ization of the glutamic acid amino group and side-chain carboxyl groups and leave the charged main-chain carboxyl groups jutting out of the tight dimer. Polyamines dispersed between such dimers effectively neutralize the carboxyl groups. However, the nature of the packing forces drives the polyamine backbone to adopt a less favourable *trans–gauche* conformation. This adaptability combined with their ability for electrostatic, hydrogen bonding and van der Waals interactions are important for their ubiquitous role as biological cations.

We thank CSIR for financial assistance. SR is an UGC SRF. Thanks are due to B. S. Neela for the molecular superposition program.

References

FREDERICK, A. C., WILLIAMS, D. L., UGHETTO, G., VAN DER MAREL, A. G., VAN BOOM, J. H., RICH, A. & WANG, J. H. A. (1990). *Biochemistry*, **29**, 2538–2549.
GAVEZZOTTI, A. (1983). *J. Am. Chem. Soc.* **105**, 5220–5225.
GIGLIO, E., LIQUORI, A. M. & PULITI, R. (1966). *Acta Cryst.* **20**, 683–688.
GUISEPPE, S. & FERIOLI, M. E. (1990). *Adv. Cancer Res.* **36**, 1–20.
KEARSLEY, S. K. (1989). *Acta Cryst.* A**45**, 208–210.
KUEHN, G. D., GARAY, B. R., BAGGA, S. & PHILLIPS, G. C. (1990). *Plant Physiol.* **94**, 855–857.
MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1984). *MULTAN*84. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.
NARDELLI, M. (1983). *Comput. Chem.* **7**, 95–98.
PATTABI, V. & CHANDRASEKAR, K. (1982). *Conformation in Biology*, edited by R. SRINIVASAN & R. H. SARMA, pp. 291–298. New York: Adenine Press.
RAMASWAMY, S. & MURTHY, M. R. N. (1990). *Curr. Sci.* **59**, 379–382.
RAMASWAMY, S. & MURTHY, M. R. N. (1991). *Curr. Sci.* **60**, 173–176.
RAMASWAMY, S., NETHAJI, M. & MURTHY, M. R. N. (1989). *Curr. Sci.* **58**, 1160–1163.
SEQUEIRA, A., RAJAGOPAL, H. & CHIDAMBARAM, R. (1972). *Acta Cryst.* B**28**, 2514–2519.
SHELDRICK, G. M. (1976). *SHELX*76. Program for crystal structure determination. Univ. of Cambridge, England.
SHELDRICK, G. M. (1986). *SHELX*86. Program for crystal structure determination. Univ. of Göttingen, Germany.
SLOCUM, R. D., SWAHNEY, R. K. & GALSTON, A. W. (1984). *Arch. Biochem. Biophys.* **235**, 283–303.
SMITH, T. A. (1985). *Annu. Rev. Plant. Physiol.* **36**, 117–143.
TABOR, C. W. & TABOR, H. (1984). *Annu. Rev. Biochem.* **53**, 749–790.

Acta Cryst. (1992). B**48**, 492–498

Positive Identification of Two Orthorhombic Polymorphs of Sulfamerazine ($C_{11}H_{12}N_4O_2S$), their Thermal Analyses and Structural Comparison

BY MINO R. CAIRA AND RIANA MOHAMED

Department of Chemistry, University of Cape Town, Rondebosch 7700, *South Africa*

(*Received* 15 *October* 1991; *accepted* 20 *January* 1992)

Abstract

The independent existence of at least two polymorphs [designated (I) and (II)] of sulfamerazine [4-amino-*N*-(4-methyl-2-pyrimidinyl)benzenesulfonamide] has been demonstrated by thermal analysis, X-ray crystallographic and spectroscopic methods. The single-crystal X-ray analysis of polymorph (I) is reported. Crystal data are: (I), $C_{11}H_{12}N_4O_2S$, $M_r = 264.3$, orthorhombic, $Pn2_1a$, $a = 14.474$ (2), $b = 21.953$ (2), $c = 8.203$ (1) Å, $V = 2606.5$ (5) Å^3, $Z = 8$, $D_m = 1.34$ (1), $D_x = 1.347$ Mg m^{-3}, m.p. = 509–511 K, Mo $K\alpha$, $\lambda = 0.7107$ Å, $\mu = 0.237$ mm^{-1}, $F(000) = 1104$, $T = 294$ K, final $R = 0.047$ for 1886 independent reflections. The structure of polymorph (II) (space group *Pbca*) was reported earlier [Acharya, Kuchela & Kartha (1982). *J. Crystallogr. Spectrosc. Res.* **12**, 369–376]. In both polymorphs, the repeating motif is a dimer [pseudocentrosymmetric in (I), centrosymmetric in (II)] formed *via* two N(amide)—H···N(pyrimidinyl) hydrogen bonds. Distinct differences in the X-ray powder patterns, infrared spectra and behaviour on heating for (I) and (II) allow their rapid identification. A phase transition from (II) to (I) occurring at 422–423 K has been detected. Experimental conditions for obtaining the individual polymorphs are described. The JCPDS File No. for sulfamerazine is 43-2000.

