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TWO NEW DITERPENE ALKALOIDS FROM *DELPHINIUM CARDIOPETALUM* DC[1]

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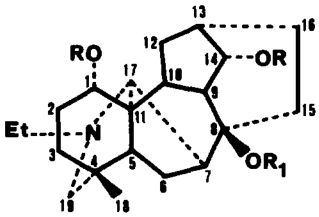
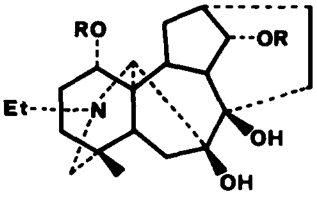
SUMMARY Chemical, spectral and X ray data are given for cardiopetaline and cardiopetalidine, two new C-19 diterpene alkaloids from the genus Delphinium.

The structure determination of cardiopetaline (1) and cardiopetalidine (4), two new minor C-19 diterpene alkaloids found in *Delphinium cardiopetalum* DC (syn. *Delphinium verdunense* Balbis)[2], collected in León, Spain, is here reported.





1 R=R1=H
2 R=Ac, R1=H
3 R=R1=Ac

4 R=H
5 R=Ac

Cardiopetaline, $C_{21}H_{33}NO_3$: mp 179-181°, $\{\alpha\}_D$-16° (c 0.22, EtOH); IR (KBr) cm^{-1} 3520, 3300 (OH), 1100, 1115 (C-O); PMR ($CDCl_3$) δ 0·88 (3H, s, C-CH_3), 1·12 (3H, t, J=7Hz, N-$CH_2\underline{C}H_3$), 3·07 (1H, s, C-17H), 3·75 (1H, m, $W_{\frac{1}{2}}$=6Hz, C-1βH, boat conformation in Ring A)[3], 4·12 (1H, dd, $J_1=J_2=4{\cdot}5$Hz, C-14βH). The MS is characteristic of alkaloids with lycoctonine skeletons: M^+ 347 (18%), M^+-CH_3 (27%), M^+-OH (base peak, loss of C-1αOH)[4], M^+-H_2O (14%) $\{M^+$-$CH_3\}$-H_2O (27%).

Treated with Ac_2O/Py, cardiopetaline gave diacetate 2 as a resin: M^+ 431 (10%), M^+-OAc (base peak, loss of C-1αOAc); IR ($CHCl_3$) cm^{-1} 3560 (OH), 1725, 1250 (acetate); PMR ($CDCl_3$) δ 2·03, 2·10 (3H each, s, acetate), 4·80 (1H, dd, J_1=J_2=5Hz, C-14βH), 4·90 (1H, q, J_1=10Hz, J_2=6Hz, C-1βH, chair conformation in ring A)[3], 2·30 (1H, s, OH, disappearing when D_2O is added).

Upon heating 2 with Ac_2O and a catalytic amount of p-toluenesulfonic acid in a steam bath, triacetate 3 was formed as a resin: M^+ 473 (2%), M^+-OAc (84%), {M^+-OAc}-HOAC (base peak, loss of C-1αOAc and acetic acid from C-8)[5]; IR ($CHCl_3$) cm^{-1} 1730, 1270 (acetate); PMR ($CDCl_3$) δ 1·94, 2·05 (3H and 6H each, s, acetate).

Cardiopetalidine (4), $C_{21}H_{33}NO_4$: mp 223-227°, $\{\alpha\}_D$+1·1° (c 0·18, EtOH); IR (KBr) cm^{-1} 3540, 3390, 3250 (OH), 1100, 1050 (C-O); PMR ($CDCl_3$) δ 0·92 (3H, s, C-CH_3), 1·10 (3H, t, J=7Hz, N-CH_2-$C\underline{H}_3$), 3·08 (1H, s, C-17H), 3·68 (1H, m, $W_{\frac{1}{2}}$=6Hz, C-1βH), 4·18 (1H, dd, J_1=J_2=4·5Hz, C-14βH); MS showed peaks at M^+ 363 (27%), M^+-CH_3 (74%), M^+-OH (base peak), M^+-H_2O (8%), {M^+-CH_3}-H_2O (15%).

