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

The Synthesis of Compounds Related to the Sex Hormones

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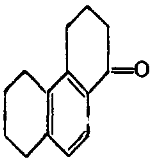
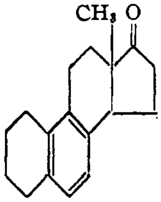
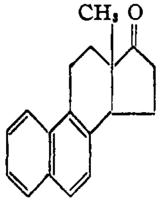
From 1-keto-*sym*-octahydrophenanthrene (I), the *cis* and *trans* forms of 1,2,3,4-tetrahydro-17-equilenone[2] (II), an isomer of desoxyestrone, were prepared by the method employed for the synthesis of equilenin[3] and related compounds. Since the configurations of the two forms of II (m. p. 72–73° and 114–115°) are not known, they are designated by the prefixes α and β. The structures of the two forms were established by dehydrogenation. When heated with sulfur the α-form of II gave the α-form of 17-equilenone[2] (III) and the β-form yielded the β-form of 17-equilenone. These reactions relate the configurations of the compounds in the two series. The new compounds should prove useful in studies of the sex hormones and compounds derivable from neoergosterol. Marker and Rohrmann[3a] prepared one of the optically active forms (m. p. 107–109°) of II from equilenin.


I



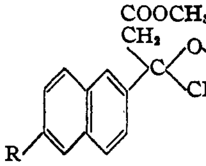
II



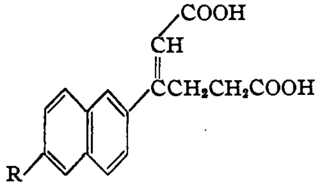
III

A number of 3-arylcyclopentenones and 3-arylcyclopentanones were synthesized from the β-3-aroylpropionic acids. In the synthesis of VIc, the methyl ester of β-6-methoxy-2-naphthoylpropionic acid was treated with zinc and methyl bromoacetate to yield the lactone (IVb) of the Reformatsky ester. When the lactone was hydrolyzed by methanolic sodium hydroxide and a solution of the resulting sodium salt was acidified, the unsaturated dicarboxylic acid (Vb) was formed. The double bond is probably in the position indicated, for the acid is reduced readily by means of sodium amalgam and water. By cyclization of the dimethyl ester of this acid by means of sodium methoxide, followed by treatment of the product with a boiling mixture of acetic acid and hydrochloric acid, a mixture of 3-(6′-hydroxy-2′-naphthyl)-cyclopenten-2-one-1 (VIc) and its methyl ether (VIb) was obtained. 3-(6′-Hydroxy-2′-naphthyl)-cyclopentanone-1 was obtained by catalytic reduction of VIc and also by cyclization of the ester of the saturated dicarboxylic acid, obtained by reduction of Vb by means of sodium amalgam and water. Banerjee[4] prepared 3-(*p*-hydroxyphenyl)-cyclohexanone by a similar procedure.

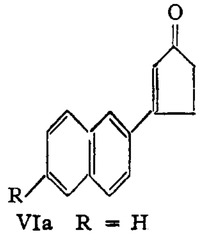
By a similar series of reactions 3-(2′-naphthyl)-cyclopenten-2-one-1 (VIa), 3-(2′-naphthyl)-cyclopentanone, 3-(5′,6′,7′,8′-tetrahydro-2′-naphthyl)-cyclopenten-2-one-1 (VII) and the corresponding cyclopentanone were prepared. By catalytic dehydrogenation, the tetralylcyclopentenone (VII) was converted to the naphthylcyclopentenone (VIa). VIa and the corresponding cyclopentanone had been prepared previously by Weidlich and Daniels by another method.[5] The 2-methyl derivatives, of VIa,[5] of VIc[6] and of the corresponding cyclopentanones have been prepared by other methods.



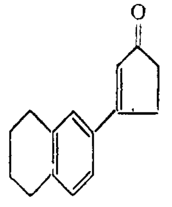
IVa R = H
IVb R = OCH$_3$



Va R = H
Vb R = OCH$_3$



VIa R = H
VIb R = OCH$_3$
VIc R = OH



VII

The ring structures of these compounds were confirmed completely by Wolf–Kishner reduction of VIa to 1-β-naphthylcyclopentene and of VIb to 1-(6′-methoxy-2′-naphthyl)-cyclopentene. Both of these reference compounds have been prepared previously by another method.[7]

Experimental

1-Keto-1,2,3,4,5,6,7,8-octahydrophenanthrene (I).—α-Naphthylamine (20 g.) was reduced by sodium and fusel oil by the procedure described for the β-isomer.[8] After all

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[1] From the Ph. D. Dissertation of R. D. Morin.

[2] For the nomenclature of these compounds see Bachmann and Wilds, THIS JOURNAL, **62**, 2084 (1940).

[3] Bachmann, Cole and Wilds, *ibid.*, **62**, 824 (1940).

