Pergamon

Tetrahedron 54 (1998) 14265–14282

TETRAHEDRON

Generation and Trapping of Allene Oxides: An Approach to Chiral, Nonracemic α-Alkoxyketones

Michael Shipman*

School of Chemistry, University of Exeter, Stocker Road, Exeter, Devon, EX4 4QD, U.K.

Heidi R. Thorpe

Department of Chemistry, Loughborough University, Loughborough, Leics., LE11 3TU, U.K.

Ian R. Clemens

Glaxo Wellcome Research & Development Ltd, Glaxo Wellcome Medicines Research Centre, Stevenage, Herts, SG1 2NY, U.K.

Received 20 August 1998; revised 7 September 1998; accepted 17 September 1998

Abstract: Epoxy mesylates **5** react with a variety of sodium alkoxides to produce the corresponding α-alkoxyketones in good yields. Evidence is presented for the involvement of transient allene oxides in these reactions. Enantiomerically enriched epoxy mesylates (2*R*,3*S*)-**5a-c** were prepared using the Sharpless asymmetric epoxidation reaction as the key step. These precursors rearrange to α-alkoxyketones without significant racemisation under modified reaction conditions (ROK, 18-crown-6, THF, -78°C). The reactions are shown to proceed with stereochemical inversion at the epoxide centre.

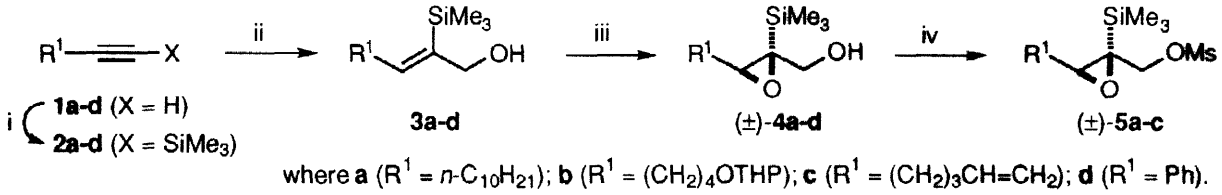
INTRODUCTION

Allene oxides are an interesting class of heterocyclic compound which formally contain the elements of an epoxide, a double bond and an enol ether. The strain energy associated with the allene oxide ring system provides a considerable driving force for a number of interesting chemical conversions including various cycloaddition and ring opening reactions.[1] Furthermore, allene oxides have been shown to be key intermediates in a number of important biological interconversions including plant lipid metabolism and marine prostaglandin biosynthesis.[2] As a consequence, there has been considerable interest in the development of reliable, mild methods for the generation of allene oxides. Perhaps the most direct method for generating these often transient species involves the selective monoepoxidation of allenes. While success has been accomplished in this area, particularly using neutral oxidants such as dimethyldioxirane, this approach often produces mixtures of products.[3] Chan and Ong reported an alternative approach to allene oxides based upon introducing the exocyclic double bond into an epoxide containing precursor *via* an elimination reaction.[4] While this method offers a very mild and neutral method for the generation of allene oxides, work in our own laboratories identified some significant limitations with the published method. Consequently, we have devised an improved elimination approach to allene oxides and used it to prepare α-alkoxyketones in both racemic and enantiomerically enriched form by subsequent *in situ* capture of the allene oxides with alcohol nucleophiles.[5,6] In this paper, we describe in detail our findings in this area.

0040-4020/98/$ - see front matter
PII: S0040-4020(98)00878-3

RESULTS AND DISCUSSION

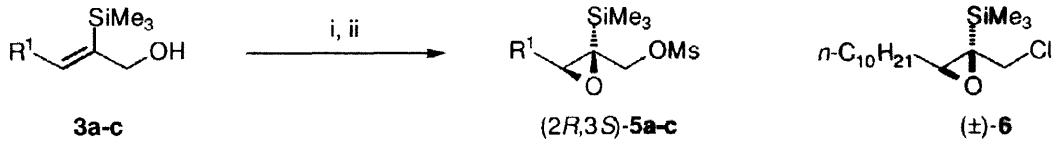
Preparation of Allene Oxide Precursors. Our own studies have determined that epoxymesylates **5** make good precursors for the generation of allene oxides (*Vide Infra*). We have found that these precursors can readily be made in four steps from the corresponding terminal acetylenes **1a-d** (Scheme 1). This reaction sequence was used to prepare a variety of compounds with different types of pendant groups. After silylation, the alkyne bond can be regioselectively hydroaluminated with DIBAL and reacted *in situ* with formaldehyde to yield the hydroxymethyl substituted alkenes **3a-d**. Hydroxyl directed epoxidation of the resultant allylic alcohols gave racemic **4a-d** and subsequent mesylation afforded epoxymesylates **5a-c** in good overall yields. It should be noted that the mesylate precursors are not very stable to acidic conditions and cannot be purified very satisfactorily by silica gel chromatography. However, this did not represent a significant problem as the mesylation reactions were sufficiently clean that the products could be used in subsequent reactions without recourse to any purification beyond a standard aqueous work up. Furthermore, with the exception of the mesylate derived from epoxyalcohol **4d** which was made and used immediately (*Vide Infra*), these mesylates were sufficiently stable to be stored in a freezer for a few days without significant degradation.



where **a** (R^1 = *n*-$C_{10}H_{21}$); **b** (R^1 = $(CH_2)_4OTHP$); **c** (R^1 = $(CH_2)_3CH{=}CH_2$); **d** (R^1 = Ph).

Scheme 1. *Reagents & Conditions:* (i) *n*-BuLi, THF, -78°C, Me_3SiCl, 53-96%; (ii) DIBAL, MeLi, CH_2O, Et_2O, 40-68%; (iii) $VO(acac)_2$, CH_2Cl_2, ^tBuOOH, 43-72%; (iv) $MeSO_2Cl$, Et_3N, CH_2Cl_2, 0°C, 76-89%.

The corresponding enantiomerically enriched precursors were prepared in an identical fashion by performing Sharpless asymmetric epoxidations on allylic alcohols **3a-c** (Scheme 2).[7] Conversion of the resultant epoxyalcohols into the corresponding MPTA esters established that they had been produced with high levels of asymmetric induction (83-85%ee). These epoxides were assigned the (2*R*,3*S*)-stereochemistry on the basis of literature precedent.[8] Subsequent mesylation gave the enantiomerically enriched mesylates (2*R*,3*S*)-**5a-c** in good yields. Racemic chloroepoxide **6**, used for comparisons with the original Chan methodology, was prepared according to the published method.[4]

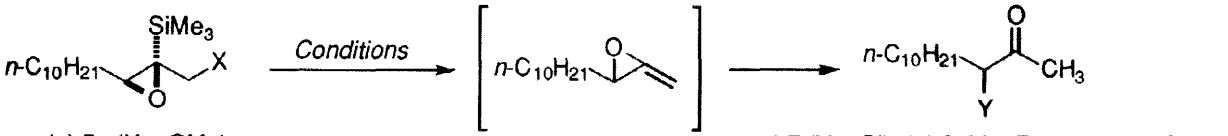


where **a** (R^1 = *n*-$C_{10}H_{21}$); **b** (R^1 = $(CH_2)_4OTHP$); **c** (R^1 = $(CH_2)_3CH{=}CH_2$)

Scheme 2. *Reagents & Conditions:* (i) $Ti(O^iPr)_4$, L-(+)-diethyl tartrate, ^tBuOOH, CH_2Cl_2, -20°C, 41-56%; (ii) $MeSO_2Cl$, Et_3N, CH_2Cl_2, 0°C, 74-95%.

Generation and Trapping of Racemic Allene Oxides with Alcohol Nucleophiles. Initially, we examined the reported conversion of chloroepoxide **6** into the corresponding α-chloroketone **7** by treatment with caesium fluoride in acetonitrile. This reaction, which is believed to proceed *via* the corresponding allene oxide, proceeded as expected to give **7** in 65% yield (Table 1, Entry 1).[4] We then began to examine the more interesting situation wherein the allene oxide intermediate is captured by an external nucleophile. Chan and Ong reported that treatment of chloroepoxide **6** with caesium fluoride in the presence of methanol (3 eq) gives α-methoxyketone **9** in 60% isolated yield.[4] Unfortunately, in our hands this result could not be reproduced and a mixture of the α-chloro, α-fluoro- and α-methoxy compounds was obtained (Table 1, Entry 2). Changing the source and purity of the caesium fluoride used in this reaction had little effect on the outcome.

We reasoned that the formation of α-chloroketone **7** would be prevented by the use of a less nucleophilic leaving group in the elimination reaction. Indeed, using the corresponding mesylate **5a** as the allene oxide precursor, we were able to obtain increased amounts of the desired α-methoxyketone **9** (Table 1, Entry 3). However, this method still lead to the formation of the α-fluoroketone **8** as the major product. The use of alternate fluoride sources such as tetra-*n*-butylammonium fluoride did not reduce the amount of α-fluoroketone produced (Table 1, Entry 4). In order to promote nucleophilic attack on the allene oxide by the added nucleophile rather than fluoride ion, we reasoned that the use of the corresponding alkoxide anion might be beneficial. Initially, we examined the use of sodium methoxide in conjunction with caesium fluoride (Table 1, Entry 5). However, further experimentation established that by using two equivalents of the sodium alkoxide, clean conversion to the α-methoxyketone could be accomplished without the addition of any caesium fluoride. Using this method, mesylate **3a** could be converted into α-methoxyketone **9** in 59% isolated yield after column chromatography (Table 1, Entry 6).



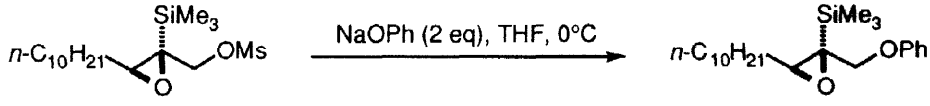
(±)-**5a** (X = OMs) or (±)-**6** (X = Cl)

(±)-**7** (Y = Cl); (±)-**8** (Y = F); (±)-**9** (Y = OMe).

Entry	Precursor	Conditions[#]	Product Ratio[§]	% Yield[¶]
1	(±)-**6**	CsF, MeCN	**7** (100)	65 (**7**)
2	(±)-**6**	CsF, MeCN, MeOH (3 eq)	**7** (71): **8** (23): **9** (6)	-
3	(±)-**5a**	CsF, MeCN, MeOH (12 eq)	**8** (61): **9** (39)	-
4	(±)-**5a**	TBAF, THF, MeOH (10 eq)	**8** (66): **9** (34)	-
5	(±)-**5a**	CsF (1 eq), NaOMe (1 eq), MeCN	**9** (100)	39 (**9**)
6	(±)-**5a**	NaOMe (2.1 eq), THF	**9** (100)	59 (**9**)

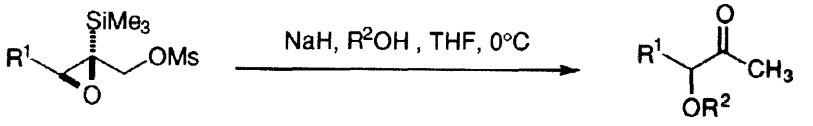
Table 1. [§]Determined by GC and/or ^{1}H nmr spectroscopic ratios on the crude reaction mixture. [¶]Yield of pure isolated material after column chromatography.

