viscous syrup (50 mg.), which was characterized as a picrate of yellow needles (from EtOH), m.p. 185~186° (decomp.). This was identical with the one obtained as above.

3-Methyl-8,9-methylenedioxy-1*H*,6*H*-5,10b-ethano-2,3,4,4a-tetrahydrophenanthridine (VI)——The hydrochloride (200 mg.) of the foregoing base was dissolved in H_2O (1 ml.), to which $NaHCO_3$ (0.2 g.) and HCHO solution (0.2 ml.) were added. The mixture was heated on a steam bath for 30 min., when an oil separated. This oil was isolated from the mixture by decantation, washed thoroughly with H_2O to remove HCHO and then heated with conc. HCl (0.2 ml., 38%) on a steam bath for 1 hr. When cooled, the product was diluted with H_2O, shaken with Et_2O, and the aqueous layer was basified with NaOH to separate the base, which was extracted with Et_2O and worked up as usual. The residue was a syrup and distilled at 170~180° (bath temp.) at 1 mm. Hg. Yield, 130 mg.
Picrate : Yellow needles (from AcOH), m.p. 188° (decomp.). *Anal.* Calcd. for $C_{23}H_{24}O_9N_4$: C, 55.20; H, 4.83; N, 11.20. Found : C, 55.04; H, 4.83; N, 11.49.

Greatful acknowledgement is offered to Prof. Emeritus, S. Sugasawa for his guidance. Thanks are also due to Dr. T. Fujisawa, the Director of this laboratory, and to Dr. M. Ohara, the Director of Osaka Research Laboratory, for their active interest in this work.

Summary

3-Methyl-8,9-methylenedioxy-1*H*,6*H*-5,10b-ethano-2,3,4,4a-tetrahydrophenanthridine, which has the skeleton of crinane, was synthesized from the ketone, 2-(3,4-methylenedioxyphenyl)-5-methylcyclohexanone, which was derived from safrole.

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66. Hiroshi Ōsaka : On Steroidal Sapogenins. V.*1 Synthesis of 11-Oxygenated Spirostanes. (3).

(*Research Laboratory, Shionogi & Co., Ltd.**2)

Several kinds of 2,3-dihydroxyspirostan-11-one were synthesized in order to examine their behavior in Huang-Minlon reduction and reported in the previous papers.[1],*1 In the present series of work, several kinds of 2-hydroxyspirostan-11-one were prepared.

There are few reports on the preparation of steroids oxygenated at 2-position of the A-ring. One of them is the report by Pataki and others[2] who obtained 2β-hydroxy (axial) derivative by reduction of 2β,3β-epoxy-25D,5α-spirostane with lithium aluminium hydride and the other is that of Sheehan and others[3] who obtained 2-oxo derivative in one step by treatment of 2β-hydroxy-3β-tosyloxycholestane with collidine. On the other hand, synthesis of monohydroxy-steroids by reduction of monotosylate of vicinal diol with lithium aluminium hydride is known.[4] Attempt was therefore made to utilize this latter reaction to effect liberation of hydroxyl group at C-3 position of several kinds of 2,3-dihydroxy-11-oxo-sapogenins obtained earlier.[1],*1

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*1 Part IV : Yakugaku Zasshi, **81**, 1662 (1961).
*2 Sagisu, Fukushima-ku, Osaka (大坂 弘).
1) Part III. K. Takeda, H. Ōsaka, N. Maezono : Yakugaku Zasshi, **81**, 1657 (1961).
2) J. Pataki, G. Rosenkranz, C. Djerassi : J. Am. Chem. Soc., **73**, 5375 (1951).
3) J. C. Sheehan, W. F. Erman : *Ibid.*, **79**, 6050 (1957).
4) (a) P. Karrer, H. Asmis, K. N. Sarren, R. Schwyzer : Helv. Chim. Acta, **34**, 1022 (1951). (b) C. W. Shoppee, D. N. Jones, G. H. R. Summers : J. Chem. Soc., **1957**, 3100.

Partial acetylation of metagenone[5] (Ia) with acetic anhydride-pyridine in chloroform affords a mixture of monoacetates (Ib and Id), whose recrystallization from chloroform-petroleum ether gives (Id) as the main product, the pure compound melting at 248.5~250.5°. The crystals obtained from its mother liquor, as recrystallized from hydrous methanol, are that of its isomer (Ib) of m.p. 222~223.5°. The analytical values of these two products agree with those of metagenone monoacetate and their infrared spectra possess absorptions for hydroxyl, carbonyl, and acetyl groups. Mixed fusion of the two monoacetates show depression of the melting point.

The monoacetate (Ib) forms a tosylate (Ic) of m.p. 237.5° (decomp.), while the other monoacetate (Id) forms a tosylate (Ie) of m.p. 183~184°. Reduction of this latter tosylate (Ie) with lithium aluminium hydride and oxidation of its product with chromium trioxide gives the known 3,11-dioxo compound (Ⅶ). Consequently, (Ic) is considered to be the objective 3-tosylate. Similar treatment as above of this tosylate (Ic) gives a diketone (Ⅵ) which shows depression of the melting point on admixture with the 3,11-dioxo compound and this has proved the foregoing assumption to be correct. On the other hand, tosylation of the mixture of the monoacetates (Ib and Id) and treatment of the product by alumina chromatography easily separates the product into the two kinds of tosylate, (Ic) and (Ie).

Reduction of the tosylate (Ic) with lithium aluminium hydride and treatment of the product by alumina chromatography affords two kinds of diol compound; (Ⅱa), m.p. 213.5~214.5°, $[\alpha]_D^{19}$ −50.8°, from the fractions eluted with 9:1 and 4:1 mixture of benzene and ether, and (Ⅲa), m.p. 211~212.5°, $[\alpha]_D^{22}$ −56.4°, from the fraction eluted with benzene-ether (1:1) mixture. Oxidation of the diol (Ⅱa) with chromium trioxide-pyridine gives 2,11-dioxo compound (Ⅳ), m.p. 204.5~205.5°, which shows depression on admixture with a sample of 3,11-dioxo compound. Acetylation of this diol (Ⅱa) gives a monoacetate (Ⅱb) of m.p. 187~188°.

Oxidation of the other diol (Ⅲa) with chromium trioxide and pyridine also gives the 2,11-dioxo compound (Ⅵ), which shows no depression of the melting point on admixture with the 2,11-dioxo compound obtained from (Ⅱa) and infrared spectra of these two samples are in good agreement. Acetylation of this diol (Ⅲa) gives a monoacetate (Ⅲb) which does not crystallize. Cathylation of (Ⅲa) gives a monocathylate (Ⅲc) of m.p. 185~187°.

