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Supporting Information

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Chiral Boron-Bridged Bisoxazolines: Readily Available Anionic Ligands for Asymmetric Catalysis

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All reactions were carried out under an inert atmosphere of argon or nitrogen, unless otherwise noted. Solvents were distilled according to standard procedures and degassed by three successive "freeze-pump-thaw" cycles prior to use. NMR spectra were recorded on 400 and 500 Bruker Avance spectrometers. Infrared spectra were obtained on Shimadzu FTIR-8400S spectrometer using neat samples. Optical rotations were measured on a Perkin Elmer polarimeter 341 equipped with a Na-lamp. Elemental analyses were obtained from the Micro-Analytical Laboratory of the Department of Chemistry of the University of Basel.

Ph_2BCl,[1] Et_2BBr,[1,2] bis[3,5-bis(trifluoromethyl)phenyl]boronchloride,[3] 2*H*-oxazolines[4] and 2,2-diphenylmalonyl dichloride[5] were prepared according to literature procedures. All other reagents were available from commercial suppliers and most of the time used without further purification. Olefins were purified by distillation from CaH_2 and finally degassed. Liquid diazoacetate precursors were degassed prior to use.

General procedure for the synthesis of ligands 6a and 6b. In a 100ml round bottom flask 2,2-diphenylmalonyldichloride (720 mg, 2.46 mmol) was dissolved in 50 ml of dry CH_2Cl_2. Triethylamine (0.75 g, 1.03 ml, 7.4 mmol) was added, followed by solid (*S*)-amino alcohol (2.56 mmol). The pale yellow solution was stirred overnight before 25ml of a saturated aqueous Na_2CO_3 solution was added. The organic layer was separated and the aqueous phase extracted with 25 ml of CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was first filtered through a plug of silica (CH_2Cl_2/MeOH 9:1) and subsequently purified by column chromatography (gradient: CH_2Cl_2/MeOH 20:1 to CH_2Cl_2/MeOH 9:1). The product was isolated as a white solid.

The β-amido alcohol (1.00 mmol) and Burgess' reagent (1.15 mmol) were dissolved in 50 mL of dry THF. The reaction mixture was refluxed overnight. After cooling to room temperature and evaporation of the volatiles, the crude mixture was dissolved in CH_2Cl_2, successively washed with HCl (1N), brine and water. The organic phases were combined and dried over $MgSO_4$. After evaporation of the solvent, the remaining yellowish oil was transferred to a silica gel column and purified by flash chromatography (CH_2Cl_2 to CH_2Cl_2/MeOH 20:1) to afford the desired product.

***N,N*-Bis[1-(hydroxymethyl)-1,1-dimethylethyl]-2,2-diphenyl-1,3-propanediamide).** Yield: 87 %; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38-7.26 (m, 10H, H_{Ar}), 3.82 (bm, 2H, CH_2-C*H*-NH), 3.68 (m, 2H, C*H*$_2$OH), 3.53 (m, 2H, C*H*$_2$OH), 2.71 (bs, 2H, OH), 1.80 (m, 2H, CH_{iPr}), 0.86 (d, 6H, $CH_{3\ iPr}$), 0.74 (d, 6H, $CH_{3\ iPr}$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.9 (C=O), 139.8 ($C_{quat\ Ar}$), 129.5 (C_{Ar}), 128.6 (C_{Ar}), 128.1 (C_{Ar}), 64.3 (CH), 58.1

(CH_2), 28.8 (CH_{iPr}), 19.6 ($CH_{3\ iPr}$), 18.1 ($CH_{3\ iPr}$). IR: 3409, 3301, 2954, 1666, 1635, 1504, 1242, 1072, 1033, 702; $[\alpha]_{20}$ = -30 (*c* = 0.11, CH_2Cl_2). MS (FAB) *m/z* (rel. intensity): [M+H^+] 427 (100). Elemental analysis calcd (%) for $C_{25}H_{34}N_2O_4$ (426.55): C 70.39, H 8.03, N 6.57; found: C 70.15, H 8.19, N 6.46.

6a (R^1 = Ph; R^2 = *i*-Pr). Yield: 96 %; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40-7.26 (m, 10H, H_{Ar}), 4.25 (m, 2H, H_{oxa}), 4.05 (m, 4H, H_{oxa}), 1.86 (m, 2H, CH_{iPr}), 0.96 (d, 6H, $CH_{3\ iPr}$), 0.90 (d, 6H, $CH_{3\ iPr}$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.2 (C=N), 139.8 ($C_{quat\ Ar}$), 129.4 (C_{Ar}), 127.7 (C_{Ar}), 127.3 (C_{Ar}), 72.0 (CH_{oxa}), 70.1 ($CH_{2\ oxa}$), 57.8 (C_{bridge}), 32.5 (CH_{iPr}), 18.9 ($CH_{3\ iPr}$), 18.1 ($CH_{3\ iPr}$). IR: 2962, 2908, 2869, 2360, 1650, 1596, 1465, 1442, 1350, 1211, 1164, 1002, 941, 871, 748. $[\alpha]_{20}$ = -119 (*c* = 0.11, CH_2Cl_2). MS (FAB) *m/z* (rel. intensity): [M+H^+] 391 (100). Elemental analysis calcd (%) for $C_{25}H_{30}N_2O_2$ (390.52): C 76.89, H 7.74, N 7.17; found: C 75.76, H 7.73, N 7.07.

