STRUCTURES OF GADENINE AND PENTAGYLINE, TWO NEW DITERPENOID ALKALOIDS

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Abstract - The structures of pentagyline and gadenine, two new diterpenoid alkaloids isolated from Delphinium pentagynum, were determined with the aid of ^1H and ^{13}C-NMR spectroscopy. A biogenetic scheme is proposed by which karakoline could afford the C-19 diterpenoid alkaloids found in this plant.

From plants of Delphinium pentagynum Lam we have isolated pentagyline (4) and gadenine (9), two new diterpenoid alkaloids.

Pentagyline had mp 198-200°C and gave an analysis corresponding to $C_{30}H_{41}NO_7$ by high resolution MS; M^+ (30%), M^+-CH_3 (100%), M^+-OH (85%) and $|M^+-CH_3|-H_2O$ (70%); IR (KBr), 3400 (OH), 1710, 1275 and 710 cm^{-1} (benzoate). The ^1H-NMR ($CDCl_3$) displayed signals at δ 1.00 (3H, *s*, CH_3), 1.03 (3H, *t*, *J*= 7Hz, N-CH_2-$C\underline{H}_3$), 3.31 and 3.38 (3H each, *s*, two OCH_3), 3.99 (1H, *d*, *J*= 8Hz, C-6βH), 4.22 (1H, *m*, $W\frac{1}{2}$ = 7Hz, C-1βH), 5.55 (1H, *t*, *J*= 4.5Hz, C-14βH), 7.50 and 8.15 (3H and 2H, *m*, benzoate).

Upon acetylation with Ac_2O-Py pentagyline yielded a monoacetate, mp 233-236°C, the ^1H-NMR spectrum of which gave a one-proton quartet centred at δ5.51 (J_1= 10Hz, J_2= 8Hz) for the C-1βH[1]. On the other hand, the ^1H-NMR signals for the C-14βH and C-1βH in our base were shifted downfield by 0.45 and 0.44 ppm, respectively, comparing the former with 14-benzoylpentagynine and the latter with dihydropentagynine (2), suggesting the presence of a tertiary hydroxyl geoup at C-10.

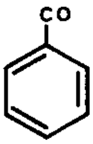
Gadenine (9) had mp 147-150°C and its molecular formula $C_{30}H_{41}NO_8$ was established by high resolution MS; M^+ (29%), M^+-CH_3 (100%), M^+-OH (87%), $|M^+-CH_3|-H_2O$ (37%); IR (KBr), 3450 (OH), 1710, 1280 and 715 cm^{-1} (benzoate). Its ^1H-NMR ($CDCl_3$) exhibited signals at δ 1.11 (3H, *s*, CH_3), 1.11 (3H, *t*, *J*= 7Hz, N-CH_2-$C\underline{H}_3$), 3.32 and 3.36 (3H each, *s*, two OCH_3), 4.02 (1H, *s*, C-6αH), 4.15 (1H, *m*, $W\frac{1}{2}$ = 7Hz, C-1βH), 5.55 (1H, *t*, *J*= 4.5Hz, C-14βH), 7.50 and 8.15 (3H and 2H, *m*, benzoate).

By acetylation gadenine yielded a monoacetate, mp 188-190°C; ^{1}H-NMR ($CDCl_3$), δ 2.05 (3H, *s*, $OCOCH_3$) and 5.45 (1H, *q*, J_1= 10Hz, J_2= 8Hz, C-1βH).

As in the case of pentagyline (4), the ^{1}H-NMR signals for the C-14βH and C-1βH in gadenine (9) appeared downfield by 0.35 and 0.50 ppm, respectively, the products for comparison being 14-benzoylgadesine and dihydrogadesine (6), again indicating the existence of a tertiary hydroxyl group at C-10.

