contacts and hydrogen bonds. Interestingly, a bifurcated hydrogen bond is found between O(2′) and N(3) at $(-x-\frac{1}{2}, -y-1, z-\frac{1}{2})$ of lengths 2·86 Å. Other noted short interactions are between O(3′) and O(5′) at $(x, y, z+1)$ of 2·72 Å; O(2) of the pyrimidine ring with N(3) $(-x-\frac{1}{2}, -y-1, z+\frac{1}{2})$ of 2·88 Å; O(4) with C(2) $(x, y, z-1)$ of 2·99 Å; O(4) with O(2) $(x, y, z-1)$ of 3·08 Å, respectively.

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Structure of the High-Melting Polymorph of the 1/1 Addition Compound Between Benzoic Acid and 2,4-Diamino-5-(3,4,5-trimethoxybenzyl)pyrimidinium Benzoate (Trimethoprim Monobenzoate–Benzoic Acid 1/1 Complex, Form I)*

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Abstract. $C_{14}H_{19}N_4O_3^+.C_7H_5O_2^-.C_7H_6O_2$, $M_r = 534{\cdot}57$, triclinic, $P\bar{1}$, $a = 14{\cdot}059\,(2)$, $b = 14{\cdot}791\,(2)$, $c = 13{\cdot}262\,(1)$ Å, $\alpha = 96{\cdot}10\,(1)$, $\beta = 90{\cdot}50\,(2)$, $\gamma = 93{\cdot}61\,(2)°$, $V = 2736{\cdot}4\,(6)$ Å^3, $Z = 4$, $D_m = 1{\cdot}30$, $D_x = 1{\cdot}298$ g cm^{-3}, $\lambda(\text{Mo}\ K\alpha) = 0{\cdot}7107$ Å, $\mu = 0{\cdot}883$ cm^{-1}, $F(000) = 1128$, $T = 296$ K, $R = 0{\cdot}0474$ for 3449 observed reflections. The asymmetric unit of the crystal of the high-melting polymorph (form I) contains two independent systems. The trimethoprim cation shows a bonding pattern to the benzoate anion different from that found in the previously described low-melting polymorph (form II). The benzoic acid molecule in system *A* is linked to the benzoate anion through a strong O—H···O hydrogen bond [2·488 (3) Å] while benzoic acid in system *B* links the two independent systems in the asymmetric unit. Molecular packing is achieved *via* N—H···N and N—H···O hydrogen bonds involving all the aminopyrimidine N atoms and benzoic acid O atoms not engaged in intraionic and intramolecular bonds. The two crystal forms exhibit conformational polymorphism due to different conformations of trimethoprim cations around the methylene bridge.

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Introduction. The occurrence of polymorphism for many organic medicinal compounds and its practical implications are well documented in the pharmaceutical literature (Doi, Yasuda, Ishida & Inoue, 1985). The crystal forms of a drug are usually characterized by means of differential scanning calorimetry, microscopy, infrared and X-ray powder diffraction patterns, but only in relatively few cases have their solid-state arrangements been examined, mainly owing to the difficulty in obtaining single crystals of each polymorph (Azibi, Draguet-Brughmans, Bouche, Tinant, Germain, Declercq & Van Meerssche, 1983; Goldberg & Becker, 1987). Investigations concerning the structural properties of a polymorphic drug system can prove to be very helpful in relation to physicochemical properties (Saito, Harada, Matsumura, Kato, Ito & Hori, 1983), stability (Thoma & Serno, 1984), pharmacological activity (Sutton & Byrn, 1987), characterization, and conformational polymorphism (Bar & Bernstein, 1985).

In a previous paper in this journal the structure of a polymorph of trimethoprim (TMP) monobenzoate–benzoic acid (BA) 1/1 complex (form II: m.p. = 398·8 K) has been described (Bettinetti, Giordano, La Manna, Giuseppetti & Tadini, 1985). As soon as the high-melting polymorph (form I: m.p. = 407·4 K) became available as single crystals its crystal structure determination was undertaken in order to achieve a more detailed picture of this polymorphic system, and the present paper deals with the results obtained.

