Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

for

Angew. Chem. Int. Ed. Z52073

69451 Weinheim, Germany

Kinetic Resolution of Epoxides *via* a C-C Bond Forming Reaction. Highly Enantioselective Addition of Indoles to *Cis*, *Trans* and *Meso* Aromatic Epoxides Catalysed by Cr(Salen) Complexes*

Marco Bandini, Pier Giorgio Cozzi,* Paolo Melchiorre and Achille Umani-Ronchi*

Dipartimento di Chimica Organica "G. Ciamician", Università di Bologna

Via Selmi 2, 40126 Bologna (Italy)

**E-mail: pgcozzi@ciam.unibo.it; umani@ciam.unibo.it*

General Methods

^{1}H-NMR spectra were recorded on Varian 200 (200 MHz) or Varian 300 (300 MHz) spectrometers. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuterochloroform: δ 7.27 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz). ^{13}C-NMR spectra were recorded on a Varian 200 (50 MHz) or Varian 300 (75 MHz) spectrometers with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal standard (deuterochloroform: δ 77.0 ppm). Mass spectra were performed at an ionizing voltage of 70 eV. Chromatographic purification was carried out using silica gel (240-400 mesh). Analytical gas-chromatography (GC) was performed on a Hewlett-Packard HP 6890 gas chromatograph with a flame ionization detector and split mode capillary injection system, using a Crosslinked 5% PH ME Siloxane (30 m) column or a Megadex-5 chiral (25 m) column (flow rate 15 mL/min, method: 50 °C for 2 min, ramp @ 10 °C/min to 250 °C for 15 min). Analytical high performance liquid chromatography (HPLC) was performed on a HP 1090 liquid chromatograph equipped with a variable wavelength UV detector (deuterium lamp 190-600 nm) and

using a Daicel Chiralcel™ OD and OF columns (0.46 cm I.D. x 25 cm) (Daicel Inc.). HPLC grade isopropanol and *n*-hexane were used as the eluting solvents. Elemental analyses were carried out by using a EACE 1110 CHNOS analyzer. IR were recorded with FT-IR instrument.

All the reactions were carried out under a nitrogen atmosphere in flame-dried glassware using standard inert techniques for introducing reagents and solvents.

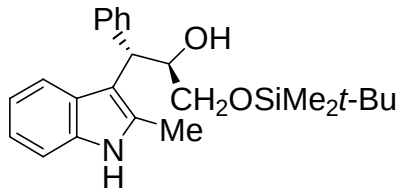
Materials

Anhydrous solvents were supplied by Fluka in Sureseal® bottles and used as received. Racemic epoxides were prepared by MCPA oxidation of the corresponding alkenes. 1-methoxy-3-phenyl-2-propene was prepared from cinnamic alcohol (NaH, MeI). 1-*t*-butyldimethylsilyloxy-3-phenyl-2-propene was prepared from cinnamic alcohol (TBMSCl, imidazole, CH_2Cl_2). *Cis*-1-phenyl-2-propene was prepared from phenyl-2-propine (Pd/C, quinoline, H_2).[1] *Cis* and *trans* stilbene, *trans*-β-phenyl propene, 3,4-dihydronaphthalene, cinnamic alcohol, cinnamic acid, styrene oxide, indole, 2-methylindole, 1-methylindole, 1,2-methylindole and 5-methoxyindole are commercially available and were used as received. (R,R)-Cr(Salen)Cl (Stream) is commercially available and used as received. Cr(Salen)SbF_6, Cr(Salen)PF_6 and Cr(Salen)BF_4 were prepared according to literature procedure.[2] Molecular sieves 4Å were activated by microwave irradiation (4 x 1 min., 500 W) before use. The product **2a**, obtained by kinetic resolution of styrene oxide with 2-methylindole catalysed by Cr(Salen)Cl, is a known compound.[3]

General Procedure for the Kinetic Resolution of Aromatic Epoxides with 2-MethylIndole (Table 1).

A flamed two necked flask equipped with a magnetic stirring bar was charged with Cr(Salen) complex (0.01 mmol) and activated molecular sieves 4Å (100 mg). Then TBME (0.2 mL) was added and the

resulting solution was stirred under nitrogen at room temperature for 5 min. The solution was cooled to 0°C and then the epoxide (0.3 mmol) and 2-methylindole (0.1 mmol) were added to the reaction mixture. Finally *t*-BuOH (0.1 mmol) was added and the reaction mixture stirred at 0°C until GC analysis indicated complete conversion of 2-methylindole. The crude reaction mixture was diluted with Et_2O and filtered trough celite. After evaporation of the solvent under reduced pressure, the product was purified by chromatography on silica gel.



(*S*,*R*)-2-(2-Methyl-3-indolyl)-1-dimethyl *t*-butylsilyloxy-2-phenylethanol

$C_{24}H_{33}NO_2Si$

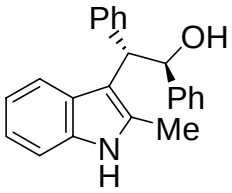
M.W. 395.61 g/mol

The product **2b** was isolated as a white solid after chromatographic purification (eluent, cyclohexane : Et_2O 7 : 3). Mp 109-111°C. Yield 96%

