Synthesis of Enantiomerically Pure Dissymmetric 2,2′-Disubstituted 9,9′-Spirobifluorenes

Frank Thiemann,[a] Torsten Piehler,[a] Detlev Haase,[a] Wolfgang Saak,[a] and Arne Lützen*[a]

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Racemic dissymmetric 2,2′-dihydroxy-9,9′-spirobifluorene was prepared and resolved by clathrate formation with (*R*,*R*)-(+)-2,3-dimethoxy-*N*,*N*,*N*′,*N*′-tetracyclohexylsuccindiamide, giving rise to both enantiomers in very good yields. The absolute stereochemistry of the resolved material could be assigned by an X-ray structure analysis of single crystals of the clathrate. Enantiomerically pure diols could be transformed into the corresponding ditriflates, which were then used as starting materials in different cross-coupling procedures to provide a number of new enantiomerically pure spiro compounds bearing versatile functional groups suitable for further elaboration, as demonstrated by some examples.

Introduction

Although now known for 75 years,[1] 9,9′-spirobifluorene (**1**) and its derivatives for a long time had to face the fate of being regarded as only another rigid, though admittedly aesthetic, hydrocarbon. However, this situation has changed dramatically.[2] After the first examples in the area of molecular recognition were reported by the groups of V. Prelog,[3] F. Diederich,[4] and others,[5] these compounds found a wide range of applications in molecular electronics,[6] macromolecular chemistry,[7] light emitting devices,[8] and other areas.[9,10,11,12]

In the course of our studies concerning the diastereoselective formation of self-assembled supramolecular helicates,[13,14] dissymmetric 2,2′-disubstituted 9,9′-spirobifluorenes attracted our interest and prompted us to evaluate the possibilities of accessing enantiomerically pure derivatives. V. Prelog prepared the first enantiomerically pure spirobifluorenes in 1969,[3a] by resolving some dicarboxylic acid derivatives through diastereoisomer formation with enantiomerically pure dehydroabietylamine.[3a] A few years later he was able to develop another method for the resolution of the 2,2′-bis(hydroxymethyl) derivative through esterification with camphanic acid, separation of the resulting diastereomers, and subsequent saponification.[3b,3c] Although both approaches have been successfully applied by others,[15,4c,4d] Prelog himself admitted that they are quite tedious. In 1996 F. Diederich reported on the use of an elaborated enantiomerically pure 9,9′-spirobifluorene-based cleft as a tool for the separation of 2,2′-dicarboxy- and 2,2′-bis(hydroxymethyl)-9,9′-spirobifluorene,[4f] although this of course needs resolved material from other approaches in advance.

For our purposes the 2,2′-dibrominated or 2,2′-diiodinated spirobifluorenes **2** and **3** seemed to be very promising candidates with respect to their potential for further functionalization. Since we had had some good experiences with resolution procedures based on clathrate formation,[16,17] we were especially interested in evaluating this approach. Unfortunately, all our attempts to obtain clathrate formation with cinchonidine derivatives or tartaric acid derivatives proved unsuccessful. In 1988, however, F. Toda had published a procedure to resolve 2,2′-dihydroxy-9,9′-spirobifluorene (**4**) through clathrate formation with (*R*,*R*)-(+)-2,3-dimethoxy-*N*,*N*,*N*′,*N*′-tetracyclohexylsuccindiamide (**5**).[18,19] Although he only reported on one enantiomer that he was able to isolate by this method and despite the fact that he was not able to assign the stereochemistry of the enantiomerically pure (+)-enantiomer, this procedure still seemed very attractive since the diol could also serve, after transformation into a corresponding disulfonate, as a suitable starting material for our studies. In this account we describe how we succeeded in the isolation of both enantiomers of **4**, the assignment of their absolute stereochemistry, and the application of the resolved compounds as substrates in transition metal-catalyzed cross-coupling reactions and some other transformations in order to gain access to a number of enantiomerically pure spiro compounds bearing versatile functional groups capable of further elaboration.

[a] University of Oldenburg, Institute of Pure and Applied Chemistry,
P. O. Box 2503, 26111 Oldenburg, Germany
Fax: +49-441-798-3706
E-mail: arne.luetzen@uni-oldenburg.de

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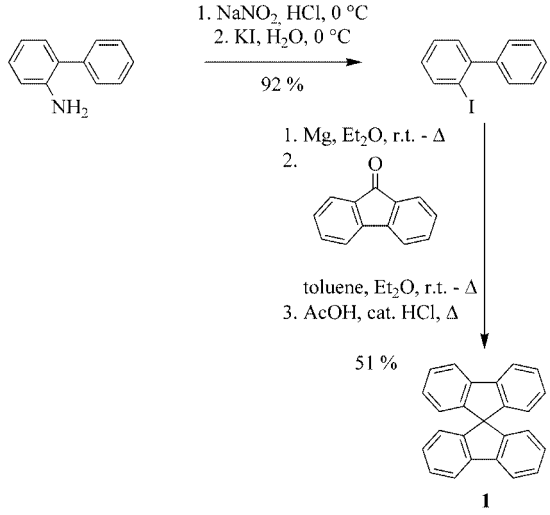
Results and Discussion

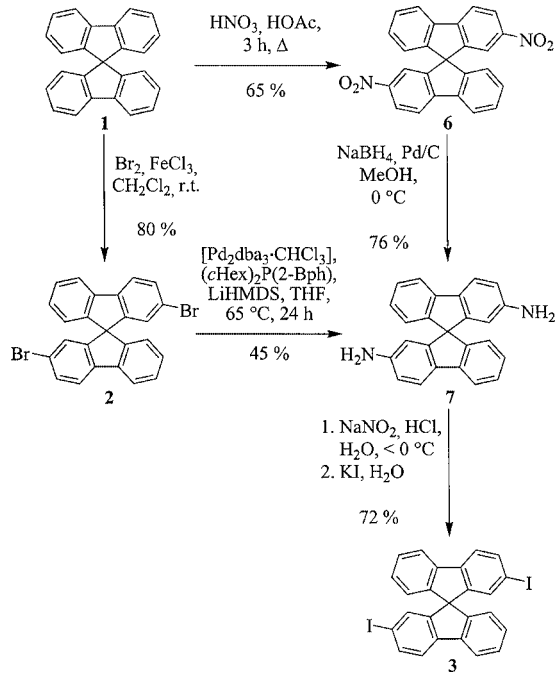
The central 9,9′-spirobifluorene (**1**) was readily prepared in three steps starting from commercially available 2-aminobiphenyl (Scheme 1). An initial Sandmeyer reaction was followed by a Grignard reaction with 9-fluorenone and subsequent condensation under acidic conditions to give **1** in an overall yield of 47%.[1]



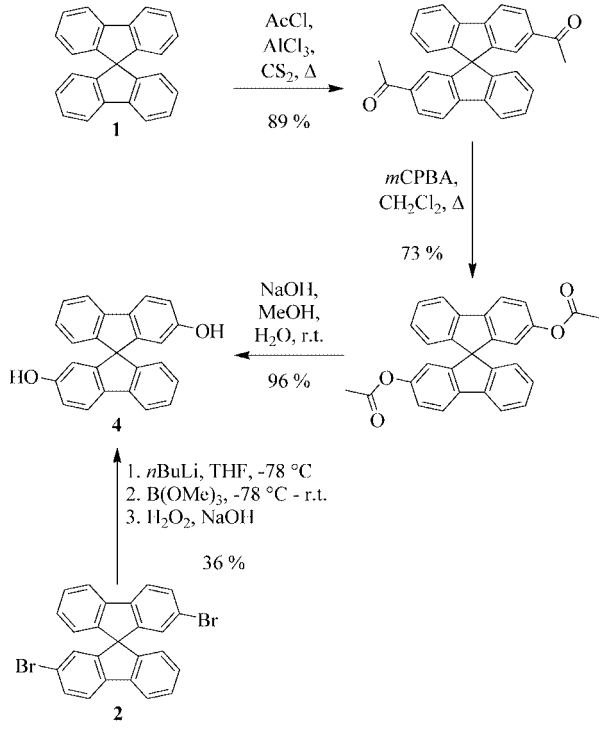
Scheme 1. Synthesis of 9,9-spirobifluorene (**1**).

By F. K. Sutcliffe's and J. H. Weisburger's procedures, **1** could easily be subjected to double electrophilic aromatic substitutions to provide 2,2′-dibromo- or 2,2′-dinitro-9,9′-spirobifluorene **2** and **6**, respectively, in a regioselective manner (Scheme 2).[20] Both **2** and **6** could be employed to synthesize 2,2′-diamino-9,9′-spirobifluorene (**7**), either by palladium-catalyzed amination[21] of the dibromide or by simple reduction of the dinitro compound with sodium borohydride and palladium on charcoal,[22] which in fact turned out to be much more efficient to produce the desired **7**. Compound **7** could then be transformed into 2,2′-diodo-9,9′-spirobifluorene (**3**) in a Sandmeyer reaction. However, all of our attempts to resolve these racemic compounds through clathrate formation with cinchonidine derivatives or tartaric acid derivatives unfortunately failed, as did our approach to the preparation of diastereomeric cross-coupling products with enantiomerically pure 2,2′-dihydroxy-1,1′-binaphthyl-derivatives, because we were not able to separate the diastereomers by column chromatography or by crystallization.

