

(+)-Lupinine-*N*-methiodide,* C₁₁H₂₂NO⁺.I⁻

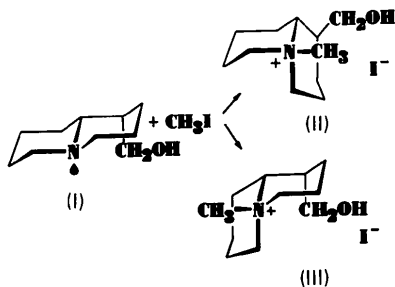
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Abstract. $M_r = 311.2$, m.p. 559 K, orthorhombic, $P2_12_12_1$, $a = 7.228$ (1), $b = 13.115$ (3), $c = 13.468$ (3) Å, $V = 1276.7$ (5) Å³, $Z = 4$, $D_m = 1.61$ (floatation in bromobenzene/CHBr₃), $D_x = 1.62$ Mg m⁻³, $\lambda(\text{Mo } K\alpha) = 0.7107$ Å, $\mu(\text{Mo } K\alpha) = 2.51$ mm⁻¹, $F(000) = 624$, room temperature. The final $R = 0.029$ for 1010 reflexions and 127 refined parameters. The quinolizidine in the *N*-methyl-lupinium cation adopts the *cis* configuration; the hydroxymethyl group is equatorial. The absolute configuration has been established as (1*R*,5*S*,10*R*).

Introduction. The free-electron pair on the amino N atom in the lupinine molecule (I) is able to be inverted. The configuration and conformation of the lupinine *N*-alkylation product is of particular interest. It is impossible to investigate the environment of the quaternary N atom using IR spectra because of the absence of the 'trans band' (2840–2600 cm⁻¹; Skolik, Krueger & Wiewirowski, 1968). The inversion of configuration in the *N*-methyl-lupinium cation, with respect to lupinine, was first deduced from an analysis of a spatial model of the molecule (Crow, 1958) and then attempts were made to confirm it by taking into consideration the CH₂OH-group position. On the basis of IR and NMR data (Sadykov, Aslanov & Kushmuradov, 1975) an equatorial orientation of the CH₂OH group has been found and only configuration (II), but not (III), can be ascribed to the *N*-methyl-lupinium cation.



This study was undertaken to determine the absolute configuration of the cation as well as its conformation.

* 1-(Hydroxymethyl)-5-methylperhydroquinolizinium iodide.

Experimental. The compound was recrystallized from methanol solution. Crystal 0.45 × 0.42 × 0.35 mm, Syntex $P2_1$ diffractometer, Mo $K\alpha$ radiation, lattice parameters by least squares from 2θ values of 12 reflexions centered on a diffractometer. 1146 independent reflexions, $2\theta_{\text{max}} = 48^\circ$, hkl range: h 0–8, k 0–14, l 0–15, background and intensity of reflexions calculated by the peak-profile-analysis method (Lehmann & Larsen, 1974; Jaskólski, 1979); semi-empirical absorption-correction factors (Syntex *XTL*, 1973) varied from 0.61 to 1.00; two standard reflexions (400, 600) monitored every 100 showed intensity variation < 5.5%. 1146 reflexions recorded, 1010 reflexions with $I \geq 1.96\sigma(I)$ [$R_1(F) = R_2(F) = 0.011$ (Syntex *XTL*)] used in the calculations. Patterson synthesis for I, other non-hydrogen atoms by Fourier method. 13 of 22 H atoms located in a difference Fourier map, coordinates of the remaining H atoms calculated assuming a tetrahedral configuration about the C atom; $B_{\text{iso}} = 4.0$ Å² for H atoms. Scattering factors with anomalous-dispersion corrections from *International Tables for X-ray Crystallography* (1974), refinement by full-matrix least squares [minimizing $\sum w(\Delta F)^2$], with $w = (F_o/F_1)^2$ if $F_o < F_1$, $w = 1$ if $F_1 \leq F_o \leq F_h$, $w = (F_h/F_o)^2$ if $F_o > F_h$ ($F_1 = 11.5$, $F_h = 51.0$), maximum shift/e.s.d. = 0.28, maximum electron density in final difference Fourier map = 0.35 e Å⁻³, final $R(+)$ = 0.029, $R_w(+)$ = 0.033, $S(+)$ = 2.30 for the first enantiomorph, and $R(-)$ = 0.031, $R_w(-)$ = 0.036, $S(-)$ = 2.51 for the second.

