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Conformational Study of a Methylating Agent: the Crystal Structure of *S*-Methyl-L-Methionine Chloride.HCl (Vitamin U Hydrochloride)

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S-Methyl-L-methionine chloride.HCl ($C_6H_{14}NO_2SCl.HCl$) is monoclinic, space group $P2_1$, with $a = 9{\cdot}500$ (8), $b = 7{\cdot}223$ (6), $c = 8{\cdot}884$ (7) Å, $\beta = 114{\cdot}9$ (2)°, $Z = 2$. The structure was refined to $R = 0{\cdot}022$ for 1684 counter reflexions. The molecules are held together by electrostatic, hydrogen-bonding and van der Waals forces. The sulphonium group is pyramidal with the C–S bonds and angles around the S atom nearly equal (mean 1·79 Å and 102·1° respectively). Intramolecular van der Waals potential-energy calculations, carried out for *S*-methyl-L-methionine (SMM), indicate the existence of several minima. The actual molecular conformation corresponds to that of the deepest if the O atoms are neglected in the calculations. Short contacts between methyl groups and Cl^- ions were found in the crystal. If this situation were reproduced in biological systems, the polarization effect of the negative counter-ions on the C–S bonds, which are thus weakened, may support the methylating ability of the sulphonium compound when it is close to a suitable acceptor. Calculations which take into account atomic charges of SMM for its cationic, zwitterionic and anionic forms show that cyclic conformations, with the carboxyl group near to the S atom, are strongly stabilized. These conformations could explain the loss of $(CH_3)_2S$ at alkaline *p*H's from SMM. The results of the potential energy calculations are qualitatively supported by NMR spectra at different *p*H's.

Introduction

Very little is known about the structure of the methylated sulphonium group (Zuccaro & McCullough, 1959; Lopez-Castro & Truter, 1964) which is present in several methylating agents that give rise to most of the methyl transfer reactions of cellular metabolism (Shapiro & Schlenk, 1965). Attempts to crystallize *S*-adenosyl-L-methionine (SAM, upper part of Fig. 1), the most versatile methyl donor in mammalian cells (Cantoni, 1952, 1953), failed. SMM (lower part of Fig. 1) is a natural sulphonium compound which occurs in a variety of higher plants (McRorie, Sutherland, Lewis, Barton, Glazener & Shive, 1954; Schlenk, 1965), resembles the active part of SAM, enzymatically reacts with homocysteine yielding two molecules of methionine (Shapiro, 1955), and gives crystals suitable for X-ray analysis. The *S*-methylmethioninesulphonium salts (vitamin U, Bukin & Khuchua, 1973) are implicated in the prevention of shay ulcers in rats (Vinci, 1959), and of ulcers and certain hepatic disorders in humans. Moreover, it has

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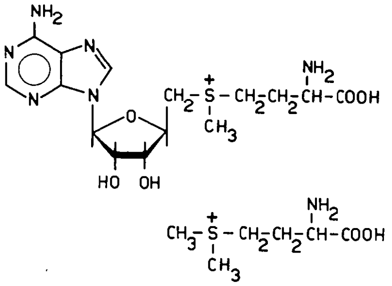

Fig. 1. Chemical structure of SAM and SMM.

been reported (Bukin & Khuchua, 1973) that the efficiency of SMM salts in the prevention and treatment of gastric ulcer may in part be ascribed to the fact that histamine would be *N*-methylated by SMM.

In order to relate the peculiar chemical behaviour of SMM with its geometry we have undertaken the determination of the crystal structure of SMM chloride.HCl, the calculation of the SMM potential energy and a NMR study in dimethyl sulphoxide and in water, the latter as a function of *p*H.

Experimental

SMM was synthesized from L-methionine, with methyl iodide as methylating agent (Toennies & Kolb, 1945). After removal of excess iodine by evaporation under reduced pressure, the SMM iodide was converted to chloride by absorption on a Dowex 50, H^+ form, column, followed by elution with 2*N* HCl.

Single crystals of SMM chloride.HCl were obtained as colourless prisms by vapour diffusion of ethyl ether in a 1:1 (v/v) methanol–ethanol mixture in which the compound was dissolved. The crystal data are reported in Table 1. The density was measured by flotation in a chloroform–ethyl ether mixture.

The crystal, 0·45 × 1·25 × 0·53 mm, was mounted with **b** nearly coincident with the polar φ axis of the goniostat. The lattice constants and intensities were measured with Mo $K\alpha$ radiation on an automatic four-circle Philips PW 1100 single-crystal diffractometer equipped with a scintillation counter, pulse-height analyser and graphite monochromator.

