110. Xylostosidine: The First of a New Class of Monoterpene Alkaloid Glycosides from *Lonicera Xylosteum* L.

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Summary

The structure of xylostosidine (**1**), a novel sulfur-containing monoterpene alkaloid glucoside, is presented.

At present, the number of substances regarded as monoterpene alkaloids[1]) is about fifty [1] and that of alkaloidal glycosides more than thirty [2]. The latter group is further subdivided into the isoquinoline and the indole series according to the nature of the non-terpene part [2]. We have studied the water-soluble constituents of *Lonicera xylosteum* L. *(Caprifoliaceae)*[2]), isolating 'xylostosidine', spectral analyses of which led to the unusual monoterpene alkaloid structure **1**.

Table. *^{13}C-NMR. Spectral data of xylostosidine* (**1**) *and related compounds*[a])

Carbon atom	1	1a	2	Carbon atom	1	1a	2
1	97.19	95.86	97.86	11	164.57	161.87	168.40
3	148.90	146.66	153.90	12	49.83	48.46	–
4	107.92	107.56	105.91	13	28.63	28.17	–
5	28.36	27.40	28.27	1′	99.39	96.10	99.58
6	32.47	31.63	25.78	2′	74.49	70.47	74.53
7	62.29	60.95	69.64	3′	78.03	72.12	78.16
8	133.52	131.60	133.23	4′	71.31	68.16	71.36
9	44.23	42.74	43.60	5′	77.67	72.20	77.69
10	120.75	120.75	120.75	6′	62.50	61.67	62.57

[a]) Chemical shifts are given in ppm downfield from TMS. Compounds **1** and **2** are recorded in CD_3OD and **1a** in $CDCl_3$.

[1]) Bakankoside (**4**) is the only exception in this group which has a glucose moiety at C(1).

[2]) There has yet been no confirmed report of the occurrence of any alkaloid in the family *Caprifoliaceae.*

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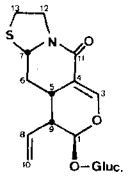
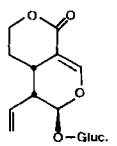
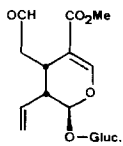


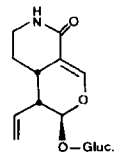
1 Xylostosidine



2 Sweroside



3 Secologanin



4 Bakankoside

Xylostosidine (**1**), $C_{18}H_{25}O_8NS$[3]), ($M^+ = 415$, EI-MS.)[4]), $[\alpha]_D^{20} = -289.37°$ ($c = 0.56$, MeOH), was obtained as a crystalline compound (aq. MeOH), m.p. 190–191°. The UV. spectrum, λ_{max} (MeOH): 238 nm ($\log \varepsilon = 4.23$), and the IR. spectrum (KBr): 1658 cm^{-1} indicated the presence of an α,β-unsaturated lactam moiety.

The MS. of xylostosidine (**1**) showed, beside the molecular-ion peak at *m/z* 415 (11%), significant fragments at *m/z* 253 (30) and 236 (14) and the base peak at 184. The ions at *m/z* 253 ($C_{12}H_{15}O_3NS$)[3]) and 236 correspond to the loss of $C_6H_{11}O_5$ (with H transfer) and $C_6H_{11}O_6$, respectively. The relative intensity (9%) of $M^+ + 2$ peak in relation to M^+ peak indicated the presence of sulfur in the molecule.

Acetylation of **1** afforded the tetraacetate **1a**, $C_{26}H_{33}O_{12}NS$ ($M^+ = 583$, EI-MS.), $[\alpha]_D^{20} = -185.35°$ ($c = 0.53$, $CHCl_3$), accounting for four acetyl functions in xylostosidine (**1**). All the hydroxyl functions in the molecule were thus associated with the glucose moiety. This was confirmed by the IR. and the ^{1}H-NMR. spectral data.

A study of the ^{13}C-NMR. spectrum of xylostosidine (**1**) proved most revealing. In CD_3OD, separate signals for all 18 C-atoms were observed and their assignment[5]) is given in the *Table*. Of these 18 signals, 15 correspond in multiplicity and approximate chemical shift to signals observed in the ^{13}C-NMR. of sweroside (**2**). Their δ-values differ by less than ± 0.5 ppm, with the exception of the signals of C(3), C(4), C(6) and C(11). The triplets (SFORD) at 49.83 and 28.63 ppm could be assigned, respectively, to N–CH_2 and S–CH_2 and the doublet at 62.29 ppm to C(7).

