New Chiral Schiff Base as Tridentate Ligand for Catalytic Enantioselective Addition of Diethylzinc to Aldehydes

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General methods. All melting points were uncorrected. ^1H and ^{13}C NMR spectra (400 and 100.6 MHz, respectively) were recorded using Me_4Si as an internal standard in CDCl_3 . Diethylzinc and dimethylzinc were kindly donated by Tosoh Finechem Co.

Synthesis of chiral Schiff bases

Oxidation of Alcohol **2** by the Pd/C—ethylene system:

A dry Schlenk tube under an ethylene atmosphere was charged with Alcohol **2** ($\text{R}^1 = \text{Ph}$, 3.9 g, 15.2 mmol) and acetonitrile (20 mL). To this mixture, 10% Pd/C (1.17 g) was added. The mixture was stirred vigorously at 80 °C for 7 h under ethylene atmosphere using a balloon (1 atm). After confirmation of completion of the reaction by TLC, the palladium precipitate was filtered off. After removal of the solvent, the residue was column chromatographed on silica-gel using hexane as an eluent to afford the corresponding ketone **3** ($\text{R}^1 = \text{Ph}$, 3.2 g, 12.6 mmol, 83%) as a yellow oil. ^1H NMR (400 MHz, CDCl_3): δ 1.47 (s, 9H), 6.79 (t, $J = 7.8$ Hz, 1H), 7.44 (dd, $J = 7.8$ Hz, 1.6 Hz, 1H), 7.50 (m, 2H), 7.57 (s, 1H), 7.66 (d, 1H, $J = 6.8$ Hz), 12.9 (brs, 1H); ^{13}C NMR (100.6 MHz, CDCl_3): δ 29.2, 34.9, 119.2, 120.6, 132.0, 134.1, 138.2, 161.2, 197.2.

(*S*)-2-[*N*-(2-hydroxy-3-*tert*-butylsalicylidene)amino-3-methylbutanol (**4a**)

Yield: 98%; R_f 0.13 (5:1 hexane—ethyl acetate); mp 57 °C (lit.¹ 57—58 °C); $[\alpha]_D^{25}$ -38.0 (c 1.0, CHCl₃) ; (lit.¹ $[\alpha]_D^{24}$ -39.8 (c 1.0, CHCl₃)) IR (KBr): $\nu_{\max}$ (cm⁻¹) 3467, 2954, 1451, 1293, 1221, 922, 755; ¹H NMR (400 MHz, CDCl₃): δ 0.94 (d, J = 6.7 Hz, 3H), 0.96 (d, J = 6.7 Hz, 3H), 1.44 (s, 9H), 1.79 (brs, 1H), 1.94 (m, 1H), 3.02 (m, 1H), 3.79 (m, 2H), 6.83 (m, 1H), 7.14 (m, 1H), 7.34 (m, 1H), 8.35 (s, 1H), 13.8 (brs, 1H); ¹³C NMR (100.6 MHz, CDCl₃): δ 18.8, 19.8, 29.4, 29.6, 30.1, 34.9, 64.7, 77.9, 117.9, 118.5, 129.6, 129.9, 137.4, 160.5, 166.7; MS m/z : 264 ($M + H^+$); Anal. Calcd for C₁₆H₂₅NO₂: C, 72.97; H, 9.57; N, 5.32. Found: C, 73.33; H, 9.83; N, 5.32.

