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The crystal structure of methacholine chloride, $C_8H_{18}ClNO_2$

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.34 × 0.34 × 0.22 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.33 mm ⁻¹
Diffractometer, scan mode:	Bruker APEX-II, φ and ω
$\theta_{\max}$, completeness:	28.3°, 99%
$N(hkl)_{\text{measured}}$:	2506, 2506, 0.027
$N(hkl)_{\text{unique}}$, R_{int} :	
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 1965
$N(\text{param})_{\text{refined}}$:	115
Programs:	Bruker [1, 2], SHELX [3], WinGX/ORTEP [4], Mercury [5], PLATON [6]

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Abstract

$C_8H_{18}ClNO_2$, monoclinic, $P2_1/c$ (no. 14), $a = 6.8110(5)$ Å, $b = 8.8779(7)$ Å, $c = 17.2774(16)$ Å, $\beta = 97.582(4)^\circ$, $V = 1035.59(15)$ Å³, $Z = 4$, $R_{\text{gt}}(F) = 0.0484$, $wR_{\text{ref}}(F^2) = 0.0922$, $T = 200$ K.

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The molecular structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Source of material

The compound was obtained commercially (Merck Schuchardt). Crystals were taken directly from the product.

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Experimental details

Carbon-bound H atoms were placed in calculated positions (C–H 0.99 Å for methylene groups and C–H 1.00 Å for methine groups) and were included in the refinement in the riding model approximation, with $U(H)$ set to $1.2U_{\text{eq}}(C)$.

The H atoms of the methyl groups were allowed to rotate with a fixed angle around the C–C bond to best fit the experimental electron density (HFIX 137 in the SHELX program suite [3]), with $U(H)$ set to $1.5U_{\text{eq}}(C)$.

The compound was refined as a two-component twin with a volume ratio of 21.3–78.7% (twin law 1.00 0.00 0.00, 0.00 –1.00 0.00, –0.67 0.00 –1.00).

Comment

The effect of size and steric pretense of large ions on chemical and spectroscopic properties of compounds have been a focus of research for many decades. Among the many effects that can be attributed to the spatial requirements of counterions have been the glass transition temperature in ionomers [7], surfactant modifying properties [8], the charge transfer in radical ions [9] and polymer-modified electrodes [10] as well as the structural and vibrational spectroscopic behaviour of DNA building blocks [11]. Furthermore, the benefit of choosing the adequate size of counterions to crystallize ionic compounds has been confirmed on many occasions [12].

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

Atom	x	y	z	U _{iso} [*] /U _{eq}
Cl1	0.26533 (10)	0.71572 (6)	0.52943 (4)	0.02950 (15)
O1	0.3911 (2)	0.10456 (17)	0.76844 (9)	0.0235 (4)
O2	0.2547 (3)	0.31055 (19)	0.81546 (11)	0.0393 (5)
N1	0.2700 (3)	0.1819 (2)	0.58946 (11)	0.0210 (4)
C1	0.1907 (4)	0.0680 (3)	0.86703 (16)	0.0347 (6)
H1A	0.086549	0.118463	0.891392	0.052 [*]
H1B	0.293308	0.030980	0.907710	0.052 [*]
H1C	0.133606	−0.016974	0.835546	0.052 [*]
C2	0.2797 (4)	0.1762 (3)	0.81622 (14)	0.0243 (5)
C3	0.5027 (4)	0.1968 (2)	0.71945 (13)	0.0220 (5)
H3	0.460099	0.304429	0.721310	0.026 [*]
C4	0.7198 (4)	0.1824 (3)	0.75162 (15)	0.0313 (6)
H4A	0.765135	0.079847	0.742729	0.047 [*]
H4B	0.737503	0.203594	0.807773	0.047 [*]
H4C	0.797300	0.254466	0.725150	0.047 [*]
C5	0.4643 (3)	0.1386 (2)	0.63639 (13)	0.0212 (5)
H5A	0.572642	0.174643	0.608123	0.025 [*]
H5B	0.472096	0.027266	0.638104	0.025 [*]
C6	0.0962 (4)	0.1179 (4)	0.62296 (16)	0.0450 (8)
H6A	−0.026059	0.143760	0.589081	0.068 [*]
H6B	0.091766	0.159938	0.675151	0.068 [*]
H6C	0.109179	0.008114	0.626588	0.068 [*]
C7	0.2671 (4)	0.1205 (3)	0.50868 (13)	0.0268 (5)
H7A	0.142003	0.147766	0.477071	0.040 [*]
H7B	0.279554	0.010570	0.511068	0.040 [*]
H7C	0.377936	0.162921	0.484992	0.040 [*]
C8	0.2516 (5)	0.3508 (3)	0.58218 (17)	0.0408 (7)
H8A	0.365221	0.390910	0.559457	0.061 [*]
H8B	0.248536	0.394959	0.633987	0.061 [*]
H8C	0.129002	0.376142	0.548370	0.061 [*]

In continuation of our interest in metrical features of large cations [13–15] the structure of the title compound has been determined. Methacholine chloride is a synthetic derivative of acetylcholine, a neurotransmitter. It is used in the bronchoprovocation test to determine the non-specific airway responsiveness. This pulmonary lung function test is one method used to assess airway responsiveness and to help diagnose asthma [16–18]. The structure of *L*-(+)-(S)-acetyl-β-methylcholine iodide is apparent in the literature [19].

The structure shows a propane derivative bearing an N(CH₃)₃ group on one of the terminal carbon atoms as well as an acetyl substituent on the central carbon atom. The positive charge caused by the tetracoordinate nitrogen atom is balanced by the presence of one chloride anion. N–C bond lengths are found in a very narrow range of 1.496(3)–1.508(3) Å with the longest bond established to the propyl chain. Carbon oxygen bond lengths of 1.461(3)° for the ethereal bond as well as 1.352(3) Å for the carbonyl group

are reminiscent of similar bond lengths in other acetyl derivatives that have been deposited with the Cambridge Structural Database [20].

In the crystal, C–H···O as well as C–H···Cl contacts are apparent whose range invariably falls by more than 0.1 Å below the sum of van-der-Waals radii of the atoms participating in them. These are supported by hydrogen atoms on two of the three nitrogen-bonded methyl groups as well as one hydrogen atom on the non-functionalized carbon atom of the central propyl chain. The latter group also gives rise to the only C–H···O contact that exclusively employs the keto-type oxygen atom acting as acceptor. In terms of graph-set analysis [21], the descriptor for these contacts is *DDDDC*₁¹(6) on the unary level.

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