[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Steroid Total Synthesis—Hydrochrysene Approach. II.[1] 1-Methoxy-8-keto-10a-methyl-5,6,8,9,10,10a,11,12-octahydrochrysene

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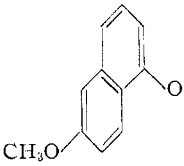
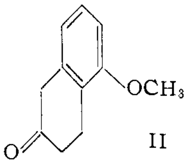
RECEIVED MAY 31, 1956

The tetracyclic ketone VI, a promising intermediate for steroid syntheses, has been prepared from 1,6-dimethoxynaphthalene (I) as follows. Sodium and alcohol reduction gave the known methoxytetralone II which was condensed in the Robinson–Mannich base reaction with 1-diethylamino-3-pentanone methiodide to give a mixture of the tricyclic ketones IV and V. Condensation of this product either with 1-diethylamino-3-butanone methiodide or methyl vinyl ketone yielded the crystalline tetracyclic ketone VI. Under mild reaction conditions the intermediary hydroxy ketone VIII was the major product. The structures of the tricyclic and tetracyclic products were proved by ultraviolet and infrared spectroscopy and by dehydrogenation studies.

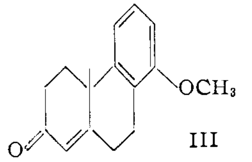
The objective of this study was to synthesize the tetracyclic ketone VI which promised to be a readily available and useful intermediate in a projected approach to the total synthesis of steroids.[1] The present paper describes our studies directed toward the preparation and proof of structure of this substance.



I



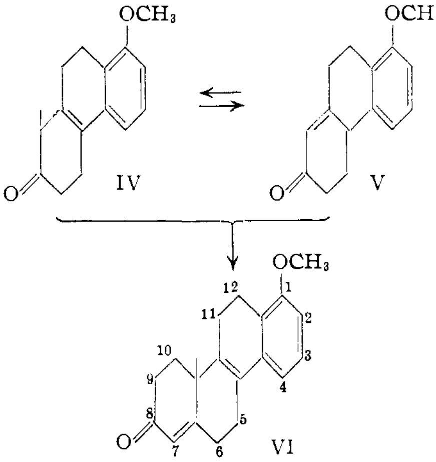
II



III

Cornforth and Robinson[6] have described an excellent method of preparing 5-methoxy-2-tetralone (II) in over 70% yield by sodium and alcohol reduction of 2,5-dimethoxynaphthalene (I) followed by acid hydrolysis of the enol ether. They also developed procedures for the monomethylation of the tetralone II at C_1 and for condensation of this product with 1-diethylamino-3-butanone methiodide in the Robinson–Mannich base reaction to produce the tricyclic intermediate III which has further been employed in a total synthesis of epiandrosterone.[7]

We have employed the Cornforth–Robinson sequence to produce an isomeric tricyclic ketone IV, which we envisaged as an intermediate constituting rings B, C and D of the steroid nucleus, rather than rings A, B and C as in the previous work.[6] In the present study the methoxytetralone II was not methylated but condensed directly with 1-diethylamino-3-pentanone methiodide. The previous procedure[6] worked well in this case, but for larger scale runs it was found advantageous to modify the procedure so that the reaction mixture was homogeneous and to employ sodium methoxide in place of potassium ethoxide as the condensing agent. The tricyclic product was thus obtained in 64% yield.



Although the tricyclic ketones III and IV differ only in the position of a methyl substituent, this structural variation has a fundamental effect on the functional properties of the molecule. In structure IV the hydrogen atom at the bridgehead of the two alicyclic rings is in the γ-position to the α,β-unsaturated ketone system. This arrangement permits the olefinic bond to migrate readily into conjugation with the aromatic nucleus in a 3-carbon tautomerism IV $\rightleftarrows$ V, a situation which is precluded in compound III by the angular methyl group at the bridgehead. It was not surprising, therefore, to find that our tricyclic product was an oily mixture consisting principally of the two tautomers IV and V. The latter form, m.p. 97°, was preponderant and could be crystallized from the mixture in about 40% yield. The ultraviolet absorption spectrum of this isomer (Fig. 1) was characteristic of the *m*-methoxystyrene chromophore with a minimum in the 240 mμ region, where the form IV, in contrast, would be expected to absorb at high intensity due to the α,β-unsaturated ketone chromophore. The spectrum of the crude (mixture) tricyclic ketone (Fig. 1) does, in fact, exhibit considerable absorption in this region indicating the presence of some of the isomer IV, which has not, as yet, been isolated in a pure state.

