Juliá–Colonna asymmetric epoxidation reactions under non-aqueous conditions: rapid, highly regio- and stereo-selective transformations using a cheap, recyclable catalyst

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The asymmetric oxidation of some enones (Table 1), selected dienones **3**–**5**, and a trienone **13** is accomplished using poly-L-leucine or poly-D-leucine and urea hydrogen peroxide under non-aqueous conditions. One of the resultant epoxy ketones **6** has been converted into the δ-lactones **19** and **22**.

Introduction and background information

There is considerable current interest in the asymmetric epoxidation of α,β-unsaturated carbonyl compounds, as succinctly summarised by Lygo and Wainwright.[1] Our contribution to this area has concentrated on the development of the Juliá–Colonna oxidation reaction.[2] Along with others,[3] we have found that the protocol is appropriate for the epoxidation of a wide range of α,β-unsaturated ketones.[4]

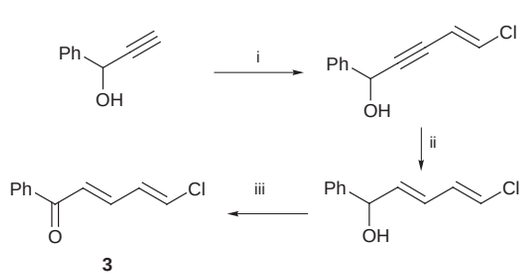
In this paper we describe the use of a non-aqueous variant of the Juliá–Colonna reaction for the epoxidation of dienones and trienones.[5]

Results and discussion

Asymmetric epoxidation reactions

The recently described non-aqueous conditions for the Juliá–Colonna oxidation allow chalcone-type enones to be oxidized rapidly to give epoxides in good to excellent enantiomeric excess (Table 1). It was of interest to investigate the transformation of dienones and trienones under similar conditions.

The dienones **1** and **2** were prepared by standard aldol condensations and subjected to non-aqueous Juliá–Colonna epoxidation conditions using poly-L-leucine as the catalyst to furnish the corresponding epoxides **6** and **7** in good yield (85–95%) and excellent enantiomeric excess (85–95%). Similarly the chloro compound **3**, prepared as outlined in Scheme 1, afforded the



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Scheme 1 *Reagents and conditions:* i, ClCHCHCl, $Pd(PPh_3)_4$, CuI, piperidine, THF, 0 °C, 1 h, 98%; ii, Red-Al®, diethyl ether, room temp., 45 min, 96%; iii, MnO_2, CH_2Cl_2, room temp., 2 h, 68%.

epoxide **8** (55% yield, 86% ee). The esters **4** and **5** were readily prepared from phenylglyoxal monohydrate in *ca.* 50% yield (Scheme 2). Epoxidation of these substrates was rapid (5 h), high yielding (80–90%) and gave products with high enantiomeric excesses (≥90%). It is noteworthy that the oxidation is

Table 1 Oxidation of some simple α,β-unsaturated ketones

Reagents and conditions: i, urea–H_2O_2, poly-L-leucine, DBU, THF.

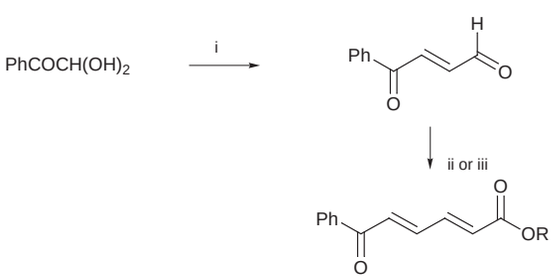
Substituent (R)	*t*/h	Yield (%)	Ee[a] (%)
Ph	0.5	90	92
2-naphthyl	0.5	91	91
$C(CH_3)_3$	6.0	71	94
$CH(CH_3)C_2H_5$	24.0	87	96
$CH_2CH_2CH_3$	24.0	85	94
CH_2CH_3	20.0	80	82

[a] Determined by chiral HPLC.

1	R^1 = Ph; R^2 = β-naphthyl	**6**
2	R^1 = 2-furyl; R^2 = β-naphthyl	**7**
3	R^1 = Cl; R^2 = Ph	**8**
4	R^1 = CO_2Me; R^2 = Ph	**9**
5	R^1 = $CO_2{}^tBu$; R^2 = Ph	**10**

regioselective; no attack of the ene ester moiety was observed under these reaction conditions.

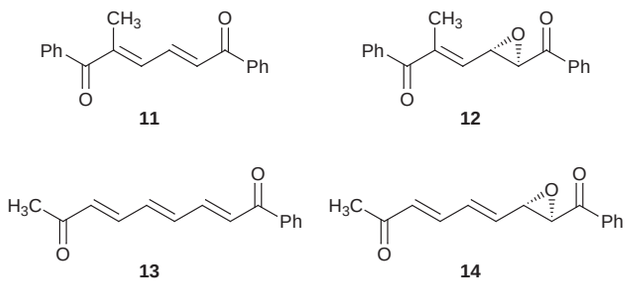
Regioselective oxidation was also observed for the dienone **11** which furnished the epoxide **12** in 70% yield (92% ee). Obviously the trisubstituted alkene unit is not as readily oxidized as the disubstituted site.



4 R = Me
5 R = ^{t}Bu

Scheme 2 *Reagents and conditions:* i, molecular sieves, $Ph_3PCHCHO$, toluene, 70%; ii, Ph_3PCHCO_2Me, toluene, 53%; iii, $Ph_3PCHCO_2{}^tBu$, toluene, 58%.

Finally the triene dione **13** is rapidly transformed under the standard oxidation conditions to afford the monoepoxide **14** in fair yield (43%) and good enantiomeric excess (90%). The modest yield may reflect the formation of a reactive diepoxide. Further oxidation of the monoepoxide **14** gave a plethora of unidentified materials.



The absolute stereochemistry of the products **6**–**10**, **12** and **14** is assumed to be that described, on the basis of literature precedent.[6]

Further transformations of the epoxy ketone 6

We have been anxious to illustrate the utility of the chiral epoxides derived from the Juliá–Colonna methodology.[7] In this context we have explored further transformations of the readily available epoxy ketone **6**.

The ketone **6** was treated with osmium tetroxide under standard dihydroxylation conditions (room temperature being 18 °C) to give a mixture of the two diols **15** and **16** in a 5:3 ratio (determined by NMR of the crude product) and 73% overall yield (Scheme 3). Clearly the presence of the epoxide group does not exercise good control over the osmylation process at the adjacent double bond. Carrying out the reaction at −40 °C gave the diols **15** and **16** in a 2:1 ratio respectively after 1 week and further decreasing the temperature to −78 °C improved the ratio to 3:1 but increased the reaction time to 18 days.

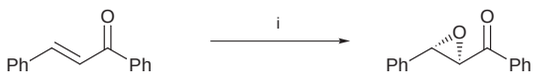
Epoxydiol **15** was obtained as a crystalline solid in 90% yield using the Sharpless AD-mix-α reagent. In complementary fashion AD-mix-β gave the epoxydiol **16** in 95% yield. Protection of the diol unit in compound **15** gave the acetonide **17** which formed the β-hydroxy ketone **18** on treatment with lithium cyanocuprate. (The latter reaction is reminiscent of the epoxy ring opening reactions promoted by samarium diiodide.[8]) Conversion of the β-hydroxy ketone **18** under Baeyer–Villiger oxidation conditions,[9] followed by treatment with acid, led to spontaneous cyclisation and formation of the lactone **19**. The non-optimised yield for the last three reactions was *ca.* 17%. The epoxide **16** gave the acetonide **20**, the ketol **21** and the lactone **22** in a similar three-step sequence. Clearly this methodology could give rise to 5-C-linked deoxyribonucleosides. The requisite starting materials are available by reaction of treatment of diene **1** with oxidant in the presence of poly-D-leucine to give the epoxide *ent*-**6** which was converted into the diols *ent*-**15** and *ent*-**16** in a 5:3 ratio respectively, using osmium tetroxide.

Repeated use of the catalyst

Flisak, Lantos *et al.* reported that poly-L-leucine can be recycled when employed in the original Juliá–Colonna conditions[10] and we have intimated that the same is true using the new non-aqueous protocol. In Table 2 we give evidence of this, using the standard chalcone reaction to monitor the long term effectiveness of the catalyst.

Clearly the catalyst, which is now commercially available in bulk,[11] suffers little damage during the transformation: the reaction time lengthens but the yield and the enantiomeric excess remain high. For oxidations which require longer reaction times, for example when using *tert*-butyl styryl ketone as the substrate (Table 3), the catalyst becomes progressively less efficient. However, it is noteworthy that the catalyst may be reactivated simply by washing with 4 M aqueous sodium hydroxide.

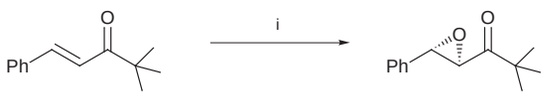
Table 2 Oxidation of chalcone using the same batch of catalyst



Reagents: i, urea–H_2O_2, diaminopropane-bound poly-L-leucine, DBU, THF. After each reaction the catalyst was recovered, dried and reused.

Run	*t*/h	Conversion (%)	Ee (%)
1	1	>95	97
2	1	>95	97
3	1	>95	98
4	1	>95	97
5	2.5	>95	97
6	>4	>95	96

Table 3 Oxidation of *tert*-butyl styryl ketone using the same batch of catalyst



Reagents: i, urea–H_2O_2, diaminopropane-bound poly-L-leucine, DBU, THF. After each reaction the catalyst was recovered, dried and reused.

