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SYNTHESIS AND DYNAMIC NMR OF HEXATHIADODECAMETHOXYMETACYCLOPHANE

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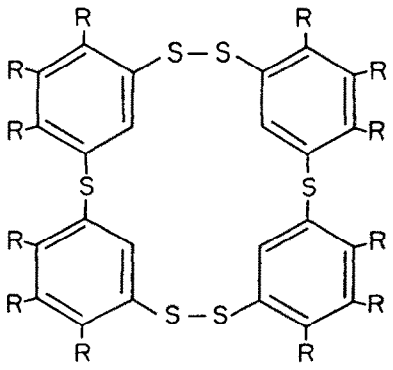
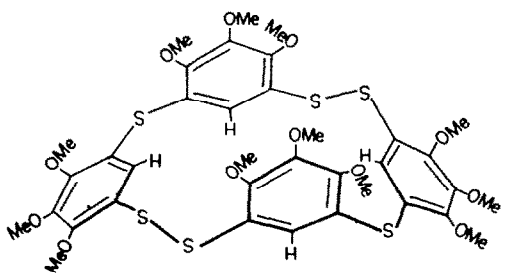
Abstract - A "one-pot" synthesis of the title compound (1) is described, which might also be suitable for other related compounds. It is shown by ^{1}H NMR that (1) has a saddle structure with C_2 symmetry. At room temperature it undergoes fast dynamic interconversion between two symmetry related structures resulting in an overall four-fold symmetry. The activation parameters for this reaction are: $\Delta E^{\ddagger}$=10.5 kcal/mole, $\Delta S^{\ddagger}$=7.1 e.u. At ~-100°C the reaction is frozen out on the NMR time scale.

In our search for macrocyclic compounds that exhibit mesomorphic properties[1] we have prepared a number of substituted thiacyclophanes and examined their phase diagram. As yet we have not found a mesogen among these compounds, however we wish to report on one of its members i.e. the 18-membered macrocycle 1,2,9,16,17,24-hexathia[2.1.2.1]-4,5,6,11,12,13,19,20,21,26,27,28-dodecamethoxy-metacyclophane (1), because (i) we found a new - "one-pot" - synthetic route for its preparation, and (ii) using proton NMR, we obtained structural and dynamic information which seem to contradict earlier conclusions concerning the conformation of 18-membered thiametacyclophanes obtained by Pappalardo et al.[2] These workers discussed the stereochemistry of a number of tetrameric metacyclophanes including 1,2,9,16,17,24-hexathia-[2.1.2.1]-4,6,8,11,13,15,19,21,23,26,28,30-dodecamethyl metacyclophane (2). Based on solution proton NMR evidence obtained in deuterated



(1) 4,5,6,11,12,13,19,20,21,26,27,28-dodecamethoxy. R=OCH_3

(2) 4,6,8,11,13,15,19,21,23,26,28,30-dodecamethyl. R=CH_3



(3)

nitrobenzene at 150°C, they concluded that this compound has a fixed crown conformation with D_{2d} symmetry. These extreme experimental conditions were necessary because of the low solubility of (2). Since the solubility of the methoxy derivative (1) is considerably higher we were able to obtain NMR spectra at much lower temperatures. The results show that the hexathiametacyclophane ring, at least in the latter compound, is highly flexible and undergoes fast interconversion between two conformations of C_2 symmetry. The interconversion process is frozen out (on the NMR time scale) at around -100°C.

RESULTS AND DISCUSSION

Examples of ^{1}H NMR spectra of ~2 wt.% solution of (1) in THF-d_8 at various temperatures are shown in Fig. 1. In the low temperature range two groups of lines are observed; (i) a doublet at $\delta \simeq 6-7$ ppm and (ii) a group of four lines around $\delta \simeq 3.9$ ppm, identified respectively with the aromatic and methoxy protons. The latter group of lines can be interpreted in terms of three

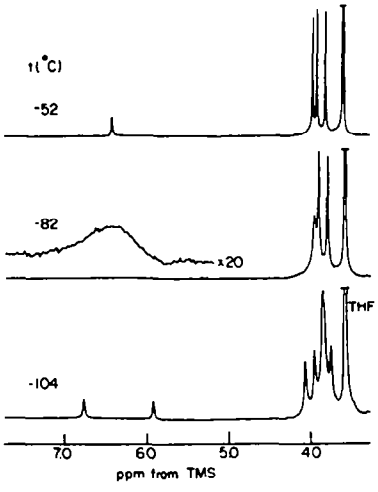


Fig. 1. ^{1}H NMR spectra of (1) in deuterated THF at the indicated temperatures. The signal due to residual protons in THF is truncated.