Experimental. Single crystal obtained by recrystallization from a 1,2-propanediol solution of the low-melting polymorph. Density measured with a helium pycnometer model 1302/1303 Micrometric Instrument Corp. Prismatic crystal (0·60 × 0·40 × 0·13 mm). Philips PW1100 four-circle diffractometer, graphite monochromator; 36 reflections ($2 < \theta < 20°$) used for measuring lattice parameters with Philips *LAT* routine. ω–2θ scan mode, scan speed 0·05° s^{-1}, scan width 2·0°, θ range 2–20° (intensities negligible at $\theta > 20°$). Three standard reflections every 180 min, mean intensity variation 1·4%, max. intensity variation 2·5%. 5080 independent data [$-13 \leq h \leq 13$, $-13 \leq k \leq 13$, $l \leq 12$, max. $(\sin\theta)/\lambda = 0{\cdot}48\,Å^{-1}$], 3449 observed with $I > 3\sigma(I)$. Corrections for Lorentz–polarization and experimental absorption, between 1·0037 and 1·0470, following North, Phillips & Mathews (1968). Structure solved by direct methods (*MULTAN*80; Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980). F magnitudes used in least-squares refinement. Coordinates of H atoms calculated by geometrical consideration (*XANADU:* Roberts & Sheldrick, 1975), confirmed by a final ΔF synthesis showing random fluctuations between 0·15 and $-0{\cdot}016\,e\,Å^{-3}$; parameters refined: coordinates and anisotropic thermal parameters for non-hydrogen atoms, scale factor and secondary-extinction value [$g = 4{\cdot}1\,(2) \times 10^{-5}$] calculated from the anisotropic coefficients following Coppens & Hamilton (1970). Final value of $R_{obs} = 0{\cdot}0474$, $R_{all} = 0{\cdot}0838$, unit weights, $S = 1{\cdot}087$. Max. $\Delta/\sigma = 0{\cdot}004$ in last cycle of refinement. Atomic scattering factors for neutral atoms from *International Tables for X-ray Crystallography* (1974). A locally modified version of *ORFLS* (Busing, Martin & Levy, 1962) and the program *PARST* (Nardelli, 1983) were used. Fig. 1 was drawn with *ORTEP*II (Johnson, 1976).

Discussion. The asymmetric unit of this polymorph contains two independent systems, whose final atomic coordinates are given in Table 1.* Interatomic bond distances and angles, and the geometry of the hydrogen bonds and contacts are listed in Tables 2 and 3. TMP is protonated at its strongest nucleophilic atom [*i.e.* N(1) in system *A* and N(40) in system *B*], as shown in Fig. 1, but it is linked to the benzoate anion in a different pattern with respect to form II (Bettinetti *et al.*, 1985). In system *A*, the aminopyrimidinium moiety H(79)—N(1)—C(2)—N(8)—H(83)$^{(+)}$ interacts with the O(22) atom of the benzoate anion and the best plane through these atoms is practically the same as that through the pyrimidine ring [angle between planes 2·4 (2)°]. A similar bonding pattern in which the TMP cation interacts with an O atom of the partner is described by Shimizu & Nishigaki (1982). O(23) of the anion is not involved in the intraionic bond but links BA through a strong O···O hydrogen bond of 2·488 (3) Å. In system *B*, the moiety H(109)—N(40)—C(41)—N(47)—H(114)$^{(+)}$ interacts with both O(70) and O(62) [hydrogen bonded through H(133)] of the benzoate anion and BA molecule, respectively. The best plane through the atoms involved in this bond [maximum displacement 0·211 (6) Å for O(62)] is nearly coincident with the plane through the respective pyrimidine ring [angle between planes 7·8 (1)°]. The BA molecule belonging to system *B* is responsible for the intramolecular bonding between the two entities in the asymmetric unit through N—H···O interaction of 2·784 (3) Å. Intermolecular bonding is achieved *via* hydrogen bonds involving aminopyrimidine N atoms, which act as donors with their H atoms not involved in intramolecular interactions. All the amino H atoms thus participate in hydrogen bonding with a contribution to the molecular packing of intermolecular $C(sp^2)$—H···O contacts (Table 3). The conformational parameters

