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Supporting Information

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Sulfur Ylide Mediated Synthesis of Highly Functionalised and Trisubstituted Epoxides with High Enantioselectivity. Application to the Synthesis of CDP 840.

Varinder K. Aggarwal,* Imhyuck Bae, Hee-Yoon Lee,* Jeffery Richardson, and David T. Williams

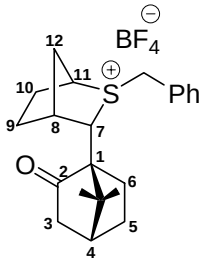
General Procedure for Salt Preparation from Corresponding Bromide[1] (Method X)

To a rapidly stirred solution of sulfide **1**[2] (1.8 g, 7.1 mmol) in freshly distilled alkyl bromide (85 mmol) was added silver tetrafluoroborate in the dark (2.2 g, 10.6 mmol) under an argon atmosphere at 0 °C. The reaction was allowed to warm to room temperature, stirred for 48 h and dichloromethane (10 mL) added. The resulting silver bromide precipitate was filtered, washed with dichloromethane and the filtrate concentrated *in vacuo*. The resulting oil was purified by column chromatography eluting with dichloromethane to 5% methanol/CH_2Cl_2 to give a pale yellow solid. This was dissolved in ethanol, stirred for 0.5 h at 40 °C over activated charcoal, filtered through celite and the filtrate concentrated *in vacuo* to give a white solid.

General Procedure for Salt Preparation from Corresponding Alcohol[3,4](Method Y)

A solution of HBF_4 in Et_2O (54% Wt., 1.35 mL, 9.0 mmol) was slowly added to a solution of alcohol (10.0 mmol) and sulfide **1** (500 mg, 2.0 mmol) in Et_2O (5 mL) under nitrogen. After 12 h, the precipitate was collected by filtration. The salt was washed with Et_2O (3×10 mL) and dried in *vacuo* to afford a white powder.

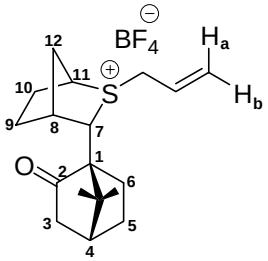
(1S,3S,4R)-2-benzyl-3-[(1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-yl]-2-thioniabicyclo[2.2.1]heptane tetrafluoroborate (2a) (Method X)



2a

White powder (92 %); R_f = 0.33 (5 % MeOH in CH_2Cl_2); ν_{max}/cm^{-1} 2968, 1736, 1056; m.p. 143-145 °C (EtOH); $[\alpha]_D^{25}$ = -36.0 (c = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 1.08 (3H, s, CH_3), 1.17 (3H, s, CH_3), 1.20-1.37 (2H, m, 2 × C*H*H), 1.53-1.69 (2H, m, C^{5}H$_2$), 1.81 (1H, dt, *J* 23.5 Hz and 2.0 Hz, C*H*H), 1.92 (1H, d, 19.0 Hz, C^{3}*H*H), 1.94-2.05 (1H, m, C*H*H), 2.04-2.20 (3H, m, C^{4}H, 2 × CH*H*), 2.23 (1H, d, *J* 13.0 Hz, C^{12}*H*H), 2.54 (1H, ddd, *J* 19.0, 5.0 and 3.0 Hz, C^{3}H*H*), 2.81 (1H, d, *J* 13.0 Hz, C^{12}H*H*), 3.20 (1H, br. s, C^{8}H), 4.21 (1H, d, *J* 5.0 Hz, C^{11}H), 4.32 (1H, d, *J* 2.5 Hz, C^{7}H), 4.39 (1H, d, *J* 13.0 Hz, SC*H*HPh), 4.66 (1H, d, *J* 13.0 Hz, SCH*H*Ph), 7.35-742 (3H, m, Ar*H*$^{meta/para}$), 7.44-7.50 (2H, m, Ar*H*^{ortho}); ^{13}C NMR (63 MHz, $CDCl_3$) 19.1, 21.9, 24.4, 26.6, 26.7, 33.3, 41.1, 43.5, 44.0, 45.1, 47.9, 49.9, 58.0, 60.0, 68.8, 128.6, 129.7, 129.9, 130.5, 215.6; *m/z* (ES+) 341 (M^+-BF_4^-, 47%), 217 (100), (Found: M^+-BF_4^-, 341.1939. $C_{22}H_{29}SO$ requires M^+-BF_4^-, 341.1927).

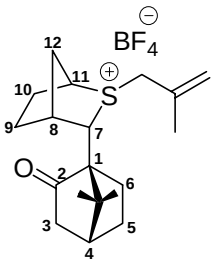
(1S,3S,4R)-2-allyl-3-[(1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-yl]-2-thioniabicyclo [2.2.1]heptane tetrafluoroborate (2b) (Method X)



2b

Pale yellow powder (83 %); R_f = 0.45 (5 % MeOH in CH_2Cl_2); ν_{max}/cm^{-1} 2938, 1735, 1038; m.p. 159-159.5 °C (CH_2Cl_2/Et_2O); $[\alpha]_D^{25}$ = -50.0 (c = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 1.13 (3H, s, CH_3), 1.22 (3H, s, CH_3), 1.38-1.46 (1H, m, C*H*H), 1.54-1.72 (3H, m, $C^{5}H_2$, C*H*H), 1.98 (1H, d, *J* 20.0 Hz, C^{3}*H*H), 2.06-2.28 (6H, m, C^{4}H, C^{12}*H*H, 4 × C*H*H) 2.59 (1H, ddd, *J* 18.5, 4.5 and 3.0 Hz, C^{3}HH), 2.64 (1H, d, *J* 14.0 Hz, C^{12}H*H*), 3.19 (1H, br. s, C^{8}H), 3.88 (1H, dd, *J* 13.5 and 7.5 Hz SC*H*HCH), 4.07 (1H, dd, *J* 13.5 and 7.5 Hz, SCH*H*CH), 4.24 (1H, d, *J* 2.0 Hz, C^{7}H), 4.34 (1H, d, *J* 4.5 Hz, C^{11}H), 5.55 (1H, d, *J* 10.0 Hz, H_b, 5.73 (1H, d, *J* 16.0 Hz, H_a), 5.80-5.93 (1H, m, C*H*=CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) 19.3, 22.0, 24.0, 26.8, 34.3, 41.1, 43.3, 44.1, 45.2, 46.3, 50.0, 57.7, 60.0, 68.9, 125.4, 126.9, 215.6; *m/z* (CI) 291 (M^+-BF_4^-, 28%), 250 (30%), 217 (100%), (Found: M^+-BF_4^- 291.1787. $C_{18}H_{27}SO$ requires M^+-BF_4^- 291.1783).

(1S,3S,4R)-3-[(1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-yl]-2-(2-methyl-2-propenyl)-2-thioniabicyclo[2.2.1]heptane tetrafluoroborate (2c) (Method X)

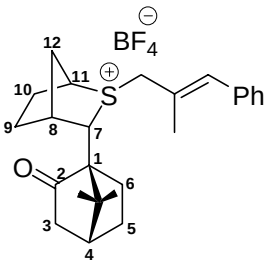


2c

White powder (91 %); R_f = 0.41 (5 % MeOH in CH_2Cl_2); (Found C, 58.05; H, 7.79; S, 7.99; $C_{19}H_{29}BF_4OS$ requires C, 58.17; H, 7.45; S, 8.17 %); ν_{max}/cm^{-1} 2932, 1734, 1029; m.p. 175-177 °C

(decom.)(CH_2Cl_2/petrol); $[\alpha]_D^{24}$ = -53.5 (c = 1.0 in MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) 1.13 (3H, s, CH_3), 1.21 (3H, s, CH_3), 1.38-1.48 (1H, m, C*H*H), 1.48-1.57 (1H, m, C*H*H), 1.57-1.76 (2H, m, C^5H_2), 1.90 (3H, s, $CH_3C{=}CH_2$), 1.99 (1H, d, *J* 19.0 Hz, C^3H*H*), 2.05-2.30 (6H, m, C^4H, C^{12}H, 4 × C*H*H), 2.56-2.69 (2H, m, C^3*H*H, C^{12}*H*H), 3.20 (1H, br. s, C^8H), 3.80 (1H, d, *J* 13.0 Hz, SC*H*HC), 4.06 (1H, d, *J* 13.0 Hz, SCH*H*C), 4.21 (1H, d, *J* 2.0 Hz, C^7H), 4.28 (1H, d, *J* 4.5 Hz, C^{11}H), 5.22 (1H, s, C=C*H*H), 5.40 (1H, s, C=CH*H*); ^{13}C NMR (100 MHz, $CDCl_3$) 19.2, 21.5, 21.9, 24.4, 26.8, 26.9, 33.8, 41.2, 43.4, 44.2, 45.2, 50.0, 51.3, 58.3, 60.1, 69.3, 121.9, 133.9, 215.4; *m/z* (FAB) 305 (M^+-BF_4^-, 100%), 217 (25%).

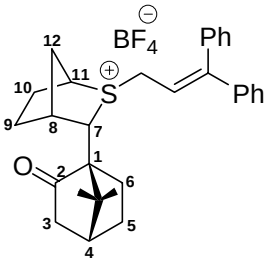
(1S,3S,4R)-3-[(1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-yl]-2-[(2E)-2-methyl-3-phenyl-2-propenyl]-2-thioniabicyclo[2.2.1]heptane tetrafluoroborate (2d) (Method Y)



2d

White powder (86 %); R_f = 0.35 (5 % MeOH in CH_2Cl_2); (Found C, 64.49; H, 7.05; S, 6.50; $C_{25}H_{33}BF_4OS$ requires C, 64.10; H, 7.10; S, 6.85 %); ν_{max}/cm^{-1} 2980, 1734, 1053, 1035; m.p. 136-138 °C; $[\alpha]_D^{24}$ = -95.7 (c = 1.0 in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) 1.11 (3H, s, CH_3), 1.21 (3H, s, CH_3), 1.32-1.43 (1H, m, C^5*H*H), 1.45-1.55 (1H, m, C^5H*H*), 1.55-1.70 (3H, m, CH_2CCH_3), 1.90-2.32 (9H, m, C^{12}*H*H, C^3*H*H, C^4H, 6 × C*H*H), 2.58 (1H, d, *J* 19.0 Hz, C^3H*H*), 2.73 (1H, d, *J* 12.5 Hz, C^{12}H*H*), 3.21 (1H, br. s, C^8H), 3.97 (1H, d, *J* 13.0 Hz, SCH*H*C), 4.24 (1H, d, *J* 13.0 Hz, SCH*H*C), 4.27 (1H, br. s, C^{11}H), 4.33 (1H, d, *J* 2.5 Hz, C^7H), 6.89 (1H, s, C=C*H*Ph), 7.24-7.38 (5H, m, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$) 17.7, 19.3, 21.9, 24.5, 26.8, 27.0, 33.9, 41.4, 43.4, 44.2, 45.2, 50.0, 54.9, 58.3, 60.2, 68.9, 125.9, 127.9, 128.5, 129.1, 135.8, 136.0, 215.6; *m/z* (FAB) 381 (M^+-BF_4^-, 46%), 131 (100%).

(1S,3S,4R)-3-[(1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-yl]-2-(3,3-diphenyl-2-propenyl)-2-thioniabicyclo[2.2.1]heptane tetrafluoroborate (2e) (Method Y)



2e

White solid (64 %); R_f = 0.35 (5 % MeOH in CH_2Cl_2); ν_{max}/cm^{-1} 2964, 1732, 1495, 1445, 764, 707; m.p. 160-161 °C (CH_2Cl_2/Et_2O); $[\alpha]_D^{25}$ = -64.4 (c = 1.9 in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) 1.06 (3H, s, C*H*$_3$), 1.12 (1H, m, C*H*H), 1.16 (3H, s, C*H*$_3$), 1.29 (1H, m, C*H*H), 1.58 (2H, m, C^{5}H$_2$), 1.90-2.23 (7H, m, C^{12}*H*H, C^{3}H*H*, C^{4}H, 4 × C*H*H), 2.44 (1H, d, *J* 13.0 Hz, C^{12}H*H*), 2.55 (1H, ddd, *J* 17.5, 5.5 and 2.0 Hz, C^{3}*H*H), 3.08 (1H, br. s, C^{8}H), 3.87 (1H, dd, *J* 13.0 and 8.5 Hz, SCH*H*CH), 4.08 (1H, d, *J* 5.0 Hz, C^{11}H), 4.20 (2H, m, C^{7}H and SCH*H*CH), 6.27 (1H, t, *J* 8.5 Hz, *H*C=C(Ph)$_2$), 7.18-7.48 (10H, m, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$) 19.3, 21.9, 24.4, 26.8, 27.1, 33.1, 41.0, 42.9, 43.0, 44.1, 45.1, 49.9, 56.8, 60.3, 68.3, 113.6, 127.6, 128.6, 128.6, 129.1, 129.3, 129.5, 137.4, 139.6, 153.3; *m/z* (FAB) 443 (M^+-BF_4^-, 40%), 193 (100%).

Tetrahydro-1-(phenylmethyl)-thiophenium tetrafluoroborate[4] (method Y)

White solid (95%); R_f = 0.15 (5% MeOH/CH_2Cl_2); m.p. 76.5-78 °C (EtOH) [lit.,[4] 79-79.5 °C (H_2O/EtOH/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) 2.21-2.37 (4H, m, CH_2), 3.39-3.60 (4H, m, CH_2), 4.55 (2H, s, C*H*$_2$Ph), 7.37-7.49 (5H, m, Ar*H*).

General Procedure for Epoxidation Using KOH as Base (Method A) [5]

To a stirred solution of the sulfonium salt (200 mg, 0.47 mmol) in a 9:1 acetonitrile/water mixture (1.25 mL) at room temperature was added the freshly distilled aldehyde or ketone (0.47 mmol) followed by powdered KOH (50.2 mg, 0.93 mmol). The reaction was then allowed to stirred at room temperature for 2 hours. Water (2 mL) was added and the aqueous phase extracted with

dichloromethane (3 x 5 mL), the combined organic layers washed with water (2 mL), dried over $MgSO_4$ and concentrated in *vacuo*. The residue was then purified by column chromatography.

General Procedure for Epoxidation at Low Temperature using P_2 Base (Method B) [6]

To a solution of the sulfonium salt (0.1 g, 0.23 mmol) in anhydrous solvent (0.8 mL) was added N,N,N′,N′,-tetramethyl-N″-[tris(dimethylamino)phosphoralidene]phosphoric triamide ethylimine[7] (0.23 mmol) at –78 °C. After stirring for 10–15 min the desired aldehyde or ketone (0.23 mmol) was added dropwise and the reaction stirred for 1 hour (aldehydes) or 2 days (ketones) at –78 °C. After addition of a saturated solution of NaCl in water (1 mL), the organic phase was separated and the aqueous phase extracted with CH_2Cl_2 (3 x 5 mL). The organic phases were combined, filtered over $MgSO_4$, and concentrated in *vacuo*.

