Juliá–Colonna stereoselective epoxidation of some α,β-unsaturated enones possessing a stereogenic centre at the γ-position: synthesis of a protected galactonic acid derivative

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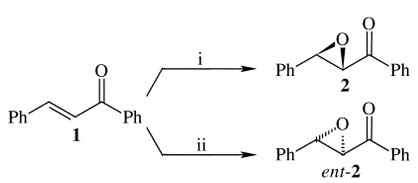
The oxidation of enones **6**–**8** using peroxide or percarbonate and polyleucines as catalysts gave the corresponding diastereomers **9**–**12** in high yield. The compound **9** was converted into the galactonic acid derivative **16** in five steps and in an overall yield of nearly 60%. Polyleucines are shown to be catalysts powerful enough to overturn the intrinsic stereocontrol in the chosen substrates.

Introduction

The stereoselective epoxidation of chalcone using aqueous hydrogen peroxide in the presence of a polyamino acid was invented by Juliá and Colonna.[1] These workers found that chalcone **1** afforded the 2*S*,3*R*-epoxide **2** in high enantiomeric excess when poly-D-leucine (PDL) was used as the stereoselective catalyst, while the enantiomeric epoxide *ent*-**2** was obtained on using poly-L-leucine (PLL) (Scheme 1).



Scheme 1 *Reagents and conditions*: i, H_2O_2, H_2O, NaOH, toluene, poly-D-leucine (PDL); ii, H_2O_2, H_2O, NaOH, toluene, poly-L-leucine (PLL).

Subsequently the Juliá–Colonna oxidation has been developed and improved. Noteworthy modifications include the following:

adsorption of the polyamino acid on silica for efficiency, ease of use, simple recovery and ready recycling;[2]

use of urea hydrogen peroxide (UHP) as the oxidant with a non-nucleophilic base (such as diazabicycloundecene (DBU)) in order to avoid aqueous hydroxide and hence to expand the substrate range;[3]

introduction of percarbonate in dimethoxyethane as a cheap oxidant/solvent for use in some polyamino acid-catalysed epoxidations.[4]

The above work has resulted in a predictive model for the enantioselective epoxidation of various (*E*)-enones on catalysis using polyleucine (Fig. 1).

With a portfolio of optimised reaction conditions available for the enantioselective epoxidation of (*E*)-enones it was of interest to test the power of the polyamino acid catalysts. One test, often used in this context previously, is to examine the ability of a catalyst to overcome the sense of diastereoselection for a reaction involving a substrate containing a pre-existing stereogenic centre. For example oxidation of the allylic alcohol **3** using *tert*-butyl hydroperoxide and titanium(IV) isopropoxide gave the epoxide **4** and its diastereomer **5** in the ratio 2.3:1. Addition of (−)-diethyl tartrate changed the ratio of **4**:**5** to 40:1 while on the other hand addition of (+)-diethyl tartrate altered the ratio to 1:14. The "matched" catalyst system

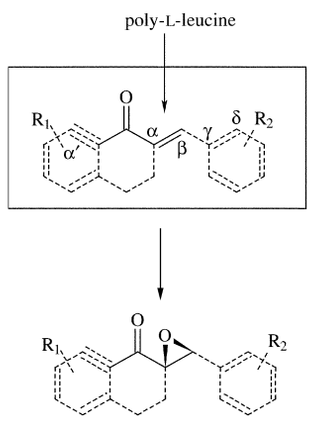
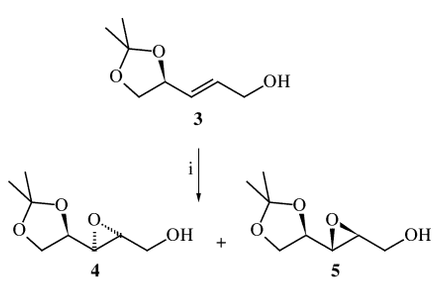


Fig. 1 Predictive model for polyleucine induced epoxidation.

employing (−)-diethyl tartrate enhances the sense of diastereoselection; the "mismatched" Katsuki–Sharpless stereoselective epoxidation is clearly able to overcome the intrinsic substrate control (Scheme 2).[5] The ability of the Juliá–Colonna catalyst



Scheme 2 *Reagents*: i, Ti(O*i*-Pr)$_4$, *t*-BuOOH.

to override the bias observed in the non-catalysed Weitz–Scheffer oxidation of chiral enones was investigated using (*E*)-enone **6**, the corresponding (*Z*)-enone **7** and epoxide **8**.[6]

Results and discussion

The ketones **6** and **7** (ratio 2:1) were prepared in 98% yield by a two-step, one-pot procedure from 1,2:5,6-di-*o*-isopropyl-

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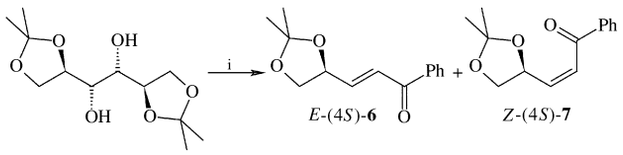
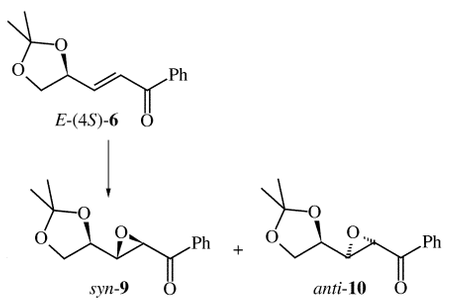
idene-D-mannitol using silica gel-supported sodium metaperiodate[7] followed by addition of the phenylcarbonylmethylenetriphenylphosphorane (Scheme 3). The two alkenes