^{1}H-NMR (200 MHz, $CDCl_3$) δ: -0.08 (3 H, s); 0.03 (3 H, s); 0.91 (9 H, s); 2.45 (3 H, s); 2.77 (1 H, d, J = 4.5 Hz); 3.45 (1 H, dd, J = 6.3, 10.2 Hz); 3.65 (1 H, dd, J = 3.6, 10.2 Hz); 4.32 (1 H, d, J = 10.2 Hz); 4.78-4.84 (1 H, m); 7.06-7.18 (5 H, m); 7.26-7.32 (2 H, m); 7.53 (1 H, dd, J = 0.9, 9 Hz); 7.63 (1 H, d, J = 7.8); 7.80 (1 H, br). **^{13}C-NMR** (50 MHz, $CDCl_3$) δ: -5.35 (2), 12.42, 18.25, 25.90 (3), 45.91, 65.62, 72.18, 110.24, 111.92, 119.32 (2), 120.82, 125.89, 127.45, 128.08 (2), 128.44 (2), 131.37, 135.23, 142.59. **GC-MS** m/z (relative intensity) 59 (8), 75 (20), 115 (10), 130 (15), 177 (15), 207 (25), 220 (100), 247 (15), 395 (10).

Elem. Anal. Calcd. for $C_{24}H_{33}NO_2Si$: C, 72.86%; H, 8.41%; N, 3.54%. Found: C, 72.96%; H, 8.30%; N, 3.49%. Enantiomeric excess was evaluated by HPLC analysis: Chiralcel OF, isocratic (*n*-hexane : *i*-PrOH 88:12), flow 0.5 mL/min; t_{minor}= 10.7min; t_{major}= 15.7min; Ee 91%

$[\alpha]^D$: +34.6° (c 0.53, $CHCl_3$).



(*S*,*R*)-2-(2-Methyl-3-indolyl)-1,2-diphenylethanol

$C_{23}H_{21}NO$

M.W. 327.42 g/mol

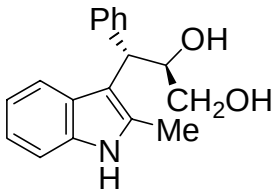
The product **2c** was isolated as a white solid after chromatographic purification (eluent, cyclohexane : AcOEt 8 : 2). Mp 142-145°C. Yield 82%.

^{1}H-NMR (200 MHz, $CDCl_3$) δ: 2.07 (3 H, s); 2.25 (1 H, d, J = 2.2 Hz); 4.47 (1 H, d, J = 10.0 Hz); 5.77 (1 H, dd, J = 2.2, 10.0 Hz); 7.01-7.37 (11 H, m); 7.53 (1 H, br); 7.53-7.71 (3 H, m). **^{13}C-NMR** (50 MHz, $CDCl_3$) δ: 11.84, 51.76, 74.89, 110.23, 112.01, 119.16, 119.59, 120.64, 125.50, 126.37 (2), 126.43, 127.29, 127.74 (2), 128.52 (2), 128.84 (2), 131.56, 135.19, 141.74, 143.13. **GC-MS** m/z (relative intensity) 51 (5), 77 (15), 91 (5), 115 (10), 152 (5), 178 (20), 204 (20), 220 (100), 294 (10), 309 (15).

Elem. Anal. Calcd. for $C_{23}H_{21}NO$: C, 84.37%; H, 6.46%; N, 4.28%. Found: C, 84.47%; H, 6.47%; N, 4.25%.

The enantiomeric excess was evaluated by HPLC analysis: Chiralcel OD, isocratic (*n*-hexane : *i*-PrOH 88:12), flow 0.5 mL/min; t_{minor}= 32.5min; t_{major}= 39.5min; Ee 86%.

$[\alpha]^D$: -60.4° (c 0.81, $CHCl_3$).



(*S*,*R*)-2-(2-Methyl-3-indolyl)-1-methylenehydroxy-2-phenylethanol

$C_{18}H_{19}NO_2$

M.W. 281.35 g/mol

The product **2d** was isolated as an oil after chromatographic purification (eluent, Cyclohexane : AcOEt, gradient from 8:2 to 1:1). Yield 93%.

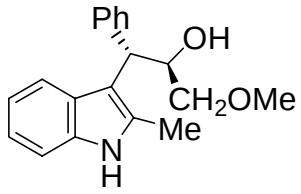
^{1}H-NMR (200 MHz, $CDCl_3$) δ: 2.42 (3 H, s), 3.61-3.70 (2 H, m); 4.28 (1 H, d, J = 10.2 Hz); 5.80-5.88 (1 H, m); 7.04-7.27 (7 H, m); 7.50 (1 H, d, J = 6.8 Hz); 7.62 (1 H, d, J = 8.8 Hz); 7.85 (1 H,

br). **^{13}C-NMR** (50 MHz, $CDCl_3$) δ: 12.39, 46.55, 65.19, 72.73, 110.42, 111.32, 119.18, 119.43, 120.92, 126.36, 127.24, 128.41 (2), 128.52 (2), 131.70, 135.25, 141.85. **GC-MS** m/z (relative intensity) 51 (5), 77 (15), 115 (10), 130 (15), 178 (20), 204 (20), 220 (100), 250 (10), 281 (10).

Elem. Anal. Calcd. for $C_{18}H_{19}NO_2$: C, 76.84%; H, 6.81%; N, 4.98%. Found: C, 76.84%; H, 6.95%; N, 5.02%.

The enantiomeric excess was evaluated by HPLC analysis: Chiralcel OD, isocratic (n-hexane : *i*-PrOH 85:15), flow 0.5 mL/min; t_{minor} = 31.3min; t_{major}= 37.1min; Ee 87%.

$[\alpha]^D$: product contaminated by traces of Salen.