We therefore decided to prepare diol **4** and to try to take F. Toda's protocol a step further and isolate both enantiomers of **4**. The synthesis of **4** started with a double Friedel–Crafts acylation of **1**, by V. Prelog's procedure,[3c] followed by a Baeyer–Villiger oxidation to give the corresponding diacetate with *meta*-chloroperbenzoic acid. Subsequent saponification of the diester gave rise to **4** in excellent yield (Scheme 3). This sequence proved superior to an alternative route starting from dibromide **2**, by which **4** was obtained in a one-pot procedure after bromine–lithium exchange, subsequent boronic acid ester formation, and immediate oxidation. Although this sequence saves one step the overall yield is still considerably lower and the reactants are also more expensive.



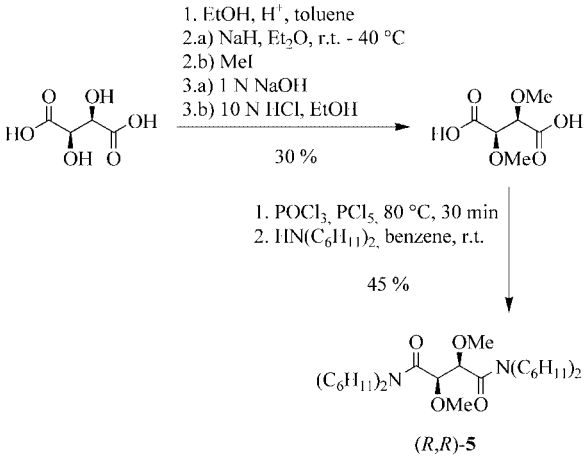
Scheme 2. Synthesis of racemic 2,2′-disubstituted 9,9′-spirobifluorene derivatives **2**, **3**, **6**, and **7**.



Scheme 3. Preparation of racemic diol **4**.

The clathrate-forming tartaric acid derivative **5** was prepared in four steps from (*R*,*R*)-tartaric acid. Thus, the tartaric acid was first transformed into the corresponding di-

ethyl ester,[23] after which the hydroxy functions were methylated with methyl iodide.[24] After saponification of the ester functions[25] the diacid was converted into the corresponding diacid chloride, which was finally treated with dicyclohexylamine to give **5** (Scheme 4).[18]



Scheme 4. Synthesis of (*R*,*R*)-2,3-dimethoxy-*N*,*N*,*N*′,*N*′-tetracyclohexylsuccindiamide [(*R*,*R*)-**5**].

With both components to hand we then studied the clathrate formation. Equimolar amounts of the resolving agent **5** and racemic **4** were dissolved in ethanol and kept at room temperature for 12 h. After that period the precipitate was collected and recrystallized twice from ethanol. The clathrate could be destroyed by dissolving in benzene and treatment with aqueous sodium hydroxide to liberate the (+)-enantiomer in a very good yield of 83% after separation of the aqueous layer, neutralization with hydrochloric acid, and subsequent extraction. The specific rotation of this material {$[a]_D^{20}$ = +27.1 (*c* = 0.39, methanol)} was in perfect agreement with that reported by F. Toda.[18,26] Furthermore, diamide **5** could be at least in part recovered from the neutralized organic phase. In order also to recover the remainder, the original ethanol solution was evaporated to dryness and the resulting residue was subjected to flash chromatography on silica gel with a 2:1 mixture of petroleum ether and ethyl acetate as eluent. After this procedure we were able to recover a total of 89% of the tartaric acid derivative **5**. Much more importantly, however, we were also able to isolate the (–)-enantiomer from this in enantiomerically pure form and in an excellent yield of 96% as revealed by its specific rotation of $[a]_D^{20}$ = –26.9 (*c* = 0.92, methanol).

Since we had been able to obtain single crystals suitable for an X-ray crystal structure analysis from the clathrate, we were also able to assign the absolute stereochemistry of the resolved enantiomers of **4** for the first time (Figure 1). Thus, the (+)-enantiomer of **4** turned out to be (*R*)-configured and the (–)-enantiomer to be (*S*)-configured by the rules of R. S. Cahn, C. Ingold, and V. Prelog.[27]

In order to gain access to further elaborated spiro compounds, especially through the use of cross-coupling reactions, the hydroxy functions in **4** had to be converted into more reactive groups. At first we tried to achieve substitution of the hydroxy groups by treatment with phosphorus pentabromide at elevated temperatures by an approach used by A. Binz and O. v. Schickh.[28] Unfortunately, we were unable to obtain the desired enantiomerically pure dibromide **2** in this way but rather observed decomposition of our starting material. We thus decided to switch to conversion to sulfonates, because these have found increasing applications in transition metal-catalyzed cross-coupling reactions over the last years.[29] We chose triflates for our purposes. Adapting a protocol by A. Abad et al.[30] we were able to prepare the desired ditriflate **8** in almost quantitative yield from **4** (Scheme 5).[31]

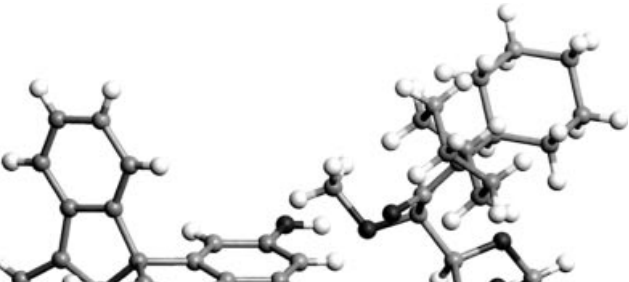
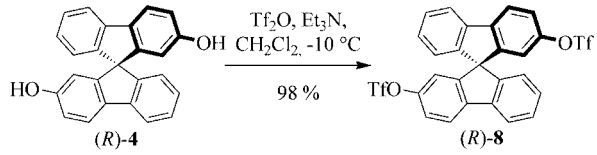


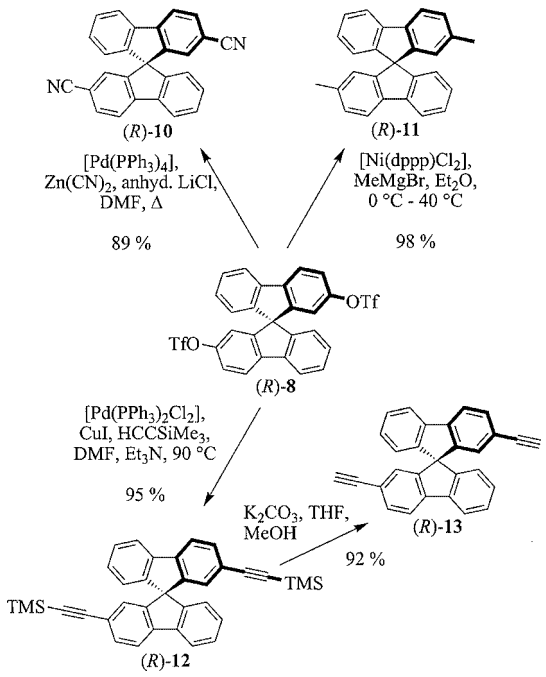
Figure 1. X-ray crystal structure analysis of the clathrate formed by tartaric acid derivative (*R*,*R*)-**5** and (*R*)-(+)-2,2′-dihydroxy-9,9′-spirobifluorene [(*R*)-**4**].



Scheme 5. Formation of bis(triflate) (*R*)-**8**.

