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AN ALTERNATE ROUTE FOR THE CONVERSION OF DITHIA[3.3]CYCLOPHANES TO CYCLOPHANE-DIENES. REACTION WITH BENZYNE FOLLOWED BY SULFOXIDE PYROLYSIS.

Tetsuo Otsubo and Virgil Boekelheide*
Department of Chemistry, University of Oregon
Eugene, Oregon 97403 U.S.A.

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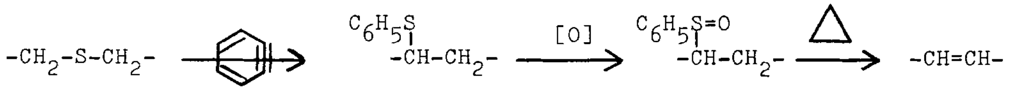
The conversion of dithia[3.3]cyclophanes to cyclophane-dienes utilizing a Stevens rearrangement followed by a Hofmann elimination has proved to be generally useful for the synthesis of [2.2]metacyclophane-1,9-dienes,[1] 15,16-dihydropyrenes,[2] [2.2]metaparacyclophane-1,9-dienes,[3] [2.2]naphthalenophane-dienes,[4,5] and various other derivatives.[6] The scope of the method has recently been extended by the discovery that the Wittig rearrangement can often be employed advantageously in place of the Stevens rearrangement.[7] However, for certain types of compounds the yields obtained in the Stevens and Wittig rearrangements may be low due to competing side reactions. Paracyclophane derivatives, in particular, undergo 1,6-elimination and so usually give the desired rearrangement products in fair to poor yield. This has stimulated us to examine alternate routes for the conversion of dithiacyclphanes to cyclophane-dienes. We now report that the reaction of dithiacyclophanes with benzyne followed by pyrolysis of the corresponding sulfoxides provides a useful alternative to the Stevens or Wittig rearrangement followed by a Hofmann elimination. The steps involved in this alternate benzyne-sulfoxide pyrolysis route are illustrated below.



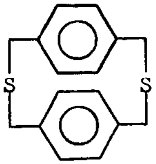
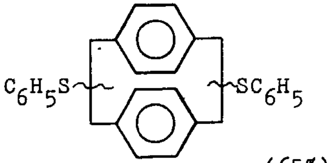
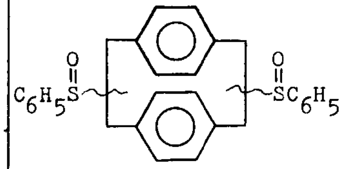
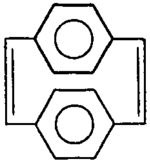
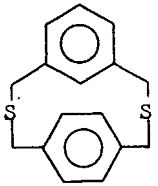
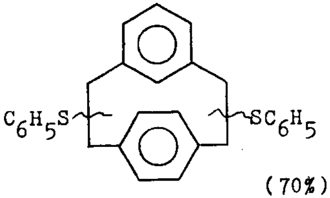
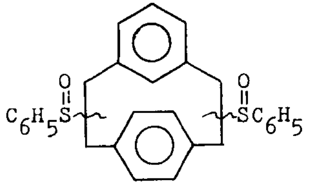
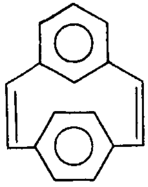
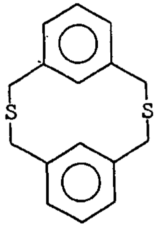
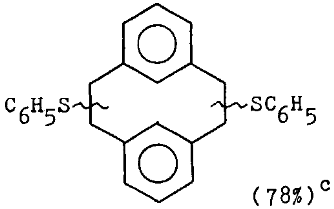
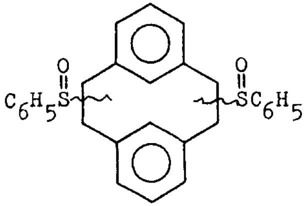
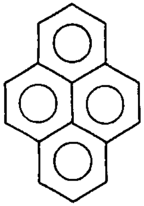
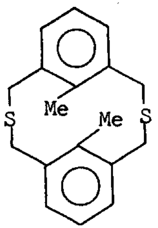
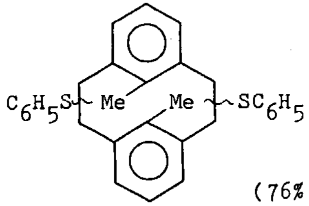
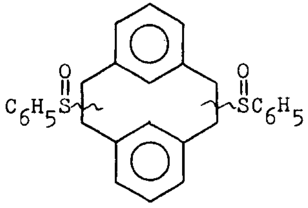
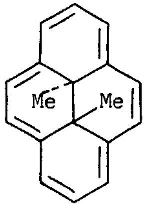
$$-CH_2-S-CH_2- \longrightarrow \overset{C_6H_5S}{-CH-CH_2-} \xrightarrow{[O]} \overset{C_6H_5S=O}{-CH-CH_2-} \xrightarrow{\Delta} -CH=CH-$$

