Supplementary Material (ESI) for Chemical Communications

Supporting Information for:

Chiral diamino-bis(*tert*-thiophene): effective ligand for asymmetric Pd and Zn-catalyzed transformations

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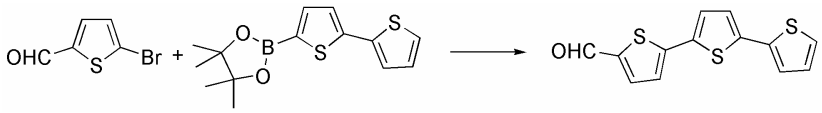
General Methods. ^{1}H-NMR spectra were recorded on Varian 200 (200 MHz), Varian 300 (300 MHz) spectrometers. Chemical shifts are reported in ppm from TMS with the solvent resonance as the internal standard (deuterochloroform: δ 7.27 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = duplet, pd = pseudo duplet, t = triplet, q = quartet, br = broad, br s = broad singlet, m = multiplet), coupling constants (Hz). ^{13}C-NMR spectra were recorded on a Varian 200 (50 MHz), Varian 300 (75 MHz) spectrometers with complete proton decoupling. Chemical shifts are reported in ppm from TMS with the solvent as the internal standard (deuterochloroform: δ 77.0 ppm). GC-MS spectra were taken by EI ionization at 70 eV on a Hewlett-Packard 5971 with GC injection. They are reported as: *m/z* (rel. intense). LC-electrospray ionization mass spectra were obtained with Agilent Technologies MSD1100 single-quadrupole mass spectrometer. Chromatographic purification was done with 240-400 mesh silica gel. IR analysis were performed with a FT-IR NICOLET 205 spectrophotometer and the spectra are expressed by wavenumber (cm^{-1}). Analytical high performance liquid chromatograph (HPLC) was performed on a liquid chromatograph equipped with a variable wave-length UV detector (deuterium lamp 190-600 nm), using a Daicel Chiralcel^{TM} AD and OD columns (0.46 cm I.D. x 25 cm). HPLC grade isopropanol (IPA) and *n*-hexane (*n*-hex) were used as the eluting solvents. 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). Optical rotations were determined in a 1 ml cell with a path length of 10 mm (Na_D line). Melting points were determined with Büchi 150 melting point unit and are not corrected.

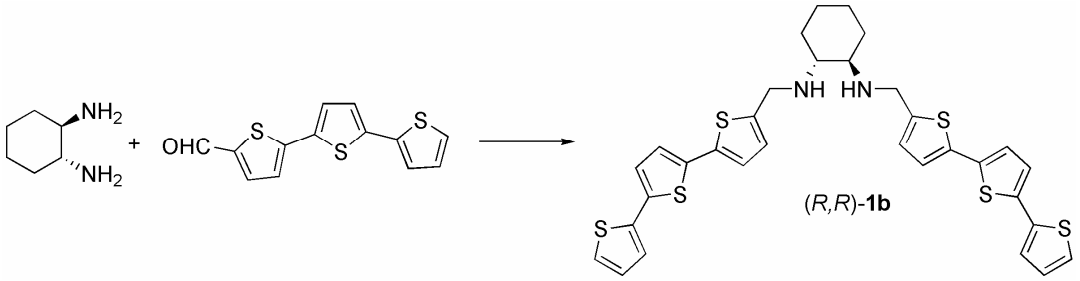
Materials. THF was supplied by Fluka in Sureseal® bottles and used as received. Enantiomerically pure (1*R*,2*R*)-diaminocyclohexane was obtained by optical resolution of the commercially available (±)-*trans*-diaminocyclohexane by standard literature procedure.[1] $[Pd_2(dba)_3]\cdot CHCl_3$ and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ was obtained from Aldrich and used as received. BSA was freshly distilled before using in asymmetric allylic substitution. The racemic allylic carbonates **3** was prepared following standard literature procedure. Ketones **6a-c** were freshly distilled before use. **6d** and **6e** were used as received.

