

Acta Cryst. (1969). B25, 1925

The Absolute Crystal Structure of (–)-Isolunine Hydrobromide Dihydrate at –150°C

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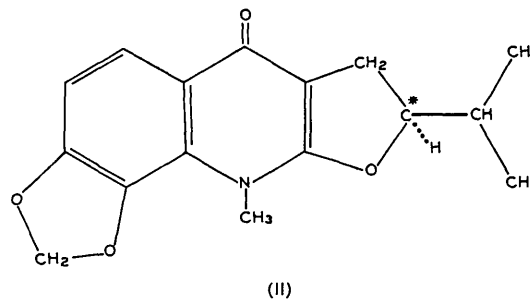
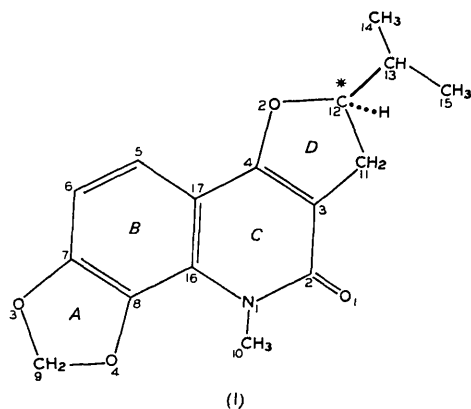
(Received 28 October 1968)

Crystals of (–)-isolunine hydrobromide dihydrate, $C_{16}H_{17}NO_4 \cdot 2H_2O \cdot HBr$, are monoclinic, space group $P2_1$, with $a=11.11$, $b=7.24$, $c=22.33$ Å, $\beta=101^\circ 11'$ at $-150^\circ C$, $Z=4$, the asymmetric unit consisting of two molecules. Application of image-seeking procedures revealed the main components of the structure, while electron density and difference syntheses led to a complete solution of the molecular skeleton. Differentiation of the nitrogen and oxygen atoms in the skeleton was assisted by a mass spectroscopic determination of the molecular weight. Refinement was by least-squares and the absolute chirality was defined by Bijvoet's technique. The crystal structure involves a short approach distance, 2.45 Å, between the lactam oxygen atom and a water molecule, the grouping being stabilized by the interpolation of a proton, H^+ . The relation of isolunine to lunine is outlined.

Introduction

The material, shown to be isolunine, was initially assumed to have a probable structure of a quite different type. Analysis of the X-ray diffraction data established the molecular skeleton but exact differentiation of certain atoms as N or O was not possible. This experience, based on film data, parallels that of Ammon & Jensen (1966) in their analysis of 1-methyl-6-[5-(1-methyl-1*H*-1-pyridinyl)]-1-azoniaindan iodide, which also initially lacked clear definition as a molecular species. In their case, the matter was resolved by reference to the improved precision of diffractometer data. In our case, supplementary evidence was provided by a mass spectrometer molecular weight determination which allowed only one interpretation for the molecular skeleton and hence the detailed chemical structure could be defined.

Having thus established that the molecular structure of the compound was (I), *i.e.* isolunine, its synthesis from lunine, (II), (Hart, Johns, & Lamberton, unpublished results) allowed its identity to be confirmed.



The crystal analysis, although it is of interest in relation to the group of isopropylidihydrofuroquinoline alkaloids (Boit, 1961), proved to be far more significant in respect of one particular detail, namely the strong hydrogen bond between isolunine (I) and a water molecule (Beecham, Hurley, Mackay, Maslen & Mathieson, 1968).

Experimental

The crystals of isolunine hydrobromide dihydrate, $C_{16}H_{17}NO_4 \cdot 2H_2O \cdot HBr$, are monoclinic with dimensions $a=11.11$, $b=7.24$, $c=22.33$ Å, $\beta=101^\circ 11'$ at *ca.* $-150^\circ C$, determined against a powder standard (Si, $a=5.4173$ Å at room temperature). The unit-cell volume, U , is 1762 Å³. The density, measured (at room temperature) in a mixture of carbon tetrachloride and petroleum spirit, was 1.48 g.cm⁻³. The space group is $P2_1$, the alternative $P2_1/m$ being excluded by the presence of optical activity. The information available at the time indicated that $Z=4$ with two molecules in the asymmetric unit.

Intensity data were recorded with filtered Cu $K\alpha$ radiation at $-150^\circ C$, the experimental conditions being as described in Fridrichsons & Mathieson (1962*a*). Equi-inclination Weissenberg photographs with 6-film packs were recorded for 0–6 layers about [010] and

0.2 about [100]. Being unstable in air, the crystals had to be coated in collodion and, since they were apparently also affected by X-radiation, only data for two layers were obtained from any one crystal. Intensities were estimated visually against a set of timed exposures of a single reflexion, 3410 of 3670 possible terms being measured, corresponding to 80% of the total for Cu $K\alpha$ radiation.

Structure analysis

At the beginning of this analysis, the compound under investigation had not been identified as isolunine and the information available at the time concerning the possible structure of the molecule was therefore misleading.

