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1-(1-Methyl-2-phenylethyl)-2-methyl-3-hydroxy-azetidinium Hydrochloride

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Abstract. $C_{13}H_{20}NO^+.Cl^-$, monoclinic, space group $P2_1$, $a=11{\cdot}064$ (6), $b=7{\cdot}385$ (6), $c=8{\cdot}446$ (5) Å, $\beta=92{\cdot}52$ (8)°, $Z=2$, $D_c=1{\cdot}16$, $D_m=1{\cdot}14$ g cm^{-3} (by flotation). The azetidine ring is non-planar. The absolute configurations at the 2- and 3-azetidine ring positions are *S* and *R*, respectively, relative to the known *S* configuration at the *N*-phenylisopropyl carbon. The azetidinium moiety is linked to two chloride ions by N–H···Cl and O–H···Cl hydrogen bonds.

Introduction. Crystals of the title compound (hereinafter AzHCl), recrystallized from a methanol–ethyl acetate solution, were obtained from E. H. Gold, Schering Corporation, Bloomfield, New Jersey. Systematic absences $0k0$, $k=2n+1$ with $Z=2$, and known optical activity, uniquely identified the space group as $P2_1$. The small, needle-like crystals were hygroscopic and were mounted in thin-walled glass capillaries. Two axes of diffraction data (b,c) were collected with nickel-filtered Cu $K\alpha$ radiation and an automated Supper–Pace diffractometer possessing Weissenberg geometry. After Lp corrections the data were correlated (Simpson, 1963) to give 1417 independent reflections, 814 of which were considered observed, having intensities greater than $2\sigma(I)$ (Parker, Flynn & Boer, 1968). An additional 242 high-angle reflections accessible with Cu $K\alpha$ radiation were not measured because of physical limitations of the diffractometer.

The structure was solved by the heavy-atom method after determination of the chlorine position from the Patterson map. Full-matrix least-squares refinement of the positions and anisotropic temperature factors of the non-hydrogen atoms with the program *ORFLS* (Busing, Martin & Levy, 1962) reduced R_1 to 0·11. A difference synthesis revealed the positions of all hydrogens except those of the methyl groups. Inclusion of the 14 hydrogens with fixed positions and an isotropic temperature factor $B=4{\cdot}0$ Å^2 in four additional cycles of full-matrix anisotropic least-squares refinement of non-hydrogen parameters produced a final $R_1=0{\cdot}097$, $wR=0{\cdot}085$. The final value of R_1 for all measured data (including zero-intensity reflections) is 0·162. R_1 and wR are defined by $R_1=\sum||F_o|-|F_c||/\sum|F_o|$ and $wR=[\sum w(|F_o|-|F_c|)^2/\sum w|F_o|^2]^{1/2}$. The weighting scheme $w=1/\sigma^2(F_o)$ was employed. Atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1968). Examination of a final difference map revealed no residual peaks exceeding 0·31 e Å^{-3} except in the region of the chlorine and the two methyl carbons. The final atomic coordinates and thermal parameters are given in Table 1.*

Table 1. *Final values of atomic coordinates* (× 10^4) *and thermal parameters* (× 10^4) *for* AzHCl

