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Synthesis, Chiral Resolution, and Absolute Configuration of C_2-Symmetric, Chiral 9,9′-Spirobifluorenes

Caroline Stobe,[a] Ryota Seto,[a] Andreas Schneider,[a] and Arne Lützen*[a]

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Racemic 2,2′-, 2,2′,7,7′-, and 2,2′,3,3′-substituted 9,9′-spirobifluorenes were synthesised and successfully resolved by HPLC on a Chiralpak IA stationary phase on both analytical and semipreparative scales. Their absolute configurations were determined by comparison of their specific optical rotations with literature data or by comparison of retention times with independently prepared enantiopure material. These compounds are versatile C_2-symmetric building blocks for the formation of more sophisticated cleft-like, chiral molecular architectures.

Introduction

Since 9,9′-spirobifluorene was first synthesised in 1930 by Clarkson and Gomberg[1] its derivatives have found a wide range of applications. After the groups of Prelog[2] and Diederich[3] had explored their use in the field of molecular recognition, 9,9′-spirobifluorenes found their way into catalysis,[4] coordination,[5] and polymer chemistry.[6] Recently, 9,9′-spirobifluorenes have attracted attention because of their unique (opto-)electronic properties.[7] In fact, today 2,2′,7,7′-tetrakis[bis(*p*-methoxyphenyl)amino]-9,9′-spirobifluorene (spiro-MeOTAD)[8] is the most widely used hole transport material (HTM) in high-performance solid-state dye-sensitised solar cells (ssDSCs).[9]

In our group, 9,9′-spirobifluorenes have proven their worth as versatile building blocks for artificial receptors[10] as well as for metallosupramolecular aggregates.[5e,5h] Being especially interested in the molecular recognition of chiral substrates and in the diastereoselective self-assembly of metallosupramolecular aggregates, dissymmetric 9,9′-spirobifluorenes attracted our interest and highlighted a need for enantiomerically pure derivatives.

In 1988, Toda published a procedure for the resolution of 2,2′-dihydroxy-9,9′-spirobifluorene through clathrate formation with (*R*,*R*)-(+)-2,3-dimethoxy-*N*,*N*,*N*′,*N*′-tetracyclohexylsuccindiamide,[11] which was refined and improved by Thiemann in 2005.[12] Although this approach has been applied successfully by us[5e,5h] and others[6e,6h,13] it is quite tedious. This is not only due to the fact that the tartaric acid derivative must be synthesised in three steps and tends to racemise during the second step. In fact, the clathrate formation and its subsequent cleavage have to be performed very carefully to obtain sufficient enantiomeric excesses for both enantiomers.

Drawing on our experience with HPLC-based resolutions[14] we tried to employ this technique for the direct separation of racemic 2,2′-disubstituted 9,9′-spirobifluorenes. HPLC on chiral stationary phases has proven to be a versatile tool for the resolution of a wide range of compounds.[15] In 2006, Zhou et al. reported on a new route to chiral dihydroxy-9,9′-spirobifluorenes. In this study Chiralpak AD-H was employed as chiral stationary phase for the preparative resolution of 3,3′- and 4,4′-dihydroxy-9,9′-spirobifluorene.[16] Nevertheless, in the case of chiral 9,9′-spirobifluorenes, HPLC has primarily been used for analytical purposes.[6h,13] The reason for this is most likely the nature of the stationary phase Chiralpak AD-H, which has been used in all resolutions of chiral 9,9′-spirobifluorenes so far. In this phase the chiral selector amylose tris(3,5-dimethylphenylcarbamate) is only physically adsorbed on the silica gel support. This limits the range of potential eluents to a great extent – in fact only alkanes, alcohols and acetonitrile can be applied without destruction of the column. Although generally exhibiting a good solubility, 9,9′-spirobifluorenes are only poorly soluble in these mobile phases. Consequently, only small amounts of racemate can be applied even on a preparative column which clearly makes this approach quite unattractive due to time-consumption and high costs. Fortunately, in chiral stationary phases of the next generation such as Chiralpak IA, the selector is immobilised – which means covalently bonded to the silica substrate. This extends the range of possible mobile phases enormously and offers new possibilities for the effective (semi)preparative chiral resolution of many compounds.

