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NMR STUDIES OF CONFORMATIONS AND DYNAMIC PROCESSES—I

[2_4]CYCLOPHANES WITH ETHYLENE BRIDGES

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Abstract—The conformations and dynamic processes in a series of relatively unstrained [2_4]paracyclophanes (with one, two or four -CH_2-CH_2-bridges) and some closely related compounds have been analysed. Their ^{1}NMR spectra have been recorded at low temperatures and the temperature dependence rationalised as being due to essentially two types of dynamic process—the torsional motion around the sp^3-sp^3 C–C bonds in the bridges, and the rotation around the sp^2-sp^3 C–C bonds adjacent to the benzene rings. The barriers to the former process are similar for the series of cyclophanes **1–6** and are due to steric and electronic interactions in the *syn*-oriented transition states. In cyclophanes **7–9**, in which *anti*-orientations of the aromatic rings are possible, the barriers are lower. The latter process, involving the rotation of the benzene rings, becomes important at temperatures below 150 K and has not been further analysed.

Multiple Wittig reactions have proved to be efficient for the synthesis of a variety of cyclophanes,[1] and we have used this method to prepare several relatively large and unstrained cyclophanes and bicyclophanes containing unsaturated bridges.[2] Catalytic hydrogenation of the double bonds then leads to cyclophanes with ethylene bridges. Careful electrochemical reduction at constant potential has enabled us to selectively reduce one, two, or three of the four double bonds in [2_4]paracyclophanetetraene and thus to prepare a series of cyclophanes with both vinylene and ethylene bridges.[3]

In the course of this work, we have become interested in the geometrics and conformational properties of the cyclophanes. We have also observed that many of them show temperature dependent NMR spectra indicative of dynamic processes. In this series of papers we have tried to collect, systematise, and rationalise our observations of low-energy conformations and dynamic processes in some selected examples of cyclophanes having a varying degree of unsaturation.

Although the actual ring size of most of the cyclophanes considered here is large, the rigidity of the benzene rings, which constitute part of the perimeters, causes a pronounced loss of mobility in the various cyclophanes. A *para*-substituted benzene ring is thus comparable to a very long single bond, a *meta*-substituted ring to a carbonyl group or a hetero-atom, and an *ortho*-substituted ring to a *cis* double bond. Thus, the cyclophanes considered here are in some respect similar to medium-sized rings in the range from 8- to 12-membered.

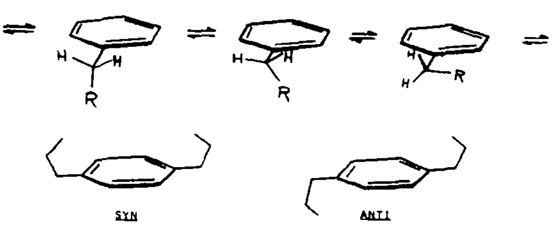
Much of the present knowledge and understanding of the structures, conformations and dynamic processes in medium-sized rings can be attributed to the work of Anet and Dale.[4,5] The complexity of the problem is apparent from a review by Dale,[5] whose methods we have tried to adopt.

BACKGROUND AND ASSUMPTIONS

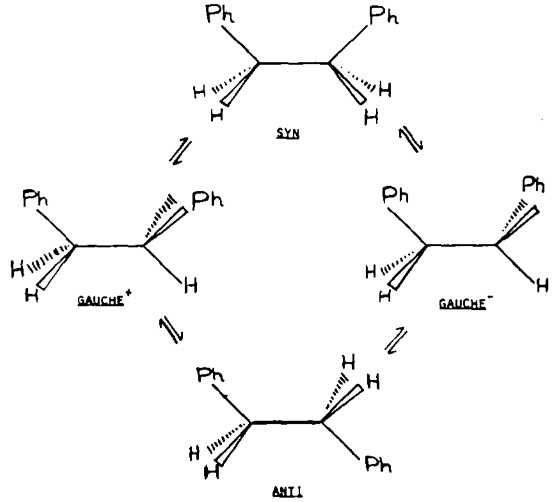
A complete analysis of the conformational properties of ring compounds of the size considered here is certainly a very complex task. Despite the valuable development of molecular mechanics calculations, this method is still too complicated if the number of compounds and conformations is large. We have instead chosen a simpler method of analysis by dividing the various conformational processes into a few general types, thus assuming that they can be treated independently. We have also found space-filling models (CPK) to be extremely useful in the evaluation of conformations and conformational barriers.

Two types of dynamic process are relevant in the cyclophanes with ethylene bridges, namely, rotation around the sp^2-sp^3 C–C bonds connecting the bridges and the aromatic rings (Scheme 1) and rotation around the sp^3-sp^3 C–C bonds in the ethylene bridges (Scheme 2). The former is expected to have a lower barrier to rotation and it is assumed that the minimum energy conformations are generally those with the ethylene groups essentially perpendicular to the benzene rings, the bridges being either *syn* or *anti* (Scheme 1).

Literature data on the rotation about the sp^2-sp^3 C–C bond in, e.g. ethylbenzene are contradictory[6,7] but we believe the above assumption to be justified, especially



Scheme 1.



Scheme 2.

for cyclophanes with *gauche* orientation of the aromatic rings.

The second type of process, rotation around the sp^3–sp^3 C–C bonds, is the more important one. In the cyclophanes considered here (with a few exceptions) *anti* orientation of the two aromatic substituents on the ethylene bridges can be ruled out for steric reasons, and *gauche* orientation should dominate. The interconversion of mirror image forms of the cyclophanes must occur via one or more *gauche*$^+$ to *gauche*$^-$ transitions, all of which involve intermediate *syn*-orientation of the two aromatic rings (Scheme 2). The barrier to this process is often measurable using NMR methods. In a few cases, *gauche*$^+$ to *anti* to *gauche*$^-$ transitions are possible and no conformational barriers should then be observable by NMR methods (Scheme 2).

The cyclophanes discussed here are large enough to be flexible by small changes in bond and torsional angles. As a result, the transition states for conformational changes will involve strong interactions at only one bridge at a time. Thus multistep conformational changes can be treated as a series of one-step conformational changes, and the observed barrier for a multistep process should be similar in height to that for each individual step. We have perhaps overemphasised this situation in order to simplify the analysis.