Compound **8** was then used as a substrate in different reactions in order to explore its potential for further elaboration to give enantiomerically pure spiro compounds with various functional groups. We used (*R*)-**8** to perform these experiments and then repeated some demonstration reactions with (*S*)-**8** in order to establish whether the stereochemical integrity remained intact during these transformations. Unfortunately, all our attempts to prepare 2,2′-dicarboxy-9,9′-spirobifluorene (**9**) or 2,2′-diamino-9,9′-spirobifluorene (**7**) by S. Cacchi's palladium-catalyzed carboxylation protocol[32] or by the palladium-catalyzed amination procedures of Y. Murakami[33] or S. L. Buchwald[21] have so far been unsuccessful, since we were only able to recover unconverted starting material or the fully defunctionalized spirobifluorene under these conditions. After several unsuccessful experiments,[34] however, we were able to achieve the synthesis of 2,2′-dicyano-9,9′-spirobifluorene (**10**)[35] in an excellent yield of 89% when we adapted a protocol used by K. C. Rice (Scheme 6).[36] It should be noted at this point,

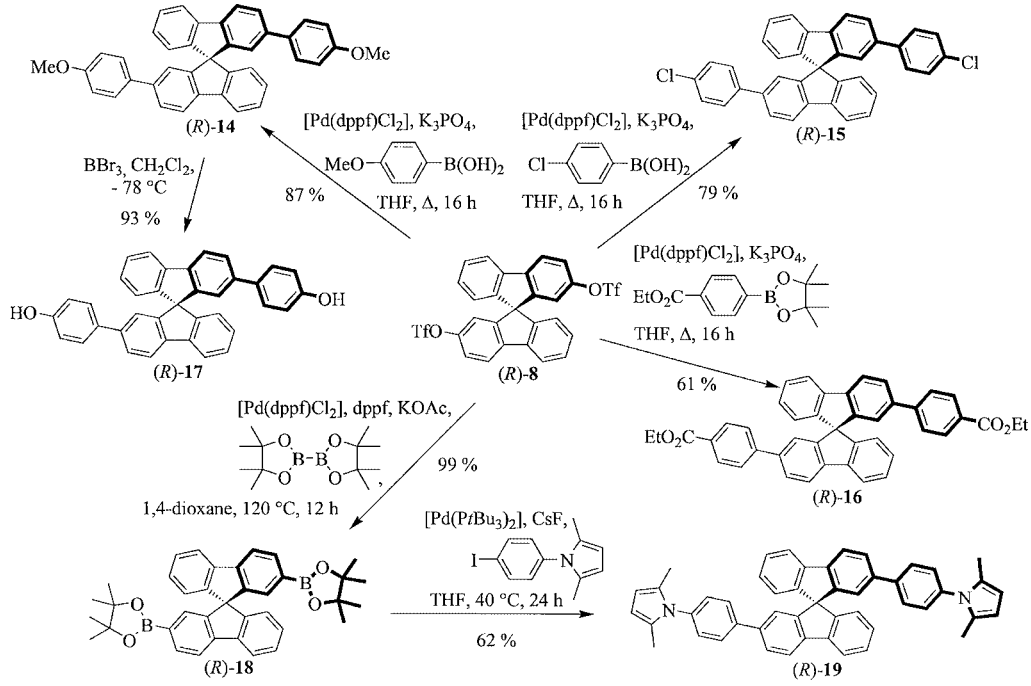
however, that the key to this success was to use carefully dried lithium chloride, because otherwise only trace amounts of desired **10** could be detected.



Scheme 6. Transition metal-catalyzed cyanation, alkylation, and ethynylation of bis(triflate) (*R*)-**8**.

Next, we were able to synthesize 2,2′-dimethyl-9,9′-spirobifluorene (**11**)[37] from **8** in almost quantitative yield by using a modified nickel-catalyzed Kumada coupling procedure reported by D. Xiao[38] with methylmagnesium bromide (Scheme 6). Besides establishing C–C bond formation between an sp^2- and an sp^3-carbon atom we were also able to achieve the coupling of an *sp*- and an sp^2-carbon atom in a palladium-catalyzed Sonogashira reaction[39] to provide bis(ethynylated) **12** in an excellent yield of 95% when we employed a protocol by M. C. Pirrung.[40] Furthermore, we were also able to synthesize fully desilylated compound **13** after standard deprotection with potassium carbonate in methanol/THF (Scheme 6).

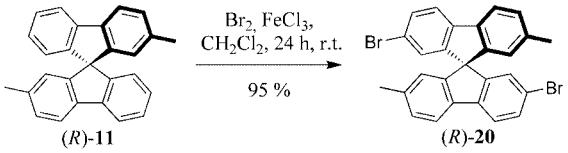
Arguably, arylations are combined like no other reaction with the rise of modern cross-coupling procedures.[29c,41] This is especially true for boron-mediated Suzuki reactions, which have seen a tremendous development recently.[29c,42] To apply this reaction to the synthesis of new derivatives of 9,9′-spirobifluorene we examined several conditions[43] and found those published by E. Vedejs[44] especially useful to provide the desired arylated compounds. By this protocol we were able to isolate compounds **14**–**16** upon treatment of some aryl boronic acid derivatives with **8**, with the newly introduced aryl groups carrying different substituents, in good to very good yields (Scheme 7). Furthermore, we were able to demonstrate that the methyl protecting groups could be removed from **14** to give **17** in an excellent yield of 93% by application of a standard demethylation procedure with boron tribromide.[45] Next we tried to prepare a diboronic acid ester from **8** in order to gain access to another widely applicable building block for the synthesis of elaborated spirobifluorenes. In fact, this kind of transformation had already been performed by other groups on various triflate substrates.[46] Among these, T. Ishiyama's conditions[46b] appeared especially appealing to us because of their usually



Scheme 7. Synthesis of borylated (*R*)-**18** and Suzuki cross-coupling reactions starting from (*R*)-**8** or (*R*)-**18**.

very high yields. Fortunately, this was also the case when we applied these conditions to the palladium-catalyzed borylation of **8** with bis(pinacolato)diboron, which provided the desired diboronic acid ester **18**[47] in almost quantitative yield (Scheme 7). To test **18**′s ability to act as a substrate in Suzuki-type reactions, a demonstration coupling with a pyrrole-protected *p*-iodoaniline was performed to provide the desired bisarylated **19**.

Finally, we wanted to see whether we could gain access to a versatile dibromide derivative of **1**, so we chose dimethylated **11** and subjected it to a double electrophilic aromatic substitution to provide 2,2′-dibromo-7,7′-dimethyl-substituted **20** in an excellent yield of 95% (Scheme 8).[48,49]



Scheme 8. Synthesis of (*R*)-2,2-dibromo-7,7′-dimethyl-9,9′-spirobifluorene [(*R*)-**20**]. Note that the stereodescriptor does not change in these spiro compounds, although the priority of the substituents is changed.

Conclusions

In summary, we have been able to demonstrate that F. Toda's resolution of racemic 2,2′-dihydroxy-9,9′-spirobifluorene (**4**) through clathrate formation with tartaric acid derivative **5** could be extended to isolate both enantiomers in very good yields, thereby also allowing recovery of the resolving agent. By X-ray diffraction analysis of single crystals of the clathrate we were also able to assign the absolute stereochemistries of (+)- and (–)-**4** for the first time. Enantiomerically pure **4** could then be successfully transformed into the corresponding bis(triflate) **8**, which was subsequently shown to be a versatile substrate in transition metal-catalyzed cyanations, borylations, and cross-coupling procedures resulting in *sp*-, sp^2-, and sp^3-sp^2 C–C bond formations and giving rise to further elaborated enantiomerically pure spiro compounds **10**–**20**, some of them carrying different functional groups for further functionalization, in one or two steps.