[a] Kekulé-Institut für Organische Chemie und Biochemie, Rheinische Friedrich-Wilhelms-Universität Bonn, Gerhard-Domagk-Str. 1, 53121 Bonn, Germany
E-mail: arne.luetzen@uni-bonn.de
http://www.chemie.uni-bonn.de/oc/forschung/arbeitsgruppen/ak_lue

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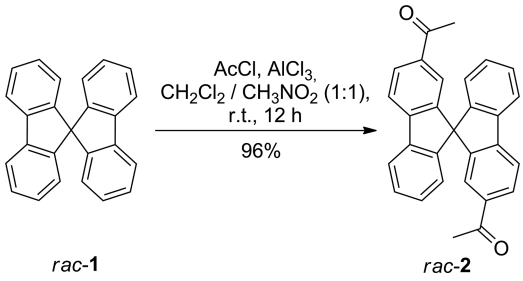
In this work, we present the synthesis and a resolution approach employing semipreparative HPLC that allowed us to improve the resolution of C_2-symmetric, chiral 9,9′-spirobifluorene derivatives with regard to yield and optical purity. The absolute configuration of the enantiomers was determined by comparison of either their optical rotation with literature data or their retention times with those of their enantiopure analogues synthesised in advance.

Results and Discussion

The starting material for the synthesis of all compounds was 2,2′-dihydroxy-9,9′-spirobifluorene (**3**). The synthesis of the diol **3** starting from 9,9′-spirobifluorene[1] (**1**) according to a procedure by Prelog[2c] is well established and has been applied in our group for years.[12] However, carbon disulfide, which is needed as solvent in the initial Friedel–Crafts acylation of **1**, is highly toxic. Moreover, the protocol using carbon disulfide requires a rather extensive workup. By utilising a mixture of dichloromethane and nitromethane we were able to both simplify the work-up and improve the yield of the Friedel–Crafts acylation (Scheme 1).



Scheme 1. Improved synthesis of 2,2′-diacetyl-9,9′-spirobifluorene (**2**).

Subsequent Baeyer–Villiger oxidation of **2** and saponification of the resulting diester finally yields racemic 2,2′-dihydroxy-9,9′-spirobifluorene (**3**). By applying our experience concerning HPLC-based chiral resolutions, we were able to establish a very efficient resolution protocol for **3**. Employing Chiralpak IA as stationary phase enabled us to use a mixture of chloroform and 2-propanol as the mobile phase. The high solubility of **3** in this eluent together with a very high selectivity value (α = 4.3) enabled the resolution of large quantities in a reasonable time (Figure 1). The absolute configuration of the enantiomers could be assigned by comparison of the specific optical rotations of the two fractions with literature data.[12]

Encouraged by this exciting result, we wanted to explore if the strategy of chiral resolution of 9,9′-spirobifluorenes via HPLC could be extended to higher substituted derivatives. Due to the orientation of the substituents and because of the multitude of possible chemical transformations, 2,2′-dibromo-7,7′-dihydroxy-9,9′-spirobifluorene (**6**) attracted our interest. In 1992, Diederich et al. published a synthetic route to racemic **6** starting from 2,2′-diacetyl-9,9′-spirobifluorene (**2**).[3c] By applying the same chiral resolution

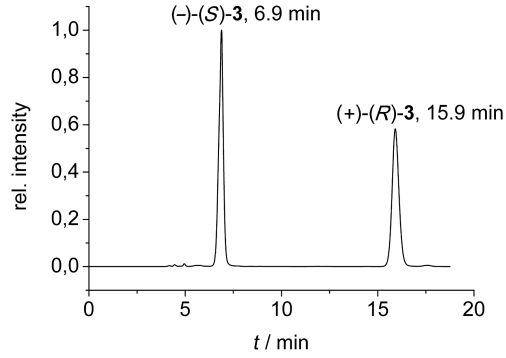


Figure 1. Chromatographic resolution of *rac*-**3** by analytical HPLC on an analytical chiral Chiralpak IA phase with chloroform/2-propanol (95:5 v/v) as eluent, a flow rate f = 0.5 mL min^{-1}, and a detection wavelength λ = 300 nm.

protocol as used for **3**, the dibromo derivative **6** was easily accessible in enantiopure form (Figure 2). Because this compound had been synthesised only in racemic form before, the absolute configuration could not be assigned by simple comparison of the optical rotations with literature data. Finding it impossible to resolve either of the compounds used in the synthesis described by Diederich or to crystallise the enantiopure dibromide **6**, we decided to synthesise both enantiomers of **6** starting from enantiopure diol **3**. This enabled us to compare the retention times and optical rotations of the synthetically obtained enantiopure compounds with those resolved by HPLC.

