mμ was then measured against the solvent as a blank. The wave length was chosen in most cases to provide an initial optical density reading in the neighborhood of 1.0. Runs were followed to at least two-thirds of completion. At least eight optical density readings, including one at infinite time, were recorded during each run. Rate constants, k, were evaluated from the slopes of the straight lines obtained by plotting log d values *vs.* t (see equation 1). At least ten minutes time was allowed for equilibration of the sample to cell housing temperature in runs in the 2 and 45° region, and zero time was then recorded as the time of the first optical density measurements. In the case of very fast runs at 25.2° timing was accomplished with a battery of stopwatches. In fast runs, in which it was necessary to establish the time of mixing diene and dienophile solutions with reference to the time of the first optical density reading, the two solutions were mixed by dropping a small beaker containing one into a larger beaker containing the other.

The optical densities measured at infinite time in these runs were always small and were presumed to result from traces of impurities in the reaction mixtures. These final readings were subtracted from individual readings taken during the runs to provide the values of d_c used in calculating rate constants by equation 1. The measured values of d_c included the absorption of both free and complexed diene. Within any one run in which the molar concentration of dienophile, (D), remained constant, d_c was related to the total concentration of both free and complexed diene, $(\mathrm{ArH})_\mathrm{T}$, by the expression

$$d_c = (\mathrm{ArH})_\mathrm{T}[\epsilon_{\mathrm{ArH}} + (\mathrm{D})K_1\epsilon_{\mathrm{ArH \cdot D}}]/[1 + K_1(\mathrm{D})] \quad (15)$$

In this equation ϵ_{ArH} and $\epsilon_{\mathrm{ArH \cdot D}}$ are the extinction coefficients of free and complexed diene, and K_1 is the equilibrium constant for formation of the complex. In some runs on dimethylanthracene and maleic anhydride the reaction rate was followed at one wave length until the diene concentration was a small fraction of its initial value. Then the wave length setting of the spectrophotometer was shifted downward to a region of more intense diene absorption and a new series of optical density measurements were made. Rate constants calculated from these two sets of data by equation 1 were always in excellent agreement with each other.

The Equilibrium Constant for Complex Formation.—A series of four or five solutions were prepared in which the dienophile concentration ranged from about 1.5–0 3 M and the diene concentrations were of the order of magnitude of 10^{-2}–10^{-3} M. The optical densities of these solutions *vs.* the solvent as blank were measured in 1 cm. absorption cells over a series of wave lengths in the 400–450 mμ region. In all cases the cell housing temperature was controlled to within 0.1° during the course of the measurements.

In solutions of dimethylanthracene and maleic anhydride Diels–Alder reaction occurred too rapidly to permit direct measurement of the optical densities of the freshly prepared solution. These were conveniently calculated by following the rates of the Diels–Alder reactions in these solutions at 450 mμ and extrapolating plots of log d_t *vs.* time back to the times of mixing.

The equilibrium constants, K_1, for complex formation were calculated by graphical analysis of the data according to the equation[20]

$$1/(\epsilon_a - \epsilon_\mathrm{D}) = 1/K_1(\mathrm{D})\,(\epsilon_{\mathrm{ArH \cdot D}} - \epsilon_\mathrm{D}) + 1/(\epsilon_{\mathrm{ArH \cdot D}} - \epsilon_\mathrm{D}) \quad (16)$$

in which $\epsilon_a = d/(\mathrm{ArH})_\mathrm{T}$. Values of ϵ_D obtained from separate measurements of diene-free solutions were generally small or zero over the wave length ranges of these investigations.

The Diels–Alder Adducts.—Product isolation experiments were designed to check the identity of two of the Diels–Alder adducts (A and B) formed under reaction conditions which were comparable to those used in the kinetic work.

(A) **9,10-Dimethyl-9,10-dihydroanthracene-9,10-endo-α,β-succinic Anhydride.**—A solution of 0.300 g. (0.00145 mole) of dimethylanthracene and 0.144 g. (0.00147 mole) of maleic anhydride in 10 cc. of chloroform was prepared at room temperature. Crystals began to precipitate from the deep orange solution almost immediately, and the solution rapidly became lighter in color. After one hour the white crystals (0.37 g.) were filtered. After recrystallization from ethyl acetate the product melted[8] from 331–333°.

(B) **9,10-Dimethyl-9,10-dihydroanthracene-9,10-endo-α-chloro-α,β-succinic Anhydride.**—A solution of 0.645 g. (0.00312 mole) of dimethylanthracene and 0.440 g. (0.00332 mole) of chloromaleic anhydride in 10 cc. of chloroform was allowed to stand overnight during which time its color changed from deep red to light yellow. The solvent was evaporated under reduced pressure, and the crystalline residue was triturated with ether to remove a yellow colored contaminant. The remaining white powder (0.54 g.) was recrystallized twice from aqueous acetic acid to yield the chlorine containing anhydride in the form of fine white needles of m.p. 173–175°.

Anal. Calcd. for $C_{20}H_{15}O_3Cl$: C, 70.90; H, 4.46. Found: C, 71.03; H, 4.53.

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[20] J. A. A. Ketelaar, C. van de Stolpe, A. Goudsmit and W. Dzcubas, *Rec. trav. chim.*, **71**, 1104 (1952).

