(1 ml) was added. The inorganic precipitate was filtered off and washed with ether (50 ml) and the filtrate was evaporated. The residue was treated with hexane and the precipitated **17** was filtered off to yield 0.90 g (90%), mp 119–120°, ir no C=O band.

17α-Hydroxy-3-methoxy-14β-estra-1,3,5(10)-trien-11-one (18). A mixture of compound **17** (1.00 g, 2.91 mmol), methanol (20 ml), and 10% hydrochloric acid (2 ml) was heated under reflux for 15 min. The solvent (15 ml) was evaporated and then compound **18** was filtered off and washed with water, giving 0.73 g (86%): mp 189–191°; NMR δ 1.10 (s, 3, CH_3), 3.80 (s, 3, CH_3O), 3.95 (br s, 1, at C-17), 6.75 (m, 2, at C-2 and C-4), 7.25 ppm (d, 1, J = 9 Hz, at C-1); ir 3500, 1705 cm^{-1}.

17α-Hydroxy-3-methoxy-14β-estra-1,3,5(10)-trien-11-one Ethylene Thioketal[10] (19). To a solution of compound **18** (1.0 g, 3.33 mmol) in 5 ml of ethanedithiol, $Et_2O \cdot BF_3$ (1 ml) was added at 10° and the mixture was allowed to stand at room temperature for 2 hr. When compound **18** could no longer be detected in the mixture (by TLC) the reaction mixture was diluted with ether and washed with 1 N sodium hydroxide solution until the ethanedithiol odor was eliminated. Upon drying and evaporation, the ether solution gave a crude mercaptal **19** (1.10 g, 88%): mp 90–91°; NMR δ 1.35 (s, 3, CH_3), 3.80 (s, 3, CH_3O), 3.95 (br s, 1, at C-17), 6.70 (m, 2, at C-2 and C-4), 8.75 ppm (d, 1, J = 9 Hz, at C-1); ir 3500 cm^{-1}, no C=O band.

Anal. Calcd for $C_{21}H_{28}S_2O_2$: C, 67.07; H, 7.45. Found: C, 67.2; H, 7.36.

3-Methoxy-14β-estra-1,3,5(10)-trien-17α-ol (20). Freshly prepared Raney nickel (from 8 g of alloy) was added to a solution of compound **19** (0.200 g, 0.532 mmol) in methanol (20 ml). The resulting suspension was heated under reflux for 5 min with rapid stirring with a magnetic bar. The nickel was then removed by filtration and the solvent was evaporated. The residue, recrystallized from methanol, yielded 0.140 g (89%) of compound **20**: mp 103–104°; NMR δ 1.04 (s, 3, CH_3), 3.76 (s, 4, CH_3O and H at C-17), 6.70 (m, 2, at C-2 and C-4), 7.25 ppm (d, 1, J = 9 Hz, at C-1); ir 3400 cm^{-1}.

Anal. Calcd for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found: C, 79.82; H, 9.10.

3-Methoxy-14β-estra-1,3,5(10)-trien-17-one (21). To a solution of **20** (0.100 g, 0.35 mmol) in 5 ml of acetone, Jones reagent[3] was added dropwise at room temperature until the time when the yellow color of the solution became permanent. When compound **20** was oxidized a few drops of 2-propanol were added and the inorganic solid was removed by filtration. Acetone was evaporated and the residue was washed with water. The precipitate was recrystallized from methanol, yielding 0.080 g (80.5%) of compound **21**, mp 120–121°, whose ir spectrum in $CHCl_3$ was identical with that described by Johnson et al.[7]

Acknowledgment. I would like to express my gratitude to Professor M. Kocór for his help and fruitful discussion, and to Dr. M. Guzewska for her help in the preparation of the manuscript.

Registry No.—**1**, 55923-92-7; **3**, 55887-37-1; **4**, 55923-93-8; **6**, 55887-38-2; **7**, 55904-18-2; **8**, 55871-08-4; **9**, 55887-39-3; **10**, 55887-40-6; **11**, 55887-41-7; **12**, 55923-94-9; **13**, 55903-63-4; **14**, 55923-95-0; **15**, 55903-64-5; **16**, 55887-42-8; **17**, 55923-96-1; **18**, 55923-97-2; **19**, 55923-98-3; **20**, 55923-99-4; **21**, 55924-00-0.

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(8) All melting points are uncorrected. The NMR spectra were determined in $CDCl_3$ unless otherwise stated with a Jeol apparatus at 100 MHz using Me_4Si as an internal standard. The ir spectra were obtained in KBr unless otherwise stated with a Unicam SP 200 spectrophotometer. All the reactions were monitored by thin layer chromatography. All the compounds were obtained as racemates and for the sake of simplicity prefixes *dl* or *rac* have been omitted.
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(10) These reactions were carried out according to J. Fried and J. A. Edwards, "Organic Reactions in Steroid Chemistry", Vol. 1, Van Nostrand-Reinhold, Princeton, N.J., 1972, pp 172–173.