(*S*)-2-[*N*-(2-hydroxy-3-*tert*-butylsalicylidene)amino-3,3-dimethylbutanol (**5a**)

Yield: 99%; R_f 0.14 (5:1 hexane—ethyl acetate); mp 58 °C (lit.¹ 55—57 °C); $[\alpha]_D^{25}$ -4.2 (c 1.0, EtOH) (lit.¹ $[\alpha]_D^{24}$ -3.8 (c 1.1, EtOH)); IR (KBr): $\nu_{\max}$ (cm⁻¹) 3495, 2974, 1576, 1432, 1327, 1243, 1225, 1213, 919, 752; ¹H NMR (400 MHz, CDCl₃): δ 0.99 (s, 9H), 1.34 (m, 1H), 1.44 (s, 9H), 2.94 (dd, J =9.4, 3.2 Hz, 1H), 3.77 (ddd, J =10.8, 10.8, 3.2 Hz, 1H), 3.94 (ddd, J =10.8, 9.4, 3.2 Hz, 1H), 6.84 (dd, J =8.0, 8.0 Hz, 1H), 7.16 (dd, J =7.6, 1.6 Hz, 1H), 7.34 (dd, J =7.6, 1.60 Hz, 1H), 8.36 (s, 1H), 13.82 (s, 1H); ¹³C NMR (100.6 MHz, CDCl₃): δ 27.1, 29.4, 33.3, 34.9, 62.6, 81.4, 117.9, 118.5, 129.5, 130.0, 137.4, 160.5, 166.8; MS m/z : 278 ($M + H^+$); Anal. Calcd for C₁₇H₂₇NO₂: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.27; H, 9.76; N, 5.06.

(*S*)-2-{*N*-[1-(2-hydroxy-3-*tert*-butylphenyl)-ethylidene]amino}-3-methyl-1-butanol (**4b**)

Yield: 52%; R_f 0.17 (5:1 hexane—ethyl acetate); $[\alpha]_D^{25}$ -67.3 (c 1.0, CHCl_3); IR (KBr): ν_{max} (cm^{-1}) 3455, 2950, 1632, 1462, 1214, 1146, 931, 754; ^1H NMR (400 MHz, CDCl_3): δ 0.98 (m, 6H), 1.26—1.28 (m, 1H), 1.44 (s, 9H), 1.97~2.02 (m, 1H), 2.41 (s, 3H), 3.73~3.90 (m, 3H), 6.73 (dd, J = 6.8, 7.3 Hz, 1H), 7.33 (d, J = 6.8 Hz, 1H); 7.46 (d, J = 7.3 Hz, 1H), 16.8 (s, 1H); ^{13}C NMR (100.6 MHz, CDCl_3): δ 15.1, 18.8, 19.6, 29.4, 30.6, 35.0, 65.0, 66.5, 116.0, 119.1, 126.5, 129.4, 138.5, 163.5, 172.8; MS m/z : 278 ($\text{M} + \text{H}^+$); Anal. Calcd for $\text{C}_{17}\text{H}_{27}\text{NO}_2$: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.50; H, 10.04; N, 4.75.

(*S*)-2-{*N*-[1-(2-hydroxy-3-*tert*-butylphenyl)-ethylidene]amino}-3,3-dimethyl-1-butanol (**5b**)

Yield: 77%; R_f 0.20 (5:1 hexane—ethyl acetate); mp 99—102 °C; $[\alpha]_D^{27}$ -80.2 (c 1.0, CHCl_3); IR (KBr): ν_{max} (cm^{-1}) 3488, 2993, 1632, 1441, 1344, 1232, 1214, 1141, 911, 742; ^1H NMR (400 MHz, CDCl_3): δ 0.98 (s, 9H), 1.42 (m, 1H), 1.45 (s, 9H), 2.39 (s, 3H), 3.66—3.77 (m, 2H), 3.92 (d, J = 10.4 Hz, 1H), 6.72 (dd, J = 8.0, 8.0 Hz, 1H), 7.32 (dd, J = 8.0, 1.6 Hz, 1H), 16.97 (s, 1H); ^{13}C NMR (100.6 MHz, CDCl_3): δ 15.0, 26.9, 29.4, 33.9, 35.0, 63.3, 69.6, 115.8, 119.0, 126.6, 129.3, 138.5, 163.9, 172.8; MS m/z : 292 ($\text{M} + \text{H}^+$); Anal. Calcd for $\text{C}_{18}\text{H}_{29}\text{NO}_2$: C, 74.18; H, 10.03; N, 4.81. Found: C, 73.89; H, 10.27; N, 4.82.

