

between the 3-cephem nucleus and the exocyclic amide group. However, the orientation of the 7 $\beta$ -phenylglycyl group with respect to the amide group is nearly constant in ampicillin, amoxycillin and cefadroxil despite different crystal-packing environments.

Although formation of the intramolecular N(18)—H $\cdots$ O(16) hydrogen bond has been suggested based on the poorly determined crystal structure of cephaloglycine (Sweet & Dahl, 1970), such a direct hydrogen bond has not been observed in any  $\beta$ -lactam compounds containing the 7 $\beta$ -phenylglycyl side chain. In cefadroxil, the amino N(18) atom is close to the exocyclic amide O(16) [N $\cdots$ O = 2.718 (6) Å, O(16)—C(15)—C(17)—N(18) = 33.0 (4) $^\circ$ ] but there is no intramolecular hydrogen bond. Instead, these two atoms are linked by hydrogen bonds mediated by a water molecule, although the N(18)—H(*a*) $\cdots$ O(*w*) hydrogen bond is very weak (see Table 3). In amoxycillin trihydrate and ampicillin trihydrate, N(14), instead of N(18), and O(16) are linked by hydrogen bonds also mediated by a water molecule. There is no intramolecular hydrogen-bonding interaction between N(18) and O(16), even in ampicillin anhydrate.

The crystal packing (Fig. 2) consists of an intricate hydrogen-bonding network. H(18*a*) of the protonated amino group is involved in a very weak three-centred hydrogen bond with O(*w*) and  $\beta$ -lactam keto O(9). The remaining two H atoms on N(18) are hydrogen-bonded to the carboxyl O(12) and O(13) atoms in the two molecules related by a twofold

screw-axis symmetry along the *c* axis. Each carboxyl O atom accepts two hydrogen bonds. There is a hydrogen bond between the phenolic O(25) and carboxyl O(12) atoms in the molecule, related by a translation along the *a* axis [O $\cdots$ H $\cdots$ O = 2.811 (5) Å]; H(25) is disordered between these two O atoms. The same phenomenon has been observed in amoxycillin trihydrate. Each water molecule is involved in four hydrogen bonds in a tetrahedral configuration.

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## Structure of 3,4-Dimethyl-5-methylamino-1,2,4-thiadiazolium Chloride Monohydrate

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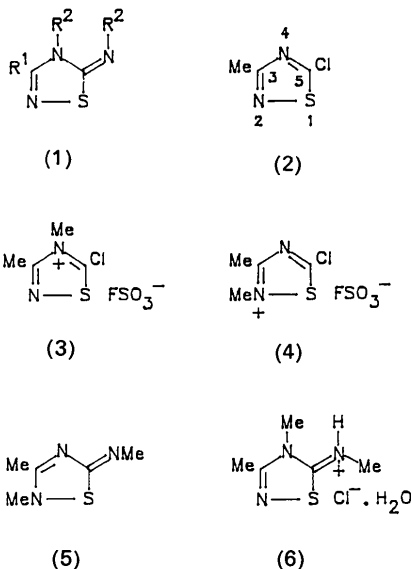
**Abstract.** C<sub>5</sub>H<sub>10</sub>N<sub>3</sub>S<sup>+</sup>.Cl<sup>-</sup>.H<sub>2</sub>O, *M*<sub>r</sub> = 197.69, monoclinic, *P*2<sub>1</sub>/*n*, *a* = 5.600 (1), *b* = 10.833 (2), *c* = 15.281 (2) Å,  $\beta$  = 97.22 (1) $^\circ$ , *V* = 919.7 (3) Å<sup>3</sup>, *Z* = 4, *D*<sub>x</sub> = 1.428 Mg m<sup>-3</sup>,  $\lambda$ (Mo *K* $\alpha$ ) = 0.71073 Å,  $\mu$  = 0.585 mm<sup>-1</sup>, *F*(000) = 416, *T* = 297 K, final *R* =

0.0454 for 1635 independent reflections [*I* > 3 $\sigma$ (*I*)]. The methyl substituent of the 5-methylamino group lies in an *E* orientation with respect to the methyl group on N(4).