Having determined conditions for the efficient conversion of **5a** into **9**, we decided to examine the scope and limitations of this method for the preparation of a variety of α-alkoxyketones. Our findings suggest that a variety of different alcohols including methanol, *iso*-propanol and benzyl alcohol can be used as the nucleophilic component in this reaction (Table 2). Various alkyl substituents can be attached to the epoxide ring without detrimental effects on the efficiency of the process, although to date we have only explored the chemistry of epoxymesylates possessing just one substituent attached to the ring. It should be noted that sodium phenoxide cannot be successfully employed in this process, instead slow displacement of the mesylate occurs yielding epoxide **10** (Scheme 3).



(±)-**5a** (±)-**10**

Scheme 3



Entry	Mesylate	Alcohol	Product	%Yield¶
1	(±)-**5a**	MeOH	**9** (R^1 = *n*-$C_{10}H_{21}$; R^2 = Me)	59
2	(±)-**5a**	BnOH	**11** (R^1 = *n*-$C_{10}H_{21}$; R^2 = Bn)	66
3	(±)-**5b**	MeOH	**12** (R^1 = $(CH_2)_4OTHP$; R^2 = Me)	61
4	(±)-**5b**	BnOH	**13** (R^1 = $(CH_2)_4OTHP$; R^2 = Bn)	63
5	(±)-**5c**	MeOH	**14** (R^1 = $(CH_2)_3CH{=}CH_2$; R^2 = Me)	55
6	(±)-**5c**	^{i}PrOH	**15** (R^1 = $(CH_2)_3CH{=}CH_2$; R^2 = ^{i}Pr)	57

Table 2. ¶Yield of pure isolated material after column chromatography.

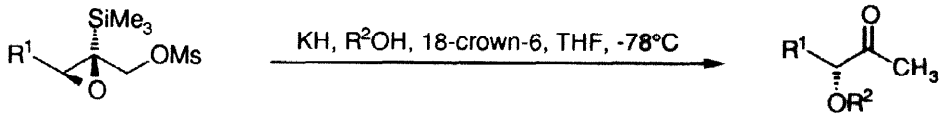
Generation and Trapping of Enantiomerically Enriched Allene Oxides with Alcohol Nucleophiles. In an extension of this work, we were interested in establishing whether homochiral α-alkoxyketones could be prepared using this method. At the outset, we were uncertain whether the strongly basic conditions required for the conversion of the epoxymesylates into the corresponding α-alkoxyketones would facilitate product racemisation. Indeed, our initial attempts at effecting the stereocontrolled conversion of epoxymesylate **5a** into α-methoxyketone **9** were unsuccessful. Treatment of (2*R*,3*S*)-**5a** (84%ee) with sodium methoxide, freshly prepared from sodium hydride and methanol, furnished *racemic* **9** in 59% yield. A series of experiments were then undertaken to establish if racemisation could be prevented by modifying the reaction conditions (Table 3). Sodium methoxide at low temperature was insufficiently reactive to facilitate rearrangement and the starting mesylate was recovered unchanged (Entry 2). While the use of potassium methoxide, freshly prepared from potassium hydride and methanol, at 0°C facilitated product racemisation, this alkoxide was sufficiently reactive to produce a modest yield of the desired ketone at low temperature (Entries 3 & 4). ^{1}H NMR analysis with (+)-Eu(hfc)$_3$ revealed that this material had been produced with little racemisation. Further experimentation established that the use of 18-crown-6 improved the yield of ketone **9** without diminishing the enantioselectivity of the process (Entry 5).

(2*R*,3*S*)-**5a** (3*R*)-**9**

Entry	Reaction Conditions	Yield¶	% ee§
1	NaOMe (2 eq), THF, 0°C to rt,	59%	0%
2	NaOMe (2 eq), THF, -78°C	no reaction	-
3	KOMe (2 eq), THF, 0°C to rt	54%	0%
4	KOMe (2 eq), THF, -78°C	26%	80%
5	KOMe (2 eq), 18-crown-6 (2 eq), THF, -78°C	50%	80%

Table 3. ¶ Yield of isolated material after column chromatography. § Determined by ^{1}H NMR spectroscopic analysis in the presence of (+)-Eu(hfc)$_3$ using racemic material for comparison purposes.

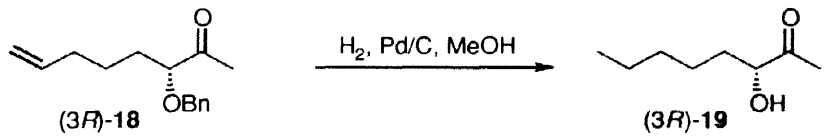
Further studies reveal that these modified reaction conditions are quite general providing access to a variety of chiral α-alkoxyketones in moderate yields (Table 4). Significantly, in each case, the enantiomeric purity of the product closely reflects that of the starting epoxide. While the reaction tolerates functionality in the epoxy mesylate, we have found that only relatively unhindered potassium alkoxides can be used. Thus, potassium *iso*-propoxide, freshly prepared from *iso*-propanol and potassium hydride, does not yield any of the desired α-*iso*-propoxy substituted ketone but simply triggers decomposition of the starting epoxide.



Entry	Precursor	R^1	R^2OH	Product[¶]	%ee[§]
1	(2*R*,3*S*)-**5a**	*n*-$C_{10}H_{21}$	MeOH	(3*R*)-**9** (50%)	80% (84%)
2	(2*R*,3*S*)-**5a**	*n*-$C_{10}H_{21}$	1-Naphthalenemethanol	(3*R*)-**16** (57%)	79% (84%)
3	(2*R*,3*S*)-**5b**	-$(CH_2)_4OTHP$	1-Naphthalenemethanol	(3*R*)-**17** (53%)	83% (83%)
4	(2*R*,3*S*)-**5c**	-$(CH_2)_3CH{=}CH_2$	$PhCH_2OH$	(3*R*)-**18** (52%)	82% (85%)

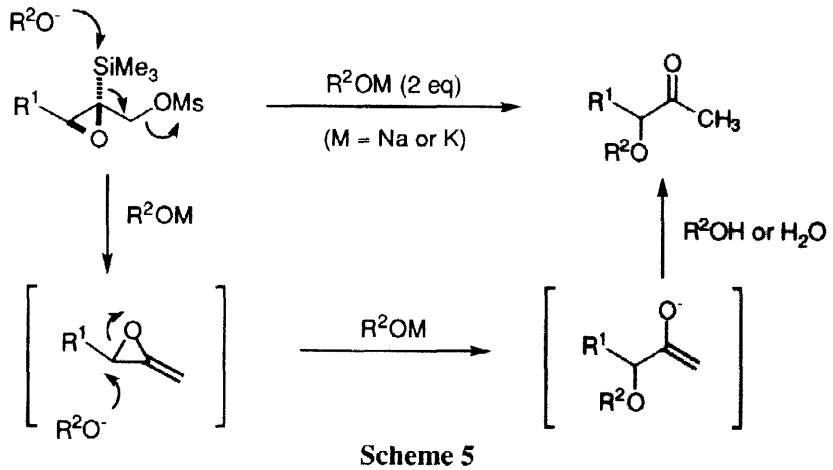
Table 4. [¶] Yield of isolated material after column chromatography given in parenthesis. [§] Enantiomeric purity of the starting material given in parenthesis. The enantiomeric excesses of the products were determined by ^1H NMR spectroscopic analysis in the presence of (+)-Eu(hfc)$_3$ (Entries 1 & 4) or by chiral HPLC analysis (Entries 2 & 3).

We envisaged that these reactions proceed with stereochemical inversion at the epoxide centre. Palladium catalysed hydrogenation of α-benzyloxyketone **18** resulted in the simultaneous removal of the benzyl ether and the alkene double bond furnishing the highly volatile α-hydroxyketone **19** in a very modest 15% yield (Scheme 4). The optical rotation of this material, $[\alpha]_J^{25}$ = -40° (*c* 0.03, $CHCl_3$) was found to be opposite in sign to the known (*S*)-enantiomer,[9] $[\alpha]_J^{25}$ = +92° (*c* 0.03, $CHCl_3$), indicating that both α-benzyloxyketone **18** and α-hydroxyketone **19** possess the (*R*)-configuration. It should be noted that while we cannot account for the discrepancy in the magnitude of these rotations, we are confident that the enantiomeric excess determined for (3*R*)-**18** by chiral HPLC analysis is reliable. This stereochemical study indicates that the alkoxide mediated reactions of epoxymesylates **5** proceed with net stereochemical inversion at C-3.



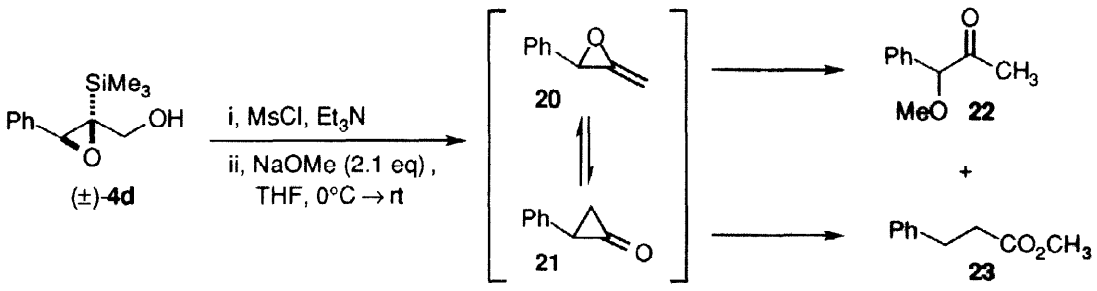
Scheme 4

Mechanistic Studies. We suggest that the observed transformation of epoxymesylates into α-alkoxyketones by reaction with two equivalents of metal alkoxides proceeds *via* initial attack by the alkoxide anion on the silicon which facilitates elimination to form the corresponding allene oxide (Scheme 5). The formation of the strong Si-O bond (*ca* 530 kJ mol^{-1}) presumably provides a powerful driving force for this reaction. Additional circumstantial evidence for initial attack on silicon is provided by the observation that anions centred on nitrogen and sulfur atoms (PhSNa, NaN_3, $PhCH_2NHLi$), which have a lower affinity for silicon, do not produce the corresponding α-substituted ketone products.[10] We speculate that the allene oxide generated by the elimination reaction is subsequently attacked by another molecule of alkoxide anion at the sp^3 epoxide ring carbon causing the epoxide ring to open to the corresponding enolate with stereochemical inversion (*Vide Supra*). Quenching of this enolate with either excess alcohol sometimes present in the reaction mixture or on aqueous work-up would account for the formation of the observed α-alkoxyketone products.