Scheme 3 *Reagents and conditions*: i, SiO_2–$NaIO_4$, $Ph_3PCHCOPh$, CH_2Cl_2.

were separated by chromatography and independently subjected to epoxidation using basic peroxide. The enantiomeric purity of enones (*E*)-(4*S*)-**6** and (*Z*)-(4*S*)-**7** was determined by comparison of the HPLC results to those obtained from the corresponding racemates.[8]

Oxidation of enone (*E*)-(4*S*)-**6** using UHP and DBU in tetrahydrofuran (THF) gave the *syn*-**9** and *anti*-**10** epoxides in the ratio 1:2.2 (94%) (Scheme 4). Addition of poly-D-leucine,



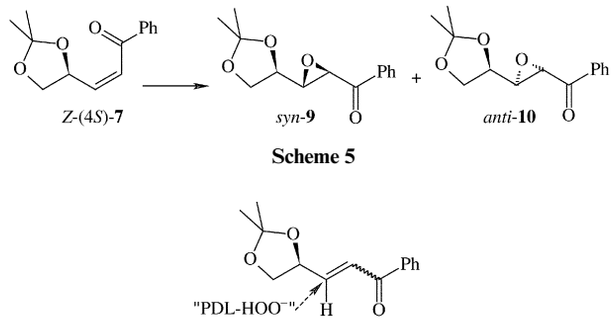
Scheme 4

expected to be the matched catalyst,[1] did indeed alter the ratio of **9** and **10** substantially in favour of the *anti*-**10** isomer (ratio 1:30) (95% yield). The major component was crystallized and the stereostructure of the compound was confirmed by X-ray analysis. The mismatched catalyst, poly-L-leucine, was initially disappointing, altering the ratio only to the extent of giving equal quantities of the two diastereoisomers. However, on using poly-L-leucine adsorbed onto silica, the ratio of *syn*-**9** to *anti*-**10** was improved to 2.2:1 (96% yield). This improvement was attributed to the greater efficiency of the silica-based catalyst, minimizing the background (non-catalysed) reaction.

In the absence of polyleucine the previously documented percarbonate conditions[4] afforded the *syn*-**9** and *anti*-**10** isomers in the ratio 1:2.7 (97%). Addition of poly-L-leucine to the reaction mixture reversed the selectivity, to give the *syn*-**9** isomer as the major component (ratio 2.4:1; 94% yield). The optimum conditions involved conducting the percarbonate reaction at a lower temperature (0 to 3 °C) whereupon, on using poly-L-leucine as the catalyst, the *syn*-**9** and *anti*-**10** isomers were obtained in a 3.8:1 ratio (95%). Recrystallization of this mixture afforded the pure *syn*-**9** isomer, as evidenced by HPLC analysis. Under the low temperature percarbonate conditions, catalysis by poly-D-leucine furnished **9** and **10** in the ratio 1:30 (90% yield).

The Juliá–Colonna stereoselective epoxidation of (*Z*)-enones has not been explored to any appreciable extent, thus it was of particular interest to include the (*Z*)-enone (4*S*)-**7** as a substrate in the present study. Oxidation of **7** in THF using DBU and UHP gave the epoxides **9** and **10** in the ratio 1:1.3 (Scheme 5). The diminished *anti*-selectivity, compared to that observed for the (*E*)-enone, is probably due to the increased importance of reaction *via* an *anti*-Felkin transition state in which 1,3-allylic strain is minimised.[9]

Conducting the reaction in the presence of poly-D-leucine enhanced the amount of the *anti*-isomer (ratio **9**:**10**, 1:8). On

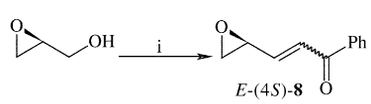


Scheme 5

Fig. 2 Selectivity for poly-D-leucine catalysed epoxidation of (*E*)-(4*S*)-**6** and (*Z*)-(4*S*)-**7**.

the other hand the reaction catalysed by poly-L-leucine afforded the diastereomers **9**:**10** in the ratio 3.6:1. The latter ratio was improved slightly (to 4:1) on conducting a repeat run at 0 °C. All three reactions gave excellent yields (>95%). It is especially noteworthy that the polyleucine-catalysed epoxidations of the (*Z*)-enone were faster than the corresponding reactions of the (*E*)-enone, precluding the possibility that addition–elimination reactions may have caused *cis*/*trans*-isomerization prior to oxidation. Thus the poly-D-leucine catalysed reaction of both the (*Z*)-enone and the (*E*)-enone involves attack of peroxide from the same (*Si*) face (Fig. 2). In the case of the (*Z*)-enone rotation about C_2–C_3 takes place prior to ring closure.

