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[18] 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.

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

Madison, Wisconsin Received June 19, 1950

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

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-

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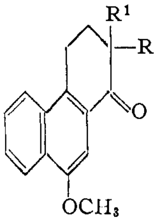
[1] Sterling–Winthrop Research Institute Fellow, 1949–1950.

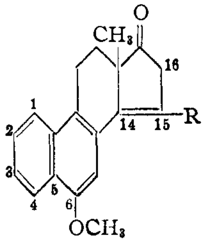
[2] Johnson, Petersen and Gutsche, This Journal, **69**, 2942 (1947).

[3] Bachmann and Holmes, *ibid.*, **62**, 2750 (1940).

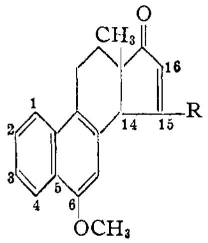
[4] Huang-Minlon, *ibid.*, **68**, 2487 (1946).



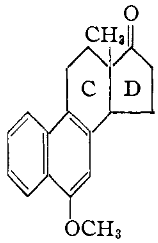
I



II



III



IV

tive and isoxazole to the pure cyano ketone I $R^1 = CH_3$, $R^2 = CN$) was effected in 78% yield, and its condensation with dimethyl succinate in the presence of potassium *t*-butoxide afforded the keto ester II ($R = COOCH_3$) in 70–78% yield. Saponification and decarboxylation gave a mixture from which the unstable compound, 6-methoxy-14,15-dehydro-17-equilenone II (R = H), m.p. 153–155°, could be separated by crystallization, but in only 10% yield. Although the isomeric 15,16-dehydro compound III (R = H) was not isolated it was probably present in the oily residues just as in the equilenin and the desoxyequilenin series.[2] If the yield of this decarboxylation step could be improved, it is apparent from the following discussion that the objective of designing a method for the production of IV (C/D *trans*) on a large scale would be realized.

The double bond in ring D of the crystalline decarboxylation product was shown to lie in the 14,15-position (formula II, R = H) through ultraviolet spectroscopy.[5] Catalytic hydrogenation of this material gave the two 6-methoxy-17-equilenones melting, after purification, at 148.5–150° and at 107–108.4°. When these specimens were admixed, respectively, with the α- (m.p. 147.5–149°) and β- (m.p. 112–113°) forms of IV of Bachmann and Holmes,[3] no depression of the melting points was observed.[6]

In the hydrogenation of II (R = H) the α-form of IV was produced in preponderance, in fact this was the only product which could be isolated (74% yield) when conditions for rapid hydrogenation were employed. By analogy to the corresponding hydrogenation step in the equilenin series which yields a preponderance of equilenin methyl ether, the α-form of IV may now be tentatively placed in the same stereochemical series as equilenin in which rings C/D are undoubtedly fused in the *trans* configuration.[7] The stereospecificity of this type of hydrogenation is further supported by the analogous behavior in the hydrogenation of 14,15-dehydro-17-equilenone to give in preponderance a product which by independent evidence appears also to belong to the same stereochemical series as equilenin.[8]

Experimental Part[9,10]

β-(4-Methoxy-1-naphthoyl)-propionic acid was prepared by the method of Bachmann and Holmes[3] with the following modifications which obviate the steam distillation. After the addition of the α-methoxynaphthalene was complete the mixture was stirred for 4 hours at room temperature and finally allowed to stand (without stirring) for 20 hours. Upon decomposition of the aluminum chloride complex with ice and concentrated hydrochloric acid, the crude keto acid precipitated from the nitrobenzene layer where it remained in suspension. After standing for a while the aqueous layer was separated and discarded. The organic suspension was then washed twice with water and the product separated by suction filtration and washed thoroughly with dilute hydrochloric acid until the washings were free of aluminum salts. After drying on a porous plate at room temperature the brown product usually melted between 170–173° and 173–174°. In a typical run the yield of such material from 490 g. of α-methoxynaphthalene was 685.5 g. or 86%. Additional material was isolated from the filtrate (which was first washed free of aluminum salts by dilute hydrochloric acid) by extraction with dilute ammonium hydroxide (1 part concentrated reagent to 5 parts of water by volume). Acidification of these extracts yielded a crude product which after crystallization from glacial acetic acid amounted to 19.5 g., m.p. 171–173°, making the total yield 88%. One recrystallization from acetic acid gave material melting at 174–175° (recovery 89%). Bachmann and Holmes reported an 83% yield of material melting at 172–174°.[3]

