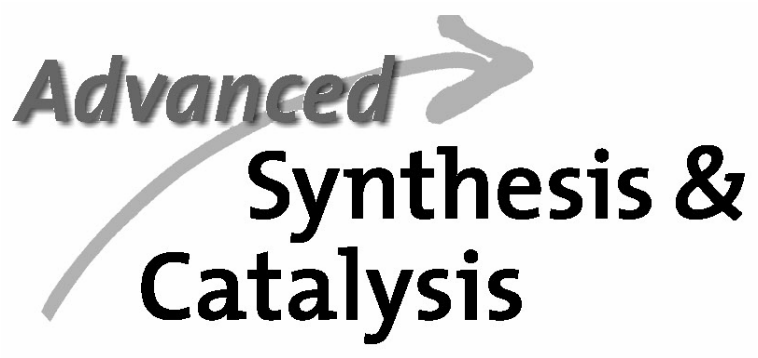


Supporting Information

Enantioselective Synthesis of Butenolide Derivatives Catalyzed by an Iodine-Substituted Chiral Phosphoric Acid

Takahiko Akiyama,* Yashuhiro Honma, Junji Itoh, and Kohei Fuchibe

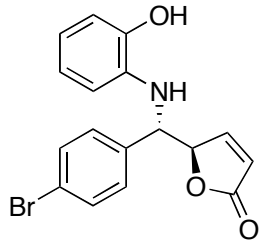
Department of Chemistry, Faculty of Science,
Gakushuin University,
Mejiro, Toshima-ku, Tokyo 171-8588, Japan
takahiko.akiyama@gakushuin.ac.jp

Supporting Information

General. NMR spectra were recorded on Unity Inova 400 instrument (Varian Inc., 400 MHz for ^{1}H, 100 MHz for ^{13}C, 189 MHz for ^{31}P) and JNM-Al300 instrument (JEOL, 300 MHz for ^{1}H, 75 MHz for ^{13}C, 121 MHz for ^{31}P, 283 MHz for ^{19}F) using $CDCl_3$ as a solvent. Tetramethylsilane (TMS) ($\delta = 0$) or $CHCl_3$ ($\delta = 7.27$) served as an internal standard for ^{1}H NMR, and $CDCl_3$ was used as an internal standard ($\delta = 77.0$) for ^{13}C NMR. H_3PO_4 was used as an external standard ($\delta = 0$) for ^{31}P NMR. C_6F_6 was used as an internal standard ($\delta = 0$) for ^{19}F NMR. IR spectra were recorded on a Shimadzu FT-IR 8600 spectrometer. EI Mass spectra were measured by GCMS-QP-5000 (Shimadzu) at an ionizing voltage of 70 eV. Fab mass spectra were measured on a JEOL JMS-700 using 3-nitrobenzyl alcohol as a matrix. Purification of the products was performed by column chromatography on silica gel (Fuji sylisia D60L or PSQ-60B) or preparative TLC on silica gel (Wako gel B-5F). All solvents were purified according to the standard procedures. Elemental analysis (EA) was carried out on EA1110 instrument (Amco Inc.).

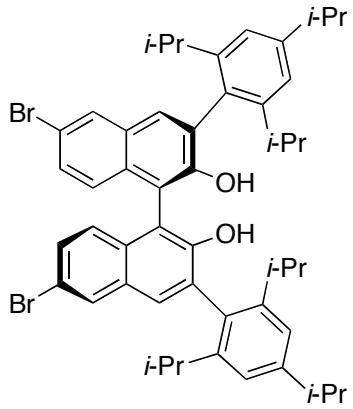
Determination of the absolute stereochemistry

The absolute and relative stereochemistry of the following compound were determined by X-ray analysis.



This compound (55% ee, Table 2, entry 3) was recrystallized from benzene to give optically pure compound, which was subjected to X-ray analysis (see, .cif).

Experimental Section

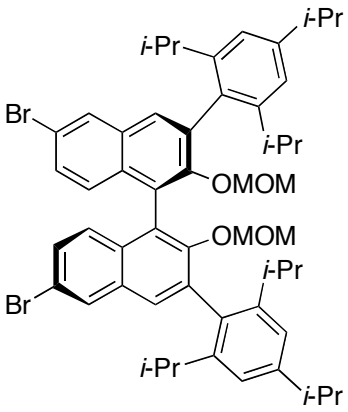


(*R*)-6,6'-Dibromo-3,3'-bis(2,4,6-triisopropylphenyl) -1,1'-binaphthol

To a solution of (*R*)-3,3'-bis(2,4,6-triisopropylphenyl)-1,1'-binaphthol[1] (0.94 g, 1.36 mmol) in CH_2Cl_2 (5 mL) at −78 ˚C was added dropwise Br_2 (0.60 g, 3.73 mmol) in CH_2Cl_2 (5 mL) for 10 min. After being stirred at room temperature for 13 h, the reaction mixture was quenched by addition of sat. Na_2SO_3. The solution was extracted with CH_2Cl_2. The combined organic layers were washed with Na_2SO_3, brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude product was purified by silica gel column chromatography (Hexane/Ethyl acetate= 20/1) to give the product (1.07 g, 1.26 mmol) in 93% yield.

R_f 0.4 (Hexane : Ethyl acetate = 20:1 v/v); $[\alpha]_D^{25}$ +72.5 (c 1.0, $CHCl_3$); IR ($CHCl_3$) 3518, 3053, 3022, 2963, 2930, 2870, 1593, 1568, 1487, 1462, 1435, 1385, 1364, 1265, 1213, 1221, 1175, 1138, 1121, 1069, 935, 903, 881 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.01 (d, 2H, *J*=2.0 Hz), 7.66 (s, 2H), 7.38 (dd, 2H, *J*= 7.0, 2.0 Hz), 7.16-7.11 (m, 6H), 4.92 (s, 2H), 3.00-2.93 (m, 2H), 2.79-2.76 (m, 2H), 2.65-2.62 (m, 2H), 1.31 (d, 12H,

J=6.8 Hz), 1.20 (d, 6H, *J*=6.8 Hz), 1.10 (d, 6H, *J*=7.0 Hz), 1.08 (d, 6H, *J*=6.8 Hz), 1.02 (d, 6H, *J*=6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ=150.7, 149.7, 148.0, 147.8, 132.0, 130.2, 130.1, 130.1, 129.9, 129.4, 129.3, 126.2, 121.5, 121.4, 117.6, 113.6, 34.4, 30.9, 30.8, 24.3, 24.0, 24.0, 23.9, 23.7.; MS(DI) m/z 853 (M^++7, 7), 852 (M^++6, 2), 851 (M^++5, 59), 850 (M^++4, 58), 848 (M^++2, 100), 847 (M^++1, 51);

