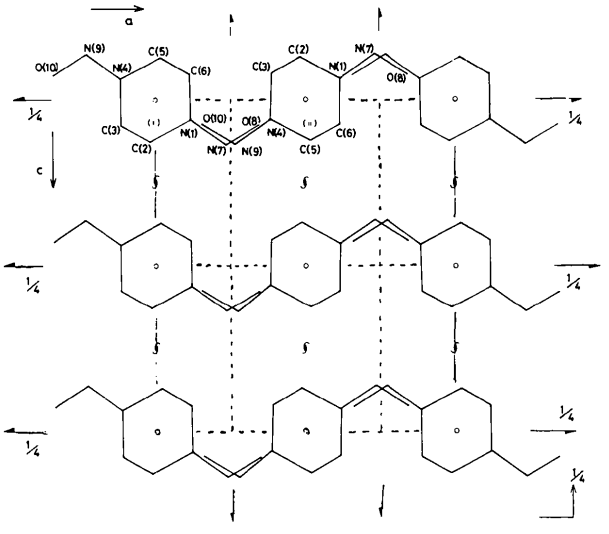

Fig. 2. The molecular packing in the unit cell viewed down the *b* axis. Symmetry codes: (i) *x*, *y*, *z*; (ii) 0·5 + *x*, 0·5 − *y*, −*z*.

found in MNA (1·234 Å). The N—N bond length of 1·336 (4) Å is in good agreement with that of 1·344 Å in MNA, and is significantly shorter than the N—N single bond (Liminga & Olovsson, 1964). This shows the N—N double-bond character. Thus the C_2NNO group results in hindered rotation about the N—N bond (Cooney, Brownstein & ApSimon, 1974).

The molecular packing viewed down the *b* axis is shown in Fig. 2. The closest non-bonded approach of 3·185 (4) Å is between N(1^{i}) and O(10^{ii}). The second-shortest contact of 3·300 (6) Å is between N(7^{i}) and N(9^{ii}). The triangular plane formed by N(1^{i}), N(7^{i}), and O(8^{i}) is approximately parallel to the neighboring triangular plane formed by N(4^{ii}), N(9^{ii}), and O(10^{ii}), the dihedral angle being 10·2 (1)°. No other short contacts can be seen in the structure. The molecules are packed together to form infinite ribbons along the [110] direction, and the ribbons are held together in the crystal by van der Waals forces.

The authors would like to thank Mr Yoshiaki Totsuka of Nippon Nyukazai Co. Ltd, Tokyo, for the supply of crystals. They are also indebted to Mr Kazumasa Maruyama and Mr Eiichi Yamamoto for their kind help in the computation.

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Structure of 2-[(Hydroxyimino)(phenylthio)methyl]-1-methylpyridinium Chloride, $C_{13}H_{13}N_2OS^+.Cl^-$

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(*Received* 27 *January* 1984; *accepted* 17 *December* 1984)

Abstract. $M_r = 280·78$, $P2_1/c$, $a = 9·30$ (1), $b = 11·433$ (7), $c = 14·02$ (2) Å, $\beta = 114·8$ (1)°, $V = 1353$ (3) Å^3, $Z = 4$, $D_x = 1·378$ Mg m^{-3}, Mo $K\alpha$, $\lambda = 0·71069$ Å, $\mu = 0·373$ mm^{-1}, $F(000) = 584$, room temperature, $R = 0·037$, 2513 unique reflections. The oxime moiety of the molecule is in the (*E*) configuration. The molecule has a folded conformation, which may be responsible for its inability to reactivate

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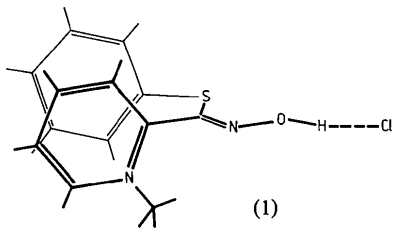
inhibited acetylcholinesterase. The cation is linked to the Cl^- anion through a hydrogen bond with an O—H···Cl distance of 2·961 (1) Å.

