

Conformational Properties of [n.2.2]- and [n.3.3]Metacyclophanes

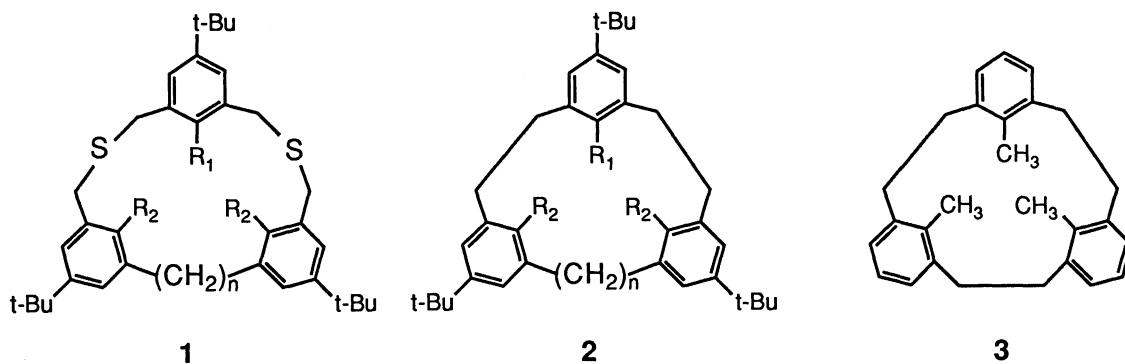
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Metacyclophanes having three aromatic rings in their skeleton were prepared. Their conformational properties were estimated by the ^1H NMR spectra and the X-ray analysis. It was proved that they assume a "folded inwards" or an "alternate" conformation depending on a slight difference in the structure of the internal substituent.

Cyclophane compounds have been attracting a great interest in many fields of chemistry.¹⁾ We have been devoting a development of the preparation routes for metacyclophanes(MCPs) and also disclosing their characteristics.²⁻³⁾ In general MCPs consisting of two aromatic rings are known to have a strained and rigid structure. On the other hand MCPs having more than four aromatic rings, including topical calixarenes,⁴⁾ are flexible and exhibit particular conformers. However it is surprising that knowledge of MCPs which have three aromatic rings in their skeleton is very limited.⁵⁾ From these points of view we have been quite interested in these kinds of MCPs. In the present study we show the conformational properties of [n.2.2]- and [n.3.3]MCPs.

Cyclophanes **1**, **2**, and **3** were prepared according to our reported method.^{3a)} Chemical shifts of terminal protons in R_1 and R_2 together with those of the corresponding R_1 -substituted benzene analogs(R_1Ph) are summarized in Table 1. Coalescence temperature(T_c) and ΔG^\neq determined by temperature-dependent ^1H NMR technique are also shown in Table 1. Terminal protons of R_1 of [2.3.3]MCPs(**1a**,**1b**,**1i**) show a remarkable upfield shift compared with those of the corresponding substituted benzenes(R_1Ph). Such considerable upfield shifts of terminal protons are observed for R_1 of dithia[1.3.3]MCPs(**1j**,**1k**) and for one of the substituents (R_1 or R_2) of



[2.2.2] and [1.2.2]MCPs. These shifts might arise from a strong shielding effect of aromatic rings, thus it is deduced that these cyclophanes adopt a "folded inwards" conformation shown in Fig.1, in which one aromatic ring folds into the cavity formed by two other aromatic rings. The assumption of this conformation can be assured by the X-ray analysis of **2I-B**⁶ (Fig.2), indicating "folded inwards"

