

The Structure of a Derivative of Indolizidine, $C_{22}H_{27}NO_3 \cdot HBr \cdot C_2H_5OH^*$

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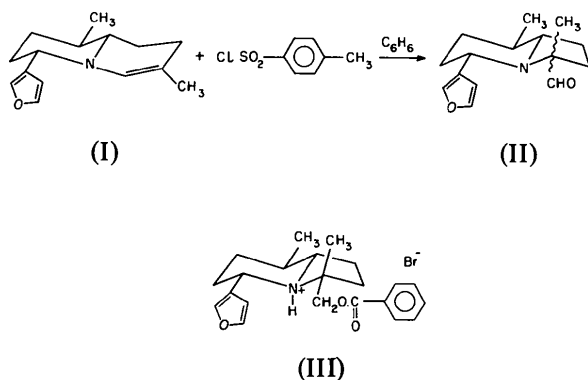
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The structure of the title compound has been determined by the heavy-atom method, and refined by block-diagonal least squares to $R = 0.057$ for 2057 observed reflexions. The unit cell is orthorhombic, $P2_12_12_1$, $a = 13.598(2)$, $b = 18.238(2)$, $c = 9.785(5)$ Å, $Z = 4$. The piperidine and pyrrolidine rings are *trans*-fused at a C–N bond. The piperidine is chair, the pyrrolidine is envelope, while the furyl and phenyl rings are planar. The crystals contain solvent molecules of ethyl alcohol, with each Br^- involved in hydrogen bonds to N^+ of the main molecule and to O of the solvent. The CH_3 of the solvent molecule appears to be disordered.

Introduction

In order to prepare α -sulphonylhemiaminals and α -thiohemiaminals, LaLonde, Tsai & Wong (1976) treated 6-dehydrodeoxynupharidine (I), which contains a quinolizidine enamine, with *p*-toluenesulphonyl chloride. In addition to the expected compounds they obtained two diastereoisomers of the indolizidine (II). Only one of these could be isolated and was extensively studied, since the induced rearrangement by the arene-sulphonyl chloride had not been described previously. The aldehyde (II) was reduced to a primary alcohol which was subsequently converted to the benzoate. The hydrobromide of this ester (III) crystallized as well-formed prisms.



The IR spectra indicated that the five- and six-membered rings in (II) and (III) are *trans*-fused and that the benzoate group is down. However, confirmation of the stereochemistry of (III) by X-rays was desirable in view of the intended further studies involving derivatives of this compound.

Experimental

Crystal and intensity data

$C_{22}H_{28}N^+O_3Br^- \cdot C_2H_5OH$, $M_r = 480.44$; orthorhombic, $P2_12_12_1$; $a = 13.598(2)$, $b = 18.238(2)$, $c = 9.785(5)$ Å; $U = 2426.7$ Å³, $Z = 4$, $D_x = 1.315$, $D_m = 1.303$ g cm⁻³ (by flotation in CCl_4 and hexane at 24 °C); $\mu(Cu K\alpha) = 27.8$ cm⁻¹; $F(000) = 1008$.

The X-ray measurements were carried out on a four-circle diffractometer with Cu radiation and a Ni filter [$\lambda(K\alpha_1) = 1.54050$, $\lambda(K\alpha_2) = 1.54435$ Å]. The crystal was an approximate cube of side 0.27 mm, mounted with a^* along the glass fibre. The cell parameters were based on the 2θ values of high-order axial reflexions. The presence of solvent molecules was first indicated by the crystal densities, and was later confirmed by Fourier and difference maps.

The integrated intensities were measured by the θ - 2θ scan procedure, and the background was recorded separately for each reflexion. The intensities of 040 and 012 were examined at regular intervals for scaling, but showed no significant variations. Of the 2353 unique reflexions within $\sin \theta/\lambda = 0.59$, 2057 (87.4%) were observed above threshold, thus providing 5.3 observations per parameter. Lorentz-polarization corrections were applied to the net intensities, but absorption corrections were ignored ($\mu_r = 0.75$).

Structure determination

The structure was determined by the heavy-atom method. The positions of Br and N were derived from a sharpened Patterson map, the other non-hydrogen atoms of the indolizidine molecule from Fourier maps. The peaks of the solvent molecule were not accepted until after the main molecule was fully located

($R = 0.18$). Since the crystals were grown from a methyl alcohol solution, only O(27) and C(28) of the solvent molecule were included at the start. However, subsequent Fourier and difference maps indicated the presence of an additional atom, C(29), in the solvent molecule, thus making it ethyl instead of methyl alcohol. This assignment also improved the agreement between the observed and calculated crystal densities. Professor LaLonde later confirmed that some crystals were first grown from ethyl alcohol. These crystals were redissolved in methyl alcohol and on evaporation produced the crystals under study. It was, however, surprising to find that the new crystals contained molecules of the original rather than the final solvent. In view of the crystallographic evidence C(29) was accepted, but on refinement it was shown to be disordered, and to have unit occupancy. All the H atoms, except those of C(28) and C(29), were located from a difference map.

