Macro Rings. VIII. Aromatic Substitution of the [6.6]Paracyclophane[1]
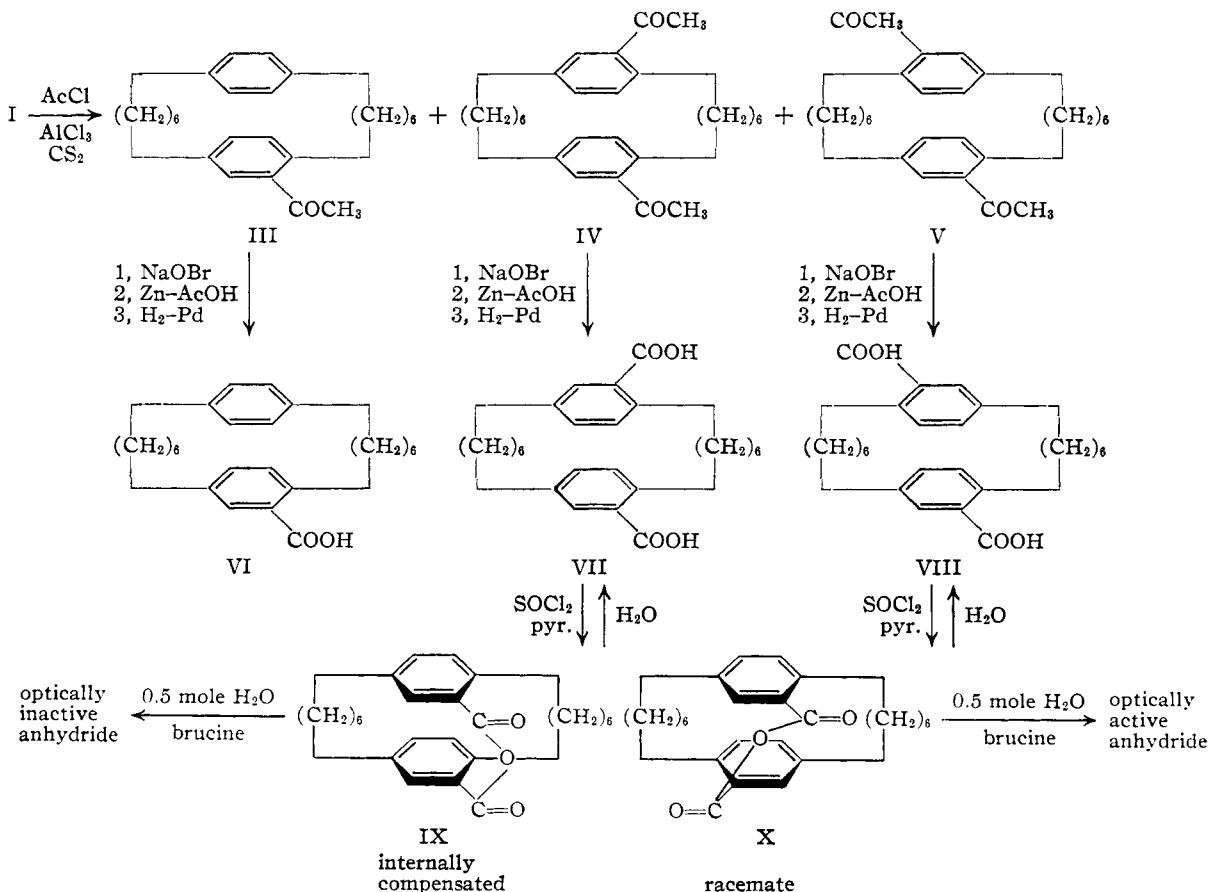
BY DONALD J. CRAM AND JARED ABELL[2]

RECEIVED AUGUST 9, 1954

Acylation experiments carried out on paracyclophane I provide the following conclusions. (1) The substitutions of the two aromatic rings of I proceed independently of one another, no transannular deactivating or directing influences being observed. (2) The spectra of the mono- and diacylated derivatives of I indicate that no transannular electronic effects are operative in these compounds. (3) The number of diacylated isomers of I (one acyl group in each ring) that were obtained is equal to the number predicted, assuming that each nucleus can rotate with respect to the other. (4) The structures of the two isomeric diacylated paracyclophanes were determined through their oxidation to the corresponding diacids, each of which provided a *trans*-nuclear anhydride, one a racemate and the other an internally compensated compound. The racemate was identified by its partial asymmetric hydrolysis. Nitration experiments provided nitroparacyclophanes which were linked through an appropriate series of interconversions to the acylated paracyclophanes.

A number of unique problems arise regarding the course of aromatic substitution of the paracyclophanes II, and the structures of the derived mono- and polysubstituted products. These problems center about possible internuclear effects, both steric and electronic, which might assert themselves in the following ways. (1) Functions substituted in one ring might either accelerate or retard the rate of substitution in the other, depending on the natures of the function and reagent involved. (2) A function substituted in one ring might exert directive influences during the substitution of the other ring. (3) The physical properties (*e.g.*, spectra) of cycles with electron-withdrawing groups in one ring and electron-releasing groups in the other might be different from those observed from open chain models. (4) The number of optical isomers obtainable from the monosubstituted and

TABLE I

ULTRAVIOLET ABSORPTION SPECTRA OF SUBSTITUTED [6,6]PARACYCLOPHANES AND THEIR MODELS[a]

Compound	λ_{max} (log ϵ), mμ	λ_{min} (log ϵ), mμ
2,5-Dimethylacetophenone		
III	214 (4.46), 250 (3.86), 295 (3.16)	232 (3.62), 279 (3.01)
IV	213 (4.68), 248 (4.14), 294 (3.45)	2.30 (3.88), 272 (3.16)
V	213 (4.68), 248 (4.14), 294 (3.45)	2.30 (3.88), 272 (3.16)
XI	220 (4.19), 260 (2.64), 265 (2.75), 274 (2.67)	210 (4.13), 237 (1.78), 262 (263), 272 (254)
XIII	220 (4.20), 260 (2.72), 265 (2.83), 274 (2.82)	244 (2.25), 262 (2.69), 272 (2.61)
XVII	214 (4.03),[b] 257 (4.18)	224 (3.12)
3-Aminoacetophenone	232 (4.35), 255 (3.86),[b] 337 (3.28)	209 (3.88), 250 (3.91),[c] 284 (2.37)
XIX	238 (4.32), 265 (3.89),[b] 338 (3.38)	213 (3.88), 260 (3.89),[c] 291 (2.91)
1,2-Diacetamidobenzene	214 (4.34), 244 (4.07),[b] 284 (2.90)[b]	240 (4.08),[c] 274 (3.13)[c]
1,4-Dimethyl-2,5-diacetamidobenzene	~208 (4.51), 245 (4.02), 282 (3.36)[b]	226 (3.87), 275 (3.50)[c]
XXIV	211 (4.52), 271 (2.86), 276 (2.82)[b]	260 (2.72), 274 (2.82)[c]
1,4-Dimethyl-2-acetamidobenzene	210 (4.39),[b] 232 (3.79),[b] 275 (2.98)	227 (3.80),[c] 273 (2.96)
XXII	208 (4.45), 240 (3.70),[b] 275 (2.88)	230 (3.80),[c] 272 (2.88)
XXV	209 (4.46), 238 (3.71),[b] 274 (3.04)	232 (3.74),[c] 272 (2.98)

[a] Taken in 95% ethanol, Cary recording spectrophotometer, model 11 MPS, quartz cells. [b] Shoulder. [c] Inflection.

of geometric isomers from the disubstituted paracyclophanes (one substituent in each ring) should be different depending on the ability of each ring to turn over with respect to the other. The detection and study of the above effects as a function of the values of m and n in II is the subject of the next few papers in this series, the previous communications[3] recording the preparation and properties of III with $m = n$ and $m = n - 1$ with values of m and n ranging from 2 to 6.

