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[5]METACYCLOPHANES
A SPECTROSCOPIC AND THEORETICAL INVESTIGATION OF STRUCTURE AND CONFORMATION

L.A.M. Turkenburg, W.H. de Wolf, and F. Bickelhaupt*
Vakgroep Organische Chemie, Vrije Universiteit
De Boelelaan 1083, 1081 HV Amsterdam, The Netherlands

W.P. Cofino
Vakgroep Analytische en Algemene Chemie
Vrije Universiteit, Amsterdam

K. Lammertsma
Hydrocarbon Research Institute and
Department of Chemistry
University of Southern California, Los Angeles

Abstract: The ^{1}H NMR spectra of [5]metacyclophane (1a) and of its 8,11-dichloro derivative 1b are reported. 1a Has a rigid conformation A between -50 and +150 °C. Conformation A is also the preferred one (85%) for 1b at -47 °C, but 1b-A is in equilibrium with a second conformer 1b-B, for which spectral parameters can be derived. A and B correspond with two energy minima predicted by MNDO calculations.

One of the most intriguing aspects of the recently synthesized small [n]para-[1] and [n]metacyclophanes[2] is their stereochemistry, in particular the question of bending of the benzene ring and the conformation of the oligomethylene bridge. Molecular mechanics[3] and MNDO[4] calculations have been reported, but X-ray crystal structures are known only for [n]paracyclophanes[5]. However, NMR spectroscopy has proven to be useful in the elucidation of their conformations. At low temperatures, both [6]para-[1b,c] and [6]metacyclophane[2a] have a frozen conformation of the bridge; on warming up, dynamic phenomena reveal a limited mobility of the bridge on one side of the aromatic ring. In addition, at higher temperatures, the bridge in [6]metacyclophane can flip to the other side of the aromatic ring, causing considerable simplification of the NMR pattern by coalescence[2a]. We here report on the structure and conformation of [5]metacyclophane (1a)[2b] and of its 8,11-dichloro derivative 1b[2e] as determined from an analysis of their ^{1}H NMR spectra and from MNDO calculations.

The 250 MHz ^{1}H NMR spectrum of 1a was essentially unchanged[2b] between -50 and 150 °C; apparently, no conformational changes occur in this temperature range. The spectrum revealed C_S symmetry and could be simulated[6] with the parameters in Table 1. Contrary to simple intuition, the two high field protons (δ=0.25 ppm) are not those of the γ-methylene group (H(7), H(8)), but belong to the β-methylene groups (H(9)). This is only possible if H(9) is shielded by the aromatic ring, as in conformation A (Fig. 2; vide infra). The low field shift of H(1) is caused by compression[2a] against H(8) and H(4).

The 250 MHz ^{1}H NMR spectrum of 1b at -47 °C (Fig. 1a) is very similar to that of 1a. The chemical shifts (Table 1) are somewhat different; major differences are found with H(4) and H(8); which are probably caused by the proximity of the chlorine at C(11). Nevertheless, the coupling constants are identical[7], implying an identical conformation of both bridges.

