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Tetrahedron 62 (2006) 3600–3609
Tetrahedron

Peracid dependent stereoselectivity and functional group contribution to the stereocontrol of epoxidation of (*E*)-alkene dipeptide isosteres

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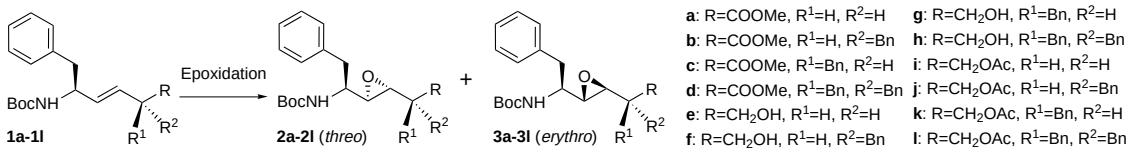
Received 19 October 2005; revised 9 January 2006; accepted 26 January 2006

Abstract—Twelve *Boc*-protected phenylalanyl-phenylalanine and phenylalanyl-glycine *trans*-vinyl isosteres were epoxidised with magnesium monoperoxyphtalate hexahydrate (MMPP) and trifluoroperacetic acid, and the results have been compared with those from earlier studies on epoxidations with *m*-CPBA. The alkenes were synthesised in high yields with high *E*/*Z*-selectivities using either the Julia or Schlosser reactions. The formation of *threo* isomers was favoured in all epoxidation reactions except with CF_3CO_3H on substrates containing two allylic/homoallylic functional groups directing the peracid to opposite faces of the alkene. The switch to *erythro* selectivity observed with CF_3CO_3H is suggested to emanate from coordination to the allylic ester functionalities via hydrogen bond donation from the peracid. The other peracid reagents seem to be preferentially coordinated to the allylic carbamate function. The contribution of individual functional groups to the stereopreference was also investigated.

1. Introduction

Stereoselective epoxidation reactions have been studied experimentally[1,2] and theoretically[3] to a great extent over the years. Peracids are still commonly used, although several novel epoxidation reagents have been developed.[4] However, these new, usually metal-based reagents, have mainly been studied using simpler mono- or non-functionalised alkenes. In a project aimed at the synthesis and use of functionalised dipeptidomimetics we have for some time studied the stereoselective epoxidation of structurally more complex alkenes. In these studies, *Boc*-protected phenylalanyl-phenylalanine (Phe-Phe) and phenylalanyl-glycine (Phe-Gly) derived epoxides (**2a–l**, **3a–l**) were synthesised by *m*-CPBA treatment of the Phe-Phe and Phe-Gly vinyl isosteres **1a–l**, possessing two stereogenic centres and different oxygen containing functional groups at the C-terminus of the pseudo-dipeptide (Scheme 1).[5] The reactions are highly stereoselective with the formation of *threo* isomers being favoured.



Scheme 1.

Keywords: Epoxidation; Peracid; Dipeptidomimetics; Stereoselectivity; Allylic functional group; Coordination.
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0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2006.01.095

The stereoselectivity has been suggested to originate from cooperative coordination of *m*-CPBA to the allylic carbamate and a suitably positioned ester or alcohol group.[6–8]

In a preliminary study on epoxidation of six Phe-Phe vinyl isosteres, we used trifluoroperacetic acid (generated from urea hydrogen peroxide (UHP) and trifluoroacetic anhydride) as oxidant in addition to *m*-CPBA.[9] It was found that the stereoselectivity was strongly dependent on the choice of peracid and the functionalities flanking the alkene, presumably by formation of different hydrogen bonding patterns between the peracid and the alkenes. Differences in stereoselectivity between the two peracids have been reported with cyclic alkenes containing one directing functional group.[10] To gain further understanding of these phenomena, we have made a more extensive study including more alkene substrates, and also added monoperoxyphthalate hexahydrate (MMPP), a peracid presumed to possess different hydrogen bonding properties compared to *m*-CPBA and trifluoroperacetic acid. A new method for the synthesis of β,γ-unsaturated esters based on the Schlosser reaction is also disclosed.

2. Results and discussion

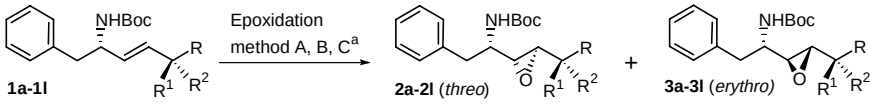
2.1. Peracid epoxidation

2.1.1. Epoxidation of 1a–h and 1k with MMPP. MMPP has been suggested as a replacement for *m*-CPBA in epoxidations and other oxidation reactions. MMPP has similar chemical properties to *m*-CPBA but it is considered safer to use in both small- and large-scale reactions.[11] We expected that MMPP might exhibit different hydrogen bonding properties to *m*-CPBA due to the additional *ortho*-positioned carboxylate. Compounds **1a–h** and **1k** were treated with MMPP in a two-phase system consisting of chloroform and water at room temperature in the presence of methyltrioctylammonium chloride as phase-transfer catalyst. Throughout, the epoxidation reactions with MMPP were much slower than those using *m*-CPBA, the alcohol derivatives **1e–h** being the most reactive (Table 1, entries 5–8). Epoxidation of methyl ester **1a** with MMPP proceeded in only ca. 50% yield even after extensively prolonged reaction times (17 days). No products were observed in epoxidation of **1b–d** and acetate **1k** after 7 days. The rate of MMPP epoxidations has been proposed to increase after addition of pyridine to the reaction medium.[11] However, in our hands, the reactions became more sluggish in the presence of catalytic amounts (0.1 equiv) of either pyridine or 4-dimethylaminopyridine or when using pyridine as the solvent. Due to the low rates of reaction of the ester derivatives, we did not consider it practical to perform the epoxidations on any other acetate derivative in the series.

The *threo*/*erythro* ratios of products in the MMPP epoxidations were about the same as those in reactions using *m*-CPBA (Table 1). Thus, the results indicate that the phthalic acid motif itself does not contribute to a change in the reagent–substrate hydrogen bonding interaction compared to *m*-CPBA. Consequently, the diastereoselectivity of the MMPP epoxidations may be rationalised by assuming the same influence of cooperative coordination as in the reactions with *m*-CPBA. This coordination may also explain the increased reactivity of the alcohols (**1e–h**) compared to the esters since additional hydrogen bonding between the substrate and the peracid should lead to an increased stability of the transition state.

2.1.2. Epoxidation of 1a–l with trifluoroperacetic acid. Trifluoroperacetic acid[11] can be generated in situ from urea-hydrogen peroxide (UHP) and trifluoroacetic anhydride. Substrates **1a–l** were epoxidised at 0 °C using a mixture of UHP, trifluoroacetic anhydride, and Na_2HPO_4 in CH_2Cl_2. Throughout, the trifluoroperacetic acid epoxidations were faster than the reactions with *m*-CPBA.

