TABLE II

Amount of water, ml.	Yield, %	Reaction period, min.
0[a]	Recovered[a]	480[a]
0[b]	80	240
0.07	90	60
.18	100	10
.36	100	15
.72	100	35
1.8	70	35[b]
7.2	55	60[c]
10.8	37	60[c]
14.4	32	60[c]

[a] Reaction procedures are different: see discussion. [b] Pyridine distilled over potassium hydroxide was used. [c] Formation of dimeric polyenes (λ_{max} 339, 375, 356 mμ) were apparent.

Anal. Calcd. for $C_{22}H_{26}O_5$: C, 71.33; H, 7.08. Found: C, 71.49; H, 7.33.

3,17α,21-Trihydroxy-19-norpregna-1,3,5(10),9(11)-tetraen-20-one 3,21-Diacetate (IVc).—A solution of 160 mg. of IVb in 4 ml. of acetic anhydride and 4 ml. of pyridine was permitted to stand at room temperature for 24 hr. The solution was poured into ice–water and the crystals collected by filtration to give 140 mg. of diacetate (IVc), as needles, m.p. 188–190°; $[\alpha]_D$ +136°; λ_{max} 226 mμ (ϵ 8500), 258.5 mμ (ϵ 16,000), 290 mμ (ϵ 2700), 299.5 mμ (shoulder); ν_{max} 3540, 1738, 1631, 1606, 1589, 1230, 1213 cm.$^{-1}$.

Anal. Calcd. for $C_{24}H_{28}O_6$: C, 69.88; H, 6.84. Found: C, 69.99; H, 6.85.

3,17α,21-Trihydroxy-19-norpregna-1,3,5(10),9(11)-tetraen-20-one (IVa).—To a solution of 100 mg. of IVb in 20 ml. of methanol was added a solution of 100 mg. of potassium bicarbonate in 2 ml. of water. The reaction mixture was allowed to stand for 24 hr. at room temperature. The mixture was neutralized with acetic acid and evaporated to dryness *in vacuo*. The residue was dissolved in methanol and undissolved inorganic substance was removed by filtration. Recrystallization from acetone gave 78 mg. of IVa, m.p. 248–250° dec.; $[\alpha]_D$ +176°; λ_{max} 262.5 mμ (ϵ 18,000), 299.5 mμ (ϵ 3000).

Anal. Calcd. for $C_{20}H_{24}O_4$: C, 73.14; H, 7.37. Found: C, 72.58; H, 7.37.

Hydrogenation of IVb to 3,17α,21-Trihydroxy-19-norpregn-1,3,5(10)-trien-20-one 21-Acetate (Vb).—A solution of 372 mg. of IVb in 30 ml. of ethyl acetate was shaken with 40 mg. of 10% palladium on charcoal for 1 hr. under hydrogen. Filtration, evaporation and recrystallization from methanol gave 340 mg. of Vb as needles, m.p. 184–186°; λ_{max} 281 mμ (ϵ 2380), 288 mμ (shoulder).

Anal. Calcd. for $C_{22}H_{28}O_5$: C, 70.94; H, 7.58. Found: C, 71.11; H, 7.59.

3,17α,21-Trihydroxy-19-norpregna-1,3,5-(10)-trien-20-one 3,-21-Diacetate (Vc).—Acetylation of Vb was carried out by the usual procedure and recrystallization from methanol afforded Vc as needles, m.p. 167–168°; λ_{max} 213 mμ (ϵ 13,400), 268.5 mμ (ϵ 1000), 275.5 mμ (ϵ 1000).

Anal. Calcd. for $C_{24}H_{30}O_6$: C, 69.54; H, 7.30. Found: C, 69.79; H, 7.24.

17α,21-Dihydroxypregna-1,4,9(11)-triene-3,20-dione BMD (VI).—To a solution of 1.5 g. of 17α,21-dihydroxypregn-1,4,9-(11)-triene-3,20-dione in 50 ml. of chloroform was added 13 ml. of concentrated hydrochloric acid and 13 ml. of 37% formalin. The mixture was shaken for 72 hr. at room temperature. The aqueous layer was separated and discarded. The chloroform solution was washed with aqueous sodium bicarbonate until it was neutralized, dried over sodium sulfate, and concentrated. Recrystallization of the residue from methylene chloride–methanol afforded 980 mg. of BMD compound (VI), m.p. 198–199°, as fine needles.

