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The Crystal Structure and Conformational Analysis of Acetylcarnitine Hydrochloride Monohydrate

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(*Received* 21 *June* 1976; *accepted* 24 *July* 1976)

Acetylcarnitine hydrochloride monohydrate, $C_9H_{17}NO_4.HCl.H_2O$, is monoclinic, space group $P2_1/c$, with $a = 12{\cdot}037\,(1)$, $b = 9{\cdot}509\,(1)$, $c = 12{\cdot}449\,(1)$ Å, $\beta = 109{\cdot}20\,(1)°$, $Z = 4$. Counter data collected with Mo $K\alpha$ radiation were used to derive the structure by direct methods. Refinement by full-matrix least squares led to an R of 0·055 for 2441 reflexions with $I > 0$. Bond distances and angles of the acetylcarnitine cation agree well with those of other β-substituted acetylcholine derivatives. The conformational analysis of the isolated molecule, performed with the force field made up by torsional barriers about single bonds and non-bonded interactions, shows three minima in the energy surface. One of these corresponds to the experimental configuration in the crystal.

Introduction

The role of carnitine (γ-trimethylammonium β-hydroxybutyrate) in fatty-acid metabolism is well documented (Bremer, 1962; Norum & Bremer, 1963; Fritz & Yue, 1963; Bressler & Katz, 1965). The currently held belief is that carnitine serves as a carrier of activated fatty acyl groups, which are transported across the mitochondrial membrane in the form of carnitine esters. The translocation of the active acetyl group of acetyl coenzyme A by acetylcarnitine from intra- to extra-mitochondrial sites has been discussed by Bressler & Katz (1965). More recently, Mueller & Strack (1973) have evaluated the hydrolysis enthalpy of some *O*-acylcarnitines and betaine esters; the relation between ΔH and the free energy indicated that the ΔG^0 value for all *O*-acylcarnitines is $-7{\cdot}90$ kcal mol^{-1}. This result confirms the statement of Friedman & Fraenkel (1955), that the ester bond of acetylcarnitine is a high-energy bond comparable to the thioester bond of acetyl coenzyme A.

We have performed an X-ray crystallographic study of acetylcarnitine hydrochloride monohydrate (ACC) to compare its conformation with that of carnitine (CAR) (Tomita, Urabe, Kim & Fujiwara, 1974). Furthermore, since ACC has muscarinic action in the nervous system (Hosein & Proulx, 1964), its structure can be compared with that of other acetylcholine-like molecules displaying the same action (Baker, Chothia, Pauling & Petcher, 1971).

Experimental

Crystals of ACC were obtained from a dilute methanolic solution of commercial acetylcarnitine hydrochloride by slow evaporation at 275 K. Cell dimensions reported in Table 1 were obtained by a least-squares fit to the $\sin^2\theta$ values of 45 hkl reflexions measured on a diffractometer. The space group $P2_1/c$ was indicated by the absences $h0l$ with l odd and $0k0$ with k odd. The density was measured by flotation in mixed solvents. For the data collection a crystal $0{\cdot}35 \times 0{\cdot}25 \times 0{\cdot}20$ mm was mounted on a computer-controlled Syntex $P\bar{1}$ diffractometer using graphite-monochromated Mo $K\alpha$ radiation ($\lambda = 0{\cdot}71069$ Å) and a variable θ–2θ scan technique. Background measurements were taken at both ends of the scan range, each for a time equal to one-half of the scan time. Two standard reflexions were checked after each 30 intensity measurements; they showed no appreciable trend. The data set consisted of 2441 observed (*i.e.* >0) out of 2652 independent reflexions measured in the range $0 < 2\theta < 52°$. Each reflexion was assigned a variance of $\sigma^2(I)$ based on counting statistics plus a term $(0{\cdot}03 \times S)^2$, where S is the scan count. Intensities and their standard deviations $[\sigma(I)]$ were corrected for Lorentz and polarization effects, but not for absorption.

