[Chem. Pharm. Bull. 22(5)1140—1144(1974)]

UDC 547.92.057 : 615.36.011.5

Syntheses of C_{20} 13α-Steroidal Progestagens[1]

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(Received September 17, 1973)

In order to examine the physiological activity the preparation of 3,17-dihydroxy-19-nor-13α-pregna-1,3,5(10)-trien-20-one 17-acetates (IIId, IXc) has been undertaken. The Grignard reaction of 13α-estrone (I) with ethynylmagnesium bromide provided two epimeric 17-ethynyl-17-ols (II, VIIIa), which on hydration were led to 3,17-dihydroxy-19-nor-13α-pregnatrien-20-ones (IIIa, IXa). Elucidation of the stereochemistry at C-17 was attained by the degradative means. First, IIIa was submitted to metal hydride reduction, usual acetylation followed by Serini reaction to afford 19-nor-13α-pregnatrien-20-one (V). Upon treatment with base V was readily transformed into the thermodynamically much more stable 17α-epimer (VIb), whose structure was confirmed by leading to the known 13α-estratriene-3,17α-diol (VIIa) employing Baeyer-Villiger reaction. The desired compounds were unequivocally obtained from the 3,17-diacetates (IIIc, IXb) by partial hydrolysis, respectively.

In a previous paper of this series we reported the syntheses of C-17 epimeric 5α,13α-pregnane derivatives. Of these compounds 17α-ethynyl-13α-testosterone exhibited a progestational potency almost equivalent to that of progesterone.[3] The result is of great theoretical interest since this is the first demonstration of a physiologically active steroid in the 13α-series. Further interest in the structure-activity relationship of the 13α-steroids prompted us to examine the 19-nor-13α-pregnane derivatives having the aromatic ring A.

The preparation of the desired compounds was undertaken along the route previously established.[3,4] 13α-Estrone (I), readily obtainable from estrone by photochemical reaction,[5] was first subjected to Grignard reaction with ethynylmagnesium bromide in tetrahydrofuran. The product could be efficiently separated by column chromatography on silica gel and then by preparative thin-layer chromatography (TLC) into two C-17 epimeric 17-ethynyl-17-ols (II and VIIIa) in a ratio of *ca.* 5 to 1. When treated with mercury-resin used as a catalyst,[6] the less polar epimer, II, was hydrated with ease to afford 3,17-dihydroxy-19-nor-13α-pregnatrien-20-one (IIIa).

The stereochemistry at C-17 was elucidated by leading to the known compound employing Serini reaction[7] followed by Baeyer-Villiger oxidation. Reduction of IIIa with lithium aluminum hydride and subsequent acetylation yielded the 17,20-glycol 20-acetate (IV), which in turn was subjected to further step without purification. When refluxed with granulated zinc in xylene, IV was led to 19-norpregnatrien-20-one (V) along the configurational inversion of the side chain. Upon brief exposure to methanolic alkali, V was easily transformed into the thermodynamically much more stable 17α-epimer (VIa). Treatment of the 3-acetate

1) This paper constitutes Part XVII of the series entitled "Studies on Cardiotonic Steroid Analogs"; Part XVI: T. Nambara and J. Goto, *Chem. Pharm. Bull.* (Tokyo), **21**, 2209 (1973).
2) Location: *Aobayama, Sendai.*
3) T. Nambara, J. Goto, A. Sasaki, and K. Sudo, *Chem. Pharm. Bull.* (Tokyo), **21**, 565 (1973).
4) T. Nambara and J. Goto, *Chem. Pharm. Bull.* (Tokyo), **19**, 1937 (1971).
5) T. Nambara, T. Kudo, H. Hosoda, K. Motojima, and S. Goya, *Chem. Pharm. Bull.* (Tokyo), **17**, 2366 (1969) and references quoted therein.
6) M.S. Newman, *J. Am. Chem. Soc.*, **75**, 4740 (1953).
7) A. Serini, W. Logemann, and W. Hildebrand, *Ber.*, **72**, 391 (1939); L.F. Fieser and Huang-Minlon, *J. Am. Chem. Soc.*, **71**, 1840 (1949).