***N,N*-Bis[1-(hydroxymethyl)-2,2-dimethylpropyl]-2,2-diphenyl-1,3-propanediamide.** Yield: 90 %; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51-7.29 (m, 10H, H_{Ar}), 3.78 (m, 2H, C*H*$_2$-OH), 3.41 (m, 2H, C*H*-NH), 2.54 (bm, 2H, OH), 0.88 (s, 18H, $CH_{3\ tBu}$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.1 (C=O), 139.9 ($C_{quat\ Ar}$), 129.6 (C_{Ar}), 128.6 (C_{Ar}), 128.0 (C_{Ar}), 63.2 (CH), 60.8 (CH_2), 33.2 ($C_{quat\ tBu}$), 26.7 ($CH_{3\ tBu}$). IR: 3409, 3355, 3278, 2954, 2877, 2360, 1666, 1643, 1512, 1465, 1365, 1242, 1188, 10566, 1002, 933, 825, 756, 702. $[\alpha]_{20}$ = -15 (*c* = 0.11, CH_2Cl_2). MS (FAB) *m/z* (rel. intensity): [M+H^+] 455 (100). Elemental analysis calcd (%) for $C_{27}H_{38}N_2O_4$ (454.61): C 71.34, H 8.42, N 6.16; found: C 70.86, H 8.45, N 6.28.

6b (R^1 = Ph; R^2 = *t*-Bu). Yield: 96 %; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45-7.28 (m, 10H, H_{Ar}), 4.21 (bt, 2H, CH_{oxa}), 4.12 (bt, 2H, CH_{oxa}) 4.00 (bt, 2H, CH_{oxa}), 0.95 (s, 18H, $CH_{3\ tBu}$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.2 (C=N), 139.8 ($C_{quat\ Ar}$), 129.6 (C_{Ar}), 127.7 (C_{Ar}), 127.3 (C_{Ar}), 75.7 (CH), 68.9 (CH_2), 57.9 (C_{bridge}), 34.1 ($C_{quat\ tBu}$), 26.1 ($CH_{3\ tBu}$). IR: 2954, 2900, 2360, 1658, 1481, 1450, 1396, 1288, 1203, 1157, 1002, 948, 871, 748, 702. $[\alpha]_{20}$ = -116 (*c* = 0.11, CH_2Cl_2). MS (FAB) *m/z* (rel. intensity): [M+H^+] 419 (100). Elemental analysis calcd (%) for $C_{27}H_{34}N_2O_2$ (418.58): C 77.48, H 8.19, N 6.69; found: C 77.17, H 8.24, N 6.60.

General procedure for the synthesis of the lithium salts (7)-Li and the ligands 9a-f. *t*-BuLi (1.7 M in hexanes, 1.78 mL, 3.03 mmol) was added at -78°C over a 10 minutes period to a solution of 2*H*-oxazoline (2.75 mmol) in 100 mL of THF, resulting in a pale yellow solution. After stirring for 30 minutes at this temperature, a solution of R_2BCl (1.38 mmol) in toluene (5 mL) was added through a cannula and the cooling bath immediately removed after addition was complete. After 4 to 12 h, the reaction was complete and the volatile compounds were removed under vacuum. The remaining foamy residue was redissolved in benzene, filtered to remove LiCl, and the solvent evaporated again. After washing with hexanes (3x20 mL) and drying, the ligand salt was isolated as a highly hygroscopic white solid.

General procedure for the conversion of the lithium salts into their protonated analogues. The lithium salt of the Bora-BOX (**7**)-Li was dissolved in a minimum amount of the eluent mixture (typically: hexanes : ethyl acetate : Et_3N = 10:1:0.5 unless otherwise mentioned) and directly transferred to a silica gel column chromatography (12 cm; Ø = 2cm). After elution and evaporation of the solvents, the product was isolated in its protonated form.

General procedure for the conversion of the protonated ligands into their lithium salts. *n*-BuLi (140 μL, 0.23 mmol) was added at 0 °C to a solution of **9a** (84 mg, 0.22 mmol) in 10 mL of THF. After 2h hours of additional stirring at room temperature, the volatiles were removed under reduced pressure. The analytically pure material (**7a**)-Li was isolated as a white solid (82 mg, 0.206 mmol, 96 % yield).

(7a)-Li (R^1 = Ph; R^2 = *i*-Pr). Yield: 67 %; ^{1}H NMR (500 MHz, $(CD_3)_2CO$): δ 7.29 (vt, 4H, $H_{Ar\text{-}m}$), 6.96 (vt, 4H, $H_{Ar\text{-}o}$), 6.87 (dd, 2H, $H_{Ar\text{-}p}$), 3.79 (m, 2H, H_{oxa}), 3.73 (m, 2H, H_{oxa}), 3.62 (m, 2H, H_{oxa}), 2.02 (m, 2H, H_{iPr}), 0.821 (s, 6H, $CH_{3\ iPr}$), 0.71 (s, 6H, $CH_{3\ iPr}$); ^{13}C NMR (125 MHz, $(CD_3)_2CO$): δ $C_{Ar\text{-}ipso}$: not detected, 209.4 ($C{=}N_{oxa}$), 134.5 ($C_{Ar\text{-}m}$), 125.7 ($C_{Ar\text{-}o}$), 123.1 ($C_{Ar\text{-}p}$), 71.1 (C_{oxa}), 65.4 (C_{oxa}), 31.6 (CH_{iPr}), 18.9 ($CH_{3\ iPr}$); 16.3 ($CH_{3\ iPr}$); ^{11}B NMR (160 MHz, $(CD_3)_2CO$): δ -12.7 (s); IR: 2962, 2877, 2360, 1635, 1589, 1465, 1388, 1265, 1157, 1103, 1033, 964, 864, 732. $[\alpha]_{20}$ = -49 (*c* = 0.11, CH_2Cl_2). MS (MALDI-TOF, 2,5-dihydroxybenzoic acid): *m/z*(%): 402 $[M+2Li]^+$, 396 $[M]^+$, 390 $[M\text{-}Li]^+$.

