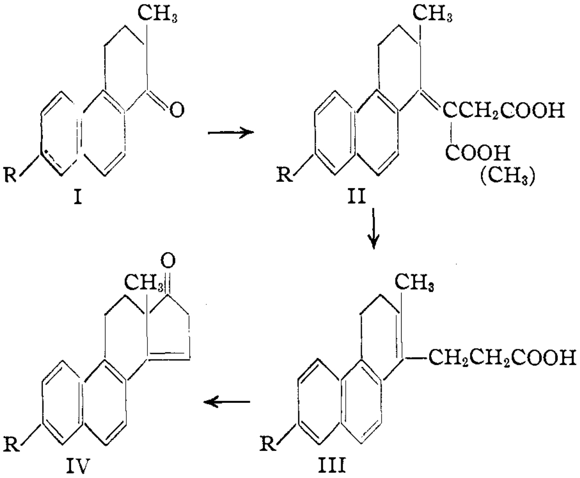
[Contribution from the Laboratory of Organic Chemistry of the University of Wisconsin]

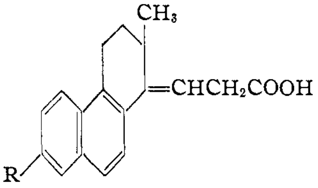
The Stobbe Condensation with 1-Keto-2-methyl-7-methoxy-1,2,3,4-tetrahydrophenanthrene. A New Synthesis of Equilenin[1]

By William S. Johnson* and Verner L. Stromberg[2]

In a recent communication[3] we described a synthesis of 14,15-dehydro-17-equilenone, IV (R = H) from 1-keto-2-methyl-1,2,3,4-tetrahydrophenanthrene, I (R = H), according to the sequence outlined in the accompanying flow sheet. This scheme has now been extended to the methoxy series (formulas I→IV, R = OCH_3). Since the product, 14,15-dehydroequilenin methyl ether (IV, R = OCH_3), is known to be convertible into equilenin,[4] this scheme constitutes another approach to the hormone. The present communication includes a description of this synthesis as well as some experiments on the elucidation of the structures of some of the intermediates involved in this and some previous studies.



The methoxy ketone I (R = OCH_3) was even less reactive than the parent compound I (R = H)[3] in the Stobbe condensation with dimethyl succinate, but by further modification of the procedure excellent yields were realized. The crude mixture of dibasic acids obtained upon saponification of the half-ester mixture was submitted directly to acid-catalyzed decarboxylation giving the monobasic acid III (R = OCH_3) in 35% over-all yield. This acid, m. p. 185° (methyl ester 99°), is evidently different from either of those m. p. 194° (methyl ester 114°) and m. p. 230° (methyl ester 137°) obtained by Haberland[5] *via* a different synthetic route and tentatively assigned by him the structures V (R = OCH_3) and III (R = OCH_3), respectively. That our 185° acid does indeed have the latter structure was suggested by the fact that the ultraviolet absorption spectrum is almost identical with that of the model compound 1,2-dimethyl-7-methoxy-3,4-dihydrophenanthrene, VI (see Fig. 1). The spectrum of the acid also resembles, but somewhat less closely, that of 14,15-dehydroequilenin methyl ether, IV (R = OCH_3), which constitutes a model for the structure V (R = OCH_3) with the bond exocyclic to the alicyclic six-membered ring. Proof that the 185° acid did not have the structure V (R = OCH_3), however, was provided by ozonization which gave none of the ketone I (R = OCH_3), but instead a keto acid which is the expected product from the structure III (R = OCH_3) with the olefinic bond in the endocyclic position. Analogous results were obtained on ozonization of the monobasic acid in the series lacking the methoxyl group and accordingly the structure III (R = H) previously tentatively proposed[3] is now confirmed.



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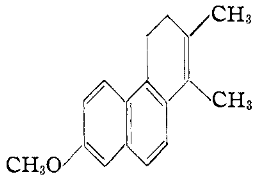

VI

Although the structures of Haberland's acids remain uncertain, there appears to be fair correlation between his lactone, m. p. 198°, produced by sulfuric acid cyclization of the keto acid VII, and the lactone m. p. 193° obtained in the present work by hydrogen fluoride cyclization of the 185° acid III (R = OCH_3), particularly since the hydroxy acids obtained by alkaline hydrolysis of each of these lactones melted at 163 and 162.5°, respectively. Haberland suggests a δ-, but we prefer the γ-lactone structure VIII, particularly in view of the easy reconversion to an unsaturated acid by the action of warm mineral acid on the sodium salt of the hydroxy acid. Since this transformation failed in the series without the methoxyl substituent[3] it becomes evident that this group labilizes the C–O bond which is reasonable only with the γ-lactone structure.[6] By

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* Harvard University Ph.D. 1940.

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[3] Johnson, Stromberg and Petersen, This Journal, **71**, 1384 (1949).

[4] Johnson, Petersen and Gutsche, *ibid.*, **69**, 2942 (1947).

[5] Haberland, *Ber.*, **72**, 1215 (1939); **76**, 621 (1943).

