Acta Chemica Scandinavica B 29 (1975) 891—903

The Crystal Structures of Carbamoylcholine Chloride, Carbamoylcholine Iodide, and the 1:1 Complex Carbamoylcholine Picrate, Picric Acid

BIRTHE JENSEN

Chemical Laboratory C, The Royal Danish School of Pharmacy, Universitetsparken 2, DK-2100 Copenhagen, Denmark

The crystal structures of carbamoylcholine chloride, CARCHL, carbamoylcholine iodide, CARIOD, and the 1:1 complex carbamoylcholine picrate, picric acid, CARPCR, have been determined from diffractometer collected three-dimensional X-ray data and refined by full-matrix least-squares techniques to R values of 0.039, 0.043, and 0.056 for CARCHL, CARIOD, and CARPCR, respectively. In all of the three crystal structures the two possible hydrogen bonds N−H···A are found, but the contacts are generally rather weak. The conformations of the carbamoylcholine ions found in the crystals of the three salts are highly different, and *trans* as well as *gauche* arrangements of the choline moiety are seen.

The crystal structures of three carbamoylcholine salts, a chloride, an iodide, and a picrate complexed with picric acid, was investigated as part of conformational studies of choline derivatives in the solid state.

Since the carbamoylcholine ion is conformationally flexible, salts forming non-isostructural crystals have been investigated in order to examine the effect of different environments on the conformation of the carbamoylcholine ion. Here the possible formation of hydrogen bonds has been of special interest. Among the large number of salts of choline derivatives, of which the crystal structures are known, only very few have any possibility of formation of hydrogen bonds. The salts have most often been halides, and few of the choline derivatives examined can act as donors for hydrogen bonds.

EXPERIMENTAL

Carbamoylcholine chloride, CARCHL. A solution of commercial CARCHL in ethanol was cooled slowly to give colourless prisms of the compound. Preliminary Weissenberg- and precession X-ray diffraction photographs showed the crystals to be orthorhombic. The systematically absent reflections are $h0l$ when h is odd and $0kl$ when $k+l$ is odd, indicating that the space group is $Pna2_1$ or $Pnam$. The unit cell parameters were refined by least-squares techniques from diffractometer measured 2θ-angles (Mo$K\alpha$ radiation, $\lambda = 0.7107$ Å) for 17 independent reflections. The density of the crystals was measured by flotation in a mixture of chlorobenzene and bromobenzene. All melting points given in this paper were determined on a Leitz hot stage microscope. Table 1 lists the unit cell parameters and other crystal data.

Three-dimensional diffraction data were measured at room temperature on a Nonius three-circle automatic diffractometer using graphite monochromated Mo$K\alpha$-radiation. The ω scan technique with a scan speed of 1.2° min^{-1} was employed, and the scan angle was 1.2°. Background counts were taken for half the scanning time at each of the scan range limits. One standard reflection was measured after every 40 reflections. All the data were measured from a single crystal with approximate dimensions $0.31 \times 0.34 \times 0.42$ mm. The crystal was sealed in a glass capillary to avoid the humidity of the air and mounted with its elongated dimension, which was parallel to the

Table 1. Crystal data.

	CARCHL	CARIOD	CARPCR
Stoichiometry	$C_6H_{15}N_2O_2Cl$	$C_6H_{15}N_2O_2I$	$C_{18}H_{20}N_8O_{16}$
Formula weight	182.65	274.10	604.40
Z	4	4	2
$F(000)$	396	540	624
Space group	*Pnam*	$P2_1/c$	$P\bar{1}$
a	10.248(3) Å	6.073(2) Å	13.020(5) Å
b	12.850(4) Å	12.616(8) Å	13.736(4) Å
c	6.809(4) Å	13.688(5) Å	7.117(2) Å
α			96.39(3)°
β		95.79(3)°	96.77(2)°
γ			91.72(4)°
Cell volume	896.66 Å^3	1043.38 Å^3	1254.66 Å^3
D_x	1.35 g cm^{-3}	1.74 g cm^{-3}	1.60 g cm^{-3}
D_m	1.35(1) g cm^{-3}	1.74(1) g cm^{-3}	1.61(1) g cm^{-3}
$\mu_{(MoK\alpha)}$	3.83 cm^{-1}	30.62 cm^{-1}	1.54 cm^{-1}
Melting point	203–208 °C (decomp.)	193–195 °C	89–91 °C

crystallographic c-axis, along the ϕ-axis of the goniostat. Out of the 1289 independent reflections within the range $2.5° \leq \theta \leq 25.0°$, 979 had $I_{net} \geq 2.5\sigma(I)$, where $\sigma(I)$ is the standard deviation from counting statistics. These were regarded as observed reflections, whereas the remaining reflections were regarded as unobserved and excluded from the refinement procedure. Lorentz and polarization corrections were applied, but no absorption corrections were made.

The statistical distribution of normalized structure factor magnitudes ($|E|$'s) indicated that the crystal structure is centrosymmetric. Consequently the space group was assumed to be *Pnam*, and this assumption was corroborated by the final structure analysis. The trial structure was obtained by the heavy-atom method.

Carbamoylcholine iodide, CARIOD. CARIOD was prepared by mixing almost saturated aqueous solutions of carbamoylcholine chloride and potassium iodide. The resulting precipitate was purified by recrystallisation from 96 % ethanol. Single crystals (colourless prisms) were grown by slow cooling of a solution in aqueous ethanol. Preliminary Weissenberg- and precession photographs showed the crystals to be monoclinic. The systematically absent reflections are $h0l$ when l is odd and $0k0$ when k is odd, indicating that the space group is $P2_1/c$. The unit cell parameters were obtained by least-squares refinement of 2θ-angles (Mo$K\alpha$ radiation) for 48 reflections, measured from precession photographs. No corrections for film shrinkage were performed. The density of the crystals was measured by flotation in a mixture of bromobenzene and methyliodide. Crystal data are listed in Table 1.

Intensity data were measured from a single crystal with approximate dimensions $0.14 \times 0.16 \times 0.42$ mm. The crystal was sealed in a glass capillary and mounted with its elongated dimension, which was parellel to the crystallographic a-axis, along the ϕ-axis of the goniostat. The experimental conditions and treatment of the data were the same as described for CARCHL. Each of the 1831 independent reflections in the range $2.5° \leq \theta \leq 25.0°$ was measured twice. 2948 of the 3562 reflections ($hk \pm l$ and $h - k \pm l$) had $I_{net} \geq 2.5\sigma(I)$. The reflections for both quadrants were used independently in the least-squares refinement.

The trial structure was obtained by the heavy-atom method.

