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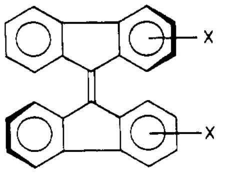
Communications

On the Chirality of Bifluorenylidenes[1]

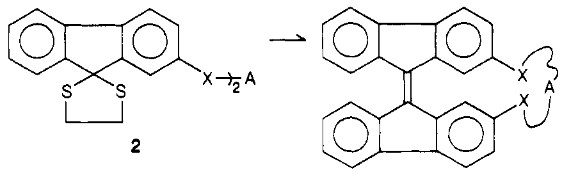
Summary: Chiral bifluorenylidenes were synthesized by intramolecular desulfurdimerization of two fluorenone dithioacetal units linked by a chiral bridge. The barrier of racemization (12 kcal/mol) for bifluorenylidene has been determined.

Sir: Bifluorenylidenes (**1**) are nonplanar[2] and therefore can be chiral. Indeed, the parent hydrocarbon has accidently been obtained in optically pure form.[2c] Other attempts to resolve the racemic mixture were unsuccessful.[3]



1

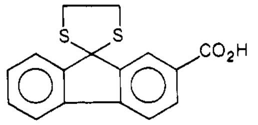
It has been envisaged that the barrier of racemization would be relatively low. However, no quantitative measurement is known. We recently reported a novel W$(CO)_6$-mediated desulfurdimerization reaction of dithioacetals leading to the carbon–carbon double bond formation.[4] Bifluorenylidenes (**1**) can be synthesized in excellent yields. The reaction, however, is nonstereoselective, and a mixture of *E*/*Z* isomers is generally obtained when a substituted fluorene dithioacetal is employed. We felt that, if two fluorenone moieties are connected with an aliphatic chain, intramolecular desulfurdimerization would yield exclusively the *Z* isomer (eq 1). Moreover, the introduction of a chiral bridge in **2** might cause optical induction[5] in the coupling step and chiral **1** might be synthesized. We now describe the first enantioselective synthesis of optically active bifluorenylidenes and the dynamics of racemization of the bifluorenylidene moiety.



2

(1)

Treatment of **3** with ditosylate **4a** under basic conditions (K_2CO_3, Bu_4NBr, DMF, 60 °C, 6 h) afforded the diester **5a** ($[\alpha]^{22}_D$ −10.2° (c 0.18, $CHCl_3$); mp 173–175 °C)[6] in 92% yield. Desulfurdimerization of **5a** with $W(CO)_6$ (4 equiv) in refluxing chlorobenzene for 48 h gave bifluorenylidene **6a** ($[\alpha]^{22}_D$ +634° (c 0.10 $CHCl_3$), mp 274–277 °C)[6-8] in 40%



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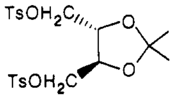
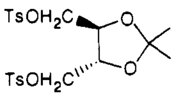
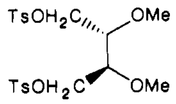


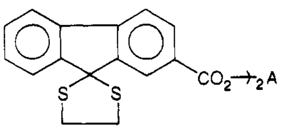
4a



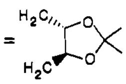
4b



4c



5a: A =



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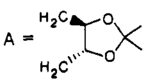

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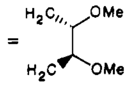

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[1] Transition Metal Promoted Reactions. 25.

[2] (a) Bailey, N. A.; Hull, S. E. *J. Chem. Soc., Chem. Commun.* **1971**, 960. (b) Bailey, N. A.; Hull, S. E. *Acta Crystallogr.* **1978**, *B34*, 3289. (c) Nyberg, S. C.; Lee, J. S. *Acta Crystallogr.* **1985**, *C41*, 560. (d) Ballester, M.; Castaner, J.; Riera, J.; de la Fuente, G.; Camps, M. *J. Org. Chem.* **1985**, *50*, 2287.

[3] (a) Bell, F. *J. Chem. Soc.* **1952**, 5047. (b) Wawzonek, S.; Henry, J. P. *J. Org. Chem.* **1953**, *18*, 1461. (c) Sandström, J., private communication.