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* Lists of structure factors, anisotropic temperature factors for non-hydrogen atoms, refined hydrogen coordinates, torsion angles, least-squares planes with deviations of the atoms from the planes, interatomic bond distances and angles involving H atoms have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44621 (41 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Fractional atomic coordinates* ($\times 10^4$) *and equivalent isotropic temperature factors* (Å^2), *with e.s.d.'s in parentheses*

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

	x	y	z	B_{eq}
System *A*				
N(1)	7131 (2)	−900 (2)	−122 (2)	3·5 (1)
C(2)	8042 (3)	−1086 (2)	−279 (3)	3·0 (1)
N(3)	8766 (2)	−482 (2)	−25 (2)	3·1 (1)
C(4)	8561 (2)	353 (2)	408 (3)	2·9 (1)
C(5)	7610 (2)	603 (2)	587 (3)	3·0 (1)
C(6)	6935 (3)	−48 (2)	295 (3)	3·6 (1)
C(7)	7379 (3)	1548 (3)	1031 (3)	3·8 (1)
N(8)	8221 (2)	−1913 (2)	−717 (3)	3·9 (1)
N(9)	9302 (2)	931 (2)	648 (3)	3·8 (1)
C(10)	7578 (2)	1786 (2)	2154 (3)	3·3 (1)
C(11)	7714 (3)	2703 (3)	2520 (3)	3·9 (1)
C(12)	7851 (3)	2947 (2)	3548 (3)	4·1 (1)
C(13)	7887 (3)	2285 (3)	4211 (3)	4·0 (1)
C(14)	7743 (3)	1373 (3)	3838 (3)	4·4 (1)
C(15)	7588 (3)	1132 (3)	2812 (3)	3·9 (1)
O(16)	7979 (2)	3825 (2)	4004 (2)	6·3 (1)
O(17)	8104 (2)	2543 (2)	5225 (2)	5·6 (1)
O(18)	7784 (3)	783 (2)	4553 (2)	7·2 (1)
C(19)	7561 (6)	−158 (4)	4261 (5)	8·7 (2)
C(20)	7372 (5)	2494 (6)	5902 (5)	8·9 (2)
C(21)	7938 (4)	4543 (3)	3390 (5)	5·9 (2)
O(22)	6324 (2)	−2605 (2)	−848 (2)	4·4 (1)
O(23)	4766 (2)	−2637 (2)	−1076 (2)	4·1 (1)
C(24)	5566 (3)	−2973 (2)	−1222 (3)	3·2 (1)
C(25)	5600 (3)	−3858 (2)	−1882 (3)	3·0 (1)
C(26)	6419 (3)	−4321 (3)	−1939 (3)	4·0 (1)
C(27)	6439 (4)	−5139 (3)	−2555 (4)	5·3 (1)
C(28)	5645 (4)	−5484 (3)	−3105 (4)	5·8 (2)
C(29)	4836 (4)	−5027 (3)	−3056 (4)	5·4 (1)
C(30)	4801 (3)	−4210 (3)	−2436 (3)	3·9 (1)
O(31)	4450 (2)	−2368 (2)	1278 (2)	4·4 (1)
