Supporting Information

Enantioselective Construction of Quaternary Stereocenter through a Reissert-Type Reaction Catalyzed by Electronically Tuned Bifunctional Catalyst: Efficient Synthesis of Various Biologically Significant Compounds

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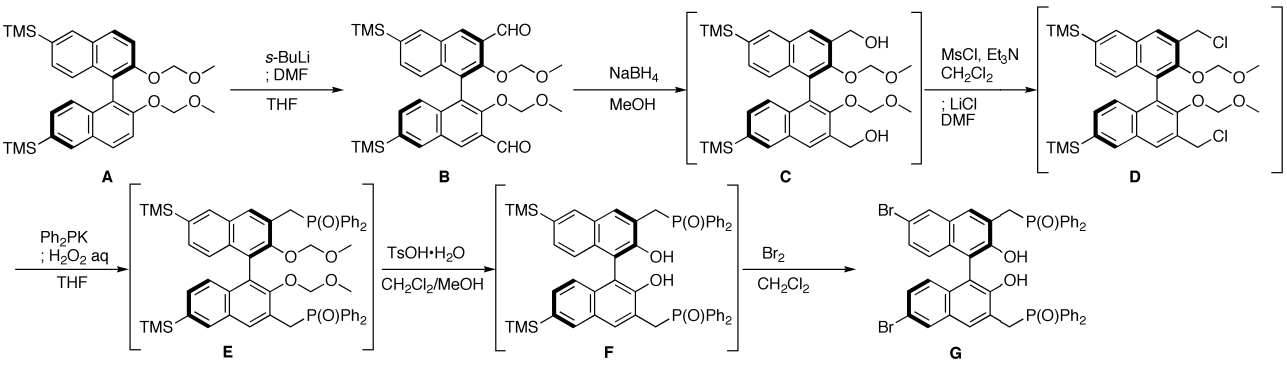
General: NMR spectra were recorded on a JEOL JNM-LA500 spectrometer, operating at 500 MHz for ^{1}H NMR, 125.65 MHz for ^{13}C NMR, and 202 MHz for ^{31}P NMR. Chemical shifts in $CDCl_3$ were reported downfield from TMS (= 0) for ^{1}H NMR. For ^{13}C NMR, chemical shifts were reported in the scale relative to $CDCl_3$ (77.00 ppm for ^{13}C NMR) as an internal reference. ^{31}P NMR were carried out with phosphoric acid (85%) as an external standard. Optical rotations were measured on a JASCO P-1010 polarimeter. Mass spectra were measured on a JEOL BU-20 spctrometer. Column chromatography were performed with silica gel Merck 60 (230-400 mesh ASTM). The enantiomeric excess (ee) were determined by HPLC analysis. HPLC analysis 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 CHIRALPAK AS, AD, or DAICEL CHIRALCEL OJ, OD, OD-H; mobile phase, hexane/2-propanol; flow rate, 1.0-1.5mL/min. In general, reactions were carried out in dry solvents under an argon atmosphere, unless otherwise specified. Tetrahydrofuran (THF) and diethyl ether were distilled from sodium benzophenone ketyl. Dichloromethane (CH_2Cl_2) was distilled from calcium hydride. Diethylaluminum chloride in hexane (1 M) and trimethylaluminium in hexane (1 M) were purchased from KANTO CHEMICAL. CO., INC., 2-8, Nihonbashi, Honcho 3-chome, Chuo-ku, Tokyo, 103-0023, Japan (fax: +813-3667-6892). Other reagents were purified by usual methods.

Synthesis of the ligand for the catalyst 6



(*R*)-2,2'-Bis(methoxymethoxy)-6,6'-bis(trimethylsilyl)-1,1'-binaphthyl (A) was prepared according to a procedure developed by Shu Kobayashi et al. (Yamshita, H.; Ishitani, H.; Shimizu, H.; Kobayashi, S. *submitted for publication*): (*R*)-2,2'-Bis(methoxymethoxy)-6,6'-dibromo-1,1'-binaphthyl (*J. Am. Chem. Soc.* **2000**, *122*, 8180–8186) in THF was treated with *n*-BuLi at -78 °C and subsequent addition of trimethylsilyl chloride at the same temperature afforded the product **A** in quantitative yield.

(*R*)-3,3'-Diformyl-2,2'-bis(methoxymethoxy)-6,6'-bis(trimethylsilyl)-1,1'-binaphthyl (B): To a solution of (*R*)-2,2'-bis(methoxymethoxy)-6,6'-bis(trimethylsilyl)-1,1'-binaphthyl (**A,** 7.95 g, 15.3 mmol) in THF (76.5 mL), was added *sec*-BuLi (45.9 mL of a 1.0 M soln. in cyclohexane, 45.9 mmol) at –78 °C. After 1 h, DMF (7.11 mL, 91.8 mmol) was added over 10 min and kept stirring for 12 h at –40 °C. Quench with satd. NH_4Cl aq, extraction with AcOEt and purification by silica gel column chromatography (hexane-Et_2O) gave the product **B** in 68% yield as a pale yellow solid. ^{1}H NMR ($CDCl_3$): δ 0.34 (s, 18H), 2.92 (s, 6H), 4.71 (dd, *J* = 22.0, 6.1 Hz, 4H), 7.19 (d, *J* = 8.2 Hz, 2H), 7.53 (dd, *J* = 8.6, 1.2 Hz, 2H), 8.21 (s, 2H), 8.62 (s, 2H), 10.55 (s, 2H); ^{13}C NMR ($CDCl_3$): δ -1.3, 57.1, 100.6, 125.0, 126.0, 128.9, 129.5, 132.4, 133.7, 136.1, 136.9, 138.8, 154.3, 190.6; $[\alpha]^{24}_{D}$ -73.4 (*c* 2.0, $CHCl_3$); IR (neat) 2954, 1692, 1610, 1582, 1389, 1248, 1159, 1097, 842 cm^{-1}; EI-MS m/z 574 (M^+); Anal. Calcd. for $C_{32}H_{38}O_6Si_2$: C, 66.86; H, 6.66. Found: C, 66.84; H, 6.76.

(*R*)-3,3'-Bis(hydroxymethyl)-2,2'-bis(methoxymethoxy)-6,6'-bis(trimethylsilyl)-1,1'-binaphthyl (C): To a solution of **B (**2.00 g, 3.48 mmol) in MeOH (11.6 mL), was added $NaBH_4$ (329 mg, 8.70 mmol) at 0 °C. Quenching with satd. NH_4Cl aq and extraction with AcOEt gave the crude product **C** in 99% approximate yield as a white solid. This crude mixture was used in the next step without further purification. ^{1}H NMR ($CDCl_3$): δ 0.32 (s, 18H), 3.23 (s, 6H), 3.43 (br, 2H), 4.47 (dd, *J* = 13.5, 6.5 Hz, 4H), 4.85 (bd, *J* = 12.2 Hz, 2H), 4.99 (bd, *J* = 12.6 Hz, 2H), 7.12 (d, *J* = 8.3 Hz, 2H), 7.38 (dd, *J* = 8.6 1.0 Hz, 2H), 8.02 (s, 2H), 8.06 (s, 2H); ^{13}C NMR ($CDCl_3$): δ -1.0, 57.4, 62.1, 99.6, 124.9, 125.1, 130.1, 130.5, 131.1, 134.2, 134.6, 137.6, 153.6; EI-MS m/z 578 (M^+).