DAVIS, CALIFORNIA

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

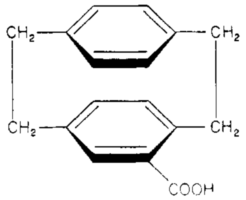
Macro Rings. XII. Stereochemical Consequences of Steric Compression in the Smallest Paracyclophane[1]

BY DONALD J. CRAM AND NORMAN L. ALLINGER

RECEIVED JUNE 28, 1955

The preparation, proof of structure and complete resolution of compound I is described, as well as the anomalous behavior of the parent hydrocarbon (II, $n = m = 2$) upon catalytic hydrogenation.

The preparation, properties and some reactions of the paracyclophanes II in which n and m have been varied from 2 to 6 have been described in previous publications.[2] When the value of either n or m became smaller than 4, the spectral properties of the compounds became abnormal, the departures from normality increasing as the two benzene rings



I

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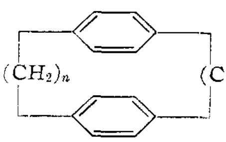
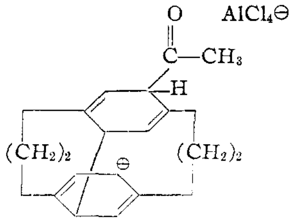
[1] This research was supported in part by a generous grant from The Upjohn Company, and in part was conducted under contract AF 33(616)-146 with the United States Air Force, the sponsoring agency being the Aeronautical Research Laboratory of the Wright Air Development Center, Air Research and Development Command.

[2] Paper XI in this series, D. J. Cram and M. Cordon, THIS JOURNAL, **77**, 4090 (1955).

were thrust closer together.[3] Certain substitution reactions of II with $n = m = 6$ were investigated,[4] and since the behavior of the aromatic nuclei of the substance proved typical of that of isolated benzene rings, the compound served as a model for comparison with the lower members of the homologous series. Experiments with II in which $n = m = 4$ indicated that in certain substitution reactions, transannular deactivating effects were present, although the ultraviolet absorption spectrum of the parent hydrocarbon was normal.[5]



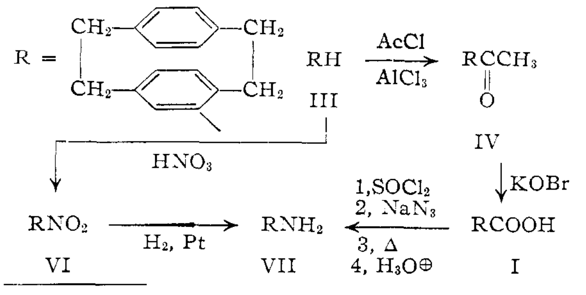
II



V

The present paper is concerned with an investigation of the chemistry of the smallest paracyclophane II, that in which $n = m = 2$. Because of the proximity of the aromatic rings in this compound, the transannular effects should be at a maximum. This feature coupled with the strain (the benzene rings are not planar)[6] inherent in the system might be expected to lead to atypical reactions.

Substitution Reactions of [2.2]Paracyclophane (III).—Acetylation of [2.2]paracyclophane had to be carried out under very mild conditions (−20°, 10 minutes), as under the conditions most suitable for acylation of the larger cycles (II, $n = m = 4$ or 6)[4,5] only polymeric products could be isolated. This non-distillable material possessed an absorption maximum in the ultraviolet (λ 252, ε 6,000) similar to that reported[7] for *p*-methylacetophenone (λ 253, ε 14,100), a fact which suggests that acetylation occurred accompanied by a ring-opening polymerization of the strained system. That the monoacetylated product IV was obtainable under conditions under which the large hydrocarbons (II, $n = m = 4$ or 6) suffered negligible reaction points to a stabilization of the transition state leading to IV, possibly through transannular resonance of the type formulated in V. Unlike the large cycles (II, $n = m = 4$ or 6), cycle III gave no detectable diacetylated material, apparently because an acetyl group in one ring thoroughly protected *both rings* from further electrophilic substitution.

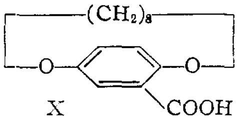


Nitration of III gave the mononitroparacyclophane VI in 33% yield plus a large number of other products of a complex nature. Attempts to nitrate the two larger cycles (II, $n = m = 4$ or 6) resulted in non-resolvable mixtures.

Evidence that the ring system (R) was preserved intact during these two substitution reactions was obtained by converting nitro compound VI and acetyl compound IV into the same amine VII through the use of conventional reactions (see formulas). Attempts to reduce the diazonium salt of amine VII to the starting paracyclophane III with both hypophosphorous acid and alkaline formaldehyde were unsuccessful. Simple 2,5-disubstituted anilines are ordinarily reduced to the corresponding hydrocarbons by either of these reducing agents,[8] but in the present case none of the desired hydrocarbon could be isolated. Instead a mixture of products was obtained from which chloride VIII and phenol IX were separated in 20 and 22% yields, respectively. The chloride was identified by comparison with a sample prepared deliberately (27% yield) from the same diazonium salt by the Sandmeyer reaction. The phenol was identified by its analysis and ultraviolet spectrum,[9] which showed a characteristic shift taken in basic as compared to acidic solution.[10]

$$\underset{\text{VII}}{R{-}NH_2} \xrightarrow[\text{HCl}]{\text{HNO}_2} (R{-}N_2^{\oplus}Cl^{\ominus}) \xrightarrow{\text{H}_3\text{PO}_2} \underset{\text{VIII}}{R{-}Cl} + \underset{\text{IX}}{R{-}OH}$$