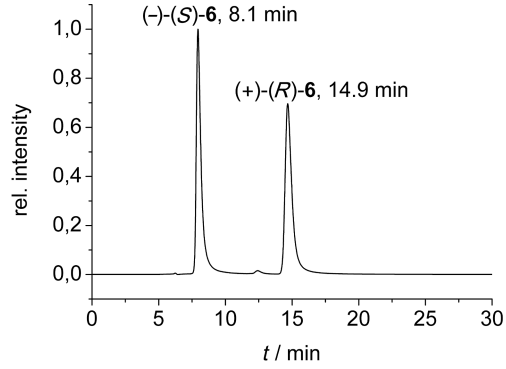
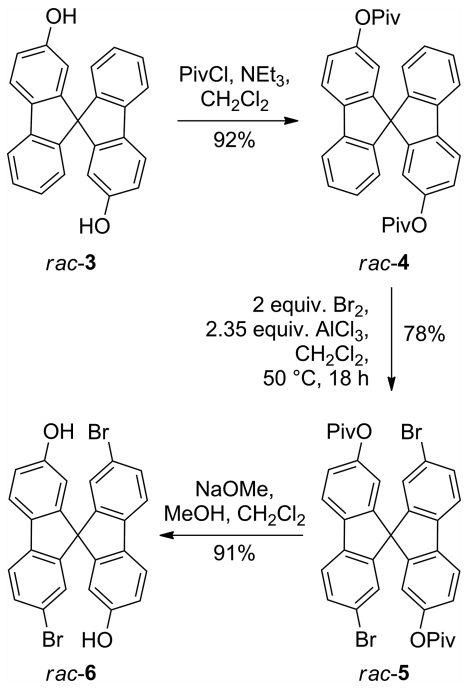


Figure 2. Chromatographic resolution of *rac*-**6** by analytical HPLC on an analytical chiral Chiralpak IA phase with chloroform/2-propanol (95:5 v/v) as eluent, a flow rate f = 0.5 mL min^{-1}, and a detection wavelength λ = 300 nm.

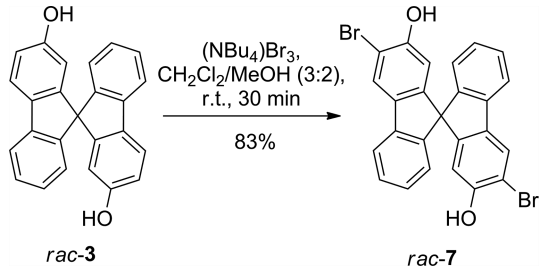
Unfortunately, direct 7,7′-selective bromination of **3** was not possible. After several unsuccessful attempts applying different halogenation protocols and alcohol protecting groups, we found that pivaloyl ester **4** was a convenient starting material. The latter ester is easily prepared from diol **3** through deprotonation with triethylamine and subsequent treatment with pivaloyl chloride in 92% yield. Establishing a reliable protocol for the regioselective bromination of **4** required some effort but was ultimately successful: By using aluminium chloride as Lewis acid and two equivalents of bromine at 50 °C for 18 h, **5** could be obtained in a very

good yield of 78%. Saponification of the bulky ester **5** required the use of sodium methoxide as base, giving **6** in 91% yield (Scheme 2).



Scheme 2. Synthesis of 2,2′-dibromo-7,7′-dihydroxy-9,9′-spirobifluorene (**6**).

To explore whether we were able to extend our concept to different substitution patterns, we synthesised 3,3′-dibromo-2,2′-dihydroxy-9,9′-spirobifluorene (**7**). This compound is easily accessible by applying a bromination protocol developed by Kajigaeshi using tetrabutylammoniumtribomide as halogenation agent (Scheme 3).[17]



Scheme 3. Synthesis of 3,3′-dibromo-2,2′-dihydroxy-9,9′-spirobifluorene (**7**).

