[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Macro Rings. XIV. Substitution Studies in the [4.4]Paracyclophane System

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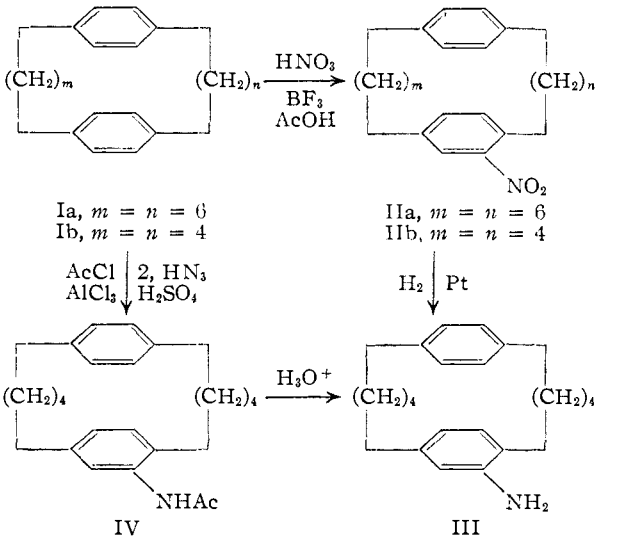
Nitration and acylation of [4.4]paracyclophane (Ib) leads to compounds, which by suitable reactions were converted to a number of substances containing unusual structural features. A two-membered methylene bridge connecting the two phenyls of [4.4]paracyclophane was constructed. In a second substance, one of the two benzene rings was converted to a quinone. A third compound was prepared in which one of the benzene rings was converted into a naphthalene nucleus. Evidence is presented suggesting that the two rings of [4.4]paracyclophane can rotate with respect to one another at ordinary temperatures. The absence of inter-ring directive influences in the acetylation of acetyl[4.4]paracyclophane was demonstrated.

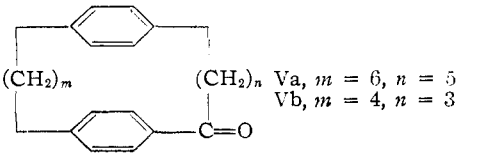
Previous papers of this series have described the preparation of a number of paracyclophanes,[2] recorded their spectral properties,[2d] and described a number of exploratory reactions which these cycles undergo.[3] These investigations have involved an assessment of the variation of inter-ring electronic and steric effects as the lengths of the methylene bridges have been systematically varied. The present paper deals with the chemistry of [4.4]-paracyclophane, in which the aromatic rings are far enough apart to allow them to act as isolated chromophores,[2d] but close enough together so that they do not behave as independent reaction sites in electrophilic substitution[3b] and catalytic reduction reactions.[3b]

Intramolecular, Molecular Complexes.—The unique structures of the paracyclophanes provide an opportunity to build compounds that might possess the characteristics of intramolecular, molecular complexes. The possibility exists that should the two aromatic rings become sufficiently dissimilar in an electronic sense because of the character of appropriately located substituents, attractive forces might draw the two rings together and the spectral properties be modified accordingly. The strong electron-withdrawing properties of the nitro and quinone groups made their incorporation into paracyclophanes desirable in connection with the possible construction of such systems.

With solutions of nitric acid and boron trifluoride in acetic acid,[4] both [4.4]- and [6.6]paracyclophane (Ia and Ib) gave mononitro derivatives in 2 and 15% yields, respectively. The structure of IIb was demonstrated by its conversion to amine III, which previously had been prepared by the route Ib → IV → III. Nitro compound IIa was prepared previously in an impure state by nitration of Ia in which one ring was fully reduced, the mononitro product being fully aromatized in a subsequent step.[3a] Accompanying the mononitro compounds in the nitration mixtures were 12 and 41% yields of ketones Va and Vb, respectively. That the carbonyl group in these compounds is conjugated with the aromatic ring is demonstrated by the position of the carbonyl bands in their infrared

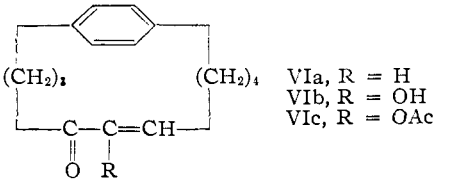


spectra (1670 cm.$^{-1}$), and by their ultraviolet absorption spectra. The ultraviolet spectrum of nitro compound IIa proved to be normal and that



of IIb somewhat abnormal. These spectra will be discussed in a future paper.

Benzoquinone is a good dienophile and Andrews and Keefer[5] have observed abnormalities in the ultraviolet absorption spectra of dienophiles in benzene. Compounds VIa, b and c all possess abnormal spectra,[6] facts which were attributed to molecular complexing. Thus compound IX might be expected to possess unusual spectral properties.



The substance was prepared as indicated in the formulations. The conversion of amine III to phenol VIII gave miserable yields of impure product identi-

(1) National Science Foundation Predoctoral Fellowship, 1954-1956.

(2) (a) D. J. Cram and H. Steinberg, THIS JOURNAL, **73**, 5691 (1951); (b) D. J. Cram and N. L. Allinger, *ibid.*, **76**, 726, 2362 (1954); (c) J. Abell and D. J. Cram, *ibid.*, **76**, 4406 (1954); (d) D. J. Cram, N. L. Allinger and H. Steinberg, *ibid.*, **76**, 6132 (1954).

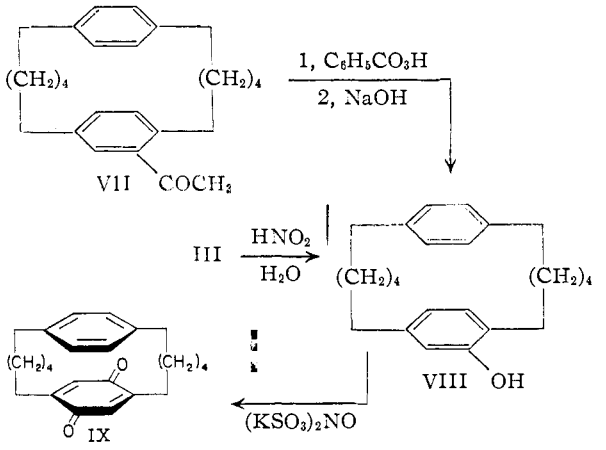
(3) (a) D. J. Cram and J. Abell, *ibid.*, **77**, 1179 (1955); (b) D. J. Cram and R. W. Kierstead, *ibid.*, **77**, 1186 (1955); (c) D. J. Cram and N. L. Allinger, *ibid.*, **77**, 6289 (1955).

(4) L. Sihlbohm, *Acta Chem. Scand.*, **5**, 1210 (1951).

(5) L. J. Andrews and R. M. Keefer, THIS JOURNAL, **75**, 3776 (1953).

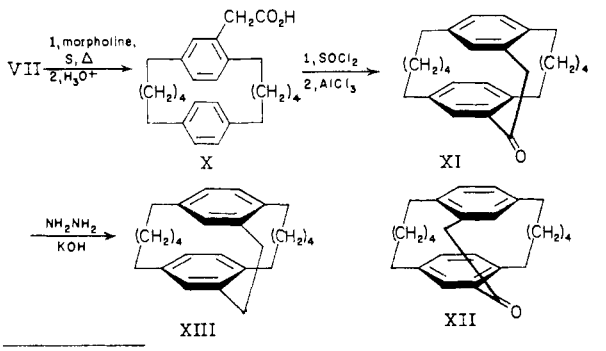
(6) (a) D. J. Cram and H. U. Daeniker, *ibid.*, **76**, 2743 (1954); (b) D. J. Cram and M. Cordon, *ibid.*, **77**, 4090 (1955).

fied by its ultraviolet absorption spectrum in acid and base. The alternate route utilizing VII[3b] and the Baeyer–Villiger reaction gave VIII (8%), which was converted to quinone IX by the elegant method of Teuber.[7] The ultraviolet spectrum of phenol VIII will be reported in a future paper. Figure 1 compares the spectrum of quinone IX and that of



2,5-dimethylbenzoquinone. A shift to longer wave lengths of the strongly absorbing band in the 265–274 mμ region is evident in the spectrum of IX, but the effect is not dramatic. The shoulder found in the spectrum of the model in the region of 290 mμ (log ε 2.4) has become a maximum (λ_{max} 288 mμ, log ε 3.11) in cycle IX. Unfortunately, not enough material was available to take the low intensity visible spectrum of IX. The above data, however, provide evidence for a weak inter-ring electronic interaction in the quinoidal paracyclophane. In all other paracyclophane systems, spectra have been found to be normal when the two chromophores could get over 3.4 Å. apart without any strain.[2d,6b,8]

Construction of Addition Bridges in [4.4]Paracyclophane.—The interesting problem arises in the paracyclophanes with regard to the direction that Friedel–Crafts acylation reactions might take with cycles carrying $-(CH_2)_nCOCl$ chains as starting material. Two such compounds (X and XV) were prepared utilizing conventional reactions. Compound X when submitted to the action of thionyl chloride and then aluminum chloride gave cyclic ketone (28% yield) whose structure is probably XI.[9] The alternative structure (XII) is improbable on steric grounds, but cannot be entirely ruled out. The spectral properties of the pseudo-conjugated ketone XI will be recorded and discussed in a future paper. The polycyclic hydrocarbon XIII was prepared by the reduction of XI. The ultraviolet spectrum of this substance along with that of the parent [4.4]paracyclophane and of [2.4]paracyclophane[2a] are recorded in Fig. 2. The abnormalities of the spectrum of this latter compound, attributed to the proximity of the π-orbitals of each benzene ring,[2d] are also found in XIII.