In 1,2-diphenylethane, which is the model compound for the cyclophanes with ethylene bridges, the symmetry number and, thus, the entropy of the *gauche* conformers and the *syn* conformer are the same. In highly symmetrical cyclophanes, the stable *gauche* conformers and the *syn*, *gauche* conformers, the latter being the assumed transition states for the conformational processes, may have different symmetry numbers and entropy, thus resulting in a lowering of the observed barrier in comparison with less symmetrical cases. The effect should be small but not completely negligible if the total barrier is 30–40 kJ mol^{-1}, as found in most cases of interconversion of highly symmetrical cyclophanes and their mirror image forms via several different reaction paths over several different barriers involving *syn* orientation of two aromatic rings.

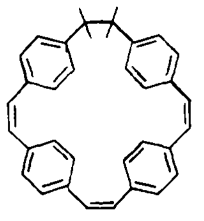
All the experimental results reported in this series of papers are based on ^{1}H NMR measurements. In a few cases, it is clear which conformation of the cyclophane has the lowest energy and thus contributes most to the observed average NMR spectrum. In most cases, however, the NMR data show that several conformations have similar energy and contribute to the average spectrum.

The absence of polar groups and substituents in the cyclophanes discussed here simplifies the analysis of the information obtainable from the chemical shifts of the various protons. The anistropy of the aromatic rings is responsible for any observed deviations from normal values. The effect of the benzene rings on the chemical shifts of nearby protons is estimated using the Johnson and Bovey equations.[8]

RESULTS AND DISCUSSION

For the present study, we have selected some $[2_4]$paracyclophanes with one, two, or four ethylene bridges, compounds **1**, **2**, **3** and **5**. A cyclophane, **4**, with a structure similar to **2** has also been included for comparison. A small progressive variation of the angles between the ethylene bridges extending from one aromatic ring is found in the series of $[2_4]$cyclophanes, **5**, **6**, **7**, **8** and **9**, in which two *para*-substituted benzene rings are exchanged for two thiophene, furan, *meta*-substituted, and finally *ortho*-substituted rings. The probability of *anti* conformations increases in this series and is greatest in **8** and **9**. The ^{1}H NMR data of the cyclophanes **1**–**9** are collected in Table 1. The 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.

$[2_4]$*Paracyclopanetriene*, **1**, is the simplest member of this series of cyclophanes, and contains only one ethylene bridge and three vinylene bridges. Cyclophane **1** should thus resemble cyclo-octatriene. Assuming that the rotation of the benzene rings is fast, two conformations with different *gauche* orientation of the benzene rings at the saturated bridge are relevant (Scheme 3). The passage of the two benzene rings over the faces of each other in the *syn* conformation is identified as the transition state for the interconversion of "outer" and "inner" hydrogens in the ethylene bridge (Scheme 3). The NMR spectrum of cyclophane **1** shows a sharp singlet



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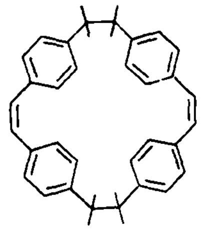

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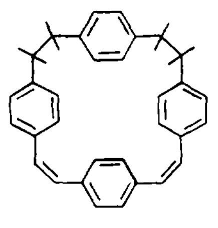

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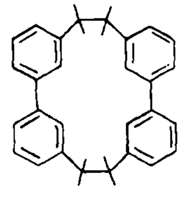

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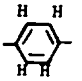
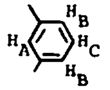
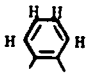
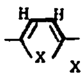
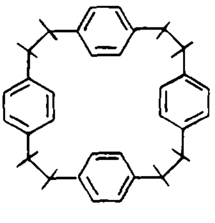
Table 1. ^{1}H NMR data of the cyclophanes 1-9 in $CDCl_3$ at room temperature at 270 MHz

	chemical shifts (δ)					
cyclophane	$-CH_2-CH_2-$	$-CH=CH-$				 X = S, O
1	2.87	6.52	7.14,6.95			
2	2.84	6.53	7.00,6.73			
3	2.87		7.09,7.08 6.81,6.71	A B C		
4	2.87			5.97, 7.19/7.01, 7.28		
5	2.85		6.72			
6	2.97,2.86	6.54,6.48	6.75			5.69
7	2.91,2.88		6.72			5.38
8	2.73		6.81	5.88,6.93,7.15		
9	2.66,2.19		6.83		7.17	



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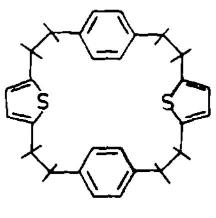

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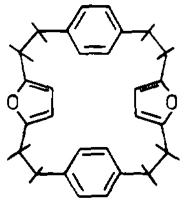

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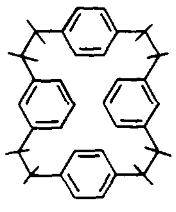

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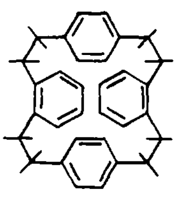

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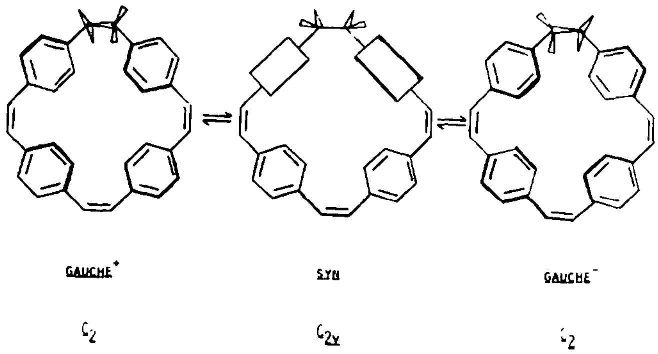
for the four ethylene protons at room temperature. On cooling the sample, the singlet broadens and becomes very broad at 173 K. On further cooling, the sample shows two broad peaks for the ethylene protons at 153 K (see Fig. 1). The signals for the aromatic and olefinic hydrogens also broaden, but to a lesser extent. From the coalescence temperature of 163 K and a shift difference of 200 Hz, extrapolated from the spectrum at 153 K, a barrier of approximately 31 kJ mol^{-1} can be calculated by the standard procedure.

[2_4]Paracyclophanediene, isomer 2, has two ethylene bridges situated opposite each other and two vinylene bridges, and should thus resemble 1,5-cyclo-octadiene. The two saturated bridges must be of the *gauche* type. Four conformations of 2 are relevant assuming rapid rotation aound the sp^2-sp^3 C–C bonds (Scheme 4). The g^+, g^+- and g^-, g^--conformations correspond to a twist boat form with D_2-symmetry and the g^+, g^-- and g^-, g^+-conformations to a chair form with C_{2h}-symmetry, respectively, of 1,5-cyclooctadiene. The conformational barriers must be of the *syn* type with a transition state of C_2-symmetry. From inspection of molecular models, it is difficult to differentiate between the conformations with regard to their free energy. The entropy term is equal for the C_{2h}- and the D_2-conformations if both the respective symmetry numbers and the optically active forms of the latter are taken into account.