(*S*,*R*)-2-(2-methyl-3-indolyl)-1-methoxymethyl-2-phenylethanol

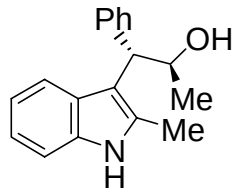
$C_{19}H_{21}NO_2$

M.W. 295.38 g/mol

The product **2e** was isolated as an oil after chromatographic purification (eluent, cyclohexane : AcOEt, 85 : 15). Yield 98%. **^{1}H-NMR** (200 MHz, $CDCl_3$) δ: 2.43 (3 H, s); 2.54 (1 H, br); 3.19-3.30 (1 H, m); 3.28 (3 H, s); 3.39-3.48 (1 H, m); 4.32 (1 H, d, J = 9.8 Hz); 4.85-5.00 (1 H, m); 7.00-7.31 (7 H, m); 7.50 (1 H, d, J = 7.4 Hz); 7.60 (1 H, d, J = 7.0 Hz); 7.79 (1 H, br). **^{13}C-NMR** (50 MHz, $CDCl_3$) δ: 12.27, 46.16, 58.94, 71.08, 75.22, 110.33, 111.95, 119.33, 119.44, 120.95, 126.13, 127.48, 128.32 (2), 128.49 (2), 131.56, 135.33, 142.18. **GC-MS** m/z (relative intensity) 51 (5), 77 (10), 115 (10), 144 (15), 178 (10), 204 (15), 220 (100), 295 (10).

Elem. Anal. Calcd. for $C_{19}H_{21}NO_2$: C, 77.26%; H, 7.17%; N, 4.74%. Found: C, 77.41%; H, 7.18%; N, 4.80%.

Enantiomeric excess was evaluated by HPLC analysis: Chiralcel OD, isocratic (*n*-hexane : *i*-PrOH 85:15), flow 0.5 mL/min; t_{minor}= 20.8 min, t_{major}= 21.1 min; Ee 86%



(*S*,*S*)-2-(2-Methyl-3-indolyl)-1-methyl-2-phenylethanol

$C_{18}H_{19}NO$

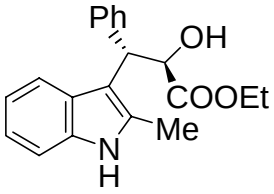
M.W. 265.35 g/mol

The product **2f** was isolated as a white solid after chromatographic purification (eluent, Cyclohexane : AcOEt, gradient from 95:5 to 8:2). Mp 130-133 °C. Yield 99%.

^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.23 (3 H, d, J = 5.8 Hz); 2.18 (1 H, s); 2.43 (3 H, s); 4.05 (1 H, d, J = 9.6 Hz); 4.95 (1 H, m); 7.06-7.33 (6 H, m); 7.49 (2 H, d, J = 7.6 Hz); 7.65 (1 H, m); 7.79 (1 H, br). **^{13}C-NMR** (50 MHz, $CDCl_3$) δ: 12.53, 21.66, 52.55, 69.29, 110.32, 112.72, 119.35, 119.46, 120.82, 126.38, 127.42, 128.36 (2), 128.57 (2), 131.49, 135.22, 142.46. **GC-MS** m/z (relative intensity) 77 (10), 91 (5), 115 (10), 130 (15), 144 (10), 178 (15), 204 (20), 220 (100), 248 (5), 265 (25). Elem. Anal. Calcd. for $C_{18}H_{19}NO$: C, 81.47%; H, 7.22%; N, 5.28%. Found: C, 81.47%; H, 7.35%; N, 5.33%.

Enantiomeric excess was evaluated by HPLC analysis: Chiralcel OD, isocratic (n-hexane : *i*-PrOH 87:13), flow 0.5 mL/min, t_{major}= 20.4 min; t_{minor} = 22.3 min; Ee 72%.

$[\alpha]^{D}$: +98.1° (c 0.71, $CHCl_3$).



(*S*,*R*)-2-(2-Methyl-3-indolyl)-1-carboxyethyl-2-phenylethanol

$C_{20}H_{21}NO_3$

M.W. 323.39 g/mol

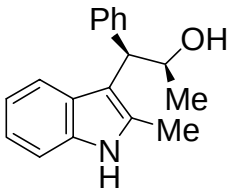
The product **2g** was isolated as a white solid after chromatographic purification (eluent, cyclohexane : AcOEt, 85 : 15). Mp 39-41 °C. Yield 85%.

^{1}H-NMR (200 MHz, $CDCl_3$) δ: 0.89 (3 H, t, J = 7.0 Hz); 2.33 (3 H, s); 3.96 (2 H, q, J = 7.0 Hz); 4.66 (1 H, d, J = 6.6 Hz); 5.00-5.10 (1 H, m); 7.00-7.40 (7 H, m); 7.40-7.50 (1 H, m); 7.57 (1 H, d, J = 7.0 Hz), 7.90 (1 H, br). **^{13}C-NMR** (50 MHz, $CDCl_3$) δ: 12.41,

13.56, 46.89, 61.25, 73.26, 110.09, 111.09, 119.36, 119.42, 120.96, 126.41, 127.45, 128.19 (2), 128.69 (2), 132.21, 135.12, 140.29, 174.06. **GC-MS** m/z (relative intensity) 51 (5), 77 (15), 91 (5), 115 (10), 130 (15), 178 (10), 204 (30), 220 (100), 250 (10), 323 (15).

Elem. An. Calcd. for $C_{20}H_{21}NO_3$: C, 74.28%; H, 6.55%; N, 4.33%. Found: C, 74.35%; H, 6.40%; N, 4.24 %.

