H); δ_C(100 MHz; $CDCl_3$) 10.9/11.1 (C-10'), 14.5/14.7 and 14.9/15.0 (C-1" and C-4"), 20.1/20.2 (C-5'), 20.64/20.66 and 20.8/21.0 (C-8' amd C-9'), 33.3/33.4 (C-6'), 47.8/48.1 and 49.0/49.1 (C-1' and C-7'), 52.8/53.0 (C-4'), 71.9/73.4, 73.6/73.8 and 74.4 (C-3, C-2" and C-3"), 85.8/86.0 (C-2'), 113.2/113.4 (C-3'), 123.36/123.42, 127.0/127.8, 140.1/140.2 and 147.3/147.5 (Ar-C), 127.4/129.2 (C=CH_2), 148.0/149.4 (C-2) and 164.7/165.0 (C-1); *m/z* 445 (M^+, 5.5%) and 55 (100).

Preparation of *3,3-[(2R,3S)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-phenylpropanoate* (255e)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl acrylate (**250**) (0.30 g, 1.0 mmol), benzaldehyde (0.12 g, 1.1 mmol) and DABCO (0.12 g, 1.1 mmol) in $CDCl_3$ (0.4 ml) were reacted as described for the synthesis of 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(3-pyridyl)propanoate (**255a**) (Method 2). After 3 months, work-up and flash chromatography [elution with hexane-EtOAc (9:1)] yielded, as a diastereomeric mixture,

*3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-phenylpropanoate* (**255e**) (0.25 g, 61%) (6% d.e. as determined by ^{1}H NMR spectroscopy) (Found: $\mathbf{M}^+$ 400.2250. $C_{24}H_{32}O_5$ requires *M*, 400.2251); ν_{max}(thin film)/cm^{-1} 3500 (OH), 1720 (C=O) and 1630 (C=C); δ_H(400 MHz; $CDCl_3$) 0.56/0.75 (3H, s, 10'-Me), 0.73/1.18 and 0.75/0.84† (6H, 2xs, 8' and 9'-Me), 0.97-1.04 (6H, complex of multiplets, 1"- and 4"-Me), 1.22-1.79 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 3.77/3.79 (1H, d, *J* 4.3/9.2, OH), 3.95-4.15 (2H, complex of multiplets, 2"- and 3"-H), 4.77/4.84 (1H, s, 2'-H), 4.42/5.77 and 6.34/6.47 (2H, 2xs, C=CH_2), 5.48/5.58 (1H, 2xm, 3-H) and 7.21-7.43 (5H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 10.9/11.1 (C-10'), 14.6/14.7 and 14.91/14.94 (C-1" and C-4"), 20.17/20.23 (C-5'), 20.6/20.7 and 20.9/21.0 (C-8' and C-9'), 33.4/33.5 (C-6'), 47.8/48.1 and 49.1/49.2 (C-1' and C-7'), 53.0/53.1 (C-4'), 72.6/74.3 (C-3), 73.5/73.6 and 74.5 (C-2" and C-3"), 85.5/85.8 (C-2'), 113.4/113.5 (C-3'), 126.1/127.0, 127.4/127.7, 128.2/128.3 (Ar-C), 126.80/127.9 (C=*C*H_2), 140.6/141.2 and 141.8/143.1 (Ar-C and C-2) and 165.4/165.5 (C-1); *m/z* 400 ($\mathbf{M}^+$, 0.2%) and 155 (100).

Preparation of *3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(4-methoxyphenyl)propanoate* (255f)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl acrylate (**250**) (0.30 g, 1.0 mmol), 4-methoxybenzaldehyde (0.15 g, 1.1 mmol) and DABCO (0.11 g, 1.0 mmol) in $CDCl_3$ (0.4 ml) were reacted as described for the synthesis of 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(3-pyridyl)propanoate (**255a**) (Method 2). After 4 months, work-up and flash chromatography [elution with hexane-EtOAc (9:1)] yielded, as a diastereomeric mixture, *3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(4-methoxy)phenylpropanoate* (**255f**) (0.18 g, 41%) (8% d.e. as determined by ^{1}H NMR spectroscopy) (Found: $\mathbf{M}^+$ 430.2348. $C_{25}H_{34}O_6$ requires *M*, 430.2355); ν_{max}(thin film)/cm^{-1} 3450 (OH), 1710 (C=O) and 1630 (C=C); δ_H(400 MHz; $CDCl_3$) 0.58/0.73 (3H, s, 10'-Me), 0.73/0.82¶ and 1.16 (6H, 2xs, 8'- and 9'-Me), 0.90-1.06 (6H, complex of multiplets, 1"- and 4"-Me), 1.21-1.80 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 3.63-3.71 (1H, complex of multiplets, OH), 3.75/3.76 (3H, s, OMe), 3.93-4.13 (2H, complex of multiplets, 2"- and 3"-H),

† There is coincidence with the 10'-Me signal.

¶ There is coincidence with the 10'-Me signal.

4.74/4.80 (1H, s, 2'-H), 5.40-5.47 (1H, complex of multiplets, 3-H), 5.52/5.76 and 6.31/6.42 (2H, 2xs, C=CH_2) and 6.78-6.88 and 7.23-7.33 (4H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 10.9/11.0 (C-10'), 14.60/14.63 and 14.82/14.84 (C-1" and C-4"), 20.1/20.2 (C-5'), 20.6/20.7 and 20.9/21.0 (C-8' and C-9'), 33.35/33.43 (C-6'), 47.8/48.0 and 49.2/49.3 (C-1' and C-7'), 53.0/53.1 (C-4'), 55.20/55.22 (OMe), 72.1/73.46, 73.55 and 74.4 (C-3, C-2", and C-3"), 85.5/85.7 (C-2'), 113.3/113.4 (C-3'), 113.58/113.63, 127.4/128.2, 132.9/134.0, 141.6/143.3 (Ar-C), 126.3/127.0 (C=*C*H_2), 159.0/159.1 (C-2) and 165.4/165.5 (C-1); *m/z* 430 ($\mathbf{M}^+$, 155%) and 1.9 (100).

Preparation of *3,3-[(2R,3S)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylenebutanoate* (255g)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl acrylate (**250**) (0.31 g, 1.1 mmol), acetaldehyde (0.082 g, 1.9 mmol) and DABCO (0.12 g, 1.1 mmol) in $CDCl_3$ (0.4 ml) were reacted as described for the synthesis of 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(3-pyridyl)propanoate (**255a**) (Method 2). After 3 months, work-up and flash chromatography [elution with hexane-EtOAc (9:1)] yielded, as a diastereomeric mixture, *3,3-[(2R,3S)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylenebutanoate* (**255g**) (0.23 g, 64%) [30% d.e. (18 % d.e.) as determined by ^{1}H NMR spectroscopy] (Found: $\mathbf{M}^+$ 338.2080. $C_{19}H_{30}O_5$ requires *M*, 338.2093); ν_{max}(thin film)/cm^{-1} 3500 (OH), 1715 (C=O) and 1640 (C=C); δ_H(400 MHz; $CDCl_3$) 0.78/0.79 (3H, s, 10'-Me), 0.83 and 1.15/1.16 (6H, 2xs, 8'- and 9'-Me), 0.99-1.06 (6H, complex of multiplets, 1"- and 4"-Me), 1.37/1.41 (3H, 2xd, *J* 6.6/6.5, 4-Me), 1.34-1.89 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 3.07/3.54 (1H, br s, OH), 3.97-4.16 (2H, complex of multiplets, 2"- and 3"-H), 4.55/4.61 (1H, m, 3-H), 4.81/4.84 (1H, s, 2'-H) 5.71/5.75 and 6.23/6.27 (2H, 2xs, C=CH_2); δ_C(100 MHz; $CDCl_3$) 11.1/11.2 (C-10'), 14.7/14.9 and 14.9/15.1[¥] (C-1" and C-4"), 20.1/20.6 (C-4), 20.2 (C-5'), 20.7 and 21.0/21.1 (C-8' and C-9'), 33.4/33.6 (C-6'), 48.0/48.1 and 49.1/49.2 (C-1' and C-7'), 53.1/53.2 (C-4'), 65.6/68.1 (C-3), 73.5/73.6 and 74.4 (C-2" and C-3"), 85.3/85.6 (C-2'), 113.4/113.5 (C-3'), 124.2/124.5 (C=*C*H_2), 143.6/143.7 (C-2) and 165.6/165.7 (C-1); *m/z* 338 ($\mathbf{M}^+$, 11.4%) and 155 (100).

[¥] There is coincidence of the C-1" and C-4" signals.

Preparation of *3,3-[(2R,3S)-2-*endo,*3-*exo-*butanedioxy]-2-*exo-*bornyl 3-hydroxy-2-methylenepentanoate* (255h)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl acrylate (**250**) (0.32 g, 1.1 mmol), propanaldehyde (0.066 g, 1.1 mmol) and DABCO (0.12 g, 1.1 mmol) in $CDCl_3$ (0.4 ml) were reacted as described for the synthesis of 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(3-pyridyl)propanoate (**255a**) (Method 2). After 3 months, work-up and flash chromatography [elution with hexane-EtOAc (9:1)] yielded, as a diastereomeric mixture, *3,3-[(2*R,*3*S*)-2-*endo,*3-*exo-*butanedioxy]-2-*exo-*bornyl 3-hydroxy-2-methylenepentanoate* (**255h**) (0.16 g, 42%) (35% d.e. as determined by ^{1}H NMR spectroscopy) (Found: $\mathbf{M}^+$ 352.2260. $C_{20}H_{32}O_5$ requires *M*, 352.2250); ν_{max}(thin film)/cm^{-1} 3500 (OH), 1715 (C=O) and 1630 (C=C); δ_H(400 MHz; $CDCl_3$) 0.78 (3H, s, 10'-Me), 0.83 and 1.15 (6H, 2xs, 8'- and 9'-Me), 0.92/0.95 (3H, t, *J* 7.45/7.50, 5-Me), 0.99-1.06 (6H, complex of multiplets, 1"- and 4"-Me), 1.34-1.80 (7H, complex of multiplets, 4'-H and 4-, 5'- and 6'-CH_2), 3.00/3.10 (1H, d, *J* 8.2/4.8, OH), 3.96-4.16 (2H, complex of multiplets, 2"- and 3"-H), 4.20-4.33 (2H, complex of multiplets, 3-H), 4.80/4.81 (1H, s, 2'-H) and 5.69/5.71 and 6.26/6.27 (1H, 2xs, C=CH_2); δ_C(100 MHz; $CDCl_3$) 10.2 (C-10'), 11.18/11.22 (C-5), 14.76/14.86 and 14.88/14.91 (C-1" and C-4"), 20.21/20.24 (C-5'), 20.7 and 21.00/21.03 (C-8' and C-9'), 27.9/29.3 (C-4), 33.4/33.6 (C-6'), 48.0/48.1 and 49.1/49.2 (C-1' and C-7'), 53.2 (C-4'), 72.1, 73.5 and 74.3/74.4 (C-3, C-2" and C-3"), 85.4/85.6 (C-2'), 113.39/113.43 (C-3'), 124.7/125.7 (C=*C*H_2), 142.2/142.6 (C-2) and 165.6/165.8 (C-1); *m/z* 352 ($\mathbf{M}^+$, 8.3%) and 155 (100).

