

Table 2. *Interatomic bond distances (Å) and bond angles (°)*

U—O(1)	1.761 (9)	O(1)—U—O(1 ⁱ)	177.0 (5)
U—O(1 ⁱ)	1.761 (9)	O(4)—U—O(3 ⁱⁱⁱ)	74.4 (3)
U—O(2)	2.438 (7)	O(3 ⁱⁱⁱ)—U—O(2)	72.3 (3)
U—O(2 ⁱ)	2.438 (7)	O(2)—U—O(2 ⁱ)	68.4 (4)
U—O(3 ⁱⁱ)	2.38 (1)	O(2 ⁱ)—U—O(3 ⁱⁱ)	72.3 (3)
U—O(3 ⁱⁱⁱ)	2.38 (1)	O(3 ⁱⁱ)—U—O(4)	74.4 (3)
U—O(4)	2.400 (9)	O(4)—U—O(1)	88.4 (3)
		O(4)—U—O(1 ⁱ)	88.4 (3)
Hydrogen bonds		O(3 ⁱⁱⁱ)—U—O(1)	87.4 (5)
O(4)—O(2 ^{iv})	2.70 (1)	O(3 ⁱⁱⁱ)—U—O(1 ⁱ)	91.8 (5)
O(4)—O(2 ^v)	2.70 (1)	O(3 ⁱⁱ)—U—O(1)	91.8 (5)
		O(3 ⁱⁱ)—U—O(1 ⁱ)	87.4 (5)
Formato group		O(2)—U—O(1)	97.9 (4)
C—O(2)	1.246 (13)	O(2)—U—O(1 ⁱ)	84.8 (4)
C—O(3)	1.242 (17)	O(2 ⁱ)—U—O(1)	84.8 (4)
		O(2 ⁱ)—U—O(1 ⁱ)	97.9 (4)
		O(2)—C—O(3)	125.4 (9)
		O(2 ^v)—O(4)—O(2 ^{iv})	119.5 (5)

Symmetry code

(i)	$-x,$	$-y,$	z	(iv)	$\frac{1}{2} + x,$	$y,$	$-\frac{1}{2} + z$
(ii)	$\frac{1}{4} - x,$	$-\frac{1}{4} + y,$	$-\frac{1}{4} + z$	(v)	$-\frac{1}{2} - x,$	$-y,$	$-\frac{1}{2} + z$
(iii)	$-\frac{1}{4} + x,$	$\frac{1}{4} - y,$	$-\frac{1}{4} + z$				

parison of the structures of these two compounds with those of other uranyl compounds, photosensitive or not, should enable us to find a clue to the phenomenon of photosensitivity in the solid state.

All the computations have been performed on an IBM 370-168 computer at Orsay (CIRCE), through the terminal of the Institut de Recherches sur la

Catalyse, Lyon, and with a program library at the Laboratoire de Chimie Analytique II.

BFM is grateful to Professor G. Thomas-David who introduced him to the Laboratoire de Chimie Analytique II, where this work has been successfully carried out.

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The Crystal and Molecular Structure of DL-Lactoylcholine Iodide

BY CYRUS CHOTHIA* AND PETER PAULING

William Ramsay, Ralph Forster and Christopher Ingold Laboratories, University College London, Gower Street, London WC12, England

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Crystals of DL-lactoylcholine iodide, $C_8H_{18}NO_3I$, are monoclinic, space group $P2_1/c$ (C_{2h}^2), $a = 9.891$ (6), $b = 12.286$ (8), $c = 10.150$ (5) Å, $\beta = 90.65$ (3)°, $Z = 4$. The values of the torsion angles $-N^+-C-C-O$ (85°) and $-C-C-O-C-$ (157°) are similar to those observed in other cholinergic agonists. The acidic end of the ester group, however, has an unusual conformation which is probably a result of the molecular packing involving hydrogen bonds to the terminal hydroxyl group.