For the chiral resolution of **7**, we had to change the separation protocol slightly with respect to the mobile phase. Instead of 2-propanol, *n*-hexane was used as a modifier. Nevertheless, the racemate could be dissolved in a chloroform/2-propanol mixture, ensuring that reasonable amounts of racemic material could be resolved efficiently (Figure 3). We applied the same strategy that was used for **7** to assign the absolute configuration of the enantiomers.

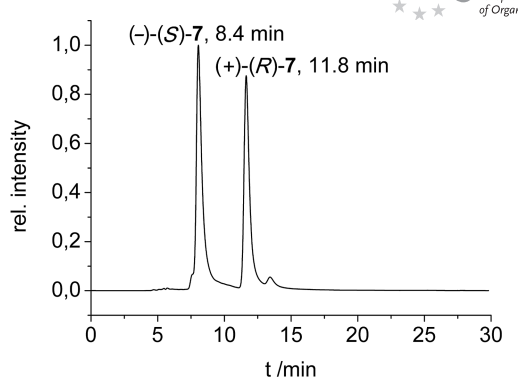


Figure 3. Chromatographic resolution of *rac*-**7** by analytical HPLC on an analytical chiral Chiralpak IA phase with chloroform/*n*-hexane (90:10 v/v) as eluent, a flow rate f = 0.5 mL min^{-1}, and a detection wavelength λ = 325 nm.

Conclusions

We were able to synthesise five different chiral dissymmetric 9,9′-spirobifluorenes. Within the scope of our attempts to access enantiopure 9,9′-spirobifluorenes, we established a new route to 2,2′-dibromo-7,7′-dihydroxy-9,9′-spirobifluorene (**6**) starting from **3**. Additionally, we synthesised a new dibromo derivative with a 2,2′,3,3′-substitution pattern **7**. Finally, we were able to resolve the racemic diols **3**, **6**, and **7** by HPLC techniques on an analytical and a semipreparative scale by using a Chiralpak IA stationary phase. The absolute configuration of the separated enantiomers was determined by comparison of their specific optical rotation and/or retention times with literature data or with those of synthetically obtained enantiopure compounds. The resolution via HPLC gave rise to all enantiomers in excellent yields and purities. These enantiopure compounds represent versatile, configurationally stable building blocks for the synthesis of more sophisticated molecular architectures based on the chiral, cleft-like structure of the 9,9′-spirobifluorene scaffold.

Experimental Section

General: Reactions under inert gas atmosphere were performed under argon by using standard Schlenk techniques and oven-dried glassware prior to use. Thin-layer chromatography was performed on aluminium TLC plates silica gel 60F_{254} from Merck. Detection was carried out under UV light (254 and 366 nm). Products were purified by column chromatography on silica gel 60 (40–60 mesh) from Merck. The ^{1}H and ^{13}C NMR spectra were recorded with a Bruker DPX 500 spectrometer at 298 K, at 500.1 and 125.8 MHz or with a Bruker AM 400 at 298 K, at 400.1 MHz and 100.6 MHz, respectively. The ^{1}H NMR chemical shifts are reported on the δ scale (ppm) relative to residual non-deuterated solvent as the internal standard. The ^{13}C NMR chemical shifts are reported on the δ scale (ppm) relative to deuterated solvent as the internal standard. Signals were assigned on the basis of ^{1}H, ^{13}C, HMQC-, and HMBC NMR experiments. Mass spectra were recorded with a Finnigan MAT 212 and data system MMS-ICIS (EI) or with a Bruker micrOTOF-Q (ESI). Elemental analyses were carried out with a