Resolution of 4-Carboxy[2.2]paracyclophane (I).—Simple monosubstituted products of III (such as I, IV, VI to IX) are potentially optically active since, as shown by models, the aromatic rings are not free to rotate and the molecules consequently contain no plane of symmetry. These compounds are in this respect analogous to X, which was prepared in optically active form by Lüttringhaus and Gralheer.[11] Evidence for the presence of these geometric restrictions in carboxylic acid I was obtained through its complete resolution. Five recrystallizations of the brucine salt of this acid gave material whose rotation did not change upon further recrystallization, and which gave a free acid with $[\alpha]^{24}\text{D}$ −157°, m.p. 211.5–213° (racemic acid, m.p. 223.5–224.5°). Attempts to obtain the other enantiomer *via* various alkaloid salts were unsuccessful, but the acid ($[\alpha]^{23}\text{D}$ +161°, m.p. 212–214°) was obtained by direct fractional crystallization of the material from the first crystallization of the brucine salt. That virtual optical purity was obtained is suggested by the proximity of the magni-



X

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[3] D. J. Cram, N. L. Allinger and H. Steinberg, THIS JOURNAL, **76**, 6132 (1954).

[4] D. J. Cram and J. Abell, *ibid.*, **77**, 1179 (1955).

[5] D. J. Cram and R. W. Kierstead, *ibid.*, **77**, 1186 (1955).

[6] C. J. Brown, *J. Chem. Soc.*, 3265 (1953).

[7] W. A. Sweeney and W. M. Schubert, THIS JOURNAL, **76**, 4625 (1954).

[8] N. Kornblum, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 262.

[9] The spectra of the compounds prepared in this paper will be recorded and discussed in a future paper of this series.

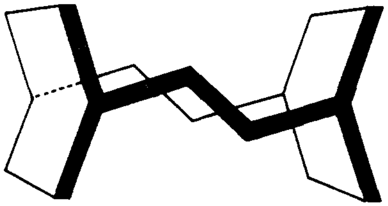
[10] H. H. Hodgson, *J. Chem. Soc.*, 380 (1943).

[11] A. Lüttringhaus and H. Gralheer, *Ann.*, **557**, 112 (1947).

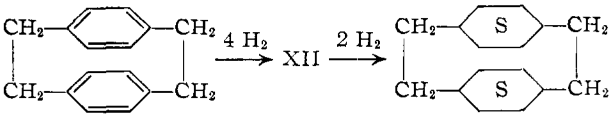
tudes of the rotations and melting points of these enantiomers.

Since the optical activity of I was due to the asymmetry introduced into the molecule by substitution, removal of the substituent from an optically active sample of acid I was expected to furnish optically inactive hydrocarbon III. Such was found to be the case. An optically pure sample of I was decarboxylated with copper powder in quinoline[12] to give a hydrocarbon in 65% yield. This hydrocarbon was identified by mixed melting point comparisons with authentic III, and by its infrared spectrum, and was found to have $[\alpha]^{25}_{\mathrm{D}}$ −0.1 ± 0.5°. This experiment demonstrated that: (1) the ring structure present in III was intact in acid I; (2) the optical activity of I was destroyed concurrent with the loss of the substituent and was thus dependent on the latter.

The Anomalous Course of the Catalytic Reduction of [2.2]Paracyclophane (III).—When cycle III was reduced exhaustively with hydrogen (platinum and glacial acetic acid), six moles of hydrogen were absorbed to give a fully saturated, nicely crystalline product. This compound was shown to be tricyclic by elemental analysis, molecular weight and by the demonstration through its infrared and ultraviolet absorption spectra that multiple bonds were absent. These facts coupled with the constitution of the starting material establish that the substance possesses structure XI, which may be looked upon as a twelve-membered carbocyclic ring carrying two two-membered methylene bridges. Since even cyclododecane itself is somewhat strained due to hydrogen–hydrogen compression,[13] the introduction of the extra two rings and four methylene groups should make XI one of the most internally crowded molecules known. Scale models suggest that in the substance a gross violation of the van der Waals radii and/or a severe distortion of bond angles must occur.[14]


XI

Three hexahydroparacyclophanes with $n = m = 4$ and 6, and with $n = 3$, $m = 4$ were prepared earlier and found to possess essentially normal ultraviolet absorption spectra,[3] a fact which is indicative of a planar aromatic ring. While in the [6.6]paracyclophane the two aromatic rings reduced quite independently of one another,[4] in the [4.4]paracyclophane the first ring hydrogenated at an appreciably greater rate than did the second.[3] Reduction of only one of the two aromatic rings of [2.2]paracyclophane should give a product carrying a badly distorted benzene ring,[15] and extrapolating from the behavior of the homolog with $n = m = 4$, the first ring should reduce much more rapidly than the second. When three moles of hydrogen was added to III, a solid waxy octahydro derivative (XII) was obtained (62% yield) along with recovered starting material (20% yield). When four moles of hydrogen was added, the octahydro compound was obtained in 91% yield. A hydrogenation curve (moles of hydrogen absorbed *vs.* time) was run, and in agreement with these results a sharp break in the curve occurred after four moles of hydrogen had been absorbed. This break in the curve was so pronounced in some runs that the reaction came to a full stop after four moles of hydrogen had been consumed.



