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AZULENOPHANE VI. CONFORMATION OF DITHIA[3.3]AZULENOPHANES

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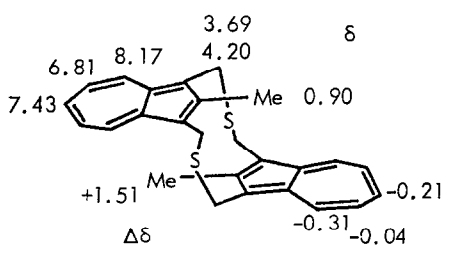
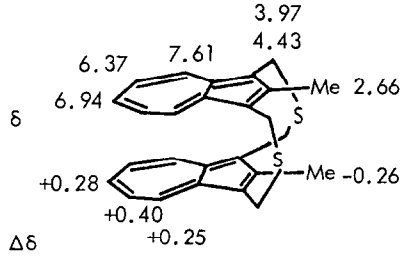
Abstract Conformation of seven dithia[3.3]azulenophanes was investigated by PMR spectroscopy to disclose the preference of syn forms for all cases. This was attributed to the tortional strain in bridges. The syn/anti ratio is also affected to minor extent by the intramolecular dipole-dipole interaction between two dipolar aromatic rings.

2,11-Dithia[3.3]metacyclophanes are known in solution to undergo dynamic processes which involve both the flipping of two aromatic rings and the conformational change in the S-containing bridges. Although 2,11-dithia[3.3]metacyclophane itself was shown to exist exclusively in syn form both in crystalline state and in solution[1], the syn/anti ratio (reflecting the free energy difference between two forms) varies from one derivative to another depending on the substituent at one of the inner positions[2]. However, as the substituent has two effects, steric and electronic, it is desirable to utilize a compound with a dipolar ring system in order to evaluate charge transfer interaction, which would affect the ratio by stabilizing syn form. Dithia[3.3]azulenophanes incorporating the dipolar azulene system would be suited for the purpose. We have carried out the PMR spectroscopic study on the conformational preference in the azulenophanes 1-6[3]. The result is described herein[4,5].

Methylsubstituted azulenophanes 1 and 2 PMR spectrum[6] of the dimethyl compound 1 clearly shows two sets of signals (1:2 intensity ratio) for all aromatic protons and four methylene protons (AB type), suggesting the presence of two discrete compounds. Although their separation was not achieved, each signal was assigned unequivocally taking advantage of their intensity and multiplicity. The chemical shifts are shown below along with their differences (Δδ; + denotes up-field shift) from those of 1,2,3-trimethylazulene. A significant up-field shift of methyl signal and small down-field shifts of aromatic protons for



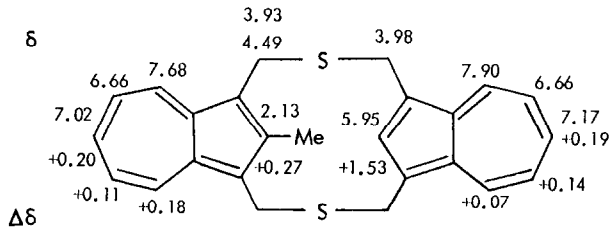
1a



1s

the minor component and the reverse trends for the major one are attributed to the structures 1a and 1s, respectively. The result is in accord with those in dithia[3.3]metacyclophane series[2,7], and would provide reference values in determining the major conformation in the flipping azulenophanes in general.

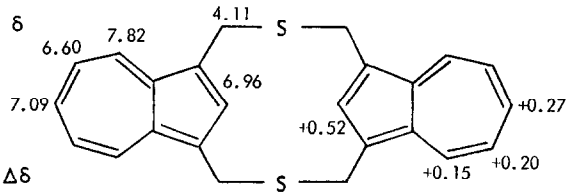
The methylene signals of the monomethyl compound 2 consist of a 4H singlet and 4H AB signals indicating that, while the methyl-carrying azulene ring is rigid, the unsubstituted azulene ring is flipping freely at room temperature. Result of analysis is shown below.