The ^{1}NMR spectrum is fairly simple. It shows an



Scheme 3.

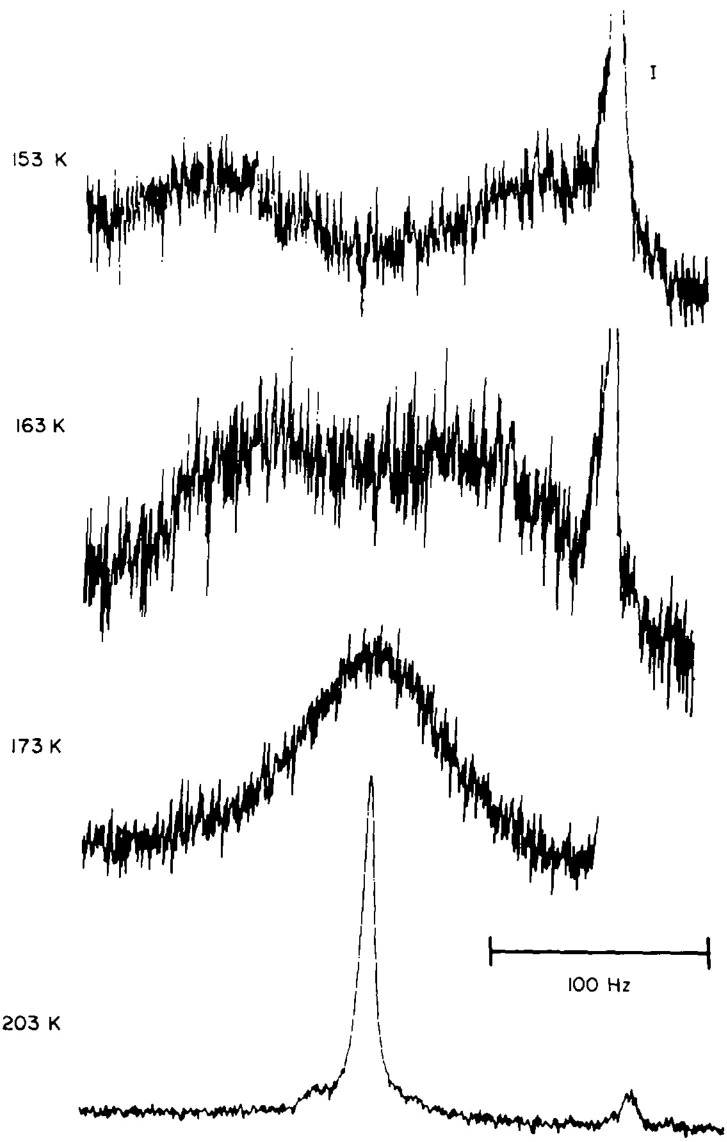
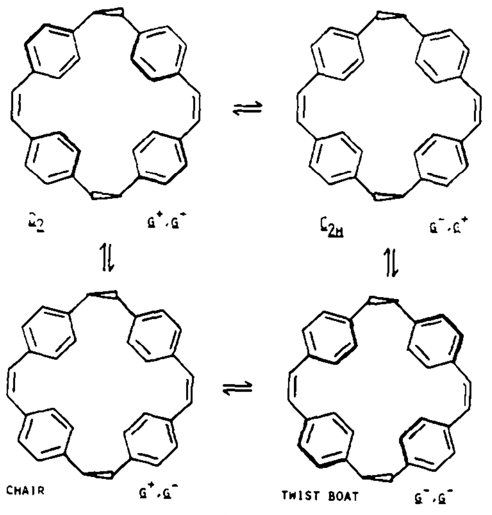


Fig. 1. 270 MHz ^{1}H NMR spectrum of [2$_4$]paracyclophanetriene, 1, in CD_2Cl_2/toluene-d_8 at various temperatures. The ethylene region is shown. The peak marked I is due to a solvent impurity.



Scheme 4.

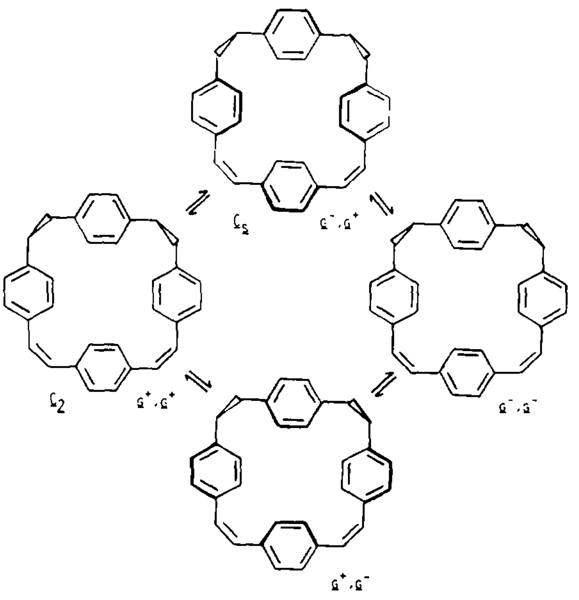
AA′XX′-pattern (almost a pair of doublets) for the aromatic protons and two singlets for the olefinic and ethylenic protons, respectively (see also Table 1). On cooling the sample, the ethylene proton peak broadens and appears, at 148 K, as two broad peaks with a shift difference of 120 Hz. The coalescence temperature is estimated to 155 K. The aromatic and olefinic protons also give broad peaks at low temperatures, indicative of slowed rotation of the aromatic rings. However, it is clear from the spectra that equilibration of the ethylene protons is much slower and has a higher barrier. It is not possible to decide whether only one conformation is dominant at low temperature, and this makes the calculation of the barrier uncertain. The simple calculation from coalescence temperature and shift difference, assuming only two equally populated exchanging sites, gives a barrier of approximately 29 kJ mol^{-1}, which is somewhat lower than the barrier in [2$_4$]paracyclophanetriene, 1.

