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SECOIRIDOID GLUCOSIDES FROM *LONICERA PERICLYMENUM*

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Key Word Index—*Lonicera periclymenum*, Caprifoliaceae, secoiridoids, secologanin, morroniside, secoxyloganin, secologanoside, dimethyl-secologanoside, ^{13}C NMR spectroscopy, FDMS

Abstract—The stems of *Lonicera periclymenum* have been investigated for secoiridoid glycosides In addition to two well-known glucosides, secologanin and morroniside, two rare secoiridoids, secoxyloganin and secologanoside, have been isolated and characterized by chemical and spectroscopic means Secologanoside has been isolated for the first time as a genuine, non-derivatized compound

INTRODUCTION

In the course of the systematic investigation of iridoid glucosides of Caprifoliaceae plants, we have isolated a new biosidic ester and two known iridoids from *Lonicera periclymenum* [1] A further examination of the methanolic extract of this plant has yielded four secoiridoid glucosides secologanin (1), morroniside (2), secoxyloganin (3) and secologanoside (4) Secologanoside (4) has been reported previously only as its dimethylester tetraacetate from *Vinca rosea* [2], in which form it was characterized by ^1H NMR spectroscopy Secoxyloganin (3) has also been isolated from *L xylosteum* [R K Chaudhuri and O Sticher, unpublished work] It was later reported in *Mentzelia* species and has been characterized by its ^1H NMR spectrum [3] In this paper, we describe the isolation and structure determination of the two secoiridoids 3 and 4 by means of more detailed spectroscopic studies

RESULTS AND DISCUSSION

The methanolic extract of stems of *L periclymenum* was fractionated by polyamide column chromatography followed by silica gel column chromatography The subsequent purification of the chromatographic fractions afforded three iridoids [1] and four secoiridoids (1–4)

The data of 1 and 2 and their acetates showed good agreement with those reported for secologanin and morroniside respectively [4, 5] Secoxyloganin (3), $C_{17}H_{24}O_{11}$ (M^+ 404, FDMS), $[\alpha]_D^{20}$ −111 7° (MeOH) and secologanoside (4), $C_{16}H_{22}O_{11}$ (M^+ 390, FDMS), $[\alpha]_D^{20}$ −103 5° (H_2O), were isolated as amorphous substances

The UV and IR absorptions of 3 [233 nm (log ε4 04), 1700 and 1620 cm^{-1}] and 4 [230 nm (log ε3 92), 1690 and 1640 cm^{-1}] were typical of an iridoid enol ether system conjugated with a carbonyl group [6] Their ^1H NMR spectra (in D_2O) were similar and, apart from a three proton singlet at δ3 75 arising from the methyl group of the carbomethoxy group for 3 (see Experimental), showed the presence of nine protons in the aglycone moieties These facts strongly suggested that 4 had a structure similar to that of 3 In both 3 and 4, the protons at C-3 of the aglycone unit were observed at δ7 54 (*s, br*) and 7 28 (*d*, J = 1 6 Hz), respectively Three vinylic protons appearing at about δ5 70 (1H, *ddd*, H-8) and between δ5 27 and 5 36 (2H, each *dd* or *d*, H-10_a and H-10_b) indicated that 3 and 4 have secologanin type secoiridoid structures In the ^1H NMR spectrum of 3, the geminal coupling ($J_{10a,10b}$) was not observed The signals which appeared at δ5 55 (*d*, J = 4 4 Hz) and 4 85 (*d*, J = 7 69 Hz) for 3 and 5 46 (*d*, J = 4 5 Hz) and 4 80 (*d*, J = 7 98 Hz) for 4 were assigned to H-1 and to the anomeric

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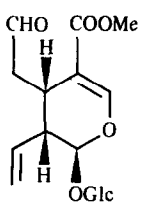

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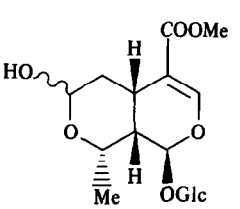

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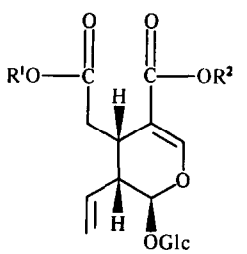

	R¹	R²
3	H	Me
4	H	H
5	Me	Me

Table 1 ^{13}C NMR spectral data of compounds 3–5 [75 47 MHz, CD_3OD (3, 5) or D_2O (4), TMS as int (3, 5) or ext (4) standard]

