Asymmetric induction in Darzens condensation by means of (−)-8-phenylmenthyl and (−)-menthyl auxiliaries

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Asymmetric Darzens condensation of benzaldehyde and various ketones has been investigated. The condensation of acetophenone, propiophenone and symmetric ketones with (−)-8-phenylmenthyl halogenoacetates 3a,b afforded the corresponding glycidic esters *cis*-12, *cis*-13 and 15–19 in 77–96% de, respectively, as the major products. Aza-Darzens condensation between *N*-benzylideneaniline and 3a occurred to give the *trans*-aziridine 21 as the major isomer in >85% de. The stereochemistry of the major diastereoisomers of *cis*-12 and 18 was confirmed by their conversion into the known optically active diols 22 and 24. The configuration of the major product of *cis*-12 was determined to be 2*R*,3*R* and that of 18 to be 2*R*. The geometric and disastereofacial selectivities were understandable in terms of the open-chain or non-chelated antiperiplanar transition state model in the initial aldol-type reaction.

Introduction

The epoxide functionality has frequently been demonstrated to be a versatile and useful moiety for organic synthesis.[1] Moreover, the elegant asymmetric epoxidation procedure reported by Sharpless and Katsuki has provided a facile approach to chiral epoxides which allows for total stereocontrol of both asymmetric centres.[2] However, there are several problems in such asymmetric syntheses. Thus, the Sharpless method has limitation arising from steric problems when substituents occupy, in particular, the 1-position of the allylic alcohol. Furthermore, the stereocontrolled direct and versatile routes to electrophilic epoxides is not developed so far compared with that of the nucleophilic epoxides such as the Sharpless epoxidation.[3]

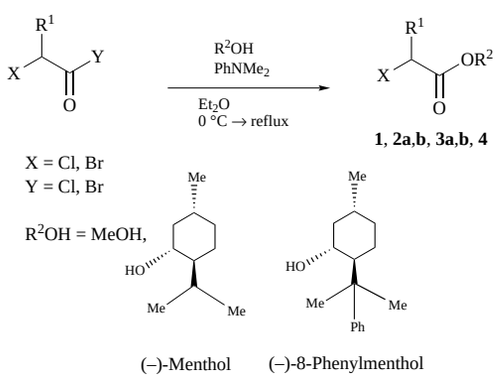
With a view to solving these problems, we have investigated the stereocontrolled route to electrophilic epoxides. Our approach to the asymmetric synthesis of epoxides is based on the well known Darzens glycidic ester condensation which has been one of the more reliable methods for the construction of α,β-epoxy esters.[4] Since the reaction formally consists of an initial aldol-type addition, followed by an intramolecular S_N2 reaction,[5–9] most of the highly stereoselective Darzens reactions have been developed only by a two-step procedure involving stereoselective aldol-type addition.[5,10] Therefore, little attention has been paid to the stereoselective Darzens reaction of ketones, especially symmetric ones.[6,7] In this paper we describe the asymmetric Darzens condensation of various carbonyl compounds with α-halogeno esters **1**–**4** by using chiral auxiliaries such as the (−)-menthyl and (−)-8-phenylmenthyl groups at the ester moiety (see Scheme 1).

The (−)-8-phenylmenthyl group is an effective chiral auxiliary and many asymmetric syntheses have been devised to make use of this ability.[11] Chiral auxiliaries in most studies of asymmetric induction have been attached to electron-poor reagents, for example, in Michael additions and Diels–Alder reactions *etc.* The origin of asymmetric introduction in such reactions has often been attributed to intramolecular π–π interaction between π-systems, and theoretical studies support this view.[12] Notwithstanding, less attention has been accorded to asymmetric induction in the reactions of electron-rich substrates such as enolate, enamine, *etc.* involving a chiral auxiliary.[13] With this in mind, asymmetric induction in the Darzens reaction where (−)-menthyl and (−)-8-phenylmenthyl groups are used as a chiral auxiliary have been investigated.[14]

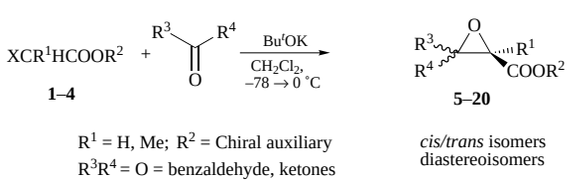
Results and discussion

α-Halogenoacetates **1**–**4** were prepared by reaction of the corresponding α-halogenoacetyl halide with (−)-menthol and (−)-8-phenylmenthol in the presence of *N*,*N*-dimethylaniline as shown in Scheme 1. The Darzens condensation of benzaldehyde and ketones with **1**–**4** in the presence of potassium *tert*-butoxide at −78–0 °C provided the glycidic esters **5**–**20** (Scheme 2). The geometric assignments were confirmed through

Halogenoacetate	X	R^1	R^2
1	Cl	H	Me
2a	Cl	H	(−)-Menthyl
2b	Br	H	(−)-Menthyl
3a	Cl	H	(−)-8-Phenylmenthyl
3b	Br	H	(−)-8-Phenylmenthyl
4	Br	Me	(−)-8-Phenylmenthyl



Scheme 1



Scheme 2

Table 1 Darzens condensations of benzaldehyde with compounds **1**–**4**

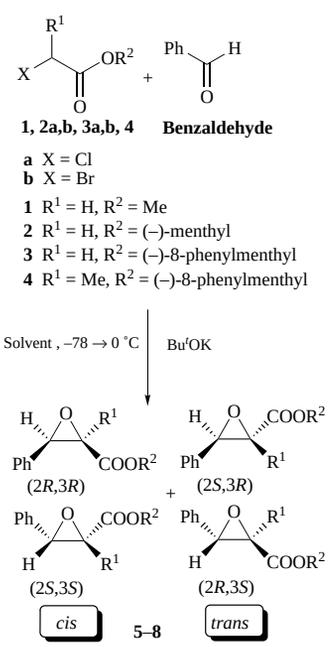
Entry	Halogenoester	Solvent	Product	Yield (%)[a]	*cis*/*trans*[b] *cis*:*trans*	% de[b] *cis*	*trans*
1	**1**	CH_2Cl_2	**5**	52	1.0:9.5	—	—
2	**2a**	Hexane	**6**	90	2.9:1.0	Low	Low
3	**2a**	CH_2Cl_2	**6**	97	1.8:1.0	Low	Low
4	**2a**	Et_2O	**6**	65	1.1:1.0	Low	Low
5	**2b**	Hexane	**6**	68	6.1:1.0	Low	Low
6	**2b**	CH_2Cl_2	**6**	81	6.1:1.0	Low	Low
7	**2b**	Et_2O	**6**	42	7.0:1.0	Low	Low
8	**3a**	Hexane	**7**	95	1.0:1.1	43	Low
9	**3a**	CH_2Cl_2	**7**	90	2.8:1.0	38	33
10	**3a**	Et_2O	**7**	90	1.0:1.3	63	23
11	**3b**	Hexane	**7**	81	5.2:1.0	31	50
12	**3b**	CH_2Cl_2	**7**	75	6.7:1.0	43	41
13	**3b**	Et_2O	**7**	26	6.7:1.0	37	50
14	**4**	CH_2Cl_2	**8**	92	4.9:1.0	29	33

[a] The yield was not optimized. [b] The diastereoselectivity and the geometric ratio were measured by ^{1}H NMR analysis of the crude product mixture.

dif-NOE analysis of the ^{1}H NMR spectra of the glycidic esters whilst the diastereoselectivity was determined by means of ^{1}H NMR and HPLC.

Darzens reaction of benzaldehyde

The Darzens reaction of benzaldehyde with α-halogeno esters **1**–**4** in the presence of Bu^{t}OK smoothly proceeded to give the glycidic esters **5**–**8** as a *cis*/*trans* mixture (Scheme 3). The geometry (*cis* and *trans*) of the glycidic esters was determined by comparisons of the coupling constants (*cis*: *J* 3.9–4.9, *trans*: *J* 1.5–2.0) between the vicinal protons of epoxide ring. The chemical shifts of protons attached at the C-2 position in the *trans* isomers were observed at higher magnetic field than those of the *cis* as a result of the magnetic anisotropic effect of the phenyl ring. The geometric isomers of some of the glycidic esters were separated as pure samples by preparative TLC on silica gel. In addition, the relative stereochemistry of **6** was confirmed by dif-NOE analysis of its ^{1}H NMR spectrum; when 3-H in the oxirane ring was irradiated, 8.2% enhancement of the signal of 2-H was observed in the *cis* diastereoisomer. The geometry of the (−)-8-phenylmenthyl glycidic ester **8** was also confirmed by the dif-NOE analysis of its ^{1}H NMR spectrum; when 3-H was irradiated, 8.4% enhancement in the intensity of signal of the 2-methyl proton was observed in the *cis* isomer but was absent in the *trans*.



Scheme 3

Table 1 shows results for the Darzens condensation of benzaldehyde with **1**, **2a**,**b**, **3a**,**b** and **4**. The Darzens reaction of benzaldehyde with methyl α-chloroacetate **1** gave preferentially the *trans*-isomer (*cis*/*trans* 0.11), as expected from the overlap control mechanism in which the *trans*-epoxide should be predominant.[5,6] However, the same reaction with (−)-menthyl and (−)-8-phenylmenthyl α-halogenoacetate (**2a**,**b**, **3a**,**b** and **4**) in CH_2Cl_2 solution gave the *cis* glycidic esters **6**, **7** and **8** respectively as the major isomers. The *cis*/*trans* ratio of the glycidic esters **6** showed a small dependence on the reaction medium (entries 2–4, 5–7). The *cis* preference in the Darzens reactions of the α-bromo derivatives was more pronounced relative to that of the α-chloro derivatives. For example, the Darzens reaction of (−)-methyl α-bromoacetate **2b** gave **6** (*cis*/*trans* 6.1–7.0; entries 5–7), while the reaction of the α-chloroacetate **2a** afforded the same product **6** (*cis*/*trans* 1.1–2.9, entries 2–4). A similar change in the *cis*/*trans* ratios was observed in the (−)-8-phenylmenthyl esters: that is, *cis*/*trans* 5.2–6.7 for the bromide **3b**; *cis*/*trans* 0.8–2.8 for the chloride **3a**.