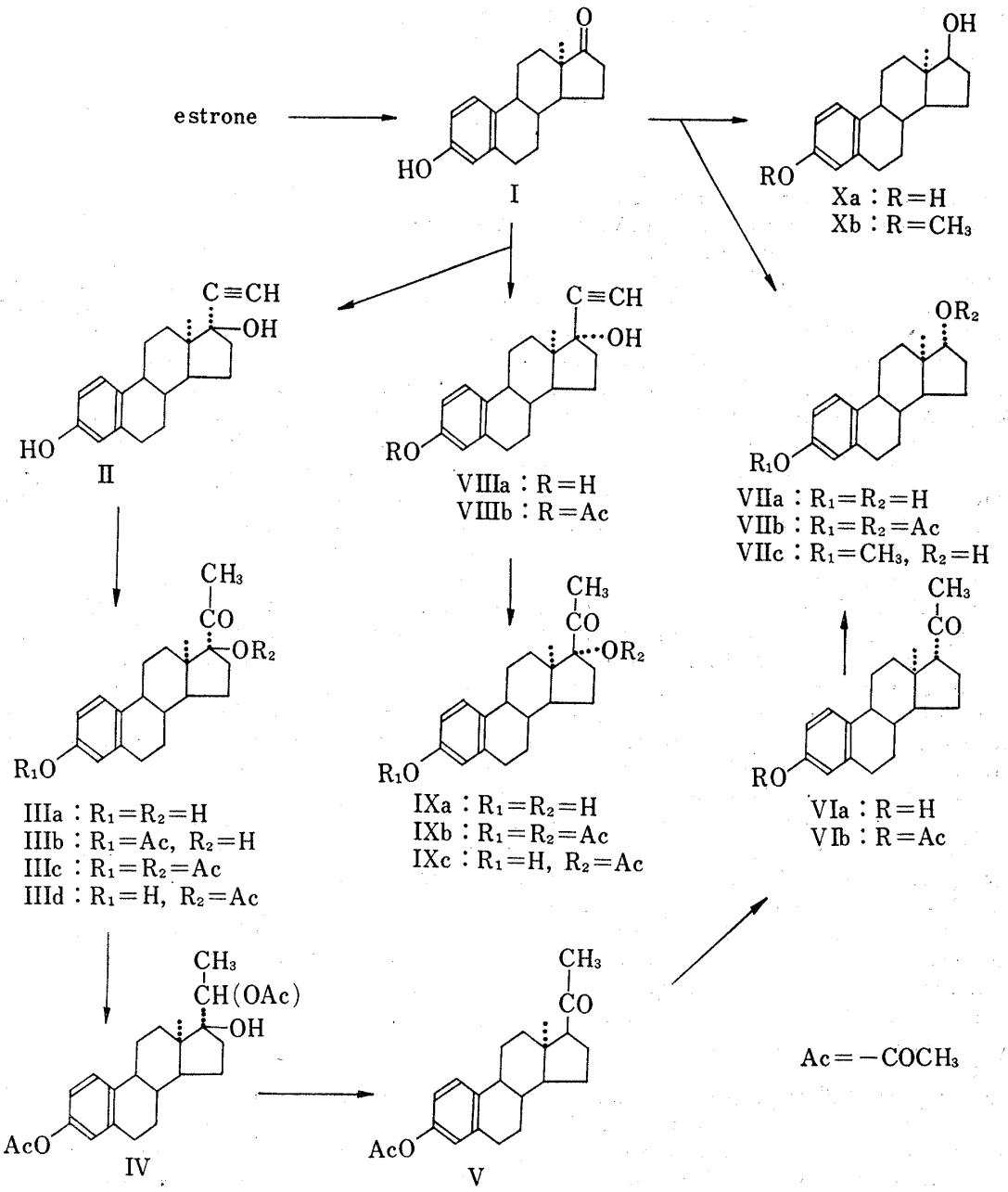

Chart 1

(VIb) with *m*-chloroperbenzoic acid furnished the 17-acetoxy derivative (VIIb) with retention of configuration at C-17.[8] Hydrolytic cleavage of the 3,17-diacetate with alkali gave 13α-estratriene-3,17α-diol (VIIa), whose structure was unambiguously characterized by direct comparison with the authentic specimen. It is evident from these results that the C-17 acetyl group in VI and hence the ethynyl group in II should be both α.