Since the hydroxyl groups in these two diols (Ⅱa and Ⅲa) are acetylable under mild conditions and both compounds form a monoacetate, the hydroxyl at the 11-position is considered to have a β-configuration.

The values of specific rotation of (Ⅱa) and (Ⅲa) are so close to each other that it is difficult to determine from it the configuration of the hydroxyl at C-2 position of these compounds.[6] However, as will be stated later, 25D,5β-spirostan-2α-ol acetate,[7] obtained by reduction of 2α,3α-epoxy-25D,5β-spirostane with lithium aluminium hydride, and the product obtained from Huang-Minlon reduction of (Ⅳa) were found to be identical, showing no depression of the melting point and the same infrared spectral curves. Consequently, (Ⅳa) is the 2α-hydroxy compound and (Ⅴa) is considered to be 2β-hydroxy compound. The foregoing evidences revealed that (Ib) was the 2-monoacetate and (Id) was the 3-monoacetate. The fact that both of the two monoacetates (Ⅱb and Ⅲb) are 2-acetates was confirmed, as will be stated later, by the formation of the same 2-oxo compound[7] by oxidation of the monohydroxyl compounds obtained by the Huang-Minlon reduction of (Ⅳa) and (Ⅴa).

Oxidation of the 2-monoacetate (Ⅱb) with chromium trioxide-pyridine gives the 11-oxo

5) K. Takeda, K. Hamamoto : This Bulletin, 8, 1004 (1960).
6) L. F. Fieser, M. Fieser : "Steroids," 177 (1958). Reinhold Publ. Co., New York.
7) H. Ōsaka : This Bulletin, **10**, 417 (1962).

compound (IVb), m.p. 177~178°, whose saponification with alkali affords 2α-hydroxy-11-oxo compound (IVa), m.p. 214~215°. On the other hand, the same oxidation of the other monoacetate (IIIb) gives the 11-oxo compound (Vb) of m.p. 160~161°, whose saponification with alkali affords 2β-hydroxy-11-oxo compound (Va) of m.p. 270.5~272.5°.

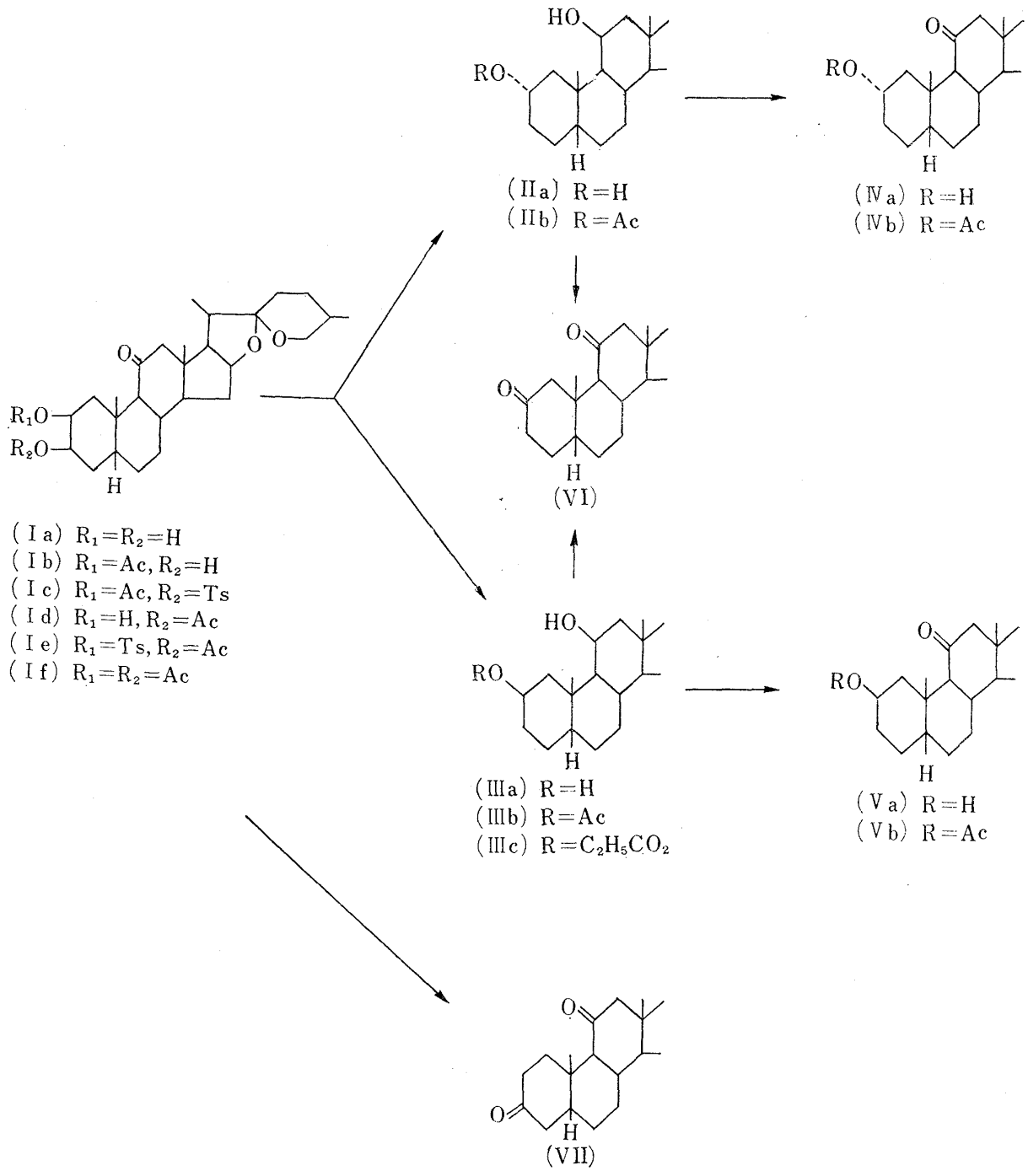

Chart 1.