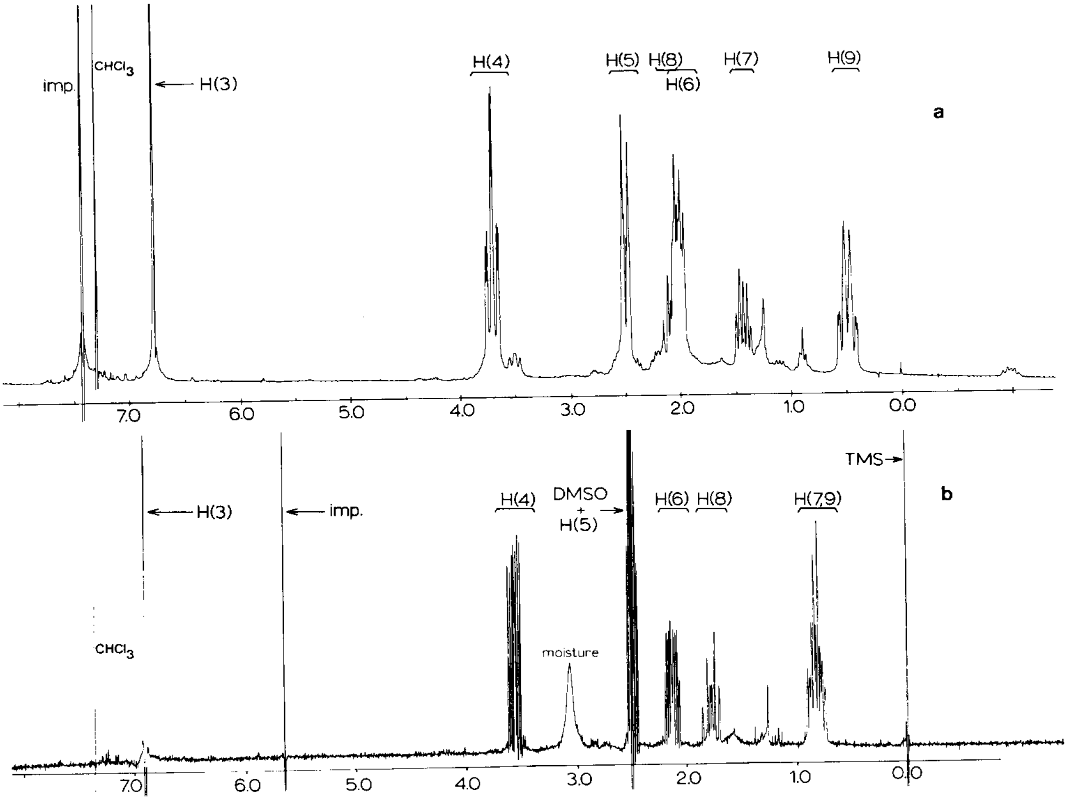

Fig.1. ^{1}H NMR Spectrum of 1b (250 MHz) (a) at -47 °C in $CDCl_3$; (b) at 125 °C in DMSO-d_6

On closer inspection , the spectrum reveals low intensity signals (originally ascribed to "impurities"), e.g. at δ=3.52 and -0.98 ppm. By spin saturation transfer[8], it was established that these signals correspond to protons which are in slow exchange on the NMR time scale with H(4) and H(7), respectively. Furthermore, and in contrast to 1a, the spectrum of 1b was reversibly temperature dependent. On warming up, the signals broaden and shift. At about 125 °C, high resolution is again observed (Fig. 1b). The new spectrum has the same degree of complexity as that at -47 °C, which means that all protons retain their identity in the dynamic process involved.

Table 1. 250 MHz ^{1}H NMR spectrum of 1a and 1b

H (No.)*	δ (ppm) 1a ($CDCl_3$;30 °C)	1b ($CDCl_3$;-47 °C)	1b (DMSO-d_6;125 °C)
1	7.83	-	-
2	7.19	-	-
3	6.81	6.76	6.92
4	2.85	3.70	3.54
5	2.54	2.50	2.51
6	1.92	≈ 2.0	2.11
7	1.67	1.44	≈ 0.8
8	1.33	2.07	1.76
9	0.25	0.49	≈ 0.8

$^3J_{HH}$ 1a (No.)*	(Hz)	(No.)*	(Hz)
1-2	<0.5	5-9	3.3
1-3	1.1	6-9	14.4
2-3	7.0	6-7	7.7
4-5	12.5	6-8	<0.5
4-6	3.0	9-7	1.1
4-9	12.3	9-8	10.6
5-6	3.3	7-8	16.2

* for numbering of the protons, see Fig. 2.

Inspection of models suggested that these observations can be explained by the occurrence of two conformations 1b-A and 1b-B of comparable energy. At -47 °C, their equilibrium is slow on the NMR time scale, and from the integral ratios of H(4) or H(7) (A:B ≈ 85:15), $\Delta\Delta G_{AB}^{-47}$ = 0.77 kcal.mol^{-1} can be derived. At 125 °C, the position of the equilibrium can be estimated from the difference in the chemical shift of H(7)^{9} to be approximately A:B = 75:25, which leads to $\Delta\Delta G_{AB}^{125}$ = 0.86 kcal.mol^{-1}, and further to $\Delta\Delta H_{AB}$ ≈ 0.7 kcal.mol^{-1} and $\Delta\Delta S_{AB}$ ≈ -0.5 e.u..

