Pbca
$a = 12.4588\ (11)$ Å
$b = 7.8993\ (5)$ Å
$c = 13.222\ (2)$ Å
$V = 1301.2\ (4)$ Å^3
$Z = 4$
$D_x = 1.216$ Mg m^{-3}
Cu $K\alpha$ radiation
$\lambda = 1.54184$ Å

$\mu = 0.60$ mm^{-1}
$T = 297$ K
Fragment
0.48 × 0.42 × 0.30 mm
Colorless
Crystal source: recrystallization from ethanol

Data collection

Enraf-Nonius CAD-4 diffractometer
ω-2θ scans
Absorption correction: empirical
$T_{\min} = 0.9294$, $T_{\max} = 0.9918$
1336 measured reflections
1336 independent reflections

1154 observed reflections $[I > 3\sigma(I)]$
$\theta_{\max} = 75°$
$h = 0 \rightarrow 15$
$k = 0 \rightarrow 9$
$l = 0 \rightarrow 16$
3 standard reflections
frequency: 167 min
intensity variation: <1%

Refinement

Refinement on F
Final $R = 0.039$
$wR = 0.063$
$S = 4.054$
1154 reflections
111 parameters
All H-atom parameters refined
$w = 4F_o^2[\sigma^2(I) + (0.02F_o^2)^2]^{-1}$
$(\Delta/\sigma)_{\max} < 0.01$

$\Delta\rho_{\max} = 0.17$ e Å^{-3}
$\Delta\rho_{\min} = -0.11$ e Å^{-3}
Extinction correction: $(I + gI_c)^{-1}$ applied to F_c
Extinction coefficient: $g = 4.0\ (4) \times 10^{-6}$
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Table 1. *Fractional atomic coordinates and equivalent isotropic thermal parameters* (Å^2)

$B_{\rm eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$

	x	y	z	$B_{\rm eq}$
O1	0.25708 (8)	0.0650 (2)	0.50833 (7)	4.74 (2)
C1	0.2980 (1)	0.1342 (2)	0.59400 (9)	3.88 (2)
C2	0.2384 (1)	0.2183 (2)	0.6668 (1)	5.28 (3)
C3	0.2885 (2)	0.2812 (2)	0.7520 (1)	6.58 (4)
C4	0.3975 (2)	0.2638 (2)	0.7652 (1)	6.64 (4)
C5	0.4572 (1)	0.1826 (2)	0.6930 (1)	5.31 (3)
C6	0.4093 (1)	0.1170 (2)	0.60610 (9)	3.82 (2)
C7	0.4722 (1)	0.0340 (2)	0.53066 (9)	3.85 (2)
C8	0.1433 (1)	0.0608 (3)	0.4975 (1)	5.96 (4)

Table 2. *Geometric parameters* (Å, °)

O1—C1	1.357 (2)	C3—C4	1.376 (3)
O1—C8	1.425 (2)	C4—C5	1.370 (2)
C1—C2	1.386 (2)	C5—C6	1.395 (2)
C1—C6	1.402 (2)	C6—C7	1.428 (2)
C2—C3	1.380 (2)	C7—C7′	1.194 (2)
C1—O1—C8	117.8 (1)	C3—C4—C5	119.6 (2)
O1—C1—C2	124.8 (1)	C4—C5—C6	121.0 (2)
O1—C1—C6	115.3 (1)	C1—C6—C5	118.8 (1)
C2—C1—C6	119.8 (1)	C1—C6—C7	120.5 (1)
C1—C2—C3	119.8 (1)	C5—C6—C7	120.7 (1)
C2—C3—C4	121.0 (2)	C6—C7—C7′	177.8 (1)

The sample was sealed in a capillary tube. Programs used were *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978), *MolEN* (Fair, 1990) and *ORTEP* (Johnson, 1965).

Lists of structure factors, anisotropic thermal parameters, H-atom coordinates, bond distances and angles involving H atoms, least-squares-planes data and torsion angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71169 (14 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: BR1031]

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Structure of (−)-Muscarone Iodide

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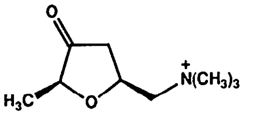
Abstract

The crystal structure of (−)-*cis*-trimethyl{[(2*S*,5*S*)-2-methyl-3-oxotetrahydro-5-furyl]methyl}ammonium iodide (muscarone iodide) is comparable to the structure obtained for the racemic mixture [Frydenvang & Jensen (1992). *Acta Cryst.* C**48**, 469-474]. The space group is different as no mirror planes can exist for the pure enantiomer. The conformation of the muscarone ion is a distorted twist, $^1T_5-^1E$ [phase = 80.2 (2)°], with the puckering amplitude $\theta_m = 35.8\ (1)°$. The quaternary ammonium group adopts an *anti* orientation [O—C—C—N 161.0 (1)°]. The crystal packing is nearly identical to that of the racemic mixture. Both crystal structures are

stabilized by electrostatic interactions and charge-charge interactions place iodide ions close to the quaternary ammonium group.

