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Synthesis and Optical Resolution of 9,9′-Spirobifluorene-1,1′-diol

Xu Cheng, Guo-Hua Hou, Jian-Hua Xie, and Qi-Lin Zhou*

State Key Laboratory and Institute of Elemento-organic Chemistry, Nankai University, Tianjin 300071, China

qlzhou@nankai.edu.cn

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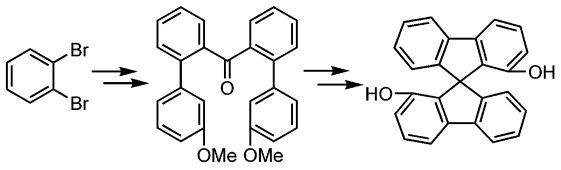
ABSTRACT



9,9′-Spirobifluorene-1,1′-diol (SBIFOL) was conveniently synthesized from 1,2-dibromobenzene and 3-bromoanisole in high yield. Both enantiomers of SBIFOL were obtained in 99% ee by inclusion resolution with 2,3-dimethoxy-*N,N,N′,N′*-tetracyclohexylsuccinamide. The absolute configurations were determined by X-ray analysis of a single crystal of molecular complex.

Molecules with a 9,9′-spirobifluorene backbone are unique in rigidity and have a wide range of applications in molecular electronics,[1] light-emitting materials,[2] enantioselective molecular recognition,[3] and other areas.[4] However, to our knowledge, chiral ligands with a 9,9′-spirobifluorene backbone for asymmetric catalysis have not yet been reported. To form efficient chelating ligands, the coordinating groups need to be introduced into 9,9′-spirobifluorene at the 1 and 1′ positions, i.e., in the "bay region". For this purpose, 9,9′-spirobifluorene-1,1′-diol is a good starting point because the OH groups can be easily converted to other coordinating groups.[5] However, although 9,9′-spirobifluorene-2,2′-diol was already reported by Prelog in 1978,[6] 9,9′-spirobifluorene-1,1′-diol is still an unknown compound. In this paper, we describe the synthesis and optical resolution of 9,9′-spirobifluorene-1,1′-diol.

Our first attempt followed the method for building the structure of 9,9′-spirobifluorene reported by Weisburger (Scheme 1).[7] The substituted biphenyl **1,** prepared from Kumada coupling of 1,2-dibromobenzene and the Grignard reagent of 3-bromoanisole, was treated with *n*-BuLi and reacted with ethyl chloroformate to give ester **2**. After hydrolysis, the obtained carboxylic acid **3** was treated with bromine followed by cyclization with PPA to give 4-bromo-1-methoxyfluoren-9-one (**5**).[8] The nucleophilic addition of

(1) (a) Tour, J. M.; Wu, R.-L.; Schumm, J. S. *J. Am. Chem. Soc.* **1990**, *112*, 5662. (b) Pei, J.; Ni, J.; Zhou, X.-H.; Cao, X.-Y.; Lai, Y.-H. *J. Org. Chem.* **2002**, *67*, 8112.

(2) (a) Bach, U.; Lupo, D.; Comte, P.; Moser, J. E.; Weissortel, F.; Salbeck, J.; Spreitzer, H.; Gratzel, M. *Nature* **1998**, *395*, 583. (b) Schartel, B.; Damerau, T.; Hennecke, M. *Phys. Chem. Chem. Phys.* **2000**, *2*, 4690. (c) Wu, C. C.; Lin, Y. T.; Chiang, H. H.; Cho, T. Y.; Chen, C. W. *Appl. Phys. Lett.* **2002**, *81*, 577. (d) Chien, Y.-Y.; Wong, K.-T.; Chou, P.-T.; Cheng, Y.-M. *Chem. Commun.* **2002**, 2874. (e) Krüger, J.; Plass, R.; Grätzel, M.; Cameron, P. J.; Peter, L. M. *J. Phys. Chem. B* **2003**, *107*, 7536. (f) Lee, J.-I.; Lee, H.; Oh, J.; Chu, H. Y.; Kim, S. H.; Yang, Y. S.; Kim, G. H.; Do, L.-M.; Zyung, T. *Curr. Appl. Phys.* **2003**, *3*, 469.

(3) (a) Smith, D. K.; Diederich, F. *J. Chem. Soc., Chem. Commun.* **1998**, 2501. (b) Lustenberger, P.; Martinborough, E.; Denti, T. M.; Diederich, F. *J. Chem. Soc., Perkin Trans. 2* **1998**, 747. (c) Smith, D. K.; Zingg, A.; Diederich, F. *Helv. Chim. Acta* **1999**, *82*, 1225. (d) Tejeda, A.; Oliva, A. I.; Simón, L.; Grande, M.; Caballero, M.-C.; Morán, J. R. *Tetrahedron Lett.* **2000**, *41*, 4563.

