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# SYNTHESES OF [2.2](2,6,2',7')NAPHTHALENOPHANE AND [2.2](2,6,2',7')NAPHTHALENOPHANE-1, 11-DIENE AND A STUDY OF THEIR CONFORMATIONAL FLIPPING

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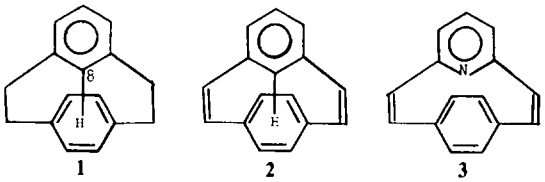
**Abstract**—Syntheses of [2.2](2,6,2',7')naphthalenophane and its corresponding diene have been accomplished by standard procedures from 2,13-dithia[3.3](2,6,2',7')naphthalenophane. The transition state for conformational flipping of [2.2](2,6,2',7')naphthalenophane requires the two naphthalene rings to become perpendicular to each other with insertion of the 1- and 8-hydrogens of one naphthalene ring into the cavity of the $\pi$-electron cloud of the other naphthalene ring. The kinetic parameters for the conformational flipping process have been measured by a selective pulse Fourier transform NMR technique.

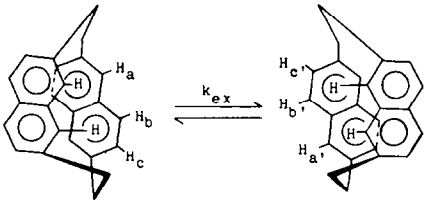
In a previous study of the conformational flipping of [2.2]metaparacyclophane(**1**) and its various derivatives,[1] it was shown that the barrier to conformational flipping in the parent compound was 20·8 kcal/mol and that the rate of conformational flipping was extremely sensitive to isotopic substitution ($k_D/k_H = 1{\cdot}20$) of the 8-hydrogen which, in the transition state, must impinge into the $\pi$-electron cloud of the *para*-bridged ring. Further, remote substituents of differing electron attraction in the *meta*-bridged ring had marked effect on the rate of conformational flipping. The extreme sensitivity of this system to slight alterations of bond angles and bond distance was shown by the fact that [2.2]metaparacyclophane-1,9-diene (**2**) undergoes conformational flipping with extreme ease, having an energy barrier of only 8·3 kcal/mol.[2] Finally, the corresponding pyridine derivative **3** has the two aromatic rings perpendicular to each other in the crystalline state, as shown by X-ray analysis.[3,4]




1 2 3

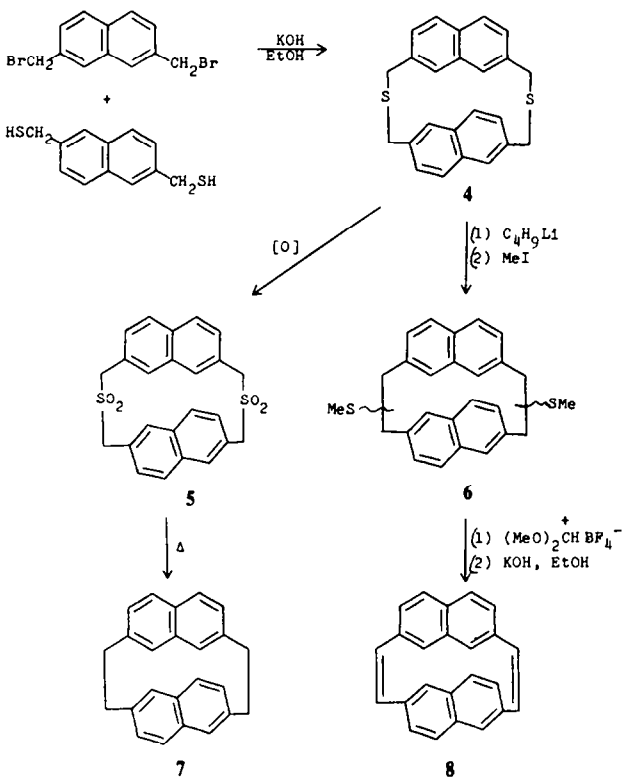
Clearly, the examination of conformational flipping rates provides an extremely sensitive test for the steric interaction of aromatic $\pi$-electron clouds. In an attempt to extend this type of probing of the behavior of aromatic $\pi$-electron clouds, we have now synthesized the two naphthalene derivatives, **7** and **8**, and have studied their rates of conformational flipping. The syntheses followed in a straight-forward fashion from methods we have reported earlier for the syntheses of cyclophanes and cyclophane-dienes,[1,5,6] and is outlined in Scheme 1. The reaction conditions and yields obtained are fairly analogous to those reported by Haenel and Staab for the closely related [2.2](2,6)naphthalenophane series.[7]