Next is the synthesis of 2-hydroxy-25D,5α-spirostan-11-one. Tosylation of 2β,3β-dihydroxy-25D,5α-spirostan-11-one*1 (VIIIa) is considered to have taken place at the equatorial C-3 position to form the 3-tosylate (VIIIb), m.p. 170~172°, and its treatment with collidine gives (XIII), m.p. 235~237°, which shows depression of the melting point on admixture with 3,11-dioxo compound and should therefore be 2,11-dioxo compound. Re-

duction of (XIII) with lithium aluminium hydride would probably result in preferential reduction of the ketone group at C-11 to 11β-hydroxyl[8] and that of 2-oxo compound to a mixture of α- and β-hydroxyls.[9] Separation of these two kinds of diols (IXa and Xa) is difficult. Acetylation of the mixture of these two diols (IXa and Xa), without separation, under mild conditions afforded a mixture of monoacetates (IXb and Xb) and its oxidation gave a mixture of 2-acetoxy-11-oxo compounds (XIb and XIIb). Treatment of this mixture by alumina chromatography separates the mixture, affording (XIb), m.p. 245 ~247°, $[\alpha]_D^{25}$ −38.1°, from the fraction eluted with petroleum ether-benzene (1:1) mixture, and (XIIb), m.p. 201.5~202°, $[\alpha]_D^{25}$ −39.1°, from the fraction eluted with benzene. Alkali saponification of (XIb) and (XIIb) affords the respective isomers of 2-hydroxy-11-oxo compound; (XIa), m.p. 201~202°, $[\alpha]_D^{20}$ −24.7°, and (XIIa), m.p. 219~220°, $[\alpha]_D^{25}$ −28.7°. The fact that these (IXb) and (Xb) are 2-monoacetates was further confirmed from the Huang-Minlon reduction product, as in the case of 5β-series.

It is difficult to determine the configuration of 2-hydroxyl group in these two compounds as the values of their specific rotation are close to each other. Therefore, attempt was made to identify the compounds by synthesis of 2β-acetoxy-11-oxo compound by another route. For this purpose, 2β,3α-dihydroxy-25D,5α-spirostan-11-one 2-acetate (XIVa) synthesized earlier*[1] was used. Treatment of (XIVa) with methanesulfonyl chloride and pyridine to form 2β-acetoxy-3α-methanesulfonyl compound (XIVb), its treatment with potassium hydroxide gave 2β,3β-epoxy-11-oxo compound[2,10] (XV), m.p. 240~241°, and its reduction with lithium aluminium hydride afforded 2β,11β-diol (Xa), m.p. 210~212°. Acetylation of (Xa) under mild conditions gave a 2-monoacetate (Xb), m.p. 208~210°, and its oxidation with chromium trioxide and pyridine finally gave 2β-acetoxy-11-oxo compound of m.p. 201.5~202°, which was found to be identical with the isomer (XIIb) described above, by mixed fusion and comparison of their infrared spectra. Consequently, this isomer (XIIb) is the 2β-acetoxy-11-oxo compound and the other (XIb) would be the 2α-acetoxy-11-oxo compound.

2α-Acetoxy-11-oxo (XIb) and 2β-acetoxy-11-oxo (XIIb) compounds are also obtained by the following process. Detosylation of the 3-tosylate (VIIIb) with lithium aluminium hydride to form 2,11-diols (IXa and Xa), acetylation as above, oxidation of the acetates, and separation of the product by alumina chromatography affords 2α-acetoxy-11-oxo (XIb) and 2β-acetoxy-11-oxo (XIIb) compounds. These are identified with the foregoing isomers by mixed fusion and comparison of their infrared spectra.

Cathylation of the mixture of 2,11-diols (IXa and Xa), obtained on treatment of (VIIIb) with lithium aluminium hydride, and treatment of its product by alumina chromatography affords a monocathylate (Xc) of m.p. 204.5~205° from the fraction eluted with benzene and a monocathylate, probably of (IXa), from the fraction eluted with benzene-ether (19:1) mixture. No detailed examination of the latter was made due to the small amount available.

Saponification of the cathylate (Xc) with alkali affords a diol (Xa), m.p. 210.5~211°, identical with that obtained from 2β,3β-epoxy-11-oxo compound (XV), through mixed fusion and comparison of their infrared absorption spectra. Oxidation of (Xa) with chromium trioxide and pyridine affords 2,11-dioxo compound (XIII), m.p. 235~237°, which was identical with the compound described earlier.

The four kinds of compounds hereby synthesized, 2-hydroxy-25D,5β-spirostan-11-one (IVa and Va) and 2-hydroxy-25D,5α-spirostan-11-one (XIa and XIIa) are new substances. The Huang-Minlon reduction of these compounds will be described in the following papers.

8) K. Hamamoto : This Bulletin, 8, 1099 (1960).
9) W.G. Dauben, E.J. Blanz Jr., J. Jiu, R.A. Micheli : J. Am. Chem. Soc., **78**, 3752 (1956).
10) A. Fuerst, Pl. A. Plattner : Helv. Chim. Acta, **22**, 275 (1949).

