and IV, ($Py\cdot^*\ Py^+ \pm Py^+, Py\cdot^*$), where $Py\cdot^*$ is a locally excited state of pyridinyl radical end. Then, this absorption band may be regarded as the shifted local excitation of the pyridinyl at ~3900 Å. Furthermore, the shortest wavelength absorption of $Py\cdot$ at ~3100 Å seems to be shifted to shorter wavelength region in the closed form cation radical, as seen in Figure 1.

As mentioned in the introductory section, the trimethylene is most efficient for intramolecular electronic interactions in excimer[8,9] and also in energy transfer.[10] The results obtained in this paper give further evidence of the importance of the trimethylene chain for the interaction of the radical and parent molecule, *e.g.*, in one type of the dimer radical $(A)_2^+$ or $(A)_2^-$; the favorable length of the trimethylene for the intramolecular interaction in dipyridinylalkanes was demonstrated in the previous paper.

Experimental Section

Materials. Three bis(pyridinium iodides)[7] were prepared from 4-carbomethoxypyridine and three corresponding diiodoalkanes. 1,1′-Trimethylenebis(4-carbomethoxypyridinium bromide) was also obtained from 1,3-dibromopropane, mp 160–163° (*Anal.* Calcd for $C_{17}H_{20}O_4N_2Br_2$: C, 42.85; H, 4.20; N, 5.88. Found: C, 42.49; H, 4.20; N, 5.42).

The acetonitrile was spectrograde. 2-Methyltetrahydrofuran and 1,2-dimethoxyethane were refluxed with potassium metal for several hours and distilled. Refluxing and distillation were repeated two or three times.

Absorption Spectra. A Cary Model 11 recording spectrophotometer was used. In the determination of low-temperature spectra, a quartz dewar was used.

Epr Spectra. Epr measurements were made with JEOLCO P-10 ESR spectrometer with 100-kc modulation.

Preparation of Cation Radicals. Bis(pyridinium iodide) (~0.1 g) and 3% sodium amalgam (~0.5 g) were sealed into the reaction tube. After evacuating to $\sim10^{-5}$ mm, degassed acetonitrile (about 10 ml) was introduced by using a vacuum line. The reaction tube was shaken some time for about 0.5 hr at 5 to −20°. After connecting the reaction tube to the vacuum line, the solvent was removed and residue washed with a small amount of MTHF (~2 ml) in order to remove the diradical. After washing two times, the cation radical was extracted with MTHF (~10 ml). A slightly greenish yellow solution of the cation radical was obtained.

Determination of concentration of cation radical and of relative spin concentration was done using the same procedures as described in the previous paper.[7]

Acknowledgment. The author wishes to express his thanks to Professor S. Nagakura for reading the manuscript and discussions. Thanks are also due to Professor T. Okamoto for his encouragement.

Macro Rings. XLI. Preparation and Reactions of [2.2]Metaparacyclophane[1,2]

Daniel T. Hefelfinger and Donald J. Cram*

Contribution No. 2744 from the Department of Chemistry of the University of California at Los Angeles, Los Angeles, California. *Received October 30, 1970*

Abstract: Treatment of [2.2]paracyclophane (I) with aluminum chloride in dichloromethane saturated with hydrogen chloride at −10° gave [2.2]metaparacyclophane (II) in 46% yield and small amounts of 1,2,2a,3,4,5-hexahydropyrene. Compound II was characterized by its spectral properties, its tetracyanoethylene complex, by its oxidation to a mixture of isophthalic and terephthalic acids, and by its reductive cleavage with potassium to *p,m′*-dimethylbibenzyl. The pattern of products of rearrangement of 4-methyl[2.2]paracyclophane (III) and of 4-bromo[2.2]paracyclophane (IV) to the corresponding [2.2]metaparacyclophanes was examined. Solution of I or II in fluorosulfonic acid–sulfuryl chloride–dichloromethane at −80 to −98° gave nmr spectra of structures in which one proton had added to a bridgehead position of the para rings. These solutions with sodium methoxide–methanol gave back only starting material. At 100° in deuteriotrifluoroacetic acid, all positions of II underwent isotopic exchange at roughly the same rate except the most hindered 8 position. Acetylation of II gave a mixture of monoacetylated [2.2]metaparacyclophanes and 1-acetyl-5,7,12,14,16(4)-tetracyclo[9.2.2.1^{4,11}.0^{8,16}]hexadecapentaene (XVI), whose structures were demonstrated. Bromination of II gave a mixture of monobrominated [2.2]metaparacyclophanes, whose structures were demonstrated. The reactivities and spectral properties of II and its derivatives are discussed in terms of the crystal structure and strain energy of II.

Since the original description of the conversion of [2.2]paracyclophane (I) to [2.2]metaparacyclophane (II),[2a] several elegant syntheses of II[3a–d] have appeared, one of which involved tetradehydro[2.2]metaparacyclophane as an intermediate.[3b] Three reports of studies of ring inversion of II have also appeared,[2b,3c,3e] one of which[2b] demonstrated that at temperatures up to 200° only the meta ring underwent rotation.

Since the structures of I and II are central to this study, they are compared here. Combustion of II by Boyd, *et al.*, demonstrated the substance possessed a strain energy of 23 kcal mol^{-1} as compared to 31 kcal mol^{-1} for I.[4] A preliminary refinement in a single

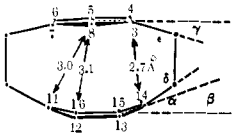
(1) The authors thank the National Science Foundation for a grant used in support of this research. D. T. H. also thanks the National Science Foundation for a Traineeship, 1965–1969.

(2) Preliminary accounts of parts of this work have already appeared: (a) D. J. Cram, R. C. Helgeson, D. Lock, and L. A. Singer, *J. Amer. Chem. Soc.*, **88**, 1324 (1966); (b) D. T. Hefelfinger and D. J. Cram, *ibid.*, **92**, 1073 (1970).

(3) (a) T. Hylton and V. Boekelheide, *ibid.*, **90**, 6886 (1968); (b) V. Boekelheide and P. H. Anderson, *Tetrahedron Lett.*, 1207 (1970); (c) F. Vögtle, *Chem. Ber.*, **102**, 1784, 3077 (1969); (d) F. Vögtle, *Angew. Chem., Int. Ed. Engl.*, **8**, 274 (1969); (e) S. Akabori, S. Hayashi, M. Nawa, and K. Shiomi, *Tetrahedron Lett.*, 3727 (1969).

(4) (a) R. H. Boyd, *Tetrahedron*, 22, 119 (1966); (b) R. H. Boyd, *J. Chem. Phys.*, **49**, 2574 (1968); (c) C. Shieh, D. McNally, and R. H. Boyd, *Tetrahedron*, **25**, 3653 (1969).

crystal X-ray structure study of II has been carried out by Trueblood and Crisp,[5a] and a highly refined structure of I has been completed by Trueblood, Bernstein, and Hope.[5b] The decrease in strain energy of 8 kcal mol^{-1} in going from I to II is a result of decentering



[2.2]Metaparacyclophane (II)

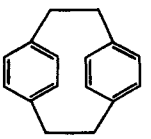
Molecule	Bond angle, deg α	β	γ	δ	ε
[2.2]Metaparacyclophane, X-ray[5a]	14	14	13	107	112
[2.2]Metaparacyclophane, predicted[4b]	14	14.6		109.5	112.4
[2.2]Paracyclophane[5b]	12.6	11.2		113.7	

the rings (decreasing the π–π repulsions) and changing bond angles. However, the para-substituted ring of II is more deformed than those of I (compare bond angles α), and the bond angles of the rings to bridges in II (β and γ) are about equal or greater than the corresponding bond angle of I (β). Boyd's angle predictions[4b] for the deformed rings of II are in close agreement with the preliminary X-ray work.[5a] Interestingly, the meta ring of II is bent into an inclined chair. Thus, carbon 8 is ~0.09 Å above and carbon 5 is ~0.07 Å below the plane of carbons 3, 4, 6, and 7.

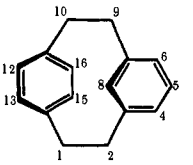
The closeness of the rings in II is revealed by the nonbonded distances between carbons of the two rings. Thus, the C-3 to C-14 distance is ~2.7 Å, the C-8 to C-12 distance is ~3.1 Å, and the C-8 to C-11 distance is ~3.0 Å. The analogous bridgehead-to-bridgehead distances in other cyclophanes are 2.78 Å in I,[5b] and 2.80 Å in 1,2,9,10-tetradehydro[2.2]paracyclophane.[5c]

The largeness of angles α and β and the closeness of the π systems of II reveal the origins of its strain. The substance contains the smallest known number of atoms (seven) forming a chain connecting the para ends of a benzene ring. The substance, [7]paracyclophane, has not yet been prepared and has been estimated to have an angle α *ca.* 25°.[6] Another known compound, 2,2a,3,3a,4,5-hexahydro-1H-cyclopent[*jkl*]-*as*-indacene,[7] can also be regarded as a [7]paracyclophane with extra bridging, and its severe deformity is expressed in its unusual chemical reactivity and spectral properties.

Anticipation of unusual behavior of II due to strain and the proximity of the two benzene rings to one another led to our studies of its preparation and chemistry. The commercial availability of I[8] made it an attractive starting material for the preparation of II. This paper reports the conversion of I to II, and derivatives of I to derivatives of II, and the pattern of aromatic substitution of II. Of immediate importance to the preparation of derivatives of II is the question of whether one or both of the two benzene rings of II can rotate with respect to one another. The next paper of this series deals specifically with this question, but from the results reported in this paper it is clear that one or the other or both rings can flip.[9]



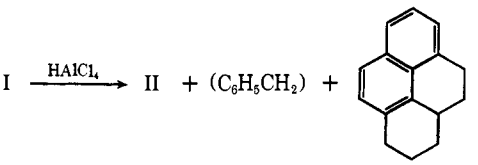
I



II

Results and Discussion

Isomerizations of [2.2]Paracyclophane to [2.2]Metaparacyclophane. Treatment of [2.2]paracyclophane (I) with a hydrogen chloride saturated solution of aluminum chloride in dichloromethane at −10° gave [2.2]-metaparacyclophane (II) in 44% yield, 1,2,2a,3,4,5-hexahydropyrene (10%), trace amounts of bibenzyl, and 7% of I. Appropriate manipulation of conditions gave 46% II free of all but easily separable polymer.



1, 2, 2a, 3, 4, 5-hexahydropyrene

Since I has ~8 kcal mol^{-1} more strain energy than II, release of strain appears to be one of the driving forces for this reaction. Another possible driving force is the well-known fact that meta-dialkylated benzenes are stronger bases than para-dialkylated benzenes toward proton acids.[10] In connection with the latter possibility, the nmr spectra of I and II in fluorosulfonic acid–sulfuryl chlorofluoride–dichloromethane (bright red solutions) were examined. This medium gave the same spectrum previously found[11] for I in sulfur dioxide–aluminum chloride–hydrogen chloride, but the resolution and integrations were better in our medium, and there were no extraneous peaks (see Experimental Section). Both solutions when quenched in methanol–sodium methoxide gave back staring material only.

The nmr spectrum of I changed upon protonation from two singlets at τ 3.5 and 6.9 of 16 protons to one that integrated well for 17 protons. This fact and the quenching experiment indicate that IH^+ must be monoprotonated at either of two positions, at a bridgehead or ortho to a bridgehead. The high symmetry of the aromatic protons (two A_2B_2 patterns) is consistent only with the indicated bridgehead-protonated structure. Protonation at this point is expected to relieve more bond angle strain, π–π repulsion, and benzylic hydrogen eclipsing strain than protonation at the position ortho to the bridgehead. This result contrasts with the observed exclusive protonation of *p*-xylene at positions ortho to the methyl group.[12] That protonation of I ortho to the bridgehead does occur reversibly was

(5) (a) K. N. Trueblood and M. J. Crisp, private communication; (b) K. N. Trueblood, J. Bernstein, and H. Hope, private communication. We thank these authors for permission to discuss these data in advance of publication; (c) C. L. Coulter and K. N. Trueblood, *Acta Crystallogr.*, 16, 667 (1963).

(6) N. L. Allinger, L. A. Freiberg, R. B. Hermann, and M. A. Miller, *J. Amer. Chem. Soc.*, 85, 1171 (1963).

(7) H. Rapoport and G. Smolinsky, *ibid.*, 82, 1171 (1960).

(8) (a) Y. L. Yeh and W. F. Gorham, *J. Org. Chem.*, 34, 2366 (1969); (b) W. F. Gorham, *J. Polym. Sci., Part A-1*, 4, 3027 (1966).

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

(10) D. A. McCauley and A. P. Lien, *ibid.*, 74, 6246 (1952).

(11) M. Sheehan, Ph.D. Dissertation, University of California at Los Angeles, 1969.

(12) (a) D. M. Brouwer, E. L. Mackor, and C. MacLean, *Recl. Trav. Chim. Pays-Bas*, 84, 1564 (1965); (b) T. Birchall and R. T. Gillespie, *Can. J. Chem.*, 42, 502 (1964).

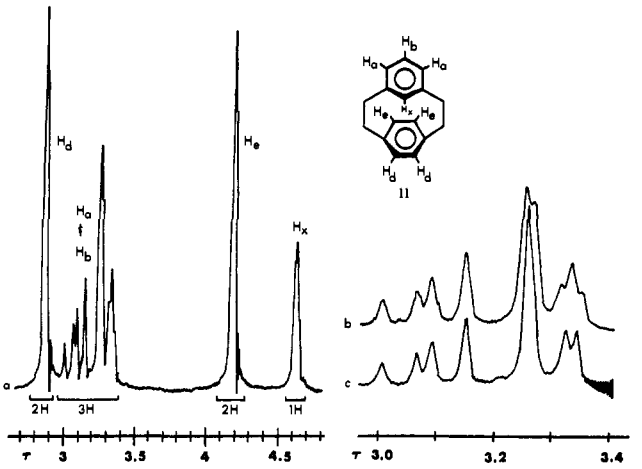
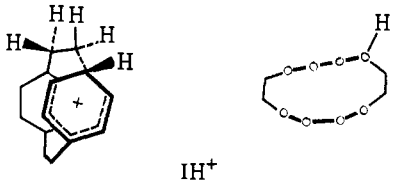


Figure 1. Aromatic proton nmr spectrum of [2.2]metaparacyclophane (100 MHz): spectrum a, aromatic region; b, H_a and H_b spectrum expanded; c, H_a and H_b spectrum with H_x decoupled (irradiated), A_2B system.

shown by isotopic exchange experiments.[11] When I was treated with sulfur dioxide–deuterium chloride–aluminum chloride at −80° and the mixture quenched, recovered I had incorporated a substantial amount of deuterium. Although no temperature variation studies were made, the spectra of solutions of I in both acidic media when warmed to −20° indicated the start of decomposition. This was just the temperature below which the reaction I → II did not occur. It is safe to say that formation of IH^+ is the first step in the production of II, and highly probable that IH^+ possesses a partially deeclipsed structure in which the protonated ring has become more planar. The tendency of I to deeclipse is evident even in its crystal form,[5b] and is expected to become more pronounced upon protonation. The energy barrier to equilibration between the two deeclipsed forms of IH^+ is expected to be small enough to produce an equilibrium spectrum at −80°.