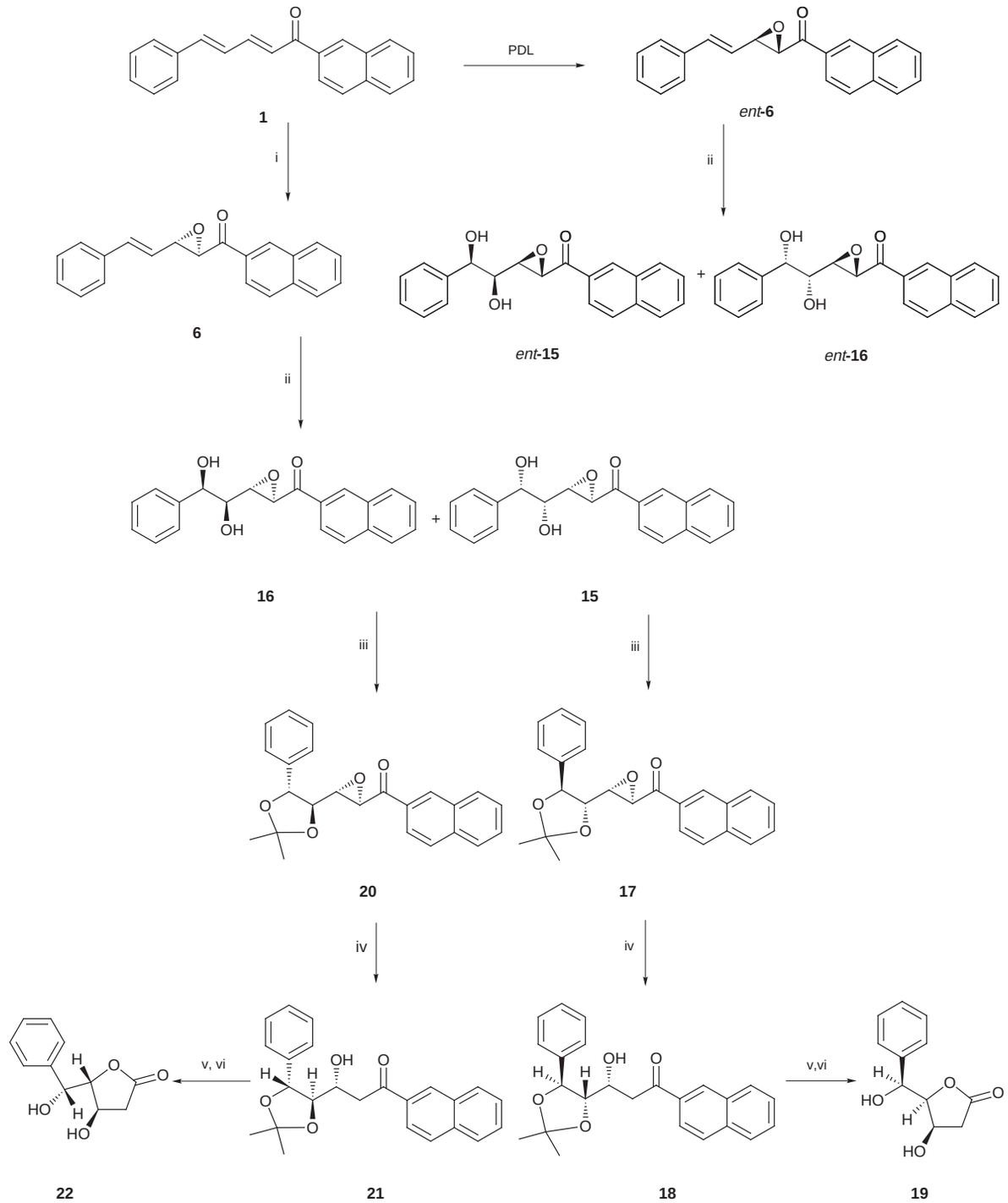
Run	*t*/h	Conversion[a] (%)	Ee (%)
1	6	99	97
2	6	100	92
3	6	66	93
4	6	48	85
5	6	49	79
			Reactivation[b]
6	6	98	96
7	6	80	91
8	6	65	88
9	6	51	78
10	6	40	75

[a] Conversion calculated by HPLC using UV detection (254 nm): the epoxide:enone absorption at this wavelength was taken as 2.0:1. [b] Old catalyst washed with 4 M aqueous NaOH and 10% fresh catalyst added to compensate weight loss.

Experimental

Dichloromethane was refluxed over and distilled from calcium hydride under dry nitrogen; light petroleum (bp 40–60 °C) was distilled before use to remove involatile fractions; tetrahydrofuran was refluxed over and distilled from sodium wire and benzophenone under dry nitrogen. All other solvents were used as supplied without prior purification. The pH 7 buffer solution was prepared by dissolving potassium phosphate (85 g, KH_2PO_4) and sodium hydroxide (14.5 g) in distilled water (950 ml).

Flash chromatography was performed using Merck 60 silica gel (40–63 μm). Thin layer chromatography (TLC) was carried out using glass plates coated with Merck 60F-254 silica gel. The plates were observed either under ultraviolet light (254 nm), or via treatment with potassium permanganate, *p*-anisaldehyde, 0.2% w/v cerium(IV) sulfate and 5% ammonium molybdate in 2 M sulfuric acid, or 0.5% ninhydrin in methanol. Chiral HPLC analyses were performed on a Gilson instrument equipped with the chiral column Chiralpak® AD, an ultraviolet detector



Scheme 3 *Reagents and conditions:* i, poly-L-leucine, THF, DBU, urea–H_2O_2, room temp.; ii, OsO_4, *N*-methylmorpholine *N*-oxide, acetone–H_2O (8 : 1), room temp.; iii, TsOH, $(CH_3)_2C(OCH_3)_2$, acetone, $CuSO_4$, room temp.; iv, CH_3Li, CuCN, CH_2Cl_2, −78 °C; v, MCPBA, CH_2Cl_2, pH 7 buffer solution, room temp.; vi, CF_3CO_2H, H_2O, room temp.

(254 nm) and a flow rate 1.0 ml min^{-1}. Chiral shift ^1H NMR experiments were performed by complexing the substrates with 0.1–0.5 equivalents of enantiomerically pure $Eu(hfc)_3$.

Melting points were recorded on an electrothermal instrument and are uncorrected.

NMR spectra (^1H and ^{13}C) were recorded on a Bruker AMX400, DRX400, AC300, AM250, AC200 and Varian 300 Gemini 2000 spectrometers. Chemical shifts (δ) are quoted in ppm and the coupling constants (J) in Hz. The spectra taken in d-chloroform or d_4-methanol were calibrated using a trace of tetramethylsilane; $^1H = 0.00$. Spectra taken in d_3-acetonitrile were calibrated using the CHD_2CN solvent peak; $^1H = 2.94$ ppm. ^{13}C spectra were calibrated using the appropriate solvent peak; chloroform = 77.7 ppm.

Infrared spectra were recorded on a Nicolet Magna-550 Fourier Transform spectrometer. For clarity, only the characteristic peaks are recorded.

Mass spectra were recorded on Kratos profile HV3, CIPOS and TRIO1000 spectrometers.

Optical rotations were measured on an Optical Activity Ltd. AA-1000 polarimeter operating at 589 nm corresponding to the sodium D line. The concentrations quoted are given in g per 100 ml.

Elemental analyses were obtained by the Departmental microanalysis service.

5-Phenyl-1-(2-naphthyl)penta-2,4-dien-1-one 1

To a solution of 2-acetonaphthone (9.9 g, 75 mmol) in metha-

nol (400 ml) was added *trans*-cinnamaldehyde (13.4 g, 5.2 mmol) and sodium methoxide (12.0 g, 225 mmol) under a nitrogen atmosphere. After 0.5 h a yellow precipitate had formed. The reaction mixture was stirred for 18 h, after which ice-cold water (100 ml) was added and the reaction stirred for a further 2 h. The reaction mixture was filtered and the precipitate washed with cold ethanol (400 ml). The precipitate was collected as a yellow solid and dried under vacuum. Purification by column chromatography (diethyl ether–light petroleum, 1 : 4) yielded 5-phenyl-1-(2-naphthyl)penta-2,4-dien-1-one **1** (14.35 g, 67% yield) as a yellow solid, mp 114 °C (ethyl acetate) (Found: C, 88.61; H, 5.67. Calculated for $C_{21}H_{16}O$: C, 88.70; H, 5.67%); δ_H (300 MHz, $CDCl_3$) 7.05 (2 H, d, *J* 9.5, H-2, H-3), 7.23 (1 H, d, *J* 6.1, H-5), 7.28–7.41 (3 H, m, Ph), 7.51 (1 H, dd, *J* 1.6, 8.4, H-4), 7.54–7.70 (4 H, m, Np, Ph), 7.87–7.99 (3 H, m, Np), 8.06 (1 H, dd, *J* 1.7, 8.6, Np), 8.49 (1 H, s, Np); δ_C (75 MHz, $CDCl_3$) 123.8, 124.9, 126.1, 126.4, 126.7, 127.2, 127.7, 127.9, 128.2, 128.6, 128.9, 129.1 (14 × CH, C-2, C-3, C-4, C-5, Np, Ph), 132.0, 134.8, 135.0, 135.6 (4 × C, Np, Ph), 141.3, 144.0 (2 × CH, Np), 189.7 (1 × C=O, C-1); *m*/*z* (EI) 284 (M^+, 88%), 207 (26), 155 (36), 127 (100).

5-(2-Furyl)-1-(2-naphthyl)penta-2,4-dienone 2

To a solution of 2-acetonaphthone (8.94 g, 53.0 mmol) in methanol (300 ml) were added sodium methoxide (8.10 g, 150.0 mmol, 3 equiv.) and *trans*-3-(2-furyl)acrolein (6.10 g, 50.0 mmol). When TLC analysis (50% Et_2O–light petroleum) indicated total consumption of starting material after stirring for 15 h, ice-cold water (~300 ml) was added and the mixture stirred for a further 2 h. The reaction mixture was filtered, washing with methanol, to yield the desired product as a yellow solid which was recrystallised from light petroleum–EtOAc (10.8 g, 79%), mp 119 °C (ethyl acetate–light petroleum) (Found: C, 82.93; H, 5.14. Calculated for $C_{19}H_{14}O_2$: C, 83.19; H, 5.14) (Found: M^+, 274.09953. $C_{19}H_{14}O_2$ requires 274.09937); ν_{max} (NaCl)/cm^{-1} 1648 (strong, C=O unsaturated ketone), 1577 (C=C); δ_H (300 MHz, $CDCl_3$) 6.42–6.49 (2 H, m, 2 × Fr), 6.76 (1 H, d, *J* 15.2, H-5), 6.93 (1 H, d, *J* 15.2, H-4), 6.97 (1 H d, *J* 15.2, H-2), 7.21 (1 H, app t, *J* 6.2 and 8.5, H-3), 7.44–7.65 (4 H, m, 4 × Np, Fr), 7.84–8.06 (4 H, m, 4 × Np), 8.46 (1 H, s, Np); δ_C (75 MHz, $CDCl_3$) 112.3, 124.5, 125.4, 125.5, 126.8, 127.8, 127.9, 128.3, 128.5, 129.6, 129.8, 132.3 (14 × CH, C-2, C-3, C-4, C-5, C-7, C-8, C-9, Np), 135.6, 136.0, 143.9, 144.3 (4 × C, Np), 172.5 (1 × C, C-6), 190.1 (1 × C=O, C-1); *m*/*z* 274 (M^+, 100), 245 (26), 155 (40), 127 (99).