Preparation of *3,3-[(2R,3S)-2-*endo,*3-*exo-*butanedioxy]-2-*exo-*bornyl 3-hydroxy-2-methylenehexanoate* (255i)

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl acrylate (**250**) (0.30 g, 1.0 mmol), butyraldehyde (0.086 g, 1.2 mmol) and DABCO (0.12 g, 1.1 mmol) in $CDCl_3$ (0.4 ml) were reacted as described for the synthesis of 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 3-hydroxy-2-methylene-3-(3-pyridyl)propanoate (**255a**) (Method 2). After 3 months, work-up and flash chromatography [elution with hexane-EtOAc (9:1)] yielded, as a diastereomeric mixture, *3,3-[(2*R,*3*S*)-2-*endo,*3-*exo-*butanedioxy]-2-*exo-*bornyl 3-hydroxy-2-methylenehexanoate* (**255i**) (0.18, 48%) [34% d.e. (29% d.e.) as determined by ^{1}H NMR spectroscopy] (Found: $\mathbf{M}^+$ 366.2406. $C_{21}H_{34}O_5$ requires *M*, 366.2418); ν_{max}(thin film)/cm^{-1} 3350 OH), 1720 (C=O) and 1635 (C=C); δ_H(400 MHz; $CDCl_3$) 0.78 (3H, s, 10'-Me), 0.83 and 1.16 (6H, 2xs, 8'- and 9'-Me), 0.87-

0.95 (3H, complex of multiplets, , 6-Me), 0.98-1.07 (6H, comples of multiplets, 1"- and 4"-Me), 1.22-1.80 (9H, complex of multiplets, 4'-H and 5'-, 6'-, 4- and 5-CH_2), 3.03/3.11 (1H, d, *J* 8.4/4.7, OH), 3.97-4.16 (2H, complex of multiplets, 2"- and 3"-H), 4.32/4.39 (1H, m, 3-H), 4.81/4.82 (1H, s, 2'-H) and 5.69/5.71 and 6.25/6.27 (2H, 2xs, C=CH_2); δ_C(100 MHz; $CDCl_3$) 11.18/11.23 (C-10'), 13.81/13.85 (C-6), 14.78/14.88 and 14.88/14.92 (C-1" and C-4"), 19.1/19.2 and 20.2/20.3 (C-5' and C-5), 20.7/21.00 and 21.04/21.1 (C-8' and C-9'), 33.4/33.6 (C-6'), 37.0/38.6 (C-4), 48.0/48.1 and 49.1/49.2 (C-1' and C-7'), 53.2 (C-4'), 70.3/72.8 (C-3), 73.6 and 74.4 (C-2" and C-3"), 85.4/85.6 (C-2'), 113.40/133.44 (C-3'), 124.5/125.5 (C=*C*H_2). 142.5/142.9 (C-2) and 165.6/165.8 (C-1); *m/z* 366 ($\mathbf{M}^+$, 7.1%) and 155 (100).

Preparation of *1-({3,3-[(2R,3S)-2-*endo,*3-*exo-*butanediol]bornane-2-exo-oxy}dimethylsilyloxy)-3,4-dihydronaphthalene* (259)

Part A.

Diisopropylamine (1.12 g, 11.0 mmol), BuLi (15% in hexane; 7.0 ml, 12 mmol), α-tetralone (1.4 g, 9.8 mmol) and Me_2SiCl_2 (1.39 g, 10.7 mmol) in dry THF (30 ml) were reacted as described for the synthesis of 1-{dimethyl(spiro[bornane-3,2'-indan]-2-*exo*-oxy)silyloxy}-3,4-dihydronaphthalene (**194**) (Method 2; Part A).

Part B.

3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-Butanedioxy]-2-*exo*-bornanol (**235a**) (2.0 g, 8.3 mmol), BuLi (15% in hexane; 5.1 ml, 8.3 mmol) in dry THF (30 ml) and the chlorosilane formed in part A, were reacted as described for the synthesis of 1-{dimethyl(spiro[bornane-3,2'-indan]-2-*exo*-oxy}silyloxy)-3,4-dihydronaphthalene (**194**) (Method 2; Part B). Work-up and flash chromatography [elution with hexane-EtOAc (49:1)] yielded, as an oil, *1-({3,3-[(2*R,*3*S*)-2-*endo,*3-*exo-*butanedioxy]bornane-2-*exo-*oxy}dimethylsilyloxy)-3,4-dihydronaphthalene* (**259**) (1.62 g, 44%) (Found: $\mathbf{M}^+$ 442.2534. $C_{26}H_{38}O_4Si$ requires *M*, 442.2539); ν_{max}(thin film)/cm^{-1} 1645 (C=C), 1255 (SiMe) and 1050 (SiO); δ_H(400 MHz; $CDCl_3$) 0.25 (6H, s, SiMe), 0.79, 0.82 and 1.16 (9H, 3xs, 8'-, 9'- and 10'-Me), 1.12 and 1.14 (6H, 2xd, *J* 5.46 and 5.41, 1"- and 4"-Me), 1.17-1.62 (4H, complex of multiplets, 5'- and 6'-CH_2), 1.73 (1H, m, 4'-H), 2.31 (2H, dt, $J_{3,4}$ 8.0 and $J_{2,3}$ 4.6, 3-CH_2), 2.74 (2H, t, $J_{3,4}$ 8.0, 4-CH_2), 3.73 (1H, s, 2'-H), 4.02 and 4.17 (2H, 2xm, 2"- and 3"-H), 5.37 (1H, t, $J_{2,3}$ 4.6, 2-H) and 7.06-7.20 and 7.44-7.46 (4H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) -2.4 and -2.0 (SiMe), 11.8, 21.0 and 21.5 (C-8', C-9' and C-10'),

15.4 and 15.5 (C-1" and C-4"), 20.5 (C-5'), 22.2 (C-3), 28.2 (C-4), 33.6 (C-6'), 48.0 and 49.4 (C-1' and C-7'), 51.7 (C-4'), 72.5 and 73.2 (C-2" and C-3"), 86.5 (C-2'), 105.8 (C-2), 113.7 (C-3'), 121.9, 126.1, 126.8, 127.1, 133.6 and 137.0 (Ar-C) and 147.4 (C-1); *m/z* 442 ($\mathbf{M}^+$, 1.1%), 297 (5.8), 221 (9.6), 204 (1.7), 203 (7.3), 176 (0.6), 95 (17.5), 75 (97.8) and 155 (100).

Preparation of *3,3-dimethyl-2-*({3,3-*[(2*R,*3*S*)-2-*endo,*3*-exo-*butanedioxy]bornane-2*-exo-*oxy}dimethylsilyloxy)but-1-ene* (260)

Part A.

Diisopropylamine (1.06 g, 10.4 mmol), BuLi (15% in hexane; 6.6 ml, 11 mmol), pinacolone (0.86 g, 8.6 mmol) and Me_2SiCl_2 (1.2 ml, 10 mmol) in dry THF (30 ml) were reacted as described for the synthesis of 1-{dimethyl(spiro[bornane-3,2'-indan]-2-*exo*-oxy)silyloxy}-3,4-dihydronaphthalene (**194**) (Method 2; Part A).

Part B.

3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]-2-*exo*-bornanol (**235a**) (0.98 g, 4.1 mmol), BuLi (15% in hexane; 2.5 ml, 4.2 mmol) in dry THF (30 ml) and the chlorosilane formed in part A, were reacted as described for the synthesis of 1-{dimethyl(spiro[bornane-3,2'-indan]-2-*exo*-oxy)silyloxy}-3,4-dihydronaphthalene (**194**) (Method 2; Part B). Work-up and flash chromatography [elution with hexane-EtOAc (49:1)] yielded, as an oil, *3,3-dimethyl-2-({3,3-[(2*R,*3*S*)-2-*endo,*3*-exo-*butanedioxy]bornane-2*-exo-*oxy}dimethylsilyloxy)but-1-ene* (**260**) (0.80 g, 49%) (Found: $\mathbf{M}^+$ 396.2692. $C_{22}H_{40}O_4Si$ requires *M*, 396.2696); $[\alpha]_D^{27}$ -3.0 (*c* 2.2 in $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1630 (C=C), 1260 (SiMe) and 1035 (SiO); δ_H(400 MHz; $CDCl_3$) 0.19 (6H, s, SiMe), 0.78, 0.83 and 1.14 (9H, 3xs, 8'-, 9'- and 10'-Me), 1.05 [9H, s, $C(CH_3)_3$], 1.10 and 1.13 (6H, 2xd, *J* 6.40 and 6.35, 1"- and 4"-Me), 1.15-1.61 (4H, complex of multiplets, 5'- and 6'-CH_2), 1.69 (1H, m, 4'-H), 3.66 (1H, s, 2'-H), 3.99 and 4.15 (2H, 2xm, 2"- and 3"-H) and 4.09 and 4.16 (2H, 2xd, *J* 1.1, 1-CH_2); δ_C(100 MHz; $CDCl_3$) -2.6 and -2.2 (SiMe), 11.9, 21.0 and 21.5 (C-8', C-9' and C-10'), 15.37 and 15.43 (C-1" and C-4"), 20.5 (C-5), 28.1 [$C(CH_3)_3$], 33.7 (C-6'), 36.4 (C-3), 48.0 and 49.4 (C-1' and C-7'), 51.8 (C-4'), 72.5 and 73.3 (C-2" and C-3"), 86.5 (C-2'), 87.1 (C-1), 113.8 (C-3'), 166.0 (C-2); *m/z* 430 ($\mathbf{M}^+$, 0.07%), 297 (0.08), 175 (0.9), 158 (0.3), 157 (1.7), 130 (1.8), 95 (7.0), 75 (1.0) and 91 (100).

Preparation of *2-({3,3-[(2R,3S)-2-endo,3-exo-butanedioxy]bornane-2-exo-oxy}dimethylsilyloxy)-1,2,3,4-tetrahydro-1-naphthalone* (261)

1-({3,3-[(2*R*,3*S*)-2-*Endo*,3-*exo*-butanedioxy]bornane-2-*exo*-oxy}dimethylsilyloxy)-3,4-dihydronaphthalene (**259**) (0.51 g, 1.2 mmol) was reacted with MCPBA (55%; 0.35 g, 1.1 mmol) and $NaHCO_3$ (0.29 g, 3.4 mmol) in CH_2Cl_2 (30 ml) at 0 °C as described for the synthesis of 2-[dimethyl(10-pinanyl)silyloxy]-1,2,3,4-tetrahydro-1-naphthalone (**159**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded an oil (0.17 g) comprising a 1:1 mixture of 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornanol (**235a**) and a diastereomeric mixture of *2-({3,3-[(2*R,3S*)-2-*endo,3-exo-*butanedioxy]bornane-2-exo-oxy}dimethylsilyloxy)-1,2,3,4-tetrahydro-1-naphthalone* (**261**) (17%) (16% d.e. as determined by ^1H NMR spectroscopy) M^+-$C_{14}H_{23}O_3$ (Found: M^+ 219.0846. $C_{12}H_{15}O_2Si$ requires *M*, 219.0841) and M^+-$C_{12}H_{15}O_2Si$ (Found: M^+ 239.1656. $C_{14}H_{23}O_3$ requires *M*, 239.1647);[4] ν_{max}(thin film)/cm^{-1} 1705 (C=O), 1255 (SiMe) and 1040 (SiO); δ_H(400 MHz; $CDCl_3$) 0.21/0.22 and 0.23/0.24 (6H, 2xs, SiMe), 0.74-1.17 (15H, complex of multiplets, 8'-, 9'-, 10'-Me, 1"- and 4"-Me), 1.06-1.17 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 2.22/2.41 (2H, m, 3-CH_2), 3.03/3.05 (2H, 2xm, 4-CH_2), 3.64/3.66 (1H, s, 2'-H), 3.92-4.20 (2H, complex of multiplets, 2"- and 3"-H), 4.60/4.72 (1H, dd, 2-CH_2) and 7.18-7.32, 7.40-7.47 and 7.97-8.04 (4H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) -2.1/-1.8 and -1.2/-0.7 (SiMe), 11.8, 20.9 and 21.5 (C-8', C-9' and C-10'), 15.48 and 15.52/15.57 (C-1" and C-4"), 20.4 (C-5'), 28.0 (C-4), 32.8/33.0 (C-3), 33.6 (C-6'), 47.9 and 49.3 (C-1' and C-7'), 51.29/51.34 (C-4'), 72.2 and 72.9 (C-2" and C-3"), 74.6/74.7 (C-2), 85.6/85.8 (C-2'), 113.7 (C-3'), 126.6, 127.6, 128.5, 131.97/131.99, 133.2 and 143.5 (Ar-C) and 197.2 (C-1); *m/z* 458 (M^+, 0.7%) and 219 (100).

Attempted preparation of *2-t-butyl-1,2,3,4-tetrahydro-1-naphthalone* (160)

A solution of 1-({3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]bornane-2-*exo*-oxy}dimethylsilyloxy)-3,4-dihydronaphthalene (**259**) (0.15 g, 0.34 mmol) and *t*-BuCl (0.08 ml, 0.8 mmol) in dry CH_2Cl_2 (5 ml) was reacted with $TiCl_4$ (0.1 M solution in CH_2Cl_2; 0.7 ml, 0.7 mmol) as described in section 3.2.2, p. 162. Work-up and flash chromatography yielded a complex mixture of products that could not be purified.

---

[4] High resolution MS data could not be obtained for the silyl enol ether (**261**). However, such data was obtained for the two fragments.