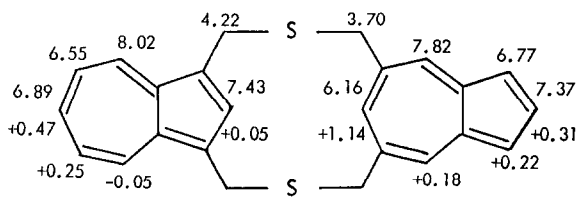
2

The methyl signal splits into two broad singlets (1.3 and 2.8 ppm) of nearly equal intensity at -110°C, revealing that anti and syn conformer have nearly equal free energy. From the coalescence temperature (-87.5°C) the activation energy for the ring flipping was calculated to be ca. 8.3 kcal/mol.

Azulenophanes 3 and 4 In both compounds, the ring flipping occurs freely at room temperature as shown by singlet nature of the methylene protons. The result of the analysis is shown below.



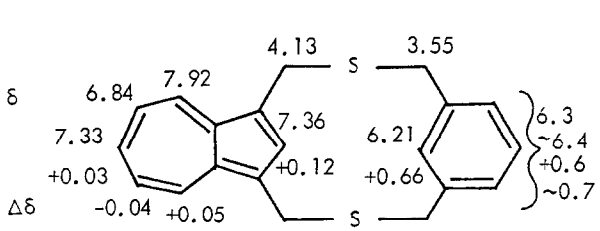
3



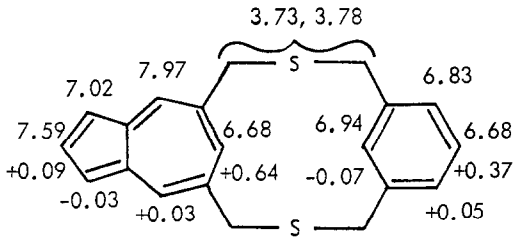
4

Judging from the shift values of the outer ring protons (larger up-field shift than those of 2, and smaller than those of 1s)[8], the predominance of syn conformer was suggested for both compounds. This was supported by the spectra at lower temperature. For 3, a singlet of 0.3H intensity appeared at 5.8 ppm at -115°C, revealing that 3 exists as a 7:3 mixture of syn and anti forms, and that the former is ca. 0.3 kcal/mol more stable than the latter. For 4, all signals appear as pairs of nearly equal intensity at -115°C. However, these must be due to two syn forms as the high-field signal expected to the inner protons of anti conformer was not detected[9]. The free energy difference between syn and anti forms should thus be larger than 1.5 kcal/mol in this case. Activation energy of the ring flipping for 4 was calculated[10] from the coalescence of methylene signals to be~12 kcal/mol.

Azulenometacyclophanes 5 and 6 Result of analysis is shown. Aromatic rings are freely flipping at room temperature. The up-field shift values of azulenic outer protons in these compounds are much smaller than in 3 and 4. However, shift values of outer benzene protons (comparable with those in



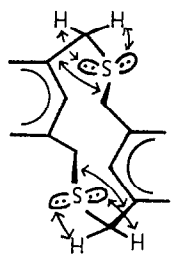
5



6

dimethyl-2,11-dithia[3.3]metacyclophane[1]) and those of the inner protons[8]) are explicable only by the preferred syn conformation. At -110°C, methylene protons of 5 became narrow AB quartets but no inner proton signal expected from anti conformation was observed. The free energy difference would therefore be more than 1.5 kcal/mol. The activation energy of the ring flipping was calculated to be ~10 kcal/mol. Although all aromatic protons of 6 appeared at -100°C as a pair with 3:2 intensity ratio, no high-field signal attributable to the inner protons of anti conformation was observed. Thus the free energy difference in this case should also be greater than 1.5 kcal/mol.

Thus, in all of the flipping dithia[3.3]phanes examined so far, syn conformations are always preferred to anti forms, and yet free energy difference between syn and anti form is different, 0.3 kcal/mol for 3 and > 1.5 kcal/mol for others. The reason for the preferred syn conformation can be rationalized by torsional strain in bridges in anti conformation. Molecular model clearly shows that a bond and two lone pairs on sulfur (in sp^3 hybridization) are always nearly eclipsed with three bonds of either one of adjacent methylenes in anti conformation (see fig.), while they are always in gauche form in syn conformation[11]. The resulted steric repulsion in anti conformation seems the major cause for the preferred syn conformation[12].



