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THE CRYSTAL STRUCTURE OF ACETYLCHOLINE PERCHLORATE

by

Vijay K. Mahajan

A THESIS SUBMITTED
IN PARTIAL FULFILLMENT OF THE
REQUIREMENTS FOR THE DEGREE OF

Doctor of Philosophy

Thesis Director's Signature

A handwritten signature in cursive script, reading "Ronald L. Sasser", is written over a horizontal line.

Houston, Texas

May, 1973

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To My Parents

Table of Contents

<u>Section:</u>	<u>Page</u>
Introduction	1
Experimental	3
Structure Determination	8
Three-Dimensional Refinement	18
Discussion	34
References	45

List of Figures

<u>Figure Number</u>	<u>Title</u>	<u>Page</u>
1	Space Group Pbca	4
2	Patterson Map ($w = 0.0$)	10
3	Patterson Map ($w = 0.5$)	11
4	The Structure of the Acetylcholine Molecule in Crystals of Acetylcholine Perchlorate	35
5	Packing Diagram, [001] Projection	44

List of Tables

<u>Table Number</u>	<u>Title</u>	<u>Page</u>
1	Symbolic Assignments, FAME	13
2	Control Parameters, MAGIC	15
3	Observed and Calculated Structure Factor Magnitudes (x10)	21
4	Final Parameters for Non-Hydrogen Atoms	30
5	Final Parameters for Hydrogen Atoms	32
6	Scale Factors for c-Axis Layers	33
7	Bond Distances Involving Non-Hydrogen Atoms	36
8	Bond Angles Involving Non-Hydrogen Atoms	37
9	Bond Distances Involving Hydrogen Atoms	39
10	Bond Angles Involving Hydrogen Atoms	40
11	Selected Torsional Angles in Acetylcholine Perchlorate, Acetylcholine Chloride and Acetylcholine Bromide	42

INTRODUCTION

For the past several years, our research group has been investigating the structural and molecular properties of various compounds active in cholinergic systems. Structures which have been studied include those of procaine hydrochloride,¹ 2-diethylaminoethyl p-methoxybenzoate hydrochloride² and 2-diethylaminoethyl p-nitrobenzoate hydrochloride.³ A primary consideration in these studies is the correlation between the conformational geometry of these molecules with that of acetylcholine, the natural intercellular effector in nerve impulse transmission. Thus, the structural features of acetylcholine must be accurately established.

Various conformational arrangements have been put forth for acetylcholine on the basis of theoretical calculations. Liquori, Damiani and DeCoen⁴ calculated minimum energy conformations of acetylcholine in terms of Van der Waals pairwise interaction between non-bonded atoms and threefold torsional potentials. They found four stable conformations separated in energy by less than 1 kcal/mole. Kier,⁵ using molecular orbital calculations predicted a single minimum energy conformation while Pullman and Courrière,⁶ using the method of perturbative configuration interaction on localized orbitals, find a single global energy minimum and a number of other local minima similar to those calculated by Liquori, et al.

The crystallographic studies of acetylcholine chloride⁷ and acetylcholine bromide⁸ give conformational parameters for acetylcholine distinctly different from each other. Each, however, corresponds to one of the several theoretically predicted molecular geometries. It

thus seems evident that the conformation of acetylcholine is strongly influenced by its environment and that more information is needed before these effects can be characterized.

The purpose of this thesis is to investigate the crystal structure of acetylcholine perchlorate and to determine the conformation that acetylcholine would assume with perchlorate anion. We are particularly interested in comparing the structures of crystalline acetylcholine chloride, acetylcholine bromide and acetylcholine perchlorate.

EXPERIMENTAL

The compound acetylcholine perchlorate was prepared by reacting acetylcholine bromide with silver perchlorate. Crystals suitable for X-ray diffraction study were obtained by ether diffusion into a 2:1 ethanol to ethyl acetate solution of the compound. The crystals were clear, colorless, and prismatic in shape, with an average diameter of 0.15 mm. From preliminary examination of several crystals, a single crystal was chosen and used throughout the analysis.

Oscillation, rotation and equi-inclination Weissenberg photographs using CuK_α radiation ($\lambda = 1.5418 \text{ \AA}$) indicated the following conditions for reflection:

$h k \ell$: No Conditions

$0 k \ell$: $k = 2n$

$h 0 \ell$: $\ell = 2n$

$h k 0$: $h = 2n$

$h 0 0$: ($h = 2n$)

$0 k 0$: ($k = 2n$)

These conditions uniquely determine the space group to be $\text{Pbca}(D_{2h}^{15})$. The features of the c-axis projection of this space group are shown in Figure 1.

The c-axis cell constant was determined from rotation photographs and the approximate values for a-axis and b-axis cell constants were obtained from zero-layer Weissenberg photographs. The reported values for a-axis and b-axis cell constants were determined by measurement on a Phillip's PAILRED diffractometer using the method of omega differences.

Figure 1. Space Group Pbca, Equivalent Positions

$$x, y, z$$

$$\frac{1}{2} + x, \frac{1}{2} - y, \bar{z}$$

$$\bar{x}, \frac{1}{2} + y, \frac{1}{2} - z$$

$$\frac{1}{2} - x, \bar{y}, \frac{1}{2} + z$$

$$\bar{x}, \bar{y}, \bar{z}$$

$$\frac{1}{2} - x, \frac{1}{2} + y, z$$

$$x, \frac{1}{2} - y, \frac{1}{2} + z$$

$$\frac{1}{2} + x, y, \frac{1}{2} - z$$

The omega angular displacements about the rotation axis which are necessary for the diffraction maxima along each axial reflection were measured. Monochromatized molybdenum K_{α} radiation ($\lambda_{\alpha_1} = 0.70926 \text{ \AA}$; $\lambda_{\alpha_2} = 0.71354 \text{ \AA}$) was used for the measurements. These omega values were substituted in the expression

$$\frac{n\lambda}{2d} = \sin(\omega + \alpha)$$

where

n = order of the diffracted beam

λ = wavelength of the radiation

α = phase angle

$\frac{1}{d}$ = reciprocal lattice spacing

By minimizing the sum of the squares of the differences of each α from the average values, the best values of $\frac{1}{d}$ were chosen. The constants, a and b , were then determined. The final cell constants and their estimated standard deviations are

$$a = 19.550(4) \text{ \AA}$$

$$b = 12.410(3) \text{ \AA}$$

$$c = 9.770(1) \text{ \AA}$$

$$\alpha = \beta = \gamma = 90^{\circ} \text{ (by symmetry)}$$

The density of crystalline acetylcholine perchlorate was measured by flotation in a mixture of chlorobenzene and bromobenzene. The calculated density of 1.38 gm/cm^3 for eight molecules per unit cell was in close agreement with the experimentally measured density of 1.36 gm/cm^3 .

Since the space group $Pbca$ has eight equivalent general positions, the asymmetric unit consists of only one molecule of acetylcholine perchlorate.

Three-dimensional intensity data were collected on a Phillip's PAILRED diffractometer using equi-inclination geometry. Silicon [111] monochromatized molybdenum K_{α} radiation ($\lambda = 0.71069 \text{ \AA}$) was used for collecting the data. The fixed counter, moving crystal technique was used. The scan range varied from 2.8° to 3.2° with a 0.5° per minute scan speed. The background time varied accordingly from 120 to 200 seconds. The counting statistical error $\Delta I/I$ ⁹ was calculated for each reflection. All intensities for which $\Delta I/I$ exceeded 0.4 were treated as being statistically absent.

$$\frac{\Delta I}{I} = \frac{(T + t^2 B)^{\frac{1}{2}}}{T - tB}$$

where

T = total number of counts for omega scan

t = ratio of scan time to background time

B = total number of background counts.