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

	x/a	y/b	z/c	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
N(1)	6292 (8)	1631 (12)	8121 (12)	113 (10)	118 (14)	105 (18)	−5 (11)	27 (11)	2 (14)
C(2)	6132 (10)	2808 (13)	6612 (16)	96 (11)	79 (24)	165 (23)	−13 (12)	28 (12)	23 (16)
C(3)	4930 (10)	1983 (15)	6312 (16)	73 (10)	160 (26)	141 (26)	10 (12)	35 (13)	− 1 (18)
C(4)	4983 (11)	1395 (17)	8029 (15)	123 (13)	162 (24)	108 (24)	27 (15)	9 (15)	14 (19)
C(5)	6910 (10)	2447 (23)	9578 (14)	119 (12)	161 (19)	118 (21)	−26 (20)	14 (12)	−30 (26)
C(6)	6788 (19)	1056 (24)	928 (18)	300 (28)	264 (35)	104 (26)	−114 (26)	18 (23)	63 (24)
C(7)	8194 (9)	3014 (17)	9313 (15)	76 (10)	221 (31)	135 (25)	33 (14)	−12 (12)	−42 (19)
C(8)	8736 (11)	3833 (19)	789 (15)	101 (12)	278 (31)	82 (22)	16 (16)	13 (15)	−32 (22)
C(9)	1697 (12)	488 (18)	8628 (17)	109 (14)	231 (30)	125 (25)	21 (17)	3 (15)	64 (25)
C(10)	1175 (15)	1227 (23)	7259 (23)	114 (15)	292 (38)	278 (42)	34 (21)	32 (20)	93 (32)
C(11)	273 (17)	435 (32)	6437 (25)	118 (17)	429 (50)	257 (44)	38 (26)	58 (24)	138 (40)
C(12)	241 (11)	3904 (30)	3019 (22)	58 (11)	486 (57)	203 (35)	−46 (22)	−9 (16)	84 (38)
C(13)	9718 (14)	3056 (22)	1611 (20)	139 (15)	339 (48)	175 (31)	−28 (22)	26 (19)	−7 (27)
C(14)	7143 (11)	2537 (29)	5393 (14)	126 (12)	297 (28)	122 (22)	62 (24)	27 (14)	4 (29)
O(15)	3942 (8)	3144 (12)	5902 (12)	126 (9)	213 (20)	189 (20)	38 (11)	5 (10)	−5 (14)
Cl	3402 (4)	2500	2334 (5)	178 (5)	115 (4)	193 (7)	−5 (5)	−37 (4)	25 (7)

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* A table of observed and calculated structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30256 (11 pp., 1 microfiche). Copies may be obtained through the Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 1 (*cont.*)

	x/*a*	*y*/*b*	*z*/*c*
H(1)	6682	280	7879
H(2)	5985	4368	6653
H(3)	5011	840	5562
H(4*A*)	4437	87	8339
H(4*B*)	4922	2483	8758
H(5)	6333	3667	9833
H(7*A*)	7893	4300	8682
H(7*B*)	8731	2353	8826
H(9)	7622	6033	645
H(10)	8333	7590	3000
H(11)	9906	6195	4464
H(12)	1016	3290	3748
H(13)	39	1829	897
H(15)	3624	3085	4930

Table 2. *Final values of interatomic distances for* AzHCl (Å)

N(1)——C(2)	1·546 (15)
N(1)——C(4)	1·457 (15)
N(1)——C(5)	1·507 (15)
C(2)——C(3)	1·474 (15)
C(2)——C(14)	1·567 (18)
C(3)——C(4)	1·512 (18)
C(3)——O(15)	1·420 (13)
C(5)——C(6)	1·545 (20)
C(5)——C(7)	1·507 (16)
C(7)——C(8)	1·489 (17)
C(8)——C(9)	1·409 (17)
C(8)——C(13)	1·387 (20)
C(9)——C(10)	1·382 (21)
C(10)——C(11)	1·327 (26)
C(11)——C(12)	1·355 (26)
C(12)——C(13)	1·442 (24)
N(1)——H(1)	1·110
C(2)——H(2)	1·164
C(3)——H(3)	1·062
C(4)——H(4*A*)	1·175
C(4)——H(4*B*)	1·017
C(5)——H(5)	1·130
C(7)——H(7*A*)	1·132
C(7)——H(7*B*)	0·884
C(9)——H(9)	1·032
C(10)——H(10)	1·169
C(11)——H(11)	0·959
C(12)——H(12)	1·129
C(13)——H(13)	1·153
O(15)——H(15)	0·880
O(15)···Cl	3·083 (11)
H(15)···Cl	2·238
N(1)····Cl	3·095 (9)
H(1)····Cl	2·062

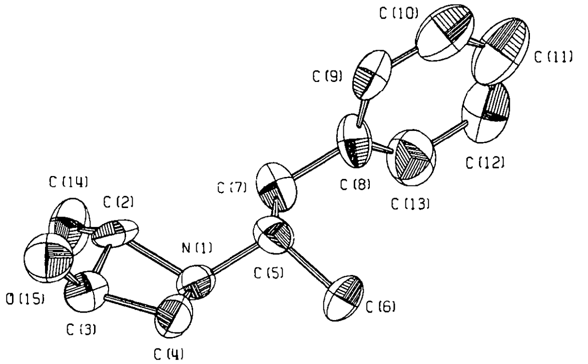

Fig. 1. An *ORTEP* (Johnson, 1970) drawing of the correct absolute configuration of AzHCl.