[4] (a) Yeung, L. L.; Yip, Y. C.; Luh, T.-Y. *J. Chem. Soc., Chem. Commun.* **1987**, 981. (b) Wong, C. S.; Leung W. S.; Yeung, L. L.; Luh, T.-Y. *J. Organomet. Chem.* **1986**, 307, C49. (c) Ng, D. K. P.; Luh, T.-Y. *Tetrahedron Lett.* **1988**, *29*, 5131.

[5] For examples: Robin, J.-P.; Landais, Y. *J. Org. Chem.* **1988**, *53*, 224. Miyano, S.; Tobita, M.; Nawa, M.; Sato, S.; Hashimoto, H. *J. Chem. Soc., Chem. Commun.* **1980**, 1233.

[6] All new compounds gave satisfactory spectroscopic data, accurate mass, and/or analysis.

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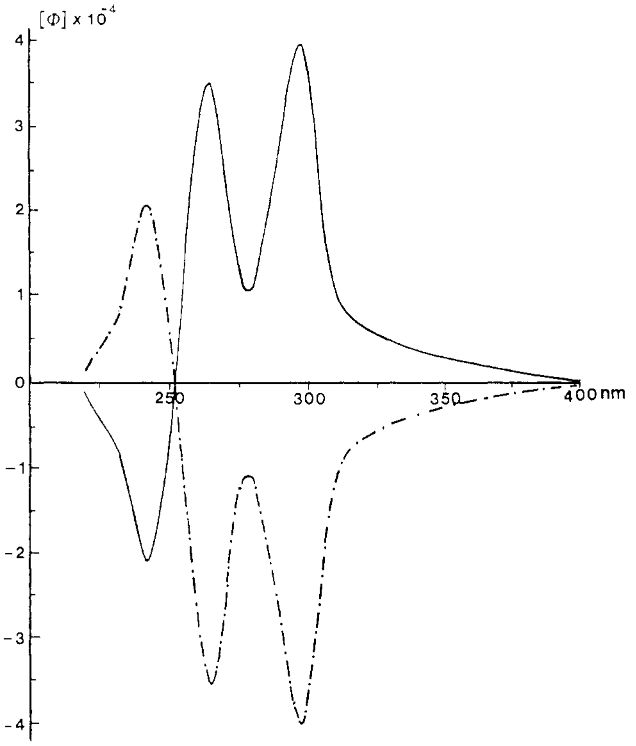


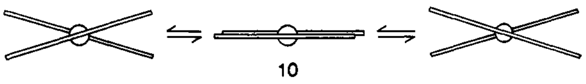
Figure 1. CD curves for **6a** (–·–·) and **6b** (—) in THF.

yield. In a similar manner, the enantioisomer **6b** ($[\alpha]^{22}_D$ −690° (*c* 0.11, $CHCl_3$), mp 275–277 °C)[6-8] was obtained from **3** and **4b** via **5b** ($[\alpha]^{22}_D$ +9.0° (*c* 0.20, $CHCl_3$), mp 174–175 °C) in an overall yield 40%. It is noteworthy that both **6a** and **6b** exhibited the same physical properties in all respects except the sign of optical rotation. The CD curves for **6a** and **6b** are shown in Figure 1. The absolute configurations for the bifluorenylidene moiety in **6a** and **6b** were accordingly assigned to be *S* and *R*, respectively, in comparison with the CD curves of related systems.[9]

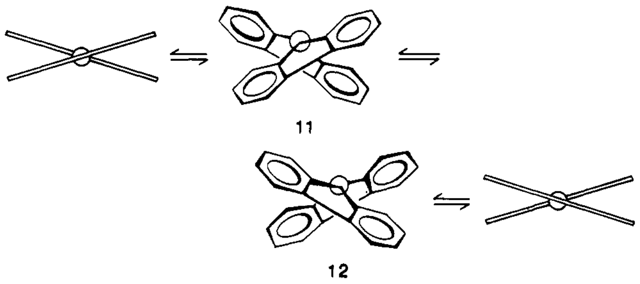
Reduction of **6a** and **6b** with $(i\text{-Bu})_2AlH$ (toluene, 0 °C) yielded quantitatively the optically inactive diol **7a**.[6,8] Base hydrolysis of **6a** and **6b** gave quantitatively the racemic diacid **7b**, which was esterified to yield methyl ester **7c**.[6,8] The *Z* configuration of **7** was established on the basis of the NOE experiments. In addition, treatment of **7b** with 1,4-dibromobutane under phase-transfer conditions (K_2CO_3, Bu_4NBr, DMF, 60 °C, 48 h) afforded **8**[6,8] in 29% yield.

