Pergamon

SCIENCE DIRECT®

Tetrahedron Letters 44 (2003) 4839–4841

TETRAHEDRON LETTERS

Homo-cholestane glycosides from *Solanum aethiopicum*

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Received 27 March 2003; revised 28 April 2003; accepted 2 May 2003

Abstract—The first naturally occurring steroidal glycosides, named aethiosides A, B and C, possessing a homo-cholestane skeleton with an aromatized ring E, were isolated from *Solanum aethiopicum*. They are presumably regarded to be derived from polyhydroxycholesterol by the conjugation of acetyl CoA or malonyl CoA.

Our ongoing search for bioactive oligoglycosides from solanaceous plants has so far resulted in the isolation of cytotoxic compounds[1] against several tumor cell lines, antifeeding substances[2] for *Thrips palmi* and important key intermediates[3] on the biosynthesis of steroidal alkaloids. In the present study, we have investigated the steroidal constituents in the respective organs of the leaves, stems and fruits of *Solanum aethiopicum* to provide three novel steroidal glycosides, named aethiosides A–C (**1**–**3**).[4] This paper deals with their structural characterization and discussing a plausible biogenesis.

The title plant was extracted with MeOH, and the resulting extract was partitioned between *n*-hexane and 80% MeOH. The lower layer was subjected to Diaion HP-20, silica gel and Chromatorex chromatographic separation to afford three glycosides.

Aethioside A (**1**), obtained as an amorphous powder, showed $[\alpha]_D$ −35.0° (MeOH) and a quasimolecular ion peak at m/z 1037 $[M-H]^-$ in the negative FABMS. The ^{1}H NMR spectrum showed the signals due to three tertiary methyls at δ 0.96, 1.12 and 2.34, a secondary methyl at δ 0.99 (d, $J=6.7$ Hz), an olefinic proton at δ 5.38 (br s), and two aromatic protons at δ 7.04 and 7.11 (each 1H, d, $J=7.3$ Hz) together with three anomeric proton signals at δ 4.87 (1H, d, $J=7.9$ Hz), 5.85 (1H, s), 6.39 (1H, s). The ^{13}C NMR signals[5] suggested the presence of a β-D-glucopyranosyl and a β-chacotriosyl

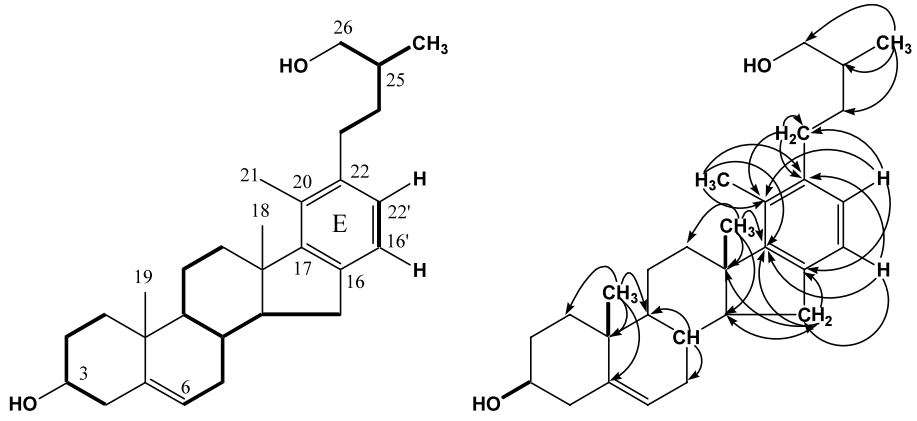

Figure 1. ^{1}H–^{1}H COSY (bold lines) and HMBC (denotes) of **4**.