The common anion VII derivable from either tautomer IV or V was expected to undergo alkyla-

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[1] Paper I, W. S. Johnson, THIS JOURNAL, **78**, 6278 (1956).

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[5] Sterling-Winthrop Research Institute Fellow, Spring, 1951; Allied Chemical and Dye Co. Fellow, 1951–1952.

[6] J. W. Cornforth and R. Robinson, *J. Chem. Soc.*, 1855 (1949).

[7] H. M. E. Cardwell, J. W. Cornforth, S. R. Duff, H. Holtermann and R. Robinson, *ibid.*, 361 (1953).

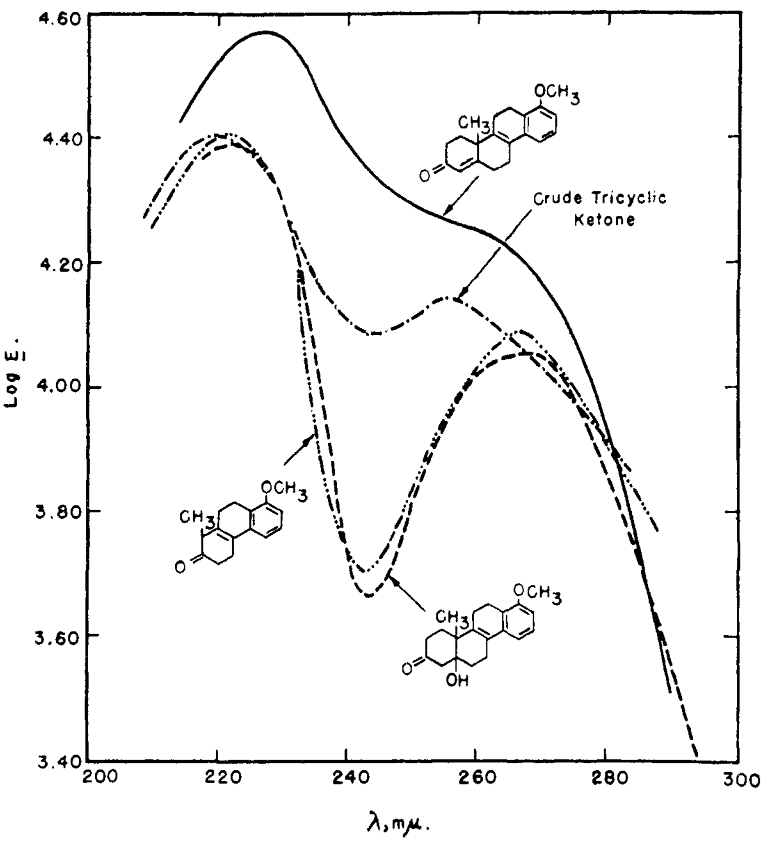
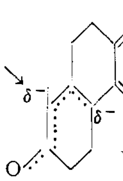


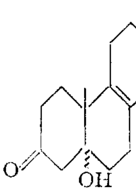
Fig. 1.

tion at C_8 (indicated by arrow) which has vinylogous β-tetralone reactivity.[8] We chose to use the



VII

system IV ⇌ V accordingly with the view to applying the Wilds principle of vinylogous activation for adding a new ring.[9] When the tricyclic ketone mixture was treated in the presence of sodium methoxide either with methyl vinyl ketone or with 1-diethylamino-3-butanone, the Michael reaction occurred at the methyne position C_8 and was followed by aldol cyclization to produce the crystalline tetracyclic ketone VI in 64% yield.



VIII

As in the case of Wilds, *et al.*,[9] mild reaction conditions yielded the intermediary aldol VIII which was obtained as a crystalline mixture of the 6a-epimers.[10] On heating with methanolic sodium methoxide, this mixture of epimers VIII was converted smoothly into the tetracyclic ketone VI.

For preparative purposes it was not necessary to isolate the tricyclic ketone mixture IV ⇌ V. The reaction mixture in which it was formed was treated directly with methyl vinyl ketone, and the sparingly soluble mixture of ketols VIII was isolated and dehydrated as described above. In this way the tetracyclic ketone VI was produced easily in 34% over-all yield from II.

