Supplementary Material (ESI) for Chemical Communications

Catalytic Enantioselective Arylation of Aldehydes: Boronic Acids as a Convenient Source of Transferable Aryl Groups

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SUPPORTING INFORMATION

General Procedures. Melting Points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded at a Brucker DPX-400 spectrometer at 400 and 100 MHz respectively, with tetramethylsilane as internal standard. High resolution mass spectra were recorded on a Brucker BioApex 70e FT-ICR (Bruker Daltonics, Billerica, USA) instrument in ESI-mode. Column chromatography was performed using Merck Silica Gel (230-400 mesh) following the methods described by Still.[1] Thin layer chromatography (TLC) was performed using Merck Silica Gel GF_{254}, 0.25 mm thickness. For visualization, TLC plates were either placed under ultraviolet light, or stained with iodine vapor, or acidic vanillin. THF was dried over sodium benzophenone ketyl and distilled prior to use. Dichloromethane and acetonitrile were distilled from phosphorus pentoxide. Toluene was distilled over sodium. All other solvents were used as purchased unless otherwise noted.

Preparation of ligands (2). Ester hydrochloride **1** (5 mmol) were added in small portions to freshly prepared Grignard reagent (25 mmol) in THF at 0 ^{o}C under argon atmosphere. The reaction was stirred at room temperature for 12 h, before being quenched pouring into 2 M NaOH. The heterogeneous mixture was filtered through a pad of Celite® and washed with dichloromethane (3 x 50mL). The combined organic phases were dried with $MgSO_4$, filtered and the solvent removed under vacuum to yield amino alcohols which were used without further purification.

[1] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem*. 1978, **43**, 2923-2925

The amino alcohols were dissolved in acetonitrile and diiodoalkane and K_2CO_3 were added subsequently. The mixture was refluxed for 24 h and then filtered and the solvent evaporated. The residue was dissolved in dichloromethane, dried under $MgSO_4$ and filtered. The solvent removed under vacuum and the crude product was purified by flash chromatography in hexanes/ethyl acetate (90:10).

(*S*)-1,1,3-Triphenyl-2-(piperidin-1-yl)propan-1-ol 2a. Pale yellow oil, Yield: 82 %; $[\alpha]_D^{20}$ +39.0 (*c* 1.0 EtOAc); ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 7.57-7.50 (m, 5H), 7.33-7.23 (m, 10H), 3.89 (dd, 1H, *J*= 11.8, *J*= 1.8), 3.22 (dd, 1H, *J*= 11.8, *J*= 1.8), 2.76-2.73 (m, 1H), 2.39-2.35 (m, 2H), 2.06-2.01 (m, 2H), 1.34-1.18 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 145.60, 144.43, 140.24, 129.28, 128.91, 128.88, 128.28, 128.19, 128.00, 127.84, 127.51, 127.29, 127.13, 126.65, 126.14, 77.50, 74.10, 52.91, 34.56, 27.55, 25.18; HRMS-ESI *m/z* calcd for $C_{26}H_{29}NO + H^+$ 372.2321, found 372.2316.

(*S*)-3-Ethyl-1-phenyl-2-(piperidin-1-yl)pentan-3-ol 2b. Pale yellow oil, Yield: 92 %; $[\alpha]_D^{20}$ -26.0 (*c* 1.0 EtOAc); ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 7.28-7.16 (m, 5H), 4.32 (m, 1H), 2.98-2.96 (m, 1H), 2.96-2.86 (m, 1H), 2.75-2.74 (m, 1H), 2.50-2.49 (m, 4H), 1.78-1.76 (m, 1H), 1.48-1.41 (m, 6H), 1.31-1.25 (m, 3H), 0.96-0.91 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 141.05, 129.01, 128.17, 125.86, 74.12, 71.12, 53.45, 32.03, 29.07, 27.56, 27.04, 24.38, 7.85, 7.64; HRMS-ESI *m/z* calcd for $C_{18}H_{29}NO + H^+$ 276.2322, found 276.2319.

(*S*)-2-Methyl-4-phenyl-3-(piperidin-1-yl)butan-2-ol 2c. Needles, Yield: 97 %; mp 57-59 ^{o}C; $[\alpha]_D^{20}$ -49.0 (*c* 1.0 EtOAc); ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 7.31-7.18 (m, 5H), 2.94-2.85 (m, 2H), 2.76-2.72 (m, 1H), 2.54-2.52 (m, 4H), 1.56-1.53 (m, 2H), 1.48-1.45 (m, 2H), 1.32-1.31 (m, 2H), 1.22-1.18 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 140.56, 129.00, 128.30, 126.02, 75.49, 70.39, 53.04, 32.17, 29.03, 26.84, 25.25, 24.24; HRMS-ESI *m/z* calcd for $C_{16}H_{25}NO + H^+$ 248.2008, found 248.2005.

