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Conformational Properties of the Ethers of Hydroxy[2_4]metacyclophanes1)

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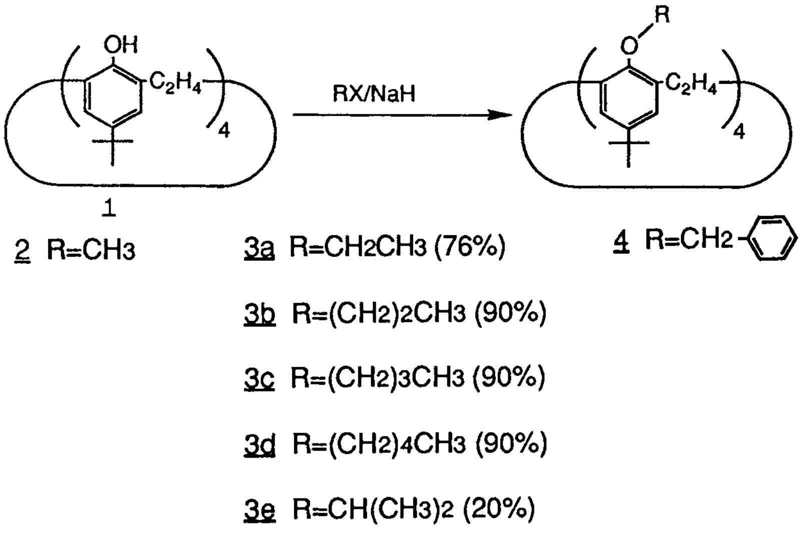
Ethyl, propyl, isopropyl, butyl, pentyl and benzyl ethers of hydroxy[2_4]metacyclophanes were prepared. One of the conformers of the benzyl ether was confirmed to assume "cone" conformation by ^{1}H NMR and X-ray analysis.

We have reported the preparation of metacyclophanes which have three or four aromatic rings in their skeleton and disclosed their some uniqe properties.2,3) On the other hand, calixarenes,4,5) consisting of several phenolic units which are linked by methylene bridge at meta positions, have attracted considerable interest in the last decade, because they are easily prepared and their derivatives are useful potentially as enzyme mimics.6) One of the most important characteristics making calixarenes a basic skeleton for practically useful molecules is conformational feature. The conformational properties of calix[n]arenes7,8) and the ethers of them9,10) have been clarified by several groups. Their studies suggested that a bulky group which was introduced into the OH group had much effect on the conformational freedom of calixarenes. Due to this restraint effect, some isomers were isolated in several cases. However, the relation between the isomer formation and the structure of calixarenes has not been clarified adequately. A structural variety in calixarene-like compounds would offer more information about this.

In the present study, we show the conformational behavior of [2_4]metacyclophane derivatives.

The parent compound 1, synthesized from anisole in several steps as reported previously,3) was treated with RX(R=Ethyl, Propyl, Butyl, Pentyl, Isopropyl, Benzyl) in the presence of NaH to give the corresponding ethers of 1. The yield of 3e was not good because a disubstituted derivative was also formed(20%). The portions of ^{1}H NMR spectra for the ethylene bridge protons in 2 and 3a-3e are shown in Fig.1. 2 showed a sharp singlet down to -100 °C ; however, 3a showed a broadened peak at -100 °C. Coalesence temperatures of 3b, 3c, and 3e are 98 °C, above 120 °C, and 0 °C,



1

2 R=CH3

3a R=CH2CH3 (76%)

3b R=(CH2)2CH3 (90%)

3c R=(CH2)3CH3 (90%)

3d R=(CH2)4CH3 (90%)

3e R=CH(CH3)2 (20%)

4 R=CH2-

respectively. The great difference of Tc between 3a and 3b (over 200 °C) was observed, suggesting that the slight difference of the length in the substituent R had much effect on the conformational inversion. 3b, 3c, and 3d give a complex multiplet at room temperature indicating less flexibility than 2 or 3a. Isopropyl derivative 3e which shows a broadened singlet is conformationally more flexible than the propyl derivative 3b. But even at low temperatures(-60 °C—100 °C), all these compounds did not show well resolved spectra enough to assign their conformers. Treatment of 1 with benzyl bromide gave 4 as a mixture of conformers in 60% yield accompanied by inseparatable materials. Interestingly, this mixture was separated into three kinds of conformers, 4-1(10%), 4-2(10%), and 4-3(20%), by using a TLC plate repeatedly. They are not interconvertible to each other at 200 °C in the solid state. The partial ^{1}H NMR for ethylene and aromatic protons in these conformers are shown in Fig 2. These spectra did not change in the range of +50 °C to -40 °C at all. In 4-1 two kinds of

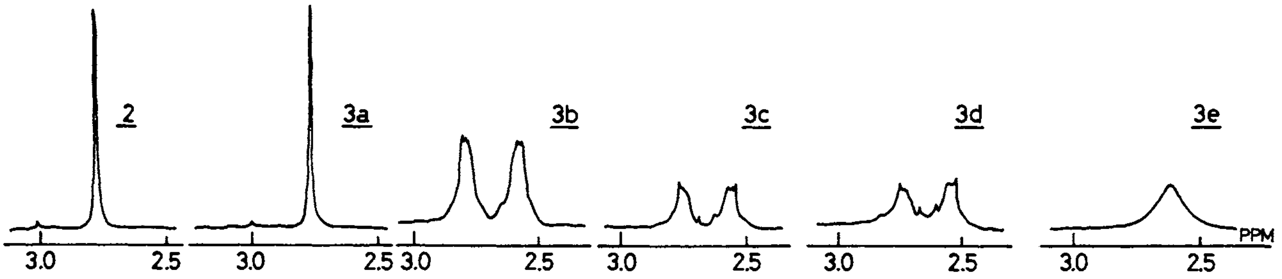


Fig.1. Partial ^{1}H NMR(100 MHz) sprctra for ethylene protons of 2 and 3 in CDCl3 (27 °C).