Similarly, hydration of the triple bond in VIIIa with mercury-resin resulted in formation of the corresponding 17β-acetyl derivative (IXa). Being treated with acetic anhydride in the presence of anhydrous *p*-toluenesulfonic acid, both IIIa and IXa were converted into the 3,17-diacetates (IIIc, IXb) in a satisfactory yield. Treatment of IIIc and IXb with potassium bicarbonate under the mild conditions effected the partial hydrolysis to provide the desired 17-monoacetates (IIId, IXc), respectively.

8) It is sufficiently substantiated that Baeyer-Villiger oxidation proceeds with retention of configuration.[9]
9) L.F. Fieser and M. Fieser, "Steroids," Reinhold Publ. Co., New York, 1959, p. 338.

The details of bioassay results on these C_{20} 13α-steroids will be reported elsewhere in near future.

Experimental[10]

Grignard Reaction of 3-Hydroxy-13α-estra-1,3,5(10)-trien-17-one (13α-Estrone) (I) with Ethynylmagnesium Bromide——To a solution of CH≡CMgBr[11] in anhydrous tetrahydrofuran (THF) (0.5N, 200 ml) was added I (2 g) and refluxed for 6 hr. The resulting solution was poured into a cold saturated NH_4Cl solution and extracted with AcOEt. The organic layer was washed with 5% HCl, H_2O and dried over anhydrous Na_2SO_4. After evaporation of solvent a crystalline product was treated with Ac_2O (12 ml) and pyridine (15 ml). On usual work-up the crude product obtained was submitted to chromatography on silica gel (40 g) and eluted with hexane–benzene (1:2 and 1:4 to 1:10). The more polar fraction was dissolved in 3% methanolic KOH (2 ml) and allowed to stand at room temperature overnight. The resulting solution was diluted with AcOEt, washed with H_2O, and dried over anhydrous Na_2SO_4. After evaporation of solvent a crystalline product obtained was recrystallized from acetone–hexane to give 17β-ethynyl-13α-estra-1,3,5(10)-triene-3,17-diol (VIIIa) (60 mg) as colorless needles. mp 184—185°. $[\alpha]_D^{25}$ +142.5° (c=0.08, MeOH). *Anal.* Calcd. for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 80.87; H, 8.20. IR ν_{max}^{KBr} cm^{-1}: 3270 (–C≡CH), 1625, 1600, 1510 (C=C). NMR (4% solution in CD_3OD) δ: 1.11 (3H, s, 18-CH_3), 2.72 (1H, s, –C≡CH), 6.43 (1H, d, J=3 Hz, 4-H), 6.51 (1H, q, J=3 and 8 Hz, 2-H), 6.98 (1H, d, J=8 Hz, 1-H).

The less polar fraction was dissolved in 3% methanolic KOH (5 ml) and allowed to stand at room temperature overnight. The resulting solution was diluted with AcOEt, washed with H_2O, and dried over anhydrous Na_2SO_4. After evaporation of solvent a crystalline product obtained was dissolved in THF (10 ml). To this solution was added $NaBH_4$ (100 mg) and allowed to stand at room temperature overnight. The resulting solution was extracted with AcOEt, washed with H_2O, and dried over anhydrous Na_2SO_4. After usual work-up a crystalline product obtained was submitted to preparative TLC on Silica gel HF using benzene–AcOEt (15:1) as developing solvent. Elution of the adsorbent corresponding to the Spot (*Rf* 0.10—0.25) with AcOEt and recrystallization of the eluate from acetone–hexane gave 17α-ethyl-13α-estra-1,3,5(10)-triene-3,17-diol (II) (295 mg) as colorless plates. mp 205—206°. $[\alpha]_D^{26}$ +75.0° (c=0.06). *Anal.* Calcd. for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 80.99; H, 8.35. IR ν_{max}^{KBr} cm^{-1}: 3300 (–C≡CH), 1615, 1600, 1510 (C=C). NMR (4% solution in CD_3OD) δ: 1.05 (3H, s, 18-CH_3), 2.72 (1H, s, –C≡CH), 6.42 (1H, d, J=3 Hz, 4-H), 6.48 (1H, q, J=3 and 8 Hz, 2-H), 7.03 (1H, d, J=8 Hz, 1-H).

