Highly Enantioselective Nitroaldol Reaction Catalyzed by New Chiral Copper Complexes.*

Marco Bandini,* Fabio Piccinelli, Simona Tommasi and Achille Umani-Ronchi,* Catarina Ventrici.

Dipartimento di Chimica Organica "G. Ciamician", Università di Bologna
Via Selmi 2, 40126 Bologna (Italy)
**E-mail: marco.bandini@unibo.it, achille.umanironchi@unibo.it*

Supporting Information

General Methods

^{1}H-NMR spectra were recorded on Varian 200 (200 MHz) or Varian 300 (300 MHz) spectrometers. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuterochloroform: δ 7.27 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = dublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz). Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal standard (deuterochloroform: δ 77.0 ppm). Chromatographic purification was carried out using silica gel (240-400 mesh). Analytical high performance liquid chromatography (HPLC) was performed on a HP 1090 liquid chromatograph equipped with a variable wavelength UV detector (deuterium lamp 190-600 nm) and using a Daicel Chiralcel^{TM} OD, AD and OJ columns (0.46 cm I.D. x 25 cm) (Daicel Inc.). HPLC grade isopropanol and *n*-hexane were used as the eluting solvents. Optical rotations were determined in a 0.6 ml cell with a path length of 10 mm (Na_D line, 23°C. 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}).

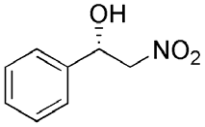
All the reactions were carried out under a nitrogen atmosphere in flame-dried glassware using standard inert techniques for introducing reagents and solvents.

The diffraction experiment for the (+/-)-DAT-$Cu(OAc)_2$ was carried out at room temperature on a Bruker APEX II CCD based diffractometer using graphite monochromated Mo-Kα radiation (λ = 0.71073 Å). Intensity data were measured over full diffraction spheres using 0.3° wide ω scans,

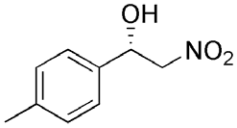
crystal-to-detector distance 5.0 cm. The software SMART[1a] was used for collecting frames of data, indexing reflections and determination of lattice parameters. The collected frames were then processed for integration by software SAINT[1a] and an empirical absorption correction was applied with SADABS.[1b] The structures were solved by direct methods (SIR 97)[1c] and subsequent Fourier syntheses, and refined by full-matrix least-squares calculations on F^2 (SHELXTL)[2] attributing anisotropic thermal parameters to the non-hydrogen atoms. The aromatic hydrogen atoms were placed in calculated positions and refined with idealized geometry C(sp^2)-H = 0.93 Å) whereas the other H atoms were located in the Fourier map and refined isotropically.

Materials

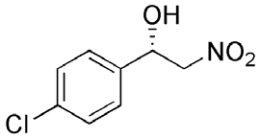
Anhydrous solvents were supplied by Fluka in Sureseal® bottles and used as received. The liquid aldehydes were freshly distilled before using.



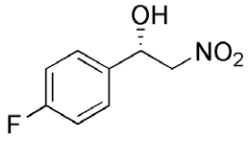
(*S*)-1-Phenyl-2-nitroethanol (2a): Yellow oil; flash chromatography *c*-CH_2Cl_2:Et_2O 9:1→8:2; yield = 98%, (conv. 99%); HPLC analysis: Chiralcel OD, isocratic (*n*-hex:IPA 90:10), flow 1.0 mL/min; t_S = 15.1 min; t_R = 18.2 min, *ee* = 96%; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.90 (1H, br); 4.50-4.67 (2H, m); 5.48 (1H, d, J = 9.4 Hz); 7.38-7.43 (5H, m). $[\alpha]^D$: +35.8 (*c* 1.31, CH_2Cl_2, *ee* = 86%), [Lit. (*R*)-**2a** *ee* = 94%, $[\alpha]^D$: -41.6 (*c* 1.03, CH_2Cl_2).[3]