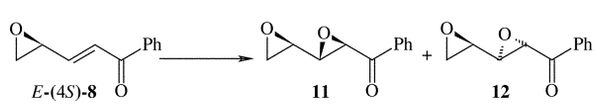
The third substrate (*E*)-(4*S*)-**8** for study was made from (*S*)-glycidol by a one-pot Swern oxidation/Wittig olefination sequence,[10] and the enantiomeric purity determined by comparison of the HPLC trace to that obtained from racemic glycidol. The crystalline enone (*E*)-(4*S*)-**8** was obtained in this way in 80% yield (Scheme 6). The (*Z*)-enone was identified in



Scheme 6 *Reagents and conditions*: i, DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2, $Ph_3PCHCOPh$.

the crude mixture by ^1H NMR spectroscopy, but it proved to be difficult to isolate in a pure state.

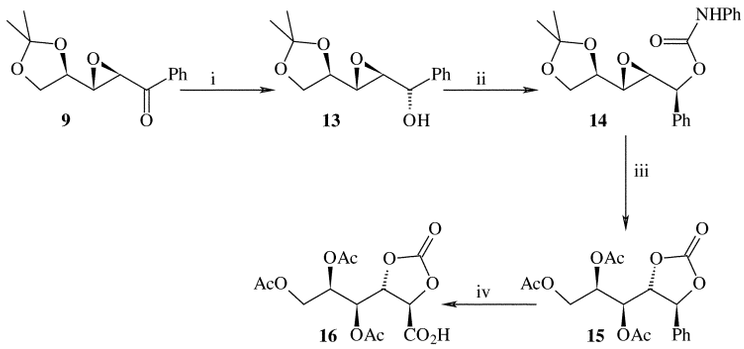
Epoxidation of enone **8** using UHP and DBU in the absence of catalyst gave the *syn*-isomer **11** and the *anti*-isomer **12** in the ratio 1:1.7 (Scheme 7). Employment of poly-D-leucine as a



Scheme 7

catalyst for the oxidation gave a mixture which was highly enriched in the *anti*-isomer **12** (ratio **11**:**12**; 1:10) such that an enantiomerically pure sample of **12** was readily obtained on recrystallization from ethanol. The X-ray crystal data served to confirm the stereostructure. Oxidation of substrate **8** under the usual UHP–DBU–THF conditions, using poly-L-leucine as the catalyst, furnished the two diastereomers **11** and **12** in the ratio 3.5:1.

The ready availability of highly functionalised compounds such as **9** or **10** prompted an investigation of some aspects of their chemistry. For example zinc borohydride reduction of the epoxyketone **9** afforded alcohol **13** in a nearly quantitative yield.[11] This alcohol was converted into the corresponding urethane **14** in 95% yield by reaction with phenyl isocyanate in the presence of pyridine.[12] The urethane was treated with boron trifluoride diethyl ether complex at −20 °C for 1 h and the intermediate iminium carbonate was then hydrolysed with



Scheme 8 *Reagents and conditions*: i, $Zn(BH_4)_2$, Et_2O; ii, PhNCO, pyridine, CH_2Cl_2; iii, (a) $BF_3(OEt_2)$, Et_2O, H_2SO_4, (b) Ac_2O, pyridine, DMAP, CH_2Cl_2; iv, $RuCl_3$, $NaIO_4$, CCl_4, CH_3CN, H_2O.

dilute sulfuric acid with concomitant removal of the isopropylidene group. The crude product was acetylated to give the triester **15** in 96% yield. Finally, treatment of the cyclic carbonate **15** in carbon tetrachloride and acetonitrile with aqueous sodium metaperiodate containing ruthenium(III) chloride or ruthenium(IV) oxide[13] furnished the carboxylic acid **16** in 65–68% yield. This acid is a differentially protected derivative of galactonic acid (Scheme 8).

Other polyoxygenated hexanoic acids would be available from (*R*)- or (*S*)-glyceraldehydes using the appropriate polyamino acid in the key oxidation step.[6] Thus in summary the polyleucine catalysts are obviously powerful enough to overcome the intrinsic senses of stereoselection to give different diastereomers as major products when employed as catalysts for the oxidation of enones **6**, **7**, and **8**. Poly-D-leucine acted as the "matched" catalyst, poly-L-leucine as the "mismatched" catalyst in each case.

Experimental

General

Melting points were measured using a Reichert-Jung Thermovar hot-stage microscope and are uncorrected. Microanalyses were determined using a Carlo Elba elemental analyser instrument. Nominal and accurate mass spectra were recorded on VG7070E, CIPOS, Kratos Profile HV3 and TRIO1000 machines. Optical rotations ($[\alpha]_D$) were measured at ambient temperature (22 ± 3 °C) from chloroform solutions using a 1 cm^3 cell with 0.1 dm path length, on a Optical Activity Ltd AA-1000 polarimeter, and are recorded in units of 10^{-1} deg cm^2 g^{-1}. Infrared spectra were recorded in chloroform solutions using a Perkin-Elmer 881 infrared spectrophotometer. All NMR spectra were recorded on a Varian 300 Gemini 2000 (300 MHz) instrument. Chiral High Pressure Liquid Chromatography was conducted using a Chiralpak AD column (*Daicel Chemical Industries*), 0.46 × 25 cm. Column chromatography was conducted with Merck Kieselgel 60: 230–400 mesh for flash chromatography, using the technique described by W. C. Still.[14]

