

GRACININE, A NEW C-19 DITERPENOID ALKALOID FROM

DELPHINIUM GRACILE DC

Antonio G. González, Rafael Díaz Acosta, and

José A. Gavín

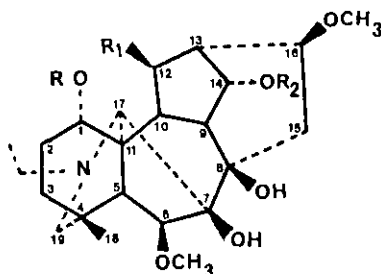
Instituto Universitario de Química Orgánica, Universidad de
La Laguna, Tenerife, Canary Islands, Spain

Gabriel de la Fuente*

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

Abstract - Gracinine, a new C-19 diterpenoid alkaloid bearing a C-12 functionality, was isolated from Delphinium gracile DC, together with the known bases gadesine, dihydrogadesine and nudicaulidine. The structure of the new compound was established by means of ^1H - and ^{13}C -nmr spectroscopy.

Continuing our work on Delphinium gracile DC¹, an endemism of the Iberian Peninsula, we have isolated, as a minor constituent, a new C-19 diterpenoid alkaloid gracinine (1). The plants were collected on a poor, sandy soil in Sardón del Duero² (Valladolid Province, Spain) during the flowering period.



1 $R = \text{H}$; $R_1 = \text{OH}$; $R_2 = \text{Bz}$

2 $R = \text{Ac}$; $R_1 = \text{OAc}$; $R_2 = \text{Bz}$

3 $R = \text{H}$; $R_1 = \text{H}$; $R_2 = \text{Bz}$

Gracinine (1), $[\alpha]_D^{25} + 37.6^\circ$ (c, 0.15, CHCl_3), was isolated as a resin and a molecular formula of $\text{C}_{30}\text{H}_{41}\text{NO}_8$ was obtained by high resolution mass spectroscopy (M^+ , m/z 543.2829 for $\text{C}_{30}\text{H}_{41}\text{NO}_8$, $\Delta - 0.1$ mmu); ir (CHCl_3), 3420 (OH), 1718, 1275, and 710 (benzoate), 1120 and 1085 (C-O).

The ms (70 eV) showed the characteristic fragmentation of a lycotoniine-type

alkaloid, giving ions at m/z , 543 (7%) M^+ , 528 (25%) M^+-CH_3 , 526 (23%) M^+-OH , 512 (25%) M^+-OCH_3 , 510 (14%) $|M^+-CH_3|-H_2O$, 508 (8%) $|M^+-OH|-H_2O$, 492 (5%) $|M^+-CH_3|-2H_2O$, 406 (7%) $|M^+-CH_3|-C_7H_6O_2$ and 404 (7%) $|M^+-OH|-C_6H_7O_2$.

The 1H -nmr spectrum (200 MHz, $CDCl_3$) shows typical signals of a lycoctonine alkaloid^{3,4} at δ 1.08 (3H, s, CH_3), 1.11 (3H, t, $J = 7.11$ Hz, $N-CH_2-\underline{CH_3}$), 3.35 (6H, s, two OCH_3), 3.79 (1H, s, disappearing when D_2O is added, OH), 3.93 (1H, s, H-6 α), 4.17 (1H, m, $W_2^1 = 6.5$ Hz, H-1 β), 5.47 (1H, t, $J = 4.8$ Hz, H-14 β), 7.45 and 8.10 (3H and 2H, respectively, m, benzoate).

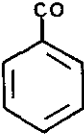
The 1H -nmr spectrum also gave signals at δ 1.98 (1H, d, $J = 1.8$ Hz) and 2.70 (1H, d, $J = 2.0$ Hz) for H-5 and H-17, respectively, in W arrangement, 1.90 (1H, dd, $J_1 = 2.7$ Hz, $J_2 = 7.8$ Hz, H-10), 2.54 (1H, d, $J = 4.7$ Hz, H-13), 3.40 (m, partially obliterated by other signals above, H-9), and 4.30 (1H, d, $J = 2.4$ Hz, H-12 α). These assignments were made taking into account the calculated coupling constants according to the dihedral angles measured on a Dreiding molecular model of gracinine, and the connectivities between H-5-H-17, H-14 β -H-9, H-14 β -H-13, H-9-H-10, and H-10-H-12 α , determined by double resonance experiments. The downfield shifts of 0.41 ppm and 0.37 ppm observed for H-1 β H and H-14 β H in the 1H -nmr spectrum of gracinine as compared with those of 14-benzoyldihydrogadesine (3)⁵ were consistent with the presence of a secondary hydroxyl group at C-12 β in the molecule.

Treatment of gracinine (1) with Ac_2O -Py afforded a diacetate (2), ms (15 eV) m/z , 612 (5%) M^+-CH_3 , 609 (15%) M^+-H_2O , and 568 (100%) M^+-OAc . Its 1H -nmr spectrum showed signals at δ 2.01 (6H, s, two $OCOCH_3$), 4.77 (1H, q, $J_1 = 9.1$ Hz, $J_2 = 8.3$ Hz, H-1 β), 5.12 (1H, d, $J = 3.5$ Hz, H-12 α), and 5.23 (1H, t, $J = 4.7$ Hz, H-14 β). As expected, a less deshielding effect on H-1 β and H-14 β is observed, caused by the acetyloxy group at C-12 β .

The structure of gracinine (1) was definitively established by ^{13}C -nmr spectroscopy. Its spectrum was very similar to that of 14-benzoyldihydrogadesine (3),⁵ and the appearance of a new doublet at δ 76.0 with the concomitant disappearance of the triplet at δ 29.7 in the spectrum of (3), and the β -effects of 12.6 ppm and 11.2 ppm observed on C-10 and C-13, respectively, confirmed the existence at C-12 of a hydroxyl group in gracinine (1). The slight γ -gauche effect of 0.8 ppm produced on C-14 by the C-12 β OH (in gracinine) is attributable to the lesser puckering of the cyclopentane ring, which is not as pronounced as in the cyclohexane ring.⁶

We have also isolated gadesine,⁷ dihydrogadesine,⁸ and 13-acetylhetisinone,⁹ identified by comparison with authentic samples, and nudicaulidine,¹⁰ identified by its ms, ¹H- and ¹³C-nmr spectra.

TABLE 1. ¹³C-nmr chemical shifts and assignments for gracinine (1) and 14-benzoyldihydrogadesine (3)

Carbon	1	3	Carbon	1	3
1	71.6	72.7	14	75.3	76.1
2	29.5	28.9	15	35.2	34.3
3	32.6	31.6	16	79.1	82.4
4	33.4	33.0	17	66.7	65.9
5	50.8	50.0	18	27.7	27.7
6	91.3	91.0	19	60.8	60.9
7	88.0	87.6	20	50.4	51.2
8	77.7	78.4	21	13.8	14.4
9	43.7	43.5	6'	58.2	58.0
10	55.6	43.0	16'	56.4	56.4
11	48.8	49.5		166.7	166.5
12	76.0	29.7		131.0	129.2
				130.1	129.8
				128.5	129.4
13	49.1	37.9		132.8	132.7

Chemical shifts in ppm downfield from TMS. Solvent deuterochloroform.

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