Supporting information for:

Synthesis and optical resolution of 9,9′-spirobifluorene-1,1′-diol

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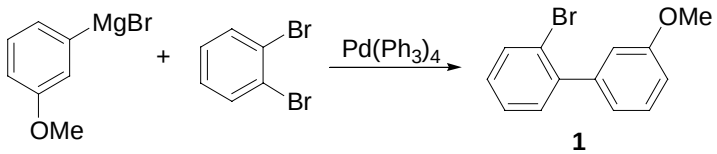
General:

All reactions and manipulations were performed using standard Schlenk techniques. THF was distilled from sodium benzophenone ketyl. CH_2Cl_2 was distilled from CaH_2. Melting points were measured on a RY-I apparatus and uncorrected. ^1H, ^{13}C and ^{31}P NMR spectra were recorded on a Varian Mercury Vx-300 spectrometer or Bruker 300 MHz. Chemical shifts were reported in ppm down field from internal Me_4Si. Optical rotations were determined using a Perkin Elmer 341 MC polarimeter. Elemental analyses were performed on the Yanaca CDRDER MT-3 instrument. Mass spectra were recorded on the VG-7070E spectrometer. HPLC analyses were performed using a Hewlett Packard Model HP 1100 Series. X-ray diffraction analysis was performed on a Bruker smart-1000 X-ray diffraction meter.

1. Synthesis of racemic 9,9′-spirobifluorene-1,1′-diol

Preparation of 2-bromo-3′-methoxybiphenyl (1)

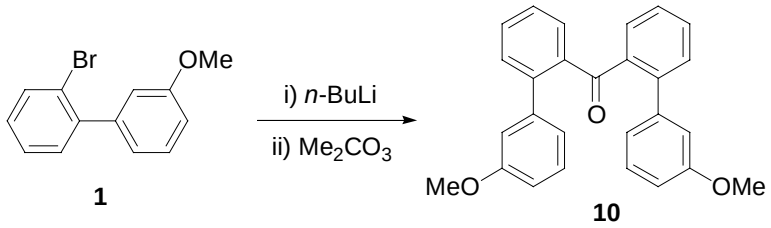


1

A solution of 3-methoxyphenylmagnesium bromide was prepared from magnesium powders (2.1 g, 89 mmol) and 1-bromo-3-methoxybenzene (16.6 g, 89 mmol) in 100 mL of THF. This solution was added to the mixture of 1,2-dibromobenzene (20.0 g, 92 mmol) and tetrakis(triphenylphosphine)palladium (1.5 g, 1.3 mmol) in 100 mL of THF. The resulted mixture was stirred for 48 h at 40 ^oC and was hydrolyzed with saturated NH_4Cl. Extraction with Et_2O, dryness over $MgSO_4$ and concentration under reduced pressure yielded the crude product. Chromatography of crude product on silica gel with PE/EA (30:1) gave compound **1** as a colorless liquid (14.0 g, 60%). ^1H NMR (300 MHz, $CDCl_3$) δ 3.87 (s, 3H, Ar-OCH_3), 6.98 (d, 1H, J = 7.5 Hz, Ar-H), 7.13-7.58 (m, 5H, Ar-H), 7.59 (d, 2H, J = 7.2 Hz, Ar-H); ^{13}C NMR

(75 MHz, $CDCl_3$) δ 55.5, 113.5, 115.3, 122.1, 122.8, 127.6, 129.0, 129.3, 131.4, 133.4, 142.6, 159.4; MS (EI) m/z 263 and 264 (M^+); Anal. Calcd for $C_{13}H_{11}BrO$: C, 59.34; H, 4.21. Found: C, 59.28; H, 4.18.

