Transformation of Sulfide Linkages to Carbon–Carbon Double Bonds. Syntheses of [2.2]Metaparacyclophane-1,9-dienes[1,2]

V. Boekelheide,* Peter H. Anderson, and Thomas A. Hylton

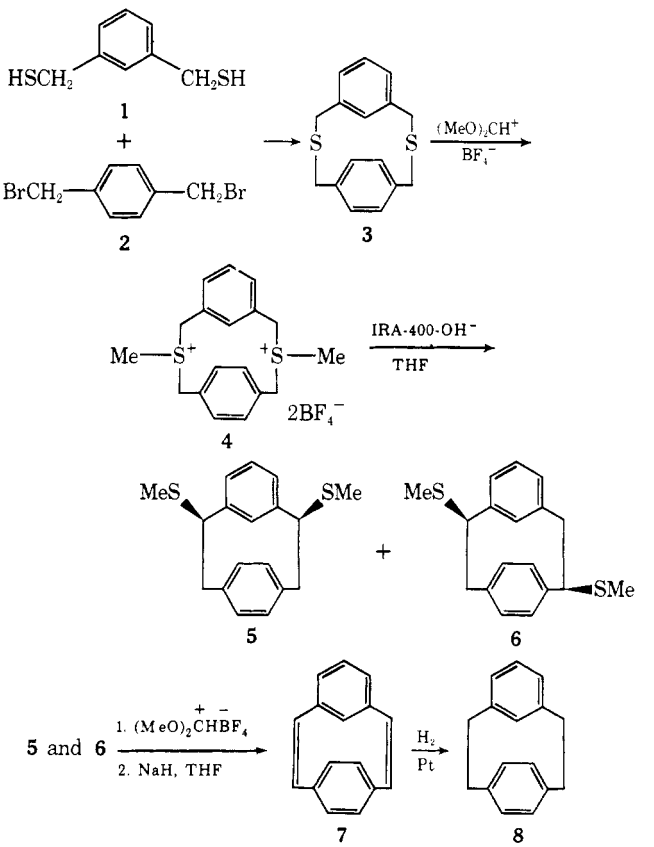
Contribution from the Department of Chemistry, University of Oregon, Eugene, Oregon 97403. *Received July 10, 1973*

Abstract: The two-step reaction sequence of a Stevens rearrangement followed by a Hofmann elimination provides a convenient synthetic route for transforming 2,11-dithia[3.3]metaparacyclophanes to [2.2]metaparacyclophane-1,9-dienes. The requisite 2,11-dithia[3.3]metaparacyclophanes are readily available in good yield by the condensation of *m*-xylylene dibromides with *p*-xylylene dimercaptans or, alternatively, by the condensation of *p*-xylylene dibromides with *m*-xylylene dimercaptans. A series of [2.2]metaparacyclophane-1,9-dienes have been prepared having fluoro, cyano, or formyl groups at the 8 position. These [2.2]metaparacyclophane-1,9-dienes are of interest because, in order for the molecule to undergo conformational flipping, the internal substituent at the 8 position is forced strongly into the aromatic π-electron cloud of the para-bridged ring and, thus, the energy barrier to conformational flipping provides an insight into the interaction of such functional groups with aromatic π-electron clouds. An alternate approach to the synthesis of cyclophanes, involving the alkylation of bis(dithianes), is described and its employment for the synthesis of [2.2]metaparacyclophane-1,9-diene is presented.

In an accompanying paper we have described a two-step reaction sequence (Stevens rearrangement and Hofmann elimination) for transforming sulfide linkages to carbon–carbon double bonds.[3] It was demonstrated that this procedure provides convenient access to a variety of [2.2]metacyclophane and 15,16-dihydropyrene derivatives. In the present report we describe the extension of this method to the synthesis of [2.2]-metaparacyclophane-1,9-dienes. In addition and for comparison we present yet another general cyclophane synthesis based on the alkylation of bis(dithianes).

The pioneer investigations of [2.2]metaparacyclophanes have been made by Cram and his collaborators,[4–7] who discovered the acid-catalyzed rearrangement of [2.2]paracyclophane to [2.2]metaparacyclophane.[8,9] Although this procedure is a very convenient one for obtaining the parent substance, it appeared likely that the Stevens rearrangement–Hofmann elimination sequence would be advantageous for preparing [2.2]metaparacyclophane-1,9-dienes as well as for preparing [2.2]metaparacyclophanes with substituents at specific positions.

As a first test of our method we investigated the preparation of [2.2]metaparacyclophane-1,9-diene (**7**).[10] Condensation of *p*-xylylene dibromide (**1**) with 1,3-bis(mercaptomethyl)benzene (**2**) gave 2,11-dithia[3.3]-metaparacyclophane (**3**) in 43% yield.[11] Treatment of **3** with dimethoxycarbonium fluoroborate[12] gave the corresponding bis(sulfonium) fluoroborate (**4**) in essentially quantitative yield. The Stevens rearrangement was carried out by stirring a solution of **4** in tetrahydrofuran with an ion exchange resin (IRA-400-OH) at room temperature for 84 hr. The product was a mixture of two isomers, **5** and **6**, formed in an overall



(1) We thank the National Science Foundation for their support of this investigation.

(2) Abstracted from the doctoral dissertation of P. H. Anderson, University of Oregon, 1971.

(3) R. H. Mitchell and V. Boekelheide, *J. Amer. Chem. Soc.*, **96**, 1547 (1974).

(4) D. T. Hefelfinger and D. J. Cram, *J. Amer. Chem. Soc.*, **93**, 4754 (1971).

(5) D. T. Hefelfinger and D. J. Cram, *J. Amer. Chem. Soc.*, **93**, 4767 (1971).

(6) D. J. Cram and J. W. Cram, *Accounts Chem. Res.*, **4**, 204 (1971).

(7) R. E. Gilman, M. H. Delton, and D. J. Cram, *J. Amer. Chem. Soc.*, **94**, 2478 (1972).

(8) D. J. Cram, R. C. Helgelson, D. Lock, and L. A. Singer, *J. Amer. Chem. Soc.*, **88**, 1324 (1966).

(9) D. T. Hefelfinger and D. J. Cram, *J. Amer. Chem. Soc.*, **92**, 1074 (1970).

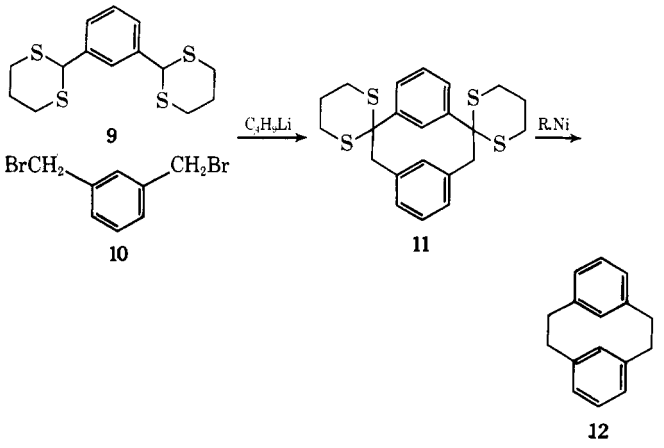
(10) For preliminary publication of this work, see V. Boekelheide and P. H. Anderson, *Tetrahedron Lett.*, 1207 (1970).

