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A NEW SELECTIVE CLEAVAGE METHOD OF GLUCURONIDE LINKAGE IN OLIGOGLYCOSIDE
LEAD TETRAACETATE OXIDATION FOLLOWED BY ALKALI TREATMENT

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During the course of the study in search of a new selective cleavage method for a certain glycoside linkage in the oligosaccharide portion of saponin, it has been found that the ultraviolet irradiation is an effective procedure for selective splitting of the glucuronide linkage in saponin.[1] This paper communicates another selective cleavage method for the glucuronide linkage, that is, lead tetraacetate oxidation followed by alkali treatment of the permethylated derivative of glucuronide-saponin possessing a free carboxyl function in the glucuronide moiety. By the present method, the methylated sapogenol and methylated carbohydrate ingredients are liberated in the excellent yields.

It has been assumed that when a glucuronide (1, possessing the free carboxyl and R being the protecting groups or the other protected carbohydrate residues) is treated with lead tetraacetate,[2] an enol ether (2) and/or acetates (3) would be derived and 2 and 3 could readily be decomposed respectively by mild acid and alkali treatment liberating the sapogenol moiety. The assumption has been realized *via* 3 as shown below.

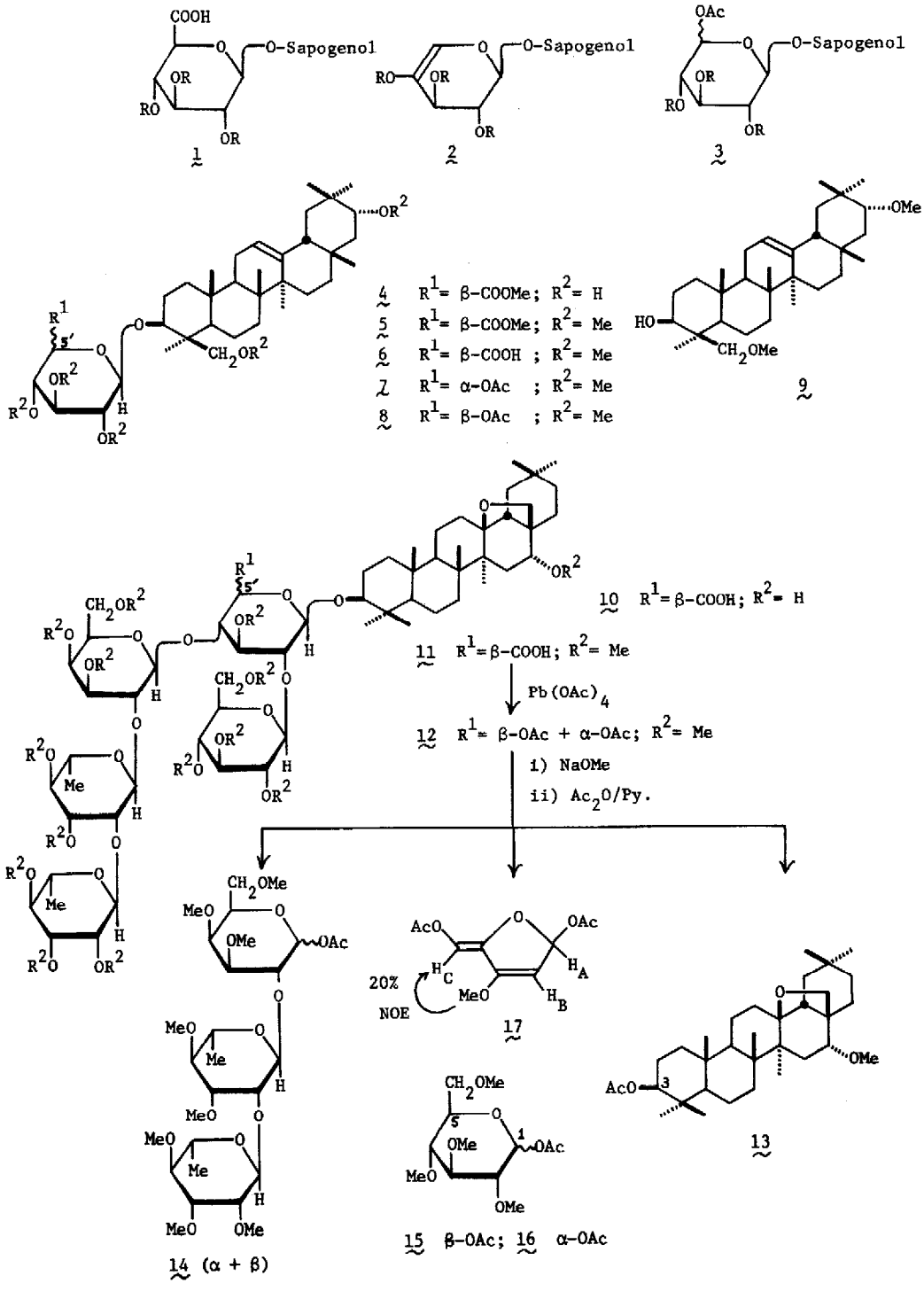
A permethylated derivative $C_{42}H_{70}O_9$[3] (5, $\nu(CCl_4)$: 1759 cm^{-1} ($COOCH_3$)) of a prosapogenol (4) of soyasaponin I (from *Glycine max* Merrill seeds)[4] was treated with aq. K_2CO_3 to give 6, $C_{41}H_{68}O_9$, which possesses a free carboxyl ($\nu(CCl_4)$: 1735 cm^{-1}). Treatment of 6 with $Pb(OAc)_4$ in benzene under reflux for one hour gave two isomeric products: 7 (45%) and 8 (42%), and no enol ether (type 2) was formed.