Enantiomeric excess was evaluated by HPLC analysis: Chiralcel OD, od: 45 min, 95:5 then 35 min. 90:10 (*n*-hexane : *i*-PrOH), flow 0.5 mL/min; t_{major}= 64.1 min; t_{minor} = 66.4 min; Ee 80%; $[\alpha]^D$: -9.8° (*c* 1.6, $CHCl_3$)



(*R*,*S*)-2-(2-Methyl-3-indolyl)-1-methyl-2-phenylethanol

$C_{18}H_{19}NO$

M.W. 265.35 g/mol

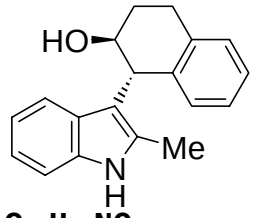
The product **2h** was isolated as a white solid after chromatographic purification (eluent, cyclohexane : Et_2O gradient from 9 : 1 to 1 : 1). Mp 52-54 °C. Yield 95%.

^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.29 (3 H, d, J = 5.8 Hz); 1.99 (1 H, s); 2.44 (3 H, s); 4.07 (1 H, d, J = 8.6 Hz); 4.87-4.96 (1 H, m); 7.08-7.30 (6 H, m); 7.49 (2 H, m); 7.75-7.80 (1 H, m); 7.92 (1 H, br). **^{13}C-NMR** (50 MHz, $CDCl_3$) δ: 12.53, 21.66, 52.55, 69.29, 110.32, 112.72, 119.35, 119.46, 120.82, 126.38, 127.42, 128.36 (2), 128.57 (2), 131.49, 135.22, 142.46. **GC-MS** m/z (relative intensity) 77 (5), 102 (8), 115 (10), 130 (10), 144 (15), 178 (15), 204 (18), 220 (100), 265 (20).

Elem. Anal. Calcd. for $C_{18}H_{19}NO$: C, 81.47%; H, 7.22%; N, 5.28%. Found: C, 81.46%; H, 7.37%; N, 5.35%.

Enantiomeric excess was evaluated by HPLC analysis: Chiralcel OD, isocratic (*n*-hexane:*i*-PrOH 85:15), flow 0.5 mL/min; t_{minor} = 19.8 min; t_{major} = 25.3 min; Ee 80%.

$[\alpha]^D$: -115.5° (*c* 0.77, $CHCl_3$).



$C_{19}H_{19}NO$

(1*R*,2*S*)-*trans*-1-(2-Methyl-1H-indol-3-il)-1,2,3,4-tetrahydronaphthalen-2-ol

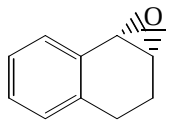
M.W. 277.36 g/mol

The product **2j** was isolated as an oil after chromatographic purification (eluent, Cyclohexane : AcOEt, gradient from 8 : 2 to 7 : 3). Yield 97%.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.89 (1 H, br); 1.96-2.01 (1 H, m); 2.31-2.38 (1 H, m); 2.43 (3 H, s); 3.08-3.15 (2 H, m); 4.14-4.28 (2 H, m); 6.85 (1 H, t, J = 8.9 Hz); 6.92-7.01 (4 H, m); 7.09 (1 H, t, J = 7.8 Hz); 7.17 (1 H, d, J = 6.0 Hz); 7.32 (1 H, d, J = 8.0 Hz); 7.94 (1 H, br). **^{13}C-NMR** (75 MHz, $CDCl_3$) δ: 12.09, 26.90, 28.66, 30.65, 46.28, 71.75, 110,28, 110, 78, 119.09, 119.32, 121.02, 125.84, 125.89, 127.08, 128.19, 129.04, 134.09, 135.58, 137.47. **IR** (nujol): 3536, 3398, 3020, 2970, 1610, 1530, 1300, 1040, 740 cm^{-1}. **GC-MS** m/z (relative intensity) 51 (5), 77 (10), 91 (5), 102 (15), 117 (25), 132 (40), 146 (30), 189 (20), 218 (100), 232 (20), 259 (18), 277 (95).

Elem. Anal. Calcd. for $C_{19}H_{19}NO$: C, 82.28%; H, 6.90%; N, 5.05%. Found: C, 82.34%; H, 6.91%; N, 5.15%.

Enantiomeric excess was evaluated by HPLC analysis: Column OD, isocratic isocratic (*n*-hexane:*i*-PrOH 80:20), flow 0.5 mL/min; t_{major}= 14.4 min; t_{minor} = 17.6 min. Ee 83%; $[\alpha]^D$: -30.0° (*c* 0.42, $CHCl_3$)



(1*S*,2*R*)-3,4-Dihydronaphthalene oxide

$C_{10}H_{10}O$

M.W. 146.19 g/mol

In a flamed two-necked flask, under a nitrogen atmosphere, (*R*,*R*)-Cr(Salen)Cl (33 mg, 0.0525 mmol) was dissolved in TBME (0.4 mL). The solution was cooled to 0°C and then 2-methylindole (89.4 mg, 0.68 mmol) and racemic 3,4-dihydronaphthalene oxide **1j** (150 mg, 1.05 mmol) were added. The consumption of indole was carefully monitored. After 24 hours the reaction goes to completion. The reaction mixture was diluted with Et_2O and filtered through celite. The solvent was evaporated and the epoxide was purified by chromatography on silica deactivated with Et_3N (eluent, Cyclohexane: AcOEt : Et_3N, 97 : 2 : 1).

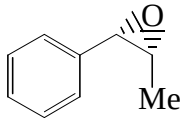
Yield 29% (84% on maximum theoretical yield).

^{1}H-NMR (200 MHz, $CDCl_3$) δ : 1.22-3.00 (m, 4 H) ; 3.31-3.73 (m, 2 H) ; 6.88-7.35 (m, 4 H).

