Synthesis and Structure of Novel 1,8-Bridged Fluorenophanes†

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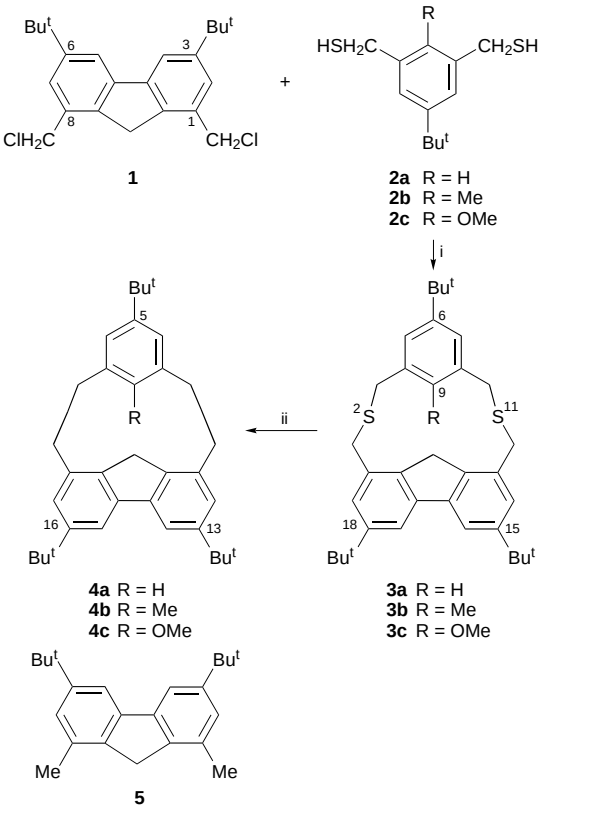
Akihiko Tsuge,*[a] Yasuhiro Ueda,[a] Tadashi Araki[a] Tetsuji Moriguchi,[a] Kazunori Sakata,[a] Keizo Koya,[b] Shuntaro Mataka[b] and Masashi Tashiro[b]

[a]*Department of Chemistry, Kyushu Institute of Technology, Tobata-ku, Kitakyushu 804, Japan*
[b]*Institute of Advance Material Study, Kyushu University, Kasuga, Fukuoka 816, Japan*

A novel 1,8-bridged fluorenophane (**4a**) is found to assume an 'inward-folded' conformation with the bulky *tert*-butyl group located in the cavity, a situation which is different from the conformation of the corresponding dithiafluorenophane (**3a**).

Cyclophanes are cyclic compounds consisting of aromatic units. Many aromatic components have been used in the cyclophane skeleton.[1] Considerable attention has been paid to particular properties of the components, because of the strained structure of the ring system and its ability to form π-electronic interactions. It is of interest to examine the properties of a fluorene unit in cyclophane compounds, because of its aromatic nature and acidic proton. To the best of our knowledge, however, [2.2](2,7)fluorenophane is the only example[2] to have been investigated so far. This is due to difficulties in introducing a functional group into sites other than the 2- and 7-positions by electrophilic reactions. In previous work[3] we found that a chloromethyl group can be introduced into the 1,8-positions of the fluorene molecule by treatment with chloromethyl methyl ether in the presence of an appropriate Lewis acid. This chloromethylated fluorene should be a precursor for the synthesis of fluorenophane compounds. Thus, we describe here the synthesis of novel 1,8-bridged fluorenophanes and their conformational properties.

Treatment of 3,6-di-*tert*-butylated fluorenophane with chloromethyl methyl ether in the presence of $TiCl_4$ gave the 1,8-bis(chloromethyl)fluorene **1** in 58% yield. Bromination of 4-*tert*-butyl-*m*-xylene with *N*-bromosuccinimide (NBS), followed by treatment with thiourea afforded the bis(thiol) **2a**. Compounds **2b** and **2c** were obtained according to reported methods.[4] Cyclization of **1** and **2a–c** using CsOH as a base under highly dilute conditions afforded the corresponding dithiafluorenophanes (**3a–c**) in 72–84% yields (Scheme 1).



Scheme 1 *Reagents and conditions:* i, CsOH, EtOH;; ii, MCPBA, then 500 °C, 2 Torr

The ^{1}H NMR spectra of **3a–c** are summarized in Table 1. Signals for the CH_2 bridge reflect the dynamic behaviour of the dithiafluorenophane. The C-9 hydrogens of **3a** show a broad singlet, indicating that inversion of the ring at room temperature is slow on the NMR time-scale. In contrast, a pair of doublets with a separation of 22 Hz was observed in the spectra of **3b** and **3c**. These results strongly suggest that the barrier to inversion in dithiafluorenophanes depends on the bulkiness of the inner substituent (R).