(11) F. Vögtle [*Chem. Ber.*, **102**, 3077 (1969)] has also reported the synthesis of **3**, indicating that the condensation of *m*-xylylene dibromide and 1,4-bis(mercaptomethyl)benzene gives **3** in only 18% yield.

(12) R. F. Borch, *J. Org. Chem.*, **34**, 627 (1969).

yield of 45%. For the Hofmann elimination the mixture of **5** and **6** was again methylated using dimethoxycarbonium fluoroborate and then treated with sodium hydride in tetrahydrofuran. This gave [2.2]metaparacyclophane-1,9-diene (**7**) in 72% yield. The assignment of structure to **7** was confirmed by its quantitative hydrogenation over platinum to give the known [2.2]metaparacyclophane (**8**).[8]

Before we discuss the properties of [2.2]metaparacyclophane-1,9-diene (**7**), it is of interest to compare this synthesis with an alternate one based on the alkylation of bis(dithianes).[13] Corey and Seebach first introduced the alkylation of dithianes as a method for converting aldehydes to ketones.[14] Since application of this procedure to aromatic dialdehydes could effect cyclization, we have investigated the potential of the method for synthesizing cyclophanes. It was found that the alkylation of isophthalaldehyde bis(dithioacetal) (**9**) with *m*-xylylene dibromide (**10**) gave the corresponding [2.2]metacyclophane derivative **11** in 28% yield.[15] The structure of **11** was readily established by its desulfurization with Raney nickel to the known [2.2]metacyclophane (**12**).



Similarly, the alkylation of **9** using *p*-xylylene dibromide (**2**) gave the corresponding [2.2]metaparacyclophane derivative **13** in 40% yield. Again, Raney nickel desulfurization of **13** to give [2.2]metaparacyclophane (**8**) established its structure. Hydrolysis of **13** in methanol using mercuric chloride as catalyst led to [2.2]metaparacyclophane-2,9-dione (**14**) in 91% yield. Reduction of **14** with sodium borohydride gave a mixture of the diastereoisomeric alcohols **15** in 97% yield. Conversion of **15** to the corresponding ditosylate **16** followed by an elimination reaction using potassium *tert*-butoxide in *tert*-butyl alcohol then gave [2.2]-metaparacyclophane-1,9-diene (**7**) in 65% overall yield. The dithiane alkylation procedure is advantageous for preparing cyclophanes with functionality in the aliphatic bridges. However, the Stevens rearrangement–Hofmann elimination sequence is shorter and more convenient for preparing cyclophane-1,9-dienes or cyclophanes with specific substituents in the aromatic rings.

(13) For a preliminary publication describing this method, see T. Hylton and V. Boekelheide, *J. Amer. Chem. Soc.*, **90**, 6887 (1968).

(14) E. J. Corey and D. Seebach, *Angew. Chem.*, **77**, 1134, 1135 (1965); D. Seebach, N. R. Jones, and E. J. Corey, *J. Org. Chem.*, **33**, 300 (1968).

(15) Recently, H. W. Gschwend [*J. Amer. Chem. Soc.*, **94**, 8430 (1972)] has reported that by using a high dilution procedure the yield in this reaction can be raised to about 70%.

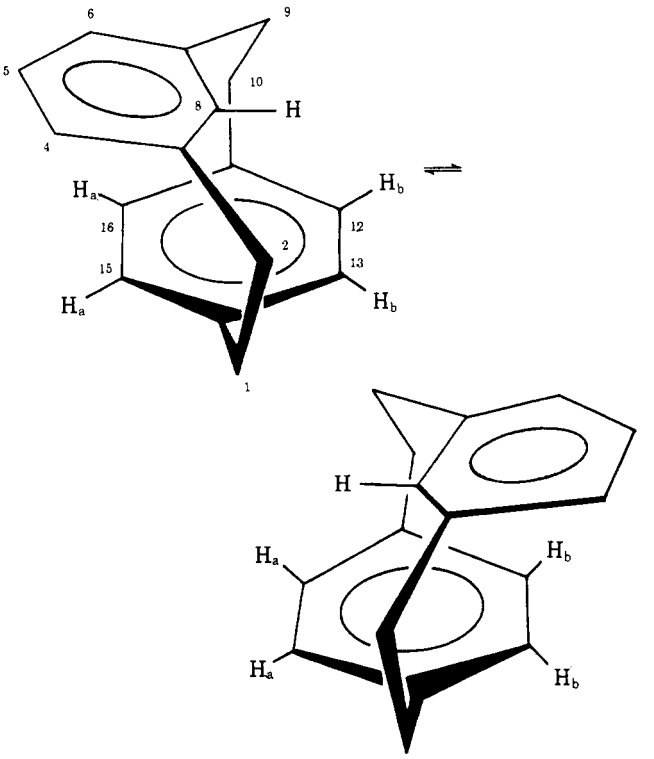
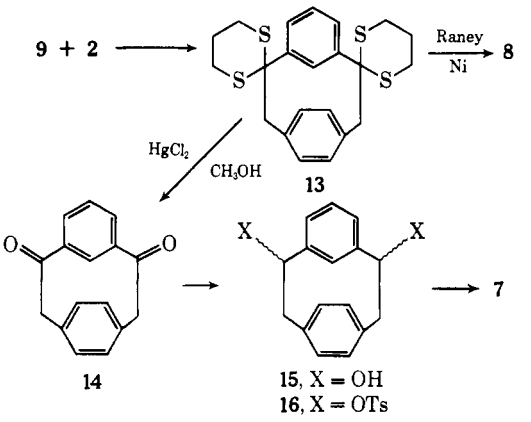


Figure 1. Conformational flipping of [2.2]metaparacyclophanes and [2.2]metaparacyclophane-1,9-dienes.



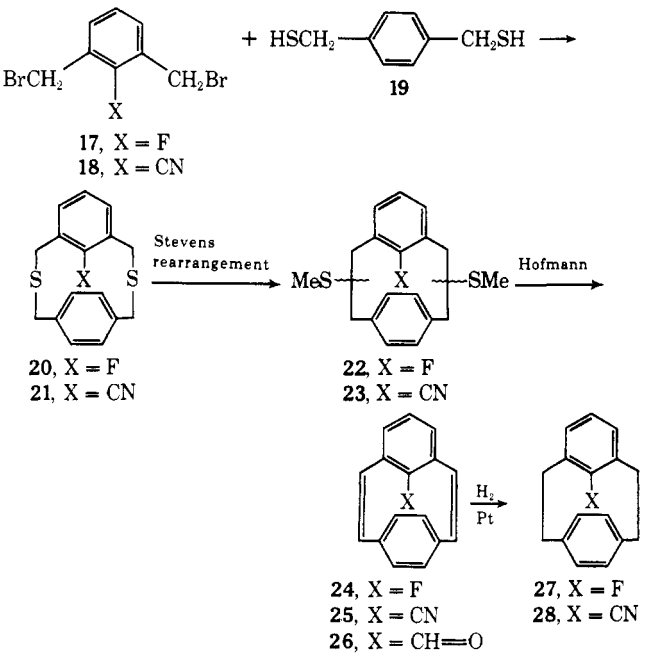
One of the interesting features of the [2.2]metaparacyclophane moiety is that its transition state for conformational flipping, as shown in Figure 1, requires the substituent at the 8 position to impinge very strongly into the aromatic π-electron cloud of the para-bridged ring. Thus, the room temperature nmr spectrum of [2.2]metaparacyclophane (**8**) shows the four para-bridged, aromatic protons as a pair of narrow multiplets centered at τ 4.30 (H_a) and 3.03 (H_b). At 60 MHz, coalescence of these two signals occurs at about 140°.[9,16] The $\Delta G^{\ddagger}_{140°}$ for the conformational flipping of **8** has been calculated to be 20.8 kcal/mol.[9] Quite in contrast, the four para-bridged, aromatic protons of [2.2]-metaparacyclophane-1,9-diene (**7**) appear as a singlet at τ 3.23, when measured at room temperature. It is only below −100° that two separate signals (H_a and H_b) are seen at τ 3.69 and 2.78. From the coalescence temperature of −96° and $\Delta\nu$ = 91.0 Hz, the value of $\Delta G^{\ddagger}_{-96}$ for the conformational flipping of **7** is calculated

