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): $\lambda_{\max}$ (mμ): 215 (4.38), 250 (3.86), 296 (3.17), $\lambda_{\min}$ (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] 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.

LOS ANGELES 24, CALIFORNIA

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

[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).

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

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

BY DONALD J. CRAM AND R. W. KIERSTEAD

RECEIVED AUGUST 9, 1954

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 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

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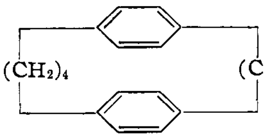
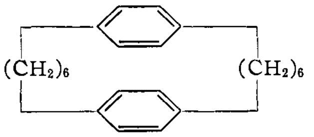
[1] This work was sponsored by the Office of Ordnance Research, U. S. Army.

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



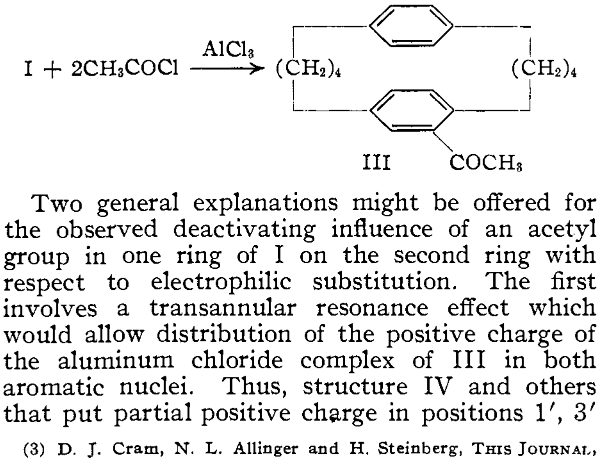
I



II

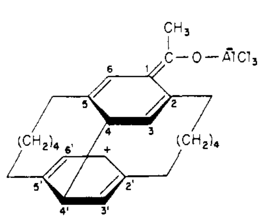
normal ultraviolet absorption spectrum,[3] and apparently in this compound, the benzene rings are just outside each other's electronic and steric environments. This paper is concerned with the question of whether the two aromatic rings of I are close enough to one another to affect one another's reactivity in the acetylation and hydrogenation reactions.

Acetylation of [4.4]Paracyclophane (I).—Acetylation of paracyclophane I with 2 moles of acetyl chloride gave a minimum of an 85% yield of monoacetyl compound III, 2% of starting material and 7% of a mixture of materials, some of which was diacetylated paracyclophane of undetermined structure. These results contrast with those obtained[2] in the [6.6]paracyclophane (II) where the approximate product balance was as follows: 1% yield monoacetyl derivative, 63% yield of diacetyl derivatives, 9% recovered starting material. Unlike the monoacetyl[6.6]paracyclophane, the rate of acetylation of III is considerably lower than the rate of acetylation of I.[4]



III

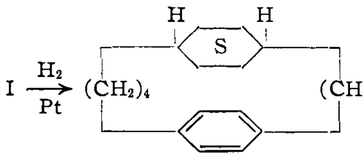
Two general explanations might be offered for the observed deactivating influence of an acetyl group in one ring of I on the second ring with respect to electrophilic substitution. The first involves a transannular resonance effect which would allow distribution of the positive charge of the aluminum chloride complex of III in both aromatic nuclei. Thus, structure IV and others that put partial positive charge in positions 1′, 3′ and 5′ as well as in positions 2, 4 and 6 would contribute to the resonance hybrid, and both rings would be deactivated toward electrophilic attack. If this explanation applies, the ultraviolet absorption spectrum of III complexed with a strong acid should be different from that of the corresponding complex with the monoacetyl[6.6]paracyclophane.[2] The spectrum of III itself in ethanol was essentially identical with that of its larger homolog,[2] and unfortunately both compounds underwent sulfonation when their spectra were determined in 96% sulfuric acid. A second consequence of transannular resonance in the complex should be that if disubstitution is forced, the second acetyl group should enter the unsubstituted ring more readily in positions 4′ and 6′ than in positions 1′ and 3′.