IH^+

Comparison of the nmr spectra (100 MHz) of [2.2]metaparacyclophane (II) and IIH^+ indicates the position of protonation in IIH^+. Figure 1 records the nmr spectrum of the aromatic region of II and Figure 2 the total spectrum of IIH^+. The combination of conformation and ring currents gives the various positions of II widely differing magnetic environments. Protons H_a, H_b, and H_d are normal benzenelike deshielded protons, whereas protons H_x and H_e are shielded since they are located above or below a π system. Although H_x is shifted considerably upfield, the diagmagnetic shielding of H′ is not as pronounced as the corresponding H_x in [2.2]metacyclophane[13] at τ 5.79. Protons H_a and H_b are slightly upfield from the normal benzene resonance (τ 2.8); this is attributable to small diamagnetic shielding by the other ring as in I. Protons H_a and H_b collapsed to a typical A_2B pattern (as in 2,6-dimethylpyridine)[14] when H_x was decoupled in an irradiation experiment. At room temperature there is no evidence of H_b and H_e becoming equivalent as at high temperatures.[2b,3c,3e,9]

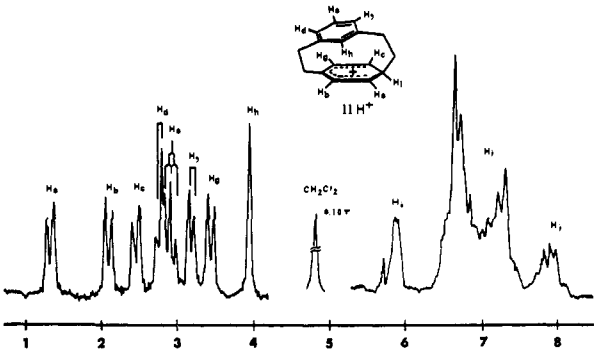
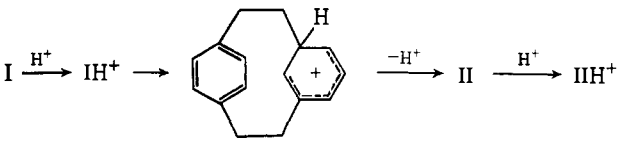


Figure 2. Protonated [2.2]metaparacyclophane nmr spectrum (100 MHz) in fluorosulfonic acid at −98° (100 MHz).

The clear red solution of [2.2]metaparacyclophane (II) in fluorosulfonic acid–sulfuryl chlorofluoride–dichloromethane at −98° gave an exceptionally clear nmr spectrum (Figure 2). Integrations showed 17 protons indicating one proton had added to II to give a single species, IIH^+. The nmr spectrum is uniquely interpretable in terms of the structure in which the proton added to the bridgehead position of the para-substituted ring. This ring is the most bent,[5b] and protonation at this position undoubtedly relieves the most bond angle strain and π–π repulsions.

If, as is likely, hydrocarbons I and II are essentially completely protonated in $HAlCl_4$–CH_2Cl_2 (as they are in the nmr solution), then the thermodynamic driving force for rearrangement came from the difference in stability between IH^+ and IIH^+, and not I and II themselves. Since IIH^+ is protonated in the para ring rather than the ordinarily more basic meta ring, the occurrence of the rearrangement is traceable mainly to the relief of π–π repulsion and not to an increased basicity in a meta-dialkylated benzene over that of a para. The overall rearrangement is formulated as an ordinary 1,2-alkyl group shift to an adjacent electron deficient center.



The origin of 1,2,2a,3,4,5-hexahydropyrene as a by-product of the rearrangement is not clear. Use of excess aluminum chloride (6 mol) and temperatures of ≦10° nearly eliminated it from the reaction, whereas addition of traces of water to the reaction mixture and use of temperatures of 10° increased its yield. The fact that [2.2]metacyclophane when treated with aluminum chloride gave the same compound[15] suggests

(13) (a) N. L. Allinger, M. A. DaRooge, and R. B. Hermann, *J. Amer. Chem. Soc.*, 83, 1974 (1961); (b) N. L. Allinger, B. J. Gorden, S. Hu, and R. A. Ford, *J. Org. Chem.*, 32, 2272 (1967).

(14) J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. 1, Pergamon Press, New York, N, Y., 1966, p 328.

(15) W. Baker, J. F. W. McOmie, and J. N. Norman, *J. Chem. Soc.*, 1114 (1951).

that II might have further rearranged to [2.2]metacyclophane which in turn gave the hydropyrene.

The ring contraction of I to II finds analogy in the ring contraction of [9]- and [10]paracyclophanes to [9]- and [10]metacyclophanes during succinoylation.[16] Here, as in our example, electrophilic attack at the bridgehead and relief of strain by rearrangement occurred.

Characterization of [2.2]Metaparacyclophane (II) and Comparison of Its Physical Properties with Those of [2.2]Paracyclophane (I). Reduction of II in dimethoxyethane with potassium produced *m,p'*-dimethylbibenzyl. Alkaline potassium permanganate oxidation of *m,p'*-dimethylbibenzyl or of II gave a mixture of isophthalic and terephthalic acids.[2a]

The ultraviolet spectrum of II (Figure 3) is very different from that of *m,p'*-dimethylbibenzyl, which serves as an open-chain model. A band appears at 240 nm, which is similar to the 244-nm band of [2.2]paracyclophane.[17] The remnants of the fine structure of the open-chain model are visible in the 270–290-nm region.

When a solution of II and tetracyanoethylene in dichloromethane and cyclohexane was allowed to evaporate, dark red crystals of a 1:1 complex were obtained. The nmr spectrum of this complex was the same as for II itself. The long wavelength charge-transfer band in the visible spectrum of the π salt in dichloromethane occurred at 455 nm. This transition is of higher energy than that of any of the other paracyclophanes,[18] and is between that of *m*-xylene (440 nm) and *p*-xylene (460 nm). This fact suggests[19] that II is a weaker π-base than either [2.2]paracyclophane (π-salt, λ_{max} 521 nm)[18a] or [2.2]metacyclophane (π-salt, λ_{max} 486 nm).[2a]

Whereas [2.2]paracyclophane (I) contains three mirror planes, [2.2]metaparacyclophane (II) has only one. This loss of symmetry is reflected in the melting point and solubility. In passing from I to II the melting point dropped *ca.* 200°, and the solubility in pentane increased from nearly zero to *ca.* 1 g/8 ml at 25°. Although both substances have waxy odors, II seemed slightly more volatile. Both substances produce similar mass spectra, the overwhelmingly predominant fragmentation occurring by benzyl–benzyl cleavage to produce a xylylene fragment (*m/e* 104).

Rearrangements of 4-Methyl[2.2]paracyclophane (III) and 4-Bromo[2.2]paracyclophane (IV). Isomerization experiments were performed on several derivatives of I. Attempted rearrangements of 4-acetyl-, 4-carbomethoxy-, and 4-cyano[2.2]paracyclophanes resulted in only high molecular weight products. However, 4-methyl[2.2]paracyclophane (III) and 4-bromo[2.2]paracyclophane (IV) were successfully isomerized to derivatives of [2.2] metaparacyclophane.

Isomerization of III gave 70% of a mixture of monomethyl[2.2]metaparacyclophanes, which by nmr analysis (see future section) was 66% 12-isomer, 12% 15-isomer, and 13% 4-isomer. The 12- and 15-isomers equilibrated at room temperature by ring rotation,[9] and the isomer mixture was not separated.

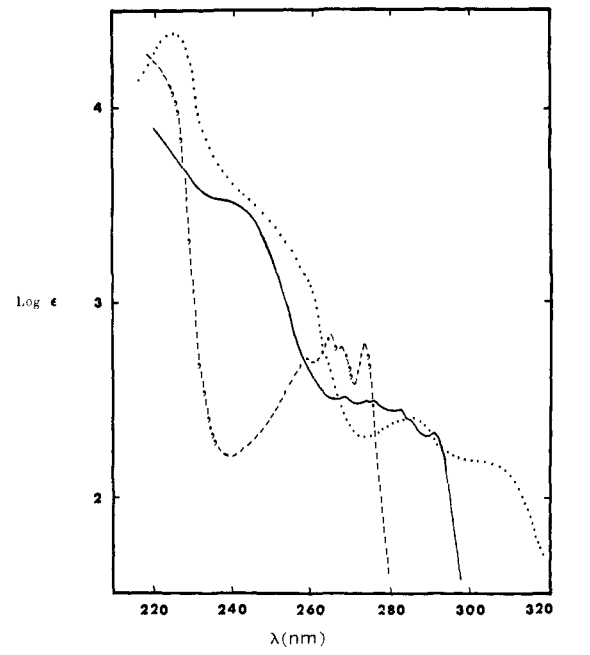
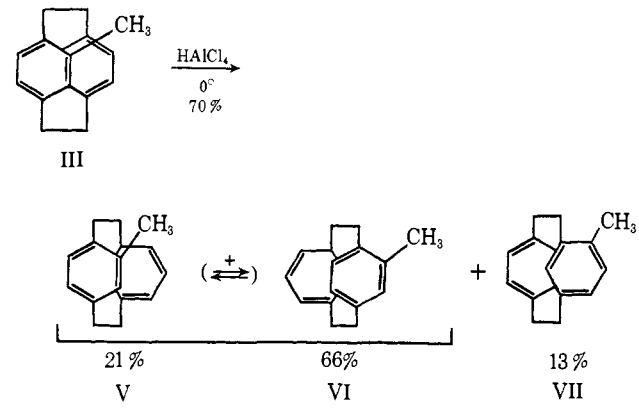


Figure 3. Ultraviolet spectra in 95% ethanol: curve ———, [2.2]metaparacyclophane; curve - - - - -, [2.2]paracyclophane; curve · · · · · ·, *m,p'*-dimethylbibenzyl.



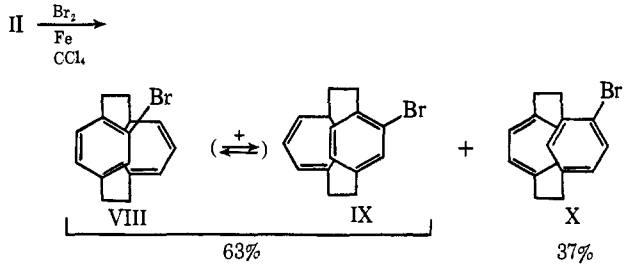
Isomerization of IV gave only a 10% yield of monobromo[2.2]metaparacyclophanes, along with 12% hydrocarbons and 12% dibrominated cyclophanes, from which was isolated pseudo-*p*-dibromo[2.2]paracyclophane.[20] Metallation of the isomeric mixture of monobromo derivatives and methylation with dimethyl sulfate of the organometallics gave 87% of a mixture composed of 22% V, 70% VI, and 8% VII, again analyzed by nmr.

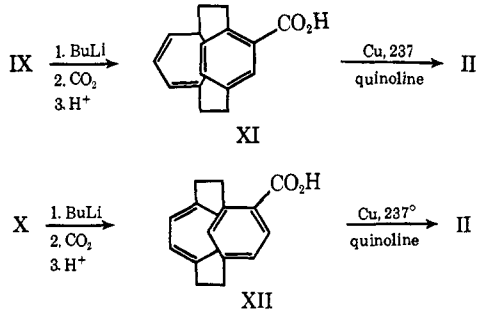
The product-determining step in these rearrangements is probably the 1,2-shift of the methylene group, and protonation of the various bridgehead positions is undoubtedly rapid and reversible. The results indicate that the 1,2-shift occurs in the nonsubstituted ring about seven to eleven times as fast as in the substituted ring, although in the case of methyl compound III the methylated ring is probably the more basic.[21] The equilibration between V and VI after formation destroys any further fruitful discussion of mechanism.

(16) A. T. Blomquist, R. E. Stahl, Y. C. Meinwald, and B. H. Smith, *J. Org. Chem.*, 26, 1687 (1961).
(17) R. C. Helgeson and D. J. Cram, *J. Amer. Chem. Soc.*, 88, 509 (1966).
(18) (a) D. J. Cram and R. H. Bauer, *ibid.*, 81, 5971 (1959); (b) M. Sheehan and D. J. Cram, *ibid.*, 91, 3553 (1969).
(19) R. E. Merrifield and W. D. Phillips, *ibid.*, 80, 2778 (1958).
(20) H. J. Reich and D. J. Cram, *ibid.*, 91, 3505 (1969).
(21) (a) D. A. McCauley and A. P. Lien, *ibid.*, 73, 2013 (1951); (b) M. Kilpatrick and F. E. Luborsky, *ibid.*, 75, 577 (1953).

Isotopic Exchange of [2.2]Metaparacyclophane (II). Reaction of II with deuteriotrifluoroacetic acid (98.5%) at 100° gave exchange of protium of the aromatic rings for deuterium. At the start of reaction the rings contained 1.9 mmol of protium and the medium contained 25 mmol of deuterium. At ~50% isotopic exchange the reverse reaction was small enough so that integrations of the spectrum of the product gave a rough estimate of the relative reactivities of the various ring positions. Exchange occurred as follows (see Figure 1): 76% H_d, 79% H_e, 66% H_a plus H_b, and 56% H_x. Thus, the rates of isotopic exchange at these sets of positions are about the same except for H_x, which is slightly slower. This hydrogen sits over the face of the para-bonded benzene, and is perhaps the most hindered of these aromatic protons.