Experimental Section

General Remarks: Bis(pinacolato)diboron, (4-chlorophenyl)boronic acid, ethyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate, *p*-iodoaniline, (4-methoxyphenyl)boronic acid, lithium hexamethyldisilazide solution (1 M in THF), methylmagnesium bromide solution (3 M in diethyl ether), [Ni(dppp)Cl_2], and trifluoromethanesulfonic anhydride were purchased from ABCR, Lancaster, Sigma–Aldrich, or Strem and were used as received. 9,9′-Spirobifluorene was prepared in three steps from commercially available 2-aminobiphenyl by the reaction sequence published by M. Gomberg.[1] (*rac*)-2,2′-Dibromo- [(*rac*)-**2**] and (*rac*)-2,2′-dinitro-9,9′-spirobifluorene [(*rac*)-**6**] could be synthesized from **1** by F. K. Sutcliffe's protocols.[20] (*rac*)-2,2′-Dihydroxy-9,9′-spirobifluorene [(*rac*)-**4**] was prepared in three steps from 9,9′-spirobifluorene (**1**) by a procedure published by V. Prelog.[3a,3c] (*R*,*R*)-2,3-Dimethoxy-*N*,*N*,*N*′,*N*′-tetracyclohexylsuccindiamide (**5**) was prepared in four steps from (*R*,*R*)-tartaric acid.[18,23–25] 1,1′-Bis(diphenylphosphanyl)ferrocene (dppf),[50] 2-(dicyclohexylphosphanyl)biphenyl [*c*Hex_2P(2-Bph)],[51] [Pd_2dba_3·$CHCl_3$],[52] [Pd(dppf)Cl_2],[53] [Pd(PPh_3)$_2Cl_2$],[53] [Pd(PPh_3)$_4$],[54] and [Pd(P*t*Bu_3)$_2$][55] were prepared by published procedures. Most solvents were dried, distilled, and stored under argon according to standard procedures. Reactions with air- and moisture-sensitive transition metal compounds were performed under argon in oven-dried glassware by standard Schlenk techniques. Unless otherwise noted, quenching, extraction, and washing operations were usually performed with 50–75 mL portions of the solvents or solutions given in the experimental details. Thin layer chromatography was performed on aluminium TLC plates (Merck silica gel 60 F_{254}). Detection was usually by UV light (254 or 366 nm); only in the case of the detection of (*R*,*R*)-**5** was the detection achieved by treatment with a 5% solution of molydophosphoric acid in ethanol. Products were purified by column chromatography on silica gel 60 (Merck, 70–230 mesh or 230–400 mesh). ^{1}H, ^{13}C, and ^{11}B NMR spectra were recorded at 300 K in $CDCl_3$ solutions on a Bruker Avance 500 spectrometer at 500.1, 125.8, and 160.5 MHz, respectively. ^{1}H NMR chemical shifts are reported on the δ scale in ppm relative to residual non-deuterated solvent as internal standard. ^{13}C NMR chemical shifts are reported on the δ scale in ppm relative to deuterated solvent as internal standard. ^{11}B NMR chemical shifts are reported on δ scale in ppm relative to BF_3·Et_2O as external standard. ^{19}F NMR spectra were recorded at 300 K in $CDCl_3$ solutions on a Bruker Avance 300 spectrometer at 282.4 MHz. ^{19}F NMR chemical shifts are reported on the δ scale in ppm relative to CCl_3F as external standard. IR spectra were recorded from potassium bromide pellets on a Bruker Vector 22 FT-IR spectrometer in the transmission mode. The mass spectra were taken on a Finnigan MAT 212 instrument with the MMS data system and ISIS processing system (EI, CI, isobutane or ammonia) or on a Finnigan MAT 95 with the DEC-Station 5000 data system (EI, HiRes-EI, CI, HiRes-CI, isobutane or NH_3). Melting points were measured with a Leitz SM-Lux hot-stage microscope and are uncorrected. Elemental analyses were carried out with a Fisons EA1108 instrument. Specific optical rotations were measured on a Perkin–Elmer Polarimeter 343 in a 10 cm cuvette.

(*rac*)-2,2′-Diiodo-9,9′-spirobifluorene [(*rac*)-3]: Compound (*rac*)-**7** (346 mg, 1 mmol) was dissolved in a mixture of conc. aq. HCl (10 mL) and water (15 mL). After the system had been cooled to 0 °C, sodium nitrite (159 mg, 2.3 mmol) dissolved in water (5 mL) was added dropwise such that the temperature did not rise above 0 °C. Stirring was maintained for another 45 min after complete addition. After that period, potassium iodide (664 mg, 4 mmol) dissolved in water (20 mL) was added and the solution was stirred for 16 h. The reaction mixture was extracted four times with diethyl ether and the combined organic phases were washed three times with hydrochloric acid (3 N) and sat. aq. sodium hydrogen carbonate solution. The organic solution was then further washed with water, $Na_2S_2O_3$ solution (10%), water again, and finally with brine. After drying with $MgSO_4$ the solvent was removed. The dark brown residue was subjected to column chromatography on silica gel with *n*-hexane/ethyl acetate (4:1 v/v) as eluent to give the desired product as an off-white solid, which can be crystallized from a mixture of *n*-hexane and dichloromethane (410 mg, 72%). M.p. 264–266 °C. – ^{1}H NMR ($CDCl_3$, 500.1 MHz): δ = 6.70 (dd, J = 7.7, 1.1 Hz, 2 H), 7.02 (d, J = 1.7 Hz, 2 H), 7.14 (ddd, J = 7.7, 7.7, 1.1 Hz, 2 H), 7.38 (ddd, J = 7.7, 7.7, 1.1 Hz, 2 H), 7.56 (d, J =

7.7 Hz, 2 H), 7.70 (dd, J = 7.7, 1.7 Hz, 2 H), 7.81 (dd, J = 7.7, 1.1 Hz, 2 H) ppm. – ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 65.4, 93.0, 120.2, 121.8, 124.0, 128.2, 128.6, 133.1, 137.1, 140.7, 141.3, 147.5, 150.0 ppm. MS (EI): m/z (%) = 567.7 (100) $[M]^{\cdot+}$. HRMS (EI) calcd. for $[C_{25}H_{14}I_2]^{\cdot+}$: 567.9185; found 567.9180. $4C_{25}H_{14}I_2{\cdot}H_2O$ ($4\times612.52 + 18.02 = 2468.10$): calcd. C 53.97, H 2.99; found C 54.26, H 2.62%.

(*rac*)-2,2′-Diamino-9,9′-spirobifluorene [(*rac*)-7]. Method A: Compound (*rac*)-**2** (948 mg, 2 mmol), $[Pd_2dba_3{\cdot}CHCl_3]$ (21 mg, 1 mol %), and cHex$_2$P(2-Bph) (17 mg, 2.2 mol %) were mixed and repeatedly (usually three times) evacuated and flushed with argon. After the mixture had been dissolved in abs. THF (10 mL), a LiHMDS solution in THF (1 M, 4.8 mL 4.8 mmol) was added by syringe. The reaction mixture was placed in an oil bath that had previously been heated to 65 °C and was kept at this temperature for 15 h. After complete consumption of the starting material the mixture was allowed to cool to room temperature and treated with hydrochloric acid (1 M, 20 mL). After stirring for 5 min the mixture was neutralized with aq. sodium hydroxide and the layers were separated. The aqueous solution was extracted four times with dichloromethane and the combined organic layers were washed with brine and dried with Na_2SO_4. After evaporation of the solvent in vacuo the resulting residue was subjected to column chromatography on silica gel with n-hexane/ethyl acetate (1:1 v/v) containing 0.5% triethylamine as eluent. The pure solid product was finally obtained after a second chromatographic separation on silica with toluene/ethyl acetate (5:1 v/v) containing 0.5% triethylamine as eluent (315 mg 45%). **Method B:** Compound (*rac*)-**6** (406 mg, 1 mmol) was repeatedly evacuated and flushed with argon. Abs. methanol (100 mL) and Pd/C (5% Pd, 50 mg) were added. The resulting suspension was cooled in an ice bath. Sodium borohydride (1.25 g, 33 mmol) was added in several portions. After complete addition the ice bath was removed and the mixture was stirred for 12 h at room temperature. After that period the mixture was filtered through celite and the filtrate was evaporated to dryness. The resulting residue was dissolved in dichloromethane (100 mL) and washed twice with water. The combined aqueous phases were then extracted with dichloromethane, and the combined organic layers were then washed with water and brine and dried with Na_2SO_4. The solid product was obtained after evaporation of the solvent and column chromatography on silica with n-hexane/ethyl acetate (1:1 v/v) containing 0.5% of triethylamine as eluent (265 mg, 76%). The analytical data were in agreement with those published by F. K. Sutcliffe.[20]

Optical Resolution of (*rac*)-2,2′-Dihydroxy-9,9′-spirobifluorene [(*rac*)-4]: Compound (*R*,*R*)-**5** (1.74 g, 3.45 mmol) and (*rac*)-**4** (1.2 g, 3.45 mmol) were dissolved in ethanol (15 mL). After 12 h at room temperature the precipitate was collected and repeatedly recrystallized from ethanol.[26] (m.p. 236–238 °C, ref.[18] 238–243 °C). As revealed by an X-ray crystal structure analysis, a 1:1 clathrate of the (*R*)-**4** and (*R*,*R*)-**5** was obtained. Addition of aq. sodium hydroxide (3 N) to a solution of the clathrate in benzene and subsequent neutralization of the aqueous phase with aq. hydrochloric acid allowed isolation of the pure (+)-enantiomer after extraction with benzene. The (–)-enantiomer of **4** could be isolated from the ethanolic filtrate of the clathrate formation after concentration in vacuo and subsequent column chromatography of the resulting residue on silica gel with n-hexane/ethyl acetate (2:1 v/v) as eluent. The enantiomerically pure products were obtained as white solids. Furthermore, two portions of (*R*,*R*)-**5** could be recovered, the first from the decomposition of the clathrate and the second from the chromatography [(+)-(*R*)-**4**: 500 mg (83%, ref.[18] 90%), (–)-(*S*)-**4**: 580 mg (96%), recovered (*R*,*R*)-**5**: 1.55 g (89%)]. M.p. 271–275 °C. (+)-(*R*)-**4** $[\alpha]_D^{20}$ = +27.1 {c = 0.39, MeOH, ref.[18] +27.1 (c = 0.88, methanol)}; (–)-(*S*)-**4** $[\alpha]_D^{20}$ = –26.9 (c = 0.92, MeOH).[26] The spectroscopic data were in agreement with those published by V. Prelog and F. Toda.[3c,18]