The refinement was carried out by block-diagonal least squares, where the quantity $\sum w(|F_o| - |F_c|)^2$ was minimized. In the final three cycles, the weights were calculated from $w = \{1/1 + [(|F_o| - 30)/23]^4\}$, where $3.3 < |F_o| < 197.5$. In the final cycle, the average parameter shift was 0.36 e.s.d. and the maximum shift was

2.30 e.s.d. The final difference map showed a distribution within $\pm 0.35 e \text{ \AA}^{-3}$ near C(29) (the disordered methyl group), and within $\pm 0.25 e \text{ \AA}^{-3}$ in the rest of the map. The final parameters are listed in Table 1, for which $R = 0.057$ and $R_w = 0.058$, $[\sum w \Delta^2 / (m - n)]^{1/2} = 1.24$ for the observed reflexions.* There were no outstanding discrepancies among the unobserved reflexions.

The scattering factors were those of Hanson, Herman, Lea & Skillman (1964) for C, O, N⁺, Br⁻, and of Stewart, Davidson & Simpson (1965) for H. All calculations were carried out with the set of programs by Ahmed, Hall, Pippy & Huber (1973).

Discussion

The molecular structure is shown in Fig. 1. It confirms the structure proposed on the basis of the IR spectra.

* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32059 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 1. The fractional coordinates ($\times 10^4$ for the non-hydrogen atoms and $\times 10^3$ for the H atoms), and the anisotropic thermal parameters ($\times 10^3 \text{ \AA}^2$) for the expression $T = \exp[-2\pi^2(U_{11}a^{*2}h^2 + \dots + 2U_{23}b^*c^*kl + \dots)]$

The B(H) values are in Å^2 . The H atoms of C(28) and C(29) were not determined.