(16) S. A. Sherrod and V. Boekelheide, *J. Amer. Chem. Soc.*, **94**, 5513 (1972).

to be 8.3 kcal/mol, using the method of Calder and Garratt.[17]

At first glance it might seem surprising that the energy barrier for conformational flipping is smaller for the diene **7** than for [2.2]metaparacyclophane (**8**) itself. However, examination of molecular models indicates that the effect of bond angle change in going from bridging sp^3 carbons to sp^2 carbons is opposite to and outweighs the effect of bond shortening. Thus, the transition state for conformational flipping of [2.2]metaparacyclophane (**8**) requires a deeper penetration into the cavity of the para-bridged, aromatic π-electron cloud by the substituent at the 8 position than is the case for the corresponding [2.2]metaparacyclophane-1,9-diene. This has also been borne out by X-ray crystallographic structure determinations of **7** and **8**.[18,19] In crystals of **7**, the aromatic rings are inclined to each other at an angle of 41°.[18] The distance between C(8) and the plane of carbons 12, 13, 15, and 16 is 2.71 Å, whereas for H(8) it is only 2.16 Å. If the meta-bridged ring is brought perpendicular to the para-bridged ring, but without otherwise distorting bond angles or bond lengths, these distances become 2.57 and 1.59 Å, respectively. Although the exact comparable figures for **8** are not available, they are even somewhat shorter. Because the conformational flipping of [2.2]metaparacyclophane derivatives requires deep penetration of the para-bridged, aromatic π-electron cloud by whatever substituent is present at the 8 position and because the rates of conformational flipping of these derivatives can readily be followed by nmr, [2.2]metaparacyclophane derivatives are exceedingly well suited for studying the interactions of various functional groups with aromatic π-electron clouds. In the remainder of the present paper we report on our studies of derivatives of [2.2]metaparacyclophane-1,9-diene having bulkier substituents than hydrogen at the 8 position. In an accompanying paper,[20] studies of the effect on the rate of conformational flipping of [2.2]metaparacyclophane derivatives having substituents at the 5 position or isotopic substitution at the 8 position are reported. In two other accompanying papers, the effects of replacing the aromatic C–H at the 8 position by a pyridine nitrogen with its lone pair are presented.[21a,b]

In the common way of categorizing substituents according to steric interaction the next larger substituent than hydrogen is usually considered to be fluorine.[22] It was of interest to see what effect an 8-fluoro substituent would have on the rate of conformational flipping of [2.2]metaparacyclophane-1,9-diene. The condensation of 2,6-bis(bromomethyl)fluorobenzene (**17**) with 1,4-bis(mercaptomethyl)benzene (**19**) gave 9-fluoro-2,11-dithia[3.3]metaparacyclophane (**20**) in 44% yield.[23] In contrast to **3**, the rate of conformational flipping for **20** is sufficiently slow at room temperature that the para-bridged aromatic protons appear as two signals at τ 3.42 and 2.93. Also, the methylene protons appear as two overlapping AB systems at τ 6.29 and 6.51. A variable temperature study of **20** at 100 MHz showed coalescence of the para-bridged, aromatic proton signals at 93° ($\Delta\nu$ = 49 Hz, $\Delta G^{\ddagger}_{93}$ = 18.2 kcal/mol). Subjection of **20** to a Stevens rearrangement gave **22** as a mixture of isomers in 52% yield. A Hofmann elimination of **22** then led to 8-fluoro[2.2]-metaparacyclophane-1,9-diene (**24**) in 92% yield. Hydrogenation of **24** over platinum proceeded in essentially quantitative yield to give 8-fluoro[2.2]metaparacyclophane (**27**).



The room temperature nmr spectrum of 8-fluoro-[2.2]metaparacyclophane-1,9-diene (**24**) shows the para-bridged, aromatic protons as two very narrow multiplets at τ 3.74 and 2.80. In a variable temperature study at 100 MHz, a solution of **24** in dimethyl-d_6 sulfoxide was heated to 150° but with no change in its nmr spectrum. When this result is compared to the coalescence temperature of −96° for conformational flipping of [2.2]-metaparacyclophane-1,9-diene (**7**), it is apparent that a small change in the steric requirements of the "internal" substituent at the 8 position has a drastic effect on the rate of conformational flipping.

A striking spectral characteristic of [2.2]metaparacyclophane-1,9-diene (**7**) is the strong upfield shift of the signal for the 8 proton due to the ring current of the para-bridged ring. The position of this signal is quite sensitive to the "average" geometry of the molecule. In a carbon disulfide solution at 35°, when there is fast conformational flipping, this signal is at τ 5.74. However, at −110°, when the conformational isomers are frozen out on the nmr time scale, the position of this signal has moved even further upfield to τ 6.00. For both **3**, where there is fast conformational flipping, and **8**, where conformational flipping is restricted, the signal for the "internal" proton is at lower field, τ 4.48 and 4.76, respectively, as shown in Table I.

Although ring current effects on neighboring protons are well known to be quite striking, there is some ques-

(17) I. C. Calder and P. J. Garratt, *J. Chem. Soc. B*, 660 (1967).
(18) A. W. Hanson, *Acta Crystallogr., Sect. B*, **27**, 197 (1971).
(19) K. N. Trueblood and M. J. Crisp, as quoted in ref 4.
(20) S. A. Sherrod, R. L. da Costa, R. A. Barnes, and V. Boekelheide, *J. Amer. Chem. Soc.*, **96**, 1565 (1974).
(21) (a) V. Boekelheide, K. Galuszko, and K. S. Szeto, *J. Amer. Chem. Soc.*, **96**, 1578 (1974); (b) L. H. Weaver and B. W. Matthews, *ibid.*, **96**, 1581 (1974).
(22) R. L. Shriner, R. Adams, and C. S. Marvel in H. Gilman, "Organic Chemistry," Wiley, New York, N. Y., 1938, Chapter 3.
(23) F. Vögtle [*Chem. Ber.*, **102**, 3077 (1969)] has also reported the preparation of **20** by the condensation of 2,6-bis(mercaptomethyl)-fluorobenzene with *p*-xylylene dibromide, but in only 14% yield.