C	3	4	5
1	97 67	99 35	97 79
3	153 56	152 31	153 79
4	110 83	114 80	110 04
5	29 26	30 97	29 25
6	36 90	38 31	35 48
7	176 60	181 35	174 85
8	134 69	135 32	134 54
9	45 41	46 19	45 47
10	120 46	123 05	120 53
11	169 15	175 30	168 88
$COO\underline{C}H_3$	51 79		51 85
$COO\underline{C}H_3$			52 20
1′	99 92	100 00	100 08
2′	74 65	75 15	74 67
3′	77 89	78 12	78 18
4′	71 59	72 16	71 59
5′	78 41	78 84	78 42
6′	62 79	63 30	62 81

proton of β-D-glucopyranosyl moiety, respectively The signals arising from 2H-6 were observed as double-doublets in both spectra The ^{13}C NMR spectra of 3 and 4 were also in good agreement, except the signal arising from the methyl group of the carbomethoxy function at C-11 (δ51 79, *q*) (Table 1)

In order to find the exact positions of the acidic functions of 3 and 4, they were esterified with diazomethane Both yielded the same substance 5, the ^{1}H NMR and ^{13}C NMR spectra of which showed the presence of two carbomethoxyl functions (δ3 70, 3 65, each *s*, and 51 85, 52 20, each *q*) (see Experimental and Table 1)

These results showed that the only difference between 3 and 4 was the extent of esterification of the carboxyl groups which were situated at C-7 and C-11 Based on these data, 3 was identified as secoxyloganin and 4 as secologanoside

EXPERIMENTAL

General procedures were as earlier described [1] ^{1}H and ^{13}C NMR spectra [δ (ppm), *J* (Hz)] were obtained at 300 13 MHz (^{1}H NMR) and at 75 47 MHz (^{13}C NMR) using a Bruker WM 300 Spectrospin instrument in Fourier transform mode

Plant material Fresh plant material of *Lonicera periclymenum* L was collected from the Forch area, Zurich, Switzerland [1] A voucher specimen is deposited in the Herbarium of the Laboratory of Pharmacognosy and Phytochemistry, School of Pharmacy, ETH Zurich

Isolation procedures Extraction and fractionation were as reported [1] In this investigation seven fractions (A_1–A_7) were collected Fr A_1 was subjected to semiprep HPLC (MeOH–H_2O, 7 13) to yield secologanin (1), which was found to be identical with an authentic sample of secologanin (^{1}H NMR, ^{13}C NMR (acetate of 1) [4]) Fr A_2 afforded 2 on semiprep HPLC (MeOH–H_2O, 3 7) Data for 2 and for its acetate derivative showed good agreement with those of morroniside [5] Fr A_4 gave secoxyloganin (3) on semiprep HPLC (MeOH–H_2O, 3 7) Fr A_7 was rechromatographed over silica gel with $CHCl_3$–MeOH–H_2O–AcOH (60 40 10 0 5) to give pure secologanoside (4)

Secoxyloganin (3) $[\alpha]_D^{20}$ −111 7° (*c* 0 521, MeOH), UV λ_{max}^{MeOH} 233 nm (log ε = 4 04), IR ν_{max}^{KBr} cm^{-1} 3400, 1700 and 1620, ^{1}H NMR (D_2O) δ2 36 (1H, *dd*, $J_{6\alpha,6\beta}$ = 16 0 Hz, $J_{6\alpha\ 5}$ = 7 5 Hz, H_α-6), 2 63 (1H, *dd*, $J_{6\alpha,6\beta}$ = 16 0 Hz, $J_{6\beta,5}$ = 4 0 Hz, H_β-6), 2 79 (1H, *m*, H-9), 3 24 (1H, *m*, H-5), 3 32–3 56 (4H, *m*, H-5′, H-3′, H-4′, H-2′), 3 75 (3H, *s*, COOMe), 3 75 (1H, H_b-6′, merged with the COOMe signal), 3 95 (1H, *d*, $J_{6\ a,6\ b}$ = 12 4 Hz, H_a-6′), 4 85 (1H, *d*, $J_{1',2}$ = 7 7 Hz, H-1′), 5 31 (1H, *d*, $J_{10a,8}$ = 9 5 Hz, H_a-10), 5 36 (1H, *d*, $J_{10b,8}$ = 16 6 Hz, H_b-10) [geminal coupling ($J_{10a,10b}$) was not observed], 5 55 (1H, *d*, $J_{1\ 9}$ = 4 4 Hz, H-1), 5 71 (1H, *ddd*, $J_{8,10a}$ (*cis*) = 9 5 Hz, $J_{8,10b}$ (*trans*) = 16 6 Hz, $J_{8,9}$ = 9 5 Hz, H-8), 7 54 (1H, *s* (*br*), H-3), ^{13}C NMR (CD_3OD) see Table 1, FDMS *m/z* 404 $[M]^+$, 405 $[M+H]^+$, 427 $[M+Na]^+$

