λ_{max}^{ether} 230 mμ (log ε 4.02) and 335 mμ (log ε 3.98), infrared λ_{max} 5.75 μ (weak), 5.96 μ (intense), 6.10 and 6.22 μ (weak) and 6.4 μ (intense). The product was reacetylated and chromatographed. Most of the product (184 mg.) was eluted from Florisil in 20:1 benzene–ether as light yellow crystals. A fraction recrystallized from methanol–acetone–water gave clusters of short needles, m.p. 186–188°, $[\alpha]^{25}D$ −145.6° ($CHCl_3$), λ_{max}^{ether} 237 mμ (log ε 4.04) and 341 mμ (log ε 4.06). The infrared spectrum was unchanged.

Anal. Calcd. for $C_{30}H_{42}O_3$: C, 79.9; H, 9.39. Found: C, 79.9; H, 9.38. The product formed a deep red 2,4-dinitrophenylhydrazone, $\lambda_{max}^{CHCl_3}$ 440 and 326 mμ.

Hydrogenation of Ketone VII under Acid Conditions.—A 50-mg. sample of VII in 10 ml. of acetic acid was subjected to hydrogenation overnight in the presence of platinum catalyst. The reaction mixture was filtered, and the product was precipitated by addition of water to the filtrate. The white solid, m.p. 96–98°, was recrystallized from ethyl acetate to give 15 mg. of plates, m.p. 106–107°, $[\alpha]^{25}D$ +17° ($CHCl_3$). The melting point on admixture with an authentic sample of 8(14)-ergostenol 3-acetate (m.p. 110–111°) was 109–110°. The infrared spectrum also was identical to that of the known compound.

8(14),22-Ergostadien-3β-ol-15-one Acetate (XI).—A solution of 168 mg. (0.37 mmole) of ketone VII in 20 ml. of ethyl acetate was added to 1 g. of Raney nickel pre-reduced in 40 ml. of ethyl acetate and subjected to hydrogenation at room temperature and atmospheric pressure. The rate of hydrogen uptake slowed down considerably after 18 ml. had been absorbed (30 minutes). The hydrogenation was stopped after 2 hr. (total uptake 22.6 ml.). The catalyst was removed by filtration and the colorless solution concentrated to dryness to give 168 mg. white solid, m.p. 130–135°, $[\alpha]^{25}D$ +81.5° ($CHCl_3$), λ_{max}^{EtOH} 257 mμ (log ε 4.00). Trituration of the crude product with methanol yielded 23 mg. of white crystalline solid, m.p. 166–168°. Recrystallization from 1 ml. of methanol gave the product (13 mg.) as short needles, m.p. 176–177°, $[\alpha]^{25}D$ +72.5° ($CHCl_3$), λ_{max}^{EtOH} 259 mμ (log ε 4.16). Comparison of this product with an authentic sample of 8(14),22-ergostadien-3β-ol-15-one acetate[13] by mixed melting point and infrared spectra showed them to be identical.

Reduction of Ketone VII with Lithium Aluminum Hydride.—Reduction of a sample (80 mg.) of acid-rearrangement product VII in 50 ml. of ether with 5 ml. of 0.5 *M* lithium aluminum hydride solution overnight gave a crude product XII, λ_{max}^{ether} 231 mμ (log ε 4.02) and 284 mμ (log ε 3.65).

BROOKLYN 6, N. Y.

[CONTRIBUTION FROM THE MERCK SHARP & DOHME RESEARCH LABORATORIES, MERCK & CO., INC.]

Synthesis of 2-Hydroxy-8-keto-5-methoxy-4a-methylperhydrophenanthrene

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2-Hydroxy-8-keto-5-methoxy-4a-methylperhydrophenanthrene (IX) and 2,5,8-trihydroxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (XIX), potential C-11 oxygenated steroid intermediates, have been synthesized.

The synthesis of 8-hydroxy-2-keto-5-methoxy-4a-methyl-2,3,4,4a,9,10-hexahydrophenanthrene (I), a potential intermediate for the synthesis of C–11 oxygenated steroids, has been reported.[1] Its conversion into two of the isomeric 2-hydroxy-8-keto-5-methoxy-4a-methylperhydrophenanthrenes (IXA) and (IXB) is described in the present paper. In addition, some reactions of these and related compounds are reported.

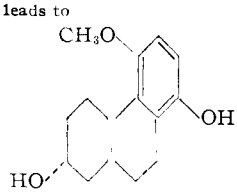
The reduction of the hexahydrophenanthrene I to give the hydroxyphenol IV was accomplished in two ways. Hydrogenation over a palladium catalyst gave a quantitative yield of one isomer of the ketophenol II. Subsequent reduction of the ketophenol II over Raney nickel yielded a single crystalline hydroxyphenol IV. This product was also obtained by hydrogenation of the hexahydrophenanthrene I in one step using Raney nickel as a catalyst.[2]

2-Acetoxy-8-hydroxy-5-methoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (VI) could be prepared directly by monoacetylation of the hydroxyphenol IV. Better yields were obtained, however, by selectively hydrolyzing the diacetoxy derivative V with an aqueous solution of potassium bicarbonate.