Discussion. Certain D-1-(α-alkylphenylethyl)-3-azetidinols and their ester and ether derivatives, including AzHCl, have been shown to exhibit both stimulant and anoretic activity (Gold, 1968). The X-ray structure

Table 3. *Final values of interatomic angles for* AzHCl (°)

C(2)—N(1)——C(4)	86·9 (0·8)
C(2)—N(1)——C(5)	118·7 (0·9)
C(4)—N(1)——C(5)	120·4 (0·9)
N(1) —C(2)——C(3)	88·8 (0·8)
N(1) —C(2)——C(14)	114·2 (0·9)
C(3)—C(2)——C(14)	120·0 (1·1)
C(2)—C(3)——C(4)	87·5 (1·0)
C(2)—C(3)——O(15)	118·1 (0·9)
C(4)—C(3)——O(15)	113·9 (1·0)
N(1) —C(4)——C(3)	90·8 (0·9)
N(1) —C(5)——C(6)	106·6 (1·2)
N(1) —C(5)——C(7)	112·7 (0·9)
C(6)—C(5)——C(7)	114·1 (1·1)
C(5)—C(7)——C(8)	109·7 (1·0)
C(7)—C(8)——C(9)	121·0 (1·2)
C(7)—C(8)——C(13)	121·9 (1·2)
C(9)—C(8)——C(13)	117·0 (1·3)
C(8)—C(9)——C(10)	119·9 (1·4)
C(9)—C(10)——C(11)	122·7 (1·6)
C(10)—C(11)——C(12)	120·5 (1·7)
C(11)—C(12)——C(13)	118·9 (1·5)
C(8)—C(13)——C(12)	120·7 (1·5)
H(1) —N(1)——C(2)	112·7
H(1) —N(1)——C(4)	106·0
H(1) —N(1)——C(5)	110·1
H(2) —C(2)——N(1)	122·9
H(2) —C(2)——C(3)	106·7
H(2) —C(2)——C(14)	104·5
H(3) —C(3)——C(2)	109·4
H(3) —C(3)——C(4)	110·0
H(3) —C(3)——O(15)	114·8
H(4*A*)-C(4)——H(4*B*)	117·7
H(4*A*)-C(4)——N(1)	127·2
H(4*A*)-C(4)——C(3)	116·9
H(4*B*)-C(4)——N(1)	88·0
H(4*B*)-C(4)——C(3)	110·7
H(5) —C(5)——N(1)	103·4
H(5) —C(5)——C(6)	108·7
H(5) —C(5)——C(7)	110·5
H(7*A*)-C(7)——H(7*B*)	115·7
H(7*A*)-C(7)——C(5)	92·5
H(7*A*)-C(7)——C(8)	98·8
H(7*B*)-C(7)——C(5)	124·9
H(7*B*)-C(7)——C(8)	111·1
H(9) —C(9)——C(8)	112·4
H(9) —C(9)——C(10)	127·6
H(10) -C(10)——C(9)	108·4
H(10) -C(10)——C(11)	128·8
H(11) -C(11)——C(10)	106·4
H(11) -C(11)——C(12)	133·0
H(12) -C(12)——C(11)	118·0
H(12) -C(12)——C(13)	122·9
H(13) -C(13)——C(8)	108·4
H(13) -C(13)——C(12)	130·6
H(15) -O(15)——C(3)	118·1
N(1) —H(1)····Cl	153·5 (0·5)
C(2)—N(1)····Cl	117·5 (0·6)
C(4)—N(1)····Cl	89·4 (0·6)
C(5)—N(1)····Cl	116·5 (0·8)
O(15) -H(15)···Cl	161·1 (0·6)
C(3)—O(15)···Cl	105·1 (0·7)

determination of AzHCl was undertaken in order to establish the absolute configuration of the molecule relative to a known *S* configuration at the *N*-phenylisopropyl carbon (Gold, 1971). The absolute configuration of AzHCl as determined by this study is *S*, *R* at C(2) and C(3), respectively, relative to the known *S* configuration at C(5).

