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Supporting Information

A Novel Asymmetric Cyanation Reaction and Sequential Asymmetric Cyanation–Nitroaldol Reaction using YLi_3 tris(binaphthoxide) (YLB) Single Catalyst Component: Catalyst Tuning by Achiral Additives

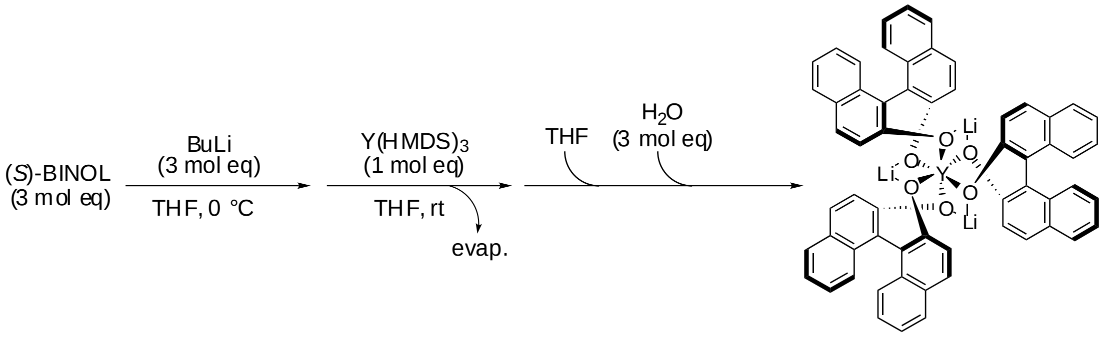
Jun Tian, Noriyuki Yamagiwa, Shigeki Matsunaga and Masakatsu Shibasaki*

Experimental Section

General: Infrared (IR) spectra were recorded on a JASCO FT/IR 410 Fourier transform infrared spectrophotometer. NMR spectra were recorded on a JEOL JNM-LA500 spectrometer, operating at 500 MHz for ^1H NMR and 125.65 MHz for ^{13}C NMR. Chemical shifts in $CDCl_3$ were reported downfield from TMS (= 0) or in the scale relative to $CHCl_3$ (7.24 ppm) for ^1H NMR. For ^{13}C NMR, chemical shifts were reported in the scale relative to $CHCl_3$ (77.0 ppm for ^{13}C NMR) as an internal reference. Optical rotations were measured on a JASCO P-1010 polarimeter. EI mass spectra were measured on JMS-BU20 GCmate. ESI mass spectra were measured on Waters-ZQ4000. Column chromatography was performed with silica gel Merck 60 (230–400 mesh ASTM). The enantiomeric excess (ee) was determined by HPLC analysis and GC analysis. HPLC was performed on JASCO HPLC systems consisting of the following: pump, 880-PU or PU-980; detector, 875-UV or UV-970, measured at 254 nm; column, DAICEL CHIRALCEL OD, OD-H, OJ, and DAICEL CHIRALPAK AD, AS, AD-H; mobile phase, hexane–2-propanol; flow rate, 1.0 mL/min. GC was performed on Shimadzu GC-14A with Varian Chirasil DEX CB column (0.25 mm x 25 m); carrier gas, nitrogen (4 kPa). Reactions were carried out in dry solvents under an argon atmosphere, unless otherwise stated. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. $Y[N(Si(CH_3)_3)_2]_3$ was purchased from Aldrich. Other reagents were purified by the usual methods.

Procedure for Preparation of the (*S*)-Yttrium-Lithium$_3$-tris(binaphthoxide) Complex (YLB 1) :

To a stirred solution of (*S*)-BINOL (1.237 g, 4.32 mmol) in THF (20 mL) at 0 °C, was added BuLi (2.72 mL, 4.32 mmol, 1.59 M in hexanes). To the resulting suspended mixture was added a solution of $Y[N(Si(CH_3)_3)_2]_3$ (820 mg, 1.44 mmol) in THF (20 mL). After stirring for 10 min at room temperature, the solvents were removed under reduced pressure. The residue was dissolved in THF (48 mL), and H_2O (78 mL, 4.23 mmol) was added to give (*S*)-YLB **1**-H_2O solution (30 mM, in THF).



YLi$_3$tris(binaphthoxide) (YLB **1**)

Preparation of tris(2,6-dimethoxyphenyl)phosphine oxide (5b):

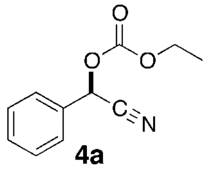
To a stirred solution of tris(2,6-dimethoxyphenyl)phosphine (12.1 g, 27.3 mmol) and Na_2HPO_4 (11.6 g, 81.9 mmol) in CH_2Cl_2 (300 mL) at 0 °C was added *m*CPBA (7.1 g, 60-70% purity, 28.8 mmol). The mixture was stirred at 0 °C for 30 min and, then *sat. aq.* $Na_2S_2O_3$ solution and sat. aq. $NaHCO_3$ solution were added. Organic layer was separated, washed with brine, and was dried over $MgSO_4$. After evaporation, the residue was purified by flash column chromatography (silica gel, acetone/2-propanol = 10/1) to give **5b** as colorless solid (10.6 g, y. 85%). **5b** was used for cyanation reaction after recrystallization from acetone; IR (KBr) ν 2935, 1586, 1465, 1249, 1184, 1098 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.52 (s, 18H), 6.49 (dd, J = 8.3, 6.4 Hz, 6H), 7.21 (t, J = 8.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 56.1, 105.0, 105.1, 131.3, 162.5; EI-MS *m/z* 481 $[M+Na]^+$, 459 (base) $[M^++1]$.