Table I. Comparison of Nmr Chemical Shifts of the Internal Proton and Fluorine in Metaparacyclophanes

Compd	Chemical shift, 8-H, τ	Compd	Chemical shift,[a] 8-F, τ
3	4.48	**20**	+118.0
6	4.65	**22**	+106.9
7	5.71	**24**	+86.4
8	4.76	**27**	+105.6

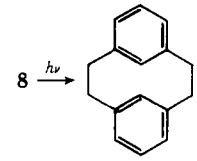
[a] Shift relative to $CFCl_3$ as an internal reference.

tion of whether such ring current effects will be overshadowed by other influences with other elements such as carbon-13 or fluorine-19.[24] To explore this question we have measured the fluorine nmr spectra of **20**, **22**, **24**, and **27**, and the results are given in Table I. In contrast to the corresponding examples with hydrogen, which show very striking ring current effects, the chemical shifts of the fluorine nmr absorptions vary widely but in no consistent pattern attributable to a ring current effect. The other factors influencing fluorine chemical shifts seem to quite outweigh any ring current effect.

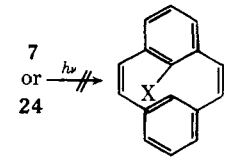
Consideration was then given to the synthesis of the corresponding 8-cyano[2.2]metaparacyclophane-1,9-diene (**25**). Although admittedly rather unlikely, the possibility that the rod-like cyano grouping might be capable of insertion into the cavity of the para-bridged π-electron cloud deserved testing. As shown, the condensation of **18** and **19** gave 8-cyano-2,11-dithia[3.3]-metaparacyclophane (**21**) in 27% yield. In this case the Stevens rearrangement gave a single isomer, 8-cyano-2,9-bis(mercaptomethyl)[2.2]metaparacyclophane (**23**), in 77% yield. Presumably, the direction of the Stevens rearrangement of **21** is strongly influenced by the activation due to the internal cyano group. Subjection of **23** to a Hofmann elimination, using an ion exchange resin (IRA-400, OH^-), then gave **25** in 63% yield. The nmr spectrum of **25** showed the para-bridged, aromatic protons as two separate signals at τ 3.85 and 2.57, indicating a very slow rate of conformational flipping on the nmr time scale. When **25** was hydrogenated over platinum, 8-cyano[2.2]metaparacyclophane (**28**) readily formed, the two signals for the para-bridged, aromatic protons of **28** appearing at τ 4.23 and 2.65.

Reduction of **25** with diisobutylaluminum hydride readily gave 8-formyl[2.2]metaparacyclophane-1,9-diene (**26**) in 61% yield. Surprisingly, the crystals of **26** are yellow and the ultraviolet absorption spectrum of **26** shows an absorption band at 349 nm (ϵ 786), suggesting an appreciable interaction between the aldehyde group and the para-bridged, aromatic π-electron cloud. As further evidence of such an interaction the aldehydic proton of **26** appears at τ 1.02, a shift of about 1 ppm to higher field than normal. A variable temperature study of **26** indicated that at lower temperatures free rotation of the aldehyde moiety is sufficiently restricted so that the two para-bridged, ring protons beneath the aldehyde group become nonequivalent. Coalescence occurs at −83°. Also, **26** is sufficiently basic to be extracted into aqueous acid.

Photochemical Experiments. The photochemical rearrangement of [2.2]metaparacyclophane (**8**) to [2.2]-metacyclophane (**29**) has recently been reported by Cram and his collaborators.[7] We have likewise investigated this photochemical rearrangement and observed the formation of [2.2]metacyclophane in yields comparable to those reported. Of particular interest to us was the possible extension of this photochemical rearrangement to the case of [2.2]metaparacyclophane-1,9-dienes, which might provide easy access to [2.2]metacyclophane-1,9-dienes (**30**) and 15,16-dihydropyrenes.



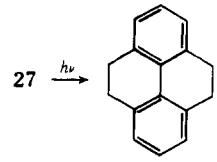
29



30

Unfortunately, prolonged irradiation of **7** led only to a complete recovery of starting material. In view of the ease of conformational flipping of **7** and the possible conjugation of the meta-bridged ring with the olefinic double bonds, the irradiation was repeated with the 8-fluoro derivate **24**, where conformational flipping is restricted. Again, only starting material was recovered.

As an additional check on the factors influencing the photochemical rearrangement, the irradiation of **27** was examined. In this case rearrangement was accompanied by loss of the elements of hydrogen fluoride to give 4,5,9,10-tetrahydropyrene (**31**) in 60% yield.



31

It is of interest that the mass spectra of all of the [2.2]metacyclophane-1,9-diene derivatives so far examined show a strong peak at *m/e* 202, corresponding to the molecular ion of pyrene. This would suggest that rearrangement of the [2.2]metaparacyclophane-1,9-diene moiety to the [2.2]metacyclophane-1,9-diene moiety does occur on electron impact.

Experimental Section[25]

2,11-Dithia[3.3]metaparacyclophane (3). A solution of 17.4 g of *p*-xylylene dibromide (**2**) in 500 ml of benzene was added from one Hershberg funnel while simultaneously and at the same rate a solution of 11.3 g of 1,3-bis(mercaptomethyl)benzene (**1**) in 500 ml of 70% aqueous ethanol containing 5.3 g of sodium hydroxide was

(24) R. H. Levin and J. D. Roberts, *Tetrahedron Lett.*, 135 (1973).

(25) Elemental and mass spectral analyses were determined by Dr. S. Rottschaefer, University of Oregon Microanalytical Laboratories. Melting points are uncorrected and were taken with a Mel-Temp apparatus; infrared spectra were measured with a Beckman IR-5a or IR-7; ultraviolet and visible spectra with a Cary 15; nmr spectra were measured with tetramethylsilane as an internal standard using a Varian A-60, T-60, HA-100, or XL-100 instrument; and mass spectra with a Consolidated Model 21-110 spectrometer. We thank the National Science Foundation for funds used toward the purchase of the Varian XL-100. All elemental analyses of new compounds gave experimental values within 0.4% of the calculated values.

being added from a second Hershberg funnel to a vigorously stirred mixture of 400 ml of ethanol and 200 ml of benzene in a Morton flask. Addition was complete in 5 hr and the reaction mixture was then concentrated under reduced pressure. The resulting solid was taken up in dichloromethane and washed successively with aqueous potassium carbonate, water, aqueous acid, and water. Concentration of the dichloromethane solution gave 16.8 g of a white solid which, after recrystallization from carbon tetrachloride, yielded 7.74 g (43%) of white crystals: mp 158.5–160.0° (lit.[11] mp 157–158°); nmr ($CDCl_3$) multiplet at τ 2.84–3.2 (3 H, Ar*H*), a singlet at 3.20 (4 H, Ar*H*), broad singlet at 4.48 (1 H, 8-H), and singlets at 6.24 (4 H, CH_2) and 6.62 (4 H, CH_2); mass spectrum (70 eV) *m/e* (rel intensity) 272 (100), 167 (15), 137 (30), 136 (22), 135 (32), 106 (22), 105 (87), and 104 (30).

