fixed position, even when (and this is contrary to previous conclusions) the indene has no substituent group in its five-membered ring.

A number of compounds prepared incidentally in exploratory syntheses are also reported.

MINNEAPOLIS, MINNESOTA RECEIVED AUGUST 17, 1943

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE UNIVERSITY OF MICHIGAN]

The Synthesis of Compounds Related to the Sex Hormones

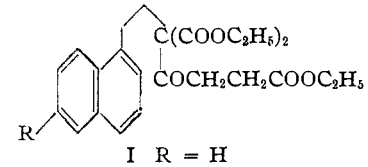
BY W. E. BACHMANN, R. A. GREGG AND E. F. PRATT[1]

In the preparation of an intermediate in the synthesis of estrone-a,[2] cyclization of the triethyl ester of 5-keto-6,6-dicarboxy-8-*m*-anisyloctanoic acid was effected by means of 100% phosphoric acid; cyclization took place to the benzene ring in a position para to a methoxy group. We were interested in determining how readily a similar cyclization would occur to the beta position of the naphthalene nucleus. Such a cyclization would offer a route to norequilenin and related compounds.

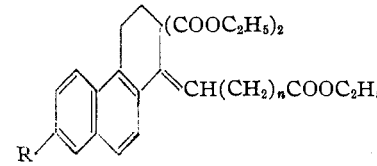
Condensation of the sodio derivative of β-1-naphthylethylmalonic ester with the acid chloride of ethyl hydrogen succinate gave the triethyl ester of 4-keto-5,5-dicarboxy-7-α-naphthylheptanoic acid (I) It was found that cyclization to II could be effected by means of 100% phosphoric acid provided that a higher temperature and a longer time were employed than were required for the anisyl derivative. Hydrolysis of the unsaturated triester yielded the corresponding tricarboxylic acid, which was decarboxylated in hot water to an unsaturated dicarboxylic acid, probably 2-carboxy-3,4-dihydrophenanthrene-1-β-propionic acid (III), although the position of the double bond has not been established. The acid was obtained in 15–23% over-all yields from I.

The dimethyl ester of III is the key compound from which the three cyclic ketones IV, V and VI were prepared. These differ in the degree of unsaturation in the C ring. By dehydrogenation of the dimethyl ester of III by means of palladium-charcoal at 310°, the dimethyl ester of 2-carboxyphenanthrene-1-β-propionic acid was obtained which was converted to 3′-keto-1,2-cyclopentenophenanthrene (IV) through Dieckmann cyclization followed by hydrolysis and decarboxylation of the resulting product. The cyclic ketone was identical with the compound which had been prepared previously by cyclization of β-1-phenanthrylpropionic acid.[3]

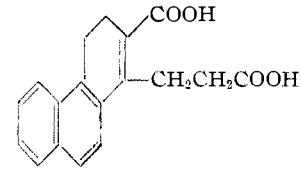
When the dimethyl ester of III was cyclized by the Dieckmann method and the resulting cyclic β-keto ester hydrolyzed and decarboxylated, 3′-keto-3,4-dihydro-1,2-cyclopentenophenanthrene (V) was produced. The position of the double bond in the compound has not been established. The compound is probably identical with the cyclic ketone obtained by Bardhan[4] by treatment of the unsaturated dicarboxylic acid (III) with acetic anhydride followed by distillation of the product and with the compound prepared by Robinson and Thompson.[5]



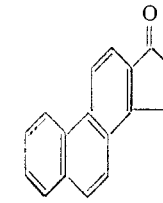
I R = H
Ia R = OCH_3



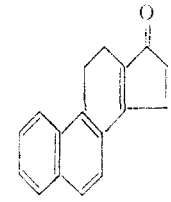
II R = H; n = 1
IIa R = OCH_3; n = 1
IIb R = H; n = 2
IIc R = OCH_3; n = 2



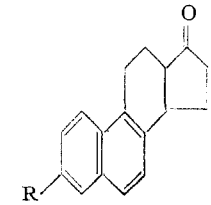
III



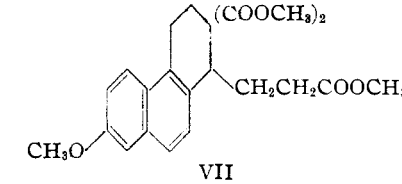
IV



V



VI R = H
VIa R = OH



VII

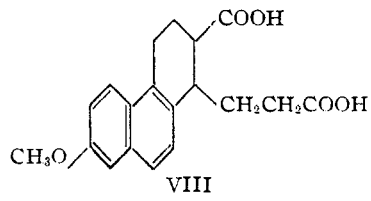
(1) From the Ph. D. dissertations of R. A. Gregg and E. F. Pratt.

