

18.64. Acetylation of VII with acetic anhydride in pyridine afforded 2,3-dideoxy-3-bromo-1,4-di-O-acetyl-6-O-tosyl- α -D-glucopyranose (VIII), m.p. 104.5~105.5°, $[\alpha]_D^{20} +60^\circ$ (c=0.5, CHCl₃). Anal. Calcd. for C₁₇H₂₁O₈SBr: C, 43.88; H, 4.55. Found: C, 43.96; H, 4.59. Reflux of VIII with potassium acetate in acetic anhydride for 1 hour gave crystals, m.p. 82°, undepressed on admixture of V, which were indistinguishable by IR with that of V.

Conclusively, the authors were able to establish an easy preparative method of compounds having the same properties with the Fischer's *Glucal-hydrobromid-diacetat* and *Triacetat*. The structures of these compounds (III and V) were assigned to be 2,3-dideoxy-3-bromo-4,6-di-O-acetyl- α -D-glucopyranose and 2,3-dideoxy-3-bromo-1,4,6-tri-O-acetyl- α -D-glucopyranose, respectively.

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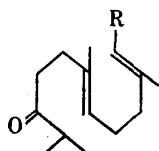
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Acid-catalyzed Cyclization of Squalene Oxide*¹

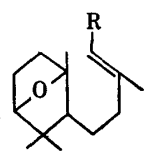
Recent report¹⁾ on the cyclization of squalene 2,3-oxide with stannic chloride in benzene solution by van Tamelen prompted us to report our results on the cyclization of the same epoxide with boron trifluoride-ether in benzene.

Squalene 2,3-oxide²⁾ in water-saturated benzene solution (0.1N) was treated with a catalytic amounts of boron trifluoride etherate for 15 hours. The reaction mixture was separated by silica-gel chromatography into three compounds, A, B and C with 9, 12 and 50% yield respectively. All of these compounds have the same molecular formula of C₃₀H₅₀O (m/e 426, mol. w. 426.70).

Structure I and II were deduced to the compounds A and B from the following spectroscopic evidences respectively.



I



II

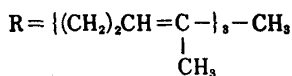
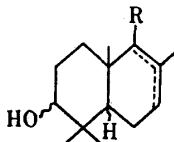
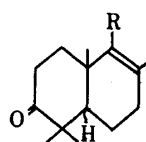


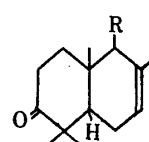
Chart 1.



III



IVa



IVb

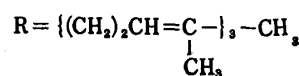


Chart 2.

*¹ From a thesis submitted to the undergraduate School of the Tohoku University in partial fulfillment of the requirement for the B. Sc. degree (1966, 3).

1) E. E. van Tamelen, J. Willet, M. Schwartz, R. Nadeau: J. Am. Chem. Soc., **88**, 5937 (1966).

2) E. E. van Tamelen, T. J. Curphey: Tetrahedron Letters, No. 3, 121 (1962).

The compound A—IR; 1715 cm^{-1} (carbonyl), NMR: δ 1.03 (6H, doublet, $J=6.5$ c.p.s., methyls of isopropyl group), 1.55 (18H, broad singlet, methyls on double bond), 5.1 (5H, broad singlet, protons on double bond).

The compound B—IR; no absorption in the carbonyl and hydroxyl regions, NMR; 0.97 and 1.01 (6H, singlets, methyls on quarternary carbon), 1.22 (3H, singlet, methyl geminal to an oxygen function), 1.55 (15H, broad singlet, methyls on double bond), 3.55 (1H, doublet, $J=4$ c.p.s., hydrogen geminal to an oxygen), 5.1 (4H, broad singlet, hydrogens on double bond).

IR spectrum of fraction C shows the presence of hydroxyl group (3350 cm^{-1}), which was converted to the corresponding ketone (IR, 1712 cm^{-1}) by chromium trioxide-pyridine oxidation.

The silica-gel-silver nitrate chromatography of fraction C gave three compounds (C_1 , C_2 , C_3).

The following results suggest the structure III for fraction C_1 .

a) absorption of about four moles of hydrogen on the catalytic reduction (PtO_2 , EtOH)*; b) appearance of three methyl groups at δ 1.00–0.70 p.p.m. and one hydrogen geminal to hydroxyl group at 3.29 as double doublet ($J=5$ and 7.5 c.p.s.) in its NMR spectrum.

Although glc (SE 30) and tlc (SiO_2) of fraction C_1 itself showed one component, TLC of the corresponding ketone obtained by the chromium trioxide-pyridine oxidation showed two closely located spots which were separated by preparative TLC (SiO_2) into two compounds (K_1 and K_2).

In NMR spectra of both K_1 and K_2 , there appeared three methyl groups attached on quarternary carbons as expected in structure Va and Vb for K_1 and K_2 , respectively.

Absorption of two moles of hydrogen on the catalytic reduction (PtO_2 , EtOH) of fraction C_2 to afford the corresponding tetrahydro derivative (m/e 430, mol. w. 430.73) which was positive to tetranitromethane, and one hydrogen geminal to hydroxyl group at δ 3.06 as double doublet ($J=6$ and 8.5 c.p.s.) in its NMR spectrum suggested the structure Va for this compound C_2 .

