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Structure of N^1-(4,6-Dimethyl-2-pyrimidinyl)sulfanilamide Methanol Solvate, $C_{12}H_{14}N_4O_2S.CH_3OH$

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Abstract. $M_r = 310{\cdot}38$, orthorhombic, $P2_12_12_1$, $a = 19{\cdot}187\ (7)$, $b = 8{\cdot}334\ (2)$, $c = 9{\cdot}749\ (3)$ Å, $V = 1558{\cdot}9\ (8)$ Å^3, $Z = 4$, $D_x = 1{\cdot}32$ g cm^{-3}, λ(Mo $K\alpha$) $= 0{\cdot}71069$ Å, $\mu = 2{\cdot}23$ cm^{-1}, $F(000) = 656$, $T = 291$ K, final $R = 0{\cdot}037$ for 1002 observed reflexions. There is one short intermolecular contact between the two molecules of the asymmetric unit. The usual conformation of 2-pyrimidinylsulfanilamide derivatives is observed.

Introduction. The present work is a part of our study of polymorphism and pseudopolymorphism in sulfamides. The structure of the unsolvated molecule of the title compound (or sulfamethazine) was elucidated by Rambaud, Maury, Pauvert, Lasserre, Berge & Audran (1983). Using physicochemical methods, these authors showed that the crystals obtained in methanol were different from those crystallized from other solvents. It is confirmed that sulfamethazine is linked to methanol by hydrogen bonds.

Experimental. Colorless crystals obtained by evaporation from methanol solution. D_m not measured. Prismatic crystal, $0{\cdot}2 \times 0{\cdot}15 \times 0{\cdot}35$ mm. Lattice parameters refined using 15 reflexions in the range $5 \leq 2\theta \leq 15°$. No absorption correction. Syntex $P2_1$ diffractometer, graphite-monochromated Mo $K\alpha$ radiation. 1296 independent *hkl* reflexions (h 0→21, k 0→9, l 0→10) with $\sin\theta/\lambda \leq 0{\cdot}561$ Å^{-1}, 1002 with $I \geq 2{\cdot}5\sigma(I)$. Standard reflexion (122) checked every 50 reflexions: no significant deviation. Structure solved by direct methods with *MULTAN*80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980). H atoms from difference Fourier synthesis except those of C(21), in computed position. Anisotropic least-squares refinement (*SHELX*76, Sheldrick, 1976) using F; H isotropic with common refined temperature factor. $w = 1/(\sigma^2 + 0{\cdot}00046F^2)$, $R = 0{\cdot}037$, $R_w = 0{\cdot}037$ for 1002 observed reflexions. Final max. shift-to-error $= 0{\cdot}64$. Max. and min. heights in final difference Fourier synthesis $= 0{\cdot}7$ and $-0{\cdot}3$ e Å^{-3}. Atomic scattering factors from *International Tables for X-ray Crystallography* (1974).

Table 1. *Atomic coordinates* ($\times 10^4$) *and equivalent isotropic temperature factors* (Å^2)

$$B_{\rm eq} = \tfrac{8}{3}\pi^2 \textstyle\sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	$B_{\rm eq}$
C(1)	1050 (3)	7448 (8)	8811 (7)	3·05 (11)
C(2)	1635 (3)	8328 (8)	8411 (7)	3·11 (12)
C(3)	1662 (3)	9080 (8)	7162 (6)	2·76 (12)
C(4)	1101 (3)	8980 (7)	6266 (6)	2·72 (11)
C(5)	519 (3)	8079 (10)	6643 (7)	3·73 (13)
C(6)	490 (4)	7331 (10)	7886 (8)	4·00 (14)
N(7)	1019 (4)	6714 (9)	10052 (6)	4·74 (13)
S(8)	1122 (1)	9925 (2)	4672 (2)	2·95 (3)
O(9)	413 (2)	10232 (6)	4272 (5)	4·10 (9)
O(10)	1602 (3)	11219 (5)	4703 (5)	4·01 (9)
N(11)	1377 (3)	8608 (7)	3517 (5)	2·96 (10)
C(12)	2043 (3)	7954 (7)	3441 (7)	2·73 (11)
N(13)	2148 (2)	6990 (6)	2380 (5)	2·88 (10)
C(14)	2792 (3)	6343 (8)	2269 (7)	3·15 (12)
C(15)	3297 (4)	6682 (9)	3243 (8)	3·71 (14)
C(16)	3133 (3)	7680 (8)	4303 (7)	3·39 (13)
N(17)	2496 (2)	8340 (6)	4428 (5)	2·91 (9)
C(18)	2925 (5)	5259 (11)	1099 (10)	5·06 (18)
C(19)	3635 (4)	8082 (15)	5462 (11)	5·49 (20)
O(20)	−295 (3)	11254 (8)	1860 (6)	4·97 (11)
C(21)	−462 (6)	9800 (14)	1239 (13)	7·59 (28)

