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Supporting information

Beneficial Effect of *ortho*-Methoxy group in the Asymmetric Ring Opening of *meso* Epoxides with Silicon Tetrachloride Catalyzed by Chiral *o*-Methoxyphenyldiazaphosphonamides Lewis Bases

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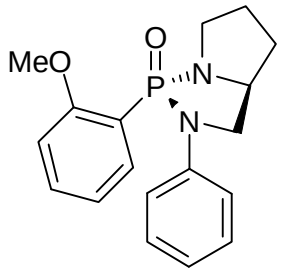
Materials and methods : ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a Bruker AC100 and AC200 spectrometer in $CDCl_3$ as solvent. The chemical shifts (ppm) were determined relative to Me_4Si (^{1}H and ^{13}C) and 85% H_3PO_4 (^{31}P). Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet), and br (broad) and coupling constants *J* are given in Hertz. Mass spectrometry was performed on a quadripolar ATI UNICAM Automass unit (Gas Chromatography performed on a capillary VARIAN 3500 unit, column SGE BPX5, 25 m, 0.25 mm, Helium). Optical rotations were taken on a Perkin–Elmer 241 MC polarimeter. Toluene, tetrahydrofuran (THF) were distilled from sodium/benzophenone ketyl immediately prior to use. Dichloromethane was distilled from P_2O_5. Silicon tetrachloride was distilled under argon immediatey prior to use. Ethylacetate and petroleum ether (35-60°C) were purchased from SDS and used without any previous purification. Column chromatography were performed on SDS silica gel (70-230 mesh).

meso-1,4-benzyloxy-2,3-epoxybutane and cycloheptene oxide were prepared by epoxidation of the corresponding alkenes with *m*-CPBA.[1] 3,4-epoxytetrahydrofuran was prepared from Payne reaction.[2] Other epoxides (cyclopentene oxide, cyclohexene oxide, cyclooctene oxide and *cis*-stilbene oxide) were purchased and used without any further purification.

Preparation of (2*S*,5*S*)-2-(2-anisyl)-3-phenyl-1,3-diaza-2-phosphabicyclo-[3.3.0]-octane 2-oxide (1)



1

Bis(dimethylammino)-*ortho*-anisylphosphine (4.6 g, 20.4 mmol) was added dropwise at 20°C to a solution of (*S*)-(+)-2-anilinomethylpyrrolidine (3.58 g, 20.4 mmol) in dry toluene (30 mL) under argon and warmed at 110°C for 3 hours. The mixture was allowed to cool to rt and then cooled at 0°C with an ice bath. *Tert*-butyl hydroperoxyde (3.7 mL, 5.5 M in decane) was slowly added and the mixture was stirred for 3 hours. After removing the solvent *in vacuo*, purification by silicagel chromatography (ethyl acetate) afforded 5.62 g of compound **1** as a white solid in 84 % yield.

mp 144°C

Optical Rotation $[\alpha]_D^{20}$ -28.9 (*c* = 1.0, CH_2Cl_2)

^{31}P NMR (40.5 MHz)

24.4

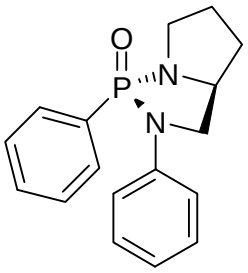
^{1}H NMR (200 MHz)

8.06 (ddd, *J* = 14.9, 7.4, 2.2, 1H), 7.38-7.32 (m, 1H), 7.16-6.93 (m, 5H), 6.84-6.71 (m, 2H), 4.14-3.72 (m, 6H), 3.47 (td, *J* = 8.2, 3.3, 1H), 3.04-2.87 (m, 1H), 2.17-1.73 (m, 4H)

^{13}C NMR (50 MHz)

160.5, 142.1 (d, *J* = 6.6), 136.6 (d, *J* = 7.3), 133.5, 128.8 (2C), 120.6, 120.3, 120.0 (d, *J* = 163), 115.8 (d, *J* = 4.4), 111.0, 110.9, 59.3 (d, *J* = 6.2), 55.8, 48.8 (d, *J* = 15.9), 45.1, 33.4, 26.5 (d, *J* = 2.5)

Preparation (2*S*,5*S*)-2,3-diphenyl-1,3-diaza-2-phosphabicyclo-[3.3.0]-octane 2-oxide 2