The structure was solved by direct methods. The positions of all non-hydrogen atoms were obtained from an E map, and those of the H atoms from difference maps calculated during the course of the refinement. Since the methyl group C(9) undergoes extensive thermal motion, the atomic parameters of its H atoms were included only in the structure factor calculations but not refined. Refinement was by full-matrix least-squares minimization of the quantity $\Sigma\, w(|F_o| - |F_c|)^2$, with weights w equal to $4F_o^2/\sigma^2(F_o^2)$. Atomic form factors for C, N, O and Cl^- were from Cromer & Waber (1965), and for H from Stewart, Davidson & Simpson (1965). In the final cycles, 213 parameters were simultaneously adjusted: coordinates and anisotropic temperature coefficients b_{ij} for the 16 heavy atoms, coordinates and isotropic B's for the 17 H atoms and a scale factor. The resulting atomic parameters are given in Tables 2 and 3.* The final R $(\Sigma||F_o| - |F_c||/\Sigma|F_o|)$ was 0·055 for 2441 reflexions showing positive net intensity [$R = 0{\cdot}032$ for 1470

Table 1. *Crystal data*

$C_9H_{17}NO_4.HCl.H_2O$	F.W. 257·72
Space group $P2_1/c$	$Z = 4$
$a = 12{\cdot}037\,(1)$ Å	$V = 1345{\cdot}7$ Å^3
$b = 9{\cdot}509\,(1)$	$D_m = 1{\cdot}26\,(1)$ g cm^{-3}
$c = 12{\cdot}449\,(1)$	$D_c = 1{\cdot}272$
$\beta = 109{\cdot}20\,(1)°$	$\mu(\text{Mo } K\alpha) = 2{\cdot}95$ cm^{-1}

Table 3. *Coordinates* ($\times 10^3$) *and isotropic temperature coefficients for the hydrogen atoms*

	x	y	z	$10B$
H(1)	−203 (2)	369 (3)	179 (2)	67 (7)
H(2)	66 (1)	224 (2)	270 (2)	46 (4)
H(3)	2 (2)	170 (2)	145 (2)	46 (5)
H(4)	114 (1)	339 (2)	84 (1)	28 (3)
H(5)	274 (1)	338 (2)	307 (1)	35 (4)
H(6)	174 (1)	458 (2)	272 (1)	35 (4)
H(7)	431 (2)	473 (2)	141 (2)	61 (5)
H(8)	329 (2)	363 (2)	85 (2)	55 (7)
H(9)	420 (2)	336 (3)	209 (2)	78 (7)
H(10)	427 (2)	499 (2)	360 (2)	71 (6)
H(11)	428 (2)	633 (2)	277 (2)	59 (6)
H(12)	329 (2)	625 (2)	335 (2)	66 (6)
H(13)	181 (2)	646 (3)	151 (2)	71 (7)
H(14)	284 (2)	656 (2)	99 (2)	63 (5)
H(15)	178 (2)	542 (3)	52 (2)	77 (7)
H(16)*	222	−84	10	90
H(17)*	295	−52	140	80
H(18)*	331	14	38	90
H(19)	−367 (3)	524 (3)	120 (2)	68 (10)
H(20)	−388 (2)	401 (2)	83 (2)	58 (6)

* From ΔF synthesis, not refined.

Table 2. *Final atomic parameters and standard deviations* (*in parentheses*)

Fractional coordinates are $\times 10^5$, thermal parameters $\times 10^4$. The anisotropic temperature coefficients are of the form $T_i = \exp[-(b_{11}h^2 + b_{22}k^2 + b_{33}l^2 + 2b_{12}hk + 2b_{13}hl + 2b_{23}kl)]$.