Total Synthesis of Steroids. VII. Synthesis of 14β-Estra-4-ene-3,11,17-trione and Related Compounds

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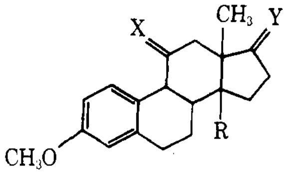
Transformation of 14β-hydroxy-3-methoxyestra-1,3,5(10)-triene-11,17-dione to 3-methoxy-14β-estra-1,3,5(10)-triene-11,17-dione, 14β-estra-4-ene-3,11,17-trione, and 3-methoxy-8α-estra-1,3,5(10)-triene-11,17-dione as well as to other compounds is described. The stereochemistry of the products was elucidated on spectral grounds and by convertion to known compounds.

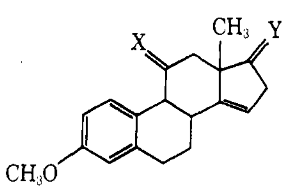
In part VI on total synthesis of steroids[1] a method of preparation of 9β,11β,14β-trihydroxy-3-methoxyestra-1,3,5(10)-trien-17-one (**12**) and 14β-hydroxy-3-methoxyestra-1,3,5(10)-triene-11,17-dione (**1**) was described. The present work is concerned with a transformation of **1** and **12** into estrane derivatives. Compound **1** can be easily dehydrated with thionyl chloride in pyridine to unsaturated diketone **2**. A catalytic hydrogenation of C-14 double bond in diketone **2** and compounds **4, 7, 9, 10** and **11** (Scheme I) leads to 3-methoxy-14β-estra-1,3,5(10)-triene-11,17-dione (**3**) irrespectively of the substitution at C-11 and C-17 by a hydroxyl, keto, or ketal function, similarly to the known reduction of 14-dehydroestrone methyl ether.[2]

In order to obtain compounds with the natural configuration at carbon atom 14 the following series of reactions was carried out (Scheme II). The known[1] triol **12** was oxidized by Collins' method[3] to diketone **13**, which was dehydrated in hot acetic acid with p-toluenesulfonic acid to pentaene **14**. This compound could also be obtained by dehydration of the known compound[4] **15**, which was produced by either a monodehydration of **13** or an oxidation of **16**. The preparation of **16** and the proof of its structure will be described later. Catalytic hydrogenation of pentaene **14** in toluene solution over $Pd/CaCO_3$ catalyst gave tetraene **17** as in the case of reduction of 3-methoxyestra-1,3,5(10),8,14-pentaen-17-one.[5] The uv spectrum of **17** was

Scheme I



1, X = Y = O; R = OH
3, X = Y = O; R = H
5, X = ξOH, ξH; Y = βOH, αH; R = H
6, X = Y = OCH_2CH_2O; R = OH
8, X = Y = OCH_2CH_2O; R = N
9a, X = OCH_2CH_2O; Y = O; R = H



2, X = Y = O
4, X = ξOH, ξH; Y = βOH, αH
7, X = Y = OCH_2CH_2O
9, X = OCH_2CH_2O; Y = O
10, X = OCH_2CH_2O; Y = βOH, αH
11, X = O; Y = βOH, αH

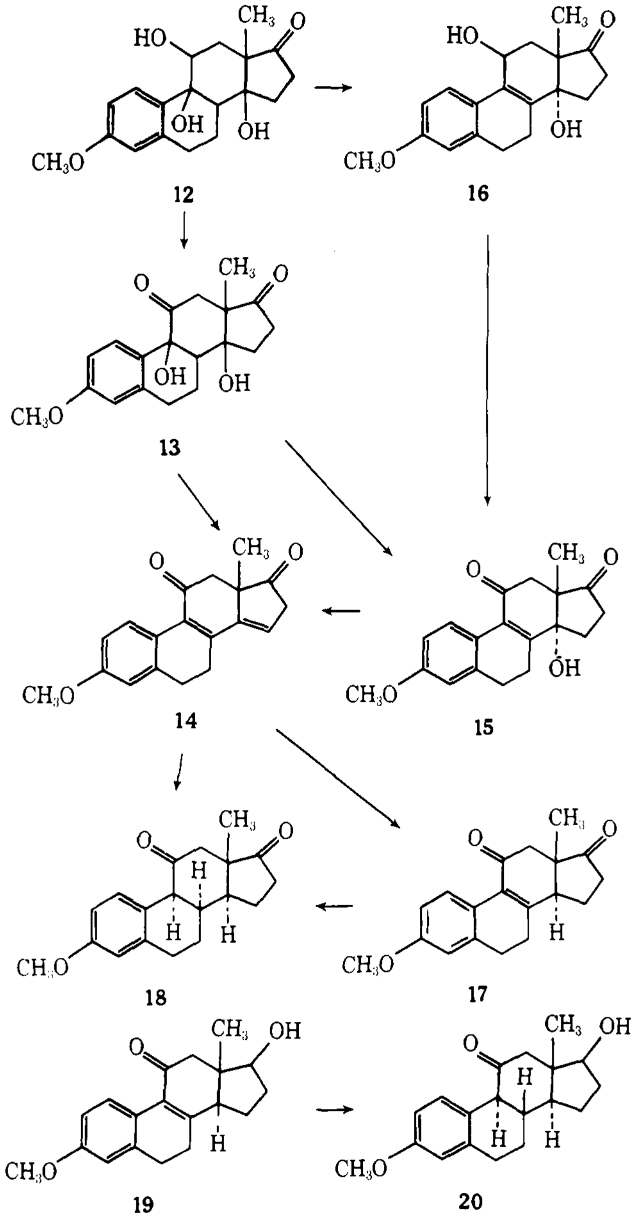
$$\begin{tikzcd}
6 \arrow[r] & 7 \arrow[r] & 8 \arrow[dd] & & \\
 & & & 9a \arrow[dl] & 9 \arrow[l] \arrow[dd] \\
1 \arrow[r] & 2 \arrow[r] \arrow[d] & 3 & & \\
 & 4 \arrow[r] & 5 \arrow[u] & 11 \arrow[ul] & 10 \arrow[l]
\end{tikzcd}$$