**Introduction.** The determination of the structure of the title compound (6) arose from work on the

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synthesis of compounds possessing structure (1) (Nicol, 1983; Lai, 1990) which were required for the construction of new types of 1,6,6a $\lambda^4$ -triheterapentalenes (Mitchell & Reid, 1982; Lai, 1990; Billing, Boeyens, Denner, Hellyar, Lai, Matthee & Reid, 1991). We have synthesized the trimethyl derivative [(1)  $R^1 = R^2 = \text{Me}$ ] (Nicol, 1983; Lai, 1990) as follows: methylation of 5-chloro-3-methyl-1,2,4-thiadiazole (2) (Goerdeler, Groschopp & Sommerladd, 1957) with methyl fluorosulfonate in dichloromethane gave a homogeneous salt in nearly quantitative yield which must be (3), arising from methylation at N(4), or (4) arising from methylation at N(2); reaction of this salt with methylamine in ethanol gave a base which must be the required compound [(1)  $R^1 = R^2 = \text{Me}$ ], derived from the salt (3), or its isomer (5) from the salt (4). The base was a low-melting solid (m.p. 313–315 K), unstable to air, and did not form crystals suitable for crystallography, but it formed stable salts with strong acids and its hydrochloride monohydrate afforded crystals suitable for an X-ray single-crystal structure determination. This has shown that the hydrochloride monohydrate possesses structure (6) and that the corresponding base accordingly possesses structure (1) ( $R^1 = R^2 = \text{Me}$ ).



**Experimental.** The base (6) was dissolved in ethanol saturated with hydrogen chloride. Gradual addition of ether to the solution precipitated title compound (6) as colourless needle-shaped crystals, m.p. 454–457 K.  $^1\text{H}$  NMR [200 MHz,  $(\text{CD}_3)_2\text{SO}$ ]:  $\delta$  2.50 (3H, 3- $\text{CH}_3$ ), 3.02 (3H, 4- $\text{CH}_3$ ), 3.60 (*vbr*,  $\text{NH} + \text{H}_2\text{O}$ ), and 3.76 (3H,  $\text{NHCH}_3$ ).  $^{13}\text{C}$  NMR [80 MHz,  $(\text{CD}_3)_2\text{SO}$ ]:  $\delta$  16.65 (3- $\text{CH}_3$ ), 33.42 (4- $\text{CH}_3$ ), 34.14 ( $\text{NHCH}_3$ ), 160.19 (3-C), and 176.59 (5-C).

Table 1. *Atomic coordinates* ( $\times 10^4$ ) and *equivalent isotropic displacement coefficients* ( $\text{\AA}^2 \times 10^3$ )

Equivalent isotropic  $U$  is defined as one third of the trace of the orthogonalized  $U_{ij}$  tensor.

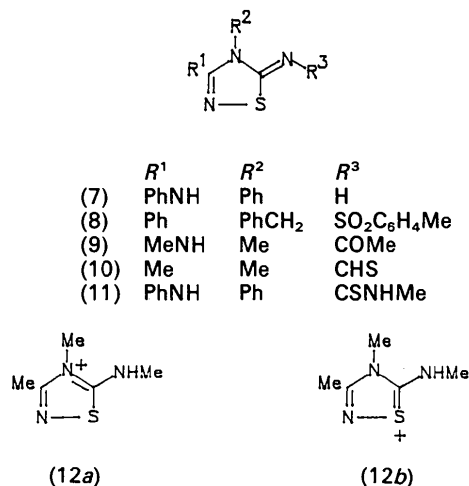
	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{eq}}$
Cl(1)	3084 (2)	7572 (1)	2465 (1)	40 (1)
S(1)	1994 (2)	9813 (1)	4162 (1)	35 (1)
N(1)	3303 (5)	8878 (3)	4960 (2)	37 (1)
N(2)	-155 (5)	7841 (3)	4451 (2)	33 (1)
N(3)	-2306 (5)	9053 (3)	3324 (2)	38 (1)
C(1)	1970 (6)	7906 (3)	5026 (2)	35 (1)
C(2)	-454 (6)	8849 (3)	3912 (2)	31 (1)
C(3)	2623 (8)	6917 (4)	5687 (3)	50 (1)
C(4)	1919 (7)	6843 (4)	4425 (3)	46 (1)
C(5)	-2445 (7)	10176 (4)	2812 (3)	51 (1)
O(1)	2785 (7)	5166 (3)	3730 (2)	72 (1)

