

Fig. 1. Perspective view of the cation with the atom-numbering scheme. Selected intramolecular non-bonding distances are: C(1)⋯C(6) 4.38 (3), N(1)⋯C(6) 3.82 (2) and N(1)⋯C(8) 6.30 (2) Å.

A perspective view of the cation, with atom-numbering scheme and selected intramolecular non-bonding distances, is presented in Fig. 1.

The C(*sp*<sup>3</sup>)—C(*sp*<sup>3</sup>) bond lengths range from 1.47 (3) to 1.58 (3) Å and the four C—N<sup>+</sup> distances are in the range 1.48 (4)—1.51 (2) Å.

The most relevant aspect of the structure of the molecule is the orientation of the cyclopentane ring with respect to the ammonium tetrahedral N. Therefore the molecular structure of TMC2 is essentially a one-parameter problem: the N(1)—C(4)—C(5)—C(6) torsion angle. The other torsion angles have threefold symmetry,  $\tau = \pm 60$  or  $180^\circ$ .  $\tau[\text{N}(1)\text{—C}(4)\text{—C}(5)\text{—C}(6)]$  is  $-167^\circ$  in TMC2, indicating that the overall conformation adopted by this cation is very similar to that found in carbon aliphatic chains and is not that

which has been suggested to be necessary for muscarinic activity in acetylcholine and its analogues (Baker, Chothia, Pauling & Petcher, 1971).

The puckering amplitude  $Q$  is 0.52 (4) Å (Cremer & Pople, 1975). In addition there is a pseudo twofold axis through C(10) and C(6)—C(7) (see Fig. 2).<sup>\*</sup> The asymmetry parameter of Duax, Weeks & Rohrer (1976),  $\Delta C_2[\text{C}(10)] = 2 (2)^\circ$ , indicates that the conformation of the ring is 'half-chair'.

The environment of the I<sup>-</sup> ions (Fig. 3)<sup>\*</sup> is approximately tetrahedral with I<sup>-</sup>⋯N<sup>+</sup> distances ranging from 4.4 to 4.7 Å, with the other packing distances as expected from van der Waals radii.

<sup>\*</sup> See previous footnote.

#### References

- BAKER, R. W., CHOTHIA, C. H., PAULING, P. J. & PETCHER, T. J. (1971). *Nature (London)*, **230**, 439–445.  
 CREMER, D. & POPLE, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1367.  
 DUAX, W. L., WEEKS, C. M. & ROHRER, D. C. (1976). *Top. Stereochem.* **9**, 284–286.  
*International Tables for X-ray Crystallography* (1974). Vol. IV, pp. 71–103. Birmingham: Kynoch Press.  
 SHELDRICK, G. M. (1976). *SHELX76*. Program for crystal structure determination. Univ. of Cambridge, England.

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## Structure of [2-(Ethylideneaminoxy)ethyl]trimethylammonium Iodide, C<sub>7</sub>H<sub>17</sub>N<sub>2</sub>O<sup>+</sup>·I<sup>-</sup>

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**Abstract.**  $M_r = 272.1$ , monoclinic,  $P2_1/c$ ,  $a = 8.188 (4)$ ,  $b = 13.748 (5)$ ,  $c = 10.174 (5)$  Å,  $\beta = 98.1 (1)^\circ$ ,  $Z = 4$ ,  $U = 1133.8 (9)$  Å<sup>3</sup>,  $D_m = 1.59$ ,  $D_x = 1.594$  Mg m<sup>-3</sup>,  $\lambda(\text{Mo } K\alpha) = 0.7107$  Å,  $\mu = 2.85$  mm<sup>-1</sup>,  $F(000) = 536$ ,  $T = 298$  K. Final  $R = 0.047$  for 1420 observed reflections. The conformation of the molecule, described by the torsion angles about the non-rigid bonds, is very similar to that found in many muscarinic agents.

**Introduction.** As a part of our investigation of the crystal structures of molecules affecting cholinergic

transmission systems we have completed the single-crystal X-ray analysis of the structure of the title compound (TMON hereinafter). This compound possesses a very interesting pharmacological activity (Groppetti, Zappia, Pirola & Rossi, 1966) and has been considered in an extensive structure–activity analysis by Pratesi (Pratesi, Villa, Ferri, De Micheli, De Amici, Grana, Santagostino Barbone, Silipo & Vittoria, 1983).