General Procedure for Epoxidation at Low Temperature using KHMDS as Base (Method C)

To a rapidly stirred suspension of the sulfonium salt (65 mg, 0.15 mmol) in anhydrous THF (0.6 mL) under an N_2 atmosphere at –78 °C, was added KHMDS (0.5 M in toluene, 300 μL, 0.15 mmol), at which point the sulfonium salt dissolved. The reaction mixture then was stirred at –78 °C for 2 h before addition of the desired carbonyl compound (0.15 mmol). Stirring was continued at –78 °C for 5 h and then a saturated solution of NaCl in water (1 mL) was added. The organic phase was separated and the aqueous phase extracted with CH_2Cl_2 (3 x 5 mL). The organic phases were combined, filtered over $MgSO_4$, and concentrated in *vacuo*.

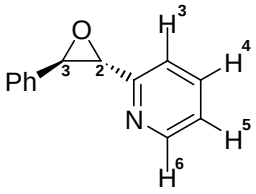
General Purification Method for Epoxides

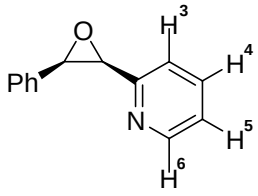
The crude epoxides were generally purified by flash column chromatography on silica gel (Merck Kieselgel $60F_{254}$, 230-400 mesh). For the acid sensitive vinyl epoxides, the crude materials were purified by basic aluminum oxide (grade 5) [prepared by addition of 15% H_2O to Fluka type 5016 A basic alumina] eluting with 1% EtOAc in petroleum ether or by Kugelröhr distillation.

2,3-Diphenyloxirane (Table 1, entry 1)[2]

Purified by column chromatography eluting with 2% EtOAc/petrol. *Trans* isomer: White solid; R_f = 0.40 (5% EtOAc/petrol); m.p. 65-66 °C (petrol) [Lit.,[8] 65-67 °C (petrol)]; ^{1}H NMR (270 MHz, $CDCl_3$) 3.87 (2H, s, 2 × CH), 7.30-7.43 (10H, m, Ar*H*). *Cis* isomer (not isolated): R_f = 0.36 (5% EtOAc/petrol); ^{1}H NMR (270 MHz, $CDCl_3$) 4.39 (2H, s, 2 × CH), 7.16-7.19 (10H, m, Ar*H*).

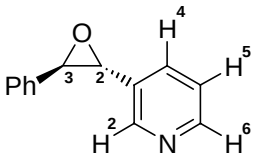
2-[(2R,3R)-3-phenyloxiran-2-yl]pyridine (Table 1, entry 2)[9,10]

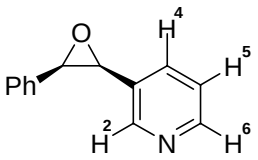




Purified by column chromatography eluting with 10% EtOAc/petrol then 20% EtOAc/petrol. *Trans isomer:* white solid; R_f = 0.22 (20% EtOAc/petrol); m.p. 51-53 °C [Lit.,[9]51-53 °C]; ^{1}H NMR (400 MHz, $CDCl_3$) 4.05 (1H, d, *J* 1.5 Hz, PhCHC*H*), 4.07 (1H, d, *J* 1.5 Hz, PhC*H*), 7.24-7.28 (2H, m, H_3, H_5), 7.31-7.40 (5H, m, Ar*H*), 7.69-7.76 (1H, dt, *J* 8.0 and 1.5 Hz, H_4), 8.60 (1H, d m, *J* 5.0 Hz, H_6); ^{13}C NMR (100 MHz) 61.9, 62.9, 120.2, 123.3, 125.8, 128.5, 128.6, 136.7, 136.9, 156.5. *cis isomer: colourless oil;* R_f = 0.10 (20% EtOAc/petrol);. $[\alpha]_D^{25}$ (*cis* isomer, 80% ee) = +25.0 (c = 0.36, benzene) [Lit.,[9] $[\alpha]_D^{25}$ (99.9% ee) = +82.0 (c = 0.36, benzene]; ^{1}H NMR (270 MHz, $CDCl_3$) 4.46 (1H, d, *J* 5.5 Hz, PhCH*CH*), 4.49 (1H, d, *J* 5.5 Hz, PhC*H*), 7.02-7.12 (2H, m, H_3, H_5), 7.12-7.30 (5H, m, Ar*H*), 7.40-7.50 (1H, dt, *J* 8.0, and *2*.5 Hz, H_4), 8.45 (1H, d m, 5.5 and 1.0 Hz, H_6).

3-(3-phenyloxiranyl)-pyridine (Table 1, entry 3)[9,10]





Purified by column chromatography using eluting with 10% EtOAc/petrol to 30% EtOAc/petrol. *Trans* isomer: Colourless oil; R_f = 0.28 (30% EtOAc/petrol); ^{1}H NMR (270 MHz, $CDCl_3$) 3.89 (1H,

d, *J* 2.0 Hz, PhCHC*H*), 3.91 (1H, d, *J* 2.0 Hz, PhC*H*), 7.30-7.44 (6H, m, Ar*H* + H_5), 7.65 (1H, dt, *J* 7.5 and 2.0 Hz, H_4), 8.59 (1H, dd, *J* 4.5 and 2.0 Hz, H_6), 8.64 (1H, d, *J* 2.0 Hz, H_2); ^{13}C NMR (100 MHz, $CDCl_3$) 60.7, 62.8, 123.5, 125.5, 128.7, 132.7, 136.4, 140.0, 147.8, 149.7. *Cis* isomer (not isolated, observed in crude reaction mixture); R_f = 0.40 (30% EtOAc/ petrol); ^{1}H NMR (400 MHz, $CDCl_3$) 4.36 (1H, d, *J* 4.5 Hz, PhCHC*H*), 4.44 (1H, d, *J* 4.5 Hz, PhC*H*), 7.02-7.21 (6H, m, Ar*H* and H_5), 7.30-7.48 (1H, m, H_4), 8.40 (1H, m, H_6), 8.49 (1H, m, H_2).

2-Butyl-3-phenyloxirane (Table 1, entry 4)[2]

Purified by column chromatography eluting with 1% EtOAc/petrol to 10% EtOAc/petrol. Mixture of *trans* and *cis isomers*. *Trans isomer*: colourless oil; R_f = 0.57 (10% EtOAc/petrol); ^{1}H NMR (400 MHz, $CDCl_3$) 0.74-0.98 (3H, m, CH_3), 1.18-1.76 (6H, m, 3 × CH_2), 2.95 (1H, td, *J* 5.5 and 2.0 Hz, CH_2C*H*), 3.60 (1H, d, *J* 2.0 Hz, PhC*H*), 7.23-7.39 (5H, m, Ar*H*). *Cis* isomer: colourless oil; R_f = 0.51 (10% EtOAc/petrol); ^{1}H NMR (400 MHz, $CDCl_3$) 0.74-0.98 (3H, m, CH_3), 1.18-1.76 (6H, m, 3 × CH_2), 3.20 (1H, m, CH_2C*H*), 4.07 (1H, d, *J* 4.0 Hz, PhC*H*), 7.23-7.39 (5H, m, Ar*H*).

2-Phenyl-3-vinyloxirane (Table 1, entry 5 and 13)[6,11,12]

Purified by Kugelröhr distillation at 50 °C / 2 mmHg. Isolated as a *cis*/*trans* mixture; *Trans* isomer: colourless oil; R_f = 0.60 (20% EtOAc/petrol); $[\alpha]_D^{25}$ (*trans* isomer, 99% ee) = +89.0 (c = 0.3, $CHCl_3$) [Lit.,[11] [*S*,*S*] enantiomer, $[\alpha]_D^{25}$ = -14.2 (c = 0.88, $CHCl_3$]; ^{1}H NMR (270 MHz, $CDCl_3$) 3.36 (1H, dd, *J* 7.5 and 2.0 Hz, PhCHC*H*), 3.77 (1H, d, *J* 2.0 Hz, PhC*H*), 5.34 (1H, dd, *J* 10.5 and 1.5 Hz, CH=C*H*H), 5.52 (1H, dd, *J* 17.0 and 1.5 Hz, CH=CH*H*), 5.65-5.85 (1H, m, C*H*=CH_2), 7.10-7.45 (5H, m, Ar*H*); ^{13}C NMR (67.5 MHz, $CDCl_3$) 60.22, 62.9, 119.5, 125.5, 128.2, 128.5, 135.1. *Cis* isomer (not isolated observed in crude reaction mixture from table 1, entry 5 method A); ^{1}H NMR (400 MHz, $CDCl_3$) 3.67 (1H, dd, *J* 6.0 and 4.0 Hz, PhCHC*H*), 4.25 (1H, d, *J* 4.0 Hz, PhC*H*), 5.20-5.85 (3H, m, C*H*=CH_2, CH=CH_2), 7.10-7.45 (5H, m, Ar*H*).

2-Phenyl-3-isopropenyloxirane (Table 1, entry 6 and 14)[12,13]

Purified by Kugelröhr distillation at 50 °C / 2 mmHg. Isolated as a *cis*/*trans* mixture; *Trans* isomer: colourless oil; R_f = 0.34 (5% EtOAc/petrol). ^{1}H NMR (270 MHz, $CDCl_3$) 1.75 (3H, t, *J* 1.5 Hz, CH_3), 3.37 (1H, d, *J* 2.0 Hz, PhCHC*H*), 3.81 (1H, d, *J* 2.0 Hz, PhC*H*), 5.04-5.08 (1H, m, C=CH*H*), 5.17-5.20 (1H, m, C=CH*H*), 7.27-7.41 (5H, m, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$) 17.0, 58.4, 64.9, 114.2, 125.6, 128.2, 128.5, 137.5, 141.1; *cis* isomer (not isolated observed in crude reaction mixture from table 1, entry 6 method A): R_f = 0.34 (5% EtOAc/petrol); ^{1}H NMR (270 MHz, $CDCl_3$) 1.45-1.54 (3H, m, CH_3), 3.67 (1H, d, *J* 5.5 Hz, PhCHC*H*), 4.19 (1H, d, *J* 5.5 Hz, PhC*H*), 4.86-4.89 (1H, m, C=C*H*H), 4.99-5.02 (1H, m, C=CH*H*), 7.27-7.41 (5H, m, Ar*H*).

2-Phenyl-3-[(E)-1-propenyl]oxirane (Table 1, entry 7)[2,12]

Purified by Kugelröhr distillation at 75 °C / 2 mmHg. Isolated as a *cis*/*trans* mixture; *Trans* isomer: colourless oil; R_f = 0.30 (5% EtOAc / 1% NEt_3 / petroleum ether); $[\alpha]_D^{25}$ (95% ee) = +87.0 (c = 0.21 in $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) 1.76 (3H, dd, *J* 7.0 and 2.0 Hz, CH_3), 3.32 (1H, dd, *J* 8.0 and 2.0 Hz PhCHC*H*), 3.76 (1H, d, *J* 2.0 Hz, PhC*H*), 5.35 (1H, ddq, *J* 15.5, 7.0 and 2.0 Hz, C*H*=CHCH$_3$), 5.98 (1H, dq, *J 15.5* and 6.5 Hz, CH=C*H*CH$_3$), 7.24-7.40 (5H, m, Ar*H*). *Cis* isomer; observed in crude reaction mixture from table 1, entry 7 method A); ^{1}H NMR (400 MHz, $CDCl_3$) 1.65 (3H, dd, *J* 7.0 and 2.0 Hz, CH_3), 3.64 (1H, dd, *J* 9.0 and 4.0 Hz PhCHC*H*), 4.21 (1H, d, *J* 4.0 Hz, PhC*H*), 5.03 (1H, ddq, *J* 15.5, 9.0 and 2.0 Hz, C*H*CHCH$_3$), 5.94-6.04 (1H, m, CHC*H*CH$_3$), 7.24-7.40 (5H, m, Ar*H*).

Tris(1-methylethyl)[(3-phenyloxiranyl)ethynyl]-silane (Table 1, entry 8)[14]

Purified by column chromatography eluting with petrol to 2% EtOAc/petrol. Mixture of *trans* and *cis isomers*. The pure *trans* isomer and a *cis*/*trans* mixture were isolated by chromatography. *Trans* isomer: colourless oil; R_f = 0.63 (2% EtOAc/petrol); $[\alpha]_D^{25}$ (*trans* isomer, 99% ee) = +96.0 (c = 0.07, CH_2Cl_2); ν_{max}(film)/cm^{-1} 3066, 3035, 2942, 2171; ^{1}H NMR (400 MHz, $CDCl_3$), 1.09 (21H, s, 3xPr^i), 3.38 (1H, d, *J* 2.0 Hz, PhCHC*H*), 4.00 (1H, d, *J* 2.0 Hz, PhC*H*), 7.25-7.45 (5H, m, Ar*H*); c*is*

isomer: R_f = 0.55 (2% EtOAc/petrol); ^{1}H NMR (400 MHz, $CDCl_3$) 0.93 (21H, s, 3 × *i*-Pr), 3.77 (1H, d, *J* 3.9 Hz, PhCHC*H*), 4.11 (1H, d, *J* 3.9 Hz, PhC*H*), 7.25-7.45 (5H, m, Ar*H*).^{13}C NMR [mixture of *trans* and *cis* 1.2:1)] (100 MHz, $CDCl_3$) 11.1, 11.2, 18.4, 18.6, 48.5, 49.7, 59.1, 60.4, 86.1, 88.0, 101.1, 103.1, 125.7, 126.9, 127.9, 128.2, 128.6, 134.1, 135.8, 137.0; *m*/z (EI) 300 (M^+, 46%), 84 (100), (Found $[M^+H]^+$ 301.1918 $C_{19}H_{28}OSi$ requires *m/z* 301.1943).

(2*R*)-2-Phenyl-1-oxaspiro[2.5]octane (Table 1, entry 9)[15-17]

Purified by column chromatography eluting with 2% EtOAc/petrol to 10% EtOAc/petrol. Colourless oil, R_f = 0.29 (5% EtOAc/petrol); $[\alpha]_D^{25}$ = +68.0 (c = 2.5, pentane) [Lit.,[15] (S) enantiomer, $[\alpha]_D^{25}$ (92% ee) = -26.5 (c = 2.5, pentane]; ^{1}H NMR (400 MHz, $CDCl_3$) 1.21-1.90 (10H, m, 5 × CH_2), 3.86 (1H, s, PhC*H*), 7.24-7.37 (5H, m, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$) 24.6, 25.4, 25.6, 28.5, 35.5, 64.6, 65.5, 126.4, 127.3, 128, 136.4.

6-*t*-Butyl-2-phenyl-1-oxa- spiro[2.5]octane (Table 1, entry 10).