[6] The mechanism of this conversion may indeed be related to the acid-catalyzed lacto-enoic tautomerism VIII $\rightleftarrows$ III like that demonstrated in a closely related series (Johnson, Petersen and Schneider, This Journal, **69**, 74 (1947)) in that a common carbonium ion intermediate is probably involved. The labilizing effect of a conjugated methoxyl group on this type of tautomerism has also been demonstrated; Johnson and Miller, *ibid.*, **72**, 511 (1950).

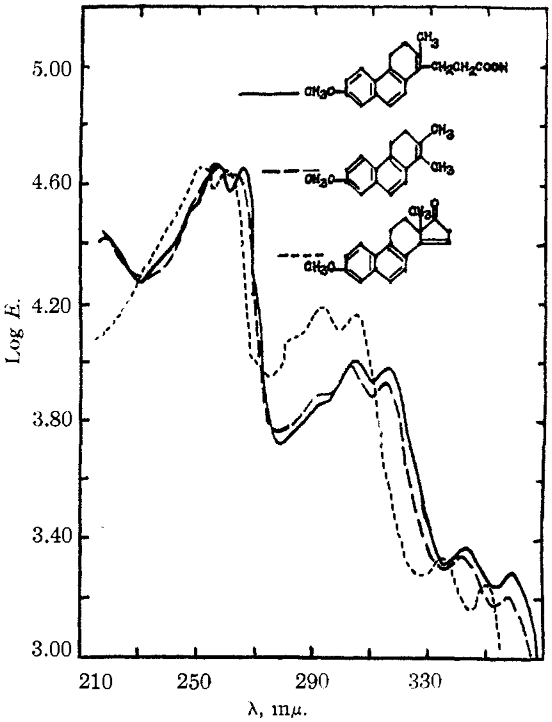
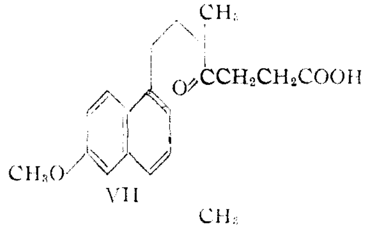
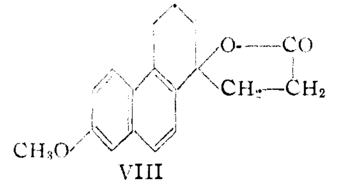


Fig. 1.———, β-(2-Methyl-7-methoxy-3,4-dihydro-1-phenanthryl)-propionic acid; — — — —, 1,2-dimethyl-7-methoxy-3,4-dihydrophenanthrene; - - - - - - - -, 14,15-dehydroequilenin methyl ether.

such isomerization of his lactone, however, Haberland obtained the 230° acid, while our experiments resulted in regeneration of the 185° acid III (R = OCH_3).



VII



VIII

Cyclization of the unsaturated acid III (R = OCH_3) with acetic anhydride containing a trace of zinc chloride gave a neutral oil from which 14,15-dehydroequilenin methyl ether, IV (R = OCH_3), was easily isolated in about 23% yield by chromatographic adsorption. This product was identified by mixed melting point determinations of the free ketone and the semicarbazone with authentic specimens. The ultraviolet absorption spectra of the two samples of the ketones were also identical.

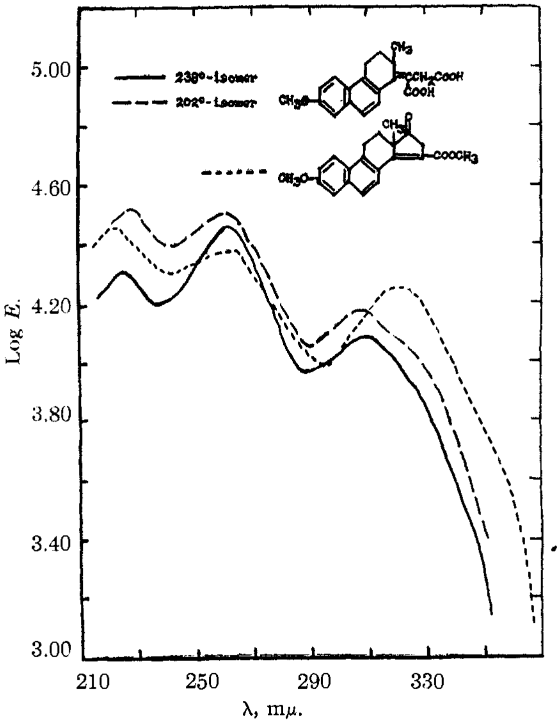
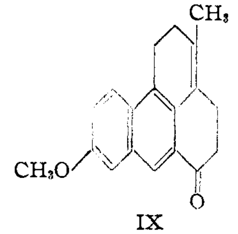
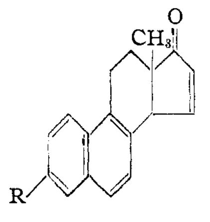


Fig. 2.—β-Carboxy-β-(2-methyl-7-methoxy-1,2,3,4-tetrahydro-1-phenanthrylidene)-propionic acid: ——, 238° isomer; — — —, 202° isomer; - - - - -, 15-carbomethoxy-14,15-dehydroequilenin methyl ether.