General Procedure for Enantioselective Cyanation Reaction of Aldehyde Promoted by (*S*)-YLB 1 with $Ar_3P(O)$ 5b:

To tris(2,6-dimethoxyphenyl)phosphine oxide (**5b**) (27.5 mg, 0.06 mmol) in a test tube was added the (*S*)-YLB **1**-H_2O solution (2.0 mL, 0.06 mmol, 30 mM in THF). The solution was stirred at room temperature. After completely dissolving **5b**, BuLi (0.06 mmol) was added to the mixture. The mixture solution was cooled down to –78 °C, aldehyde **2a** (0.6 mmol) and ethyl cyanoformate **3** (0.72 mmol) was added and stirred at –78 °C. After stirring for 2 h, 1 M HCl was added to the solution and organic component was extracted with diethyl ether. Organic layer was washed with brine, dried over Na_2SO_4. After evaporating solvent, the residue was purified by silica gel flash column chromatography to give the product **4a** (120.6 mg, 0.59 mmol, y. 98%) as colorless oil. Enantiomeric excess was determined by HPLC (DAICEL CHIRALCEL OD, 2-

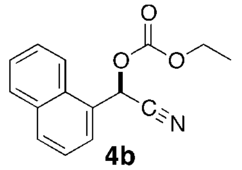
propanol/hexane 1/99, flow 1.0 mL/min, detection at 254 nm) t_R 12.4 min (*R*) and 16.2 min (*S*).

(*R*)-2-Ethoxycarboxy-2-phenylacetonitrile (4a):


4a

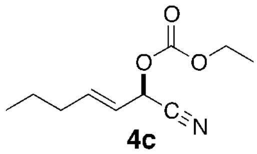
colorless oil; IR (neat) ν 1757, 1249 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.34 (dd, J = 7.2, 7.2 Hz, 3H), 4.24-4.34 (m, 2H), 6.27 (s, 1H), 7.44-7.56 (m, 5H); ^{13}C NMR (CDCl$_3$) δ 14.1, 65.6, 66.4, 115.7, 127.9, 129.27, 130.63, 131.22, 153.42; EI-MS *m/z* 205 [M]$^+$; $[\alpha]_D^{21.7}$ +16.2 (*c* 2.8, CH$_3$Cl) (94% ee), [lit. $[\alpha]_D^{16}$ +13.7 (c 2.8, CHCl$_3$) for *R* enantiomer in 75% ee]; Anal. Calcd for $C_9H_{11}O_3N$; C, 64.38; H, 5.40; N, 6.83; O, 24.39. Found: C, 64.34; H, 5.59; N, 6.64; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 1/99, flow 1.0 mL/min, detection at 254 nm) t_R 12.4 min (*R*) and 16.2 min (*S*). Absolute configuration was determined by from the sign of optical rotation.Lit. Y. Hamashima, D. Sawada, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **1999,** *121*, 2641.

(*R*)-2-Ethoxycarboxy-2-(1-naphthyl)acetonitrile (4b):


4b

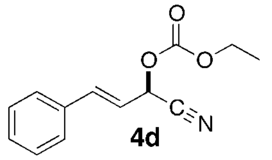
colorless oil; IR (neat) ν 1755, 1248 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.31 (dd, J = 7.5, 7.5 Hz, 3H), 4.23-4.34 (m, 2H), 6.87 (s, 1H), 7.49-8.07 (m, 7H); ^{13}C NMR (CDCl$_3$) δ 13.3, 64.1, 64.9, 115.0, 121.84, 124.25, 125.76, 126.91, 127.03, 128.34, 129.24, 130.94, 133.15, 152.73.; EI-MS *m/z* 255 [M]$^+$, 165 [M–HCO$_2$Et]$^+$; $[\alpha]_D^{23.0}$+36.2 (*c* 2.00 , CH$_3$Cl) (90% ee); HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 1/99, flow 1.0 mL/min, detection at 254 nm) t_R 12.4 min (*R*) and 16.2 min (*S*). Absolute configuration was determined after converting into corresponding 2-hydroxyacid methyl ester. **Methyl (*R*)-2-hydroxy-2-(1-naphthyl)acetate**; colorless oil; ^{1}H NMR (CDCl$_3$) δ 3.72 (s, 3H), 5.81 (s, 1H), 7.43-7.56 (m, 4H), 7.84 (d, J = 7.9 Hz, 1H), 7.87 (d, J = 7.9 Hz, 1H), 8.13 (d, J = 8.5 Hz, 1H);^{13}C NMR (CDCl$_3$) δ 53.0, 71.4, 123.6, 125.2, 125.9, 126.6, 128.8, 129.5, 131.0, 133.9, 134.0, 174.7; $[\alpha]_{435}^{25.9}$ –223 (c 1.25, acetone). [lit. $[\alpha]_{435}^{16}$ +319 (*c* 1.5816, acetone) for *S* enantiomer]. Lit. A. McKenzie, W. S. Dennler, *Ber.* **1937**, *60,* 220.

(*R*)-2-Ethoxycarboxy-3-heptenenitrile (4c):


4c

colorless oil; IR (neat) ν 1757, 1251 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 0.90 (t, J = 7.3 Hz, 3H), 1.32 (dd, J = 7.2, 7.2 Hz, 3H), 1.40-1.47 (m, 2H), 2.07-2.12 (m, 2H), 4.21-4.30 (m, 2H), 5.54-5.59 (m, 1H), 5.65 (dd, J = 6.7, 0.9 Hz, 1H), 6.16 (ddt, J = 15.3, 6.7, 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.7, 14.3, 21.6, 34.1, 65.1, 65.5, 115.5, 119.9, 141.3, 153.5; EI-MS *m/z* 197 $[M]^+$, 169 $[M–CH_2CH_2]^+$; $[\alpha]_D^{23}$ –11.5 (*c* 2.17 , CH_3Cl) (92% ee); Anal. Calcd for $C_{10}H_{15}O_3N$; C, 60.90; H, 7.67; N, 7.10; O, 24.33. Found: C, 60.88; H, 7.78; N, 7.07; GC, injection temp. 120 ℃; initial column temp. 230 ℃; detection temp. 250 ℃; retention time (t_R) of 14.4 min (major), 15.9 min (minor). Absolute configuration was determined after converting into **4e** by hydrogenation.