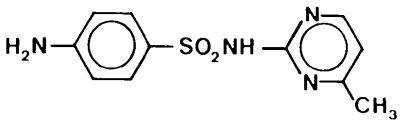
Introduction

Owing to a variety of possible hydrogen-bonding arrangements and ring-stacking modes, sulfonamides are predisposed to polymorphism (Yang & Guillory, 1972; Byrn, 1982). Numerous studies aimed at the isolation and characterization of individual

0108-7681/92/040492-07$06.00

polymorphs of sulfonamides have been undertaken because the bioavailability of solid dosage forms may be affected, depending on which polymorph of a given drug is used. Recent studies of this kind include the characterization of polymorphs of sulfapyridine (Bar & Bernstein, 1985) and sulfathiazole (Anwar, Tarling & Barnes, 1989).

The present study relates to the question of polymorphism in sulfamerazine, 4-amino-*N*-(4-methyl-2-pyrimidinyl)benzenesulfonamide (see scheme below) a constituent of the triple sulfa drug combination which contains, in addition, sulfamethazine [4-amino-*N*-(4,6-dimethyl-2-pyrimidinyl)benzenesulfonamide] and sulphadiazine (4-amino-*N*-2-pyrimidinylbenzenesulfonamide).



Earlier thermomicroscopic studies indicated the existence of at least two polymorphs of sulfamerazine (Kuhnert-Brandstätter & Wunsch, 1969; Kuhnert-Brandstätter, 1971). However, more recent studies have been unsuccessful in detecting more than one crystalline form, despite the use of different solvents and conditions for recrystallization (Yang & Guillory, 1972; Woolfenden, 1977; Deo, Tiwari & Singh, 1980; Maury, Rambaud, Pauvert, Berge, Lasserre & Audran, 1986). Maury *et al.* (1986) have attempted to explain the lack of polymorphism in sulfamerazine, sulfadiazine and sulfadimethoxine by comparing their crystal structures and infrared spectra with those of sulfonamides which are known to display polymorphism. A report on the crystal structure analysis of sulfamerazine (Acharya, Kuchela & Kartha, 1982) makes no reference to the term 'polymorphism'. Thus, the impression we gain from the recent literature relating to this drug is that the existence of only one polymorph is acknowledged.

In this study, we present unequivocal evidence based on X-ray crystallographic, thermoanalytical and spectroscopic data for the existence of at least two polymorphs of sulfamerazine and discuss their thermodynamic and structural relationships. Both polymorphs have, in fact, been investigated previously and independently by different methods, but it appears that their relationship has been overlooked. We describe the structure of a polymorph of sulfamerazine belonging to the space group $Pn2_1a$, designated (I) here. The second polymorph, referred to as (II) here, whose crystal structure has already been reported (Acharya *et al.*, 1982), belongs to the space group *Pbca*.

Crystals of polymorphs (I) and (II) are readily distinguished on the basis of their morphology, X-ray powder patterns, infrared spectra and behaviour on heating. In view of the speculation surrounding the question of polymorphism in sulfamerazine and the importance in pharmaceutical manufacture of ensuring reproducibility, we describe procedures we used to obtain the individual polymorphs in the form of single crystals of good quality.

Experimental

General

Anhydrous sulfamerazine in powder form was obtained from the Sigma Chemical Company, Missouri, USA. Solvents used for crystallization included methanol and acetonitrile, both A. R. grade and dried over molecular sieves. Crystals of (I) exclusively ($Pn2_1a$ polymorph) were obtained by adding 0.281 g of sulfamerazine to 50 cm^3 dry MeOH and heating to 318 K with stirring for 5 min. The filtered solution was left to cool spontaneously to ambient temperature (291 K) and after four days yielded colourless crystals of (I) with rhombic prismatic habit, elongated (up to 2 mm) parallel to **c**. Density determination was by repeated flotation in C_6H_6–CCl_4 at 292 K, and for measurement, an Anton Paar density meter DMA 35 was used. Crystals of (II) exclusively (*Pbca*) were obtained by adding 0.050 g of sulfamerazine to 7 cm^3 dry MeCN and heating to 323 K with stirring for 10 min. Filtering and spontaneous cooling to 291 K followed and large colourless crystals with tabular six-sided habit were collected after one week.

Characterization included microanalyses in a Heraeus universal combustion analyser Model CHN-Rapid and thermomicroscopy using a Linkam TH600 hot stage coupled to a CO600 temperature controller. Infrared spectra were recorded as Nujol mulls between CsI plates on a Perkin–Elmer 983 spectrophotometer (4000–200 cm^{-1}). Thermogravimetric (TGA) and differential scanning calorimetric (DSC) traces were obtained using a Perkin–Elmer PC7-series thermal analysis system calibrated with indium and zinc standards. Sample masses for TGA (scan rate 10 K min^{-1}) were 3–4 mg and for DSC (scan rate 5 K min^{-1}) 10–16 mg. Samples were placed in vented pans and a N_2 purge at 40 cm^3 min^{-1} was used. Melting or other temperature ranges reported are from the extrapolated onset to the peak temperature and were reproducible within ± 1 K. For X-ray powder diffraction, samples were triturated and sieved (≤ 63 μm), packed in Al sample holders and mounted on a Philips PW1050/80 diffractometer using Ni-filtered Cu $K\alpha$ radiation (λ = 1.5418 Å). Step scans (0.02° 2θ, 2 s counting times) were performed between 2θ 8–16° using 0.5°

divergence and receiving slits and between 2θ 16–60° with slit widths 1° each. Calculated powder patterns were generated from single-crystal X-ray data with the program *LAZY PULVERIX* (Yvon, Jeitschko & Parthé, 1977). Space groups and preliminary unit-cell data were determined from X-ray precession photographs. For (I), systematic absences $hk0$ for $h = 2n + 1$, and $0kl$ for $k + l = 2n + 1$ indicated the space group to be either *Pnma* or $Pn2_1a$ (alternative setting of $Pna2_1$).