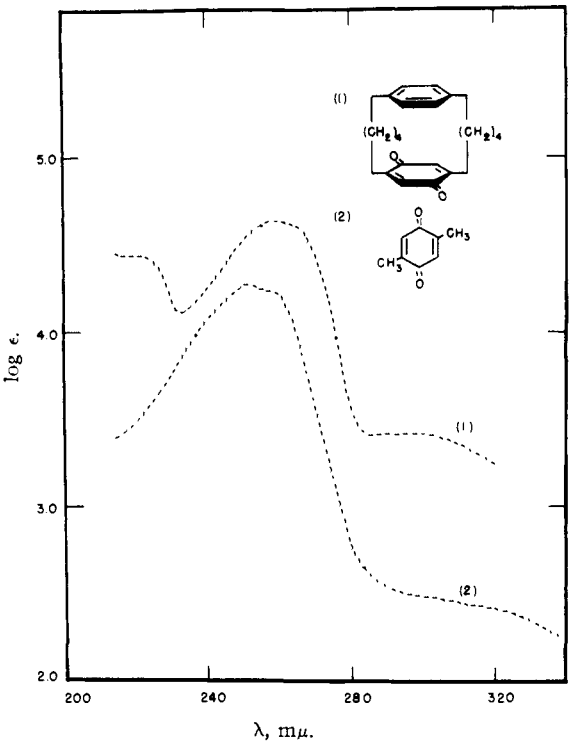


Fig. 1.—Ultraviolet absorption spectra in 95% ethanol, Cary spectrophotometer, model 11 MPS. Curve 1 is displaced upward by 0.5 unit.

The ring closure of [4.4]paracyclophane carrying a four-carbon chain (XV) assumed a different steric course. When treated with polyphosphoric acid, XV gave ketone XVI (24% yield), which indicated that electrophilic substitution had occurred in the ring carrying the side chain rather than the second benzene ring. The structure of XVI was demonstrated through its conversion to the fully aromatic compound carrying a naphthalene nucleus (XVIII). Figure 3 compares the ultraviolet absorption spectrum of XVIII with that of an equimolar mixture of *p*-xylene and 1,4-dimethylnaphthalene. The two curves are similar but not identical.

Attempted Resolution of a Substituted [4.4]-Paracyclophane.—Evidence will be presented in a later section of this paper that the two rings in [4.4]paracyclophane can turn over with respect to one another at ordinary temperatures. It seemed of interest to determine if the blocking ability of an ethyl and a carboxyl *para* to one another on one of the rings of the cycle would permit resolution of the system into optical antipodes. Compound XXI was prepared as indicated in the formulations.

(7) H. J. Teuber and W. Rau, *Ber.*, **86**, 1036 (1953).
(8) D. J. Cram and N. L. Allinger, THIS JOURNAL, **78**, 2518 (1956).
(9) The authors are indebted to Dr. R. W. Kierstead who first prepared X and XI.

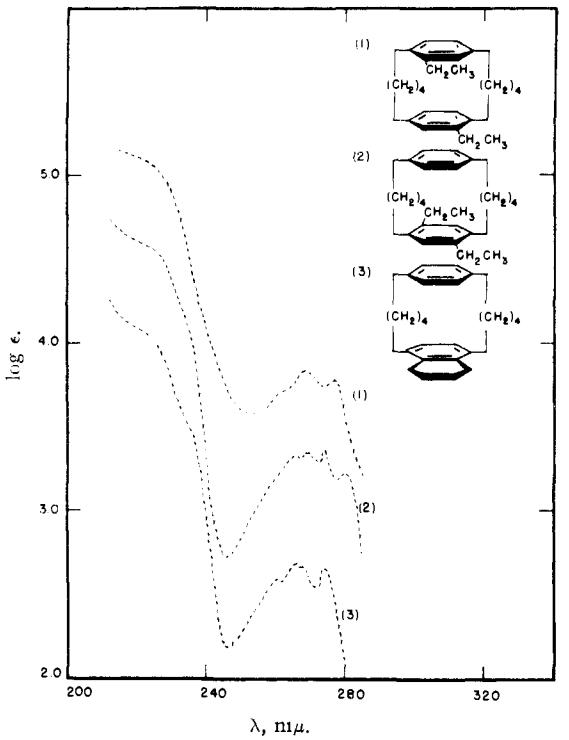


Fig. 2.—Ultraviolet absorption spectra in 95% ethanol, Cary spectrophotometer, model 11 MPS. Curves 2 and 1 are displaced upward by 0.5 unit from the curve immediately below.

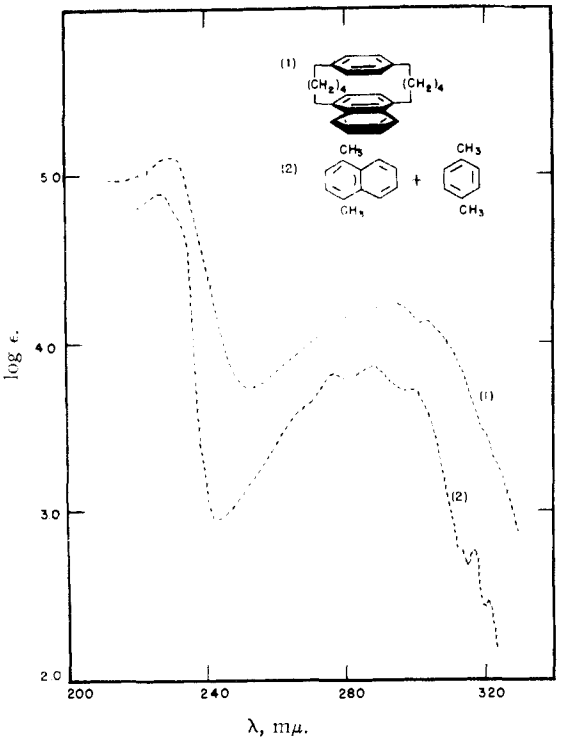
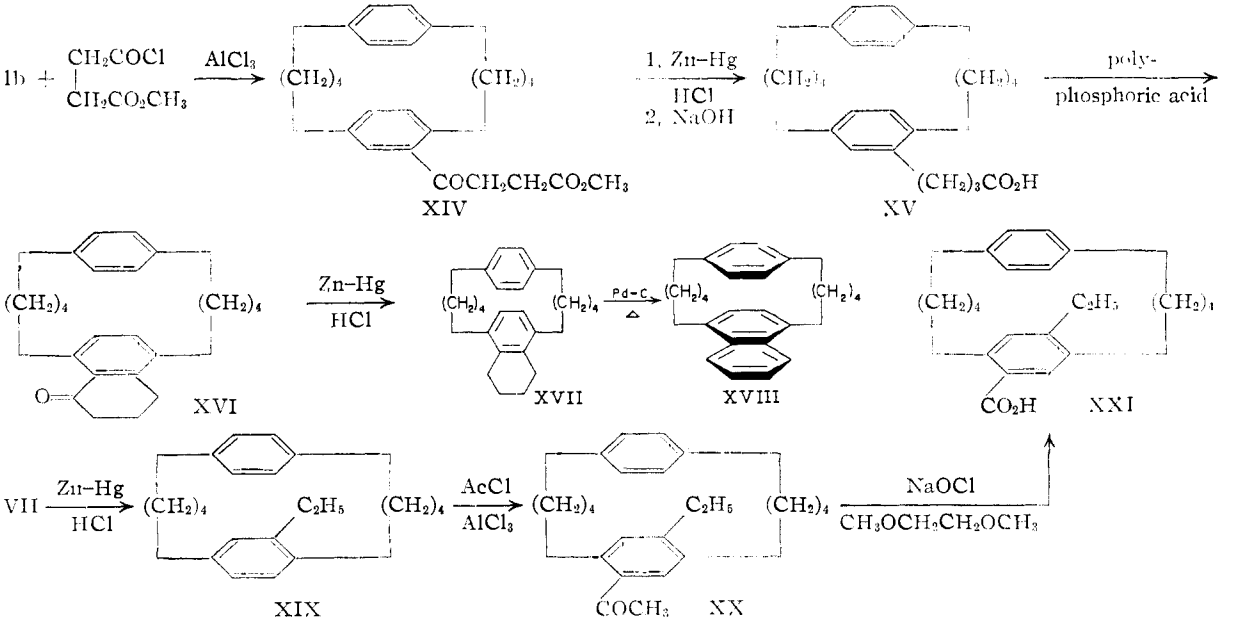


Fig. 3.—Ultraviolet absorption spectra in 95% ethanol, Cary spectrophotometer, model 11 MPS. Curve 1 is displaced upward by 0.5 unit.