9a (R^1 = Ph; R^2 = *i*-Pr). Yield: 63 %; ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.76 (bs, $1H_{NHN}$), 7.32 (bt, 4H, $H_{Ar\text{-}m}$), 7.21 (dd, 4H, $H_{Ar\text{-}o}$), 7.14 (dd, 2H, $H_{Ar\text{-}p}$), 4.40 (m, 2H, H_{oxa}), 4.11 (m, 2H, H_{oxa}), 3.86 (m, 2H, H_{oxa}), 1.78 (m, 2H, H_{iPr}), 1.05 (s, 6H, $CH_{3\ iPr}$), 0.96 (s, 6H, $CH_{3\ iPr}$); ^{13}C NMR (125 MHz, $CDCl_3$): δ $C_{Ar\text{-}ipso}$ and $C{=}N_{oxa}$ not detected, 133.8 ($C_{Ar\text{-}m}$), 127.1 ($C_{Ar\text{-}o}$), 125.2 ($C_{Ar\text{-}p}$), 72.1 (C_{oxa}), 67.3 (C_{oxa}), 32.9 (CH_{iPr}), 18.9 ($CH_{3\ iPr}$); 18.8 ($CH_{3\ iPr}$); ^{11}B NMR (160 MHz, $CDCl_3$): δ -13.5 (s); IR: 2954, 2877, 1581, 1465, 1411, 1311, 1272, 1218, 1164, 1033, 964, 933, 725. $[\alpha]_{20}$ = -66 (*c* = 0.11, CH_2Cl_2). Elemental analysis calcd (%) for $C_{24}H_{31}BN_2O_2$ (390.33): C 73.85, H 8.00, N 7.18; found: C 73.75, H 7.91, N 7.15. MS (FAB) *m/z* (rel. intensity): $[M+H^+]$ 391 (100), $[M$ - oxa + $H^+]$ 278 (57.83). Rf = 0.43.

(7b)-Li (R^1 = Ph; R^2 = *t*-Bu). Yield: 88 %; ^{1}H NMR (500 MHz, $(CD_3)_2CO$): δ 7.32 (dd, 4H, $H_{Ar\text{-}m}$), 6.95 (vt, 4H, $H_{Ar\text{-}o}$), 6.86 (vt, 2H, $H_{Ar\text{-}p}$), 3.76 (m, 2H, H_{oxa}), 3.68 (m, 2H, H_{oxa}), 3.63 (m, 2H, H_{oxa}), 0.71 (s, 18H, $CH_{3\ tBu}$); ^{13}C NMR (125 MHz, $(CD_3)_2CO$): δ $C_{Ar\text{-}ipso}$: not detected, 209.4 ($C{=}N_{oxa}$), 134.6 ($C_{Ar\text{-}m}$), 125.6 ($C_{Ar\text{-}o}$), 123.1 ($C_{Ar\text{-}p}$), 75.1 (C_{oxa}), 65.6 (C_{oxa}), 33.6 ($C_{quat\text{-}tBu}$), 25.7 ($CH_{3\ tBu}$); ^{11}B NMR (160 MHz, $(CD_3)_2CO$): δ -12.5 (s); IR: 2954, 2869, 2360, 1581, 1473, 1411, 1365, 1288,m 1211, 1164, 1033, 964, 848, 702; $[\alpha]_{20}$ = -50 (*c* = 0.11, CH_2Cl_2). MS (MALDI-TOF, 2,5-dihydroxybenzoic acid): *m/z* (%): 425 $[M+H]^+$, 419 $[M\text{-}Li+H]^+$.

9b (R^1 = Ph; R^2 = *t*-Bu). Yield: 72 %; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.62 (bs, $1H_{NHN}$), 7.35 (vt, 4H, $H_{Ar\text{-}m}$), 7.23 (dd, 4H, $H_{Ar\text{-}o}$), 7.16 (vt, 2H, $H_{Ar\text{-}p}$), 4.32 (vt, 2H, H_{oxa}), 4.21 (vt, 2H, H_{oxa}), 3.90 (vt, 2H, H_{oxa}), 0.98 (s, 18H, $CH_{3\ tBu}$); ^{13}C NMR (125 MHz, $CDCl_3$): δ $C_{Ar\text{-}ipso}$: not detected, 194.5 (very broad signal, $C{=}N_{oxa}$), 134.0 ($C_{Ar\text{-}m}$), 127.2 ($C_{Ar\text{-}o}$),

125.2 ($C_{Ar\text{-}p}$), 70.8 (C_{oxa}), 70.1 (C_{oxa}), 33.4 ($C_{quat\text{-}tBu}$), 25.8 ($CH_{3\ tBu}$); ^{11}B NMR (160 MHz, $CDCl_3$): δ -13.4 (s); IR: 2954, 2869, 2360, 1581, 1473, 1411, 1365, 1288,m 1211, 1164, 1033, 964, 848, 702. $[\alpha]_{20}$ = -89 (*c* = 0.11, CH_2Cl_2). Elemental analysis calcd (%) for $C_{26}H_{35}BN_2O_2$ (418.38): C 74.64, H 8.43, N 6.70; found: C 74.41, H 8.52, N 6.83. MS (FAB) *m/z* (rel. intensity): [M+H$^+$] 419 (100), [M - oxa + H$^+$] 292 (55.07). Rf = 0.46.