Intensity data collection and structure solution of (I)

Data were collected at 294 K on an Enraf–Nonius CAD-4 diffractometer operating in the ω–2θ scan mode with graphite-monochromated Mo $K\alpha$ radiation ($\lambda = 0.7107$ Å). Accurate cell dimensions were obtained by least-squares analysis of the setting angles of 24 reflections in the range $32 \le 2\theta \le 34°$. A final intensity acceptance limit of 20σ at 20° min^{-1} in ω was used with a maximum recording time of 60 s. Data were collected to $(\sin\theta/\lambda)_{max} = 0.595$ Å^{-1}. The intensities of three standard reflections (11,2,1, 1,16,3, 276), monitored every hour, showed negligible intensity decay (< 2%). Orientation control was performed every 200 measured reflections. Data were corrected for Lp effects and for absorption. Azimuthal scans for nine reflections with χ near 90° were used for the latter and absorption corrections were from program *EAC* (Enraf–Nonius, 1979). Crystal data, data-collection and refinement details for (I) are listed in Table 1.

The structure was solved by direct methods using *SHELXS*86 (Sheldrick, 1985) assuming the space group $Pn2_1a$ with two molecules in the asymmetric unit. The solution revealed the two independent molecules as being related by an almost exact centre of symmetry. Since the intensity statistics did not identify the space group unambiguously, attempts were made to refine the structure in *Pnma*. These attempts were not fruitful, leading to abnormally short intermolecular contacts. Full-matrix least-squares refinement on F using *SHELX*76 (Sheldrick, 1976) and minimizing $\sum w|F_o - kF_c|^2$ followed for the 30 non-H atoms initially treated isotropically. All H atoms were located from difference Fourier syntheses and, in particular, the presence of the amido tautomeric form for both molecules [*i.e.* with H atoms on N(11) and N(29)] was confirmed. These H atoms were coplanar with their S—N—C moeities but as their positions tended to drift somewhat during refinement, they were added in idealized positions with U_{iso} fixed at 0.20 Å^2 and N—H at 1.00 Å. Phenyl and methyl H atoms were also added in idealized positions (C—H = 1.00 Å) with variable common U_{iso} values for chemically similar groups. Only the amino-H atoms refined freely. All non-H atoms were treated anisotropically in the final refinement.* The final weighting scheme yielded a constant distribution of $\sum w(\Delta F)^2$ with $\sin\theta$ and with $(F/F_{max})^{1.2}$. Complex neutral-atom scattering factors for non-H atoms were employed (Cromer & Mann, 1968) and for H atoms, those of Stewart, Davidson & Simpson (1965). Dispersion corrections were from Cromer & Liberman (1970). Other programs used included *PARST* (Nardelli, 1983) and *PLUTO*89 (Motherwell, 1989).

Table 1. *Crystal data, experimental and refinement parameters for polymorph* (I)

Crystal dimensions (mm)	0.50 × 0.40 × 0.25
Range scanned θ (°)	$1 \le \theta \le 25$
Index range	h 0, 17; k 0, 26; l 0, 9
Scan width (°)	0.80 + 0.35tanθ
Vertical aperture (mm)	4
Aperture width (mm)	1.12 + 1.05tanθ
No. of reflections collected	2637
No. of unique reflections	2171
R_{int}	0.01
No. of reflections with $I > 2\sigma(I)$	1886
No. of LS parameters	349
wR	0.048
w	$[\sigma^2(F_o) + 5.21 \times 10^{-3}F_o^2]^{-1}$
S	0.809
Shift/e.s.d. max., average	0.6, 0.03
$(\Delta\rho)_{max}$ final (e Å^{-3})	0.58
$(\Delta\rho)_{min}$ final (e Å^{-3})	−0.50
Absorption corrections min., max., average	0.8047, 0.9984, 0.9030

Results and discussion

To avoid ambiguity, samples of sulfamerazine recrystallized from MeOH and MeCN respectively were checked microscopically and representative specimens were identified by single-crystal X-ray photography prior to the analyses whose results are described below. The species obtained from MeOH and crystallizing in space group $Pn2_1a$ was designated (I).

The species designated (II) obtained from MeCN, was found to have the same cell dimensions and space group (*Pbca*) as the species whose crystal structure was reported by Acharya *et al.* (1982), who stated that they obtained their crystals by slow evaporation from acetone.

TGA traces for the raw material, (I) and (II) showed no mass loss over the temperature range 298–523 K. Elemental analyses for all three samples yielded values of %C, %H and %N in accord with

* Tables of structure factors, anisotropic thermal parameters, H-atom parameters, least-squares planes and torsion angles for (I), and powder diffraction data for polymorph (II) have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 54904 (47 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: AB0256]

Table 2. *Fractional atomic coordinates* ($\times 10^4$) *and equivalent isotropic thermal parameters* ($Å^2 \times 10^3$) *with e.s.d.'s in parentheses for polymorph* (I)