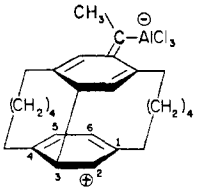
Figure 4 records the ultraviolet absorption spectrum of ketones VII and XX. The fact that acylation of XIX occurred in the ring carrying the ethyl group is indicated by the movement of the lower wave length band of VII (λ_{max} 252 mμ) to longer wave lengths in XX (λ_{max} 262 mμ). Had acylation occurred in the other benzene ring, the spectrum of the product would have been almost identical to that of VII. Final proof of the structure of XXI, and therefore of ketone XX, was obtained by permanganate oxidation of XXI to a tetraacid identified through its tetramethyl ester as the ester of pyromellitic acid.

Acid XXI (m.p. 234–236°) proved to be extremely insoluble even in basic solution and could be obtained by the hypochlorite oxidation of XX only with 1,2-dimethoxyethane as solvent. No optically active acid could be isolated from attempts to resolve XXI with brucine. The acid was so insolu-



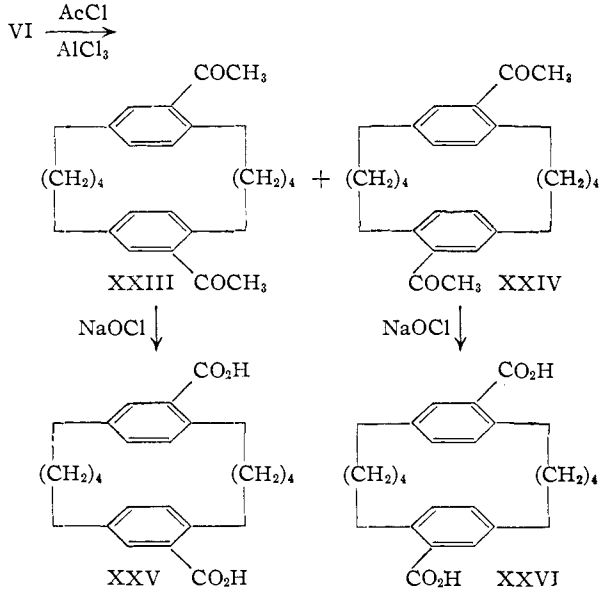
ble in the solvents used that only by maintaining a fourfold molar excess of brucine in solution through all recrystallizations could the acid be prevented from crystallizing in place of the salt. By this method a well defined salt was obtained which yielded on hydrolysis nearly the equivalent amount of inactive acid. No change of the rotation of a solution of the salt with time occurred. Unsuccessful attempts to resolve the acid with quinine also were made. We consider it probable that the bulk of the carboxyl group is not sufficient to prevent the ring carrying this substituent from turning through the center of the paracyclophane ring at ordinary temperatures.

The Problem of Inter-ring Directive Influences.—The fact that an acetyl group in one ring of [4.4]paracyclophane somewhat deactivates both rings toward further electrophilic attack suggests that in the aluminum chloride complex of ketone VII, some positive charge can be distributed in both rings, with structures such as XXII contributing to the resonance hybrid. This possibility leads to the second question of whether any



XXII

inter-ring directive influences are operative. This problem was pursued by subjecting ketone VII to acetylating conditions under which a second acetyl group was introduced into the molecule (higher temperatures). The reaction products proved to be similar to those obtained utilizing [4.4]paracyclophane as the starting material with twice as much acylating agent and the same reaction conditions. Two bis-acetyl compounds were isolated, the same techniques being employed for their separation as were used for the products from the diacetylation of [6.6]paracyclophane.[3a]



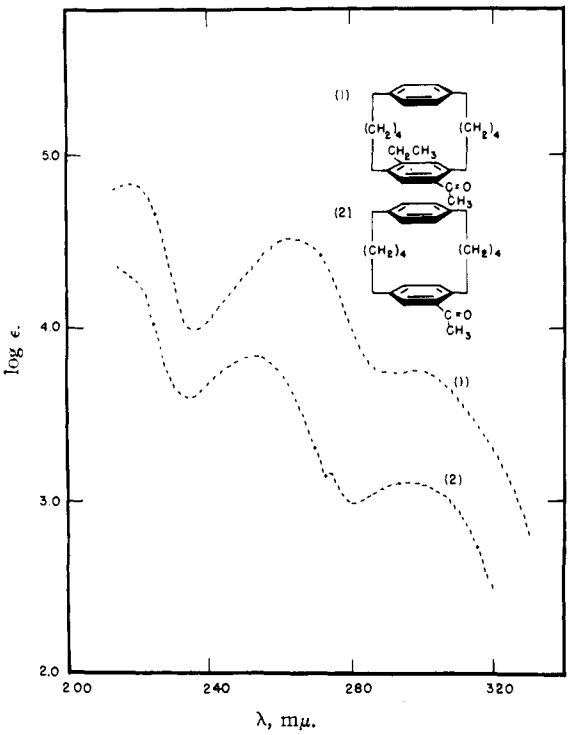
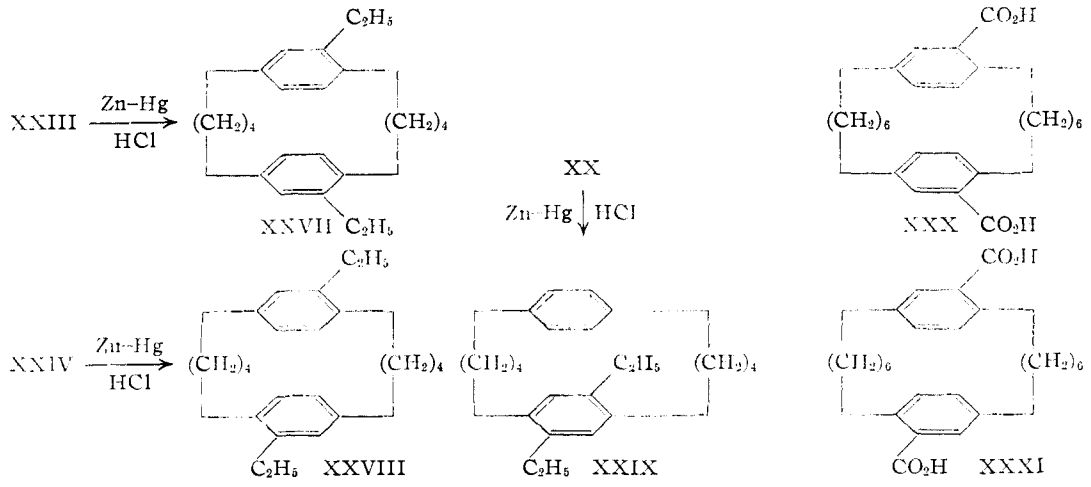


Fig. 4.—Ultraviolet absorption spectra in 95% ethanol, Cary spectrophotometer, model 11 MPS. Curve 1 is displaced upward by 0.5 unit.

The two compounds were isolated in approximately equal amounts and probably possess structures XXIII and XXIV. Their ultraviolet absorption spectra are identical to one another and almost identical to that of the two bis-acetylated [6.6]paracyclophanes,[3a] and to that of VI (these spectra will be recorded in a later paper). These facts make it highly improbable that either of the two bis-acetylated [4.4]paracyclophanes carry two acetyl groups in the same ring. This possibility was further diminished by reducing both substances to the corresponding bis-ethyl derivatives XXVII and XXVIII, and demonstrating both of them to be different from the bis-diethyl compound XXIX obtained by the reduction of ketone XX, whose structure has been elucidated. Minor but distinct ultraviolet absorption spectral differences are exhibited by compounds XXVII and XXVIII (spectra identical) on the one hand and XXIX and XIV on the other (see Fig. 5). Ketones XXIII and XXIV were oxidized to their corresponding bis-acids XXV and XXVI which failed to form intramolecular anhydrides when subjected to the same conditions under which their homologs in the [6.6]paracyclophane series gave anhydrides.

Although the assignment of structures XXIII and XXIV to the two diacetyl[4.4]paracyclophane isomers cannot be made with certainty, several empirical correlations of the individual properties of these ketones and of their derived acids XXV and XXVI with the corresponding compounds in the [6.6]paracyclophane series permit a tentative assignment of structure to be made. The lower melting diketone was eluted first in chromatography



in both series. The lower melting diketone in each series yielded the higher melting diacid. The infrared spectra of all four of the diacids in question are remarkably similar in the region from 950 to 4000 cm.$^{-1}$. In each pair of isomers, however, a difference appears in a band appearing between 900 and 925 cm.$^{-1}$. In XXX this band appears at 925 cm.$^{-1}$, in XXXI at 910 cm.$^{-1}$. A similar shift is found in the infrared spectra of acids XXV and XXVI, and in such a way as to lead to structural assignments in harmony with those based on the melting point and chromatographic behavior. A band near 935 cm.$^{-1}$ has been attributed to the out-of-plane deformation mode of the hydroxyl carried by a carboxyl group. According to Bellamy,[10] "It would seem likely that this band is a reasonably characteristic one for carboxylic acids and that it arises from the OH deformation. As such it would be expected to show marked changes associated with changes of state which may alter the degree of hydrogen bonding." Since the degree of intramolecular hydrogen bonding in these diacids would depend on the relative positions of the two carboxyl groups, the position of this infrared band could reasonably provide a significant indication of the structural relationships of the diacids between the [4.4]- and [6.6]paracyclophane series. The structures of the diacids and diketones have been assigned on this basis.