White solid; R_f = 0.35 (5 % EtOAc in petroleum ether); (Found C, 83.52; H, 10.20; $C_{17}H_{24}O$ requires C, 83.55; H, 9.90 %); ν_{max}/cm^{-1} 2953, 1367, 742, 697; m.p. 61-63 °C; $[\alpha]_D^{25}$ (>99% ee) = –6.8 (c = 1.0 in MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) 0.89 (9H, s, 3 × C*H*$_3$), 1.02-0.13 (1H, m, C*H*), 1.22-1.39 (3H, m, C*H*), 1.39-1.53 (2H, m, 2 × C*H*), 1.69-1.80 (1H, m, C*H*), 1.80-1.88 (1H, m, C*H*), 1.91-2.01 (1H, m, C*H*), 3.90 (1H, s, PhC*H*), 7.24-7.37 (5H, m, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$) 24.9, 25.1, 27.7, 28.5, 32.6, 35.2, 47.8, 64.2, 65.0, 126.4, 127.3, 128.0, 136.5. *m*/z (EI) 244 (M^+, 13%), 226 (7), 215 (8), 169 (49), 141 (13), 128 (6), 115 (8), 105 (19), 91 (64), 84 (100), 57 (41); (Found M^+ 244.1834 $C_{17}H_{24}O$ requires *m/z* 244.1827).

2-Methyl-2,3-diphenyloxirane (Table 1, entry 11)[18,19]

Colourlesss oil; major product c*is;* confirmed by nOe experiment. Purified by chromatography on aluminium oxide (grade 5) eluting with 2 % EtOAc/petroleum ether as the *trans* isomer was

unstable on silica gel. Mixture of *trans* and *cis isomers was isolated*. *Trans isomer*: R_f = 0.45 (10% EtOAc in petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) 1.47 (3H, s, C*H*$_3$), 3.98 (1H, s, C*H*), 7.30 – 7.50 (10H, m, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$) 16.7, 63.0, 67.0, 126.5, 126.9, 127.4, 127.6, 128.1, 128.4, 135.9, 142.3; *cis isomer*: observed in crude reaction mixture from table 1, entry 11 method B); R_f = 0.42 (10% EtOAc in petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) 1.78 (3H, s, C*H*$_3$), 4.15 (1H, s, C*H*), 7.00 – 7.20 (10H, m, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$) 25.6, 65.5, 65.9, 125.1, 126.4, 127.0, 127.2, 127.5, 127.7, 135.5, 138.4.

(2*S*,3*R*)-2-Methyl-2-(4-nitrophenyl)-3-phenyloxirane (Table 1, entry 12)[17]

Purified by column chromatography eluting with 10% EtOAc/petrol to 20% EtOAc/petrol. *Cis* configuration confirmed by nOe experiment. White crystalline solid; R_f = 0.42 (20% EtOAc/petrol); m.p. 74-75 °C (EtOAC/petrol)[Lit.(racemate),[17] (126-128 °C)]; $[\alpha]_D^{25}$ (*cis* isomer, 71% ee) = -49.0 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 1.82 (3H, s, CH_3), 4.25 (1H, s, PhC*H*), 7.0 – 7.42 (7H, m, Ar*H*), 8.02-8.07 (2H, m, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$) 24.8, 65.3, 65.8, 123.2, 126.3, 127.8, 127.9, 128.0, 134.6, 145.9, 147.1.

(2*R*,3*R*)-2-[(E)-1-Methyl-2-phenylethenyl]-3-phenyl-oxirane (Table 1, entry 15)

Purified by chromatography on aluminium oxide (grade 2) eluting with petroleum ether to petroleum ether/CH_2Cl_2 (7:3) as epoxide was unstable on silica gel. *Trans isomer*: Colourless oil; R_f = 0.38 (5% EtOAc in petroleum ether); ν_{max}(film)/cm^{-1} 3025, 2985, 1600, 1495, 1455, 1013, 845, 750, 695; $[\alpha]_D^{25}$ (*trans* isomer) = +337.3 (c = 1.0 in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) 1.88 (3H, d, *J* = 1.3 Hz, C*H*$_3$), 3.49 (1H, dd, *J* = 1.3 Hz, 1.9 Hz, C*H*), 3.89 (1H, *J* = 1.9 Hz, C*H*), 6.68 (1H, br. s, C*H*), 7.30-7.37 (10H, m, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$) 12.8, 58.5, 66.7, 125.6, 126.9, 128.3, 128.6, 128.7, 129.0, 133.7, 137.1, 137.5; *m*/z (CI) 237 (M^++1, 25 %); (Found $[M+H]^+$ 237.1278. $C_{17}H_{17}O$ requires *m/z*, 237.1279).

2-(2,2-Diphenylethenyl)-3-phenyl-oxirane (Table 1, entry 16)[2]

Purified by chromatography on aluminium oxide (grade 5) eluting with 1 % CH_2Cl_2/petroleum ether as the epoxide isomer was unstable on silica gel. Yellow crystalline solid; R_f = 0.53 (20 % EtOAc in petroleum ether); m.p. 71-74 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *Trans isomer*: 3.46 (1H, dd, *J* = 8.9, 2.1 Hz, OC*H*), 3.95 (1H, d, *J* = 2.1 Hz, OC*H*Ph), 5.85 (1H, d, *J* = 8.5 Hz, C*H*), 7.20-7.45 (15H, m, Ar*H*); ^{13}C NMR (63 MHz, $CDCl_3$) 60.6, 60.8, 126.4, 127.6, 128.4, 136.8, 138.5, 141.4, 148.0; ^{1}H NMR (400 MHz, $CDCl_3$); *cis isomer*: 3.72 (1H, dd, *J* = 9.2, 4.5 Hz, OC*H*), 4.25 (1H, d, *J* = 4.3 Hz, OC*H*Ph), 5.61 (1H, d, *J* = 9.2 Hz, C*H*), 7.20-7.45 (15H, m, Ar*H*); ^{13}C NMR (63 MHz, $CDCl_3$) 57.4, 60.0, 121.9, 127.6-128.4, 135.3, 138.8, 149.5; *m/z* (CI) 299 (M^++1, 20%); (Found $[M+H]^+$ 299.1421 $C_{22}H_{18}O$ requires *m/z*, 299.1426).

Total Synthesis of CDP-840

3-Hydroxy-4-methoxybenzaldehyde[20]

Isovanillin (1 g, 6.5 mmol) and oven dried potassium carbonate (1.38 g, 10 mmol) were added to DMF (6 mL) at room temperature. The mixture was heated to 60 °C and cyclopentyl bromide (1.12 mL, 10.5 mmol) was added slowly. The mixture was stirred overnight at the same temperature and then cooled to room temperature. Water was added and the aqueous layer was extracted with petroleum ether (3×10 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo.* The residual oil was purified by flash chromatography (10 % EtOAc in petroleum ether, R_f = 0.11) to give the aldehyde as a yellow oil (1.38 g, 97 %); ν_{max}(film)/cm^{-1} 2958, 1683, 1507, 1259, 1237, 1130; ^{1}H NMR (400 MHz, $CDCl_3$) 1.55-2.10 (8H, m, 4 x CH_2), 3.93 (3H, s, OCH_3), 4.86 (1H, m, C*H*), 6.96 (1H, d, *J* = 8 Hz, Ar*H*), 7.37-7.46 (2H, m, Ar*H*), 9.84 (1H, s, C*H*O); ^{13}C NMR (100 MHz, $CDCl_3$) 24.1, 32.8, 56.2, 80.6, 110.9, 112.4, 126.3, 130.1, 148.4, 155.5, 191.0; *m/z* (EI) 220 (M^+, 11 %), 168 (30), 152 (100), 137 (7), 123 (9), 109 (11), 95 (11), 84 (82), 69 (19), 57 (24).

[3-(Cyclopentyloxy)-4-methoxyphenyl]methanol (6)

To a MeOH (5 mL) solution of 3-hydroxy-4-methoxybenzaldehyde (880 mg, 4.0 mmol), $NaBH_4$ (150 mg, 4.0 mmol) was slowly added at 0 °C. The solution was stirred for 1 h, and then the solvent was evaporated. Water (10 mL) was added and the aqueous layer extracted with EtOAc (3×10 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Flash chromatography (33 % EtOAc in petroleum ether) gave **5** as a colorless oil (890 mg, 100 %); R_f = 0.41 (50 % EtOAc in petroleum ether); (Found C, 70.32; H, 8.33; $C_{13}H_{18}O_3$ requires C, 70.24; H, 8.16); ν_{max}(film)/cm^{-1} 3379, 1511, 1257, 1232, 1157, 1024, 990; ^{1}H NMR (400 MHz, $CDCl_3$) 1.65-2.00 (8H, m, $4 \times CH_2$), 3.84 (3H, s, OCH_3), 4.60 (2H, s, $ArCH_2OH$), 4.79 (1H, m, C*H*), 6.84(1H, d, *J* = 8.1 Hz, Ar*H*), 6.87 (1H, dd, *J* = 8.1, 1.2 Hz, Ar*H*), 6.92 (1H, d, *J* = 1.2 Hz, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$) 24.0, 32.9, 56.2, 65.3, 65.4, 80.5, 112.1, 114.3, 119.3, 133.6, 147.9, 149.8; *m/z* (EI) 222 (M^+, 14 %), 154 (92), 137 (26), 125 (22), 93 (24), 84 (100), 67 (20); (Found M^+ 222.1256 $C_{13}H_{18}O_3$ requires *m/z* 222.1256).

2-(3-Cyclopentyloxy-4-methoxybenzyl)-3-[(1S)-7,7-dimehtyl-2-oxo-bicyclo[2.2.1]hept-1-yl]-(3R)-2-thionia-bicyclo[2.2.1]heptane tetrafluoroborate (5)

A 54 wt % HBF_4 solution in Et_2O (105 μL, 0.75 mmol) was slowly added to a solution of alcohol **5** (111 mg, 0.5 mmol) and sulfide ent-**1** (250 mg, 1.0 mmol) in Et_2O (3 mL) under nitrogen. After 4 h, the precipitated was collected by filtration. The salt was washed with Et_2O (3×5 mL) and then dried under vacuum. Salt **4** was obtained as a white solid (217 mg, 80%); R_f = 0.14 (10 % MeOH in CH_2Cl_2); (Found C, 61.78; H, 7.19; S, 5.83; $C_{28}H_{39}BF_4SO_3$ requires C, 61.99; H, 7.25; S, 5.91 %); ν_{max}/cm^{-1} 2956, 1740, 1515, 1263, 1027; m.p. 133-135 °C (decom.); $[\alpha]_D^{24}$ = +40.4 (c = 1 in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) 1.09 (3H, s, CH_3), 1.16 (3H, s, CH_3), 1.15-1.32 (2H, m), 1.50-2.30 (17H, m), 2.54 (1H, ddd, *J* = 18.6, 4.4, 2.7 Hz, COCH*H*), 2.77 (1H, d, *J* = 12.7 Hz, SCHCH*H*), 3.19 (1H, br s, SCHC*H*), 3.82 (3H, s, OCH_3), 4.21(1H, d, *J* = 4.4 Hz, $SCHCH_2$), 4.24 (1H, d, *J* = 1.5 Hz, SC*H*CH), 4.36 (1H, d, *J* = 13.2 Hz, ArCH*H*S), 4.60 (1H, d, *J* = 13.2 Hz,

ArCH*H*S), 4.84 (1H, m, OC*H*), 6.81 (1H, d, *J* = 8.3 Hz, Ar*H*), 6.95-7.05 (2H, m, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$) 19.1, 21.9, 24.1, 24.5, 26.7, 26.8, 32.8, 33.5, 41.2, 43.5, 44.1, 45.3, 48.5, 49.8, 56.2, 58.0, 60.1, 68.7, 80.8, 112.6, 116.5, 120.5, 123.2, 148.6, 151.4, 215.4; m/z (FAB) 455 (M^+-BF_4^-, 10 %) 205 (100).

4-{3-[3-(Cyclopentyloxy)-4-methoxyphenyl]oxiran-2-yl}pyridine (4)

To a stirred solution of **4** (240 mg, 0.44 mmol) in CH_2Cl_2 (5 mL) was added N,N,N′,N′,-tetramethyl-N″-[tris(dimethylamino)phosphoralidene]phosphoric triamide ethylimine (142 μL, 0.44 mmol) at –78 °C under nitrogen. After 10 min, 4-pyridinecarboxaldehyde (150 μL, 0.45 mmol) was added to the solution. After an additional 1 h stirring, the mixture was warmed to room temperature and then saturated NaCl solution (10 mL) was added. The organic layer was separated and the aqueous layer extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude mixture was purified on basic alumina (grade 5) (5% EtOAc in petroleum ether) to give a mixture of *trans*:*cis* = 7:3 (120 mg, 89 %); R_f = 0.30 (2% EtOAc in petroleum ether on Al_2O_3); (Found C, 73.10; H, 6.62; N, 4.31; $C_{19}H_{21}NO_3$ requires C, 73.29; H, 6.80; N, 4.50 %); ν_{max}/cm^{-1} 2958, 1513, 1257, 1133; ^{1}H NMR *trans isomer* : 1.48-2.01 (8H, m, 4 × C*H*$_2$), 3.78 (1H, d, *J* = 1.6 Hz C*H*), 3.83 (1H, d, *J* = 1.6 Hz C*H*), 3.86 (3H, s, OC*H*$_3$), 4.79 (1H, m, C*H*), 6.83 (1H, s, Ar*H*), 6.87 (1H, d, *J* = 8.1 Hz, Ar*H*), 6.89 (1H, dd, *J* = 8.1, 1.3 Hz, Ar*H*), 7.27 (2H, d, *J* = 5.8Hz, Ar*H*), 8.61 (2H, d, *J* = 5.8Hz, Ar*H*); *cis isomer* : 1.48-2.01 (8H, m, 4 × C*H*$_2$), 3.75 (3H, s, OC*H*$_3$), 4.26 (1H, d, *J* = 4.2 Hz, C*H*), 4.36 (1H, d, *J* = 4.2 Hz, C*H*), 4.57 (1H, m, C*H*), 6.59 (1H, d, *J* = 1.6 Hz, Ar*H*), 6.69 (1H, d, *J* = 8.1 Hz, Ar*H*), 6.73 (1H, dd, *J* = 8.1, 1.6 Hz, Ar*H*), 7.12 (2H, d, *J* = 6.1 Hz, Ar*H*), 8.43 (2H, d, *J* = 6.1 Hz, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$) 24.0, 32.8, 32.9, 56.0, 56.2, 58.5, 59.7, 61.1, 63.1, 80.5, 80.7, 111.6, 111.8, 112.1, 113.6, 118.4, 119.5, 120.4, 121.9, 122.2, 125.7, 128.6, 143.9, 146.3, 147.3, 148.2, 149.3, 149.9, 150.0, 150.1, 150.7, 151.3; *m/z* (EI) 311(M^+, 65 %), 282 (24), 271 (33), 214 (24), 137 (61), 84 (100); (Found M^+ 311.1521 $C_{19}H_{21}NO_3$ requires *m/z* 311.1521).

