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SELECTIVE CLEAVAGE OF ESTER TYPE GLYCOSIDE-LINKAGES AND ITS APPLICATION TO STRUCTURE DETERMINATION OF NATURAL OLIGOGLYCOSIDES

Kazuhiro Ohtani, Kenji Mizutani, Ryoji Kasai and Osamu Tanaka*
Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine
Kasumi, Minami-ku, Hiroshima 734 Japan

Abstract: On treatment with anhydrous LiI, 2,6-lutidine and anhydrous methanol, an ester type glycosyl linkage of acidic tri- and di-terpenes was selectively cleaved without decomposition of a reducing terminal of the resulting sugar moiety to give an anomeric mixture of methyl glycosides along with an aglycone or a pro-aglycone in quantitative yield. In this reaction, no hydrolysis of any other glycoside linkages took place.

A number of glycosides having an ester type glycoside-linkage have been found in nature, namely, saponins of acidic triterpenes etc. It has been known that a glycosyl ester of less hindered fatty acids is readily saponified even by mild alkaline treatment, affording both aglycone and sugar moieties. However, saponification of a glycosyl ester of a hindered carboxylic acid such as 28-carboxylic acid of oleanane, ursane or lupane type triterpenes requires a relatively strong alkaline condition which is accompanied by the decomposition of a reducing terminal of the resulting sugar unit, yielding no intact sugar moiety. Accordingly, for structural elucidation, the glycosides of this type have been subjected to careful permethylation followed by $LiAlH_4$ reduction and the resulting permethylated alditol (or permethylated glycosyl-alditol) has been analyzed for the identification of a sugar moiety which is linked with an aglycone carboxylic acid. The present communication reports the simple, selective and quantitative cleavage of an ester type glycoside-linkage which is promising for the rapid structure determination of the glycosides of this type.

Elsinger et al.[1] and Dean[2] reported the selective cleavage of a small alcoholic ester linkage such as methyl ester by treating with LiI and DMF (or 2,6-lutidine). By this procedure, the strongly hindered methyl ester linkage of methyl 3-O-acetyloleanolate(**1**) was selectively cleaved to yield 3-O-acetyloleanolic acid(**2**) in fairly good yield. In the present study, it was demonstrated that, treatment of β-D-glucopyranosyl oleanolate(**3**)[3,4] under the same condition yielded no free glucose but gave 1,6-anhydroglucose (**4**) which was identified by comparison with an authentic sample. Treatment of α-L-arabinopyranosyl 3-O-acetyloleanolate(**5**)[5] under this condition afforded

3-O-acetyloleanolic acid(2) but no sugar unit could be identified due to the simultaneous decomposition. A similar negative result was observed for β-D-xylopyranosyl and α-L-rhamnopyranosyl esters(6 and 7)[5] of 2. This would be due to the instability of the probable intermediate, the sugar iodide such as 8 formed in this reaction.

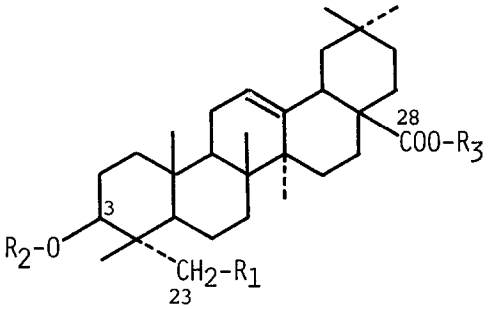
In order to obtain a sugar moiety in a stable form, it was attempted to convert the sugar iodide into a methyl glycoside by conducting the reaction in anhydrous methanol, leading to the desired result; a solution of 5(50 mg) and anhydrous LiI*(30 mg) in 2,6-lutidine(2 ml) and anhydrous methanol(1 ml) was refluxed under N_2 gas for 16hr. After diluting with 50% methanol, the reaction mixture was deionized by passing through a column of Amberlite MB-3 and then chromatographed on highly porous polymer, Diaion HP-20 (Mitsubishi Chem. Ind. Co.Ltd., Tokyo) to give methyl L-arabinopyranoside(9, 11 mg) by elution with water and 2(35 mg) by subsequent elution with methanol. In a similar manner, 6, 7 and β-D-glucopyranoside(10) of 2 afforded methyl D-xylopyranoside(11), L-rhamnopyranoside(12) and D-glucopyranoside(13), respectively, in almost quantitative yields, together with 2 without cleavage of the 3-O-acetyl linkage. The anomeric ratio of the resulting methyl glycosides was determined by gas chromatography as a trimethylsilyl ether for 13 and by ^{1}H-NMR for 9, 11 and 12. These results are summarized in Table I. It is notable that the ratio of the α-anomer is significantly lower for 11 than for the other cases.