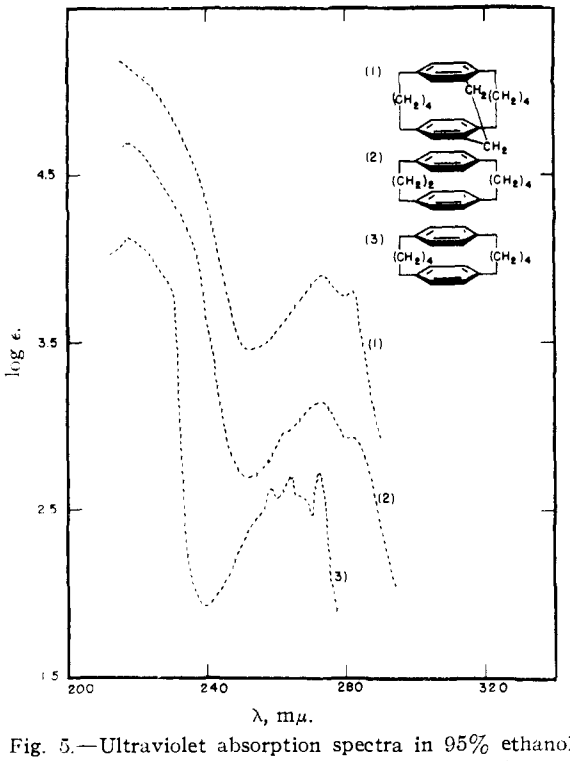
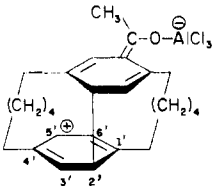


Fig. 5.—Ultraviolet absorption spectra in 95% ethanol, Cary spectrophotometer, model 11 MPS. Curves 2 and 1 are displaced upward by 0.5 unit from the curve immediately below.

The fact that only two diketones were obtained in acylation of VII favors the idea that the two rings of [4.4]paracyclophane can turn over with respect to one another, at least at ordinary temperatures. Should such rotation be restricted, the number of possible isomers would increase to four. Since the two diacetyl[4.4]paracyclophanes were produced in essentially equal amounts, no inter-ring directive influences appear to operate in this particular system. This observation is not incompatible with the fact that deactivating influences operate. Contributions of structures such as XXII to the resonance hybrid place partial positive charge in positions 2′,4′ and 6′ of the unsubstituted ring, suggesting that electrophilic substitution in that ring might be directed toward positions 3′ and 5′ to give a predominance of XXIV when VII is further acetylated. However, molecular models of [4.4]paracyclophane indicate not only that the two aromatic rings can turn over with respect to one another, but also that the two rings can occupy a variety of geometries in which the two aromatic nuclei occupy parallel planes. Thus XXII is only one of a family of structures, members of which include such structures as XXXII, which might direct electrophilic attack to the 2- and 6-positions. The problem of inter-ring directive influences is being studied in the smaller paracyclophanes in which the methylene bridges are short enough to remove this structural ambiguity.

(10) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen and Co., Ltd., London, 1954 p. 148.



XXXII

Experimental Part

Nitration of [4.4]Paracyclophane (Ib).—[4.4]Paracyclophane (1.00 g., 0.00379 mole) was dissolved in glacial acetic acid (15 ml.) containing boron trifluoride (0.45 g.), and the solution was heated to 90°. A solution of fuming nitric acid (91%, 0.265 g., 0.00379 mole) and boron trifluoride (0.4 g.) in glacial acetic acid (4 ml.) was added dropwise during three minutes to the hot solution of the hydrocarbon, giving a dark brown solution. The solution was immediately poured with stirring into crushed ice, giving a yellow precipitate. The mixture was allowed to warm to room temperature and was then extracted with ether, giving two clear phases. The ether solution was washed three times with water, three times with sodium bicarbonate solution (wash very yellow), and twice with water. The solution was dried and concentrated to give a brown semicrystalline material (1.14 g.). This material was adsorbed on a column of neutral activity I alumina (50 g.) made up with 10% ether–pentane. Elution of the column with 10% ether–pentane gave, first, starting material (0.21 g., 21%) and, after a blank fraction, a white solid, 6-nitro[4.4]paracyclophane (IIb) (0.175 g., 15%). Elution of the column with 50% ether–pentane gave a white solid, crude 1-keto[4.4]paracyclophane (0.44 g., 42%), or Vb.

6-Nitro[4.4]paracyclophane was distilled in a short-path still at 130° (bath temperature) (1 mm.) to give a white powder. Two crystallizations of the material from methanol gave white prisms, m.p. 92.4–94.3°.

Anal. Calcd. for $C_{20}H_{23}O_2N$: C, 77.64; H, 7.49. Found: C, 77.86; H, 7.57.

Catalytic reduction of 6-nitro[4.4]paracyclophane gave 6-amino[4.4]paracyclophane (III), m.p. 138–142°, undepressed on admixture with an authentic sample.[3b]

Crude 1-keto[4.4]paracyclophane showed only one band in the carbonyl region of the infrared spectrum, at 1670 $cm.^{-1}$. One crystallization of the ketone from hexane and four crystallizations from methanol gave colorless prisms, m.p. 113.6–114.5°.

Anal. Calcd. for $C_{20}H_{22}O$: C, 86.28; H, 7.97. Found: C, 86.28; H, 7.87.

Nitration of [6.6]Paracyclophane.—[6.6]Paracyclophane (1.00 g., 0.00312 mole) was dissolved in glacial acetic acid (15 ml.) containing boron trifluoride (0.7 g.), and the solution was heated to 90°. A solution of fuming nitric acid (91%, 0.218 g., 0.00312 mole) and boron trifluoride (0.4 g.) in glacial acetic acid (4 ml.) was added in small portions during three minutes to the hot solution of the hydrocarbon. The color of the solution after each addition became dark brown and quickly faded to light tan. The solution was immediately poured with stirring into crushed ice, giving a very gummy yellow precipitate. The mixture was allowed to warm to room temperature and was then extracted with ether, giving two clear phases. The ether solution was washed with water, sodium bicarbonate solution, and again with water. The solution was dried and concentrated to give a brown oil (1.11 g.). This oil was adsorbed on a column of neutral activity I alumina (90 g.) made up with pentane. Elution of the column with pentane gave starting material (0.20 g., 20%). Elution with 20% ether–pentane gave an oil, 8-nitro[6.6]paracyclophane (IIa) (0.015 g., 1.3%). Elution with 50% ether–pentane gave a white solid, crude 1-keto[6.6]paracyclophane (Va) (0.126 g., 12%).

8-Nitro[6.6]paracyclophane was distilled in a short-path still at 140° (bath temperature) (1 mm.) to give a yellow gum.

Anal. Calcd. for $C_{24}H_{31}O_2N$: C, 78.86; H, 8.55. Found: C, 79.18; H, 8.45.

1-Keto[6.6]paracyclophane was recrystallized three times from methanol to give very fine white needles, m.p. 77.8–78.9°.

Anal. Calcd. for $C_{24}H_{30}O$: C, 86.18; H, 9.04. Found: C, 86.37; H, 9.18.

Preparation of 6-Hydroxy[4.4]paracyclophane (VIII) by Diazotization of 6-Amino[4.4]paracyclophane (III).—6-Amino[4.4]paracyclophane (0.200 g., 0.000718 mole) was stirred at 0° with dilute sulfuric acid (2 *N*, 10 ml.). Sodium nitrite (0.052 g., 0.00075 mole) in water (2 ml.) was added, and the yellow mixture was stirred for 30 minutes at 0°. The ice-bath was removed and the mixture was stirred until all of the diazonium salt had decomposed. The mixture was extracted with ether, and the ether solution was washed with dilute sodium hydroxide solution and then with water. Acidification of the sodium hydroxide wash gave only a faint turbidity. The ether solution was dried and concentrated to give an oily yellow solid (0.175 g.). Sublimation of the material at 125° (1 mm.) gave a yellow solid (0.125 g.). Five recrystallizations of the compound from pentane gave white plates, 6-hydroxy[4.4]paracyclophane (0.016 g., 8%), m.p. 169–175°.

Anal. Calcd. for $C_{20}H_{24}O$: C, 85.67; H, 8.63. Found: C, 84.97; H, 8.54.

Although this material is obviously impure, its ultraviolet absorption spectrum was essentially identical with the more pure material prepared in the next section.