Comment

Muscarone (I) is an agonist in the muscarinic as well as the nicotinic part of the cholinergic nervous system. It has been observed recently that muscarone shows the same high degree of stereospecificity (De Amici *et al.*, 1992) as other muscarinic agonists. The enantiomer (-)-(2*S*,5*S*)-muscarone is the most potent agonist. The absolute configuration is known to be that of the (2*S*,5*S*) enantiomer.



(I)

The structure determination was performed in order to confirm the observations found for the racemic mixture of muscarone iodide (Frydenvang & Jensen, 1992). The crystal structure of the racemic mixture showed disorder. Each equivalent position in the unit cell could be occupied by either a (-)- or a (+)-muscarone ion, because some of the atoms were situated on a mirror plane. The pure (-)-muscarone iodide was expected to have the same crystal packing without the disorder, as there is no mirror plane present, so the equivalent positions will therefore always be occupied by the (-)-muscarone ion. The final result is given in Tables 1 and 2, and the muscarone ion is shown in Fig. 1.

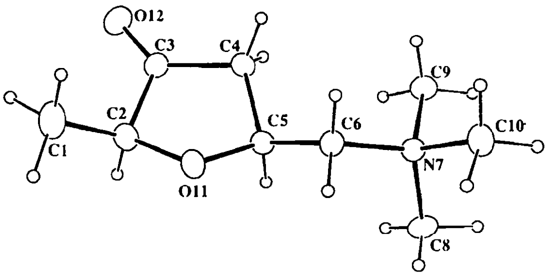


Fig. 1. The muscarone ion with atomic labelling and displacement ellipsoids at the 50% probability level (*ORTEP*II; Johnson, 1976).

The conformation of the muscarone ion is a distorted twist, $^1T_5-^1E$ (Table 2), and the quaternary ammonium group adopts an *anti* orientation (O—C—C—N). This is approximately the same overall conformation as for the muscarone ion in the racemic mixture. The maximum change in bond lengths is 0.03 Å (C6—N7). The largest differences in geometry are observed for the quaternary ammonium group, especially for dimensions involving C8. Bond angles for C8 and C10 are quite different for the two structure determinations, the differences being −10.6 and 11.2°, respectively. This may be because of the mirror plane in the racemic mixture, where C10 is generated from C8 by a symmetry operation.

The crystal packing is stabilized by electrostatic interactions. The positive charge of the quaternary ammonium group is delocalized and no single short contact was observed, but several weaker interactions were found (Table 3). The contacts from the C atoms of the quaternary ammonium group to the iodide ion (C—H···I) are nearly linear and may be weak hydrogen bonds (Taylor & Kennard, 1982). Contacts between muscarone ions are observed between the carbonyl O atom and the C atoms of the quaternary ammonium group. The N—C···O angle is nearly linear, giving close contact to more than one H atom.

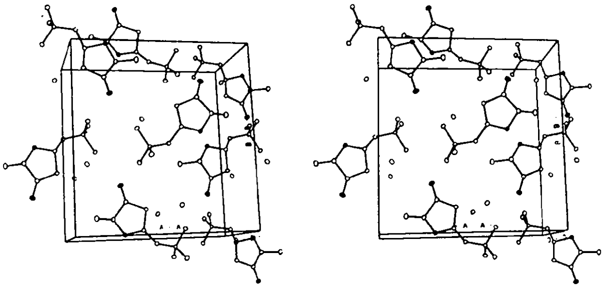


Fig. 2. Stereo drawing of the crystal packing of (-)-muscarone iodide; *x* horizontal, *y* vertical, *z* into the plane of the paper.