4,5-Isopropylidenedioxy-1-phenylpent-2-en-1-ones 6 and 7

1,2:5,6-Di-*o*-isopropylidene-D-mannitol (1 g, 3.8 mmol) was added to a vigorously stirred suspension of silica gel-supported sodium metaperiodate[7] (7.6 g) in anhydrous dichloromethane (40 cm^3), followed by the addition of phenylcarbonylmethylenetriphenylphosphorane (3 g, 7.9 mmol). The mixture was stirred for 2 h and then filtered over a pad of Na_2SO_4, which was washed with dichloromethane. The filtrate was evaporated under reduced pressure to afford a crude residue (6 g). Flash chromatography of the residue over silica gel (100 g) with ethyl acetate–hexane (2:3) as the eluent afforded a *E*/*Z* mixture of (4*S*)-**6** and (4*S*)-**7** (1.72 g, 98%, *E*:*Z* [2:1] by ^{1}H NMR). Flash chromatography of the residue over silica gel (300 g) with ethyl acetate–hexane (1:9) as the eluent afforded (*Z*)-(4*S*)-**7** (>99% ee [chiral HPLC: ethanol–hexane (1:9); R_t = 13.5 min]), mp 58–59 °C (from ethyl acetate) (Found: C, 72.5; H, 7.0. $C_{14}H_{16}O_3$ requires C, 72.4; H, 6.9%); $[\alpha]_D$ 173 (*c* = 1, $CHCl_3$); ν_{max}(film)/cm^{-1} 1743 (ketone CO); δ_H (300 MHz, $CHCl_3$) 1.40 and 1.48 (2 × 3H, 2 × s, $C(CH_3)_2$), 3.70 (1H, dd, *J* 6.9 and 8.4 Hz, 5-H), 4.52 (1H, dd, *J* 7.2 and 8.4 Hz, 5-H), 5.37 (1H, m, 4-H), 6.49 (1H, dd, *J* 6.6 and 11.7 Hz, 3-H), 6.96 (1H, dd, *J* 1.5 and 11.7 Hz, 2-H), 7.38–7.94 (5H, m, C_6H_5); δ_C (75 MHz, $CHCl_3$) 25.3 and 26.6 ($C(CH_3)_2$), 69.7 (C-5), 74.6 (C-4), 109.8 ($C(CH_3)_2$), 124.8 (C-2), 128.5, 128.8, 133.2 and 137.7 (C_6H_5), 149.0 (C-3) and 190.9 (C-1); *m*/*z* (EI) 232 (M^+), (CI) 233 $[M + H]^+$ and 250 $[M + NH_4]^+$, followed by (*E*)-(4*S*)-**6** (>99% ee [chiral HPLC: ethanol–hexane (1:9); R_t = 9.2 min]), mp 48 °C (from ethyl acetate–hexane); $[\alpha]_D$ 21 (*c* = 1, $CHCl_3$), ν_{max}($CHCl_3$)/cm^{-1} 1673 (ketone CO); δ_H (300 MHz, $CDCl_3$) 1.45 and 1.49 (2 × 3H, 2 × s, $C(CH_3)_2$), 3.73 (1H, dd, *J* 7.2 and 8.4 Hz, 5-H), 4.24 (1H, dd, *J* 6.6 and 8.4 Hz, 5-H), 4.80 (1H, m, 4-H), 6.97 (1H, dd, *J* 5.1 and 15.0 Hz, 3-H), 7.19 (1H, dd, *J* 1.2 and 15.0 Hz, 2-H), 7.48–7.96 (5H, m, C_6H_5); δ_C (75 MHz, $CDCl_3$) 25.7 and 26.4 ($C(CH_3)_2$), 68.9 (C-5), 75.5 (C-4), 110.3 ($C(CH_3)_2$), 126.0 (C-2), 128.7, 133.1 and 137.7 (C_6H_5), 144.6 (C-3) and 190.3 (C-1); *m*/*z* (EI) 232 $[M]^+$, (CI) 233 $[M + H]^+$ and 250 $[M + NH_4]^+$.

4,5-Epoxy-1-phenylpent-2-en-1-one 8

Dimethyl sulfoxide (2.55 cm^3, 35.9 mmol) was added dropwise to a solution of oxalyl chloride (8.5 cm^3, 2.4 mol dm^{-3} solution in dichloromethane) in anhydrous dichloromethane (38 cm^3) at −78 °C and under nitrogen. The mixture was vigorously stirred for 5 min, after which a solution of racemic glycidol (1.11 cm^3, 16.67 mmol) in anhydrous dichloromethane (15 cm^3) was added. The mixture was stirred for 15 min at −70 °C and then triethylamine (10.5 cm^3) was added. The mixture was stirred for a further 5 min at −70 °C and then raised to room temperature over a 1 h period. Phenylcarbonylmethylenetriphenylphosphorane (7 g, 18.4 mmol) and a further portion of anhydrous dichloromethane (20 cm^3) was added and the mixture stirred for a further 20 h at room temperature. Water (80 cm^3) was added and the mixture was extracted with chloroform (40 cm^3 × 3), and the combined extracts were washed with brine, dried (Na_2SO_4) and evaporated under reduced pressure to afford a crude residue (11 g). Selective recrystallisation of the phosphine oxide was not possible. Flash chromatography of the residue over silica gel (300 g) with ethyl acetate–petroleum ether (3:17) as the eluent afforded an uncharacterised product (100 mg), followed by *epoxide* (*E*)-*rac*-**8** (2 g, 70%; the racemate was separated on chiral HPLC: isopropyl alcohol–hexane (1:99); R_t = 44 and 55 min respectively); ν_{max}($CHCl_3$)/cm^{-1} 1670 (ketone CO); δ_H (300 MHz, $CDCl_3$) 2.76 (1H, dd, *J* 2.4 and 5.7

