The Crystal Structure of a New Alkaloid, Stemofoline, from *Stemona japonica*

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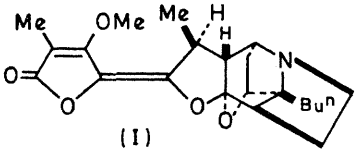
Summary The structure (I) of a new alkaloid, stemofoline isolated from the stems and leaves of *Stemona japonica* has been determined by *X*-ray crystallographic analysis of its hydrobromide monohydrate.

WE recently found that the stems and leaves of *Stemona japonica* Miq. contain a hitherto unknown alkaloid which we named stemofoline, $C_{22}H_{29}NO_5$, m.p. 87—89° (after drying), M^+ 387, $[\alpha]_D$ +273° (MeOH), λ_{max} (EtOH) 296 nm (ϵ 24,200), ν_{max} (KBr disc) 1745, 1691, and 1622 cm^{-1}, n.m.r. ($CDCl_3$) τ 5·75 (broad s, 1H; CH geminal to an ether oxygen), 5·87 (s, 3H; OMe), 7·93 (s, 3H; olefinic Me), 8·63 (d, 3H, J 6·5 Hz; secondary Me), and 9·09 (t, 3H, J 6·0 Hz; primary Me).



(I)

Although the amount of stemofoline isolated was too small to allow an extensive chemical study, the structure determination was achieved by the *X*-ray crystallographic analysis of well formed needle-like single crystals of stemofoline hydrobromide monohydrate, $C_{22}H_{29}NO_5$,HBr,H_2O, m.p. 224° (decomp.) D_m 1·392 g cm^{-3}, which were obtained from an ethanol solution. The crystals are orthorhombic, space group $P2_12_12_1$ with $Z = 4$, $a = 11{\cdot}80$, $b = 25{\cdot}94$, $c = 7{\cdot}61$ Å, $V = 2328$ Å^3, D_x 1·390 g cm^{-3}. The *X*-ray intensity data around *a* and *c* crystallographic axes were measured visually from equi-inclination Weissenberg photographs taken with Cu-K_α radiation. Though the position of a Br atom in the unit-cell was $x = 0{\cdot}7915$, $y = 0{\cdot}5924$, $z = 0{\cdot}2622$—close to the special position ($z = 1/4$), the crystal structure was solved by the usual heavy-atom method and refined by a full-matrix least-squares method. The absolute configuration of the molecule was determined from the anomalous *X*-ray dispersion effect of Br atoms on the Weissenberg films. The reliability index *R* was 12·7% for 2140 non-zero independent reflections. A perspective view of the molecular structure along the [101] direction in the crystal is shown in the Figure.

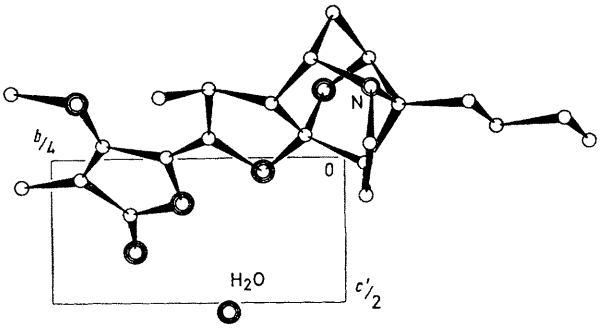


FIGURE. *The molecule viewed in projection along the* [101] *axis.* c'=c *cos*(*tan*$^{-1}$ a/c). *Open, double, and triple circles represent carbon, nitrogen, and oxygen atoms, respectively.*

From the established structure of stemofoline (I), it can be seen that stemofoline is closely related to protostemonine[1] in that both have in common a furo[3,2-*c*]pyrrolo[1,2-*a*]-azepine ring system which is attached to 4-hydroxy-3-methoxy-2-methylcrotonolactone by a double bond. In contrast to protostemonine, however, stemofoline has two additional annelations which cause the molecule to adopt a rigid cage structure of a new type. Another characteristic structural feature of stemofoline is the presence of an n-butyl grouping instead of the γ-lactone ring present in protostemonine, tuberostemonine,[2] and oxotuberostemonine[3] in the position α to the nitrogen of the pyrrolidine ring.

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[2] H. Harada, H. Irie, N. Masaki, K. Osaki, and S. Uyeo, *Chem. Comm.*, 1967, 460.
[3] C. P. Huber, S. R. Hall, and E. N. Maslen, *Tetrahedron Letters*, 1968, 4081.