From an examination of molecular models, the conformational flipping of [2.2](2,6,2',7')naphthaleneophane (**7**) would appear to involve a movement of the 2,7-bridged naphthalene from a coplanar orientation through perpendicularity to the opposite coplanar orientation. In the perpendicular transition state the 1- and 8-hydrogens of the 2,7-bridged naphthalene are forced into the aromatic $\pi$-electron cloud of the 2,6-bridged naphthalene. This is illustrated below.




In contrast to [2.2]metaparacyclophane (**1**), one might expect that the naphthalene derivative **7**, where two hydrogens impinge into an aromatic $\pi$-electron cloud during conformational flipping, would have a much higher energy barrier to flipping. In fact, an obvious prediction would be no conformational flipping. On the other hand, the sensitivity of the conformational flipping process to small changes in bond angles and bond distances, as seen in the case of **2**, might suggest that the larger size of the bridges in the naphthalene series would offer more opportunity for relief of strain by incremental small changes in bond angles and bond distances. Thus, the two obvious effects that characterize the naphthalene series, as compared to the [2.2]metaparacyclophanes, would be predicted to operate in opposing directions and it was the interest in determining the net balance of these two effects that prompted the present study.

In the process of conformational flipping, it is apparent that exchange occurs between the aromatic protons under the 2,7-bridged naphthalene and those aromatic protons opposite and away from the 2,7-bridged naphthalene. Thus, any one of the three sets of aromatic protons undergoing exchange could be used for a kinetic analysis of the conformational flipping rate. In our study of the conformational flipping of [2.2]metaparacyclophane derivatives, a kinetic analysis of proton exchange was made by a continuous-wave, double-irradiation NMR technique devised by Forsen and Hoffman.[8] Recently, though, Dahlquist, Longmuir and DuVernet have introduced a selective-pulse, Fourier-transform NMR method for kinetic analysis of chemical exchange processes.[9] The selective pulse method has marked advantages in convenience and in allowing the determination of both the




Scheme 1.

longitudinal relaxation time and the exchange rate constant in a single experiment. The selective pulse method was employed, therefore, for kinetic analysis of the conformational flipping of [2.2](2,6,2',7')naphthalenophane (**7**).

First of all, it was shown that the NMR spectrum of **7** was temperature dependent, having a coalescence temperature of 160°C using a 100-MHZ instrument. Measurements of the exchange rate were made at three temperatures and are summarized in Table 1. From the exchange rate constants at these three temperatures have been calculated $\Delta H^{\ddagger} = 18{\cdot}8 \pm 0{\cdot}5$ kcal/mol; $\Delta S^{\ddagger} = -5{\cdot}6 \pm 1{\cdot}0$ eu; and $\Delta G^{\ddagger}_{25°} = 20{\cdot}6$ kcal/mol. These values are amazingly close to those ($\Delta H^{\ddagger} = 17{\cdot}0 \pm 0{\cdot}5$ kcal/mol, $\Delta S^{\ddagger} = -8{\cdot}8 \pm 2{\cdot}4$ eu, and $\Delta G^{\ddagger}_{25°} = 20{\cdot}8$ kcal/mol) found for [2.2]metaparacyclophane. Apparently, the changes in going from [2.2]metaparacyclophane to [2.2](2,6,2',7')-naphthalenophane result in opposing effects that almost exactly counterbalance each other.

