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The Crystal Structure of Lucidusculine Hydriodide

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Crystals of lucidusculine hydriodide (C24H35O4N. HI) are orthorhombic, with space group P212121 and lattice parameters a = 15.94, b = 14.29, c = 10.20 Å, containing four molecules in the unit cell. The structure was solved by the heavy atom method using three-dimensional Fourier and difference Fourier syntheses. The refinement was carried out by full-matrix least-squares calculations including isotropic temperature factors. The final R index for 1092 nonzero reflexions was 0.133. The absolute configuration was established by the anomalous dispersion method.

The molecule is composed of four six-membered rings, three of which have the boat configuration and one the chair configuration. The jodine atom lies between the two alcoholic hydroxyl groups of the same molecule, and a hydrogen-bonded chelate structure is suggested. Within the crystal, the molecules are linked together by hydrogen bonds in the a direction, forming a chain which is packed sideways by van der Waals forces.

Introduction

The diterpene alkaloid lucidusculine was extracted from Aconitum lucidusculum by Majima & Morio (1931, 1932). Later, the chemical structure of this compound was studied by Suginome, Amiya & Shima (1959) who suggested the presence of an allyl acetate group, a secondary hydroxyl group and an N-ethyl group. Amiya (1960, 1961) obtained a phenanthrene derivative by selenium oxide reduction and proposed a partial structure. Further study by chemical methods was suspended owing to difficulties in getting enough of the sample. The present X-ray study is therefore undertaken in order to determine the molecular structure of lucidusculine.

Experimental

We isolated lucidusculine from Aconitum yoesoensis Nakai and purified it in the form of the quaternary ammonium perchlorate. In order to determine the molecular structure, a heavy atom salt, the hydriodide,

was prepared by exchanging the anion ClO₄ with the I- anion over the ion exchange resin Amberlite IRA-410. The crystals of lucidusculine hydriodide were recrystallized from aqueous methanol. They are colorless prisms with well developed {110} planes and elongated along the c axis. The density was measured by the flotation method with a mixture of benzene and carbon tetrachloride. The cell dimensions and space group were determined from rotation and Weissenberg photographs taken with Cu $K\alpha$ radiation.

Crystal data

Lucidusculine hydriodide C₂₄H₃₅O₄N . HI.

Mol.wt. 529·0

m.p. 249-250°C

Orthorhombic

 $a = 15.94 \pm 0.02$, $b = 14.29 \pm 0.02$, $c = 10.20 \pm 0.015$ Å

 $U = 2349.8 \text{ Å}^3$

 $D_m = 1.478 \text{ g.cm}^{-3}$, $D_x = 1.496 \text{ g.cm}^{-3}$, Z = 4Linear absorption coefficient for Cu $K\alpha$ radiation, $\mu = 128.5 \text{ cm}^{-1}$

F(000) = 1088

Absent reflexions: h00 when h is odd, 0k0 when k is odd, 00l when l is odd

Space group $P2_12_12_1$

The three-dimensional reflexions of $h0l \sim h3l$ and $hk0 \sim hk6$ were recorded with Cu $K\alpha$ radiation on equinclination Weissenberg photographs taken about the b and c axes using the multiple-film technique. The intensities of reflexions were visually estimated by using a standard scale. The c axis X-ray specimen prepared

for the intensity measurements was a cylindrical rod crystal elongated along the c axis and 0.133 mm in diameter. Since the μR value was about 1.0 the absorption correction was not applied. During the exposure of X-rays, the thin rod-like specimen bent plastically under its own weight, so that the sizes of the reflexion spots varied with the reflexion position of the crystal. A spot size correction was therefore necessary for the measurement of integrated intensities. All intensity data were then corrected for Lorentz and polarization factors. The resulting values were put on a single scale and a total of 1803 structure factors were finally evaluated. A Wilson plot was then made using the hk0 reflexions, which gave an approximate scale factor and an overall temperature factor B with the value 4.5 Å².

