Tetrahedron Letters Vol. 21, pp 3775 - 3778
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0040-4039/80/0922-3775$02.00/0

# LABDANE DITERPENE GLYCOSIDES WITH 6-DEOXY-L-IDOSE FROM *ASTER SPATHULIFOLIUS* MAXIM.

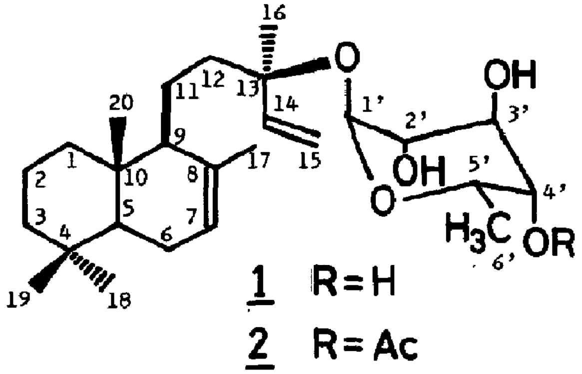
Y. Uchio, M. Nagasaki, S. Eguchi, A. Matsuo, M. Nakayama and S. Hayashi[1]
Department of Chemistry, Faculty of Science, Hiroshima University, Hiroshima 730, Japan

*Summary:* Three labdane type diterpene glycosides (1, 2 and 3) with 6-deoxy-L-idose have been isolated from *Aster spathulifolius* Maxim. and their structures have been determined on the basis of chemical and spectral data.

Among eight theoretically possible pairs of optically active 6-deoxyhexoses only 6-deoxyidose has not been known[2] in nature. We now isolated the sugar as a common component of three labdane diterpene glycosides during our studies on diterpenoids of *Aster spathulifolius* Maxim. The present communication deals with the isolation and structure of these glycosides containing 6-deoxyidose.

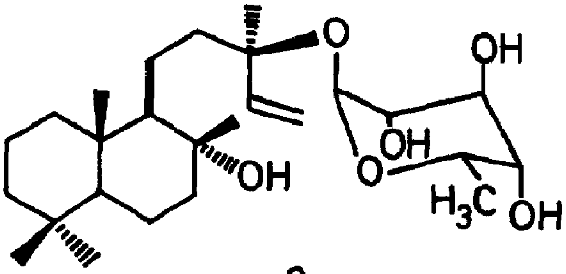
Methanolic extract of the fresh aerial parts of the plant was chromatographed on silica gel using chloroform with increasing amounts of methanol, and three closely related glycosides (1, 2 and 3) were isolated along with three diterpenoids, labda-7,14-dien-13β-ol (7),[3] 7α-hydroxymanool[4] and sclareol (8).[5]

The glycoside 1,[6] $C_{26}H_{44}O_5$ ($M^{+\cdot}$ 436), amorphous powder, $\{\alpha\}_D$ -61.0°(MeOH), was characterized as a 6-deoxyhexoside of a diterpene alcohol based on 26 carbon signals of the $^{13}C$ NMR spectrum (Table 1). Oxidation of 1 with sodium periodate in EtOH furnished a diterpene alcohol, $C_{20}H_{34}O$ ($M^{+\cdot}$ 290); $\{\alpha\}_D$ -2.4°(MeOH), coinciding with 7 isolated from this plant in spectral data (IR, $^1H$ NMR, $^{13}C$ NMR, MS) and $\{\alpha\}_D$. Acetylation of 1 with $Ac_2O$/Pyridine gave a tri-O-acetyl derivative (4), $C_{32}H_{50}O_8$ ($M^{+\cdot}$ 582); $\{\alpha\}_D$ -45.2°($CHCl_3$); δ 2.06 (6H, s), 2.10 (3H, s), and also methylation with $CH_3I$/NaH-DMSO[7] gave a tri-O-methyl derivative (6), $C_{29}H_{50}O_5$ ($M^{+\cdot}$ 478); $\{\alpha\}_D$ -38.1°($CHCl_3$); δ 3.40, 3.52, 3.54 (each 3H, s). The $^1H$ NMR spectra of 1, 4 and 6 showed the presence of a secondary methyl and a proton on a methine group forming an O-glycoside linkage at δ 1.20 (3H, d, J=7.0 Hz) and 4.42 (1H, dq, J=7.0, 3.5), 1.18 (3H, d, J=7.0) and 4.42 (1H, dq, J=7.0, 3.5), and 1.16 (3H, d, J=7.0) and 4.15 (1H, m), respectively. From these chemical and spectral data the structure of 1 was confirmed to be a 6-deoxypyranoside of 7. Six $^{13}C$ NMR resonances of sugar moiety of 1 clearly differed from those of reported commonly occurring 6-deoxysugars(rhamnose, fucose, quinovose) and their methyl glycosides.[8] In addition to the above fact, no formation of acetonide of 1 strongly suggested the presence of 6-deoxyidopyranosyl moiety, the three hydroxyl groups of which were situated in *trans* relationship each other in the molecule of 1. Therefore, a search has been made to isolate the sugar moiety of 1. Methanolysis of 1 using a strongly acidic ion exchange resin[9] and subsequent acetylation ($Ac_2O$/Pyridine) afforded two methyl 6-deoxyhexoside triacetates,[10] $C_{13}H_{20}O_8$ ($M^{+\cdot}$-1, 303), oil, $\{\alpha\}_D$ -148.0°($CHCl_3$), and $C_{13}H_{20}O_8$ ( $M^{+\cdot}$-1, 303), mp 97.5-98.0°, $\{\alpha\}_D$ +46.9°($CHCl_3$), which were assigned to the α[11] and β-anomeric pyranosides, respectively, based on the $^1H$ chemical shifts[12] of each secondary methyls (δ 1.20 in