Examination of the NMR spectrum of [2.2](2,6,2',7')naphthalenophane-1,11-diene (**8**) showed a symmetrical pattern, indicating that either the two naphthalene rings are perpendicular or conformational flipping is occurring so rapidly that the exchanging protons are equivalent. No change in the NMR spectrum of **8** was observed on lowering the temperature to −120°C, the limit experimentally available to us. Thus, for **8** it is clear that conformational flipping is easier than for the corresponding diene in the [2.2]metaparacyclophane series.[2] The conclusion from these experiments that seems apparent is that steric crowding of aromatic $\pi$-electron clouds is relieved more effectively by small, incremental changes in many bond angles and/or bond lengths than by larger such changes with fewer bonds.

## EXPERIMENTAL

2,13-*Dithia*[3.3](2,6,2',7')*naphthalenophane*, **4**. A soln of 2,7-bis(bromomethyl)naphthalene[10] (3·14 g; 0·01 mol) and 2,6-bis-(mercaptomethyl)naphthalene[7] (2·2 g; 0·01 mol) in 500 ml benzene was added dropwise with vigorous stirring over 72 hr to a soln of KOH (1·70 g) in 1 l 95% EtOH boiling under reflux. After concentration, chloroform and water were added. The organic layer was separated, dried and concentrated. The residual solid was taken up in chloroform and chromatographed over silica gel. From the main fraction of eluate there was isolated 2·5 g (67%) of white crystals; m.p. 230–231°; NMR ($CDCl_3$), a multiplet at $\tau$ 2·40–2·80 (10 H, ArH), a broad singlet at 4·18 (2 H, ArH), a singlet at 5·90 (4 H, –CH–S–) and a singlet at 6·22 (4 H, –CH–S–). (Found, C, 77·68; H, 5·48. Calc. for $C_{24}H_{20}S_2$: C, 77·40; H, 5·41%).

2,2,13,13 - *Tetraoxo* - 2,13 - *dithia*[3.3](2,6,2',7')-*naphthalenophane*, **5**. To a soln of **4** (65 mg) in 30 ml $CH_2Cl_2$

Table 1. Longitudinal relaxation times and ring-flipping rates

| Compd | Temp °C | $k_{ex}$ $sec^{-1}$ | $1/T \times 10^3$ $sec^{-1}$ |
|---|---|---|---|
| [2.2](2,6,2',7')Naph-thalenophane (7) | 60.7 ± 0.3 | 0.199 ± 0.005 | 2.995 ± 0.003 |
| | 71.2 ± 0.3 | 0.490 ± 0.01 | 2.905 ± 0.003 |
| | 81.7 ± 0.3 | 1.218 ± 0.04 | 2.818 ± 0.003 |

*m*-chloroperbenzoic acid 150 mg) was added in portions with shaking. When the addition was complete, the mixture was stirred overnight at room temp. After the mixture had been washed successively with dil. NaOH aq and water, it was dried and concentrated to give 40 mg (50%) of a white powder; m.p. > 400°; (mol wt: Found (High resolution mass spectrum): 436·079; Calc. for $C_{24}H_{20}S_2O_4$: 436·080).

[2.2](2,6,2',7')*Naphthalenophane*, **7**. In a pyrolysis flow system, modeled after that of Haenel and Staab,[11] **5** (40 mg) was placed. The first furnace was set at 350° with the second at 500°, and the flow rate was such that the pyrolysis was complete in 48 hr. On the cold finger, there collected 18 mg (65%) of white crystals; m.p. 170–172°; NMR ($CCl_2$=CClCCl=$CCl_2$), a multiplet at $\tau$ 2·20–3·10 (7 H, ArH), a multiplet at 3·62–4·00 (3 H, internal ArH), singlets at 4·16 and 4·48 (2 H, internal ArH), and a multiplet at 6·50–7·70 (8 H–Ar$CH_2$–); mass spectrum (70 eV), *m/e* at 308. (Found, C, 93·22; H, 6·53; Calc. for $C_{24}H_{20}$; C, 93·46; H, 6·54%).