Carbamoylcholine picrate, picric acid, CARPCR. CARPCR was prepared by mixing aqueous solutions of carbamoylcholine chloride and picric acid. After standing for some minutes yellow prisms were formed. These were purified by recrystallisation from water, and single crystals were grown by slow cooling of an aqueous solution. Preliminary Weissenberg- and precession photographs showed the crystals to be triclinic. The unit cell parameters were refined by least-squares techniques from diffractometer measured 2θ-angles (Mo$K\alpha$ radiation) for 43 independent reflections. The density of the crystals was measured by flotation in a mixture of bromobenzene and methyl iodide. Crystal data are listed in Table 1.

Intensity data were measured from a single crystal with approximate dimensions $0.20 \times 0.22 \times 0.38$ mm. The crystal was mounted on a glass fiber with its elongated dimension, which was parallel to the crystallographic c-axis, along the ϕ-axis of the goniostat. The experimental conditions and treatment of the data were the same as described for CARCHL. Out of the 4436 independent reflections within the range $2.5° \leq \theta \leq 25.0°$ 2751 had $I_{net} \geq 2.5\sigma(I)$.

Table 2. Final positional and thermal parameters for non-hydrogen atoms. The estimated standard deviations, referring to the last significant figure, are given in parentheses. Thermal parameters are $\times 10^2$.
The temperature factor is defined by: $\exp[-2\pi^2(U_{11}h^2a^{*2}+\cdots+2U_{12}hka^*b^*+\cdots)]$.

Atom	x/a	y/b	z/c	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
CARCHL									
N(1)	.9997(2)	.3788(2)	.2500(−)	3.74(11)	2.94(10)	4.61(13)	−0.20(9)	0.0(−)	0.0(−)
C(2)	.9214(2)	.4617(2)	.2500(−)	3.35(11)	2.97(11)	2.27(11)	0.23(9)	0.0(−)	0.0(−)
O(3)	.8027(2)	.4593(1)	.2500(−)	2.96(8)	3.45(9)	5.23(12)	0.31(7)	0.0(−)	0.0(−)
O(4)	.9895(2)	.5523(1)	.2500(−)	2.85(8)	2.55(8)	4.81(11)	−0.02(7)	0.0(−)	0.0(−)
C(5)	.9071(2)	.6427(2)	.2500(−)	2.87(10)	2.48(11)	4.35(15)	0.06(9)	0.0(−)	0.0(−)
C(6)	1.0026(2)	.7334(2)	.2500(−)	2.48(10)	2.52(10)	3.43(13)	−0.09(9)	0.0(−)	0.0(−)
N(7)	.9378(2)	.8389(2)	.2500(−)	2.37(8)	2.52(9)	2.54(10)	0.14(7)	0.0(−)	0.0(−)
C(8)	1.0454(2)	.9193(2)	.2500(−)	3.16(11)	2.88(12)	4.10(15)	0.80(9)	0.0(−)	0.0(−)
C(9)	.8565(2)	.8551(2)	.0695(3)	3.67(8)	4.00(9)	3.51(10)	−0.23(7)	1.09(7)	0.45(8)
Cl^-	.8271(1)	.1558(1)	.2500(−)	3.39(3)	3.38(3)	4.10(4)	−0.12(3)	0.0(−)	0.0(−)
CARIOD									
N(1)	.9146(8)	−.0508(4)	.6144(3)	7.2(3)	6.3(3)	3.5(2)	1.1(2)	1.9(2)	0.7(2)
C(2)	.7587(8)	.0243(4)	.5916(3)	4.8(3)	3.7(2)	3.2(2)	−0.6(2)	0.6(2)	−0.4(2)
O(3)	.7301(6)	.0714(3)	.5153(2)	5.7(2)	4.9(2)	3.0(2)	0.2(2)	1.1(1)	0.4(1)
O(4)	.6356(6)	.0370(3)	.6671(2)	5.6(2)	4.7(2)	3.1(2)	1.1(2)	1.2(1)	0.3(1)
C(5)	.4693(9)	.1183(4)	.6551(3)	4.8(3)	4.1(2)	3.3(2)	0.8(2)	0.1(2)	0.1(2)
C(6)	.3361(8)	.1149(4)	.7423(4)	3.3(2)	4.2(2)	4.2(3)	0.0(2)	0.1(2)	0.1(2)
N(7)	.4527(7)	.1509(3)	.8398(3)	4.1(2)	4.2(2)	3.8(2)	0.2(2)	1.4(2)	−0.8(2)
C(8)	.6230(12)	.0700(7)	.8785(5)	6.3(4)	10.1(6)	4.1(3)	3.3(4)	−1.2(3)	−1.1(3)
C(9)	.5518(15)	.2570(6)	.8328(6)	10.1(6)	6.8(4)	7.0(4)	−4.9(4)	3.9(4)	−2.9(4)
C(10)	.2829(12)	.1563(6)	.9118(5)	7.2(4)	6.4(4)	6.0(4)	−0.5(3)	4.1(3)	−0.8(3)
I^-	−.05069(5)	.15367(2)	.13618(2)	4.47(2)	4.42(2)	3.93(2)	0.32(2)	0.63(1)	−0.14(2)
CARPCR									
N(1)	−.0214(2)	.0975(2)	.3450(4)	4.0(2)	4.7(2)	6.8(2)	0.5(1)	0.1(1)	1.1(1)
C(2)	.0815(2)	.1006(2)	.3608(5)	4.5(2)	3.0(2)	4.5(2)	0.3(1)	0.3(2)	−0.5(1)
O(3)	.1368(2)	.0452(2)	.4469(3)	4.2(1)	4.6(1)	6.5(2)	0.5(1)	−0.1(1)	1.2(1)
O(4)	.1180(2)	.1698(2)	.2644(3)	4.9(1)	4.5(1)	6.0(2)	0.6(1)	1.2(1)	1.0(1)
C(5)	.2276(3)	.1915(2)	.2886(5)	5.7(2)	4.5(2)	5.6(2)	−1.4(2)	1.2(2)	−0.8(2)
C(6)	.2665(3)	.1915(2)	.0971(5)	5.3(2)	3.1(2)	5.3(2)	−0.6(1)	1.2(2)	−0.1(1)
N(7)	.2903(2)	.0915(2)	.0020(4)	4.2(2)	3.4(1)	4.1(2)	−0.6(1)	0.2(1)	−0.3(1)
C(8)	.1961(3)	.0240(2)	−.0379(6)	5.1(2)	4.3(2)	7.1(3)	−1.2(2)	0.6(2)	−1.6(2)
C(9)	.3286(3)	.1057(3)	−.1845(6)	7.2(3)	7.0(3)	5.3(2)	−0.9(2)	1.8(2)	−0.2(2)

Table 2. Continued.

