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THE WITTIG REARRANGEMENT OF SOME THIACYCLOPHANES.

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The route to cyclophane dienes from dithia[3,3]cyclophanes utilizing a Stevens rearrangement followed by a Hofmann elimination has been applied with success both by ourselves[1] and other workers[2]. We have however encountered examples in which the Stevens rearrangement step is temperamental; the yields obtained being sensitive to both the nature of the base used and its concentration, as well as to the starting thiacyclophane. This has been particularly important since we have now improved significantly the yields of the starting dithia[3,3]cyclophanes (see below) and hence have been investigating reactions on a larger scale.

Since it has been noticed[3] that mechanistically there are many similarities between the Stevens and Wittig rearrangements, and more recently[4] the Wittig rearrangement of dibenzyl sulfide has been reported, and gives the same products as the Stevens rearrangement on the corresponding methyl sulfonium salt reported earlier.[1,5] We thought it worthwhile to investigate the Wittig rearrangement of some dithia[3,3]cyclophanes.

Treatment of 2,11-Dithia[3,3]metacyclophane **1a** with either n-butyllithium or lithium diisopropylamide in dry tetrahydrofuran at 0°C followed by methylation of the resulting thiolate with methyl iodide gave the [2,2]metacyclophane **1b** in better than 94% yield after purification. The results with a variety of other thiacyclophanes are shown in Table 1.

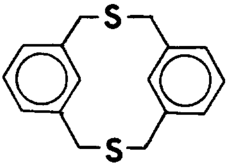
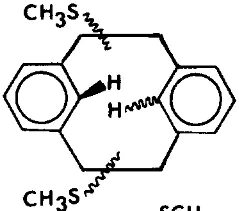
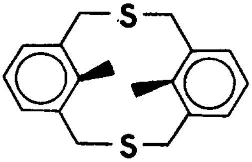
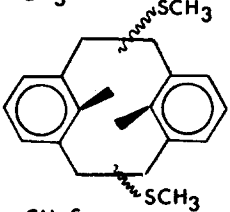
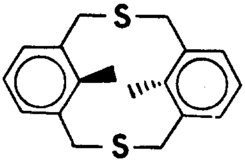
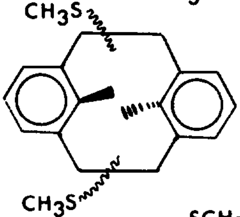
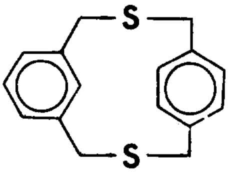
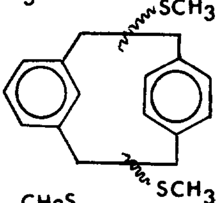
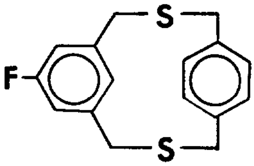
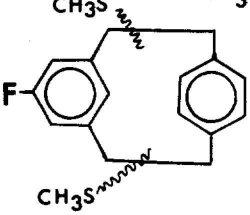
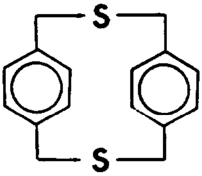
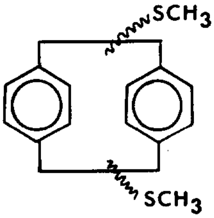
Reactant		Product		Yield (after purification)
	1a		1b	94% [70 anti : 30 syn]
	2a		2b	59% [98 anti (3b) : 2 syn (2b)]
	3a		3b	99% [100 anti]
	4a		4b	65%
	5a		5b	63%
	6a		6b	24%

TABLE 1

In all cases the Wittig rearrangement occurs more rapidly and is more convenient to conduct than the analogous Stevens rearrangements. In the case of the paracyclophane **6a**, where 1,6-elimination is a competing side reaction, the Wittig rearrangement using iPr_2NLi gives the desired product in 24% yield, whereas in our hands none of the desired product was obtained from the Stevens rearrangement. In the reactions involving **1a**, **3a**, **4a** or **5a** the product isomer ratios were the same in the Wittig rearrangements as in the corresponding Stevens rearrangement, whereas those from **2a** were not, more of the anti isomer being formed. This might indicate a longer lived intermediate in this reaction, allowing the syn isomers to ring flip to the thermodynamically more stable anti isomers. The distribution of the $-SCH_3$ groups in the product isomers was shown to be essentially the same as obtained in the Stevens rearrangements by comparison of the pmr spectra for the separated products (previously reported in detail).[1] In the case of **6b** however, no definite assignment has yet been possible.

It is noteworthy that the following experimental procedure was applied in all cases: To a solution of 2 mmoles of the thiacyclophane in 10 ml dry THF under N_2 was added 5 mmoles of BuLi in hexane or 5 mmoles of iPr_2NLi in hexane/THF (10 ml) with ice cooling. After 2-3 mins, 10 mmole of MeI was added, which caused an immediate dissolution of any precipitated salts and decolourization of the solution. The reaction mixture was worked up by addition of H_2O and CH_2Cl_2, and the products were purified by filtration through silica gel. When this procedure is scaled up, the yields are maintained.

The initial coupling to produce the dithia[3,3]cyclophanes has been markedly improved to give the coupling product in about 80% yield in the following manner: A mixture of the xylylene bromide and xylylene dithiol (<0.1 mole/litre) in benzene is added dropwise over 70-100 hours to a <0.1M solution of KOH in 90% ethanol (at RT or reflux) under N_2. After removal of solvent and crystallization/chromatography of the product, the following yields have been obtained: **1a**, RT, 82%; **2a** and **3a**, reflux: 76% (11% syn, 65% anti); **4a**, RT, 81%.

The net result of these two procedures is that substituted [2,2]cyclophanes (**1b**-**6b**) are much more readily available than previously. Desulfurization with Raney Nickel can then be used to give the [2,2]cyclophanes themselves,[1] or employment of the Hofmann elimination procedure can be used to give the cyclophane dienes. In the case of **3a**, the end product is *trans*-15,16-dimethyl-15,16-dihydropyrene, the tautomer of the cyclophanediene, and this can now be prepared in about 65% overall yield from 2,6-bis(bromomethyl)toluene, a considerable improvement from the original synthesis.[6]

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3. See for example A. R. Lepley "Molecular Rearrangements and Miscellaneous Reactions", chap. 8 in Chemically Induced Magnetic Polarization, Ed. by A. R. Lepley and G. L. Closs, Wiley, New York, 1973.
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