On the Enantioselective Opening of meso Epoxides with Silicon Tetrachloride Catalyzed by Chiral Phosphonamides: A Response to Brunel, Legrand, Reymond and Buono

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General Experimental

$^1$H NMR spectra and $^{13}$C NMR spectra were recorded on either Varian Unity 400 (400 MHz, $^1$H; 100 MHz, $^{13}$C) or Varian Unity 500 (500 MHz, $^1$H; 126 MHz, $^{13}$C) spectrometers. Spectra are referenced to residual chloroform $\delta$ 7.26 ppm, $^1$H; $\delta$ 77.0 ppm, $^{13}$C) in CDCl$_3$ unless otherwise stated. Chemical shifts are reported in ppm ($\delta$); multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet) and br (broad). Coupling constants, $J$, are reported in Hertz. Optical rotations were obtained on a Jasco DIP-360 digital polarimeter and are reported as follows: $\left[\alpha\right]_D^T$, temperature (T), concentration ($c = g/100$ mL) and solvent. Elemental analyses were performed by the University of Illinois Microanalytical Service Laboratory.

All reactions were performed in oven and/or flame dried glassware under an atmosphere of dry nitrogen. All reported reaction temperatures were measured by internal monitoring with thermocouples. Dichloromethane (CH$_2$Cl$_2$) was distilled from P$_2$O$_5$, SiCl$_4$ was refluxed for 6-10 h then distilled
immediately before use from a still. Solvents for chromatography and extraction were technical grade and distilled from the indicated drying agents: hexane, pentane, and dichloromethane (CaCl₂); ethyl acetate (K₂CO₃). Analytical thin-layer chromatography was performed on Merck silica gel plates with QF-254 indicator. Column chromatography was performed using EM Science 230-400 mesh silica gel by the method of Still. Analytical supercritical fluid chromatography (SFC) was performed on a Berger Instruments packed-column SFC with built-in photometric detector (λ = 220 nm) using Daicel Chiralpak AS column. Retention times (tᵣ) and peak ratios were determined with a Hewlett Packard 3396 Series II integrator. Analytical capillary gas chromatography (GC) was performed using a Hewlett Packard 5890 Series II instrument. Chiral analyses were performed using an Astec G-TA (ChiralDEX™) 30-m trifluoroacetyl γ-cyclodextrin or Astec B-PH (ChiralDEX™) 30-m permethylated β-cyclodextrin. The injector temperature was 225 °C, the detector temperature was 300 °C. Temperature programs are reported in the form: initial temperature [time (min)], temperature ramp rate (deg/min), final temperature [time (min)]. Retention times (tᵣ) and integrated ratios were obtained from a Hewlett Packard 3393A integrator. Kugelrohr distillations were performed on a Büchi GKR-50 Kugelrohr; boiling points (bp) correspond to uncorrected air-bath temperatures (ABT). Epoxide 3 was prepared by epoxidation of cis-stilbene with oxone. Epoxides 4, and 5 were purchased and distilled prior to use.

**Preparation of Catalyst (R,R)-2.**

**Preparation of Bis(dimethylamino)chlorophosphine (9) and Bis(dimethylamino)-2-**
methoxyphenylphosphine (10)\(^{[2]}\)

Phosphorus trichloride (3.19 g, 23.2 mmol) was added to 7.58 g hexamethylphosphorous triamide (46.4 mmol, 2 equiv) in a flame-dried 25-mL round-bottomed flask under \(\text{N}_2\). The solution was heated to 100 \(\text{°C}\) for 20 min and then was allowed to cool. The yellow liquid was distilled (bp. 80 \(\text{°C}\)/12 mm Hg) to afford 9.3 g (86% yield) of 9 clear, colorless oil which was used directly in the next step.

2-Bromoanisole (10.5 g, 56.6 mmol) was dissolved in 100 mL of THF in a flame-dried. 250-mL round-bottomed flask under \(\text{N}_2\). The solution was then cooled to -78 \(\text{°C}\) in a dry-ice-acetone bath. To this solution was added dropwise \(n\)-butyllithium (1.56 M in hexane, 36.3 mL, 56.6 mmol, 1 equiv) and the solution was stirred for 20 min A solution of chlorobi(s(dimethylamino)phosphine (9.2 g, 59.4 mmol, 1.05 equiv) in 10 mL of THF was added dropwise. The reaction mixture was then slowly warmed up to rt and was stirred for 12 h. The reaction mixture was filtered under an inert atmosphere to remove LiCl and the filtrate was concentrated by simple distillation at atmospheric pressure. The dark yellow liquid was distilled (bp 98 \(\text{°C}\)/1.5 mm Hg) to afford 6.9 g (54% yield) of 10 as a clear, colorless oil.

