

Lunarine

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LUNARINE, $C_{25}H_{31}N_3O_4$, the principal alkaloid of *Lunaria biennis*¹ and *Lunaria rediviva*² is a monoacid base containing a benzene ring, a ketonic carbonyl function and two ethylenic bonds.³ Alkali fusion of the alkaloid yields spermidine, $H_2N[CH_2]_3NH[CH_2]_4NH_2$,⁴ 2,4-dihydroxybiphenyl-3',5-dicarboxylic acid,⁵ the lactone (I), and 3-methyl-, 3-ethyl-, and 3-n-propyl-4-methylbenzoic acid.⁶ On the basis of the degradative evidence and the spectroscopic properties of lunarine the alkaloid was formulated as (II) or the alternative structure in which the spermidine portion is reversed.⁶

Independent crystal-structure analyses of lunarine hydrobromide monohydrate (at Urbana)

and lunarine hydriodide monohydrate (at Glasgow) have now been performed and our results unambiguously establish that the alkaloid has the constitution and relative stereochemistry shown in (III). Biogenetically, this structure can arise from *p*-hydroxycinnamic acid by oxidative phenolic coupling,⁷ followed (or preceded) by amidation with spermidine and reduction of a double bond. A close analogy is provided by Pummerer's ketone (IV) which is obtained by oxidation of *p*-cresol. Attempts at synthesis of lunarine by this scheme are in progress.

Crystals of lunarine hydrobromide monohydrate belong to the monoclinic system, space group $P2_1$, with two units of $C_{25}H_{32}N_3O_4Br \cdot H_2O$ in a cell of

¹ E. Steinegger and T. Reichstein, *Pharm. Acta Helv.*, 1947, **22**, 258; O. R. Hansen, *Acta Chem. Scand.*, 1947, **1**, 657; H. G. Boit, *Chem. Ber.*, 1954, **87**, 1082; M.-M. Janot and J. LeMen, *Bull. Soc. chim. France*, 1956, 1841.

² S. Huneck, *Naturwiss.*, 1962, **49**, 233.

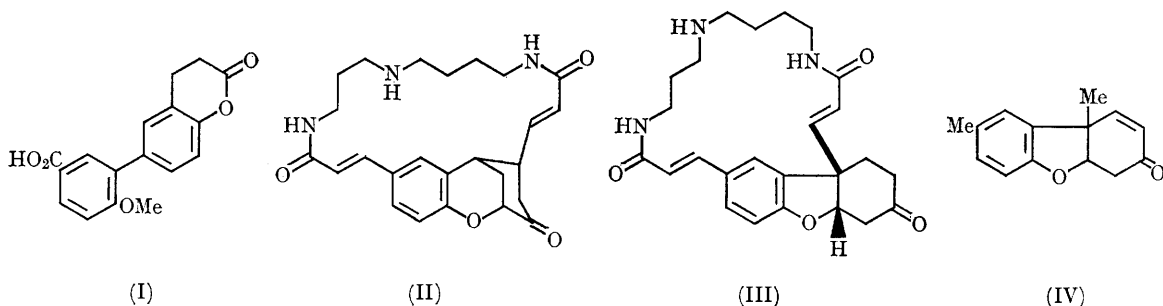
³ P. Potier and J. LeMen, *Bull. Soc. chim. France*, 1959, 456; P. Bladon, R. Ikan, F. S. Spring, and A. D. Tait, *Tetrahedron Letters*, 1959, No. 9, 18.

⁴ P. Potier, J. LeMen, M.-M. Janot, and P. Bladon, *Tetrahedron Letters*, 1960, No. 18, 36.

⁵ P. Bladon, M. Chaigneau, M.-M. Janot, J. LeMen, P. Potier, and A. Melera, *Tetrahedron Letters*, 1961, 321.

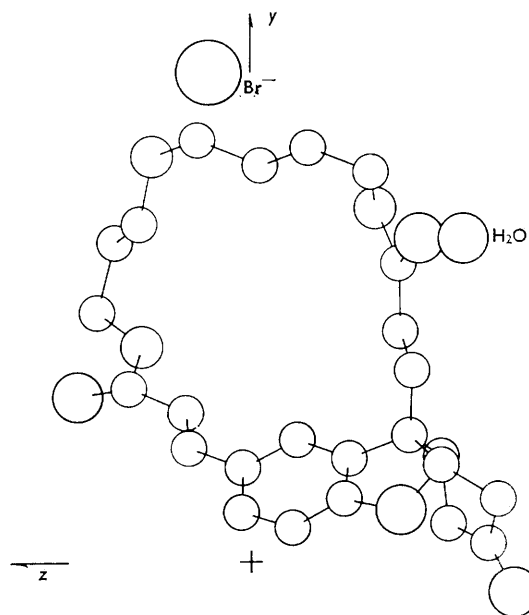
⁶ P. Potier, J. LeMen, M.-M. Janot, P. Bladon, A. G. Brown, and C. S. Wilson, *Tetrahedron Letters*, 1963, 293.

⁷ D. H. R. Barton and T. Cohen, "Festschrift A. Stoll", Birkhauser, Basle, 1957, p. 117; A. I. Scott, *Quart. Rev.*, 1965, **19**, 1.



dimensions $a = 11.37$, $b = 10.96$, $c = 12.41 \text{ \AA}$, $\beta = 120.3^\circ$. The hydride is orthorhombic, space group $P2_12_12_1$, with four units of $C_{25}H_{32}N_3O_4 \cdot H_2O$ in a cell of dimensions $a = 11.60$, $b = 16.53$, $c = 14.01 \text{ \AA}$. For both compounds three-dimensional X-ray intensity data were recorded on equi-inclination Weissenberg photographs and estimated visually. The atoms, apart from hydrogen, were located in three-dimensional electron-density distributions. With phases based on the bromide ion alone the initial Fourier synthesis for lunarine hydrobromide inevitably displayed a false plane of symmetry and this, together with the large amount of spurious detail caused by the approximate phases, made the choice of atomic sites hazardous. A considerable improvement in definition was obtained by weighting the coefficients in the Fourier series according to Sim's method⁸ and a large fraction of the structure was delineated in this electron-density distribution. The atomic co-ordinates were subsequently refined by the method of least squares and the value of R is 13.7%. The co-ordinates yield satisfactory bond lengths and valency angles.

The atomic arrangement in lunarine hydrobromide hydrate as viewed along the a axis of the crystal is shown in the Figure.



The molecular structure of lunarine hydrobromide monohydrate as viewed along the a axis of the crystal.

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⁸ G. A. Sim, *Acta Cryst.*, 1959, **12**, 813; 1960, **13**, 511; "Computing Methods and the Phase Problem in X-Ray Crystal Analysis", ed. R. Pepinsky, J. M. Robertson, and J. C. Speakman, Pergamon Press, Oxford, 1961, p. 227.