Using F^2 data, sharpened by the modification function, $\cosh(as) \exp(-\pi^2 s^2/p)$ (Wunderlich, 1965), the $H(u, \frac{1}{2}, w)$ section and generalized Patterson syntheses (Cochran & Dyer, 1952) for the six layers about [010], yielded the x, y, z parameters of both Br atoms in the asymmetric unit. Image-seeking procedures (Fridrichsons & Mathieson, 1962b) were applied with variation of scale and modification function to make atom site location more straightforward, but little significant improvement was achieved in the resultant distributions. This procedure revealed the main components of the structure – two independent molecular skeletons each containing 21 atoms. Similarity in relative atom disposition permitted the preliminary assumption that the two components of the asymmetric unit were identical. Each molecule comprised two six-membered rings and two five-membered rings, the former, with their substituents constituting an essentially planar system. In addition, there were four well-defined peaks, which, by their relatively isolated locations, appeared most likely to be oxygen atoms of water molecules.

Differentiation of the light atoms in the molecule as C, N or O was rendered difficult by uncertainties, still evident at this stage, as to the exact number of N and O atoms in the molecular skeleton. Refinement procedures tended to show a consistent pattern in which atoms, later allocated as O(1), O(2), O(3) and O(4) showed greater scattering power. Least-squares refinements in which atom occupancies were varied (with temperature factors stabilized) did indicate a possible differentiation of nitrogen and oxygen. When set as carbon, some occupancies grouped in the range 1.30–1.55 while one was at 1.25 but a clear distinction was not possible (see also Ammon & Jensen, 1966) particularly since the earlier chemical information, presumed applicable, prevented an unbiased assessment of the situation. Differentiation of the nitrogen and oxygen atoms was assisted by a mass spectrometric determination of the molecular weight, 287, compatible, for this molecular skeleton, only with the structure (I).

With conventional least-squares procedures, involving anisotropic temperature factors for the Br atoms and isotropic for all others, a final reliability index,

$R=0.12$, was obtained.* Final difference syntheses with data limited to $\sin \theta < 0.60$ gave no thoroughly convincing demonstration of H atom sites. They were therefore omitted from the calculation.

The final electron density distribution, as superimposed sections parallel to [010], for the molecules *A* and *B*, are shown in Fig. 1 while line diagrams projected down [010] and [100] are shown in Figs. 2(a) and (b) respectively. Atomic parameters and temperature factors are listed in Table 1. The resultant bond lengths

* The table, presenting the comparison of observed and calculated values of structure factors, is not given here. Copies can be obtained from either author, on request.

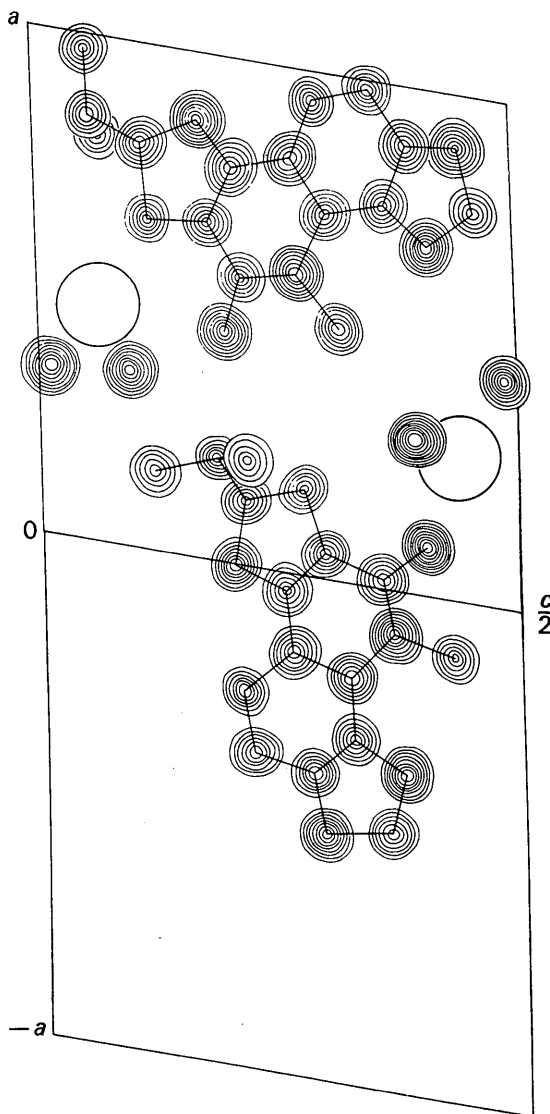


Fig. 1. Molecular structure of isolunine hydrobromide dihydrate. Superimposed are sections of the final electron density distribution showing molecules *A* and *B*.