	x	y	z	b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
C(1)	−5493 (17)	35882 (23)	17162 (16)	57 (2)	111 (3)	55 (2)	−8 (2)	15 (1)	0 (2)
C(2)	3873 (18)	24909 (23)	19102 (19)	61 (2)	94 (3)	70 (2)	−5 (2)	19 (1)	6 (2)
C(3)	14223 (17)	29732 (20)	15627 (16)	55 (2)	88 (2)	50 (1)	6 (2)	18 (1)	6 (2)
C(4)	22059 (17)	39530 (21)	24348 (15)	53 (2)	91 (2)	46 (1)	5 (2)	21 (1)	1 (2)
C(5)	37649 (27)	40844 (29)	15354 (27)	100 (3)	119 (3)	117 (3)	−3 (3)	78 (3)	−3 (3)
C(6)	37665 (23)	57001 (28)	30416 (22)	71 (2)	114 (3)	86 (2)	−20 (2)	18 (2)	−7 (2)
C(7)	22913 (26)	59386 (27)	11803 (22)	96 (3)	108 (3)	77 (2)	0 (2)	24 (2)	23 (2)
C(8)	18244 (22)	10139 (23)	5369 (19)	108 (3)	111 (3)	68 (2)	1 (2)	37 (2)	−4 (2)
C(9)	26541 (40)	−1733 (35)	6319 (30)	208 (5)	142 (4)	93 (3)	67 (4)	47 (3)	−17 (3)
N(1)	29924 (13)	49046 (16)	20330 (12)	58 (1)	84 (2)	56 (1)	0 (1)	26 (1)	1 (1)
O(1)	−14914 (15)	30959 (20)	18969 (16)	58 (1)	160 (3)	147 (2)	12 (2)	46 (1)	48 (2)
O(2)	−4692 (12)	47605 (15)	14004 (12)	75 (1)	98 (2)	100 (1)	2 (1)	33 (1)	7 (1)
O(3)	21247 (11)	17480 (13)	15196 (11)	71 (1)	97 (2)	62 (1)	11 (1)	21 (1)	−9 (1)
O(4)	10215 (17)	13323 (19)	−2866 (13)	160 (2)	178 (3)	68 (1)	31 (2)	8 (1)	−20 (2)
O(5)	−34218 (15)	44724 (24)	13272 (16)	65 (2)	140 (3)	103 (2)	9 (2)	12 (1)	−23 (2)
Cl(1)	−51384 (5)	26815 (5)	−5903 (5)	81 (1)	99 (1)	78 (1)	−1 (1)	13 (1)	−17 (1)

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* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32077 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

reflexions having $I > 3\sigma(I)$]. $R_w = [\Sigma\, w(|F_o| - |F_c|)^2/\Sigma\, wF_o^2]^{1/2}$ was 0·034, and the goodness-of-fit, $[\Sigma\, w(|F_o| - |F_c|)^2/(m-n)]^{1/2}$, was 0·99 for $n = 213$ parameters and $m = 2441$ observations of non-zero weight.

Discussion

Molecular dimensions

The atomic-numbering scheme and the configuration of the cation as observed in the crystal are shown in Fig. 1. In Table 4 the bond distances and angles involving nonhydrogen atoms are compared with those found in CAR (Tomita *et al.*, 1974). Bond lengths in the two molecules are closely similar, with the possible exception of C(3)–O(3) which is longer in ACC. Values reported by Scheraga (1968) for a C–O bond (1·45 in esters and 1·42 Å in alcohols) are consistent with those found in ACC and CAR.

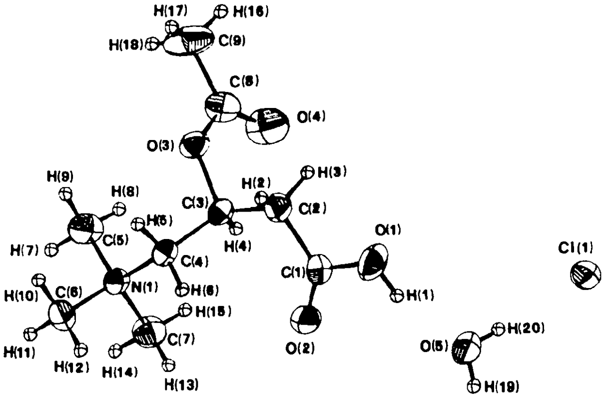

Fig. 1. A perspective drawing of acetylcarnitine hydrochloride monohydrate, showing atomic numbering. The atoms are represented by temperature-factor ellipsoids drawn at the 40% probability level (Johnson, 1965).

A strict similarity is also observed between the corresponding bond angles of the two molecules, except for two angles at C(3): O(3)–C(3)–C(4) and C(2)–C(3)–C(4). Their values presumably depend on the conformation of the N$^+$–C–C–O system, essentially defined by the torsion angle N(1)–C(4)–C(3)–O(3) (τ_0 in Table 5). When τ_0 is in the range 81–86° the N$^+\cdots$O Coulombic attraction (Sundaralingam, 1968) produces a deformation of O(3)–C(3)–C(4), whose value in alcohols and esters is usually found to lie in the range 110–115°. The narrowing of this angle, on the other hand, is not necessary when τ_0 is close to 60°, since in this case the quaternary N and the electronegative O are already brought in close contact.

Both ACC and CAR show a value for N(1)–C(4)–C(3) significantly larger than the expected value of 113°. This is a feature common to most of the acetylcholine-like molecules, and is presumably due to the need for a lengthening of the contact between the H atom at C(3) and one of the H atoms of the C(7) methyl group. In ACC the shortest contact is H(4)$\cdots$H(15), 2·17 Å.