Table 1. Reaction conditions, yields and stereochemical results from epoxidations of the olefinic substrates **1a–l**[a]



Entry	Substrate	R	R_1	R_2	Ratio **2**:**3** (*threo*:*erythro*)[b]			Isolated yield (%)			Reaction time (h)		
					A	B[c]	C	A	B[c]	C	A	B[c]	C
1	**1a**	COOMe	H	H	88:12	89:11	84:16	46[d]	81	79	408	48	0.5
2	**1b**	COOMe	H	Bn	[e]	62:38	37:63	0[e]	80	75	168	44	0.5
3	**1c**	COOMe	Bn	H	[e]	91:9	87:13	0[e]	77	81	168	40	0.5
4	**1d**	COOMe	Bn	Bn	[e]	88:12	87:13	0[e]	90	86	168	24	0.5
5	**1e**	CH_2OH	H	H	79:21	88:12	85:15	57	68	78	24	12	0.5
6	**1f**	CH_2OH	H	Bn	63:37	60:40	48:52	71	89	63	26	6	0.5
7	**1g**	CH_2OH	Bn	H	88:12	87:13	88:12	76	89	82	30	5	0.5
8	**1h**	CH_2OH	Bn	Bn	64:36	76:24	78:22	70	94	76	24	5	0.5
9	**1i**	CH_2OAc	H	H		83:17	82:18		87	53		12	0.5
10	**1j**	CH_2OAc	H	Bn		68:32	36:64		84	71		45	0.5
11	**1k**	CH_2OAc	Bn	H	[e]	86:14	76:24	0[e]	80	81	168	24	0.5
12	**1l**	CH_2OAc	Bn	Bn		79:21	61:39		84	67		48	0.5

[a] A: MMPP, $(C_8H_{17})_3NMeCl$, $CHCl_3/H_2O$, rt; B: *m*-CPBA, CH_2Cl_2, rt; C: CF_3CO_3H, CH_2Cl_2, 0 °C.
[b] The relative ratios of epoxide isomers were determined by HPLC and NMR spectroscopy of the crude reaction product.
[c] Data on *m*-CPBA epoxidations are taken from Ref. 5c.
[d] 54% starting material was recovered after 408 h.
[e] No products were obtained even after long reaction times.

Most substrates followed the general trend affording mainly *threo* epoxide isomers in yields comparable to those obtained with *m*-CPBA, but a somewhat lower diastereoselectivity was obtained (Table 1). Interestingly, two substrates (methyl ester **1b** and acetate **1j**) afforded preferentially *erythro* products with *threo*/*erythro* diastereomeric ratios of 37:63, and 36:64, respectively. In contrast, *m*-CPBA epoxidation of **1b** and **1j** produced epoxides in a diastereomeric ratio of 62:38, and 68:32, respectively (Table 1, entries 2 and 10). In the trifluoroperacetic acid epoxidation reaction of the alcohol derivative **1f**, which has the same absolute configuration at the stereogenic centres as the ester derivatives **1b** and **1j**, stereoselectivity was essentially lost; however, the difference in *threo*/*erythro* ratio from that obtained with *m*-CPBA was small (Table 1, entry 6).

By-products were formed if the reaction time was prolonged. An isomeric mixture of by-products from the epoxidation reaction of **1b** with trifluoroperacetic acid was separated by column chromatography and the structures of the isomers were determined by NMR spectroscopy to be oxazolidinone derivatives **4a** and **4b**,[12] probably formed via an intramolecular ring opening of the corresponding epoxides by the carbamate carbonyl oxygen. The epoxide ring opening is probably catalysed by trifluoroacetic acid generated in the epoxidation reaction. The minor oxazolidinone isomer (**4b**) was analysed by X-ray crystallography,[13] which established the stereochemistry at C-4 and C-5 (Fig. 1). The 4*S*,5*S* stereochemistry also established that **4b** was formed from the *threo* epoxide isomer **1b**. Both the *threo* and *erythro* epoxides can undergo the cyclisation/ring opening reaction to form oxazolidinones, but the reaction rate of the *erythro* isomer seems to be considerably higher than that of the *threo* isomer since a change in the *threo*/*erythro* ratio of epoxides was observed over time. Epoxidation of **1b** gave after 30 min a *threo*/*erythro* ratio of 2:3, which changed to 2:1 after 120 min. This is probably due to formation of by-products preferentially from the *erythro* isomer. A decrease of the temperature in the trifluoroperacetic acid epoxidation suppressed the by-product formation, that is, epoxidation of **1f** produced 10–20% of by-products at 0 °C but no by-products were observed when the reaction was run at −78 °C.

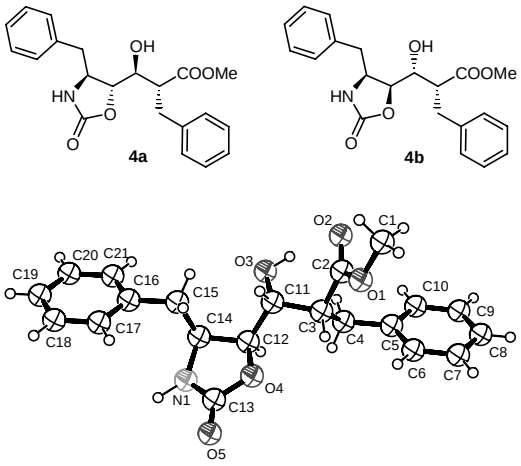


Figure 1. Perspective ORTEP view of the crystal structure of **4b** (CCDC no. 102769),[13] showing 50% probability displacement ellipsoids. Hydrogens are included to clarify the absolute configuration of chiral atoms.

The observed change of stereoselectivity for **1b** and **1j** indicates that the *threo* directing effect of the allylic carbamate is weaker with trifluoroperacetic acid and that the directing effect from the ester group is dominating. To gain further information on the directing role of each functionality, compounds **8a–e** having only one directing functional group, were synthesised and epoxidised.

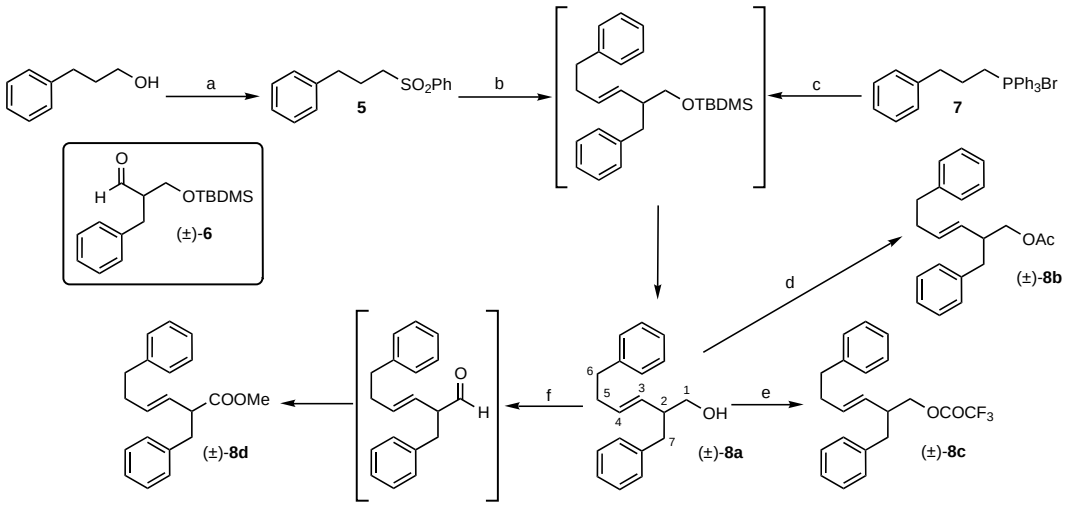
2.2. Directing effect contribution of allylic functional groups to the stereoselectivity of *m*-CPBA and trifluoroperacetic acid in epoxidation reactions

2.2.1. Synthesis of the alkenes 8a–e. To investigate the relative influence of the different functional groups on the stereoselectivity, analogues of **1** with only one functionality were synthesised and epoxidised. In previous studies,[5a,b] we have relied on the Julia olefination reaction[14] as a reliable method for the construction of (*E*)-alkene peptide isosteres (i.e., **1**). The reaction has good *E*-selectivity, whilst preserving the stereochemistry at C-5. The method was suitable also for the synthesis of the alkenes **8a–d** (Scheme 2) and the allylic carbamate **8e** (Table 2) as described previously.[5c] The anion of sulfone **5** and DIBAL·OMe-activated aldehyde **6**[5b] were reacted followed by desulfonylation and deprotection to give the *E*/*Z*-isomers of allylic alcohol **8a** in a ratio of 88:12 and 33% total yield.

