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NMR STUDIES OF CONFORMATIONS AND DYNAMIC PROCESSES—III

CYCLOPHANES WITH UNSATURATED BRIDGES

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Abstract—Three cyclophanes, each displaying a different type of dynamic process, have been studied by NMR methods. The barriers to these processes are attributed mainly to the decrease in π-electron overlap between the benzene rings and adjacent double bonds which occurs in the transition state for each process. In [5$_2$] paracyclophanetetraene, two successive flippings of the benzene rings interconvert the two hydrogens in the methylene groups (Scheme 1). In tetramethyl [2$_4$] paracyclophanetetraene, the passage of one methyl group through the central cavity of the molecule interconverts two conformations of similar, but not equal, free energy (Scheme 2). In [2$_6$] orthoparacyclophanehexaene, the orthosubstituted rings change sides by passing through the centre of the cyclophane (Scheme 3).

In the preceeding papers[1,2] we have discussed the conformational processes in some unstrained cyclophanes with ethylene bridges. The important, and measurable, barriers were all caused by the same type of interaction as that which occurs between the aryl groups in *syn* 1,2-diarylethane. The barriers to rotation about the sp^2–sp^3 C—C bonds were assumed to be smaller and were observable only at very low temperatures. In the cyclophanes with unsaturated bridges discussed here, the situation is different. Delocalisation of π-electrons is possible in relatively planar conformations, and the geometry of the cyclophanes with unsaturated bridges is determined by the balance between the resonance energy available from delocalisation of the π-electrons and the steric interactions present in the relatively planar conformations. The barriers to the rotation of the benzene rings are essentially due to the loss of π-electron overlap which occurs on rotation.

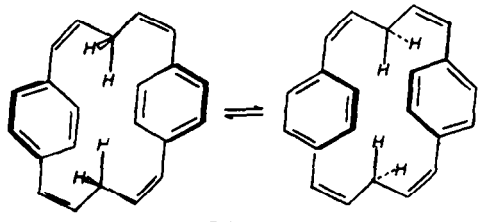
Three types of dynamic process are discussed in this paper; the passage of a methylene group between the faces of two benzene rings in [5$_2$] paracyclophanetetraene (Scheme 1); the rotation of the aromatic rings in [2$_4$] paracyclophane-tetraenes (Scheme 2); and the passage of *ortho*-substituted benzene rings through the centre of [2$_6$] orthoparacyclophane-hexaene, an inversion-like process (Scheme 3). Similar types of process have been reported separately for some [2$_4$] naphthalenophanes[3] and [2$_4$] ferrocenophanes.[4]

RESULTS AND DISCUSSION

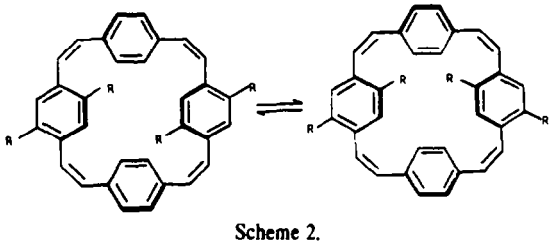
[5$_2$] *Paracyclophanetetraene*, 1

The cyclophane 1 was prepared by a fourfold Wittig reaction between benzene-1,4-dicarbaldehyde and the bistriphenylphosphonium salt from 1,3-dibromopropane. The ^{1}H NMR spectrum of 1 in toluene-d_8/CD_2Cl_2 at room temperature showed the expected simple pattern with a small upfield shift of the aromatic protons (δ 6.75) and the signals from the methylene protons (δ 3.08). Low temperature spectra in the same solvent showed two multiplets, at 3.63 and 2.22, for the methylene protons and two singlets, at 6.81 and 6.43, for the aromatic protons. The methylene signals coalesced at *ca* 200K, the aromatic ones at *ca* 190K. Simple calculation of the barrier from the coalescence temperatures and shift differences gives 37 kJ mol^{-1} for both the methylene and the aromatic signals. Thus, one process with a barrier of *ca* 37 kJ mol^{-1} nicely explains the NMR data and the observations are consistent with the process outlined in Scheme 1. The two singlets (without *ortho* couplings) observed for the aromatic protons at 158 K show that there must be an apparent plane of symmetry perpendicular to the longest axis in 1. Molecular models of the cyclophane 1 do not indicate any unfavourable steric interactions in the sandwich-like conformer 1D (Scheme 4) which is one possible model for the transition state for the dynamic process. It thus seems reasonable to assume that loss of π-electron overlap between the benzene rings and the vinyl groups determines the barrier.