[2,2';5',2'']Terthiophene-5-carbaldehyde



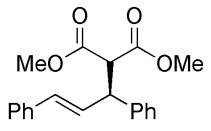
To a solution of 35 mg (0.17 mmol) of $[PdCl_2(PPh_3)_2]$ in 18 mL of anhydrous DME, 238 µL (2.6 mmol) of commercially available 5-bromo-thiophene-2-carbaldehyde were added and the reaction mixture was stirred for 5 min. Then 7 mL of ethanol, 760 mg (3.4 mmol) of 5-(4,4,5,5-tetramethyl-1,3,2-dioxoborolan-2-yl)-2,2'-bithiophene and 6 mL of Na_2CO_3 (2M) were added and the solution was refluxed for 48 h. Then 15 mL of water were added, DME and ethanol removed and the product was extracted with CH_2Cl_2 (3 x 10 mL). Evaporation of the solvent afforded crude **7**, which was purified by chromatography on silica using *c*-hex/Et_2O 95/5. The product was isolated as yellow-orange powder 349 mg (55% yield).[2]

(1*R*,2*R*)-*N*,*N*'-Bis-[2,2';5',2'']terthiophen-5-ylmethyl-cyclohexane-1,2-diamine (1b)

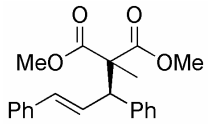


In a 50 mL two-necked flask (2,2';5',2")-*ter*thiophene-5-carbaldehyde **2** (1.49 mmol, 411 mg) and (1*R*,2*R*)-diaminocyclohexane (0.74 mmol, 85 mg) were dissolved in 15 mL of dry CH_2Cl_2 under N_2 atmosphere. $MgSO_4$ (6 mmol, 534 mg) was added and the mixture was stirred rt for 48 h. The crude was filtered, the solvent evaporated under reduced pressure giving 396 mg (85% yield) of intermediate imine as a yellow solid (purity > 95% by ^1H NMR). To a solution of imine (390 mg, 0.62 mmol) in dry THF (6 mL), under nitrogen atmosphere, were added at once 615 µL of anhydrous solution of HCl in Et_2O (2 M, 1.23 mmol). The flask was cooled to 0°C and $NaBH_3CN$ (117 mg, 1.86 mmol) was added. The ice bath was then removed and the reaction mixture allowed stirring overnight at room temperature. NaOH (0.1 M, 10 mL) was added, the volatiles were removed under reduced pressure and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). Dried with Na_2SO_4 and concentrated under vacuum. The crude was purified by triturating the residue in *c*-hex. Yellow solid (338 mg, 72% yield, two steps).[2] Further purification can be carried out by flash chromatography (CH_2Cl_2: MeOH 99:1).

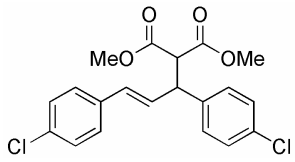
Pd-catalyzed AAA, (method A): A 25 mL two necked flask was charged, under a nitrogen atmosphere, with $[Pd_2(dba_3)\cdot CHCl_3]$ (2.6 mg, $2.5\cdot10^{-3}$ mmol), diamine **1b** (3.2 mg, $5\cdot10^{-3}$ mmol) and 1.5 ml of anhydrous THF. The mixture was stirred at rt for 5 min (the colour of the solution gradually turned from purple to brown) then **3** (0.05 mmol), **4** (29 µL, 0.25 mmol), BSA (12 µL, 0.05 mmol) and a catalytic amount of KOAc were sequentially added. The reaction mixture was stirred overnight at rt. Judged complete by TLC, the reaction was quenched with 3 ml of H_2O. The two phases were separated and the aqueous layer extracted with CH_2Cl_2 (3 x 5 mL). Finally, the organic layers were collected, dried with Na_2SO_4 and concentrated under vacuum.



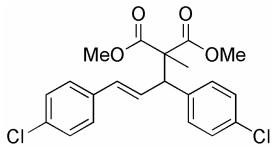
(*S*)-**5aa:** Pale yellow oil. Yield: 99% (*c*-hex/Et_2O 9/1). Ee: 99% (HPLC, Chiralcel AD: IPA/*n*-hex 10/90, 1.0 mL/min flow, 214 nm, Rt_R: 9.3 min.; Rt_S: 12.6 min.). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7-21-7.7.34 (m, 10H), 6.48 (d, *J* = 15.9 Hz, 1H), 6.33 (dd, *J* = 8.7, 15.9 Hz, 1H), 4.29 (dd, *J* = 8.7, 11.1 Hz, 1H), 3.95 (d, *J* = 11.1 Hz, 1H), 3.72 (s, 3H), 3.53 (s, 3H). $[\alpha]_D$ = -9.0 (*c* 0.7, $CHCl_3$), lit. (*R*)-**5aa** $[\alpha]_D$ = +19.2 (*c* 1.3, $CHCl_3$).[3]



