*UDC 547.92 : 582.572.7*

## The Structure of Tokorogenin

In a previous report[1] from these Laboratories it was described that a new steroidal sapogenin "tokorogenin" was isolated from rhizomes of *Dioscorea tokoro* MAKINO and was shown to be degraded to a triacetoxypregn-16-en-20-one via the pseudosapogenin followed by chromic acid oxidation.

The present communication reports the elucidation of the structure of tokorogenin to be 1$\beta$,2$\beta$,3$\alpha$-trihydroxy-25D-5$\beta$-spirostane (I) by the following reactions.

Chromic acid oxidation of (I) in acetic acid gave tokorogenic acid (II), m.p. 250°; $[\alpha]_D^{23}$ −26.3° (*Anal.* Calcd. for $C_{26}H_{40}O_6$ : C, 69.61; H, 8.99. Found : C, 69.65; H, 9.43). With acetic anhydride, (II) was converted to acid anhydride (III), m.p. 268°; $\nu_{max}^{Nujol}$ 1800 and 1755 $cm^{-1}$ (*Anal.* Calcd. for $C_{26}H_{38}O_5$ : C, 72.52; H, 8.90. Found : C, 72.47; H, 9.09). By the action of diazomethane, (II) afforded dimethyl ester (IV), m.p. 157°, but with methanolic hydrochloric acid and (II) $\alpha$-monomethyl ester (V), m.p. 185°, was obtained. (V) also resulted from (III) and sodium methoxide. The alkaline hydrolysis of (IV), on the contrary, produced the isomeric $\beta$-monomethyl ester (VI), m.p. 208°. Similar observations have been made in camphoric acid[2] and etiobilienic acid,[3] thus providing an evidence that tokorogenic acid (II) possesses one carboxylic group attached to the tertiary carbon atom at C-10 and hence tokorogenin would be 1,2,3-trihydroxysapogenin.