almost identical with that of **15**. In order to prove that the hydrogenation of the 14(15) double bond took place from the α side, tetraene **17** was hydrogenated in an alcoholic solution and gave the known compound **18** identical in all respects with an authentic sample.[6] Compound **18** was also prepared by a direct hydrogenation of pentaene **14** over palladium catalyst in an alcoholic solution.

The reduction of the 8(9) double bond of compound **19** to **20** with the natural configuration was carried out by Smith[7] and by Birch.[8] These authors obtained a 60% yield of compound **20**, but their substrate **19** had the β-hydroxyl group at C-17 instead of the keto group which is present in compound **17**. We have shown[1] that the treatment of triol **12** with $Et_2O{\cdot}BF_3$ gives diketone **1** but the acidification of the same triol **12** with *p*-toluenesulfonic acid in alcoholic solution yields the unsaturated compound **16** in which a change of configuration at C-14 takes place. TLC showed that the first step of this reaction was a dehydration and the second step was a change of configuration at C-14. The mechanism of this reaction was not investigated further but it is probable that a change of configuration at C-14 takes place through the SN1 type reaction to the thermodynamically favored diastereoisomer. It is known[9] that cinnamyl alcohol exchanges the hydroxyl group under acidic conditions. The acetyl derivative **22** was obtained by acetylation of **16** and by dehydration of known monoacetate[1] **23** (Scheme III).

These reactions proved that there was no change of configuration at C-11. Catalytic hydrogenation of **16** gave compound **24** as the major product and compounds **25** and **26** as by-products. The known[10] compound **27** was obtained by oxidation of **24** with Jones[11] reagent. The structure of **27** was established unambiguously. It was shown earlier[1] that the configuration of the hydroxyl group at C-11 could not be demonstrated by NMR, owing to a flexibility of the steroidal nucleus at the cis B/C and C/D ring junctions. Confirmation of the β configuration of the hydroxyl group at C-11 in triol **12** and other related compounds was obtained from the NMR spectrum of compound **29**. Compound **29** has a double bond between C-14 and C-15 and consequently has only one chair conformation. The signal of the proton at C-11 (5.62 ppm) in the NMR spectrum of **29** has a total width of 10 Hz, clearly showing the axial β geometry of the hydroxyl at C-11.