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

	x	y	z	U_{eq}
C(1)	189 (3)	7347 (2)	−1855 (5)	36 (1)
C(2)	−718 (3)	7555 (2)	−1837 (6)	39 (1)
C(3)	−1172 (3)	7654 (2)	−3279 (6)	42 (1)
C(4)	−732 (4)	7562 (3)	−4768 (6)	48 (2)
C(5)	179 (4)	7352 (3)	−4777 (6)	55 (2)
C(6)	632 (3)	7246 (3)	−3332 (6)	50 (2)
N(7)	−1203 (4)	7650 (3)	−6179 (6)	74 (2)
S(8)	778 (1)	7209	−54 (1)	38 (0)
O(9)	357 (3)	7554 (2)	1214 (4)	51 (1)
O(10)	1751 (2)	7279 (2)	331 (5)	50 (1)
N(11)	686 (3)	6479 (2)	351 (6)	47 (1)
C(12)	−131 (3)	6172 (2)	630 (6)	41 (2)
N(13)	−899 (3)	6485 (2)	842 (5)	47 (2)
C(14)	−1669 (4)	6169 (3)	1135 (8)	57 (2)
C(15)	1634 (4)	5541 (3)	1252 (12)	84 (3)
C(16)	−807 (5)	5260 (3)	970 (13)	88 (3)
N(17)	33 (3)	5571 (2)	675 (7)	61 (2)
C(18)	2540 (4)	6527 (4)	1347 (11)	82 (3)
C(19)	2065 (3)	4035 (2)	1779 (5)	36 (1)
C(20)	2958 (3)	3796 (2)	1808 (6)	40 (1)
C(21)	3403 (3)	3727 (3)	3249 (6)	40 (1)
C(22)	2984 (4)	3881 (2)	4723 (6)	43 (2)
C(23)	2081 (4)	4118 (3)	4673 (6)	47 (2)
C(24)	1637 (3)	4190 (3)	3231 (6)	45 (2)
N(25)	3432 (3)	3816 (3)	6161 (6)	58 (2)
S(26)	1474 (1)	4135 (1)	43 (1)	39 (0)
O(27)	1899 (3)	3784 (2)	1279 (4)	52 (1)
O(28)	502 (2)	4071 (2)	234 (4)	51 (1)
N(29)	1564 (3)	4863 (2)	498 (6)	46 (1)
C(30)	2383 (3)	5186 (2)	−725 (7)	45 (2)
N(31)	3154 (3)	4871 (2)	−888 (5)	46 (1)
C(32)	3926 (4)	5200 (3)	−1116 (7)	55 (2)
C(33)	3904 (4)	5818 (3)	−1186 (10)	78 (3)
C(34)	3065 (4)	6098 (3)	−979 (12)	82 (3)
N(35)	2278 (3)	5783 (2)	−713 (7)	60 (2)
C(36)	4798 (4)	4843 (4)	1288 (10)	78 (3)

the theoretical values (50.0, 4.6 and 21.2 respectively) for $C_{11}H_{12}N_4O_2S$. Together, these data preclude solvates, indicating instead the presence of polymorphic forms.

X-ray powder patterns for the raw material and species (I) were found to be identical, but differed from the pattern for (II). Following the recommendations of Bar & Bernstein (1985) who suggest that the powder pattern computed from a single-crystal structure represents the best model for the pure polymorph, we have generated patterns for (I) and (II) using, respectively, our cell dimensions, space-group data and atomic parameters (Table 2), and those of Acharya *et al.* (1982). These line patterns are superimposed on the experimental patterns for (I) and (II) in Figs. 1(*a*) and 1(*b*) respectively. Close agreement between experimental and calculated 2θ values serves to indicate that neither (I) nor (II) undergoes a transformation on grinding. The pattern for (I) matches that previously reported for sulfamerazine crystallized from various solvents (Yang & Guillory, 1972; Woolfenden, 1977) and a listing of the 2θ and intensity values for this phase is therefore omitted here. A search of the JCPDS (1990) powder diffraction file for sulfamerazine revealed that the powder pattern for (II) has not been reported previously. Powder data for (II) obtained in this study have been deposited.*

DSC traces for the raw material and (I) were identical (Fig. 2*a*), showing only one endothermic peak (*P*) which corresponds to the fusion of sulfamerazine at 509–511 K. The enthalpy and entropy of fusion from repeated runs yielded ranges of 38.5–40.3 kJ mol^{-1} and 75.6–79.1 J K^{-1} mol^{-1} respectively. Yang & Guillory (1972) reported values of 36.3 kJ mol^{-1} and 71.5 J K^{-1} mol^{-1}, while more recent estimates by Maury *et al.* (1986) are 41.6 kJ mol^{-1} and 80.9 J K^{-1} mol^{-1} for ΔH_f and ΔS_f respectively. The DSC trace for (II) (Fig. 2*b*) yielded a fusion peak (*P*) with the same characteristics as those for (I), but revealed an additional

* See deposition footnote.