Table 1. Chemical shifts,^{a)} T_c, and ΔG[≠] of cyclophanes

	(R ₁)	δ/ppm		T _c /°C	ΔG [≠] /kcal mol ⁻¹	A:B ^d
		R ₁ ^{b,c)}	R ₂			
1(R ₂ =CH ₃ , n=2)	a (CH ₃)	0.15(2.38) ^{3a)}	2.19	-5	13.1	
	b (CH ₂ CH ₃)	0.06(1.20)	2.11	27	14.8	
	c ((CH ₂) ₂ CH ₃)	0.91(0.92)	2.23	>140	-	
	d (OCH ₃)	3.49(3.88)	1.28	-5	12.9	
	e (OCH ₂ CH ₃)	1.34(1.38)	1.23	135	20.4	
	f (O(CH ₂) ₂ CH ₃)	1.03(1.00)	1.21	>140	-	
	g (O(CH ₂) ₄ CH ₃)	0.95(0.92)	0.95	>140	-	
1(R ₂ =OCH ₃ , n=2)	h (OCH ₃)	3.64(3.88)	3.45	5	13.7	
	i (CH ₃)	0.32(2.38)	3.60	30	14.8	
1(R ₂ =CH ₃ , n=1)	j (CH ₃)	0.17(2.38)	2.31	0	13.0	
	k (OCH ₃)	2.52(3.88)	2.00	5	13.5	
1(R ₂ =OCH ₃ , n=1)	l (OCH ₃)	3.38(3.88)	3.90	25	14.6	
2(R ₂ =CH ₃ , n=2)	a (CH ₃)	0.60, 1.63				
	b (CH ₂ CH ₃)	0.63	1.62			
	d (OCH ₃)-A	1.42	1.72			1:2.5
	d -B	3.44	0.62, 1.53			
	e (OCH ₂ CH ₃)	1.24	0.57, 1.50			
	f (O(CH ₂) ₂ CH ₃)	0.96	0.55, 1.46			
	g (O(CH ₂) ₄ CH ₃)	0.92	0.56, 1.45			
2(R ₂ =OCH ₃ , n=2)	h (OCH ₃)	1.46	3.44			
	i (CH ₃)-A	0.60	3.25			1:2
	i -B	1.68	1.41, 3.42			
2(R ₂ =CH ₃ , n=1)	j (CH ₃)-A	0.51	1.66			1:2
	j -B	1.44	0.28, 1.66			
	k (OCH ₃)	3.28	0.56, 1.68			
2(R ₂ =OCH ₃ , n=1)	l (OCH ₃)-A	1.21	3.44			1:2
	l -B	2.64, 3.17, 3.24				
3(R ₂ =CH ₃ , n=2)	(CH ₃)	0.72, 1.68 ^{3a)}				

a) In CDCl₃, 27 °C. b) Chemical shifts of terminal protons. c) Corresponding chemical shifts of R₁-substituted benzenes(R₁Ph) are shown in the parentheses. d) Ratio of two conformers.

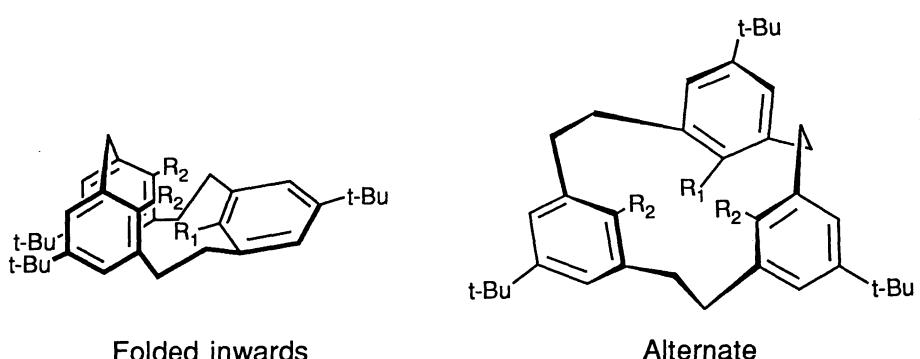
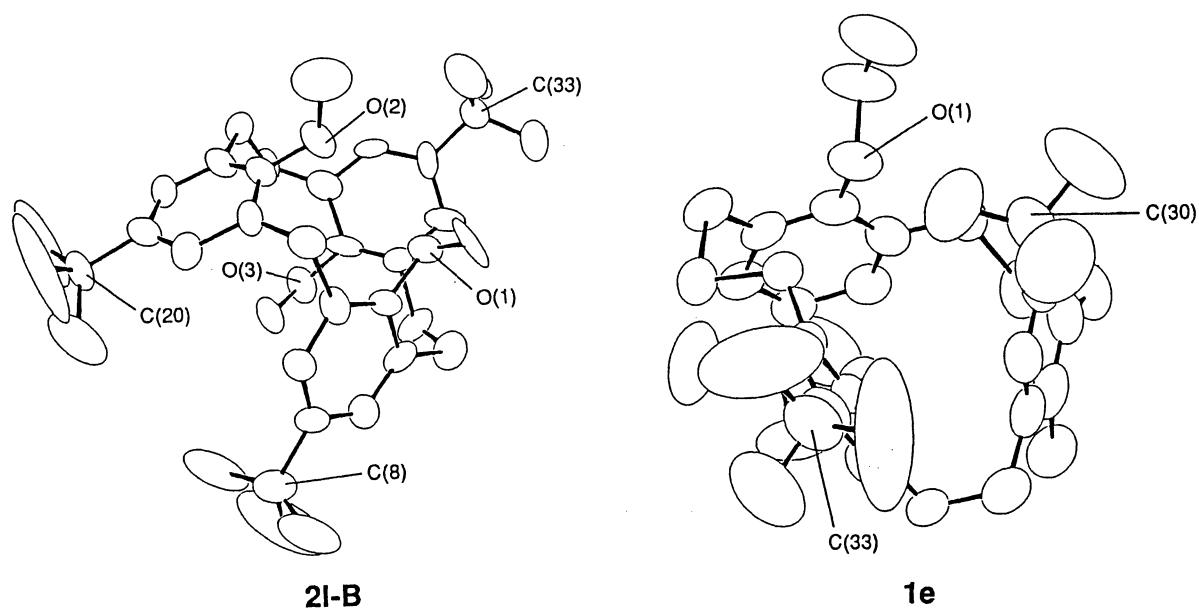