(7c)-Li (R^1 = Cy; R^2 = *i*-Pr). Yield: 40 %; ^{1}H NMR (500 MHz, $(CD_3)_2CO$): δ 3.73 (m, 2H, H_{oxa}), 3.67 (m, 2H, H_{oxa}), 3.60 (m, 2H, H_{oxa}), 1.65 (m, 2H, H_{iPr}), 1.61-1.48 (m, 6H_{Cy}), 1.28 (bd, 4H, H_{Cy}), 1.15-0.9 (m, 12H, H_{Cy}), 0.83 (s, 6H, $CH_{3\ iPr}$), 0.75 (s, 6H, $CH_{3\ iPr}$); ^{13}C NMR (125 MHz, $(CD_3)_2CO$): δ 209.4 (C=N_{oxa}), 71.1 (C_{oxa}), 64.9 (C_{oxa}), 53.5 (broad signal, C_{Cy}), 31.6 (CH_{iPr}), 29.0 (C_{Cy}), 20.5 (C_{Cy}), 29.4 (C_{Cy}), 19.6 ($CH_{3\ iPr}$); 16.7 ($CH_{3\ iPr}$); ^{11}B NMR (160 MHz, $(CD_3)_2CO$): δ -12.9 (s); IR: 2954, 2908, 2839, 1650, 1581, 1465, 1442, 1411, 1265, 1180, 1110, 1049, 1018, 964, 902, 871. $[\alpha]_{20}$ = -45 (*c* = 0.11, CH_2Cl_2). MS (MALDI-TOF, 2,5-dihydroxybenzoic acid): *m/z* (%): 402 [M-Li]$^+$.

9c (R^1 = Cy; R^2 = *i*-Pr). Yield: 70 %; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.09 (bs, 1H_{NHN}), 4.37 (m, 2H, H_{oxa}), 4.00 (m, 2H, H_{oxa}), 3.75 (m, 2H, H_{oxa}), 1.61-1.48 (m, 6H_{Cy}), 1.43 (bd, 4H, H_{Cy}), 1.15 (m, 2H, H_{iPr}), 0.98 (s, 6H, $CH_{3\ iPr}$), 0.92 (s, 6H, $CH_{3\ iPr}$) 1.21-0.28 (m, 12H, H_{Cy}); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.5 (C=N_{oxa}), 71.3 (C_{oxa}), 67.1 (C_{oxa}), 32.9 (CH_{iPr}), 31.5 (C_{Cy}), 31.3 (C_{Cy}), 29.1 (C_{Cy}), 27.9 (C_{Cy}), 19.1 ($CH_{3\ iPr}$); 18.9 ($CH_{3\ iPr}$); ^{11}B NMR (160 MHz, $CDCl_3$): δ -12.9 (s); IR: 2962, 2908, 2839, 1573, 1465, 1442, 1411, 1311, 1203, 1018, 956, 933, 864; $[\alpha]_{20}$ = -63 (*c* = 0.11, CH_2Cl_2). Elemental analysis calcd (%) for $C_{24}H_{43}BN_2O_2$ (402.43): C 71.63, H 10.77, N 6.96; found: C 71.53, H 10.75, N 6.90. MS (FAB) *m/z* (rel. intensity): [M+H$^+$] 403 (100), [M -oxa -Cy +H$^+$] 307 (17.63). Rf = 0.3.

(7d)-Li (R^1 = Cy; R^2 = *t*-Bu). Yield: 34 %; ^{1}H NMR (500 MHz, $(CD_3)_2CO$): δ 3.73 (m, 4H, H_{oxa}), 3.58 (m, 2H, H_{oxa}), 1.62-1.48 (m, 6H_{Cy}), 1.36 (bd, 4H, H_{Cy}), 1.12-0.5 (m, 12H, H_{Cy}), 0.78 (s, 18H, $CH_{3\ tBu}$); ^{13}C NMR (125 MHz, $(CD_3)_2CO$): δ 209.3 (C=N_{oxa}), 75.3 (C_{oxa}), 64.8 (C_{oxa}), 53.5 (broad signal, C_{Cy}), 29.0 (C_{Cy}), 33.1 ($C_{quat\text{-}tBu}$), 20.5 (C_{Cy}), 29.4 (C_{Cy}), 29.2 ($CH_{3\ tBu}$), 29.0 (C_{Cy}); ^{11}B NMR (160 MHz, $(CD_3)_2CO$): δ -13.2 (s); IR: 2908, 2839, 1634, 1573, 1473, 1442, 1396, 1365, 1203, 1126, 1103, 1049, 1010, 972, 894, 864, 786. $[\alpha]_{20}$ = -45° (*c* = 0.11, CH_2Cl_2). MS (MALDI-TOF, 2,5-dihydrobenzoic acid): *m/z* (%):436 [M]$^+$, 430 [M-Li]$^+$, 402 [M-Li]$^+$.