All acceptable intensities were corrected for Lorentz, polarization and Tunell factors. Intensity measurements for both hkl and $\bar{h}\bar{k}\bar{l}$ reflections were collected and averaged. The intensities were averaged if and only if both the equivalent reflections had the statistical counting error less than 0.4. A single value was used when only one of the equivalent reflections passed this test. Those intensities for which neither equivalent reflection passed were not used in the analysis.

The maximum value of μ_R was 0.03. Nor corrections for absorption or extinction were made.

The c-axis layers, $l = 0 - 12$, were collected. Layers 0 - 3 were collected to an upsilon value (counter elevation angle) of 61° , layers 4 - 10 were collected up to upsilon equals 47° and 11 - 12 layers were collected only to an upsilon value of 32° . Selected reflections were monitored after each layer to test any crystal deterioration and the alignment of the crystal. The crystal was manually realigned whenever either test showed a deviation from the original value by more than twice the standard deviation (based on counting statistics). No noticeable decrease in the intensities of monitored reflections was observed during the process of data collection.

A total of 5635 reflections were measured on the diffractometer. Finally, 1068 averaged intensities corrected for Lorentz, polarization and Tunell factors were used in the determination and refinement of the structure.

STRUCTURE DETERMINATION

The chlorine atom position was determined by using a Patterson map. Other atom positions were determined by using an E-map derived from symbolic addition procedures and Fourier maps.

The Patterson function is defined as:

$$P(u, v, w) = \frac{1}{V} \sum_h \sum_k \sum_{\ell}^{\infty} |F_{hkl}|^2 \exp 2\pi i(hu + kv + \ell w)$$

A Fourier calculation can thus be carried out using the phaseless quantities $|F|^2$ as coefficients, which in turn are directly derivable from X-ray intensities. The Patterson function is a map of all interatomic vectors translated to a common origin. The weight of a peak in the Patterson map depends upon the number of electrons in the atoms between which the vector occurs and is approximately proportional to the product of their atomic numbers. Thus, a peak at the point u, v, w in a Patterson map indicates that there are atoms at x_1, y_1, z_1 and x_2, y_2, z_2 such that

$$u = x_1 - x_2, v = y_1 - y_2, w = z_1 - z_2$$

In space group Pbca, the interatomic vectors between equivalent atoms (one of which has coordinates x, y, z) are:

$$\frac{1}{2}, \frac{1}{2} \pm 2y, \pm 2z$$

$$\pm 2x, \frac{1}{2}, \frac{1}{2} \pm 2z$$

$$\frac{1}{2} \pm 2x, \pm 2y, \frac{1}{2}$$

$$\frac{1}{2}, 0, \frac{1}{2} \pm 2z$$

$$\begin{aligned} & \frac{1}{2} \pm 2x, \frac{1}{2}, 0 \\ & 0, \frac{1}{2} \pm 2y, \frac{1}{2} \\ & \pm 2x, \pm 2y, \pm 2z \end{aligned}$$

Since each chlorine has seventeen electrons compared to the six, seven, and eight electrons of carbon, nitrogen, and oxygen, the greatest contribution to the Patterson function will be from interatomic vectors between equivalent chlorine atoms.

The chlorine atom in acetylcholine perchlorate was located from three Harker sections (Figures 2 and 3). Thus,

a. Harker section at $u = \frac{1}{2}$;

peak found $\frac{26}{52}, \frac{35}{79}, \frac{1}{2}$

assigned $\frac{1}{2}, \frac{1}{2} - 2y, 2z$ so $y = \frac{2.25}{79}, z = \frac{1}{4}$

b. Harker section at $v = \frac{1}{2}$;

peak found $\frac{15}{52}, \frac{39.5}{79}, 0$

assigned $2x, \frac{1}{2}, \frac{1}{2} - 2z$ so $x = \frac{7.5}{52}, z = \frac{1}{4}$

c. Harker section at $w = \frac{1}{2}$;

peak found $\frac{11}{52}, \frac{4.5}{79}, \frac{1}{2}$

assigned $\frac{1}{2} - 2x, 2y, \frac{1}{2}$ so $x = \frac{7.5}{52}, y = \frac{2.25}{79}$

Other large peaks were found at $w = 0$ and $w = \frac{1}{2}$ sections, which correlated well with these special chlorine-chlorine interatomic vectors. Thus, the chlorine atom as located from the Patterson map was assigned the coordinates, $x = .144, y = .028, z = .250$.

Because the chlorine atom is located near a special position in the cell, the Fourier maps calculated on the basis of these phases will have additional symmetry as compared to the true space group. At this

ACCL04 MATTERSON

V IN 70TMS

U IN 52NDS

W = 1 2NDS

0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	
0	239	238	222	194	146	113	109	108	106	113	137	173	194	194	185	168	151	139	125	124	132	133	153	192	220	239	249	239
1	236	232	222	195	146	112	106	105	103	111	138	177	196	193	186	170	150	137	123	121	128	131	152	191	219	236	244	236
2	224	225	221	195	146	109	98	96	97	107	140	186	201	191	187	174	148	130	117	113	118	123	147	188	215	225	229	225
3	206	210	212	189	142	103	87	84	86	99	143	197	204	184	185	178	144	119	106	100	103	111	138	178	203	206	205	206
4	175	146	192	172	130	93	75	69	72	88	142	204	201	171	178	178	137	103	90	83	86	96	122	155	180	177	172	177
5	147	154	160	143	111	80	62	55	56	73	136	200	189	151	162	169	124	85	71	64	67	78	100	125	146	140	133	140
6	112	117	119	106	85	64				55	120	181	164	125	138	149	105	62				60	76	94	106	100	92	100
7	77	79	77	67	56						94	147	131	96	108	118	78											
8											61	104	93	68	75	80												
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28																												
29	02	55																										
30	136	97																										
31	203	149	64																									
32	274	206	98																									
33	335	256	129	55																								
34	373	292	158	76																								
35	381	306	179	96																								
36	345	303	193	115	67																							
37	338	288	201	130	84	52																						
38	305	271	205	143	96	64																						
39	288	261	206	149	103	71	50	58																				
40	288	261	206	149	103	71	50	58																				
41	305	271	205	143	96	64																						
42	338	288	201	130	84	52																						
43	366	303	193	115	67																							
44	381	306	179	96																								
45	373	292	158	76																								
46	335	256	129	55																								
47	274	206	98																									
48	283	149	64																									
49	136	97																										
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72	77	79	77	67	56																							
73	112	117	119	106	85	64																						
74	147	154	160	143	111	80	62	55	56	73	136	200	189	151	162	169	124	85	71	64	67	78	100	129	146	140	133	140
75	179	186	192	172	130	93	75	69	72	88	142	204	201	171	178	178	137	103	90	83	86	96	122	159	180	177	172	177
76	206	210	212	189	142	103	87	84	86	99	143	197	204	184	185	178	144	119	106	100	103	111	138	178	203	206	205	206
77	224	225																										

Figure 3

stage, it was decided to try the symbolic addition technique to locate possible positions of other atoms and thereby remove this pseudosymmetry element created by chlorine.

