Preparation and Conformational Properties of 1,8-Bridged Fluorenophanes

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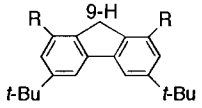
Novel 1,8-bridged fluorenophanes consisting of benzene, benzoquinone, or naphthalene ring have been prepared. Their conformational properties are clarified by the NMR spectra and the X-ray analysis, especially in terms of a shielding effect on 9-protons of the fluorene unit. The dynamic structure was also examined by the variable-temperature NMR spectroscopy.

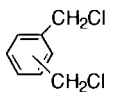
Cyclophanes are cyclic compounds consisting of aromatic units. Various aromatic components have been employed in the cyclophane skeleton.[1] Considerable attention has been paid to what components can be introduced since unique properties of cyclophanes based on their strained structure and specific π-electronic interaction are much dependent on the components. It is of interest to examine the property of a fluorene unit existing in cyclophane system because of its aromatic nature and acidic protons. To the best of our knowledge, however, [2.2](2,7) fluorenophane is the only example[2] to have been investigated so far. This must be due to difficulties in introducing a functional group into sites other than the 2- and 7-positions of the fluorene by electrophilic reactions. In previous works[3] we found out that a chloromethyl group can be introduced into the 1- and 8-positions of fluorene by treatment with chloromethyl methyl ether in the presence of an appropriate Lewis acid. This chloromethylated fluorene should be a potential precursor[4] for the synthesis of fluorenophane compounds.

Thus, we describe here the synthesis of novel 1,8-bridged fluorenophanes and their conformational properties.

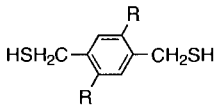
Treatment of **1a** with chrolomethyl methyl ether in the presence of $TiCl_4$ gave **1b** in 68% yield. **1b** was reacted with thiourea in DMSO to afford **1c** in 89% yield. Cyclization of **1c** and **2a-b**, or **1b** and **3a-b**[5] using CsOH as a base under highly



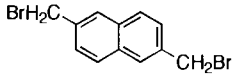
1a; R=H
1b; R=CH_2Cl
1c; R=CH_2SH
1d; R=CH_3



2a; ortho
2b; meta



3a; R=H
3b; R=OCH_3



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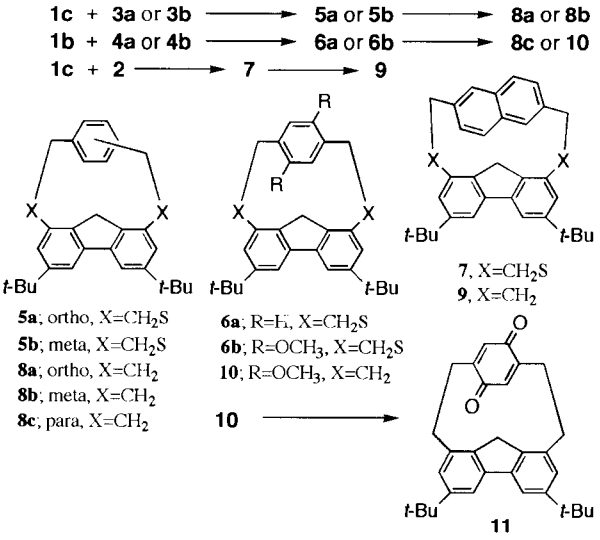
dilute conditions afforded the corresponding dithiafluorenophanes (**5a-b**, **6a-b**) in 65-85% yields. The dithiafluorenophane **7** was prepared by the coupling of **1c** and **4**[6] in 58% yield. After oxidation of **5a-b** and **6a** with MCPBA, pyrolysis was carried out in order to obtain the fluorenophanes **8a-c**. However, all attempts to prepare **8a** resulted in failure, and in most cases a small amount of **1d** was isolated. This may be due to the strained structure of **8a** because of the bridges connecting to the ortho positions. On the other hand in the cases of **5b** and **6a** the desired fluorenophanes **8b** and **8c** were obtained in 24% and 40% yields,



respectively. The compound **7** was transformed into the fluorenophane **9** by oxidation, followed by pyrolysis in 35% yield. The fluoreno-phane **10** was prepared from **6b** similarly to **8c**, then oxidized with CAN to give the fluorenophane **11** in 47% yield.

Table 1. Chemical shifts[a] of 9-protons of fluorenophanes

Compound	9-proton (δ / ppm)	Compound	9-proton (δ / ppm)
1a	3.95(s)	**8c**	0.00(d, J=20Hz)
5a	3.26(s)		2.38(d, J=20Hz)
5b	2.76(brs)	**9**	-0.69(d, J=21Hz)
6a	2.37(s)		2.11(d, J=21Hz)
6b	2.60(s)	**10**	0.53(d, J=20Hz)
7	1.57(s)		2.57(d, J=20Hz)
8b	3.12(d, J=19Hz)	**11**	3.41(d, J=20Hz)
	3.54(d, J=19Hz)		3.68(d, J=20Hz)

[a]In $CDCl_3$ at 27 °C.

Signals of the CH_2 bridge (9-protons) in the ^1H NMR spectra reflect a conformational process of the fluorenophanes. The chemical shifts of 9-protons in the fluorenophanes are summarized together with **1a** in Table 1.

The 9-protons in the dithiafluorenophanes are observed as a singlet, indicating that flipping of the aromatic component is fast at room temperature on the NMR time-scale. The upfield shifts of 9-protons in **6a** and **6b** from the position at δ 3.95 in **1a** could be due to the conformation in which these protons exist in the shielding region of the benzene ring. However, such a shielding effect is not observed in **5a**, since flipping of the benzene ring has little effect on the fluorene unit. On the contrary slow flipping

must occur in **5b** because the 9-protons appear as a broad singlet. Naphthalene ring could offer stronger shielding effect than a benzene ring as clearly indicated by the shielded 9-protons at δ 1.57 in **7**.