2

Bis(dimethylamino)phenylphosphine (4.6 g, 20.4 mmol) was added dropwise at 20°C to a solution of (*S*)-(+)-2-anilinomethylpyrrolidine (3.58 g, 20.4 mmol) in dry toluene (30 mL) under argon and warmed at 110°C for 3 hours. The mixture was allowed to cool to rt and then cooled at 0°C with an ice bath. *Tert*-butyl hydroperoxyde (3.7 mL, 5.5 M in decane) was slowly added and the mixture was stirred for 3 hours. The solvent was evaporated under reduced pressure. The crude product was purified by flash chromatography on a silica gel column (eluent : ethyl acetate) to afford **2** as a white solid in 80% yield.

mp 194 °C

Optical Rotation $[\alpha]^{20}_{D}$ = -28.4 (*c* = 0.25, CH_2Cl_2)

^{31}P NMR (40.5 MHz)

26.5

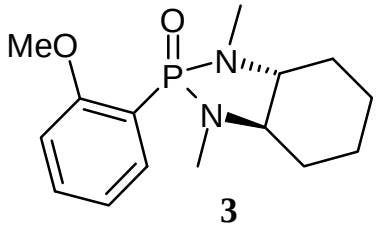
^{1}H NMR (200 MHz)

1.74-2.09 (m, 4H), 2.86-2.95 (m, 1H), 3.44-3.51 (m, 1H), 3.73-3.98 (m, 3H), 6.79 (t, *J* = 7.1, 1H), 6.95-7.19 (m, 4H), 7.29-7.37 (m, 3H), 7.73 (ddd, *J* = 13.7, *J* = 6.1, *J* = 1.9, 2H)

^{13}C NMR (50 MHz)

26.2 (d, *J* = 2.1), 32.0 (d, *J* = 1.0), 44.5 (d, *J* = 0.9), 49.0 (d, *J* = 13.9), 59.1 (d, *J* = 4.5), 116.0 (d, *J* = 4.6, 2C), 120.8, 128.1 (d, *J* = 14.3, 2C), 128.8 (2C), 131.3 (d, *J* = 3.0), 131.5 (d, *J* = 10.3, 2C), 132.9 (d, *J* = 166.7), 141.5 (d, *J* = 6.6)

Preparation of (1*R*,6*R*)-7,9-Dimethyl-8-(2-methoxyphenyl)-7,9-diaza-8-phosphabicyclo-[4.3.0]-nonane 8-oxide (3)



3

Bis(dimethylammino)-*ortho*-anisylphosphine (1.55 g, 6.9 mmol) was added dropwise at 20°C to a solution of (1*R*,2*R*)-N,N'-dimethylcyclohexane-1,2-diamine (977 mg, 6.9 mmol) in dry toluene (15 mL) under argon and warmed at 110°C for 3 hours. The mixture was allowed to cool to rt and then cooled at 0°C with an ice bath. *Tert*-butyl hydroperoxyde (1.25 mL, 5.5 M in decane) was slowly added and the mixture was stirred for 3 hours. After removing the solvent *in vacuo*, purification by silicagel chromatography (ethylacetate) afforded compound **3** as white solid in 91% chemical yield.

mp 115 °C

Optical Rotation $[\alpha]_D^{20}$ -28.3 (*c* = 1.0, CH_2Cl_2)

^{31}P NMR (40.5 MHz)

32.2

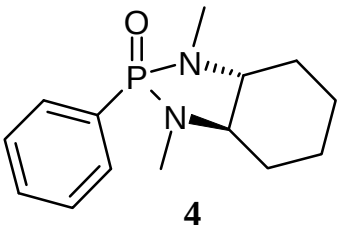
^{1}H NMR (200 MHz)

8.00 (ddd, *J* = 13.9, 7.6, 1.8, 1H), 7.49-7.37 (m, 1H), 6.98 (td, *J* = 7.4, 2.6, 1H), 6.87 (dd, 8.2, 6.0, 1H), 3.89 (s, 3H), 2.80-3.00 (m, 2H), 2.45 (d, *J* = 12, 2H), 2.35 (d, *J* = 11.6, 2H), 2.10-1.85 (m, 4H), 1.5-1.2 (m, 4H)

^{13}C NMR (50 MHz)

160.9, 138.0 (d, *J* = 5.9), 133.7, 120.5 (d, *J* = 12.9), 118.0 (d, *J* = 152.0), 111.0 (d, *J* = 7.7), 64.8 (d, *J* = 5.8), 64.0 (d, *J* = 8.7), 55.5, 29.6, 28.9 (d, *J* = 11.0), 28.5 (d, *J* = 8.3), 28.3 (d, *J* = 5.8), 24.8, 24.7