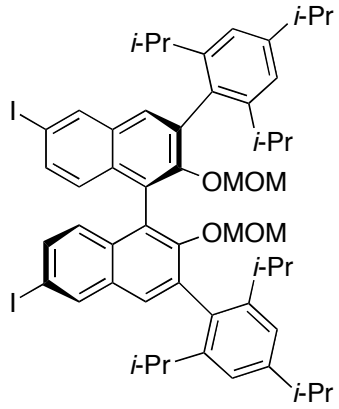


(*R*)-6,6'-Dibromo-3,3'-bis(2,4,6-triisopropylphenyl)-2,2'-bis(methoxymethoxy)-1,1'-binaphthyl

To a solution of NaH (0.19 g, 4.80 mmol) in DMF (7 mL) at 0 ˚C was added dropwise (*R*)-6,6'-dibromo-3,3'-bis(2,4,6-triisopropylphenyl)-1,1'-binaphthol (1.60 g, 1.36 mmol) in DMF (7 mL). After being stirred at 0 ˚C for 1 h, to the solution was added dropwise MOMCl (340 μL, 4.48 mmol) for 6 min. After being stirred at room temperature for 7 h, the reaction mixture was quenched by addition of H_2O, EtOAc, 1N HCl. The solution was extracted with Ethyl acetate. The combined organic layers were washed with 1N HCl, 6N HCl and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude product was purified by silica gel column chromatography (Hexane/CH_2Cl_2= 5/1) to give the product (1.67 g, 1.79 mmol) in 95% yield.

R_f 0.4 (Hexane : CH_2Cl_2= 5:1); $[\alpha]_D^{24}$ +12.8 (c 1.0, $CHCl_3$); IR ($CHCl_3$) 3030, 2963, 2930, 2870, 1607, 1585, 1568, 1462, 1425, 1385, 1364, 1350, 1317, 1238, 1157, 1121, 1069, 1005, 972, 907, 880, 864, 818 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=8.00 (d, 2H, *J*=2.0 Hz), 7.70 (s, 2H), 7.39 (dd, 2H, *J*=7.9, 2.0 Hz), 7.22 (d, 2H, *J*=7.9 Hz), 7.09 (dd, 4H, *J*=11.7, 1.6 Hz), 4.24 (d, 2H, *J*=5.7 Hz), 4.20 (d, 2H, *J*=5.7 Hz), 2.96-2.92 (m, 2H), 2.80-2.74 (m, 4H), 2.26 (s, 6H), 1.30-1.18 (m, 30H), 1.00 (d, 6H, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ=152.7, 148.7, 147.2, 146.8, 135.5, 132.5, 131.9, 131.5, 130.2, 129.7, 129.5, 127.9, 125.8, 120.9, 120.7, 119.0, 97.7, 55.3, 34.3, 31.1, 30.8, 25.8, 25.3,

24.2, 24.1, 23.3, 23.1.; MS(DI) m/z 941 (M^++7, 41), 940 (M^++6, 65), 937 (M^++3, 33), 863 (20), 862 (46), 861 (44), 860 (73), 858 (36), 831 (11), 821 (24), 820 (55), 819 (61), 818 (100), 816 (53), 393 (11).

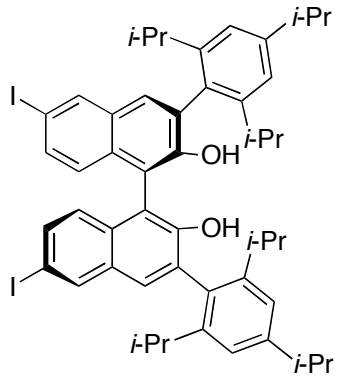


(*R*)-6,6'-Diiodo-3,3'-bis(2,4,6-triisopropylphenyl)-2,2'-bis(methoxymethoxy)-1,1'-binaphthyl

To a solution of (*R*)-6,6'-dibromo-3,3'-bis(2,4,6-triisopropylphenyl)-2,2'-bis(methoxymethoxy)-1,1'-binaphthyl (1.65 g, 1.76 mmol) in THF (10 mL) at –78 ˚C was added dropwise *n*-BuLi (4.4 mL, 7.04 mmol) for 7 min. The reaction mixture was stirred at –78 ˚C for 2 h. To the reaction mixture was added dropwise I_2 (2.74 g, 10.80 mmol) in THF (10 mL) over 15 min. After being stirred at –78 ˚C for 3 h, the reaction mixture was quenched by dropwise addition of MeOH, EtOAc, H_2O at –78 ˚C. The solution was extracted with EtOAc. The combined organic layers were washed with $NaHSO_3$, brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude product was purified by silica gel column chromatography (Hexane/CH_2Cl_2= 3/1) to give the product (1.28 g, 1.25 mmol) in 71% yield.

R_f 0.5 (Hexane: CH_2Cl_2= 3:1); $[\alpha]_D^{26}$ +108.0 (c 1.0, $CHCl_3$); IR ($CHCl_3$) 2963, 2928, 2870, 1605, 1578, 1462, 1427, 1385, 1362, 1315, 1238, 1157, 1119, 1099, 1080, 1003, 972, 926, 907, 880 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.22 (s, 2H), 7.66 (s, 2H), 7.54 (dd, 2H, *J*=7.3, 1.6 Hz), 7.10 (s, 2H), 7.08-7.06 (m, 4H), 4.22 (d, 2H, *J*=5.7 Hz), 4.20 (d, 2H, *J*=5.7 Hz), 2.96-2.92 (m, 2H), 2.79-2.73 (m, 4H), 2.26 (s, 6H), 1.32-1.18 (m, 32H), 0.99 (d, 4H, *J*=7.0 Hz).; ^{13}C NMR (75 MHz, $CDCl_3$) δ=152.8, 148.7, 147.2, 146.8, 136.4, 135.3, 134.7, 132.5, 132.2, 132.0, 130.1, 127.7, 125.7, 120.9, 120.6, 97.7, 90.6,