In this technique, the phases of several larger reflections can be determined to a calculated degree of probability by using known relationships between the reflections. The programmed symbolic addition procedure used consists of four main segments, FAME, MAGIC, LINK and SYMPL.¹⁰

The observed data for acetylcholine perchlorate was reduced to a set of E values (normalized structure factors) using the FAME routine. Seven theta intervals were used to calculate a Wilson plot. The 25 largest E's, along with their interactions, were listed. A total of eight symbolic phases were assigned to this group. The symbols assigned are listed in Table 1. The value of sigma (probability factor required in MAGIC) was calculated from the expression,

$$\sigma = \frac{\sigma_3}{\sigma_2^{3/2}},$$

where

$$\sigma_3 = \sum_i^N n_i^3,$$

$$\sigma_2 = \sum_i^N n_i^2$$

and n_i is the fraction of the scattering power represented by the i th atom. This value of sigma was .1144.

TABLE 1

SYMBOLIC ASSIGNMENTS, FAME

<u>h</u>	<u>k</u>	<u>l</u>	<u> E </u>	<u>Symbol</u>
2	5	2	3.0994	A
4	8	1	2.4116	B
2	3	1	3.7222	C
4	2	2	3.1198	D
2	3	4	3.3478	E
14	4	1	2.4116	F
4	1	1	3.4467	G
0	2	2	4.3800	H

A total of 250 phases from the 1068 E's were determined by MAGIC. Five iterations were required to accomplish this. The decision parameters were altered automatically during the program in order to calculate all the phases. The minimum probability level was required to be at least .9945. The results are summarized in Table 2.

LINK assigned the following positive origin phases:

h k l	Symbol	Value
2 3 1	C	+
2 3 4	E	+

The remaining symbols were tried in every combination of plus one and minus one. For each combination, the relative number of "inconsistencies" were calculated according to the formula

$$\text{weighted index} = \sum_i^S \frac{1}{(1 + \text{PARAM} - P)(\text{Iteration \#})},$$

where P is the probability of that sign determination. PARAM is an input parameter, usually equal to 0.000001, and S is the number of signs determined. The weighted index had a range from 123.3 to 5,846,260.5. It was found that two groups of symbol equivalences had the same low index values. The results are shown below.

TABLE 2

CONTROL PARAMETERS, MAGIC

Parameter Values at End of Iteration					
ITERATION	TOTAL SIGNS	PROBABILITY 'P'	CONTRIBUTORS*	INCONSISTENCIES*	RATIO C/I*
Initial	8	0.9995	0	0	0.0
1	16	0.9995	0	0	0.0
2	22	0.9995	2	1	7.0
3	50	0.9945	0	2	7.0
4	102	0.9945	2	1	7.0
5	239	0.9945	4	1	7.0

* For any one sign determination during an iteration:

Contributors: Minimum number of contributors with $P_{\text{sign}} \geq 'P'$ necessary for sign acceptance.

Inconsistencies: Contributors with opposite sign and $P_{\text{sign}} \geq 'P'$. Minimum number that can be tolerated.

Ratio C/I: Ratio of contributors to inconsistencies.

Symbol	Sign Value	
	Combination I	Combination II
A	-	-
B	+	+
C*	0	0
D	+	+
E*	0	0
F	+	-
G	+	-
H	-	-

* indicates an origin phase.

0 $\equiv$ sign fixed as positive.

Because of inconsistencies in sign determination, ten E's were excluded from the decks punched by SYMPL for combinations I and II. The E-maps were computed for both combinations I and II. It was possible to locate three additional atoms from the E-map using the Combination II. No physically meaningful model could be fitted to the peaks in the Combination I model.

A three-dimensional electron density map was calculated using phases based upon the positions of these three atoms plus the chlorine atom. A three-dimensional model was constructed based upon the largest peaks in the map. From this model, it was possible to locate the remaining atoms of the acetylcholine fragment. Three cycles of least squares refinement were then performed yielding an R factor,

$$R = \left[\frac{\sum_j w_j (F_j^{\text{obs}} - F_j^{\text{calc}})^2}{\sum_j w_j (F_j^{\text{obs}})^2} \right]^{\frac{1}{2}}$$

of 0.255.

Electron density maps of the region around the chlorine atom showed diffuse peaks of lower than normal heights for oxygen atoms ($2 - 4 \text{ e}/\text{\AA}^3$), a feature which appears to be characteristic of the perchlorate group in the solid state.^{11,12,13,14} An initial series of refinements were carried out excluding the perchlorate oxygen atoms. A difference Fourier map was then computed. Two disordered sets of tetrahedrally arranged oxygen atoms about the chlorine atom were located and included in an isotropic least squares refinement; the oxygen atoms were weighted proportionally to observed map peak heights. A new difference Fourier map was calculated based on this refinement. Regions of very high electron density were interpreted as fractional oxygen atoms and their previous population parameters were readjusted so that the total of all fractional oxygens around the chlorine atom was four. This procedure was repeated until the difference Fourier map had no regions of electron density greater than $0.5 \text{ e}/\text{\AA}^3$ in the vicinity of the perchlorate ion.

This refinement was performed on an IBM 7094 computer, using the FOURR and ORFLS programs of X-RAY-63.¹⁵

THREE-DIMENSIONAL REFINEMENT

A total of 1068 reflections were used in the three-dimensional full-matrix least squares refinement of the structure. The trial parameters, x_i , obtained above were adjusted so as to minimize the function

$$\sum_j \left[\sqrt{w_j} (F_j^{\text{obs}} - F_j^{\text{calc}}) - \sqrt{w_j} \sum_i \frac{\partial F_j}{\partial x_i} \Delta x_i \right]^2$$

The reliability index,

$$R = \frac{\sum_j |F_j^{\text{obs}} - F_j^{\text{calc}}|}{\sum_j |F_j^{\text{obs}}|},$$

was taken as a measure of the agreement between the observed and calculated data.

The calculations were carried out using an IBM 7094 computer and the least squares program "ORFLS" written by Busing, Martin and Levy.¹⁶ Scattering factors used for non-hydrogen atoms are those of Cromer and Waber.¹⁷ The hydrogen atom scattering factors are those of Stewart, Davidson and Simpson.¹⁸ Individual weights were assigned to the observed reflections employing the weighting scheme of Evans:¹⁹

$$w = L_p(T - B)/q(T + B) = L_p(1 - b)/q(1 + b)$$

where

L_p = Lorentz, polarization and Tunell factors

T = total number of counts in a peak

B = number of counts corresponding to background

$$b = B/T$$

q = changes in conditions of measurements from
one reflection to another

Since it was evident from the Fourier map that the oxygen atoms about the chlorine atom were badly disordered, an initial series of refinements were carried out on only the acetylcholine fragment. The reliability index R was reduced to 0.290 after three cycles of refinement on the positional parameters and thirteen layer to layer scale factors.

Two disordered sets of tetrahedrally arranged oxygen atoms were assigned to the perchlorate group in the refinement. Three cycles of full-matrix least squares refinement varying all positional parameters, scale factors and individual isotropic temperatures lowered the R value to 0.176. A cycle of scale factor refinement and four cycles of anisotropic temperature refinement dropped R to 0.135.

A three-dimensional Fourier difference map was synthesized at this stage. It was possible to identify all the hydrogen atom positional parameters. Isotropic temperature factors ranging from 5.0 to 7.0 were assigned to the hydrogen atoms from an examination of the peaks in the difference map. Addition of the hydrogen atoms dropped the R factor to 0.134. The weighted R was 0.065. Four cycles of least squares refinement on positional parameters and anisotropic temperatures (keeping hydrogen atom positions and temperatures fixed) dropped the unweighted R to 10. The weighted R was lowered to 0.042.

