2260, 1731, 1653, 1196. *Anal.* Calcd. for $C_{20}H_{29}O_2N$: C, 76.15; H, 9.27. Found : C, 76.38; H, 9.02.

2-Hydroxyimino-A-norandrost-3(5)-ene-1β,17β-diol (XIII)——a) By reduction of XIIa with $NaBH_4$: To a solution of the oxime (XIIa) (151 mg.) in EtOH (40 ml.), $NaBH_4$ (75 mg.) was added and the mixture was refluxed for 2 hr. After cooling, a few drops of dil. HCl were added to decompose the excess reagent. The reaction mixture was diluted with H_2O and concentrated *in vacuo* to about a half volume. The precipitated crystals were collected by filtration, washed with H_2O and dried (84 mg.). Recrystallization from EtOH gave fine needles (46 mg.) of XIII, m.p. 235~236° (decomp.), which was identified by a mixed melting point and by comparison of the IR spectra with an authentic sample prepared by the method b) described below.

b) By treatment of IIa with hydroxylamine : To a solution of the ketol (IIa) (60 mg.) dissolved in EtOH (4 ml.) was added a solution of hydroxylamine hydrochloride (30 mg.) and AcONa (40 mg.) in H_2O (2 ml.). The mixture was refluxed for 40 min. and evaporated *in vacuo*. Addition of H_2O afforded a crystalline material (40 mg.), m.p. 224~230° (decomp.). Recrystallization from EtOH gave XIII (17 mg.) as fine needles, m.p. 235~236° (decomp.), $[\alpha]_D$ −42° (c=0.53, dioxane). UV : λ_{max} 252 mμ (ε 13,600). IR ν_{max}^{Nujol} cm^{-1} : 3260, 1642, 1625. *Anal.* Calcd. for $C_{18}H_{27}O_3N$: C, 70.79; H, 8.91; N, 4.59. Found : C, 70.78; H, 8.93; N, 4.73.

The authors express their deep gratitude to Dr. Ken'ichi Takeda, Director of this Laboratory, for his helpful guidance throughout the course of this work.

Summary

Reactions of 17β-hydroxy-A-norandrost-3(5)-ene-1,2-dione (Ia) and its 17-propionate (Ib) with several reagents have been examined. Treatment of I with zinc-acetic acid or lithium-liquid ammonia resulted in the reduction of only the C_1-carbonyl group giving 1β,17β-dihydroxy-A-norandrost-3(5)-en-2-one (II). On the contrary, reaction of I with carbonyl reagents in the usual condition afforded the corresponding derivatives which were condensed at only the C_2-carbonyl group with the reagents. Lithium aluminum hydride or sodium borohydride reduction of I gave the glycols, (IV) and (V), epimeric at C-2 with the 1β-hydroxyl group.

(Received November 9, 1964)

[Chem. Pharm. Bull. 13(2) 165~172 (1965)] UDC 547.923.07

22. Keiji Yoshida and Tokuo Kubota : Studies on A-Norsteroids. III.*1 Hydrogenations of A-Nor-$\Delta^{3(5)}$-steroids Substituted at C_1 and C_2-Positions.

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It has been described, in the preceding paper,*1 that the treatment of 17β-hydroxy-A-norandrost-3(5)-ene-1,2-dione with zinc and acetic acid resulted in the formation of 1β,17β-dihydroxy-A-norandrost-3(5)-en-2-one (VIIa) which on the reduction with metal hydrides afforded the unsaturated 1β,2β,17β- and 1β,2α,17β-triols, (I) and (II). The present report deals with an interesting result from catalytic hydrogenations of the $\Delta^{3(5)}$ double bond in the A-norsteroids, (I), (II) and (VIIa), bearing substituents at the C_1- and C_2-positions.

*1 Part II : This Bulletin, **13**, 156 (1965).

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The above-mentioned A-norandrost-3(5)-ene-1β,2β,17β-triol (I) and 1β,2α,17β-triol (II)*[1] were subjected to catalytic reduction for the purpose of furnishing the corresponding, saturated triols. In the first attempt, which was carried out using palladium-charcoal in a mixture of methanol and ethyl acetate, both the unsaturated triols (I) and (II) gave an identical, saturated diol, $C_{18}H_{30}O_2$, m.p. 145~147°, after uptake of two equivalents of hydrogen. Acetylation of the diol afforded the diacetate, m.p. 150~152°, which on alkaline hydrolysis regenerated the diol. This diol has now been deduced to be the 1β,17β-diol, which was formed by simultaneous hydrogenolysis of the allylic C-2 hydroxyl group and hydrogenation of the double bond in the unsaturated triols. Since it has been shown in many examples[1~3] that hydrogenations of A-nor-$\Delta^{3(5)}$-steroids with palladium-charcoal afforded A-nor-5β-steroids, the diol was predicted to have 5β structure as IIIa. This assumption was supported by the nuclear magnetic resonance (NMR) spectrum, which showed a doublet signal at 6.02 τ (J=5 c.p.s.) being attributable to the proton on the hydroxy-bearing C-1 as well as a second-order quartet signal at 6.39 τ due to the proton at C-17. In examination of molecular models, the 1α-proton in 1β,17β-dihydroxy-A-norsteroids can be expected to appear as a doublet in 5β-series, but as a quartet in 5α-isomer, by using Karplus' correlation.[4]