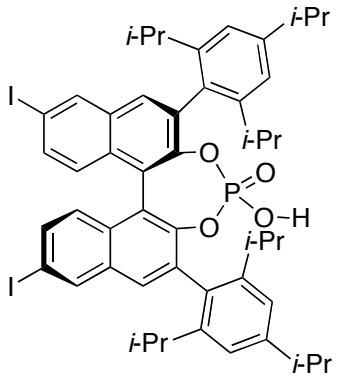
55.3, 34.3, 31.1, 30.8, 25.8, 25.3, 24.1, 23.2, 23.1



(*R*)-6,6'-Diiodo-3,3'-bis(2,4,6-triisopropylphenyl)-1,1'-binaphthol

To a solution of (*R*)-6,6'-diiodo-3,3'-bis(2,4,6-triisopropylphenyl)-2,2'-bis(methoxymethoxy)-1,1'-binaphthyl (1.12 g, 1.09 mmol) in EtOH (80 mL) was added conc. HCl (20 mL) at room temperature. The reaction mixture was heated at 50 ˚C for 28 h. After evaporation of EtOH under vacuum, the solution was extracted with CH_2Cl_2. The combined organic layers were successively washed with brine, dried over anhydrous Na_2SO_4, and concentrated to dryness. The crude product was purified by silica gel column chromatography (Hexane/CH_2Cl_2= 5/1) to give the product (0.83 g, 0.88 mmol) in 80% yield.

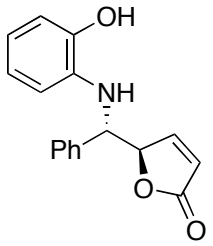
R_f 0.4 (Hexane : CH_2Cl_2= 5:1); $[\alpha]_D^{27}$ +185.9 (c 1.0, $CHCl_3$); IR ($CHCl_3$) 3518, 3028, 3005, 2964, 2930, 2870, 1605, 1587, 1568, 1483, 1462, 1433, 1385, 1364, 1317, 1306, 1263, 1209, 1202, 1188, 1175, 1140, 1121, 1103, 1065, 997, 932, 907, 881 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.22 (s, 2H), 7.62 (s, 2H), 7.53 (dd, 2H, *J*=8.2, 1.7 Hz), 7.13 (d, 4H, *J*=9.0 Hz), 6.97 (d, 2H, *J*=8.2 Hz), 4.89 (s, 2H), 2.97-2.94 (m, 2H), 2.77-2.74 (m, 2H), 2.64-2.60 (m, 2H), 1.31 (d, 12H, *J*=6.8 Hz), 1.19 (d, 6H, *J*=7.0 Hz), 1.09 (d, 6 H, *J*=7.0 Hz), 1.07 (d, 6 H, *J*=7.0 Hz), 1.01 (d, 6H, *J*=6.8 Hz).; ^{13}C NMR (100 MHz, $CDCl_3$) δ=150.8, 149.7, 148.0, 147.8, 136.7, 135.0, 132.3, 130.7, 130.0, 129.3, 129.2, 126.2, 121.5, 121.4, 113.4, 88.8, 34.4, 30.9, 30.8, 24.3, 24.0, 24.0, 23.9, 23.7.; MS(DI) m/z 949 (M^++7, 11), 946 (M^++4, 100), 872 (10), 816 (28), 772 (6), 688 (8).



(*R*)-6,6'-Diiodo-3,3'-bis(2,4,6-triisopropylphenyl)-1,1'-binaphthyl phosphate (2b)

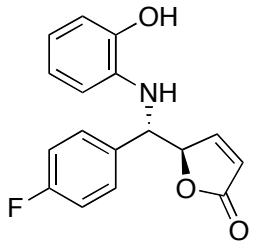
To a solution of (*R*)-6,6'-diiodo-3,3'-bis(2,4,6-triisopropylphenyl)-1,1'-binaphthol (557.5 mg, 0.59 mmol) in pyridine (8 mL) was added phosphorus oxychloride (80 μL, 0.86 mmol) at room temperature. After stirring at room temperature for 2 h, the reaction mixture was heated at reflux for 2 h. The reaction mixture was quenched by addition of H_2O (145 μL) at 0 ˚C and stirred for overnight at room temperature. After evaporation of pyridine under vacuum, 6N HCl (14 mL) was added to the residue at 0 ˚C. The mixture was refluxed for 2 h. After cooling to room temperature, The solution was extracted with CH_2Cl_2. The combined organic layers were successively washed with 6N HCl and brine, dried over anhydrous Na_2SO_4, and concentrated to dryness. The crude product was purified by silica gel column chromatography (Hexane/EtOAc= 1/2) to give the product (524.0 mg, 0.52 mmol) in 88% yield.

R_f 0.3 (Hexane : Ethyl acetate = 1:2); $[\alpha]_D^{24}$ –15.7 (c 1.00, $CHCl_3$); IR ($CHCl_3$) 3022, 2964, 2930, 2870, 1607, 1583, 1483, 1462, 1418, 1385, 1364, 1313, 1281, 1232, 1223, 1200, 1099, 1065, 1003, 972, 957, 939, 908, 895, 862 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.26 (s, 1 H), 8.26 (s, 1 H), 7.68 (s, 2 H), 7.58 (dd, 2 H, *J*=9.0, 1.6 Hz), 6.99 (d, 2 H, *J*=9.0 Hz), 6.95 (s, 2 H), 6.93 (s, 2 H), 3.52 (brs, 1 H), 2.86-2.82 (m, 1 H), 2.51-2.44 (m, 2 H), 1.22 (d, 12 H, *J*=6.8 Hz), 1.01-0.98 (m, 12 H), 0.89 (d, 6 H, *J*=6.6 Hz), 0.69 (d, 6 H, *J*=6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ=148.8, 148.0, 147.5, 146.3, 146.2, 136.8, 135.0, 133.4, 132.5, 131.5, 131.1, 130.9, 128.6, 121.8, 121.2, 120.3, 91.4, 34.3, 31.0, 30.7, 26.4, 24.9, 24.1, 23.9, 23.2, 22.7.; ^{31}P NMR (121 MHz, $CDCl_3$) δ=2.24; Found: C, 59.77; H, 5.48%. Calcd for $C_{50}H_{55}I_2O_4P$: C, 59.77; H, 5.52%.