(4) (a) Fournier, J.-H.; Maris, T.; Wuest, J. D. *J. Org. Chem.* **2003**, *68*, 241. (b) Poriel, C.; Ferrand, Y.; Le Maux, P.; Raul-Berthelot, J.; Simonneaux, G. *Chem. Commun.* **2003**, 1105. (c) Poriel, C.; Ferrand, Y.; Le Maux, P.; Paul, C.; Rault-Berthelot, J.; Simonneaux, G. *Chem. Commun.* **2003**, 2308. (d) Pei, J.; Ni, J.; Zhou, X.-H.; Cao, X.-Y.; Lai, Y.-H. *J. Org. Chem.* **2002**, *67*, 4924. (e) Shu, C.-F.; Wu, S.-C. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41*, 1160. (f) Reddy, D. S.; Chou, C.-H.; Shu, C.-F.; Lee, G.-H. *Polymer* **2003**, *44*, 557.

(5) (a) Cai, D.; Payack, J. F.; Bender, D. R.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. J. *J. Org. Chem.* **1994**, *59*, 7180. (b) Cai, D.; Payack, J. F.; Bender, D. R.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. J. *Org. Synth.* **1998**, *76*, 6. (c) Yuyet, T. M. T.; Harada, T.; Hashimoto, K.; Hatsuda, M.; Oku, A. *J. Org. Chem.* **2000**, *65*, 1335.

(6) (a) Prelog, V. *Pure Appl. Chem.* **1978**, *50*, 893. (b) Prelog, V.; Bedeković, D. *Helv. Chim. Acta* **1979**, *62*, 2285.

(7) Weisburger, J. H.; Weisburger, E. K.; Ray, F. E. *J. Am. Chem. Soc.* **1950**, *72*, 4250.

(8) PPA = polyphosphoric acid.

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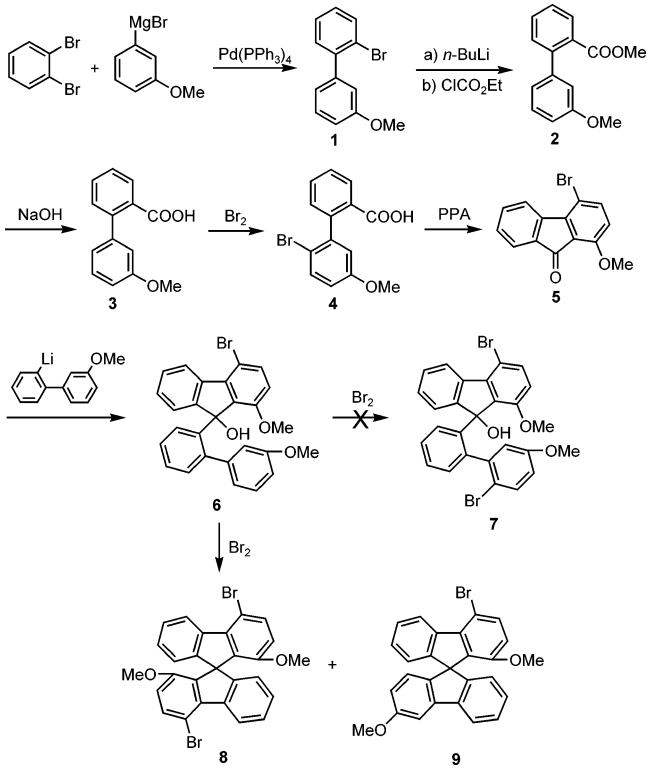
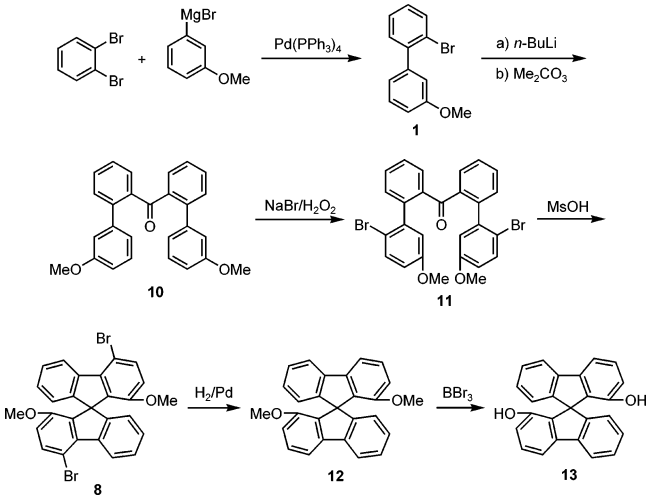
Scheme 1. Synthesis of 9,9′-Spirobifluorene-1,1′-diol through a Separated Ring-Closing Route