IV

The second possible explanation for III not undergoing further acetylation (as did its higher homolog) involves the electrostatic effect of a positive charge resonating in the substituted ring on the tendency of the other ring to undergo electrophilic substitution.[5] If this effect applies, the unsubstituted ring of IV might undergo electrophilic attack with less discrimination between positions 1′ and 3′ on the one hand and positions 4′ and 6′ on the other. These alternatives are being investigated.

Catalytic Reduction of [4.4]Paracyclophane (I).—When reduced with platinum and 3 moles of hydrogen in glacial acetic acid, cycle I gave a 71% yield of the hexahydro derivative V and a mixture of V, fully reduced, and starting material. This result contrasts with the higher homolog II giving in the same reaction a 13% yield of half-reduced, 6% yield of fully reduced and 17% yield of starting material.[6] Thus, either the cyclohexane ring of V inhibits the reduction of the second ring, or the presence of a second aromatic ring in I enhances the reduction of the first. In the larger homolog, the two rings appear to reduce independently of one another.



V (*cis*)

Demonstration of the Structure of Monoacetyl-[4.4]paracyclophane (III).—The possibility that rearrangements occurred during the Friedel–Crafts

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

(4) The rate difference can be estimated as follows (the authors are indebted to Dr. W. G. McMillan for this analysis). If the acylation reactions are assumed to be bimolecular and irreversible, and are competitive and consecutive, the following kinetic situation applies. If A is acetyl chloride, B is [4.4]paracyclophane, C is monoacetyl paracyclophane, D is diacetyl paracyclophane and E is HCl, then

$$\mathrm{A} + \mathrm{B} \xrightarrow{k_1} \mathrm{C} + \mathrm{E} \quad \mathrm{d}C/\mathrm{d}t = k_1AB - k_2AC$$

$$\mathrm{A} + \mathrm{C} \xrightarrow{k_2} \mathrm{D} + \mathrm{E} \quad \mathrm{d}D/\mathrm{d}t = k_2AC$$

and

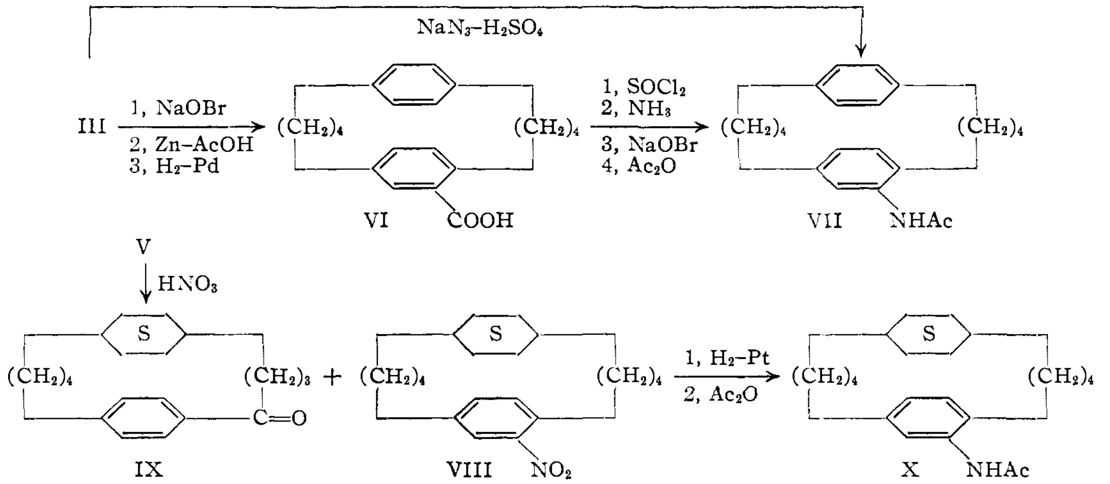
$$(\alpha - 1)\ln(1 - D/B_0) = \ln[1 - C/(B_0 - D)] - \alpha \ln [1 - C/\alpha(B_0 - D)]$$

where $\alpha = k_1/k_2$. If $k_1/k_2 \gg 1$ and $C < (B_0 - D)$, then, $k_1/k_2 = 1 + [C/(B_0 - D) + \ln B/(B_0 - D)]/\ln(1 - D/B_0)$