The next three cycles of least squares refinement were performed varying the positional parameters of hydrogen atoms. After a series of

successive least squares refinement, the R factors were reduced to 0.096 and 0.038. No attempt was made to refine on the hydrogen atom temperature factors.

It became apparent at this stage that 24 reflections had a very poor agreement between the observed and calculated structure factors. These reflections have a high value of $\sin\theta/\lambda$. They were excluded from the final refinement on the basis of unreliability in intensity measurements, yielding a final R value of 0.088. The observed and final calculated structure factors are shown in Table 3. An * indicates that the reflection was not included in the final refinement. Final positional and thermal parameters of non-hydrogen atoms, together with their standard deviations, are listed in Table 4. Final positional and isotropic temperature factors for hydrogen atoms, along with their standard deviations, are listed in Table 5. The final scale factors for each c-axis layer are shown in Table 6.

TABLE 3

Observed and Calculated Structure Factor Magnitudes (x10)

K	FO	FC	K	FO	FC	K	FO	FC	K	FO	FC
0,K,0			8,K,0			16,K,0			2,K,1		
2	1841	1848	0	767	-768	1	208	-200	2	241	225
4	325	334	1	280	277	2	202	-175	3	1788	1725
6	484	-501	3	239	-196	3	274	250	4	179	-155
8	373	371	4	86	-15	5	140	156	5	696	732
10	454	-459	5	591	593	6	131	118	6	91	-85
12	168	-180	6	432	435	7	285	265	8	90	99
16	114	-135	7	232	191	8	178	177	9	111	-95
2,K,0			8	196	-189	11	95	106	11	156	-195
2	219	-201	9	357	393	18,K,0			13	191	-278
3	2337	2320	11	88	88	3,K,1					
4	688	-694	12	125	-168	0	356	-329	1	271	-281
5	62	133	15	101	-97	1	233	-229	2	457	-428
6	120	-79	10,K,0			2	90	-97	3	103	92
7	408	405	0	126	-146	3	193	-250	4	318	305
8	161	133	1	343	-343	4	218	-194	5	221	-224
9	112	-167	2	367	-366	5	120	-88	6	213	236
4,K,0			3	360	-335	20,K,0			11	98	110
0	3384	-3389	5	425	376	2	257	121	4,K,1		
2	1219	-1216	6	284	-279	3	151	-153	1	1762	-1747
3	536	-538	9	220	217	5	120	-104	2	567	550
4	147	-189	11	133	113	22,K,0			3	201	-215
5	801	-792	12	186	223	0	103	79	6	118	140
7	248	-226	13	135	113	5	91	55	7	200	-212
9	233	-236	12,K,0			24,K,0			8	528	501
10	258	273	0	171	156	2	114	-96	10	370	382
11	135	-132	1	238	257	0,K,1			11	137	147
12	146	187	2	288	255	2	648	-653	13	91	114
16	103	135	5	298	-263	4	355	-351	5,K,1		
6,K,0			6	280	-272	6	325	-348	1	66	62
0	303	-281	7	367	-363	8	640	-579	2	206	227
1	49	9	8	125	-121	10	496	-503	3	64	74
2	786	776	9	179	-191	12	127	-114	4	279	-281
3	54	29	14,K,0			1,K,1			5	90	-97
4	291	290	0	544	533	2	341	-319	10	106	112
5	822	-835	1	390	365	3	219	-249	12	84	-72
6	394	377	2	96	81	4	466	476	6,K,1		
7	121	-83	3	237	252	5	74	-42	1	837	-855
8	188	-165	4	311	287	6	148	128	2	177	-154
9	126	-110	7	92	-117	9	116	100	3	629	-617
10	89	-80	10	155	-173	12	87	96	4	67	57
11	101	-79	12	103	-124				5	154	-171
12	130	-167							6	196	-207
13	168	-191							7	68	-35

K	FO	FC	K	FO	FC	K	FO	FC	K	FO	FC
8	250	-245	3	248	231		18,K,1			3,K,2	
9	80	70	5	67	-38						
11	109	130	6	86	-63	1	183	-188	0	131	-151
13	163	205	11	84	97	2	157	178	1	482	469
	7,K,1			12,K,1		4	165	190	2	380	410
1	205	159	1	162	-155	6	128	143	3	193	195
2	339	336	2	269	216	8	113	110	4	469	456
3	235	-201	3	383	-383	11	107	104	5	65	-110
4	157	-125	5	165	-162		20,K,1		6	74	63
5	181	187	7	157	201	1	179	-199	7	145	178
6	70	-76	9	182	222	3	132	-97	8	152	-157
11	95	-99		13,K,1		4	89	-117	9	176	175
	8,K,1					6	120	-120		4,K,2	
1	441	469	1	69	-42		22,K,1		0	1490	1475
2	242	-238	2	104	84				1	289	308
3	485	509	4	102	-91	1	139	125	2	1393	1341
4	170	153	8	100	-52		24,K,1		3	517	537
5	205	242		14,K,1					5	103	125
6	104	-117				4	95	78	7	324	314
8	275	-257	2	374	-363		0,K,2		8	185	-187
9	173	-187	3	119	-156				9	178	195
10	95	-102	4	429	-422				10	168	-185
11	133	-147	6	324	-308	2	3112	-3118	11	134	144
	9,K,1		7	120	141	4	952	945	14	92	-126
2	165	-179	8	208	-217	6	189	-246		5,K,2	
4	167	107	11	99	-104	8	355	365	0	269	257
5	173	191		15,K,1		10	80	86	1	516	489
6	77	-44				12	173	201	2	110	-89
8	75	66	1	92	81	14	95	114	3	125	107
	10,K,1		3	118	-141		1,K,2		5	247	-232
1	263	293	6	80	72				6	217	205
2	323	274		16,K,1		2	427	439	11	85	-24
3	316	337	1	309	312	3	189	-190	13	87	-47
4	373	341	2	192	-158	4	407	428		6,K,2	
6	421	391	3	244	219	5	223	227	0	578	-586
7	97	-143	6	100	138	8	133	-134	1	73	-102
8	260	259	8	86	71	11	79	47	2	76	19
10	95	92		17,K,1		14	96	-65	3	511	531
	11,K,1						2,K,2		4	456	-481
1	224	-213	2	88	-73	2	195	200	5	351	361
2	102	-115	3	79	-89	3	197	-235	6	73	-64
			5	85	-59	4	193	175	7	365	342
						5	1073	-1089	9	81	45
						7	74	88	10	230	242
						9	179	-163	11	211	218
						10	93	-93			