While in CAR C(1), C(2), O(1) and O(2) are coplanar within experimental error, the corresponding atoms in ACC are not: C(1) deviates from the best least-squares plane by 0·012 Å, six times the e.s.d. A similar situation occurs in the acetyl group, where C(8) and C(9) deviate from the mean plane, in opposite directions, by 0·011 and 0·009 Å respectively. The extensive thermal motion of the two atoms, however, makes these last values only marginally significant.

Table 4. *Bond lengths* (Å) *and angles* (°) *involving non-hydrogen atoms*

	ACC*	CAR†		ACC*	CAR†
C(1)–O(1)	1·313 (3)	1·324 (10)	N(1)–C(5)	1·495 (3)	1·487 (12)
C(1)–O(2)	1·196 (3)	1·203 (10)	N(1)–C(6)	1·499 (3)	1·499 (13)
C(1)–C(2)	1·496 (3)	1·507 (11)	N(1)–C(7)	1·489 (3)	1·475 (12)
C(2)–C(3)	1·518 (3)	1·529 (11)	C(3)–O(3)	1·451 (2)	1·419 (10)
C(3)–C(4)	1·504 (3)	1·519 (11)	O(3)–C(8)	1·350 (3)	—
C(4)–N(1)	1·509 (2)	1·518 (10)	C(8)–O(4)	1·194 (3)	—
			C(8)–C(9)	1·486 (5)	—
O(1)–C(1)–O(2)	123·8 (2)	123·3 (8)	C(4)–N(1)–C(5)	111·6 (2)	111·4 (7)
O(1)–C(1)–C(2)	111·8 (2)	111·8 (7)	C(4)–N(1)–C(6)	108·1 (2)	107·1 (7)
O(2)–C(1)–C(2)	124·4 (2)	124·9 (7)	C(4)–N(1)–C(7)	111·2 (2)	112·3 (7)
C(1)–C(2)–C(3)	112·9 (2)	111·5 (6)	C(5)–N(1)–C(6)	108·1 (2)	108·1 (7)
C(2)–C(3)–C(4)	111·1 (2)	107·2 (6)	C(5)–N(1)–C(7)	109·5 (2)	109·5 (7)
O(3)–C(3)–C(4)	106·8 (2)	111·3 (7)	C(6)–N(1)–C(7)	108·3 (2)	108·4 (7)
C(2)–C(3)–O(3)	108·1 (2)	108·7 (7)	C(8)–O(3)–C(3)	117·6 (2)	—
C(3)–C(4)–N(1)	116·4 (2)	116·8 (7)	O(4)–C(8)–O(3)	123·2 (2)	—
			C(9)–C(8)–O(3)	110·4 (2)	—

* Acetylcarnitine, this investigation.
† Carnitine hydrochloride, Tomita *et al.* (1974).

Table 5. *The geometry of the* N^+–C–C–O *system in ACC and in other similar compounds*

	ACC$^{(a)}$	CAR$^{(b)}$	ACBMCH$^{(c)}$	OMBEMTM1$^{(d)}$	BEMTM1$^{(e)}$	
					A	*B*
τ_0 = [N(1)–C(4)–C(3)–O(3)]	83·6 (2)°	66·4 (7)°	85 (3)°	85·7 (3)°	51·6°	80·7°
N(1)–C(4)–C(3)	116·4 (2)	116·8 (7)	114 (3)	115·4 (3)	117·8	114·4
O(3)–C(3)–C(4)	106·8 (2)	111·3 (7)	107 (3)	105·7 (3)	116·8	105·4
C(2)–C(3)–C(4)	111·1 (2)	107·2 (6)	116 (3)	110·2 (3)	107·0	107·8
C(2)–C(3)–O(3)	108·1 (2)	108·7 (7)	110 (3)	109·6 (3)	112·4	110·4
O(3)···N(1)	3·173 (2) Å	3·07 (1) Å	3·17 (4) Å	3·160 (4) Å	3·013 Å	3·104 Å
O(3)···C(5)	2·968 (2)	3·07 (1)	2·97 (4)	2·950 (6)	3·055	2·899

(*a*) Acetylcarnitine, this investigation. (*b*) Carnitine hydrochloride, Tomita *et al.* (1974). (*c*) L-(+)-Acetyl-β-methylcholine iodide, Chothia & Pauling (1969). (*d*) *o*-Methyl β-methylphenylcholine ether bromide, Kneale, Geddes & Sheldrick (1974). (*e*) β-Methylphenylcholine ether bromide, two molecules (*A* and *B*) per asymmetric unit. E.s.d.'s in the range 0·010–0·023 Å in bond lengths and 0·65–1·21° in bond angles. Hamodrakas, Geddes & Sheldrick (1974).