(2) Bachmann, Kushner and Stevenson, THIS JOURNAL, **64**, 974 (1942).

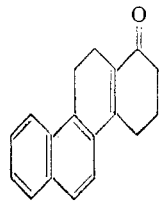
(3) Bachmann and Kloetzel, *ibid.*, **59**, 2207 (1937).

(4) Bardhan, *J. Chem. Soc.*, 1848 (1936).

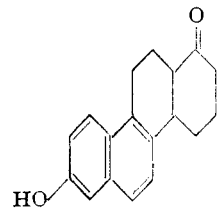
(5) Robinson and Thompson, *ibid.*, 1739 (1939).



VIII



IX



X

By hydrogenation of the dimethyl ester of III in the presence of palladium on charcoal, a crystalline saturated ester was obtained in 80% yield. Cyclization by the Dieckmann method followed by hydrolysis and decarboxylation of the product yielded one of the forms of 3′-keto-1,2,3,4-tetrahydro-1,2-cyclopentenophenanthrene (VI). It is probably identical with the compound prepared by Koebner and Robinson[6] by another procedure.

The same methods of synthesis proved applicable for the preparation of 3′-keto-7-hydroxy-1,2,3,4 - tetrahydro - 1,2 - cyclopentenophenanthrene (VIa), which possesses the structure of equilenin except for the angular methyl group. The triethyl ester of 4-keto-5,5-dicarboxy-7-(6′-methoxy-1′-naphthyl)-heptanoic acid (Ia) was cyclized to IIa under much milder conditions and in better yield than obtained for the desmethoxy compound. The methoxy group exerted a favorable influence on the *beta* position of the naphthalene nucleus and cyclization took place about as readily as it did in the anisyl derivative. The product was an uncrystallizable oil, but the corresponding tricarboxylic acid and the trimethyl ester of the latter were crystalline solids. The latter result suggested the use of methyl esters in the preceding steps in order to obtain a crystalline product on cyclization, but this has not yet been tried. The trimethyl ester was reduced by hydrogen in the presence of palladium on charcoal to the saturated ester (VII), which was hydrolyzed to the corresponding tricarboxylic acid. On decarboxylation of this acid at 180°, there was a possibility of obtaining both the *cis* and *trans* forms of the dicarboxylic acid (VIII), but only one form was isolated. It was converted to its dimethyl ester which was cyclized by the Dieckmann method to a crystalline cyclic β-keto ester in 84% yield. When this compound was heated with a mixture of hydrochloric acid and acetic acid, demethylation of the ether group as well as hydrolysis and decarboxylation of the ester group took place, and the phenolic ketone (VIa) was produced. Methylation of the product gave the methyl ether which possessed the same melting point as the *x*-norequilenin methyl ether of Koebner and Robinson.[7]

By an analogous series of reactions, in which the acid chloride of ethyl hydrogen glutarate was used in the first step, the 1-ketohexahydrochrysene IX (or the isomer with the double bond extending to the 4-position) and the 1-keto-8-hydroxyoctahydrochrysene X were prepared. Cyclization of the triethyl ester of 5-keto-6,6-dicarboxy-8-α-naphthyloctanoic acid to IIb was difficult and the product was formed only in poor yield, It is planned to study the effect of other cyclizing agents such as aluminum chloride, hydrogen fluoride and stannic chloride, on these and related ketones. The 1-ketohexahydrochrysene was obtained through the Dieckmann method or more simply by refluxing a mixture of IIb, hydrochloric acid and acetic acid, a method found to be suitable for the preparation of 7-methoxy-1 - keto - 1,2,3,4,9,10 - hexahydrophenanthrene.[2] The unsaturated cyclic ketone is probably identical with that prepared by Chuang, Huang and Ma[8] by a different method. The hydrochrysene structure and the position of the carbonyl group in the molecule were established by conversion of the compound to 1-methylchrysene by treatment with methylmagnesium iodide, followed by dehydration and dehydrogenation of the methyl carbinol at 300–310° in the presence of palladium on charcoal.