[3a] Marker and Rohrmann, *ibid.*, **61**, 3314 (1939).

[4] Banerjee, *Science and Culture*, **5**, 566 (1940).

[5] Weidlich and Daniels, *Ber.*, **72**, 1590 (1939).

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

[7] Bachmann and Kloetzel, THIS JOURNAL, **60**, 2204 (1938).

[8] Waser and Möllering, "Organic Syntheses," Coll. Vol. I, 1941, 2nd ed., p. 499.

the sodium had reacted, the hot mixture was poured into water and after separation of the layers, the organic layer was acidified with hydrochloric acid. Six such runs were combined and concentrated by distillation until the *ar*-tetrahydro-α-naphthylamine hydrochloride began to crystallize from the hot solution. The cooled solution was filtered and the crystalline hydrochloride was washed several times with ether to remove colored impurities; the product obtained was sufficiently pure for the next step; yield, 131 g. (84%).

Diazotization and conversion to 1-iodo-5,6,7,8-tetrahydronaphthalene was carried out according to the directions for 1-iodo-6-methoxynaphthalene.[9] From 110 g. of *ar*-tetrahydro-α-naphthylamine, 102 g. (66%) of 1-iodo-5,6,7,8-tetrahydronaphthalene, b. p. 153–158° (20 mm.), was obtained.

The Grignard reagent of the iodotetralin was prepared and allowed to react with ethylene oxide according to the procedure described for *m*-iodoanisole.[10] From 51.6 g. of the 1-iodotetralin, 20 g. (57%) of β-(5,6,7,8)-tetrahydro-1-naphthylethyl alcohol was obtained as a viscous yellow oil; b. p. 125–135° (0.4 mm.).

Conversion of the alcohol to β-5,6,7,8-tetrahydro-1-naphthylethyl bromide by means of phosphorus tribromide was carried out in the same manner as described for a similar case.[3] From 35.2 g. of alcohol, 30 g. (62%) of the bromide was obtained; b. p. 113–118° (0.05 mm.).

To the cooled mixture of sodio-malonic ester obtained from 10 g. of sodium powder, 30 cc. of absolute alcohol, 25 cc. of dry benzene and 100 g. of malonic ester was added 71.7 g. of the tetrahydronaphthylethyl bromide. The reaction was carried out and worked up as described for a similar case.[3] The substituted malonic acid was decarboxylated at 180° to γ-5,6,7,8-tetrahydro-1-naphthylbutyric acid. After recrystallization from ligroin, the acid melted at 94–95°; yield, 42 g. (65%). The acid was identical with the product prepared in 45% yield from 1-chloroacetyltetralin by the procedure of Schroeter.[11] In one step of his process, the precipitation of a mixture of the substituted malonic acid and its potassium salt was avoided by adding the aqueous solution of the dipotassium salt to concentrated hydrochloric acid.

The butyric acid was cyclized to 1-keto-1,2,3,4,5,6,7,8-octahydrophenanthrene by the action of stannic chloride on the acid chloride according to the procedure described by Wilds[10] for γ-1-naphthylbutyric acid. From 21.8 g. of the acid 17.6 g. (88%) of ketone was obtained; m. p. 80.5–82°. Schroeter obtained an 80% yield of the ketone (m. p. 81–82°) by simply heating the acid chloride.

Methyl 1-Keto-1,2,3,4,5,6,7,8-octahydrophenanthrene-2-glyoxalate.—The condensation of 20 g. of the cyclic ketone with methyl oxalate was carried out in the manner described for a similar compound.[3] Recrystallization of the glyoxalate from methanol gave 25.5 g. (89%) of bright yellow prisms; m. p. 101–102°. A sample after two more recrystallizations melted at 103–104°. It gave a dark purple-brown color with alcoholic ferric chloride.

Anal.[12] Calcd. for $C_{17}H_{18}O_4$: C, 71.3; H, 6.3. Found: C, 71.4; H, 6.3.

1-Keto-2-carbomethoxy-1,2,3,4,5,6,7,8-octahydrophenanthrene.—Following the procedure described,[3] 10 g. of the glyoxalate and 5 g. of powdered soft glass were heated at 180° for exactly one-half hour. The product was separated from the glass with hot benzene and the benzene solution was washed with 2% aqueous sodium hydroxide to remove any unreacted glyoxalate. The product after recrystallization from methanol was suitable for the next step; yield, 7.95 g. (88%); m. p. 81–84°. A sample after three more recrystallizations formed stout colorless prisms which melted at 83–85°. It gave an immediate dark blue-green color with alcoholic ferric chloride.

Anal.[12] Calcd. for $C_{16}H_{18}O_3$: C, 74.4; H, 7.0. Found: C, 74.3; H, 7.1.