Secologanoside (4) $[\alpha]_D^{20}$ −103 5° (*c* 0 546, H_2O), UV λ_{max}^{MeOH} 230 nm (log ε 3 92), IR ν_{max}^{KBr} cm^{-1} 3400, 1690 and 1640, ^{1}H NMR (D_2O) δ2 27 (1H, *dd*, $J_{6\alpha\ 6\beta}$ = 16 0 Hz, $J_{6\alpha\ 5}$ = 9 5 Hz, H_α-6), 2 75 (1H, *dd*, $J_{6\beta,6\alpha}$ = 16 0 Hz, $J_{6\beta\ 5}$ = 4 9 Hz, H_β-6), 2 79 (1H, *ddd*, $J_{9,1}$ = 4 5 Hz, $J_{9,5}$ = 4 9 Hz, $J_{9,8}$ = 9 6 Hz, H-9), 3 17 (1H, *m*, H-5), 3 29–3 53 (4H, *m*, H-5′, H-3′, H-4′, H-2′), 3 72 (1H, *dd*, $J_{6\ b,6\ a}$ = 12 4 Hz, $J_{6\ b,5}$ = 5 70 Hz, H_b-6′), 3 91 (1H, *dd*, $J_{6\ a,6\ b}$ = 12 4 Hz, $J_{6\ a,5}$ = 1 97 Hz, H_a-6′), 4 80 (1H, *d*, $J_{1\ 2}$ = 7 98 Hz, H-1′), 5 27 [1H, *dd*, $J_{10a,10b}$ (gem) = 1 4 Hz, $J_{10a,8}$ = 10 0 Hz, H_a-10], 5 30 [1H, *dd*, $J_{10b,10a}$ (gem) = 1 4 Hz, $J_{10b,8}$ = 17 0 Hz, H_b-10], 5 46 [1H, *d*, $J_{1\ 9}$ = 4 5 Hz, H-1], 5 69 [1H, *ddd*, $J_{8,10a}$ (*cis*) = 10 0 Hz, $J_{8,10b}$ (*trans*) = 17 0 Hz, $J_{8,9}$ = 9 6 Hz, H-8], 7 28 (1H, *d*, $J_{3,5}$ = 1 6 Hz, H-3), ^{13}C NMR (D_2O) see Table 1, FDMS *m/z* 390 $[M]^+$ 413 $[M+Na]^+$

Dimethyl-secologanoside (5) Compounds 3 and 4 afforded after esterification with CH_2N_2 dimethyl-secologanoside (5) ^{1}H NMR (CD_3OD) δ2 37 (1H, *dd*, $J_{6\alpha,6\beta}$ = 16 2 Hz, $J_{6\alpha,5}$ = 8 4 Hz, H_α-6), 2 76 (1H, *ddd*, $J_{9\ 1}$ = 5 4 Hz, $J_{9\ 8}$ = 9 2 Hz, $J_{9\ 5}$ = 4 8 Hz, H-9), 2 85 (1H, *dd*, $J_{6\beta,6\alpha}$ = 16 2 Hz, $J_{6\beta\ 5}$ = 5 64 Hz, H_β-6), 3 22 (1H, *m*, H-5), 3 28–3 40 (4H, *m*, H-5′, H-3′, H-4′, H-2′), 3 67 (1H, *dd*, $J_{6\ b,6\ a}$ = 12 0 Hz, $J_{6\ b,5}$ = 5 0 Hz, H_b-6′), 3 89 (1H, *dd*, $J_{6\ a,6\ b}$ = 12 0 Hz, $J_{6\ a,5}$ = 1 8 Hz, H_a-6′), 3 65 and 3 70 (each 3H, *s*, 2 × COOMe), 4 66 (1H, *d*, $J_{1\ 2}$ = 7 8 Hz, H-1′), 5 22 [1H, *dd*, $J_{10a,10b}$ (gem) = 1 8 Hz, $J_{10a\ 8}$ = 10 2 Hz, H_a-10], 5 24 [1H, *dd*, $J_{10b,10a}$ (gem) = 1 8 Hz, $J_{10a,8}$ = 18 0 Hz, H_b-10], 5 48 (1H, *d*, $J_{1\ 9}$ = 5 4 Hz, H-1), 5 63 (1H, *ddd*, $J_{8,10a}$ = 10 2 Hz, $J_{8,10b}$ = 18 0 Hz, $J_{8\ 9}$ = 9 2 Hz, H-8), 7 47 (1H, *d*, $J_{3\ 5}$ = 1 7 Hz, H-3), ^{13}C NMR (CD_3OD) see Table 1

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