Anal. Calcd. for $C_{21}H_{15}ON$: C, 84.82; H, 5.08; N, 4.71. Found: C, 84.61; H, 5.33; N, 4.91.

A solution of 0.025 g. of this isocyanate in 25 ml. of absolute alcohol was refluxed for 20 hours. Ethyl 9,10-dimethyl-1,2-benzanthryl-3-carbamate (XA) was isolated in 63% yield as described above for X. The pale yellow needles melted at 113.3–114.1°; a mixture with the isocyanate (IXA) melted considerably lower.

Anal. Calcd. for $C_{23}H_{21}O_2N$: N, 4.07. Found: N, 3.91.

3-Methoxy-9-methyl-10-phenyl-1,2-benzanthracene (XI).—One liter of a benzene solution of crude anthrone (IV) prepared from 25 g. of the substituted benzoic acid (III) was added to 1 l. of an ethereal solution, containing 0.125 mole of phenylmagnesium bromide. The mixture was refluxed 12 hours and the crude tertiary alcohol isolated in the same general fashion as for VA. The product obtained upon dehydration on the hot-plate and purification *via* chromatographic adsorption applied to the picrate, as before, resisted attempts at crystallization. Molecular distillation gave 23 g. (81%, calculated from III) of an orange, glassy solid which had no definite melting point, but which analyzed satisfactorily.

Anal. Calcd. for $C_{28}H_{20}O$: C, 89.62; H, 5.78; CH_3O–8.90. Found: C, 89.84; H, 6.04; CH_3O–, 8.93.

3-Methoxy-9-methyl-10-ethyl-1,2-benzanthracene (XII).—This compound was prepared in the same general fashion as described for XI. Crystallization from a large volume of 30–60° petroleum ether gave a 60% yield (calcd. from III) of fine rosettes which melted at 86.4–87.2°.

Anal. Calcd. for $C_{22}H_{20}O$: C, 87.96; H, 6.67; CH_3O–, 10.33. Found: C, 87.97; H, 6.77; CH_3O–, 10.26.

Acknowledgment.—The authors are grateful to Professor N. L. Drake for his helpful interest in this work.

Summary

9-Methyl- and 9,10-dimethyl-1,2-benzanthryl-3-isocyanates have been prepared from α-methoxynaphthalene by nine-step syntheses. Good yields were obtained in each step, the over-all yield being about 28% in each case.

COLLEGE PARK, MARYLAND RECEIVED JULY 17, 1950

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Structure and Hydrogenation of Key Intermediates in the Equilenin Synthesis[1,2]

BY WILLIAM S. JOHNSON, C. DAVID GUTSCHE,[3] RALPH HIRSCHMANN[4] AND VERNER L. STROMBERG[5]

In the equilenin synthesis developed in this Laboratory,[1] the product of the pivotal reaction, *viz.*, the condensation of dimethyl succinate with 2-cyano-1-keto-7-methoxy-2-methyl-1,2,3,4-tetrahydrophenanthrene, was formulated as 15-carbomethoxy-14,15-dehydroequilenin methyl ether, I ($R^1 = OCH_3$, $R^2 = H$, $R^3 = CH_3$). This structure was proved conclusively except for the position of the ethylenic bond, which might alternately be located in the 15,16-position, formula II ($R^1 = OCH_3$, $R^2 = H$, $R^3 = CH_3$).[6] The ultraviolet absorption spectrum of this ester has been determined and found to be compatible with the structure I ($R^1 = OCH_3$, $R^2 = H$, $R^3 = CH_3$) on the basis of the high maximum at 323 mμ presumably arising from the extended conjugation in the 6-methoxy-2-naphthylacrylic acid system.[7] Surprisingly the acid, which is obtained in practically quantitative yield by the saponification of I ($R^1 = OCH_3$, $R^2 = H$, $R^3 = CH_3$), has a spectrum (Fig. 1) which is strikingly different from that of the ester in that the high maximum at 323 mμ had vanished. We were, therefore, forced to the conclusion that the bond had shifted from the 14,15- to the 15,16-position during the alkali treatment. This 3-carbon tautomeric shift evidently was essentially complete since the spectrum of the crude saponification product (Fig. 1) showed no indication of the high maximum at 323 mμ. That an isomerization had occurred was further demonstrated by treatment of the acid with diazomethane to produce a new methyl ester, m.p, 136–137°, which was different from the original ester I ($R^1 = OCH_3$, $R^2 = H$, $R^3 = CH_3$), m.p. 170–171°. The spectrum of the lower-melting ester (Fig. 1), moreover, was similar to that of the acid which is now formulated as 15-carboxy-15,16-dehydroequilenin methyl ether, II ($R^1 = OCH_3$, $R^2 = R^3 = H$) instead of the 14,15-dehydro compound.

