REFINEMENT OF THE CRYSTAL STRUCTURE OF (RS)-CARNITINE HYDROCHLORIDE

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A single crystal of (RS)-carnitine hydrochloride has been obtained, and its crystal structure has been refined by an x-ray structural experiment.

Carnitine (γ-trimethylamino-β-hydroxybutyrobetaine) is present both in plant and animal tissues (in the form of the L-enantiomer). It is known as vitamin B_T and possesses a manifold medicinal action, particularly in myocardial ischemia [1, 2], and also a muscarinic stimulating action on the nervous system [3]. Compounds possessing anabolic and immunostimulating properties have been obtained from carnitine, and the refinement of its structure is therefore of interest in connection with the purposeful search for effective new drugs.

The crystal structure of the hydrochloride of racemic carnitine has been determined previously by the photo method with limited accuracy (R = 0.13) [6]. As a result of our investigations the structure of carnitine hydrochloride has been established more accurately (R = 0.048).

The molecule is constructed of cations of protonated [at the carboxylic O(2) atom] carnitine and of Cl^- anions linked in a zigzag chain (along the z axis; neighboring ions of the same type are linked with a glide plane by O(1)–H(O1)···Cl and O(2)–H(O2)···Cl hydrogen bonds (distances: O···Cl 3.08 and 3.00 Å; H···Cl 2.25 and 2.05 Å; and angles O–H–Cl 173 and 171°, respectively).

The geometry of the cation agrees with that found in [6] (see Fig. 1 and Table 1). The conformation of its chain is close to the anti-anti type [torsional angles: N(1)C(1)-C(2)C(3) 175.2°, C(1)C(2)C(3)C(4) −166.7°, C(2)C(3)C(4)O(2) −156.7°], which agrees well with hypotheses [1, 7] on the link between the geometry and bioactivity of such compounds. The conformation of the zwitterionic carnitine differs from that given practically only by the torsional angle C(2)C(3)C(4)O(2) (58.5°). The orientation of the NMe group relative to the main chain is skew, the torsional angle C(5)N(1)C(1)C(2) being −44.4°.

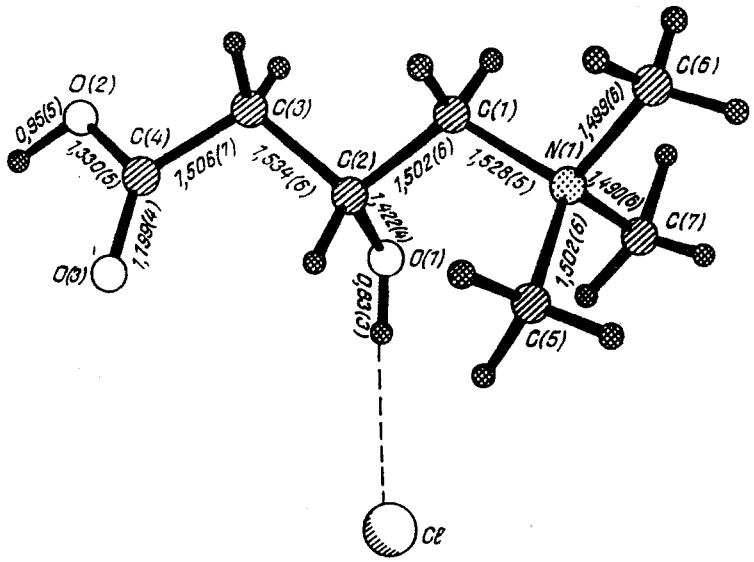

Fig. 1. Cation (with bond lengths) and anion in a carnitine hydrochloride crystal.

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TABLE 1. Valence Angles ω (deg.)

Angle	ω	Angle	ω
C(6)N(1)C(7)	109.0(4)	O(1)C(2)C(1)	111.9(3)
C(5)N(1)C(7)	109.6(3)	C(1)C(2)C(3)	106.9(3)
C(5)N(1)C(6)	108.8(3)	O(1)C(2)C(3)	107.9(3)
C(1)N(1)C(7)	111.3(3)	C(2)C(3)C(4)	111.3(3)
C(1)N(1)C(6)	106.9(3)	O(3)C(4)C(3)	125.1(4)
C(1)N(1)C(5)	111.2(3)	O(2)C(4)C(3)	111.7(3)
N(1)C(1)C(2)	116.5(3)	O(2)C(4)O(3)	123.1(4)

TABLE 2. Coordinates of the Atoms (×10⁴, for H ×10³) in the Structure of (I)

Atom	x	y	z	Atom	x	y	z
Cl	2436(2)	2113(1)	784(1)	C2	6762(6)	627(3)	3142(3)
O1	6647(5)	1765(2)	2722(2)	C3	7292(6)	769(3)	4282(3)
O2	5958(4)	1755(3)	5339(2)	C4	5361(7)	1226(3)	4440(3)
O3	7500(4)	1131(3)	3841(2)	C5	6023 7)	−855(4)	1366(3)
N1	8294(5)	−436(3)	2001(2)	C6	9852(7)	−1421(4)	2123(3)
C1	8580(6)	−91(3)	3073(3)	C7	8825 (8)	560(4)	1475(3)
H1	854(7)	−88(4)	338(3)	H6	1137(7)	−101(4)	253(3)
H1′	1012(6)	36(3)	338(3)	H6′	918(6)	−218(4)	238(3)
H2	522(7)	20(4)	276(3)	H6″	998(7)	−169(4)	155(3)
H3	859(7)	135(4)	410(3)	H7	767(7)	115(4)	138(3)
H3′	768(6)	−11(4)	458(3)	H7′	1052(7)	82(4)	193(3)
H5	605(7)	−120(4)	78(3)	H7″	894(7)	30(4)	100(3)
H5′	552(7)	−150(4)	175(3)	H10	546(6)	182(3)	222(3)
H5″	491(7)	−011(4)	119(3)	H20	474(7)	209(4)	541(3)

EXPERIMENTAL

The x-ray diffraction experiment was conducted on a Syntex P2 automatic four-circle diffractometer at 20°C (CuK_α radiation, graphite monochromator), and the calculations were made on a personal computer by the SELX-76 program.

The crystals were monoclinic: a = 6.750 (1), b = 11,414 (2), c = 14.381 (c) Å, β = 114.38 (2)°, V = 1009.2 (4) Å³, sp. gr. $P2_1/c$, Z = 4, $C_7H_{16}NO_3^+Cl^-$, d_{calc} = 1.30 g/cm³. In [6], an uncorrected set was used: d = 6.77 (1), b = 11.41 (2), c = 15.10 (3) Å, β = 120.1 (1)°, V = 1008.9 Å³, sp. gr. $P2_1/c$, which can be obtained from that which we used by the transformation $c = c - 2a$.

The intensities of 1428 independent reflections with $F < 5\sigma(F)$ and $2\theta \leq 124°$ were measured by the $\theta/2\theta$ scanning method. The structure was interpreted by the direct method. All the nonhydrogen atoms were refined by the MLS in the anisotropic approximation, and all the H atoms (revealed by a difference synthesis) in the isotropic approximation to R = R_w = 0.048. The coordinates of the atoms are given in Table 2.

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