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(*R*)-(+)-*O*-Isopropyl-*S*-(trimethylammonioethyl)methylphosphonothioate Iodide

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Abstract. $C_9H_{23}NO_2IPS$, $M_r = 367{\cdot}24$, orthorhombic, $P2_12_12_1$, $a = 7{\cdot}784$ (8), $b = 33{\cdot}62$ (3), $c = 6{\cdot}217$ (3) Å, $Z = 4$, $D_x = 1{\cdot}50$ g cm^{-3} (D_m not determined). The structure and absolute configuration were determined from single-crystal X-ray data. The final R is 0·046.

Introduction. The title compound $(CH_3)_2CHO(CH_3)P(O)SCH_2CH_2N(CH_3)_3^+.I^-$ (hereinafter TPI+) was synthesized by Boter (1970), who kindly provided the sample. Crystals were grown from a solution of TPI+ in methanol–acetone (1:1).

The cell parameters were obtained by least-squares techniques from the diffractometer-measured θ angles of 25 reflexions.

The crystal used for data collection was irregularly shaped; the boundary planes and distances (mm) from an arbitrary point inside the crystal were:

(010) 0·045 (301) 0·095 ($\bar{1}$42) 0·110

(0$\bar{1}$0) 0·045 ($\bar{3}$0$\bar{1}$) 0·095 (12$\bar{5}$) 0·081.

The crystal was mounted in a glass capillary and oriented with **b** parallel to the φ axis of the goniostat. Intensities were measured on a Nonius three-circle diffractometer with graphite-monochromated Mo $K\alpha$ radiation ($\lambda = 0{\cdot}71069$ Å). The ω-scan technique with scan speed 1·2° min^{-1} was employed. The θ range was limited to 2·5–17·0° because of a rapid decline in intensity with increasing θ. 928 independent reflexions were measured, having $|F_{rel}|$ values in the range 0–300; 732 reflexions with $I > 2\sigma(I)$ were used in the refinement. The data were corrected for Lorentz–polarization effects and for absorption (Coppens, 1970). The transmittance factor varied from 0·66 to 0·83.

The structure was solved by the heavy-atom method. Least-squares refinement of the positional and isotropic thermal parameters of all non-hydrogen atoms converged at $R = 0{\cdot}09$. The quantity minimized was $\Sigma w(|F_o| - |F_c|)^2$, with unit weights. At this stage 23 H atom positions were calculated and included as a fixed contribution. In the final refinement anisotropic tem-

Table 1. *Atomic parameters* (×10^4)

	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
I	6301 (2)	1917 (1)	3687 (3)	73 (1)	87 (1)	80 (1)	−5 (1)	2 (1)	17 (1)
S(1)	1468 (11)	726 (2)	1752 (10)	182 (7)	66 (4)	67 (5)	31 (5)	−5 (6)	0 (4)
P(1)	1818 (8)	662 (2)	5003 (11)	80 (5)	63 (5)	79 (4)	13 (4)	−1 (4)	1 (4)

	x	y	z	U		x	y	z	U
O(1)	1287 (22)	1018 (4)	6179 (28)	94 (4)	C(4)	−199 (29)	1924 (8)	−1610 (44)	98 (8)
O(2)	3679 (24)	526 (3)	5363 (19)	82 (4)	C(5)	2862 (27)	1979 (7)	−1530 (43)	92 (8)
N(1)	1326 (25)	1897 (6)	−226 (22)	69 (5)	C(6)	699 (25)	222 (6)	5713 (32)	78 (8)
C(1)	478 (30)	1257 (8)	1443 (52)	114 (9)	C(7)	5145 (34)	805 (8)	5113 (49)	104 (10)
C(2)	1890 (35)	1460 (9)	551 (48)	131 (11)	C(8)	6048 (49)	828 (9)	7225 (46)	146 (12)
C(3)	1245 (31)	2167 (6)	1639 (37)	80 (6)	C(9)	6333 (40)	645 (7)	3523 (47)	116 (8)
H(11)	216	1368	2898	80	H(53)	3906	1968	−595	80
H(12)	−481	1249	372	80	H(61)	1145	−5	4837	80
H(21)	2344	1306	−704	80	H(62)	−555	259	5423	80
H(22)	2821	1483	1653	80	H(63)	877	165	7275	80
H(31)	894	2438	1148	80	H(71)	4727	1073	4665	80
H(32)	2401	2181	2337	80	H(81)	7044	1015	7105	80
H(33)	386	2064	2697	80	H(82)	6470	558	7640	80
H(41)	−419	2208	−1984	80	H(83)	5234	928	8346	80
H(42)	−1216	1813	−831	80	H(91)	7323	832	3347	80
H(43)	0	1768	−2957	80	H(92)	5726	614	2115	80
H(51)	2764	2249	−2188	80	H(93)	6764	380	4016	80
H(52)	2961	1775	−2695	80					