Table 1. The final fractional atomic coordinates, temperature factors and their standard deviations

				-	•			
	x/a	$\sigma(x/a)$	y/b	$\sigma(y/b)$	z/c	$\sigma(z/c)$	$B(\text{\AA}^2)$	$\sigma B(\text{Å}^2)$
I(1)/2	0.10914	0.00042	0.38553	0.00049	-0.05255	0.00081	4.93	0.18
I(2)/2	0.09944	0.00042	0.37845	0.00049	-0.11443	0.00081	4.85	0.18
C(1)	-0.09094	0.0023	-0.01131	0.0023	0.12176	0.0039	4.27	0.84
C(2)	-0.12206	0.0023	0.06468	0.0025	0.23438	0.0041	4.67	0.92
C(3)	0.04376	0.0023	0.11828	0.0032	0.28657	0.0043	5.53	0.92
C(4)	0.01704	0.0021	0.15714	0.0022	0.19301	0.0039	3.55	0.73
C(5)	0.18458	0.0025	0.17035	0.0028	0.11569	0.0047	5.46	1.05
C(6)	0.27718	0.0022	0.16472	0.0024	0.05919	0.0045	5.36	0.89
C(7)	0.28521	0.0019	0.11261	0.0026	-0.07640	0.0041	4.43	0.74
C(8)	0.19952	0.0020	0.11146	0.0028	-0.14068	0.0038	4.48	0.78
C(9)	0.06685	0.0019	0.00257	0.0021	-0.09856	0.0041	3.55	0.72
C(10)	0.03675	0.0023	−0.07588	0.0025	-0.00707	0.0042	4.73	0.93
C(11)	0.00655	0.0021	-0.02105	0.0022	0.12189	0.0039	3.51	0.76
C(12)	0.04446	0.0020	0.08348	0.0023	0.10060	0.0044	3.98	0.81
C(13)	0.14234	0.0017	0.06783	0.0019	0.09611	0.0039	2.40	0.64
C(14)	0.15749	0.0022	0.03358	0.0025	-0.05764	0.0045	4.99	0.90
C(15)	-0.13656	0.0020	<i>−</i> 0·09975	0.0025	0.15297	0.0038	4.07	0.86
C(16)	-0 ⋅11886	0.0023	0.02456	0.0024	-0.00954	0.0039	4.19	0.86
C(17)	0.02773	0.0019	0.09842	0.0022	-0.05975	0.0040	4.11	0.98
C(18)	0.30491	0.0022	0.01236	0.0024	-0.04900	0.0041	4.77	0.89
C(19)	0.22423	0.0021	- 0·04788	0.0024	-0.06498	0.0044	4.88	0.83
C(20)	0.37926	0.0026	-0.02051	0.0027	0.00734	0.0041	6.01	1.02
C(21)	-0.08435	0.0019	0.11055	0.0024	-0.22658	0.0036	3.74	0.75
C(22)	-0.04517	0.0030	0.20015	0.0035	-0.27756	0.0052	7.77	1.34
C(23)	0.23414	0.0032	-0.21005	0.0037	-0.00595	0.0061	7.96	1.37
C(24)	0.24133	0.0019	-0.26823	0.0021	0.11705	0.0037	4.06	0.72
N(1)	-0.07036	0.0014	0.10209	0.0018	-0.08114	0.0032	3.92	0.60
O(1)	-0.02475	0.0015	0.23260	0.0016	0.12346	0.0025	4.20	0.57
O(2)	0.29335	0.0015	0.26603	0.0017	0.03270	0.0026	5.52	0.64
O(3)	0.22072	0.0013	-0.11519	0.0018	0.04484	0.0024	4.97	0.53
O(4)	0-22297	0.0022	-0.22619	0.0026	-0.11384	0.0042	9.77	0.99

Mean standard deviations

	$\sigma(x/a)$		$\sigma(y/b)$		$\sigma(z/c)$
I	0.00042	C	0.00049		0.00081
	$\sigma(x) \ (0.0064 \ \text{Å})$	$\sigma(y)$ (0)·0056 Å)	$\sigma(z)$	(0.0081 Å)
С	0.0022	(0.0026		0.0042
	(0·035 Å)	(()·040 Å)		(0·035 Å)
N	0.0014	ď)·0018		0.0032
	(0·022 Å)	(0)·025 Å)		(0·032 Å)
О	0.0016	ď	0.0019		0.0029
	(0·025 Å)	(()·027 Å)		(0·029 Å)
I	$\sigma(r) = 0.006 \text{ Å}$	С	$\sigma(r) = 0.038$	Å	
N	$\sigma(r) = 0.027 \text{ Å}$	О	$\sigma(r) = 0.027$	Å	