O(32)	4859 (2)	−1314 (2)	255 (2)	3·8 (1)
C(33)	4633 (3)	−1568 (3)	1128 (3)	3·4 (1)
C(34)	4603 (2)	−822 (2)	1976 (3)	3·0 (1)
C(35)	4460 (2)	−1044 (3)	2943 (3)	4·3 (1)
C(36)	4426 (4)	−382 (3)	3751 (3)	5·2 (1)
C(37)	4568 (3)	523 (3)	3589 (3)	5·1 (1)
C(38)	4718 (3)	756 (3)	2638 (3)	4·8 (1)
C(39)	4741 (3)	93 (3)	1819 (3)	3·5 (1)
System *B*				
N(40)	7985 (2)	4909 (2)	455 (2)	3·6 (1)
C(41)	7148 (3)	4467 (2)	154 (3)	3·2 (1)
N(42)	6322 (2)	4841 (2)	273 (2)	3·1 (1)
C(43)	6321 (3)	5704 (2)	715 (3)	2·9 (1)
C(44)	7181 (3)	6223 (2)	1049 (3)	3·0 (1)
C(45)	7988 (3)	5794 (3)	897 (3)	3·7 (1)
C(46)	7195 (3)	7195 (3)	1526 (3)	3·5 (1)
N(47)	7157 (3)	3653 (2)	−285 (3)	4·4 (1)
N(48)	5475 (2)	6038 (2)	808 (3)	3·6 (1)
C(49)	7155 (3)	7302 (2)	2682 (3)	2·9 (1)
C(50)	6291 (3)	7317 (2)	3159 (3)	3·4 (1)
C(51)	6246 (3)	7430 (2)	4212 (3)	3·3 (1)
C(52)	7081 (3)	7549 (2)	4792 (3)	3·2 (1)
C(53)	7953 (3)	7528 (2)	4300 (3)	3·6 (1)
C(54)	7989 (3)	7394 (3)	3259 (3)	3·8 (1)
O(55)	5351 (2)	7477 (2)	4629 (2)	4·6 (1)
O(56)	7024 (2)	7799 (2)	5818 (2)	4·4 (1)
O(57)	8727 (2)	7688 (2)	4937 (2)	5·4 (1)
C(58)	5142 (4)	6961 (4)	5453 (4)	5·9 (2)
C(59)	7400 (4)	7198 (4)	6457 (4)	6·6 (2)
C(60)	9642 (4)	7770 (5)	4516 (5)	7·6 (2)
O(61)	9992 (2)	2723 (2)	1195 (2)	4·7 (1)
O(62)	9550 (2)	3852 (2)	361 (2)	4·8 (1)
C(63)	9913 (3)	3542 (3)	1128 (3)	3·8 (1)
C(64)	10242 (3)	4215 (2)	2009 (3)	3·4 (1)
C(65)	10392 (3)	3911 (3)	2936 (3)	5·0 (1)
C(66)	10685 (4)	4525 (3)	3759 (4)	6·1 (2)
C(67)	10861 (4)	5431 (3)	3653 (4)	6·3 (2)
C(68)	10716 (3)	5728 (3)	2728 (4)	5·3 (1)
C(69)	10399 (3)	5128 (3)	1903 (3)	4·0 (1)
O(70)	8768 (4)	2477 (3)	−978 (3)	13·6 (2)
O(71)	10283 (4)	2394 (2)	−1313 (3)	10·8 (2)
C(72)	9444 (5)	2099 (4)	−1367 (4)	7·8 (2)
C(73)	9210 (3)	1178 (3)	−1989 (3)	4·2 (1)
C(74)	9944 (4)	680 (3)	−2320 (4)	5·6 (2)
C(75)	9744 (5)	−170 (5)	−2864 (5)	9·0 (2)
C(76)	8787 (9)	−455 (5)	−3037 (5)	12·5 (4)
C(77)	8122 (6)	39 (6)	−2678 (6)	12·0 (3)
C(78)	8311 (4)	845 (5)	−2167 (5)	7·9 (2)