(2*E*,4*E*)-5-Chloro-1-phenylpenta-2,4-dien-1-one 3[12]

A solution of 1-phenylprop-2-yn-1-ol (1.01 g, 7.65 mmol) in dry THF (8 ml) was added dropwise to a stirred mixture of *trans*-1,2-dichloroethylene (3.5 ml, 45 mmol), tetrakis(triphenylphosphine)palladium(0) (0.52 g, 0.45 mmol), cuprous iodide (0.17 g, 0.9 mmol) and piperidine (1.8 ml, 18 mmol) cooled to 0 °C. The resulting mixture was allowed to stir at room temperature for 1 h. Saturated aqueous ammonium chloride (20 ml) was added, the organic phase separated and combined with ethereal extracts (3 × 20 ml) of the aqueous phase. The combined organic extracts were dried and the solvent removed. The residue was purified by flash chromatography; elution with 30% ethyl acetate in light petroleum provided (1*E*)-1-chloro-5-phenylpent-1-en-3-yn-5-ol (1.45 g, 98%) as a red oil (Found: M^+, 192.0337. $C_{11}H_9ClO$ requires *M*, 192.0342); ν_{max} (NaCl)/cm^{-1} 3591 (broad OH); 1729 (C=C); 1602, 1492 (C=C Ar); δ_H (300 MHz, $CDCl_3$) 2.38 (1 H, br s, OH exchanges with D_2O), 5.56 (1 H, br s, H-1) 6.01 (1 H, d, $J_{4,5}$ 13.6, H-4), 6.59 (1 H, d, $J_{5,4}$ 13.6, H-5), 7.31–7.53, (5 × H, m, Ph); δ_C (75 MHz, $CDCl_3$) 65.0 (1 × CH, C-5), 81.6 (1 × CH, C-4), 91.5 (1 × C, C-3), 113.2 (1 × C, Ph), 126.7 (2 × CH, Ph), 128.6 (1 × CH, Ph), 128.8 (2 × CH, Ph), 131.4 (1 × CH, C-1), 140.3 (1 × C, C-2); *m*/*z* 192–194 (M, 2%), 15 (11), 157 (100), 139 (16), 129 (36), 128 (58), 127 (30), 113 (17).

Red-Al® (3.22 M in toluene; 1.60 ml, 5.15 mmol) was added slowly to a stirred solution of the enyne (0.62 g, 3.22 mmol) in dry ether (15 ml) cooled to −25 °C. The mixture was stirred at ambient temperature for 45 min then quenched by the careful addition of ice-cooled water (10 ml). The organic phase was separated and combined with the ethereal extracts of the aqueous phase. The combined organic extracts were dried and the solvent removed to give (1*E*,3*E*)-1-chloro-5-phenylpenta-1,3-dien-5-ol (0.60 g, 96%) as a yellow oil, ν_{max} (NaCl)/cm^{-1} 3602 (broad, OH), 1647, 1600 (C=C diene), 1584, 1492 (C=C Ar); δ_H (300 MHz, $CDCl_3$) 2.26 (1 H, br s exchanges with D_2O, OH), 5.20 (1 H, d, *J* 6.2, H-1), 5.86 (1 H, dd, *J* 6.2, 15.0, H-2), 6.22 (2 H, m, H-3, H-5), 6.44 (1 H, dd, *J* 10.8, 13.2, H-4), 7.2–7.3 (5 H, m, Ph); δ_C (75 MHz, $CDCl_3$) 74.4, 121.6, 126.4, 128.0, 128.8, 132.9, 136.1 (10 × CH, C-1, C-2, C-3, C-4, C-5, Ph), 142.5 (1 × C, Ph); *m*/*z* 194–196 (M, 15%), 159 (10), 158 (68), 157 (28), 130 (36), 129 (100), 128 (83), 127 (37), 115 (48), 77 (25).

The dienol was found to be highly light- and moisture-sensitive, and on standing cyclised to form 2-phenyl-2*H*-pyran.

A mixture of the dienol (0.60 g, 3.08 mmol), activated manganese dioxide (5.36 g, 61.7 mmol) and dry dichloromethane was stirred at room temperature for 2 h. The mixture was filtered through a small pad of Celite and the solvent removed. The residue was recrystallised from dichloromethane–light petroleum to give the *dienone* **3** (406 mg, 68%) as yellow prisms, mp 68–69 °C (dichloromethane–light petroleum) (Found: M^+, 192.0342. $C_{11}H_9ClO$ requires *M*, 192.0342); ν_{max} (NaCl)/cm^{-1} 1661 (C=O), 1645, 1599 (C=C diene), 1577 (C=C Ar); δ_H (300 MHz, $CDCl_3$) 6.70 (2 H, m, H-3, H-4), 7.00 (1 H, d, *J* 15.0, H-2), 7.34 (1 H, ddd, *J* 6.0, 10.8, 15.0, H-5), 7.47 (2 H, m, Ph), 7.56 (1 H, tt, *J* 1.5, 7.2, Ph), 7.93 (2 H, m, Ph); δ_C (75 MHz, $CDCl_3$) 126.0, 128.5, 128.8, 130.5, 132.4, 133.1, 137.9 (9 × CH, C-2, C-3, C-4, C-5, Ph), 140.0 (1 × C, Ph), 190.2 (1 × C=O, C-1); *m*/*z* 192–194 (M, 30%), 158 (13), 157 (100), 129 (37), 128 (37), 127 (14), 115 (20), 105 (35), 77 (71).

Methyl 6-oxo-6-phenylhexanoate 4 and *tert*-butyl 6-oxo-6-phenylhexanoate 5

Phenyl glyoxal monohydrate (1.0 g, 6.57 mmol) was pre-stirred with molecular sieves (200 mg) in anhydrous toluene (50 ml), under an atmosphere of nitrogen for 30 minutes. Formylmethylenetriphenylphosphorane (2.0 g, 6.57 mmol) was added in one portion and stirring continued at room temperature for 16 h, after which time TLC analysis (50% Et_2O–light petroleum) indicated total consumption of starting material. The reaction mixture was filtered to remove the molecular sieves and the filtrate was washed with water (3 × 50 ml). The organic extract was dried ($MgSO_4$) and concentrated *in vacuo* to yield a brown solid. Purification by gradient flash column chromatography (silica/0–15% Et_2O–light petroleum) yielded the desired product (*E*)-PhCOCHCHCHO as a yellow solid, which turned a rusty brown colour upon standing (743 mg, 4.64 mmol, 71%) (Found: C, 75.10; H, 5.06. Calculated for $C_{10}H_8O_2$: C, 74.99; H, 5.03); ν_{max} (NaCl)/cm^{-1} 1687 (C=O, ketone), 1663 (C=O, aldehyde); δ_H (300 MHz, $CDCl_3$) 6.99 (1 H, dd, $J_{3,4}$ 7.5 and $J_{3,2}$ 15.9, H-3), 7.49–7.58 (2 H, m, Ph), 7.63–7.75 (2 H, m, H-2 and Ph), 7.99 (2 H, d, *J* 7.7, Ph), 9.88 (1 H, d, $J_{4,3}$ 7.4, H-4); δ_C (75 MHz, $CDCl_3$) 128.9, 129.1, 134.2, 136.4, 139.1, 142.2, (8 × CH, C-2, C-3, Ph), 189.9 (1 × C=O, C-1), 192.9 (1 × C=O, C-4); *m*/*z* 160 (M^+, 49%), 130 (M^+-CHO, 12), 105 (PhCO, 100).

A smaller amount of the (*Z*)-isomer was isolated from later fractions.

(Methoxycarbonylmethylene)triphenylphosphorane (10.0 g, 30.0 mmol) and the above aldehyde (4.30 g, 27.0 mmol) were stirred at room temperature in toluene (100 ml), under an atmosphere of nitrogen. After 16 hours, TLC analysis (50% Et_2O–light petroleum) indicated completion of the reaction.

Thus, the reaction mixture was diluted with ethyl acetate (30 ml) and washed with water (3 × 30 ml). The organic extract was dried ($MgSO_4$) and concentrated *in vacuo* to give a yellow oil. Purification by gradient flash column chromatography (silica/0–15% Et_2O–light petroleum) yielded methyl 6-oxo-6-phenylhexanoate **4** as a pale yellow solid (3.1 g, 14.4 mmol, 53%) (The remainder of the material isolated was contaminated with Ph_3P=O.) Mp 141 °C (ethyl acetate) (Found: M^+, 216.07831. $C_{16}H_{18}O_3$ requires *M*, 216.07864); ν_{max} (NaCl)/cm^{-1} 1704 (s, C=O ester), 1657 (C=O, ketone); δ_H (300 MHz, $CDCl_3$) 3.81 (3 H, s, OCH_3), 6.30 (1 H, d, *J* 13.8, H-2), 7.38–7.61 (6 H, m, H-3, H-4, H-5, Ph), 7.76 (2 H, d, *J* 7.3, Ph); δ_C (75 MHz, $CDCl_3$) 51.9 (1 × CH_3, O*C*H_3), 128.5, 128.6, 128.8, 131.9, 132.1, 132.2, 133.4, 137.5, 140.6, 141.7 (10 × CH, C-2, C-3, C-4, C-5, Ph), 166.5 (1 × C=O, C-1), 189.9 (1 × C=O, C-6); *m*/*z* 216 (M^+, 34%), 201 (M^+, CH_3, 12), 185 ($M^+ - OCH_3$, 9), 157 ($M^+ - CH_3CO_2$, 100), 129 (157 − CH_2=CH_2, 47), 105 (PhCO, 72).