9d (R^1 = Cy; R^2 = *t*-Bu). Yield: 51 %; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.40 (bs, 1H_{NHN}), 4.30 (m, 2H, H_{oxa}), 4.09 (m, 2H, H_{oxa}), 3.82 (m, 2H, H_{oxa}), 1.62-1.33 (m, 8H_{Cy}), 1.19-0.6 (m, 14H, H_{Cy}), 0.91 (s, 18H, $CH_{3\ tBu}$); ^{13}C NMR (125 MHz, $CDCl_3$): δ $C_{Ar\text{-}ipso}$ and $C_{C=N}$ not detected, 70.5 (C_{oxa}), 69.3 (C_{oxa}), 33.0 ($C_{quat\text{-}tBu}$), 31.7 (C_{Cy}), 31.4 (C_{Cy}), 29.1 (C_{Cy}), 27.9 (C_{Cy}), 25.9 ($CH_{3\ tBu}$); ^{11}B NMR (160 MHz, $CDCl_3$): δ -13.5 (s); IR: 2954, 2908, 2839, 1581, 1473, 1442, 1404, 1203, 1149, 1018, 964, 856, 709; $[\alpha]_{20}$ = -35 (*c* = 0.11, CH_2Cl_2). Elemental analysis calcd (%) for $C_{26}H_{47}BN_2O_2$ (430.48): C 72.54, H 11.00, N 6.51; found: C 72.40, H 10.80, N 6.36. MS (FAB) *m/z* (rel. intensity): [M+H$^+$] 431 (100), [M - oxa - Cy + H$^+$] 222 (15.58). Rf = 0.39.

(7e)-Li (R^1 = Et; R^2 = *t*-Bu). Yield: 44 %; ^{1}H NMR (500 MHz, d_8-THF): δ 3.74 (bt, 2H, H_{oxa}), 3.66 (bt, 2H, H_{oxa}), 3.50 (m, 2H, H_{oxa}), 0.79 (s, 18H, $CH_{3\ tBu}$), 0.58 (t, 6H, $CH_{3\ Et}$),

0.36 (t, 2H, $CH_{2\ Et}$), 0.23 (bm, 2H, $CH_{2\ Et}$); ^{13}C NMR (125 MHz, d_8-THF): δ 171.5 ($C{=}N_{oxa}$), 76.7 (C_{oxa}), 66.0 (C_{oxa}), 33.9 ($C_{qat\ tBu}$), 26.5 ($CH_{3\ iPr}$), 17.4 ($CH_{2\ Et}$), 13.1 ($CH_{3\ Et}$); ^{11}B NMR (160 MHz, d_8-THF): δ -16.9 (s); IR: 2947, 2869, 2815, 1581, 1473, 1411, 1365, 1288, 1164, 1041, 1018, 964, 933, 848. $[\alpha]_{20}$ = -65 (*c* = 0.11, CH_2Cl_2). MS (MALDI-TOF, matrix name): *m/z* (%): 328 $[M+Li]^+$, 322 $[M]^+$.

9e (R^1 = Et; R^2 = *t*-Bu). Yield: 65 %; ^1H NMR (500 MHz, $CDCl_3$): δ 9.39 (bs, 1H, N-H-N), 4.29 (dd, 2H, $CH_{2\ oxa}$), 4.13 (dd, 2H, $CH_{2\ oxa}$), 3.82 (dd, 2H, CH_{oxa}), 0.89 (s, 18H, $CH_{3\ tBu}$), 0.66 (t, 6H, $CH_{3\ Et}$), 0.38 (bm, 4H, $CH_{2\ Et}$); ^{13}C NMR (125 MHz, $(CD_3)_2CO$): δ 198.3 ($C{=}N_{oxa}$), 70.7 (CH_{oxa}), 69.5 ($CH_{2\ oxa}$), 33.1 ($C_{qat\ tBu}$), 25.6 ($CH_{3\ iPr}$), 14.4 ($CH_{2\ Et}$), 11.9 ($CH_{3\ Et}$); ^{11}B NMR (160 MHz, $CDCl_3$): δ -15.7 (s). IR: 2947, 2869, 2815, 2360, 1589, 1473, 1411, 1365, 1319, 1288, 1211, 1164, 1018, 964, 933, 848. $[\alpha]_{20}$ = -80 (*c* = 0.11, CH_2Cl_2). Elemental analysis calcd (%) for $C_{18}H_{35}BN_2O_2$ (322.29): C 67.08, H 10.95, N 8.69; found: C 67.21, H 10.93, N 8.74. MS (FAB) *m/z* (rel. intensity): $[M+H^+]$ 323 (100), $[M - oxa + H^+]$ 196 (8.43).

(7f)-Li (R^1 = 3,5-bis(trifluoromethyl)phenyl; R^2 = *t*-Bu). Yield: 98 %; ^1H NMR (500 MHz, C_6D_6): δ 8.28 (bs, 4H, $H_{Ar\text{-}o}$), 7.80 (bs, 2H, $H_{Ar\text{-}p}$), 3.38-3.26 (m, 6H, H_{oxa}), 0.60 (s, 18H, $CH_{3\ tBu}$); ^{13}C NMR (125 MHz, C_6D_6): δ $C_{Ar\text{-}ipso}$ and $C{=}N_{oxa}$ not detected, 134.2 ($C_{Ar\text{-}o}$), 118.7 ($C_{Ar\text{-}p}$), 75.2 (C_{oxa}), 66.4 (C_{oxa}), 33.2 ($C_{quat\text{-}tBu}$), 25.4 ($CH_{3\ tBu}$); ^{11}B NMR (160 MHz, C_6D_6): δ -12.5 (s); ^{19}F NMR (376.5 MHz, C_6D_6): δ -63.2 (s); IR: 2962, 2877, 1635, 1596, 1473, 1657, 1272, 1118, 1049, 972, 894, 810, 678. $[\alpha]_{20}$ = -36 (*c* = 0.11, CH_2Cl_2). MS (MALDI-TOF, 2,5-dihydrobenzoic acid): *m/z* (%):706 $[M+3Li-2H]^+$, 696 $[M+Li]^+$, 402 $[M]^+$.