C(10)	.3740(3)	.0458(3)	.1226(6)	5.5(2)	5.0(2)	7.3(3)	0.8(2)	−0.7(2)	0.1(2)
C(11)	.2576(3)	.7813(2)	.3291(5)	6.0(2)	3.8(2)	4.1(2)	0.5(2)	1.5(2)	0.7(1)
C(12)	.1750(3)	.7160(2)	.2480(5)	5.1(2)	4.7(2)	3.9(2)	0.5(2)	1.1(2)	0.7(2)
C(13)	.1842(3)	.6159(2)	.2168(5)	7.3(3)	4.5(2)	4.2(2)	−0.5(2)	2.2(2)	0.2(2)
C(14)	.2791(3)	.5794(2)	.2712(5)	8.3(3)	3.7(2)	5.2(2)	0.8(2)	3.2(3)	0.6(2)
C(15)	.3633(3)	.6384(3)	.3469(5)	7.4(3)	5.5(2)	4.3(2)	1.7(2)	2.0(2)	1.0(2)
C(16)	.3526(3)	.7385(2)	.3721(5)	5.9(2)	4.8(2)	3.9(2)	0.5(2)	1.2(2)	0.5(2)
O(11)	.2516(2)	.8771(2)	.3680(4)	6.7(2)	3.9(1)	7.4(2)	0.7(1)	0.7(1)	0.4(1)
N(12)	.0733(2)	.7537(2)	.1891(4)	6.3(2)	6.3(2)	5.1(2)	−0.1(2)	0.7(2)	0.5(2)
O(121)	.0614(2)	.8427(2)	.2223(4)	6.9(2)	6.5(2)	8.2(2)	2.0(1)	0.3(2)	−0.1(1)
O(122)	.0055(2)	.6966(2)	.1104(5)	7.2(2)	8.6(2)	9.5(2)	−1.3(2)	−1.4(2)	0.3(2)
N(14)	.2901(3)	.4720(2)	.2392(5)	11.8(3)	4.9(2)	7.7(2)	2.3(2)	5.3(2)	1.2(2)
O(141)	.2210(3)	.4225(2)	.1357(5)	13.6(3)	4.8(2)	11.0(3)	−0.5(2)	4.9(2)	−1.1(2)
O(142)	.3686(3)	.4401(2)	.3175(6)	16.0(4)	6.4(2)	13.2(3)	5.0(2)	3.2(3)	1.7(2)
N(16)	.4472(2)	.7986(2)	.4459(4)	6.3(2)	6.7(2)	5.6(2)	0.4(2)	1.1(2)	−0.1(2)
O(161)	.5140(2)	.7603(2)	.5415(5)	7.2(2)	10.4(2)	9.3(2)	2.7(2)	−1.2(2)	−2.0(2)
O(162)	.4561(2)	.8796(2)	.4010(5)	8.3(2)	7.8(2)	11.8(3)	−2.0(2)	0.2(2)	1.6(2)
C(21)	.7947(2)	.3073(2)	.2220(4)	3.5(2)	3.3(2)	3.7(2)	0.1(1)	0.3(1)	0.1(1)
C(22)	.8536(2)	.3986(2)	.2863(4)	3.2(2)	3.6(2)	3.9(2)	−0.0(1)	0.2(1)	−0.0(1)
C(23)	.8141(3)	.4897(2)	.2894(5)	5.3(2)	3.4(2)	4.3(2)	−0.2(1)	0.6(2)	−0.0(1)
C(24)	.7086(3)	.4972(2)	.2368(5)	5.5(2)	3.6(2)	4.0(2)	1.1(2)	0.4(2)	0.1(1)
C(25)	.6443(2)	.4149(3)	.1804(5)	3.9(2)	5.8(2)	3.5(2)	1.0(2)	0.2(1)	0.3(2)
C(26)	.6857(2)	.3240(2)	.1763(4)	3.6(2)	4.2(2)	3.4(2)	−0.2(1)	0.4(1)	0.0(1)
O(21)	.8333(2)	.2265(2)	.1952(4)	4.7(1)	3.4(1)	7.2(2)	0.6(1)	−0.7(1)	−0.1(1)
N(22)	.9639(2)	.3932(2)	.3516(4)	4.0(2)	4.3(2)	5.4(2)	−0.4(1)	0.5(1)	−1.0(1)
O(221)	.9903(2)	.3306(2)	.4530(4)	4.9(2)	5.6(1)	7.5(2)	0.7(1)	−1.2(1)	0.1(1)
O(222)	1.0231(2)	.4546(2)	.3049(4)	4.9(2)	7.2(2)	8.8(2)	−2.1(1)	1.5(1)	0.1(1)
N(24)	.6656(3)	.5929(2)	.2387(4)	8.5(2)	5.0(2)	5.6(2)	2.7(2)	0.8(2)	0.0(1)
O(241)	.7250(3)	.6650(2)	.2963(4)	12.6(3)	4.0(1)	8.6(2)	1.9(2)	0.1(2)	−0.6(1)
O(242)	.5748(2)	.5992(2)	.1809(5)	8.2(2)	8.0(2)	10.7(3)	4.8(2)	−0.5(2)	0.2(2)
N(26)	.6155(2)	.2395(2)	.1209(4)	3.8(2)	5.7(2)	4.8(2)	−0.9(1)	0.3(1)	0.6(1)
O(261)	.5379(2)	.2466(2)	.0164(5)	6.7(2)	10.6(2)	10.4(3)	−3.2(2)	−3.4(2)	2.8(2)
O(262)	.6352(2)	.1619(2)	.1897(4)	6.0(2)	4.4(1)	10.5(2)	−0.6(1)	1.3(2)	−0.2(1)

The statistical distribution of normalized structure factor magnitudes indicated that the crystal structure is centrosymmetric, and the experimental density indicated that the unit cell contains two formula units of CARPCR. Consequently the space group was assumed to be $P\bar{1}$; this assumption was corroborated by the final structure analysis. A trial structure was obtained by direct methods with the use of MULTAN, *ed.* 1970,[1] in combination with intensive calculations by hand.

REFINEMENT OF THE TRIAL STRUCTURES

The trial structures were refined by full-matrix least-squares techniques. The quantity minimized was $\sum w(|F_o|-|F_c|)^2$ where weights were initially taken as unity but later changed as follows: For CARCHL $w=1/(1+((F_o-B)/A)^2)$ where $A=10.0$ and $B=15.0$. For CARIOD $w=(F_o/A)^2$ when $F_o \leq A$ and else $w=(A/F_o)^2$, where $A=25.0$. For CARPCR $w=1/(1+((F_o-B)/A)^2)$, where $A=10.0$ and $B=20.0$. The scattering factors for the iodide ion were those published by Cromer and Mann.[2] The scattering factors for all other atoms were taken from *International Tables for X-Ray Crystallography*.[3] All nitrogen and oxygen atoms were treated as uncharged. All hydrogen atoms were located in difference Fourier maps calculated during the latter stages of refinement. The final cycles of refinement included positional parameters for all atoms and anisotropic thermal parameters for all non-hydrogen atoms while temperature parameters of hydrogen atoms were fixed at arbitrary values. On the last cycles of refinement of the respective structures shifts of all parameters were less than one third of their estimated standard deviations. The final R index $(\sum||F_o|-|F_c||/\sum|F_c|)$ is 0.039 for CARCHL, 0.043 for CARIOD, and 0.056 for CARPCR. The calculations were performed on a GIER computer and an IBM 360/75 computer, using INDIFF,[4] a local version of *The N.R.C. 2A Picker Data Reduction Program*,[5] *The X-Ray System*,[6] and *ORTEP*.[7] The observed and calculated structure factor data are available from the author on request.