HeraeusVario EL. The HPLC analysis was performed by using three different systems: The Prominence console from Shimadzu (binary recycling system) consisting of three pumps (2 × LC20-AT, 1 × LC20-AD), degasser (DGU-20A3), diode array detector (SPD-M20A), and a fraction collector (FRC-10A). The analytical KNAUER system (Smartline series) consisting of one S-1000 pump (with 10 mL pump head), autosampler S-3945, column oven Jetstream, photodiode array detector S-2800, chiral detector of IBZ Meßtechnik and a refraction index detector Ri101 of Shodex. The semi-preparative KNAUER system (Smartline series) was composed of a two-channel degasser, two pumps S-1000 (50 mL pump head), a injection assistant 6000 with a feed pump S-100, a mixing chamber Smartmix 350, an UV-detector S-2500 and a refraction index detector (Ri)S-2400. Chiral analytical (5 μm, 4.6 × 250 mm) and semipreparative (5 μm, 250 × 10 mm) stationary phases Chiralpak IA from DAICEL were applied, and solvent mixtures of *n*-hexane, chloroform and 2-propanol (HPLC quality) were used. Optical purities were determined by analytical HPLC analysis of resolved material. Most solvents were dried, distilled and stored under argon according to standard procedures. All chemicals were used as received from commercial sources. 9,9′-Spirobifluorene,[1] *rac*-2,2′-diacetoxy-9,9′-spirobifluroene,[2c] *rac*-2,2′-dihydroxy-9,9′-spirobifluorene,[2c] and tetrabutylammonium tribromide[18] were prepared according to literature protocols.

***rac*-2,2′-Diacetyl-9,9′-spirobifluorene (*rac*-2):** Aluminium chloride (2.53 g, 19.0 mmol) was dissolved in nitromethane (6 mL) and cooled to 0 °C. Acetyl chloride (1.42 mL, 1.49 g, 18.9 mmol) was slowly added by using a syringe while the temperature was kept below 0 °C. A solution of 9,9′-spirobifluorene (2.00 g, 6.23 mmol) in anhydrous dichloromethane (6 mL) was then added over 15 min. The solution was stirred for 1 h at 0 °C, then the solution was warmed to room temperature and stirred for another 12 h. The solution was poured over ice and hydrochloric acid (1.0 M, 50.0 mL), the layers were separated, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with hydrochloric acid (1.0 M), water and brine, and dried with Na_2SO_4. After evaporation of the solvents, the residue was taken up in a small amount of dichloromethane. Cyclohexane was added until the product started to precipitate. After standing in the freezer overnight, the precipitate was filtered off, washed with cyclohexane and dried in vacuo, yield 2.40 g (5.99 mmol, 96%). The analytical data were in accordance with reported data.[2c]

Separation of Enantiomers of *rac*-3: HPLC conditions: chiral phase (semipreparative), Chiralpak IA; $CHCl_3$/2-propanol, 95:5; f = 2.3 mL min^{-1}; sample solvent: $CHCl_3$/2-propanol, 10:1 (v/v); loading per run: 40 mg of racemic material.

Compound (–)-(*S*)-3: Retention time: 8.51 min; $[\alpha]_D^{20}$ –20.3 (c = 2.93 mg mL^{-1}, $CHCl_3$); 99.9% *ee*.

Compound (+)-(*R*)-3: Retention time: 14.6 min; $[\alpha]_D^{20}$ +20.4 (c = 2.46 mg mL^{-1}, $CHCl_3$); 99.9% *ee*.