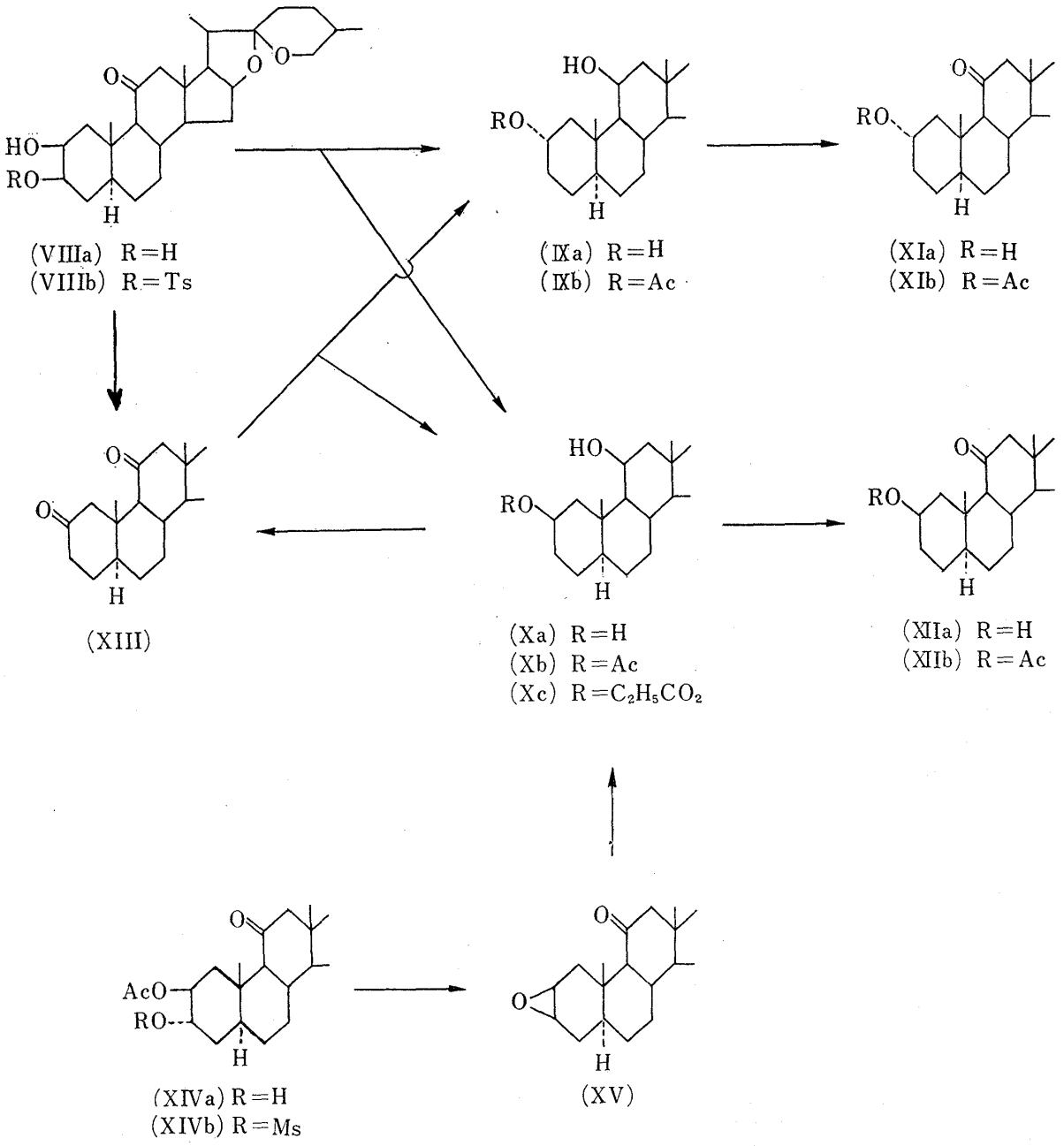

Chart 2.

Experimental

Metagenone Monoacetates (Ib and Id)——To a solution of 3 g. of metagenone (Ia) dissolved in a mixture of 100 cc. each of pyridine and $CHCl_3$, 25 cc. of Ac_2O was added dropwise with ice cooling and the mixture was allowed to stand for 18 hr. in a refrigerator. The mixture was diluted with H_2O and extracted with $CHCl_3$. The extract was washed consecutively with 10% H_2SO_4, 10% Na_2CO_3, and H_2O, dried over Na_2SO_4, and $CHCl_3$ was evaporated, leaving 3.255 g. of yellow syrupy substance. This was submitted to chromatography through alumina and elution with 9:1 and 1:1 mixture of benzene and Et_2O afforded 876 mg. of a diacetate (If) of m.p. 239~242°. Recrystallization from $CHCl_3$-MeOH mixture raised the m.p. to 241.5~245°, undepressed on admixture with an authentic specimen.[5]

From the fraction eluted with Et_2O, 1.858 g. of a syrupy mixture of monoacetates (Ib and Id) was obtained and crystallized from MeOH, m.p. 216~221°. Recrystallization of this mixture from

$CHCl_3$-petr. ether afforded needles (Id), m.p. 248.5~250.5°. $[\alpha]_D^{25}$ −50.6°(c=1.024). *Anal.* Calcd. for $C_{29}H_{44}O_6$: C, 71.28; H, 9.08. Found: C, 71.25; H, 9.14. IR ν_{max}^{Nujol} cm^{-1}: 1690(CO), 1743, 1242(AcO), 3560(OH).

From its mother liquor, crystals were obtained and recrystallized from hydr. MeOH to prisms (Ib), m.p. 222~223.5°. $[\alpha]_D^{15}$ −51.4°(c=1.051). *Anal.* Calcd. for $C_{29}H_{44}O_6$: C, 71.28; H, 9.08. Found: C, 71.03; H, 9.03. IR ν_{max}^{Nujol} cm^{-1}: 3480~3460(OH), 1734, 1260, 1248(AcO), 1707(CO).

From the fraction eluted with MeOH, 400 mg. of metagenone (Ia), m.p. 249.5~251.5°, was recovered.

2β-Acetoxy-3β-tosyloxy-25D, 5β-spirostan-11-one (Ic)——A mixture of 622 mg. of the 2-monoacetate (Ib), 15 cc. of pyridine, and 1.5 g. of tosyl chloride was allowed to stand overnight at room temperature, poured into ice water, and extracted with Et_2O. The extract was washed consecutively with 10% H_2SO_4, 10% Na_2CO_3 and H_2O, dried over Na_2SO_4, and Et_2O was evaporated, leaving 858 mg. of a residue. This residue was purified through alumina chromatography. From the fraction eluted with benzene and benzene-Et_2O (4 : 1) mixture, 521 mg. of (Ic), m.p. 236.5°(decomp.), was obtained and recrystallized from $CHCl_3$-petr. ether mixture to plates, m.p. 237.5°(decomp.). $[\alpha]_D^{21}$ −61.1°(c=1.025). *Anal.* Calcd. for $C_{36}H_{50}O_8S$: C, 67.26; H, 7.84; S, 4.99. Found: C, 67.35; H, 7.87; S, 5.13. IR ν_{max}^{Nujol} cm^{-1}: 1705(CO), 1744, 1245, 1237(AcO), 1602, 1496, 1177(tosylate).

3β-Acetoxy-2β-tosyloxy-25D, 5β-spirostan-11-one (Ie)——A mixture of 165 mg. of the 3-monoacetate (Id), 3 cc. of pyridine, and 0.5 g. of tosyl chloride was allowed to stand overnight at room temperature and treated in the usual manner to obtain 243 mg. of a residue, which was purified through alumina chromatography. The fraction eluted with benzene and benzene-Et_2O (4 : 1) mixture gave 244 mg. of a syrupy product, m.p. 182~183°, as crystallized from MeOH. Further crystallization from MeOH gave needles (Ie), m.p. 183~184°. $[\alpha]_D^{27}$ −59.0°(c=1.096). *Anal.* Calcd. for $C_{36}H_{50}O_8S$: C, 67.26; H, 7.84; S, 4.99. Found: C, 67.24; H, 7.92; S, 4.78. IR ν_{max}^{Nujol} cm^{-1}: 1709(CO), 1738, 1243(AcO), 1605, 1502, 1180(tosylate).