RESULTS AND DISCUSSION

Tables 2 and 3 list final parameters and estimated standard deviations for non-hydrogen atoms and for hydrogen atoms, respectively. The calculated bond lengths and angles involving only non-hydrogen atoms are given in Table 4.

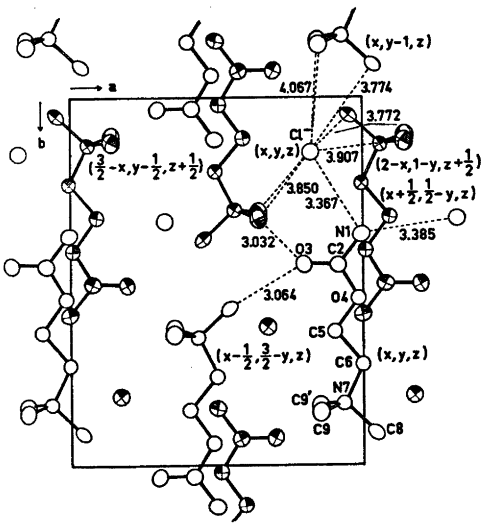

Fig. 1. CARCHL. The numbering system of the non-hydrogen atoms is given together with some *inter*molecular contacts. The structure is viewed in a direction deviating 5° from the direction of the c-axis to allow C(9) as well as C(9') to be seen. The thermal ellipsoids are drawn at the 50 % probability level. Atoms drawn as open ellipsoids are situated in or about the layer $z=1/4$, and the rest of the atoms are situated in or about the layer $z=3/4$.

Packing arrangements

CARCHL. Fig. 1 shows the crystal packing, the atomic numbering and some *inter*molecular contacts. The structure is very similar to that of 3-chloro- and 3-iodopropyltrimethylammonium iodide (mixed crystal),[8] and to that of carbamoylcholine bromide,[9] although the last compound was found to crystallize in the acentric space group $Pna2_1$. The chloride ion and all the non-hydrogen atoms of the carbamoylcholine ion with the exception of C(9) are situated in the mirror plane, while C(9) (and its mirror image C(9')), in the other carbamoylcholine salts named C(10)) occupy a general position. Two weak N–H···Cl⁻ contacts, N(1)–H(11)···$Cl^-_{(x,y,z)}$, and N(1)–H(12)···$Cl^-_{(x+\frac{1}{2},\frac{1}{2}-y,z)}$, link the ions together

Table 3. Final positional parameters for hydrogen atoms and the thermal parameters ($\times 10^2$) used. The estimated standard deviations (referring to the last significant figure) are given in parentheses.

Atom	*x/a*	*y/b*	*z/c*	*U*
CARCHL				
H(11)	.960(4)	.321(3)	.25(−)	3.8
H(12)	1.086(4)	.386(3)	.25(−)	3.8
H(5)	.849(2)	.643(2)	.132(4)	3.8
H(6)	1.058(2)	.731(2)	.124(4)	3.8
H(81)	.993(4)	.988(3)	.25(−)	3.8
H(82)	1.098(2)	.908(2)	.133(4)	3.8
H(91)	.819(2)	.927(2)	.080(4)	3.8
H(92)	.786(2)	.802(2)	.069(4)	3.8
H(93)	.914(2)	.846(2)	−.042(4)	3.8
CARIOD				
H(11)	1.083(11)	−.060(5)	.578(5)	5.1
H(12)	.882(12)	−.088(6)	.667(6)	5.1
H(51)	.549(13)	.185(6)	.643(5)	5.1
H(52)	.370(13)	.113(6)	.599(6)	5.1
H(61)	.217(13)	.164(5)	.737(5)	5.1
H(62)	.292(11)	.044(6)	.760(5)	5.1
H(81)	.519(11)	−.014(6)	.867(5)	5.1
H(82)	.720(13)	.075(6)	.837(6)	5.1
H(83)	.668(12)	.088(6)	.952(6)	5.1
H(91)	.616(13)	.280(6)	.893(5)	5.1
H(92)	.470(14)	.301(7)	.815(6)	5.1
H(93)	.681(12)	.241(6)	.790(5)	5.1
H(101)	.171(13)	.205(6)	.895(5)	5.1
H(102)	.205(12)	.083(6)	.917(5)	5.1
H(103)	.373(12)	.184(6)	.975(6)	5.1
CARPCR				
H(11)	−.054(3)	.144(3)	.299(6)	5.1
H(12)	−.053(3)	.051(3)	.410(6)	5.1
H(51)	.241(3)	.256(3)	.343(6)	5.1
H(52)	.260(3)	.141(3)	.363(6)	5.1
H(61)	.217(3)	.220(3)	−.002(6)	5.1
H(62)	.331(3)	.230(3)	.115(6)	5.1
H(81)	.174(3)	.012(3)	.082(6)	6.3
H(82)	.147(3)	.062(3)	−.105(6)	6.3
H(83)	.216(3)	−.035(3)	−.115(6)	6.3
H(91)	.270(3)	.135(3)	−.260(6)	6.3
H(92)	.387(3)	.152(3)	−.156(6)	6.3
H(93)	.346(3)	.035(3)	−.235(6)	6.3
H(101)	.435(3)	.095(3)	.147(6)	6.3
H(102)	.338(3)	.026(3)	.234(6)	6.3
H(103)	.396(3)	−.014(3)	.053(6)	6.3
H(13)	.127(3)	.577(3)	.168(6)	5.1
H(15)	.431(3)	.609(3)	.381(6)	5.1
H(111)	.176(4)	.891(4)	.332(7)	7.6
H(23)	.858(3)	.548(3)	.330(6)	5.1
H(25)	.575(3)	.418(3)	.145(6)	5.1

Table 4. Bond lengths (Å) and angles (°) involving only non-hydrogen atoms and their estimated standard deviations, referring to the last significant figure, in parentheses. The dimensions found for the carbamoylcholine ion in the crystal structure of carbamoylcholine bromide,[9] CARBRO, are given for comparison.