Anal. Calcd. for $C_{23}H_{28}O_5$: C, 71.85; H, 7.34. Found: C, 71.49; H, 7.14.

3,17α,21-Trihydroxy-19-norpregna-1,3,5(10),9(11)-tetraen-20-one BMD (VII).—A mixture of 400 mg. of VI and 15 g. of zinc dust in 20 ml. of pyridine was heated under reflux for 3 hr. After the usual work-up, recrystallization of the residue from methylene chloride afforded 300 mg. of VII, m.p. 247–248°, which was used for the next step without further purification.

Hydrolysis of VII with Aqueous Acetic Acid.—A mixture of 200 mg. of VII, 20 ml. of acetic acid, and 20 ml. of water was purged with nitrogen and heated to reflux for 6 hr. under nitrogen atmosphere. After standing at room temperature overnight the solvent was evaporated *in vacuo* to dryness. The residue was dissolved in 3 ml. of pyridine and 3 ml. of acetic anhydride. After storing at room temperature overnight, the solution was poured into ice–water. The aqueous suspension was extracted with methylene chloride, washed with water, and dried. Evaporation of the solvent and recrystallization of the residue from methanol afforded 65 mg. of 3,17α,21-trihydroxy-19-norpregn-1,3,5(10),-9(11)-tetraen-20-one, 3,21-diacetate (IVc), m.p. 183–184°. The melting point was undepressed on admixture with the sample prepared directly.

Acknowledgment.—The authors are indebted to Misses H. Yamanouchi and K. Hayashi for the microanalyses and to Miss K. Arimoto for the infrared spectral data. One of the authors (S. N.) is grateful to the Japan Society for Promotion of Science for the award of research fellowship.

An Aromatization Reaction of a Cross-conjugated Dienone System with Zinc. IV. Synthesis of 11-Hydroxyisoequilin and Aromatization of the Steroidal 1,4,8-Triene-3,11-dione System[1]

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11β-Hydroxyandrosta-1,4,8-triene-3,17-dione was prepared by the action of N-bromosuccinimide of 11β-hydroxyandrosta-1,4,9(11)-triene-3,17-dione and followed by dehydrobromination with collidine. The former was aromatized with zinc to give rise to 3,11β-dihydroxyestra-1,3,5(10)-trien-17-one, which was converted to equilenin by acid and estradiol with lithium in liquid ammonia. Refluxiug androsta-1,4,8-triene-3,11,17-trione with zinc in dimethylformamide afforded 3-hydroxyestra-1,3,5(10),8-tetraene-11,17-dione and 3-hydroxy-9,10-seco-androsta-1,3,5,X-tetraene-11,17-dione.

In a previous paper[3] of this series, it was reported that androsta-1,4,9(11)-triene-3,17-dione (I) was easily converted to 9-dehydroestrone (II) with zinc by the aromatization of ring A with concomitant elimination of the C-19 angular methyl group in excellent yield.

(1) This paper constitutes Part XXXIX of a series entitled "Steroid Studies" by K. Tsuda.

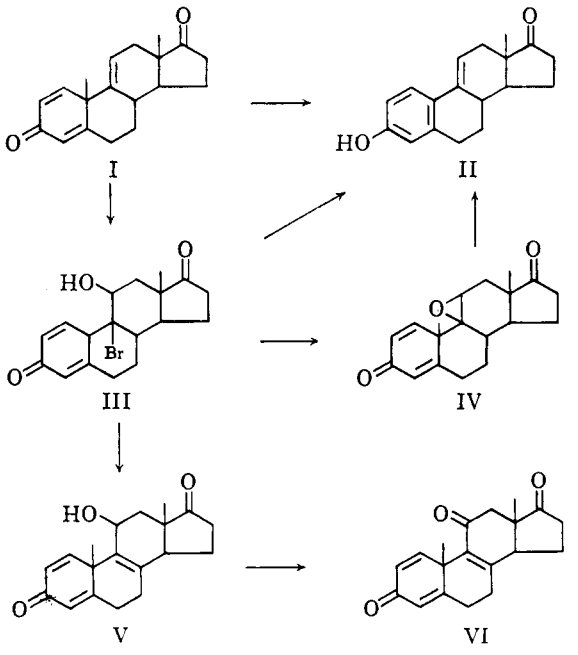
(2) Sankyo Co., Ltd., Shinagawa, Tokyo, Japan.