As an application of this procedure to natural bisdesmosides chemistry, the selective cleavage of the ester type glycoside-linkages of the following saponins was conducted: chikusetsusaponin V(14) from *Panax japonicus*,[6] mukurozisaponin Y_1(15) from pericarps of *Sapindus mukurossi*[7] and Huzhangoside B(16) from *Anemone rivularis*[8]. On treatment with this reagent, 14, 15 and 16 yielded 13, methyl sophoroside(17) (an anomeric mixture) and methyl α-L-rhamnopyranosyl-(1→4)-β-D-glucopyranosyl-(1→6)-(α and β)-D-glucopyranoside(18), respectively in good yield, along with the corresponding prosapogenins(monodesmoside), 19, 20 and 21 without cleavage of any other glycoside-linkages. Methyl oligoglycoside 18 was also obtained from chiisanoside(22) which is the glycosyl ester of 3,4-seco-lupane type triterpene isolated from *Acanthopanax chiisanensis*.[9] The identification of each methyl glycoside was substantiated by comparison with authentic samples for 14 and 17 and by the ^{13}C-NMR spectrum as well as the sequence analysis (GC-MS analysis of the derived methylated alditol acetates) for 18.[8] Recently, the structure of hemsloside H_1(23), the bisdesmoside (β-gentiobiosyl ester) from *Hemsleya chinensis*[10] was elucidated by means of the present procedure.

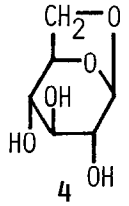
Selective cleavage in quantitative yield was also achieved for sweet diterpene glycosides, stevioside(24) and rebaudioside E(25) obtained from the leaves of *Stevia rebaudiana*.[11] 24 and 25 afforded 13 and 17, respectively together with steviolbioside(26) without cleavage of any other glycoside-linkages.

Table I Anomeric Ratio of Resulting Methyl Glycoside

Reactant	Me-Gly	α(%)	β(%)
5	**9**	59	41
6	11	22	78
7	12	87	13
10	13	61	39



	R1	R2	R3
1	-H	-Ac	-Me
2	-H	-Ac	-H
3	-H	-H	β-D-Glc
5	-H	-Ac	α-L-Ara
6	-H	-Ac	β-D-Xyl
7	-H	-Ac	α-L-Rha
10	-H	-Ac	β-D-Glc
14	-H	β-D-GlcUA(2β)-D-Glc	β-D-Glc
15	-OH	α-L-Ara(2α)-L-Rha(3β)-D-Xyl	β-D-Glc(2β)-D-Glc
16	-H	α-L-Ara(2α)-L-Rha(3β)-D-Rib	β-D-Glc(6β)-D-Glc(4α)-L-Rha
19	-H	β-D-GlcUA(2β)-D-Glc	-H
20	-OH	α-L-Ara(2α)-L-Rha(3β)-D-Xyl	-H
21	-H	α-L-Ara(2α)-L-Rha(3β)-D-Rib	-H
23	-H	β-D-GlcUA(2β)-D-Glc, (3α)-L-Ara	β-D-Glc(6β)-D-Glc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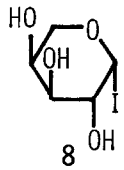
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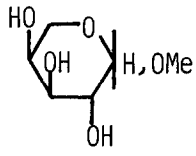
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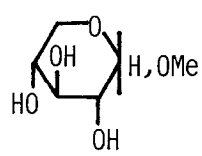
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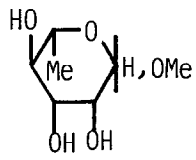
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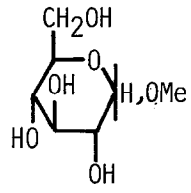
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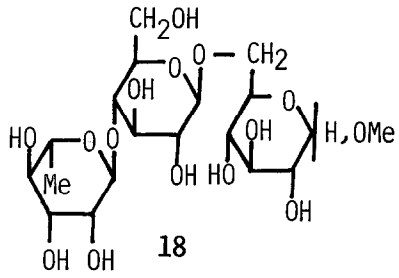
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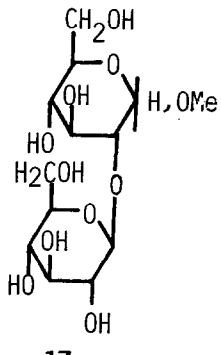
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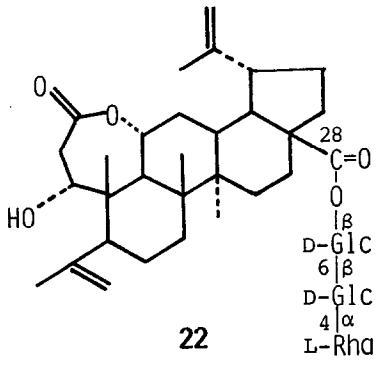

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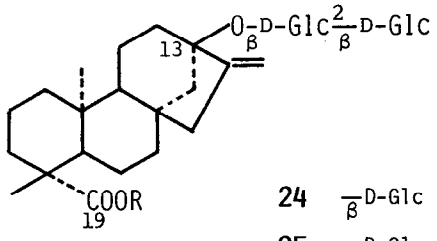

24 $\frac{}{\beta}$D-Glc

25 $\frac{}{\beta}$D-Glc $\frac{2}{\beta}$D-Glc

26 -H

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*;Anhydrous LiI from commercial $LiI \cdot 3H_2O$ by drying at 150°C *in vacuo* for 2hr.

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