Hz, 5-H), 3.10 (1H, dd, *J* 4.2 and 5.7 Hz, 5-H), 3.57 (1H, dddd, *J* 0.6, 2.4, 4.2 and 6.9 Hz, 4-H), 6.76 (1H, dd, *J* 6.9 and 15.3 Hz, 3-H), 7.25 (1H, dd, *J* 0.6 and 15.3 Hz, 2-H), 7.48–7.95 (5H, m, C_6H_5); δ_C (75 MHz, $CDCl_3$) 49.6 (C-5), 50.8 (C-4), 127.7 (C-2), 128.7, 133.1 and 137.4 (C_6H_5), 144.7 (C-3) and 189.6 (C-1); *m*/*z* (EI) 174 $[M]^+$ (Found: $[M]^+$, 174.0680. $C_{11}H_{10}O_2$ requires [*M*], 174.0681).

The above reaction was repeated for enantiopure (*S*)-glycidol (1.11 cm^3) to afford (*E*)-(4*S*)-**8** (2.3 g, 78%, >99% ee-chiral HPLC: as above) mp 69 °C (from ethyl acetate–hexane) (Found: C, 76.0; H, 5.8. $C_{14}H_{16}O_5$ requires C, 75.8; H, 5.8%); $[a]_D$ −4.5 ($c = 2$, $CHCl_3$).

General epoxidation procedures

Biphasic conditions. To a solution of substrate (0.86 mmol, >99% ee) and activated polyleucine (400 mg) in anhydrous tetrahydrofuran (1 cm^3) was added urea hydrogen peroxide (243 mg, 2.59 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.3 cm^3, 2.50 mmol). The mixture was stirred at room temperature for 4 h, and then filtered. The solid residue (polyleucine) was washed with ethyl acetate (10 cm^3 × 3) and water (20 cm^3). The filtrate was extracted with ethyl acetate (20 cm^3 × 3), and the combined extracts were dried (Na_2SO_4), and evaporated under reduced pressure to afford a residue. Chromatography over silica gel gave crude product which was analysed by HPLC. Yields and isomer ratios are detailed in the discussion.

Percarbonate ($Na_2CO_3 \cdot 1.5H_2O_2$) conditions. To a mixture of dimethoxyethane and water (1:2, 1 cm^3) was added the substrate (50 mg, 0.215 mmol) and polyleucine (400 mg). The mixture was stirred for 10 min at room temperature, and then $Na_2CO_3 \cdot 1.5H_2O_2$ (56 mg, 0.36 mmol) was added. The mixture was stirred for 30 min and then worked up as above. Chromatography over silica gel afforded crude product which was analysed by HPLC. Yields and isomer ratios are given in the discussion.

Silica adsorbed polyleucine (*SCAT*) conditions. To a solution of silica adsorbed immobilized polyleucine (600 mg) and substrate (100 mg, 0.43 mmol, >99% ee) in anhydrous tetrahydrofuran (2 cm^3) was added urea hydrogen peroxide (81 mg, 0.86 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.06 cm^3, 0.43 mmol). The mixture was stirred at room temperature for 30 min, and then filtered. The solid residue was washed with ethyl acetate (10 cm^3 × 3). The filtrate was washed with water, and the organic extract dried (Na_2SO_4), and evaporated under reduced pressure to afford a residue. Chromatography over silica gel afforded crude product which was analysed by HPLC. Yields and isomer ratios are detailed in the discussion.

(4*R*)-*syn*- and *anti*-2,3-Epoxy-4,5-isopropylidenedioxy-1-phenylpentan-1-one

Reaction of enone **6** in the absence of catalyst, with work-up as prescribed afforded a residue. Purification by silica gel flash chromatography (ethyl acetate–hexane 1:4) afforded epoxides **9** and **10** (201 mg, 94%, *syn*:*anti* [1:2.2]-chiral HPLC: ethanol–hexane (1:9); R_t = 14 and 22 min respectively).

(2*R*,3*S*,4*R*)-2,3-Epoxy-4,5-isopropylidenedioxy-1-phenylpentan-1-one 9. Reaction of enone **6** with poly-L-leucine under percarbonate conditions, with work-up as described, afforded a residue. Purification by silica gel flash chromatography (ethyl acetate–hexane 1:4) afforded **9** and **10** in the ratio 3.8:1 (203 mg, 95%); recrystallization afforded pure **9**; mp 64 °C (ethyl acetate–hexane) (HPLC: *anti*:*syn* >99:1); $[a]_D$ −35.9 ($CHCl_3$, $c = 1$); δ_H (300 MHz, $CDCl_3$) 1.40 and 1.44 (2 × 3H, 2 × s, $C(CH_3)_2$), 3.27 (1H, dd, *J* 2.1 and 3.3 Hz, 3-H), 3.97 (1H, dd, *J* 6.0 and 8.4 Hz, 5-H), 4.19 (1H, dd, *J* 6.6 and 8.4 Hz, 5-H), 4.30 (1H, d, *J* 2.1 Hz, 2-H), 4.31–4.37 (1H, m, 4-H), 7.51–8.04 (5H, m, C_6H_5); δ_C (75 MHz, $CDCl_3$) 25.6 and 26.0 ($C(CH_3)_2$), 54.1 (C-3), 58.6 (C-2), 66.0 (C-5), 73.7 (C-4), 110.5 ($C(CH_3)_2$), 128.5, 128.9, 134.1 and 135.4 (C_6H_5) and 194.0 (C-1).

