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132. Shoji Shibata,[*1] Mitiiti Fujita,[*1] Hideji Itokawa,[*2] Osamu Tanaka,[*1] and Tatsuo Ishii[*1] : Studies on the Constituents of Japanese and Chinese Crude Drugs. XI.[*3] Panaxadiol, A Sapogenin of Ginseng Roots. (1).

(*Faculty of Pharmaceutical Sciences, University of Tokyo*[*1])

As described in the earlier communication by Fujita, Itokawa, and Shibata,[1] on acid hydrolysis of the saponin isolated from Ginseng roots (the roots of *Panax ginseng* C. A. Meyer) a sapogenin, $C_{30}H_{52}O_3$, m.p. 250°, was obtained and designated panaxadiol.

The unity of the sapogenin was established by gas-chromatography, and the molecular weight was determined by mass-spectroscopy as being 460.

The infrared spectrum of panaxadiol showed the presence of hydroxyl and the absence of carbonyl and double bond. Panaxadiol possesses two hydroxyls, one of which is hindered to result mono-acetate, $C_{32}H_{54}O_4$, m.p. 215°, on acetylation. On oxidation with chromic acid, the monoacetate of panaxadiol afforded a ketonic compound, panaxanolone acetate, $C_{32}H_{52}O_4$, m.p. 183~184° (IR $\nu_{max}^{CS_2}$ cm^{-1} : 1743, 1720; no OH band).

By the Wolff-Kishner reduction modified by Barton,[2] panaxanolone acetate was converted into panaxanol, $C_{30}H_{52}O_2$, m.p. 154°, which yielded monoacetate, $C_{32}H_{54}O_3$, m.p. 198°.

Three oxygen atoms of panaxadiol have accounted for two hydroxyls non-bonded and hindered, and an ethereal oxygen.

The oxygen bridge was cleaved when panaxanol was heated with hydrochloric acid in glacial acetic acid. The resulted acetate, $C_{32}H_{52}O_2$, m.p. ca. 100°, was hydrolyzed to give anhydropanaxanol, $C_{30}H_{50}O$, m.p. 141~144°.

The infrared spcetra of anhydropanaxanol and its acetate which resembled those of isotirucallenol[3] and its acetate, respectively, except the presence of terminal methylene band at 885 cm^{-1} (KBr) in the former compounds, suggested the resembled basic skeleton of panaxadiol and its derivatives with that of isotirucallenol.

Consequently, the products of catalytic hydrogenation of anhydropanaxanol and its acetate were proved by the infrared spectra and gas-chromatography to be identical with isotirucallenol (X) and its acetate (IX), respectively.

The evidence for the position of hindered hydroxyl was provided as follows : The product which was deduced by treatment of panaxanolone acetate with sulfuric acid in glacial acetic acid gave UV : λ_{max}^{EtOH} 267.5 mμ (log ε 3.85) and IR $\nu_{max}^{CS_2}$ cm^{-1} : 1738 (acetate C=O), 1677, and 1608 (-C=C-C=O); IR δ_{max}^{KBr} cm^{-1} : 890 (terminal methylene).

Comparing with the ultraviolet spectrum of betulafolien (13,17)-dione (3,12)[4] (XII) (UV : (λ_{max}^{EtOH} 265 mμ (log ε 3.88), IR ν_{max}^{KBr} cm^{-1} : 1706($C_{(3)}$=O), 1670 ($C_{(12)}$=O), 1612 $\Delta^{13(17)}$), the presence of a keto group in the 12-position of panaxanolone acetate has been proved. Thus panaxadiol should have the non-hindered hydroxyl in the 3-position and the hindered one in the 12-position.

*1 Hongo, Tokyo (柴田承二, 藤田路一, 糸川秀治, 田中 治, 石井達郎).
*2 The present address : Tokyo College of Science.
*3 Part X : This Bulletin, **11**, 382 (1963).

1) M. Fujita, S. Itokawa, S. Shibata : Yakugaku Zasshi, **82**,1638 (1962).
2) D. H. R. Barton, D. A. J. Ives, B. R. Thomas : J. Chem. Soc., **1955**, 2056.
3) D. Arigoni, O. Jeger, L. Ruzicka : Helv. Chim. Acta, **88**, 222 (1955); J. B. Barbour, W. A. Lourens, F. L. Warren, K. H. Watling : J. Chem. Soc., **1955**, 2194.
4) F. G. Fischer, N. Seiler : Ann., **626**, 185 (1959); *Ibid.*, **644**, 162 (1961).