Bromination of [2.2]Metaparacyclophane (II). When II was brominated in carbon tetrachloride with ferric bromide catalyst, 75% monobromides and 6% polybromides were formed, and the two groups were separated by chromatography. The isomer distribution of the monobromides was determined by converting the mixture to the mixture of monomethyl derivatives (metallation and alkylation) and analyzing by nmr integration (see future section). The results are formulated. Since VIII and IX equilibrate at room temperature,[9] the sum of their per cent contributions to the product is recorded. The equilibrating mixture in solution deposited only isomer IX in crystalline form. Isomer X (oil) was isolated and purified as its π–π salt of 2,4,5,7-tetranitrofluorenone. Bromides IX and X were converted to their corresponding carboxylic acids (XI and XII) which were decarboxylated to give back initial starting material, II. These reaction cycles demonstrated that bromination occurred without skeletal rearrangement.

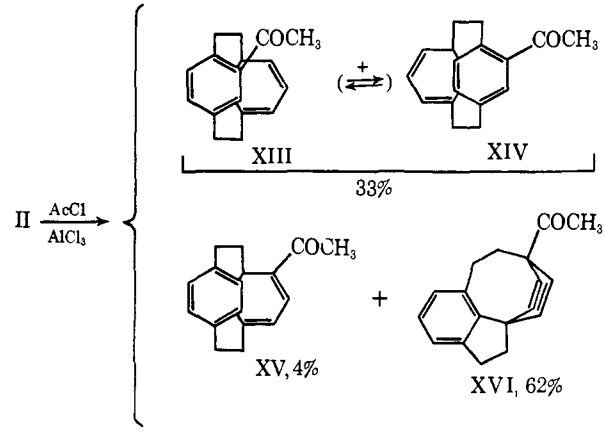




Bromination of II in carbon tetrachloride with iodine in place of iron as catalyst gave the same isomer distribution. When carried out in *n*-hexane in the dark with iron as catalyst, the same isomer distribution was observed, but the yield of monobromides increased to 90–95%. Bromination of II in dichloromethane with iodine catalyst gave >90% yield of monobromides, but the isomer distribution was altered to 15% VIII ⇄ IX and 85% X. With nitromethane as solvent and no catalyst, a similar ratio was observed (52% monobromides), but a tetrabromide (XIII) of condensed ring structure was also produced (22%). What is known about XIII is discussed in a future section. The monobromides consisted of 8% VIII ⇄ IX and 92% X.

Under brominating conditions, all 4 positions of the para ring of II are ortho to a methylene group, in effect equivalent since meta ring rotation is probably faster than bromination. The meta ring of II has two positions ortho to a methylene bridge. Thus, if bromination showed no selectivity between ortho positions in the two rings, monobrominated product should be 67% VIII ⇄ IX and 33% X. The distribution observed with carbon tetrachloride–iron–bromine, carbon tetrachloride–iodine–bromine, and *n*-hexane–iron–bromine approached this statistical pattern. However, in the more polar solvents and with less reactive forms of bromine, fairly high selectivity was observed. When corrected for the number of positions available, meta ring/para ring bromination in methylene dichloride–iodine was ~11, whereas in the even more polar nitromethane, 2[(per cent meta ring brominated)/(per cent para ring brominated)] ~ 22. That selectivity increases with more polar media and less reactive brominating agents has been well established in less complicated systems.[22] The difference in steric situations in the two rings of II, the possible transannular transfer of the proton leaving from the σ intermediate (as was observed in bromination of I[20,23]), and the differences in activity of the electrophile are all mechanistic features that contribute to changes in substitution patterns with changes in medium.

Acetylation of [2.2]Metaparacyclophane (II). With acetyl chloride and aluminum chloride in dichloromethane at −25°, II gave 61% yield of monoacetylated derivatives, XIII, XIV, XV, and XVI. Ketone XVI will be referred to as the tetracyclic ketone, since its IUPAC name,[24] 1-acetyl-5,7,12,14,16(4)-tetracyclo[9.2.-2.1^{4,11}.0^{8,16}]hexadecapentaene, is long. The structure proof of XVI is given in a later section. Isomers XIII and XIV exist an an equilibrium mixture in solution at room temperature,[9] but only XIV deposits on crystal-



(22) R. O. C. Norman and R. Taylor, "Electrophilic Substitution in Benzenoid Compounds," Elsevier Publishing Co., New York, N. Y., 1965, Chapters 1, 5, and 11.
(23) H. J. Reich and D. J. Cram, *J. Amer. Chem. Soc.*, 91, 3527 (1969).
(24) IUPAC 1597 Rules, *tbid.*, 82, 5557 (1960).

Table I. Partial Mass Spectra of Cyclophanes and Derivatives

Compound	Mol wt	*m/e* of base peak (rel int = 100)	Relative intensity of peaks			
			Parent, P	P − 104	104	103
[2.2]PCP[a] (I)	208	104	16	100	100	100
[2.2]MPCP[b] (II)	208	104	44	100	100	100
4-Bromo[2.2]MPCP[b] (X)	286	207	28	49	29	49
4-Methyl[2.2]MPCP[b] (VII)	222	118	45	100	0	100
12-Acetyl[2.2]MPCP[b] (XIV)	250	145	45	17	19	17
Tetracyclic ketone (XVI)	250	207	38	0	1	0

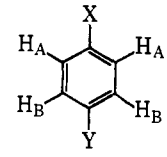
[a] PCP = paracyclophane. [b] MPCP = metaparacyclophane.

lization. Ketone XV was not isolated pure (only a derivative), and the amount present was determined by nmr analysis (see future section). The yields indicate that about 96% of the isolated products arose by attack on the para ring. When acetic anhydride was substituted for acetyl chloride in the acetylation, 54% of the ketonic mixture was obtained, but the yield picture changed: XIII ⇄ XIV, 84%; XV, 5%; and XVI, 11%.

Ketone XIV was oxidized to acid XI, also prepared from II through the bromide IX. Likewise, an impure sample of XV was oxidized to acid XII, also prepared from II through bromide IX. Both acids XI and XII were further characterized as their esters. Since acids XI and XII were both decarboxylated to II, the acetylations of II to give XIV and XV must have occurred without skeletal rearrangement.

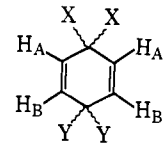
In both acetylations, attack on the para ring of II gave the major products. Compound XVI undoubtedly arose by attack of an acetyl group at the bridgehead of the para ring (see next section). Thus, para ring substitution dominated over meta ring substitution with acetyl chloride by a factor of >20, and by a factor of ~15 with acetic anhydride. These results contrast with the brominations, in which the para ring was only slightly favored in nonpolar solvents, and greatly disfavored in polar media. These two substitution reactions taken together offer convenient entrance into two of the four substitutable positions of [2.2]metaparacyclophane. No evidence of substitution at either the 5 or 8 positions in the meta ring of II was observed.

Structure Elucidation of Tetracyclic Ketone XVI. Analytical and mass spectral data established the compound to have the same molecular composition as the monoacetyl[2.2]metaparacyclophanes, but the 104 and P − 104 mass peaks due to benzyl–benzyl fragmentation (typical of I, II, and its derivatives) were completely absent (Table I). The infrared absorption spectrum of XVI gave a carbonyl absorption at 1712 cm^{-1} characteristic of an unconjugated ketone, which compares with 12-acetyl[2.2]metaparacyclophane's (XIV) band at 1675 cm^{-1} and 4-acetyl[2.2]metaparacyclophane's (XV) band at 1678 cm^{-1}. The pmr spectrum of XVI (60 MHz) exhibited the following: τ 3.0 (m, 3, ArH), 3.78 and 3.94 (AB quartet, 4, J = 9.5 Hz, HC=CH), 6.84–7.13 (m, 4, $ArCH_2$), 7.66–8.05 (m, 4, aliphatic CH_2), and 7.79 (s, 3, $COCH_3$). The A_2B_2 quartet at τ ~3.9 suggested the molecule possessed a plane of symmetry passing through either a para-substituted benzene ring or a dienic ring (at least six membered)[25] illustrated in A and B. The three proton multiplet in the aromatic region of XVI was far more complicated than the A_2B system of II (seven resolved signals, see Figure 1), at least 12 lines being visible. The resonance of τ 7.78 of the methyl group indicated



A

J_{AB} = 6–9 Hz



B

J_{AB} = 7–12 Hz

the carbonyl group was not conjugated. A natural abundance ^{13}C nmr spectrum with ^1H decoupled was determined[26] in dioxane, and Table II records the results. Sixteen singlets corresponding to 16 different *kinds* of carbon atoms compose the spectrum, two of which are of double intensity (total of 18 carbons). The chemical shifts correspond to one carbonyl carbon (C-1), eight other different kinds of sp^2 carbons (C-2 through C-9), and seven different kinds of sp^3 carbons (C-10 through C-16). Of the eight different kinds of sp^2 carbons, C-5 and C-7 are of double intensity. Carbonyl carbons of conjugated ketones absorb at *ca.* δ_{CS_2} −4 (*e.g.*, acetophenone) and for nonconjugated ketones at *ca.* δ_{CS_2} −12 (*e.g.*, acetone).[27] The occurrence of a band at δ_{CS_2} −15 (C-1) confirms the carbonyl group of

Table II. Natural Abundance ^{13}C Nmr Spectral Data at 15.08 MHz, Solvent Dioxane, ^1H Decoupled of the Tetracyclic Ketone (XVI)

Carbon no.	ν, Hz	$\delta_{O(CH_2CH_2)_2O}$	δ_{CS_2}	Intensity
1	5278	−140.8	−15.2	1
2	4397	−82.4	43.1	1
3	4281	−74.7	50.8	1
4	4206	−69.7	55.8	1
5	4193	−68.8	56.7	2
6	4105	−63.0	62.5	1
7	4102	−62.8	62.7	2
8	4056	−59.7	65.8	1
9	4003	−56.2	69.3	1
10	2985	11.3	136.8	1
11	2928	15.1	140.6	1
12	2715	29.2	154.7	1
13	2682	31.4	156.9	1
14	2647	33.7	159.2	1
15	2609	36.2	161.2	1
16	2533	41.2	166.7	1

(25) S. Sternhell, *Quart. Rev., Chem. Soc.*, 23, 236 (1969).

(26) We warmly thank Dr. H. J. Reich for this spectrum and its interpretation. We profited greatly from discussions about the structure of XVI with Professor F. A. L. Anet and wish to thank him.

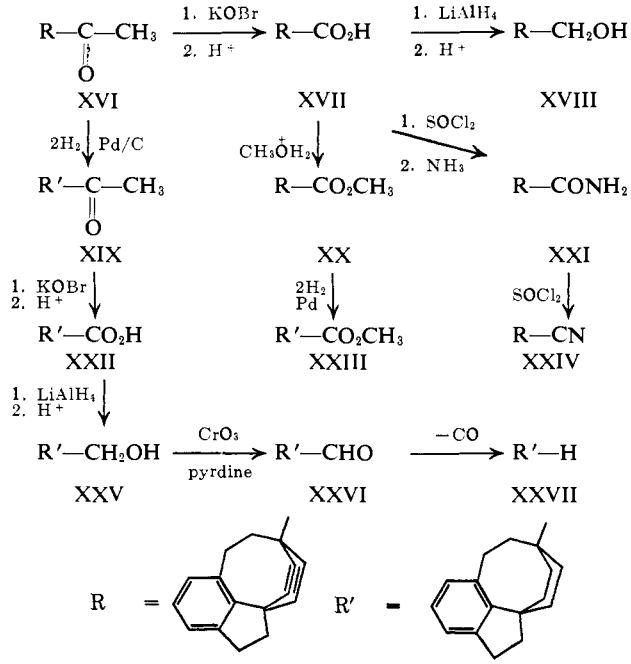
(27) Reference 14, Vol. II, Chapter 12, p 988.

XVI is not conjugated. The ten sp^2 carbons (two pairs identical) allow for only one benzene ring and two double bonds, and the seven sp^3 carbons indicate that two of the sp^2 carbons of [2.2]metaparacyclophane have become aliphatic in production of XVI. The presence of two pairs of identical sp^2 carbons confirms the plane of symmetry required by the AB quartet of the pmr spectrum, and the spectra taken together indicate the presence of unit B in the molecule.

The reactions of tetracyclic ketone XVI are outlined. The absorption of 2 mol of hydrogen in reactions XVI → XIX and XX → XXIII confirmed the presence of two aliphatic double bonds in XVI. Ester XX was also observed to rapidly absorb 2 equiv of bromine in carbon tetrachloride as well. Degradative oxidation of acid XVII with alkaline permanganate gave only 1,2,3-benzenetricarboxylic acid. No benzenedicarboxylic acids were detected.

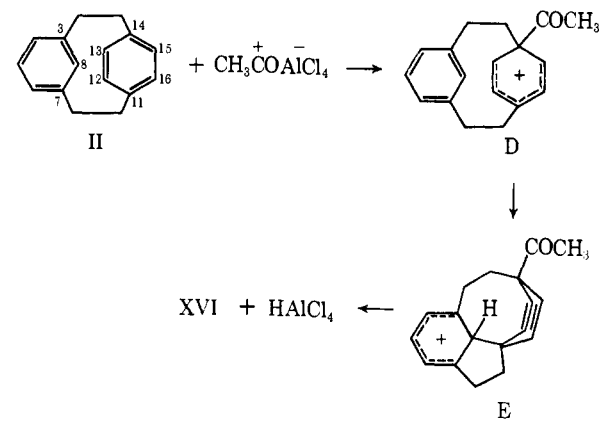
These facts taken together demonstrate that tetracyclic ketone XVI has the structure formulated. The spectral properties of the derived compounds, XVII through XXVII, were consistent with what was expected based on the assigned structure of XVI.