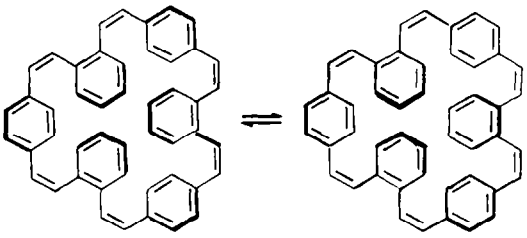
Regarding the structure of the most stable conformation, closer inspection of models reveals that there are



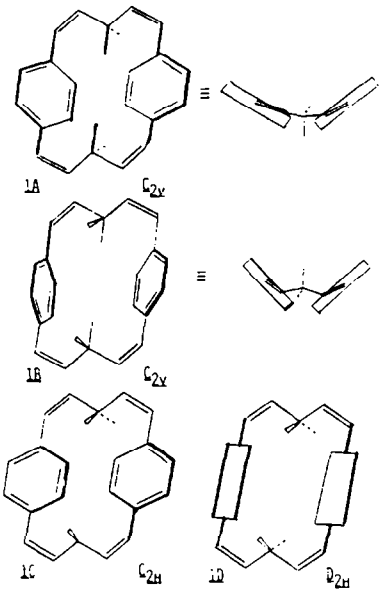
Scheme 1.



Scheme 2.



Scheme 3.



Scheme 4.

two possibilities which are consistent with the above-mentioned criteria of maximum planarity and minimum steric interactions, namely, structures **1A** and **1B**, which differ in the orientation of the methylene groups (Scheme 4). The large difference between the shifts of the geminal methylene protons at low temperature is best explained by structure **1A**, in which one of the methylene protons is shielded by the benzene rings, and the other is deshielded. In structure **1B**, one of the methylene protons is located in a neutral zone of the anisotropy of the benzene rings. Structure **1A** is more crowded than **1B**, however. The conformational barrier to the interconversion of the geminal methylene hydrogens must come from the decrease of the π-electron overlap in the transition state for the inversion process. The highly symmetrical sandwich conformation **1D** (D_{2h}-symmetry) in which the overlap of the π-electrons in the benzene rings and the vinyl groups is lost, is thus not a necessary intermediate for the dynamic process. Instead, successive flippings of the benzene rings in **1A** (or **1B**) via **1C** to **1B** (or **1A**) followed by rapid equilibration to **1A** (or **1B**) will interconvert the geminal hydrogens in the methylene groups as well as "outer" and "inner" aromatic protons. If so, the barrier should be roughly twice the torsional barrier in styrene, calculated[5] to *ca* 18 kJ mol^{-1}, but considered to be smaller from experimental results.[6]

Tetramethyl [2$_4$] paracyclophanetetraene, 2 R = -CH$_3$

In [2$_4$] paracyclophanetetraenes the delocalisation of π-electrons around the perimeter of the molecule is possible if the structure is relatively planar. An X-ray structure determination[7] and a molecular mechanics calculation[8] both show that the benzene rings in [2$_4$] paracyclophanetetraene, **2** R = H, are twisted, on average, 35° out of the molecular plane. Formally, the number of π-electrons around the perimeter is 24 and thus no extra resonance stabilisation is to be expected.