The pure tetracyclic ketone melted at 175°, and its ultraviolet spectrum (Fig. 1) corresponded to a superposition of the absorption of the α,β-unsaturated ketone chromophore (λ_{max} *ca.* 240 mμ) on that of the *m*-methoxystyrene system (*cf.* the spectrum of VIII, Fig. 1) and is therefore consistent with the structure VI. The semicarbazone exhibited a typical λ_{max} at 271 mμ (log ε 4.62) for the α,β-unsaturated system.[11] Evidence for the nuclear structure was provided by dehydrogenation over 30% palladium-on-carbon at 345–360°, which gave a mixture from which chrysene was isolated. The loss of the methoxyl group during dehydrogenation has been reported previously[12] and has also been observed upon dehydrogenation of the ketone IX[13] under similar conditions to give chrysene. In another dehydrogenation experiment on the product obtained by lithium aluminum hydride reduction of VI, a small amount of 1-methoxychrysene was isolated and shown to be identical (mixed m.p. and ultraviolet spectrum) with authentic material.

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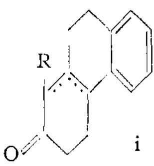
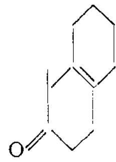
(8) Stork and Worrall (see W. S. Worrall, Ph.D. Thesis, Harvard University, 1949) for example, have demonstrated in a closely related system i (R = H) that ethylation of the enolate yields the product i (R = C_2H_5).

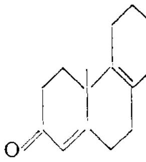


i

(9) *Cf.* A. L. Wilds, J. W. Ralls, W. C. Wildman and K. E. McCaleb, This Journal, **72**, 5794 (1950). We are indebted to Prof. Wilds for telling us of his ideas, previous to their reduction to practice (see reference above), for the conversion of the diketone ii with methyl vinyl ketone to the tricyclic compound iii.



ii



iii

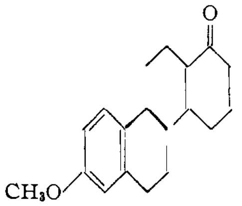
(10) See paper IV, W. S. Johnson, J. Ackerman, J. F. Eastham and H. A. DeWalt, Jr., *ibid.*, **78**, 6302 (1956), for proof of structure.

(11) *Cf.* the λ_{max} 273 mμ (log ε 4.42) of cholestenone semicarbazone, W. Menschick, I. H. Page and K. Bossert, *Ann.*, **495**, 225 (1932).

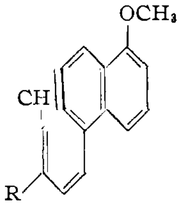
(12) *E.g.*, L. Ruzicka, K. Hofmann and J. Frei, *Helv. Chim. Acta*, **19**, 386 (1936); W. Cocker, B. E. Cross, A. K. Fateen, C. Lipman, E. R. Stuart, W. H. Thompson and D. R. A. Whyte, *J. Chem. Soc.*, 1781 (1950).

(13) W. S. Johnson, D. K. Banerjee, W. P. Schneider, C. D. Gutsche, W. E. Shelberg and L. J. Chinn, This Journal, **74**, 2832 (1952).

Evidence for the nuclear structure of the tricyclic ketone was provided by dehydrogenation experiments on the product formed by reduction of the keto group and dehydration. A substance was isolated which agreed in properties with those reported for 1-methoxy-8-methylphenanthrene (X, R = H).[14] Dehydrogenation of the tricyclic ketone directly with sulfur resulted in retention of the keto oxygen atom and after methylation yielded a product which was undoubtedly 1,7-dimethoxy-8-methylphenanthrene (X, R = OCH_3), m.p. 183°.



IX



X

Acknowledgment.—We wish to thank the agencies mentioned in references 1–5 for their generous assistance. We are indebted to the Sterling-Winthrop Research Institute also for providing large amounts of starting materials, and to S. Darling and R. Hindersinn for their help in producing quantities of the intermediates described herein for use in studies reported in the sequel.

Experimental Part[15,16]

Reaction of 5-Methoxy-2-tetralone (II) with 1-Diethylamino-3-pentanone Methiodide.—For small-scale runs, the procedure of Cornforth and Robinson[6] for the condensation of 1-methyl-5-methoxy-2-tetralone with 1-diethylamino-3-butanone methiodide gave satisfactory results; but for the larger runs it was necessary to modify the conditions as described below so that the reaction was conducted under essentially homogeneous conditions.