Numerous methods for hydrogenation of the aromatic ring of the acetoxyphenol VI were studied. In general, conditions satisfactory for obtaining complete reduction of the ring also brought about varying amounts of hydrogenolysis of the oxygen functions. Early in this work the only satisfactory system for obtaining the desired result was the palladium-catalyzed reaction described by Cornforth and Robinson[3] for the reduction of 2-acetoxy-8-hydroxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene. It was later found that hydrogenation at about 15,000 p.s.i. over a ruthenium–Darco catalyst was more satisfactory. Almost

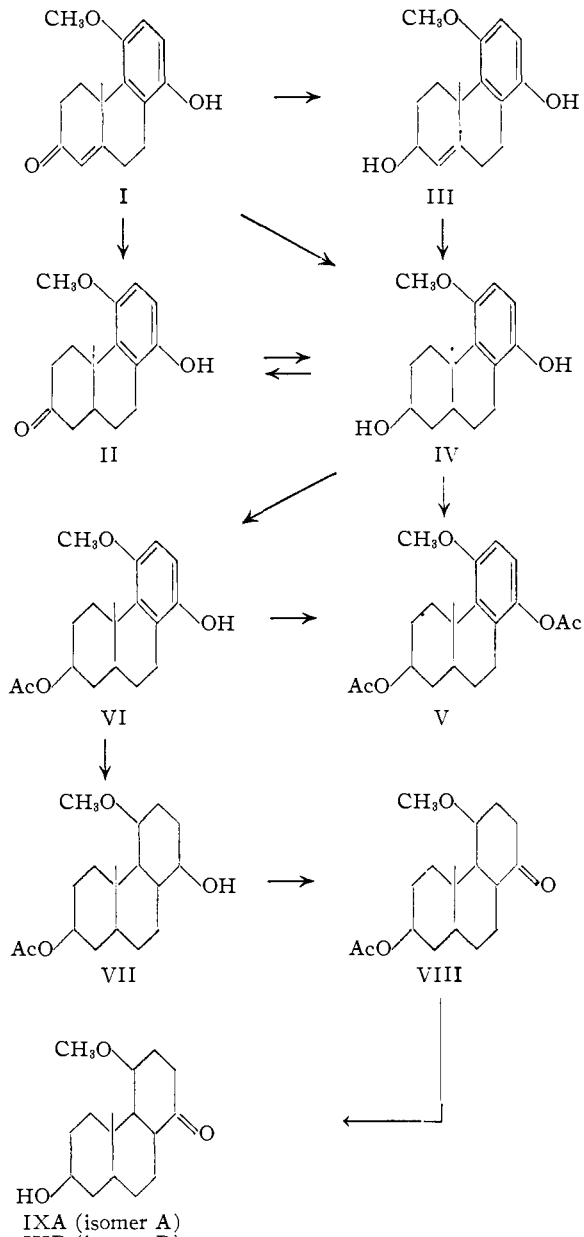
(1) W. F. Newhall, S. A. Harris, F. W. Holly, E. L. Johnston, J. W. Richter, E. Walton, A. N. Wilson and K. Folkers, THIS JOURNAL, **77**, 5646 (1955).

(2) An A/B-*cis* structure is postulated for these reduction products by analogy to neutral hydrogenations of cholestenone (H. Grashof, *Z. physiol. Chem.*, **223**, 249 (1934)) and of 2-keto-10-methyl-$\Delta^{1(9)}$-octalin (R. P. Linstead, A. F. Millidge and A. L. Walpole, *J. Chem. Soc.*, 1140 (1937); V. C. E. Burnop and R. P. Linstead, *ibid.*, 720 (1940); E. C. du Feu, F. J. McQuillan and R. Robinson, *ibid.*, 53 (1937)). In addition, a closer analogy may be drawn to the neutral reduction of 8-hydroxy-2-keto-4a-methyl-2,3,4,4a,9,10-hexahydrophenanthrene to yield the corresponding A/B-*cis* octahydrophenanthrene (J. W. Cornforth and R. Robinson, *ibid.*, 676 (1946); *Nature*, **160**, 737 (1947)). The neutral reduction of the 2-keto function probably gives rise to a secondary hydroxyl having a *trans* relation to the angular methyl; *cf.* acidic and neutral reductions of coprostanone: H. Grassoff, *Z. physiol. Chem.*, **225**, 197 (1934), and L. Ruzicka, H. Brungger, E. Eichenberger and J. Meyer, *Helv. Chim. Acta*, **17**, 1407 (1934). The above reasoning leads to



as a tentative stereochemical representation of the hydroxyphenol IV.

(3) J. W. Cornforth and R. Robinson, *J. Chem. Soc.*, 1855 (1949).

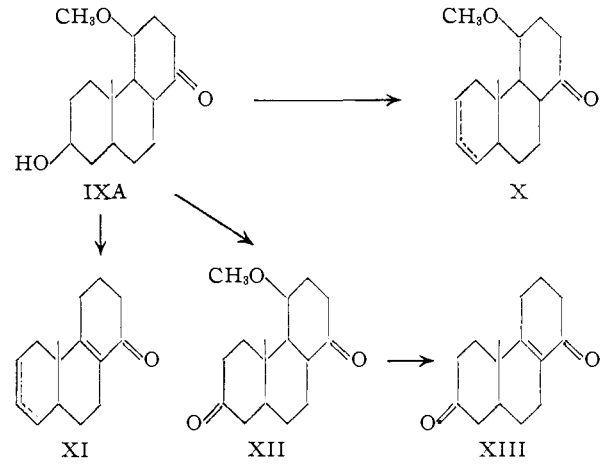


complete saturation of the aromatic ring could be obtained with practically no hydrogenolysis.[4]

The mixture of isomeric[5] acetoxyalcohols VII was oxidized with chromium trioxide in acetic acid to give the corresponding acetoxyketones VIII. The acetyl group was saponified by alcoholic potassium hydroxide which also converted the products into a mixture of B/C-*trans*[6] isomers of 2-hydroxy-8-keto-5-methoxy-4a-methylperhydrophenanthrene. From this mixture only two stereoisomeric hydroxyketones, IXA and IXB, were isolated.[7] 2,4-Diketo-5-methoxy-4a-methylperhydrophenanthrene (XII) was prepared by oxidizing the hydroxyketone IXA in acetic acid with chromium trioxide.

