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Structure of 2,11-Dioxa[3.3]orthocyclophane

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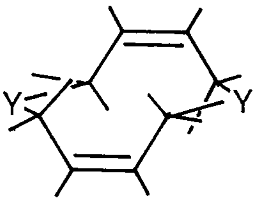
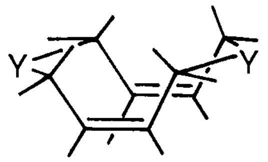
Conformational analysis of the title compound using an X-ray diffraction, molecular mechanics and ring current calculations is presented. The chair type structure found in its crystalline state is almost identical to that of its dithia analogue. However, the structure in solution is quite different from its crystalline structure.

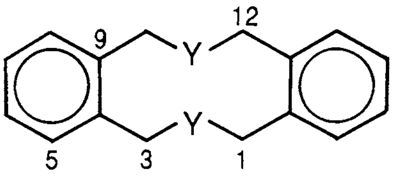
The conformations of cis,cis-1,6-cyclodecadiene and its derivatives have been of particular interest for the past two decades.1-3) They were discussed in terms of chair (A) and boat (B) conformations. The chair form has been claimed to be predominant. However, it is still unclear whether or not the chair form is the only predominantly stable conformer. The lack of efficient method for the analysis of the conformational behavior in solution is one of the main obstacles in studying a conformationally flexible molecule.



A



B



1 Y=O
2 Y=S
3 Y=Se

Recently, we have developed a new and efficient method for predicting the most stable conformation of macrocycles containing aromatic rings,4) which utilizes the calculation of secondary induced magnetic field due to an aromatic ring current. Using this method we could clarify that the most stable conformer of 4,9-dithiadibenzo-1,6-cyclodecadiene (2,11-dithia[3.3]orthocyclophane (**2**)) was not the reported boat2) but the chair form.3) With continuous interest in the application of our ring current method for the conformational analysis of flexible macrocycles, we have examined the most stable conformer of 2,11-dioxa[3.3]orthocyclophane (**1**). In this paper, we report our result which clarifies that the most stable conformation of **1** in solution is not the generally accepted chair form as was found in both **2** and **3**.

In order to obtain information about the precise molecular geometry in the solid state, an X-ray crystallographic analysis of **1** was preformed.5) The molecular structure is presented in Fig. 1. As is clearly seen in this figure, **1** has anti type chair structure in the crystalline state. This structure is quite similar to those of

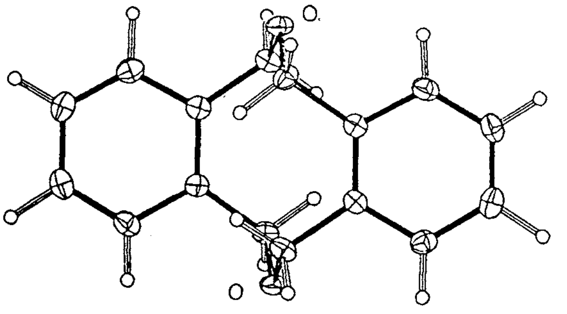


Fig.1. ORTEP drawing of **1**.

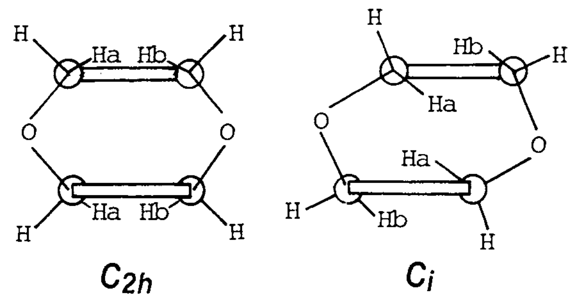


Fig.2. Side view of the C_{2h} and C_i structures of **1**.

2 and **3** in their crystalline state.[3)] Molecular mechanics calculation (MM2)[6)] predicted the highly symmetrical structure (C_{2h}) for this chair form. Slight but clear deviations from C_{2h} form are observed in the X-ray structure. Sliding of two benzene rings is one of the most prominent deviations and it is common to the three structures (**1**-**3**) in their crystalline state. The magnitude of the sliding, which is the distance between the center of each benzene rings along the short axis, is 0.32 Å in **1**, while those of **2** and **3** are 0.75 and 0.97 Å, respectively.

These structural features can be interpreted by the release of intramolecular steric repulsion. In the C_{2h} form, close contact between two hydrogens (Ha and Hb) of the two methylenes is present (Fig. 2). In order to reduce this steric repulsion, these two hydrogens must shift away from each other. This can be attained by rotating two bonds (C3-C4 and C9-C10) in a conrotatory fashion. This rotation can also give the sliding of the two benzenes. On the other hand, as the result of this rotation, the distance between the one of the methylene hydrogens and facing benzene ring became smaller, and hence repulsive interaction between them became larger. Since the distance of C-hetero bonds in the bridging chains of **1** is the shortest(C-O 1.430 Å) among the three (C-S 1.822 Å; C-Se 1.973 Å), the resulting perpendicular distance between the two benzene rings is the smallest (**1**, 2.36 Å; **2**, 2.63 Å; **3**, 2.69 Å). As the result, the degree of rotation and hence the magnitude of the sliding motion of **1** is limited to have smaller value than **2** and **3**.

While the structure of **2** in solution is known to be identical to that found in the crystalline state, that of **1** is quite different from the structure obtained by the above analysis. ^{1}H-NMR spectral data for **1** and **2** and shift differences from their reference compounds; 1,2-bis(methoxymethyl)benzene (**4**), 1,2-bis[(methylthio)methyl]-

Table 1. ^{1}H-NMR chemical shifts (δ_{CDCl_3}, ppm) of **1** and **2** and shift differences[a)] from those of **4** and **5**

Compound	CH2	Aromatic	
		ortho-	meta-
1	4.74[b)]	7.25	7.25
$\Delta\delta_{1-4}$	0.23	-0.11	-0.02
2	3.44[b)]	7.61	7.27
$\Delta\delta_{2-5}$	-0.41	0.39	0.08

a) - denotes up-field shift. b) Singlet.

