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GENUINE SAPOGENINS OF THREE PRIMULACEOUS PLANTS

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In the previous paper[1], we reported the sapogenin constituents of five Japanese Primulaceous plants : (i) Primula sieboldi E.Morren, roots (Japanese : sakura-sō), (ii) Lysimachia clethroides Duby, roots (okatoranoō), (iii) L.japonica Thunb., roots (konasubi), (iv) P.japonica A.Gray, roots (kurin-sō), and (v) L.mauritiana Lam., fruits (hamabossu), demonstrating that on acid hydrolysis of saponins the former three plants afforded primulagenin A (I) while the latter two gave camelliagenin A[2,3,4] (=dihydropriverogenin A[4,5,6]) (II) as the major sapogenins respectively.

In connection with some Primulaceous sapogenins : cyclamiretin A[7] (III), cyclamigenin B[8] (IV), and priverogenin B acetate[4,5] (V), possessing the 13,28-epoxy moiety, we have sought the genuine sapogenins of three plant materials, (i) (iv) and (v), by virtue of the modified Smith degradation[9] and reached a conclusion as described in the present report that the genuine sapogenins of (i) and (v) possess the epoxide moiety such as (VI) and (VII), while that of (iv) has the open structure, i.e. (II).

P.sieboldi roots sapogenin : On repeated treatment with the modified Smith degradation ($NaIO_4$ oxidation followed by 3% KOH-EtOH treatment at reflux under N_2 atmosphere), the saponin[1] of (i) afforded as the major product a new aglycone, now named protoprimulagenin A (VI), $C_{30}H_{50}O_3$, mp. 272~273°, $[\alpha]_D$ + 13° (c, 1.0 in $CHCl_3$), IR ($CHCl_3$) : 3640, 3560 cm^{-1}, in addition to a ketonic compound (VIII) (minor), $C_{30}H_{48}O_3$, mp. 257.5~258°, $[\alpha]_D$ -25° (c, 1.0 in $CHCl_3$), IR ($CHCl_3$) : 3620, 3470 (br.), 1700 cm^{-1}, and a trace amount of primulagenin A (I). Although the latter two are presumably derivable from protoprimulagenin A during the procedure, the soil bacterial hydrolysis[10] to attain the further elucidation is currently under study. Acid treatment of protoprimulagenin A gave smoothly I in a high yield, whereas on acetylation with Ac_2O-pyridine it furnished a monoacetate (IX), $C_{32}H_{52}O_4$, mp. 266~267°, $[\alpha]_D$ + 15° (c, 1.0 in $CHCl_3$), IR ($CHCl_3$) : 3620, 3450 (br.), 1720 cm^{-1}, whose NMR data (Table I) support the reasonable formulation of the new aglycone as 3β,16α-dihydroxy-13β,28-epoxy-oleanane (VI). The existence of the 13,28-epoxide linkage is suggested in particular

Table I (τ values in $CDCl_3$ at 100 Mc., J in cps.)

	IX	VIII
C-methyls	9.13 (6H), 9.10 (6H), 9.03, 3.85, 8.80 (3H each), (all s.)	9.23, 9.14, 9.11, 9.06, 9.03, 8.98, 8.77 (3H each., s.)
$-OCOCH_3$	7.99 (3H, s.)	——
$>C_{(3)}\underline{H}OR$	5.55 (1H, t.-like) (R=Ac)	6.85 (1H, t.-like) (R=H)
$>C_{(15)}H_2$	——*	7.45, 7.19 (2H, ABq., J=8)
$>C_{(16)}\underline{H}OH$	6.08 (1H, d., J=6)	——
$-C_{(28)}H_2-O-$	6.88, 6.56 (2H, ABq., J=8)	6.60, 6.18 (2H, ABq., J=8)

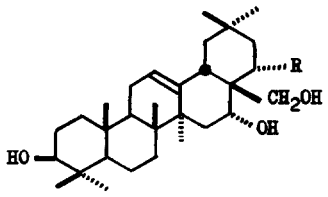
* not assigned

by the AB quartet signal at τ 6.88, 6.56 (J=8 cps.) assignable to a methylene at $C_{(28)}$[12,13] and also by lacking the signal due to a olefinic proton of $C_{(12)}$. The oxidation of the acetate (IX) with CrO_3-pyridine yielded a monoketo-acetate (X), $C_{32}H_{50}O_4$, mp. 274~276°, $[\alpha]_D$ -20° (c, 1.0 in $CHCl_3$), IR (KBr) : 1730, 1700, 1243 cm^{-1}, which was further transformed to a keto-γ-lactone (XI), $C_{32}H_{48}O_5$, mp. 276~277°, $[\alpha]_D$ -107° (c, 1.0 in $CHCl_3$), IR (KBr) : 1773, 1730, 1713, 1243 cm^{-1} via RuO_4 oxidation, thus additionally proving the 13,28-epoxy moiety in VI.