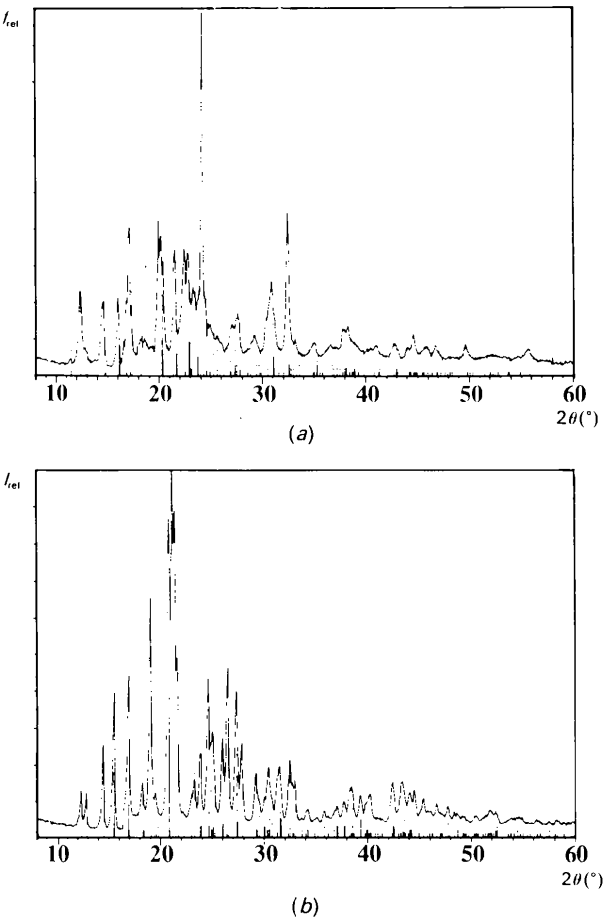


Fig. 1. Experimental and calculated X-ray powder patterns for (*a*) polymorph (I), (*b*) polymorph (II). (Intensity scaling based on matching experimental and calculated intensities for the most intense peak.)

endotherm (Q) at 422–423 K with a ΔH_t of 1.4 (2) kJ mol^{-1}. Peak Q was tentatively assumed to indicate a phase transition from (II) to (I). This was confirmed by observing large single crystals of (I) and (II) simultaneously on the hot stage at a heating rate of 2 K min^{-1} in the temperature range 373–523 K. While the crystal of (I) maintained its initial appearance until fusion, that of (II) appeared to undergo extensive fracture into slender microcrystals near 393 K, and at approximately 423 K no longer transmitted light. The two specimens melted simultaneously at 512 K. Further confirmation of the transition was obtained by heating a triturated sample of (II) at 453 K for 4 h. The resultant powder, after cooling, gave a diffractogram matching that of (I), Fig. 2(*a*), indicating complete irreversible transformation.

While the infrared spectra for the raw material and (I) were identical, distinctly different features appeared in the spectrum of (II), especially in the regions 3500–3400 and 1640 cm^{-1}, which are associated with the amino N—H stretching and —NH_2 scissoring vibrational modes (Woolfenden, 1977). These differences are reconciled below with differences in the crystal structures of (I) and (II).

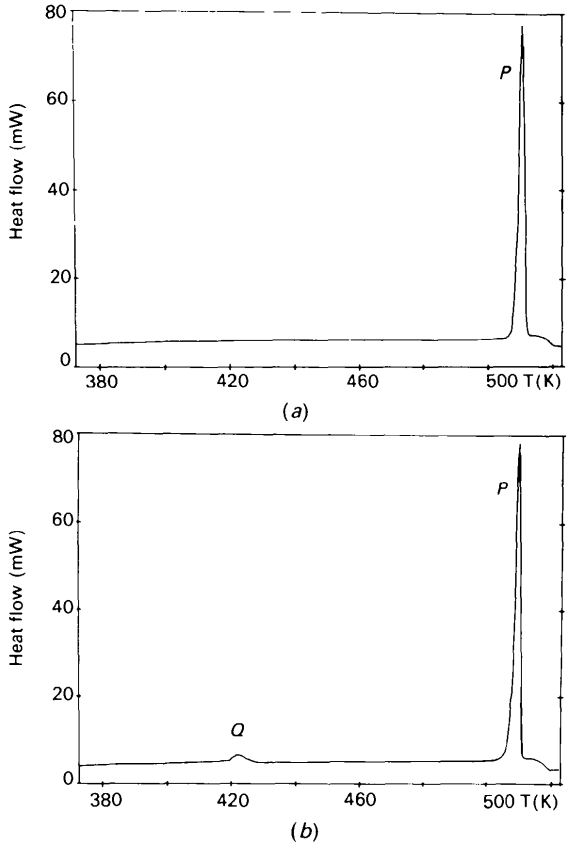


Fig. 2. DSC curves for (*a*) polymorph (I), $Pn2_1a$; (*b*) polymorph (II), *Pbca*.

On the basis of these findings, the raw material and polymorph (I) are seen to be the same phase, while (II) is a distinct polymorph. The relatively small value of ΔH_t (about 4% of ΔH_f) for the transition from (II) to (I) may account for the fact that only one sulfamerazine polymorph is generally recognized. We found that the endotherm corresponding to this transition was readily discernible in the DSC only with relatively large sample masses, so that if (II) had been encountered in earlier thermal studies, either pure or as a mixture with (I), this endotherm may have escaped detection. On the basis of thermomicroscopic data, Kuhnert-Brandstätter (1971) reported the existence of two polymorphs of sulfamerazine, designated Mod. (I) and Mod. (II), with melting points 508–511 K and ~501 K respectively. The latter species evidently arises under circumstances which suggest partial decomposition of the drug (Yang & Guillory, 1972).