During bromination of II in nitromethane, a 22% yield of a tetrabromide, $C_{16}H_{14}Br_4$ (XIII), was produced. Since its structure is probably related to that of XVI, what little is known about XIII will be mentioned here. The mass spectrum of XIII gave a parent peak at *m/e* 526. Like XVI, oxidation of XIII with alkaline permanganate gave only 1,2,3-benzenetricarboxylic acid. The nmr spectrum of the substance showed the presence

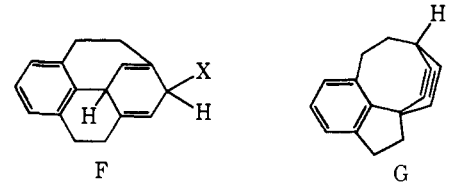


of only three aromatic protons. Solution of XIII in bromine–carbon tetrachloride did not decolorize the bromine. Addition of XIII to sodium iodide in acetone liberated iodine. When reduced with hydrogen in ethanol over palladium–carbon, a crystalline hydrocarbon, $C_{16}H_{20}$ (XXVIII), was produced in 95% yield. The nmr spectrum of XXVIII showed only three aromatic protons and 17 highly coupled aliphatic protons. Comparison of the nmr, mass, uv, and ir spectra of compounds XXVII and XXVIII indicated the compounds to be of similar but not identical structures.

The formation of tetracyclic ketone XVI by acetylation of II provides an interesting example of a relayed, double electrophilic substitution reaction. From the structure of XVI it is clear that an acetyl cation was donated to a bridgehead position of the para ring, and that the dienyl cation (D) thus generated attacked the meta ring at its closest hydrogen-carrying position to give a new dienyl cation (E), which lost a proton to give XVI. This reaction course involves initial electro-



philic attack at the sp^2 carbon of II subject to the greater bond angle and π–π repulsion strain to give D, whose positive charge is probably somewhat delocalized into the meta ring. Although the C-7 to C-11 bond distance (~2.7 Å)[5a] is shorter than the C-8 to C-11 distance (~3.0 Å),[5a] formation of a full bond at C-8 to C-11 can result in a rearomatization of the meta ring and lead to XVI. Electrophilic attack at C-15 and bond formation between C-12 and C-8 can also be envisioned, in which case F would be ultimately generated. The C-12 to



C-8 bond distance in II is about 3.1 Å.[5a] The bridgehead double bonds of F probably inhibit its formation. Conceivably, tetrabromide XIII started with the carbon skeleton of F, and the double bond strain of the system was relieved by halogen addition and possible rearrangement. The formation of XVI from II finds analogy in the formation of hydropyrenes by treatment of [2.2]metacyclophane with electrophiles.[6,15]

A number of attempts were made to form the parent tetracyclic compound, G, by treatment of II with acid in various media. These failed, possibly because the equilibrium constant between II and G favors II.

Use of Nuclear Magnetic Resonance Spectra for Determining the Position of Substitution in [2.2]Metaparacyclophane (II). The isomeric monosubstituted derivatives of II each give distinctly different nmr spectra since the magnetic environments of the molecule are so position dependent. The spectrum of the parent hydrocarbon II (Figure 1) suggests this should be so, since the aromatic proton of each position possesses such a unique chemical shift.

In the nmr spectrum of the 4-substituted [2.2]metaparacyclophanes, protons a and b on the meta ring

appear as an AB pattern further perturbed by H_x. For nmr spectral comparisons, 4-hydroxymethylene-[2.2]metaparacyclophane (XXIX) and 4-carbomethoxy-[2.2]metaparacyclophane (XXX) were prepared from acid XII. Figure 4 records the spectra of the three 4-substituted derivatives, XXIX, XXX, and bromo compound X. For XXX, the protons H_a and H_b form an AB pattern (J_{ab} = 8 Hz) with H_a downfield since it is ortho to the ester group, and with H_b coupled to H_x ($J_{bx} \sim 2$ Hz, J_{ax} was too small to resolve). For XXIX, a similar pattern is visible except that H_a is not shifted so far downfield. For X the pattern again resembles that of ester XXIX except that now the two H_e protons feel sufficiently different magnetic environments due to the transannular bromine atom to form another AB pattern. A similar transannular effect was noted in the bromo[2.2]paracyclophanes.[28]

Introduction of a group into the 12 or 15 position has a complicating effect on the nmr spectra of II since the two isomers equilibrate in solution,[9] and the spectrum obtained is the sum of the two spectra. The observed spectrum is usually nearly the same as that for the parent II with either one less H_e or H_d proton. If the group is halogen or contains a carbonyl, the proton ortho to that group is shifted downfield. These effects are illustrated in the spectrum of acetyl compounds, XIII ⇄ XVI (Figure 4).

Since the magnetic environment is so position dependent, all the monomethyl[2.2]metaparacyclophane and acetyl[2.2]metaparacyclophane isomers were identifiable by the chemical shifts of their methyl protons. Table III records the methyl resonances for the isomers

Table III. Methyl Proton Resonances of the Monomethyl- and Monoacetyl[2.2]metaparacyclophanes, and Reference Compounds (60 MHz)

Compound	Compd no.	Hz downfield from TMS	τ, ppm
12-Methyl[2.2]MPCP[a]	VI	144	7.60
4-Methyl[2.2]MPCP[a]	VII	134	7.77
16-Methyl[2.2]MPCP[a]	V	101	8.32
Toluene		140	7.67
4-Methyl[2.2]PCP[b,c]	III	121	7.98
5-Methyl[3.3]PCP[b,d]		129	7.85
8,6-Dimethyl[2.2]MCP[e,f]		34	9.44
12-Acetyl[2.2]MPCP[a]	XIV	156	7.40
4-Acetyl[2.2]MPCP[a]	XV	150	7.50
16-Acetyl[2.2]MPCP[a]	XIII	125	7.92
Acetophenone		155	7.41
Acetone		130	7.83
4-Acetyl[2.2]PCP[b]		144	7.60

[a] MPCP is metaparacyclophane. [b] PCP is paracyclophane. [c] Reference 23. [d] Data taken from ref 18b. [e] Data taken from D. J. Wilson, V. Boekelheide, and R. W. Griffin, Jr., *J. Amer. Chem. Soc.*, **82**, 6302 (1960). [f] MCP is metacyclophane.

of the two classes of compounds, and shows how the ring currents affected the chemical shifts. These differences in chemical shift were the basis of the analytical tool for determining isomer distributions in the substitution and rearrangement reactions.

(28) H. J. Reich and D. J. Cram, *J. Amer. Chem. Soc.*, **91**, 3534 (1969).

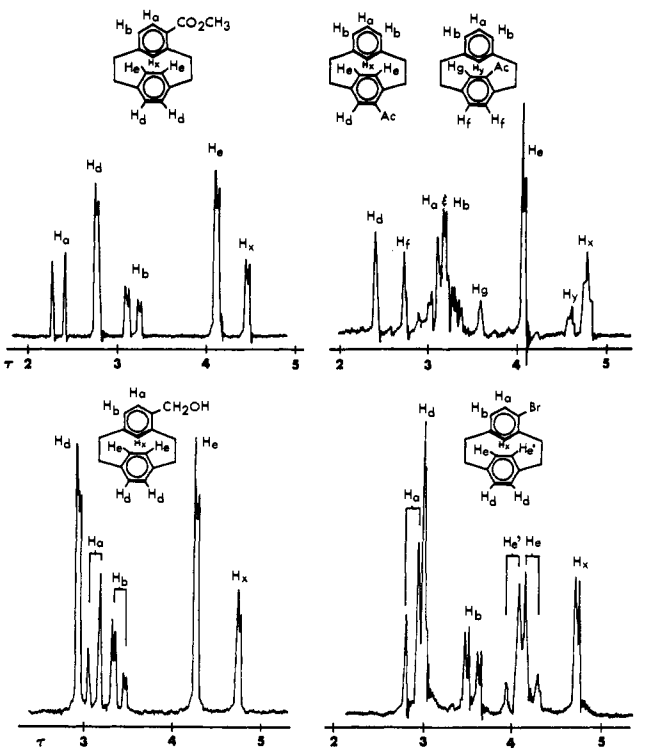
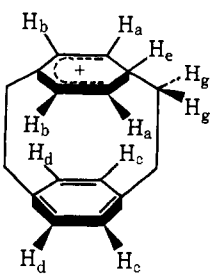


Figure 4. Aromatic proton nmr spectrum (60 MHz) of monosubstituted [2.2]metaparacyclophanes.

Experimental Section

General. All melting points are uncorrected and were taken on a Thomas-Hoover Uni-Melt capillary apparatus. Solvents are reagent grade unless otherwise specified. Infrared spectra were determined in chloroform on a Beckman IR-5 spectrometer. Ultraviolet spectra were run in absolute ethanol on a Cary 14 spectrometer. The mass spectra were obtained with an AEI Model MS-9. Thin-layer chromatography was performed using Brinkman silica gel G coated on glass plates which were developed in ether–pentane mixtures and spotted in an iodine chamber. Gas–liquid chromatography (glc) was performed on an F & M Model 720 instrument. Nmr determinations were made with a Varian A-60D or a Varian HA-100 spectrometer using dilute solutions (*ca.* 10%). Unless specified otherwise all spectra were run in deuteriochloroform with tetramethylsilane as an internal standard. In descriptions of nmr spectral data, s = singlet, d = doublet, t = triplet, m = multiplet, and the numbers following these letters indicate the number of protons the signal represents. For multiplets the chemical shift of the strongest peak is reported rather than the center of weight.

Protonation and Deuteration of [2.2]Paracyclophane (I). (a) Fluorosulfonic acid (distilled, 0.1 ml) was added to an nmr tube which was cooled to −78°. Sulfuryl chlorofluoride (SO_2ClF, 0.2 ml) was condensed in the nmr tube and stirred using a glass rod. Powdered [2.2]paracyclophane (20 mg) was added to the nmr tube followed by 5 drops of dichloromethane. Stirring with a glass rod produced a clear red solution. The nmr spectrum was recorded at −80° (60 MHz). The bands observed were assigned as follows: τ 1.73 (1.9), H_a; 2.41 (2.0), H_b; 2.82 (2.0), H_c; 3.12 (2.1), H_d; 5.89 (1.0), H_e; 6.40 (6.3), H_f; 7.20 (2.0), H_g.



(b) A solution of 1.0 g (0.75 mmol) of aluminum chloride and 1.0 g (0.48 mmol) of [2.2]paracyclophane in 15 ml of sulfur dioxide at −50° was stirred 15 min and then saturated with hydrogen chloride.[11] An aliquot of this solution was transferred by a cold pipet to a −50° nmr tube containing 1 drop of dichloromethane. The tube was then sealed and nmr spectrum recorded. In the experiment employing deuterium chloride the gas was generated by addition of deuterium oxide (99.8% D) to acetyl chloride maintained at 30–40°, and the generated gas was passed through a cold trap (−78°) and drying train.[11] Quenching was done by adding the cold solution of carbonium ions to methanol or methanol–sodium methoxide solutions (−78°). After washing with water and sodium bicarbonate solutions the solvents were evaporated and nmr spectra were recorded.

Protonation of [2.2]Metaparacyclophane (II). Almost the same procedure as used in (a) above was employed. The only difference was that II was first dissolved in 5 drops of dichloromethane and then added to the fluorosulfonic acid–sulfuryl chlorofluoride mixture. In the following resonance assignments, the structure in Figure 2 designates the positions of the hydrogens: τ 1.20 (1, J = 9.2 Hz), H_a; 1.98 (1, J = 9 Hz), H_b; 2.34 (1, J = 8.5 Hz), H_c; 2.66 (1, J = 7 Hz), H_d; 2.78 (1, J = 7 Hz), H_e; 3.06 (1, J = 7 Hz), H_f; 3.32 (1, J = 8.5 Hz), H_g; 3.82 (1, J = 0 Hz), H_h; 5.76 (1), H_i; 6.52 (7.1), H_j; 7.78 (1), H_j.

Rearrangement of [2.2]Paracyclophane (I) to [2.2]Metaparacyclophane (II). The following procedure can be improved for production of II by using a 6:1 mole ratio of aluminum chloride to I and stirring the solution at −10° for 2 hr. Product II is isolated by sublimation and crystallization. The following preparations were made to identify the side products.

A suspension of 10.0 g (75 mmol) of aluminum chloride in 400 ml of dry dichloromethane was saturated with dry hydrogen chloride at 0°. To this solution was added 5.0 g (24 mmol) of powdered I, and the resulting deep red solution was stirred magnetically at 0° for 30 min. The solution was then poured into 400 ml of ice water and extracted with dilute hydrochloric acid and sodium bicarbonate solution. The organic layer was dried ($MgSO_4$) and chromatographed on 50 g of alumina with pentane, to give 3.75 g of hydrocarbons. Crystallization of the mixture gave 145 mg of I, mp 285–287°, undepressed by admixture with an authentic sample. Preparative glc (6 ft × 0.75 in. column, 20% 1001 Epon on firebrick, 165°, 15 psi helium) of mother liquors produced 2.2 g (44%) of II, 48 min; 350 mg (7%) of I, 63 min; 0.5 g (10%) of 1,2,2a,3,4,5-hexahydropyrene, 128 min; and traces of bibenzyl at 15 min.

A sample of II was recrystallized from ether–methanol to give plates, mp 81.2–81.7°. The ultraviolet spectrum in 95% ethanol produced λ_{max} 292 nm (ϵ 230), 284 (280), 278 and 274 (320), and sh 244 (3000). The following fragments in the mass spectrum were found: 70 eV, m/e (rel intensity) 208 (44), 193 (35), 104 (100), 103 (38), 78 (37). *Anal.* Calcd for $C_{16}H_{16}$: C, 92.26; H, 7.74. Found: C, 92.39; H, 7.60.

The nmr spectrum of II (Figure 1) exhibited four groups of aromatic signals and a broad and highly coupled aliphatic region ($CDCl_3$, TMS as internal standard): τ 2.87 (d, 2 H, $J \sim 1.5$ Hz, assigned as H_d), 3.23 (mult, 3 H, H_a and H_b), 4.19 (d, 2 H, $J \sim 1.5$ Hz, H_e), 4.63 (broad singlet, 1 H, H_x), 6.80–8.00 (multiplet, aliphatic).

The hexahydropyrene compound was recrystallized from ethanol and sublimed (85°, 0.5 mm) to give material, mp 102.5–103.3° (lit.[15] 103–105°). The ultraviolet spectrum in ethanol gave maxima at 326 nm (ϵ 910), 320 (430), 310 (700), 294 (2800), 284 (3900), 278 (3300), and 232 (82,000). The nmr spectrum in carbon tetrachloride consisted of τ 2.82 (center of five-proton multiplet, aromatic), 6.75–7.5 (m, 5, benzylic), and 7.65–8.95 ppm (m, 6, aliphatic). *Anal.* Calcd for $C_{16}H_{16}$: C, 92.26; H, 7.74. Found: C, 92.40; H, 7.72.