The same tosylation of 263 mg. of a mixture of monoacetates (Ib and Id) afforded 172 mg. of (Ic) and 113 mg. of (Ie).

Reduction of 3β-Acetoxy-2β-tosyloxy-25D, 5β-spirostan-11-one (Ie) with Lithium Alminium Hydride——A suspension of 5 g. of $LiAlH_4$ in 200 cc. of dehyd. tetrahydrofuran, added with 3 g. of the tosylate (Ie), was refluxed for 6 hr., excess $LiAlH_4$ was decomposed with H_2O, and tetrahydrofuran was distilled off. 10% H_2SO_4 was added to the residue which was extracted with Et_2O, and the extract was washed with H_2O and dried. Evaporation of Et_2O left 2.7 g. of a syrupy substance and this was purified through alumina chromatography.

From the fraction eluted with benzene-Et_2O (1 : 1) mixture, 1.744 g. of a syrupy substance, assumed to be a 3,11-diol, was obtained. To 400 mg. of this syrupy product, 400 mg. of CrO_3 and 4 cc. of pyridine were added and the mixture was allowed to stand overnight at room temperature to effect oxidation. Usual after-treatment gave 153 mg. of crystals (VII) which were purified by alumina chromatography. The crystals, m.p. 186.5~191.5°, thereby obtained were recrystallized from $CHCl_3$-petr. ether mixture to crystals of m.p. 204~206°, undepressed on admixture with authentic sample of the 3,11-dioxo compound.

From the fraction eluted with $CHCl_3$-MeOH (1 : 1) mixture, 770 mg. of unidentified syrupy substance was obtained but no detailed examination of this substance was made.

25D, 5β-Spirostane-2α, 11β-diol (IIa) and -2β, 11β-diol (IIIa)——To a solution of 1.809 g. of the 2β-acetoxy-3ε-tosylate compound (Ic) dissolved in 400 cc. of dehyd. Et_2O, 3.5 g. of $LiAlH_4$ suspended in dehyd. Et_2O was added and the mixture was refluxed for 5 hr. When cooled, excess $LiAlH_4$ was decomposed by addition of H_2O, the hydroxide that precipitated out was dissolved by addition of dil. HCl, and the solution was extracted with Et_2O. The extract was washed with H_2O, dried over Na_2SO_4, and Et_2O was evaporated. The residue was purified by alumina chromatography and the fractions eluted with benzene-Et_2O (9 : 1 and 4 : 1) mixture afforded 614 mg. of crystals (IIa). Recrystallization from hydr. MeOH gave cubic crystals, m.p. 213.5~214.5°. $[\alpha]_D^{19}$ −50.8°(c=1.019). *Anal.* Calcd. for $C_{27}H_{44}O_4$: C, 74.94; H, 10.25. Found: C, 74.70; H, 10.24. IR ν_{max}^{Nujol} cm^{-1}: 3560(OH).

From the fraction eluted with benzene-Et_2O (1 : 1) mixture, 468 mg. of a syrupy substance (IIIa) was obtained and crystallized from MeOH, m.p. 207~211°. Recrystallization from MeOH gave needles, m.p. 211~212.5°. $[\alpha]_D^{22}$ −56.4°(c=1.020). *Anal.* Calcd. for $C_{27}H_{44}O_4 \cdot \frac{1}{2}H_2O$: C, 73.43; H, 10.27. Found: C, 73.38; H, 10.30. IR ν_{max}^{Nujol} cm^{-1}: 3550(OH), 1645(H_2O).

25D, 5β-Spirostane-2, 11-dione (VI)——a) To a solution of 139 mg. of the 2α, 11β-diol (IIa) dissolved in 3 cc. of pyridine, a solution of 100 mg. of CrO_3 in 2 cc. of pyridine was added and the mixture was allowed to stand at room temperature for 18 hr. The mixture was poured into H_2O, extracted with Et_2O, and the extract was washed consecutively with 10% H_2SO_4, 10% Na_2CO_3, and H_2O. After drying over Na_2SO_4, Et_2O was evaporated, and 89 mg. of the syrupy residue so obtained was purified by alumina chromatography. From the fraction eluted with benzene-Et_2O (9 : 1) mixture, 60 mg. of (VI) was obtained and recrystallized from petr. ether-$CHCl_3$ to needles, m.p. 204.5~205.5°.

$[\alpha]_D^{23}$ −30.6° (c=0.874). *Anal.* Calcd. for $C_{27}H_{40}O_4$: C, 75.66; H, 9.41. Found: C, 75.77; H, 9.37. IR ν_{max}^{Nujol} cm^{-1}: 1710 (CO).

This substance showed depression of melting point on admixture with 25D, 5β-spirostane-3, 11-dione.

b) A solution of 102 mg. of the 2β, 11β-diol (IIIa) dissolved in 3 cc. of pyridine and a solution of 90 mg. of CrO_3 in 2 cc. of pyridine were treated as in the foregoing method (a) and 89 mg. of a syrupy product crystallized from MeOH, m.p. 176~182°. Purification through alumina chromatography gave 71 mg. of (VI), m.p. 204~205°, as recrystallized from $CHCl_3$-MeOH, and identified with the above-described 2, 11-dioxo compound by admixture and comparison of infrared spectra.

25D, 5β-Spirostane-2α, 11β-diol 2-Acetate (IIb)——A mixture of 327 mg. of the 2α, 11β-diol (IIa), 4 cc. of pyridine, and 4.5 cc. of Ac_2O was allowed to stand for 48 hr. at room temperature. Usual after-treatment afforded 369 mg. of a syrupy product which crystallized from MeOH, m.p. 184.5~187°. Recrystallization from hydr. MeOH gave (IIb) as plates, m.p. 187~188°. $[\alpha]_D^{21}$ −44.7° (c=0.992). *Anal.* Calcd. for $C_{29}H_{46}O_5$: C, 73.38; H, 9.77. Found: C, 73.36; H, 9.76. IR ν_{max}^{Nujol} cm^{-1}: 1732, 1270 (AcO), 3580 (OH).