[2$_4$]*Paracyclophanediene, isomer* 3, has the two saturated bridges at adjacent positions and thus resembles 1,3-cyclo-octadiene. There are two pairs of conformations with C_s-symmetry (g^+, g^- and g^-, g^+) and C_2-symmetry (g^+, g^+ and g^-, g^-), respectively. The equilibrium of "inner" and "outer" hydrogens in each methylene group requires the passage over two *syn* barriers (with C_1-symmetry) as in the previous case (Scheme 5). The higher symmetry number for the C_2-conformations is offset by the presence of optically active forms, which leads to the same entropy as that of the C_s-conformations.

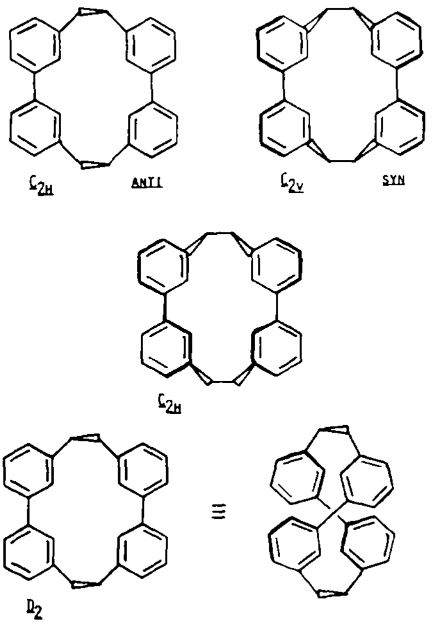
The ^{1}H NMR spectrum of **3** is somewhat more complex than that of isomer **2**. It shows two singlets and two doublets (AA'XX'-patterns) for the atomatic protons, an AB-pattern for the olefinic protons, and a sharp singlet for the ethylene protons which apparently, all have the same shift at room temperature (see also Table 1). On cooling the sample the ethylene peak broadens, but more slowly than in the two previous cases. At 163 K it is still one broad peak which becomes very broad at 143 K, which might be close to the coalescence temperature. However, the aromatic protons also give broadened peaks at this temperature and it is difficult to separate the two types of process. By comparison with the previous two sets of temperature dependent spectra it is clear that the same type of rotation around the sp^3–sp^3 C–C bonds over *syn* barriers occurs, probably with a lower barrier in **3** than in **1** and **2**. The ethylene protons in **3** should give an ABCD-spectrum at low temperature which should change to an AA'BB'-spectrum at higher temperatures. A line-shape analysis of spectra at different temperatures would be required to give a reliable barrier height.

It may seem somewhat surprising that the barriers in **2** and **3** are lower than that in **1**. There are, however, two factors which could be responsible for the observed order. One is the entropy factor of the transition states. In **1** the transition state has C_{2v}-symmetry whereas both *gauche* conformations have C_2-symmetry only (Scheme 3). This leads to a relative increase in the free energy of the transition state in comparison with the situation in **2** and **3**. In the latter two cyclophanes, the transition states for the conformational processes have no symmetry elements whereas the *gauche* conformations are of higher symmetry (Schemes 4 and 5). Another factor which should be of importance is the π-electron overlap between the benzene rings and the adjacent double bonds. In **1** both the benzene rings which pass each other in the transition state (the *syn* barrier) must twist out of conjugation whereas one of the benzene rings in **3** is not conjugated with the rest of the π-system and thus is easier to twist. The situation in **2** is similar to that in **1**. Although both factors discussed here, if taken together, can rationalise the experimental results, it is necessary to remember that small differences in relative energy (2–4 kJ mol^{-1}) will affect the observed barriers and coalescence temperatures (10–20 K).

[2$_2$](3,3')*Biphenylophane*, **4**, has the same number of ethylene bridges as **2** and **3** but is somewhat less flexible. The rotation of the *meta*-substituted benzene rings is hindered for geometrical reasons but inversion-like processes are possible. Four conformations with different orientations of the benzene rings are reasonable from inspection of molecular models (Scheme 6). The first two have essentially planar biphenyl units and might be called *syn* (C_{2h}-symmetry) and *anti* (C_{2v}-symmetry). These conformations have been considered previously by Vögtle[9] and also by Reiss *et al.*[10] The steric repulsion between the *ortho* hydrogens in the planar biphenyl units is unfavourable, however, and thus the conformations of C_{2h}-symmetry and D_2-symmetry, with a larger twist angle between the benzene rings, may be of lower energy. An increase of the twist angle in the biphenyl units leads to a decrease in the π-electron overlap. The steric and electronic factors are nicely balanced in the D_2-conformation in which the twist angle is small enough (*ca* 30°) to allow considerable overlap but large enough to minimise H-H interactions. In the D_2-conformation, which has the symmetry of a two-bladed propeller, the isolated hydrogens (H$_A$ in Table 1) are located just above the face of another benzene ring, which explains the unusual shift observed for these protons (δ5.97). In the other three conformations shown in Scheme 6, a downfield shift of the same protons would be expected.



Scheme 5.

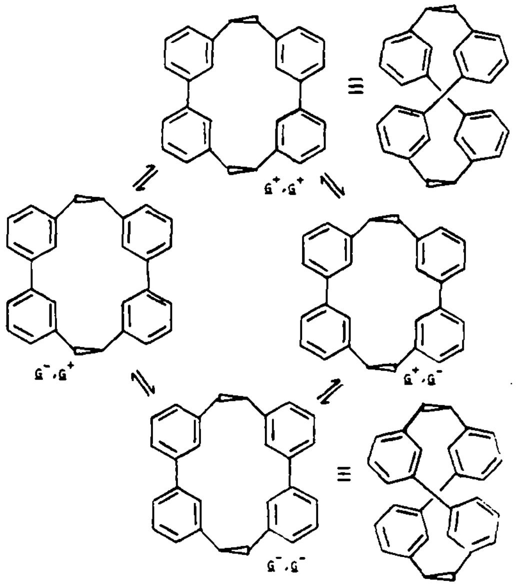


Scheme 6.

In the D_2-conformation, the ethylene bridges are of g^+, g^+ or g^-, g^- orientation.

The interconversion of the two mirror image forms, which leads to equivalence of the outer and inner hydrogens in the ethylene bridges, should involve two *syn* barriers with a minimum in between. There are several possible routes between the mirror image forms, but the one that passes the *anti* conformation (C_{2h}-symmetry) seems to be the most favourable (Scheme 7).