Bond distances and angles involving H atoms are reported in Table 6. The average length of the 17 C–H bonds is 0·97 Å; that of the two O–H bonds in the water molecule, 0·80 Å, agrees with the values found in arginine hydrochloride monohydrate, 0·83 Å (Dow, Jensen, Mazumdar, Srinivasan & Ramachandran, 1970), and in 7-methylxanthine hydrochloride monohydrate, 0·76 Å (Kistenmacher & Sorrell, 1975).

Table 6. *Bond lengths* (Å) *and angles* (°) *involving hydrogen atoms*

O(1)–H(1)	0·84 (2)	C(6)–H(11)	1·00 (2)
C(3)–H(4)	0·94 (2)	C(7)–H(14)	0·98 (2)
C(5)–H(7)	0·94 (2)	C(9)–H(17)	0·96
C(6)–H(10)	1·02 (2)	O(5)–H(20)	0·81 (2)
C(7)–H(13)	0·95 (3)	C(2)–H(3)	0·96 (2)
C(9)–H(16)	0·94	C(4)–H(6)	0·96 (2)
O(5)–H(19)	0·79 (3)	C(5)–H(9)	0·99 (3)
C(2)–H(2)	0·96 (2)	C(6)–H(12)	0·94 (2)
C(4)–H(5)	1·00 (2)	C(7)–H(15)	0·98 (3)
C(5)–H(8)	0·96 (2)	C(9)–H(18)	0·98
H(1)–O(1)–C(1)	114 (2)	H(2)–C(2)–C(1)	109 (1)
H(2)–C(2)–C(3)	109 (1)	H(2)–C(2)–H(3)	111 (2)
H(3)–C(2)–C(1)	106 (1)	H(3)–C(2)–C(3)	109 (1)
H(4)–C(3)–C(2)	109 (1)	H(4)–C(3)–C(4)	112 (1)
H(4)–C(3)–O(3)	109 (1)	H(5)–C(4)–C(3)	109 (1)
H(5)–C(4)–N(1)	106 (1)	H(5)–C(4)–H(6)	110 (1)
H(6)–C(4)–C(3)	110 (1)	H(6)–C(4)–N(1)	105 (1)
H(7)–C(5)–N(1)	106 (1)	H(7)–C(5)–H(8)	113 (2)
H(7)–C(5)–H(9)	109 (2)	H(8)–C(5)–N(1)	109 (1)
H(8)–C(5)–H(9)	109 (2)	H(9)–C(5)–N(1)	109 (2)
H(10)–C(6)–N(1)	108 (1)	H(10)–C(6)–H(11)	109 (2)
H(10)–C(6)–H(12)	114 (2)	H(11)–C(6)–N(1)	107 (1)
H(11)–C(6)–H(12)	109 (2)	H(12)–C(6)–N(1)	109 (1)
H(13)–C(7)–N(1)	109 (2)	H(13)–C(7)–H(14)	111 (2)
H(13)–C(7)–H(15)	108 (2)	H(14)–C(7)–N(1)	108 (1)
H(14)–C(7)–H(15)	113 (2)	H(15)–C(7)–N(1)	109 (1)
H(16)–C(9)–C(8)	104	H(16)–C(9)–H(17)	114
H(16)–C(9)–H(18)	108	H(17)–C(9)–C(8)	111
H(17)–C(9)–H(18)	110	H(18)–C(9)–C(8)	109
H(19)–O(5)–H(20)	104 (3)		

Conformation

The most convenient parameters for the description of the molecular conformation are the torsion angles reported in Table 7, where the values found in ACC and CAR are compared with the corresponding ones in other β-methyl derivatives of choline. There is an evident relationship between the values of τ_0 and τ_1: when the trimethylammonium group is symmetrically arranged with respect to C(4)–C(3) (*i.e.* τ_1 is close to 180°, as in ACC), steric interference between O(3) and one of the methyl groups at N(1) constrains τ_0 to be about midway between synclinal (60°) and anticlinal (120°). On the other hand, if τ_1 is significantly far from 180° and positive (as in CAR and in molecule *A* of BEMTM1), the N^+–C–C–O system can assume almost exactly the more stable *gauche* conformation.