2,2′-Dipivaloyl-9,9′-spirobifluorene (4): Compound **3** (1.00 g, 2.90 mmol) was dissolved in dichloromethane (86 mL), triethylamine (2.00 mL, 1.45 g, 14.4 mmol) was added by using a syringe, and the solution was cooled to –10 °C. A solution of pivaloyl chloride (0.90 mL, 0.87 g, 7.18 mmol) in dichloromethane (4 mL) was added over 20 min, then the solution was warmed to room temperature and stirred overnight. Ice-cold aq. hydrochloric acid (2.0 M, 50.0 mL) was added, the layers were separated, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with saturated aq. $NaHCO_3$ and brine and dried with Na_2SO_4. After evaporation of the solvents, the crude product was purified by column chromatography on silica gel (cyclohexane/ethyl acetate, 5:1 v/v; R_f = 0.56), yield 1.38 g (2.67 mmol, 92%). ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 1.28 (s, 18 H, CH_3), 6.50 (dd, $^4J_{1,3}$ = 2.2, $^5J_{1,4}$ = 0.4 Hz, 2 H, 1-H), 6.75 (ddd, $^3J_{7,8}$ = 7.4, $^4J_{6,8}$ = 1.0, $^5J_{5,8}$ = 0.7 Hz, 2 H, 8-H), 7.11–7.14 (m, 4 H, 3-H, 7-H), 7.38 (ddd, $^3J_{6,7}$ = 7.5, $^3J_{5,6}$ = 7.7, $^4J_{6,8}$ = 1.0 Hz, 2 H, 6-H), 7.82 (ddd, $^3J_{5,6}$ = 7.7, $^4J_{5,7}$ = 1.1, $^5J_{5,8}$ = 0.7 Hz, 2 H, 5-H), 7.84 (dd, $^3J_{3,4}$ = 8.4, $^5J_{1,4}$ = 0.4 Hz, 2 H, 4-H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 27.2 (C-16), 39.1 (C-15), 66.0 (C-9), 117.5 (C-1), 120.0 (C-5), 120.6 (C-4), 121.6 (C-3), 124.3 (C-8), 128.0 (C-7), 128.1 (C-6), 139.3 (C-11), 141.0 (C-12), 148.6 (C-13), 149.6 (C-10), 151.0 (C-2), 176.9 (C-14) ppm. MS (ESI): *m*/*z* (%) = 1055.4 (14) $[C_{70}H_{32}O_4 + Na]^+$, 539.2 (100) $[C_{35}H_{32}O_4 + Na]^+$, 517.2 (3) $[C_{35}H_{32}O_4 + H]^+$, 433.2 (11) $[C_{30}H_{24}O_3 + H]^+$. HRMS (EI): *m*/*z* calcd. for $[C_{35}H_{32}O_4]^{+\cdot}$ 516.2301; found 516.2300. $C_{35}H_{32}O_4$ (516.63): calcd. C 81.37, H 6.24; found C 81.17, H 6.71.

Compound (+)-(*R*)-4: $[\alpha]_D^{20}$ +30.4 (c = 3.64 mg mL^{-1}, $CHCl_3$).

Compound (–)-(*S*)-4: $[\alpha]_D^{20}$ –30.4 (c = 3.65 mg mL^{-1}, $CHCl_3$).

2,2′-Dibromo-7,7′-dipivaloyl-9,9′-spirobifluorene (5): Compound **4** (2.00 g, 3.87 mmol) and aluminium chloride (1.21 g, 9.10 mmol) were dissolved in anhydrous dichloromethane (43 mL) and stirred at 50 °C for 1 h. A bromine solution (1 M in dichloromethane, 7.75 mL, 7.75 mmol) was added by using a syringe and the resulting mixture was stirred at 50 °C for 18 h. The mixture was cooled to room temperature, poured into ice water and acidified with hydrochloric acid (5 M). After phase separation, the aqueous layer was extracted with dichloromethane (3 × 50 mL) and the combined organic layers were washed with saturated aq. $NaHCO_3$, water and brine and dried with Na_2SO_4. The solvent was evaporated and the crude product was purified by column chromatography on silica gel [*n*-heptane/THF, 20:1 → 10:1 (v/v); R_f = 0.23 for 10:1 (v/v)], yield 2.04 (3.02 mmol, 78%). ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 1.27 (s, 18 H, CH_3), 6.47 (d, $^4J_{7,8}$ = 2.1 Hz, 2 H, 8-H), 6.84 (d, $^4J_{1,3}$ = 1.8 Hz, 2 H, 1-H), 7.14 (dd, $^3J_{5,6}$ = 8.3, $^4J_{6,8}$ = 2.1 Hz, 2 H, 6-H), 7.51 (dd, $^3J_{3,4}$ = 8.2, $^4J_{1,3}$ = 1.8 Hz, 2 H, 3-H), 7.67 (d, $^3J_{3,4}$ = 8.2 Hz, 2 H, 4-H), 7.80 (d, $^3J_{5,6}$ = 8.3 Hz, 2 H, 5-H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 27.2 (C-16), 39.2 (C-15), 65.6 (C-9), 117.5 (C-8), 120.9 (C-5), 121.5 (C-4), 121.7 (C-2), 122.2 (C-6), 127.4 (C-1), 131.6 (C-3), 138.2 (C-12), 140.0 (C-11), 148.5 (C-13), 149.8 (C-10), 151.4 (C-7), 176.8 (C-14) ppm. MS (EI): *m*/*z* (%) = 674.1 (60) $[C_{35}H_{30}Br_2O_4]^{+\cdot}$, 590.0 (75) $[C_{30}H_{22}Br_2O_3]^+$, 505.9 (80) $[C_{25}H_{13}Br_2O_2]^+$. MS (ESI): *m*/*z* (%) = 697.1 (100) $[C_{35}H_{30}Br_2O_4 + Na]^+$. HRMS (ESI): *m*/*z* calcd. for $[C_{35}H_{30}Br_2O_4 + Na]^+$ 697.0386; found 697.0381. $C_{35}H_{30}Br_2O_4 \cdot 1/2H_2O$: calcd. C 61.51, H 4.57; found C 61.50, H 4.77.