γ-(4-Methoxy-1-naphthyl)-butyric Acid.—When the reduction procedure of Huang-Minlon[4] was applied to the above keto acid, there was extensive demethylation attended by considerable oxidation of the resulting phenolic product so that the yield of reduced material, m.p. 119–124° (after remethylation) never exceeded 67%. Such behavior is possibly responsible for the relatively low yields realized by Huang-Minlon in the reduction of β-(*p*-methoxybenzoyl)-propionic acid, and may be expected in general when this procedure is used with keto compounds containing phenolic ether groups which are susceptible to cleavage by alkali. The following modification of the Huang-Minlon procedure gave improved yields and promises to be of general use for related substances. The main innovations involve exclusion of air and a shortened reaction period.

In a 1-l., two-necked, round-bottomed flask were placed 75.0 g. (0.29 mole) of the keto acid described above, m.p. 174–175°, 395 ml. of diethylene glycol, 58.5 g. of 85% potassium hydroxide pellets and 39.5 ml. of 85% hydrazine hydrate. One neck of the flask was fitted with a thermometer immersed below the level of the liquid, and the other with a take-off condenser,[11] the top of which was connected to a T-tube leading to a mercury trap and to a source of nitrogen and reduced pressure. The system was evacuated and filled with nitrogen, and then, while protected from the atmosphere by engaging the mercury trap, the mixture was boiled under reflux for about 2 hours, 58 ml. of the condensate being removed through the take-off attachment during the last 23 minutes of this heating period. Refluxing was then continued for an additional 2 hours, the temperature of the reaction mixture remaining between 204–215°. The dark mixture was cooled, about 300 ml. of water added and the whole was washed with ether to remove some non-acidic material. The aqueous layer was acidified with hydrochloric acid and the dark brown oily organic acid which separated was taken up in ether. The product obtained on evaporation of the ether was dissolved in 350 ml. of 7.5% sodium hydroxide solution and methylated with a total of

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[5] See Johnson, Gutsche, Hirschmann and Stromberg, This Journal, **73**, 322 (1951).

[6] We are indebted to Professor W. E. Bachmann of the University of Michigan for kindly performing these determinations.

[7] See Bachmann and Dreiding, This Journal, **72**, 1323 (1950); Stork and Singh, *Nature*, **165**, 816 (1950).

[8] *Cf.* Bachmann and Wilds, This Journal, **62**, 2084 (1940); Wilds, Beck and T. Johnson, *ibid.*, **68**, 2161 (1946).

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

[10] We wish to thank B. Buell, R. Hunt, V. Miller and E. Shiner for carrying out the microanalyses reported herein.

[11] Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., Boston, Mass., 1941, p. 323.

150 ml. of dimethyl sulfate, added from a dropping funnel in 50-ml. portions. The reaction mixture was maintained at 0° and stirred vigorously for 15 minutes between each addition. The solution was maintained alkaline (to litmus) at all times by the addition of sodium hydroxide solution as required. After the methylation was complete, 55.0 g. of sodium hydroxide was added and the mixture boiled under reflux for 2 hours. The solution was cooled, washed with ether, then added slowly with stirring and chilling to an excess of concentrated hydrochloric acid, whereupon the desired acid precipitated. The neutral material obtained on evaporation of the ether washings was resaponified as above giving additional product on acidification. The total yield of buff-colored crystals thus produced amounted to 57.0 g. (80%), m.p. 121–126°. This material was satisfactory for the next step in the synthesis. The Clemmensen method of reduction of the keto acid is reported to give a product melting at 127–129° in 60% yield on a 25-g. scale.[3]

The above method has been carried out successfully on a scale as large as 200 g.

1-Keto-9-methoxy-1,2,3,4-tetrahydrophenanthrene (I, $R^1 = R^2 = H$).—A 9.4-g. sample of the crude methoxynaphthylbutyric acid, m.p. 120–129°, was treated for 3 hours at room temperature with an excess of hydrogen fluoride by the usual procedure.[12] The neutral material was isolated by extraction with ether–benzene and amounted to 8.0 g., m.p. 89–95°. After distillation at 210–211° (0.015 mm.) and recrystallization from dilute alcohol there was obtained 7.3 g. (84% yield) of nearly colorless crystals, m.p. 100.2–100.8°. Starting with fairly pure acid, m.p. 127–129°, Bachmann and Holmes[3] obtained the ketone, m.p. 99–100° in 92% yield *via* the Friedel–Crafts stannic chloride procedure. With our crude material this procedure gave the ketone, m.p. 96–97°, in 68% yield.