Preparation of *1-hydroxy-4,4-dimethyl-1-phenyl-3-pentanone* (163)

3,3-Dimethyl-2-({3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]bornane-2-*exo*-oxy}dimethylsilyloxy)but-1-ene (**260**) (0.37 g, 0.92 mmol), $TiCl_4$ (1.0 M solution in CH_2Cl_2, 1.1 ml, 1.1 mmol) and PhCHO (0.11 ml, 1.1 mmol) in dry CH_2Cl_2 (10 ml) were reacted as described in Section 3.2.2, p. 163. Work-up and flash chromatography yielded, as oils, 3,3-[(2*R*,3*S*)-2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornanol (**235a**) (0.05 g, 19%) and 1-hydroxy-4,4-dimethyl-1-phenyl-3-pentanone (**163**) (0.05 g, 24%).

The enantiomeric excess was determined as follows:

i) The addition of $Eu(hfc)_3$ (17 mg) to the enantiomeric mixture of 1-hydroxy-4,4-dimethyl-1-phenyl-3-pentanone (**163**) (14 mg) in $CDCl_3$ resulted in a downfield shift and resolution of the *t*-Bu signals in the ^1H NMR spectrum. The enantiomeric excess was determined to be 20% by integration of the signals.

ii) The addition of $Pr(hfc)_3$ (11 mg) to the enantiomeric mixture of 1-hydroxy-4,4-dimethyl-1-phenyl-3-pentanone (**163**) (14 mg) in $CDCl_3$ resulted in an upfield shift and resolution of the *t*-Bu signals in the ^1H NMR spectrum. The enantiomeric excess was determined to be 20% by integration of the signals.

iii) The optical rotation of the enantiomeric mixture of 1-hydroxy-4,4-dimethyl-1-phenyl-3-pentanone (**163**) was determined as $[\alpha]_D^{21}$ -4.8 (*c* 0.7 in $CHCl_3$) [lit.,[259, 260] $[\alpha]_D^{25}$ +45.9 ($CHCl_3$), for 75% e.e. (*R*)]. From this data, the enantiomeric excess was determined to be 8%.

3.2.6 The camphor-derived chiral auxiliary (262)

Preparation of *3,3-[(R,R)-2,3-butanedioxy]-2-bornanone* (262)

A mixture of camphorquinone (**223**) (1.97 g, 11.9 mmol), (*R,R*)-(-)-2,3-butanediol (**233b**) (2.00 g, 22.2 mmol) and *p*-toluenesulfonic acid (0.5 g) in benzene (20 ml) was placed in a reaction vessel fitted with a Dean-Stark trap and boiled under reflux for 1 week. During this period, approximately 0.5 ml of H_2O was collected. The reaction mixture was then treated with 1M NaOH (20 ml), washed with H_2O (2x20 ml) and dried (anhyd. $MgSO_4$). The solvent was removed *in vacuo* and flash chromatography of the residual oil [elution with hexane-EtOAc (19:1)] yielded *3,3-[(R,R)-2,3-butanedioxy]-2-bornanone* (**262**) (2.14 g, 75%) (Found: M^+ 238.1568. $C_{14}H_{22}O_3$ requires *M*, 238.1569); $[\alpha]_D^{21}$ +23.7 (*c* 0.5); ν_{max}(thin film)/cm^{-1} 1760 (C=O);

δ_H(400 MHz; $CDCl_3$) 0.88, 0.95 and 1.01 (9H, 3xs, 8-, 9- and 10-Me), 1.22 and 1.27 (6H, 2xd, *J* 6.1 and 6.1, 1'- and 4'-Me), 1.47-2.04 (5H, complex of multiplets, 4-H and 5- and 6-CH_2) and 3.53 and 4.20 (2H, 2xm, 2'- and 3'-H); δ_C(100 MHz; $CDCl_3$) 9.2, 19.2 and 21.5 (C-8, C-9 and C-10), 16.7 and 17.2 (C-1' and C-4'), 21.1 (C-5), 30.7 (C-6), 43.5 and 58.1 (C-1 and C-7), 52.6 (C-4), 78.4 and 80.3 (C-2' and C-3'), 106.8 (C-3) and 218.3 (C-2); *m/z* 238 (M^+, 0.8%) and 127 (100).

Preparation of *3,3-[(R,R)-2,3-butanedioxy]-2-*exo-*bornanol* (263)

3,3-[(*R,R*)-2,3-butanedioxy]-2-bornanone (**262**) (1.84 g, 7.76 mmol) was treated with $LiAlH_4$ (0,16 g, 4.2 mmol) in dry Et_2O (5 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornanol (**172**). Work-up and flash chromatography of the residual oil [elution with hexane-EtOAc (9:1)] yielded, as white crystals, *3,3-[(R,R)-2,3-butanedioxy]-2-*exo-*bornanol* (**263**) (1.16 g, 62%), m.p. 38-40 °C (Found: M^+ 240.1723. $C_{14}H_{24}O_3$ requires *M*, 240.1725); $[\alpha]_D^{21}$ -13.0 (*c* 2.0); ν_{max}(thin film)/cm^{-1} 3500 (OH); δ_H(400 MHz; $CDCl_3$) 0.78, 0.87 and 1.04 (9H, 3xs, 8-, 9- and 10-Me), 1.22 and 1.24 (6H, 2xd, *J* 6.1 and 6.2, 1'- and 4'-Me), 1.42-1.74 (5H, complex of multiplets, 4-H and 5- and 6-CH_2), 2.45 (1H, d, *J* 6.0, OH), 3.30 (1H, d, *J* 6.0, 2-H) and 3.53 and 3.64 (2H, 2xm, 2'- and 3'-H); δ_C(100 MHz; $CDCl_3$) 10.9, 21.2 and 21.6 (C-8, C-9 and C-10), 20.6 (C-5), 16.6 and 17.5 (C-1' and C-4'), 33.4 (C-6), 47.5 and 49.2 (C-1 and C-7), 53.9 (C-4), 77.7 and 79.7 (C-2' and C-3'), 85.6 (C-2) and 114.6 (C-3); *m/z* 240 (M^+, 15.1%) and 155 (100).

Preparation of *3,3-[(R,R)-2,3-butanedioxy]-2-*exo-*bornyl 3,3-dimethylbutanoate* (264)

3,3-[(*R,R*)-2,3-Butanedioxy]-2-*exo*-bornanol (**263**) (0.73 g, 3.7 mmol) was treated with butyllithium (15% solution in hexane, 1.9 ml; 3.1 mmol) and 3,3-dimethylbutanoyl chloride (0.52 ml, 3.7 mmol) in dry Et_2O (20 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 3,3-dimethylbutanoate (**179**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (19:1)] yielded, as an oil, *3,3-[(R,R)-2,3-butanedioxy]-2-*exo-*bornyl 3,3-dimethylbutanoate* (**264**) (0.64 g, 63%) (Found: M^+ 338.2446. $C_{20}H_{34}O_4$ requires *M*, 338.2457); $[\alpha]_D^{23}$ -46.8 (*c* 1.7); ν_{max}(thin film)/cm^{-1} 1735 (C=0); δ_H(400 MHz; $CDCl_3$) 0.79 (3H, s, 10'-Me), 0.81 and 1.11 (6H, 2xs, 8'- and 9'-Me), 1.03 [9H, s, $C(CH_3)_3$], 1.15 and 1.20 (6H, 2xd, *J* 5.7 and 5.7, 1"- and 4"-Me), 1.29-1.83 (5H, complex of multiplets, 4'-H and 5'- and 6'-CH_2), 2.22 (2H, s, 2-CH_2), 3.37-3.48 (2H, complex of multiplets, 2"- and 3"-H) and 4.49 (1H, s, 2'-H); δ_C(100 MHz; $CDCl_3$) 11.6 (C-10'), 16.5 and 17.1 (C-1' and C-4'), 20.6 (C-5'), 20.9 (C-8' and C-

9'),‡ 29.7 [C(*C*H$_3$)$_3$], 30.7 (C-3), 33.6 (C-6'), 47.9 and 48.9 (C-1' and C-7'), 48.3 (C-2), 55.0 (C-4'), 77.7 and 79.5 (C-2" nd C-3"), 86.4 (C-2'), 113.9 (C-3') and 171.7 (C-1); *m/z* 338 (M$^+$, 5.9%) and 155 (100).

Preparation of *3,3-[(R,R)-2,3-butanedioxy]-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate* (265)

3,3-[(*R,R*)-2,3-Butanedioxy]-2-*exo*-bornyl 3,3-dimethylbutanoate (**264**) (0.50 g, 1.5 mmol) was reacted with LDA [generated from diisopropylamine (0.25 ml, 1.8 mmol) and butyllithium (15% in hexane; 1.2 ml, 1.9 mmol)] and benzyl bromide (0,21 ml, 1.8 mmol) in dry THF (5 ml) as described for the synthesis of 3-*exo*-(α-methoxybenzyl)-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate (**181**). Work-up and flash chromatography of the residue [elution with hexane-EtOAc (49:1)] yielded an oil (0.34 g) comprising a 2:3 mixture of the starting material, 3,3-[(*R,R*)-2,3-butanedioxy]-2-*exo*-bornyl 3,3-dimethylbutanoate (**264**) and a diastereomeric mixture of *3,3-[(R,R)-2,3-butanedioxy]-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate* (**265**) (32%) (25% d.e. as determined by ^{1}H NMR spectroscopy). Further purification by PLC [elution with hexane-EtOAc (49:1)] yielded, as white crystals, a single diastereomer of *3,3-[(R,R)-2,3-butanedioxy]-2-*exo*-bornyl 2-benzyl-3,3-dimethylbutanoate* (165) m.p. 98-100 °C (Found: M$^+$ 428.2911. $C_{27}H_{40}O_4$ requires *M*, 428.2927); $[\alpha]_D^{22}$ -53.2 (*c* 1.7); ν_{max}(thin film)/cm^{-1} 1725 (C=O); δ_H(400 MHz; $CDCl_3$) 1.70-1.25 [24H, complex of multiplets, C(C*H*$_3$)$_3$, 8'-, 9'-, 10'-, 1"- and 4"-Me), 1.36-1.75 (5H, 4'- and 5'- and 6'-C*H*$_2$), 2.53 (1H, dd, *J* 3.9 and 11.0, 2-H), 2.82-2.89 (2H, complex of multiplets, PhC*H*$_2$), 3.34-3.50 (2H, complex of multiplets, 2"- and 3"-H), 4.14 (1H, s, 2'-H), 7.08-7.23 (5H, complex of multiplets, Ar-H); δ_C(100 MHz; $CDCl_3$) 10.7 (C-10'), 16.3 and 17.1 (C-1' and C-7'), 20.4 (C-5'), 20.8 and 20.9 (C-8' and C-9'), 28.0 [C(*C*H$_3$)$_3$], 33.1 (C-3), 33.5 (C-6'), 34.3 (PhC*H*$_2$), 47.8 and 48.5 (C-1' and C-7'), 55.1 (C-4'), 58.8 (C-2), 77.7 and 79.1 (C-2" and C-3"), 86.8 (C-2'), 133.8 (C-3'), 126.0, 128.2, 128.9, 140.4 (Ar-C) and 173.8 (C-1); *m/z* 428 (M$^+$, 8.3%) and 155 (100).

‡ There is coincidence of C-8' and C-9' signals in the ^{13}C NMR spectrum.