Diastereoselectivity in the reactions of benzaldehyde was moderate (23–63% de) with the (−)-8-phenylmenthyl group as a chiral auxiliary (entries 8–13), and very low for a (−)-menthyl auxiliary (entries 2–7).

Darzens reactions of ketones

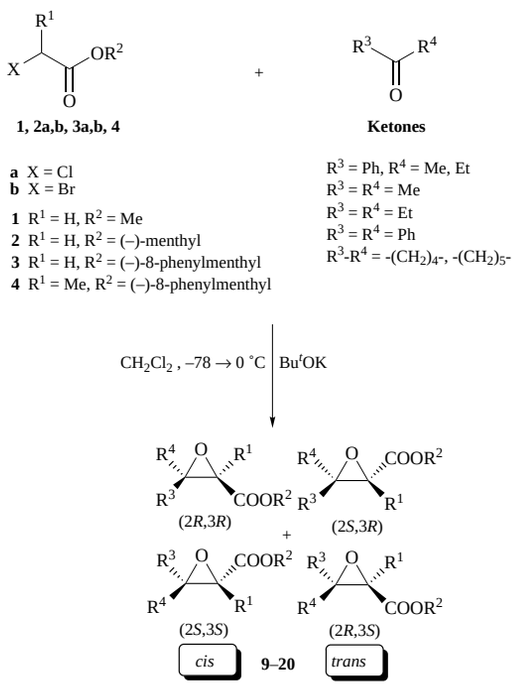
The Darzens reaction of α-halogenoacetate with various ketones gave the corresponding glycidic esters **9**–**20**, respectively (see Scheme 4); the isomeric ratios for each stereoisomer are summarised in Table 2. Geometric assignments were made on the basis of dif-NOE analysis of the ^{1}H NMR spectra; some of *cis*/*trans* isomers were separated by preparative TLC on silica gel and the assigned relative stereochemistry was confirmed by the enhancement of intensity of the methyl proton signal upon irradiation of 2-H through dif-NOE measurements. For the methyl *cis*-glycidate **9**, the intensity of the methyl proton signal was enhanced by 2.5%. For the methyl *trans*-glycidate **9**, there was no enhancement of the corresponding signal. For the major diastereoisomer of *cis*-**12**, the intensity of the methyl proton signal was enhanced by 3.2%. For the major diastereoisomer of *trans*-**12**, there was no enhancement of the corresponding signal. For **13**, the intensity of the methylene proton signal of the ethyl group was enhanced by 5.7% in the *cis* isomer. In the ^{1}H NMR spectra of **9**–**12**, the signal of the methine proton at C-2 of the *trans* isomer series appeared at higher magnetic field than that of the *cis* series.

The *cis*/*trans* ratios in the glycidic esters **9** and **10** derived from acetophenone and propiophenone with **1** were 1.3 and 1.4, respectively (entries 1, 2), preference for the *trans* isomer being

Table 2 Darzens condensations of ketones with compounds **1**–**4** in CH_2Cl_2

Entry	Halogenoester	Ketone	Product	Yield (%)[a]	*cis*/*trans*[b] *cis* : *trans*	% de[b] *cis*	*trans*
1	**1**	Acetophenone	**9**	66	1.0 : 1.3	—	—
2	**1**	Propiophenone	**10**	58	1.0 : 1.4	—	—
3	**2a**	Acetophenone	**11**	83	8.3 : 1.0	38	<10
4	**3a**	Acetophenone	**12**	79	7.6 : 1.0	93	52
5	**3b**	Acetophenone	**12**	56	5.6 : 1.0	>95	21
6	**3a**	Propiophenone	**13**	47	4.5 : 1.0	87	78
7	**3b**	Propiophenone	**13**	43	4.2 : 1.0	>95	>95
8	**2a**	Acetone	**14**	39	—	14	
9	**3a**	Acetone	**15**	64	—	87	
10	**3a**	Pentan-3-one	**16**	47	—	81	
11	**3a**	Cyclopentanone	**17**	45	—	80	
12	**3a**	Cyclohexanone	**18**	45	—	96	
13	**3a**	Benzophenone	**19**	45	—	77	
14	**4**	Cyclohexanone	**20**	18	—	36	

[a] The yields were not optimized. [b] The diastereoselectivity and the geometric ratio were determined by ^{1}H NMR analysis of the crude mixture.



Scheme 4

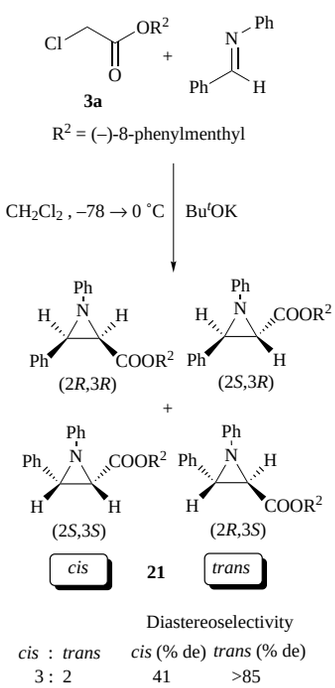
much smaller compared with that in the reaction of benzaldehyde. The Darzens reaction of ketones with the α-halogenoacetates **2a**,**b** and **3a**,**b** preferentially produced the *cis* isomers of **11**–**13** as the major isomer (*cis*/*trans* 4.2–8.3; entries 3–7). The geometric ratios were little affected by a change in the halogeno substituent (X = Cl or Br) (entries 4, 5 and 6, 7).

Whereas the observed diastereoselectivity in the reaction of acetophenone with **2a** was moderate to low (38% de for the *cis* isomer; <10% de for the *trans* isomer, entry 3), it was high (93, >95% de for the *cis*-isomers) in the reaction of acetophenone with the (−)-8-phenylmenthyl esters **3a**,**b** (entries 4,5).

Reaction of (−)-menthyl α-chloroacetate **2a** with acetone afforded the glycidic ester **14** with fair diastereoselectivity (39% de, entry 8). Reaction of (−)-8-phenylmenthyl α-chloroacetate **3a** with acetone gave the glycidic ester **15** in 64% yield and 87% de (entry 9). It is noticeable that considerably high diastereoselectivity (77–96% de) was observed in the reaction of the other symmetric ketones (pentan-3-one, cyclopentanone, cyclohexanone and benzophenone) with (−)-8-phenylmenthyl α-chloroacetate **3a** to give the glycidic esters **16**–**19** (entries 10–13). However, the Darzens reaction of the symmetric ketones with **4** also afforded the glycidic esters **20** with moderate diastereoselectivity (36% de, entry 14).

Asymmetric aza-Darzens condensation

The aza-Darzens reaction of (−)-8-phenylmenthyl α-chloroacetate **3a** with *N*-benzylideneaniline afforded the aziridine **21** in 40% yield as a stereoisomeric mixture (Scheme 5).



Diastereoselectivity

cis : *trans*	*cis* (% de)	*trans* (% de)
3 : 2	41	>85

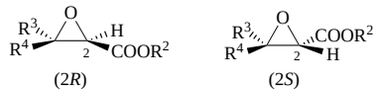
Scheme 5

The geometry (*cis*-series or *trans*-series) in each isomer of aziridine **21** was determined by comparisons of the coupling constants (*cis*: *J* 6.8, *trans*: *J* 2.4) between vicinal protons of the azidirine ring.[15] One of the geometric isomers of **21** was separated by preparative TLC on silica gel and the relative stereochemistry was confirmed by the difference NOE analysis of the ^{1}H NMR spectrum; irradiation of 2-H in the aziridine ring gave a 10.7% enhancement in the 3-H signal for the *cis* isomer. The *trans* isomer, however, demonstrated only 1.7% enhancement of the 3-H signal. The *cis*/*trans* selectivity was 1.5 : 1 and the diastereoselectivity of the *trans* aziridine was high (>85% de). Recently, almost identical results were shown independently for the other chiral auxiliary, the camphorsultam group.[15b]

Absolute configuration of the glycidic esters

The absolute configuration of the glycidic ester **12** was determined as follows (Scheme 6). Reduction of *cis*-**12** with $LiAlH_4$ gave 3-phenylbutane-1,3-diol **22** with $[\alpha]_D^{25}$ −65.8 (*c* 0.137, ben-

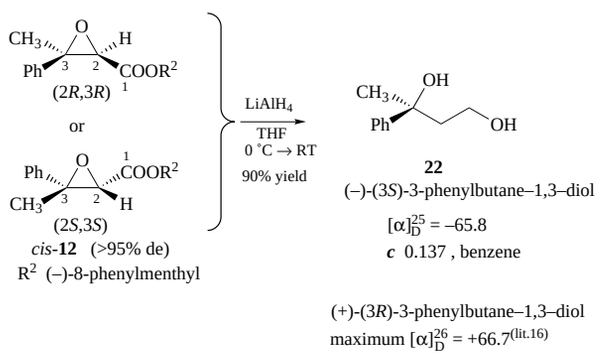
Table 3 The ^{1}H NMR chemical shifts (δ) of 2-H in the diastereoisomers of the glycidic esters **12**–**19**