The cycle with $m = n = 6$ was chosen for the initial aromatic substitution experiments for these reasons. The substance is obtainable in reasonable amounts,[3a] possesses symmetry properties making all potential substitution sites equivalent, and possesses a geometry that allows the two aromatic rings to turn over with respect to one another so that a minimum of disubstituted (one substituent in each ring) derivatives might be obtained. Besides the above practical advantages, the substitution experiments in this system in which the two aromatic rings are far from one another serve as models for the behavior of the smaller paracyclophanes in which transannular effects might be observed.

Acylation Experiments.—Acylation of compound I with one mole of acetyl chloride resulted in a mixture of one mono- and two diacylated products, as well as recovered starting material. The ultraviolet absorption spectra of these acyl compounds as well as that of 2,5-dimethylacetophenone which serves as a model are closely similar (see Table I). This fact indicates that in the two diacylated paracyclophanes IV and V, each aromatic ring carries one substituent, and that no transannular electronic effects are evident in these compounds. The yield data indicate that in the acylation, the presence of an acetyl group in one ring does not deactivate the other ring toward electrophilic substitution. Finally, the isolation of two and only two isomeric disubstituted products suggests that each aromatic ring can turn over with respect to the other, a conclusion also supported by the geometry of scale molecular models. Should rotation of the

two aromatic rings be restricted, four isomers would be possible.[4]

Each of the three solid (sharp melting) acyl paracyclophanes (III, IV and V) were oxidized to the corresponding acids (VI, VII and VIII) with sodium hypobromite, the bromine introduced into the benzyl positions being removed with first zinc and acetic acid, and then with palladium and hydrogen. These acids, although analytically pure, melted over a range, and were therefore converted to their corresponding methyl esters. The two diesters were sharp melting compounds, but when reconverted to the parent diacids gave materials melting over the same range as before. The mono ester (an oil) was chromatographed carefully and reconverted to the parent monoacid VI whose properties remained unchanged. These three acids appear to be a mixture of polymorphic crystalline modifications.

The structural identity of each of the two dibasic acids (VII and VIII) was demonstrated as follows. Each substance was converted to a mixture of linear (polymeric) and cyclic (monomeric) anhydrides[5] which were separated by molecular distillation. The monomeric anhydrides IX and X differ in their symmetry and hence optical properties, IX being internally compensated and X a racemate. Each anhydride was partially destroyed with water in the presence of a brucine catalyst, and the remaining anhydride was examined for optical activity. One of these possessed a rotation of $[\alpha]^{25}D$ $-4.2°$ (CHCl₃, 4.5), this optical activity disappearing when the anhydride was completely hydrolyzed. The other remaining anhydride showed no optical activity. This experiment demonstrates three things: the identity of each series of disubstituted paracyclophanes; the fact that each aromatic ring in these compounds can rotate with respect to the other; the already accepted fact[6] that amines become involved in the

(3) (a) D. J. Cram and H. Steinberg, THIS JOURNAL, 73, 5691 (1951); (b) H. Steinberg and D. J. Cram, ibid., 74, 5388 (1952); (c) D. J. Cram and N. L. Allinger, ibid., 76, 726 (1954); (d) N. L. Allinger and D. J. Cram, ibid., 76, 2362 (1954); (e) J. Abell and D. J. Cram, ibid., 77, 4406 (1955); (f) D. J. Cram, N. L. Allinger and H. Steinberg, ibid., 76, 6132 (1954).

(4) The absence of other isomers in the product was indicated by the pattern of elution of the mixture from a carefully prepared chromatogram (see Experimental).

(5) F. H. Carpenter, THIS JOURNAL, 70, 2964 (1948).

(6) A. Leman [Bull. soc. chim., France, [5] 16, 246 (1949)] reports that the rate of hydrolysis of acetic anhydride by water is enhanced markedly by the presence of pyridine. Possibly a somewhat similar type of catalysis is involved in the asymmetric synthesis of cyanohydrins through the agency of optically active amine catalysts [see G. Bredig and M. Minaeff, Biochem. Z., 249, 241 (1932)].

transition state of the amine-catalyzed hydrolysis of anhydrides.[7]

Nitration Experiments.—When nitrated in the usual way with nitric–acetic acid mixtures, paracyclophane I produced an exceedingly complicated mixture of oxidation and nitration products, ketone XI being the only compound isolated in a pure state. The structure of this compound was assigned on the basis shown.
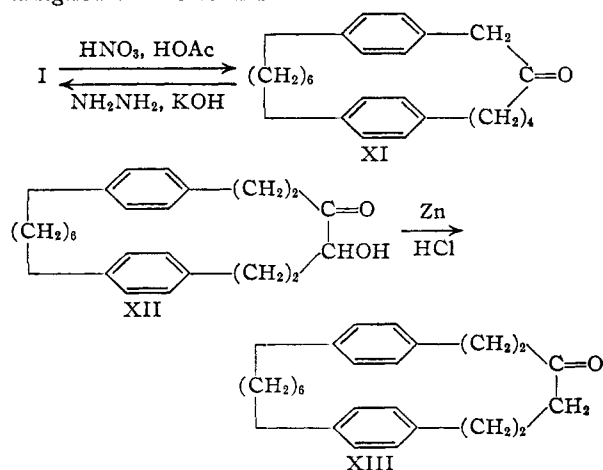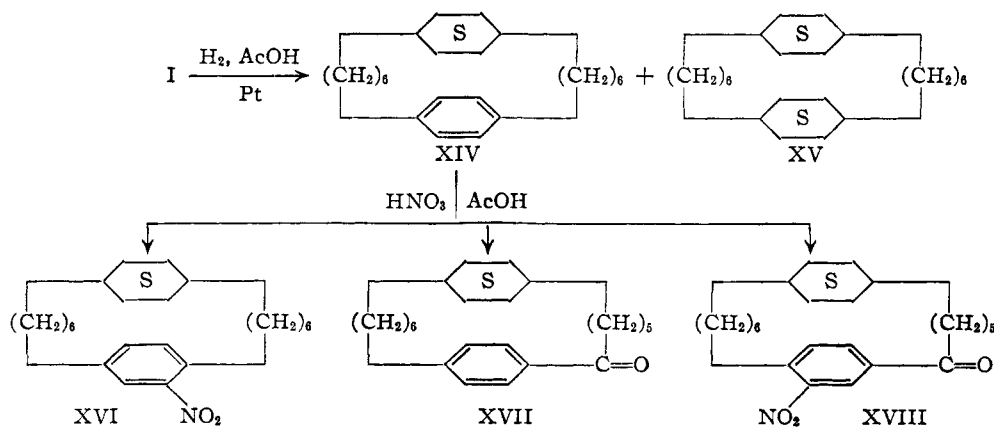

The parent hydrocarbon was obtained when the ketone was submitted to a Wolff–Kishner reduction. Three structures appear possible for this ketone: XI, XIII and the paracyclophane in which a ketone group is conjugated with one of the benzene rings. The ketone obtained from the oxidation proved by direct comparison to be different from XIII, which had been prepared previously.[3e] The ultraviolet absorption spectrum of the substance (see Table I) is inconsistent with that expected from a conjugated ketone, and thus structure XI must apply.

following approach. Cycle I was submitted to catalytic hydrogenation to give (after the absorption of three moles of hydrogen) the mixture of starting material, half reduced XIV and fully reduced XV material expected if the reduction of each proceeded completely independently of the other. These three substances were separated chromatographically, no evidence of the presence of any isomeric materials being obtained. It appears probable that XIV possesses the *cis* and XV the *cis–cis* configuration. Both of these substances were dehydrogenated readily[3c] with palladium to give back the parent aromatic, I. When submitted to nitration experiments, XIV gave three products, XVI, XVII and XVIII. The structure of ketone XVII was demonstrated by its ultraviolet absorption spectrum (the carbonyl group is conjugated with the benzene ring; see Table I). The structure of the nitroketone XVIII was assigned through a comparison of the ultraviolet absorption spectrum of the derived aminoketone XIX and that of *m*-aminoacetophenone (see Table I).[8]
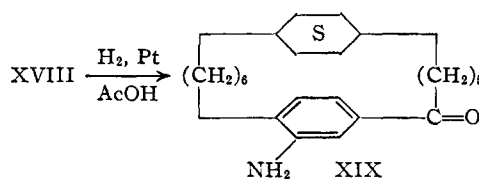
The major product of the nitration reaction, XVI, was fully aromatized with palladium in the presence of a hydrogen acceptor (ethyl cinnamate) to give XX.