K	FO	FC	K	FO	FC	K	FO	FC	K	FO	FC
7,K,2			11,K,2			6 152 -168			2,K,3		
0	225	-219	1	170	130	7	95	-81	2	246	252
1	250	-272	4	79	-110	8	84	-84	3	174	143
2	197	-218	6	119	-139	9	135	-142	4	99	-120
4	84	117	7	95	64	17,K,2			5	283	-276
6	82	91	9	85	65	7 85 68			6	95	-65
7	182	-162	10	97	84	18,K,2			7	235	-189
9	181	-179	12,K,2			2 243 249			9	104	103
8,K,2			0	234	-240	3	242	249	11	298	332
0	114	-145	2	125	-109	4	98	60	13	121	163
1	253	268	3	71	-67	6	109	97	3,K,3		
2	147	113	4	83	92	20,K,2			1	229	228
3	423	-416	5	304	296	0 142 -128			2	259	234
4	450	-507	6	198	232	5	95	82	3	133	144
5	84	-72	7	331	328	22,K,2			4	174	-157
7	475	-484	8	147	108	0 94 -113			6	373	-373
8	93	-65	9	168	201	23,K,2			7	129	110
9	215	-231	13,K,2			4* 95 -1			8	121	-144
10	202	223	0	298	334	24,K,2			9	155	-201
11	145	-164	2	125	-80	0 94 100			10	97	-121
9,K,2			4	210	-245	0,K,3			4,K,3		
0	637	-628	8	96	93	2 385 353			1	275	283
1	243	-246	14,K,2			4 88 161			2	68	-76
2	88	83	0	169	-164	6 178 182			3	250	223
3	68	-116	1	80	-94	8 606 565			4	276	-320
4	166	174	2	459	-464	10 382 372			5	63	74
5	85	73	3	311	-348	12 122 141			6	269	-277
6	74	-79	4	138	-99	1,K,3			7	89	-75
9	75	-74	6	207	-163	2 117 129			8	482	-459
13*	85	36	12	99	142	3 472 481			10	240	-224
10,K,2			15,K,2			4 284 -296			11	106	-108
0	528	547	0	232	265	5 333 319			12	112	-121
1	189	199	1	116	-119	6 455 -453			13	96	-81
2	154	201	2	87	93	7 217 -239			5,K,3		
3	93	-37	5	101	103	10 83 -74			1	72	-65
4	375	370	16,K,2			2 117 129			2	117	-96
6	113	108	0	186	180	3 472 481			3	142	-111
7	257	-270	1	161	-149	4 284 -296			4	254	250
9	95	-124	5	308	-309	5 333 319			6	265	272
10	177	-211				6 455 -453			7	170	209
11	194	-189				7 217 -239			8	189	-210
12	107	-139				10 83 -74					

K	FO	FC	K	FO	FC	K	FO	FC	K	FO	FC
	6,K,3		2	232	-248		17,K,3		10	98	56
1	766	769	3	152	-175				11	106	117
2	189	-147	4	531	-502	2	98	83			
3	144	209	5	131	-85	3	99	136		3,K,4	
4	354	328	6	397	-388	5	97	123	0	62	51
5	326	337	8	212	-211	6	101	-77	2	298	-307
6	341	301		11,K,3			18,K,3		3	216	-243
7	83	45							4	543	-550
8	167	136	1	307	314	3	120	81	5	93	-51
11	181	-237	2	96	64	4	116	-128	6	105	81
	7,K,3		4	89	68	6	105	-135	7	234	-198
1	231	-236	6	85	68		19,K,3		8	222	184
2	294	-314	7	147	156				9	164	-160
3	131	-147	8	147	162	2	84	49		4,K,4	
5	75	-77	9	89	-83		20,K,3		0	536	-563
6	141	181		12,K,3					1	391	-390
7	109	-101	1	508	501	1	124	135	2	494	-503
8	98	-43	2	76	49		23,K,3		4	395	-390
9	187	189	3	335	335				6	328	339
	8,K,3		4	201	-167	1*	93	19	7	137	-151
1	562	-608	5	131	135		0,K,4		8	156	148
2	183	-160	9	113	-154				9	255	-280
3	437	-469	11	94	-93					5,K,4	
4	371	361		13,K,3		2	103	-120	0	180	163
5	153	-127	6	172	163	4	675	639	1	62	-52
6	253	234	7	86	55	6	732	-709	2	135	-138
7	144	137		14,K,3		8	134	-103	3	242	-258
8	209	209	1	83	57	9*	77	-0	6	76	-66
9	120	123	2	258	254	10	113	-143	7	77	53
11	124	137	4	366	348		1,K,4			6,K,4	
13	97	81	6	255	275	2	146	-152	1	565	-580
	9,K,3		8	143	142	3	204	197	2	307	301
1	110	100	11*	87	38	4	423	-417	3	437	-413
3	133	-126		15,K,3		5	74	89	5	273	-227
4	90	-83				6	112	83	6	235	232
5	153	-162	1	105	-120	8	176	183	7	198	-182
6	145	-145	3	90	131		2,K,4		8	122	-123
7	118	-111	4	108	-87	3	1182	1160	9	323	-323
8	108	101	5	93	137	4	110	122	10	100	-109
9	84	83		16,K,3		5	167	156	12	127	-150
	10,K,3					6	76	-62		7,K,4	
1	463	-473	1	299	-293	7	486	441	0	271	264
			3	155	-172	9	135	112	1*	68	-53

K	FO	FC	K	FO	FC	K	FO	FC	K	FO	FC
3	131	134		12,K,4			19,K,4		4	236	230
5	71	60							6	538	534
6	127	-125	0	159	185	0	87	119	8	185	166
7	339	320	2*	68	-3				9	138	138
9	237	202	3	142	-124		20,K,4		10	227	245
10	96	75	4	182	-224						
			5	205	-209	1	83	-51		5,K,5	
	8,K,4		6	153	-137	2	89	78			
			7	255	-279	3	90	-82	1	109	99
0	79	109	9	162	-172				2	121	-103
1	332	315					0,K,5		3	110	80
2	566	567		13,K,4					4	228	-211
4	162	152				2	93	94	5	72	-97
5	305	303	3	83	36	4	82	-81	6	73	-55
6	172	136	4	194	200	6	474	-469	7	116	-163
7	249	259				8	300	-309			
8	124	-124		14,K,4		10	280	-319		6,K,5	
9	291	315				12	97	-111			
10	89	70	0	317	348				1	372	-378
12	98	-101	2	196	199		1,K,5		2	135	-143
			3	95	115				3	214	-203
	9,K,4		4	333	332	2	42	45	4	331	-325
0*	64	-30	5	197	191	3	256	-249	5	101	-82
2	87	76				6	153	161	6	341	-334
3	80	83		15,K,4		7	97	125	7	210	-231
4	164	-178	0	161	-195	8	214	207	8	100	-93
			2	134	-138				9	163	196
	10,K,4		3	88	89		2,K,5		10	97	-72
0	211	-209	10*	95	46				11	91	82
1	296	269				3	101	-76			
2	473	-477		16,K,4		4	131	159		7,K,5	
4	323	-314				5	81	73			
6	193	-187	0	155	-218	6	166	163	1	231	241
7	88	69	2	126	-131	7	331	338	2	75	83
8	100	118	3	178	180	9	129	-150	3	371	345
9	251	263	4	106	122	11	182	-198	4	127	113
12	133	146	7	169	191				5	138	133
			9	101	86		3,K,5		7	114	-147
	11,K,4			17,K,4		3	201	-231		8,K,5	
2	105	98				4	86	-75			
3	145	-155	5	102	-121	5	146	-140	1	508	497
4	141	142				6	171	178	3	280	273
6	94	106		18,K,4		7	98	117	4	243	-230
7	124	-116				8	268	267	6	409	-418
8	95	-49	0	148	-174	10	110	91	9	125	-134
9	87	-70	3	84	-102				10	102	-118
			4	136	-149		4,K,5				
			5	120	-119					9,K,5	
			8*	88	-33	2	83	-72			
						3	149	-150	1	141	-103