From a more highly adsorbed fraction of the chromatogram a second crystalline ketone was isolated in about 18% yield. This compound was different from but isomeric with both 14,15- (IV, R = OCH_3) and 15,16- (X, R = OCH_3) dehydroequilenin methyl ether, and is therefore tentatively assigned the structure IX arising from cyclization into the aromatic nucleus. This new ketone, m. p. 159°, is evidently different from that, m. p. 207°, Haberland obtained by cyclization of his 230° acid, and also tentatively assigned the structure IX.[5] The true structure of these substances must await further experimentation.



IX



X

Some study has been devoted to the nature of the products of the Stobbe condensation described above. From the crude mixture of half-esters it was possible to isolate a pure isomer, m. p. 211°, in 20% yield by crystallization. Two homogeneous dibasic acids melting at 238° and at 202° were isolated, the former by saponi-

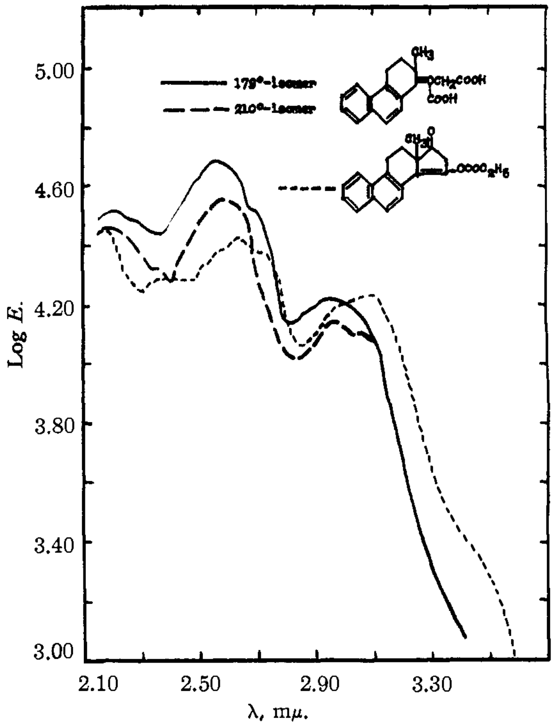


Fig. 3.—β-Carboxy-β-(2-methyl-1,2,3,4-tetrahydro-1-phenanthrylidene)-propionic acid: ——, 179° isomer; — — —, 210° isomer; ------, 15-carbethoxy-14,15-dehydro-17-equilenone.

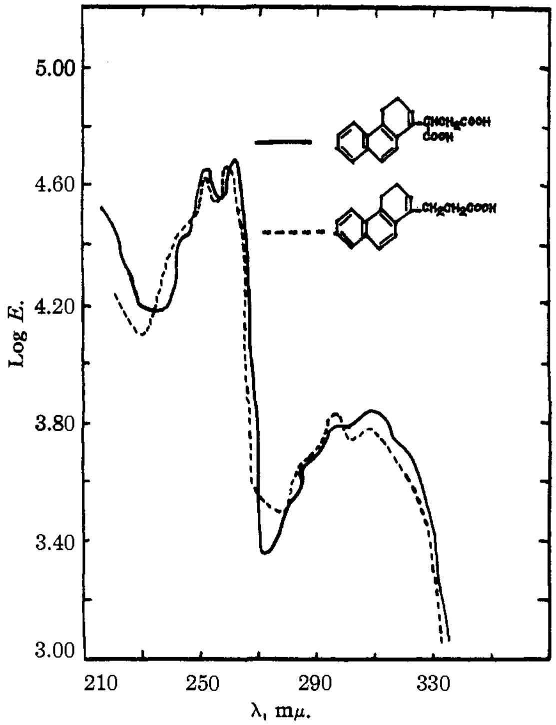
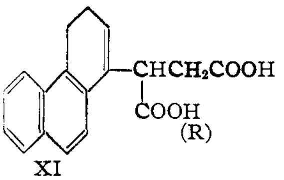


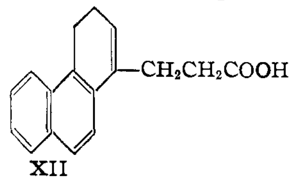
Fig. 4.———, β-Carboxy-β-(3,4-dihydro-1-phenanthryl)-propionic acid; -----, β-(3,4-dihydro-1-phenanthryl)-propionic acid.