Table 2. *Bond distances* (Å) *and angles* (°) *with e.s.d.'s in parentheses*

System *A*		System *B*	
N(1)–C(2)	1·341 (5)	N(40)–C(41)	1·345 (5)
N(1)–C(6)	1·366 (5)	N(40)–C(45)	1·376 (5)
C(2)–N(3)	1·328 (4)	C(41)–N(42)	1·321 (5)
C(2)–N(8)	1·337 (5)	C(41)–N(47)	1·334 (5)
N(3)–C(4)	1·354 (4)	N(42)–C(43)	1·347 (4)
C(4)–C(5)	1·425 (5)	C(43)–C(44)	1·430 (5)
C(4)–N(9)	1·320 (5)	C(43)–N(48)	1·319 (5)
C(5)–C(6)	1·333 (5)	C(44)–C(45)	1·340 (6)
C(5)–C(7)	1·513 (5)	C(44)–C(46)	1·507 (5)
C(7)–C(10)	1·513 (6)	C(46)–C(49)	1·527 (5)
C(10)–C(11)	1·392 (5)	C(49)–C(50)	1·374 (6)
C(10)–C(15)	1·371 (6)	C(49)–C(54)	1·386 (5)
C(11)–C(12)	1·381 (6)	C(50)–C(51)	1·391 (5)
C(12)–C(13)	1·387 (6)	C(51)–C(52)	1·389 (5)
C(12)–O(16)	1·373 (4)	C(51)–O(55)	1·382 (5)
C(13)–C(14)	1·388 (5)	C(52)–C(53)	1·394 (5)
C(13)–O(17)	1·384 (5)	C(52)–O(56)	1·375 (4)
C(14)–C(15)	1·381 (6)	C(53)–C(54)	1·376 (5)
C(14)–O(18)	1·359 (5)	C(53)–O(57)	1·364 (5)
O(16)–C(21)	1·409 (6)	O(55)–C(58)	1·420 (7)
O(17)–C(20)	1·374 (8)	O(56)–C(59)	1·414 (7)
O(18)–C(19)	1·419 (6)	O(57)–C(60)	1·411 (6)
O(22)–C(24)	1·241 (4)	O(61)–C(63)	1·236 (5)
O(23)–C(24)	1·266 (5)	O(62)–C(63)	1·275 (5)
C(24)–C(25)	1·500 (5)	C(63)–C(64)	1·501 (5)
C(25)–C(26)	1·375 (6)	C(64)–C(65)	1·372 (6)
C(25)–C(30)	1·379 (5)	C(64)–C(69)	1·378 (5)
C(26)–C(27)	1·387 (6)	C(65)–C(66)	1·385 (6)
C(27)–C(28)	1·368 (7)	C(66)–C(67)	1·370 (7)
C(28)–C(29)	1·358 (7)	C(67)–C(68)	1·364 (7)
C(29)–C(30)	1·392 (6)	C(68)–C(69)	1·385 (6)
O(31)–C(33)	1·233 (5)	O(70)–C(72)	1·223 (8)
O(32)–C(33)	1·291 (5)	O(71)–C(72)	1·230 (9)
C(33)–C(34)	1·491 (5)	C(72)–C(73)	1·532 (6)
C(34)–C(35)	1·371 (6)	C(73)–C(74)	1·354 (7)
C(34)–C(39)	1·393 (5)	C(73)–C(78)	1·337 (7)
C(35)–C(36)	1·375 (6)	C(74)–C(75)	1·391 (8)
C(36)–C(37)	1·380 (7)	C(75)–C(76)	1·394 (14)
C(37)–C(38)	1·358 (7)	C(76)–C(77)	1·287 (14)
C(38)–C(39)	1·385 (6)	C(77)–C(78)	1·318 (11)
C(2)–N(1)–C(6)	118·8 (4)	C(41)–N(40)–C(45)	118·9 (4)
N(1)–C(2)–N(8)	118·2 (4)	N(40)–C(41)–N(47)	118·4 (4)
