The X-Ray Crystal Structure and Absolute Configuration of Vertaline

Jean A. Hamilton* and L. K. Steinrauf

Contribution from the Department of Biochemistry,
Indiana University Medical School, Indianapolis, Indiana 46202.
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Abstract: The X-ray crystal structure of the Lythraceae alkaloid vertaline has been determined as the hydrobromide salt. The space group was $P2_12_12_1$ with four molecules per unit cell, and a = 7.94 Å, b = 23.47 Å, and c = 13.23 Å. Data were collected by diffractometer to include Bijvoet pairs, and the absolute configuration was determined using the anomalous dispersion of the bromine atom.

The structure of vertaline (Figure 1) represents an important link in the biogenesis of the Lythraceae alkaloids.[1a,d] The X-ray crystal structure was undertaken to provide a reference in the biogenesis scheme to which other members could be compared by nmr spectra. Crystals of the hydrobromide salt of vertaline were provided us by Dr. James Ferris. A preliminary note on the X-ray structure determination has been published.[1e]

Experimental Section

The crystals were needle shaped and not too well formed. The crystal selected for data collection was cut to give as even dimensions as possible in each direction (0.2 mm × 0.1 mm × 0.1 mm). Since no solvent loss or gain was observed the crystal was mounted open to the air on the tip of a glass fiber. Cell dimensions were estimated from Weissenberg films calibrated with aluminum powder lines, and intensity data were collected using the Supper-Pace autodiffractometer and Mo Kα radiation using techniques previously described.[2] The unique part of the data numbered 1834 nonzero reflections, and 1049 Bijvoet pairs were also measured. Absorption corrections were small and ignored. The crystal data are shown in Table I.

Table I. Crystal Data

$C_{26}H_{32}NO_5Br$
Mol wt, 518.46
Space group $P2_12_12_1$
$Z = 4$
$a = 7.94 \pm 0.01$ Å
$b = 23.47 \pm 0.01$ Å
$c = 13.23 \pm 0.01$ Å
$D_{\text{obsd}} = 1.39$ g/cm³ (by flotation in carbon tetrachloride and hexane)
$D_{\text{calcd}} = 1.41$ g/cm³
μ (Mo Kα) = 1.83 cm^{-1}

Structure Determination and Refinement. The coordinates of the bromide ion were obtained from a three-dimensional Patterson map. A three-dimensional Patterson superposition was calculated using the bromine positions, and peaks common to this and a Fourier map based on phases calculated from the bromine position were assumed to be valid. Inclusion of these positions in the phasing calculations followed by two further cycles of Fourier analysis gave the complete structure. The atomic coordinates were then refined using a block-diagonal least-squares program[3] and the unique part of the data. A difference Fourier map indicated significant anisotropy only in the case of the bromide ion. The temperature parameter of this atom was allowed to become anisotropic in the least-squares refinement. When the refinement had settled the imaginary contribution to the scattering curve for bromine was inserted in the least-squares program, and refinement of the unique data plus the Bijvoet pair data continued. The structure with the absolute configuration as shown in Figure 2 refined to a final R value of 9.45%. The mirror image refined to only 11.27%. Thus the absolute configuration in Figure 2 is correct. The numbering system, although unconventional for crystallography, is used to conform with the accompanying chemical papers. The final atomic parameters for the molecule as its absolute configuration are listed in Table II.[4]

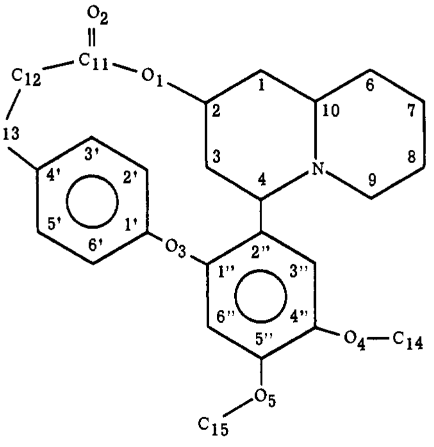

Figure 1. The structure of vertaline.