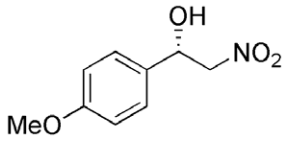
(*S*)-1-(4-Methylphenyl)-2-nitroethanol (2b): Yellow oil; flash chromatography *c*-Hex:AcOEt 9:1→8:2; yield = 75%, (conv. 80%); HPLC analysis: Chiralcel OD, isocratic (*n*-hex:IPA 90:10), flow 0.5 mL/min; t_S = 32.3 min; t_R = 41.0 min, *ee* = 90%; ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 2.39 (3H, s); 2.79 (1H, br); 4.75-4.69 (2H, m); 5.45 (1H, d, J = 9.0 Hz); 7.21-7.35 (4H, m). $[\alpha]^D$: +18.5 (*c* 0.8, EtOH, *ee* = 86%), [Lit. (*R*)-**2b** *ee* = 62%, $[\alpha]^D$: -13.5 (*c* 0.92, EtOH).[4]



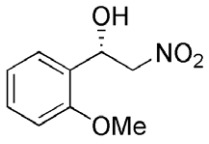
(*S*)-1-(4-Chlorophenyl)-2-nitroethanol (2c): Yellow oil; flash chromatography *c*-hex:AcOEt 9:1; yield = 68%, (conv. 79%); HPLC analysis: Chiralcel OD, isocratic (*n*-hex:IPA 80:20), flow 0.5 mL/min; t_S = 17.5 min; t_R = 20.0 min, *ee* = 92%; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.85 (1H, br); 4.50-4.60 (2H, m); 5.47 (1H, d, J = 9.0 Hz); 7.32-7.41 (4H, m); $[\alpha]^D$: +17.3 (*c* 0.55, CH_2Cl_2, *ee* = 88%), [Lit. (*R*)-**2c** *ee* = 88%, $[\alpha]^D$: -40.4 (*c* 0.27, CH_2Cl_2).[5]



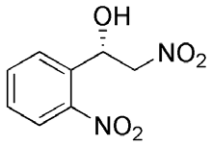
(*S*)-1-(4-Fluorophenyl)-2-nitroethanol (2d): Yellow oil; flash chromatography *c*-Hex:AcOEt 9:1→8:2; yield = 71%, (conv. 80%); HPLC analysis: Chiralcel OD, isocratic (*n*-hex:IPA 90:10), flow 1.0 mL/min; t_S = 13.6 min; t_R = 16.2 min, *ee* = 94%; ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 2.98 (1H, br); 4.47-4.66 (2H, m); 5.47 (1H, dd, J = 3.4, 8.8 Hz); 7.10 (2H, t, J = 8.6 Hz); 7.37-7.44 (2H, m); $[\alpha]^D$: +53.3 (*c* 0.9, CH_2Cl_2, *ee* = 94%), [Lit. (*R*)-**2d** *ee* = 92%, $[\alpha]^D$: -44.8 (*c* 1.05, CH_2Cl_2).[3]



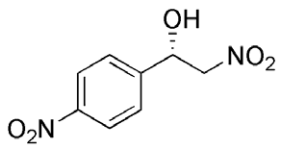
(*S*)-1-(4-Methoxyphenyl)-2-nitroethanol (2e): Yellow oil; flash chromatography *c*-hex:AcOEt 7:3; (conv. 95%); HPLC analysis: Chiralcel OD, isocratic (*n*-hex:IPA 85:15), flow 0.7 mL/min; t_S = 22.0 min; t_R = 28.5 min, *ee* = 94%; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.83 (3H, s); 4.47-4.69 (2H, m); 5.45 (1H, d J, = 9.9 Hz); 7.00 (2H, d, J = 8.4 Hz), 7.85 (2H, d, J = 8.4 Hz).



