Bismuth Triflate-Chiral Bipyridine Complexes as Water-Compatible Chiral Lewis Acids

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Supporting Information

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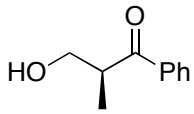
Experimental

General: Melting points were uncorrected. ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-LA300, JNM-LA400, ECX-400 or ECX-600 spectrometer in $CDCl_3$ unless otherwise noted. Tetramethylsilane (TMS) served as an internal standard (δ = 0 ppm) for ^1H NMR and $CDCl_3$ as an internal standard (δ = 77.0 ppm) for ^{13}C NMR. Preparative thin-layer chromatography was carried out using Wakogel B-5F. An aqueous solution of formaldehyde was purchased from Wako Pure Chemical Industries, Ltd.

Typical Experimental Procedure for the Hydroxymethylation of Propiophenone-derived Silicon Enolate: A mixture of $Bi(OTf)_3$ (14 mg, 0.020 mmol) and **1** (20 mg, 0.060 mmol) in DME (1 mL) was stirred at room temperature for 30 min to afford 20 mM of a catalyst solution. A reaction vessel charged with the catalyst solution (150 μL) was cooled at 0 °C for 10 min, and an 81 mM solution of 2,2'-bipyridine in DME (185 μL) was added. Then an aqueous solution of formaldehyde (129 mg, 35% w/w, 1.5 mmol) and the silicon enolate (62 mg, 0.30 mmol) were added to the mixture. The whole was stirred until the silicon enolate disappeared completely (checked by TLC). The reaction was quenched with saturated aqueous $NaHCO_3$. The resultant mixture was extracted with dichloromethane (3 times), and the combined organic layers were dried over anhydrous Na_2SO_4. The solvents were evaporated, and the residue was purified by preparative TLC (silica gel, hexane/ethyl acetate (2/1)) to give the hydroxymethylated adduct. The enantiomeric excess of the product was determined by chiral HPLC analysis.

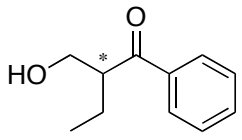
Characterization Data of the Hydroxymethylated Adducts

(*S*)-3-Hydroxy-2-methyl-1-phenylpropan-1-one[1]



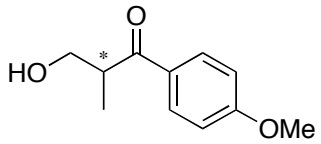
^{1}H NMR ($CDCl_3$) δ 1.24 (d, 3H, *J* = 7.1 Hz), 2.35 (brs), 3.68 (ddq, 1H, *J* = 4.3, 7.0, 7.1 Hz), 3.80 (dd, 1H, *J* = 4.3, 11.1 Hz), 3.94 (dd, 1H, *J* = 7.0, 11.1 Hz), 7.48 (dd, 2H, *J* = 7.3, 8.5 Hz), 7.58 (t, 1H, *J* = 7.3 Hz), 7.97 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR ($CDCl_3$) δ 14.5, 42.9, 64.5, 128.4, 128.7, 133.3, 136.1, 204.4; HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 19/1, flow rate = 1.0 mL/min) t_R = 17.5 min (major, *S*), t_R = 20.3 min (minor, *R*).

2-(Hydroxymethyl)-1-phenylbutan-1-one[3]



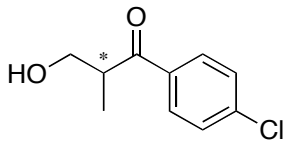
^{1}H NMR ($CDCl_3$) δ 0.95 (t, 3H, *J* = 7.4 Hz), 1.61-1.83 (m, 2H), 2.40 (brs), 3.52-3.58 (m, 1H), 3.84 (dd, 1H, *J* = 3.9, 11.0 Hz), 3.98 (dd, 1H, *J* = 6.8, 11.0 Hz), 7.45-7.50 (m, 2H), 7.56-7.60 (m, 1H), 7.95-7.97 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 11.8, 22.3, 49.5, 62.6, 128.3, 128.7, 133.2, 136.8, 204.6; IR (neat) 3435, 2966, 1678, 1043, 704 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{11}H_{14}O_2Na$ ($[M+Na]^+$): 201.0891, found: 201.0889; $[\alpha]^{24}_D$ –0.6 (*c* 0.75, $CHCl_3$) (91% ee); HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 19/1, flow rate = 1.0 mL/min) t_R = 18.8 min (major), t_R = 22.4 min (minor).