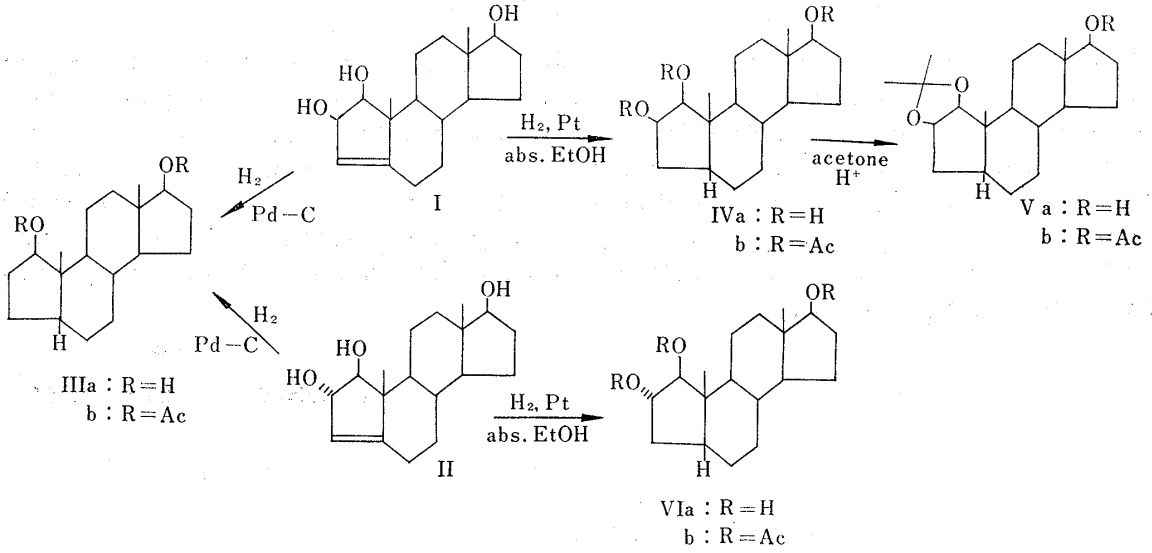

Chart 1.

In order to prevent the hydrogenolysis of the C-2 hydroxyl group, hydrogenation of the unsaturated triols (I) and (II) was carried out with Adams' catalyst in absolute alcohol solutions. With this condition, the $\Delta^{3(5)}$-1β,2β,17β-triol (I) gave the saturated triol, m.p. 111~113°, which furnished on acetylation the triacetate, m.p. 135~136°, and on treatment with acetone and *p*-toluenesulfonic acid the acetonide, m.p. 140~141°. In the same way, hydrogenation of the $\Delta^{3(5)}$-1β,2α,17β-triol (II) gave the corresponding, saturated triol, m.p. 214~215°, which on acetylation gave the triacetate, m.p. 130~131°, accompanied with the above-mentioned diol (IIIa). Concerning the A/B ring fusion of these two saturated triols, the 5β-configuration shown as IV and VI was expected from the above-mentioned facts[1~3] and this will be elucidated later.

1) *a*) H. Lettre : Z. Physiol. Chem., **221**, 73 (1933). *b*) R. Hanna, T. Rüll, G. Ourisson : Bull. soc. chim. France, **1960**, 9. *c*) W. G. Dauben, G. A. Boswell, W. H. Templeton : J. Am. Chem. Soc., **83**, 5006 (1961).
2) F. L. Weisenborn, H. E. Applegate : J. Am. Chem. Soc., **81**, 1960 (1959).
3) R. Hanna, T. Rüll, G. Ourisson : Bull. soc. chim. France, **1961**, 1209.
4) *a*) M. Karplus : J. Phys. Chem., **31**, 11 (1959). *b*) M. Karplus : J. Am. Chem. Soc., **85**, 2870 (1963).

Hydrogenation of 1β,17β-dihydroxy-A-norandrost-3(5)-en-2-one (VIIa)*[1] with palladium on charcoal, followed by chromatography over silica gel afforded a saturated dihydroxy-one, m.p. 190~192°, in 70% yield. Its NMR spectrum showed a singlet signal at 6.37 τ, as expected for the 1-hydroxy-2-one structure, in the region of bands due to the protons on hydroxy-bearing carbon atoms. The optical rotatory dispersion exhibited a negative Cotton curve suggesting the A/B ring *cis*-fusion.[5] Acetylation of the compound with acetic anhydride and pyridine gave the diacetate, m.p. 152~154°, which also showed a singlet signal at 5.08 τ arising from the proton on C-1 bearing an acetoxyl group in its NMR spectrum and a negative Cotton curve in the optical rotatory dispersion. Moreover, its infrared spectrum (CCl_4) showed an absorption at 1412 cm^{-1} due to a methylene adjacent to a carbonyl group. The diacetate was finally subjected to the reductive removal of the acetoxyl group in the α-ketol acetate moiety with zinc in refluxing glacial acetic acid containing acetic anhydride. The resulting monoacetoxy-ketone was identified, as expected, by direct comparison with an authentic sample of 17β-hydroxy-A-nor-5β-androstan-2-one acetate (IXb)[3] prepared by the known procedure, that is hydrogenation of A-nortestosterone (X) with palladium on charcoal[2] followed by acetylation.

From the above results, the saturated dihydroxy-ketone, derived from the hydrogenation of 1β,17β-dihydroxy-A-norandrost-3(5)-en-2-one (VIIa) with palladium catalyst, has been proved to be the A-nor-5β-steroid bearing a 1,17β-dihydroxy-2-oxo function and its C-1 hydroxyl group is expected to have the original β-configuration as in VIIa. The reliable evidence for this assignment was provided in the experiment described below, since it is well-known[6] that α-ketols are often rearranged to more stable isomers under a mild condition.*[3]

Reduction of the ketol (VIIa) with lithium aluminum hydride yielded a mixture of isomeric triols, which on treatment with acetone and *p*-toluenesulfonic acid and chromatography on silica gel afforded an acetonide, m.p. 140~141°, and a triol, m.p. 214~215°, in a ratio of 1:1.2. These two products were identified, as expected, with the 1β,2β,17β-triol acetonide (Va) and the 1β,2α,17β-triol (VIa), respectively, obtained from the catalytic reductions of the unsaturated triols (I) and (II). From these results, the correctness of the 1β-hydroxyl configuration in the afore-mentioned ketol (VIIa) as well as of the 5β-configuration in the saturated triols (IVa) and (VIa) has been confirmed without any doubt.