perature parameters were introduced for the I, S and P atoms, a weighting scheme $w = 1/\{[\sigma(F_o)]^2 + 0{\cdot}0005F_o^2\}$ was applied, and the structure factors were corrected for anomalous dispersion. The final R is 0·046. Table 1 lists the atomic parameters.*

The computations were performed on an IBM 370/165 computer with a local version of *DATAPH* (Coppens, 1970), the XRAY system (Stewart, Kundell & Baldwin, 1970) and *ORTEP* (Johnson, 1965). The

* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32681 (16 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

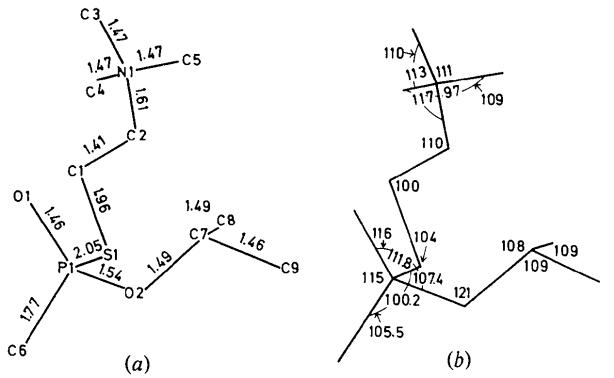

Fig. 1. (*a*) The numbering of the atoms and bond lengths (Å) between non-hydrogen atoms. E.s.d.'s are 0·01–0·04 Å. (*b*) Bond angles (°) between non-hydrogen atoms. E.s.d.'s are 0·6–2·5°.

Table 2. *Analysis of the* 310 *pairs of reflexions showing anomalous dispersion*

Sign (ΔF_o^2) = sign (ΔF_c^2)

$h\,k\,l$	ΔF_o^2	ΔF_c^2	$\frac{\|\|F_o(h)\| - \|F_o(\bar{h})\|\|}{\sigma\|F_o(h)\|}$
1 9 2	−1896	−1590	18
1 1 1	−1471	−1420	22
1 6 1	1238	1627	14
1 9 1	−1092	−849	12
4 6 1	−983	−774	10
$\sum_1^{247}\|\Delta F^2\|$	58842	51070	

Sign $(\Delta F_o^2) \neq$ sign (ΔF_c^2)

$h\,k\,l$	ΔF_o^2	ΔF_c^2	$\frac{\|\|F_o(h)\| - \|F_o(\bar{h})\|\|}{\sigma\|F_o(h)\|}$
1 12 1	−354	56	3·9
1 10 2	−321	147	4·5
1 16 4	234	−31	2·6
4 4 1	−215	157	2·2
1 4 1	203	−554	2·0
$\sum_1^{63}\|\Delta F^2\|$	4981	5823	