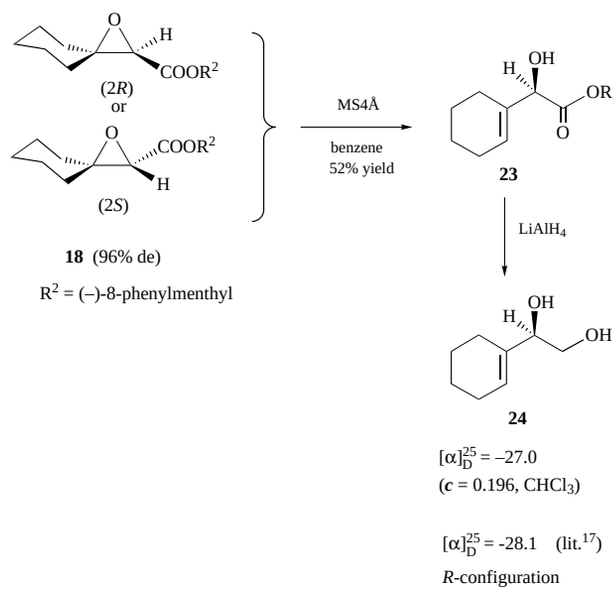
R^2 = (–)- menthyl, (–)-8-phenylmenthyl
R^3 = Ph, R^4 = Me, Et or R^3 = Me, Et, R^4 = Ph
R^3 = R^4 = Me, Et, -$(CH_2)_4$-, -$(CH_2)_5$-, Ph

Compound	R^3	R^4	Chiral auxiliary	Chemical shift, δ for *cis* major	minor	for *trans* major	minor
12	Ph	Me	Phenylmenthyl	3.31[a]	2.62	3.07	2.32
13	Ph	Et	Phenylmenthyl	3.36	2.50	3.16	2.36
				Major		Minor	
14	Me	Me	Menthyl	3.32		3.33	
15	Me	Me	Phenylmenthyl	2.84		2.19	
16	Et	Et	Phenylmenthyl	3.00		2.14	
17	$-(CH_2)_4-$		Phenylmenthyl	3.01		2.44	
18	$-(CH_2)_5-$		Phenylmenthyl	2.96[b]		2.18	
19	Ph	Ph	Phenylmenthyl	3.65		2.80	

[a] The configuration of the major product of *cis*-diastereoisomer in **12** was the 2*R*,3*R*-configuration. [b] The configuration of the major product **18** was 2*R*.



Scheme 6



Scheme 7

zene) in 90% yield. The optical rotation of a pure 3*R* sample of the 1,3-diol **22** was reported to be $[\alpha]_D^{25}$ +66.7.[16] So, the configuration of *cis*-**12** derived in the present Darzens condensation must be 2*R*,3*R*.

The absolute configuration of **18** was also determined by conversion into a known compound as shown in Scheme 7. Cleavage of the epoxide ring of **18** in the presence of MS 4 Å afforded the oxy ester **23**, which upon reduction with $LiAlH_4$ gave the 1,3-diol **24**. The optical rotation value $[\alpha]_D^{25}$ −27.0 (*c* 0.196, $CHCl_3$) of the present 1,3-diol **24** was consistent with that reported for (2*R*)-1,3-diol **24** {$[\alpha]_D^{25}$ −28.1 (*c* 1.02, $CHCl_3$)}.[17] The *R* absolute configuration was confirmed by analogy to the reported optical rotation for (*R*)-2-cyclohexylethane-1,2-diol {$[\alpha]_D^{20}$ −4.17 (*c* 1.73, $CHCl_3$)}.[18] Therefore, the absolute stereochemistry of the glycidic ester **18** was estimated to be the 2*R* configuration.

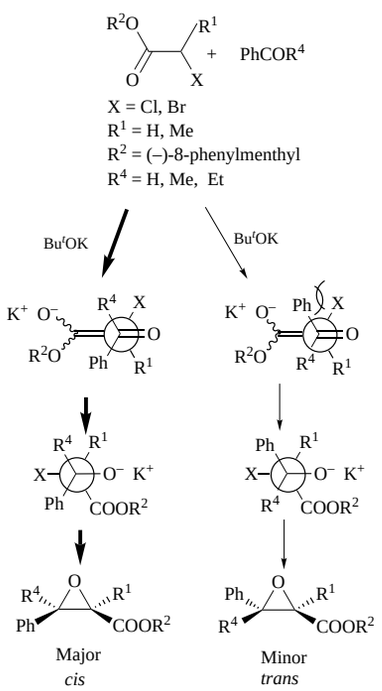
Table 3 shows the characteristic ^{1}H NMR chemical shifts assigned to the epoxy proton at C-2 position of the glycidic esters **12**–**19**. While the differences ($\Delta\delta$ 0.01) of the chemical shifts between the two diastereoisomers of **14** are very small, the differences ($\Delta\delta$ 0.57–0.86) between the two isomers for **12** and **13** are remarkably large. The epoxide ring proton of the major diastereoisomer except that of menthyl ester **14** was observed at lower magnetic field than that of the corresponding minor diastereoisomer when the (−)-8-phenylmenthyl group was utilised as a chiral auxiliary. On the basis of the absolute configuration (2*R*,3*R*) of the major diastereoisomer of **12**, it is reasonable that the absolute configuration at C-2 and C-3 in the major diastereoisomers of **13** is estimated to be 2*R* and 3*R*, respectively.

The chemical shifts of the major diastereoisomers of **15**–**19** derived from symmetric ketones were also observed at lower magnetic field than those of the minor diastereoisomers. Since the absolute configuration of the major diastereoisomer of **18** was also determined to be 2*R* through its conversion into the known compound (*R*)-**24**, the absolute configuration at C-2 of the other major diastereoisomers of **15**–**17** and **19** is also estimated to be 2*R*.

Stereochemical considerations of the geometric selectivity

The present Darzens reactions of benzaldehyde and the unsymmetric ketones with methyl α-chloroacetate preferentially afforded as the major isomer, the corresponding *trans* isomer for each of the glycidic esters **5**, **9** and **10**.[19] The *trans* selectivity coincides with the overlap control model in which epoxide C–O bond formation is the rate-determining step.[5,6] The geometric selectivity in the production of **5** from benzaldehyde was more remarkable than that observed in the preparation of **9** and **10** from ketones. On the other hand, the Darzens reactions of the α-halogenoacetates **2a**,**b** and **3a**,**b** containing chiral auxiliaries such as (−)-menthyl and (−)-8-phenylmenthyl groups at the

alkoxy moiety preferentially gave the *cis* glycidic esters of **6**, **7**, **11** and **12** *etc.* as the major isomer (Table 2). Judging from the facts of the *cis* preference in the present Darzens reactions, it is considered that the stereo-determining step would be the initial aldol type reaction rather than the final C–O bond-formation step in the oxirane ring. Furthermore, the aldol type reaction proceed *via* the open-chain or non-chelated antiperiplanar transition state model, in which the potassium enolate and carbonyl moieties are aligned in an antiperiplanar fashion as shown in Scheme 8.[20] For both the *E*- and *Z*-enolates, the



Scheme 8

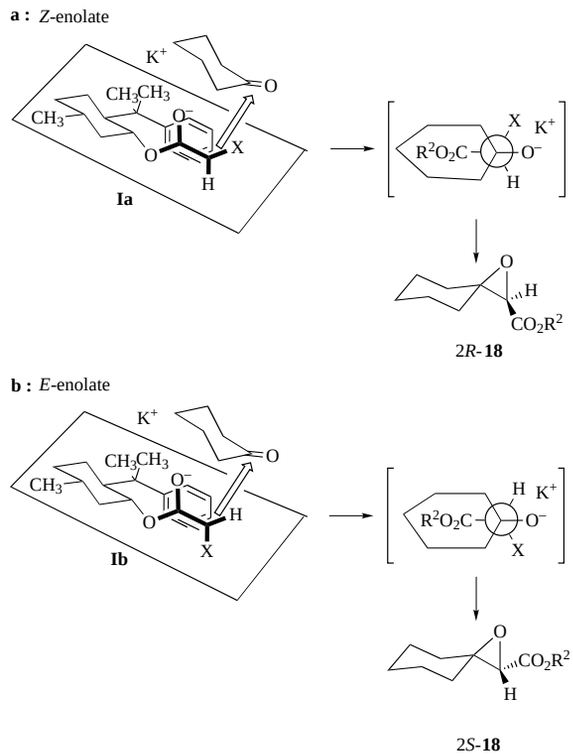
transition state leading to the *trans* oxirane product is destabilized through the steric repulsion between the halogen and phenyl groups. Recently *ab initio* calculations suggest that the open-chain transition state model is favoured for metal-free enolates.[21]

According to the open-chain transition state model, it is understandable that α-bromoacetate with benzaldehyde (R^4 = H) was more effective in the *cis* selectivity than that of α-chloroacetate because of greater repulsion between the phenyl and bromo groups relative to that of the chloro group (Table 1; entries 2, 3, 5 and 6). The explanation is not inconsistent with the smaller difference of *cis*/*trans* selectivity in the acetophenone series (R^4 = Me) in changing halogen from a bromo to a chloro group (Table 2; entries 4,5). Moreover, it is reasonable that the more efficient leaving ability of bromide ion relative chloride ion results a smoother epoxide C–O bond formation process for the bromide series compared with the chloride series.