Scheme 5

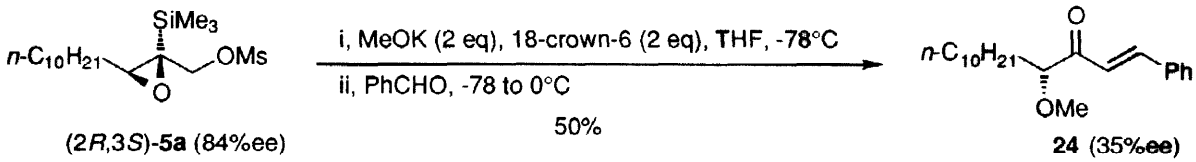
To help substantiate and develop these mechanistic ideas, we set about trying to gain evidence for this reaction pathway. Since we had already determined that epoxymesylate **5a** undergoes methoxide induced rearrangement to α-methoxyketone **9** (*Vide Supra*), we attempted to gain direct evidence for an allene oxide intermediate in this reaction. Thus, **5a** dissolved in d_8-THF containing 18-crown-6 was treated with potassium methoxide at -70°C. Analysis of the reaction mixture by ^{1}H NMR spectroscopy at this temperature failed to reveal resonances that could be assigned to an allene oxide intermediate. In hindsight, it is perhaps not surprising that we were unable to detect the reactive intermediate in the presence of the highly nucleophilic alkoxide anion. However, we do believe that we have obtained indirect evidence for the involvement of allene oxide intermediates in these reactions. Conversion of epoxyalcohol **4d** into the corresponding mesylate and subsequent treatment with sodium methoxide produced both α-methoxyketone **22** and dihydrocinnamate **23** in 14% and 17% yields respectively (Scheme 6). It has been noted previously that the nature of the substituents attached to C-1 of an allene oxide can have a profound effect on their reactivity.[1a] While allene oxides bearing an alkyl group are quite stable and can be directly captured by nucleophiles, allene oxides bearing an aromatic residue exhibit a tendency to rearrange to the corresponding cyclopropanone. Thus, the conversion of aryl substitutent precursor **4d** into two isomeric products **22** and **23** suggests the involvement of allene oxide **20**. Direct opening of this intermediate with methoxide anion accounts for the formation of ketone **22**, while the expected tautomerisation of allene oxide **20** to cyclopropanone **21** and subsequent nucleophilic attack and ring opening explains the formation of dihydrocinnamate **23**. We are unable to suggest any alternative mechanistic pathways that can successfully account for the formation of both of these products.



Scheme 6

In an effort to further probe the mechanism and extend the scope of this reaction, we reasoned that provided no excess of the alcohol nucleophile was present, it may be possible to introduce electrophiles into the reaction mixture and effect further bond forming processes using the sodium or potassium enolates which we speculated must be present in the reaction mixture (see Scheme 5). To test this hypothesis, mesylate

(2*R*,3*S*)-**5a** (84%ee) was reacted with two equivalents of potassium methoxide, then benzaldehyde was added and the solution allowed to warm to 0°C. Gratifyingly, this reaction gave enone **24** in 50% yield *via* a one-pot, three component coupling (Scheme 7). Dehydration of the initial aldol adduct occurs exclusively to give the *trans* isomer as determined by ^{1}H NMR coupling constants. Unfortunately, partial racemisation of the stereogenic centre was observed under these reaction conditions. We believe that the racemisation occurs as the mixture is slowly warmed to 0°C, an observation which is consistent with our earlier findings (see Table 3). Disappointingly, enone **24** was not produced when the reaction was attempted while maintaining the reaction temperature at -78°C for the duration of the experiment. Attempts have been made to try and capture the presumed potassium enolate with other highly reactive electrophiles such as trimethylsilyl chloride. Unfortunately, reaction of **5a** with potassium methoxide (MeOK, 18-crown-6, THF) then TMSCl at -78°C led solely to the production of α-methoxyketone **9**. These findings suggest that either the enolate is unreactive at low temperatures or that quenching of the enolate by a unidentified proton source is occurring. Thus, while we have obtained evidence in support of the mechanistic pathway presented in Scheme 5, not all of our experimental findings are fully consistent with the proposal. Despite our lack of understanding of the full mechanistic details of this process, this chemistry does provide a novel and potentially useful approach to a range of α-alkoxyketones in both racemic and enantiomerically enriched form.



(2*R*,3*S*)-**5a** (84%ee) **24** (35%ee)

Scheme 7

EXPERIMENTAL

General. Potassium hydride was purchased as a dispersion in mineral oil which was removed prior to use by repeated washing with light petroleum. Dichloromethane (DCM) was distilled from phosphorus pentoxide prior to use. Anhydrous tetrahydrofuran (THF) and diethyl ether were prepared by distillation from sodium benzophenone ketyl under nitrogen immediately prior to use, or alternatively, purchased from Aldrich in Sure/Seal™ bottles. All reactions were performed using oven dried glassware under an atmosphere of nitrogen unless otherwise stated. ^{1}H and ^{13}C NMR spectra were recorded at 250 MHz and 62.9 MHz respectively on a Bruker AC-250 instrument or at 400 MHz and 100 MHz respectively on a Bruker DPX-400 instrument. Spectra were recorded in deuterochloroform unless otherwise stated and residual protic solvent (7.26 ppm) was used as the internal standard. Infra-red spectra were recorded on a Nicolet FT-205 spectrometer or a Perkin-Elmer Paragon 1000 spectrometer with internal calibration. High and low resolution mass spectra were recorded on a Kratos 80 mass spectrometer under EI conditions unless otherwise stated. High resolution CI spectra were performed by Dr J. A. Ballantine and his staff at the EPSRC Mass Spectrometry Centre, Swansea.

General procedure for the preparation of 1-(trimethylsilyl)acetylenes (2a-d). To the appropriate terminal acetylene **1a-d** dissolved in THF at -78°C was added *n*-butyllithium dropwise. The mixture was stirred for 30 min and then chlorotrimethylsilane was added dropwise. After a further 20 min at -78°C, the reaction was quenched with saturated aqueous NH_4Cl (5-10 ml) and the solution allowed to warm to 0°C. The mixture was poured into water (200 ml) and the layers separated. The aqueous layer was extracted with diethyl ether (2 x 50 ml), the combined organic extracts dried over $MgSO_4$ and the solvent removed under reduced pressure. Purification of the product was accomplished by column chromatography.

1-(Trimethylsilyl)-1-dodecyne (2a). Treatment of 1-dodecyne **1a** (7.47 g, 45.0 mmol) with *n*-butyllithium (2.5 M in hexanes, 19.8 ml, 49.5 mmol) in THF (225 ml) and then chlorotrimethylsilane (14.7 g, 135 mmol), as described above, and subsequent column chromatography (light petroleum) gave **2a** (10.3 g, 96%) as a colourless oil; ν_{max} (film) 2958, 2855, 2176, 1466, 1249, 842 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 2.21 (2H, t, 7.1 Hz), 1.50 (2H, m), 1.27 (14H, m), 0.89 (3H, t, 6.5 Hz), 0.15 (9H, s); δ_C (62.9 MHz, $CDCl_3$) 107.6 (s), 84.2 (s), 31.7 (t), 29.4 (t), 29.3 (t), 29.1 (t), 28.9 (t), 28.6 (t), 28.5 (t), 22.5 (t), 19.7 (t), 13.9 (q), 0.0 (q); *m/z* 238 (M^+), 73, 58, 41; Observed (M^+): 238.2107; $C_{15}H_{30}Si$ requires: 238.2117.

1-(Tetrahydropyranyloxy)-6-(trimethylsilyl)-5-hexyne (2b). Treatment of 6-(tetrahydropyranyloxy)-1-hexyne[11] **1b** (11.43 g, 45.0 mmol) with *n*-butyllithium (1.6 M in hexanes, 30.9 ml, 49.5 mmol) in THF (225 ml) and then chlorotrimethylsilane (14.7g, 135 mmol), as described above, and subsequent column chromatography (10% ethyl acetate / light petroleum) gave **2b** (6.06 g, 53%) as a colourless oil; ν_{max} (CH_2Cl_2) 2956, 2174, 1034, 840 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 4.44 (1H, t, 3.4 Hz), 3.78-3.56 (2H, m), 3.41-3.22 (2H, m), 2.12 (2H, t, 7.1 Hz), 1.76-1.30 (10H, m), 0.10 (9H, s); δ_C (62.9 MHz, $CDCl_3$) 107.1 (s), 98.6 (d), 84.6 (s), 66.8 (t), 62.1 (t), 30.6 (t), 28.7 (t), 25.34 (t), 25.31 (t), 19.53 (t), 19.49 (t), 0.0 (q); *m/z* (CI) 272 (MNH_4^+), 255 (MH^+), 102; Observed (MH^+): 255.1783; $C_{14}H_{27}O_2Si$ requires: 255.1780.

1-(Trimethylsilyl)-6-hepten-1-yne (2c).[12] Treatment of 1-hepten-6-yne **1c** (2.63 g, 28.0 mmol) with *n*-butyllithium (2.5 M in hexanes, 12.3 ml, 30.1 mmol) in THF (100 ml) and then chlorotrimethylsilane (9.12 g, 84.0 mmol), as described above, and subsequent column chromatography (light petroleum) gave **2c** (3.30 g, 71%) as a colourless oil. ν_{max} (film) 2175, 1640, 1245, 1020, 990, 912, 840, 755 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 5.82 (1H, m), 5.15 (2H, m), 2.26-2.11 (4H, m), 1.93-1.51 (2H, m), 0.27 (9H, s). Spectroscopic data were consistent with literature values.[12]

1-Phenyl-2-(trimethylsilyl)ethyne (2d). Treatment of phenylacetylene **1d** (4.60 g, 45.0 mmol) with *n*-butyllithium (1.6 M in hexanes, 30.9 ml, 49.5 mmol) in THF (225 ml) and then chlorotrimethylsilane (14.7 g, 135 mmol), as described above, and subsequent Kugelrohr distillation of the orange residue gave **2d** (7.37 g, 94%) as a colourless oil (b.p. 150°C at 15 mmHg); ν_{max} (film) 3081, 2959, 2160, 1488, 1250 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.39 (2H, m), 7.23 (3H, m), 0.18 (9H, s); δ_C (62.9 MHz, $CDCl_3$) 129.9 (d), 126.5 (d), 126.2 (d), 121.3 (s), 103.4 (s), 92.2 (s), -2.0 (q); *m/z* (CI) 192 (MNH_4^+), 135; Observed (MNH_4^+): 192.1209, $C_{11}H_{18}NSi$ requires: 192.1208.

General procedure for the preparation of (*Z*)-2-(trimethylsilyl)propen-3-ols (3a-d). The appropriate 1-(trimethylsilyl)acetylene **2a-d** was dissolved in diethyl ether and cooled to 0°C. Di-*iso*-butylaluminium hydride (1.5 M in toluene) was added and the mixture was heated to reflux for 1 h. The mixture was cooled to 0°C and methyllithium (1.4 M in diethyl ether) was added gradually and the mixture was stirred for a further 30 min. Paraformaldehyde was cracked at 150-160°C and the gas passed into the reaction mixture using a stream of nitrogen. When the paraformaldehyde had all been consumed, the reaction mixture was poured into a stirred solution of ethyl acetate (15 ml per mmol of di-*iso*-butylaluminium hydride) and water (1.5 ml per mmol of di-*iso*-butylaluminium hydride). An excess of anhydrous Na_2SO_4 was added and the mixture was stirred for 1-2 h and then filtered. The solvent was removed under reduced pressure and the residue purified by column chromatography.

(Z)-2-(Trimethylsilyl)-2-tridecen-1-ol (3a). Treatment of 1-(trimethylsilyl)-1-dodecyne **2a** (5.71 g, 24.0 mmol) in diethyl ether (100 ml) with di-*iso*-butylaluminium hydride (24.0 ml, 36.0 mmol), methyllithium (26.0 ml, 36.0 mmol) and paraformaldehyde (10.8 g, 0.36 mol), as described above, and subsequent column chromatography (10% ethyl acetate / light petroleum) gave **3a** (4.21 g, 65%) as a colourless oil; ν_{max} (film) 3468, 2956, 2855, 1617, 1466, 1373, 1246, 1047, 839 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 6.21 (1H, t, 7.5 Hz), 3.94

(2H, m), 1.96 (2H, m), 1.22-1.09 (17H, m), 0.71 (3H, t, 6.2 Hz), 0.01 (9H, s); δ_C (62.9 MHz, $CDCl_3$) 144.8 (d), 138.8 (s), 69.1 (t), 31.9 (t), 31.8 (t), 29.8 (t), 29.6 (t), 29.4 (t), 29.3 (t), 22.6 (t), 14.1 (q), 0.0 (q) (two carbons in the alkyl chain were unresolved); *m/z* (CI) 270 (MNH_4^+-H_2O); Observed (MNa^+): 293.2281; $C_{16}H_{34}OSiNa$ requires: 293.2277.

