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Patrinoside, a New Iridoid Glycoside from *Patrinia scabiosaefolia*[1)]

The authors wish to report in this communication on the structure of a new iridoid glycoside obtained from *Patrinia scabiosaefolia* FISCHER (Japanese name: Ominaeshi, Valerianaceae). The methanol extract of the dried root and rhizome was chromatographed on charcoal with water and methanol. The methanol eluates were rechromatographed on silica gel with a mixture of chloroform and methanol to give a new iridoid glycoside named patrinoside (I).

I is a hygroscopic amorphous substance and gives a strong odor of isovaleric acid, which was identified by gas chromatography, with mineral acid. Acetylation of I with acetic anhydride and pyridine afforded a hexaacetate (III), $C_{33}H_{46}O_{17}$, mp 130—131.5°,[2)] $[\alpha]_D$ −45.7° (in EtOH) as colorless needles. The nuclear magnetic resonance (NMR) spectrum of III showed the presence of two secondary methyls attributed to the geminal dimethyls of isovaleryl group, six acetyl methyls and a vinyl proton (NMR data of the compounds derived from I are listed in Table I). One proton at δ 5.86 (doublet, J=5 Hz) was assigned to an acylated acetal proton of the iridoid compound from its chemical shift.[3)] Enzymatic hydrolysis of I with β-glycosidase (Worthington Biochemical Corp. Freehold, New Jersey) afforded glucose and an aglycone (II) as colorless needles, $C_{15}H_{24}O_6$, mp 111—113°, $[\alpha]_D$−85.7° (in MeOH), Mass Spectrum *m/e*: 300 (M^+), 198 (M^+−$(CH_3)_2CHCH_2COOH$), 180 (198—H_2O), 162 (180—H_2O), 144 (162—H_2O), 111 (M^+−189). Infrared (IR) spectrum of II showed the presence of ester linkage (1740 cm^{-1} in KBr) and a vinyl ether (1658 cm^{-1}). II was not oxidised by periodite, showing the hydroxy groups were not located at the adjacent position each other. Acetylation of II with acetic anhydride and pyridine afforded a triacetate (IV) as colorless oil, $C_{21}H_{30}O_9$, $[\alpha]_D$−45.6° (in EtOH), Mass Spectrum *m/e*: 324 (M^+−$(CH_3)_2CHCH_2COOH$), 264 (324—CH_3COOH), 204 (264—CH_3COOH), 144 (204—CH_3COOH), 153 (M^+−273). The signals at δ 3.90, 4.04, 4.49 in the NMR spectrum of II shifted to δ 4.42 (2H, d, J=7 Hz), 4.65 (2H, q, J=12 Hz) and 5.36 (1H, q-like) in that of IV, showing the presence of two hydroxymethylene groups (>$CHCH_2OH$, and =$\dot{C}CH_2OH$) and a secondary hydroxy group in II. An iridoid framework for II assumed by the fact that the NMR spectrum of IV was favorably comparable with that of didrovaltrate (X).[3a)] Catalytic hydrogenation of II over palladized charcoal in methanol afforded a colorless oil (V) $C_{15}H_{24}O_5$, Mass Spectrum *m/e*: 284 (M^+), 182 (284−$(CH_3)_2CHCH_2COOH$), 164 (182—H_2O), 146 (164—H_2O), 95 (M^+−189).

1) A part of this paper was presented at the 93th Annual Meeting of the Pharmaceutical Society of Japan, Tokyo, April, 1973.
2) All melting points were uncorrected.
3) *a*) P.W. Thies, *Tetrahedron*, **24**, 313 (1968); *b*) P.W. Thies, E. Finner and F. Rosskpf, *ibid.*, **29**, 3213 (1973).

From the above data and the biogenetic consideration, the structure of the aglycone was assumed to be II. The mass spectra of II and its derivatives (IV—VI) supported this assumption.[4] The location of the secondary hydroxy group was decided by the decoupling experiment of IV. Upon the irradiation of C-5 proton, the doublet at δ 6.42 (C-3 proton) was found to change into singlet, but the quartet at δ 5.36 was found no change, indicating that acetoxy group was linked to the C-7 carbon atom.

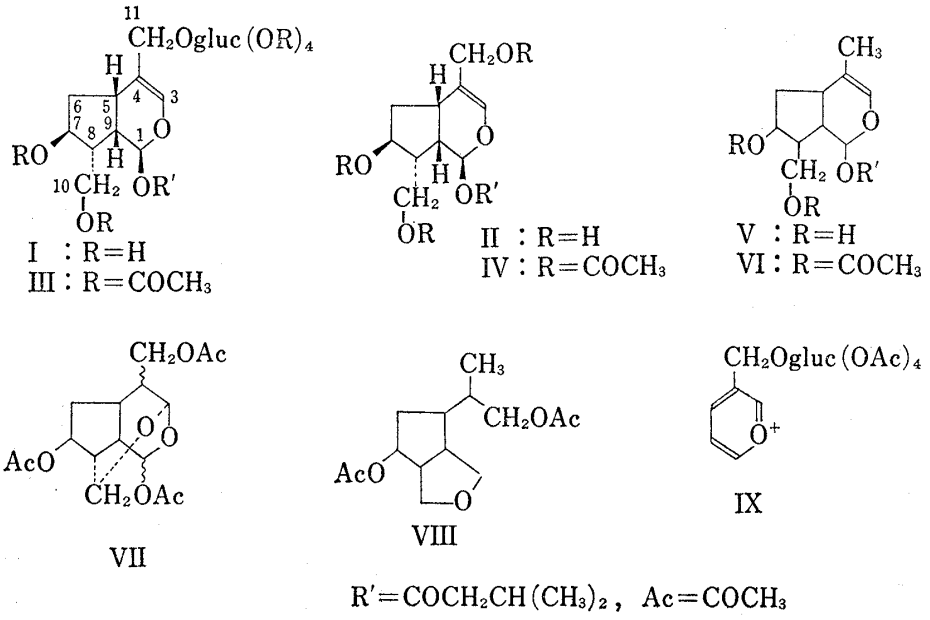

Chart 1

TABLE I. NMR Data of II—VI and X (δ Value at 60 MHz in $CDCl_3$)