Analogous behavior was noted in the parent series lacking the ring methoxyl as shown by a comparison of the spectrum of 15-carbethoxy-14,15-dehydro-17-equilenone, I ($R^1 = R^2 = H$, $R^3 = C_2H_5$), with that of the acid obtained on saponification (Fig. 2). Since the latter curve lacks the peak at 309 mμ characteristic of the β-2-naphthylacrylic acid system and resembles closely that of 15,16-dehydro-17-equilenone in which the naphthalene nucleus is not conjugated with the ethylenic bond, the acid is now assigned the structure of 15-carboxy-15,16-dehydro-17-equilenone (II) ($R^1 = R^2 = R^3 = H$).

Similarly 6-methoxy-15-carbomethoxy-14,15-dehydro-17-equilenone[8] (I) ($R^1 = H$, $R^2 = OCH_3$, $R^3 = CH_3$), was converted on saponification to the acid II ($R^1 = H$, $R^2 = OCH_3$, $R^3 = H$) having the bond shifted to the 15,16-position. The spectrum of the acid and its methyl ester differ markedly from that of the starting keto ester, the latter exhibiting absorption at longer wave lengths (Fig. 3), but this difference is not as striking as in the cases described above. The curve of the 15,16-dehydro keto ester resembles very closely that of 6-methoxy-15-carboxy-17-equilenone produced by hydrogenation of II ($R^1 = H$, $R^2 = OCH_3$, $R^3 = H$). This similarity is reasonable only if the double bond of the dehydro acid is in the 15,16-position, because the principal absorption of the isolated O=C—C=C—COOH system as it is contained

(1) Johnson, Petersen and Gutsche, THIS JOURNAL, **69**, 2942 (1947).

(2) This work was assisted in part by the Research Committee of the Graduate School from funds supplied by the Wisconsin Alumni Research Foundation.

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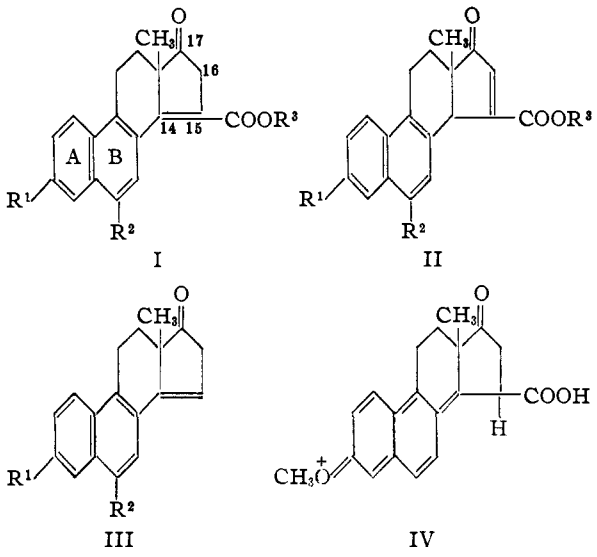
(6) See footnote 23, ref. 1.

(7) Johnson and Stromberg, THIS JOURNAL, **72**, 505 (1950).

(8) Hirschmann and Johnson, *ibid.*, **73**, 326 (1951).



in the five-membered ring would be expected to appear in the region of end absorption and would, therefore, not be apparent. The α,β-unsaturated cyclopentenone system should have $\lambda_{max.}$ *ca.* 215 mμ,[9] and the β-carboxy substituent would be expected to induce at most a small bathochromic increment, and therefore should not alter the spectrum appreciably in the region above 220 mμ.[10] This premise is supported by the similarity of the spectrum of the acid II ($R^1 = R^2 = R^3 = H$) with that of 15,16-dehydro-17-equilenone (Fig. 2). The 15,16-dehydro compounds examined in this and previous work,[1] thus show absorption above 220 mμ which is produced largely from the substituted naphthalene nucleus.