(*R*)-**5ab:** Pale yellow oil. Yield: 95% (*c*-hex/AcOEt 9/1). Ee: 85% (HPLC, Chiralcel AD: IPA/*n*-hex 0.6/99,4 0.5 mL/min flow, 214 nm, Rt_S: 47.5 min.; Rt_R: 49.1 min.). LC-ESI: 360 (M+Na); ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7-29-7.39 (m, 10H), 6.72 (dd, *J* = 9.0, 15.6 Hz, 1H), 6.50 (d, *J* = 15.6 Hz, 1H), 4.34 (d, *J* = 9.0 Hz, 1H), 3.74 (s, 3H), 3.66 (s, 3H), 1.52 (s, 3H). $[\alpha]_D$= +11.9 (*c* = 0.7, CH_2Cl_2), lit (*R*)-**5ab** $[\alpha]_D$= +60.1 (*c* = 1.2, CH_2Cl_2).[4]



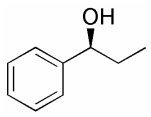
(-)-**5ba:** Pale yellow oil. Yield: 80% (*c*-hex/Et_2O 9/1). Ee: 94% (HPLC, Chiralcel AD: IPA/*n*-hex 15/85, 1.0 mL/min flow, 214 nm, Rt_{minor}: 12.2 min.; Rt_{major}: 17.8 min.). ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7-27-7.35 (m, 8H), 6.22-6.45 (m, 2H), 4.26 (dd, *J* = 7.6, 10.6 Hz, 1H), 3.92 (d, *J* = 10.6 Hz, 1H), 3.74 (s, 3H), 3.58 (s, 3H). $[\alpha]_D$= -2.9 (*c* = 1.5, $CHCl_3$), lit (-)-**5ba** $[\alpha]_D$= -2.8 (*c* = 1.12, $CHCl_3$), 93% ee.[5]



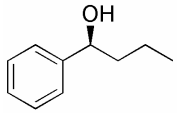
(+)-**5bb:** Pale yellow oil. Yield: 99% (*c*-hex/AcOEt 9/1). Ee: 97% (HPLC, Chiralcel AD: IPA/*n*-hex 10/90, 0.5 mL/min flow, 214 nm, Rt_{major}: 16.6 min.; Rt_{minor}: 18.0 min.). LC-ESI: 429 (M+Na); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7-28-7.32 (m, 8H), 6.64 (dd, *J* = 9.0, 15.9 Hz, 1H), 6.40 (d, *J* = 16.9 Hz, 1H), 4.27 (d, *J* = 9.0 Hz, 1H), 3.73 (s, 3H), 3.67 (s, 3H), 1.49 (s, 3H). $[\alpha]_D$= +38.1 (*c* = 1.1, CH_2Cl_2).

Pd-catalyzed AAA, (method B): A 25 mL two necked flask was charged, under a nitrogen atmosphere, with $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (2.2 mg, $6\cdot10^{-3}$ mmol), diamine **1b** (7,6 mg, 0.012 mmol) and 1.5 ml of anhydrous THF. The mixture was stirred at rt for 15 min then $AgSbF_6$ (4 mg, 0.012 mmol). After a few minutes stirring (with formation of AgCl), **3c** (19 μL, 0.12 mmol) was added then the reaction flask was cooled at 0°C and finally **4a** (69 μL, 0.6 mmol) and Cs_2CO_3 (78 mg, 0.24 mmol) were sequentially added. The reaction mixture was stirred for 4 days at 0°C, then quenched with 3 ml of H_2O. The two phases were separated and the aqueous one extracted with CH_2Cl_2 (3 x 5 mL). Finally, the organic layers were collected, dried with Na_2SO_4 and concentrated under vacuum. The desired product (*S*)-**5ca** was isolated as a yellow oil after flash chromatography (*c*-hex/AcOEt 95/5); yield: 14 mg (55%). Ee: 91%. GC with a chiral column (flow rate 15 mL/min; Rt_S: 47.1 min.; Rt_R: 49.0 min. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 5.53 (dd, *J* = 4.6, 10.6 Hz, 1H), 5.35 (dd, *J* = 6.4, 10.6 Hz, 1H), 2.73 (s, 3H), 2.70 (s, 3H), 2.27 (d, *J* = 6.0 Hz, 1H), 2.86-2.95 (m, 1H), 1.64 (dd, *J* = 1.0, 4.2 Hz, 3), 1.06 (d, *J* = 4.6 Hz, 3H). GC-MS (relative intensity): 59 (19), 69 (90), 81 (22), 100 (12), 109 (23), 125 (100), 141 (36), 200 (5, M). $[\alpha]_D$ = -15.0 (*c* 0.34, $CHCl_3$), lit. $[\alpha]_D$ = -27.9 (*c* 1.1, $CHCl_3$).[6]