**Experimental.** Single crystals obtained by slow evaporation of a solution in absolute ethanol, under reduced constant pressure in a dry atmosphere,  $D_m$  measured by flotation; approximate unit-cell parameters estimated from preliminary Weissenberg

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and precession photographs, crystal  $\sim 0.1 \times 0.2 \times 0.5$  mm, Philips PW 1100 four-circle diffractometer, graphite monochromator; accurate unit-cell parameters and crystal-orientation matrices (together with their estimated standard errors) obtained from least-squares refinement of the  $2\theta$ ,  $\omega$ ,  $\chi$  and  $\varphi$  values of 20 carefully centered high-angle reflections,  $\theta$ - $2\theta$  scan, scan speed  $0.03^\circ \text{ s}^{-1}$ ,  $2\theta$  range  $4$ - $50^\circ$ ; two standard reflections ( $\bar{1} 3 2, 2 1 1$ ) every 180 min; 1989 data measured, 1420 with  $I \geq 3\sigma(I)$ ; Lorentz and polarization corrections, intensities placed on an absolute scale by Wilson's method, experimental absorption correction applied (North, Phillips & Mathews, 1968); maximum and minimum transmission factors 1.5 and 0.3 respectively; trial structure obtained by heavy-atom method, refined by full-matrix least squares,  $\sum w(|F_o| - |F_c|)^2$  minimized,  $w = 1.336[\sigma^2(F_o) + 0.002 F_o^2]^{-1}$ ; adequacy of weighting scheme confirmed by an analysis of the variation of the mean  $w(|F_o| - |F_c|)^2$  with  $|F_o|$  and  $\lambda^{-1} \sin\theta$ ; scattering factors from *International Tables for X-ray Crystallography* (1974), both real and imaginary components of anomalous dispersion included for I only (*International Tables for X-ray Crystallography*, 1974); refinement carried out allowing all non-H atoms to vibrate anisotropically; although most H atoms could be located from a difference Fourier map, all included in their calculated idealized positions ( $\text{C-H} = 1.0 \text{ \AA}$ ) as a fixed contribution; final conventional  $R = 0.047$ ,  $R_w = 0.054$  for 1420 observed reflections; calculations carried out on the CYBER 76 computer of CINECA with *SHELX76* (Sheldrick, 1976).

**Discussion.** A perspective view of the cation with the atom-numbering scheme is presented in Fig. 1. The final positional parameters are given in Table 1;\* interatomic distances and interbond angles with e.s.d.'s calculated from the full variance-covariance matrix are in Table 2.

The most important parameters of the structure are the  $\text{C}(3)\text{--N}(1)\text{--C}(4)\text{--C}(5) = -173.9$  (8),  $\text{N}(1)\text{--C}(4)\text{--C}(5)\text{--O}(1) = 77.1$  (9),  $\text{C}(4)\text{--C}(5)\text{--O}(1)\text{--N}(2) = 92.5$  (9),  $\text{C}(5)\text{--O}(1)\text{--N}(2)\text{--C}(6) = -164.9$  (9) and  $\text{O}(1)\text{--N}(2)\text{--C}(6)\text{--C}(7) = 3$  (2) $^\circ$  torsion angles.

\* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38416 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

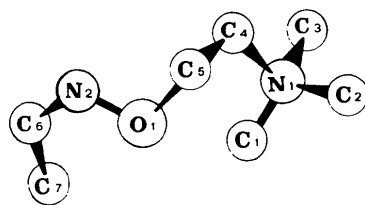


Fig. 1. Perspective view of the cation with the atom-numbering scheme.

Table 1. Final atomic coordinates ( $\times 10^4$ ) and equivalent isotropic thermal parameters ( $\text{\AA}^2 \times 10^3$ ) with e.s.d.'s in parentheses

$$U_{eq} = \frac{1}{3} \sum_i \sum_j U_{ij} a_i^* a_j^* a_i a_j$$

	x	y	z	$U_{eq}$
I(1)	1857 (1)	764 (1)	2503 (1)	64 (1)
N(1)	3055 (7)	4256 (4)	1956 (7)	52 (3)
N(2)	6348 (11)	3327 (8)	5230 (9)	123 (6)
O(1)	5367 (8)	3016 (5)	4145 (6)	93 (4)
C(1)	4443 (10)	3753 (7)	1420 (8)	64 (6)
C(2)	1492 (10)	3730 (7)	1481 (9)	66 (5)
C(3)	2916 (12)	5280 (7)	1456 (10)	76 (5)
C(4)	3366 (11)	4301 (7)	3469 (9)	66 (5)
C(5)	3716 (10)	3359 (8)	4171 (8)	74 (5)
C(6)	7834 (14)	3233 (11)	5095 (14)	128 (8)
C(7)	8591 (15)	2901 (9)	4004 (13)	116 (8)