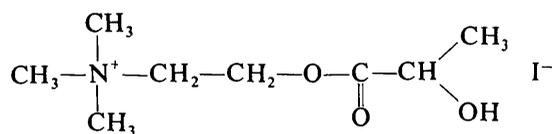
Introduction

Rama Sastry, Lasslo & Pfeiffer (1958, 1960) synthesized the enantiomers of lactoylcholine and

* To whom correspondence should be addressed at: Chemistry Department, University College London, 20 Gordon Street, London WC1.

measured their activities at cholinergic synapses. The nicotinic activities are similar to those of acetylcholine [reciprocal relative activities of $D(-):L(+):ACh$ are 0.69:3.45:1.00] but the muscarinic activities are slight [reciprocal relative activities of $D(-):L(+):ACh$ are 850:4700:1]. Here we describe the single-crystal

structure analysis of crystals of DL-lactoylcholine iodide.



Experimental results

Crystals of DL-lactoylcholine iodide provided by Dr B. V. Rama Sastry were used without further recrystallization. They were colourless hygroscopic plates. An optical examination showed that the extinction directions are parallel to the plate face but have no simple relation to the plate edges, suggesting that the crystals are monoclinic. Isogyres cross the interference figure as the crystal is rotated indicating that the crystals are biaxial.

Because most crystals were split or dendritic, a crystal suitable for the collection of X-ray intensity data was found by smashing a large crystal and examining the diffraction patterns of the fragments, which were coated in Formvar to protect them from moisture.

Crystal data

DL-Lactoylcholine iodide, $C_8H_{18}NO_3I$, $M_r = 303.15$, $a = 9.891(6)$, $b = 12.286(8)$, $c = 10.150(5)$ Å, $\beta = 90.65(3)^\circ$; $Z = 4$, $d_c = 1.63$ g cm $^{-3}$. Laue symmetry $2/m$; monoclinic; systematic absences in diffraction pattern: $0k0:k = 2n + 1$; $h0l:l = 2n + 1$. Space group $P2_1/c$.

Diffraction data were collected from a crystal of dimensions $0.15 \times 0.10 \times 0.08$ mm. Seven layers of data, $hk0-hk6$, were collected with the equi-inclination multiform-pack Weissenberg technique. Cu $K\alpha$ radiation was used from an X-ray tube run at 28 mA and 35 kV, with a Ni filter. The layers $h0l$ and $0kl$ were collected on a precession camera with Zr-filtered Mo $K\alpha$ radiation. The intensities were measured on a Joyce-Loebl flying-spot densitometer. Any reflexion that gave a consistent reading above its background was accepted as significant. The data were processed with a program which calculates interfilm scale factors by the method of Hamilton, Rollett & Sparks (1965); the averaged intensities were corrected for Lorentz and polarization factors. Approximate interlayer scale factors were calculated by comparison of the data from the $hk0-hk6$ layers with the $h0l$ and $0kl$ intensity data.

Structure analysis

A three-dimensional Patterson synthesis calculated with F_o as coefficients clearly showed peaks due to the

vectors between symmetry-related I atoms; the I atom position was determined as $x = 0.225$, $y = 0.050$, $z = 0.192$. A Fourier synthesis with F_o^2 as coefficients, and phases calculated from the position of the I atom

Table 1. DL-Lactoylcholine iodide: final atomic positions ($\times 10^4$) and temperature factors

	x	y	z	B (Å 2)
I	2741 (2)	501 (2)	1860 (2)	*
N(1)	1877 (22)	-786 (18)	2752 (23)	2.7
C(1)	3310 (33)	-628 (32)	2367 (34)	5.3
C(2)	1147 (38)	-1564 (33)	1850 (39)	6.2
C(3)	1767 (34)	-1359 (30)	4029 (37)	5.2
C(4)	1157 (26)	309 (24)	2858 (29)	3.0
C(5)	1092 (30)	968 (25)	1545 (32)	3.6
C(6)	2332 (34)	2491 (31)	716 (37)	4.9
C(7)	3770 (36)	2990 (29)	645 (37)	5.2
C(8)	4528 (34)	2573 (30)	-459 (34)	5.1
O(1)	2368 (21)	1563 (17)	1520 (21)	4.3
O(2)	1322 (26)	2754 (21)	87 (24)	6.0
O(3)	3612 (25)	4133 (21)	372 (25)	6.6