Table 1(a). *Atomic parameters of the asymmetric unit together with their estimated standard deviation, multiplied by 10⁴, and individual isotropic temperature factors applied to the light atoms*

Molecule <i>A</i>	<i>x/a</i> ($\sigma x/a$)	<i>y/b</i> ($\sigma y/b$)	<i>z/c</i> ($\sigma z/c$)	<i>B</i>
Br	4697 (7)	0000	0676 (4)	
C(2)	5713 (60)	4566 (111)	2148 (31)	1.32 Å ²
C(3)	6691 (63)	4833 (141)	1806 (32)	1.90
C(4)	7866 (60)	4484 (108)	2075 (32)	1.28
C(5)	9458 (63)	3289 (113)	2933 (32)	1.29
C(6)	9819 (63)	2565 (114)	3497 (33)	1.27
C(7)	8870 (59)	2301 (112)	3840 (31)	1.01
C(8)	7640 (62)	2832 (116)	3598 (32)	1.24
C(9)	7802 (80)	1901 (155)	4569 (41)	2.87
C(10)	5089 (63)	3981 (123)	3121 (32)	1.43
C(11)	6601 (74)	5435 (126)	1152 (38)	2.51
C(12)	8036 (61)	5534 (105)	1115 (32)	1.44
C(13)	8376 (69)	4420 (121)	0605 (35)	1.97
C(14)	8166 (79)	2336 (144)	0669 (39)	2.60
C(15)	9725 (73)	4820 (159)	0584 (35)	2.64
C(16)	7291 (65)	3547 (117)	3015 (33)	1.49
C(17)	8244 (64)	3736 (121)	2689 (33)	1.32
O(1)	4614 (37)	4904 (86)	1951 (19)	1.10
O(2)	8685 (41)	4819 (90)	1717 (21)	1.52
O(3)	8955 (45)	1554 (89)	4389 (23)	1.76
O(4)	6952 (47)	2348 (84)	4024 (24)	1.93
O(5)	3307 (56)	3694 (106)	0112 (29)	3.09
O(6)	3548 (43)	6071 (100)	0978 (23)	2.03
N(1)	6083 (49)	4026 (97)	2735 (26)	1.12

Molecule <i>B</i>	<i>x/a</i> ($\sigma x/a$)	<i>y/b</i> ($\sigma y/b$)	<i>z/c</i> ($\sigma z/c$)	<i>B</i>
Br	2878 (6)	0960 (19)	4375 (4)	
C(2)	0234 (59)	7239 (114)	3584 (30)	0.97
C(3)	0517 (61)	7685 (114)	3001 (32)	1.23
C(4)	9656 (67)	8494 (118)	2584 (33)	1.57
C(5)	7502 (58)	9416 (101)	2167 (30)	0.93
C(6)	6283 (66)	9586 (120)	2227 (34)	1.85
C(7)	6078 (66)	9025 (129)	2802 (35)	1.66
C(8)	6939 (64)	8381 (114)	3281 (33)	1.41
C(9)	5180 (61)	8726 (118)	3611 (31)	1.19
C(10)	8863 (61)	6984 (119)	4319 (32)	1.17
C(11)	1715 (72)	7642 (131)	2788 (37)	2.08
C(12)	1280 (63)	8120 (120)	2104 (33)	1.34
C(13)	2007 (65)	9604 (120)	1847 (33)	1.76
C(14)	2058 (82)	1483 (141)	2140 (41)	2.96
C(15)	1537 (68)	9844 (148)	1170 (35)	2.33
C(16)	8139 (64)	8204 (119)	3237 (33)	1.40
C(17)	8382 (59)	8673 (110)	2640 (30)	0.85
O(1)	1024 (39)	6550 (70)	4049 (20)	0.99
O(2)	9988 (45)	8878 (86)	2071 (23)	1.80
O(3)	4943 (42)	9112 (81)	2973 (22)	1.39
O(4)	6378 (47)	7986 (88)	3766 (24)	1.87
O(5)	4447 (44)	7149 (87)	4858 (23)	1.72
O(6)	3040 (37)	5238 (72)	3967 (19)	0.92
N(1)	9073 (49)	7491 (89)	3686 (25)	0.82

and angles in molecules *A* and *B*, with their mean values, are shown in Table 2 and Fig. 3 while selected inter-molecular approach distances are given in Fig. 2 and Table 3.

Table 1(b). *Anisotropic temperature factor components applied to the bromine atoms A and B multiplied by 10⁴*

$$T = \exp [-(h^2 B_{11} + k^2 B_{22} + l^2 B_{33} + 2hk B_{12} + 2kl B_{23} + 2hl B_{13})].$$

	<i>B</i> ₁₁	<i>B</i> ₂₂	<i>B</i> ₃₃	<i>B</i> ₁₂	<i>B</i> ₂₃	<i>B</i> ₁₃
Br(<i>A</i>)	44	117	12	5	6	0
Br(<i>B</i>)	22	96	22	3	5	-1

Table 2(a). *Bond lengths for the two molecules in the asymmetric unit*

	<i>d</i> (Å) Molecule <i>A</i>	<i>d</i> (Å) Molecule <i>B</i>	<i>d</i> (Å) Average
C(13)—C(14)	1.54	1.51	1.52 ₅
C(13)—C(15)	1.54	1.50	1.52
C(12)—C(13)	1.50	1.52	1.51
C(11)—C(12)	1.62	1.54	1.58
C(11)—C(3)	1.50	1.51	1.50 ₅
C(3)—C(4)	1.35	1.34	1.34 ₅
C(4)—O(2)	1.35	1.29	1.32
O(2)—C(12)	1.49	1.53	1.51
C(3)—C(2)	1.45	1.43	1.44
C(2)—O(1)	1.24	1.31	1.27 ₅

Table 2(a) (cont.)

