Notes

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The Isomers of 25D,5β-spirostane-2,3-diol.

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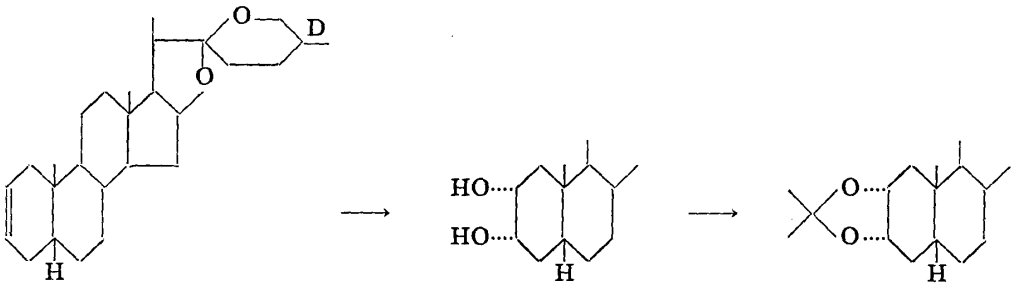
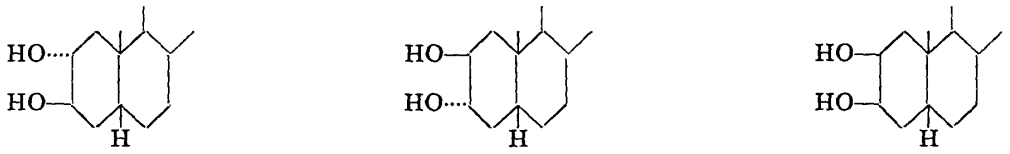
The four possible diols epimeric at C-2 and C-3 in 25D,5α-spirostane-2,3-diols have all been synthesized in the course of structural elucidation of gitogenin (25D,5α-spirostane-2α,3β-diol), by Djerassi,[1,3] Sondheimer[2] and their co-workers.

However, in regard to the 25D,5β-spirostane-2,3-diols, it was only known formerly that samogenin,[4] first isolated from *Samuela carnerosana* TREL., has the stauctures of 25D,-5β-spirostane-2β,3β-diol (IV)[5] and that epimerisation of this sapogenin with sodium and alcohol gave *epi*-samogenin,[4] which was assumed to be the corresponding 2β,3α-diol.



(I)



(II) (III) (IV)

Yonogenin Samogenin

Recently,[6] a new sapogenin, yonogenin, was isolated from the epigenous part of *Dioscorea tokoro* MAKINO and the structure of this sapogenin was clarified as 2β,3α-diol (III), identical with *epi*-samogenin. In the present series of experiments, acetolysis of 2β,3β-epoxy-25D,5β-spirostane followed by saponification yielded another *trans*-isomer, the 2α,3β-diol (II) which differed from yonogenin.

To complete the series of 25D,5β-spirostane-2,3-diols, partial synthesis of the fourth possible isomer, the 2α,3α-diol (I), has now been accomplished. 25D,5β-Spirost-2-ene,[6] derived from yonogenin dimesylate, was submitted to the silver acetate-iodine oxidation, which was reported by Woodward[7] for the preparation of a *cis*-glycol of opposite configuration to that obtained with osmium tetroxide oxidation. It yielded as the major

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1) J. Pataki, G. Rosenkranz, C. Djerassi : J. Am. Chem. Soc., **73**, 5375(1951).
2) J. Herran, G. Rosenkranz, F. Sondheimer : *Ibid.*, **76**, 5531(1954).
3) C. Djerassi, L. B. High, T. T. Grossnickle, R. Ehrlich, J. A. Moore, R. B. Scott : Chem. & Ind. (London), **1955**, 474.
4) R. E. Marker, *et al.* : J. Am. Chem. Soc., **69**, 2194(1947).
5) C. Djerassi, J. Fishman : *Ibid.*, **77**, 4291(1955).
6) K. Takeda, T. Okanishi, A. Shimaoka : This Bulletin, **6**, 532(1958).
7) R. B. Woodward, F. V. Brutcher, Jr. : J. Am. Chem. Soc., **80**, 209(1958).

product a new diol, m.p. 202~204°, $[\alpha]_D$ −75° (diacetate, m.p. 152~154°, $[\alpha]_D$ −70°), which formed an acetonide of m.p. 184°. This diol was proved to be different in physical constants and infrared spectrum from those of the above-mentioned three isomers and is therefore believed to be the expected 2α,3α-diol (I).

