

## CONFORMATION OF DITHIA[3.3]- AND [2.2]AZULENO(2,6)PYRIDINOPHANES<sup>1)</sup>

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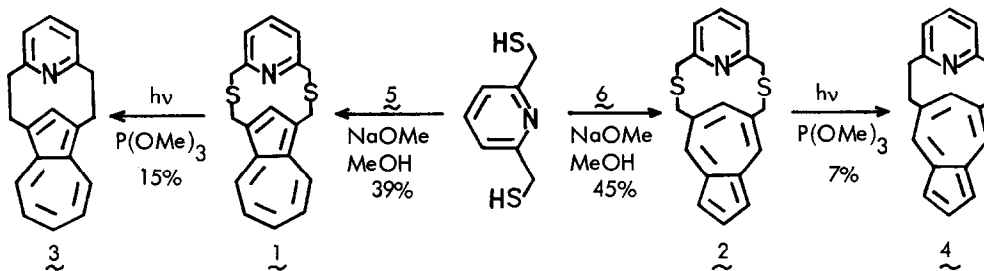
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**Abstract:** Four azuleno(2,6)pyridinophanes (1-4) were synthesized and their conformations were found by NMR spectroscopy to be very similar to those of the corresponding azulenometacyclophanes. A transverse conformational change was observed for [2.2](5,7)azuleno(2,6)pyridinophane.

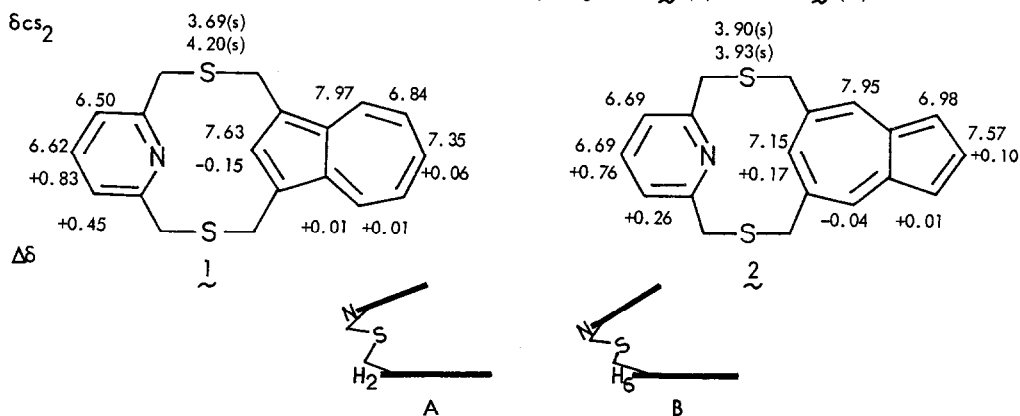
There has been considerable interest over the decade in the conformationally mobile [m.n]meta-cyclophanes and their analogs<sup>2)</sup>. In the studies on conformation of dithia[3.3]azulenophanes with meta-type bridges<sup>1)</sup>, we have shown that all such phanes studied preferred the syn conformation, presumably due to Pitzer strain in the bridges, and that the dipole-dipole interaction between two azulene rings contributes to the stability of the syn conformation and thus controls the syn-anti ratio. We have extended our study to azulenopyridinophanes in order to compare their conformations with those of the corresponding azulenometacyclophanes. The former may assume different conformations from the latter through the disposition of a pyridine ring in the proximity of an azulene, so varying the extent of dipole-dipole interaction or the interaction between the pyridine nitrogen and the 7-membered ring of azulene<sup>3)</sup>. The results for two dithia[3.3]azuleno(2,6)pyridinophanes (1, 2) and two [2.2]azuleno(2,6)-pyridinophanes (3, 4) are described herein.

**Synthesis** As shown in the scheme below, 2,6-bis(mercaptomethyl)-pyridine<sup>4)</sup> was coupled in the presence of a base with azulene-1,3- or -5,7-bis(methyltrimethylammonium)diiodides<sup>5,6)</sup> to give the corresponding dithia[3.3]azuleno(2,6)pyridinophanes, 1 and 2, respectively. Photodesulfurization



of 1 and 2 gave the corresponding [2.2]azuleno(2,6)pyridinophanes, 3 and 4, respectively<sup>7</sup>).

Conformation of 1 and 2 As shown in the figures, PMR spectra of both 1 and 2 show two singlet methylene signals, indicating that the aromatic rings in these compounds are flipping freely at room temperature. The chemical shift ( $\delta$ ) of their aromatic outer hydrogens and their difference ( $\Delta\delta$ ; + denotes up-field shift) from the reference compounds (2,6-lutidine, and 1,3- and 5,7-dimethylazulenes) clearly indicate the preferred syn conformations for both cases although  $\Delta\delta$ s in azulene protons are generally smaller than those in pyridine rings. Opposite sign of  $\Delta\delta$  between inner hydrogens of 1 and 2 would reflect the difference in the relative positions of the pyridine ring with respect to the azulene ring; the pyridine ring would lean more towards the inner hydrogen in 2 (B) than in 1 (A).