In the preparation of IIc it was observed again that the methoxy group in the 6-position of the naphthalene nucleus activated the 2-position, for cyclization to form IIc took place readily. The tricarboxylic acid corresponding to IIc was reduced, the saturated tricarboxylic acid was decarboxylated to a dicarboxylic acid and the dimethyl ester of the latter was cyclized by the Dieckmann method. As with previous compounds containing the β-naphthol methyl ether nucleus, demethylation of the methyl ether of X took place in a boiling mixture of acetic acid and hydrochloric acid. Only one of the two possible forms of the 1-keto-8-hydroxyoctahydrochrysene was obtained. This compound is a structural isomer of equilenin.

Experimental

Triethyl Ester of 4-Keto-5,5-dicarboxy-7-α-naphthylheptanoic Acid (I).—Absolute alcohol (80 cc.) was added in portions to a suspension of 16.7 g. of powdered sodium in 50 cc. of dry benzene; after only a few minutes of refluxing all of the sodium had reacted. To the mixture was added 175 cc. of ethyl malonate and after one-half hour of refluxing, 118 g. of β-naphthylethyl bromide in 150 cc. of benzene was added to the cooled mixture. After being kept warm in a water-bath for eleven hours and then heated on a steam cone for four hours, the mixture was worked up in the usual manner. The β-1-naphthylethylmalonic ester was obtained as a viscous liquid distilling at 170–175° and 0.05 mm.; yield, 141 g. (89%).

A mixture of 100 g. of ethyl hydrogen succinate and 73 cc. of purified thionyl chloride was allowed to stand at room temperature for three and one-half hours and then heated

(6) Koebner and Robinson, *J. Chem. Soc.*, 566 (1941).

(7) Koebner and Robinson, *ibid.*, 1994 (1938).

(8) Chuang, Huang and Ma, *Ber.*, **72B**, 713 (1939).

on a steam-bath for one hour. Distillation gave 109 g. (97%) of the acid chloride boiling at 94–96° and 2 mm.

A solution of 21.2 g. of β-1-naphthylethylmalonic ester in 45 cc. of benzene was added to 1.6 g. of powdered sodium in 30 cc. of benzene. After two hours of refluxing, when all of the sodium had reacted, the mixture was cooled in an ice-bath and treated with a solution of 22 cc. of the acid chloride of ethyl hydrogen succinate in 15 cc. of benzene. After the mixture had stood for twelve hours, it was treated with water, the benzene solution was washed with sodium bicarbonate solution, dried and fractionated. Fourteen grams of the desired product (b. p. 180–195° at 0.02 mm.) was obtained; in addition, 9.5 g. of the original substituted malonic ester was recovered.

2-Carboxy-3,4-dihydrophenanthrene-1-β-propionic Acid (III).—A mixture of 2.5 g. of the aforementioned keto-triester and 12.5 g. of 100% orthophosphoric acid was kept at 64° (boiling methanol bath) for thirty-six to forty-eight hours; during this period the mixture was swirled occasionally to effect mixing; the pale yellow gel gradually turned to a clear dark red solution. Four such mixtures were poured onto ice, the product was extracted with ether, the ethereal layer was washed with dilute sodium bicarbonate solution and then with a little water, and the ether was evaporated. The crude product containing the cyclic triester (II) was a dark amber sirup which did not crystallize. It was hydrolyzed by heating it with 25 cc. of 45% aqueous potassium hydroxide and an equal volume of methanol for three hours. The methanol was removed in a current of air and the residue was added dropwise to 1:3 hydrochloric acid. The resulting tricarboxylic acid was extracted with ether, the ether solution was treated with Norite and then evaporated and the acid, which did not crystallize, was heated with 200 cc. of water on a steam cone for twelve hours. The tricarboxylic acid went into solution, carbon dioxide was evolved and the unsaturated dicarboxylic acid (III) precipitated from the solution in solid form along with some oil. The product was extracted with ether, the ether was removed, the residue was dissolved in acetone and the solution was decolorized. Some benzene was added and as the acetone was removed in a current of air the dicarboxylic acid precipitated; yield, 1.0–1.5 g.; m. p. 220–225°. By recrystallization from acetone–benzene it was obtained as colorless crystals melting at 234–236°. It is probably identical with the compound prepared by Bardhan who reported a melting point of 226–227°[9] and 237–238°.[4]