Keywords: *Solanum aethiopicum*; steroidal glycoside; homo-cholestane; acetyl CoA; malonyl CoA; biogenesis.
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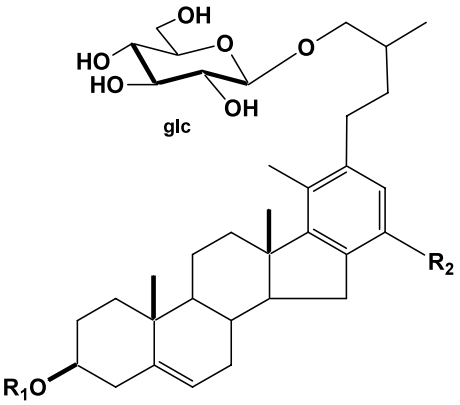
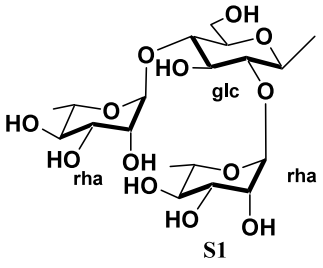
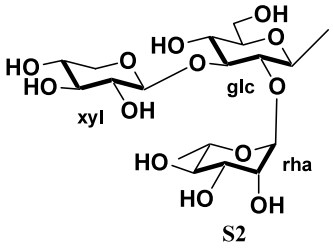
doi:10.1016/S0040-4039(03)01147-X



Aethioside A (**1**) R_1=S1; R_2=H
B (**2**) R_1=S2; R_2=H
C (**3**) R_1=S1; R_2=COOH





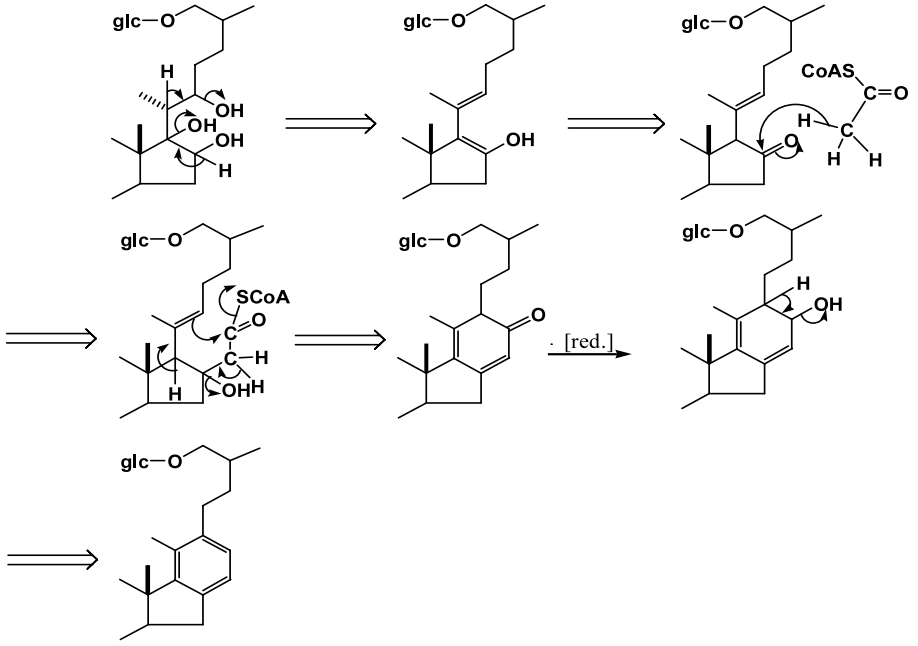


Chart 1. Plausible biosynthesis of **1**.

