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1,4-Addition of Vinylmagnesium Bromide to α,β-Unsaturated Steroidal Ketones. I. Reaction of 16-En-20-oxo and 19-Nor-4-en-3-oxo Steroids

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The reaction of 16-en-20-oxo and 19-nor-4-en-3-oxo steroids with vinylmagnesium bromide in the presence of cupric acetate afforded 16α-vinyl-20-oxo and 19-nor-5β-vinyl-3-oxo steroids. In order to establish the configuration of vinyl group introduced by the reaction and to study the streochemical relationship between the reaction with vinylmagnesium bromide and that with a saturated Grignard reagent, some transformations of vinyl compounds derived by the reaction were undertaken. The stereochemical course of reactions was found to be identical with that of a saturated Grignard reagent.

It is well known that methyl-Grignard reagent reacts with some α,β-unsaturated steroidal ketones to give 1,4-addition products. Thus, 20-oxo-16-ene (I),[2] 3-oxo-4-ene (II),[3] A/B-*trans*-3-oxo-1-ene (III),[4] A/B-*cis*-3-oxo-1-ene (IV)[5] and 3β-hydroxy-6-oxo-4-ene (V)[6] may be transformed into the corresponding 1,4-addition products, 16α-methyl-20-one (VI), 5β-methyl-3-one (VII), A/B-*trans*-1α-methyl-3-one (VIII), A/B-*cis*-1β-methyl-3-one (IX) and A/B-*trans*-3β-hydroxy-4β-methyl-6-one (X), by treatment with a methyl-Grignard reagent

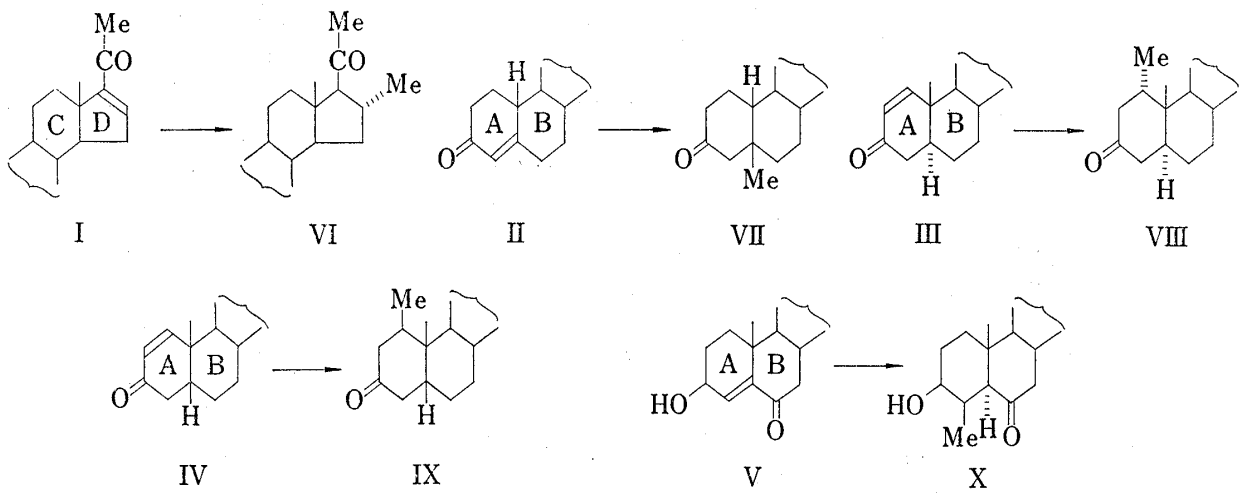

Chart 1

1) Location: *1604 Shimosakunobe, Takatsu-ku, Kawasaki.*
2) R.E. Marker and H.M. Crooks, Jr., *J. Am. Chem. Soc.*, **64**, 1280 (1942); K. Heusler, J. Kebrle, C. Meystre, H. Ueberwasser, P. Wieland, G. Anner, and A. Wettstein, *Helv. Chim. Acta*, **42**, 2043 (1959); E.P. Oliveto, R. Rausser, A.L. Nussbaum, W. Gebert, E.B. Hershberg, S. Tolksdorf, M. Eisler, and P.L. Perlman, *J. Am. Chem. Soc.*, **80**, 4428 (1958); G.E. Arth, D.B.R. Johnston, J. Fried, W.W. Spooneer, D.R. Hoff, and L.H. Sarett, *ibid.*, **80**, 3160 (1958).
3) H. Mori, *Chem. Pharm. Bull.* (Tokyo), **10**, 382 (1962); A.J. Birch and M. Smith, *Proc. Chem. Soc.*, **1962**, 356.
4) H. Mori, *Chem. Pharm. Bull.* (Tokyo), **10**, 386 (1962); R. Wiechert, U. Kerb, and K. Kieslich, *Chem. Ber.*, **96**, 2765 (1963).
5) D. Bertin and Perrannet, *Bull. Soc. Chim. France*, **11**, 2782 (1964) [*C.A.*, 62, 7826*a* (1965)]; W.J. Wechter, *J. Org. Chem.*, **29**, 163 (1964); W.J. Wechter, G. Slomp, and F.A. Mackllar, *Tetrahedron*, **21**, 1625 (1965).
6) H. Mori, *Chem. Pharm. Bull.* (Tokyo), **12**, 1224 (1964).

in the presence of cuprous chloride or cupric acetate. Stereochemical course of 1,4-addition is discussed in the literature and it is concluded that the methyl group introduced by the reaction is usually axially oriented.[6,7] This and the following papers describe the reaction of vinyl-Grignard reagent with α,β-unsaturated steroidal ketones and the stereochemistry of their products.