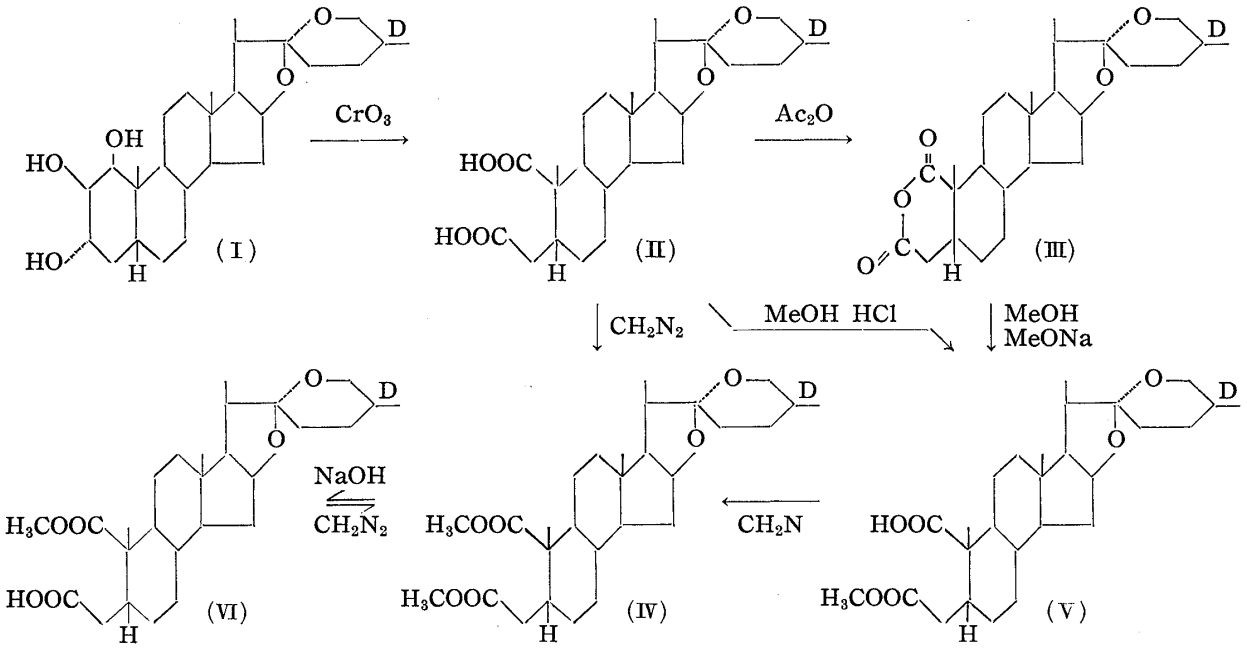



Chart 1.

Tokorogenin forms the acetonide (VII), m.p. 303°(decomp.) (*Anal.* Calcd. for $C_{30}H_{48}O_5$: C, 73.73; H, 9.90. Found : C, 73.50; H, 9.90), which is readily changed to (I) in boiling aqueous acetic acid. With pyridine and *p*-toluenesulfonyl chloride, (VII) gave the acetonide tosyl ester (VIII), m.p. 203°(decomp.), which then converted to (IX), m.p. 190°(de comp.), on boiling in aqueous acetic acid. With methanolic potassium hydroxide, (IX)

1) M. Nishikawa, K. Morita, H. Hagiwara, M. Inoue : J. Pharm. Soc. Japan, **74**, 1165(1954).
2) J. Simonsen : "The Terpenes," Vol. II, 485(1949).
3) S. Kuwada : J. Pharm. Soc. Japan, **56**, 78(1936).

yielded the epoxide (X), m.p. 235° (*Anal.* Calcd. for $C_{27}H_{42}O_4$ : C, 75.31; H, 9.83. Found: C, 75.44; H, 9.88), which was oxidized with pyridine-chromium trioxide into $\alpha,\beta$-epoxyketone (XI), m.p. 236° (*Anal.* Calcd. for $C_{27}H_{40}O_4$ : C, 75.66; H, 9.41. Found : C, 75.35; H, 9.40). (XI) was treated with chromous chloride and the resulting $\alpha,\beta$-unsaturated ketone (XII), m.p. 219°, $\lambda_{max}$ 225 mμ ($\varepsilon$ 7690), was catalytically hydrogenated over palladium-charcoal to the ketone (XIII), m.p. 182°, and (XIII) was finally reduced by the Huang-Minlon reaction to give the known 25D-5$\beta$-spirostane (XIV), m.p. 137° (*Anal.* Calcd. for $C_{27}H_{44}O_2$ : C, 80.94; H, 11.07. Found : C, 80.62; H, 11.05).