Generation of benzyne in situ provides for ease of operation and allows for increasing the scale of the reaction without exceptional hazard. A typical experimental procedure for the benzyne reaction is as follows. A solution of 1 mmole of anthranilic acid in 20 ml of 1,2-dichloroethane was added dropwise over a period of 2.5 hr. to a solution of 0.4 mmole of a dithiacyclophane and an excess (420 mg) of isoamyl nitrite in 20 ml of 1,2-dichloroethane boiling under reflux in a nitrogen atmosphere. After concentration of the reaction mixture under reduced pressure, the residual oil was taken up in either carbon tetrachloride or a 1:1 benzene-hexane mixture and chromatographed over a column of silica gel. The main fraction of eluate gave either a colorless oil or a semi-solid. Nmr analysis showed this product to be a mixture of stereoisomers corresponding to the desired Stevens rearrangement product.

The yields obtained in the benzyne-Stevens rearrangement are summarized in Table I. For the paracyclophane case the benzyne reaction is clearly superior to the normal Stevens or to the Wittig rearrangement, giving the desired rearrangement product in 65% yield as compared to 24% in the Wittig rearrangement and a very low yield in the normal Stevens. For the metaparacyclophane case the benzyne reaction is still slightly better with a yield of 70% as compared to 65% in the Wittig and 57% in the normal Stevens. For the metacyclophane derivatives, where 1,6-elimination is not a possibility, the normal Stevens or Wittig rearrangements are superior proceeding in essentially quantitative yields.

Since phenyl sulfides are not well suited for a Hofmann elimination, it was necessary to find an alternate method for removal of sulfur with concomitant introduction of a carbon-carbon double bond. It was also desirable that such an alternate method be different in mechanistic pathway and steric requirements so that it could be complementary to the present Hofmann elimination route. Kingsbury and Cram first studied the thermal elimination of sulfoxides and showed that, at low temperatures at least, the stereospecificity of the reaction was in accord with a mechanism involving concerted cis elimination.[8] Considerable interest has developed recently in synthetic applications of sulfoxide eliminations to give olefins.[9-11] We now report that this is a useful method for introducing carbon-carbon double bonds into [2.2]cyclophanes. The various Stevens rearrangement products from the benzyne reaction shown in Table I were converted in essentially quantitative yield to their corresponding bisulfoxides and these, in turn, on pyrolysis gave the desired cyclophane-dienes, or their transformation products, in fair to good yield. The following description is typical of the experimental procedure employed. A solution of 0.25 mmole of Stevens rearrangement product and two equivalents of m-chloroperbenzoic acid in 10 ml of chloroform was allowed to stand at room temperature for one day under a nitrogen atmosphere. After the solution had been washed with a saturated, aqueous sodium bicarbonate solution, it was dried and concentrated to give a colorless solid. Nmr analysis indicated that the mixture of stereoisomers of the corresponding bissulfoxides was essentially pure and had formed in quantitative yield. Pyrolysis of the sulfoxides was accomplished either by a) heating 0.25 mmole of the bissulfoxide in 50 ml of xylene under reflux for 20 hr. and then concentrating; or b) heating the bissulfoxide under vacuum (5×10^{-4}mm) in a gradient sublimator and collecting the product in a cold trap. In either case the crude product was taken up in carbon tetrachloride, or a 1:1 benzene-hexane mixture, and

TABLE I

Dithia[3.3]-cyclophanes	Benzyne Products (Yield)	Sulfoxides	Pyrolysis Products (Yield a, xylene; b, vacuum)
	 (65%)		 (a, 54%; b, 31%)[d]
	 (70%)		 (a, 24%)
	 (78%)[c]		 (b, 37%)
	 (76%)		 (b, 34%)

[c] nmr analysis indicated 39% syn and 61% anti conformation. [d] mp. 233.5-234.5 (ref.12, mp. 230-231°); nmr analysis ($CDCl_3$); singlet at τ 2.80 (4H, -CH=CH-) and a singlet at τ 3.50 (8H, Ar<u>H</u>).

chromatographed over silica gel. The resulting solid was then recrystallized from a benzene-hexane mixture to give a pure crystalline product on which the yields in Table I are based. Identification in each case was then made by direct comparison with an authentic sample or, in the case of [2.2]paracyclophane-1,9-diene by comparison with data from the literature.[12]

A comparison of the benzyne-sulfoxide route with the Stevens-Hofmann route would indicate that the older method is superior in yield for metacyclophanes, although the benzyne-sulfoxide route may be easier to execute experimentally. For paracyclophane derivatives, though, the benzyne-sulfoxide route is superior and is clearly the method of choice for preparing [2.2]paracyclophane-1,9-diene.

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