The **methyl ester,** prepared in excellent yield by means of diazomethane, crystallized from petroleum ether in large colorless plates; m. p. 69–71°. A sample after evaporative distillation at low pressure and recrystallization melted at 73–74° (reported,[4] 75°).

Dimethyl Ester of 2-Carboxyphenanthrene-1-β-propionic Acid.—A mixture of 150 mg. of the dimethyl ester of III and 40 mg. of palladium-charcoal catalyst[10] was heated at 310–320° in a nitrogen atmosphere for one-half hour. The product was separated from the catalyst and evaporatively distilled at 180–200° and 0.01 mm.; yield, 60 mg.; m. p. 107–112°. A sample after recrystallization from methanol melted at 114–116°.

Anal. Calcd. for $C_{20}H_{18}O_4$: C, 74.6; H, 5.6. Found: C, 75.1; H, 5.6.

3'-Keto-1,2-cyclopentenophenanthrene (IV).—Sixty mg. of the aforementioned compound was cyclized in benzene by means of sodium methoxide (two hours of warming).[11] The cyclic keto ester was a solid which gave a dark green color with an alcoholic solution of ferric chloride. It was heated with a mixture of acetic acid and hydrochloric acid in the manner described for a similar compound.[11] The cyclic ketone was sublimed and then recrystallized from acetone–methanol, from which it separated in long colorless plates; m. p. 196–197° alone and when mixed with the compound prepared by another method.[3]

3'-Keto-3,4-dihydro-1,2-cyclopentenophenanthrene (V).—Two-tenths gram of the dimethyl ester of III was cyclized by sodium methoxide in benzene (eleven hours refluxing).[11] The product after recrystallization from ligroin weighed 0.16 g. and melted at 137–142°. A sample after recrystallization from benzene–acetone formed faintly yellow prismatic needles; m. p. 142–144°. With alcoholic ferric chloride the **2'-carbomethoxy-3'-keto-3,4-dihydro-1,2-cyclopentenophenanthrene** gave an olive-green color.

Anal. Calcd. for $C_{19}H_{16}O_3$: C, 78.1; H, 5.5. Found: C, 78.4; H, 5.5.

A mixture of 75 mg. of the cyclic keto ester and 6 cc. of a solution of water, hydrochloric acid and acetic acid in the ratio of 1:5:10 was refluxed in a nitrogen atmosphere for three hours. The product (V) was evaporatively distilled at 170–200° and 0.01 mm.; yield, 59 mg. (98%) of colorless rhombohedral prisms; m. p. 214–216° (reported, 210°[4] and 212–213°[5]).

3'-Keto-1,2,3,4-tetrahydro-1,2-cyclopentenophenanthrene (VI).—A solution of 0.6 g. of the dimethyl ester of III in 25 cc. of ethyl acetate was shaken with 0.1 g. of palladium-charcoal catalyst[10] in the presence of hydrogen until one mole equivalent of hydrogen had been absorbed. Evaporation of the solution gave a colorless sirup which gradually crystallized; trituration with petroleum ether yielded 0.445 g. of crystals melting at 81–84° and 0.03 g. of only slightly less pure product. From petroleum ether the **dimethyl ester of 2-carboxy-1,2,3,4-tetrahydrophenanthrene-1-β-propionic acid** crystallized in colorless needles; m. p. 88–89°.

Anal. Calcd. for $C_{20}H_{22}O_4$: C, 73.6; H, 6.8. Found: C, 73.1; H, 6.9.

