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The Structure of 2-Methylamino-1-(spiro[cyclopentane-1,1′-inden]-3′-yl)ethanol Hydrochloride

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Abstract. $C_{16}H_{21}NO.HCl$, triclinic, $P\bar{1}$, $a = 15{\cdot}394$, $b = 7{\cdot}324$, $c = 7{\cdot}430$ Å, $\alpha = 91{\cdot}81$, $\beta = 99{\cdot}15$, $\gamma = 113{\cdot}69°$, $V = 752{\cdot}90$ Å^3, $D_m = 1{\cdot}230$, $D_x = 1{\cdot}234$ g cm^{-3}, $Z = 2$, μ(Cu $K\alpha$) = 21·747 cm^{-1}, no systematic absences. The structure was determined by the Patterson method and refined by a full-matrix least-squares procedure to an R value of 0·040 for 2593 reflexions collected on an automatic four-circle diffractometer. The molecule consists of a maximally extended side chain and two mutually perpendicular rings, the indene ring system and the cyclopentane ring, the latter showing an envelope conformation. Three types of hydrogen bonds, N—H···O, N—H···Cl and O—H···Cl, form columns running in the *b* direction. In the other directions the structure is held together by van der Waals forces only.

Introduction. In search of new sympathomimetic amines the pharmaceutical company Kabi AB has synthesized a series of compounds with an indene ring system connected by a spiro carbon atom to a cyclopentane ring. The title compound, hereinafter referred to as KABI 2023, shows a pronounced adrenergic activity (Jönsson, Kempe, Mikiver & Sparf, 1977) and the crystal structure determination was undertaken as a part of a research project on biologically active amines. At the time of this work, only the racemic mixture of the compound could be obtained. However, recently Kabi AB has isolated the active isomer of KABI 2023, which will be the object of a subsequent crystal structure determination.

All attempts to recrystallize the material obtained from Kabi AB by evaporation of different solutions were fruitless. An aqueous solution for instance gave nothing but a polycrystalline solid and slow evaporation of a methanol solution resulted in distorted crystals often markedly curved. However, if the methanol solution was enclosed in a surrounding of ethanol and the ethanol was allowed to diffuse into the methanol solution, large, transparent crystals were obtained. One optically perfect crystal was chosen and reshaped by partial dissolution to an almost perfect sphere with a radius of 0·2 mm. Preliminary unit-cell dimensions were derived from Weissenberg photographs using a method for determining triclinic cell parameters from one crystal setting (Hebert, 1978). Accurate cell dimensions were obtained by least-squares refinement of the setting angles of 25 accurately centred reflexions. The density was measured by flotation in a xylene–chloroform mixture.

The crystal was mounted on a Philips PW 1100 computer-controlled diffractometer and the ω–2θ scan technique was employed to measure reflexions out to $\theta = 70°$ at a scan speed of 0·02° s^{-1} with a scan width of 1·6°. Using graphite-monochromatized Cu $K\alpha$ radiation ($\lambda = 1{\cdot}5418$ Å) 2870 unique reflexions were measured. Reference reflexions recorded at regular intervals during the data collection showed no significant change in intensity. As the crystal was approximately spherical an absorption correction program for spherical crystals could be applied on the primary data and the net intensities thus obtained were corrected for Lorentz and polarization factors. The corrected structure amplitudes were then placed on an approximately absolute scale by Wilson statistics.

The position of the Cl atom could easily be located from the three-dimensional Patterson maps. Three subsequent electron density calculations revealed the non-hydrogen atoms of the KABI 2023 molecule. The refinement was carried out by a full-matrix least-squares procedure. After two cycles of isotropic and one cycle of anisotropic refinement of the non-hydrogen atoms the conventional R value ($R = \sum||F_o| - |F_c||/\sum |F_o|$) was 0·089. In a difference synthesis calculated at this stage all the 22 H atoms could easily be located. One cycle of refinement of the non-hydrogen atoms with the H atoms fixed in the positions found in the difference maps lowered the R value to 0·067. Weights were then applied to $|F_o|$ according to $w = 1/(a + |F_o| + c|F_o|^2 + d|F_o|^3)$ with $a = 5$, $c = 0{\cdot}1$ and $d = 0{\cdot}001$. Three cycles of refinement of the positional parameters of the H atoms with their temperature factors locked at 3·5 Å^2 and three cycles of refinement of the non-hydrogen atoms concluded the refinement procedure.* The average of the positional