In acetylcholine-like molecules τ_4 shows several different values (Baker *et al.*, 1971), but in β-substituted derivatives this angle is always close to −155°. Chothia & Pauling (1969) have suggested that this is due to steric interference of O(4) with the H atoms at C(3) and C(2).

The most significant conformational difference between ACC and CAR concerns the position of the carboxyl group with respect to the rest of the molecule, and is visualized by the values of τ_8 and τ_9. Obviously ACC cannot assume the roughly *trans* zigzag skeletal configuration of CAR, since in this conformation O(4) would strongly interfere with O(2). Of particular interest is the question of whether the conformation of ACC found in the crystal is mainly due to intramolecular energy effects or is dictated by packing and hydrogen bonds. We have performed a conformational analysis of the isolated molecule of ACC, following the 'molecular-mechanics' or force-field method. As intramolecular contributions to the total energy, we considered only the torsional barriers to internal rotation about single bonds and the non-bonded interactions. Bond lengths and angles were fixed at their experimental values, on the assumption (Scheraga, 1968) that inclusion of the possibility of distortion of geometry in the calculations will not make much difference to the positions of local minima in the energy surface, but only to the relative energies of these minima. Functional forms for the potential and appropriate barrier heights for the calculation of the torsion energies were from Scheraga (1968) and Allinger, Tribble & Miller (1972). The non-bonded interactions were calculated by Lennard–Jones '6–12' potential functions, the parameters of which were taken from Table 16 of Scheraga (1968). A systematic variation of τ_9 [O(3)–C(3)–C(2)–C(1)] in the range 0–360° (steps of 5°), leaving all other torsion angles fixed at their experimental values, showed two minima of approximately equal values in the energy surface, at $\tau_9 = 55$ and $-170°$ respectively. The calculations were then repeated, allowing τ_{10} [C(3)–C(2)–C(1)–O(2)] to vary: at each fixed value of τ_9, the best value for τ_{10} was obtained by minimization of the energy by steepest descents. Besides the previously determined two minima, which were confirmed (with corresponding τ_{10} values of 3·8 and −2·2° respectively), a third minimum appeared, at $\tau_9 = -65°$ and $\tau_{10} = -114{\cdot}2°$. The conformation corresponding to the second minimum is almost coincident with the crystallographic one, while the value of τ_9 in the third minimum is only slightly different from that found in CAR. The energy barrier separating the first two minima is about 7 kcal, while the other two barrier heights are both $\simeq$ 4 kcal.

Eventually, the experimental configuration of the whole molecule was optimized with respect to all the torsion angles; convergence was assumed when the energy change in two subsequent cycles of the minimization procedure was less than 0·5 kcal. The greatest variation (7·5°) occurred at τ_0 [N(1)–C(4)–C(3)–O(3)], which assumed a final value of 76·1°; the trimethylammonium group was rotated by less than 1° about N(1)–C(4), and the staggered conformation of the three methyl groups at N(1) was left almost unchanged, the maximum rotation being about C(7)–N(1), 2·8°. The acetyl group was moved by a similar amount (2·6°) and the optimal values for τ_9 and τ_{10} were −172·8 and 1·3° respectively. In summary, since the average change in torsion angles was as low as 3°, the intermolecular effects on the conformation of the molecule in the crystal can be assumed to be negligible, and hence we can expect that a very similar configuration could be adopted by the molecule *in vivo*.

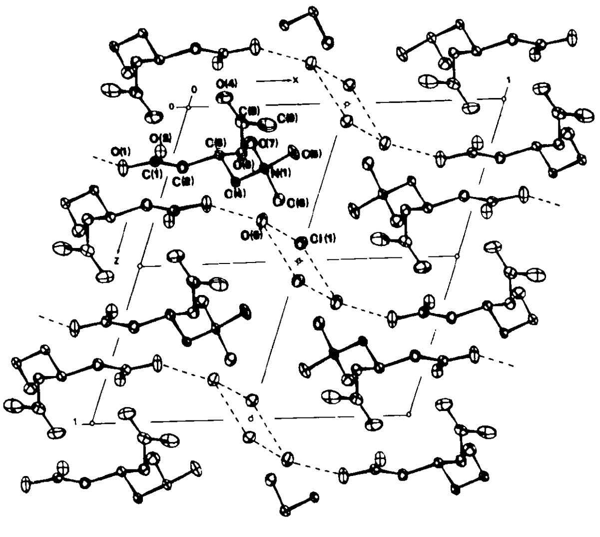

Fig. 2. A drawing of the structure viewed along **b**.