The intensities were collected within the range $4° \le 2\theta \le 60°$ by the ω-scan technique. Each reflexion was scanned once at a rate of 3·6° $\min^{-1}$ over a range of 1·2°. Background counts were taken for a time equal to that of the scan. 1684 independent reflexions with $I > 3\sigma(I)$ out of a total of 1730 were recorded. Three standard reflexions, monitored every 3 h, remained essentially constant, showing only the deviations from the mean predicted by counting statistics. The data were corrected for counting losses (Arndt & Willis, 1966), with $t = 2{\cdot}5 \times 10^{-6}$ s and $K = 1$, and for background. Standard deviations were assigned according to $\sigma(I) = [P + B(pI)^2]^{1/2}$ where P is the total integrated peak count, B the total background count, $I = P - B$ and p is the 'ignorance factor' (Corfield, Doedens & Ibers, 1967) fixed as 0·06. Lorentz and polarization factors were applied (Azaroff, 1955). No absorption correction was applied $[\mu(\text{Mo } K\alpha) = 7{\cdot}2\ \text{cm}^{-1}]$. All calculations were carried out on the Univac 1110 computer of the Università di Roma.

Table 1. *Crystal data* (*room temperature*) *of SMM chloride*.HCl

$\lambda = 0{\cdot}7107$ Å
$a = 9{\cdot}500$ (8)
$b = 7{\cdot}223$ (6)
$c = 8{\cdot}884$ (7)
$\beta = 114{\cdot}9$ (2)°
$Z = 2$

Systematic absences $0k0: k \ne 2n$
Space group $P2_1$
$M_r = 236{\cdot}2$
$D_x = 1{\cdot}39$ g cm^{-3}
$D_m = 1{\cdot}39$

The NMR spectra were recorded on Varian XL-100-15 and on Bruker 270 spectrometers.

Structure solution and refinement

The structure was solved from a Patterson map. A Fourier synthesis phased on the Cl and S atoms revealed all the non-hydrogen atoms. Refinement was by isotropic and anisotropic full-matrix least squares with all observed reflexions. Scattering factors for Cl^-, S, O, N and C were from Cromer & Mann (1968) and for H from Hanson, Herman, Lea & Skillman (1964). The function minimized was $\Sigma\, w(|F_o| - |F_c|)^2$, w being equal to $(a + b|F_o| + c|F_o|^2)^{-1}$ with $a = 3{\cdot}000$, $b = 1{\cdot}000$ and $c = 0{\cdot}014$. The correction for the anomalous dispersion due to Cl^- and S was taken into account. A difference synthesis showed all the H atoms at expected positions. These were included in the last three cycles of refinement with an overall isotropic B of 4 Å^2, keeping fixed their positional parameters. The refinement was considered to be complete when the parameter shifts were less than 10% of the estimated standard deviations.

The sum of the square of the ratios between the parameter shifts and the estimated standard deviations is 0·62. The adequacy of the weighting scheme was checked by inspection of the mean of $w|\Delta F^2|$ as a function of the $|F_o|$ and $\sin\theta/\lambda$ ranges: in both cases the function was nearly constant. The final R and R_w are 0·022 and 0·040, respectively, for the observed reflexions. The final atomic coordinates are reported in Table 2.*

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* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32661 (15 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 2. *Final fractional coordinates* ($\times 10^4$; *for* H $\times 10^3$) *with their standard deviations in parentheses*

	x	*y*	*z*
Cl(1)	3169 (1)	3000*	160 (1)
Cl(2)	8131 (1)	3158 (1)	4818 (1)
S(1)	2364 (0)	7511 (1)	1179 (1)
O(1)	6325 (2)	8400 (3)	6285 (2)
O(2)	8842 (2)	7972 (4)	6917 (2)
N(1)	8293 (2)	7247 (3)	3749 (2)
C(1)	7536 (2)	8185 (3)	5934 (2)
C(2)	7048 (2)	8201 (3)	4056 (2)
C(3)	5497 (2)	7259 (3)	3022 (2)
C(4)	4117 (2)	8528 (3)	2698 (2)
C(5)	961 (2)	9252 (4)	935 (3)
C(6)	2606 (2)	7753 (4)	−701 (2)
H1(O1)	672	841	741
H1(N1)	920	770	435
H2(N1)	835	597	391
H3(N1)	809	731	272
H1(C2)	705	947	367
H1(C3)	540	616	356
H2(C3)	552	692	199
H1(C4)	394	862	357
H2(C4)	416	977	227
H1(C5)	3	895	2
H2(C5)	94	939	170
H3(C5)	873	531	945
H1(C6)	176	730	852
H2(C6)	322	688	930
H3(C6)	310	902	926

* This coordinate was kept fixed during the refinement.