	$d(\text{\AA})$ Molecule A	$d(\text{\AA})$ Molecule B	$d(\text{\AA})$ Average
C(2)—N(1)	1.36	1.36	1.36
N(1)—C(10)	1.53	1.52	1.52 ₅
N(1)—C(16)	1.41	1.40	1.40 ₅
C(16)—C(17)	1.41	1.44	1.42 ₅
C(17)—C(4)	1.45	1.45	1.45
C(17)—C(5)	1.41	1.39	1.40
C(5)—C(6)	1.34	1.39	1.36 ₅
C(6)—C(7)	1.44	1.42	1.43
C(7)—C(8)	1.42	1.37	1.39 ₅
C(8)—C(16)	1.38	1.37	1.37 ₅
C(7)—O(3)	1.31	1.39	1.35
O(3)—C(9)	1.44	1.43	1.43 ₅
C(9)—O(4)	1.42	1.41	1.41 ₅
O(4)—C(8)	1.38	1.37	1.37 ₅

Table 2(b). Bond angles for the two molecules in the asymmetric unit

	Molecule A	Molecule B	Average
C(14)—C(13)—C(15)	111°	108°	109 ₅ °
C(12)—C(13)—C(15)	108	111	109 ₅
C(12)—C(13)—C(14)	113	116	114 ₅
O(2)—C(12)—C(13)	110	107	108 ₅
O(2)—C(12)—C(11)	104	104	104
C(11)—C(12)—C(13)	115	116	115 ₅
C(3)—C(11)—C(12)	101	101	101
C(4)—C(3)—C(11)	111	110	110 ₅
C(4)—C(3)—C(2)	120	119	119 ₅
C(2)—C(3)—C(11)	129	131	130
N(1)—C(2)—C(3)	116	120	118
N(1)—C(2)—O(1)	119	116	117 ₅
O(1)—C(2)—C(3)	126	124	125
C(16)—N(1)—C(2)	126	122	124

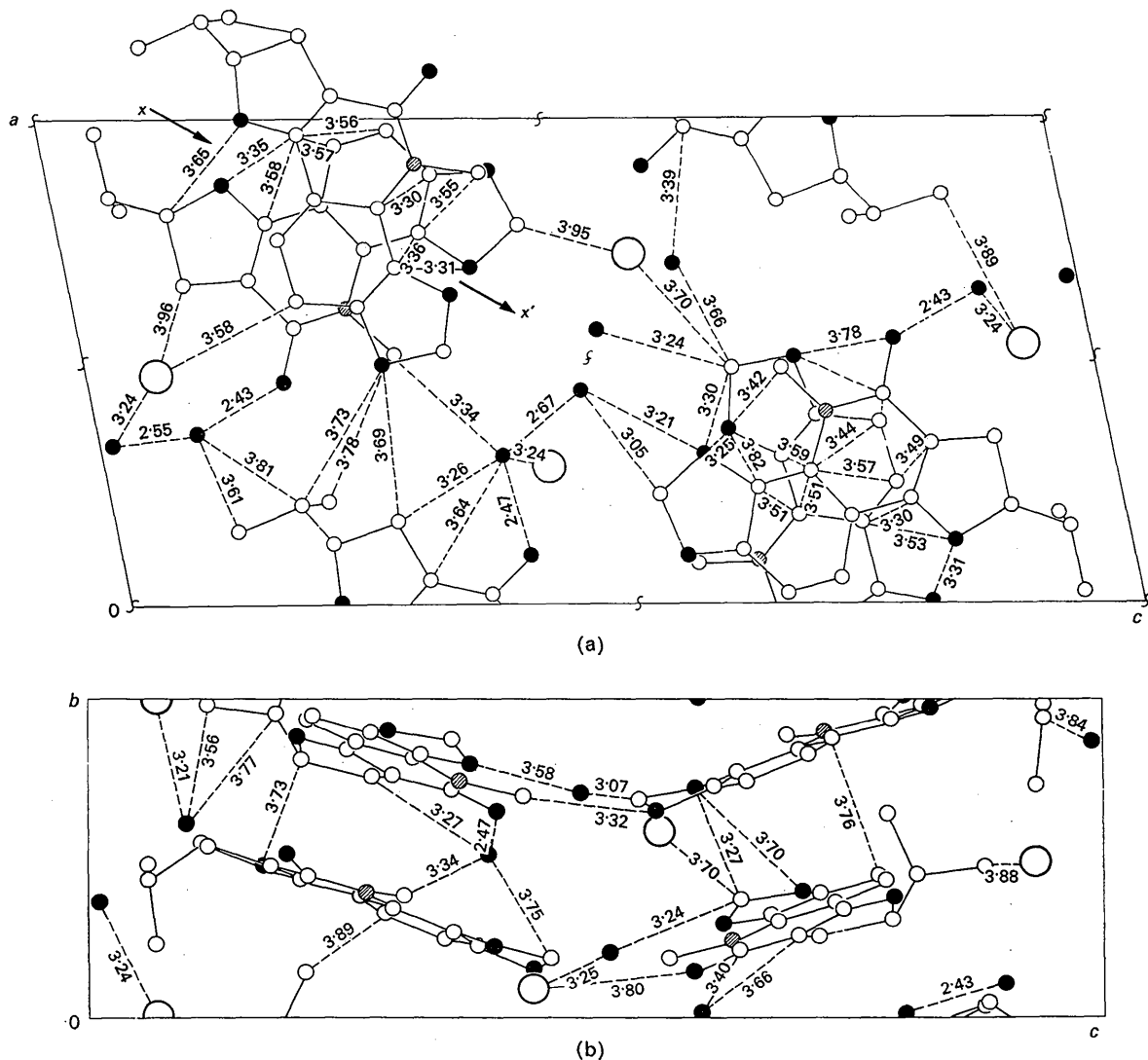


Fig. 2. Molecular structure of isolunine hydrobromide dihydrate. Diagram of the structure projected down (a) [010] and (b) [100]. Selected approach distances are indicated. Larger open circles, Br; small open circles, C; small filled circles, O; small lined circles, N.