(*S*)-2-{*N*-[(2-hydroxy-3-*tert*-butylphenyl)-phenyl-methylene]amino}-3-methyl-1-butanol (**4c**)

Yield: 94%; R_f 0.32 (5:1 hexane—ethyl acetate); mp 47 °C ; $[\alpha]_D^{25}$ -54.0 (c 1.0, CHCl_3); IR (KBr): ν_{max} (cm^{-1}) 3466, 2940, 1565, 1422, 1321, 1265, 1254, 1212, 1133, 736; ^1H NMR (400 MHz, CDCl_3): δ 0.86 (d, J = 6.8 Hz, 3H), 0.94 (d, J = 6.8 Hz, 3H), 1.48 (s, 9H), 1.57 (m, 1H), 1.91 (m, 1H), 3.28 (m, 1H), 3.71—3.81 (m, 2H), 6.57 (t, J = 7.8 Hz, 1H), 6.63 (dd, J = 7.8, 1.6 Hz, 1H), 7.17 (m, 1H), 7.30 (dd, J = 8.0, 1.2 Hz, 1H), 7.42—7.50 (m, 4H), 16.12 (s, 1H); ^{13}C NMR (100.6 MHz, CDCl_3): δ 18.9, 19.6, 29.5, 33.4, 35.0, 65.0, 67.8, 116.2, 119.6, 127.9, 128.2, 128.3, 128.4, 128.6, 129.5, 130.2, 134.5, 137.9, 163.0, 175.8; MS m/z : 340 ($\text{M} + \text{H}^+$); Anal. Calcd for $\text{C}_{22}\text{H}_{29}\text{NO}_2$: C, 77.84; H, 8.61; N, 4.13. Found: C, 77.70; H, 8.90; N, 4.05.

(*S*)-2-{*N*-[(2-hydroxy-3-*tert*-butylphenyl)-phenyl-methylene]amino}-3,3-dimethyl-1-butanol (**5c**)

Yield: 92%; R_f 0.30 (5:1 hexane—ethyl acetate); mp 143—144 °C; $[\alpha]_D^{29}$ -44.2 (c 1.0, CHCl_3); IR (KBr): ν_{max} (cm^{-1}) 3476, 2960, 1593, 1442, 1324, 1288, 1254, 1214, 1141, 919, 752, 706; ^1H NMR (400 MHz, CDCl_3): δ 0.93 (s, 9H), 1.36 (t, J = 6.4 Hz, 1H), 1.48 (s, 9H), 3.25 (dd, J = 9.6, 4.8 Hz, 1H), 3.79—3.87 (m, 2H), 6.56 (t, 1H, J = 7.8 Hz), 6.63 (dd, J = 7.8, 1.8 Hz, 1H), 7.16 (m, 1H), 7.30 (dd, J = 7.6, 2.0 Hz, 1H), 7.37 (m, 1H), 7.45 (m, 3H), 16.25 (s, 1H); ^{13}C NMR (100.6 MHz, CDCl_3): δ 27.1, 29.5, 33.9, 35.0, 63.5, 70.9, 116.2, 119.7, 128.0, 128.2, 128.3, 128.6, 129.0, 129.4, 130.3, 134.5, 137.9, 163.0, 175.9; MS m/z : 354 ($\text{M} + \text{H}^+$); Anal. Calcd for $\text{C}_{23}\text{H}_{31}\text{NO}_2$: C, 78.15; H, 8.84; N, 3.96. Found: C, 78.21; H, 8.97; N, 4.02.