The Grignard reaction of 3β-acetoxy-5α-pregn-16-en-20-one (XI) with vinylmagnesium bromide in the presence of cupric acetate afforded a saturated ketone. In nuclear magnetic resonance (NMR) spectrum, a vinyl group appears at 4.6—5.9 ppm as a multiplet. Since a saturated carbonyl band was observed in its infrared (IR) absorption spectrum, the product was considered as a 1,4-addition product, 16-vinyl-20-oxo compound. This compound exhibits a positive Cotton effect curve in optical rotatory dispersion (ORD), which is coincident with that of the usual 20-oxopregnane compound.[8] In addition to these spectral data some transformations demonstrated its structure to be 16α-vinyl-3β-hydroxy-5α-pregnan-20-one (XII). The reduction of XII with lithium aluminum hydride gave the 20β-hydroxyl compound (XIVa). The configuration of 20-hydroxyl group was assigned tentatively on analogy

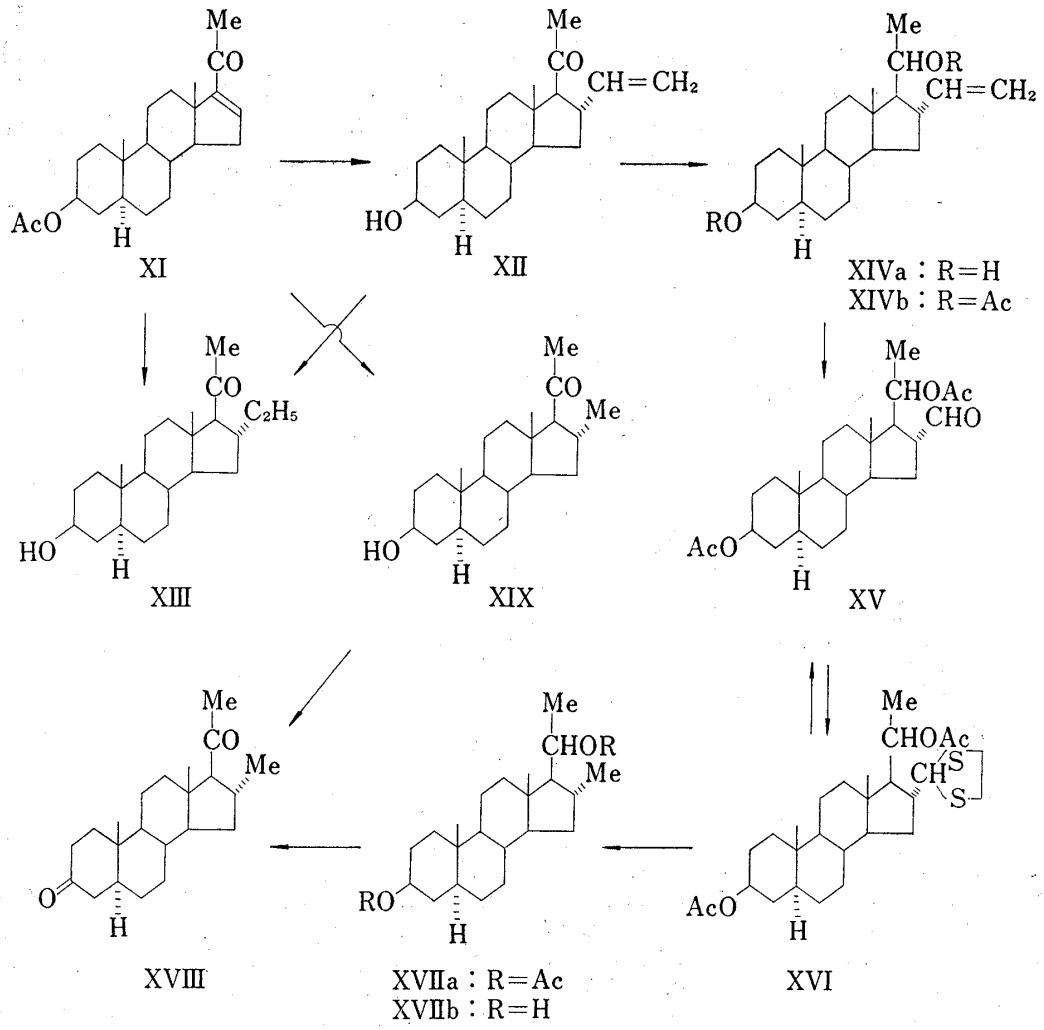

Chart 2

7) H.O. House and H.W. Thompson, *J. Org. Chem.*, **28**, 360 (1963).
8) P. Crabbe, "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," Holden-Day, San Francisco, 1965, p. 134.