Perbenzoic Acid Oxidation of 6-Acetyl[4.4]paracyclophane (VII).—A wet chloroform solution of perbenzoic acid was prepared and found to contain 0.0511 g. of peracid per milliliter of solution.[3c] 6-Acetyl[4.4]paracyclophane (0.477 g., 0.00146 mole) in chloroform (3 ml.) was added to the perbenzoic acid solution (7.00 ml., 0.00260 mole). The reaction mixture was allowed to stand for twelve days in the dark at room temperature. Titration of an aliquot of the solution and of a blank solution similarly prepared indicated that the reaction had proceeded to 91% completion. The chloroform solution was well washed with sodium bicarbonate solution and water. The solution was dried and concentrated to give a yellow oil (0.454 g.) which was partially soluble in pentane. The pentane-soluble portion (0.280 g.) was adsorbed on neutral activity IV alumina made up in pentane. Elution of the column with pentane gave a colorless oil (0.196 g.) which solidified partially on standing. Five crystallizations of the product from aqueous methanol gave 6-acetoxy[4.4]paracyclophane as white plates, m.p. 103.5–104.8°.

Anal. Calcd. for $C_{22}H_{26}O_2$: C, 81.95; H, 8.13. Found: C, 81.29; H, 8.20.

Crude ester (0.119 g.) was refluxed for six hours with a solution of sodium hydroxide (0.2 g.) in water (5 ml.) and ethanol (5 ml.). The cooled solution was extracted with ether, and the ether solution was washed with dilute hydrochloric acid and then with water. The ether solution was dried and concentrated to give a yellow oil (0.097 g.) which partially solidified. The oil was adsorbed on a column of neutral activity IV alumina made up with pentane. 6-Hydroxy[4.4]paracyclophane (VIII) (0.020 g., 4.6%) was eluted with 20% ether–pentane. Crystallization of the solid from pentane gave white needles, m.p. 179–183°.

Anal. Calcd. for $C_{20}H_{24}O$: C, 85.67; H, 8.63. Found: C, 85.56; H, 8.56.

Preparation of Potassium Nitrosodisulfonate, NO-$(SO_3K)_2$.—Potassium nitrosodisulfonate was prepared according to directions supplied by Teuber.[11] Sodium nitrite solution (5 *M*, 50 ml.) was cooled in an ice–salt-bath. Ice (100 g.) was added to the solution. Sodium bisulfite solution (5 *M*, 50 ml.) was then added with stirring. Glacial acetic acid (10 ml.) was added and the solution began to turn yellow. After three minutes a 25% ammonium hydroxide solution (12.5 ml.) was added. Potassium permanganate solution (6.4 g. of $KMnO_4$, 200 ml. of water) was added with stirring during five minutes. The precipitated manganese dioxide was collected, the filtrate being cooled in ice. To the cold filtrate was added an equal volume of potassium chloride solution (saturated at room temperature), and the solution was placed in the refrigerator. The yellow precipitate was collected and dissolved at 45° in a potassium hydroxide solution (2 *N*, 600 ml.). The solution was filtered and the purple filtrate was placed in the

(11) H. J. Teuber, private communication.

refrigerator. After standing overnight, the yellow-orange crystals of potassium nitrosodisulfonate (10 g.) were filtered, washed three times with methanol and stored under vacuum over calcium chloride.

Oxidation of 6-Hydroxy[4.4]paracyclophane (VIII) with Potassium Nitrosodisulfonate.—A solution of potassium nitrosodisulfonate (0.155 g., 0.00058 mole) in water (12 ml.) containing sodium acetate (0.25 g.) was added to a solution of crude 6-hydroxy[4.4]paracyclophane (VIII) (m.p. 150–175°, 0.070 g., 0.000265 mole) in ether (6 ml.). Shaking of the mixture for two hours produced no apparent reaction. Methanol (7 ml.) was added and the shaking of the mixture was continued for two hours. The solution was extracted with ether, and the ether solution was washed with water. The solution was dried and concentrated to give a yellow solid (0.041 g.) which could not be induced to crystallize. Its ultraviolet spectrum indicated it to be a mixture of quinone and other materials.

On standing overnight, the aqueous solution which had been extracted with ether contained a precipitate. This precipitate was extracted into ether, and the ether solution was washed with water and dried. The solution was concentrated to give a yellow solid which was sublimed at 155° (1 mm.) to give a yellow powder. Crystallization of the material from hexane–chloroform gave the quinone IX as fine yellow needles (0.006 g.), m.p. 217–223° (slight decomposition).

Anal. Calcd. for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.44; H, 7.56.

6-Ethyl[4.4]paracyclophane (XIX).—Mossy zinc (20 g.), mercuric chloride (2.0 g.), water (40 ml.) and concentrated hydrochloric acid (2.0 ml.) were swirled together for five minutes. The liquid was decanted and the amalgamated zinc was washed with water. 6-Acetyl[4.4]paracyclophane (VII) (2.70 g., 0.0102 mole) dissolved in glacial acetic acid (40 ml.) was added, followed by concentrated hydrochloric acid (40 ml.). The mixture was refluxed for 30 hours with addition of portions of concentrated hydrochloric acid (10 ml.) at 8-hour intervals. The mixture was cooled, poured into water, and extracted with ether. The ether solution was washed with water, sodium bicarbonate solution, and again with water. The ether solution was dried and concentrated to give a colorless oil (2.50 g.) which was adsorbed on a column of neutral activity I alumina (100 g.) made up in pentane. 6-Ethyl[4.4]paracyclophane (XIX) (2.18 g., 85%) was eluted with pentane as a colorless oil which rapidly solidified. For analysis the material was distilled at 205–210° (bath temperature) (1.5 mm.) to give a colorless oil which solidified, m.p. 57–62°.

Anal. Calcd. for $C_{22}H_{28}$: C, 90.35; H, 9.65. Found: C, 90.37; H, 9.82.

Acetylation of 6-Ethyl[4.4]paracyclophane (XIX).—Acetyl chloride (0.79 g., 0.0100 mole) was added to a stirred suspension of aluminum chloride (1.20 g., 0.0090 mole) in carbon disulfide (50 ml.). 6-Ethyl[4.4]paracyclophane (2.18 g., 0.00746 mole) dissolved in carbon disulfide (20 ml.) was added, and the mixture was stirred at room temperature for one hour. The mixture was poured with stirring into crushed ice and hydrochloric acid, and this mixture was allowed to stand overnight. The mixture was extracted with ether and the ether solution was washed with water, sodium bicarbonate solution, and again with water. The ether solution was dried and concentrated to give a tan solid (2.39 g.). This solid was adsorbed on a column of neutral activity I alumina (100 g.) made up in pentane. Starting material (0.22 g., 10%) was eluted with pentane. 6-Ethyl-9-acetyl[4.4]paracyclophane (XX) (1.83 g., 74%) was eluted with 30% ether–pentane as a white solid, m.p. 127–129°. A solid mixture of diacetylated 6-ethyl[4.4]-paracyclophane isomers (0.18 g., 6%) was eluted with ether, m.p. 88–97°. For analysis, XX was recrystallized five times from methanol to give white triangles, m.p. 129.0–130.0°.

Anal. Calcd. for $C_{24}H_{30}O$: C, 86.18; H, 9.04. Found: C, 86.09; H, 9.29.

The diacetylated material was distilled in a short-path still at 170° (bath temperature) (1 mm.) to give a solid which was crystallized from aqueous methanol to give small white prisms, m.p. 95.6–103.2°.

Anal. Calcd. for $C_{26}H_{32}O_2$: C, 82.93; H, 8.57. Found: C, 82.81; H, 8.46.

6-Ethyl-9-carboxy[4.4]paracyclophane (XXI).—A solution of hypochlorite was prepared from calcium hypochlorite (5 g.) as described in the preparation of XXV (see future section). To this solution (30 ml.) solid potassium hydroxide was added (4 g.). 6-Ethyl-9-acetyl[4.4]paracyclophane (0.200 g., 0.00060 mole) dissolved in 1,2-dimethoxyethane (25 ml.) was added, and the two-phase mixture was stirred very vigorously for 30 minutes at room temperature. The mixture was then stirred for one hour at 70° and for 14 hours at 32°. The mixture was extracted with ether. The ether solution was extracted with Claisen alkali and washed with water. The ether solution was dried and concentrated to give starting material (0.070 g., 35%). The Claisen alkali extract was diluted with water and acidified with hydrochloric acid, giving a white precipitate. The mixture was extracted with ether, and the ether solution was washed with water. The ether solution was dried and concentrated to give a white solid. One crystallization of the material from ether gave 6-ethyl-9-carboxy[4.4]paracyclophane (XXI) (0.088, g., 44%) as tiny white needles, m.p. 233–236°. For analysis, three crystallizations of the brucine salt followed by hydrolysis gave white needles, m.p. 233.8–236.2°.

Anal. Calcd. for $C_{23}H_{28}O_2$: C, 82.10; H, 8.39. Found: C, 81.85; H, 8.43.