Scheme II

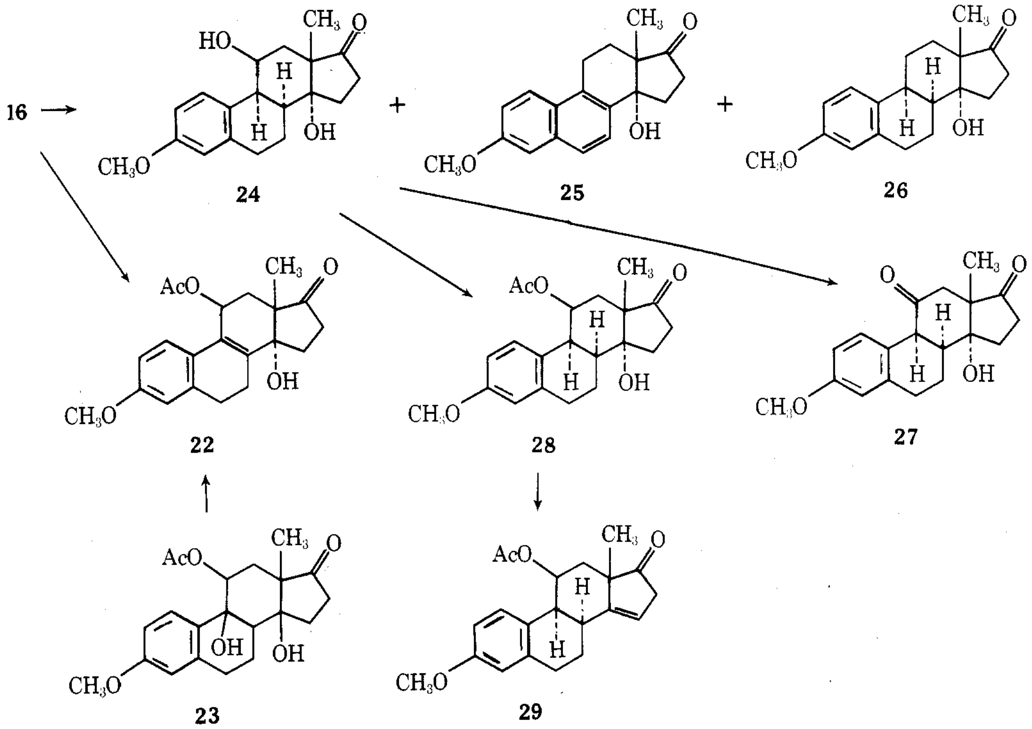


In order to obtain some other new 19-norsteroids, diketals **6** and **8** were reduced by sodium in liquid ammonia and the products were hydrolyzed to the hitherto unknown triketones **31**, **32**, and **34** (Scheme IV). The hydrogen atom at C-10 was assumed to have the trans configuration with respect to the hydrogen atom at C-9.[12]

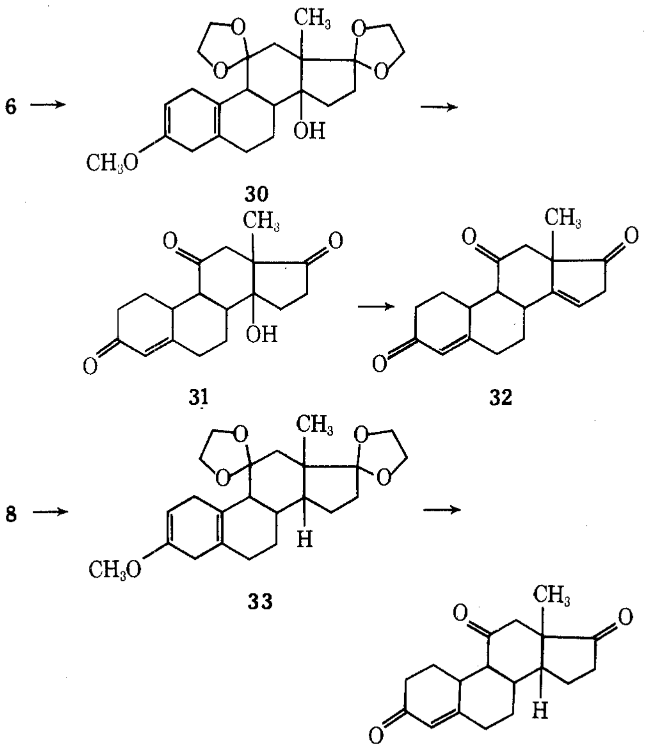
Experimental Section[13,14]

3-Methoxyestra-1,3,5(10),14-tetraene-11,17-dione (2). To a solution of **1** (1.00 g, 3.19 mmol) in dry pyridine, 0.5 ml of $SOCl_2$ was added at 0°. The mixture was stirred for 5 min and water (25 ml) was added. The crystalline product was filtered off and washed with water and cold methanol. The yield of **2** was 0.81 g (86%). Crude **2** melted at 143–145°; NMR δ 1.2 (s, 3, CH_3), 2.55 (s, 2, at

Scheme III



Scheme IV



C-16), 3.55 (d, 1, J = 12 Hz, at C-9), 3.8 (s, 3, CH_3O), 5.87 (t, 1, at C-15), 6.7 (m, 2, at C-2 and C-4), 7.05 ppm (d, 1, J = 9 Hz, at C-1); ir 1710, 1735 cm^{-1}.

Anal. Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.94; H, 6.83.

3-Methoxy-14β-estra-1,3,5(10)-triene-11,17-dione (3) via Compounds 4 and 5. To a solution of **2** (1.00 g, 3.38 mmol) in ether (50 ml), 200 mg (5.26 mmol) of $LiAlH_4$ was added at room temperature. The mixture was stirred for 10 min and water (2 ml) was added. The inorganic precipitate was filtered off and washed with ether (50 ml). The filtrate was evaporated, and the crystalline compound **4** (ir showed the absence of C=O band) was hydrogenated without purification to compound **5** over palladium on charcoal under atmospheric pressure in ethyl alcohol solution. The standard Jones oxidation[11] of **5** afforded 0.60 g of **3**: mp 202–205°; NMR δ 1.1 (s, 3, CH_3), 3.75 (s, 3, CH_3O), 3.85 (d, 1, J = 12 Hz, at C-9), 6.55 (m, 2, at C-2 and C-4), 7.05 ppm (d, 1, J = 9 Hz at C-1); ir 1710, 1738 cm^{-1}.

Anal. Calcd for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43. Found: C, 76.50; H, 7.39.

