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CONFORMATION OF DITHIA[3.3]AZULENOFURANO- AND -THIOPHENOPHANES1)

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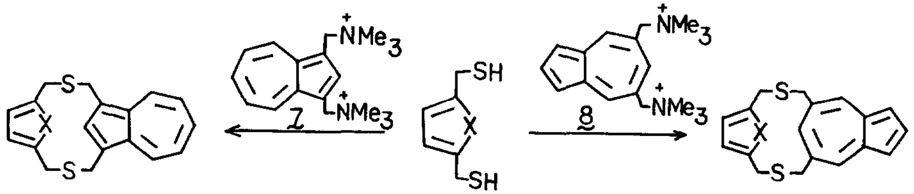
Abstract: Preferred conformation of the dithia[3.3]azulenofurano- (**1** and **2**) and thiophenophanes (**3** and **4**) were examined by PMR and X-ray crystallographic analysis. While the furanophanes prefer syn conformation, the thiophenophanes exist mainly in anti form. Free energy of activation for flipping of azulene and thiophene was evaluated separately for the latters.

Although extensive studies on conformation of dithia[3.3]metacyclophane and its analogs were conducted2), little is known about the stereochemistry of the structurally related dithia[3.3]heterophanes3). We have previously shown that dithia[3.3]azuleno(2,6)pyridinophanes prefer the syn conformation, because the Pitzer strain in the 2-thiapropano bridges overwhelms the dipole-dipole interaction between azulene and pyridine1,4). Apparently, the nitrogen lone pair, being smaller in steric bulkiness than C-H5) when situated at an inner position, did not change the conformational preference. Conversely, the introduction of a larger hetero atom to the inner position may increase the repulsion between inner groups and overcome the Pitzer strain6). In this context, we have synthesized four dithia[3.3]azulenoheterophanes (**1**-**4**) containing furan and thiophene rings. Through the NMR studies and X-ray crystallographic analysis, the thiophenophanes **3** and **4** have been shown, for the first time in dithia[3.3]phanes, to exist in preferred anti conformations, while furanophanes **1** and **2** prefer syn forms. Furthermore, free energy of activation for each flipping of the two aromatic rings in **3** was evaluated separately for the first time in a phane system.

Synthesis The synthetic scheme is shown on the next page. 2,5-bis(mercaptomethyl)furan (**5**)7) and -thiophene (**6**)8) were coupled with the 1,3- or 5,7-bisammonium salts, **7** and **8** 9), to give the corresponding dithia[3.3]azuleno(2,5)furanophanes **1** and **2**, and their thiophene analogs **3** and **4**, respectively10).

Dithia[3.3]azuleno(2,5)furanophanes **1** and **2** Two sharp singlets due to methylene signals at room temperature suggest a rapid flipping of two aromatic rings in both cases. Fairly large up-field shifts of furan hydrogens and small shifts (both up-field and down-field) of azulene ring hydrogens10) revealed the predominance of the syn conformation in both cases as in the [3.3]phanes in general1,11). At -100°C,



1 X = O
3 X = S

5 X = O
6 X = S

2 X = O
4 X = S

methylene singlets of 1 changed to two AB quartets (flipping frozen) but the aromatic hydrogens remained unchanges, showing no signal assignable to the minor anti isomer. This suggests a free energy difference (ΔGo) between syn and anti conformers > 1.5 kcal/mol. The free energy of activation ($\Delta G^{\ddagger}$) for the ring flipping was estimated, applying the coalescence temperature method, to be 9.4 kcal/mol. Spectra of 2 showed practically no change down to -102°C, suggesting free flipping even at -102°C. The $\Delta G^{\ddagger}$ for the ring flipping was then estimated to be < 8 kcal/mol in this case.

Dithia[3.3](1,3)azuleno(2,5)thiophenophane 3 The PMR spectrum of 3 10) at room temperature exhibits two sets of AB quartets due to methylene hydrogens indicating that the flipping of at least one of the rings has slowed on the nmr time scale. The ring hydrogens show rather unusual shifts: the thiopene hydrogens (H_T) show an up-field shift ($\Delta\delta$, +0.26 ppm) from those of 2,5-dimethylthiophene, suggesting that they are above the plane of the azulene ring. However, the inner azulenic hydrogen (H_2) also exhibits a fairly large up-field shift (+0.58 ppm), implying that it is located also above the plane of the thiophene ring. These two contradicting $\Delta\delta$ values, together with small $+\Delta\delta$ for H_4 and small $-\Delta\delta$ for H_5 and H_6 (azulene numbering), are explicable either by an off-parallel orientation of the aromatic rings (syn form) or by the co-existence of the syn and the anti conformations with a rapid flipping of one of the aromatic rings.