Preparation of (3a\(R\),7a\(R\))-1H-Octahydro-2-(2-methoxyphenyl)-1,3-dimethyl-1,3,2-benzodiazaphosphole 2-Oxide (\((R,R)-2\)).

![Reaction diagram](image_url)
(1R,2R)-N,N'-Dimethylcyclohexane-1,2-diamine (4.31 g, 30.3 mmol) was dissolved in 65 mL of toluene in a 100-mL round-bottomed flask. Bis(dimethylamino)-2-methoxphenylphosphine (6.86 g, 30.3 mmol) was added dropwise. The solution was heated to 110 °C for three hours. The solution was allowed to cool to room temperature before it was cooled to 0 °C in an ice bath. tert-Butyl hydroperoxide[^3](5.53 M, 5.48 mL, 30.3 mmol) was then added dropwise. The solution was stirred at 0 °C for three hours, then was allowed to warm to room temperature and was stirred for an additional 12 h. The solvent was removed in vacuo and the white residue was purified by silica gel chromatography in two batches (7% MeOH/EtOAc) to afford 3.0 g and 3.8 g of a white solid (76% yield combined). The white solid was purified by crystallization (toluene/heptane) in two batches to yield 3.90 g and 1.0 g of white crystals (55%). The spectroscopic data matched those reported by Buono.[^4]

Analytical Data for (R,R)-2 (Batch A):

m.p. 115-116 °C

[α]_D^{22} = -26.7 (c = 0.99, CH₂Cl₂)

Analysis: C₁₅H₂₃N₂O₂P (294.33)

Calculated: C: 61.21% H: 7.88% N: 9.52% P: 10.52%

Found: C: 61.27% H: 7.89% N: 9.43% P: 10.33%

Analytical Data for (R,R)-2 (Batch B):

m.p. 115-116 °C

¹H NMR: (500 MHz, CDCl₃)

8.03 (ddd, J = 13.9, 7.5, 1.7, 1H), 7.46 (tdd, J = 9.0, 1.7, 0.6, 1H), 7.02 (tdd, J = 8.4, 2.5, 0.9, 1H), 6.89 (dd, J = 6.0, 8.1, 1H), 3.84 (s, 3H), 2.89-2.83 (m, 2H), 2.48 (d, J = 12, 2H), 2.40 (d, J = 11.6, 2H),
2.07-2.00 (m, 2H), 1.86-1.84 (m, 2H), 1.38-1.30 (m, 3H), 1.20-1.16 (m, 2H)

$^{13}$C NMR: (126 MHz, CDCl$_3$)
161.06, 138.29 (d, $J = 6.4$), 133.81, 120.75 (d, $J = 13$), 118.05 (d, $J = 150$), 111.20 (d, $J = 8.3$), 64.95 (d, $J = 6.5$), 64.18 (d, $J = 8.2$), 55.63, 29.58, 29.07 (d, $J = 10.1$), 28.65 (d, $J = 8.2$), 28.41 (d, $J = 5.5$), 24.77, 24.67.

IR: (CHCl$_3$)
2980 (m), 2941 (s), 2868 (m), 1591 (w), 1477 (s), 1465 (s), 1433 (w), 1275 (w), 1252 (s), 1171 (s), 1082 (w), 1026 (w), 923 (w), 819 (w)

$^{31}$P NMR: (202 MHz, CDCl$_3$)
34.21

$[\alpha]_D^{22} = -23.5$ (c = 1.10, CH$_2$Cl$_2$)

Analysis: C$_{15}$H$_{23}$N$_2$O$_2$P (294.33)
Calculated: C: 61.21% H: 7.88% N: 9.52% P: 10.52%
Found: C: 61.05% H: 7.91% N, 9.31% P: 10.04%

Preparation of Racemic Chlorohydrins.

