crief & Lipscomb (1966) in the LCR methiodide structure. The chemical formula of the other part is in agreement with the latest ^{13}C n.m.r. studies (Rasoanaivo *et al.*, 1974), except for the position of the *cis* double bond included in the 11-membered ring: C′(20)–C′(21) = 1·34 (2) Å. Another intramolecular hydrogen bond links the indole nitrogen N′(1) to the carbonyl oxygen O′(25) [2·65 (1) Å], stabilizing the conformation of the $COOCH_3$ group which is substituted at C′(16) (one end of the C(10)–C′(16) bridge between the two halves of the molecule). As frequently observed, the terminal methyl of the ethyl chain is disordered [C′(18)–C′(19) = 1·34 (5) Å], but the shortening effect seems to be enhanced by the misplacing of C′(19): C′(19)–C′(20) = 1·64 (3) Å. All the other distances are in good agreement with standard values within experimental r.m.s. deviation (0·03 Å). Table 2 gives the mean values of the bond lengths, classified schematically according to the hybridization of the carbon atoms. The end of the other ethyl chain, C(18), is not far from the aldehyde oxygen O′(26): 3·57 (2) Å, so that the general conformation of the catharine molecule is rather compact. The acetone molecule is inserted into the hollow formed by the catharine molecule: C′(17)–O*A*(4) = 3·05 (2) Å. No intermolecular hydrogen bond was found.

Table 2. *Mean values of the bond lengths* (Å), *with the corresponding root mean square deviations, calculated with respect to those mean values*

N is the number of distances.

Bond type	Mean	σ	*N*
C_{ar}–C_{ar}	1·39	4	14
C_{sp3}–C_{sp3}	1·54	3	12*
C_{sp3}–N	1·47	2	6
C_{sp2}–N	1·40	1	5
C_{sp3}–C_{sp2}	1·51	2	14†
C_{sp2}–C_{sp2}	1·33	2	2
C=O	1·21	1	6
C_{sp3}–O	1·44	5	5
C_{sp2}–O	1·36	1	4

* Excluding C′(18)–C′(19).
† Excluding C′(19)–C′(20).

References

Abraham, D. J., Farnsworth, N. R., Blomster, R. N. & Rhodes, R. E. (1967). *J. Pharm. Sci.* **56**, 401–407.

Doyle, P. A. & Turner, P. S. (1968). *Acta Cryst.* A**24**, 390–397.

Germain, G., Main, P. & Woolfson, M. M. (1971). *Acta Cryst.* A**27**, 368–376.

Johnson, C. K. (1965). *ORTEP*. Oak Ridge National Laboratory Report ORNL-3794.

Karle, J. (1968). *Acta Cryst.* B**24**, 182–186.

Karle, J. & Karle, I. L. (1966). *Acta Cryst.* **21**, 849–859.

Moncrief, J. W. & Lipscomb, W. N. (1966). *Acta Cryst.* **21**, 322–331.

Rasoanaivo, P. (1974). Thesis, p. 173.

Rasoanaivo, P., Ahond, A., Cosson, J. -P., Langlois, N., Potier, P., Guilhem, J., Ducruix, A., Riche, C. & Pascard, C. (1974). *C. R. Acad. Sci. Paris*, **279**, 75–77.

Riche, C. (1973). *Acta Cryst.* A**29**, 133–137.

Svoboda, G. H., Gorman, M., Neuss, N. & Barnes, A. (1961). *J. Pharm. Sci.* **50**, 409–413.