with the reduction of the usual 20-oxo compound.[9] After acetylation of XIVa, ozonolysis followed by treatment with zinc dust and acetic acid afforded the aldehyde (XV). Since the aldehyde was difficult to be crystallized and was considered to be unstable, the crude oily product was treated with ethanedithiol and boron trifluoride etherate to afford the thioketal (XVI). Isomerization of the aldehyde at C-16 in this reaction was excluded by the experimental evidence that the aldehyde (XV) was recovered after hydrolysis of the thioketal (XVI) by the catalysis of mercuric chloride and yellow mercuric oxide.[10] The reductive desulfurization of the thioketal (XVI) with Raney nickel gave the 16-methyl compound (XVIIa), which exhibits a signal for 16-methyl group at 1.07 ppm as a doublet in its NMR spectrum.

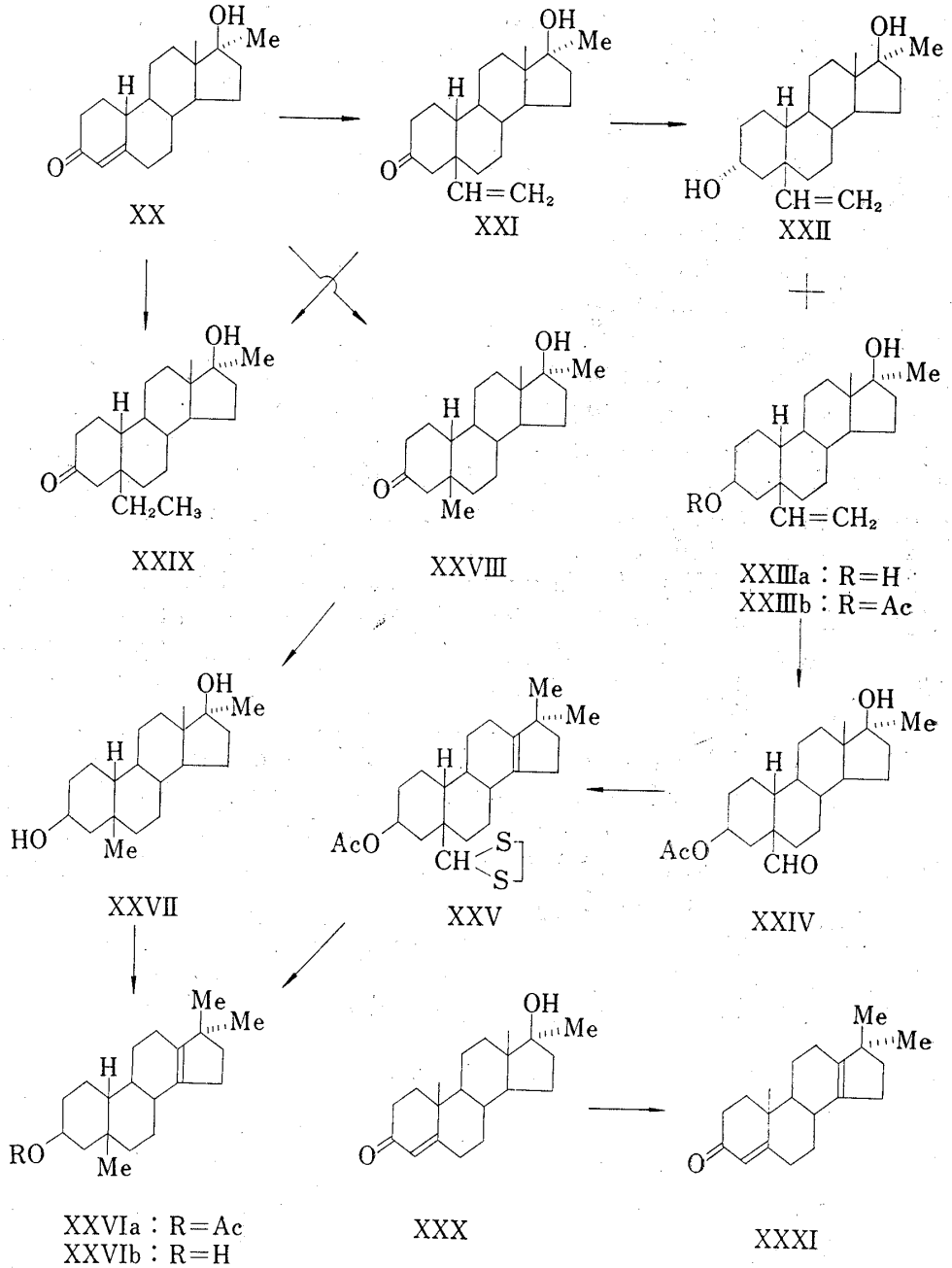

Chart 3

9) W. Klyne and E. Miller, *J. Chem. Soc.*, **1950**, 1972; D.N. Kirk, "Steroid Reaction Mechanisms," Elsevier Publishing Co., Amsterdam, 1960, p. 49.
10) W.G. Overend, M. Stacey, and J. Stanek, *J. Chem. Soc.*, **1949**, 2841.