(*R*)-3,3'-Bis(chloromethyl)-2,2'-bis(methoxymethoxy)-6,6'-bis(trimethylsilyl)-1,1'-binaphthyl (D): To a solution of crude mixture **C (**1.99 g, <3.44 mmol) in CH_2Cl_2 (6.9 mL), was added Et_3N (1.68 mL, 12.0 mmol) and then methanesulfonyl chloride (799 μL, 10.3 mmol) at 0 °C, and the mixture was stirred for 20 min. DMF (6.9 mL) and LiCl (874 mg, 20.6 mmol) were added subsequently to the mixture, which was further stirred for 3 h. Quenching with satd. $NaHCO_3$ aq and extraction with AcOEt gave the crude product **D** in 87% approximate yield as a colorless oil. This crude mixture was used in the next step without further purification. ^{1}H NMR ($CDCl_3$): δ 0.32 (s, 18H), 3.02 (s, 6H), 4.57 (dd, *J* = 51.6, 5.8 Hz, 4H), 4.97 (dd, *J* = 22.6, 11.9 Hz, 4H), 7.14 (d, *J* = 8.7 Hz, 2H), 7.40 (dd, *J* = 8.6, 1.0 Hz, 2H), 8.05 (s, 2H), 8.12 (s, 2H); ^{13}C NMR ($CDCl_3$): δ -1.0, 42.6, 57.1, 99.7, 125.0, 125.3, 130.2, 131.2, 131.5, 134.1, 134.5, 137.7, 152.6; EI-MS m/z 614 (M^+).

(*R*)-3,3'-Bis(diphenylphosphinoylmethyl)-2,2'-bis(methoxymethoxy)-6,6'-bis(trimethylsilyl)-1,1'-binaphthyl (E): To a solution of crude mixture **D (**900 mg, <1.46 mmol) in THF (6.4 mL), was added potassium diphenylphosphide (6.43 mL of a 0.5 M soln in THF, 3.22 mmol) at 0 °C, and the mixture was stirred for 20 min. Quenching with satd. NH_4Cl aq. and oxidation with excess H_2O_2 aq (30-35%), extraction with AcOEt gave the crude product **E** as a pale yellow oil. This crude mixture was used in the next step without further purification. ^{1}H NMR ($CDCl_3$): δ 0.29 (s, 18H), 2.88 (s, 6H), 4.10 (dt like, *J* = 95.0, 15.3 Hz, 4H), 4.20 (m, 4H), 6.82 (d, *J* = 13.3 Hz, 2H), 7.25 (d, *J* = 8.3 Hz, 2H), 7.41–7.51 (m, 14H), 7.80 (dd, *J* = 11.3, 7.3 Hz, 4H), 7.92 (m, 4H), 8.00 (s, 2H), 8.36 (d, *J* = 2.1 Hz, 2H); ^{31}P NMR ($CDCl_3$): δ 31.5.

(*R*)-3,3'-Bis(diphenylphosphinoylmethyl)-2,2'-dihydroxy-6,6'-bis(trimethylsilyl)-1,1'-binaphthyl (F): To a solution of crude mixture **E (**1.4 g, <1.46 mmol) in CH_2Cl_2/MeOH (1/1, 10 mL), was added *p*-toluenesulfonic acid monohydrate (55.6 mg, 0.292 mmol) at room temperature, and the mixture was stirred for 4.5 h. Extraction with AcOEt gave the crude product **F** as a pale yellow oil. This crude mixture was used in the next step without further purification. ^{1}H NMR ($CDCl_3$): δ 0.27 (s, 18H), 3.92–4.06 (m, 4H), 6.86 (d, *J* = 8.2 Hz, 2H), 7.25 (s, 2H), 7.42–7.53 (m, 14H), 7.76–7.83 (m, 10H), 7.85 (s, 2H); ^{31}P NMR ($CDCl_3$): δ 34.9.

(*R*)-6,6'-Dibromo-3,3'-bis(diphenylphosphinoylmethyl)-2,2'-dihydroxy-1,1'-binaphthyl (G): To a solution of the crude mixture **F** (1.3 g, <1.46 mmol) in CH_2Cl_2 (7.3 mL), was added Br_2 (187 μL, 3.65 mmol) at 0 °C. The reaction mixture was stirred for 20 min, then an excess of Na_2SO_3 aq was added. Extraction with AcOEt and filtration over celite, recrystallization (CH_2Cl_2-Et_2O) gave the product **G** in 54% yield from **D** (3 steps) as a white solid. ^{1}H NMR ($CDCl_3$): δ 3.97 (dt like, *J* = 57.4, 14.0 Hz, 4H), 6.75 (d, *J* = 9.2 Hz, 2H), 7.21 (dd, *J* = 9.2, 1.9 Hz, 2H), 7.44–7.56 (m, 14H), 7.74–7.77 (m, 10H); ^{13}C NMR ($CDCl_3$): δ 34.8 (d, *J* = 66.1 Hz), 117.4, 118.4, 123.2, 123.3, 126.6, 128.8, 128.9, 129.5, 129.6, 130.0, 130.2, 130.3, 131.0, 131.06, 131.11, 131.13, 131.9, 132.4, 132.5, 132.5, 152.1 (d, *J* = 4.1 Hz); ^{31}P NMR ($CDCl_3$): δ 36.1; $[\alpha]^{25}_D$ +39.7 (*c* 0.65, $CHCl_3$); IR (neat) 1590, 1487, 1438, 1388, 1333, 1157, 1122, 1069, 933, 900, 748, 693 cm^{-1}; FAB-MS m/z 1005 (M + Cs^+); FAB-HRMS Calcd. for $C_{46}H_{34}{}^{79}Br^{81}BrCsO_4P_2$ (M + Cs^+) 1004.9333, Found 1004.9333.

A representative procedure for the preparation of the catalysts 3-9 (Y = Cl)
Preparation of the catalyst 6 (Y = Cl)

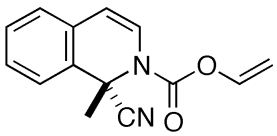
To a solution of ligand **G** (13.1 mg, 0.015 mmol) in CH_2Cl_2 (3.0 mL), was added Et_2AlCl (16.1 μL of a 0.93 M soln in hexane, 0.015 mmol) at ambient temperature and the resulting solution was stirred for 1 h.

A representative procedure for the preparation of the catalysts 3-9 (Y = OTf)
Preparation of the catalyst 6 (Y = OTf)

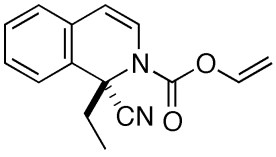
To a solution of ligand **G** (13.1 mg, 0.015 mmol) in CH_2Cl_2 (2.75 mL), was added Me_3Al (15.3 μL of a 0.98 M soln in hexane, 0.015 mmol) at ambient temperature and the resulting solution was stirred for 1 h. Trifluoromethanesulfonic acid (250 μL of a 0.0585 M soln in CH_2Cl_2, 0.146 mmol, 97.5 mol % to Me_3Al) was added and the mixture was stirred for 30 min. A white precipitate often generated, which was then completely dissolved when the isoquinoline was added. The catalysts **6** with Y = NTf_2 and BF_4 were also prepared from the ligand, Me_3Al, and HY.

General procedure for the catalytic enantioselective Reissert-type reaction .

To the catalyst solution (or suspension), as prepared above, was added a solution of isoquinoline **1** (0.600 mmol) in CH_2Cl_2 (2.25 mL), followed by TMSCN (160 μL, 1.20 mmol) and vinyl chloroformate (91.8 μL, 1.08 mmol) at −60 °C. After 48 h, 5% NH_3 aq was added. Extraction with AcOEt and purification by silica gel column chromatography (hexane–AcOEt) gave the product **2**. For the reactions with 1-phenylisoquinoline (**1g**) and 1-(2-bromo-phenyl)isoquinoline (**1h**), CH_2Cl_2 was used for both extraction and chromatography instead of AcOEt. The enantiomeric excess were determined by chiral HPLC analysis. The absolute configurations of **2h** and **2i** were determined by comparison of the optical rotation after conversion into the known compounds **10** and **12** respectively. The absolute configurations of **2a-g** were assigned tentatively.