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* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33664 (18 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

parameter shifts of the last cycle expressed as fractions of their e.s.d.'s was 0·53. The final R value was 0·046 with all the 2870 collected reflexions included and 0·040 when 277 low-intensity reflexions with $|F_o|/|F_c| < 0·7$ or $|F_o|/|F_c| > 1·3$ were given zero weight and were excluded from the calculations. The atomic fractional coordinates are given in Tables 1 and 2. The atom scattering factors were those of *International Tables for X-ray Crystallography* (1974) and the computations were performed on an IBM 370/165 computer using our program system (Bergin, 1971*a*) except for the stereo pictures which were produced by the plotting program *ORTEP* (Johnson, 1965).

Table 1. *Final fractional coordinates* ($\times 10^4$) *for non-hydrogen atoms*

E.s.d.'s in parentheses are in units of the least significant digit.

	x	*y*	*z*
Cl	146 (1)	1580 (1)	2410 (1)
O	−1096 (1)	3087 (2)	−244 (1)
N	440 (1)	2964 (2)	−1851 (2)
C(1)	−2574 (1)	1724 (2)	−5069 (2)
C(2)	−2395 (1)	527 (2)	−6317 (2)
C(3)	−2935 (1)	92 (3)	−8095 (2)
C(4)	−3629 (1)	806 (3)	−8597 (2)
C(5)	−3813 (1)	1996 (3)	−7352 (2)
C(6)	−3283 (1)	2445 (2)	−5578 (2)
C(7)	−3334 (1)	3679 (2)	−3973 (2)
C(8)	−4330 (1)	2978 (3)	−3396 (3)
C(9)	−4253 (1)	4766 (4)	−2152 (3)
C(10)	−3479 (1)	6625 (3)	−2705 (3)
C(11)	−3116 (1)	5900 (3)	−4245 (2)
C(12)	−2574 (1)	3535 (2)	−2504 (2)
C(13)	−2132 (1)	2471 (2)	−3124 (2)
C(14)	−1295 (1)	2164 (2)	−2070 (2)
C(15)	−410 (1)	3142 (2)	−2949 (2)
C(16)	1322 (1)	3826 (3)	−2662 (2)

Table 2. *Final fractional coordinates* ($\times 10^3$) *for hydrogen atoms having a temperature factor B of* 3·5 Å^2

E.s.d.'s in parentheses are in units of the last digit.

	x	*y*	*z*
H(2)	−189 (2)	5 (3)	−600 (3)
H(3)	−280 (2)	−79 (3)	−883 (3)
H(4)	−401 (2)	46 (3)	−989 (3)
H(5)	−435 (1)	243 (3)	−778 (3)
H(8*A*)	−450 (2)	168 (3)	−281 (3)
H(8*B*)	−486 (2)	264 (3)	−452 (3)
H(9*A*)	−402 (1)	457 (3)	−72 (3)
H(9*B*)	−487 (2)	501 (3)	−234 (3)
H(10*A*)	−374 (2)	757 (3)	−304 (3)
H(10*B*)	−290 (2)	728 (3)	−166 (3)
H(11*A*)	−351 (2)	589 (3)	−545 (3)
H(11*B*)	−238 (2)	667 (3)	−424 (3)
H(12)	−244 (2)	421 (3)	−123 (3)
H(14)	−147 (2)	64 (3)	−205 (3)
H(O)	−82 (2)	254 (3)	47 (3)
H(15*A*)	−51 (1)	250 (3)	−415 (3)
H(15*B*)	−26 (2)	459 (3)	−305 (3)
H(N*A*)	31 (2)	165 (3)	−177 (3)
H(N*B*)	57 (2)	363 (3)	−67 (3)
H(16*A*)	120 (1)	330 (3)	−387 (3)
H(16*B*)	183 (1)	345 (3)	−192 (3)
H(16*C*)	154 (1)	527 (3)	−261 (3)

