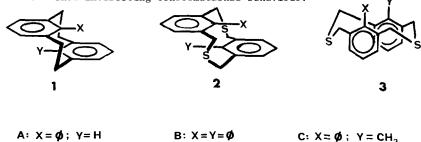
THE SYNTHESIS AND CONFORMATIONAL BEHAVIOUR OF 2,11-DITHIA[3,3]METACYCLOPHANES WITH INTERNAL PHENYL SUBSTITUENTS.¹ Reginald H. Mitchell* and Willem Anker Department of Chemistry, University of Victoria Victoria, BC V8W 2Y2 Canada.

Summary: The synthesis of syn- and anti-9-methyl-18-phenyl- and anti-9, 18diphenyl2,ll dithia[3,3]metacyclophanes is described, together with their variable temperature ¹Hmr spectra. Only partial rotation of the phenyl substituents ($\Delta G_c^{\ddagger} \sim 50$ kJ. mol⁻¹) is believed to occur.

The synthesis and stereochemical aspects of cyclophanes have been of particular interest over the last two decades.² More recently, the size of internal substituents X, Y, in [2,2] metacyclophanes 1 and 2,11 dithia [3,3]metacyclophanes 2, has attracted attention²c,³ since steric effects are especially marked when these groups are forced into close proximity, e.g. by the rigid geometry of cyclophane systems. In this respect, $V\delta gtle^3$ has most elegantly pointed out that internal phenyl groups are more attractive to study than most other substituents. Thus far, the only successful³ preparation of a cyclophane having an internal phenyl group also had a small co-substituent, a hydrogen atom, 1A and 2A. At that time, $V\delta gtle^4$ reported that the compound 2B, with two internal phenyl groups could not be obtained⁵ from the cyclisation of 2,6-bis(bromomethyl)biphenyl 4, and 2,6-bis(mercaptomethyl)biphenyl 5.

In this paper, we report that we have successfully isolated **2B** and **3B** from this reaction and that, furthermore, the compounds with one internal methyl group **2C**, **3C** can be analogously prepared, and all show interesting conformational behaviour.



A priori the assignment of stereochemistry to a compound such as **2B** or **3B** is not simple, since in **2B** the substituent phenyl ring could be shielded by the opposite cyclophane ring,

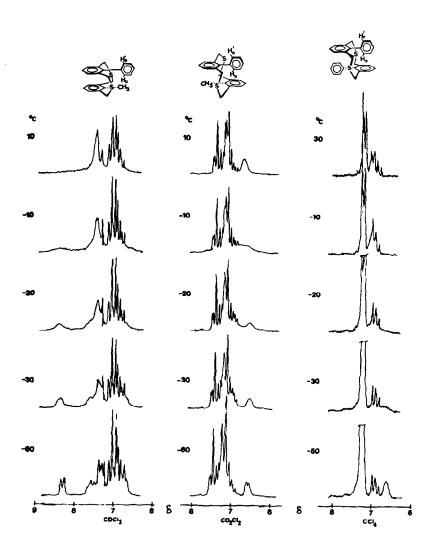
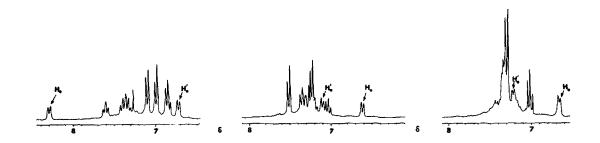


Figure 1: 90 MHz ¹Hmr Variable Temperature Spectra for aryl proton region of

250 MHz $^1\mathrm{Hmr}$ spectra at -60°C for aryl proton region



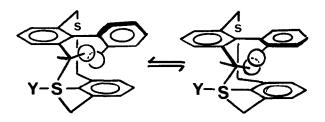
and in **3B** it could be shielded by the opposite substituent ring. The magnitude of these two effects might, however, be different since it is possible for the substituent ring to twist somewhat out of the plane of the cyclophane rings. Nevertheless, we first decided to synthesise the compounds with one internal methyl group, the presence of which has normally made assignment of stereochemistry much easier.⁶

Thus, cyclization⁷ of 5^8 and 2,6-bis(bromomethyl)toluene^{6a}, **6**, at 60°C gave a 40% yield⁹ of the syn, anti- mixture **2C**, **3C** in about a 4:1 ratio. Chromatography over silica gel followed by crystallization yielded pure¹⁰ anti-**2C**, mp 164.5-165° and pure syn-**3C**, mp 170°C. Assignment of stereochemistry was readily made on the basis of the low temperature (-60°C) ¹Hmr spectra, when both compounds were in frozen conformations. The anti- compound **2C** shows its internal methyl protons at $\delta 1.46$, strongly shielded by the opposite cylophane ring, consistent with other anti- cyclophanes.⁶ Whereas syn-**3C** shows its methyl protons at $\delta 2.37$, almost normal for a toluene, and only marginally shielded from other syn- cyclophanes⁶ by the opposite phenyl substituent, which indicates that this ring must be more or less edge on (see also below). Further support for this assignment is derived from the chemical shift of the ortho-protons of the phenyl substituent, H₀, H'₀: in the anti- compound **2C**, H₀($\delta 6.55$) is shielded somewhat from H'₀ ($\delta 7.10$) by the opposite cyclophane ring, whereas in syn-**3C**, H₀ is strongly deshielded to $\delta 8.31$ by steric compression with the opposite methyl group.¹¹

Reaction of bromide **4** with thiol **5** yielded about 1% yield of **2B**, **3B** in a 10:1 ratio, from which pure¹⁰ anti-**2B**, mp248-249°C (lit³mp **220-226**°C), could be separated by chromatography. On the basis of its (-60°C) ¹Hmr spectrum, it was assigned the anti- stereochemistry since H_o and H'_o appeared at very similar chemical shift ($\delta 6.63$ and 7.30) to those of anti- **2C**. This was subsequently confirmed by X-ray crystallography.¹²

The 90 MHz ¹Hmr variable temperature spectra for the aryl proton region of **2B**, **2C**, and **3C** are shown in Figure 1, together with the -60°C, 250 MHz spectra (which allow definitive placement of H_o and H'_o). The data used to obtain ΔG_c^{\ddagger} values are given in Table 1. It is of extreme interest that these three values are very similar. From molecular models, and X-ray data of **2B**, it seems to us very unlikely that free rotation of the internal phenyl substituent can occur, more likely a flipping (twisting) process, such as shown in Figure 2 is

FIGURE 2: CONFORMATIONAL FLIPPING (TWISTING) PROCESS OF 2(3)



occurring in which $H_0(H'_0)$ flips from one side of the methylene bridge protons to another. This would be consistent with the similarity of the three barriers, and closeness to that of $IA(\Delta G_c^4 = 54 \text{ kJ. mol}^{-1})$.³ In due course, we hope to be able to make more detailed comments on this process from complete lineshape analyses, and further nmr and X-ray measurements which are now underway.

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Table 1:	90MHz Data	Used to Calculate ¹³	∆G [∓] c
Compound			
Δv (Hz)	141.6	44.3	50.1
$T_{c}(K)$	265	262	243
ΔG_{c}^{\dagger} (kJ. mol ⁻¹)	52.0	53.9	49.6

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