1-Keto-2-methyl-2-carbomethoxy-1,2,3,4,5,6,7,8-octahydrophenanthrene.—A solution of 10.32 g. (0.04 mole) of the aforementioned keto ester in 50 cc. of dry benzene was added to a solution of sodium methoxide prepared from 4.6 g. of sodium and 90 cc. of absolute methanol. After being warmed for one-half hour and then cooled, the mixture was treated with 14 cc. of methyl iodide and kept at room temperature until nearly all of the sodio derivative had disappeared. An additional 14 cc. of methyl iodide was added and within thirty minutes all of the solid had reacted. The product was isolated according to the procedure described[3] and recrystallized from methanol; yield, 9.42 g. (86%) of nearly colorless material sufficiently pure for the next step; m. p. 72–75°. A sample after two more recrystallizations formed colorless prisms which melted at 77–78°. It gave no color with alcoholic ferric chloride.

Anal.[12] Calcd. for $C_{17}H_{20}O_3$: C, 74.9; H, 7.4. Found: C, 74.3; H, 7.3.

A mixture of 262 mg. of the compound, 3 cc. of 45% aqueous potassium hydroxide and 10 cc. of methanol was refluxed on a steam-bath for two hours. The oil that formed solidified when the contents of the flask were cooled and diluted with water. The **1-keto-2-methyl-1,2,3,4,5,6,7,8-octahydrophenanthrene** crystallized from methanol in colorless prismatic rods; m. p. 87–88°; yield, 171 mg. (80%).

Anal.[12] Calcd. for $C_{15}H_{17}O$: C, 84.0; H, 8.5. Found: C, 83.6; H, 8.6.

Dimethyl Ester of 2-Methyl-2-carboxy-1-hydroxy-1,2,3,-4,5,6,7,8-octahydrophenanthrene-1-acetic Acid.—The Reformatsky reaction between the methyl keto ester (5.44 g.), zinc and methyl bromoacetate was carried out as described for a similar compound,[3] except that extremely vigorous stirring was employed. The product crystallized from methanol in stout colorless prisms; yield, 5.3–5.6 g. (76–81%); m. p. 100–101°. A sample after two more recrystallizations melted at 102–103°.

Anal.[12] Calcd. for $C_{20}H_{26}O_5$: C, 69.3; H, 7.6. Found: C, 69.5; H, 7.7.

When a mixture of 346 mg. of the Reformatsky ester, 3 cc. of 45% aqueous potassium hydroxide and 10 cc. of methanol was refluxed on a steam-bath for two hours, 150 mg. (after recrystallization from methanol) of 1-keto-2-methyl-1,2,3,4,5,6,7,8-octahydrophenanthrene; m. p. 87–88°, was obtained.

Conversion of the Reformatsky Ester to the Unsaturated Acids.—The hydroxy ester (1.52 g.) was converted to the chloride by means of thionyl chloride and pyridine and the product was treated with aqueous alcoholic potassium hydroxide in the manner described.[3] The **2-methyl-2-carboxy-1,2,3,4,5,6,7,8-octahydrophenanthrylidene-1-acetic acid** which precipitated on acidification of the aqueous solution of the potassium salt weighed 1.21 g. (92%); m. p. 137–140°. It crystallized from acetone–ligroin in colorless prisms; m. p. 140–141° with evolution of gas.

Anal. Calcd. for $C_{18}H_{20}O_4$: C, 72.0; H, 6.7. Found: C, 71.8; H, 6.7.

Preparation of α- and β-2-Methyl-2-carboxyl-1,2,3,4,5,-6,7,8-octahydrophenanthrene-1-acetic Acid.—Usually the Reformatsky ester (6.92 g.) was converted directly to the α- and β-reduced acids without isolation of the unsaturated acid. The aqueous solution of the potassium salts of the unsaturated acids was shaken vigorously for one-half hour with 150 g. of 2% sodium amalgam. The dried mixture of reduced acids (5.5–5.7 g.) was dissolved in a hot mixture of 20 cc. of acetic acid and 30 cc. of xylene. Without filtering, the solution was allowed to cool; 2.4–2.6 g. (40–43%) of the α acid crystallized; m. p. 208–211°. A sample crystallized from acetic acid in short stout colorless prisms; m. p. 218–219°.

By evaporation of the filtrate and recrystallization of the residue from benzene, 2.8–3.0 g. (46–50%) of the β acid

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(9) Cohen, Cook, Hewett and Girard, *J. Chem. Soc.*, 653 (1934).

(10) Bachmann and Thomas, THIS JOURNAL, **64**, 95 (1942); see also Wilds, *ibid.*, **64**, 1424 (1942).

(11) Schroeter, *Ber.*, **57**, 2029 (1924).

(12) Microanalysis by T. S. Ma.

was obtained; m. p. 160–161°. A sample of the β acid crystallized from ethyl acetate–ligroin in small colorless prisms; m. p. 162–163°.

Anal. Calcd. for $C_{18}H_{22}O_4$: C, 71.5; H, 7.3. Found: (α-form) C, 71.4; H, 7.4; (β-form) C, 71.6; H, 7.4.