(2*R*)-2-[3-(Cyclopentyloxy)-4-methoxyphenyl]-2-phenyl-1-(4-pyridyl)ethanol (3)[20]

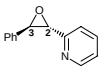
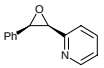
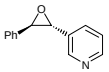
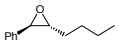
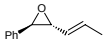
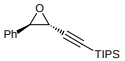
To a stirred solution of CuI (19 mg, 0.1 mmol) in THF (1 mL) was slowly added PhMgBr (1.0 mL, 1.0M solution in THF) at −40 °C under nitrogen. After 10 min, **3** (120 mg, 0.39 mmol) in THF (2 mL) was slowly added *via* canula. The stirring was continued for 15 h during which time the reaction mixture was allowed to rise to room temperature. A saturated NH_4Cl solution/35 % NH_4OH solution (2:1, 10 mL) was added and the mixture stirred for an additional 1 h. The organic layer was separated and the aqueous layer extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude mixture was purified by flash chromatography (EtOAc) to give the alcohol as an oil (*syn*:*anti* = 3:7), (130 mg, 85 %); R_f = 0.29 (EtOAc); ν_{max}(film)/cm^{-1} 3028, 2957, 1602, 1509, 1260, 1137, 728, 700; ^{1}H NMR (400 MHz, $CDCl_3$) *anti isomer* : 1.50-1.92 (8H, m, 4 × C*H*$_2$), 3.60 (1H, br, O*H*), 3.79 (3H, s, OC*H*$_3$), 4.09 (1H, d, *J* = 7.8 Hz, C*H*), 4.68 (1H, m, C*H*), 5.29 (1H, d, *J* = 7.8 Hz, C*H*), 6.76-6.88 (3H, m, Ar*H*), 7.00–7.40 (7H, m, Ar*H*), 8.30 (2H, br s, Ar*H*) *syn isomer* : 1.50-1.92 (8H, m, 4 × C*H*$_2$), 3.73 (3H, s, OC*H*$_3$), 4.07 (1H, d, *J* = 9.0 Hz, C*H*), 4.56 (1H, m, C*H*), 5.26 (1H, d, *J* = 9.0 Hz, C*H*), 6.58 (1H, d, *J* = 1.5 Hz, Ar*H*), 6.61 (1H, dd, *J* = 8.3, 1.5 Hz, Ar*H*), 6.65 (1H, d, *J* = 8.3 Hz, Ar*H*), 7.00 – 7.40 (7H, m, Ar*H*), 8.30 (2H, br s, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$) 24.1, 32.7, 32.8, 32.9, 59.2, 59.4, 75.4, 75.7, 80.6, 112.1, 112.3, 116.2, 116.5, 120.9, 121.2, 121.9, 122.0, 122.1, 126.8, 126.9, 127.1, 128.5, 128.8, 128.9, 132.1, 133.4, 140.5, 141.3, 147.4, 147.8, 149.0, 149.1, 149.4, 152.1; *m/z* (EI) 389 (*M*$^+$, 28 %), 281 (100), 213 (72), 181 (30), 152 (40), 86 (42), 84 (50); (Found *M*$^+$ 389.2000 $C_{25}H_{27}NO_3$ requires *m/z* 389.1991).

(2*R*)-1-[3-(Cyclopentyloxy)-4-methoxyphenyl]-1-phenyl-2-(4-pyridyl)ethane, CDP 840[21]

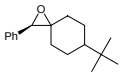
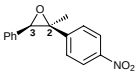
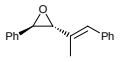
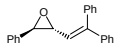
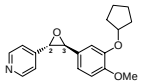
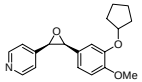
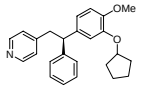
Triethylamine (100 μL, 0.65 mmol) was added to (2*R*)-2-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-phenyl-1-(4-pyridyl)ethanol (130 mg, 0.33 mmol) in CH_2Cl_2 (3 mL) at 0 °C. Methanesulfonyl chloride (40 μL) was added to this stirring solution and the solution was aged 30 min. The solvent was evaporated *in vacuo*, the residue was dissolved in acetic acid (1 mL), and zinc dust (65 mg,

1.0 mmol) was added. The mixture was stirred at room temperature for 5 h and was then diluted with methyl *t*-butyl ether (5 mL) and water (5 mL). A 5N NaOH solution was added dropwise until pH 11 and the organic phase was concentrated *in vacuo*. The residual oil was purified by flash chromatography (33 % EtOAc in petroleum ether), to give CDP-840 as a colourless oil (97 mg, 79 %). R_f = 0.29 (EtOAc); ν_{max}(film)/cm^{-1} 2954, 1507, 1258, 1135, 699; $[\alpha]_D^{23}$ = +38.6 (c = 1.0 in MeOH); [Lit., +37.0 (c = 1.5 in EtOH)][22]; ^{1}H NMR (400 MHz, $CDCl_3$) 1.48-1.64 (2H, m, C*H*$_2$), 1.70-1.89 (6H, m, 3 × C*H*$_2$), 3.31 (2H, d, *J* = 7.3 Hz, C*H*$_2$), 3.78 (3H, s, OC*H*$_3$), 4.14 (1H, t, *J* = 7.7 Hz, C*H*), 4.65 (1H, m, C*H*), 6.65 (1H, d, *J* = 1.7 Hz, Ar*H*), 6.68 (1H, dd, *J* = 8.3, 1.7 Hz, Ar*H*), 6.74 (1H, d, *J* = 8.3 Hz, Ar*H*), 6.92 (2H, d, *J* = 5.3Hz, Ar*H*), 7.14-7.30 (5H, m, Ar*H*), 8.38 (2H, d, *J* = 5.3 Hz, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$) 24.1, 32.8, 32.9, 41.7, 51.6, 56.1, 80.6, 112.1, 115.6, 120.1, 124.6, 126.5, 127.8, 128.6, 136.1, 144.0, 147.5, 148.9, 149.5; *m/z* (EI) 373 (*M*$^+$, 24 %), 305 (10), 281 (42), 213 (100), 197 (6), 181 (22), 169 (6), 165 (12), 152 (30), 141 (14), 115 (12), 93 (6), 69 (12), 65 (6)

$[\alpha]_D$ and HPLC Conditions for Determining Absolute Configuration.

Structure of major epoxides	*conditions*			*retention times*		*optical rotation*	*literature conditions*			*retention times*		*optical rotation*
	mL/min	Hx:IPA	column	minor	major		mL/min	Hx:IPA	Column			
	2.0	99:1	OD	4.9 (2S, 3S)	10.8[a] (2R, 3R)		2.0	99:1	OD[d] [1]	3.5 (2S, 3S)	5.9 (2R, 3R)	
	1.0	90:10	OD-H[d]	8.7 (2S, 3S)	14.1[a] (2R, 3R)		1.0	90:10	OD-H[2]	9.9 (2S, 3S)	16.9 (2R, 3R)	
	1.0	98:2	OJ[d]	16.8 (2R, 3S)	34.1[b] (2S, 3R)	+ 25.0 (c=0.36, PhH)	1.0	90:10	AS[d]	11.5 (2R, 3S)	7.7 (2S, 3R)	+ 82.0 (2S, 3R)[2] (c=0.36, PhH)
	1.0	90:10	OD-H[d]	20.8 (2S, 3S)	17.6[a] (2R, 3R)		1.0	90:10	OD-H[d][2]	26.0 (2S, 3S)	23.6 (2R, 3R)	
	1.0	99.5:0.5	OD	25.6 (2S, 3S)	30.7[c] (2R, 3R)							
	0.5	99.5:0.5	OD	12.1 (2S, 3S)	16.8[b] (2R, 3R)	+ 89.0 (c=0.3, $CHCl_3$)						-14.2 (2S, 3S)[3] (c=0.88, $CHCl_3$)
	1.0	98:2	OD	4.7 (2S, 3S)	6.1[c] (2R, 3R)							
	0.5	99.5:0.5	OD	13.5 (2S, 3S)	22.8[c] (2R, 3R)	+ 87.0 (c=0.21, $CHCl_3$)						
	0.7	99.9:0.1	OD	12.4 (2S, 3S)	13.5[c] (2R, 3R)	+ 96.0 (c=0.07, CH_2Cl_2)						
	0.5	99:1	OD	10.1 (S)	11.8[b] (R)	+ 68.0 (R) (c=2.5, pentane)						-26.5 (S)[4] (c=2.5, pentane)

[1] V. K. Aggarwal, J. G. Ford, S. Fonquerna, H. Adams, R. V. H. Jones, R. Fieldhouse, *J. Am. Chem. Soc.* **1998**,*120*, 8328-8339.
[2] A. Solladié-Cavallo, M. Roje, T. Isarno, V. Sunjic, V. Vinkovic, *Eur. J. Org. Chem.* **2000**. 1077-1080.
[3] U. M. Lindström, P. Somfai, *Synthesis* **1998**, 109-117.
[4] T. Durst, R. Viau, R. Van Den Elzen, C. H. Nguyen, *J. Chem. Soc., Chem. Commun.* **1971**, 1334-1335.

	1.5	99.5:0.5	OD	14.8 (S)	12.1[c] (R)	- 6.8 (c=1, MeOH)					
	1.0	99:1	OJ[d]	11.4 (2S, 3S)	16.1[a] (2R, 3R)		1.0	80:20	OD[5]	5.3 (2S,3S)	12.6 (2R,3R)
	1.0	99:1	OJ[d]	13.0 (2R, 3S)	7.6[c] (2S, 3R)						
	1.0	99:1	OD-H[d]	14.2 (2R, 3S)	12.4[c] (2S, 3R)	- 49.0 (c=1, $CHCl_3$)					
	1.0	99:1	OD	10.7 (2S, 3S)	15.8[c] (2R, 3R)	+ 337.3 (c=1, CH_2Cl_2)					
	1.0	99:1	OD	14.6 (2S, 3S)	11.7[c] (2R, 3R)						
	1.5	95:5	OD	15.6 (2R, 3R)	22.9[c] (2S, 3S)						
	1.5	95:5	OD	14.5 (2S, 3R)	12.9[c] (2R, 3S)						
	1.0	90:10	OD	14.3 (S)	12.3[b] (R)	+ 38.6 (c=1, MeOH)					+ 37[6] (c=1.5, EtOH)

[a] Absolute configuration assigned by comparison of HPLC retention times with literature.

[b] Absolute configuration assigned by comparison of optical rotation with literature.

[c] Absolute configuration assigned by analogy with other epoxides given in table.

[d] Adequate separation could not be obtained using OD column.

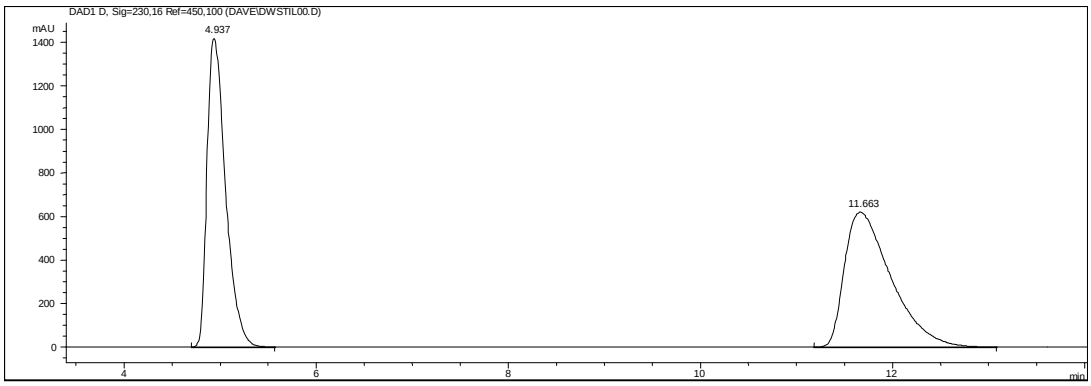
[5] Z.-X. Wang, Y. Tu, M. Frohn, J.-R. Zhang, Y. Shi, *J. Am. Chem. Soc.* **1997**, *119*, 11224-11235.
[6] Celltech Therapeutics Ltd, US Patent No. 5,622,977.

HPLC traces

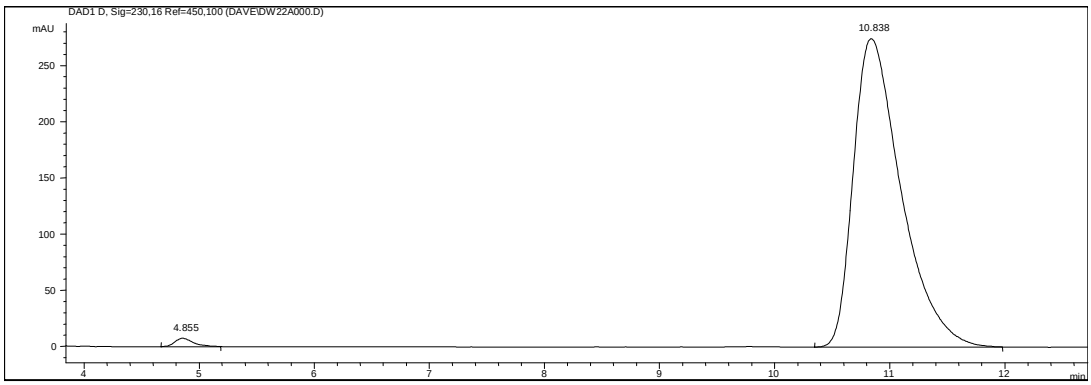
(2*R*, 3*R*)-2,3-Diphenyloxirane

OD Chiralcel. 2mL/min. 99:1 hexane:IPA, 20 °C.