When temperature was lowered, the methylene singlets of 1 broadened, and one of them changed to a clean AB type at  $-102^\circ\text{C}$ , suggesting that the ring flipping froze out. Free energy of activation of this process was estimated to be 10.6 kcal/mol by the application of the coalescence temperature method<sup>8</sup>). At this temperature, signals of aromatic hydrogens remained unchanged, and no signal expected from the anti conformation was observed. Hence, the free energy difference between syn and anti conformers is more than 1.5 kcal/mol. The same behavior is true for 2 except two closely situated singlet methylenes became one broad singlet at  $-90^\circ\text{C}$ , and ring flipping was not frozen at  $-102^\circ\text{C}$ . Hence the free energy of activation is less than 9 kcal/mol.

The failure to detect the anti form in both cases<sup>9</sup>) suggests that the incorporation of the dipolar pyridine ring is not sufficient for the enhanced dipole-dipole repulsion in the syn form of 1 to overcome the Pitzer strain in the bridge.

Structure of [2.2]azuleno(2,6)pyridinophanes 3 and 4 Complex multiplets (AGMX) at 2-4 ppm of bridge hydrogens in PMR spectra of 3 and 4 suggested their fixed geometries at room temperature. The large up-field shift of inner aromatic hydrogens and small down-field shift of outer ones, clearly shown by the  $\delta$  and  $\Delta\delta$  values in Table 1, revealed the stepped conformation in both cases. Furthermore, the fact that  $\Delta\delta$  values of azulene hydrogens are very similar to those of [2.2](1,3)- and (5,7)azulenometacyclophanes, 7<sup>10</sup>) and 8<sup>6</sup>) respectively (Table 1), suggests that all of these compounds have very similar geometries in solution, with no sizable interaction between the nitrogen and azulene ring. The conclu-

sion was further verified by the similarity of CMR spectra and electronic spectra of 3 and 7, and 4 and 8. Their CMR chemical shifts are listed in Table 2.

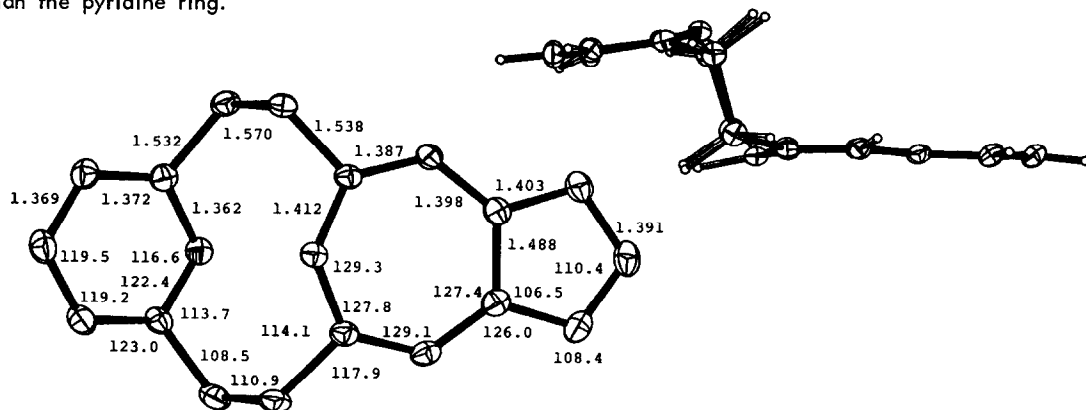
Table 1. PMR chemical shift ( $\delta$  in  $\text{CDCl}_3$ ) and  $\Delta\delta$  (in parentheses) of aromatic hydrogens in 3, 4, 7 and 8

position	Azulene Hydrogens (azulene numbering)					Pyridine (benzene) Hydrogens (pyridine numbering)		
	1	2	4	5	6	1'	3'	4'
<u>3</u>	C	5.11 (+2.37)	8.26 (-0.28)	6.98 (-0.13)	7.48 (-0.07)	N	7.09 (-0.14)	7.22 (+0.23)
<u>7</u>	C	5.12 (+2.36)	8.23 (-0.25)	6.95 (-0.10)	7.45 (-0.04)	3.10 (+3.77)	7.04~7.37 (-0.2~-0.3)	
<u>4</u>	7.22 (-0.23)	7.77 (-0.09)	8.27 (-0.36)	C	5.28 (+2.04)	N	7.13 (-0.18)	7.67 (-0.22)
<u>8</u>	7.25 (-0.26)	7.81 (-0.13)	8.25 (-0.34)	C	4.84 (+2.48)	5.21 (+1.66)	7.11 (-0.13)	7.37 (-0.32)