The programs of Domenicano, Spagna & Vaciago (1969) were used for the crystallographic calculations.

Molecular geometry and conformation

Bond distances and angles are reported in Fig. 2. The sulphonium group is pyramidal. The three bond lengths and angles are nearly equal, mean 1·788 Å and 102·1° respectively. The geometry is similar to that in other methylated sulphonium groups (Zuccaro & McCullough, 1959; Lopez-Castro & Truter, 1964). Very similar bond distances and angles are also displayed by L-methionine (Torii & Iitaka, 1973) and L-methionyl-L-methionine (Stenkamp & Jensen, 1975), in which the S atom is not charged.

A significant difference is shown by the two C—O distances (1·322 and 1·188 Å) in the carboxyl group. This large difference can be ascribed in part to the fact that O(1) is engaged in a hydrogen bond with a Cl^- ion. The angle C(1)—C(2)—C(3) is larger (115·1°) than the regular tetrahedral value, probably owing to the O(1)···H1(C4) intramolecular contact, 2·53 Å, only slightly shorter than the 2·60 Å van der Waals distance listed for an O···H contact. Another slightly short intramolecular distance, 2·45 Å, occurs between O(2) and H1(N1), so that a weak intramolecular hydrogen bond might be supposed to be formed, the N(1)···O(2) distance being 2·69 Å.

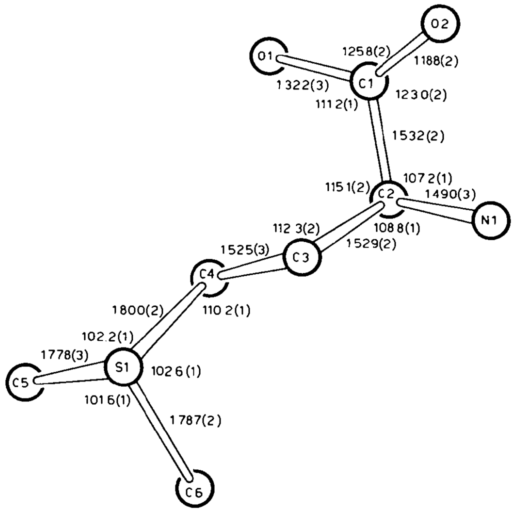

Fig. 2. SMM bond distances and angles with the estimated standard deviations in parentheses.

The conformation is described (Klyne & Prelog, 1960) by four internal rotation angles ψ_1, ψ_2, ψ_3 and ψ_4 (Fig. 3) which represent the dihedral angles O(2)—C(1)—C(2)—C(3), C(1)—C(2)—C(3)—C(4), C(2)—C(3)—C(4)—S(1) and C(3)—C(4)—S(1)—C(6) respectively. The actual conformation is given by ψ_1 = 141·8, ψ_2 = 82·5, ψ_3 = 169·6, ψ_4 = 287·8°: Table 3 lists all the torsion angles. N(1), C(2), C(3), C(4), S(1) and C(5) form a distorted *trans*-planar chain. The conformation is very similar to that found by Torii & Iitaka (1973) in one of the two crystallographically

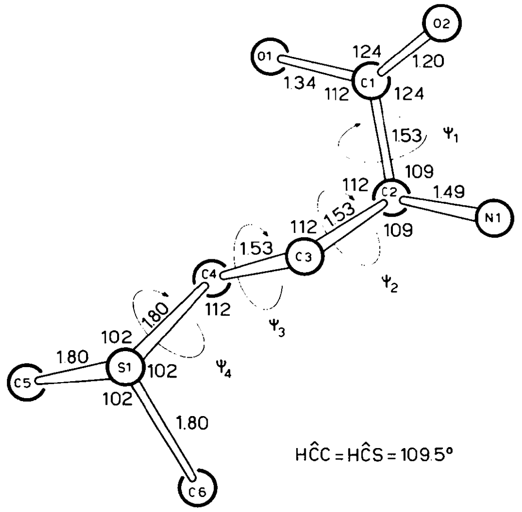

Fig. 3. Intramolecular bond distances and angles assumed in the conformational analysis of SMM. The arrows indicate the bonds around which the rotations occur.

Table 3. *Internal rotation angles (°) of SMM found in the crystal*

Some relevant values of L-methionine (two molecules in the asymmetric unit) are reported in parentheses.