Stereochemical considerations of the diastereoselectivity

The Darzens reactions of the (−)-menthyl and (−)-8-phenylmenthyl α-halogenoacetates **2a**,**b**, **3a**,**b** and **4** with benzaldehyde and various ketones afforded glycidic esters **6**–**8** and **11**–**20** with 0–95% de. In the Darzens reaction of unsymmetric and symmetric ketones, quite high diastereoselectivity was observed when the (−)-8-phenylmenthyl esters **3a**,**b** were utilised. However, the (−)-menthyl chiral auxiliary was not so effective in the present asymmetric induction. Therefore, it is considered that high diastereofacial attack would be controlled in the initial aldol type step as a result of the steric and/or electronic effects of the phenyl group in the chiral auxiliary.[12]

The Darzens condensation of cyclohexanone with (−)-8-phenylmenthyl α-chloroacetate **3a** proceeded with high stereoselectivity (96% de) to give the glycidic ester **18**. The stereochemistry at C-2 was 2*R*. The stereochemical outcome is understandable in terms of the open-chain transition state model as illustrated in Scheme 9. Thus, cyclohexanone attacks the

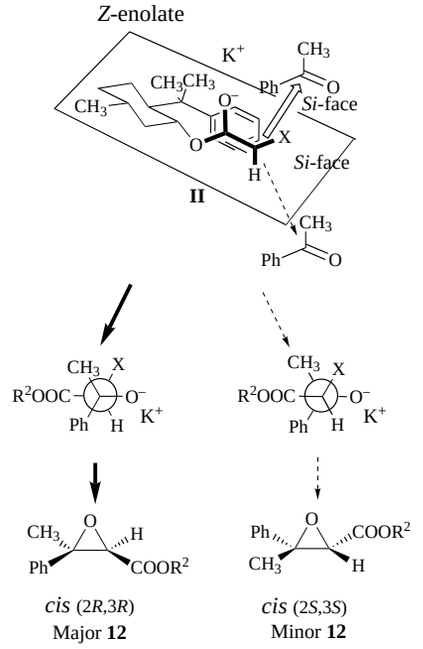


Scheme 9

Z-enolate of **3a** from the front side to give the 2*R*-glycidic ester of **18**, while the *E*-enolate gives the 2*S*-ester of **18** by a similar type of attack. In fact, the present Darzens condensation gave (2*R*)-**18** as the major diastereoisomer. Therefore, the initial step of the Darzens reaction should occur exclusively from the *Si*-face on the intermediate **Ia**, followed by cyclization to give (2*R*)-**18**. According to these considerations, the *Z*-enolate in **Ia** must be more predominant and/or reactive than the *E*-enolate in the reaction intermediate **Ib**. It has been widely accepted that the most stable *Z*-isomer is the one obtained under thermodynamic control.[22] Recently it was reported that the use of potassium *tert*-butoxide should favour the transition state leading to the *Z*-isomer in the deprotonation of 8-phenylmenthyl *N*-[bis-(methylthio)methylene]glycinate.[13f]

It seems reasonable that the π–π interaction between the benzene ring of the chiral auxiliary and the ester moiety in the intermediate **Ia** stabilises the transition state of the stereo-determining step.[11] Within this conformation, the rear face of the enolate double bond is blocked by the benzene ring leading to the result that ketone approaches from the front side (*Si*-face) of **Ia** to give the 2*R*-glycidic ester **18**. That the methylene hydrogens of the ester moiety of **3a** are observed as two doublets at δ 3.35 and 3.01 shifted to higher magnetic field relative to their counterparts in **2a** (δ 4.00 and 4.07) is the direct consequence of the aromatic shielding of the methylene hydrogen atoms by the benzene ring in the chiral auxiliary, or (−)-8-phenylmenthyl group.

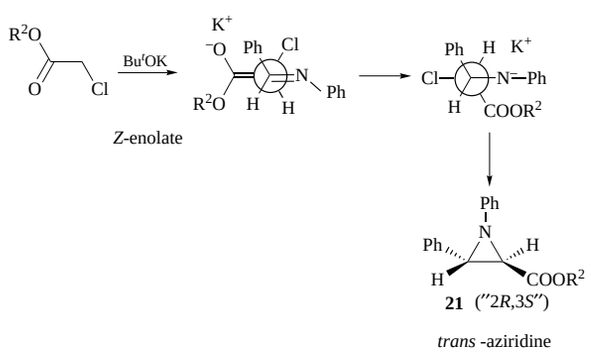
On the basis of the above explanation, it is considered (as illustrated in Scheme 10) that acetophenone attacks the *Z*-enolate of **3a** from the front side to give the *cis*-2*R*,3*R*-glycidic ester **12**. Thus, the initial step of the Darzens reaction should occur exclusively between the *Si*-face on the intermediate **II** and the *Si*-face of acetophenone (*lk*-attack).



Scheme 10

The diastereoselectivity in the Darzens reaction between (−)-8-phenylmenthyl α-halogenoacetates **3a**,**b** and ketones, was higher than that in the reaction with benzaldehyde. Thus, in terms of the reactivity–selectivity rule the difference of the selectivity between the carbonyl compounds is remarkable. It seems reasonable that the reaction of the aldehyde proceeds through a more reactant-like transition state compared than that of ketones. Therefore, the asymmetric induction is higher in the present Darzens condensation with the chiral auxiliary than in the corresponding reactions of the ketone series.

Following analogous reasoning to that in the above explanation, the absolute configuration of the major diastereoisomer of *trans*-**21** is expected to be 2*R*,3*S* as illustrated in Scheme 11.



Scheme 11 Speculation as to the configuration was based on consideration of the analogous Darzens condensation.

Conclusion

A *cis*-glycidic ester with high diastereoselectivity was obtained by the Darzens reaction of (−)-8-phenylmenthyl α-chloro-(and α-bromo-)acetate with various ketones. The high level of both the *cis* selectivity and the diatereoselectivity can be understood in terms of both the open-chain or non-chelated antiperiplanar transition model with the facial selective attack of ketones on the *Si*-face of the *Z*-enolate in which the phenyl ring of the chiral auxiliary and the enolate portion are in a face-to-face conformation.

Experimental

All reactions were carried out under N_2. Dry THF was prepared by distillation after being refluxed over Na/benzophenone. Dry CH_2Cl_2 was obtained by distillation over CaH_2. Silica gel $60F_{254}$ was used for preparative TLC with a UV lamp being used to detect spots.

NMR spectra were recorded on JEOL GSX-270 instruments and ^1H and ^{13}C NMR spectra were observed in $CDCl_3$ solution with TMS as internal reference. MS spectra were recorded on SHIMADZU GCMS-QP2000A and JEOL SX-102A instruments. FAB spectra were obtained with glycerol as a matrix and EI data were obtained at 70 eV. Optical rotations were recorded on JASCO DIP-360 polarimeter and are given in units of 10^{-1} deg cm^2 g^{-1}. Melting points were recorded on YANAGIMOTO melting-point apparatus. Recycling HPLC was carried out using a JASCO LC-908 and a JAIGEL-1H and 2H column ($CHCl_3$).

General procedure for the preparation of α-halogenoacetates

(−)-Menthyl α-chloroacetate 2a. *N*,*N*-Dimethylaniline (35 ml, 276 mmol) was added to a solution of (−)-menthol (39.9 g, 0.28 mol) in Et_2O (100 ml) at 0 °C and this was followed by chloroacetyl chloride (20 ml, 0.25 mol) added at the same temperature. After being stirred for 3 h, the reaction mixture was warmed and then refluxed for 3 h. After solvent removal under reduced pressure from the mixture, CH_2Cl_2 (100 ml) and water (80 ml) were added to the residue. The organic layer was separated, washed with water (3 × 80 ml) and brine (3 × 100 ml), dried ($MgSO_4$) and evaporated to leave a yellow oil. Distillation of this at 90–100 °C/2 mmHg afforded **2a** as a colourless oil (50.7 g, 87%) [lit.,[23] bp 104–105 °C/4 mmHg]; δ_H(270 MHz, $CDCl_3$) 0.77 (d, *J* 6.8, 3 H), 0.80–1.13 (m, 3 H), 0.90 (d, *J* 6.8, 3 H), 0.92 (d, *J* 6.4, 3 H), 1.37–1.52 (m, 2 H), 1.65–1.72 (m, 2 H), 1.81–1.99 (m, 1 H), 2.00–2.06 (m, 1 H), 4.00 (d, *J* 14.7, 1 H), 4.07 (d, *J* 14.7, 1 H) and 4.76 (dt, *J* 10.9, 4.6, 1 H).

(−)-Menthyl α-bromoacetate 2b. The general procedure was followed using (−)-menthol (5.3 g, 34 mmol) and *N*,*N*-dimethylaniline (4.5 ml, 36 mmol). Distillation of the product at 95–100 °C/1.0 mmHg gave **2b**[24] as a colourless oil (7.2 g, 77%); δ_H(270 MHz, $CDCl_3$) 0.77 (d, *J* 6.8, 3 H), 0.81–1.13 (m, 3 H), 0.90 (d, *J* 6.8, 3 H), 0.91 (d, *J* 6.4, 3 H), 1.38–1.59 (m, 2 H), 1.66–1.71 (m, 2 H), 1.85–2.03 (m, 2 H), 3.78 (d, *J* 12.2, 1 H), 3.83 (d, *J* 12.2, 1 H) and 4.73 (dt, *J* 10.7, 4.4, 1 H).

(−)-8-Phenylmenthyl α-chloroacetate 3a. The general procedure was followed using (−)-8-phenylmenthol (1.1 g, 4.4 mmol) and *N*,*N*-dimethylaniline (0.6 ml, 4.7 mmol). Recrystallization of the crude product from hexane gave a pure sample (0.92 g, 67%) as colourless crystals; mp 81–82 °C [lit.,[25] mp 82–83 °C]; δ_H(270 MHz, $CDCl_3$) 0.86–1.05 (m, 2 H), 0.89 (d, *J* 6.3, 3 H), 1.11–1.26 (m, 1 H), 1.20 (s, 3 H), 1.31 (s, 3 H), 1.42–1.55 (m, 1 H), 1.66–1.75 (m, 1 H), 1.79–1.93 (m, 2 H), 2.08 (ddd, *J* 12.1, 10.8, 3.4, 1 H), 3.01 (d, *J* 14.9, 1 H), 3.35 (d, *J* 14.9, 1 H), 4.90 (dt, *J* 10.7, 4.4, 1 H), 7.11–7.19 (m, 1 H) and 7.26–7.33 (m, 4 H) (Found: C, 69.88; H, 8.14. $C_{18}H_{25}O_2Cl$ requires C, 70.00; H, 8.16%).