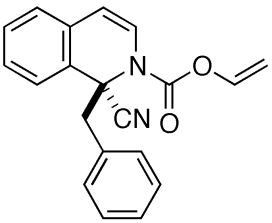


(+)-1-Cyano-1-methyl-1,2-dihydroisoquinoline-2-carboxylic acid vinyl ester (2a): colorless oil; ^{1}H NMR ($CDCl_3$): δ 1.94 (s, 3H), 4.68 (dd, J = 6.1, 1.7 Hz, 1H), 5.03 (d, J = 13.5 Hz, 1H), 5.77 (d, J = 8.3 Hz, 1H), 6.87 (d, J = 8.2 Hz, 1H), 7.02–7.05 (m, 1H), 7.25–7.29 (m, 3H), 7.57–7.59 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 28.5, 56.9, 98.3, 106.5, 119.0, 122.7, 125.4, 126.1, 127.4, 128.2, 129.4, 130.2, 141.4, 149.5; $[\alpha]^{25}_D$ +146 (*c* 0.72, $CHCl_3$, 89% ee); HPLC (DAICEL CHIRALCEL OD-H, hexane/2-propanol 98/2, 1.2 mL/min) t_R 8.5 min and 13.5 min; IR (neat) 1734, 1649, 1454, 1328, 1265, 1217, 1141, 1094, 775, 755 cm^{-1}; EI-MS m/z 241 (M^++1), 240 (M^+); EI-HRMS Calcd. for $C_{14}H_{13}N_2O_2$(M^++^{1}H) 241.0977, Found 241.0968.

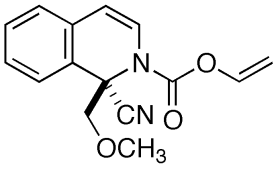


(+)-1-Cyano-1-ethyl-1,2-dihydroisoquinoline-2-carboxylic acid vinyl ester (2b): colorless oil; ^{1}H NMR ($CDCl_3$): δ 0.87 (t, J = 7.3 Hz, 3H), 2.11 (m, 1H), 2.60 (m, 1H), 4.68 (dd, J = 6.2, 1.8 Hz, 1H), 5.02 (d, J = 12.8 Hz,

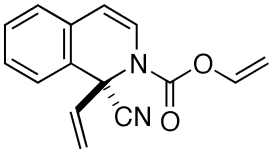
1H), 5.73 (d, *J* =8.3 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 7.02–7.07 (m, 1H), 7.26–7.34 (m, 3H), 7.52–7.55 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 33.0, 59.9, 97.2, 105.7, 117.4, 122.8, 124.2, 125.7, 126.8, 126.8, 127.7, 128.4, 140.4, 148.4; $[\alpha]^{25}_{D}$ +201 (*c* 3.0, $CHCl_3$, 87% ee); HPLC (DAICEL CHIRALCEL OD-H, hexane/2-propanol 9/1, 1.0 mL/min) t_R 6.4 min and 7.6 min; IR (neat) 1735, 1650, 1495, 1455, 1384, 1324, 1256, 1202, 1147, 941, 870, 774, 751, 600 cm^{-1}; EI-MS m/z 251 (M^+); EI-HRMS Calcd. for $C_{15}H_{14}N_2O_2$(M^+) 254.1055, Found 254.1059.



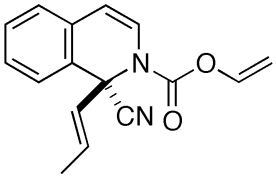
(+)-1-Benzyl-1-cyano-1,2-dihydroisoquinoline-2-carboxylic acid vinyl ester (2c): colorless oil; ^{1}H NMR ($CDCl_3$): δ 3.32 (d, *J* = 13.2 Hz, 1H), 3.66 (br, 1H), 4.67 (dd, *J* = 6.1, 2.1 Hz, 1H), 5.01 (d, *J* = 12.2 Hz, 1H), 5.50 (br, 1H), 6.72–6.76 (m, 3H), 6.93 (d, *J* = 7.3 Hz, 1H), 7.10–7.28 (m, 7H); ^{13}C NMR ($CDCl_3$): δ 45.0, 61.0, 98.2, 106.6, 117.9, 123.2, 125.0, 127.2, 127.3, 127.6, 127.9, 128.7, 129.5, 130.6, 132.4, 141.3, 149.4; $[\alpha]^{24}_{D}$ +195 (*c* 0.72, $CHCl_3$, 90% ee); HPLC (DAICEL CHIRALPAK AS, hexane/2-propanol 9/1, 1.0 mL/min) t_R 7.5 min and 12.5 min; IR (neat) 3030, 2242, 1732, 1651, 1575, 1496, 1455, 1384, 1335, 1266, 1237, 1146, 877, 770, 702 cm^{-1}; EI-MS m/z 316 (M^+); EI-HRMS Calcd. for $C_{20}H_{16}N_2O_2$(M^+) 316.1212, Found 316.1208.



(+)-1-Cyano-1-methoxymethyl-1,2-dihydroisoquinoline-2-carboxylic acid vinyl ester (2d): colorless oil; ^{1}H NMR ($CDCl_3$): δ 3.30 (s, 3H), 3.82 (d, *J* = 6.1 Hz, 1H), 3.97 (d, *J* = 9.5 Hz, 1H), 4.70 (dd, *J* = 14.8, 2.0 Hz, 1H), 5.03 (d, *J* = 13.8 Hz, 1H), 5.78 (d, *J* = 8.3 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 7.07 (dd, *J* = 8.9, 1.6 Hz, 1H), 7.24-7.34 (m, 3H), 7.64 (dd J = 7.6, 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ59.8, 59.9, 75.3, 98.2, 106.7, 117.0, 123.3, 125.2, 125.2, 126.5, 127.2, 127.6, 128.5, 129.6, 141.3, 149.4; $[\alpha]^{25}_{D}$ +188 (*c* 0.60, $CHCl_3$, 73% ee); HPLC (DAICEL CHIRALPAK AS, hexane/2-propanol 9/1, 1.0 mL/min) t_R 8.1 min and 12.7 min; IR (neat) 1736, 1651, 1455, 1383, 1330, 1255, 1207, 1146, 945, 876, 776, 757 cm^{-1}; EI-MS m/z 270 (M^+); EI-HRMS Calcd. for $C_{15}H_{14}N_2O_3$(M^+) 270.1004, Found 270.1003.

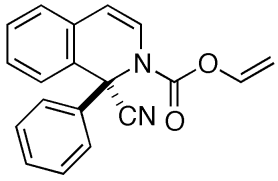


(+)-1-Cyano-1-vinyl-1,2-dihydroisoquinoline-2-carboxylic acid vinyl ester (2e): white solid; ^{1}H NMR ($CDCl_3$): δ 4.68 (dd, *J* = 6.1, 2.2 Hz, 1H), 5.03 (dd, *J* = 14.0, 2.1 Hz, 1H), 5.35 (d, *J* = 10.0 Hz, 1H), 5.55 (d, *J* = 16.8 Hz, 1H), 5.76 (d, *J* = 8.2 Hz, 1H), 6.11 (dd, *J* = 16.8, 10.1 Hz, 1H), 6.96 (d, *J* = 8.2 Hz, 1H), 7.06 (dd, *J* = 7.3, 1.5 Hz, 1H), 7.22-7.32 (m, 3H), 7.47–7.51 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 61.3, 98.3, 106.0, 116.5, 116.9, 122.9, 125.6, 127.4, 127.6, 127.8, 127.9, 129.7, 134.1, 141.2, 149.5; $[\alpha]^{24}_{D}$ +144 (*c* 0.98, $CHCl_3$, 84% ee); HPLC (DAICEL CHIRALCEL OD-H, hexane/2-propanol 9/1, 1.0 mL/min) t_R 6.6 min and 8.1 min; IR (neat) 1737, 1651, 1495, 1454, 1324, 1259, 1197, 1145, 976, 943, 875 cm^{-1}; EI-MS m/z 252 (M^+); EI-HRMS Calcd. for $C_{15}H_{12}N_2O_2$(M^+) 252.0899, Found 252.0907.