The following operations were conducted under strictly anhydrous conditions. To a chilled (ice-bath) solution of 221 g. of 1-diethylamino-3-pentanone[17] in 750 ml. of dry thiophene-free benzene was added slowly, with stirring, 219 g. of dry methyl iodide over a period of 1 hour. Stirring was continued with cooling for 4 hours; then the mixture was allowed to stand for about 18 hours at 0°. The pasty methiodide was dissolved by the addition of 350 ml. of anhydrous methanol and while still cold this solution was employed in the reaction described below.

A 5-l., 3-necked, round-bottomed flask was fitted with a rubber-sealed wire stirrer, a pressure-equalized Hershberg dropping funnel,[18] and a reflux condenser which was connected at the top through a 3-way stopcock to a source of vacuum and dry nitrogen.[19] The system was evacuated, flame-dried, and dry nitrogen was admitted. The flask was then charged with 1150 ml. of anhydrous methanol, and 48.5 g. of sodium was added slowly with the usual precautions. After the sodium was dissolved, a solution of 248 g. of 5-methoxy-2-tetralone[6] in 550 ml. of dry thiophene-free benzene was placed in the dropping funnel. The system was evacuated until the solvent began to boil, then filled with dry nitrogen, the process being repeated once to ensure the removal of air. The ketone solution was then added rapidly to the stirred sodium methoxide solution with cooling (ice-bath). The dropping funnel was next charged (in an escaping stream of nitrogen) with the cold solution of Mannich base methiodide prepared as described above. The methiodide solution was then added over a period of 140 minutes with stirring and cooling to 2–5°. Stirring was continued for 3.5 hours; then the ice-bath was replaced by a heating mantle and the mixture was boiled under reflux for 1 hour. The mixture was cooled, acidified with 1600 ml. of 2 *N* sulfuric acid, diluted with 1 l. of water, and stirred thoroughly. The aqueous layer was then separated, and extracted with three portions of ether. The combined ether and benzene solutions were washed thoroughly with saturated salt solution; then the solvent was removed by distillation under reduced pressure. The residual oil was distilled through a 12 × 2-cm. Vigreux column with a short air condenser to yield the following fractions: (1) b.p. 60–140° (0.8–1.3 mm.), 27.6 g. consisting mainly of recovered 5-methoxy-2-tetralone; (2) b.p. 140–158° (1.2–1.3 mm.), 11.3 g. containing some of the tricyclic ketone; (3) b.p. 158–203° (mostly at 200°) (0.6 mm.), 218 g. (64% yield) of the tricyclic ketone. Fraction (3) was a pale green oil which mostly solidified on seeding with the solid isomer described below. A sample of the mixture of tricyclic ketones produced in another run boiling at 155–188° (0.08–0.2 mm.) showed λ_{max} 222 mμ (log *E* 4.40), 255 (4.14), λ_{min} 242 (4.09).

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.55; H, 7.81.

A **2,4-dinitrophenylhydrazone**, m.p. 227.5–229° (dec.) was isolated by crystallization and chromatography of the mixture of derivatives produced from the crude tricyclic ketone. This isomer was obtained as silky orange needles from chloroform–methanol and was probably derived from the β,γ-isomer V.

Anal. Calcd. for $C_{22}H_{22}N_4O_5$: C, 62.55; H, 5.25. Found: C, 62.59; H, 5.39.

A 38-g. sample of tricyclic ketone, b.p. 190–195° (0.25 mm.), prepared as described above was crystallized from 100 ml. of ethanol. The colorless product melted at 90–95° and amounted to 16.0 g. Recrystallization from ethanol gave 14.8 g. of colorless prisms of **1-methyl-2-keto-8-methoxy-1,2,3,4,9,10-hexahydrophenanthrene** (V), m.p. 96.5–97°; λ_{max} 222 mμ (log *E* 4.41), 267 (4.08), λ_{min} 243 (3.72).

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 78.94; H, 7.55.