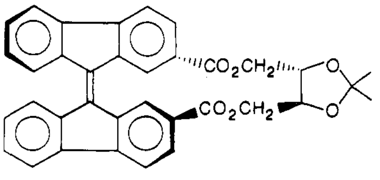
The fact that none of these products **7a–c** and **8** exhibited any optical rotation is striking. Apparently, rapid racemization would cause such observation. In other words, the bridging moiety in **6a** and **6b** might be rigid and, therefore, prohibit the interconversion of bifluorenylidene moieties leading to their diastereoisomers **6a′** and **6b′**, respectively.

Scheme I

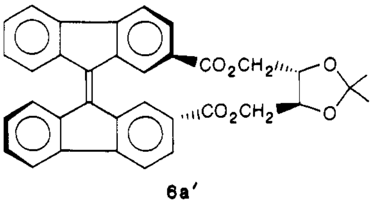


Scheme II

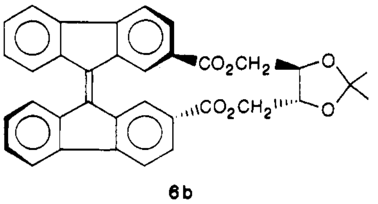




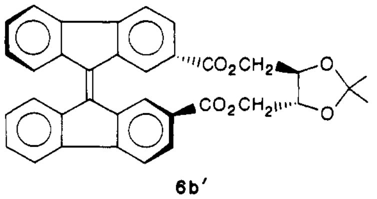
6a



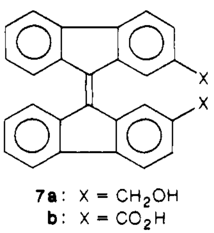
6a′



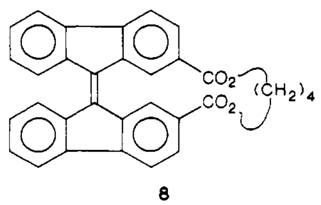
6b



6b′



7a: X = CH_2OH
b: X = CO_2H
c: X = CO_2Me



8

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(7) The reaction was in fact stereospecific. The corresponding diastereoisomers **6a′** and **6b′** were not detected at all from these reactions.