Bis(sulfonium) Fluoroborate (4). To a solution of 2.00 g of 2,11-dithia[3.3]metaparacyclophane (**3**) in 100 ml of dichloromethane held at −78° there was added 4.76 g of dimethoxycarbonium fluoroborate.[12] After the mixture had warmed to room temperature, it was stirred overnight and the resulting solid was collected by filtration followed by trituration with ethyl acetate. This gave 3.47 g (100%) of white crystals of which a portion, recrystallized from water, melted at 210° dec.

Stevens Rearrangement of 4 to give 5 and 6. A mixture of 3.47 g of **4** and an excess of ion exchange resin (IRA-400, OH^- form) in 250 ml of tetrahydrofuran was stirred at room temperature under a nitrogen atmosphere for 84 hr. After filtration to remove the ion exchange resin which was then washed thoroughly with dichloromethane, the combined filtrate and washings were concentrated to give 2.35 g of a yellow oil. This was adsorbed on a silica gel column and eluted with a 1:3 benzene–petroleum ether (30–60°) mixture. The main fraction of eluate contained 1.053 g (45%) of an oil, whose nmr spectrum indicated it to be a mixture of **5** and **6**.

Anal. Calcd for $C_{18}H_{20}S_2$: C, 71.95; H, 6.71. Found: C, 72.30; H, 6.98.

Careful chromatography of this oil over silica gel using a 0.5% mixture of acetone in petroleum ether (30–60°) gave two separate compounds as colorless oils. The first compound to be eluted was **6**, whose nmr spectrum ($CDCl_3$) showed a doublet at τ 2.32 (1 H, J = 8 Hz, *m*-Ar*H*), a multiplet at 2.64–3.30 (4 H, *m*- and *p*-Ar*H*), a multiplet at 4.14 (2 H, *p*-Ar*H*), a triplet at 4.65 (1 H, J = 0.5 Hz, 8-H), multiplet at 6.1–7.0 (4 H, $-CH_2-$), a multiplet at 7.5–8.1 (2 H, $-CHS-$), a singlet at 7.80 (3 H, SCH_3), and a singlet at 8.03 (3 H, SCH_3). The second to be eluted was **5**, whose nmr spectrum ($CDCl_3$) showed a multiplet at τ 2.60–2.90 (3 H, *m*-Ar*H*), doublets at 2.87 and 4.14 (2 H each, J = 1 Hz, *p*-Ar*H*), a triplet at 4.64 (1 H, J = 2 Hz, 8-H), multiplet at 6.56 (4 H, $-CH_2-$), multiplet at 7.46–7.8 (2 H, –CHS–), and a singlet at 8.02 (6 H, SCH_3). The mixture of **5** and **6** showed absorption maxima (cyclohexane) at 245 nm (ϵ 4740, sh), 281 (500, sh), and 290 (300); mass spectrum (70 eV) *m/e* (rel intensity) 300 (53), 253 (34), 198 (84), 151 (84), 150 (32), 105 (100), and 104 (31).

Bis(sulfonium) Fluoroborate of the Mixture of 5 and 6. To a solution of 890 mg of the mixture of **5** and **6** from the above experiment in 75 ml of dichloromethane held at −78° there was added with stirring 1.44 g of dimethoxycarbonium fluoroborate. After the addition, the mixture was allowed to warm to room temperature and was then stirred for 5 hr. The white precipitate was collected, triturated with ethyl acetate, and dried to give 1.37 g (92%) of a white solid. Crystallization of a portion of this solid from water gave white crystals, mp 236° dec.

Hofmann Elimination to Give 7. A mixture of 440 mg of the bis(sulfonium) fluoroborate of the mixture of **5** and **6** and 420 mg of sodium hydride in 100 ml of tetrahydrofuran was boiled under reflux for 8 hr. After the mixture had cooled, it was diluted with 200 ml of dichloromethane, washed successively with dilute aqueous acid and water, and then dried. Concentration gave an oil which was taken up in petroleum ether (30–60°) and chromatographed over silica gel. The main fraction of eluate yielded white crystals which, after sublimation, gave 130 mg (72%) of white crystals: mp 57–58°; uv (cyclohexane) 232.5 nm (ϵ 26,700) and 258 nm (10,000, sh); nmr (CCl_4) a multiplet at τ 3.0–3.2 (3 H, *m*-Ar*H*), a singlet at 3.19 (4 H, *p*-Ar*H*), an AB system centered at 2.83 and 3.40 (4 H, J = 10 Hz, $-CH{=}CH-$), and a singlet at 5.71 (1 H, 8-H); mass spectrum (70 eV) *m/e* (rel intensity) 205 (12), 204 (98), 203 (52), 202 (100), and 102 (27).

Hydrogenation of [2.2]Metaparacyclophane-1,9-diene (7). A solution of 9 mg of **7** in 4 ml of methanol was subjected to hydrogenation over a 5% palladium-on-charcoal catalyst at room temperature and atmospheric pressure. After removal of the catalyst and solvent, the residual solid was recrystallized from methanol to give 9 mg of white crystals, mp 80–81°. The nmr spectrum of this product, as well as its melting point, are identical with the values recorded for [2.2]metaparacyclophane (**8**).[4]

Bis(1,3-propane dithioketal) (11). To a solution of 3.14 g of the bis(1,3-propane dithioacetal) of isophthalaldehyde (**9**) in 700 ml of anhydrous tetrahydrofuran, kept at −30° under a nitrogen atmosphere, there was added 12.5 ml of a 1.6 *N* solution of *n*-butyllithium in hexane. To the resulting reddish mixture there was added dropwise over a period of 3 hr a solution of 2.64 g of *m*-xylylene dibromide (**10**) in 100 ml of tetrahydrofuran. Concentration of the reaction mixture gave an oily residue which was taken up in chloroform and washed with water and dried. Concentration of the chloroform extract gave a solid that was taken up in benzene and chromatographed over silica gel. The crystals from the main fraction of eluate were then recrystallized from a benzene–hexane mixture to give 1.15 g (28%) of white rhomboids: mp 242–243°; nmr ($CDCl_3$) an A_2BC multiplet at τ 1.87, 2,44, and 3.30 (4 H, ArH adjacent to dithiane), a broad singlet at 2.75 (3 H, Ar*H*, positions 4, 5, and 6), a broad singlet at 5.97 (1 H, Ar*H* at C-8), an AB quartet at 6.65 and 7.52 (4 H, J = 12 Hz, $-CH_2-$), and a complex at 6.5–8.3 (12 H, $-S(CH_2)_3S-$).