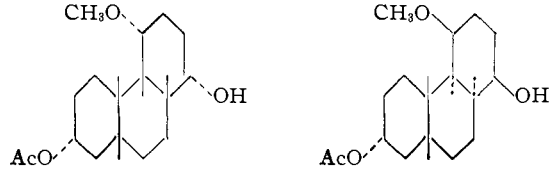
Attempts to obtain compounds for comparison with intermediates[8] of known stereochemistry by demethylation of the hydroxyketone IXA and the diketone XII were unsuccessful.[9]

When the hydroxyketone IXA was treated with concentrated sulfuric acid, both dehydration at the 2-position and demethanolation at the 5-position occurred to yield a dienone XI. When the hydroxyketone IXA was heated with 6 *N* sulfuric acid, only dehydration took place, and a methoxyketone X was obtained. 2,8-Diketo-5-methoxy-4a-methylperhydrophenanthrene (XII), when treated with concentrated sulfuric acid, yielded an unsaturated diketone XIII. The ultraviolet absorption spectra of the 2,4-dinitrophenylhydrazones of the above products are consistent[10] with the proposed structures.



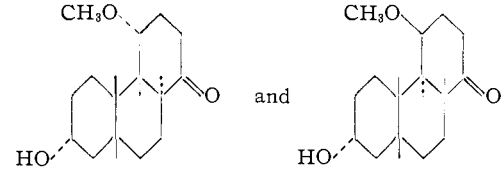
(4) It has been shown by (a) W. B. Renfrow and J. W. Cornforth, THIS JOURNAL, **75**, 1347 (1953), and (b) J. W. Cornforth, O. Karder, J. E. Pike and R. Robinson, *J. Chem. Soc.*, 3348 (1955), that catalytic hydrogenation of similar compounds having a *trans* A/B junction gives good yields of almost exclusively *trans-anti-trans* products.

(5) The catalytic hydrogenation of the benzenoid ring probably results in B/C-*cis* products (R. P. Linstead, W. E. Doering, S. B. Davis, P. Levine and R. R. Whetstone, THIS JOURNAL, **64**, 1985 (1942)). This concept would allow for only two stereochemical products from the hydrogenation and together with previous conclusions (reference 4) these products may be represented by the structures,



(6) See W. Hückel, *Ann.*, **441**, 1 (1925).

(7) As there is only one enolizable hydrogen in the acetoxyketone, and if only two all-*cis* products result from the hydrogenation (reference 5), then only two B/C-*trans* hydroxyketones should be obtained after alkaline hydrolysis and epimerization. All attempts to isolate more than two hydroxyketones were unsuccessful. The probable stereochemical nature of the products may then be shown as

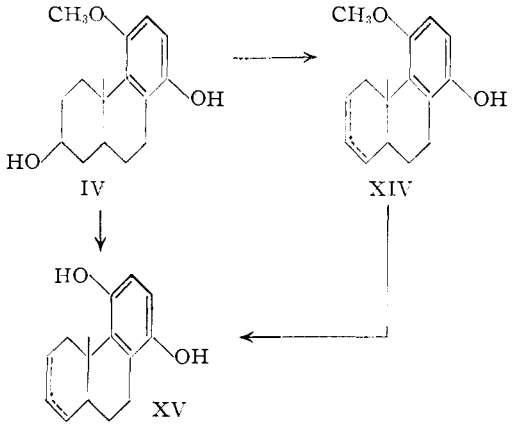


(8) The stereochemistry of similarly substituted perhydrophenanthrenes has been established by G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, THIS JOURNAL, **75**, 422 (1953).

(9) Renfrow and Cornforth (reference 4a) have converted methoxy in the 2- and 8-positions to hydroxyl using similar compounds.

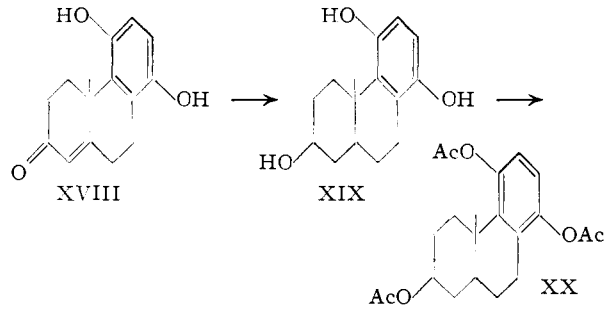
(10) See F. A. Braude and E. R. H. Jones, *J. Chem. Soc.*, 498 (1945).

In experiments designed to prepare 2,5,8-trihydroxy - 4a - methyl - 1,2,3,4,4a,9,10,10a - octahydrophenanthrene (XIX) by demethylating the 5-methoxyoctahydrophenanthrene IV, results similar to those in the perhydrophenanthrene series were obtained. Although cleavage of the ether could be accomplished by means of pyridine hydrochloride, dehydration at the 2-position occurred to yield an unsaturated diol XV.



In one reaction an 8-hydroxy-5-methoxyhexahydrophenanthrene XIV was isolated indicating that dehydration occurs before demethylation. Although the position of the double bond in the A ring has not been determined, the Δ^1-products would be expected as the thermodynamically most stable for a *cis* A/B ring junction.[11]

Although the triol XIX was not obtained by demethylation of the hydroxyphenol IV, it was prepared by hydrogenating 5,8-dihydroxy-2-keto-4a-methyl - 2,3,4,4a,9,10 - hexahydrophenanthrene (XVIII)[1] in the presence of Raney nickel catalyst. 2,5,8-Trihydroxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (XIX) was acetylated to give the corresponding triacetate XX. Ring hydrogenations of these products would lead to a second group of perhydrophenanthrenes which should be useful as steroid precursors.



Acknowledgments.—The authors wish to thank Mr. R. N. Boos and associates for microanalyses, Dr. N. R. Trenner and Mr. R. W. Walker for infrared spectral measurements and interpretation and Dr. W. H. Jones and associates for high-pressure hydrogenation reactions. The authors also wish to thank Drs. G. E. Arth, R. E. Beyler and G. I. Poos for helpful discussion of certain aspects of the stereochemistry.

(11) D. Taylor, *Chem. and Ind.*, 250 (1954).