Acta Cryst. (1976). B**32**, 938

(—)-3(*a*)-Trimethylammonio-2(*a*)-acetoxy-*trans*-decalin Iodide

By Byungkook Lee and George M. Henry

Department of Chemistry, University of Kansas, Lawrence, Kansas 66045, *U.S.A.*

(*Received* 30 *June* 1975; *accepted* 30 *October* 1975)

Abstract. $C_{15}H_{28}NO_2I$, M.W. 381·3, orthorhombic, $P2_12_12_1$, $Z=4$, $a=16{\cdot}079$ (3), $b=14{\cdot}373$ (3), $c=7{\cdot}585$ (1) Å, $D_x=1{\cdot}44$ g cm^{-3}, λ(Mo $K\alpha$) = 0·7107 Å, μ(Mo $K\alpha$) = 18·5 cm^{-1}, $R=0{\cdot}031$ for 2030 observed reflections. This acetylcholine analog is the biologically inactive isomer. Its absolute configuration was determined using the anomalous dispersion effect of iodine. It has the 2(*R*)-3(*R*) configuration. The biologically active dextrorotatory isomer must, therefore, have the 2(*S*)-3(*S*) configuration.

Introduction. The title compound was synthesized, purified, and crystallized by Smissman, Schowen, Paske & Magarian (manuscript in preparation). The X-ray photographs of the needle-shaped crystals showed orthorhombic symmetry and systematic absences consistent with the space group $P2_12_12_1$ ($h00$ reflections absent when h odd, $0k0$ absent when k odd, and $00l$ absent when l odd). Three-dimensional data were collected using a specimen 0·15 × 0·15 × 0·20 mm, a Syntex $P\bar{1}$ diffractometer, graphite-monochromated Mo $K\alpha$ radiation, and a θ–2θ scan procedure, the details of which have been reported (Seccombe, Lee & Henry, 1975). Intensities were measured for all 2314 independent reflections with $2\theta \le 55°$. Of these, 2030 reflections had $I > 3\sigma(I)$ and were used for the structure analysis. The intensity data were reduced to the structure factors by the application of Lorentz and polarization corrections. No absorption or extinction correction was applied. The neglect of the absorption effect could cause a maximum error of about 10% in the intensity of some reflections, but for most reflections error from this source is expected to be much smaller.

The structure was determined by the heavy-atom technique and refined using the least-squares procedure. The computer programs used were the same as those used by Seccombe, Lee & Henry (1975). All non-hydrogen atoms were assigned anisotropic temperature factors. The hydrogen atoms were included at fixed calculated positions assuming a C–H distance of 0·95 Å (Churchill, 1973) and with fixed isotropic temperature factors. The absolute configuration of the molecule was determined by the use of the anomalous scattering effect of iodine. Initially the structure was refined until convergence using normal atomic scattering factors from Cromer & Mann's (1968) table and the real part of the anomalous scattering factors for iodine from *International Tables for X-ray Crystallography* (1962). The discrepancy indices were $R=\sum||F_o|-|F_c||/\sum|F_o|=0{\cdot}034$ and $R'=\{\sum w(|F_o|-|F_c|)^2/\sum w|F_o|^2\}^{1/2}=0{\cdot}043$. When the imaginary part of the anomalous scattering factors for iodine (*International Tables for X-ray Crystallography*, 1962) was included, the 2(*R*)-3(*R*) isomer could be refined to give $R=0{\cdot}031$ and $R'=0{\cdot}037$ whereas the 2(*S*)-3(*S*) structure refined to $R=0{\cdot}038$ and $R'=0{\cdot}047$. The difference in R' is statistically highly significant: Hamilton's (1964) R factor ratio test rejects the 2(*S*)-3(*S*) isomer at a significance level better than 0·5%. It is concluded, therefore, that this levorotatory isomer has the 2(*R*)-3(*R*) configuration.