(*tert*-Butoxycarbonylmethylene)triphenylphosphorane (400 mg, 1.06 mmol) and the above aldehyde (298 mg, 1.86 mmol, 1.75 eq) were stirred at room temperature in toluene (20 ml), under an atmosphere of nitrogen. After 16 hours, TLC analysis (50% Et_2O–light petroleum) indicated completion of reaction. The reaction mixture was diluted with ethyl acetate (30 ml) and washed with water (3 × 30 ml). The organic extract was dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Purification by gradient flash column chromatography (silica/0–15% Et_2O–light petroleum) yielded *tert*-butyl 6-oxo-6-phenylhexanoate **5** as a pale yellow solid (157 mg, 0.61 mmol, 58%). Unreacted starting material was isolated (8%), as was the *cis,trans* product (10%). Physical data for compound **5**: mp 142 °C (diethyl ether) (Found: C, 74.22; H, 7.05. Calculated for $C_{16}H_{18}O_3$: C, 74.40; H, 7.02) (Found: M^+, 258.12552. $C_{16}H_{18}O_3$ requires *M*, 258.12561); ν_{max} (NaCl)/cm^{-1} 1694 (C=O, ester), 1654 (C=O, ketone); δ_H (300 MHz, $CDCl_3$) 1.51 [9 H, s, C(CH_3)$_3$], 6.22 (1 H, d, *J* 14.7, H-2), 7.22–7.44 (3 H, m, H-3, H-4, H-5), 7.50 (2 H, app t, *J* 7.1 and 7.7, Ph), 7.58–7.62 (1 H, m, Ph), 7.96 (2 H, d, *J* 8.5, Ph); δ_C (75 MHz, $CDCl_3$) 28.1 [3 × CH_3, C(*C*H_3)$_3$], 81.2 [1 × C, *C*(CH$_3$)$_3$], 128.6, 128.8, 131.5, 133.3 (7 × CH, C-2, C-3, C-4, C-5, Ph), 137.7 (1 × C, Ph), 140.4, 140.9 (2 × CH, Ph), 165.2 (1 × C=O, C-1), 190.0 (1 × C=O, C-6); *m*/*z* 258 (M^+, 2%), 203 [$M^+ - C(CH_3)_3$, 33], 157 (203 − CO_2, 100), 129 (157 − CH_2=CH_2, 38), 105 (PhCO, 61).

(2*E*,4*E*)-2-Methyl-1,6-diphenylhexa-2,4-diene-1,6-dione 11

A mixture of α-bromopropiophenone (5 g, 23.5 mmol), triphenylphosphine (6.15 g, 23.5 mmol) and dry acetonitrile (60 ml) was refluxed under an atmosphere of nitrogen for 30 h. The mixture was cooled and the volume of the solution reduced by 50% on a rotary evaporator. The resulting precipitate was filtered and washed well with acetonitrile and acetone. The phosphonium salt (9.16 g, 82%) was obtained as a white powder, mp 246.5–248.5 °C (Found: MBr, 395.1560. $C_{27}H_{24}OP$ requires *MBr*, 395.1565); *m*/*z* (FAB^+) 395 (MBr, 100%), 279 (9), 262 (11), 183 (17), 154 (7), 136 (8), 105 (8), 89 (7), 77 (10).

Potassium *tert*-butoxide (70 mg, 0.63 mmol) was added in one portion to a stirred suspension of the phosphonium salt (300 mg, 0.63 mmol) in dry THF (5 ml) and the resulting mixture was stirred at room temperature under an atmosphere of nitrogen for 30 min. A solution of the ketoaldehyde PhCOCH-CHCHO (100 mg, 0.63 mmol) in dry THF (1 ml) was added dropwise and the mixture stirred at room temperature for 4 h. Water (10 ml) was added and the organic phase separated and combined with the ethereal extracts of the aqueous phase. The combined organic extracts were dried and the solvent removed. The residue was purified by flash chromatography; elution with 20% ethyl acetate in light petroleum provided the *dienedione* **11** (74 mg, 43%) as a yellow powder, mp 113–114 °C (ethyl acetate) (Found: M^+, 276.1153. $C_{19}H_{16}O_2$ requires *M*, 276.1150); δ_H (300 MHz, $CDCl_3$) 2.19 (3 H, s, CH_3), 6.80 (1 H, d, *J* 11.5, H-3), 7.12 (1 H, d, *J* 15.4, H-5), 7.3–7.9 (10 H, m, C-4 and Ph); δ_C (75 MHz, $CDCl_3$) 13.9 (1 × CH_3), 128.5, 128.6, 128.8, 129.5, 130.5, 132.3, 137.3, 137.7, 138.3, 144.3 (13 × CH, C-3, C-4, C-5, Ph), 190.0, 198.3 (2 × C=O, C-1, C-6); *m*/*z* 277 (MH^+, 7%), 276 (M, 37), 172 (12), 171 (100), 128 (15), 105 (47), 77 (53%).

(4*E*)-1-Phenylnon-4-ene-2,6-diyne-1,8-diol

A solution of (1*E*)-1-chloro-5-phenylpent-1-en-3-yn-5-ol (0.20 g, 1.04 mmol) in piperidine (3 ml) was purged with nitrogen for 10 min. Bis(benzonitrile)dichloropalladium(II) (20 mg, 0.052 mmol) was added and the mixure stirred at ambient temperature for 15 min. The mixture was cooled to 0 °C and but-3-yn-2-ol (0.12 ml, 1.56 mmol) and cuprous iodide (20 mg, 0.104 mmol) were added. The resulting heterogeneous mixture was allowed to stir at 0 °C for 1 h and at room temperature for 1 h. Saturated aqueous ammonium chloride (5 ml) was added and the mixture extracted with ether (4 × 15 ml). The combined organic extracts were dried and the solvent removed. The residue was purified by flash chromatography; elution with 50% ethyl acetate in light petroleum afforded the *enediyne* (0.10 g, 43%) as an orange oil (Found: M^+, 226.0994. $C_{15}H_{14}O_2$ requires *M*, 226.0994); ν_{max} (NaCl)/cm^{-1} 3598 (broad, OH); 1643 (C=C); 1601, 1491 (C=C Ar); δ_H (300 MHz, $CDCl_3$) 1.45 (3 H, d, *J* 6.5, C-9), 4.64 (1 H, q, *J* 6.5, H-8) 5.58 (1 H, s, H-1), 6.04 (2 H, s, C-2, C-3), 7.3–7.4 (3 H, m, Ph), 7.5 (2 H, m, Ph) [OH not visible]; δ_C (75 MHz, $CDCl_3$) 24.1 (1 × CH_3, C-9), 58.8 (1 × CH, C-8); 65.0 (1 × CH, C-1), 82.0, 84.6 (2 × C, C-6, C-7), 93.9, 96.5 (2 × C, C-4, C-5), 120.5, 121.2, 126.7, 128.6, 128.8, 140.4 (6 × CH, Ph); *m*/*z* 226 (M, 3%), 207 (12), 179 (66), 178 (53), 166 (18), 165 (100), 153 (28), 152 (34), 115 (32), 105 (96), 77 (55).

(2*E*,4*E*,6*E*)-1-Phenylnona-2,4,6-triene-1,8-dione 13

The enediyne (0.10 g, 0.44 mmol) and Red-Al® (3.22 M in toluene; 0.44 ml, 1.42 mmol) in ether were reacted following the procedure described above for the reduction of 1-chloro-5-phenylpent-1-en-3-yn-5-ol. The *trienediol* (0.10 g, 98%) was obtained as a yellow oil and was oxidized without further purification. Thus, a mixture of the trienediol (32 mg, 0.14 mmol), activated manganese dioxide (0.48 g, 5.57 mmol) and dry dichloromethane was stirred at room temperature for 2.5 h. The reaction mixture was filtered through a small pad of Celite and the solvent removed. The residue was purified by recrystallisation from dichloromethane–light petroleum to give the *dione* **13** (17 mg, 54%) as yellow prisms, mp 119–120 °C (dichloromethane–light petroleum) (Found: M^+, 226.0994. $C_{15}H_{14}O_2$ requires *M*, 226.0994); ν_{max} (NaCl)/cm^{-1} 1665 (2 × C=O), 1640 (C=C), 1600 (C=C Ar); δ_H (300 MHz, $CDCl_3$) 2.32 (3 H, s, CH_3), 6.32 (1 H, d, *J* 15.6, H-7), 6.82 (2 H, m, H-4, H-5), 7.13 (1 H, d, *J* 15.0, H-2), 7.23 (1 H, dd, *J* 5.4, 15.9, H-3), 7.4–7.6 (4 H, m, H-6, Ph), 7.96 (2 H, d, *J* 7.2, Ph); δ_C (75 MHz, $CDCl_3$) 27.8 (*C*H_3), 128.5, 128.8, 133.1, 137.9, 138.5 (9 × CH, C-2, C-3, C-4, C-5, C-6, C-7, Ph), 138.6 (1 × C, Ph), 141.2, 142.6 (2 × C, Ph), 190.1 (C=O), 198.0 (C=O); *m*/*z* 227 (MH^+, 7%), 226 (M, 43), 183 (62), 165 (15), 155 (18), 121 (69), 105 (100), 77 (87).

Typical procedure for the non-aqueous Juliá–Colonna epoxidations

To a suspension of the immobilised poly-L-leucine (100 mg) in THF (0.8 ml) was added the enone substrate (0.24 mmol), DBU (3 drops) and urea–H_2O_2 (27 mg, 0.28 mmol, 1.2 equiv.). The reagents were stirred at room temperature until TLC analysis (20% EtOAc–light petroleum) indicated completion of reaction. [In those instances where the reaction did not reach completion within the initial 16 hours, a further amount of urea–H_2O_2 (27 mg, 1.2 equiv.) was added to the reaction mixture]. The reaction mixture was diluted with EtOAc (1 ml)

and the poly-L-leucine was removed by suction filtration, washing with EtOAc. The filtrate was then washed with H_2O (3 × 10 ml), dried ($MgSO_4$) and concentrated *in vacuo* to give a brown oil. Purification by gradient flash column chromatography (silica/0–15% EtOAc–light petroleum) if required yielded the desired epoxides, possessing physical characteristics as described below.

trans-(−)-2,3-Epoxy-5-phenyl-1-(2-naphthyl)pent-4-en-1-one **6** was obtained without chromatography (0.18 g, 87% yield) as a yellow crystalline solid, mp 97–99 °C (diethyl ether); $[\alpha]_D^{25}$ −110.0 (*c* 1.0 in $CHCl_3$) (Found: $[M - H_2O + NH_4^+]$ 300.11507. $C_{21}H_{16}O_2$ requires $MNH_4^+ - H_2O$, 300.11505); ν_{max} (KBr)/cm^{-1} 1670 (strong, C=O ketone), 1623 (C=C); δ_H (400 MHz; $CDCl_3$) 3.81 (1 H, dd, $J_{3,2}$ 1.8 and $J_{3,4}$ 7.9, H-3), 4.44 (1 H, d, $J_{2,3}$ 1.9, H-2), 6.10 (1 H, dd, $J_{4,3}$ 7.9 and $J_{4,5}$ 16.0, H-4), 6.90 (1 H, d, $J_{5,4}$ 16.0, H-5), 7.28–7.39 (3 H, m, Ph), 7.44–7.46 (2 H, m, Ph), 7.57–7.68 (2 H, m, Np), 7.90–8.09 (4 H, m, Np), 8.59 (1 H, s, Np); δ_C (100 MHz; $CDCl_3$) 59.2, 60.0 (2 × CH, C-2 and C-3), 123.5, 124.5 (2 × CH, C-4 and C-5), 126.6, 127.1, 127.9, 128.6, 128. 7, 128.8, 129.1, 129.7, 130.4, 136.5 (12 × CH, Np and Ph), 132.4, 132.9, 135.5, 135.9 (4 × C, Ph-ipso, Np-1, Np-3 and Np-8), 194.0 (1 × C, C-1); *m*/*z* (NH_3, EI): 301 (MH^+, 4%), 300 ($MNH_4^+ - H_2O$, 18%), 155 ($NpCO^+$, 100%); ee (found by HPLC using 10% ethanol in hexanes as the eluent) 85% for the crude product, >95% after recrystallisation from diethyl ether.