2-Hydroxymethylene-1-keto-9-methoxy-1,2,3,4-tetrahydrophenanthrene.—The condensation of 15.05 g. of the above ketone, m.p. 100–101°, with 10.0 g. of ethyl formate was carried out in the presence of 7.2 g. of commercial sodium methoxide (Mathieson Alkali Works), and a total of 155 ml. of benzene essentially as previously described for the 7-methoxy isomer. Due to the low solubility of the sodio derivative in water the product was isolated by treating the gelatinous reaction mixture with excess hydrochloric acid and ice. This mixture was shaken vigorously until no solid remained, then the benzene layer was separated and evaporated, leaving 16.8 g. of crude yellow hydroxymethylene ketone, m.p. 93–113°. This product was satisfactory for preparing the isoxazole (see below).

A sample of the hydroxymethylene ketone prepared exactly as in the equilenin series, was obtained in 92% yield as yellow crystals, m.p. 113.5–117°. Repeated recrystallization from benzene afforded yellow prisms, m.p. 117–118.5°, giving a deep green color with alcoholic ferric chloride. During the purification process an unstable polymorphic modification, m.p. 120–122.5°, was encountered.

Anal. Calcd. for $C_{16}H_{14}O_3$: C, 75.37; H, 5.55. Found: C, 75.23; H, 5.58.

10,11-Dihydro-5-methoxyphenanthro[2,1-*d*]isoxazole was prepared according to a procedure already described.[2] In a typical run there was obtained from 16.8 g. of the crude hydroxymethylene ketone (m.p. 93–113°) and 6.85 g. of hydroxylamine in 360 ml. of acetic acid, 15.7 g. (94.5% yield) of nearly colorless isoxazole, m.p. 160.5–162.5°. A sample purified by sublimation at 120° (0.13 mm.) followed by recrystallization twice from ethyl acetate was obtained as colorless needles, m.p. 163–164.5°.

Anal. Calcd. for $C_{16}H_{13}O_2N$: C, 76.47; H, 5.21. Found: C, 76.65; H, 5.07.

2-Cyano-1-keto-9-methoxy-2-methyl-1,2,3,4-tetrahydrophenanthrene (I, $R^1 = CH_3$, $R^2 = CN$).—The following procedure is an adaptation of an unpublished method developed by Dr. Eugene Woroch for the large-scale production of the 7-methoxy isomer based on the published procedure.[2] This modification eliminates the use of potassium metal.

To a stirred solution of sodium *t*-butoxide in *t*-butyl alcohol was added 8.0 g. of the isoxazole described above, m.p. 160.5–162.5°, while the temperature was maintained at 75–80°. After stirring and heating for 15 minutes, 12 ml. of methyl iodide was added dropwise to the thick crystalline suspension of sodio derivative of the cyano ketone (I, $R^1 = H$, $R^2 = CN$). After the addition was complete (20 minutes), stirring and heating was continued for an additional 45 minutes. The solvent was then largely removed at the steam-bath in a current of air, water was added, and the organic material extracted with benzene. The combined benzene solutions were washed successively with water, dilute potassium hydroxide solution, and again with water. The solid suspended at the interface of the layers was separated by filtration and amounted to 3.2 g. of cyano ketone of good purity, m.p. 172–172.5°. From the filtrate 4.7 g. of the same product, m.p. 167–169°, was isolated by evaporation of the benzene layer, making the total yield 7.9 g. (94%). A sample, m.p. 164.5–171°, was recrystallized four times (activated carbon being used the third time) from alcohol giving colorless prisms, m.p. 171.8–172.4°.

Anal. Calcd. for $C_{17}H_{15}O_2N$: C, 76.96; H, 5.70. Found: C, 77.10; H, 5.42.

In occasional runs no precipitate of the intermediary sodio derivative of the cyano ketone I ($R^1 = H$, $R^2 = CN$) formed even upon prolonged heating. In these cases the yield of final product usually dropped to about 85%.

When the procedure previously described for the 7-methoxy isomer,[2] using potassium *t*-butoxide, was applied to the present isoxazole, the methylated cyano ketone was obtained in 93% yield, m.p. 164.5–171°. Recrystallization from alcohol gave in 88.5% recovery material melting at 171–172°.