Mean estimated standard deviations in bond lengths $\sigma(C-C) = 0.05 \text{ Å}$ $\sigma(C-N) = 0.04 \text{ Å}$ $\sigma(C-O) = 0.04 \text{ Å}$

Mean estimated standard deviations in tetrahedral bond angles $\sigma(\text{C-C-C}) = 2 \cdot 8^{\circ}$

Determination of the structure

The positions of iodine atoms were determined by the calculation of the three-dimensional sharpened Patterson sections at $u=\frac{1}{2}$, $v=\frac{1}{2}$ and $w=\frac{1}{2}$. The first three-dimensional Fourier synthesis utilizing the phase angles given by the contributions of the iodine atoms revealed twelve light atoms as well-defined peaks. The electron density map also showed a pronounced anisotropic thermal vibration of the iodine atom. A Wilson plot using the h0l data gave a large B value of 6.5 Å^2 compared with that obtained from the hk0 data and, this fact suggested a kind of anisotropy of the iodine atoms. The effect of such an anisotropy in thermal vibrations on the structure factor calculation was allowed for by placing two iodine atoms of one half multiplicity along the c axis. The above mentioned twelve peaks were then

included in the next structure factor calculation assuming all were carbon atoms, and thus we found four more atoms in the second Fourier map. A third set of calculations showed a further ten atoms. However, a subsequent difference Fourier synthesis, including the contributions of the above twenty-six light atoms besides two iodine half atoms, indicated that one of these atoms was improperly located. The fifth set of similar calculations showed two further atoms and the sixth set showed the last one. On the basis of peak height considerations and the result of chemical investigation, it was possible to distinguish all oxygen atoms from carbon and nitrogen, except the O(4) atom of the acetate group, which was tentatively identified because of the shorter interatomic distance. Later, in the course of least-squares refinement, fairly large changes took place in the bond lengths C(23)-O(4) and C(23)-C(24),

Table 2. Observed and calculated structure factors

1	0.00 116.39 116.39 -0.1% 0.00 0.04 1 0.00 35.92 35.97 5.70 0.70 9.50 0.00-130.39 130.05 7.53 0.70 25.40 0.00-25.40 25.40 0.00 25.40 25.40 0.00 25.40 25.40 0.00 3.50 0.00 3.50 0.00 3.50 0.00 3.50 0.00 3.50 0.00 3.50 0.00 3.50 0.00 3.50 0.00 3.60 0.00 3.60 0	7	0 2-79 1.00 12-41 1-41 1-41 1-41 1-41 1-41 1-41 1-4	A-33 113 1-46 215 1-46 2	0 25.51 0.00 -15.60 25.71 -12.92 0.00 0 0.00 0.00 2.01 0 1.20 2.02 0 1.20 2.02	0 29-24 0 76-69 0 76-69 0 76-69 0 76-69 1 10-03 1 1	10 3 3 112 3 3 112 3 3 112 3 3 112 3 3 112 3 3 112 3 3 112 3 3 112 3 3 112 3 3 112 3 3 112 3 3 112 3 3 112 3 3 112 3 3 112 3 3 112 3 3 112 3 3 3 3		-14-7 -3-59 -11-53 6-75 -2-91 -2-99 -161-20 -5-99 -49-39 -74-57 -74-57 -74-57 -12-60 -61-07 -41-72	3:1020 1 1266237533643671 11 1 75664866366331121
19 11 12 2 2 0 0 10 0 1 1 2 1 2 1 1 1 1 1		1 9 0 64-4 5 9 0 0 75-7 5 9 0 0 75-7 5 9 0 0 75-7 5 9 0 0 75-7 5 9 0 0 10-1 10 9 0 10-1 10 9 0 10-1 10 9 0 10-1 10 10 0	11 3.00 - 0.00 1	2-25 4 16 10 16 17 16 16 17 17 16 16	0 25.71 0.00 -10.60 0 25.71 -12.92 0.00 0 -0.00 0.00 0.00 0 7.90 1.20 0.00 0 18.27 0.00 9.50 0 6.12 7.69 0.00 0 13.62 0.00 -8.21 0 0.00 -2.62 0.00 0 16.57 0.00 -17.51 0 0.00 -2.61 0.00 0 0.00 -2.61 0.00 0 7.12 0.77 0.00		1 23 4 3 5 7 7 9 7 1 3 1 3 1 3 1 3 1 3 1 3 3 4 3 5 7 7 9 9 0 1 1 1 1 1 3 8 3 5 5 5 5 5 5 7 7 7 7 7 7 7 7 7 7 7 7 7	George G	1100 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	5644863663311217 1 13 46042272332121 1110056136920742721111 5433334307 129111 1 2402169837151111

and the assignment of C(24) and O(4) was therefore changed as described later. The nitrogen atom was identified from the chemical consideration that the nitrogen atom is to be bonded to an ethyl group.