Compound	C-1	C-3	C-5	C-6	C-7	C-8	C-9	C-10	C-11	OH	-$COCH_3$	-$COCH_2CH(CH_3)_2$
II	5.86 (d,J=5)	6.38 (d,J=1)	2.7—3.2 m	−2.2 m	4.49 (q-like)	−2.0 m		3.90 m	4.04 m,h/2=3	3.20 (3H,br.s)	—	0.96 (d,J=6)
III	5.86 (d,J=6)	6.25 (d,J=1.5)	2.7—3.2 m	−2.2	—	—		4.05—4.20[a]		—	1.95—2.10	0.96 (d,J=6)
IV	6.05 (d,J=4.5)	6.42 (d,J=1)	2.7—3.2 m	−2.2 m	5.36 (q-like)	−2.0 m		4.42 (d,J=7)	4.68 4.42 (q,J=12)	—	2.0—2.1 (3×-$COCH_3$)	0.98 (d,J=6)
V	5.91 (d,J=4)	6.03 (d,J=2)	2.7—3.2 m	−2.2 m	4.38 (q-like)	−2.0 m		3.75 3.96 (*ABX* octet J=4/6)	1.57 (d,J=1.5)	2.83 (2H,br,s)	—	0.97 (d,J=6)
VI	6.03 (d,J=4.5)	6.07 (d,J=1)	2.4—2.8 m	−2.2 m	5.33 (q-like)	−2.0 m		4.21 (d,J=7)	1.57 (d,J=1)	—	2.05 (2×-$COCH_3$)	0.98 (d,J=6)
X[b]	5.81 (d,J=5)	6.50 (d,J=1)	−2.0 m	−2.0 m	4.92 (t,J=6)	−2.70 (q,J=8/5)		3.04 2.80 (AB q, J=5)	4.68 4.42 (AB q, J=12.5)	—	—	—

a) Signal patterns are unclear due to the overlapping with C-6′ protons of sugar moiety.
b) P.W. Thies, *Tetrahedron*, **24**, 313 (1968)
J values are given in Hz
d=doublet, m=multiplet, q=quartet, s=singlet, t=triplet

4) T.W. Bentley, R.A.W. Johnstone and J. Grimshow, *J. Chem. Soc.* (*C*), **1967**, 2234.

The *cis* ring junction was suggested from the simirality of the C-5 proton signals of IV and didrovaltrate iodohydrine in their NMR spectra.[3b] The *trans* relationship between the protons on C-7 and C-8 was proved by the decoupling experiment of IV ($J_{7,8}$=4 Hz, $\phi_{7,8}$≒120°). Treatment of II with sodium methoxide in absolute methanol followed by acetylation afforded an oily substance (VII) $C_{16}H_{22}O_8$ (*m/e*, 342 (M^+)), NMR (in $CDCl_3$): δ, 2.0—2.2 (3×$-COCH_3$), 3.46—4.56 (4H, m, H-10 and H-11), 5.10 (1H, d, J=4 Hz, H-3), 5.46 (1H, m, H-7), 6.23 and 6.35 (1H, each *d*-like, H-1). Further, catalytic hydrogenation of II over platinum oxide in acetic acid followed by acetylation gave a colorless oil (VIII), $C_{14}H_{22}O_5$, Mass Spectrum *m/e*: 210 (M^+-CH_3COOH). 150 (210—CH_3COOH), 135 (150—CH_3), NMR (in $CDCl_3$) δ: 0.82 (3H, d, J=6 Hz, $-\dot{C}HC\underline{H}_3$), 1.93—2.13 (6H, s, 2×$COCH_3$), 3.41—4.83 (6H, m, 3×$-OC\underline{H}_2\dot{C}H-$, each ABX), 5.20—5.58 (1H, m, $-\dot{C}HOCOCH_3$).[5] The formation of VII and VIII indicated α-orientation of the hydroxymethylene group at C-8. The acetal proton on C-1 (δ 6.03) of methoxybromide (C_3–OCH_3, C_4–Br) of III showed coupling constant of 8 Hz, indicating the *trans* relationship between the protons on C-1 and C-9.

The formula II was thus given for the aglycone of patrinoside (I). II was also isolated from this plant. The location of glucose in I was proved by the following evidence. Catalytic hydrogenation of I over palladized charcoal in methanol afforded V and glucose in good yield, and the mass spectrum of III showed the fragment ion at *m/e* 441 (IX), indicating that glucose must be linked to C-11 hydroxy group of II. The β-configuration for glucose was indicated by the signal of the anomeric proton in NMR spectrum of III (δ 4.47, J=7 Hz). The structure of patrinoside was thus formulated as I. I and II were also isolated from the whole plant of *Valeriana flaccidissima* Maxim. (Japanese name; Tsurukanokosō, Valerianaceae) and the presence of I in *Patrinia triloba* Miq. var. *triloba* (Japanese name: Kokinreika, Valerianaceae) was proved by thin-layer chromatography.

It is interesting that I is the third example of iridoid glycosides whose glucose links to C-11 hydroxy group and this type of iridoid glycosides (villoside[6] and valerosidate[7]) have been isolated from the plants of Valerianaceae.

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