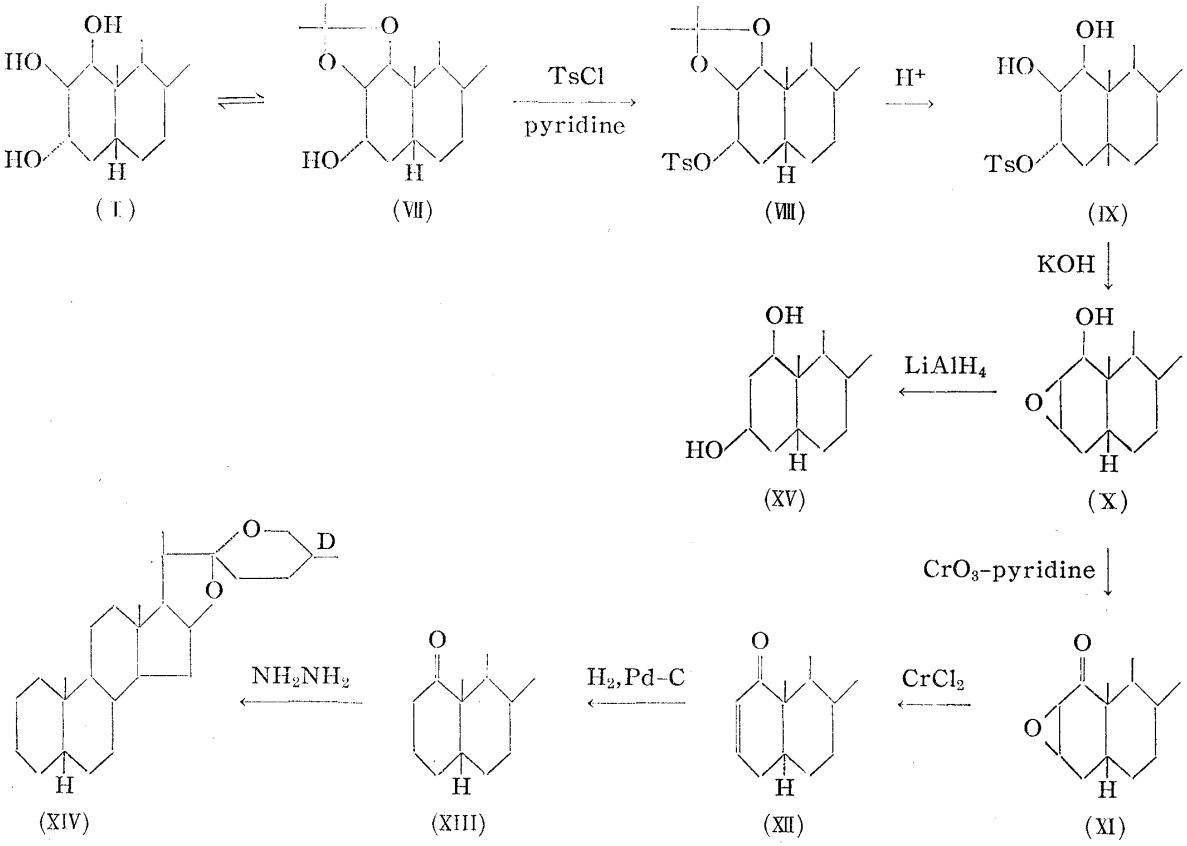
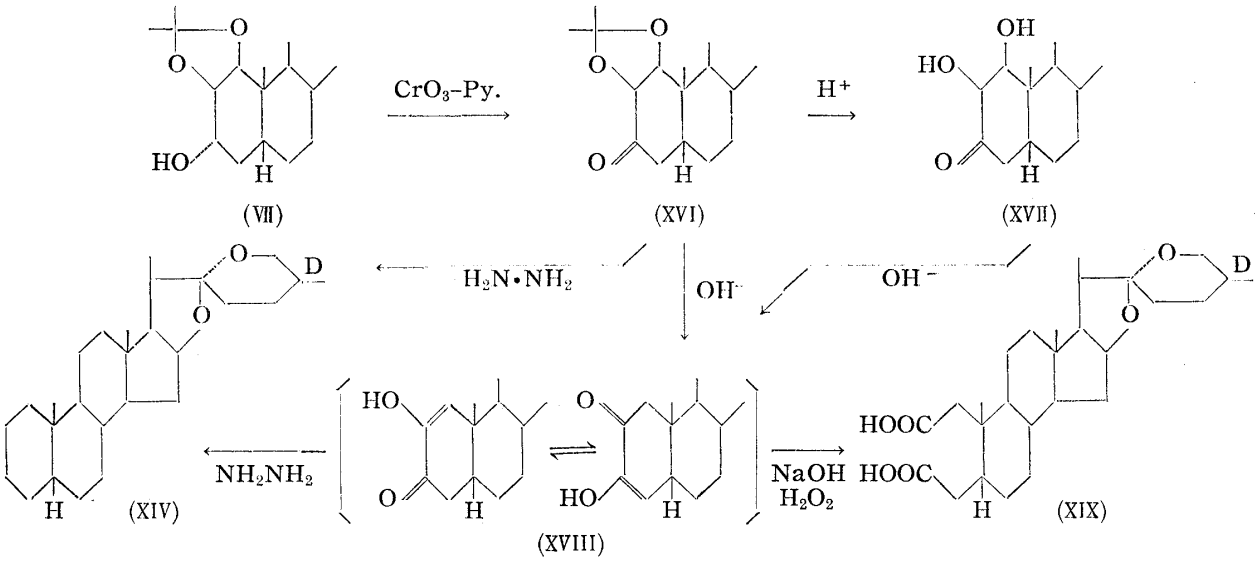