Preparation of trans-2-Chlorocyclohexan-1-ol ((±)-7) [Procedure I]

To a stirred solution of cyclohexene oxide (510 L, 5.0 mmol) in CH$_2$Cl$_2$ (50 mL) was added HMFA (87 µL, 0.50 mmol, 0.1 equiv) at rt. The stirred
solution was cooled to -75 °C and then SiCl₄ (630 µL, 5.5 mmol, 1.1 equiv) was added dropwise over 1 min. After the addition was completed, the mixture was stirred at -75 °C for 20 min and then was quenched by pouring into cold (0 °C), rapidly stirring sat. aq. NaHCO₃ solution (100 mL) and was allowed to warm to rt. The resulting mixture was filtered through Celite, and the pad was rinsed with CH₂Cl₂ (4 x 20 mL). The Celite/silicon polymer was washed again with CH₂Cl₂ (3 x 50 mL). The combined organic extracts were washed with brine (30 mL) and the brine wash was back extracted with CH₂Cl₂ (2 x 20 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and evaporated under reduced pressure. The resulting pale-yellow liquid was purified by silica gel chromatography (4/1 pentane/Et₂O) to afford 0.64 g (95%) of trans-2-chlorocyclohexan-1-ol. The spectral data from 7 matched those previously reported.

¹H NMR: (400 MHz)

\[ \begin{align*}
3.72 \text{ (ddd, } J = 11.8, 9.3, 4.5, 1 \text{ H}), & \quad 3.56-3.45 \text{ (m, 1 H)}, & \quad 2.55 \text{ (d, } J = 2.2, 1 \text{ H}), & \quad 2.80-2.18 \text{ (m, 1 H)}, & \quad 2.14-2.06 \text{ (m, 1 H)}, & \quad 1.80-1.58 \text{ (m, 3 H)}, \\
1.40-1.22 \text{ (m, 3 H)}
\end{align*} \]

Preparation of (R*,R*)-2-Chloro-1,2-diphenylethan-1-ol (±)-6

Following Procedure I with 196 mg (1.0 mmol) of cis-stilbene oxide, CH₂Cl₂ (10 mL), SiCl₄ (126 µL, 1.10 mmol, 1.1 equiv), HMPA (17 µL, 0.10 mmol, 0.1 equiv), 2 h at -78 °C, quenched with (1/1) sat. KF / 1M KH₂PO₄.
Purification by silica gel chromatography (5/1 pentane/Et$_2$O) afforded 0.101 g (43%) of (R*,R*)-2-chloro-1,2-diphenylethan-1-ol. The spectral data from 6 matched those previously reported.

SFC: $t_R$ (S,S)-6, 4.77 min (50.1%); $t_R$ (R,R)-6, 5.90 min (49.9%) (Chiralpak AS, 150 bar, 40 °C, 5% CH$_3$OH in CO$_2$, 2.5 mL min$^{-1}$)

**Preparation of trans-2-Chlorocyclooctan-1-ol ((±)-8) (BGJ1/92)**

Following procedure I with 127 mg (1.00 mmol) of cyclooctene oxide, CH$_2$Cl$_2$ (2 mL), SiCl$_4$ (126 µL, 1.10 mmol, 1.1 equiv), HMPA (17 µL, 0.10 mmol, 0.1 equiv), 2 h at rt, quenched with (1/1) sat. KF / 1M KH$_2$PO$_4$. Purification by silica gel chromatography (9/1 pentane/Et$_2$O), followed by distillation (bulb-to-bulb) afforded 0.145 g (89%) of trans-2-chlorocyclooctan-1-ol. The spectral data from 8 matched those previously reported.

$^1$H NMR: (500 MHz)

4.13-4.07 (m, 1 H), 3.88-3.82 (m, 1 H), 2.50 (br s, 1 H), 2.24-2.16 (m, 1 H), 2.04-1.88 (m, 2 H), 1.84-1.68 (m, 3 H), 1.68-1.52 (m, 4 H), 1.50-1.40 (m, 2 H)

**Preparation of trans-1-Chloro-2-trifluoroacetoxycyclohexane ((±)-11)**
To a stirred solution of 7 (640 mg, 4.75 mmol) in CH₂Cl₂ (4.5 mL) was added trifluoroacetic anhydride (3.8 mL, 27 mmol, 5.7 equiv) at rt. After the addition was completed, the mixture was stirred at rt for 20 min and then was concentrated in vacuo. Purification of the residue by silica gel chromatography (pentane), followed by distillation (bulb-to-bulb) afforded 0.641 g (58%) of 1-chloro-2-trifluoroacetoxycyclohexane.