(3) K. Tsuda, E. Ohki, S. Nozoe, and N. Ikekawa, *J. Org. Chem.*, **26**, 2614 (1961).

Those results led us to extend this aromatization reaction to a steroidal 1,4,8-trien-3-one system which renders the C_{10}—C_{19} linkage triply allylicyl activated.

In order to prepare a 1,4,8-trien-3-one system, androsta - 1,4,9(11) - triene - 3,17 - dione (I) was treated with N-bromosuccinimide, using acetone containing dilute perchloric acid.[4] That the resulting bromohydrin has the 9α-bromo 11β-hydroxy configuration is now clear by analogy to related compounds.[5] The bromohydrin (III) was converted to the 9β,11β-epoxide (IV) by potassium acetate in methanol. When both the bromohydrin (III) and the epoxide (IV) were treated with zinc in pyridine, the same product, m.p. 255–257°, was obtained. This compound was characterized as a 9-dehydroestrone by direct comparison with an authentic sample. The formation of 9-dehydroestrone from both compounds may be assumed to proceed by regeneration of the double bond at the 9–11-position with zinc[6] to form compound I, followed by aromatization in a manner similar to that which we reported previously.[7]

Treatment of the bromohydrin (III) with collidine afforded in good yield a dehydrobromination product (V), which was also obtained in 40% yield by the action of silver nitrate in dioxane[5] at room temperature. Compound V, on chromium trioxide oxidation in acetic acid afforded androsta-1,4,8-triene-3,11,17-trione (VI). The oxidation product (VI) was characterized by an increase of the molecular extinction coefficient at 240 mμ to 22,300, and also by the characteristic infrared absorption band of the new α,β-unsaturated carbonyl function at 1666 cm.$^{-1}$, thereby proving the structure of 11β-hydroxyandrosta-1,4,8-triene-3,17-dione (V).

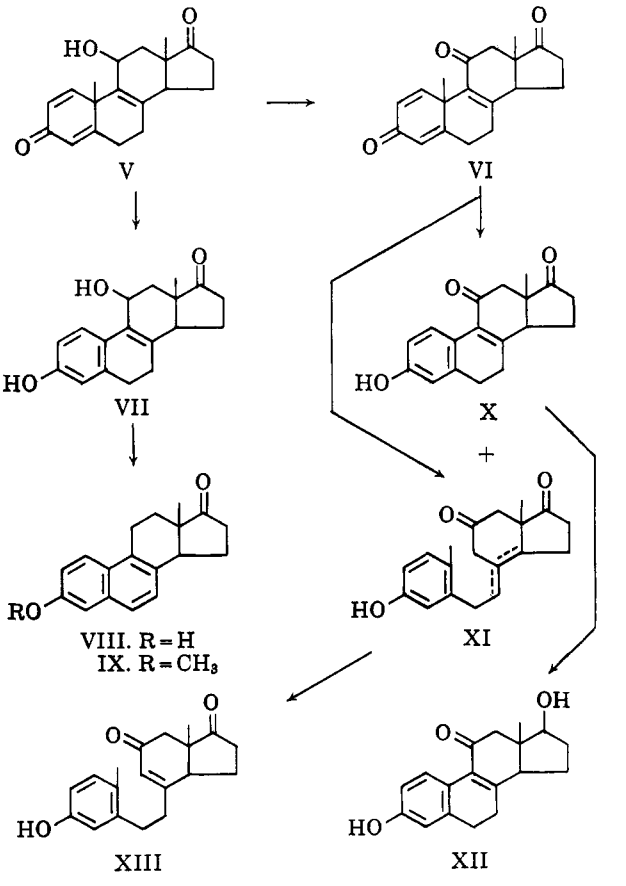


Reaction of trienone (V) with zinc in dimethylformamide yielded a phenolic product (VII), m.p. 187–189°, whose infrared spectrum exhibited a characteristic aromatic band, an *o*-phenylene band at 810 cm.$^{-1}$ and two bands associated with the hydroxyl group at 3520 and 3340 cm.$^{-1}$. The ultraviolet absorption maximum at 278 mμ[8] was analogous to that of Δ^8-isoequilin.[9] On the basis of the spectral data and of elemental analysis the phenolic product (VII) was assigned the structure of 3,11β-dihydroxyestra-1,3,5(10),8-tetraen-17-one.