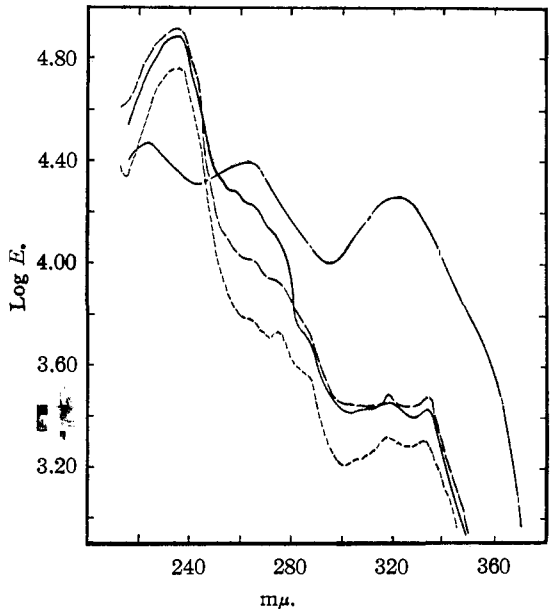


Fig. 1.— Pure ——, crude — —, 15-carboxy-15,16-dehydroequilenin methyl ether (II, $R^1 = OCH_3$, $R^2 = R^3 = H$); — — —, 15-carbomethoxy-14,15-dehydroequilenin methyl ether (I, $R^1 = OCH_3$, $R^2 = H$, $R^3 = CH_3$); — — — —, 15-carbomethoxy-15,16-dehydroequilenin methyl ether (II, $R^1 = OCH_3$, $R^2 = H$, $R^3 = CH_3$).

(9) See ref. 1, footnote 13.

(10) *Cf.* the absorption of crossed conjugated systems, Fieser and Fieser, "Natural Products Related to Phenanthrene," 3rd ed., Reinhold Publishing Corp., New York, N. Y., 1949, p. 198.

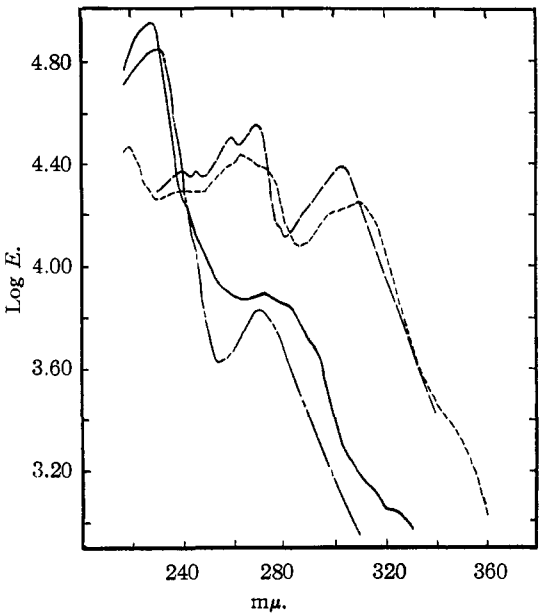


Fig. 2.— 15,16-Dehydro-17-equilenone-15-carboxylic acid ——, (II, $R^1 = R^2 = R^3 = H$); — — — —, ethyl 14,15-dehydro-17-equilenone-15-carboxylate (I, $R^1 = R^2 = H$, $R^3 = C_2H_5$); — — —, 15,16-dehydro-17-equilenone[1]; — —, methyl β-1-naphthylacrylate.

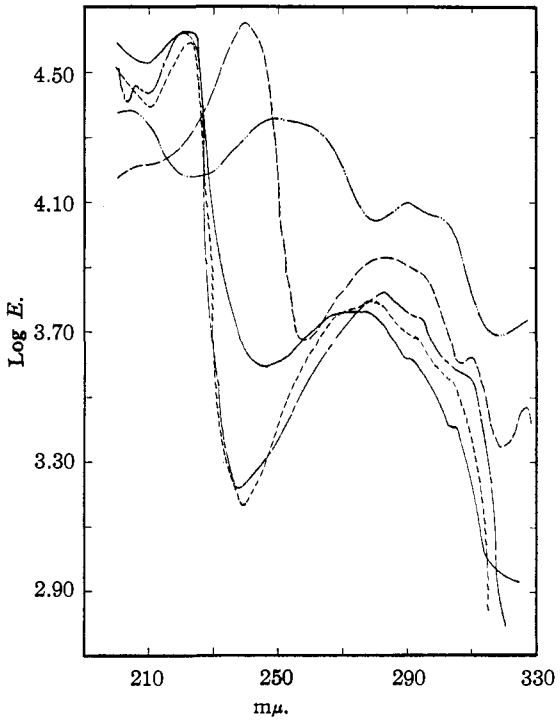


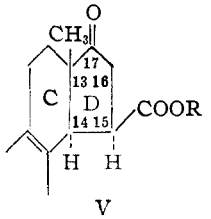
Fig. 3.— Methyl 6-methoxy-15,16-dehydro-17-equilenone-15-carboxylate ——, (II, $R^1 = H$, $R^2 = OCH_3$, $R^3 = CH_3$); · · — · ·, methyl 6-methoxy-14,15-dehydro-17-equilenone-15-carboxylate (I, $R^1 = H$, $R^2 = OCH_3$, $R^3 = CH_3$); — —, 6-methoxy-14,15-dehydro-17-equilenone (III, $R^1 = H$, $R^2 = OCH_3$); — — —, α-6-methoxy-17-equilenone; — — — — —, 6-methoxy-17-equilenone-15-carboxylic acid.