Experimental

2,8-Dihydroxy-5-methoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (IV).—A solution of 103 g. (0.4 mole) of 2-keto-4a-methyl-5-methoxy-8-hydroxy-2,3,4,4a,-9,10-hexahydrophenanthrene (I)[1] in 1500 ml. of absolute alcohol was shaken at room temperature under a hydrogen atmosphere using about 3 teaspoons of Raney nickel[12] as a catalyst. When the theoretical amount of hydrogen had been absorbed, the catalyst was filtered and the solvent was removed under reduced pressure.

The residue was dissolved in 700 ml. of chloroform at room temperature, and the product crystallized on standing. It was filtered, washed with chloroform and dried in a vacuum oven at 60°. The weight of product, m.p. 165.5–168°, was 98 g. It contained chloroform of crystallization. The chloroform was removed by heating the product at 100°. The dried material, m.p. 168–170°, weighed 68 g. (64%). A sample twice recrystallized from alcohol–water melted at 171–172°.

Anal. Calcd. for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.10; H, 8.33.

8-Hydroxy-2-keto-5-methoxy-4a-methyl-1,2,3,4,4a,9,10-10a-octahydrophenanthrene (II).—A solution of 11.8 g. (0.0457 mole) of 8-hydroxy-2-keto-5-methoxy-4a-methyl-1,2,3,4,4a,9,10-hexahydrophenanthrene (I) in 200 ml. of methanol was hydrogenated in the presence of 2 g. of palladium (5% on Darco) catalyst.[13] In 3 hr. the theoretical amount of hydrogen had been absorbed and the catalyst was removed by filtration. The solvent was removed under reduced pressure. The residue, m.p. 125–127°, weighed 11.8 g. (100%). A sample recrystallized from a benzene–petroleum ether mixture melted at 127–128°.

Anal. Calcd. for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.73; H, 7.29.

2-Ethylenedioxy-8-hydroxy-5-methoxy-4a-methyl-1,2,3-4,4a,9,10,10a-octahydrophenanthrene.—A mixture of 5.0 g. (0.019 mole) of 8-hydroxy-2-keto-5-methoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (II), 1.31 g. (0.021 mole) of ethylene glycol, 10 mg. of *p*-toluenesulfonic acid monohydrate and 40 ml. of benzene was heated under reflux for 1 hr. The water produced in the reaction was removed azeotropically. The solution was cooled and washed with sodium bicarbonate solution, with water and was dried. The benzene was removed under reduced pressure. The residual oil crystallized when it was triturated with carbon tetrachloride. It was recrystallized from 10 ml. of carbon tetrachloride. The yield of dioxolane derivative, m.p. 123–124°, was 4.9 g. (85%).

Anal. Calcd. for $C_{18}H_{24}O_4$: C, 71.02; H, 7.95. Found: C, 70.71; H, 7.62.

2,8-Dihydroxy-5-methoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (IV). From II.—A solution of 380 mg. (0.0015 mole) of 8-hydroxy-2-keto-5-methoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (II) in 50 ml. of ethanol was shaken with hydrogen and 1/8 teaspoon of Raney nickel[12] as a catalyst. The catalyst was filtered, and most of the solvent was removed under reduced pressure. The residue was diluted with water and the product crystallized. The yield of product, m.p. 168–170°, was 200 mg. (53%). The melting point of a mixture of this material with the hydroxyphenol described above was not depressed.

2-Acetoxy-8-hydroxy-5-methoxy-4a-methyl-1,2,3,4,4a,9,-10,10a-octahydrophenanthrene (VI).—A mixture of 62.5 g. (0.24 mole) of 2,8-dihydroxy-5-methoxy-4a-methyl-1,2,3,4,-4a,9,10,10a-octahydrophenanthrene (IV) in 180 ml. of acetic acid and 75 ml. (0.73 mole) of acetic anhydride was heated on the steam-bath for 4–5 hr. The still hot solution was poured into about 3 l. of water and allowed to stand at room temperature until the gummy precipitate which formed had solidified.

The entire mixture was extracted with a total of 1 l. of chloroform. The chloroform extract was washed with sodium bicarbonate solution, with water and was dried. The solvent was removed under reduced pressure to give a residue consisting mostly of 2,8-diacetoxy-5-methoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (V). A portion

(12) W-4: H. Adkins and A. A. Pavlic, THIS JOURNAL, **69**, 3039 (1947).

(13) "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1950, p. 685, procedure B.

solidified when it was triturated with petroleum ether. Two recrystallizations from benzene–petroleum ether produced a purified sample, m.p. 119.5–121°.

Anal. Calcd. for $C_{20}H_{26}O_5$: C, 69.34; H, 7.57. Found: C, 69.46; H, 7.14.

The rest of the 2,8-diacetoxy derivative V was dissolved in 300 ml. of ethanol, and a solution of 18 g. of potassium carbonate in 250 ml. of water was added. The reaction mixture was heated under reflux for 0.5 hr. The product began to separate from solution, and a little more water was added in small portions to reduce the solubility of the compound. The mixture was cooled to room temperature and the solution was acidified with dilute hydrochloric acid. After about 2 hr. the product was filtered, washed with water and dried. The yield of acetoxyphenol, m.p. 182–184°, was 65.5 g. (90%). Two recrystallizations from a mixture of acetic acid and water yielded the purified product, m.p. 186–187°.

Anal. Calcd. for $C_{18}H_{24}O_4$: C, 71.03; H, 7.95. Found: C, 70.87; H, 7.72.

8-Hydroxy-2-keto-5-methoxy-4a-methyl-1,2,3,4,4a,9,10,-10a-octahydrophenanthrene (II). From IV.—One gram of 2,8-dihydroxy-5-methoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (IV) was dissolved in a mixture of 80 ml. of benzene and 40 ml. of acetone. Two grams of aluminum *t*-butoxide was added and the mixture was heated under reflux overnight. It was cooled and acidified with dilute sulfuric acid. The aqueous layer was extracted several times with ether. The combined organic layers were washed with water, dried and concentrated to dryness under reduced pressure. The yield of residue, m.p. 105–110°, was 0.6 g. (60%). It was recrystallized from a mixture of alcohol and water to give the pure ketophenol, m.p. 127–128°. The melting point of a mixture of this material with that of an authentic sample showed no depression.

