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THE SYNTHESIS AND FLUXIONAL BEHAVIOUR OF THE FIRST [2.1.2.1] METACYCLOPHANE

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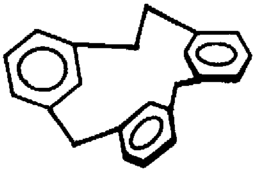
Summary : 8,15,23,30-Tetramethyl[2.1.2.1]metacyclophane, **4** , is synthesised. Variable temperature ^{1}Hmr and ^{13}Cmr spectra indicate that **4e** is the most likely conformation and that at temperatures above 50°C the molecule is fluxional ($\Delta G^{\ddagger}_{323}$ = 15.4 kcal/mole).

The synthesis and stereochemical aspects of cyclophanes have been of particular interest over the last two decades,[1] with particular attention[1b] paid to [2.2]metacyclophanes, which possess an *anti*-stepped conformation. The higher [2^n]metacyclophanes have also been well examined[2] and when n $\gtrsim$ 3 appear to be conformationally mobile. However [2.1.1]metacyclophane appears to have[3] a fixed conformation **1**, as does [2.2.0]metacyclophane **2**, whereas [2.0.2.0]metacyclophane **3** again appears to be mobile.[4] Introduction of intra-annular substituents such as -CH_3, increases the barriers to conformational flipping,[5] for example both *syn*- and *anti*-9,18-dimethyl-2,11-dithia[3.3]metacyclophane exists as discrete compounds, whereas 2,11-dithia-[3.3]-metacyclophane itself is conformationally mobile.[3,6] Surprisingly, few of the higher metacyclophanes containing internal methyl substituents appear to have been studied[8] despite the fact that the chemical shift of the -CH_3 group provides a convenient probe by ^{1}Hmr of any possible conformational changes.



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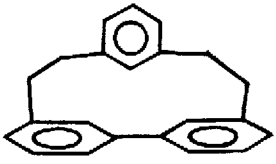

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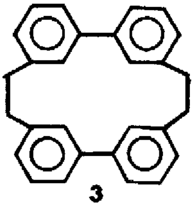

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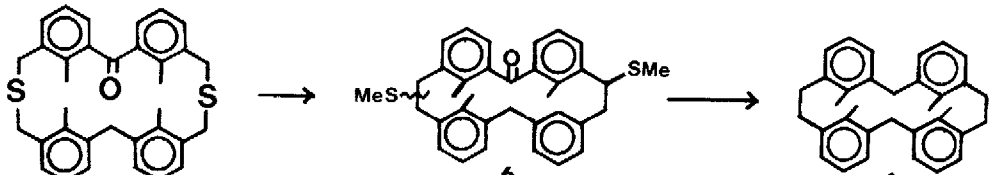
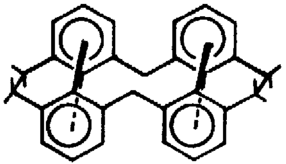
From the previous results, it is not obvious whether a [2.1.2.1]metacyclophane with intra-annular methyl groups will be mobile or not. Molecular models indicate that several interesting conformations might exist. This paper thus describes the synthesis and fluxional properties of 8,15,23,30-tetramethyl[2.1.2.1]metacyclophane **4**.

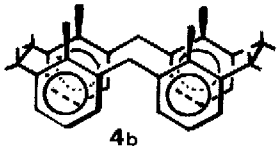
In order to examine new annelated annulenes,[9] we had reason to prepare[10] the thiacyclophane **5** which provides a convenient starting point to synthesise **4**. The ^{1}Hmr spectrum (90 MHz, $CDCl_3$) of **5**, a [3.1.3.1]metacyclophane; indicated that it had no fixed conformation, and showed peaks at δ 7.6-7.0 (m, 12H, Ar-H), 3.96 (s, 2H, Ar-CH_2-Ar), 3.74 (s, 8H, -CH_2S-) and 1.97 and 1.87 (s, 6H each, -CH_3). Stevens rearrangement[6] (t-BuOK-THF) of the bis methyl sulfonium tetrafluoroborate of **5** gave a 48% yield of the [2.1.2.1]cyclophane **6**, which on treatment with W-7 Raney Ni (see the following accompanying communication) gave the desired cyclophane **4** in 85% yield,[11] as colourless crystals from cyclohexane mp 282-284°C. Its variable temperature ^{1}Hmr spectrum is shown in Figure 1. Clearly at room temperature and below it exists in a fixed conformation which shows fluxional behaviour at higher temperatures. Examination of molecular models indicates that several conformers **4a**-**4e** might be considered. The two different types of $-CH_3$ group however, indicate that **4** cannot be the *anti,anti*-conformer **4a** or the *syn,syn*-conformer



