Development of the Juliá asymmetric epoxidation reaction. Part 1. Application of the oxidation to enones other than chalcones

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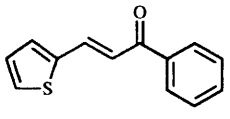
Asymmetric epoxidation of a variety of enones 3, 6, 8, 10, 12, 14, 16, 18, 21, 22, 26, 28–30 and 36 gives the corresponding oxiranes in good to excellent yield and optical purity. The oxidation medium consists of basic peroxide or sodium perborate or sodium percarbonate or *tert*-butylhydroperoxide and the preferred catalyst is polyleucine, conveniently prepared from the *N*-carboxyanhydride using 1,3-diaminopropane.

Introduction

The asymmetric epoxidation of chalcones (Scheme 1), discovered by Juliá, involves the use of basic peroxide in the

Scheme 1 *Conditions:* i, NaOH, H_2O_2, poly-(L)-leucine, hexane or CH_2Cl_2

presence of a polyamino acid such as poly-(L)-leucine.[1] The reaction was explored further by Juliá and Colonna[2] who showed, *inter alia*, that a range of compounds of the type ArCH=CHCOAr could be oxidized to optically active epoxides, often in high yield and excellent enantiomeric excess. Included in these data was one example of the oxidation of a heterocyclic system, namely the enone **1**. Polyoxygenated chalcone epoxides



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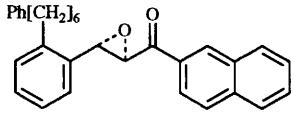

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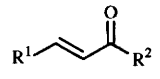
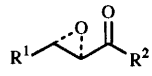
were produced in optically active form by Bezuidenhoudt and Ferreira[3] using the same methodology, in investigations aimed at the enantioselective synthesis of flavanoids.[4] More recently the Juliá asymmetric epoxidation was used to prepare the epoxide **2** *en route* to a potent leukotriene antagonist.[5] The latter work, by Flisak and co-workers, established some interesting principles: first, the catalyst [poly-(L)-leucine] was prepared and used on a large (> 200 g) scale. Secondly, the catalyst was found to be reusable, without detrimental effect on yield or enantiomeric excess. Thirdly, the preferred use of naphthyl (arylalkenyl) ketones was emphasized. In an earlier paper some α,β-unsaturated ketones other than chalcones were studied as electrophiles, without success.[6] However, we did not accept that the transformation was, of necessity, limited to chalcones and hence we set up a programme of research to investigate the full versatility of the reaction. We report some of our early results in this paper.[7]

Results and discussion

Variation of the starting enone

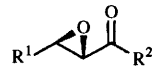
Initially, poly-(L)-leucine was prepared from pure-(L)-leucine-*N*-carboxyanhydride (mp 76–78 °C) using a humidity cabinet.[5] Poly-(D)-leucine was synthesised from (D)-leucine-*N*-carboxyanhydride in a similar manner. The epoxidation of the enone **3** was





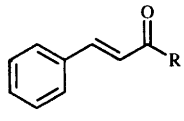
3 R^1 = Ph, R^2 = 2-naphthyl
6 R^1 = 2-furyl, R^2 = 2-naphthyl
8 R^1 = 2-pyridyl, R^2 = Ph
10 R^1 = 3-pyridyl, R^2 = Ph
12 R^1 = 4-pyridyl, R^2 = 2-naphthyl

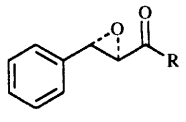
4 R^1 = Ph, R^2 = 2-naphthyl
7 R^1 = 2-furyl, R^2 = 2-naphthyl
9 R^1 = 2-pyridyl, R^2 = Ph
13 R^1 = 4-pyridyl, R^2 = 2-naphthyl



5 R^1 = Ph, R^2 = 2-naphthyl
11 R^1 = 3-pyridyl, R^2 = Ph

studied using both catalysts (Table 1). The reaction catalysed by poly-(L)-leucine gave rise to the epoxide **4** of good optical purity, the reaction catalysed by poly-(D)-leucine furnished the epoxide **5** in slightly lower yield but with the same optical purity. Thus as demonstrated previously,[8] switching from poly-(L)-leucine to poly-(D)-leucine changes the configuration of the major enantiomer formed in the reaction.





14 R = 2-furyl **15**
16 R = 2-pyridyl **17**

A range of heterocyclic enones behave in a similar fashion. Thus, oxidation of the chosen enone in a three-phase system, comprising aqueous phase, organic solvent and (insoluble) catalyst gave rise, after *ca.* one day, to the corresponding optically active epoxide in good to excellent yield and enantiomeric excess. Note that none of the reactions were optimized.

Dienone **18** afforded the mono-epoxide **19** using poly-(L)-leucine and the enantiomer **20** using poly-(D)-leucine (Table 2), while the dienones **21** and **22** gave bis(epoxides) **23** and **24**/**25**, respectively. The tetraene **26** reacts, not surprisingly given the

Table 1 Epoxidation of the enones **3**, **6**, **8**, **10**, **12**, **14** and **16**