The adsorbent of the area corresponding to *Rf* 0.05—0.10 was eluted with AcOEt. To a solution of the eluate (800 mg) in CH_2Cl_2 (70 ml) was added pyridine (12.5 ml)-CrO_3 (1.7 g) complex at 0° and stirred at room temperature for 3 hr. The precipitate was removed by decantation and washed with ether. The supernatant and washings were combined and evaporated. The residue was taken up in ether, washed with 5% NaOH, 5% HCl, 5% $NaHCO_3$, and H_2O, successively, and dried over anhydrous Na_2SO_4. After evaporation of solvent a crude product obtained was recrystallized from MeOH to give unchanged I (400 mg) as colorless prisms.

3,17β-Dihydroxy-19-nor-13α-pregna-1,3,5(10)-trien-20-one (IIIa)——To an ethanolic solution (6 ml) of II (190 mg) were added Hg-Dowex 50 (1.85 g) and H_2O (0.6 ml) and refluxed for 1.5 hr. The reaction mixture was filtered and the filtrate was diluted with AcOEt, washed with H_2O, and dried over anhydrous Na_2SO_4. After evaporation of solvent a crystalline product obtained was recrystallized from benzene to give IIIa (134 mg) as colorless needles. mp 194—196°. $[\alpha]_D^{25}$ +123.1° (c=0.13). *Anal.* Calcd. for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34. Found: C, 76.76; H, 8.48. IR ν_{max}^{KBr} cm^{-1}: 1705 (C=O), 1615, 1600, 1510 (C=C). NMR (4% solution in $CDCl_3$) δ: 0.98 (3H, s, 18-CH_3), 2.29 (1H, s, 21-CH_3), 6.52 (1H, d, J=3 Hz, 4-H), 6.58 (1H, q, J=3 and 8 Hz, 2-H), 7.10 (1H, d, J=8 Hz, 1-H).

3,17β-Dihydroxy-19-nor-13α-pregna-1,3,5(10)-trien-20-one 3-Acetate (IIIb)——Treatment of IIIa (30 mg) with Ac_2O (0.5 ml) and pyridine (1 ml) in the usual manner followed by recrystallization from acetone–hexane gave IIIb (27 mg) as colorless plates. mp 101—103°. $[\alpha]_D^{25}$ +103.3° (c=0.15). *Anal.* Calcd. for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92. Found: C, 74.17; H, 7.84. IR ν_{max}^{KBr} cm^{-1}: 1770, 1710 (C=O), 1615, 1590, 1505 (C=C). NMR (4% solution in $CDCl_3$) δ: 0.97 (3H, s, 18-CH_3), 2.25 (3H, s, 3-$OCOCH_3$), 2.28 (3H, s, 21-CH_3), 6.73 (1H, d, J=3 Hz, 4-H), 6.80 (1H, q, J=3 and 8 Hz, 2-H), 7.23 (1H, d, J=8 Hz, 1-H).

3,17β-Dihydroxy-19-nor-13α-pregna-1,3,5(10)-trien-20-one Diacetate (IIIc)——A solution of IIIa (170 mg) in Ac_2O (8 ml) was stirred with anhydrous *p*-TsOH (170 mg) at room temperature for 2 hr. The

10) All melting points were taken on a micro hot-stage apparatus and are uncorrected. Optical rotations were measured in $CHCl_3$ unless otherwise specified. Infrared (IR) spectra were run on JASCO Model IRA-1 spectrometer. Nuclear magnetic resonance (NMR) spectra were recorded on Hitachi Model R-20A spectrometer at 60 MHz using tetramethylsilane as an internal standard. Abbreviation used s=singlet, d=doublet, q=quartet, and m=multiplet.

11) T. Nambara, J. Goto, Y. Fujimura, and Y. Kimura, *Chem. Pharm. Bull.* (Tokyo), **19**, 1137 (1971).

reaction mixture was poured into ice-water and extracted with AcOEt. The organic layer was washed with 5% $NaHCO_3$, H_2O and dried over anhydrous Na_2SO_4. After evaporation of solvent a crystalline product obtained was recrystallized from acetone–hexane to give IIIc (178 mg) as colorless needles. mp 125—126°. $[\alpha]_D^{25}$+95.5° (c=0.11). *Anal.* Calcd. for $C_{24}H_{30}O_5$: C, 72.33; H, 7.59. Found: C, 72.41; H, 7.64. IR ν_{max}^{KBr} cm^{-1}: 1770, 1735, 1725 (C=O), 1610, 1590, 1500 (C=C). NMR (4% solution in $CDCl_3$) δ: 0.88 (3H, s, 18-CH_3), 2.01 (3H, s, 17β-OCOCH_3), 2.14 (3H, s, 21-CH_3), 2.27 (3H, s, 3-OCOCH_3), 6.76 (1H, d, J=3 Hz, 4-H), 6.83 (1H, q, J=3 and 8 Hz, 2-H), 7.27 (1H, d, J=8 Hz, 1-H).