Using poly-D-leucine, *trans*-(+)-2,3-epoxy-5-phenyl-1-(2-naphthyl)pent-4-en-1-one, *ent*-**6** was obtained without chromatography (0.9 g, 85% yield) as a yellow crystalline solid, mp 96–98 °C (diethyl ether); $[\alpha]_D^{25}$ +110.0 (*c* 1.0 in $CHCl_3$) (Found: C, 83.80; H, 5.41. Calculated for $C_{21}H_{16}O_2$: C, 83.98; H, 5.41. Found: $[M - H_2O+NH_4^+]$ 300.11507. $C_{21}H_{16}O_2$ requires $M + NH_4 - H_2O$, 300.11505); ee (found by HPLC using 10% ethanol in hexanes as eluent) 87% for the crude product; ee >95% after recrystallisation from diethyl ether.

Epoxide **7** was obtained as an unstable oil (79% yield) (Found: M^+, 290.09439. $C_{16}H_{18}O_4$ requires *M*, 290.09430); δ_H (200 MHz, $CDCl_3$) 3.75 (1 H, dd, $J_{3,2}$ 2.0, $J_{3,4}$ 8.0, H-3), 4.42 (1 H, d, $J_{2,3}$ 2.0, H-2), 6.05 (1 H, dd, $J_{4,3}$ 8.0, $J_{4,5}$ 16.0, H-4), 6.35–6.44 (2 H, m, Ph), 6.71 (1 H d, $J_{5,4}$ 16.0, H-5), 7.54 (1 H, s, Ph), 7.57–7.68 (3 H, m, Ph), 7.88–8.08 (8 H, m, Ph), 8.59 (1 H, s, Ph); *m*/*z* 290 (M^+, 7), 172 (23), 155 (100), 127 (68); ee (found by HPLC using 5% propan-2-ol in hexanes as the eluent) 95%.

Epoxide **8** was formed (300 mg, 55% yield) as a white solid which was recrystallised from dichloromethane–light petroleum to give white needles, mp 78–80 °C (dichloromethane–light petroleum) (Found: M^+, 208.0292. $C_{11}H_9ClO_2$ requires *M*, 208.0291); $[\alpha]_D^{23}$ −164.0 (*c* 1.0 in $CHCl_3$); δ_H (300 MHz, $CDCl_3$) 3.53 (1 H, dd, $J_{3,2}$ 1.7 and $J_{3,4}$ 7.7, H-3), 4.14 (1 H, d, $J_{2,3}$ 1.7, H-2), 5.78 (1 H, dd, $J_{4,3}$ 7.7 and $J_{4,5}$ 13.7, H-4), 6.46 (1 H, d, $J_{5,4}$ 13.7, H-5), 7.45 (3 H, m, Ph), 7.93 (2 H, d, *J* 8.2, Ph); δ_C (75 MHz, $CDCl_3$) 56.9, 58.3 (2 × CH, C-2, C-3), 125.3, 128.4, 129.0, 129.3, 134.2, 135.5 (8 × CH, C-4, C-5, Ph), 193.1 (1 × C=O, C-1); *m*/*z* 208–210 (M, 0.5%), 115 (9), 105 (100), 77 (63); ee (found by HPLC using 10% ethanol in hexanes as the eluent) 86% for the crude product; after recrystallisation ee >99%.

Epoxide **9** was obtained as a colourless solid (90% yield), mp 58–59 °C (ethyl acetate); $[\alpha]_D^{23}$ −80.4 (*c* 1.15 in $CHCl_3$) (Found: M^+, 232.07331. $C_{13}H_{12}O_4$ requires *M*, 232.07356); ν_{max} (NaCl)/cm^{-1} 1722 (C=O ester), 1689 (C=O aldehyde), 1231 (C–O epoxide); δ_H (300 MHz; $CDCl_3$) 3.71 (1 H, dd, $J_{4,5}$ 1.8 and $J_{4,3}$ 7.2, H-4), 3.78 (3 H, s, OCH_3), 4.24 (1 H, d, $J_{5,4}$ 1.8, H-5), 6.28 (1 H, d, $J_{2,3}$ 15.7, H-2), 6.78 (1 H, dd, $J_{3,4}$ 7.2 and $J_{3,2}$ 15.7, H-3), 7.49–7.54 (2 H, m, Ph), 7.62–7.67 (1 H, m, Ph), 8.01 (2 H, d, *J* 7.0, Ph); δ_C (75 MHz; $CDCl_3$) 51.9 (1 × CH_3, OCH_3), 56.9, 58.7 (2 × CH, C-4, C-5), 125.6, 128.4 (2 × CH, C-2, C-3), 129.0, 134.3, 135.4, 142.2 (6 × CH, Ph), 165.7 (1 × C=O, ester), 192.63 (1 × C=O, ketone); *m*/*z* (EI) 232 (M^+, 1%), 217 ($M^+ - CH_3$, 3), 201 (217 − O, 2), 105 (PhCO, 100); ee [determined by Eu(hfc)$_3$ chiral shift] 90%.

Epoxide **10** was obtained as a pale yellow solid (95% yield), mp 82 °C (ethyl acetate); $[\alpha]_D^{23}$ −75.0 (*c* 0.24 in $CHCl_3$) (Found: M^+, 274.12024. $C_{16}H_{18}O_4$ requires *M*, 274.12051); ν_{max} (NaCl)/cm^{-1} 1710 (C=O, ester), 1656 (C=O, ketone), 1597 (C=C), 1259 (C–O); δ_H (300 MHz, $CDCl_3$) 1.43 [9 H, s, $C(CH_3)_3$], 3.61 (1 H, ddd, $J_{4,2}$ 0.7, $J_{4,5}$ 1.9 and $J_{4,3}$ 7.3, H-4), 4.17 (1 H, d, $J_{5,4}$ 1.9, H-5), 6.13 (1 H, dd, $J_{2,4}$ 0.7 and $J_{2,3}$ 15.7, H-2), 6.58 (1 H, dd, $J_{3,4}$ 7.3 and $J_{3,2}$ 15.7, H-3), 7.50 (2 H, app t, *J* 6.6 and *J* 7.4, Ph), 7.58–7.62 (1 H, m, Ph), 7.93 (2 H, dd, *J* 1.2 and *J* 8.4, Ph); δ_C (75 MHz, $CDCl_3$) 27.1 [3 × CH_3, $C(CH_3)_3$], 56.2, 57.7 (2 × C, C-4, C-5), 80.4 [1 × C, $C(CH_3)_3$], 127.1, 127.5, 128.0, 133.3 (6 × C, C-2, C-3, *meta*, *ortho*-Ph), 134.4 (1 × C, *ipso*-Ph), 139.7 (1 × C, *para*-Ph), 163.6 (1 × C=O, C-1), 191.8 (1 × C=O, C-6); *m*/*z* 274 (M^+, 2%), 218 [$M^+ - C(CH_3)_3$, 4%], 173 (218 − CO_2, 4%), 105 (PhCO, 100); ee [determined by Eu(hfc)$_3$ chiral shift] 90%.

The *monoepoxide* **12** was isolated in 70% yield as a pale yellow oil (Found: M^+, 292.1096. $C_{19}H_{16}O_3$ requires *M*, 292.1100); δ_H (300 MHz, $CDCl_3$) 2.11 (3 H, d, $J_{Me,4}$ 1.6, CH_3), 3.95 (1 H, dd, $J_{3,2}$ 1.7 and $J_{3,4}$ 8.8, H-3), 4.20 (1 H, d, $J_{2,3}$ 1.7, H-2), 5.87 (1 H, dd, $J_{4,Me}$ 1.6 and $J_{4,3}$ 8.8, H-4), 7.3–7.7 (8 H, m, Ph), 7.97 (2 H, d, *J* 7.1, Ph); δ_C (75 MHz, $CDCl_3$) 13.4 (1 × CH_3, CH_3), 55.6, 58 (2 × CH, C-2, C-3), 128.5, 128.8 (2 × CH, C-4, C-5), 129.1, 129.5, 132.4 (8 × CH, Ph), 134.3, 135.4 (2 × C, *ipso*-Ph), 137.1, 142.8 (2 × CH, Ph), 193.1, 197.4 (2 × C=O, C-1, C-6); *m*/*z* 292 (M, 3%), 263 (3), 187 (10), 159 (7), 158 (40), 157 (7), 129 (18), 106 (9), 105 (100), 77 (58); ee (found by HPLC using 10% ethanol in hexanes as the eluent) 92%.