The physical constants of the four isomeric 25D,5β-spirostane-2,3-diols and their acetates are shown in Table I.

Table I.

	Genin		Acetate		Acetonide	
	m.p. (°C)	$[\alpha]_D$	m.p. (°C)	$[\alpha]_D$	m.p. (°C)	$[\alpha]_D$
25D,5β-spirostane-2α,3α-diol (I)	202~204	−75°	154	−70°	184	—
-2α,3β-diol (II)	198	−60°	168	−78°	—	—
-2β,3α-diol (III)	238~240	−56°	212	−26°	—	—
-2β,3β-diol (IV)	207	−80°	195	−73°	167~170	−72°

Although investigation on the infrared spectra of these four isomeric diacetates was also carried out in this laboratory, details will be reported elsewhere.

Experimental*2

25D,5β-Spirostane-2α,3α-diol—To a slurry of 398 mg. of 25D,5β-spirost-2-ene[6] and 376 mg. of AgOAc in 22 cc. of glacial AcOH, 267 mg. of powdered I_2 was added in small portions during 30 min. under vigorous stirring at room temperature. After stirring for an additional 1 hr., 4.5 cc. of glacial AcOH containing 1 drop of H_2O was added. The reaction mixture was then heated at 90~95° for 3 hr. with stirring. The reaction mixture was cooled, treated with 1 g. of NaCl, and filtered. The precipitate was thoroughly washed with hot benzene and the combined filtrate was evaporated under a reduced pressure. The residue was dissolved in 30 cc. of MeOH, neutralized with KOH-MeOH, and then 0.75 g. of KOH dissolved in 4 cc. of MeOH was added in N_2 atmosphere. The mixture was allowed to stand at room temperature overnight and neutralized with dil. HCl under cooling in an ice bath. The product was extracted with Et_2O, the Et_2O solution was washed with H_2O, dried over Na_2SO_4, and evaporated to give 407 mg. of a solid residue which afforded crystals of the crude diol on triturating with a small amount of MeOH.

A part of this crude diol was further recrystallized from MeOH to 25D,5β-spirostane-2α,3α-diol (I) as needles, m.p. 202~204°, $[\alpha]_D^{30}$ −75°. *Anal.* Calcd. for $C_{27}H_{44}O_4$: C, 74.95; H, 10.25. Found: C, 74.65; H, 10.37.

The remainder (180 mg.) of the above crude diol was acetylated by heating with 2 cc. of pyridine and 4 cc. of Ac_2O for 30 min. on a steam bath. The acetate, separated with Et_2O in the usual manner, was chromatographed over alumina to yield the following fractions: (A) Petr. ether-benzene (4:1 to 1:1) eluate, m.p. 110~122°, 80 mg.; (B) benzene eluate, m.p. 185~192°, 20 mg.; and (C) benzene-$CHCl_3$ (1:1) eluate, m.p. 115~120°, 60 mg.

Fraction (A) on recrystallization from MeOH furnished the 2α,3α-diacetate as prisms. After drying *in vacuo* at 60° for 5 hr., the analytical sample showed the following constants: m.p. 152~154°, $[\alpha]_D^{30}$ −70°. IR cm^{-1}: $\nu_{C=O}$ 1745, ν_{C-O} 1241, 1222 (CS_2). *Anal.* Calcd. for $C_{31}H_{48}O_6$: C, 72.06; H, 9.36. Found: C, 72.21; H, 9.39.

Alkaline hydrolysis of this diacetate and recrystallization of the product from MeOH gave the 2α,3α-diol (I) as needles, m.p. 202~204°, which was identical with a sample obtained by direct recrystallization of the crude diol from MeOH.

Fraction (B) from the above chromatography was recrystallized from MeOH to needles, m.p. 192~194°. No depression of melting point was observed on admixture with an authetic sample of samogenin diacetate and infrared spectra of the two substances were identical. *Anal.* Calcd. for $C_{31}H_{48}O_6$: C, 72.06; H, 9.36. Found: C, 72.58; H, 9.43.