Table 2. CMR chemical shift ( $\delta$  in  $\text{CDCl}_3$ ) of azulene ring (azulene numbering)

position	1	2	4	5	6	8a
<u>3</u>	127.4	147.9	132.4	120.8	137.1	137.7
<u>7</u>	127.3	147.9	132.3	120.7	137.0	137.7
<u>4</u>	115.9	135.5	136.4	130.5	144.9	139.3
<u>8</u>	116.0	136.1	137.1	131.6	143.8	139.1

Precise molecular geometry of 4 obtained by an X-ray crystallography is shown below<sup>11)</sup>; averaged bond lengths and angles in azulene ring are very similar to those in [2.2]azulenophanes<sup>6)</sup>. Some distortion is apparent in the side view; the 7-membered ring of azulene is distorted to a boat form more so than the pyridine ring.



Although the PMR spectrum of 3 remained unchanged up to 130°C, the methylene signals of 4 showed significant change; each of two groups of multiplets became broad at 120°C and broadened further at 130°C. Unfortunately, however, the compound decomposed rapidly at higher temperatures, preventing estimation of accurate energy of activation in this dynamic process<sup>12</sup>. Since aromatic hydrogen signals of 4 remained practically unchanged at all temperatures measured, the dynamic process observed is a transverse conformational change (anti  $\rightleftharpoons$  planar  $\rightleftharpoons$  anti), but not ring flipping (anti  $\rightleftharpoons$  syn). This is the first observation of such a change for the N, CH combination of the inner atomic group in [2.2]phanes with carbon bridge<sup>14</sup>.

## References and notes

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- 2) R.H. Mitchell in "Cyclophanes", P.M. Keehn and S.M. Rosenfeld, Ed., Vol. 1, pp. 239-310. Academic Press, Inc., New York, N.Y. (1983).
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- 6) Y. Fukazawa, M. Sobukawa and S. Itô, Tetrahedron Letters, 23, 2129 (1982).
- 7) New compounds appeared in this paper have the following properties in addition to those described in the text.  
 $\underline{1}$ : Blue plates; m.p. 216°C (decomp.);  $\lambda_{\text{max}}^{\text{MeCN}}$  300 (log  $\epsilon$  4.39), 383 (3.58), 640 nm (2.42);  $\nu_{\text{KBr}}$  1572, 735 cm<sup>-1</sup>.  $\underline{2}$ : Blue plates; m.p. 157°C (decomp.);  $\lambda_{\text{max}}^{\text{MeCN}}$  295 (log  $\epsilon$  4.58), 370 (3.75), 590 nm (2.54);  $\nu_{\text{KBr}}$  1566, 743 cm<sup>-1</sup>.  $\underline{3}$ : Blue plates; m.p. 144°C (decomp.);  $\lambda_{\text{max}}^{\text{cyclohexane}}$  301 (log  $\epsilon$  4.23), 363 (3.40), 656 nm (2.00);  $\nu_{\text{KBr}}$  1565, 745 cm<sup>-1</sup>.  $\underline{4}$ : Blue plates; m.p. 182.5°C (decomp.);  $\lambda_{\text{max}}^{\text{cyclohexane}}$  303.5 (log  $\epsilon$  4.62), 355 (3.74), 610 nm (2.55);  $\nu_{\text{KBr}}$  1586, 752 cm<sup>-1</sup>.
- 8) R.J. Kurland, M.B. Rubin and W.B. Wise, J. Chem. Phys., 40, 2426 (1964).
- 9) Exclusive syn conformation in crystals was revealed for  $\underline{1}$  and  $\underline{2}$  by X-ray crystallographic analysis. Y. Fukazawa, T. Shiokawa, J. Tsuchiya and S. Itô, to be published.
- 10) Y. Nesumi, T. Nakazawa and I. Murata, Chemistry Letters, 771 (1979).
- 11) The compound 4 crystallizes in orthorhombic system of space group Pcab with 8 molecules in a unit cell of dimensions  $\underline{a}$ =25.431(5),  $\underline{b}$ =11.178(2),  $\underline{c}$ =9.896(2)Å. The final R value was 4.6%. Final crystallographic coordinates have been deposited in the Cambridge crystallographic Data Center.
- 12) If the coalescence is assumed to occur at 140°C, the  $\Delta G^\ddagger$  for the process is calculated to be ~23 kcal/mol, which is considerably smaller than that ( $\Delta G^\ddagger > 27$  kcal/mol) of [2.2](2,6)pyridinometacyclophane (ref. 13), thus the effect of ring size on this dynamic process is revealed.
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(Received in UK 29 July 1985)