The *monoepoxide* **14** was isolated in 43% yield, as a pale yellow oil (Found: M^+, 242.0940. $C_{15}H_{14}O_3$ requires *M*, 242.0943) δ_H (300 MHz, $CDCl_3$) 2.27 (3 H, s, CH_3-9), 3.64 (1 H, dd, $J_{3,2}$ 2.2 and $J_{3,4}$ 7.7, H-3), 4.21 (1 H, d, $J_{2,3}$ 2.2, H-2), 5.95 (1 H, dd, $J_{4,3}$ 7.7 and $J_{4,5}$ 15.4, H-4), 6.19 (1 H, d, $J_{7,6}$ 15.4, H-7), 6.61 (1 H, dd, $J_{5,6}$ 11.0 and $J_{5,4}$ 15.4, H-5), 7.10 (1 H, dd, $J_{6,5}$ 11.0 and $J_{6,7}$ 15.4, H-6) 7.54 (3 H, m, Ph), 7.97 (2 H, d, *J* 7.1, Ph); δ_C (75 MHz, $CDCl_3$) 27.6 (1 × CH_3, C-9), 58.3, 59.1 (2 × CH, C-2, C-3), 128.4, 129.0, 132.2, 133.7, 134.2, 135.5, 136.9 (9 × CH, C-4, C-5, C-6, C-7, Ph), 140.5 (1 × C, *ipso*-Ph), 193.1, 198.2 (2 × C=O, C-1, C-8); *m*/*z* 243 (MH^+, 0.2%), 242 (M^+, 1), 213 (3), 199 (8), 147 (2), 137 (12), 105 (100), 77 (46), 43 (41); ee [determined by Eu(hfc)$_3$ chiral shift] 90%.

Synthesis of diols 15 and 16

Method 1. *trans*-(−)-2,3-Epoxy-5-phenyl-1-(2-naphthyl)pent-4-en-1-one **6** (3.00 g, 10 mmol) and *N*-methylmorpholine *N*-oxide (1.76 g, 15 mmol) were dissolved in an acetone–water (30 ml, 8 : 1) mixture. Osmium tetroxide (0.033 g, catalytic) was added in a single portion and the solution stirred at room temperature. After 18 h, TLC (ethyl acetate–light petroleum, 1 : 1) showed no starting material (R_f 0.9), a major product (R_f 0.4) and a minor product (R_f 0.3). The reaction was cooled to 0 °C and quenched with saturated aqueous sodium hydrogen sulfite (20 ml). The acetone was evaporated *in vacuo*, and the aqueous mixture was extracted three times with ethyl acetate. The combined organic layers were dried (magnesium sulfate), filtered and evaporated to dryness. The residue was purified by flash chromatography (ethyl acetate–light petroleum, 1 : 3). The major product, (2*S*,3*S*,4*R*,5*S*)-(+)-2,3-epoxy-4,5-dihydroxy-5-phenyl-1-(2-naphthyl)pentan-1-one **15** was collected (1.52 g, 46% yield) as a colourless crystalline solid, mp 136–137 °C (ethyl acetate); $[\alpha]_D^{29}$ +45.1 (*c* 1.02 in CH_3OH) (Found: MH^+, 335.12901. $C_{21}H_{18}O_4$ requires *MH*, 335.12833); ν_{max} (NaCl)/cm^{-1} 3444 (broad, OH), 3059 (weak, CH), 1682 (strong, C=O ketone); δ_H (400 MHz; d_4-methanol) 3.33 (1 H, dd, $J_{3,2}$ 2.1 and $J_{3,4}$ 2.9, H-3), 4.09 (1 H, app t, H-4), 4.64 (1 H, d, $J_{2,3}$ 2.0, H-2), 4.89 (1 H, d, $J_{5,4}$ 4.0, H-5), 7.10–7.27 (3 H, m, Ph), 7.43–7.44 (2 H, m, Ph), 7.64–7.73 (2 H, m, Np), 7.98–8.11 (4 H, m, Np), 8.70 (1 H, s, Np); δ_C (75 MHz; d_4-methanol) 52.1, 59.1 (2 × CH, C-2 and C-3), 70.9, 72.9 (2 × CH, C-4 and C-5), 121.5, 124.9, 125.2, 125.7, 126.0, 126.2, 126.8, 127.3, 128.1, 129.3 (12 × CH, Ph and

Np), 131.1, 134.6, 137.0, 139.9 (4 × C, Ph-*ipso*, Np-1, Np-3, Np-8), 193.9 (1 × C=O, C-1); *m*/*z* (FAB$^+$) 335 (MH$^+$, 22%), 199 (22), 155 (NpCO$^+$, 100).

The minor product (R_f 0.3), (2*S*,3*S*,4*S*,5*R*)-(+)-2,3-epoxy-4,5-dihydroxy-5-phenyl-1-(2-naphthyl)pentan-1-one **16** was obtained (0.89 g, 27% yield) as a colourless solid, mp 135–136 °C (ethyl acetate); $[\alpha]_D^{28}$ +110.5 (*c* 1.05 in CH_3OH) (Found: MH$^+$, 335.12868. $C_{21}H_{18}O_4$ requires *MH*, 335.12833); ν_{max} (NaCl)/cm^{-1} 3488 (broad, OH), 3202 (broad, OH), 3062 (weak, CH), 1674 (strong, C=O ketone); δ_H (400 MHz; d_4-methanol) 3.05 (1 H, dd, $J_{3,2}$ 2.0 and $J_{3,4}$ 6.1, H-3), 3.77 (1 H, app t, H-4), 4.39 (1 H, d, $J_{2,3}$ 2.0, H-2), 4.74 (1 H, d, $J_{5,4}$ 7.0, H-5), 6.97–7.19 (3 H, m, Ph), 7.40–7.42 (2 H, m, Ph), 7.63–7.73 (2 H, m, Np), 7.87–8.07 (4 H, m, Np), 8.46 (1 H, s, Np); δ_C (75 MHz; d_4-methanol) 55.3, 61.0 (2 × CH, C-2 and C-3), 69.9, 77.1 (2 × CH, C-4 and C-5), 124.9, 128.1, 128.3, 128.4, 129.1, 129.3, 129.9, 130.5, 131.1, 132.0 (12 × CH, Ph and Np), 134.6, 135.3, 137.0, 140.9 (4 × C, Ph-*ipso*, Np-1, Np-3 and Np-8), 193.9 (1 × C=O, C-1); *m*/*z* (FAB$^+$) 335 (MH$^+$, 23%), 155 (NpCO$^+$, 100%).

Method 2. The AD-mix-α (2.8 g) and methanesulfonamide (0.19 g, 2 mmol) were dissolved in *tert*-butyl alcohol (10 ml) and water (10 ml). The mixture was stirred at room temperature until both phases were clear and then cooled in an ice bath whereupon the inorganic salts partially precipitated. *trans*-(−)-2,3-Epoxy-5-phenyl-1-(2-naphthyl)pent-4-en-1-one **6** (0.6 g, 2 mmol) was added and the mixture stirred vigorously and the ice bath removed. The reaction mixture was stirred at room temperature for 48 h, after which TLC (ethyl acetate–light petroleum, 1:1) showed no starting material (R_f 0.9), a major product (R_f 0.4) and a trace of a minor product (R_f 0.3). The reaction mixture was cooled in an ice bath, quenched with sodium sulfite, (1.5 g) warmed to room temperature and stirred for 1 h. The reaction mixture was extracted from ethyl acetate and the combined organic layers washed with 2 M potassium hydroxide (50 ml), dried (magnesium sulfate), filtered and evaporated *in vacuo*. The residue was purified by flash chromatography (ethyl acetate–light petroleum, 1:2) to afford (2*S*,3*S*,4*R*,5*S*)-(+)-2,3-epoxy-4,5-dihydroxy-5-phenyl-1-(2-naphthyl)pentan-1-one **15** (0.601 g, 90% yield) as a colourless crystalline solid, which was identical in all respects to the major product obtained in Method 1.

The AD-mix-β (2.8 g) and methanesulfonamide (0.19 g, 2 mmol) were dissolved in *tert*-butyl alcohol (10 ml) and water (10 ml). The mixture was stirred at room temperature until both phases were clear and then cooled in an ice bath whereupon the inorganic salts partially precipitated. *trans*-(−)-2,3-Epoxy-5-phenyl-1-(2-naphthyl)pent-4-en-1-one **6** (0.6 g, 2 mmol) was added, the mixture stirred vigorously and the ice bath removed. The reaction mixture was stirred at room temperature for 48 h, after which time TLC (ethyl acetate–light petroleum, 1:1) showed no starting material (R_f 0.9), a major product (R_f 0.3) and a trace of a minor product (R_f 0.4). The reaction mixture was cooled in an ice bath, quenched with sodium sulfite, (1.5 g) warmed to room temperature and stirred for 1 h. The reaction mixture was extracted from ethyl acetate and the combined organic layers washed with 2 M potassium hydroxide (50 ml), dried (magnesium sulfate), filtered and evaporated *in vacuo*. The residue was purified by flash chromatography (ethyl acetate–light petroleum, 1:2) to afford a diol (0.637 g, 95% yield) as a colourless solid, which was identical in all respects to the minor product obtained in Method 1.

Synthesis of diols *ent*-15 and *ent*-16

Method 1. *trans*-(+)-2,3-Epoxy-5-phenyl-1-(2-naphthyl)-pent-4-en-1-one (*ent*-6) (0.551 g, 1.84 mmol) and *N*-methylmorpholine *N*-oxide (0.323 g, 2.76 mmol) were dissolved in 11 ml (8:1) of acetone–water. Osmium tetroxide (2.5% wt *tert*-butyl alcohol solution, 0.5 ml, 11.7 mg) was added and the solution stirred at room temperature. After 18 h, TLC (ethyl acetate–light petroleum, 1:1) showed no starting material (R_f 0.9), a major product (R_f 0.4) and a minor product (R_f 0.3). After cooling over an ice bath, the reaction was quenched with saturated aqueous sodium hydrogen sulfite (10 ml). Most of the acetone was evaporated *in vacuo*, and the aqueous mixture was extracted three times with ethyl acetate. The combined organic layers were dried (magnesium sulfate), filtered and evaporated *in vacuo*. The residue was purified by flash chromatography (ethyl acetate–light petroleum, 1:3). The major product, (2*R*,3*R*,4*S*,5*R*)-(−)-2,3-epoxy-4,5-dihydroxy-5-phenyl-1-(2-naphthyl)pentan-1-one *ent*-**15** was obtained (0.252 g, 41% yield) as a colourless crystalline solid, mp 135–137 °C (ethyl acetate); $[\alpha]_D^{28}$ −45.0 (*c* 1.00 in CH_3OH) (Found: MH$^+$, 335.12901. $C_{21}H_{18}O_4$ requires *MH*, 335.12833).