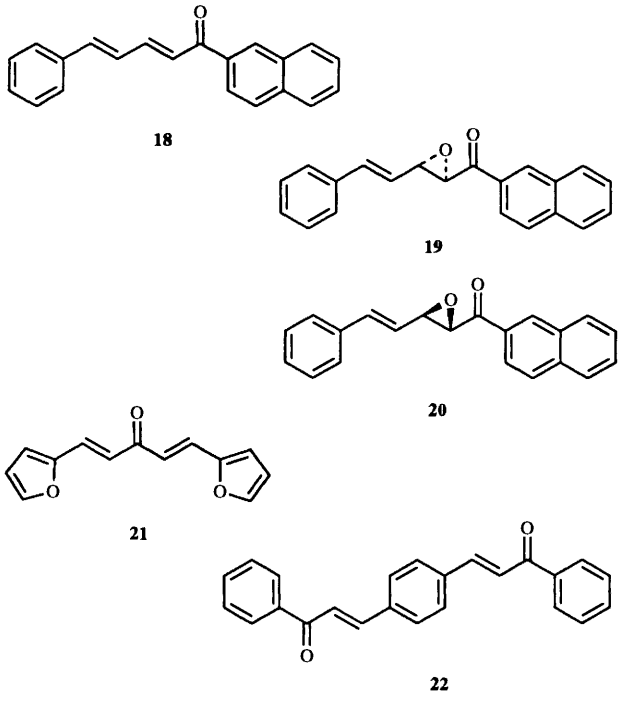
Starting enone	Catalyst[a]	Solvent	Time/h	Product	Yield (%)	Enantiomeric excess (%)
3	pLl	CH_2Cl_2	30	**4**	90	93
3	pDl	CH_2Cl_2	38	**5**	67	93
6	pLl	CH_2Cl_2	50	**7**	75	>96
8	pLl	CH_2Cl_2	16	**9**	84	72
10	pDl	CH_2Cl_2	18	**11**	70	94
12	pLl	CH_2Cl_2	16	**13**	67	>96
14	pLl	CH_2Cl_2	18	**15**	85	87
14	pDl	CH_2Cl_2	18	**15**	98	93
16	pLl	CH_2Cl_2	18	**17**	74	79

[a] pLl = poly-(L)-leucine; pDl = poly-(D)-leucine

Table 2 Epoxidation of the enones **18**, **21**, **22** and **26**

Starting enone	Catalyst	Solvent	Time/h	Product	Yield (%)	Enantiomeric excess (%)
18	pLl	hexane	72	**19**	78	>96
18	pDl	hexane	74	**20**	76	>96
21	pLl	CH_2Cl_2	60	**23**	60	90
22	pLl	CH_2Cl_2	46	**24**[a]	74	>99
22	pDl	CH_2Cl_2	42	**25**[a]	91	>99
26	pLl	CH_2Cl_2	60	**27**	50	80

[a] Diastereoisomeric excess >88%. The *meso*-compound was also obtained.



foregoing results, to give the bis(epoxide) **27** in modest yield but good enantiomeric excess.

In order to broaden the scope of this asymmetric epoxidation reaction we were anxious to remove unsaturated moieties attached to C-1 and/or C-3 of the enone unit and we can report the first successes in this endeavour. Thus, the enones **28** and **29**, as well as the dienone **30**, all containing a *tert*-butyl group in place of one or other of the unsaturated units, have been oxidized to the corresponding epoxides **31**–**35**, with good to excellent stereocontrol (Table 3).

Variation of the oxidant

In all the literature reports describing the Juliá oxidation and in all the oxidations described above, an excess of hydrogen peroxide and sodium hydroxide have been used as the oxidation medium. Other, milder oxidants can be employed in many of the cases. For example, enone **3** was oxidized to the epoxide **4** using sodium perborate (2 equiv.) and sodium hydroxide (1 equiv.) in the presence of poly-(L)-leucine and a phase transfer catalyst (aliquat 336) in excellent yield and good enantiomeric excess (Table 4). Other examples of asymmetric perborate oxidations are included in Table 4; the oxidation of dienedione **36** is particularly interesting since the bis(epoxides) **37** and **38** cannot be obtained using the $NaOH–H_2O_2$ medium.

Oxidation of the enone **3** with sodium percarbonate ($Na_2CO_3 \cdot 1.5\ H_2O_2$; excess) in water and dichloromethane containing poly-(L)-leucine and aliquat 336 gave after 63 h the epoxide **4** in 87% yield and 83.5% enantiomeric excess. Finally, oxidation of the enone **3** with *tert*-butylperoxide and hydroxide [9] gave the epoxide **4** in modest optical purity (47% ee using hexane as solvent). The latter reaction is being optimised.

Variation in the method of preparation of the catalyst

Poly-amino acids have been prepared from the *N*-carboxyanhydride using amines (such as butylamine) alkoxides and water (using a humidity cabinet). We concur with the view of Lantos and Novak that the protocol using a humidity cabinet is advantageous in terms of time of preparation and quality of the catalyst. However, we have found that 1,3-diaminopropane gives a catalyst of excellent quality; production time is less than three days. Other diamines are less effective in producing good quality catalyst in a short period of time (Table 5).

The possibility of making optically active dendrimers from (cyclic) polyamines is intrigueing.

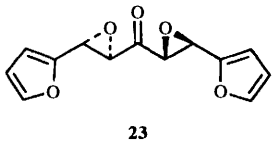
Conclusions

The Juliá asymmetric epoxidation protocol is not limited to chalcones. The essential catalyst [*e.g* poly-(L)-leucine] can be made from the chosen *N*-carboxyanhydride by a heterogeneous method (humidity cabinet) or a homogeneous method (1,3-diaminopropane). The oxidants that can be utilized include basic peroxide, sodium perborate, sodium percarbonate and *tert*-butylhydroperoxide anion.

Table 3 Epoxidation of the enones **28**, **29** and **30**

Starting material	Catalyst	Solvent	Time/h	Product	Yield (%)	Enantiomeric excess (%)
28	pLl	CH_2Cl_2	18	**31**	92	>98[a]
28	pDl	CH_2Cl_2	18	**32**	90	>86
29	pLl	CH_2Cl_2	18	**33**	85	90
29	pDl	CH_2Cl_2	18	**34**	86	76
30	pLl	CH_2Cl_2	30	**35**	90	>97

[a] After one recrystallization.