The residue from the distillation of tricyclic ketone prepared as described above contained higher boiling material which consisted in part of **1-methoxy-7,10a-dimethyl-8-keto-5,6,8,9,10,10a,11,12-octahydrochrysene** (formula VI with CH_3 at position 7) produced by further action of the Mannich base methiodide on the tricyclic ketone. Thus the pot residue (86 g.) from a run using 300 g. of methoxytetralone was redistilled and a 21.2-g. fraction of material b.p. 229–230° (0.15–0.2 mm.) was obtained. Two grams of this oil was crystallized from methanol yielding 0.50 g. of colorless rods, m.p. 133–137°. A sample, m.p. 136.4–137.2°, obtained by recrystallization from methanol was evidently converted upon evaporative distillation at 0.15 mm. into a higher melting polymorphic modification obtained as colorless needles from methanol, m.p. 143.2–143.8°, undepressed on admixture with authentic material prepared as described below, λ_{max} 221 mμ (log *E* 4.41), 255 (4.35), λ_{min} 241.5 (4.29).

Anal. Calcd. for $C_{21}H_{24}O_2$: C, 81.78; H, 7.84. Found: C, 82.02; H, 8.09.

The oxime crystallized from ethanol as colorless rods, m.p. 208.5–209.5°.

Anal. Calcd. for $C_{21}H_{25}O_2N$: C, 77.98; H, 7.79. Found: C, 78.09; H, 7.64.

Authentic 1-methoxy-7,10a-dimethyl-8-ketoöctahydrochrysene was prepared from 4.84 g. of distilled tricyclic ketone in 40 ml. of benzene and the methiodide formed from 3.24 g. of diethylaminopentanone and 3.08 g. of methyl iodide. The procedure of Cornforth and Robinson[6] was used except that sodium methoxide (from 0.69 g. of sodium and 30 ml. of methanol) was employed instead of potassium ethoxide. Crystallization of the crude oily product from methanol gave 4.1 g. (67% yield) of nearly colorless crystals, m.p. 133–134.5°. Further purification as described above raised the m.p. to 142.8–143.6°.

1-Methoxy-8-keto-10a-methyl-5,6,8,9,10,10a,11,12-octahydrochrysene (VI).—A solution of the Mannich base

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[14] G. A. R. Kon and H. R. Soper, *J. Chem. Soc.*, 790 (1939).

[15] All melting points are corrected for stem exposure.

[16] Ultraviolet absorption spectra were determined with a Beckman quartz spectrophotometer; 95% alcohol was employed as the solvent.

[17] Prepared by the unpublished procedure of A. L. Wilds, K. E. McCaleb and G. E. Inglett of this Laboratory.

[18] *Org. Syntheses*, **18**, 16 (1938).

[19] *Ibid.*, **30**, 19 (1950), Fig. 1.

methiodide was prepared from 38.3 g. of 1-diethylamino-3-pentanone and 38.0 g. of methyl iodide. The procedure was essentially the same as described above except that ether (150 ml.) was used as the solvent and 0.5 ml. of benzyl alcohol was added to catalyze the quaternary salt formation. After reaction was complete, the ether was removed under reduced pressure and the crystalline salt dissolved in 61 ml. of anhydrous methanol (dried over magnesium methoxide). This solution was employed in a condensation with 45.0 g. of 5-methoxy-2-tetralone. The procedure described above was followed except that anhydrous methanol was employed as the solvent, 95 ml. being used to dissolve the tetralone, and 200 ml. for the dissolution of the sodium (8.40 g.). After the addition of the methiodide was complete (140–170 minutes), the solution was stirred for 2 hours in the cold, then 1 hour with the cooling bath removed, and finally was boiled under reflux for 2 hours. The mixture was cooled, a solution of 7.85 g. of sodium in 200 ml. of anhydrous methanol was added rapidly (under nitrogen), and then a solution of 26.9 g. of dry methyl vinyl ketone[20] in 175 ml. of anhydrous methanol was dropped in slowly over a period of 2 hours with stirring and cooling to 2–5°. During this period the hydroxy ketone began to precipitate. After standing at room temperature for 18 hours the mixture was cooled to 15°, 50 ml. of acetic acid was added and the colorless crystalline product was separated by filtration; yield 30.0 g. This product apparently consisted of the hydroxy ketone VIII contaminated with unsaturated ketone VI, which was undoubtedly present in varying amounts depending on the run as the melting point was found to vary between values as low as 169–172° (presumably mostly unsaturated ketone) up to about 200°. Such material, however, was entirely satisfactory for the preparation of pure unsaturated ketone. Additional crude hydroxy ketone can be obtained by working up the filtrate as described in another experiment below.