3,17β-Dihydroxy-19-nor-13α-pregna-1,3,5(10)-trien-20-one 17-Acetate (IIId)——A solution of IIIc (140 mg) in 1% $KHCO_3$/aq. MeOH (25 ml) was allowed to stand at room temperature for 50 min. The resulting solution was diluted with AcOEt, washed with H_2O, and dried over anhydrous Na_2SO_4. After evaporation of solvent a crystalline product was recrystallized from acetone–hexane to give IIId (113 mg) as colorless prisms. mp 111—113°. $[\alpha]_D^{25}$+113.3° (c=0.15). *Anal.* Calcd. for $C_{22}H_{28}O_4$: C, 74.13: H, 7.92. Found: C, 74.62; H, 8.14. IR ν_{max}^{KBr} cm^{-1}: 1740, 1700 (C=O), 1623, 1590, 1510 (C=C). NMR (4% solution in $CDCl_3$) δ: 0.88 (3H, s, 18-CH_3), 1.99 (3H, s, 21-CH_3), 2.16 (3H, s, 17β-OCOCH_3), 6.56 (1H, d, J=3 Hz, 4-H), 6.63 (1H, q, J=3 and 8 Hz, 2-H), 7.24 (1H, d, J=8 Hz, 1-H).

3-Hydroxy-19-nor-13α,17α-pregna-1,3,5(10)-trien-20-one (VIa)——To a solution of IIIa (428 mg) in anhydrous THF (30 ml) was added $LiAlH_4$ (270 mg) and refluxed for 2.5 hr. To this solution was added moistened ether to decompose the excess reagent, diluted with AcOEt, and acidified with 5% HCl. The organic layer was separated, washed with H_2O, and dried over anhydrous Na_2SO_4. After evaporation of solvent an oily residue was treated with Ac_2O (2.5 ml) and pyridine (3 ml) in the usual manner. On usual work-up 19-nor-13α,17α-pregna-1,3,5(10)-triene-3,17,20-triol 3,20-diacetate (IV) was obtained as an oily product. To a solution of IV in xylene (13 ml) was added granulated Zn (6.4 g) and refluxed under a stream of N_2 gas for 17 hr. The reaction mixture was filtered and the filtrate was evaporated. An oily residue obtained was submitted to preparative TLC on Silica gel HF using benzene–AcOEt (20: 1) as developing solvent. The adsorbent of the area corresponding to Rf 0.50—0.60 was eluted with AcOEt. On usual work-up 3-hydroxy-19-nor-13α-pregna-1,3,5(10)-trien-20-one acetate (V) (252 mg) was obtained as an oily product. NMR (4% solution in CD_3OD) δ: 1.33 (3H, s, 18-CH_3), 2.16 (3H, s, 21-CH_3), 2.21 (3H, s, 3-OCOCH_3). A solution of V (250 mg) in 3% methanolic KOH (6 ml) was allowed to stand at room temperature for 6.5 hr. The resulting solution was diluted with AcOEt, washed with H_2O, and dried over anhydrous Na_2SO_4. After evaporation of solvent a crystalline product was recrystallized from aq. MeOH to give VIa (148 mg) as colorless plates. mp 173—175°. $[\alpha]_D^{25}$−34.6° (c=0.13, MeOH). *Anal.* Calcd. for $C_{20}H_{26}O_2$: C, 80.49; H, 8.78. Found: C, 80.63; H, 8.90. IR ν_{max}^{KBr} cm^{-1}: 1685 (C=O), 1625, 1590, 1510 (C=C). NMR (4% solution in CD_3OD) δ: 0.86 (3H, s, 18-CH_3), 2.11 (3H, s, 21-CH_3), 6.46 (1H, d, J=3 Hz, 4-H), 6.53 (1H, q, J=3 and 8 Hz, 2-H), 7.11 (1H, d, J=8 Hz, 1-H).