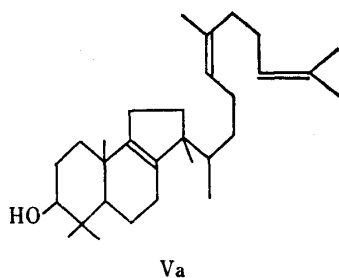


Chart 3.

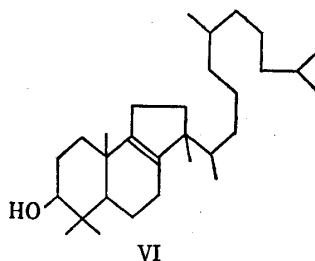
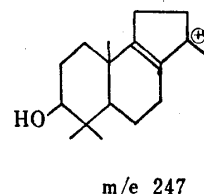


Chart 4.



The structure Va is supported by mass spectra of compound C_2 and its tetrahydro derivative (VI), in both cases fragment ions such as m/e 247 and 229 are observed as relatively intense peaks.⁹⁾ Fragment ion of m/e 247 might have the above structure.

It was thus found that cyclization of squalene 2,3-oxide proceeded also with boron trifluoride-etherate in water saturated benzene solution.

Authors express their great acknowledge to professor E. E. van Tamelen for his kind discussion and one of authors (T.K.) is indebted to professor A.I. Scott for his kind guidance at the earlier stage of this study at University of British Columbia.

*2 Mass spectrum of the reduction product showed the presence of hexahydro and octahydroderivatives.

3) The compound C_2 was found to be same with the van Tamelen's tricyclic alcohol by comparison of mass spectra of both compounds through the courtesy of Professor E. E. van Tamelen. Details of fragmentation patterns will be discussed in the full paper.

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Total Synthesis of Hydroxyhopanone

Hydroxyhopanone is a typical representative of naturally occurring triterpenoid which belongs to hopane group. In 1958 Schaffner, *et al.*¹⁾ synthesized one of its acidic dehydration product, hopenone-I (VI), starting from α -onocerin. However, in their synthesis the asymmetries at C₁₇ and C₂₁ had been lost and regeneration of these asymmetries producing a natural triterpenoid was hitherto unsuccessful. We now report the synthesis of the compound which possesses all asymmetries and oxygenated functions identical with those of natural triterpenoid, hydroxyhopanone (IIa).

The key-intermediate of the synthesis is gammaceran-3-on-21-ol (Ia) which can be derived from α -onocerin according to the methods by Schaffner, *et al.*¹⁾ or more conveniently by Tsuda, *et al.*²⁾ On tosylation with *p*-toluenesulfonyl chloride and pyridine or on mesylation with methanesulfonyl chloride and pyridine, it easily formed a tosylate (Ic), m.p. 150°, C₃₇H₅₆O₄S, and mesylate (Ib), m.p. 200~201°, C₃₁H₅₂O₄S, respectively. The tosylate (Ic) was then subjected to solvolysis under reflux 20 hours in dioxane-water with presence of CaCO₃,³⁾ and the product was separated by alumina chromatography into a hydroxy-fraction (~20%) and an unsaturated fraction (~80%). The hydroxy-fraction when crystallized from methanol formed colorless needles (~15%), m.p. 247~250°, which was proved to be completely identical (melting point and mixed melting point, IR, NMR, and TLC comparisons.) with natural hydroxyhopanone (IIa) crystallized from the same solvent.*¹

The unsaturated fraction was further separated by AgNO₃-silica gel chromatography into two compounds. One of them (III) (~20%) was found to be identical with hopenone-a,*² a dehydration product of hydroxyhopanone by POCl₃-pyridine. The other compound (IV) (~40%), m.p. 267~271°, C₃₀H₄₈O, was elucidated as gammacer-20-en-3-one (IV) since it showed two olefinic protons at δ 5.42 and 5.38 in its nuclear magnetic resonance (NMR) spectrum. Hydrogenation of this in acetic acid over PtO₂ gave, as expected, tetrahymanol (V), m.p. 312~314°, being identified with the specimen obtained by the alternative synthesis.²⁾ Careful examination of the mother liquor from III and IV by combination of gas chromatography and thin-layer chromatography (TLC) over AgNO₃-silica gel plate

*¹ The m.p. and crystalline form of hydroxyhopanone depend on the solvent of crystallization. For example, the specimen crystallized from CHCl₃-MeOH showed m.p. 268~271°, fine needles.

*² The reported specimens⁴⁾ of hopenone-a (III) and hopenone-b (VIIa) seem to be impure. They were now obtained in pure forms, m.p. 207~209° and m.p. 219~220°, respectively, by AgNO₃-silica gel chromatography.

1) K. Schaffner, L. Caglioti, D. Arigoni, O. Jeger : *Helv. Chim. Acta*, **41**, 152 (1958).

2) Y. Tsuda, A. Morimoto, T. Sano, Y. Inubushi, F. B. Mallory, J. T. Gordon : *Tetrahedron Letters*, No. 19, 1427 (1965).

3) J-F. Biellmann, G. Ourisson : *Bull. soc. chim. France*, **1962**, 331.

4) W. J. Dunstan, H. Fazakerley, T. G. Halsall, E. R. H. Jones : *Croat. Chem. Acta*, **29**, 173 (1957).