(−)-8-Phenylmenthyl α-bromoacetate 3b. The general procedure was followed using (−)-8-phenylmenthol (960 mg, 4.13 mmol) and *N*,*N*-dimethylaniline (0.6 ml, 4.6 mmol). Recrystallization of the crude product from hexane afforded a pure sample of **3b**[26] as colourless crystals (915 mg, 63%); mp 62–63 °C; δ_H(270 MHz, $CDCl_3$) 0.84–1.01 (m, 2 H), 0.89 (d, *J* 6.4, 3 H), 1.05–1.25 (m, 1 H), 1.20 (s, 3 H), 1.31 (s, 3 H), 1.42–1.52 (m, 1 H), 1.66–1.73 (m, 1 H), 1.79–1.91 (m, 2 H), 2.02–2.12 (m, 1 H), 2.96 (d, *J* 12.7, 1 H), 3.05 (d, *J* 12.7, 1 H), 4.86 (dt, *J* 10.7, 4.9, 1 H), 7.11–7.17 (m, 1 H) and 7.26–7.33 (m, 4 H) (Found: C, 61.24; H, 7.16. $C_{18}H_{25}O_2Br$ requires C, 61.19; H, 7.13%).

(−)-8-Phenylmenthyl α-Bromopropionate 4. The general procedure was followed using (−)-8-phenylmenthol (2.3 g, 9.98

mmol) and *N*,*N*-dimethylaniline (1.4 ml, 11 mmol). The crude product was purified by preparative TLC (silica gel, hexane–AcOEt, 13:1) to give **4** (3.60 g, 98%) as a colourless oil; δ_H(270 MHz, $CDCl_3$) 0.78–1.18 (m, 3 H), 0.88 and 0.89 (d, *J* 6.8, 3 H), 1.21 and 1.23 (s, 3 H), 1.30 and 1.34 (s, 3 H), 1.38–1.54 (m, 1 H), 1.55 and 1.56 (d, *J* 6.8, 3 H), 1.55–1.75 (m, 1 H), 1.79–1.93 (m, 2 H), 1.98–2.15 (m, 1 H), 3.22 and 3.77 (q, *J* 6.8, 1 H), 4.84 (dt, *J* 10.7, 4.2, 1 H), 7.12–7.16 (m, 1 H) and 7.26–7.30 (m, 4 H) [Found (HRMS): M^+, 368.1159. $C_{19}H_{27}O_2{}^{81}Br$ requires *M*, 368.1174].

General procedure for Darzens condensation

Methyl 3-phenyloxirane-2-carboxylate 5. A solution of **1** (0.3 ml, 3.4 mmol) in CH_2Cl_2 (2 ml) was added to a suspension of potassium *tert*-butoxide (412 mg, 3.78 mmol) in CH_2Cl_2 (3 ml) at −78 °C. After being stirred at −78 °C for 3 h, the mixture was treated with a solution of benzaldehyde (0.5 ml, 5 mmol) in CH_2Cl_2 (2 ml), added dropwise, and then slowly warmed from −78 to 0 °C over 8 h. After the reaction mixture had been stirred at 0 °C for 16 h, it was diluted with water (60 ml) and ether (60 ml). The aqueous layer was separated and extracted with Et_2O (3 × 60 ml) and the combined organic layer and extracts were washed with brine (2 × 60 ml), dried (Na_2SO_4) and evaporated. The residue was subjected to preparative TLC (silica gel, hexane–AcOEt, 13:1) to give a mixture of *cis*- and *trans*-**5** [1e] as a colourless oil (375 mg, 52%; *cis*/*trans* 1.0:9.5); δ_H(270 MHz, $CDCl_3$) 3.52 (d, *J* 2.0, *trans*-2-H), 3.56 (s, *cis*-O–CH_3), 3.83 (s, *trans*-O–CH_3), 3.85 (d, *J* 4.9, *cis*-2-H), 4.10 (d, *J* 2.0, *trans*-3-H), 4.27 (d, *J* 4.9, *cis*-3-H) and 7.26–7.40 (m, 5 H).

(−)-Menthyl 3-phenyloxirane-2-carboxylate 6. The general procedure was followed using Bu^{t}OK (325 mg, 2.90 mmol), **2a** (0.65 ml, 2.8 mmol) and benzaldehyde (0.3 ml, 3 mmol). The crude product was subjected to preparative TLC (silica gel, hexane–AcOEt, 6:1) to give *cis*-**6** and *trans*-**6** (diastereoisomeric mixture) as a colourless oil (829 mg, 97%, *cis*/*trans* 1.8:1.0). Use of **2b** (0.5 ml, 2.2 mmol) under the reaction conditions [Bu^{t}OK (249 mg, 2.28 mmol) and benzaldehyde (0.25 ml, 2.5 mmol)] gave *cis*- and *trans*-**6**, a mixture of diastereoisomers, as a colourless oil (67 mg, 81%; *cis*/*trans*, 6.1:1.0); *cis*-**6** (diastereoisomeric mixture): δ_H(270 MHz, $CDCl_3$) 0.32 [d, *J* 6.8, minor-CH(CH_3)$_2$], 0.62 (d, *J* 6.8, minor-CH_3), 0.67 [d, *J* 6.8, minor-CH(CH_3)$_2$], 0.76 [d, *J* 6.8, major-CH(CH_3)$_2$], 0.78 (d, *J* 6.8, major-CH_3), 0.83 [d, *J* 6.8, major-CH(CH_3)$_2$], 0.86–0.99 (m, 1 H), 1.14–1.70 (m, 6 H), 3.80–3.83 (m, 1 H), 3.81 (d, *J* 4.9, minor-2-H), 3.82 (d, *J* 3.9, major-2-H), 4.26 (d, *J* 4.9, minor-3-H), 4.26 (d, *J* 3.9, major-3-H), 4.54 (dt, *J* 10.7, 4.4, minor-O–CH), 4.58 (dt, *J* 11.0, 4.4, major-O–CH) and 7.26–7.42 (m, 5 H); *trans*-**6** (diastereoisomeric mixture): δ_H(270 MHz, $CDCl_3$) 0.77–0.82 (m, 3 H), 0.88–0.94 (m, 7 H), 0.97–1.14 (m, 2 H), 1.38–1.67 (m, 2 H), 1.71–1.80 (m, 1 H), 1.83–2.00 (m, 1 H), 2.02–2.08 (m, 1 H), 3.49 (d, *J* 1.5, minor-2-H), 3.49–3.51 (m, 1 H), 3.50 (d, *J* 2.0, major-2-H), 4.06 (d, *J* 1.5, minor-3-H), 4.07 (d, *J* 2.0, major-3-H), 4.82 (dt, *J* 10.7, 4.4, major-O–CH), 4.83 (dt, *J* 10.9, 4.4, minor-O–CH) and 7.26–7.41 (m, 5 H).

(−)-8-Phenylmenthyl 3-phenyloxirane-2-carboxylate 7. The general procedure was followed using Bu^{t}OK (38 mg, 0.33 mmol), **3a** (99 mg, 0.32 mmol) and benzaldehyde (0.05 ml, 0.5 mmol). Preparative TLC (silica gel, hexane–AcOEt, 6:1) of the crude product afforded a mixture of *cis*- and *trans*-**7** as a colourless oil (109 mg, 90%; *cis*/*trans* 2.8:1.0; *cis*: 38% de, *trans*: 33% de). Use of **3b** (100 mg, 0.29 mmol) under similar reaction condition [Bu^{t}OK (35 mg, 0.31 mmol) and benzaldehyde (0.05 ml, 0.5 mmol)], gave a mixture of *cis*- and *trans*-**7** as a colourless oil (81 mg, 75%; *cis*/*trans* 6.7:1.0; *cis*: 43% de, *trans*: 41% de): geometric and diastereoisomeric mixture of **7**; δ_H(270 MHz, $CDCl_3$) 0.66–2.14 (m, 17 H), 2.49 (d, *J* 1.5, *trans*-minor-2-H), 2.67 (d, *J* 4.9, *cis*-minor-2-H), 2.72 (d, *J* 2.0, *trans*-major-2-H), 3.46 (d, *J* 4.4, *cis*-major-2-H), 3.74 (d, *J* 1.5, *trans*-minor-3-H), 3.93 (d, *J* 2.0, *trans*-major-3-H), 3.99 (d, *J* 4.9, *cis*-minor-3-H), 4.16 (d, *J* 4.4, *cis*-major-3-H), 4.58 (dt, *J* 10.7, 4.4, *trans*-major-O–CH), 4.71 (dt, *J* 10.7, 4.4, *trans*-minor-O–CH), 4.86 (dt, *J* 10.7, 4.4, *cis*-major-O–CH), 4.96 (dt, *J* 10.7, 4.4, *cis*-minor-O–CH) and 7.15–7.67 (m, 10 H); δ_C(68 MHz, $CDCl_3$) 21.5, 21.5, 22.6, 25.3, 26.0, 26.7, 27.4, 29.5, 30.9, 31.1, 34.2, 34.3, 39.3, 39.8, 41.0, 41.1, 42.7, 50.2, 50.3, 55.3, 55.7, 56.8, 57.4, 67.0, 74.5, 76.2, 125.0, 125.2, 125.4, 125.5, 126.4, 126.9, 127.8, 128.0, 128.1, 128.3, 132.8, 150.6, 151.7, 165.3 and 165.9 [Found (HRMS): M^+, 378.2181. $C_{25}H_{30}O_3$ requires *M*, 378.2195].