fication of the pure half-ester and the latter *via* similar treatment of the residual oily mixtures of half-esters. That these acids represent the two geometrical isomers of the alkylidenesuccinic acid II (R = OCH_3) was suggested by the similarity of their ultraviolet absorption spectra (Fig. 2) which also closely resemble that of 15-carbomethoxy-14,15-dehydroequilenin methyl ether containing the same conjugated methoxynaphthylacrylic acid system. Additional evidence for the alkylidenesuccinic acid structure II was supplied by ozonization of the pure half-ester (which has the same bond structure as the corresponding (238°) dibasic acid as shown by its practically identical spectrum except for the expected slight bathochromic shift induced by the ester group) to produce the methoxy ketone I (R = OCH_3). Decarboxylation experiments gave the acid III (R = OCH_3) from both the 238° and the 202° acid, thus proving that the bond shifts during the reaction, very likely *via* lactonization of the expected β,γ-unsaturated acid, followed by isomerization of the lactone to the γ,δ-acid in a lacto-enoic tautomerism, VIII $\rightleftarrows$ III (R = OCH_3).[7]

Further study in the series without the methoxy group[3] has resulted in the discovery of a completely analogous set of compounds. In addition to the previously described 210° dibasic acid produced by saponification of the crystalline half-ester, we have now isolated a lower-melting (179°) isomer. The comparison of the absorption spectra with each other and with 15-carbethoxy-14,15-dehydro-17-equilenone (see Fig. 3), indicate that these two acids are geometrical isomers of the alkylidene succinic acid II (R = H). Ozonization of the 210° dibasic acid, moreover, gave the expected ketone I (R = H). On this basis the previous assignment of the alkenylsuccinic acid structures (double bond endocyclic) to the 210° dibasic acid and to the corresponding 160° half-ester must be revised. These structures had been tentatively proposed[8] by analogy to the probable structures of the homologous dibasic acid (XI) and the corresponding half-ester which is the exclusive product of the Stobbe condensation with 1-keto-1,2,3,4-tetrahydrophenanthrene.[8] In view of the apparent failure of the analogy, it seemed necessary to obtain conclusive evidence for the alkenylsuccinic acid structure XI in the series lacking the 2-methyl substituent. The absorption spectrum of the dibasic acid (see Fig. 4) was indeed quite different from that (Fig. 3) of the higher homolog now



XI



XII

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[7] *Cf.* Johnson and Heinz, This Journal, **71**, 2913 (1949).

[8] Johnson and Petersen, *ibid.*, **67**, 1366 (1945).

shown to have the alkylidenesuccinic acid structure (see above), and very similar to that of the decarboxylation product XII which has now been shown to have the olefinic bond in the endo- rather than exo-cyclic position by ozonization experiments described in the experimental part.

Experimental Part[9, 10]

Condensation of 1-Keto-2-methyl-7-methoxy-1,2,3,4-tetrahydrophenanthrene with Dimethyl Succinate.—When the condensation was carried out exactly as previously described for 1-keto-2-methyl-1,2,3,4-tetrahydrophenanthrene, the yield of crude half-ester mixture was 61%. By increasing the reaction temperature from 50° to reflux temperature and the time from five to seven hours, the yield was considerably improved. Thus from 8.58 g. of the ketone,[11] m. p. 108.5–110°, in 20 ml. of *t*-butyl alcohol, 38.70 g. of dimethyl succinate and a solution of 9.06 g. of potassium in 189 ml. of dry *t*-butyl alcohol there was obtained 10.86 g. (86% yield) of crude mixture of half-esters, m. p. 101–150°. Recrystallization first from benzene–petroleum ether (60–68°), then from dilute methanol gave 2.61 g. of **β-carbomethoxy-β-(2-methyl-7-methoxy-1,2,3,-4-tetrahydro-1-phenanthrylidene)-propionic acid**, m. p. 211–211.5°. Repeated recrystallization from the same solvent gave colorless microscopic needles, m. p. 214.5–216°.

Anal. Calcd. for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26; neut. equiv., 354. Found: C, 71.56; H, 6.41; neut. equiv., 358.

β-Carboxy-β-(2-methyl-7-methoxy-1,2,3,4-tetrahydro-1-phenanthrylidene)-propionic Acid, II (R = OCH_3). (*a*) *The 238° Isomer.*—Saponification of 2.61 g. of the crystalline half-ester described above by refluxing for two hours with 29 g. of barium hydroxide octahydrate in 168 ml. of water and 210 ml. of alcohol, gave 2.55 g. of crude dibasic acid, m. p. 182–185° (dec.), which after recrystallization from acetone–benzene amounted to 1.71 g. (68% yield) of colorless material, m. p. 237–238° (slow dec.). It was necessary to conduct the acidification of the barium salt in the cold (10°), otherwise some decarboxylation resulted. A sample repeatedly recrystallized from the same solvent pair melted at 237.5–238° (slow dec.), exhibiting a polymorphic change from needles to smaller crystals at about 202°. A sample introduced into the bath at 210° immediately melted and then resolidified, remelting at 237.5–238° (slow dec.).

Anal. Calcd. for $C_{20}H_{20}O_5$: C, 70.57; H, 5.92; neut. equiv., 170. Found: C, 70.27; H, 6.17; neut. equiv., 171.