(*R*)-2,2′-Bis(trifluoromethylsulfoxy)-9,9′-spirobifluorene [(*R*)-8]: (*R*)-2,2′-Dihydroxy-9,9-spirobifluorene [(*R*)-**4**, 400 mg, 1.14 mmol] dissolved in abs. dichloromethane (75 mL) was mixed with absol. triethylamine (0.8 mL, 5.7 mmol), and the mixture was cooled to –10 °C. Trifluoromethanesulfonic anhydride (0.5 mL, 2.9 mmol) dissolved in abs. dichloromethane (25 mL) was then added dropwise over a period of 1–2 h. After complete addition the reaction mixture was stirred for 1 h at –10 °C. The mixture was allowed to warm up to room temperature and stirred at this temperature for 15 h, after which the reaction was quenched by pouring into ice cold hydrochloric acid (5%). The layers were separated and the aqueous phase was extracted three times with dichloromethane. The combined organic layers were washed with sat. aq. sodium hydrogen carbonate solution and brine and dried with Na_2SO_4, and the solvents were evaporated to dryness under reduced pressure. The resulting product was further purified by column chromatography on silica gel with hexane/ethyl acetate (5:1, v/v) as eluent. The pure product was obtained as an amorphous, white, resinous solid (690 mg, 98%). $[\alpha]_D^{20}$ = +4.9 (c = 1.0, THF). ^{1}H NMR ($CDCl_3$, 500.1 MHz): δ = 6.59 (d, J = 1.2 Hz, 2 H), 6.73 (dd, J = 7.7, 1.1 Hz, 2 H), 7.18 (ddd, J = 7.7, 7.7, 1.1 Hz, 2 H), 7.32 (dd, J = 8.2, 1.2 Hz, 2 H), 7.42 (ddd, J = 7.7, 7.7, 1.1 Hz, 2 H), 7.85 (dd, J = 7.7, 1.1 Hz, 2 H), 7.90 (d, J = 8.2 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 65.8, 117.3, 118.6 (q, J(C,F) = 321 Hz), 120.7, 121.4, 121.5, 124.1, 128.6, 129.0, 139.8, 142.0, 147.7, 149.0, 149.7 ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz): δ = –72.8 ppm. IR $\tilde{\nu}$ (cm^{-1}): 1426, 1212 (RSO_2OR'). MS (CI, isobutane) m/z (%): 613.3 (100) $[MH]^+$. HRMS (CI, isobutane): calcd. for $C_{27}H_{15}F_6O_6S_2$ $[MH]^+$ 613.0214; found 613.0195. $2C_{27}H_{14}F_6O_6S_2{\cdot}H_2O$ ($2\times612.52 + 18.02 = 1243.06$): calcd. C 52.18, H 2.43; found C 52.16, H 2.46%.

(*S*)-2,2′-Bis(trifluoromethylsulfoxy)-9,9′-spirobifluorene [(*S*)-8]: Compound (*S*)-**8** was prepared according to the procedure given for the synthesis of its antipode in 97% yield. $[\alpha]_D^{20}$ = –5.0 (c = 1.01, THF).

(*R*)-9,9′-Spirobifluorene-2,2′-dicarbonitrile [(*R*)-10]: Anhydrous lithium chloride (62 mg, 1.46 mmol), (*R*)-**8** (150 mg, 0.25 mmol), $[Pd(PPh_3)_4]$ (22 mg, 10 mol %), and zinc cyanide (112 mg, 0.95 mmol) were mixed and repeatedly evacuated and flushed with argon. Abs. dimethylformamide (5 mL) was added by syringe and the solution was heated to 120 °C for 36 h. After cooling to room temperature the reaction mixture was partitioned between sat. aq. sodium hydrogen carbonate solution and dichloromethane. The phases were separated and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried with $MgSO_4$, and the solvent was removed in vacuo. The resulting residue was subjected to column chromatography on silica gel with n-hexane/ethyl acetate (5:1, v/v) as eluent. The pure product was obtained as a white solid (80 mg, 89%). M.p. 230–240 °C. $[\alpha]_D^{20}$ = +95.4 (c = 1.00, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500.1 MHz): δ = 6.74 (dd, J = 7.7, 1.1 Hz, 2 H), 6.95 (d, J = 1.5 Hz, 2 H), 7.24 (ddd, J = 7.7, 7.7, 1.1 Hz, 2 H), 7.46 (ddd, J = 7.7, 7.7, 1.1 Hz, 2 H), 7.70 (dd, J = 7.7, 1.5 Hz, 2 H), 7.91 (d, J = 7.7 Hz, 2 H), 7.96 (d, J = 7.7 Hz, 2 H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 65.5, 111.2, 118.7, 120.9, 121.4, 124.2, 127.6, 128.8, 130.0, 132.6, 139.8, 146.2, 147.8, 148.1 ppm. IR $\tilde{\nu}$ (cm^{-1}): 2222 (C≡N). MS (CI, ammonia) m/z (%): 384.2 (100) $[MNH_4]^+$. HRMS (CI, ammonia): calcd. for $C_{27}H_{18}N_3$ $[MNH_4]^+$

384.1501; found 384.1494. $4C_{27}H_{14}N_2$·ethyl acetate·*n*-hexane[56] (4×366.41 + 88.11 + 86.18 = 1639.93): calcd. C 86.42, H 4.79, N 6.83; found C 86.81, H 4.43, N 6.61%.

(*R*)-2,2′-Dimethyl-9,9′-spirobifluorene [(*R*)-11]: Compound (*R*)-**8** (153 mg, 0.25 mmol) and [Ni(dppp)Cl_2] (14 mg, 10 mol %) were repeatedly evacuated and flushed with argon, and abs. diethyl ether (25 mL) was added by syringe. After the system had been cooled to 0 °C, a solution of methylmagnesium bromide in diethyl ether (3 M, 1 mL, 3 mmol) was added dropwise over a period of approx. 15 min. After complete addition the reaction mixture was heated to reflux for 24 h. The mixture was carefully quenched with water at 0 °C and was then diluted with aq. hydrochloric acid (5%). The aqueous layer was then extracted three times with diethyl ether, and the combined organic phases were washed consecutively with water, sat. aq. sodium hydrogen carbonate solution, and brine. After drying with $MgSO_4$, the solvent was removed in vacuo and the residue was subjected to column chromatography on silica gel with hexane/ethyl acetate (5:1, v/v) as eluent. The pure product was obtained as a white solid (84 mg, 98%). M.p. 179–182 °C. $[\alpha]_D^{20}$ = +14.3 (*c* = 0.61, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500.1 MHz): δ = 2.20 (s, 6 H), 6.54 (s, 2 H), 6.70 (d, *J* = 7.7 Hz, 2 H), 7.07 (ddd, *J* = 7.7, 7.7, 1.1 Hz, 2 H), 7.17 (m, 2 H), 7.34 (ddd, *J* = 7.7, 7.7, 1.1 Hz, 2 H), 7.72 (d, *J* = 7.7 Hz, 2 H), 7.79 (d, *J* = 7.7 Hz, 2 H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 21.5, 65.7, 119.6, 119.6, 124.0, 124.6, 127.3, 127.5, 128.5, 137.8, 139.1, 141.8, 148.9, 149.2 ppm. MS (CI, isobutane) *m*/*z* (%): 345.3 (100) $[MH]^+$. HRMS (CI, isobutane): calcd. for $C_{27}H_{21}$ $[MH]^+$ 345.1643; found 345.1622. $3C_{27}H_{20}$·H_2O (3×344.45 + 18.02 = 1051.37): calcd. C 92.53, H 5.94; found C 92.15, H 6.32%.

(*S*)-2,2′-Dimethyl-9,9′-spirobifluorene [(*S*)-11]: Compound (*S*)-**11** was prepared according to the procedure given for the synthesis of its antipode in 99% yield. $[\alpha]_D^{20}$ = –14.2 (*c* = 0.61, $CHCl_3$).