Methyl 6-Methoxy-14,15-dehydro-17-equilenone-15-carboxylate (II, R = $COOCH_3$).—When the condensation of the above cyano ketone, m.p. 171–172°, with dimethyl succinate was carried out exactly as described in the equilenin series, on a 4.00-g. scale the crude keto ester was produced in yields of 75–78%, with the m.p. ranging from 134–143° to 133–137°. The ammonia produced[2] in these runs amounted to 82–86% of the theoretical. In other runs (0.4-g. scale) a product, m.p. 141–146°, was produced in 70% yield.

The condensation was also studied with crude cyano ketone, m.p. 159–167.5°. Good results were obtained when the dimethyl succinate was added to the reaction mixture all at once, and only the *t*-butoxide solution added slowly. In a typical run, 6.0 g. of the crude cyano ketone and 23 ml. of dimethyl succinate were placed in the reaction flask and treated with a solution of 6.0 g. of potassium in 128 ml. of *t*-butyl alcohol essentially as described in the equilenin series.[2] The crude product thus obtained amounted to 5.60 g. (74% yield), m.p. 128–142°.

While the crude products produced by any of the above procedures were generally satisfactory for conversion to the keto acid III (R = COOH), they were quite difficult to purify as the ester, presumably because of contamination by the less soluble, higher-melting starting cyano ketone. A sample of the 128–142° material was submitted to two successive sublimations at 140–145° ($<10^{-4}$ mm.) and then recrystallized twice from methanol. In this way a pure sample of the keto ester was obtained as pale yellow prisms, m.p. 148–149.5°.

Anal. Calcd. for $C_{21}H_{20}O_4$: C, 74.98; H, 5.99. Found: C, 75.15; H, 6.02

The crude keto ester, m.p. 120–147°, was also prepared in 61% yield directly from the isoxazole as described in the equilenin synthesis (part b).[2]

It is noteworthy that in none of these condensation experiments did the reaction mixture become as thick as in the equilenin series.

6-Methoxy-15,16-dehydro-17-equilenone-15-carboxylic Acid (III, R = COOH).[13]—Saponification of the keto ester II (R = $COOCH_3$) was carried out with barium hydroxide by essentially the same procedure previously described in the equilenin series, except that the acid was obtained from the barium salt by pouring the hot alcoholic solution into excess dilute hydrochloric acid. In a typical run 3.15 g. of crude keto ester, m.p. 120–147°, was treated with 3.15 g. of barium hydroxide octahydrate in 46 ml. of alcohol and 36 ml. of water, to yield 2.92 g. of crude keto acid, m.p. 201–205°.

In another run the reaction was carried out as described

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[12] See Adams, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N.Y., 1944, p. 158.

[13] See ref. 5 for proof of structure.

above except that the whole process including the acidification was effected in an atmosphere of nitrogen, the alkaline solutions never being exposed to the atmosphere. From 0.997 g. of keto ester, m.p. 141–146°, there was thus obtained after dissolution in sodium bicarbonate, reprecipitation with acid, and recrystallization from benzene, 0.714 g. (74% yield) of yellow keto acid, m.p. 217–220° (dec.). An additional 0.120 g., m.p. 217–219°, was obtained from the mother liquor making the total yield 87%. A sample of acid (m.p. 210–219°) in ether solution was purified by chromatographic adsorption on a column of -80 mesh activated magnesium sulfate heptahydrate. The main fraction eluted with benzene melted at 213.5–220.5°, and after precipitation from an ether–benzene solution by the addition of petroleum ether it was obtained as pale yellow crystals, m.p. 220.5–222°.

Anal. Calcd. for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63. Found: C, 74.29; H, 5.85.

6-Methoxy-14,15-dehydro-17-equilenone (II, R = H).—Like 15,16-dehydro-17-equilenone-15-carboxylic acid,[2,13] the keto acid III (R = COOH) was more resistant to decarboxylation than the 3-methoxy isomer. The decarboxylation product, moreover, appeared to be even more sensitive to air and heat than in the two previous cases, thus making the isolation and purification difficult. The long treatment required in both the hydrochloric–acetic acid method and the pyridine hydrochloride–hydrochloric acid method resulted in extensive demethylation and considerable decomposition. In one experiment by the former procedure, however, it was possible to isolate from the sodium carbonate-insoluble fraction, after evaporative distillation at 155° ($<10^{-4}$ mm.) and chromatographic purification, a semi-solid product which upon hydrogenation over 5% palladium-on-carbon catalyst[14] gave in low yield a phenolic product melting at 238–241.5° (vac.) after purification through the sodium salt. This melting point is in good agreement with that (238–240°, vac.) reported for α-6-hydroxy-17-equilenone.[3]