3-(Hydroxy)-2-methyl-1-(4-methoxyphenyl)propan-1-one



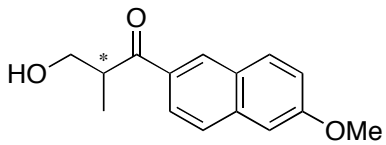
^{1}H NMR ($CDCl_3$) δ 1.22 (d, 3H, *J* = 7.1 Hz), 2.60 (brs), 3.62 (ddq, 1H, *J* = 4.3, 7.0, 7.1 Hz), 3.78 (dd, 1H, *J* = 4.3, 11 Hz), 3.87 (s, 3H), 3.91 (dd, 1H, *J* = 7.0, 11 Hz), 6.95 (d, 2H, *J* = 8.9 Hz), 7.95 (d, 2H, *J* = 8.9 Hz); ^{13}C NMR ($CDCl_3$) δ 14.7, 42.4, 55.4, 64.6, 113.8, 129.0, 130.7, 163.6, 202.9; IR (neat) 3438, 2933, 1667, 1597, 1251, 1173, 1047, 975, 843 cm^{-1}; MS m/z 194 (M^+); Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. found: C, 67.88; H, 7.33; $[\alpha]^{24}_D$ +4.2 (*c* 1.5, $CHCl_3$) (88% ee); HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 19/1, flow rate = 1.0 mL/min) t_R = 30.7 min (major), t_R = 38.9 min (minor).

3-(Hydroxy)-2-methyl-1-(4-chlorophenyl)propan-1-one



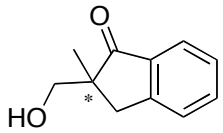
^{1}H NMR ($CDCl_3$) δ 1.21 (d, 3H, *J* = 7.3 Hz), 2.52 (brs), 3.62 (ddq, 1H, *J* = 4.3, 7.2, 7.3 Hz), 3.77 (dd, 1H, *J* = 4.3, 11 Hz), 3.87 (s, 3H), 3.93 (dd, 1H, *J* = 7.2, 11 Hz), 7.44 (d, 2H, *J* = 8.5 Hz), 7.90 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR ($CDCl_3$) δ 14.4, 43.0, 64.4, 129.0, 129.8, 134.4, 139.7, 203.0; IR (neat) 3424, 2937, 1682, 1590, 1401, 1092, 976, 841 cm^{-1}; MS m/z 198 (M^+); Anal. Calcd for $C_{10}H_{11}ClO_2$: C, 60.48; H, 5.58. found: C, 60.18; H, 5.85; $[\alpha]^{24}_D$ +4.1 (*c* 1.05, $CHCl_3$) (89% ee); HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 19/1, flow rate = 1.0 mL/min) t_R = 18.6 min (major), t_R = 28.7 min (minor).

3-Hydroxy-1-(2-methoxynaphthalen-6-yl)-2-methylpropan-1-one



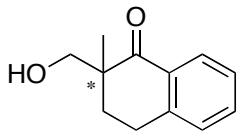
^{1}H NMR ($CDCl_3$) δ 1.28 (d, 3H, *J* = 6.9 Hz), 2.60 (s, 1H), 3.78-3.86 (m, 2H), 3.93 (s, 3H), 3.98 (m, 1H), 7.13 (m, 1H), 7.20 (m, 1H), 7.75 (m, 1H), 7.83 (m, 1H), 7.98 (m, 1H), 8.40 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 14.8, 42.7, 55.4, 64.7, 105.7, 119.7, 124.7, 127.2, 127.8, 130.1, 131.2, 131.4, 137.4, 159.8, 204.1; IR (neat) 3444, 1665, 1622, 1477, 1268, 1187, 1028 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{15}H_{17}O_3$ ($[M+H]^+$): 245.1178, found: 245.1166; $[\alpha]^{24}_D$ +2.3 (*c* 1.84, $CHCl_3$) (92% ee); HPLC (Daicel Chiralcel OD, hexane/*i*-PrOH = 19/1, flow rate = 1.0 mL/min) t_R = 30.7 min (minor), t_R = 36.6 min (major).