(2*S*,3*R*,4*R*)-2,3-Epoxy-4,5-isopropylidenedioxy-1-phenylpentan-1-one 10. Reaction of enone **6** using poly-D-leucine under biphasic conditions and work up as prescribed above gave a residue. Purification by silica gel flash chromatography (ethyl acetate–hexane 1:4) afforded **10** and **9** in the ratio 30:1 (203 mg, 95%); recrystallization furnished pure **10**; mp 65 °C (from ethyl acetate–hexane) (HPLC: *syn*:*anti* 1:>99) (Found: C, 67.9; H, 6.5. $C_{14}H_{16}O_4$ requires C, 67.7; H, 6.5%); $[a]_D$ −12.5 ($CHCl_3$, $c = 1$); $\nu_{max}(CHCl_3)/cm^{-1}$ 1694 (ketone CO); δ_H (300 MHz, $CDCl_3$) 1.39 and 1.46 (2 × 3H, 2 × s, $C(CH_3)_2$), 3.25 (1H, dd, *J* 1.8 and 5.4 Hz, 3-H), 4.02 (1H, dd, *J* 4.8 and 8.1 Hz, 5-H), 4.09 (1H, ddd, *J* 4.8, 5.4 and 6.0 Hz, 4-H), 4.21 (1H, dd, *J* 6.0 and 8.1 Hz, 5-H), 4.23 (1H, d, *J* 1.8 Hz, 2-H), 7.51–8.04 (5H, m, C_6H_5); δ_C (75 MHz, $CDCl_3$) 25.1 and 26.6 ($C(CH_3)_2$), 55.6 (C-3), 59.2 (C-2), 67.0 (C-4), 75.3 (C-5), 110.4 ($C(CH_3)_2$), 128.4, 128.9, 134.1 and 135.5 (C_6H_5) and 193.6 (C-1); *m*/*z* (CI) 249 $[M + H]^+$ and 266 $[M + NH_4]^+$. X-Ray crystal data for compound **9** are published elsewhere.[15]

(4*R*)-*syn*- and *anti*-2,3:4,5-Diepoxy-1-phenylpentan-1-one

Reaction of enone **8** under biphasic conditions, but in the absence of catalyst, with work up as described, gave a residue. Purification by silica gel flash chromatography (ethyl acetate–hexane 3:7) afforded a mixture of **11** and **12** (25 mg, 94%, ratio *syn*-**11**:*anti*-**12** [1:1.7] by ^1H NMR).

(2*S*,3*R*,4*S*)-2,3:4,5-Diepoxy-1-phenylpentan-1-one 12. Reaction of enone **8** (196 mg) under biphasic conditions, using poly-D-leucine as catalyst and with work up as described, gave a residue. Purification by silica gel flash chromatography (ethyl acetate–hexane 3:7) afforded a crystalline residue (203 mg, 95%, *syn*-**11**:*anti*-**12** [1:10] by ^1H NMR); recrystallization afforded pure **12**; mp 58 °C (from ethanol) (Found: C, 69.3; H, 5.3. $C_{11}H_{10}O_3$ requires C, 69.5; H, 5.3%); $[a]_D$ −6 ($CHCl_3$, $c = 1$); $\nu_{max}(CHCl_3)/cm^{-1}$ 1692 (ketone CO); δ_H (300 MHz, $CDCl_3$) 2.79 (1H, dd, *J* 2.7 and 5.1 Hz, 5-H), 2.94 (1H, dd, *J* 4.2 and 5.1 Hz, 5-H), 3.12 (1H, m, 4-H), 3.21 (1H, dd, *J* 2.1 and 4.8 Hz, 3-H), 4.25 (1H, d, *J* 2.1 Hz, 2-H), 7.51–8.02 (5H, m, C_6H_5); δ_C (75 MHz, $CDCl_3$) 45.5 (C-4), 50.0 (C-5), 54.7 (C-3), 58.1 (C-2), 128.4, 129.0, 134.2 and 135.4 (C_6H_5) and 193.3 (C-1); *m*/*z* (CI) 191 ($[M + H]^+$) and 208 ($[M + NH_4]^+$).