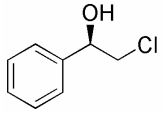
Synthesis of 1c-[Pd(η^3Ph$_2$C$_3$H$_3$)][PF$_6$]: To a solution of **1b** (28 mg, 0.057 mmol) in a degassed THF:CH_2Cl_2 mixture (6:1, 5.7 mL), [Pd-(η^3-$Ph_2C_3H_3$)Cl]$_2$ (15 mg, 0.022 mmol) was added and the resulting yellow slurry was stirred for 4h at rt. After that, 7.2 mg of NH_4PF_6 (0.044 mmol) were added and the mixture stirred overnight. The insoluble NH_4Cl was removed by filtration and the filtrate was concentrated under vacuum to give yellow solid that was washed with anhydrous Et_2O. Yield: 87% (41 mg). ^{1}H NMR (CD_2Cl_2, 300 MHz) δ: (fluxional, mixture of two η^3-Pd adducts, diagnostic signals) 7.69-7.82 (m, 2H), 7.26-7.45 (m, 10H), 6.90-7.11 (m, 2H), 6.65-6.80 (m, 1H), 5.43 (d, *J* = 9.2 Hz, 1H), 4.62 (d, *J* = 9.2 Hz, 1H), 3.97-4.15 (m, 1H), 3.76 (br, 1H), 3.29 (br, 1H), 2.13 (br, 4H), 1.92 (br, 2H), 1.56 (br, 1H), 1.25-1.36 (m, 1H), 1.05-1.27 (m, 1H), 0.88 (br, 2H).



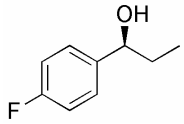
(*S*)-1-Phenyl-propanol (**7a**): Pale yellow oil. Conv. > 98%. Yield 73% (*c*-hex/Et_2O 85/15). Ee 83% (HPLC: Chiralcel OD: IPA/*n*-hex 1/99→5/95 in 10 min, 0.5 mL/min flow, 214 nm, Rt$_R$: 19.7 min.; Rt$_S$: 20.4 min.). ^{1}H NMR ($CDCl_3$, 200 MHz) δ:7.29-7.38 (m, 5H), 4.62 (t, *J* = 4.4 Hz, 1H), 1.77-1.87 (m, 2H), 0.96 (t, *J* = 4.4 Hz, 3H). GC-MS (relative intensity): 51 (10), 77 (48), 79 (85), 107 (100), 136 (12, M). $[\alpha]_D$ = -27.2 (*c* 0.5, $CHCl_3$), lit. (*S*)-**7b** $[\alpha]_D$ = -45.6 (*c* 1.3, $CHCl_3$).[7]



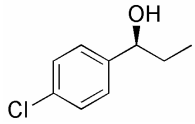
(*S*)-1-Phenyl-butanol (**7b**): Pale yellow oil. Conv. > 98%. Yield 75% (*c*-hex/Et_2O 95:5→8/2). Ee 82% (HPLC: Chiralcel OD: IPA/*n*-hex 2/98 0.5 mL/min flow, 214 nm, Rt$_R$: 25.7 min.; Rt$_S$: 27.2 min.). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.22-2.37 (m, 5H), 4.69 (dd, *J* = 2.7, 7.5 Hz, 1H), 1.67-1.82 (m, 2H), 1-25-1-55 (m, 2H), 0.94 (t, *J* = 6.0 Hz, 3H). GC-MS (relative intensity): 51 (10), 79 (100), 91 (7), 117 (18), 150 (21, M). $[\alpha]_D$ = -25.2 (*c* 1.3, $CHCl_3$), lit. (*R*)-**7c** $[\alpha]_D$ = +55.0 (*c* 5.0, $CHCl_3$).[8]