(*S*)-1-(2-Methoxyphenyl)-2-nitroethanol (2f): Yellow oil; flash chromatography *c*-hex:AcOEt 9:1; yield = 88%, (conv. 95%); HPLC analysis: Chiralcel OD, isocratic (*n*-hex:IPA 90:10), flow 1.0 mL/min; t_S = 13.0 min; t_R = 15.1 min, *ee* = 94%; ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 3.91 (3H, s); 4.61-4.71 (2H, m), 5.67 (1H, d, J = 6.6 Hz); 6.94 (1H, d, J = 8.4 Hz); 7.00-7.08 (1H, m); 7.32-7.40 (1H, m); 7.47 (1H, d, J = 8.4 Hz). $[\alpha]^D$: +40.4 (*c* 3.3, CH_2Cl_2), [Lit. (*R*)-**2f** *ee* = 93%, $[\alpha]^D$: -44.5 (c 1.00, CH_2Cl_2].[3]

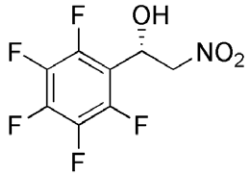


(*S*)-1-(2-Nitrophenyl)-2-nitroethanol (2g): Yellow oil; flash chromatography *c*-hex:AcOEt 9:1→7:3; yield = 92%, (conv. 95%); HPLC analysis: Chiralcel OD, isocratic (*n*-hex:IPA 90:10), flow 0.7 mL/min; t_S = 27.5 min; t_R = 31.0 min, *ee* = 94%; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 4.59 (1H, br); 4.90 (1H, d, J 10.5 Hz); 6.09 (1H, br); 7.56 (1H, t, J = 7.8 Hz); 7.76 (1H, t, J = 7.2 Hz); 7.98 (1H, d, J = 7.2 Hz); 8.09 (1H, d, J = 7.8 Hz); $[\alpha]^D$: -232.0 (*c* 1.8, CH_2Cl_2), [Lit. (*R*)-**2g** *ee* = 89%, $[\alpha]^D$: +227.1 (c 1.00, CH_2Cl_2].[3]

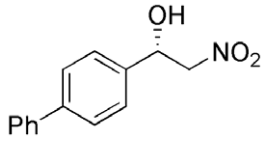


(*S*)-1-(4-Nitrophenyl)-2-nitroethanol (2h): Yellow oil; flash chromatography *c*-hex:AcOEt 8:2; yield = 81%, (conv. 99%); HPLC analysis: Chiralcel OD, isocratic (*n*-hex:IPA 85:15), flow 0.7 mL/min; t_S =

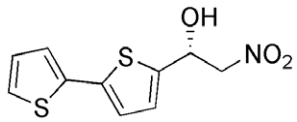
21.0 min; t_R = 26.0 min, *ee* = 81%; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 4.58-4.62 (2H, m); 5.61 (1H, dd, J = 4.8, 7.8 Hz); 7.64 (2H, d, J = 9.0 Hz); 8.27 (2H, d, J = 9.0 Hz); $[\alpha]^D$: +22.5 (*c* 3.1, CH_2Cl_2), [Lit. (*R*)-**2h** *ee* = 78%, $[\alpha]^D$: -31.6 (c 1.05, CH_2Cl_2)].[3]



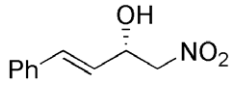
(*S*)-1-(2,3,4,5,6-Pentafluorophenyl)-2-nitroethanol (2i): Yellow oil; flash chromatography *c*-hex:AcOEt 8:2; yield = 62%, (conv. 80%); HPLC analysis: Chiralcel OJ, isocratic (*n*-hex:IPA 90:10), flow 0.5 mL/min; t_S = 21.4 min; t_R = 24.2 min, *ee* = 90%; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.08 (1H, br); 4.60 (1H, d, J = 13.5 Hz); 5.02 (1H, dd, J = 7.1, 13.5 Hz); 5.87 (1H, d, J = 7.1 Hz); $[\alpha]^D$: +8.9° (c 0.8, CH_2Cl_2).



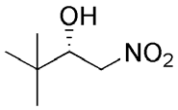
(*S*)-1-(4-Phenylphenyl)-2-nitroethanol (2j): Pale yellow solid; mp: 126-128°C; flash chromatography *c*-hex:AcOEt 9:1→8:2; yield = 92% (conv. 99%%); HPLC analysis: Chiralcel OD, isocratic (*n*-hex:IPA 80:20), flow 1.0 mL/min; t_S = 12.9 min; t_R = 15.0 min, *ee* = 87%; ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 2.85 (1H, d = 2.8 Hz); 4.54-4.72 (2H, m); 5.52-5.68 (1H, m); 7.44-7.69 (9H, m); $[\alpha]^D$: +35.4 (*c* 0.48, CH_2Cl_2), [Lit. (*R*)-**2j** *ee* = 91%, $[\alpha]^D$: -36.1 (*c* 1.35, CH_2Cl_2).[3]