(1*S*,2*S*,3*S*,4*R*)-2,3-Epoxy-4,5-isopropylidenedioxy-1-phenylpentan-1-ol 13

Zinc borohydride (4.5 cm^3, 0.0629 mol dm^{-3} ethereal solution) was added to a solution of *syn*-**9** (187 mg, 0.75 mmol) in anhydrous ether (10 cm^3), at 0 °C and under argon. The mixture was stirred at 0 °C for 10 min. Thereafter the mixture was stirred at room temperature for 2 h. Water was added and the resultant mixture stirred for 1 h after which time saturated aqueous ammonium chloride (20 cm^3) was added. The mixture was extracted with ethyl acetate (20 cm^3 × 4), and the combined extracts dried (Na_2SO_4) and evaporated under reduced pressure to afford a crude residue (420 mg). Flash chromatography of the residue over silica gel (35 g) with ethyl acetate–hexane (2:3) as the eluent afforded *epoxy alcohol* **13** (180 mg, 95%) as an oil; $[a]_D$ 53 ($CHCl_3$, $c = 1$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3451 (OH stretch); δ_H (300 MHz, $CDCl_3$) 1.31 and 1.36 (2 × 3H, 2 × s, $C(CH_3)_2$), 2.73 (1H, br s, exchanged by D_2O, OH), 3.16 (1H, dd, *J* 2.1 and 2.7 Hz, 2-H), 3.27 (1H, dd, *J* 2.1 and 4.2 Hz, 3-H), 3.71 (1H, dd, *J* 5.7 and 7.8 Hz, 5-H), 3.93–4.04 (2H, m, 4-H and 5-H), 4.88 (1H, d, *J* 2.7 Hz, 1-H) and 7.27–7.4 (5H, m, C_6H_5); δ_C (75 MHz, $CDCl_3$) 25.4 and 26.3 ($C(CH_3)_2$), 54.5 (C-3), 58.3 (C-2), 65.9 (C-5), 70.5 (C-4), 75.2 (C-1), 110.2 ($C(CH_3)_2$), 126.4, 128.4, 128.7 and 139.5 (C_6H_5).

(1*S*,2*R*,3*S*,4*R*)-2,3-Epoxy-4,5-isopropylidenedioxy-1-phenyl-1-[(*N*-phenyl)carbamoyloxy]pentane 14

Phenyl isocyanate (0.75 cm^3, 6.6 mmol) was added to a solution of the epoxy alcohol **13** (670 mg, 2.68 mmol) in anhydrous dichloromethane (21 cm^3) and anhydrous pyridine (5.5 cm^3). The mixture was stirred for 24 h. The mixture was evaporated under reduced pressure to afford a crude residue. The residue was dissolved in acetone and water (2.5 cm^3) was added. The mixture was vigorously stirred and the organic solvents were removed by evaporation under reduced pressure. Chloroform (20 cm^3) was added and the resultant mixture filtered to remove the insoluble portion. Water (20 cm^3) was added to the filtrate and the mixture was extracted with chloroform (20 $cm^3 \times 3$), and the combined extract dried (Na_2SO_4) and evaporated under reduced pressure to afford a crude residue (1.5 g). Flash chromatography of the residue over silica gel (50 g) with ethyl acetate–hexane (3:7) as the eluent afforded the *carbamate* **14** (970 mg, 95%) as an amorphous solid, mp 163 °C (from acetone-hexane) (Found: C, 68.4; H, 6.3; N, 3.8. $C_{21}H_{23}NO_5$ requires C, 68.3; H, 6.3; N, 3.8%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1737 (CO), 2401 (CN) and 3438 (NH); δ_H (300 MHz, $CDCl_3$) 1.34 and 1.38 (2 × 3H, 2 × s, $C(CH_3)_2$), 3.04 (1H, dd, *J* 2.1 and 3.9 Hz, 3-H), 3.33 (1H, dd, *J* 2.1 and 4.2 Hz, 2-H), 3.82 (1H, dd, *J* 6.3 and 7.8 Hz, 5-H), 4.02–4.15 (2H, m, 4-H and 5-H), 5.84 (1H, d, *J* 4.2 Hz, 1-H), 6.73 (1H, br s, NH) and 7.04–7.42 (10H, m, 2 × C_6H_5); *m*/*z* (CI) 370 $[M + H]^+$.