(−)-8-Phenylmenthyl 2-methyl-3-phenyloxirane-2-carboxylate 8. The general procedure was followed using Bu^{t}OK (51 mg, 0.45 mmol), **4** (83 mg, 0.23 mmol) and benzaldehyde (1.1 ml, 11 mmol). Preparative TLC (silica gel, hexane–AcOEt, 13:1) afforded *trans*-**8** (major diastereoisomer) and a diastereoisomeric mixture of *cis*-**8** together with *trans*-**8** (minor diastereoisomer), as a pale yellow oil (78 mg, 92%; *cis*/*trans* 4.9:1.0, *cis*: 29% de, *trans*: 33% de): the mixture of *cis*-**8** (diastereoisomeric mixture) and *trans*-**8** (minor diastereoisomer): δ_H(270 MHz, $CDCl_3$) 0.59 (d, *J* 6.5, *cis*-minor-CH_3), 0.60–1.87 (m, 8 H), 0.75 (d, *J* 6.3, *cis*-major-CH_3), 0.89 (d, *J* 6.4, *trans*-minor-CH_3), 0.95 [s, *cis*-major-C(CH_3)$_2$], 1.00 (s, *trans*-minor-2-CH_3), 1.07 [s, *cis*-major-C(CH_3)$_2$], 1.19 [s, *cis*-minor-C(CH_3)$_2$], 1.29 [s, *trans*-minor-C(CH_3)$_2$], 1.31 [s, *cis*-minor-C(CH_3)$_2$], 1.39 [s, *trans*-minor-C(CH_3)$_2$], 1.40 (s, *cis*-minor-2-CH_3), 1.52 (s, *cis*-major-2-CH_3), 3.93 (s, *cis*-minor-3-H), 3.95 (s, *cis*-major-3-H), 4.18 (s, *trans*-minor-3-H), 4.52 (dt, *J* 10.7, 4.4, *cis*-major-O–CH), 4.68 (dt, *J* 10.7, 4.4, *cis*-minor-O–CH), 4.91 (dt, *J* 16.1, 4.4, *trans*-minor-O–CH), 7.11–7.23 (m, 2 H) and 7.24–7.52 (m, 8 H); [Found (HRMS): M^+, 392.2350. $C_{26}H_{32}O_3$ requires *M*, 392.2351; *trans*-**8** (pure diastereoisomer): δ_H(270 MHz, $CDCl_3$) 0.81–1.70 (m, 6 H), 0.89 (d, *J* 6.4, CH_3, 3 H), 0.95 (s, 2-CH_3, 3 H), 1.25 [s, C(CH_3)$_2$, 3 H], 1.38 [s, C(CH_3)$_2$, 3 H], 1.87–1.92 (m, 1 H), 2.05–2.15 (m, 1 H), 4.01 (s, 3-H, 1 H), 5.04 (dt, *J* 10.6, 4.7, O–CH, 1 H) and 7.21–7.44 (m, 10 H) [Found (HRMS): M^+, 392.2342. $C_{26}H_{32}O_3$ requires *M*, 392.2351].

Methyl 3-methyl-3-phenyloxirane-2-carboxylate 9. The general procedure was followed using Bu^{t}OK (412 mg, 3.68 mmol), **1** (0.30 ml, 3.4 mmol) and acetophenone (0.6 ml, 5 mmol). Preparative TLC (silica gel, hexane–AcOEt, 15:1) of the crude product afforded *cis*- and *trans*-**9** [27] as a colourless oil (435 mg, 66%; *cis*/*trans*, 1.0:1.3): *cis*-**9**: δ_H(270 MHz, $CDCl_3$) 1.75 (s, 3 H), 3.45 (s, 3 H), 3.70 (s, 1 H) and 7.26–7.41 (m, 5 H); *m*/*z* (EI) 192 (M^+); *trans*-**9**: δ_H(270 MHz, $CDCl_3$) 1.77 (s, 3 H), 3.47 (s, 1 H), 3.84 (s, 3 H) and 7.26–7.39 (m, 5 H); *m*/*z* (EI) 192 (M^+).

Methyl 3-ethyl-3-phenyloxirane-2-carboxylate 10. The general procedure was followed using Bu^{t}OK (415 mg, 3.70 mmol), **1** (0.3 ml, 3.4 mmol) and propiophenone (0.07 ml, 5 mmol). Preparative TLC (silica gel, hexane–AcOEt, 13:1) of the crude product afforded *cis*-**10** and *trans*-**10** as a colourless oil (414 mg, 58%; *cis*/*trans*, 1.0:1.4). The ^{1}H NMR data of **10** were in accord with those in the literature: [28] *cis*-**10**: δ_H(270 MHz, $CDCl_3$) 0.93 (t, *J* 7.3, 3 H), 1.82 (dq, *J* 14.5, 7.3, 1 H), 2.18 (dq, *J* 14.5, 7.3, 1 H), 3.43 (s, 3 H), 3.71 (s, 1 H) and 7.25–7.38 (m, 5 H); *m*/*z* (EI) 206 (M^+); *trans*-**10**: δ_H(270 MHz, $CDCl_3$) 0.94 (t, *J* 7.3, 3 H), 1.88 (dq, *J* 14.3, 7.3, 1 H), 2.17 (dq, *J* 14.3, 7.3, 1 H), 3.48 (s, 1 H), 3.83 (s, 3 H) and 7.40–7.27 (m, 5 H); *m*/*z* (EI) 206 (M^+).

(−)-Menthyl 3-methyl-3-phenyloxirane-2-carboxylate 11. The general procedure was followed using Bu^{t}OK (325 mg, 2.82 mmol), **2a** (0.65 ml, 2.8 mmol) and acetophenone (0.4 ml, 3.4 mmol). Preparative TLC (silica gel, hexane–AcOEt, 15:1) of the crude product afforded *cis*-**11** and *trans*-**11** as a mixture of diastereoisomers, [29] in the form of a colourless oil (737 mg, 83%; *cis*/*trans*, 8.3:1.0; *cis*: 38% de, *trans*: <10% de): *cis*-**11** (diastereoisomeric mixture): δ_H(270 MHz, $CDCl_3$) 0.46 [d, *J* 6.8, major-CH(CH_3)$_2$], 0.53 [d, *J* 6.8, minor-CH(CH_3)$_2$], 0.64–1,01 (m, 3 H), 0.74 [d, *J* 6.8, minor-CH(CH_3)$_2$], 0.77 [d, *J* 6.8, major-CH(CH_3)$_2$], 0.77 (d, *J* 6.3, major-CH_3), 0.79 (d, *J* 6.3, minor-CH_3), 1.15–1.60 (m, 6 H), 1.73 (s, minor-3-CH_3), 1.76 (s, major-3-CH_3), 3.65 (s, major-2-H), 3.68 (s, minor-2-H), 4.47

(dt, *J* 10.7, 4.4, major-O–CH), 4.52 (dt, *J* 10.7, 4.4, minor-O–CH) and 7.22–7.41 (m, 5 H) [Found (HRMS): M^+, 316.2036. $C_{20}H_{28}O_3$ requires *M*, 316.2039]; *trans*-**11** (diastereoisomeric mixture): δ_H(270 MHz, $CDCl_3$) 0.77–2.05 (m, 21 H), 3.44 (s, minor-2-H), 3.45 (s, major-2-H), 4.84 (dt, *J* 10.7, 4.4, minor-O–CH), 4.87 (dt, *J* 10.7, 4.4, major-O–CH) and 7.24–7.38 (m, 5 H) [Found (HRMS) M^+, 316.2030. $C_{20}H_{28}O_3$ requires *M*, 316.2039].

(−)-8-Phenylmenthyl 3-methyl-3-phenyloxirane-2-carboxylate 12. The general procedure was followed using Bu′OK (74 mg, 0.66 mmol), **3a** (201 mg, 0.65 mmol) and acetophenone (0.15 ml, 1.3 mmol). Preparative TLC (silica gel, hexane–AcOEt, 8 : 1) of the crude product gave *cis*-**12** (major diastereoisomer), *trans*-**12** (major diastereoisomer) and *trans*-**12** (minor diastereoisomer) as the pure samples and all as colourless oils (201 mg, 79%; *cis*/*trans* 7.6 : 1.0, *cis*: 93% de, *trans*: 52% de). Use of **3b** (150 mg, 0.43 mmol) under the reaction conditions [Bu′OK (49 mg, 0.44 mmol) acetophenone (0.05 ml, 0.4 mmol)], gave *cis*- and *trans*-**12** as a mixture of diastereoisomers in the form of a colourless oil (94 mg, 56%, *cis*/*trans* 5.6 : 1.0, *cis*: >95% de, *trans*: 21% de): *cis*-**12** (major diasteroisomer): δ_H(270 MHz, $CDCl_3$) 0.30 (q, *J* 12.2, 1 H), 0.61–1.21 (m, 4 H), 0.67 (d, *J* 6.4, 3 H), 1.10 (s, 3 H), 1.25 (s, 3 H), 1.37–1.47 (m, 2 H), 1.67 (s, 3 H), 1.75–1.83 (m, 1 H), 3.31 (s, 1 H), 4.50 (dt, *J* 10.7, 4.4, 1 H) and 7.13–7.40 (m, 10 H); δ_C(68 MHz, $CDCl_3$) 21.4, 24.6, 25.6, 26.6, 27.4, 30.9, 34.2, 40.4, 50.1, 60.6, 63.2, 125.2, 125.5, 126.6, 127.7, 127.8, 127.9, 128.2, 137.1, 150.5 and 166.4 [Found (HRMS): M^+, 392.2371. $C_{26}H_{32}O_3$ requires *M*, 392.2351]; *trans*-**12** (major diastereoisomer): δ_H(270 MHz, $CDCl_3$) 0.30 (q, *J* 12.2, 1 H), 0.61–1.21 (m, 4 H), 0.67 (d, *J* 6.4, 3 H), 1.10 (s, 3 H), 1.25 (s, 3 H), 1.34–1.47 (m, 2 H), 1.67 (s, 3 H), 1.75–1.83 (m, 1 H), 3.31 (s, 1 H), 4.50 (dt, *J* 10.7, 4.4, 1 H) and 7.13–7.40 (m, 10 H); δ_C(68 MHz, $CDCl_3$) 17.3, 21.7, 26.0, 26.8, 27.3, 31.3, 34.4, 40.0, 41.7, 50.4, 61.5, 61.8, 76.3, 125.3, 125.4, 127.9, 128.0, 128.4, 140.3, 150.7 and 166.9 [Found (HRMS): M^+, 392.2335. $C_{26}H_{32}O_3$ requires *M*, 392.2351]; *trans*-**12** (minor diastereoisomer): δ_H(270 MHz, $CDCl_3$) 0.85–1.88 (m, 7 H), 0.89 (d, *J* 6.4, 3 H), 1.22 (s, 3 H), 1.34 (s, 3 H), 1.63 (s, 3 H), 2.02–2.11 (m, 1 H), 2.32 (s, 1 H), 4.96 (dt, *J* 10.7, 4.4, 1 H), 7.01–7.07 (m, 1 H) and 7.18–7.37 (m, 9 H) [Found: (HRMS): M^+, 392.2365. $C_{26}H_{32}O_3$ requires *M*, 392.2351.