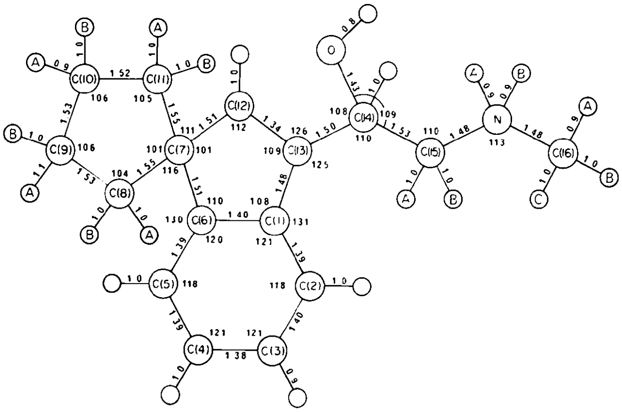

Fig. 1. Schematic drawing of the KABI 2023 molecule showing the numbering of the atoms. Distances in Å, angles in degrees.

Table 3. *Intramolecular bond distances* (Å) *and angles* (°) *with estimated standard deviations in parentheses*

C(1)–C(2)	1·389 (2)	C(2)–H(2)	0·97 (1)
C(2)–C(3)	1·396 (2)	C(3)–H(3)	0·94 (2)
C(3)–C(4)	1·375 (2)	C(4)–H(4)	1·01 (2)
C(4)–C(5)	1·388 (2)	C(5)–H(5)	1·01 (1)
C(5)–C(6)	1·388 (2)	C(8)–H(8*A*)	1·01 (2)
C(6)–C(1)	1·398 (1)	C(8)–H(8*B*)	1·02 (2)
C(6)–C(7)	1·506 (2)	C(9)–H(9*A*)	1·10 (2)
C(7)–C(8)	1·545 (1)	C(9)–H(9*B*)	1·03 (1)
C(8)–C(9)	1·532 (3)	C(10)–H(10*A*)	0·95 (2)
C(9)–C(10)	1·526 (3)	C(10)–H(10*B*)	1·02 (2)
C(10)–C(11)	1·519 (2)	C(11)–H(11*A*)	0·99 (2)
C(11)–C(7)	1·550 (2)	C(11)–H(11*B*)	1·04 (1)
C(7)–C(12)	1·508 (2)	C(12)–H(12)	1·01 (2)
C(12)–C(13)	1·336 (1)	C(14)–H(14)	1·04 (2)
C(13)–C(1)	1·480 (2)	O–H(O)	0·84 (2)
C(13)–C(14)	1·498 (1)	C(15)–H(15*A*)	0·95 (2)
C(14)–O	1·426 (2)	C(15)–H(15*B*)	1·00 (2)
C(14)–C(15)	1·525 (1)	N–H(N*A*)	0·91 (2)
C(15)–N	1·483 (1)	N–H(N*B*)	0·95 (2)
N–C(16)	1·483 (1)	C(16)–H(16*A*)	0·92 (2)
		C(16)–H(16*B*)	1·02 (2)
		C(16)–H(16*C*)	0·97 (2)

C(6)–C(1)–C(2)	120·9 (1)	C(11)–C(7)–C(12)	110·8 (1)
C(13)–C(1)–C(2)	131·4 (1)	C(7)–C(8)–C(9)	104·4 (2)
C(6)–C(1)–C(13)	107·8 (1)	C(8)–C(9)–C(10)	106·5 (2)
C(1)–C(2)–C(3)	117·9 (1)	C(9)–C(10)–C(11)	106·4 (2)
C(2)–C(3)–C(4)	121·2 (2)	C(10)–C(11)–C(7)	104·8 (1)
C(3)–C(4)–C(5)	121·0 (2)	C(7)–C(12)–C(13)	112·3 (1)
C(4)–C(5)–C(6)	118·5 (2)	C(12)–C(13)–C(14)	126·1 (1)
C(5)–C(6)–C(1)	120·5 (1)	C(12)–C(13)–C(1)	108·5 (1)
C(5)–C(6)–C(7)	129·5 (1)	C(1)–C(13)–C(14)	125·3 (1)
C(1)–C(6)–C(7)	110·0 (1)	C(13)–C(14)–O	108·0 (1)
C(6)–C(7)–C(8)	115·8 (1)	C(13)–C(14)–C(15)	109·8 (1)
C(6)–C(7)–C(11)	115·7 (1)	O–C(14)–C(15)	109·4 (1)
C(6)–C(7)–C(12)	101·4 (1)	C(14)–C(15)–N	110·5 (1)
C(8)–C(7)–C(11)	101·2 (1)	C(15)–N–C(16)	113·4 (1)
C(8)–C(7)–C(12)	112·5 (1)		