The structure of the molecule and the atom numbering scheme are shown in Fig. 1. The final atomic coordinates and thermal parameters are given in Table 1 and bond lengths and angles are given in Tables 2 and 3.*

---

* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31493 (7 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 1. *Positional and thermal parameters* (× 10⁴) *and their estimated standard deviations*

The atomic coordinates are given in the fractional crystallographic coordinate system. The anisotropic temperature factor is given in terms of the thermal parameters by $\exp[-(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^2+2\beta_{12}hk+2\beta_{13}hl+2\beta_{23}kl)]$.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
I	1094·0 (2)	846·2 (3)	290·5 (5)	43·4 (1)	74·3 (2)	152·7 (6)	–5·4 (2)	–0·6 (3)	–11·9 (3)
O(1)	5819 (2)	1631 (2)	2821 (4)	41 (1)	47 (2)	134 (6)	–2 (1)	–10 (2)	–17 (3)
O(2)	4915 (3)	2378 (3)	4538 (6)	62 (2)	78 (2)	252 (9)	–27 (2)	–15 (4)	–54 (5)
N	3818 (3)	1314 (3)	433 (6)	37 (2)	50 (2)	199 (8)	8 (2)	–18 (4)	–6 (4)
C(1)	5572 (3)	99 (3)	1806 (6)	36 (2)	40 (2)	124 (8)	3 (2)	–3 (3)	9 (4)
C(2)	5154 (3)	1028 (3)	2191 (6)	37 (2)	42 (3)	120 (8)	0 (2)	0 (3)	–10 (3)
C(3)	4759 (3)	1526 (3)	613 (6)	37 (2)	41 (2)	165 (10)	4 (2)	–10 (4)	–3 (4)
C(4)	5276 (3)	1398 (3)	–1065 (7)	51 (2)	40 (2)	132 (8)	8 (2)	–4 (4)	8 (4)
C(5)	6136 (3)	398 (4)	–3096 (6)	48 (2)	58 (3)	125 (8)	3 (2)	5 (4)	7 (4)
C(6)	6499 (3)	–564 (4)	–3403 (7)	43 (2)	63 (3)	152 (9)	2 (2)	16 (4)	–27 (4)
C(7)	7023 (3)	–876 (4)	–1846 (7)	34 (2)	57 (3)	200 (10)	3 (2)	2 (3)	–20 (6)
C(8)	6522 (3)	–857 (3)	–140 (6)	36 (2)	40 (2)	166 (9)	5 (2)	–5 (3)	–1 (5)
C(9)	6115 (3)	109 (3)	179 (5)	32 (1)	36 (2)	119 (7)	–4 (2)	–6 (4)	–4 (3)
C(10)	5624 (3)	418 (3)	–1490 (6)	36 (2)	42 (2)	109 (8)	–3 (2)	–3 (3)	5 (3)
C(11)	5608 (4)	2270 (3)	4025 (7)	59 (3)	46 (3)	144 (9)	14 (2)	–21 (4)	–11 (4)
C(12)	6346 (4)	2820 (4)	4601 (9)	76 (3)	48 (2)	206 (11)	–4 (2)	–29 (6)	–18 (5)
C(13)	3601 (3)	307 (4)	345 (10)	42 (2)	55 (3)	237 (13)	–5 (2)	6 (5)	–3 (6)
C(14)	3371 (4)	1722 (6)	1978 (12)	41 (2)	138 (7)	466 (25)	20 (4)	–2 (7)	–161 (11)
C(15)	3482 (4)	1744 (6)	–1223 (12)	54 (3)	93 (5)	454 (24)	–5 (3)	–78 (7)	91 (9)