The foregoing observations provide a basis for assigning the 14,15-dehydro structure III (R^1 = H, R^2 = OCH_3) to the product, which was isolated from the decarboxylation of II (R^1 = H, R^2 = OCH_3, R^3 = H).[8] If the olefinic bond were in the 15,16-position, the spectrum would be expected to resemble closely that of the dihydro compound or of the 15-carbomethoxy compound II (R^1 = H, R^2 = OCH_3, R^3 = CH_3). That this is not the case is readily seen from an examination of Fig. 3. The bathochromic shift of the principal maximum exhibited by III (R^1 = H, R^2 = OCH_3) is probably due to the 4-methoxy-2-vinylnaphthalene system.

The decarboxylation of the acids II to produce a ketone with the bond preponderantly in the 14,15-position is undoubtedly associated with a relatively mobile three carbon tautomerism. The fact that the acid II (R^1 = OCH_3, R^2 = R^3 = H) with the methoxyl at position 3 is considerably more susceptible to acid-catalyzed decarboxylation than the acids II (R^1 = R^2 = R^3 = H) and II (R^1 = H, R^2 = OCH_3, R^3 = H), suggests the possibility that decarboxylation may be preceded, at least in part, by an acid- and heat-catalyzed shift of the bond to the 14,15-position, thus enabling the methoxyl group to exert a labilizing influence on the carboxyl group. According to the β-carbonium ion mechanism of acid-catalyzed decarboxylation[11] this influence can be rationalized by the contribution of the form IV to the transition-state.

Hydrogenation Experiments

Until it was shown that the olefinic bond in ring D of the ester I (R^1 = OCH_3, R^2 = H, R^3 = CH_3) and the acid II (R^1 = OCH_3, R^2 = R^3 = H) occupied different positions, the results of the hydrogenation experiments described below appeared to be hopelessly complex, and defied rationalization. These experiments are now completely clarified on the basis of the new concept, and thus additional evidence for the structures now assigned to the keto esters and acids described above is provided.



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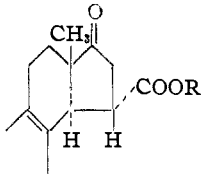

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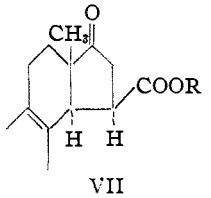
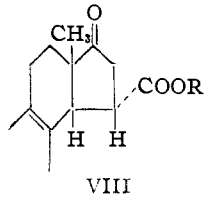


VII



VIII

Hydrogenation of the keto ester I (R^1 = OCH_3, R^2 = H, R^3 = CH_3) over palladium catalyst gave in 75% yield a dihydro ester, m.p. 161–162.5° after purification, designated the "α-ester." Saponification with barium hydroxide afforded a good yield of carboxylic acid, m.p. 236–237.5° which belonged to a different stereochemical series, since esterification with diazomethane yielded a new methyl ester, m.p. 195–196°. The 237° acid was therefore called the "β-acid" and the 196° ester, the "β-ester." Undoubtedly the α-ester is epimeric with the β-ester at C-15, inversion having occurred at this position during saponification *via* an enol anion. The most likely stereochemical course for the addition of hydrogen to the 14,15-double bond is to produce rings C/D fused in the *trans* configuration as in the case of the reduction of 14,15-dehydroequilenin methyl ether.[1] The possibility that the carbomethoxy group alters the stereochemical course of the attack of hydrogen at C-14 cannot be excluded, but seems improbable on the basis of the results of the hydrogenation of the keto acid II (R^1 = OCH_3, R^2 = R^3 = H), which leads to a different series of compounds that probably have rings C/D *cis* (see below). If *cis* addition of hydrogen to the double bond is assumed to be the more likely course of reaction, then the α-compound is best represented by formula V and the β- by VI. However, these configurations may possibly be reversed.