Hydrolysis of XVIIa followed by oxidation with the Jones reagent gave the diketone (XVIII). This compound was identical with the compound derived from the known 16α-methyl compound (XIX) by oxidation with the Jones reagent. Thus, the configuration at C-16 and C-17 was confirmed as described above.

The reaction of XI with ethylmagnesium bromide yielded the 16-ethyl compound (XIII). The catalytic hydrogenation of XII with palladium-charcoal gave a compound identical with XIII. Accordingly, the stereochemical courses are all the same in the reactions with methyl-, ethyl- and vinyl-Grignard reagents.

The 19-nor-3-oxo-4-ene steroid (XX) was treated with vinylmagnesium bromide in a similar manner as described above to give a saturated ketone. The presence of a six-membered carbonyl group and vinyl group was proved from IR and NMR data. A negative Cotton effect curve in its ORD showed that A/B-ring juncture is *cis*.[11] These data suggest that the compound must be formulated as 17β-hydroxy-17-methyl-5β-vinylestran-3-one (XXI). This conclusion was also supported by chemical transformations as will be described below. Reduction of XXI with sodium borohydride gave a mixture of 3-epimers, from which the diols (XXII and XXIIIa) were isolated by thin-layer chromatography. The product with higher melting point (mp 182—183°), XXIIIa, was considered to be a 3β-epimer, because a smaller half-band width of the signal of 3-proton was observed in its NMR spectrum.[12] Accordingly, another epimer must be the 3α-epimer. The acetate (XXIIIb) derived from XXIIIa was ozonized and treated with zinc dust and acetic acid to give the aldehyde (XXIV). The thioketalization of the aldehyde (XXIV) gave a thioketal (XXV). Since its IR spectrum showed the absence of a hydroxyl group in this thioketal, this reaction should be accompanied by the reaction in ring D. The Wagner-Meerwein rearrangement of a 17β-hydroxyl steroid with potassium hydrogen sulfate in acetic acid, in which C-18 angular methyl group migrates from C-13 to C-17β, was reported.[13] It is natural to consider that such a rearrangement would occur in this thioketalization reaction. In fact, it was found that the treatment of 17α-methyltestosterone (XXX) with boron trifluoride etherate in acetic acid, which is the same reaction condition as in thioketalization except for the absence of ethanedithiol, afforded the known rearrangement product, XXXI.[14] Thus, the structure of XXV should be given to the thioketal. The reductive desulfuration of XXV with Raney nickel afforded the 5β-methyl compound (XXVIa), which on hydrolysis with alkali gave 3β-hydroxyl compound (XXVIb). The known 5β-methyl compound (XXVIII),[2] easily derived from XX, was reduced with sodium borohydride to 3β-hydroxyl compound (XXVII). The treatment of XXVII with boron trifluoride etherate in acetic acid gave the rearrangement product identical with the compound (XXVIa) described above. Accordingly, the configuration at C-5 in XXI and XXVIII was proved by chemical means.

The 1,4-addition of ethylmagnesium bromide in XX yielded XXIX, which was also obtained by the hydrogenation of XXI over palladium-charcoal. Here again the stereochemical courses of 1,4-addition in methyl-, ethyl-, and vinyl-magnesium bromide are the same.

Experimental

Melting points were taken on a melting point apparatus Mettler FP21. Optical rotations were measured in chloroform solution unless otherwise stated. Infrared spectra were measured with a spectrometer Hitachi EPI G_2 in a KBr disk. Nuclear magnetic resonance spectra were determined at 60 MHz with a spectrometer Hitachi R-20A in deuteriochloroform solution unless otherwise stated with tetramethylsilane as an internal standard.

11) C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., Inc., New York, 1960, p. 49.
12) N.S. Bhacca and D.H. Williams, "Application of NMR Spectroscopy in Organic Chemistry," Holden-Day, San Francisco. 1964, p. 79.
13) A. Cohen, J.W. Cook, and C.L. Hewwtt, *J. Chem. Soc.*, **1935**, 445.
14) E. Caspi and D.M. Piatak, *Can. J. Chem.*, **41**, 2294 (1963).