Introduction. The compound (1) is a derivative of the well known drug 2-(hydroxyiminomethyl)-1-methylpyridinium (2-PAM), which reactivates acetylcholinesterase (AChE) that has been inhibited by various toxic organophosphorus esters (Korolkovas & Burckhalter, 1976).



(1)

The phenylthio substituent was introduced as a potential lipophilic group, which could increase the tissue penetration by the drug molecules and make their passage from the serum to the central nervous system easier (Kenley, Howd, Mosher & Winterle, 1981; de Jong, Benschop, Van den Berg, Wolring & de Korte, 1981). Unfortunately, this derivative was found to be inactive (Serafinowa, 1981) and X-ray structure analysis was undertaken in order to establish hypothetical geometrical reasons for such behaviour.

Experimental. The crystals were supplied by Professor B. Serafinowa (Technical University, Warsaw).

Space group determined from systematic absences, $h0l$: $l = 2n + 1$, $0k0$: $k = 2n + 1$, on Weissenberg photographs (Cu-filtered radiation). Unit-cell parameters refined by least squares from θ angles, measured on Nonius CAD-4 diffractometer (graphite-monochromated Mo $K\alpha$ radiation), for 15 reflections. Details of data collection and structure refinement are given in Table 1.*

Table 1. *Data collection and refinement conditions*

Crystal size (mm)	0·45 × 0·25 × 0·45
Scan mode	$\omega/2\theta$
Scan range (°)	$1 \le \theta \le 27$
hkl range	$0 \le h \le 11$ $0 \le k \le 14$ $-17 \le l \le 17$
Scan width (°)	$0{\cdot}80 + 0{\cdot}40 \tan\theta$
Control reflections	255, 363
Changes in control intensities	<3·5%, *i.e.* $<6\sigma(I)$
Number of independent reflections	2782
Criterion for observed reflections	$\lvert F_o\rvert \ge 3\sigma(F_o)$
Number of observed reflections	2513
Corrections applied	Lorentz, polarization effects
Atomic scattering factors	as in *SHELX*76
Computer programs	*SHELX*76 (Sheldrick, 1976)
Solution	automatic centrosymmetric direct methods with *SHELX*76
Refinement method	full-matrix least squares on $\lvert F_o\rvert$'s
Parameters refined	228
non-hydrogen atoms	positional and anisotropic thermal
hydrogen atoms	positional and isotropic thermal*
Weighting scheme	$w = k[\sigma^2(F_o) + g(F_o)^2]^{-1}$, k and g converged to 2·2204 and 0·00016, respectively
R, wR	0·037, 0·039
Av., max. Δ/σ	
non-hydrogen atoms	0·02, 0·15
hydrogen atoms	0·11, 0·35
Max., min. height in final difference Fourier synthesis (e Å^{-3})	0·36, −0·25

* Initial positional parameters of most hydrogen atoms were calculated from the geometry of the molecule, those for H atoms of hydroxyl and disordered methyl groups were found from difference Fourier maps.

Discussion. The final positional parameters and equivalent isotropic U values are given in Table 2. Bond lengths and angles are listed in Table 3. A view of the molecule with its numbering scheme is shown in Fig. 1.

The oxime moiety adopts the (*E*) configuration, which is the same as that found in 2-PAM (Carlström, 1966; Van Havere, Lenstra, Geise, Van den Berg & Benschop, 1982) and in 1-benzyl-2-(hydroxyiminomethyl)pyridinium (benzyl-P_2A) methylsulphonate and bromide (Van Havere, Lenstra & Geise, 1982), which are effective reactivators of phosphorylated AChE. All the bond lengths and angles have values similar to the aforementioned structures. There is no sign of π-bond localization in the phenyl and pyridinium rings and the C(7)—N(2) bond clearly has a double-bond character. As indicated by the deviations of the atoms from the best planes through the phenyl and pyridinium rings* and by the values of the torsion angles in the oxime moiety (Table 3), these three parts of the molecule are individually planar.