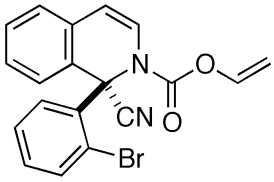


(+)-1-Cyano-1-(1-(*E*)-propenyl)-1,2-dihydroisoquinoline-2-carboxylic

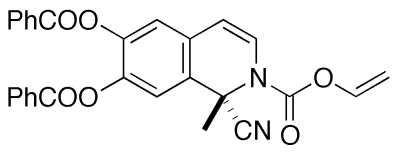
acid vinyl ester (2f): colorless oil; ^{1}H NMR ($CDCl_3$): δ 1.72 (dd, *J* = 6.6, 1.7 Hz, 3H), 4.67 (dd, *J* = 6.1, 2.2 Hz, 1H), 5.00 (dd, *J* = 13.7, 2.1 Hz, 1H), 5.74 (d, *J* = 8.3 Hz, 1H), 5.78 (dq, *J* = 15.3, 1.7 Hz, 1H), 5.91-5.98 (dq like, *J* = 15.3, 6.6 Hz, 1H), 6.93 (d, *J* = 8.2 Hz, 1H), 7.04 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.22-7.31 (m, 3H), 7.46-7.48 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 17.1, 60.7, 98.0, 106.0, 117.4, 122.9, 125.4, 127.6, 127.8, 128.2, 128.8, 129.4, 141.3, 149.4; $[\alpha]^{25}_D$ +113 (*c* 0.52, $CHCl_3$, 87% ee); HPLC (DAICEL CHIRALPAK AS, hexane/2-propanol 9/1, 1.0 mL/min) t_R 6.3 min and 9.2 min; IR (neat) 1737, 1650, 1575, 1495, 1454, 1382, 1322, 1258, 1194, 1146, 952, 876, 775, 703 cm^{-1}; EI-MS m/z 266 (M^+); EI-HRMS Calcd. for $C_{16}H_{14}N_2O_2$(M^+) 266.1055, Found 266.1064.



(+)-1-Cyano-1-phenyl-1,2-dihydroisoquinoline-2-carboxylic acid vinyl ester (2g): colorless oil; ^{1}H NMR ($CDCl_3$): δ 4.55 (dd, *J* = 6.6, 2.1 Hz, 1H), 4.86 (d, *J* = 13.4 Hz, 1H), 5.83 (d, *J* = 8.2 Hz, 1H), 7.03–7.22 (m, 5H), 7.28–7.37 (m, 3H), 7.60–7.62 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 62.9, 98.2, 105.3, 117.7, 123.4, 125.0, 125.7, 126.9, 128.1, 128.4, 128.7, 128.8, 129.3, 130.3, 141.2, 142.2, 149.5; $[\alpha]^{25}_D$ +195 (*c* 0.60, $CHCl_3$, 95% ee); HPLC (DAICEL CHIRALPAK AD, hexane/2-propanol 98/2, 1.0 mL/min) t_R 12.1 min and 14.3 min; IR (neat) 1737, 1652, 1495, 1453, 1382, 1323, 1259, 1194, 1143, 943, 876, 762, 695 cm^{-1}; EI-MS m/z 302 (M^+); EI-HRMS Calcd. for $C_{19}H_{14}N_2O_2$(M^+) 302.1055, Found 302.1055.



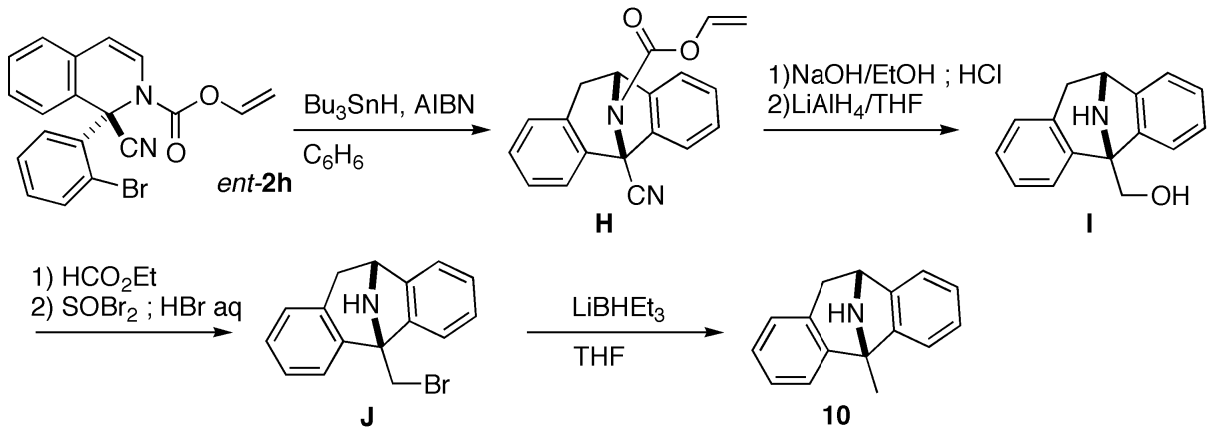
(+)-(*R*)-1-（2-Bromo-phenyl）-1-cyano-1,2-dihydroisoquinoline-2-carboxylic acid vinyl ester (2h): colorless oil; ^{1}H NMR ($CDCl_3$): δ 4.73 (d, *J* = 4.9 Hz, 1H), 4.95 (bs, 1H), 6.20 (d, *J* = 8.2 Hz, 1H), 6.69 (d, *J* = 7.9 Hz, 1H), 7.06 (dd, *J* = 6.1, 13.7 Hz, 1H), 7.17-7.23 (m, 2H), 7.31 (dd, *J* =1.5, 7.6 Hz, 1H), 7.38 (dt, *J* = 0.9, 7.5 Hz, 1H), 7.45 (dt, *J* = 1.5, 7.6 Hz, 1H), 7.68-7.75 (m, 2H), 8.20 (dd, *J* = 1.5, 7.7 Hz, 1H); ^{13}C NMR (DMSO): δ 63.8, 99.1, 105.9, 117.0, 119.6, 123.5, 125.6, 126.9, 127.4, 127.6, 128.1, 129.0, 129.8, 130.9, 131.0, 135.5, 137.3, 141.4, 148.8; $[\alpha]^{26}_D$ +148 (*c* 0.23, $CHCl_3$, 98% ee); HPLC (DAICEL CHIRALCEL OD-H, hexane/2-propanol 98/2, 1.0 mL/min) t_R 10.0 min and 13.7 min; IR (neat) 1731, 1651, 1454, 1383, 1314, 1256, 1197, 1143, 940, 878, 757 cm^{-1}; EI-MS m/z 380 (M^+); EI-HRMS Calcd. for $C_{19}H_{13}{}^{79}BrN_2O_2$($M^+$) 380.0160, Found 380.0162.



(+)-(*S*)-6,7-Bis(benzoyloxy)-1-cyano-1-methyl-1,2-dihydroisoquinoline-2-carboxylic acid vinyl ester (2i): colorless oil; ^{1}H NMR ($CDCl_3$): δ 2.02 (s, 3H), 4.71 (dd, *J* = 6.6, 2.2 Hz, 1H), 5.05 (d, *J* = 13.8 Hz, 1H), 5.79 (d, *J* = 8.3 Hz, 1H), 6.94 (d, *J* = 7.9 Hz, 1H), 7.13 (s, 1H), 7.26–7.30 (m, 1H), 7.35–7.40 (m, 4H), 7.52–7.57 (m, 2H), 7.64 (s, 1H), 8.02 (m, 4H); ^{13}C NMR ($CDCl_3$): δ 27.4, 55.6, 97.6, 104.5, 117.6, 119.2, 120.9, 122.5, 125.6, 127.2, 127.30 ,127.34, 127.5, 129.1, 129.2, 132.9, 140.4, 140.9, 142.4, 148.4, 162.8, 162.9; $[\alpha]^{25}_D$ +81.3 (*c* 1.9, $CHCl_3$, 94% ee); HPLC (DAICEL CHIRALPAK AS, hexane/2-propanol 8/2, 1.3 mL/min) t_R 9.2 min and 20.2 min; IR (neat) 1740, 1651, 1507, 1327, 1259, 1185, 1057, 760, 704 cm^{-1}; EI-MS

m/z 481 (M^++1), 480 (M^+); EI-HRMS Calcd. for $C_{28}H_{21}N_2O_6$(M^++^{1}H) 481.1400, Found 481.1409.