Reduction of the nitro compound XVI gave amine XXI, which was characterized as its *p*-nitrobenzamide and acetamide (XXII) derivatives. Attempts to resolve the amine XXI as its *d*-camphor-10-sulfonate salt failed, although excellent


The problem of nitration was simplified by the

yields of a well-defined salt were obtained. This fact suggests that the aromatic ring of XXI can turn over with respect to the cyclohexane ring, a notion consistent with the geometry of molecular models. Amine XXI was found to react readily with bromine to produce after acetylation (poor yield) what is probably dibromide XXIII, which

(7) Two other instances of isomer identification through partial asymmetric destruction of a racemate have been reported. H. J. Lucas and C. W. Gould [THIS JOURNAL, **64**, 601 (1942)] stereospecifically destroyed d,l-2,3-dibromobutane with brucine to form (at different rates) the diastereomerically related alkylated brucines. S. J. Cristol [ibid., **71**, 1894 (1949)] demonstrated that α-d,l-benzene hexachloride could be stereospecifically destroyed by brucine, and that partial resolution could be accomplished by interrupting the reaction before all the starting material was destroyed. A number of cases where stereospecific E₂ reactions failed are recorded by D. J. Cram and F. A. Abd Elhafez [ibid., **74**, 5851 (1952)].
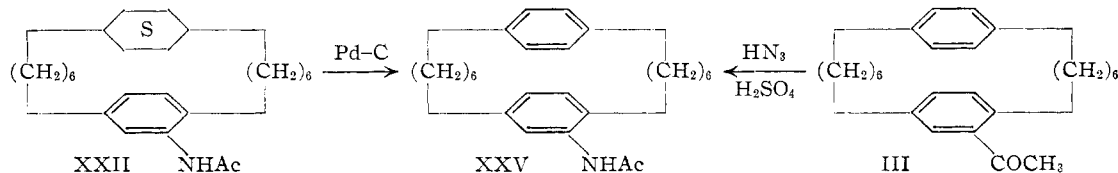
(8) The differences in spectra between o- and p-aminoacetophenone [H. Dannenberg, Z. Naturforsch, **4b**, 327 (1949)] on the one hand and of m-aminoacetophenone on the other allows this assignment to be made.
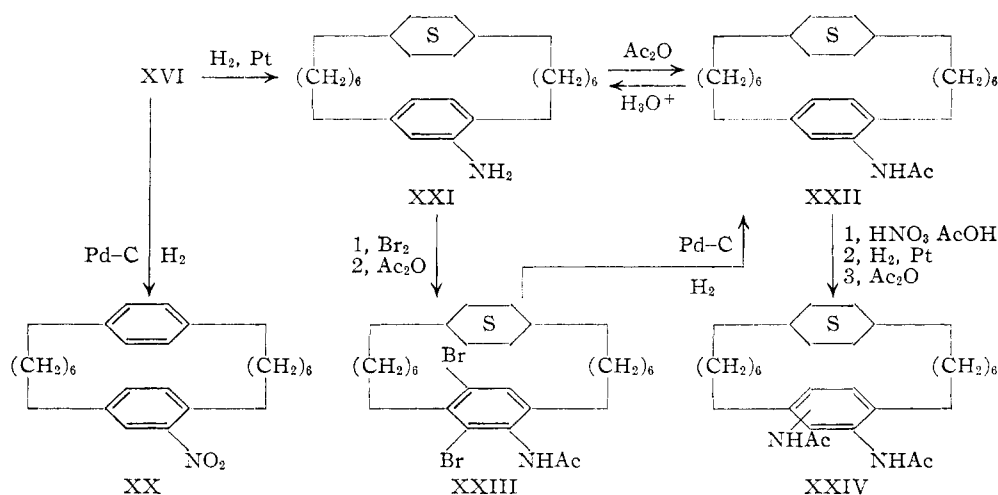
readily was reconverted by hydrogenolysis back to the parent acetamide XXII. In an attempt to provide a substance in which the rotation of the aromatic ring with respect to the cyclohexane ring is blocked by bulky substituents, amide XXII was nitrated, the product being reduced and acetylated to give a diamide XXIV. The structure of this substance is uncertain. Its spectrum (Table I) is different from that of both 1,4-diacetamido-2,5-dimethylbenzene and 1,2-diacetamidobenzene. If the two acetamido groups of XXIV are *ortho* to one another, the resulting steric inhibition of resonance probably would seriously modify the spectrum, probably in the direction of the parent aromatic molecule. Thus the spectrum of XXIV is not inconsistent with the *o*-diamide structure.

Attempts to acylate the half-reduced para-cyclophane XIV gave a good yield of an oil which analyzed well for a monoacetyl compound. Although this material was submitted to a large number of interconversions, the products were all oils and appeared to be mixtures of isomers, possibly arising out of alkyl migrations occurring during the Friedel–Crafts acylation reaction.

The Linking of the Acylation and Nitration Experiments.—The possibility of molecular rearrangements occurring during the Friedel–Crafts acetylation reaction[9] was set aside through the conversion

Nomenclature.—The compounds described in this, in previous and in future papers of this series present new problems in nomenclature. A scheme will be employed for naming these compounds which is essentially that suggested by Schubert and Sweeney.[11] For example, compound I is called [6.6]paracyclophane, the numerical values referring to the length of the methylene bridges, the number of digits designating the number of bridges (and hence 1,4-dialkylated benzene rings) in the system. The term, *paracyclophane*, as suggested earlier,[3a] names a family of compounds in which one or more benzene rings are built into a carbocyclic system and in which the *p*-positions of the benzene rings are part of the ring system. The numbering of the various positions can be illustrated through the use of the hypothetical compound XXVI.
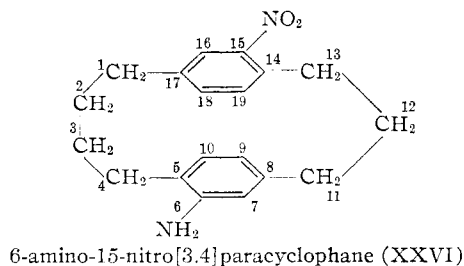

6-amino-15-nitro[3.4]paracyclophane (XXVI)

of the products of the nitration and acylation into the same substance. Thus amide XXII when submitted to aromatizing dehydrogenation provided the fully aromatic amide XXV. The same compound was obtained in 80% yield through the submission of ketone III to the Schmidt reaction.[10] Table I summarizes the spectrum of amides XXII, XXV and 2,5-dimethylacetanilide.