The ^{1}H NMR spectrum of **4** shows a triplet, two doublets of doublets and a triplet for the four types of aromatic proton and a sharp singlet for the ethylene protons (see also Table 1). On cooling the sample, the ethylene singlet broadens and then reappears, at 163 K, as two broad peaks with a separation of 160 Hz (see also Fig. 2). The peaks in the aromatic region also broaden slightly, below 183 K, but show the same pattern as the room temperature spectrum. The triplet originally at δ5.97 is shifted slightly upfield at low temperatures. The coalescence temperature of the two ethylene peaks is 180 K, and there is no indication of more than one pair of conformations below coalescence. The presence of one conformation of D_2-symmetry having distinctly lower energy than the others is thus consistent with the observed spectrum and its temperature dependence. The barrier for the equilibration of the ethylene protons can be calculated to 34.5 kJ mol^{-1} from the shift difference and the coalescence temperature. It is slightly higher than the values for **1**-**3**, reported above. Although the symmetry of the transition states is, also in this case, lower than that of the reactant and product, as in **2** and **3**, the relative decrease of π-electron overlap in the transition state must be the more important factor. Further, the interconversion of mirror image forms of **4** must also involve the rotation of the biphenyl units, which should also increase the barrier somewhat.



Scheme 7.

A line-shape analysis of the low-temperature NMR spectra was carried out by comparison of measured and calculated spectra. The calculations were performed with

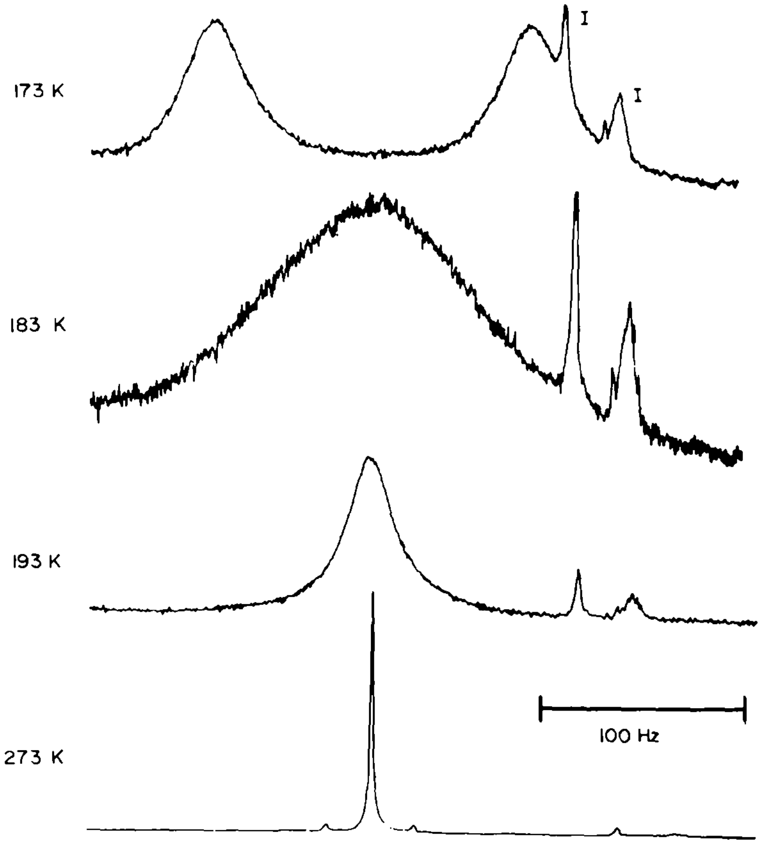


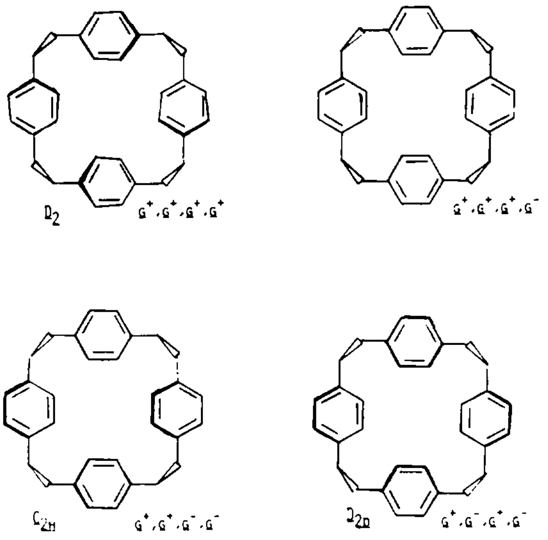
Fig. 2. 270 MHz ^{1}H NMR spectrum of [2$_2$](3,3')biphenylophane, **4**, in CD_2Cl_2/toluene-d_8 at various temperatures. The ethylene region is shown. The peaks marked I are due to solvent impurities.

the DNMR 3 program,[11] assuming an AA'BB'-spin system changing to an A_4-spin system. The best fit was obtained with the following shifts and coupling constants: $\Delta\nu_{AB}$ 175 Hz; $J_{AA'} = J_{BB'} - 13$ Hz, J_{AB} 12 Hz, $J_{AB'} = J_{A'B} = J_{A'B'}$ 3 Hz; relaxation time 0.5 s. These data gave an average barrier of 34.8 kJ mol^{-1} from five temperatures between 173 K and 193 K.

[2_4]*Paracyclophane*, **5**, has previously been investigated by Tabushi *et al.*[12] They observed a conformational barrier of 38 kJ mol^{-1} for the exchange of "axial" and "equatorial" hydrogens in the ethylene groups. However, neither the origin of the barrier nor the probable low-energy conformations were further analysed.

[2_4]Paracyclophane should resemble cyclo-octane. However, some of the conformations which, in cyclooctane, would have severe H–H repulsion are possible for **5**. If the orientation of the benzene rings is neglected in the first approximation, only four combinations of *gauche* bridges (and their mirror image forms) are possible due to the symmetry of the molecule (Scheme 8). As inspection of models shows, none of the conformations with only *gauche* bridges is apparently strained, whereas conformations with *anti* bridges are severely strained and can thus be omitted from the discussion.