2,3-Dihydro-2-(hydroxymethyl)-2-methylinden-1-one[3]



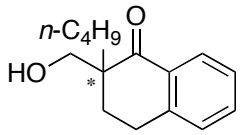
^{1}H NMR ($CDCl_3$) δ 1.26 (s, 3H), 2.91 (d, 1H, *J* = 7.2 Hz), 3.24 (d, 1H, *J* = 7.2 Hz), 3.64 (d, 1H, *J* = 11 Hz), 3.83 (d, 1H, *J* = 11 Hz), 7.35-7.41 (m, 1H), 7.45-7.48 (m, 1H), 7.59-7.64 (m, 1H), 7.64-7.77 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 20.7, 38.0, 50.8, 67.8, 124.2, 126.7, 127.5, 135.2, 135.8, 153.2, 211.1; IR (KBr) 3473, 2962, 2921, 2866, 1703 cm^{-1}; Mp 83-89 °C; Anal. calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. found: C, 74.80; H, 7.05; $[\alpha]^{24}_D$ +1.6 (*c* 0.95, $CHCl_3$) (88% ee); HPLC (Daicel Chiralcel OB-H, hexane/*i*-PrOH = 100/1, flow rate = 1.0 mL/min) t_R = 39.6 min (major), t_R = 50.0 min (minor).

3,4-Dihydro-2-(hydroxymethyl)-2-methylnaphthalen-1(2*H*)-one[3]



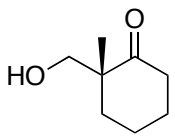
^{1}H NMR ($CDCl_3$) δ 1.23 (s, 3H), 1.78 (ddd, 1H, *J* = 3.7, 4.9, 13.4 Hz), 2.24 (ddd, 1H, *J* = 5.1, 12.0, 13.4 Hz), 2.77 (brs), 2.94 (ddd, 1H, *J* = 3.7, 5.1, 17.3 Hz), 3.15 (ddd, 1H, *J* = 4.9, 12.0, 17.3 Hz), 3.65 (d, 1H, *J* = 11.2 Hz), 3.74 (d, 1H, *J* = 11.2 Hz), 7.24-7.26 (m, 1H), 7.29-7.33 (m, 1H), 7.47-7.50 (m, 1H), 8.00-8.03 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 18.2, 25.0, 31.3, 46.3, 69.0, 126.7, 127.7, 128.7, 131.4, 133.6, 143.4, 204.0; IR (neat) 3456, 2931, 1678, 1047, 742 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{12}H_{14}O_2Na$ ([M+Na]$^+$): 213.0891, found: 213.0881; $[\alpha]^{24}_D$ –1.4 (*c* 1.3, $CHCl_3$) (95% ee); HPLC (Daicel Chiralcel OD, hexane/*i*-PrOH = 100/1, flow rate = 1.0 mL/min) t_R = 28.6 min (major), t_R = 34.3 min (minor).

2-Butyl-3,4-dihydro-2-(hydroxymethyl)naphthalen-1(*2H*)-one



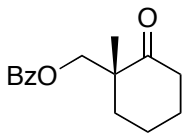
^{1}H NMR ($CDCl_3$) δ; ^{13}C NMR ($CDCl_3$) δ 13.9, 23.2, 24.9, 25.8, 28.0, 29.9, 49.5, 66.5, 126.7, 127.7, 128.7, 131.6, 133.5, 143.4, 204.4; IR (neat) 3443, 1672, 1458, 1227, 1053, 742 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{15}H_{21}O_2Na$ ([M+Na]$^+$): 255.1356, found: 255.1362; $[\alpha]^{24}_D$ –2.8 (*c* 0.75, $CHCl_3$) (93% ee); HPLC (Daicel Chiralcel OD, hexane/*i*-PrOH = 100/1, flow rate = 1.0 mL/min) t_R = 20.6 min (major), t_R = 23.6 min (minor).

(*R*)-2-(Hydroxymethyl)-2-methylcyclohexanone[2]



^{1}H NMR ($CDCl_3$) δ 1.19 (s, 3H), 1.54-1.96 (m, 5H), 2.00-2.07 (m, 1H), 2.24-2.30 (m, 1H), 2.52 (ddd, 1H, *J* = 6.1, 12.9, 14.4 Hz), 3.48 (d, 1H, *J* = 11.5 Hz), 3.52 (d, 1H, *J* = 11.5 Hz); ^{13}C NMR ($CDCl_3$) δ 20.2, 20.7, 27.3, 35.5, 38.9, 50.1, 69.0, 218.1.

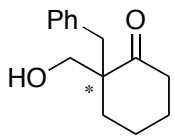
[(*R*)-1-Methyl-2-oxocyclohexyl]methyl benzoate[3]



To a solution of 2-(hydroxymethyl)-2-methylcyclohexanone (14 mg, 0.099 mmol) in CH_2Cl_2 (0.99 mL) were added benzoyl chloride (23 μL, 0.20 mmol) and pyridine (40 μL, 0.49 mmol) at room temperature. After stirring for 2 h, the reaction was quenched with water. The resultant mixture was extracted with CH_2Cl_2 (twice), and the combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. The solvents were evaporated, and the residue was purified by preparative TLC (silica gel, hexane/ethyl acetate (6/1)) to give the desired product (75% yield).