9f (R^1 = 3,5-bis(trifluoromethyl)phenyl; R^2 = *t*-Bu). Yield: 89 %; ^1H NMR (500 MHz, $CDCl_3$): δ 12.62 (bs, 1H, N<u>H</u>N), 7.67 (s, 6H, $H_{Aro\text{-}p}$), 4.37 (vt, 2H, H_{oxa}), 4.28 (vt, 2H, H_{oxa}), 3.98 (vt, 2H, H_{oxa}), 0.97 (s, 18H, $CH_{3\ tBu}$); ^{13}C NMR (125 MHz, $CDCl_3$): δ $C_{Ar\text{-}ipso}$ and $C{=}N_{oxa}$ not detected, 133.4 ($C_{Ar\text{-}o}$), 119.9 ($C_{Ar\text{-}p}$), 70.9 (C_{oxa}), 70.6 (C_{oxa}), 33.4 ($C_{quat\text{-}tBu}$), 25.5 ($CH_{3\ tBu}$); ^{11}B NMR (160 MHz, $CDCl_3$): δ -13.1 (s); ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -63.2 (s); IR: 2962, 2908, 1604, 1481, 1357, 1272, 1118, 964, 894, 840, 709, 678. $[\alpha]_{20}$ = -42 (*c* = 0.11, CH_2Cl_2). Elemental analysis calcd (%) for $C_{30}H_{31}BF_{12}N_2O_2$ (690.37): C 52.19, H 4.53, N 4.06; found: C 52.33, H 4.61, N 4.11. Rf = 0.31.

9g (R^1 = Et; R^2 = Bn). Yield: 78 %; ^1H NMR (500 MHz, $CDCl_3$): δ 10.31 (bs, 1H, N<u>H</u>N), 7.31 (m, 4 H, $C_{Ar\text{-}m}$), 7.25 (m_c, 2 H, $C_{Ar\text{-}p}$), 7.17 (m_c, 4 H, $C_{Ar\text{-}o}$), 4.34 (t, 2 H, H_{oxa}), 4.71 ('dq', 2 H, H_{oxa}), 4.11 (dd, 2 H, H_{oxa}), 2.88 (dd, 2 H, PhC<u>H</u>H), 2.70 (dd, 2 H, PhCH<u>H</u>), 0.65 (bt, 6 H, $CH_{3\text{-}Et}$), 0.44 (m, 4 H, $CH_{2\text{-}Et}$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 198.6 (C=N), 137.4 ($C_{Ar\text{-}i}$), 129.1 ($C_{Ar\text{-}o}$), 128.6 ($C_{Ar\text{-}m}$), 126.8 ($C_{Ar\text{-}p}$), 72.8 (CH_{2oxa}), 62.3 (CH_{oxa}), 42.2 (Ph*C*H_2), 14.5 (b, $CH_{2\text{-}Et}$), 11.9 ($CH_{3\text{-}Et}$); ^{11}B NMR (160.5 MHz, $CDCl_3$): δ -15.6. IR: 3140w, 3032w, 2932s, 2893s, 2854s, 2824m 1566s 1488m, 1450m, 1396m, 1350w, 1327w, 1288m, 1242w, 1203m, 1157m, 1026s. 1003s, 964m, 895s, 833m, 748s, 733s, 702vs. $C_{24}H_{31}BN_2O_2$ (390.33): calculated: C 73.85, H 8.01, N 7.18; found: C 73.74, H 7.85, N 7.03. MS (FAB) *m/z* (rel. intensity): $[M+H^+]$ 391 (100), $[M - oxa + H^+]$ 230 (17.72). Rf = 0.30.

9h (R^1 = 3,5-bis(trifluoromethyl)phenyl; R^2 = Bn): yield: 44 %; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.82 (bs, 1H, NHN). 7.68 (bs, 2H, $C_{Ar\text{-}pF}$), 7.60 (bs, 4H, $C_{Ar\text{-}oF}$), 7.29 (m, 4 H, $C_{Ar\text{-}mBn}$), 7.14 (m, 4H, $C_{Ar\text{-}oBn}$), 7.24 (m, 2H, $C_{Ar\text{-}pBn}$), 4.20 (m, 2H, $CH_{2\ oxa}$), 4.44 (m, 4H, $CH_{2\ oxa}$, OCH_{oxa}), 2.86 (m, 4 H, $PhCH_2$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 191.8 (b, C=N), 149.7 (b, $C_{Ar\text{-}i}$), 136.2 ($C_{Ar\text{-}Bn}$), 133.3 (b, $C_{Ar\text{-}o}$), 130.0 (q, $^2J_{CF}$ = 32.2 Hz, $C_{Ar\text{-}CF3}$), 129.0 ($C_{Ar\text{-}oBn}$), 128.7 ($C_{Ar\text{-}mBn}$), 127.2 ($C_{Ar\text{-}pBn}$), 124.0 (q, $^1J_{CF}$ = 272.5 Hz, CF_3), 119.9 (sept, $^3J_{CF}$ = 3.8 Hz, $C_{Ar\text{-}p}$), 73.6 ($CH_{2\ oxa}$), 62.3 (CH_{oxa}), 41.2 ($PhCH_2$); ^{11}B NMR (160.5 MHz, $CDCl_3$): δ -14.1. IR: 3070vw, 3032vw, 2962w, 2924w, 1597m, 1497w, 1473w, 1450w, 1420w, 1358m, 1273s, 1119vs, 964m, 887m, 841m, 748m, 702s, 679s. MS (FAB) *m/z* (rel. intensity): [M+H$^+$] 759 (75), [M - CH_2Ph + H$^+$] 667 (5.15), [M - oxa + H$^+$] 598 (17.33). $C_{36}H_{27}BF_{12}N_2O_2$ (758.20): calculated: C 57.01, H 3.59, N 3.69; found: C 57.04, H 3.73, N 3.65. Rf = 0.34.