The torsion angle N(2)—C(7)—C(5)—C(4) of 105·1 (3)° differs significantly from that found in benzyl-P_2A salts [32·5 (4)° for methylsulphonate and 3·9 (5) for bromide] and 2-PAM chloride [−7·6 (1)°]. This difference, despite packing considerations, may be explained by steric hindrance between the methyl group and the phenyl ring in phenylthio-2-PAM.

The overall shape of the molecule (see Fig. 1 and torsion angles in Table 3) may be described as a folded conformation, which is rather rare in crystalline structures since, for compounds with a two-atom link between two aromatic rings, an extended conformation seems to be more favourable (Fontecilla-Camps, Bugg, Temple, Rose, Montgomery & Kisliuk, 1979). For phenylthio-2-PAM the extended conformation would be energetically forbidden because of too short an

* Lists of structure factors, anisotropic thermal parameters of non-H atoms, results for H atoms, and atom deviations from the best planes have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39980 (17 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

* See deposition footnote.

Table 2. *Fractional coordinates* ($\times 10^4$) *of non-*H *atoms and equivalent isotropic thermal parameters* ($Å^2 \times 10^4$) *with e.s.d.'s in parentheses*

$U_{eq} = \frac{1}{3}\sum_i\sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
C(1)	435 (2)	6484 (1)	6398 (1)	446 (4)
C(2)	1687 (2)	5768 (1)	6544 (1)	497 (4)
C(3)	3194 (2)	6176 (2)	7090 (1)	496 (4)
C(4)	3430 (2)	7292 (1)	7498 (1)	424 (4)
C(5)	2148 (2)	7993 (1)	7350 (1)	326 (4)
C(6)	−749 (2)	8298 (2)	6691 (1)	503 (4)
C(7)	2366 (2)	9190 (1)	7790 (1)	354 (4)
C(8)	3103 (2)	7967 (1)	9620 (1)	388 (4)
C(9)	4576 (2)	7466 (2)	10168 (1)	465 (4)
C(10)	4681 (2)	6345 (2)	10557 (2)	543 (4)
C(11)	3335 (2)	5722 (2)	10403 (1)	532 (4)
C(12)	1868 (2)	6238 (2)	9868 (1)	533 (4)
C(13)	1744 (2)	7362 (2)	9484 (1)	460 (4)
N(1)	666 (2)	7578 (1)	6800 (1)	350 (4)
N(2)	2121 (2)	10037 (1)	7142 (1)	447 (1)
O	2424 (2)	11108 (1)	7659 (1)	517 (4)
S	2998·4 (7)	9418·4 (4)	9142·4 (4)	536 (2)
Cl	2417·8 (5)	12832·4 (4)	6082·5 (4)	477 (2)

Table 3. *Bond lengths* (Å) *and angles* (°) *with e.s.d.'s in parentheses, and relevant torsion angles* (°) *with e.s.d.'s* 0·3°

C(1)–C(2)	1·367 (2)	N(2)–O	1·390 (2)
C(2)–C(3)	1·367 (2)	C(7)–S	1·754 (2)
C(3)–C(4)	1·379 (2)	S–C(8)	1·777 (2)
C(4)–C(5)	1·378 (2)	C(8)–C(9)	1·384 (2)
C(5)–C(7)	1·480 (2)	C(9)–C(10)	1·380 (3)
C(5)–N(1)	1·353 (2)	C(10)–C(11)	1·377 (3)
N(1)–C(1)	1·352 (2)	C(11)–C(12)	1·384 (3)
N(1)–C(6)	1·481 (2)	C(12)–C(13)	1·379 (3)
C(7)–N(2)	1·281 (2)	C(13)–C(8)	1·383 (2)
N(1)–C(1)–C(2)	121·0 (1)	C(7)–N(2)–O	111·0 (1)
C(1)–C(2)–C(3)	119·3 (2)	N(2)–C(7)–S	122·3 (1)
C(2)–C(3)–C(4)	119·7 (2)	C(5)–C(7)–S	120·9 (1)
C(3)–C(4)–C(5)	119·9 (1)	C(7)–S–C(8)	102·1 (1)
C(4)–C(5)–N(1)	119·5 (1)	S–C(8)–C(9)	118·7 (1)
C(1)–N(1)–C(6)	118·0 (1)	C(8)–C(9)–C(10)	119·5 (2)
C(1)–N(1)–C(5)	120·5 (1)	C(9)–C(10)–C(11)	120·7 (2)
C(5)–N(1)–C(6)	121·5 (1)	C(10)–C(11)–C(12)	119·3 (2)
N(1)–C(5)–C(7)	119·4 (1)	C(11)–C(12)–C(13)	120·8 (2)
C(4)–C(5)–C(7)	121·1 (1)	C(12)–C(13)–C(8)	119·4 (1)
C(5)–C(7)–N(2)	116·8 (1)	C(13)–C(8)–S	120·9 (1)