(9) To minimize this possibility, in all cases a minimum amount of aluminum chloride *was added* to the mixture of reactants, and the conditions of the reactions were kept as mild as possible.

(10) P. A. S. Smith, THIS JOURNAL, **76**, 431 (1954).

Experimental

Acetylation of [6.6]Paracyclophane (I).—Aluminum chloride (10 g., 0.075 mole) was added to a stirred mixture of 5.0 g. (0.0152 mole) of [6.6]paracyclophane (I), 2.5 ml. (0.0375 mole) of acetyl chloride and 50 ml. of carbon disulfide. The mixture was allowed to reflux for 20 minutes and was then poured over a mixture of ice and hydrochloric acid. The mixture was then extracted with ether, the ether layer was washed with water, with sodium bicarbonate solution and again with water. The ether solution was dried and evaporated to give 6.0 g. of oil which was absorbed on a 500-

(11) W. M. Schubert, W. A. Sweeney and H. K. Latourette, *ibid.*, **76**, 5462 (1954).

g. column of neutral activated alumina made up in pentane. The material was successively eluted with pentane, 10% ether–pentane and 30% ether–pentane, the volume of column filtrate per fraction collected amounting to 75 ml. When the weight of solute per fraction is plotted against the fraction number, four maxima are observed. Recovered hydrocarbon (fractions 6 and 7) amounted to 0.44 g. (8.8%), and the monoacylated material (8-acetyl[6.6]paracyclophane or III) found in fractions 9–11 amounted to 0.07 g. (1.2%). Fractions 18–24 contained 1.89 g. (31%) of one diacylated product (8,21-diacetyl[6.6]paracyclophane or IV), and fractions 27–30 contained 1.93 g. (32%) of the other (8,20-diacetyl[6.6]paracyclophane or V). Fractions 25–26 contained 0.80 g. (13%) of a mixture IV and V, and fractions 31–35 a yellow gum that was discarded.

Monoacetyl compound III was distilled at a pot temperature of 250° (1 mm. pressure) to give 0.03 g. of colorless oil that solidified on standing, m.p. 37–42°, recrystallization of which from pentane gave material m.p. 40.4–42°.

Anal. Calcd. for $C_{26}H_{34}O$: C, 86.13; H, 9.45. Found: C, 86.11; H, 9.70.

Diacetyl compound IV was recrystallized from hexane to yield 1.46 g. of white needles, m.p. 103.5–105°. A small sample was recrystallized three times from hexane to give white needles, m.p. 104.4–105.2°.

Anal. Calcd. for $C_{28}H_{36}O$: C, 83.12; H, 8.97. Found: C, 82.90; H, 9.02.

Diacetyl compound V was recrystallized twice from hexane to give 0.98 g. of white crystals, m.p. 113.5–115.2°. Three additional recrystallizations of the substance from hexane gave prisms, m.p. 114.8–115.4°.

Anal. Calcd. for $C_{28}H_{36}O$: C, 83.12; H, 8.97. Found: C, 83.09; H, 9.02.

The acetylation was repeated using equal molar quantities of the hydrocarbon I and acetyl chloride. The reaction, as well as the isolation procedure, was carried out as above. From 9.20 g. (0.0287 mole) of I, 2.25 g. (0.0287 mole) of acetyl chloride and 7.7 g. (0.055 mole) of aluminum chloride in 75 ml. of carbon disulfide was obtained the following products: (1) 4.25 g. (46%) of recovered hydrocarbon I; (2) 0.49 g. (5%) of monoacetylated material III; (3) 5.06 g. (44%) of diacetylated material IV and V.

8,20-Dicarboxy[6.6]paracyclophane (VIII).—Bromine (7.5 g. or 0.048 mole) was added dropwise to a solution of 4.8 g. (0.12 mole) of sodium hydroxide in 40 ml. of water cooled in an ice-bath. Compound V (1.62 g., 0.004 mole) in 100 ml. of dioxane was added, and the resulting mixture was stirred for 3 hours. The excess hypobromite was destroyed with sodium bisulfite, and the alkaline solution was washed with ether. The aqueous phase was then acidified, extracted with chloroform, and the extract was washed with water, dried and evaporated to give 1.6 g. of a white solid. This material was dissolved in 60 ml. of acetic acid, the solution was mixed with 4 g. of zinc dust, and the resulting mixture was held at reflux for 10 hours. The mixture was cooled, diluted with water, and the deposited solid was collected and dissolved in 100 ml. of dioxane. Potassium carbonate (0.5 g.) and 0.3 g. of 10% palladium-on-carbon were added, and the mixture was stirred in an atmosphere of hydrogen, 18 ml. being absorbed (30 minutes). The mixture was filtered, the solvent distilled, and the residual solid was recrystallized from acetic acid to yield 1.17 g. (71%) of white crystals, m.p. 195–211.5°. Two additional recrystallizations of the material from acetic acid gave VIII, m.p. 196–212.5°.

Anal. Calcd. for $C_{26}H_{32}O_4$: C, 76.44; H, 7.89. Found: C, 76.23; H, 7.90.

The dimethyl ester of this diacid (8,20-dicarbomethoxy-[6.6]paracyclophane) was prepared by adding 0.5 g. of VIII to an excess of diazomethane in ether. The excess diazomethane was destroyed with acetic acid, the solvent was evaporated and the 0.5 g. of residual oil was adsorbed on 50 g. of activated alumina (neutral) made up in pentane. The ester was eluted with 40% ether in pentane to give 0.5 g. of colorless oil which was crystallized from pentane to yield 0.32 g. (60%) of white rosettes, m.p. 41–45°. Three recrystallizations from pentane gave m.p. 43.2–45.6°.

Anal. Calcd. for $C_{28}H_{36}O_4$: C, 77.03; H, 8.31. Found: C, 77.13; H, 8.60.

A mixture of 0.175 g. of this ester, 0.4 g. of sodium hydroxide, 5 ml. of water and 3 ml. of ethanol was held at re-

flux for 1 hour. The mixture when cooled, acidified and diluted with water deposited a white solid which, when recrystallized from acetic acid, amounted to 0.147 g. (92%) of white crystals, m.p. 195–212.5°. This melting point was unchanged by admixture with the original acid or by melting and remelting.

8,21-Dicarboxy[6.6]paracyclophane (VII).—This substance was prepared from the corresponding diacetyl compound IV in a manner completely analogous to that employed in the synthesis of diacid VIII (see above). From 1.80 g. (0.0046 mole) of IV was obtained 1.12 g. (60%) of VII, m.p. 235–248° (slight decomposition). Three additional recrystallizations of this material from acetic acid gave white crystals, m.p. 237–248° (slight decomposition).

Anal. Calcd. for $C_{26}H_{32}O_4$: C, 76.44; H, 7.89. Found: C, 76.19; H, 8.12.

A mixed melting point of diacids VII and VIII gave 185–207°.

8,21-Dicarbomethoxy[6.6]paracyclophane.—This diester was prepared from the corresponding diacid VII in the same way that the diester of VIII was prepared. From 0.30 g. of VII was obtained 0.20 g. (60%) of diester (white plates), m.p. 78.4–79.2°. One recrystallization from pentane gave plates, m.p. 78.4–79.2°.

Anal. Calcd. for $C_{28}H_{36}O_4$: C, 77.03; H, 8.31. Found: C, 76.82; H, 8.48.

Hydrolysis of 0.065 g. of the above ester gave 0.062 g. (95%) of diacid, m.p. 235–249°, undepressed by admixture with the original diacid.