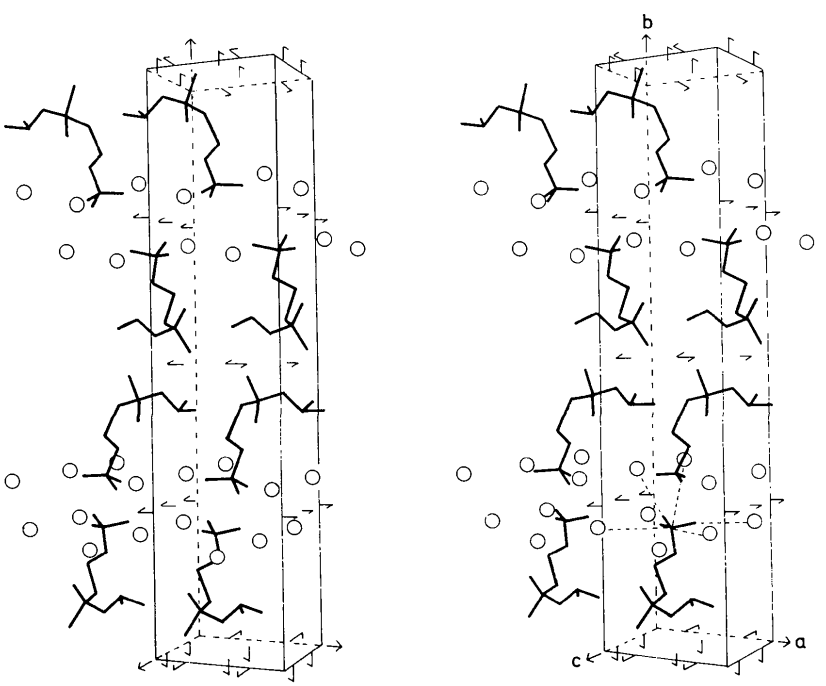

Fig. 2. Stereodiagram illustrating the molecular packing. The circles denote iodide ions. Unit-cell outline and screw axes are indicated.

scattering factors of Cromer & Mann (1968) were used for I^-, S, P, O, N, and C, and those of Stewart, Davidson & Simpson (1965) for H.

The absolute configuration was determined by an analysis of the differences between the reflexions *hkl* and $\bar{h}kl$ measured with Cu $K\alpha$ radiation. Real and imaginary dispersion corrections were introduced for all atoms except H (*International Tables for X-ray Crystallography*, 1974). The two enantiomers were independently refined, giving a final R of 0·054 for the (R) configuration and 0·071 for the (S). The 310 pairs of reflexions calculated for the (R) configuration were further analysed (Table 2). The table lists $\Delta F_o^2 = F_o(h)^2 - F_o(\bar{h})^2$ and the corresponding calculated values for five reflexions showing the most pronounced anomalous dispersion effect. For comparison are listed five reflexions showing the largest ΔF_o^2 and ΔF_c^2 values having opposite signs. The absolute configuration is on this basis assigned as (R).

Discussion. The two enantiomers of this highly toxic acetylcholinesterase inhibitor act upon the enzyme with different speeds, the (−) isomer reacting approximately 1000 times faster than the (+) isomer (Boter & Platenburg, 1967). From stereospecific syntheses the (+) isomer was assigned the configuration (R) (van den Berg, Platenburg & Benschop, 1972). Earlier the (S) configuration was suggested for the same compound (Benschop, van den Berg & Boter, 1968). The purpose of the present work was to confirm the chemical results and to contribute to the knowledge of the geometry of the binding site of the enzyme.

The conformation of the molecule including bond lengths and angles is shown in Fig. 1. The high thermal parameters for S(1), C(1), C(2), C(7), C(8), and C(9), and the anomalous bond lengths between these atoms may indicate a slight disorder in the structure, which also agrees with the rapid decline of the intensities with increasing θ. The dihedral angle of the thiocholine group is 171°. A similar antiperiplanar conformation was found in acetyl- and propionylthiocholine salts (Shefter, Mautner & Smissman, 1969).

The packing is shown in Fig. 2. The polar groups are situated about $y = \frac{1}{4}$ and $\frac{3}{4}$, the non-polar groups filling the spaces between. Each quaternary ammonium ion is surrounded by six I^- ions, geometrically placed in two groups: $I^- \cdots C(x)$–N(1) for x = 2,4,5 and $I^- \cdots$ N(1)–C(x) for x = 3,4,5.

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