Refinement of the structure

Further refinement of the structure was carried out on an IBM 7090 computer using the full-matrix least-squares program ORFLS (Busing, Martin & Levy, 1962). Since the main purpose of the present determination was the elucidation of the molecular structure of lucidusculine, the refinement with individual anisotropic temperature factors was considered to be not necessary except for the iodine atom. The iodine atom was therefore divided into two atoms of one half multiplicity separated by 0.5 Å from each other. The struc-

ture now contains 31 atoms in an asymmetric unit (excluding hydrogen atoms) and the number of parameters came out to be 125. The program was then modified to vary blocks of parameters successively during each cycle of refinement. The parameters were divided into two blocks, the first containing one scale factor and the parameters of 24 atoms (constituting the A. B, C and E rings), and the second containing those of other atoms. The experimentally unobserved reflexions were not included in the refinement. The hydrogen atoms were also excluded from the calculation. The weighting system was chosen so that the program gave unit weight to each observation. After three cycles of refinement with 1092 reflexions, the R value dropped from 0.222 to 0.133. Comparison with the initial values showed that a few parameters had changed by amounts about 2-3 times their final estimated standard

Table 2 (cont.)

3 12 1 1 1 2 2 2 1 1 1 1 2 2 2 1 1 1 1 1		4 1 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	1 10-43 -7-7 0.00 7.77 1 10-43 -7-7 0.00 17.77 1 10-43 -7-7 0.00 17.77 1 10-43 -7-7 0.00 17.77 1 10-43 -7-7 0.00 17.77 2 10-43 11-43 0.00 17.47 2 10-43 11-43 0.00 17.47 2 10-43 11-43 0.00 17.47 2 10-43 11-43 0.00 17.47 2 10-43 11-43 0.00 17.47 2 10-43 11-43 0.00 17.47 2 10-43 11-43 0.00 17.47 2 10-43 11-43 0.00 17.47 2 10-43 11-43 0.00 17.47 2 10-43 11-43 0.00 17.47 2 10-43 11-43 0.00 17.47 2 10-43 11-43 0.00 17.47 2 10-43 11-43 0.00 17.47 2 10-43 11-43 0.00 17.47 2 10-43 11-43 0.00 17.47 2 10-43 11-43 0.00 17.47 2 10-43 11-43 0.00 17.47 2 10-43 11-43 0.00 17.47 2 10-43 11-43 0.00 17.47 2 11-43 0.00 17.47 2 11-43 0.00 17.4	11 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1. 1. 1. 1. 1. 1. 1. 1.	17. % 1 1 1 1 1 1 1 1 1 1		1
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deviations and consequently some of the bond lengths changed by amounts of about 0.10 Å.

At this stage, the final Fourier synthesis was computed. The resulting superimposed contour sections, illustrating the three-dimensional electron density distribution, drawn parallel to (010), are shown in Fig. 1. The final fractional atomic coordinates and temperature factors are given in Table 1, together with their standard deviations.

The averages of the standard deviations of the positional parameters in Å may be estimated as: for iodine atoms $\sigma(r) = 0.006$ Å, for carbon atoms $\sigma(r) = 0.038$ Å, for oxygen atoms $\sigma(r) = 0.027$ Å and for nitrogen atoms $\sigma(r) = 0.027$ Å. The observed and calculated structure factors are listed in Table 2. The atomic scattering factors used for the present structure determination were: for iodine, those of Thomas & Umeda (1957),

and for oxygen, nitrogen and carbon, those of Berghuis, Haanappel, Potters, Loopstra, MacGillavry & Veenendaal (1955).