3-Methoxy-14β-estra-1,3,5(10)-triene-11,17-dione (3) by Hydrogenation of 2, 7, and 9. The hydrogenation of **2**, **7**, or **9** was carried out at atmospheric pressure in toluene solution over 10% Pd/$CaCO_3$. Compounds **3**, **8**, and **9a** were obtained in 95% yield. The hydrolysis of the ketal groups of compounds **8** and **9a** was carried out in boiling methanol containing some 10% hydrochloric acid. In both the cases compound **3** was obtained. Compound **9a** was identical in all respects with that described earlier.[1] Compound **8**: mp 161–162; NMR δ 1.1 (s, 3, CH_3), 3.8 (s, 3, CH_3O), 3.95 (s, 8, ketal groups), 6.7 (m, 2, at C-2 and C-4), 8.0 ppm (d, 1, at C-1); ir no C=O band.

Anal. Calcd for $C_{23}H_{30}O_5$: C, 71.48; H, 7.82. Found: C, 71.35; H, 7.91.

11,11,17,17-Bis(ethylenedioxy)-3-methoxyestra-1,3,5(10),14-tetraene (7). To a solution of **6** (0.500 g, 1.24 mmol) in dry pyridine (5 ml), $SOCl_2$ (0.3 ml) was added at 0°. The mixture was stirred for 10 min at 0° and water (10 ml) was added dropwise. The crystalline product **7** was filtered off and washed with water and cold methanol: yield 0.43 g (90%); mp 151–153°; NMR δ 1.25 (s, 3, CH_3), 3.8–4.0 (m, 11, CH_3O and ketal groups), 5.4 (s, 1, at C-15), 6.72 (m, 2, at C-2 and C-4), 8.0 ppm (d, 1, at C-1).

Anal. Calcd for $C_{23}H_{28}O_5$: C, 71.85; H, 7.34. Found: C, 71.69; H, 7.40.

3-Methoxy-14β-estra-1,3,5(10)-triene-11,17-dione (3) by Transformation of 10. The reduction of the 14(15) double bond of compound **10** was carried out under atmospheric pressure in toluene solution over 10% Pd/$CaCO_3$. The resulting saturated compound was hydrolyzed without isolation with 10% hydrochloric acid in a methanolic solution. Methanol and hydrochloric acid were removed and the residue was oxidized with Jones reagent[11] to compound **3**. Also the ketal group in compound **10** was hydrolyzed before the hydrogenation and the resulting compound **11** was hydrogenated without purification over 10% Pd/$CaCO_3$ in toluene solution. The crude product was oxidized by Jones reagent to the same compound **3**.

11,11-Ethylenedioxy-3-methoxyestra-1,3,5(10),14-tetraen-17-ol (10). To a solution of **9** (0.80 g, 2.2 mmol) in 20 ml of THF and 20 ml of methanol, $NaBH_4$ (0.050 g) was added at room temperature. At the end of the reaction one-half of the solvent was evaporated under reduced pressure and the residue was diluted with water. The solid **10** was recrystallized from a mixture of benzene and hexane to give 0.60 g (74.5%) of **10:** mp 138–140°; NMR δ 1.1 (s, 3, CH_3), 3.8 (s, 3, CH_3O), 3.9 (m, 5, OCH_2CH_2O and at C-17), 5.25 (s, 1, at C-15), 6.7 (m, 2, at C-2 and C-4), 8.0 ppm (d, 1, J = 9 Hz, at C-1); ir 3550 cm^{-1}.

Anal. Calcd for $C_{21}H_{26}O_4$: C, 73.66; H, 7.66. Found: C, 73.50; H, 7.71.

9β,14β-Dihydroxy-3-methoxyestra-1,3,5(10)-triene-11,17-dione (13). A mixture of CrO_3 (3 g, 30.0 mmol) and pyridine (4.75 g) in 60 ml of methylene chloride was stirred under reflux for 1 hr and compound **12** (1.00 g, 3.1 mmol) in 50 ml of methylene chloride was added. When the oxidation of **12** was complete (1 hr) the reaction mixture was filtered in order to remove the chromium salts and the last traces of them were removed by passing through a 5-cm layer of alumina. The solvent was evaporated and the residue was recrystallized from acetone–hexane mixture and gave 0.71 g (71.4%) of **13:** mp 201–203; NMR [$(CD_3)_2SO$] δ 1.0 (s, 3, CH_3), 3.82 (s, 3, CH_3O), 6.82 (m, 2, at C-2 and C-4), 7.12 ppm (d, 1, J = 9 Hz, at C-1); ir 1730, 3450 cm^{-1}.

Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 68.86; H, 6.76.

3-Methoxyestra-1,3,5(10),8(9),14-pentaene-11,17-dione (14). A mixture of **13** (0.500 g, 1.51 mmol) and *p*-toluenesulfonic acid (0.050 g) in 5 ml of acetic acid was heated under nitrogen up to 110° for 40 min. After cooling, the mixture was diluted with 5 ml of water, and the blue precipitate of **14** was filtered and washed with water and cold methanol. It was used without further purification for the hydrogenation: yield 0.39 g (87.5%); mp of crude 155–160°; uv max (95% EtOH) 255 nm (ε 12,000), 371 (5100); NMR δ 1.3 (s, 3, CH_3), 3.22 (2 d, 2, at C-16), 3.80 (s, 3, CH_3O), 6.3 (t, 1, at C-15), 6.75 (m, 2, at C-2 and C-4), 8.0 ppm (d, 1, at C-1).