(Z)-7-(Tetrahydropyranyloxy)-2-(trimethylsilyl)-2-hepten-1-ol (3b). Treatment of 1-(tetrahydropyranyloxy)-6-(trimethylsilyl)-5-hexyne **2b** (5.33 g, 21.0 mmol) in diethyl ether (100 ml) with di-*iso*-butylaluminium hydride (21.0 ml, 31.5 mmol), methyllithium (22.5 ml, 31.5 mmol) and paraformaldehyde (9.4 g, 0.31 mol), as described above, and subsequent column chromatography (20% ethyl acetate / light petroleum) gave **3b** (4.08 g, 68%) as a colourless oil; ν_{max} (film) 3419, 2945, 2867, 1617, 1454, 1441, 1249, 1022, 839 cm^{-1}; δ_H (250MHz, $CDCl_3$) 6.19 (1H, t, 8.0 Hz), 4.58 (1H, t, 4.3 Hz), 4.12 (2H, s), 3.92-3.65 (2H, m), 3.56-3.34 (2H, m), 2.20 (2H, q, 7.2 Hz), 1.86-1.23 (11H, m), 0.18 (9H, s); *m/z* (CI) 304 (MNH_4^+), 271, 201, 169; Observed (MH^+): 287.2047; $C_{15}H_{31}O_3Si$ requires: 287.2042.

(Z)-2-(Trimethylsilyl)-2,7-octadien-1-ol (3c). Treatment of 1-(trimethylsilyl)-6-hepten-1-yne **2c** (3.15 g, 19.0 mmol) in diethyl ether (80 ml) with di-*iso*-butylaluminium hydride (19.0 ml, 28.5 mmol), methyllithium (20.3 ml, 28.5 mmol) and paraformaldehyde (8.7 g, 0.29 mol), as described above, and subsequent column chromatography (10% ethyl acetate / light petroleum) gave **3c** (1.96 g, 52%) as a colourless oil; ν_{max} (film) 3340, 2952, 2926, 1641, 1617, 1249, 853 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 6.19 (1H, t, 6.2 Hz), 5.87-5.73 (1H, m), 5.06-4.94 (2H, m), 4.13 (2H, bs), 2.21-2.07 (4H, m), 1.48 (2H, m), 0.92 (1H, bs), 0.17 (9H, s); δ_C (62.9 MHz, $CDCl_3$) 144.3 (d), 139.4 (s), 138.5 (d), 114.7 (t), 69.2 (t), 33.4 (t), 31.2 (t), 29.0 (t), 0.18 (q); *m/z* (CI) 216 (MNH_4^+), 198 (MNH_4^+-H_2O), 109; Observed (MNH_4^+): 216.1784; $C_{11}H_{26}NSiO$ requires: 216.1784.

(Z)-1-Phenyl-2-(trimethylsilyl)-1-propen-3-ol (3d). Treatment of 1-phenyl-2-(trimethylsilyl)ethyne **2c** (3.31 g, 19.0 mmol) in diethyl ether (80 ml) with di-*iso*-butylaluminium hydride (1.5 M in toluene, 19.0 ml, 28.5 mmol), methyllithium (1.4 M in diethyl ether, 20.3 ml, 28.5 mmol) and paraformaldehyde (8.7 g, 0.29 mol), as described above, and subsequent column chromatography (10% ethyl actetate/light petroleum) gave **3c** (1.55 g, 40%) as a colourless oil; ν_{max} (film) 3350, 3058, 2955, 1596, 1492, 1249 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.38-7.20 (6H, m), 4.36 (2H, br s), 1.42 (1H, br, s), 0.01 (9H, s); δ_C (62.9 MHz, $CDCl_3$) 143.5 (s), 141.6 (d), 139.6 (s), 129.0 (d), 128.6 (d), 127.0 (d), 68.8 (t), -0.26 (q); *m/z* (CI) 224 (MNH_4^+), 206 (MNH_4^+-H_2O), 189, 117; Observed (MNH_4^+) 224.1471, $C_{12}H_{22}NSiO$ requires: 224.1471.

General procedure for the preparation of (2*R,3*S**)-2,3-epoxy-2-(trimethylsilyl)propan-1-ols (4a-d).** To stirred solution of the appropriate alkene **3a-d** and vanadyl acetoacetonate (0.1 eq) in DCM (5.0 ml/mmol) at 0°C was added dropwise *tert*-butyl hydroperoxide (2.0 eq) dissolved in DCM (0.5 ml/mmol). The mixture was allowed to warm gradually to room temperature and was stirred for 2 h. The reaction mixture was poured into water (2 x volume of solvent used) and filtered into a separating funnel. The layers were separated and the aqueous layer was extracted with DCM. The combined organic extracts were washed successively with 5% aqueous ferrous sulfate, water and brine then dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography.

(2*R, 3*S**)-2,3-Epoxy-2-(trimethylsilyl)tridecan-1-ol (4a).** Treatment of (*Z*)-**3a** (4.05 g, 15.0 mmol) dissolved in DCM (75 ml) with vanadyl acetoacetonate (397 mg, 1.50 mmol) and *tert*-butyl hydroperoxide (70% in water, 3.86 g, 30.0 mmol) in DCM (30 ml), as described above, and subsequent column chromatography (20% ethyl acetate/light petroleum) gave (2*R**, 3*S**)-**4a** (3.09 g, 72%) as a colourless oil; ν_{max} (film) 3255, 2954, 2919, 2850, 1463, 844 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 3.55 (1H, d, 12.2 Hz), 3.46 (1H, d, 12.3 Hz), 2.91 (1H, dd, 6.2, 4.7 Hz), 2.05 (1H, br s), 1.49-1.05 (18H, m), 0.73 (3H, t, 6.2 Hz), 0.00 (9H, s); δ_C ($CDCl_3$, 62.9 MHz) 66.1 (t), 62.4 (d), 59.1 (s), 33.5 (t), 31.9 (t), 31.2 (t), 31.5 (t), 31.1 (t), 30.9 (t), 30.7 (t),

28.8 (t), 24.3 (t), 15.7 (q), 0.0 (q); *m/z* (CI) 304 (MNH_4^+), 270, 197; Observed (MNH_4^+): 304.2670; $C_{16}H_{38}NO_2Si$ requires: 304.2672.

(2*R, 3*S**)-2,3-Epoxy-7-(tetrahydropyranyloxy)-2-(trimethylsilyl)heptan-1-ol (4b).** Treatment of (*Z*)-**3b** (3.43 g, 12.0 mmol) dissolved in DCM (60 ml) with vanadyl acetoacetonate (318 mg, 1.20 mmol) and *tert*-butyl hydroperoxide (3.0 M in 2,2,4-trimethylpentane, 8.0 ml, 24.0 mmol) in DCM (24 ml), as described above and subsequent column chromatography (25% ethyl acetate/light petroleum) gave (2*R**, 3*S**)-**4b** (1.57 g, 43%) as a colourless oil; ν_{max} (CH_2Cl_2) 3449, 2943, 2867, 1350, 1249, 1032, 842 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 4.59 (1H, t, 3.4 Hz), 3.92-3.36 (6H, m), 3.09 (1H, t, 4.6 Hz), 1.87-1.45 (13H, m), 0.16 (9H, s); δ_C (62.9 MHz, $CDCl_3$) 98.8 (d), 67.2 (t), 64.3 (t), 62.3 (t), 60.6 (d), 57.0 (s), 30.7 (t), 30.2 (t), 29.6 (t), 25.4 (t), 24.0 (t), 19.6 (t), -1.6 (q); *m/z* (CI) 320 (MNH_4^+), 303 (MH^+), 201, 129; Observed (MH^+): 303.1995, $C_{15}H_{31}O_4Si$ requires: 303.1992.

(2*R, 3*S**)-2,3-Epoxy-2-(trimethylsilyl)-7-octen-1-ol (4c).** Treatment of (*Z*)-**3c** (1.68 g, 8.5 mmol) dissolved in DCM (40 ml) with vanadyl acetoacetonate (225 mg, 0.85 mmol) and *tert*-butyl hydroperoxide (70% in water, 2.18 g, 17.0 mmol) in DCM (17 ml), as described above, and subsequent column chromatography (20% ethyl acetate/light petroleum) gave (2*R**, 3*S**)-**4c** (1.08 g, 60%) as a yellow oil; ν_{max} (film) 3448, 2931, 2860, 1641, 1414, 1251, 1079, 912 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 5.87-5.71 (1H, m), 5.05-4.93 (2H, m), 3.69 (1H, d, 12.2 Hz), 3.59 (1H, d, 12.2 Hz), 3.05 (1H, m), 2.08 (2H, m), 1.91 (1H, br s), 1.69-1.42 (4H, m), 0.14 (9H, s); δ_C (62.9 MHz, $CDCl_3$) 139.8 (d), 116.5 (t), 66.1 (t), 62.2 (d), 58.7 (s), 35.0 (t), 31.4 (t), 28.1 (t), 0.0 (q); *m/z* (CI) 232 (MNH_4^+), 215 (MH^+), 176, 160, 136, 90; Observed (MH^+): 215.1467; $C_{11}H_{23}O_2Si$ requires: 215.1467.

(1*S, 2*R**)-1,2-Epoxy-1-phenyl-2-(trimethylsilyl)propan-3-ol (4d).** Treatment of (*Z*)-**3d** (1.55 g, 7.0 mmol) dissolved in DCM (35 ml) with vanadyl acetoacetonate (186 mg, 0.7 mmol) and *tert*-butyl hydroperoxide (70% in water, 1.80 g, 14.0 mmol) in DCM (14 ml), as described above, and subsequent column chromatography (20% ethyl acetate/light petroleum) gave (1*S**, 2*R**)-**4d** (847 mg, 55%) as a colourless oil; ν_{max} (film) 3429, 3063, 3031, 2956, 1449, 1399, 1250, 842 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.29 (5H, m), 4.29 (1H, s), 3.93 (1H, dd, 12.5, 3.7 Hz), 3.79 (1H, dd, 12.5, 8.6 Hz), 1.80 (1H, dd, 8.8, 4.0 Hz), -0.17 (9H, s); δ_C (62.9 MHz, $CDCl_3$) 136.9 (s), 127.7 (d), 127.2 (d), 125.8 (d), 63.8 (t), 59.9 (s), 59.4 (d), -2.4 (q); *m/z* (CI) 240 (MNH_4^+), 150, 133, 90; Observed (MNH_4^+): 240.1420; $C_{12}H_{22}NO_2Si$ requires: 240.1419.