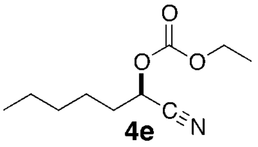
(*R*)-2-Ethoxycarboxy-4-phenyl-3-butenenitrile (4d):



4d

colorless oil; IR (neat) ν 1756, 1250 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.34 (dd, J = 7.0, 7.0 Hz, 3H), 4.24-4.33 (m, 2H), 5.88 (dd, J = 6.8, 1.3 Hz, 1H), 6.22 (dd, J = 15.9, 6.8, 1H), 6.98 (d, J = 15.9 Hz, 1H), 7.31-7.37 (m, 3H) 7.41-7.42 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.1, 65.0, 65.1, 115.1, 117.8, 127.2, 128.9, 129.5, 134.2, 138.4, 153.4.; $[\alpha]_D^{22.4.}$ –17.2 (*c* 2.02, $CHCl_3$) (88% ee); Anal. Calcd for $C_{13}H_{13}O_3N$; C, 67.52; H, 5.67; N, 6.06; O, 20.75. Found: C, 67.25; H, 5.83; N, 5.96; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 1/99, flow 1.0 mL/min, detection at 254 nm) t_R 52.0 min (*S*) and 68.7 min (*R*). Absolute configuration was determined after converting into corresponding 2-hydroxyacid methyl ester; **Methyl (*R*)-2-hydroxy-4-phenyl-3-butenoate:** colorless oil; ^{1}H NMR ($CDCl_3$) δ 3.72 (brs, 1H), 3.82 (s, 3H), 4.83 (dd, J = 5.6, 1.6 Hz, 1H), 6.22 (dd, J = 15.6, 5.6, 1H), 6.79 (dd, J = 15.6, 1.6 Hz, 1H), 7.23-7.26 (m, 1H) 7.29-7.32 (m, 2H), 7.37-7.38 (m, 2H);^{13}C NMR ($CDCl_3$) δ 53.0, 71.28, 125.2, 126.7, 128.1, 128.6, 132.4, 136.0, 173.8.; $[\alpha]_D^{24.4.}$ –32.8 (*c* 0.9, $CHCl_3$))、[lit. $[\alpha]_D^{24.4}$ –67.7 (*c* 0.05 M, $CHCl_3$ for *R* enantiomer). Lit. H.-T. Yu, H. Simon, *Tetrahedron,* **1991**, *47,* 9035.

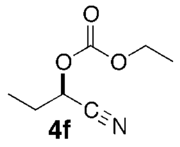
(*R*)-2-Ethoxycarboxyheptanenitrile (4e):



4e

colorless oil; IR (neat) ν 2959, 1758, 1256 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.87-0.90 (m, 3H), 1.31-1.32 (m, 7H), 1.46-1.54 (m, 2H), 1.89-1.94 (m, 2H), 4.22-4.29 (m, 2H), 5.17 (dd, J = 6.7, 6.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.8, 14.1, 22.3, 24.1, 30.9, 32.3, 64.7, 65.4, 116.6, 153.6; EI-MS *m/z* 200 $[M+H^+]$; $[\alpha]_D^{23}$ +61.7 (*c* 2.02 , $CHCl_3$) (94% ee); GC, injection temp. 110 ℃; initial column temp. 230 ℃; detection temp. 250 ℃; retention time (t_R) of 20.0 min (major), 23.1 min (minor). Absolute configuration was determined after converting into corresponding 2-hydroxyacid methyl ester; **Methyl (*R*)-2-hydroxyheptanoic acid**: colorless oil; ^{1}H NMR (C_6D_6) δ 0.83 (t, *J* = 7.0 Hz ,3H), 1.12-1.27 (m, 4 H), 1.37-1.47 (m, 2H), 1.49-1.56 (m, 1H), 1.65-1.72 (m, 1H) 2.64 (brs, 1H), 3.05 (s, 3H), 4.03 (br, 1H); ^{13}C NMR (C_6D_6) δ 14.1, 22.8, 24.8, 31.8, 34.7, 51.7, 70.5, 175.8; $[\alpha]_D^{27.4}$ –7.12 (*c* 2.21, $CHCl_3$), [lit. $[\alpha]_D^{24}$ +12.8 (*c* 2.35, $CHCl_3$ for *S* enantiomer), E. J. Corey, J. O. Link, *Tetrahedron Lett.* **1992**, *33*, 3431]

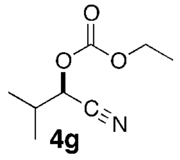
(*R*)-2-Ethoxycarboxybutanenitrile (4f):



4f

colorless oil; IR (neat) ν 1758, 1257 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.11 (dd, J = 7.3, 7.3 Hz, 3H), 1.33 (dd, J = 7.0, 7.0 Hz, 3H), 1.90-2.03 (m, 2H), 4.23-4.29 (m, 2H), 5.13 (dd, J = 6.6, 6.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.2, 13.5, 25.3, 64.7, 65.1, 115.7, 153.0; GC, injection temp. 80 °C; initial column temp. 200 °C; detection temp. 250 °C; retention time (t_R) of 13.1 min (major), 17.8 min (minor).