(*b*) *The 202° Isomer.*—The oily residue (3.66 g.) obtained on evaporation of the benzene–petroleum ether mother liquors from the first recrystallization of the crude mixture of half-esters (see above) was saponified by the procedure described above for the 238° acid. The crude product amounted to 3.57 g., m. p. 165–168° (dec.), and recrystallization from benzene–acetone gave 1.25 g. of colorless needles, m. p. 202–202.5° (dec.). Further recrystallization did not raise the m. p. That this substance was not the lower-melting polymorph of the 238° isomer was demonstrated by a mixed melting point determination (189–195°).

Anal. Calcd. for $C_{20}H_{20}O_5$: C, 70.57; H, 5.92; neut. equiv., 170. Found: C, 70.53; H, 5.95; neut. equiv., 172.

A third dibasic acid, melting at 187.5–188° (dec.), was similarly obtained in very low yield by saponification of the residues obtained from the second recrystallization of the half-ester. This substance appeared to be homogeneous, and was different from the 238 and the 202° acid as indicated by mixed melting point determinations. Due to the limited quantity available further investigation was not made.

Anal. Calcd. for $C_{20}H_{20}O_5$: C, 70.57; H, 5.92; neut. equiv., 170. Found: C, 70.31; H, 6.03; neut. equiv., 170.

β-(2-Methyl-7-methoxy-3,4-dihydro-1-phenanthryl)-propionic Acid, III (R = OCH_3). (*a*) *From the 238° Dibasic Acid.*—The decarboxylation of 0.446 g. of the dibasic acid was carried out as described in another series,[3] with 7.4 ml. of pyridine, 12 ml. of concentrated hydrochloric acid and 4.1 g. of oxalic acid. After heating for twenty-five minutes the calculated amount of gas was evolved. The crude acidic material, isolated in the usual way, amounted to 0.290 g., m. p. 170–177°. A single recrystallization from dilute methanol gave 0.223 g. (57% yield) of colorless transparent plates m. p. 182.5–184.5°. Repeated recrystallization raised the m. p. to 184–185°.

Anal. Calcd. for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80; neut. equiv., 296. Found: C, 77.17; H, 6.80; neut. equiv., 299.

The methyl ester was prepared by the conventional method with an ether solution of diazomethane. It crystallized from dilute methanol in the form of colorless flakes, m. p. 98.5–99°.

Anal. Calcd. for $C_{20}H_{22}O_3$: C, 77.39; H, 7.15. Found: C, 77.59; H, 7.30.

(*b*) *From the 202° Dibasic Acid.*—A 0.439-g. sample of this acid was decarboxylated exactly as described above, except that fifty minutes was required for evolution of the calculated amount of gas. The crude product amounted to 0.254 g., m. p. 150–161°, and after two recrystallizations from dilute alcohol, 0.135 g. (35% yield) of colorless material, m. p. 182–183.5°.

(*c*) *From the Crude Mixture of Dibasic Acids.*—The total crude mixture of half-esters obtained just as described above by the Stobbe condensation with 7.0 g. of 1-keto-2-methyl-7-methoxy-1,2,3,4-tetrahydrophenanthrene, was directly saponified with 153 g. of barium hydroxide octahydrate. This gave 9.7 g. (98% over-all yield) of a solid mixture of dibasic acids, m. p. 120–135° (dec.), which was decarboxylated with 160 ml. of pyridine, 260 ml. of concentrated hydrochloric acid and 89 g. of oxalic acid as described above. After one and three-quarters hours the calculated amount of gas was evolved. Trituration of the crude semi-solid acidic fraction (6.49 g.) with methyl alcohol gave 3.49 g. of colorless material, m. p. 173–177°. A single recrystallization from dilute methanol produced 3.05 g. (35% yield) of colorless plates, m. p. 184–185°. This product was of satisfactory purity for the cyclization experiments described below.

Lactone (VIII) of β-(1-Hydroxy-2-methyl-7-methoxy-1,2,3,4-tetrahydro-1-phenanthryl)-propionic Acid.—A 0.095-g. sample of the above monobasic acid III (R = OCH_3) was treated with hydrogen fluoride for one minute in the cold approximately as previously described for the lactonization of III (R = H).[3] The neutral residues amounted to 0.082 g. (86% yield) of crude lactone, m. p. 182–184°. Repeated recrystallization from methanol gave colorless prisms, m. p. 192–193°.

Anal. Calcd. for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.72; H, 6.80.

β-(1-Hydroxy-2-methyl-7-methoxy-1,2,3,4-tetrahydro-1-phenanthryl)-propionic acid was prepared essentially by the procedure of Haberland.[5] The lactone (0.100 g.) was warmed with 8 ml. of 2 *N* sodium hydroxide until solution was complete. The sodium salt which precipitated on chilling, was separated and treated with cold dilute acetic acid, which liberated 0.065 g. (61% yield) of colorless hydroxy acid, m. p. 148–155° (dec.). Repeated recrystallization from dilute acetone gave almost colorless needles, m. p. 161.5–162.5° (dec.).

Anal. Calcd. for $C_{19}H_{22}O_4$: C, 72.59; H, 7.06. Found: C, 72.85; H, 7.20.