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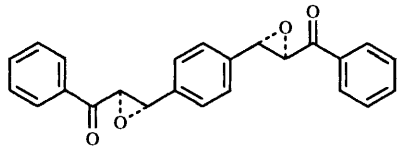

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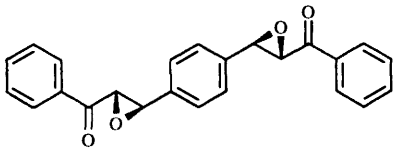

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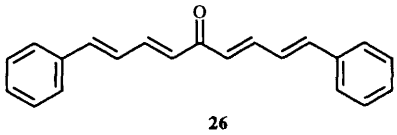

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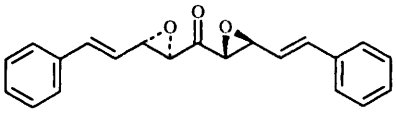

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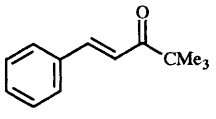

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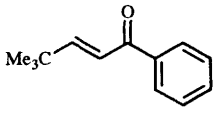

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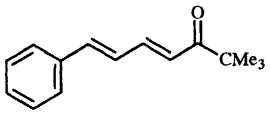

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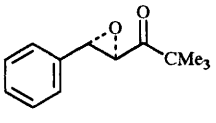

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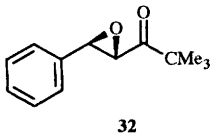

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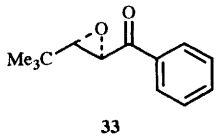

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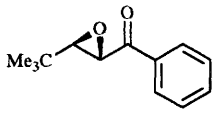

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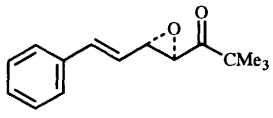

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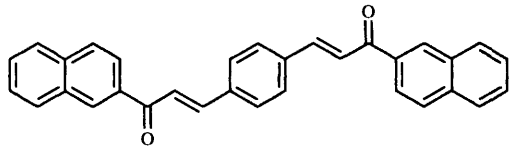

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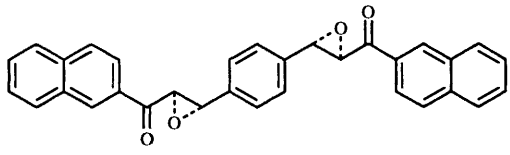

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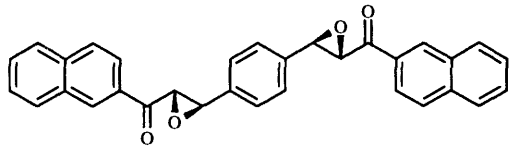

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Experimental

General

Flash column chromatography was carried out using silica gel (Merck 60, 40–63 μm). TLC was carried out on commercially available pre-coated plates (Merck silica gel 60 F254). Chiral HPLC was performed using a Chiralpak AD column. Mps were recorded with a Gallenkamp melting point apparatus and are uncorrected. IR spectra were determined with a Nicolet Magna-IR 550 infrared spectrometer. ^1H and ^{13}C NMR spectra were recorded on Bruker AM 300 or Bruker DRX 400 spectrometers. Chemical shifts are quoted in parts per million; *J*-values are given in Hz. High and low resolution mass spectra were recorded with a Kratos Profile HV 3000 spectrometer. Optical rotations were measured with a AA-1000 polarimeter. Microanalysis were carried out at Butterworths.

General procedure for the preparation of racemic epoxides

To a solution of NaOH (12 equiv.) in distilled water (0.5 cm^3 $mmol^{-1}$ substrate) at 0 °C were added toluene (4.7 cm^3 $mmol^{-1}$ substrate), EDTA (0.025 equiv.), the enone (1 equiv.) and aliquat 336 (0.1 equiv.). 30% Aqueous H_2O_2 (21 equiv.) was then added dropwise to the mixture and the whole was allowed to stir at room temperature until completion. The resulting mixture was diluted with diethyl ether and the aqueous phase was separated and extracted with diethyl ether. The combined organic phase was washed with water and brine and dried ($MgSO_4$). Removal of the solvent under reduced pressure afforded the racemic epoxide which was further purified by recrystallisation or column chromatography and analysed using chiral HPLC.

Table 4 Epoxidation of the enones **3**, **18** and **36** using sodium perborate–sodium hydroxide

Starting material	Catalyst	Solvent	Time/h	Product	Yield (%)	Enantiomeric excess (%)
3	pLl	CH_2Cl_2	24	**4**	98	88
3	pDl	CH_2Cl_2	22	**5**	96	90
18	pLl	CH_2Cl_2	120	**19**	77	96
36	pLl	CH_2Cl_2	120	**37**	82	>98[a]
36	pDl	CH_2Cl_2	144	**38**	64	>98[a]

[a] Diastereoisomeric excess >99%.

Table 5 Epoxidation of the enone **3** using different polyamino acids[a]

Substrate	Product	Amine used to initiate polymerization	Molar ratio of *N*-carboxyanhydride to diamine	Time for epoxide formation/h	Yield of epoxide (%)	Enantiomeric excess of epoxide (%)
3	**4**	1,3-Diaminopropane	60:1	20	87	95
3	**4**	1,6-Diaminohexane	60:1	37	87	92
3	**4**	1,12-Diaminododecane	60:1	62	84	80
3	**4**	Humidity cabinet	—	21	86	90

[a] All reactions were carried out in hexane.