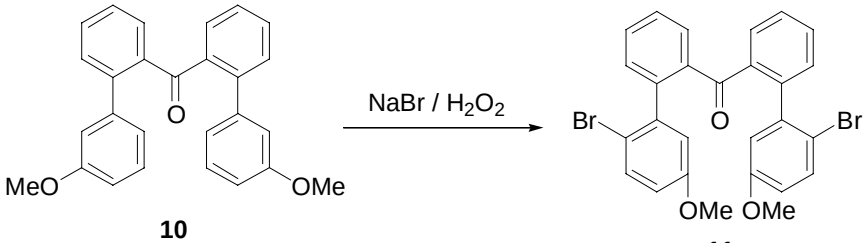
Preparation of bis(3′-methoxybiphenyl-2-yl)methanone (10)



1 **10**

To a solution of **1** (15.1 g, 57.4 mmol) in 120 mL of THF was added *n*-BuLi (34.3 mL, 60 mmol, 1.8 M in Hexane) at -78 °C, and the mixture was stirred for 0.5 h. After slowly addition of methyl carbonate (2.3 g, 25.7 mmol) in 40 mL of THF, this reaction mixture was gradually warmed to -45~ -40 °C and kept at this temperature for 3 h to give a yellow slurry. This slurry was warmed to room temperature, hydrolyzed with saturated NH_4Cl and evaporated under reduced pressure to remove the solvent. The residue was dissolved in CH_2Cl_2, washed with dilute HCl and brine, dried over $MgSO_4$, concentrated under reduced pressure to offer a yellow solid. The solid was recrystallized with EA to give compound **10** as a white solid (7.1 g, 75%). M.p. 159~160 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.74 (s, 6H, Ar-OCH_3), 6.64 (s, 2H, Ar-H), 6.69 (t, 4H, *J* = 7.5 Hz, Ar-H), 7.06-7.20 (m, 6H, Ar-H), 7.29-7.39 (m, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.1, 112.7, 114.5, 121.5, 126.7, 128.9, 129.9, 130.4, 130.5, 139.1, 141.2, 141.8, 158.9, 200.5; MS (EI) m/z 394 (M^+); Anal. Calcd for $C_{27}H_{22}O_3$: C, 82.21; H, 5.62. Found: C, 82.26; H, 5.71.

Preparation of bis(2′-bromo-5′-methoxybiphenyl-2-yl)methanone (**11)**

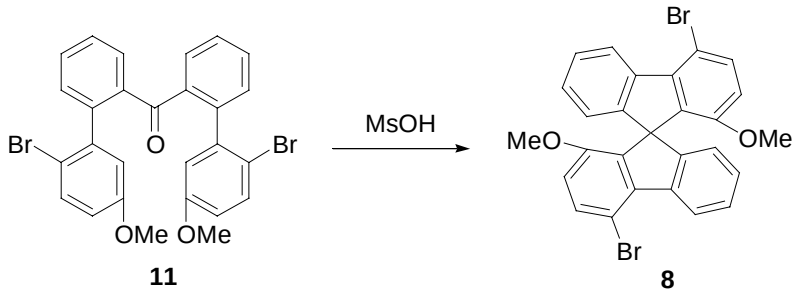


10 **11**

Sodium bromide (5.2 g, 50.8 mmol) and the well-powdered **10** (10.0 g, 25.4 mmol) were added to 300 mL of acetic acid to give a suspension. Hydrogen peroxide (30% aqueous, 15 mL, 0.44 mol) was added to this suspension. After vigorously stirring for 6 h, the mixture was diluted with water and extracted with CH_2Cl_2 (3×30 mL). The combined organic phase was washed with aqueous $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated under reduced pressure to give a light-yellow solid **11** (14.2 g, 100%). M.p. 158~160 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.69 (s, 3H, Ar-OCH_3), 3.37 (s, 3H, Ar-OCH_3), 6.63-6.69 (m, 4H, Ar-H), 7.19-7.21

(m, 4H, Ar-H), 7.34-7.50 (m, 5H, Ar-H), 7.59 (d, 1H, *J* = 7.8 Hz, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.4, 113.7, 113.8, 114.4, 115.3, 116.5, 116.7, 127.2, 127.3, 129.1, 130.0, 130.4, 130.7, 131.0, 131.1, 132.8, 133.0, 137.9, 139.6, 139.7, 140.6, 141.8, 142.4, 158.3, 196.4; MS (EI) m/z 473 (M^+-Br); Anal. Calcd for $C_{27}H_{20}Br_2O_3$: C, 58.72; H, 3.65. Found: C, 58.54; H, 3.50.