Fig.1. Schematic illustration of conformers.

Fig.2. Perspective view of **2I-B** and **1e**: t-butyl carbon and oxygen atoms are numbered.

conformation with one methoxy group which obviously plunges into the cavity. We already reported^{3c}) the reactivity of **2I** toward BBr_3 in which it was shown **2I-A** also adopted a "folded inwards" conformation. On the other hand in dithia[2.3.3]MCPs when R_1 is propyl group(**1c**), or ether group(**1d-h**) terminal protons of R_1 do not show upfield shifts as seen in **1a** or **1b**, from which it is expected that they adopt a different conformation. In fact an "alternate" conformation is regarded by X-ray analysis of **1e**⁷)(Fig.2). This conformation illustrated in Fig.1 is consistent with the result that no shielded portion exist. Although methoxy group and ethyl group are of almost same size, conformation of **1b** is totally different from that of **1d**. Some dithiaMCPs exhibit T_c . As shown in Table 1 the substituent R_1 plays a decisive role on the inversion barrier. It is also found that the difference of one methylene in R_1 could cause the increase of T_c by ca. 100 °C (comparing

1b with **1c**, or **1d** with **1e**), however, the substituent R_2 alters the conformational mobility to a negligible extent. On the contrary T_c was not observed in any [2.2.2] or [1.2.2]MCPs, indicating they are very rigid. One example of de-tert-butylatedMCP **3** is also shown in Table 1. It is postulated that conformational properties are little affected by the substituents locating outside of the ring. The substituent R_1 in the dithiaMCPs is inevitably folding because of the flexible thioether connector. However for the MCPs carrying different substituents as R_1 and R_2 two kinds of conformers(**A** and **B**) are supposed to exist. One of them(**A**) has the folded R_1 and the other(**B**) has the folded R_2 , in fact, they were identified for **2d**, **2i**, **2j** and **2l**. Ratio of two conformers(**A**:**B**) estimated from the 1H NMR is shown in Table 1. Considering they have one R_1 and two R_2 , this value(1:2) is reasonable.

In conclusion MCPs having three aromatic rings can adopt a "folded inwards" or an "alternate" conformation, especially the former one is very specific.

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- 6) Crystal data for **2l-B**: $C_{38}H_{52}O_3$, $M=556.84$, monoclinic, space group $Pna21$, $a=22.5437(55)$, $b=8.4266(22)$, $c=18.0367(37)$ Å, $\beta=90.00$ deg., $U=3424.75$ Å 3 , $Z=4$, $D_c=1.080$ g cm $^{-3}$, $\mu(Mo-K\alpha)=0.60$ cm $^{-1}$, Enraf-Nonius CAD-4 diffractometer, 1830 reflections with $I_0>3\sigma(I_0)$, $R=9.5\%$.
- 7) Crystal data for **1e**: $C_{40}H_{50}OS_2$, $M=617.02$, monoclinic, space group $P2_1/c$, $a=10.157(2)$, $b=16.830(3)$, $c=22.386(6)$ Å, $\beta=91.12(2)$ deg., $U=3826.2$ Å 3 , $Z=4$, $D_c=1.071$ g cm $^{-3}$, $\mu(Cu-K\alpha)=14.2$ cm $^{-1}$, Enraf-Nonius CAD-4 diffractometer, 5739 reflections with $I_0>3\sigma(I_0)$, $R=9.9\%$.

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