	CARCHL	CARIOD	CARPCR	CARBRO
N(1)–C(2)	1.334(3)	1.354(7)	1.329(4)	1.40(3)
C(2)–O(3)	1.217(3)	1.198(6)	1.227(4)	1.22(2)
C(2)–O(4)	1.358(3)	1.346(6)	1.340(4)	1.34(3)
O(4)–C(5)	1.436(3)	1.437(6)	1.435(4)	1.45(3)
C(5)–C(6)	1.522(3)	1.508(7)	1.509(5)	1.55(3)
C(6)–N(7)	1.509(3)	1.516(6)	1.520(4)	1.50(3)
N(7)–C(8)	1.511(3)	1.511(9)	1.495(4)	1.52(3)
N(7)–C(9)	1.500(2)	1.475(9)	1.502(5)	1.55(3)
N(7)–C(10)		1.498(8)	1.503(5)	1.51(3)
N(1)–C(2)–O(3)	125.5(2)	125.8(5)	124.8(3)	124(2)
N(1)–C(2)–O(4)	112.1(2)	109.6(4)	111.5(3)	112(2)
O(3)–C(2)–O(4)	122.4(2)	124.6(4)	123.6(3)	124(2)
C(2)–O(4)–C(5)	113.0(2)	115.8(4)	118.2(3)	112(2)
O(4)–C(5)–C(6)	104.0(2)	108.4(4)	110.2(3)	101(2)
C(5)–C(6)–N(7)	113.9(2)	116.7(4)	115.3(3)	114(2)
C(6)–N(7)–C(8)	107.1(2)	110.4(4)	111.8(3)	109(2)
C(6)–N(7)–C(9)	111.7(1)	111.8(4)	107.9(3)	113(2)
C(6)–N(7)–C(10)		107.6(4)	110.7(2)	110(2)
C(8)–N(7)–C(9)	108.1(1)	111.5(5)	108.2(3)	107(2)
C(8)–N(7)–C(10)		107.0(4)	109.9(3)	107(2)
C(9)–N(7)–C(10)	110.1(2)	108.3(5)	108.2(3)	110(2)

CARPCR

The picric acid molecule		The picrate ion	
C(11)–C(12)	1.406(5)	C(21)–C(22)	1.450(4)
C(12)–C(13)	1.378(5)	C(22)–C(23)	1.368(4)
C(13)–C(14)	1.377(6)	C(23)–C(24)	1.390(5)
C(14)–C(15)	1.364(5)	C(24)–C(25)	1.379(5)
C(15)–C(16)	1.379(5)	C(25)–C(26)	1.374(5)
C(16)–C(11)	1.401(5)	C(26)–C(21)	1.449(4)
C(11)–O(11)	1.321(4)	C(21)–O(21)	1.237(4)
C(12)–N(12)	1.468(5)	C(22)–N(22)	1.463(4)
N(12)–O(121)	1.237(4)	N(22)–O(221)	1.214(4)
N(12)–O(122)	1.205(4)	N(22)–O(222)	1.225(4)
C(14)–N(14)	1.481(5)	C(24)–N(24)	1.443(5)
N(14)–O(141)	1.228(5)	N(24)–O(241)	1.240(4)
N(14)–O(142)	1.222(6)	N(24)–O(242)	1.214(5)
C(16)–N(16)	1.471(5)	C(26)–N(26)	1.444(4)
N(16)–O(161)	1.210(5)	N(26)–O(261)	1.195(4)
N(16)–O(162)	1.200(5)	N(26)–O(262)	1.244(4)
C(11)–C(12)–C(13)	123.2(3)	C(21)–C(22)–C(23)	125.0(3)
C(12)–C(13)–C(14)	117.6(3)	C(22)–C(23)–C(24)	118.7(3)
C(13)–C(14)–C(15)	122.5(3)	C(23)–C(24)–C(25)	121.3(3)
C(14)–C(15)–C(16)	118.7(4)	C(24)–C(25)–C(26)	119.1(3)
C(15)–C(16)–C(11)	122.4(3)	C(25)–C(26)–C(21)	124.5(3)
C(16)–C(11)–C(12)	115.6(3)	C(26)–C(21)–C(22)	111.2(2)
O(11)–C(11)–C(16)	119.1(3)	O(21)–C(21)–C(26)	124.1(2)
O(11)–C(11)–C(12)	125.3(3)	O(21)–C(21)–C(22)	124.5(3)
N(12)–C(12)–C(11)	120.0(3)	N(22)–C(22)–C(21)	117.7(2)
N(12)–C(12)–C(13)	116.9(3)	N(22)–C(22)–C(23)	117.3(3)
O(121)–N(12)–C(12)	118.4(3)	O(221)–N(22)–C(22)	118.3(3)
O(122)–N(12)–C(12)	118.5(3)	O(222)–N(22)–C(22)	117.3(3)
O(121)–N(12)–O(122)	123.1(3)	O(221)–N(22)–O(222)	124.4(3)
N(14)–C(14)–C(13)	118.2(3)	N(24)–C(24)–C(23)	119.4(3)

Table 4. Continued.

N(14)–C(14)–C(15)	119.2(4)	N(24)–C(24)–C(25)	119.3(3)
O(141)–N(14)–C(14)	118.0(3)	O(241)–N(24)–C(24)	117.5(3)
O(142)–N(14)–C(14)	116.6(3)	O(242)–N(24)–C(24)	119.1(3)
O(141)–N(14)–O(142)	125.4(3)	O(241)–N(24)–O(242)	123.3(3)
N(16)–C(16)–C(15)	116.2(3)	N(26)–C(26)–C(25)	117.5(3)
N(16)–C(16)–C(11)	121.4(3)	N(26)–C(26)–C(21)	118.0(3)
O(161)–N(16)–C(16)	117.0(3)	O(261)–N(26)–C(26)	119.6(3)
O(162)–N(16)–C(16)	119.0(3)	O(262)–N(26)–C(26)	119.0(3)
O(161)–N(16)–O(162)	124.0(3)	O(261)–N(26)–O(262)	121.3(3)

Table 5. Distances and angles for possible hydrogen bonds (with estimated standard deviations referring to the last significant figure in parentheses).