The ^{1}H NMR spectrum of **2** R = H shows a singlet for the aromatic protons, even at 150 K. The rotation or flippings of the benzene rings must therefore be fast on the NMR time scale even at low temperature. In the radical anion,[9] as well as in the di- and tetra-anions,[10] the delocalisation of the π-electrons is more important and the barrier to rotation is much higher. There should be two types of energy maximum on rotation of the benzene rings in **2** R = H; one, due to decreased π-electron overlap, when the benzene ring is perpendicular to the adjacent vinylene bridges and another when the benzene ring is coplanar with the vinylene bridges, leading to steric repulsions between the inner hydrogens. The former maximum should be higher in **2** R = H. However, in tetrasubstituted [2$_4$] paracyclophanetetraenes, **2** R ≠ H, the latter maximum could be higher and two conformers might be observable and amenable to study by NMR methods (Scheme 2). By our standard procedure, such cyclophanes can readily be prepared by fourfold Wittig reactions using relatively simple aromatic dialdehydes and bisphosphonium salts from bis(halomethyl)benzenes. We have prepared [2$_4$] paracyclophanetetraenes with four methoxy-,[11] methyl-,[12] ethyl-, chloro-, bromo- and iodo-substituents.[13] In most cases, the difference in the NMR spectra (270 MHz) of the two conformers is small or, alternatively, the rotation of the substituted benzene rings too fast. However, we found the tetramethyl derivative suitable for our purpose. The ^{1}H NMR spectrum of **2** R = -CH$_3$ shows two separate singlets for the methyl protons at 273 K in the approximate ratio of 2:1 (δ 2.10 and 2.05). The different intensities of the signals rule out the possibility of inner and outer Me groups and must arise from the expected two conformers which can interconvert only by the passage of one methyl group through the cavity in the centre of the molecule. At higher temperatures, the NMR singlets broaden, coalesce, and finally appear as one singlet. The coalescence temperature is *ca* 318 K. The signals from the aromatic and olefinic protons show a similar behaviour but are less well-separated.

It is not clear which of the two conformers, **2A** or **2B**, is of lower free energy (Scheme 5). No conclusion can be drawn from the small difference in the chemical shifts. Conformer **2A** has a twofold axis of symmetry and can exist in two mirror image forms, whereas conformer **2B** has only a mirror plane. Thus, on the basis of statistical factors (the respective symmetry numbers and mirror image forms) there is no difference in the free energy. Inspection of molecular models indicates that **2A** could be somewhat less strained than **2B**. It may also be noted that in the tetraethyl derivative, **2** R = -Et, two conformations seem to be present at room temeprature, one of which is dominant (>90%). By analogy, it seems reasonable to assume that steric effects are decisive and that **2A** is the more stable conformer.

The structures of **2A** and **2B** are uncertain. By analogy

with **2** R = H, a relatively planar arrangement of the benzene rings is favourable. However, the chemical shifts for the protons in the unsubstituted rings in **2** R = -Me are somewhat different than in **2** R = H, δ 6.97 and 7.32, respectively. More significant is the large difference in the rate of hydrogenation of **2** R = -Me and **2** R = H. The latter is quantitatively hydrogenated over Pd/C at room temperature in benzene or ethanol at atmospheric pressure in a few hours, whereas **2** R = -Me is only partially hydrogenated over Pd/C in ethanol at 120° and 12 atm. pressure after 48 hr. The difference in the electrochemical reduction potentials of the two compounds[12] is too small to explain the enormous difference in rate of hydrogenation. However, if the tetramethyl derivative, **2** R = -Me, strongly perfers the helix-like conformations in Scheme 5 (with D_2- and C_2-symmetries), then the interaction of the double bonds with a transition metal would be difficult and thus explain the slow rate of hydrogenation.

[2$_6$] *Orthoparacyclophanehexaene*, **3**

[2$_6$] Orthoparacyclophanehexaene, **3**, was prepared from benzene-1,2-dicarbaldehyde and the bistriphenylphosphonium salt from 1,4-bis(bromomethyl)benzene (by a sixfold Wittig reaction.[14] The ^{1}H NMR spectrum is simple, showing a singlet and an AA'BB'-pattern for the aromatic protons and an AB-pattern for the olefinic protons (Fig. 1), consistent with a threefold axis of symmetry in the molecule. Models (CPK) show that the *ortho*-substituted rings in the centre come close together and that two conformers are possible, **3A** and **3B** in Scheme 3, with all three and two *ortho*-substituted rings on the same side of the average molecular plane, respectively. Conformer **3A** has a bowl-shaped structure with a threefold axis of symmetry (C_{3v}) while conformer **3B** is less symmetrical (C_s). The difference in symmetry and thus, in symmetry numbers, affects the entropy and should lead to a threefold excess of **3B** over **3A** if steric and electronic effects were the same.

