Supplementary Material (ESI) for Chemical Communications

Supporting Information

Enantioselective nitroaldol (Henry) reaction using Copper (II) complexes of (-)-Sparteine

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General Remarks

All chemicals were purchased from Aldrich and were used as received. All solvents used were analytical grade and were used as received from Merck India Pvt. Ltd. Commercial column chromatography grade silica gel (60-120 mesh) was first calcined at 200˚C for 6h prior to use. No high purity nitrogen was used and all reactions were conducted at 0˚C in methanol. Purification of reaction products was carried out by flash chromatography using calcined silica gel, and a mixture of ethyl acetate and hexanes as eluting agent. All products were characterized by ^{1}H-NMR spectroscopy. The ^{1}H spectra of samples were recorded on a Gemini 200 MHz, and/or a Bruker-Avance-300 MHz Spectrometer using TMS as an internal standard in $CDCl_3$. High performance liquid chromatography (HPLC) was performed using an Agilent-1100 series liquid chromatograph equipped with a single pump and UV detector (fixed at 215 nm) using a CHIRALCEL OD-H, OJ-H and AD columns with 2-propanol/hexane as eluting agent. Optical rotations were obtained on an automated JASCO P-1020 polarimeter, and the values were reported in absolute rotations: $[\alpha]_D^T$ [concentration *c* in g/100 mL of solvent]. Elemental Analysis of complexes was carried out on ELEMENTAR VARIO-EL CHNS analyzer. The r.m.s overlay of X-ray structures (**1** and **2**) was obtained by calculations involving published X-ray crystal structure data[1] using Mercury software (Version 1.4.1).[2]

Preparation of diacetato[(-)-sparteine-N,N']copper(II) (1)

Copper(II) acetate (380 mg, 2mmol) and (-)-sparteine (469 mg, 2 mmol) were taken in an oven dried 25mL RB flask containing 6mL of ethanol-triethylorthoformate (5:1) solution. This mixture was stirred under nitrogen atmosphere for 4 hrs. A blue precipitate settled out, which was filtered to yield 775 mg (91% yield) of blue microcrystalline diacetato[(-)-sparteine-N,N']copper(II) complex. Analytically pure compound was obtained by recrystallization from hot methanol. Anal. calcd. for $C_{19}H_{32}N_2O_4Cu$: C, 54.78; H, 7.69; N, 6.73. Found: C, 54.28; H, 8.02; N, 6.93.

Preparation of dichloro[(-)-sparteine-N,N']copper(II) (2)

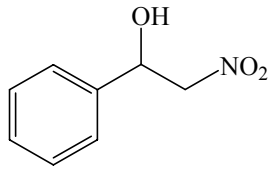
Copper(II) chloride (342mg, 2 mmol) was first dehydrated by heating at 110^{o}C under vacuum for several hours, which was then taken in an oven dried 25mL RB flask containing a solution of (-)-sparteine (469mg, 2 mmol) in methanol (6 ml). This

mixture was stirred under nitrogen atmosphere for 4 hrs. An olive green precipitate quickly precipitated out, which was filtered to yield 692 mg (89% yield) of dichloro[(-)-sparteine-N,N']copper(II) complex. Analytically pure compound was obtained by recrystallization from hot methanol. Anal. calcd. for $C_{15}H_{26}N_2Cl_2Cu$: C, 48.78; H, 7.05; N, 7.59. Found: C, 48.28; H, 7.22; N, 7.43.

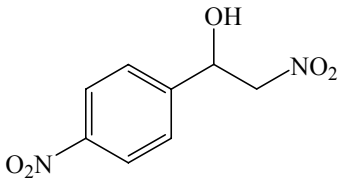
General procedure for dichloro[(-)-sparteine-N,N']copper(II) (2) catalyzed direct nitroaldol reaction of nitromethane with aldehydes.