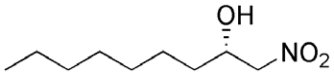
(*R*)-1-(5-(2,2'-bithienyl))-2-nitroethanol (2k): Orange solid; mp = 72-73°C; flash chromatography *c*-hex:AcOEt 9:1; yield = 42%, (conv. 58%); HPLC analysis: Chiralcel OD, isocratic (*n*-hex:IPA 80:20), flow 1.0 mL/min; t_S = 18.5 min; t_R = 23.2 min, *ee* = 88%; ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 3.05 (1H, d, J = 3.0 Hz); 4.58-4.92 (2H, m); 5.69 (1H, dd, J = 4.7, 7.9 Hz); 7.08-7.18 (5H, m); Configuration assignment by analogy: $[\alpha]^D$: +14.2 (c 0.40, CH_2Cl_2, *ee* = 80%).



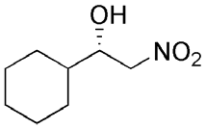
(*S*)-1-Nitro-4-phenyl-but-3-en-2-ol (2l): Yellow oil; flash chromatography *c*-hex:AcOEt 9:1→8:2; yield = 71%, (conv. 78%); HPLC analysis: Chiralcel OD, isocratic (*n*-hex:IPA 85:15), flow 1.0 mL/min; t_S = 28.4 min; t_R = 31.4 min, *ee* = 92%; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.76 (1H, br); 4.56 (2H, d, J = 5.7 Hz); 5.09 (1H, pq, J = 6.6 Hz); 6.19 (1H, dd, J = 5.7, 16.5 Hz), 6.82 (1H, d, J = 16.5 Hz), 7.30-7.45 (5H, m); Configuration assignment by analogy: $[\alpha]^D$: +6.9 (c 0.3, CH_2Cl_2, *ee* = 92%).



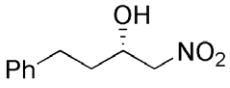
(*S*)-3,3-Dimethyl-1-nitro-butan-2-ol (2m): Pale yellow oil; flash chromatography *c*-hex:AcOEt 95:5; yield = 75%, (conv. 90%); HPLC analysis: Chiralcel OD, isocratic (*n*-hex:IPA 95:5), flow 0.5 mL/min; t_S = 19.2 min; t_R = 22.9 min, *ee* = 97%; ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 0.99 (9H, s); 2.41 (1H, d, J = 4.4 Hz); 4.02-4.08 (1H, m); 4.32-4.58 (2H, m); $[\alpha]^D$: +36.1(*c* 0.6, CH_2Cl_2), [Lit. (*R*)-**2n** *ee* = 90%, $[\alpha]^D$: -35.9 (c 1.01, CH_2Cl_2].[3]



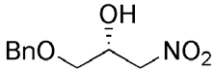
(*S*)-1-Nitro-nonan-2-ol (2n): Yellow oil; flash chromatography *c*-hex:AcOEt 99:1; yield = 78%, (conv. 95%); HPLC analysis: Chiralcel AD, isocratic (*n*-hex:IPA 98:2), flow 0.8 mL/min; t_S = 33.2 min; t_R = 49.5 min, *ee* = 99%; ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 0.89 (3H, t, J = 9.0 Hz); 1.26-1.35 (10H, m); 3.98-4.10 (1H, m); 4.34-4.48 (2H, m); Configuration assignment by analogy: $[\alpha]^D$: +16.6 (*c* 0.33, CH_2Cl_2).