O(1)–C(1)–C(2)–N(1)	201·7	
O(1)–C(1)–C(2)–C(3)	322·9	
O(2)–C(1)–C(2)–N(1)	20·5	(342·5, 325·7)
O(2)–C(1)–C(2)–C(3)	141·8	
C(1)–C(2)–C(3)–C(4)	82·5	
N(1)–C(2)–C(3)–C(4)	202·8	(194·0, 194·4)
C(2)–C(3)–C(4)–S(1)	169·6	(174·2, 73·6)
C(3)–C(4)–S(1)–C(5)	182·7	(179·7, 73·6)
C(3)–C(4)–S(1)–C(6)	287·8	

independent molecules of L-methionine; the corresponding values of some torsion angles are reported in Table 3. The methyl groups of L-methionine and SMM give rise to *trans*, *gauche* or *gauche** conformations.

The O(2)–C(1)–C(2)–N(1) torsion angle in SMM is remarkably different from those in L-methionine, the differences being 38·0 and 54·8°. These permissible conformations may be mainly stabilized by inter- and, probably weak, intra-molecular hydrogen-bonding forces.

Crystal packing and hydrogen-bonding

The molecular arrangement along **b** is shown in Fig. 4. The crystal packing is stabilized mainly by electrostatic, van der Waals and hydrogen-bonding forces. S(1), C(5) and C(6) are engaged in very strong interactions with surrounding atoms and ions (Fig. 5). S(1), C(5) and C(6) are connected by thick lines. The thin lines indicate the contacts of S(1) and the dotted and the dashed refer to the contacts of the two methyl groups. Strong Coulombic interactions exist between three Cl^- ions and the positively charged S(1): the strongest is established with Cl(1) located on the same side of the S(1) lone pair. S(1) is also engaged in a good van der Waals contact with one methyl group. One of the methyl groups is surrounded by four Cl^- ions, one O atom and one methyl group. The other strongly interacts with three Cl^- ions, one charged S atom, two O atoms and two methyl groups (Table 4). Three

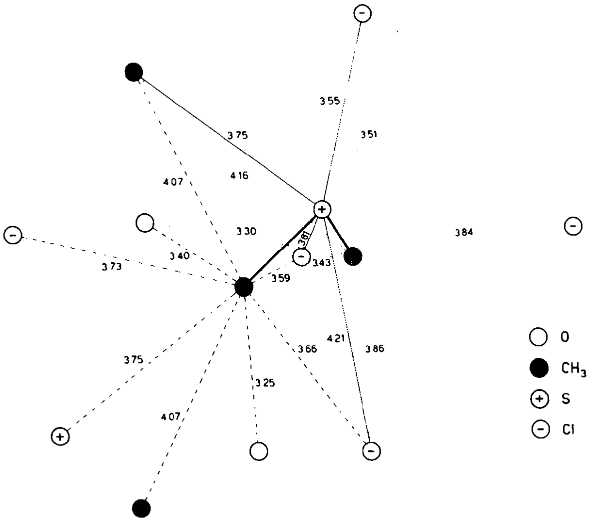

Fig. 5. The most relevant intermolecular contacts of the $-\overset{+}{S}(CH_3)_2$ group viewed approximately along **c**.

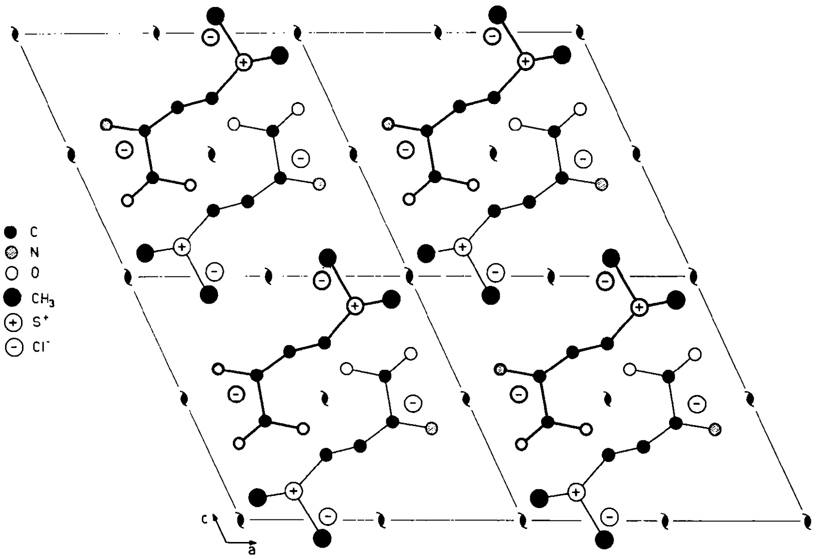

Fig. 4. Crystal packing of SMM chloride.HCl viewed along **b**. The thick lines indicate the upper molecules.