The application of the \mathcal{R} test (Hamilton, 1965) indicates that the first enantiomorph is correct [$\mathcal{R} = R_w(-)/R_w(+)$ = 1.0909; $\mathcal{R}_{1,883,0^{\circ}005} \approx 1.0044$].

Discussion. The final positional parameters are given in Table 1.† The absolute configuration of the *N*-methyl-lupinium cation (Fig. 1) was established as (1*R*,5*S*,10*R*). The quinolizidine system of the cation is *cis*, both rings having the chair conformation. The CH₂OH group is equatorially bonded to the C(1) atom (Table 2c).

† Lists of structure factors, anisotropic thermal parameters and H-atom coordinates have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38537 (15 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Coordinates for non-hydrogen atoms ($\times 10^4$; $\times 10^5$ for I atom) and isotropic B values ($B_{iso} = \frac{1}{3} \sum B_{ii}$)

	x	y	z	B_{iso} (\AA^2)
I	9909 (6)	18223 (4)	24972 (6)	3.80 (3)
O(1)	-2985 (9)	1851 (4)	3947 (4)	3.9 (4)
C(11)	-3083 (12)	2822 (6)	4399 (6)	3.1 (6)
C(1)	-4502 (10)	3510 (6)	3876 (6)	2.9 (5)
C(2)	-3875 (12)	3824 (6)	2835 (5)	3.5 (6)
C(3)	-5308 (11)	4498 (6)	2336 (6)	3.6 (7)
C(4)	-5840 (12)	5409 (6)	2976 (6)	3.3 (5)
N(5)	-6438 (8)	5084 (5)	4009 (5)	2.7 (4)
C(5)	-8235 (11)	4521 (6)	3942 (6)	3.5 (6)
C(6)	-6870 (13)	6034 (6)	4612 (7)	3.7 (7)
C(7)	-5189 (15)	6651 (7)	4878 (7)	4.4 (7)
C(8)	-3762 (14)	6013 (6)	5430 (7)	4.1 (7)
C(9)	-3280 (12)	5077 (6)	4808 (6)	3.3 (6)
C(10)	-4963 (10)	4433 (6)	4524 (5)	2.4 (5)

The *N*-methylupininium cation exhibits skeleton geometry similar to that of the nupharidinium cation (Ohrt, Parthasarathy, La Londe & Wong, 1973).

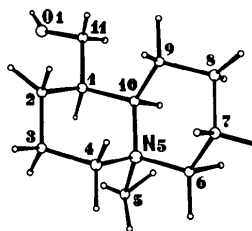


Fig. 1. The *N*-methylupininium cation. The unlabelled atoms are C atoms.

Table 2. Geometry of cation

(a) Bond lengths (\AA)

C(1)–C(2)	1.531 (10)	C(6)–C(7)	1.503 (14)
C(2)–C(3)	1.519 (12)	C(7)–C(8)	1.522 (14)
C(3)–C(4)	1.521 (11)	C(8)–C(9)	1.527 (12)
C(4)–N(5)	1.518 (10)	C(9)–C(10)	1.529 (11)
N(5)–C(6)	1.520 (10)	C(10)–C(1)	1.529 (10)
N(5)–C(5)	1.497 (10)	C(1)–C(11)	1.537 (11)
N(5)–C(10)	1.532 (9)	C(11)–O(1)	1.412 (9)

(b) Bond angles ($^\circ$)

C(2)–C(1)–C(11)	112.3 (6)	C(5)–N(5)–C(10)	110.8 (6)
C(10)–C(1)–C(11)	110.4 (6)	C(5)–N(5)–C(10)	111.0 (6)
C(2)–C(1)–C(10)	112.0 (6)	N(5)–C(6)–C(7)	113.7 (7)
C(1)–C(2)–C(3)	111.1 (7)	C(6)–C(7)–C(8)	111.6 (8)
C(2)–C(3)–C(4)	112.3 (7)	C(7)–C(8)–C(9)	109.1 (7)
C(3)–C(4)–N(5)	111.8 (6)	C(8)–C(9)–C(10)	113.6 (7)
C(4)–N(5)–C(5)	109.3 (6)	N(5)–C(10)–C(9)	111.0 (6)
C(4)–N(5)–C(6)	108.6 (6)	N(5)–C(10)–C(1)	109.5 (6)
C(4)–N(5)–C(10)	111.9 (6)	C(9)–C(10)–C(1)	114.0 (6)
C(5)–N(5)–C(6)	105.0 (6)	C(1)–C(11)–O(1)	111.5 (6)