5-[[(2-Hydroxyphenyl)amino]-phenylmethyl]furan-2(5*H*)-one (5a)

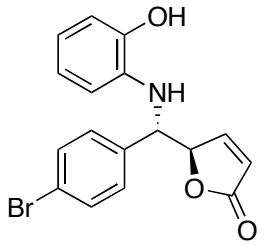
R_f 0.4 (Hexane : Ethyl acetate = 1:1 v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ =7.54-7.25 (m, 6H), 6.79-6.43 (m, 4H), 6.13 (dd, 1H, *J*=5.7, 1.8 Hz, *syn*) , 6.08 (dd, 1H, *J*=5.8, 1.2 Hz, *anti*), 5.46-5.45 (m, 1H, *anti*), 5.30-5.28 (m, 1H, *syn*), 4.84 (d, 1H, *J*=4.0 Hz, *anti*), 4.48 (d, 1H, *J*=7.0 Hz, *syn*); ^{13}C NMR (75 MHz, CD_3OD) δ=175.2(*syn*), 175.1(*anti*), 156.9(*syn*), 156.5(*anti*), 146.1, 138.9, 136.6, 129.4, 128.7, 128.4, 123.1, 121.1, 119.1, 114.1, 113.8, 87.9(*syn*), 87.4(*anti*), 61.0(*syn*), 60.6(*anti*); IR ($CHCl_3$) 3601, 3371, 3020, 3013, 2962, 2860, 1761, 1612, 1599, 1512, 1269, 1225, 1163, 1105, 1089, 1042, 901, 816 cm^{-1}; MS(DI) m/z 281(M^+, 11), 198(100), 172(25), 120(75), 115(12), 109(27), 104(11), 91(30); Found: C, 72.68; H, 5.22; N, 4.63%. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98%; HPLC: Daicel Chiralcel OJ-H, Hexane/*i*-PrOH=1/1, Flow rate= 0.4 mL/min, UV=254 nm, *anti*; t_R=34.5 min (minor), t_R= 43.9 min (major), *syn*; t_R=28.8 min (major), t_R= 49.2 min (minor).



5-[(4-Fluorophenyl)-[(2-hydroxyphenyl)amino]methyl]furan-2(5*H*)-one (5b)

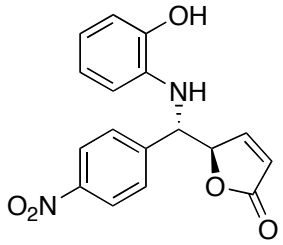
R_f 0.5 (Hexane: Ethyl acetate = 1:1); IR ($CHCl_3$) 3597, 3300, 3024, 3009, 2855, 1763, 1609, 1510, 1448, 1346, 1265, 1229, 1225, 1209, 1159, 1097, 1041 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=7.40 (dd, 1H, *J*=5.9, 1.5 Hz), 7.32-7.26 (m, 2H), 7.06-6.87 (m, 2H), 6.77-6.58 (m, 3H), 6.42 (d, 1H, *J*=7.7 Hz), 6.08 (brs, 1H), 6.08 (dd, 1H, *J*=5.1, 2.0 Hz), 5.47(brs, 1H), 4.82 (brs, 1H, major), 4.80 (brs, 1H); ^{13}C NMR (75 MHz, CD_3OD)

δ=175.0, 165.4, 162.1, 156.5, 146.2, 136.4, 134.9(d, J_{F-C}=3.5 Hz), 130.6(d, J_{F-C}=8.3 Hz), 123.2, 121.1, 119.3, 116.1(d, J_{F-C}=22.1 Hz), 114.9, 113.9, 87.3, 60.0; ^{19}F-NMR (376 MHz, $CDCl_3$) δ□51.79 (m, *anti*), 48.01 (m, *syn*); MS(DI) m/z 299(M^+, 27), 217(100), 214(64), 190(53), 170(22), 146(11), 133(27), 120(93), 109(100), 93(18), 80(16); Found: C, 68.48; H, 4.64; N, 4.76%. Calcd for $C_{17}H_{14}FNO_3$: C, 68.22; H, 4.71; N, 4.68%; HPLC: Daicel Chiralcel OJ-H, Hexane/EtOH = 5/1, Flow rate=0.8 mL/min, UV=254 nm, *anti*; t_R=48.9 min (major), t_R= 66.0 min (minor), *syn*; t_R= 41.3 min (major), t_R= 46.9 min (minor).



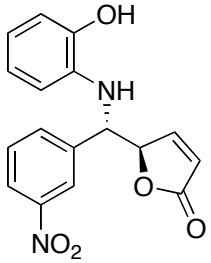
5-[(4-Bromophenyl)-[(2-hydroxyphenyl)amino]methyl]furan-2(5*H*)-one (5c)

$[\alpha]_D^{23}$ 143.3 (c 1.02, $CHCl_3$); R_f 0.4 (Hexane: Ethyl acetate = 1:1); m.p. 135.0-136.0 ˚C (Benzene); IR ($CHCl_3$) 3598, 3402, 3026, 3013, 2856, 1763, 1612, 1599, 1514, 1487, 1448, 1406, 1346, 1265, 1240, 1198, 1159, 1105, 1074, 1011, 905, 816 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=7.38-7.13 (m, 5H), 6.77-6.56 (m, 3H), 6.39-6.37 (m, 1H), 6.05 (d, 1H, *J*=5.9, 2.0 Hz), 5.44-5.41 (m, 1H), 4.87 (brs, 1H), 4.78 (d, 1H, *J*=3.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ=173.5, 153.8, 144.2, 136.0, 134.8, 132.3, 132.1, 129.2, 123.4, 122.4, 121.2, 119.0, 114.8, 113.2, 85.6, 59.3; MS(DI) m/z 361(M^++2, 11), 359(M^+, 12), 279(26), 278(100), 277(43), 276(100), 253(34), 252(100), 251(35), 250(100), 171(22), 169(13), 143(22), 120(47), 115(75), 109(100), 89(34), 80(27); Found: C, 56.91; H, 4.04; N, 3.90%. Calcd for $C_{17}H_{14}BrNO_3$: C, 56.69; H, 3.92; N, 3.89%; HPLC: Daicel Chiralpak AD-H, Hexane/EtOH=9/1, Flow rate=1.0 mL/min, UV=254 nm, *anti*; t_R=40.1 min (major), t_R= 43.2 min (minor), *syn*; t_R=50.6 min (minor), t_R=61.2 min (major).