Table 4. *Most relevant distances* (Å) *involving Coulombic, van der Waals and hydrogen-bonding interactions in SMM chloride*.HCl

Coulombic		van der Waals	
Cl(1)–S(1)	3·55	Cl(1)–C(5$^{\rm i}$)	3·66
Cl(1)–S(1$^{\rm i}$)	4·21	Cl(1)–C(5$^{\rm v}$)	3·73
Cl(2)–S(1$^{\rm ii}$)	3·81	Cl(1)–C(6)	3·51
Cl(2)–N(1$^{\rm i}$)	4·39	Cl(1)–C(6$^{\rm i}$)	3·86
		Cl(1)–C(6$^{\rm iii}$)	3·84
Hydrogen-bonding		Cl(2)–C(5$^{\rm ii}$)	3·59
		Cl(2)–C(6$^{\rm iii}$)	3·43
Cl(1)–O(1$^{\rm ii}$)	3·00	S(1)–C(5$^{\rm v}$)	3·75
Cl(1)–N(1$^{\rm iii}$)	3·20	O(2)–C(5$^{\rm vi}$)	3·40
Cl(2)–N(1)	3·13	O(2)–C(5$^{\rm ii}$)	3·25
Cl(2)–N(1$^{\rm iv}$)	3·15	O(2)–C(6$^{\rm vi}$)	3·30
		C(5)–C(5$^{\rm vii}$)	4·07
		C(5)–C(5$^{\rm v}$)	4·07
		C(5)–C(6$^{\rm vii}$)	4·16

Symmetry code

(i)	x,	$1+y$,	z	(ii)	$1-x$,	$\frac{1}{2}+y$,	$1-z$
(iii)	$1-x$,	$\frac{1}{2}+y$,	$-z$	(iv)	$2-x$,	$\frac{1}{2}+y$,	$1-z$
(v)	$-x$,	$\frac{1}{2}+y$,	$-z$	(vi)	$1+x$,	y,	$1+z$
(vii)	$-x$,	$-\frac{1}{2}+y$,	$-z$				

strong interactions are formed among the Cl$^-$ ions and the methyl groups of the sulphonium group. The corresponding distances, 3·43, 3·51 and 3·59 Å, are all shorter than the sum of the van der Waals radii. These and the Cl(1)$\cdots$C(5$^{\rm i}$), Cl(1)$\cdots$S(1) and Cl(2)$\cdots$S(1$^{\rm ii}$) interactions could produce a strong polarization effect on the methyl–sulphur bonds, thus causing a weakening of the bond strength.

Cl(1) forms a good hydrogen bond with O(1$^{\rm ii}$), the distances Cl(1)$\cdots$O(1$^{\rm ii}$), H1(O1$^{\rm ii}$)$\cdots$Cl(1), O(1)–H1(O1) and the angle O(1$^{\rm ii}$)–H1(O1$^{\rm ii}$)$\cdots$Cl(1) being 3·00, 2·14, 0·91 Å and 159·2° respectively.

N(1) shows an almost regular tetrahedral coordination with C(2), H1(N1), H2(N1) and H3(N1). Moreover, N(1) forms three hydrogen bonds with Cl$^-$ ions, located at 3·13, 3·15 and 3·20 Å from N(1) (Table 4) and approximately along the N–H directions. The angles Cl$\cdots$N–C are 96·0, 103·7 and 129·3°.

Conformational analysis of SMM

The conformational analysis was carried out in two stages. Firstly, the intramolecular van der Waals energy was computed and, subsequently, the energy calculations were performed by considering atomic charges (Del Re, 1958).

The assumed geometry is shown in Fig. 3. The C–H distances were taken as 1·08 Å. H1(O1) was generated in the plane of the carboxyl group, with O(1)–H1(O1) = 1·00 Å and C(1)–O(1)–H1(O1) 109·5°. The H atoms bound to N(1) form regular tetrahedral angles with N(1) and C(2) and bond lengths of 1·00 Å. One of them is *trans* with respect to C(3). No rotation was applied round C(1)–O(1) and C(2)–N(1). The methyl group was treated as one atom.

The charge distributions for the cationic, zwitterionic and anionic forms are reported in Figs. 6, 7 and 8

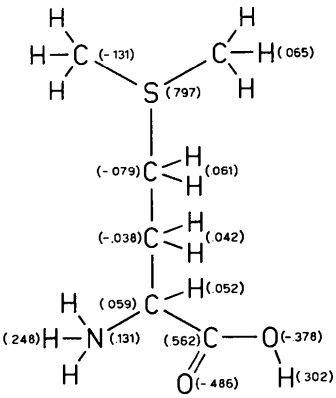

Fig. 6. Atomic charges for the cationic form of SMM.

