GRACININE, A NEW C-19 DITERPENOID ALKALOID FROM *DELPHINIUM GRACILE* DC

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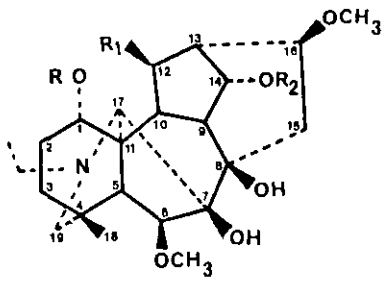
Abstract - Gracinine, a new C-19 diterpenoid alkaloid bearing a C-12 functionality, was isolated from *Delphinium gracile* DC, together with the known bases gadesine, dihydrogadesine and nudicaulidine. The structure of the new compound was established by means of ^{1}H- and ^{13}C-nmr spectroscopy.

Continuing our work on *Delphinium gracile* DC[1], 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 Duero[2] (Valladolid Province, Spain) during the flowering period.



1 R = H; R_1 = OH; R_2 = Bz
2 R = Ac; R_1 = OAc; R_2 = Bz
3 R = H; R_1 = H; R_2 = Bz

Gracinine (1), $[\alpha]_D$ + 37.6° (c, 0.15, $CHCl_3$), was isolated as a resin and a molecular formula of $C_{30}H_{41}NO_8$ was obtained by high resolution mass spectroscopy (M^+, m/z 543.2829 for $C_{30}H_{41}NO_8$, Δ - 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 lycoctonine-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 ^{1}H-nmr spectrum (200 MHz, $CDCl_3$) shows typical signals of a lycoctonine alkaloid[3,4] at δ1.08 (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-6α), 4.17 (1H, m, $W_{\frac{1}{2}}$ = 6.5 Hz, H-1β), 5.47 (1H, t, J = 4.8 Hz, H-14β), 7.45 and 8.10 (3H and 2H, respectively, m, benzoate).

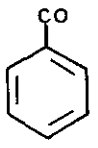
The ^{1}H-nmr spectrum also gave signals at δ1.98 (1H, d, J = 1.8 Hz) and 2.70 (1H, d, J = 2.0 Hz) for H-5 and H-17, respectively, in W arrangement, 1.90 (1H, dd, J_1 = 2.7 Hz, J_2 = 7.8 Hz, H-10), 2.54 (1H, d, J = 4.7 Hz, H-13), 3.40 (m, partially obliterated by other signals above, H-9), and 4.30 (1H, d, J = 2.4 Hz, H-12α). 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-14β-H-9, H-14β-H-13, H-9-H-10, and H-10-H-12α, determined by double resonance experiments. The downfield shifts of 0.41 ppm and 0.37 ppm observed for H-1βH and H-14βH in the ^{1}H-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-12β 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 ^{1}H-nmr spectrum showed signals at δ2.01 (6H, s, two $OCOCH_3$), 4.77 (1H, q, J_1 = 9.1 Hz, J_2 = 8.3 Hz, H-1β), 5.12 (1H, d, J = 3.5 Hz, H-12α), and 5.23 (1H, t, J = 4.7 Hz, H-14β). As expected, a less deshielding effect on H-1β and H-14β is observed, caused by the acetyloxy group at C-12β.

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 δ76.0 with the concomitant disappearance of the triplet at δ29.7 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-12βOH (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, ^{1}H- and ^{13}C-nmr spectra.

TABLE 1. ^{13}C-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
				131.0	129.2
12	76.0	29.7		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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