	Donor	Acceptor	D···A	H···A	D-H···A Angle
CARCHL	N(1)–H(11)	$Cl^-_{(x,y,z)}$	3.367(2) Å	2.53(4) Å	176(4)°
	N(1)–H(12)	$Cl^-_{(x+\frac{1}{2},\frac{1}{2}-y,z)}$	3.385(3)	2.52(4)	162(3)
CARIOD	N(1)–H(11)	$O(3)_{(2-x,-y,1-z)}$	2.940(5)	1.79(7)	160(5)
	N(1)–H(12)	$I^-_{(1-x,-y,1-z)}$	3.669(5)	2.91(8)	144(6)
CARPCR	N(1)–H(11)	$O(21)_{(x-1,y,z)}$	2.829(4)	2.00(4)	163(4)
	N(1)–H(12)	$O(3)_{(-x,-y,1-z)}$	3.048(4)	2.11(4)	174(3)
	O(11)–H(111)	$O(121)_{(x,y,z)}$	2.578(4)	1.69(5)	145(4)
	O(11)–H(111)	$O(3)_{(x,1+y,z)}$	2.829(4)	2.28(5)	113(3)

within the plane. The nitrogen-chlorine distances are 3.367(2) Å and 3.385(3) Å for the two contacts. The geometry of the possible hydrogen bonds in all three crystals are given in Table 5. The carbonyl oxygen atom O(3) is involved in three close contacts to methyl-carbon atoms: one within the layer $O(3)\cdots C(8)_{(x-\frac{1}{2},1\frac{1}{2}-y,z)}$, 3.064(3) Å, and two to adjacent layers $O(3)\cdots C(9)_{(1\frac{1}{2}-x,y-\frac{1}{2},z-\frac{1}{2})}$ and $O(3)\cdots C(9)_{(1\frac{1}{2}-x,y-\frac{1}{2},z+\frac{1}{2})}$, 3.032(2) Å. A number of weak contacts between the chloride ion and methyl- and methylene-carbon atoms within the layer and in the adjacent layers are found, *cf.* Fig. 1.

CARIOD. The crystal packing is illustrated in Fig. 2 and in Fig. 3, in which the atomic numbering and some *inter*molecular contacts are also given. The iodide ions form puckered layers close to (100), and between these layers columns of carbamoylchline ions, related by the screw-axes, are situated. There are no close contacts between the carbamoylcholine ions within

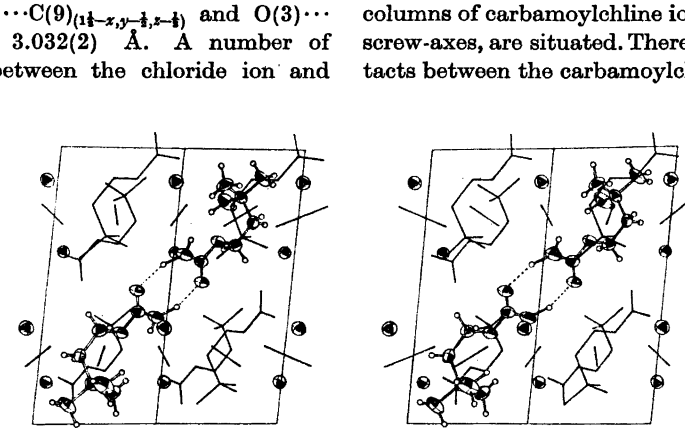

Fig. 2. CARIOD. Stereo drawing showing the packing. The *a*-axis is→, the *c*-axis is↙, and the $-b$-axis is pointing into the paper. The N–H···O hydrogen bonds are drawn with broken lines.

Table 6. Least squares planes and angles between them. The equations of the planes are in direct (unit cell) space. Distances (Å) to atoms defining the plane are asterisked.

Planes of parts of the molecule of picric acid (I) and the picrate ion (II)		Interplanar angles	
I	$-4.5975x-2.4453y+6.8828z+0.8469=0$		
I2	$-5.1159x-3.2127y+6.7506z+1.5206=0$	I–I2	4.3°
I4	$7.3710x+2.6615y-6.2410z-1.9056=0$	I–I4	11.4°
I6	$6.7592x-3.7225y-5.9515z+2.5851=0$	I–I6	27.1°
II	$-3.6191x-2.0992y+7.0122z+1.9399=0$		
II2	$-3.0300x+7.3597y+5.4908z-1.9155=0$	II–II2	41.2°
II4	$-4.4285x-2.0201y+6.9219z+2.5009=0$	II–II4	3.7°
II6	$7.7972x-2.9018y-5.7994z-3.3885=0$	II–II6	29.4°

Atom	I	I2	I4	I6
C(11)	0.017*			
C(12)	−0.001*	−0.000*		
C(13)	−0.014*			
C(14)	0.014*		0.001*	
C(15)	0.004*			
C(16)	−0.019*			0.005*
O(11)	0.078			
H(111)	0.14			
N(12)	−0.031	0.001*		
O(121)	0.034	−0.000*		
O(122)	−0.122	0.000*		
N(14)	0.005		−0.004*	
O(141)	−0.267		0.001*	
O(142)	0.261		0.001*	
N(16)	−0.093			−0.019*
O(161)	0.352			0.007*
O(162)	−0.641			0.007*
H(13)	0.01			
H(15)	−0.00			
	II	II2	II4	II6
C(21)	−0.025*			
C(22)	0.021*	0.003*		
C(23)	−0.005*			
C(24)	−0.008*		−0.002*	
C(25)	0.002*			
C(26)	0.014*			−0.004*
O(21)	−0.183			
N(22)	0.092	−0.012*		
O(221)	0.838	0.004*		
O(222)	−0.579	0.004*		
N(24)	−0.040		0.008*	
O(241)	−0.003		−0.003*	
O(242)	−0.130		−0.003*	
N(26)	0.057			0.015*
O(261)	−0.409			−0.005*
O(262)	0.631			−0.005*
H(23)	0.00			
H(25)	−0.00			

Planes through the four atoms N(1), C(2), O(3), and O(4) of the carbamoylcholine ions

CARCHL	$z-1.7023=0$
CARIOD	$3.6263x+8.9432y+4.2881z-5.4987=0$
CARPCR	$-0.9065x+7.7483y+5.3827z-2.6360=0$

Table 6. Continued.

Atom	CARBAC	CARIOD	CARPCR
N(1)	0.0*	−0.002*	−0.004*
C(2)	0.0*	0.007*	0.012*
O(3)	0.0*	−0.003*	−0.004*
O(4)	0.0*	−0.002*	−0.005*
C(5)	0.0*	0.067	0.195

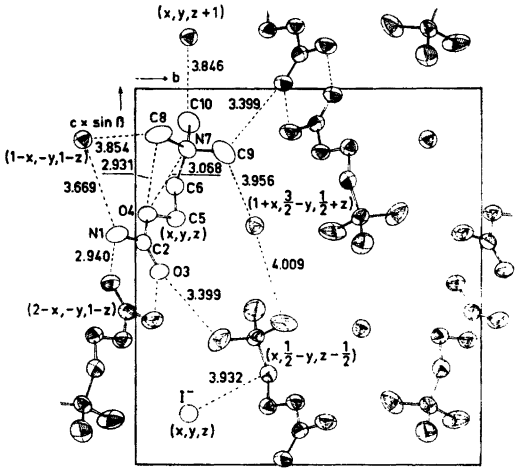

Fig. 3. CARIOD. Projection along the *a*-axis giving the numbering system of the non-hydrogen atoms together with some non-bonded distances. The ellipsoids are drawn at the 50 % probability level.

a column. Hydrogen bonds N(1)−H(11)···O(3) link carbamoylcholine ions related by a center of symmetry together in pairs. The distance $N(1)\cdots O(3)_{(2-x,-y,1-z)}$ is 2.940(5) Å. One more contact, $N(1)\cdots I^-_{(1-x,-y,1-z)}$, may be described as a hydrogen bond. The distance N(1)···I⁻ is 3.699(5) Å. A number of rather weak contacts between the iodide ion and methyl carbon atoms of adjacent carbamoylcholine ions are found, *cf.* Fig. 3. The packing in the CARIOD structure is at first glance remarkably similar to the packing in the crystal structures of succinylcholine perchlorate[10] and of (2-carbamoyloxyethyl)-*N*,*N*-dimethyl ethylammonium bromide.[9] This similarity is illustrated in Fig. 4. The space group of all three structures is $P2_1/c$. Only two of the structures are, however, isostructural, as the direction of the *b*- and *c*-axes are interchanged in the CARIOD structure compared to the directions of these axes in the two other structures.