In order to determine for **3a** the coalescence temperature and the free energy of activation for inversion, the temperature-dependent ^{1}H NMR technique was employed. The measured barrier for the observed dynamic process is 11.54 kcal mol^{-1} at -15 °C in $CDCl_3$.‡

In contrast, there were no changes in the NMR signals for **3b** or **3c**, even at 150 °C in [$^2H_6$]Me_2SO, indicating that **3b** and **3c** have rigid structures.

We have already prepared various metacyclophanes consisting of three aromatic rings and confirmed their 'inward-folded' conformation, which is characterized by one aromatic ring being folded into the cavity produced by the other two aromatic rings.[5]

Taking into account these results and the chemical shifts of the *tert*-butyl protons, it may be deduced that the dithiafluorenophanes **3a–c** assume a conformation in which the substituent R of the benzene ring is accommodated inside the cavity. After oxidation of **3a–c** with *m*-chloroperbenzoic acid (MCPBA), pyrolysis was carried out in order to obtain the fluorenophanes **4a–c** (Scheme 1). However, in spite of repeated trials, all attempts to prepare **4b** and **4c** resulted in failure, in most cases only the dimethyl compound **5** being isolated from very complex mixtures. In contrast, in the case of **3a** the desired fluorenophane **4a** was obtained in 29% yield. This is certainly due to steric hindrance of the substituent R during recombination of radical intermediates in pyrolysis: even when hydrogen was the substituent, the yield was not good.

Data for the ^{1}H NMR spectrum of **4a** are also shown in Table 1. In **4a** it is noted that the protons of the *tert*-butyl group attached to the benzene ring show an unexpectedly upfield shift, suggesting a conformation in which the *tert*-butyl group is located in the cavity formed by the π-cloud of the fluorene ring. This is in fairly good agreement with a considerable upfield shift of the aromatic protons adjacent to

*To receive any correspondence (*e-mail*: tsuge@che.kyutech.ac.jp).
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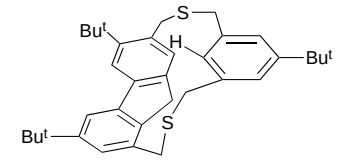
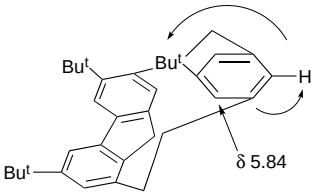
‡1 cal = 4.184 J.

Table 1 ^{1}H NMR spectra of fluorenophanes [δ values ($CDCl_3$)]

Compound	Bu^t	R	9-H
1	1.41 (18 H)		3.95 (s)
3a	1.33 (9 H) 1.37 (18 H)	7.09 (Ar-H)	2.69 (br s)
3b	1.32 (9 H) 1.36 (18 H)	2.39 (CH_3)	1.89 (d, *J* 22 Hz) 2.90 (d, *J* 22 Hz)
3c	1.32 (9 H) 1.36 (18 H)	3.86 (OCH_3)	2.03 (d, *J* 22 Hz) 3.20 (d, *J* 22 Hz)
4a	0.69 (9 H) 1.37 (18 H)	7.09 (Ar-H)	3.07 (d, *J* 19 Hz) 3.80 (d, *J* 19 Hz)



3a



4a

Scheme 2

the *tert*-butyl group. Inversion of one aromatic ring occurs during the transformation into a smaller cyclic system (Scheme 2).

Further investigations of other types of 1,8-bridged fluorenophanes are in progress.

Experimental

All melting points are uncorrected. ^{1}H NMR spectra were recorded at 500 MHz on a Nippon Denshi JEOL α-500 spectrometer in $CDCl_3$ with Me_4Si as an internal reference. Mass spectra were obtained on a Nippon Denshi JEOL DX-300 spectrometer at 75 eV using a direct-inlet system. Elemental analyses were carried out on a Yanaco MT-3 spectrometer. Column chromatography was performed on silica gel (Wako gel, C-300).

(3-tert-*Butyl*-5-*sulfanylmethylphenyl*)*methanethiol* **2a**.—A solution of 1,3-bis(bromomethyl)-5-*tert*-butylbenzene (30 g, 93 mmol) and thiourea (18.0 g, 0.24 mol) in DMSO (450 ml) was stirred at room tempearture for 15 h under an argon stream. After the reaction mixture had been poured into cold 10% aqueous NaOH (500 ml) and acidified with 10% hydrochloric acid, it was extracted with CH_2Cl_2. The extract was washed with water, dried over $MgSO_4$, and evaporated *in vacuo* to leave a residue which was distilled to afford the *bis*(*thiol*) **2a** (16.5 g, 79%) as a colourless liquid, bp 140–145 °C at 2 Torr (Found: C, 63.86; H, 8.13. $C_{12}H_{18}S_2$ requires C, 63.65; H, 8.03%); *m*/*z* 226 (M^+); δ_H 1.31 (9 H, s), 1.75 (2 H, t, *J* 8 Hz), 3.70 (4 H, d, *J* 8 Hz), 7.12 (1 H, s), 7.19 (2 H, s).