Catalytic enantioselective synthesis of (+)-MK801 (dizocilpine) (10):



(5*S*, 10*R*)-(+)-*N*-Carboxylic acid vinyl ester-5-cyano-10,11-dihydro-5*H*-dibenzo[*a*,*d*]-cyclopenten-5,10-imine (H): A solution of dihydroisoquinoline (*ent*-**2h**) (200 mg, 0.52 mmol), AIBN (4.6 mg, 0.026 mmol) and Bu_3SnH (198 μL, 0.735 mmol) in benzene (80 mL) was warmed under reflux for 1.5 hour. The reaction mixture was cooled to room temperature, the volatiles were removed under reduced pressure and a column chromatography (SiO_2, EtOAc/Hx, 1/5) afforded **H** as a colorless oil in 85% yield (135 mg). ^{1}H NMR (DMSO): δ 2.83 (d, J = 17.6 Hz, 1H), 3.58 (bd, J = 17.4 Hz, 1H), 4.75 (d, J = 4.6 Hz, 1H), 5.01 (bs, 1H), 5.74 (bs, 1H), 7.14-7.20 (m, 2H), 7.30-7.35 (m, 2H), 7.38-7.44 (m, 1H), 7.46-7.49 (m, 2H), 7.58-7.62 (m, 1H), 7.65 (d, J = 7.3 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 24.1, 58.5, 95.8 (bs), 96.6 (bs), 118.1, 118.5, 120.9, 121.5 (bs), 122.3 (bs), 125.9, 127.5, 128.2, 128.5, 130.1, 135.1, 137.3 (bs), 140.5 (bs), 140.7 (bs); $[\alpha]^{23}_D$ +100 (*c* 0.20, $CHCl_3$); IR (neat) 1729, 1650, 1461, 1353, 1299, 1197, 1151, 1049, 872, 746, 669 cm^{-1}; MS m/z 302 (M^+); EI-HRMS Calcd. for $C_{19}H_{14}N_2O_6$ (M^+) 302.1055, Found 302.1047.

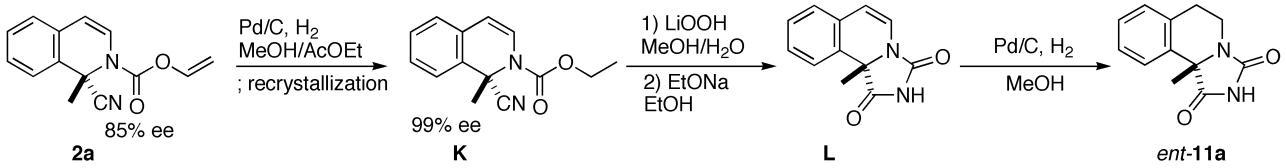
(5*S*, 10*R*)-(+)-5-(Hydroxymethyl)-10,11-dihydro-5*H*-dibenzo[*a*,*d*]-cyclohepten-5-,10-imine (I): A solution of **H** (135 mg, 0.44 mmol) in EtOH (10 mL) and aq. NaOH (3.5 mL, 4N) was heated at reflux overnight. After cooling to room temperature, the reaction mixture was acidified to pH = 1 by careful addition of aq. HCl 1N and washed with Et_2O. Water was removed under reduced pressure affording the corresponding amino-acid hydrochloride salt. A suspension of this salt in THF (20 mL) at room temperature was treated with a solution of $LiAlH_4$ in THF (0.8 mL, of a 1.0 M solution) and the resulting mixture was allowed to stir for 40 hours. Acid-base extraction gave the amino-alcohol as a white solid in 89% yield (85 mg). This compound is spectroscopically identical with the reported data in the literature (J. A. Monn, A. Thurkauf, M. V. Mattson, A. E. Jacobson, K. C. Rice, *J. Med. Chem.* **1990**, *33*, 1069). ^{1}H NMR (DMSO): δ 2.62 (d, J = 16.9 Hz, 1H), 3.44 (dd, under H_2O signal, 1H), 4.26 (dd, J = 5.2, 11.2 Hz, 1H), 4.48 (dd, J = 5.2, 11.2 Hz, 1H), 4.68 (d, J = 5.2 Hz, 1H), 4.94 (t, J = 5.2 Hz, 1H), 6.97 (d, J = 7.2 Hz, 1H), 7.05-7.15 (m, 5H),

7.26 (dd, *J* = 1.1, 7.3 Hz, 1H), 7.38 (d, *J* = 7.3 Hz, 1H); $[\alpha]^{25}_{D}$ +138 (*c* 0.21, $CHCl_3$); $[\alpha]^{24}_{D}$ +146 (*c* 0.20, EtOH); EI-MS m/z 237 (M^+).

(5*S*, 10*R*)-(+)-5-(Bromomethyl)-10,11-dihydro-5*H*-dibenzo[*a*,*d*]-cyclohepten-5-,10-imine (J): The synthesis of this compound was reported in the literature in two steps from **I** in racemic form (J. A. Monn, A. Thurkauf, M. V. Mattson, A. E. Jacobson, K. C. Rice, *J. Med. Chem.* **1990**, *33*, 1069). Using this procedure **J** was obtained in 81% yield and presented identical spectroscopic data. $[\alpha]^{25}_{D}$ +134 (*c* 0.22, $CHCl_3$).

(5*S*, 10*R*)-(+)-5-Methyl-10,11-dihydro-5*H*-dibenzo[*a*,*d*]-cyclohepten-5,10-imine (MK801, 10): To a solution of **J** (10 mg, 0.033 mmol) in THF (1.5 mL) was added $LiBHEt_3$ (66 µL, 1N) and the mixture was warmed at 60 °C for 3 hours. Extraction ($EtOAc/H_2O$) followed by a column chromatography (SiO_2, EtOAc) gave the title compound as a pale yellow oil and crystallize upon addition of hexane. (6.3 mg, 85% yield). The data are identical with those reported in the literature (see ref. 8 in this communication). ^{1}H NMR ($CDCl_3$): δ 1.91 (s, 3H), 2.72 (d, *J* = 16.7 Hz, 1H), 3.44 (dd, *J* = 5.5, 16.7 Hz, 1H), 4.68 (d, *J* = 5.5 Hz, 1H), 6.91-6.94 (m, 1H), 7.01-7.11 (m, 5H), 7.24-7.29 (m, 1H); $[\alpha]^{24}_{D}$ +155 (*c* 0.081, EtOH); EI-MS m/z 221 (M^+); EI-HRMS Calcd. for $C_{16}H_{15}N$ (M^+) 221.1204, Found 221.1207.