Although it was mentioned above that 1β,17β-dihydroxy-A-norandrost-3(5)-en-2-one (VIIa) on the hydrogenation with palladium on charcoal gave the A-nor-5β-steroid (VIIIa), catalytic reduction of VIIa in absolute alcohol over Adams' catalyst unexpectedly afforded another saturated dihydroxy-one, m.p. 218~221° as a sole crystalline product. The NMR spectrum of the new compound showed a singlet signal at 6.23 τ as expected for the C-1 proton in the 1-hydroxy-2-one structure, whereas its optical rotatory dispersion exhibited a positive Cotton curve suggesting the 5α-structure,[5] in contrast with that of VIIa. The dihydroxy-one was acetylated with acetic anhydride and pyridine giving an oily diacetate, which was led to the known 17β-hydroxy-A-nor-5α-androstan-2-one acetate (XII)[7] by treatment with zinc in acetic acid and acetic anhydride. On the other hand,

*3 This ketol (VIIa) was actually rearranged to another isomer by chromatography on neutral alumina and to the third isomer with methanolic alkali. These rearrangements will be described as the next paper of this series in near future.

5) W. Klyne : Tetrahedron, **13**, 29 (1961).
6) *a*) N. S. Leeds, D. K. Fukushima, T. F. Gallagher : J. Am. Chem. Soc., **76**, 2943 (1954). *b*) W. S. Johnson, H. Gastambide, R. Pappo : J. Am. Chem. Soc., **79**, 1991 (1957). *c*) W. R. Biggerstaff, T. F. Gallagher : J. Org. Chem., **22**, 1220 (1957). *d*) J. Fishman : J. Am. Chem. Soc., **82**, 6143 (1960). *e*) T. Nambara, J. Fishman : J. Org. Chem., **27**, 2131 (1962).
7) T. Rüll, G. Ourisson : Bull. soc. chim. France, **1958**, 1573.

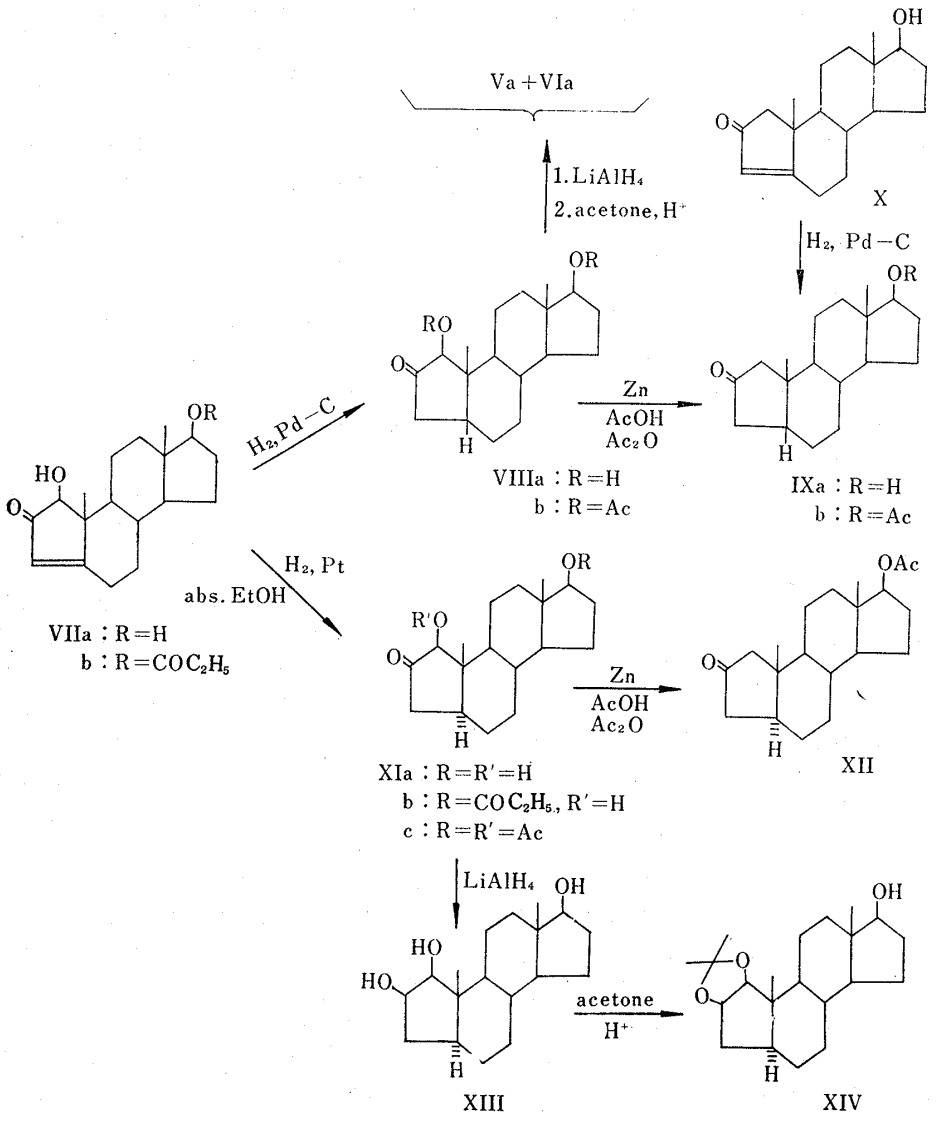

Chart 2.

reduction of the dihydroxy-one with lithium aluminum hydride furnished a triol, m.p. 213~214°, which was indicated to have a 2β-hydroxyl group by a positive digitonin test.[8] The triol showed a band at 3567 cm^{-1} due to an intramolecular hydrogen bonding besides a free hydroxyl absorption at 3628 cm^{-1} in its infrared spectrum*4 and gave the acetonide (XIV) by treatment with acetone and *p*-toluenesulfonic acid. From the above results, the triol can be defined as A-nor-5α-androstane-1β,2β,17β-triol (XIII) and consequently the dihydroxy-one, obtained from the hydrogenation of VIIa with Adams' catalyst, has now been proved to be 1β,17β-dihydroxy-A-nor-5α-androstan-2-one (XIa).