5-[[(2-Hydroxyphenyl)amino]-(4-nitrophenyl)methyl]furan-2(5*H*)-one (5d)

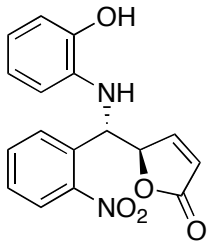
R_f 0.4 (Hexane: Ethyl acetate = 1:1); IR ($CHCl_3$) 3597, 3396, 3030, 3020, 3009, 2858, 1763, 1611, 1522, 1493, 1448, 1350, 1269, 1232, 1157, 1105, 1041, 858, 818 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.10 (d, 2H, *J*=8.8 Hz), 7.51 (d, 2H, *J*=8.8 Hz), 7.45 (dd, 1H, *J*=6.8, 1.6 Hz), 6.79-6.61 (m, 4H), 6.35 (dd, 1H, *J*=6.8, 1.4 Hz), 6.12 (dd, 1H, *J*=5.7, 2.0 Hz), 5.52 (brs, 1H), 4.93 (brs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=173.0, 153.5, 147.7, 144.3, 143.9, 134.2, 128.5, 123.9, 123.4, 121.2, 119.1, 114.7, 112.7, 85.0, 59.2; MS(DI) m/z 326(M^+, 5), 243(100), 217(51), 197(15), 115(14), 109(23), 80(13); Found: C, 62.46; H, 4.51; N, 8.41%. Calcd for $C_{17}H_{14}N_2O_5$: C, 62.57; H, 4.32; N, 8.59%; HPLC: Daicel Chiralpak AD-H, Hexane /EtOH = 5/1, Flow rate = 1.0 mL/min, UV=254 nm, *anti*; t_R=38.6 min (major), t_R= 40.7 min (minor), *syn*; t_R=45.5 min (minor), t_R=63.4 min (major).



5-[[(2-Hydroxyphenyl)amino]-(3-nitrophenyl)methyl]furan-2(5*H*)-one (5e)

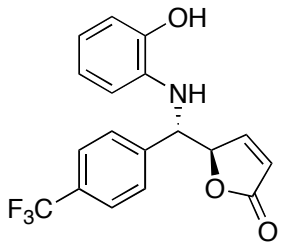
R_f 0.5 (Hexane: Ethyl acetate= 1:1); IR ($CHCl_3$) 3599, 3373, 3034, 2856, 1763, 1612, 1525, 1514, 1448, 1352, 1265, 1232, 1201, 1157, 1089, 1041, 897 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.81-8.17 (m, 1 H), 8.07 (ddd, 1 H, *J*=8.2, 2.8, 1.0 Hz), 7.68 (d, 1 H, *J*=7.7 Hz), 7.50 (dd, 1 H, *J*=5.8, 1.7 Hz), 7.30-7.26 (m, 1 H), 6.73 (dd, 1 H, *J*=7.9, 1.5 Hz), 6.69 (dt, 1 H, *J*=7.6, 1.5 Hz), 6.60 (dt, 1 H, *J*=7.6, 1.5 Hz), 6.39 (dd, 1 H, *J*=7.9, 1.5 Hz), 6.11 (dd, 1 H, *J*=5.8, 2.0 Hz), 5.54 (ddd, 1 H, *J*=3.9, 2.0, 1.7 Hz), 5.06 (brs, 1 H), 4.95 (brs, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=172.7(*syn*), 172.6(*anti*), 153.5(*syn*), 153.2(*anti*), 148.6(*syn*), 148.3(*anti*), 144.2(*syn*), 144.0(*anti*), 140.8(*syn*), 139.5(*anti*),

134.5(*syn*), 134.2(*anti*), 133.5(*anti*), 130.0(*syn*), 129.9(*anti*), 123.6(*anti*), 123.4(*anti*), 123.3(*syn*), 122.4(*anti*), 122.2(*syn*), 121.3(*syn*), 121.2(*anti*), 121.1(*syn*), 120.1(*syn*), 119.4(*syn*), 119.2(*anti*), 117.4(*syn*), 115.4(*syn*), 114.8(*anti*), 113.3(*syn*), 113.0(*anti*), 85.2(*syn*), 85.0(*anti*), 59.8(*syn*), 59.4(*anti*); MS(DI) m/z 326(M^+, 5), 243(100), 217(78), 197(22), 120(38), 109(46), 80(12); Found: C, 62.36; H, 4.32; N, 8.45%. Calcd for $C_{17}H_{14}N_2O_5$: C, 62.57; H, 4.32; N, 8.59%; HPLC: Daicel Chiralpak IA, Hexane/EtOH=9/1, Flow rate=1.0 mL/min, UV=254 nm, *anti*; t_R=34.6 min (major), t_R= 38.5 min (minor), *syn*; t_R=42.8 min (major), t_R=47.7 min (minor).



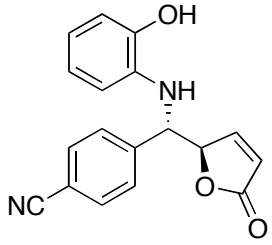
5-[[(2-Hydroxyphenyl)amino]-(2-nitrophenyl)methyl]furan-2(5*H*)-one (5f)

R_f 0.4(*anti*), 0.5(*syn*) (Hexane: Ethyl acetate = 1:1); IR ($CHCl_3$) 3599, 3404, 3024, 3013, 1763, 1611, 1529, 1448, 1350, 1294, 1265, 1240, 1161, 1105, 1090, 1040 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ= 7.87 (d, 1H, *J*=8.2 Hz), 7.64-7.62 (m, 1H), 7.58 (d, 1H, *J*=7.9 Hz), 7.22-7.18 (m, 1H), 6.85-6.81 (m, 1H), 6.70-6.53 (m, 3H), 6.38 (d, 1H, *J*=7.7 Hz), 6.00 (dd, 1H, *J*=5.9, 2.0 Hz), 5.93-5.91 (m, 1H), 5.76-5.74 (m, 1H), 5.45 (brd, 1H, *J*=9.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ=173.8, 155.1, 148.9, 144.0, 135.4, 134.4, 134.3, 129.8, 129.2, 125.3, 123.0, 121.5, 119.2, 114.9, 112.6, 85.7, 53.6; MS(DI) m/z 326(M^+, 18), 243(100), 217(10), 196(38), 135(11), 119(59), 109(100), 92(44), 82(71); Found: C, 62.35; H, 4.37; N, 8.47%. Calcd for $C_{17}H_{14}N_2O_5$: C, 62.57; H, 4.32; N, 8.59%; HPLC: Daicel Chiralpak IA, Hexane/EtOH=10/1, Flow rate=0.5 mL/min, UV=254 nm, *anti*; t_R=57.1 min (major), t_R= 75.1 min (minor), *syn*; t_R=46.2 min (major), t_R=54.8 min (minor).