Employing the yield data obtained when the reaction was interrupted ($C = 0.88$, $B = 0.02$, $D = 0.07$, and $B_0 = 1.00$), $k_1/k_2 \cong 40$. Since $B = 0.02$ and $D = 0.07$ are maximum values (weights of impure chromatographic fractions), the ratio of k_1/k_2 might be considerably higher than 40. See A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 165, for types of solutions to the general kinetic problem.

(5) An elegant demonstration of the importance of this "field effect" on chemical reactivity of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids has been provided by J. D. Roberts and W. T. Moreland Jr. [THIS JOURNAL, **75**, 2167 (1953)].

(6) These low yields reflect the difficulty in separating the mixture into its components. Elution patterns of chromatograms indicated that approximately 50% of the material went to half-reduced, 25% to fully reduced and that 25% of the starting compound remained.



acylation of I was set aside through the following series of interconversions. The acetyl compound III was oxidized to the corresponding carboxylic acid VI, whose amide was submitted to the Hofmann rearrangement to give acetamido compound VII. Much better yields of XII were obtained directly from III through use of the modified Schmidt rearrangement.[7]

In a second series of interconversions, the half-reduced paracyclophane V was nitrated to give nitro compound VIII (54%) and ketone IX. Reduction of VIII and acetylation of the resulting amine provided the half-reduced acetamidoparacyclophane X, dehydrogenation of which provided the fully aromatic acetamidoparacyclophane VII. These conversions of the products of acetylation and nitration into a common substance VII point to the absence of rearrangements in the acetylation reaction.

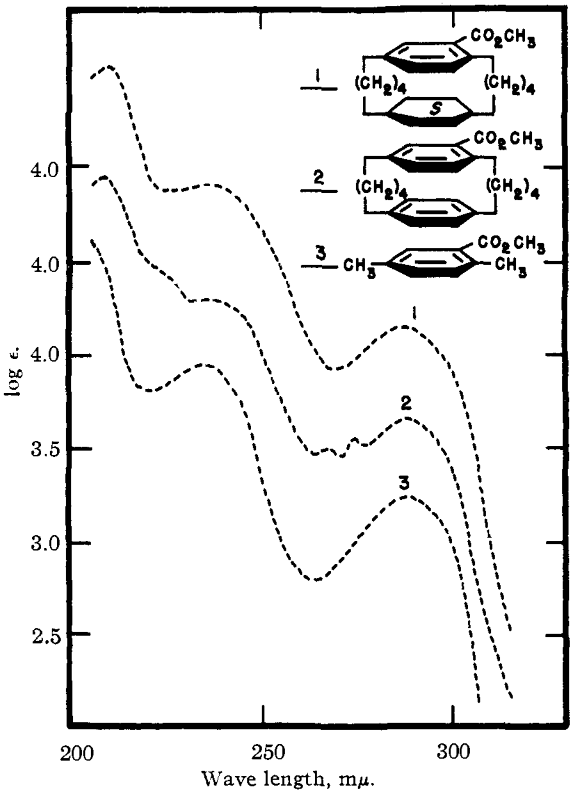


Fig. 1.—Ultraviolet absorption spectra in 95% ethanol, Cary recording spectrophotometer model 11MPS. Spectra 2 and 1 are displaced upward on the vertical axis by successive increments of 0.5 log unit.