A solution of 42 mg of **11** in 10 ml of ethanol containing 1 ml of an ethanolic slurry of Raney nickel was boiled under reflux for 1 hr. After removal of the catalyst and solvent, the residual solid was recrystallized from methanol to give 13 mg (62%) of white crystals, mp 133–134°, identical in all respects with crystals of an authentic specimen of [2.2]metacyclophane.[26]

[2.2]Metacyclophane-1,10-dione. A mixture of 2.75 g of **11**, 6.0 g of mercuric chloride, and 5 ml of methanol in 25 ml of tetrahydrofuran was heated in a sealed tube for 7 hr. The contents was then poured into water and extracted with chloroform. The chloroform extract was washed successively with water, aqueous potassium iodide solution, and water. After the extract had been dried, it was concentrated to give the bis(dimethyl ketal) of [2.2]metacyclophane-1,10-dione. This was dissolved in 100 ml of acetone containing 5 ml of concentrated hydrochloric acid and boiled under reflux for 3 hr. After concentration the residual solid was taken up in benzene and chromatographed over silica gel. The material from the main fraction of eluate was recrystallized from a benzene–hexane mixture to give 650 mg of [2.2]metacyclophane-1,10-dione as white needles: mp 144–145°; ir ($CHCl_3$) 5.90 μ (C=O); uv (EtOH) 307 nm (log ϵ 2.42) and 267 (2.81 sh); nmr ($CDCl_3$) a complex at τ 2.3–3.0 (6 H, Ar*H*), a broad singlet at 4.10 (1 H, Ar*H* at C-8), a broad singlet at 5.79 (1 H, Ar*H* at C-16), and an AB quartet at 6.05 and 6.53 (4 H, J = 14 Hz, $-CH_2-$).

Bis(1,3-propane dithioketal) of [2.2]Metaparacyclophane-1,10-dione (13). To a 1 l. of tetrahydrofuran boiling under reflux while being rapidly stirred there was added dropwise and simultaneously a solution of 2.64 g of *p*-xylylene dibromide (**2**) in 1 l. of tetrahydrofuran from one Hershberg funnel and a solution of 3.14 g of **9** in 1 l. of tetrahydrofuran containing 13 ml of a 1.6 *N* *n*-butyllithium solution in hexane from a second Hershberg funnel. When addition was complete (6 hr), the mixture was concentrated. The residual solid was taken up in benzene, washed with water, dried, and chromatographed over silica gel using benzene for elution. Recrystallization of the product from the main eluate fraction from benzene gave 1.51 g (36%) of white rhomboids: mp 244–246°; nmr ($CDCl_3$) AB_2S multiplet at τ 2.26, 2.80, and 7.15 (4 H, Ar*H*), narrow multiplets at 2.67 (2 H, Ar*H*) and 4.15 (2 H, Ar*H*), an AB quartet at 6.53 and 7.27 (4 H, J = 14 Hz, $-CH_2-$), and a complex multiplet at 7.0–8.4 (12 H, $-S(CH_2)_3S-$).

A solution of 245 mg of **13** and 5 ml of an ethanolic slurry of Raney nickel in 250 ml of absolute ethanol was boiled under reflux for 2 hr. After removal of the catalyst and solvent, the residual oil was taken up in hexane and chromatographed over silica gel to give 20 mg of white crystals which, after recrystallization from methanol, melted at 79–81°, identical in all respects with the specimen of [2.2]metaparacyclophane prepared earlier.

[2.2]Metaparacyclophane-2,9-dione (14). A mixture of 500 mg of **13**, 1.5 g of mercuric chloride, and 5 ml of methanol in 15 ml of tetrahydrofuran was heated in a sealed tube at 130° for 12 hr. The contents was then poured into water and extracted with chloroform. After the chloroform extract had been washed successively with water, aqueous potassium iodide solution, and water, it was dried and concentrated. The residual solid was taken up in benzene and chromatographed over silica gel to give 258 mg (91%) of white

(26) W. S. Lindsay, P. Stokes, L. G. Humber, and V. Boekelheide, *J. Amer. Chem. Soc.*, **83**, 943 (1961).

crystals. Recrystallization from a chloroform–hexane mixture gave white needles: mp 129.5–130.0°; ir ($CHCl_3$) 5.90 μ (C=O); uv (EtOH) 315 nm (log ϵ 2.46) and 285 (2.71, sh); nmr ($CDCl_3$) a narrow A_2BX multiplet at τ 2.8 (3 H, Ar*H*) and 4.36 (1 Ar*H*, at C-8), a singlet at 2.93 (4 H, Ar*H* of para-bridged ring), and a singlet at 6.11 (4 H, $-CH_2-$).

[2.2]Metaparacyclophane-1,9-diol (15). A solution of 240 mg of **14** and 76 mg of sodium borohydride in 75 ml of absolute ethanol was stirred at room temperature for 2 hr. The excess borohydride was then destroyed by addition of aqueous acid and the mixture was extracted with ether. After the extract had been washed with water, it was dried and concentrated to give a white solid. Recrystallization of this from a chloroform–hexane mixture gave 236 mg (97%) of fine, white needles, mp 186–191°.

Ditosylate of [2.2]Metaparacyclophane-2,9-diol (16). A solution of 94 mg of **15** and 600 mg of tosyl chloride in 3 ml of pyridine was heated on a steam bath for 8 hr. After concentration, the residue were taken up in chloroform and chromatographed over silica gel. The crystals from the main fraction of eluate were recrystallized from a benzene–hexane mixture to give 205 mg (95%) of white needles, mp 178–184°.

Conversion of 16 to [2.2]Metaparacyclophane-1,9-diene (7). A solution of 278 mg of **16** in 15 ml of a 1 *N* solution of potassium *tert*-butoxide in *tert*-butyl alcohol was boiled under reflux for 2 hr. This was then poured into water and extracted with ether. After the ether solution had been washed with water, it was dried and concentrated. The residual oil was taken up in hexane and chromatographed over silica gel. The solid from the main fraction of eluate was recrystallized from methanol to give 71 mg (68%) of white crystals, mp 58–59°, identical in all respects with the specimen of [2.2]metacyclophane-1,9-diene described previously.

9-Fluoro-2,11-dithia[2.2]metaparacyclophane (20). To a vigorously stirred solution of 200 ml of benzene and 400 ml of ethanol there was added dropwise and simultaneously a solution of 3.40 g of 1,4-bis(mercaptomethyl)benzene **(19)** and 1.60 g of sodium hydroxide in 200 ml of a 60% aqueous ethanol solution from one Hershberg funnel and a solution of 5.63 g of 2,6-bis(bromomethyl)-fluorobenzene **(17)** in 200 ml of benzene from a second Hershberg funnel. When the addition was complete (3.5 hr), the mixture was concentrated and water and dichloromethane were added. After the dichloromethane extract had been washed successively with aqueous base, water, aqueous acid, and water, it was dried and concentrated. The residual solid was taken up in a 20% benzene in hexane mixture and chromatographed over silica gel. The solid from the main fraction of eluate was recrystallized from carbon tetrachloride to give 2.50 g of white crystals: mp 177–178° (lit.[23] mp 172–173°); uv (cyclohexane) 230 nm (ϵ 8800, sh), 268 nm (1050, sh), and 277 nm (630, sh); nmr ($CDCl_3$) a doublet at τ 2.93 (2 H, Ar*H* of para-bridged ring), a multiplet at 2.95 (3 H, Ar*H* of meta-bridged ring), a doublet at 3.42 (2 H, Ar*H* of para-bridged ring), an AB quartet at 6.29 (4 H, J = 13 Hz, $-CH_2-$), and an AB quartet at 6.51 (4 H, J = 16 Hz, $-CH_2-$); mass spectrum (70 eV) *m/e* (rel intensity) 290 (100), 153 (19), 123 (26), and 104 (17).