Fig. 1 is an *ORTEP* (Johnson, 1970) drawing of AzHCl. Final values of bond distances and angles and their estimated standard errors (*ORFFE*, Busing, Martin & Levy, 1964) are given in Tables 2 and 3. The azetidine ring is non-planar with a dihedral angle of 154 (1)° between the planes C(2)–N(1)–C(4) and C(2)–C(3)–C(4). This deviation from planarity is significantly greater than that observed in studies of three non-planar azetidine compounds in which dihedral angles of 169, 166 and 169° were observed (Towns & Trefonas, 1971; McGandy, Berman, Burgner & VanEtten, 1969; Berman, McGandy, Burgner & VanEtten, 1969). The equations of and the atomic displacements from several calculated least-squares planes are given in Table 4. The angle between the normals to the best least-squares plane of the azetidine ring and that of the phenyl group is 90°. Fig. 2 is a stereoscopic drawing (Johnson, 1970) of the unit cell of AzHCl. The azetidinium moiety is linked to two twofold screw-related chloride ions by O–H···Cl and N–H···Cl hydrogen bonds having O(15)···Cl and N(1)···Cl distances of 3·083 (11) and 3·095 (9) Å.

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Table 4. *Calculated least-squares planes and atomic displacements for* AzHCl

Equations of least-squares planes (Cartesian coordinates).

(*a*) $0{\cdot}6593X+0{\cdot}5167Y-0{\cdot}5462Z=7{\cdot}4713$
(*b*) $0{\cdot}2947X-0{\cdot}8560Y-0{\cdot}4248Z=1{\cdot}5947$
(*c*) $0{\cdot}4367X-0{\cdot}7231Y-0{\cdot}5353Z=3{\cdot}0483$
(*d*) $0{\cdot}1303X-0{\cdot}9497Y-0{\cdot}2847Z=0{\cdot}2233$
(*e*) $0{\cdot}4454X-0{\cdot}8579Y-0{\cdot}2561Z=2{\cdot}0305$
(*f*) $0{\cdot}1289X-0{\cdot}8132Y-0{\cdot}5675Z=0{\cdot}8269$

Atomic displacements from least-squares planes (Å).

	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	(*f*)
N(1)		0·120*	0·000*	0·000*	0·474	0·000*
C(2)		−0·119*	0·000*	−0·479	0·000*	0·000*
C(3)		0·121*	0·000*	0·000*	0·000*	0·467
C(4)		−0·123*	−0·463	0·000*	0·000*	0·000*
C(5)		−0·732	−0·819	−0·840	−0·078	−1·106
C(7)	−0·011					
C(8)	−0·019*					
C(9)	0·014*					
C(10)	0·012*					
C(11)	−0·031*					
C(12)	0·023*					
C(13)	−0·002*					
C(14)		0·832	1·204	0·156	0·954	0·897
O(15)		−0·782	−0·905	−0·856	−1·123	−0·170

* Atoms defining least-squares planes.

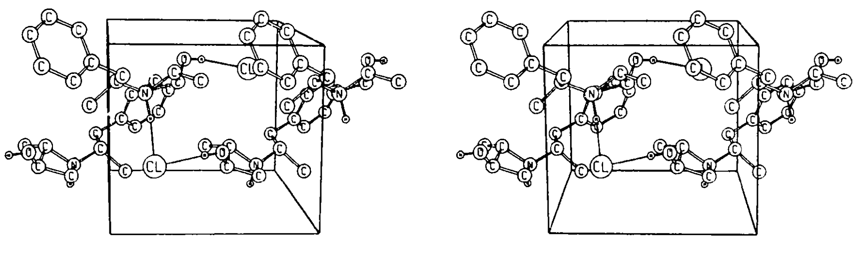

Fig. 2. A stereoscopic drawing (Johnson, 1970) of the unit cell of AzHCl. Hydrogen bonds O–H···Cl and N–H···Cl are shown as darker solid lines. The vertical axis is *b* and the horizontal axis is *a*.

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Crystal Structure of α-Glucuronamide

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Abstract. $C_6H_{11}NO_6$, monoclinic, $P2_1$, $a = 9{\cdot}229$ (12), $b = 5{\cdot}179$ (4), $c = 8{\cdot}261$ (8) Å, $\beta = 102{\cdot}9$ (2)°, $Z = 2$, $D_x = 1{\cdot}67$ g cm^{-3}. The structure was solved by routine application of the symbolic addition procedure and refined to a final R index of 5·1 %.