Dimethyl Ester of 2-Methyl-2-carboxy-1,2,3,4,5,6,7,8-octahydrophenanthrene-1-acetic Acid.—The α-form of this compound, prepared in 97% yield from the α-acid by means of diazomethane, crystallized from methanol in stout colorless prisms; m. p. 70–71.5°. A sample after one more recrystallization melted at 70.5–71°.

The β-form, prepared from 6.04 g. of the β-acid and diazomethane, crystallized from methanol in colorless prisms; yield, 6.07 g. (92%); m. p. 79–81°. After two more recrystallizations a sample melted at 81.5–82.5°.

Anal.[12] Calcd. for $C_{20}H_{26}O_4$: C, 72.7; H, 7.9. Found: (α-form) C, 73.0; H, 7.6; (β-form) C, 73.3; H, 7.8.

2-Methyl-2-carbomethoxy-1,2,3,4,5,6,7,8-octahydrophenanthrene-1-acetic Acid.—A mixture of 4.62 g. of the dimethyl ester, 100 cc. of methanol and 14.3 cc. of *N* sodium hydroxide was refluxed for two hours, the methanol was removed and the residue dissolved in about 25 cc. of warm water. About 3 cc. of ethyl acetate was added and the mixture was acidified. The acid ester, which gradually crystallized as the ethyl acetate evaporated, was sufficiently pure for the next step.

In this manner 4.21 g. (95%) of the α-form melting at 120–122° was obtained. A sample after two recrystallizations from acetone–ligroin formed colorless prisms; m. p. 121–122°.

The β-form was obtained in 98% yield; m. p. 136–139°. From ethyl acetate it crystallized in small colorless prisms melting at 141–142°.

Anal. Calcd. for $C_{19}H_{24}O_4$: C, 72.2; H, 7.6; neut. equiv., 316. Found: (α-form) C, 72.3; H, 7.7; neut. equiv., 317. (β-form) C, 72.0; H, 7.6; neut. equiv., 318.

Arndt–Eistert Reaction on the Acid Esters.—This was carried out on 1.58 g. of the acid esters as described for a similar compound.[3] The solution of the product obtained by the action of silver oxide on the diazoketone in methanol was filtered and evaporated, and the residue was evaporatively distilled at 180° (0.05 mm.).

The **dimethyl ester of α-2-methyl-2-carboxy-1,2,3,4,5,6,7,8-octahydrophenanthrene-1-β-propionic acid** crystallized from methanol in small colorless prisms; yield, 1.29 g. (75%); m. p. 63.5–64.5°.

Anal.[12] Calcd. for $C_{21}H_{28}O_4$: C, 73.2; H, 8.2. Found: (α-form) C, 73.0; H, 8.0.

The β-isomer, a pale yellow liquid, was used directly in the next step; yield, 1.59 g.

1,2,3,4-Tetrahydro-16-carbomethoxy-17-equilenone.—Cyclization of 1.38 g. of the aforementioned esters by sodium methoxide in benzene (ten hours of refluxing) was accomplished by the procedure described.[3]

The α-form crystallized from methanol in fine colorless needles; yield, 1.12 g. (90%); m. p. 124–124.5°. After two more recrystallizations a sample melted at 124–125°. The compound gave a dark green color with alcoholic ferric chloride.

By recrystallization from methanol the β-form was obtained as colorless prisms; yield, 1.08 g. (85%); m. p. 118–121°. After three recrystallizations a sample melted at 121–122°. The compound gave an immediate greenish-brown color with alcoholic ferric chloride.

Anal.[12] Calcd. for $C_{20}H_{24}O_3$: C, 76.9; H, 7.8. Found: (α-form) C, 76.8; H, 7.7; (β-form) C, 76.9; H, 8.1.

1,2,3,4-Tetrahydro-17-equilenone (II).—A mixture of 0.9 g. of the 16-carbomethoxy derivative, 45 cc. of acetic acid, 22 cc. of concentrated hydrochloric acid and 4 cc. of water was refluxed for two hours in an atmosphere of nitrogen. The residue remaining after removal of the solvents under reduced pressure was dissolved in benzene and washed with 2% aqueous sodium hydroxide. The benzene solution was concentrated and the residue was dissolved in hot methanol from which the product crystallized.

The α-form crystallized in stout colorless prisms; yield, 0.65 g. (88%); m. p. 72–73°. After evaporative distillation at 100° (0.05 mm.) and two recrystallizations from methanol it melted at the same temperature.

The β-form crystallized in small colorless prisms; yield, 0.60 g. (79%); m. p. 113–114°. After evaporative distillation at 110° (0.05 mm.) and two recrystallizations from methanol, it melted at 114–115° (vac.).

Anal.[12] Calcd. for $C_{18}H_{22}O$: C, 85.0; H, 8.6. Found: (α-form) C, 84.7; H, 8.3; (β-form) C, 84.4; H, 8.4.