Determination of the absolute configuration

The absolute configuration of lucidusculine has not yet been studied by chemical methods. The present study has determined the absolute structure, using the anomalous dispersion method (Bijvoet, Peerdeman & van Bommel, 1951). The dispersion correction for the iodine scattering factor for Cu $K\alpha$ radiation was given by Dauben & Templeton (1955) as $\Delta f' = -1.1$ and $\Delta f'' = 7.2$. The structure factors were calculated from the atomic parameters of Table 1 by assuming a right handed set of axes. Of the 48 pairs of reflexions in hk1 and hk2, for which the intensity differences in I(hk1)

Table 2 (cont.)

Table 2 (cont.)

2 1 1	5 63.71 0.00 -65.74 65.	S I 13 S	5 0.00 11.75 -7.56	14.05	1 2 0 1	13.79 -10.05 0.00 10.95	1 4 7	\$ 15-51 -11-55 11-17 16-07
	5 14-51 -0-55 5-41 5-		5 40-75 0-00 44-57	45-57	301	3.51 -9.53 0.33 5.43		\$ 20-50 5-15 12-10 14-55
3 1 1	15.52 -15.71 -35.46 53			23.53	4 3 1		1 7 7	\$ 4.09 -2.01 -5-25 6.47
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11 1 7	5 15-12 15-99 11-46 19-			18.42	13 0 1			6 19.79 -7.05 14.70 17.75
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17 2 1	5 15.51 -21.59 -7.10 22.	p 19	5 10+75 3+00 -1+21	3 - 24	3 2 4	23-21 -10-05 -21-34 23-62	90	7 14.70 0.20 -4.55 4.55
2 3 9	10.07 0.00 -79.70 79.	9 9		41-85	4 2 5	10-56 -2-65 -4-07 4-85	10 0	
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2 3 7	5 23-16 23-73 1-50 23-			20-14	5 2 5		12 2	
	21.46 6.71 17.40 14.	9 5 9	5 17.36 -15.07 -3.32	19-15				
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5 5 5	9.46 4.74 -4.12 10.	2 3 3		17-07	9 6 5	11-21 11-24 9-41 14-69	1 1 1 1	2.20 11.24 4.25 11.95
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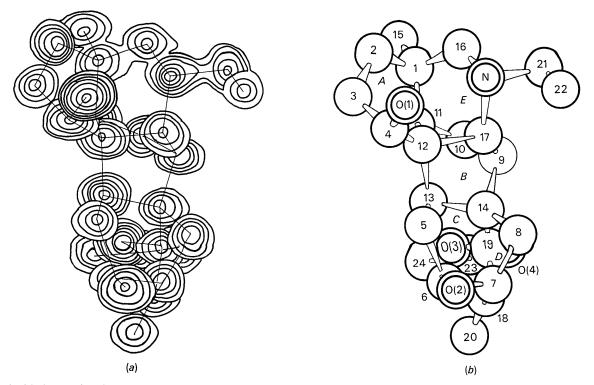


Fig. 1. (a) Composite electron density map of the molecule viewed downwards along the b axis. Contours are drawn at 2, 3, 4,... e.Å⁻³. (b) A molecule viewed downwards along the b axis.

and $I(h\bar{k}l)$ are expected to be measurable, 44 pairs showed significant differences in the c-axis Weissenberg photographs of the first and the second layers. Some of the results are shown in Table 3. A comparison of the observed and calculated intensity differences led to the absolute configuration shown in Fig. 1.

Table 3. Comparison of the observed and calculated intensity differences used for the establishment of absolute configuration

	$F_c^2(hkl)$	$I_o(hkl)$
hkl	$\overline{F_c^2(h\bar{k}l)}$	$\overline{I_o(h k l)}$
111	0.480	< 1
211	0.726	< 1
311	0.755	< 1
611	1.608	>1
811	0.520	< 1
521	1.577	> 1
621	1.938	> 1
112	1.754	>1
612	1.447	> 1
1012	0.760	< 1
322	1.706	> 1
332	0.726	< 1
832	1.493	>1
442	0.546	< 1
252	2.252	> 1
652	0.752	< 1
762	2.364	> 1
272	0.534	< 1
472	1.938	> 1

Discussion of the structure

The molecular structure

Intramolecular bond distances and angles, calculated from the coordinates given in Table 1, are shown in Figs. 2 and 3. The mean estimated standard deviations in the bond distances are 0.05 Å in C-C and 0.04 Å

in C-N and 0.04 Å in C-O bonds, and those in bond angles are 2.8° in tetrahedral C-C-C bonds. In Table 4, the bond distances and angles are listed in groups of similar type, together with their average values.