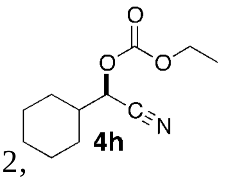
(*R*)-2-Ethoxycarboxy-3-methylbutanenitrile (4g):



4g

colorless oil; IR (neat) ν 1758, 1254 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (d, J = 6.7 Hz, 3H), 1.11 (d, J = 7.0 Hz, 3H), 1.32 (dd, J = 7.0, 7.0 Hz, 3H), 2.13-2.22 (m, 1H), 4.20-4.29 (m, 2H), 5.01 (d, J = 5.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.1, 16.2, 16.6, 30.2, 64.3, 68.9, 114.6, 152.7; EI-MS *m/z* 171 $[M]^+$; $[\alpha]_D^{24.9}$ +80.9 (c 2.210 , $CHCl_3$) (98% ee); Anal. Calcd for $C_8H_{13}O_3N$; C, 56.13; H, 7.65; N, 8.18; O, 28.04. Found: C, 55.91; H, 7.71; N, 7.98; GC, injection temp. 80 °C; initial column temp. 200 °C; detection temp. 250 °C; retention time (t_R) of 16.2 min (*R*), 20.4 min (*S*). Absolute configuration was determined after converting into corresponding 2-hydroxyacid. **(*R*)-2-hydroxy-3-methylbutanoic acid**; ^1H NMR ($CDCl_3$) δ 0.90 (d, J = 7.0 Hz, 3H), 1.04 (d, J = 7.0 Hz, 3H), 2.10-2.19 (ttd, J = 7.0, 7.0, 3.4 Hz, 1H), 4.13 (d, J = 3.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 15.8, 18.7, 32.0, 74.8; $[\alpha]_D^{22.4.}$ –13.7 (*c* 1.11, $CHCl_3$) [lit. $[\alpha]_D^{18}$ +19 (*c* 1.0, $CHCl_3$ for *S* enantiomer)]

(*R*)-2-Ethoxycarboxy-2-cyclohexylacetonitrile (4h):

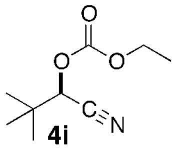


4h

colorless oil; IR (neat) ν 1757, 1254 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04-1.28 (m, 5H), 1.26 (dd, J = 7.2, 7.2 Hz, 3H), 1.61-1.64 (m, 1H), 1.72-1.86 (m, 5H), 4.16 (dq, J = 7.2, 10.4, 1H), 4.20 (dq, J = 7.2, 10.4 Hz, 1H), 4.95 (d, J = 6.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1, 25.2, 25.3, 25.7, 27.8, 28.0, 40.2, 65.4, 69.3 ,115.8, 153.8; EI-MS *m/z* 211 $[M]^+$; $[\alpha]_D^{24.9}$ +53.4 (*c* 2.02 , $CHCl_3$) (96% ee); GC, injection temp. 130 °C; initial column temp. 250 °C; detection temp. 250 °C; retention time (t_R) of 20.2 min (*R*), 21.3 min (*S*). Absolute configuration was determined after converting into corresponding 2-hydroxyacid. **(*R*)-2-hydroxy-2-cyclohexylacetic acid**; ^1H NMR ($CDCl_3$) δ 1.04-1.40 (m, 6H), 1.50-

1.51 (m, 1H), 1.64-1.81 (m, 5H), 4.10 (d, J = 3.4 Hz, 1H); $[\alpha]_D^{\cdot}$ –18.7 (*c* 1.6, CH_3COOH)、 [lit. $[\alpha]_D^{18}$ +23 (*c* 1.0, CH_3COOH for *S* enantiomer)]

(*R*)-2-Ethoxycarboxy-3,3-dimethylbutanenitrile (4i):


4i

colorless oil; IR (neat) ν 2972, 1758, 1258 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09 (s, 9H), 1.32 (dd, J = 7.2, 7.2 Hz, 3H), 4.25 (m, 2H), 4.89 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.0, 24.0, 33.8, 64.2, 72.1, 114.6, 152.8; $[\alpha]_D^{23.1}$+75.6 (χ 2.2 , CH_3Cl) (87% ee); Anal. Calcd for $C_9H_{15}O_3N$; C, 58.36; H, 8.16; N, 7.56; O, 25.92. Found: C, 58.20; H, 8.12; N, 7.36; GC, injection temp. 80 °C; initial column temp. 200 °C; detection temp. 250 °C; retention time (t_R) of 16.9 min (*R*), 18.5 min (*S*). Absolute configuration was determined after converting into corresponding cyanohydrin. **(*R*)-2-hydroxy-3,3-dimethylbutanenitrile**; ^1H NMR ($CDCl_3$) δ 1.05 (s, 9H), 4.10 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 25.1, 35.6, 70.7, 119.3; $[\alpha]_D^{25.1}$ +17.3 (*c* 1.25, $CHCl_3$)、[lit. $[\alpha]_D^{24}$ +14.5 (*c* 1.0, $CHCl_3$) for *R* enantiomer in 70% ee]. Lit. M. Hayashi, Y. Miyamoto, T. Inoue, N. Oguni, *J. Org. Chem.* **1993**, *58*, 1515.

General Procedure for Catalytic Asymmetric Nitroaldol Reaction Promoted by (*S*)-YLB 1:

To a stirred solution of (*S*)-YLB **1**-H_2O solution (2.0 mL, 30 mM in THF, 0.06 mmol). at –40 °C was added aldehyde **2a** (61 μL, 0.60 mmol) and then, CH_3NO_2 (325 μL, 6.0 mmol). The reaction mixture was stirred at –40 °C. After stirring for 20 h, 1 M aq. HCl was added to the solution and organic component was extracted with diethyl ether. Organic layer was washed with brine, dried over Na_2SO_4. After evaporating solvent, the residue was purified by flash column chromatography (silica gel, hexane/ethyl acetate = 6/1) to give the product **7a** (82 mg, 0.492 mmol, y. 82%, 62% ee).