Data for (±)-11:

bp: 130 °C (12 mmHg) ABT

¹H NMR: (400 MHz)

5.10-4.90 (m, 1 H), 4.00-3.88 (m, 1 H), 2.40-2.26 (m, 1 H), 2.24-2.12 (m, 1 H), 1.90-1.70 (m, 3 H), 1.60-1.30 (m, 3 H)

GC: tR (R,R)-11, 3.55 min (50.0%); tR (S,S)-11, 4.30 min (50.0%) (G-TA, 14.0 psi, isothermal 85 °C).

Preparation of trans-1-Chloro-2-trifluoroacetoxycyclooctane ((±)-12)

To a stirred solution of 8 (145 mg, 0.89 mmol, 1.0 equiv) in CH₂Cl₂ (1.0 mL) was added trifluoroacetic anhydride (1.0 mL, 7.1 mmol, 8.0 equiv) at rt. After the addition was completed, the mixture was stirred at rt for 20 min and then concentrated in vacuo. Purification of the residue by silica gel chromatography (98/2 pentane/Et₂O), followed by distillation (bulb-to-bulb) afforded 0.164 g (80%) of 1-chloro-2-trifluoroacetoxycyclooctane ((±)-12).
Data for (±)-12:

bp: 112 °C (1.0 mmHg)

$^1$H NMR: (500 MHz)

5.30 (ddd, $J = 9.7$, 7.1, 2.7, 1 H), 4.25 (ddd, $J = 9.3$, 6.8, 2.6, 1 H),
2.28-2.19 (m, 1 H), 2.07-1.99 (m, 1 H), 1.96-1.83 (m, 3 H), 1.81-1.52 (m, 5 H), 1.47-1.36 (m, 2 H)

GC: $t_R$ 12, 11.9 min; $t_R$ 12', 12.5 min (B-PH, 16 psi, isothermal 85 °C).
Epoxide Opening Experiments.

Reaction of cis Stilbene Oxide. Preparation of (+)-2-Chloro-1,2-diphenylethan-1-ol (6).

In a flame dried 2-neck flask under nitrogen 12.6 mg (0.043 mmol 0.1 equiv) of catalyst (R,R)-2 was dissolved in 6 mL of dry dichloromethane. The resulting solution was cooled to -75°C and then 49 µL (73 mg, 0.43 mmol) of SiCl₄ was added to the reaction mixture. The mixture was stirred at this temperature for five minutes followed by slow addition of 84 mg (0.43 mmol) of cis-stilbene oxide as a solution in 1 mL of CH₂Cl₂. The resulting reaction mixture was allowed to stir under nitrogen for 3.5 h. The reaction mixture was then poured directly into 15 mL of a chilled (-3°C) solution of 1/1 sat. aq. KF/1.0 M KH₂PO₄ with vigorous stirring. The biphasic mixture was allowed to slowly warm to RT over 2.5h. The mixture was then washed 4 x 20 mL CH₂Cl₂. The combined organic extracts were dried (Na₂SO₄), filtered, and evaporated under reduced pressure. The resulting pale-yellow liquid was purified by silica gel chromatography (85/15 pentane/Et₂O) to afford 87 mg (87%) of (+)-2-chloro-1,2-diphenylethan-1-ol ((+)-6).

Data for (+)-6

$^1$H NMR: (500 MHz)

7.25-7.13 (m, 8 H), 7.13-7.07 (m, 2 H), 5.01 (d, $J = 8.3$ Hz, 1 H), 4.95 (dd, $J = 8.3$, 2.7 Hz, 1 H), 3.02 (d, $J = 2.7$ Hz, 1 H)

$^{13}$C NMR: (126 MHz)
138.89, 137.86, 128.72, 128.49, 128.37, 128.32, 128.15, 127.15, 78.90, 70.80

**SFC:** $t_R$ (S,S)-6, 4.76 min (52.5%); $t_R$ (R,R)-6, 5.87 min (47.5%) (Chiralpak AS, 150 bar, 40 °C, 5% CH$_3$OH in CO$_2$, 2.5 mL min$^{-1}$)

**Run #2:** (TAWIII77) Following the procedure outlined above with 29 mg (0.10 mmol 0.1 equiv) of catalyst (R,R)-2, 114 µL (170 mg, 1.0 mmol) of SiCl$_4$, and 196 mg, (1.0 mmol) of trans-stilbene oxide in 14 mL of dichloromethane yielded 174 mg (75% yield) of (+)-2-chloro-1,2-diphenylethan-1-ol. Spectral data were identical to run #1.