1 R=H

2 R=Ac



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α-anomer and δ 1.30 in β-anomer, each d, J=7.0 Hz). The β-anomer obtained was identified to be methyl 2,3,4-tri-O-acetyl-β-L-idopyranoside by the mixed mp, $\{\alpha\}_D$ and spectral (IR, $^1$H NMR, MS) comparison with those of synthetic material,[13] thus confirming the occurrence of 6-deoxy-L-idopyranose in the molecule of 1

Table 2. Comparative $^1$H NMR data[a] of sugar moieties of 1, 2 and 3 in $CD_3OD$ (δ from TMS, 90 MHz).

| | 1 | Coupling (Hz) | 2 | Coupling (Hz) | 3 | Coupling (Hz) |
|---|---|---|---|---|---|---|
| H-1' | 4.83 (d) | $J_{1,2}=3.5$ | 4.78 (d) | $J_{1,2}=4.5$ | 4.81 (d) | $J_{1,2}=4.5$ |
| H-2' | 3.35-3.45 (overlaps with H-4', m) | $J_{2,3}=J_{3,4}=5.5$ | 3.39 (dd) | $J_{2,3}=J_{3,4}=7.0$ | 3.38 (dd) | $J_{2,3}=J_{3,4}=6.0$ |
| H-3' | 3.69 (t) | | 3.68 (t) | | 3.68 (t) | |
| H-4' | 3.35-3.45 (overlaps with H-1', m) | $J_{4,5}=3.5$ | 4.76 (dd) | $J_{4,5}=4.0$ | 3.46 (dd) | $J_{4,5}=3.5$ |
| H-5' | 4.24 (dq) | | 4.32 (dq) | | 4.24 (dq) | |
| H-6' | 1.20 (d) | $J_{5,6}=7.0$ | 1.13 (d) | $J_{5,6}=7.0$ | 1.19 (d) | $J_{5,6}=7.0$ |
| $CH_3CO$ | | | 2.08 (s) | | | |

[a] The assignment was made by comparison with the spectrum of 6-deoxy-β-L-idopyranoside and its triacetate in ref. 13.