Acetylation of the half-reduced paracyclophane V gave an oil (53% yield) which analyzed well for monoacetylated material. The oxime of this material was a gum, and the semicarbazone was a solid that melted over a wide range. The monoacetylated material was oxidized to the carboxylic acid, which was also an oil, and which gave an ester (oil) that gave a good analysis. Since these results indicated the monoacetylated material to be a mixture of isomers, the derived carboxylic acid was oxidized with alkaline permanganate to the derived benzenetricarboxylic acid. The only identified product of the oxidation was 1,2,4-benzenetricarboxylic acid. It appears likely that during the acetylation reaction, an aluminum chloride-catalyzed rearrangement of the aliphatic side chain occurred. Figure 1 reports the ultraviolet absorption spectra of the methyl esters of 2,5-dimethylbenzoic acid, of fully aromatic acid VI, and of the non-homogeneous hexahydro acid. The close similarity of these spectra. taken in conjunction with the above oxidation experiments, suggests that migration of the side chain around the ring in the acetylation of V did not occur to an appreciable extent.[8]

Experimental Part[9]

Acylation of [4.4]Paracyclophane (I).—To a mixture of 3.55 g. (0.0452 mole) of acetyl chloride and 5.5 g. (0.0411 mole) of aluminum chloride in 40 ml. of carbon disulfide was added 5.42 g. (0.0205 mole) of hydrocarbon (I), and the resulting suspension was stirred at room temperature for 70 minutes. The suspension was then poured onto ice and concentrated hydrochloric acid. The product was extracted into ether, the resulting ether solution was washed with water, dilute base, dried and evaporated. The resulting

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[7] P. A. S. Smith, THIS JOURNAL, **76**, 431 (1954).

[8] The close similarity of the spectrum of the open-chain ester and of the ester of acid VI points to the absence of transannular electronic effects in the latter compound.

[9] Melting points are corrected, and boiling points are uncorrected. Ultraviolet absorption spectra were determined in 95% ethanol (Cary recording spectrophotometer, model 11 PMS).

oil was chromatographed (acid-washed alumina) in 20% ether–pentane, and the column filtrates gave 106 mg. (2%) of recovered starting material, 5.55 g. (88%) of 6-acetyl-[4.4] paracyclophane (III)[10] and 496 mg. (7%) of a mixture of solids, possibly diacetylated material. Distillation of the monoacetylated product gave 5.35 g. (85%) of a colorless oil, b.p. 170° (bath temp.) (0.1 mm.), which slowly solidified. Crystallization of the substance from aqueous methanol gave a colorless solid, m.p. 51–53°; $\lambda_{\max.}$ 215 mμ (ε 23,600), $\lambda_{\min.}$ 234 mμ (ε, 3,500), $\lambda_{\max.}$ 252 mμ (ε, 6,430), $\lambda_{\text{inflection}}$ 273 mμ (ε, 1,370), $\lambda_{\max.}$ 274 mμ (ε, 980), $\lambda_{\max.}$ 295 mμ (ε, 1,340).

Anal. Calcd. for $C_{22}H_{26}O$: C, 86.23; H, 8.55. Found: C, 86.19; H, 8.57.

Hypobromite Oxidation of 6-Acetyl[4.4]paracyclophane (III).—A solution of sodium hypobromite was prepared from 2.10 g. (0.0525 mole) of sodium hydroxide and 3.50 g. (0.022 mole) of bromine in 30 ml. of water. To this cooled solution (0°) was added 2.23 g. (0.00729 mole) of the ketone III dissolved in 50 ml. of dioxane. The resulting mixture (2 layers) was agitated vigorously at room temperature for 1 hour (homogeneous) and then allowed to stand at 0° for 1 hour. The excess hypobromite was then decomposed with sodium bisulfite, the solution was acidified to congo red and the product was extracted into ether. The ether solution was washed with water, dried and evaporated. Since the residual solid gave a positive test for halogen (Beilstein), it was boiled for 3 hours in glacial acetic acid containing zinc dust. The mixture was cooled, diluted with water and extracted with ether. Removal of the ether gave 1.92 g. (85%) of crude 6-carboxy[4.4]paracyclophane (VI), which on crystallization from acetic acid gave needles, weight 1.52 g. (68%), m.p. 206–208°.