In excellent agreement with these experimental data, MNDO^{10} calculations also reveal two conformations A and B of minimal energy for 1a and 1b (Fig. 2), with A (1a-A : ΔH_f = 45.7 kcal.mol^{-1}; 1b-A : ΔH_f = 34.7 kcal.mol^{-1}) slightly favoured over B (1a-B : ΔH_f = 46.9 kcal.mol^{-1}; 1b-B : ΔH_f = 35.1 kcal.mol^{-1}). As both A and B are very rigid, it is reasonable to find $\Delta\Delta S_{AB}$ ≈ 0; for 1b, the calculated value of $\Delta\Delta H_{AB}$ = 0.4 kcal.mol^{-1} is in good agreement with the experimental one. A tentative calculation of the transition barrier between A and B revealed a maximum for the planar conformation of the bridge with $\Delta H^{\ddagger}$ = 18.9 and 19.0 kcal.mol^{-1} for 1a and 1b, respectively. This value is in the range expected for the observed coalescence phenomena of 1b; it is at present not understood why 1a, having the same calculated barrier as 1b, occurs in conformation A only.

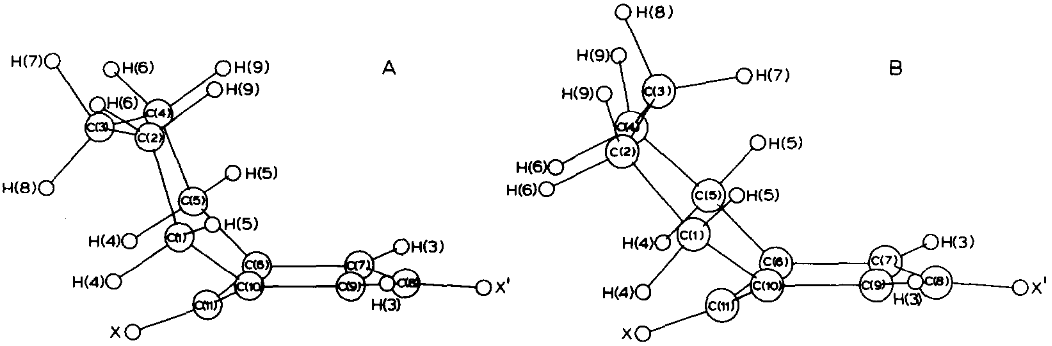

Fig.2. Calculated conformations A and B of 1a (X=H(1), X'=H(2)) and 1b (X=X'=Cl).

The experimental δ and J values are in good agreement with the calculated structures^{11}. The most spectacular change from A to B is the upfield shift of H(7) (Δδ=-2.44 ppm), which moves from an unshielded position into the shielding cone of the aromatic ring. An impressive downfield shift is observed for H(9) (Δδ=+1.47 ppm) which makes the opposite movement.

Finally, it is of interest to mention that the MNDO optimized structures of 1a and 1b reveal considerable distortion of the benzene ring which has a boat shape. This deviation from planarity and the consequent loss of resonance energy is reflected in the observed high reactivity of 1a[2d,f]; presumably for electronic reasons, 1b is somewhat less reactive[2e].

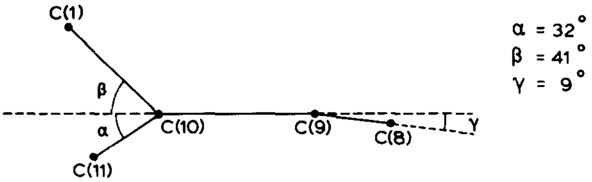

Fig.3. Side view of 1a-A

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6. Spectrum simulation was performed with the ITRCAL program.
7. The only difference was observed for $J_{H(4)H(9)}$: J=12.3 Hz in 1a, J=12.5 Hz in 1b!
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9. A correction has to be applied for the change from $CDCl_3$ to DMSO-d_6; at 65 °C, this correction was determined for H(7) to be $\Delta\delta \approx + 0.02$ ppm. The correction varies for the different protons and inevitably introduces some degree of uncertainty in both δ and ΔG. This will be discussed in more detail in a full paper.
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11. For 1b-B, δ and J values can be derived from the values of Table 1, accounting for solvent corrections[9]; they will be discussed in a full paper.

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