III XI

The structure of this octahydro derivative is of interest since this is the first reported case of a partial catalytic reduction of a classically isolated benzene ring. The compound proved to be rather unstable; a sample polymerized when left at room temperature for eight hours, but it could be stored for two days under the nitrogen in the dark at −20° with little deterioration. Elemental analysis of the substance confirmed the empirical formula inferred from the uptake of hydrogen during its formation, and its relative volatility (b.p. *ca.* 150°, 5 mm.) suggests a monomeric structure. This octahydro compound upon further reduction absorbed two additional moles of hydrogen to give the fully saturated tricycle XI. The ultraviolet absorption spectrum of this diene XII possesses no maximum above 208 mμ and therefore the double bonds are presumed to be unconjugated.[16] Distortion of a conjugated diene from a planar configuration would exert a small hypsochromic effect, but no physically reasonable amount of distortion in the ring system possessed by diene XII could shift the maximum out of the observable region.[17] The end absorption shown by diene XII is as follows: λ_{220}, ϵ 1,860; λ_{215}, ϵ 4,020; λ_{210}, ϵ 6,460. The corresponding absorption has been measured in many steroidal olefins,[18] and for those which are trisubstituted the constants are: λ_{220}, ϵ 200–1,600; λ_{215}, ϵ 780–3,100; λ_{210}, ϵ 1,950–4,300. If the double bonds in XII are electronically independent and their absorption is additive, the absorption for each double bond is half the total, and these values lie within the range defined by the model compounds. A structure for

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(12) D. M. Hughes and J. C. Reid, *J. Org. Chem.*, **14**, 516 (1949).

(13) V. Prelog, *J. Chem. Soc.*. 420 (1950).

(14) The crystal structure of XI is currently being investigated in this Laboratory by Dr. K. N. Trueblood by the X-ray method.

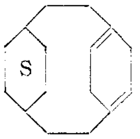
(15) As the 1,4-carbons of a benzene ring are pulled together to form a boat, the Dewar and Ladenburg formulas for benzene might be expected to make greater contributions to the resonance hybrid.

(16) A six-membered ring carrying two double bonds and two alkyl substituents can be calculated to have $\lambda_{\max}$ 268–273 mμ (L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," 3rd Ed., Reinhold Publishing Corp., New York, N. Y., 1949, p. 187).

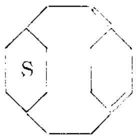
(17) A. T. Blomquist and A. Goldstein, THIS JOURNAL, **77**, 998 (1955), have reported that *cis-trans*-1,3-cyclodecadiene has no maximum above 215 mμ in the ultraviolet. Such a phenomenon is not expected in the present case, as the double bonds are necessarily more nearly in the same plane, and the bathochromic effect of a homocyclic diene in a six-membered ring is quite large compared to that observed in a ten-membered ring [see also E. A. Braude, *Chemistry and Industry*, 1557 (1954); R. W. Fawcett and J. O. Harris, *J. Chem. Soc.*, 2673 (1954)].

(18) P. Bladon, H. B. Henbest and G. W. Wood, *Chemistry & Industry*, **866** (1951); *J. Chem. Soc.*, 2737 (1952).

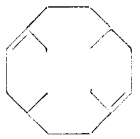
XII in which the double bonds were disubstituted should lie well out of this range.[18] The infrared spectrum of XII is also in agreement with the presence of trisubstituted double bonds. The strongest band between 7 and 15 μ was located at 12.40 μ, which is within the range in which the out-of-the-plane hydrogen bonding is found for trisubstituted olefins.[19] A medium band at 6.02 μ was also observed (C═C stretching). No bands which could be attributed to other kinds of substituted olefins were observed. The spectrographic evidence thus appears to limit the likely structures for diene XII to XIIa, and to structural types represented by XIIb (exocyclic) and XIIc (heteroannular). Of these, only XIIa can be constructed with scale molecular models. The relative freedom of structure XIIa from strain coupled with the decided drop in hydrogenation rate of paracyclophane III after XII was formed makes XIIa possibly the best hypothetical structure for the diene XII. Chemical degradative work on XII is in progress.



XIIa

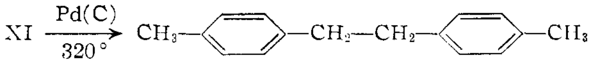


XIIb



XIIc

The results of dehydrogenation of the fully saturated tricycle XI with palladium-on-charcoal also afforded chemical evidence for the ring strain present in III and its hydrogenated derivatives. The isolable product of the reaction, XIII, resulted from both hydrogenolysis and dehydrogenation of III. No paracyclophane III could be detected in the reaction product, although unique properties of III make its presence in mixtures easily discernible.