Anal. Calcd. for $C_{21}H_{24}O_2$: C, 81.78; H, 7.84. Found: C, 81.78; H, 8.13.

A hypochlorite oxidation of the above ketone gave an acid which was contaminated by chlorinated products and was extremely difficult to purify.

The methyl ester was prepared with diazomethane and was crystallized from aqueous methanol to give shiny plates, m.p. 63–64.5°.

Anal. Calcd. for $C_{22}H_{26}O_2$: C, 81.95; H, 8.13. Found: C, 81.81; H, 8.17.

***cis*-5,6,7,8,9,10-Hexahydro[4.4]paracyclophane (V).**—Paracyclophane I, 0.95 g. (0.0036 mole), was hydrogenated with 0.1 g. of platinum oxide in a mixture of 10 ml. of acetic acid and 20 ml. of ethyl acetate. The theoretical amount of hydrogen was absorbed in 4 hours. The solution was filtered free of catalyst and was poured into pentane. The pentane phase was washed, dried and the solvents were removed in vacuum. The residual oil was dissolved in pentane and absorbed on 125 g. of alumina of activity I.[11] The column was washed with pentane and the eluate was collected in 25-ml. fractions. Fractions 1–3 contained nothing, fraction 4 contained 0.08 g. of oil, fractions 5–8 contained 0.70 g. of half-reduced paracyclophane V, fractions 9–12 (eluted with ether) gave 0.17 g. of recovered starting material. The product from fractions 5–8, 0.70 g. (71%), had m.p. 47.8–48.4°. For analysis, a sample was crystallized from ethanol (needles), m.p. 48.0–48.6°.

Anal. Calcd. for $C_{20}H_{30}$: C, 88.82; H, 11.18. Found: C, 89.04; H, 11.10.

Acylation of *cis*-5,6,7,8,9,10-Hexahydro[4.4]paracyclophane (V).—To a mixture of 244 mg. (0.00311 mole) of acetyl chloride and 450 mg. (0.0034 mole) of aluminum chloride was added 400 mg. (0.00148 mole) of hydrocarbon V, and the resulting mixture was stirred at room temperature for 10 hours. The wine-colored mixture was poured onto a mixture of ice and concentrated hydrochloric acid. The product was extracted into ether, washed with water, dilute base and was dried, and the solvent was evaporated. The residual yellow oil was chromatographed (neutral alumina) with 30% ether–pentane to give 246 mg. (53%) of monoacetylated product (colorless oil), b.p. 190° (bath temp.) (0.1 mm.); $\lambda_{\max.}$ 217 mμ (ε 24,300), $\lambda_{\min.}$ 235 mμ (ε 4,350), $\lambda_{\max.}$ 254 mμ (ε, 8,000), $\lambda_{\min.}$ 286 mμ (ε, 1,490), $\lambda_{\max.}$ 298 mμ (ε, 1,600).

Anal. Calcd. for $C_{22}H_{32}O$: C, 84.56; H, 10.32. Found: C, 84.70; H, 10.27.

The oxime of the above ketone was obtained as a viscous oil which could not be crystallized. The semicarbazone, after several crystallizations from aqueous methanol, melted over a wide range (m.p. 80–100°).

Further elution of the above column with methanol gave 235 mg. (45%) of diacetylated products, which on distillation gave a yellow gum, b.p. 235° (bath temp.) (0.1 mm.); $\lambda_{\max.}$ 216 mμ (ε, 24,000), $\lambda_{\min.}$ 234 mμ (ε 6,220), $\lambda_{\max.}$ 253 mμ (ε, 9,200), $\lambda_{\text{shoulder}}$ 284 mμ (ε, 2,220).

Anal. Calcd. for $C_{24}H_{34}O_2$: C, 81.31; H, 9.67. Found: C, 81.34; H, 9.30.