The Julia reaction has some disadvantages as the procedure is laborious, and desulfonylation is accomplished using sodium amalgam. To avoid the hazardous handling of molten sodium and mercury, an alternative phosphorous ylide based strategy for forming the double bond from similar components was investigated. A standard Wittig reaction between the ylide generated from deprotonation of phosphonium salt **7**[15] with *n*-butyllithium and aldehyde **6** (Scheme 2) was expected[16] to give predominantly the *Z*-isomer of **8a** which was indeed found to be the case, the resulting *E*/*Z*-ratio was 12:88. An increased reaction temperature may sometimes give higher *E*-selectivity in the Wittig reaction;[16] performing the reaction at 0 °C resulted in a slightly higher yield of (*E*)-**8a** (*E*/*Z* 22:78).

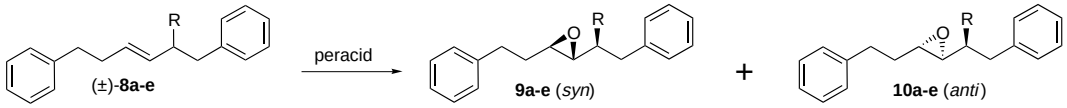
To gain further *E*-selectivity, the Schlosser modification[16] of the Wittig reaction was tried (Scheme 2). Deprotonation of **7** with *n*-butyllithium at −78 °C and addition of aldehyde **6**, was followed by a second equivalent of *n*-butyllithium at −41 °C and the β-oxido ylide was protonated with *tert*-butanol. No improvement of the *E*-selectivity was found, the *E*/*Z*-ratio was 19:81. Attempts to further optimise the reaction by trying different temperatures were made, but it was not until the base was changed to phenyllithium that any change in selectivity was found, the *E*/*Z*-ratio was essentially reversed to 87:13 and the alcohol **8a** was obtained in 61% total yield (Scheme 2). An explanation of the dependence of *E*-selectivity on the choice of alkyllithium was presented by Schlosser and co-workers during the course of this study.[17]

Alcohol **8a** was further transformed into acetate **8b** and trifluoroacetate **8c** by treatment with acetic anhydride and trifluoroacetic anhydride, respectively (Scheme 2). Methyl ester **8d** was prepared by oxidation of **8a** in two steps, first with the Dess–Martin periodinane to the corresponding



Scheme 2. Reagents, reaction conditions and yields: (a) (1) MsCl, Et_3N, CH_2Cl_2, 0 °C; (2) PhSH, NaOMe, THF/MeOH, rt; (3) *m*-CPBA, CH_2Cl_2, 0 °C–rt (73% over three steps). (b) (1) (i) *n*-BuLi, THF, −78 °C; (ii) **6**·DIBAL·OMe; (2) Na(Hg), Na_2HPO_4, MeOH, 0 °C; (3) HF, ACN, rt (33% over three steps, *E*/*Z* 88:12). (c) (1) (i) PhLi, THF, −60 °C; (ii) **6**, −60 to −41 °C; (iii) PhLi; (iv) MeOH; (v) *t*-BuOK −41 °C–rt; (2) TBAF, THF, rt (61% over two steps, *E*/*Z* 87:13). (d) Ac_2O, DMAP, Et_3N, rt (94%). (e) $(CF_3CO)_2O$, Et_3N, CH_2Cl_2, rt (81%). (f) (1) Dess–Martin periodinane, ACN/CH_2Cl_2, 0 °C–rt; (2) PDC, MeOH, DMF, rt (40% over two steps).

Table 2. Reaction conditions[a] and results of epoxidation of alkenes **8a–e** with *m*-CPBA and CF_3CO_3H



Entry	Substrate	R	Ratio **9**:**10** (*syn*/*anti*)[b]		Isolated yield (%)		Reaction time (h)	
			m-CPBA	CF_3CO_3H	*m*-CPBA	CF_3CO_3H	*m*-CPBA	CF_3CO_3H
1	(±)-**8a**	CH_2OH	71:29	72:28	93	74	2	0.5
2	(±)-**8b**	CH_2OAc	60:40	69:31	82	68	5	2
3	(±)-**8c**	CH_2OCOCF_3	63:37	64:36	82[c]	88[c]	15	5
4	(±)-**8d**	COOMe	67:33	79:21	86	80	24	4
5	(±)-**8e**	NHBoc	76:24[d]	66:33[e]	80	79	29	0.5

[a] Reactions with *m*-CPBA were performed at room temperature and reactions with CF_3CO_3H at 0 °C.
[b] Determined by HPLC and NMR of the crude reaction product.
[c] The yields refer to the crude product.
[d] Data taken from Ref. 5c.
[e] The reaction was run at −78 °C since the *anti* isomer was unstable at 0 °C.

aldehyde (oxidation with PCC gave substantial decomposition of the product), which was reacted with PDC and methanol[18] to form the unstable β,γ-unsaturated ester **8d**. Formation of the corresponding carboxylic acid had to be avoided since it was found to decompose immediately by decarboxylation.

2.2.2. Epoxidation of the alkenes 10a–e. The alkenes **8a–e** were reacted with trifluoroperacetic acid and *m*-CPBA to give diastereomeric mixtures of epoxides **9a–e** (*syn*) and **10a–e** (*anti*). The results are listed in Table 2. The stereochemical assignment of epoxides **9** and **10** was based on NMR-data. Consistent chemical shift differences between signals of the epoxide isomers observed in earlier studies[5b,c] was used also in the assignments of **9** and **10**. Diagnostic NMR spectral data of epoxide **9a–b** and **10a–b** are given in Table 3 and NMR data used for identification of epoxides **9d** and **10d** are given in Table 4. Epoxides **9c** and **10c** were identified by chemical correlation with **9a** and **10a** via methanolysis.