Preparation of (1*R*,6*R*)-7,9-Dimethyl-8-phenyl-7,9-diaza-8-phosphabicyclo-[4.3.0]-nonane 8-oxide (4)



4

Bis(dimethylammino)phenylphosphine (4.6 g, 20.4 mmol) was added dropwise at 20°C to a solution of (*S*)-(+)-2-anilinomethylpyrrolidine (3.58 g, 20.4 mmol) in dry toluene (30 mL) under argon and warmed at 110°C for 3 hours. The mixture was allowed to cool to rt and then cooled at 0°C with an ice bath. *Tert*-butyl hydroperoxyde (3.7 mL, 5.5 M in decane) was slowly added and the mixture was stirred for 3 hours. The solvent was evaporated under reduced pressure. The crude product was purified by flash chromatography on a silica gel column (eluent : ethyl acetate) to afford **4** as a white solid in 80% yield.

mp 125 °C

Optical Rotation $[\alpha]_D^{20}$ -2.5 (*c* = 0.15, CH_2Cl_2)

^{31}P NMR (40.5 MHz)

32.5

^{1}H NMR (200 MHz)

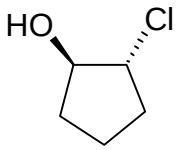
1.19-1.40 (m, 4H), 1.85-2.08 (m, 2 H), 2.24 (d, *J* = 11, 3H), 2.50 (d, *J* = 11, 3H), 2.60-2.70 (m, 1H), 2.87-2.91 (m, 1H), 7.41-7.47 (m, 3H), 7.69-7.79 (m, 2H)

^{13}C NMR (50 MHz)

160.9, 141.2, 132.8 (d, *J* = 8.8), 131.6 (d, *J* = 2.2), 128.4, 128.2, 65.6 (d, *J* = 7.1), 63.7 (d, *J* = 7.3), 28.9 (d, *J* = 6.8), 28.2 (d, *J* = 7.4), 24.4, 24.3

General procedure for the preparation of chiral chlorohydrins: To a stirred solution of catalyst **1-4** (0.1 equiv.) in CH_2Cl_2 or THF (6 mL) at -78°C under argon, is added $SiCl_4$ (1 equiv.). After 5 min, epoxide (1 equiv.) is added. After the addition is completed, the mixture was stirred at -78°C for 20 min to 3.5 h (depending on the nature of the epoxide) and then quenched by pouring into cold (-78°C), rapidly stirring sat. $NaHCO_3$ or 1/1 sat. KF/sat. KH_2PO_4 (15 mL) and allowed to warm to rt. The resulting mixture was extracted with CH_2Cl_2 (2 × 15 mL) and the combined organic extracts are washed with water (10 mL), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue is purified by silica gel chromatography.

Preparation of (1*R*,2*R*)-2-chlorocyclopentan-1-ol



Following the general procedure : catalyst **1** (40 mg, 0.122 mmol), cyclopentene oxide (107 µL, 1.22 mmol), CH_2Cl_2 (6 mL), $SiCl_4$ (140 µL, 1.22 mmol), 20 minutes at -78°C, quenched with sat. $NaHCO_3$ (15 mL). Purification by silica gel chromatography (85/15 petroleum ether/diethyl ether) afforded 133.8 mg (91 %) of *(1R,2R)*-2-chlorocyclopentan-1-ol.

Optical Rotation $[\alpha]_D^{20} = -7.2°$ (*c* = 1.0, CH_2Cl_2) ee =24%

^{1}H NMR (200 MHz)

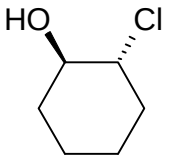
4.19-4.11 (m, 1H), 3.97-3.90 (m, 1H), 2.50 (br s, 1H), 2.28-2.02 (m, 2H), 1.88-1.67 (m, 3H), 1.58-1.35 (m, 1H)

^{13}C NMR (50 MHz)

