

NEVADENINE AND NEVADENSINE, TWO NEW DITERPENOID ALKALOIDS
FROM ACONITUM NEVADENSE VECSTR.

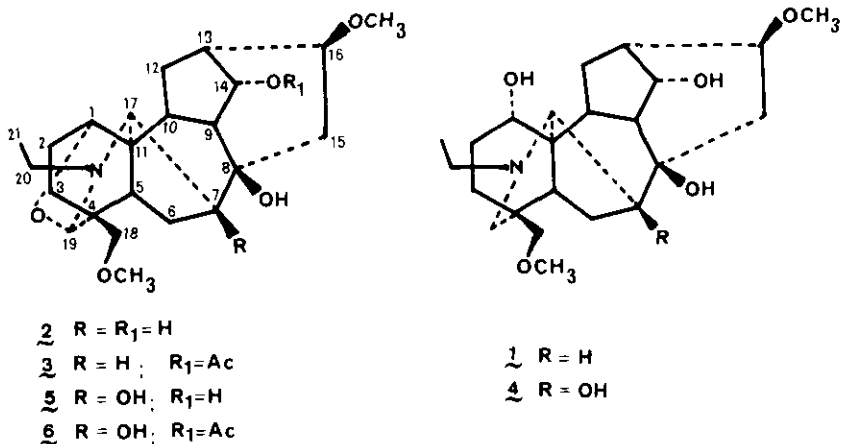
Antonio G. González,^{*a)} Gabriel de la Fuente,^{b)} Tomás Orribo,^{b)}
and Rafael Díaz Acosta^{a)}

a) Instituto Universitario de Química Orgánica, Universidad de
La Laguna, Tenerife, Canary Islands, Spain

b) Instituto de Productos Naturales Orgánicos, CSIC, La Laguna,
Tenerife, Canary Islands, Spain

Abstract - Neoline, chasmanine, isotalatizidine, and two new C-19
diterpenoid alkaloids, nevadenine and nevadensine, were isolated from
Aconitum nevadense. The structures of the new bases were established
by ¹H and ¹³C-nmr spectroscopy, and chemical derivation to known
alkaloids.

From the aerial parts of plants of Aconitum nevadense Vechtr., collected in
Sierra Nevada, Granada, Spain, we have isolated two new C-19 diterpenoid alkaloids,
nevadenine (2) and nevadensine (5) as minor constituents.



Nevadenine was isolated as a resin, and its elemental composition C₂₃H₃₅NO₅
established by high resolution mass measurement; M⁺ (6%), M⁺-CH₃ (5%), M⁺-OCH₃
(100%), M⁺-C₃H₄O (63%) and |M⁺-OCH₃| - C₃H₄O (60%). The loss of acrolein in the
ms¹ and the ir (KBr) adsorptions at 995 and 815 cm⁻¹ ² indicated the presence
of the carbinolamine inner ether in the molecule. The ¹H-nmr spectrum (200 MHz,
CDCl₃) displayed signals at δ1.04 (3H, t, J = 7 Hz, N-CH₂-CH₃), 2.70 (2H, q,

$J = 7$ Hz, $N-CH_2-CH_3$), 3.29 and 3.33 (3H each, s, two OCH_3), 3.67 (1H, m, $W_{\frac{1}{2}} = 7.5$ Hz, C-1 β H), 3.78 (1H, s, C-19H) and 4.17 (1H, t, $J = 5$ Hz, C-14 β H). Treated with Ac_2O-Py , nevadenine gave a monoacetate (3) as a resin, M^+ 447 (1%); ir (KBr) 1730 and 1230 cm^{-1} (acetate). Its 1H -nmr spectrum gave signals at δ 2.06 (3H, s, acetate) and 4.85 (1H, t, $J = 4.8$ Hz), indicating that the C-14 α OH group was acetylated.

Nevadensine (5) was also isolated as a resin and gave an analysis corresponding to $C_{23}H_{35}NO_6$ by high resolution ms; M^+ (3%), M^+-CH_3 (8%), M^+-OCH_3 (32%), $M^+-C_3H_4O$ (100%), $|M^+-OCH_3| - C_3H_4O$ (85%). As in the case of nevadenine the ms peaks caused by ejection of acrolein and the ir (KBr) adsorptions at 890 and 990 cm^{-1} suggested the presence of the C-1-O-C-19 inner ether in the new base. The 1H -nmr spectrum ($CDCl_3$) exhibited signals at δ 1.04 (3H, t, $J = 7.2$ Hz, $N-CH_2-CH_3$), 3.25 and 3.30 (3H each, s, two OCH_3), 3.60 (1H, m, $W_{\frac{1}{2}} = 8$ Hz, C-1 β H), 3.89 (1H, s, C-19H) and 4.14 (1H, t, $J = 4.8$ Hz, C-14 β H).

Upon acetylation with Ac_2O-Py nevadensine yielded a monoacetate (6) as a resin, M^+ 463 (2%), ir (KBr) 1730 and 1240 cm^{-1} (acetate). The acetate group was located at C-14 as inferred by the signals at δ 2.00 (3H, s) and 4.79 (1H, t, $J = 4.8$ Hz) in the 1H -nmr spectrum.