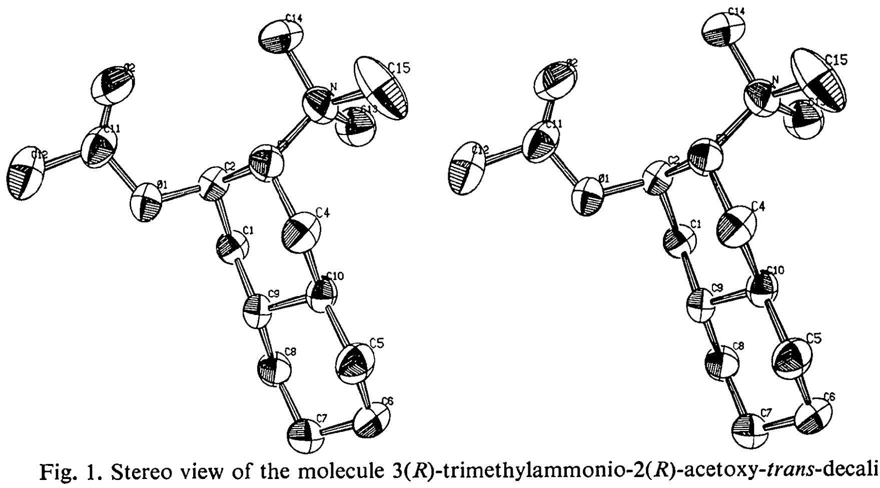

Fig. 1. Stereo view of the molecule 3(*R*)-trimethylammonio-2(*R*)-acetoxy-*trans*-decalin.

Table 2. *Bond lengths* (Å)

C(1)—C(2)	1·524 (6)	N-C(3)	1·548 (6)
C(2)—C(3)	1·532 (6)	N-C(13)	1·491 (6)
C(3)—C(4)	1·532 (7)	N-C(14)	1·495 (8)
C(4)—C(10)	1·538 (6)	N-C(15)	1·500 (8)
C(10)-C(5)	1·521 (7)		
C(5)—C(6)	1·519 (7)	C(11)-O(1)	1·339 (6)
C(6)—C(7)	1·518 (8)	C(11)-O(2)	1·190 (7)
C(7)—C(8)	1·525 (7)	C(11)-C(12)	1·492 (8)
C(8)—C(9)	1·553 (6)	C(2)—O(1)	1·457 (5)
C(9)—C(1)	1·512 (6)		
C(9)—C(10)	1·508 (6)		

Table 3. *Bond angles* (°)

C(9)—C(1)-C(2)	113·8 (4)	C(3)—N-C(13)	115·1 (3)
C(1)—C(2)-C(3)	116·2 (4)	C(3)—N-C(14)	108·9 (4)
O(1)—C(2)-C(1)	105·1 (4)	C(3)—N-C(15)	110·2 (5)
O(1)—C(2)-C(3)	106·5 (3)	C(13)-N-C(14)	107·6 (6)
C(2)—C(3)-C(4)	111·6 (3)	C(13)-N-C(15)	106·2 (5)
N——C(3)-C(2)	112·5 (4)	C(14)-N-C(15)	108·7 (5)
N——C(3)-C(4)	115·7 (4)		
C(3)—C(4)-C(10)	116·6 (4)	C(2)-O(1)--C(11)	116·5 (4)
C(10)-C(5)-C(6)	110·8 (4)	O(1)-C(11)-C(12)	111·2 (5)
C(5)—C(6)-C(7)	111·3 (4)	O(2)-C(11)-C(12)	125·5 (5)
C(6)—C(7)-C(8)	111·2 (4)	O(2)-C(11)-O(1)	123·4 (5)
C(7)—C(8)-C(9)	111·8 (4)		
C(1)—C(9)-C(8)	111·2 (3)	C(4)-C(10)-C(5)	110·9 (4)
C(1)—C(9)-C(10)	110·6 (3)	C(4)-C(10)-C(9)	109·0 (4)
C(8)—C(9)-C(10)	111·1 (4)	C(5)-C(10)-C(9)	112·5 (4)

Discussion. This compound is a 'conformationally rigid' analog of the neurotransmitter acetylcholine (Triggle, Moran & Barnard, 1971). The racemic mixture of this and its optical isomer is an active cholinergic agent (Smissman, Nelson, Lapidus & Day, 1966) and its crystal structure has been reported (Shefter & Smissman, 1971). When the individual optical isomers of this mixture were separated and their activities tested, it was found that the dextrorotatory isomer was about twice as active as the racemic mixture on an equimolar basis whereas the levorotatory isomer was completely inactive (Schowen, Smissman & Stephen, 1975). The crystal structure studies reported herein establish unambiguously that the exclusive biological activity of the dextrorotatory isomer is associated with the 2(*S*)-3(*S*) configuration.