Various other methods of decarboxylation were investigated, but the best results were realized with simple thermal decarboxylation procedure already described for the 3-methoxy isomer.[2] A 0.685-g. sample of III (R = COOH), m.p. 216–217°, thus heated at 223 ± 4° at 27 mm. for 1 hour and 25 minutes, then at 220° (0.4 mm.) for 1 hour and 10 minutes, gave a yellow oily distillate which was dissolved in ether and extracted with sodium bicarbonate solution to remove undecarboxylated material. Acidification of the bicarbonate solutions gave back about 18% of crude starting acid III (R = COOH), m.p. about 188–191°. Evaporation of the dried ether solution in a current of nitrogen gave an amorphous red residue which on crystallization from ethanol yielded the crude 14,15-dehydro compound (m.p. about 120–142°). This material was evaporatively distilled at 160° (0.05 mm.) and recrystallized from ethanol to give 0.094 g. (16% yield), m.p. 149–152°. A second recrystallization gave (63% recovery) pink prisms, m.p. 153–155° with previous softening. This product gave no depression of the m.p. on admixture with the analytical specimen described below. An alternate method of purification involved chromatographic adsorption (which could be carried out upon the total crude bicarbonate-insoluble fraction) on acid-washed alumina in 1:1 benzene–petroleum ether (b.p. 60–68°) solution. The main fraction eluted by this solvent pair was obtained, after recrystallization from ethanol, as red crystals, m.p. 144–152°. Sublimation at 122–129° ($<10^{-4}$ mm.) gave a colorless sublimate melting at 149–150.5° (micro hot stage), $\lambda_{\max}$ 259.5 mμ (log E 4.65), which on standing in air gradually darkened. Note that the recrystallized product described above has a higher m.p.

Anal. Calcd. for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52. Found: C, 82.19; H, 6.70.

The 6-Methoxy-17-equilenones.—A 0.1103-g. sample of 6-methoxy-14,15-dehydro-17-equilenone, m.p. 153–155°, in 17 ml. of dioxane[15] was hydrogenated over 0.150 g. of 30% palladium-on-carbon catalyst[16] at atmospheric pressure and room temperature. After 20 minutes the reaction subsided, the uptake of gas being approximately the calculated quantity. The oily residue obtained on evaporation of the filtered solution was crystallized from methanol giving 0.073 g. of the pure α-isomer, m.p. 148–150°. An additional 0.009 g. of material m.p. 142–145° was obtained from the mother liquors making the total yield 74%. Further crystallization of the residue gave lower-melting fractions which undoubtedly contained some of the β-isomer (see below). The purest sample of the α-isomer, which was obtained by repeated recrystallization, melted at 148.5–150°, and showed no m.p. depression on admixture with a specimen of the α-isomer of Bachmann and Holmes,[3] m.p. 147–148°.[6]

The β-isomer was isolated from the hydrogenation of a less pure sample of II (R = H), m.p. 145–155°, over 5% palladium-on-carbon.[14] The hydrogenation was much slower, requiring 20 hours for absorption of 80% of the calculated amount of gas, which probably accounted for the formation of a higher proportion of the β-(*cis*) form.[17] In this case the crude α-isomer, m.p. 143–148°, was isolated in only 46% yield, and from the mother liquors there was obtained in 23% yield a product, m.p. 101–106° which after recrystallization from methanol melted at 107–108.5°. A mixture with a sample of authentic β-isomer[3] (m.p. 113–114°), melted at 106–113°.[6]

Summary

The two racemic forms of 6-methoxy-17-equilenone of Bachmann and Holmes[3] have been prepared by the method developed in this Laboratory for the synthesis of equilenin.[2] Because of certain stereospecific features of this synthesis, some evidence has been provided for the assignment of configurations to these stereoisomers.

MADISON, WISCONSIN RECEIVED JUNE 19, 1950

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[14] Catalyst C; Mozingo, *Org. Syn.*, **26**, 77 (1946).

[15] Purified according to Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., Boston, Mass., 1941, p. 368.

[16] Linstead and Thomas, *J. Chem. Soc.*, 1127 (1940).

[17] Similar behavior has been noted in the hydrogenation of 14,15-dehydroequilenin methyl ether during large-scale reductions carried out by Woroch and Buell. When impure starting material or a small amount of catalyst was employed so that the reaction was slow, a higher proportion of isoequilenin methyl ether was produced, possibly formed *via* an isomerization of the 14,15- to the 15,16-dehydro compound the latter giving exclusively the *cis* form on reduction (see ref. 2). The argument for the configurations of the α- and β-forms of IV is thus strengthened by this analogy.