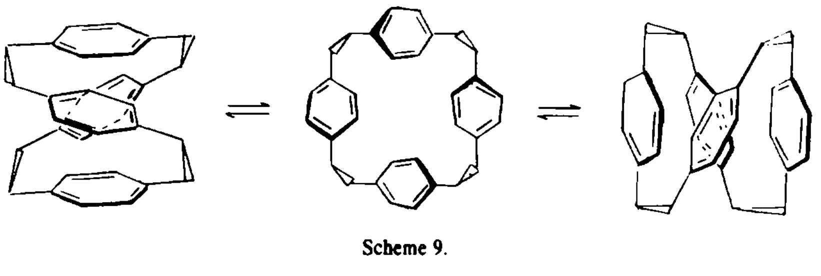
It is certainly very difficult, from inspection of molecular models, to guess correctly the relative energies of the four conformations shown in Scheme 8. It seems as if steric interactions are minimised in symmetrical conformations, leading to lower free energy, which is partly offset by the high symmetry number and, thus, low entropy. In the conformation with lowest symmetry, g^+, g^+, g^+, g^-, all four ethylene bridges cannot be oriented perpendicular to the nearest benzene rings as assumed in the introduction. C_{2h}- and D_{2d}-conformations are similar to each other. In the former, two of the benzene rings are sandwiched between the other two and thus have little mobility, which seems unfavourable. In both these conformations there is a cavity in the molecule, which is absent in the all-g^+-conformation. In the latter, all four benzene rings can not be accommodated in a crown-like structure with D_4-symmetry. A helix-like structure with D_2-symmetry is more probable (see also Scheme 9). The ethylene bridges extend *anti* from two of the benzene rings and *syn* from the other two (see Schemes 1 and 9).



Scheme 8.

The ^{1}H NMR spectrum of **5** shows a singlet for the aromatic protons and a singlet for the ethylene protons (Table 1). On cooling the sample, both signals are shifted slightly upfield and the latter, after broadening, eventually resharpen to a rather broad AA'XX'-pattern at 173 K. Thus the low temperature spectrum of **5** is still rather simple. If one assumes that the rotation of the benzene rings is rapid, the spectrum is consistent with the D_{2d}-conformation but not with the other three, less symmetrical, conformations in Scheme 8. In the D_2-conformation, which has a helix-like structure, the benzene rings are pairwise identical and the four ethylene hydrogens in the bridges are all different. However, rotation about the sp^2–sp^3 C–C bonds and a twist of the whole molecule can interconvert the two sets of benzene rings and, simultaneously, interconvert the ethylene protons into two sets without pasing over a *syn* barrier (Scheme 9). Thus the D_{2d}- and D_2-conformations, but not the other two conformations in Scheme 8, are compatible with the low temperature NMR spectra. The observed chemical shifts are not suitable for distinction betwen these two conformers.

Tabushi and Yamada have published a paper on the temperature dependent NMR spectra of a series of monosubstituted [2_4]paracyclophanes.[13] They observed a rather unusual temperature dependence of the signals from the protons *meta* and *para* to the substituent. A clear upfield shift was observed for the nitro-, cyano-, aceto- and bromo-cyclophanes, whereas hydroxy-, acetoxy- and dimethylamino-groups had smaller effects. The shifts and their temperature dependence can be rationalised nicely by assuming that the D_2-conformation has lowest energy and that the benzene rings carrying substituents can prefer either the sandwiched position or the outer position (Scheme 9). Apparently, benzene rings with electron-withdrawing substituents prefer the sandwiched positions and will, at lower temperatures, spend most of the time there. This will result in an upfield shift of the signals from the *meta* and *para* protons because they must be located between the faces of the two outer benzene rings. Benzene rings with electron-donating substituents show no preference for the sandwiched



Scheme 9.

positions and thus will not cause an upfield shift of the signals from the *meta* and *para* protons. It is more difficult to rationalise the temeprature dependent NMR spectra of the monosubstituted [2_4]paracyclophanes if the D_{2d}-type of conformation has the lowest energy.

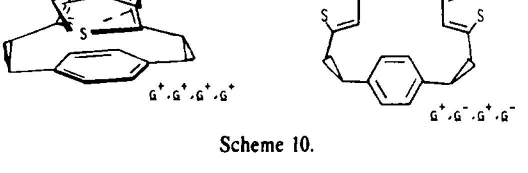
The same preference for a helix-type conformation (D_2 of **5**) over a more planar conformation (D_{2d} of **5**) best explained the observed low-temperature spectrum of [2_4](1,4)naphthalenoparacyclophane.[14] The problem will be treated again the discussion of the thiophene and furan analogues of **5** below.

The angle between the saturated bridges extending from two of the aromatic rings decreases gradually in the series of cyclophanes **5**–**9**, as does the energy of *anti* conformations. In this series of cyclophanes, *anti* orientations at the ethylene bridges will first be important as the transition states for the interconversions of all-*gauche* conformations and, in the later members, in the most stable conformations. This should result in a decrease of the conformational barriers in the series.

For [2_4](2,5)*thiophenoparacyclophane*, **6**, the number of conformations increases rapidly as compared to **5** because of the two possible orientations of the thiophene rings. However, the same types of barrier are still probable as the rotation of the thiophene rings should be at least as fast as that of the benzene rings. The ^{1}H NMR spectrum of cyclophane **6** is simple (see also Table 1). The aromatic protons give two sharp singlets and the ethylene protons give an AA'BB'-pattern. The large upfield shift of the thiophene (δ5.69) is consistent with both the all-g^+- and the g^+, g^-, g^+, g^--conformations if the sulphur atoms point outwards from the centre of the cyclophane as shown in Scheme 10.

On cooling the sample, the NMR spectrum changes. The ethylene peaks first broaden and then, at 163 K, reappear as three broad peaks in the ratio 1:1:2 (see also Fig. 3). The aromatic proton signals broaden somewhat, but at 163 K give the same simple pattern as observed at room temperature, with a small upfield shift of both singlets. Further cooling leads to broadening of both the ethylene peaks and the aromatic peaks, consistent with a slower rotation of the aromatic rings. The cyclophane **6** behaves similarly to **5** with essentially the same barrier for the equilibration of the outer and inner protons in the ethylene bridges.

A line-shape analysis of the low-temperature spectra was carried out. Calculated spectra (see cyclophane **4**) and measured spectra were compared and the best fit was obtained assuming an ABCD-spin system changing to an AA'BB'-system with the following relative shifts and coupling constants: $\Delta\nu_{AB}$ 50 Hz, $\Delta\nu_{AC}$ 135 Hz, $\Delta\nu_{AD}$ 140 Hz; J_{AB} 0 Hz, $J_{AC} = J_{BD} - 13$ Hz, J_{AD} 12 Hz, $J_{BC} = J_{CD}$ 3 Hz; relaxation time 0.5 s. These data gave an average barrier of 34 kJ mol^{-1} from five temperatures between 163 K and 183 K.



G^+, G^+, G^+, G^+

G^+, G^-, G^+, G^-

Scheme 10.