Compound (–)-(*R*)-5: $[\alpha]_D^{20}$ –1.4 (c = 5.55 mg mL^{-1}, $CHCl_3$).

Compound (+)-(*S*)-5: $[\alpha]_D^{20}$ +1.8 (c = 3.51 mg mL^{-1}, $CHCl_3$).

2,2′-Dibromo-7,7′-dihydroxy-9,9′-spirobifluorene (6): Compound **5** (0.80 g, 1.19 mmol) was dissolved in anhydrous dichloromethane (36 mL) and a solution of sodium methoxide (5.4 M in methanol, 5.30 mL) was slowly added by using a syringe. After stirring at room temperature overnight, the mixture was neutralised by adding hydrochloric acid (2 M). The layers were separated and the aqueous phase was extracted with dichloromethane (3 × 50 mL). The combined organic phases were washed with saturated aq. $NaHCO_3$, water and brine, and dried with $MgSO_4$. After evaporation of the solvents, the crude product was subjected to column chromatography on silica gel [cyclohexane/ethyl acetate, 2:1 (v/v); R_f = 0.42], yield 0.551 g (1.09 mmol, 91%). ^{1}H NMR (500.1 MHz, [D$_6$]acetone): δ = 6.21 (dd, $^4J_{6,8}$ = 2.3, $^5J_{5,8}$ = 0.4 Hz, 2 H, 8-H), 6.80 (dd, $^4J_{1,3}$ = 1.9, $^5J_{1,4}$ = 0.4 Hz, 2 H, 1-H), 6.92 (dd, $^3J_{5,6}$ = 8.3, $^4J_{6,8}$ =

2.3 Hz, 2 H, 6-H), 7.53 (dd, $^3J_{3,4}$ = 8.2, $^4J_{1,3}$ = 1.9 Hz, 2 H, 3-H), 7.80 (dd, $^3J_{3,4}$ = 8.2, $^5J_{1,4}$ = 0.4 Hz, 2 H, 4-H), 7.83 (dd, $^3J_{5,6}$ = 8.2, $^5J_{5,8}$ = 0.4 Hz, 2 H, 5-H), 8.50 (br. s, 2 H, O*H*) ppm. ^{13}C NMR (125.8 MHz, [D$_6$]acetone): δ = 66.2 (C-9), 111.4 (C-8), 116.6 (C-6), 120.1 (C-2), 121.9 (C-4), 122.6 (C-5), 127.3 (C-1), 132.0 (C-3), 133.0 (C-11), 142.2 (C-12), 150.9 (C-10, C-13), 159.2 (C-7) ppm. MS (EI): *m*/*z* (%) = 506.0 (100) $[C_{25}H_{14}Br_2O_2]^{+\cdot}$, 425.1 (40) $[C_{25}H_{14}BrO_2]^+$, 345.1 (20) $[C_{25}H_{13}O_2]^+$. HRMS (EI): *m*/*z* calcd. for $[C_{25}H_{14}Br_2O_2]^{+\cdot}$ 503.9361; found 503.9358. $C_{25}H_{14}Br_2O_2 \cdot 3/4C_4H_8O_2$: calcd. C 58.77, H 3.52; found C 58.80, H 3.55.