Table 2. *Bond lengths* ( $\text{\AA}$ ) and *bond angles* ( $^\circ$ )

S(1)—N(1)	1.680 (3)	S(1)—C(2)	1.727 (3)
N(1)—C(1)	1.302 (5)	N(2)—C(1)	1.389 (4)
N(2)—C(2)	1.365 (4)	N(2)—C(4)	1.462 (5)
N(3)—C(2)	1.302 (4)	N(3)—C(5)	1.444 (5)
C(1)—C(3)	1.486 (6)		
N(1)—S(1)—C(2)	93.3 (1)	S(1)—N(1)—C(1)	110.0 (2)
C(1)—N(2)—C(2)	111.8 (3)	C(1)—N(2)—C(4)	125.2 (3)
C(2)—N(2)—C(4)	122.9 (3)	C(2)—N(3)—C(5)	120.1 (3)
N(1)—C(1)—N(2)	116.5 (3)	N(1)—C(1)—C(3)	122.7 (3)
N(2)—C(1)—C(3)	120.8 (3)	S(1)—C(2)—N(2)	108.4 (2)
S(1)—C(2)—N(3)	126.3 (3)	N(2)—C(2)—N(3)	125.3 (3)

A colourless chunk-like crystal of dimensions 0.72  $\times$  0.36  $\times$  0.32 mm was selected for X-ray analysis. A Siemens  $R3m/V$  diffractometer was used with graphite-monochromated  $\text{Mo } K\alpha$  radiation:  $\theta/2\theta$  scan technique; scan width  $1.00^\circ + K\alpha$  separation; scan speed  $2.93\text{--}14.65^\circ \text{ min}^{-1}$ . Cell parameters were determined from least-squares procedure on 19 reflections ( $15.17 < 2\theta < 31.06^\circ$ ). Systematic absences:  $h0l$ ,  $h + l = 2n + 1$ ;  $0k0$ ,  $k = 2n + 1$ . A total of 2041 reflections were measured up to  $2\theta = 50^\circ$  and in the range  $-6 \leq h \leq 6$ ,  $0 \leq k \leq 12$ ,  $0 \leq l \leq 18$ . There was no significant variation in intensities of three standards monitored every 50 reflections. 1364 unique structure amplitudes with  $I \geq 3.0\sigma(I)$  were corrected for absorption (Alcock, 1974), Lorentz and polarization effects. The structure was solved by direct methods and refined by full-matrix least squares based on  $F$  values. All non-H atoms were refined with anisotropic temperature factors. All the H atoms were deduced from difference electron-density maps and refined with fixed  $U$  values ( $0.08 \text{\AA}^2$ ). At convergence  $R = 0.0454$ ,  $wR = 0.0567$ ,  $w = [\sigma^2(F) + 0.0027F^2]^{-1}$ ,  $\sigma^2(F)$  based on counting statistics,  $(\Delta/\sigma)_{\text{max}} = 0.001$ ,  $S = 1.53$ ,  $(\Delta\rho)_{\text{max}} = 0.62$ ,  $(\Delta\rho)_{\text{min}} = -0.36 \text{ e \AA}^{-3}$ . Scattering factors were taken from *International Tables for X-ray Crystallography* (1974, Vol. IV). All calculations were performed on a DEC MicroVAX II computer system using the *SHELXLTL-Plus* programs (Sheldrick, 1990).