	X	Y	Z	U11	U22	U33	2U23	2U13	2U12
Br-	2538 (1)	1498 (0)	1287 (1)	69 (0)	68 (0)	71 (0)	8 (1)	37 (1)	-16 (1)
C (1)	5389 (6)	1535 (5)	10076 (10)	61 (4)	74 (5)	102 (6)	-12 (11)	-52 (9)	-13 (9)
C (2)	5116 (6)	2312 (4)	9639 (9)	69 (5)	57 (5)	72 (5)	5 (8)	-28 (9)	-17 (8)
C (3)	4435 (5)	2250 (4)	8400 (8)	37 (3)	55 (4)	63 (4)	-5 (7)	8 (7)	-18 (6)
N* (4)	4017 (4)	1467 (3)	8597 (6)	46 (3)	46 (3)	49 (3)	6 (6)	6 (5)	-9 (5)
C (5)	3461 (5)	1083 (4)	7458 (8)	50 (4)	56 (4)	59 (4)	-23 (7)	27 (7)	-3 (7)
C (6)	3156 (6)	344 (4)	7985 (9)	63 (5)	46 (4)	95 (6)	-15 (8)	-3 (9)	-31 (7)
C (7)	3991 (7)	-128 (4)	8526 (10)	86 (5)	47 (4)	87 (6)	-9 (9)	-30 (11)	6 (7)
C (8)	4556 (6)	283 (4)	9653 (9)	75 (5)	55 (4)	82 (6)	7 (8)	-16 (10)	23 (8)
C (9)	4899 (5)	1018 (4)	9082 (8)	53 (4)	63 (4)	61 (5)	9 (7)	19 (7)	19 (7)
C (10)	5004 (7)	2301 (5)	7049 (9)	79 (5)	76 (5)	75 (5)	26 (9)	37 (10)	-55 (9)
C (11)	3611 (5)	2816 (4)	8432 (9)	53 (4)	44 (3)	73 (5)	-3 (7)	7 (8)	-13 (6)
C (12)	4091 (3)	3482 (2)	8830 (6)	53 (2)	46 (2)	98 (4)	-14 (6)	2 (6)	-10 (4)
C (13)	3517 (5)	4073 (4)	8987 (10)	56 (4)	49 (4)	95 (6)	22 (8)	0 (9)	-13 (7)
O (14)	2681 (4)	4077 (3)	8664 (8)	54 (3)	67 (3)	175 (6)	-31 (8)	-76 (9)	7 (5)
C (15)	4055 (5)	4689 (4)	9635 (8)	44 (4)	44 (4)	81 (5)	17 (8)	1 (8)	-6 (7)
C (16)	3526 (6)	5307 (5)	10016 (11)	50 (4)	56 (4)	132 (8)	-16 (10)	-5 (10)	6 (8)
C (17)	3959 (7)	5883 (5)	10682 (12)	87 (6)	53 (4)	135 (8)	-37 (11)	-16 (12)	-2 (9)
C (18)	4952 (7)	5851 (5)	11002 (9)	90 (6)	74 (5)	76 (6)	-3 (9)	-16 (10)	-40 (9)
C (19)	5471 (7)	5227 (5)	10674 (10)	64 (5)	74 (5)	96 (6)	4 (10)	-25 (10)	-20 (9)
C (20)	5039 (6)	4654 (4)	10000 (9)	58 (4)	58 (4)	80 (5)	36 (8)	-9 (9)	0 (8)
C (21)	2631 (5)	1517 (4)	6918 (7)	36 (3)	55 (3)	57 (3)	-19 (7)	-7 (6)	-8 (7)
C (22)	2493 (7)	1729 (5)	5631 (8)	81 (5)	94 (6)	72 (4)	17 (8)	-1 (12)	15 (11)
O (23)	1597 (5)	2044 (4)	5467 (6)	80 (4)	103 (4)	84 (4)	18 (7)	-23 (7)	45 (7)
C (24)	1161 (6)	2005 (5)	6713 (10)	52 (4)	75 (5)	95 (6)	2 (10)	-2 (9)	3 (8)
C (25)	1730 (6)	1690 (4)	7604 (8)	59 (4)	68 (5)	64 (5)	9 (8)	-12 (8)	-13 (7)
C (26)	5465 (8)	-160 (5)	10116 (15)	78 (6)	74 (6)	181 (11)	64 (14)	-16 (15)	43 (10)
O (27)	3821 (5)	2550 (4)	3229 (8)	74 (4)	114 (5)	122 (5)	-6 (9)	-32 (8)	-28 (7)
C (28)	3179 (10)	3184 (6)	3494 (13)	155 (10)	91 (7)	123 (9)	22 (14)	12 (18)	-32 (14)
C (29)	3047 (13)	3640 (7)	2358 (14)	212 (14)	116 (9)	107 (9)	22 (15)	-21 (18)	-36 (18)

	X	Y	Z	B	X	Y	Z	B	
H (1, 1)	506 (5)	139 (4)	1108 (8)	5.6 (1.6)	H (11, 1)	326 (5)	290 (3)	750 (6)	4.3 (1.5)
H (1, 2)	602 (5)	141 (4)	1015 (8)	7.6 (2.1)	H (11, 2)	298 (5)	270 (4)	914 (7)	4.7 (1.5)
H (2, 1)	488 (5)	236 (4)	1038 (7)	8.2 (2.4)	H (16)	288 (4)	536 (3)	964 (6)	3.2 (1.2)
H (2, 2)	567 (5)	268 (4)	943 (8)	7.0 (2.0)	H (17)	341 (5)	628 (4)	1076 (8)	8.7 (2.4)
H (4)	364 (4)	146 (3)	924 (6)	2.8 (1.1)	H (18)	527 (5)	622 (4)	1157 (8)	5.9 (1.7)
H (5)	385 (4)	101 (3)	675 (5)	1.8 (1.0)	H (19)	622 (6)	532 (5)	1077 (8)	7.5 (2.1)
H (6, 1)	283 (5)	7 (3)	747 (6)	3.3 (1.4)	H (20)	539 (6)	414 (4)	973 (8)	6.4 (1.8)
H (6, 2)	269 (5)	37 (4)	860 (7)	4.9 (1.4)	H (22)	293 (5)	173 (4)	488 (7)	4.3 (1.4)
H (7, 1)	371 (6)	-63 (5)	895 (9)	6.9 (1.9)	H (24)	72 (5)	223 (4)	657 (8)	7.1 (1.9)
H (7, 2)	432 (6)	-46 (4)	778 (8)	7.2 (2.0)	H (25)	173 (4)	168 (3)	850 (6)	3.6 (1.3)
H (8)	420 (6)	46 (5)	1052 (9)	7.3 (2.0)	H (26, 1)	510 (6)	-58 (4)	1040 (8)	10.4 (2.7)
H (9)	523 (4)	95 (3)	822 (6)	3.5 (1.3)	H (26, 2)	583 (6)	-36 (5)	923 (8)	6.4 (1.8)
H (10, 1)	523 (6)	282 (4)	706 (8)	3.7 (1.3)	H (26, 3)	616 (6)	12 (4)	1033 (9)	7.2 (2.2)
H (10, 2)	471 (5)	218 (4)	618 (8)	8.0 (2.1)	H (27)	341 (6)	234 (5)	248 (9)	7.6 (2.1)
H (10, 3)	558 (6)	222 (4)	746 (8)	7.5 (2.1)					