The hydrogenation of the keto acid II (R^1 = OCH_3, R^2 = R^3 = H) yielded a mixture of two dihydro compounds: the "γ-acid," m.p. 210–211°, formed in preponderance, and the "δ-acid," m.p. 227.5–229°. Both the γ-methyl ester, m.p. 119.8–121.7° and the δ-methyl ester, m.p. 170.5–171°, yielded the γ-acid on saponification indicating that they are epimeric about C-15. The δ-ester is most conveniently prepared by hydrogenation of the 15,16-dehydro ester II (R^1 = OCH_3, R^2 = H, R^3 = CH_3) obtained by the action of diazomethane on the unsaturated keto acid. Although the γ-ester is produced in preponderance, the δ-ester is less soluble and is isolated easily in 30% yield by crystallization. Since the C/D ring system with a 15,16-double bond is probably stable only in the *cis* configuration,[1] the γ- and δ-acids probably belong to the C/D *cis* series provided no bond migration occurs during hydrogenation. It is noteworthy that the hydrogenation of the 15,16-dehydro ester proceeded relatively rapidly. These reduction products, therefore, are assigned the formulas VII and VIII (or the reverse) as the most likely configurations on the basis of the existing evidence. In one experiment on the hydrogenation of I (R^1 = OCH_3, R^2 = H, R^3 = CH_3), a small amount of the δ-ester was isolated from the mother liquors. This product may have been formed *via* some 15,16-dehydro ester produced by a slow isomerization and shown above to give the δ-ester. It is also possible that the addition of hydrogen to the 14,15-double bond is not stereospecific.[12]

Experimental Part[13,14,15]

15-Carbomethoxy-14,15-dehydroequilenin Methyl Ether (I, R^1 = OCH_3, R^2 = H, R^3 = CH_3).—Material prepared

(11) Johnson and Heinz, THIS JOURNAL, 71, 2913 (1949).

(12) *Cf.* The hydrogenation of 14,15-dehydroequilenin methyl ether, ref. 1.

(13) All melting points are corrected.

(14) Microanalyses were kindly performed by B. Buell, R. Graber and E. Shiner.

(15) Ultraviolet absorption spectra were determined in alcohol solution on a Beckman quartz spectrophotometer.

by Johnson, Petersen and Gutsche[1] was employed. The ultraviolet spectrum is reported elsewhere.[7]

15-Carboxy-15,16-dehydroequilenin Methyl Ether (II, $R^1 = OCH_3$, $R^2 = R^3 = H$), m.p. 196–197°, was prepared by saponification of the above ester.[1] This product was previously formulated tentatively as the 14,15-dehydro compound[1]; λ_{max} 235 mμ (log E 4.89), 318 (3.46), 333.5 (3.43).[15]

15-Carbomethoxy-15,16-dehydroequilenin Methyl Ether (II, $R^1 = OCH_3$, $R^2 = H$, $R^3 = CH_3$).—A 0.014-g. sample of the acid described above was treated with excess diazomethane in ether solution. Evaporation of the ether gave 0.014 g. of crude ester, m.p. 133–136°. Repeated recrystallization from methanol yielded almost colorless needles, m.p. 136–137°: λ_{max} 235 mμ (log E 4.76), 275 (3.73), 318 (3.32), 332.5 (3.32).[15]

Anal. Calcd. for $C_{21}H_{20}O_4$: C, 74.98; H, 5.99. Found: C, 74.70; H, 5.93.

Ethyl 14,15-dehydro-17-equilenone-15-carboxylate (I, $R^1 = R^2 = H$, $R^3 = C_2H_5$) from previous work[1] was employed. The ultraviolet spectrum is reported elsewhere.[7]

15,16-Dehydro-17-equilenone-15-carboxylic acid (II, $R^1 = R^2 = R^3 = H$), m.p. 236–238°, was prepared by saponification of the above ester.[1] This product was previously formulated tentatively as the 14,15-dehydro compound[1]; λ_{max} 228 mμ (log E 4.95), 272.5 (3.89).[15]

Methyl β-1-Naphthylacrylate.—β-1-Naphthylacrylic acid, m.p. 204–207°, was prepared in 82% yield by the condensation of β-naphthaldehyde[16] with malonic acid in pyridine containing 4% piperidine. Recrystallization from dilute alcohol raised the m.p. to 206–207° (reported,[17] 209°). Esterification with diazomethane yielded colorless plates, m.p. 92–93°, after repeated recrystallization from 60–68° petroleum ether, $\lambda_{max.}$ 240.5 mμ (log E 4.36), 245.5 (4.36), 259 (4.49), 268.5 (4.54), 303.5 (4.38).[15]

Anal. Calcd. for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 79.55; H, 5.85.

Methyl 6-methoxy-14,15-dehydro-17-equilenone-15-carboxylate (I, $R^1 = H$, $R^2 = OCH_3$, $R^3 = CH_3$), m.p. 148–149.5°,[8] showed $\lambda_{max.}$ 213 mμ (log E 4.39), 223.5 (4.40), 268.5 (4.38), 310.5 (4.11), 354 (3.77).[15]

6-Methoxy-15,16-dehydro-17-equilenone-15-carboxylic acid (II, $R^1 = R^3 = H$, $R^2 = OCH_3$), m.p. 220.5–222°,[8] showed $\lambda_{max.}$ 214.5 mμ (log E 4.60), 243 (4.64), 296 (3.77), 327 (3.51).[15]

Methyl 6-methoxy-15,16-dehydro-17-equilenone-15-carboxylate (II, $R^1 = H$, $R^2 = OCH_3$, $R^3 = CH_3$) was prepared by the action of diazomethane in ether on the acid described above. After purification by evaporative distillation at 105–115° (<10^{-4} mm.) and repeated recrystallization from methanol it was obtained as pale yellow needles, m.p. 141.5–143°, $\lambda_{max.}$ 241.5 mμ (log E 4.62), 296.5 (3.77), 325 (3.41).[15] On admixture with the 14,15-dehydro isomer (m.p. 148–149.5°) the m.p. was depressed to 110–135°.