Bis(sulfonium) Fluoroborate of 20. To a solution of 1.13 g of **20** in 50 ml of dichloromethane kept at −78° there was added 2.28 g of dimethoxycarbonium fluoroborate. The mixture was allowed to warm to room temperature and was held there with stirring for 8 hr. The precipitate was collected by filtration, triturated with ethyl acetate, and dried to give 1.75 g (91%) of white crystals, mp 195° dec.

Stevens Rearrangement to Give 22. To a solution of 1.12 g of potassium *tert*-butoxide in 125 ml of tetrahydrofuran there was added 1.62 g of the bis(sulfonium) fluoroborate of **20**. After the mixture had been allowed to stir overnight at room temperature, it was diluted with 200 ml of ether and washed with water. After concentration, the residual oil was taken up in a 10% benzene in petroleum ether (30–60°) mixture and chromatographed over silica gel. The main fraction of eluate gave 540 mg (52%) of a colorless oil: uv (cyclohexane) 235 nm (ϵ 6400, sh), 274 (675), and 280 (660); nmr ($CDCl_3$) a doublet at τ 2.36 (2 H, J = 9 Hz, Ar*H*), a multiplet at 2.6–3.4 (5 H, Ar*H*), a doublet at 4.10 (2 H, J = 0.5 Hz, Ar*H*), a multiplet at 5.8–6.24 (2 H, –CH–), a multiplet at 7.1–8.05 (4 H, $-CH_2-$), a singlet at 7.84 (3 H, SCH_3), and a singlet at 9.06 (3 H, SCH_3); mass spectrum (70 eV) *m/e* (rel intensity) 318 (45), 270 (47), 168 (100), and 153 (29). A portion of the oil crystallized from cyclohexane as white crystals, mp 103–104°.

Bis(sulfonium) Fluoroborate of 22. To a solution of 470 mg of the oily mixture represented by **22** in 50 ml of dichloromethane held at −78° there was added with stirring 860 mg of dimethoxycarbonium fluoroborate. The mixture was allowed to warm to room temperature and stand overnight with stirring. Then the precipitate was collected, triturated with ethyl acetate, and dried to give 720 mg (92%) of white crystals, mp 280° dec.

8-Fluoro[2.2]metaparacyclophane-1,9-diene (24). To a solution of 410 mg of potassium *tert*-butoxide in 100 ml of tetrahydrofuran there was added with stirring 630 mg of the bis(sulfonium) fluoroborate of **22**. The mixture was stirred at room temperature for 8 hr and then diluted with 150 ml of ether. After the solution had been washed successively with water, aqueous dilute acid, and water, it was dried and concentrated. The residual solid was taken up in petroleum ether (30–60°) and chromatographed over silica gel. The material from the main fraction of eluate was sublimed to give 245 mg (92%) of white crystals: mp 73–74°; uv (cyclohexane) 231 nm (ϵ 19,860) and 265 (6670); nmr ($CDCl_3$) a singlet at τ 2.80 (2 H, Ar*H* of para-bridged ring), an AB quartet at 3.22 (4 H, J = 10 Hz, –CH=CH–), multiplet at 3.30 (3 H, Ar*H*), and a singlet at 3.74 (2 H, Ar*H* of para-bridged ring); mass spectrum (70 eV) *m/e* (rel intensity) 223 (18), 222 (100), 221 (15), 220 (37), 203 (11), and 202 (49).

8-Fluoro[2.2]metaparacyclophane (27). A solution of 30 mg of **24** in 5 ml of ethyl acetate was subjected to hydrogenation over platinum oxide at room temperature and atmospheric pressure. After removal of the catalyst and solvent, the residual solid was sublimed to give 30 mg (99%) of white crystals: mp 136–137° (lit.[23] mp 138–139°); uv (cyclohexane) 236 nm (ϵ 3877), 273.5 (425), 278 (420), and 288 (163, sh); nmr ($CDCl_3$) a doublet at τ 2.85 (2 H, J = 1 Hz, Ar*H* of para-bridged ring), a multiplet at 3.28 (3 H, Ar*H*), a doublet at 4.09 (2 H, J = 1 Hz, Ar*H* of para-bridged ring), and a multiplet at 6.7–7.8 (8 H, $-CH_2-$); mass spectrum (70 eV) *m/e* (rel intensity) 226 (95), 122 (100), and 104 (11).

Anal. Calcd for $C_{16}H_{15}F$: mol wt, 226.116. Found (high resolution mass spectrometry): mol wt, 226.115.

8-Cyano-2,11-dithia[3.3]metaparacyclophane (21). To a vigorously stirred solution of 100 ml of benzene and 150 ml of ethanol there was added dropwise and simultaneously a solution of 3.4 g of 1,4-bis(mercaptomethyl)benzene **(19)** and 1.60 g of sodium hydroxide in 200 ml of a 60% aqueous ethanol solution from one Hershberg funnel and a solution of 5.78 g of 2,6-bis(bromomethyl)-benzonitrile **(18)** in 200 ml of benzene from a second Hershberg funnel. When the addition was complete (45 min), the mixture was concentrated and water and dichloromethane were added. After the dichloromethane extract had been washed with water, it was dried and concentrated. The residual solid was taken up in a 40% benzene in petroleum ether (30–60°) mixture and chromatographed over silica gel. The crystals from the main fraction of eluate were recrystallized from cyclohexane to give 1.59 g (27%) of white crystals: mp 219.5–220.5°; uv (cyclohexane) 219 nm (ϵ 17,400, sh), 225 (16,300, sh), 268 (1720, sh), 291 (1740), and 301.5 (2080); ir ($CHCl_3$) 2,210 cm^{-1} (–C≡N); nmr ($CDCl_3$) a multiplet at τ 2.71 (3 H, Ar*H*), a doublet at 2.80 (2 H, J = 1.5 Hz, Ar*H* of para-bridged ring), a doublet at 3.54 (2 H, J = 1.5 Hz, Ar*H* of para-bridged ring), an AB quartet at 6.13 (4 H, J = 12 Hz, $-CH_2-$), and an AB quartet at 6.29 (4 H, J = 17 Hz, CH_2); mass spectrum (70 eV) *m/e* (rel intensity) 297 (54), 193 (100), and 104 (36).

Bis(sulfonium) Fluoroborate of 21. To a solution of 595 mg of **21** in 50 ml of dichloromethane held at −78° there was added 1.29 g of dimethoxycarbonium fluoroborate with stirring. The mixture was allowed to warm to room temperature and stirring was continued for 5 hr. The crystalline precipitate was collected, trituated with ethyl acetate, and dried. Recrystallization from water gave 1.03 g (100%) of white needles, mp 220° dec.