We observed that the epoxidations of **8b–d** using trifluoroperacetic acid were more *syn*-stereoselective than when using *m*-CPBA (Table 2, entries 2–4), which is in accord with an earlier report.[10] However, the *syn*-directing effect of the allylic carbamate group in **8e** was significantly decreased in the trifluoroperacetic acid epoxidation (Table 2, entry 5). No significant difference in stereoselectivity between the peracid in epoxidation of alcohol **8a** was found (Table 2, entry 1). These results again suggest that the two peracids have different preferences of coordination to different functional groups. Apparently, trifluoroperacetic acid coordinates more favourably to the methyl ester than to the allylic carbamate, alcohol, and acetate moieties. In contrast, *m*-CPBA coordinates better to the allylic carbamate than to the alcohol or ester functions. This is in line with the results found in our previous study of epoxidations of derivatives of **1f** in which the functional groups direct the peracid to different faces of the alkene.[9]

Table 3. Selected ^{1}H and ^{13}C NMR shifts (in ppm) for assignment of the relative stereochemistry of epoxides **9a**, **10a**, **9b** and **10b**[a,b]

Compound	Rel. stereochem.	H-1	H-4	C-1	C-7
2f	*syn*	3.67	2.63	63.06	32.94
3f	*anti*	3.46	2.98	62.43	34.92
2g	*syn*	3.67	2.56	63.50	34.22
3g	*anti*	3.54	3.07	62.66	35.34
9a	*syn*	3.71	2.56	64.11	31.73
10a	*anti*	3.45	2.96	62.50	34.69
2j	*syn*	4.11	2.48	64.49	34.52
3j	*anti*	3.90	2.85	63.56	34.92
2k	*syn*	4.12	2.72	64.78	34.81
3k	*anti*	3.95	2.77	63.83	35.13
9b	*syn*	4.15	2.45	64.82	34.89
10b	*anti*	3.97	2.85	63.78	34.99

[a] Data for compounds **2f**,**g**,**j**,**k** and **3f**,**g**,**j**,**k** are from Ref. 5b and c.
[b] See Scheme 2 for atom numbering. For compounds **2f**, **g**,**j**,**k** and **3f**,**g**,**j**,**k** this implies the corresponding atoms.

Table 4. Selected ^{1}H NMR shifts (in ppm) for assignment of the relative stereochemistry of epoxides **9d** and **10d**[a,b]

Compound	Rel. stereochem.	H-5
9a	*syn*	1.63–1.76
10a	*anti*	1.78–1.99
9b	*syn*	1.60–1.71
10b	*anti*	1.77–1.89
9d	*syn*	1.63–1.72
10d	*anti*	1.82–1.90
9e	*syn*	1.67–1.75
10e	*anti*	1.68–1.83

[a] Data for compounds **9e** and **10e** are from Ref. 5c
[b] See Scheme 2 for atom numbering.

Obviously, there are several factors that control the face selectivity in peracid epoxidation of acyclic alkenes with directing groups, of which the most important are; (i) the conformational preferences in the transition state, (ii) the directing effect, which is due to hydrogen bonding between the coordinating functionality and the peracid. The steric preferences in the transition state have been a matter of discussion. Extensive theoretical work on 1,2 asymmetric induction[19] and empirical studies on epoxidation of cyclic allylic alcohols[8c,20] support a staggered model (Fig. 2), but a model where the hydrogen is eclipsed with the double bond (Fig. 2) has also been used, and possibly there are different transition states depending on the substitution pattern of the alkene.[6c,21] The interpretation of our results is not affected by choice of model. Regarding the directing effect, the hydrogen bond donor–acceptor capability of the reactants, and the distance between the alkene and the coordinating group should influence the stereoselectivity.

The mode of hydrogen bonding between the peracid and the coordinating group can influence the stereoselectivity in the peracid epoxidations. For allylic alcohols it is believed that the face selectivity is due to hydrogen bonding from OH to O-3 in the peracid (A, Fig. 2).[22] Similarly, allylic carbamates can direct the peracid via hydrogen bonding from NH to O-3 in the peracid (B, Fig. 2).[5b,8d] However, there is also evidence for a directing effect via reverse hydrogen bonding, that is, the peracid is donating a hydrogen bond to the carbonyl oxygen of the carbamate group. This was proposed by Kočovský and Starý who showed that an allylic carbamate group with a disubstituted

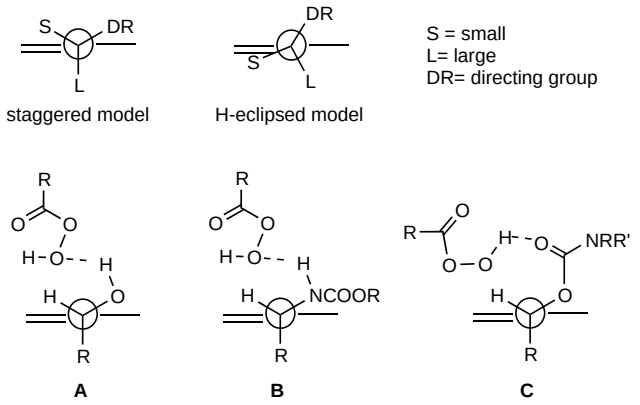
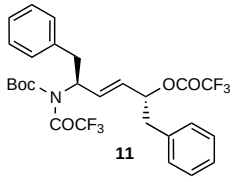


Figure 2. Top: proposed transition state models for epoxidation of alkenes by peracids. Bottom: different modes of hydrogen bonding interactions of peracids with allylic functional groups.

nitrogen atom also gives a strong *syn* direction (C, Fig. 2).[8d] Analogously, de Sousa et al. found evidence that homoallylic silyl ethers are moderate *syn*-directors by reverse hydrogen bonding.[23] A similar observation has been made by us when alkene **11** was treated with trifluoroperacetic acid.[9] The trifluoroacetylated carbamate is a hydrogen bond acceptor, and the directing carbonyl group appears to be more basic than that of the trifluoroacetate, resulting in epoxide products with a *threo*/*erythro* ratio of 81:19. Hence, reverse hydrogen bonding may well explain the directing effects of the acetate and methyl ester functions in the present study.



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The acidity of the peracid should influence the direction of the hydrogen bonding; the more acidic the peracid the stronger the hydrogen bond donating capability. Thus, trifluoroperacetic acid ($pK_a = 3.7$) is more prone to coordinate to different functional groups through hydrogen bond donation than *m*-CPBA ($pK_a = 7.57$). This hypothesis is supported by the current study in that the acetate function in **8b** directs trifluoroperacetic acid more strongly than *m*-CPBA to the *syn* face of the alkene (Table 2), and that the acetate is a better hydrogen bond acceptor than the trifluoroacetate of **8c**, for which no significant difference between the peracids was found.

3. Conclusions

Suitable reaction conditions for efficient synthesis of β,γ-unsaturated esters using the *E*-selective Schlosser reaction were identified. Careful monitoring of the temperature and the use of phenyllithium as the base allowed the production of *E*-alkenes in high yield and high *E*/*Z*-selectivity. The peracid epoxidation of the synthesised *E*-alkene dipeptidomimetics was highly stereoselective, and the formation of the *threo*-isomers was favoured in most reactions. The results strongly suggest a powerful directing effect from the

carbamate function, which is difficult to overcome by changing the peracid or the reaction conditions. However, the second functional group also exhibited strong directing effects. Employing trifluoroperacetic acid as the epoxidation reagent we obtained a reversed stereoselectivity in the epoxidation of two vinylic dipeptide isosteres (**1b** and **1j**). This change in stereodirection probably emanates from a stronger coordination of the peracid to the ester function than to the carbamate moiety. The ester functionality in **1b** and **1j** would direct the epoxidation to the *erythro* face of the alkene. This change of directing properties is supposed to be due to differences in peracid acidity and thereby differences in hydrogen bond donating capacity.