The piperidine and pyrrolidine rings are *trans*-fused at the N(4)—C(9) bond, and the benzoate group projects on the same side of the double ring assembly as the furyl ring. The bond lengths and angles, not corrected for thermal vibration, are presented in Fig. 2. C(28)—C(29), 1.40 Å, is obviously erroneous due to

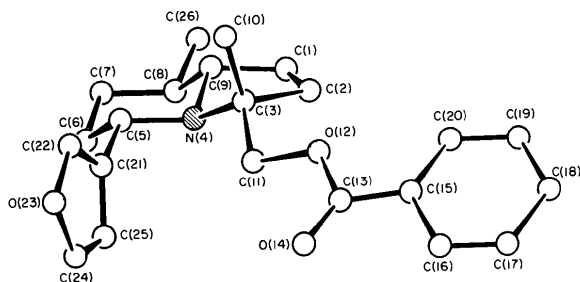


Fig. 1. A view of the main molecule showing its conformation.

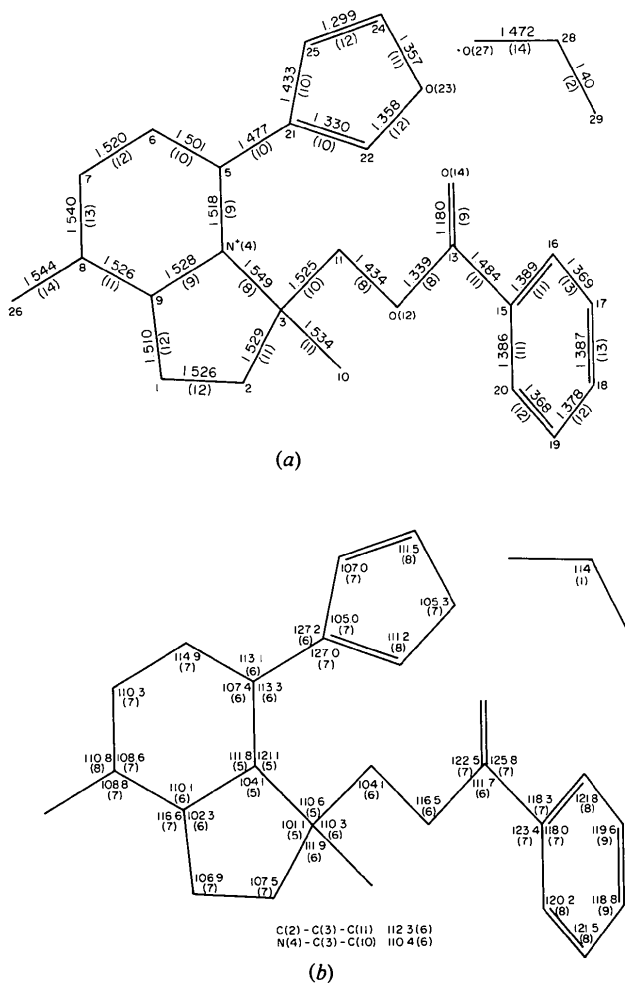


Fig. 2. The bond lengths (Å) and valency angles (°), and their estimated standard deviations in parentheses.

the disorder of C(29). C(3)—N(4), 1.549 (8) Å, is considerably longer than C(5)—N(4) and C(9)—N(4), 1.518 (9) and 1.528 (9) Å respectively. There are no other outstanding anomalies in the remaining bond lengths and angles. The C—H values are in the range 0.75–1.12 Å, mean 0.98 Å; O(27)—H(27) = 1.00 Å and N(4)—H(4) = 0.82 Å.