5-[[(2-Hydroxyphenyl)amino]-(4-trifluoromethylphenyl)methyl]furan-2(5*H*)-one (5g)

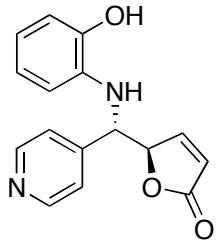
R_f 0.3 (Hexane: Ethyl acetate=1:1); IR ($CHCl_3$) 3597, 3290, 3026, 2856, 1767, 1612, 1599, 1514, 1448, 1420, 1327, 1267, 1224, 1215, 1169, 1132, 1107, 1069, 1042, 1018, 903, 816 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.45-7.32 (m, 5H), 6.74-6.56 (m, 3H), 6.38 (d, 1H, *J*=7.9 Hz), 6.06 (dd, 1H, *J*=5.8, 1.9 Hz), 5.51-5.50 (m, 1H), 5.00 (brs, 1H), 4.89 (d, 1H, *J*=3.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ=173.1, 153.3, 143.9, 140.8, 134.4, 130.3 (q, J_{F-C}=32.6 Hz), 127.7, 125.6 (q, J_{F-C}=3.4 Hz), 123.7 (q, J_{F-C}=272.3 Hz), 123.3, 121.0, 118.9, 114.6, 112.8, 85.2, 59.2; ^{19}F-NMR (376 MHz, $CDCl_3$) δ=99.07 (s, *anti*), 99.14 (s, *syn*); MS(DI) m/z 349(M^+, 9), 266(100), 240(77), 184(19), 171(24), 159(25), 115(60), 109(87), 80(41); Found: C, 62.03; H, 4.26; N, 3.86%. Calcd for $C_{18}H_{14}F_3NO_3$: C, 61.89; H, 4.04; N, 4.01%. HPLC: Daicel Chiralcel OD-H, Hexane/EtOH=7/1, Flow rate=1.0 mL/min, UV=254 nm, *anti*; t_R=42.0 min (major), t_R= 59.8 min (minor), *syn*; t_R=34.1 min (minor), t_R=35.5 min (major).



5-[(4-Cyanophenyl)-[(2-hydroxyphenyl)amino]methyl]furan-2(5*H*)-one (5h)

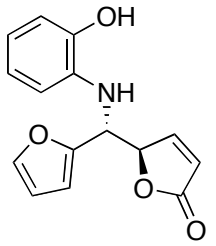
R_f 0.4 (Hexane: Ethyl acetate=1:1); IR ($CHCl_3$) 3603, 3294, 3026, 2978, 2360, 2341, 2233, 1769, 1611, 1514, 1448, 1340, 1240, 1209, 1157, 1105, 1090, 1043, 1020, 877, 818 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=7.43 (dd, 1H, *J*=5.8, 1.7 Hz), 7.39 (d, 2H, *J*=8.3 Hz), 7.32 (d, 2H, *J*=8.3 Hz), 6.73-6.56 (m, 3H), 6.34-6.31 (m, 1H), 6.07 (dd, 1H, *J*=5.8, 2.0 Hz), 5.52 (ddd, 1H, *J*=3.9, 2.0, 1.7 Hz), 5.09 (brs, 1H), 4.89 (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ =172.8, 153.2, 143.8, 142.3, 134.1, 132.4, 128.2, 123.3,

121.0, 118.9, 118.3, 114.6, 112.6, 112.0, 84.9, 59.3; MS(DI) m/z 306(M^+, 14), 234(10), 223(50), 197(48), 141(100), 115(55), 80(50); Found: C, 70.37; H, 4.87; N, 9.36%. Calcd for $C_{18}H_{14}N_2O_3$: C, 70.58; H, 4.61; N, 9.15%; HPLC: Daicel Chiralpak IA, Hexane/EtOH=7/1, Flow rate=1.0 mL/min, UV=254 nm, *anti*; t_R=31.3 min (major), t_R= 34.8 min (minor), *syn*; t_R=37.1 min (major), t_R=43.7 min (minor).



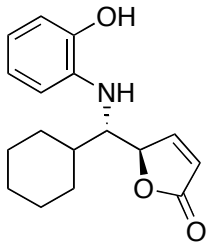
5-[[(2-Hydroxyphenyl)amino]-(4-pyridyl)methyl]furan-2(5*H*)-one (5i)

R_f 0.3 (Ethyl acetate); IR ($CHCl_3$) 3597, 3393, 3020, 3013, 2963, 2930, 2856, 1767, 1599, 1514, 1448, 1418, 1375, 1362, 1339, 1313, 1247, 1225, 1159, 1105, 1094, 1043, 901, 814, 804 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.53-8.48 (m, 2H), 7.43-7.38 (m, 1H), 7.32-7.28 (m, 2H), 6.73-6.55 (m, 3H), 6.34 (d, 1H, *J*=7.7 Hz), 6.11 (d, 1H, *J*=5.7 Hz), 5.43 (d, 1H, *J*=4.2 Hz), 4.79 (d, 1H, *J*=4.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ=172.0, 152.8, 149.2, 147.7, 144.6, 134.5, 123.5, 122.9, 120.5, 119.0, 114.6, 112.4, 84.5, 59.1; MS(DI) m/z 282(M^+, 63), 271(30), 255(14), 239(42), 238(100), 237(52), 223(33), 209(19), 199(100), 197(100), 196(100), 173(100), 160(51), 132(17), 120(38), 117(42), 109(100), 91(20), 80(33); Found: C, 68.14; H, 4.76; N, 9.74%. Calcd for $C_{16}H_{14}N_2O_3$: C, 68.07; H, 5.00; N, 9.92%. HPLC: Daicel Chiralcel OJ-H, Hexane/EtOH=9/1, Flow rate=1.0 mL/min, UV=254 nm, *anti*; t_R=24.3 min (major), t_R=64.8 min (minor), *syn*; t_R=39.4 min (major), t_R=51.4 min (minor).