The **semicarbazones** were prepared with semicarbazide hydrochloride in a mixture of absolute alcohol and pyridine. The α-form crystallized from alcohol in colorless prisms; m. p. 243–244°. The β-form was obtained in colorless prisms; m. p. 274–275° (vac.).

Anal. Calcd. for $C_{19}H_{25}ON_3$: N, 13.5. Found: (α-form) N, 13.3; (β-form) N, 13.4.

Dehydrogenation of 1,2,3,4-Tetrahydro-17-equilenone.—A mixture of 50 mg. of II and 15 mg. of sulfur was heated at 210° for two hours. The product was purified by sublimation at 100° (0.05 mm.) and recrystallization from methanol. The α-form gave 20 mg. of α-17-equilenone (41%) melting at 97–98.5°; when mixed with α-17-equilenone (III) (m. p. 100–101°)[2] it melted at 98–99°. The β-form gave 24 mg. (49%) of β-17-equilenone melting at 186–187.5° (vac.); when mixed with β-17-equilenone (m. p. 188.5–189.5°) it melted at 187–188.5° (vac.).

Lactone of the Monomethyl Ester of β-Hydroxy-β-(6-methoxy-2-naphthoyl)-adipic Acid (IVb).—β-Naphthyl methyl ether (158 g.) and 110 g. of succinic anhydride were brought into reaction according to the procedure of Short, Stromberg and Wiles.[13] Fractional crystallization of the mixture of isomeric acids from acetone gave 49 g. of β-(6-methoxy-2-naphthoyl)-propionic acid (m. p. 147–148°). Esterification of this acid by alcoholic hydrogen chloride yielded 52.5 g. of the ethyl ester (m. p. 107.5–108°). By esterification of the mixture of acids in the acetone mother liquor an additional 40 g. of the ethyl ester was obtained.

The Reformatsky reaction on the above keto ester (8.05 g.) was carried out in the manner previously described[3] except that vigorous stirring was employed; in working up the reaction mixture washing with ammonium hydroxide was omitted in order to avoid hydrolysis of the product. The lactone ester crystallized from methanol in yellowish prisms; yield, 8.02 g. (84%); m. p. 115–119°. This was sufficiently pure for the next step. A sample after evaporative distillation at 115° (0.05 mm.) crystallized from methanol in fine colorless prisms; m. p. 121–122°.

Anal.[12] Calcd. for $C_{18}H_{18}O_5$: C, 68.8; H, 5.8. Found: C, 69.2; H, 5.7.

3-(6′-Methoxy-2′-naphthyl)-2-hexendioic Acid (Vb).—A mixture of 12.4 g. of the above crude lactone ester, 300 cc. of methanol and 80 cc. of *N* sodium hydroxide was refluxed for three hours on a steam-bath. The methanol was removed in a current of air, some water was added to the residue, and this solution was filtered and acidified. The unsaturated acid which precipitated was filtered and dried; yield, 11.27 g. (98%); m. p. 194–195°. A sample crystallized from acetone–ligroin in small colorless prisms which melted at the same temperature.

Anal. Calcd. for $C_{17}H_{16}O_5$: C, 68.0; H, 5.3. Found: C, 68.2; H, 5.4.

3-(6′-Hydroxy-2′-naphthyl)-cyclopenten-2-one-1 (VIc).—Ethereal diazomethane was added to 4.2 g. of the above unsaturated acid to form the dimethyl ester. The product was an oil which was purified by evaporative distillation at 190° (0.05 mm.). Cyclization of 3.28 g. of the ester was accomplished by the procedure described[3] (twelve hours of refluxing). The cyclic keto ester crystallized from methanol as a light tan powder; yield, 2.36 g. (80%); m. p. 123–125°. A sample of the **3-(6′-methoxy-2′-naphthyl)-5-carbomethoxycyclopenten-2-one-1** after three more recrystallizations from methanol formed small colorless prisms; m. p. 125–126°.

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(13) Short, Stromberg and Wiles, *J. Chem. Soc.*, 320 (1936).

Anal. Calcd. for $C_{18}H_{16}O_4$: C, 73.0; H, 5.4. Found: C, 73.1; H, 5.5.

Two grams of the crude material was refluxed for ten hours with a mixture of 75 cc. of acetic acid, 37 cc. of concentrated hydrochloric acid and 7 cc. of water in an atmosphere of nitrogen. The cooled solution was poured into one liter of water. The crystalline product was filtered off, dissolved in 100 cc. of hot 2.5% aqueous potassium hydroxide and the solution was filtered from a small amount of the methyl ether. The **3-(6′-hydroxy-2′-naphthyl)-cyclopenten-2-one-1** (**VIc**) obtained by acidification of the alkaline solution was purified by sublimation at 200° (0.05 mm.) and subsequent recrystallization from methanol; yield, 0.22 g. of small stout prisms; m. p. 252–253° (vac.) to red liquid. The m. p. was unchanged after two more recrystallizations.