[2_4](2,5)*Furanoparacyclophane*, **7**, is similar to its thiophene analogue **6**. The angle between the bridges extending from the furan is slightly smaller, however, which leads to a decrease in the energy of conformations with *anti* orientations at ethylene bridges. The ^{1}H NMR spectrum of **7** is similar to that of **6** with a large upfield shift for the heteroaromatic proton signal (δ5.38, see also Table 1). On cooling the sample, the peaks from the ethylene protons broaden, but at lower temperature than in the previous case (Fig. 4).

At very low temperatures, broadening of the peaks from the aromatic protons also occurs (153 K), and it is not possible to separate the torsional motion around the sp^3–sp^3 C–C bonds from the rotation around the sp^2–sp^3 C–C bonds. However, it seems clear that there must be two different processes, the one with the higher barrier being similar to those observed in the previous cases. The barrier could well involve *anti* conformations which would explain why it is lower in **7** than in **5** and **6**.

In [2_4]*metaparacyclophane*, **8**, the angle between the bridges extending from the *meta*-substituted rings is 120°. The molecule is less symmetrical than **5** and five different all-*gauche* conformations are possible. Besides, two conformations with two *gauche* and two *anti* bridges are possible (Scheme 11). A complete scheme with all the reasonable conformations and their routes of interconversion becomes rather complex. Fortunately, the NMR spectrum of **8** shows an unusually large upfield shift of the aromatic protons situated between the bridges in the *meta*-substituted rings (δ5.88, see also Table 1), which means that they must be located over the face of an adjacent benzene ring. This occurs only in three of the conformations in Scheme 11, the two with *anti* bridges, and the all-*gauche*$^+$ conformation. In the latter, the *meta*-substituted rings are sandwiched between the *para*-substituted rings in a compact conformation which resembles those of the bicyclophanes discussed in the following paper.[15]

The ^{1}H NMR spectrum of **8** shows a sharp singlet for the ethylene protons (see also Table 1). The singlet broadens somewhat on cooling the sample, but much less so than in the previous cases. At 163 K it is still a broad singlet, as is the peak from the protons in the *para*-substituted rings. The triplet originally at 5.88 has shifted slightly upfield and become broad and structureless. There is no indication of a measurable barrier to the equilibration of outer and inner hydrogens in the ethylene bridges in **8**. Thus, it seems reasonable to assume that the conformations with *anti* bridges are either of lowest energy or represent low-energy conformational barriers.

In [2_4]*orthoparacyclophane*, **9**, the angle between the bridges extending from the *ortho*-substituted rings is only 60° and conformations with two *anti* bridges are relatively unstrained. The ^{1}H NMR spectrum shows an unusual upfield shift for the ethylene signals which appear as an AA'XX'-pattern (δ2.66 and 2.19, see also Table 1), showing that two of the hydrogens in each ethylene bridge must spend a large part of the time over a face of a benzene ring. This is not consistent with any of the all-*gauche* conformations but is nicely explained by assuming that the dominant conformations are one, or both, of the a, g^+, a, g^+- and a, g^+, a, g^--conformations (Scheme 12). The equilibration of the ethylene hydrogens to two types requires at least two processes, both of which can be fast on the NMR time scale. In one of the processes the *gauche* and *anti* bridges are exchanged, which reduces the number of different ethylene

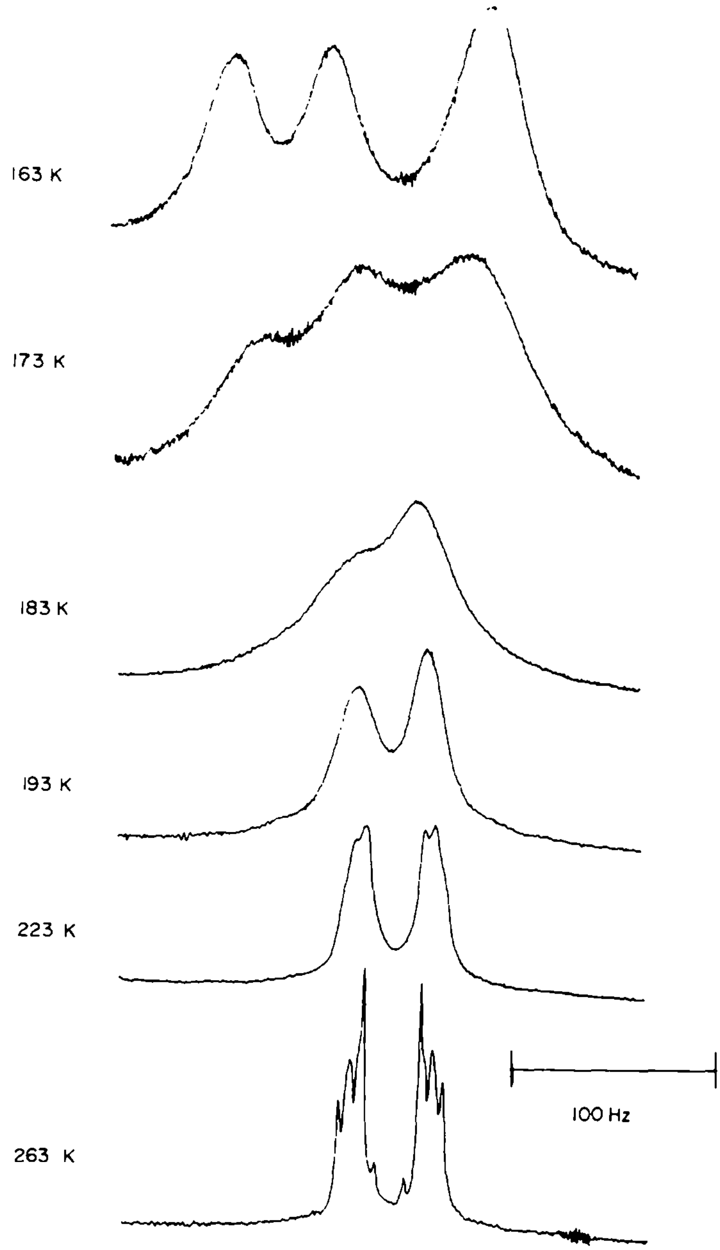


Fig. 3. 270 MHz ^{1}H NMR spectrum of $[2_4](2,5)$thiophenoparacyclophane, **6**, in CD_2Cl_2/toluene-d_8 at various temperatures. The ethylene region is shown.

hydrogens in each of the conformations in Scheme 12 from eight to four, two outer and two inner hydrogens. A second process interconverts the outer and inner hydrogens in the ethylene bridges, as well as the two conformations, by successive rotation of the ethylene bridges around the sp^2–sp^3 C–C bonds when the benzene substituents are *anti* oriented (Scheme 13).