On catalytic reduction in the same way, the 17-propionate (VIIb) of the unsaturated dihydroxy-one gave the corresponding, saturated product (XIb) in 55% yield, which on reduction with lithium aluminum hydride was led to the formation of the same triol (XIII) as that derived from XIa. Saponification of XIb with refluxing methanolic sodium

*4 Infrared spectra for this purpose were obtained with a LiF prism and a 20 mm. cell by a Perkin-Elmer Single-beam Infrared Spectrophotometer Model 12 C.

8) *a*) R. E. Marker, O. Kamm, D. M. Jones, L. W. Mixon : J. Am. Chem. Soc., 59, 1362 (1937). *b*) T. Kawasaki : Yakugaku Zasshi, 57, 1058 (1937). *c*) W. G. Dauben, G. A. Boswell, W. H. Templeton : J. Am. Chem. Soc., 83, 5006 (1961).

hydroxide afforded the free dihydroxy-one (Xa), in which no ketol rearrangement took place.

It is remarkable that the catalytic reduction of 1β,17β-dihydroxy-A-norandrost-3(5)-en-2-one (VIIa) over Adams' catalyst in absolute alcohol has afforded stereoselectively the A-nor-5α-steroid (Xa), in contrast to the formation of the A-nor-5β-steroid (VIIIa) on the hydrogenation over palladium-charcoal. As far as the authors are aware, there is no instance that an A-nor-5α-steroid has been predominantly obtained by reduction of A-nor-$\Delta^{3(5)}$-steroids. On the other hand, it has been described that A-norcholest-3(5)-en-2-one gave exclusively A-nor-5β-cholestan-2-one by the catalytic hydrogenations over Adams' catalyst in acetic acid[9] as well as over palladium-charcoal in alkaline methanol.[1c] Furthermore, as mentioned above, the A-nor-$\Delta^{3(5)}$-1β,2β,17β-triol (I) and 1β,2α,17β-triol (II) on the hydrogenation over Adams' catalyst in absolute ethanol, that is the same condition as the unsaturated ketol (VIIa) has been transformed to the A-nor-5α-steroid (Xa), have afforded the corresponding 5β-steroids (IVa) and (VIa). Accordingly, neither steric feature of the molecule nor affinity of the catalyst for oxygen atoms[10] appears to be a factor which controlled the hydrogenation from the α-side on VIIa and an explanation for this experimental result is left in further investigations.

Experimental

All melting points were uncorrected. Optical rotations were measured, unless otherwise stated, in dioxane solutions at ca. 25° with a Rudolf Photoelectric Polarimeter Model 200. Unless otherwise stated, IR spectra were recorded with a NaCl prism on a Koken Infrared Spectrophotometer Model DS 301. NMR spectra were determined at 60 Mc. in $CDCl_3$ solutions containing tetramethylsilane as an internal reference using a Varian A-60 Analytical NMR Spectrometer. Optical rotatory dispersion (ORD) curves were run in dioxane solutions with a Rudolf Recording Spectropolarimeter.

A-Nor-5β-androstane-1β,17β-diol (IIIa)——a) From A-nor-androst-3(5)-ene-1β,2β,17β-triol (I): A solution of I (200 mg.) in MeOH (10 ml.) and AcOEt (10 ml.) was shaken with 5% Pd-C (500 mg.) in an atmosphere of H_2. Hydrogenation was completed after 1 hr. with uptake of 2 mol equivalents of H_2. The catalyst was removed by filtration and the solvent was evaporated. The residue was chromatographed on silica gel (4 g.) and the eluate (196 mg.) with benzene-$CHCl_3$ (8:2) and $CHCl_3$ was recrystallized from Me_2CO yielding A-nor-5β-androstane-1β,17β-diol (IIIa) (113 mg.), m.p. 143~146°, as needles. The analytical sample was obtained by further recrystallization from the same solvent. m.p. 145~147°, $[\alpha]_D$ +17° (c=0.54). IR: ν_{max}^{Nujol} 3365 cm^{-1}. NMR (τ): 6.02 (doublet, J=5 c.p.s., C_1-proton), 6.39 (second order quartet, C_{17}-proton), 9.02 (singlet, C_{19}-CH_3), 9.27 (singlet, C_{18}-CH_3). *Anal.* Calcd. for $C_{18}H_{30}O_2$: C, 77.65; H, 10.86. Found; C, 77.48; H, 10.89.

b) From A-norandrost-3(5)-ene-1β,2α,17β-triol (II): Hydrogenation of II (100 mg.) in MeOH (8 ml.) and AcOEt (8 ml.) over 5% Pd-C (250 mg.) was carried out in the same manner as mentioned in a). Chromatography of the crude product (94 mg.) over silica gel (1.5 g.) and recrystallization of the eluate (84 mg.) from Me_2CO afforded needles (59 mg.), m.p. 145~147°, which was identical with the 1β,17β-diol (IIIa) obtained from I in a) in all respects.