Anal.[12] Calcd. for $C_{15}H_{12}O_2$: C, 80.3; H, 5.4. Found: C, 79.8; H, 5.4.

The **semicarbazone** melted at 260–262° (vac.).

Anal. Calcd. for $C_{16}H_{15}O_2N_3$: N, 14.9. Found: N, 15.1.

The **methyl ether** (**VIb**) after evaporative distillation at 190° (0.05 mm.) crystallized from methanol in fine needles; m. p. 169–170°.

Anal. Calcd. for $C_{16}H_{14}O_2$: C, 80.7; H, 5.9. Found: C, 80.4; H, 6.0.

The **semicarbazone of the methyl ether** melted at 250–251° (vac.).

Anal. Calcd. for $C_{17}H_{17}O_2N_3$: N, 14.2. Found: N, 14.0.

A mixture of 118 mg. of the semicarbazone and a solution of sodium methoxide prepared from 0.3 g. of sodium and 6 cc. of absolute alcohol was heated in a sealed tube at 180° for twenty hours. From the reaction mixture 34 mg. (37%) of 1-(6′-methoxy-2-naphthyl)-cyclopentene was obtained; m. p. 141–142°, alone and when mixed with an authentic specimen.[7]

3-(6′-Hydroxy-2′-naphthyl)-cyclopentanone.—A solution of 3.0 g. of the substituted hexendioic acid (Vb) in 1.75 cc. of 45% aqueous potassium hydroxide and 20 cc. of water was shaken with 75 g. of 2% sodium amalgam for one-half hour. The **β-(6-methoxy-2-naphthyl)-adipic acid** obtained by acidification of the filtered solution crystallized from acetone–ligroin in colorless prisms; yield, 3.01 g. (99%); m. p. 164–165°.

Anal. Calcd. for $C_{17}H_{18}O_5$: C, 67.5; H, 6.0. Found: C, 67.8; H, 6.1.

The liquid dimethyl ester of the acid, prepared by means of diazomethane, was evaporatively distilled at 180–190° (0.05 mm.). Cyclization of 1.98 g. of the ester and hydrolysis, decarboxylation and demethylation were accomplished as previously described for similar cases.[3] A solution of the phenolic product in 125 cc. of hot 2.5% potassium hydroxide was filtered and acidified. The **3-(6′-hydroxy-2′-naphthyl)-cyclopentanone** after evaporative distillation at 200° (0.05 mm.) crystallized from methanol in small colorless prisms; yield, 1.14 g. (83%); m. p. 176–176.5°. The m. p. remained unchanged after two more recrystallizations.

The same compound was obtained by shaking a solution of 100 mg. of VIc in 10 cc. of acetic acid with 25 mg. of palladium–charcoal catalyst[14] and hydrogen for four hours. The filtered solution was evaporated and the residue was crystallized from methanol; yield, 70 mg. (70%); m. p. 176–176.5°.

Anal.[12] Calcd. for $C_{15}H_{14}O_2$: C, 77.9; H, 6.2. Found: C, 77.5; H, 6.3.

The **semicarbazone** crystallized in cream-colored prisms; m. p. 212–213°.

Anal. Calcd. for $C_{16}H_{17}O_2N_3$: N, 14.8. Found: N, 15.1.

3-(2′-Naphthyl)-cyclopenten-2-one-1.—The Reformatsky reaction was carried out on 7.5 g. of methyl-β-2-naphthoylpropionate (m. p. 74–75°), which was prepared from the acid in quantitative yield by means of diazomethane. The **lactone of the monomethyl ester of β-hydroxy-β-(2-naphthyl)-adipic acid** (**IVa**) (5.7 g.; m. p. 106–108°) was sufficiently pure for the next step. A sample after evaporative distillation at 170° (0.05 mm.). followed by two recrystallizations from methanol formed fine colorless needles; m. p. 111–112°.

Anal.[12] Calcd. for $C_{17}H_{16}O_4$: C, 71.8; H, 5.7. Found: C, 72.0; H, 5.5.

A mixture of 8.9 g. of the crude lactone ester, 150 cc. of methanol and 63 cc. of *N* sodium hydroxide was refluxed for three hours. The **3-(2′-naphthyl)-2-hexendioic acid** (**Va**) was isolated as described for the methoxy compound; yield, 8.06 g. (96%); m. p. 179–180°. The crude product was pure enough for the next step. After two recrystallizations from acetone–ligroin a sample was obtained as colorless prisms with the same m. p.

Anal. Calcd. for $C_{16}H_{14}O_4$: C, 71.0; H, 5.2. Found: C, 71.3; H, 5.2.

