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RIBASINE, A NEW CLASS OF PAPAVERACEAE ALKALOIDS[9]

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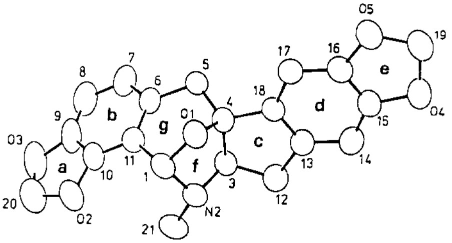
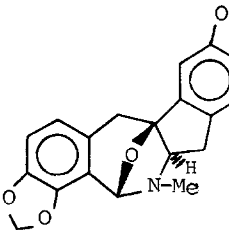
Abstract:The structure (including absolute stereochemistry) of ribasine, a new class of papaveraceae alkaloids with an indanobenzazepine skeleton, has been established. It was isolated from Sarcocapnos crassifolia and Corydalis claviculata.

Plants of the genera Sarcocapnos and Corydalis (Papaveraceae) have proved to be sources of cularine, benzophenanthridine and protopine alkaloids[1]. In the present communication we wish to report the isolation and structure of ribasine, the first example of a new class of alkaloids with an indanobenzazepine skeleton.

Ribasine was obtained from Sarcocapnos crassifolia and Corydalis claviculata as a white , crystalline, optically active substance,mp 194-195°(EtOH),$|\alpha|_D$=+126 (c=1.3 g/l,$CHCl_3$). Its molecular formula,$C_{20}H_{17}NO_5$, was established by elemental analysis and confirmed by MS (M^+,97%; f:351.1080;c:351.1106).Its UV spectrum showed λ_{max}(EtOH)(log ε):213(4.37),240 sh(4.01) and 292 (4.07) nm;no appreciable change was observed in it upon addition of acid and base.The pmr (200 MHz,$CDCl_3$) exhibited in the aromatic region two one proton singlets at δ 6.87 and 6.66 ppm and an AB_q at δ_A=6.74 and δ_B=6.64 (J_{AB}=9Hz),two methylendioxy groups centred at 5.95(m),one proton singlet at 5.67,an AB_q atδ_A=3.57 and δ_B=2.69 (J=16.1 Hz), an ABC system between 3.08 and 2.85 and an N-Me group at 2.33 ppm.Its C-13 NMR revealed as the most significant signals a quaternary carbon at δ 93.65 and two methine groups at 89.55 and 69.73 ppm.Two isomeric structures,1 and 2 are compatible with the above data.X-ray analysis of ribasine showed the new alkaloid actually to possess structure 1.

Ribasine 1,crystallizes in the space group $P2_12_12_1$,Z=8,with a=15.420(2),b=15.095(1) and c=13.983(1) Å. The molecular weight is 351.36 and the calculated density is 1.434 g cm^{-3}. A single crystal of 0.3x0.2x0.1 mm was used to measure the intensities of 3121 independent Friedel pairs,alternately collected in the range of 2°<θ<65° on a computer-controlled four-circle diffractometer.Some experimental details are:ω/2θ scan mode,1.30° scan width, 3 degrees mm^{-1} scan speed, with the same measurement time for both background and peak.Graphite-monochromated CuK_α radiation (1.5418 Å) was used.No crystal decomposition was observed during the data collection process. After the usual correction for Lorentz and polarization effects, 2392 Friedel pairs were considered as observed according to the criterion I>3σ(I) and were used in the least-squares refinement[2] . No absorption correction was applied.The atomic scattering factors and the anomalous dispersion corrections were taken from reference[3] . The structure was solved by direct methods[4] . The hydrogen atoms were placed at their expected positions,but they were checked in a Fourier difference map and included as fixed isotropic contributions in the refinement.For the last refinement $<\Delta^2F>$ was weighted with $w=w_1.w_2$, where $w_1=1/(a+b|Fo|)^2$ and $w_2=1/(c+d\ \sin\theta/\lambda)$ with coefficients calculated so as to prevent bias in $<w\Delta^2F>$ vs. $<|Fo|>$ and $<\sin\theta/\lambda>$[5] . Several cycles of weighted anisotropic refinement including both hkl and $\overline{h}\overline{k}\overline{l}$ reflexions gave for the right enantiomer the following unweighted and weighted discrepancy





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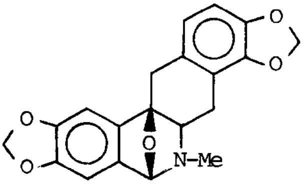

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Fig.1:Molecular structure of ribasine(1)

indices:R=0.043 and R_w=0.052. The absolute configuration[6] ,shown in fig.1,was determined by comparing the 81 Bijvoet pairs with $|\Delta F_c|>0.12$, giving the average Bijvoet difference $\Sigma|(Fo(+h)-Fo(-h)-(Fc(+h)-Fc(-h))|/N$ as 0.579 for the right enantiomer as against 0.700 for the reverse structure.

The ribasine crystal is built up with dimers of two crystallographically independent molecules with the same absolute configuration. One of them is shown in fig.1. The conformations of the two molecules are very similar[7] except for rings a and e, which are envelopes with the methylene groups at the flap, and with different out-of-plane deviations. Nevertheless rings f and g are the most interesting structural features of this compound, with a seven membered ring bridge spanning between C1 and C4. Ring g presents a half-chair conformation in both molecules and ring f is an envelope[8]. Both molecules can be described in terms of two planes:I, 1-11-10-O_2-O_3-9-8-7-6-5 and II, O_4-15-14-13-12-3-4-18-17-16-O_5, which atoms do not deviate by more than 0.06A from the best planes. The dihedral angles between planes I and II are 63° and 67°for molecules A and B,respectivel

The biogenesis of ribasine can plausibly be envisaged as involving rearrengement of stylopine or protopine which we have also isolated from S.crassifolia and C.claviculata. Further support for this pathway is at present being sought.

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8 Ring conformational parameters.

Ring	Aa	Ba	Ae	Be	Ac	Bc	Af	Bf	Ag	Bg
q (Å)	.16	.07	.01	.18	.03	.04	.49	.48	.65	.65
φ°	286	295	173	286	171	198	333	332	78	84
θ°									52	49

Calculations have been done with the following origins and sense:a,C_9-C_{10}; e,C_{15}-C_{16}; c,C_3-C_4; f,O_1-C_4; g,C_1-O_1.

9 Dedicated to Professor I.Ribas on the occasion of his 82nd birthday.

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