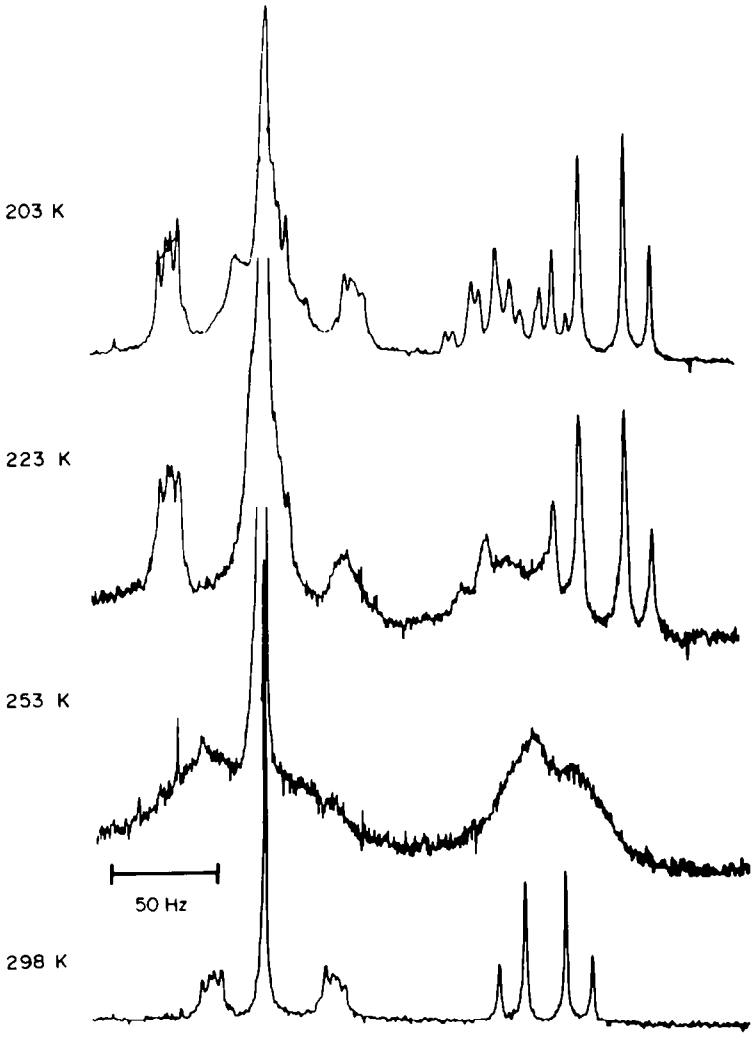
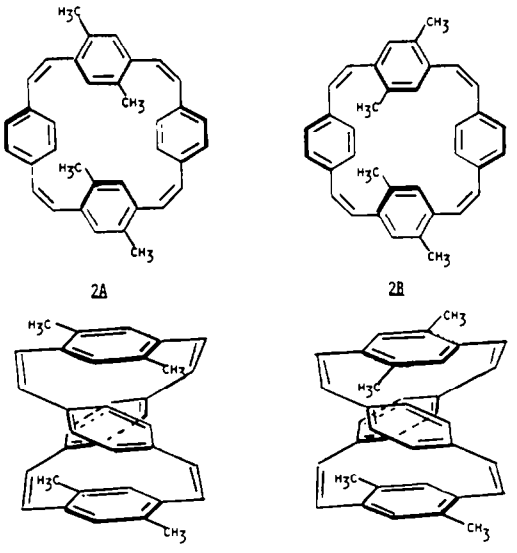


Fig. 1. ^{1}H NMR spectrum of [2$_6$] orthoparacyclophanehexaene, **3**, in CD_2Cl_2 at different temperatures. The aromatic/olefinic region is shown.