Further proof of the structure of compound VII was secured by its conversion to equilenin and equilenin methyl ether with hydrochloric acid and dimethyl sulfate, respectively. The formation of the naphthol structure may be assumed to proceed by 1,4-elimination of water to form a 1,3,5(10),7,9(11)-pentaene system followed by migration to the conjugated position to furnish equilenin and its methyl ether in both reactions. Furthermore, compound VII gave estradiol in excellent yield on reduction with lithium in liquid ammonia, the identity of which was confirmed by the direct comparison with the natural hormone. The formation of estradiol came about by hydrogenolysis of the allylic hydroxyl group,[10] reduction of the 17-carbonyl group, and subsequent hydrogenation of the tetra-substituted double bond to the 8β-H, 9α-H configuration, *trans* B/C juncture.

On the other hand, similar reaction of V with zinc in ethylene glycol was found to give equilenin directly as was indicated by the change of ultraviolet spectrum to the characteristic six peaks.

During the purification of the phenolic product (VII), the solution of the reaction mixture was observed to de-



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velop deep violet coloration which changed to dark green in alkaline media.

Finally, androsta-1,4,8-triene-3,11,17-trione (VI), obtained from V on chromium trioxide oxidation, was treated with zinc in dimethylformamide to yield a mixture of two phenolic products, which were separated by Florisil column chromatography. Elution with benzene–ether (5%) yielded 35% of a phenolic product (XI), m.p. 170–178°, and with benzene–ether (20%), a second phenolic product (X), m.p. 225–228°, in 30% yield. The former showed a characteristic absorption maximum at 281 mμ (ε 3000) for a nonconjugated phenolic chromophore. Its infrared spectrum exhibited a band corresponding to an aromatic ring, two adjacent hydrogen atoms on that ring, and saturated five- and six-membered ring carbonyl absorption. Elemental analysis of this compound supported a 19 carbon skeleton, which indicated that no elimination of the angular methyl group had occurred. On the basis of the above evidence and from mechanistic grounds, this phenol is assumed to have structure XI.[11] Further support for the structural assignment of this phenol was proved by the double bond migration from the β,γ- to the α,β-position of the carbonyl function on treatment with alkali. Treatment of XI with sodium methoxide in methanol afforded a compound (XIII), m.p. 125–129°, which showed the characteristic ultraviolet absorption maximum of a nonconjugated phenolic chromophore at 280 mμ (ε 3300), along with a new band at 240 mμ (ε 11,100), corresponding to an unsaturated carbonyl group. The presence of the conjugated carbonyl group was further supported by the shift of the carbonyl band from 1700 cm.$^{-1}$ to 1660 cm.$^{-1}$ in the infrared. The lack of conjugation of the double bond at the 8-position and aromatic ring A indicated the product (XI) has a 9,10-seco structure.

In contrast to the former, the latter product (X), m.p. 225–228°, exhibited ultraviolet absorption maxima at 245 (ε 1500), 288 (shoulder), 297 (ε 4070), 319 mμ (ε 4300) and characteristic unsaturated ketone absorption at 1660 cm.$^{-1}$ in the infrared which indicates that an aromatic ring, a double bond at the 8-position and an 11-carbonyl group are in conjugation. The elemental analysis corresponded to $C_{18}H_{18}O_3$. From the above physical data the structure of (X) is derived as 3-hydroxy-estra-1,3,5(10),8-tetraene-11,17-dione, resulting from aromatization of ring A with concomitant elimination of the angular methyl group.

As suggested previously,[7] the presence of the C_9—C_{11} double bond probably influences the reaction course by allylic activation of the C_{10}—C_{19} linkage. This view was supported somewhat by the formation of compounds VII and X from the corresponding 1,4,8-trien-3-one systems (V) and (VI), respectively. While compound VI also gave a seco type of phenol (XI), its formation could be explained (see col. 2).

The contribution of π-electrons through the unsaturated keto group as in (A) renders the C_9—C_{10} linkage as weak as the C_{10}—C_{19} linkage in intermediate (B). Consequently (C) is formed as well as the desmethyl compound (X). Further investigation of this aromatization is now underway and will be published at a later data.