CARPCR. The crystal packing is illustrated in Fig. 5 and in Fig. 6, in which the atomic numbering and some *inter*molecular contacts

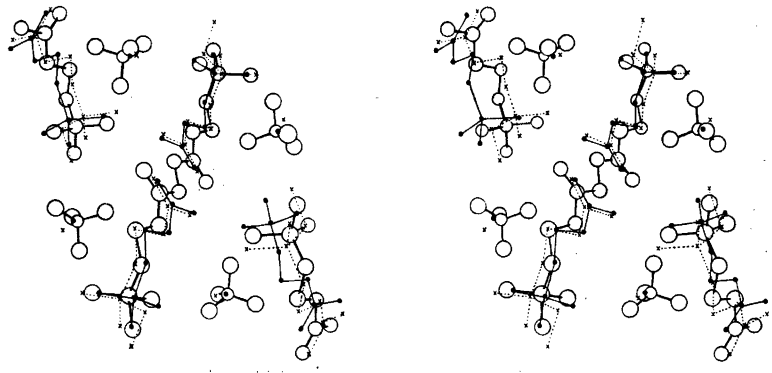

Fig. 4. Stereo drawing showing the structures of CARIOD, (●) succinylcholine perchlorate,[10] (O) and (2-carbamoyloxyethyl)-*N*,*N*-dimethylethylammonium bromide,[9] (×). The centers of symmetry in the middle of the drawing occupy a common point. All structures are viewed along the *a**-axis. For CARIOD the *b*-axis is →, and the *c*-axis is ↑. These directions are interchanged for the other two structures.

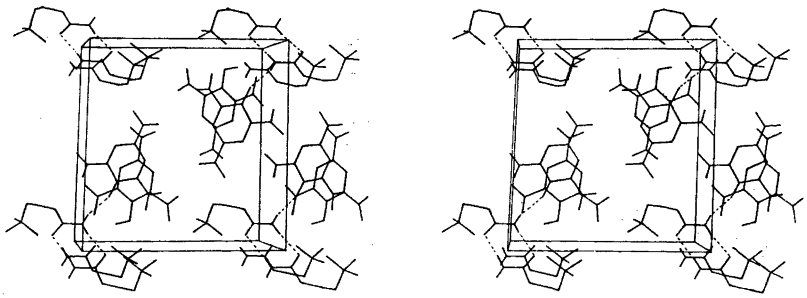

Fig. 5. CARPCR. Stereo drawing showing the packing. The *a*-axis is→, the *b*-axis is ↓, and the *c*-axis is pointing into the paper. Hydrogen bonds are indicated with broken lines. H(11) and H(12), the two hydrogen atoms attached to the amide nitrogen atom N(1) are drawn and so is H(111), the hydroxyl hydrogen atom of the molecule of picric acid. All other hydrogen atoms have been omitted.

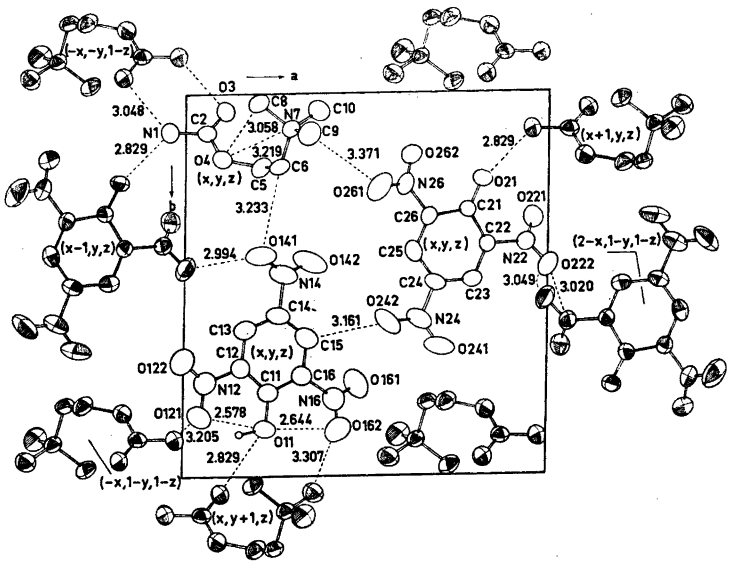

Fig. 6. CARPCR. Projection along the *c**-axis giving the numbering system of the non-hydrogen atoms together with some non-bonded distances. The ellipsoids are drawn at the 50 % probability level.

are also given. Carbamoylcholine ions related by a center of symmetry are linked together in pairs by weak hydrogen bonds N(1)−H(12)···O(3). The distance N(1)···O(3)$_{(-x,-y,1-z)}$ is 3.048(4) Å. The shortest distance between a carbamoylcholine ion and the one on top of it in the *c*-direction is O(3)···C(9)$_{(x,y,z+1)}$, 3.414(5) Å. A number of contacts between the carbamoylcholine ions and adjacent picrate ions and picric acid molecules are found. The distance between N(1) and the phenoxide oxygen atom O(21)$_{(x-1,y,z)}$ is 2.829(4) Å, and the position of H(11) is in agreement with the existence of a hydrogen bond N(1)−H(11)···O(21), *cf.* Table 5. The distance O(3)···O(11)$_{(x,y-1,z)}$ is also 2.829(4) Å, but here the dimensions given in Table 5 do not indicate the existence of a hydrogen bond O(11)−H(111)···O(3).[11]

The picrate ions are stacked alternating with

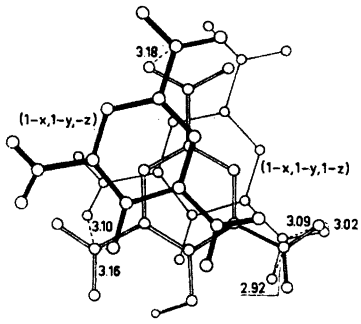

Fig. 7. One molecule of picric acid (O=O) together with the two neighbouring picrate ions. The stack is viewed perpendicular to the plane of the ring of the molecule of picric acid.

molecules of picric acid to form columns in the c-direction. The angle between ring plane I of the picric acid molecule and ring plane II of the picrate ion is 5.0°, while the angles between [001] and planes I and II are 23.6° and 18.7°, respectively. The overlap within a column is illustrated in Fig. 7. The *inter*planar spacing in the regions of overlap is approximately equal to 3.4 Å. A number of closer contacts between the atoms of the nitro groups of a picric acid molecule and of the adjacent picrate ions are pointed out in Fig. 7.