Discussion

The absolute configurations at positions 2 and 4 are consistent with chemical data and also with the

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(1) (a) J. P. Ferris, C. B. Boyce, and R. C. Briner, *J. Amer. Chem. Soc.*, **93**, 2942 (1971); (b) J. P. Ferris, R. C. Briner, and C. B. Boyce, *ibid.*, **93**, 2953 (1971); (c) J. P. Ferris, R. C. Briner, and C. B. Boyce, *ibid.*, **93**, 2958 (1971); (d) J. P. Ferris, C. B. Boyce, R. C. Briner, U. Weiss, I. H. Qureshi, and N. E. Sharpless, *ibid.*, **93**, 2963 (1971); (e) J. A. Hamilton and L. K. Steinrauf, *Tetrahedron Lett.*, **42**, 5121 (1966).

(2) J. M. H. Pinkerton and L. K. Steinrauf, *J. Org. Chem.*, **32**, 1828 (1967).

(3) D. Harris, "World List of Crystallographic Computer Programs," 2nd ed, Rotterdam, Netherlands, Bronder-Offset, 1966, p 23.

(4) The observed and calculated structure have been deposited with the ASIS National Auxiliary Publication Service, c/o CCM Information Corp., 909 Third Ave., New York, N. Y. 10022, as Document No. 01327. A copy may be obtained by citing the document number and remitting $2.00 for microfiche or $5.00 for photocopies. Advance payment is required. Make checks or money orders payable to: CCMIC-NAPS.

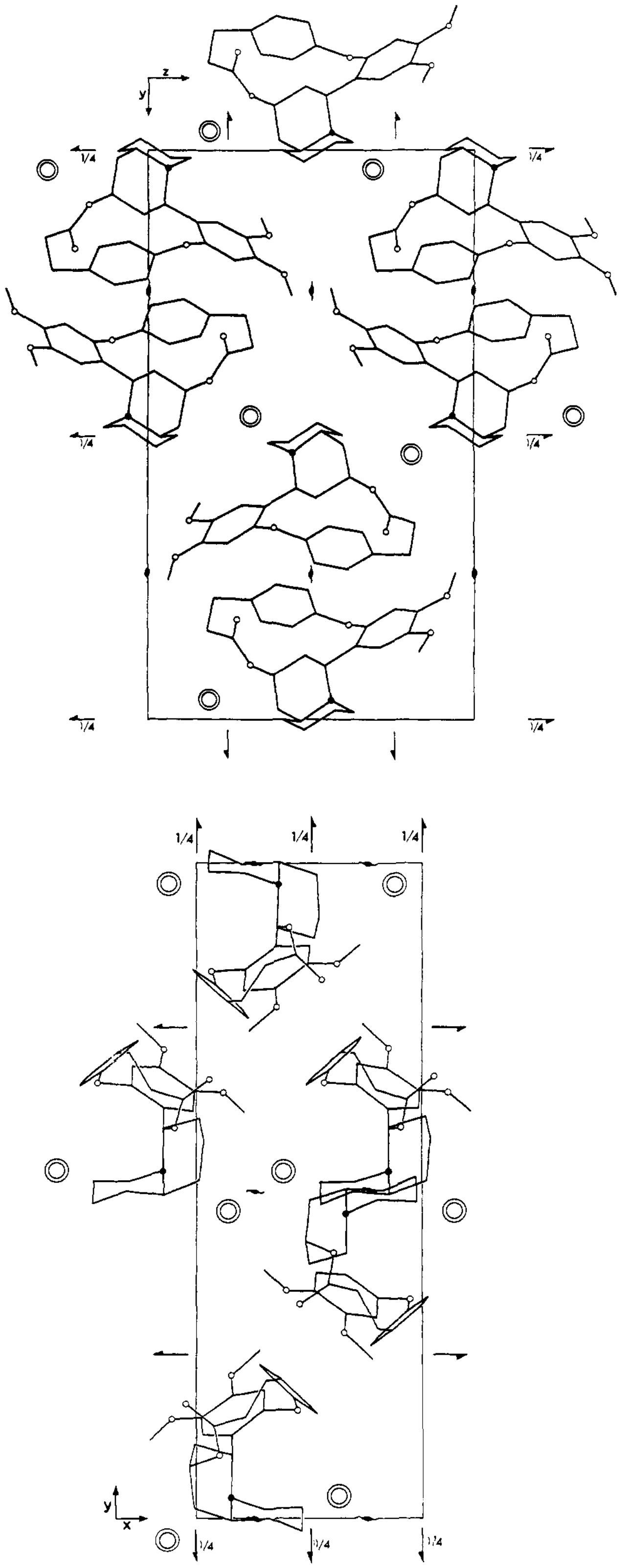

Figure 2. Drawings showing the packing of the molecules in the unit cell looking down the *X* and *Z* axes, respectively.