2,5,8-Trihydroxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (XIX).—A solution of 6.3 g. (0.026 mole) of 5,8-dihydroxy-2-keto-4a-methyl-2,3,4,4a,9,10-hexahydrophenanthrene (XVIII) in 200 ml. of methanol was shaken with hydrogen (40 p.s.i.) in the presence of Raney nickel.[12] In 1 hr. 86% of the theoretical amount of hydrogen required had been taken up. The catalyst was removed and the filtrate concentrated at reduced pressure. The residue was crystallized from methanol–tetrachloroethane to yield 3.75 g. of the product, m.p. 199–201°. A 2.0-g. portion was recrystallized from acetone to yield 1.24 g. (36%) of the triol XIX, m.p. 211–214°. A portion recrystallized from acetone had a melting point of 213–214°. This sample was dried at 125° for analysis.

Anal. Calcd. for $C_{13}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.96; H, 8.00.

2,5,8-Triacetoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (XX).—A mixture of 0.35 g. (0.0014 mole) of 2,5,8-trihydroxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (XIX), 3 ml. of acetic anhydride and 2 drops of pyridine was refluxed for 3 hr. The mixture was cooled and diluted with 3 ml. of water and stirred at room temperature for 1 hr. The mixture was concentrated at reduced pressure and the residue was dissolved in ether. The ether solution was washed with water, dilute aqueous sodium bicarbonate and water; dried over anhydrous sodium sulfate; filtered and concentrated at reduced pressure. The residue (0.35 g.) was crystallized from ether and then ethanol to yield 0.17 g. of the triacetoxyoctahydrophenanthrene XX, m.p. 146–148°.

Anal. Calcd. for $C_{21}H_{26}O_6$: C, 67.37; H, 7.00. Found: C, 66.92; H, 6.90.

Reaction of 2,8-Dihydroxy-5-methoxy-4a-methyl-1,2,3,4,-4a,9,10,10a-octahydrophenanthrene (IV) with Pyridine Hydrochloride.—A mixture of 5 g. (0.019 mole) of 2,8-dihydroxy-5-methoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (IV) and 15 g. of pyridine hydrochloride was heated under nitrogen at 155° for 5 hr. The cooled reaction mixture was dissolved in 50 ml. of water and extracted 4 times with ether. The ether extracts were washed with water, 1 *N* hydrochloric acid and aqueous sodium bicarbonate. The ether solution was dried over anhydrous sodium sulfate, filtered and concentrated at reduced pressure to yield 4 g. of an oil. Part of the oil crystallized from benzene to yield 1.9 g. (43%) of 5,8-dihydroxy-4a-methyl-1(or 3),-4,4a,9,10,10a-hexahydrophenanthrene (XV), m.p. 159–162°. Several recrystallizations from ethylene dichloride yielded a purified product, 5,8-dihydroxy-4a-methyl-1(or 3), 4,4a,9,10,10a-hexahydrophenanthrene (XV), m.p. 168–170°.

Anal. Calcd. for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.23; H, 7.71.

The benzene filtrates were concentrated to yield 1.64 g. of residual oil. The oil was chromatographed on acid-washed alumina using chloroform–carbon tetrachloride (1:5). A fraction (0.45 g., 10%) crystallized from carbon tetrachloride–petroleum ether to yield the product, 8-hydroxy-5-methoxy-4a-methyl-1(or 3),4,4a,9,10,10a-hexahydrophenanthrene (XIV), m.p. 78–79°.

Anal. Calcd. for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25; CH_3O–, 12.70. Found: C, 78.71; H, 8.23; CH_3O–, 10.99.

Reduction of 2-Acetoxy-8-hydroxy-5-methoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (VI). A. Using a Palladium Catalyst.—A mixture of 10 g. (0.033 mole) of 2-acetoxy-8-hydroxy-5-methoxy-4a-methyl-1,2,3,4,4a,-9,10,10a-octahydrophenanthrene (VI), 400 ml. of methylcyclohexane and 85 g. of palladium–strontium carbonate catalyst (2.5% palladium)[3] was shaken with hydrogen (4000 p.s.i.) at 200° for 5 hr. The catalyst was removed by filtration and washed with one l. of dry ether. The filtrate and washings were concentrated at reduced pressure to yield an oil. The oil was distilled at 0.1 mm. and 2 fractions were obtained: (1) 3.7 g., b.p. <110°; (2) 5.3 g., b.p. 110–148°.

Fraction 2 (5.3 g.) was dissolved in 50 ml. of glacial acetic acid, cooled to 0° and treated slowly with a solution of 1.25 g. of chromium trioxide in a little water and 50 ml. of glacial acetic acid. The mixture was kept at room temperature for 16 hr., diluted with water and extracted 3 times with ether. The combined ether extracts were washed with water, aqueous sodium bicarbonate and water. The ether solution was concentrated at reduced pressure to yield a mixture of isomers of 2-acetoxy-9-keto-5-methoxy-4a-methylperhydrophenanthrene (VIII) as an oil.

A solution of this oil in 100 ml. of 0.4 *N* alcoholic potassium hydroxide was refluxed for 1 hr. The warm hydrolysis mixture consisting of isomers of 2-hydroxy-8-keto-4-methoxy-4a-methylperhydrophenanthrene (IX) was treated with 2.6 g. of semicarbazide hydrochloride and 2.6 g. of anhydrous sodium acetate. The solution yielded, after being cooled, 1.34 g. (12.5%)[14] of the semicarbazone of 2-hydroxy-8-keto-4-methoxy-4a-methylperhydrophenanthrene (IXA). The product was washed with water and warm ethanol to give the pure derivative, m.p. 245–250°.