General procedure for the asymmetric epoxidation of (*Z*)-2-(trimethylsilyl)-2-propen-1-ols (3a-c). To DCM containing 4Å molecular sieves at -20°C was added titanium tetra-*iso*-propoxide then L-(+)-diethyl tartrate and the mixture stirred for 5 min. Anhydrous *tert*-butyl hydroperoxide (5.0-6.0 M decane) was added dropwise and the mixture was stirred for 30 min. The appropriate (*Z*)-2-(trimethylsilyl)-2-propen-1-ol **3a-c** dissolved in DCM was added to the stirred mixture while the temperature was maintained at -20°C. When the reaction was estimated to be complete by TLC, the mixture was poured into a pre-cooled solution of ferrous sulfate (1.2 mmol/mmol) and citric acid (0.6 mmol/mmol) in water (1 ml/mmol). After stirring for 5 min, the layers were separated and the aqueous layer extracted with diethyl ether. The combined organic extracts were washed with brine then poured into a 10% solution of NaOH in brine (10 ml/mmol) and stirred for 30 min. The layers were separated and the aqueous layer extracted with diethyl ether. The combined organic extracts were washed again with brine then dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue purified by column chromatography.

(2*R*,3*S*)-2,3-Epoxy-2-(trimethylsilyl)tridecan-1-ol (4a). Treatment of **3a** (3.78 g, 14.0 mmol) with titanium tetra-*iso*-propoxide (312 µl, 1.05 mmol), L-(+)-diethyl tartrate (220 µl, 1.28 mmol) and *tert*-butyl hydroperoxide (5.0-6.0 M decane, 8.40 ml, *ca* 42.0 mmol) in DCM (14 ml) containing 4Å molecular sieves

(1.4 g) at -20°C for 20 h, according to method described above, and subsequent column chromatography (20% ethyl acetate/light petroleum) gave (2*R*,3*S*)-**4a** (2.10 g, 53%, 84%ee) as a colourless oil; $[\alpha]_D^{20}$ = -10.2 (*c* 1.0, $CHCl_3$). Other spectroscopic data consistent with that reported for the racemic compound.

(2*R*,3*S*)-2,3-Epoxy-7-(tetrahydropyranyloxy)-2-(trimethylsilyl)heptan-1-ol (4b). Treatment of **3b** (601 mg, 2.10 mmol) with titanium tetra-*iso*-propoxide (47.0 µl, 0.16 mmol), L-(+)-diethyl tartrate (33.0 µl, 0.19 mmol) and *tert*-butyl hydroperoxide (5.0-6.0 M decane, 1.26 ml, *ca* 6.30 mmol) in DCM (3 ml) containing 4Å molecular sieves (160 mg) at -20°C for 20 h, according to method described above, and subsequent column chromatography (25% ethyl acetate/light petroleum) gave (2*R*,3*S*)-**4b** (356 mg, 56%, 83%ee) as a colourless oil; $[\alpha]_D^{20}$ = -9.6 (*c* 1.0, $CHCl_3$). Other spectroscopic data consistent with that reported for the racemic compound.

(2*R*,3*S*)-2,3-Epoxy-2-(trimethylsilyl)-7-octen-1-ol (4c). Treatment of **3c** (2.32 g, 11.7 mmol) with titanium tetra-*iso*-propoxide (262 µl, 0.88 mmol), L-(+)-diethyl tartrate (184 µl, 1.07 mmol) and *tert*-butyl hydroperoxide (5.0-6.0 M decane, 7.02 ml, *ca* 35.1 mmol) in DCM (15 ml) containing 4Å molecular sieves (890 mg) at -20°C for 16 h, according to the method described above, and subsequent column chromatography (20% ethyl acetate/light petroleum) gave (2*R*,3*S*)-**4c** (1.04 g, 41%, 85%ee) as a yellow oil; $[\alpha]_D^{20}$ = -13.3 (*c* 1.0, $CHCl_3$). Other spectroscopic data consistent with that reported for the racemic compound.

Preparation of (2*R,3*S**)-2,3-Epoxy-1-(methanesulfonyloxy)-2-(trimethylsilyl)tridecane (5a).** To a stirred solution of (2*R**,3*S**)-**4a** (572 mg, 2.0 mmol) in DCM (9 ml) containing triethylamine (0.42 ml, 3.01 mmol) at 0°C was added methanesulfonyl chloride (0.17 ml, 2.20 mmol) in DCM (1 ml). The ice-bath was removed and the mixture stirred for 30 min then poured into ice/water. The layers were separated and the aqueous layer extracted with DCM. The combined organic extracts were washed successively with 2M hydrochloric acid, saturated aqueous $NaHCO_3$ and brine then dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give (2*R**,3*S**)-**5a** (646 mg, 89%) as a slightly yellow oil which was used without further purification; δ_H (250 MHz, $CDCl_3$) 4.18 (1H, d, 11.2 Hz), 4.17 (1H, d, 11.2 Hz), 3.02 (3H, s), 2.96 (1H, dd, 6.7, 4.5 Hz), 1.47-1.25 (18H, m), 0.87 (3H, t, 6.3 Hz), 0.19 (9H, s).

Preparation of (2*R*,3*S*)-2,3-Epoxy-1-(methanesulfonyloxy)-2-(trimethylsilyl)tridecane (5a). To a stirred solution of (2*R*,3*S*)-**4a** (143 mg, 0.50 mmol) in DCM (1.5 ml) containing triethylamine (0.10 ml, 0.72 mmol) at 0°C was added methanesulfonyl chloride (43 µl, 0.56 mmol) in DCM (0.5 ml). The ice-bath was removed and the mixture stirred for 30 min then poured into ice/water. The layers were separated and the aqueous layer extracted with DCM. The combined organic extracts were washed successively with 2M hydrochloric acid, saturated aqueous $NaHCO_3$ and brine then dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give (2*R*,3*S*)-**5a** (173 mg, 95%) as a slightly yellow oil which was used without further purification.

Preparation of (2*R,3*S**)-2,3-Epoxy-1-(methanesulfonyloxy)-7-(tetrahydropyranyloxy)-2-(trimethylsilyl)heptane (5b).** To a stirred solution of (2*R**,3*S**)-**4b** (604 mg, 2.0 mmol) in DCM (6 ml) containing triethylamine (0.42 ml, 3.0 mmol) at 0°C was added methanesulfonyl chloride (0.18 ml, 2.2 mmol) in DCM (1 ml). The ice-bath was removed and the mixture stirred for 30 min then poured into ice/water. The layers were separated and the aqueous layer extracted with DCM. The combined organic extracts were washed successively with 2M hydrochloric acid, saturated aqueous $NaHCO_3$ and brine then dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give (2*R**,3*S**)-**5b** (581 mg, 76%) as a yellow oil which was used without further purification; δ_H (250 MHz, $CDCl_3$) 4.59 (1H, t, 3.4 Hz), 4.23 (1H, d, 11.4 Hz), 4.17 (1H, d, 11.4 Hz), 3.92-3.72 (2H, m), 3.56-3.36 (2H, m), 3.04 (3H, s), 2.99 (1H, m), 1.89-1.42 (12H, m), 0.20 (9H, s).

Preparation of (2*R*,3*S*)-2,3-Epoxy-1-(methanesulfonyloxy)-7-(tetrahydropyranyloxy)-2-(trimethylsilyl)-heptane (5b). To a stirred solution of (2*R*,3*S*)-**4b** (304 mg, 1.01 mmol) in DCM (3 ml) containing triethylamine (0.21 ml, 1.50 mmol) at 0°C was added methanesulfonyl chloride (85 µl, 1.1 mmol) in DCM (1 ml). The ice-bath was removed and the mixture stirred for 30 min then poured into ice/water. The layers were separated and the aqueous layer extracted with DCM. The combined organic extracts were washed successively with 2M hydrochloric acid, saturated aqueous $NaHCO_3$ and brine then dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give (2*R*,3*S*)-**5b** (280 mg, 74%) as a slightly yellow oil which was used without further purification.

Preparation of (2*R,3*S**)-2,3-Epoxy-1-(methanesulfonyloxy)-2-(trimethylsilyl)-7-octene (5c).** To a stirred solution of (2*R**,3*S**)-**4c** (321 mg, 1.5 mmol) in DCM (4.5 ml) containing triethylamine (0.31 ml, 2.25 mmol) at 0°C was added methanesulfonyl chloride (0.13 ml, 1.68 mmol) in DCM (0.5 ml). The ice-bath was removed and the mixture stirred for 30 min then poured into ice/water. The layers were separated and the aqueous layer extracted with DCM. The combined organic extracts were washed successively with 2M hydrochloric acid, saturated aqueous $NaHCO_3$ and brine then dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give (2*R**,3*S**)-**5c** (345 mg, 79%) as a yellow oil which was used without further purification; δ_H (250 MHz, $CDCl_3$) 5.86-5.74 (1H, m), 5.07-4.96 (2H, m), 4.23 (1H, d, 11.1 Hz), 4.17 (1H, d, 11.4 Hz), 3.03 (3H, s), 2.99 (1H, m), 2.13 (2H, m), 1.71-1.37 (4H, m), 0.19 (9H, s).

Preparation of (2*R*,3*S*)-2,3-Epoxy-1-(methanesulfonyloxy)-2-(trimethylsilyl)-7-octene (5c). To a stirred solution of (2*R*,3*S*)-**4c** (642 mg, 2.99 mmol) in DCM (6 ml) containing triethylamine (0.63 ml, 4.52 mmol) at 0°C was added methanesulfonyl chloride (0.26 ml, 3.36 mmol) in DCM (2 ml). The ice-bath was removed and the mixture stirred for 30 min then poured into ice/water. The layers were separated and the aqueous layer extracted with DCM. The combined organic extracts were washed successively with 2M hydrochloric acid, saturated aqueous $NaHCO_3$ and brine then dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give (2*R*,3*S*)-**5c** (751 mg, 86%) as a slightly yellow oil which was used without further purification.

Reaction of (2*S,3*S**)-1-chloro-2,3-epoxy-2-(trimethylsilyl)tridecane (6) with caesium fluoride and methanol.** Caesium fluoride (46.0 mg, 0.30 mmol) was weighed directly into a round bottom flask that had been oven-dried and cooled under an atmosphere of nitrogen. (±)-**6** (91.0 mg, 0.30 mmol) dissolved in acetonitrile (5 ml) was added to the flask followed by methanol (40 µl, 0.90 mmol). The mixture was stirred for 2 h at room temperature, then diluted with diethyl ether. The white solid was filtered off and the solvent removed under reduced pressure. ^1H NMR analysis of the resulting residue indicated a mixture of 3-chloro-2-tridecanone **7**; δ_H (250 MHz, $CDCl_3$) 4.17 (1H, dd, 7.8, 6.2 Hz), 2.32 (3H, s), 1.90 (2H, m), 1.42-1.26 (16 H, m), 0.88 (3H, t, 6.4 Hz); 3-fluoro-2-tridecanone **8**; δ_H 4.55 (1H, ddd, 50.3, 7.5, 4.9 Hz), 2.09 (3H, d, 6.7 Hz), 1.63 (2H, m), 1.30 (2H, m), 1.11 (14H, m), 1.74 (3H, t, 6.8 Hz) and 3-methoxy-2-tridecanone **9**; δ_H 3.54 (1H, t, 6.2 Hz), 3.35 (3H, s), 2.15 (3H, s), 1.58 (2H, m), 1.36-1.25 (16H, m), 0.88 (3H, t, 6.3 Hz) had been produced. The mixture was analysed by gas chromatography (25 m Cidex B column, 150°C) which determined the following relative yields: 3-chloro-2-tridecanone **7** (71%); 3-fluoro-2-tridecanone **8** (23%); 3-methoxy-2-tridecanone **9** (6%).