Catalytic enantioselective total synthesis of the phenytoin analog (*ent*-11a)



(+)-1-Cyano-1-methyl-1,2-dihydroisoquinoline-2-carboxylic acid ethyl ester (K): To a solution of the Reissert product **2a** (125 mg, 0.516 mmol, 85% ee) in AcOEt/MeOH (1/1, 8.0 mL), was added 10% Pd/C (10 mg) and the flask was filled with H_2 (1 atm). After 20 min, the Pd/C was filtered off and solvents were evaporated. Single recrystallization (hexane–AcOEt) gave the product **K** in 63% yield (99% ee) as colorless prisms. ^{1}H NMR ($CDCl_3$): δ 1.40 (t, *J* = 7.7 Hz, 3H), 1.92 (s, 3H), 4.38 (m, 2H), 5.68 (d, *J* = 8.3 Hz, 1H), 6.86 (d, *J* = 8.3 Hz, 1H), 7.00–7.03 (m, 1H), 7.23–7.31 (m, 2H), 7.56–7.59 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 12.9, 27.2, 55.4, 62.1, 103.8, 118.1, 122.2, 123.7, 124.7, 126.4, 126.6, 127.9, 129.0, 150.8; $[\alpha]^{24}_{D}$ +182 (*c* 0.50, $CHCl_3$, 99% ee); HPLC (DAICEL CHIRALPAK AS, hexane/2-propanol 98/2, 1.5 mL/min) t_R 6.5 min and 13.0 min; IR (neat) 1718, 1646, 1455, 1396, 1373, 1318, 1263, 1095 cm^{-1}; EI-MS m/z 242 (M^+); EI-HRMS Calcd. for $C_{14}H_{14}N_2O_2$(M^+) 242.1055, Found 242.1067.

(+)-10b-Methyl-10b*H*-imidazo[5,1-*a*]isoquinoline-1,3-dione (L): To a solution of **K** (82 mg,

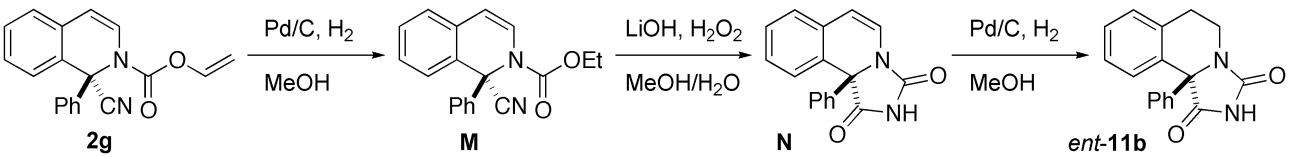
0.338 mmol) in MeOH (3.0 mL), were added H_2O_2 aq (30-35%, 192 μL, ~1.7 mmol) and LiOH・H_2O (28 mg, 0.676 mmol), and the reaction mixture was stirred for 30 min at room temperature. Addition of 10% Na_2SO_3 aq and 10% citric acid aq, extraction with AcOEt and purification by silica gel column chromatography (hexane–AcOEt) gave 1-carbamoyl-1-methyl-1,2-dihydroisoquinoline-2-carboxylic acid ethyl ester in 95% yield and **L** in 3% yield. This carbamide and EtONa (32.8 mg, 0.482 mmol) was dissolved in EtOH (3.0 mL) and stirred for 5 min. Addition of 10% citric acid aq, extraction with AcOEt and silica gel column chromatography (hexane–AcOEt) gave the product **L** in 92% yield. Thus **L** was obtained in 90% yield from **K**.

(-)-1-Carbamoyl-1-methyl-1,2-dihydroisoquinoline-2-carboxylic acid ethyl ester; colorless oil;^{1}H NMR ($CDCl_3$): δ 1.31 (t, *J* = 7.2 Hz, 3H), 1.72 (s, 3H), 4.25 (q, *J* = 7.0 Hz, 2H), 5.67 (d, *J* = 8.3 Hz, 1H), 5.87 (bs, 1H), 6.94–6.96 (m, 2H), 7.07–7.17 (m, 2H), 7.24–7.27 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 14.1, 24.5, 62.9, 65.9, 105.3, 124.5, 124.8, 124.9, 127.4, 127.9, 128.1, 133.5, 174.7; $[\alpha]^{23}_D$ -22.3 (*c* 0.84, $CHCl_3$); IR (neat) 1694, 1645, 1601, 1495, 1454, 1397, 1374, 1319, 1263, 1216, 1145, 1068, 1047, 777 cm^{-1}; EI-MS m/z 260 (M^+); EI-HRMS Calcd. for $C_{14}H_{16}N_2O_3$(M^+) 260.1160, Found 260.1160.

(+)-10b-Methyl-10b*H*-imidazo[5,1-*a*]isoquinoline-1,3-dione (**K**); colorless oil; ^{1}H NMR ($CDCl_3$): δ 1.60 (s, 3H), 6.15 (d, *J* = 7.3 Hz, 1H), 6.83 (d, *J* = 7.3 Hz, 1H), 7.13–7.15 (m, 1H), 7.26–7.28 (m, 2H), 7.87–7.90 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 26.7, 62.7, 113.4, 119.9, 123.1, 126.2, 128.0, 128.3, 129.1, 130.8, 152.9, 174.7; $[\alpha]^{23}_D$ +433 (*c* 3.8, $CHCl_3$); IR (neat) 1775, 1716, 1625, 1486, 1459, 1412, 1382, 1108, 781, 763, 642 cm^{-1}; EI-MS m/z 214 (M^+); EI-HRMS Calcd. for $C_{12}H_{10}N_2O_2$(M^+) 214.0744, Found 214.0748.

(+)-10b-Methyl-6,10b-dihydro-5*H*-imidazo[5,1-*a*]isoquinoline-1,3-dione (*ent*-11a): To a solution of **L** (29 mg, 0.135 mmol) in MeOH (2.7 mL), was added 10% Pd/C (5.0 mg) and the flask was filled with H_2 (1 atm). After 20 min, the Pd/C was removed by filtration and evaporation of the solvent gave the product *ent*-**11a** in quantitative yield as a white solid. ^{1}H NMR ($CDCl_3$): δ 1.75 (s, 3H), 2.73 (dd, *J* = 16.4, 3.4 Hz, 1H), 3.03-3.09 (m, 1H), 3.18 (td, *J* = 12.3, 4.2 Hz, 1H), 4.30 (dd, *J* = 13.4, 6.1 Hz, 1H), 7.10 (d, *J* = 7.4 Hz, 1H), 7.22–7.26 (m, 2H), 7.74 (d, *J* = 7.7 Hz, 1H), 9.32 (bs, 1H); ^{13}C NMR ($CDCl_3$): δ26.3, 28.0, 35.2, 63.3, 126.1, 127.0, 127.8, 129.3, 132.6, 133.7, 155.9, 175.8; $[\alpha]^{23}_D$ +132 (*c* 1.45, $CHCl_3$, 99% ee); HPLC (DAICEL CHIRALCEL OJ, hexane/2-propanol 7/3, 1.3 mL/min) t_R 5.0 min and 7.0 min; IR (neat) 1761, 1715, 1655, 1463, 1426, 1297, 1116 cm^{-1}; EI-MS m/z 216 (M^+); EI-HRMS Calcd. for $C_{12}H_{12}N_2O_2$ (M^+) 216.0899, Found 216.0897.

Catalytic enantioselective synthesis of the phenytoin analog (*ent*-11b):

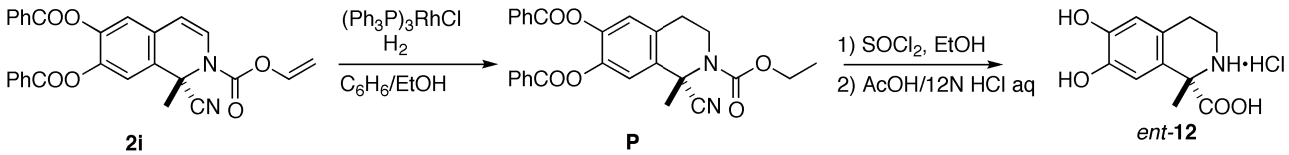


(+)-1-Cyano-1-phenyl-1,2-dihydroisoquinoline-2-carboxylic acid ethyl ester (M): To a stirred solution of **2g** (180 mg, 0.595 mmol, 95% ee) in MeOH/EtOAc (10 mL, 1/1) was added Pd/C 10% (10 mg) and the mixture was stirred 15 min under H_2 (1 atm). The Pd/C was removed by filtration on celite and the solvent evaporated to afford the title compound as a colorless oil in 98% yield (175 mg). ^{1}H NMR ($CDCl_3$): δ 1.12 (t, *J* = 7.0 Hz, 3H), 4.10-4.15 (m, 2H), 5.73 (d, *J* = 8.3 Hz, 1H), 7.00-7.02 (m, 1H), 7.05-7.09 (m, 2H), 7.12-7.18 (m, 2H), 7.27-7.35 (m, 3H), 7.57-7.59 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 12.8, 61.9, 62.4, 103.0, 117.1, 123.3, 123.9, 124.5, 126.3, 126.7, 127.4, 127.7, 128.1, 129.5, 142.1, 151.3; $[\alpha]^{23}_D$ +200 (*c* 0.185, $CHCl_3$); IR (neat) 1730, 1641, 1493, 1452, 1318, 1254, 1019, 928, 769, 639 cm^{-1}; EI-MS m/z 304 (M^+); EI-HRMS Calcd. for $C_{19}H_{16}N_2O_2$ (M^+) 304.1212, Found 304.1197.