General Procedure for Catalytic Asymmetric Nitroaldol Reaction Promoted by (*S*)-YLB 1 with $Ar_3P(O)$ 5b:

To tris(2,6-dimethoxyphenyl)phosphine oxide (**5b**) (27.5 mg, 0.06 mmol) in a test tube was added the (*S*)-YLB **1**-H_2O solution (2.0 mL, 30 mM in THF, 0.06 mmol). The solution was stirred at room temperature. After completely dissolving **5b**, the mixture solution was cooled down to –40 °C. Aldehyde **2a** (61 μL, 0.60 mmol) and then, CH_3NO_2 (325 μL, 6.0 mmol) were added and the reaction mixture was stirred at –40 °C. After stirring for 20 h, 1 M aq. HCl was added to the solution and organic component was extracted with diethyl ether. Organic layer was washed with brine, dried over Na_2SO_4. After evaporating solvent, the residue was purified by flash column chromatography (silica gel, hexane/ethyl acetate = 6/1) to give the product **7a** (68 mg, 0.408 mmol, y. 68%, 11% ee).

General Procedure for Catalytic Asymmetric Nitroaldol Reaction Promoted by (*S*)-YLB 1 with $Ar_3P(O)$ 5b and $LiBF_4$:

To tris(2,6-dimethoxyphenyl)phosphine oxide (**5b**) (27.5 mg, 0.06 mmol) and $LiBF_4$ (16.9 mg, 0.18 mmol) in a test tube was added the (*S*)-YLB 1-H_2O solution (2.0 mL, 30 mM in THF, 0.06 mmol). The solution was stirred at room temperature. After completely dissolving **5b**, the mixture solution was cooled down to –40 °C. Aldehyde **2a** (61 µL, 0.60 mmol) and then, CH_3NO_2 (325 µL, 6.0 mmol) were added and the reaction mixture was stirred at –40 °C. After stirring for 20 h, 1 M aq. HCl was added to the solution and organic component was extracted with diethyl ether. Organic layer was washed with brine, dried over Na_2SO_4. After evaporating solvent, the residue was purified by flash column chromatography (silica gel, hexane/ethyl acetate = 6/1) to give the product **7a** (84 mg, 0.504 mmol, y. 84%, 59% ee).

Spectra data of nitroaldol adducts (**7a**, **7j**) were identical with literature data.

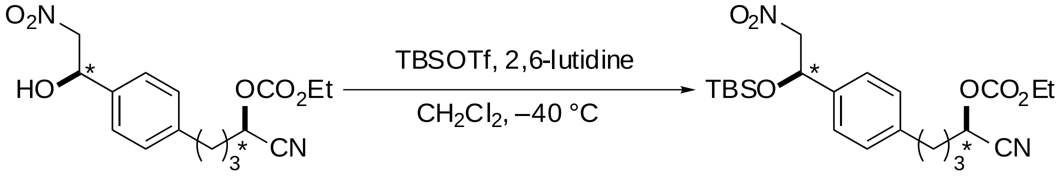
(*R*)-2-Nitro-1-phenylethanol (7a):
$[\alpha]_D^{28.0}$ –26.5 (*c* 2.5, $CHCl_3$) (62% ee). Absolute configuration of **7a** was determined to be *R* from retention time in HPLC analysis reported in the literature.

(*R*)-2-Nitro-1-(4-methylphenyl)ethanol (7j):
$[\alpha]_D^{27.8}$–13.5 (*c* 0.92, CH_3CH_2OH) (62% ee) [lit. $[\alpha]_D^{25}$–23.0 (*c* 0.95, CH_3CH_2OH) for *R* enantiomer in 98% ee]. Absolute configuration of **7j** was determined to be *R* from the sign of optical rotation.

lit. M. Watanabe, K. Murata, T. Ikariya, *J. Org. Chem.* **2002**, *67*, 1712.

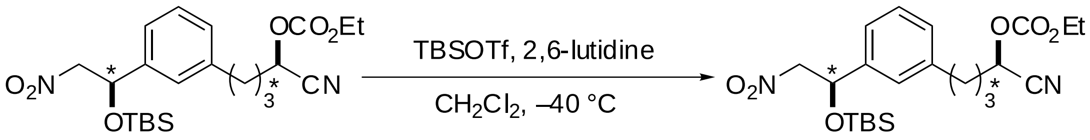
General Procedure for Sequential Asymmetric Cyanation-nitroaldol Reaction Promoted by (*S*)-YLB 1 with $Ar_3P(O)$ 5b and $LiBF_4$:

To tris(2,6-dimethoxyphenyl)phosphine oxide (**5b**) (27.6 mg, 0.06 mmol) in a test tube was added the (*S*)-YLB **1**-H_2O solution (2.0 mL, 30 mM in THF, 0.06 mmol). The solution was stirred at room temperature. After completely dissolving **5b**, BuLi (0.06 mmol) was added to the mixture. This catalyst solution was cooled down to –78 ℃, dialdehyde **8a** (0.6 mmol) and ethyl cyanoformate **3** (0.66 mmol) was added and stirred at –78 ℃. After stirring for 3 h, $LiBF_4$ (90 µL, 2.0 M in THF, 0.18 mmol) was added and the mixture was stirred at –50 °C for 30 min. Then, CH_3NO_2 (325 μL, 6.0 mmol) was added and the reaction mixture was stirred at –50 °C. After stirring for 20 h, 1 M aq. HCl was added to the solution and organic component was extracted with diethyl ether. Organic layer was washed with brine, dried over Na_2SO_4. After evaporating solvent, the residue was purified by flash column chromatography (silica gel, hexane/ethyl acetate = 6/1) to give the product **10a** (156.6 mg, 0.465 mmol, y. 78%, dr = 2.6/1, 93% ee for major diastereomer) as colorless oil. Diastereomeric ratio and enantiomeric excesses were determined by HPLC and NMR analysis after protecting **10a** and **10b** with TBS. Enantiomeric pairs in HPLC chart were determined by ^{1}H-NMR analysis after separating each enantiomer by chiral HPLC.