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[9] All melting points are corrected.

[10] We are indebted to Virginia D. Miller and Richard H. Hunt for the microanalyses reported herein.

[11] Prepared by the procedure of Wilds and Close, THIS JOURNAL, **69**, 3079 (1947).

Conversion of the Lactone VIII to the Unsaturated Acid III (R = OCH_3).—The sodium salt produced from 0.100 g. of the lactone VIII exactly as described in the preceding preparation was treated with 5 ml. of 5% hydrochloric acid. The mixture was heated to boiling, then cooled and the colorless solid separated; yield 0.043 g., m. p. 184–185°. The m. p. was not raised on recrystallization, and was not depressed on admixture with the sample of the unsaturated acid III (R = OCH_3) described above.

Cyclization of β-(2-Methyl-7-methoxy-3,4-dihydro-1-phenanthryl)-propionic Acid.—The conditions for this reaction proved to be quite critical. Those employed successfully in the series lacking the methoxyl group,[3] failed to give the desired product, but by slight modification the following satisfactory procedure was developed.

To a solution of 0.100 g. of the acid in 10 ml. of freshly distilled acetic anhydride was added 3 drops of a solution of anhydrous zinc chloride in acetic anhydride (20 mg./ml.) which was freshly prepared by allowing the salt to dissolve at room temperature. The mixture was boiled under reflux in an atmosphere of nitrogen for four hours, then the excess anhydride was decomposed by the dropwise addition of 10 ml. of water to the hot, red solution. The acetic acid was removed in a current of nitrogen at steam bath temperature, and the oily residue treated with water and taken up in ether where it was washed thoroughly with ammonium hydroxide, then dried over anhydrous sodium sulfate. Evaporation of the ether gave 0.093 g. of a red semi-crystalline glass, which was dissolved in benzene. An equal volume of 60–68° petroleum ether was added to the solution which was then adsorbed on an 8 × 120 mm. wet-packed column of 80–200 mesh, acid-washed, activated alumina. Elution with a 1 to 3 mixture of 60–68° petroleum ether–benzene gave 0.022 g. (23% yield) of crude yellow 14,15-dehydroequilenin methyl ether, m. p. 153–159°. A single crystallization from methanol gave 0.019 g. of pale yellow plates, m. p. 160–161°, undepressed on admixture with an authentic specimen of the same m. p. prepared by another method.[4]

The **semicarbazone** of the above ketone was prepared by the conventional method from semicarbazide hydrochloride and pyridine in ethanol. It crystallized from pyridine in the form of colorless crystals, m. p. 251–252.5° (dec.), introduced in bath at 240°. This derivative prepared from authentic 14,15-dehydroequilenin methyl ether[4] had the same melting point alone or when mixed with the above semicarbazone.

Anal. Calcd. for $C_{20}H_{21}O_2N_3$: C, 71.62; H, 6.31. Found: C, 72.16; H, 6.21.

Further elution of the column with pure benzene gave 0.010 g. of an orange oil (fraction no. 2) from which no solid ketonic derivatives could be prepared. Elution next with benzene containing 5% ether afforded a second orange oil (fraction no. 3) which after trituration with petroleum ether (60–68°) was converted to a brown solid, m. p. 156–158°; yield 0.017 g. (18%). Recrystallization from methanol gave 0.013 g. of brown needles, m. p. 158–159°. Further recrystallization did not raise the m. p. which was depressed to 120–125° on admixture with 14,15-dehydroequilenin methyl ether.

Anal. Calcd. for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52. Found: C, 82.00; H, 6.51.

The **semicarbazone** obtained by the pyridine–alcohol method crystallized from pyridine–water in the form of fine yellow needles, m. p. 241–242° (dec.), introduced in bath at 230°. The m. p. was depressed to 227–233° on admixture with the semicarbazone of 14,15-dehydroequilenin methyl ether.

Anal. Calcd. for $C_{20}H_{21}O_2N_3$: C, 71.62; H, 6.31. Found: C, 71.58; H, 6.17.

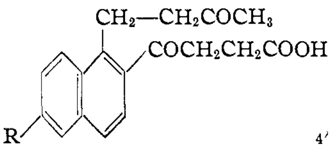
Further elution of the column with more polar solvents gave only intractable oils.

In another cyclization experiment carried out exactly as described above with the same quantities except that the amount of organic acid was doubled, the yield of 14,15-dehydroequilenin methyl ether dropped to 10%. It was also discovered that the solution of zinc chloride in acetic anhydride became more effective as a catalyst for the cyclization after standing at room temperature for some time. A cyclization conducted with such a solution which had stood for one week and had gradually turned quite dark, gave the maximum yield (20%) of 14,15-dehydroequilenin methyl ether after a reaction period of only one and one-half hours.