***trans*-(±)-2,3-Epoxy-3-(2-furyl)-1-(2-naphthyl)propan-1-one 7.** (45%), Mp 76–77.5 °C (from diethyl ether–hexane); ν_{max}(KBr)/cm^{-1} 1683 (C=O), 1278 and 781 (C–O); δ_H(400 MHz; $CDCl_3$) 4.18 [1 H, d, *J* 2, C*H*(O)CHC=O], 4.91 [1 H, d, *J* 2, CH(O)C*H*C=O], 6.44 (1 H, dd, *J* 3.3 and 1.8, 4-H furyl), 6.62 (1 H, dd, *J* 3.3 and 0.7, 3-H furyl), 7.44 (1 H, d, *J* 1.8, 5-H furyl), 7.56–7.67 (2 H, m, 6-H and 7-H naphthyl), 7.90 (1 H, d, *J* 5-H or 8-H naphthyl), 7.94 (1 H, d, *J* 8.5, 4-H naphthyl), 8.00 (1 H, d, *J* 8, 5-H or 8-H naphthyl), 8.08 (1 H, dd, *J* 8.5 and 1.8, 3-H naphthyl) and 8.62 (1 H, s, 1-H naphthyl); δ_C(100.6 MHz; $CDCl_3$) 52.9 and 57.8 (C epoxide), 111.1 (CH), 111.6 (CH), 123.7 (CH), 127.1 (CH), 127.9 (CH), 128.9 (CH), 129.1 (CH), 129.8 (CH), 130.6 (CH), 132.4 (C), 132.8 (C), 136.0 (C), 143.5 (C-5 furyl), 148.2 (C-2 furyl) and 193.0 (C=O); *m*/*z* 264 (M^+, 19.8) and 155 (100%) (Found: M^+, 264.0795. $C_{17}H_{12}O_3$ requires *M*, 264.0786). Chiral HPLC (5:95, isopropanol–hexane, 1 cm^3 min^{-1}): 32.7 and 36.6 min.

***trans*-(±)-2,3-Epoxy-1-phenyl-3-(2-pyridyl)propan-1-one 9.** (85%), Mp 92 °C (from dichloromethane–hexane); ν_{max}(KBr)/cm^{-1} 1687 (C=O) and 1232 (C–O); δ_H(300 MHz; $CDCl_3$) 4.21 [1 H, d, *J* 2, C*H*(O)CHC=O], 4.57 [1 H, d, *J* 2, CH(O)C*H*C=O], 7.30 (1 H, ddd, *J* 8, 5 and 1, 5-H pyridyl), 7.39 (1 H, br d, *J* 8, 3-H pyridyl), 7.44–7.52 (2 H, m, PhH), 7.61 (1 H, tt, *J* 8 and 1, 4-H phH), 7.74 (1 H, ddd, *J* 8, 8 and 1, 4-H pyridyl), 7.97–8.03 (2 H, m, PhH) and 8.60 (1 H, ddd, *J* 5, 2 and 1, 6-H pyridyl); δ_C(75.5 MHz; $CDCl_3$) 59.3 and 59.4 (C epoxide), 121.1 (CH), 123.8 (CH), 128.4 (2 × CH), 128.8 (2 × CH), 133.9 (CH), 135.4 (C), 136.9 (CH), 149.9 (CH), 154.7 (C) and 193.0 (C=O); *m*/*z* 225 (M^+, 2.1) and 120 (100%) (Found: M^+ 225.0799. $C_{14}H_{11}O_2N$ requires *M*, 225.0789). Chiral HPLC (20:80, isopropanol–hexane, 1 cm^3 min^{-1}): 13.2 and 15.4 min.

***trans*-(±)-2,3-Epoxy-1-phenyl-3-(3-pyridyl)propan-1-one 11.** (56%), Mp 78–80 °C (from dichloromethane–hexane); ν_{max}(KBr)/cm^{-1} 1690 (C=O) and 884 (C–O); δ_H(300 MHz; $CDCl_3$) 4.10 [1 H, d, *J* 2, C*H*(O)CHC=O], 4.31 [1 H, d, *J* 2, CH(O)C*H*C=O], 7.34 (1 H, dd, *J* 8 and 5, 5-H pyridyl), 7.45–7.53 (2 H, m, PhH), 7.59–7.68 (2 H, m, 4-H pyridyl and 4-H PhH), 7.98–8.03 (2 H, m, PhH), 8.62 (1 H, br d, *J* 5, 6-H pyridyl) and 8.65 (1 H, br s, 2-H pyridyl); δ_C(75.5 MHz; $CDCl_3$) 57.2 and 60.6 (C epoxide), 128.4 (2 × CH), 128.9 (2 × CH), 132.6 (CH), 132.9 (C), 133.1 (CH), 134.2 (CH), 135.3 (C), 147.9 (CH), 150.3 (CH) and 192.5 (C=O); *m*/*z* 225 (M^+, 12.2) and 105 (100%) (Found: M^+, 225.0785. $C_{14}H_{11}O_2N$ requires *M*, 225.0789). Chiral HPLC (20:80, isopropanol–hexane, 1 cm^3 min^{-1}): 14.9 and 26.2 min.

***trans*-(±)-2,3-Epoxy-1-(2-naphthyl)-3-(4-pyridyl)propan-1-one 13.** (79%), Mp 140–142 °C (from dichloromethane–hexane); ν_{max}(KBr)/cm^{-1} 1677 (C=O), 1245 and 782 (C–O); δ_H(300 MHz; $CDCl_3$) 4.16 [1 H, d, *J* 2, C*H*(O)CHC=O], 4.36 [1 H, d, *J* 2, CH(O)C*H*C=O], 7.31–7.40 (2 H, m, pyridyl), 7.57 (1 H, ddd, *J* 8, 8 and 2, 6-H or 7-H naphthyl), 7.63 (1 H, ddd, *J* 8, 8 and 1.5, 6-H or 7-H naphthyl), 8.03 (1 H, dd, *J* 8 and 2, 3-H naphthyl), 7.91–7.98 (2 H, m, 8-H and 5-H naphthyl), 7.89 (1 H, br d, *J* 8, 4-H naphthyl), 8.55 (1 H, br s, 1-H naphthyl) and 8.64–8.70 (2 H, m, pyridyl); δ_C(75.5 MHz; $CDCl_3$) 57.6 and 60.6 (C epoxide), 120.5 (CH), 123.6 (2 × CH), 127.2 (CH), 127.9 (CH), 129.0 (CH), 129.2 (CH), 129.7 (CH), 130.6 (CH), 132.4 (C), 132.6 (C), 136.0 (C), 144.6 (C), 150.2 (2 × CH) and 192.2 (C=O); *m*/*z* 275 (M^+, 20.6) and 83 (100%) (Found: M^+, 275.0948. $C_{18}H_{13}O_2N$ requires *M*, 275.0946). Chiral HPLC (20:80, isopropanol–hexane, 1 cm^3 min^{-1}): 18.3 and 30.0 min.