Dithiafluorenophanes **3**. *General Procedure: Preparation of* 6,15,18-*tri*-tert-*butyl*-2,11-*dithia*[3]*metacyclo*[3](1,8)*fluorenophane* **3a**.—A solution of **1**[3] (1.09 g, 2.9 mmol) and **2a** (0.70 g, 3.1 mmol) in EtOH–benzene (1:1; 300 ml) was added dropwise from a Hershberg funnel with stirring to a solution of CsOH (1.21 g, 8.07 mmol) and $NaBH_4$ (0.12 g, 3.2 mmol) in EtOH (2 l) for 1 h. After solvents had been evaporated, the residue was extracted with CH_2Cl_2. The extract was washed with water, dried over $MgSO_4$, and evaporated *in vacuo* to give **3a** (1.22 g, 79%) as colourless *prisms*, mp 234–235 °C (from hexane) (Found: C, 79.32; H, 8.41. $C_{35}H_{44}S_2$ requires C, 79.47; H, 8.40%); *m*/*z* 528 (M^+); δ_H 1.34 (9 H, s), 1.38 (18 H, s), 2.70 (2 H, br s), 3.70 (4 H, s), 3.74 (4 H, s), 7.17 (2 H, d, *J* 1.5 Hz), 7.19 (2 H, s), 7.45 (1 H, s), 7.62 (2 H, d, *J* 1.5 Hz).

6,15,18-*Tri*-tert-*butyl*-2,11-*dithia*[3]*metacyclo*[3](1,8)*fluorenophane* **3b**.—**3b** was obtained according to the general procedure. Thus **1**[3] (0.53 g, 1.41 mmol) and **2b**[4] (0.35 g, 1.46 mmol) gave **3b** (0.64 g, 84%) as colourless *prisms*, mp 189–191 °C (from hexane) (Found: C, 79.83; H, 8.49. $C_{36}H_{46}S_2$ requires C, 79.63; H, 8.56%); *m*/*z* 542 (M^+); δ_H 1.32 (9 H, s), 1.36 (18 H, s), 1.90 (1 H, d, *J* 22 Hz), 2.39 (3 H, s), 2.90 (1 H, d, *J* 22 Hz), 3.48 (2 H, d, *J* 12 Hz), 3.74 (2 H, d, *J* 14 Hz), 3.95 (2 H, d, *J* 14 Hz), 3.99 (2 H, d, *J* 12 Hz), 7.14 (2 H, s), 7.15 (2 H, d, *J* 1.5 Hz), 7.61 (2 H, d, *J* 1.5 Hz).

6,15,18-*Tri*-tert-*butyl*-9-*methoxy*-2,11-*dithia*[3]*metacyclo*[3]-(1,8)*fluorenophane* **3c**.—**3c** was obtained according to the general procedure. Thus **1**[3] (0.32 g, 0.85 mmol) and **2c**[4] (0.23 g, 0.90 mmol) gave **3c** (0.34 g, 72%) as colourless *prisms*, mp 191–193 °C (from hexane) (Found: C, 77.58; H, 8.50. $C_{36}H_{46}S_2O$ requires C, 77.35; H, 8.31%); *m*/*z* 558 (M^+); δ_H 1.32 (9 H, s), 1.35 (18 H, s), 2.03 (1 H, d, *J* 22 Hz), 3.21 (1 H, d, *J* 22 Hz), 3.51 (2 H, d, *J* 12 Hz), 3.60 (2 H, d, *J* 14 Hz), 3.86 (3 H, s), 3.93 (2 H, d, *J* 14 Hz), 3.99 (2 H, d, *J* 12 Hz), 7.13 (2 H, d, *J* 1.5 Hz), 7.18 (2 H, s), 7.58 (2 H, d, *J* 1.5 Hz).

5,13,16-*Tri*-tert-*butyl*[2]*metacyclo*[2](1,8)*fluorenophane* **4a**.—The sulfone derivative of **3a** (0.52 g, 0.88 mmol) was pyrolysed at 500 °C under reduced pressure (2 Torr) in a horizontal quartz tube. The resultant product was chromatographed with hexane as an eluent to afford **4a** (0.12 g, 29%) from the first fraction as colourless *needles*, mp 296–298 °C (from hexane) (Found: C, 90.16; H, 9.66. $C_{35}H_{44}$ requires C, 90.44; H, 9.54%); *m*/*z* 464 (M^+); δ_H 0.69 (9 H, s), 1.37 (18 H, s), 2.93–3.86 (8 H, m), 3.07 (1 H, d, *J* 19 Hz), 3.80 (1 H, d, *J* 19 Hz), 5.83 (2 H, s), 6.91 (2 H, d, *J* 1.5 Hz), 7.09 (1 H, s), 7.23 (2 H, d, *J* 1.5 Hz).

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