16α-Vinyl-3β-hydroxy-5α-pregnan-20-one (XII)——The Grignard reagent prepared from Mg (11 g), vinyl bromide (7 g) and tetrahydrofuran (THF) (220 ml) was added dropwise to a solution of 3β-acetoxy-5α-pregn-16-en-20-one (XI, 4.0 g) and cupric acetate (1.0 g) in THF (60 ml). After stirring was continued for 3 hr at room temperature, water was carefully added to decompose excess Grignard reagent. The organic layer was separated and the aqueous phase was extracted with ether. The combined organic solution was washed with 10% NH_4Cl, 5% Na_2CO_3 and water, and dried over Na_2SO_4. After evaporation of the solvent, recrystallization of the product from acetone gave 16α-vinyl-3β-hydroxy-5α-pregnan-20-one (XII, 1.03 g) as colorless needles, mp 181—182°. $[\alpha]_D^{26}$ +54° (c=1.00). IR cm^{-1}: 3450 (–OH), 1690 (C=O). NMR δ: 0.65 (3H, s, 18-CH_3), 0.79 (3H, s, 19-CH_3), 4.6—5.9 (3H, m, 16-CH_2=CH–). ORD (c=0.277, EtOH) $[\alpha]^{25}$ (mμ): +34° (700), +58° (589), +2340° (310), (peak), +2310° (312), −2530° (264), (trough), −2460°(260), −2300° (255). *Anal.* Calcd. for $C_{23}H_{36}O_2$: C, 81.18; H, 10.52. Found: C, 79.96; H, 10.62.

16α-Ethyl-3β-hydroxy-5α-pregnan-20-one (XIII)——a) To a solution of 3β-acetoxy-5α-pregnan-16-en-20-one (XI, 2.0 g) and cupric acetate (0.50 g) in THF (100 ml), the Grignard reagent prepared from Mg (4.8 g), C_2H_5Br (21.8 g) and THF (100 ml) was dropwise added with vigorous stirring at 0°. Stirring was continued at room temperature for 2 hr and the reaction mixture was worked up in the same manner described above to give 16α-ethyl-3β-hydroxy-5α-pregnan-20-one (XIII, 0.62 g) as colorless needles (from acetone), mp 177—182°. $[\alpha]_D^{22.5}$ 52° (c=1.00). IR cm^{-1}: 3400 (–OH), 1703, 1685 (C=O). NMR δ: 0.62 (3H, s, 18-CH_3), 0.81 (3H, s, 19-CH_3), 2.11 (3H, s, 21-CH_3). ORD (c=0.16, EtOH) $[\alpha]^{25}$ (mμ): +40° (700), +56° (589), +2320° (312), (peak), 2254° (314), +358° (290), −2550° (260), (trough), −2220° (312), −1887° (255). *Anal.* Calcd. for $C_{23}H_{38}O_2$: C, 79.72; H, 11.07. Found: C, 79.62; H, 11.19.

b) A mixture of 16α-vinyl-3β-hydroxy-5α-pregnan-20-one (XII, 0.10 g), 5% Pd-C (0.05 g) and EtOH (20 ml) was shaken in H_2 atmosphere (at atmospheric pressure). Hydrogen uptake was completed in 30 min. Catalyst was removed by filtration and the filtrate was evaporated to give XIII, the IR spectrum of which was the same as that for the compound obtained above.

16α-Vinyl-5α-pregnane-3β,20β-diol (XIVa)——A solution of 16α-vinyl-3β-hydroxy-5α-pregnan-20-one (XII, 1.61 g) in THF (60 ml) was treated with lithium aluminum hydride (0.40 g) for 2 hr at room temperature. Water was carefully added to decompose excess lithium aluminum hydride, the organic layer was separated and the aqueous phase was extracted with ether. The combined organic solution was washed with water and dried over Na_2SO_4. The solvent was evaporated and the product was purified by preparative thin layer chromatography (silica gel Merck GF_{254}: $CHCl_3$–acetone 9: 1) to give 16α-vinyl-5α-pregnane-3β,20β-diol (XIVa, 1.26 g) as colorless needles (from acetone–ether), mp 152—153°. $[\alpha]_D^{20}$ −24° (c=1.00). IR cm^{-1}: 3400 (–OH). *Anal.* Calcd. for $C_{23}H_{38}O_2 \cdot 1/2H_2O$: C, 77.69, H, 11.06. Found: C, 77.84; H, 11.09.

3β,20β-Diacetoxy-16α-methyl-5α-pregnane (XVIIa)——A solution of 16α-vinyl-5α-pregnane-3β,20β-diol (XIVa, 1.26 g) in pyridine (20 ml) and Ac_2O (10 ml) was allowed to stand at room temperature overnight. The reaction mixture was poured into ice water and the product was extracted with ether. The ethereal extract was washed with 10% HCl, 5% Na_2CO_3, and water, and dried over Na_2SO_4. After evaporation of the solvent the residue was recrystallized from ether–petroleum ether to give 3β,20β-diacetoxy-16α-vinyl-5α-pregnane (XIVb, 1.31 g). IR cm^{-1}: 1700 (C=O). NMR δ: 0.68 (3H, s, 18-CH_3), 0.80 (3H, s, 19-CH_3), 2.00 (6H, s, 3β- and 20β-OAc), 4.5—6.0 (3H, m, 16α-CH_2=CH–).