Hypobromite Oxidation of 16(?)-Acetyl-*cis*-5,6,7,8,9,10-hexahydro[4.4]paracyclophane.—A solution of sodium hypobromite was prepared from 1.75 g. (0.0437 mole) of sodium hydroxide and 2.88 g. (0.018 mole) of bromine in 25 ml. of water. To the cooled (0°) solution was added the above ketone dissolved in 90 ml. of dioxane (2 layers), and the resulting mixture was vigorously agitated at room temperature for 8 hours. The mixture was treated with sodium bisulfite solution, acidified to congo red and the products were extracted into ether. The acidic products were extracted into base, the basic layer was acidified and extracted with ether. Removal of the ether gave a brown oil which was boiled with zinc and acetic acid to remove bromine. The zinc was collected, the filtrate was diluted with water, extracted with ether, and the ethereal solution was well washed with water and dried. Removal of the ether gave 1.75 g. (93%) of product as a "glass" which could not be crystallized. The acid (1.73 g., 0.0055 mole) was esterified with diazomethane to give 1.80 g. (99%) of ester which was chromatographed with pentane–ether on alumina (previously washed with ethyl acetate) of activity I. Although a total of 40 fractions were collected, it was not possible to detect the presence of more than one component. Distillation of the product gave a colorless oil (ester), b.p. 175° (bath temp.) (0.1 mm.).

Anal. Calcd. for $C_{22}H_{32}O_2$: C, 80.44; H, 9.82. Found: C, 80.19; H, 9.58.

Permanganate Oxidation of 16(?)-Carboxy-*cis*-5,6,7,8,-9,10-hexahydro[4.4]paracyclophane.—The acid (see above), 480 mg. or 1.5 mmoles, in 3 ml. of 10% sodium hydroxide was heated under reflux for 21 hours with 6.3 g. of potassium permanganate in 110 ml. of water. After cooling, the mixture was acidified, treated with sulfur dioxide, and the resulting aqueous solution was extracted continuously with ether (12 hours). Removal of the ether gave a semi-solid which was esterified with diazomethane. The resulting product was distilled (bath temp. 100°, 0.1 mm.) to give 120 mg. of colorless oil which was hydrolyzed with alcoholic potassium hydroxide to yield 94 mg.of solid (m.p. 207–210°) which was boiled with ethyl acetate and then filtered to yield 45 mg. of colorless solid, m.p. 216–220° dec. (lit.[12] m.p. of trimellitic acid, 238° dec.). The sample was sublimed at 170° (0.05 mm.) to yield 34 mg. of anhydrotrimellitic acid, m.p. 165–167° (lit.[13] m.p. 162.5–163.5°).

Anal. Calcd. for $C_9H_4O_5$: C, 56.26; H, 2.10. Found: C, 56.18; H, 2.30.

The residue from the ethyl acetate was sublimed (140° (0.1 mm.)) with decomposition to yield several milligrams of colorless solid, which melted over a wide range (m.p. 153–195°).

16-Nitro-*cis*-5,6,7,8,9,10-hexahydro[4.4]paracyclophane (VIII).—To a cooled (0°) mixture of acetic acid (1.0 ml.) and fuming nitric acid (2.50 g.) (sp. gr. 1.50) was added 270 mg. (0.0010 mole) of hydrocarbon V over a period of 20 minutes. The resulting mixture was stirred at 0° for 1 hour, then at room temperature for 2.5 hours. The yellow solution was poured onto ice, extracted with ether, the ether solution was washed with water and base and dried. Removal of the ether gave a yellow oil which was chromatographed (alumina) with 15% ether–pentane to yield 172 mg. (55%) of nitro compound VIII as a pale yellow oil, b.p. 200° (bath temp.) (0.15 mm.); $\lambda_{\max.}$ 215 mμ (ε 13,500), $\lambda_{\min.}$ 246 mμ (ε, 3,660), $\lambda_{\text{shoulder}}$ 310 mμ (ε, 1,540).

Anal. Calcd. for $C_{20}H_{29}O_2N$: C, 76.15; H, 9.27; N, 4.43. Found: C, 76.17; H, 8.88; N, 4.33.