When distilled tricyclic ketone (203 g.) was employed in the condensation with methyl vinyl ketone[20] (88.2 g.) and sodium methoxide (from 14.4 g. of sodium) as described above, 142 g. of crude hydroxy ketone was obtained in the first crop. The filtrate was evaporated under reduced pressure, sufficient water added to dissolve the sodium acetate and the mixture extracted with benzene. The benzene layer was evaporated under reduced pressure and the gummy residue triturated with ether and allowed to stand overnight. In this way an additional 30 g. of colorless crystalline crude hydroxy ketone was obtained.

The unsaturated ketone was easily obtained from the crude hydroxy ketone as follows. The 30.0 g. of first crop material obtained without isolation of the tricyclic ketone (see above) was treated with a solution of 3.5 g. of sodium in 500 ml. of methanol. After refluxing for 4 hours under an atmosphere of nitrogen, the mixture was chilled and 9.5 ml. of acetic acid was added. The colorless product was separated by filtration, washed with ether followed by water and dried in a vacuum oven at 100°. The yield of tetracyclic ketone, m.p. 174–175°, was 25.6 g. (34% based on methoxytetralone).

A sample of the tetracyclic ketone purified by sublimation at 170° (0.05 mm.) followed by recrystallization from ethanol was obtained as colorless rhombs, m.p. 174.2–175.2°.

Anal. Calcd. for $C_{20}H_{22}O_2$: C, 81.59; H, 7.53. Found: C, 81.48; H, 7.61.

The semicarbazone crystallized from ethanol as colorless short rods, m.p. 246–249° (dec.) with darkening at 237°; λ_{max} 223.5 mμ (log *E* 4.47), 271 (4.62), λ_{min} 242 (4.21).

Anal. Calcd. for $C_{21}H_{25}O_2N_3$: C, 71.77; H, 7.17. Found: C, 71.55; H, 7.30.

The alternative preparation of the tetracyclic ketone VI by the use of the Mannich base methiodide was carried out as follows. The Mannich base methiodide was prepared from 15.3 g. of 1-diethylamino-3-butanone in 50 ml. of benzene and 16.4 g. of methyl iodide under essentially the same conditions as described above for the higher homolog. After standing for 90 hours in the refrigerator the solvent was removed through a sintered glass filter disk and the residual salt was washed with dry ether (yield 29.7 g., 97%). The methiodide was dissolved in 50 ml. of methanol and 50 ml. of benzene, and this solution was employed in condensation with 26.15 g. of distilled tricyclic ketone mixture (dissolved in 220 ml. of benzene) in the presence of a solution of 3.73 g. of sodium in 110 ml. of methanol. The procedure was essentially the same as that described above for the condensation of the Mannich base methiodide with 5-methoxy-2-tetralone. The addition time for the methiodide was 2 hours, stirring was continued for 1 hour in the cold, then the mixture was refluxed for 25 minutes, cooled, and acidified with 200 ml. of 2 *N* sulfuric acid. The orange benzene layer was separated, and the aqueous layer extracted with benzene. The combined benzene solutions were washed thoroughly with water, and concentrated under reduced pressure. The orange solid residue was crystallized from 100 ml. of *n*-butyl acetate to give 20.4 g. (64% yield) of tetracyclic ketone, m.p. 169–172.5°.

Dehydrogenation Studies. (a) Of the Tetracyclic Ketone VI.—A mixture of 0.200 g. of the tetracyclic ketone and 0.25 g. of 30% palladium-on-carbon[21] was heated at 345–360° for 1 hour and 40 minutes in the Heymann type of apparatus.[22] A total of 2.8 moles of gas per mole of ketone was liberated. The crystals which had sublimed onto the cold finger amounted to 0.080 g. Two recrystallizations from benzene–methanol gave 0.007 g. of colorless plates, m.p. 254.2–255°. On admixture with an authentic sample of chrysene, m.p. 252–253°, the m.p. was 251.8–253°. An additional 0.008 g. of material, m.p. 252–253°, was obtained from the mother liquors.

Anal. Calcd. for $C_{18}H_{12}$: C, 94.70; H, 5.30. Found: C, 94.42; H, 5.56.