Anhydride of 8,20-Dicarboxy[6.6]paracyclophane (X).—Diacid VIII (0.368 g. or 0.00090 mole) was suspended in 5 ml. of tetrachloroethane and the mixture was dried by distillation of a small amount of the solvent. To the suspension held at 40°, pyridine (0.074 ml. or 0.00081 mole) and thionyl chloride (0.082 ml. or 0.00099 mole) were added, and the mixture was held at reflux for 2 minutes. The clear solution was poured over ice, the mixture was extracted with chloroform, and the chloroform extract was washed with dilute hydrochloric acid, water, sodium bicarbonate solution and again with water. The solution was dried, and the chloroform was evaporated to give 0.35 g. of a yellow gum. Sublimation of this material at 2×10^{-5} mm. and a pot temperature of 250–300° gave 0.225 g. (61%) of pale yellow solid. This material was characterized by its infrared spectrum (13% in CCl_4, NaCl prism), the following bands being observed: 3.27(m), 3.38(s), 3.73(w), 5.08(w), 5.60(s),[12] 5.76(s),[12] 6.18(w), 6.36(w), 6.70(m), 6.86(m), 7.02(w), 7.38(w), 7.82(m), 8.06(s), 8.26(m), 8.54(s), 9.64(m), 10.04(s), 10.54(w), 10.98(m), 11.47(m).

Anhydride of 8,21-Dicarboxy[6.6]paracyclophane (IX).—By the same procedure (see above), 0.785 g. of diacid VII was obtained 0.526 g. (70%) of distilled gum which solidified on standing. This material was characterized by its infrared spectrum (12% in CCl_4, NaCl prism), the following bands being observed: 3.27(m), 3.38(s), 3.72(w), 5.16(w), 5.58(s),[12] 5.75(s),[12] 6.18(w), 6.36(w), 6.66(m), 6.86(m), 7.02(w), 7.38(w), 7.90(m), 8.06(s), 8.27(m), 8.54(s), 8.66(s), 9.70(s), 10.02(s), 10.56(m), 11.04(m), 11.47(m).

Asymmetric Hydrolysis of the Two Anhydrides.—A mixture of 0.235 g. (0.00060 mole) of the anhydride prepared from 8,20-dicarboxy[6.6]paracyclophane (X) was mixed with 1.2 g. (0.003 mole) of carefully purified anhydrous brucine, 5.5 mg. (0.0003 mole) of water and 7 ml. of pure dry benzene. The mixture was then heated at 75–80° for 30 minutes (homogeneous) and diluted with water. The mixture was extracted with chloroform, the organic layer was washed three times with dilute hydrochloric acid, twice with sodium bicarbonate solution and twice with water. Acidification of the bicarbonate extract gave 40 mg. (16%) of diacid VIII. The chloroform solution was dried, and the solvent was evaporated to give 0.0185 g. (80%) of colorless anhydride as an oil, $[\alpha]^{25}D$ $-6.7°$ (c 6.2, $CHCl_3$). This material was dissolved in chloroform, and the solution was washed three times with dilute hydrochloric acid. The solution was dried, and the solvent evaporated to give 0.0160 g. of colorless anhydride, $[\alpha]^{25}D$ $-4.3°$ (c 5.3,

(12) The spectra of anhydrides are characterized by two strong bands, 5.36–5.75 μ and 5.61–5.93 μ. These bands are always separated by about 0.2 μ [H. M. Randall, R. G. Fowler, N. Fuson and J. R. Dangl, "Infrared Determination of Organic Structures," D. Van Nostrand Co., Inc., New York, N. Y., 1949, p. 20].

CHCl$_3$). Repetition of the washing procedure gave 0.135 g. of anhydride, $[\alpha]^{25}$D $-4.2°$ (c 4.5, CHCl$_3$). A mixture of this anhydride, 20 ml. of ethanol and 0.5 ml. of hydrochloric acid was held at reflux for 3 hours. Most of the solvent was distilled, and 10 ml. of chloroform was added. The solution was completely evaporated to give 0.0100 g. of oil which was completely optically inactive. To this oil was added 10 ml. of ethanol, 7 ml. of water and 0.4 g. of sodium hydroxide, and the resulting solution was held at reflux for 4 hours. The solution was cooled, diluted with water, acidified and extracted with chloroform. The extract was washed with water, dried, evaporated and the residual solid (70 mg.) was esterified with an ethereal solution of diazomethane. The ether was evaporated, and the residual oil was crystallized from pentane to give 10 mg. of 8,20-dicarbomethoxy[6.6]paracyclophane, m.p. 42–45°, undepressed by admixture with an authentic sample of diester.

A mixture of 0.235 g. (0.00060 mole) of anhydride prepared from 8,21-dicarboxy[6.6]paracyclophane (IX), 1.2 g. of carefully purified brucine, 11 mg. (0.00060 mole) of water and 7 ml. of pure dry benzene was submitted to the same procedure as that recorded above. Diacid VII (60 mg. or 24%) was recovered from the bicarbonate washes, and 0.0158 g. (67%) of anhydride was recovered from the chloroform solution, $[\alpha]^{25}$D $-0.35°$ (c 5.3, CHCl$_3$). This material was dissolved in chloroform, the solution was washed three times with dilute hydrochloric acid, and the anhydride was recovered (0.0155 g.), $[\alpha]^{25}$D 0.00° (c 5.2, CHCl$_3$).

A mixture of 0.28 g. of the anhydride prepared from VII, 1 g. of sodium hydroxide, 10 ml. of water and 15 ml. of ethanol was held at reflux for 1 hour. The solution was cooled, diluted with water, acidified and extracted with chloroform. This extract was washed, dried and evaporated to give a white solid that was mixed with an ethereal solution of diazomethane. The solution was evaporated, and the resulting oil was crystallized from pentane to give 0.17 g. of white needles, m.p. 78.5–79.0°, undepressed by admixture with authentic 8,21-dicarbomethoxy[6.6]paracyclophane. A second crop gave 20 mg. more diester (60% total yield).

8-Carboxy[6.6]paracyclophane (VI).—A mixture of 8-acetyl[6.6]paracyclophane (0.37 g. or 0.0010 mole), 15 ml. of dioxane, 0.60 g. of sodium hydroxide and 0.94 g. (0.006 mole) of bromine and 8 ml. of water was stirred for 3.5 hours. The reaction was carried through and the acid isolated by the same procedure as that recorded above for the conversion of V to VIII. Crystallization of the product from acetic acid gave 0.185 g. (50%) of white solid, m.p. 103–124°. An additional recrystallization from acetic acid followed by two recrystallizations from hexane gave 0.072 g. of VI, m.p. 104–126°.

Anal. Calcd. for C$_{25}$H$_{32}$O$_2$: C, 82.37; H, 8.85. Found: C, 82.13; H, 8.87.

8-Carbomethoxy[6.6]paracyclophane.—Acid VI (50 mg.) was esterified with an ethereal solution of diazomethane to give 50 mg. of colorless oil. This material was chromatographically absorbed on 10 g. of activated alumina (neutral) and eluted with 10% ether in pentane. The pentane was evaporated and the residue distilled at 1 mm. and a pot temperature of 230° to give 30 mg. of colorless ester (oil).

Anal. Calcd. for C$_{26}$H$_{34}$O$_2$: C, 82.49; H, 9.05. Found: C, 82.51; H, 9.07.

The above ester (0.13 g.) was mixed with 0.40 g. of sodium hydroxide, 3 ml. of ethanol, and 5 ml. of water. The mixture was held at reflux for 1.5 hours and then was cooled and was acidified. The precipitate which formed was collected and was recrystallized from hexane to give 0.073 g. (55%) of white crystals, m.p. 104–126°, undepressed by admixture with VI.