As seen in the table, the C-C single bond distances vary from 1.47 Å [C(3)-C(4)] to 1.67 Å [C(12)-C(17)]. The mean value of the twenty-five C-C bonds found in the molecule, 1.56₁ Å, is slightly longer than the normal carbon-carbon single bond distance, but the difference is within the limit of experimental error.

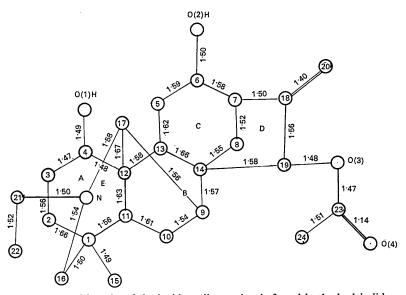
Table 4. The bond distances and angles arranged in groups of similar type

•	<i>J</i> 1 <i>J</i>	71	
C-C single bonds		C = C double bond	
C(1)— $C(2)$	1∙66 Å	C(18)-C(20)	1·40 Å
C(2)-C(3)	1.56		
C(3)-C(4)	1.47	C-O single bonds	
C(4)-C(12)	1.48	C(4)-O(1)	1·49 Å
C(5) - C(6)	1.59	C(6) - O(2)	1.50
C(5) - C(13)	1.62	C(19)-O(3)	1.48
C(6) - C(7)	1.58	C(23)— $O(3)$	1.47
C(7)— $C(8)$	1.52	Mean value	1.485
C(7)— $C(18)$	1.49		
C(8) - C(14)	1.55	C-N single bonds	
C(9)—C(10)	1.54	C(16)-N	1∙54 Å
C(9)—C(14)	1.57	C(17)-N	1.58
C(9)-C(17)	1.56	C(21)-N	1.50
C(10)-C(11)	1.61	Mean value	1.54_{0}
C(11)-C(1)	1.56		
C(11)-C(12)	1.63	C = O double bond	
C(12)-C(13)	1.58	C(23)-O(4)	1.14
C(12)-C(17)	1.67		
C-C single bonds			
C(13)-C(14)	1.66		
C(14)-C(19)	1.58		
C(15)-C(1)	1.49		
C(16)-C(1)	1.50		
C(18)-C(19)	1.56		

1.52

1.51

 1.56_{1}

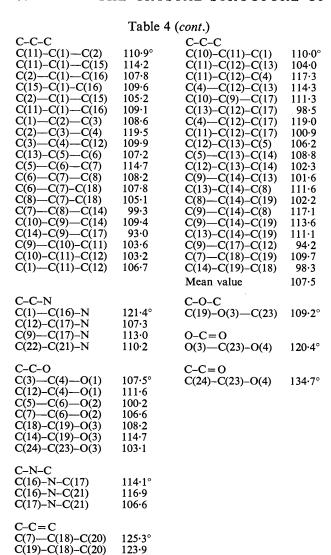


C(21)-C(22)

C(23)-C(24)

Mean value

Fig. 2. Bond lengths of the lucidusculine molecule found in the hydriodide.



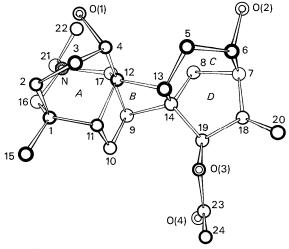


Fig. 4. A view of the molecule along the c axis.

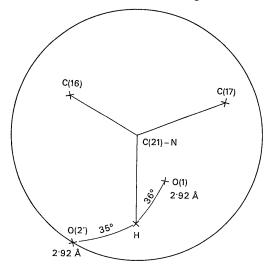
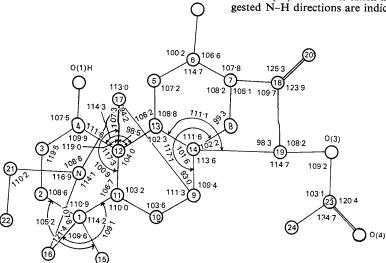


Fig. 5. Stereographic projection showing the distribution of atoms around the nitrogen atom. For oxygen atoms, the distances from the nitrogen atom are given. The direction of the C(21)-N bond is taken as the polar axis and the suggested N-H directions are indicated.



O(2)H

Fig. 3. Bond angles.

Some of the bond distances and angles involved in the B ring differ significantly from the normal values and indicate a considerable strain existing in the ring.