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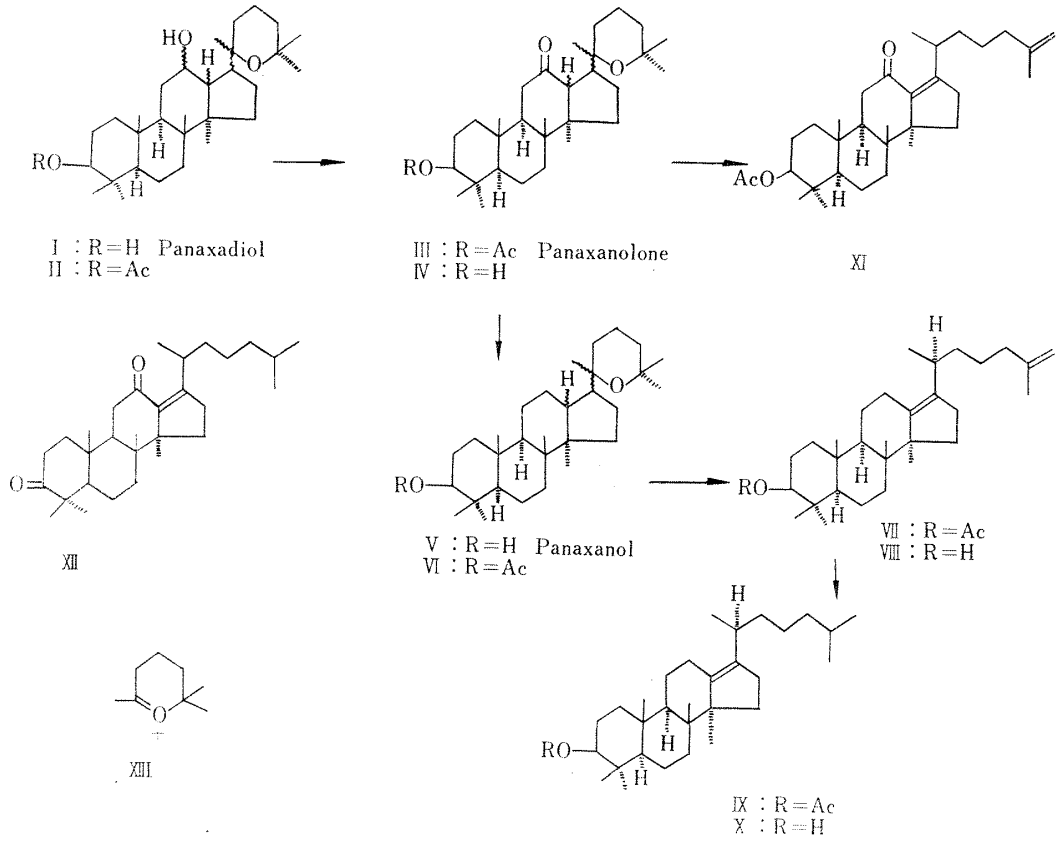
On the other hand, dammarandiol acetate[5] and 20-hydroxybetulafolian-3,12-dione[4] liberated 20-hydroxyl to form a double bond at 13(17) on treatment with acid under the same condition adopting to panaxanol and panaxanolone acetate to form an isopropenyl group.

It would therefore be reasonable to propose the formula (I) to represent panaxadiol, and the reactions mentioned above would be illustrated by the scheme (II～XI).



The mass-spectrum of panaxadiol showed a base peak at m/e 127 which corresponded to the fragment (XIII) (Fig. 1). The nuclear magnetic resonance spectra of panaxadiol and its acetate gave 6 signals of CH_3 group in the region of τ-value 8.70～9. 20 (Fig. 2) whose areal intensities corresponded to 8 CH_3 groups to support the formula (I) of panaxadiol.