K	FO	FC	K	FO	FC	K	FO	FC	K	FO	FC
2	177	184	16,K,5			5,K,6			10,K,6		
3	69	69									
4	228	210	1	222	199	0	165	-184	0	163	189
5	133	127	3	107	143	1	49	65	1	68	45
10,K,5			4*	83	-5	2	149	-141	2	167	178
			17,K,5			3	73	57	3	86	-81
1	307	307				5	128	94	4	285	319
2	254	250	3	104	-76	6	109	-101	5	90	67
3	121	111	0,K,6			9	113	-120	7	101	-116
4	329	324				6,K,6			11,K,6		
6	299	294	2	514	-502	0	268	-285	0	69	-63
7	155	156	6	86	-90	1	129	118	1	72	53
8	118	126	8	261	275	2	128	-145	2	83	-81
9	91	-91	1,K,6			3	355	370	4	148	-156
10	91	92				4	263	-260	5	137	157
11,K,5			2	228	250	7	233	231	9*	94	36
			3	60	-49	9	127	166	12,K,6		
1	230	-234	5	221	-194	7,K,6					
3	117	-119	9	103	106				3	85	103
4	114	-89	10	87	-117	0	66	-70	4	148	178
6	167	-194	2,K,6			2	61	-78	5	154	162
7	103	100				4	129	134	7	102	152
8	96	-96	2	58	93	5	306	-335	9	103	127
12,K,5			3	395	-377	7	226	-235	13,K,6		
			5	452	-464	9	123	-59			
1	507	-507	7	232	-218	8,K,6			0	88	-110
3	224	-229	9	277	-322				2	108	-106
6	140	124	3,K,6			0	364	-384	6	89	-96
8	100	-78				1	101	117	14,K,6		
11	92	72	0	144	165	2	132	-136			
13,K,5			2	254	255	3	152	-165	2	172	-207
			5	318	325	4	248	-262	3	94	-85
1	89	38	7	181	178	5	132	-152	4	113	-80
2	76	-31	4,K,6			6	76	88	6	99	-111
4	106	-112				7	225	-257	15,K,6		
14,K,5			0	327	316	9	81	-85			
			1	61	-35	11	97	-84	0	84	107
1	87	-109	2	361	365	9,K,6			16,K,6		
2	116	-94	3	57	42						
4	198	-216	4	136	140	0	155	159			
5	95	93	5	60	53	2	155	164			
6	162	-185	7	147	191	6	113	106	0	151	231
7	108	-74	8	93	-93	9	87	68	1	101	-113
			9	83	105				5	93	-120
									9	105	-145

K	FO	FC	K	FO	FC	K	FO	FC	K	FO	FC
	17,K,6			5,K,7		6	105	-116	5	241	240
4*	85	17	1	150	-146	8	110	-140	7	227	254
	0,K,7		2	266	269		11,K,7			3,K,8	
2	62	-67	4	137	126	1	147	159	0	374	-352
4	219	195	5	101	124	3	157	161	1	57	81
5	232	258		6,K,7		4	121	130	2	78	-85
7*	84	-0	1	149	135	6	137	164	3	103	-106
8	227	270	2	234	224		12,K,7		5	215	-214
10	118	130	3	134	96	1	289	270	7	131	-139
	1,K,7		4	230	232	3	122	132		4,K,8	
3	163	-144	5	195	198	8	94	-65	0	311	-309
5	139	-169	6	145	133		13,K,7		2	210	-228
6	145	-117	8	183	152	0*	85	-0	3	69	49
7	74	44	11	101	-94	1	137	-81	5	97	-78
8	179	-180		7,K,7		2	123	109	6	82	-63
	2,K,7		1	278	-272	4	87	75		5,K,8	
2	98	-97	3	266	-267		14,K,7		0	228	233
3	292	-259	4	93	-128	2	91	30	2	132	117
4	127	-132	5	86	-54	4	108	93	3	102	-92
5	247	-252	6	88	-127		16,K,7		4	141	142
6	97	-86	7	92	137	1	114	-107		6,K,8	
7	78	-75		8,K,7		3	120	-135	0	132	143
11	123	115	1	284	-289		0,K,8		1	88	-101
	3,K,7		2	79	103	2	150	143	2	219	213
1	137	114	3	73	-91	4	182	217	4	87	94
2	98	96	4	219	222	10	115	-129	5	190	-198
3	268	253	5	87	-51		1,K,8		7	90	-99
5	124	128	8	133	145	2	141	-141		7,K,8	
6	87	-69		9,K,7		3	164	150	0	113	121
7	83	-104	1	129	110	5	74	59	1	119	-125
8	173	-174	2	261	-259	10	95	96	4	90	-53
	4,K,7		4	131	-134		2,K,8		5	201	206
1	98	90	5	85	-61	2	117	-110	7	127	148
3	73	72	8	93	-49	3	296	311		8,K,8	
4	255	-249		10,K,7					0	124	131
5	91	90	1	95	-91				2	214	215
6	190	-184	2	157	-129				5	166	152
7	88	-52	4	174	-158				6	110	79
8	183	-223	5	94	-65				7	96	62

K	FO	FC	K	FO	FC	K	FO	FC	K	FO	FC
9,K,8			1,K,9			8,K,9			3 99 -92		
0	175	-194	3	189	187	1	77	88	5	91	-80
1	77	-72	5	85	85	2	149	-160	2,K,10		
2	75	-48	6	142	140	3	82	102	3 101 -93		
4	93	-78	2,K,9			9,K,9			5	186	-187
10,K,8			2,K,9			1	82	-85	3,K,10		
2	113	-125	2	75	57	2	135	147	0 104 128		
3	115	-82	3	247	250	4	90	93	2	70	87
4	81	-76	4	71	70	6	114	78	3	105	83
5	99	99	5	125	141	10,K,9			5	122	113
6	92	-79	9*	96	-7	3	81	65	8	121	-69
11,K,8			3,K,9			6	101	107	4,K,10		
1	88	71	1	152	-155	11,K,9			0	159	200
2	86	88	2	80	-77	1	113	-117	2	72	75
3	78	-47	3	159	-174	3	91	-77	4	94	68
12,K,8			6	119	83	4	97	-93	5,K,10		
3	99	-87	4,K,9			11*	111	15	0 112 -92		
9	121	-81	2	101	107	12,K,9			2	164	-145
13,K,8			3	71	-84	1	123	-128	3	82	57
0	132	114	6	87	84	3	106	-100	4	122	-96
14,K,8			7	83	26	8*	181	30	6,K,10		
0	100	95	8	116	95	13,K,9			0	165	-143
7*	93	-4	5,K,9			1	88	79	1	94	-86
15,K,8			1	66	86	14,K,9			2	84	-60
2	93	-77	2	156	-149	1*	173	-2	3	84	64
16,K,8			3	92	-69	16,K,9			5	95	78
3	97	82	4	81	-79	1	97	86	7,K,10		
0,K,9			6	100	-107	0,K,10			10*	126	-12
6	97	-82	6,K,9			7,K,9			8,K,10		
8	102	-139	2	129	-116	2	87	-129	0	221	-212
			3	147	-155	4	74	-60	3*	90	-39
			4	105	-102	1,K,10			4	93	-47
			6	102	-99	2 119 140			10	128	37
			7,K,9			9,K,10			2 122 92		
			1	199	215						
			3	91	120						
			4	91	109						
			9	95	-78						