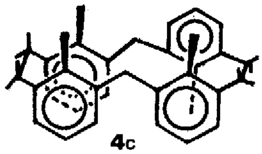
5 **6** **4**



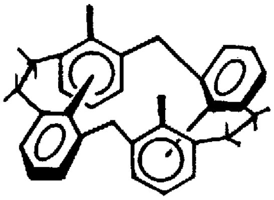
4a



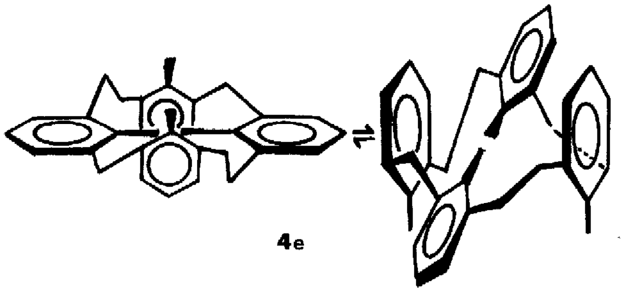
4b



4c



4d

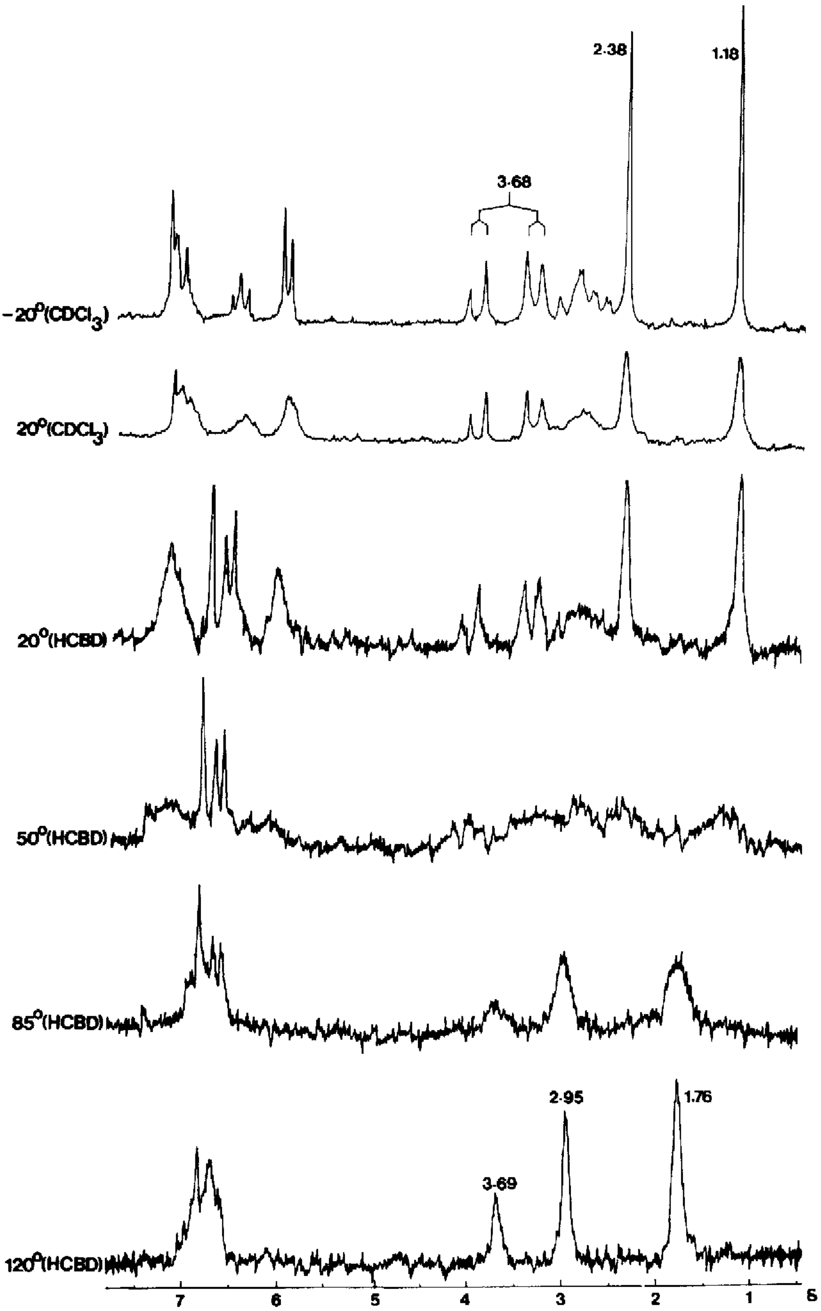


4e

4b . Consideration of the aromatic hydrogens rules out **4d** which would not be expected to have six shielded aromatic hydrogens characteristic of two *syn*-benzene rings, (possessed by **4c** and **4e**). The appearance of these hydrogens in the low temperature spectrum is as an AB_2 spectrum which seems more likely for **4e**, whereas **4c** from models should show more differentiation between the chemical shifts of the three sets of hydrogens, i.e. an ABC spectrum. Unfortunately, the AA'BB' spectrum of the bridge $-CH_2CH_2-$ is not clearly enough resolved to positively distinguish between **4c** (one set *syn*, one set *anti*) and **4e** (both sets *anti*). The ^{13}Cmr spectrum (-30°C) however shows twelve types of aromatic carbon, two different bridge ($-CH_2CH_2-$) carbons, a single type of $-CH_2-$ bridge carbon and two $-CH_3$ carbons. This is clearly consistent with the more symmetrical **4e**, since from models **4c** should show four different ($-CH_2CH_2-$) carbons, two different $-CH_2-$ carbons and four $-CH_3$ carbons.

In the high temperature spectrum each peak occurs at the average (± .02 ppm) position of the corresponding peaks in the low temperature spectrum, indicating a true fluxional process,

Figure 1: Variable Temperature ^{1}Hmr spectrum (**Hexachlorobutadiene** or $CDCl_3$-90 MHz) of the [2.1.2.1]cyclophane **4** .



consistent with **4e** ⇌ **4e** , rather than one conformer going to a different conformer. Application of the Gutowsky-Holm equation[13] to the separation of the -CH_3 groups ($\Delta\nu$ = 108 Hz; T_c = 50°C) leads to a value of $\Delta G^{\ddagger}_{323}$ = 15.4 kcal/mole. It will be interesting to compare this result with other methyl substituted cyclophanes as they become available, and with other families of cyclophanes.[14]

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