When cardiopetalidine (4) was treated with Ac_2O/Py, diacetate 5 was afforded as a resin: M^+ 447 (3%), M^+-OAc (base peak); IR (KBr) cm^{-1} 3500 (OH), 1735, 1250 (acetate); PMR ($CDCl_3$) δ 2·03, 2·10 (3H each, s, acetate), 4·75 (1H, q, J_1=10Hz, J_2=6Hz, C-1βH), 4·80 (1H, dd, J_1=J_2=4·5Hz, C-14βH).

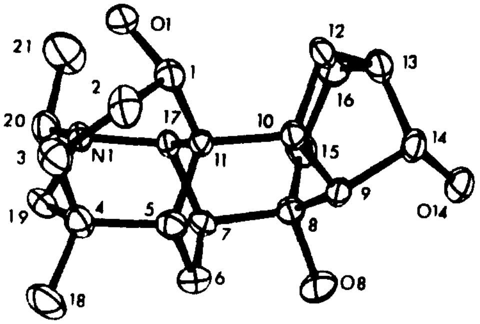
Biogenetic considerations and the above chemical and spectroscopic data led to the tentative assignment of structures 1 and 4 to cardiopetaline and cardiopetalidine, respectively. In order to confirm these structures an x-ray analysis was carried out.

Compound 1 crystallized in the orthorhombic system, space group $P2_12_12_1$, four molecules in a cell: a=12·755(3), b=15·494(5), c=9·215(2) Å. All intensity data were collected by the θ:2θ scanning technique using a variable scan speed and a graphite monochromator. Room-temperature lattice parameters were refined by a least-squares procedure utilizing 15 reflections the angles of which were measured by a Syntex $P2_1$ diffractometer centring routine. Periodically monitored reflections showed no significant change in intensity. Of the 1870 independent reflections taken, 1675 were accepted as observed {2σ(I)} after correction for Lorentz and polarization effects. No absorption effects were taken into account.

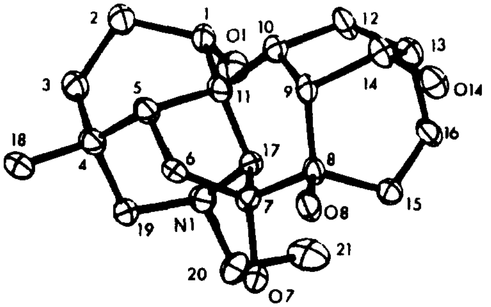
Compound 4 crystallized in the orthorhombic system, space group $P2_12_12_1$, with four molecules in a cell: a=14·21(2), b=14·98(2), c=8·35(2) Å. A total of 1803 independent reflections were measured and 1345 had intensities greater than $2\sigma(I)$ after correction for polarization and Lorentz. No significant intensity decay was observed.

The direct-methods MULTAN[6] was used to calculate phases from which both structures were deduced. The thermal and atomic positional parameters were refined by a least-squares procedure. The refinement was monitored by examining the R factor which is defined as $R= \Sigma|Fo|-|Fc|/\Sigma|Fo|$. The function minimized in the refinement was $\Sigma w(|Fo|-|Fc|)^2$ where $w=\{1/\sigma(Fo)\}^2$ was determined from counting statistics. Final agreement factors were R=0·097 for 1 and R=0·131 for 4, with only C, N and O atoms[7]

To our knowledge these compounds are the *first diterpene alkaloids with a lycoctonine skeleton which do not have an oxygen function at C-16.* Like ranaconitine and lappaconitine[8], they show that one plant can yield both aconitine-type and lycoctonine-type alkaloids. It seems probable from the evidence of such pairs of substances that the former alkaloid converts directly into the second type by biological oxidation.



compound 1



compound 4

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7 The structures will be further refined and the hydrogen atom parameters determined.

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