**SFC:** $t_R$ (S,S)-6, 4.66 min (52.7%); $t_R$ (R,R)-6, 5.81 min (47.3%) (Chiralpak AS, 150 bar, 40 °C, 5% CH$_3$OH in CO$_2$, 2.5 mL min$^{-1}$)

**Run #3:** (TAWIII74) Following the procedure outlined above with 12.6 mg (0.043 mmol 0.1 equiv) of catalyst (R,R)-2, 49 µL (73 mg, 1.0 mmol) of SiCl$_4$, and 84 mg, (0.43. mmol) of trans-stilbene oxide in 6 mL of dichloromethane yielded 65 mg (65% yield) of (+)-2-chloro-1,2-diphenylethan-1-ol. Spectral data were identical to run #1.

**SFC:** $t_R$ (S,S)-6, 3.82 min (54.1%); $t_R$ (R,R)-6, 4.76 min (45.9%) (Chiralpak AS, 150 bar, 40 °C, 5% CH$_3$OH in CO$_2$, 3.0 mL min$^{-1}$)

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**Chemical Structure:**

![Chemical Structure](attachment:structure.png)

**Reaction of Cyclohexene Oxide. Preparation of trans-2-Chlorocyclohexan-1-ol (7).**
Run #1: In a flame dried 2-neck flask under nitrogen 36 mg (0.12 mmol 0.1 equiv) of catalyst (R,R)-2 was dissolved in 6 mL of dry dichloromethane. The resulting solution was cooled to -75°C and then 140 µL (207 mg, 1.22 mmol) of SiCl₄ was added to the reaction mixture. The mixture was stirred at this temperature for five minutes followed by slow addition (over 2 min) of 124 µL (120 mg, 1.22 mmol) of cyclohexene oxide (neat). The resulting reaction mixture was allowed to stir at -75 °C (internal temp.) under nitrogen for 20 min. The reaction mixture was then poured directly into 15 mL of a chilled (-3°C) sat. aq. solution of NaHCO₃ with vigorous stirring. The biphasic mixture was allowed to slowly warm to rt over 2.5 h. The mixture was then filtered through a pad of Celite and the aqueous layer was washed 4 x 20 mL CH₂Cl₂. The combined organic layers were dried over Na₂SO₄. Removal of the solvent in vacuo was followed by distillation (bulb to bulb) to yield 148 mg (90% yield) of trans-2-chlorocyclohexan-1-ol ((+) -7).

Data for (+)-7

bp: 110 °C ABT (10 mmHg)

¹H NMR: (400 MHz)

3.72 (ddd, J = 11.8, 9.3, 4.5 Hz, 1 H), 3.56-3.45 (m, 1 H), 2.55 (d, J = 2.2 Hz, 1 H), 2.80-2.18 (m, 1 H), 2.14-2.06 (m, 1 H), 1.80-1.58 (m, 3 H), 1.40-1.22 (m, 3 H)

¹³C NMR: (100 MHz)

75.57, 67.81, 35.36, 33.29, 25.89, 24.18

GC: Chiral analysis of 7 was performed on the trifluoroacetate derivative 11

tₚ (R,R)-11, 3.53 min (47.7%); tₚ (S,S)-11, 4.28 min (52.3%) (G-TÅ, 14.0 psi, isothermal 85 °C).
Run #2: (TAWIII76) Following the above procedure with 59 mg (0.2 mmol 0.1 equiv) of catalyst (R,R)-2, 229 µL (339.8 mg, 2.0 mmol) of SiCl₄, and 202 µL (196 mg, 2.0 mmol) of cyclohexene oxide in 10 mL of dichloromethane yielded 240 mg (90% yield) of trans-2-chlorocyclohexan-1-ol. Spectral data were identical to run #1.

GC: Chiral analysis of 7 was performed on the trifluoroacetate derivative 11.

\[ t_R (R,R)-11, \quad 3.52 \text{ min (47.2%); } t_R (S,S)-11, \quad 4.25 \text{ min (52.8%)} \text{ (G-TA, 14.0 psi, isothermal 85 °C).} \]

Run #3: (TAWIII73) Following the above procedure 36 mg (0.12 mmol 0.1 equiv) of catalyst (R,R)-2, 140 µL (207 mg, 1.22 mmol) of SiCl₄, and 124 µL (120 mg, 1.22 mmol) of cyclohexene oxide in 6 mL of dichloromethane yielded 123 mg (75% yield) of trans-2-chlorocyclohexan-1-ol. Spectral data were identical to run #1.