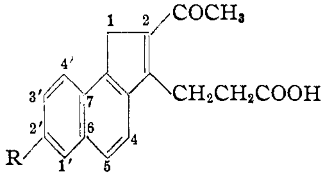
Ozonization Experiments. (*a*) *With the 210° Isomer of β-Carboxy-β-(2-methyl-1,2,3,4-tetrahydro-1-phenananthrylidene)-propionic Acid, II* (R = H).—Ozone produced by a U. S. Air Ozonizer from oxygen flowing at the rate of 10 liters per hour, was introduced for a period of ten minutes through a sintered glass disk near the bottom of a chilled (ice-bath) reaction tube containing a solution of 0.176 g. of pure 210° dibasic acid II (R = H) in 30 ml. of ethyl acetate. The solvent was then evaporated on the steam-bath in a current of air, and the residue heated on the steam-bath with 0.200 g. of powdered zinc, 10 ml. of water and 0.5 ml. of acetic acid for fifteen minutes. The mixture was extracted with ethyl acetate and the combined extracts were washed thoroughly with 1 *N* ammonium hydroxide. Acidification of the aqueous alkaline solutions gave 0.035 g. of starting acid. Evaporation of the ethyl acetate left 0.029 g. (30% yield based on recovered acid) of crude colorless 1-keto-2-methyl-1,2,3,4-tetrahydrophenanthrene, m. p. 63–65°. The m. p. was raised to 72.5–73.5° by a single recrystallization from petroleum ether (60–68°) and was not depressed on admixture with an authentic specimen of the ketone, m. p. 73–74°.

(*b*) *With β-(2-methyl-3,4-dihydro-1-phenanthryl)-propionic Acid, III* (R = H).—A solution of 0.142 g. of the pure acid III (R = H) in 30 ml. of methylene chloride was treated with ozone for twenty-five minutes, and the product treated with zinc and isolated as described above, part (a). The neutral fraction amounted to 0.017 g. of colorless oil which gave no semicarbazone. The acidic portion amounted to 0.100 g. of colorless oil which on treatment in alcohol with semicarbazide hydrochloride and pyridine afforded 0.067 g. of an acidic derivative, m. p. 226–227° (dec.). The melting point was not raised by recrystallization from dilute alcohol. The analysis corresponds with the semicarbazone (or pyrazoline) of β-(2-acetyl-6,7-benz-3-indenyl)-propionic acid (formula B, R = H) which could arise from the expected diketo acid A (R = H) by a cyclodehydration of the aldol type.

Anal. Calcd. for $C_{19}H_{19}O_3N_3$: C, 67.64; H, 5.68. Found: C, 67.86; H, 5.52.



A



B

(*c*) *With β-Carbomethoxy-β-(2-methyl-7-methoxy-1,2,3,4-tetrahydrophenanthrylidene)-propionic Acid.*—The half-ester was ozonized just as described above, part (a), except that a flow rate of 11 liters per hour of oxygen and a reaction time of seven and one-half minutes were used. The acidic fraction of the product amounted to 0.070 g. of starting material, and the neutral fraction, 0.049 g. (56% yield based on recovered acid) of crude colorless 1-keto-2-methyl-7-methoxy-1,2,3,4-tetrahydrophenanthrene, m. p. 88–90°. Two recrystallizations from methanol gave material m. p. 107–108°, undepressed on admixture with authentic ketone, m. p. 107–108°.

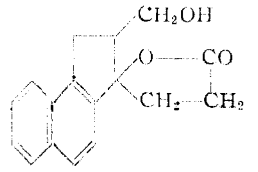
(*d*) *With β-(2-Methyl-7-methoxy-3,4-dihydro-1-phenanthryl)-propionic Acid, III* (R = OCH_3).—Ozonolysis of a 0.167-g. sample of the acid was carried out just as described above, part (*b*), for III (R = H). Treatment of the acid fraction with semicarbazide gave 0.043 g. of a tan product, m. p. 222.5–223°, possibly the semicarbazone (or pyrazoline) of B (R = OCH_3). Recrystallization from alcohol did not raise the m. p.

Anal. Calcd. for $C_{20}H_{21}O_4N_3$: C, 65.38; H, 5.76. Found: C, 64.91; H, 5.75.

(*e*) *With β-(3,4-Dihydro-1-phenanthryl)-propionic Acid.*—Ozonization of 0.146 g. of this acid was carried out as described in part (*a*) except that air instead of oxygen was employed in the ozonizer, the reaction period was extended to seventy-five minutes, and the zinc was omitted in the decomposition of the ozonide. The crude product was a pale yellow solid amounting to 0.125 g., m. p. 150–155°. Recrystallization from benzene–acetone gave 0.050 g. of colorless needles, m. p. 257–259°. Two additional recrystallizations from acetone raised the m. p. to 258–260°.

Anal. Calcd. for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 76.09; H, 6.20.

This product behaved like a lactone, dissolving in dilute alkali only on warming, and did not give a 2,4-dinitrophenylhydrazone. The analysis is compatible with formula C, a reasonable, but definitely tentative structure which could arise from the expected aldehydo keto acid (formula A with H instead of CH_3, and R = H) by intramolecular aldol condensation followed by lactonization of the resulting γ-hydroxy acid, and disproportionation of the aldehyde group. In any case the failure to find any 1-keto-1,2,3,4-tetrahydrophenanthrene in the neutral fraction reasonably precludes the location of the ethylenic bond in the endocyclic position.