Scheme 2. Synthesis of 9,9′-Spirobifluorene-1,1′-diol through a Continuous Ring-Closing Route



lithium reagent to **5** produced alcohol **6**. Compound **6** was so unstable under the bromination conditions that it dehydrated immediately to offer the desired 9,9′-spirobifluorene compound **8** and byproduct **9** in a 1:3 ratio.[9] Because byproduct **9** could not be converted to the desired compound **8** and was also not easy to separate from compound **8**, a very low overall yield can be expected in the preparation of 9,9′-spirobifluorene-1,1′-diol by this separated ring-closing method.

To avoid unwanted ring-closing compounds and to facilitate the purification of product, a new strategy was designed as shown in Scheme 2. The Kumada coupling product **1** was treated with *n*-BuLi and reacted with 0.5 equiv of dimethyl carbonate to produce ketone **10** in 70% yield. This ketone was brominated with NaBr in the presence of H_2O_2 to give dibromoketone **11** in a quantitative yield. The brominations took place exclusively para to the CH_3O groups. In the ring-closing step, PPA was initially tested to cyclize ketone **11** and 9,9′-spirobifluorene compound **8** was produced in 50% yield. However, the workup of the reaction mixture was rather troublesome because an emulsion always occurred during extraction of product. Our second approach was to use methanesulfonic acid (MsOH), which was reported to be a good ring-closing reagent in the synthesis of fluoren-9-ones.[10] In MsOH, ketone **11** was cyclized to 9,9′-spirobifluorene compound **8** in 73% yield at 40−50 °C for 5 h, and the workup of the reaction mixture was very simple. Having the key intermediate **8** at hand, the following debromination by Pd/C-catalyzed hydrogenation and the demethylation by tribromoboron were easily achieved using standard conditions.[11] The target molecule, 9,9′-spirobifluorene-1,1′-diol (**13**), was finally obtained in 27% overall yield from dibromobenzene.

Inclusion crystallization is an effective method for the separation of enantiomers of racemic chiral compounds and is much simpler than traditional diastereomeric resolution.[12] The choice of chiral host is most important for achieving differentiation between diastereoisomeric inclusion complexes formed in resolution. After screening different chiral resolving reagents, 2,3-dimethoxy-*N*,*N*,*N*′,*N*′-tetracyclohexylsuccinamide (**14**)[13] was found to have the greatest potential in the resolution of 9,9′-spirobifluorene-1,1′-diol (**13**). When (2*R*,3*R*)-**14** and racemic diol **13**, in a molar ratio of 1:1, were dissolved in ethanol at rt, a white precipitate appeared after a few minutes. This slurry was stirred overnight, and crystal complexes were collected by filtration. The decomposition of the inclusion complex with 1 N NaOH gave (+)-**13** in 85% yield (based on one enantiomer) in 80% ee. The enantiomeric excess of (+)-**13** was further increased to 99% by repeating the procedure of inclusion crystallization as mentioned above. The enantiomer (−)-**13** (99% ee) was obtained by inclusion resolution using (2*S*,3*S*)-**14**.

(9) Though excess pyridine was present, the ring closure is complete at 0 °C in 5 min.

(10) Tilly, D.; Samanta, S. S.; Faigl, F.; Mortier, J. *Tetrahedron Lett.* **2002**, *43*, 8347.

(11) (a) Birman, V. B.; Rheingold, A. L.; Lam, K.-C. *Tetrahedron: Asymmetry* **1999**, *10*, 125. (b) Zhu, S.-F.; Fu, Y.; Xie, J.-H.; Liu, B.; Xing, L.; Zhou, Q.-L. *Tetrahedron: Asymmetry* **2003**, *14*, 3219.

(12) (a) *Inclusion Compounds*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Eds.; Academic Press: London, 1984; Vols. 1−111; Oxford University Press: Oxford, 1991; Vols. IV, V. (b) *Molecular Inclusion and Molecular Recognition-Clathrates I and II*; Weber, E., Ed.; Topics in Current Chemistry; Springer: Berlin, 1987, 1988; Vols. 140, 149. (c) Tanaka, K.; Okada, T.; Toda, F. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1147. (d) Toda, F.; Tanaka, K.; Stein, Z.; Goldberg, I. *J. Org. Chem.* **1994**, *59*, 5748. (e) Toda, F.; Tanaka, K., *Chem. Commun*. **1997**, 1087. (f) Ding, K.; Wang, Y.; Yun, H.; Liu, J.; Wu, Y.; Terada, M.; Okubo, Y.; Mikami, K. *Chem. Eur. J.* **1999**, *5*, 1734. (g) Periasamy, M.; Venkatraman, L.; Thomas, K. R. J. *J. Org. Chem.* **1997**, *62*, 4302.