14α-Hydroxy-3-methoxyestra-1,3,5(10),8(9)-tetraene-11,17-dione (15). A mixture of **13** (0.50 g, 1.51 mmol) and *p*-toluenesulfonic acid (0.050 g) in 5 ml of acetic acid was stirred at room temperature until the substrate **13** disappeared. Then it was diluted with water (5 ml). The precipitate **15** was filtered and washed with water and cold methanol. After recrystallization from ether 0.30 g (63.5%) of **15** was obtained. It was identical in all respects with the compound described earlier.[4] Compound **15** was also obtained by an oxidation of **16** with Jones reagent[11] which gave an 85% yield.

11β,14α-Dihydroxy-3-methoxyestra-1,3,5(10),8(9)-tetraen-17-one (16). To a solution of **12** (0.500 g, 1.50 mmol) in 5 ml of 90% ethanol, 0.05 g of *p*-toluenesulfonic acid was added at room temperature. After 2 hr the substrate **12** almost disappeared, and 2 ml of water was added. The precipitated **16** was filtered and was recrystallized from aqueous acetone: yield of **16** 0.30 g (63.5%); mp 185–196°; NMR (CD_3SOCD_3) δ 1.05 (s, 3, CH_3), 3.75 (s, 3, CH_3O), 4.34 (m, 1, at C-11), 6.7 (m, 2, at C-2 and C-4), 7.25 ppm (d, 1, J = 9 Hz, at C-1); ir 3350, 1730 cm^{-1}; uv max (95% EtOH) 276 nm (ε 16,000).

Anal. Calcd for $C_{19}H_{22}O_4$: C, 72.59; H, 7.05. Found: C, 72.62; H, 6.96.

3-Methoxyestra-1,3,5(10),8(9)-tetraene-11,17-dione (17). The hydrogenation of **14** (1.00 g, 3.4 mmol) was carried out under atmospheric pressure in a toluene solution using 1.00 g of 10% Pd/$CaCO_3$. When the hydrogen absorption ceased, the catalyst was removed by filtration and the toluene was evaporated under reduced pressure. Methanol (5 ml) was added to the residue, and the precipitate was filtered and washed with cold methanol. After drying it gave 0.80 g (80%) of the product **17:** mp 143–146°; NMR δ 0.97 (s, 3, CH_3), 3.77 (s, 3, CH_3O), 6.70 (m, 2, at C-2 and C-4), 7.84 ppm (d, 1, J = 9 Hz, at C-1); uv max (95% EtOH) 247 nm (ε 16,400), 287 (3730), 297 (3990), 322 (4170).

3-Methoxy-8α-estra-1,3,5(10)-triene-11,17-dione (18). The hydrogenation of **17** (0.500 g, 1.69 mmol) was carried out under atmospheric pressure in ethanol solution using 0.50 g of 10% Pd/$CaCO_3$. At the end of the reaction the catalyst and ethanol were removed and the residue was recrystallized from methanol to give 0.40 g (80%) of **18** which turned out to be identical in all respects with a sample kindly supplied by Professor H. Smith of Wyeth Laboratories.[6]

11β-Acetoxy-14α-hydroxy-3-methoxyestra-1,3,5(10),8(9)-tetraen-17-one (22). Method A. A solution of **16** (0.200 g, 0.638 mmol) in pyridine (2 ml) and acetic anhydride (2 ml) was allowed to stand overnight at room temperature and was evaporated under reduced pressure. The residue was dissolved in chloroform (10 ml) and was washed with water, then dried and evaporated to dryness. After recrystallization from an acetone–hexane mixture it gave 0.20 g (88%) of **22:** mp 180–190°; NMR δ 1.2 (s, 3, CH_3), 2.0 (s, 3, CH_3CO), 3.8 (s, 3, CH_3O), 5.75 (t, 1, at C-11), 6.8 ppm (m, 3, at C-1, C-2, and C-4); ir 3500, 1740, 1715 cm^{-1}; uv max (95% EtOH) 278 nm (ε 16,000).

Anal. Calcd for $C_{21}H_{24}O_5$: C, 70.76; H, 6.79. Found: C, 70.69; H, 6.81.

Method B. A solution of **23** (0.500 g, 1.33 mmol) and *p*-toluenesulfonic acid (0.100 g) in 90% ethanol (10 ml) was allowed to stand at room temperature. After 2 hr the substrate disappeared, 2 ml of water was added, and the precipitated **22** (0.300 g, 63.2%) was filtered and recrystallized from an acetone–hexane mixture.