Attempted Nitration of [6.6]Paracyclophane; Isolation of 2-Keto[6.6]paracyclophane (XI).—To a stirred mixture of 5.0 g. (0.0155 mole) of [6.6]paracyclophane, 75 ml. of acetic acid and 50 ml. of acetic anhydride was added during 45 minutes 1.1 ml. (0.017 mole) of concentrated nitric acid dissolved in 25 ml. of acetic acid. The mixture was stirred for two hours and poured over ice. The oil that separated was dissolved in ether, the solution was washed with water, sodium bicarbonate solution, and again with water. The solution was dried and evaporated to give 6.0 g. of a yellow oil.

Extensive chromatographic separations of the fractions of this oil indicated it to be a complex mixture of nitration and oxidation products. One of the numerous fractions crystallized and was recrystallized from hexane to yield 0.15 g. of oily solid. Alternate recrystallizations from hexane and methanol provided 55 mg. of white rosettes of IX, m.p. 109.8–110.4°. A mixed melting point of this substance with 3-keto[6.6]paracyclophane[3e] gave 96–113°.

Anal. Calcd. for C$_{24}$H$_{30}$O: C, 86.17; H, 9.04. Found: C, 86.03; H, 9.18.

A semicarbazone prepared in the usual manner melted at 93.2–94.4°.

A small amount of this ketone was reduced to the parent hydrocarbon as follows. A mixture of 3 mg. of ketone, 0.15 ml. of 85% hydrazine hydrate, 0.2 g. of potassium hydroxide and 1 ml. of diethylene glycol was held at reflux for 2 hours and then distillate was removed until the pot temperature reached 210°. The mixture was held at reflux for 8 hours, cooled, poured onto ice and extracted with pentane. The pentane was washed with water, dried, evaporated and the residual solid was recrystallized from methanol to give white needles 90–97°, m.m.p. with authentic [6.6]paracyclophane, 90–99°.

7,8,9,10,11,12-Hexahydro[6.6]paracyclophane (XIV).—A mixture of 9.0 g. (0.028 mole) of [6.6]paracyclophane, 1.0 g. of platinum oxide and 200 ml. of acetic acid was allowed to absorb 2.25 liters (0.084 mole) of hydrogen during 70 minutes. The catalyst was removed by filtration, water was added and the mixture was extracted with pentane. The extract was washed, dried and evaporated to give 9.5 g. of colorless oil. This oil was dissolved in pentane, chromatographically absorbed on 500 g. of neutral activated alumina, and eluted with pentane, 75-ml. fractions being taken. Fractions 5 and 6 (A) gave 1.9 g., fractions 7 through 15 gave 4.8 g. (B), and fractions 16 through 23 (C) gave 2.4 g. of white solid.

Fraction C (m.p. 93.6–96.5°) was recrystallized from methanol to give 1.5 g. of white needles, m.p. 96.5–98°. Admixture with starting hydrocarbon I gave no melting point depression.

Fraction A (m.p. 94.0–96.7°) was recrystallized from ethanol to give 0.95 g. of white needles, m.p. 98–100°. Three more recrystallizations of this material from ethanol gave 0.56 g. of 7,8,9,10,11,12,19,20,21,22,23,24-duodecahydro[6.6]paracyclophane (XV), m.p. 101–101.6°, m.m.p. with starting material, 80–90°.

Anal. Calcd. for C$_{24}$H$_{44}$: C, 86.66; H, 13.34. Found: C, 86.58; H, 13.22.

Fraction B was recrystallized from ethanol to give 2.73 g. of white needles, m.p. 51.5–55.7°. Five recrystallizations of this material from ethanol gave 1.2 g. of 7,8,9,10,-11,12-hexahydro[6.6]paracyclophane (XIV), m.p. 57.3–58.4°.

Anal. Calcd. for C$_{24}$H$_{38}$: C, 88.27; H, 11.73. Found: C, 88.39; H, 11.44.

Nitration of 7,8,9,10,11,12-Hexahydro[6.6]paracyclophane (XIV).—To a stirred solution of 20 ml. of fuming nitric acid in 10 ml. of acetic acid held at 0° was added 4.0 g. (0.012 mole) of hydrocarbon XIV. The mixture was stirred at 0° for 15 hours, poured over ice, and extracted with ether. The solution was washed, dried, and evaporated to give 4.5 g. of a yellow oil. This oil was chromatographically adsorbed on 200 g. of neutral activated alumina made up in pentane. The adsorbed material was eluted as follows. A solution of 10% ether in pentane gave 3.1 g. (70%) of yellow oil (A); 50% ether in pentane gave 0.1 g. of yellow solid (B); ether gave two fractions (yellow oils), 0.7 g. of C and 0.5 g. of D.

Fraction A (1.0 g.) was distilled at 1 mm. and a pot temperature of 235–237° to give 0.9 g. of 7,8,9,10,11,12-hexahydro-20-nitro[6.6]paracyclophane (XVI) as a yellow oil, n^{25}D 1.5360.

Anal. Calcd. for C$_{24}$H$_{37}$O$_2$N: C, 77.61; H, 10.04. Found: C, 77.57; H, 10.11.

Fraction B was recrystallized from methanol to give 0.3 g. of needles, m.p. 82–84°. Four more recrystallizations from methanol gave 1-keto-7,8,9,10,11,12-hexahydro[6.6]-paracyclophane (XVII) as white needles (0.14 g.), m.p. 84.8–85.6°.

Anal. Calcd. for C$_{24}$H$_{36}$O: C, 84.64; H, 10.66. Found: C, 84.65; H, 10.77.

An oxime of ketone XVII was prepared by the usual

method (white needles from a mixture of hexane and benzene), m.p. 182.8–184.8°.

Anal. Calcd. for $C_{24}H_{37}ON$: C, 81.07; H, 10.49. Found: C, 80.97; H, 10.55.

Fraction C was hydrogenated in ethanol in the presence of platinum, approximately 6 moles of hydrogen being absorbed. The mixture was filtered and shaken with a mixture of pure pentane and water, and the pentane layer was washed with water, dried, and evaporated to give 0.66 g. of a yellow oil. Acetylation of this material with acetic anhydride and pyridine gave an oil from which no crystalline products could be isolated.

Fraction D was submitted to the same hydrogenation procedure as C, 3 moles of hydrogen being absorbed and 0.5 g. of yellow solid being obtained. This material was recrystallized from a mixture of hexane and benzene to yield 0.365 g. of 1-keto-7,8,9,10,11,12-hexahydro-20-amino-[6.6]paracyclophane (XIX) as yellow needles, m.p. 139–141.5°. Three additional recrystallizations of this material from the same solvent gave 0.15 g. of pale yellow needles, m.p. 142.4–143.4°. The compound gave a positive test for a carbonyl group with 2,4-dinitrophenylhydrazine.

Anal. Calcd. for $C_{24}H_{37}ON$: C, 81.09; H, 10.59. Found: C, 81.07; H, 10.49.

8-Nitro[6.6]paracyclophane (XX).—A mixture of 0.115 g. (0.00031 mole) of XVI, 40 mg. of 10% palladium-on-charcoal and 2 ml. of ethyl cinnamate was held at reflux for 2 hours. The mixture was cooled and shaken with a mixture of ether and water. The ether layer was washed with water, dried, and evaporated, the residual oil being distilled at 1 mm. and a pot temperature of 255–260°. The distillate collected at this temperature (94 mg. of yellow oil) was chromatographed on a column of 10 g. of activated alumina made up in pentane. The column was developed with 50% ether in pentane to give a column eluant of 40 mg. of yellow oil. Distillation of this oil provided 9 mg. of yellow oil XX, pot temperature 250–255° at 1 mm. pressure.