(*S*)-2-{*N*-[(2-hydroxy-3-*tert*-butylphenyl)-4-*tert*-butylphenyl-methylene]amino}-3-methyl-1-butanol (**4d**)

Yield: 76%; R_f 0.44 (5:1 hexane–ethyl acetate); mp 86 °C; $[\alpha]_D^{26}$ -45.3 (c 1.0, CHCl_3); ν_{max} (cm^{-1}) 3415, 2961, 1593, 1444, 1326, 1292, 1281, 746; ^1H NMR (400 MHz, CDCl_3): δ 0.87 (d, J = 6.8 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H), 1.38 (s, 9H), 1.48 (s, 9H), 1.60 (brs, 1H), 1.89—1.94 (m, 1H), 3.29—3.34 (m, 1H), 3.74—3.80 (m, 2H), 6.55 (m, 1H), 6.66 (d, J = 7.1 Hz, 1H), 7.05—7.21 (m, 2H), 7.27 (d, 1H, J = 9.8 Hz), 7.45 (d, J = 8.1 Hz, 1H), 16.3 (brs, 1H); ^{13}C NMR (100.6 MHz, CDCl_3): δ 18.8, 19.7, 29.5, 30.4, 30.9, 31.3, 31.6, 34.8, 35.0, 65.0, 67.6, 116.1, 119.8, 125.1, 125.2, 127.6, 128.0, 129.4, 130.3, 131.4, 137.8, 151.6, 163.1, 176.3; MS m/z : 396 ($\text{M} + \text{H}^+$); Anal. Calcd for $\text{C}_{26}\text{H}_{37}\text{NO}_2$: C, 78.94; H, 9.43; N, 3.54. Found: C, 79.06; H, 9.37; N, 3.21.

(*S*)-2-{*N*-[(2-hydroxy-3-*tert*-butylphenyl)-2-naphthyl-methylene]amino}-3-methyl-1-butanol (**4e**)

Yield: 82%; R_f 0.37 (5:1 hexane–ethyl acetate); mp 79—81 °C; $[\alpha]_D^{25}$ -42.3 (c 1.0, CHCl_3); IR (KBr): ν_{max} (cm^{-1}) 3431, 2948, 1601, 1420, 1274, 747; ^1H NMR (400 MHz, CDCl_3): δ 0.85—0.98 (m, 6H), 1.26 (s, 1H), 1.49 (s, 9H), 1.92 (m, 1H), 3.32—3.35 (m, 1H), 3.74—3.85 (m, 2H), 6.53 (t, J = 7.60 Hz, 1H), 6.65 (m, 1H), 7.27—7.94 (m, 9H), 16.17 (s, 1H); ^{13}C NMR (100.6 MHz, CDCl_3): δ 18.9, 19.6, 29.5, 30.4, 35.0, 65.0, 68.0, 116.3, 125.5, 126.0, 126.8, 126.9, 127.2, 127.8, 127.8, 127.9, 128.1, 128.2, 128.5, 129.5, 130.3, 137.9, 162.9, 175.8; MS m/z : 390 ($\text{M} + \text{H}^+$); Anal. Calcd for $\text{C}_{26}\text{H}_{31}\text{NO}_2$: C, 80.17; H, 8.02; N, 3.60. Found: C, 79.88; H, 8.21; N, 3.36.

(*S*)-2-{*N*-[(2-hydroxy-3-*tert*-butylphenyl)-2-naphthyl-methylene]amino}-3,3-dimethyl-1-butanol (**5e**)

