

Bellendine, the First Proteaceous Alkaloid, a γ -Pyrone-tropane: X-Ray Structure Determination by Direct Methods

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Summary Bellendine, the first alkaloid isolated from a proteaceous plant, has been shown to have a γ -pyrone-tropane structure by direct methods of X-ray determination.

BELLENDINE¹ (I) occurs in the flowers of the monotypic shrub *Bellendena montana*, endemic on Tasmanian mountain plateaux, and constitutes the first alkaloid from the *Proteaceae*, a large family especially well-represented in the southern hemisphere. Extraction of the fresh flowers with Prollius solution² followed by standard methods of fractionation gave a benzene concentrate which was chromatographed on silica gel. The major alkaloid, bellendine, was obtained in 0.0013% yield together with at least two other bases whose structures have not yet been studied in detail.

Bellendine forms colourless crystals, $[\alpha]_D^{20} + 168.5^\circ$ (CHCl₃), m.p. 162–163°, from ether-petroleum, or by sublimation. Mass spectrometry established the formula C₁₂H₁₅NO₂, and the n.m.r. spectrum showed the presence of an *N*-methyl group, and a *C*-methyl attached to an

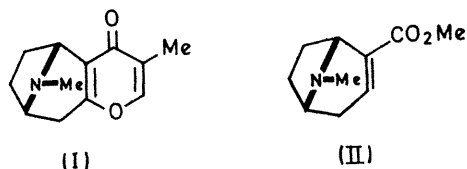
olefinic carbon. Both the i.r. and the u.v. spectra suggested the presence of a conjugated carbonyl [ν_{\max} 1650 cm⁻¹; λ_{\max} (EtOH) 258, 213 nm (ϵ_{\max} 10,680, 10,290)], and the chemical shift of the *C*-methyl group (τ 8.11) pointed to its being substituted α to the carbonyl group. The *C*-methyl is coupled allylically to the only olefinic proton present, the chemical shift of which (τ 2.42) indicated that it was attached to a carbon bearing an oxygen or a nitrogen atom; however, the basicity of bellendine (pK_a 7.3) precluded the possibility of it being a vinologous amide. The evidence is thus in accord with a γ -pyrone structure with a 3-methyl group, and is further supported by the fact that in CF₃CO₂H solution, the allylic coupling in the n.m.r. spectrum is lost due to the increased aromatic character of the ring.

An intense *M* - 29 peak in the mass spectrum was shown by high resolution to be due to loss of C₂H₅; however, the n.m.r. spectrum showed the absence of an ethyl group as such. The formation of this strong ion suggested the presence of a 6-membered nitrogen-containing ring which on electron impact aromatises with loss of an ethylene bridge and hydrogen transfer to the neutral fragment. These

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observations are in complete accord with a tropane system.

The absolute stereochemistry has not yet been determined, and is written arbitrarily as (I) to correspond with the structurally analogous naturally-occurring *Coca* alkaloid methyl ecgonidine (II).



The structure of bellendine was established by an *X*-ray diffraction analysis of the crystals using direct mathematical methods³ with no chemical assumptions.

Crystal data: Bellendine $C_{12}H_{15}NO_2$, M 205, orthorhombic, $a = 9.733 \pm 0.008$, $b = 12.624 \pm 0.008$, $c = 8.507 \pm 0.007$ Å, $D_c = 1.305$ g cm⁻³, $Z = 4$, space group $P2_12_12_1$, $F(000) = 440$.

The intensities of 1010 reflexions were measured in about 10 days with an automatic diffractometer operating in the $\theta-2\theta$ scan mode. The corrected intensities were converted into $|E|$ values and the highest 153 were input to a computer program⁴ which selects reflexions to be given symbolic phases in the tangent formula method of solution. Three symbolic reflexions and one origin selecting reflexion were chosen by the program. These were input to an iterative tangent formula calculation^{5,6} which generated 32 sets of phases for 153 of the highest $|E| > 1.396$. A

Karle map computed with the phased *E* of the set with lowest *R* (Karle) (19.4%) revealed the complete molecule

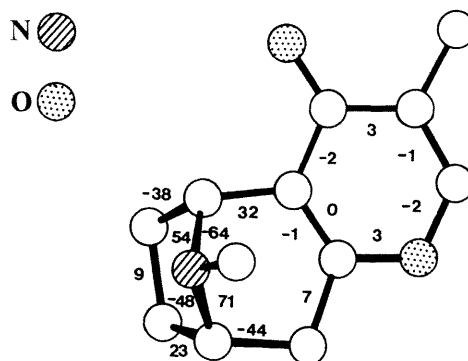


FIGURE. A perspective view of the bellendine molecule with intramolecular torsion angles. Numbers refer to the relevant torsion angles in degrees.

as (I). The atomic positions, taken from the Karle map, were refined through two cycles of isotropic and two of anisotropic full-matrix least-squares calculations. Hydrogen positions were calculated where possible by using the heavier atom co-ordinates. The current reliability factor is 7.3%. The solution and refinement of the structure was completed in approximately 2.5 h on an IBM 360/44 computer.

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² Prolius, *Arch. Pharm.*, [3], 1881, **19**, 85.

³ J. Karle and I. L. Karle, *Acta Cryst.*, 1966, **21**, 849.

⁴ Program developed by W. D. S. Motherwell and N. W. Isaacs, to be published in *Acta Cryst.*

⁵ Program Manual, Crystallography Group, University Chemical Laboratory, Cambridge, 1969.

⁶ G. Germain and M. M. Woolfson, *Acta Cryst.*, 1968, **B24**, 91.