(1*S*,2*S*,3*S*,4*R*)-1,2-Carbonyldioxy-3,4,5-triacetoxy-1-phenylpentane 15

Boron trifluoride–diethyl ether (0.074 cm^3, 0.60 mmol) was added to a solution of the epoxy urethane **14** (200 mg, 0.54 mmol) in anhydrous ether (12 cm^3), at −20 °C and under argon. The mixture was stirred for 1 h at −20 °C. Dilute aqueous sulfuric acid (10 cm^3, 1 mol dm^{-3}) was added and the mixture stirred for a further 5 h. The mixture was extracted with ethyl acetate (20 $cm^3 \times 3$) and chloroform (20 $cm^3 \times 1$) and the combined extracts were dried (Na_2SO_4) and evaporated under reduced pressure to afford a crude residue (250 mg). The residue was dissolved in anhydrous dichloromethane (8 cm^3) and acetic anhydride (0.6 cm^3, 6.4 mmol), anhydrous pyridine (0.4 cm^3, 4.9 mmol) and 4-dimethylaminopyridine (10 mol%) were added. The mixture was stirred for 24 h, saturated aqueous sodium hydrogen carbonate (30 cm^3) was added. The mixture was extracted with chloroform (20 $cm^3 \times 3$), and the combined extracts washed with dilute aqueous hydrochloric acid (10 cm^3, 2 mol dm^{-3}), dried (Na_2SO_4) and evaporated under reduced pressure to afford a crude residue (290 mg). The residue was flash chromatographed over silica (35 g); elution with ethyl acetate–petroleum ether (3:17) afforded an unidentified product (60 mg), followed by the title compound **15** (196 mg, 96%), as an oil; $[\alpha]_D$ −20 ($CHCl_3$, $c = 1$); $\nu_{max}(CHCl_3)/cm^{-1}$ 1700–1840 (br CO stretch); δ_H (300 MHz, $CDCl_3$) 2.02, 2.03 and 2.09 (3 × 3H, 3 × s, 3 × OAc), 3.98 (1H, dd, *J* 6 and 11.7 Hz, 5-H), 4.24 (1H, dd, *J* 6 and 11.7 Hz, 5-H), 4.74 (1H, t, *J* 2 × 6 Hz, 2-H), 5.37 (1H, dt, *J* 3.9 and 2 × 6 Hz, 4-H), 5.53 (1H, d, *J* 6 Hz, 1-H), 5.56 (1H, dd, *J* 3.9 and 6 Hz, 3-H) and 7.32–7.49 (5H, m, C_6H_5); δ_H (300 MHz, C_6D_6) 1.48, 1.50 and 1.57 (3 × 3H, 3 × s, 3 × OAc), 3.81 (1H, dd, *J* 6 and 11.7 Hz, 5-H), 4.17 (1H, dd, *J* 5.4 and 11.7 Hz, 5-H), 4.35 (1H, t, *J* 2 × 6 Hz, 2-H), 5.19 (1H, d, *J* 6 Hz, 1-H), 5.28–5.38 (2H, m, 3-H and 4-H) and 6.89–6.94 (5H, m, C_6H_5); δ_C (75 MHz, $CDCl_3$) 20.4, 20.5 and 20.6 (3 × $COCH_3$), 61.0 (C-5), 68.7 and 70.1 (C-3 and C-4), 78.0 (C-1 and C-2), 126.5, 129.5, 130.2 and 135.5 (C_6H_5), 153.1 (CO_3), 169.5, 169.6 and 170.3 ($COCH_3$); δ_C (75 MHz, C_6D_6) 19.5, 19.5 and 19.8 (3 × $COCH_3$), 61.2 (C-5), 68.8 and 70.3 (C-3 and C-4), 79.6 and 80.0 (C-1 and C-2), 126.5, 129.1, 129.6 and 136.0 (C_6H_6), 152.8 (CO_3), 168.9, 168.9 and 169.5 ($COCH_3$); *m*/*z* (CI) 398 $[M + NH_4]^+$ (Found: $[M + NH_4]^+$, 398.1439. $C_{18}H_{24}NO_9$ requires $[M + NH_4]^+$, 398.1451).

(2*S*,3*S*,4*S*,5*R*)-2,3-Carbonyldioxy-4,5,6-triacetoxyhexanoic acid 16

Sodium metaperiodate (2.8 g, 13.4 mmol) was added to a stirred mixture of the phenyl carbonate **15** (340 mg, 0.89 mmol), carbon tetrachloride (3.7 cm^3), acetonitrile (3.7 cm^3) and water (5.2 cm^3). Ruthenium(III) chloride (414 mg, 2 mmol) was added and the resultant mixture stirred for 24 h at room temperature, at which point there was complete consumption of the phenyl carbonate (TLC). The mixture was diluted with an excess of diethyl ether, with vigorous stirring for 10 min to precipitate ruthenium(IV) oxide. Anhydrous magnesium sulfate was added to the mixture. The resultant mixture was filtered over anhydrous magnesium sulfate and washed thoroughly with an excess of diethyl ether. The resultant filtrate was washed with saturated aqueous sodium thiosulfate and evaporated under reduced pressure to afford the title compound **16** (212 mg, 68%, 0.61 mmol) as an oil; $\nu_{max}(CHCl_3)/cm^{-1}$ 1755 (CO stretch of COOH), 1831 (CO stretches of OAc), and 2400 to 3500 (br OH stretch of COOH dimer); δ_H (300 MHz, $CDCl_3$) 2.06, 2.11 and 2.17 (3 × 3H, 3 × s, 3 × OAc), 4.04 (1H, dd, *J* 6.0 and 11.7 Hz, 6-H), 4.30 (1H, dd, *J* 5.7 and 11.7 Hz, 6-H), 4.92 (1H, t, *J* 2 × 4.2 Hz, 3-H), 5.18 (1H, d, *J* 4.2 Hz, 2-H), 5.40 (1H, ddd, *J* 3.3, 5.7 and 6.0 Hz, 5-H), 5.57 (1H, dd, *J* 3.3 and 4.2 Hz, 4-H), and 8.42 (1H, br s, exchanged by D_2O, $COOH$); δ_C (75 MHz, $CDCl_3$) 20.3, 20.6 and 20.7 (3 × $COCH_3$), 61.4 (C-6), 68.9 and 69.6 (C-4 and C-5), 73.4 and 77.7 (C-2 and C-3), 152.8 (CO_3), 169.0 ($COOH$), 169.8, 170.3 and 171.0 ($COCH_3$); *m*/*z* (CI) 366 $[M + NH_4]^+$ (Found: $[M + NH_4]^+$, 366.1045. $C_{13}H_{20}NO_{11}$ requires $[M + NH_4]^+$, 366.1036).

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