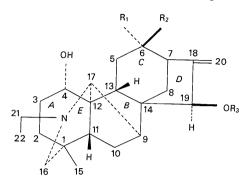


Fig. 6. Chemical formulae of lucidusculine, songorine, and luciculine, together with their absolute configurations.

I. $R_1 = OH$, $R_2 = H$, $R_3 = COCH_3$, lucidusculine. II. R_1 , $R_2 = 0$, $R_3 = H$, songorine.

III. $R_1 = OH$, $R_2 = H$, $R_3 = H$, luciculine.

A bridge between C(9) and C(12) probably causes such deformations. The angle at the bridgehead [C(9)–C(17)– C(12)] is 94.2°, which is of the same order of magnitude as that found in the tricyclo-octane nucleus (Macdonald & Trotter, 1965).

As for the structure of the molecule of lucidusculine found in the crystals of its hydriodide, the following points are well established (Fig. 4):

- (a) The conformation of ring A is a boat form.
- (b) The conformation of ring B is a boat form.
- (c) Rings A and B are trans-fusion.
- (d) Ring C has a boat form.
- (e) The ring-juncture of B and C is cis.
- (f) C(4)-O(1)H is axially oriented from the A ring, i.e. O(1)H takes the α -alcohol conformation.
- (g) C(6)-O(2)H is equatorial and takes the α -alcohol conformation.
- (h) The bonds C(7)-C(18) and C(14)-C(19) are both axially oriented from ring C.
- (i) C(19)–O(3) is a β -conformation.

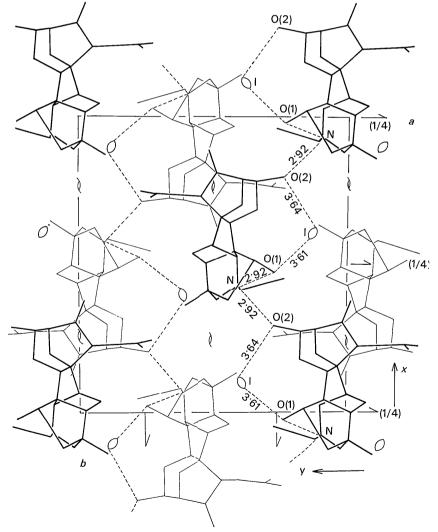


Fig. 7. Projection of the structure along the c axis (c axis upwards). Hydrogen bonds are shown by broken lines.

(j) The C-C=C group formed by C(7), C(18), C(19),

C(20) and the acetyl group C(23), C(24), O(3), O(4) both have planar configurations.

- (k) Ring E has the chair form and the ring-juncture of B and E is cis-fusion.
- (1) The angles subtended at the apex of the pyramid formed by N-R₁R₂R₃ are 106.6, 114.1 and 116.9°, and the N-ethyl bond turns to the trans side of the A ring. The nitrogen atom takes a tetrahedral coordination HN-R₁R₂R₃ with a hydrogen atom attached through the fourth bond. In Fig. 5, the arrangement of electronegative atoms around the nitrogen atom is shown by the stereographic projection, in which the direction of the C(21)-N bond is taken as the polar axis and a suggested N-H direction is also indicated. It is seen that the hydrogen atom is situated on the line nearly bisecting the angle $O(1) \cdots N \cdots O(2')$ and forms a bifurcated hydrogen bond. The present structure analysis on the HI salt has shown that the A ring is in the boat form and C(4)-O(1)H is axial. This axial OH group should be situated at a shorter distance than would be observed if the A ring were in the chair form and C(4)-O(1)H were equatorial. It is clear that the boat conformation is stabilized by the hydrogen bonding between N and O(1)H.

Absolute configuration

Recently, the absolute configuration of some of the diterpene alkaloids such as lycoctonine (Przybylska, 1961), aconitine (Przybylska, 1961) and hetisine (Przybylska, 1963) has been determined by X-ray methods. The present study has provided direct evidence that lucidusculine (Fig. 6, I) takes the same absolute configuration as that found in the above mentioned diterpene alkaloids, and, besides, important information on the absolute configuration of an aconite alkaloid, songorine (Fig. 6, II). For years the structure of songorine $(C_{22}H_{31}O_3N, \text{ m.p. } 198 \sim 202^{\circ}C)$ had been a subject of intensive investigations (Yunsov, 1948; Kuzovkov, 1953; Sugasawa, 1956; Wiesner, Ito & Valenta, 1958). In 1956, Sugasawa proposed the structural formula except for its absolute configuration. Upon completion of the present study, Okamoto, Natsume, Iitaka, Yoshino & Amiya (1965) showed that the reduction product of songorine is really identical with luciculine $(C_{22}H_{33}O_3N \cdot H_2O, m.p. 117-118.5^{\circ}C, Fig. 6, III), a$ hydrolysis product of lucidusculine, and established the structural relationship between them together with the absolute configuration of songorine.