The minor product (R_f 0.3), (2*R*,3*R*,4*R*,5*S*)-(−)-2,3-epoxy-4,5-dihydroxy-5-phenyl-1-(2-naphthyl)pentan-1-one *ent*-**16** was obtained (0.208 g, 34% yield) as a colourless crystalline solid, mp 136–138 °C (ethyl acetate); $[\alpha]_D^{28}$ −110.0 (*c* 1.00 in CH_3OH) (Found: C, 74.89; H, 5.35. Calculated for $C_{21}H_{18}O_4$: C, 75.43; H, 5.43; Found: MH$^+$, 335.12901. $C_{21}H_{18}O_4$ requires *MH*, 335.12833).

(2*S*,3*S*,4*R*,5*S*)-(−)-2,3-Epoxy-4,5-*O*-isopropylidene-5-phenyl-1-(2-naphthyl)pentan-1-one 17 and isomer 20

Anhydrous copper sulfate (0.3 g) was heated (~500 °C) *in vacuo* for 10 min. Toluene-*p*-sulfonic acid (0.07 g, catalytic 0.4 mmol) was added to the same vessel and both were left to dry *in vacuo* for 1 h. (2*S*,3*S*,4*R*,5*S*)-(+)-2,3-Epoxy-4,5-dihydroxy-5-phenyl-1-(2-naphthyl)pentan-1-one **15** (1.34 g, 4.01 mmol) was dried *in vacuo* for 1 h and added to the reaction vessel in anhydrous acetone (25 ml). The reagents were stirred vigorously under an atmosphere of nitrogen and 2,2-dimethoxypropane (0.74 ml, 6.03 mmol) was added to the reaction mixture. After 20 mins, TLC (ethyl acetate–light petroleum, 1:2) showed no starting material (R_f 0.2) and a single product (R_f 0.8). The reaction was quenched with potassium carbonate (0.2 g, 1.44 mmol) and the solvents were removed *in vacuo*. The residue was dissolved in diethyl ether and washed with saturated aqueous sodium hydrogen carbonate, brine and water. The organic solvent was dried (magnesium sulfate), filtered and evaporated *in vacuo*. The residue was purified by flash chromatography (ethyl acetate–light petroleum, 1:3) to afford (2*S*,3*S*,4*R*,5*S*)-(+)-2,3-epoxy-4,5-O-isopropylidene-5-phenyl-1-(2-naphthyl)pentan-1-one **17** (1.42 g, 95% yield) as a white solid, mp 167–169 °C (diethyl ether); $[\alpha]_D^{28}$ +20.9 (*c* 1.05 in $CHCl_3$) (Found: MH$^+$, 375.15979. $C_{24}H_{22}O_4$ requires *MH*, 375.15963); ν_{max} (NaCl)/cm^{-1} 3059, 2986, 2933 (weak, CH), 1685 (strong, C=O ketone); δ_H (400 MHz; $CDCl_3$) 1.60, 1.64 [2 × 3 H, 2 × s, $(CH_3)_2C$], 3.50 (1 H, dd, $J_{3,2}$ 2.0 and $J_{3,4}$ 5.2, H-3), 3.96 (1 H, dd, $J_{4,3}$ 5.2 and $J_{4,5}$ 8.1, H-4), 4.40 (1 H, d, $J_{2,3}$ 2.0, H-2), 5.08 (1 H, d, $J_{5,4}$ 8.1, H-5), 7.35–7.51 (5 H, m, Ph), 7.58–7.65 (2 H, m, Np), 7.86–8.04 (4 H, m, Np), 8.53 (1 H, s, Np); δ_C (100 MHz; $CDCl_3$) 26.7, 26.9 [2 × CH_3, $(CH_3)_2C$], 54.8, 58.3 (2 × CH, C-2 and C-3), 81.0, 81.7 (2 × CH, C-4 and C-5), 110.4 [1 × C, $(CH_3)_2C$], 123.4, 126.5, 127.0, 127.8, 128.5, 128.5, 128.6, 128.7, 129.0, 129.6, 130.5 (12 × CH, Np and Ph), 132.3, 132.6, 135.9, 137.1 (4 × C, Np and Ph-*ipso*), 193.0 (1 × C=O, C-1); *m*/*z* (FAB$^+$) 375 (MH$^+$, 5%), 317 (MH$^+$ − CH_3CO, 8), 183 (NpCOCO$^+$, 12), 155 (NpCO$^+$, 100).

(2*R*,3*R*,4*S*,5*R*)-(−)-2,3-Epoxy-4,5-dihydroxy-5-phenyl-1-(2-naphthyl)pentan-1-one *ent*-**15**, when treated under the same conditions produced (2*R*,3*R*,4*S*,5*R*)-(−)-2,3-epoxy-4,5-*O*-isopropylidene-5-phenyl-1-(2-naphthyl)pentan-1-one *ent*-**17** (52 mg, 92% yield) as a white solid, mp 166–167 °C (diethyl ether); $[\alpha]_D^{28}$ −21.0 (*c* 1.00 in $CHCl_3$) (Found: M$^+$, 374.15220. $C_{24}H_{22}O_4$ requires *M*, 374.15179).

(2*S*,3*S*,4*S*,5*R*)-(+)-2,3-Epoxy-4,5-dihydroxy-5-phenyl-1-(2-naphthyl)pentan-1-one **16**, when treated under the same

conditions, produced (2*S*,3*S*,4*S*,5*R*)-(+)-2,3-epoxy-4,5-*O*-isopropylidene-5-phenyl-1-(2-naphthyl)pentan-1-one **20** (1.051 g, 92% yield) as a white solid, mp 149–153 °C (ethyl acetate); $[a]_D^{28}$ +17.1 (*c* 1.05 in $CHCl_3$) (Found: MH^+, 375.16053. $C_{24}H_{22}O_4$ requires *MH*, 375.15963); ν_{max} (NaCl)/cm^{-1} 2987 (weak, CH), 1685 (strong, C=O ketone); δ_H (400 MHz; $CDCl_3$) 1.56, 1.64 [2 × 3 H, 2 × s, $(CH_3)_2C$], 3.38 (1 H, dd, $J_{3,2}$ 2.0 and $J_{3,4}$ 3.8, H-3), 3.98 (1 H, dd, H-4, $J_{4,3}$ 3.8 and $J_{4,5}$ 8.6, H-4), 4.32 (1 H, d, $J_{2,3}$ 2.0, H-2), 5.01 (1 H, d, $J_{5,4}$ 8.6, H-5), 7.35–7.45 (5 H, m, Ph), 7.55–7.64 (2 H, m, Np), 7.86–7.96 (4 H, m, Np), 8.39 (1 H, s, Np); δ_C (100 MHz; $CDCl_3$) 26.4, 27.1 [2 × CH_3, $(CH_3)_2C$], 53.7, 57.2 (2 × CH, C-2 and C-3), 80.1, 81.4 (2 × CH, C-4 and C-5), 110.4 [1 × C, $(CH_3)_2C$], 123.5, 126.6, 126.9, 127.8, 128.7, 128.7, 128.8, 129.0, 129.7, 130.5 (12 × CH, Np and Ph), 132.2, 132.6, 135.8, 136.8, (4 × C, Np and Ph-*ipso*), 193.2 (1 × C=O, C-1); *m*/*z* (FAB^+) 375 (MH^+, 13%), 155 ($NpCO^+$, 100).

(2*R*,3*R*,4*R*,5*S*)-(−)-2,3-Epoxy-4,5-dihydroxy-5-phenyl-1-(2-naphthyl)pentan-1-one *ent*-**16** under the same conditions produced (2*R*,3*R*,4*R*,5*S*)-(−)-2,3-epoxy-4,5-*O*-isopropylidene-5-phenyl-1-(2-naphthyl)pentan-1-one *ent*-**20** (1.051 g, 92% yield) as a white solid, mp 149–153 °C (ethyl acetate); $[a]_D^{28}$ −17.1 (*c* 1.05 in $CHCl_3$) (Found: MH^+, 375.16055. $C_{24}H_{22}O_4$ requires *MH*, 375.15963).

(3*R*,4*S*,5*R*)-3-Hydroxy-4,5-*O*-isopropylidene-5-phenyl-1-(2-naphthyl)pentan-1-one 21

Copper cyanide (1.6 g, 17.9 mmol) was stirred vigorously at −78 °C in dry dichloromethane (20 ml) under an atmosphere of nitrogen. Methyllithium (12 ml, 5% in diethyl ether solution) was added dropwise, and the solution was observed to change from pale yellow to colourless. (2*S*,3*S*,4*S*,5*R*)-(−)-2,3-Epoxy-4,5-*O*-isopropylidene-5-phenyl-1-(2-naphthyl)pentan-1-one **20** (1.16 g, 3.1 mmol) was added dropwise in a dry solution of dichloromethane (20 ml). The solution was allowed to stir for 6 h. The temperature was raised to −10 °C, a brown precipitate slowly formed and the reaction mixture was quenched with saturated aqueous ammonium chloride (50 ml), upon which a bright orange colour was formed that slowly turned blue. The mixture was diluted with diethyl ether (150 ml), the solvents partitioned and the organic fraction washed with saturated aqueous ammonium chloride until a blue colour was no longer apparent in the aqueous layer. The organic layer was washed with water, dried (magnesium sulfate) and evaporated *in vacuo*. The residue was purified by flash chromatography (diethyl ether–light petroleum, 1:4) to afford (3*R*,4*S*,5*R*)-3-hydroxy-4,5-*O*-isopropylidene-5-phenyl-1-(2-naphthyl)pentan-1-one **21** (0.82 g, 71% yield) as a white solid, mp 130–132 °C (diethyl ether); $[a]_D^{28}$ +49.5 (*c* 1.01 in $CHCl_3$) (Found: M^+, 376.16691. $C_{24}H_{24}O_4$ requires *M*, 376.16748); ν_{max} (NaCl)/cm^{-1} 3484 (broad, OH), 3060, 3036, 2985, 2933, 2904 (weak, CH), 1675 (strong, C=O ketone), 1627 (C=C); δ_H (400 MHz; $CDCl_3$) 1.56, 1.61 [2 × 3 H, 2 × s, $(CH_3)_2C$], 3.27 (1 H, dd, $J_{2,3}$ 8.7 and $J_{2,2'}$ 17.7, H-2), 3.40 (1 H, dd, $J_{2',3}$ 2.9 and $J_{2',2}$ 17.7, H-2′), 3.47 (1 H, br d, OH, exchangeable with D_2O, *J* 3.34), 4.08 (1 H, dd, $J_{4,3}$ 6.3 and $J_{4,5}$ 7.6, H-4), 4.52 (1 H, ddd, $J_{3,2'}$ 2.9, $J_{3,4}$ 6.3 and $J_{3,2}$ 8.9, H-3), 5.12 (1 H, d, $J_{5,4}$ 7.7, H-5), 7.28–7.32 (1 H, m, Ph-*para*), 7.36–7.40 (2 H, m, Ph), 7.52–7.55 (2 H, m, Ph), 7.55–7.63 (2 H, m, Np), 7.85–7.97 (4 H, m, Np), 8.37 (1 H, s, Np); δ_C (100 MHz; $CDCl_3$) 27.1, 27.2 [2 × CH_3, $(CH_3)_2C$], 41.6 (1 × CH_2, C-2), 69.0 (1 × CH, C-3), 81.0 (1 × CH, C-4), 84.5 (1 × CH, C-5), 109.5 [1 × C, $(CH_3)_2C$], 123.4, 126.8, 127.3, 127.7, 128.1, 128.3, 128.4, 128.6, 129.5, 130.0 (12 × CH, Np and Ph), 132.3, 133.8, 135.7, 138.9 (4 × C, Np and Ph), 199.8 (1 × C=O, C-1); *m*/*z* (CI^+) 376 (M^+, 0.11%), ($M^+ - H_2O$, 1.96), 155 ($NpCO^+$, 100).