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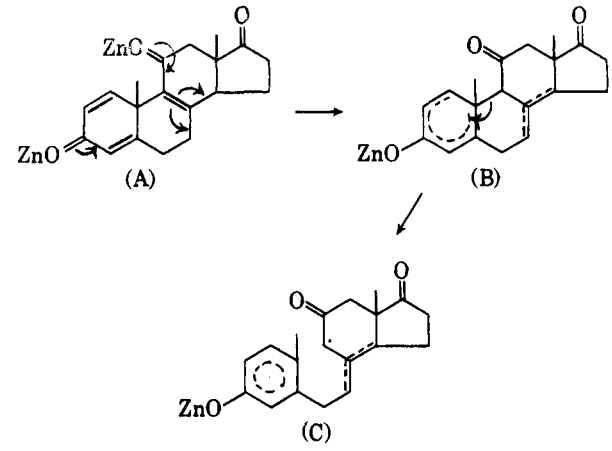

Experimental[12]

9α-Bromo-11β-hydroxyandrosta-1,4-diene-3,17-dione (III).—To a stirred solution of 2.82 g. of androsta-1,4,9(11)-triene-3,17-dione in 40 ml. of acetone maintained at 0° was added 2.5 g. of N-bromosuccinimide, followed by 24 ml. of cold 0.2 *N* aqueous perchloric acid added dropwise over a period of 20 min. The reaction mixture was stirred at 0° for 4 hr. Aqueous sodium bisulfite was added under cooling to the suspension to destroy excess N-bromosuccinimide. The reaction mixture then was poured into a large amount of ice–water and stirred for another hour at 0°. The precipitate was filtered, washed with water, and dried to give 3.5 g. of bromohydrin, m.p. 168–170° dec. Recrystallization from acetone afforded analytically pure sample, m.p. 178–180°, $[\alpha]_D$ +158° (*c* 0.68); ν_{max} 3320, 1744, 1660, cm.$^{-1}$.

Anal. Calcd. for $C_{19}H_{23}O_3Br$: C, 60.16; H, 6.11. Found: C, 59.92; H, 6.07.

9β,11β-Epoxyandrosta-1,4-diene-3,17-dione (IV).—To a stirred suspension of 1.6 g. of bromohydrin (III) in 20 ml. of methanol under nitrogen was added 1 ml. of 1 *N* methanolic sodium methoxide solution to give a clear red solution. The mixture was stirred at room temperature for 10 min. under nitrogen, then the color changed from red to yellow. After 15 min. the solution was neutralized with acetic acid, then poured into a large amount of water. The product was taken up in ether. The ether extract was washed with aqueous sodium bicarbonate and water, dried, and evaporated *in vacuo* to dryness. Recrystallization of the residue from acetone–ether afforded epoxide (IV) as prisms with m.p. 164–169°; $[\alpha]_D$ +88° (*c* 0.71); ν_{max} 1743, 1662, 1624, 1605 cm.$^{-1}$.

Anal. Calcd. for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43. Found: C, 76.36; H, 7.39.

3-Hydroxy-estra-1,3,5(10),9(11)-tetraen-17-one (II).—(1) A mixture of 500 mg. of III in 20 ml. of pyridine and 10 g. of zinc dust was heated under reflux for 2 hr. After filtration of zinc from the reaction mixture the filtrate was poured into water and extracted with ether. The extract was washed successively with dilute hydrochloric acid, dilute sodium bicarbonate solution, and water. Evaporation of the solvent and trituration of the residue from acetone–*n*-hexane afforded 280 mg. of crude 9-dehydroestrone, m.p. 232–246°, as leaflets. Recrystallization from methanol–ether raised the m.p. to 255–256°, undepressed on admixture with authentic sample. The infrared and ultraviolet spectra of this compound were identical with those of an authentic sample.

(2) Aromatization of epoxide IV was carried out in the same manner as described above and gave 9-dehydroestrone (II).

11β-Hydroxyandrosta-1,4,8-triene-3,17-dione (V). (1) **With Collidine.**—A suspension of 5 g. of bromohydrin (III) in 20 ml. of collidine was heated under reflux for 5 min. After cooling, 20 ml. of ether was added and the resulting suspension was kept in a refrigerator overnight. The separated crystals were filtered, washed with ether to remove the free collidine, then with water to remove the collidine hydrochloride, and dried, to afford 3.2 g. of V. An additional 400 mg. of V with the same melting point was isolated from the mother liquors. Recrystallization from

(12) All melting points are uncorrected and, unless noted otherwise, all rotations were measured in chloroform solution at 25°. Methanol was used for the ultraviolet spectra and Nujol paste for the infrared spectra.

acetone gave an analytically pure sample of V, m.p. 204–208° dec.; $[\alpha]_D$ +11° (*c* 1.05); ν_{max} 3420, 1737, 1662, 1617, 1600 cm.$^{-1}$.