Table 2. Bond distances ( $\text{\AA}$ ) and angles ( $^\circ$ ) with e.s.d.'s in parentheses

N(1)–C(1)	1.497 (11)	C(5)–O(1)	1.435 (11)
N(1)–C(2)	1.490 (10)	O(1)–N(2)	1.340 (11)
N(1)–C(3)	1.496 (11)	N(2)–C(6)	1.250 (15)
N(1)–C(4)	1.526 (11)	C(6)–C(7)	1.421 (20)
C(4)–C(5)	1.487 (14)		
C(1)–N(1)–C(2)	108.6 (6)	N(1)–C(4)–C(5)	116.3 (7)
C(1)–N(1)–C(3)	109.6 (7)	C(4)–C(5)–O(1)	113.3 (7)
C(2)–N(1)–C(3)	109.0 (7)	C(5)–O(1)–N(2)	109.7 (7)
C(1)–N(1)–C(4)	111.0 (6)	O(1)–N(2)–C(6)	110.9 (10)
C(2)–N(1)–C(4)	111.1 (6)	N(2)–C(6)–C(7)	131.1 (12)
C(3)–N(1)–C(4)	107.4 (6)		

The group of atoms C(3)–N(1)–C(4)–C(5) forms an approximately antiperiplanar extended chain with a torsion angle very similar to that expected from a consideration of van der Waals forces and steric-hindrance effects (Chothia & Pauling, 1970). The group N(1)–C(4)–C(5)–O(1) adopts the *synclinal* conformation, a factor which is commonly observed in acetylcholine-like molecules (Baker, Chothia, Pauling & Petcher, 1971). It has been suggested (Sundaralingam, 1968) that this conformation is a result of electrostatic attraction between the positively charged quaternary group and the electronegative O atom. The C(1)···O(1) and N(1)···O(1) distances of 2.95 (1) and 3.20 (1)  $\text{\AA}$  in TMON agree with these contentions. The most relevant difference between TMON and other cholinergic agonists involves the value of  $\tau[\text{C}(4)\text{--C}(5)\text{--O}(1)\text{--N}(2)]$  which is not in the range of  $140$ – $180^\circ$  observed for many agonists. Nevertheless, values close to  $90^\circ$  are observed in acetylcholine bromide and in the crystals of some weakly active or inactive muscarinic agonists (Baker *et al.*, 1971). In addition, for many muscarinic agonists the energy barriers and the energy differences between different conformers are low (Pullman & Port, 1973). The conclusions are summarized in Table 3, which lists three torsion angles of the conformation of acetylcholine-like molecules calculated by conformational analyses (Liquori, Damiani & De Coen, 1968; Kier, 1967), as concluded from the NMR study (Culvenor & Ham, 1966) and observed in acetylcholine bromide

Table 3. *Theoretical and observed torsion angles ( $^{\circ}$ ) of acetylcholine-like molecules*

	Reference	O(2)—C(6)—O(1)—C(5)	C(6)—O(1)—C(5)—C(4)	O(1)—C(5)—C(4)—N
Acetylcholine bromide	(a)	4.10	78.90	78.44
Lactoylcholine iodide	(b)	1	157	85
L-(+)-Muscarine iodide	(c)	—	144	73
NMR	(d)	$\sim 0$	$\sim 180$	$\sim 60$
van der Waals TTGT	(e)	0	178	74
van der Waals TGGT	(e)	0	75	72
Molecular orbital	(f)	$\sim 0$	$\sim 180$	$\sim 80$

References: (a) Svinning & Sörum (1975); (b) Chothia & Pauling (1977); (c) Jellinek (1957); (d) Culvenor & Ham (1966); (e) Liquori *et al.* (1968); (f) Kier (1967).

(Svinning & Sörum, 1975), lactoylcholine iodide (Chothia & Pauling, 1977) and muscarine iodide (Jellinek, 1957). The torsion angle  $\tau[\text{C}(6)\text{—O}(1)\text{—C}(5)\text{—C}(4)]$  can be either  $\pm 60^{\circ}$  or about  $180^{\circ}$ . Both have been observed crystallographically and both are stable according to the van der Waals energy analysis. The  $180^{\circ}$  value has been concluded from the NMR study and from the molecular-orbital-energy analysis and correlates well with the structure of L-(+)-muscarine. Liquori *et al.* (1968) found the energy difference between the two conformations to be  $1.3 \text{ kJ mol}^{-1}$  with the  $180^{\circ}$  value slightly more stable. Chothia & Pauling (1968) estimated from Liquori's results and others that the energy barrier between the two forms is about  $13 \text{ kJ mol}^{-1}$ . These two forms are those which allow a maximum interaction between an H atom on C(1) and either of the two tetrahedral electron pairs of the ether O atom.