Fig. 1 is a schematic drawing of the KABI 2023 molecule showing the numbering of the atoms. The bond lengths and angles between atoms, uncorrected for thermal motion, given in this figure and in Table 3, show no significant deviations from standard values and are close to those found in earlier determinations of indene derivatives (Dreissig, Luger, Rewicki & Tuchscherer, 1973; Declercq, Germain & Van Meerssche, 1975; Carlström, 1976). The conformation around the spiro atom C(7) is slightly distorted. Thus two of the angles, C(6)–C(7)–C(12) and C(8)–C(7)–C(11), are somewhat smaller than would be expected from a perfect tetrahedral arrangement.

As can be seen from the stereoscopic pair in Fig. 2 the molecule consists of three approximately planar parts constituting the three-dimensional structure. The deviations of the atoms from these planes are given in Table 4. The exocyclic atom C(14) is 0·11 Å out of the indene ring system which is planar within the limits of error. Almost perpendicular (88·7°) to this plane, connected by the spiro atom C(7), is the cyclopentane ring which shows an envelope conformation with C_s symmetry. The third plane consists of the atoms C(13)–C(15) and N forming the ethylamine side chain. The C(16) atom is well within this plane which is inclined at 61·5° to the indene ring system, a conformation found in many biologically active phenethylamines and indoleamines (Carlström, Bergin & Falkenberg, 1973). The N atom is 1·6 Å above the indene nucleus. This distance is in accordance with the value found by Bergin (1971*b*) for sympathomimetic amines acting directly on the receptor. The overall structure of the title compound exhibits no significant differences from the related substance KABI 1847 (Carlström, 1976) which is similar but lacks the hydroxyl group attached to the side chain.

A stereoscopic drawing of the molecular packing and the hydrogen-bonding system is shown in Fig. 3. Table 5 gives pertinent distances and angles for the hydrogen bonds. The Cl ions together with the positively charged N atoms and the O atoms of the KABI 2023 molecule

Table 4. *Least-squares planes and deviations in Å of individual atoms*

The equations of the planes are in the form $AX + BY + CZ = D$, where X, Y, Z are coordinates in orthogonal ångström space along a, b, c respectively. Asterisks indicate atoms not included in the calculations of the planes.

Plane of the indene ring system

$$-0{\cdot}4428X - 0{\cdot}8537Y + 0{\cdot}2740Z = -0{\cdot}6189$$

C(1)	−0·0024	C(6)	−0·0002	H(2)*	−0·021
C(2)	0·0073	C(7)	0·0002	H(3)*	0·068
C(3)	0·0019	C(12)	0·0130	H(4)*	0·000
C(4)	0·0000	C(13)	−0·0150	H(5)*	0·030
C(5)	−0·0047	C(14)*	−0·1139	H(12)*	0·030

Plane of the cyclopentane ring

$$0{\cdot}7186X - 0{\cdot}1879Y + 0{\cdot}6695Z = -7{\cdot}2140$$

C(8)	−0·0008	C(1)	0·0008
C(9)	0·0012	C(7)*	0·6228
C(10)	−0·0012		

Plane of the side chain

$$0{\cdot}1924X - 0{\cdot}8071Y - 0{\cdot}5582Z = -0{\cdot}9393$$

C(13)	−0·0221	N	−0·0224
C(14)	0·0218	C(16)*	0·0213
C(15)	0·0226		

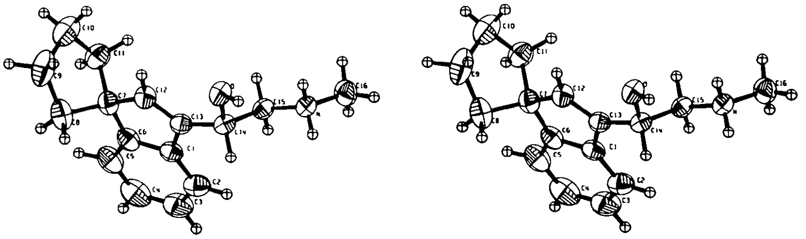

Fig. 2. Stereoscopic drawing of the KABI 2023 molecule. Heavy atoms are represented by thermal ellipsoids of 50% probability. Hydrogen atoms are depicted as small spheres.