Fraction (C) was recrystallized from MeOH to the analytical sample, m.p. 125~128°. IR (Nujol) cm^{-1}: ν_{OH} 3496, $\nu_{C=O}$ 1731, ν_{C-O} 1270, 1245. This substance was assumed to be the 2α,3α-diol 3-monoacetate, because it gave the 2α,3α-diol (I), m.p. 202~204°, identical with the above-mentioned sample, by saponification. *Anal.* Calcd. for $C_{29}H_{46}O_5$: C, 73.38; H, 9.77. Found: C, 73.45; H, 10.12.

25D,5β-Spirostane-2α,3α-diol Acetonide—25D,5β-Spirostane-2α,3α-diol (I) (30 mg.) was refluxed for

*2 All melting points are uncorrected. Specific rotations were measured in $CHCl_3$.

5 hr. with 15 cc. of acetone containing 10 mg. of *p*-toluenesulfonic acid. The solution was neutralized with Na_2CO_3 solution and concentrated under reduced pressure. The product was extracted with Et_2O, the extract was washed with H_2O, and dried over Na_2SO_4. After removal of the solvent, the crystalline residue, m.p. 140~155°, was chromatographed on alumina. Elution with petr. ether (b.p. 40~60°)-benzene (4:1) furnished 15 mg. of the acetonide, which was recrystallized from MeOH to needles, m.p. 184°. *Anal.* Calcd. for $C_{30}H_{48}O_4$: C, 76.22; H, 10.24. Found: C, 76.03; H, 10.31.

Summary

Partial synthesis of 25D,5β-spirostane-2α,3α-diol, the only unknown isomer of 25D,5β-spirostane-2,3-diols, is described.

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Hiroshi Tanida: Quinoline and Related Compounds. III.[1] The Direct N-Methylphenylamination of Quinoline 1-Oxide.

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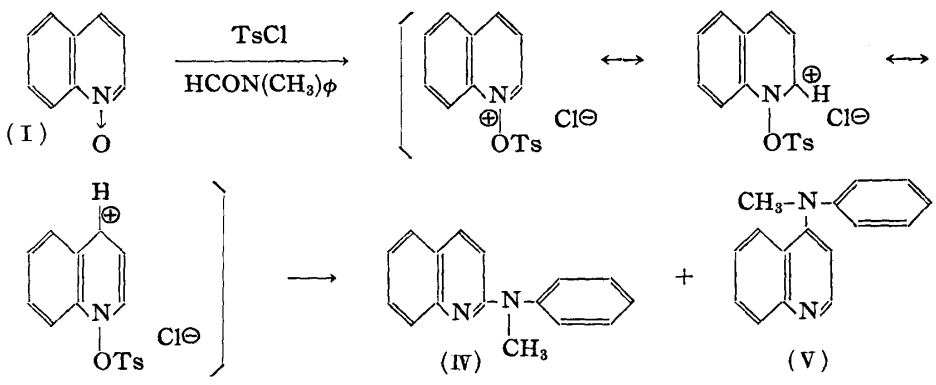
In the previous paper[2] dealing with the reaction between quinoline 1-oxide and tosyl chloride in dimethylformamide, it was shown that 2- and 4-dimethylaminoquinolines were prepared directly from quinoline 1-oxide. According to the mechanism described in that paper, it is possible to apply this reaction to various dialkylaminoformamides. The present work is one example to which this reaction was applied.

When quinoline 1-oxide (I) was heated with tosyl chloride in N-methylformanilide in the presence of boric trifluoride, a colorless oil (IV), $b.p_{0.1}$ 135~140° (Picrate: Cubic crystals, m.p. 167~168°) and a slightly yellow oil (V) (picrate of needles, m.p. 177~178°) were obtained. The composition of both picrates agreed with $C_{16}H_{14}N_2 \cdot C_6H_3O_7N_3$, and the ultraviolet absorption curves exhibited the additive curve of aminoquinoline and aniline. On the basis of these data, it seems reasonable to assume that (IV) and (V) are 2- and 4-(N-methylanilino)quinolines, respectively. The chemical proof was furnished by admixture with an authentic sample, which was prepared from chloroquinoline and methylaniline. The yield of those products was 31% of (IV) and 20% of (V).



*1 Imafuku, Amagasaki, Hyogo-ken (谷田 博).

1) Part II: This Bulletin, 7, 887(1959).
2) H. Tanida: Yakugaku Zasshi, 78, 608(1958).