$[\alpha]^D$: -91.3° (c 2.12, $CHCl_3$).

Lit.[4] (1*R*,2*S*)-3,4-Dihidronaphthalene oxide $[\alpha]^D$: +88° (c 0.36, $CHCl_3$).

Enantiomeric excess was evaluated by chiral CG analysis. Isotherm 120 °C, (*S*,*R*): 12.3 min, (*R*,*S*): 13.9 min. Ee 99.2%



(1*S*,2*R*)-*cis*-β-Methylstyrene oxide

$C_9H_{10}O$

M.W. 134.18g/mol

A flamed two necked flask equipped with a magnetic stirring bar was charged with Cr(Salen)SbF_6 (12.5 mg, 0.015 mmol) and activated molecular sieves 4Å (100 mg). Then TBME (0.2 mL) was added and the resulting solution was stirred under nitrogen at room temperature for 5 min. The solution was cooled to 0°C and then the epoxide **1h** (40.2 mg, 0.3 mmol) and 2-methylindole (27.5 mg, 0.21 mmol) were

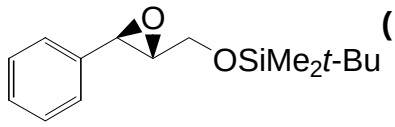
added to the reaction mixture. Finally *t*-BuOH (0.020 mL, 0.21 mmol) was added and the reaction mixture stirred at 0°C until GC analysis indicated complete conversion of 2-methyl indole. After 30 hours the reaction goes to completion. The reaction mixture was diluted with Et_2O and filtered through celite. The solvent was evaporated and the epoxide was purified by chromatography on silica deactivated with Et_3N. (eluent, Cyclohexane : Et_2O 100 : 0 to 9 : 1).

Yield 24% (80% on maximum theoretical yield).

^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.08 (3 H, d, J 5.5 Hz); 3.34 (1 H, dq, J = 4.3, 5.5 Hz); 4.06 (1 H, d, J = 4.4 Hz); 7.2-7.4 (5 H, m).

$[\alpha]^D$ = +31.5° (*c* 1.52, $CHCl_3$). Lit.[5] *cis*-(1*S*,2*R*)-β-Methylstyrene oxide $[\alpha]^D$ = +47.5° (*c* 1.17, $CHCl_3$)

Enantiomeric excess was evaluated by Chiral CG analysis. Isotherm 70 °C, (*S*,*R*): 42.28 min, (*R*,*S*): 32.45 min. Ee > 99.8%



(1*R*,2*R*)-*trans*-2-[(*tert*-Butyldimethylsiloxy)]-3-phenyloxirane

$C_{15}H_{24}O_2Si$

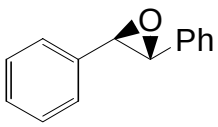
M.W. 264.44 g/mol

A flamed two necked flask equipped with a magnetic stirring bar was charged with Cr(Salen)SbF_6 (30 mg, 0.036 mmol) and activated molecular sieves 4Å (200 mg). Then TBME (0.4 mL) was added and the resulting solution was stirred under nitrogen at room temperature for 5 min. The solution was cooled to 0°C and then the epoxide **1b** (312 mg, 1.18 mmol) and 2-methylindole (93 mg, 0.708 mmol) were added to the reaction mixture. Finally *t*-BuOH (0.067 mL, 0.708 mmol) was added and the reaction mixture stirred at 0°C until GC analysis indicated complete conversion of 2-methylindole. After 24 hours the reaction goes to completion. The reaction mixture was diluted with Et_2O and filtered through celite. The solvent was evaporated and the epoxide was purified by chromatography on silica deactivated with Et_3N. (eluent, Cyclohexane : AcOEt : Et_3N, 97:2:1).

Yield 36% (90% on maximum theoretical yield).

^{1}H-NMR (200 MHz, $CDCl_3$) δ: 0.12 (3 H, s); 0.13 (3 H, s); 0.92 (9 H, s); 3.14 (1 H, ddd, J = 1.8, 3.0, 3.9 Hz); 3.21 (1 H, d, J = 1.8 Hz); 3.82 (1 H, dd, J = 3.9, 12.0 Hz); 3.97 (1 H, dd, J = 3.0, 12 Hz); 3.19-3.40(5 H, m).

$[\alpha]^D$ = +31.5° (c 1.52, $CHCl_3$). Lit.[6] (1*R*,2*R*)-*trans*-2-[(*tert*-butyldimethylsiloxy)]-3-phenyloxirane $[\alpha]^D$ = +40.0° (*c* 0.47, $CHCl_3$) Enantiomeric excess was evaluated by chiral CG analysis. Isotherm 130 °C, (*R*,*R*): 46.2 min, (*S*,*S*): 47.5 min. Ee 96%.



(1*R*,2*R*)-*trans*-stilbene oxide

$C_{14}H_{12}O$

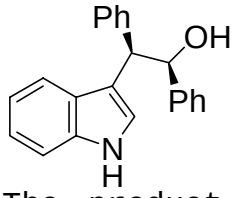
M.W. 196.24 g/mol

A flamed two necked flask equipped with a magnetic stirring bar was charged with Cr(Salen)SbF_6 (16.6 mg, 0.02 mmol) and activated molecular sieves 4Å (100 mg). Then TBME (0.4 mL) was added and the resulting solution was stirred under nitrogen at room temperature for 5 min. The solution was cooled to 0°C and then the epoxide **1c** (78.4 mg, 0.4 mmol) and 2-methylindole (35 mg, 0.268 mmol) were added to the reaction mixture. Finally *t*-BuOH (0.023 mL, 0.268 mmol) was added and the reaction mixture stirred at 0°C until GC analysis indicated complete conversion of 2-methylindole. After 48 hours the reaction goes to completion. The reaction mixture was diluted with Et_2O and filtered through celite. The solvent was evaporated and the epoxide was purified by chromatography on silica deactivated with Et_3N (eluent, Cyclohexane: Et_2O, gradient polarity from 1:0 to 9:1). Yield 27% (82% on maximum theoretical yield).