Anal. Calcd. for $C_{17}H_{29}N_3O_3$: C, 63.13; H, 9.04; N, 12.99; CH_3O–, 9.59. Found: C, 63.56; H, 9.00; N, 12.40; CH_3O–, 9.74.

The filtrate from the preparation of the semicarbazone of isomer A was concentrated at reduced pressure to remove most of the alcohol. The oil which separated was extracted into ether. The ether extracts were washed with water, dried and concentrated at reduced pressure to yield 2.6 g. of mixed semicarbazones as an oil. The oil was dissolved in 20 ml. of warm methanol and was treated with a solution of 1.59 g. of 2,4-dinitrophenylhydrazine in 20 ml. of methanol, 6 ml. of water and 2 ml. of concentrated sulfuric acid. The reaction mixture was concentrated and the residual oil was extracted into benzene. The benzene extract was washed with water, dried and concentrated to yield 3.1 g. of oily 2,4-dinitrophenylhydrazones.

The 3.1 g. of oil in benzene was chromatographed on an alumina column using one l. of benzene for column development. A red band at the top of the column was followed by a narrow and a wide orange band. The column was extruded and the wide orange band was eluted with methanol. The methanol solution was concentrated to yield a 1.96-g. residue. The residue was rechromatographed, developing with 3 l. of ether followed by one l. of benzene. The ether removes an impurity not removed by benzene alone. The column was extruded and the wide orange band was again eluted with methanol. The methanol solution was concentrated to yield a 1.1-g. residue. The residue was crystallized from benzene–methanol to yield a total of 0.6 g. (5%) of the 2,4-dinitrophenylhydrazone of 2-hydroxy-8-keto-5-methoxy-4a-methylperhydrophenanthrene (IXB), m.p. 204–

(14) The yield in other preparations was as high as 24%.

206°. Recrystallization from benzene–methanol yielded a purified sample, m.p. 210–211°.

Anal. Calcd. for $C_{22}H_{30}N_4O_6$: C, 59.18; H, 6.77. Found: C, 59.65; H, 6.96.

2-Hydroxy-8-keto-5-methoxy-4a-methylperhydrophenanthrene (IXA).—A solution of 6.24 g. of the semicarbazone of IX A in 50 ml. of acetic acid and 6.3 g. of 43% aqueous pyruvic acid was refluxed for 1 hr. The reaction mixture was concentrated at reduced pressure, and the residue was diluted with water. The oil which separated was extracted into ether. The ether extract was washed with aqueous sodium bicarbonate and water and concentrated to an oily residue. The residue was dissolved in a solution of 2.5 g. of potassium hydroxide in 100 ml. of ethanol. After being heated under nitrogen at the reflux temperature for 1 hr., the reaction mixture was concentrated to 50 ml. and diluted with 500 ml. of water. The solution was acidified with 25 ml. of 2.5 *N* hydrochloric acid and extracted five times with ether. The combined ether extracts were washed with aqueous sodium bicarbonate and water. The solvent was removed at reduced pressure to give 4.98 g. (97%) of the hydroxyketone IXA as a very viscous oil. A sample was heated at 100° (<1 mm.) for 3 hr. prior to analysis.

Anal. Calcd. for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84. Found: C, 72.95; H, 9.53.

2-Hydroxy-8-keto-5-methoxy-4a-methylperhydrophenanthrene (IXB).—A mixture of 0.475 g. of the 2,4-dinitrophenylhydrazone of the hydroxyketone IXB in 40 ml. of acetic acid containing 1 g. of 43% pyruvic acid was warmed to obtain complete solution. The solution was kept at room temperature for 48 hr. The crystalline 2,4-dinitrophenylhydrazone of pyruvic acid was removed, and the filtrate was concentrated at reduced pressure. The residue was dissolved in ether, and the ether solution was washed repeatedly with aqueous sodium bicarbonate, with water and dried. The ether solution was concentrated to yield an oil which crystallized from methylcyclohexane to yield 0.1 g. of hydroxyketone IXB, m.p. 144–145° (dried at 100°).

Anal. Calcd. for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84. Found: C, 72.05; H, 9.89.

The Semicarbazone of 2-Hydroxy-8-keto-5-methoxy-4a-methylperhydrophenanthrene (IXB).—A solution of 0.11 g. (0.00041 mole) of the hydroxyketone IXB in alcohol was treated with an aqueous solution of equal weights of semicarbazide hydrochloride and sodium acetate. No precipitate was obtained. The reaction mixture was extracted several times with ether and the ether extracts were combined, dried and concentrated. The residual oil crystallized after being kept at room temperature for several days. The product was recrystallized from alcohol to yield the semicarbazone of the hydroxyketone IXB, m.p. 225–227° dec. A mixture with the semicarbazone of the hydroxyketone IXA (m.p. 248–250° dec.) melted at 222–225° dec.

Anal. Calcd. for $C_{17}H_{29}N_3O_3$: C, 63.13; H, 9.04; N, 12.99. Found: C, 63.29; H, 8.82; N, 12.87.

Reduction of 2-Acetoxy-8-hydroxy-5-methoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (VI). B. Using a Ruthenium Catalyst.—A solution of 5 g. (0.016 mole) of 2-acetoxy-8-hydroxy-5-methoxy-4a-methyl-1,2,3,4,4a,-9,10,10a-octahydrophenanthrene in 75 ml. of methylcyclohexane was shaken with hydrogen (15,000 p.s.i.) and 1 g. of ruthenium[15] (10% on Darco) at 125° for 5 hr.[16] The reduction mixture was filtered and the catalyst was washed with a large volume of acetone. The filtrate and washings were concentrated to yield 5.0 g. of 2-acetoxy-8-hydroxy-5-methoxy-4a-methylperhydrophenanthrene. The oil showed only 1.5% of the typical phenolic absorption of starting material in the ultraviolet and contained no low boiling hydrogenolysis products.