11β,14α-Dihydroxy-3-methoxy-8α-estra-1,3,5(10)-trien-17-one (24), 14α-Hydroxy-3-methoxyestra-1,3,5,6,8(9)-pentaen-17-one (25), and 14α-Hydroxy-3-methoxy-8α-estra-1,3,5(10)-trien-17-one (26). The hydrogenation of **16** (1.00 g, 1.32 mmol) was carried out under atmospheric pressure in ethanol over 1.0 g of 10% Pd/C. The reaction mixture was separated by column chromatography on silica gel 100–200 mesh using a mixture of hexane–ethyl acetate (2:1) as eluent. After chromatography three compounds, **24** (0.71 g), **25** (0.080 g), and **26** (0.070 g), were isolated. **24:** mp 158–160°; NMR δ 1.3 (s, 3, CH_3), 3.72 (s, 3, CH_3O), 4.12 (m, 1, at C-11), 6.65 (m, 2, at C-2 and C-4), 7.0 ppm (d, 1, J = 9 Hz, at C-1); ir 3500, 1730 cm^{-1}.

Anal. Calcd for $C_{19}H_{24}O_4$: C, 72.12; H, 7.65. Found: C, 72.07; H, 7.59.

25: mp 151–153°; NMR δ 1.1 (s, 3, CH_3), 3.9 (s, 3, CH_3O), 7.5 ppm (m, 5, at C-1, C-2, C-4, C-6, and C-7); ir 3500, 1725 cm^{-1}; uv max (95% EtOH) 267 nm (ε 5180), 278 (5290), 287 (3460), 319 (1235), 333 (1630); mass spectrum *m/e* 296. **26:** mp 145–149°; NMR δ 1.1 (s, 3, CH_3), 3.8 (s, 3, CH_3O), 6.75 (m, 3, at C-2 and C-4), 7.12 ppm (d, 1, J = 8 Hz, at C-1); ir 3550, 1735 cm^{-1}; uv max (95% EtOH) 279 nm (ε 2180), 287 (1920); mass spectrum *m/e* 300.

14α-Hydroxy-3-methoxy-8α-estra-1,3,5(10)-triene-11,17-dione (27). Compound **27** was obtained by an oxidation of **24** with Jones reagent[11] using the standard procedure. It was identical in all respects with the compound described earlier.[10]

11β-Acetoxy-14α-hydroxy-3-methoxy-8α-estra-1,3,5(10)-trien-17-one (28). A mixture of **24** (0.500 g, 1.58 mmol), pyridine, and acetic acid anhydride (2 ml) was refluxed for 1 hr, during which the substrate disappeared. Then water (5 ml) was added, and the precipitated **28** was filtered and recrystallized from ether. The yield of **28** was 0.49 g (86.5%): mp 193–195°; NMR δ 1.3 (s, 3, CH_3), 1.8 (s, 3, CH_3CO), 3.8 (s, 3, CH_3O), 5.38 (q, 1, at C-11), 6.7 (m, 2, at C-2 and C-4), 7.1 ppm (d, 1, J = 9 Hz, at C-1); ir 3450, 1730, 1710 cm^{-1}.

Anal Calcd for $C_{21}H_{26}O_5$: C, 70.37; H, 7.31. Found: C, 70.10; H, 7.23.

11β-Acetoxy-3-methoxy-8α-estra-1,3,5(10),14-tetraen-17-one (29). To a solution of **28** (0.250 g, 0.70 mmol) in pyridine (2 ml), 2 drops of $SOCl_2$ was added at 0°. When the substrate disappeared, water (3 ml) was added, and the precipitated **29** was filtered and recrystallized from methanol. The yield of **29** was 0.220 g (93%): mp 143–144°; NMR δ 1.4 (s, 3, CH_3), 1.78 (s, 3, CH_3CO), 3.8 (s, 3, CH_3O), 5.58 (q, 1, at C-11), 5.9 (t, 1, at C-15), 6.75 (m, 2, at C-2 and C-4), 7.1 ppm (d, 1, J = 8.5 Hz, at C-1); ir 1735 cm^{-1}.

Anal. Calcd for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 73.97; H, 7.23.

11,11,17,17-Bis(ethylenedioxy)-3-methoxyestra-2,5(10)-dien-14β-ol (30). A solution of **6** (1.00 g, 2.49 mmol) in *tert*-butyl alcohol (15 ml) and THF (30 ml) was added to liquid ammonia (200 ml) and 1.0 g of metallic sodium was added in small portions. After 4 hr the solution was treated with methanol until a disappearence of blue color and 3 g of NH_4Cl was added. Ammonia was allowed to evaporate, water (100 ml) was added, and the solvents, THF, *tert*-butyl alcohol, and some water, were distilled off under reduced pressure. The precipitated **30** was filtered and was washed with water and methanol. The yield of **30** was 0.925 g (92.5%): mp of crude product 193–203°; ir 3500 cm^{-1}; NMR δ 1.05 (s, 3, CH_3), 3.55 (s, 3, CH_3O), 4.0 (m, 8, OCH_2CH_2O), 4.62 ppm (t, 1, at C-2).