^{1}H-NMR (200 MHz, $CDCl_3$) δ: 3.88 (s, 2 H) ; 7.45-7.30 (10 H, m). $[\alpha]^D$ = +232.5° (*c* 0.78, C_6H_6). Lit.[6] (1R,2R)-*trans* stilbene oxide $[\alpha]^D$ = +257.2° (*c* 1.10, C_6H_6). Enantiomeric excess was evaluated by Chiral CG analysis. Isotherm 150 °C, (*R*,*R*): 24.9 min, (*S*,*S*): 26.3 min. Ee 91%.

General Procedure for the Asymmetric Ring Opening (ARO) Reaction of *meso* Stilbene Oxide with Indoles.

A flamed two necked flask equipped with a magnetic stirring bar was charged with Cr(Salen)Cl (0.01 mmol) and TBME (0.2 mL). Then *meso* stilbene oxide (0.1 mmol) was added to the brown solution. The mixture was stirred few minutes then indole (0.15 mmol) was added. The reaction mixture was stirred for 30-36 hours (checked by HPLC). Then the reaction mixture was diluted with Et_2O and filtered through celite. The solvent was evaporated and the indolyl derivative was purified by chromatography on silica gel (eluent, Cyclohexane : AcOEt).



(*R*,*R*)-2-(3-Indolyl)-1,2-diphenylethanol

$C_{22}H_{19}NO$

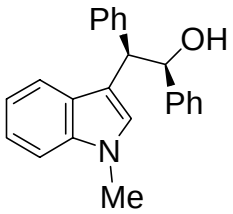
M.W. 313.39 g/mol

The product **4a** was isolated after flash chromatography (eluent, cyclohexane : AcOEt 8 : 2) as a white solid: mp 142-146°C. Yield 98%

^{1}H-NMR (200 MHz, $CDCl_3$) δ: 2.49 (1 H, br); 4.61 (1 H, d, J = 8.1 Hz); 5.36 (1 H, d, J = 8.1 Hz); 7.01-7.48 (m, 15 H); 8.16 (1 H, br). **^{13}C-NMR** (50 MHz, $CDCl_3$) δ: 52.09, 77.61, 111.03, 115.26, 119.37, 119.59, 122.29, 122.35, 126.25, 126.66 (2), 127.26, 127.49, 127.84 (2), 128.05 (2), 128.54 (2), 136.21, 141.61, 142.27. **IR** (nujol) 3540, 3295, 3060, 1600, 1455, 1370, 1340, 1250, 1100, 1030, 915, 740, 700 cm^{-1}. **GC-MS** m/z (relative intensity) 51 (10), 77 (15), 79 (15), 105 (10), 130 (15), 178 (30), 206 (100), 295 (10), 313 (5).

Elem. An. Calcd. for $C_{22}H_{19}NO$: C, 84.31%; H, 6.11%; N, 4.47%. Found: C, 84.43%; H, 6.21%; N, 4.51%.

The enantiomeric excess was determined by HPLC analysis: Chiralcel OF, isocratic (*n*-hexane : *i*-PrOH 85:15), flow 0.5 mL/min; temperature of the column 35°C. (1*S*,2*S*): 37.3 min; (1*R*,2*R*): 21.9 min. Ee 93%. $[\alpha]^D$ = -68.8° (*c* 1.12, $CHCl_3$).



(*R*,*R*)-2-(1-Methyl-3-indolyl)-1,2-diphenylethanol

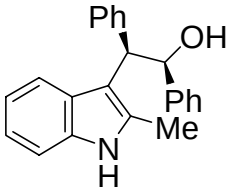
$C_{23}H_{21}NO$

M.W. 327.42 g/mol

The product **4b** was isolated after chromatographic purification (eluent, cyclohexane : Et_2O, 85:15) as a white solid. Mp 36-39°C. Yield 96%

^{1}H-NMR (200 MHz, $CDCl_3$) δ: 2.53 (1 H, brs); 3.81 (3 H, s); 4.58 (1 H, d, J = 8.0 Hz); 5.34, (1 H, d, J = 8.0 Hz); 7.02-7.31 (14 H, m); 7.46 (1H, d, J = 7.0 Hz). **^{13}C-NMR** (75 MHz, $CDCl_3$) δ:32.81, 52.18, 77.64, 109.20, 113.73, 119.13, 119.49, 121.87, 126.22, 126.76 (2), 127.15, 127.29, 127.88 (2), 128.00, 128.08 (2), 128.56 (2), 137.11, 141.96, 142.49. **IR** (nujol): 3500, 3360, 3050, 1610, 1455, 1240, 1030, 740, 700 cm^{-1}. **GC-MS** m/z (relative intensity) 51 (5), 77 (15), 91 (5), 115 (10), 178 (20), 204 (30), 220 (100), 309 (5), 327 (8). Elem. An. Calcd. for $C_{23}H_{21}NO$: C, 84.37%; H, 6.46%; N, 4.28%. Found: C, 84.38%; H, 4.39%; N, 4.33 %.