(−)-8-Phenylmenthyl 3-ethyl-3-phenyloxirane-2-carboxylate 13. The general procedure was followed using Bu′OK (37 mg, 0.33 mmol), **3a** (101 mg, 0.33 mmol) and propiophenone (0.05 ml, 0.4 mmol). Preparative TLC (silica gel, hexane–AcOEt, 13 : 1) afforded *cis*-**13** and *trans*-**13** as a mixture of diastereoisomers in the form of a colourless oil (63 mg, 47%; *cis*/*trans* 4.5 : 1.0, *cis*: 87% de, *trans*: 78% de). Use of **3b** (94 mg, 0.26 mmol) under the reaction conditions [Bt′OK (33 mg, 0.30 mmol) and propiophenone (0.05 ml, 0.4 mmol)], gave *cis*- and *trans*-**13** as a mixture of diastereoisomers in the form of a colourless oil (46 mg, 43%; *cis*/*trans* 4.2 : 1.0, *cis*: >95% de, *trans*: >95% de): *cis*-**13** (diastereoisomeric mixture): δ_H(270 MHz,$CDCl_3$) 0.20 (q, *J* 12.5, 1 H), 0.58–1.45 (m, 6 H), 0.65 (d, *J* 6.4, 3 H), 0.88 (t, *J* 7.3, 3 H), 1.14 (s, 3 H), 1.28 (s, 3 H), 1.65–1.80 (m, 2 H), 2.17 (dq, *J* 14.7, 7.3, 1 H), 3.36 (s, 1 H), 4.49 (dt, *J* 10.6, 4.4, 1 H) and 7.13–7.37 (m, 10 H) [Found (HRMS): M^+, 406.2537. $C_{27}H_{34}O_3$ requires *M*, 406.2508]; *trans*-**13** (diastereoisomeric mixture): δ_H(270 MHz, $CDCl_3$) 0.77–1.56 (m, 6 H), 0.87 (d, *J* 6.4, 3 H), 0.95 (t, *J* 7.3, 3 H), 1.29 (s, 3 H), 1.39 (s, 3 H), 1.85–2.05 (m, 3 H), 2.17 (dq, *J* 14.2, 7.3, 1 H), 3.16 (s, 1 H), 4.89 (dt, *J* 14.2, 4.1, 1 H), 7.04–7.10 (m, 1 H) and 7.20–7.38 (m, 9 H) [Found (HRMS): M^+, 406.2537. $C_{27}H_{34}O_3$ requires *M*, 406.2508].

(−)-Menthyl 3,3-dimethyloxirane-2-carboxylate 14. The general procedure was followed using Bu′OK (34 mg, 0.31 mmol), **2a** (0.1 ml, 0.43 mmol) and acetone (0.05 ml, 0.7 mmol). Preparative TLC (silica gel, hexane–AcOEt, 13 : 1) afforded **14** as a mixture of diastereoisomers in the form of a colourless oil (30 mg, 39%, 14% de). For the major diastereoisomer, the ^1H NMR data of **14** were in accord with those of the literature:[3b] δ_H(270 MHz, $CDCl_3$) 0.75 (d, *J* 6.8, 3 H), 0.90 (d, *J* 6.8, 3 H), 0.91 (d, *J* 6.8, 3 H), 0.97–1.14 (m, 3 H), 1.36 (s, 3 H), 1.43 (s, 3 H), 1.44–1.54 (m, 2 H), 1.64–1.74 (m, 2 H), 1.81–1.94 (m, 1 H), 1.95–2.05 (m, 1 H), 3.32 (s, 1 H) and 4.83 (dt, *J* 11.2, 4.4, 1 H); for the minor diastereoisomer: δ_H(270 MHz, $CDCl_3$) 0.77 (d, *J* 6.8, 3 H), 0.91 (d, *J* 6.8, 3 H), 0.91 (d, *J* 6.8, 3 H), 0.94–1.14 (m, 3 H), 1.32–1.63 (m, 2 H), 1.38 (s, 3 H), 1.43 (s, 3 H), 1.64–1.73 (m, 2 H), 1.80–1.91 (m, 1 H), 1.92–2.05 (m, 1 H), 3.33 (s, 1 H) and 4.80 (dt, *J* 11.2, 4.4, 1 H).

(−)-8-Phenylmenthyl 3,3-dimethyloxirane-2-carboxylate 15. The general procedure was followed using Bu′OK (38 mg, 0.34 mmol), **3a** (101 mg, 0.33 mmol) and acetone (0.05 ml, 0.7 mmol). Preparative TLC (silica gel, hexane–AcOEt, 13 : 1) afforded **15** as a mixture of diastereoisomers in the form of a colourless oil (70 mg, 64%; 87% de): for the major diastereoisomer: δ_H(270 MHz, $CDCl_3$) 0.77–1.15 (m, 3 H), 0.87 (d, *J* 6.4, 3 H), 1.23 (s, 3 H), 1.31 (s, 3 H), 1.33 (s, 3 H), 1.37 (s, 3 H), 1.40–1.65 (m, 3 H), 1.92–2.00 (m, 1 H), 2.06 (ddd, *J* 12.2, 10.8, 3.4, 1 H), 2.84 (s, 1 H), 4.87 (dt, *J* 10.8, 4.4, 1 H), 7.12–7.29 (m, 5 H) [Found (HRMS): M^+, 330.2229. $C_{21}H_{30}O_3$ requires *M*, 330.2195].

(−)-8-Phenylmenthyl 3,3-dimethyloxirane-2-carboxylate 16. The general procedure was followed using Bu′OK (36 mg, 0.32 mmol), **3a** (99 mg, 0.32 mmol) and pentan-3-one (0.05 ml, 0.5 mmol). Preparative TLC (silica gel, hexane–AcOEt, 13 : 1) of the crude product afforded **16** as a mixture of diastereoisomers in the form of a colourless oil (54 mg, 47%; 81% de): for the major diastereoisomer; δ_H(270 MHz, $CDCl_3$) 0.73–1.09 (m, 3 H), 0.86 (d, *J* 6.8, 3 H), 0.89, (t, *J* 7.3, 3 H), 1.00 (t, *J* 7.3, 3 H), 1.25 (s, 3 H), 1.34 (s, 3 H), 1.39–1.75 (m, 3 H), 1.63 (q, *J* 7.3, 2 H), 1.67 (q, *J* 7.3, 2 H), 1.94–2.04 (m, 1 H), 2.01 (ddd, *J* 12.2, 10.7, 3.4, 1 H), 3.00 (s, 1 H), 4.87 (dt, *J* 10.7, 4.4, 1 H) and 7.12–7.29 (m, 5 H) [Found: M^+, 358.2531. $C_{21}H_{34}O_3$ requires *M*, 358.2508].

(−)-8-Phenylmenthyl spiro[cyclopentane-1,2′-oxirane]-3′-carboxylate 17. The general procedure was followed using Bu′OK (34 mg, 0.30 mmol), **3a** (91 mg, 0.29 mmol) and cyclopentanone (0.05 ml, 0.6 mmol). Preparative TLC (silica gel, hexane–AcOEt, 13 : 1) of the crude product afforded **17** as a mixture of diastereoisomers in the form of a colourless oil (49 mg, 45%; 80% de): for the major diastereoisomer: δ_H(270 MHz, $CDCl_3$) 0.77–1.14 (m, 3 H), 0.87 (d, *J* 6.3, 3 H), 1.23 (s, 3 H), 1.31 (s, 3 H), 1.40–2.00 (m, 4 H), 1.57–1.62 (m, 2 H), 1.62–1.66 (m, 2 H), 1.76–1.87 (m, 4 H), 2.05 (ddd, *J* 12.2, 10.7, 2.9, 1 H), 3.01 (s, 1 H), 4.86 (dt, *J* 12.2, 10.7, 4.4, 1 H) and 7.12–7.28 (m, 5 H) [Found (HRMS): M^+, 356.2346. $C_{23}H_{32}O_3$ requires *M*, 356.2352].

(−)-8-Phenylmenthyl spiro[cyclohexane-1,2′-oxirane]-3′-carboxylate 18. The general procedure was followed using Bu′OK (36 mg, 0.32 mmol), **3a** (93 mg, 0.30 mmol) and cyclohexanone (0.05 ml, 0.5 mmol). Preparative TLC (silica gel, hexane–AcOEt, 13 : 1) of the crude product afforded **18** as a mixture of diastereoisomers in the form of a colourless oil (50 mg, 45%; 96% de): for the major diastereoisomer: δ_H(270 MHz, $CDCl_3$) 0.74–1.10 (m, 3 H), 0.86 (d, *J* 6.8, 3 H), 1.24 (s, 3 H), 1.24–1.34 (m, 2 H), 1.34 (s, 3 H), 1.37–1.75 (m, 3 H), 1.52–1.57 (m, 2 H), 1.65–1.72 (m, 6 H), 1.93–2.02 (m, 1 H), 2.02 (ddd, *J* 12.2, 10.7, 3.4, 1 H), 2.96 (s, 1 H), 4.88 (dt, *J* 10.7, 4.4, 1 H) and 7.13–7.30 (m, 5 H); δ_C(68 MHz, $CDCl_3$) 21.5, 24.4, 24.6, 25.1, 25.6, 26.7, 27.4, 28.2, 31.1, 34.2, 34.7, 39.8, 41.4, 50.1, 59.2, 64.4, 75.8, 125.0, 125.2, 127.7, 150.5 and 167.3 [Found (HRMS): M^+, 370.2543. $C_{24}H_{34}O_3$ requires *M*, 370.2508].