Anal. Calcd. for $C_{21}H_{20}O_4$: C, 74.98; H, 5.99. Found: C, 75.24; H, 6.06.

6-Methoxy-14,15-dehydro-17-equilenone (III, $R^1 = H$, $R^2 = OCH_3$), m.p. 149–150.5°,[8] showed $\lambda_{max.}$ 259.5 (log E 4.65), 302 (3.94), 330 (3.62), 347 (3.47).[15]

α-6-Methoxy-17-equilenone, m.p. 148.5–150°,[8] showed $\lambda_{max.}$ 225 mμ (log E 4.46), 240 (4.63), 303 (3.81).[15]

Hydrogenation Experiments

α-15-Carbomethoxyequilenin Methyl Ether.—A solution of 1.381 g. of the dehydro ester I ($R^1 = OCH_3$, $R^2 = H$, $R^3 = CH_3$),[1] m.p. 169–172°, in 150 ml. of purified ethyl acetate[18] was stirred with three-fourths teaspoonful of Raney nickel at room temperature. The mixture was filtered and the filtrate stirred with 0.200 g. of 30% palladium-on-carbon[19] and hydrogen at room temperature and atmospheric pressure. Two additional 0.200-g. portions of catalyst were added when the reaction became very slow. After about 80 hours of stirring the reaction stopped, 90% of the calculated volume of gas having been absorbed. The mixture was filtered, the filtrate evaporated in a current of air on the steam-bath, and the oily residue crystallized from ethanol yielding 1.05 g. (75% yield) of nearly colorless crystals, m.p. 159–161°. Repeated recrystallization from methanol gave colorless needles, m.p. 161–162.5° (dec.).

Anal. Calcd. for $C_{21}H_{22}O_4$: C, 74.52; H, 6.55. Found: C, 74.26; H, 6.49.

The oxime was prepared with hydroxylamine hydrochloride and pyridine in ethanol. It was obtained from benzene as colorless crystals, m.p. 229.5–231.3° (vac.).

Anal. Calcd. for $C_{21}H_{23}O_4N$: C, 71.36; H, 6.56. Found: C, 71.41; H, 6.52.

β-15-Carboxyequilenin Methyl Ether.—A mixture of 0.120 g. of the α-ester (described above), 0.120 g. of barium hydroxide octahydrate, 5 ml. of alcohol and 3 ml. of water was boiled under reflux in an atmosphere of nitrogen for 1 hour. The barium salt was decomposed without exposure to the atmosphere by the addition of a solution of 7.5 ml. of concd. hydrochloric acid in 25 ml. of water, and the mixture was heated for an additional hour in an atmosphere of nitrogen. The acid was separated by filtration; yield 0.105 g., m.p. 232–237.5° (dec.). Crystallization from ethanol (activated carbon) and recrystallization from dilute alcohol gave colorless needles, m.p. 236–237.5°.

Anal. Calcd. for $C_{20}H_{20}O_4$: C, 74.05; H, 6.22. Found: C, 73.83; H, 6.53.

The oxime, prepared as described above for the ester was obtained as colorless crystals from dilute alcohol, m.p. 234–235° (dec.).

Anal. Calcd. for $C_{20}H_{21}O_4N$: C, 70.78; H, 6.24. Found: C, 70.41; H, 6.30.

β-Carbomethoxyequilenin Methyl Ether.—A sample of the β-acid described above was dissolved in benzene–ether and treated with an excess of ethereal diazomethane. The crude product obtained on evaporation of the ether melted at 191–194°. Recrystallization from methanol yielded pale pink blades, m.p. 195–196°.

Anal. Calcd. for $C_{21}H_{22}O_4$: C, 74.52; H, 6.55. Found: C, 74.22; H, 6.40.