The enantiomeric excess was determined by HPLC analysis: Chiralcel OF, isocratic (*n*-hexane : *i*-PrOH 91:9), flow 0.5 mL/min; temperature of the column 35°C. (1*S*,2*S*): 32.9 min; (1*R*,2*R*): 38.*3min*. Ee 96%. $[\alpha]_D$ = -65.5° (*c* 2.23, $CHCl_3$).



(*R*,*R*)-2-(2-methyl-3-indolyl)-1,2-diphenylethanol

$C_{23}H_{21}NO$

M.W. 327.42g/mol

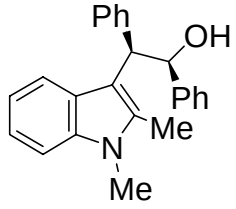
The product **4c** was isolated after chromatographic purification (cyclohexane : AcOEt 85:15) as a white solid: mp 148-152°C. Yield 98%

^{1}H-NMR (200 MHz, $CDCl_3$) δ: 2.19 (3H, s); 2.46 (1H, d = J 3.6 Hz); 4.45 (1H, d, J = 8.0 Hz); 5.75 (1H, dd, J = 3.6, 8.0 Hz); 7.11-7.30 (m, 13H); 7.68 (1H, d, J = 7.2Hz), 7.89 (1H, br). **^{13}C-NMR** (50 MHz, $CDCl_3$) δ: 12.08, 52.39, 76.04, 109.48, 110.48, 119.48, 119.81, 121.10, 125.98, 126.78 (2), 127.28, 127.87(2), 127.97 (2), 128.48

(2), 133.70; 135.36; 141.86; 142.82. **IR** (nujol) 3500, 3305, 3065, 1605, 1450, 1340, 1300, 1050, 820, 750, 700 cm^{-1}. **GC-MS** m/z (relative intensity) 51 (8), 77 (15), 91 (5), 115 (10), 130 (20), 145 (25), 217 (30), 230 (25), 294 (25), 309 (100). Elem. An. Calcd. for $C_{23}H_{21}NO$: C, 84.37%; H, 6.46%; N, 4.28%. Found: C, 84.42%; H, 6.47%; N, 4.31%.

The enantiomeric excess was determined by HPLC analysis: Chiralcel OD, isocratic (*n*-hexane : *i*-PrOH 80:20), flow 0.5 mL/min; (1*S*,2*S*): 24.30 min; (1*R*,2*R*): 34.1min. Ee 98%.

$[\alpha]^D$ = -153.5° (*c* 0.68, $CHCl_3$).



(*R*,*R*)-2-(1,2-Dimethyl-3-indolyl)-1,2-diphenylethanol

$C_{24}H_{23}NO$

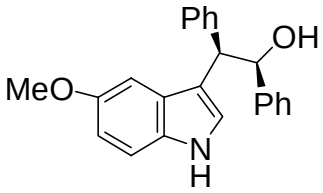
M.W. 341.45g/mol

The product **4d** was isolated after flash chromatography (Cyclohexane : AcOEt 85:15) as a white solid: mp 147-150°C. Yield 95% .

^{1}H-NMR (200 MHz, $CDCl_3$) δ: 2.33 (3 H, s); 2.53 (1 H, d, J = 3.4 Hz); 3.68 (3 H, s); 4.50 (1 H, d, J = 8.0 Hz); 5.78 (1 H, dd, J = 3.4, 8.0 Hz); 7.11-7.30 (m, 13 H); 7.78 (1 H, d, J = 8.4 Hz). **^{13}C-NMR** (50 MHz, $CDCl_3$) δ: 10.46; 29.69; 53.00; 75.99; 108.74; 108.89; 119.43 (2); 120.66; 125.90; 126.85 (2); 127.24; 127.83 (2); 127.92 (2); 128.03; 128.44 (2); 135.64; 136.87; 142.08; 142.84. **IR** (nujol) 3510, 3050, 1600, 1460, 1315, 1200, 1040, 755, 705 cm^{-1}. **GC-MS** m/z (relative intensity) 56 (10), 77 (15), 91 (5), 115 (10), 130 (20), 176 (5), 204 (8), 218 (10), 234 (100), 323 (5), 341 (5). Elem. An. Calcd. for $C_{24}H_{23}NO$: C, 84.42%; H, 6.79%; N, 4.10%. Found: C, 84.39%; H, 6.82%; N, 4.11 %.

The enantiomeric excess was determined by HPLC analysis: Chiralcel OD, isocratic (*n*-hexane : *i*-PrOH 80:20), flow 0.5 mL/min; (1*S*,2*S*): 19.2 min; (1*R*,2*R*): 54.2min. Ee 97%.

$[\alpha]^D$ = -142.1° (*c* 0.81, $CHCl_3$).



(R,R)-2-(5-Methoxy-3-indolyl)-1,2-diphenylethanol

$C_{23}H_{21}NO_2$

M.W. 343.42

The product **4e** was isolated after flash chromatography (Cyclohexane : AcOEt 8:2) as a white solid mp 158-160°C. Yield 95%.