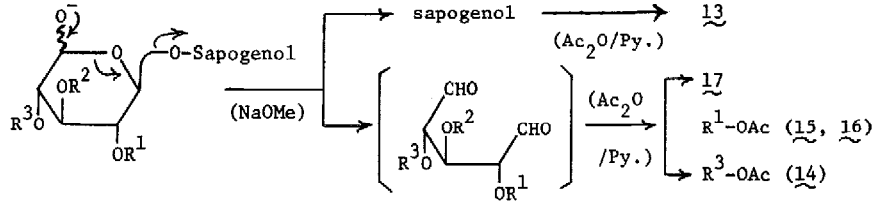
7, $C_{42}H_{70}O_9$, is assigned the structure having an α-axial acetoxyl while 8, $C_{42}H_{70}O_9$, with a β-equatorial acetoxyl at C-5' as based on the IR and PMR spectra: $\nu(CCl_4)$: 1762, 1226 cm^{-1} and $\delta(CDCl_3)$: 2.11 (3H, s, OAc) and 6.21 (1H, d, J= 3.5 Hz, 5'-H) in 7; $\nu(CCl_4)$: 1768, 1222 cm^{-1} and $\delta(CDCl_3)$: 2.10 (3H, s, OAc) and 5.43 (1H, m,[5] 5'-H) in 8. Respective treatment of 7 and 8 with 0.1% $NaOCH_3$ in CH_3OH at room temperature for 30 min. furnished 21,24-di-O-methyl-soyasapogenol B (9)[4] in the excellent yield (95% from 7 and 91% from 8).