A-Nor-5β-androstane-1β,17β-diol Diacetate (IIIb)——The 1β,17β-diol (IIIa) (125 mg.) in Ac_2O (1.3 ml.) and pyridine (3 ml.) was allowed to stand at room temperature overnight. The reaction mixture was worked up in the usual manner and recrystallization of the crude product (158 mg.) from hexane gave the diacetate (IIIb) (100mg.) as needles, m.p. 150~152°, $[\alpha]_D$ −8° (c=0.55). IR ν_{max}^{Nujol} cm^{-1}: 1739, 1727, 1252, 1236, 1223. *Anal.* Calcd. for $C_{22}H_{34}O_4$: C, 72.89; H, 9.49. Found: C, 72.93; H, 9.28.

This diacetate (IIIb) (98 mg.) was saponified by refluxing in MeOH (8 ml.) and 40% NaOH (1 ml.) for 30 min. Crystals (81 mg.) extracted with $CHCl_3$, on recrystallization from Me_2CO, afforded needles (57 mg.) of the original 1β,17β-diol (IIIa) m.p. 145~147°.

Hydrogenation of I with Adams' Catalyst——A suspension of $PtO_2 \cdot H_2O$ (60 mg.) in abs. EtOH (8 ml.) was shaken in an atmosphere of H_2. The solvent was decanted and the catalyst was washed thoroughly with abs. EtOH. A solution of I (127 mg.) in abs. EtOH (27 ml.) was added to the above catalyst and the mixture was shaken in a H_2 atmosphere. Hydrogenation was complete in 40 min. with absorption of 13.4 ml. of H_2. The catalyst was removed by filtration and the solvent was evaporated leaving a semi-

9) T. L. Jacobs, N. Takahashi: J. Am. Chem. Soc., **80**, 4865 (1958).
10) S. Mitsui, Y. Senda, K. Konno: Chem. & Ind. (London), **1963**, 1354.

solid material. Recrystallization from AcOEt-petr. ether afforded A-nor-5β-androstane-1β,2β,17β-triol (IVa) (61 mg.), m.p. 105~113°, as clusters of small plates. Concentration of the mother liquor gave the second crop (36 mg.), m.p. 102~112°. For analysis, the first crop was recrystallized from AcOEt-petr. ether giving clusters of small plates melted at 111~113° after moistened at 105°. $[\alpha]_D$ +8° (c=0.49). IR ν_{max}^{Nujol} cm^{-1} : 3355, 3280; $\nu_{max}^{CCl_4}$ cm^{-1}*4 : 3630, 3621, 3566. *Anal.* Calcd. for $C_{18}H_{30}O_3$: C, 73.43; H, 10.27. Found : C, 73.40; H, 10.26.

A-Nor-5β-androstane-1β,2β,17β-triol 1,2-Acetonide (Va)——In the same manner as described in the preceding experiment, I (95 mg.) was hydrogenated with Adams' catalyst (45 mg.) and abs. EtOH (20 ml.). After removals of the catalyst and the solvent, the crude saturated triol (IVa) was treated with refluxing Me_2CO (24 ml.) containing *p*-toluenesulfonic acid (12 mg.) for 5 hr. The reaction mixture was neutralized with 5% $NaHCO_3$, concentrated under reduced pressure and extracted with AcOEt. The extract was washed with H_2O, dried and evaporated giving an oily residue, which was purified by chromatography on silica gel (2.5 g.). The eluate (72 mg.) with benzene-$CHCl_3$ (1:1) was recrystallized from hexane to afford needles (50 mg.) of A-nor-5β-androstane-1β,2β,17β-triol 1,2-acetonide (Va), m.p. 140~141°, $[\alpha]_D$ +20° (c=0.50). IR $\nu_{max}^{CCl_4}$ cm^{-1} : 3640, 3500, 1382, 1374. *Anal.* Calcd. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found : C, 75.59; H, 10.26.

A-Nor-5β-androstane-1β,2β,17β-triol Triacetate (IVb)——A mixture of the triol (IVa) (40 mg.), Ac_2O (0.8 ml.) and pyridine (1.2 ml.) was allowed to stand at room temperature overnight. The crude product, isolated with Et_2O in the usual manner, on recrystallization from hexane afforded plates (24 mg.) of the triacetate (IVb), m.p. 135~136°, $[\alpha]_D$ −7° (c=0.53). IR ν_{max}^{Nujol} cm^{-1} : 1741, 1247. *Anal.* Calcd. for $C_{24}H_{36}O_6$: C, 68.54; H, 8.63. Found : C, 68.66; H, 8.73.

A-Nor-5β-androstane-1β,2β,17β-triol 1,2-Acetonide 17-Acetate (Vb)——A mixture of the acetonide (Va) (40 mg.), Ac_2O (0.5 ml.) and pyridine (1 ml.) was allowed to stand at room temperature overnight. The crude product, isolated in the usual manner, was recrystallized from hexane giving the acetate (Vb) (34 mg.), m.p. 188~189°, as prisms, $[\alpha]_D$ +12° (c=0.60), IR ν_{max}^{Nujol} cm^{-1} : 1728, 1253. *Anal.* Calcd. for $C_{23}H_{36}O_4$: C, 73.36; H, 9.64. Found : C, 73.24; H, 9.65.