GC: Chiral analysis of 7 was performed on the trifluoroacetate derivative 11.

\[ t_R (R,R)-11, \quad 3.53 \text{ min (47.4%); } t_R (S,S)-11, \quad 4.25 \text{ min (52.6%)} \text{ (G-TA, 14.0 psi, isothermal 85 °C).} \]

Preparation of trans-1-Chloro-2-trifluoroacetoxycyclohexane ((±)-11).

Run#1: To a stirred solution of 7 (From TAWII85) (148 mg, 1.1 mmol) in CH₂Cl₂ (1.0 mL) was added trifluoroacetic anhydride (1.0 mL, 7.1 mmol, 6.4 equiv) at rt. After the addition was completed, the mixture was stirred at rt for 3 h
and then concentrated in vacuo. Purification of the residue by silica gel chromatography (pentane), followed by distillation (bulb-to-bulb) afforded 0.165 g (71%) of 1-chloro-2-trifluoroacetoxycyclohexane ((±)-11).

**Data for (±)-11:**

bp: 130 °C ABT (10 mmHg)
\[ \text{1H NMR: (400 MHz)} \]

5.10–4.90 (m, 1 H), 4.00–3.88 (m, 1 H), 2.40–2.26 (m, 1 H), 2.24–2.12 (m, 1 H), 1.90–1.70 (m, 3 H), 1.60–1.30 (m, 3 H)

**GC:** See previous section.

Run #2: (TAWIII80) Following the procedure outlined above using 240 mg (1.78 mmol) of \( 7 \) (From TAWIII76) and 1 mL trifluoroacetic anhydride (7.1 mmol, 4.0 equiv.) in 1.0 mL of dichloromethane yielded 301 mg (73%) of 1-chloro-2-trifluoroacetoxycyclohexane. Spectral data were identical to run #1.

Run #3: (TAWIII75) Following the procedure outlined above using 100 mg (0.74 mmol) of \( 7 \) (From TAWIII73) and 1 mL trifluoroacetic anhydride (7.1 mmol, 10.0 equiv.) in 1.0 mL of dichloromethane yielded 119 mg (70%) of 1-chloro-2-trifluoroacetoxycyclohexane. Spectral data were identical to run #1.

**Preparation of (±) trans-2-Chlorocyclooctan-1-ol (8).**

\[ \text{Run #1: In a flame dried 2-neck flask under nitrogen 122 mg (0.427 mmol 0.1 equiv) of catalyst (R,R)-2 was dissolved in 20 mL of dry dichloromethane. The resulting solution was cooled to \(-75^\circ C\) and then 490 } \mu \text{L (724 mg, 4.27 mmol) of SiCl}_4 \text{ was added to the reaction mixture. The mixture was stirred at this temperature for five minutes followed by slow addition of 540 mg (4.27 mmol) of cyclooctene oxide as a solution in 1 mL of CH}_2\text{Cl}_2. \text{ The resulting reaction mixture was allowed to stir at } \text{\(-75^\circ C\)} \text{ (internal temp) under nitrogen for 3.5 h. The reaction mixture was then poured directly into 40 mL of a chilled} \]
(-3°C) solution of 1/1 sat. aq. KF/1.0 M KH$_2$PO$_4$ with vigorous stirring. The biphasic mixture was allowed to slowly warm to rt over 2.5h. The mixture was then washed 4 x 50 mL CH$_2$Cl$_2$. The combined organic extracts were dried (Na$_2$SO$_4$), filtered, and evaporated under reduced pressure. The resulting liquid was purified by silica gel chromatography (90/10 pentane/Et$_2$O), and distilled (bulb to bulb) to afford 20 mg (3%) of (±)-2-chloro-1,2-diphenylethan-1-ol ((±)-8) and 448 mg 83% of recovered cyclooctene oxide.

Data for 8
bp: 135 °C ABT (4.5 mmHg)

$^1$H NMR: (500 MHz)

4.13-4.07 (m, 1 H), 3.88-3.82 (m, 1 H), 2.50 (br s, 1 H), 2.24-2.16 (m, 1 H), 2.04-1.88 (m, 2 H), 1.84-1.68 (m, 3 H), 1.68-1.52 (m, 4 H), 1.50-1.40 (m, 2H)

GC: Chiral analysis of 8 was performed on the trifluoroacetate derivative 12 (vide infra) $t_R$ 12, 11.93 min (50.6%); $t_R$ 12', 12.55 min (49.4%) (B-PH, 16 psi, isothermal 85 °C).