***trans*-(±)-2,3-Epoxy-3-phenyl-1-(2-furyl)propan-1-one 15.** (87%), Mp 59–60 °C (from diethyl ether–hexane) (Found: C, 72.87; H, 4.43. $C_{13}H_{10}O_3$ requires C, 72.89; H, 4.70%); ν_{max}(KBr)/cm^{-1} 1680 (C=O), 1271 and 888 (C–O); δ_H(300 MHz; $CDCl_3$) 4.13 [1 H, d, *J* 1.8, C*H*(O)CHC=O], 4.15 (1 H, d, *J* 1.8, CH(O)C*H*C=O], 6.60 (1 H, dd, *J* 3.6 and 1.8, 4-H furyl), 7.32–7.41 (5 H, m, PhH), 7.46 (1 H, dd, *J* 3.6 and 0.6, 3-H furyl) and 7.68 (1 H, dd, *J* 1.8 and 0.6, 5-H furyl); δ_C(75.5 MHz; $CDCl_3$) 59.5 and 60.0 (C epoxide), 112.6 (CH), 119.5 (CH), 125.8 (2 × CH), 128.7 (2 × CH), 129.0 (CH), 135.4 (C), 147.6 (C-5 furyl), 151.2 (C-2 furyl) and 182.0 (C=O); *m*/*z* 214 (M^+, 18.1) and 95 (100%) (Found: M^+, 214.0639. $C_{13}H_{10}O_3$ requires *M*, 214.0630). Chiral HPLC (10:90, isopropanol–hexane, 1 cm^3 min^{-1}): 15.3 and 16.8 min.

***trans*-(±)-2,3-Epoxy-3-phenyl-1-(2-pyridyl)propan-1-one 17.** (93%), Mp 94–95 °C (from dichloromethane–hexane); ν_{max}(KBr)/cm^{-1} 1696 (C=O), 885 and 787 (C–O); δ_H(300 MHz; $CDCl_3$) 4.08 [1 H, d, *J* 2, C*H*(O)CHC=O], 5.11 [1 H, d, *J* 2, CH(O)C*H*C=O], 7.30–7.40 (5 H, m, PhH), 7.49 (1 H, ddd, *J* 8, 5 and 1, 5-H pyridyl), 7.85 (1 H, ddd, *J* 8, 8 and 1, 4-H pyridyl), 8.08 (1 H, ddd, *J* 8, 1 and 1, 3-H pyridyl) and 8.64 (1 H, ddd, *J* 5, 2 and 1, 6-H pyridyl); δ_C(75.5 MHz; $CDCl_3$) 50.3 and 59.2 (C epoxide), 122.3 (CH), 126.1 (2 × CH), 127.8 (CH), 128.6 (2 × CH), 128.9 (CH), 136.5 (C), 137.0 (CH), 149.3 (CH), 152.8 (C) and 193.9 (C=O); *m*/*z* 225 (M^+, 25.6) and 78 (100%) (Found: M^+, 225.0784. $C_{14}H_{11}O_2N$ requires *M*, 225.0789). Chiral HPLC (20:80, isopropanol–hexane, 1 cm^3 min^{-1}): 9.3 and 11.8 min.

***trans*-(±)-2,3-Epoxy-5-phenyl-1-(2-naphthyl)pent-4-en-1-one 19 or 20.** (35%), Mp 131–134 °C (from diethyl ether); ν_{max}(KBr)/cm^{-1} 1664 (C=O), 1626 (C=C), 1234 and 888 (C–O); δ_H(300 MHz; $CDCl_3$) 3.82 [1 H, dd, *J* 8 and 2, CH=CHC*H*(O)CH], 4.43 [1 H, d, *J* 2, CH=CHCH(O)C*H*], 6.11

[1 H, dd, *J* 16 and 8, CH=C*H*CH(O)CH], 6.93 [1 H, d, *J* 16, C*H*=CHCH(O)CH], 7.28–7.46 (5 H, m, PhH), 7.54–7.68 (3 H, m, PhH), 7.87–8.02 (2 H, m, PhH), 8.06 (1 H, dd, *J* 8.5 and 2, 3-H naphthyl) and 8.60 (1 H, s, 1-H naphthyl); δ_C(75.5 MHz; $CDCl_3$) 59.4 and 59.8 (C epoxide), 123.7 and 124.5 (CH=CH), 126.7 (2 × CH), 127.0 (CH), 127.9 (CH), 128.6 (CH), 128.7 (2 × CH), 128.8 (CH), 129.0 (CH), 129.7 (CH), 130.4 (CH), 132.4 (C), 132.9 (C), 135.6 (C), 135.9 (C), 136.4 (CH) and 193.4 (C=O); *m*/*z* 300 (M^+, 6) and 127 (100%) (Found: M^+, 300.1153. $C_{21}H_{16}O_2$ requires *M*, 300.1150). Chiral HPLC (2:98, isopropanol–hexane, 1.3 cm^3 min^{-1}): 52.7 and 60.3 min.

***trans*-(±)-1,2:4,5-Bis(epoxy)-1,5-(2-furyl)-pentan-3-one 23.** (45%); Chiral HPLC (5:95 ethanol–hexane, 0.5 cm^3 min^{-1}): 7.5 and 8.8 min; *meso* diepoxide: 8.1 min.