The picrate anion and the molecule of picric acid

The dimensions of the benzene ring of the picric acid molecule show some deviations from the dimensions of an unsubstituted benzene ring, *cf.* Table 4. The two bonds C(11)–C(12) and C(11)–C(16) are slightly longer than the ideal aromatic carbon-carbon distance,[12] and significant deviations from 120° are found for the valency angles in the ring. The same pattern is found for the dimensions of the picrate ion, although the deviations from the dimensions of benzene are greater here, as could be expected. The benzene rings of the picric acid molecule as well as of the picrate ion are slightly non-planar. The greater deviations from planarity are found for the picrate ion, *cf.* Table 6. The N(12) nitro group of the picric acid molecule is tilted only 4.3° out of the plane of the benzene ring, and one of the oxygen atoms of this nitro group is acceptor in an *intra*molecular hydrogen bond O(11)–H(111)···O(121). The distance O(11)···O(121) is 2.578(4) Å. The angles between the planes of all the nitro groups and the pertinent benzene rings are listed in Table 6.

The carbamoylcholine ion

The bond lengths and angles found for the carbamoylcholine ions of the three structures are very similar, but significant differences for a few of the valency angles are observed, *cf.* Table 4. The dimensions found for the carbamoylcholine ion in the crystal structure of carbamoylcholine bromide [9] are given for comparison. The bonds and angles found for the carbamoylcholine ions are hardly significantly different from those found for the corresponding bond lengths and angles of the acetylcholine ions [13–15] and of the succinylcholine ions.[10,16] The different conformations of the three carbamoylcholine ions of the present paper are visualized in Fig. 8, and Table 7 lists the torsion angles. Pullman and Courière [17] have studied the conformation of the carbamoylcholine ion and have performed PCILO calculations *based on the dimensions of CARBRO*. These authors predicted a pronounced flexibility of the car-

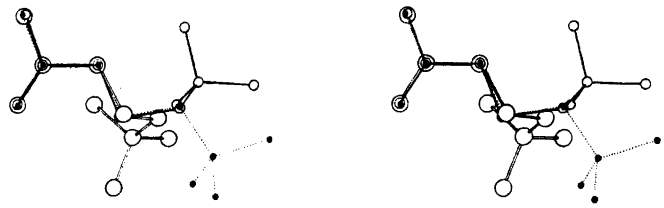

Fig. 8. A stereo view of the carbamoylcholine ions of CARCHL(●), CARIOD (o), and CARPCR (O). The ions are viewed perpendicular to the plane of the carbamoyl group, and C(2)–O(4) is defined to be common for the three ions.

Table 7. Selected torsion angles of the carbamoylcholine ions as found in the three crystal structures of the present paper and in the crystal structure of carbamoylcholine bromide.[9]

	CARCHL	CARIOD	CARPCR	CARBRO
N(1)–C(2)–O(4)–C(5)	180°	±177°	±171°	±177°[a]
C(2)–O(4)–C(5)–C(6)	180°	±175°	±131°	±173°
O(4)–C(5)–C(6)–N(7)	180°	±70°	±84°	±178°

[a] Calculated from the published [9] coordinates.

bamoylcholine ion. The conformations of the ions found in the four crystal structures of different carbamoylcholine salts are some of the many which could be expected from the theoretical energy map. The calculated energy barrier between the *gauche* and *trans* conformations of the carbamoylcholine ion was only 1 kcal/mol.[17] Thus weak interactions from the environments may cause a change from one conformation to another. It is a common feature in the crystal structures of the carbamoylcholine salts, and in salts of related compounds derived from carbamoylcholine by replacing one or more methyl groups by other substituents,[9] that although both of the two possible N–H···A hydrogen bonds are always found, these are generally of lengths indicating rather weak contacts. In accordance with the strong delocalisation of the positive charge of choline derivatives [18] no other single dominating contacts between the carbamoylcholine ion and the environments are seen in any of the structures, while a number of weaker contacts are always found.

REFERENCES

1. Germain, G., Main, P. and Woolfson, M. M. *Acta Crystallogr. A 27* (1971) 368.
2. Cromer, D. and Mann, J. *Acta Crystallogr. A 24* (1968) 321.
3. *International Tables for X-Ray Crystallography*, Kynoch Press, Birmingham 1962, Vol. III.
4. Sørensen, A. M. *INDIFF, An Algol Nonius Three-circle Diffractometer Input Data Program*, Chemical Laboratory C, The Royal Danish School of Pharmacy, DK-2100 Copenhagen 1968.
5. Ahmed, F. R. *N. R. C. Crystallographic Program System*, National Research Council Ottawa, Canada 1968.
6. Stewart, J. M., Kruger, G. J., Amman, H. L., Dickinson, C. and Hall, S. R. *X-Ray 72* Crystal Structure Calculation System, Computer Science Center, University of Maryland, June 1972.
7. Johnson, C. K. *ORTEP, A Fortran Thermal Ellipsoid Plot Program for Crystal Structure Illustrations*, Oak Ridge National Laboratory, Oak Ridge 1965.
8. Mallard, D. J. H., Vaughan, D. P. and Hamor, T. A. *Acta Crystallogr. B 30* (1974) 2825.
9. Barrans, Y. *Thèse*, L'Université de Bordeaux 1971.
10. Jensen, B. *Acta Chem. Scand. 25* (1971) 3388.
11. Kvick, Å. *Acta Universitatis Upsaliensis 322* (1974) 43.
12. Sutton, L. E. *Tables of Interatomic Distances and Configurations in Molecules and Ions*, Supplement 1956–1959, The Chemical Society, London 1965.
13. Herdklotz, J. K. and Sass, R. L. *Biochem. Biophys. Res. Commun. 40* (1970) 583.
14. Jensen, B. *Acta Chem. Scand. B 29* (1975) 531.
15. Svinning, T. and Sørum, H. *Acta Crystallogr. B 31* (1975) 1581.
16. Jensen, B. *Acta Chem. Scand. B 29* (1975) 115.
17. Pullman, B. and Courière, P. *Mol. Pharmacol. 8* (1972) 612.
18. Pullman, B. and Courière, P. *Theor. Chim. Acta 31* (1973) 19.

Received February 26, 1975.