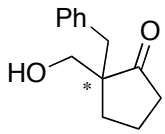
^{1}H NMR ($CDCl_3$) δ 1.26 (s, 3H), 1.73-1.98 (m, 6H), 2.42-2.54 (m, 2H), 4.38 (d, 1H, *J* = 11.0 Hz), 4.46 (d, 1H, *J* = 11.0 Hz), 7.41-7.45 (m, 2H), 7.53-7.58 (m, 1H), 7.99-8.01 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 20.8, 21.0, 27.2, 36.4, 38.8, 48.9, 69.1, 128.3, 129.5, 130.0, 133.0, 166.3, 212.9; IR (neat) 2937, 1718, 1274, 1115, 714 cm^{-1}; Anal. calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. found: C, 73.24; H, 7.54; $[\alpha]^{18}_D$ –0.2 (*c* 0.50, $CHCl_3$) (for *R*, 77% ee); HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 100/1, flow rate = 0.5 mL/min) t_R = 39.7 min (major, *R*), t_R = 42.3 min (minor, *S*).

2-Benzyl-2-(hydroxymethyl)cyclohexanone[3]



^{1}H NMR ($CDCl_3$) δ 1.40-1.48 (m, 1H), 1.60-1.78 (m, 3H), 1.91-2.11 (m, 2H), 2.35-2.41 (m, 1H), 2.55-2.80 (m, 2H), 2.88 (d, 1H, *J* = 13.4 Hz), 3.08 (d, 1H, *J* = 13.4 Hz), 3.34 (d, 1H, *J* = 11.6 Hz), 3.46 (d, 1H, *J* = 11.6 Hz), 7.21-7.31 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 20.6, 27.0, 31.5, 37.0, 39.3, 53.8, 65.6, 126.6, 128.2, 130.5, 135.9, 217.9; IR (neat) 3452, 2941, 1699, 1454, 1061, 706 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{14}H_{18}O_2Na$ ($[M+Na]^+$): 241.1204, found: 241.1204; $[\alpha]^{24}_D$ –8.2 (*c* 1.25, $CHCl_3$) (82% ee); HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 40/1, flow rate = 1.0 mL/min) t_R = 22.1 min (major), t_R = 29.8 min (minor).

2-Benzyl-2-(hydroxymethyl)cyclopentanone



^{1}H NMR ($CDCl_3$) δ 1.56-1.88 (m, 3H), 1.94 (m, 1H), 2.11-2.31 (m, 2H), 2.41 (br, 1H), 2.81 (dd, 2H, *J* = 13, 28 Hz), 3.55 (m, 2H), 7.16 (m, 2H), 7.20-7.30 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 19.0, 29.8, 37.9, 39.1, 54.3, 65.7, 126.6, 128.3, 130.2, 136.8, 224.5; IR (neat) 3438, 1727, 1160, 1053, 757, 705 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{10}H_{16}O_2Na$ ([M+Na]$^+$): 227.1043, found: 227.1040; $[\alpha]^{24}_D$ –4.5 (*c* 0.85, $CHCl_3$) (79% ee); HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 19/1, flow rate = 1.0 mL/min) t_R = 15.1 min (major), t_R = 19.0 min (minor).