Stevens Rearrangement to Give 23. A mixture of 1.03 g of the bis(sulfonium) fluoroborate of **21** and an excess of ion exchange resin (IRA-400 (OH^-), 20 ml, 26 mequiv) in 50 ml of tetrahydrofuran was boiled under reflux for 2 hr. Removal of the ion exchange resin and the solvent left an oily residue. This was taken up in a 33% benzene in petroleum ether (30–60°) mixture and chromatographed over silica gel. The material from the main fraction of eluate was sublimed to give 500 mg (77%) of white crystals: mp 125–126°; ir ($CHCl_3$) 2210 cm^{-1} (–C≡N); uv (cyclohexane) 230 nm (ϵ 10,400) and 299 (1060); nmr ($CDCl_3$) a multiplet at τ 2.38–2.78 (3 H, Ar*H*), a narrow multiplet at 2.68 (2 H, Ar*H* on para-bridged ring), a narrow multiplet at 4.19 (2 H, Ar*H* on para-bridged ring), an ABC system at 5.80 (2 H, J_{AB} = 6.5 Hz, J_{AC} = 10.5 Hz, –CH–), 6.35 (2 H, J_{AB} = 6.5 Hz, J_{BC} = 12 Hz, CH_2), and 7.58 (2 H, J_{AC} = 10.5 Hz, J_{BC} = 12 Hz, $-CH_2-$), and a singlet at 7.96 (6 H, SCH_3); mass spectrum (70 eV) *m/e* (rel intensity) 325 (46), 221 (100), and 191 (34).

Bis(sulfonium) Fluoroborate of 23. To a solution of 464 mg of **23** in 50 ml of dichloromethane held at −78° there was added 923

mg of dimethoxycarbonium fluoroborate with stirring. The mixture was allowed to warm to room temperature and was stirred an additional 5 hr. The crystalline precipitate was collected, triturated with ethyl acetate, and recrystallized from water, to give 750 mg (100%) of white crystals, mp 279° dec.

8-Cyano[2.2]metaparacyclophane-1,9-diene (25). A mixture of 800 mg of the bis(sulfonium) fluoroborate of **23** and an excess of ion exchange resin (IRA-400 (OH^-), 20 ml, 26 mequiv) in 50 ml of tetrahydrofuran was boiled under reflux for 5 hr. After removal of the ion exchange resin and solvent, the residual solid was taken up in benzene and chromatographed over silica gel to give 220 mg (63%) of white crystals. A portion was recrystallized from cyclohexane to give white crystals: mp 184–185°; ir ($CDCl_3$) 2210 cm^{-1} (–C≡N); uv (cyclohexane) 227 nm (ε 17,700), 263 (7660), and 325 (692, sh); nmr ($CDCl_3$) a doublet at τ 2.57 (2 H, J = 1 Hz, Ar*H* on para-bridged ring), a triplet at 2.78 (1 H, J = 7 Hz, Ar*H* on meta-bridged ring), an AB quartet at 2.96 (4 H, J = 10 Hz, –C*H*=C*H*–), a doublet at 3.17 (2 H, J = 7 Hz, Ar*H* on meta-bridged ring) and a doublet at 3.85 (2 H, J = 1 Hz, Ar*H* on para-bridged ring); mass spectrum (70 eV) *m/e* (rel intensity) 230 (2), 229 (26), 228 (6), 203 (6), 202 (16), and 106 (100).

8-Cyano[2.2]metaparacyclophane (28). A solution of 25 mg of **25** in 5 ml of ethyl acetate was subjected to hydrogenation over a platinum catalyst at room temperature and atmospheric pressure. After removal of the catalyst and solvent, the residual solid was recrystallized from cyclohexane to give 26 mg (100%) of white crystals: mp 228–230°; ir ($CHCl_3$) 2210 cm^{-1} (–C≡N); uv (cyclohexane) 233 nm (ε, 9325), 285 (697, sh), 291 (773), and 296 (701, sh); nmr ($CDCl_3$), a doublet at τ 2.65 (2 H, J = 0.5 Hz, Ar*H* on para-bridged ring), an AB_2 system at 2.86 (1 H, J = 8 Hz, Ar*H* on meta-bridged ring) and 3.09 (2 H, J = 8 Hz, Ar*H* on meta-bridged ring), a doublet at 4.23 (2 H, J = 0.5 Hz, Ar*H* on para-bridged ring), and multiplets at 6.68 (2 H, $-CH_2-$) and 7.0–7.6 (6 H, $-CH_2-$); mass spectrum (70 eV) *m/e* (rel intensity) 233 (100), 232 (43), 129 (131), and 104 (18).

8-Formyl[2.2]metaparacyclophane-1,9-diene (26). To a solution of 100 mg of 8-cyano[2.2]metaparacyclophane-1,9-diene (**25**) in 25 ml of benzene there was added 350 mg of a 20% solution of diisobutylaluminum hydride. The resulting yellow mixture was stirred at room temperature for 3 hr. It was then diluted with dichloromethane and washed successively with water, aqueous acid, and water. The acidic washings were neutralized with potassium carbonate and extracted with dichloromethane, which moved the yellow color, due to the aldehyde **26**, into the organic layer. The combined organic extracts were dried and concentrated. Sublimation of the residual solid gave 62 mg (61%) of light yellow crystals: mp 171–172°; ir ($CHCl_3$) 1684 cm^{-1} (–C=O); uv cyclohexane) 219 nm (ε 21,400), 263 (7890, sh), and 349 (786); nmr ($CDCl_3$) a singlet at τ 1.02 (1 H, CH=O), a doublet at 2.96 (2 H, J = 1 Hz, Ar*H* on para-bridged ring), an AB quartet at 3.10 (4 H, J_{AB} = 8 Hz, C*H*=C*H*), a multiplet at 2.8–3.33 (3 H, Ar*H* on meta-bridged ring), and a doublet at 3.76 (2 H, J = 1 Hz, Ar*H* on para-bridged ring); mass spectrum (70 eV) *m/e* (rel intensity) 233 (21), 232 (100), 231 (7), 203 (68), and 202 (96).

Photochemical Rearrangement of [2.2]Metaparacyclophane (8) to [2.2]Metacyclophane (29). A solution of 17 mg of **8** in 5 ml of cyclohexane in a quartz tube was irradiated with light of 2537 Å for 43 hr. Monitoring of the reaction by nmr indicated that the ratio of [2.2]metacyclophane (**29**) to [2.2]metaparacyclophane (**8**) was 55:45. Chromatography over silica gel led to the isolation of 7 mg (45%) of **29** as white crystals, mp 132–133°, identical in all respects with an authentic specimen.[26]

Irradiation of a sample of [2.2]metaparacyclophane-1,9-diene (**7**) in cyclohexane under the same conditions led to a complete recovery of unchanged **7**. Similarly, irradiation of 8-fluoro[2.2]-metacyclophane-1,9-diene (**24**) under these conditions led only to recovery of starting material.

Photochemical Rearrangement of 8-Fluoro[2,2]metaparacyclophane (27) to 4,5,9,10-Tetrahydropyrene (31). A solution of 15 mg of 8-fluoro[2.2]metaparacyclophane (**27**) in 6 ml of cyclohexane in a quartz tube was irradiated with 2537-Å light for 48 hr. After removal of the solvent, the residual solid was taken up with petroleum ether and chromatographed over silica gel to give 6 mg (44%) of white crystals, mp 139–140°, identical in all respects when compared with an authentic specimen of 4,5,9,10-tetrahydropyrene prepared by the procedure of Sato, *et al.*[27]

(27) T. Sato, M. Wakabayashi, S. Hayashi, and K. Hata, *Bull. Chem. Soc. Jap.*, **42**, 773 (1969).