Hydrogenation of II with Adams' Catalyst——Hydrogenation of II (50 mg.) in abs. EtOH (10 ml.) over Adams' catalyst (32 mg.) was carried out in the same manner as described above for hydrogenation of I and completed in 30 min. with uptake of H_2 (5.7 ml.). After removals of the catalyst and the solvent, the crude product was chromatographed on Al_2O_3 (2 g.). The fractions (13 mg.), eluted with $CHCl_3$, were recrystallized from Me_2CO giving the 1β,17β-diol (IIIa), m.p. 145~147°, identical with an authentic sample described above. The next fractions (23 mg.) eluted with $CHCl_3$-MeOH (20:1) afforded, on recrystallization from Me_2CO, needles (11 mg.), m.p. 207~209°. Further recrystallization from Me_2CO afforded A-nor-5β-androstane-1β,2α,17β-triol (VIa) as needles, m.p. 214~215°, $[\alpha]_D$ +23° (c=0.51). IR : ν_{max}^{Nujol} 3315 cm^{-1}; $\nu_{max}^{CCl_4}$ 3620 cm^{-1}.*4 *Anal.* Calcd. for $C_{18}H_{30}O_3$: C, 73.43; H, 10.27. Found : C, 73.42; H, 10,27.

A-Nor-5β-androstane-1β,2α,17β-triol Triacetate (VIb)——A mixture of the 1β,2α,17β-triol (VIa) (20 mg.), Ac_2O (0.5 ml.) and pyridine (0.5 ml.) was allowed to stand at room temperature overnight. The product, extracted with Et_2O in the usual way, was recrystallized from hexane giving the triacetate (VIb) as needles, in nearly quantitative yield, m.p. 130~131°, $[\alpha]_D$ +14° (c=0.50). IR ν_{max}^{Nujol} cm^{-1} : 1737, 1254, 1230. *Anal.* Calcd. for $C_{24}H_{36}O_6$: C, 68.54; H, 8.63. Found : C, 68.78; H, 8.68.

1β,17β-Dihydroxy-A-nor-5β-androstan-2-one (VIIIa)——A solution of 1β,17β-dihydroxy-A-nor-androst-3(5)-en-2-one (VIIa) (436 mg.) in MeOH (20 ml.) and AcOEt (20 ml.) was hydrogenated at room temperature over 5% Pd-C (1.09 g.). After equimolar H_2 was absorbed, the mixture was filtered and the filtrate was evaporated to dryness. The crystalline residue was chromatographed over silica gel (7 g.). The eluate (404 mg.) with $CHCl_3$-MeOH (100:1) gave, on recrystallization from Me_2CO, VIIIa (153 mg.), m.p. 190~192°, as plates. Concentration of the mother liquor gave the second crop (151 mg.), m.p. 177~186°. The first crop showed the following constants : $[\alpha]_D$ −78° (c=0.56). IR $\nu_{max}^{CHCl_3}$ cm^{-1} : 3625, 1743. NMR (τ) : 6.37 (singlet, C_1-proton), 6.50 (second order quartet, C_{17}-proton), 8.93 (singlet, C_{19}-CH_3), 9.24 (singlet, C_{18}-CH_3). ORD (c=0.56) : $[\alpha]_{342}$ −1842°, $[\alpha]_{297}$ +1099°. *Anal.* Calcd. for $C_{18}H_{28}O_3$: C, 73.93; H, 9.65. Found : C, 74.15; H, 9.81.

1β,17β-Dihydroxy-A-nor-5β-androstan-2-one Diacetate (VIIIb)——A mixture of VIIIa (52 mg.), Ac_2O (0.5 ml.) and pyridine (0.7 ml.) was allowed to stand at room temperature overnight. The product, isolated in the usual way, was recrystallized from Me_2CO-hexane giving the diacetate (VIIIb) (53 mg.), m.p. 151~152°, as plates. The analytical sample was obtained by further recrystallization from the same solvent and melted at 152~154°. $[\alpha]_D$ −137° (c=0.49). IR $\nu_{max}^{CCl_4}$ cm^{-1} : 1753, 1743, 1412, 1242, 1226. NMR (τ) : 5.08 (singlet, C_1-proton), 5.47 (second order quartet, C_{17}-proton), 9.00 (singlet, C_{19}-CH_3), 9.20 (singlet, C_{18}-CH_3). ORD (c=0.21) : $[\alpha]_{700}$ −120°, $[\alpha]_{343}$ −2650°, $[\alpha]_{336}$ −2320°, $[\alpha]_{331}$ −2510°, $[\alpha]_{288}$ +2350°, $[\alpha]_{245}$ +700°. *Anal.* Calcd. for $C_{22}H_{32}O_5$: C, 70.18; H, 8.57. Found : C, 70.08; H, 8.66.

17β-Hydroxy-A-nor-5β-androstan-2-one Acetate (IXb)——a) From VIIIb : A solution of the diacetate (VIIIb) (51 mg.) in AcOH (10 ml.) and Ac_2O (1 ml.) was stirred and Zn dust (2.6 g.) was added portionwise during 15 min. After refluxing for 18 hr., the reaction mixture was filtered and the precipitate was washed with AcOEt. The combined filtrates were evaporated and AcOEt was added. The organic solution was

washed with 5% $NaHCO_3$ and H_2O, dried over Na_2SO_4 and evaporated. The residue (50 mg.) was chromatographed on Al_2O_3 (1.5 g.) and elution with petr. ether–benzene and benzene yielded a crystalline material (41 mg.). Recrystallization from Me_2CO–hexane gave plates (20 mg.), m.p. 146~148°. No depression was observed on admixture with a sample of 17β-hydroxy-A-nor-5β-androstan-2-one acetate (Xb), m.p. 146~148°, prepared by the following method b), and the IR sprctra of the specimens were identical.