The ester (0.25 g.) was cyclized by means of sodium methoxide in benzene according to the procedure described[11] (eleven hours of refluxing). Evaporation of the benzene solution, after treatment with dilute acid, water and sodium bicarbonate solution, gave colorless crystals of **2' - carbomethoxy - 3' - keto - 1,2,3,4 - tetrahydro - 1,2-cyclopentenophenanthrene;** these were digested with a little ligroin and filtered; yield, 0.205 g. (91%); m. p. 133–135°. After recrystallization from acetone–methanol, in which little loss was experienced, the compound melted at 134–135°. It gave an immediate purple color with an alcoholic solution of ferric chloride.

Anal. Calcd. for $C_{19}H_{18}O_3$: C, 77.6; H, 6.2. Found: C, 77.8; H, 6.4.

Hydrolysis and decarboxylation of 100 mg. of the compound by acetic acid and hydrochloric acid was carried out as described for the preceding cyclic keto ester. The cyclic ketone (VI) was obtained as colorless plates by evaporative distillation at 145–175° and 0.01 mm.; yield, 74 mg. (92%); m. p. 112–113° (reported,[6] 111–112°).

Trimethyl Ester of 2,2-Dicarboxy-7-methoxy-1,2,3,4-tetrahydrophenanthrylidene-1-β-propionic Acid.—An 80% yield of β-6-methoxy-1-naphthylethylmalonic ester (b. p. 193–198° at 0.02 mm.) was obtained from β-6-methoxy-1-naphthylethyl bromide and the sodio derivative of malonic ester by the method employed for the desmethoxy derivative. Condensation of the sodio derivative of the substituted malonic ester (31.6 g.) with the acid chloride of ethyl hydrogen succinate (30 cc.) was carried out similarly. Because of its high boiling point the resulting keto-triester (Ia) (41 g.) was used in the next step without distillation, after the solvent had been removed at 100° under reduced pressure.

Cyclization of 2.5-g. batches of Ia with five times the weight of 100% orthophosphoric acid was carried out as described for the desmethoxy compound except that a temperature of 42° was employed and four to five hours were allowed for the reaction to take place. The resulting product (IIa) was an oil; it was hydrolyzed with potassium hydroxide to the tricarboxylic acid, which crystallized from acetone–benzene as a light yellow powder; yield, 3.61 g. (45% based on β-6-methoxy-1-naphthylethylmalonic ester); m. p. 148–150°. After a second recrystallization, it melted at 150–151°. It was converted to its trimethyl

(9) Bardhan, *Nature*, **134**, 217 (1934).

(10) Zelinsky and Turowa-Pollak, *Ber.*, **58**, 1295 (1925).

(11) Bachmann, Cole and Wilds, THIS JOURNAL, **62**, 824 (1940).

ester by short treatment with diazomethane; m. p. 157–158°. A sample of the ester crystallized from methanol in hexagonal prisms; m. p. 159–160°.

Anal. Calcd. for $C_{23}H_{24}O_7$: C, 67.0; H, 5.9. Found: C, 67.2; H, 5.8.

Dimethyl Ester of 2-Carboxy-7-methoxy-1,2,3,4-tetrahydrophenanthrene-1-β-propionic Acid (VIII).—The equivalent of one mole of hydrogen was absorbed in three hours when a solution of 0.89 g. of the aforementioned unsaturated trimethyl ester in 90 cc. of ethyl acetate was shaken with hydrogen in the presence of 0.135 g. of 30% palladium charcoal catalyst.[10] The liquid saturated trimethyl ester (VII) was hydrolyzed by heating it with a mixture of 10 cc. of 45% aqueous potassium hydroxide and 10 cc. of methanol for five hours and yielded 0.75 g. (93%) of **2,2-dicarboxy-7-methoxy-1,2,3,4-tetrahydrophenanthrene 1-β-propionic acid**, m. p. 193–195°. A sample crystallized from acetone–benzene in colorless needles.

Anal. Calcd. for $C_{20}H_{20}O_7$: C, 64.5; H, 5.41. Found: C, 64.9; H, 5.8.

The tricarboxylic acid (0.75 g.) was decarboxylated at 180–185° (twenty-five minutes), the product was dissolved in acetone, the solution was decolorized with Norite, benzene was added and the solution was concentrated in a current of air, yielding 0.63 g. (95%) of 2-carboxy-7-methoxy-1,2,3,4-tetrahydrophenanthrene-1-β-propionic acid (VIII); m. p. 150–155°. This acid was treated with diazomethane and the product was digested with ligroin and filtered; yield, 0.54 g.; m. p. 54–57°. The dimethyl ester crystallized from methanol in colorless rosets; m. p. 60–61°.