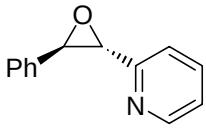
Racemic



Asymmetric, 98% *ee*

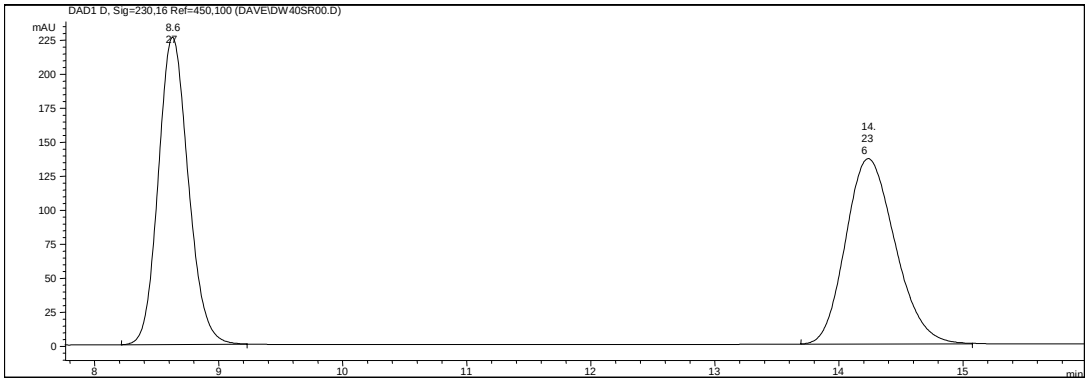


2-[(2R,3R)-3-Phenyloxiran-2-yl]pyridine

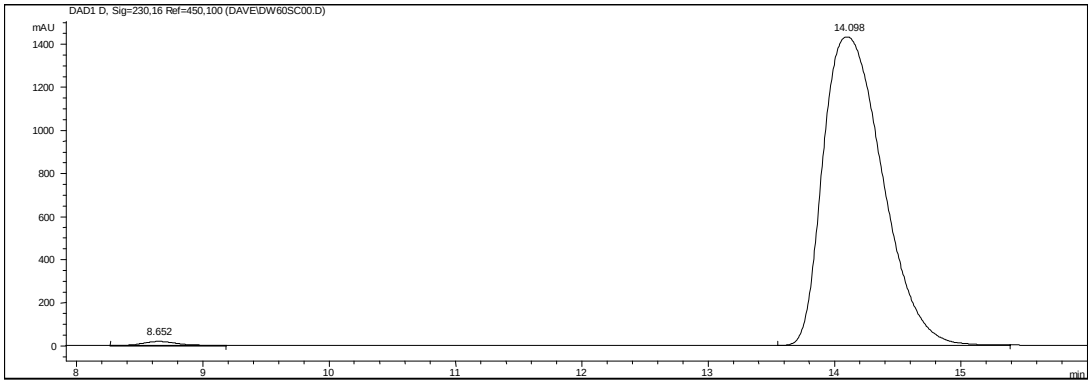


ODH Chiralcel. 1mL/min. 90:10 Hexane:IPA, 20 °C.

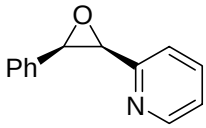
Racemic



Asymmetric, 99% *ee*

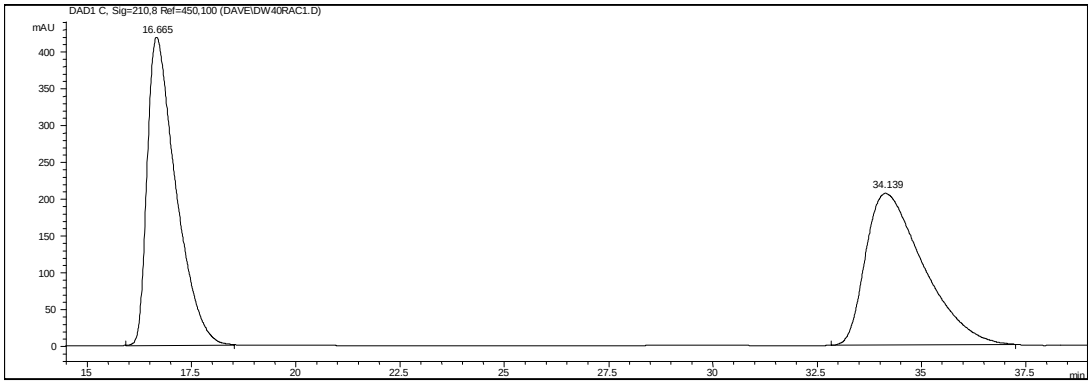


2-[(2S,3R)-3-Phenyloxiran-2-yl]pyridine

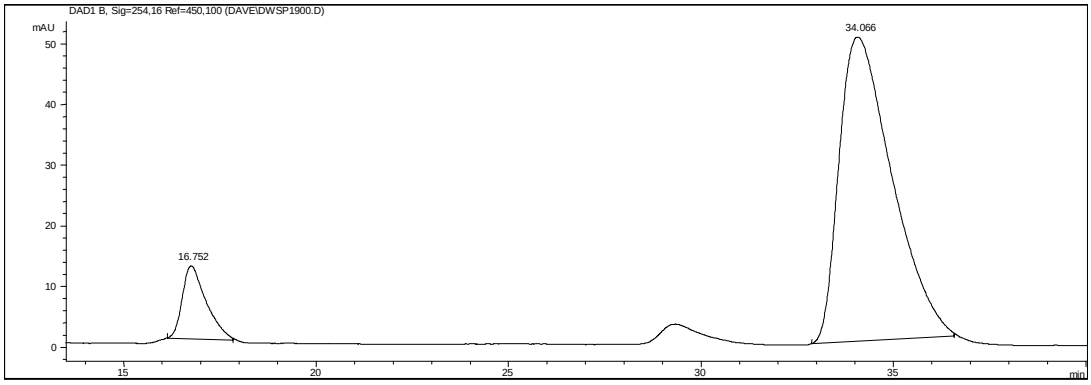


OJ Chiralcel. 1mL/min. 98:2 Hexane:IPA, 10 °C.

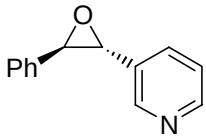
Racemic



Asymmetric, 80% *ee*

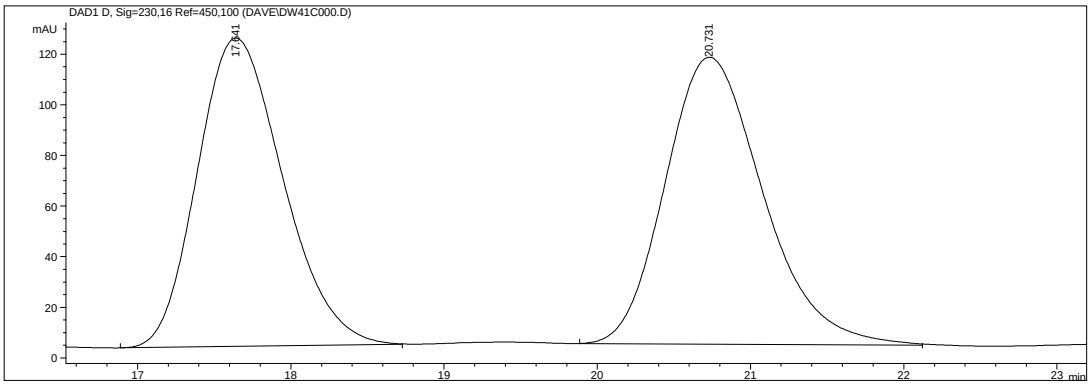


3-[(2R,3R)-3-Phenyloxiran-2-yl]pyridine

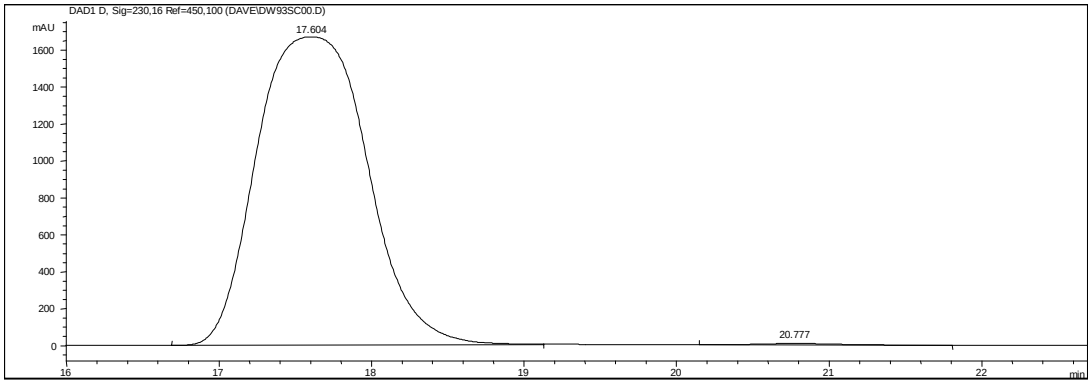


ODH Chiralcel. 1mL/min. 90:10 Hexane:IPA, 20 °C.

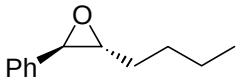
Racemic



Asymmetric, >99% *ee*

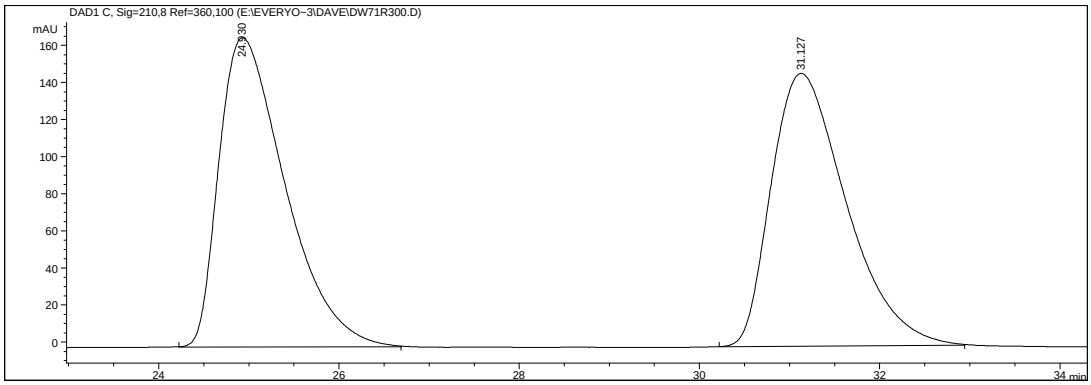


(2R,3R)-2-*n*-Butyl-3-phenyl-oxirane

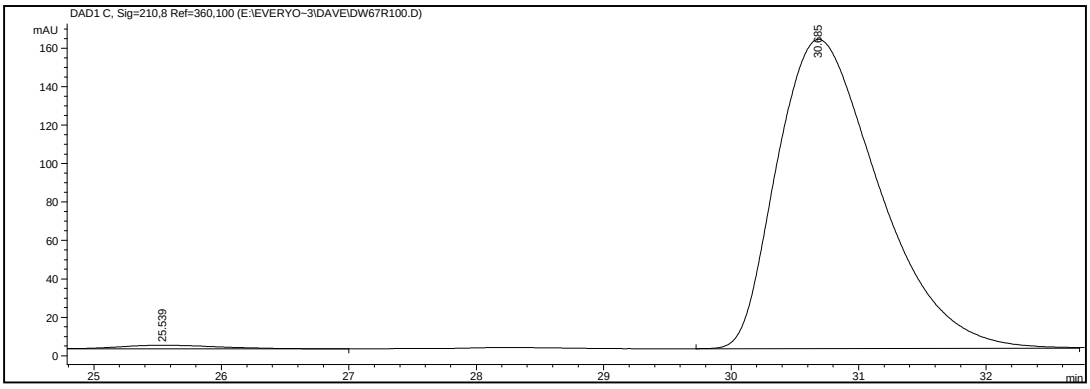


OD Chiralcel. 1 mL/min. 99.5:0.5 Hexane:IPA, 20 °C.

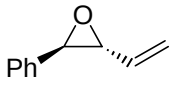
Racemic



Asymmetric, 97% *ee*

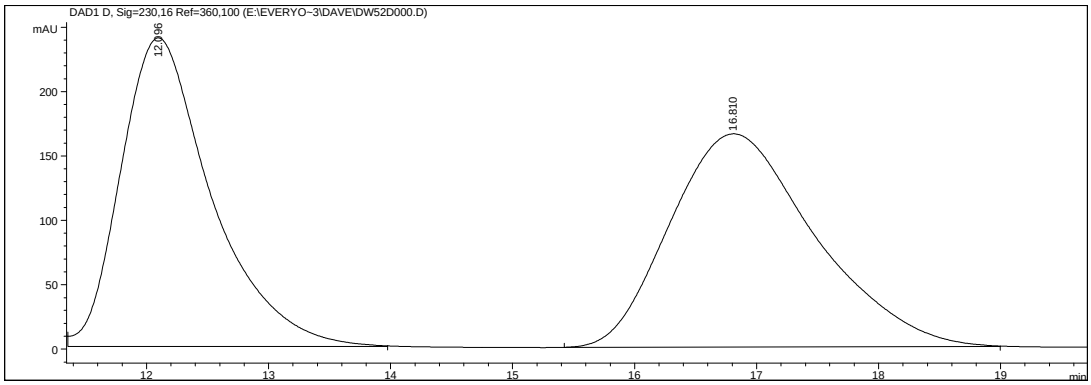


(2R,3R)-2-Phenyl-3-vinyloxirane

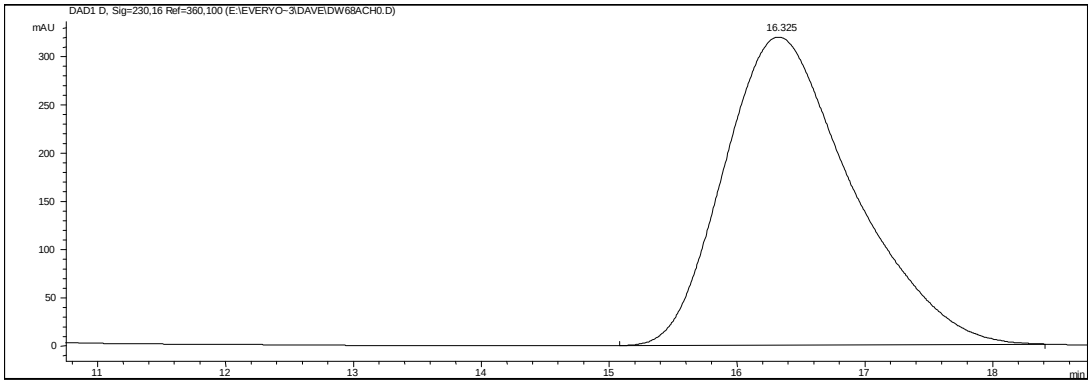


OD Chiralcel. 0.5 mL/min. 99.5:0.5 Hexane:IPA, 20 °C.