K	FO	FC	K	FO	FC
	10,K,10			5,K,12	
0	99	85	0	64	69
			2	76	79
	13,K,10		4	69	70
			5	77	-41
3	113	-42			
				9,K,12	
	1,K,11				
			4	85	-65
5	96	-83			
				10,K,12	
	2,K,11				
			0*	158	-26
3	80	-102			
	3,K,11				
1	85	120			
	5,K,11				
4	113	109			
	6,K,11				
1	71	42			
7	106	-6			
	7,K,11				
1	126	-127			
	8,K,11				
2	97	60			
	0,K,12				
2	40	52			
	1,K,12				
5	77	75			
	2,K,12				
6*	87	-1			

TABLE 4

Final Positional and Thermal Parameters for Non-hydrogen Atoms and Their Estimated Standard Deviations

The values in the table have been multiplied by 10^4 . The temperature factors are of the form:

$$T = \exp(-\beta_{11}h^2 - \beta_{22}k^2 - \beta_{33}l^2 - 2\beta_{12}hk - 2\beta_{13}hl - 2\beta_{23}kl)$$

Atom	X	Y	Z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Cl(1)	1441(1)	5369(2)	2632(2)	30(1)	69(2)	104(3)	7(2)	5(2)	14(3)
N(1)	945(3)	- 810(4)	2704(5)	26(3)	56(6)	67(7)	3(3)	- 4(4)	- 10(6)
O(1)	1297(2)	1446(4)	1463(5)	27(2)	55(5)	118(7)	4(3)	-10(3)	10(5)
O(2)	758(3)	2529(5)	- 31(6)	37(3)	87(6)	198(11)	9(5)	- 6(5)	50(7)
O(3)	1269(11)	4612(12)	1640(14)	174(22)	136(25)	175(27)	-29(21)	22(22)	-130(24)
O(4)	1688(10)	6246(11)	2112(15)	145(19)	96(18)	207(35)	-17(15)	2(19)	39(22)
O(5)	1785(9)	4969(14)	3722(14)	68(13)	265(42)	221(32)	-33(17)	-55(15)	144(33)
O(6)	916(8)	5436(18)	3571(16)	45(9)	403(58)	251(33)	-34(19)	51(15)	-134(42)
O(7)	1846(6)	5117(14)	1455(14)	37(7)	232(39)	250(33)	38(13)	- 8(13)	- 49(27)
O(8)	908(6)	6011(10)	2243(15)	25(6)	149(19)	331(41)	46(9)	31(13)	75(23)

Table 4 - continued

Atom	X	Y	Z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
O(9)	1248(16)	4619(16)	3033(31)	201(34)	185(47)	592(126)	- 7(31)	-209(33)	24(58)
O(10)	1969(7)	5817(18)	3487(21)	39(7)	423(56)	428(68)	-101(18)	19(17)	-267(53)
C(1)	1681(5)	- 799(8)	2312(14)	29(3)	91(10)	376(25)	19(5)	- 9(9)	21(15)
C(2)	843(8)	-1490(9)	3969(11)	79(5)	75(9)	119(12)	8(6)	- 5(7)	21(9)
C(3)	518(5)	-1302(9)	1604(11)	44(4)	104(11)	209(16)	12(6)	- 41(7)	- 47(11)
C(4)	719(5)	328(8)	3046(7)	41(4)	93(10)	110(11)	8(6)	3(5)	- 15(10)
C(5)	635(4)	1120(7)	1937(8)	21(3)	105(11)	150(13)	12(5)	17(5)	39(10)
C(6)	1289(5)	2190(5)	416(6)	58(5)	32(8)	116(11)	- 6(5)	- 5(7)	- 31(8)
C(7)	2006(4)	2451(9)	- 41(10)	30(3)	102(9)	175(13)	- 11(7)	11(7)	28(9)

TABLE 5

Final Positional and Thermal Parameters for Hydrogen Atoms

The values for the coordinates have been multiplied
by 10^4 .

Atom	X	Y	Z	B
H(1,1)	1615(32)	- 659(52)	1214(66)	7.0
H(1,2)	1854(30) σ	-1443(49)	2536(73)	7.0
H(1,3)	1941(31)	- 395(52)	2853(67)	7.0
H(2,1)	961(32)	-2089(45)	3750(66)	7.0
H(2,2)	1196(31)	-1085(47)	4626(64)	7.0
H(2,3)	265(32)	-1194(55)	4115(65)	7.0
H(3,1)	100(33)	-1200(58)	2015(68)	7.0
H(3,2)	735(33)	-1875(51)	1427(69)	7.0
H(3,3)	621(32)	- 744(54)	727(69)	7.0
H(4,1)	276(30)	124(53)	3330(62)	5.6
H(4,2)	912(31)	641(48)	3741(60)	5.6
H(5,1)	360(32)	856(49)	1178(60)	5.6
H(5,2)	311(28)	1725(42)	2462(62)	5.6
H(7,1)	2366(33)	2186(52)	643(58)	7.0
H(7,2)	2160(31)	3242(49)	68(70)	7.0
H(7,3)	2102(29)	2527(58)	-1004(65)	7.0

TABLE 6

Scale Factors for c-Axis Layers

<u>Layer</u>	<u>Scale Factors</u>
hk0	3.0606
hk1	2.9685
hk2	2.9949
hk3	3.1453
hk4	3.1983
hk5	3.3183
hk6	3.3367
hk7	3.7194
hk8	3.7233
hk9	3.9215
hk10	4.7377
hk11	4.9287
hk12	4.0869

DISCUSSION

A drawing of acetylcholine perchlorate (excluding hydrogen atoms and perchlorate group) is shown in Figure 4. The distance in angstroms of each atom from the plane containing C(7)-C(6)-O(2)-O(1)-C(5)-C(4) is indicated. The bond distances and angles of non-hydrogen atoms and their estimated standard deviations are listed in Tables 7 and 8. Bond distances and angles involving hydrogen atoms, along with their standard deviations, are given in Tables 9 and 10.

The bond distances and angles for acetylcholine fragment are essentially normal and agree with similar dimensions observed in a variety of related compounds.²⁰ The range of values obtained for seven of the eight Cl-O bond distances in perchlorate ion was from 1.29 to 1.43 Å. One Cl-O distance had an unusually low value of 1.08 Å. The position of this oxygen atom corresponded to a diffuse region in the difference maps. This atom was clearly incorrectly placed on the long arc of electron density which persistently marked its position on the maps. The bond angles for the perchlorate ion had a range of from 82° to 119°. These values indicate that the ion is disordered, as is often observed, and it is apparent that the anisotropic approximation has not provided an adequate description. The accepted Cl-O bond distance is in the range of from 1.43 to 1.48 Å, and bond angle is tetrahedral.²¹

Table 11 presents a comparison of selected torsional angles for acetylcholine perchlorate, along with acetylcholine chloride and acetylcholine bromide. All three structures show the nitrogen atom to be gauche to the ether oxygen [angle N(1)-C(4)-C(5)-O(1)]. This structural feature is present in the calculated minimum energy

Figure 4. The Structure of the Acetylcholine
Molecule in Crystals of Acetylcholine
Perchlorate

TABLE 7

Bond Distances Involving Non-Hydrogen Atoms
and Their Estimated Standard Deviations