C

The 179° Isomer of β-Carboxy-β-(2-methyl-1,2,3,4-tetrahydro-1-phenanthrylidene)-propionic Acid.—The brown oily half-ester mixture remaining after separation of the crystalline half-ester described in a previous communication[3] was saponified with barium hydroxide as described above and the crude dibasic acid was repeatedly recrystallized from acetone–benzene. The pure acid was thus obtained in poor yield as colorless needles, m. p. 178–179° (dec.).

Anal. Calcd. for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85. Found: C, 73.20; H, 5.92.

Ultraviolet Absorption Spectra.—These determinations were carried out in ethanol solution on a Beckman ultraviolet spectrophotometer, employing analytical samples described in this paper or in the reference indicated.

1,2-Dimethyl-7-methoxy-3,4-dihydrophenanthrene (VI) was prepared from 1.0 g. of 1-keto-2-methyl-7-methoxy-1,2,3,4-tetrahydrophenanthrene by the action of excess methylmagnesium iodide. The crude carbinol obtained on hydrolysis of the addition compound with ammonium chloride was dehydrated by heating at 180–200° for fifteen minutes. Evaporative distillation at 0.5 mm. gave 0.882 g. of colorless solid, m. p. 95–97°. Repeated recrystallization from methanol gave colorless needles, m. p. 109–110°.

Anal. Calcd. for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.33; H, 7.49.

β-(2-Methyl-7-methoxy-3,4-dihydro-1-phenanthryl)-propionic Acid (III, R = OCH_3).—λ max. 219.5 mμ (log *E* 4.35), 256 (4.68), 265 (4.68), 303 (4.02), 315.5 (3.99), 342 (3.39), 357.5 (3.30). **1,2-Dimethyl-7-methoxy-3,4-dihydrophenanthrene** (VI).—λ max. 256 mμ (log *E* 4.68), 302.5 (3.99), 314.5 (3.94), 341.5 (3.45), 357.5 (3.22). **14,15-Dehydroequilenin Methyl Ether** (IV, R = OCH_3).[4]—λ max. 253 mμ (log *E* 4.67), 261.5 (4.66), 293.5 (4.20), 304.5 (4.17), 333 (3.34), 349.5 (3.24). **β-Carbomethoxy-β-(2-methyl-7-methoxy-1,2,3,4-tetrahydro-1-phenanthrylidene)-propionic Acid** (II, R = OCH_3).—λ max. 226 mμ (log *E* 4.42), 266 (4.54), 313 (4.23). **β-Carboxy-β-(2-methyl-7-methoxy-1,2,3,4-tetrahydro-1-phenanthrylidene)-propionic Acid** (II, R = OCH_3). **238° Isomer.**—λ max. 226 mμ (log *E* 4.32), 262.5 (4.48), 309.5 (4.09). **202° Isomer.**—λ max. 227.5 mμ (log *E* 4.54), 262.5 (4.52), 309.5 (4.19). **The 188° Dibasic Acid.**—λ max., 261.5 mμ (log *E* 4.64), 307.5 (4.13). **15-Carbomethoxy-14,15-dehydroequilenin Methyl Ether.**[4]—λ max. 223 mμ (log *E* 4.48), 264.5 (4.40), 323 (4.26). **β-Carbomethoxy-β-(2-methyl-1,2,3,4-tetrahydro-1-phenanthrylidene)-propionic Acid** (II, R = H).—λ max. 219.5 mμ (log *E* 4.52), 259 (4.59), 297.5 (4.23). **β-Carboxy-β-(2-methyl-1,2,3,4-tetrahydro-1-phenanthrylidene)-propionic Acid** (II, R = H). **210° Isomer.**—λ max. 260 mμ (log *E* 4.56), 298 (4.15), 307 (4.11). **179° Isomer.**—λ max. 221 mμ (log *E* 4.51), 257 (4.66), 297.5 (4.21). **15-Carbethoxy-14,15-dehydro-17-equilenone.**[4]—λ max. 219 mμ (log *E* 4.47), 242.5 (4.30), 246.5 (4.30), 264 (4.43), 309.5 (4.25). **β-Carboxy-β-(3,4-dihydro-1-phenanthryl)-propionic Acid.**[8]—λ max. 253 mμ (log *E* 4.68), 262.5 (4.70), 310 (3.85). **β-(3,4-Dihydro-1-phenanthryl)-propionic Acid.**[8]—λ max. 253 mμ (log *E* 4.46), 260 (4.67), 297 (3.82), 308 (3.77).

Summary

A synthetic scheme involving the Stobbe condensation, previously developed for the production of steroid-like structures from 1-keto-2-methyl-1,2,3,4-tetrahydrophenanthrene, has now been extended to the 7-methoxy compound to give 14,15-dehydroequilenin methyl ether. Since this substance is known to be convertible into equilenin, the present study constitutes a new total synthesis of this naturally occurring steroid.

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