REFERENCES

1. J. D. Morrison and H. S. Mosher, *Asymmetric Organic Reactions*, American Chemical Society, Washington, 1976, p. 4.
2. R. K. Mackie, D. M. Smith and R. A. Aitken, *Guidebook to Organic Synthesis*, Longman, 1990.
3. G. R. Stevenson and J. -P. Genet, in *Advanced Asymmetric Synthesis*, ed. G. R. Stevenson, Chapman & Hall, London, 1996, p. 3.
4. C. R. Eck, G. L. Hodgson, D. F. MacSweeney, R. W. Mills and T. Money, *J. Chem. Soc., Perkin Trans. 1*, 1974, 1938.
5. S. G. Davies, *Chem. Br.*, 1989, **25**, 268.
6. D. Enders, P. Fey and H. Kipphardt, *Org. Synth.*, 1987, **65**, 173.
7. D. Enders, H. Kipphardt and P. Fey, *Org. Synth.*, 1987, **65**, 183.
8. D. Enders, in *Asymmetric Synthesis*, ed. J. D. Morrison, Academic Press, Orlando, 1984, vol. 3, p. 275.
9. A. I. Meyers, G. Knaus and K. Kamata, *J. Am. Chem. Soc.*, 1974, **96**, 268.
10. K. A. Lutomski and A. I. Meyers, in *Asymmetric Synthesis*, ed. J. D. Morrison, Academic Press, Orlando, 1984, vol. 3, p. 213.
11. T. Katsuki and K. B. Sharpless, *J. Am. Chem. Soc.*, 1980, **102**, 5974.
12. K. B. Sharpless, in *Asymmetric Synthesis*, ed. J. D. Morrison, Academic Press, Orlando, 1985, vol 5, p. 193.
13. V. S. Martin, S. S. Woodard, T. Katsuki, Y. Yamada, M. Ikeda and K. B. Sharpless, *J. Am. Chem. Soc.*, 1981, **103**, 6237.
14. S. Miyano, L. D. -L. Lu, S. M. Viti and K. B. Sharpless, *J. Org. Chem.*, 1983, **48**, 3608.
15. A. Miyashita, A. Yasuda, H. Takaya, K. Toriumi, T. Ito, T. Souchi and R. Noyori, J. Am. Chem. Soc., 1980, **102**, 7932.
16. H. Takaya, K. Mashima, K. Koyano, M. Yagi, H. Kumobayashi, T. Taketomi, S. Akutagawa and R. Noyori, *J. Org. Chem.*, 1986, **51**, 629.
17. R. Noyori, M. Ohta, Y. Hsiao, M. Kitamura, T. Ohta and H. Takaya, *J. Am. Chem. Soc.*, 1986, **108**, 7117.

18. R. Noyori and H. Takaya, *Acc. Chem. Res.*, 1990, **23**, 345.

19. K. Tanaka, H. Ushio, Y. Kawabata and H. Suzuki, *J. Chem. Soc., Perkin Trans. 1*, 1991, 1445.

20. K. Tanaka and H. Suzuki, *J. Chem. Soc., Chem. Commun.*, 1991, 101.

21. K. Tanaka, H. Ushio and H. Suzuki, *J. Chem. Soc., Chem. Commun.*, 1990, 795.

22. K. Tanaka, J. Matsui, Y. Kawabata, H. Suzuki and A. Watanabe, *J. Chem. Soc., Chem. Commun.*, 1991, 1632.

23. T. Money, *Nat. Prod. Rep.*, 1985, 253.

24. H. E. Armstrong and T. M. Lowry, *J. Chem. Soc.*, 1902, **81**, 1441.

25. A. McKenzie, *J. Chem. Soc.*, 1906, **85**, 365.

26. A. McKenzie and H. Wren, *J. Chem. Soc.*, 1906, **85**, 688.

27. V. Prelog, O. Ceder and M. Wilhelm, *Helv. Chim. Acta*, 1955, **35**, 303 and references cited therein.

28. A. Streitwieser, Jr. and J. R. Wolfe, Jr., *J. Am. Chem. Soc.*, 1957, **79**, 903.

29. K. Sisido, K. Kumazawa and H. Nozaki, *J. Am. Chem. Soc.*, 1960, **82**, 125.

30. M. H. Palmer and J. A. Reid, *J. Chem. Soc.*, 1962, **141**,1762.

31. A. Gilbert, T. W. Heritage and N. S. Isaacs, *Tetrahedron: Asymmetry*, 1991, **2**, 969.

32. P. T. Kaye and R. A. Learmonth, *S. Afr. J. Chem.*, 1990, **43**, 114.

33. P. T. Kaye and R. A. Learmonth, *Synth. Commun.*, 1990, **20**, 1333.

34. J. M. McIntosh and P. Mishra, *Can. J. Chem.*, 1986, **64**, 726.

35. J. M. McIntosh and R. K. Leavitt, *Tetrahedron Lett.*, 1986, **27**, 3839.

36. J. Yaozhong, L. Guilan, L. Jinchu and Z. Changyou, *Synth. Commun.*, 1987, **17**, 1545.

37. J. Yaozhong, Z. Changyou, G. Lan and L. Guilan, *Synth. Commun.*, 1989, **19**, 1297.

38. J. Yaozhong, Z. Changyou and P. Huri, *Synth. Commun.*, 1989, **19**, 881.

39. J. Yaozhong, L. Guilan and D. Jingen, *Synth. Commun.*, 1988, **18**, 1291.

40. S. -Y Po, H. -H. Liu and B. -J. Uang, *Tetrahedron: Asymmetry*, 1990, **1**, 143.

41. P. D. Bartlett and L. H. Knox, *Org. Synth.*, 1965, **45**, 55.

42. T. Kunieda, T. Ishizuka, T. Higuchi and M. Hirobe, *J. Org. Chem.*, 1988, **53**, 3381.

43. T. Ishizuka, S. Ishibuchi and T. Kunieda, *Tetrahedron Lett.*, 1989, **30**, 3449.

44. R. A. Chittenden and G. H. Cooper, *J. Chem. Soc.*, 1970, **149**, 49.

45. T. R. Kelly and A. Arvanitis, *Tetrahedron Lett.*, 1984, **25**, 39.

46. P. Zhang and R. E. Gawley, *Tetrahedron Lett.*, 1992, **33**, 2945.

47. R. E. Gawley and P. Zhang, *J. Org. Chem.*, 1996, **61**, 8103.

48. K. Tanaka, H. Osuga and H. Suzuki, *Tetrahedron: Asymmetry*, 1993, **4**, 1843.

49. E. L. Eliel and W. J. Frazee, *J. Org. Chem.*, 1979, **44**, 3598.

50. M. Isobe, J. Obeyama, Y. Funabashi and T. Goto, *Tetrahedron Lett.*, 1988, **29**, 4773.

51. O. De Lucchi, C. Marchioro, G. Valle and G. Modena, *J. Chem. Soc., Chem. Commun.*, 1985, 878.

52. O. De Lucchi, V. Lucchini, C. Marchioro, G. Valle and G. Modena, *J. Org. Chem.*, 1986, **51**, 1457. Corrections seen in *J. Org. Chem.*, 1989, **54**, 3245.

53. Y. Arai, K. Hayashi, T. Koizumi, M Shiro and K. Kuriyama, *Tetrahedron Lett.*, 1988, **29**, 6143.

54. Y. Arai, M. Matsui and T. Koizumi, *J. Chem. Soc., Perkin Trans. 1*, 1990, 1233.

55. Y. Arai, M. Matsui and T. Koizumi, *Synthesis*, 1990, 320.

56. Y. Arai, K. Hayashi, M. Matsui, T. Koizumi, M. Shiro and K. Kuriyama, *J. Chem. Soc., Perkin Trans. 1*, 1991, 1709.

57. S. G. Pyne, P. Bloem and R. Griffith, *Tetrahedron*, 1989, **45**, 7013.

58. C. E. Dixon, K. Hellmund and S. G. Pyne, *J. Chem. Res. (S)*, 1996, 372.

59. K. Nishide, Y. Shigeta, K. Obata and M. Nobe, *J. Am. Chem. Soc.*, 1996, **118**, 13103.

60. B. M. Eschler, R. K. Haynes, S. Kremmydas and D. D. Ridley, *J. Chem. Soc., Chem. Commun.*, 1988, 137.

61. A. K. McFarlane, G. Thomas and A. Whiting, *Tetrahedron Lett.*, 1993, **34**, 2379.

62. S. -M Hung, D. -S. Lee and T. -K. Yang, *Tetrahedron: Asymmetry*, 1990, **1**, 873.

63. G. -S. Yang, Y. Li, Z. -Q. Fang, X. Xiao, Y. -Z. Jiang and T. -K. Yang, *Hecheng Huaxue*, 1994, **2**, 154.

64. T. -K. Yang, R. -Y. Chen, D. -S. Lee, W. -S. Peng, Y. -Z. Jiang, A. -Q. Mi and T. -T. Jong, *J. Org. Chem.*, 1994, **59**, 914.

65. N. P. Singh, B. Metz and J. F. Biellmann, *Bull. Soc. Chim. Fr.*, 1990, **127**, 98.

66. T. Herold and R. W. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 768.

67. R. W. Hoffmann and H. -J. Zeiss, *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 218.

68. R. W. Hoffmann, H. -J. Zeiβ, W. Ladner and S. Tabche, *Chem. Ber.*, 1982, **115**, 2357.

69. T. Herold, U. Schrott and R. W. Hoffmann, *Chem. Ber.*, 1981, **114**, 359.

70. M. García-Valverde, R. Pedrosa and M. Vicente, *Tetrahedron: Asymmetry*, 1995, **6**, 1787.

71. M. Caballero, M. García-Valverde, R. Pedrosa and M. Vicente, *Tetrahedron: Asymmetry*, 1996, **7**, 219.

72. P. T. Kaye and W. Molema; Unpublished data.

73. D. F. Taber and K. Raman, *J. Am. Chem. Soc.*, 1983, **105**, 5935.

74. D. F. Taber, K. Raman and M. D. Gaul, *J. Org. Chem.*, 1987, **52**, 28.

75. S. R. Wilson, A. M. Venkatesan, C. E. Augelli-Szafran and A. Yasmin, *Tetrahedron Lett.*, 1991, **32**, 2339.

76. D. F. Taber, J. F. Mack, A. L. Rheingold and S. J. Geib, *J. Org. Chem.*, 1989, **54**, 3831.

77. P. Somfai, D. Tanner and T. Olsson, *Tetrahedron*, 1985, **41**, 5973.

78. W. Oppolzer, M. Kurth, D. Reichlin, C. Chapuis, M. Mohnhaupt and F. Moffatt, *Helv. Chim. Acta*, 1981, **64**, 2802.

79. T. Arnold and H. -U. Reissig, *Synlett*, 1990, 514.

80. W. Oppolzer, C. Chapuis, G. M. Dao, D. Reichlin and T. Godel, *Tetrahedron Lett.*, 1982, **23**, 4781.

81. W. Oppolzer and C. Chapuis, *Tetrahedron Lett.*, 1983, **24**, 4665.

82. W. Oppolzer, C. Chapuis, D. Dupuis and M. Guo, *Helv. Chim. Acta*, 1985, **68**, 2100.

83. W. Oppolzer and C. Chapuis, *Tetrahedron Lett.*, 1984, **25**, 5383.

84. S. W. Remiszewski, J. Yang and S. M. Weinreb, *Tetrahedron Lett.*, 1986, **27**, 1853.

85. W. Oppolzer, R. Moretti, T. Godel, A. Meunier and H. Löher, *Tetrahedron Lett.*, 1983, **24**, 4971.

86. W. Oppolzer, R. Pitteloud, G. Bernardinelli and K. Baettig, *Tetrahedron Lett.*, 1983, **24**, 4975.

87. W. Oppolzer and T. Stevenson, *Tetrahedron Lett.*, 1986, **27**, 1139.

88. X. Verdaguer, A. Moyano, M. A. Pericàs, A. Riera, A. E. Greene, J. F. Piniella and A. Alvarez-Larena, *J. Organomet. Chem.*, 1992, **433**, 305.