On lowering the temperature, H_T and H_2 became broad and shifted toward each other, overlapped at -72°C, then crossed over, and sharpened again to become two sharp singlets (Fig. 1). At -112°C the $\Delta\delta$ value of H_2 is +1.26 ppm and that of H_T -0.36 ppm, clearly suggesting a single anti form. From the coalescence temperature (-82°C), $\Delta G^{\ddagger}$ of the dynamic process was estimated to be ~9 kcal/mol, the value nearly the same as those obtained for dithia[3.3]azulenophanes 9). Hence, the dynamic process disclosed here was concluded to be due to the azulene flipping.

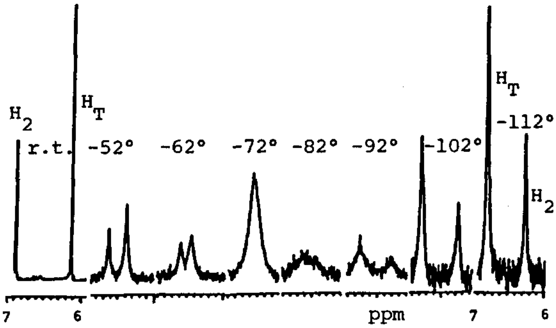


Fig. 1 Variable temperature PMR spectra of 3

The change of the chemical shifts of H_T and H_2 by temperature (Fig. 2) is rather unusual. This is explicable by the temperature dependency of the equilibrium constant $[K_T=(\delta H_2^{anti}-\delta H_2^{obs})/(\delta H_2^{anti}-\delta H_2^{syn})]$ between anti and syn conformers. While the chemical shift of the anti conformer, δH_2^{anti} (6.24 ppm) in

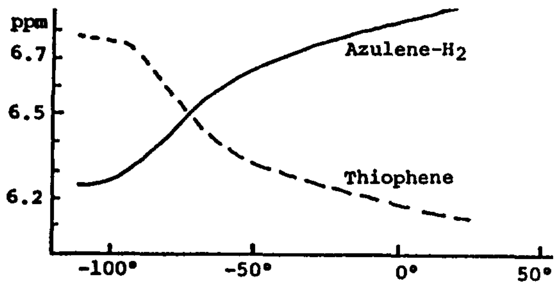


Fig. 2 Temperature dependent chemical shift of thiophene (H_T) and azulenic hydrogens (H_2) in **3**

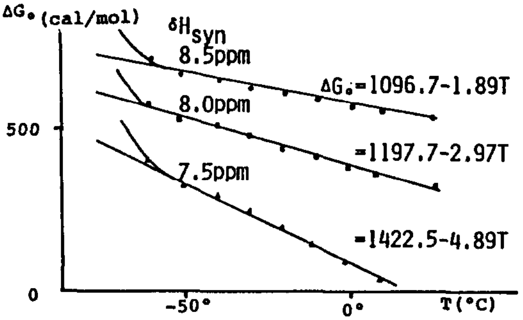


Fig. 3 Variation of ΔGo of **3** as a function of temperature

the equation, was obtained directly from the spectrum at -112°C, H_2^{syn} could not be deduced experimentally as no syn isomer was detected. Therefore, K_T was calculated for three cases, using values 7.5, 8.0 and 8.5 ppm for H_2^{syn}. These values are based on the observed chemical shift (7.91 ppm) of H_2 in **1**, which exists exclusively in the syn conformation. The free energy difference (ΔGo= $-RT\ln K_T$) for the three cases were plotted against temperature (Fig. 3). From the linear part of the plots, enthalpy difference (ΔHo) was estimated to be 1.1-1.4 kcal/mol and that of entropy 1.0-2.5 eu.

In order to estimate $\Delta G^{\ddagger}$ for the flipping of thiophene ring, PMR spectra were measured at higher temperatures in hexachlorobutadiene. While the aromatic hydrogens remained practically unchanged, the methylene signals (AB quartet) coalesced at ~70°C and became sharp singlets at 90°C. From the coalescence temperature, $\Delta G^{\ddagger}$ for thiophene ring flipping was estimated to be 18.1 kcal/mol. Thus the entire dynamic process of **3** can be visualized in Fig. 4. To the best of our knowledge, it is the first instance that the individual free energy of activation for the flipping of two rings has been obtained separately in a phane system.