Table 2(b) (cont.)

	Molecule A	Molecule B	Average
C(16)—N(1)—C(10)	118	122	120
C(10)—N(1)—C(2)	116	116	116
N(1)—C(16)—C(17)	119	120	119 ₅
N(1)—C(16)—C(8)	125	125	125
C(8)—C(16)—C(17)	115	114	114 ₅
C(16)—C(17)—C(4)	115	115	115
C(16)—C(17)—C(5)	122	124	123
C(4)—C(17)—C(5)	123	121	122
C(17)—C(4)—C(3)	125	123	124
C(17)—C(4)—O(2)	121	121	121
C(3)—C(4)—O(2)	114	115	114 ₅
C(6)—C(5)—C(17)	124	120	122
C(5)—C(6)—C(7)	116	113	114 ₅
C(6)—C(7)—C(8)	120	127	123 ₅
C(6)—C(7)—O(3)	129	124	126 ₅
O(3)—C(7)—C(8)	111	110	110 ₅
C(7)—C(8)—O(4)	106	109	107 ₅
C(7)—C(8)—C(16)	123	121	122
O(4)—C(8)—C(16)	131	130	130 ₅
C(7)—O(3)—C(9)	106	105	105 ₅
C(8)—O(4)—C(9)	106	107	106 ₅
O(3)—C(9)—O(4)	107	107	107

Table 3. Some intermolecular approach distances

	$d(\text{Å})$		$d(\text{Å})$
O(2A)····C(4B)	3·35	O(6B)····C(2B)	3·39
C(16B)····C(7A)	3·30	O(4A)····C(9B)	3·30
C(8A)····C(8B)	3·36	O(4A)····O(4B)	3·25
O(4A)····C(8B)	3·31	O(4B)····C(10A)	3·42
C(11B)····O(6B)	3·26	C(8A)····C(16B)	3·51
O(6B)····C(10A)	3·34	C(16B)····C(16A)	3·51
O(5B)····C(9B)	3·24	C(16A)····C(6B)	3·44
O(5B)····O(4A)	3·21	C(5B)····C(3A)	3·49
O(5B)····C(9A)	3·05	C(17B)····C(4A)	3·30
O(2A)····O(2B)	3·31	O(1B)····O(6B)	2·47
O(4A)····C(9B)	3·30	O(5A)····O(6A)	2·55
O(5B)····C(9B)	3·24	O(5B)····O(6B)	2·67
O(6B)····C(11B)	3·26	Br(A)····O(6B)	3·21
C(10B)····O(3A)	3·31	Br(B)····O(6B)	3·24
O(5B)····C(9A)	3·05	Br(A)····O(5A)	3·24
O(1A)····O(6A)	2·43	Br(B)····O(5B)	3·25

Absolute configuration

The absolute configuration of the structure has been determined by application of Bijvoet's technique (Bijvoet, Peerdeman & van Bommel, 1951) with the anomalous scatter of Cu $K\alpha$ radiation by the Br atoms. Components f'' and f''' were from Dauben & Templeton (1955).

The reflexions selected as most advantageous for visual comparison are given in Table 4 with tabulated values of $A_0B_{Br} - B_0A_{Br}$, as given in (2) (Patterson, 1963) in accord with a right-handed set of axes,

$$D_f = \frac{1}{2} \{ |F_{hkl}^+|^2 - |F_{hkl}^-|^2 \} = - \frac{2Af'''}{f} (A_0B_{Br} - B_0A_{Br}). \quad (2)$$

Table 4. Comparison of intensities $I(hkl)$ and $I(\bar{h}\bar{k}\bar{l})$ with the values $(A_0B_{Br} - B_0A_{Br})$ for absolute configuration determination

A_0 and B_0 refer to structure factor components for the complete structure and A_{Br} and B_{Br} to the Br ions only, based on a right-handed set of axes.

Index	$I(hkl) \gtrless I(\bar{h}\bar{k}\bar{l})$	$(A_0B_{Br} - B_0A_{Br})$
0, 1, 6	<	226
0, 1, 9	>	-510
0, 1, 10	<	496
0, 1, 17	<	321
1, 1, 6	<	860
1, 1, 13	<	151
1, 1, 14	>	-297
1, 2, 4	<	700
1, 2, 9	>	-816
1, 2, 10	>	-234
1, 2, 11	>	-297
1, 2, 12	>	-950

Discussion

The two molecules of isoleucine in the asymmetric unit are shown by the X-ray analysis to be structurally identical. In respect of the assessment of dimensional accuracy and, indirectly, of the validity of the assessment of standard deviations in conventional least-squares refinement procedures, this identity has certain advantages, as noted e.g. for gliotoxin (Fridrichsons &