* Anisotropic temperature factors for iodine are:

b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
0.0102	0.0075	0.0104	0.0047	-0.0004	0.0023

Table 2. DL-Lactoylcholine iodide: intramolecular torsion angles ($^\circ$)

These values are for the L(+)*S* lactate enantiomer. For the D(-)*R* enantiomer the torsion angles are of the opposite sign.

C(1)[C(2),C(3)]-N-C(4)-C(5)	-61 (+66, +176)
N-C(4)-C(5)-O(1)	+85
C(4)-C(5)-O(1)-C(6)	+157
C(5)-O(1)-C(6)-C(7)[O(1)]	+173 (+1)
O(2)-C(6)-C(7)-C(8)	+88
O(2)-C(6)-C(7)-O(3)	-35

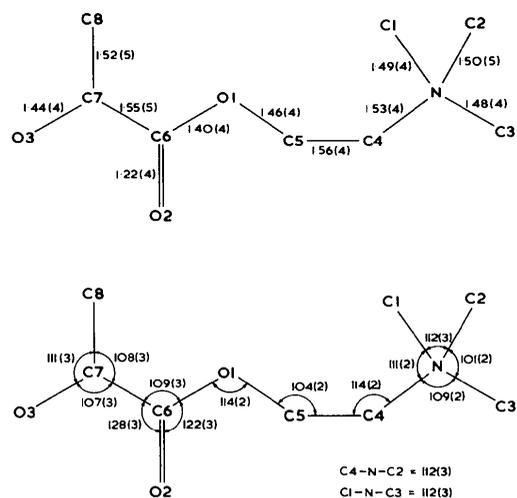


Fig. 1. Lactoylcholine: bond angles ($^\circ$) and lengths (Å).

clearly showed all the non-hydrogen atoms. This structure was refined by least-squares analysis. The scattering factors used were those of Cromer & Waber (1965) and the anomalous dispersion of I for Cu $K\alpha$ radiation was that of Cromer (1965). The program used in the refinement was written by Dr G. Shearing and his colleagues at the University of Manchester, and was adopted for use on the London Atlas Computer by Dr R. W. Baker. The program allows each structure factor the weight w given by the expression

$$w = (W_1 + W_2F_o + W_3F_o^2)/(W_4 + W_5F_o + W_6F_o^2),$$

where $W_1 \dots W_6$ are parameters provided by the user and F_o is $F(\text{observed})$. Initially unit weights were used. After a few cycles of least squares, a graph of $w(F_o - F_c)$ against F_o was calculated and weighting parameters were devised to give a constant value of $w(F_o - F_c)$ for all ranges of F_o . These parameters are: $W_1 = 7200$, $W_2 = 0$, $W_3 = 0$, $W_4 = 10\,500$, $W_5 = -114$, $W_6 = 1$. Refinement of positional parameters, with anisotropic thermal parameters for I and isotropic thermal parameters for the other atoms, resulted in a final conventional R of 0.072 for the 617 independent, observed diffraction maxima.* Interlayer scale factors were refined separately from the other parameters. The principal features of the final difference synthesis were ridges of electron density whose maximum value is equivalent to about one electron. The position of these ridges around the I atom suggests that they arise from the effects of series termination. Other features on the map were less than one electron. There were no significant sets of peaks that could be related to the presumed position of H atoms. The final positional and thermal parameters are given in Table 1. The bond lengths and angles are illustrated in Fig. 1 and the torsion angles of the observed conformation are listed in Table 2.