Synthesis of (7a)$_2$-Cu. $CuSO_4{\cdot}H_2O$ (21 mg, 0.132 mmol) in 10 mL of H_2O was combined with a solution of (**7a**)-Li (105 mg, 0.265 mmol) in 20 mL of CH_2Cl_2 under vigorous stirring at room temperature. After 25 minutes, 5 mL of a saturated aqueous solution of $NaHCO_3$ was added. After stirring for additional 25 minutes, during which time the organic phase changed from blue to green, the organic phase was extracted, filtered through a plug of Celite and evaporated. The green crystalline solid was then redissolved in a minimum amount of CH_2Cl_2-Et_2O (1 mL) and layered with hexanes. After 2 days, blue-green plates started to grow. They were collected and subjected to single crystal analysis.

Elemental analysis calcd (%) for $C_{48}H_{60}B_2CuN_4O_4$ (842.19): C 68.46, H 7.18, N 6.65; found: C 68.78, H 7.23, N 6.60. $[\alpha]_{20}$ = -931 (*c* = 0.11, CH_2Cl_2). MS (MALDI-TOF, 2,5-dihydrobenzoic acid): *m/z* (%): 842 [M+H]$^+$.

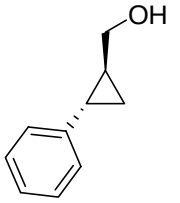
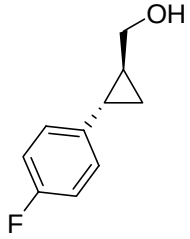
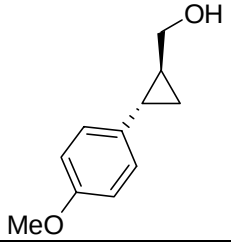
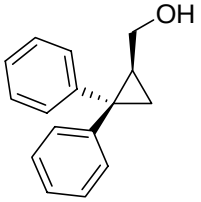
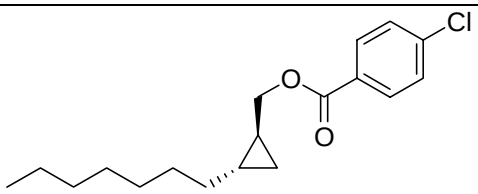
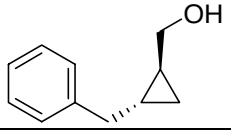
Synthesis of (6a)-CuCl$_2$. $CuCl_2$ (15.2 mg, 0.113 mmol) and one equivalent of **6a** (44.2 mg, 0.113 mmol) were dissolved in dry CH_2Cl_2 (1mL) under vigorous stirring at room temperature. After 2 hours, the solution was transferred in a long narrow tube and layered with hexanes. After 1 day, long thick green needles started to grow. They were collected and subjected to X-Ray crystallographic analysis. $[\alpha]_{20}$ = -253 (c = 0.11, CH_2Cl_2); MS (FAB): *m/z* (rel. intensity): [(**6a**)$_2$-Cu]$^+$ 843 (17.84), [M-Cl]$^+$ 488 (40.10), [M-2Cl] $^+$ 453 (91.89), [**6a**+H]$^+$ 391 (100).

General procedure for the cyclopropanation of styrene using ethyl diazoacetate or *tert*-butyl diazoacetate. Ligand (**7**)-Li (0.012 mmol) and $[Cu(OTf)]_2$-0.5(C_6H_6) (2.5mg, 0.005 mmol) were dissolved in 1 mL of 1,2-dichloroethane and the resulting solution was stirred at room temperature for 30 minutes before 125 μL (1.0 mmol) of styrene were then added. After further 30 minutes, a solution of the diazoester (1.2 mmol) in anhydrous 1,2-dichloroethane (1 mL) was added over the course of ~6h via a syringe pump. After the addition was complete, the reaction was stirred for an additional 12h. The reaction mixture was then concentrated in vacuo to afford the crude product. Flash chromatography using hexanes-ethylacetate (9:1 when ethyl diazoacetate was used (R_f of *cis*/*trans* mixture = 0.45); 14:1 when *tert*-butyldiazoacetate was used (R_f = 0.40) afforded a *cis:trans* mixture of the cyclopropane carboxylates. The *cis/trans* ratio as well as the enantiomeric excesses were determined by GC analysis (the cyclopropanes derived from

tert-butyl diazoacetate were converted to the ethyl esters by a standard transesterification protocol prior to analysis[6]).