γ-15-Carboxyequilenin Methyl Ether.—A solution of 3.69 g. of the keto acid II ($R^1 = OCH_3$, $R^2 = R^3 = H$) (see above), m.p. 192–194.4°, in 200 ml. of ethyl acetate[18] was treated with Raney nickel, then hydrogenated over 0.300 g. of 30% palladium-on-carbon[19] as described above for the preparation of the α-ester. The reaction ceased after 61% of the calculated volume of hydrogen was absorbed (30 hours) and did not resume on introducing additional catalyst. Crystallization of the crude product from methanol gave 1.30 g. (35% yield) of pink γ-acid, m.p. 206–209° with previous softening. A pure sample was obtained as colorless prisms, m.p. 210–211°, by repeated recrystallization from ethanol.

Anal. Calcd. for $C_{20}H_{20}O_4$: C, 74.05; H, 6.22. Found: C, 74.09; H, 6.39.

The oxime, prepared as described above for the α-ester oxime, was obtained from benzene as colorless needles, m.p. 230–231° (dec.) when introduced in bath at 225°.

Anal. Calcd. for $C_{20}H_{21}O_4N$: C, 70.78; H, 6.24. Found: C, 70.73; H, 6.18.

In another reduction experiment with dehydro acid, m.p. 194–196°, the reaction was still continuing slowly after the calculated amount of hydrogen was absorbed. The stirring was stopped and the product worked up as described above to give a 16% yield of crude γ-acid, m.p. 202–208°. From the mother liquors there was isolated in very low yield a new acid, **δ-15-carboxyequilenin methyl ether**, as colorless plates, m.p. 227.5–229°, after recrystallization from methanol.

Anal. Calcd. for $C_{20}H_{20}O_4$: C, 74.05; H, 6.22. Found: C, 73.87; H, 6.28.

Esterification of a sample of the δ-acid with ethereal diazomethane gave after crystallization from methanol, colorless prisms, m.p. 170–171.5°, undepressed on admixture with the δ-ester obtained by reduction of I ($R^1 = OCH_3$, $R^2 = H$, $R^3 = CH_3$) (see below).

γ-15-Carbomethoxyequilenin Methyl Ether.—Treatment of the γ-acid with ethereal diazomethane gave after two recrystallizations from methanol (activated carbon) nearly colorless prisms, m.p. 119.8–121.7°.

Anal. Calcd. for $C_{21}H_{22}O_4$: C, 74.52; H, 6.55. Found: C, 74.75; H, 6.65.

δ-15-Carbomethoxyequilenin Methyl Ether.—(*a*) *From I* ($R^1 = OCH_3$, $R^2 = H$, $R^3 = CH_3$).—In one experiment on

(16) Williams, *Org. Syn.*, **23**, 63 (1943).

(17) Fulton and Robinson, *J. Chem. Soc.*, 200 (1939).

(18) Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., Boston, Mass., 1941, p. 364.

(19) Linstead and Thomas, *J. Chem. Soc.*, 1127 (1940).

the hydrogenation of I(R^1 = OCH_3, R^2 = H, R^3 = CH_3) as described at the beginning of the section on hydrogenation experiments, the α-ester was contaminated with a higher-melting product which was isolated in low yield by recrystallization from ethyl acetate. The purified product was obtained as a mixture of colorless blades and rhombs, m.p. 170.5–171°.

Anal. Calcd. for $C_{21}H_{22}O_4$: C, 74.52; H, 6.55. Found: C, 74.22; H, 6.40.

The oxime was prepared as described above for the α-isomer. It was obtained from benzene as colorless crystals, m.p. 184–186° when introduced in bath at 175°.

Anal. Calcd. for $C_{21}H_{23}O_4N$: C, 71.36; H, 6.56. Found: C, 71.59; H, 6.59.

(*b*) *From II* (R^1 = OCH_3, R^2 = H, R^3 = CH_3).—A solution of 1.00 g. of the 15,16-dehydro ester, m.p. 138–140.4°, prepared by the action of diazomethane on II, R^1 = OCH_3, R^2 = R^3 = H (see above), in 50 ml. of ethyl acetate[15] was treated with Raney nickel and then hydrogenated over 0.300 g. of 30% palladium-on-carbon[19] as described above for the reduction of I (R^1 = OCH_3, R^2 = H, R^3 = CH_3). The reaction proceeded relatively rapidly, the calculated volume of gas being absorbed in 50 minutes. Crystallization of the crude product from benzene–petroleum ether (b.p. 60–68°) gave 0.300 g. (30% yield) of crude δ-ester, m.p. 162–169° with previous softening. A single recrystallization from benzene raised the m.p. to 169–171°, which was undepressed on admixture with the specimen of the δ-ester described above. From the mother liquors of the first crystallization a total of 0.500 g. (50% yield) of crude γ-ester, m.p. 113–117°, was isolated. A single recrystallization from methanol gave material m.p. 115–118°, undepressed on admixture with the sample of the γ-ester described above.