(c) Torsion angles ($^\circ$)

O(1)–C(11)–C(1)–C(2)	-69.2 (8)	C(6)–C(7)–C(8)–C(9)	55.3 (10)
O(1)–C(11)–C(1)–C(10)	165.0 (7)	C(7)–C(8)–C(9)–C(10)	-55.7 (8)
C(10)–C(1)–C(2)–C(3)	-55.4 (8)	C(8)–C(9)–C(10)–N(5)	54.1 (8)
C(1)–C(2)–C(3)–C(4)	53.1 (8)	C(9)–C(10)–N(5)–C(6)	-50.8 (8)
C(2)–C(3)–C(4)–N(5)	-53.2 (8)	C(10)–N(5)–C(6)–C(7)	53.0 (8)
C(3)–C(4)–N(5)–C(10)	54.9 (8)	C(5)–N(5)–C(4)–C(3)	-68.3 (8)
C(4)–N(5)–C(10)–C(1)	-56.1 (7)	C(5)–N(5)–C(10)–C(1)	66.2 (7)
N(5)–C(10)–C(1)–C(2)	56.4 (7)	C(5)–N(5)–C(6)–C(7)	172.8 (8)
N(5)–C(6)–C(7)–C(8)	-55.9 (10)	C(5)–N(5)–C(10)–C(9)	-167.0 (7)

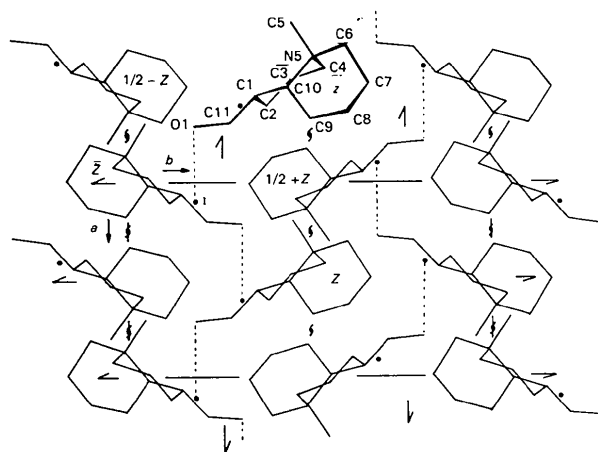


Fig. 2. A view of the crystal structure along c . The O(1)–H(1)···I⁻ hydrogen-bond geometry: O(1)···I⁻ 3.475 (6), O(1)–H(1) 1.27, H(1)···I⁻ 2.23 \AA , \angle O(1)–H(1)···I⁻ 165 $^\circ$. The other contacts (\AA) between the I⁻ anion and the cation C atoms: C(4ⁱ) 4.016 (9), C(5ⁱⁱ) 4.078 (8), C(5ⁱⁱⁱ) 4.103 (8), C(7^{iv}) 4.098 (9), C(11) 4.117 (8). Symmetry code: (i) $1-x, \frac{1}{2}+y, \frac{1}{2}-z$; (ii) $1-x, y, z$; (iii) $-1-x, \frac{1}{2}+y, \frac{1}{2}-z$; (iv) $-\frac{1}{2}-x, 1-y, \frac{1}{2}+z$.

Table 3. Conformation and configuration of the lupinine molecule and its derivatives