The liquid dimethyl ester of the unsaturated dicarboxylic acid, prepared by means of diazomethane, was evaporatively distilled at 170–180° (0.05 mm.). Cyclization of 1.64 g. of the ester and hydrolysis and decarboxylation of the product was carried out as described.[8] The **3-(2′-naphthyl)-cyclopenten-2-one-1** (**VIa**) was evaporatively distilled at 160–170° (0.05 mm.) and then recrystallized twice from methanol; yield, 0.93 g. (81%) of small colorless prisms; m. p. 126–127° (reported,[5] 126–127°).

Anal.[12] Calcd. for $C_{15}H_{12}O$: C, 86.6; H, 5.8. Found: C, 87.2; H, 5.9.

The **semicarbazone** melted at 240–241° (reported, 244°[5]).

Anal. Calcd. for $C_{16}H_{15}ON_3$: N, 15.8. Found: N, 16.0.

The Wolff–Kishner reduction of 115 mg. of the above semicarbazone was carried out exactly as described for the methoxy compound and yielded 40 mg. (49%) of 1-(2′-naphthyl)-cyclopentene; m. p. 84.5–86° (reported,[7] 85–86°).

3-(2′-Naphthyl)-cyclopentanone.—Reduction of 3.24 g. of the naphthylhexendioic acid by 2% sodium amalgam was carried out as described for the methoxy derivative; yield, 3.14 g. (96%) of **β-(2-naphthyl)-adipic acid** sufficiently pure for the next step; m. p. 151–153°. After two recrystallizations from acetone–ligroin a sample formed colorless prisms; m. p. 153–154°.

Anal. Calcd. for $C_{16}H_{16}O_4$: C, 70.6; H, 5.9. Found: C, 70.7; H, 5.9.

The liquid dimethyl ester of the acid prepared by means of diazomethane was evaporatively distilled at 180° (0.05 mm.). Cyclization of 2.4 g. of the diester and hydrolysis and decarboxylation of the cyclic keto ester were carried out as described. The **3-(2′-naphthyl)-cyclopentanone** after evaporative distillation at 150° (0.05 mm.) followed by two recrystallizations from methanol formed small colorless prisms; yield, 1.47 g. (87%); m. p. 65–66° (reported,[5] 61°).

The same compound was obtained in 75% yield by catalytic hydrogenation of 200 mg. of VIa in acetic acid in the presence of 50 mg. of palladium-charcoal catalyst.

Anal.[12] Calcd. for $C_{15}H_{14}O$: C, 85.7; H, 6.7. Found: C, 85.7; H, 6.7.

The **semicarbazone** crystallized in colorless prisms; m. p. 199–199.5° (reported,[5] 196–197°).

Anal. Calcd. for $C_{16}H_{17}ON_3$: N, 15.7. Found: N, 15.5.

3-(5′,6′,7′,8′-Tetrahydro-2′-naphthyl)-cyclopenten-2-one-1 (**VII**).—A malonic ester synthesis was carried out on 104.5 g. of 2-chloroacetyl-5,6,7,8-tetrahydronaphthalene as described[11] except that benzene was used as the solvent and one hour of refluxing was employed. By adding the aqueous solution of the potassium salt of the substituted malonic acid to concentrated hydrochloric acid, the free

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[14] Zelinsky and Turowa-Pollak, *Ber.*, **58**, 1295 (1925).

acid was obtained. After decarboxylation of the substituted malonic acid at 150–170°, the β-(5,6,7,8-tetrahydro-2-naphthoyl)-propionic acid was recrystallized from benzene using Norite; yield, 94.5 g. (85%); m. p. 120.5–121.5° (reported,[11] 121–122°). The methyl ester, prepared from 23 g. of the acid by means of diazomethane, solidified after distillation (b. p. 168–173° at 0.1 mm.) to a colorless solid; yield, 22 g.; m. p. 31–32° (reported,[15] 31°).

A Reformatsky reaction was carried out on 7.38 g. of the methyl ester as described. The product was an oil which was purified by evaporative distillation at 180° (0.05 mm.) and heated with 50 cc. of *N* sodium hydroxide in 50 cc. of methanol for three hours. The **3-(5′,6′,7′,8′-tetrahydro-2′-naphthyl)-2-hexendioic acid** (4.9 g., m. p. 183–185°) was sufficiently pure for the next step. A sample twice recrystallized from acetone–ligroin formed colorless prisms which melted at 185–186°.

Anal. Calcd. for $C_{16}H_{18}O_4$: C, 70.1; H, 6.6. Found: C, 70.0; H, 6.7.

The liquid dimethyl ester, prepared by means of diazomethane was evaporatively distilled at 180° (0.05 mm.); and 2.8 g. of it was cyclized as described. The cyclic keto ester was hydrolyzed and decarboxylated by heating with hydrochloric and acetic acids,[8] and the **3-(5′,6′,7′,8′-tetrahydro-2′-naphthyl)-cyclopenten-2-one-1** (VII) was evaporatively distilled at 150° (0.05 mm.) and recrystallized twice from methanol from which it crystallized in small colorless prisms; yield, 1.64 g. (77%); m. p. 82–82.5°.