(*S*)-3-Phenyl-2-(piperidin-1-yl)propan-1-ol 2d. Needles, Yield: 93 %; mp 49 °C; $[\alpha]_D^{20}$ -15,0 (*c* 1.0 EtOAc); ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 7.26-7.10 (m, 5H), 3.42 (s, 1H), 3.33-3.31 (m, 2H), 2.94-2.90 (m, 2H), 2.72-2.68 (m, 2H), 2.43-2.41 (m, 2H), 2.30-2.26 (m, 2H), 1.61-1.45 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 139.21, 128.44, 127.94, 125.54, 67.22, 59.32, 48.91, 31.48, 26.22, 24.35; HRMS-ESI *m/z* calcd for $C_{14}H_{21}NO + H^+$ 220.1695, found 220.1691

(*S*)-3-Ethyl-1-phenyl-2-(pyrrolidin-1-yl)pentan-3-ol 2e. Pale yellow oil, Yield: 78 %; $[\alpha]_D^{20}$ -35.0 (*c* 1.01 EtOAc); ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 7.32-7.09 (m, 5H), 4.02-4.01 (m, 1H), 3.33-3.32 (m, 1H), 2.87-2.81 (m, 2H), 2.70-2.69 (m, 2H), 2.55-2.53 (m, 2H), 1.56-1.54 (m, 4H), 1.44-1.41 (m, 2H), 1.29-1.15 (m, 2H), 0.96-0.89 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 140.84, 129.04, 128.24, 125,86, 73.95, 65.34, 56.22, 31.39, 27.29, 24.02, 23.32, 7.78, 7.64; HRMS-ESI *m/z* calcd for $C_{17}H_{27}NO + H^+$ 262.2165, found 262.2161.

(*S*)-3-Ethyl-5-methyl-4-(piperidin-1-yl)hexan-3-ol 2f. Pale yellow oil, Yield: 92 %; $[\alpha]_D^{20}$ +25.0 (*c* 1.0 EtOAc); ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 2.92-2.91 (m, 2H), 2.67-2.65 (m, 2H), 2.21-2.19 (m, 1H), 2.02-1.99 (m, 2H), 1.88-1.69 (m, 2H), 1.57-1.43 (m, 6H), 1.43-1.31 (m, 1H), 1.06-0.84 (m, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 74.20, 73.15, 52.82, 29.25, 28.60, 28.27, 27.27, 24.72, 23.82, 22.32, 8.11, 7.80; HRMS-ESI *m/z* calcd for $C_{14}H_{29}NO + H^+$ 228.2321, found 229.2320.

(4*S*)-3-Ethyl-5-methyl-4-(piperidin-1-yl)heptan-3-ol 2g. Pale yellow oil, Yield: 88 %; $[\alpha]_D^{20}$ +21.0 (*c* 1.0 EtOAc); ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 2.92-2.91 (m, 2H), 2.63-2.61 (m, 2H), 2.34-2.32 (m, 1H), 1.79-1.77 (m, 4H), 1.54-1.41 (m, 5H), 1.23-1.21 (m, 4H), 0.97-0.84 (m, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 73.61, 71.82, 52.90, 34.41, 29.05, 28.38, 27.34, 26.79, 24.73, 17.73, 10.80, 8.14, 7.75; HRMS-ESI *m/z* calcd for C15H31NO + H^+ 242.2478, found 242.2477

(*S*)-3-Ethyl-6-methyl-4-(piperidin-1-yl)heptan-3-ol 2h. Pale yellow oil, Yield: 84 %; $[\alpha]_D^{20}$ +6.0 (*c* 2.3 EtOAc); ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 2.85-2.80 (m, 2H), 2.60-2.58 (m, 3H), 1.72-1.66 (m, 3H), 1.55-1.54 (m, 4H), 1.36-1.30 (m, 6H), 0.95-0.83 (m, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 74.01, 66.76, 35.96, 28.71, 27.47, 27.03, 26.54, 26.13, 24.73, 24.28, 21.21, 7.77, 7.46; HRMS-ESI *m/z* calcd for C15H31NO + H^+ 242.2478, found 242.2476

General Procedure for the asymmetric arylation of aldehydes. Diethylzinc (3.6 mmol, toluene solution) was dropwise added to a solution of boronic acid (1.2 mmol) in toluene (2 mL) under an argon atmosphere. After stirring for 12 h at 60 ^{o}C, the mixture is cooled to room temperature and a toluene solution of chiral amino alcohol (10 mol%) was introduced. The reaction is stirred for additional 15 min and the aldehyde (0.5 mmol) was subsequently added. After stirring overnight the reaction was quenched with water and the aqueous layer was extracted with dichloromethane. The combined organic layers were dried with $MgSO_4$, filtered and the solvents evaporated. Purification by flash chromatography eluting with a mixture of hexanes/ethyl acetate (90:10) afforded the pure diarylmethanols.

HPLC-Analyses

All measurements were performed at a 20 ^{o}C column temperature using a UV detector at 254 nm.

Phenyl(*p*-tolyl)methanol (**4a**):

Chiralcel OD, hexane/*i*-PrOH 90:10, 0.5 mL/min, (*R*): 19.1 min, (*S*): 21.1 min

Phenyl(*o*-tolyl)methanol (**4b**):

Chiralcel OB-H, hexane/*i*-PrOH 95/5, 1 mL/min, (*R*): 43.9 min, (*S*): 56.5 min

(4-Methoxyphenyl)(phenyl)methanol (**4c**):

Chiralcel AD-H, hexane/*i*-PrOH 90/10, 1 mL/min, (*R*): 24.5 min, (*S*): 26.7 min

(2-Methoxyphenyl)(phenyl)methanol (**4d**):

Chiralcel OD, hexane/*i*-PrOH 98:2, 0.5 mL/min, (*R*): 76.3 min, (*S*): 85.2 min

(4-Chlorophenyl)(phenyl)methanol (**4e**):

Chiralpak AD-H, hexane/*i*-PrOH 90:10, 1 mL/min, (*R*): 13.7 min, (*S*): 15.2 min

(2-Chlorophenyl)(phenyl)methanol (**4f**):

Chiralcel OD, hexane/*i*-PrOH 90:10, 0.5 mL/min, (*R*): 15.9 min, (*S*): 19.8 min

(2-Bromophenyl)(phenyl)methanol (**4g**):

Chiralcel OD, hexane/*i*-PrOH 90:10, 0.8 mL/min, (*R*): 11.6 min, (*S*): 14.9 min