25D, 5β-Spirostane-2β, 11β-diol 2-Acetate (IIIb)——A mixture of 346 mg. of the 2β, 11β-diol (IIIa), 10 cc. of pyridine, and 5 cc. of Ac_2O was allowed to stand for 48 hr. at room temperature. Usual after-treatment afforded 311 mg. of a syrupy product which was purified through alumina chromatography. The fraction eluted with petr. ether-benzene (1 : 1) mixture gave 284 mg. of a syrupy substance (IIIb) which did not crystallize.

25D, 5β-Spirostane-2β, 11β-diol 2-Cathylate (IIIc)——To a solution of 118 mg. of (IIIa) dissolved in 6 cc. of pyridine, 0.5 cc. of ethyl chlorocarbonate was added dropwise with ice-cooling and the mixture was allowed to stand for 24 hr. at room temperature. The mixture was poured into H_2O, extracted with Et_2O, and the extract was washed consecutively with 10% H_2SO_4, 10% Na_2CO_3, and H_2O. After drying over Na_2SO_4, Et_2O was evaporated and 134 mg. of a syrupy residue so obtained was purified through alumina chromatography. The fractions eluted with petr. ether-benzene (1 : 1) mixture and benzene afforded 104 mg. of syrupy (IIIc). Recrystallization from $CHCl_3$-MeOH gave cubic crystals, m.p. 185~187°. $[\alpha]_D^{22}$ −42.7° (c=0.999). *Anal.* Calcd. for $C_{30}H_{48}O_6$: C, 71.39; H, 9.59. Found: C, 71.57; H, 9.61. IR ν_{max}^{Nujol} cm^{-1}: 3540 (OH), 1746, 1580, 1260, 790 (cathylate).

The recrystallization mother liquor was concentrated and 32 mg. of a syrupy residue so obtained was dissolved in 1 cc. of 10% MeOH-KOH. This solution was refluxed for 3 hr. to effect saponification, MeOH was evaporated, the residue was diluted with H_2O, and 22 mg. of crystals (IIIa) that precipitated out was collected. Recrystallization from $CHCl_3$-MeOH gave crystals of m.p. 197~200°, undepressed on admixture with an authentic sample of the 2β-ol (IIIa) but depressed on admixture with 2α-ol (IIa).

2α-Acetoxy-25D, 5β-spirostan-11-one (IVb)——A mixture of 262 mg. of crude (IIb), 200 mg. of CrO_3, and 4 cc. of pyridine was allowed to stand for 48 hr. at room temperature and usual after-treatment afforded 262 mg. of a syrupy product. This was purified by alumina chromatography and the fraction eluted with petr. ether-benzene (1 : 1) mixture gave 154 mg. of a syrupy substance which crystallized on treatment with MeOH. Recrystallization from hydr. MeOH gave (IVb) as needles, m.p. 177~178°. $[\alpha]_D^{21}$ −20.5° (c=0.805). *Anal.* Calcd. for $C_{29}H_{44}O_5$: C, 73.69; H, 9.38. Found: C, 73.61; H, 9.38. IR ν_{max}^{Nujol} cm^{-1}: 1706 (CO), 1743, 1730, 1250, 1228 (AcO).

2α-Hydroxy-25D, 5β-spirostan-11-one (IVa)——A mixture of 172 mg. of (IVb) and 18 cc. of 10% MeOH-KOH was refluxed for 1 hr. to effect saponification, MeOH was evaporated, the residue was diluted with H_2O, and extracted with Et_2O to afford 136 mg. of a crude product, m.p. 212~214.5°. Purification through alumina chromatography and elution with benzene and benzene-Et_2O (9 : 1) mixture gave 125 mg. of (IVa). Recrystallization from $CHCl_3$-petr. ether gave needles, m.p. 214~215°. $[\alpha]_D^{23}$ −27.2° (c=0.937). *Anal.* Calcd. for $C_{27}H_{42}O_4$: C, 75.31; H, 9.83. Found: C, 75.12; H, 9.88. IR ν_{max}^{Nujol} cm^{-1}: 1700, 1690 (CO), 3540 (OH).

2β-Acetoxy-25D, 5β-spirostan-11-one (Vb)——A solution of 231 mg. of (IIIb) dissolved in 4 cc. of pyridine and added with 200 mg. of CrO_3 and 3 cc. of pyridine was allowed to stand at room temperature for 2 days. Usual after-treatment afforded 228 mg. of a syrupy product which was purified through alumina chromatography. From the fraction eluted with petr. ether-benzene (1 : 1) mixture, a syrupy substance (Vb) was obtained and crystallized from MeOH, m.p. 159~160.5°. Recrystallization from $CHCl_3$-MeOH gave needles, m.p. 160~161°. $[\alpha]_D^{20}$ −41.9° (c=1.022). *Anal.* Calcd. for $C_{29}H_{44}O_5$: C, 73.69; H, 9.38. Found: C, 73.70; H, 9.41. IR ν_{max}^{Nujol} cm^{-1}: 1708 (CO), 1730, 1248 (AcO).

2β-Hydroxy-25D, 5β-spirostan-11-one (Va)——A mixture of 80 mg. of (Vb) and 10% MeOH-KOH was refluxed for 1 hr. on a water bath and usual after-treatment gave 58 mg. of crude (Va). Recrystallization from $CHCl_3$-MeOH gave needles, m.p. 270.5~272.5° $[\alpha]_D^{21}$ −43.7° (c=0.974). *Anal.* Calcd. for $C_{27}H_{42}O_4$: C, 75.31; H, 9.83. Found: C, 75.60; H, 9.96. IR ν_{max}^{Nujol} cm^{-1}: 3590 (OH), 1690 (CO).

2β, 3β-Dihydroxy-25D, 5α-spirostan-11-one 3-Tosylate (VIIIb)——A solution of 4 g. of 2β, 3β-dihydroxy-25D, 5α-spirostan-11-one (VIIIa) dissolved in 40 cc. of pyridine and added with 8 g. of tosyl chlo-

ride was allowed to stand overnight at room temperature, poured into H_2O, and crystals that precipitated out were collected by filtration. After washing with H_2O, the crystals were dried and recrystallized from MeOH to 3.9 g. of (VIIIb), m.p. 169~170° (decomp.). Recrystallization from MeOH twice gave needles, m.p. 170~172° (decomp.). $[\alpha]_D^{25}$ −16.0° (c=1.050). *Anal.* Calcd. for $C_{34}H_{48}O_7S$: C, 67.97; H, 8.05; S, 5.34. Found: C, 67.88; H, 8.08; S, 5.47. IR ν_{max}^{Nujol} cm^{-1}: 3600 (OH), 1700 (CO), 1603, 1498, 1177 (tosylate).