A dry and nitrogen flushed 5 mL flask, equipped with a magnetic stirring bar, was charged with dichloro[(-)-sparteine-N,N']copper(II) (**2**) catalyst (44mg, 0.1 mmol), and freshly distilled methanol (1 mL) at room temperature. Corresponding aldehyde (0.5 mmol), and nitromethane (0.1 mL, 2.0 mmol) were then added successively, and the resulting blue solution was stirred for an additional 10 minutes at room temperature. After cooling the mixture to 0 °C, 0.2 mL of 1.0 vol% solution of triethylamine in methanol (~3-mol.% relative to aldehyde) was added by a syringe, and the mixture was stirred at the same temperature till the completion of reaction. The reaction was quenched with a saturated aqueous solution of NH4Cl (10 mL), extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried using anhydrous Na_2SO_4, filtered, and the solvent was removed by evaporation. The crude product was purified by column chromatography (silica gel: 100-200 mesh using ethyl acetate and hexanes) to give corresponding Henry adduct. Enantiomeric excess was determined by HPLC using Chiralcel OD-H, OJ-H, or AD columns using isopropanol and hexanes as eluting agent. The absolute configuration of the Henry products were assigned by comparison with optical rotation data of known compounds.[3-5]

Analytical Data for Henry Adducts:

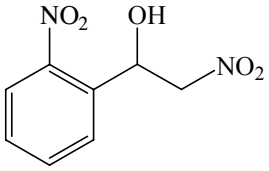


(*R*)-1-Phenyl-2-nitroethanol (3a).. ^{1}H NMR (300 MHz, $CDCl_3$) 2.91 (d, 1 H, *J*=3.9 Hz), 4.54 (dd, 1 H, *J*=13.4, 3.1 Hz), 4.59-4.50 (dd, 1 H, *J*=13.2, 9.8 Hz), 5.40-5.41 (m, 1 H), 7.50-7.38 (m, 5 H); Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (85:15 hexane:isopropanol, 1.0 mL/min, 215 nm); major enantiomer t_r = 9.8 min, minor enantiomer t_r = 11.7 min; 79% ee; $[\alpha]_D^{28}$ –35.3 (*c* 1.0, CH_2Cl_2)[Lit[3] $[\alpha]_D^{21}$ –41.6 (*c* 1.03, CH_2Cl_2; 94%ee, (R)-isomer)

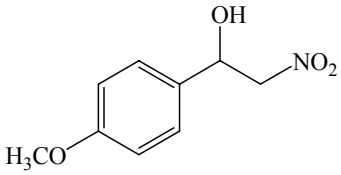


(*R*)-2-Nitro-1-(4-nitrophenyl)ethanol (3b). ^{1}H NMR (200MHz, $CDCl_3$) 3.12 (d, 1 H, *J*=4.0 Hz), 4.54-4.50 (m, 2 H), 5.58 (dd, 1H, J=8.0, 4.0 Hz), 7.58-7.55 (m, 2 H), 8.18-

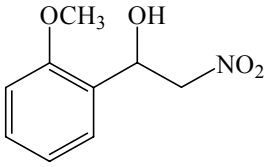
8.14 (m, 2H); Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (85:15 hexane:isopropanol, 0.8 mL/min, 215 nm); major enantiomer t_r = 15.8 min, minor enantiomer t_r = 19.9 min; 86% ee; $[\alpha]_D^{29}$ –31.8 (*c* 1.05, CH_2Cl_2) [Lit[3] $[\alpha]_D^{21}$ –31.6 (*c* 1.05, CH_2Cl_2; 78%ee, (R)-isomer).



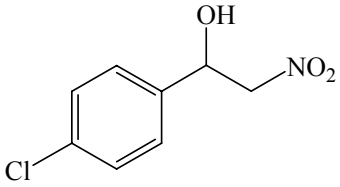
(*R*)-1-(2-nitrophenyl)-2-nitroethanol (3c). ^{1}H NMR (200 MHz, $CDCl_3$) 3.2 (d, 1 H, *J*= 4.2 Hz,), 4.63 (dd, 1 H, *J*=13.7, 8.8 Hz), 4.50 (dd, 1 H, J=13.9, 2.2 Hz), 6.15 (ddd,1 H, J=8.8, 4.3, 2.0 Hz), 8.15-7.55(m, 4 H); Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (90:10 hexane:isopropanol, 1 mL/min, 215 nm); major enantiomer t_r = 14.1 min, minor enantiomer t_r = 16.4 min; 89% ee; $[\alpha]_D^{23}$ +220.8 (*c* 1.00, CH_2Cl_2) [Lit[3] $[\alpha]_D^{21}$ +227.1 (*c* 1.00, CH_2Cl_2; 89%ee, (R)-isomer).