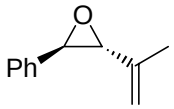
Racemic



Asymmetric, >99% *ee*

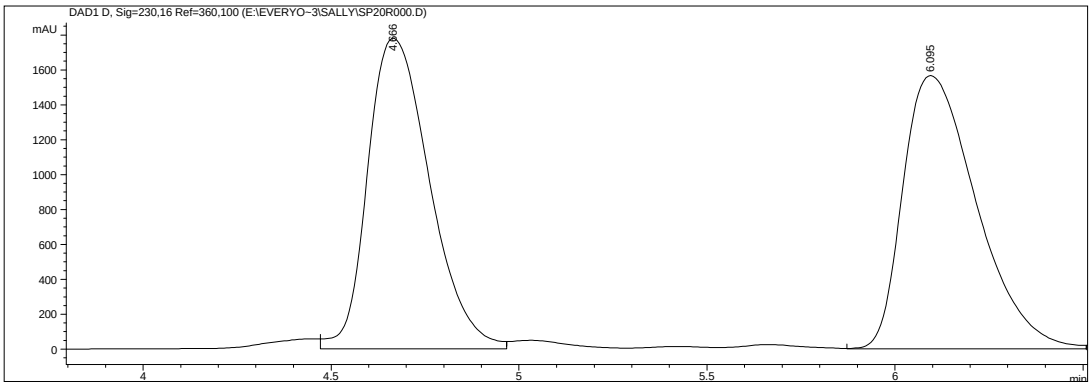


(2R,3R)-2-Phenyl-3-isopropenyloxirane

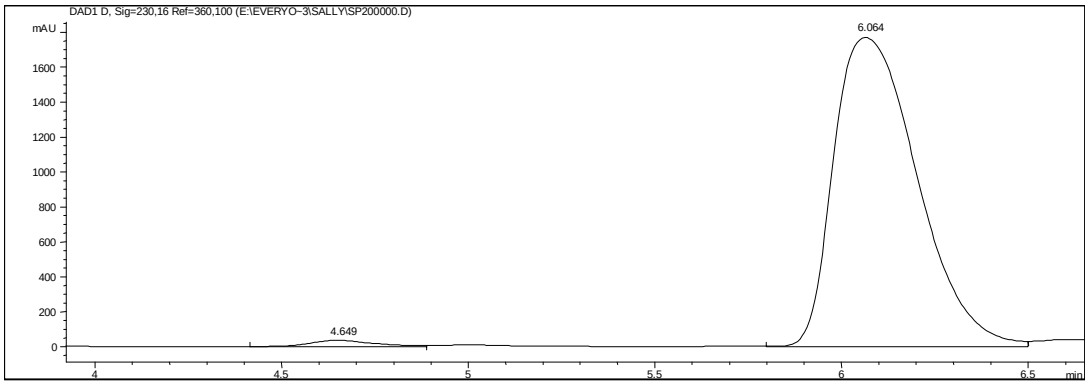


OD Chiralcel. 1 mL/min. 98:2 Hexane:IPA, 20 °C.

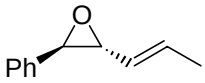
Racemic



Asymmetric, 96% *ee*

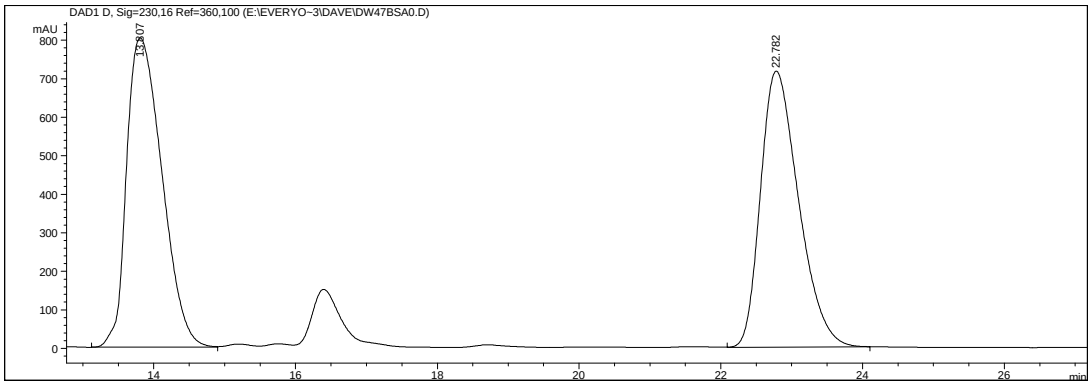


(2R,3R)-2-Phenyl-3-[(E)-1-propenyl]oxirane

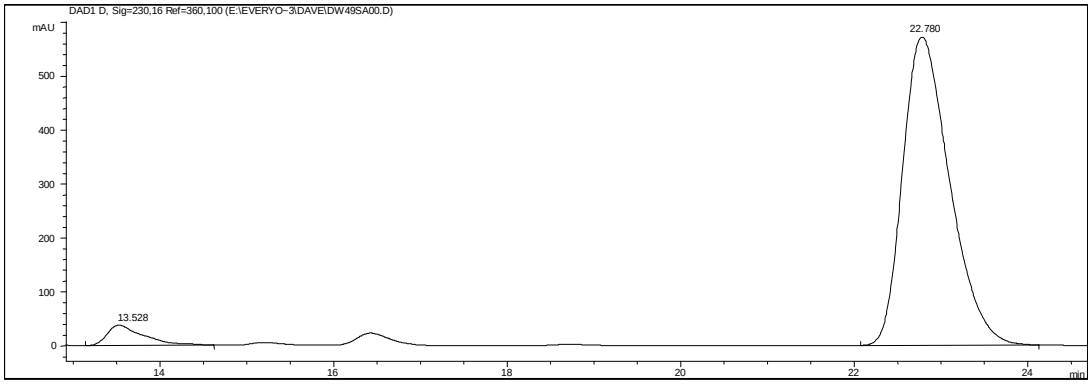


OD Chiralcel. 0.5 mL/min. 99.5:0.5 Hexane:IPA, 20 °C.

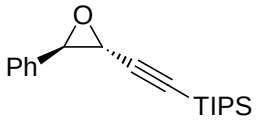
Racemic



Asymmetric, 90% *ee*

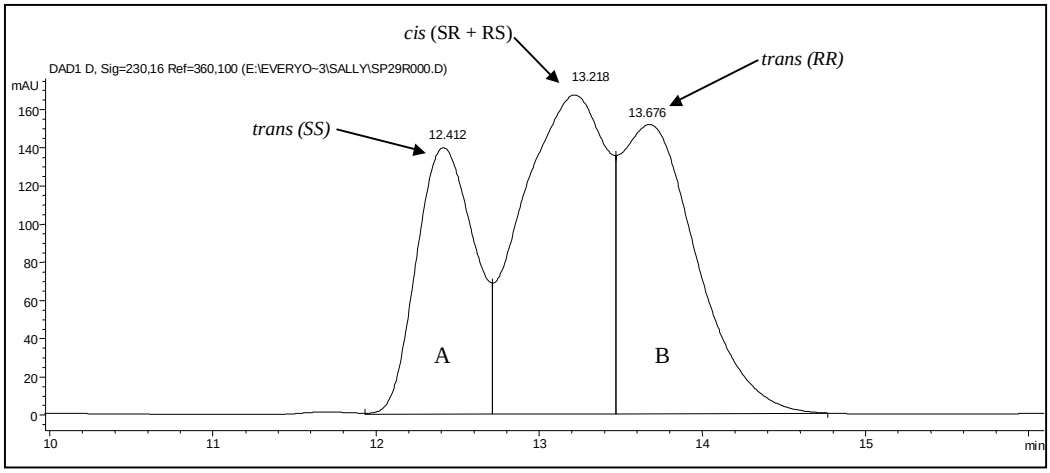


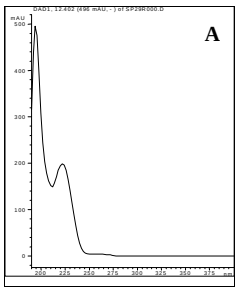
Tris(1-methylethyl)[[(2*R*,3*R*)-3-phenyloxiranyl]ethynyl]-silane

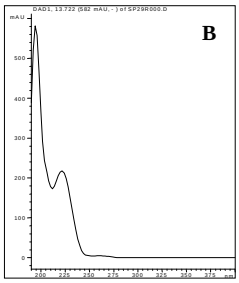


OD-H Chiralcel. 0.7 mL/min. 99.9:0.1 Hexane:IPA, 10 °C.

Racemic

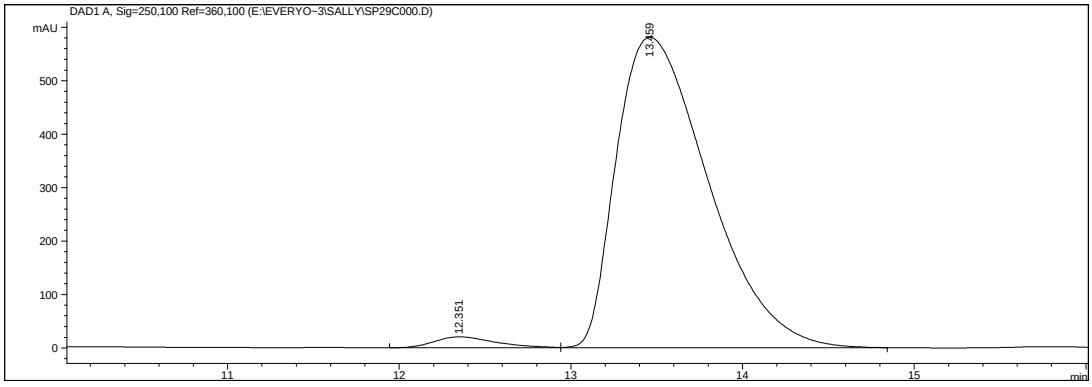




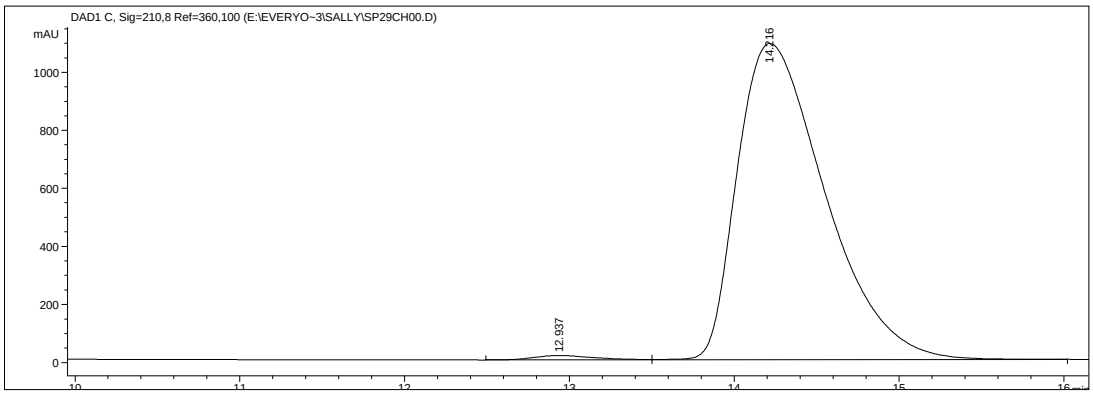


A: UV of peak at 12.4 B: UV of peak at 13.7

Asymmetric, 95 % *ee* KOH

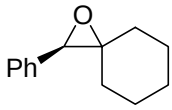


Asymmetric, 99 % *ee* EtP_2



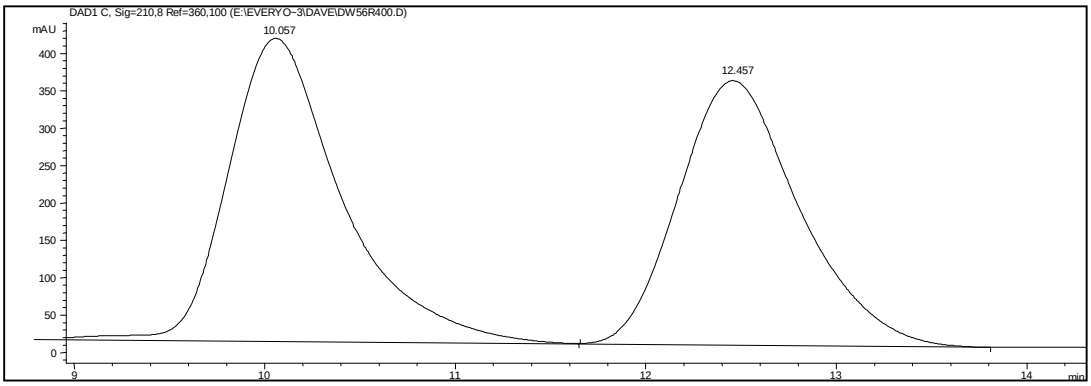
Related TMS and TBDMS acetylenic epoxides have also been separated on a chiralcel OD column.[23] In both cases the *R,R*-epoxide has a greater retention time than the *S,S* enantiomer.

(2R)-2-Phenyl-1-oxaspiro[2.5]octane

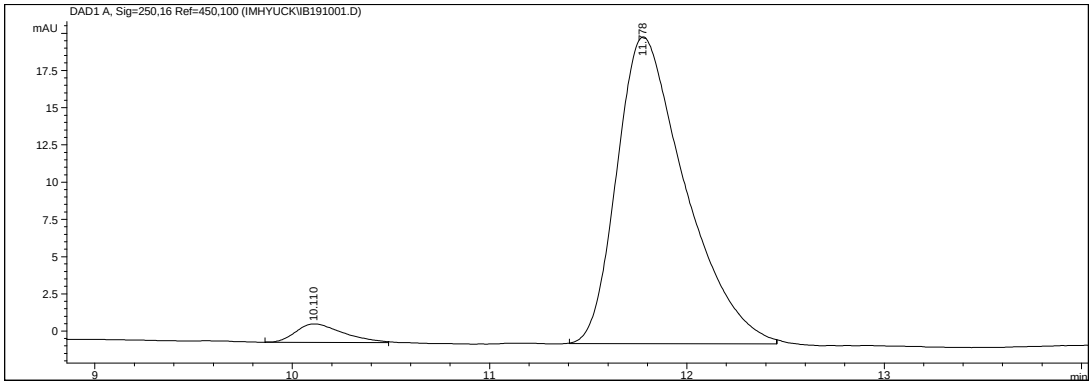


OD Chiralcel. 0.5 mL/min. 99:1 Hexane:IPA, 20 °C.