4. Experimental

4.1. General methods

Melting points were determined with a Tomas–Hoover apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer 241 polarimeter at ambient temperature. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-EX270 spectrometer at 270 and 68 MHz, respectively, or a JEOL Eclipse 400 spectrometer at 400 and 100 MHz, respectively, in $CDCl_3$. Chemical shifts are reported in ppm with the solvent residual peak as internal standard ($CHCl_3$ δ^{H} 7.26, $CDCl_3$ δ^{C} 77.0). 2D COSY, HMQC and HMBC NMR spectroscopy was used to validate structural assignment of the signals. Analytical thin-layer chromatography was performed on Merck silica gel, grade 60 F_{254} and the spots were visualised by UV light (254 nm) and treatment with 5% phosphomolybdic acid in ethanol and heating. Flash chromatography was performed on Merck silica gel SI-60 Å. For analytical HPLC a Hitachi system (L-4000 UV detector at 254 nm and L-6200 pump with flow rate 1.5 mL/min) fitted with a LiChroCART 4× 250 mm 5 μm LiChrospher Si 60 column was used. Infrared spectra were recorded on a Perkin-Elmer 298 or 16PC FT-IR spectrometer and only the major peaks are listed. Elemental analyses were conducted by MikroKemi AB, Uppsala, Sweden. High-resolution mass analysis was performed by Stenhagen analyslab AB, Mölndal, Sweden. The synthesis of the olefins **1a–l**, data for epoxides **2a–l** and **3a–l**, and the analysis procedure of isomeric ratios of epoxides using NMR-spectroscopy and HPLC are described in Ref. 5b and 5c The synthesis and the epoxidation of olefin **8e** are described in Ref. 5c, and the preparation of aldehyde **6** in Ref. 5b. Phosphonium salt **7** was prepared according to literature procedures.[15]

4.2. General procedures for epoxidation reactions

4.2.1. Epoxidation with MMPP (method A). MMPP (2 equiv) was added to a solution of the substrate (0.13 M) and trioctylmethylammonium chloride (0.05 equiv) in a two-phase system consisting of $CHCl_3$ and H_2O (1:1). After stirring at room temperature for the reaction time specified in Table 1, the mixture was poured into satd aq $Na_2S_2O_3$ and the phases were separated. The organic phase was further washed with 1 M aq HCl, satd aq $NaHCO_3$ and brine. The organic layer was dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The crude products were purified by column chromatography as described earlier.[5b,c]

4.2.2. Epoxidation with *m*-CPBA (method B). *m*-CPBA (1.5 equiv) was added to a solution of the substrate (0.2 M) in CH_2Cl_2. After stirring at room temperature for the reaction time specified in Table 1, the reaction was worked up as described above for method A.

4.2.3. Epoxidation with trifluoroperacetic acid (method C). Trifluoroacetic acid anhydride (4 equiv) was added to a solution of urea–hydrogen peroxide (15 equiv, 3 M) and Na_2HPO_4 (10 equiv) in CH_2Cl_2. After stirring at 0 °C for 30 min, substrate was added. Stirring was continued (see Table 1 for reaction times) at the same temperature after which the reaction was quenched immediately by addition of satd aq $NaHCO_3$ and the phases were separated. The organic phase was further washed with satd aq $Na_2S_2O_3$, 1 M aq HCl and brine. The organic layers were dried ($MgSO_4$), filtered and the solvent was removed. The crude products were purified by column chromatography as described earlier.[5b,c]

4.3. Data for the oxazolidinones (4). (4*S*,5*R*)-4-Benzyl-5-[(1*S*)-hydroxy-(2*R*)-methoxycarbonyl-3-phenylpropyl]-1,3-oxazolidin-2-one (4a) and (4*S*,5*S*)-4-benzyl-5-[(1*R*)-hydroxy-(2*R*)-methoxycarbonyl-3-phenylpropyl]-1,3-oxazolidin-2-one (4b)

The compounds were isolated from the trifluoroperacetic acid-mediated epoxidation reaction of **1b** after chromatography using ether/pentane 1:3 as eluent (see method C).

4.3.1. Compound 4a. Mp 115–117 °C; $[\alpha]_D^{20}$ −46.3 (*c* 0.50, $CHCl_3$); ^{1}H NMR (270 MHz) δ 7.35–7.16 (m, 10H), 4.94 (bs, 1H), 4.11 (dd, 1H, J=8.5, 4.6 Hz), 3.98 (dt, 1H, J=9.3, 4.8 Hz), 3.66 (s, 3H), 3.58 (m, 2H), 3.15–2.94 (m, 4H), 2.74 (t, 1H, J=13.6 Hz); ^{13}C NMR (68 MHz) δ 175.8, 157.4, 137.4, 136.1, 129.1 (2C), 129.0 (4C, s), 128.7 (2C), 127.3, 126.9, 81.3, 71.8, 57.0, 52.1, 46.8, 42.3, 35.4; IR (KBr) 3343, 1748 cm^{-1}. Anal. Calcd for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28; N, 3.79. Found: C, 68.28; H, 6.17; N, 3.87.

4.3.2. Compound 4b. Mp 188–190 °C. $[\alpha]_D^{20}$ −40.5 (*c* 0.74, $CHCl_3$); ^{1}H NMR (270 MHz) δ 7.38–7.18 (m, 10H), 4.92 (bs, 1H), 4.64 (dd, 1H, J=10.1, 7.3 Hz), 4.35 (dd, 1H, J=10.0, 2.2 Hz), 4.07 (ddd, 1H, J=12.0, 7.2, 3.2 Hz), 3.65 (bs, 1H), 3.52 (s, 3H), 3.33–3.08 (m, 4H), 2.64 (t, 1H, J=13.0 Hz); ^{13}C NMR (68 MHz) δ 176.1, 157.6, 138.1, 136.7, 129.1 (4C), 129.0 (2C), 128.5 (2C), 127.2, 126.6, 76.7, 68.0, 56.3, 51.9, 48.4, 35.9, 31.2; IR (KBr) 3373, 1744 cm^{-1}. Anal. Calcd for $C_{21}H_{23}NO_5\times0.5H_2O$: C, 66.65; H, 6.39; N, 3.70. Found: C, 66.74; H, 6.31; N, 3.59. The stereochemistry of this compound was established by X-ray crystallography.[13]

4.4. Synthesis of the alkenes 8a–d

4.4.1. Phenyl-(3-phenylpropyl)sulfone (5). 3-Phenylpropanol (15.0 g, 110 mmol) and Et_3N (6.0 mL, 330 mmol) were dissolved in CH_2Cl_2 (450 mL). Methanesulfonyl chloride (21.5 g, 275 mmol) was added drop wise at 0 °C. After 2 h H_2O was added and the mixture was extracted three times with CH_2Cl_2. The combined organic phases

were dried ($MgSO_4$) and concentrated in vacuo without heating to afford a crude oil, which was used in next step without further purification.

Thiophenol (73.0 mL, 716 mmol) was added to a solution of $NaOCH_3$ (38.65 g, 716 mmol) in THF/MeOH (5:1, 300 mL). The mixture was stirred for 30 min at room temperature and the mesylate from the previous step was added as an oil. The reaction mixture was stirred at room temperature overnight. The day after, satd aq $NaHCO_3$ was added and the organic solvent was evaporated. The mixture was partitioned between H_2O and ether, and the aqueous phase was extracted three times with ether. The combined ether layers were dried ($MgSO_4$) and concentrated to afford a yellow-brown oil. Purification by column chromatography (petroleum ether) gave phenyl-(3-phenylpropyl)sulfide (24.37 g, 97% over two steps): ^1H NMR data were in agreement with those reported;[24] ^{13}C NMR (68 MHz) δ 141.2, 136.5, 129.0 (2C), 128.8 (2C), 128.4 (2C), 128.3 (2C), 125.9, 125.7, 34.6, 32.8, 30.5.