(±)-Compound 24 or 25. (42%), Mp 163–166 °C (from diethyl ether–hexane); ν_{max}(KBr)/cm^{-1} 1689 (C=O), 1233 and 894 (C–O); δ_H(300 MHz; $CDCl_3$) 4.11 [2 H, d, *J* 2, C*H*(O)CHC=O], 4.29 [2 H, d, *J* 2, CH(O)C*H*C=O], 7.42 (4 H, m, PhH), 7.50 (4 H, distorted t, PhH), 7.63 (2 H, m, PhH_{para}) and 8.02 (4 H, distorted dd, PhH; H_{ortho}); δ_C(75.5 MHz; $CDCl_3$) 58.9 and 61.0 (C epoxide), 126.3 (CH), 128.4 (CH), 128.9 (CH), 134.1 (Ph_{para}), 135.4 (C), 136.6 (C) and 192.8 (C=O); *m*/*z* 370 (M^+, 3.3) and 105 (100%) (Found: M^+, 370.1204. $C_{24}H_{18}O_4$ requires *M*, 370.1205). Chiral HPLC (40:60, isopropanol–hexane, 1 cm^3 min^{-1}): 31.2 and 39.3 min; *meso* diepoxide: 29.9 min.

***trans*-(±)-3,4:6,7-Bis(epoxy)-1,9-diphenylnona-1,6-diene-5-one 27.** (40%); Chiral HPLC (1:99, isopropanol–hexane, 1 cm^3 min^{-1}): 7.8 and 9.1 min.

***trans*-(±)-2,3-Epoxy-3-phenyl-1-(*tert*-butyl)propan-1-one 31 or 32.** (75%); Chiral HPLC (5:95 ethanol–hexane, 1 cm^3 min^{-1}): 9.6 and 14.1 min.

***trans*-(±)-2,3-Epoxy-3-(*tert*-butyl)-1-phenylpropan-1-one 33 or 34.** (70%); Chiral HPLC (5:95 isopropanol–hexane, 0.5 cm^3 min^{-1}): 16.0 and 19.2 min.

***trans*-(±)-2,3-Epoxy-5-phenyl-1-(*tert*-butyl)pent-4-en-1-one 35.** (78%); Chiral HPLC (2:98 isopropanol–hexane, 1 cm^3 min^{-1}): 19.1 and 32.0 min.

(±)-Compound 37 or 38. (37%), Mp 189–191 °C (from diethyl ether); ν_{max}(KBr)/cm^{-1} 1669 (C=O), 1277 and 879 (C–O); δ_H(400 MHz; $CDCl_3$) 4.20 [2 H, d, *J* 2, C*H*(O)CHC=O], 4.45 [2 H, d, *J* 2, CH(O)C*H*C=O], 7.48 (4 H, s, PhH), 7.58 (2 H, distorted dt, 6-H or 7-H naphthyl), 7.65 (2 H, distorted dt, 6-H or 7-H naphthyl), 7.88–8.00 (6 H, m, 4-H, 5-H, 8-H naphthyl), 8.07 (2 H, dd, *J* 8.5 and 1.8, 3-H naphthyl) and 8.59 (2 H, s, 1-H naphthyl); δ_C(100.6 MHz; $CDCl_3$) 59.1 and 61.1 (C epoxide), 123.7 (CH), 126.4 (4 × CH, Ph), 127.1 (CH), 127.9 (CH), 128.9 (CH), 129.1 (CH), 129.7 (CH), 130.5 (CH), 132.4 (C), 132.8 (C), 136.0 (C), 136.7 (C) and 192.7 (C=O); *m*/*z* 470 (M^+, 0.1), 452 ($M - H_2O$) and 14 (100%) (Found: M^+, 470.1492. $C_{32}H_{22}O_4$ requires *M*, 470.1518). Chiral HPLC (60:40, isopropanol–hexane, 1 cm^3 min^{-1}): 34.4 and 37.9 min.

General procedure for the epoxidation of enones using peroxide

To a solution of NaOH (206 mg, 5.15 mmol) in distilled water (0.5 cm^3), cooled in an ice–water bath, were added CH_2Cl_2 or hexane (1.8 cm^3), poly-L-leucine or poly-D-leucine (111 mg) and 30% aqueous H_2O_2 (1 cm^3, 9 mmol). The mixture was allowed to warm to room temperature and stirred for 6 h to allow the polymer to swell. The α,β-unsaturated ketone (0.43 mmol) was then added to the mixture. If after 18 h the reaction was incomplete, a solution of NaOH (30 mg) in 30% aqueous H_2O_2 (0.3 cm^3) was added to the reaction mixture and stirring was continued until the reaction was complete. After diluting the reaction mixture with ethyl acetate the catalyst was filtered off and the filtrate was washed with water and brine, dried ($MgSO_4$) and the solvent removed under reduced pressure to afford the crude product, which was analysed using chiral HPLC to determine the enantiomeric excess.

Modification for enones 9, 11, 13 and 17. Distilled water (1.8 cm^3) was used instead of 0.5 cm^3.

***trans*-(−)-2,3-Epoxy-3-(2-furyl)-1-(2-naphthyl)propan-1-one 7.** (75%), Mp 72–73 °C; $[\alpha]_D$ −135 (*c* 1 in $CHCl_3$); Chiral HPLC (5:95, isopropanol–hexane, 1 cm^3 min^{-1}): 32.7 min.

***trans*-(−)-2,3-Epoxy-1-phenyl-3-(2-pyridyl)propan-1-one 9.** (84%), Mp 74 °C (dichloromethane–hexane); $[\alpha]_D$ −161 (*c* 1.04 in $CHCl_3$); Chiral HPLC (20:80, isopropanol–hexane, 1 cm^3 min^{-1}): 13.2 min.

***trans*-(+)-2,3-Epoxy-1-phenyl-3-(3-pyridyl)propan-1-one 11.** (70%), Mp 75 °C (dichloromethane–hexane); $[\alpha]_D$ +155 (*c* 1.04 in $CHCl_3$); Chiral HPLC (20:80, isopropanol–hexane, 1 cm^3 min^{-1}): 26.2 min.