[2.2](2,6,2',7')*Naphthalenophane*, **8**

(a) *Wittig rearrangement of* **4** *to give* **6**. To a soln of **4** (540 mg; 1·5 mmol) in 30 ml freshly-distilled THF *n*-BuLi (4 mmol) in hexane was added. After the mixture had been stirred for 20 min MeI (0·8 ml) was added, followed by 30 ml water. Extraction of the mixture with chloroform, followed by drying and concentration of the extract gave 600 mg (100%) of a yellow oil (mol wt: Found (high resolution mass spectrum) 400·132; Calc. for $C_{26}H_{24}S_2$: 400·133). The NMR spectrum of this oil was in accord with its being a mixture of stereoisomers corresponding to **6**.

(b) *Hofmann elimination to give* **8**. A soln of **6** (300 mg) in 10 ml $CH_2Cl_2$ was added with stirring to a suspension of dimethoxycarbonium fluoroborate[12] (324 mg) in 10 ml $CH_2Cl_2$ held at −78°. After the mixture had been stirred for 5 hr, EtOAc (20 ml) was added and the mixture was stirred an additional 4 hr. The crystalline ppt was collected, triturated with EtOAc, and dried to give 190 mg (50%) of a solid, which was used directly. To a soln of KOH (84 mg) in 30 ml ab EtOH the bis(methofluoroborate) salt (252 mg) was added. The resulting mixture was boiled under reflux for 14 hr. After concentration, the residue was taken up in benzene and washed successively with water, dilute aqueous acid and water. The resulting benzene extract was then dried and concentrated. The residual solid was taken up in hexane and chromatographed over silica gel. The main fraction of eluate gave 8 mg (6%) of white crystals; m.p. 247–248°; NMR ($CD_3COCD_3$), a doublet at $\tau$ 2·15 (4 H, ArH, $J_{a,b}$ = 8 Hz), a doublet of doublets at 2·70 (4 H ArH, $J_{a,b}$ = 8 Hz; $J_{b,c}$ = 1·7 Hz), a broad singlet at 2·84 (4 H, ArH), and a singlet at 3·28 (4 H, –CH=CH–); mass spectrum (70 eV), *m/e* 304. (Found: C, 94·70; H, 5·31; Calc. for $C_{24}H_{16}$: C, 94·70; H, 5·30%).

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## REFERENCES

[1]S. A. Sherrod, R. L. daCosta, R. A. Barnes and V. Boekelheide, *J. Am. Chem. Soc.* **96**, 1565 (1974).
[2]V. Boekelheide, P. H. Anderson and T. A. Hylton, *Ibid.* **96**, 1558 (1974).
[3]V. Boekelheide, K. Galuszko and K. S. Szeto, *Ibid.* **96**, 1578 (1974).
[4]L. H. Weaver and B. W. Mathews, *Ibid.* **96**, 1581 (1974).
[5]R. H. Mitchell and V. Boekelheide, *Ibid.* **96**, 1547 (1974).
[6]R. H. Mitchell, T. Otsubo and V. Boekelheide, *Tetrahedron Letters* 219 (1975).
[7]M. Haenel and H. Staab, *Chem. Ber.* **106**, 2203 (1973).
[8]S. Forseń and R. A. Hoffman, *Acta Chem. Scand.* **17**, 1787 (1963); *J. Chem. Phys.* **39**, 2892 (1963); **40**, 1189 (1964).
[9]F. W. Dahlquist, K. L. Longmuir and R. B. DuVernet, *J. Mag. Res.* **17**, 406 (1975).
[10]J. R. Davy and J. A. Reiss, *Tetrahedron Letters* 3639 (1972).
[11]M. Haenel and H. Staab, *Ibid.* 3585 (1970).
[12]R. F. Borch, *J. Org. Chem.* **34**, 627 (1969).