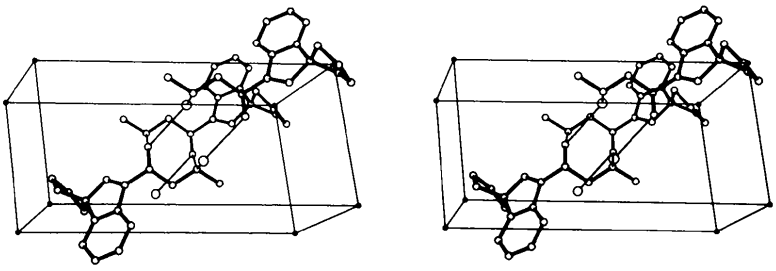

Fig. 3. Stereoscopic drawing of the molecular packing as seen along *b*. Thin lines represent hydrogen bonds.

Table 5. *Hydrogen-bonded interactions*

The columns labelled x', y', z' give the symmetry of the acceptor atom Y'. Reference molecule in x, y, z.

X	H	Y'	x'	y'	z'	$X\cdots Y'$	$\mathrm{H}\cdots Y'$	X–H$\cdots Y'$
N	H(N*B*)	O	$-x$	$1-y$	$-z$	2·95 Å	2·25 Å	130°
N	H(N*A*)	Cl	$-x$	$-y$	$-z$	3·07	2·19	164
O	H(O)	Cl	$-x$	$-y$	$-z$	3·06	2·24	170

form a network of hydrogen bonds running in the *b* direction. A molecule is connected in one direction directly to a centrosymmetrically related molecule through pairs of N—H···O bonds. In the opposite direction the molecules are held together by the intercalated Cl ions through pairs of N—H···Cl and O—H···Cl hydrogen bonds. The side chain of the molecule is in this way tightly locked through the hydrogen-bonding system, while the hydrophobic parts of the molecule, *i.e.* the indene ring system and the cyclopentane ring, are not taking part in any intermolecular bonding. This gives rise to the proportionately high thermal vibration of this part of the molecule. In the *a* and *c* directions there are no connexions other than van der Waals contacts holding the structure together. This explains the rod shape of the crystals with the long direction corresponding to the *b* axis. No distances violating ordinary packing requirements are found in the structure apart from the hydrogen bonds.

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Sparteine *N*(16)-Oxide Monoperchlorate

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Abstract. $C_{15}H_{27}N_2O^+.ClO_4^-$, $M_r = 350{\cdot}9$, orthorhombic, $P2_12_12_1$, $a = 16{\cdot}089$ (2), $b = 12{\cdot}656$ (2), $c = 8{\cdot}314$ (2) Å, $V = 1687{\cdot}7$ Å^3, $Z = 4$, $D_c = 1{\cdot}38$ g cm^{-3}, $R = 0{\cdot}047$, $R_w = 0{\cdot}052$ for 1279 reflections. The four rings in the sparteine cation are in the chair conformation. There is a very strong intramolecular hydrogen bond between N(1) and O(16), of length 2·492 (6) Å.

Introduction. From the IR and NMR investigations (Wiewiórowski & Baranowski, 1967; Baranowski, Skolik & Wiewiórowski, 1964; Skolik, Łangowska & Wiewiórowski, 1972, 1975) and from p*Ka* values it is known that the sparteine *N*(16)-oxide cation (I.H$^+$) of the title compound has an all-chair conformation in both the solid and liquid states. The all-chair conformation of the cation I.H$^+$ is stabilized by a strong intramolecular hydrogen bond shown in Fig. 1. The chemical and spectroscopic results were confirmed by the X-ray analysis of sparteine *N*(16)-oxide sesquiperchlorate [2I.3HClO$_4$, Fig. 2(*a*)] (Srivastava & Przybylska,