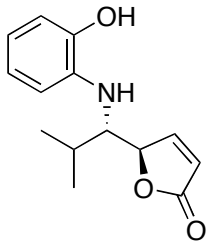
5-[(4-Furyl)-[(2-hydroxyphenyl)amino]methyl]furan-2(5*H*)-one (5j)

R_f 0.4 (Hexane: Ethyl acetate= 1:1); IR ($CHCl_3$) 3599, 3383, 3028, 3009, 1755, 1611, 1514, 1448, 1346, 1321, 1269, 1232, 1201, 1122, 1107, 1088, 1043, 897, 812 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=7.48 (d, 1H, *J*=5.3 Hz, *anti*), 7.40 (d, 1H, *J*=5.5 Hz, *syn*), 7.34 (d, 1H, *J*=20.7 Hz), 6.65-6.60 (m, 4H), 6.28 (d, 2H, *J*=20.7 Hz), 6.11 (d, 1H, *J*=5.3 Hz, *anti*), 6.06 (d, 1H, *J*=5.5 Hz, *syn*), 4.89 (d, 1H, *J*=3.8 Hz, *anti*), 4.77 (d, 1H, *J*=4.9 Hz, *syn*), 4.58 (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ =173.3(*syn*), 173.2(*anti*), 153.9(*syn*), 153.6(*anti*), 150.7(*syn*), 150.6(*anti*), 145.1(*syn*), 144.8(*anti*), 142.8(*syn*), 142.5(*anti*), 134.5(*syn*), 134.5(*anti*), 123.0(*anti*), 122.5(*syn*), 121.0(*anti*), 121.0(*syn*), 120.0(*syn*), 119.8(*anti*), 114.9(*anti*), 114.8(*syn*), 114.4(*anti*), 110.7(*syn*), 110.6(*anti*), 108.5(*syn*), 108.5(*anti*), 84.2(*anti*), 84.1(*syn*), 55.2(*syn*), 54.6(*anti*); MS(DI) m/z 271(M^+, 13), 188(100), 170(13), 162(56), 120(57), 109(55), 81(70); Found: C, 66.69; H, 4.92; N, 5.16%. Calcd for $C_{15}H_{13}NO_4$: C, 66.41; H, 4.83; N, 5.16%; HPLC: Daicel Chiralcel OD-H, Hexane/EtOH= 10/1, Flow rate=1.0 mL/min, UV=254 nm, *anti*; t_R=30.0 min (major), t_R=38.1 min (minor), *syn*; t_R=17.6 min (major), t_R=26.5 min (minor).



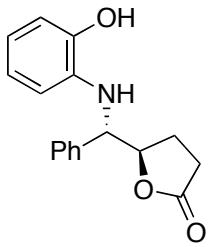
5-[(4-Cyclohexycly)-[(2-hydroxyphenyl)amino]methyl]furan-2(5*H*)-one (5k)

R_f 0.5 (Hexane: Ethyl acetate = 1:1); IR($CHCl_3$) 3599, 3301, 3028, 3016, 3007, 2856, 1753, 1610, 1514, 1450, 1352, 1265, 1164, 1099, 1084, 903, 818 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=7.47 (dd, 1H, *J*=5.8, 1.6 Hz), 6.80-6.49 (m, 4H), 6.13 (dd, 1H, *J*=5.8, 1.8 Hz), 5.30 (brs, 1H), 5.09 (ddd, 1H, *J*=8.4, 1.8, 1.6 Hz), 3.33 (brs, 1H), 1.93-1.61 (m, 6H), 1.34-1.22 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=173.2, 156.3, 142.8, 136.5, 121.9, 117.6, 114.6, 112.1, 83.9, 61.1, 40.5, 30.4, 26.9, 26.3, 26.2, 26.1; MS(DI) m/z 287(M^+, 2), 204(100), 120(48), 109(15); Found: C, 71.22; H, 7.13; N, 4.62%. Calcd for $C_{17}H_{21}NO_3$: C, 71.06; H, 7.37; N, 4.87%; HPLC: Daicel Chiralcel OJ-H Hexane/EtOH = 10/1 Flow rate = 1.0 mL/min, UV=254 nm, *anti*; t_R=24.0 min (major), t_R=49.3 min (minor), *syn*; t_R=16.9 min (minor), t_R=21.9 min (major).



5-[[(2-Hydroxyphenyl)amino]-(isopropyl)methyl]furan-2(5*H*)-one (5l)

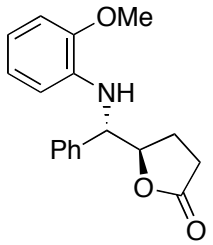
R_f 0.3 (Hexane: Ethyl acetate = 2:1); IR ($CHCl_3$) 3601, 3308, 3032, 3024, 3010, 2876, 1751, 1611, 1514, 1448, 1373, 1263, 1164, 1094, 1078, 1036, 903, 816 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=7.8 (dd, 1H, *J*=5.7, 1.3 Hz), 6.81-6.49 (m, 4H), 6.13 (dd, 1H, *J*=5.9, 1.8 Hz), 5.04 (d, 1H, *J*=8.2 Hz), 4.12 (brs, 1H), 3.33-3.31 (m, 1H), 2.23-2.19 (m, 1H), 1.07 (d, 3H, *J*=7.0 Hz), 1.02 (d, 3H, *J*=6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ=173.7, 156.7, 143.1, 136.6, 121.7, 121.4, 117.6, 114.6, 111.9, 84.6, 61.2, 30.4, 19.9, 16.3; MS(DI) m/z 247(M^+,38), 204(15), 164(100), 109(51), 80(16); Found: C, 67.98; H, 7.01; N, 5.74%. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66%; HPLC: Daicel Chiralcel OJ-H Hexane/EtOH=10/1 Flow rate = 1.0 mL/min, UV=254 nm, *anti*; t_R=35.9 min (major), t_R=59.7 min (minor), *syn*; t_R=33.2 min (minor), t_R=49.4 min (major).