(−)-8-Phenylmenthyl 3,3-dimethyloxirane-2-carboxylate 19. The general procedure was followed using Bu′OK (39 mg, 0.35 mmol), **3a** (107 mg, 0.35 mmol) and benzophenone (92 mg, 0.50 mmol). Preparative TLC (silica gel, hexane–AcOEt, 13 : 1) of the crude product afforded **19** as a mixture of diastereoisomers in the form of a colourless oil (71 mg, 45%; 77% de): for the major diastereoisomer: δ_H(270 MHz, $CDCl_3$) 0.28 (q, *J* 12.2,

1 H), 0.56–0.98 (m, 2 H), 0.69 (d, *J* 6.3, 3 H), 1.17 (s, 3 H), 1.18–1.52 (m, 4 H), 1.33 (s, 3 H), 1.80 (ddd, *J* 12.2, 10.7, 3.4, 1 H), 3.65 (s, 1 H), 4.60 (dt, *J* 10.7, 3.9, 1 H), 7.07–7.26 (m, 5 H), 7.28–7.31 (m, 5 H) and 7.46–7.52 (m, 5 H) [Found (HRMS): M^+, 454.2531. $C_{31}H_{34}O_3$ requires *M*, 454.2508].

(−)-8-Phenylmenthyl 3′-methylspiro[cyclohexane-1,2′-oxirane]-3′-carboxylate 20. The general procedure was followed using Bu′OK (68 mg, 0.60 mmol), **4** (103 mg, 0.28 mmol) and cyclohexanone (33 mg, 0.34 mmol). Preparative TLC (silica gel, hexane–AcOEt, 13 : 1) of the crude product afforded a mixture of 2*R*- and 2*S*-**20** as a colourless oil (7 mg, 18%; 36% de): δ_H(270 MHz, $CDCl_3$) 0.84–2.09 (m, 30 H), 4.84 (dt, *J* 10.7, 4.4, major-O–CH), 4.98 (dt, *J* 10.7, 4.4, minor-O–CH), 7.15–7.20 (m, 1 H) and 7.26–7.31 (m, 4 H) [Found (HRMS): M^+, 384.2662. $C_{25}H_{36}O_3$ requires *M*, 384.2664].

(−)-8-Phenylmenthyl 1,3-diphenylaziridine-2-carboxylate 21. The general procedure for the Darzens reaction was followed using Bu′OK (86 mg, 0.77 mmol), **2a** (101 mg, 0.33 mmol) and *N*-benzylideneaniline (85 mg, 0.47 mmol). Preparative TLC (silica gel, hexane–AcOEt, 13 : 1) afforded *cis*-**21** (major diastereoisomer) and a mixture of *cis*-**21** (minor diastereoisomer) together with *trans*-**21** (diastereoisomeric mixture) (57 mg, 38%, *cis*/*trans* 1.5 : 1.0; *cis*: 41% de, *trans*: >85% de): *cis*-**21** (pure diastereoisomer): δ_H(270 MHz, $CDCl_3$) 0.41–0.54 (m, 1 H), 0.67 (d, *J* 6.3, CH_3, 3 H), 0.73–0.92 (m, 2 H), 0.97–1.13 (m, 1 H), 1.14–1.31 (m, 1 H), 1.20 [s, $C(CH_3)_2$, 3 H], 1.34 [s, $C(CH_3)_2$, 3 H], 1.54–1.62 (m, 1 H), 1.67–1.78 (m, 1 H), 1.92–2.02 (m, 1 H), 2.34 (d, *J* 7.1, 3-H, 1 H), 3.33 (d, *J* 7.1, 2-H, 1 H), 4.71 (dt, *J* 10.8, 4.7, O–CH, 1 H), 6.95–7.15 (m, 3 H) and 7.21–7.42 (m, 12 H) [Found (HRMS): MH^+, 454.2697. $C_{31}H_{36}O_2N$ requires *M*H, 454.2746]; *trans*-**21** (diastereoisomeric mixture) and *cis*-**21** (minor diastereoisomer): δ_H(270 MHz, $CDCl_3$) 0.59–2.16 (m, 17 H), 2.15 (d, *J* 2.7, *trans*-major-3-H), 2.75 (d, *J* 2.4, *trans*-minor-3-H), 2.90 (d, *J* 6.5, *cis*-minor-3-H), 3.53 (d, *J* 6.5, *cis*-minor-2-H), 3.55 (d, *J* 2.4, *trans*-minor-2-H), 3.61 (d, *J* 2.7, *trans*-major-2-H), 4.61 (dt, *J* 10.8, 4.4, *trans*-minor-O–CH), 4.78 (dt, *J* 10.7, 4.4, *trans*-major-O–CH), 4.82 (dt, *J* 10.8, 4.7, *cis*-minor-O–CH) and 6.64–7.31 (m, 15 H) [Found (HRMS): MH^+, 454.2757. $C_{31}H_{36}O_2N$ requires *M*H, 454.2746].

3-Phenylbutane-1,3-diol 22. To a suspension of $LiAlH_4$ (80 mg, 2.1 mmol) in THF (4 ml) at 0 °C was slowly added a solution of *cis*-**12** (105 mg, 0.27 mmol). The reaction mixture was stirred at 0 °C for 5 h and then warmed to 25 °C. After 17 h, the mixture was cooled to 0 °C and diluted with ether (30 ml) and water (1 ml) added carefully. The resulting precipitate was filtered off and washed with Et_2O. The combined filtrate and washings were washed with water, dried (Na_2SO_4) and evaporated. The crude product was purified with preparative TLC (silica gel, hexane–AcOEt, 10 : 3) to afford **22** as a colourless oil {34 mg, 76%, $[\alpha]_D^{25}$ −65.8 (*c* 0.137, benzene)} {lit.,[16] (+)-(3*R*)-**22**: $[\alpha]_D^{25}$ +66.7 (maximum, benzene)}; δ_H(270 MHz, $CDCl_3$) 1.57 (s, 3 H), 2.00 (ddd, *J* 14.7, 5.3, 3.9, 1 H), 2.10 (ddd, *J* 14.7, 8.6, 4.4, 1 H), 2.85 (br s, 1 H), 3.60–3.44 (m, 1 H), 3.80 (br s, 1 H), 3.80–3.64 (m, 1 H), 7.27–7.20 (m, 1 H), 7.37–7.31 (m, 2 H) and 7.44–7.40 (m, 2 H) [Found (HRMS): M^+, 166.1010. $C_{10}H_{14}O_2$ requires *M*, 166.0994].

(−)-8-Phenylmenthyl α-(Cyclohex-1-enyl)-α-hydroxyacetate 23. A mixture of **18** (317 mg, 0.855 mmol) and MS 4 Å (5.6 g) in benzene was refluxed for 12 h after which it was cooled and filtered. The precipitate was washed with CH_2Cl_2 and the combined filtrate and washings were evaporated. Preparative TLC (silica gel, hexane–AcOEt, 9 : 1) of the crude product afforded **23** (166 mg, 52%); δ_H(270 MHz, $CDCl_3$) 0.80–1.10 (m, 3 H), 0.87 (d, *J* 6.8, 3 H), 1.22 (s, 3 H), 1.31 (s, 3 H), 1.41–1.75 (m, 8 H), 1.94–2.08 (m, 5 H), 4.20 (d, *J* 3.4, 1 H), 4.88 (dt, *J* 10.7, 4.4, 1 H), 5.75–5.80 (m, 1 H), 7.16–7.22 (m, 1 H) and 7.24–7.35 (m, 4 H); δ_C(68 MHz, $CDCl_3$) 21.6, 21.9, 22.1, 23.4, 25.0, 25.8, 26.9, 27.2, 31.3, 34.3, 39.8, 41.4, 50.2, 76.3, 76.7, 125.2, 125.4, 128.0, 128.2, 134.1, 151.0 and 172.1 [Found (HRMS): M^+, 370.2550. $C_{24}H_{34}O_3$ requires *M*, 370.2508].

1-(Cyclohex-1-enyl)-ethane-1,2-diol 24. A solution of **23** (303 mg, 0.82 mmol) in THF (4 ml) was added at 0 °C to a suspension of $LiAlH_4$ (552 mg, 14.6 mmol) in THF (5 ml). The reaction mixture was stirred at 25 °C for 12 h, after which it was cooled to 0 °C, and carefully diluted with water. The resulting precipitate was filtered off and washed with CH_2Cl_2. The combined organic layer and washings were dried ($MgSO_4$) and evaporated. Preparative TLC (silica gel, hexane–AcOEt, 2 : 1) of the crude product afforded the diol **24** along with (−)-8-phenylmenthol (153 mg, 85%). A pure sample of **12** was obtained by recycling-HPLC (JAIGEL-1H and 2H, $CHCl_3$) as colourless crystals (15 mg, 13%) {$[\alpha]_D^{25}$ −27.0 (*c* 0.196, $CHCl_3$) [lit.,[17] (1*R*)-**24**: $[\alpha]_D^{25}$ −28.1]}; δ_H(270 MHz, $CDCl_3$) 1.54–1.83 (m, 4 H), 1.84–1.93 (m, 2 H), 1.94–2.11 (m, 4 H), 3.53–3.81 (m, 2 H), 4.05–4.15 (m, 1 H) and 5.75–5.85 (m, 1 H); δ_C(68 MHz, $CDCl_3$) 22.4, 22.5, 24.8, 24.9, 63.4, 76.2, 124.0 and 136.7; [Found (HRMS): M^+, 142.0994. $C_8H_{14}O_2$ requires *M*, 142.0994].

Acknowledgements

We are indebted to the Instrument Center for Chemical Analysis, Hiroshima University for measurements of NMR, MS and optical rotation measurements using JEOL GSX-270, JEOL SX-102A and JASCO DIP-360 instruments, respectively.

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Paper 7/07310K
Received 9*th October* 1997
Accepted 18*th November* 1997