Data for 5 (cyclooctene oxide)
bp: 110 °C ABT (4.5 mmHg)

$^1$H NMR: (500 MHz)

2.89 (ddd $J = 11.2, 4.5, 3.2$ Hz, 2H), 2.13(pseudo dq $J = 13.7, 4.1$ Hz, 2H), 1.64-1.39 (m, 8H), 1.30-1.22 (m 2H)

$^{13}$C NMR: (126 MHz)

55.84, 26.72, 26.45, 25.76
Run #2: (TAWIII87) Following the procedure outlined above with 36 mg (0.12 mmol 0.1 equiv) of catalyst \((R,R)\)-2, 140 µL (207 mg, 1.22 mmol) of SiCl₄, and 154 mg, (1.2 mmol) of cyclooctene oxide in 6 mL of dichloromethane yielded 4 mg (2.5% yield) of (±)-2-chloro-1,2-diphenylethan-1-ol and 124 mg (81% recovery) of cyclooctene oxide. Spectral data were identical to run #1. GC: Chiral analysis of 8 was performed on the trifluoroacetate derivative 12 (vide infra) \(t_R\) 12, 11.97 min (51.7%); \(t_R\) 12', 12.55 min (48.3%) (B-PH, 16 psi, isothermal 85 °C).

Run #3: (TAWIII82) Following the procedure outlined above with 36 mg (0.12 mmol 0.1 equiv) of catalyst \((R,R)\)-2, 140 µL (207 mg, 1.22 mmol) of SiCl₄, and 154 mg, (1.2 mmol) of cyclooctene oxide in 6 mL of dichloromethane and a reaction time of 3d yielded 12 mg (6% yield) of (±)-2-chloro-1,2-diphenylethan-1-ol and 110 mg (70% recovery) of recovered cyclooctene oxide. Spectral data were identical to run #1. GC: Chiral analysis of 8 was performed on the trifluoroacetate derivative 12 (vide infra) \(t_R\) 12, 11.89 min (53.8%); \(t_R\) 12', 12.55 min (46.2%) (B-PH, 16 psi, isothermal 85 °C).

Preparation of trans-1-Chloro-2-trifluoroacetoxycyclooctane ((±)-12).

To a stirred solution of 8 (20 mg, 0.12 mmol, 1 equiv) in CH₂Cl₂ (0.4 mL) was added trifluoroacetic anhydride (0.2 mL, 1.4 mmol, 11 equiv) at rt. After the addition was completed, the mixture was stirred at rt for 2 h
and then concentrated in vacuo. Purification of the residue by silica gel chromatography (98/2 pentane/Et₂O), followed by distillation (bulb-to-bulb) afforded 24 mg (77%) of 1-chloro-2-trifluoroacetoxycyclooctane (±-\textit{12}).

**Data for (±)-\textit{12}:**

bp: 115 °C ABT (1.5 mmHg)

$^1$H NMR: (400 MHz)

5.30 (ddd, $J = 9.7$, 7.1, 2.7 Hz, 1 H), 4.25 (ddd, $J = 9.3$, 6.8, 2.6 Hz, 1 H), 2.28-2.19 (m, 1 H), 2.07-1.99 (m, 1 H), 1.96-1.83 (m, 3 H), 1.81-1.52 (m, 5 H), 1.47-1.36 (m, 2 H)

GC: see previous section

**Run #2:** (TAWII89) Following the procedure outlined above using 4 mg (0.02 mmol) of 8 (From TAWII87) and 0.1 mL trifluoroacetic anhydride (0.7 mmol, 35 equiv.) in 0.2 mL of dichloromethane yielded 4 mg (80%) of 1-chloro-2-trifluoroacetoxycyclooctane. Spectral data were identical to run #1.

**Run #3:** (TAWII88) Following the procedure outlined above using 12 mg (0.07 mmol) of 8 (From TAWII82) and 0.2 mL trifluoroacetic anhydride (1.4 mmol, 20 equiv.) in 0.2 mL of dichloromethane yielded 11 mg (61%) of 1-chloro-2-trifluoroacetoxycyclooctane. Spectral data were identical to run #1.