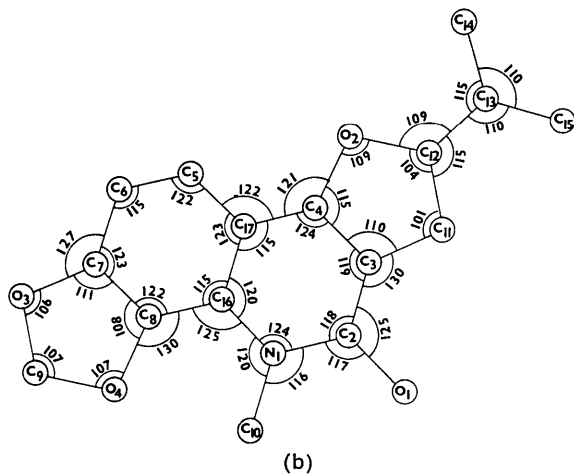
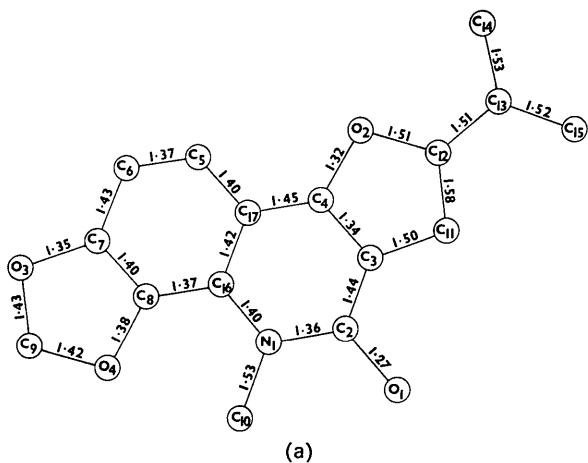


Fig. 3. Values of bond lengths (a) and angles (b) for isoleucine corresponding to the mean of the two entities in the asymmetric unit.

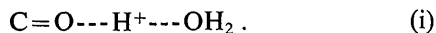
Mathieson, 1967) and α -bromo-isotutinone (Mackay & Mathieson, 1965). From this internal evidence, it appears probable that the standard deviation of bond lengths is of the order of 0.03–0.04 Å.

The structure of the molecule is given as (I), the rings *B* and *C* forming a quinoline system which, with its direct substituent atoms, is essentially planar, within ± 0.07 Å [see Fig. 2(b)] compatible with the sp^2 hybridization in this component. Only C(9) of ring *A* and C(12), C(13), C(14) and C(15) of the terminal isobutyl group deviate markedly from the main plane of the molecule, rings *A* and *D* having an envelope conformation.

The aromatic C–C bond lengths in ring *B* are normal while the bond lengths in ring *C* reflect the association of the double bond C(3)–C(4) (1.34 Å), the lactam group C(3), C(2), O(1), N(1), C(10), C(16) (with its short central bond C(2)–N(1), 1.36 Å) and ring *B*, the sp^2 hybridization reducing the bonds C(3)–C(2) and C(4)–C(17) to ~ 1.45 Å. For the C–O bonds, those involving C(sp^3) have a mean of 1.45 Å, those with C(sp^2) 1.35 Å.

In this crystal structure, layers of *A* molecules are interleaved with layers of *B* molecules, the layers being at a small angle to [010] (Fig. 2). The environment of each molecule in the asymmetric unit is similar with respect to water molecules and Br ions, molecule *A* and molecule *B* being related by an approximate non-crystallographic twofold symmetry axis, XX' in Fig. 2(a). Hydrogen bonds involving the Br ions, water molecules and the lactam oxygen atom O(1) hold together the separate arrays of *A* and *B* molecules but no such bonding links the two arrays. These two independent hydrogen bonding systems form spiral chains running throughout the structure approximately parallel to [010], essential features in one such system being represented in Fig. 4.

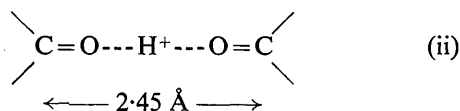
Certain details of the results are of some chemical relevance in that no simple cation–anion relationship is indicated by the crystal structure. The inter-molecular approach distances, Table 3, reveal no close association between the Br ion and the organic molecule, the closest approaches being Br(*A*)...O(1*A*), 3.79 Å; Br(*A*)...C(9*B*), 3.70 Å; Br(*A*)...C(6*B*), 3.76 Å; Br(*B*)...C(6*A*), 3.59 Å and Br(*B*)...C(15*A*), 3.90 Å, Fig. 2. The only approach distances which appear significant in respect to the Br ion are Br...O(5) and Br...O(6), both of 3.24 Å. The feature which is striking is the close approach of the water oxygen atom O(6) to the lactam oxygen atom, O(1), 2.45 Å, constituting a strong hydrogen bond which can arise only owing to the existence of a proton near the mid-point. From the dimension, there seems little doubt that the potential has a single minimum and presumably the proton, H^+ , at the mid-point, the situation being as indicated in (i).



As a result, the lactam C=O bond length, mean 1.27 Å, is found to be significantly longer than the normal value

of 1.19–1.20 Å (Sutton, 1965). It may also be worth comment that the O(1)–H–O(6) bond lies approximately in the lactam plane with the angle C(2)–O(1)–O(6), *circa* 130°.