Ozone was introduced to a solution of the diol XIVb (0.99 g) in CH_2Cl_2 (60 ml) and pyridine (0.18 ml) until the peak of 909 cm^{-1} in IR spectrum was disappeared (for about 30 min). Zinc dust (1.5 g) was added to the reaction mixture and the suspension was stirred for 1 hr at room temperature. Zinc dust was removed by filtration and filtrate was washed with 5% Na_2CO_3 and water, and dried over Na_2SO_4. The solvent was evaporated *in vacuo* to give 3β,20β-diacetoxy-16α-formyl-5α-pregnane (XV, 1.17 g) as an oily product. IR cm^{-1} (in $CHCl_3$): 1720, 1710 (C=O). NMR δ: 0.71 (3H, s, 18-CH_3), 0.81 (3H, s, 19-CH_3), 2.01 (6H, s, 3β- and 20β-OAc), 9.58 (1H, d, J=3 Hz, 16α-CHO).

To a solution of the aldehyde XV (1.17 g) in AcOH (20 ml) was added ethanedithiol (2 ml) and boron trifluoride etherate (2 ml). After standing overnight at room temperature, the reaction mixture was poured into water and the product was extracted with ether. The ethereal layer was washed with 10% NaOH and water, and dried over Na_2SO_4. The solvent was evaporated to give the thioketal XVI (1.32 g) as an oily material. NMR δ: 0.78 (3H, s, 18-CH_3), 0.80 (3H, s, 19-CH_3), 2.00 (6H, s, 3β- and 20β-OAc), 3.1—3.5 (4H, m, –SCH_2CH_2S–).

A mixture of the thioketal XVI (1.17 g), Raney nickel (18 g) and EtOH (100 ml) was refluxed for 5 hr. Catalyst was removed by filtration and the filtrate was evaporated *in vacuo* to give 3β,20β-diacetoxy-16α-methyl-5α-pregnane (XVIIa, 0.68 g) as colorless needles (from ether–*n*-hexane), mp 98—101°. $[\alpha]_D^{26}$ +7° (c=1.00). IR cm^{-1}: 1715 (C=O). NMR δ: 0.66 (3H, s, 18-CH_3), 0.81 (3H, S, 19-CH_3), 1.07 (3H, d, J=6 Hz, 16α-CH_3), 1.23 (3H, d, J=6 Hz, 21-CH_3), 2.00 (6H, s, 3β- and 20β-OAc). *Anal.* Calcd. for $C_{26}H_{42}O_4$: C, 74.60; H, 10.11. Found: C, 74.33; H, 10.22.

Hydrolysis of the Thioketal XVI——To a solution of the thioketal XVI (0.10 g) in acetone (10 ml) was added mercuric chloride (0.30 g) and yellow mercuric oxide (0.30 g), and the suspension was refluxed for 15 min. After filtration of the reaction mixture and addition of pyridine (3.0 ml), the solution was allowed to stand overnight at room temperature. The resulting precipitate was filtered off and the filtrate was evapo-

rated *in vacuo* to give the formyl compound XV identical with the product obtained above in its IR and NMR spectra.

16α-Methyl-5α-pregnane-3,20-dione (XVIII)——a) A solution of 3β,20β-diacetoxy-16α-methyl-5α-pregnane (XVIIa, 0.30 g) in 5% ethanolic KOH (20 ml) was refluxed for 30 min. The reaction mixture was diluted with ether, and the ethereal layer was washed with water and dried over Na_2SO_4. The solvent was evaporated *in vacuo* to give 16α-methyl-5α-pregnane-3β,20β-diol (XVIIb, 0.23 g) mp 195—198°. IR cm^{-1}: 3300 (-OH).

To a solution of the diol XVIIb (0.23 g) in AcOH (20 ml) was added a solution of CrO_3 (0.24 g) in water (3 drops) and the resulting solution was stored for 1 hr at room temperature. After the reaction mixture was poured into water, the product was extracted with ether and the ethereal layer was washed with 5% Na_2CO_3 and water, and dried over Na_2SO_4. The solvent was evaporated *in vacuo* to give 16α-methyl-5α-pregnane-3,20-dione (XVIII, 0.18 g). Recrystallization from acetone gave colorless needjles, mp 139—140°. $[\alpha]_D^{26}$ +93° (c=1.04). IR cm^{-1}: 1705 (C=O). NMR δ: 0.65 (3H, s, 18-CH_3), 0.94 (3H, d, J=7 Hz, 16α-CH_3), 1.00 (3H, s, 19-CH_3), 2.10 (3H, s, 21-CH_3). *Anal.* Calcd. for $C_{22}H_{34}O_2$: C, 79.95; H, 10.37. Found: C, 79.88; H, 10.67.

b) A solution of CrO_3 (0.12 g) in AcOH (5 ml) and a few drops of water was added to a solution of 3β-hydroxy-16α-methyl-5α-pregnane-20-one (XIX, 0.11 g) in AcOH (5 ml). The mixture was stored for 1 hr at room temperature and poured into water. The product was extracted with ether and the ethereal layer was washed with 5% Na_2CO_3 and water, and dried over Na_2SO_4. The solvent was removed to give the dione XVIII (0.04 g) identical with the product obtained above.