Finally in TMON, while the value of  $\tau[\text{C}(5)\text{—O}(1)\text{—N}(2)\text{—C}(6)]$  is very close to the angle expected on the basis of steric hindrance and van der Waals interactions, the value of  $\tau[\text{O}(1)\text{—N}(2)\text{—C}(6)\text{—C}(7)]$  is unusual because the *trans* configuration would be more

stable. Nevertheless, in this way the terminal methyl C(7) atom is allowed to be at a distance of  $5.07 (1) \text{ \AA}$  from the ammonium tetrahedral N(1).  $\text{N}^+\cdots\text{methyl}$  distances in the range  $5\text{--}6 \text{ \AA}$  are typical of acetylcholine-like molecules (Baker *et al.*, 1971).

The crystal packing, as viewed down **b**, is depicted in Fig. 2 and it is mainly determined by Coulombic and van der Waals forces. The intermolecular non-bonding distances are as expected for standard van der Waals values. The environment of the  $\text{I}^-$  ions is approximately tetrahedral with  $\text{I}^-\cdots\text{N}^+$  distances ranging from  $4.50$  to  $4.95 \text{ \AA}$ .

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#### References

- BAKER, R. W., CHOTHIA, C. H., PAULING, P. J. & PETCHER, T. J. (1971). *Nature (London)*, **230**, 430–445.
- CHOTHIA, C. H. & PAULING, P. J. (1968). *Nature (London)*, **219**, 1156–1157.
- CHOTHIA, C. H. & PAULING, P. J. (1970). *Proc. Natl Acad. Sci. USA*, **65**, 477–482.
- CHOTHIA, C. H. & PAULING, P. J. (1977). *Acta Cryst.* **B33**, 1851–1854.
- CULVENOR, C. C. J. & HAM, N. S. (1966). *Chem. Commun.* pp. 537–539.
- GROPETTI, A., ZAPPÀ, M. L., PIROLA, O. & ROSSI, S. (1966). *Farmaco Ed. Sci.* **21**, 51.
- International Tables for X-ray Crystallography* (1974). Vol. IV, pp. 71–103. Birmingham: Kynoch Press.
- JELLINEK, F. (1957). *Acta Cryst.* **10**, 277–280.
- KIER, L. B. (1967). *Mol. Pharmacol.* **3**, 487–489.
- LIQUORI, A. M., DAMIANI, A. & DE COEN, J. L. (1968). *J. Mol. Biol.* **33**, 439–445.
- NORTH, A. C. T., PHILLIPS, D. C. & MATHEWS, F. S. (1968). *Acta Cryst.* **A24**, 351–359.
- PRATESI, P., VILLA, L., FERRI, V., DE MICHELI, C., DE AMICI, M., GRANA, E., SANTAGOSTINO BARBONE, M. G., SILIPO, C. & VITTORIA, A. (1983). In preparation.
- PULLMAN, A. & PORT, G. N. J. (1973). *Theor. Chim. Acta*, **32**, 77–79.
- SHELDRIK, G. M. (1976). *SHELX76*. Program for crystal structure determination. Univ. of Cambridge, England.
- SUNDARALINGAM, M. (1968). *Nature (London)*, **217**, 35–37.
- SVINNING, T. & SÖRUM, H. (1975). *Acta Cryst.* **B31**, 1581–1586.

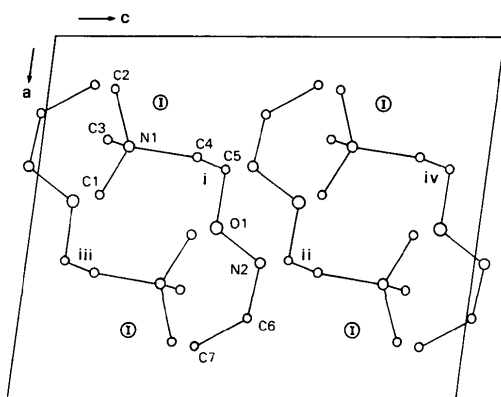


Fig. 2. The crystal structure projected down **b**. The symbols represent the equivalent positions in space group  $P2_1/c$  (No. 14) [i.e. (i)  $x, y, z$ ; (ii)  $1-x, \bar{y}, 1-z$ ; (iii)  $1-x, \frac{1}{2}+y, \frac{1}{2}-z$ ; (iv)  $x, \frac{1}{2}-y, \frac{1}{2}+z$ ].