The piperidine ring has a chair form with N(4), C(5), C(7) and C(8) nearly coplanar ($\chi^2 = 1.5$), C(6) at -0.64 and C(9) at 0.71 Å from the seat of the chair. The five-membered pyrrolidine has the envelope conformation with its four C atoms coplanar ($\chi^2 = 3.6$) and N(4) at -0.63 Å from the plane of the C atoms. The conformation angles of these two

Table 2. Torsion angles (°) of the two non-planar rings of the main molecule

Pyrrolidine ring

C(9)—C(1)—C(2)—C(3)	1.6
C(1)—C(2)—C(3)—N(4)	23.4
C(2)—C(3)—N(4)—C(9)	-40.0
C(3)—N(4)—C(9)—C(1)	41.6
N(4)—C(9)—C(1)—C(2)	-26.4

Piperidine ring

C(9)—N(4)—C(5)—C(6)	57.1
N(4)—C(5)—C(6)—C(7)	-55.3
C(5)—C(6)—C(7)—C(8)	56.1
C(6)—C(7)—C(8)—C(9)	-55.2
C(7)—C(8)—C(9)—N(4)	58.6
C(8)—C(9)—N(4)—C(5)	-61.4

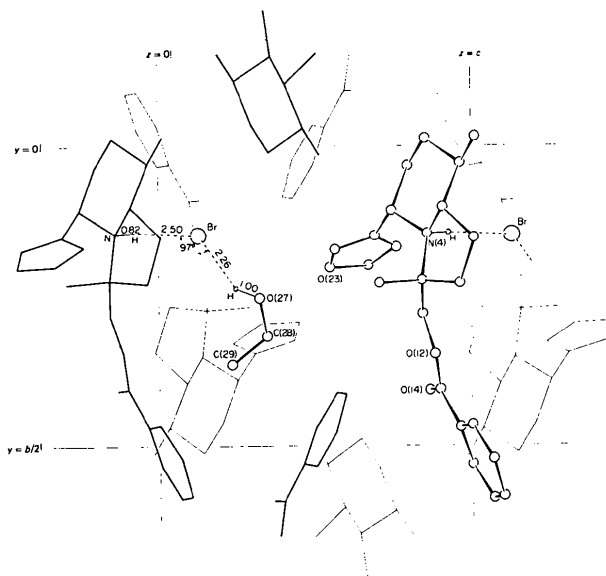


Fig. 3. A projection of the unit-cell contents along *a*, showing the cavity occupied by the solvent molecule and the hydrogen bonds connecting it to the main molecule.

rings are listed in Table 2. Their two mean planes form an angle of 7.3° . The phenyl ring is planar ($\chi^2 = 10.2$), as is the five-membered furyl ring ($\chi^2 = 7.4$).

The Br⁻ is involved in two hydrogen bonds, one to N⁺(4) of the main molecule and the other to O(27) of the solvent (Fig. 3). The corresponding dimensions are: Br...H(4) 2.50, Br...N(4) 3.31 Å, Br...H(4)—N(4) 175° ; Br...H(27) 2.26, Br...O(27) 3.22 Å, Br...H(27)—O(27) 159° . There are no other short intermolecular contacts.

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An Electron Density Study of $NaCN \cdot 2H_2O$ at 150 K

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The crystal structure of $NaCN \cdot 2H_2O$ has been refined from X-ray data measured at 150 K on a four-circle diffractometer. The CN group is found to be inverted compared with a previously reported study [LeBihan, *Acta Cryst.* (1958), **11**, 770–773]. The cyanide group is bonded mainly through the N atom to the Na atom, while the C atom is involved in two hydrogen bonds with hydrate molecules. Results of an all-data refinement and a high-order refinement are compared. Considerable lone-pair density is observed at the back of the C atom in the deformation maps. Analyses of the charge distribution show a net charge on the CN group of $-0.50 e$. The Na atom is almost neutral, while the positive charge in the crystal is concentrated on the hydrate molecules.

Introduction

The crystal structure of $NaCN \cdot 2H_2O$ was first determined by LeBihan (1958) and it was concluded that, in contrast to many simple cyanides where the CN group is disordered, an ordered CN group is present in $NaCN \cdot 2H_2O$ as a result of interactions of this group with hydrogen bonds.

Determination of the electron density seemed of considerable interest, because the cyanide ion is small and can be relatively easily studied theoretically, and because of the insight into the nature of the water molecule binding in crystalline hydrates that may be obtained. It was therefore decided to undertake an ac-

curate redetermination of its structure. In order to reduce thermal motion the study was performed at reduced temperature.

Experimental

Single crystals of $NaCN \cdot 2H_2O$ were grown from an aqueous solution of NaCN. A crystal of approximately $0.30 \times 0.30 \times 0.35$ mm was selected for data collection and sealed in a glass capillary as the crystals rapidly decomposed in the air. The crystal was cooled with a stream of cold nitrogen gas. A temperature of 150 K was chosen for the experiment. Below this temperature ice formation became a serious problem. The space group $P2_1/c$, reported earlier (LeBihan, 1958), was confirmed. Crystallographic information is repor-

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