Separation of Enantiomers: HPLC conditions: chiral phase (semi-preparative), Chiralpak IA; $CHCl_3$/2-propanol, 95:5; *f* = 2.3 mL min^{-1}; sample solvent: $CHCl_3$/2-propanol, 10:1 (v/v); loading per run: 20 mg of racemic material.

Compound (–)-(*S*)-6: Retention time: 6.60 min; $[\alpha]_D^{20}$ –20.4 (*c* = 3.44 mg mL^{-1}, $CHCl_3$); 99.9% *ee*.

Compound (+)-(*R*)-6: Retention time: 16.0 min; $[\alpha]_D^{20}$ +19.0 (*c* = 2.16 mg mL^{-1}, $CHCl_3$); 99.9% *ee*.

3,3′-Dibromo-2,2′-dihydroxy-9,9′-spirobifluorene (7): Compound **3** (0.40 g, 1.15 mmol) was dissolved in methanol (12 mL) and dichloromethane (18 mL), then tetrabutylammonium tribromide (1.11 g, 2.30 mmol) was added in small portions. The solution was stirred for 30 min until decolouration of the orange solution occurred. The solvents were evaporated and the waxy residue was taken up in water and diethyl ether. The layers were separated and the aqueous layer was extracted twice with diethyl ether. The combined organic layers were washed with brine and dried with $MgSO_4$. After removal of the solvent, the crude product was purified by column chromatography on silica gel [cyclohexane/ethyl acetate, 5:1 (v/v); R_f = 0.73], yield 0.482 g (0.95 mmol, 83%). ^{1}H NMR (400.1 MHz, [D$_6$]acetone): δ = 2.90 (br. s, 2 H, O*H*), 6.33 (s, 2 H, 1-H), 6.68 (dd, $^3J_{7,8}$ = 7.6, $^4J_{6,8}$ = 0.7 Hz, 2 H, 8-H), 7.11 (ddd, $^3J_{7,8}$ = 7.6, $^3J_{6,7}$ = 7.5, $^4J_{5,7}$ = 1.1 Hz, 2 H, 7-H), 7.38 (ddd, $^3J_{6,7}$ = 7.5, $^3J_{5,6}$ = 7.6, $^4J_{6,8}$ = 0.7 Hz, 2 H, 6-H), 7.91 (dd, $^3J_{5,6}$ = 7.6, $^4J_{5,7}$ = 1.1 Hz, 2 H, 5-H), 8.08 (s, 2 H, 4-H) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]acetone): δ = 66.2 (C-9), 110.5 (C-3), 112.4 (C-1), 120.6 (C-5), 124.5 (C-8), 125.6 (C-4), 128.1 (C-7), 129.0 (C-6), 136.0 (C-11), 141.6 (C-12), 148.9 (C-13), 150.6 (C-10), 154.7 (C-2) ppm. MS (EI): *m*/*z* (%) = 505.8 (100) $[C_{25}H_{14}Br_2O_2]^{+\cdot}$, 488.8 (45) $[C_{25}H_{13}Br_2O]^+$, 424.9 (15) $[C_{25}H_{14}BrO_2]^+$. HRMS (EI): *m*/*z* calcd. for $[C_{25}H_{14}Br_2O_2]^{+\cdot}$ 503.9361; found 503.9362. $C_{25}H_{14}Br_2O_2 \cdot 1/6C_6H_{12}$: calcd. C 60.03, H 3.10; found C 59.94, H 3.30.

Separation of Enantiomers: HPLC conditions: chiral phase (semi-preparative), Chiralpak IA; $CHCl_3$/*n*-hexane, 95:5; *f* = 2.3 mL min^{-1}; sample solvent: $CHCl_3$/2-propanol, 10:1 (v/v); loading per run: 20 mg of racemic material.

Compound (–)-(*S*)-7: Retention time: 7.90 min; $[\alpha]_D^{20}$ –34.8 (*c* = 3.80 mg mL^{-1}, $CHCl_3$); 94.5% *ee*.

Compound (+)-(*R*)-7: Retention time: 11.6 min; $[\alpha]_D^{20}$ +34.3 (*c* = 3.67 mg mL^{-1}, $CHCl_3$); 99.1% *ee*.[19]

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra of compounds **4**–**7**.

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