The sulfide (1.50 g, 6.57 mmol) was dissolved in CH_2Cl_2 (75 mL) and *m*-CPBA (5.18 g, 21.0 mmol) was added at 0 °C. The mixture was allowed to reach room temperature while stirring overnight. The reaction was quenched by slow addition of aq NaOH (10%, 25 mL) saturated with $NaHSO_3$. After filtration and dilution, the aqueous phase was extracted four times with CH_2Cl_2. The combined organic layers were extracted once with 1 M NaOH, dried ($MgSO_4$) and concentrated. The crude product was recrystallised (CH_2Cl_2/hexane) to afford sulfone **5** (1.24 g, 72%). ^1H NMR data and melting point were in agreement with those reported;[25] ^{13}C NMR (68 MHz) δ 139.7, 138.9, 133.6 (2C), 129.2 (2C), 128.5 (2C), 128.3 (2C), 127.9, 126.3, 55.3, 33.9, 24.1.

4.4.2. 2-Benzyl-6-phenyl-(*E*)-3-hexen-1-ol (8a). *By Julia olefination with* **5**. Sulfone **5** (0.64 g, 2.46 mmol) was dissolved in dry THF (20 mL) under N_2 atmosphere. The solution was cooled to −78 °C and *n*-butyllithium (1.6 M in hexane, 1.84 mL, 2.95 mmol) was added. The solution was stirred for 30 min at −78 °C. In a separate flask, aldehyde **6** (1.03 g, 3.69 mmol) was treated with DIBAL-methoxide (1.16 M, 3.18 mL) at −78 °C in THF (10 mL). The solution of the activated aldehyde was added immediately to the solution of the sulfone anion, and the mixture was stirred for 30 min at −78 °C. The reaction was quenched by addition of satd aq NH_4Cl and allowed to reach room temperature. After removal of THF by evaporation, the mixture was extracted five times with CH_2Cl_2. The organic phase was dried ($MgSO_4$) and concentrated to afford a colourless oil.

The crude oil was dissolved in MeOH (75 mL) and Na_2HPO_4 (3.49 g, 24.6 mmol) and 6% Na(Hg) (9.43 g) were added at 0 °C. After 4 h, H_2O and 1 M HCl were added and the insoluble material was filtered off. MeOH was removed by evaporation and the mixture was extracted with CH_2Cl_2 four times. The organic phase was dried ($MgSO_4$) and concentrated. Purification by column chromatography (ether/petroleum ether 1:19) gave an *E*/*Z* mixture of 2-benzyl-1-[(*tert*-butyldimethylsilyl)oxy]-6-phenyl-3-hexene.

The crude product (500 mg, 1.31 mmol) was dissolved in acetonitrile (40 mL) containing 2% HF (2 mL of a 40% aqueous HF solution) at room temperature. After 1 h H_2O was added and the mixture was extracted with CH_2Cl_2. The organic phase was dried ($MgSO_4$) and concentrated to afford 470 mg of a crude oil. The *E*/*Z* ratio was 88:12 according to GC and NMR (33% combined yield over two steps). The isomers were separated by repeated column chromatography (CH_2Cl_2/MeOH/hexane 4:1:25) to afford **8a** as a colourless oil: HPLC (0.5% EtOH in hexane), t_R 13.2 min; ^1H NMR (270 MHz) δ 7.30–7.11 (m, 10H), 5.48 (app dt, 10H, J=6.6, 15.4 Hz), 5.21 (ddt, 1H, J=1.1, 8.1, 15.4 Hz), 3.51 (ddd, 1H, J=4.7, 8.1, 10.7 Hz), 3.33 (ddd, 1H, J=4.3, 7.7, 10.7 Hz), 2.74–2.51 (m, 4H), 2.50–2.40 (m, 1H), 2.38–2.26 (m, 2H), 1.22 (app ddd, 1H, J=1.1, 4.3, 8.1 Hz); ^{13}C NMR (68 MHz) δ 141.6, 139.8, 132.8, 131.3, 129.1 (2C), 128.4 (2C), 128.3 (2C), 128.2 (2C), 125.9, 125.8, 65.0, 47.1, 37.7, 35.7, 34.3; IR (neat) 3370, 3020, 2920, 1600, 1490, 1450 cm^{-1}. Anal. Calcd for $C_{19}H_{22}O$: C, 85.7; H, 8.3. Found: C, 85.6; H, 8.5.

By Schlosser olefination with **7**. Phosphonium salt **7** (1.19 g, 2.58 mmol) was suspended by magnetic stirring in dry THF (5 mL) under N_2. The vessel was cooled to −60 °C and phenyllithium (2.0 M in dibutyl ether, 1.36 mL, 2.72 mmol) was added. The reaction was allowed to warm to room temperature and was stirred for 30 min during which an orange colour solution developed. The reaction was again cooled to −60 °C and a solution of **6** (0.72 g, 2.59 mmol) in THF (2 mL) was added drop wise at which the colour faded. The reaction was allowed to warm to −41 °C and was left with stirring for 30 min. Another equivalent of phenyllithium was added to yield a dark violet solution which was stirred for 30 min. Addition of MeOH (0.105 mL, 2.29 mmol) gave a slight yellow solution, which was stirred for 30 min at −41 °C. *t*-BuOK (0.29 g, 2.59 mmol) was added in one portion and the reaction was stirred for 30 min and was then allowed to reach room temperature. The reaction was quenched by addition of diethyl ether (15 mL) and satd aq NH_4Cl (25 mL). The mixture was stirred briefly and the phases were separated. The aqueous phase was extracted with diethyl ether (25 mL) and the combined organic phases were washed with H_2O and brine, dried over $MgSO_4$ and evaporated. The product, 2-benzyl-1-[(*tert*-butyldimethylsilyl)oxy]-6-phenyl-3-hexene (mixture of *E*/*Z*-isomers), was purified by column chromatography as described above.

The crude product was dissolved in THF (4 mL) and TBAF (1 M in THF, 6.9 mL, 6.9 mmol) was added and the resulting mixture was stirred for 26 h. The mixture was diluted with diethyl ether (60 mL) and washed with 10% aq citric acid solution (60 mL), satd aq $NaHCO_3$ (60 mL) and brine (60 mL), dried over $MgSO_4$, filtered and evaporated. The crude product was purified by gradient column chromatography (EtOAc/hexanes 1:20–1:10) to yield the title compound with an *E*/*Z*-ratio of 87:13 (0.42 g, 61% combined yield over two steps). The *E*/*Z*-isomers were separated as indicated above.