89. S. E. Denmark and M. E. Schnute, *J. Org. Chem.*, 1991, **56**, 6738.

90. E. Ade, G. Helmchen and G. Heiligenmann, *Tetrahedron Lett.*, 1980, **21**, 1137.

91. R. Schmierer, G. Grotemeier and G. Helmchen, *Angew. Chem., Int. Ed. Engl.*, 1981, **20**, 207.

92. R. Gamboni and C. Tamm, *Helv. Chim. Acta*, 1986, **69**, 615.

93. G. Helmchen and R. Schmierer, *Angew. Chem., Int. Ed. Engl.*, 1981, **20**, 205.

94. T. Poll, G. Helmchen and B. Bauer, *Tetrahedron Lett.*, 1984, **25**, 2191.

95. F. Effenberger, T. Beisswenger and H. Isak, *Tetrahedron Lett.*, 1985, **26**, 4335.

96. M. Shimizu, Y. Teramoto and T. Fujisawa, *Tetrahedron Lett.*, 1995, **36**, 729.

97. G. Helmchen and R. Wierzchowski, *Angew. Chem., Int. Ed. Engl.*, 1984, **23**, 60.

98. G. Helmchen and R. Schmierer, *Tetrahedron Lett.*, 1983, **24**, 1235.

99. U. Schmidt and W. Siegel, *Tetrahedron Lett.*, 1987, **28**, 2849.

100. G. Helmchen and G. Wegner, *Tetrahedron Lett.*, 1985, **26**, 6047.

101. G. Helmchen and G. Wegner, *Tetrahedron Lett.*, 1985, **26**, 6051.

102. G. Helmchen, U. Leikauf and I. Taufer-Knöpfel, *Angew. Chem., Int. Ed. Engl.*, 1985, **24**, 874.

103. R. Gamboni, P. Mohr, N. Waespe-Šarčevič and C. Tamm, *Tetrahedron Lett.*, 1985, **26**, 203.

104. D. Dorsch, E. Kunz and G. Helmchen, *Tetrahedron Lett.*, 1985, **26**, 3319.

105. R. Gamboni and C. Tamm, *Tetrahedron Lett.*, 1986, **27**, 3999.

106. T. Langer, M. Ilich and G. Helmchen, *Tetrahedron Lett.*, 1995, **36**, 4409.

107. W. Oppolzer, C. Chapuis and M. J. Kelly, *Helv. Chim. Acta*, 1983, **66**, 2358.

108. W. Oppolzer, C. Chapuis and G. Bernardinelli, *Tetrahedron Lett.*, 1984, **25**, 5885.

109. W. Oppolzer and J. Marco-Contelles, *Helv. Chim. Acta*, 1986, **69**, 1699.

110. W. Oppolzer, P. Dudfield, T. Stevenson and T. Godel, *Helv. Chim. Acta*, 1985, **68**, 212.

111. W. Oppolzer and P. Dudfield, *Helv. Chim. Acta*, 1985, **68**, 216.

112. W. Oppolzer and P. Dudfield, *Tetrahedron Lett.*, 1985, **26**, 5037.

113. D. Hernanz, F. Camps, A. Guerrero and A. Delgado, *Tetrahedron: Asymmetry*, 1995, **6**, 2291.

114. W. Oppolzer, R. Pedrosa and R. Moretti, *Tetrahedron Lett.*, 1986, **27**, 831.

115. D. Basavaiah, V. V. L. Gowriswari, P. K. S. Sarma and P. D. Rao, *Tetrahedron Lett.*, 1990, **31**, 1621.

116. K. N. Jensen and G. H. P. Roos, *S. Afr. J. Chem*, 1992, **45**, 112.

117. C. -Y. Hsu, Y. -S. Lin and B. -J. Uang, *Tetrahedron: Asymmetry*, 1990, **1**, 219.

118. H. -P. Buser and F. Spindler, *Tetrahedron: Asymmetry*, 1993, **4**, 2451.

119. R. McCague, M. Jarman, M. G. Rowlands, J. Mann, C. P. Thickitt, D. W. Clissold, S. Neidle and G. Webster, *J. Chem. Soc., Perkin Trans. 1*, 1989, 196.

120. F. A. Davis, P. Zhou and G. S. Lal, *Tetrahedron Lett.*, 1990, **31**, 1653.

121. F. A. Davis, P. Zhou and P. J. Carroll, *J. Org. Chem.*, 1993, **58**, 4890.

122. K. H. Ahn, S. Lee and A. Lim, *J. Org. Chem.*, 1992, **57**, 5065.

123. K. H. Ahn, A. Lim and S. Lee, *Tetrahedron: Asymmetry*, 1993, **4**, 2435.

124. T. -H. Yan, V. -V. Chu, T. -C. Lin, W. -H. Tseng and T. -W. Cheng, *Tetrahedron Lett.*, 1991, **32**, 5563.

125. T. -H. Yan, V. -V. Chu, T. -C. Lin, C. -H. Wu and L. -H. Liu, *Tetrahedron Lett.*, 1991, **32**, 4959.

126. T. -H. Yan, C. -W. Tan, H. -C. Lee, H. -C. Lo and T.-Y. Huang, *J. Am. Chem. Soc.*, 1993, **115**, 2613.

127. T. -H Yan, H. -C. Lee and C. -W. Tan, *Tetrahedron Lett.*, 1993, **34**, 3559.

128. Y. -C. Wang, A. -W. Hung, C. -S. Chang and T. -H. Yan, *J. Org. Chem.*, 1996, **61**, 2038.

129. T. -H. Yan, A. -W. Hung, H. -C. Lee and C. -S. Chang, *J. Org. Chem.*, 1994, **59**, 8187.

130. T. -H. Yan, A. -W. Hung, H. -C. Lee, C. -S. Chang and W. -H. Liu, *J. Org. Chem.*, 1995, **60**, 3301.

131. M. P. Bonner and E. R. Thornton, *J. Am. Chem. Soc.*, 1991, **113**, 1299.

132. M. R. Banks, A. J. Blake, J. I. G. Cadogan, I. M. Dawson, I. Gosney, K. J. Grant, S. Gaur, P. K. G. Hodgson, K. S. Knight, G. W. Smith and D. E. Stevenson, *Tetrahedron*, 1992, **48**, 7979.

133. K. Tanaka, H. Uno, H. Osuga and H. Suzuki, *Tetrahedron: Asymmetry*, 1993, **4**, 629.

134. W. A. Noyes and R. S. Potter, *J. Am. Chem. Soc.*, 1915, **37**, 189.

135. R. K. Boeckman, Jr., S. G. Nelson and M. D. Gaul, *J. Am. Chem. Soc.*, 1992, **114**, 2258.

136. R. K. Boeckman, Jr., A. T. Johnson and R. A. Musselman, *Tetrahedron Lett.*, 1994, **35**, 8521.

137. R. K. Boeckman, Jr. and S. T. Wrobleski, *J. Org. Chem.*, 1996, **61**, 7238.

138. R. K. Boeckman, Jr. and S. G. Nelson, *Diss. Abstr. Int.*, 1992, **53**, 853.

139. R. K. Boeckman, Jr. and Y. Liu, *J. Org. Chem.*, 1996, **61**, 7984.

140. S. G. Davies, J. M. Brown, A. J. Pratt and G. Fleet, *Chem. Br.*, 1989, **25**, 259.

141. S. C. Stinson, *Chem. Eng. News*, 1992, **70**, 46.

142. S. C. Stinson, *Chem. Eng. News*, 1995, **73**, 44.

143. M. E. C. Polywka, *Chim. Oggi*, 1992, **10**, 33.

144. F. A. Davis, M. S. Haque, T. G. Ulatowski and J. C. Towson, *J. Org. Chem.*, 1986, **51**, 2402.

145. I. Mergelsberg, D. Gala, D. Scherer, D. DiBenedetto and M. Tanner, *Tetrahedron Lett.*, 1992, **33**, 161.

146. F. A. Davis and A. C. Sheppard, *Tetrahedron*, 1989, **45**, 5703.

147. F. A. Davis and B. -C. Chen, *Chem. Rev.*, 1992, **92**, 919.

148. F. A. Davis and M. S. Haque, *J. Org. Chem.*, 1986, **51**, 4085.

149. F. A. Davis, J. C. Towson, M. C. Weismiller, S. Lal and P. J. Carroll, *J. Am. Chem. Soc.*, 1988, **110**, 8477.

150. F. A. Davis and M. C. Weismiller, *J. Org. Chem.*, 1990, **55**, 3715.

151. W. Oppolzer, C. Chapuis and G. Bernardinelli, *Helv. Chim. Acta*, 1984, **67**, 1397.

152. W. Oppolzer, *Tetrahedron*, 1987, **43**, 1969.

153. W. Oppolzer, *Pure Appl. Chem.*, 1990, **62**, 1241.

154. W. Oppolzer, *Pure Appl. Chem.*, 1988, **60**, 39.

155. B. H. Kim and D. P. Curran, *Tetrahedron*, 1993, **49**, 293.

156. W. Oppolzer, *Angew. Chem., Int. Ed. Engl.*, 1984, **23**, 876.

157. W. Oppolzer, I. Rodriguez, J. Blagg and G. Bernardinelli, *Helv. Chim. Acta.*, 1989, **72**, 123.

158. W. Oppolzer and D. Dupuis, *Tetrahedron Lett.*, 1985, **26**, 5437.

159. M. Vandewalle, J. Van der Eycken, W. Oppolzer and C. Vullioud, *Tetrahedron*, 1986, **42**, 4035.

160. W. Oppolzer and J. -P. Barras, *Helv. Chim. Acta.*, 1987, **70**, 1666.

161. W. Oppolzer, G. Poli, A. J. Kingma, C. Starkemann and G. Bernardinelli, *Helv. Chim. Acta*, 1987, **70**, 2201.

162. W. Oppolzer, R. J. Mills, W. Pachinger and T. Stevenson, *Helv. Chim. Acta*,, 1986, **69**, 1542.

163. W. Oppolzer and P. Schneider, *Helv. Chim. Acta*, 1986, **69**, 1817.

164. W. Oppolzer, J. Blagg, I. Rodriguez and E. Walther, *J. Am. Chem. Soc.*, 1990, **112**, 2767.

165. W. Oppolzer, C. Starkemann, I. Rodriguez and G. Bernardinelli, *Tetrahedron Lett.*, 1991, **32**, 61.

166. W. Oppolzer and P. Lienard, *Tetrahedron Lett.*, 1993, **34**, 4321.

167. W.Oppolzer, R. Moretti and S. Thomi, *Tetrahedron Lett.*, 1989, **30**, 5603.

168. W. Oppolzer, R. Moretti and S. Thomi, *Tetrahedron Lett.*, 1989, **30**, 6009.

169. W. Oppolzer, R. Moretti and C. Zhou, *Helv. Chim. Acta*, 1994, **77**, 2363.

170. Y. Elemes and U. Ragnarsson, *J. Chem. Soc., Perkin Trans. 1*, 1995, 537.

171. W. Oppolzer and O. Tamura, *Tetrahedron Lett.*, 1990, **31**, 991.

172. W. Oppolzer, O. Tamura and J. Deerberg, *Helv. Chim, Acta*, 1992, **75**, 1965.

173. W. Oppolzer, P. Cintas-Moreno and O. Tamura, *Helv. Chim. Acta*, 1993, **76**, 187.

174. W. Oppolzer and E. Merifield, *Helv. Chim. Acta*, 1993, **76**, 957.

175. W. -X. Wu, A. T. McPhail and N. A. Porter, *J. Org. Chem.*, 1994, **59**, 1302.

176. A. A. Cantrill, L. D. Hall, A. N. Jarvis, H. M. I. Osborn, J. Raphy and J. B. Sweeney, *J. Chem. Soc., Chem. Commun.*, 1996, 2631.

177. P. T. Kaye and R. A. Learmonth, *Synth. Commun.*, 1989, **19**, 2337.

178. P. T. Kaye, R. A. Learmonth and S. S. Ravindran, *Synth. Commun.*, 1993, **23**, 437.

179. P. T. Kaye and S. S. Ravindran, *S. Afr. J. Chem.*, 1994, **47**, 17.

180. P. T. Kaye and S. S. Ravindran, *S. Afr. J. Chem.*, 1995, **48**, 64.

181. M. D. Evans, P. T. Kaye and R. A. Learmonth, *J. Chem. Res. (S)*, 1994, 314.

182. G. Helmchen, A. Selim, D. Dorsch and I. Taufer, *Tetrahedron Lett.*, 1983, **24**, 3213.

183. H. O. House, L. J. Czuba, M. Gall and H. D. Olmstead, *J. Org. Chem.*, 1969, **34**, 2324.

184. R. D. Walkup and N. U. Obeyesekere, *J. Org. Chem.*, 1988, **53**, 920.

185. G. M. Rubottom and M. I. Lopez, *J. Org. Chem.*, 1973, **38**, 2097.

186. S. Murai, T. Aya and N. Sonoda, *J. Org. Chem.*, 1973, **38**, 4354.

187. S. Miyano, Y. Izumi, H. Fugii and H. Hashimoto, *Synthesis*, 1977, 700.

188. H. E. Simmons, E. P. Blanchard and R. D. Smith, *J. Am. Chem. Soc.*, 1964, **86**, 1347.

189. J. M. Denis, C. Girard and J. M. Conia, *Synthesis*, 1972, 549.

190. D. Wang and T. H. Chan, *Tetrahedron Lett.*, 1983, **24**, 1573.

191. T. Aoki, K. Shinohara and E. Oikawa, *Makromol. Chem., Rapid Commun.*, 1992, **13**, 565. (*Chem. Abstr.*, 1993, **118**, 104043).