The glycoside 2,[6] $C_{28}H_{46}O_6$ ($M^{+\cdot}$ 478), amorphous powder, $\{\alpha\}_D$ -46.8°(MeOH), which contained an acetoxyl group ($^1$H: δ 2.08, 3H, s, in $CD_3OD$. $^{13}$C: δ 170.4, s, δ 20.7, q, in $C_5D_5N$), was proved to be a monoacetate of 1 since $^{13}$C NMR signals of aglycone moieties of 1 and 2 appeared at almost the same positions as listed in Table 1 and on acetylation ($Ac_2O$/Pyridine) 2 gave a triacetate coinciding with 4 in spectral data (IR, $^1$H NMR, $^{13}$C NMR, MS) and $\{\alpha\}_D$. Comparison of the $^1$H NMR spectra of 1 and 2 (the signals of only sugar parts were listed in Table 2), and decoupling experiment revealed the site of the acetoxyl group of 2 to be at C-4'; the signals due to H-2' and H-3', respectively, appeared at δ 3.39 (dd) and δ 3.68 (t) which were essentially the same positions as those of 1, while the signal of H-4' being deshielded on acetylation shifted to a lower field of δ 4.76 which on irradiation caused the triplet (δ 3.68, H-3') into a doublet (J=7.0 Hz).

The minor component, glycoside 3,[6] $C_{26}H_{46}O_6$ ($M^{+\cdot}$-18, 436), $\{\alpha\}_D$ -33.2°(MeOH), on acetylation ($Ac_2O$/Pyridine) provided a tri-O-acetyl derivative (5), $C_{32}H_{52}O_9$ ($M^{+\cdot}$ 580), $\{\alpha\}_D$ -20.2°($CHCl_3$); δ 2.04 (6H, s), δ 2.06 (3H, s) in which one hydroxyl group remained unaffected (IR, $^1$H NMR and $M^{+\cdot}$-18 peak) indicating its tertiary nature. Comparative study of the $^{13}$C and $^1$H NMR spectra of

Table 1. $^{13}$C chemical shifts[a] and glycosylation shifts[b] of aglycone moieties.

| | | in $C_5D_5N$ | | | | | | in $CDCl_3$ | |
|---|---|---|---|---|---|---|---|---|---|
| | | 1[c] | (Δδ)[b] | 2[c] | (Δδ)[b] | 3[c] | (Δδ)[b] | 4[c] | 5[c] |
| C-1 | | 39.3 | ( 0.0) | 39.3 | ( 0.0) | 39.9 | (-0.1) | 39.2 | 39.8 |
| 2 | | 19.0 | (-0.1) | 19.0 | (-0.1) | 18.7 | (-0.1) | 20.4 | 18.9 |
| 3 | | 42.5 | ( 0.0) | 42.5 | ( 0.0) | 42.1 | (-0.1) | 42.4 | 42.1 |
| 4 | | 33.0 | ( 0.0) | 33.0 | ( 0.0) | 33.2 | (-0.1) | 32.9 | 33.2 |
| 5 | | 55.4 | ( 0.0) | 55.4 | ( 0.0) | 56.3 | (-0.2) | 55.2 | 56.2 |
| 6 | | 24.0 | ( 0.0) | 24.0 | ( 0.0) | 20.7 | (-0.2) | 23.8 | 20.7 |
| 7 | | 122.3 | (+0.2) | 122.3 | (+0.2) | 44.3[e] | (-0.8) | 122.4 | 43.8[e] |
| 8 | | 135.4 | (-0.3) | 135.5 | (-0.2) | 73.8 | (+0.3) | 135.4 | 74.3 |
| 9 | | 50.3 | (-0.1) | 50.3 | (-0.1) | 62.1 | ( 0.0) | 50.2 | 62.0 |
| 10 | | 37.2 | (-0.1) | 37.2 | (-0.1) | 39.4 | (-0.1) | 37.1 | 39.1 |
| 11 | γ | 21.3 | (-0.4) | 21.4 | (-0.3) | 19.7 | (-0.4) | 21.0 | 20.7 |
| 12 | β | 44.9 | (-0.9) | 44.9 | (-0.9) | 44.1[e] | (-2.3) | 44.7 | 42.8[e] |
| 13 | α | 80.4 | (+7.7) | 79.9 | (+7.2) | 80.5 | (+7.4) | 80.4 | 80.2 |
| 14 | β | 143.0 | (-3.8) | 143.8 | (-3.0) | 144.2 | (-3.4) | 142.1 | 143.0 |
| 15 | γ | 111.5 | (+4.2) | 115.0 | (+3.8) | 114.1 | (+3.3) | 116.0 | 114.4 |
| 16 | β | 22.7 | (-5.8) | 23.2 | (-5.3) | 23.1 | (-5.1) | 22.3 | 23.6 |
| 17 | | 22.4 | (-0.1) | 22.4 | (-0.1) | 24.3 | (-0.3) | 22.3 | 24.3 |
| 18 | | 33.3 | ( 0.0) | 33.2 | (-0.1) | 33.4 | (-0.2) | 33.2 | 33.2 |
| 19 | | 21.9 | ( 0.0) | 21.9 | ( 0.0) | 21.6 | (-0.1) | 21.9 | 21.5 |
| 20 | | 13.8 | (+0.1) | 13.8 | (+0.1) | 15.0 | (-0.6) | 13.6 | 14.9 |
| C-1' | | 96.6 | ( - ) | 96.9 | ( - ) | 95.8 | ( - ) | 93.2 | 92.5 |
| 2' | | 71.9[d] | ( - ) | 73.8[d] | ( - ) | 72.6[d] | ( - ) | 69.3[d] | 69.7[d] |
| 3' | | 72.5[d] | ( - ) | 71.8[d] | ( - ) | 72.8[d] | ( - ) | 70.1[d] | 70.1[d] |
| 4' | | 71.6[d] | ( - ) | 75.9 | ( - ) | 72.5[d] | ( - ) | 68.8[d] | 68.9[d] |
| 5' | | 65.6 | ( - ) | 65.8 | ( - ) | 67.3 | ( - ) | 63.3 | 64.2 |
| 6' | | 15.7 | ( - ) | 14.3 | ( - ) | 15.6 | ( - ) | 15.1 | 15.5 |
| | | | Ac | 170.4 | ( - ) | | 3 x Ac | 170.0 | 3 x Ac 169.9 |
| | | | | 20.7 | ( - ) | | | 169.5 | 169.6 |
| | | | | | | | | 169.3 | 169.3 |
| | | | | | | | | 20.8 | 20.7 |