80.1, 65.6, 33.2, 31.2, 20.5

Enantiomeric excess determined by GC analysis after derivatization of the chlorohydrins by trifluoroacetic anhydride. 100 mg (0.83 mmol) of chlorohydrin in 1 mL of CH_2Cl_2 was added trifluoroacetic anhydride (150 µL, 1.06 mmol). The mixture was stirred at 30°C for 15 min and then concentrated *in vacuo*. t_R (1*R*,2*R*) 14.2 min (62 %); t_R (1*S*,2*S*) 16.7 min (38 %), (Lipodex E, 30 KPa, isothermal 80°C, 0.1 µL)

Preparation of (1*R*,2*R*)-2-chlorocyclohexan-1-ol



Following the general procedure : catalyst **1** or **3** (0.122 mmol), cyclohexene oxide (124 µL, 1.22 mmol), CH_2Cl_2 (6 mL), $SiCl_4$ (140 µL, 1.22 mmol), 20 minutes at -78°C, quenched with sat. $NaHCO_3$ (15 mL). Purification by silica gel chromatography (80/20 petroleum ether/diethylether) afforded 139.4 mg (85 %) (with **1**) and 137.8 mg (84 %) (with **3**) of predominantly (1*R*,2*R*)-2-chlorocyclohexan-1-ol.

Optical Rotation with **1** : $[\alpha]_D^{20} = -30$ (*c* = 1.0, CH_2Cl_2) ee = 61%

with **3** : ee = 82%

^{1}H NMR (200 MHz)

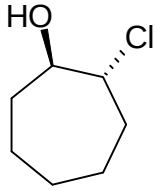
3.73-3.61 (m, 1H), 3.51-3.39 (m, 1H), 3.27 (br s, 1H), 2.19-1.98 (m, 2H), 1.69-1.49 (m, 3H), 1.38-1.04 (m, 3H)

^{13}C NMR (50 MHz)

74.9, 66.9, 34.9, 33.0, 25.3, 23.7

Enantiomeric excess determined by ^{13}C NMR analysis after derivatization of the chlorohydrins with fluorinated lactic acid.[4]

Preparation of (1*R*,2*R*)-2-chlorocycloheptan-1-ol



Following the general procedure : catalyst **1** or **3** (0.122 mmol), cycloheptene oxide (137 mg, 1.22 mmol), CH_2Cl_2 (6 mL), $SiCl_4$ (140 µL, 1.22 mmol), 3 hours at -78°C, quenched with 1/1 sat. KF/sat. KH_2PO_4. Purification by silica gel chromatography (80/20 petroleum ether/diethylether) afforded 143 mg (79 %) (with **1**) and 136 mg (75 %) (with **3**) of predominantly (1*R*,2*R*)-2-chlorocycloheptan-1-ol.

Optical Rotation with **1** : $[\alpha]_{436}^{20}$ = -4.0 (*c* = 1.0, CH_2Cl_2) ee = 79%
with **3** : $[\alpha]_{436}^{20}$ = -3.0 (*c* = 1.0, CH_2Cl_2) ee = 75%

^{1}H NMR (200 MHz)

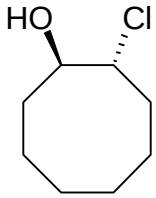
3.98-3.84 (m, 1H), 3.78-3.63 (m, 1H), 3.4-3.12 (m, 1H), 2.27-1.3 (m, 10H)

^{13}C NMR (50 MHz)

78.5, 71.2, 34.3, 32.1, 26.5, 23.6, 21.8

Enantiomeric excess determined by ^{13}C NMR analysis after derivatization of the chlorohydrins with fluorinated lactic acid.[4]

Preparation of (1*R*,2*R*)-2-chlorocyclooctan-1-ol



Following the general procedure : catalyst **1** or **3** (0.122 mmol), cyclooctene oxide (154 mg, 1.22 mmol), CH_2Cl_2 (6 mL), $SiCl_4$ (140 µL, 1.22 mmol), 3.5 hours at -78°C, quenched with 1/1 sat. KF/sat. KH_2PO_4. Purification by silica gel chromatography (90/10 petroleum ether/diethylether) afforded 184 mg (93 %) (with **1**) and 178 mg (90 %) (with **3**) of predominantly (1*R*,2*R*)-2-chlorocyclooctan-1-ol.