Anal. Calcd. for $C_{21}H_{24}O_5$: C, 70.8; H, 6.7. Found: C, 70.9; H, 6.6.

3′-Keto-7-hydroxy-1,2,3,4-tetrahydro-1,2-cyclopentenophenanthrene (VIa).—The aforementioned dimethyl ester (0.275 g.) was cyclized in benzene by a means of sodium methoxide in an atmosphere of nitrogen (eleven hours) and the mixture was worked up in the usual manner.[11] The product crystallized when scratched with ligroin containing a trace of methanol; yield, 0.21 g.; m. p. 130–136°. The **2′-carbomethoxy-3′-keto-7-methoxy-1,2,3,4-tetrahydrophenanthrene** was obtained as colorless rectangular prisms by recrystallization with little loss from acetone–methanol; m. p. 139–141°. With alcoholic ferric chloride it gave a deep purple color.

A mixture of the cyclic β-keto ester (0.137 g.), 1 cc. of water, 5 cc. of concentrated hydrochloric acid and 10 cc. of acetic acid was refluxed in a nitrogen atmosphere for fourteen hours; after removal of the solvents, the product was sublimed under reduced pressure; yield, 0.095 g. (89%); m. p. 242–246°. After purification through solution in aqueous sodium hydroxide and recrystallization from methanol, the compound (IX) formed long colorless plates; m. p. 245–247° (vac). Koebner and Robinson[6] probably had this compound but they reported no m. p. or analysis.

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 81.0; H, 6.4. Found: C, 80.7; H, 6.4.

The methyl ether was prepared by means of sodium hydroxide and methyl sulfate; the product was evaporatively distilled at 200° and 0.01 mm. and recrystallized from methanol from which it was obtained as colorless glistening plates; yield, 78%; m. p. 116–117°. Koebner and Robinson[3] report the same m. p. for their *x*-norequilenin methyl ether which was prepared by a different method.

1-Keto-1,2,3,4,11,12-hexahydrochrysene (IX).—To 1.6 g. of powdered potassium in 100 cc. of benzene was added 12.6 g. of β-1-naphthylethylmalonic ester. When the formation of the potassio derivative was complete, 9.6 g. of the acid chloride of ethyl hydrogen glutarate was added to the cooled mixture. The mixture was heated on a steam-bath for one hour and then worked up as described for the preparation of I. Since the product was found to decompose on distillation (195–200° at 0.03 mm.), it was used after some impurities had been removed by distillation at 100° and 0.01 mm. and then at 200° for a brief time; there remained 13.1 g. of a viscous liquid.

Cyclization of the triethyl ester of 5-keto-6,6-dicarboxy-8-α-naphthyloctanoic acid by means of 100% phosphoric acid was tried under various conditions; at temperature ranging from 42 to 120° and times up to forty hours. When four hours at 42° were allowed for reaction, β-1-naphthylethylmalonic acid was obtained in excellent yield when the mixture was hydrolyzed with methanolic potassium hydroxide and acidified. Cyclization by sulfuric acid likewise gave poor results.

The desired cyclic ketone was obtained most readily by the following procedure. A mixture of 2 g. of the ester and 10 g. of 100% orthophosphoric acid was heated at 100° for ten hours. After treatment with water, the mixture of esters which contained IIb was evaporatively distilled at 0.01 mm. and the distillate was refluxed in a nitrogen atmosphere for one and one-half hours with 10 cc. of acetic acid and 5 cc. of hydrochloric acid. The acids were removed by distillation, the residue was dissolved in ether, the ethereal solution was washed well with aqueous sodium hydroxide, the ether was evaporated, and the residue was evaporatively distilled at 200° and 0.01 mm.; yield, 0.09 g.; m. p. 159–160°. By recrystallization from acetone–methanol the compound (IX) was obtained in the form of prismatic needles which possessed a light cream color; m. p. 160.5–161.7°. Chuang, Huang and Ma[8] report their compound as a yellow substance with m. p. 160–161°.