(*R*)-2,2′-Bis[(trimethylsilyl)ethynyl]-9,9′-spirobifluorene [(*R*)-12]: Compound (*R*)-**8** (150 mg, 0.25 mmol), [$PdCl_2(PPh_3)_2$] (18 mg, 0.025 mmol, 10 mol %), and CuI (5 mg, 0.025 mmol, 10 mol %) were mixed and repeatedly evacuated and flushed with argon. Then abs. dimethylformamide (20 mL) and abs. triethylamine (1 mL) were added by syringe. After the system had been stirred for 5 min at room temperature, trimethylsilylacetylene (0.14 mL, 1 mmol) was added by syringe and the reaction mixture was stirred for 10 h at 90 °C. After complete consumption of the starting material the reaction mixture was quenched with brine (20 mL), filtered through celite, and extracted with dichloromethane. The combined organic layers were washed with water and brine, dried with Na_2SO_4, concentrated in vacuo, and the residue was subjected to column chromatography on silica gel with *n*-hexane/ethyl acetate (5:1, v/v) as eluent. The pure product was obtained as a white solid (120 mg, 95%). M.p. 180–183 °C. $[\alpha]_D^{20}$ = +26.0 (*c* = 1.00, THF). ^{1}H NMR ($CDCl_3$, 500.1 MHz): δ = 0.15 (s, 18 H), 6.70 (dd, *J* = 7.7, 1.1 Hz, 2 H), 6.81 (d, *J* = 1.6 Hz, 2 H), 7.11 (ddd, *J* = 7.7, 7.7, 1.1 Hz, 2 H), 7.37 (ddd, *J* = 7.7, 7.7, 1.1 Hz, 2 H), 7.49 (dd, *J* = 7.7, 1.6 Hz, 2 H), 7.76 (d, *J* = 7.7 Hz, 2 H), 7.81 (dd, *J* = 7.7, 1.1 Hz, 2 H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = –0.1, 65.5, 94.5, 105.2, 119.8, 120.3, 122.2, 124.1, 127.6, 128.0, 128.3, 132.0, 141.0, 142.1, 148.1, 148.5 ppm. IR $\tilde{\nu}$ (cm^{-1}): 2154 (C≡C), 732 ($SiMe_3$). MS (CI, isobutane) *m*/*z* (%): 508.8 (100) $[MH]^+$. HRMS (CI, isobutane): calcd. for $C_{35}H_{33}Si_2$ $[MH]^+$ 509.2120; found 509.2119. $C_{35}H_{32}Si_2$: calcd. C 82.62, H 6.34; found C 82.60, H 6.61%.

(*S*)-2,2′-Bis[(trimethylsilyl)ethynyl]-9,9′-spirobifluorene [(*S*)-12]: Compound (*S*)-**12** was prepared according to the procedure given for the synthesis of its antipode in 96% yield. $[\alpha]_D^{20}$ = –25.3 (*c* = 0.98, THF).

(*R*)-2,2′-Diethynyl-9,9′-spirobifluorene [(*R*)-13]: (*R*)-2,2′-Bis[(trimethylsilyl)ethynyl]-9,9′-spirobifluorene [(*R*)-**12**, 50 mg, 0.108 mmol] and potassium carbonate (105 mg, 0.757 mmol) were mixed with THF/MeOH (1:1, 20 mL) and stirred for 3 h at room temperature. After complete consumption of the starting material the mixture was diluted with dichloromethane (40 mL). The solution was washed with water, dried with Na_2SO_4, and concentrated in vacuo. The resulting residue was subjected to column chromatography on silica gel with *n*-hexane/ethyl acetate (5:1, v/v) as eluent. The pure product was obtained as a slightly brown solid (32 mg, 92%). M.p. 240 °C (decomposition). $[\alpha]_D^{20}$ = +158.7 (*c* = 1.06, THF). ^{1}H NMR ($CDCl_3$, 500.1 MHz): δ = 2.96 (s, 2 H), 6.72 (dd, *J* = 7.7, 1.1 Hz, 2 H), 6.84 (d, *J* = 1.1 Hz, 2 H), 7.13 (ddd, *J* = 7.7, 7.7, 1.1 Hz, 2 H), 7.38 (ddd, *J* = 7.7, 7.7, 1.1 Hz, 2 H), 7.51 (dd, *J* = 8.2, 1.1 Hz, 2 H), 7.79 (d, *J* = 8.2 Hz, 2 H), 7.83 (dd, *J* = 7.7, 1.1 Hz, 2 H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 65.5, 77.4, 83.8, 120.0, 120.4, 121.2, 124.1, 127.8, 128.1, 128.5, 132.1, 140.9, 142.4, 148.2, 148.4 ppm. IR $\tilde{\nu}$ (cm^{-1}): 2102 (C≡C). MS (CI, isobutane) *m*/*z* (%): 365.5 (100) $[MH]^+$. HRMS (CI, isobutane): calcd. for $C_{29}H_{17}$ $[MH]^+$ 365.1330; found 365.1315. $C_{29}H_{16}$·H_2O (364.44 + 18.02 = 382.46): calcd. C 94.03, H 4.53; found C 94.01, H 4.51%.

(*S*)-2,2′-Diethynyl-9,9′-spirobifluorene [(*S*)-13]: Compound (*S*)-**13** was prepared according to the procedure given for the synthesis of its antipode in 94% yield. $[\alpha]_D^{20}$ = –160.0 (*c* = 1.02, THF).

(*R*)-2,2′-Bis(4-methoxyphenyl)-9,9′-spirobifluorene [(*R*)-14]: Compound (*R*)-**8** (153 mg, 0.25 mmol), (4-methoxyphenyl)boronic acid (114 mg, 0.75 mmol), [$PdCl_2$(dppf)] (10 mg, 5 mol %), and potassium phosphate (212 mg, 1 mmol) were mixed and repeatedly evacuated and flushed with argon. Abs. THF (5 mL) was then added by syringe and the reaction mixture was heated under reflux for 16 h. After cooling to room temperature the reaction mixture was partitioned between sat. aq. sodium hydrogen carbonate solution and dichloromethane. The phases were separated and the aqueous phase was extracted three times with dichloromethane. The combined organic layers were washed with water and brine, dried with Na_2SO_4, and concentrated in vacuo. The resulting residue was subjected to column chromatography on silica gel with *n*-hexane/ethyl acetate (5:1, v/v) as eluent. The pure product was obtained as an off-white solid (115 mg, 87%). M.p. 212–215 °C. $[\alpha]_D^{20}$ = +262.1 (*c* = 1.01, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500.1 MHz): δ = 3.76 (s, 6 H), 6.77 (dd, *J* = 7.7, 0.7 Hz, 2 H), 6.83 (d, *J* = 8.8 Hz, 4 H), 6.94 (d, *J* = 1.8 Hz, 2 H), 7.10 (ddd, *J* = 7.7, 7.7, 0.7 Hz, 2 H), 7.36 (d, *J* = 8.8 Hz, 4 H), 7.37 (ddd, *J* = 7.7, 7.7, 0.7 Hz, 2 H), 7.57 (dd, *J* = 8.1, 1.8 Hz, 2 H), 7.85 (dd, *J* = 7.7, 0.7 Hz, 2 H), 7.88 (d, *J* = 8.1 Hz, 2 H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 55.3, 66.1, 114.0, 119.9, 120.2, 122.3, 124.1, 126.4, 127.7, 127.7, 128.1, 133.5, 140.5, 140.6, 141.5, 149.1, 149.5, 159.0 ppm. MS (CI, isobutane) *m*/*z* (%): 529.3 (100) $[MH]^+$. HRMS (CI, isobutane): calcd. for $C_{39}H_{29}O_2$ $[MH]^+$ 529.2168; found 529.2154. $2C_{39}H_{28}O_2$·ethyl acetate[56] (2×528.64 + 88.11 = 1145.39): calcd. C 85.99, H 5.63; found C 86.12, H 5.79%.

(*R*)-2,2′-Bis(4-chlorophenyl)-9,9′-spirobifluorene [(*R*)-15]: Compound (*R*)-**8** (153 mg, 0.25 mmol), (4-chlorophenyl)boronic acid (94 mg, 0.6 mmol), [$PdCl_2$(dppf)] (10 mg, 5 mol %), and potassium phosphate (212 mg, 1 mmol) were mixed and repeatedly evacuated and flushed with argon. Abs. THF (5 mL) was then added by syringe and the reaction mixture was heated to reflux for 16 h. After cooling to room temperature the reaction mixture was partitioned between sat. aq. sodium hydrogen carbonate solution and dichloromethane. The phases were separated and the aqueous phase was extracted three times with dichloromethane. The combined organic layers were washed with water and brine, dried with Na_2SO_4, and

the solvent was removed in vacuo. The residue was subjected to column chromatography on silica gel with *n*-hexane/ethyl acetate (5:1, v/v) as eluent. The pure product was obtained as a white solid (106 mg, 79%). M.p. 154–157 °C. $[\alpha]_D^{20}$ = +267.9 (*c* = 0.97, $CHCl_3$). ^1H NMR ($CDCl_3$, 500.1 MHz): δ = 6.78 (dd, *J* = 7.7, 0.7 Hz, 2 H), 6.94 (d, *J* = 1.4 Hz, 2 H), 7.13 (ddd, *J* = 7.7, 7.7, 0.7 Hz, 2 H), 7.26 (d, *J* = 8.4 Hz, 4 H), 7.35 (d, *J* = 8.4 Hz, 4 H), 7.40 (ddd, *J* = 7.7, 7.7, 0.7 Hz, 2 H), 7.59 (dd, *J* = 8.1, 1.4 Hz, 2 H), 7.89 (dd, *J* = 7.7, 0.7 Hz, 2 H), 7.92 (d, *J* = 8.1 Hz, 2 H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 66.1, 120.2, 120.5, 122.5, 124.1, 126.8, 127.9, 128.1, 128.3, 128.7, 133.2, 139.3, 139.7, 141.2, 141.4, 149.0, 149.5 ppm. MS (CI, isobutane) *m*/*z* (%): 537.3 (100) $[MH]^+$. HRMS (CI, isobutane): calcd. for $C_{37}H_{23}Cl_2$ $[MH]^+$ 537.1177; found 537.1177. $3\,C_{37}H_{22}Cl_2$·ethyl acetate[56] (3 × 537.48 + 88.11 = 1700.55): calcd. C 81.22, H 4.39; found C 81.14, H 4.38%.