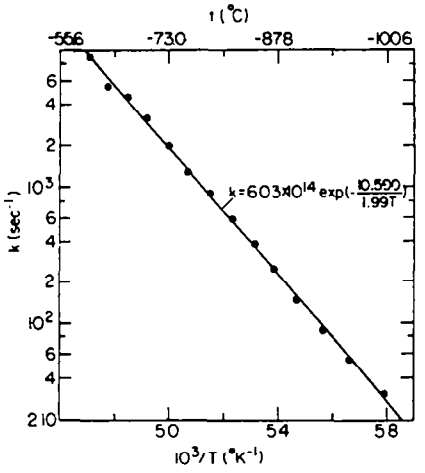


Fig. 2. An Arrhenius plot of the interconversion rate of (1) as derived from the aromatic protons lineshape.

equally intense doublets due to the three inequivalent methoxy groups. The relevant chemical shift data are summarized in the Table. As the temperature is increased the two groups of peaks coalesce to a one- and three-line pattern, with overall relative intensity of 1 to 9. The chemical shift of the latter correspond approximately to the mid-points of the various doublets of the low temperature spectra (see Table).

Proton chemical shifts (in ppm) of (1) at -104°C and at room temperature

	aromatic protons		methoxy protons					
-104°C	6.764	5.918	4.053	3.841	3.936	3.841	3.841	3.741
rel.int.[a]	1	1	3	3	3	3	3	3
average	6.341		3.947		3.889		3.791	
R.T.	6.488		3.948		3.897		3.807	

[a]relative intensity (rounded figures).

The fact that two equally intense peaks due to the aromatic (and each of the methoxy) protons are observed indicate that the stable conformations of (1) must have C_2 symmetry. A likely structure is the saddle conformation (3) in which two phenyl rings are strongly inclined while the two others are more nearly parallel to the molecular C_2 axis. This geometry will cause the aromatic protons of the tilted rings to be shielded by the ring currents of the other pair, hence the relatively large shift between the two types of aromatic protons.

Using molecular models it can be seen that the proposed conformation (3) gives a torsional angle for the S-S bond of about 90°. This value was found in a number of X-ray studies of compounds possessing a disulfide moiety and seems to correspond to a minimum in its potential energy

curve.[3,4] The molecular topology of (1) allows two equivalent conformations of type (3) corresponding to the two possibilities in which oppositely positioned phenyl rings are inclined with respect to the C_2 axis. The NMR results show that at room temperature these two conformations rapidly interconvert to yield an overall four-fold symmetry. On cooling a coalescence temperature is reached at around -80°C. A quantitative analysis of the dynamic lineshapes of the aromatic protons yields interconversion rates as plotted in Fig. 2, with the activation parameters: $\Delta E^{\#}$=10.5 kcal/mole; $\Delta H^{\#}$=9.9 kcal/mole; $\Delta S^{\#}$=7.1 e.u.. It appears that the high rate of the reaction reflects the large and positive activation entropy associated with a highly flexible transition state.

On the basis of these results it is felt that if a suitable low temperature solvent is employed a similar spectrum corresponding to a conformer with C_2 symmetry will also be found for compound(2) at low temperatures.[2]

EXPERIMENTAL SECTION

Synthesis - The synthesis of 1 was performed as follows: While stirring at room temperature, a solution of sulfurdichloride (12.2g,0.118 mole) in 50ml CH_3CN was added to a 13.1g solution of 1,2,3-trimethoxybenzene (13.1g, 0.08 mole) in 100ml of the same solvent within 1 h. Stirring was then continued for 4 more h. The resulting crystalline mass was filtered and repeatedly washed with CH_3CN. The compound was finally crystallized from ethanol/CH_3CN, yielding 4.8g (28%); m.p.=236-237°C. TLC over silica/$CHCl_3$ gave a single spot. The high resolution mass spectrum of (1) gave strong ion peaks at m/e=856.0843,100%, corresponding to the ion molecule, and at half m/e (428.0499,61%) corresponding to $C_{18}H_{20}S_3O_6^+$ as would be expected from fragmentation by cleavage of the S-S bonds.[2] Elementary analysis $C_{30}H_{40}S_6O_{12}$: C, 50.18; H, 4.75; S, 22.30; (Calc.: C, 50.44, H, 4.70; and S, 22.44, respectively).

NMR measurement - ^1H NMR measurements were made on a Bruker WH 270 using a B-VT 1000 temperature controller. Samples of (1) in deuterated THF were studied in the temperature range -105°C to room temperature. Chemical shifts were measured relative to the solvent peaks and converted to the standard TMS scale using δ_1=1.73 ppm and δ_2=3.58 ppm for THF. The chemical shifts of (1) at room temperature and at -104°C are given in the Table.

REFERENCES

1. H. Zimmermann, R. Poupko, Z. Luz and J. Billard, Z.Naturforsch. 40a, 149 (1985); 41a, 1137 (1986).
2. S. Pappalardo, F. Bottino and G. Ronsisvalle, Phosphorus and Sulfur, 19, 327 (1984).
3. N.B. Pakor, M. Calligaris, L. Randaccio, F. Bottino and S. Pappalardo, Gazz.Chim.Ital. 110, 227 (1980).
4. B.A. Katz and A. Kossiakoff, J.Biol.Chem. 261, 15480 (1986).