XIII

Experimental[20]

4-Nitro[2.2]paracyclophane (VI).—Hydrocarbon III,[21] 2.60 g., was dissolved in 260 ml. of boiling acetic acid and the resulting solution was rapidly cooled to 70° with vigorous shaking. Fuming nitric acid, 32.5 ml., was then added to the fine suspension in one portion and, after shaking for 1 minute, the clear dark solution was poured rapidly with stirring into 800 ml. of cold water. After a few minutes the yellow solid was collected and washed with water. The material was then taken up in ether, the ether layer was washed and dried, and the ether was evaporated. The residual solid was dissolved in 20 ml. of ether and placed on a chromatographic column containing 50 g. of alumina (activity III).[22] The column was then washed with ether-pentane, 4:1, 30-ml. fractions being collected. Fractions 3–6 contained a total of 0.72 g. of crude nitro compound, m.p. 145–150°. Later fractions were eluted with progressively more polar solvents, up to pure methanol, but only tars were obtained. Fractions 1 and 2 were combined and rechromatographed using chloroform:pentane, 1:4, as eluent. Fraction 1 contained 0.11 g. of starting material, m.p. 277–281°. Fraction 2 was a mixture, wt. 0.05 g., m.p. 150–240°. Fractions 3–6 gave an additional 0.61 g. of crude nitro compound. The total nitro compound, 1.33 g., was crystallized from ethanol to yield faintly yellow needles, wt. 1.06 g. (33%), m.p. 155.5–156.5°. The infrared spectrum showed bands at 6.27 μ (medium), 6.60 μ (very strong), 6.87 μ (medium), 7.45 μ (very strong), 11.08 and 11.46 μ (medium).

Anal. Calcd. for $C_{16}H_{15}NO_2$: C, 75.56; H, 6.34. Found: C, 75.50; H, 6.09.

4-Amino[2.2]paracyclophane (VII).—The nitro compound VI, 0.40 g., was reduced with 30 mg. of platinum oxide in 20 ml. of absolute methanol. The theoretical amount of hydrogen was taken up in 10 minutes, the catalyst was collected and the filtrate was concentrated to a volume of 10 ml. After cooling this solution to −10°, the product that separated was collected, slightly brownish plates or granules, m.p. 239–241.5° dec., wt. 0.24 g. A second crop of the same melting point brought the total yield to 0.31 g. (88.5%). The infrared spectrum of the amine possessed the following bands: 2.92 and 2.98 μ (medium) (N–H str.); 6.19 μ (very strong) (N–H def.); 6.66 and 7.01 μ (strong); 7.82 μ (medium); 8.30 μ (strong); 10.25 and 10.80 μ (medium); 11.23 and 11.58 μ (medium).

Anal. Calcd. for $C_{16}H_{17}N$: C, 86.05; H, 7.68. Found: C, 86.09; H, 7.69.

4-Acetyl[2.2]paracyclophane (IV).—To a solution of 9.5 g. of powdered anhydrous aluminum chloride and 6.25 g. of acetyl chloride in 75 ml. of *sym*-tetrachloroethane at −30° was added in one portion 8.32 g. of [2.2]paracyclophane. The mixture was kept at −15 to −20° with stirring for 10 minutes, and was then cooled to −40° while 30 ml. of *N* hydrochloric acid was added. The aqueous phase was separated and extracted with chloroform. The organic phases were washed with water, dilute bicarbonate solution and water. After drying the organic phase, the solvent was evaporated and the product was distilled at a bath temperature of 190–205° (4 mm.). The crude product, 7.96 g., solidified and was crystallized from aqueous ethanol to yield 7.52 g. of white plates (71%), m.p. 106.8–108.2°. The analytical sample was twice recrystallized, m.p. 109.7–110.4°. The infrared spectrum showed the following bands: 5.96 μ (very strong) (conj. C═O str.); 6.29 μ and 6.45 μ (medium) (benzoyl); 6.65 μ (medium) (phenyl); 7.93 μ (very strong); 8.42 μ (strong); 10.52 μ (medium); 11.15 μ (medium) (1,3,4-trisubstituted phenyl); 11.76 μ (medium) (*p*-substituted phenyl); 12.64 μ (medium); 13.81 μ (strong) (the region above 12 μ in carbon disulfide).

The ketone was found to crystallize in another polymorphic form when, in another run similar to that described above, the product was obtained as minute needles, m.p. 91.9–92.7°. That the compounds were polymorphs was shown by converting each form into the other by recrystallizing each form by seeding with the other.

Anal. Calcd. for $C_{18}H_{18}O$: C, 86.36; H, 7.25. Found: C, 86.56; H, 7.43.

The filtrates from the crystallization of IV were concentrated, and the organic material was extracted with ether. The ether phase was washed and dried and the ether was evaporated. The remaining oil, 0.14 g., was chromatographed on alumina, and the resulting fractions were converted to dinitrophenylhydrazones. The derivative of the last fraction weighed 20 mg., m.p. 125–140°. Two recrystallizations of this material gave 5 mg. of orange needles, m.p. 165.8–167.1°. This compound was not identified.

Anal. Found: C, 63.18; H, 5.59.

Dinitrophenylhydrazone of IV.—The usual procedure gave red-orange needles, m.p. 196.4–198.2° after two crystallizations from ethanol, λ 381, ϵ 23,500 (chloroform).

Anal. Calcd. for $C_{24}H_{22}O_4N_4$: C, 66.96; H, 5.15. Found: C, 67.19; H, 5.27.

The infrared and ultraviolet spectra of the residue remaining after the original distillation of the ketone were recorded: λ 252, ϵ 6,000 (chloroform); 5.97 μ (strong).

4-Carboxy[2.2]paracyclophane (I).—Bromine, 14.6 g., was added during 10 minutes to a stirred solution of 11.5 g. of potassium hydroxide in 60 ml. of water at 0°. A solution of 6.94 g. of ketone IV in 105 ml. of pure dioxane was then added to the hypobromite solution during a similar period

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(19) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, p. 31.