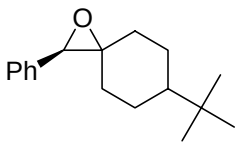
Racemic



Asymmetric, 92% *ee*

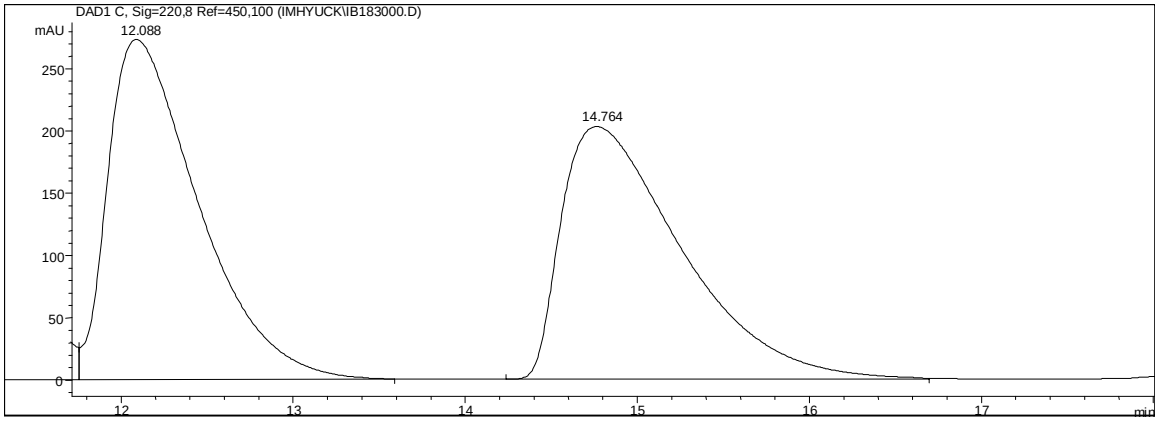


(2*R*)-6,-(1,1-Dimethylethyl)-2-phenyl-1-oxaspiro[2.5]octane

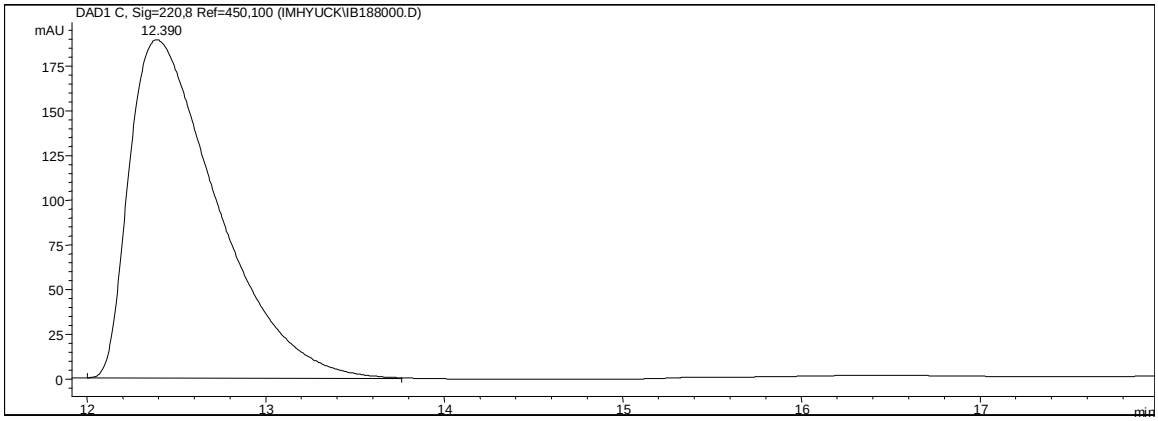


OD Chiralcel. 1.5 mL/min. 99.5:0.5 Hexane:IPA 20 °C.

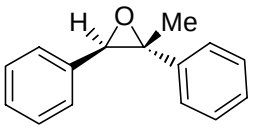
Racemic



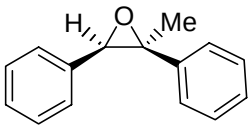
Asymmetric, >99 % *ee*



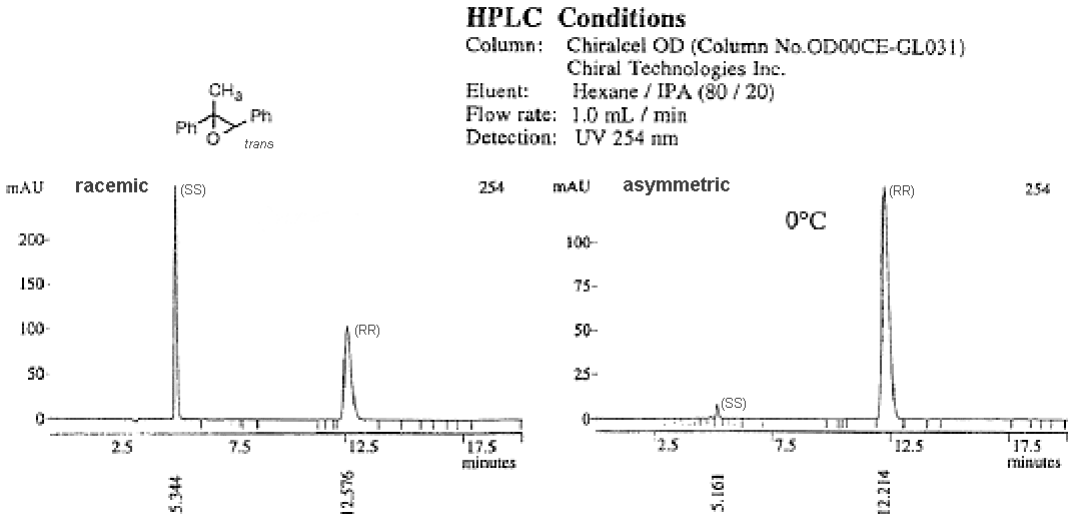
2-Methyl-2,3-diphenyloxirane



Trans



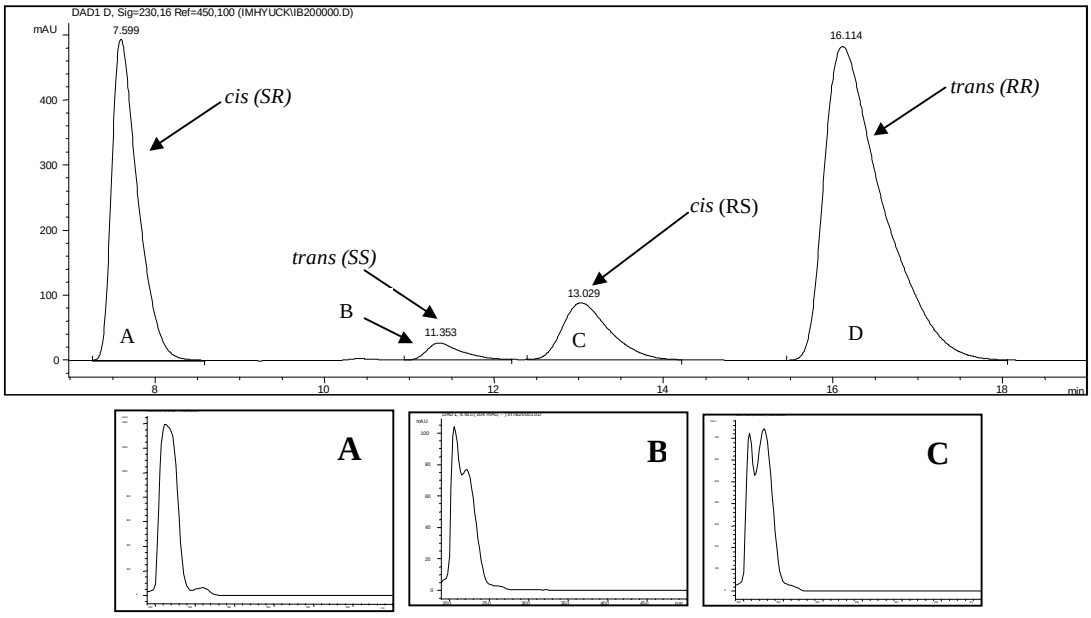
Cis



Taken from: Wang, Z.-X.; Tu, Y.; Frohn, M.; Zhang, J.-R.; Shi, Y. *J. Am. Chem. Soc.* **1997**, *119*, 11224-11235. (Supplementary material).

OD Chiralcel. 1.0 mL/min. 80:20 Hexane:IPA, 20 °C.

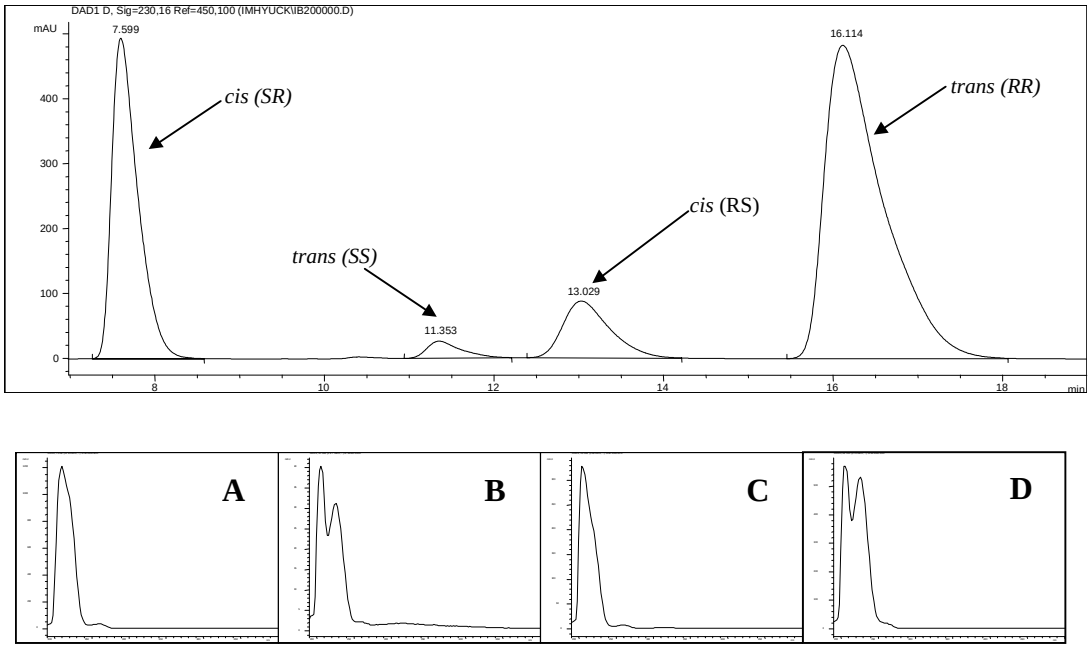
Asymmetric (2:1 *cis:trans*)



A: UV of peak at 4.1 (*R*,*R*), **B**: UV of peak at 4.4 (*cis* + *S*,*S*), **C**: UV of peak at 7.9 (*cis*).

OJ Chiralcel. 1.0 mL/min. 99:1 Hexane:IPA 20 °C. (2:1 *cis:trans*)

trans: 93% *ee*, *cis*: 50% *ee*



A: UV of peak at 7.6 (*S*,*R*).

B: UV of peak at 11.4 (*S*,*S*).

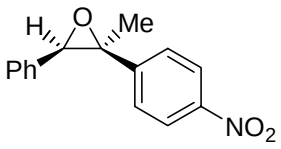
C: UV of peak at 13.0 (*R*,*S*).

D: UV of peak at 16.1 (*R*,*R*).

HPLC of the 2:1 *cis:trans* mixture using literature conditions for the *trans* epoxide resulted in overlapping. Using the OD column[24] the (*R, R*) *trans* epoxide eluted at 7.9 minutes. The (*S, S*) *trans* epoxide eluted at 4.1 minutes together with the *cis* epoxide.

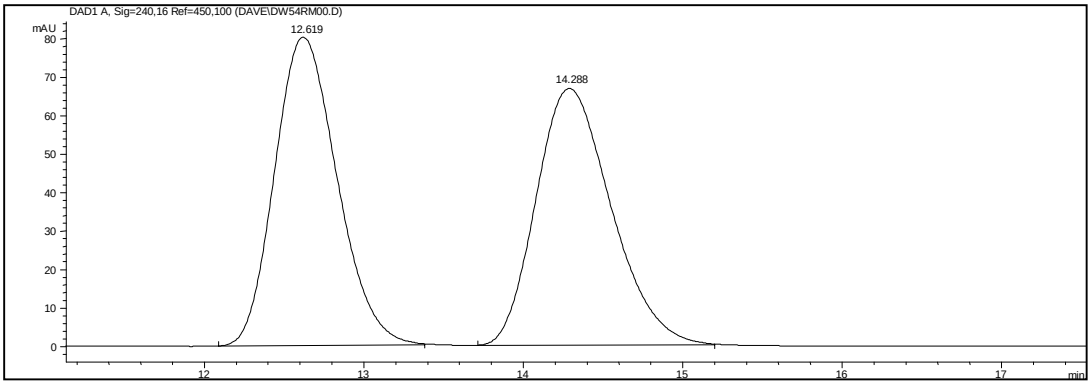
Separation of the *cis* and trans epoxides was achieved using an OJ column. Assignment of *cis* and *trans* epoxides was accomplished by comparison of UV traces from the OJ column with the UV traces from the OD column. This was clarified by independent synthesis of a racemic *trans* sample that also eluted at 11.4 and 16.1 minutes on the OJ column. The peaks at 7.6 and 13.0 minutes therefore correspond to the *cis* epoxide.

(2S,3R)-2-Methyl-2-(4-nitrophenyl)-3-phenyloxirane

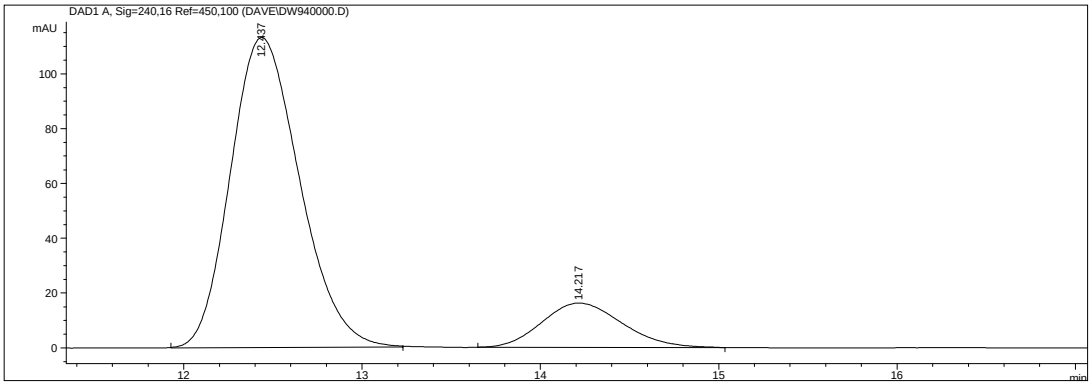


ODH Chiracel. 1 mL/min. 99:1 Hexane:IPA, 10 °C.