(+)-10b-Phenyl-10b*H*-imidazo[5,1-*a*]isoquinoline-1,3-dione (N): To a solution of **M** (175 mg, 0.575 mmol) in MeOH (5 mL), were added $LiOH \cdot H_2O$ (48 mg, 1.15 mmol) and H_2O_2 aq (0.28 mL, ~30%, ~2.87 mmol) in H_2O (1.5 mL) at room temperature. Stirring was continued for 1 hour, and an extraction ($EtOAc/H_2O$) followed by a column chromatography (SiO_2, EtOAc/Hx, 1/2) gave **N** as a colorless oil in 87% yield (139 mg). ^{1}H NMR ($CDCl_3$) δ 6.11 (d, *J* = 7.3 Hz, 1H), 6.95 (d, *J* = 7.3 Hz, 1H), 7.15 (d, *J* = 7.6 Hz, 1H), 7.20-7.31 (m, 5H), 7.33 (dt, *J* = 1.5, 7.6 Hz, 1H), 7.39 (dt, *J* = 1.5, 7.6 Hz, 1H), 7.66 (bs, 1H), 8.17 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 66.6, 113.6, 119.4, 123.7, 124.7, 125.6, 126.8, 127.7, 127.8, 127.9, 129.2, 129.3, 136.1, 151.8, 173.0; $[\alpha]^{25}_D$ +22 (*c* 0.16, $CHCl_3$); IR (neat) 3204, 1778, 1724, 1627, 1482, 1455, 14077, 1104, 782 cm^{-1}; EI-MS m/z 276 (M^+); EI-HRMS Calcd. for $C_{17}H_{12}N_2O_2$ (M^+) 276.0899, Found 276.0894.

(-)-10b-Phenyl-6,10b-dihydro-5*H*-imidazo[5,1-*a*]isoquinoline-1,3-dione (*ent*-11b): The compound **N** (135 mg, 0.489 mmol) was dissolved in MeOH (6 mL) and the flask was charged with Pd/C 10% (10 mg). Stirring was continued for 1 hour under H_2 (1 atm) to afford *ent*-**11b** as a white solid (96%, 130 mg). The spectroscopic data obtained are identical with those reported in the literature (*J. Heterocyclic Chem.* **1974**, *11*, 803). ^{1}H NMR ($CDCl_3$): δ 2.64-2.69 (m, 1H), 3.00-3.05 (m, 1H), 3.22-3.30 (m, 1H), 3.99-4.05 (m, 1H), 7.17-7.25 (m, 3H), 7.29-7.35 (m, 5H), 7.84-7.86 (m, 1H), 8.20 (bs, 1H) ; $[\alpha]^{25}_D$ -107 (*c* 0.12, $CHCl_3$); EI-MS m/z 278 (M^+); EI-HRMS Calcd. for $C_{17}H_{14}N_2O_2$ (M^+) 278.1055, Found 278.1052.

Catalytic enantioselective total synthesis of (+)-(*S*)-salsolinol-1-carboxylic acid (*ent*-12)



(*S*)-(+)-6,7-Bis(benzoyloxy)-1-cyano-1-methyl-1,2,3,4-tetrahydroisoquinoline-2-carboxylic acid ethyl ester (P): 6,7-Bis(benzoyloxy)-1-cyano-1-methyl-1,2-dihydroisoquinoline-2-carboxylic acid vinyl ester (**2i**, 50 mg, 0.104 mmol) and chlorotris(triphenylphosphine)rhodium (47.9 mg, .0.518

mmol) were dissolved in benzene/EtOH (5/1, 2.5 mL) in a sealed tube under H_2 (90 atm). After 48 h, the pressure was lowered to ambient pressure and purification by preparative scale silica gel TLC gave the product **P** in 38% yield as a colorless oil. 6,7-Bis(benzoyloxy)-1-cyano-1-methyl-1,2-dihydroisoquinoline-2-carboxylic acid ethyl ester was recovered in 59% yield. ^{1}H NMR ($CDCl_3$): δ 1.38 (t, *J* = 7.2 Hz, 3H), 2.05 (s, 3H), 2.89–2.98 (m, 2H), 3.71–3.88 (m, 2H), 4.33 (q, *J* = 7.2 Hz, 2H), 7.27 (s, 1H), 7.36–7.42 (m, 4H), 7.53-7.58 (m, 2H), 7.64 (s, 1H), 8.03–8.08 (m, 4H) ^{13}C NMR ($CDCl_3$): δ 14.4, 29.1, 29.8, 40.9, 54.6, 62.6, 120.3, 122.4, 123.5, 128.4, 128.5, 130.15, 130.19, 132.7, 133.5, 133.8, 133.9, 141.7, 142.3, 154.9, 163.99, 164.04; $[\alpha]^{24}_D$ +15.5 (*c* 1.06, $CHCl_3$, 93% ee); HPLC (DAICEL CHIRALPAK AS, hexane/2-propanol 8/2, 1.3 mL/min) t_R 13.2 min and 20.9 min; IR (neat) 1748, 1705, 1647, 1507, 1452, 1407, 1379, 1347, 1260, 1177, 1059, 1024, 707 cm^{-1}; EI-MS m/z 484 (M^+); EI-HRMS Calcd. for $C_{28}H_{24}N_2O_6$(M^+) 484.1634, Found 484.1635.

(*S*)-(+)-6,7-Dihydroxy-1-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylic acid hydrochloride salt (salsolinol-1-carboxylic acid hydrochloride salt, *ent*-12): To a solution of **P** (15 mg, 0.031 mmol) in EtOH (2.5 mL), was added thionyl chloride (365 μL, 5 mmol) and the reaction mixture was stirred for 3 h at 90 °C in a sealed tube. After evaporation of solvent, AcOH (2.0 mL) and 12N HCl aq (2.0 mL) were added and the reaction mixture was stirred for further 7 h at 90 °C in a sealed tube. Evaporation and partial purification by reverse phase preparative scale TLC (Merck, RP-8 F_{254}s) gave the product *ent*-**12** in 80-90% yield. The ^{1}H-NMR was identical to a compound prepared by a literature procedure (*Tetrahedron Asymm*. **1997**, *8*, 1487-1490). A precise value of the optical rotation was difficult to determine due to a partial contamination with the stationary phase. ^{1}H NMR (CD_3OD): δ 1.90 (s, 3H), 2.90-3.02 (m, 2H), 3.47-3.62 (m, 2H), 6.61 (s, 1H), 7.06 (s, 1H).

Preparation of the substrates for the catalytic enantioselective Reissert-type reaction

1-Methylisoquinoline (1a) is commercially available (Tokyo Chemical Industry co., ltd.). **1a** was also prepared by a literature procedure in 70–80% yield except that benzoyl chloride was used instead of polymer-supported aroyl chloride. (*J. Org. Chem*. **1998**, *63*, 2244–2250).