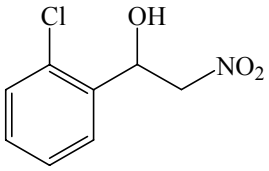
(R)-1-(4-Methoxyphenyl)-2-nitroethanol (3d): ^{1}H NMR (300 MHz, $CDCl_3$) 3.1 (d, 1H, *J*=4.1 Hz), 3.8 (s, 3H), 4.64-4.55 (m, 2H), 5.60 (dd, 1H, J= 7.9 4.1 Hz), 7.60-8.30(m, 4H). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (85:15 hexane:isopropanol, 0.8 mL/min, 215 nm); major enantiomer t_r = 16.4 min, minor enantiomer t_r = 20.5 min; 80% ee; $[\alpha]_D^{25}$ -29.8 (c 1.0, CH_2Cl_2) [Lit[4] $[\alpha]_D^{25}$ +29.7 (*c* 1.0, CH_2Cl_2; 85%ee, (S)-isomer).



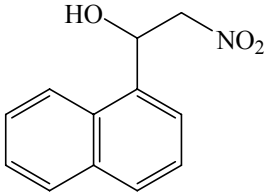
(*R*)-1-(2-Methoxyphenyl)-2-nitroethanol (3e). ^{1}H NMR (200 MHz, $CDCl_3$) 3.16(d, 1 H, *J*=6.1 Hz,), 3.89 (s, 3 H, OCH_3), 4.61 (dd, 1 H, *J* =13.25, 9.1 Hz), 4.61 (dd, 1 H, J= 13.1, 3.4 Hz), 5.69 (ddd,1 H, J=9.2, 6.1, 3.4 Hz), 6.95-7.50(m, 4 H);;Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (90:10 hexane:isopropanol, 0.8 mL/min, 215 nm); major enantiomer t_r = 13.6 min, minor enantiomer t_r = 16.17 min; 97% ee; $[\alpha]_D^{30}$ -45.3 (*c* 1.00, CH_2Cl_2) [Lit[3] $[\alpha]_D^{21}$ –44.5 (*c* 1.03, CH_2Cl_2; 94% ee, (R)-isomer).



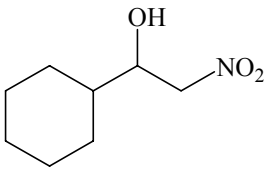
(*R*)-1-(4-Chlorophenyl)-2-nitroethanol (3f). ^{1}H NMR (300 MHz, $CDCl_3$,) 3.14(d, 1 H, *J*=4.1 Hz), 4.51 (dd, 1 H, *J*=13.3, 2.9 Hz), 4.55 (dd, 1 H, *J*=13.3, 9.5 Hz), 5.42-5.38 (m, 1 H), 7.38-7.32(m,4 H) Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (85:15 hexane:isopropanol, 1 mL/min, 215 nm); major enantiomer t_r = 9.3 min, minor enantiomer t_r = 11.4min; 81% ee; $[\alpha]_D^{23}$ -37.1 (*c* 2.0, CH_2Cl_2) [Lit[3] $[\alpha]_D^{23}$ –37.6 (*c* 2.03, CH_2Cl_2; 90% ee, (R)-isomer).



(*R*)-1-(2-Chlorophenyl)-2-nitroethanol (3g). ^{1}H NMR (300 MHz, $CDCl_3$ 3.02(d, 1 H, *J*=4.6 Hz), 4.43 (dd, 1 H, *J*=13.7, 9.8 Hz), 4.65 (dd, 1 H, *J*=13.7, 2.5 Hz), 5.84-5.81 (m, 1 H), 7.64-7.27(m,4 H); Enantiomeric excess was determined by HPLC with a Chiralcel OJ-H column (90:10 hexane:isopropanol, 1 mL/min, 215 nm); major enantiomer t_r =13.2 min, minor enantiomer t_r = 14.6 min; 96% ee; $[\alpha]_D^{27}$ -52.3 (*c* 1.0, CH_2Cl_2) [Lit[3] $[\alpha]_D^{23}$ –52.7 (*c* 1.21, CH_2Cl_2; 91% ee, (R)-isomer).

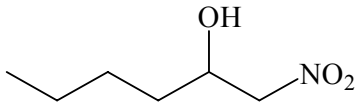


(*R*)-1-(1-Naphthyl)-2-nitroethanol (3h). ^{1}H NMR (300MHz, $CDCl_3$) 3.07 (d,1H, 2.9 Hz,); 4.64-4.57 (m, 2H,), 6.21-6.17 (m, 1H,) 7.48-8 (m, 7H,), Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (85:15 hexane:isopropanol, 0.8 mL/min, 215 nm); major enantiomer t_r = 13.6 min, minor enantiomer t_r = 20.6 min; 73% ee; $[\alpha]_D^{28}$ -19.9 (*c* 1.08, CH_2Cl_2) [Lit[3] $[\alpha]_D^{23}$ -24.9 (*c* 1.08, CH_2Cl_2; 92% ee, (R)-isomer).