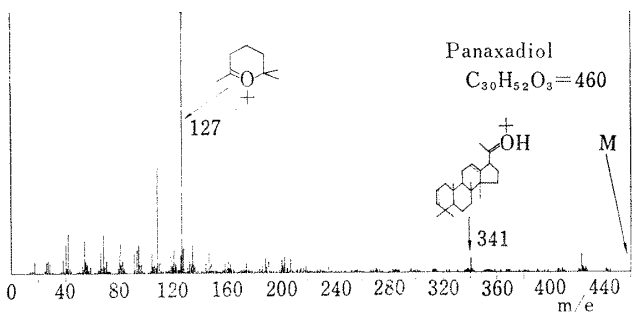


Fig. 1.

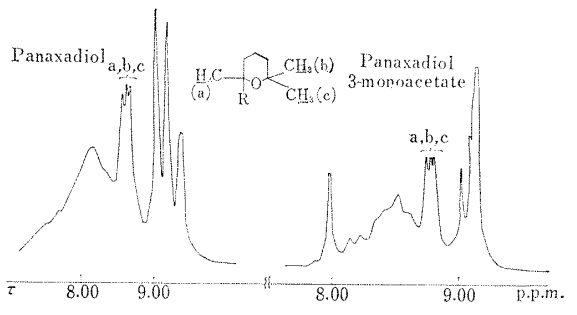


Fig. 2.

5) J. S. Mills : J. Chem. Soc., **1956**, 2196.

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Nuclear magnetic resonance spectra were measured in chloroform using Varian Associates 4300-C spectrometer at 60 Mc.
Panaxadiol : τ=8.71 (1 Me), 8.76 (1 Me), 8.80 (1 Me), 9.00 (2 Me), 9.10 (2Me), 9.20 (1 Me).
Panaxadiol 3-monoacetate : τ=8.71 (1 Me), 8.76 (1 Me), 8.81 (1 Me), 9.01 (1 Me), 9.09 (1 Me), 9.14 (3 Me).

Experimental

Treatment of Panaxanolone Acetate (III) with H_2SO_4 in Acetic Acid——A solution of panaxanolone acetate (III) (1.1 g.) in AcOH (33 cc.) containing 2*N* H_2SO_4 (1.1 cc.) was refluxed for 2 hr. The reaction mixture was diluted with H_2O and extracted with Et_2O. The ethereal solution was washed with aq. $NaHCO_3$ solution and H_2O, dried over anhyd. Na_2SO_4 and evaporated to dryness to afford yellow syrup (UV : λ_{max}^{EtOH} 265 mμ). The chromatographical separation of this syrup on neutral alumina (Grade I) gave colorless crystalline powder as the main fraction, which showed the absorption maximum at 267.5 mμ (log ε 3.85 in EtOH) in the UV spectrum and the bands at 1735 (acetyl), 1677, 1608 (-C=C-C=O) and 890 cm^{-1} (terminal methylene) in the IR spectrum (in CS_2).

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Summary

Panaxadiol, $C_{30}H_{52}O_3$, a sapogenin of Ginseng roots was acetylated to afford monoacetate, $C_{32}H_{54}O_4$, which was oxidized with chromium trioxide to give panaxanolone acetate, $C_{52}H_{52}O_4$. On Wolff-Kishner reduction, panaxanolone acetate was converted into panaxanol, $C_{30}H_{52}O_2$, which was heated with hydrochloric acid in glacial acetic acid to furnish anhydropanaxanol acetate, $C_{32}H_{52}O_2$. On catalytic hydrogenation of anhydropanaxanol, isotirucallenol (X) was obtained, which was established by infrared and gas-chromatography. A trimethyltetrahydropyrane ring system in panaxadiol was proved by mass-spectrometry, and the oxygen ring was cleaved by the action of hydrochloric acid on panaxanol.

The α,β-unsaturated ketonic system was proved ultraviolet spectroscopically in the product derived from panaxanolone acetate by the action of sulfuric acid in glacial acetic acid. Thus the hindered hydroxyl of panaxadiol should be present at the 12-position.

Consequently, it has been concluded that panaxadiol is a new tetracyclic triterpene of dammarane series having hydroxyls at the 3- and 12-positions and trimethyltetrahydropyrane ring at $C_{(17)}$, as represented by the formula (I).

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