Syntheses of Cyclophanes by Photochemical Extrusion of Sulphur

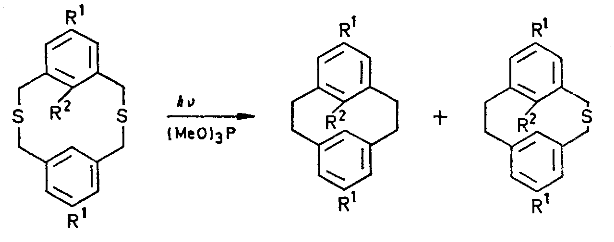
By Virgil Boekelheide,* I. David Reingold, and Mark Tuttle
(*Department of Chemistry, University of Oregon, Eugene, Oregon* 97403)

Summary Irradiation of dithiacyclophanes in the presence of trimethyl phosphite gives the corresponding cyclophanes in good yield, and this procedure has allowed the synthesis of [2,2](2,6)pyridinoparacyclophane (**8**).

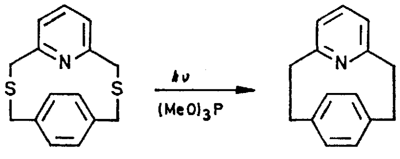
Until recently, the only good general method for synthesizing cyclophanes has been the Wurtz reaction.[1] The formation of dithiacyclophanes generally occurs in excellent yield, and they have been used as precursors for syntheses of cyclophanes in two ways: (i) the extrusion of sulphur has been accomplished by a two-step reaction sequence of a Stevens rearrangement followed by a Hofmann elimination;[2] (ii) the extrusion of sulphur has been accomplished by conversion into the corresponding bis-sulphone followed by elimination of sulphur dioxide on pyrolysis.[3] It had been reported that irradiation of sulphides alone in the presence of trivalent phosphorus derivatives leads to extrusion of sulphur.[4] We now report that irradiation of dithiacyclophanes in the presence of trimethyl phosphite provides a convenient, high-yield, single-step synthesis of cyclophanes.

For example, the condensation of 3,5-bis(bromomethyl)-toluene and 3,5-bis(mercaptomethyl)toluene gave *anti*-6,15-dimethyl-2,11-dithia[3,3]metacyclophane (**1**), m.p. 98–99°, in 45% yield.† Irradiation of (**1**) (300 mg) in trimethyl phosphite (8 ml) at 24° using Vycor tubing and a Hanovia 450 w high-pressure mercury lamp for 18 h gave (**3**), identical in all respects with a known sample,[5] in 85% yield. When the irradiation was carried out for shorter periods, the yield of (**3**) was lower and the intermediate product (**5**), m.p. 116—117°, corresponding to a single extrusion of sulphur was isolated.

Similarly, the condensation of 2,6-bis(bromomethyl)-toluene with 1,3-bis(mercaptomethyl)benzene gave (**2**), m.p. 104—105°, in 38% yield. Irradiation of (**2**) in trimethyl phosphite at room temperature for 48 h gave (**4**),[6] in 49% yield. At shorter irradiation times, n.m.r. monitoring showed the presence of the intermediate monosulphide, (**6**).



(1) R¹ = Me, R² = H
(2) R¹ = H, R² = Me
(3) R¹ = Me, R² = H
(4) R¹ = H, R² = Me
(5) R¹ = Me, R² = H
(6) R¹ = H, R² = Me



(7) (8)

Sutherland and his co-workers have studied the comparative steric requirements of the pyridine nitrogen lone pair *versus* a benzene carbon–hydrogen bond with respect to conformational flipping in the [2,2]metacyclophane series.[7] In contrast to [2,2]metacyclophane, which shows no change in its n.m.r. spectrum up to 200°, the corresponding [2,2]metaparacyclophane exhibits n.m.r. coalescence at 157° using a 100 MHz spectrometer.[8] It was of interest to see whether the present procedure might provide (**8**), the pyridine analogue of [2,2]metaparacyclophane,

---

† Satisfactory elemental analyses and spectral data have been obtained for all new compounds.

and if so, to examine the n.m.r. spectrum of (**8**) and its temperature dependence.

Condensation of 2,6-bis(mercaptomethyl)pyridine and *p*-xylylene dibromide gave (**7**), m.p. 177—178°, in 48% yield. Irradiation of (**7**) in trimethyl phosphite gave (**8**), m.p. 83—84°. At room temperature the four *para*-bridged aromatic protons of (**8**) appear as a singlet. Separation into the two separate signals corresponding to the respective conformational isomers is observed only at quite low temperatures, with coalescence occurring at $-50°$, using a 100 MHz spectrometer. Although the transition state for conformational flipping in the case of the [2,2]metaparacyclophane skeleton is probably different to that for the [2,2]metacyclophanes, the conclusion is that the pyridine nitrogen lone pair has appreciably smaller steric requirements than an aromatic carbon–hydrogen bond.

We thank the National Science Foundation for their support of this work.

(*Received*, 17*th April* 1973; *Com.* 552.)

[1] B. H. Smith, 'Bridged Aromatic Compounds,' Academic Press, New York, 1964.
[2] R. H. Mitchell and V. Boekelheide, *Tetrahedron Letters*, 1970, 1197.
[3] F. Vögtle, *Angew. Chem.*, 1969, **81**, 258.
[4] E. H. Corey and E. Block, *J. Org. Chem.*, 1969, **34**, 1233.
[5] V. Boekelheide and R. W. Griffin, *J. Org. Chem.*, 1969, **34**, 1960.
[6] H. Blaschke, C. E. Ramey, I. Calder, and V. Boekelheide, *J. Amer. Chem. Soc.*, 1970, **92**, 3675.
[7] I. Gault, B. J. Price, and I. O. Sutherland, *Chem. Comm.*, **1967**, 540; J. R. Fletcher and I. O. Sutherland, *ibid.*, **1969**, 1504.
[8] S. A. Sherrod and V. Boekelheide, *J. Amer. Chem. Soc.*, 1972, **94**, 5513.