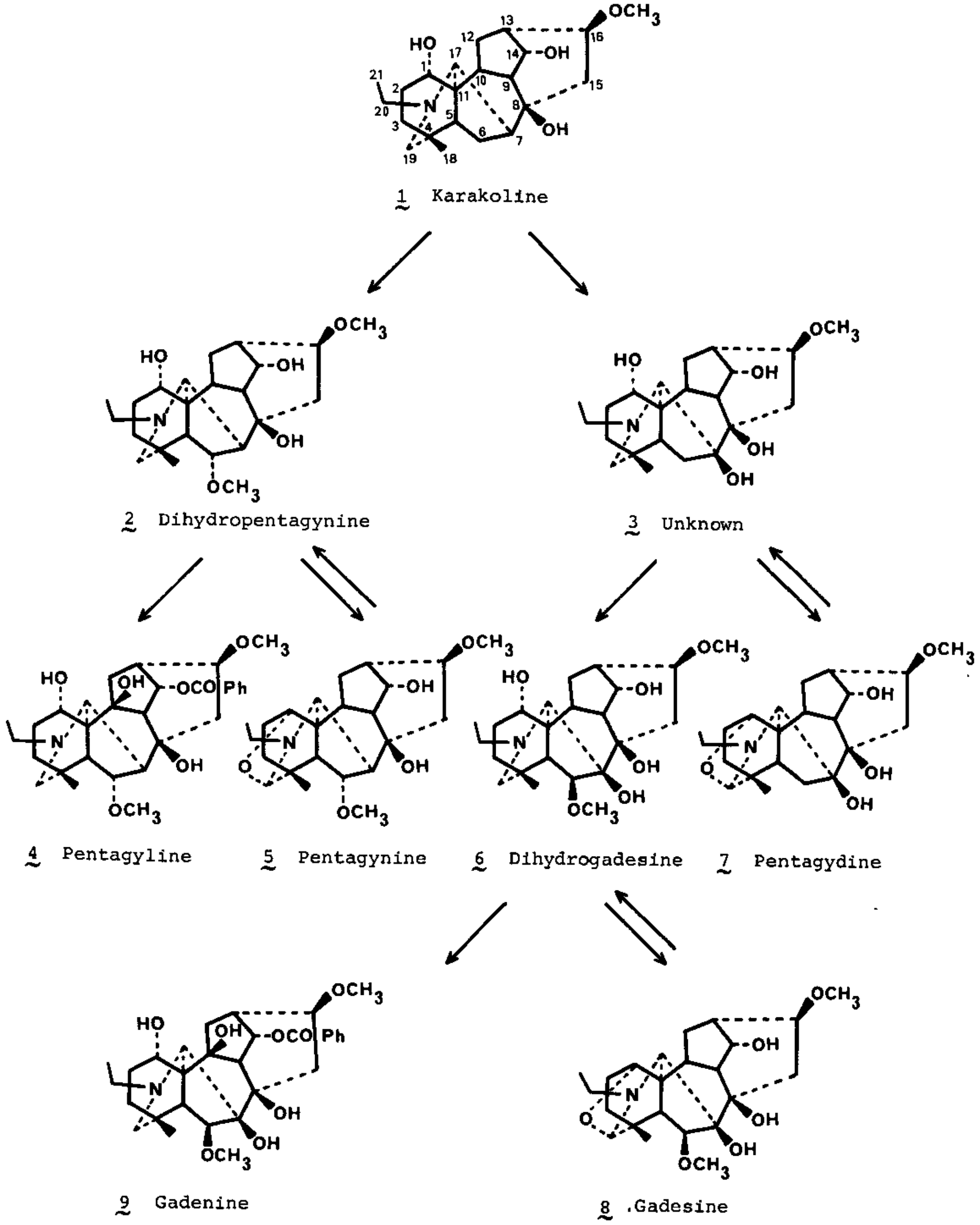
The structures of pentagyline (4) and gadenine (9) were definitively established by their ^{13}C-NMR spectra. Assignments were made by comparison with the spectra of neoline (10)[2] and 14-acetyldelcaroline (11)[3] and other published ^{13}C-NMR data for related diterpenoid alkaloids. The singlets at 82.4 and 81.7 ppm in the spectra of pentagyline and gadenine, respectively, confirmed the presence of a teritary hydroxyl group at C-10 in both bases.