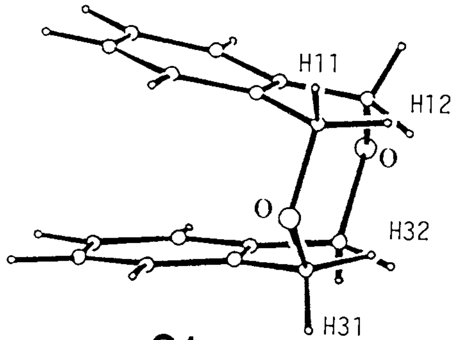
benzene (5) are collected in Table 1. Although 2 shows shift differences ($\Delta\delta_{2-5}$); upfield shift of CH_2 signal and down field shift of aromatic hydrogens, characteristic to the chair conformation3) the shift differences of 1 ($\Delta\delta_{1-4}$) are completely reverse, namely methylene signals show down field shift and aromatic hydrogens show upfield shift. 7) These shift values cannot be explained by the chair conformer found in its crystalline state. The characteristic downfield shift of methylene hydrogens suggested that these hydrogens should be located in deshielding zone of the magnetic anisotropy of the opposite benzene ring.

In order to find correct structure in solution, all the plausible structures were generated by MM2 calculation with the aid of our MMRS program,8) which generates all the possible initial geometries by the use of a tree search type ring closure algorithm.9) The above calculation gave us three syn and 11 anti structures as candidates. The shift values for individual methylene hydrogens of every structures were estimated by ring current method.10) The results of some of the structures are summarized in Table 2. Since 1 has dynamic processes

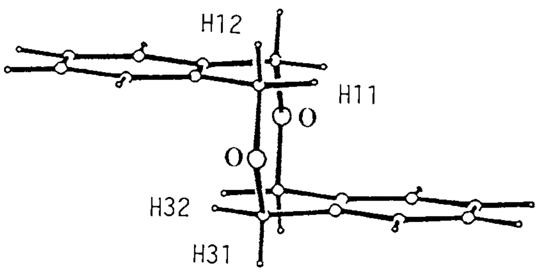
Table 2. The calculated shift differencesa) for indivisual methylene hydrogen of the selected conformers from the observed chemical shift of 4.

	S1	A1(X-ray)	A2	A3
H11	-0.054	-0.967	-0.939	0.275
H12	0.026	-0.130	0.003	0.182
H31	-0.053	-0.122	0.210	0.276
H32	0.026	-0.930	0.113	0.183
av.	-0.017	-0.539	-0.146	0.231

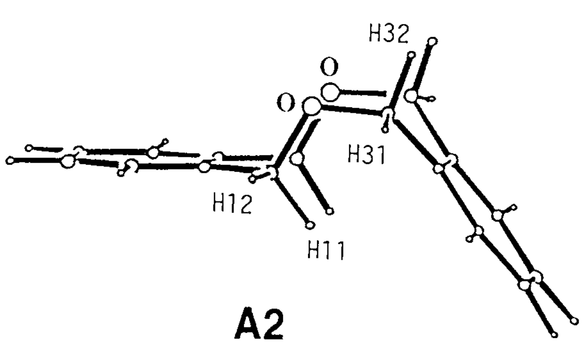
a) - denotes up-field shift.



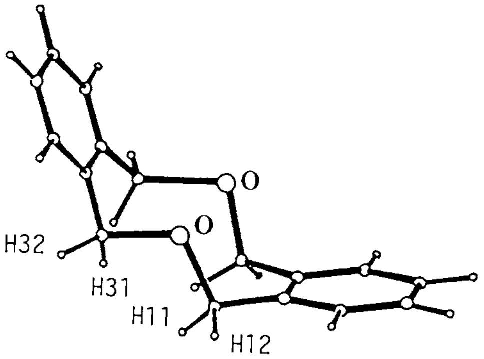
S1



A1(X-ray)



A2



A3

which equalize all the methylene hydrogens, these values should be averaged for comparison with the observed shift value. While the value of the X-ray structure (**A1**) is opposite in its sign, that for **A3** conformer is very close to the observed one (0.23 ppm). And none of the other conformers can give shift value compatible to the observed shift. The close agreement of the two values can be the evidence for the predominance of **A3** conformer in the solution.[11] Throughout this study we have exemplified that the combination of molecular mechanics and our ring current calculations can be a useful tool for the conformational analysis of flexible molecules containing aromatic rings.

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5) The crystallographic data for **1** are as follows: Monoclinic, $P2_1/n$, a=11.389(3), b=6.661(1), c=8.009(3) Å, β=95.12(3)°, z=4, R=0.041.

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7) The nmr spectrum of **1** in CD_2Cl_2 is not temperature dependent down to -70 °C, suggesting that a single conformer is predominant.

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10) The aromatic hydrogens especially ortho to the methoxymethyl group of **4** are susceptible to various influences such as steric compression and magnetic anisotropy effect of the C-O bond of the substituent. From this reason the comparison of the observed and calculated shift values may give misleading conclusion, since it is very difficult to identify the most stable conformer of **4**.

11) The same conclusion is true in various solvents, since the observed shift values of the methylene signals of **1** are almost the same in different solvents($\Delta\delta_{1\text{-}4}$; CCl_4, 0.20; $CDCl_3$, 0.23; CD_3COCD_3, 0.20; CD_3OD, 0.20 ppm).

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