The above data guided by biogenetic considerations lead to **1** as the most logical structure (including the configuration at C(1), C(5) and C(9) as given in the formula) for xylostosidine. The chemical shift difference at C(3), C(4), C(6), C(7) and C(11) as well as the multiplicity of C(7) as compared with **2** can easily be explained on the basis of structure **1**.

Independent evidence for structure **1** as well as the configuration at C(1), C(5), C(7) and C(9) can be obtained from the 360-MHz-^{1}H-NMR. spectra[6]) of

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[3]) Determined by accurate mass measurement.

[4]) Further confirmed by FD.-MS.

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

[6]) ^{1}H-NMR. **1** (CD_3OD): 7.41 (*d*, $J_{3,5} = 2.7$, H–C(3)); 5.53 (*d* × *t*, $J_{8,10} = 17$, $J_{8,9} = J_{8,10'} = 10$, H–C(8)); 5.49 (*d*, $J_{1,9} = 1.9$, H–C(1)); 5.30 (*m*, $J_{8,10} = 17$, $J_{10,10'} = 2$, H–C(10)); 5.25 (*m*, $J_{8,10'} = 10$, $J_{10,10'} = 2$, H–C(10')); *ca.* 4.8 (H–C(7) partly overlapping with the HDO signal); 4.67 (*d*, $J_{1',2'} = 8.8$, *H*–C(1')); 4.13 and *ca.* 3.6 (2 H–C(12) the latter overlapping with H–C(6')); *ca.* 3.1 (*m*, H–C(5)

1 and **1a**. The H–C(5) and H–C(7) are *cis* to each other since both show a large *trans*-coupling to H_{ax}–C(6) ($J_{5,6ax}=13$, $J_{6ax,7}=11$ Hz). The vicinal coupling constants $J_{5,9}=5.5$ Hz and $J_{1,9}\sim 2$ Hz are very similar to those of **2** (5.5 and 1.8 Hz)[7]) and thus confirm the configuration at C(1), C(5) and C(9) since the configuration of **2** is known [5].

The co-occurrence of loganin [6], sweroside (**2**) [6] and xylostosidine (**1**) in *L. xylosteum* L. could be taken as circumstantial evidence that **1** might be biosynthesized from a secologanin (**3**) (or equivalent) unit [7] and the amino acid cysteine. If so, we could expect to find more members of this new class of monoterpene alkaloid glycosides. Work to this end is currently under way in our laboratory.

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overlapping with H–C(2')); *ca.* 3.1 (*m*, 2 H–C(13)); 2.69 (*m*, $J_{8,9}=10$, $J_{5,9}=5.5$, $J_{1,9}=1.9$, H–C(9)); 2.18 ($d\times t$, $J_{6,6}=12.5$, $J_{5,6}=J_{6,7}=3.5$, H_{eq}–C(6)); 1.49 (*m*, $J_{5,6}=13$, $J_{6,6}=12.5$, $J_{6,7}=11$, H_{ax}–C(6)). **1a** ($CDCl_3$): 7.42 (*d*, $J_{3,5}=2.4$, H–C(3)); 5.48 (*m*, H–C(8)); 5.23–5.31 (*m*, 2 H–C(10)); 5.27 (*d*, $J_{1,9}=1.7$, H–C(1)); 4.91 (*d*, $J_{1',2'}=8.5$, H–C(1')); 4.78 ($d\times d$, $J_{6ax,7}=11$, $J_{6eq,7}=3$, H–C(7)); 4.34 and 3.55 (*m*, 2 H–C(12)); 3.00 (*m*, 2 H–C(13)); 2.82 (*m*, H–C(5)); 2.67 (*m*, $J_{8,9}=10$, $J_{5,9}=5.5$, $J_{1,9}=1.7$, H–C(9)); 1.96–2.08 (*s*, 4 OAc); 2.10 ($d\times t$, H_{eq}–C(6) overlapping with a OAc signal); 1.54 (*m*, H_{ax}–C(6) overlapping with the H_2O signal).

[7]) Coupling constants are obtained by a 360-MHz-^{1}H-NMR. analysis of **2**.