17β-Hydroxy-17-methyl-5β-vinylestran-3-one (XXI)——The Grignard reagent prepared from Mg (6.4 g), CH_2=CHBr (30 g) and THF (170 ml) was added to a solution of 19-normethyltestosterone (XX, 5.0 g) and cupric acetate (1.0 g) in THF (100 ml) for 30 min with vigorous stirring at 0°. Stirring was continued for an additional 3 hr at room temperature. The excess Grignard reagent was decomposed by addition of ice, and the organic layer was separated and aqueous phase was extracted with ether. The combined organic solution was washed with 10% NH_4Cl, 5% Na_2CO_3 and water, and dried over Na_2SO_4. After evaporation of the solvent the residue was chromatographed on alumina (100 g). Elution with benzene gave 17β-hydroxy-17-methyl-5β-vinylestran-3-one (XXI). Recrystallization from MeOH gave colorless prisms (2.6 g), mp 188—190°. $[\alpha]_D^{26}$ −25° (c=1.00). IR cm^{-1}: 3450 (-OH), 1700 (C=O). NMR δ: 0.89 (3H, s, 18-CH_3), 1.23 (3H, s, 17α-CH_3), 4.7—6.0 (3H, m, 5β-CH=CH_2). ORD (c=0.269, EtOH) $[\alpha]^{25}$ (mμ): −17° (700), −26° (589), −479° (308), −487° (306) (trough), +200° (270), +200° (268) (peak). *Anal.* Calcd. for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.50; H, 10.14.

5β-Ethyl-17β-hydroxy-17-methylestran-3-one (XXIX)——To a solution of 19-normethyltestosterone (XX, 4.36 g) in THF (40 ml) was added cupric acetate (0.20 g) and the mixture was stirred vigorously. The Grignard reagent prepared from Mg (0.97 g), C_2H_5Br (4.36 g) and THF (40 ml) was added to the mixture described above and the reaction mixture was treated as the same manner described above to give 5β-ethyl-17β-hydroxy-17-methylestran-3-one (XXIX, 1.18 g) as colorless needles (from acetone–n-hexane), mp 148.5—150°. $[\alpha]_D^{22.5}$ +6° (c=1.00). NMR δ: 0.90 (3H, s, 18-CH_3), 1.24 (3H, s, 17α-CH_3). IR cm^{-1}: 3490 (-OH), 1695 (C=O). ORD (c=0.274, EtOH) $[\alpha]^{25}$ (mμ): +25° (700), +23° (589), −166° (310), −201° (306) (trough), −169° (302), +79° (300) (peak), −7° (270). *Anal.* Calcd. for $C_{21}H_{34}O_2$: C, 79.11; H, 10.76. Found: C, 70.90; H, 10.90.

b) A mixture of 17β-hydroxy-17-methyl-5β-vinylestran-3-one (XXI, 0.20 g), 5% Pd-C (0.05 g) and EtOH (20 ml) was shaken in H_2 atmoshere (at atmospheric pressure). Hydrogen uptake was completed in 30 min. Catalyst was removed by filtration and the filtrate was evaporated to give the 5β-ethyl compound (XX, 0.15 g), the IR spectrum of which was the same as that for the compound obtained above.

17α-Methyl-5β-vinylestrane-3α,17-diol (XXII) and 17α-Methyl-5β-vinylestrane-3β,17-diol (XXIIIa)——To a solution of 17β-hydroxy-17-methyl-5β-vinylestran-3-one (XXI, 1.0 g) in MeOH (50 ml) was added sodium borohydride (0.40 g) and the mixture was stirred for 1 hr at room temperature. A few drops of AcOH was added and the solvent was removed by distillation *in vacuo*. The residue was diluted with water and the product was extracted with ether. The ethereal layer was washed with 5% Na_2CO_3 and water, and dried over Na_2SO_4. After evaporation of the solvent, the reduction product (0.98 g) was submitted to preparative thin layer chromatography (silica gel Merck GF_{254}, $CHCl_3$–acetone 9: 1). The product with high Rf value was recrystallized from acetone to give 17α-methyl-5β-vinylestrane-3β,17-diol (XXIIIa, 0.57 g) as colorless needles, mp 138—139°. $[\alpha]_D^{28}$ −21° (c=1.00,). IR cm^{-1}: 3400 (-OH). NMR δ: 0.87 (3H, s, 18-CH_3), 1.23 (3H, s, 17α-CH_3), 3.95—4.15 (1H, m, 3α-H), 4.95—6.40 (3H, m, 5β-CH=CH_2). *Anal.* Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76. Found: C, 79.09; H, 10.80.

The product with low Rf value was recrystallized from acetone to give 17α-methyl-5β-vinylestrane-3α,17-diol (XXII, 0.41 g) as colorless needles, mp 170—174°. $[\alpha]_D^{29}$ −19° (c=1.01). IR cm^{-1}: 3350 (-OH). NMR δ: 0.84 (3H, s, 18-CH_3), 1.22 (3H, s, 17α-CH_3), 3.50—4.20 (1H, m, 3β-H), 4.80—6.00 (3H, m, 5β-CH=CH_2). *Anal.* Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76. Found: C, 78.89; H, 10.85.