Anal. Calcd. for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43; Found: C, 76.73; H, 7.45.

(2) **With Silver Nitrate.**—To a solution of 5 g. of the bromohydrin (III) in 50 ml. of dioxane was added a solution of 2 g. of silver nitrate in 30 ml. of water with stirring. The mixture was allowed to remain at room temperature in the dark for 24 hr. The precipitate was removed by filtration and the filtrate was poured into 250 ml. of water. The product was isolated by extraction with methylene chloride. The extract was washed with water and dried. After evaporation of the solvent the crystalline residue was recrystallized from acetone to give 2 g. of crude V. Recrystallization from acetone afforded pure material, which, on admixture with the sample prepared by dehydrobromination with collidine, did not depress the melting point.

Androsta-1,4,8-triene-3,11,17-trione (VI).—To a stirred solution of 865 mg. of 11β-hydroxyandrosta-1,4,8-triene-3,17-dione (V) in 50 ml. of acetic acid was added dropwise 213 mg. of chromium trioxide in 20 ml. of acetic acid containing 2 drops of water over a period of 10 min. at room temperature. The dark green reaction mixture was allowed to stand for 1 hr. and 1 ml. of methanol was added. The mixture was poured into a large amount of water and neutralized with sodium bicarbonate. The product was isolated by extraction with ether. Evaporation of ether and trituration of the residue by acetone gave 711 mg. of crude VI. Recrystallization from acetone–ether yielded an analytical sample of VI, m.p. 167–169° (brown melt); $[\alpha]_D$ +428° (*c* 0.75); λ_{max} 239 mμ (ε 22,500), ν_{max} 1745, 1666, 1656, 1626, 1605, 1587 cm.$^{-1}$.

Anal. Calcd. for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.96; H, 6.74.

3,11β-Dihydroxyestra-1,3,5(10),8-tetraen-17-one (VII).—A mixture of 1 g. of 11β-hydroxyandrosta-1,4,8-triene-3,17-dione (V) in 30 ml. of dimethylformamide containing 0.2 ml. of water and 20 g. of zinc was heated under reflux for 1 hr. with stirring. After the usual work-up, the solvent was evaporated to dryness and the resulting oily substance triturated with acetone. Filtration and recrystallization from acetone–ether gave 400 mg. of VII, m.p. 187–189° dec. The dark green filtrates were combined and evaporated to dryness. The residue was dissolved in methylene chloride and passed through a silica gel column. Elution with methylene chloride afforded an additional 200 mg. of VII with the same melting point; $[\alpha]_D$ +107° (*c* 0.67 in dioxane); ν_{max} 3510 (broad), 3330, 1737, 1613, 1581, 817 cm.$^{-1}$.

Anal. Calcd. for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.21; H, 7.06.

Equilenin (VIII).—(1) To a solution of 100 mg. of VII in 20 ml. of methanol was introduced dry hydrogen chloride gas at room temperature for 20 min. After evaporation of the methanol, the residue was dissolved in ether. The ether solution was washed with aqueous sodium bicarbonate, with water and dried. Evaporation of the ether afforded a brown oil, which was purified by silica gel chromatography. Elution of the column with methylene chloride afforded equilenin, which after crystallization from acetone melted at 252–254° (red melt) (lit.,[13] 256–258°); λ_{max} mμ, (ε): 230, 259.5, 270, 281, 292.5, 327.5, and 340 (5000, 3630, 4600, 5020, 3330, 2000, 2300).

(2) A mixture of 50 mg. of V in 10 ml. of ethylene glycol containing 0.05 ml. of water and 1 g. of zinc was heated under reflux for 1 hr. with stirring. After the usual work-up the crude product was obtained, which showed the characteristic ultraviolet absorption spectrum of equilenin.