Yield: 63%; R_f 0.34 (5:1 hexane–ethyl acetate); mp 208 °C; $[\alpha]_D^{25}$ -38.0 (c 1.0, CHCl_3); IR (KBr): ν_{max} (cm^{-1}) 3429, 2956, 1595, 1440, 1284, 751; ^1H NMR (400 MHz, CDCl_3): δ 0.92 (s, 9H), 1.45 (s, 1H), 1.50 (s, 9H), 3.27—3.33 (m, 1H), 3.84 (m, 2H), 6.52 (dd, J = 8.0, 8.0 Hz, 1H), 6.63 (dd, J = 8.4, 5.2 Hz, 1H), 7.24—7.94 (m, 9H), 16.27 (s, 1H); ^{13}C NMR (100.6 MHz, CDCl_3): δ 27.1, 29.5, 33.8, 35.0, 63.4, 71.0, 116.2, 125.8, 126.6, 126.7, 126.9, 127.5, 127.7, 127.8, 127.9, 128.2, 128.5, 128.6, 129.4, 130.4, 137.9, 162.9, 175.7; MS m/z : 405 ($\text{M} + \text{H}^+$); Anal. Calcd for $\text{C}_{27}\text{H}_{33}\text{NO}_2$: C, 80.36; H, 8.24; N, 3.47. Found: C, 80.10; H, 8.42; N, 3.49.

Enantioselective addition of diethylzinc to aldehydes

General procedure for asymmetric ethylation (Table. 2): To a solution of chiral Schiff base (0.018 mmol) in solvent (4 mL) at -40 °C was added diethylzinc (0.37mL, 3.6 mmol). The solution was warmed up to 0 °C, stirred for 30 min and then cooled to -40 °C again, when aldehyde (1.8 mmol) was added. The mixture was stirred for 24 h at 0 °C and was then quenched by 1N HCl *aq.* (20 mL). After extraction with diethylether (20 mL x 3), silica-gel column chromatography [eluent, hexane–ethyl acetate (10:1)] and Kugelrohr distillation, a product was obtained. The ee was determined by HPLC analysis using chiral column.

1-Phenyl-1-propanol: $[\alpha]_D^{29} = +41.9$ (c 1.00, CHCl_3) (lit.² $[\alpha]_D^{20} = +42.9$ (c 3.58, CHCl_3 , 87.5% ee (R))). The ee of the product was determined as 96% ee by HPLC analysis. : t_R of R -isomer, 11.07 min; t_R of S -isomer, 13.36 min [column, CHIRALCEL OD-H (DAICEL): eluent, hexane-2-propanol (97.5:2.5), 1.0 mL/min].

検出器 A-254 nm ピーク番号	保持時間	面積	面積%
1	11.086	14084120	97.81
2	13.440	315756	2.19
Total		14399876	100.00

1-(4-Chlorophenyl)-1-propanol: $[\alpha]_D^{28} = +24.1$ (c 1.00, benzene) (lit.² $[\alpha]_D^{20} = +26.4$ (c 5.27, benzene, 96.9% ee (R))). The ee of the product was determined as 90% ee by HPLC analysis. : t_R of R -isomer, 15.10 min; t_R of S -isomer, 13.96 min [column, CHIRALCEL OD-H (DAICEL): eluent, hexane-2-propanol (95:5), 0.5 mL/min].

検出器 A-254 nm ピーク番号	保持時間	面積	面積%
1	13.960	54348	4.82
2	15.099	1073396	95.18
Total		1127744	100.00

1-(4-Methoxyphenyl)-1-propanol: $[\alpha]_D^{28} = +25.7$ (c 1.00, benzene) (lit.² $[\alpha]_D^{20} = +31.3$ (c 4.84, benzene, 95.8% ee (*R*))). The ee of the product was determined as 80% ee by HPLC analysis. : t_R of *R* –isomer, 19.57 min; t_R of *S* –isomer, 23.09 min [column, CHIRALCEL OD-H (DAICEL): eluent, hexane–2-propanol (95:5), 0.5 mL/min].

(*E*)-1-Phenylpent-1-en-3-ol: $[\alpha]_D^{28} = +6.1$ (c 1.01, CHCl_3) (lit.² $[\alpha]_D^{20} = +5.2$ (c 1.91, CHCl_3 , 81.3% ee (*R*))). The ee of the product was determined as 75% ee by HPLC analysis. : t_R of *R* –isomer, 12.23 min; t_R of *S* –isomer, 20.79 min [column, CHIRALCEL OD-H (DAICEL): eluent, hexane–2-propanol (95:5), 1.0 mL/min].