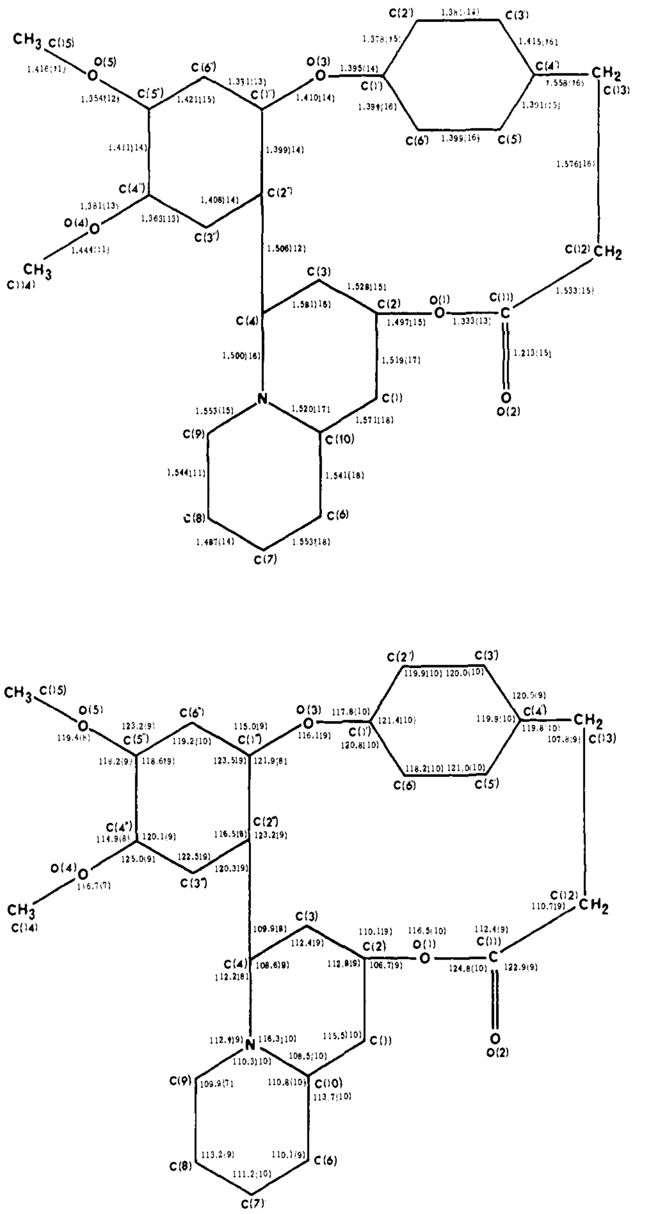

Figure 3. Diagrams illustrating the bond lengths and angles for the molecule. Standard deviations are given in parentheses.

absolute configuration of a similar alkaloid, lythridine methiodide, determined by Chu, Jeffrey, *et al.*,[5] from X-ray data. The ring fusion in the quinolizidine ring is cis, and the lactone group and biphenyl ether are linked to the quinolizidine ring in the axial and equatorial positions, respectively. The bond lengths and angles are shown in Figure 3. None are significantly different from expected values, the differences being within three times the estimated standard deviation. In the area of the lactone group atoms C(11), O(1), O(2) the bond C(11)—O(1) shows partial double bond character. The length of 1.333 ± 0.013 Å for the C(11)—O(1) bond agrees with that of 1.36 ± 0.01 Å for shortened single bonds.[6] Similarly the length of 1.213 ± 0.015 Å for the C(11)—O(2) bond is compatible with that of 1.23 ± 0.01 Å found for carbonyl groups.[6] The packing in the unit cell provides a confortably large distance between the smaller ions, the bromides. The bromine to nitrogen distance of 3.190 ± 0.013 Å could indicate a weak hydrogen bond. There are no interactions between the benzene rings of neighboring mole-

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(5) S. C. Chu and G. A. Jeffrey, *et al.*, *Chem. Ind.* (*London*), 1795 (1966).

(6) "Interatomic Distances and Configuration in Molecules and Ions," The Chemical Society, London, 1958.