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(10) See ref. 2 for explanation of nomenclature.

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

(12) G. T. Morgan and E. A. Coulson, *J. Chem. Soc.*, 2554 (1929).

(13) W. Schultze, *Ann.*, **359**, 142 (198).

Further elution of the column with methanol gave 65 mg. of yellow gum which was not investigated further.

In another experiment, in which the temperature was allowed to rise to 50°, a white solid was isolated in approximately 35% yield. This is probably 1-keto-*cis*-5,6,7,8,9,10-hexahydro[4.4]paracyclophane, arising from oxidation of the benzyl position. One crystallization from methanol gave needles, m.p. 73.5–74.5°; $\lambda_{\text{min.}}$ 225 mμ (ϵ, 2,100), $\lambda_{\text{max.}}$ 253 mμ (ϵ, 12,100), $\lambda_{\text{shoulder}}$ 305 mμ (ϵ, 300).[14]

Anal. Calcd. for $C_{20}H_{28}O$: C, 84.45; H, 9.92. Found: C, 84.25; H, 9.74.

16-Amino-*cis*-5,6,7,8,9,10-hexahydro[4.4]paracyclophane.—A solution of nitro compound VIII (0.304 g., 0.000965 mole) in 95% ethanol (20 ml.) was shaken in hydrogen in the presence of 50 mg. of platinum oxide until absorption of hydrogen ceased (73.7 ml. at 22° (748 mm.), 103%). The catalyst and solvent were removed, the residue was dissolved in ether, and the solution was washed with water and dried. Removal of the ether gave 274 mg. (99%) of the amine, b.p. 200° (bath temp.) (0.1 mm.).

Anal. Calcd. for $C_{20}H_{31}N$: C, 84.15; H, 10.95; N, 4.91. Found: C, 84.36; H, 10.97; N, 4.98.

16-Acetamido-*cis*-5,6,7,8,9,10[4.4]paracyclophane (X).—The above amine (175 mg.) was heated under reflux for 25 minutes with 1 ml. of acetic anhydride, and the mixture was diluted with water. The resulting soapy solid was taken up in ethanol water (3:1) and filtered to give 141 mg. (70%) of crude amide, m.p. 184–186°. One crystallization from ethanol gave 119 mg. (needles) of X, m.p. 186–187°; $\lambda_{\text{shoulder}}$ 234 mμ (ϵ 7,350), $\lambda_{\text{shoulder}}$ 273 mμ (ϵ 885).

Anal. Calcd. for $C_{22}H_{33}ON$: C, 80.68; H, 10.16. Found: C, 80.84; H, 10.02.

6-Acetamido[4.4]paracyclophane (VII).—Acetamido compound X (172 mg.) was dehydrogenated with 35 mg. of 10% palladium-on-charcoal by heating at 280–300° until the evolution of hydrogen ceased. During this operation, a large amount of solid sublimed into the neck of the flask, thus making it impossible to ensure complete dehydrogenation. The product was then taken up in ethyl acetate and filtered. Removal of the ethyl acetate gave a solid which was crystallized once from aqueous methanol and once from cyclohexane to yield 73 mg. (43%) of the aromatic amide VII, m.p. 172–174°. The compound sublimed at 138° (0.05 mm.) to yield prisms, m.p. 173–174.5°; $\lambda_{\text{shoulder}}$ 233 mμ (ϵ, 5,660), $\lambda_{\text{inflection}}$ 273 mμ (ϵ, 997), $\lambda_{\text{max.}}$ 274 mμ (ϵ, 1,050).

Anal. Calcd. for $C_{22}H_{27}ON$: C, 82.20; H, 8.47; N, 4.36. Found: C, 82.09; H, 8.31; N, 4.50.