(*S*)-1-Cyclohexyl-2-nitroethanol (2o): Yellow oil; flash chromatography *c*-hex:AcOEt 9:1; yield = 72%, (conv. 97%); HPLC analysis: Chiralcel AD, isocratic (*n*-hex:IPA 97:3), flow 0.8 mL/min; t_S = 27.5 min; t_R = 29.3 min, *ee* = 93%; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.10-1.29 (5H, m); 1.50 (1H, br); 1.68-1.72 (2H, m); 1.79-1.89 (3H, m); 4.14 (1H, br), 4.49 (2H, br). $[\alpha]^D$: +16.9 (*c* 2.1, CH_2Cl_2), [Lit. (*R*)-**2p** *ee* = 93%, $[\alpha]^D$: -21.1 (c 1.33, CH_2Cl_2].[3]

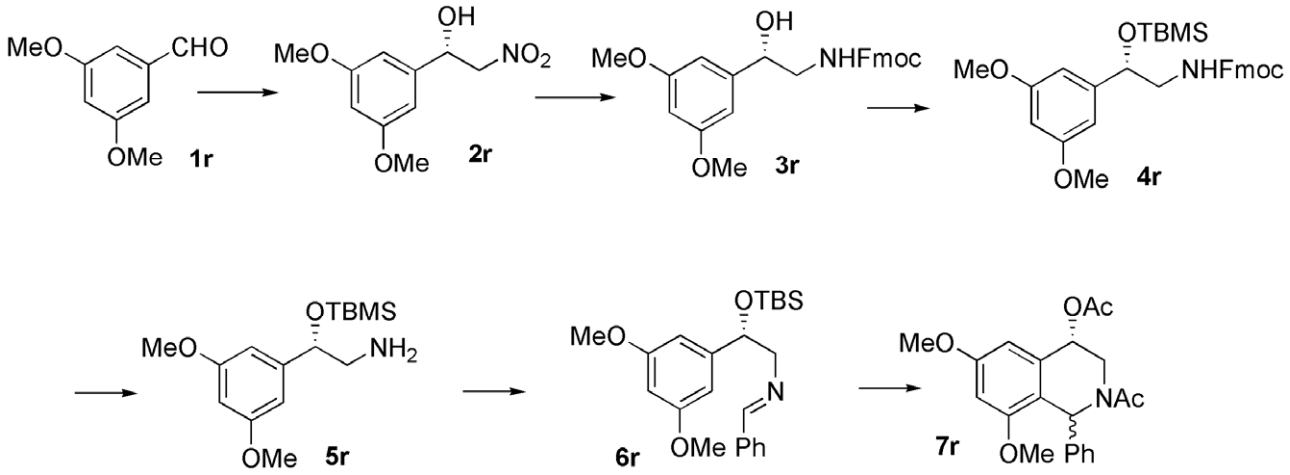


(*S*)-1-Nitro-4-phenylbutan-2-ol (2p): White solid; mp: 102-103°C; flash chromatography *c*-hex:AcOEt 9:1; yield = 53%, (conv. 80%); HPLC analysis: Chiralcel AD, isocratic (*n*-hex:IPA 90:10), flow 1.0 mL/min; t_S = 10.5 min; t_R = 14.5 min, *ee* = 87%; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.78-1.90 (2H, m); 2.70-2.78 (2H, m); 2.82-2.90 (1H, m); 4.30-4.38 (1H, m); 4.40-4.44 (2H, m); 7.38-7.43 (5H, m); $[\alpha]^D$: -10.9 (*c* 1.3, CH_2Cl_2, *ee* = 87%), [Lit. (*R*)-**2q** *ee* = 90%, $[\alpha]^D$: +15.0 (c 1.33, CH_2Cl_2)].[3]



(*R*)-1-Benzyloxy-3-nitropropan-2-ol (2q): Yellow oil; flash chromatography *c*-hex:AcOEt 9:1; yield = 62%, (conv. 85%); HPLC analysis: Chiralcel OD, isocratic (*n*-hex:IPA 85:15), flow 1.0 mL/min; t_S = 14.0 min; t_R = 15.7 min, *ee* = 80%; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.59 (2H, d, J = 3.6 Hz); 4.54-4.60 (5H, m); 7.34-7.37 (5H, m); $[\alpha]^D$: +1.5 (*c* 0.9, CH_2Cl_2, *ee* = 80%), [Lit. (*R*)-**2q** *ee* = 86%, $[\alpha]^D$: +0.52 (c 0.59, CH_2Cl_2)].[6]

Synthesis of 7r.



