THE STRUCTURE OF GRACILINE, A NEW DITERPENOID ALKALOID FROM DELPHINIUM GRACILE

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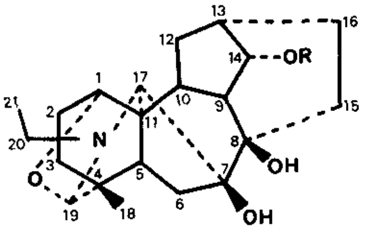
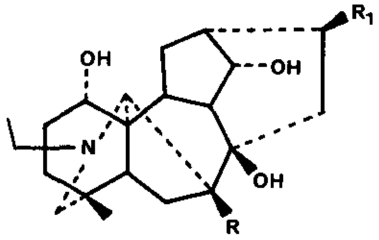
Abstract - Besides hetisinone, 13-acetylhetisinone, cardiopetamine, and atisinium chloride, a new diterpenoid alkaloid graciline was isolated from Delphinium gracile, and its structure elucidated. The ^{13}C-NMR chemical shifts for graciline, cardiopetaline and cardiopetalidine are presented.

We report here the structure elucidation of graciline (1), a new lycoctonine-type diterpenoid alkaloid, isolated from Delphinium gracile DC., collected in Cadiz, Spain.



1 R=H
2 R=Ac



3 R=H R$_1$=OCH$_3$
4 R=R$_1$=
5 R=OH R$_1$=H

Graciline had mp 98-100°C. Its high resolution MS was characteristic of alkaloids with lycoctonine skeleton[1]: M^+ 361.2258 amu (3%), $C_{21}H_{31}NO_4$ (calc. 361.2253), M^+-CH_3 (14%), $M^+-C_3H_4O$ (100%), and $|M^+-C_3H_4O|-CH_3$ (13%). The ^{1}H-NMR ($CDCl_3$) gave signals at δ 0.89 (3H, *s*, CH_3), 1.11 (3H, *t*, *J* = 7Hz, N-CH_2-$\underline{CH_3}$), and 4.07 (1H, *t*, *J* = 4.5Hz, C-14βH). The loss of a molecule of acrolein in the MS[1], the IR absorptions at 978 and 875 cm^{-1}[2], and the ^{1}H-NMR signals at δ 3.73 (1H, *m*, $W_{\frac{1}{2}}$ = 7Hz, C-1βH) and 3.85

(1H, *s*, C-19H), pointed out the presence of the C-1-C-19 inner ether in the new base. Treatment of graciline (1) with acetic anhydride in pyridine afforded a monoacetate (2) as a resin, M^+ 403. IR ($CHCl_3$), 1725 and 1255 cm^{-1} (acetate). Its ^1H-NMR spectrum exhibited a one-proton triplet centered at δ 4.76 (J = 4.5Hz), indicating that the C-14αOH group was acetylated.

TABLE 1

Carbon	1	3	4	5	Carbon	1	3	4	5
1	89.3	72.4	72.3	72.7	12	30.6	29.3	32.8	32.0
2	28.9	29.6	29.7	29.6	13	35.5	44.1	34.9	34.8
3	22.8	31.3	31.3	31.9	14	74.6	75.6	76.3	75.8
4	38.1	32.9	32.9	33.5	15	27.5	42.5	32.6	26.7
5	36.4	45.1	46.3	47.5	16	23.0	82.4	25.1	24.9
6	33.1	25.2	25.6	34.0	17	64.5	63.0	63.0	64.0
7	87.1	46.7	46.7	87.2	18	19.8	27.6	27.6	27.4
8	76.2	74.3	77.2	78.4	19	68.7	60.3	60.4	59.4
9	46.8	46.7	46.9	48.0	20	48.0	48.3	48.3	50.5
10	45.3	40.4	44.1	43.8	21	14.3	13.0	13.0	13.5
11	48.0	48.9	49.0	50.2	16'		56.2		

^{13}C Chemical shifts in ppm downfield from TMS and assignments using deuteriochloroform as solvent.

The ^{13}C-NMR spectrum of graciline (1) showed twenty signals for twenty-one carbon atoms in the molecule, and the assignments were made by comparison with the spectra of karakoline (3)[3], cardiopetaline (4), cardiopetalidine (5)[4], and other published ^{13}C-NMR data for related diterpenoid alkaloids. The chemical shift pattern in graciline (1) was very close to that of cardiopetalidine (5). As in the case of 18-methoxygadesine[5], the appearance of a new doublet at 68.7 ppm, the disappearance of a triplet at ∿ 60 ppm, the downfield shift of C-1, and the β or γ effects observed on the resonances of C-3, C-4, C-5 and C-18 in the spectrum of graciline (1) with respect to that of the other alkaloids considered, afforded evidence for the presence of a C-1-C-19 inner ether in (1).

On the other hand, it is interesting to note the α and β substituent effect of ∿ 58 ppm and ∿ 9 ppm, respectively, produced upon replacement of C-16βH by OCH_3, and the upfield shift of C-15 by ∿ 5.5 ppm in graciline (1) and cardiopetalidine (5) with respect to cardiopetaline (4) due to the γ effect of C-7OH.

The oxidation of cardiopetalidine (5) with $KMnO_4$[6] led to graciline (1) in 83% yield (mp, IR, ^{1}H-NMR and MS identical), and therefore its structure was definitively established.

We have also isolated hetisinone[7], 13-acetylhetisinone[8], cardiopetamine[9], and atisinium chloride[10] from this plant, all of which were identified by comparison with authentic samples.

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