Discussion

The molecular structure

All the bond lengths are within one standard deviation of expected values and the bond angles within less than three (Fig. 1). The high values of the standard deviations, caused by the presence of the I atom, mean that the precise values of bond lengths and angles do not warrant further discussion.

The conformational parameters of the lactoylcholine molecule can be expressed in terms of the torsion angles $\tau\{C(3)C(1),C(2)-N^+-C(4)-C(5)\}$, $\tau[N^+-C(4)-C(5)-O(1)]$, $\tau[C(4)-C(5)-O(1)-C(6)]$ and

$\tau\{C(1)O(2)-C(6)-C(7)-O(3)C(8)\}$ (Fig. 1). The value of $\tau\{C(5)-O(1)-C(6)-O(2)C(7)\}$ is fixed at 0° (180°) by the partial double bond $O(1)-C(6)$. As is commonly observed in similar structures, steric hindrance between C(5) and the methyl groups on N forces the methyl group into the staggered position so that $\tau[C(3)-N-C(4)-C(5)]$ is antiplanar (Baker, Chothia, Pauling & Petcher, 1971).

In this structure, $\tau[N^+-C(4)-C(5)-O(1)]$ is 85° and the $C(1)-O(1)$ distance $2.97(4)$ Å. The synclinal value for this torsion angle is generally found in $N^+-C-C-O$ systems (Sundaralingam, 1968). A careful X-ray structure analysis of xylocholine bromide, 2,6-dimethylphenylcholine bromide (Coggon, McPhail & Roe, 1969), has shown that none of the hydrogens on C(1) are in a position to form hydrogen bonds with O(1) and therefore the stability of synclinal $N^+-C-C-O$ conformations is a result of electrostatic attraction between the positively charged quaternary group and the electronegative O atom. A similar conclusion was reached in the neutron diffraction study of erythro-acetyl- α,β -dimethylcholine (Brennan, Ross, Hamilton & Sheffer, 1970). The $\tau[C(4)-C(5)-O(1)-C(6)]$ and $\tau\{C(1)O(2)-C(6)-C(7)-O(3)C(8)\}$ torsion angles will be discussed together. In cholinergic compounds the observed value of the former angle varies between $+76$ and -148° . The value observed depends upon intramolecular steric strain, the substituents on C(4) or C(5), and crystal packing forces (Baker *et al.*, 1971). The value here for $\tau[O(2)-C(6)-C(7)-C(8)]$ (88°) is unusual. In esters of simple unsubstituted acids the C atom corresponding to C(8) is usually synplanar to O(2); $\tau[O(2)-C(6)-C(7)-C(8)]$ is $\sim 0^\circ$ (P. J. Pauling, to be published). An examination of the crystal structure, however, suggests that there is a hydrogen bond between the hydroxyl group [O(3)] and the iodide ion. Hydrogens were not found on the final difference Fourier map so the existence of an O-H-I hydrogen bond cannot be stated with certainty, but the short $O(3) \dots I$ distance [$3.39(3)$ Å], the $C(7)-O(3) \dots I$ angle (111°) which would allow a hydrogen on O(3) to be in a position to form a hydrogen bond, and the necessity for an intermolecular attraction to explain the unusual value of $\tau[O(2)-C(6)-C(7)-C(8)]$ suggest convincingly that the hydroxyl group [O(3)] is hydrogen bonded to the iodide ion. This hydrogen bond and the antiplanar value of $\tau[C(4)-C(5)-O(1)-C(6)]$ allow the formation of linear chains of molecules which facilitate crystal packing.