A picrate of the substance was formed by adding 20 mg of hexahydropyrene to 20 mg of picric acid in 5 ml of ethanol. Recrystallization of the orange picrate from ethanol gave crystals, mp 150.4–150.6° (lit.[15] mp 147–148°).

Bibenzyl, mp 49–50°, was undepressed upon admixture with an authentic sample.

Reduction of [2.2]Metaparacyclophane (II) to *m,p'*-Dimethylbibenzyl. To a solution of 200 mg of II in dimethoxyethane was added 2 equiv of potassium metal (75 mg). The solution was stirred for 5 days, quenched with water, and extracted with dichloromethane. After drying the organic layer ($MgSO_4$), evaporating the solvents, and submitting the residue to preparative glc (same conditions as for preparation of II) 60 mg (29%) of *m,p'*-dimethylbibenzyl was obtained. The nmr spectrum in carbon tetrachloride gave the following signals: τ 3.03 (s, 4, para ring), multiplet centered at 3.06 (4, meta ring), 7.22 (s, 4, methylene), 7.74 ppm (s, 6, methyl). The ultraviolet spectrum in ethanol possessed maxima at 274 nm (ϵ 620), 268 (596), 265 (677), 259 (517), and sh 220 (16,780). A trace of II (<2%) was present in the oil which gave the following analysis. *Anal.* Calcd for $C_{16}H_{18}$: C, 91.37; H, 8.63. Found: C, 91.53; H, 8.62.

Oxidation of *m,p'*-Dimethylbibenzyl to Benzenedicarboxylic Acids. A 50-mg sample of the hydrocarbon, 150 mg of sodium carbonate, 0.4 g of potassium permanganate, and 15 ml of water were brought to reflux. Three more 0.4-g samples of potassium permanganate were added periodically during 10 hr of reflux. The solution was cooled and acidified with dilute sulfuric acid, and the manganese dioxide was reduced with sodium bisulfite. This aqueous mixture was extracted with ether for 2 days in a continuous extractor to produce 30 mg of diacids which were esterified with diazomethane. The mixture of esters analyzed to be approximately equal quantities of dimethyl isophthalate and terephthalate by glc and tlc, where R_f values differ significantly for all benzenedicarboxylic acid esters and benzenetricarboxylic acid esters.[29] When the same oxidation and esterification procedure was applied to [2.2]metaparacyclophane (II), the same esters were obtained.

Rearrangement of 4-Bromo[2.2]paracyclophane (X). To 1200 ml of dichloromethane cooled to 0° and saturated with dry hydrogen chloride, 29.0 g (0.21 mol) of aluminum chloride was added. Powdered 4-bromo[2.2]paracyclophane (IV)[28] (10.0 g, 0.035 mol) was then added and the reaction mixture was stirred at 0° for 60 min. The reaction was poured onto 400 ml of ice water, and the organic layer was washed with water, dilute hydrochloric acid, and saturated sodium bicarbonate, dried ($MgSO_4$), and stripped of solvent to yield 9.2 g of a yellow oil. Chromatography of the oil on 150 g of alumina with 5% ether–95% pentane yielded 7.1 g of white solids. Preparative glc (180°, 20% SE-30 gum rubber) gave 0.83 g of hydrocarbons, 2.70 g of monobromides, and 1.38 g of dibromides. The hydrocarbons were chromatographed on alumina to yield 0.72 g of II and 80 mg of I (analyzed by melting point and nmr). The monobromides were chromatographed on alumina to produce 0.90 g of an isomeric mixture of bromo[2.2]metaparacyclophanes, mp 62–63°. The nmr spectrum showed this mixture to be mostly 12- and 15-bromo derivatives. Recrystallization from ether–pentane gave white, solid 12-bromo[2.2]metaparacyclophane (IX), mp 65.5–67.2°. *Anal.* Calcd for $C_{16}H_{15}Br$: C, 66.94; H, 5.23. Found: C, 67.13; H, 5.06.

Further chromatography gave 1.0 g of 4-bromo[2.2]paracyclophane (IV), mp 137–138°. The dibromide glc fraction was fractionally crystallized from dichloromethane to give pseudo-*p*-dibromo[2.2]paracyclophane,[20] mp 249–250°, undepressed by admixture with an authentic sample.

Conversion of Bromo[2.2]metaparacyclophanes to Methyl[2.2]metaparacyclophanes. Into 20 ml of dry ether under nitrogen was syringed 0.84 ml (1.26 mmol) of *n*-butyllithium. The solution was cooled to 0° and the bromo[2.2]metaparacyclophane mixture (mp 62–63°, 0.42 mmol) from above was added. The solution was warmed to reflux and let stir for 30 min. Dimethyl sulfate, 0.24 ml (2.5 mmol), was then added by syringe and the reaction was stirred for 20 min. Water and a few milliliters of aqueous ammonia then were added to decompose the excess dimethyl sulfate. The ethereal layer was washed with water and saturated sodium bicarbonate solution, dried ($MgSO_4$), and evaporated to dryness. Analysis of the nmr spectrum of the solid showed the composition to be 70% 12-methyl-, 22% 15-methyl-, and 8% 4-methyl[2.2]metaparacyclophanes. Sublimation of the solid produced 79 mg (85%) of a waxy solid, mp 40–45°, which gave an identical nmr spectrum, including integrations of methyl singlets (see Table III).

Preparation of 4-Methyl[2.2]paracyclophane (III). Our most recent modification of the preparation of this compound has been reported.[20] The original preparation using methyl iodide as the methylating agent was less satisfactory. When 4-bromo[2.2]paracyclophane was converted to the lithio derivative[20] and treated with methyl iodide, a 48% yield of 4-methyl[2.2]paracyclophane (III) was obtained. However, a second metal–halogen interchange apparently occurs and a 35% yield of 4-iodo[2.2]paracyclophane,[29] mp 143–144°, was obtained.

Rearrangement of 4-Methyl[2.2]paracyclophane (III). The isomerization was performed identically as for 4-bromo[2.2]paracyclophane (IV) except the reaction time was 165 min in order to

(29) D. J. Cram and H. P. Fischer, *J. Org. Chem.*, 30, 1815 (1965).

consume all starting material. Aliquots were checked periodically by glc analysis for starting material concentrations and also for disproportionation products (which did not appear). When 7.1 g (54 mmol) of aluminum chloride, 2.0 g (9 mmol) of III, and 300 ml of dichloromethane saturated with hydrogen chloride were allowed to react, a viscous yellow oil was produced which on work-up afforded 1.4 g of oily solid after being passed through 60 g of alumina with pentane. Nmr analysis of this mixture and on a 0.9-g sample (mp 42–44°) obtained by recrystallization from ethanol showed both samples to be 66% 12-methyl-, 21% 15-methyl-, and 13% 4-methyl[2.2]metaparacyclophanes (see Table III). The nmr spectrum demonstrated the absence of starting material, and glc showed that no dimethylated (disproportionation) products were present. *Anal.* Calcd for $C_{17}H_{18}$: C, 91.84; H, 8.16. Found: C, 91.74; H, 8.24.

Acetylation of [2.2]Metaparacyclophane (II) with Acetyl Chloride. A solution of 5.56 g (26.7 mmol) of II in 300 ml of dichloromethane was cooled to −55°. Then a 25° mixture of 300 ml of dichloromethane, 2.4 ml (33.4 mmol) of acetyl chloride, and 4.94 g (37.4 mmol) of aluminum chloride was decanted into the above cold solution (any undissolved aluminum chloride was withheld). Immediately, a dark red color developed and the resulting temperature was −25°. The stirred reaction mixture was maintained at −25° for 15 min. The mixture was poured onto ice–dilute hydrochloric acid slurry, and enough ether was added to make the organic layer float. The organic layer was washed twice with 10% hydrochloric acid, twice with saturated bicarbonate, and twice with saturated sodium chloride. The oily reaction mixture (8% starting material and no diacetylated material by glc) was adsorbed onto 15 g of silica gel and chromatographed on 140 g of silica gel. Pentane (1 l.) afforded 0.69 g of starting material (by nmr and tlc). The next 4 l. of 2–6% ether–pentane gave 5.87 g (87%) of ketonic oil. Nuclear magnetic resonance and glc showed the ketonic oil to be 62% tetracyclic ketone (XVI), 26% 12-acetyl[2.2]metaparacyclophane (XIV), 8% 15-acetyl[2.2]metaparacyclophane (XIII), and *ca.* 4% 4-acetyl[2.2]metaparacyclophane (XV). The glc retention times were 9.1 and 10.5 min, acetyl[2.2]metaparacyclophane isomers and tetracyclic ketone (XVI), respectively (column temperature 200°, 10 ft × 1/8 in. o.d., 5% SE 30 gum rubber on firebrick, 15 psi helium).

This oil partially crystallized on standing and yielded from ether–pentane 2.47 g (37%) of XVI, colorless hexagonal plates, mp 87.0–88.6°. Ketone XVI gave the following spectral data: ir 3004 (HC=), 2932 and 2747 (CH), 1710 (C=O), 1517 cm^{-1}; uv λ_{max} 278 nm (ϵ 590), 270 (630), sh 235 (4320); nmr τ 3.0 (m, 3, ArH), 3.78 and 3.94 (AB quartet, 4, J = 9.5 Hz, HC=C), 6.84–7.13 (m, 4, benzylic CH_2), 7.66–8.05 (m, 4, aliphatic CH_2), and 7.79 ppm (s, 3, $COCH_3$). The ^{13}C nmr of XVI gave signals in dioxane recorded in Table II.

The mass spectrum of ketone XVI exhibited the following fragments at 70 eV: *m/e* (rel int) 251 (8), 250 (38), 235 (11), 208 (18), 207 (100), 206 (8), 205 (28), 192 (12), 191 (14), 179 (12), 178 (11), 165 (15). *Anal.* Calcd for $C_{18}H_{18}O$: C, 86.36; H, 7.25. Found: C, 86.35; H, 7.34.

Later crops gave 1.33 g (20%) of white buttons, mp 67–78°, of 12-acetyl[2.2]metaparacyclophane (XIV). Purification by further crystallizations and the use of Girard's "T" reagent did not narrow the broad melting point range. The spectral data for the 12-isomer (XIV) was as follows (15-acetyl[2.2]metaparacyclophane, XIII, is in equilibrium with the 12-isomer in solutions): ir 3005 (aromatic CH), 2920 and 2750 (CH), 1675 cm^{-1} (C=O); uv λ_{max} 320 nm (ϵ 1240), 260 (6060), 230 (13,000); nmr for **12-isomer** (XIV) τ 2.43 (s, 1, *p*-ArH), 3.22 (m, 3, *m*-ArH), 4.09 (s which may be an AB quartet, 2, *p*-ArH), 4.8 (broad s, 1, *m*-ArH), 6.0–8.0 (m, 8, CH_2CH_2), 7.40 ppm (s, 3, $COCH_3$); **15-isomer** (XIII) τ 2.75 (m, 2, *p*-ArH), 3.22 (m, 3, *m*-ArH), 3.6 (s, 1, *p*-ArH), 4.6 (s, 1, *p*-ArH), 6.0–8.0 (m, 8, CH_2CH_2), and 7.89 ppm (s, 3, $COCH_3$). The ratio of the methyl peaks was 3.9:1.0 for 12- to 15-isomer. The mass spectrum for ketone XIV at 70 eV exhibited these fragments: *m/e* (rel int) 251 (9), 250 (45), 146 (12), 145 (100), 105 (23), 104 (19), 103 (18), 78 (13).

Although 4-acetyl[2.2]metaparacyclophane (XV) was never isolated, the following details offer proof of its presence. When the mother liquors from the acetylation of II (both methods) were subjected to a bromoform reaction followed by esterification in methanol–sulfuric acid, the 4-methyl ester was isolated along with the previously isolated 12-isomer and tetracyclic isomer (XX). These three esters were separated from one another by means of chromatography on silica gel impregnated with silver nitrate. The silica gel was made by dissolving 10 g of silver nitrate in 300 ml of water, adding 100 g of silica gel, and removing the water at reduced pressure and elevated temperatures on a rotary evaporator.

The 12-carbomethoxy[2.2]metaparacyclophane (mp 75–76°) was eluted with 5% ether–pentane (beginning elution with pure pentane) and 4-carbomethoxy[2.2]metaparacyclophane soon followed. The tetracyclic ester (XX, mp 94–95°) was not eluted until 25% ether, 0.5% methanol, and 74.5% pentane were used. The 12-isomer and tetracyclic isomer were identical with samples prepared below. The 4-carbomethoxy[2.2]metaparacyclophane had mp 81.0–82.5° and gave the following nmr signals: τ 2.37 (d, 1, J = 8 Hz, *m*-ArH), 2.78 (m, 2, *p*-ArH), 3.20 (doublet of doublets, 1, J = 8 Hz, J = 2 Hz, *m*-ArH), 4.13 (m, 2, *p*-ArH), 4.47 (d, 1, J = 2 Hz, *m*-ArH), 6.12 (s, 3, CO_2CH_3), 6.2–8.1 ppm (m, 8, CH_2CH_2). *Anal.* Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.25; H, 6.95.

Acetylation of [2.2]Metaparacyclophane (II) with Acetic Anhydride. The procedure was the same as for acetyl chloride with the following changes. (1) The aluminum chloride and dichloromethane were cooled to *ca.* −40° before the acetic anhydride was added since the reaction between anhydride and aluminum chloride was more exothermic than that of acetyl chloride and aluminum chloride in dichloromethane. (2) Reaction time was 20 min as the solution warmed from −20 to −10°. In a sample reaction were used 8.34 g (40.2 mmol) of II, 31.8 g (240 mmol) of aluminum chloride, 12.2 ml (120 mmol) of acetic anhydride, and 600 ml of dichloromethane. Analysis of the product by glc showed 0% starting material, 91% monoacetylated material, and 9% higher retention time material, *ca.* 2.3 times the retention time of monoacetylated material. From the nmr methyl integrations of the spectrum of the ketone mixture, the content was found to be 64% XIV, 20% XIII, 11% XVI, and 5% XV. Silica gel chromatography of the total reaction mixture gave the following materials: (a) an unknown compound (3%) with an R_f value of a hydrocarbon, ir 1450 cm^{-1}, mass spectrum P = 440 (possibly $(C_{16}H_{15})_2C{=}CH_2$); (b) monoacetylated compounds, 5.4 g (54%). Crystallization of the semisolid ketone from ether–pentane gave: crop 1, 0.61 g of ketone XVI, plates, mp 87.2–88.5°; crop 2, 1.33 g of button-shaped crystals (mp 66–77°) and plates (mp 75–86°). Recrystallization of the buttons combined with the mother liquors gave 3.0 g of XIV, buttons, mp 67–78°.