1-Phenylpent-1-yn-3-ol: $[\alpha]_D^{28} = +12.5$ (c 1.00, Et₂O) (lit.³ $[\alpha]_D = +7.8$ (c 2.12, Et₂O, 38% ee (*R*))). The ee of the product was determined as 61% ee by HPLC analysis. : t_R of *R*-isomer, 8.54 min; t_R of *S*-isomer, 21.55 min [column, CHIRALCEL OD-H (DAICEL): eluent, hexane-2-propanol (95:5), 1.0 mL/min].

1-Phenyl-3-pentanol: $[\alpha]_D^{29} = -23.4$ (c 1.00, EtOH) (lit.³ $[\alpha]_D = -21.2$ (c 7.72, EtOH, 94% ee (*R*))). The ee of the product was determined as 81% ee by HPLC analysis. : t_R of *R*-isomer, 9.51 min; t_R of *S*-isomer, 13.60 min [column, CHIRALCEL OD-H (DAICEL): eluent, hexane-2-propanol (95:5), 1.0 mL/min].

3-Octanol: $[\alpha]_D^{28} = -7.4$ (c 1.00, CHCl_3) (lit.⁴ $[\alpha]_D^{20} = +12.5$ (c 1.29, CHCl_3 , 56% ee (S))). The ee of the product was determined as 83% ee by HPLC analysis of its benzoate. : t_R of R -isomer, 14.17 min; t_R of S -isomer, 13.76 min [column, CHIRALCEL OD-H (DAICEL): eluent, hexane-2-propanol (99.94:0.06), 0.5 mL/min].

1-Cyclohexyl-1-propanol: $[\alpha]_D^{28} = +4.5$ (c 1.00, CHCl_3) (lit.² $[\alpha]_D^{20} = +6.35$ (c 3.00, CHCl_3 , 94.8% ee (R))). The ee of the product was determined as 93% ee by HPLC analysis of its benzoate. : t_R of R -isomer, 9.48 min; t_R of S -isomer, 11.50 min [column, CHIRALCEL AD-H (DAICEL): eluent, hexane-2-propanol (99.9:0.1), 1.0 mL/min].

1-Furyl-1-propanol: $[\alpha]_D^{26} = +25.9$ (c 2.10, CHCl_3) (lit.² $[\alpha]_D^{20} = +14.3$ (c 2.20, CHCl_3 , 78% ee (R))). The ee of the product was determined as 90% ee by HPLC analysis of its benzoate. : t_R of R -isomer, 11.07 min; t_R of S -isomer, 12.60 min [column, CHIRALCEL AD-H (DAICEL): eluent, hexane-2-propanol (98:2), 0.5 mL/min].

1-Thienyl-1-propanol: $[\alpha]_D^{28} = +26.4$ (c 2.20, CHCl_3) (lit.² $[\alpha]_D^{20} = +25.3$ (c 2.24, CHCl_3 , 94.9% ee (R))). The ee of the product was determined as 95% ee by HPLC analysis of its benzoate. : t_R of R -isomer, 6.81 min; t_R of S -isomer, 8.91 min [column, CHIRALCEL AD-H (DAICEL): eluent, hexane-2-propanol (98:2), 0.5 mL/min].

Enantioselective addition of dimethylzinc to benzaldehydes

1-Phenyl-1-ethanol: $[\alpha]_D^{28} = +29.7$ (c 1.01, CH_2Cl_2) (lit.⁵ $[\alpha]_D^{21} = +43.6$ (neat, 98.8% ee (R))). The ee of the product was determined as 64% ee by HPLC analysis. : t_R of R – isomer, 13.65 min; t_R of S – isomer, 17.95 min [column, CHIRALCEL OD-H (DAICEL): eluent, hexane–2-propanol (97.5:2.5), 1.0 mL/min].

NMR spectra of zinc-Schiff base complex

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