C(9)–C(8)–S–C(7)	[τ_1]	106·5
C(4)–C(5)–C(7)–N(2)	[τ_3]	105·1
S–C(7)–C(5)–C(4)		−72·7
N(1)–C(5)–C(7)–S		106·8
S–C(7)–N(2)–O		0·0
C(7)–N(2)–O–H(O)		165·8
C(8)–S–C(7)–C(5)		−3·2
C(8)–S–C(7)–N(2)	[τ_2]	180·0

intramolecular contact between the oxygen atom of the oxime moiety and the plane of the phenyl ring (about 2·03 Å).

The potential energy for the isolated molecule in the atom–atom approximation (Motherwell, 1974) was calculated as a function of three torsion angles, τ_1, τ_2, τ_3, defined in Table 3. The energy maps revealed four minima related to one another, which correspond to the observed folded conformation with calculated values $\tau_1 = 80·3$, $\tau_2 = 149·3$ and $\tau_3 = 89·7°$.

The mechanism of AChE reactivation is believed to be a two-step process (Kenley, Howd, Mosher & Winterle, 1981). In the first step a complex between the reactivator and the inhibited enzyme is formed, while in the second step the complex decomposes with nucleophilic displacement of the phosphoryl residue from the enzyme to the reactivator. In phenylthio-2-PAM the folded conformation could be considered to be responsible for its inability to reactivate phosphorylated AChE through formation of a relatively stable intermediate complex. A similar situation was established for a complex of a folded conformer of methotrexate with dihydrofolate reductase in the bacteria *E. coli* and *L. casei* (Camerman, Mastropaolo & Camerman, 1982). In contrast to the phenylthio derivative, the methylthio derivative of 2-PAM* was found to be an active reactivator of AChE (Serafinowa, 1981).

* The structure will be published later.

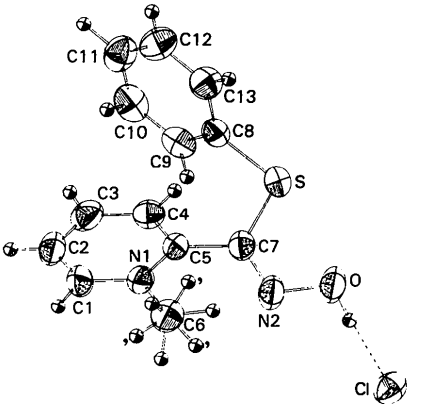


Fig. 1. *ORTEP* (Johnson, 1965) drawing of the molecule with atom numbering. Thermal ellipsoids are shown at the 35% probability level. Hydrogen atoms are shown as spheres of arbitrary size. The methyl group is disordered.