The variable-temperature NMR technique was employed to examine the dynamic process. For example, as the temperature is lowered the signal of 9-protons in **5b** splits into two doublets at -90 ℃ through a coalescence point at -30 ℃. From these results the barrier at the coalescence temperature was estimated to be 40.9 kJ/mol. The data of such a dynamic process for other dithiafluorenophanes are also summarized in Table 2. The 9-protons of **5a** appear as a sharp singlet down to -80 ℃, and hence flipping in this system is fast. Both **6a** and **7** coalesce at -50 ℃. Thus, the dithiabenzofluorenophanes seem to assume more flexible conformation in order of meta-, para-, and ortho derivatives.

Table 2. Dynamic process of fluorenophanes

Compound	Tc / °C	$\Delta G^{\neq}$ / kJ mol^{-1}
5a	< -80	-
5b	-30	40.9
6a	-50	38.5
7	-50	39.1

In contrast there were no obvious changes in the NMR signals for the fluorenes (**8a-c**, **9**) even at 150 ℃, suggesting that they have rigid structures. As shown in Table 1 two doublets for 9-protons can be seen in the fluorenophanes. One of them in **8c**, **9**, and **10** is subject to large upfield shift, which is caused by the shielding of the opposite benzene ring. The difference in this shielding effect is likely dependent on conformational geometries and the electronic nature of the aromatic component. For example one of the 9-protons in **8c** seems to direct toward the aromatic ring and hence appears more shielded at δ 0.00 than that in **10**.

The X-ray analysis of **8c**[7] strongly supports the plausible geometry in which the aromatic ring is located right upon the 9-protons (Figure 1). On the other hand it can be considered that **8b** exists in the folded conformation in which 9-protons are not located in the cavity of the π-cloud of the aromatic ring. This is in fairly good agreement with the result of the X-ray analysis of **8b**[8] as shown in Figure 2.

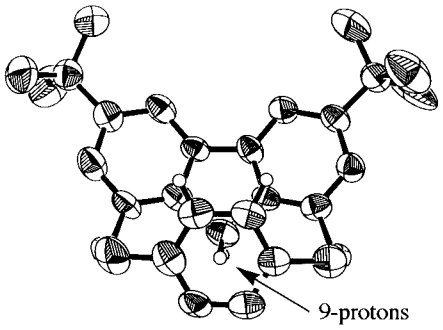


Figure 1. Perspective view of **8c**.

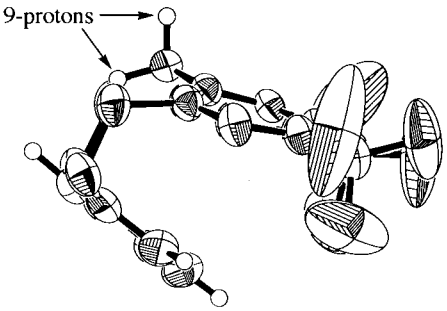


Figure 2. Perspective view of **8b**.

The effect of the electronic nature of the aromatic ring on the 9-protons by a through-space interaction is also interesting. No upfield shift of the 9-protons in **11** was observed, which can be explained by through-space electronic effect of the benzoquinone. One of the 9-protons in **9** appears at δ -0.69 in extremely upfield region as a result of the strong shielded effect of the naphthalene ring.

The investigation of anionic derivatives of 1,8-bridged fluorenophanes is in progress.

References and Notes

1 For example, see: F. Vögtle, "Supramolecular Chemistry," Weiley, Chichester, (1989); F. Diederich, "Cyclophanes," The Royal Society of Chemistry, Cambridge, (1991); F. Vögtle, "Cyclophane Chemistry," Weiley, Chichester, (1989).
2 M. W. Haenel, *Tetrahedron Lett.*, **1976**, 3121; **1997**, 1273.
3 A. Tsuge, T. Yamasaki, T. Moriguchi, T. Matsuda, Y Nagano, H. Nago, S. Mataka, S. Kajigaeshi, and M. Tashiro, *Synthesis*, **1993**, 205.
4 A. Tsuge, Y. Ueda, T. Araki, T. Moriguchi, K. Sakata, K. Koya, S. Mataka, and M. Tashiro, *J.Chem.Res(S).*, **1997**, 168.
5 M. Tashiro, K. Koya, and T. Yamato, *J.Am.Chem.Soc.*, **105**, 6650 (1983).
6 Reduction of 2,6-naphthalenedicarboxylic acid dimethyl ester with $LiAlH_4$, followed by treatment with PBr_3 gave **4** in 72 % yield.
7 Crystal Data for **8c**: $C_{31}H_{36}$, M=408.63, monoclinic, space group $P2_1/a$(No.14), a=19.316(5), b=5.814(5), c=23.176(4) Å, β=109.80(1)°, V=2449(2) Å^3, Z=4, D_{calc}=1.108 g/cm^3, μ(CuKα)=4.59 cm^{-1}, Rigaku AFC7R diffractometer, 1890 reflections with $I>3.00\sigma(I)$, R=0.090, R_w=0.071.
8 Crystal Data for **8b**: $C_{31}H_{36}$, M=408.63, monoclinic, space group $P2_1/a$(No.14), a=11.203(2), b=18.397(2), c=12.538(1) Å, β=106.14(1)°, V=2482.2(5) Å^3, Z=4, D_{calc}=1.093 g/cm^3, μ(CuKα)=4.53 cm^{-1}, Rigaku AFC7R diffractometer, 3226 reflections with $I>3.00\sigma(I)$, R=0.081, R_w=0.075.