5β,17,17-Trimethyl-13-gonen-3β-ol (XXVIb) and Its Acetate (XXVIa)——a) 17α-Methyl-5β-vinylestrane-3β,17-diol (XXIIIa, 2.04 g) was acetylated with Ac_2O–pyridine to give 3β-acetoxy-17α-methyl-5β-vinylestrane (XXIIIb, 1.26 g) as colorless needles (from ether–n-hexane), mp 151—152°. IR cm^{-1}: 3400

(–OH), 1710 (C=O). NMR δ: 0.87 (3H, s, 18-CH_3), 1.22 (3H, s, 17α-CH_3), 1.98 (3H, s, 3β-OAc), 4.75—6.35 (4H, 5β-CH=CH_2 and 3α-H).

To a solution of the acetate (XXIIIb, 1.02 g) in CH_2Cl_2 (60 ml) and pyridine (0.18 ml) was bubbled ozone at −78° until peaks at 954 and 921 cm^{-1} in IR spectrum was disappeared (for about 20 min). AcOH (1.7 ml) and zinc dust (1.27 g) were added in the reaction mixture and the suspension was treated as described above to give 3β-acetoxy-5β-formyl-17α-methylestran-17-ol (XXIV, 0.84 g) as crystalline material. IR cm^{-1}: 3450 (–OH), 1705 (–CHO and –OAc). NMR δ: 0.87 (3H, s, 18-CH_3), 1.22 (3H, s, 17α-CH_3), 2.00 (3H, s, 3β-OAc), 4.93—5.25 (1H, m, 3α-H), 9.39 (1H, s, 5β-CHO).

A solution of the formyl compound (XXIV, 0.84 g) was treated with ethanedithiol (1.7 ml) and boron trifluoride etherate (1.7 ml) in the same manner as described above to give thioketal derivative (XXV, 0.81 g) as oily material. IR cm^{-1} (in $CHCl_3$ solution): 1720 (C=O).

A mixture the thioketal (XXV, 0.81 g), Raney Ni (13 g) and EtOH (100 ml) was refluxed for 1 hr. After filtration, the filtrate was evaporated to dryness to give 3β-acetoxy-5β,17,17-trimethyl-13-gonene (XXVIa, 0.21 g) as oily material. IR cm^{-1} (in $CHCl_3$ solution): 1710 (C=O). NMR δ: 0.96 (6H, s, 17,17-diCH_3), 1.23 (3H, s, 5β-CH_3), 2.03 (3H, s, 3β-OAc), 4.95—5.20 (1H, m, 3α-H).

b) A solution of 5β,17α-dimethylestrane-3β,17-diol (XXVII, 0.05 g) in Ac_2O (0.5 ml) and boron trifluoride etherate (0.5 ml) was allowed to stand overnight at room temperature. The reaction mixture was poured into water and the product was extracted with ether. The ethereal layer was washed with 5% Na_2CO_3 and water, and dried over Na_2SO_4. The solvent was evaporated to dryness *in vacuo* to give the acetate (XXVIa, 0.04 g), the IR and NMR spectrum of which was identical with that of the acetate obtained above.

A solution of the acetate (XXVIa 0.21 g) in 5% ethanolic KOH (10 ml) was refluxed for 30 min and poured into 10% HCl. The product was extracted with ether and the ethereal layer was washed with 5% Na_2CO_3 and water, and dried over Na_2SO_4. The solvent was evaporated and the residue (0.17 g) was recrystallized from ether to give 5β,17,17-trimethyl-13-gonen-3β-ol (XXVIb) as colorless needles, mp 158—159°. $[\alpha]_D^{24}$ −29° (c=1.02). IR cm^{-1}: 3300 (–OH). NMR δ: 0.98 (6H, s, 17,17-diCH_3), 1.22 (3H, s, 5β-CH_3), 4.05—4.30 (1H, m, 3α-H). Mass Spectrum *m/e*: 288 (M^+). *Anal.* Calcd. for $C_{20}G_{32}O$: C, 83.27; H, 11.18. Found: C. 83.33; H, 11.11.

5β,17α-Dimethylestrane-3β,17-diol (XXVII)——To a solution of 5β,17α-dimethyl-17-hydroxyestran-3-one (XXVIII, 0.15 g) in MeOH (20 ml) was added sodium borohydride (0.08 g) portionwise. The mixture was stirred for 1 hr at room temperature. After usual work-up the crude product (0.16 g) was submitted to preparative thin-layer chromatography (silica gel Merck GF_{254}, $CHCl_3$–acetone 9: 1) to give 5β,17α-dimethylestrane-3β,17-diol (XXVII) as colorless prisms (from acetone–ether), mp 179—180°. $[\alpha]_D^{29}$ +36° (c=1.07). IR cm^{-1}: 3400 (–OH). NMR δ: 0.85 (3H, s, 18-CH_3), 1.21 (6H, s, 5β-CH_3 and 17α-CH_3), 4.05—4.30 (1H, m, 3α-H). *Anal.* Calcd. for $C_{20}H_{34}O_2$: C, 78.37; H, 11.18. Found: C, 78.22; H, 11.19.

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