Anal. Calcd. for $C_{18}H_{16}O$: C, 87.1; H, 6.5. Found: C, 87.5; H, 6.4.

A solution of 24 mg. of the cyclic ketone was added to the Grignard reagent prepared from 0.5 cc. of methyl iodide, the mixture was refluxed for two hours, 15 cc. of benzene was added and refluxing was continued for two hours. The methyl carbinol obtained on hydrolysis was heated with 3 mg. of palladium-charcoal[10] for twenty minutes at 210°; then the temperature was raised to 310° during the next twenty minutes. The material which had sublimed on the sides of the tube was washed down with a little benzene and the residue was heated for fifteen minutes at 310°. The product (13 mg.) melted at 249–250° alone and when mixed with authentic 1-methylchrysene[12]; mixed with chrysene (m. p. 248–249°) it melted at 242–245°.

7-Methoxy-2,2-dicarboxy-1,2,3,4-tetrahydrophenanthrylidene-1-γ-butyric Acid.—The triethyl ester of 5-keto-6,6-dicarboxy-8-(6′-methoxy-1′-naphthyl)-octanoic acid was prepared from the potassio derivative of 13.75 g. of β-6-methoxy-1-naphthylethylmalonic ester and 9.2 g. of the acid chloride of ethyl hydrogen glutarate by the method described. The product which was obtained after addition of water and cold dilute acid was kept at 200° and 0.04 mm. until low-boiling material was distilled from it and the residue (15–17 g.) was then employed in the next step.

For cyclization, a mixture of 2.5 g. of the viscous liquid and 10 g. of 100% orthophosphoric acid was warmed until a clear liquid was obtained and this was then allowed to stand at room temperature for fifteen hours. Water was then added and the product was extracted with ether, the solution was washed with dilute alkali, the solvent was removed, and the residue was evaporatively distilled at 200–220° and 0.02 mm. The slightly yellow distillate containing IIc was saponified by methanolic potassium hydroxide. The acid obtained on acidification of an aqueous solution of the salt was extracted with ether and the ethereal solution was washed with water; on slow evaporation of the ether, the acid crystallized. Colored oily impurities were removed by digestion of the product with benzene and then with a 10% solution of acetone in benzene; yield, 0.56–0.73 g.; m. p. 196°. It was difficult to recrystallize the compound without decomposing it partially. Best results were obtained by adding benzene to a solution of the acid in cold acetone, and evaporating part of the acetone. In this manner the unsaturated tricarboxylic acid was obtained as a white powder which melted in a sealed tube at 202–203° with vigorous evolution of gas, when the tube was put in the bath at 190°. The compound reduced potassium permanganate readily.

(12) Bachmann and Struve, *J. Org. Chem.*, **5**, 416 (1940).

Anal. Calcd. for $C_{21}H_{22}O_7$: C, 65.5; H, 5.3. Found: C, 66.1; H, 5.3.

The **trimethyl ester** prepared by means of diazomethane crystallized from methanol in colorless prisms; m. p. 114–115°.

Anal. Calcd. for $C_{24}H_{26}O_7$: C, 67.6; H, 6.1. Found: C, 67.6; H, 5.9.

Dimethyl Ester of 7-Methoxy-2-carboxy-1,2,3,4-tetrahydrophenanthrene-1-γ-butyric Acid.—A mixture of 1.54 g. of recrystallized unsaturated tricarboxylic acid, 0.22 g. of palladium-charcoal catalyst,[10] 40 cc. of absolute alcohol and 10 cc. of acetic acid was shaken with hydrogen at room temperature and atmospheric pressure; the unsaturated acid went into solution as hydrogenation took place. One mole equivalent of hydrogen was absorbed in three hours. The resulting **7-methoxy-2,2-dicarboxy-1,2,3,4-tetrahydrophenanthrene-1-γ-butyric acid** (1.51 g.; m. p. 205–206°) obtained by evaporation of the solvents at room temperature was saturated to potassium permanganate. A pure sample was obtained by making the trimethyl ester by means of diazomethane, evaporatively distilling the ester under reduced pressure and hydrolyzing the distillate; m. p. 216–217° with evolution of gas.

Anal. Calcd. for $C_{21}H_{22}O_7$: C, 65.3; H, 5.7. Found: C, 66.0; H, 5.8.