The structure of this optical isomer is essentially the same as that reported for the racemic mixture (Shefter & Smissman, 1971). The qualitative features of the structure discussed below are present in the racemic structure as well.

There are numerous structural studies of the substituted cyclohexanes, but this structure appears to be the first example wherein a t-butyl or trimethylammonium group is *axially* attached to the cyclohexane moiety. In such a structure, because of the proximity of one of the methyl groups to two axial hydrogens of the ring, it may be expected that the ring flattens and/or the substituent group bends outwards, away from the ring. Both of these features can be detected in the present structure (see below). The actual experimental contact distances in the structure are C(13)–H(C1), 3·371 (7) and C(13)–H(C10), 3·519 (7) Å.

A comparison of the ring bond angles and the ring dihedral angles for the adjacent ring (the cyclohexane ring that carries the trimethylammonium and the acetoxy groups) and the distal ring of the decalin moiety shows that the former is flatter. Thus the average ring bond angle is 113·0 (4)° for the adjacent ring compared to 111·5 (4)° for the distal ring. (If bond angles were all regular tetrahedral, this angle would be 109·5°, whereas for a completely flat ring this angle is 120°.) The average ring dihedral angle is 49·1 (5)° for the adjacent ring and 54·8 (5)° for the distal ring. (This angle is 60° for an unflattened ideal cyclohexane ring.) The pattern of bond angle values (Table 3) indicates that the flattening of the adjacent ring occurs mainly by folding the C(4)–C(3)–C(2) triangle away from the rest of the ring along the C(4)–C(2) line.

That the trimethylammonium group is bent outward is seen from the 26·8° angle that the C(3)–N bond makes with the normal of the mean plane of the adjacent ring. By comparison, the C(2)–O(1) bond makes only a 9·6° angle with the same normal.

An upshot of these structural features is that the dihedral angle O(1)–C(2)–C(3)–N is –148·3 (3)° and not 180° as one might expect from an inspection of, say, a Dreiding model.

Other structural features that may be noted are as follows: (1) The four atoms O(1), C(11), C(12) and O(2) of the acetoxy group lie in one plane (the r.m.s. deviation of the atoms from their mean plane is 0·011 Å). Since the dihedral angle C(3)–C(2)–O(1)–C(11) is 88·7 (4)°, this plane is nearly perpendicular to the O(1)–C(2)–C(3) plane; (2) the three methyl groups of the trimethylammonium group are rotated around the N–C(3) bond by about 10° from the perfectly staggered position.

This work was supported by the National Institutes of Health through the Health Science Advancement Award to the University of Kansas, RR 06147.

References

Churchill, M. R. (1973). *Inorg. Chem.* **12**, 1213–1214.

Cromer, D. T. & Mann, J. B. (1968). *Acta Cryst.* **A24**, 321–324.

Hamilton, W. C. (1964). *Statistics in Physical Sciences.* New York: Ronald Press.

International Tables for X-ray Crystallography (1962). Vol. III, 2nd ed., Tables 3.3.1A and 3.3.2C. Birmingham: Kynoch Press.

Schowen, K. B., Smissman, E. E. & Stephen, W. F. Jr (1975). *J. Med. Chem.* **18**, 292–300.

Seccombe, R. C., Lee, B. & Henry, G. M. (1975). *Inorg. Chem.* **14**, 1147–1153.

Shefter, E. & Smissman, E. E. (1971). *J. Pharm. Sci.* **60**, 1364–1367.

Smissman, E. E., Nelson, W. L., Lapidus, J. B. & Day, J. L. (1966). *J. Med. Chem.* **9**, 458–465.

Triggle, D. J., Moran, J. F. & Barnard, E. A. (1971). *Cholinergic Ligand Interactions.* New York: Academic Press.