Bromoform Oxidation of Tetracyclic Ketone (XVI) to Tetracyclic Acid (XVII). To a solution of 15.15 g (0.27 mol) of potassium hydroxide in 40 ml of water maintained at 0° was added 2.2 ml of bromine (0.04 mol) with stirring. Then 2.3 g (0.009 mol) of ketone XVI dissolved in 40 ml of dioxane was added to the above hypobromite solution. (The reagent grade dioxane was further purified by passing through 80 ml of act. 1 alumina.) The cooling bath was removed and the reaction was allowed to stir at room temperature for 2.5 hr. Sodium bisulfite solution was then added to destroy excess hypobromite, the mixture was extracted three times with 10 ml of dichloromethane, and the aqueous layer was acidified with 6 *N* HCl to yield a cream-colored precipitate of 2.27 g of crude acid XVII, mp 182–184°. Crystallization from ether afforded 2.1 g (90%) of white crystalline rods of XVII, mp 184.8–186.0°. This compound gave the following spectral data: ir 1700 cm^{-1} (C=O), broad band 3400–2250 cm^{-1} (CH and OH); nmr τ −2.0 (s, 1, COOH), 3.0 (m, 3, ArH), 3.67 and 3.81 (AB quartet, 4, J = 9.5 Hz, HC=C), 7.0 (m, 4, CH_2), and 7.83 ppm (m, 4, CH_2). *Anal.* Calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 80.83; H, 6.40.

Tetracyclic Ester (XX). Esterification was complete after 2 days of refluxing 350 mg of XVII, 0.14 ml of sulfuric acid, 1.2 ml of methanol, and 4 ml of 1,2-dichloroethane. After the reaction was cooled and water and ether were added, the ethereal layer was extracted three times with water, three times with 5% Na_2CO_3 (gave no precipitate on acidification), and once with saturated sodium chloride. The ethereal layer was dried (Na_2SO_4), the solvent was removed, and crystallization from ether–pentane gave 279 mg (75%) of ester XX, rods, mp 94.8–95.5°. Ester XX had a carbonyl absorption in the ir at 1730 cm^{-1} and an nmr spectrum which was the same as XVI except for the methyl signal ($COCH_3$) at τ 6.27. *Anal.* Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.03; H, 6.84.

Tetracyclic Amide (XXI). Acid XVII, 0.9 g (4 mmol), was combined with 6 ml of benzene and 1.5 g (1 ml) of thionyl chloride and refluxed 1 hr. The solvent was evaporated and 5 ml of dry acetone was added to make a solution which then was cooled to 0°. Concentrated ammonium hydroxide, 6 ml, was added with swirling. A precipitate formed which was filtered to give 0.4 g of XXI, mp 167–168°. In the ir spectrum absorptions appeared at 3470 and 3380 (NH), 1675 (C=O), and 1584 cm^{-1}. *Anal.* Calcd for $C_{17}H_{17}NO$: C, 81.24; H, 6.82. Found: C, 81.14; H, 6.98.

Tetracyclic Nitrile (XXIV). Dehydration of amide XXI was achieved by refluxing 350 mg of XXI in 10 ml of benzene and 0.7 ml of thionyl chloride for 3 hr. The solvents were evaporated at reduced pressure to leave a solid, which was chromatographed on silica gel (3.0 g) and eluted with 2% ether–pentane. Exactly 80 mg (25%) of fluffy white solid (XXIV), mp 138–139°, was obtained. The ir spectrum of XXIV possessed a peak at 2240 cm^{-1} (C≡N); the nmr spectrum was like XVI with no methyl absorption. *Anal.* Calcd for $C_{17}H_{15}N$: C, 87.51; H, 6.48. Found: C, 87.60; H, 6.29.

Alkaline Permanganate Oxidation of Tetracyclic Acid (XVII). A mixture of 550 mg of XVII, 1.5 g of sodium carbonate, and 30 ml of water was brought to reflux. Potassium permanganate, 5.6 g, was added slowly in four portions over 2 hr. The purple color persisted and sodium bisulfite was added to decompose the excess oxidant. The reaction was made distinctly acidic with sulfuric acid at which point the manganese dioxide was reduced by the acidic bisulfite solution and went into solution. Some sodium chloride was dissolved in this solution and the solution was extracted in a lighter-than-water extractor for 3 days with ether. The extraction produced 279 mg (50%) of solid, mp 195–200° (pure 1,2,3-benzenetricarboxylic acid, mp 196–197°, anhydride mp 197°). Esterification of the triacid with 40 ml of 1,2-dichloroethane, 12 ml of methanol, and 1.4 ml of sulfuric acid produced a semisolid which produced on silica gel chromatography 157 mg of white solid, mp 100.5–101.5° (authentic trimethyl ester of the 1,2,3-triacid, mp 100.3–101.0°), mmp 100–101°. The R_f value of the ester on tlc was identical with authentic sample and different from authentic isomeric tri- and diesters.

Catalytic Hydrogenation of Tetracyclic Ester (XX). A stirred mixture of 15 mg of 10% Pd/C and 20 ml of absolute ethanol was saturated with 1 atm of hydrogen. A 5-ml solution of ethanol and 0.266 g (1 mmol) of ester XX was syringed into the above flask through a ground glass joint fitted on the end with a rubber serum cap. After 1.5 hr of stirring at 25°, 2.17 mmol (54.0 ml) of hydrogen was absorbed. The solution was filtered through Celite, and solvent was removed to yield 0.26 g of XXIII as a clear oil. Ester XXIII provided the following spectral data: ir 3003 (ArH), 2924 and 2857 (CH), 1712 (C=O), 1451 cm^{-1} (ArC=C); nmr τ 3.05 (m, 3, ArH), 6.38 (s, 3, CO_2CH_3), 7.17 (m, 4 H, benzylic CH_2), 8.20 ppm (m, 12, CH_2). Ester XXIII exhibited the mass spectral data shown in Table IV. Isotopic content calculated for $C_{18}H_{22}O_2$,

Table IV

Rel peak int	P	P + 1	P + 2	P + 1/P + 2
Calcd	1	0.19	0.022	8.75
Obsd	1	0.197	0.022	8.65

parent ion = *m/e* 270. *Anal.* Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 80.12; H, 8.33.

Bromoform Oxidation of 12-Acetyl[2.2]metaparacyclophane (XIV). This reaction was performed identically with the preparation of acid XVII *via* the bromoform reaction. The reactants were 1.50 g of XIV, 1.45 ml of bromine, 11.90 g of potassium hydroxide, 30 ml of water, and 25 ml of distilled dioxane passed through alumina. Crystallization of the crude oil gave 1.2 g (80%) of 12-carboxy[2.2]metaparacyclophane (XI), mp 163–163.5°. The nmr spectrum of XI exhibited signals at τ −1.93 (broad s, 1, CO_2H), 2.0 (s, 1, ArH), 2.70–3.35 (m, 3, ArH), 4.0 (narrow m, 2, ArH), 4.70 (s, 1, ArH), 5.67–5.97 and 6.70–8.00 ppm (m, 8, CH_2). *Anal.* Calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 81.02; H, 6.45.

Alkaline Permanganate Oxidation of 12-Carboxy[2.2]metaparacyclophane (XI). The same procedure used in the oxidation of XVII was used here. Chromatography of the crude esters produced only 50 mg of white needles (from 300 mg of 12-acid), mp 65–65.8°. Pure 1,3-benzenedicarboxylic acid melts at 65.5–66.2°, and the mixture melting point was 65.5–66.5°. Tlc gave the correct R_f value which was also different from other isomeric benzenedicarboxylic acid methyl esters.

12-Carbomethoxy[2.2]metaparacyclophane. An ethereal solution of diazomethane was added to a solution of acid XI until the yellow diazomethane color persisted. The ether was evaporated to give the 12-ester which was recrystallized from pentane to give crystals, mp 75–76.3°. Its nmr spectrum contained signals at τ 2.20 (s, 1, *p*-ArH), 2.80–3.38 (m, 3, *m*-ArH), 4.09 (m, 2, *p*-ArH), 4.75 (s, 1, *m*-ArH), 5.85–6.00 and 6.70–8.00 (m, 8, CH_2CH_2), 6.09 and 6.32 ppm (s, 3, CO_2CH_3, the latter value being the 16-isomer whose methyl peak integrated to be one-seventh of the 12-isomer). *Anal.* Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.39; H, 6.80.

12-Hydroxymethyl[2.2]metaparacyclophane. The reduction of acid XI was performed in ether with lithium aluminum hydride using the procedure used for the reduction of acid XVII. The product was an oil which was very slow to crystallize and did so only after standing several weeks. The solid was sublimed to give white solid, mp 88–90°. The alcohol possessed the following ultraviolet spectrum: λ_{max} sh 295 nm (ϵ 278), 285 (350), sh 277 (374), sh 245 (3300). The nmr spectrum was composed of two superimposed spectra, namely the 12- and 15-isomers in a ratio of 2.21:1.00, respectively. The following signals were present: **12-isomer**, τ 2.8–3.5 (m, 4, *p*-ArH), 2.90–3.45 (m, 3, *m*-ArH), 4.20 (s, 2, *p*-ArH), 4.73 (broad s, 1, *m*-ArH), 5.12 and 5.27 (AB quartet, 2, J = 12.5 Hz, CH_2OH), 6.5–8.1 (m, 8, CH_2CH_2), 8.27 ppm (s, 1, OH); **15-isomer**, τ 2.8–3.5 (m, 5, ArH), 4.00 (s, 2, *p*-ArH), 5.70 and 6.18 (AB quartet, 2, J = 12.5 Hz, CH_2OH), 6.5–8.1 (m, 8, CH_2CH_2), 8.27 ppm (s, 1, OH). *Anal.* Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.66; H, 7.67.

Bromination of [2.2]Metaparacyclophane (II) with Ferric Bromide Catalyst in Carbon Tetrachloride. To a mixture of 0.1 g of iron dust and 20 ml of carbon tetrachloride (dried over molecular sieves) was added one-tenth of a solution of bromine (0.28 ml, 5.3 mmol) in carbon tetrachloride (80 ml). The mixture was stirred for 2.5 hr, and then about 80 ml of carbon tetrachloride was added followed by 1.0 g (4.8 mmol) of II. The bulk of the bromine color disappeared quickly and the remaining bromine solution was added over 1 hr with stirring. The bromine color did not intensify, implying a rapid consumption of bromine. At this point an aliquot was removed from the reaction, worked up, and analyzed by glc. Approximately one-third of the starting material remained, and no products other than monobromides were seen. Additional bromine (0.09 ml) was added and the reaction continued for 0.5 hr. The reaction was extracted with aqueous sodium bisulfite, aqueous sodium bicarbonate, and saturated salt solution, dried ($MgSO_4$), and evaporated until free of solvent. The product was passed through 20 g of alumina with pentane eluent to give after evaporation an oil (1.1 g, 75%) which by glc analysis was found to be 1% II, 4–8% of compound(s) with retention time longer than the monobromides, the remainder being monobromides. Analysis by nmr showed this mixture to be roughly 60% 12-bromo[2.2]metaparacyclophane (IX) and 40% 4-isomer (X). The spectrum of the 15-isomer (VIII) could not be quantitatively separated from the spectrum of the 12-isomer. This mixture was converted to methyl[2.2]metaparacyclophanes (conversion of bromine to methyl) to give 49 ± 5% of the 12-isomer, 14 ± 1% of the 15-isomer, and 37 ± 5% of the 4-isomer of methyl[2.2]metaparacyclophanes (by nmr integration of methyl signals). Thus, about 63% of isomers having bromine on the para ring and 37% on the meta ring must have been formed in the bromination reaction.

The reaction mixture was chromatographed using preparative glc (20% silicone gum rubber, SE-30, on crushed firebrick, 6 ft × 0.75 in. i.d., 180°, 15 psi helium) to give 0.6 g of monobromides (monobromides did not ever separate on glc) which had the same nmr spectrum as before glc. Chromatography of this oil on silica gel with pentane did not give complete separation but forefractions were sufficiently enriched that they crystallized to give 0.1 g of IX as a white solid, mp 65.5–67.2°. The nmr spectrum of the compound gives two superimposed spectra since the 12- and 15-isomers equilibrate in solution at 25° (composition equals 90–83% 12-isomer and 10–17% 15-isomer by integrations). The spectrum showed these signals for the 12-bromide: τ 2.65 (s, 1, *p*-ArH), 3.18 (m, 3, *m*-ArH), 4.20 (m, 2, *p*-ArH), 4.52 (broad s, 1, *m*-ArH), 6.5–8.0 ppm (m, 8, CH_2CH_2). *Anal.* Calcd for $C_{16}H_{15}Br$: C, 66.94; H, 5.23. Found: C, 67.13; H, 5.06.

From the remaining 0.5 g of monobromides the 4-bromo[2.2]metaparacyclophane (X) was isolated by formation of a π acid–base complex. To 0.5 g of the monobromides dissolved in 1 ml of acetone, 0.63 g of 2,4,5,7-tetranitrofluorenone (TNF) dissolved in 8 ml of acetone was added. The solution changed from the yellow color of TNF to a dark yellow-orange. This solution was cooled to −78° at which point an orange precipitate formed. Characterization of this solid orange complex proved difficult because it appeared to be a mixture of TNF–cyclophane plus TNF crystals (complex mp 188–200°, pure TNF 250–253°). The orange precipitate was redissolved in acetone and then reprecipitated in the cold to purify the complex further. When the orange complex

was mixed with ether, the color changed back to yellow leaving a TNF precipitate. When the ethereal extracts were passed through alumina, a colorless, clear oil (0.12 g) was obtained which was characterized as 4-bromo[2.2]metaparacyclophane (X). The following nmr signals were exhibited by X: τ 2.88 (d, 1, J_{AB} = 8 Hz, $J_{AX} < 1$ Hz, H_A of ABX system of meta ring), 3.0 (broad s, 2, *p*-ArH), 3.52 (doublet of doublets, 1, J_{AB} = 8 Hz, J_{BX} = 2 Hz, H_B of meta ring), 4.02 and 4.17 (ab quartet, 2, J_{ab} = 8 Hz, *p*-ArH), 4.68 (d, 1, J_{BX} = 2 Hz, $J_{AX} < 1$ Hz, H_X of meta ring), 6.8–8.2 ppm (m, 8, CH_2CH_2). The mass spectrum of X at 70 eV gave *m/e* (rel intensity) 288 (28), 286 (28), 207 (100), 192 (20), 184 (47), 182 (49), 104 (29), 103 (62), 77 (36). *Anal.* Calcd for $C_{16}H_{15}Br$: C, 66.94; H, 5.23. Found: C, 67.12; H, 5.35.