moieties.[6] Signals due to six sp^2 carbons were observed at δ 122.9, 127.5, 131.3, 139.8, 140.8, 151.9 besides two sp^2 carbon signals due to the C-5,6-double bond. The measurements of the HMBC spectrum revealed the correlations between H_3-21 and sp^2 carbons at C-17/-20/-22, H_3-18 and sp^2 carbon at C-17, an aromatic proton at δ 7.04 and C-16/-20, and an aromatic proton at δ 7.11 and C-17/-22, suggesting the presence of a benzene ring at E-ring. Furthermore, the H_2-26 correlated with the anomeric carbon of the glucopyranosyl moiety, simultaneously indicating the attaching of the β-chacotriosyl moiety to the hydroxyl group at C-3. To confirm the structure of sapogenol, **1** was hydrolyzed with 1N HCl–MeOH to afford a sapogenol (**4**),[7]

obtained as colorless needles, mp 221–224°C, which showed a quasimolecular ion peak at m/z 515 due to $[M+glycerol+H]^+$ in the positive FABMS. The ^1H–^1H COSY and HMBC showed the correlations as illustrated in Figure 1. Thus, the structure of **4** was verified and **1** was determined as shown in the formula. As regards to the production of **1** it was plausibly deduced as shown in Chart 1, that is, starting from the conjugation of polyhydroxycholesterol[8] and acetyl CoA resulting in the formation of a benzene ring at E-ring. The structures of aethiosides B (**2**)[9] and C (**3**)[10] were also analogously determined by the spectroscopic studies. In case of **3**, a malonyl CoA was deduced to be impregnated into the cholesterol molecule to give a carboxyl benzene ring. These three glycosides were for the first time isolated as the steroids with a novel skeleton carrying a benzene ring at E-ring by conjugation of cholesterol derivative and acetyl CoA or malonyl CoA.

Acknowledgements

We are grateful to Mr. N. Ogata and Ms. Y. Kaneko for cultivation of the plant in the botanical garden in Kumamoto University.