3-Hydroxy-19-nor-13α,17α-pregna-1,3,5(10)-trien-20-one Acetate (VIb)——Treatment of VIa (34 mg) with Ac_2O (0.5 ml) and pyridine (1 ml) in the usual manner followed by recrystallization from acetone–hexane gave VIb (25 mg) as colorless plates. mp 102—103.5°. $[\alpha]_D^{25}$+50.0° (c=0.06). *Anal.* Calcd. for $C_{22}H_{28}O_3$: C, 77.61; H, 8.29. Found: C, 77.32; H, 8.39. NMR (4% solution in CD_3OD) δ: 0.87 (3H, s, 18-CH_3), 2.11 (3H, s, 21-CH_3), 2.22 (3H, s, 3-OCOCH_3), 6.72 (1H, d, J=3 Hz, 4-H), 6.78 (1H, q, J=3 and 8 Hz, 2-H), 7.22 (1H, d, J=8 Hz, 1-H).

Baeyer-Villiger Oxidation of VIb——To a solution of VIb (30 mg) in $CHCl_3$ (3 ml) was added m-chloroperbenzoic acid (120 mg) and stirred at 35° for 30 hr. The reaction mixture was diluted with $CHCl_3$, washed with 5% $NaHSO_3$, 5% $NaHCO_3$, and H_2O, successively, and dried over anhydrous Na_2SO_4. After usual work-up an oily residue obtained was submitted to preparative TLC on Silica gel HF using benzene–AcOEt (15: 1) as developing solvent. The adsorbent of the area corresponding to Rf 0.40—0.60 was eluted with AcOEt. Evaporation of solvent gave 13α-estra-1,3,5(10)-triene-3,17α-diol diacetate (VIIb) as an oily product, which in turn was treated with 3% methanolic KOH (2 ml) at room temperature overnight. The resulting solution was diluted with AcOEt, washed with H_2O, and dried over anhydrous Na_2SO_4. After evaporation of solvent a crystalline product obtained was recrystallized from acetone-hexane to give 13α-estra-1,3,5(10)-triene-3,17α-diol (VIIa) (10 mg) as colorless prisms. mp 197—200°. Mixed melting point on admixture with the authentic sample showed no depression and IR spectra of two samples were entirely identical in every respect.

17β-Ethynyl-13α-estra-1,3,5(10)-triene-3,17-diol 3-Acetate (VIIIb)——Treatment of VIIIa (20 mg) with Ac_2O (0.5 ml) and pyridine (1 ml) in the usual manner followed by recrystallization from acetone–hexane gave VIIIb (16 mg) as colorless plates. mp 119—120°. $[\alpha]_D^{25}$+123.3° (c=0.15). *Anal.* Calcd. for $C_{22}H_{26}O_3$: C, 78.07; H, 7.74. Found: C, 78.23; H, 7.93. NMR (4% solution in $CDCl_3$) δ: 1.16 (3H, s, 18-CH_3), 2.26 (3H, s, 3-OCOCH_3), 2.48 (1H, s, -C≡CH), 6.76 (1H, d, J=3 Hz, 4-H), 6.82 (1H, q, J=3 and 8 Hz, 2-H), 7.21 (1H, d, J=8 Hz, 1-H).

3,17α-Dihydroxy-13α-pregna-1,3,5(10)-trien-20-one (IXa)——To an ethanolic solution (5 ml) of VIIIa (100 mg) were added Hg-Dowex 50 (1 g) and H_2O (0.5 ml) and refluxed for 1 hr. The reaction mixture was processed in the manner as described in IIIa. A crystalline product obtained was recrystallized from acetone–hexane to give IXa (62 mg) as colorless plates. mp 205—208°. $[\alpha]_D^{25}$+104.5° (c=0.11, MeOH). *Anal.* Calcd. for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34. Found: C, 76.16; H, 8.49. IR ν_{max}^{KBr} cm^{-1}: 1700 (C=O), 1617, 1590, 1507

(C=C). NMR (4% solution in CD_3OD) δ: 1.23 (3H, s, 18-CH_3), 2.21 (3H, s, 21-CH_3), 6.42 (1H, d, J=3 Hz, 4-H), 6.50 (1H, q, J=3 and 8 Hz, 2-H), 6.93 (1H, d, J=8 Hz, 1-H).