10a: *p*-substituted

11a: *p*-substituted



10b: *m*-substituted

11b: *m*-substituted

(*2R,1”R*)-2-Ethoxycarboxy-5-[4’-(1”-hydroxy-2”-nitro-ethyl)-phenyl]-pentanenitrile (10a):

(*2R,1”R*)-isomer (major diastereomer):

colorless oil; IR (neat) ν 3515, 2937, 1755, 1553, 1375, 1257 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.33 (t, J = 7.0 Hz, 3H), 1.75-1.84 (m, 2H), 1.85-1.91 (m, 2H), 2.69 (t, J = 7.4 Hz, 2H), 4.15-4.25 (m, 2H), 4.49 (dd, J = 13.4, 3.1 Hz, 1H), 4.59 (dd, J = 13.4, 9.8 Hz, 2H), **5.162 (t, J = 6.4 Hz, 1H),** 5.43 (brdd, J = 9.8, 3.1 Hz, 1H), 7.19 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 13.0, 24.8, 30.6, 33.4, 63.3, 64.4, 69.7, 80.1, 115.3, 125.1, 125.1, 127.9, 127.9, 1 35.1, 140.6, 152.4; ESI-MS *m/z* 359 (base) [M+Na]$^+$.

(*2R,1”S*)-isomer (minor diastereomer):

colorless oil; IR (neat) ν 3515, 2937, 1755, 1553, 1375, 1257 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.33 (t, J = 7.0 Hz, 3H), 1.75-1.84 (m, 2H), 1.85-1.91 (m, 2H), 2.69 (t, J = 7.4 Hz, 2H), 4.15-4.25 (m, 2H), 4.49 (dd, J = 13.4, 3.1 Hz, 1H), 4.59 (dd, J = 13.4, 9.8 Hz, 2H), **5.158 (t, J = 6.4 Hz,1H),** 5.43 (brdd, J = 9.8, 3.1 Hz, 1H), 7.19 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H); ^{13}C NMR (CDCl$_3$) δ 13.0, 24.8, 30.6, 33.4, 63.3, 64.4, 69.7, 80.1, 115.3, 125.1, 125.1, 127.9, 127.9, 135.1, 140.6, 152.4; ESI-MS *m/z* 359 (base) [M+Na]$^+$.

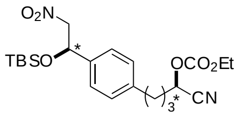
2-Ethoxycarboxy-5-[4’-(1”-tert-butyldimethylsilyloxy-2”-nitro-ethyl)-phenyl]-pentanenitrile (11a):

(*2R,1”R*)-isomer (major diastereomer):

colorless oil; IR (neat) ν 2931, 1759, 1556, 1376, 1257 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ –0.18 (s, 3H), –0.01 (s, 3H), 0.81 (s, 9H), 1.33 (t, J = 7.0 Hz,3H), 1.81-1.87 (m, 2H), 1.89-1.96 (m, 2H), 2.67 (t, J = 7.4 Hz, 2H), 4.20-4.29 (m, 2H), 4.33 (dd, J = 11.9, 3.1 Hz, 1H), 4.50 (dd, J = 11.9, 10.4 Hz, 2H), **5.168 (t, J = 6.4 Hz,1H),** 5.37 (dd, J = 10.4, 3.1 Hz, 1H), 7.16 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H); ^{13}C NMR (CDCl$_3$) δ –6.4, –5.7, 13.3, 17.2, 24.7, 25.0, 31.7, 34.5, 64.4, 65.4, 72.4, 82.7, 116.3, 126.3, 126.3, 128.7, 128.7, 137.2, 141.2, 153.5 ; ESI-MS *m/z* 473 [M+Na]$^+$, 390 (base) [M–CO$_2$Et]$^+$; HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/hexane 1/9, flow 1.0 mL/min, detection at 254 nm) t$_R$ 12.1 min (major) and 54.6 min (minor).

(*2R,1”S*)-(minor diastereomer):

colorless oil; IR (neat) ν 2931, 1759, 1556, 1376, 1257 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ –0.18 (s, 3H), –0.01 (s, 3H), 0.81 (s, 9H), 1.33 (t, J = 7.0 Hz,3H), 1.81-1.87 (m, 2H), 1.89-1.96 (m, 2H), 2.67 (t, J = 7.4 Hz, 2H), 4.20-4.29 (m, 2H), 4.33 (dd, J = 11.9, 3.1 Hz, 1H), 4.50 (dd, J = 11.9, 10.4 Hz, 2H), **5.172 (t, J = 6.4 Hz,1H),** 5.37 (dd, J = 10.4, 3.1 Hz, 1H), 7.16 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H); ^{13}C NMR (CDCl$_3$) δ –6.4, –5.7, 13.3, 17.2, 24.7, 25.0, 31.7, 34.5, 64.4, 65.4, 72.4, 82.7, 116.3, 126.3, 126.3, 128.7, 128.7, 137.2, 141.2, 153.5 ; ESI-MS *m/z* 473 [M+Na]$^+$, 390 (base) [M–CO$_2$Et]$^+$; HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/hexane 1/9, flow 1.0 mL/min, detection at 254 nm) t$_R$ 13.8 min (minor) and 31.9 min (major).