The NMR spectrum (Table I) of the above-mentioned minor ketonic aglycone, $C_{30}H_{48}O_3$, mp. 257.5~258°, along with its IR absorption bands provides the possible formulation as VIII. identical structure with aegicerin which was previously established by Rao.[11] Although the direct comparison has not been available, the identity (mixed mp., IR., TLC) of a monoacetate derived from the ketone with the monoketo-acetate (X) substanciates the correctness of the structure VIII.

P.japonica roots sapogenin : On the Smith degradation as above, the saponin[1] of (iv) furnished camelliagenin A (II) as the major aglycone, which was identical with the one obtained by acid hydrolysis of the same saponin.

Interestingly in this case, although no aglycone of priverogenin B or its derivative was obtained, protoprimulagenin A (VI) was isolated as a minor. This proves that primulagenin A (I), a minor sapogenin of (iv)[1], attaches to a saponin in a 13,28-epoxy form (VI) similarly as found in the saponin of (i). To exclude the possible epoxide-ring opening during the procedure of either drying the roots or extraction with MeOH at reflux, the fresh roots were extracted with MeOH containing 0.5% pyridine at reflux (to avoid the effects of acidic components in the plant meterial) as performed by Kubota and Hinoh[13] in case of Bupleurum falcatum L. roots saponin, and the saponin thus obtained was submitted to the Smith degradation as well. Here again it was found that the



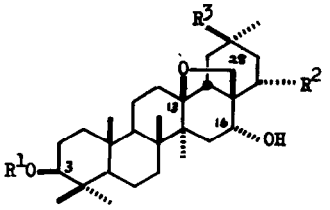
I R=H

primulagenin A

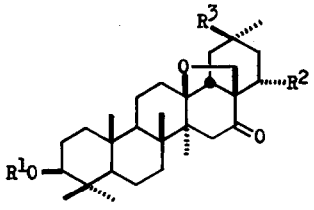
II R=OH

camelliagenin A

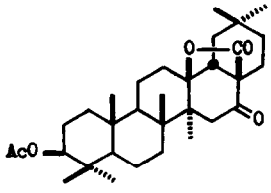
(=dihydropriverogenin A)



	R^1	R^2	R^3	
III	H	H	CHO	cyclamiretin A
V	H	OAc	CH_3	
VI	H	H	CH_3	protoprimulagenin A
VII	H	OH	CH_3	priverogenin B
IX	Ac	H	CH_3	



	R^1	R^2	R^3	
IV	H	H	CHO	cyclamigenin B
VIII	H	H	CH_3	aegicerin
X	Ac	H	CH_3	



XI

open structure (II) was a genuine form in the roots of (iv).

L.mauritiana fruits sapogenin : Although the acid hydrolysis of saponin of (v) afforded camelliagenin A (II) as the major aglycone[1], the Smith degradation as above furnished a compound, mp. 275.5~276°, IR (KBr) 3450 cm^{-1}, which was found identical with authentic priverogenin B[4,5] (VII) kindly provided by Prof. R.Tschesche.

It is noteworthy to point out that the major genuine sapogenins of (iv) and (v) differ whether the 13,28-oxide bridge is open or closed, whereas the major sapogenins obtained by the acid hydrolysis of both saponins are identical. The finding might be ascribed either to the difference of genera or to the different parts (roots or seeds) of the plant materials, and the examination in this connection is in progress.

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Literatures

1) I.Kitagawa, A.Matsuda, T.Nishimura, S.Hirai, I.Yosioka : Chem. Pharm. Bull.(Tokyo), 15 1435 (1967).

2) H.Itokawa, N.Sawada, T.Murakami : Tetrahedron Letters, 1967 597.

3) S.Ito, M.Kodama, M.Konoike : Tetrahedron Letters, 1967 591.

4) I.Yosioka, T.Nishimura, N.Watani, I.Kitagawa : Tetrahedron Letters, 1967 5343.

5) R.Tschesche, B.T.Tjoa, G.Wulff : Liebig's Ann., 696 160 (1966); Tetrahedron Letters, 1968 183.

6) M.Kodama, S.Ito : Chem. & Ind., 1967 1647.

7) R.Tschesche, H.Striegler, H.-W.Fehlhaber : Liebig's Ann., 691 165 (1966).

8) R.O.Dorchai, J.B.Thomson : Tetrahedron, 24 1377 (1968) ; Tetrahedron Letters, 1965 2223.

9) J.J.Dugan, P.de Mayo : Can.J.Chem., 43 2033 (1965).

10) I.Yosioka, M.Fujio, M.Osamura, I.Kitagawa : Tetrahedron Letters, 1966 6303 ;
I.Yosioka, K.Imai, I.Kitagawa : Tetrahedron Letters, 1967 2577.

11) K.V.Rao : Tetrahedron , 20 973 (1964).

12) N.Aimi, H.Fujimoto, S.Shibata : Chem. Pharm. Bull.(Tokyo), 16 641 (1968).

13) T.Kubota, H.Hinoh : Tetrahedron, 24 675 (1968).