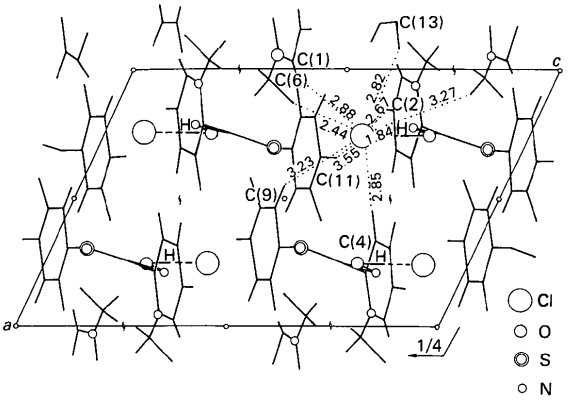
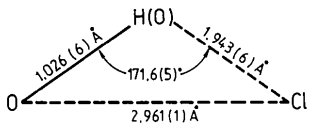


Fig. 2. Molecular packing viewed along **b**. The hydrogen bond is marked with a dashed line and other Cl contacts shorter than 3·35 Å with dotted lines. For the sake of clarity only one position of the disordered methyl group is drawn.

The packing in the structure is shown in Fig. 2. The 2-[(hydroxyimino)(phenylthio)methyl]-1-methylpyridinium cations and chloride anions are linked through a hydrogen bridge, O—H(O)···Cl, with the geometry illustrated in (2).



(2)

The existence of such a bond between halide anions and the oxygen of the oxime group has been postulated earlier in 2-(hydroxyiminomethyl)-1-methylpyridinium (2-PAM) iodide (Carlström, 1966) and in 1-benzyl-2-(hydroxyiminomethyl)pyridinium bromide (Van Havere, Lenstra & Geise, 1982), and confirmed recently in 2-(hydroxyiminomethyl)-1-methylpyridinium chloride (Van Havere, Lenstra, Geise, Van den Berg & Benschop, 1982).

We would like to thank Professor B. Serafinowa and Dr A. M. Glazer for helpful discussions. We also thank the X-ray Laboratory of SLAFiBS, Kraków, for making the diffractometer available.

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Acta Cryst. (1985). C**41**, 746–749

Absolute Structure of (+)-8α-Acetoxy-12-(4-bromobenzoyloxy)-13,14,15,16-tetranorlabdane,* $C_{25}H_{35}BrO_4$ (I), and Structure of (−)-8α,12-Dihydroxy-13,14,15,16-tetranor-9-epilabdane,† $C_{16}H_{30}O_2$ (II)

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Abstract. (I): $M_r = 479{\cdot}5$, orthorhombic, $P2_12_12_1$, $a = 6{\cdot}1383\ (7)$, $b = 17{\cdot}093\ (3)$, $c = 22{\cdot}912\ (5)$ Å, $V = 2404{\cdot}0\ (5)$ Å^3, $Z = 4$, $D_x = 1{\cdot}325$ Mg m^{-3}, Mo $K\alpha$, $\lambda = 0{\cdot}71069$ Å, $\mu = 1{\cdot}717$ mm^{-1}, $F(000) = 1008$, room temperature, $R = 8{\cdot}5\%$ for 1828 observed reflections (mostly Friedel pairs), $[\alpha]_D^{20°C} = +2{\cdot}1°$ (1·38% in $CHCl_3$), m.p. 361–363·5 K. (II): $M_r = 254{\cdot}4$, orthorhombic, $P2_12_12_1$, $a = 7{\cdot}235\ (1)$, $b = 11{\cdot}931\ (3)$, $c = 17{\cdot}064\ (4)$ Å, $V = 1473{\cdot}0\ (4)$ Å^3, $Z = 4$, $D_x = 1{\cdot}147$ Mg m^{-3}, Mo $K\alpha$, $\lambda = 0{\cdot}71069$ Å, $\mu = 0{\cdot}068$ mm^{-1}, $F(000) = 568$, room temperature, $R = 3{\cdot}7\%$ for 624 observed reflections (mostly Friedel pairs), $[\alpha]_D^{20°C} = -13{\cdot}6°$ (1·54% in $CHCl_3$), m.p. 383–384 K. The absolute configuration for chiral centres of (I) was confirmed by least-squares refinement. For the two structures, the six-membered rings are *trans*-fused and both are in the chair conformation. There are no unusual bond distances or angles.

* (+)-12-(4-Bromobenzoyloxy)-13,14,15,16-tetranorlabdan-8α-yl acetate.

† (−)-13,14,15,16-Tetranor-9β-labdane-8α,12-diol.

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