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STRUCTURES OF TWO NOVEL MONOTERPENE ALKALOID GLUCOSIDES FROM *LONICERA XYLOSTEUM L.*

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Summary - The structures of loxylostosidine A and B, two new sulfoxide - containing monoterpene alkaloid glucosides, are described.

We recently[1] determined structure 1 for xylostosidine, the first of a new class of monoterpene alkaloid glycosides, from *Lonicera xylosteum L.*. Subsequently, we made a search for the presence of further members of this class of compounds in *L. xylosteum* that led to the isolation of two additional alkaloid glucosides[2]. In this communication we report the structures of these two compounds, named loxylostosidine A (2) and loxylostosidine B (3), respectively.

Loxylostosidine A (2) $[\alpha]_D^{20}$ = -248.32 (c= 0.65, MeOH) was obtained as an amorphous substance. The compound was found to possess the composition $C_{18}H_{25}O_9NS$ ($M^{+\cdot}$ = 431, FD-MS), one oxygen atom more than xylostosidine (1). In contrast to the latter, loxylostosidine A failed to provide a satisfactory $M^{+\cdot}$ peak in the EI-MS. The UV-spectrum λ_{max} (MeOH): 241 (log ε = 4.04) and the IR spectrum (KBr) at 1660 cm^{-1}, showed that loxylostosidine A, like xylostosidine, also possessed an β-alkoxyacrylamide function.

The compound 2 afforded a tetraacetate, $C_{26}H_{33}O_{13}NS$, accounting for four acetyl functions in the molecule (^{1}H-NMR), and thus all the hydroxyl functions, as in xylostosidine (1), were associated with the glucose moiety.

The ^{13}C-NMR spectrum of 2 (Table) displayed 18 signals, 14 of which are virtually identical in chemical shift and multiplicity with signals observed in the ^{13}C-NMR spectrum of 1. Three of the remaining four signals appeared as triplets (SFORD) at 27.83, 44.0 and 49.55 ppm and were assigned[3] to C(6), C(12) and C(13), respectively. The fourth, a doublet at 83.40 ppm, was assigned to C(7). The configuration at the S-atom was deduced from the chemical shift difference of C(6) between 2 and 1 (-4.64 ppm). This small γ-effect is only compatible with a trans arrangement of C(6) and the O-atom of the sulfoxide group[4].

The 360 MHz ^{1}H-NMR spectrum[7] of 2 is rather similar to that of 1. The following differences, however, corroborate[8] the assignment of the configuration at the S-atom made with the aid of the ^{13}C-NMR data: H_{eq}-C(6) is shifted downfield by 0.33 ppm with respect to 1, indicating that this proton is quasi synaxial[8] to the O-atom, and H-C(7) shows a high field shift of ca. 0.5 ppm as compared with H-C(7) in 1. H-C(5) and H-C(7) are cis to each other as in 1 (cf. the large trans couplings to H_{ax}-C(6)[7]). The vicinal coupling constants $J_{5,9}$ and $J_{1,9}$ amount to 5.5 and 2 Hz, resp., proving that the configuration at C(1), C(5) and C(9) is the same as in 1, sweroside[9] or bakankoside[10]. On the basis of the data presented, structure 2 is proposed for loxylostosidine A.

Loxylostosidine B (3), $[\alpha]_D^{20}$= -286.97 (c= 0.42, MeOH) is a minor metabolite and was obtained in pure form only after repeated chromatography over a reversed phase C_{18} column using MeOH/H_2O. The compound 3, like loxylostosidine A, was found to possess the composition $C_{18}H_{25}O_9NS$ ($M^{+\cdot}$= 431, FD-MS) but displayed a different TLC and HPLC behaviour. The UV and IR spectra were very similar to that of 2.

The ^{13}C-NMR (Table) and the ^{1}H-NMR[11] spectra indicated that loxylostosidine B differs from 2 only by the configuration at the S-atom. This assignment is based on the following observations: (i) The chemical shift difference of C(6) between 3 and 1 is -8.12 ppm (syn-γ-effect[4]), (ii) H_{ax}-C(6) is shifted downfield by 0.23 ppm whereas H_{eq}-(6) is unchanged in respect to 1 (cf. lit.[8]), (iii) finally, the lactam carbonyl C(11) appeared at lower field (166.55 ppm) than in 1 or 2; we interpret this downfield shift as a consequence of the change in the configuration at the S-atom, making an axial orientation of the O-atom probable. The above data can only be satisfactorily explained with structure 3 for loxylostosidine B.

An obvious inference from the structures of loxylostosidine A (2) and loxylostosidine B (3) is that their biogenetic precursor would have to be xylostosidine (1), from which they are formed by simple S-oxidation. Despite a detailed search for it's presence, C(7)-epi-xylostosidine and it's two sulfoxides have so far eluded isolation from *L. xylosteum*. This search, however, was rewarding as it resulted in the isolation of lonicerosidin[12], yet another novel compound belonging to the secoiridoid glycosides.

