Tetrahedron Letters No. 1, pp 79 - 80.
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0040-4039/79/0101-0079$02.00/0

GADESINE, A NEW C-19 DITERPENE ALKALOID FROM DELPHINIUM PENTAGYNUM LAM

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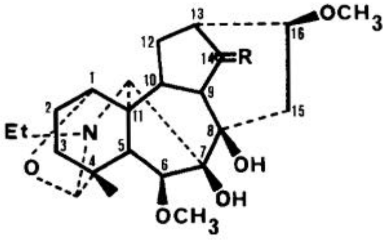
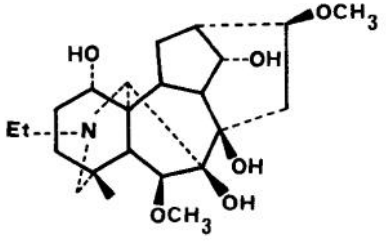
We should like to report the structure determination of gadesine (I), a C-19 diterpene alkaloid isolated from the plant Delphinium pentagynum Lam, collected in Cadiz (Southern Spain).



I, R=αOH, βH
II, R=αOAc, βH
III, R=O



IV

Gadesine, $C_{23}H_{35}NO_6$: mp 174-177°, $\{\alpha\}_D$+76° (c 0·27, EtOH); IR (KBr), cm^{-1} 3520, 3400 (OH), 1125, 1090 (ether linkage), 1000 and 900 (carbinolamine inner ether[1]); PMR ($CDCl_3$), δ 1·00 (3H, s, C-CH_3), 1·09 (3H, t, J=7Hz, N-CH_2-$C\underline{H}_3$), 3·35, 3·37 (3H each, s, OCH_3), 3·69 (1H, m, $W_{\frac{1}{2}}$=7Hz, C-1βH), 3·78 (1H, s, C-19H), 3·82 (1H, d, J=1Hz, C-6αH), 3·97 (1H, dd, $J_1=J_2$=4·5Hz, C-14βH) and 2·99, 3·91 and 3·92 which disappear when D_2O is added (1H each, s, OH). The MS is characteristic of alkaloids with lycoctonine skeletons: M^+ 421 (4%), M^+-CH_3 (82%, loss of a methyl group from N-ethyl), $\{M^+-CH_3\}-H_2O$ (base peak), M^+-CH_3OH (24%) and M^+-56 (12%, ejection of acrolein from ring A owing to the carbinolamine inner ether)[2].

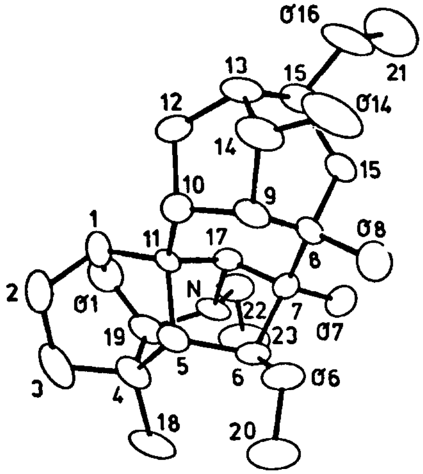
Treated with Ac_2O/Py, gadesine gave monoacetate II as a resin: M^+ 463; IR (KBr), cm^{-1} 3450 (OH), 1730 and 1250 (acetate); PMR ($CDCl_3$), δ 2·08 (3H, s, $OCOCH_3$) and 4·84 (1H, dd, J=4 5Hz, C-14βH). Oxidation of I with Cornforth's reagent yielded 14-ketogadesine (III): mp 157-160°, $\{\alpha\}_D$+51° (c 0·2, EtOH); M^+ 419; IR (KBr), cm^{-1} 3450 (OH) and 1745 (pentacyclic ketone). $LiAlH_4$ reduction of I gave the amino-alcohol IV: mp 80-82°, $\{\alpha\}_D$+32° (c 0·1, EtOH); IR (KBr), cm^{-1} 3400 and 3120 (OH) did not show the absorption proper to the carbinolamine inner ether; PMR ($CDCl_3$), δ 3·73 (1H, m, $W_{\frac{1}{2}}$=6Hz, C-1βH, boat conformation in ring A)[3]; MS, M^+ 423 (21%), M^+-OH (61%, loss of C-1αOH). This spectrum was very like those of delsoline, delcosine and acetyldelcosine[4] underlining the structural similarity of these bases. IV was converted in 75% yield to gadesine (mmp, IR, PMR, MS) by $KMnO_4$ oxidation[5], thus confirming the presence of C-1αOH in IV and of the C-1-C-9 ether in gadesine.

The above chemical and spectroscopic data and biogenetic considerations led to structure I being tentatively assigned to gadesine. In order to confirm this structure an X ray analysis was performed. Crystal data: monoclinic space group $P2_1$ with two molecules of I per unit cell, dimensions a=12·320(3), b=8·652(1), c=10·148(2)Å and β=104·72(1)°. 2702 reflections within the range $2<\Theta<28°$ were recorded on a 4-circle diffractometer with monochromated MoKα radiation (λ=0·7107Å). There was 39% intensity decay in 50h experiment so two crystals were used. 1963 reflections were considered observed $\{I>2\sigma(I)\}$. The crystal structure was solved by direct methods and refined anisotropically (isotropically for H atoms), with unit weight, by least-squares analysis to R=7·8% and R_W=7·5%[6].

Ring A is stabilized in the skew form through the ether bridge C1-O1-C19, contributing to a very rigid unit, C1-C2-C3-C4-C19-N-C17-C11, bridged twice through O1 and C5. Two intramolecular H bonds are formed between O8-H8...O6 (2·68Å) and O14-H14...O16 (3·11Å).

Gadesine is an interesting alkaloid from the biogenetic point of view, being, like delcosine, 14-dehydrodelcosine, mono-acetyldelcosine[7] and delcorine[8] a lycoctonine-type alkaloid with C-1α and C-6β substituents.

FINAL X-RAY MODEL FOR GADESINE



ACKNOWLEDGEMENT We are grateful to Prof S García-Blanco for the use of his Dept's automatic diffractometer and to Dr J Rivera for taking the high resolution MS.

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(Received in UK 31 October 1978)