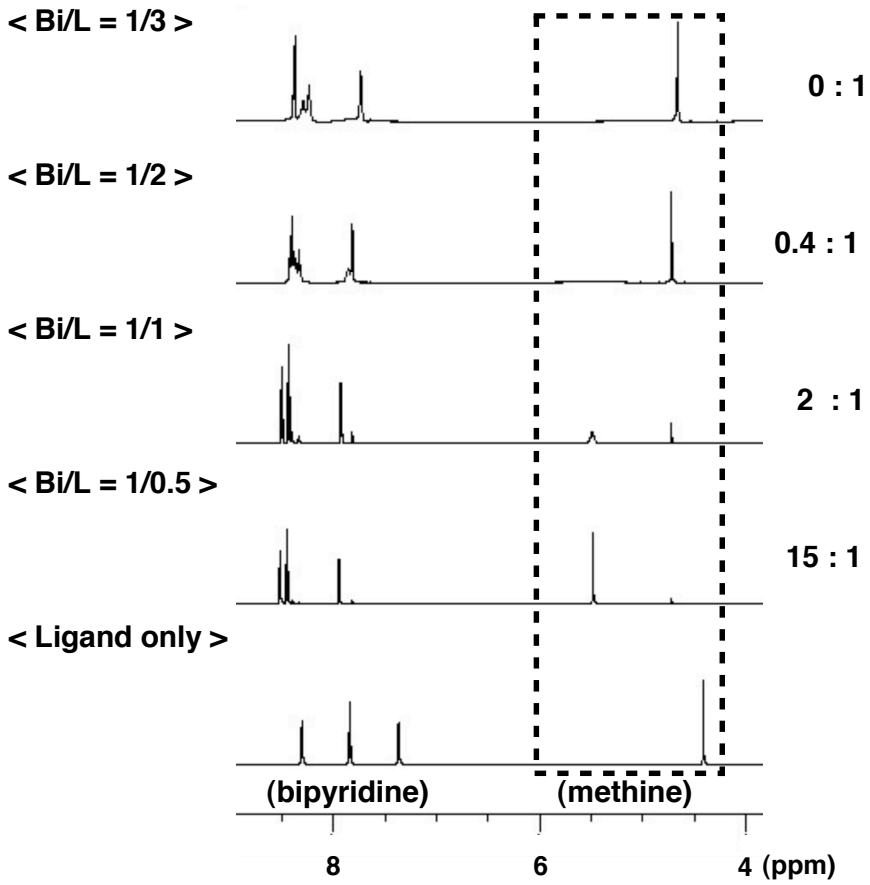
Crystallization of [$BiBr_3$•1]•(H_2O)$_2$•DME complexes

Crystallization of **[$BiBr_3$•1]•(H_2O)$_2$•DME** was carried out as follows: To a yellow solution of $BiBr_3$ (20.2 mg, 45 μmol) in DME (20 μL) was added **1** (14.8 mg, 45 μmol) at room temperature. The solution was warmed to 75 °C (oil bath temperature). Then, a white precipitate was gradually formed, and was dissolved by addition of DME (630 μL). The resulting solution was allowed to stand at room temperature under DME vapor to give the crystals.

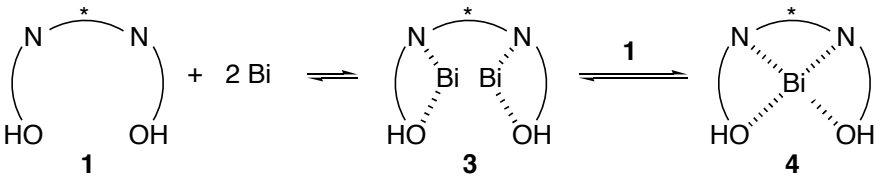
NMR analysis of the catalyst structure

NMR experiments were conducted to obtain some information about the catalyst structure when the Bi(OTf)$_3$-**1** ratio were 1:0.5, 1:1, 1:2 and 1:3 (Figure S-1). When the Bi(OTf)$_3$ and **1** were combined at the ratio of 1:0.5, a signal at 5.49 ppm was dominant. On the other hand, another signal at 4.72 ppm increased when the ratio of **1** to Bi(OTf)$_3$ increased, and finally the former signal disappeared when Bi(OTf)$_3$ was combined with three equivalents of **1**. These results indicate that two equivalents of Bi(OTf)$_3$ and one equivalent of **1** formed complex **3**, and that complex **4** consisting of one equivalent of Bi(OTf)$_3$ and one equivalent of **1** was generated when excess amount of **1** was added (Scheme S-1).

Figure S-1. ^{1}H NMR analysis of the catalyst structure.



Scheme S-1.



Representative Procedure for NMR Experiments: [$Bi(OTf)_3$:**1** = 1:1] A solution of $Bi(OTf)_3$ (24 mg, 0.036 mmol) and **1** (12mg 0.036 mmol) in CD_3CN (900 μL) was stirred at 0 °C for 10 min. D_2O (100 μL) was added to the mixture, and the solution was stirred for 30 min at 0 °C. NMR experiments were conducted at 0 °C using ECX-600 NMR spectrometer. The deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc. and used without further purification.

References

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(2) Miyaoka, H.; Kajiwara, Y.; Hara, M.; Suma, A.; Yamada, Y. *Tetrahedron: Asymmetry* **1999**, *10*, 3189.

(3) Ishikawa, S.; Hamada, T.; Manabe, K.; Kobayashi, S. *J. Am. Chem. Soc.* **2004**, *126,* 12236.