Crystal structure of polymorph (I) *and comparison with polymorph* (II)

Fractional atomic coordinates and equivalent isotropic thermal parameters for (I) are listed in Table 2 and bond lengths, bond angles and hydrogen-bond data in Table 3. The structure of the asymmetric unit is shown in Fig. 3. It consists of two sulfamerazine molecules linked together by two N—H···N hydrogen bonds. The crystallographically independent molecules are related by a pseudo-centre of symmetry. While there are no significant differences between chemically equivalent bond lengths and angles in the two molecules, small but significant conformational differences exist. The principal torsion angles, namely those associated with rotation about the bonds in the C—N—S—C chain, are listed in Table 4, which includes the τ values we have calculated from the data of Acharya *et al.* (1982) for polymorph (II). It is evident that for the polymorphs of sulfamerazine, τ_1 shows the least variation in magnitude while τ_2 and τ_3 vary over a range of approximately 10°. Though not explicitly stated or discussed in the report of Acharya *et al.* (1982), sulfamerazine in polymorph (II) also exists in the form of a hydrogen-bonded dimer with, however, an exact centre of symmetry, in space group *Pbca*. The extent of hydrogen bonding is comparable for (I) and (II), which is consistent with the small value of ΔH_t accompanying the solid–solid transformation. In each case, apart from the N—H···N hydrogen bonds linking the molecules into dimers, each of the amino groups associated with a dimer engages in a single intermolecular N—H···O hydrogen bond (Table 3).

For a dimer of (I), which possesses only a pseudo-centre of symmetry, there are thus four unique hydrogen bonds (two N—H···N and two N—H···O)

Table 3. *Bond lengths* (Å), *bond angles* (°) *and hydrogen-bond geometry* (Å, °) *with e.s.d.'s in parentheses for polymorph* (I)

C(1)—C(2)	1.390 (6)	C(19)—C(20)	1.397 (6)
C(1)—C(6)	1.389 (6)	C(19)—C(24)	1.385 (7)
C(1)—S(8)	1.732 (4)	C(19)—S(26)	1.736 (4)
C(2)—C(3)	1.371 (7)	C(20)—C(21)	1.354 (7)
C(3)—C(4)	1.391 (7)	C(21)—C(22)	1.394 (7)
C(4)—C(5)	1.399 (8)	C(22)—C(23)	1.407 (8)
C(4)—N(7)	1.357 (7)	C(22)—N(25)	1.354 (7)
C(5)—C(6)	1.374 (7)	C(23)—C(24)	1.355 (7)
S(8)—O(9)	1.424 (4)	S(26)—O(27)	1.414 (4)
S(8)—O(10)	1.435 (3)	S(26)—O(28)	1.431 (3)
S(8)—N(11)	1.642 (4)	S(26)—N(29)	1.646 (5)
N(11)—C(12)	1.379 (6)	N(29)—C(30)	1.394 (6)
C(12)—N(13)	1.317 (6)	C(30)—N(31)	1.320 (6)
C(12)—N(17)	1.330 (6)	C(30)—N(35)	1.319 (6)
N(13)—C(14)	1.334 (7)	N(31)—C(32)	1.344 (7)
C(14)—C(15)	1.383 (9)	C(32)—C(33)	1.358 (9)
C(14)—C(18)	1.496 (9)	C(32)—C(36)	1.492 (9)
C(15)—C(16)	1.365 (10)	C(33)—C(34)	1.372 (9)
C(16)—N(17)	1.335 (9)	C(34)—N(35)	1.350 (8)
C(6)—C(1)—S(8)	119.3 (3)	C(24)—C(19)—S(26)	119.3 (3)
C(2)—C(1)—S(8)	120.9 (4)	C(20)—C(19)—S(26)	121.3 (3)
C(2)—C(1)—C(6)	119.9 (4)	C(20)—C(19)—C(24)	119.5 (4)
C(1)—C(2)—C(3)	119.7 (4)	C(19)—C(20)—C(21)	119.8 (4)
C(2)—C(3)—C(4)	121.1 (5)	C(20)—C(21)—C(22)	121.6 (5)
C(3)—C(4)—N(7)	120.0 (5)	C(21)—C(22)—N(25)	121.5 (5)
C(3)—C(4)—C(5)	118.9 (5)	C(21)—C(22)—C(23)	117.9 (5)
C(5)—C(4)—N(7)	121.0 (5)	C(23)—C(22)—N(25)	120.6 (5)
C(4)—C(5)—C(6)	120.1 (5)	C(22)—C(23)—C(24)	120.6 (5)
C(1)—C(6)—C(5)	120.3 (5)	C(19)—C(24)—C(23)	120.7 (5)
C(1)—S(8)—N(11)	107.7 (2)	C(19)—S(26)—N(29)	106.2 (2)
C(1)—S(8)—O(10)	109.2 (2)	C(19)—S(26)—O(28)	109.6 (2)
C(1)—S(8)—O(9)	108.6 (2)	C(19)—S(26)—O(27)	109.5 (2)
O(10)—S(8)—N(11)	102.5 (2)	O(28)—S(26)—N(29)	102.1 (3)
O(9)—S(8)—N(11)	109.7 (2)	O(27)—S(26)—N(29)	109.4 (2)
O(9)—S(8)—O(10)	118.6 (2)	O(27)—S(26)—O(28)	119.2 (2)
S(8)—N(11)—C(12)	125.3 (4)	S(26)—N(29)—C(30)	126.3 (4)
N(11)—C(12)—N(17)	113.4 (4)	N(29)—C(30)—N(35)	114.0 (4)
N(11)—C(12)—N(13)	119.5 (4)	N(29)—C(30)—N(31)	117.8 (4)
N(13)—C(12)—N(17)	127.1 (4)	N(31)—C(30)—N(35)	128.2 (4)
C(12)—N(13)—C(14)	117.3 (5)	C(30)—N(31)—C(32)	115.8 (5)
N(13)—C(14)—C(18)	116.9 (6)	N(31)—C(32)—C(36)	115.7 (6)
N(13)—C(14)—C(15)	120.0 (5)	N(31)—C(32)—C(33)	121.6 (5)
C(15)—C(14)—C(18)	123.1 (6)	C(33)—C(32)—C(36)	122.7 (6)
C(14)—C(15)—C(16)	118.1 (6)	C(32)—C(33)—C(34)	117.6 (6)
C(15)—C(16)—N(17)	122.4 (6)	C(33)—C(34)—N(35)	122.5 (6)
C(12)—N(17)—C(16)	115.1 (5)	C(30)—N(35)—C(34)	114.2 (5)