A solution of the oil in 75 ml. of glacial acetic acid was cooled and was oxidized by the addition of a solution of 1.32 g. (20% excess) of chromium trioxide in 5 ml. of water. The solution was kept at room temperature for 16 hr. The reaction solution was diluted with water and extracted 5 times with ether. The combined ether extracts were washed with aqueous sodium bicarbonate and then with water. The ether was removed at reduced pressure to yield 4.5 g. of a mixture of isomers of 2-acetoxy-8-keto-5-methoxy-4a-methylperhydrophenanthrene (VIII).

The 4.5 g. of mixed acetoxyketones was refluxed under nitrogen in 70 ml. of ethanol (95%) containing 2.5 g. of potassium hydroxide. The reaction solution was diluted with water, acidified and extracted several times with ether. The combined ether extracts were washed with aqueous sodium bicarbonate and water. After being dried, the ether solution was concentrated at reduced pressure to yield 3.5 g. of a mixture of isomers of 2-hydroxy-8-keto-5-methoxy-4a-methylperhydrophenanthrene (IX).

The mixture of hydroxyketones (3.5 g.) was dissolved in 15 ml. of hot ethanol and a solution of 2 g. of semicarbazide hydrochloride and 2 g. of sodium acetate in 15 ml. of ethanol–water was added. On cooling, the solution yielded a total of 2.25 g. (43%) of the semicarbazone of 2-hydroxy-8-keto-5-methoxy-4a-methylperhydrophenanthrene (IXA), m.p. 244–246° dec. The filtrate from the above semicarbazone was diluted with water; an oil separated which was crystallized from methanol to yield 0.16 g. (3%) of the semicarbazone of 2-hydroxy-8-keto-5-methoxy-4a-methylperhydrophenanthrene (IXB), m.p. 218–223° dec.

Reaction of 2-Hydroxy-8-keto-5-methoxy-4a-methylperhydrophenanthrene (IXA) with Sulfuric Acid.—Three hundred and sixty milligrams (0.0014 mole) of 2-hydroxy-8-keto-5-methoxy-4a-methylperhydrophenanthrene (IXA) was dissolved in 4–5 ml. of concentrated sulfuric acid, and the solution was allowed to stand overnight at room temperature. It was poured into an excess of cold water and this solution was extracted three times with ether. The ether solution was washed with sodium bicarbonate solution, with water and was dried and concentrated.

The oily residue (210 mg.) was treated with 2,4-dinitrophenylhydrazine in alcohol and hydrochloric acid. A deep-red solid crystallized and was twice recrystallized from a mixture of alcohol and water to yield a 2,4-dinitrophenylhydrazone of 8-keto-4a-methyl-1(or 3),4,4a,5,6,7,8,9,10,10a-decahydrophenanthrene (XI), m.p. 190° dec.; $\lambda_{max}^{CHCl_3}$ 2590 Å. (ϵ 16500), $\lambda_{max}^{CHCl_3}$ 3890 Å. (ϵ 26000).

Anal. Calcd. for $C_{21}H_{24}N_4O_4$: C, 63.62; H, 6.10; N, 14.13. Found: C, 63.43; H, 6.34; N, 13.98.

A solution of 1.13 g. (0.0043 mole) of 2-hydroxy-8-keto-5-methoxy-4a-methylperhydrophenanthrene (IXA) in 15 ml. of glacial acetic acid and 15 ml. of 6 *N* sulfuric acid was heated under reflux for 16 hr. The reaction mixture was cooled and diluted with 200 ml. of water. The mixture was extracted twice with ether. The ether extracts were then washed with sodium bicarbonate solution, with water and dried and concentrated.

The residual oil (0.9 g.) was converted to a 2,4-dinitrophenylhydrazone with 0.9 g. of 2,4-dinitrophenylhydrazine in a mixture of 40 ml. of alcohol and 3–4 ml. of concentrated hydrochloric acid. The product was recrystallized from alcohol, but it was contaminated with the 2,4-dinitrophenylhydrazone of the starting material.

The mother liquor was diluted with water and 0.18 g. of the orange 2,4-dinitrophenylhydrazone of 8-keto-5-methoxy-4a-methyl-1(or 3),4,4a,4b,5,6,7,8,8a,9,10,10a-dodecahydrophenanthrene (X) separated, m.p. 150°; $\lambda_{max}^{CHCl_3}$ 2590 Å. (ϵ 11000), $\lambda_{max}^{CHCl_3}$ 3655 Å. (ϵ 24000).

Anal. Calcd. for $C_{21}H_{28}N_4O_5$: C, 61.67; H, 6.59; N, 13.08; CH_3O–, 7.24. Found: C, 61.82; H, 6.43; N, 12.98; CH_3O–, 7.11.

Reaction of 2,8-Diketo-5-methoxy-4a-methylperhydrophenanthrene (XII) with Sulfuric Acid.—Four hundred and twenty milligrams (0.0016 mole) of 2,8-diketo-5-methoxy-4a-methylperhydrophenanthrene (XII) was dissolved in 8 ml. of concentrated sulfuric acid. The solution was kept overnight at room temperature and was then poured into 200 ml. of cold water. The cloudy solution was extracted three times with ether. The ether extracts were washed with sodium bicarbonate solution, with water and were dried and concentrated.

The oily residue (350 mg.) was converted to a 2,4-dinitrophenylhydrazone in alcoholic solution in the usual manner to yield 650 mg. of the derivative, m.p. 200–203°. It was recrystallized three times from ethyl acetate to yield the

(15) I. D. Webb and G. T. Borcherdt, THIS JOURNAL, **73**, 752 (1951).