***trans*-(−)-2,3-Epoxy-1-(2-naphthyl)-3-(4-pyridyl)propan-1-one 13.** (67%), Mp 127 °C (dichloromethane–hexane); $[\alpha]_D$ −91 (*c* 1.05 in $CHCl_3$); Chiral HPLC (20:80, isopropanol–hexane, 1 cm^3 min^{-1}): 18.3 min.

***trans*-(−)-2,3-Epoxy-3-phenyl-1-(2-furyl)propan-1-one 15.** (85%), Mp 58–60 °C; $[\alpha]_D$ −205 (*c* 1 in $CHCl_3$); Chiral HPLC (10:90, isopropanol–hexane, 1 cm^3 min^{-1}): 16.8 min.

***trans*-(+)-2,3-Epoxy-3-phenyl-1-(2-furyl)propan-1-one 15.** (98%), Mp 56–57 °C; $[\alpha]_D$ +218 (*c* 1 in $CHCl_3$); Chiral HPLC (10:90, isopropanol–hexane, 1 cm^3 min^{-1}): 15.3 min.

***trans*-(−)-2,3-Epoxy-1-phenyl-3-(2-pyridyl)propan-1-one 17.** (74%), Mp 70 °C (dichloromethane–hexane); $[\alpha]_D$ −128 (*c* 1 in $CHCl_3$); Chiral HPLC (20:80, isopropanol–hexane, 1 cm^3 min^{-1}): 9.2 min.

***trans*-(−)-2,3-Epoxy-5-phenyl-1-(2-naphthyl)pent-4-en-1-one 19.** (78%), Mp 95–97 °C; $[\alpha]_D$ −153 (*c* 1 in $CHCl_3$); Chiral HPLC (2:98, isopropanol–hexane, 1.3 cm^3 min^{-1}): 52.7 min.

***trans*-(+)-2,3-Epoxy-5-phenyl-1-(2-naphthyl)pent-4-en-1-one 20.** (76%), Mp 97–99 °C; $[\alpha]_D$ +159 (*c* 1 in CH_2Cl_2); Chiral HPLC (2:98, isopropanol–hexane, 1.3 cm^3 min^{-1}): 60.3 min.

***trans*-(−)-1,2:4,5-Bis(epoxy)-1,5-bis(2-furyl)pentane-3-one 23.** (60%); ν_{max}(neat)/cm^{-1} 1670 (C=O), 1278 (C–O); $[\alpha]_D$ −140 (*c* 0.05 in $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 4.16 [2 H, d, *J* 1.9, C*H*(O)CHC=O], 4.43 [2 H, d, *J* 1.9, CH(O)C*H*C=O], 7.26, 7.43 (6 H, m, 3-H furyl, 4-H furyl, 5-H furyl); *m*/*z* 246 (M^+, 2.7) and 91 (100%) (Found: M^+, 246.0528, $C_{13}H_{10}O_5$ requires *M*, 246.0804). Chiral HPLC (5:95, ethanol–hexane, 0.5 cm^3 min^{-1}): 8.8 min.

Compound 24. (74%), Chiral HPLC (40:60, isopropanol–hexane, 1 cm^3 min^{-1}): 39.3 min.

Compound 25. (91%), Chiral HPLC (40:60, isopropanol–hexane, 1 cm^3 min^{-1}): 31.2 min.

***trans*-(−)-3,4:6,7-Bis(epoxy)-1,9-diphenylnona-1,6-dien-5-one 27.** (50%), ν_{max}(neat)/cm^{-1} 1653 (C=O), 1525 (C=C) and 1275 (C–O); $[\alpha]_D$ −23 (*c* 0.48 in $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 4.16 [2 H, d, *J* 1.9, C*H*(O)CHC=O], 4.44 [2 H, d, *J* 1.9, CH(O)C*H*C=O] and 7.00–7.59 [14 H, m, PhH, CH=C*H*CH(O)CH, C*H*=CH-CH(O)CH]; *m*/*z* 318 (M^+, 0.3) and 57 (100%) (Found: M^+, 318.1256. $C_{12}H_{18}O_3$ requires *M*, 318.1266). Chiral HPLC (1:99, isopropanol–hexane, 1 cm^3 min^{-1}): 8.0 min.

***trans*-(−)-2,3-Epoxy-3-phenyl-1-(*tert*-butyl)propan-1-one 31.** (92%), Mp 68–70 °C (from diethyl ether–hexane); ν_{max}(KBr)/cm^{-1} 1706 (C=O), 1240 and 881 (C–O); $[\alpha]_D$ −162 (*c* 0.63 in $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 1.24 (9 H, s, CCH_3), 3.86 [2 H, d, *J* 1.9, C*H*(O)CHC=O and CH(O)C*H*C=O] and 7.29–7.38 (5 H, m, PhH); δ_C(100.6 MHz; $CDCl_3$) 25.7 (CCH_3), 43.6 (CCH_3), 59.1 and 59.3 (C epoxide), 125.6 (2 × CH), 128.7 (2 × CH), 128.9 (CH), 135.7 (C) and 208.1 (C=O); *m*/*z* 204. (M^+, 31) and 57 (100%) (Found: M^+, 204.1150. $C_{13}H_{16}O_2$ requires *M*, 204.1160). Chiral HPLC (5:95 ethanol–hexane, 1 cm^3 min^{-1}): 9.5 min.

***trans*-(+)-2,3-Epoxy-3-phenyl-1-(*tert*-butyl)propan-1-one 32.** (90%), mp 69.5–71.5 °C (from diethyl ether–hexane); $[\alpha]_D$ +209 (*c* 0.2 in $CHCl_3$); Chiral HPLC (5:95 ethanol–hexane, 1 cm^3 min^{-1}): 17.8 min.