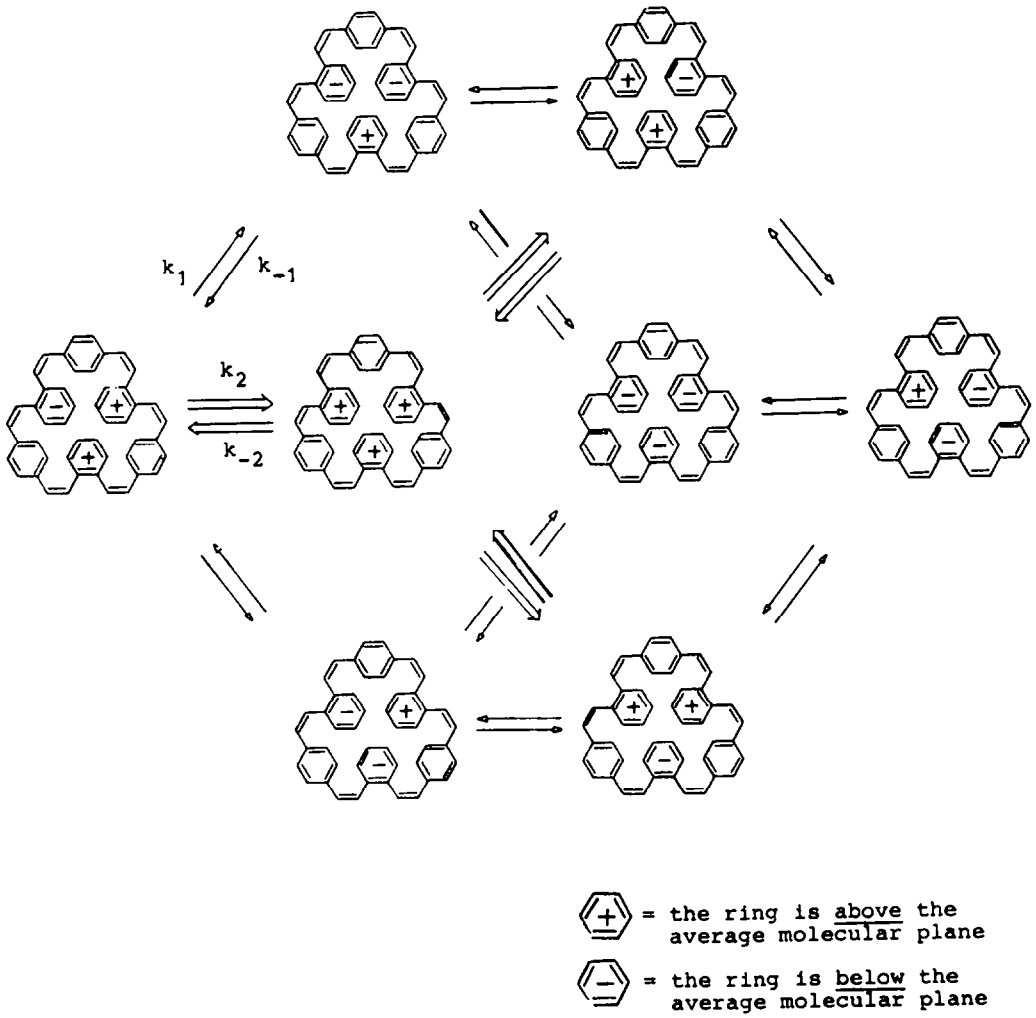


Scheme 5.

A complete sheme for the interconversion of the conformers **3A** and **3B** is rather complex (Scheme 6). It is characterised by four rate constants, k_1, k_{-1}, k_2 and k_{-2}, two of which are equal ($k_1 = k_{-1}$). Two slightly different barriers are possible, one for the interconversion of two conformers of type **3B** and another for the interconversion of conformers of type **3A** and **3B** (Scheme 6).