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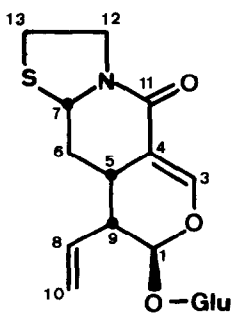
Table. ^{13}C-NMR Spectral Data of Alkaloid Glucosides of *L. xylosteum*[a]

C-Atom	1[b]	2	3	C-Atom	1[b]	2	3
C-1	97.19	97.26	97.45	C-11	164.57	164.28	166.55
C-3	148.90	149.85	149.35	C-12	49.83	44.00	47.40[c]
C-4	107.92	107.39	107.62	C-13	28.63	49.55	46.02[c]
C-5	28.36	27.17	27.34	C-1'	99.39	99.45	99.58
C-6	32.47	27.83	24.35	C-2'	74.49	74.49	74.72
C-7	62.29	83.40	76.74	C-3'	78.03	78.08	78.26
C-8	133.52	133.28	133.40	C-4'	71.31	71.32	71.50
C-9	44.23	44.19	44.58	C-5'	77.67	77.63	77.90
C-10	120.75	121.18	121.21	C-6'	62.50	62.55	62.61

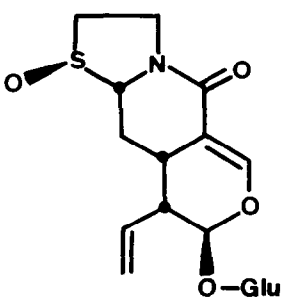
[a] Chemical shifts are given in ppm downfield from TMS. All compounds are recorded in CD_3OD.

[b] Data taken from Ref. 1

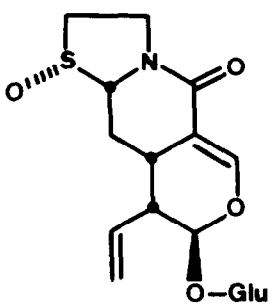
[c] Assignments are interchangeable



1. Xylostosidine



2. Loxylostosidine A



3. Loxylostosidine B

References and Notes

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[2] For leading references see: R.S. Kapil and R.T. Brown, in "The Alkaloids", Eds. R.H.F. Manske and R.G.A. Rodrigo, Academic Press Inc., New York, San Francisco, London, Vol. XVII, 1979, p.546.

[3] Assignment is based on (i) multiplicity of the signal in the SFORD spectrum, (ii) literature data on chemical shifts of SO containing compounds[4] and (iii) comparison of the spectra of 1, 2 and 3 with related compounds[5,6].

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[7] ^{1}H-NMR of loxylostosidine A, (2) [CD_3OD, δ-values in ppm from TMS internal ref., assignments were aided by double resonance experiments]: 7.43 [d, $J_{3,5}$= 2.5, H-C(3)], 5.52 [d, $J_{1,9}$= 2, H-C(1)], 5.52 [m, H-C(8)], 5.24-5.37 [m, 2H-C(10)], 4.66 [d, $J_{1',2'}$= 8, H-C(1')], 4.66 & 3.76 [m, 2H-C(12)], 4.29 [dd, $J_{6ax,7}$= 12.5, $J_{6eq,7}$= 4, H-C(7)], ca. 3.2 [m, H-C(2'), H-C(5), H-C(13)], 2.98 [m, H-C(13)], 2.76 [m, $J_{8,9}$= 9.5, $J_{5,9}$= 5.5, $J_{1,9}$= 2, H-C(9)], 2.51 [dt, $J_{6,6}$= 12.5, $J_{5,6}$= $J_{6,7}$= 4, H_{eq}-C(6)], 1.65 [q, $J_{5,6}$= $J_{6,6}$= $J_{6,7}$= 12.5, H_{ax}-C(6)].

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[11] ^{1}H-NMR of loxylostosidine B, (3) [CD_3OD, δ-values in ppm from TMS internal ref.]: 7.44 [d, $J_{3,5}$= 2.5, H-C(3)], 5.56 [dt, $J_{8,10}$= 17, $J_{8,9}$= $J_{8,10'}$= 10, H-C(8)], 5.52 [d, $J_{1,9}$= 1.8, H-C(1)], 5.34 [dd, $J_{8,10}$= 17, $J_{10,10'}$= 2, H-C(10)], 5.27 [dd, $J_{8,10'}$= $J_{10,10'}$= 2, H'-C(10)], 4.68 [d, $J_{1',2'}$= 8, H-C(1')], 4.61 [dd, $J_{6ax,7}$= 11.5, $J_{6eq,7}$= 3.5, H-C(7)], 4.32 & 3.94 [m, 2H-C(12)], 3.0-3.4 [m, H-C(5) & H-C(13)], overlapping with H-C(2') to H-C(5') and CD_2HOD), 2.76 [m, $J_{8,9}$= 10, $J_{5,9}$= 5.5, $J_{1,9}$= 1.8, H-C(9)], 2.19 [dt, $J_{6,6}$= 12.5, $J_{5,6}$= $J_{6,7}$= ca. 3.5, H_{eq}-C(6)], 1.72 [m, $J_{5,6}$= 13.5, $J_{6,6}$= 12.5, $J_{6,7}$= 11.5, H_{ax}-C(6)].

[12] R.K. Chaudhuri and O. Sticher, unpublished results.

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