N(11)···N(35)	2.899 (6)	H(11)···N(35)	1.989 (6)	N(11)—H(11)···N(35)	150 (1)
N(29)···N(17)	2.947 (6)	H(29)···N(17)	2.085 (7)	N(29)—H(29)···N(17)	143 (1)
N(7)···O(9^{i})	3.116 (7)	H(72)···O(9^{i})	2.28 (6)	N(7)—H(72)···O(9^{i})	166 (6)
N(25)···O(27^{ii})	3.056 (6)	H(252)···O(27^{ii})	2.17 (6)	N(25)—H(252)···O(27^{ii})	149 (5)

Symmetry code: (i) $x, y, z-1$; (ii) $x, y, z+1$.

whereas for (II), where the dimer lies on an inversion centre, these degenerate into one unique N—H···N and one unique N—H···O hydrogen bond. The lower symmetry of the dimer of (I) is borne out by the infrared spectral results. Peaks assignable to ν_{as} NH_2 (Woolfenden, 1977) are split for (I), appearing at 3493 and 3478 cm^{-1}, whereas for (II) only a single peak at 3453 cm^{-1} is observed. Similarly, the $-NH_2$ scissoring vibration in (I) appears as a split peak (1626, 1639 cm^{-1}) while for (II) a single peak at 1642 cm^{-1} appears. The S—O stretching vibrations in the regions 550, 570 and 1150 cm^{-1} are relatively unaffected.

Molecular-packing schemes for the two polymorphs are shown in Figs. 4 and 5. Differences in packing arise because different pairs of sulfonyl O atoms in the dimers of (I) and (II) serve as donors in the N—H···O hydrogen bonds. Inspection of Fig. 3 reveals that atoms O(10)' and O(28) are nearly coplanar with the N—H···N hydrogen-bonded pyrimidine ring planes, whereas atoms O(9) and O(27) deviate significantly [−0.762 (3) and 0.662 (3) Å from their respective pyrimidine rings]. In polymorph (I), the latter pair of O atoms engages in N—H···O hydrogen bonding (Fig. 4), while in (II), it is the former pair (Fig. 5). In (I), the dimers are linked by these hydrogen bonds in infinite chains parallel to the z direction, which is the longest crystal-growth direction.

The solid–solid transition observed in the DSC is accompanied by a decrease in crystal density from 1.43 g cm^{-3} for (II) to 1.35 g cm^{-3} for (I). A simple deformation mechanism involving translations and rotations of individual dimers seems unlikely since visual observations of the transformation (II)→(I) do not suggest a single-crystal to single-crystal transformation (Richardson, Yang, Novotny-Bregger & Dunitz, 1990).

Finally, we note that crystals of polymorph (I), whose structure was determined in this study, are

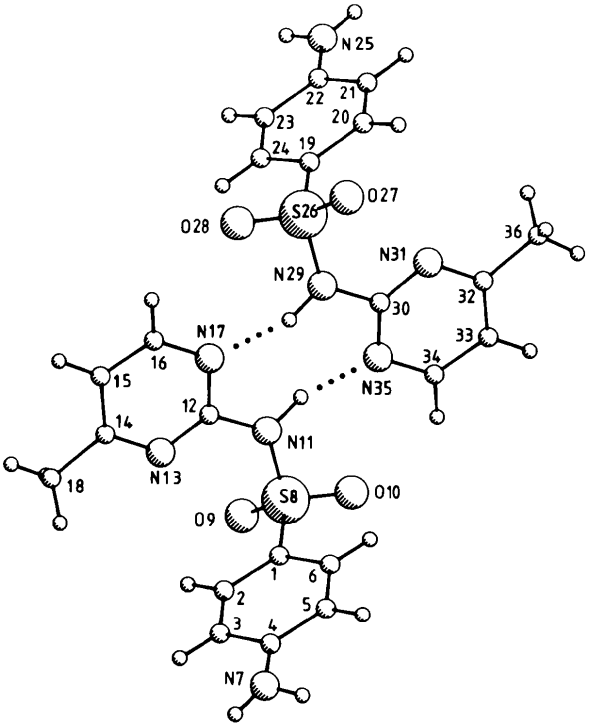


Fig. 3. Structure and nomenclature of the asymmetric unit in polymorph (I). Circles labelled with numerals only are C atoms. Dotted lines indicate hydrogen bonds.

Table 4. *Principal torsion angles (°) for sulfamerazine*

	Polymorph (I)*		
	Molecule *A*	Molecule *B*	Polymorph (II)†
τ_1	C(6)—C(1)—S(8)—N(11) −83.8 (4)	C(24)—C(19)—C(26)—N(29) 80.1 (4)	79.7 (7)
τ_2	C(1)—S(8)—N(11)—C(12) −61.5 (5)	C(19)—S(26)—N(29)—C(30) 58.5 (5)	71 (1)
τ_3	S(8)—N(11)—C(12)—N(17) 170.0 (4)	S(26)—N(29)—C(30)—N(35) −165.4 (4)	−176.6 (6)

* Present study.