Bromination of [2.2]Metaparacyclophane Using Iodine Catalyst in Dichloromethane. To a mixture of 300 mg (1.44 mmol) of II, 20 mg (0.08 mmol) of iodine crystals, and 40 ml of dichloromethane was added in one portion 0.17 ml (3.31 mmol) of bromine dissolved in 17 ml of dichloromethane. This reaction mixture was allowed to stir for 2.75 hr at 25° at which time an aliquot was removed and determined by glc to contain no starting material, 95% monobromides, and 5% dibromides. The reaction mixture was extracted with aqueous sodium bisulfite and aqueou ssodium bicarbonate, dried over anhydrous sodium carbonate, and chromatographed on 15 g of alumina with pentane to yield 423 mg of clear oil (97% crude yield). Conversion of the bromine to a methyl group in these monobromides (previously described) gave a mixture of 5% II, 87% methyl[2.2]metaparacyclophanes, and 8% dimethyl derivatives. Nmr spectra before and after preparative glc gave the following isomer distribution for the methyl[2.2]metaparacyclophanes: 85 ± 1% 4-isomer and 15% 12- plus 15-isomers. Purification of the bromides *via* a tetranitrofluorenone complex, as in the iron-catalyzed bromination above, gave a sample of the 4-bromo[2.2]metaparacyclophane (X), an oil, which was pure by nmr analysis.

Bromination of [2.2]Metaparacyclophane (II) Using Iodine Catalyst and Carbon Tetrachloride Solvent. This reaction was performed identically with the ferric bromide catalyst reaction in carbon tetrachloride by changing the catalyst to iodine. However, in this case the reaction was very slow and a manyfold excess of bromine was needed to achieve a 70% yield in 10 hr at 25°. Approximately 7% dibromides were formed and the composition of the monobromides was determined by nmr to be the same as in the ferric bromide–carbon tetrachloride reaction.

Bromination of [2.2]Metaparacyclophane (II) in *n*-Hexane in the Dark Using Ferric Bromide Catalyst. After finding that bromine would not react (uncatalyzed) with II in *n*-hexane in the dark, ferric bromide was prepared *in situ*, and the reaction was allowed to proceed to 90–95% completion in 45 min at 25° with little or no dibromide formation. The nmr spectrum showed the composition of the monobromides to be the same as in the ferric bromide–carbon tetrachloride reaction.

12-Methyl[2.2]metaparacyclophane (VI). Into a dry flask under a positive pressure of nitrogen was syringed 25 ml of ether and 0.84 ml (1.26 mmol) of *n*-butyllithium in hexane. After a brief period of reflux (to ensure a dry flask) the contents were cooled and 12-bromo[2.2]metaparacyclophane (120 mg, 0.42 mmol) was added directly in one portion. After stirring at 25° for 30 min (pale yellow color developed) the solution was again cooled and the dimethyl sulfate (0.30 cc, 3.00 mmol) was added by syringe. Immediately the yellow color disappeared and a white precipitate appeared. After stirring the reaction mixture for 15 min, 3 ml of water and 0.5 ml of concentrated aqueous ammonia were added to destroy the excess methylating agent. The ethereal solution was washed with water and dried, and the solution evaporated. The reaction mixture was crystallized from methanol and sublimed to give 43 mg of 12-methyl[2.2]metaparacyclophane (VI), mp 44–45°. The nmr spectrum gave the following signals. In solution this compound is an equilibrium mixture of two isomers, 3.3:1.0 for the 12-:15-isomers. Since the 15-isomer is not present in large amounts, integrations were carried out only for the 12-isomer: τ 2.83–3.40 (m, 4, ArH), 4.15–4.35 (m, 2, *p*-ArH), 4.72 (m, 1, *m*-ArH), 6.60 (m, 8, CH_2CH_2), 7.60 (s, 3, CH_3 for 12-isomer), and 8.32 ppm (15-isomer methyl singlet). *Anal.* Calcd for $C_{17}H_{18}$: C, 91.84; H, 8.16. Found: C, 91.74; H, 8.24.

Preparation of 4-Methyl[2.2]metaparacyclophane (VII). This preparation was carried out identically with the preparation of 12-methyl[2.2]metaparacyclophane *via* the 12-bromide. In this case the following reagents were used: 0.40 g (1.39 mmol) of 4-bromo[2.2]metaparacyclophane, 1.95 ml (2.78 mmol) of *n*-butyllithium (1.5 *M* in hexane), 0.55 ml (5.56 mmol) of dimethyl sulfate, and 50 ml of anhydrous ether. The time of formation of the lithio derivative was 1 hr at 25° and the methylation time was 2 hr at 25°. The reaction product (284 mg) contained 7% II, 91% VII, and 2% dimethyl derivatives by analytical glc. Preparative glc on a 20% silicone gum rubber, SE-30, on firebrick column (6 ft × 0.75 in. i.d.) at 180° gave II at 30–36 min, the 4-methyl derivative at 38–52 min, and the dimethyl derivatives at 70–80 min. The 4-methyl[2.2]metaparacyclophane appeared pure (free of other isomers) by nmr and gave the following signals: τ 2.92 (d, 2, $J \sim 2$ Hz, *p*-ArH), 3.30 (d, 1, J_{AB} = 8 Hz, H_A of ABX system of *m*-ArH), 3.43 (doublet of doublets, 1, J_{AB} = 8 Hz, J_{BX} = 1.6 Hz, H_B of *m*-ArH), 4.23 (d, 2, $J \sim 2$ Hz, *p*-ArH), 4.75 (d, 1, $J_{XB} = J_{BX}$ = 1.6 Hz, H_X of *m*-ArH), 6.8–8.3 (m, CH_2CH_2), 7.80 ppm (s, 3, CH_3). The mass spectrum at 70 eV *m/e* (rel int) 222 (45), 207 (30), 118 (100), 117 (26), 115 (12), 103 (14), 91 (14). *Anal.* Calcd for $C_{17}H_{18}$: C, 91.84; H, 8.16. Found: C, 91.74; H, 8.24.

Preparation of 4-Carboxy[2.2]metaparacyclophane (XII) from Iodine-Catalyzed Bromination Products. To a dry flask under a positive pressure of dry nitrogen was added 40 ml of ether, 3.4 ml (5.1 mmol) of 1.5 *M* *n*-butyllithium in hexane, and 0.500 g (1.74 mmol) of monobromo[2.2]metaparacyclophanes. The monobromides had the composition of 85% 4-bromide (X) and 15% of isomers with bromine on the para ring (VIII and IX). The reaction mixture was allowed to stir for 1 hr at 25°. At this point the ethereal solution of the lithio derivative was poured directly onto freshly sublimed carbon dioxide (50 g) and allowed to stir until all Dry Ice had disappeared. Pentane was added to the milky ethereal solution containing a precipitate, and this mixture was extracted three times with 30-ml portions of the following basic solution: 10% sodium hydroxide, 40% methanol, and 50% water. The basic extracts were extracted with ether and acidified with 6 *N* hydrochloric acid to give a milky precipitate which coagulated overnight to form solid particles. The solid material was filtered and pumped to dryness to yield 320 mg of solid (73%). The solid was recrystallized from ether–pentane twice to give 100 mg of white solid (XII), mp 192–193°. The nmr spectrum showed the typical ABX spectrum for the meta ring reminiscent of the 4-bromide (X). The signals were τ −0.38 (broad s, 1, CO_2H), 2.22 (d, 1, J_{AB} = 8 Hz, *m*-ArH), 2.78 (d, 2, $J \sim 1.5$ Hz, *p*-ArH), 3.17 (doublet of doublets, 1, J_{AB} = 8 Hz, $J_{BX} \sim 2$ Hz, *m*-ArH), 4.10 (d, 2, $J \sim 1.5$ Hz, *p*-ArH), 4.45 (d, 1, $J_{BX} \sim 2$ Hz, *m*-ArH), 6.1–8.2 ppm (m, 8, CH_2CH_2). *Anal.* Calcd for $C_{17}H_{18}O_2$: C, 91.84; H, 8.16. Found: C, 91.74; H, 8.24.

Preparation of 12-Carboxy[2.2]metaparacyclophane (XI) from Iron-Catalyzed Bromination Products. The procedure used here is identical with the preceding procedure (for the 4-acid, XII). The bromides used here were composed of 37% 4-isomer and 63% isomers with bromine on the para ring (VIII and IX). When 1.6 g of bromides was converted to acids, a 92% crude yield of acids was obtained. Recrystallization of this material from ether–pentane gave 400 mg of XI, mp 160–161.5°. This acid was identical by nmr with the acid obtained in the bromoform reaction of 12-acetyl[2.2]metaparacyclophane (XIV). The mother residue was a mixture of XI and XII by nmr.

Decarboxylation of 4-Carboxy[2.2]metaparacyclophane (XII). In a 5-ml flask equipped with a condenser, 60 mg of acid XII, 30 mg of copper powder, 30 mg of basic copper carbonate,[30] and 1.5 ml of quinoline (bp 237°) were heated to reflux in a 260° Wood's metal bath for 0.75 hr. The mixture was cooled, ether was added, and the solution was extracted with 20% aqueous potassium hydroxide solution. Acidification of the hydroxide extracts gave no acid precipitate. The ethereal layer was washed six times with 6 *N* hydrochloric acid, once with water, and once with saturated sodium chloride solution and evaporated to dryness. An oily yellow solid remained which was passed through 1 g of alumina with pentane and then sublimed three times to yield 26 mg of white solid, mp 79.2–80.8° (actual mp 81.2–81.7°). The nmr spectrum was identical with that of II, and no extraneous peaks were present.

Decarboxylation of 12-Carboxy[2.2]metaparacyclophane (XI). A mixture of 60 mg of 12-acid, 30 mg of copper powder, 30 mg of basic copper carbonate,[31] and 2 ml of quinoline was refluxed in a 258° Wood's metal bath for 1.25 hr. The mixture was cooled, ether was added, and the mixture was extracted with 15% potassium hydroxide (acidification gave no starting material). The ethereal layer was extracted several times with 6 *N* hydrochloric acid which removed nearly all discolored material. The mixture was washed

(30) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Wiley, New York, N. Y., 1968, p 163.

with sodium bicarbonate solution and dried (Na_2SO_4), and the solvent was removed to give an oily solid which had some odor of quinoline. Sublimation at 80° (10 μ) gave II, mp 81.5–83°. The nmr spectrum was identical with that of authentic sample and no peaks were present below τ 2.8, showing no quinoline or other aromatic impurities.

Bromination of [2.2]Metaparacyclophane (II) with Molecular Bromine in Nitromethane. In a dry flask 350 mg (1.7 mmol) of II was dissolved in 40 ml of nitromethane (spectral grade over molecular sieves). A 1-ml sample of 1 ml of bromine diluted to 10 ml (or 0.1 ml of neat bromine or 1.95 mmol) in nitromethane was added to the above flask, and the mixture was stirred for 3 hr, at which point glc analysis of an aliquot showed 75% of the starting material remained. More bromine, 0.8 ml of the above nitromethane solution, was added and glc analysis showed after 5 hr that 34% of the starting material remained and 65% of the mixture was monobromides (assuming everything was being detected by the instrument). At this point 0.4 equiv of the bromine solution was added and 3 hr later only 10% of the starting material remained. After a total of 8.5 hr of stirring with a total of 2.5 equiv of bromine, a solution of sodium bisulfite was added to the reaction followed by enough ether to make the organic layer float. The organic layer was then extracted with 2 *N* potassium hydroxide (heat evolution) until no more nitromethane was present. The nitromethane was also successfully evaporated under reduced pressure. The ether solution was washed with bicarbonate and chromatographed on silica gel (45 g) beginning with pentane eluent. Of the 75-ml fractions, fractions 3–9 produced an oil, 253 mg (52%), which was predominantly monobromides and a little starting material. An nmr spectrum showed these bromides to be nearly entirely 4-bromo-[2.2]metaparacyclophane (X). Conversion of the bromides to methyl derivatives produced a mixture of 92% 4-methyl[2.2]metaparacyclophane (VII) and 8% of the isomers with methyl on the para ring (V and VI).

At fraction 11 the eluent was changed to 2% ether–pentane and fractions 17–20 afforded 190 mg (22%) of a white crystalline tetrabromide (XIII), mp 174.5–176°. The mass spectrum of XIII gave a parent peak of *m/e* 526, in agreement with a molecular formula of $C_{16}H_{14}Br_4$. The ultraviolet spectrum in ethanol showed only a steady increase in absorption from 300 to 210 nm with the only detail being the following shoulders: sh 277 nm (ε 865), sh 270 (1350), sh 250 (5040), sh 220 (16,800). A 100-MHz proton nmr spectrum exhibited the following signals: τ 3.03 (m, 3, aromatic), 4.12 (s with fine splitting, 1), 4.39 (doublet, 1, J = 2 Hz, some overlap with next signal), 4.45 (d, 1, J = 2 Hz), 5.35 (t, 1, J = 8 Hz), 5.93 (broad s, 1), 6.5–6.9 (m, 3), 6.96 (doublet of doublets, 1, J = 8 Hz, $J \sim$ 8.5 Hz), 7.45 (doublet of doublets, 1, J = 8 Hz, $J \sim$ 8.5 Hz), 8.90 ppm (doublet of doublets, 1, J = 16 Hz, J = 11 Hz). *Anal.* Calcd for $C_{16}H_{14}Br_4$: C, 36.54; H, 2.68. Found: C, 36.59; H, 2.74.