(20) All m.p.'s are corrected, b.p.'s are uncorrected. Ultraviolet spectra were determined on a Cary recording spectrophotometer, model 11 PMS, in 95% ethanol, and infrared spectra were recorded on a Perkin-Elmer recording spectrophotometer, model 21, 10% in $CHCl_3$ unless otherwise specified.

(21) D. J. Cram and H. Steinberg, THIS JOURNAL, **73**, 5691 (1951).

(22) H. Brockmann and H. Schodder, *Ber.*, **74B**, 73 (1941).

with continued cooling and stirring. After an additional 10 minutes the ice-bath was removed, and the solution was allowed to warm and stand at room temperature for 1.5 hours. The excess oxidizing agent was destroyed by adding a solution of 2 g. of sodium bisulfite in 250 ml. of water. After extracting the mixture with chloroform, the aqueous phase was acidified, and the crude product was collected, a white powder, m.p. 222.5–224°, wt. 7.20 g. The crude acid was dissolved in 80 ml. of boiling acetic acid, and the solution was filtered free of a little salt. After addition of a little water to the solution, the compound crystallized as stout needles, m.p. 223.5–224.5° with previous sintering, wt. 6.30 g. (90%).

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 80.78; H, 6.43.

Resolution of 4-Carboxy[2.2]paracyclophane.—The quinine salt of I was nicely crystalline, but gave no resolution upon crystallization from acetone. Only the free alkaloid crystallized from solutions of the cinchonine salt in various solvents. The brucine and cinchonidine salts both gave the (−)-form of the acid, with the former resolving more rapidly.

The salt was prepared by dissolving 5.67 g. of (±)-I and 10.5 g. of brucine in 250 ml. of acetone. The solution was allowed to stand 18 hours at room temperature and 4 hours at 0°. The first crop of salt was collected as fine needles, wt. 4.4 g. The filtrate was diluted with 150 ml. of water, and after standing at −10° for 18 hours, was filtered to yield a second crop of crystals, wt. 4.6 g. These crops of crystals were fractionally recrystallized, four recrystallizations of the first crop furnishing 1.1 g. of the optically pure salt. The second crop and filtrates, after several recrystallizations, yielded an additional 1.65 g. of the pure salt, which was obtained as stout needles, m.p. 212–216° dec. The melting point was not a useful criterion of optical purity, but the resolution could be followed by measuring the rotation of the salt; the pure salt had $[\alpha]^{22}\mathrm{D}$ −96.1 ± 0.9° (chloroform 0.9–1.1%). The free acid was obtained from 2.60 g. of the pure salt by shaking the latter with 30 ml. of *N* hydrochloric acid and 100 ml. of ether. The aqueous phase was separated and extracted with ether. The ether extracts were washed with *N* hydrochloric acid, water and were dried. The residue remaining after evaporation of the solvent was crystallized from acetic acid to yield white plates of (−)-I, wt. 1.46 g. (54%), m.p. 211.5–213°, $[\alpha]^{24}\mathrm{D}$ −157° (chloroform, 0.93). That this material does not correspond to a eutectic mixture is shown by the fact that a sample of the partially resolved acid which had $[\alpha]^{24}\mathrm{D}$ −106° showed m.p. 205–207°.

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 80.85; H, 6.48.

The filtrates from the above resolution were combined, and the acid was recovered from the salt in a manner similar to that described above. The acid obtained, 3.48 g., had $[\alpha]^{21}\mathrm{D}$ +56°, m.p. 206–215°. A sample of this material, 0.96 g., was crystallized from acetic acid to yield poorly defined crystals, 0.72 g., m.p. 217–222°, $[\alpha]^{23}\mathrm{D}$ +39°. The filtrate was diluted with water, and a second crop of crystals was taken. The latter proved to be essentially optically pure (+)-I, plates, m.p. 212–214°, $[\alpha]^{23}\mathrm{D}$ +161° (chloroform, 0.943).

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 80.82; H, 6.50.

Decarboxylation of (+)-4-Carboxy[2.2]paracyclophane.—A mixture of 98 mg. of the pure acid, $[\alpha]^{23}\mathrm{D}$ +161°, 0.1 g. of copper powder and 2 ml. of quinoline was heated under reflux for 1.5 hours. The solution was then filtered and diluted with 10 ml. of chloroform. The chloroform solution was washed with *N* hydrochloric acid and water, dried and the solvent was evaporated. The residual solid was crystallized from acetic acid to give 53.4 mg. (66%) of crude hydrocarbon III, m.p. 278–281°. This material was taken up in 10 ml. of chloroform and the solution was poured on a column of 15 g. of alumina (I).[22] The column was washed with 20% chloroform in pentane. The first 30-ml. fraction collected was evaporated to dryness, and the residue was crystallized from acetic acid to yield pure III, m.p. 281–284°, wt. 39.7 mg. (49%). A pure authentic sample of III had m.p. 283–285.7°, mixed m.p. 282–285.4°. The two samples had identical infrared spectra. The optical rotation of the sample from the decarboxylation was measured, $[\alpha]^{25}\mathrm{D}$ −0.1 ± 0.5° (chloroform, 0.716).