Reaction of (2*R,3*S**)-2,3-epoxy-1-(methanesulfonyloxy)-2-(trimethylsilyl)tridecane (5a) with caesium fluoride and methanol.** Caesium fluoride (76.0 mg, 0.50 mmol) was weighed directly into an oven-dried round-bottomed flask which had been cooled to room temperature under an atmosphere of nitrogen. (±)-**5a** (183 mg, 0.50 mmol) dissolved in acetonitrile (5 ml) was added followed by methanol (240 µl, 6.00 mmol). The mixture was stirred for 24 h at room temperature during which time a white precipitate formed. The mixture was diluted with diethyl ether (10 ml) and the solid was filtered off. The solvent was removed under

reduced pressure and the residue was purified by column chromatography (30% diethyl ether/light petroleum) to give as the least polar fraction, 3-fluoro-2-tridecanone **8** (60.0 mg, 55%) as a colourless oil: ν_{max} (film) 2955, 2926, 2855, 1727, 1467, 1420, 1358, 1124, 1084 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.55 (1H, ddd, 50.3, 7.5, 4.9 Hz), 2.09 (3H, d, 6.7 Hz), 1.63 (2H, m), 1.30 (2H, m), 1.11 (14H, m), 1.74 (3H, t, 6.8 Hz); δ_C (100 MHz, $CDCl_3$) 205.2 [s, (J_{CF} = 26 Hz)], 92.8 [d, (J_{CF} =183 Hz)], 31.9 (t), 29.6 (t), 29.53 (t), 29.47 (t), 29.32 (t), 29.28 (t), 29.15 (t), 25.8 (q), 24.5 (t), 22.7 (t), 14.1 (q); δ_F (376 MHz, $CDCl_3$, referenced to TMS at 0.00 ppm) -189.65 to -189.98 (m); *m/z* (CI) 234 (MNH_4^+), 154, 117; Observed (MNH_4^+): 234.2233; $C_{13}H_{29}FNO$ requires: 234.2233. Further elution gave 3-methoxy-2-tridecanone **9** (39.4 mg, 35%) as a colourless oil; ν_{max} (film) 2926, 2855, 2826, 1716, 1466, 1354, 1129, 1109 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 3.54 (1H, t, 6.2 Hz), 3.35 (3H, s), 2.15 (3H, s), 1.58 (2H, m), 1.36-1.25 (16H, m), 0.88 (3H, t, 6.3 Hz); δ_C (62.9 MHz, $CDCl_3$) 211.3 (s), 87.5 (d), 58.0 (q). 31.8 (t), 29.5 (t), 29.4 (t), 29.3 (t), 29.2 (t), 25.0 (t), 22.6 (q), 14.0 (q) (3 methylene carbons of the alkyl chain were not resolved); *m/z* (CI) 246 (MNH_4^+), 229 (MH^+); Observed (MH^+): 229.2168; $C_{14}H_{29}O_2$ requires: 229.2168.

General procedure for the rearrangement of (2*R,3*S**)-2,3-epoxy-1-(methanesulfonyloxy)-2-(trimethylsilyl)propanes to α-alkoxyketones.** The appropriate alcohol (3-10 eq) was added dropwise to sodium hydride (2 eq) stirred in THF at 0°C. When gas evolution was complete the appropriate mesylate dissolved in THF was added dropwise and the reaction mixture was gradually allowed to warm to room temperature. After the reaction was judged to be complete by TLC, the mixture was poured into water, the layers were separated and the aqueous layer extracted with diethyl ether. The combined organic extracts were washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue purified by column chromatography.

3-Methoxy-2-tridecanone (9). Mesylate (±)-**5a** (439 mg, 1.20 mmol) dissolved in THF (4 ml) was treated with a solution of sodium methoxide, prepared from methanol (0.48 ml, 11.9 mmol) added dropwise to sodium hydride (60 mg, 2.5 mmol) in THF (8 ml) as described above. After 1.5 h, work up and subsequent column chromatography (20% diethyl ether / light petroleum) gave (±)-**9** (162 mg, 59%) as a colourless oil. The spectroscopic data were in accordance with those previously described.

3-Benzyloxy-2-tridecanone (11). Mesylate (±)-**5a** (437 mg, 1.20 mmol) dissolved in THF (2 ml) was treated with a solution of sodium benzoxide, prepared from benzyl alcohol (0.37 ml, 3.6 mmol) and sodium hydride (60 mg, 2.50 mmol) in THF (5 ml) as described above. After 2.5 h, work up and and subsequent column chromatography (20% diethyl ether / light petroleum) gave (±)-**11** (242 mg, 66%) as a yellow oil; ν_{max} (film) 3021, 2952, 2925, 2854, 1716, 1466, 1455, 1353, 1099, 734 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.35 (5H, m), 4.58 (1H, d, 11.7 Hz), 4.42 (1H, d, 11.7 Hz), 3.75 (1H, dd, 7.5, 5.3 Hz), 2.18 (3H, s), 1.67 (2H, m), 1.36-1.26 (16H, m), 0.89 (3H, t, 6.2 Hz); δ_C (62.9 MHz, $CDCl_3$) 212.2 (s), 138.3 (s), 128.4 (d), 127.8 (d), 127.8 (d), 85.1 (d), 72.3 (t), 31.9 (t), 31.8 (t), 29.5 (t), 29.47 (t), 29.34 (t), 29.28 (t), 29.2 (t), 25.2 (q), 25.1 (t), 22.6 (t), 14.0 (q); *m/z* (C.I.$^+$, thermospray) 322 (MNH_4^+), 170, 108; Observed (MNH_4^+): 322.2748; $C_{20}H_{36}NO_2$ requires: 322.2746.

7-(Tetrahydropyranyloxy)-3-methoxyheptan-2-one (12). Mesylate (±)-**5b** (266 mg, 0.70 mmol) dissolved in THF (2 ml) was reacted with a solution of sodium methoxide, prepared from methanol (283 µl, 6.99 mmol) and sodium hydride (33 mg, 1.38 mmol) in THF (5 ml) as described above. After 2.5 h, work up and subsequent column chromatography (25% ethyl acetate / light petroleum) gave (±)-**12** (105 mg, 61%) as a colourless oil; ν_{max} (film) 2939, 2869, 1715, 1353, 1200, 1121, 1035 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 4.56 (1H, t, 3.6 Hz), 3.90-3.68 (2H, m), 3.56 (1H, t, 6.8 Hz), 3.55-3.32 (2H, m), 3.36 (3H, s), 2.17 (3H, s), 1.90-1.36 (12H, m); δ_C (62.9 MHz, $CDCl_3$) 211.5 (s), 98.9 (d), 87.4 (d), 67.2 (t), 62.4 (t), 58.1 (q), 31.7 (t), 30.8 (t), 29.5 (t),

25.5 (t), 25.1 (q), 22.0 (t), 19.7 (t); *m/z* (C.I.$^+$, thermospray) 245 (MH^+), 161, 142, 111; Observed (MNa^+): 267.1569; $C_{13}H_{24}NaO_4$ requires: 267.1572.

7-(Tetrahydropyranyloxy)-3-benzyloxyheptan-2-one (13). Mesylate (±)-**5b** (176 mg, 0.46 mmol) dissolved in THF (1 ml) was treated with a solution of sodium benzoxide, prepared from benzyl alcohol (178 µl, 1.65 mmol) and sodium hydride (26 mg, 1.07 mmol) in THF (4 ml) as described above. After 2.5 h, work up and subsequent column chromatography (20% ethyl acetate / light petroleum) gave (±)-**13** (93.0 mg, 63%) as a colourless oil; ν_{max} (film) 3042, 2940, 2867, 1714, 1352, 1121, 1027 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.40-7.28 (5H, m), 4.59 (1H, d, 12.9 Hz), 4.55 (1H, m), 4.41 (1H, d, 12.9 Hz), 3.90-3.68 (3H, m), 3.48 (1H, m), 3.36 (1H, m), 2.18 (3H, s), 1.86-1.40 (12H, m); δ_C (62.9 MHz, $CDCl_3$) 211.4 (s), 137.5 (s), 128.5 (d), 127.9 (d), 127.9 (d), 98.8 (d), 85.1 (d), 72.4 (t), 67.2 (t), 62.3 (t), 31.8 (t), 30.7 (t), 29.4 (t), 25.5 (t), 25.3 (q), 22.0 (t), 19.6 (t); *m/z* (C.I.$^+$, thermospray) 321 (MH^+), 237, 228, 128 ; Observed (MNa^+): 343.1882; $C_{19}H_{28}NaO_4$ requires: 343.1885.

3-Methoxy-7-octen-2-one (14). Mesylate (±)-**5c** (321 mg, 1.10 mmol) dissolved in THF (2 ml) was treated with a solution of sodium methoxide, prepared from methanol (445 µl, 11.0 mmol) and sodium hydride (53.0 mg, 2.21 mmol) in THF (4 ml) as described above. After 1.5 h, work up and subsequent column chromatography (20% ethyl acetate / light petroleum) gave (±)-**14** (94 mg, 55%) as a colourless oil; ν_{max} (film) 2935, 2866, 2827, 1716, 1641, 1457 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 5.70-5.63 (1H, m), 4.93-4.83 (2H, m), 3.44 (1H, m), 3.24 (3H, s), 2.04 (3H, s), 1.94 (2H, m), 1.54-1.49 (2H, m), 1.40-1.34 (2H, m); δ_C (62.9 MHz, $CDCl_3$) 211.7 (s), 138.5 (d), 115.3 (t), 87.7 (d), 58.4 (q), 33.7 (t), 31.5 (t), 25.4 (q), 24.8 (t); *m/z* (C.I.$^+$, thermospray) 174 (MNH_4^+); Observed (MNH_4^+): 174.1494; $C_9H_{20}NO_2$ requires: 174.1450.

3-(1-Methylethyloxy)-7-octen-2-one (15). Mesylate (±)-**5c** (146 mg, 0.50 mmol) dissolved in THF (1 ml) was treated with a solution of sodium *iso*-propoxide, prepared from *iso*-propyl alcohol (150 µl, 1.96 mmol) and sodium hydride (25.0 mg, 1.04 mmol) in THF (3 ml) as described above. After 2.5 h, work up and subsequent column chromatography (25% diethyl ether / light petroleum) gave (±)-**15** (52.0 mg, 57%) as a colourless oil; ν_{max} (film) 3078, 2974, 2934, 1714, 1641, 1457, 1376, 1354, 1120, 913 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 5.63-5.54 (1H, m), 4.84-4.74 (2H, m), 3.50 (1H, m), 3.33 (1H, m), 1.96 (3H, s), 1.87 (2H, m), 1.38-1.22 (4H, m), 0.99 (3H, d, 6.1 Hz), 0.95 (3H, d, 6.0 Hz); δ_C (100 MHz, $CDCl_3$) 214.5 (s), 139.7 (d), 116.4 (t), 85.0 (d), 73.3 (d), 34.8 (t), 33.5 (t), 26.6 (q), 26.2 (t), 24.4 (q), 23.1 (q); *m/z* (C.I.$^+$) 202 (MNH_4^+); Observed (MNH_4^+): 202.1807; $C_{11}H_{24}NO_2$ requires: 202.1807.