(*R*)-2-Chloro-1-phenylethan-1-ol (**7c**): Pale yellow oil. Conv. > 80%. Yield 55% (*c*-hex/Et_2O 9/1). Ee 72% (HPLC: Chiralcel OD: IPA/*n*-hex 7/93, 0.5 mL/min flow, 214 nm, Rt$_s$: 17.7 min.; Rt$_R$: 20.7 min.). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.31-7.48 (m, 5H), 4.82 (dd, *J* = 3.6, 9.0 Hz, 1H), 3.76 (dd, *J* = 3.6, 11.7 Hz, 1H), 3.65 (dd, *J* = 9.0, 11.7 Hz, 1H), 2.64 (br, 1H). GC-MS (relative intensity): 51 (22), 77 (70), 79 (89), 91 (10), 107 (100), 156 (10, M). $[\alpha]_D$ = -27.5 (*c* 1.5, $CHCl_3$), lit. (*R*)-**7c** $[\alpha]_D$ = -56.2 (*c* 1.3, $CHCl_3$).[5]

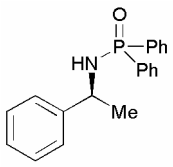


(*S*)-1-(4'-Fluorophenyl)ethan-1-ol (**7d**): Pale yellow oil. Conv. > 98%. Yield 60% (*c*-hex/Et_2O 9/1). Ee 80% (GC analysis (method: 100°C isoterm, Rt$_R$: 17.5 min.; Rt$_S$: 22.6 min). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.30-7.32 (m, 2H), 7.01-7.07 (m, 2H), 4.60 (t, *J* = 6.6 Hz, 1H), 1.74-1.83 (m, 2H), 0.91 (t, *J* = 7.5 Hz, 3H). GC-MS (relative intensity): 51 (10), 77 (35), 95 (25), 97 (65), 125 (100), 154 (19, M). $[\alpha]_D$ = -35.9 (*c* 1.0, $CHCl_3$), lit. (*R*)-**7d** $[\alpha]_D$ = 51.2 (*c* 2.5, $CHCl_3$).[9]



(*S*)-1-(4'-Chlorophenyl)ethan-1-ol (**7e**): pale yellow oil. Conv. > 98%. Yield 52% (*c*-hex/Et_2O 9/1). Ee 80% (GC analysis (method: 130°C isoterm, Rt$_R$: 11.9 min.; Rt$_S$: 14.0 min). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.30-7.34 (m, 4H), 4.60 (t, *J* = 6.6 Hz, 1H), 1.73-1.81 (m, 2H), 0.91 (t, *J* = 7.5 Hz, 3H). GC-MS (relative intensity): 51 (15), 75 (9), 77 (81), 113 (21), 141 (100), 170 (15, M). $[\alpha]_D$ = -20.1 (*c* 1.5, C_6H_6), lit. (*S*)-**7e** $[\alpha]_D$ = -23.5 (*c* 0.8, C_6H_6).[10]

Typical procedure for stereoselective hydrosilylation of 8: a flamed 25 mL two necked flask was charged with diamine **1b** (6.2 mg, 0.01 mmol), 800 μL of anhydrous THF and 9.1 μL of Et_2Zn (1.1 M, toluene). The mixture was stirred at rt for 1h, and after cooling to 0°C, **8**[11] (0.2 mmol, 62 mg), PMHS (65 μL, 0.6 mmol) and distilled MeOH (200 μL) were sequentially added. The reaction was stirred at 0 °C for 3h when it was judged complete by GC-MS. After that, the mixture was quenched (3 ml of NaOH, 10%, wt.), and extracted with AcOEt (3 x 5 mL). Finally, the collected organic phases were dried over Na_2SO_4 and concentrated under vacuum. The desired products **9** were purified by flash chromatography.



(*S*)-(-)-*N*-(1-Phenylethyl)-diphenylphosphinamide (**9**): White solid. Conv. > 98%. Yield 70% (*c*-hex/AcOEt 7/3). Ee 97% (HPLC: Chiralcel OD: IPA/*n*-hex 7/93 0.5 mL/min flow, 214 nm, Rt_S: 18.1 min.; Rt_R: 24.6 min.). ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.76-7.93 (m, 5H), 7.29-7.44 (m, 10H), 4.37 (q, *J* = 6.6 Hz, 1H), 3.16 (br, 1H); 1.55 (d, *J* = 6.6 Hz, 3H). GC-MS (relative intensity): 51 (10), 77 (38), 120 (100), 201 (77), 306 (48), 320 (5, M). $[\alpha]_D$ = -32.0 (*c* 0.8, MeOH, ee = 80%), lit. (*S*)-**9a** $[\alpha]_D$ = -35.5 (*c* 0.8, MeOH).[12]

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