(−)-4-Amino[2.2]paracyclophane (VII).—Acid I, $[\alpha]^{24}\mathrm{D}$ −157°, 1.33 g., was converted to the acid chloride by mixing it with 1.15 g. of phosphorus pentachloride in 5 ml. of benzene. The mixture was heated on the steam-bath for 15 minutes, and the volatile materials were then removed in vacuum. The crystalline acid chloride thus obtained was dissolved in 30 ml. of C.P. acetone, and after the solution had been cooled to 0°, it was added in one portion to a stirred solution of 1.31 g. of sodium azide in a mixture of 15 ml. of water and 10 ml. of acetone also at 0°. The mixture was allowed to stand at room temperature for 20 minutes, then 80 ml. of water was added and after cooling the mixture to 0°, the azide was collected and dried under vacuum at room temperature, white plates, wt. 1.38 g. The azide was then dissolved in 25 ml. of toluene and was converted to the isocyanate by heating the solution under reflux for 20 minutes. Approximately the theoretical amount of nitrogen was evolved. Thirty ml. of concentrated hydrochloric acid was then added to the solution, and the mixture was heated under reflux for 48 hours. The cooled solution was filtered, and the solid amine hydrochloride, 0.8 g., was removed by filtration. The toluene layer was separated, extracted with dilute hydrochloric acid and discarded. The acid extracts were combined and made basic with solid potassium hydroxide and, after the resulting solution had been cooled, the amine was filtered. The solid amine hydrochloride obtained above was heated under reflux for a few minutes with a mixture of 50 ml. each of chloroform and of 10% potassium hydroxide. The chloroform layer was separated, washed and dried and the solvent was evaporated. The residual amine was combined with that obtained above and crystallized from hexane to furnish a tan solid, wt. 0.71 g. (60%), m.p. 239–241.5° dec., $[\alpha]^{24}\mathrm{D}$ −71.5° (chloroform, 0.845).

Anal. Calcd. for $C_{16}H_{17}N$: C, 86.05; H, 7.68. Found: C, 86.09; H, 7.69.

(−)-4-Acetamido[2.2]paracyclophane.—Amine VII, $[\alpha]^{24}\mathrm{D}$ −71.5°, 35 mg., was heated on the steam-bath for 1 hour with 2 ml. each of acetic anhydride and pyridine. The solution was cooled, diluted with water and the product was filtered. Recrystallization of the material from benzene–pentane gave poorly defined crystals, m.p. 208–210°, $[\alpha]^{22}\mathrm{D}$ −177° (chloroform, 0.31).

Anal. Calcd. for $C_{18}H_{19}NO$: C, 81.47; H, 7.22. Found: C, 81.52; H, 7.30.

(±)-4-Amino[2.2]paracyclophane.—The racemic amine was prepared from racemic I by the Curtius reaction as described for preparation of the optically active amine. The product had m.p. 239–242°, and showed no mixed melting point depression with a sample prepared from the nitro compound VI.

(±)-4-Acetamido[2.2]paracyclophane.—The acetylation of the racemic amine was carried out in a manner similar to that described for acetylation of the optically active form. From 25 mg. of the amine was obtained 22 mg. of the acetamido compound as white needles, m.p. 206.7–207.6°.

Anal. Calcd. for $C_{18}H_{19}NO$: C, 81.47; H, 7.22. Found: C, 81.36; H, 7.22.

(±)-4-Chloro[2.2]paracyclophane (VIII).—Amine VII racemic, 300 mg., was suspended in 5 ml. of concentrated hydrochloric acid, and after stirring for a few minutes, the mixture was cooled to 0°. A solution of 97.5 mg. of sodium nitrite in 2 ml. of water was added dropwise, and after stirring an additional 5 minutes at 0°, the mixture was added to 0.4 g. of cuprous chloride[23] dissolved in 5 ml. of concentrated hydrochloric acid also at 0°. The resulting mixture was allowed to warm to room temperature and stand for 3 hours and was then warmed on the steam-bath for 30 minutes. The mixture was then extracted with ether, the ether layer was washed and dried and the solvent was evaporated. The residue was dissolved in 10 ml. of ether and the solution was placed on a column of 30 g. of alumina III. The elution was carried out with 10% ether in pentane, 25-ml. fractions being collected. Fractions 1 and 2 were combined and recrystallized from aqueous ethanol to yield VIII as plates, wt. 90 mg. (27%), m.p. 160–162°.

Anal. Calcd. for $C_{16}H_{15}Cl$: C, 79.16; H, 6.23. Found: C, 79.07; H, 6.34.

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(23) C. S. Marvel and S. M. McElvain, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1948, p. 170.

Attempted Conversion of VII to III.—The diazonium salt from 108 mg. of racemic amine VII was prepared as described under the preparation of chloride VIII. To the resulting solution at 0° was added 2.70 g. of hypophosphorous acid (30%) precooled to 0°. The resulting solution was left at 0° overnight, after which time the brown solid which had separated was filtered. Sublimation of the material gave two fractions as yellow solids: (1) wt. 50 mg., bath temp. 110–140° (2 mm.); and (2) wt. 20 mg., bath temp. 270° (1 mm.). No definite compounds were isolable from fraction 2 upon chromatography. Fraction 1 was chromatographed on 15 g. of alumina III[22] with pentane, 25-ml. fractions being collected. Fraction 1 contained nothing. Fraction 2 contained 20 mg. (20%) of chloride VIII. Crystallization of this material from aqueous ethanol gave plates, m.p. 154–159°, undepressed by admixture with an authentic sample of VIII. Fractions 3–5 contained nothing. Fractions 6–7, eluted with ether, furnished 20 mg. (22%) of what proved to be crude 4-hydroxy[2.2]paracyclophane. Crystallization of this material from aqueous ethanol furnished 8 mg. of fine needles, m.p. 225–229°.