Table II. Fractional Atomic Coordinates and Thermal Parameters for Vertaline Hydrobromide with Standard Deviations

	x	($\sigma \times 10^4$)	y	($\sigma \times 10^4$)	z	($\sigma \times 10^4$)	B, Å^2	($\sigma \times 10$)
Br	0.6290	(2)	0.0331	(1)	−0.3116	(1)	[a]	
C(1)	−0.0095	(17)	0.0138	(5)	−0.0979	(9)	3.3	(3)
C(2)	−0.0300	(16)	0.0775	(5)	−0.1142	(9)	2.9	(3)
C(3)	−0.0118	(15)	0.1120	(4)	−0.0160	(8)	2.6	(2)
C(4)	0.4665	(15)	0.0140	(4)	0.0734	(7)	4.7	(2)
C(6)	0.3154	(15)	−0.0010	(5)	−0.0910	(8)	4.1	(2)
C(7)	0.4628	(18)	−0.0198	(5)	−0.0215	(9)	4.9	(3)
C(8)	0.4665	(10)	−0.0140	(3)	0.0734	(5)	4.7	(1)
C(9)	0.2981	(10)	0.0126	(3)	0.1317	(5)	3.7	(1)
C(10)	0.1473	(17)	−0.0045	(5)	−0.0332	(9)	3.0	(3)
C(11)	0.0720	(15)	0.1418	(4)	−0.2420	(7)	3.7	(2)
C(12)	0.2090	(15)	0.1536	(5)	−0.3208	(8)	3.6	(2)
C(13)	0.3013	(15)	0.2116	(5)	−0.2975	(8)	3.9	(2)
C(14)	−0.2602	(9)	0.1211	(3)	0.3412	(5)	4.6	(1)
C(15)	0.2728	(9)	0.2579	(3)	0.4401	(5)	4.8	(1)
C(1′)	0.4237	(16)	0.1846	(5)	0.0158	(8)	2.4	(2)
C(2′)	0.5246	(15)	0.1604	(4)	−0.0571	(7)	3.6	(2)
C(3′)	0.4962	(16)	0.1721	(4)	−0.1579	(8)	3.4	(2)
C(4′)	0.3642	(16)	0.2094	(5)	−0.1861	(8)	3.4	(2)
C(5′)	0.2735	(15)	0.1271	(4)	−0.1108	(8)	3.5	(2)
C(6′)	0.3043	(16)	0.2259	(5)	−0.0086	(9)	3.3	(2)
C(1′′)	0.2923	(13)	0.1623	(4)	0.1724	(7)	2.6	(2)
C(2′′)	0.1569	(13)	0.1278	(4)	0.1435	(6)	2.2	(2)
C(3′′)	0.0201	(14)	0.1252	(4)	0.2110	(7)	2.6	(2)
C(4′′)	0.0198	(14)	0.1530	(4)	0.3014	(7)	2.7	(2)
C(5′′)	0.1569	(14)	0.1880	(4)	0.3287	(7)	2.8	(2)
C(6′′)	0.2946	(15)	0.1928	(4)	0.2607	(7)	3.1	(2)
O(1)	0.1026	(14)	0.0949	(4)	−0.1884	(7)	3.1	(2)
O(2)	−0.0498	(14)	0.1723	(4)	−0.2311	(7)	5.0	(2)
O(3)	0.4415	(13)	0.1654	(4)	0.1149	(7)	3.2	(2)
O(4)	−0.1097	(11)	0.1513	(3)	0.3710	(5)	3.4	(1)
O(5)	0.1484	(11)	0.2167	(4)	0.4173	(6)	3.5	(2)
N	0.1526	(17)	0.0322	(5)	0.0614	(9)	2.5	(3)

[a] Anisotropic thermal parameters for the bromine atom of the form: $\exp[-\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + \beta_{12}hk + \beta_{13}hl + \beta_{23}kl)]$. $\beta_{11} = 0.0086(2)$; $\beta_{22} = 0.0030(0.2)$; $\beta_{33} = 0.0092(0.7)$; $\beta_{12} = -0.0010(2)$; $\beta_{13} = -0.0011(3)$; $\beta_{23} = -0.0041(0.7)$; $\sigma + 10^4$ is given in parentheses.

cules. The crystal is otherwise held together by van der Waals forces, and there are no unusual intermolecular contacts. The packing in the unit cell is shown in Figure 2.

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