General procedure for the reaction of (2*R*,3*S*)-2,3-epoxy-1-(methanesulfonyloxy)-2-(trimethylsilyl)propanes (5a-c) with potassium alkoxides at low temperature. The appropriate (2*R*,3*S*)-2,3-epoxy-1-(methanesulfonyloxy)-2-(trimethylsilyl)propane and 18-crown-6 were dissolved in THF and cooled to -78°C. A 1.0 M solution of the potassium alkoxide in THF was prepared from potassium hydride and the appropriate alcohol (R^2OH). The potassium alkoxide solution was added dropwise to the reaction mixture which was stirred at -78°C until the reaction was estimated to be complete by TLC. The reaction was quenched with diethyl ether containing 1% acetic acid and allowed to warm to 0°C. The mixture was poured into water and the layers separated. The aqueous layer was extracted with diethyl ether and the combined organic extracts washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue purified by column chromatography.

Reaction of (2*R*,3*S*)-2,3-epoxy-1-(methanesulfonyloxy)-2-(trimethylsilyl)tridecane (5a) with potassium methoxide. Treatment of (2*R*,3*S*)-**5a** (145 mg, 0.40 mmol) dissolved in THF (0.8 ml) containing 18-crown-6 (211 mg, 0.80 mmol) with potassium methoxide [1.0 M in THF, 0.8 ml, 0.8 mmol, prepared from potassium

hydride (80 mg, 2.0 mmol) and methanol (81 μl, 2.0 mmol) in THF (2.0 ml)] for 2 h, as described above and subsequent column chromatography (25% diethyl ether/light petroleum) gave (3*R*)-3-methoxytridecan-2-one **9** (45 mg, 50%) as a colourless oil $[\alpha]_D^{20}$ = +59.7 (*c* 0.6, $CHCl_3$). Other spectroscopic data consistent with those reported for the racemic compound. The enantiomeric excess was estimated to be 80%ee from the integration of the two methyl resonances in the ^1H NMR in the presence of (+)-Eu(hfc)$_3$. The NMR solution was prepared from (3*R*)-3-methoxytridecan-2-one (2.2 mg) and (+)-Eu(hfc)$_3$ (4.8 mg) in $CDCl_3$ (1.0 ml).

Reaction of (2*R*,3*S*)-2,3-epoxy-1-(methanesulfonyloxy)-2-(trimethylsilyl)tridecane (5a) with potassium 1-naphthalenemethoxide. Treatment of (2*R*,3*S*)-**5a** (291 mg, 0.80 mmol) dissolved in THF (1.6 ml) containing 18-crown-6 (422 mg, 1.60 mmol) with potassium 1-naphthalenemethoxide [1.0 M in THF, 1.6 ml, 1.60 mmol, prepared from potassium hydride (120 mg, 3.0 mmol) and 1-naphthalenemethanol (474 mg, 3.0 mmol) in THF (3.0 ml)] for 2 h, as described above, and subsequent column chromatography (25% diethyl ether/light petroleum) gave (3*R*)-3-(1-naphthylenemethoxy)-tridecan-2-one **16** (161 mg, 57%, 79%ee) as a yellow oil; ν_{max} (film) 3049, 2925, 2854, 1715, 1599, 1512, 1466, 1353, 1168, 1098, 793 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.20 (2H, m), 7.75 (2H, m), 7.44-7.33 (3H, m), 4.95 (1H, d, 11.9 Hz), 4.76 (1H, d, 11.9 Hz), 3.73 (1H, dd, 8.0, 4.9 Hz), 2.05 (3H, s), 1.60-1.48 (2H, m), 1.23-1.06 (16H, m), 0.78 (3H, t, 6.7 Hz); δ_C (100 MHz, $CDCl_3$) 213.6 (s), 135.8 (s), 135.0 (s), 133.7 (s), 130.9 (d), 130.6 (d), 128.8 (d), 128.2 (d), 127.9 (d), 127.1 (d), 126.0 (d), 86.8 (d), 72.8 (t), 34.0 (t), 33.9 (t), 31.5 (t), 31.5 (t), 31.3 (t), 31.3 (t), 31.2 (t), 27.4 (q), 27.1 (t), 24.7 (t), 16.1 (q); *m/z* (C.I.$^+$, thermospray) 372 (MNH_4^+); Observed (MNH_4^+): 372.2902; $C_{24}H_{38}NO_2$ requires 372.2903; $[\alpha]_D^{20}$ = +29.6 (*c* 1.0, $CHCl_3$). The enantiomeric excess was determined to be 79%ee by HPLC using a Chiralcel OD HPLC column (λ = 254 nm, 0.3% *iso*-propanol/hexane, 0.6 ml/min): 31.90 min (minor), 34.12 min (major).

Reaction of (2*R*,3*S*)-2,3-epoxy-1-(methanesulfonyloxy)-7-(tetrahydropyranyloxy)-2-(trimethylsilyl)-heptane (5b) with potassium 1-naphthalenemethoxide. Treatment of (2*R*,3*S*)-**5b** (280 mg, 0.74 mmol) dissolved in THF (2.0 ml) containing 18-crown-6 (407 mg, 1.54 mmol) with potassium methoxide [1.0 M in THF, 1.54 ml, 1.54 mmol, prepared from potassium hydride (80 mg, 2.0 mmol) and 1-naphthalenemethanol (316 mg, 2.0 mmol) in THF (2.0 ml)] for 2 h, as described above and subsequent column chromatography (25% diethyl ether/light petroleum) gave (3*R*)-3-(1-naphthalenemethoxy)-7-(tetrahydropyranyloxy)heptan-2-one **17** (143 mg, 53%, 83%ee) as a yellow oil ; ν_{max} (film) 3048, 3007, 2942, 2868, 1713, 1598, 1511, 1453, 1440, 1353, 1137, 1033 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.13 (1H, m), 7.85 (2H, m), 7.55-7.43 (4H, m), 5.05 (1H, dd, 11.9, 2.1 Hz), 4.88 (1H, d, 11.9 Hz), 4.52 (1H, m), 3.85 (2H, m), 3.65 (1H, m), 3.48 (1H, m), 3.28 (1H, m), 2.15 (3H, s), 1.81-1.42 (12H, m); δ_C (62.9 MHz, $CDCl_3$) 211.3 (s), 133.7 (s), 132.9 (s), 131.6 (s), 128.9 (d), 128.4 (d), 126.6 (d), 126.2 (d), 125.8 (d), 125.2 (d), 123.9 (d), 98.7 (d), 84.6 (d), 70.7 (t), 67.0 (t), 62.2 (t), 31.7 (t), 30.1 (t), 29.3 (t), 25.4 (t), 25.4 (q), 21.9 (t), 19.5 (t); *m/z* (E.I.$^+$) 287, 243, 141 (100%), 85, 67, 55, 43, 27; Observed (M^+): 370.2142; $C_{23}H_{30}O_4$ requires: 370.2144; $[\alpha]_D^{20}$ = +26.7 (*c* 0.95, $CHCl_3$). The enantiomeric excess was determined to be 83%ee by HPLC using a Chiralcel OD HPLC column (λ = 254 nm, 2.0% *iso*-propanol/hexane, 2.0 ml/min): 9.83 min (major), 11.21 min (minor).

Reaction of (2*R*,3*S*)-2,3-epoxy-1-(methanesulfonyloxy)-2-(trimethylsilyl)-7-octene (5c) with potassium benzoxide. Treatment of (2*R*,3*S*)-**5c** (292 mg, 1.0 mmol) dissolved in THF (2.0 ml) containing 18-crown-6 (503 mg, 1.9 mmol) with potassium benzoxide [1.0 M in THF, 2.0 ml, 2.0 mmol, prepared from potassium hydride (120 mg, 3.0 mmol) and benzyl alcohol (310 μl, 3.0 mmol) in THF (3.0 ml)] for 3 h, according to the procedure described above, and subsequent column chromatography (25% diethyl ether/light petroleum) gave (3*R*)-3-benzyloxy-7-octen-2-one **18** (120 mg, 52%, 82%ee) as a colourless oil; ν_{max} (film) 3066, 3032, 2976, 2936, 2863, 1714, 1641, 1497, 1455, 1354, 1101, 912 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.22-7.14, (5H, m), 5.59

(1H, m), 4.80 (2H, m), 4.42 (1H, d, 11.6 Hz), 4.26 (1H, d, 11.7 Hz), 3.60 (1H, dd, 7.7, 5.0 Hz), 2.01 (3H, s), 1.88 (2H, m), 1.53-1.30 (4H, m); δ_C (100 MHz, $CDCl_3$) 210.0 (s), 136.4 (d), 135.7 (s), 126.6 (d), 126.2 (d), 113.3 (t), 83.2 (d), 70.7 (t), 31.6 (t), 29.6 (t), 23.6 (q), 22.7 (t) (one of the aromatic carbon signals was not resolved); *m/z* (C.I.$^+$, thermospray) 250 (MNH_4^+); Observed (MNH_4^+): 250.1807; $C_{15}H_{24}NO_2$ requires: 250.1807; $[\alpha]_D^{20}$ = +43.1 (*c* 1.0 , $CHCl_3$). The enantiomeric excess was estimated to be 82% from the integration of the two methyl resonances in the ^1H NMR spectrum which resolve in the presence of (+)-Eu(hfc)$_3$. The NMR solution was prepared from (3*R*)-3-benzoxy-7-octen-2-one (4.6 mg) and (+)-Eu(hfc)$_3$ (9.6 mg) in $CDCl_3$ (1.0 ml).

Determination of the absolute configuration: Palladium catalysed hydrogenation of (3*R*)-3-benzyloxy-7-octen-2-one (18). (3*R*)-3-benzyloxy-7-octen-2-one **18** (100 mg, 0.43 mmol) was dissolved in methanol (1 ml) and added to 10% palladium on activated carbon (52 mg) in methanol (3 ml). The flask was evacuated and filled with hydrogen *via* a balloon. The mixture was stirred under a positive pressure of hydrogen at room temperature and the reaction followed by TLC. After 20 h, the catalyst was filtered off through a pad of celite. The solvent was removed under reduced pressure and the residue purified by column chromatography (20% ethyl acetate/light petroleum) to give as the most polar fraction (3*R*)-3-hydroxyoctan-2-one **19** (9.3 mg, 15%), $[\alpha]_D^{20}$ = -37.1 (*c* 1.0, $CHCl_3$); δ_H (250 MHz, $CDCl_3$) 4.18 (1H, m), 3.45 (1H, d, 4.7 Hz), 2.20 (3H, s), 1.62 (2H, m), 1.57-1.31 (6H, m), 0.89 (3H, t, 6.2 H); δ_C (100 MHz, $CDCl_3$) 210.4 (s), 77.7 (d), 33.9 (t), 32.0 (t), 25.6 (q), 24.8 (t), 22.9 (t), 14.4 (q). Data are consistent with the literature values.[9] The optical rotation was measured on the J-line (mercury 578 nm) $[\alpha]_J^{25}$ = -40.0 (*c* 0.03, $CHCl_3$) to compare it with (+)-(3*S*)-3-hydroxyoctan-2-one [lit.,[9] $[\alpha]_J^{25}$ = +91 (*c* 0.03, $CHCl_3$)].