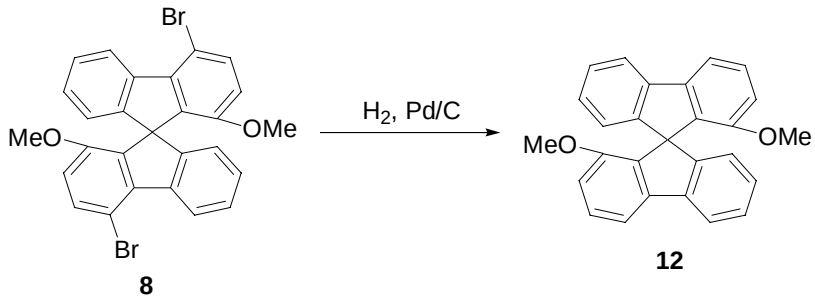
Preparation of 4,4′-dibromo-1,1′-dimethoxy-9,9′-spirobifluorene (8)



11 **8**

The compound **11** (14.2 g, 25.7 mmol) was added to 400 mL of methanesulfonic acid and was stirred vigorously at 40~50 °C for 5 h. The reaction mixture was poured into ice-cold water, extracted with CH_2Cl_2 (3×30 mL). The organic phase was washed with aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, concentrated under reduced pressure to offer a yellow solid. This solid was washed with EA to give compound **8** as a white powder (10.0 g, 73%). M.p. 158~160 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.22 (s, 6H, Ar-OCH_3), 6.54 (d, 2H, *J* = 8.4 Hz, Ar-H), 6.63 (d, 2H, *J* = 7.2 Hz, Ar-H), 7.11 (t, 3H, *J* = 7.5 Hz, Ar-H), 7.36 (t, 3H, *J* = 7.5 Hz, Ar-H), 7.47 (d, 2H, *J* = 8.7 Hz, Ar-H), 8.63 (d, 2H, *J* = 7.5 Hz, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.0, 103.2, 107.6, 112.4, 119.6, 122.6, 123.1, 126.9, 128.0, 133.6, 137.0, 141.3, 148.0, 155.0; MS (EI) m/z 534 (M^+); Anal. Calcd for $C_{27}H_{18}Br_2O_2$: C, 60.70; H, 3.40. Found: C, 60.72; H, 3.46.

Preparation of 1,1′-dimethoxy-9,9′-spirobifluorene (12)

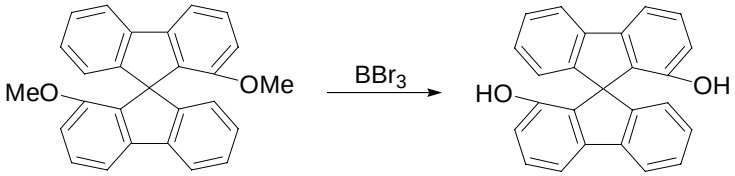


8 **12**

To a solution of the compound **8** (7.2 g, 13.5 mmol) in 120 mL of THF was added tetrabutylammonium bromide (2.9 g, 9 mmol), potassium carbonate (13.1 g, 95 mmol) in 58 mL distilled water and palladium on coal (0.95 g, 10%, 0.9 mmol). The mixture was stirred and hydrogenated by bubbling hydrogen at 35~40 °C for 4 h. After cooling to room