In another experiment 0.200 g. of the tetracyclic ketone in 10 ml. of benzene was added to a solution of 0.1 g. of lithium aluminum hydride in 50 ml. of ether. The mixture was refluxed for 20 minutes, allowed to stand at room temperature for 15 minutes, and water was added, followed by 15 ml. of 2 *N* sulfuric acid. The aqueous phase was extracted with ether, and the combined ether layers dried over anhydrous sodium sulfate. The oil obtained on evaporation of the solvent was heated with 0.25 g. of palladium-on-carbon[21] at 310–360° for 1 hour and 43 minutes. A total of 2.54 moles of gas per mole of compound was evolved, and 0.09 g. of sublimate was collected. Recrystallization from benzene–methanol gave a first crop, m.p. 196–200° (soft at 156°), and a second, m.p. 155–168°. Recrystallization of the second crop from methanol gave 0.005 g. of plates, m.p. 167–168°, undepressed on admixture with 1-methoxychrysene prepared as described below. The ultraviolet absorption spectra of the two substances were also essentially identical. Cook and Schoental[23] report the m.p. 167–168° for 1-methoxychrysene.

A sample of 1-methoxychrysene was synthesized from 1-keto-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysene prepared by W. P. Schneider according to the procedure for producing the corresponding 8-methoxy derivative.[13] A 0.36-g. sample of the crude mixture of stereoisomeric ketones (m.p. 128–133°) was heated with 0.3 g. of 30% palladium-on-carbon[21] at 295–320° for 1 hour and 15 minutes. A total of 3.75 moles of gas per mole of compound was evolved. The phenol which sublimed was methylated by the procedure of Cook and Schoental[23] giving material melting at 167–168° after recrystallization from benzene–petroleum ether; λ_{max} 226.5 mμ (log *E* 4.53), 267 (5.00), 293 (4.03), 304 (4.16), 318 (4.09), 345 (3.38); λ_{min} 243 (4.41), 288 (3.98), 297.5 (4.01), 311 (4.03), 342 (3.35), 357 (2.82), 363 (3.26).

(b) **Of 1-Keto-8-methoxydodecahydrochrysene (IX).**—A 1-g. sample of the α-isomer, m.p. 169–170°[13] (prepared by W. P. Schneider), was heated with 1 g. of 30% palladium-on-carbon[21] at 313–350° for 2 hours and 20 minutes. Crystallization of the sublimate from benzene gave 0.30 g. of material, m.p. 251–253°. Recrystallization from benzene (Norit) gave colorless plates with a strong violet fluores-

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[20] The azeotrope containing 85% methyl vinyl ketone supplied by E. I. du Pont de Nemours and Co. was dried by treatment with excess anhydrous potassium carbonate. The organic layer was separated, chilled in an ice bath and dried first over calcium chloride, then potassium carbonate. Distillation at reduced pressure gave material b.p. 30–32° (120 mm.) or 35–36° (140 mm.), $n^{23}D$ 1.4086.

(21) R. P. Linstead and S. L. S. Thomas, *J. Chem. Soc.*, 1127 (1940).

(22) L. F. Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., Boston, Mass., 1941, p. 461.

(23) J. W. Cook and R. Schoental, *J. Chem. Soc.*, 288 (1945).

cence, m.p. 257.5–259° (after drying at 78° (0.5 mm.) for 2 hours), undepressed on admixture with chrysene.

Anal. Calcd. for $C_{18}H_{12}$: C, 94.70; H, 5.30. Found: C, 94.91; H, 5.63.

(c) **Of the Tricyclic Ketone.**—A 0.5-g. sample of the distilled tricyclic ketone was treated with 0.5 g. of lithium aluminum hydride in a total of 150 ml. of anhydrous ether. After refluxing for 15 minutes and standing at room temperature for 1 hour, water was added followed by 70 ml. of 2 *N* sulfuric acid. The product was extracted with ether, the solvent evaporated, and the residual oil dehydrated by heating with 0.5 g. of potassium bisulfate at 160° for 7 minutes under an atmosphere of nitrogen. Evaporative distillation at 140–180° (0.1 mm.) gave 0.45 g. of pale yellow oil which was heated with 0.3 g. of 30% palladium-on-carbon[21] at 348–352° for 2 hours and 25 minutes. A total of 1.9 moles of gas per mole of compound was evolved. The product was separated from the catalyst by dissolution in ether and filtration. Evaporation of the filtrate gave 0.217 g. of semi-solid material which was treated with 0.223 g. of picric acid in 3 ml. of a saturated solution of picric acid in ethanol. On cooling 0.17 g. of a picrate separated, m.p. 128–132°. Recrystallization from ethanol raised the m.p. to 138–144°. This material (0.1 g.) was dissolved in ethanol and passed through a column of alumina to decompose the picrate. The product was eluted with ethanol, the eluate evaporated, and the residue crystallized from methanol to give 0.025 g. of crystals, m.p. 114–118° (softening at 110°). Recrystallization from 95% alcohol then again from dilute alcohol raised the m.p. to 119.8–121°.