Saponification of δ-15-Carbomethoxyequilenin Methyl Ether.—A 0.040-g. sample of the δ-ester was saponified with 0.040 g. of barium hydroxide octahydrate as described above for the α-isomer. The crude acid, which amounted to 0.037 g., melted at about 100°, resolidifying at 110°, then remelting about 180–207°. Crystallization from methanol gave 0.020 g. of crude γ-acid, m.p. 204–209°. Crystallization of the crude material from benzene gave material, m.p. 207.5–209.5°, undepressed on admixture with the analytical sample of the γ-acid described above.

Since the m.p. behavior of the crude product indicated it to be quite impure, an effort was made to find the δ-isomer. The residues from the isolation of the γ-acid in a similar experiment were combined and treated with diazomethane. Crystallization of the crude ester from benzene–petroleum ether (b.p. 40–60°) gave crude γ-ester, m.p. 111–114°, which may have contained some of the δ-ester as recrystallization raised the m.p. to 108–140°. The amount, however, was too small to carry further.

6-Methoxy-17-equilenone-15-carboxylic Acid.—A 0.426-g. sample of 6-methoxy-15,16-dehydro-17-equilenone-15-carboxylic acid (II, R^1 = R^3 = H, R^2 = OCH_3),[8] m.p. 211–214°, was hydrogenated in ethyl acetate over 5% palladium-on-carbon[20] as described above. About 90% of the calculated volume of gas was absorbed after 34 hours. The crude product amounted to 0.365 g., m.p. 168–180°. Recrystallization twice from ethanol, once from benzene and twice again from ethanol gave colorless crystals, m.p. 203.5–204.5°, $\lambda_{max.}$ 243 mμ (log *E* 4.59), 300 (3.79).[15]

Anal. Calcd. for $C_{20}H_{20}O_4$: C, 74.05; H, 6.22. Found: C, 73.62; H, 6.35.

Summary

Ultraviolet spectroscopy and hydrogenation experiments have provided conclusive evidence (1) that the olefinic bond of the 15-carbalkoxydehydro-17-equilenones produced by the condensation of succinic ester with the appropriate α-cyano ketones lies in the 14,15-position as represented by formula I (R^3 = alkyl), and (2) that this olefinic bond shifts to the 15,16-position upon saponification to produce keto acids of the formula II (R^3 = H). This phenomenon has been observed in the parent series (R^1 = R^2 = H), in the 3-methoxy (equilenin) series (R^1 = OCH_3, R^2 = H), and in the 6-methoxy series (R^1 = H, R^2 = OCH_3).

The hydrogenation studies in the equilenin series have given rise to four stereoisomeric 15-carboxyequilenin methyl ethers. The manner of their formation has made it possible to draw some conclusion regarding the configurations of these products.

(20) "Catalyst C," Mozingo, *Org. Syn.*, **26**, 77 (1946).

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A New Synthesis of the 6-Methoxy-17-equilenones and Some Stereochemical Considerations

BY RALPH HIRSCHMANN[1] AND WILLIAM S. JOHNSON

The experiments recorded herewith describe the application of the equilenin synthesis developed in this Laboratory[2] to the preparation of the two racemic 6-methoxy-17-equilenones (IV) of Bachmann and Holmes.[3] It was hoped that these ketones, in particular the isomer with ring C/D *trans*, would thus be made readily available for use as starting materials in a proposed conversion into some of the natural hormones. Since our synthetic scheme embodies certain stereospecific features (see below), it was also hoped that some evidence would be provided for the assignment of configurations to the two racemic forms of IV.

The steps involved in the synthesis were analogous to those already described in detail for the synthesis of equilenin.[2] The starting material, 1-keto-9-methoxy-1,2,3,4-tetrahydrophenanthrene, I (R^1 = R^2 = H), was prepared by the method of Bachmann and Holmes[3] except that the reduction of β-4-methoxy-1-naphthoylpropionic acid to γ-4-methoxy-1-naphthylbutyric acid was effected by the Huang-Minlon modification of the Wolff–Kishner method,[4] and that the cyclization of the latter was performed with hydrogen fluoride. It is noteworthy that in the reduction step extensive decomposition by what is presumed to be air oxidation of demethylated (phenolic) material, could be obviated by conducting the reaction in an atmosphere of nitrogen. The ketone I (R^1 = R^2 = H) thus was produced on a fair scale in 53% over-all yield from α-methoxynaphthalene. The conversion of this ketone *via* the hydroxymethylene deriva-

(1) Sterling-Winthrop Research Institute Fellow, 1949–1950.
(2) Johnson, Petersen and Gutsche, THIS JOURNAL, **69**, 2942 (1947).
(3) Bachmann and Holmes, *ibid.*, **62**, 2750 (1940).
(4) Huang-Minlon, *ibid.*, **68**, 2487 (1946).