Equilenin Methyl Ether (IX).—To a solution of 50 mg. of 11β-hydroxyestra-1,3,5(10),8-tetraen-17-one (VII) in 2 ml. of ethanol and 0.6 ml. of water containing 0.5 g. of potassium hydroxide was added a total of 0.6 ml. of dimethyl sulfate. When the reaction was completed, the ethanol was removed by evaporation and water was added. The product was isolated by extraction with ether. The extract was washed with aqueous sodium bicarbonate and water. Evaporation of the solvent followed by chromatography on silica-gel afforded crude equilenin methyl ether. Recrystallization from ether gave equilenin methyl ether, m.p. 191–193° (red melt) (lit.,[14] 196–196.5°); λ_{max} mμ (ε), 267.5, 278, 289, 322.5, 337.5 (5000, 5460, 3800, 2100, 2540).

3-Hydroxyestra-1,3,5(10),8-tetraene-11,17-dione (X) and 3-Hydroxy-9,10-secoandrosta-1,3,5(10),x-tetraene-11,17-dione (XI).—A mixture of 3 g. of VI in 50 ml. of dimethylformamide containing 1 ml. of water and 30 g. of zinc dust was heated under reflux for 2 hr. with stirring. After the usual work-up 2.1 g. of crude product was crystallized from methanol. Recrystallization from methanol afforded a mixture of two kinds of crystals having the different shapes, which were mechanically separated into pale brown prisms and colorless needles. The former was recrystallized from methanol furnishing 500 mg. of X, m.p. 226–229° (violet melt); $[\alpha]_D$ +223° (*c* 0.58, in dioxane); ν_{max} 3510 (broad), 1740, 1660, 1614, 1600, 1573, 1496, 837 cm.$^{-1}$.

Anal. Calcd. for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43. Found: C, 76.79; H, 6.43.

The latter was chromatographed over Florisil and eluted with benzene. Elution with benzene–ether (5%) afforded colorless needles, m.p. 168–175°. Recrystallization from methanol furnished 700 mg. of XI, m.p. 170–178° (brown melt); $[\alpha]_D$ +186° (*c* 0.5, in dioxane); λ_{max} 220 mμ (ε 11,100) 281 mμ (ε 3300); ν_{max} 3330 (broad), 1735, 1685, 1608, 1577, 1492, 812 cm.$^{-1}$.

Anal. Calcd. for $C_{19}H_{22}O_2$: C, 76.48; H, 7.43. Found: C, 76.44; H, 7.43.

Continued elution of the column with benzene–ether (20%) afforded 170 mg. of X, which, after crystallization from methanol, melted at 225–228°.

Isomerization of XI with Methanolic Potassium Hydroxide.—A solution of 50 mg. of XI in 5 ml. of methanol containing 500 mg. of potassium hydroxide was refluxed for 1 hr. to give a violet solution. After evaporation of the solvent, 10 ml. of water added. The mixture was acidified with 1% hydrochloric acid and extracted with ethyl acetate. The extract was washed with aqueous sodium bicarbonate and water. Evaporation of the solvent and purification of the residue by silica gel chromatography yielded pale yellow crystals, m.p. 122–125°. Recrystallization from ether gave XIII, m.p. 125–129°; λ_{max} 227 mμ (ε 14,700), 242 mμ (ε 11,100), 280 mμ (ε 3300); ν_{max} 3240 (broad), 1745, 1638, 1611, 1584, 1500, 814 cm.$^{-1}$.

Hydrogenation of X.—One mole equivalent of hydrogen was consumed in 2 hr. when a solution of 141 mg. of 3-hydroxyestra-1,3,5(10),8-tetraene-11,17-dione (X) in 20 ml. of ethanol was shaken with 20 mg. of platinum oxide under hydrogen. Filtration, evaporation, and recrystallization from methanol afforded 98 mg. of 3,17-dihydroxyestra-1,3,5(10),8-tetraen-11-one (XII), m.p. 251–254°; $[\alpha]_D$ +130° (*c* 0.63, in dioxane); λ_{max} 278 mμ (ε 16,000), 273 mμ (shoulder); ν_{max} 3340 (broad), 1631, 1595, 1573, 1495, 821 cm.$^{-1}$.

Anal. Calcd. for $C_{18}H_{20}O_3$: C, 76.07; H, 7.09. Found: C, 75.99; H, 7.00.

Acknowledgment.—The authors are indebted to Dr. S. Akagi, of Sankyo Co., Ltd., for helpful discussions, to Misses H. Yamanouchi and K. Hayashi for elemental analyses, and to Misses N. Kurosawa, N. Tohata, and K. Arimoto for infrared spectra measurements.

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