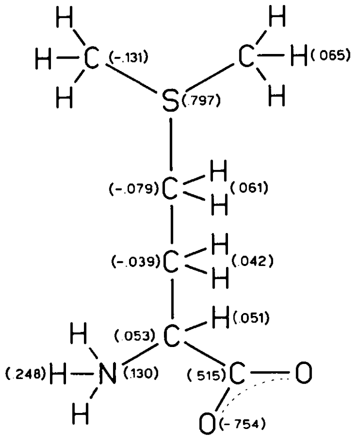

Fig. 7. Atomic charges for the zwitterionic form of SMM.

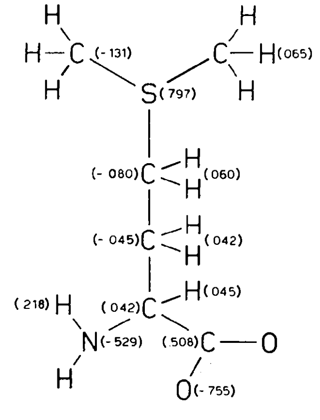

Fig. 8. Atomic charges for the anionic form of SMM.

respectively. The coefficients of the van der Waals potentials (Coiro, Giglio & Quagliata, 1972; Pavel, Quagliata & Scarcelli, 1976) in the generalized form:

$$V(r) = a\exp(-br)/r^d - cr^{-6},$$

where r is the interatomic distance, are reported in Table 5. Coulombic interactions were calculated from

$$V_{\text{el}}(r_{ij}) = q_i q_j / D r_{ij},$$

where q_i and q_j are the partial charges centred at the atoms i and j, r_{ij} is the interatomic distance and D is the dielectric constant taken as unity. The van der Waals and Coulombic energies were computed as a function of the four internal rotation angles ψ_1, ψ_2, ψ_3 and ψ_4, giving angular increments of 20 and, subsequently, of 10°. The van der Waals energy section at $\psi_1 = 70$ and $\psi_2 = 80°$ shows the deepest minima (Fig. 9). The black spot indicates the actual conformation of SMM with the exception of the ψ_1 value which is about 140 instead of 70°. Reasonably, the coordinates of the O atoms are mainly influenced by the possibility that O(1) and O(2) form inter- and intra-molecular hydrogen bonds with Cl(1) of the asymmetric unit at $(1 - x, \frac{1}{2} + y, 1 - z)$ and N(1).

Table 5. *The coefficients of the potential functions*

The energy is in kcal per atom pair if the interatomic distance is in Å.

Interaction	$a \times 10^{-3}$	b	c	d
H–H	6·6	4·080	49·2	0
H–C	44·8	2·040	125·0	6
H–N	52·1	2·040	132·0	6
H–O	42·0	2·040	132·7	6
H–CH$_3$	49·1	3·705	380·5	0
H–S	40·5	3·851	265·2	0
C–C	301·2	0·000	327·2	12
C–N	340·0	0·000	340·0	12
C–O	278·7	0·000	342·3	12
C–CH$_3$	291·1	1·665	981·1	6
C–S	255·4	1·811	684·0	6
N–O	316·2	0·000	356·0	12
N–CH$_3$	325·9	1·665	1020·5	6
N–S	288·6	1·811	711·5	6
O–CH$_3$	272·7	1·665	1026·3	6
O–S	239·2	1·811	715·5	6

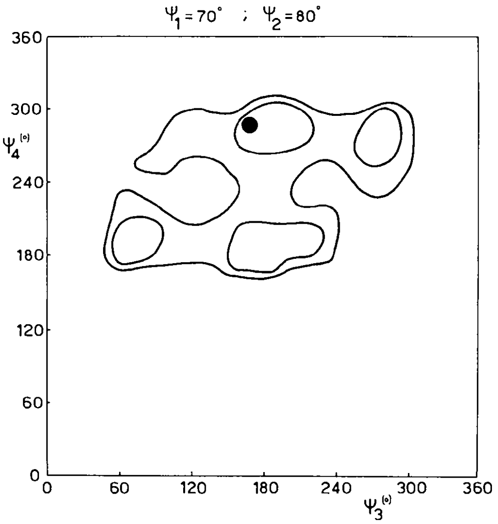

Fig. 9. Section of the van der Waals energy map of SMM at $\psi_1 = 70$ and $\psi_2 = 80°$. The contour lines are drawn at arbitrary intervals. The black spot corresponds to the actual conformation except for ψ_1.