192. G. Yi, D. Wang and T. H. Chen, *Youji Huaxue*, 1988, **8**, 115. (*Chem. Abstr.*, 1989, **110**, 75615).

193. T. G. Selin and R. West, *J. Am. Chem. Soc.*, 1962, **84**, 1863.

194. *One-dimensional and Two-dimensional NMR Spectra by Modern Pulse Techniques*, ed. K. Nakanishi, University Science Books, Mill Valley, 1990.

195. L. A. Paquette, H. -S. Lin and J. C. Gallucci, *Tetrahedron Lett.*, 1987, **28**, 1363.

196. T. H. Chan, I. Paterson and J. Pinsonnault, *Tetrahedron Lett.*, 1977, **48**, 4183.

197. C. H. Heathcock, S. K. Davidsen, K. T. Hug and L. A. Flippin, *J. Org. Chem.*, 1986, **51**, 3027.

198. L. M. Sweeting, D. C. Crans and G. M. Whitesides, *J. Org. Chem.*, 1987, **52**, 2273.

199. T. Mukaiyama, *Angew. Chem., Int. Ed. Engl.*, 1977, 817.

200. J. -P. Pillot, G. Dèlèris, J. Dunogués and R. Calas, *J. Org. Chem.*, 1979, **44**, 3397.

201. L. Cappi, A. Ricci and M. Taddei, *Tetrahedron Lett.*, 1987, **28**, 965.

202. L. Cappi, A. Mordini and M. Taddei, *Tetrahedron Lett.*, 1987, **28**, 969.

203. T. G. Selin and R. West, *J. Am. Chem. Soc.*, 1962, **84**, 1860.

204. H. C. Brown and P. K. Jadhav, in *Asymmetric Synthesis*, ed. J. D. Morrison, Academic Press, Orlando, 1983, vol 2, p. 1.

205. K. Ishihara, H. Yamamoto and C. H. Heathcock, *Tetrahedron Lett.*, 1989, **30**, 1825.

206. A. Mori, I. Arai and H. Yamamoto, *Tetrahedron*, 1986, **42**, 6447.

207. I. Mori, K. Ishihara, L. A. Flippin, K. Nozaki, H. Yamamoto, P. A. Bartlett and C. H. Heathcock, *J. Org. Chem.*, 1990, **55**, 6107.

208. H. C. Brown and S. Krishnamurthy, *J. Am. Chem. Soc*, 1972, **94**, 7159.

209. H. C. Brown and K. Ichikawa, *J. Am. Chem. Soc.*, 1962, **84**, 373.

210. L. W. Trevoy and W. G. Brown, *J. Am. Chem. Soc.*, 1949, **71**, 1675.

211. S. J. Angyal and R. J. Young, *J. Am. Chem. Soc.*, 1959, **81**, 5467.

212. J.-C. Richer and A. Rossi, *Can. J. Chem.*, 1972, **50**, 1376.

213. B. -I. Seo, I. -H. Suh, W. P. Jensen and D. E. Lewis, L. K. Wall and R. A. Jacobson, *Tetrahedron: Asymmetry*, 1992, **3**, 367.

214. V. L. Tweedie and M. Cuscurida, *J. Am. Chem. Soc.*, 1957, **79**, 5463.

215. W. J. Bailey and F. Marktscheffel, *J. Org. Chem.*, 1960, **25**, 1797.

216. S. Fonquerna, A. Moyano, M. A. Pericàs and A. Riera, *Tetrahedron*, 1995, **51**, 4239.

217. K. Nordström and C. Moberg, *Tetrahedron Lett.*, 1994, **35**, 7267.

218. T. Oshikawa and M. Yamashita, *Bull. Chem. Soc. Jpn.*, 1989, **62**, 3177. (*Chem. Abstr.*, **112**, 217058).

219. H. Sakaguchi, Y. Jokura, T. Kamiya, T. Kitsuki and Y. Fujikura, Japanese patent 04,221,305 (Cl.A61K7/00), 1992; (*Chem. Abstr.*, **118**, 27489h).

220. D. A. Evans, in *Asymmetric Synthesis*, ed. J. D. Morrison, Academic Press, Orlando, 1984, vol. 3, p. 83.

221. R. E. Ireland, P. Wipf and J. D. Armstrong, III, *J. Org. Chem.*, 1991, **56**, 650.

222. P. Sykes, *A Guidebook to Mechanism in Organic Chemistry*, Longman, London, p. 237.

223. J. Toullec and J. E. Dubois, *J. Am. Chem Soc.*, 1974, **96**, 3524.

224. B. C. Taverner, J. M. Smith, D. P. White and N. J. Coville, *S. Afr. J. Chem.*, 1997, **50**, 59.

225. C. Nativi, N. Ravidà, A. Ricci, G. Seconi and M. Taddei, *J. Org. Chem.*, 1991, **56**, 1951.

226. E. J. Corey and C. Rücker, *Tetrahedron Lett.*, 1984, **25**, 4345.

227. P. Sampson and D. F. Wiemer, *J. Chem. Soc., Chem. Commun.*, 1985, 1746.

229. T. H. Chan, A. Baldassarre and D. Massuda, *Synthesis*, 1976, 801.

229. R. T. Taylor, C. R. Degenhardt, W. P. Melega and L. A. Paquette, *Tetrahedron Lett.*, 1977, **18**, 159.

230. W. E. Fristad, T. R. Bailey and L. A. Paquette, *J. Org. Chem.*, 1978, **43**, 1620.

231. L. A. Paquette, W. E. Fristad, D. S. Dime and T. R. Bailey, *J. Org. Chem.*, 1980, **45**, 3017.

232. F. Ameer, S. E. Drewes, R. Hoole, P. T. Kaye and A. T. Pitchford, *J. Chem. Soc., Perkin Trans. I*, 1985, 2713.

233. S. S. Ravindran, PhD Thesis, Rhodes University, 1995.

234. M. R. Agharahimi and N. A. LeBel, *J. Org. Chem.*, 1995, **60**, 1856.

235. P. F. Cirillo and J. S. Panek, *J. Org. Chem.*, 1994, **59**, 3055.

236. I. Fleming and A. P. Thomas, *J. Chem. Soc., Chem. Commun.*, 1985, 411.

237. J. G. Smith, S. E. Drozda, S. P. Petraglia, N. R. Quinn, E. M. Rice, B. S. Taylor and M. Viswanathan, *J. Org. Chem.*, 1984, **49**, 4112.

238. G. H. Posner, *Org. Reactions*, 1975, **22**, 253.

239. B. H. Lipshutz, *Synthesis*, 1986, 325.

240. E. Azzari, C. Faggi, N. Gelsomini and M. Taddei, *J. Org. Chem.*, 1990, **55**, 1106.

241. E. Azzari, C. Faggi, N. Gelsomini and M. Taddei, *Tetrahedron Lett.*, 1989, **30**, 6067.

242. B. H. Lipshutz and R. S. Wilhelm, *J. Am. Chem. Soc.*, 1981, **103**, 7672.

243. B. S. Furniss, A. J. Hannaford, P. W. G. Smith and A. R. Tatchell, *Vogel's Textbook of Practical Organic Chemistry*, 5th Edition, Longman Scientific & Technical, London, 1989, p.527.

244. J. Casanova, Jr. and E. J. Corey, *Chem. Ind.*, 1961, 1664.

245. L. Cook, personal communication.

246. D. Basavaiah, P. D. Roa and R. S. Hyma, *Tetrahedron*, 1996, **52**, 8001.

247. S. E. Drewes and G. H. P. Roos, *Tetrahedron*, 1988, **44**, 4653.

248. A. R. Banks, R. F. Fibiger and T. Jones, *J. Org. Chem.*, 1977, **42**, 3965.

249. R. A. Learmonth, PhD Thesis, Rhodes University, 1990.

250. D. R. Dimmel and J. Wolinsky, *J. Org. Chem.*, 1967, **32**, 410.

251. D. S. Weinberg and C. Djerassi, *J. Org. Chem.*, 1966, **31**, 115.

252. W. C. Still, M. Kahn and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923.

253. A. Magata, J. Iyoda and I. Shiihara, *Kogyo Kagaku Zisshi*, 1966, **60**, 1957. (*Chem. Abstr.*, **68**, 69145x).

254. C. Girard and J. -M. Conia, *J. Chem. Res. (M)*, 1978, 2348.

255. A. J. Ragauskas and J. B. Stothers, *Can. J. Chem.*, 1985, **63**, 2969.

256. Available from Petrarch Chemicals.

257. M. T. Reetz, W. F. Maier, I. Chatziiosifidis, A. Giannis, H. Heimbach and U. Löwe, *Chem. Ber.*, 1980, **113**, 3741.

258. H. O. House, D. S. Crumrine, A. Y. Teranishi and H. D. Olmstead, *J. Am. Chem. Soc.*, 1973, **95**, 3310.

259. M. Muraoka, H. Kawasaki and K. Koga, *Tetrahedron Lett.*, 1988, **29**, 337.

260. P. V. Ramachandran, W. -C Xu and H. C. Brown, *Tetrahedron Lett.*, 1996, **37**, 4911.

261. R. D. Clark and C. H. Heathcock, *J. Org. Chem.*, 1976, **41**, 1396.

262. B. S. Furniss, A. J. Hannaford, P. W. G. Smith and A. R. Tatchell, *Vogel's Textbook of Practical Organic Chemistry*, 5th Edition, Longman Scientific & Technical, London, 1989, p.692.

263. *Handbook of Chemistry and Physics*, 61st Edition, ed. R. C. Weast and M. J. Astle, CRC Press, Baco Raton, 1980-1981.

264. *Dictionary of Organic Compounds*, ed. J. R. A. Pollock and R. Stevens, Eyre and Spottiswood Publishers, London, 1965, vol. 4.

265. W. Oppolzer, I. Rodriguez, C. Starkemann and E. Walther, *Tetrahedrom Lett.*, 1990, **31**, 5019.

266. R. H. Pickard and J. Yates, *J. Chem. Soc.*, 1916, **95**, 1011.

267. A. M. Aguiar, C. J. Morrow, J. D. Morrison, R. E. Burnett, W. F. Masler and N. S. Bhacca, *J. Org. Chem.*, 1976, **41**, 1545.

268. W. Kirmse, P. Feyen, W. Gruber and W. Kapmeyer, *Chem. Ber.*, 1975, **108**, 1839.

269. H. Sakurai and A. Hosomi, *J. Am. Chem. Soc.*, 1970, **92**, 7507.

270. L. F. Fieser and M. Feiser, *Reagents for Organic Synthesis*, John Wiley & Sons, New York, 1967, vol. 1, p. 1185.

271. R. O. Hutchins, C. A. Milewski and B. E. Maryanoff, *J. Am. Chem. Soc.*, 1973, **95**, 3662.

272. D. H. R. Barton, F. S. Guziec and I. Shahak, *J. Chem. Soc., Perkin Trans. 1*, 1974, 1794.

273. I. Fleming and R. B. Woodard, *J. Chem. Soc. (C)*, 1968, 1289.

274. B. S. Furniss, A. J. Hannaford, P. W. G. Smith and A. R. Tatchell, *Vogel's Textbook of Practical Organic Chemistry*, 5th Edition, Longman Scientific & Technical, London, 1989, p.559.

275. B. Pfrunder and C. Tamm, *Helv. Chim. Acta*, 1969, **52**, 1630.

276. I. Fleming, T. W. Newton and F. Roessler, *J. Chem. Soc., Perkin Trans. I*, 1981, 2527.

277. M. B. Watson and G. W. Youngson, *J. Chem. Soc. (C)*, 1968, 258.

APPENDIX

Crystollographic Data for *3,3-[(2R,3S)-2-endo,3-exo-butanedioxy]-2-exo-bornyl 2,4-dinitrobenzoate* (238)

TABLE 1. Crystal data and structure refinement for 3,3-[(2*R*,3*S*)2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 2,4-dinitrobenzoate (**238**).