Experimental

Crystal data

$C_9H_{18}NO_2^+.I^-$
M_r = 299.2
Orthorhombic
$P2_12_12_1$
a = 12.708 (1) Å
b = 13.131 (1) Å
c = 7.444 (1) Å
V = 1242.2 (4) Å^3
Z = 4
D_x = 1.599 Mg m^{-3}

Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 19 reflections
θ = 20.44–22.79°
μ = 2.525 mm^{-1}
T = 122 K
Rectangular
0.30 × 0.30 × 0.12 mm
Colourless

Data collection

Enraf-Nonius CAD-4 diffractometer
ω-2θ scans
Absorption correction: *ABSCOR* (*SDP*; Frenz, 1982)
$T_{\min}$ = 0.5301, $T_{\max}$ = 0.8635
11 106 measured reflections
10 030 independent reflections
7300 observed reflections [$I > 3\sigma(I)$]

$R_{\rm int}$ = 0.037
$\theta_{\max}$ = 45.0°
$h = 0 \rightarrow 25$
$k = 0 \rightarrow 26$
$l = -14 \rightarrow 14$
3 standard reflections monitored every 300 reflections
intensity variation: −8.4% (corrected)

Refinement

Refinement on F
Final $R = 0.031$
$wR = 0.037$
$S = 1.505$
7297 reflections
190 parameters
All H-atom parameters refined
Calculated weights
$w = 1/[\sigma^2(F) + (0.03F)^2/4]$
$(\Delta/\sigma)_{\max} = 0.31$
$\Delta\rho_{\max} = 2.25$ e Å^{-3}
$\Delta\rho_{\min} = -2.56$ e Å^{-3}
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV, Table 2.2)

Table 1. *Fractional atomic coordinates and equivalent isotropic thermal parameters* (Å^2)

$$B_{eq} = (4/3)\Sigma_i\Sigma_j\beta_{ij}\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	B_{eq}
I	0.56838 (1)	0.64333 (1)	0.50195 (2)	1.518 (1)
C1	0.6505 (2)	0.8938 (2)	−0.0160 (4)	2.35 (3)
C2	0.7536 (2)	0.8978 (2)	0.0837 (3)	1.60 (3)
C3	0.8253 (2)	0.8079 (1)	0.0416 (2)	1.41 (2)
C4	0.9354 (1)	0.8498 (1)	0.0107 (3)	1.48 (2)
C5	0.9231 (1)	0.9624 (1)	0.0573 (2)	1.28 (2)
C6	0.9780 (1)	1.0380 (1)	−0.0663 (2)	1.28 (2)
N7	1.0924 (1)	1.0585 (1)	−0.0272 (2)	1.16 (2)
C8	1.1066 (2)	1.1136 (2)	0.1471 (3)	1.62 (3)
C9	1.1567 (1)	0.9624 (1)	−0.0235 (2)	1.46 (3)
C10	1.1319 (2)	1.1253 (2)	−0.1771 (3)	1.66 (3)
O11	0.8130 (1)	0.98489 (9)	0.0295 (2)	1.58 (2)
O12	0.7985 (1)	0.7198 (1)	0.0336 (2)	1.97 (2)

Table 2. *Bond lengths* (Å), *bond angles* (°), *selected torsion angles* (°) *and pseudorotational parameters* (°)

	(-)-Muscarone	(±)-Muscarone
C1—C2	1.507 (3)	1.505 (5)
C2—C3	1.525 (3)	1.520 (4)
C2—O11	1.429 (2)	1.427 (4)
C3—C4	1.522 (2)	1.521 (4)
C3—O12	1.207 (2)	1.206 (3)
C4—C5	1.528 (2)	1.545 (3)
C5—C6	1.522 (2)	1.516 (4)
C5—O11	1.444 (2)	1.450 (3)
C6—N7	1.507 (2)	1.534 (3)
N7—C8	1.497 (2)	1.484 (2)
N7—C9	1.503 (2)	1.506 (3)
N7—C10	1.505 (2)	1.484 (2)*
C1—C2—C3	113.0 (2)	113.3 (3)
C1—C2—O11	110.4 (2)	110.5 (3)
C3—C2—O11	104.2 (1)	104.0 (2)
C2—C3—C4	107.5 (1)	108.6 (2)
C2—C3—O12	125.7 (2)	125.0 (3)
C4—C3—O12	126.8 (2)	126.4 (2)
C3—C4—C5	102.9 (1)	101.8 (2)
C4—C5—C6	116.5 (1)	114.4 (2)
C4—C5—O11	105.3 (1)	101.8 (3)
C6—C5—O11	102.9 (1)	103.0 (2)
C5—C6—N7	116.3 (1)	113.4 (2)
C6—N7—C8	111.7 (1)	122.3 (2)
C6—N7—C9	112.2 (1)	111.4 (2)
C6—N7—C10	106.4 (1)	95.2 (2)*
C8—N7—C9	108.9 (1)	109.0 (1)
C8—N7—C10	108.7 (1)	108.6 (2)*
C9—N7—C10	108.7 (1)	109.1 (1)*
C2—O11—C5	107.9 (1)	108.4 (2)
C3—C2—O11—C5	−31.9 (2)	−30.9 (3)
O11—C2—C3—C4	15.1 (2)	12.2 (3)
C2—C3—C4—C5	5.9 (2)	9.3 (2)
C3—C4—C5—O11	−24.8 (2)	−27.4 (2)
C4—C5—O11—C2	36.4 (2)	37.7 (3)
C6—C5—O11—C2	159.0 (1)	±157.5 (2)
O11—C5—C6—N7	161.0 (1)	±157.5 (2)
Phase, P	80.2 (2)	75.0
Amplitude, θ_m	35.8 (1)	36.6
	$^1T_5-^1E$	$^1T_5$