[HPLC chart of **11a**] 

racemic **11a** (dr =1/1 mixture)

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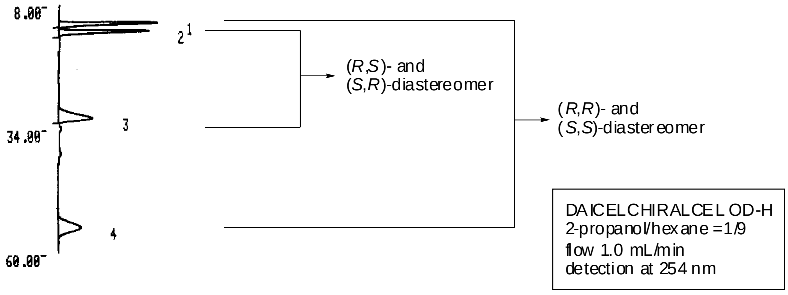

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 2                   13.793     2226361     M         25.2477
 3                   31.886     2155776     M         24.4472
 4                   54.646     2199251               24.9402

       TOTAL                    8818067              100.0000
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chiral **11a** (dr =2.6/1)

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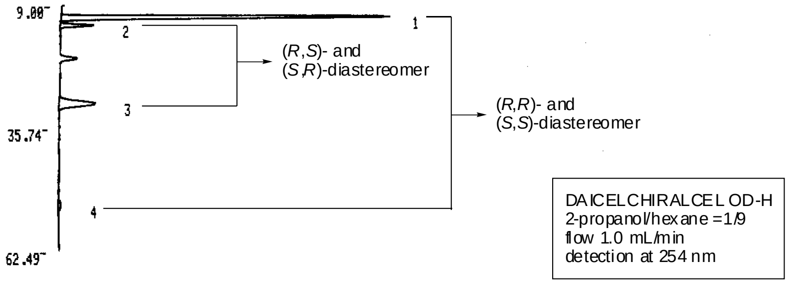

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CAL . METHOD    00
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NO .     NAME          RT        A OR H     MK          CONC

 1                   11.766     1690636               69.7289
 2                   13.460      188150                7.7601
 3                   30.406      488656               20.1542
 4                   52.806       57139                2.3566

       TOTAL                    2424582              100.0000
```

Enantiomeric pairs in the HPLC chart were determined by ^{1}H-NMR analysis after separating each enantiomer by chiral HPLC.

(*2R,1”R*)-2-Ethoxycarboxy-5-[3’-(1”-hydroxy-2”-nitro-ethyl)-phenyl]-pentanenitrile (10b):

(*2R,1”R*)-isomer (major diastereomer):
colorless oil; IR (neat) ν 3508, 2934, 1758, 1556, 1375, 1258 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J = 7.0 Hz, 3H), 1.77-1.83 (m, 2H), 1.84-1.91 (m, 2H), 2.65 (t, J = 7.6 Hz, 2H), 4.14-4.24 (m, 2H), 4.46 (dd, J = 13.5, 3.1 Hz, 1H), 4.54 (dd, J = 13.5, 9.5 Hz, 2H), **5.116 (t, J = 6.4 Hz,1H),** 5.33 (brdd, J = 9.5, 3.1 Hz, 1H), 7.08 (d, J = 7.7 Hz, 1H), 7.15 (d, J = 7.7 Hz, 1H), 7.16 (s, 1H), 7.23 (dd, J = 7.7 Hz, 1H);^{13}C NMR ($CDCl_3$) δ 13.2, 25.0, 30.8, 33.9, 63.6, 64.7, 70.1, 80.4, 115.5, 123.0, 125.0, 128.1, 128.4, 137.6, 140.7, 152.7; ESI-MS m/z 359 (base) [M+Na]$^+$.

(*2R,1”S*)-isomer (minor diastereomer):
colorless oil; IR (neat) ν 3508, 2934, 1758, 1556, 1375, 1258 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J = 7.0 Hz, 3H), 1.77-1.83 (m, 2H), 1.84-1.91 (m, 2H), 2.65 (t, J = 7.6 Hz, 2H), 4.14-4.24 (m, 2H), 4.46 (dd, J = 13.5, 3.1 Hz, 1H), 4.54 (dd, J = 13.5, 9.5 Hz, 2H), **5.108 (t, J = 6.4 Hz,1H),** 5.33 (brdd, J = 9.5, 3.1 Hz, 1H), 7.08 (d, J = 7.7 Hz, 1H), 7.15 (d, J = 7.7 Hz, 1H), 7.16 (s, 1H), 7.23 (dd, J = 7.7 Hz, 1H);^{13}C NMR ($CDCl_3$) δ 13.2, 25.0, 30.8, 33.9, 63.6, 64.7, 70.1, 80.4, 115.5, 123.0, 125.0, 128.1, 128.4, 137.6, 140.7, 152.7; ESI-MS *m/z* 359 (base) [M+Na]$^+$.

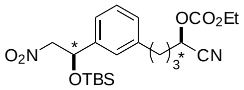
2-Ethoxycarboxy-5-[3’-(1”-tert-butyldimethylsilyloxy-2”-nitro-ethyl)-phenyl]-pentanenitrile (11b):

(*2R,1”R*)-isomer (major diastereomer):
colorless oil; IR (neat) ν 2931, 1758, 1556, 1376, 1258 cm^{-1}; ^{1}H NMR (C_6D_6) δ –0.14 (s, 3H), –0.08 (s, 3H), 0.90 (s, 9H), 1.33-1.37 (m, 2H), 1.40-1.47 (m, 2H), 2.15 (t, J = 7.4 Hz, 2H), 3.71-3.81 (m, 2H), **3.670 (dd, J = 4.3, 11.9 Hz, 1H),** 4.17 (dd, J = 11.9, 10.0 Hz, 2H), 4.79 (t, J = 6.4 Hz,1H), 5.27 (dd, J = 10.0, 4.3 Hz, 1H), 6.74 (d, J = 7.6 Hz, 2H), 6.83 (s, 1H), 6.86 (d, J = 7.6 Hz, 1H), 6.99 (dd, J = 7.6 Hz, 1H); ^{13}C NMR (C_6D_6) δ –5.6, –4.9, 14.0, 18.0, 25.5, 25.9, 31.7, 34.7, 64.3, 65.4, 72.6, 82.7, 116.3, 124.1, 126.0, 128.7, 128.9, 139.6, 141.3, 153.5 ; ESI-MS *m/z* 473 [M+Na]$^+$, 390 (base) [M–CO_2Et]$^+$; HPLC (DAICEL CHIRALPAK AD-H, 2-propanol/hexane 1/150, flow 1.0 mL/min, detection at 254 nm) t_R 31.7 min (major) and 34.6min (minor).

(*2R,1”S*)- (minor diastereomer):

colorless oil; IR (neat) ν 2931, 1758, 1556, 1376, 1258 cm^{-1}; ^{1}H NMR (C_6D_6) δ –0.14 (s, 3H), –0.08 (s, 3H), 0.90 (s, 9H), 1.33-1.37 (m, 2H), 1.40-1.47 (m, 2H), 2.15 (t, J = 7.4 Hz, 2H), 3.71-3.81 (m, 2H), **3.663 (dd, J = 4.3, 11.9 Hz, 1H),** 4.17 (dd, J = 11.9, 10.0 Hz, 2H), 4.79 (t, J = 6.4 Hz,1H), 5.27 (dd, J = 10.0, 4.3 Hz, 1H), 6.74 (d, J = 7.6 Hz, 2H), 6.83 (s, 1H), 6.86 (d, J = 7.6 Hz, 1H), 6.99 (dd, J = 7.6 Hz, 1H); ^{13}C NMR (C_6D_6) δ –5.6, –4.9, 14.0, 18.0, 25.5, 25.9, 31.7, 34.7, 64.3, 65.4, 72.6, 82.7, 116.3, 124.1, 126.0, 128.7, 128.9, 139.6, 141.3, 153.5 ; ESI-MS *m/z* 473 [M+Na]$^+$, 390 (base) [M–CO_2Et]$^+$; HPLC (DAICEL CHIRALPAK AD-H, 2-propanol/hexane 1/150, flow 1.0 mL/min, detection at 254 nm) t_R 27.5 min (major) and 39.1 (minor).

[HPLC chart of **11b**]



racemic **11b** (dr =1/1 mixture)

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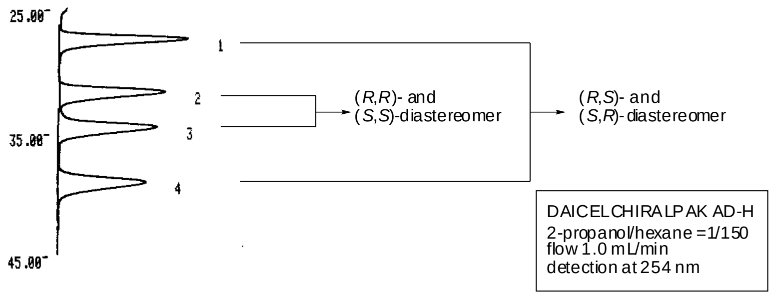

DAICELCHIRALPAK AD-H
2-propanol/hexane =1/150
flow 1.0 mL/min
detection at 254 nm