Molecular packing

The packing of DL-lactoylcholine in crystals of the iodide consists of chains of molecules running parallel to **b** (Fig. 2). Each chain consists of molecules related by b translations and linked by iodide ions. The iodide ion probably forms a hydrogen bond with OH [O(3)] of one molecule ($I \dots O$ is 3.39 Å) and an ionic link

* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32366 (4 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

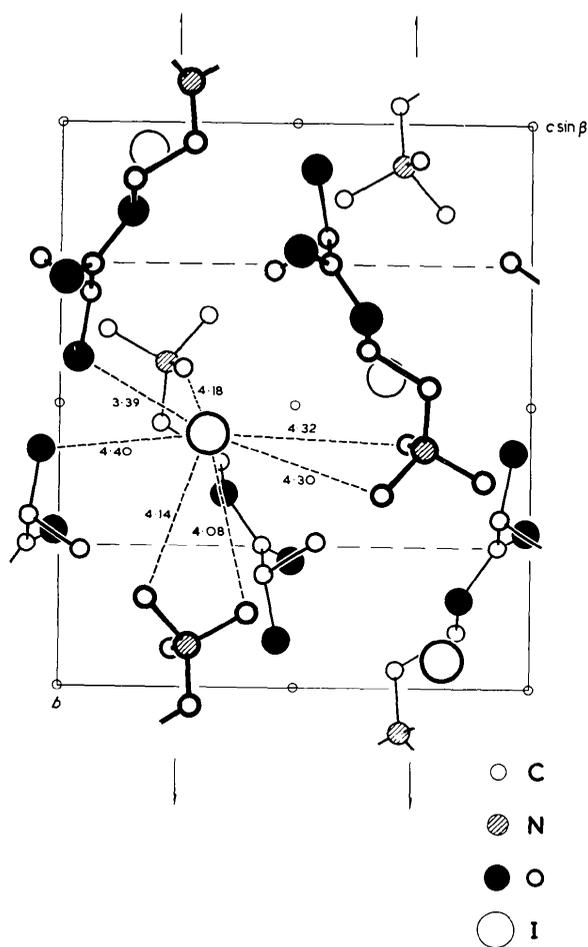


Fig. 2. Lactoylcholine iodide: a view of the unit cell in the *a* direction.

with C(2) (4.14 Å) and C(3) (4.08 Å) of the quaternary group in the next molecule in the chain (Fig. 2).

The iodide ions of one chain are associated with four molecules in adjacent chains. In the $\pm x$ directions, adjacent chains are related by the screw axis. This symmetry operator gives a C(1)–I distance of 4.18 Å in one direction and a contact C(5)–I of 3.85 Å (in the other direction). The association between the iodide ions and the two adjacent chains in the $\pm z$ directions is much weaker. These chains are related by the *c* glide plane. In one direction C(1) and C(2) are 4.32 Å and

Table 3. *Lactoylcholine iodide: intermolecular contacts (Å)*

		Symmetry and translation of second atom
C(1)–O(3)	3.56	$x, \frac{1}{2} - y, \frac{1}{2} + z$
C(3)–O(3)	3.55	$x, \frac{1}{2} - y, \frac{1}{2} + z$
C(4)–O(2)	3.29	$x, \frac{1}{2} - y, \frac{1}{2} + z$
C(4)–O(3)	3.57	$x, \frac{1}{2} - y, \frac{1}{2} + z$
C(1)–C(7)	3.89	$-x, \frac{1}{2} + y, \frac{1}{2} - z, +a, -b$
C(1)–C(8)	3.65	$x, \frac{1}{2} + y, \frac{1}{2} - z, +a, -b$
C(2)–C(3)	3.89	$x, \frac{1}{2} - y, \frac{1}{2} + z$
C(3)–O(2)	3.37	$-x, \frac{1}{2} + y, \frac{1}{2} - z, -b$
O(3)–O(3)	3.56	$-x, -y, -z, +a, +b$

4.30 Å from I, and in the other direction C(3) is 4.40 Å from I. In contrast to the weak ionic association between the iodide ions and the quaternary ammonium groups in the $\pm z$ direction, the lactoylcholine molecules have many van der Waals contacts (Table 3).

The biological implications of this structure are discussed elsewhere (Chothia & Pauling, 1968, 1969; Chothia, 1970).

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