Anal. Calcd. for $C_{16}H_{16}O$: C, 85.67; H, 7.19. Found: C, 85.41; H, 7.05.

An attempt to reduce the diazonium salt from 26 mg. of VII with alkaline formaldehyde gave only 4 mg. of sublimable material, m.p. 260–268°. Recrystallization of this material was unsuccessful.

Perhydro[2.2]paracyclophane (XI).[24]—Hydrocarbon III, 204 mg., was hydrogenated in 20 ml. of acetic acid in the presence of one gram of pre-reduced platinum. The theoretical amount of hydrogen was taken up in 24 hours. The product had partly crystallized and was dissolved by the addition of ether. The catalyst was removed by filtration, and after concentration of the solution, the product crystallized and was collected. Recrystallization of the product from ethanol gave plates, m.p. 113.5–114.2°, wt. 138 mg. (64%). The ultraviolet spectrum of this compound showed no absorption above 215 mμ. The infrared showed no absorption in the 6 μ region attributable to C=C stretching.

Anal. Calcd. for $C_{16}H_{28}$: C, 87.19; H, 12.81; mol. wt., 220. Found: C, 87.19; H, 12.64; mol. wt. (Rast), 200.

Octahydro[2.2]paracyclophane (XII).—Hydrocarbon III, 428 mg., was reduced using 0.2 g. of platinum oxide catalyst in a solvent mixture containing 50 ml. of ethyl acetate and 25 ml. of acetic acid. The reaction was interrupted after 4 moles of hydrogen had been added (12 hours). The catalyst was removed by filtration and the solvent was evaporated. The residue was distilled at a bath temperature of 150° (5 mm.), and solidified to a waxy solid, m.p. 94–97°, wt. 400 mg. (91%). Chromatography on alumina indicated that the material was homogeneous. The ultraviolet spectrum showed no maximum above 208 mμ, and end absorption was as follows: λ_{230}, ϵ 259; λ_{220}, ϵ 1,860; λ_{215}, ϵ 4,020; λ_{210}, ϵ 6,460. The infrared spectrum showed bands at 6.02 μ (medium) and 12.40 μ (strong) (carbon disulfide). The compound was sweet-smelling, showed no Bayer test for unsaturation and reacted with bromine only very slowly and with concurrent evolution of hydrogen bromide. The compound dissolved in concentrated sulfuric acid to give a yellow solution from which a hydrocarbon layer was obtained upon dilution with water. The compound could be stored in the dark under nitrogen at −20° for a day or two. After a day in the room, it was largely converted to a pentane-insoluble white glass. The material gave poorly defined crystals from ethanol.

Anal. Calcd. for $C_{16}H_{24}$: C, 88.83; H, 11.17. Found: C, 88.69; H, 11.20.

In another experiment, with 390 mg. of III, the reaction was carried out as above only it was interrupted after 3 moles of hydrogen had been taken up. The crude product was obtained as previously, and was boiled briefly with 20 ml. of pentane. The insoluble starting material, 65 mg., was removed by filtration, and the pentane solution was chromatographed on 60 g. of alumina I, 20-ml. fractions being collected. Fractions 2–5 gave a total of 243 mg. (62%) of the octahydro compound. The column was then washed with chloroform to yield an additional 20 mg. of starting material. The total recovered III was thus 85 mg. (22%).

When a methylene chloride solution of the octahydro compound was treated with ozone at 0°, an insoluble polymer separated shortly before completion of the reaction. The solution and polymer were treated with hydrogen peroxide, but the latter remained unreacted, and no ketonic derivative could be obtained from the solution with dinitrophenylhydrazine. The reaction was repeated at −80° with identical results.

The octahydro compound, 200 mg., in 25 ml. of acetone, was heated with 1 g. of potassium permanganate for 8 hours. The mixture was filtered and the acetone was evaporated from the filtrate. The residue, a white waxy solid, weighed 180 mg., and had an ultraviolet spectrum identical with that of the starting material.

Dehydrogenation of Perhydro[2.2]paracyclophane (XI).—A sample of XI, 126 mg., and 10 mg. of palladium-on-charcoal were heated at 210–320° during 45 minutes. After this time the hydrogen evolution had ceased, a total of 38 ml. (45%) having been evolved. The residue was dissolved in chloroform and the solution was filtered free of catalyst. The chloroform was evaporated from the filtrate and the residue was taken up in pentane and chromatographed on 20 g. of alumina I, 10-ml. fractions being collected. Fractions 1–3 combined yielded 32 mg. of a white solid, which when recrystallized had m.p. 110.5–112°, and was shown to be starting material by mixed melting point and lack of ultraviolet spectrum. Fractions 5 and 6 contained a white solid, 43 mg., which was recrystallized to yield 4,4′-dimethylbibenzyl (XIII) as plates, m.p. 77–79°. An authentic sample[21] had m.p. 81.5–82.3°, and the mixed m.p. was 78–80.5°. The ultraviolet spectrum of this substance was superimposable on that reported for the authentic compound.

A similar dehydrogenation was carried out on XII, and a similar work-up procedure gave a 72% yield of XIII and oily materials which were not investigated.

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[24] The authors are indebted to I. Lieberman who first prepared this compound.