5-[[(2-Hydroxyphenyl)amino]-phenylmethyl]-dihydrofuran-2-one

To a suspension of 5-[[(2-hydroxyphenyl)amino]-phenylmethyl]furan-2(5*H*)-one (**5a**) (423.3 mg, 1.51 mmol, *anti*/*syn*=91 (77% ee)/9 (23% ee)) and Pd/C (45.5 mg, 10 wt. %) in Ethyl acetate (23 mL) was purged with H_2 (1 atm) and the mixture was stirred at room temperature for 4 h. After filtration over Celite, the filtrate was concentrated to dryness in vacuo. The crude product was purified by silica gel column chromatography (Hexane/EtOAc= 2/1) to give the product (416.4 mg, 1.47 mmol) in 97% yield

R_f 0.5 (Hexane : Ethyl acetate = 1:1); IR ($CHCl_3$) 3601, 3383, 3030, 3013, 1774, 1742, 1611, 1599, 1512, 1495, 1454, 1375, 1352, 1319, 1267, 1228, 1213, 1205, 1175, 1153, 1128, 1088, 1040, 1028, 1002, 928, 914 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ =7.41-7.24 (m, 5H), 6.77-6.57 (m, 3H), 6.48 (dd, 1H, *J*=7.8, 1.4 Hz), 5.03-5.00 (m, 1H), 4.53 (d, 1H, *J*=3.5 Hz), 2.54-2.45 (m, 1H), 2.29-2.21 (m, 1H), 2.13-2.06 (m, 1H), 1.90-1.83 (m, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ=179.9, 146.2, 139.7, 136.8, 129.5, 129.3, 128.9, 121.0, 118.9, 114.8, 114.0, 84.3, 62.0, 28.7, 25.0; MS(DI) m/z 283(M^+, 14), 199(41), 198(100), 196(12), 120(12), 91(15); Found: C, 72.07; H, 6.02; N, 4.67%. Calcd for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05; N, 4.94%

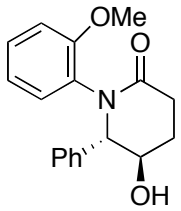


5-[[(2-Methoxyphenyl)amino]-phenylmethyl]-dihydrofuran-2-one

To a suspension of 5-[[(2-hydroxyphenyl)amino]-phenylmethyl]-dihydrofuran-2-one (188 mg, 0.66 mmol) and K_2CO_3 (500 mg, 3.62 mmol) in acetone (11.5 mL) was added methyl iodide (2.3 mL) and the mixture was stirred at room temperature for 17 h. The reaction mixture was quenched by addition of water at 0 ˚C and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4. After filtration of the drying agent, the filtrate was concentrated to dryness in vacuo. The crude product was purified by silica gel column chromatography (Hexane/EtOAc= 1/1) to give the product (193.3 mg, 0.65 mmol) in 98% yield and with *anti*/*syn*=93 (77% ee)/7 (25% ee), which was determined by chiral HPLC analysis on a Daicel Chiralcel AD-H column.

R_f 0.5 (Hexane : Ethyl acetate = 1:1); IR ($CHCl_3$) 3524, 3423, 3067, 3032, 3011, 2961, 2939, 2870, 2837, 1778, 1732, 1603, 1560, 1514, 1456, 1431, 1373, 1350, 1304, 1265, 1244, 1209, 1178, 1151, 1134, 1047, 1028, 928, 908 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ =7.38-7.24 (m, 5H), 6.74 (dd, 1H, *J*=7.7, 1.5 Hz), 6.70-6.60 (m, 2H), 6.39 (dd, 1H, *J*=7.7, 1.5 Hz), 5.19 (brs, 1H), 4.99-4.94 (m, 1H), 4.52 (brs, 1H), 3.86 (s, 1H), 2.31-2.20 (m, 2H), 2.11-2.02 (m, 1H), 1.87-1.75 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ=176.9, 147.0, 137.1, 135.9, 128.7, 128.0, 127.9, 120.8, 117.2, 111.1, 109.4, 82.3, 60.4, 55.3,

27.6, 23.7; MS(DI) m/z 297(M^+, 26), 213(60), 212(100), 197(13), 196(54), 120(52), 104(10), 91(31), 77(16); Found: C, 72.93; H, 6.32; N, 4.47%. Calcd for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71%; HPLC: Daicel Chiralpak AD-H Hexane/EtOH=5/1 Flow rate = 0.3 mL/min, UV=254 nm, *anti*; t_R=41.7 min (major), t_R=43.5 min (minor), *syn*; t_R=7.8 min (major), t_R=51.3 min (minor).



5-Hydroxy-*N*-(2-methoxyphenyl)-6-phenyl-piperidin-2-one (6)

To a suspension of 5-[[(2-methoxyphenyl)amino]-phenylmethyl]-dihydrofuran-2-one (68.0 mg, 0.23 mmol) in benzene (2 mL) was added *t*-BuOK (32.8 mg, 0.29 mmol) and the mixture was stirred at room temperature for 0.5 h. The reaction mixture was quenched by addition of sat. NH_4Cl at 0 ˚C and extracted with ethyl acetate. The combined organic layers were washed with sat. NH_4Cl and brine, dried over anhydrous Na_2SO_4. After filtration of the drying agent, the filtrate was concentrated to dryness in vacuo. The crude product was purified by silica gel column chromatography (Hexane/EtOAc= 1/1) to give the product (57.9 mg, 0.20 mmol) in 85% yield and with *anti*/*syn*=92 (78% ee)/8 (23% ee), which was determined by chiral HPLC analysis on a Daicel Chiralcel OD-H column.

R_f 0.5 (Ethyl acetate); IR ($CHCl_3$) 3510, 3431, 3065, 3043, 3007, 2937, 2961, 2872, 2837, 1709, 1603, 1512, 1456, 1431, 1344, 1244, 1213, 1178, 1132, 1101, 1086, 1070, 1051, 1030, 943, 927, 916 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ =7.38-7.20 (m, 5H), 6.75 (dd, 1H, *J*=7.7, 1.5), 6.69 (ddd, 1H, *J*=7.7, 7.7, 1.5 Hz), 6.62 (ddd, 1H, *J*=7.7, 7.7, 1.5 Hz), 6.40 (dd, 1H, *J*=7.7, 1.5 Hz), 4.42 (d, 1H, *J*=4.6 Hz), 4.00-3.96 (m, 1H), 3.86 (s, 3H), 2.56-2.40 (m, 2H), 1.92-1.80 (m, 1H), 1.63-1.54 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ=179.3, 147.1, 138.9, 136.5, 128.6, 127.6, 127.5, 121.0, 117.1, 111.4, 109.4, 73.8, 62.3, 55.4, 30.7, 28.1; MS(DI) m/z 297(M^+, 4), 213(15), 212(100); Found: C, 72.90; H, 6.72; N, 4.53%. Calcd for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71%; HPLC: Daicel Chiralcel OD-H Hexane/EtOH=5/1 Flow rate = 0.5 mL/min, UV=254 nm, *anti*; t_R=45.4 min (minor), t_R=68.3 min (major), *syn*; t_R=23.8 min (minor), t_R=31.7 min (major).

Reference

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