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.8; H, 7.6. Found: C, 84.6; H, 7.5.

The **semicarbazone** melted at 235–236°.

Anal. Calcd. for $C_{16}H_{19}ON_3$: N, 15.6. Found: N, 15.8.

A mixture of 50 mg. of VII and 10 mg. of palladium-charcoal catalyst was heated for fifteen minutes at 320° in an atmosphere of nitrogen. The 3-(2′-naphthyl)-cyclopenten-2-one-1 was evaporatively distilled at 150° (0.05 mm.); yield, 30 mg. (61%); m. p. 125–126°, alone and when mixed with a sample of VIa.

3-(5′,6′,7′,8′-Tetrahydro-2′-naphthyl)-cyclopentanone.—Reduction of 2.0 g. of the tetralylhexendioic acid by 2% sodium amalgam gave 2.0 g. (98%) of **β-(5,6,7,8-tetrahydro-2-naphthyl)-adipic acid** sufficiently pure for the next step; m. p. 159–160°. After two recrystallizations from acetone–ligroin a sample formed small colorless prisms which melted at 159.5–160°.

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.5; H, 7.2. Found: C, 69.8; H, 7.2.

The liquid dimethyl ester, prepared by means of diazomethane, was evaporatively distilled at 160° (0.05 mm.), 1.06 g. of it was cyclized (eight hours of refluxing), and the cyclic keto ester was hydrolyzed and decarboxylated as described.[8] The ketone was evaporatively distilled at 170° (0.05 mm.) and recrystallized twice from methanol; yield, 0.63 g. (83%) of colorless prisms; m. p. 73–74°. The same compound was formed in 74% yield when VII was hydrogenated in acetic acid in the presence of palladium–charcoal.

Anal. Calcd. for $C_{15}H_{18}O$: C, 84.1; H, 8.4. Found: C, 83.6; H, 8.5.

The **semicarbazone** crystallized in colorless prisms; m. p. 207–208°.

Anal. Calcd. for $C_{16}H_{21}ON_3$: N, 15.5. Found: N, 15.3.

Summary

The *cis* and *trans* forms of 1,2,3,4-tetrahydro-17-equilenone, an isomer of desoxyestrone, have been synthesized from 1-keto-*sym*-octahydrophenanthrene. The compounds were dehydrogenated by sulfur to the *cis* and *trans* forms of 17-equilenone (desoxyequilenin).

Three 3-arylcyclopentenones and the corresponding 3-arylcyclopentanones were prepared in which the aryl groups were 2′-naphthyl-, 2′-tetralyl- and 6′-methoxy-2′-naphthyl.

ANN ARBOR, MICHIGAN RECEIVED DECEMBER 31, 1943

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(15) Newman and Zahm, THIS JOURNAL, 65, 1099 (1943).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF IOWA STATE COLLEGE]

Relationship between Solution Viscosity and Molecular Weight in the Amylose Series[1]

BY JOSEPH F. FOSTER[2] AND R. M. HIXON

Data on the solution viscosities of a series of amyloses prepared from various starch sources have recently been given.[3] Investigations of the osmotic behavior of some of these materials have been carried out with a view to establishing a relationship between molecular weight and viscosity for this series of glucose polymers. Unfortunately, it has been necessary to discontinue these investigations, temporarily, in the present rather preliminary stage.

Attempts to relate the solution viscosities of high polymers with their molecular weights through simple equations, of which that of Staudinger is best known, have been complicated by several factors. In the first place it is essential that the polymers be either linear or, if branched, have a constant degree of branching, so that the length or axial ratio may be expressed as a simple function of molecular weight. Much confusion has been caused in attempting to apply the Staudinger equation to starch and its degradation products, due to the fact that this polymer apparently consists of two types of molecules,[3,4,5] the one highly branched and the other linear. Obviously the same equations could not be expected to apply to both types of polymer.

In the second place it is now recognized that viscosity measurements on high polymers yield not a simple number average molecular weight as in the case of osmotic studies but one which is weighted in some manner.[6] Therefore it is essen-

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[1] Journal Paper No. J-1139 of the Iowa Agricultural Experiment Station, Ames, Iowa; Project No. 817. Supported in part by a grant from the Corn Industries Research Foundation.

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[3] Foster and Hixon, THIS JOURNAL, 65, 618 (1943).

[4] K. H. Meyer, "Natural and Synthetic High Polymers," Interscience Publishers, Inc., New York, N. Y., 1942, pp. 387–417.

[5] Bates, French and Rundle, THIS JOURNAL, 65, 142 (1943).

[6] Kraemer and Lansing, *J. Phys. Chem.*, 39, 153 (1935); Flory, THIS JOURNAL, 65, 372 (1943).