The tricarboxylic acid (0.42 g.) was converted to the dicarboxylic acid (0.37 g.) by keeping it at 220° for six minutes when no more carbon dioxide was evolved. The product was dissolved in methanol, the solution was decolorized with Norite and the solvent was evaporated; the cream colored solid melted at 191–193°. After recrystallization from acetone–benzene the **7-methoxy-2-carboxy-1,2,3,4-tetrahydrophenanthrene-1-γ-butyric acid** melted at 193–194°.

Anal. Calcd. for $C_{20}H_{22}O_5$: C, 70.2; H, 6.4. Found: C, 69.9; H, 6.4.

The **dimethyl ester,** prepared by means of diazomethane, was a waxy solid which was evaporatively distilled at 200° and 0.02 mm. After several recrystallizations from methanol a sample melted at 59–62°.

Anal. Calcd. for $C_{22}H_{26}O_5$: C, 71.3; H, 7.1. Found: C, 71.0; H, 6.8.

1-Keto-8-hydroxy-1,2,3,4,4a,11,12,12-octahydrochrysene (X).—A Dieckmann cyclization was carried out on 0.72 g. of the aforementioned dimethyl ester by means of sodium methoxide in benzene in a nitrogen atmosphere (three hours refluxing) and worked up in the manner described.[11] The product was recrystallized from acetone–methanol from which it was obtained as colorless crystals; yield, 0.5 g. melting at 167.5–168° and 0.08 g. of less pure product. The **2-carbomethoxy derivative of the cyclic ketone** gave a purplish green color with alcoholic ferric chloride.

Anal. Calcd. for $C_{21}H_{22}O_4$: C, 74.5; H, 6.6. Found: C, 74.9; H, 6.5.

A mixture of 0.19 g. of this compound, 9 cc. of concentrated hydrochloric acid, 1.5 cc. of water and 20 cc. of acetic acid was refluxed in a nitrogen atmosphere for four hours. One-half of the liquids was removed by distillation, an equal volume of water was added and the solid (0.13 g.) which precipitated was filtered; m. p. 258–269°. It was insoluble in cold *N* sodium hydroxide but most of it dissolved in 30 cc. of hot 2% potassium hydroxide. The solution was filtered from about 20 mg. of the methyl ether which escaped demethylation and poured into dilute hydrochloric acid, and the regenerated phenol was recrystallized from acetone; yield, 80 mg.; m. p. 268–270° under nitrogen. By a second recrystallization from acetone–methanol, the **cyclic ketone (X)** was obtained in fine colorless needles; m. p. 273–275° to a reddish-brown liquid in a nitrogen atmsophere.

When moistened with concentrated sulfuric acid, the compound gave a burnt-orange color, then dissolved to give a yellow solution, which fluoresced slightly green when warmed.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.2; H, 6.8. Found: C, 81.2; H, 6.9.

The **methyl ether** which was obtained above was purified by evaporative distillation at 180–200° and 0.01 mm., and crystallization from methanol; yield, 11 mg.; m. p. 139–140°. It was prepared also by methylation of the phenolic compound in alkaline solution. From acetone–methanol it crystallized in fine colorless rods; m. p. 140.5–141.5° in nitrogen.

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.4; H, 7.2. Found: C, 81.4; H, 7.1.

The **benzoate** was prepared by adding 8 drops of benzoyl chloride to a solution of 15 mg. of X in 1.5 cc. of dry benzene and 0.5 cc. of pyridine. After ten hours, an additional 10 drops of benzoyl chloride were added and the mixture was warmed for five minutes. The mixture was worked up in the usual manner and the product was evaporatively distilled at 200° (0.01 mm.) and crystallized from acetone; yield, 12 mg.; m. p. 204–208° with previous softening.

Anal. Calcd. for $C_{25}H_{22}O_3$: C, 81.1; H, 6.0. Found: C, 81.0; H, 6.0.

Summary

The method developed for the preparation of key intermediates in the synthesis of estrone-a has now been extended to the preparation of several analogs of equilenin, including *x*-norequilenin. In addition two compounds containing a six-membered D ring have been prepared, one of which is a structural isomer of equilenin.

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