**Discussion.** Final atomic coordinates and bond distances and angles are listed in Tables 1 and 2.\* The structure of 3,4-dimethyl-5-methylamino-1,2,4-thiadiazolium chloride monohydrate (6) is shown in Fig. 1, which also defines the crystallographic numbering scheme. The cation in (6) is nearly planar, with maximum deviations from planarity not exceeding 0.0352 Å.



The dimensions of the heterocycle in (6) are similar to those of five 5-imino-4,5-dihydro-1,2,4-thiadiazoles whose structures have previously been determined, namely (7) (Butler, Glidewell & Liles, 1978), (8) (L'abbé, Verhelst, Toppet, King & Briers, 1976), (9) (Sato, Kinoshita, Hata & Tamura, 1972), (10) (Glidewell & Liles, 1981) and (11) (Cuthbertson & Glidewell, 1981). The lengths of the ring bonds and the exocyclic N(3)—C(2) bond in the salt (6) all lie in the range found for the corresponding bonds in

\* Lists of structure factors, anisotropic thermal parameters, H-atom parameters and least-squares-planes data have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55015 (9 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

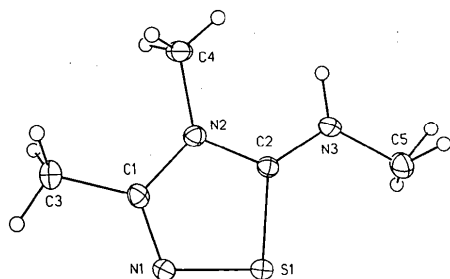


Fig. 1. Molecular structure and atom-numbering scheme of the cation in the title compound.

compounds (7)–(11). The lengths of these bonds in compound (6) are especially close to those of the corresponding bonds in compounds (8) and (9); for compounds (6), (8) and (9) the bond length ranges are: S(1)—N(1) 0.01, N(1)—C(1) 0.012, N(2)—C(1) 0.001, N(2)—C(2) 0.005, S(1)—C(2) 0.01, N(3)—C(2) 0.008 Å.

Comparison of the bond lengths of the cation in (6) with those of the structurally closely related imine (7) shows that whereas the lengths of the S(1)—N(1), the N(1)—C(1), and the N(2)—C(1) bonds in (6) [S(1)—N(1) 1.68 (3), N(1)—C(1) 1.302 (5), N(2)—C(1) 1.389 (4) Å] are almost identical with those of the corresponding bonds in the imine (7) [S(1)—N(1) 1.691 (3), N(1)—C(1) 1.294 (4), N(2)—C(1) 1.386 (4) Å], the N(2)—C(2) and the S(1)—C(2) bonds in (6) are shorter [N(2)—C(2) 1.365 (4), S(1)—C(2) 1.728 (3) Å] than the corresponding bonds in the imine (7) [N(2)—C(2) 1.402 (4), S(1)—C(2) 1.761 (4) Å], but the exocyclic N(3)—C(2) bond in (6) [1.302 (4) Å] is longer than that in the imine (7) [1.264 (5) Å]. The shortening of the N(2)—C(2) and the S(1)—C(2) bonds and the lengthening of the N(3)—C(2) bond in (6) relative to the corresponding bonds in the imine (7) can be attributed to delocalization of the charge in the cation in (6) as expressed by the contributing structures (12a) and (12b). The N(3)—C(2) bond is nevertheless still a short bond and restricted rotation about this bond allows two possible arrangements of the substituents on N(3). The observed arrangement in which the smaller group H is closer to the methyl group on N(2), minimizes the steric repulsion between the methyl group on N(2) and its neighbouring group on N(3). The water molecule resides in the lattice without forming any hydrogen bonds.

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