Evidence for Allene Oxide Intermediates: Formation of methyl 3-phenylpropanoate (23) and 1-methoxy-1-phenylpropan-2-one (22). To a stirred solution of (±)-**4d** (333 mg, 1.50 mmol) in DCM (5 ml) containing triethylamine (313 µl, 2.25 mmol) at 0°C was added methanesulfonyl chloride (128 µl, 1.65 mmol). The ice-bath was removed and the solution allowed to warm to room temperature. After 30 min, the mixture was poured into ice/water. The layers were separated and the aqueous layer extracted with DCM. The combined organic extracts were washed successively with 2M hydrochloric acid, saturated aqueous $NaHCO_3$ and brine, and then dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give crude mesylate (374 mg) as a yellow oil which was used without further purification. This mesylate was contaminated with some starting alcohol **4d** (*ca* 30%). To sodium hydride (35.0 mg, 1.45 mmol) in THF (4 ml) at 0°C was added methanol (279 µl, 6.90 mmol) and the mixture stirred until gas evolution ceased. A portion of the crude mesylate (316 mg) in THF (2 ml) was added dropwise and the mixture allowed to warm slowly to room temperature. After 2 h, the mixture was poured into water, the layers separated and the aqueous layer extracted with diethyl ether. The combined organic extracts were washed with brine, dried over $MgSO_4$ and the solvent removed under reduced pressure. Column chromatography (30% diethyl ether/light petroleum) gave as the least polar fraction methyl 3-phenylpropanoate **23**[13] (36.0 mg, 17%) as a yellow pungent oil; ν_{max} (film) 3064, 3029, 2952, 1739, 1497, 1454, 1364, 1279, 1163, 735 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.42 (3H, m), 7.35 (2H, m), 3.81 (3H, s), 3.10 (2H, t, 7.6 Hz), 2.78 (2H, t, 8.1 Hz); δ_C (62.9 MHz, $CDCl_3$) 175.3 (s), 142.5 (s), 130.5 (d), 130.3 (d), 128.5 (d), 53.5 (q), 37.7 (t), 32.9 (t); *m/z* (C.I.$^+$, thermospray) 182 (MNH_4^+); Observed (MNH_4^+): 182.1181; $C_{10}H_{16}NO_2$ requires: 182.1181. Further elution gave 1-methoxy-1-phenylpropan-2-one **22**[14] (28.4 mg, 14%) as a yellow oil; ν_{max} (film) 3063, 3031, 2992, 2936, 1719, 1494, 1454, 1419, 1196, 1103, 735 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.49 (5H, m), 4.78 (1H, s), 3.51 (3H, s), 2.24 (3H, s); δ_C (62.9 MHz, $CDCl_3$) 207.0 (s), 136.3 (s), 129.2 (d), 128.9 (d), 127.3 (d), 89.8 (d), 57.6 (q), 25.4 (q); *m/z* (C.I.$^+$, thermospray) 182 (MNH_4^+), 165; Observed (MNH_4^+): 182.1181; $C_{10}H_{16}NO_2$ requires: 182.1181.

Reaction of (2*R*,3*S*)-2,3-epoxy-1-(methanesulfonyloxy)-2-(trimethylsilyl) tridecane (5a) with potassium methoxide and benzaldehyde. (2*R*,3*S*)-**5a** (158 mg, 0.43 mmol) and 18-crown-6 (227 mg, 0.86 mmol) were dissolved in THF (1 ml) and cooled to -78°C. A 1.0 M solution of the potassium methoxide in THF (2 ml) was prepared from potassium hydride (80 mg, 2.0 mmol) and methanol (81 μl, 2.0 mmol). A portion of the potassium methoxide solution (0.86 ml, 0.80 mmol) was added dropwise to the mixture and the reaction followed by TLC. After 4 h, the starting material had been consumed, then benzaldehyde (0.10 ml, 1.03 mmol) was added and the reaction mixture allowed to warm gradually to 0°C over *ca* 16 h. The mixture was quenched with saturated $NaHCO_3$ (2 ml) then poured into water (5 ml). The layers were separated and the aqueous layer extracted with diethyl ether (3 x 5 ml). The combined organic extracts were washed with brine (20 ml) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue purified by column chromatography (25% diethyl ether/light petroleum) to give (4*R*)-4-methoxy-1-phenyl-1-tetradecen-3-one **24** (68 mg, 50%) as a colourless oil; ν_{max} (film) 3082, 3062, 3028, 2925, 2825, 1689, 1608, 1576, 1496, 1450, 1330, 1202, 1108, 990 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.58 (1H, d, 16.0 Hz), 7.43 (2H, m), 7.23 (3H, m), 6.94 (1H, d, 16.0 Hz), 3.58 (1H, dd, 7.6, 5.6 Hz), 3.20 (3H, s), 1.51 (2H, m), 1.25 (2H, m), 1.09 (14H, m), 0.69 (3H, t, 6.7 Hz); δ_C (100 MHz, $CDCl_3$) 202.2 (s), 144.4 (d), 135.0 (s), 131.1 (d), 130.0 (d), 129.3 (d), 120.8 (d), 87.5 (d), 58.5 (q), 32.9 (t), 32.3 (t), 30.0 (t), 29.9 (t), 29.85 (t), 29.8 (t), 29.7 (t), 25.6 (t), 23.1 (t), 14.5 (q); *m/z* (C.I.$^+$, thermospray) 317 (MH^+); Observed (MH^+): 317.2481; $C_{21}H_{33}O_2$ requires: 317.2481; the enantiomeric excess was determined to be 35%ee by HPLC using a Chiralcel OD HPLC column (λ = 254 nm, 0.5% *iso*-propanol/hexanes, 1.0 ml/min): 8.21 (minor), 8.93 (major).

ACKNOWLEDGEMENTS

We thank Professor TH Chan (Montreal) for providing us with further experimental details for his original procedure. We are grateful to the EPSRC for a CASE award (to HRT), The Royal Society and Glaxo Group Research Ltd for their generous financial support. We are indebted to Dr J.A. Ballantine and his staff at the EPSRC Mass Spectrometry Service for high resolution mass spectra and Dr D.S. Ennis at Smithkline Beecham Pharmaceuticals, Harlow for assistance with some of the optical rotation measurements.

REFERENCES AND NOTES

1. For reviews on the chemistry of allene oxides, see (a) Chan, T.H.; Ong, B.S. *Tetrahedron*, **1980**, *36*, 2269; (b) L'Abbe, G. *Angew. Chem., Int. Ed. Engl.*, **1980**, *19*, 276; (c) Stang, P.J. *The Chemistry of Functional Groups, Supplement E: The Chemistry of Ethers, Crown Ethers, Hydroxyl Groups and their Analogues*; Patai, S., Ed.; Wiley: New York, 1983; pp 859-879; (d) Smadja, W. *Chem. Rev.*, **1983**, *83*, 263.
2. For some leading references, see (a) Brash, A.R. *J. Am. Chem. Soc.*, **1989**, *111*, 1891; (b) Hamberg, M.; Fahlstadius, P. *Arch. Biochem. Biophys.*, **1990**, *276*, 518; (c) Song, W.-C.; Brash, A.R. *Science*, **1991**, *253*, 781; (d) Brash, A.R.; Hughes, M.A.; Hawkins, D.J.; Boeglin, W.E.; Song, W.-C.; Meijer, L. *J. Biol. Chem.*, **1991**, *266*, 22926; (e) Lau, S.-M.C.; Harder, P.A.; O'Keefe, D.P. *Biochemistry*, **1993**, *32*, 1945; (f) Brash, A.R.; Song, W.-C. *J. Lipid Mediators Cell Signalling*, **1995**, 12, 275; (g) Laudert, D.; Pfannschmidt, U.; Lottspeich, F.; Holländer-Czytko, H.; Weiler, E.M. *Plant Molecular Biology*, **1996**, *31*, 323.
3. For illustrative examples, see (a) Crandall, J.K.; Machleder, W.H.; Thomas, M.J. *J. Am. Chem. Soc.*, **1968**, *90*, 7346; (b) Crandall, J.K.; Machleder, W.H. *J. Am. Chem. Soc.*, **1968**, *90*, 7347; (c) Camp, R L.; Greene, F.D. *J. Am. Chem. Soc.*, **1968**, 7349; (d) Bertrand, M.; Dulcere, J. P.; Gil, G.; Grimaldi, J.; Sylvestre-Panthet, P. *Tetrahedron Lett.*, **1976**, 1507; (e) Kim, S. J.; Cha, J. K. *Tetrahedron Lett.*, **1988**,

29, 5613; (f) Marshall, J.A.; Tang, Y. *J. Org. Chem.*, **1994**, *59*, 1457; (g) Sakaguchi, S.; Watase, S.; Katayama, Y.; Sakata, Y.; Nishiyama, Y.; Ishii, Y. *J. Org. Chem.*, **1994**, *59*, 5681; (h) Crandall, J.K.; Rambo, E. *Tetrahedron Lett.*, **1994**, *35*, 1489; (i) Crandall, J.K.; Reix, T. *Tetrahedron Lett.*, **1994**, *35*, 2513.

4. (a) Ong, B.S.; Chan, T.H. *Tetrahedron Lett.*, **1976**, *37*, 3257; (b) Chan, T.H.; Ong, B.S. *J. Org. Chem.*, **1978**, *43*, 2994.
5. (a) Clemens, I.R.; Shipman, M.; Thorpe, H.R. *Synlett*, **1996**, 1065; (b) Clemens, I.R.; Shipman, M.; Thorpe, H.R. *Tetrahedron Lett.*, **1997**, *38*, 897.
6. For further examples of allene oxides generated by elimination reactions, see (a) Corey, E.J.; Ritter, K.; Yus, M.; Nájera, C. *Tetrahedron Lett.*, **1987**, 28, 3547; (b) Vergne, F.; Aitken, D.J.; Husson, H.-P. *J. Chem. Soc., Perkin Trans. 1*, **1991**, 1346; (c) Kabat, M.M. *Tetrahedron: Asymmetry*, **1993**, *4*, 1417; (d) Kabat, M.M. *Tetrahedron Lett.*, **1993**, *34*, 8543; (e) Konoike, T.; Hayashi, T.; Araki, Y. *Tetrahedron: Asymmetry*, **1994**, *5*, 1559; (f) Kabat, M.M. *J. Org. Chem.*, **1995**, *60*, 1823; (g) Kabat, M.M. *Tetrahedron Lett.*, **1996**, 37, 7437.
7. Gao, Y.; Hanson, R.M.; Klunder, J.M.; Ko, S.Y.; Masamune, H.; Sharpless, K.B. *J. Am. Chem. Soc.*, **1987**, *109*, 5765.
8. (a) Takeda, Y.; Matsumoto, T.; Sato, F. *J. Org. Chem.*, **1986**, *51*, 4728; (b) Katsuki, T.; Martin, V.S. *Org. React.*, **1996**, *48*, 1.
9. Bel-Rhlid, R.; Fauve, A.; Veschambre, H. *J. Org. Chem.*, **1989**, *54*, 3221.
10. Thorpe, H.R. PhD Thesis, Loughborough University, 1997.
11. Sharma, S.; Oehlschlager, A.C. *J. Org. Chem.*, **1989**, *54*, 5064.
12. Negishi, E.; Holmes, S.J.; Tour, J.M.; Miller, J.A.; Cederbaum, F.E.; Swanson, D.R.; Takahashi, T.; *J. Am. Chem. Soc.*, **1989**, *111*, 3336.
13. Barton, P.; Laws, A.P., Page, M.I. *J. Chem. Soc., Perkin Trans. 2*, **1994**, 2021.
14. (a) Sonawane, H.R.; Nanjuniah, B.S.; Kulkarni, D.G.; Ahuja, J.R. *Tetrahedron*, **1988**, 44, 7319; (b) Tokunaga, Y.; Ihara, M.; Fukumoto, K. *J. Chem. Soc., Perkin Trans. 1*, **1997**, 207.