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3. Ohmura, E.; Nakamura, T.; Tian, R.; Yahara, S.; Yoshimitsu, H.; Nohara, T. *Tetrahedron Lett.* **1995**, *36*, 8443–8444.
4. Aethiosides A–C (**1**–**3**) were obtained from the fresh leaves (5.2×10^{-4}%) and fruits (2.6×10^{-3}%)/stems (8.3×10^{-4}%), and the fruits (1.3×10^{-4}%), respectively.
5. The ^{13}C NMR spectrum of **1**: (in pyridine-d_5) δ: Aglycone moiety C-1-27, C-16′, and C-22′: 37.4, 30.2, 78.6, 39.1, 141.1, 121.8, 32.5, 31.0, 50.6, 37.2, 21.3, 37.0, 47.2, 57.7, 32.0, 140.8, 151.9, 17.4, 19.4, 131.3, 14.7, 139.8, 31.3, 35.5, 34.2, 75.0, 16.6, 122.9, 127.5; β-D-glc·pyr C-1-6: 100.3, 78.2, 76.9, 78.0, 77.8, 61.4, α-L-rha·pyr C-1-6: 102.1, 72.5, 72.8, 74.2, 69.5, 18.5, α-L-rha·pyr C-1-6: 103.0, 72.6, 72.9, 73.9, 70.5, 18.7, 26-*O*-β-D-glc·pyr C-1-6: 105.0, 75.3, 78.7, 71.8, 78.8, 62.9.
6. Mahato, S. B.; Sahu, N. P.; Gaguly, A. N.; Kasai, R.; Tanaka, O. *Phytochemistry* **1980**, *19*, 2017–2020.
7. The ^{13}C NMR spectrum of **4**: (in pyridine-d_5) δ: C-1-27, C-16′, and C-22′: 37.7, 32.7, 71.3, 43.5, 142.3, 121.0, 32.5, 31.1, 50.7, 37.1, 21.5, 37.2, 47.3, 57.9, 32.1, 140.8, 151.9, 16.7, 19.6, 131.3, 14.7, 140.1, 31.6, 35.5, 36.8, 37.5, 17.3, 123.0, 127.4.
8. Zhu, X.-H.; Tsumagari, H.; Honbu, T.; Ikeda, T.; Ono, M.; Nohara, T. *Tetrahedron Lett.* **2001**, *42*, 8043–8046.
9. Aethioside B (**2**), $[\alpha]_D$ −36.8°(MeOH), a quasimolecular ion peak at m/z 1023 $[M-H]^-$ in the negative FABMS. The ^1H NMR spectrum (in pyridine-d_5) δ: 0.95 (3H, s, H_3-18), 1.06 (3H, d, $J=6.7$ Hz, H_3-27), 1.14 (3H, s, H_3-19), 1.77 (3H, d, $J=6.1$ Hz, rha H_3-6), 2.34 (3H, s, H_3-21), 4.87 (1H, d, $J=7.9$ Hz, 26-*O*-glc H-1), 5.39 (1H, br s, H-6), 6.33 (1H, s, rha H-1), 7.04 (1H, d, $J=7.3$ Hz, H-16′), 7.12 (1H, d, $J=7.3$ Hz, H-22′). The ^{13}C NMR spectrum of **2**: (in pyridine-d_5) δ: Aglycone moiety C-1-27, C-16′, and C-22′: 37.4, 30.2, 78.5, 38.8, 141.1, 121.9, 32.5, 31.1, 50.6, 37.2, 21.3, 37.1, 47.2, 57.8, 31.3, 140.8, 151.9, 17.4, 19.4, 131.3, 14.7, 139.8, 32.0, 35.5, 34.2, 75.0, 16.6, 122.9, 127.5; β-D-glc·pyr C-1-6: 100.1, 77.8, 88.3, 77.5, 74.7, 62.5, α-L-rha·pyr C-1-6: 102.4, 72.4, 72.9, 74.2, 69.5, 18.5, β-D-xyl·pyr C-1-5: 105.4, 75.0, 78.0, 70.7, 67.3, 26-*O*-β-D-glc pyr C-1-6: 105.0, 75.3, 78.5, 71.9, 78.7, 63.0.
10. Aethioside C (**3**), $[\alpha]_D$ −63.8°(MeOH), a quasimolecular ion peak at m/z 1081 $[M-H]^-$, 1105 $[M+Na]^+$ in the negative and positive FABMS. Positive HR-FAB-MS (m/z): 1105.5190 $[M+Na]^+$ ($C_{54}H_{82}O_{22}Na$, calcd for 1105.5195). The ^1H NMR spectrum (in pyridine-d_5) δ: 0.99 (3H, s, H_3-18), 1.07 (3H, d, $J=6.7$ Hz, H_3-27), 1.11 (3H, s, H_3-19), 1.62 (3H, d, $J=6.1$ Hz, rha H_3-6), 1.78 (3H, d, $J=6.1$ Hz, rha′ H_3-6), 2.40 (3H, s, H_3-21), 4.87 (1H, d, $J=7.9$ Hz, 3-*O*-glc H-1), 4.96 (1H, d, $J=6.7$ Hz, 26-*O*-glc H-1), 5.39 (1H, br s, H-6), 5.79 (1H, s, rha H-1), 6.32 (1H, s, rha′ H-1), 8.14 (1H, s, H-22′). The ^{13}C NMR spectrum: (in pyridine-d_5) δ: Aglycone moiety C-1-27, C-16′, C-22′ and COOH at C-16′: 37.4, 30.2, 78.3, 38.9, 141.0, 121.9, 33.3, 31.0, 50.5, 37.1, 21.3, 36.9, 46.9, 57.2, 32.0, 143.4, 153.3, 16.5, 19.4, 135.0, 15.1, 140.2, 31.3, 35.3, 34.1, 75.1, 17.3, 123.0, 129.5, 170.7; β-D-glc·pyr C-1-6: 100.2, 78.1, 76.7, 78.0, 77.7, 61.3, α-L-rha·pyr C-1-6: 102.0, 71.7, 72.2, 73.9, 69.5, 18.4, α-L-rha′·pyr C-1-6: 102.8, 72.4, 72.6, 73.6, 70.4, 18.6, 26-*O*-β-D-glc·pyr C-1-6: 104.7, 75.0, 78.9, 71.7, 78.9, 62.7.