In fact, the H1(N1)···O(2) and N(1)···O(2) distances are 2·45 and 2·69 Å, respectively, so that a weak intramolecular hydrogen bond could stabilize the actual conformation. However, the section at $\psi_1 = 140$ and $\psi_2 = 80°$ has a shape very similar to that of Fig. 9 and the observed conformation fits a relative minimum. The van der Waals energy results suggest that ψ_2 can assume mainly values within the range of the *gauche* or *trans* conformations, as supported by our and other experimental data (Torii & Iitaka, 1973). A large region, 60 to 300°, is allowed for ψ_3. Finally, the best energy values are generally observed when ψ_4 has values near 180 and 280°.

The conversion path from one minimum to the other is not hindered by a high energy barrier (see, for example, Fig. 9). Therefore, as far as the van der Waals energy is concerned, SMM exhibits a remarkable

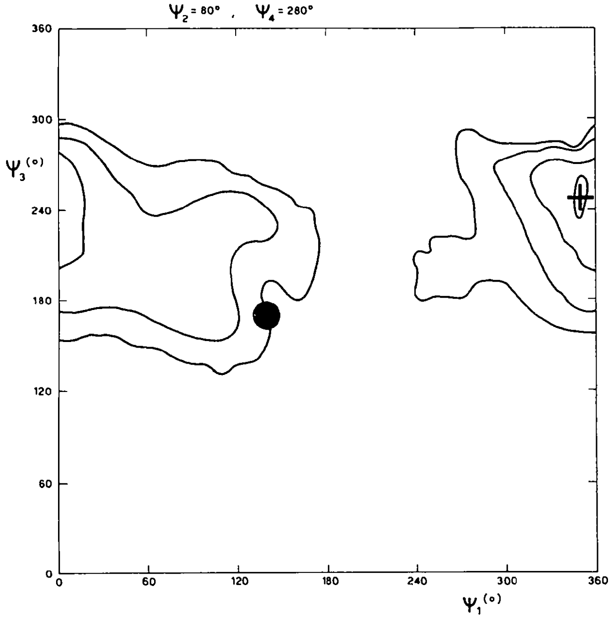

Fig. 10. Section of the energy map of the SMM cationic form at $\psi_2 = 80$ and $\psi_4 = 280°$. The contour lines are drawn at arbitrary intervals. The black spot and the cross correspond to the actual conformation and the deepest calculated minimum respectively.

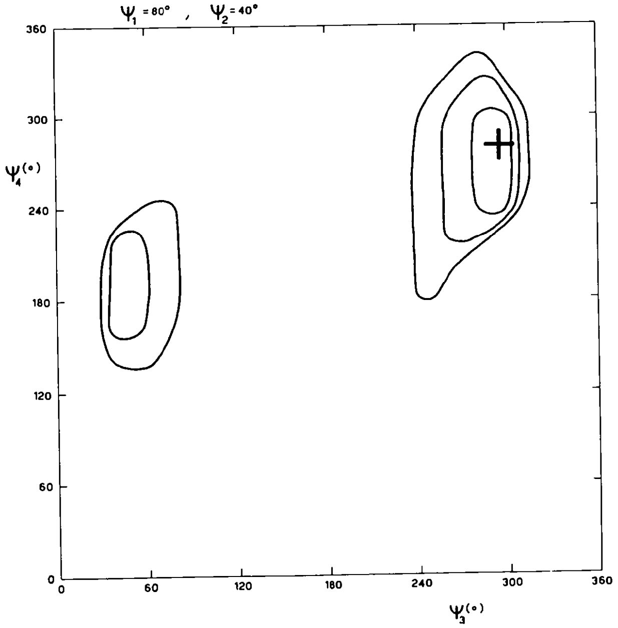

Fig. 11. Section of the energy map of the SMM anionic form at ψ_1 = 80 and ψ_2 = 40°. The contour lines are drawn at arbitrary intervals. The cross corresponds to the deepest calculated minimum.

conformational flexibility, so that many conformers may exist.

The Coulombic and van der Waals potential energy was computed for the cationic, zwitterionic and anionic forms with the charges reported in Figs. 6, 7 and 8. Two relevant sections of the maps for the cationic and anionic forms are shown in Figs. 10 and 11.

The zwitterionic has a behaviour very similar to the anionic form and no section is reported. The internal rotation angles corresponding to the lowest minima are listed in Table 6. ψ_2 and ψ_4 are in good agreement with the observed values, whereas ψ_1 and ψ_3 differ significantly. It is clear that the inclusion of the atomic partial charges favours a cyclic conformation with the positive S atom near the negative carboxyl group, especially for the anionic and zwitterionic forms. This conformation may be a suitable model to explain the degradation of a basic aqueous solution of SMM salts in dimethyl sulphide and homoserine, *via* its lactone (Schlenk, 1965; Ramirez, Finnan & Carlson, 1973). It is interesting to note that the same reaction occurs by means of a bacterial enzyme (Mazelis, Levin & Mallinson, 1965).