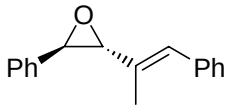
Racemic



Asymmetric, 71% *ee*

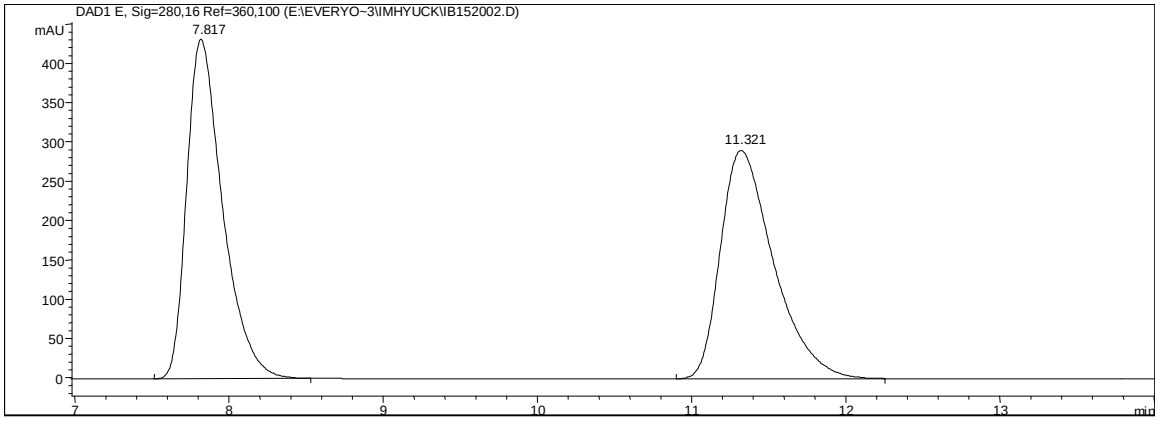


(2R,3R)-2-[(E)-1-Methyl-2-phenylethenyl]-3-phenyl-oxirane

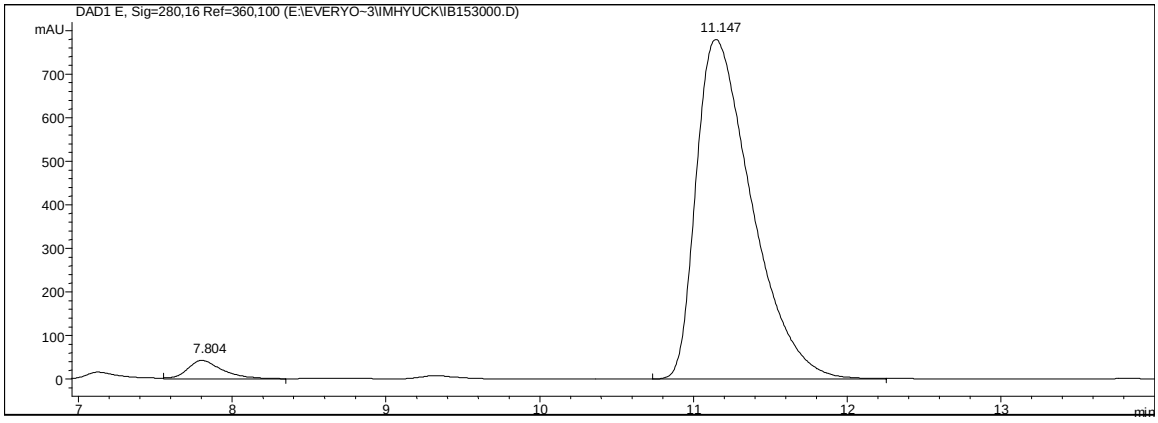


OD Chiralcel. 1.0 mL/min. 99:1 Hexane:IPA 20 °C.

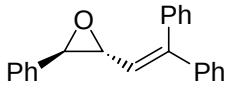
Racemic



Asymmetric, 90 % *ee*

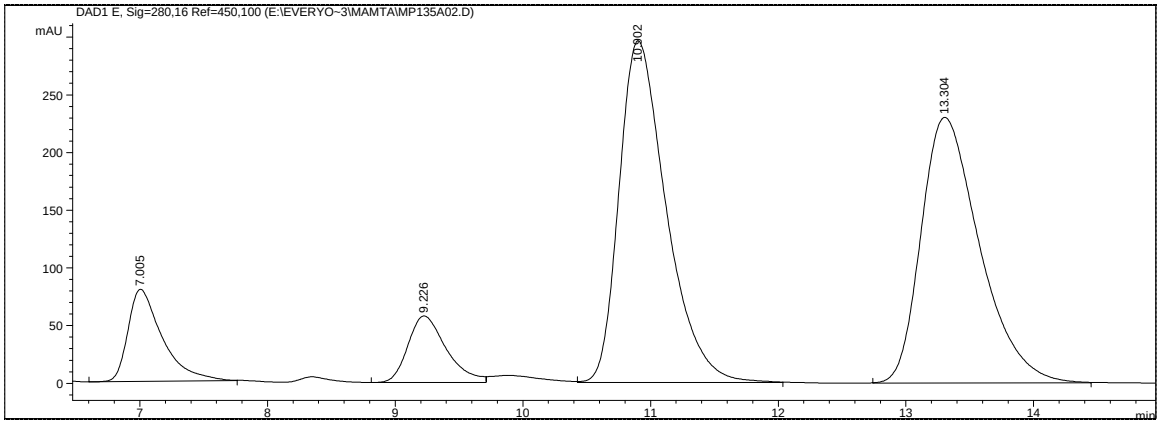


(2R,3R)-2-(2,2-Diphenylethenyl)-3-phenyl-oxirane

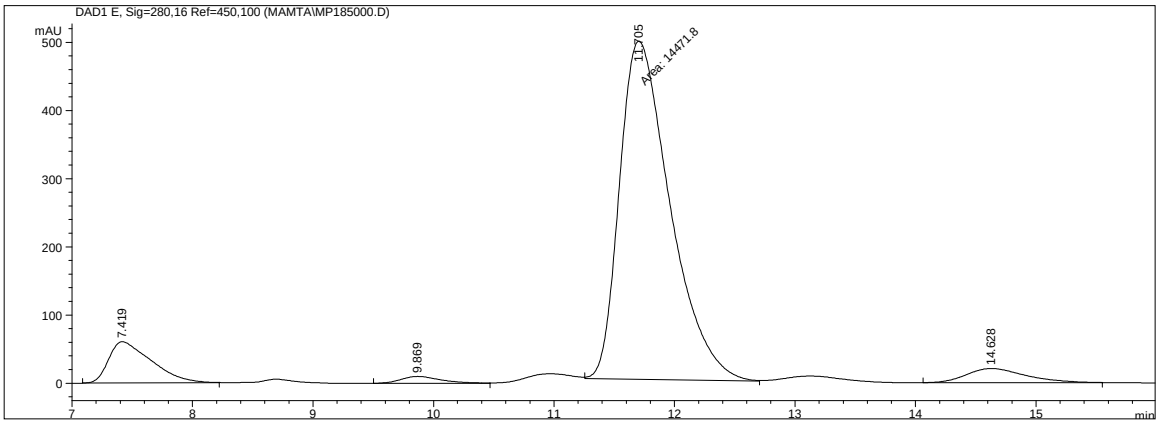


OD Chiralcel. 1.0 mL/min. 99:1 Hexane:IPA 20 °C.

Racemic

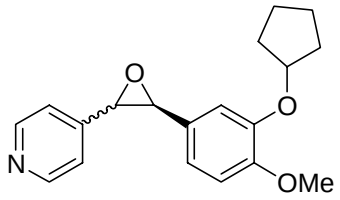


Asymmetric, 90 % *ee*



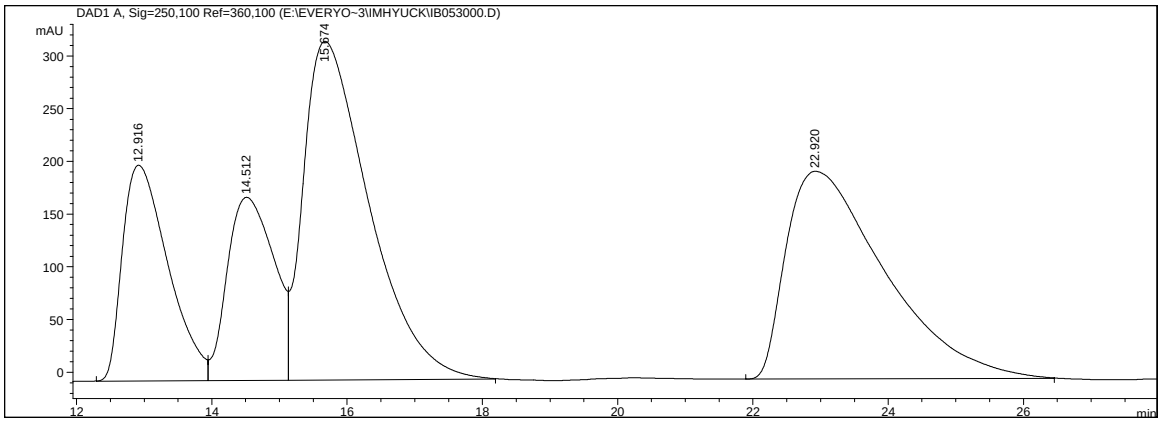
This material is difficult to purify. Peaks at 11.7 and 14.6 correspond to the *trans* epoxide and we believe that the peaks at 7.4 and 9.9 correspond to the *cis* epoxide.

4-{3-[3-(Cyclopentyloxy)-4-methoxyphenyl]oxiran-2-yl}pyridine

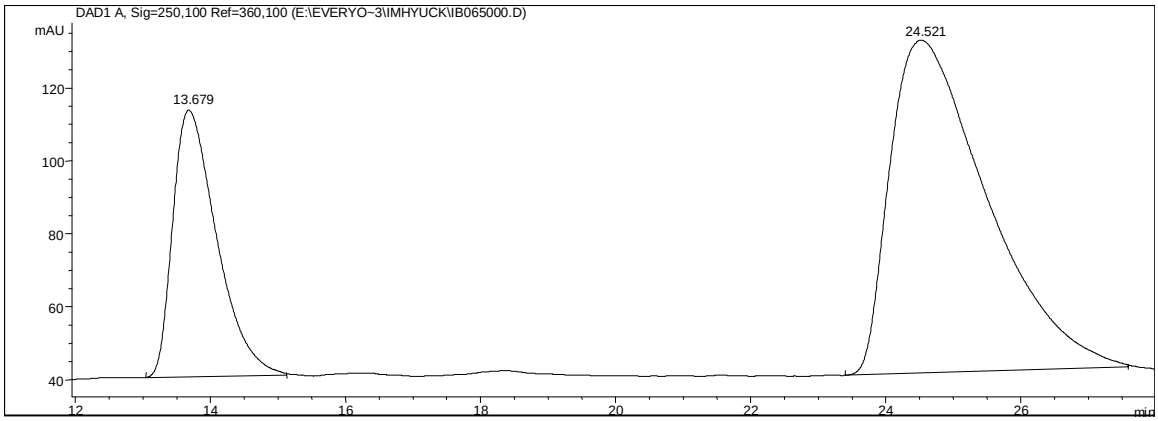


OD Chiralcel. 1.5 mL/min. 95:5 Hexane:IPA 20 °C.

Racemic

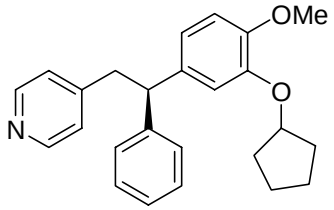


Asymmetric *trans* : 99 % *ee*, *cis* : 99 % *ee*



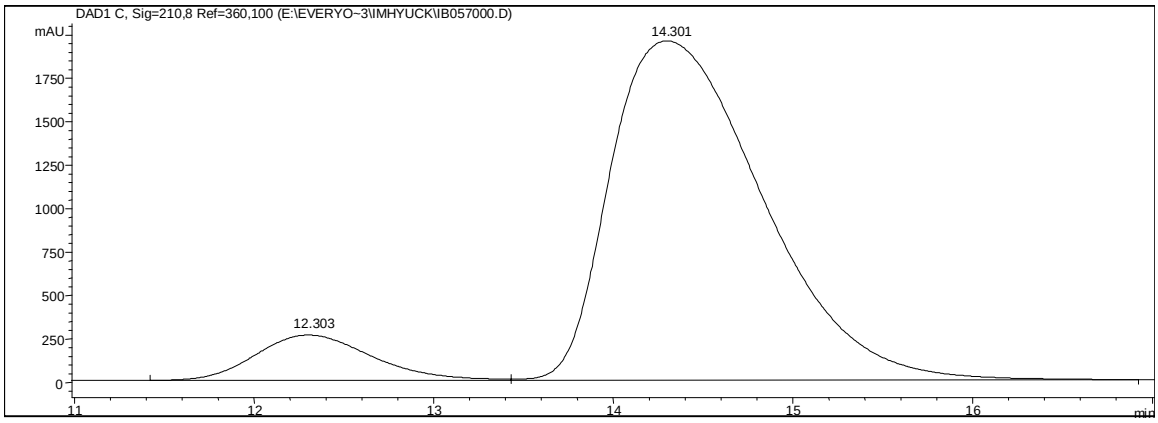
The peaks at 12.9 and 14.5 correspond to the *cis* epoxide and the peaks at 15.6 and 22.9 correspond to the *trans* epoxide.

(2R)-1-[3-(Cyclopentyloxy)-4-methoxyphenyl]-1-phenyl-2—(4-pyridyl)ethane, CDP-840

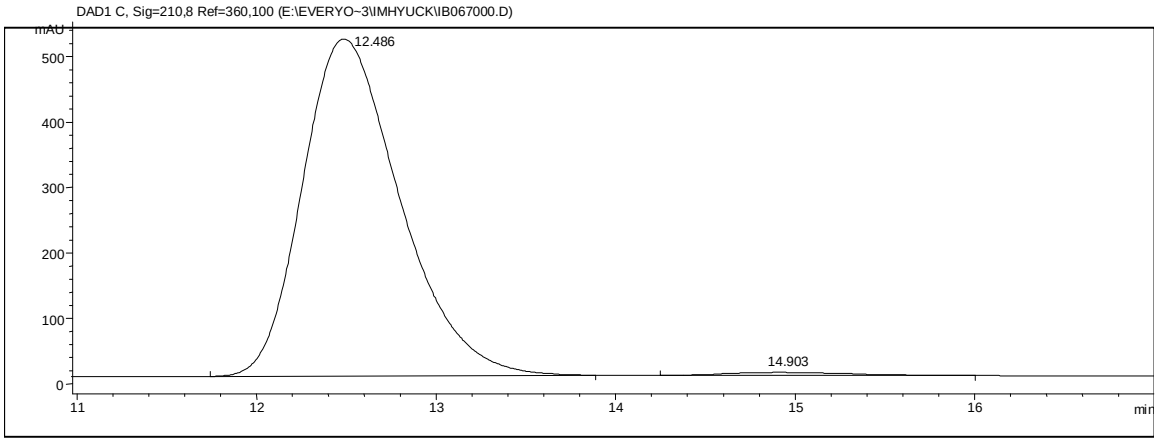


OD Chiralcel. 1 mL/min. 90:10 Hexane:IPA 20 °C.

91:9 enantiomeric mixture



Asymmetric, 99 % *ee*



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