b) From A-nortestosterone (X): The hydrogenation of X with 5% Pd-C was carried out, according to the procedure of Weisenborn and Applegate,[2] to give 17β-hydroxy-A-nor-5β-androstan-2-one (Xa) as plates, m.p. 194~195°, $[\alpha]_D$ −78° (c=0.53, EtOH). (reported[2] m.p. 196.5~197°, $[\alpha]_D$ −72° (EtOH)). IR ν_{max}^{Nujol} cm^{-1}: 3440, 1724. ORD (c=0.48): $[\alpha]_{323}$ −2672°, $[\alpha]_{276}$ +2408°. *Anal.* Calcd. for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found: C, 77.92; H, 10.26. Acetylation of Xa with Ac_2O and pyridine in usual manner gave the 17-acetate (Xb) as plates, m.p. 147~148°, $[\alpha]_D$ −71° (c=0.56, EtOH). (reported[3] m.p. 147~148°, $[\alpha]_D$ −116° (EtOH)). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1743, 1739, 1407, 1244. ORD (c=0.49): $[\alpha]_{324}$ −2400°, $[\alpha]_{276}$ +2264°. *Anal.* Calcd. for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found: C, 75.30; H, 9.51.

Reduction of 1β,17β-Dihydroxy-A-nor-5β-androstan-2-one (VIIIa) with Lithium Aluminum Hydride——A suspension of $LiAlH_4$ (119 mg.) in dry tetrahydrofuran (12 ml.) was refluxed with stirring and a solution of VIIIa (119 mg.) in dry tetrahydrofuran (12 ml.) was added dropwise over a period of 10 min. The mixture was continued to reflux for 3 hr. After cooling, the complex was decomposed with careful addition of a small portion of H_2O and dil. HCl. The mixture was extracted with AcOEt and the organic solution was washed with 5% Na_2CO_3 and H_2O, dried and evaporated. The resulting semisolid (123 mg.) was dissolved in Me_2CO (24 ml.) containing *p*-toluenesulfonic acid (12 mg.). The solution was refluxed for 5 hr., neutralized with 5% $NaHCO_3$, concentrated under reduced pressure and extracted with AcOEt. The extract was washed with H_2O, dried and evaporated giving the oily residue (139 mg.), which was chromatographed over silica gel (3 g.). The fractions (42 mg.), eluted with benzene–$CHCl_3$ (1:1), afforded on recrystallization from hexane needles (37 mg.), m.p. 140~141°, identical with an authentic sample of A-nor-5β-androstan-1β,2β,17β-triol 1,2-acetonide (Va) mentioned above. The fractions (52 mg.), eluted with $CHCl_3$–MeOH (50:1 to 20:1) were recrystallized from Me_2CO giving needles (39 mg.) of the above-mentioned A-nor-5β-androstane-1β,2α,17β-triol (VIa), m.p. 214~215°. Identity with an authentic sample was established by the IR comparison and a mixed melting point determination.

Hydrogenation of 1β,17β-Dihydroxy-A-norandrost-3(5)-en-2-one (VIIa) with Adams' Catalyst——A solution of the unsaturated dihydroxy-one (VIIa) (93 mg.) in abs. EtOH (20 ml.) was added to a suspension of prereduced PtO_2 catalyst (47 mg.) in abs. EtOH (10 ml.). The mixture was shaken in H_2 for 40 min. until equimolar H_2 was absorbed. The catalyst was filtered and the filtrate was evaporated leaving a semicrystalline mush, which was chromatographed on silica gel (4 g.). The crystalline fractions (63 mg.) eluted with benzene–$CHCl_3$ (8:1 to 1:1) gave, on recrystallization from Me_2CO, 1β,17β-dihydroxy-A-nor-5α-androstan-2-one (XIa) (38 mg.), m.p. 219~221°, as plates, $[\alpha]_D$ +132° (c=0.49). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3625, 3525, 1742, NMR (τ): 6.23 (singlet, C_1-proton), 6.36 (second order quartet, C_{17}-proton). 9.25 (singlet, C_{19}-CH_3), 9.29 (singlet, C_{18}-CH_3). ORD (c=0.49): $[\alpha]_{700}$ +89°, $[\alpha]_{323}$ +3931°, $[\alpha]_{278.5}$ −4337°, $[\alpha]_{255}$ −2828°. *Anal.* Calcd. for $C_{18}H_{28}O_3$: C, 73.93; H, 9.65. Found: C, 73.85; H, 9.72.

Hydrogenation of 1β,17β-Dihydroxy-A-norandrost-3(5)-en-2-one 17-Propionate (VIIb) with Adams' Catalyst——The unsaturated ketol (VIIb) (223 mg.) in abs. EtOH (15 ml.) was hydrogenated with Adams' catalyst (87 mg.) in the same manner as described above. The crude product (234 mg.) was chromatographed on silica gel (4 g.). The fractions (198 mg.) eluted with benzene–$CHCl_3$ (1:1) gave, on recrystallization from Me_2CO, 1β,17β-dihydroxy-A-nor-5α-androstan-2-one 17-propionate (XIb) (124 mg.) as plates, m.p. 202~204°, $[\alpha]_D$ +106° (c=0.57). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3528, 1748, 1738, 1417, 1185. NMR (τ): 6.22 (singlet, C_1-proton), 5.40 (second order quartet, C_{17}-proton), 9.20 (singlet, C_{19}-CH_3), 9.30 (singlet, C_{18}-CH_3). ORD (c=0.17): $[\alpha]_{324.5}$ +3416°, $[\alpha]_{278}$ −3897°. *Anal.* Calcd. for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26. Found: C, 72.23; H, 9.23.

Alkaline Hydrolysis of XIb——A mixture of the foregoing XIb (100 mg.), MeOH (8 ml.) and 40% NaOH (1 ml.) was refluxed for 30 min. in N_2 stream. Working up in the usual manner and recrystallization of the crude product (84 mg.) from Me_2CO afforded plates (54 mg.), m.p. 218~221°. Identity with a sample of 1β,17β-dihydroxy-A-nor-5α-androstan-2-one (XIa) prepared in the above-mentioned experiment was established by the IR spectra and mixed melting point determination.