The observation concerning the lactam oxygen–proton–water oxygen group proves to have a much wider significance than at first appears. In fact, it appears to be a central observation in a series of similar groupings involving oxygen atoms in surprisingly different states. Thus, consideration of the crystal structure of the 2:1 adduct of mesitaldehyde–perchloric acid by Fisher, Jensen & Schubert (1965) revealed that the two molecules of mesitaldehyde are linked by the intermediary of the proton, the dimensional pattern and the conformation detail relative to the carbonyl group in isolunine being repeated, (ii),



with the inter-oxygen distance, 2.45 Å and the C–O–O angle being again $\sim 130^\circ$. Also the inductive effect on the C–O bond length is again indicated, the mean C=O being 1.25 Å. Thus the pattern is revealed between two carbonyl groups and between a carbonyl and a water molecule. The question arose as to whether a similar situation had been detected where two water molecules are associated with a proton. An example appeared

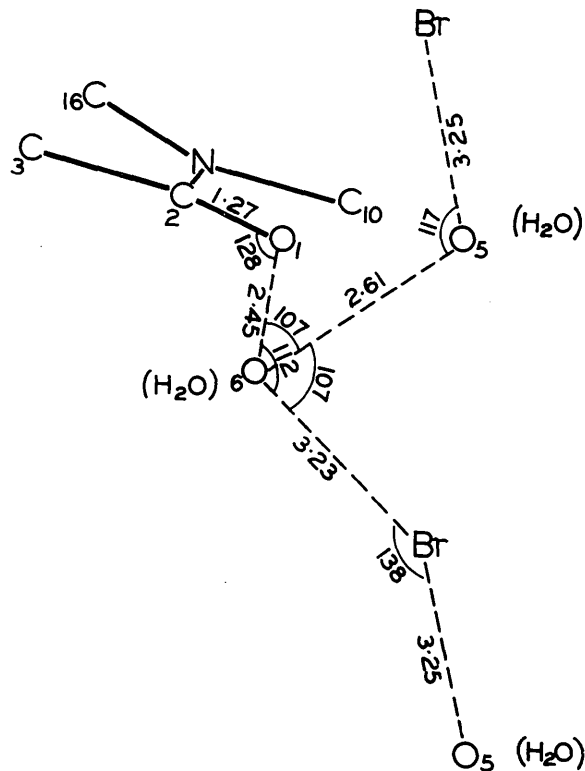
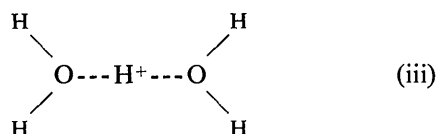


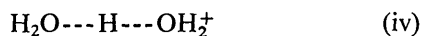
Fig. 4. Details of hydrogen-bonding in isolunine hydrobromide dihydrate.

shortly afterwards when Williams (1967) reported on a neutron diffraction study of a compound studied earlier by X-ray (Nakahara, Saito & Kuroya, 1965) and revealed the existence of the entity ($\text{H}_2\text{O}-\text{H}^+-\text{OH}_2$) with the inter-oxygen distance, $2.50 \pm 0.03 \text{ \AA}$. Additional data established this observation in the analyses of $\text{HCl} \cdot 2\text{H}_2\text{O}$ (Lundgren & Olovson, 1967*a*) and $\text{HCl} \cdot 3\text{H}_2\text{O}$ (Lundgren & Olovsson, 1967*b*) with $d(\text{O}-\text{O})$ of 2.44 and 2.45 \AA (values corrected for independent motion) respectively, (iii).



The question as to whether small changes occur in the O-H bond lengths of the water molecules (*i.e.* other than those involving the proton) is an interesting one in respect of the likely inductive effect of the O-H⁺-O group. These dimensional details warrant careful investigation in future.

The examples above referred to what may be described as neutral oxygen atoms. It is therefore intriguing to note the summary of observations which Speakman (1967) has made as a result of 7(+1) very careful refinements of carboxylic acid salts of the type $\text{M}^+\text{H}^+\text{X}_2^-$. He reports that the inter-oxygen distance is 2.446 \AA (with a standard deviation of 0.003 \AA) and a subsequent report (Ferguson, Sime, Speakman & Young, 1968) buttresses this pattern of constancy. It is therefore evident that even with oxygen atoms bearing a full or partial real charge (depending on the precise description of the charge allocation) the constancy of interatomic distance is retained. The implications of these observations are being followed up. One proposal arising from these observations is that the *bioxonium* ion, (iv),



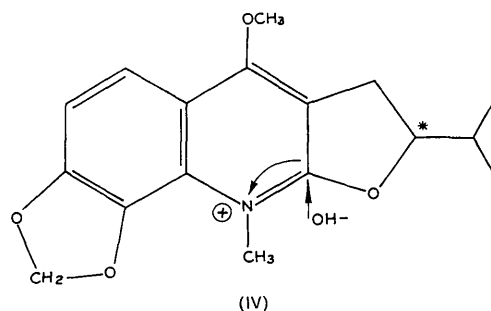
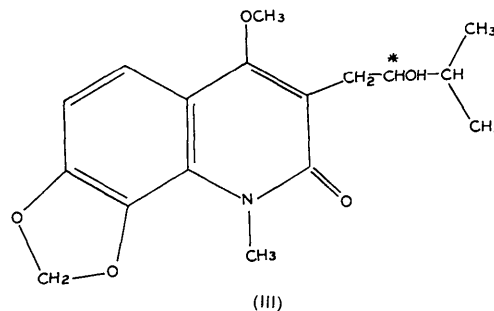
is a stable entity in aqueous solutions of acids (Beecham *et al.*, 1968). The further implications of this proposal for the reassessment of the kinetic and electrical mobility behaviour of hydrated protons in solutions appear to be considerable. It appears likely that the present observations may lead to further valuable conclusions.