^{1}H-NMR (200 MHz, $CDCl_3$) δ:2.53 (1 H, d, J = 3.4 Hz); 3.74 (3 H, s); 4.57 (1 H, d, J = 7.4 Hz); 5.37 (1 H, dd, J = 3.4, 7.4 Hz); 6.78-6.86 (2 H, m); 7.11-7.30 (11 H, m); 8.08 (1 H, br). **^{13}C-NMR** (50 MHz, $CDCl_3$) δ: 52.03; 55.78; 77.35; 101.23; 111.68; 112.47; 114. 84; 123.27; 126.25; 126.61 (2); 127.23; 127.86 (2); 127. 95; 128.06 (2); 128.51 (2); 131.38; 141.47; 142.49; 153.91. **IR** (nujol) 3360, 3040, 1610, 1450, 1300, 1050, 916, 730, 700 cm^{-1}. **GC-MS** m/z (relative intensity) 51 (10), 77 (20), 89 (5), 107 (10), 139 (5), 165 (15), 204 (20), 220 (15), 236 (100), 325 (5), 343 (8). Elem. An. Calcd. For $C_{23}H_{21}NO_2$: C, 80.44%; H, 6.16%; N, 4.08%. Found: C, 80.56%; H, 5.95%; N, 4.10%. The enantiomeric excess was determined by HPLC analysis: Chiralcel OD, isocratic (*n*-hexane : *i*-PrOH 70:30), flow 0.5 mL/min; (1*S*,2*S*): 38.6 min; (1*R*,2*R*): 51.2min.

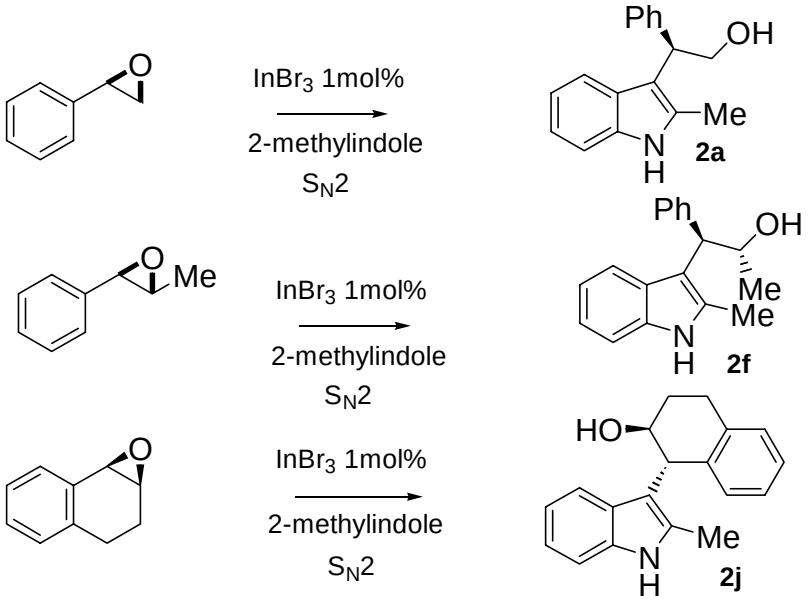
$[\alpha]^D$ = -24.1° (c 0.28, $CHCl_3$). Ee 90%.

Stereochemical assignement for 2a, 2f, 2j.

The absolute configuration was established for the products **2a**, **2f** and **2j**.

We have reported in a previous work[3] that the $InBr_3$ catalysed the ring-opening of optically pure aromatic epoxides with indoles without racemization *via* an S_N2 mechanism. To assign the absolute configuration of the ring-opened product **2a** obtained in the kinetic resolution catalysed by Cr(Salen)Cl, we performed the reaction of 2-methylindole with the enantiopure (*R*)-(+)-styrene oxide in the presence of a catalytic amount (1 mol%) of $InBr_3$. We have established the (*R*) absolute configuration for **2a** by comparison with analytical data of the known product.[3]

In order to establish the absolute configuration of the other ring-opened products **2b-j**, we have chosen two representative substrates for *cis* and *trans* epoxides. Optically pure (1*R*,2*R*)-(+)-1-phenyl-propene oxide, commercially available, (Aldrich), instead (1*R*,2*S*)-(+)-3,4-dihydronaphthalene oxide was prepared using the Jacobsen's epoxidation (83% ee).[4] The two epoxides reacted with 2-methylindole in the presence of a catalytic amount (1 mol%) of $InBr_3$, affording the corresponding indolyl derivatives in 99 and 83% ee, respectively.



The absolute configuration of the products **2f** and **2j** obtained in the kinetic resolution catalysed by Cr(Salen) complexes, were assigned by comparison of their retention times in HPLC (Chiralcel OD) with the samples obtained in the reaction performed with $InBr_3$. For all the other ring-opened products **2**, the absolute configuration was assigned by analogy.

In order to assign the absolute configuration of the ring-opened products **4a-e** obtained in the asymmetric ring-opening of *meso* aromatic epoxide catalyzed by Cr(Salen)Cl, we have assumed that the *meso* stilbene oxide is structurally related to a *cis* aromatic epoxide. Consequently, the attack of indoles to *meso* stilbene oxide and to *cis* aromatic epoxides occurred with the same stereochemical outcome.

1 E. N Jacobsen, L. Deng, Y. Furukawa, L. E. Martínez, *Tetrahedron* **1994**, *50*, 4323.

2 S. E., Schaus, J. Brånalt, E. N. Jacobsen, *J. Org. Chem.* **1998**, *63*, 403.

3 M. Bandini, P. G. Cozzi, P. Melchiorre, A. Umani-Ronchi, *J. Org. Chem.* **2002**, *67*, 5386.

4 C. M. Bellucci, A. Bergamini, P. G. Cozzi, A. Papa, E. Tagliavini, A. Umani-Ronchi, *Tetrahedron:Asymmetry* **1997**, *8*, 895.

5 B. Witkop, C. M. Foltz, *J. Am. Chem. Soc.* **1957**, *79*, 197.

6 L. Shu, Y. Shi, *Tetrahedron* **2001**, *57*, 5213.