2-Acetoxy-25D, 5α-spirostan-11-one (XIb and XIIb)——a) Reduction of 25D, 5α-Spirostane-2, 11-dione with $LiAlH_4$: A solution of 0.5 g. of $LiAlH_4$ in 40 cc. of dehyd. Et_2O was added to a solution of 0.4 g. of the 2, 11-dione (XIII) dissolved in 60 cc. of dehyd. Et_2O and the mixture was stirred for 1 hr. at room temperature. Excess $LiAlH_4$ was decomposed by addition of 60 cc. of 20% H_2SO_4 under ice-cooling, Et_2O layer was separated, and washed with $NaHCO_3$ solution and H_2O. Evaporation of Et_2O left 398 mg. of a mixture of diols (IXa and Xa), m.p. 198~201°. Without purification, this mixture was allowed to stand with 5 cc. each of Ac_2O and pyridine at room temperature overnight to effect acetylation. Usual treatment gave 445 mg. of a mixture of monoacetates (IXb and Xb), m.p. 191~194°.

This mixture of monoacetates was dissolved in 10 cc. of pyridine, 0.45 g. of CrO_3 and 5 cc. of pyridine were added, and the mixture was allowed to stand overnight at room temperature. Usual aftertreatment afforded 405 mg. of a mixture of 2-acetoxy-11-oxo compounds (XIb and XIIb), m.p. 165~180°, which was purified through alumina chromatography. The fraction eluted with benzene-petr. ether mixture afforded 121 mg. of 2α-acetoxy-11-oxo compound (XIb), m.p. 191~220°. Recrystallization from $CHCl_3$-MeOH gave needles, m.p. 245~247°. $[\alpha]_D^{25}$ −38.1° (c=1.031). *Anal.* Calcd. for $C_{29}H_{44}O_5$: C, 73.69; H, 9.38. Found: C, 73.44; H, 9.36. IR ν_{max}^{Nujol} cm^{-1}: 1705 (CO), 1737, 1243 (AcO).

From the benzene fraction, 204 mg. of 2β-acetoxy-11-oxo compound (XIIb), m.p. 189~191°, was obtained. Recrystallization from $CHCl_3$-MeOH gave scaly crystals, m.p. 201.5~202°. $[\alpha]_D^{25}$ −39.1° (c=1.032). *Anal.* Calcd. for $C_{29}H_{44}O_5$: C, 73.69; H, 9.38. Found: C, 73.52; H, 9.42. IR ν_{max}^{Nujol} cm^{-1}: 1700 (CO), 1730, 1242 (AcO).

b) Reduction of (VIIIb) with $LiAlH_4$: A solution of 5.2 g. of 2β, 3β-dihydroxy-25D, 5α-spirostan-11-one 3-tosylate (VIIIb) dissolved in 400 cc. of dehyd. Et_2O was added to a solution of 6 g. of $LiAlH_4$ in 100 cc. of dehyd. Et_2O and the mixture was refluxed for 5 hr. Subsequent acetylation and oxidation of its product as in the foregoing (a) afforded 0.77 g. of (XIb) and 1.6 g. of (XIIb), which were identified with the same substances obtained as above, through mixed fusion and comparison of infrared spectra.

25D, 5α-Spirostane-2β, 11β-diol 2-Cathylate (Xc)——A solution of 5 g. of $LiAlH_4$ dissolved in 500 cc. of dehyd. Et_2O was added to a solution of 3.4 g. of the 3-tosylate (VIIIb) dissolved in 350 cc. of dehyd. Et_2O and the mixture was refluxed for 5 hr. The usual after-treatment gave 2.55 g. of a mixture of diols (Xa and IXa), m.p. 194~200°.

A mixture of 2.55 g. of this diol mixture, 30 cc. of pyridine, and 6 cc. of ethyl chlorocarbonate was allowed to stand overnight at room temperature, poured into H_2O, and extracted with $CHCl_3$. The extract was washed consecutively with dil. H_2SO_4, dil. Na_2CO_3, and H_2O, and $CHCl_3$ was evaporated, leaving 3.347 g. of an orange product. This product was purified by alumina chromatography and the fraction eluted with benzene gave 2.125 g. of (Xc), m.p. 178~186°. Recrystallization from MeOH gave needles, m.p. 204.5~205°. $[\alpha]_D^{29}$ −42.5° (c=1.007). *Anal.* Calcd. for $C_{30}H_{48}O_6$: C, 71.39; H, 9.59. Found: C, 71.25; H, 9.57. IR ν_{max}^{Nujol} cm^{-1}: 3580 (OH), 1715, 1277, 798 (cathylate).

The fraction eluted with benzene-EtO_2 (19 : 1) mixture gave 285 mg. of a product melting at 166~169°, which was recrystallized from MeOH to needles, m.p. 194°, which showed depression on admixture with the foregoing (Xc). This was assumed to be the 2α-cathylate but no detailed examination was made. *Anal.* Calcd. for $C_{30}H_{48}O_6$: C, 71.39; H, 9.59. Found: C, 71.39; H, 9.55. IR ν_{max}^{Nujol} cm^{-1}: 3540 (OH), 1753, 1265, 793 (cathylate).

25D, 5α-Spirostane-2β, 11β-diol (Xa)——a) A solution of 800 mg. of the 2β, 3β-epoxy-11-oxo compound (XV) dissolved in 40 cc. of dehyd. Et_2O was added to the solution of 1.60 g. of $LiAlH_4$ in 50 cc. of dehyd. Et_2O and the mixture was refluxed for 4 hr. on a water bath. The usual treatment of the reaction mixture gave 800 mg. of jellylike substance which was recrystallized from Et_2O-hexane to needles, m.p. 210~212°. $[\alpha]_D^{26}$ −42.3° (c=1.024). *Anal.* Calcd. for $C_{27}H_{44}O_4 \cdot \frac{1}{2}H_2O$: C, 73.43; H, 10.27. Found: C, 73.60; H, 10.35. IR ν_{max}^{Nujol} cm^{-1}: 3400~3550 (OH), 1640 (H_2O).

b) A mixture of 1 g. of the cathylate (Xc) in 10% MeOH-KOH was refluxed for 1 hr., MeOH was evaporated, and the residue was diluted with H_2O. The crystals that precipitated out were collected by filtration, washed with H_2O, and dried to 0.907 g. of (Xa), m.p. 204~208°. Recrystallization from MeOH gave needles, m.p. 210~212°, undepressed on admixture with (Xa) obtained as in above (a). Their infrared spectra were also in good agreement.