3,17α-Dihydroxy-13α-pregna-1,3,5(10)-trien-20-one Diacetate (IXb)——A solution of IXa (45 mg) in Ac_2O (2 ml) was stirred with anhydrous *p*-TsOH (45 mg) at room temperature for 2 hr. The reaction mixture was processed in the manner as described in IIIc to give IXb (48 mg) as an oily product. NMR (4% solution in $CDCl_3$) δ: 1.30 (3H, s, 18-CH_3), 2.10 (6H, s, 17α-$OCOCH_3$ and 21-CH_3), 2.24 (3H, s, 3-$OCOCH_3$).

3,17α-Dihydroxy-13α-pregna-1,3,5(10)-trien-20-one 17-Acetate (IXc)——A solution of IXb (45 mg) in 1% $KHCO_3$/aq. MeOH (2.5 ml) was allowed to stand at room temperature for 80 min. The resulting solution was diluted with AcOEt, washed with H_2O, and dried over anhydrous Na_2SO_4. After evaporation of solvent a crystalline product obtained was recrystallized from acetone–hexane to give IXc (30 mg) as colorless plates. mp 208—209°. $[\alpha]_D^{26}$+75.0° (c=0.10). *Anal.* Calcd. for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92. Found: C, 74.04; H, 8.01. IR ν_{max}^{KBr} cm^{-1}: 1710, 1700 (C=O), 1614, 1594, 1505 (C=C). NMR (4% solution in $CDCl_3$) δ: 1.39 (3H, s, 18-CH_3), 2.10 (6H, s, 21-CH_3 and 17α-$OCOCH_3$), 6.45 (1H, d, J=3 Hz, 4-H), 6.54 (1H, q, J=3 and 8 Hz, 2-H), 6.96 (1H, d, J=8 Hz, 1-H).

Reduction of I with Sodium Borohydride——To a stirred solution of I (118 mg) in THF (8 ml) was added $NaBH_4$ (60 mg) at 0° and allowed to stand at room temperature for 1 hr. After decomposition of excess $NaBH_4$ with AcOH (2 drops) the reaction mixture was diluted with AcOEt, washed with 5% $NaHCO_3$ and H_2O, and dried over anhydrous Na_2SO_4. After evaporation of solvent a crystalline product obtained was submitted to preparative TLC using benzene–AcOEt (2: 1) as developing solvent. Elution of the adsorbent corresponding to the spot (*Rf* 0.60—0.65) with AcOEt and recrystallization of the eluate from acetone–hexane gave 13α-estra-1,3,5(10)-triene-3,17α-diol (VIIa) (22 mg) as colorless prisms. mp 199—201°. $[\alpha]_D^{25}$−34.6° (c=0.13, MeOH). *Anal.* Calcd. for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.20; H, 9.01.

Elution of the adsorbent corresponding to the spot (*Rf* 0.70—0.75) with AcOEt and recrystallization of the eluate from acetone–hexane gave 13α-estra-1,3,5(10)-triene-3,17β-diol (Xa) (35 mg) as colorless needles. mp 190—192°. $[\alpha]_D^{24}$+28.1° (c=0.06, MeOH). *Anal.* Calcd. for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.54; H, 8.98.

3-Methoxy-13α-estra-1,3,5(10)-trien-17α-ol (VIIc)——Treatment of VIIa with Me_2SO_4 and KOH in the usual manner followed by recrystallization from aq. MeOH gave VIIc as colorless needles. mp 132—136°. Mixed melting point on admixture with the authentic sample[5] showed no depression and IR spectra of two samples were entirely identical in every respect.

3-Methoxy-13α-estra-1,3,5(10)-trien-17β-ol (Xb)——Treatment of Xa with Me_2SO_4 and KOH in the usual manner followed by recrystallization from aq. MeOH gave Xb as colorless needles. mp 75—78°. Mixed melting point on admixture with the authentic sample[5] showed no depression and IR spectra of two samples were entirely identical in every respect.

Acknowledgement The authors are indebted to all the staffs of central analytical laboratory of this Institute for elemental analyses and spectral measurements.