Next, the cleavage method was applied to saponin which possesses a glucuronide linkage directly connected to the sapogenol. A derivative 11, $C_{74}H_{126}O_{27}$, $\nu(CCl_4)$: 1750, 1740 cm^{-1}, prepared from sakurasō-saponin (10)(from *Primula sieboldi* E.Morren root)[6] was first treated with $Pb(OAc)_4$ as above to afford a mixture of two acetates (12): $\nu(CCl_4)$: 1762, 1228 cm^{-1}; $\delta(CDCl_3)$: 1.99, 2.04 (totally 3H, each s, OAc), 5.52, 6.05 (totally 1H, each d, J= 8 and 4 Hz, 5'-H), which, without further separation, was subjected to $NaOCH_3/CH_3OH$ treatment followed by Ac_2O/Py. acetylation. Separation of the products was effected by chromatography to furnish 3-O-acetyl-16-O-methyl-protoprimulagenin A (13, 90%), $C_{33}H_{54}O_4$: $\nu(CCl_4)$: 1730, 1238 cm^{-1} and $\delta(CCl_4)$: 1.94 (3H, s, OAc), 3.21 (3H, s, OMe), 4.39 (1H, t-like, 3α-H), a trisaccharide (14, 92 %): $\nu(CCl_4)$: 1767, 1225 cm^{-1} (the structure being determined by PMR analysis and methanolysis), 15: $\nu(CCl_4)$: 1770, 1224 cm^{-1} and $\delta(CDCl_3)$: 2.11 (3H, s, OAc), 5.42 (1H, d, J= 7 Hz, 1-H), 16: $\nu(CCl_4)$: 1764, 1227 cm^{-1} and $\delta(CDCl_3)$: 2.07 (3H, s, OAc), 6.14 (1H, d, J= 3 Hz, 1-H)(70% for 15 + 16), and a dienic compound $C_{10}H_{12}O_6$ (17, 32%).[7]

On methanolysis, 15 and 16 gave methyl 2,3,4,6-tetra-O-methyl-glucopyranoside and the structure 17 has been based on the spectroscopic evidence. Thus, the presence of acetoxyls and a diene chromophore has been shown by the IR spectrum: $\nu(CCl_4)$: 1765, 1738, 1615, 1235, 1217 cm^{-1} and by the UV spectrum: max (EtOH): 238.5 nm (ε= 12600). In the PMR spectrum, are observed the signals due to two acetoxyls (δ2.14, 6H, s), one methoxyl (δ3.91, 3H, s), two olefinic protons (δ5.24, 1H, d, J= 3 Hz, H_B and δ5.46, 1H, s, H_C), and a methine proton (δ5.88, 1H, d, J= 3 Hz, H_A), the latter being proved to be adjacent to H_B by the decoupling experiments. In addition, the 20% NOE enhancement was observed between the methoxyl protons and H_C. The mass fragmentation pattern also supports the formulation 17 which will be reported elsewhere.

It has been shown that a methylated saponin possessing a glucuronide linkage (with a free carboxyl) directly connected to the sapogenol is readily split to the methylated sapogenol and the methylated carbohydrate ingredients in the excellent yields. It is also noted here that the acid-labile 13β,28-oxide moiety in the sapogenol portion of 10 was kept unaffected


1
2
3
4 R1= β-COOMe; R2= H
5 R1= β-COOMe; R2= Me
6 R1= β-COOH ; R2= Me
7 R1= α-OAc ; R2= Me
8 R1= β-OAc ; R2= Me
9
10 R1= β-COOH; R2= H
11 R1= β-COOH; R2= Me
Pb(OAc)4
12 R1= β-OAc + α-OAc; R2= Me
i) NaOMe
ii) Ac2O/Py.
13
14 (α + β)
15 β-OAc; 16 α-OAc
17
20%
NOE



throughout the reactions. In order to examine the general applicability, the present degradation method has similarly been applied to soyasaponin I,[4] desacyl-jegosaponin (from *Styrax japonica* Sieb. et Zucc. pericarps),[8] and desacyl-boninsaponin A (from *Schima mertensiana* Koidz. bark),[9] all of which possess a glucuronide moiety directly attached to the sapogenol, and the corresponding methylated sapogenols and methylated carbohydrate ingredients have been isolated in addition to 17 as expected. As for the reaction pathway, a scheme shown above seems to be attractive. Although the β-elimination reactions under the basic conditions have often been utilized to cleave at the glucuronide moiety in polysaccharide,[10] the present method also seems to be applicable to the selective cleavage of the uronide linkage in polysaccharide and to be a useful tool for the structure study in the field.

REFERENCES AND FOOTNOTES

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3) All the compounds given with the chemical formulae gave the satisfactory analytical values.

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5) The PMR measurements of 8 in the various solvents (d_6-benzene, d_6-acetone, d_5-pyridine, and CCl_4) have disclosed the multiplicity of the signal being due to the virtual coupling.

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7) The low yield is due to the instability of 17.

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