Optical Rotation with **1** : $[\alpha]_{365}^{20}$ = -1.4 (*c* = 1.0, CH_2Cl_2) ee>99%

with **3** : $[\alpha]_{365}^{20}$ = -1.4 (c = 1.0, CH_2Cl_2) ee>99%

^{1}H NMR (200 MHz)

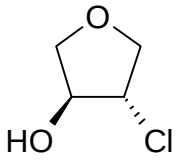
4.11 (ddd, *J* = 9.2, 7.3, 2.8, 1H), 3.86 (ddd, *J* = 9.2, 6.9, 2.1, 1H), 2.63 (br s, 1H), 2.29-2.13 (m, 1H), 2.07-1.30 (m, 11H)

^{13}C NMR (50 MHz)

76.2, 71.2, 32.3, 32.0, 25.7, 25.7, 24.9, 24.1

Enantiomeric excess determined by GC analysis after derivatization of the chlorohydrins by trifluoroacetic anhydride. 100 mg (0.62 mmol) of chlorohydrin in 1 mL of CH_2Cl_2 was added trifluoroacetic anhydride (113 µL, 0.80 mmol). The mixture was stirred at 30°C for 15 min and then concentrated *in vacuo*. t_R (1*R*,2*R*) 29.4 min (> 99%); t_R (1*S*,2*S*) 37.2 min (<1%), (Lipodex E, 30 KPa, isothermal 130°C, 0.1 µL)

Preparation of (-)-*trans*-4-chlorotetrahydrofuran-3-ol



Following the general procedure : catalyst **1** or **3** (0.122 mmol), 3,4-epoxytetrahydrofuran (105 mg, 1.22 mmol), CH_2Cl_2 (6 mL), $SiCl_4$ (140 µL, 1.22 mmol), 3 hours at -78°C, quenched with 1/1 sat. KF/sat. KH_2PO_4. Purification by silica gel chromatography (70/30 petroleum ether/ethylacetate) afforded 61 mg (41 %) (with **1**) and 66 mg (44 %) (with **3**) of predominantly (-)-4-chlorotetrahydrofuran-3-ol.

Optical Rotation with **1** : $[\alpha]_D^{20}$ = -2.7 (*c* = 1.0, CH_2Cl_2) ee = 48%

with **3** : $[\alpha]_D^{20}$ = -1.6 (*c* = 1.0, CH_2Cl_2) ee = 37%

^{1}H NMR (100 MHz)

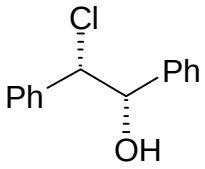
4.50-3.72 (m, 5H), 2.70 (br s, 1H), 1.35-1.12 (m, 1H)

^{13}C NMR (50 MHz)

78.5, 74.0, 73.4, 61.9

Enantiomeric excess determined by GC analysis after derivatization of the chlorohydrins by trifluoroacetic anhydride. 50 mg (0.41 mmol) of chlorohydrin in 1 mL of CH_2Cl_2 was added trifluoroacetic anhydride (75 µL, 0.53 mmol). The mixture was stirred at 30°C for 15 min and then concentrated *in vacuo*. t_R 22.5 min (**1**: 74 %, **3**: 69 %); t_R 25.9 min (**1**: 26 %, **3**: 31 %), (Lipodex E, 30 KPa, isothermal 80°C, 0.1 µL)

Preparation of (2*S*,3*S*)-2-chloro-1,2-diphenylethan-1-ol



Following the general procedure : catalyst **1** (THF, 6 mL) or **3** (CH_2Cl_2, 6 mL), (0.043 mmol), stilbene oxide (100 mg, 0.43 mmol), $SiCl_4$ (49 µL, 0.43 mmol), 3.5 hours at -78°C, quenched with 1/1 sat. KF/sat. KH_2PO_4. Purification by silica gel chromatography (80/20 petroleum ether/diethylether) afforded 68 mg (68 %) (with **1**) and 71 mg (71 %) (with **3**) of predominantly (1*S*,2*S*)-2-chloro-1,2-diphenylethan-1-ol.

Optical Rotation with **1** : $[\alpha]_D^{20}$ = +10.2 (*c* = 1.0, CH_2Cl_2) ee = 92%

with **3** : $[\alpha]_D^{20}$ = +6.7 (*c* = 1.0, CH_2Cl_2) ee = 60%

^{1}H NMR (200 MHz)

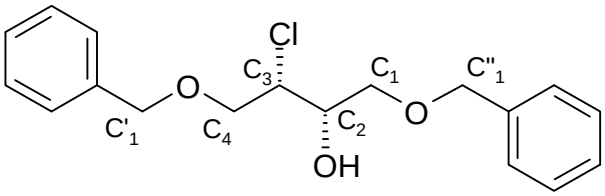
7.36-7.13 (m, 10H), 5.10-4.95 (m, 2H), 3.1-2.7 (m, 1H)