Compound	Reference	Absolute configuration	Quinolizidine	Orientation of substituent at C(1) atom	Torsion angles ($^\circ$)	
					C(10)–C(1)–C(11)–O(1)	C(2)–C(1)–C(11)–O(1)
(-)-Lupinine	(a)	1 <i>R</i> ,5 <i>R</i> ,10 <i>R</i>	<i>trans</i>	Axial	-174.8 (4)	-50.0 (4)
(-)-Lupinine.HCl	(b)	1 <i>R</i> ,5 <i>R</i> ,10 <i>R</i>	<i>trans</i>	Axial	-177.6 (4)	-50.6 (5)
(-)-Iodolupinane.HClO ₄ *	(c)	1 <i>R</i> ,5 <i>R</i> ,10 <i>R</i>	<i>trans</i>	Axial	173 (1)	-59 (1)
(-)-Tosyloxylupinane <i>p</i> -toluenesulfonate†	(d)	1 <i>R</i> ,5 <i>R</i> ,10 <i>R</i>	<i>trans</i>	Axial	173.6 (6)	-59.6 (7)
(+)-Epilupinine	(e)	1 <i>S</i> ,5 <i>R</i> ,10 <i>R</i>	<i>trans</i>	Equatorial	-177.0 (5)	58.9 (7)
(+)-Lupinine- <i>N</i> -methiodide	(f)	1 <i>R</i> ,5 <i>S</i> ,10 <i>R</i>	<i>cis</i>	Equatorial	165.0 (7)	-69.2 (8)

References: (a) Kozioł, Kosturkiewicz & Podkowińska (1978); (b) Kozioł, Gdaniec & Kosturkiewicz (1980a); (c) Kozioł & Kosturkiewicz (1980); (d) Kozioł & Podkowińska (1983); (e) Kozioł, Gdaniec & Kosturkiewicz (1980b); (f) this paper.

* Torsion angles C(10)–C(1)–C(11)–I and C(2)–C(1)–C(11)–I.

† Torsion angles C(10)–C(1)–C(11)–O(6) and C(2)–C(1)–C(11)–O(6).

Comparison with other derivatives of lupinine (Table 3) shows that (i) neither N protonation nor any substituent on the C(11) atom causes inversion of the *trans*-quinolizidine, (ii) N alkylation leads to conformational and configurational changes in the lupinine molecule, (iii) the substituent at the C(1) atom in the equatorial orientation is chemically more stable than the axial one [R. K. Hill in Pelletier (1970)] and more susceptible to intermolecular interactions in the solid state.

Bond lengths and angles (Table 2) are as expected. The mean $N^+—C$ bond distance of 1.517 (7) Å is in good agreement with values found for quaternary amino salts.

In the crystal structure (Fig. 2) cations and anions are linked together by the interionic $O—H…I^-$ hydrogen bonds and by electrostatic $N^+—CH_3…I^-$ attractions.

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Antischistosomal Analogs of Hycanthone. III.* Structure of the 1:1 Chloroform Solvate of 8-Chloro-2-[2-(diethylamino)ethyl]-2H-[1]benzothiopyrano[4,3,2-*cd*]indazole-5-methanol, $C_{20}H_{22}ClN_3OS.CHCl_3$ †

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Abstract. $M_r = 507.312$, monoclinic, $P2_1/n$, $a = 10.312$ (1), $b = 30.502$ (2), $c = 8.683$ (1) Å, $\beta = 120.046$ (6)°, $V = 2364.1$ Å³, $Z = 4$, $D_x = 1.425$ g cm⁻³, $\lambda(Cu K\alpha_1) = 1.54056$ Å, $\mu = 54.93$ cm⁻¹, $F(000) = 1046$, $T = 296$ (1) K. Final $R(F) = 0.056$ for 2865 counter reflections. All H atoms were located and their parameters refined. Bond lengths and angles are all within the ranges of expected values, and the fused four-ring system is nearly planar. The terminal N atom is not protonated and is hydrogen bonded to the H atom of the chloroform molecule *via*

$N…H—C$, with $N…H$ distance 2.31 (4) Å and $N…H—C$ angle 160 (3)°. The ring nitrogen, not connected to the side chain, acts as an acceptor in a $N…H—O$ hydrogen bond with a neighboring translation-related molecule, while the hydroxyl O atom in turn donates its H atom to the same N atom of another translation-related molecule, thus forming an infinite hydrogen-bonded chain in the [101] direction, the $N…H$ length and $N…H—O$ angle being 2.03 (6) Å and 163 (5)°, respectively. In the chloroform molecule, the average C—Cl and Cl…Cl distances are 1.753 (3) and 2.881 (1) Å; the average Cl—C—Cl angle is 110.6 (2)°. Stereochemical evidence suggests two alternative configurations for the $-CH_2OH$ group having different occupancies (ratio roughly 9:1).

* Part II: Wei (1982).

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