(8) **6a** and **6b**: ^1H NMR ($CDCl_3$) δ 9.00 (s, 2 H, H_1, $H_{1'}$), 8.42 (d, *J* = 8 Hz, 2 H, H_8, $H_{8'}$), 8.16 (d, *J* = 8 Hz, 2 H, H_3, $H_{3'}$), 7.80 (d, *J* = 8 Hz, 2 H, H_4, $H_{4'}$), 7.74 (d, *J* = 8 Hz, 2 H, H_5, $H_{5'}$), 7.36 (dd, *J* = 8, 6.5 Hz, H_6, $H_{6'}$), 7.24 (dd, *J* = 6.5, 8 Hz, H_7, $H_{7'}$), 4.52 (m, 2 H), 4.30 (m, 4 H), 1.48 (s, 6 H); the signal at δ 4.30 became two multiplets at δ 4.02 and 4.50 at −60 °C; other signals remained unchanged at low temperature; ^{13}C NMR ($CDCl_3$) δ 166.1, 145.6, 141.0, 140.3, 138.9, 137.6, 131.7, 129.9, 128.3, 128.0, 127.4, 127.3, 120.8, 120.0, 111.4, 77.5, 64.0, 28.7. **7a**: ^1H NMR ($CDCl_3$) δ 8.55 (s, 2 H, H_1, $H_{1'}$), 8.41 (d, *J* = 8 Hz, 2 H, H_8, $H_{8'}$), 7.70 (d, *J* = 8 Hz, 2 H, H_4, $H_{4'}$), 7.65 (d, *J* = 8 Hz, 2 H, H_5, $H_{5'}$), 7.35 (t, *J* = 8 Hz, 2 H, H_6, $H_{6'}$), 7.23 (m, 4 H, H_3, $H_{3'}$, H_7, $H_{7'}$), 4.67 (s, 4 H). **7c**: ^1H NMR ($CDCl_3$) δ 9.05 (s, 2 H, H_1, $H_{1'}$), 8.35 (d, *J* = 8 Hz, 2 H,H_8, $H_{8'}$), 8.06 (d, *J* = 8 Hz, 2 H, H_3, $H_{3'}$), 7.80 (m, 4 H, H_4, $H_{4'}$, H_5, $H_{5'}$), 7.41 (dd, *J* = 8, 6.5 Hz, H_6, $H_{6'}$), 7.34 (dd, *J* = 6.5, 8 Hz, H_7, $H_{7'}$), 3.90 (s, 6 H, Me). **8**: ^1H NMR ($CDCl_3$) δ 9.14 (d, *J* = 2 Hz, 2 H, H_1, $H_{1'}$), 8.44 (d, *J* = 8 Hz, 2 H, H_8, $H_{8'}$), 8.14 (dd, *J* = 2, 8 Hz, 2 H, H_3, $H_{3'}$), 7.82 (d, *J* = 8 Hz, 2 H, H_4, $H_{4'}$), 7.76 (d, *J* = 8 Hz, 2 H, H_5, $H_{5'}$), 7.38 (t, *J* = 8 Hz, H_6, $H_{6'}$), 7.24 (t, *J* = 8 Hz, H_7, $H_{7'}$), 4.35 (m, 4 H), 1.87 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 166.9, 145.4, 140.6, 139.1, 137.8, 131.4, 129.8, 129.3, 127.9, 127.7, 127.4, 120.7, 119.8, 63.8, 24.9. **9**: ^{13}C NMR ($CDCl_3$) δ 166.3, 145.5, 141.1, 140.6, 139.0, 137.7, 131.4, 129.9, 128.9, 128.3, 128.0, 127.4, 120.8, 120.0, 79.0, 61.6, 58.7.

(9) (a) Wynberg, H.; Feringa, B. *J. Am. Chem. Soc.* **1977**, *99*, 602. (b) Feringa, B.; Wynberg, H. *Recl. Trav. Chim. Pay-Bays* **1978**, *97*, 249. (c) Meurer, K. P.; Vögtle, F. *Top. Curr. Chem.* **1985**, *127*, 1.

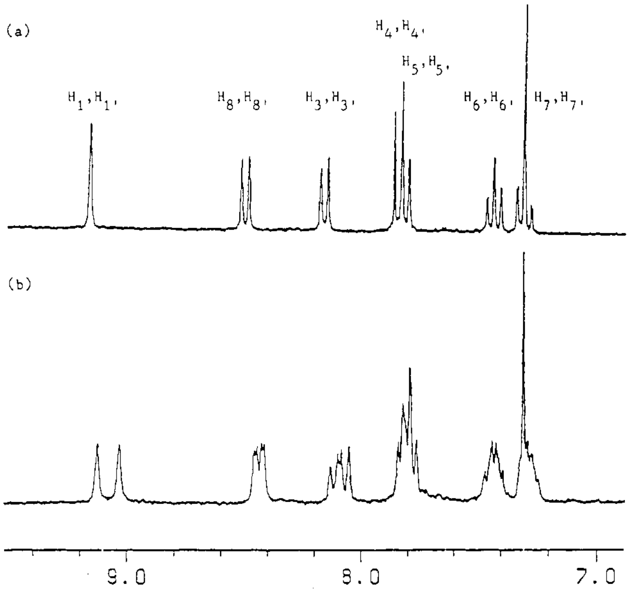
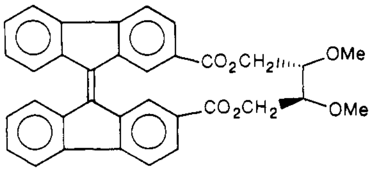
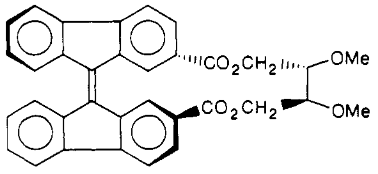


Figure 2. The partial ^{1}H NMR spectra of **9** at (a) 20 °C and (b) −60 °C. The singlet at δ 7.26 in both spectra is due to residual CHCl$_3$ absorption. Other signals: (a) (20 °C) 4.40–4.60 (br m, 4 H), 3.70–3.80 (br m, 2 H), 3.49 (s, 6 H); (b) (−60 °C) 5.05 (m, 1 H), 4.82 (m, 1 H), 4.15 (m, 1 H), 4.05 (m, 1 H), 3.79 (m, 1 H), 3.55 (m, including a singlet at 3.56, 4 H), 3.44 (s, 3 H).