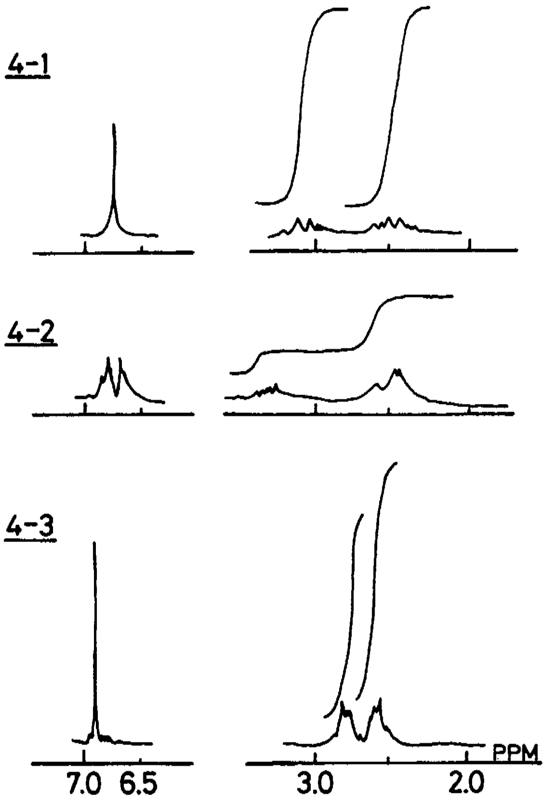


Fig.2. Partial ^{1}H NMR(270 MHz) spectra for ethylene and aromatic protons of 4 in CDCl$_3$ (27 °C).

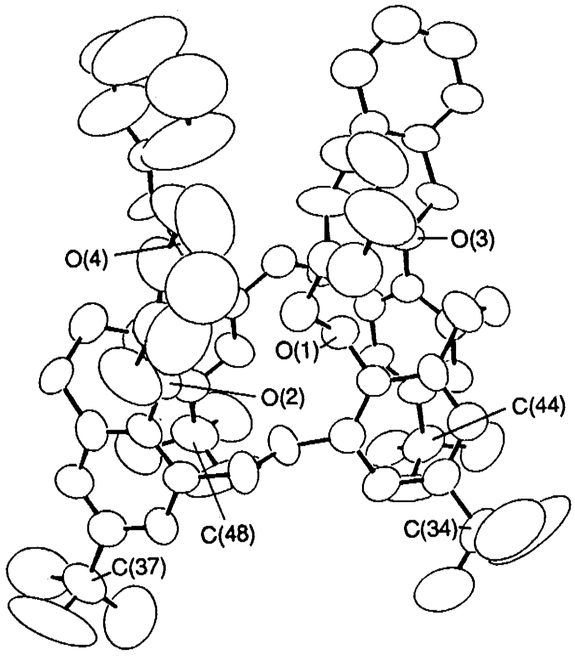


Fig.3. Perspective view of 4-1 : t-butyl carbon and oxygen atoms are numbered.

peaks in the ratio of 1:1 in the methylene region and singlet arising from aromatic protons are observed, which can be interpreted in terms of a "cone" conformation. This is also strongly suggested by X-ray analysis[11] shown in Fig.3. 4-2 is considered to assume "1,2-alternate" conformation because of two kinds of peaks in the ratio of 1:3 in the methylene region and two broad singlets in the aromatic region. On the other hand the spectrum of 4-3 is similar to that of 4-1 which assumes "cone" conformation. Thus, 4-3 seems to assume "1,3-alternate" conformation ; however, at present time it is not successful to get the crystal appropriate for X-ray analysis.

Gutsche et al.[9] have reported that the benzyl ether of calix[6]arene existed as a mixture of conformers at -60 °C and the benzyl ether of calix[4]arene did as a rigid "cone" conformation. From these results it is postulated that the mobility of 4 is intermediary between the calix[4]arene and the calix[6]arene.

In conclusion we demonstrated that the [2_4]metacyclophanes assume the conformation similar to that of calixarenes, and an introduction of a bulky group makes the conformational flexibility restricted in the $[2_4]$metacyclophane system. The present study also indicates that the concept of calixarene would be extended to other macrocyclic metacyclophanes.

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11) Crystal data for 4-1:$C_{76}H_{88}O_4$, M=1065.53, monoclinic, space group C2/c, a=49.184(18), b=14.227(9), c=19.765(7) Å, β=109.34(3)deg., U=13052.2 $Å^3$, Z=8, Dc=1.085 g cm^{-3}, $\mu(Mo\text{-}K_\alpha)$=0.60 cm^{-1}, Enraf-Nonius CAD-4 diffractmeter, 3527 reflections with $I_0>3\sigma(I_0)$, R=10.4%.

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