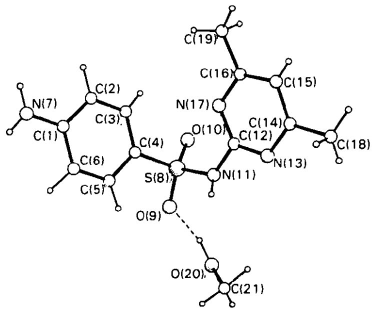

Fig. 1. View of the sulfamethazine–methanol complex.

Discussion. The atomic parameters are given in Table 1.* Fig. 1 is a view of the complex between sulfamethazine and methanol, giving the numbering of the atoms; Fig. 2 shows the packing in the unit cell (drawn with *PLUTO*, Motherwell & Clegg, 1978). Bond distances and angles are given in Table 2. They are in good agreement with the values observed in isolated sulfamethazine (Rambaud *et al.*, 1983): the mean absolute differences are respectively 0·01 Å and 0·8°. The two S—O bond lengths differ significantly, the largest one corresponding to an oxygen atom [O(9)] involved in a hydrogen bond.

The two six-membered rings are planar. The conformation of such molecules can be completely defined by three torsional angles: τ_1 = C(3or5)—C(4)—S(8)—N(11), τ_2 = C(4)—S(8)—N(11)—C(12), τ_3 = S(8)—N(11)—C(12)—N(13or17). In Table 3, these angles are compared for various molecules containing the 2-pyrimidinylsulfanilamide fragment. It can be seen that in spite of some flexibility, the conformations are quite comparable.

The cohesion of the crystal is stabilized by four hydrogen bonds described in Table 4.* As can be seen on Fig. 2, the methanol appears in cavities between the sulfamethazine molecules. It is linked to the sulfone atom O(9) and the amide atom N(11) of two different sulfamethazine molecules.

Note added in proof: The structure of the unsolvated molecule of sulfamethazine has also been elucidated by Basak, Mazumdar & Chaudhuri (1983) and Tiwari, Haridas & Singh (1984). The results obtained by the present authors are in good agreement with those of Basak *et al.* (1983).

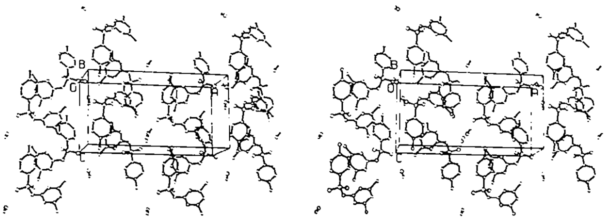

Fig. 2. Stereoview of the packing in the unit cell.

Table 2. *Bond distances* (Å) *and angles* (°)

C(2)—C(1)	1·397 (7)	C(6)—C(1)	1·406 (8)
N(7)—C(1)	1·357 (7)	C(3)—C(2)	1·370 (8)
C(4)—C(3)	1·390 (7)	C(5)—C(4)	1·394 (7)
S(8)—C(4)	1·743 (5)	C(6)—C(5)	1·364 (8)
O(9)—S(8)	1·438 (4)	O(10)—S(8)	1·418 (4)
N(11)—S(8)	1·647 (5)	C(12)—N(11)	1·391 (6)
N(13)—C(12)	1·325 (6)	N(17)—C(12)	1·337 (6)
C(14)—N(13)	1·353 (7)	C(15)—C(14)	1·386 (8)
C(18)—C(14)	1·477 (9)	C(16)—C(15)	1·364 (8)
N(17)—C(16)	1·344 (7)	C(19)—C(16)	1·522 (10)
C(21)—O(20)	1·391 (10)		