(*S*)-1-(3,5-Dimethoxyphenyl)-2-nitroethanol (2r): Yellow oil; flash chromatography *c*-hex:AcOEt 80:20; yield = 83%, (conv. 95%); HPLC analysis: Chiralcel AD, isocratic (*n*-hex:IPA 90:10), flow 1.0 mL/min; t_S = 15.6 min; t_R = 20.1 min, *ee* = 84%; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.91 (1H, d, J = 3.6 Hz); 3.81 (6H, s); 4.48-4.64 (2H, m); 5.40 (1H, dt, J = 3.0, 9.3 Hz); 6.44 (1H, t, J = 2.4 Hz); 6.55 (2H, d, J = 2.4 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 55.4(2C); 71.0; 81.2; 100.7; 103.8(2C); 140.5; 161.3(2C); Configuration assignment by analogy: $[\alpha]^D$: +11.0 (*c* 0.6, CH_2Cl_2).

(*S*)-*N*-Fmoc-3r. (*S*)-**2r** (290 mg, 1.5 mmol, *ee* = 84%) was reduced with 10% Pd/C (42 mg) in MeOH (10 mL) under H_2 (1 atm) for 16h, to provide the corresponding amino alcohol as a yellow viscous oil (purity > 90% by ^{1}H-NMR); ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.81-2.88 (1H, m); 2.98-3.02 (1H, m); 3.36 (3H, br); 3.78 (6H, s); 4.64-4.66 (1H, m); 6.33 (1H, s); 6.50 (2H, s); LC-ESI-MS: 198(M+1). A flamed two-necked round-bottom flask was charged with anhydrous CH_2Cl_2 (8 mL), crude (*S*)-amino alcohol[7] (70 mg, 0.35 mmol) and TEA (93 μL, 0.7 mmol). To the cooled solution (0°C), 96 mg of Fmoc-Cl (0.7 mmol) were added. After 16h stirring at rt, the reaction was quenched with a saturated solution of $NaHCO_3$ (5 mL) and the two phases separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL), dried with Na_2SO_4 and concentrated under reduced pressure. Flash chromatography *c*-hex:AcOEt 70:30; yield = 61% (90 mg, two steps), white solid; mp = 124-125°C; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.29-3.36 (1H, m); 3.54-3.63 (1H, m); 3.79 (6H, s); 4.23 (1H, t, J = 6.9 Hz); 4.43 (2H, d, J = 6.9 Hz); 4.78-4.80 (1H, br); 5.24 (1H, br s); 6.39 (1H, t,

J = 2.1 Hz); 6.54 (2H, s); 7.32 (2H, t, J = 7.8 Hz); 7.41 (2H, t, J = 7.8 Hz); 7.59 (2H, d, J = 7.2 Hz); 7.77 (2H, d, J = 7.2 Hz); ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 47.2; 48.5; 55.4(2C); 66.9; 73.7; 99.9; 103.7(2C); 120.0(2C); 125.0(2C); 127.4(2C); 127.7(2C); 141.3(2C); 143.8(2C); 144.0, 150.9, 161.0(2C); HPLC analysis: Chiralcel AD, isocratic (*n*-hex:IPA 80:20), flow 1.0 mL/min; t_R = 11.9 min; t_S = 15.5 min, *ee* = 84%; $[\alpha]^D$: +14.9 (*c* 0.47, CH_2Cl_2).