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[a] The spectra were taken on a Hitachi R-42FT spectrometer at 22.6 MHz and reported in ppm relative to TMS: assignment were aided by off-resonance decoupling of each compound.

[b] Change in carbon chemical shift on glycosylation[14]: Δδ=δ(glycoside)-δ(aglycone), in ppm.

[c] The assignment of aglycone moieties refered to labdane diterpenoids.[17] [d,e] Values within a column may be interchanged.

3 with those of 1 and 8 co-occurred in the same plant enabled us to determine the structure of 3. Namely, $^{13}$C signals due to both aglycone and sugar moieties of 3 resonated at virtually the same positions as those of 1, except for the signals of C-7 and C-8, as well as those of 4 and 5 ( Table 1), and a good agreement was also obtained in the $^{1}$H chemical shifts and J values of sugar parts of 1 and 3 (Table 2). Taken together, these data supported the structure of 3 which was a glycoside of sclareol (8) containing 6-deoxy-L-idose as a sugar component. The attachment of the sugar moiety to the *tert*-OH at C-13 of 3 could be established by difference of the $^{13}$C chemical shifts with those of corresponding aglycone (8); characteristic signal shifts[14] were observed in the α, β and γ-positions of the OH group in which the glycosylation occurred as well as those of 1 and 2, as shown in parentheses of Table 1. Lastly, the anomeric proton doublets of 1, 2 and 3 showed respectively the coupling constants of 3.5, 4.5 and 4.5 Hz, these values of which were closely similar to those of methyl α-idopyranosiduronic acid (4.0 Hz)[15] and methyl α-D-idopyranoside (4.0 Hz).[16]

Based on the results mentioned above, the structures of three glycosides isolated from *A. spathulifolius* have been represented by formulae 1, 2 and 3, whose anomeric carbons were determined to be all in α configurations.

*Acknowledgement*--We thank Professor R. Tanaka, Botanical Institute, Hiroshima University, for collection and identification of the plant material.

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11. $^{13}$C NMR data(CDCl$_3$); $CH_3$: 15.6; $CH$: 62.8, 68.0, 68.6, 69.9; anomeric $CH$: 99.2; $CH_3CO$: 20.7 ( x3); $CH_3CO$: 170.0 (x2), 169.4; $CH_3O$: 55.5 ppm. The spectrum exhibited a good correspondence with those of sugar part of 4 listed in Table 1, except for the signals due to C-1' and CH$_3$O.
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**(Received in Japan 20 June 1980)**