***trans*-(−)-2,3-Epoxy-3-(*tert*-butyl)-1-phenylpropan-1-one 33.** (85%); ν_{max}(KBr)/cm^{-1} 1692 (C=O), 1231 and 881 (C–O); $[\alpha]_D$ −14 (*c* 0.20 in $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 1.02 (9 H, s, CCH_3), 2.94 [1 H, d, *J* 2.2, C*H*(O)CHC=O], 4.09 [1 H, d, *J* 2.2,

CH(O)C*H*C=O], 7.45–7.60 (3 H, m, PhH) and 7.97–8.01 (2 H, m, PhH); δ_C(100.6 MHz; $CDCl_3$) 54.9 and 67.6 (C epoxide), 128.2 (2 × CH), 128.8 (2 × CH), 133.7 (CH), 135.6 (C) and 195.0 (C=O); *m/z* 204 (M^+, 0.1) and 105 (100%) (Found: M^+, 204.1150. $C_{13}H_{16}O_2$ requires *M*, 204.1149). Chiral HPLC (5:95 isopropanol–hexane, 0.5 cm^3 min^{-1}): 16.1 min.

***trans*-(+)-2,3-Epoxy-3-(*tert*-butyl)-1-phenylpropan-1-one 34.** (86%); $[\alpha]_D$ +10 (*c* 0.53 in $CHCl_3$); Chiral HPLC (5:95 isopropanol–hexane, 0.5 cm^3 min^{-1}): 20.5 min.

***trans*-(−)-2,3-Epoxy-5-phenyl-1-(*tert*-butyl)pent-4-en-1-one 35.** (90%); ν_{max}(neat)/cm^{-1} 1682 (C=O), 1618 (C=C), 1286 and 754 (C–O); $[\alpha]_D$ −14 (*c* 0.5 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 1.25 (9 H, s, CCH_3), 3.52 [1 H, dd, *J* 1.5 and 7.9, C*H*(O)CHC=O], 3.88 [1 H, d, *J* 1.5, CH(O)C*H*C=O], 5.95 [1 H, dd, *J* 7.9 and 16.0, CH=C*H*CH(O)CH], 6.85 [1 H, d, *J* 16.0, C*H*=CHCH(O)CH] and 7.29–7.40 (5 H, m, PhH); δ_C(100.6 MHz; $CDCl_3$) 25.5, 25.6 (CCH_3), 43.6 (CCH_3), 57.1 and 59.7 (C epoxide), 124.5 [CH=*C*HCH(O)CH], 126.6 (2 × CH), 128.6 (2 × CH), 128.7 (CH), 135.5 (C), 136.1 [*C*H=CHCH(O)CH] and 208.6 (C=O); *m/z* 230 (M^+, 14.2) and 57 (100%) (Found: M^+, 230.1301. $C_{15}H_{18}O_2$ requires *M*, 230.1309). Chiral HPLC (2:98 isopropanol–hexane, 1 cm^3 min^{-1}): 18.9 min.

General procedure for the epoxidation of enones using perborate

To a 0.43 mol dm^{-3} solution of NaOH (1 cm^3, 0.43 mmol) were sequentially added distilled water (1 cm^3), $NaBO_3 \cdot 4H_2O$ (132 mg, 0.86 mmol), CH_2Cl_2 (2 cm^3), poly-L-leucine or poly-D-leucine (111 mg) and aliquat 336 (1 drop). The mixture was stirred at room temperature for 6 h and the α,β-unsaturated ketone (111 mg, 0.43 mmol) was added to it. The reaction was followed by TLC and stirring was continued until completion. After diluting the reaction mixture with ethyl acetate the catalyst was filtered off and the filtrate was washed with water and brine, dried and evaporated to afford the crude product, which was analysed using chiral HPLC to determine the enantiomeric excess.

Compound 37. (82%), Mp 181–184 °C; $[\alpha]_D$ −264 (*c* 1 in CH_2Cl_2); Chiral HPLC (60:40, isopropanol–hexane, 1 cm^3 min^{-1}): 37.9 min.

Compound 38. (82%), Mp 178–183 °C; $[\alpha]_D$ +252 (*c* 1 in CH_2Cl_2); Chiral HPLC (60:40, isopropanol–hexane, 1 cm^3 min^{-1}): 34.4 min.

Epoxidation of enone 3 using percarbonate

To a mixture of distilled water (1 cm^3), $Na_2CO_3 \cdot 1.5H_2O_2$ (46 mg, 0.44 mmol relative to H_2O_2) and CH_2Cl_2 (0.9 cm^3) were added poly-L-leucine (56 mg) and aliquat 336 (1 drop). The mixture was stirred at room temperature for 6 h and **3** (56 mg, 0.22 mmol) was added to the mixture. After 20 h $Na_2CO_3 \cdot 1.5H_2O_2$ (92 mg, 0.88 mmol) was added to it and the mixture was stirred for a further 42 h. After diluting the reaction mixture with ethyl acetate the catalyst was filtered off and the filtrate was washed with water and brine, dried and evaporated to afford **4** as a white solid, which was analysed using chiral HPLC.

Epoxidation of enone 3 using *tert*-butyl hydroperoxide

As for the general procedure for the epoxidation of enones using hydrogen peroxide except that 3 mol dm^{-3} *tert*-butyl hydroperoxide in isooctane (approx. 7 equiv.) was used instead of hydrogen peroxide.

With dichloromethane as solvent the yield of compound **4** was 62% (36% ee); with hexane as solvent 71% (47% ee) as determined by chiral HPLC *vide supra*.

General polymerization procedure

To a solution of 0.50 g (3.18 mmol) L-leucine-*N*-carboxyanhydride in CH_2Cl_2 (anhydrous; 15 cm^3) were added 0.053 mmol of the diamine. After stirring for three days under an argon atmosphere at ambient temperature the solvent was removed under reduced pressure. The residue was washed with diethyl ether and dried *in vacuo* to yield polymerized L-leucine (340 mg).

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