temperature, the reaction mixture was filtrated through celite and extracted with CH_2Cl_2 (3×30 mL). The organic phase was dried over $MgSO_4$, passed through a silica gel pad. Evaporation of solvent under reduced pressure produced compound **12** as a white solid (5.4 g, 100%). M.p. 214~216 ^oC; ^1H NMR (300 MHz, d_6-acetone) δ 3.24 (s, 6H, Ar-OCH_3), 6.52 (d, 2H, *J* = 7.5 Hz, Ar-H), 6.76 (d, 2H, *J* = 8.1 Hz, Ar-H), 7.06 (t, 2H, *J* = 7.5 Hz, Ar-H), 7.29-7.40 (m, 4H, Ar-H), 7.57 (d, 2H, *J* = 7.5 Hz, Ar-H), 7.89 (d, 2H, *J* = 7.8 Hz, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.8, 111.1, 112.6, 119.8, 122.9, 127.0, 127.4, 129.0, 134.6, 142.0, 144.2, 148.2, 156.1; MS (EI) m/z 376 (M^+); Anal. Calcd for $C_{27}H_{20}O_2$: C, 86.14; H, 5.36. Found: C, 85.96; H, 5.47.

Preparation of 1,1′-dihydroxy-9,9′-spirobifluorene (13)



12 **13**

Tribromoboron (7.2 mL, 44 mmol) in 18 mL of CH_2Cl_2 was added dropwise to a solution of the compound **12** (4.0 g, 11 mmol) in 74 mL of CH_2Cl_2 at –78 ^oC. The mixture was stirred overnight and warmed spontaneously during the reaction. The reaction mixture was diluted with CH_2Cl_2 (50 mL), washed with aqueous $NaHSO_3$ and brine successively, and dried over $MgSO_4$. Concentration under reduced pressure offered a brown solid. Recrystallization of the crude product with acetone and petroleum ether gave the compound **13** as a white solid (3.0 g, 81%). M.p. 289~291 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ 3.98 (s, 2H, Ar-OH), 6.68 (d, 2H, *J* = 6.6 Hz, Ar-H), 6.78 (d, 2H, *J* = 7.5 Hz, Ar-H), 7.16 (t, 2H, *J* = 7.5 Hz, Ar-H), 7.33-7.43 (m, 4H, Ar-H), 7.50 (d, 2H, *J* = 7.5 Hz, Ar-H), 7.86 (d, 2H, *J* = 8.7 Hz, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.0, 113.2, 116.1, 120.8, 123.7, 128.5, 128.6, 129.1, 130.6, 141.0, 142.9, 145.5, 152.5; MS (EI) m/z 348 (M^+); Anal. Calcd for $C_{25}H_{16}O_2$: C, 86.19; H, 4.63. Found: C, 85.99; H, 4.66.

2. Resolution of racemic 1,1′-dihydroxy-9,9′-spirobifluorene

The well-powdered racemic diol **13** (2.0 g, 5.7 mmol) and (2*R*,3*R*)-N,N,N′,N′-tetracyclohexyl- 2,3-dimethoxysuccinamide (**14**) (2.9 g, 5.7 mmol) were added to 16 mL of ethanol, and the mixture was stirred rapidly to give a clear solution. After a few minutes, white precipitate appeared. This slurry was stirred overnight and filtrated to give a white powder. The powder was dissolved in 50 mL of Et_2O and washed with 1N NaOH. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to recover the resolving reagent. The aqueous layer was acidified by concentrated HCl to pH = 3 and extracted with CH_2Cl_2 (3×20 mL). The CH_2Cl_2 phase was dried with $MgSO_4$ and concentrated under reduced pressure to give the **13** (0.85 g, 85% based on one enantiomer) in 80% ee with *R* configuration.

By repeating the procedures of the inclusion and the decomposition mentioned above, (*R*)-(+)-**13** (0.6 g, 60%) in 99% ee was obtained as a white solid. M.p. 290 ^{o}C; $[\alpha]^{25}_{D}$ = +39.2 (*c* 0.50, $CHCl_3$).