* C10 does not exist in the racemic mixture. C10 is C8 after symmetry operation $x, y, \frac{1}{2}-z$ (Frydenvang & Jensen, 1992).

Table 3. *Intermolecular contacts* (Å, °)

A—$B\cdots C$	$A\cdots C$	$B\cdots C$	A—$B\cdots C$	Symmetry
Muscarone to iodide				
I···C4	4.003 (2)			v
I···C5	4.013 (2)			v
C6—H61···I	4.184 (2)	3.37 (3)	149 (2)	i
C8—H83···I	4.037 (2)	3.21 (3)	161 (3)	ii
C9—H92···I	3.984 (2)	3.10 (3)	167 (2)	i
C10—H101···I	4.033 (2)	3.08 (4)	159 (3)	iii
Muscarone to muscarone				
C8—H81···O12	3.009 (2)	2.53 (3)	105 (2)	iii
C8—H82···O12	3.009 (2)	3.01 (3)	81 (2)	iii
C8—H83···O12	3.009 (2)	2.98 (3)	84 (2)	iii
C9—H91···O12	2.997 (2)	2.85 (3)	91 (2)	i
C9—H92···O12	2.997 (2)	2.85 (3)	90 (2)	i
C9—H93···O12	2.997 (2)	2.96 (3)	83 (2)	i
C10—H101···O12	3.061 (3)	2.96 (4)	86 (2)	iv
C10—H102···O12	3.061 (3)	3.10 (3)	78 (2)	iv
C10—H103···O12	3.061 (3)	2.68 (3)	105 (2)	iv

Symmetry codes: (i) $\frac{1}{2}+x, \frac{3}{2}-y, -z$; (ii) $\frac{3}{2}-x, 2-y, z-\frac{1}{2}$; (iii) $2-x, \frac{1}{2}+y, \frac{1}{2}-z$; (iv) $2-x, \frac{1}{2}+y, -z-\frac{1}{2}$; (v) $x-\frac{1}{2}, \frac{3}{2}-y, 1-z$.

Single crystals were obtained from vapour diffusion of dimethoxymethane into a solution of the compound in ethanol. The absolute configuration is known to be the (2*S*,5*S*) enantiomer and was confirmed by Hamilton's *R*-value test (Rogers, 1981). The (2*S*,5*S*) enantiomer is the correct one [significance level $\alpha \ll 10^{-10}$, $R(+) = 0.03133$, $wR(+) = 0.03726$, $R(-) = 0.03612$, $wR(-) = 0.04634$]. Both maximum and minimum residual electron densities were observed close to the location of the iodide ion. Pseudorotational parameters were calculated by *PLATON* (Spek, 1991) according to the method described by Rao, Westhof & Sundaralingam (1981). Data collection: Enraf-Nonius (1985) CAD-4 diffractometer control program. Cell refinement: Enraf-Nonius CAD-4 diffractometer control program. Data reduction: *SDP BEGIN* (Frenz, 1982). Program(s) used to solve structure: *SDP DIRDIF*. Program(s) used to refine structure: *SDP LSFM*. Molecular graphics: *ORTEP* (Johnson, 1976).

The compound was kindly donated by Dr M. De Amici, Milano, Italy.

Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and complete geometry have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71266 (42 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: AB1062]

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Acta Cryst. (1993). C**49**, 1837–1840

Structure Determinations of (*dl*)-*trans*-3-Hydroxy-5-iodomethyl-2,2-diphenyltetrahydrofuran and (*dl*)-*trans*-*N*,*N*,*N*-Trimethyl-(3-hydroxy-2,2-diphenyltetrahydro-5-furyl)methylammonium Iodide

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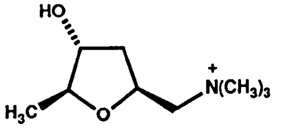
Abstract

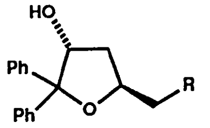
The conformation of the five-membered ring in muscarine-related compounds was studied. The conformations observed in the two title compounds, (1) 5-iodomethyl-2,2-diphenyltetrahydrofuran-3-ol and (2) trimethyl[(3-hydroxy-2,2-diphenyltetrahydro-5-furyl)methyl]ammonium iodide, are slightly different. In the iodomethyl compound the ring adopts an E_3 envelope conformation in which the C atom connected to the hydroxy group is out of the best plane through the remaining ring atoms. The ring adopts a $^4T_3$ twist conformation in the iodide salt with the C atom connected to the hydroxy group and the methylene C atom out of the plane of the ring. In both cases, the hydroxy group is in an axial orientation. The puckering amplitudes are of the same magnitude (40.8 and 41.5°, respectively). The crystal packing in the iodomethyl compound is stabilized by van der Waals contacts and that of the iodide salt by van der Waals contacts and electrostatic interactions. In the latter, a hydrogen bond is also observed between the hydroxy group and the iodide ion.

Comment

The structure determinations of the two title compounds were performed in order to study the conformations of the five-membered rings and to obtain information about the relative orientations, *cis* or *trans*, of the ring substituents. A series of cholinergic compounds has been analyzed in order to obtain information about the dependence of the flexibility of the five-membered ring on the substituents (Jellinek, 1957; Frydenvang & Jensen, 1990, 1993). A five-membered ring is present in many cholinergic compounds, agonists as well as antagonists. Muscarine is an agonist in parts of the cholinergic nervous system whereas compound (2) is expected to be an antagonist on the basis of earlier studies of oxathiolane compounds (Angeli *et al.*, 1986).

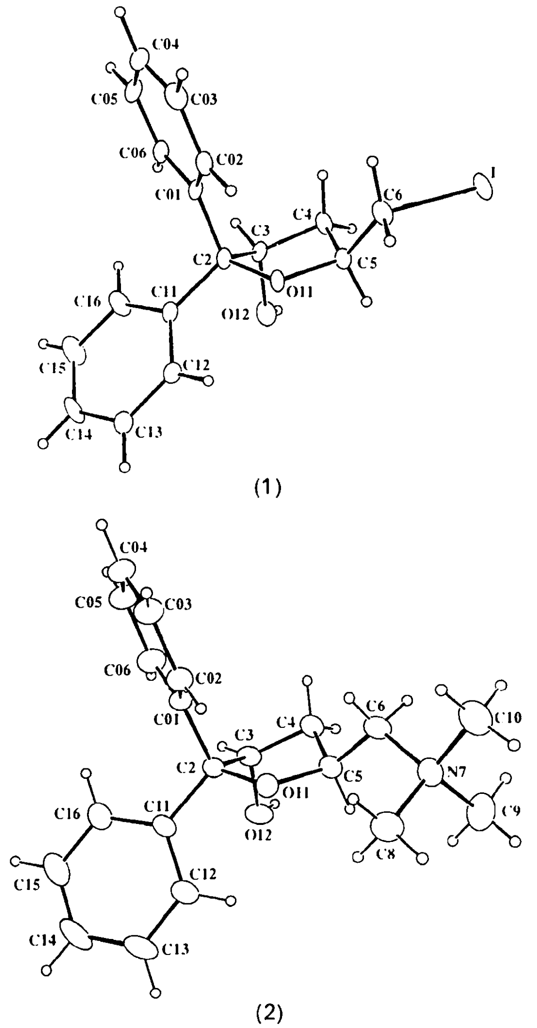


Muscarine



(1) R = I
(2) R = $^+N(CH_3)_3$

The final results of the structure determinations are given in Table 1 and 2, and the compounds are shown in Fig. 1. The substituents on the five-membered ring



(1)

(2)

Fig. 1. The title compounds shown with displacement ellipsoids and atomic labelling (*ORTEP*; Johnson, 1976).