(*S*)-4r. A flamed two-necked round-bottom flask was charged with anhydrous DMF (2 mL), (*S*)-*N*-Fmoc-**3r** (80 mg, 0.19 mmol) and imidazole (32 mg, 0.48 mmol). To the stirred mixture, 59 mg of TBSCl (0.39 mmol) were added and the mixture stirred overnight. The reaction were judged complete by TLC, then H_2O (5 ml) and EtOAc (5 mL) were added. The phases separated and the organic layer washed with H_2O. After dryness (Na_2SO_4), the volatiles were evaporated under reduced pressure to leave desired *O*-silyl compound was obtained as a pale yellow oil Flash chromatography *c*-hex:AcOEt 90:10→80:20; yield = 63% (57 mg). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: -0.04 (3H, s); 0.07 (3H, s); 0.94 (9H, s); 3.15-3.23 (1H, m); 3.41-3.58 (1H, m); 3.79 (6H, s); 4.23 (1H, t, J = 7.2 Hz, 1H); 4.40 (2H, d, J = 7.2 Hz); 4.70-4.79 (1H, m); 5.01-5.10 (1H, m); 6.39 (1H, t, J = 1.8 Hz); 6.52 (2H, br s); 7.31 (2H, t, J = 7.2 Hz); 7.41 (2H, t, J = 7.2 Hz); 7.59 (2H, d, J = 7.5 Hz); 7.79 (2H, d, J = 7.5 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: -3.0; 1.0, 18.2, 25.7(3C); 47.2; 49.3; 55.3(2C); 66.8; 73.8, 99.7, 103.9(2C); 120.0, 125.1, 127.0(2C); 127.7(2C); 141.3(2C), 144.0(2C), 144.8(2C), 156.3, 160.8(2C). HPLC analysis: Chiralcel AD, isocratic (*n*-hex:IPA 90:10), flow 0.5 mL/min; t_S = 13.1 min; t_R = 16.0 min, *ee* = 84%; $[\alpha]^D$: +16.3 (*c* 0.30, CH_2Cl_2, *ee* = 84%).

(*S*)-5r. A 25 mL round-bottom flask was charged with crude O-TBS,*N*-Fmoc derivative **4r** (55 mg, 0.10 mmol) and 1 mL of Me_2NH (2M, THF). After stirring for 15 min at rt the volatiles were removed under reduced pressure and the treatment was repeated a second time. ^{1}H-NMR check confirmed a conversion > 95%. The desired amino compound **5r** was purified by flash chromatography (CH_2Cl_2:MeOH 99:1→95:5) to give (*S*)-**5r** as a pale yellow oil in 74% yield (24 mg). HPLC analysis: Chiralcel OD, isocratic (*n*-hex:IPA 97:3), flow 1.0 mL/min; t_R = 8.9 min; t_S = 14.2 min, *ee* = 84%; ^{1}H-NMR (200 MHz, $CDCl_3$) δ: -0.04 (3H, s); 0.08 (3H, s); 0.93 (9H, s); 2.81-2.83 (2H, m); 3.79 (6H, s); 4.60 (1H, t, J = 5.1 Hz); 6.36 (1H, t, J = 2.4 Hz); 6.48 (2H, J = 2.4 Hz); ^{13}C-NMR (50 MHz, $CDCl_3$) δ: -4.5; -4.6; 18.2, 25.8(3C); 50.8; 55.3(2C); 99.2: 104.0(2C); 145.6; 160.6. GC-MS (*m/z*: 51(5); 73(95); 89(10); 127(12); 153(18); 180(10); 193(11); 209(12); 225(7); 237(8); 254(25); 282(100); 296(10); $[\alpha]^D$: +25.0 (*c* 0.80, CH_2Cl_2, *ee* = 53%).

(*S*)-6r. To a solution of **5r** (20 mmol, 0.06 mmol) in dry CH_2Cl_2 (2 mL), freshly distilled PhCHO (6 μL, 0.06 mmol) and $MgSO_4$ (22 mg, 0.18 mmol) were added in sequence. The reaction mixture was stirred at rt overnight then the $MgSO_4$ was filtered off through a pad of celite. After evaporation the

crude imine **6r** was obtained in high chemical purity (judged >95% by ^{1}H NMR) and used without further purification. Pale yellow viscous oil (30 mg); ^{1}H-NMR (200 MHz, $CDCl_3$) δ: -0.07 (6H, s); 0.82 (9H, s); 3.53 (1H, dd, J = 8.8, 11.4 Hz); 3.80 (6H, s); 4.00 (1H, d, J = 10.2 Hz); 5.02 (1H, dd, J = 3.0, 8.8 Hz); 6.37 (1H, t = 2.6 Hz); 6.60 (2H, d, J = 2.6 Hz); 7.41-7.45 (3H, m); 7.71-7.77 (2H, m); 8.22 (1H, s); ^{13}C-NMR (50 MHz, $CDCl_3$) δ: -4.8 (2C); 18.2, 25.7 (3C); 55.3 (2C); 70.8, 74.3, 99.3, 103.9 (2C); 128.1 (2C); 128.6 (2C); 136.2, 146.3, 160.6 (2C); 163.1.