TABLE 1

Carbon	10	11	4	9	Carbon	10	11	4	9
1	72.3	78.1	69.8	70.0	16	82.3	82.0	81.8	81.5
2	29.5	26.2	29.7	30.0	17	63.6	65.3	65.2	66.3
3	29.9	32.2	31.4	31.5	18	80.3	77.4	27.9	27.7
4	38.2	38.0	32.2	32.7	19	57.2	52.8	61.5	61.0
5	44.9	45.3	46.5	46.0	20	48.2	51.3	48.7	50.4
6	83.3	91.1	82.7	91.5	21	13.0	14.2	12.7	13.4
7	52.3	87.6	50.7	87.0	1'		55.5		
8	74.3	75.6	73.9	76.8	6'	57.8	57.6	57.8	58.2
9	48.3	54.5	54.4	53.0	16'	56.3	56.3	56.1	56.2
10	40.7	81.8	82.4	81.7	18'	59.1	59.1		
11	49.6	52.8	53.8	54.3				166.6 130.6 129.9 128.3 132.6	166.6 130.5 130.0 128.4 132.8
12	29.8	38.3	40.5	40.5					
13	44.3	38.8	38.4	38.2					
14	75.9	74.8	75.6	75.5					
15	42.7	34.6	41.6	35.24					

^{13}C Chemical shifts in ppm downfield from TMS and assignments.

Solvent deuterochloroform.


1 Karakoline
2 Dihydropentagynine
3 Unknown
4 Pentagyline
5 Pentagynine
6 Dihydrogadesine
7 Pentagydine
9 Gadenine
8 .Gadesine
HO
OH
OCH3
-OH
-OCO Ph
N
O
1
2
3
4
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8
9
10
11
12
13
14
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16
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21

SCHEME 1

Together with pentagyline (4) and gadenine (9), we have also isolated karakoline (1), dihydropentagynine (2), pentagynine (5), dihydrogadesine (6), pentagydine (7) and gadesine (8)[4] from this plant. We suggest that karakoline could biogenetically afford all the other alkaloids by the oxidation sequence outlined in Scheme 1. As inferred from the oxygenation pattern found till now in the C-19 diterpenoid alkaloids[5], hydroxylation at C-1α, C-8, C-14α and C-16β seems to take place at an early stage in their biogenesis. In our hypothesis karakoline (1) leads to the lycoctonine-type alkaloids by hydroxylation, first at C-7 and then at C-6β, and to the aconitine-type bases, hydroxylation beginning at C-6α. However, heteratisine, heterophylline [5] and the alkaloids A and B[6], pointed to the possibility of a C-6β hydroxylation without a previous one at C-7, in certain cases.

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REFERENCES

1. S.W. Pelletier, Z. Djarmati, S. Lajsić, and W.H. De Camp, *J. Am. Chem. Soc.*, 1976, **98**, 2617.
2. S.W. Pelletier and Z. Djarmati, *J. Am. Chem. Soc.*, 1976, **98**, 2626.
3. S.W. Pelletier, N.V. Mody, and R.C. Desai, *Heterocycles*, 1981, **16**, 747.
4. A.G. González, G. de la Fuente, R. Díaz, P.G. Jones, and G.M. Sheldrick, *Tetrahedron Letters*, 1983, **22**, 959 and references cited therein.
5. S.W. Pelletier and N.V. Mody in "The Alkaloids", ed.: R.H.F. Manske and R. Rodrigo, Academic Press Inc., New York, 1979, vol. 17, p.1.
6. P.W. Codding, K.A. Kerr, M.H. Benn, A.J. Jones, S.W. Pelletier, and N.V. Mody, *Tetrahedron Letters*, 1980, **21**, 127.

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