Anal. Calcd. for $C_{24}H_{31}O_2N$: C, 78.86; H, 8.55. Found: C, 79.12; H, 8.97.

7,8,9,10,11,12-Hexahydro-20-amino[6.6]paracyclophane (XXI) and Derivatives.—Nitro compound XVI (1.0 g., 0.0027 mole) was shaken with a mixture of 50 mg. of platinum oxide (prereduced) and 10 ml. of ethanol until 223 ml. of hydrogen (3 moles) was absorbed (40 minutes). The mixture was filtered and shaken with water and ether. The ether layer was washed with water, dried, and evaporated to give 1.0 g. of a pink oil (crude amine, XXI).

This amine was converted to its acetamide derivative as follows. A mixture of 2 ml. of acetic anhydride, the above amine, and 5 ml. of pyridine was heated at 95° for 1.5 hours. The mixture was poured over ice and then extracted with ether. The ether layer was washed with water, dilute acid, again with water, dried, and evaporated to give 1.1 g. of a yellow oil. This material crystallized from hexane to give 0.81 g. of white needles, m.p. 114.6–116.5°. Recrystallization of the material from hexane gave 0.71 g. (70%) of needles, m.p. 117–118°. A small sample was recrystallized three times from hexane to give 7,8,9,10,11,12-hexahydro-21-acetamido[6.6]paracyclophane (XXII) as white needles, m.p. 118.6–119.2°.

Anal. Calcd. for $C_{26}H_{41}ON$: C, 81.40; H, 10.77. Found: C, 81.27; H, 10.89.

Amine XXI was converted to its *p*-nitrobenzamide derivative with *p*-nitrobenzoyl chloride and pyridine by the usual method. From 0.2 g. of amine was obtained 0.12 g. of yellow needles of amide (yellow needles from a mixture of hexane and benzene), m.p. 164–166°. Three more recrystallizations of this material from the same solvent gave 70 mg. of pale yellow needles, m.p. 163.5–164.5°.

Anal. Calcd. for $C_{31}H_{42}O_3N_2$: C, 75.88; H, 8.63. Found: C, 75.83; H, 8.57.

The attempt to resolve amine XXI was made as follows. A solution of 0.41 g. (0.0018 mole) of *d*-camphor-10-sulfonic acid in aqueous methanol was added to 0.62 g. (0.0018 moles) of crude amine XXI. The oily solid that separated was recrystallized twice from acetone to give 0.42 g. of white solid which decomposed above 200°. This material was recrystallized six times from acetone to yield 0.24 g. of pure salt.

Anal. Calcd. for $C_{34}H_{55}O_4NS$: C, 71.16; H, 9.66. Found: C, 71.11; H, 9.71.

The mother liquors from the original crystallization were evaporated, and the residue was shaken with a mixture of sodium hydroxide and ether. The ether was washed with water, dried, and evaporated to give 0.26 g. of oil, $[\alpha]^{25}D$ 0.00°, (c 26, C_6H_6).

7,8,9,10,11,12-Hexahydro-20,21-diacetamido[6.6]paracyclophane? (XXIV).—Acetamido compound XXII (1.0 g., 0.0026 mole) was nitrated with a mixture of 10 ml. of fuming nitric acid and 10 ml. of glacial acetic acid at 0° over a period of 11 hours. The procedure was analogous to that employed for the preparation of XVI (see above). The product, 1.1 g. of yellow oil, was chromatographically absorbed on a column of 50 g. of activated neutral alumina made up in pentane. Elution of the material with 50% ether in pentane gave 1.0 g. of a yellow oil that could not be crystallized. This oil was hydrogenated in the presence of platinum (in ethanol), 95% (214 ml.) of 3 moles of hydrogen being absorbed. The solution was filtered, the solvent was evaporated, and the residual oil (0.90 g.) was heated at 100° for 1.5 hours with a mixture of 0.6 ml. of acetic anhydride and 3 ml. of pyridine. The resulting mixture was shaken with a mixture of ether and water, the ether layer was washed with water, with dilute acid, and again with water. The solution was dried and evaporated to give 0.6 g. of an oily solid. This material was submitted to chromatographic separation on neutral alumina with ether as a developer. One of the central fractions of the column filtrate gave upon evaporation a solid (0.15 g.), which upon recrystallization from hexane–benzene gave 61 mg. of material, m.p. 260–266° dec. Three additional recrystallizations of the substance from the same solvents gave 25 mg. of XXIV, m.p. 263–268° dec.

Anal. Calcd. for $C_{28}H_{44}O_2N_2$: C, 76.32; H, 10.06. Found: C, 76.35; H, 9.95.

7,8,9,10,11,12-Hexahydro-20,23-dibromo-21-acetamido-[6.6]paracyclophane (XXIII).—Amine XXI was converted to its dibromo derivative by treatment with an excess of bromine in acetic acid (10% solution). From 0.9 g. of amine was obtained 1.0 g. of dibromo derivative (an oil). This oil was subjected to the usual acetylating conditions (acetic anhydride) and in turn gave 1.3 g. of very crude (XXIII) (an oil). Crystallization of the material from hexane gave 0.15 g. of white solid, m.p. 140–160°. Five recrystallizations from hexane gave 0.05 g. (4%) of fluffy white needles, m.p. 166.2–168.5°.

Anal. Calcd. for $C_{26}H_{33}ONBr_2$: C, 57.67; H, 7.26. Found: C, 57.68; H, 7.56.

Evaporation of the solvent from the mother liquors left 1.0 g. of oil. Part of this oil (0.5 g.) was hydrogenated in ethanol in the presence of 0.15 g. of 10% palladium-on-carbon and 0.2 g. of potassium carbonate, 46 ml. of hydrogen being absorbed during 1 hour. The catalyst was removed by filtration and the solution was diluted with water. An ether extract was obtained and on evaporation yielded a white solid. Two recrystallizations from hexane 0.31 g. (83%) of white crystals, m.p. 117.0–118.2°, undepressed by admixture with XXII. Similar treatment with 75 mg. of pure, crystalline XXIII gave 40 mg. of pure XXII.

8-Acetamido[6.6]paracyclophane (XXV) from 7,8,9,10,11,-12-Hexahydro-20-acetamido[6.6]paracyclophane (XXII).—A mixture of 1.0 g. (0.0026 mole) of compound XXII and 0.2 g. of 10% palladium-on-carbon was heated from 250–295° during 30 minutes and 3 moles (190 ml.) of hydrogen was evolved. The mixture was cooled, extracted with hot benzene, and the catalyst was collected. The filtrate was evaporated to give 1.0 g. of colorless oil which was crystallized from hexane to give 0.80 g. of white prisms, m.p. 117.4–119.0°. A second crop also was obtained (0.06 g.), m.p. 114.5–118° (88% yield, total). A small sample was recrystallized four times from hexane to give needles, m.p. 118.2–119.3°.

Anal. Calcd. for $C_{26}H_{35}ON$: C, 82.71; H, 9.35. Found: C, 82.74; H, 9.18.

8-Acetamido[6.6]paracyclophane (XXV) from 8-Acetyl-[6.6]paracyclophane (III).—A mixture of 0.10 g. (0.00027 mole) of acetyl compound III, 0.038 ml. (0.00081 mole) of sulfuric acid and 0.08 g. of trichloroacetic acid was maintained at 60° in a water-bath. Sodium azide (30 mg., 0.00047 mole) was added during 30 minutes. After an ad-

ditional 30 minutes, the mixture was poured over ice. The product was extracted with ether, the ether extract was washed with water, with sodium bicarbonate solution, and again with water. The solution was dried, evaporated, and the 0.1 g. of residual oil was crystallized from hexane to give 86 mg. (85%) of colorless prisms, m.p. 117.5–118.8°, undepressed by admixture with XXV prepared above.