**References**


[3] t-Butyl hydroperoxide was dried and purified according to K. B. Sharpless, T. Verhoeven, Aldrichima Acta 1979, 4, 63.

## DIRECTORY OF SPECTRAL AND ANALYTICAL DATA

<table>
<thead>
<tr>
<th>page</th>
<th>experiment</th>
<th>data</th>
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<tbody>
<tr>
<td>18</td>
<td>preparation of ((R,R) - 2)</td>
<td>(^1)H NMR spectrum of ((R,R) - 2)</td>
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<td>19</td>
<td>preparation of ((R,R) - 2)</td>
<td>(^{13})C NMR spectrum of ((R,R) - 2)</td>
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<td>preparation of ((R,R) - 2)</td>
<td>(^{31})P NMR spectrum of ((R,R) - 2)</td>
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<td>preparation of ((R,R) - 2)</td>
<td>(^1)H NMR spectrum of ((R,R) - 1,2)-cyclohexanediamine toluamide</td>
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<td>preparation of ((R,R) - 2)</td>
<td>SFC trace of racemic (1,2)-cyclohexanediamine toluamide</td>
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<td>preparation of ((R,R) - 2)</td>
<td>SFC trace of enantiopure ((R,R) - 1,2)-cyclohexanediamine toluamide</td>
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<td>(^1)H NMR spectrum of 6</td>
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<td>25</td>
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<td>(^{13})C NMR spectrum of 6</td>
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<td>Opening Cyclooctene Oxide (Run #1)</td>
<td>GC Trace of Racemic $12$</td>
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<td>opening cyclooctene oxide (run #1)</td>
<td>GC trace of racemic $12$</td>
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<td>39</td>
<td>opening cyclooctene oxide (run #1)</td>
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</table>
Data column, 15% MeOH, 3 ml/min. racemic cyclohexyl diamine derivative

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Acq. Method: ADTEST.M
Acq. Operator: jellerichs
Injection Date: 12/8/00 11:30:29 PM
Sample Name: BAJ-1-94
Injection Volume: Unknown

Analysis Method: C:\BERGER\METHODS\ADTEST.M
(modified after loading)

VWD1 A, Wavelength=220 nm of JELLERICH-96007D

---

Area Percent Report

---

Sorted by signal
Multiplier: 1.000000

Signal 1: VWD1 A, Wavelength=220 nm

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Totals: 2613.31201  133.76312

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*** End of Report ***
Sample Name: RQJ-1-12

Acq. Method : ATEST.M
Acq. Operator : Jellerichs
Injection Date : 11/19/2000 22:04:14 PM
Sample Name : RQJ-1-12

Analysis Method : C:\Jellerichs\METHODS\ADTEST.M

[^Graph^]

Area Percent Report

Sorted by Signal
Multiplier : 1.000000

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Totals : 9160.4477 349.77962

*** End of Report ***
Sorted by Signal
Multiplier : 1.000000

Signal 1: VWD1 A, Wavelength=220 nm

Peak   RT [min] Type Width [min] Area [mAU*sec] Height [mAU] Area %
1 4.770  BS 0.241 110.50571 33.92469 50.1430
2 6.863  BS 0.160 108.73405 26.94181 45.8570

Totals : 629.24036 55.56521

*** End of Report ***
as 2.5 ml/min 150 bar 40 dry 5 % MeOH stilbene chloroh yatin boiling cat.

Acq. Method : ASTEST.M
Acq. Operator : wynn
Injection Date : 11/20/30 3:08:26 PM
Sample Name : tawi177

Analysis Method : C:\BERGER\\METHODS\ASTEST.M
(modified after loading)

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**Area Percent Report**

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**Totals**: 12039.97656 1473.95593

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***End of Report***

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SPC 3D system Monday, November 20, 2000 3:15:31 PM by wynn
Aastec Chiraldeo GT-A
95 °C Isothermal
14 psi head pressure

Closing signal file M: SIGNAL .RAW
RUN 46 NOV 20, 2006 19:29:21

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END OF SIGNAL

RUN#  47    DEC 2, 2000  14:55:50

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TOTAL AREA = 78687
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Asten Chiralux BP-H
85 °C isothermal
16 psi head pressure

END OF SIGNAL

TOTAL AREA 232275
NUCL. FACTOR=1.00000E+00
Closing signal file M-SIGNAL.RAW
RUN 60 DEC 6, 2000 15:05:52

SIGNAL FILE: M-SIGNAL.RAW

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