(*R*)-2,2′-Bis[4-(ethoxycarbonyl)phenyl]-9,9′-spirobifluorene [(*R*)-16]: Compound (*R*)-**8** (153 mg, 0.25 mmol), ethyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (0.15 mL, 0.58 mmol), [$PdCl_2$(dppf)] (10 mg, 5 mol %), and potassium phosphate (212 mg, 1 mmol) were mixed and repeatedly evacuated and flushed with argon. Abs. THF (5 mL) was then added by syringe and the reaction mixture was heated to reflux for 16 h. After cooling to room temperature the reaction mixture was partitioned between sat. aq. sodium hydrogen carbonate solution and dichloromethane. The phases were separated and the aqueous phase was extracted three times with dichloromethane. The combined organic layers were washed with water and brine, dried with Na_2SO_4, and the solvent was removed in vacuo. The residue was subjected to column chromatography on silica gel twice, first with *n*-hexane/ethyl acetate (5:1, v/v) and then with THF/toluene (1:1 v/v) and 5% of triethylamine as eluent. The pure product was obtained as a yellow solid (93 mg, 61%). M.p. 185–188 °C. $[\alpha]_D^{20}$ = +269.1 (*c* = 1.02, $CHCl_3$). ^1H NMR ($CDCl_3$, 500.1 MHz): δ = 1.36 (t, *J* = 7.1 Hz, 6 H), 4.34 (q, *J* = 7.1 Hz, 4 H), 6.77 (dd, *J* = 7.7, 0.7 Hz, 2 H), 7.01 (d, *J* = 1.7 Hz, 2 H), 7.14 (ddd, *J* = 7.7, 7.7, 0.7 Hz, 2 H), 7.40 (ddd, *J* = 7.7, 7.7, 0.7 Hz, 2 H), 7.48 (d, *J* = 8.2 Hz, 4 H), 7.66 (dd, *J* = 8.2, 1.7 Hz, 2 H), 7.89 (dd, *J* = 7.7, 0.7 Hz, 2 H), 7.94 (d, *J* = 8.2 Hz, 2 H), 7.96 (d, *J* = 8.2 Hz, 4 H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 14.3, 60.9, 66.1, 120.3, 120.5, 122.8, 124.1, 126.9, 127.3, 128.0, 128.2, 129.1, 129.9, 139.8, 141.1, 141.9, 145.1, 149.0, 149.4, 166.4 ppm. IR $\tilde{\nu}$ (cm^{-1}): 1715 (C=O). MS (CI, isobutane) *m*/*z* (%): 613.2 (100) $[MH]^+$. HRMS (CI, isobutane): calcd. for $C_{43}H_{33}O_4$ $[MH]^+$ 613.2379, found 613.2380. $2\,C_{43}H_{32}O_4$·*n*-hexane·H_2O[56] (2 × 612.71 + 86.18 + 18.02 = 1329.61): calcd. C 83.11, H 6.06; found C 83.05, H 6.03%.

(*S*)-2,2′-Bis[4-(ethoxycarbonyl)phenyl]-9,9′-spirobifluorene [(*S*)-16]: Compound (*S*)-**16** was prepared according to the procedure given for the synthesis of its antipode in 60% yield. $[\alpha]_D^{20}$ = –267.6 (*c* = 1.10, $CHCl_3$).

(*R*)-2,2′-Bis(4-hydroxyphenyl)-9,9′-spirobifluorene [(*R*)-17]: Compound (*R*)-**14** (132 mg, 0.25 mmol) was repeatedly evacuated and flushed with argon. Abs. dichloromethane (5 mL) was then added by syringe and the solution was cooled to –78 °C. At that temperature, a boron tribromide solution in dichloromethane (1 M, 1 mL, 1 mmol) were added by syringe. The cooling bath was removed and the mixture was stirred for 5 h at room temperature. After complete consumption of the starting material the mixture was quenched with aq. sodium hydroxide solution (2 N). After addition of THF (10 mL) the mixture was acidified (pH 1–2) with hydrochloric acid (6 M) and the aqueous phase was extracted three times with dichloromethane. The combined organic layers were washed with water, sat. aq. sodium hydrogen carbonate solution, and brine, dried with Na_2SO_4, and concentrated in vacuo. The residue was subjected to column chromatography on silica gel with *n*-hexane/ethyl acetate (1:2, v/v) as eluent. The pure product was obtained as an off-white solid (116 mg, 93%). M.p. 163–165 °C. $[\alpha]_D^{20}$ = +259.3 (*c* = 0.96, $CHCl_3$). ^1H NMR ($CDCl_3$, 500.1 MHz): δ = 4.84 (br. s, 2 H), 6.74–6.76 (m, 6 H), 6.91 (d, *J* = 1.7 Hz, 2 H), 7.09 (ddd, *J* = 7.7, 7.7, 0.7 Hz, 2 H), 7.30 (d, *J* = 8.8 Hz, 4 H), 7.36 (ddd, *J* = 7.7, 7.7, 0.7 Hz, 2 H), 7.55 (dd, *J* = 8.2, 1.7 Hz, 2 H), 7.85 (dd, *J* = 7.7, 0.7 Hz, 2 H), 7.87 (d, *J* = 8.2 Hz, 2 H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 66.1, 115.4, 119.9, 120.2, 122.3, 124.1, 126.4, 127.7, 127.7, 128.3, 133,7, 140.5, 140.5, 141.5, 149.1, 149.5, 155.0 ppm. MS (CI, isobutane) *m*/*z* (%): 501.2 (100) $[MH]^+$. HRMS (CI, isobutane): calcd. for $C_{37}H_{25}O_2$ $[MH]^+$ 501.1855; found 501.1859. $3\,C_{37}H_{24}O_2$·*n*-hexane[56] (3 × 500.59 + 86.18 = 1587.95): calcd. C 88.50, H 5.46; found C 88.21, H 5.42%.

(*R*)-2,2′-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-9,9′-spirobifluorene [(*R*)-18]: Anhydrous potassium acetate (147 mg, 1.5 mmol), (*R*)-**8** (153 mg, 0.25 mmol), bis(pinacolato)diboron (140 mg, 0.55 mmol), [$PdCl_2$(dppf)] (19 mg, 10 mol %), and dppf (14 mg, 10 mol %) were mixed, repeatedly evacuated, and flushed with argon. Abs. 1,4-dioxane (5 mL) was then added by syringe and the reaction mixture was heated to reflux for 12 h. After cooling to room temperature the reaction mixture was partitioned between water and dichloromethane. The phases were separated and the aqueous phase was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried with Na_2SO_4, and the solvent was removed in vacuo. The residue was subjected to column chromatography on silica gel with *n*-hexane/ethyl acetate (5:1, v/v) as eluent. The product was obtained as an off-white solid (129 mg, 91%). M.p. 176–178 °C. $[\alpha]_D^{20}$ = +53.1 (*c* = 0.96, $CHCl_3$). ^1H NMR ($CDCl_3$, 500.1 MHz): δ = 1.25 (s, 24 H), 6.65 (dd, *J* = 7.7, 0.7 Hz, 2 H), 7.08 (ddd, *J* = 7.7, 7.3, 0.7 Hz, 2 H), 7.16 (s, 2 H), 7.34 (ddd, *J* = 7.7, 7.3, 0.7 Hz, 2 H), 7.84 (d, *J* = 7.7 Hz, 2 H), 7.85 (m, 2 H), 7.85 (d, *J* = 7.7 Hz, 2 H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 24.8, 65.9, 83.6, 119.3, 120.4, 124.1, 127.6, 128.3, 128.3, 130.4, 134.7, 141.5, 145.0, 147.5, 149.5 ppm. ^{11}B NMR ($CDCl_3$, 160.5 MHz): δ = 29.5 ppm. IR $\tilde{\nu}$ (cm^{-1}): 1355 (RB(OR′)$_2$). MS (CI, ammonia) *m*/*z* (%): 586.3 (100) $[MNH_4]^+$. HRMS (CI, ammonia): calcd. for $C_{37}H_{42}B_2NO_4$ $[MNH_4]^+$ 586.3300; found 586.3299.