7,8,9,10,11,12-Hexahydro-20-acetyl[6.6]paracyclophane. —A mixture of 1.0 g. (0.003 mole) of 7,8,9,10,11,12-hexahydro[6.6]paracyclophane (XIV), 0.5 ml. (0.003 mole) of acetyl chloride and 15 ml. of carbon disulfide was prepared at ice temperature and allowed to stand at 0° for 30 minutes. The temperature was then allowed to rise to 20° during 1 hour. The reaction mixture was maintained at 20° for an additional 2 hours and then was poured into a mixture of ice and hydrochloric acid. The mixture was extracted with ether, the ether layer was washed with water, dried, and evaporated to give 1.2 g. of a yellow oil. This material was adsorbed on a chromatograph column of 50 g. of activated neutral alumina made up in pentane, the product being eluted with 20% ether in pentane to give 0.82 g. of colorless oil. This product was distilled at a pressure of 1 mm. and a pot temperature of 230–235° to yield 0.6 g. of colorless oil, ultraviolet spectrum (95% ethanol): λ_{max} (mμ): 215 (4.38), 250 (3.86), 296 (3.17), λ_{min} (mμ): 232 (3.61), 277 (3.03).

Anal. Calcd. for $C_{26}H_{40}O$: C, 84.72; H, 10.94. Found: C, 84.86; H, 10.98.

Preparation of Compounds that Serve as Spectral Models. 2,5-Dimethylacetophenone.—With 14.5 g. (0.11 mole) of aluminum chloride, 75 ml. of carbon disulfide, 10.6 g. (0.10 mole) of *p*-xylene and 7.8 g. (0.10 mole) of acetyl chloride, 6.3 g. of crude 2,5-dimethylacetophenone was prepared (b.p. 90° at 20 mm.) utilizing the same procedure as that recorded for the acylation of [6.6]paracyclophane. This crude oil was adsorbed on a chromatograph column of 150 g. of neutral activated alumina, and the product was eluted with 10% ether in pentane to give 4.8 g. of product, b.p. 106–107° (12 mm.), n^{25}D 1.5266, n^{30}D 1.5250 (literature[13] b.p. 101 at 9 mm., n^{30}D 1.5245).

This material was purified further as follows. A mixture of 1 g. of 2,5-dimethylacetophenone, 1.33 g. of semicarbazide hydrochloride, 2.0 g. of sodium acetate and 30 ml. of ethanol was heated under reflux for 15 minutes. The mixture was cooled, diluted with water, and the precipitate was collected and recrystallized from benzene to give 1.0 g. of white solid, m.p. 163–164°. Four recrystallizations from benzene gave 0.6 g. of material, m.p. 165.5–166.5° (literature,[13]

(13) C. T. Lester and E. C. Suratt, THIS JOURNAL, **71**, 2262 (1949).

m.p. 168–169°). This material was dissolved in 2 ml. of pyruvic acid and allowed to stand for 24 hours. Recovery of the ketone by the usual method gave 0.5 g. of colorless oil, boiling at a pot temperature of 120° at 20 mm., n^{25}D 1.5268.

1,4-Dimethyl-2-nitrobenzene.—This compound was prepared from 15 g. (0.141 mole) of *p*-xylene and 37.5 g. of fuming nitric acid by the reported procedure,[14] 15 g. of product (n^{25}D 1.5391) being obtained.

2,5-Dimethylacetanilide.—A mixture of 2.0 g. of 1,4-dimethyl-2-nitrobenzene, 0.1 g. of platinum oxide and 60 ml. of ethanol was stirred in the presence of hydrogen until the theoretical amount of hydrogen (980 ml.) was absorbed. The amine was isolated in the usual way and heated at 100° for 2.5 hours with a mixture of 5 ml. of acetic anhydride and 10 ml. of pyridine. The resulting amide was isolated and recrystallized from hexane–benzene to give 1.3 g. (83%) of white crystals, m.p. 139–141°. Two recrystallizations of this material from aqueous methanol gave 2,5-dimethylacetanilide, m.p. 141–142° (literature m.p. 139°).[15]

1,4-Dimethyl-2,5-diacetamidobenzene.—From 0.50 g. of 2,5-dimethylacetanilide, 0.47 ml. of concentrated nitric acid and 0.95 ml. of concentrated sulfuric acid was obtained 0.27 g. (42%) of 4-nitro-2,5-dimethylaniline as yellow crystals, m.p. 139–142° (literature m.p. 144–145°).[16] This procedure has been reported already.[16] A mixture of 0.2 g. of 4-nitro-2,5-dimethylaniline, 50 mg. of platinum oxide and 25 ml. of ethanol was shaken in an atmosphere of hydrogen until the theoretical amount of hydrogen was absorbed (90 ml.). The solution was filtered, evaporated, and the brown solid that remained was recrystallized three times from benzene to give 47 mg. of yellow needles of 1,4-diamino-2,5-dimethylbenzene, m.p. 141–144° (literature m.p. 150).[17] This material was heated at 100° for 30 minutes with a mixture of 0.35 ml. of acetic anhydride and 1.0 ml. of pyridine. The mixture was cooled, diluted with water, and the precipitate collected. The product was recrystallized three times from glacial acetic acid to give 20 mg. of a white powder (1,4-dimethyl-2,5-diacetamidobenzene) which did not melt below 320°.

Anal. Calcd. for $C_{12}H_{16}O_2N_2$: C, 65.43; H, 7.32. Found: C, 65.24; H, 7.45.

(14) H. R. Snyder and F. J. Pilgrim, *ibid.*, **70**, 3787 (1948).

(15) I. M. Heilbron and H. M. Bunbury, "Dictionary of Organic Compounds," Vol. III, Oxford University Press, New York, N. Y., 1938, p. 933.

(16) C. H. Fisher and C. T. Walling, THIS JOURNAL, **57**, 1701 (1935).

(17) E. Noelting and G. Thesmar, *Ber.*, **35**, 641 (1902).

LOS ANGELES 24, CALIFORNIA

Macro Rings. IX. Transannular Deactivating Influence in the Aromatic Substitution of [4.4]Paracyclophane[1]

BY DONALD J. CRAM AND R. W. KIERSTEAD

Acetylation of the [4.4]paracyclophane (I) gave an 85% yield of the monoacetyl derivative and very little either diacetylated or non-acetylated material. This behavior contrasts with that of the [6.6]paracyclophane which under the same conditions undergoes ready acetylation in both aromatic rings. In the smaller cycle, an acetyl group in one aromatic ring deactivates the other toward electrophilic substitution. Catalytic hydrogenation of [4.4]paracyclophane with three moles of hydrogen gave a 70% yield of product containing one cyclohexane ring, whereas a similar experiment with [6.6]paracyclophane gave a statistical distribution of starting material, half-reduced, and fully reduced cycles. In the smaller paracyclophane, the first ring reduces faster than the second. Nitration experiments on the half-reduced [4.4]paracyclophane provided nitro compound which was linked through an appropriate series of interconversions to the acetylated paracyclophane.

The previous paper in this series[2] reported the results of acetylation, nitration, and hydrogenation experiments carried out on [6.6]paracyclophane (II). In these reactions, each aromatic ring

(2) D. J. Cram and J. Abell, THIS JOURNAL, **77**, 1179 (1955).

behaved essentially independently of the other, and neither transannular deactivating nor directive influences of one ring on the other was evident. These results were expected since in II the benzene rings are thoroughly separated by rather long methylene bridges. On the other hand, compound I is the smallest cycle of its class that possesses a