On cooling the sample, the ^{1}H NMR spectrum of **3** changes. At low temperature (200 K) the olefinic protons give two sets of signals. One set is similar to the room temperature spectrum with a small upfield shift and can be interpreted as originating from conformer **3A**. The other set is more complex but can be interpreted as due to conformer **3B**, as it contains three slightly different AB-patterns. At low temperature, the aromatic region of the spectrum becomes rather complex, as expected, with a distinct broadening of the signals from the *para*-substituted rings in conformer **3A** (see also Fig. 1).

A complete analysis of the dynamic process for the complex spin systems has not been carried out. However, a qualitative interpretation of the spectra indicates that the assumption of two rapidly interconvert-



Scheme 6.

ing conformers, **3A** and **3B**, fits the experimental data. It seems as if the rate of interconversion of conformers of type **3B**, k_1, is larger than k_2 and k_{-2}, which are the rates of interconversion of types **3A** and **3B** (Scheme 6). The equilibrium constant k_2/k_{-2} is *ca* 0.4 at 200 K in CD_2Cl_2 and *ca* 0.2 in $CDCl_3$. Thus, the difference in enthalpy between the conformers **3A** and **3B** is small.

The conformational barriers in **3** are higher than expected from inspection of molecular models. The passage of an *ortho*-substituted ring through the centre of the molecule causes the adjacent *para*-substituted rings to twist out of conjugation with the rest of the π-system, and this is probably the main factor causing the observed barriers. This assumption is supported by the observation of considerable line-broadening of the signals from the *para*-substituted benzene rings at low temperature, indicative of slow rotation or flipping.

The dynamic processes discussed in this paper all involve the rotation or flipping of an aromatic ring out of conjugation with a larger π-system, and in this respect are similar to previously observed processes concerning the rotation of 1,5-naphthalene groups in [2.4] naphthalenophanes[3] and 1,1'-ferrocene groups in [2.4] ferrocenoparacyclophanes.[4]

EXPERIMENTAL

The ^{1}H NMR spectra were obtained at 270 MHz on a Bruker WH-270 spectrometer equipped with a standard Bruker B-ST 100/700 variable temperature system.

[5.2] *Paracyclophanetetraene*, **1**. Dry DMSO (Riedel-De Haën) and ^{n}BuLi (Merck) were handled and stored under an atmosphere of dry N_2. The Wittig reaction was also conducted under N_2.

The bisphosphonium salt (2.18 g, 3 mmol) from triphenyphosphine and 1,3-dibromopropane was dissolved in dry DMSO (25 ml) in a Schlenk tube. ^{n}BuLi (3.75 ml of a 1.6 M hexane solution) was then added via syringe and the vessel shaken thoroughly for 10 min. The resultant deep red soln was then added dropwise to a magnetically stirred soln of benzene-1,4-dicarbaldehyde (0.40 g, 3 mmol) in dry DMSO (50 ml). The mixture was then stirred for several hr at room temp, during which time its colour gradually changed to pale yellow. This mixture was then diluted with three times its own volume of cold water and then extracted thoroughly with diethyl ether. The combined ether extracts were washed with water (3 × 100 ml), dried ($MgSO_4$), and evaporated to dryness. The desired product was then isolated by plc (silica gel coated plates, dichloromethane as eluent) as a colourless, viscous oil. (17 mg, 4%). ^{1}H NMR ($CDCl_3$): δ 6.86 (s, 8H, aromatic protons), 6.55 (d of t, 4H, J 11.5 and 1.5 Hz) and 5.79 (d of t, 4H, J 11.5 and 8 Hz) olefinic protons and 3.17 (t of t, 4H, J 8 and 1.5 Hz, methylene protons). MS (AEI MS 902): *m/e* 284 (M^+, 61%), 179 (100), 178 (72), 167 (52), 165 (42), 143 (46), 141 (70), 128 (55), 115 (57), 107 (56), 63 (92), and 45 (70). Only peaks stronger than 40% of the base peak are listed. Abs. mass 284.1565, calc. for $C_{22}H_{20}$ 284.1566.

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