<u>Atoms</u>	<u>Distance in Angstroms</u>
N(1)---C(1)	1.491(11)
N(1)---C(2)	1.510(12)
N(1)---C(3)	1.491(12)
N(1)---C(4)	1.517(11)
O(1)---C(5)	1.433(9)
O(1)---C(6)	1.378(8)
O(2)---C(6)	1.202(10)
C(4)---C(5)	1.472(12)
C(6)---C(7)	1.506(13)
Cl(1)--O(3)	1.391(15)
Cl(1)--O(4)	1.294(15)
Cl(1)--O(5)	1.353(15)
Cl(1)--O(6)	1.379(15)
Cl(1)--O(7)	1.431(13)
Cl(1)--O(8)	1.366(12)
Cl(1)--O(9)	1.078(23)
Cl(1)--O(10)	1.439(17)

TABLE 8

Bond Angles Involving Non-Hydrogen Atoms
and Their Estimated Standard Deviations

<u>Apex</u>	<u>End</u>	<u>End</u>	<u>Angle in Degrees</u>
N(1)	C(2)	C(1)	110.03(.83)
N(1)	C(3)	C(1)	111.06(.71)
N(1)	C(3)	C(2)	106.76(.71)
N(1)	C(4)	C(2)	107.59(.61)
N(1)	C(4)	C(3)	112.14(.59)
N(1)	C(4)	C(1)	109.16(.59)
O(1)	C(6)	C(5)	114.79(.60)
C(6)	C(7)	O(2)	128.35(.68)
C(6)	C(7)	O(1)	110.73(.72)
C(6)	O(2)	O(1)	120.91(.75)
C(5)	C(4)	O(1)	109.00(.63)
C(4)	C(5)	N(1)	119.49(.62)
C1(1)	O(3)	O(4)	112.58(.90)
C1(1)	O(3)	O(5)	114.86(.99)
C1(1)	O(3)	O(6)	108.88(1.14)
C1(1)	O(4)	O(5)	115.65(1.08)
C1(1)	O(4)	O(6)	119.26(1.21)
C1(1)	O(5)	O(6)	82.41(.97)

Table 8 - continued

<u>Apex</u>	<u>End</u>	<u>End</u>	<u>Angle in Degrees</u>
C1(1)	O(7)	O(8)	109.03(.84)
C1(1)	O(7)	O(9)	107.28(1.66)
C1(1)	O(7)	O(10)	98.91(.88)
C1(1)	O(8)	O(9)	109.64(1.72)
C1(1)	O(8)	O(10)	118.92(.99)
C1(1)	O(9)	O(10)	111.99(1.84)

TABLE 9

Bond Distances Involving Hydrogen Atoms
and Their Estimated Standard Deviations

<u>Atoms</u>	<u>Distance in Angstroms</u>
C(1) --H(1,1)	1.094(66)
C(1) --H(1,2)	.895(62)
C(1) --H(1,3)	.887(64)
C(2) --H(2,1)	.807(12)
C(2) --H(2,2)	1.067(62)
C(2) --H(2,3)	1.198(65)
C(3) --H(3,1)	.919(66)
C(3) --H(3,2)	.846(65)
C(3) --H(3,3)	1.120(68)
C(4) --H(4,1)	.944(59)
C(4) --H(4,2)	.869(60)
C(5) --H(5,1)	.973(61)
C(5) --H(5,2)	1.108(56)
C(7) --H(7,1)	1.025(62)
C(7) --H(7,2)	1.033(61)
C(7) --H(7,3)	.963(64)

TABLE 10

Bond Angles Involving Hydrogen Atoms
and Their Estimated Standard Deviations

<u>Apex</u>	<u>End</u>	<u>End</u>	<u>Angle in Degrees</u>
C(1)	H(1,1)	N(1)	98.02(3.3)
C(1)	H(1,2)	N(1)	107.05(4.0)
C(1)	H(1,3)	N(1)	113.86(4.1)
C(1)	H(1,1)	H(1,2)	115.18(5.8)
C(1)	H(1,1)	H(1,3)	124.23(5.5)
C(1)	H(1,2)	H(1,3)	98.19(5.9)
C(2)	H(2,1)	N(1)	105.05(1.0)
C(2)	H(2,2)	N(1)	98.30(3.4)
C(2)	H(2,3)	N(1)	92.83(3.2)
C(2)	H(2,1)	H(2,2)	114.18(3.5)
C(2)	H(2,1)	H(2,3)	125.71(3.6)
C(2)	H(2,2)	H(2,3)	113.15(4.6)
C(3)	H(3,1)	N(1)	97.19(4.3)
C(3)	H(3,2)	N(1)	102.13(4.5)
C(3)	H(3,3)	N(1)	101.39(3.4)
C(3)	H(3,1)	H(3,2)	130.66(6.4)
C(3)	H(3,1)	H(3,3)	114.22(5.5)
C(3)	H(3,2)	H(3,3)	105.79(5.7)
C(4)	H(4,1)	N(1)	94.69(4.0)
C(4)	H(4,2)	N(1)	117.54(4.1)
C(4)	H(4,1)	C(5)	107.02(3.9)

Table 10 - continued

<u>Apex</u>	<u>End</u>	<u>End</u>	<u>Angle in Degrees</u>
C(4)	H(4,2)	C(5)	108.98(4.0)
C(4)	H(4,1)	H(4,2)	106.78(5.5)
C(5)	H(5,1)	O(1)	110.39(0.6)
C(5)	H(5,2)	O(1)	118.32(2.9)
C(5)	H(5,1)	C(4)	113.43(3.7)
C(5)	H(5,2)	C(4)	100.15(3.1)
C(5)	H(5,1)	H(5,2)	105.35(4.7)
C(7)	H(7,1)	C(6)	112.14(3.5)
C(7)	H(7,2)	C(6)	116.43(3.5)
C(7)	H(7,3)	C(6)	119.44(3.6)
C(7)	H(7,1)	H(7,2)	92.15(5.1)
C(7)	H(7,1)	H(7,3)	122.33(4.9)
C(7)	H(7,2)	H(7,3)	87.11(5.7)

TABLE 11

Selected Torsional Angles In Crystalline Acetylcholine Perchlorate,
Acetylcholine Chloride and Acetylcholine Bromide

<u>Angle</u>	<u>Perchlorate</u>	<u>Chloride</u>	<u>Bromide</u>
C(2)-N(1)-C(4)-C(5)	168.3°	171.4°	~180°
N(1)-C(4)-C(5)-O(1)	73.7°	84.7°	77°
C(4)-C(5)-O(1)-C(6)	179.8°	-166.9°	79°
C(5)-O(1)-C(6)-O(2)	0.8°	5.2°	0°

geometries reported in all of the theoretical studies on acetylcholine. The major difference between acetylcholine perchlorate and acetylcholine bromide is the C(4)-C(5)-O(1)-C(6) torsion angle: 179.8° in the perchlorate and 79° in the bromide.

The N(1)-O(1) non-bonded interatomic distance for acetylcholine perchlorate is 3.13 Å. The values for this distance in acetylcholine chloride and bromide are 3.26 Å and 3.29 Å, respectively. The C(1)-O(1) non-bonded interatomic distance of 3.00 Å is comparable to the values of 3.17 Å and 3.02 Å in acetylcholine chloride and bromide, respectively.

Figure 5 is a [001] projection of the unit cell indicating the crystal packing. The range of Cl-N distance varies from 4.84 to 5.31 Å. The two closest N-N distances are 6.44 Å and 7.22 Å. The chlorine and nitrogen atoms are nearly stacked upon each other in the c-axis direction. All intermolecular contact distances are not significantly different from accepted Van der Waals values.

Figure 5. Packing Diagram [001] Projection

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