C(6)—C(1)—C(2)	118·1 (5)	N(7)—C(1)—C(2)	121·4 (6)
N(7)—C(1)—C(6)	120·5 (5)	C(3)—C(2)—C(1)	121·3 (5)
C(4)—C(3)—C(2)	120·1 (5)	C(5)—C(4)—C(3)	119·2 (5)
S(8)—C(4)—C(3)	121·0 (4)	S(8)—C(4)—C(5)	119·8 (4)
C(6)—C(5)—C(4)	120·9 (5)	C(5)—C(6)—C(1)	120·5 (6)
O(9)—S(8)—C(4)	107·5 (2)	O(10)—S(8)—C(4)	109·9 (2)
O(10)—S(8)—O(9)	119·0 (2)	N(11)—S(8)—C(4)	108·4 (2)
N(11)—S(8)—O(9)	102·4 (2)	N(11)—S(8)—O(10)	109·1 (2)
C(12)—N(11)—S(8)	124·8 (4)	N(13)—C(12)—N(11)	114·8 (4)
N(17)—C(12)—N(11)	117·7 (5)	N(17)—C(12)—N(13)	127·5 (5)
C(14)—N(13)—C(12)	116·3 (4)	C(15)—C(14)—N(13)	120·2 (5)
C(18)—C(14)—N(13)	117·6 (5)	C(18)—C(14)—C(15)	122·2 (6)
C(16)—C(15)—C(14)	118·9 (5)	N(17)—C(16)—C(15)	121·9 (5)
C(19)—C(16)—C(15)	123·4 (5)	C(19)—C(16)—N(17)	114·7 (5)
C(16)—N(17)—C(12)	115·3 (5)		

Table 3. *Comparison of the conformations of 2-pyrimidinylsulfanilamide fragments*

Compound	τ_1 (°)	τ_2 (°)	τ_3 (°)
(*a*)	95 (1)	−68 (1)	4 (1)
(*b*)	129	−82	34
(*c*)	107	−53	−34
(*d*)	113	−58	−28
	105	−58	−17
(*e*)	136	−65	−12
(*f*)	121	−77	16
(*g*)	102	−71	−5
Mean	113	−66	−9

(*a*) This molecule. (*b*) Isolated sulfamethazine (Rambaud *et al.*, 1983). (*c*) Sulfadiazine.Ag^+ (Cook & Turner, 1975). (*d*) N^1-(5-Methoxy-2-pyrimidinyl)sulfanilamide (form I) (Giuseppetti, Tadini, Bettinetti & Giordano, 1977). (*e*) As (*d*), form III. (*f*) Sulfadiazine (Shin, Ihn, Kim & Koo, 1974). (*g*) Sulfamerazine (Acharya, Kuchela & Kartha, 1982).

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* Lists of structure factors, anisotropic thermal parameters, H-atom coordinates, bond distances and angles involving H, and Table 4 have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39496 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

* Deposited.

References

Acharya, K. R., Kuchela, K. N. & Kartha, G. (1982). *J. Crystallogr. Spectrosc. Res.* **12**(4), 369–376.

Basak, A. K., Mazumdar, S. K. & Chaudhuri, S. (1983). *Acta Cryst.* C**39**, 492–494.

Cook, D. S. & Turner, M. F. (1975). *J. Chem. Soc. Perkin Trans.* 2, pp. 1021–1025.

Giuseppetti, G., Tadini, C., Bettinetti, G. P. & Giordano, F. (1977). *Cryst. Struct. Commun.* **6**, 263–274.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press.

Main, P., Fiske, S. J., Hull, S. E., Lessinger, L., Germain, G., Declercq, J.-P. & Woolfson, M. M. (1980). *MULTAN80. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. of York, England, and Louvain-la-Neuve, Belgium.

Motherwell, W. D. S. & Clegg, W. (1978). *PLUTO*. Program for plotting molecular and crystal structures. Univ. of Cambridge, England.

Rambaud, J., Maury, L., Pauvert, B., Lasserre, Y., Berge, G. & Audran, M. (1983). *J. Pharm. Sci.* Submitted for publication.

Sheldrick, G. M. (1976). *SHELX76*. Program for crystal structure determination, Univ. of Cambridge, England.

Shin, H. S., Ihn, G. S., Kim, H. S. & Koo, C. H. (1974). *J. Korean Chem. Soc.* **18**, 329–340.

Tiwari, R. K., Haridas, M. & Singh, T. P. (1984). *Acta Cryst.* C**40**, 655–657.