4.4.3. 2-Benzyl-6-phenyl-(*E*)-3-hexenylacetate (8b). Alcohol **8a** (50 mg, 0.188 mmol) and Et_3N 131 μL, 0.938 mmol) were dissolved in CH_2Cl_2 (5 mL). Acetic

anhydride (89 μL, 0.938 mmol) and a catalytic amount of DMAP were added. The reaction was stirred at room temperature overnight. The mixture was extracted with 1 M HCl and satd aq $NaHCO_3$. The organic phase was dried ($MgSO_4$), filtered and concentrated. Purification of the crude oil by column chromatography (ether/pentane 1:12) afforded the title compound (54.6 mg, 94%): HPLC (10% EtOAc in hexane), t_R 4.6 min, ^{1}H NMR (270 MHz) δ 7.29–7.09 (m, 10H), 5.42 (app dt, 1H, J=6.4, 15.4 Hz), 5.28 (app dd, 1H, J=7.5, 15.4 Hz), 4.02–3.91 (m, 2H), 2.78–2.51 (m, 5H), 2.31–2.23 (m, 2H), 2.02 (s, 3H); ^{13}C NMR (68 MHz) δ 171.0, 141.7, 139.4, 131.7, 130.3, 129.2 (2C), 128.4 (2C), 128.2 (4C), 126.0, 125.7, 66.8, 43.3, 38.2, 35.8, 34.3, 20.9; IR (neat) 3020, 2930, 1740, 1490, 1450, 1240 cm^{-1}. Anal. Calcd for $C_{21}H_{24}O_2$: C, 81.8; H, 7.8. Found: C, 81.7; H, 7.9.

4.4.4. 2-Benzyl-6-phenyl-(*E*)-3-hexenyltrifluoroacetate (8c). Alcohol **8a** (150 mg, 0.563 mmol) and Et_3N (235 μL, 1.69 mmol) were dissolved in CH_2Cl_2 (10 mL) and trifluoroacetic anhydride (86 μL, 0.619 mmol) was added. The reaction was stirred at room temperature. More Et_3N and trifluoroacetic anhydride were added twice since there was starting material left after 2 and 4 h, respectively. After 5 h, the reaction mixture was extracted with 1 M aqueous HCl and saturated aqueous $NaHCO_3$. The organic phase was dried ($MgSO_4$) and concentrated. Purification of the crude oil by column chromatography (ether/pentane 1:4) afforded the title compound (166 mg, 81%) as a colourless oil: HPLC (2% EtOAc in hexane), t_R 4.8 min; ^{1}H NMR (270 MHz) δ 7.31–7.08 (m, 10H), 5.49 (dt, 1H, J=6.5, 15.4 Hz), 5.32–5.23 (m, 1H), 4.26–4.15 (m, 2H), 2.74–2.58 (m, 5H), 2.33–2.25 (m, 2H); ^{13}C NMR (68 MHz) δ 157.4 (q, J_{CCF}= 42 Hz), 141.6, 138.5, 133.0, 129.1, 128.9 (2C), 128.4 (4C), 128.2 (2C), 126.4, 125.8, 114.5 (q, J_{CF}=285 Hz), 69.8, 43.1, 37.7, 35.6, 34.3; IR (neat) 3020, 2930, 1780, 1490, 1450, 1220, 1160 cm^{-1}. Anal. Calcd for $C_{21}H_{21}F_3O_2$: C, 69.60; H, 5.84. Found: C, 69.57; H, 5.90.

4.4.5. Methyl 2-benzyl-6-phenyl-(*E*)-3-hexenoate (8d). Alcohol **8a** (110 mg, 0.413 mmol) was dissolved in CH_2Cl_2 (1.5 mL) and acetonitrile (2 mL) under a N_2 atmosphere and cooled to 0 °C. Dess–Martin periodinane (15 wt% solution in CH_2Cl_2, 1.46 g solution, 0.516 mmol) was added drop wise to the stirred solution. The reaction was stirred for 30 min at 0 °C and another 3 h at rt. The solvent volume was reduced to half by rotary evaporation without heating, and the remaining solution was cooled to 0 °C, and cold satd aq $Na_2S_2O_3$ solution was added and stirring was continued for 20 min. The mixture was extracted three times with diethyl ether, and the combined organic layers were washed with cold satd aq $NaHCO_3$, dried over $MgSO_4$, filtered and evaporated. The product was purified by rapid chromatography on a short column (EtOAc/hexanes 1:20) to yield the unstable compound *E*-2-benzyl-6-phenyl-3-hexenal as a crude oil (95 mg), which was used immediately in the next step. ^{1}H NMR (400 MHz) δ 9.57 (d, 1H, J=1.8 Hz), 7.32–7.10 (m, 10H), 5.61–5.54 (m, 1H), 5.32 (dd, 1H, J=8.4, 15.8 Hz), 3.25 (q, 1H, J=7.4 Hz), 3.11 (dd, 1H, J=6.2, 13.9 Hz), 2.74 (dd, 1H, J=7.7, 13.9 Hz), 2.68–2.62 (m, 2H), 2.38–2.32 (m, 2H).

The crude aldehyde (approx 0.36 mmol) was dissolved in dry DMF (2 mL) under a N_2 atmosphere and MeOH (106 μL, 2.6 mmol) was added. The mixture was stirred for 10 min and subsequently PDC (0.982 g, 2.20 mmol) was added. The reaction was quenched after 19 h by adding the reaction solution in small portions to a vigorously stirred mixture of H_2O (25 mL) and diethyl ether (75 mL). The resulting suspension was filtered through Celite and the filtrate was washed with H_2O. The aqueous layer was washed extracted twice with ether and the combined organic phases were washed with brine, dried over $MgSO_4$, filtered and evaporated. Purification of the unstable product was done by rapid chromatography on a short column (EtOAc/hexanes 1:100) to yield the title compound (49 mg, 40% over two steps, repeated attempts gave comparable yields). ^{1}H NMR (400 MHz) 7.30–7.09 (m, 10H), 5.52–5.48 (m, 2H), 3.63 (s, 3H), 3.31–3.23 (m, 1H), 3.06 (dd, 1H, J=7.7, 13.6 Hz), 2.79 (dd, 1H, J=7.3, 13.6 Hz), 2.63 (dt, 2H, J= 3.3, 7.7 Hz), 2.33–2.27 (m, 2H); ^{13}C NMR (100 MHz) 174.2, 141.6, 138.8, 133.0, 129.0 (2C), 128.4 (2C), 128.2 (4C), 127.6, 126.3, 125.8, 51.7, 51.0, 38.8, 35.5, 34.2; IR (neat) 3027, 2928, 1735, 1449, 1160 cm^{-1}; HRMS (FAB) calcd for $C_{20}H_{23}O_2$ (MH^+) 295.170, found 295.167.

4.5. Epoxidation of the alkenes 8a–d

Epoxidations were performed as described above (method B and C). Data on isomeric ratios, yields and reaction times are given in Table 2.

4.5.1. (2*R,3*S**,4*R**)-2-Benzyl-3,4-epoxy-6-phenyl-hexan-1-ol (9a) and (2*R**,3*R**,4*S**)-2-benzyl-3,4-epoxy-6-phenyl-hexan-1-ol (10a).** Purification by column chromatography (CH_2Cl_2/MeOH/hexane 4:1:12) afforded **9a** and **10a**.