The oxidation of isotalatizidine (1)³ with $KMnO_4$ ⁴ led to nevadenine (2) in 80% yield and the $NaBH_4$ reduction of nevadensine (5) gave virescensine (4)⁵ in 90% yield (mp, ir, ms and 1H -nmr identical). Therefore the structures of the new alkaloids were firmly established.

Additional support for these structures was also derived from ^{13}C -nmr.

Assignments were made by comparison with the spectrum of isotalatizidine (1)⁶ and virescensine (4)⁵, taking into account the α - and β -effects produced upon acetylation. As in the case of pentagynine,⁷ 18-methoxygadesine,⁸ and graciline,⁹ the new doublet at \sim 69 ppm, and the β - or γ -effects observed on the C-3, C-4, C-5 and C-18 resonances in the spectra of nevadenine (2) and nevadensine (5), compared with those of the other alkaloids considered, corroborated the existence of the C-1-O-C-19 ether in the new compounds.

The published assignments for C-10 and C-13 in virescensine (4) have been reversed on the basis of the chemical shifts observed in nevadensine (5) and its acetate (6), and the reported values for delcosine.¹⁰

Neoline,¹¹ chasmanine,¹¹ and isotalatizidine³ were also found in this plant, and identified by their mp, ms, and 1H and ^{13}C -nmr spectra.

^{13}C Chemical shifts and assignments

Carbon	1	2	3	4	5	6
1	72.7	87.6	87.4	72.4	85.3	85.3
2	28.8	24.3	24.3	28.5	25.9	25.9
3	30.6	22.8	22.9	29.3	22.3	22.3
4	37.8	42.9	42.8	37.7	42.7	42.6
5	42.2	37.2	36.8	41.9	36.7	36.5
6	25.6	25.8	25.8	33.5	32.5	32.6
7	45.5	44.5	44.0	86.1	86.7	85.3
8	74.2	72.3	72.9	76.2	74.1	74.7
9	47.4	45.8	43.9	48.0	46.7	43.4
10	44.8	54.9	55.9	43.6	43.9	43.7
11	49.1	47.8	48.0	49.4	47.2	47.9
12	27.8	27.1	29.0	26.9	27.3	29.4
13	40.7	38.6	36.5	39.7	38.9	37.9
14	76.3	75.7	76.7	75.5	75.5	76.1
15	43.1	39.7	41.9	36.0	35.3	35.0
16	82.6	82.1	82.2	81.9	81.9	82.5
17	64.1	62.1	61.2	64.9	64.4	63.8
18	79.3	74.4	74.3	78.7	73.9	73.9
19	56.9	69.4	69.4	55.8	69.0	69.2
20	48.6	48.2	48.0	50.5	47.9	47.8
21	13.2	14.6	14.5	13.9	14.1	14.2
16'	55.9	56.6	56.2	56.4	56.6	56.3
18'	59.1	59.5	59.5	59.4	59.5	59.5
CO			170.7			171.2
CH ₃			21.4			21.5

Chemical shifts in ppm downfield from TMS.

Solvent deuteriochloroform.

ACKNOWLEDGEMENT

This work has been partially financed by a grant from the Comisión Asesora de Investigación Científica y Técnica of Spain. We thank Professor S.W. Pelletier for a sample of virescenine.

REFERENCES

1. S.W. Pelletier and S.W. Page, 'Chemistry of Diterpene Alkaloids' in "The Alkaloids", ed. by J.E. Saxon, The Chem. Soc., London, 1973, vol. 3, p. 235.
2. R. Auct, D. Clayton, and I. Marion, Can. J. Chem., 1957, 35, 397.
3. S.W. Pelletier, L.H. Keith, and P.C. Parasarathy, J. Am. Chem. Soc., 1967, 89, 4146.
4. O. Achmatowicz, T. Tsuda, and L. Marion, Can. J. Chem., 1965, 43, 2336.
5. S.W. Pelletier, N.V. Nady, A.P. Venkov, and S.B. Jones, Heterocycles, 1979, 12, 779.
6. V. Boido, O.E. Edwards, K.L. Handa, R.J. Kolt, and K.K. Purushothaman, Can. J. Chem., 1984, 62, 778.
7. A.G. González, G. de la Fuente, and R. Díaz, Phytochemistry, 1982, 21, 1781.
8. A.G. González, G. de la Fuente, and O. Munguía, Heterocycles, 1983, 20, 409.
9. A.G. González, G. de la Fuente, M. Reina, and I. Timón, Heterocycles, 1984, 22, 667.
10. B.S. Joshi, J.A. Glinski, H.P. Chokski, S. Chen, S.K. Srivastava, and S.W. Pelletier, Heterocycles, 1984, 22, 2037.
11. S.W. Pelletier, Z. Djarmati, S. Lajsic, and W.H.D. Camp, J. Am. Chem. Soc., 1976, 98, 2617.

Received, 5th July, 1985