Chart 2.

It is obvious from the above experiments that the two vicinal hydroxyl groups in tokorogenin are *cis* and the other one is *trans* to the former two. Furthermore, the treatment of (X) with $LiAlH_4$ yielded dihydroxysapogenin (XV), m.p. 238°, which neither formed the acetonide nor suffered oxidation by periodic acid, and hence, the 1$\beta$,3$\beta$-diol structure was assigned to this compound from the consideration that $LiAlH_4$-reduction of the epoxide gives rise to axial hydroxyl groups.

Another approach to the elucidation of the structure of tokorogenin again started from tokorogenin acetonide (VII). (VII) was oxidized with pyridine-chromium trioxide to give the keto acetonide (XVI), m.p. 229°, which was then boiled in aqueous acetic acid to furnish dihydroxyketone (XVII), m.p. 225° (*Anal.* Calcd. for $C_{27}H_{42}O_5$ : C, 72.65; H, 9.42. Found : C, 72.54; H, 9.57). With alkali, (XVII) afforded $\alpha$-diketone (enol-form) (XVIII), m.p. 225°, $\lambda_{max}$ 269 mμ ($\varepsilon$ 6900). Both (XVI) and (XVIII), when reacted with hydrazine hydrate and alkali, yielded the known 25D-5$\beta$-spirostane (XIV). With alkali, (XVI) was directly converted to (XVIII), which was then oxidized with alkali and hydrogen peroxide to give the known samogenic acid (XIX), m.p. 270°, $[\alpha]_D^{23}$ −37°, and its dimethyl ester, m.p. 147°. In conclusion, the structure of 1$\beta$,2$\beta$,3$\alpha$-trihydroxy-25D-5$\beta$-spirostane (I) should be assigned to tokorogenin.




This work was carried out as a part of Nishikawa's papers entitled "Studies in Steroids." (All melting points are not corrected.) The author appreciates the valuable advice and encouragement of Prof. Y. Asahina, Dr. S. Kuwada, and Dr. T. Matsukawa.

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## Solubilization of Fat-soluble Vitamins with Sucrose Monoester of Fatty Acids*

As is well known, fat-soluble vitamins are solubilized with nonionic surfactants having polyoxyethylene radical as the hydrophilic group, but the surfactants are not permitted to be used in the field of food, as polyoxyethylene is far different from substances found in nature or from biological materials. Aqueous solutions of fat-soluble vitamins produced by the aid of nonionic surfactants are generally sensitive and exhibit clouding formation on warming, especially when polar substances are solubilized. As each of these nonionic surfactants is not a single substance and difficult to purify, studies on the mechanism of solubilization meet with many difficulties.

Investigation was made to find out a more suitable solubilizer to overcome these weak points and it was found that clear aqueous solutions of fat-soluble vitamins are obtained with the aid of sucrose monoesters of fatty acid, which were synthesized according to Osipow's report.[1)]

Minimum amount of these esters required to solubilize the fat-soluble vitamins is shown in Table I.

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* This constitutes a part of a series entitled "Studies on the Pharmaceutical Preparations" by A. Watanabe.

1) Osipow, *et al.*; Ind. Eng. Chem., 48, 1459(1956).