Anal. Calcd. for $C_{16}H_{14}O$: C, 86.45; H, 6.35. Found: C, 86.40; H, 6.54.

The trinitrobenzene complex was obtained as yellow needles from ethanol, m.p. 177.1–178.3°. Kon and Soper[14] report that 1-methoxy-8-methylphenanthrene melts at 121–121.5° and the trinitrobenzene derivative at 177–178°.

The dehydrogenation of 0.300 g. of the distilled tricyclic ketone with 0.0818 g. of sulfur was carried out between 170–215° for 47 minutes, then the temperature was raised to 250° during a 10-minute period and maintained there for 15 minutes. Evaporative distillation of the black product at 180–220° (1–2 mm.) gave 0.12 g. of a viscous oil which solidified immediately, m.p. 60–80°. It was dissolved in 15 ml. of 10% sodium hydroxide, filtered, 3 ml. of dimethyl sulfate was added, and the mixture shaken for 10 minutes, then heated on the steam-bath for 30 minutes. The organic material was taken up in chloroform, dried over calcium chloride and, after evaporation of the solvent, sublimed at 140–160° (0.05 mm.). The sublimate (0.012 g.) was recrystallized twice from alcohol to give **1,7-dimethoxy-8-methylphenanthrene** (X, R = CH_3) as colorless rods, m.p. 182–183.2°.

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 81.09; H, 6.77.

MADISON, WISCONSIN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Steroid Total Synthesis—Hydrochrysene Approach. III.[1] Reduction of the Olefinic Bonds and of the Carbonyl Group in 1-Methoxy-8-keto-10a-methyl-5,6,8,9,10,10a,11,12-octahydrochrysene

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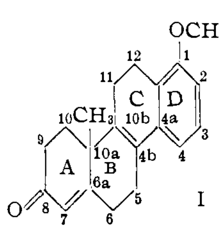
RECEIVED MAY 31, 1956

Reduction of the olefinic bonds and the carbonyl group of the tetracyclic ketone I has been studied. Stereoselective reduction of the 6a,7-bond has given the A/B *trans-* and A/B *cis*-dihydro ketones IV and XI. The former on catalytic hydrogenation of the 4b,10b-(styrene) bond gives the *trans-anti-cis* ketone-A, and on lithium–alcohol–ammonia reduction of the corresponding ketal, V affords upon acid hydrolysis the *trans-anti-trans* ketone-B. The alcohol IX derived from ketone-B can be produced in a single step by lithium–alcohol–ammonia reduction of I. Similarly XI has led to the *cis-syn-cis* ketone-C and the *cis-anti-trans* ketone-D. In the reduction of the ketal XII a second isomer (XIV) was produced which afforded on hydrolysis what is probably the *cis-syn-trans* ketone-E. Some other approaches to these tetrahydro ketones or their reduction products are also reported, and the general stereochemical problem is discussed. The present study along with that described in paper IV has thus led to the synthesis and configurational assignment of 6 of the 8 possible 4b,6a,7,10b-tetrahydro derivatives of the tetracyclic ketone I.

In the preceding paper[1] the three-step synthesis (from 1,6-dimethoxynaphthalene) and the proof of structure of the tetracyclic ketone I are described. The present work is a report of a study of the selective reduction of the double bonds at the 6a,7- and the 4b,10b-position as well as of the carbonyl group at C_8.



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The reduction of the 6a,7-bond is first considered. By analogy to the conversion of cholestenone into cholestanone (A/B *trans*),[11] the tetracyclic ketone was treated with ethyl orthoformate to produce the crystalline enol ethyl ether II, m.p. 136°, with λ_{max} 227 mμ (log ϵ 4.58), which is characteristic of the diene structure II and shows that the styrene

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(1) Paper II, W. S. Johnson, J. Szmuszkovicz, E. R. Rogier, H. I. Hadler and H. Wynberg, THIS JOURNAL, **78**, 6285 (1956).

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(11) H. H. Inhoffen, G. Stoeck, G. Kölling and U. Stoeck, *Ann.*, **568**, 52 (1950).