

Molecular Structure of Veratrobazine

Sir:

We report an X-ray diffraction determination of the structure and stereochemistry, except for absolute configuration, of the steroid alkaloid veratrobazine ($C_{27}H_{41}O_3N$), which is present in the perennial *Veratrum album* (the European hellebore).¹ This determination establishes the correct empirical formula, proves that an N-methyl group is *not* present, and helps to elucidate the relationships of veratrobazine to the other *Veratrum* alkaloids, particularly to jervine.

The space group is $P2_12_12_1$, and there are four molecules in a unit cell of dimensions $a = 8.385$, $b = 15.773$, and $c = 18.037$ Å. Of the 3105 unique diffraction maxima, within reciprocal space accessible to Cu radiation, 3077 were recorded by the multiple-film Weissenberg method, and visual estimates were obtainable for all but 378 of these.² In the course of several years of investigation, a number of crystallographic methods failed to provide a solution of this structure.² The structure was finally solved by the symbolic addition procedure of Karle and Karle,³ in which phases were assigned to three reflections to fix the origin, phases of six other structure invariants were obtained from the Σ_1 formula,⁴ and two phases were assigned symbols of unknown values, one of which determined the enantiomorph. The 52 phases determined by symbolic addition were used as input to the tangent formula⁵ by which phases were assigned to 636 reflections having normalized structure factors, E , greater than 1.1. Convergence was achieved in 14 min on an IBM 7094 computer with the use of a program written in this laboratory (by G. N. R.). Refinement, first with the use of the tangent formula⁵ and then by Fourier and least-squares methods, has reached a value of 0.11 for the R factor ($R = \sum |F_o| - |F_c| / \sum |F_o|$) after inclusion of all hydrogen atoms and assumption of isotropic thermal parameters. At this stage of refinement, bond distances and angles are near expected values: for example, the average $C(sp^3)-C(sp^3)$ distance is 1.53 ± 0.02 Å.

The identity of the N and O atoms was established with certainty by refinements in which all non-H atoms were assumed to be carbon, and the behavior of atom multipliers and apparent thermal parameters was examined. Difference electron density maps and interatomic distances were also examined.

The structure (Figure 1) has a bonding skeleton like that of jervine except that veratrobazine has a hydroxyl group at C_{11} whereas jervine has a keto group. This hydroxyl group is strongly indicated by the bond angles about C_{11} and by the C-O distance of 1.46 Å. Both veratrobazine and jervine contain the highly unusual C-nor-D-homo steroid ring system. It remains to be shown whether the stereochemistry of the two molecules is identical at corresponding asymmetric centers. Although the absolute configuration was not established in this study, we have chosen for the A and B rings the

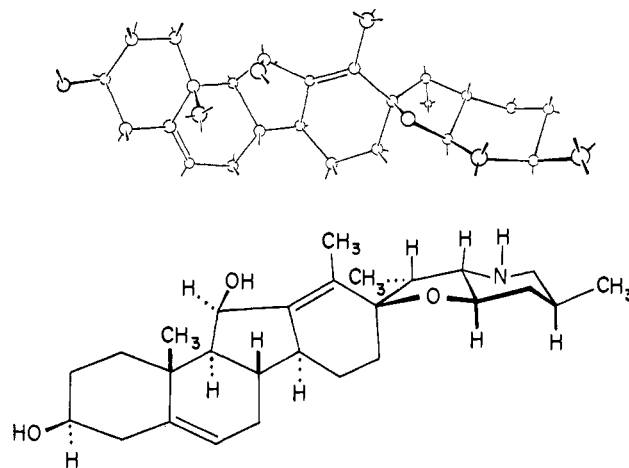


Figure 1. (a) Stereochemical drawing from a model of the veratrobazine molecule (upper); (b) conventional chemical representation of the stereochemistry of veratrobazine (lower).

configuration which occurs in normal steroids, such as cholesterol.

An apparent difficulty in measurements of the molecular weight has led to reports of the incorrect empirical formula, $C_{24}H_{37}O_3N$.^{1,6,7} Hitherto, the veratrobazine molecule has been believed^{1,6} to contain an N-methyl group as a tertiary amine, which is at variance with the monobenzylation reaction.⁶ Our structure determination shows that the N-methyl group is not present and thereby provides a basis for the explanation of some of the more puzzling chemical results.⁶

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(6) A. Stoll, D. Stauffacher, and E. Seebeck, *Helv. Chim. Acta*, **38**, 1964 (1955).

(7) L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, pp 867-879.

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A Novel Bidentate π -Bonding Ligand Derived from 1,2-Dicarba-closo-dodecaborane(12)

Sir:

A variety of transition metal complexes with eleven-particle icosahedral carborane fragments have been reported.¹ We wish to report a complex containing

(1) A. Stoll and E. Seebeck, *J. Am. Chem. Soc.*, **74**, 4728 (1952).

(2) R. Lewin, Ph.D. Thesis, Harvard University, 1964. The primary X-ray data are available in this thesis.

(3) J. Karle and I. L. Karle, *Acta Cryst.*, **21**, 849 (1966); I. L. Karle and J. Karle, *ibid.*, **17**, 835 (1964).

(4) J. Karle and H. Hauptman, *ibid.*, **9**, 635 (1956).

(5) I. L. Karle, J. Karle, and J. A. Estlin, *ibid.*, **23**, 494 (1967).

(1) (a) M. F. Hawthorne, D. C. Young, T. D. Andrews, D. V. Howe, R. L. Pilling, A. D. Pitts, M. Reintjes, L. F. Warren, Jr., and P. A. Wegner, *J. Am. Chem. Soc.*, **90**, 879 (1968); (b) D. E. Hyatt, J. L. Little, J. T. Moran, F. R. Scholer, and L. J. Todd, *ibid.*, **89**, 3342 (1967); (c) L. F. Warren, Jr., and M. F. Hawthorne, *ibid.*, **89**, 470 (1967); (d) W. H. Knoth, *ibid.*, **89**, 3342 (1967); (e) P. A. Wegner and M. F. Hawthorne, *Chem. Commun.*, 861 (1966); (f) M. F. Hawthorne and T. D. Andrews, *ibid.*, 443 (1965); (g) A. Zalkin, T. E. Hopkins, and