The crystal structure

The projection of the structure viewed along the c axis is shown in Fig. 7, where suggested hydrogen bonds are represented by broken lines. Fig. 8 is another projection of the structure viewed along \mathbf{b} , in which some

of the intermolecular short distances less than 3.80 Å are shown by broken lines.

As seen in the figure, the I⁻ ion lies between the two alcoholic hydroxyl groups of the same molecule [O(1)H] and O(2)H. Chelation to the I⁻ ion may be suggested by the formation of the hydrogen bond system, $O(1)H \cdots I^{-} \cdots HO(2)$, the hydrogen bond distances being 3.61 Å and 3.64 Å respectively.

There is another hydrogen bond between the molecules, i.e., $NH \cdots O(2')$ of 2.92 Å, which links the molecules in the a direction to form a chain of the molecules. Within the crystal, these chains are bound together sideways by van der Waals forces.

As noted in the previous section, the plastic deformation of the crystal often disturbed the experimental work. This deformation seems to occur by a slip on the (001) plane. The pronounced anisotropic

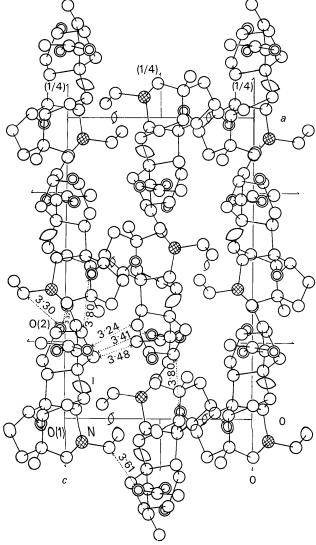


Fig. 8. Projection of the structure along the b axis (b axis downwards), showing the packing of the chains of molecules. Some of the shorter intermolecular interatomic distances less than 3.80 Å are shown by broken lines.

thermal vibrations of the iodine atoms were also observed along **c**. These facts indicate that the structure of the crystal has no strong intermolecular force in the **c** direction.

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Relationships among Structure Factors due to Identical Molecules in Different Crystallographic Environments

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Restraints on phases are imposed when a molecule crystallizes in different crystal forms or occurs more than once per asymmetric unit. These restrictions are expressed by the equations

$$|F_p| \exp \{i\alpha_p\} = \frac{U}{V} \sum_{h=-\infty}^{+\infty} |F_h| \exp \{i\alpha_h \sum_{n=1}^{N} G_{hpn} \exp \{i\varphi_{hpn}\}.$$

Here $|F_p|$, α_p , $|F_h|$, and α_h are the structure factors and their phases at the reciprocal lattice points \mathbf{p} and \mathbf{h} in either the same or different crystals. G_{hpn} and φ_{hpn} are simple functions of the rotation and translation parameters relating the molecules in the structures concerned. These equations have been tested in both one and three dimensions. In the one-dimensional case the same arbitrary electron density distribution was repeated several times at irregular intervals within the unit cell. All chosen distributions led to equations that could be solved correctly, suggesting that in general there is a unique solution. Refinement of initial approximate translation parameters during phase solution was also successful.

Introduction

When there are chemically identical molecules in different crystallographic environments, the phase problem may be approached in three distinct stages. The first stage involves determining the three rotation parameters that relate any two molecules. The rotation fuction (Rossmann & Blow, 1962; Sasada, 1964) has

proved successful for this purpose in a number of cases (Blow, Rossmann & Jeffery, 1964; Prothero & Rossmann, 1964; Dodsen, Harding, Hodgkin & Rossmann, 1966; Palmer, Palmer & Dickerson, 1964). The second stage involves determining the translation parameters that relate these molecules. A method of determining these parameters has been worked out in a special situation when the independent molecules are within the