```
CAL . METHOD    00
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        .100000₁₀+03  .100000₁₀+01  .100000₁₀+01

NO .    NAME          RT        A OR H    MK          CONC

 1                27 .500      495865              25 .1667
 2                31 .740      490889              24 .9142
 3                34 .593      486220              24 .6772
 4                39 .060      497344              25 .2417

        TOTAL                 1970320             100 .0000
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chiral **11b** (dr =3.7/1)

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SAMPLE 359                19:32   MAY   28 2002
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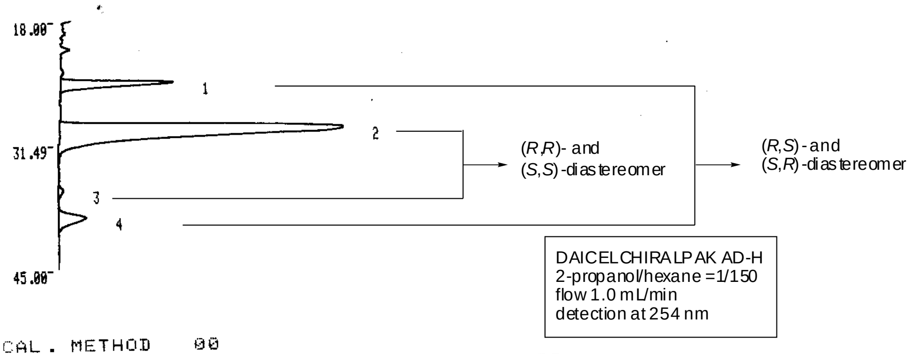

DAICELCHIRALPAK AD-H
2-propanol/hexane =1/150
flow 1.0 mL/min
detection at 254 nm

```
CAL . METHOD    00
                  SF              PA              PB
        .100000₁₀+03  .100000₁₀+01  .100000₁₀+01

NO .    NAME          RT        A OR H    MK          CONC

 1                24 .940      394812              14 .8926
 2                29 .993     2067801              77 .9993
 3                36 .766       25203               0 .9506
 4                39 .606      163232               6 .1572

        TOTAL                 2651049             100 .0000
```

Enantiomeric pairs in HPLC chart were determined by ^{1}H-NMR analysis after separating each enantiomer by chiral HPLC.