(13) Toda, F.; Tanaka, K. *J. Org. Chem.* **1988**, *53*, 3607.

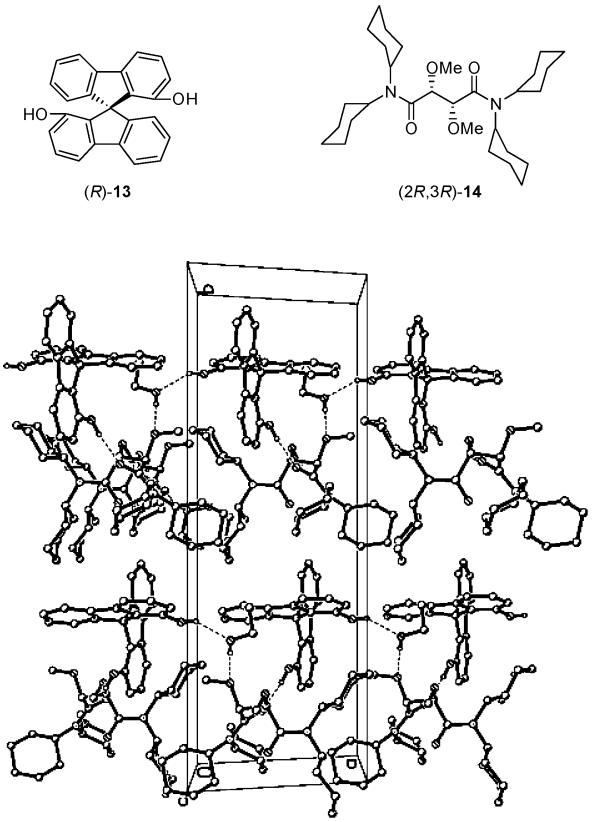


Figure 1. Crystal structure of the molecular complex of (*R*)-**13** and (2*R*,3*R*)-**14**.

To determine the absolute configurations of diols **13**, a single crystal of the molecular complex was prepared from ethanol and subjected to X-ray diffraction analysis. The perspective view of the molecular complex is shown in Figure 1.[14] In the crystal, each block was constructed of one (2*R*,3*R*)-**14** and one (+)-**13** through a hydrogen bond between the hydroxy group of the diol and the carbonyl group of the amide. The blocks were linked by ethanol as a bridge in a zigzag manner. The length of the hydrogen bond between the diol and the carbonyl of the amide OH···O was 1.82 Å and the angle of the bonds O−H···O was 173°, which indicated the existence of a strong hydrogen bond in the block. The two hydrogen bonds held by ethanol were 2.10 Å long and the two O−H···O angles were 179° and 150°, respectively. These two hydrogen bonds kept the supermolecule big enough to precipitate out of ethanol. The absolute configuration of (+)-**13** was assigned to be *R* unambiguously by relating it to the configuration of (2*R*,3*R*)-**14**.

In conclusion, we have developed a new strategy toward the synthesis of 9,9′-spirobifluorene-1,1′-diol with continuous ring-closing as a feature. The enantiomers of 9,9′-spirobifluorene-1,1′-diol were obtained by inclusion resolution. This new member of the 9,9′-spirobifluorene family will provide a potential backbone for chiral ligands and synthetic material.

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Supporting Information Available: The procedure for the preparation of racemic 9,9′-spirobifluorene-1,1′-diol and resolution. The analysis data of **1**, **7**, and **9**−**12** and the structure information of crystal complexes. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) Crystal data for [(*R*)-**13**·(2*R*, 3*R*)-**14**·EtOH]: $C_{57}H_{74}N_2O_7$, M_r = 899.18, T = 293 K, radiation = Mo Kα, λ = 0.710 73 Å, crystal dimensions = 0.22 × 0.20 × 0.18 mm, monoclinic, space group $P2(1)$, a = 9.718(3) Å, b = 25.585 (8) Å, c = 11.268 (4) Å, V = 2561.0(14) Å^3, Z = 2, 8644 unique reflections, R_1 = 0.0687. For crystallographic data for the structure, see the Supporting Information.