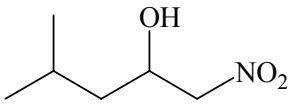


(*R*)-1-Cyclohexyl-2-nitroethanol (3i). ^{1}H NMR (300 MHz, $CDCl_3$) 1.27-0.98(m, 5 H). 1.46-1.37 (m, 1 H), 1.73-1.64 (m, 2 H), 1.82-1.73 (m, 3 H), 2.77 (d, 1H, J=4.9 Hz), 4.1 (m, 1 H), 4.42 (dd, 1 H, J=12.8, 9.0Hz), 4.46 (dd, 1 H, J= 12.8, 2.9 Hz);

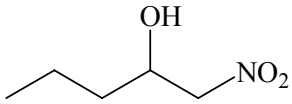
Enantiomeric excess was determined by HPLC with a Chiralcel AD column (97:3 hexane:isopropanol, 0.8 mL/min, 215 nm); major enantiomer t_r = 26.0 min, minor enantiomer t_r = 27.9 min; 85% ee; $[\alpha]_D^{29}$ -19.1 (*c* 1.33, $CHCl_3$) [Lit[3] $[\alpha]_D^{20}$ -17.6 (*c* 1.57, $CHCl_3$; 90% ee, (R)-isomer).



(*R*)-1-Nitrohexan-2-ol (3j). ^{1}H NMR (300 MHz, $CDCl_3$) 0.92 (t, 3 H, J= 6.3Hz), 1.31-1.60 (m, 6 H), 2.80 (bs, 1 H), 4.3 (m, 1 H), 4.36(dd, 1H, J= 13.1, 8.6 Hz), 4.41 (dd, 1H, J= 13.1, 2.9 Hz).Enantiomeric excess was determined by HPLC with a Chiralcel AD column (98:2 hexane:isopropanol, 0.8 mL/min, 215 nm); major enantiomer t_r = 30.3 min, minor enantiomer t_r = 41.2 min; 78% ee; $[\alpha]_D^{31}$ -8.76 (*c* 2.73, CH_2Cl_2) [Lit[3] $[\alpha]_D^{23}$ -9.3 (*c* 2.73, CH_2Cl_2; 93% ee, (R)-isomer).



(*R*)-4-Methyl-1-nitropentan-2-ol (3k). ^{1}H NMR (300 MHz, CDCl3) 0.94 (app t, 6H, *J* = 6.8 Hz), 1.24-1.19 (m, 1H), 1.51-1.45 (m, 1H), 1.85- 1.77 (m, 1H), 2.75 (d, 1H, *J* = 4.4 Hz,), 4.41-4.32 (m, 3H,), Enantiomeric excess was determined by HPLC with a Chiralcel AD column (98:2 hexane:isopropanol, 0.6 mL/min, 215 nm); major enantiomer tr = 35.7 min, minor enantiomer tr = 39.2 min; 90% ee; $[\alpha]_D^{30}$ +2.62 (*c* 3.28, CH2Cl2) [Lit[3] $[\alpha]_D^{23}$ +2.63 (*c* 3.28, CH_2Cl_2; 92% ee, (R)-isomer).



(R)-1-nitropentan-2-ol (3l). ^{1}H NMR (300 MHz, CDCl3)) 1.02 (t, 3H, *J*= 6.8 Hz,) 1.63-1.29 (m, 4H,) 3.03-2.77 (b, 1H,) 4.44-4.32 (m, 1H), 4.51-4.36 (m, 2H,), Enantiomeric excess was determined by HPLC with a Chiralpak AD column (98:2 hexane: isopropanol, 1.0 ml/min, 215 nm); major enantiomer t_r =28.8 min; minor enantiomer t_r = 48.4 min; 81% ee; $[\alpha]_D^{30}$ -16.2 (*c* 2.3, CH2Cl2) [Lit[5] $[\alpha]_D^{25}$ -18.3 (*c* 2.3, CH_2Cl_2 92% ee, (R)-isomer).

References

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