The mother liquid of the resolution was concentrated under reduced pressure to give the **13**, with *S* isomer being predominant. The inclusion complex was decomposed by the procedure referred above and subjected to the resolution by (2*S*,3*S*)-**14** to offer the (*S*)-**13** (0.73, 73% based on one isomer) in 99% ee.

The ee values of the resolution products were determined by HPLC analysis on DAICEL OD-H column: Hex/*i*-PrOH = 85:15, flow = 0.7 mL/min, t_R = 17.0 min, t_S = 26.3 min).

3. X-ray analysis of inclusion complex

A single crystal of inclusion complex suitable for X-ray analysis was prepared by the recrystallization of the complex in ethanol. M.p. 184~186 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.06-1.88 (m, 43H, hexyl and methyl in ethanol), 2.34-2.50 (m, 4H, N-CHR_2), 3.41(s, 6H, OCH_3), 3.68-3.76 (m, 2H, CH_2 in ethanol), 4.14 (s, 2H, HC-CO), 4.57 (s, 2H, Ar-OH), 6.68 (d, 2H, *J* = 8.1 Hz, Ar-H), 6.78 (d, 2H, *J* = 7.5 Hz, Ar-H), 7.16 (t, 2H, *J* = 7.5 Hz, Ar-H), 7.2-7.48 (m, 4H, Ar-H), 7.49 (d, 2H, *J* = 7.5 Hz, Ar-H), 7.85 (d, 2H, *J* = 7.8 Hz, Ar-H); Anal. Calcd for $C_{55}H_{68}N_2O_6$: C, 60.70; H, 3.40. Found: C, 60.72; H, 3.36. The structure and the crystal data are in Figure 1 and Table 1. The bond lengths and the bond angles are in cif file.

Figure 1 X-Ray structure of inclusion complex of (*R*)-**13** and (2*R*,3*R*)-**14**

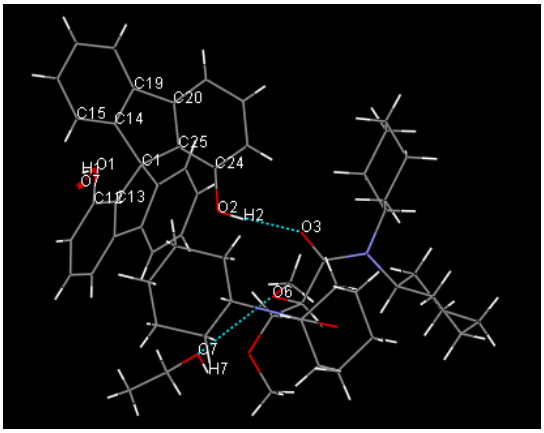


Table 1. Crystal data and structure refinement for inclusion complex (*R*)-**13** and (2*R*,3*R*)-**14**

Empirical formula	$C_{57}\ H_{74}\ N_2\ O_7$
Formula weight	899.18
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)
Unit cell dimensions	a = 9.718(3) Å $\alpha = 90^o$
	b = 25.585(8) Å $\beta = 113.919(7)^o$
	c = 11.268(4) Å $\gamma = 90^o$
Volume	2561.0(14) $Å^3$
Z, Calculated density	2, 1.166 $Mg.m^3$
Absorption coefficient	0.076 mm^{-1}
F(000)	972
Crystal size	0.22 x 0.20 x 0.18 mm
Theta range for data collection	2.29 to 25.00^o
Limiting indices	$-11\leq h\leq 11$, $-30\leq k\leq 30$, $-13\leq l\leq 7$
Reflections collected / unique	13219 / 8644 [R(int) = 0.0754]
Completeness to theta = 25.00	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9865 and 0.9836
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8644 / 1 / 601
Goodness-of-fit on F^2	0.951
Final R indices [I>2sigma(I)]	R1 = 0.0687, wR2 = 0.0785
R indices (all data)	R1 = 0.2024, wR2 = 0.1083
Absolute structure parameter	2.6(14)
Largest diff. peak and hole	0.154 and -0.148 $e.Å^{-3}$