(16) At higher temperatures (150–225°) extensive hydrogenolysis occurred. Eight hours at 125° also produced extensive hydrogenolysis.

orange-red 2,4-dinitrophenylhydrazone of 2,8-diketo-4a-methyl - 1,2,3,4,4a,5,6,7,8,9,10,10a - dodecahydrophenanthrene (XIII), m.p. 228–230°; $\lambda_{max}^{CHCl_3}$ 2590 Å. (ε 27400); $\lambda_{max}^{CHCl_3}$ 3710 Å. (ε 48000).

Anal. Calcd. for $C_{27}H_{26}N_8O_8$: C, 54.72; H, 4.76; N, 18.91; CH_3O–, 0. Found: C, 55.26; H, 5.21; N, 17.80; CH_3O–, 0.3.

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[CONTRIBUTION FROM THE MCPHERSON CHEMICAL LABORATORY, THE OHIO STATE UNIVERSITY]

The Synthesis and Resolution of Hexahelicene[1]

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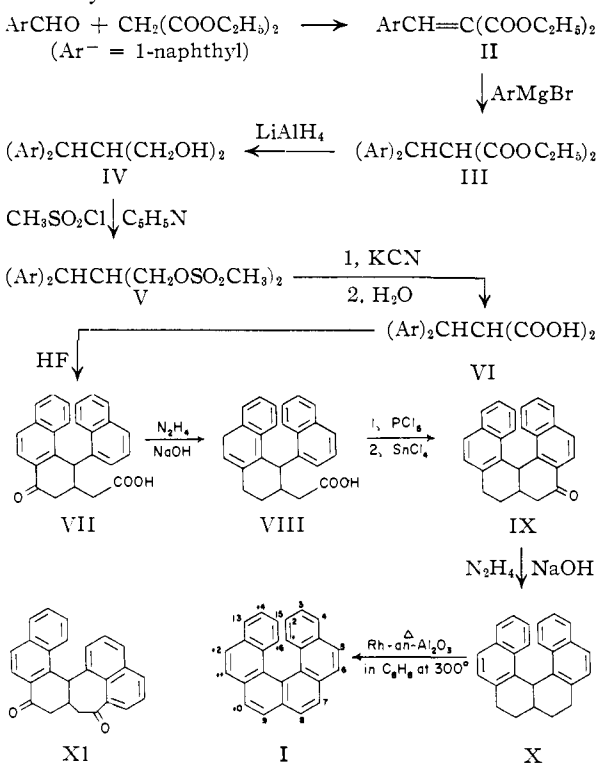
The synthesis and resolution of hexahelicene (I) is described.

In continuation of work on the synthesis and resolution of compounds which owe their asymmetry to intramolecular overcrowding[3] we report the synthesis and resolution of hexahelicene (I).[4] This compound represents the first example of a purely aromatic hydrocarbon which owes its asymmetry to intramolecular overcrowding. The preferred synthesis is outlined in the chart.



The condensation of 1-naphthaldehyde with ethyl malonate afforded II in 70% yield. The yields of III by addition of the Grignard reagent from 1-bromonaphthalene to II varied unpredictably between 35 and 56%. Reduction of III afforded pure IV in 90% yield. Conversion of the latter to VI was carried out in high over-all yield without purification of V or the corresponding dinitrile. Interestingly, the hydrolysis of the dinitrile by sulfuric in acetic acid was incomplete even after prolonged refluxing. However, alkaline hydrolysis for one hour in ethylene glycol at reflux afforded the acid VI in high yield. Cyclization of VI to VII by anhydrous hydrogen fluoride proceeded in 65–70% yield, the remaining product being a neutral glass. When pure VII was dissolved in hydrogen fluoride it could be quantitatively recovered. The only fair yield obtained in this type of cyclization which ordinarily proceeds in high yield foreshadowed the increasing difficulties which were to be met in the synthesis because of the increasing steric strains gradually being introduced into the molecule.

The ketoacid VII was reduced to VIII in 87% yield by the Huang-Minlon procedure. We have found in this case, as well as in several others, that the long periods of heating often recommended[5] are not necessary. After the water is distilled and the temperature begins to rise rapidly, if the apparatus is connected to an azotometer, it is seen that the gas evolution, usually nearly theoretical, is complete in 15–30 minutes. Further heating after this point is useless or harmful.

The cyclization of the reduced acid VIII proved difficult. The ring closure of the acid chloride of VIII to IX in 55% yield was finally accomplished by heating at 90° for one hour with stannic chloride in *o*-dichlorobenzene. When one contrasts this with the rapid cyclization of substituted γ-phenylbutyryl chlorides using stannic chloride[6] (2–12 minutes at about 5°) the great resistance toward formation of the hydrohexahelicene ring system is illustrated.

The conversion of IX to hexahelicene (I) was effected by several different routes, the best of which comprised reduction to the hexahydro derivative X followed by hydrogen transfer to benzene[7] over 5% rhodium-on-alumina[8] at 300°. The

(1) A systematic name is phenanthro[3,4-c]phenanthrene. However, a proposal to create the systematic name *helicene* for nuclei of the continuously coiled type is at present being considered by American and International nomenclature committees. The prefixes, penta, hexa and hepta, etc., would be used for five, six and seven, etc., ring compounds. The numbering preferred by the authors is shown on I.

(2) Holder of National Science Foundation Predoctoral Fellowships during the years 1952–1955. The material herein presented is taken from the Ph.D. thesis, O.S.U., 1955.

(3) For a review of recent accomplishments in this field see M. S. Newman and R. M. Wise, THIS JOURNAL, **78**, 450 (1956).

(4) For a preliminary communication see M. S. Newman, W. B. Lutz and D. Lednicer, *ibid.*, **77**, 3420 (1955).

(5) D. Todd, "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1948, Vol. IV, p. 385.

(6) M. S. Newman, H. V. Anderson and K. H. Takemura, THIS JOURNAL, **75**, 347 (1953).

(7) Compare H. Adkins, L. M. Richards and J. W. Davis, *ibid.*, **63**, 1320 (1941).

(8) Catalyst supplied by the Baker Company, Philadelphia, Pa.