1-Ethylisoquinoline (1b) and **1-benzylisoquinoline (1c)** were prepared by a literature procedure except that benzoyl chloride was used instead of polymer-supported aroyl chloride. Yields are 70–80% for 3 steps. (*J. Org. Chem*. **1998**, *63*, 2244–2250). Another general method for preparation of 1-alkylisoquinoline has been reported (*Org. Synth.* **1977**, *56*, 19–25).

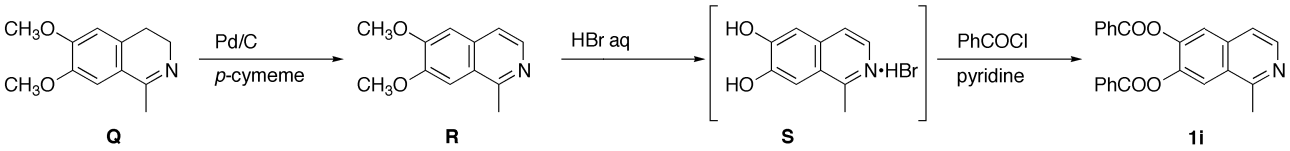
1-Methoxymethylisoquinoline (1d) was prepared according to a literature procedure except that benzoyl chloride was used instead of polymer-supported aroyl chloride and chloromethyl methyl ether was used as alkylating reagent in 75–85% yield (*J. Org. Chem*. **1998**, *63*, 2244–2250). colorless oil; ^{1}H NMR ($CDCl_3$): δ 3.48 (s, 3H), 5.07 (s, 2H), 7.60-7.63 (m, 2H), 7.67-7.71 (m, 1H), 7.83 (d, *J* = 8.3 Hz, 1H), 8.32 (d, *J* = 8.3 Hz, 1H), 8.48 (d, *J* = 5.8 Hz, 1H); ^{13}C NMR ($CDCl_3$):

δ 58.5, 74.9, 121.0, 125.5, 127.06, 127.10, 127.4, 130.1, 136.4, 141.5, 156.9; IR (neat) 1626, 1587, 1565, 1501, 1456, 1350, 1189, 1102, 956, 828, 750 cm^{-1}; EI-MS m/z 174 (M^++1), 173 (M^+); EI-HRMS Calcd. for $C_{11}H_{11}NO$ (M^+) 173.0841, Found 173.0839.

1-Vinylisoquinoline (1e) (*Aust. J. Chem*. **1989**, *42*, 279–285), **1-(1-(*E*)-propenyl)isoquinoline (1f)** (*J. Pharm. Sci.* **1978**, *67*, 740–742), **1-phenylisoquinoline (1g)** (*J. Org. Chem.* **1949**, *14*, 650–654) were prepared according to the corresponding literature procedure.

1-(2-Bromo-phenyl)isoquinoline (1h): To a stirred solution of (±)-2-amino-1-phenylethanol (3.14 g, 22.8 mmol) and Et_3N (3.19 mL, 22.8 mmol) in CH_2Cl_2 (50 mL) at 0 °C was added 2-bromobenzoyl chloride (5.00 g, 22.8 mmol) dropwise. Stirring was continued for 2 hours, and an extraction (CH_2Cl_2/H_2O) afforded 2-bromo-*N*-(2-hydroxy-2-phenylethyl)-benzamide as a white solid (7.28 g, quant. yield). A part of this amide (4.00 g, 12.5 mmol) was heated at reflux overnight in a mixture of toluene/xylene (150 mL, 1/1) with P_2O_5 (10 g, 35.2 mmol) and $POCl_3$ (14 mL, 150 mmol). The reaction mixture was then cooled to room temperature and quench by addition of MeOH. Addition of NaOH pellets until pH = 11 followed by an extraction with EtOAc gave the crude title compound. Purification by a first filtration on silica gel (EtOAc/Hx, 1/4), a subsequent acid-base extraction and a final column chromatography (SiO_2, EtOAc/Hx, 1/5) afforded **1h** as a pure colorless oil (2.30 g, 8.12 mmol) with 65% overall yield. ^{1}H NMR ($CDCl_3$): δ 7.34 (dt, *J* = 2.1 , 6.9 Hz, 1H), 7.42-7.48 (m, 2H), 7.52 (t, *J* = 7.0 Hz, 1H), 7.62 (d, *J* = 8.5 Hz, 1H), 7.65-7.74 (m, 3H), 7.90 (d, *J* = 8.2 Hz, 1H), 8.62 (d, *J* = 5.7 Hz, 1H); ^{13}C NMR ($CDCl_3$):δ 119.6, 121.9, 125.9, 126.0, 126.2, 126.3, 126.4, 128.9, 129.2, 130.2, 131.8, 135.3, 139.3, 141.1, 159.0; IR (neat) 1621, 1583, 1560, 1498, 1427, 1386, 1321, 1028, 872 cm^{-1}; EI-MS m/z 285, 283 (M^+); EI-HRMS Calcd. for $C_{16}H_{10}{}^{81}BrN$ (M^+) 284.9976, Found 284.9971.

6,7-Bis(benzoyloxy)-1-methylisoquinoline (1i)



3,4-Dihydro-6,7-dimethoxy-1-methylisoquinoline (Q) was prepared according to a literature procedure (*Org. Synth.* **1977**, *56*, 3–7).

6,7-Dimethoxy-1-methylisoquinoline (R): To a solution of **Q** (12.2 g, 59.3 mmol) in *p*-cymene (120 mL), was added Pd/C (10%, 1.0 g) and the reaction mixture was stirred for 30 h at 176 °C. Filtration of Pd/C, extraction with 2N HCl aq and neutralization, purification by silica gel column chromatography (AcOEt-MeOH) and recrystallization (hexane-AcOEt) gave the product **Q** in 80–90% yield as a brown solid. Spectra of the synthesized compound were identical with those in the literature (*Die Pharmazie* **1984**, *39*, 387–388).

6,7-Dihydroxy-1-methylisoquinoline hydrobromide (S): R (500 mg, 2.46 mmol) in 48% HBr aq (5.0 mL), was stirred for 27 h at 100 °C. Evaporation of solvent gave the crude product **S** in almost quantitive yield as a brown solid. This crude mixture was used in the next step without further purification. ^{1}H NMR (CD_3OD): δ 3.03 (s, 3H), 7.40 (s, 1H), 7.65 (s, 1H), 7.91 (d, *J* = 6.7 Hz, 1H),

8.04 (d, J = 6.7 Hz, 1H).

6,7-Bis(benzoyloxy)-1-methyl-isoquinoline (1i) To a solution of crude mixture of **S** (128 mg, <0.50 mmol) in dichloromethane (1.0 mL), were added pyridine (242 μL, 3.0 mmol) and benzoyl chloride (174 μL, 1.5 mmol) at 0 °C and the reaction mixture was stirred overnight at room temperature. Quench with H_2O, extraction with AcOEt and silica gel column chromatography (hexane-AcOEt) gave the product **1i** in 82% yield for 2 steps as a light brown solid.. Reaction conditions are not fully optimized. ^{1}H NMR ($CDCl_3$): δ 2.98 (s, 3H), 7.35-7.41 (m, 4H), 7.53-7.58 (m, 3H), 7.88 (s, 1H), 8.06-8.10 (m, 4H), 8.14 (s, 1H), 8.44 (d, J = 6.6 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 22.4, 118.9, 119.6, 120.5, 125.7, 128.37, 128.42, 128.5, 128.6, 130.2, 133.9, 134.8, 142.0, 142.3, 145.0, 158.1, 164.0, 164.4; IR (neat) 1736, 1715, 1639, 1505, 1452, 1415, 1363, 1217 cm^{-1}; EI-MS m/z 383 (M^+); EI-HRMS Calcd for $C_{24}H_{17}NO_4$(M^+) 383.1158, Found 383.1157.