17β-Hydroxy-A-nor-5α-androstan-2-one Acetate (XII)——1β, 17β-Dihydroxy-A-nor-5α-androstan-2-one (XIa) (50 mg.) was acetylated with Ac_2O (0.5 ml.) and pyridine (0.7 ml.) by standing at room temperature overnight. The reaction mixture was worked up in the usual manner yielding the oily diacetate (XIc) (67 mg.). This product was dissolved in AcOH (19 ml.) and Ac_2O (1.3 ml.) and to the stirred solution Zn dust (3.4 g.) was added portionwise during 15 min. After refluxing for 18 hr., the reaction mixture was filtered and the filtrate was evaporated and extracted with AcOEt. The AcOEt extract was washed with 5% $NaHCO_3$ and H_2O and dried. After removal of the solvent, the resulting semisolid (63 mg.) was chromatographed on Al_2O_3 (2 g.). The crystalline fractions (31 mg.) eluted with petr. ether–benzene (1:1) to benzene–$CHCl_3$ (9:1) afforded, on recrystallization from hexane, the acetate (XII) (17 mg.) as leaflets, m.p. 112~114°, $[\alpha]_D$ +133° (c=0.50). (reported[7]; m.p. 114~115°, $[\alpha]_D$ +166° ($CHCl_3$)). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1744,

1412, 1246. ORD (c=0.20) : $[\alpha]_{700}$ +114°, $[\alpha]_{325}$ +4271°, $[\alpha]_{276.5}$ −3415°. *Anal.* Calcd. for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found : C, 75.41; H, 9.52.

A-Nor-5α-androstane-1β,2β,17β-triol (XIII)——a) From 1β,17β-dihydroxy-A-nor-5α-androstan-2-one (XIa). To a suspension of $LiAlH_4$ (79 mg.) in dry tetrahydrofuran (8 ml.), a solution of XIa (79 mg.) in dry tetrahydrofuran (10 ml.) was added dropwise over a period of 10 min. with stirring and the mixture was refluxed for 3 hr. After cooling, the excess reagent was decomposed by careful addition of H_2O and dil. HCl. The mixture was extracted with AcOEt and the organic layer was washed with 5% $NaHCO_3$ and H_2O and dried over Na_2SO_4. After removal of the solvent, the residue (85 mg.) was chromatographed on silica gel (1.7 g.). The eluate (77 mg.) with $CHCl_3$ and $CHCl_3$–MeOH (100:1), was recrystallized from Me_2CO giving A-nor-5α-androstane-1β,2β,17β-triol (XIII) (47 mg.), m.p. 213~214°, as plates, $[\alpha]_D$ −16° (c=0.55). IR : ν_{max}^{Nujol} 3350 cm^{-1}; $\nu_{max}^{CCl_4}$ cm^{-1} *4 : 3628, 3567. *Anal.* Calcd. for $C_{18}H_{30}O_3$: C, 73.43; H, 10.27. Found : C, 73.68; H, 10.33.

To a solution of this triol (XIII) (4 mg.) in 95% EtOH (0.1 ml.) was added digitonin (20 mg.) in 70% EtOH (0.5 ml.). After standing at room temperature for 20 min. the digitonide precipitated.

b) From the 17-propionate (XIb). A solution of XIb (60 mg.) in dry tetrahydrofuran (8 ml.) was treated with $LiAlH_4$ (60 mg.) in dry tetrahydrofuran (6 ml.) in the same manner as described in a). Chromatography of the crude product (55 mg.) over silica gel (1 g.) and recrystallization of the eluate (53 mg.) from Me_2CO gave plates (25 mg.), m.p. 213~214°, identical with a sample of the 1β,2β,17β-triol (XIII) prepared in a) by comparison of the IR spectra and a mixed melting point determination.

A-Nor-5α-androstane-1β,2β,17β-triol 1,2-Acetonide (XIV)——A solution of the 1β,2β,17β-triol (XIII) (60 mg.) and *p*-toluenesulfonic acid (6 mg.) in Me_2CO (12 ml.) was refluxed for 5 hr. After cooling, the mixture was neutralized with 5% $NaHCO_3$, concentrated and extracted with Et_2O. The Et_2O layer was washed with H_2O, dried and evaporated *in vacuo* and the residue (68 mg.) was chromatographed on silica gel (1 g.). Elution with benzene–$CHCl_3$ (9:1 to 1:1) and recrystallization of the eluate (65 mg.) from Me_2CO gave the acetonide (XIV) (46 mg.), m.p. 187~188°, as needles, $[\alpha]_D$ −46° (0.51). IR $\nu_{max}^{CCl_4}$ cm^{-1} : 3635, 1382, 1374. *Anal.* Calcd. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found : C, 75.51; H, 10.37.

The authors express their deep gratitude to Dr. Ken'ichi Takeda, Director of this Laboratory, for his helpful guidance throughout the course of this work.

Summary

Catalytic hydrogenations of the A-nor-$\Delta^{3(5)}$-steroid derivatives have been described. The unsaturated 1β,2β,17β- (I) and 1β,2α,17β- (II) triols on hydrogenation with palladium-charcoal afforded the saturated 1β,17β-diol (IIIa) accompanied with hydrogenolysis of their allylic C_2-hydroxyl group, while with Adams' catalyst gave the respective trihydroxy-5β-steroids (IVa) and (Va). The unsaturated 1β,17β-dihydroxy-2-one (VIa) was hydrogenated over palladium-charcoal into the corresponding 5β-steroid (VIIa), but with Adams' catalyst to yield exclusively the 5α-steroid (XIa).

(Received November 9, 1964)