(*S*)-2,2′-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-9,9′-spirobifluorene [(*S*)-18]: Compound (*S*)-**18** was prepared by the procedure given for the synthesis of its antipode in 99% yield. $[\alpha]_D^{20}$ = –53.7 (*c* = 1.17, $CHCl_3$).

1-(2,5-Dimethyl-1*H*-pyrrol-1-yl)-4-iodobenzene:[57] 4-Iodoaniline (657 mg, 3 mmol), hexane-2,5-dione (0.37 mL, 3.2 mmol), and *p*-TsOH·H_2O (10 mg, 0.05 mmol) were dissolved in toluene (8 mL) and heated in a Dean–Stark apparatus for 3 hours. After cooling, the reaction mixture was washed with sat. aq. sodium hydrogen carbonate solution, five times with water, and with brine. After the mixture had been dried with $MgSO_4$, the solvent was removed in vacuo and the residue was subjected to column chromatography on silica gel with *n*-hexane/ethyl acetate (5:1, v/v) as eluent. The pure product was obtained as a slightly brownish solid (871 mg, 87%). M.p. 72–76 °C. ^1H NMR ($CDCl_3$, 500.1 MHz): δ = 2.02 (s, 6 H), 5.89 (s, 2 H), 6.95 (d, *J* = 8.2 Hz, 2 H), 7.78 (d, *J* = 8.2 Hz, 2 H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 13.0, 92.9, 106.1, 128.6, 130.1, 138.3, 138.7 ppm. MS (CI, isobutane) *m*/*z* (%): 298.1 (100) $[MH]^+$. HRMS (CI, isobutane): calcd. for $C_{12}H_{13}IN$ $[MH]^+$ 298.0093, found 298.0082. $6\,C_{12}H_{12}IN$·*n*-hexane (6 × 297.13 + 86.18 = 1868.98): calcd. C 50.13, H 4.64, N 4.50; found C 50.27, H 4.44, N 4.43%.

(*R*)-2,2′-Bis[4-(2,5-dimethyl-1*H*-pyrrol-1-yl)phenyl]-9,9′-spirobifluorene [(*R*)-19]: Anhydrous CsF (221 mg, 1.45 mmol), (*R*)-**18** (125 mg, 0.22 mmol), 1-(2,5-dimethyl-1*H*-pyrrol-1-yl)-4-iodobenzene (157 mg, 0.53 mmol), and $[Pd(PtBu_3)_2]$ (5 mg, 4 mol %) were mixed, repeatedly evacuated, and flushed with argon. Abs. THF (5 mL) was then added by syringe and the reaction mixture was heated to reflux for 24 h. After the system had been cooled to room temperature, dichloromethane was added and the mixture was washed twice with sat. aq. sodium carbonate solution. After separation of the phases the aqueous layer was extracted with dichloromethane. The combined organic layers were washed with brine, dried with Na_2SO_4, and the solvent was removed in vacuo. The residue was subjected to column chromatography on silica gel with *n*-hexane/ethyl acetate (5:1, v/v) as eluent. The pure product was obtained as a white solid (90 mg, 62%). M.p. 151–154 °C. $[a]_D^{20}$ = +273.7 (*c* = 0.52 $CHCl_3$). ^1H NMR ($CDCl_3$, 500.1 MHz): δ = 1.97 (s, 12 H), 5.87 (br. s, 4 H), 6.79 (dd, *J* = 7.7, 1.1 Hz, 2 H), 7.04 (d, *J* = 1.6 Hz, 2 H), 7.13–7.15 (m, 6 H), 7.41 (ddd, *J* = 7.7, 7.7, 1.1 Hz, 2 H), 7.52 (d, *J* = 8.2 Hz, 4 H), 7.68 (dd, *J* = 8.2, 1.6 Hz, 2 H), 7.89 (dd, *J* = 7.7, 1.1 Hz, 2 H), 7.95 (d, *J* = 8.2 Hz, 2 H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 13,0, 66.1, 105.7, 120.2, 120.5, 122.6, 124.2, 126.9, 127.6, 127.9, 128.1, 128.3, 128.8, 138.0, 139.9, 140.1, 141.3, 141.4, 149.0, 149.5 ppm. MS (CI, isobutane) *m*/*z* (%): 655.3 (100) $[MH]^+$. HRMS (CI, isobutane): calcd. for $C_{49}H_{39}N_2$ $[MH]^+$ 655.3113; found 655.3108. $C_{49}H_{38}N_2$·dichloromethane·2 H_2O[56] (654.84 + 84.93 + 36.04 = 775.81): calcd. C 77.41, H 5.72, N 3.61; found C 77.34, H 5.95, N 3.29%.

(*R*)-2,2′-Dibromo-7,7′-dimethyl-9,9′-spirobifluorene [(*R*)-20]: Compound (*R*)-**11** (120 mg, 0.35 mmol) was dissolved in dichloromethane (4.5 mL), and iron(III) chloride hexahydrate (0.3 mg, 0.3 mol %) was added. The flask was covered with aluminium foil to protect the reaction from light. Bromine (38 μL, 119 mg, 0.74 mmol) dissolved in dichloromethane (0.5 mL) was then added and the mixture was stirred for 24 h. After cooling, the mixture was washed consecutively with sat. aq. sodium hydrogen carbonate solution (10 mL), with sat. aq. sodium thiosulfate solution (10 mL), and water (10 mL), dried with Na_2SO_4, and the solvent was removed in vacuo. The resulting residue was subjected to column chromatography on silica gel with *n*-hexane/ethyl acetate (5:1, v/v) as eluent. The pure product was obtained as a white solid (167 mg, 95%). Suitable single crystals to perform an X-ray crystal structure analysis were obtained from *n*-hexane.[49] M.p. 241–246 °C. $[a]_D^{20}$ = +19.2 (*c* = 0.77, $CHCl_3$). ^1H NMR ($CDCl_3$, 500.1 MHz): δ = 2.21 (s, 6 H), 6.98 (s, 2 H), 6.80 (d, *J* = 1.7 Hz, 2 H), 7.18 (d, *J* = 7.7 Hz, 2 H), 7.47 (dd, *J* = 7.7, 1.7 Hz, 2 H), 7.64 (d, *J* = 7.7 Hz, 2 H), 7.68 (d, *J* = 7.7 Hz, 2 H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 21.5, 65.4, 119.9, 120.9, 121.1, 124.7, 127.2, 129.1, 131.0, 138.0, 138.5, 140.8, 148.1, 150.1 ppm. MS (CI, isobutane) *m*/*z* (%): 501.0 (67) $[MH]^+$ containing $2\times{}^{79}Br$, 503.0 (100) $[MH]^+$ containing ^{79}Br and ^{81}Br, 501.0 (45) $[MH]^+$ containing $2\times{}^{81}Br$. HRMS (CI, isobutene): calcd. for $C_{27}H_{18}{}^{79}Br_2$ $[MH]^+$ 500.9854; found 500.9851. $C_{27}H_{18}Br_2$·H_2O (502.24 + 18.02 = 520.26): calcd. C 62.33, H 3.87; found C 62.33, H 3.67%.

(*S*)-2,2′-Dibromo-7,7′-dimethyl-9,9′-spirobifluorene [(*S*)-20]: Compound (*S*)-**20** was prepared according to the procedure given for the synthesis of its antipode in 94% yield. $[a]_D^{20}$ = –19.5 (*c* = 0.29, $CHCl_3$).

X-ray Crystallographic Study of the Clathrate Formed from (*R*)-4 and (*R*,*R*)-5: Crystal data: $C_{55}H_{68}N_2O_6$, M_r = 853.11, *a* = 9.1776(6), *b* = 9.1776(6), *c* = 55.718(6) Å, $\alpha = \beta = \gamma = 90°$, *V* = 4693.1(6) Å^3, *Z* = 4, $\rho_{calcd.}$ = 1.207 mg m^{-3}, tetragonal, space group $P4_122$. Data collection: STOE-IPDS-diffractometer, Mo-K_α radiation, graphite monochromator, imaging plate, crystal dimensions: 0.45 × 0.32 × 0.31 mm, *T* = 193 K, *F*(000) = 1840, Θ_{max} = 22.45°, $-9 < h < 9$; $-9 < k < 9$; $-59 < l < 59$, 26125 measured reflections, 3025 independent reflections (R_{int} = 0.1300), μ = 0.077 mm^{-1}, max. and min. transmission 0.9764 and 0.9660. Structural analysis and refinement: All non-hydrogen atoms were anisotropically refined and the H atoms were inserted in the calculated positions. 2720 reflections $I > 2\sigma(I)$ and 289 refined parameters, GOF(F^2) = 1.119, final *R* indices: R_1 = 0.0469, wR_2 = 0.0907, max./min. residual electron density 0.177 and –0.225 e Å^{-3}. The structures were solved by direct phase determination (SHELXS-97[58]) and refined on F^2. CCDC-253521 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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