CONCLUSIONS

The experimental results reported above clearly show that conformational changes with measurable barriers occur in a series of $[2_4]$cyclophanes. Despite the complexity and size of the molecules it seems as if the experiments can be rationalised by the methods used by Dale and others, and by assuming that the molecular motions can be divided into a few general types. The presence of symmetry elements in the molecules simplifies the analysis. The important process here is the passage of two aromatic rings on adjacent C atoms, as in the *syn* conformation of 1,2-diphenylethane for which the barrier can not be measured directly. The nature of the aromatic rings seems to influence the barrier (cyclophanes **5**, **6** and **7** in Table 2). The presence of thiophene or furan rings decreases the barrier successively, but in the latter case an alternative explanation with *anti* orientations of the aromatic rings in the transition state cannot be ruled out.

The conclusions arrived at in this paper should be further verified by molecular mechanics calculations on a few selected cases to gain a better understanding of the factors which determine the energy involved in torsional motions of substituted ethanes.

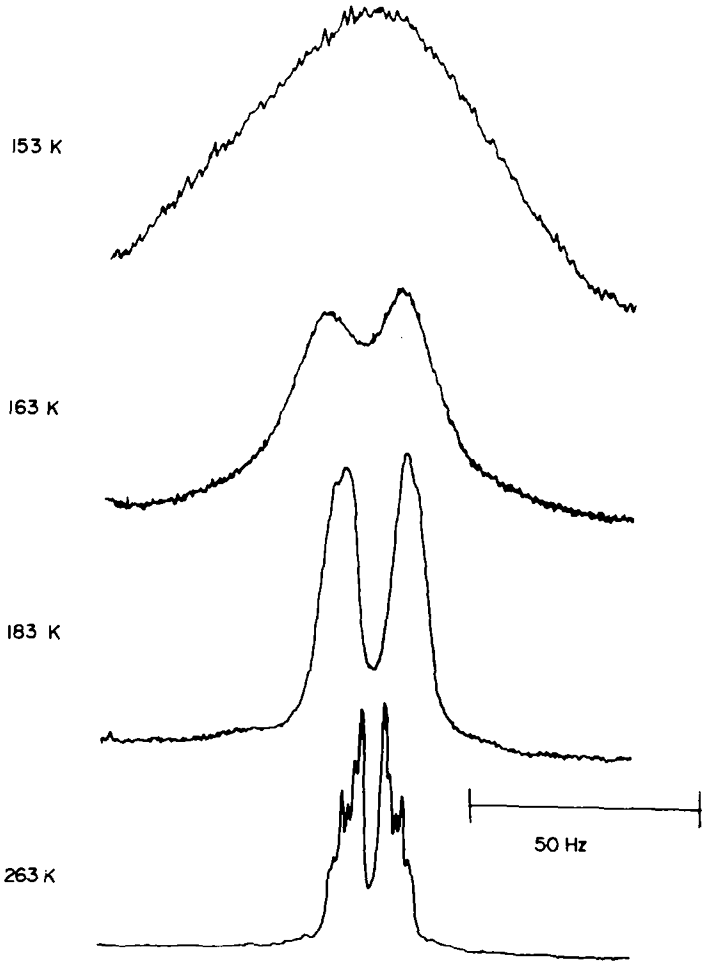
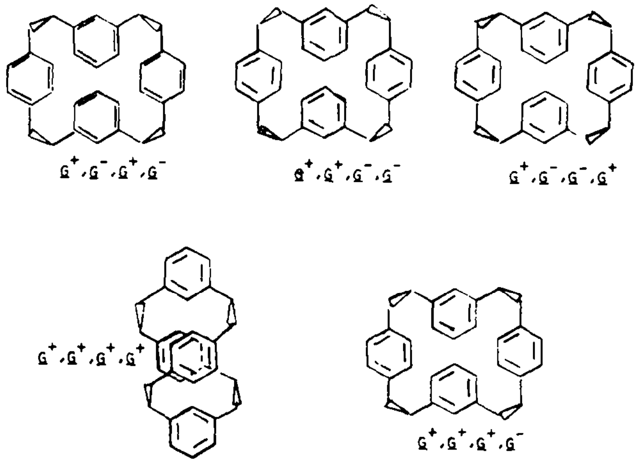


Fig. 4. 270 MHz ^{1}H NMR spectrum of [2$_4$](2,5)furanoparacyclophane, 7, CD_2Cl_2/toluene-d_8 at various temperatures. The ethylene region is shown.



Scheme 11.

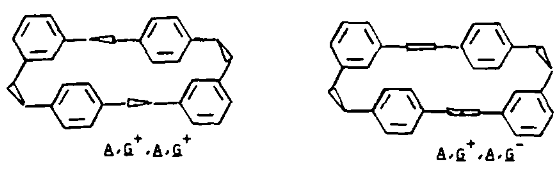
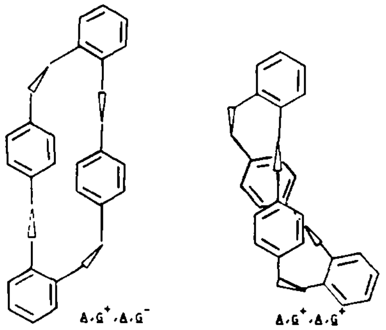
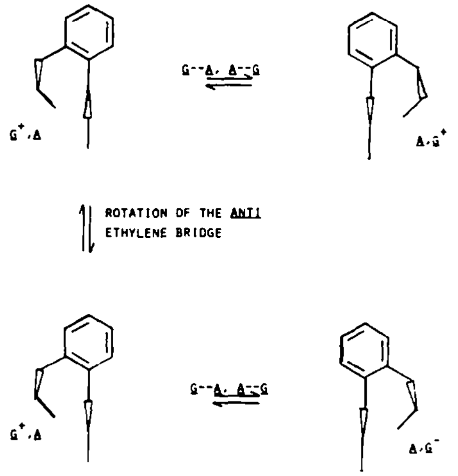


Table 2. Measured barriers to the torsional motion around the sp^3-sp^3 C–C bonds in cyclophanes with ethylene bridges

compound	barrier, kJ mol^{-1}	comments
1	31	from coalescence temp.
2	29	-"-
3		too low to measure
4	34.8	from line-shape analysis
5	38	from coalescence temp. and ref 11
6	34	from line-shape analysis
7		too low to measure
8		no barrier observed
9		-"-



Scheme 12.



Scheme 13.

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