25D, 5α-Spirostane-2, 11-dione (XIII)——a) From the 3-Tosylate (VIIIb): A mixture of 900 mg. of (VIIIb) and 7 cc. of collidine was refluxed for 6 hr., collidine was distilled off almost completely, the residue was diluted with H_2O, and dil. H_2SO_4 was added. The crystals that precipitated out were collected by filtration, washed with H_2O, and dried. Purification through alumina chromatography

and elution with benzene and benzene-Et_2O mixture gave 530 mg. of (XIII). Recrystallization from $CHCl_3$-hexane afforded needles, m.p. 235~237°. $[\alpha]_D^{25}$ −11.3°(c=0.995). *Anal.* Calcd. for $C_{27}H_{40}O_4$: C, 75.65; H, 9.41. Found: C, 75.73; H, 9.47. IR ν_{max}^{Nujol} cm^{-1}: 1695(CO). This product showed depression of melting point on admixture with 25D, 5α-spirostane-3, 11-dione.

b) From the 2β, 11β-Diol (Xa): A mixture of 100 mg. of (Xa), 5 cc. of pyridine, and 800 mg. of CrO_3 was allowed to stand for 38 hr. at room temperature. The usual treatment gave 68 mg. of (XIII), m.p. 229~232°, which was recrystallized from MeOH to scales, m.p. 235~237°, undepressed on admixture with the 2, 11-dione compound obtained as above. The infrared spectra of the two were also in good agreement.

25D, 5α-Spirostane-2β, 11β-diol 2-Acetate (Xb)——A mixture of 1 g. of the 2β, 11β-diol (Xa), 10 cc. of Ac_2O, and 24 cc. of pyridine was allowed to stand overnight at room temperature, poured into H_2O, and the crystals that separated out were collected by filtration. The crystals were washed with H_2O and dried to 0.913 mg. of crystals, m.p. 185~195°, which were recrystallized from MeOH to (Xb) as scales, m.p. 208~210°. $[\alpha]_D^{26}$ −41.3°(c=1.012). *Anal.* Calcd. for $C_{29}H_{46}O_5$: C, 73.38; H, 9.77. Found: C, 73.19; H, 9.79. IR ν_{max}^{Nujol} cm^{-1}: 3550(OH), 1735, 1240, 1250(AcO).

2β-Acetoxy-25D, 5α-spirostan-11-one (XIIb)——A mixture of 500 mg. of the 2β-acetoxy-11-hydroxy compound (Xb), 400 mg. of CrO_3, and 25 cc. of pyridine was allowed to stand overnight at room temperature, poured into H_2O, and the solution was filtered. The filtrate was extracted with Et_2O, the extract was washed consecutively with 10% H_2SO_4, 10% Na_2CO_3, and H_2O, dried over Na_2SO_4, and evaporation of Et_2O left 424 mg. of a product. This was purified through alumina chromatography and fractions eluted with petr. ether-benzene (1 : 1) mixture and benzene afforded 337 mg. of crude crystals melting at 196~197.5°. Recrystallization from MeOH afforded (XIIb) as scales, m.p. 201.5~202°, undepressed on admixture with the authentic sample obtained earlier. The infrared spectra of the two substances were also in good agreement.

2α-Hydroxy-25D, 5α-spirostan-11-one (XIa)——A mixture of 0.48 g. of the 2α-acetoxy-11-oxo compound (XIb) and 10% MeOH-KOH was refluxed for 1.5 hr. and usual treatment gave 0.32 g. of (XIa) as needles, m.p. 201~202°, recrystallized from MeOH. $[\alpha]_D^{20}$ −24.7°(c=0.673). *Anal.* Calcd. for $C_{27}H_{42}O_4$: C, 75.31; H, 9.83. Found: C, 75.04; H, 9.80. IR ν_{max}^{Nujol} cm^{-1}: 1690(CO), 3530(OH).

2β-Hydroxy-25D, 5α-spirostan-11-one (XIIa)——A mixture of 0.99g. of the 2β-acetoxy-11-oxo compound (XIIb) and 10% MeOH-KOH was refluxed for 1.5 hr. and usual after-treatment gave 0.60 g. of needles (from $CHCl_3$-MeOH), m.p. 219~220°. $[\alpha]_D^{25}$ −28.7°(c=1.033). *Anal.* Calcd. for $C_{27}H_{42}O_4$: C, 75.31; H, 9.83. Found: C, 75.37; H, 9.89. IR ν_{max}^{Nujol} cm^{-1}: 3450(OH), 1704(CO).

2β, 3β-Epoxy-25D, 5α-spirostan-11-one (XV)——To a solution of 3.2 g. of syrupy 25D, 5α-spirostane-2β, 3α-diol 2-acetate (XIVb) dissolved in 15 cc. of pyridine, 6 cc. CH_3SO_2Cl was added in small portions and the mixture was allowed to stand for 44 hr. at room temperature. The mixture was acidified with dil. HCl, extracted with $CHCl_3$, and the usual treatment of the extract afforded a dark brown, syrupy product. This was purified through alumina chromatography and 3.5 g. of yellow syrupy (XIVb) was obtained from the fraction eluted with benzene. IR ν_{max}^{Nujol} cm^{-1}: 1741, 1238(AcO), 1706 (CO), 1179(mesylate).

A solution of 3.5 g. of (XIVb) and 2.1 g. of KOH dissolved in 800 cc. of MeOH was refluxed for 2 hr. on a water bath, MeOH was evaporated in a reduced pressure, and the residue was extracted with $CHCl_3$. Usual treatment of the $CHCl_3$ extract gave 2.7 g. of powdery (XV), which was recrystallized from Me_2CO to needles, m.p. 240~241°. *Anal.* Calcd. for $C_{27}H_{40}O_4$: C, 75.65; H, 9.41. Found: C, 75.35; H, 9.31. IR ν_{max}^{Nujol} cm^{-1}: 1694(CO), 815(epoxide).

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Summary

In order to examine the Huang-Minlon reduction of the 11-ketone group in steroids, 2-hydroxy-25D,5β- and -5α-spirostan-11-one of various configurations were synthesized from 2,3-dihydroxyspirostan-11-one.

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