Permanganate Oxidation of 6-Ethyl-9-carboxy[4.4]paracyclophane (XXI).—6-Ethyl-9-carboxy[4.4]paracyclophane (0.311 g., 0.00093 mole) was heated under reflux for 48 hours with a solution of potassium permanganate (6.6 g.) in water (110 ml.) and 10% sodium hydroxide solution (3 ml.). The solution was cooled and acidified with hydrochloric acid. Sulfur dioxide was bubbled into the mixture until a colorless solution was obtained. The solution was extracted with a small amount of ether to remove any readily ether-soluble compounds. A small amount of precipitate (0.010 g.) was collected and dissolved in 10% sodium hydroxide solution. Acidification of the solution with hydrochloric acid gave no precipitate. The filtrate was extracted continuously with ether for 36 hours. The ether extract was dried and concentrated to give a white powder (0.170 g.) decomposing from 180–230°. This material was suspended in a mixture of methylene chloride and ether and was treated with a solution of diazomethane (large excess). A considerable amount of the material remained insoluble during the reaction. The excess diazomethane was decomposed with dilute hydrochloric acid, and the solution was extracted with ether. The ether solution was washed with water. The ether solution was dried and concentrated to give a slightly yellow solid (0.100 g.), m.p. 132–138° (softens 124°). The solid was adsorbed on a column of neutral activity I alumina (20 g.) made up in ether. Ether eluted a white solid (0.038 g.), m.p. 138–140° (softens 133°). The solid was dissolved in boiling methanol, and the solution was filtered free of a small amount of insoluble material and placed in the refrigerator. Pyromellitic acid tetramethyl ester (0.025 g., 9%) was deposited as white plates, m.p. 140.6–142.5°, reported m.p. 141.5°.[12]

Anal. Calcd. for $C_{14}H_{14}O_8$: C, 54.19; H, 4.55. Found: C, 54.46; H, 4.70.

Attempted Resolution of 6-Ethyl-9-carboxy[4.4]paracyclophane with Brucine.—Brucine (1.13 g., 0.00286 mole) and 6-ethyl-9-carboxy[4.4]paracyclophane (0.240 g., 0.000715 mole) was heated in absolute ethanol (25 ml.) until a clear solution was obtained. After standing eight hours, clumps of fine needles (0.442 g.) deposited from the mixture, m.p. 226–228° (decomposition from 194°). This material was recrystallized three times from absolute ethanol, each time three moles of brucine per mole of salt being added. The final recrystallization of the substance gave the salt (0.151 g.) with melting point unchanged. A portion of the salt was hydrolyzed by shaking with ether and dilute hydrochloric acid to give the acid as a white solid, 90% of the theoretical amount of acid based on the weight of pure salt. No solvent except Claisen alkali could be found to dissolve enough acid to take the rotations; $[\alpha]^{25}D$ 0.00° (*c* 1.5, Claisen alkali).

6-Carboxymethylene[4.4]paracyclophane (X).—6-Acetyl-[4.4]paracyclophane (VII) (2.00 g., 0.00654 mole) was dissolved in morpholine (2.95 g., 0.0344 mole), and sulfur

(12) J. D. Roberts and W. T. Moreland, THIS JOURNAL, **75**, 3167 (1953).

(0.313 g., 0.0098 mole) was added. The solution was heated at reflux for 24 hours (dark brown). The solution was concentrated under vacuum, and the residue was refluxed for 20 hours with a solution of potassium hydroxide (6 g.) in water (6 ml.) and ethanol (25 ml.). The solution was cooled and poured into water (50 ml.). The cloudy mixture was acidified with hydrochloric acid and extracted with ether. The ether solution was washed with water and extracted with Claisen alkali. The Claisen alkali solution was diluted with water and acidified with hydrochloric acid. The acidified solution was extracted with ether, and the ether extract was washed with water. The ether solution was dried and concentrated to give a brown gum (1.04 g.). This gum was refluxed for four hours with a solution of absolute methanol (10 ml.) and concentrated sulfuric acid (0.5 ml.). The solution was cooled, poured into water (50 ml.), and the mixture was extracted with ether. The ether solution was dried and concentrated to give a brown oil (1.05 g.) which was adsorbed on a column of neutral activity I alumina (70 g.) made up in 10% ether–pentane. Crude 6-carbomethoxymethylene[4.4]paracyclophane (0.46 g., 21%) was eluted with 25% ether–pentane as a slightly yellow oil which solidified to a waxy solid, m.p. 50–55°. For analysis, the ester was crystallized from aqueous methanol and distilled in a short-path still at 160° (bath temperature) (1 mm.) to give a white powder, m.p. 56.4–58.3°.

Anal. Calcd. for $C_{23}H_{28}O_2$: C, 82.10; H, 8.39. Found: C, 82.19; H, 8.32.

The crude ester (0.38 g.) was refluxed for eight hours with a solution of potassium hydroxide (1 g.) in water (1 ml.) and ethanol (10 ml.). The solution was cooled and poured into water. The clear aqueous solution was acidified with hydrochloric acid giving a white precipitate, and the mixture was extracted with ether. The ether extract was washed with water and dried. Concentration of the ether solution gave a white solid which on crystallization from methanol gave 6-carboxymethylene[4.4]paracyclophane [X] (0.300 g., 14% from the ketone) as tiny white needles, m.p. 147–153°. For analysis the acid was crystallized from aqueous ethanol to give white plates, m.p. 151–153°.

Anal. Calcd. for $C_{22}H_{26}O_2$: C, 81.95; H, 8.13. Found: C, 82.26; H, 8.18.

6,17-Ketomethylene[4.4]paracyclophane (XI).—6-Carboxymethylene[4.4]paracyclophane (X) (0.206 g., 0.00064 mole) was mixed with thionyl chloride (0.60 ml.). The compound dissolved immediately. The solution was stirred at room temperature for 10 minutes and then at 70° for 10 minutes. The excess thionyl chloride was removed under vacuum. Carbon disulfide (4 ml.) dissolved the residue, and to this stirred solution aluminum chloride (0.092 g., 0.00069 mole) was added, giving an immediate gummy, brown precipitate. The mixture was stirred for 15 minutes at room temperature and then refluxed for 15 minutes. The mixture was poured with stirring into crushed ice and concentrated hydrochloric acid, and this was allowed to stand overnight. The mixture was extracted with ether, and the ether solution was washed with water, 5% potassium hydroxide solution, and again with water. The ether solution was dried and concentrated to give an oil (0.15 g.) which solidified on standing. This material was adsorbed on a column of neutral activity I alumina made up in 50% ether–pentane. Elution with 50% ether–pentane gave a white solid (0.086 g.), m.p. 134–139°. The material was distilled in a short-path still at 145° (0.5 mm.) to give a white solid which was crystallized from ether–pentane to give 6,17-ketomethylene[4.4]paracyclophane (XI) (0.055 g., 28%) as beautiful white feathers, m.p. 138.2–140.4°.

Anal. Calcd. for $C_{23}H_{26}O$: C, 86.80; H, 7.95. Found: C, 86.88; H, 7.94.

6,17-Dimethylene[4.4]paracyclophane (XIII).—Potassium hydroxide (0.5 g.) and 85% hydrazine hydrate (0.3 g.) were dissolved in diethylene glycol (6 ml.). 6,17-Ketomethylene[4.4]paracyclophane (0.042 g., 0.000138 mole) was added and the mixture was heated at 155° for 3 hours. The condenser was removed and the temperature was raised to 210° during 30 minutes. The condenser was replaced and heating was continued at 210° for 3 hours. The solution was cooled, diluted with water, and extracted with ether. The ether solution was washed with water, dried, and concentrated to give a partially crystalline yellow solid (0.043 g.). This solid was adsorbed on a column of neutral activity I alumina made up in pentane. A white solid (0.028 g.) was eluted with pentane. This solid was distilled in a short-path still at 120° (bath temperature) (0.5 mm.) to give a white powder (0.026 g.), m.p. 99.7–110.1°. Six crystallizations of the substance from 95% ethanol gave 6,17-dimethylene[4.4]paracyclophane (XIII) as thin needles (0.008 g., 20%), m.p. 109.1–109.8°.

Anal. Calcd. for $C_{22}H_{26}$: C, 90.97; H, 9.03. Found: C, 90.91; H, 8.78.

β-{6[4.4]Paracyclophanoyl}-propionic Acid.—Succinic anhydride (0.96 g., 0.0096 mole) was added to a stirred suspension of aluminum chloride (2.50 g., 0.0192 mole) in *sym*-tetrachloroethane (20 ml.). The resulting solution was stirred for 10 minutes at room temperature and then cooled to 0°. [4.4]Paracyclophane (2.00 g., 0.0076 mole) dissolved in *sym*-tetrachloroethane (12 ml.) was added to the stirred solution during 8 minutes. Stirring was continued for 3 minutes at 0°, and for 30 minutes after removal of the ice-bath. The solution was poured with stirring into crushed ice and concentrated hydrochloric acid, and the mixture was allowed to warm to room temperature. The mixture was extracted with ether, and the ether solution was washed with water and dried. The ether was removed on the steam-bath and the tetrachloroethane was distilled off at reduced pressure. The residue was crystallized from hexane to give β-{6[4.4]paracyclophanoyl}-propionic acid (1.8 g., 66%) as white rosettes, m.p. 126–128°. For analysis, the acid was again crystallized from hexane, m.p. 127–128°.