Compound **9a**. HPLC (3% EtOH in hexane), t_R 9.9 min; ^{1}H NMR (270 MHz) δ 7.32–7.09 (m, 10H), 3.75–3.68 (m, 2H), 2.82 (dd, 1H, J=6.8, 13.7 Hz), 2.70 (dd, 1H, J=2.4, 7.7 Hz), 2.66–2.43 (m, 4H), 2.07 (br s, 1H), 1.76–1.63 (m, 3H); ^{13}C NMR (68 MHz) δ 141.1, 139.2, 129.1 (2C), 128.9 (2C), 128.4 (2C), 128.2 (2C), 126.3, 126.0, 64.1, 60.9, 57.8, 45.0, 34.9, 33.5, 31.7; IR (neat) 3440, 3020, 2920, 1600, 1490, 1450 cm^{-1}. Anal. Calcd for $C_{19}H_{22}O_2 \times 0.1H_2O$: C, 80.3; H, 7.8. Found: C, 80.3; H, 8.0.

Compound **10a**. HPLC (3% EtOH in hexane, t_R 8.6 min; ^{1}H NMR (270 MHz) δ 7.33–7.15 (m, 10H), 3.53–3.37 (m, 2H), 2.96 (app dt, 1H, J=2.3, 5.8 Hz), 2.88–2.69 (m, 4H), 2.61 (dd, 1H, J=8.6, 13.7 Hz), 1.99–1.78 (m, 3H), 1.67–1.63 (m, 1H); ^{13}C NMR (68 MHz) δ 141.1, 139.0, 129.0 (2C), 128.5 (2C), 128.4 (2C), 128.3 (2C), 126.2, 126.1, 62.5, 61.1, 56.9, 43.9, 34.7, 33.6, 32.1; IR (neat) 3440, 3020, 2920, 1600, 1490, 1450 cm^{-1}. Anal. Calcd for $C_{19}H_{22}O_2$: C, 80.8; H, 7.9. Found: C, 80.7; H, 7.7.

4.5.2. (2*R,3*S**,4*R**)-2-Benzyl-3,4-epoxy-6-phenyl-hexanyl acetate (9b) and (2*R**,3*R**,4*S**)-2-benzyl-3,4-epoxy-6-phenyl-hexanyl acetate (10b).** Purification by column chromatography (diethyl ether/pentane 1:9) afforded **9b** and **10b**.

Compound **9b**. HPLC (10% EtOAc in hexane), t_R 18.1 min; ^{1}H NMR (270 MHz) δ 7.32–7.10 (m, 10H), 4.22–4.09

(m, 2H), 2.77 (dd, 1H, J=6.5, 13.5 Hz), 2.68–2.64 (m, 1H), 2.61–2.48 (m, 3H), 2.47–2.43 (m, 1H), 2.09 (s, 3H), 1.86–1.73 (m, 1H), 1.71–1.60 (m, 2H); ^{13}C NMR (68 MHz) δ 171.0, 141.1, 138.8, 128.9 (2C), 128.5 (2C), 128.4 (2C), 128.2 (2C), 126.4, 126.0, 64.8, 59.2, 58.0, 42.9, 34.9, 33.5, 31.8, 20.9; IR (neat) 3020, 2930, 1740, 1490, 1450, 1240 cm^{-1}. Anal. Calcd for $C_{21}H_{24}O_3$: C, 77.8; H, 7.5. Found: C, 77.6; H, 7.6.

Compound **10b**. HPLC (10% EtOAc in hexane), t_R 12.7 min; ^{1}H NMR (270 MHz) δ 7.32–7.15 (m, 10H), 4.00–3.94 (m, 2H), 2.93 (dd, 1H, J=5.0, 13.7 Hz), 2.85 (app dt, 1H, J=2.3, 5.8 Hz), 2.83–2.63 (m, 4H), 2.01 (s, 3H), 1.89–1.77 (m, 3H); ^{13}C NMR (68 MHz) δ 170.8, 141.0, 138.4, 129.1 (2C), 128.5 (4C), 128.3 (2C), 126.4, 126.0, 63.8, 59.9, 58.0, 42.5, 35.0, 33.8, 32.1, 20.8; IR (neat) 3020, 2930, 1740, 1490, 1450, 1240 cm^{-1}. Anal. Calcd for $C_{21}H_{24}O_3$: C, 77.8; H, 7.5. Found: C, 77.7; H, 7.5.

4.5.3. (2*R,3*S**,4*R**)-2-Benzyl-3,4-epoxy-6-phenyl-hexanyl trifluoroacetate (9c) and (2*R**,3*R**,4*S**)-2-benzyl-3,4-epoxy-6-phenyl-hexanyl trifluoroacetate (10c).** The epoxides **9c** and **10c** were not isolated, instead the crude mixture was treated with K_2CO_3 in MeOH to produce a mixture with unchanged ratio of the corresponding alcohol epoxides **9a** and **10a**.

4.5.4. Methyl (2*R,3*S**,4*R**)-2-benzyl-3,4-epoxy-6-phenyl-hexanoate (9d) and methyl (2*R**,3*R**,4*S**)-2-benzyl-3,4-epoxy-6-phenyl-hexanoate (10d).** Purification by gradient column chromatography (EtOAc/hexanes 1:33–1:20) afforded **9d** and **10d**.

Compound **9d**. HPLC (5% EtOH in hexane), 1.5 mL/min, t_R 14.4 min; ^{1}H NMR (400 MHz) δ 7.31–7.08 (m, 10H), 3.71 (s, 3H), 3.06 (dd, 1H, J=7.0, 13.9 Hz), 2.94 (dd, 1H, J=2.2, 8.4 Hz), 2.80 (dd, 1H, J=8.8, 13.9 Hz), 2.67–2.58 (m, 1H), 2.56–2.48 (m, 1H), 2.48–2.41 (m, 2H), 1.72–1.63 (m, 2H); ^{13}C NMR (100 MHz) δ 173.2, 141.0, 138.0, 128.8 (2C), 128.6 (2C), 128.4 (2C), 128.2 (2C), 126.7, 126.0, 58.5, 58.1, 52.0, 50.3, 35.3, 33.3, 31.7; IR (neat) 3027, 2949, 1732, 1604, 1495, 1454, 1200, 1165. Anal. Calcd for $C_{20}H_{22}O_3$: C, 77.4; H, 7.1. Found: C, 77.5; H, 7.3.

Compound **10d**. HPLC (5% EtOAc in hexane), 1.5 mL/min, t_R 8.4 min; ^{1}H NMR (400 MHz) δ 7.34–7.20 (m, 10H), 3.61 (s, 3H), 3.06 (app d, 2H, J=7.0 Hz), 2.94–2.89 (m, 2H), 2.82–2.68 (m, 2H), 2.53 (app q, 1H, J=7.3 Hz), 1.89–1.84 (m, 2H); ^{13}C NMR (100 MHz) δ 172.4, 141.0, 138.0, 128.9 (2C), 128.4 (4C), 128.3 (2C), 126.6, 126.0, 58.4, 57.9, 51.8, 50.2, 35.7, 33.5, 32.1; IR (neat) 3027, 2949, 1738, 1604, 1496, 1454, 1201, 1164 cm^{-1}; HRMS (FAB) calcd for $C_{20}H_{23}O_3$ (MH^+) 311.165, found 311.167

Acknowledgements

Financial support was obtained from the Knut and Alice Wallenberg Foundation and the Swedish Research Council. The authors thank Professor Uli Hacksell for his interest in this work and for valuable discussions.

Supplementary data

NMR spectral assignments of characterised compounds. ^{1}H and ^{13}C NMR spectra of **8d** and **10d**. Experimental details, selected details of the final structure refinement and crystal data of **4b**.

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2006.01.095

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