Table 6. *Internal rotation angles* (°) *of the SMM energy minima compared with the experimental values*

	Experimental	Cationic	Zwitterionic	Anionic
ψ_1	142	0	80	80
ψ_2	83	60	60	40
ψ_3	170	240	300	300
ψ_4	288	280	280	280

NMR study of SMM solutions

The results of the conformational calculations are also supported by NMR data. SMM was studied by proton magnetic resonance spectroscopy both in DMSO$_{d6}$ and in aqueous solutions over the *p*H range 1 to 12. SMM is quite stable at acidic and neutral *p*H values, at room temperature, whereas at *p*H's higher than 10 (*i.e.* higher than *pK*$_2$) it loses $(CH_3)_2S$ rather easily (Ramirez, Finnan & Carlson, 1973).

The same phenomenon occurs in DMSO, probably owing to the property of this solvent of enhancing the nucleophilic character of the carboxyl group. An indirect confirmation of this behaviour might come from the observation of conformational changes of the SMM molecular skeleton in going from low to high *p*H's. It was our intention to extract this information from a measurement of the coupling constants of the grouping $>CH-CH_2-CH_2-$ in aqueous solutions at various *p*H's. In fact it would be possible to correlate such data directly with the findings of the energy calculations. Unfortunately, the spectrum of the $>CH-CH_2-$ grouping appears deceptively simple both at acidic and neutral *p*H's. Thus it was not possible to extract meaningful coupling constants. Nevertheless it is interesting to note that the spectrum of very basic solutions [prior to any loss of $(CH_3)_2S$] is drastically different from those at acidic or neutral *p*H's, in a way that is qualitatively consistent with the conformational changes predicted by the energy calculations.

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Molekül- und Kristallstruktur von *N*-Benzyl-*syn*-benzamidoxim

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N-Benzyl-*syn*-benzamidoxime, $C_{14}H_{14}N_2O$, is a new self-condensation product of *syn*-benzaldoxime. It crystallizes from methanolic solution in the monoclinic space group $P2_1/a$ with $a = 12{\cdot}513\ (8)$, $b = 13{\cdot}288\ (8)$, $c = 7{\cdot}332\ (4)$ Å, $\beta = 91{\cdot}88\ (2)°$. 2299 independent reflexions were measured on an automatic diffractometer. The structure was solved by direct methods and refined by a least-squares method yielding a final R index of 0·06 for 1802 observed reflexions. The molecular geometry is compared with analogous compounds. The molecule contains an intramolecular hydrogen bond which builds up a five-membered ring. This H-bridge is formed by the amide H as donor and the oxime OH group as acceptor ($N-H\cdots OH$ 2·04 Å). In the crystal structure two molecules related by a centre of symmetry form a hydrogen-bridged dimer with two $O-H\cdots N(OH)$ hydrogen bonds ($O\cdots N$ 2·73 Å; $H\cdots N$ 1·77 Å).

Einleitung

Die Thermolyse von *syn*-Benzaldoxim (1) ist eine seit langer Zeit bekannte Reaktion (Petraczek, 1883). Als Reaktionsprodukte treten Ammoniumbenzoat, Benzamid, Benzoesäure und Benzonitril auf. Führt man jedoch diese Reaktion unter Zusatz von katalytischen Mengen bestimmter Übergangsmetallverbindungen in Gegenwart wasserentziehender Mittel durch, so entsteht ein neuartiges Kondensationsprodukt des *syn*-Benzaldoxims, welches, wie Elementaranalyse und Massenspektrum zeigten, die Summenformel $C_{14}H_{12}N_2O$ besitzt (Gieren, Dederer. Ugi & Stüber, 1977). Dieses Produkt (2*a* oder 2*b*) musste also unter Wasserabspaltung aus zwei Molekülen von (1) entstanden sein. Spektroskopische Befunde deuteten zunächst auf die Struktur (2*b*) eines Dioximäthers hin. Gegen diesen Strukturvorschlag sprach jedoch die Tatsache, dass bei der Hydrierung von (2) mit Natriumdihydro-bis(2-methoxy-äthoxy)-aluminat (Red-Al) nur eine C=N-Doppelbindung angegriffen wurde. Das Hydrierungsprodukt (3) der Alternative (2*a*) konnte aber auf chemischem und spektroskopischem Wege ebenfalls nicht eindeutig charakterisiert werden.

Zur Aufklärung der neuen metallkatalysierten Selbstkondensation haben wir zunächst das Primärprodukt (2) röntgenographisch untersucht. Da sich die Kristalle von (2) jedoch für eine Röntgenstrukturanalyse als