Anal. Calcd. for $C_{24}C_{28}O_3$: C, 79.09; H, 7.74. Found: C, 79.08; H, 8.01.

Methyl β-{6[4.4]Paracyclophanoyl}-propionate (XIV).—[4.4]Paracyclophane (2.00 g., 0.0076 mole) and carbomethoxypropionyl chloride (1.22 g., 0.0082 mole) were dissolved in *sym*-tetrachloroethane (50 ml.) and the solution was cooled to −5°. Aluminum chloride was added to the stirred solution in portions during one hour. The orange mixture which resulted was stirred for 30 minutes at −5°, and then allowed to warm to room temperature with stirring during 90 minutes. The mixture was poured with stirring into crushed ice and concentrated hydrochloric acid, and this was allowed to stand overnight. The mixture was extracted with ether, and the ether solution was washed with water, sodium bicarbonate solution and again with water. The solvent was evaporated on the steam-bath, and the remaining tetrachloroethane was removed under reduced pressure. The residual liquid was adsorbed on a column of neutral activity I alumina (90 g.) made up with pentane. Starting material (0.45 g., 22%) was eluted with pentane. Methyl β-{6[4.4]paracyclophanoyl}-propionate (XIV) (1.75 g., 61%) was eluted with 80% ether–pentane as a colorless, very viscous liquid. For analysis, the liquid was distilled at 270° (bath temperature) (2.5 mm.).

Anal. Calcd. for $C_{25}H_{30}O_3$: C, 79.33; H, 7.99. Found: C, 79.46; H, 7.94.

γ-{6[4.4]Paracyclophanyl}-butyric Acid (XV).—Mossy zinc (15 g.), mercuric chloride (1.5 g.), water (30 ml.) and concentrated hydrochloric acid (1.5 ml.) were swirled together in a flask for 5 minutes. The liquid was decanted, and the amalgamated zinc was washed with water. Methyl β-{6[4.4]paracyclophanoyl}-propionate (1.75 g., 0.00464 mole) dissolved in glacial acetic acid (30 ml.) was added, followed by concentrated hydrochloric acid (30 ml.). The mixture was refluxed for 44 hours with addition of portions of concentrated hydrochloric acid (10 ml.) at 12-hour intervals. The mixture was cooled and poured into water. The resulting mixture was extracted with ether, and the ether solution was washed with water, sodium bicarbonate solution, and again with water. The solution was dried and concentrated to give an oil (1.66 g.) which rapidly solidified. This solid was added to a solution of potassium hydroxide (4 g.) in water (5 ml.) and ethanol (18 ml.), and the solution was refluxed for five hours. The solution was poured into water, acidified with hydrochloric acid, and extracted with ether. The ether solution was washed with water and extracted with Claisen alkali. The Claisen alkali extract was diluted with water, acidified with hydrochloric acid, and extracted with ether. The ether solution was washed with water and dried. Concentration of the

solution gave a colorless liquid (1.56 g.) which rapidly solidified, m.p. 100–108° (not clear). The material was crystallized from acetone–hydrochloric acid–water to give γ-{6[4.4]paracyclophanyl}-butyric acid (XV) (1.23 g., 72%), m.p. 100–108°. For analysis, the material was distilled in a short-path still at 200° (bath temperature) (1 mm.), crystallized three times from aqueous methanol, again distilled at 180° (bath temperature) (1 mm.), and crystallized from aqueous methanol to give tiny white needles, m.p. 103.5–108.0°.

Anal. Calcd. for $C_{24}H_{30}O_2$: C, 82.24; H, 8.63. Found: C, 82.02; H, 8.65.

Polyphosphoric Acid Cyclization of γ-{6[4.4]Paracyclophanyl}-butyric Acid.—Phosphorus pentoxide (10.3 g.) and 85% orthophosphoric acid (7.0 ml.) were heated on the steam-bath for two hours. γ-{6[4.4]Paracyclophanyl}-butyric acid (0.425 g., 0.00122 mole) was added, and heating was continued for 27 hours. The resulting gummy mass was stirred with crushed ice, and this mixture was allowed to stand overnight. The mixture was extracted with ether, and the ether solution was washed with water, sodium bicarbonate solution, again with water, and it was then extracted with Claisen alkali. The Claisen alkali extract was diluted with water, acidified with hydrochloric acid, and the resulting white precipitate was taken up in ether. The ether solution was washed with water, dried, and concentrated to give starting material (0.17 g., 40%). The original ether extract was washed with water and dried. Concentration of the solution gave yellow crystals which were dissolved, and adsorbed on a column of neutral activity I alumina made up with 50% ether–pentane. The white solid which was eluted with 50% ether–pentane was crystallized from methanol to give 6,7-tetramethylene-21-keto-[4.4]paracyclophane (XVI) (0.097 g., 24%), m.p. 98–101°. For analysis, the material was crystallized again from methanol, m.p. 99.5–101.0°.

Anal. Calcd. for $C_{24}H_{28}O$: C, 86.70; H, 8.49. Found: C, 86.49; H, 8.34.

6,7-Tetramethylene[4.4]paracyclophane (XVII).—Amalgamated zinc was prepared from mossy zinc (2 g.). To the amalgamated zinc was added 6,7-tetramethylene-21-keto-[4.4]paracyclophane (XVI) (0.095 g., 0.000295 mole) dissolved in glacial acetic acid (6 ml.). The mixture was heated at reflux for 30 hours with addition of portions of concentrated hydrochloric acid (2 ml.) at 8-hour intervals. The reaction mixture was cooled, diluted with water, and extracted with ether. The ether solution was washed with water, sodium bicarbonate solution, and again with water. The ether solution was dried and concentrated to give a colorless liquid (0.088 g.). This liquid was adsorbed on a column of neutral activity I alumina (20 g.) made up in pentane. 6,7-Tetramethylene[4.4]paracyclophane (XVII) (0.067 g., 74%) was eluted with pentane as a colorless liquid which solidified on standing, m.p. 76–79°. The material was crystallized from 95% ethanol to give long, broad needles, m.p. 81.0–82.3°.

Anal. Calcd. for $C_{24}H_{30}$: C, 90.50; H, 9.50. Found: N, 90.67; H, 9.36.

Benzo[4.4[paracyclophane (XVIII).—6,7-Tetramethylene[4.4]paracyclophane (XVII) (0.035 g., 0.00110 mole) was powdered with 10% palladium-on-carbon and placed in a 30-cm. length of 8-mm. glass tubing. A slightly smaller glass rod was held slightly above the mixture which was then heated at 210–250° for 2 hours, the heating being discontinued occasionally to allow the distilling liquid to run back into contact with the catalyst. The tube was cooled and washed out with ether. The ether solution was filtered and concentrated to give a white solid (0.020 g.). This material was crystallized from 95% ethanol to give very long, white needles (0.010 g., 29%), m.p. 119.3–122.1°.

Anal. Calcd. for $C_{24}H_{26}$: C, 91.66; H, 8.34. Found: C, 91.55; H, 8.59.

Acetylation of 6-Acetyl[4.4]paracyclophane (VII).—Acetyl chloride (0.155 g., 0.00196 mole) was added to a mixture of aluminum chloride (0.458 g., 0.00344 mole) and carbon disulfide (10 ml.) stirred at room temperature. 6-Acetyl-[4.4]paracyclophane (0.500 g., 0.00164 mole) was added, and the mixture was stirred for 7 hours at room temperature. The mixture was poured with vigorous stirring into crushed ice and concentrated hydrochloric acid, and the mixture was allowed to warm to room temperature. The mixture was extracted with ether, and the ether layer was washed with water, sodium bicarbonate solution, and again with water. The ether solution was dried and concentrated to give a semi-crystalline solid which was adsorbed on a column of activity I neutral alumina (80 g.) made up in 25% ether–pentane. The column was eluted successively with 25% ether–pentane, ether and methanol. Starting material (0.164 g., 33%) was eluted with 25% ether–pentane. A mixture of diacetyl isomers XXIII and XXIV (0.169 g., 44% based on unrecovered starting material) was eluted with ether. Elution with methanol gave, after separation from alumina by solution in ether, an unidentified oil (0.050 g.).

Separation of Diacetyl[4.4]paracyclophane Isomers (XXIII and XXIV).—A mixture of the diacetyl isomers (2.4 g.) obtained from acetylation of [4.4]paracyclophane was adsorbed on a column of neutral activity I alumina (400 g., column 34 cm. high and 5 cm. in diameter) made up with 30% ether–pentane. Fractions 1–25 (75 ml. each) of 30% ether–pentane containing a small amount of oil (0.13 g.). The diacetyl isomers were eluted with 40% ether–pentane. Fractions 31–45 gave white solids which were crystallized from methanol to give white needles, partially melting at 110–115°, partially resolidifying, and completely melting at 140°. Short path distillation of the material at 150° (bath temperature) (1 mm.) gave quantitatively a white powder, 6,17-diacetyl[4.4]paracyclophane (XXIII), m.p. 138.8–140.0° (0.90 g.).