14β-Hydroxyestra-4-ene-3,11,17-trione (31). A solution of **30** (0.800 g, 1.98 mmol) in methanol (50 ml) and 10% HCl (5 ml) was refluxed for 0.5 hr and methanol was evaporated under reduced pressure. The precipitated **31** was filtered and was washed with water. It was recrystallized from acetone–hexane mixture and gave 0.480 g (80%) of **31:** mp 205–207°; NMR δ 1.05 (s, 3, CH_3), 5.82 ppm (s, 1, at C-4); ir 3450, 1730, 1710, 1660, 1620 cm^{-1}; uv max (95% EtOH) 240 nm (ε 14,000).

Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.25; H, 7.54.

Estra-4,14-diene-3,11,17-trione (32). To a solution of **31** (0.400 g, 1.32 mmol) in dry pyridine, $SOCl_2$ (0.1 ml) was added at −10°. The mixture was stirred at this temperature for 10 min and water (5 ml) was added. The solvent was evaporated to dryness under reduced pressure and the crystalline **32** was washed with water and recrystallized from benzene–hexane mixture. The yield of **32** was 0.300 g (80%): mp 130–132°; NMR δ 1.13 (s, 3, CH_3), 3.1 (s, 2, at C-16), 5.9 ppm (s, 2, at C-4 and C-15); ir 1740, 1705, 1660, 1625 cm^{-1}; uv max (95% EtOH) 238 nm (ϵ 16,500).

Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 75.93; H, 7.15.

14β-Estra-4-ene-3,11,17-trione (34). The diketal **8** was reduced by the Birch method by the procedure used in the case of compound **30**. The intermediate **33** was not isolated in pure form, but was hydrolyzed to compound **34** in methanol containing some 10% hydrochloric acid. The yield of **34** was 85%: mp 173–175°; NMR δ 1.18 (s, 3, CH_3), 5.9 ppm (s, 1, at C-4); ir 1730, 1700, 1660, 1620 cm^{-1}; uv max (95% EtOH) 239 nm (ϵ 16,000).

Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.49; H, 7.74. Found: C, 75.38; H, 7.82.

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(14) All the compounds were obtained as racemates and for the sake of simplicity, prefixes *dl* or *rac* have been omitted. For the preparation of optically active compounds see part VIII, *J. Org. Chem.*, **40**, 3135 (1975). Compounds **1**, **6**, **9**, and **12** were obtained according to procedures described in ref 1.

Total Synthesis of Steroids. IX.[1] Synthesis of 11-Oxidized 19-Norandrostanes

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Reactions of *rac*-3-methoxy-14α-hydroxy-8α-estra-1,3,5(10)-triene-11,17-dione (**1a**) leading to *rac*-11-keto-8,14-bisdehydroestradiol 3-methyl ether (**20**) and analogous compounds are described. The Birch reduction of **20** followed by hydrolysis and Jones oxidation produced *rac*-19-norandrost-4-ene-3,11,17-trione (**22**), having the natural geometry at all chiral centers.

The total synthesis of a mixture of *rac*-3-methoxy-14α-hydroxy-8α-estra-1,3,5(10)-triene-11,17-dione (**1a**) and its epimer **1b** was described earlier.[2] This mixture gave on ketalization a single diketal **2** (Scheme I), whose further transformations are the subject of our present communication.

The diketal **2** was dehydrated with thionyl chloride in pyridine to form the unsaturated intermediate **3**, which was subsequently catalytically hydrogenated to the saturated diketal **4**. The latter compound was then reduced by the Birch method and yielded on hydrolysis the 19-norsteroid **6** with cis geometry of C/D ring junction. Acid hydrolysis of the diketal **4** afforded an unseparable mixture of diketones **7a** and **7b** epimeric at C-9. Birch reduction of the diketal **2**, followed by acid hydrolysis produced the 19-nor compound **9**, which was dehydrated to the diene trione **10**.

The synthesis of the 17-hydroxy 19-norsteroid **12** was achieved by Birch reduction, followed by acid treatment, of the monohydroxy ketal **11** (Scheme II); the latter compound has been prepared from the diketal **2** as described before.[2] In all cases of Birch reduction described above and below, a new chiral center was created at carbon 10. According to the literature,[3] such a reduction of the aromatic A ring, followed by acid hydrolysis of the enol ether groups, leads predominantly to products with trans geometry of the hydrogen at C-10 with respect to H-9; consequently the compound **6** is a racemic mixture of 13-isoestranes (or 19-nor-13-isoandrostanes, respectively), and therefore compounds **9**, **10**, and **12** have also the geometry as presented.

In order to secure the possibility of changing the configuration at carbon atoms 8 and 9, we attempted the introduction of the double bond at the B/C ring junction. In fact, dehydrogenation of **1a,b** with DDQ gave the desired compound[4] **15** (Scheme III), but only in poor yield (22%); the main reaction product was a 8,14-seco compound, **16**. This disappointing result can be explained in the following way. As is known from the literature,[5] the DDQ dehydrogenation of saturated ketones consists of β-axial hydride ion abstraction from the ketone enolate, followed by the stabilization of the intermediate carbonium ion by reorganization of electrons to α,β-unsaturated ketone. In our case, however, the intermediate carbonium ion **14** formed from the enolate **1c** can stabilize in two competing ways, a and b, as depicted in Scheme III. The tricyclic compound **16** was re-