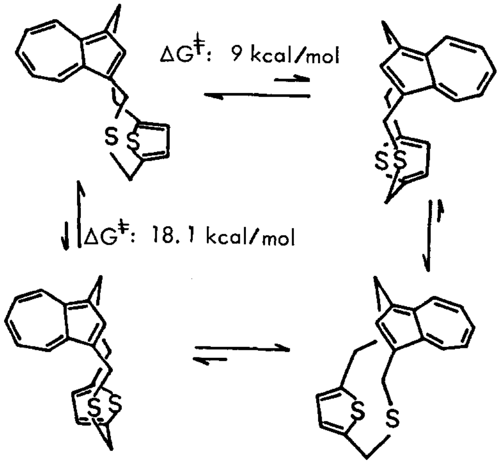


Fig. 4 Dynamic processes of **3**

In crystals, **3** exists exclusively in the anti conformation (Fig. 5), though the thiophene ring is tilted significantly, as disclosed by an X-ray crystallographic study[12]. Thus, **3** is the first dithia[3.3]phane with no inner substituent shown to possess the preferred anti conformation both in the solution and in the crystalline state[11].

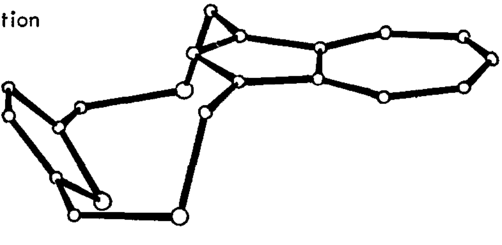


Fig. 5 Molecular structure of **3**

Dithia[3.3](5,7)azuleno(2,5)thiophenophane **4**   At room temperature, **4** also exhibits two sets of AB quartet[10], suggesting azulene flipping. Predominance of the anti conformation in this case also was concluded from $\Delta\delta$ of aromatic hydrogens (H_T -0.06 ppm, H_6 +1.16 ppm). Although NMR spectra at higher temperature allowed the estimation of $\Delta G^{\ddagger}$ of 17.9 kcal/mol for thiophene flipping, poor solubility of **4** precluded the estimation of the value for azulene flipping.

References and Notes

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10) Compounds **1**-**4** were properly characterized. Electronic and PMR spectra were measured in CH_2Cl_2 and CS_2, respectively. **1**: blue prisms, m.p. 143°C (decomp.); λmax (log ε) 295 (4.54), 379 (3.73), 630 nm (2.47); δ 3.53 (4H, s), 4.20 (4H, s), 5.16 (2H, s), 6.91 (2H, t, J=9.5), 7.40 (1H, t, J=9.5), 7.83 (1H, s), 8.01 (2H, d, J=9.5). **2**: blue prisms, m.p. 136°C (decomp.); λmax (log ε) 288 (4.72), 368 (3.87), 600 nm (2.65); δ 3.67 (4H, s), 3.90 (4H, s), 5.51 (2H, s), 7.04 (2H, d, J=3.7), 7.05 (1H, s), 7.62 (1H, t, J=3.7), 8.01 (2H, d, J=1.8). **3**: blue plates, m.p. 145°C (decomp.); λmax (log ε) 303 (4.43), 384 (3.62), 628 nm (2.31); δ 3.77 (2H, d, J=15), 3.95 (2H, d, J=15), 4.06 (2H, d, J=15), 4.16 (2H, d, J=15), 6.09 (2H, s), 6.90 (1H, s), 6.90 (2H, t, J=10), 7.40 (1H, t, J=10), 7.94 (2H, d, J=10). **4**: blue plates, m.p. 117°C (decomp.); λmax (log ε) 289 (4.67), 352 (3.75), 608 nm (2.60); δ 3.70 (2H, d, J=14), 3.88 (2H, d, J=14), 3.92 (2H, d, J=14), 3.94 (2H, d, J=14), 6.16 (1H, t, J=2), 6.41 (2H, s), 7.04 (2H, d, J=3.7), 7.62 (2H, t, J=3.7), 7.95 (2H, d, J=2).

11) One other case which has the anti structure only in crystalline state, is known. T.L. Chan, C.K. Chan, K.W. Ho, J.S. Tse and T.C.W. Mak, J. Cryst. Mol. Struct., **7**, 199 (1977).

12) The compound **3** crystallizes in orthorhombic system of space group $P2_12_12_1$ with 4 molecules in a unit cell of dimension a=16.886(10), b=14.825(8), c=6.158(5)Å. The final R factor was 9.8%. Final crystallographic coordinates have been deposited in the Cambridge Crystallographic Data Center.

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