† Calculated from coordinates of Acharya *et al.* (1982) for one of the two centrosymmetrically related molecules.

probably identical to those isolated by Deo *et al.* (1980) from acetone at 298 K. Their reported cell dimensions match those given here for polymorph (I), but whereas they reported the space group as $Pca2_1$, we determined it as $Pn2_1a$ (alternative setting $Pna2_1$). Polymorph (I) was also obtained from acetone by Yang & Guillory (1972). The fact that acetone also yields polymorph (II) (Acharya *et al.*, 1982) emphasizes the need for judicious selection of solvents and careful monitoring of experimental conditions for the crystallization of the individual polymorphs.

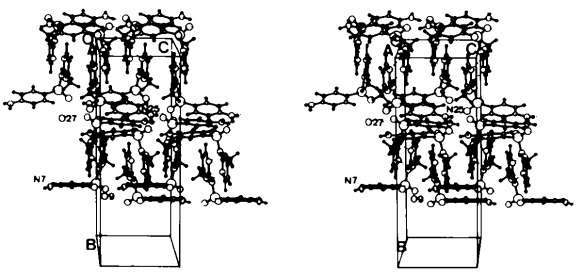


Fig. 4. Stereoscopic view of the molecular packing in polymorph (I). Dotted lines indicate hydrogen bonds.

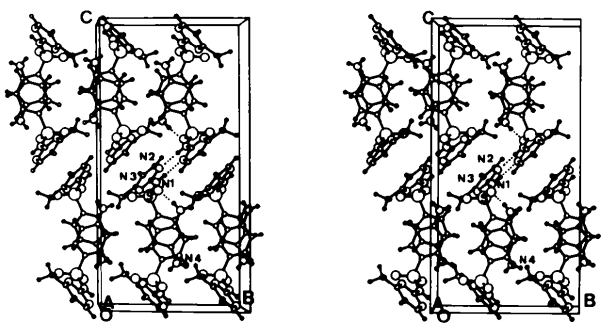


Fig. 5. Stereoscopic view of the molecular packing in polymorph (II). Representative hydrogen bonds are indicated by dotted lines. [Prepared from the data of Acharya *et al.* (1982).]

We thank the University of Cape Town and the Foundation for Research Development (Pretoria) for research grants. Assistance with data collection and computations from M. L. Niven, D. C. Liles, P. Terblanche and L. J. Barbour is gratefully acknowledged.

References

ACHARYA, K. R., KUCHELA, K. N. & KARTHA, G. (1982). *J. Crystallogr. Spectrosc. Res.* **12**, 369–376.

ANWAR, J., TARLING, S. E. & BARNES, P. (1989). *J. Pharm. Sci.* **78**, 337–342.

BAR, I. & BERNSTEIN, J. (1985). *J. Pharm. Sci.* **74**, 255–263.

BYRN, S. R. (1982). *Solid-State Chemistry of Drugs*, pp. 103–116. London: Academic Press.

CROMER, D. T. & LIBERMAN, D. (1970). *J. Chem. Phys.* **53**, 1891–1898.

CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* A**24**, 321–325.

DEO, N., TIWARI, R. K. & SINGH, T. P. (1980). *J. Sci. Res. (Bhopal, India)*, **2**, 137–139.

Enraf–Nonius (1979). *Structure Determination Package*. Enraf–Nonius, Delft, The Netherlands.

JCPDS (1990). Pattern Nos. 8-514 and 8-803. Joint Committee on Powder Diffraction Standards, PA, USA.

KUHNERT-BRANDSTÄTTER, M. (1971). *Thermomicroscopy in the Analysis of Pharmaceuticals*, pp. 34–42. Oxford: Pergamon Press.

KUHNERT-BRANDSTÄTTER, M. & WUNSCH, S. (1969). *Mikrochim. Acta*, **6**, 1308–1321.

MAURY, L., RAMBAUD, J., PAUVERT, B., BERGE, G., LASSERRE, Y. & AUDRAN, M. (1986). *Farmaco Ed. Prat.* **41**, 26–35.

MOTHERWELL, W. D. S. (1989). *PLUTO*89. Program for plotting molecular and crystal structures. Univ. of Cambridge, England.

NARDELLI, M. (1983). *Comput. Chem.* **7**, 95–98.

RICHARDSON, M. F., YANG, Q.-C., NOVOTNY-BREGGER, E. & DUNITZ, J. D. (1990). *Acta Cryst.* B**46**, 653–660.

SHELDRICK, G. M. (1976). *SHELX*76. Program for crystal structure determination. Univ. of Cambridge, England.

SHELDRICK, G. M. (1985). *SHELXS*86. *Crystallographic Computing* 3, edited by G. M. SHELDRICK, C. KRÜGER & R. GODDARD, pp. 175–189. Oxford Univ. Press.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

WOOLFENDEN, R. D. G. (1977). *Analytical Profiles of Drug Substances*, Vol. 6, edited by K. FLOREY, pp. 515–517. New York: Academic Press.

YANG, S. S. & GUILLORY, J. K. (1972). *J. Pharm. Sci.* **61**, 26–40.

YVON, K., JEITSCHKO, W. & PARTHÉ, E. J. (1977). *J. Appl. Cryst.* **10**, 73–74.