Relationship of isolunine to lunine

The compound on which the X-ray analysis was carried out has been shown to be identical with (-)-isolunine derived from the alkaloid, (-)-lunine (II), isolated from *Lunasia quercifolia* (Warb.) Lauterb. and K. Schum. (Goodwin, Shooley & Johnson, 1959; Hart & Price, 1966).

The probable relationship of lunine to isolunine is indicated by the following reactions. In alkaline solution, (-)-lunine methiodide yields (+)-lunidine (III) which, on heating in aqueous acid, affords the laevoro-

tatory, more weakly basic isomer of lunine, isolunine (I), which is therefore the angular isomer of lunine. The formation of isolunine from lunine follows the analogous sequence by which (-)-lunacrine methiodide is converted *via* (+)-lunacridine to (+)-lunacrine and the corresponding laevorotatory angular isomer of lunacrine. It has been argued that the hydrolysis of (-)-lunacrine (and consequently that of (-)-lunine) proceeds without inversion at the asymmetric centre, *, according to the mechanism indicated in relation to (IV) and that the cyclization step involves inversion (Goodwin & Hornig, 1959; Price, 1959). If the interpretation on the basis of this mechanism is correct, normally occurring (-)-lunine should have an absolute configuration opposite to that determined for (-)-isolunine, (I), and be represented by (II). An absolute configuration determination has not been previously reported for any of the alkaloids of the isopropylidihydrofuroquinoline group (Boit, 1961) having an asymmetric centre in the isoprenyl group for any derivatives.



We are grateful to Dr J.A. Wunderlich* for the mass-spectrometric measurements on the material (I), and their interpretation. Also to Drs. J.A. Lamberton* and S.R. Johns* for the synthesis of (-)-isolunine from (-)-lunine. We would like to express appreciation to Dr J.C.B. White† for making available his modified version of the structure-factor least-squares program (ORFLS) of Busing & Levy and for his Fourier synthesis program MUF2.

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The Crystal Structure of Calcium Sodium Hypophosphite, $\text{CaNa}(\text{H}_2\text{PO}_2)_3$

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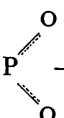
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(Received 3 October 1968)

The crystal structure of $\text{CaNa}(\text{H}_2\text{PO}_2)_3$, a double salt of calcium and sodium hypophosphites, has been determined. The crystal belongs to the cubic system, space group $P2_13$, $Z=4$, with the lattice constant $a=9.720 \pm 0.003 \text{ \AA}$. Refinement of the structure was carried out by the full-matrix least-squares method including anisotropic thermal parameters. The final R value for 705 observed reflexions was 0.097. The structure consists of two kinds of octahedral groups, one with a calcium atom and the other with a sodium atom. Each oxygen atom of the hypophosphite ions is coordinated to each one of the calcium and sodium atoms to form the octahedra. The present structure is considered to be typical of the double salts of hypophosphorous acid. The structural similarities with langbeinite, $\text{Mg}_2\text{K}_2(\text{SO}_4)_3$, are discussed.

Introduction

In the course of a study on the structures of nucleic acid constituents, in which the infrared characteristic ab-

sorption bands of the P  - groups in various hypo-

phosphites were investigated, we found a new form of a hypophosphite, crystallized in the cubic system. The hypophosphites whose crystal structures have been studied so far are $\text{NH}_4\text{H}_2\text{PO}_2$ (orthorhombic; Zachariasen & Mooney, 1934), $\text{Mg}(\text{H}_2\text{PO}_2)_2 \cdot 6\text{H}_2\text{O}$ (tetragonal; Pedrazuela, Garcia-Blanco & Rivoir, 1953), $\text{Ca}(\text{H}_2\text{PO}_2)_2$ (monoclinic; Loopstra, 1958) and KH_2PO_2

(monoclinic; Akimoto, 1965). The present crystal possesses the highest symmetry of these salts and it seemed to be interesting to determine its crystal structure. The result showed that the compound is actually a double salt of calcium and sodium hypophosphites having the chemical formula of $\text{CaNa}(\text{H}_2\text{PO}_2)_3$.

Experimental

The crystals of $\text{CaNa}(\text{H}_2\text{PO}_2)_3$ were obtained by slow evaporation of an aqueous solution prepared by adding $\text{Ca}(\text{H}_2\text{PO}_2)_2$ to the saturated aqueous solution of $\text{Na}(\text{H}_2\text{PO}_2) \cdot \text{H}_2\text{O}$. They crystallize in the form of a cubic dodecahedron with well developed $\{110\}$ faces. The lattice constant was measured on a powder diffractometer with the use of silicon powder as an internal