Identification code	mel56_13
Empirical formula	C_{21} H_{26} N_2 O_8
Formula weight	434.44
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system	monoclinic
Space group	$P2_1$
Unit cell dimensions	a = 12.7892(10) A alpha = 90 deg.
	b = 10.6562(9) A beta = 91.533(2) deg.
	c = 16.1864(13) A gamma = 90 deg.
Volume, Z	2205.2(3) A^3, 4
Density (calculated)	1.309 Mg/m^3
Absorption coefficient	0.101 mm^{-1}
F(000)	920
Theta range for data collection	1.26 to 28.27 deg.
Limiting indices	-16<=h<=15, -14<=k<=13, -20<=l<=18
Reflections collected	12196
Independent reflections	7819 [R(int) = 0.0544]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7819 / 1 / 569
Goodness-of-fit on F^2	1.105
Final R indices [I>2sigma(I)]	R1 = 0.1117, wR2 = 0.2021
R indices (all data)	R1 = 0.2328, wR2 = 0.2542
Absolute structure parameter	-2(2)
Largest diff. peak and hole	0.186 and -0.181 e.A-3

TABLE 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x10^3) for 3,3-[(2*R*,3*S*)2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 2,4-dinitrobenzoate(**238**).[a, b] U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
O(1A)	-8643(5)	-8683(8)	8667(5)	115(3)
N(1)	-3177(6)	539(10)	6720(6)	90(2)
N(1A)	-8357(6)	-9607(10)	8321(5)	80(2)
C(1A)	-6600(6)	-9285(7)	8902(5)	59(2)
C(1)	-1485(6)	711(8)	6095(5)	68(2)
O(1)	-3445(6)	1481(8)	6389(6)	125(3)
O(2A)	-8932(5)	-10276(7)	7889(5)	118(3)
N(2)	-486(9)	-2673(9)	7172(5)	89(2)
N(2A)	-5514(8)	-12552(8)	7754(5)	82(2)
O(2)	-3722(5)	-91(8)	7169(5)	115(3)
C(2)	-2117(6)	40(8)	6580(5)	62(2)
C(2A)	-7239(6)	-10002(8)	8406(5)	60(2)
C(3A)	-6911(7)	-11059(8)	8014(4)	58(2)
O(3)	-1089(7)	-3262(9)	7564(6)	145(3)
O(3A)	-6099(7)	-13084(9)	7287(6)	158(4)
C(3)	-1816(7)	-1056(9)	952(5)	65(2)
O(4)	413(7)	-2994(8)	7088(5)	120(3)
O(4A)	-4598(7)	-12838(7)	7892(4)	106(2)
C(4A)	-5893(7)	-11405(7)	8156(5)	59(2)
C(4)	-846(8)	-1485(8)	6780(5)	65(2)
O(5A)	-5161(4)	-7984(6)	9972(4)	82(2)
O(5)	-29(5)	1965(7)	5075(5)	100(2)
C(5)	-150(6)	-833(8)	6302(4)	63(2)
C(5A)	-5203(6)	-10719(7)	8642(4)	57(2)
O(6A)	-3895(4)	-9278(5)	9586(3)	59(1)
O(6)	1178(4)	515(6)	5433(4)	89(2)
C(6)	-477(6)	276(8)	5956(4)	59(2)
C(6A)	-5562(6)	-9640(7)	9034(4)	51(2)
O(7A)	-2427(4)	-6591(5)	9711(3)	71(2)
O(7)	2220(6)	1868(7)	6497(4)	107(2)
C(7A)	-4875(6)	-8874(8)	9587(5)	54(2)
C(7)	233(6)	1029(9)	5425(6)	67(2)
O(8A)	-2589(4)	-8001(5)	8663(3)	73(2)
O(8)	2529(4)	3262(6)	5478(4)	78(2)
C(8A)	-3100(5)	-8648(7)	10073(4)	49(2)
C(8)	2018(6)	1157(9)	5049(5)	71(2)
C(9A)	-2384(6)	-9601(7)	10515(4)	54(2)
C(9)	2842(7)	224(10)	4731(7)	89(3)
C(10A)	-2956(7)	-10707(9)	10896(6)	89(3)

C(10)	2460(10)	-441(12)	3973(7)	141(5)
C(11A)	-1782(6)	-8827(7)	11171(5)	61(2)
C(11)	3103(9)	-651(12)	5440(8)	114(4)
C(12A)	-1015(6)	-8050(9)	10657(5)	74(2)
C(12)	3733(10)	143(13)	6045(7)	130(5)
C(13A)	-1289(6)	-8468(7)	9767(5)	60(2)
C(13)	3744(7)	s1481(11)	5626(6)	96(3)
C(14A)	-1550(6)	-9879(7)	9872(5)	64(2)
C(14)	3816(8)	1081(10)	4731(6)	91(3)
C(15A)	-610(7)	-10616(10)	10234(6)	103(3)
C(15)	3725(8)	2181(10)	4142(5)	101(3)
C(16A)	-1926(7)	-10569(9)	9069(5)	90(3)
C(16)	4818(8)	360(12)	4552(7)	130(4)
C(17A)	-2341(6)	-7899(8)	9529(4)	54(2)
C(17)	2610(7)	1957(10)	5691(6)	80(3)
C(18A)	-2210(7)	-5938(8)	8945(6)	75(3)
C(18)	2044(8)	3111(13)	6807(6)	100(3)
C(19A)	-2557(8)	-4596(9)	9023(6)	107(4)
C(19)	867(8)	3346(11)	6864(7)	121(4)
C(20A)	-2789(7)	-6781(8)	8318(5)	71(2)
C(20)	2625(8)	3936(11)	6226(7)	94(3)
C(21A)	-3932(7)	-6529(11)	8166(6)	104(3)
C(21)	2222(10)	5268(11)	6100(7)	128(4)

[a] For atom labelling, see Figure 18. [b] Estimated standard deviations in parenthesis.

TABLE 3. Bond lengths [A] and angles [deg] for 3,3-[(2*R*,3*S*)2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 2,4-dinitrobenzoate (**238**).[a, b]

O(1A)-N(1A)	1.194(10)
N(1)-O(1)	1.185(10)
N(1)-O(2)	1.220(10)
N(1)-C(2)	1.479(11)
N(1A)-O(2A)	1.229(9)
N(1A)-C(2A)	1.493(11)
C(1A)-C(2A)	1.364(10)
C(1A)-C(6A)	1.391(9)
C(1)-C(2)	1.348(10)
C(1)-C(6)	1.394(10)
N(2)-O(3)	1.190(10)
N(2)-O(4)	1.211(10)
N(2)-C(4)	1.483(12)
N(2A)-O(3A)	1.193(9)
N(2A)-O(4A)	1.225(10)
N(2A)-C(4A)	1.472(11)
C(2)-C(3)	1.365(11)
C(2A)-C(3A)	1.364(11)
C(3A)-C(4A)	1.368(11)
C(3)-C(4)	1.357(11)
C(4A)-C(5A)	1.376(10)
C(4)-C(5)	1.383(11)
O(5A)-C(7A)	1.198(9)
O(5)-C(7)	1.191(10)
C(5)-C(6)	1.368(11)
C(5A)-C(6A)	1.398(10)
O(6A)-C(7A)	1.325(8)
O(6A)-C(8A)	1.436(8)
O(6)-C(7)	1.327(9)
O(6)-C(8)	1.429(9)
C(6)-C(7)	1.499(11)
C(6A)-C(7A)	1.482(10)
O(7A)-C(17A)	1.430(9)
O(7A)-C(18A)	1.456(9)
O(7)-C(17)	1.412(10)
O(7)-C(18)	1.437(13)
O(8A)-C(17A)	1.433(8)
O(8A)-C(20A)	1.434(10)
O(8)-C(20)	1.410(11)
O(8)-C(17)	1.436(11)
C(8A)-C(9A)	1.532(10)
C(8A)-C(17A)	1.549(10)
C(8)-C(17)	1.529(13)
C(8)-C(9)	1.547(12)

C(9A)-C(10A)	1.526(11)
C(9A)-C(11A)	1.536(10)
C(9A)-C(14A)	1.539(10)
C(9)-C(10)	1.488(14)
C(9)-C(11)	1.509(14)
C(9)-C(14)	1.545(13)
C(11A)-C(12A)	1.543(10)
C(11)-C(12)	1.51(2)
C(12A)-C(13A)	1.539(10)
C(12)-C(13)	1.580(14)
C(13A)-C(17A)	1.516(10)
C(13A)-C(14A)	1.550(11)
C(13)-C(14)	1.515(13)
C(13)-C(17)	1.543(12)
C(14A)-C(15A)	1.539(11)
C(14A)-C(16A)	1.559(11)
C(14)-C(15)	1.513(12)
C(14)-C(16)	1.528(12)
C(18A)-C(19A)	1.503(12)
C(18A)-C(20A)	1.532(12)
C(18)-C(20)	1.499(14)
C(18)-C(19)	1.530(13)
C(20A)-C(21A)	1.499(11)
C(20)-C(21)	1.522(14)
O(1)-N(1)-O(2)	124.9(10)
O(1)-N(1)-C(2)	119.4(9)
O(2)-N(1)-C(2)	115.7(10)
O(1A)-N(1A)-O(2A)	124.0(9)
O(1A)-N(1A)-C(2A)	119.5(8)
O(2A)-N(1A)-C(2A)	116.5(10)
C(2A)-C(1A)-C(6A)	119.5(8)
C(2)-C(1)-C(6)	119.3(8)
O(3)-N(2)-O(4)	122.8(10)
O(3)-N(2)-C(4)	118.7(10)
O(4)-N(2)-C(4)	118.5(10)
O(3A)-N(2A)-O(4A)	125.2(9)
O(3A)-N(2A)-C(4A)	117.9(9)
O(4A)-N(2A)-C(4A)	116.8(9)
C(1)-C(2)-C(3)	123.0(8)
C(1)-C(2)-N(1)	117.7(9)
C(3)-C(2)-N(1)	119.3(9)
C(3A)-C(2A)-C(1A)	123.3(7)
C(3A)-C(2A)-N(1A)	119.7(8)
C(1A)-C(2A)-N(1A)	117.0(8)
C(2A)-C(3A)-C(4A)	116.6(7)
C(4)-C(3)-C(2)	116.5(8)
C(3A)-C(4A)-C(5A)	123.1(8)
C(3A)-C(4A)-N(2A)	118.2(8)

C(5A)-C(4A)-N(2A)	118.7(9)
C(3)-C(4)-C(5)	123.4(8)
C(3)-C(4)-N(2)	118.3(9)
C(5)-C(4)-N(2)	118.1(9)
C(6)-C(5)-C(4)	118.0(8)
C(4A)-C(5A)-C(6A)	118.9(7)
C(7A)-O(6A)-C(8A)	120.2(5)
C(7)-O(6)-C(8)	119.6(7)
C(5)-C(6)-C(1)	119.7(8)
C(5)-C(6)-C(7)	120.9(8)
C(1)-C(6)-C(7)	119.4(8)
C(1A)-C(6A)-C(5A)	118.5(7)
C(1A)-C(6A)-C(7A)	119.5(7)
C(5A)-C(6A)-C(7A)	122.0(7)
C(17A)-O(7A)-C(18A)	105.9(6)
C(17)-O(7)-C(18)	108.8(8)
O(5A)-C(7A)-O(6A)	124.1(7)
O(5A)-C(7A)-C(6A)	124.4(7)
O(6A)-C(7A)-C(6A)	111.5(7)
O(5)-C(7)-O(6)	126.4(9)
O(5)-C(7)-C(6)	123.7(8)
O(6)-C(7)-C(6)	109.8(8)
C(17A)-O(8A)-C(20A)	110.2(6)
C(20)-O(8)-C(17)	106.5(7)
O(6A)-C(8A)-C(9A)	110.6(6)
O(6A)-C(8A)-C(17A)	111.9(6)
C(9A)-C(8A)-C(17A)	103.4(5)
O(6)-C(8)-C(17)	109.6(7)
O(6)-C(8)-C(9)	111.3(7)
C(17)-C(8)-C(9)	104.8(7)
C(10A)-C(9A)-C(8A)	114.4(6)
C(10A)-C(9A)-C(11A)	111.9(6)
C(8A)-C(9A)-C(11A)	104.4(6)
C(10A)-C(9A)-C(14A)	118.2(7)
C(8A)-C(9A)-C(14A)	103.2(6)
C(11A)-C(9A)-C(14A)	103.1(6)
C(10)-C(9)-C(11)	113.2(10)
C(10)-C(9)-C(14)	121.9(9)
C(11)-C(9)-C(14)	101.8(8)
C(10)-C(9)-C(8)	111.7(9)
C(11)-C(9)-C(8)	106.4(8)
C(14)-C(9)-C(8)	100.2(8)
C(9A)-C(11A)-C(12A)	103.3(6)
C(12)-C(11)-C(9)	104.5(10)
C(13A)-C(12A)-C(11A)	102.5(6)
C(11)-C(12)-C(13)	103.7(9)
C(17A)-C(13A)-C(12A)	107.5(6)
C(17A)-C(13A)-C(14A)	102.9(6)