Experimental. Glucuronamide is the amide of glucuronic acid which is one of the components of the polysaccharide heparin. The crystal was selected from a commercial sample (Sigma Chemical Company). The 699 independent reflections were collected from a small crystal ($\sim 0{\cdot}34 \times 0{\cdot}12 \times 0{\cdot}07$ mm) on an automatic diffractometer using Cu $K\alpha$ radiation ($\lambda = 1{\cdot}54178$ Å, Ni filter). The θ–2θ scan mode of data collection was used (maximum $\sin \theta/\lambda = 0{\cdot}567$ Å^{-1}).

The structure was solved by the symbolic addition procedure for non-centrosymmetric crystals (Karle & Karle, 1966). Full-matrix least-squares methods (Busing *et al.*, 1971) were used to refine the structure. The atomic scattering factors used were those listed in *International Tables for X-ray Crystallography* (1962). The function minimized was $\sum w(|F_o| - |F_c|)^2$ where the weights were calculated according to the procedure outlined by Gilardi (1973). The final R index is 0·051 ($R_w = 0{\cdot}050$). The hydrogen atoms were located in a difference map. Positional parameters for the hydrogen atoms were included in the refinement. Hydrogen thermal factors (set equal to the final isotropic value for the atom to which they were bonded) were not refined. Table 1 lists the final coordinates and thermal

Table 1. *Fractional coordinates and thermal parameters with standard deviations*

The thermal parameters are of the form $T = \exp\,[\frac{1}{4}(B_{11}h^2a^{*2} + B_{22}k^2b^{*2} + B_{33}l^2c^{*2} + 2B_{12}hka^*b^* + 2B_{13}hla^*c^* + 2B_{23}klb^*c^*)]$.

Standard deviations are based solely on least-squares parameters.

	x	y	z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
N(1)	0·3546 (6)	0·6226 (13)	−0·0444 (6)	3·9 (2)	1·7 (2)	3·0 (2)	−0·8 (2)	1·6 (2)	−0·1 (2)
C(1)	0·0692 (6)	0·6069 (16)	0·2666 (6)	2·3 (2)	1·8 (2)	2·9 (2)	0·0 (2)	1·2 (2)	−0·2 (2)
C(2)	0·1801 (6)	0·5506 (13)	0·4309 (6)	2·6 (2)	1·2 (3)	2·7 (2)	−0·0 (2)	0·9 (2)	0·1 (2)
C(3)	0·2622 (6)	0·2968 (13)	0·4205 (7)	2·4 (2)	1·6 (2)	2·0 (2)	0·1 (2)	0·3 (2)	−0·3 (2)
C(4)	0·3342 (6)	0·3082 (13)	0·2730 (7)	2·4 (2)	1·5 (2)	2·3 (2)	−0·1 (2)	0·7 (2)	−0·2 (2)
C(5)	0·2152 (5)	0·3674 (13)	0·1144 (6)	2·1 (2)	1·9 (3)	2·4 (2)	0·4 (2)	0·6 (2)	−0·3 (2)
C(6)	0·2898 (5)	0·3961 (14)	−0·0295 (6)	2·1 (2)	2·4 (3)	2·4 (2)	−0·1 (2)	0·5 (2)	0·3 (2)
O(1)	−0·0435 (4)	0·4226 (11)	0·2436 (5)	2·2 (1)	2·7 (2)	3·5 (2)	−0·2 (2)	0·5 (1)	0·7 (2)
O(2)	0·1069 (4)	0·5276 (12)	0·5642 (4)	3·6 (2)	2·8 (2)	2·7 (2)	0·6 (2)	1·5 (1)	0·0 (2)
O(3)	0·3761 (4)	0·2542 (11)	0·5641 (4)	2·4 (2)	2·6 (2)	2·0 (1)	0·2 (2)	0·4 (1)	0·0 (1)
O(4)	0·4031 (4)	0·0696 (10)	0·2453 (4)	3·1 (2)	2·2 (2)	2·1 (1)	1·0 (2)	0·5 (1)	−0·0 (1)
O(5)	0·1442 (4)	0·6078 (0)	0·1335 (4)	2·7 (2)	1·3 (2)	2·5 (2)	0·4 (1)	1·0 (1)	0·3 (1)
O(6)	0·2939 (4)	0·2094 (11)	−0·1259 (4)	3·3 (2)	2·1 (2)	2·1 (1)	−0·2 (2)	0·8 (1)	−0·4 (1)