General procedure for the cyclopropanation of styrene using 2,6-di-*tert*-butyl-4-methylphenyldiazoacetate. Ligand (**7f**)-Li (8.4 mg, 0.012 mmol) and $[Cu(OTf)]_2$-$0.5(C_6H_6)$ (2.5 mg, 0.005 mmol) were dissolved in 1 mL of 1,2-dichloroethane and the resulting solution was stirred at room temperature for 30 minutes before 125 μL (1.0 mmol) of styrene were then added. After further 30 minutes, 0.4 equiv. of 2,6-di-*tert*-butyl-4-methylphenyldiazoacetate was added to the reaction mixture. The remaining 0.8 equiv. was added in batches of 0.4 equivalents at 10 hours intervals. After the addition was complete, the reaction was stirred for an additional 18h at room temperature. The reaction mixture was then concentrated in vacuum to afford the crude product. Flash chromatography using hexanes-$CHCl_3$ (60:40) afforded a *cis:trans* mixture of the cyclopropane carboxylates. The relative *cis*/*trans* ratio was established by ^{1}H NMR spectroscopy, before the products were reduced into the corresponding alcohols[7] in order to determine the enantiomeric puritiy. Spectroscopic analyses of the cyclopropanation products are in good agreement with published data.[8,9].

HPLC analyses of the cyclopropanation products.

Cyclopropane	ee assay	conditions	$t_{R\ maj}$	$t_{R\ min}$
	HPLC Chiralcel OD-H	*i*-PrOH-Hept (90:10) 0.5mL/min ; 20°C	19.61	14.57
	HPLC Chiralcel OD-H	*i*-PrOH-Hept (90:10) 0.5mL/min ; 20°C	12.57	11.49
	HPLC Chiralcel OD-H	*i*-PrOH-Hept (90:10) 0.5mL/min ; 20°C	19.05	16.92
	HPLC Chiralcel OD-H	*i*-PrOH-Hept (90:10) 0.5mL/min ; 20°C	17.52	14.78
	HPLC Chiralcel OD-H	*i*-PrOH-Hept (99.95:0.05) 1.0mL/min ; 20°C	15.55	19.05
	HPLC Chiralcel OD-H	*i*-PrOH-Hept (90:10) 0.5mL/min ; 20°C	12.20	10.73

General procedure for the asymmetric desymmetrization of *meso*-1,2-diols. Ligand **9g** (3.8 mg, 0.0052 mmol) and $CuCl_2$ (2.5 mg, 0.005 mmol) were dissolved in 2.5 mL of dichloromethane and the resultant solution was stirred at room temperature for 2-3 hours before the appropriate *meso*-1,2-diol (0.5 mmol) was added at room temperature. After cooling the reaction mixture to 0°C, 86μl of *N*-diisoprylethylamine (0.5 mmol) and 60μL of Benzoylchloride (0.51 mmol) were successively added. The reaction was slowly warmed up to room temperature and stirred for further 12 hours. The reaction mixture was then concentrated in vacuum to afford the crude product. Flash chromatography using hexanes-EtOAc (3:1) afforded the desired pure monobenzoylated alcohols. The enantiomeric excess was assessed by HPLC and the absolute configuration assigned based on the retention times by comparison with the literature.[10,11]

Spectroscopic analysis of monobenzoylated products were in good agreement with the published data.[10,11]

Table 3, entries 1-3: **(*1R,2S*)-2-hydroxycyclopentyl benzoate**: Chiralcel OJ, Heptane:*i*-PrOH = 95:05, 40°C, 0.5 ml/min, retention time: 16.2 (minor), 18.9 (major).

Table 3, entries 3-6: **(*1R,2S*)-2-hydroxycyclohexyl benzoate**: HPLC Chiralcel OJ, Heptane:*i*-PrOH = 95:05, 40°C, 1.0 ml/min, retention time: 18.1 (minor), 21.6 (major).

Table 3, entries 6-9: **(*2R,3S*)-3-hydroxybutan-2-yl benzoate**: Chiralcel AD-H, Heptane:*i*-PrOH = 95:05, 40°C, 0.7 ml/min, retention time: 14.7 (minor), 17.2 (major).

References

[1] R. Köster, P. Binger, *Inorg. Synth.* **1974**, *15*, 149-153.
[2] R. Köster, M. A. Grassberger, *Liebigs, Ann. Chem.* **1968**, *719*, 169-186.
[3] a) D. J. Parks, W. E. Piers, G. P. A. Yap, *Organometallics* **1998**, *17*, 5492-5503. b) J. C. Thomas, J. C. Peters, *Inorg. Chem.* **2003**, *42*, 5055-5073.
[4] a) W. R. Leonard, J. L. Romine, A. I. Meyers, *J. Org. Chem.* **1991**, *56*, 1961-1963; K. Kamata, I. Agata, A. I. Meyers, *J. Org. Chem.* **1998**, *63*, 3113-3116.
[5] 2,2-diphenylmalonyl dichloride was prepared according to: H. Staudinger, O Göhring, M. Schöller, *Chem. Ber.* **1914**, *47*, 40-48.
[6] H. Fritschi, U. Leutenegger, A. Pfaltz, *Helv. Chim. Acta* **1988**, *71*, 1553-1565.
[7] A. V. Malkov, D. Pernazza, M. Bell, M. Bella, A. Massa, F. Teply, P. Meghani, P. Kocovsky, *J. Org. Chem.* **2003**, *68*, 4727-4742.
[8] M. M.-C. Lo, G. C. Fu, *J. Am. Chem. Soc.* **1998**, *120*, 10270-10271.
[9] M. P. A. Lyle, P. D. Wilson, *Org. Lett.* **2004**, *6*, 855-857.
[10] S. Mizuta, M. Sadamori, T. Fujimoto, I. Yamamoto, *Angew. Chem. Int. Ed.* **2003**, *42*, 3383-3385
[11] F. Iwasaki, T. Maki, W. Nakashima, Y. Matsumura, *J. Org. Chem.* **2000**, *65*, 996-1002.