The following qualitative tests were performed. When the tetrabromide was dissolved in acetone and mixed with sodium iodide in acetone, iodine was liberated. Treatment of the tetrabromide with ethanolic silver nitrate gave a precipitate. Treatment of the tetrabromide with bromine in carbon tetrachloride did not decolorize the bromine solution. Attempted dehydrobromination in a *tert*-butyl alcohol solution of potassium *tert*-butoxide gave a rapid formation of a black amorphous precipitate.

Catalytic Hydrogenation of $C_{16}H_{14}Br_4$ (XIII). Exactly 250 mg of XIII, 40 mg of palladium on charcoal (10%), and 20 ml of ethanol were added to a hydrogenator flask and stirred magnetically under 1 atm of hydrogen. Within 1 hr 44 ml of hydrogen was absorbed. At this point the flask was opened and 250 mg of potassium hydroxide was added.[31] It was found experimentally that the addition of hydroxide causes the small amount of side products to go on to the major product. The hydrogenation was continued for 3 hr and *ca.* 9 ml of additional hydrogen was absorbed. The solution was filtered through Celite and analyzed by glc and tlc. Glc showed one peak and tlc showed one fast-moving spot and none of the two slower moving side products obtained when hydroxide was omitted. After a filtration chromatograph of the reaction mixture on silica gel and sublimation of the product at 70° (35μ), 100 mg (95%) of a white crystalline compound, XXVIII, was obtained, mp 62–64°. The spectral characteristics of XXVIII were uv λ_{max} 269 nm (ε 167), 262 (228), sh 255 (180), minimum 240 (73), sh 220 (6970); nmr τ 3.12 (m, 3, ArH), 6.5–9.3 ppm (m, 17, aliphatic). *Anal.* Calcd for $C_{16}H_{20}$: C, 90.50; H, 9.50. Found: C, 90.53; H, 9.51.

(31) R. L. Augustine, "Catalytic Hydrogenation," Marcel Dekker, New York, N. Y., 1965, Chapter 6.

Permanganate Degradation of $C_{16}H_{14}Br_4$ (XIII). A slurry of the tetrabromide was made by dissolving 0.7 g (1.33 mmol) of XIII in 6 ml of hot pyridine followed by the addition of 20 ml of water. A potassium permanganate solution (9.0 g, 57 mmol, in 40 ml of hot water) was then added over 1 hr by pipet to the aqueous slurry maintained at reflux. After 3 more hr at reflux the reaction was cooled and a bisulfite solution was added. The manganese dioxide was filtered by means of a glass frit, and the cake was extracted with dilute potassium hydroxide. This extract was added to the filtrate and the entire aqueous layer was extracted with three 40-ml portions of ether. The aqueous layer was acidified with sulfuric acid and extracted with ether in a lighter than water continuous extractor for 2 days. A solid was obtained which was esterified in refluxing methanol with a trace of sulfuric acid for 3 days. At this point 5 g of anhydrous sodium carbonate and 40 ml of ether were added to the esterification mixture followed by filtration. The filtrate, when compared by glc to the pure methyl esters of the benzenedicarboxylic and benzenetricarboxylic acids, showed only 1,2,3-benzenetricarboxylic acid trimethyl ester. Chromatography of the ester on 7 g of silica gel with 35% ether–pentane gave 89 mg of fluffy white solid, mp 91–97°. Tlc showed a contaminant (slower moving) but glc did not. Recrystallization of this material from cold ether gave 43 mg (15%) of ester, mp 100.0–100.6° (authentic mp 100.3–101.0°). This ester was identical with the 1,2,3-trimethyl ester by mixture melting point and by tlc and glc comparisons with authentic samples.

Tetracyclic Ketone (XIX) *via* Hydrogenation. Into a hydrogenator flask was placed 1.51 g (5.7 mmol) of XVI, 40 ml of ethanol, and 150 mg of palladium on charcoal (10%). While stirred under 1 atm of hydrogen *ca.* 300 ml of hydrogen uptake occurred (11.4 mmol of hydrogen would correspond to 280 ml). The reaction was filtered, and the solvent was removed to give an oil which crystallized (1.57 g, mp 80–83.5°). Tlc showed only one spot which was faster moving than starting material. Recrystallization from ether–pentane gave XIX, mp 83.5–85.0°. *Anal.* Calcd for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 84.92; H, 8.51.

Tetracyclic Acid XXII. The necessary hypobromite solution was prepared as follows. A solution of 8.24 g (150 mmol) of potassium hydroxide in 20 ml of water was cooled to 0° and 1.24 ml (24.2 mmol) of bromine was added all at once with stirring. A solution of 1.3 g (4.8 mmol) of XVI in freshly purified *p*-dioxane was then added in one portion to the hypobromite solution. The purification of the dioxane was achieved by passing 50 ml of dioxane from a freshly opened bottle through 40 ml of Activity 1 alumina and using the first 20 ml that came through. After the addition, the cooling bath was removed and the reaction was stirred for 2.25 hr at 25°. A bisulfite solution was added followed with enough water to dissolve the salts. The reaction was extracted with three 30-ml portions of ether and the aqueous layer was acidified with 12 *M* hydrochloric acid. A precipitate formed which was filtered, washed with water, and dried to give 1.0 g (78%) of white solid, mp 192.5–193.5°. Crystallization from ether gave XXII, mp 193–195°. *Anal.* Calcd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 79.55; H, 7.96.

Tetracyclic Hydroxymethylene Compound XXV. A reaction mixture composed of 200 ml of ether, 1.0 g (26 mmol) of lithium aluminum hydride, and 800 mg (3.12 mmol) of XXII was stirred for 24 hr and then treated with enough saturated potassium carbonate to destroy the excess hydride. The ethereal solution was filtered, dried ($MgSO_4$), and evaporated to yield 747 mg of oil. The oil had traces of an impurity (tlc) and was distilled to give an analytical sample. *Anal.* Calcd for $C_{17}H_{22}O$: C, 84.25; H, 9.15. Found: C, 84.08; H, 9.22.

Tetracyclic Aldehyde XXVI. To 60 ml of pyridine cooled to 10°, 1.26 g (12.6 mmol) of chromium trioxide was added with stirring in 15 min in five portions (caution, fire hazard). Alcohol XXV (600 mg, 2.48 mmol) was dissolved in 10 ml of pyridine and pipetted into the 20° chromium trioxide–pyridine complex solution. A hot air gun was used to heat the mixture to 60–65° over a 4-min period and then the heating was stopped. The reaction was stirred for an additional 1.5 min and then dumped onto ice water. The mixture was then extracted with three 100-ml portions of 6 *N* hydrochloric acid, water, 1 *N* potassium hydroxide (acidification of this extract gave only traces of acid), and bicarbonate solution, dried ($MgSO_4$), and freed of solvent. The crude product was an oil and contained two impurities by tlc (slower moving). The product was chromatographed on silica gel and gave 452 mg (76%) of aldehyde XXVI (mp 69.8–71°) using 4% ether–pentane eluent. *Anal.* Calcd for $C_{17}H_{20}O$: C, 84.95; H, 8.39. Found: C, 84.85; H, 8.37.

Tetracyclic Hydrocarbon XXVII. Xylene, 20 ml, was first deaerated by bubbling through nitrogen and then 120 mg (0.5 mmol) of aldehyde XXVI and 486 mg (0.5 mmol) of tristriphenylphosphinerhodium(I) chloride were added. The mixture was refluxed under nitrogen for 29 hr. The xylene was then evaporated under reduced pressure and the mixture was chromatographed on 12 g of silica gel in pentane. After 100 ml of pentane, 62 mg of XXVII, an oil, was eluted. Glc analysis showed the hydrocarbon XXVII to have a shorter retention time than the hydrogenated tetrabromide product XXVIII. The uv and nmr spectra of XXVII were also different but similar to XXVIII. The spectral data of XXVII were nmr τ 2.97 (m, 3, ArH), 7.18 (m, 4, aliphatic), and 8.18 ppm (m, 13, aliphatic); uv λ_{max} 274.5 nm (ϵ 455), sh 270 (390), 266 (490), sh 260 (362), minimum 236 (56), sh 220 (10,200). *Anal.* Calcd for $C_{16}H_{20}$: C, 90.50; H, 9.50. Found: C, 90.64; H, 9.57.

Tetracyclic Hydroxymethylene Compound XVIII. Lithium aluminum hydride, 0.8 g (20 mmol), was added slowly to a solution of 1.5 g (6 mmol) of XVII in 200 ml of ether. The reaction was stirred overnight with a drying tube on the flask. Excess hydride was destroyed with saturated sodium carbonate solution. The solution was filtered and washed successively with dilute potassium hydroxide solution, sodium bicarbonate solution, and saturated sodium chloride solution. The ethereal solution of the alcohol was adsorbed onto silica gel and chromatographed. Elution with 20% ether–pentane produced 1.17 g of a thick oil of XVIII, with the following spectral properties: uv λ_{max} 278 nm (ϵ 496), 270 (563), sh 265 (458), sh 230 (4770); nmr τ 3.07 (m, 3, ArH), 3.88 and 4.13 (AB quartet, 4, J = 9.0 Hz), 6.47 (s, 2, CH_2OH), 7.03 (m, 4, CH_2CH_2), 7.70 (s, 1, OH), 7.87 (m, 2, CH_2), 8.32 ppm (m, 2, CH_2). *Anal.* Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.78; H, 7.40.

Formation of the 3,5-dinitrobenzoate ester of XVIII using 3,5-dinitrobenzoyl chloride in pyridine produced an orange solid, mp 157.5–159°. *Anal.* Calcd. for $C_{24}H_{20}N_2O_6$: C, 66.65; H, 4.66. Found: C, 66.69; H, 4.89.

Macro Rings. XLII. Ring Rotation in [2.2]Metaparacyclophane[1,2]

Daniel T. Hefelfinger and Donald J. Cram*

Contribution No. 2739 from the Department of Chemistry, University of California at Los Angeles, Los Angeles, California 90024.
Received November 12, 1970

Abstract: With nmr and stereochemical techniques the ring rotation of [2.2]metaparacyclophane (I) and its derivatives have been studied. Crystallization of monosubstituted derivatives of I with the substituent in the para ring provides only the 12-isomer (substituent anti to the meta ring). When dissolved at −50° in deuteriochloroform, only the nmr spectra of the 12-isomers were visible. When warmed to 37°, the spectra became those of a mixture of the 12- and 15-isomers (substituent syn to the meta ring) by rotation of either the meta or para ring (or both). At 37°, K_{equil} = (15-isomer)/(12-isomer) were measured for para ring derivatives: CO_2CH_3, K = 0.14; $COCH_3$, K = 0.26; CH_3, K = 0.31; CH_2OH, K = 0.45; CHO, K = 0.48; H, K = 1. For CHO as substituent, k_1 and k_{-1} at −13.5° were determined for 12-isomer ⇄ 15-isomer (τ −0.32 for 12-isomer and 0.52 for 15-isomer), and were $k_1 = 1.72 \times 10^{-4}$ sec^{-1} and $k_{-1} = 3.83 \times 10^{-4}$ sec^{-1}. The same rate constants were also determined at the coalescence temperature (T_c = 140°) of the aldehyde proton: k_1 = 85 sec^{-1}, k_{-1} = 175 sec^{-1} ($K_{140°}$ = 0.48). The activation parameters were calculated from these rate constants: $\Delta H^{\ddagger}$ 17.7 ± 0.3 kcal mol^{-1}, $\Delta G_{140°}{}^{\ddagger}$ = 20.8 ± 0.4 kcal mol^{-1}, $\Delta S_{140°}{}^{\ddagger}$ = −7.8 ± 2.2 eu from k_1's; $\Delta H^{\ddagger}$ = 17.6 ± 0.3 kcal mol^{-1}, $\Delta G_{140°}{}^{\ddagger}$ = 20.2 ± 0.4 kcal mol^{-1}, $\Delta S^{\ddagger}$ = −6.1 ± 2.4 eu from k_{-1}'s. The parent hydrocarbon's nmr spectrum in hexachlorobutadiene also was temperature dependent. Protons at C-12 (C-13) and C-15 (C-16) coalesced at 146°. When heated to *ca.* 185° these protons formed a sharp singlet, and the aliphatic protons went from a complex multiplet to an AA'BB' pattern. With $\Delta\nu$ = 75 Hz, at 146° k = 167 sec^{-1} and $\Delta G_{146°}{}^{\ddagger}$ = 20.6 ± 0.3 kcal mol^{-1}. To determine whether only one or both rings rotated, 12-carbomethoxy[2.2]metaparacyclophane was prepared optically pure. When heated to 200° and recovered, optically pure material retained its optical purity. Clearly only one ring rotated, undoubtedly the meta ring. *Had both rings rotated racemic* material *would have resulted.*

In the previous paper,[3] it was reported that pure crystalline derivatives of [2.2]metaparacyclophane (I)[4] could be prepared with substituents in the 12 position (II). When dissolved at room temperature, these substances exhibited nmr spectra that indicated isomers II had equilibrated by ring rotation with isomers III. The system offered the unusual advantage for study of ring rotation phenomena in which one of the two components of an equilibrating mixture could be isolated, and its rate of equilibration measured. The system also poses the interesting and answerable questions of whether just one (which one) or both of the benzene rings of the [2.2]metaparacyclophane rotate with respect to one another. We therefore undertook to study the rates and equilibria involving II and III, as well as the ring inversion of the parent hydrocarbon (I). This system possesses the advantages that the chemical shifts of the different protons of I, II, and III show considerable sensitivity to their positions in the molecule, and ring rotation is easily followed. After our work was completed,[2] reports of two other studies of ring rotation of hydrocarbon I appeared.[5]

(1) The authors thank the National Science Foundation for a grant used in support of this research. D. T. Hefelfinger also thanks the National Science Foundation for a Traineeship, 1965–1969. The authors warmly acknowledge Professor F. A. L. Anet's suggestions concerning the nmr spectral parts of the work.

(2) A preliminary account of this work has appeared: D. T. Hefelfinger and D. J. Cram, *J. Amer. Chem. Soc.*, **92**, 1073 (1970).

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

(4) D. J. Cram, R. C. Helgeson, D. Lock, and L. A. Singer, *ibid.*, **88**, 1324 (1966).

(5) (a) F. Vögtle, *Chem. Ber.*, **102**, 3077 (1969); (b) S. Akabori, S. Hayashi, M. Nawa, and K. Shiomi, *Tetrahedron Lett.*, 3727 (1969).