(3*R*,4*R*,5*S*)-3-Hydroxy-4,5-*O*-isopropylidene-5-phenyl-1-(2-naphthyl)pentan-1-one 18

Copper cyanide (0.12 g, 1.3 mmol) was stirred vigorously at −78 °C in dry dichloromethane (5 ml) under an atmosphere of nitrogen. Methyllithium (0.9 ml, 5% in diethyl ether solution) was added dropwise, and the solution was observed to change from pale yellow to colourless. (2*S*,3*S*,4*R*,5*S*)-(−)-2,3-Epoxy-4,5-*O*-isopropylidene-5-phenyl-1-(2-naphthyl)pentan-1-one **17** (0.10 g, 0.3 mmol) was added dropwise in a dry solution of dichloromethane (5 ml). The solution changed to a yellow-orange colour and was allowed to stir for 2 h. After a work up as described above, the residue was purified by flash chromatography (ethyl acetate–light petroleum, 1:9) to afford (3*R*,4*R*,5*S*)-3-hydroxy-4,5-*O*-isopropylidene-5-phenyl-1-(2-naphthyl)pentan-1-one **18** (73 mg, 73% yield) as a colourless oil, $[a]_D^{28}$ +45.6 (*c* 0.98 in $CHCl_3$) (Found: MH^+, 377.17481. $C_{24}H_{24}O_4$ requires *MH*, 377.17529); ν_{max} (NaCl)/cm^{-1} 3498 (broad, OH), 3060, 2984, 2933, (CH), 1674 (strong, C=O ketone); δ_H (400 MHz; $CDCl_3$) 1.59, 1.62 [2 × 3 H, 2 × s, $(CH_3)_2C$], 3.18 (1 H, dd, $J_{2,3}$ 3.1 and $J_{2,2'}$ 17.4, H-2), 3.21 (1 H, br s, OH, exchangeable with D_2O), 3.48 (1 H, dd, $J_{2',3}$ 9.0 and $J_{2',2}$ 17.4, H-2′), 3.88 (1 H, dd, $J_{4,5}$ 8.6 and $J_{4,3}$ 1.8, H-4), 4.36 (1 H, app dt, H-3), 5.17 (1 H, d, $J_{5,4}$ 8.6, H-5), 7.30–7.34 (1 H, m, Ph-*para*), 7.37–7.41 (2 H, m, Ph), 7.47–7.49 (2 H, m, Ph), 7.53–7.66 (2 H, m, Np), 7.85–7.98 (4 H, m, Np), 8.40 (1 H, s, Np); δ_C (75 MHz; $CDCl_3$) 26.9, 27.3 [2 × CH_3, $(CH_3)_2C$], 43.0 (1 × CH_2, C-2), 65.2 (1 × CH, C-3), 78.8 (1 × CH, C-4), 85.6 (1 × CH, C-5), 109.5 [1 × C, $(CH_3)_2C$], 123.7, 126.9, 127.9, 128.5, 128.6, 128.8, 129.7, 130.1 (12 × CH, Np, Ph), 132.5, 134.2, 135.9, 137.9 (4 × C, Np and Ph), 199.5 (1 × C=O, C-1); *m*/*z* (FAB^+) 377 (MH^+, 12%), 361 (MH^+-O, 15), 319 [$MH^+ - (CH_3)_2CO$, 100], 301 [$MH^+ - (CH_3)_2CO - H_2O$, 46].

4-Hydroxy-5-(1′-hydroxybenzyl)tetrahydrofuran-2-one 19

(3*R*,4*R*,5*S*)-3-Hydroxy-4,5-*O*-isopropylidene-5-phenyl-1-(2-naphthyl)pentan-1-one **18** (0.95 g, 0.253 mmol) and *m*-chloroperoxybenzoic acid (0.218 g, 1.26 mmol, 57–86% purity) were stirred in chloroform (3 ml) and pH 7 buffer solution (2 ml) for 12 h. More *m*-chloroperoxybenzoic acid (0.2 g, 1.16 mmol) was added and the solution was stirred for 6 h, after which time the reaction mixture was diluted with diethyl ether (30 ml) and water (20 ml) and the solvents partitioned. The organic layer was washed with a saturated solution of sodium hydrogen carbonate, dried (magnesium sulfate), filtered and evaporated. The residue was dissolved in water (10 ml) and trifluoroacetic acid (1 ml) and stirred for 1 h. At this point TLC (diethyl ether–light petroleum, 1:1) showed no starting material (R_f 0.7), and one major product (R_f 0.1). The solvents were removed *in vacuo*. The residue was purified by flash chromatography (ethyl acetate–light petroleum, 1:1) to afford 4-hydroxy-5-(1′-hydroxybenzyl)tetrahydrofuran-2-one **19** (11 mg, 31% yield) as a colourless crystalline solid, mp 134–137 °C (ethyl acetate) (Found: $M+NH_4^+$ 226.10824. $C_{11}H_{12}O_4$ requires $M+NH_4$, 226.10793); ν_{max} (NaCl)/cm^{-1} 3417 (broad, 2 × OH), 2945, 2929, (weak, CH), 1778 (s, C=O saturated 5-membered ring lactone); δ_H (400 MHz; d_3-acetonitrile) 2.48 (1 H, dd, $J_{2,3}$ 1.9 and $J_{2,2'}$ 17.6, H-2), 2.82 (1 H, dd, $J_{2',3}$ 5.7 and $J_{2',2}$ 17.5, H-2′), 3.92 (1 H, br s, OH, exchangeable with D_2O), 3.95 (1 H, br s, OH, exchangeable with D_2O), 4.27 (1 H, ddd, $J_{3,2}$ 1.9, $J_{3,4}$ 4.2 and $J_{3,2'}$ 5.8, H-3), 4.57 (1 H, dd, $J_{4,3}$ 4.1 and $J_{4,5}$ 6.4, H-4), 5.08 (1 H, d, $J_{5,4}$ 6.4, H-5), 7.34–7.51 (5 H, m, Ph); δ_C (100 MHz; d_3-acetonitrile) 39.3 (1 × CH_2, C-2), 68.2 (1 × CH, C-3), 71.6 (1 × CH, C-4), 86.5 (1 × CH, C-5), 127.1 (2 × CH, Ph), 127.8 (1 × CH, Ph-*para*), 128.2 (2 × CH, Ph), 140.5 (1 × C, Ph-*ipso*), 175.7 (1 × C=O, C-1); *m*/*z* (NH_3, CI^+) 226 (MNH_4^+, 100%), 208 ($MNH_4^+ - H_2O$, 44).

4-Hydroxy-5-(1′-hydroxybenzyl)tetrahydrofuran-2-one 22

(3*R*,4*S*,5*R*)-3-Hydroxy-4,5-*O*-isopropylidene-5-phenyl-1-(2-naphthyl)pentan-1-one **21** (0.95 g, 0.253 mmol) was oxidized using *m*-chloroperoxybenzoic acid (0.218 g, 1.26 mmol, 57–86% purity) in chloroform (3 ml) and a pH 7 buffer solution (2 ml) as described above to afford 4-hydroxy-5-(1′-hydroxybenzyl)-

tetrahydrofuran-2-one **22** (13 mg, 38% yield) as a colourless crystalline solid, mp 134–137 °C (ethyl acetate) (Found: $M+NH_4^+$ 226.10825. $C_{11}H_{12}O_4$ requires *M*+*NH*$_4$, 226.10793); ν_{max} (NaCl)/cm^{-1} 3371 (broad, OH), 2945, 2925 (weak, CH), 1764 (s, C=O saturated 5-membered ring lactone), 1360, 1193, 1070; δ_H (400 MHz; d_3-acetonitrile) 2.28 (1 H, dd, $J_{2,3}$ 2.1 and $J_{2,2'}$ 18.1, H-2), 2.69 (1 H, dd, $J_{2',3}$ 6.7 and $J_{2',2}$ 18.1, H-2′), 3.92 (1 H, br s, OH, exchangeable with D_2O), 3.95 (1 H, br s, OH, exchangeable with D_2O), 4.47 (1 H, ddd, $J_{3,2}$ 1.9, $J_{3,4}$ 2.2 and $J_{3,2'}$ 6.7, H-3), 4.49 (1 H, dd, $J_{4,3}$ 1.8 and $J_{4,5}$ 3.4, H-4), 4.87 (1 H, *d*, $J_{5,4}$ 3.5, H-5), 7.34–7.51 (5 H, m, Ph); δ_C (100 MHz; d_3-acetonitrile) 38.6 (1 × CH_2, C-2), 69.4 (1 × CH, C-3), 73.1 (1 × CH, C-4), 92.0 (1 × CH, C-5), 127.6 (2 × CH, Ph), 128.8 (1 × CH, Ph-*para*), 129.3 (2 × CH, Ph), 141.7 (1 × C, Ph-*ipso*), 178.0 (1 × C=O, C-1); *m*/*z* (NH_3, CI^+) 226 (MNH_4^+, 100%), 209 (MH^+, 5), 208 ($MNH_4^+ - H_2O$, 44).

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