C(12A)-C(13A)-C(14A)	102.8(7)
C(14)-C(13)-C(17)	103.8(8)
C(14)-C(13)-C(12)	99.1(9)
C(17)-C(13)-C(12)	104.4(8)
C(9A)-C(14A)-C(15A)	112.9(7)
C(9A)-C(14A)-C(13A)	92.4(6)
C(15A)-C(14A)-C(13A)	111.6(7)
C(9A)-C(14A)-C(16A)	116.8(7)
C(15A)-C(14A)-C(16A)	107.3(7)
C(13A)-C(14A)-C(16A)	115.3(7)
C(13)-C(14)-C(15)	112.2(9)
C(13)-C(14)-C(16)	113.2(9)
C(15)-C(14)-C(16)	108.7(8)
C(13)-C(14)-C(9)	95.5(7)
C(15)-C(14)-C(9)	114.3(8)
C(16)-C(14)-C(9)	112.5(9)
O(7A)-C(17A)-O(8A)	105.0(6)
O(7A)-C(17A)-C(13A)	114.2(6)
O(8A)-C(17A)-C(13A)	113.0(6)
O(7A)-C(17A)-C(8A)	109.4(6)
O(8A)-C(17A)-C(8A)	113.0(6)
C(13A)-C(17A)-C(8A)	102.4(6)
O(7)-C(17)-O(8)	105.2(8)
O(7)-C(17)-C(8)	114.2(8)
O(8)-C(17)-C(8)	110.2(7)
O(7)-C(17)-C(13)	113.4(8)
O(8)-C(17)-C(13)	111.3(8)
C(8)-C(17)-C(13)	102.7(8)
O(7A)-C(18A)-C(19A)	108.7(7)
O(7A)-C(18A)-C(20A)	100.6(6)
C(19A)-C(18A)-C(20A)	118.4(8)
O(7)-C(18)-C(20)	103.7(8)
O(7)-C(18)-C(19)	109.6(9)
C(20)-C(18)-C(19)	116.6(10)
O(8A)-C(20A)-C(21A)	112.9(8)
O(8A)-C(20A)-C(18A)	101.3(6)
C(21A)-C(20A)-C(18A)	117.1(8)
O(8)-C(20)-C(18)	101.9(8)
O(8)-C(20)-C(21)	109.8(9)
C(18)-C(20)-C(21)	117.3(10)

[a] For atom labelling, see Figure 18. [b] Estimated standard deviations in parenthesis.

TABLE 4. Anisotropic displacement parameters (A^2 x 10^3) for 3,3-[(2*R*,3*S*)2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 2,4-dinitrobenzoate (**238**).[a,b] The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a^{*2} U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
O(1A)	52(4)	127(7)	166(7)	-31(6)	-9(4)	19(4)
N(1)	72(6)	99(7)	98(7)	5(5)	17(5)	-13(6)
N(1A)	60(5)	99(7)	80(6)	23(5)	-19(4)	-7(6)
C(1A)	60(5)	49(5)	68(5)	4(4)	4(4)	5(4)
C(1)	59(6)	69(6)	75(6)	7(5)	-5(4)	-4(5)
O(1)	83(5)	116(7)	179(8)	30(6)	29(5)	20(5)
C(2A)	78(5)	128(6)	145(6)	-14(6)	-50(4)	-26(5)
N(2)	100(7)	84(7)	82(6)	7(5)	5(5)	-3(6)
N(2A)	101(7)	73(6)	73(5)	-30(5)	23(5)	-12(6)
O(2)	77(5)	155(7)	116(5)	18(5)	28(4)	-5(5)
C(2)	54(5)	64(6)	70(6)	-12(5)	9(4)	-7(5)
C(2A)	55(5)	59(6)	65(5)	12(5)	-9(4)	-19(5)
C(3A)	70(6)	57(6)	47(5)	-2(4)	-12(4)	-32(5)
O(3)	139(7)	128(7)	168(8)	72(6)	21(6)	-3(6)
O(3A)	132(6)	161(8)	182(8)	-125(7)	15(6)	-42(6)
C(3)	78(6)	72(6)	46(5)	-1(5)	5(4)	-14(5)
O(4)	134(7)	117(6)	110(6)	26(5)	2(5)	35(6)
O(4A)	134(6)	87(5)	96(5)	-24(4)	11(5)	15(5)
C(4A)	76(6)	54(5)	46(5)	2(4)	4(4)	-35(5)
C(4)	87(7)	62(6)	46(5)	-11(4)	-5(5)	-3(5)
O(5A)	52(3)	82(4)	113(5)	-47(4)	-8(3)	12(3)
O(5)	71(4)	101(5)	129(6)	45(5)	0(3)	6(4)
C(5)	72(6)	78(6)	39(5)	4(4)	-2(4)	3(5)
C(5A)	67(5)	55(5)	49(5)	17(4)	19(4)	7(5)
O(6A)	42(3)	61(3)	74(3)	-26(3)	-11(2)	1(3)
O(6)	67(4)	93(5)	108(5)	32(4)	19(3)	0(4)
C(6)	59(5)	70(6)	47(5)	7(4)	-13(4)	-13(5)
C(6A)	50(5)	46(5)	58(5)	4(4)	-6(4)	-9(4)
O(7A)	84(4)	50(4)	78(4)	-1(3)	-4(3)	2(3)
O(7)	137(6)	116(6)	72(4)	1(4)	41(4)	6(5)
C(7A)	42(5)	57(6)	63(5)	-12(4)	9(4)	0(4)
C(7)	45(5)	71(7)	85(7)	1(5)	-5(5)	4(5)
O(8A)	99(4)	64(4)	55(3)	1(3)	-9(3)	14(3)
O(8)	81(4)	89(5)	65(4)	-1(4)	5(3)	-1(4)
C(8A)	45(4)	46(5)	55(4)	-19(4)	0(4)	6(4)
C(8)	62(5)	80(7)	73(6)	16(5)	15(5)	0(5)
C(9A)	59(5)	45(5)	57(5)	4(4)	-9(4)	5(4)
C(9)	80(7)	85(7)	104(8)	15(7)	31(6)	10(6)

C(10A)	99(7)	69(7)	99(7)	10(6)	-2(6)	-16(6)
C(10)	203(14)	107(10)	114(10)	-30(8)	18(9)	26(10)
C(11A)	54(5)	61(5)	66(5)	-2(4)	-12(4)	-2(4)
C(11)	104(9)	108(9)	131(11)	35(8)	16(7)	17(8)
C(12A)	55(5)	76(6)	90(6)	-11(5)	-4(4)	2(5)
C(12)	116(9)	171(13)	103(9)	60(10)	32(7)	58(10)
C(13A)	48(5)	70(6)	62(5)	1(4)	13(4)	3(4)
C(13)	72(6)	143(10)	73(7)	26(7)	-1(5)	15(7)
C(14A)	60(5)	59(6)	73(6)	-9(5)	0(4)	23(5)
C(14)	83(7)	104(8)	87(8)	33(6)	27(5)	32(6)
C(15A)	88(7)	111(8)	109(8)	-20(7)	-17(6)	42(7)
C(15)	105(7)	121(9)	77(7)	30(6)	36(5)	1(7)
C(16A)	99(7)	86(7)	84(7)	-36(6)	-14(5)	34(6)
C(16)	112(9)	155(11)	125(10)	24(9)	39(7)	43(9)
C(17A)	50(5)	59(6)	54(5)	-9(4)	-3(4)	16(4)
C(17)	73(6)	90(7)	77(7)	24(6)	21(5)	8(6)
C(18A)	77(6)	61(6)	88(7)	22(5)	13(5)	1(5)
C(18)	91(7)	157(11)	51(6)	-26(7)	-6(5)	-11(8)
C(19A)	143(9)	75(8)	105(8)	37(6)	33(7)	3(7)
C(19)	108(9)	121(10)	135(10)	-34(8)	31(7)	-10(8)
C(20A)	94(7)	69(6)	51(5)	11(5)	8(5)	7(6)
C(20)	77(7)	112(9)	93(8)	-1(7)	1(6)	-16(6)
C(21A)	78(7)	115(9)	118(8)	19(7)	-17(6)	17(7)
C(21)	169(11)	100(10)	113(9)	-32(8)	-6(8)	-23(9)

[a] For atom labelling, see Figure 18. [b] Estimated standard deviations in parenthesis.

TABLE 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for 3,3-[(2*R*,3*S*)2-*endo*,3-*exo*-butanedioxy]-2-*exo*-bornyl 2,4-dinitrobenzoate (**238**).[a,b]

	x	y	z	U(eq)
H(1A)	-6857(6)	-8565(7)	9149(5)	70
H(1)	-1719(6)	1456(8)	5854(5)	81
H(3A)	-7357(7)	-11520(8)	7667(4)	70
H(3)	-2252(7)	-1487(9)	7305(5)	78
H(5)	520(6)	-1139(8)	6217(4)	76
H(5A)	-4509(6)	-10970(7)	8709(4)	68
H(8A)	-3421(5)	-8092(7)	10476(4)	58
H(8)	1749(6)	1684(9)	4595(5)	85
H(10A)	-3392(38)	-11105(37)	10481(11)	133
H(10B)	-3381(39)	-10412(12)	11335(26)	133
H(10C)	-2455(7)	-11301(29)	1112(35)	133
H(10D)	2178(68)	158(15)	3584(24)	212
H(10E)	1925(53)	-1029(65)	4115(11)	212
H(10F)	3031(19)	-882(73)	3731(33)	212
H(11A)	-1409(6)	-9366(7)	11561(5)	73
H(11B)	-2250(6)	-8286(7)	11470(5)	73
H(11C)	2472(9)	-961(12)	5689(8)	137
H(11D)	3511(9)	-1361(12)	5254(8)	137
H(12A)	-1130(6)	-7157(9)	10728(5)	89
H(12B)	-294(6)	-8247(9)	10807(5)	89
H(12C)	4437(10)	-183(13)	6121(7)	156
H(12D)	3403(10)	175(13)	6577(7)	156
H(13A)	-739(6)	-8300(7)	9372(5)	72
H(13)	4291(7)	2057(11)	5828(6)	115
H(15A)	-61(22)	-10630(59)	9841(19)	155
H(15B)	-821(16)	-11460(22)	10353(42)	155
H(15C)	-361(36)	-10218(40)	10734(25)	155
H(15D)	4363(22)	2656(38)	4166(32)	151
H(15E)	3154(36)	2708(37)	4298(27)	151
H(15F)	3601(54)	1878(11)	3590(8)	151
H(16A)	-1355(15)	-10635(53)	8698(17)	135
H(16B)	-2485(35)	-10103(33)	8807(21)	135
H(16C)	-2168(46)	-11393(24)	9205(7)	135
H(16D)	4862(37)	-369(49)	4900(42)	195
H(16E)	5412(9)	890(31)	4662(54)	195
H(16F)	4808(34)	106(75)	3983(16)	195
H(18A)	-1458(7)	-5965(8)	8847(6)	90
H(18)	2367(8)	3182(13)	7360(6)	120
H(19A)	-2138(36)	-4184(20)	9442(31)	161

H(19B)	-3279(17)	-4572(9)	9171(43)	161
H(19C)	-2476(53)	-4174(20)	8504(14)	161
H(19D)	752(8)	4139(39)	7128(49)	181
H(19E)	558(14)	2689(46)	7182(46)	181
H(19F)	553(14)	3356(82)	6319(8)	181
H(20A)	-2436(7)	-6723(8)	7789(5)	86
H(20)	3364(8)	3967(11)	6402(7)	113
H(21A)	-4264(13)	-6410(71)	8685(7)	156
H(21B)	-4246(14)	-7230(33)	7881(42)	156
H(21C)	-4016(7)	-5787(42)	7835(40)	156
H(21D)	2245(66)	5706(28)	6619(12)	191
H(21E)	1513(25)	5241(11)	5889(52)	191
H(21F)	2652(43)	5697(28)	5714(42)	191

[a] For atom labelling, see Figure 18. [b] Estimated standard deviations in parenthesis.