Table 7. *Some torsion angles of interest*

The values found in ACC are compared with those of other acetylcholine-like molecules. Symbols of molecules and references are as in Table 5.

	ACC	CAR	ACBMCH	OMBEMTM1	BEMTM1	
					A	*B*
τ_0 N(1)–C(4)–C(3)–O(3)	83·6	66·4	85	85·7	51·6	80·7
τ_1 C(6)–N(1)–C(4)–C(3)	−175·3	163·0	†	−174·7	166·0	−174·3
τ_2 C(5)–N(1)–C(4)–C(3)	−56·6	−79·1	†	−56·1	−78·5	−56·0
τ_3 C(7)–N(1)–C(4)–C(3)	65·9	44·2	†	67·0	43·8	69·3
τ_4 C(4)–C(3)–O(3)–C(8)	−153·2	−145·1*	−147	−156·9	−167·5	−158·3
τ_5 C(3)–O(3)–C(8)–C(9)	178·3	–	175	179·3	−163·3	180·0
τ_6 C(3)–O(3)–C(8)–O(4)	0·5	–	14	−0·1‡	12·1‡	−3·7‡
τ_7 N(1)–C(4)–C(3)–C(2)	−158·8	−174·8	−152	−156·4	178·6	−161·4
τ_8 C(4)–C(3)–C(2)–C(1)	76·9	166·2	–	–	–	–
τ_9 O(3)–C(3)–C(2)–C(1)	−166·2	−73·4	–	–	–	–
τ_{10} C(3)–C(2)–C(1)–O(2)	−5·2	−22·7	–	–	–	–
τ_{11} C(3)–C(2)–C(1)–O(1)	172·6	156·7	–	–	–	–

* C(8) of ACC is replaced by an H atom in CAR.

† Not available, since the atomic coordinates were not reported.

‡ O(4) of ACC is replaced by a C atom in OMBEMTM1 and BEMTM1.

Table 8. *Intermolecular contact distances* (Å)

For each pair of atoms, the coordinates of the second atom are transformed as shown.

O(2) · · · H(15)	$-x$,	$1-y$,	$-z$	2·40
Cl(1) · · · H(5)	$-1+x$,	$\frac{1}{2}-y$,	$-\frac{1}{2}+z$	2·75
Cl(1) · · · H(7)	$-x$,	$1-y$,	$-z$	2·96
Cl(1) · · · H(9)	$-1+x$,	$\frac{1}{2}-y$,	$-\frac{1}{2}+z$	2·90
Cl(1) · · · H(10)	$-1+x$,	$\frac{1}{2}-y$,	$-\frac{1}{2}+z$	2·74
Cl(1) · · · H(19)*	$-1-x$,	$1-y$,	$-z$	2·41
Cl(1) · · · H(20)*	x,	y,	z	2·29
O(5) · · · H(1)*	x,	y,	z	1·75

* Hydrogen bond.

The analogous treatment of the CAR molecule gave very similar results: there were three energy minima when τ_9 was systematically varied, and the corresponding values of this torsion angle were 50, −160 and −75° respectively; no optimization procedures were adopted for τ_{10}, fixed at the experimental value of −22·7°. The barrier height between the second and third minima was here only 3 kcal. After optimization of the whole molecular conformation in the same way as for ACC, the average deformation in torsion angles was 4°, the greatest change occurring at τ_{10} [O(2)–C(1)–C(2)–C(3)], which converged at −14·1°.

Packing and hydrogen bonds

The structure viewed along [010] is shown in Fig. 2, where the H atoms are omitted for clarity. The lengths of the hydrogen bonds, represented by dashed lines, are: O(1) · · · O(5) 2·556; O(5) · · · Cl(1) 3·102; and O(5) · · · Cl(1)($-1-x$, $1-y$, $-z$) 3·182 Å. The corresponding values of the H · · · O(5) and H · · · Cl(1) distances are reported in Table 8, together with other intermolecular contacts less than the sum of the van der Waals radii. All distances listed involve H atoms, since there are no unusual short contacts between nonhydrogen atoms.

We are grateful to Dr A. Gavezzotti for the use of his program for conformational-analysis calculations.

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