^{13}C NMR (50 MHz)

138.8, 128.6, 128.4, 128.2, 128.0, 127.0, 78.8, 70.7

HPLC t_R (2*S*,3*S*) 10.63 min (**1**: 96 %, **3**: 80 %); t_R (2*R*,3*R*) 11.30 min (**1**: 4 %, **3**: 20 %), ((*S*,*S*)-Whelk-O 1, Hexane/*i*-PrOH, 90/10, 0.5 mL/min, 254 nm)

Preparation of (2*S*,3*S*)-3-chloro-1,4-bis-(benzyloxy)-butan-2-ol



Following the general procedure : catalyst **1** or **3** (0.122 mmol), 1,4-benzyloxy-2,3-epoxybutane (346.5 mg, 1.22 mmol), CH_2Cl_2 (6 mL), $SiCl_4$ (140 µL, 1.22 mmol), 3.5 hours at -78°C, quenched with 1/1 sat. KF/sat. KH_2PO_4. Purification by silica gel chromatography (ethyl acetate) afforded 303 mg (78%) (with **1**) and 370 mg (95 %) (with **3**) of predominantly (2*S*,3*S*)-3-chloro-1,4-bis-(benzyloxy)-butan-2-ol.

Optical Rotation with **1** : $[\alpha]_{365}^{20}$ = +1.2 (*c* = 1.0, CH_2Cl_2) ee = 94%

with **3** : $[\alpha]_{365}^{20}$ = +1.0 (*c* = 1.4, CH_2Cl_2) ee = 90

^{1}H NMR (200 MHz)

7.20-7.12 (m, 10H), 4.51-4.34 (m, 4H), 4.13-3.97 (m, 1H), 3.69-3.35 (m, 5H), 3.17-3.11 (m, 1H)

^{13}C NMR (50 MHz)

128.5 (Ph), 127.9 (Ph), 73.5 (C'_1), 73.2 (C''_1), 71.5 (C_4), 71.1 (C_1), 69.9 (C_2), 60.8 (C_3)

HPLC t_R (2*S*,3*S*) 22.3 min (**1**: 97 %, **3**: 95%); t_R (2*R*,3*R*) 26.6 min (**1**: 3 %, **3**: 5%), (Chiralcel-OD-H, hexane/EtOH, 96/4, 0.5 mL/min, 254 nm)

References

Preparation of racemic chlorohydrins

To a stirred solution of HMPA (175 µL, 1 mmol) in CH_2Cl_2 (15 mL) at -78°C under argon, was added $SiCl_4$ (1.26 mL, 11 mmol). After 5 min, the desired epoxide (873 µL, 10 mmol) was added. After the addition was completed, the mixture was stirred at -78°C for 20 min, quenched by pouring into cold (-78°C), rapidly stirring sat. $NaHCO_3$ (15 mL) and allowed to warm to rt. The resulting mixture was extracted with CH_2Cl_2 (2 × 15 mL) and the combined organic extracts were washed with water (10 mL), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The resulting liquid was purified by silica gel chromatography to the expected chlorohydrin.

(1) To a solution of *m*-CPBA (5.74 mmol) in CH_2Cl_2 (40 mL) was added the desired olefin (3.16 mmol). The reaction was strirred overnight at rt and then quenched with sat. Na_2SO_3 (40 mL). The resulting mixture was extracted with CH_2Cl_2 (2 × 20 mL) and the combined organic extracts were washed with sat. Na_2SO_3 (20 mL) and twice with water (20 mL), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The resulting compound was purified by silica gel chromatography to afford the expected epoxide.

(2) To a stirred mixture of methanol (50 mL), with acetonitrile (232 mmol, 12.1 mL) is added 2,5-dihydrofurane (116 mmol, 8.12 g) and $NaHCO_3$ (116 mmol, 9.75 g). 30 % H_2O_2 (40 mL) was added dropwise. After the addition was completed, the mixture was stirred for 12 h at rt, and then 4 h at 35°C. The resulting mixture was filtered and extracted with CH_2Cl_2 (2 × 40 mL) and the combined organic extracts were washed twice with sat. Na_2SO_3 (20 mL) and water (40 mL), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. 3,4-epoxytetrahydrofuran was obtained in 50% yield but without any byproducts and used without any further purification.

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