Anal. Calcd. for $C_{24}H_{28}O_2$: C, 82.70; H, 8.10. Found: C, 82.93; H, 8.38.

Fractions 46–56 gave a mixture of XVIII and XXIV. Fractions 57–89 gave white solids which were crystallized once from methanol to give white needles, 6,16-diacetyl-[4.4]paracyclophane (XXIV), m.p. 151.4–153.0° (0.90 g.). A mixed melting point of XXIII and XXIV was 105–130°.

Anal. Calcd. for $C_{24}H_{28}O_2$: C, 82.70; H, 8.10. Found: C, 82.43; H, 7.94.

6,17-Dicarboxy[4.4]paracyclophane (XXV).—A solution of hypochlorite was prepared by a modification of the method described by Newman and Holmes.[13] HTH (commercial calcium hypochlorite) (10 g.) was heated on the steam-bath with water (40 ml.). A solution of potassium carbonate (7 g.) and potassium hydroxide (2 g.) in water (20 ml.) was added and the gel originally formed was shaken for 5 minutes until it was quite fluid. The solution was filtered and the precipitate was washed with water (5 ml.). Solid potassium hydroxide (8 g.) was added. 6,17-Diacetyl-[4.4]paracyclophane (XXIII) (0.59 g., 0.00170 mole) dissolved in 1,2-dimethoxyethane (50 ml.) was added, and the resulting two-phase mixture was stirred vigorously for one hour at room temperature. The basic solution was extracted with ether, and the aqueous phase was acidified with hydrochloric acid, giving a white precipitate. The precipitate was taken up slowly in ether by repeated extractions of the aqueous emulsion, until finally on the last extraction two clear layers were obtained. The combined ether extracts were washed with water and dried. Concentration of the ether solution gave a white solid which was sublimed at 235° (1×10^{-4} mm.) to give a white powder, 6,17-dicarboxy[4.4]paracyclophane (XXV) (0.50 g., 83%). For analysis, the material was crystallized from glacial acetic acid to give small white prisms, m.p. 317–322° (slight decomposition from 295°).

Anal. Calcd. for $C_{22}H_{24}O_4$: C, 74.98; H, 6.86. Found: C, 74.76; H, 6.91.

6,16-Dicarboxy[4.4]paracyclophane (XXVI).—A hypochlorite solution was prepared from HTH (10 g.) as described in the preceding experiment. A solution of 6,16-diacetyl[4.4]paracyclophane (XXIV) (0.396 g., 0.00114 mole) in 1,2-dimethoxyethane was added, and the two-phase system was stirred vigorously at room temperature for two hours. The temperature was then raised to 70° for one hour, and stirring was continued at room temperature for 27 hours. The mixture was extracted with ether, and the aqueous phase was acidified with hydrochloric acid. The resulting white precipitate was readily extracted into ether. The ether solution was washed with water and dried. Concentration of the ether solution gave a white solid which

(13) M. S. Newman and H. L. Holmes, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 429.

was sublimed at 230° (6×10^{-4} mm.) to give a white powder, 6,16-dicarboxy[4.4]paracyclophane (XXVI) (0.306 g., 76%). For analysis, the material was crystallized from glacial acetic acid to give tiny white prisms, m.p. 297–302° (slight decomposition from 285°).

Anal. Calcd. for $C_{22}H_{24}O_4$: C, 74.98; H, 6.86. Found: C, 74.94; H, 6.92.

Clemmensen Reduction of 6-Ethyl-9-acetyl[4.4]paracyclophane (XX).—Amalgamated zinc was prepared from mossy zinc (5 g.). 6-Ethyl-9-acetyl[4.4]paracyclophane (0.096 g., 0.000287 mole) dissolved in glacial acetic acid (10 ml.) was added, followed by concentrated hydrochloric acid (10 ml.), and the mixture was heated at reflux for 30 hours, with addition of portions of concentrated hydrochloric acid (3 ml.) at 8-hour intervals. The mixture was cooled, poured into water, and extracted with ether. The ether solution was washed with water, sodium bicarbonate solution, and again with water. The solution was dried and concentrated to give a white solid which was absorbed on a column of neutral activity I alumina (20 g.) made up in pentane. 6,9-Diethyl[4.4]paracyclophane (0.062 g., 60%) was eluted with pentane as a white solid, m.p. 108.5–111°. Two crystallizations of the material from 95% ethanol gave fat white needles, m.p. 109.9–111.6°.

Anal. Calcd. for $C_{24}H_{32}$: C, 89.93; H, 10.07. Found: C, 89.73; H, 10.00.

Clemmensen Reduction of 6,16-Diacetyl[4.4]paracyclophane.—Amalgamated zinc was prepared from mossy zinc (8 g.). 6,16-Diacetyl[4.4]paracyclophane (0.110 g., 0.000316 mole) dissolved in glacial acetic acid (10 ml.) was added, followed by concentrated hydrochloric acid (10 ml.). The mixture was refluxed for 75 hours, with addition of portions of concentrated hydrochloric acid (2.5 ml.) at 8-hour intervals. The mixture was cooled, poured into water, and extracted with ether. The ether solution was washed with water, sodium bicarbonate solution, and again with water. The solution was dried and concentrated to give a colorless oil which was catalytically reduced in ethanol. There was little or no hydrogen absorbed. The ethanol solution was poured into water, and the mixture was extracted with ether. The ether solution was washed with water and dried. The solution was concentrated to give an oil which was adsorbed on a column of neutral activity I alumina (20 g.) made up in pentane. 6,16-Diethyl[4.4]-paracyclophane (0.057 g., 56%) was eluted with pentane as a colorless liquid. For analysis, the liquid was distilled at 115° (bath temperature) (0.5 mm.).

Anal. Calcd. for $C_{24}H_{32}$: C, 89.93; H, 10.07. Found: C, 89.65; H, 10.18.

Clemmensen Reduction of 6,17-Diacetyl[4.4]paracyclophane.—Amalgamated zinc was prepared from mossy zinc (5 g.). 6,17-Diacetyl[4.4]paracyclophane (0.110 g., 0.000316 mole) dissolved in glacial acetic acid (10 ml.) was added, followed by concentrated hydrochloric acid (10 ml.). The mixture was heated at reflux for 30 hours, with addition of portions of concentrated hydrochloric acid (3 ml.) at 8-hour intervals. The mixture was cooled, poured into water, and extracted with ether. The ether solution was washed with water, sodium bicarbonate solution, and again with water. The solution was dried and concentrated to give an oil which was adsorbed on a column of neutral activity I alumina made up in pentane. 6,17-Diethyl[4.4]paracyclophane (0.054 g., 54%) was eluted with pentane as a colorless liquid. For analysis, the liquid was distilled at 110° (bath temperature) (0.5 mm.).

Anal. Calcd. for $C_{24}H_{32}$: C, 89.93; H, 10.07. Found: C, 89.75; H, 10.02.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Macro Rings. XV. The Synthesis and Properties of Six New Paracyclophanes Carrying One Methylene in One of the Bridges[1]

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A series of six homologous paracyclophanes (I) have been prepared in which one of the two bridges carries one methylene and the other, 7, 8, 9, 10, 11 and 12 methylene groups. The smallest cycle preparable through use of the acyloin reaction on diester carrying *two aromatic rings* was [1.8]paracyclophane (I, $m = 1$, $n = 8$). The smallest cycle preparable through use of the acyloin reaction on diester carrying *two cyclohexane rings* was the [1.7]paracyclophane. The benzene rings of the latter compound are probably bent from their normal planar geometry. The ultraviolet absorption spectra of this series of compounds exhibit an even progression of λ_{max} toward longer wave lengths as the benzene rings are drawn toward one another, the smallest cycle possessing an entirely different spectrum from that of the open chain model. These spectral changes are attributed to transannular interactions between the π-electrons of the two benzene rings, the effects becoming more serious as the π-orbitals of each ring are pressed more and more into each other's environment.

The preparation,[2] spectral properties[2a,e] and reactions[3,4] of the more symmetrical paracyclophanes (I with n or m = 2 to 6) have been reported in earlier papers of this series. The sandwich-like geometry of the aromatic portions of these more symmetrical cycles places the π-orbitals of each ring end to end, as indicated in II. This paper is concerned with the construction and properties of compounds shaped more like clams (III), in which at one end of the molecule the π-orbitals of the two benzene rings are orthogonal to one another. The synthesis of III with $n = 8$ has been previously reported.[2d]

Synthesis.—All of the cycles except [1.7]paracyclophane were prepared by the general synthetic sequence outlined in Chart I. Table I reports the physical constants and analyses of the compounds involved, and the Experimental reports typical procedures employed. Compounds XXII, XXVIII, XXXIII, XXXVIII, XLIV, XLV and XLVI have been reported previously. In some cases intermediates (*e.g.*, XI) were not characterized but were used directly in the next step. These syntheses were greatly facilitated by the interesting fact that diphenylmethane can be acylated to give either mono- or bis-substituted product in good yield, depending on the number of moles of acylating agent employed. Clearly an acyl group

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