Smaller free energy difference for 3 may be attributed to the dipole-dipole interaction between two azulene rings, which destabilizes the syn form of 3, while no such an interaction is anticipated in anti form. The same interaction should stabilize the syn form of 4, but unfortunately precise situation was not disclosed experimentally. In this context, it is interesting that the difference in activation energy for the ring flipping, 8 kcal/mol for 2, ~10 kcal/mol for 5 and ~12 kcal/mol for 4, fall in the order. This may reflect the stability of the respective syn forms. Thus, considering steric factor of the bridge as the major factor and the dipole-dipole interaction as the minor one, the conformations of dithia[3.3]azulenophanes can be explained satisfactorily.

References and Notes

1) W. Anker, G.W. Bushnell and R.H. Mitchell, Can. J. Chem., 57, 3080 (1979) and the references cited therein.

2) F. Vögtle and P. Neumann, Tetrahedron, 26, 5299 (1970). F. Vögtle, W. Wieder and H. Förster, Tetrahedron Letters, 4361 (1974).

3) Synthesis of 3, 5 and 6 has been reported. 3: Y. Fukazawa, M. Aoyagi and S. Itô, Tetrahedron Letters, 1055 (1979). 5: Y. Nesumi, T. Nakazawa and I. Murata, Chemistry Letters, 771 (1979).

6: Y. Fukazawa, M. Sobukawa and S. Itô, Tetrahedron Letters, 23, 2129 (1982). Synthesis of 1 and 2 followed the general route used for that of 3, coupling reaction yielded the desired compounds in 35% and 30% yield, respectively. 2: green plates, m.p. 161.5-163° (dec.); m/e 386 (M^+), 341, 200, 198, 185, 168 (b.p.), 166, 155; ν_{KBr} 1570, 1488, 1480, 1428, 902, 743, 732, 688. (M. Sobukawa, MS Thesis, Tohoku University (1981)). For the synthesis of 4, 1,3-bis(mercaptomethyl)-azulene was coupled with trimethyl ammonium iodide of 5,7-bis(aminomethyl)azulene in 35% yield. Its synthesis, physical properties and the reactions will be reported elsewhere.

4) Although the dynamic process observed consists of the flipping of aromatic rings and conformational change in S-containing bridges, the present discussion is mainly concerned with the former. The latter process was always found to have smaller activation energy, so that it was sometimes not frozen at the lowest temperature measured.

5) Preliminary and general account of this study has been presented at the 4th International Symposium on the Chemistry of Novel Aromatic Compounds, Jerusalem, Aug. 1981. Cf. S. Itô, Pure and Appl. Chem., 54, 957 (1982).

6) Spectra were measured at 90 MHz or 200 MHz in CS_2 or CS_2+CD_2Cl_2 solution.

7) R.H. Mitchell and V. Boekelheide, Tetrahedron Letters, 1197 (1970). Idem, J. Am. Chem. Soc., 96, 1547 (1974).

8) Throughout the compounds measured, the inner protons on the larger ring have always larger shift values This is probably concerned with the time-averaged position of the hydrogen in question relative to the facing ring.

9) Since the methylene protons can be analyzed as four sets of quartets at this temperature, both syn forms must have symmetrical structures in S-containing bridges.

10) R.J. Kurland, M.B. Rubin and W.B. Wise, J. Chem. Phys., 40, 2426 (1964).

11) Molecular mechanics calculations (MMPI) for 2,11-dithia[3.3]metacyclophane disclosed that syn conformations are ca. 3 kcal/mol more stable than anti forms. The torsional strain originated from the bridge part in the anti form was calculated to be 1.7 kcal/mol.

12) This type of rationalization can also be applied to the preferred syn conformation in [3.3]metacyclophane [T. Otsubo, M. Kitasawa and S. Misumi, Bull. Chem. Soc. Jpn., 52, 1515 (1979)].

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