6-Carboxyamido[4.4]paracyclophane.—A mixture of 308 mg. (0.001 mole) of acid VI and 1.5 ml. of thionyl chloride was heated on the steam-bath for 30 minutes, the excess thionyl chloride then being removed under vacuum. The residue, on treatment with cold concentrated ammonia, gave a viscous oil which slowly solidified. One crystallization of the compound from aqueous ethanol and recrystallization from cyclohexane gave 177 mg. (57.5%) of the amide of acid VI, m.p. 180–182°.

Anal. Calcd. for $C_{21}H_{25}ON$: N, 4.56. Found: N, 4.34.

Rearrangement of the Preceding Amide to 6-Acetamido-[4.4]paracyclophane (VII).—To a solution prepared from 14 mg. (0.6 mmole) of sodium and 0.4 ml. of methanol was added 92 mg. (0.3 mmole) of the preceding amide, followed by 48 mg. (0.3 mmole) of bromine, the resulting mixture being heated on the steam-bath for 10 minutes. The solvent was then removed under reduced pressure, and the residue was taken up in ether. The solution was washed with water, dried and evaporated to give an oil which partially solidified. This material was heated under reflux for 6 hours with 0.12 g. of potassium hydroxide in aqueous methanol in order to hydrolyze any unreacted starting material. The basic solution was diluted with water and extracted with ether. Removal of the ether gave an oil which was heated under reflux for 1 hour with 0.3 ml. of acetic anhydride and 0.4 ml. of pyridine. This solution was diluted with water and extracted with ether. The ethereal extract was washed with dilute acid and dilute base, dried, and evaporated. The residual solid on sublimation (140° (0.06 mm.)) gave 35 mg. (36%) of amide VII, m.p. 172–174°, undepressed upon admixture with the authentic specimen described above.

Schmidt Reaction with 6-Acetyl[4.4]paracyclophane (III).—Ketone III (0.708 g., 2.31 mmoles) was added to 7 g. of trichloroacetic acid and 0.68 g. of concentrated sulfuric acid, the resulting mixture being maintained at approximately 60° while 0.265 g. (4.1 mmoles) of sodium azide was added over a period of 25 minutes. After 90 minutes, the mixture was cooled, diluted with water and extracted with ether. The ethereal solution was washed with water and dilute base and dried. Removal of the ether gave 618 mg. of solid which was crystallized from 12 ml. of cyclohexane–benzene (3:1) to yield 513 mg. (69%) of the amide VII, m.p. 170–171.5°, undepressed upon admixture with the authentic specimen described above.

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[14] Compare the spectrum of this compound with that of 1-keto-7,8,9,10,11,12-hexahydro[6.6]paracyclophane (ref. 2.)

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF BIRKBECK COLLEGE]

The Structure of the Caryophyllene-Maleic Anhydride "Adduct"

BY ALEX NICKON[1]

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The compound formed on combination of caryophyllene and maleic anhydride is shown to have the structure XI. Formulas for derived rearrangement products are proposed.

In 1935 Ruzicka and Zimmermann[2] reported that treatment of caryophyllene ($C_{15}H_{24}$) with maleic anhydride in hot benzene solution produced a crystalline (m.p. 98°), 1:1 addition product. Even though the constitution of caryophyllene itself was unknown at that time, their findings became of considerable interest when subsequent work revealed that the two double bonds in the original hydrocarbon were not conjugated.[3] Furthermore, the catalytic hydrogenation experiments of Ruzicka, Plattner and Balla[4] later revealed that the maleic anhydride addition product still retained two double bonds, and so indicated that this "adduct" was not one of the usual Diels–Alder type.

The nature of this unusual reaction became more understandable through an important fundamental discovery by Alder, Pascher and Schmitz in 1943.[5] These investigators found that many mono-unsaturated olefins combined with maleic anhydride at elevated temperatures (*ca.* 200°) to form products in which the anhydride residue was attached to the saturated carbon of an allylic system. The adjoin-

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[4] L. Ruzicka, P. A. Plattner and G. Balla, *ibid.*, **24**, 1219 (1941).

[5] K. Alder, F. Pascher and A. Schmitz, *Ber.*, **76B**, 27 (1943).