7r (mixture of diastereoisomers). A dried two-necked bottom flask connected to the nitrogen line, was charged with 18 mg of crude (*S*)-**6r** (≈ 0.07 mmol) dissolved in anhydrous CH_3CN (2 mL), and the mixture was cooled to 0°C. Then, AcCl (8 μL, 0.11 mmol) and lutidine (13 μL, 0.11 mmol) were added. After stirring overnight at 0°C the reaction was judged complete by ^{1}H NMR. Usual work-up (H_2O, CH_2Cl_2, brine, Na_2SO_4) provided the crude **7** that was purified by flash chromatography (*n*-hex:AcOEt 80:20). Yield = 63%; dr: 5.3:1 by LC-HPLC; HPLC analysis; LC-ESI: 441 (M+1), 464 (M+Na); 905 (2M+Na); Chiralcel AD, isocratic (*n*-hex:IPA 95:5), flow 0.5 mL/min; t_1 = 12.6 min; t_2 (major) = 14.3 min, *ee* = 84%, t_3 (major) = 16.9 min; t_4 = 18.5 min, *ee* = 84%; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: (major isomer, major conformer) 0.027 (3H, s); 0.08 (3H, s); 0.90 (9H, s); 2.21 (3H, s); 3.40-3.48 (1H; m); 3.58-3.65 (1H, m); 3.83 (6H, s); 4.69 (1H, t, J = 3.3 Hz); 6.40 (1H, d, J = 1.5Hz); 6.50 (1H, d, J = 1.5Hz); 6.67 (1H, s); 7.10-7.25 (5H, m); (major isomer, minor conformer, diagnostic signals) 2.18 (3H, s); 3.67 (6H, s); 4.62 (1H, dd, J = 5.7, 9.6Hz); 6.37 (1H, s); 6.47 (1H, s); (minor isomer, diagnostic signals) 4.79 (1H, dd, J = 5.8, 10.0 Hz); 6.68 (1H, s); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: (major isomer, major conformer, diagnostic signals) -4.52 (2C); 18.1; 25.8 (3C); 49.8; 53.8; 55.3(2C); 66.8; 97.8: 103.4 (2C); 117.1; 125.7; 127.1 (2C); 128.0 (2C); 138.6; 141.2; 159.7 (2C); 169.7; (major isomer, minor conformer, diagnostic signals) -4.2 (2C); 18.2; 26.9 (3C); 48.6; 55.5 (2C); 66.2; 97.3; 100.7; 116.7; 126.9 (2C); 128.5 (2C); 140.8; 141.4; 157.1; 170.5; . (minor isomer, diagnostic signals): -5.2(2C); 47.9; 55.7 (2C); 67.2; 100.0; 127.4 (2C); 155.7;

Crystal data for complex (+/-)-DAT2-Cu(OAc)$_2$: collected on a Bruker APEX II CCD diffractometer (Mo-K_α radiation, λ = 0.71073 Å) Empirical absorption correction was applied, initial structure model by direct methods. Anisotropic full-matrix least-squares refinement on F^2. Data for (+/-)-DAT2/($Cu(OAc)_2$): $C_{28}H_{32}N_2S_4Cu_1O_4$, M_r = 652.34, monoclinic, Cc, a = 20.9769(19), b = 13.9008(12), c = 12.2335(11)Å, β = 123.8310(10)°, V = 2963.2(5) Å^3, Z = 4, D_x = 1.462 Mg/m^3, μ = 1.055 mm^{-1}, F(000) = 1356, T = 293(2) K, theta max 28.65°, 12621 reflections collected, 5113 reflections $I > 2\sigma(I)$. Final agreement indices R_1 = 0.0602 and wR_2 = 0.1887.

Goodness-of-fit = 1.044. CCDC 299401 contains the supplementary crystallographic data for this structure. These data can be obtained online free of charge (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

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