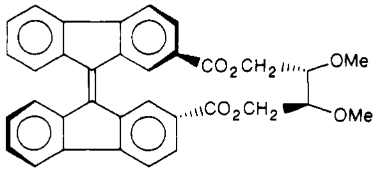
In order to clarify this point, we synthesized a less rigid chiral bridged bifluorenylidene **9** ($[\alpha]^{22}_D$ +7.3° (c 0.19, CHCl$_3$), mp 265–285 °C)[6,8] from **3** in 30% yield by the usual manner.[10] It is important to note that **9** exhibited only one set of NMR absorptions at ambient temperature but two sets of signals at low temperature (Figure 2).[11] The coalescent temperature was −20 °C, which corresponds to a barrier[12] of 12 kcal/mol. These results clearly demonstrate that **9** consisted of a pair of diastereoisomers **9a** and **9b** which underwent rapid equilibrium. The wide range of the melting point of **9** further supports such fast interconversion.



9



9a



9b

The mechanism for the racemization of bifluorenylidenes is interesting. Direct interconversion via a planar bifluorenylidene transition state **10** (Scheme I) seems unlikely since the steric interaction between hydrogens at C$_1$ and C$_{1'}$ and between hydrogens at C$_8$ and C$_{8'}$ in **10** would be severe and the barrier should be much higher[3c] than that obtained in this investigation. Alternatively, pyramidalization[13] at C$_9$ and/or C$_{9'}$ might occur to give **11**, which might undergo rapid twist along the C$_9$–C$_{9'}$ bond to yield **12** followed by "depyramidalization" to afford the inversion product (Scheme II). The barrier for such an interconversion might be expected to be lower than that depicted in Scheme I.

In summary, we have demonstrated the first enantioselective synthesis of bifluorenylidenes and the activation barrier for the racemization of one such bifluorenylidene. Our results indicate that bifluorenylidene molecules could be chiral in rigid systems.

Acknowledgment. We thank the Croucher Foundation for generous support and X.W. thanks Beijing–Hong Kong Academic Exchange Centre for financial aid. Thanks are also due to Professor L.-X. Dai for the arrangement to measure CD curves and to Professor J. Sandström for helpful discussion.

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(10) Treatment of **3** with **4c** (K$_2$CO$_3$, Bu$_4$NBr, DMF, 60 °C) yielded **5c** (90%, mp 202–204 °C, $[\alpha]^{22}_D$ +1.6° (c 0.38, CHCl$_3$)). Desulfurdimerization of **5c** with W(CO)$_6$ (4 equiv) afforded **9** (33%).

(11) It is noted that the chemical shifts were slightly different at different temperatures. The signals between δ 9.0 and 9.2 were employed for the coalescent study.

(12) Atta-ur-Rahman *Nuclear Magnetic Resonance: Basic Principles*; Springer Verlag: New York, 1986; p 133.

(13) (a) Khan, A. Z.-Q.; Sandström, J. *J. Am. Chem. Soc.* **1988**, *110*, 4843 and references therein. (b) Sakurai, H.; Ebata, K.; Sakamoto, K.; Nakadaira, Y.; Kabuto, C. *Chem. Lett.* **1988**, 965.

(14) On leave from the Institute of Chemistry, Academia Sinica, Beijing.

General Methods for Alkaloid Synthesis via Intramolecular Diels–Alder Reactions. A Concise Formal Total Synthesis of (±)-Dendrobine

Summary: The tricyclic enone **2**, which previously served as a key intermediate in the total synthesis of (±)-dendrobine (**1**), has been prepared by a novel strategy that features the stereoselective, intramolecular Diels–Alder cycloaddition of the olefinic dienamide **13** to give **14**; several model studies related to this cyclization were performed.

Sir: The ornamental orchid "Jinchai Shihu" (*Dendrobium nobile* LINDL.) has been employed in traditional herbal

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