N(1)–C(2)–N(3)	122·7 (3)	N(40)–C(41)–N(42)	123·0 (3)
N(3)–C(2)–N(8)	119·2 (4)	N(42)–C(41)–N(47)	118·8 (4)
C(2)–N(3)–C(4)	117·8 (3)	C(41)–N(42)–C(43)	118·3 (3)
N(3)–C(4)–N(9)	115·7 (4)	N(42)–C(43)–N(48)	115·3 (3)
N(3)–C(4)–C(5)	122·7 (3)	N(42)–C(43)–C(44)	122·2 (3)
C(5)–C(4)–N(9)	121·6 (3)	C(44)–C(43)–N(48)	122·5 (3)
C(4)–C(5)–C(7)	122·7 (4)	C(43)–C(44)–C(46)	122·9 (4)
C(4)–C(5)–C(6)	114·9 (4)	C(43)–C(44)–C(45)	115·6 (3)
C(6)–C(5)–C(7)	122·4 (4)	C(45)–C(44)–C(46)	121·3 (4)
N(1)–C(6)–C(5)	123·1 (4)	N(40)–C(45)–C(44)	122·0 (4)
C(5)–C(7)–C(10)	116·5 (3)	C(44)–C(46)–C(49)	114·6 (3)
C(7)–C(10)–C(15)	122·1 (4)	C(46)–C(49)–C(54)	120·2 (4)
C(7)–C(10)–C(11)	118·0 (4)	C(46)–C(49)–C(50)	120·2 (4)
C(11)–C(10)–C(15)	120·0 (4)	C(50)–C(49)–C(54)	119·5 (4)
C(10)–C(11)–C(12)	119·6 (4)	C(49)–C(50)–C(51)	120·7 (4)
C(11)–C(12)–O(16)	125·2 (4)	C(50)–C(51)–O(55)	116·9 (4)
C(11)–C(12)–C(13)	120·5 (4)	C(50)–C(51)–C(52)	120·0 (4)
C(13)–C(12)–O(16)	114·3 (4)	C(52)–C(51)–O(55)	123·0 (3)
C(12)–C(13)–O(17)	119·4 (4)	C(51)–C(52)–O(56)	118·9 (4)
C(12)–C(13)–C(14)	119·4 (4)	C(51)–C(52)–C(53)	118·8 (3)
C(14)–C(13)–O(17)	121·1 (4)	C(53)–C(52)–O(56)	121·8 (4)
C(13)–C(14)–O(18)	114·6 (4)	C(52)–C(53)–O(57)	114·2 (3)
C(13)–C(14)–C(15)	120·0 (4)	C(52)–C(53)–C(54)	120·8 (4)
C(15)–C(14)–O(18)	125·6 (4)	C(54)–C(53)–O(57)	125·1 (4)
C(10)–C(15)–C(14)	120·6 (4)	C(49)–C(54)–C(53)	120·2 (4)
C(12)–O(16)–C(21)	118·2 (4)	C(51)–O(55)–C(58)	117·7 (4)
C(13)–O(17)–C(20)	117·5 (4)	C(52)–O(56)–C(59)	116·0 (3)
C(14)–O(18)–C(19)	118·6 (4)	C(53)–O(57)–C(60)	118·9 (4)
O(22)–C(24)–O(23)	123·3 (3)	O(61)–C(63)–O(62)	123·9 (4)
O(23)–C(24)–C(25)	118·4 (4)	O(62)–C(63)–C(64)	117·7 (3)
O(22)–C(24)–C(25)	118·3 (4)	O(61)–C(63)–C(64)	118·4 (4)
C(24)–C(25)–C(30)	119·6 (4)	C(63)–C(64)–C(69)	121·3 (4)
C(24)–C(25)–C(26)	120·6 (4)	C(63)–C(64)–C(65)	119·2 (4)
C(26)–C(25)–C(30)	119·9 (4)	C(65)–C(64)–C(69)	119·5 (4)
C(25)–C(26)–C(27)	119·8 (4)	C(64)–C(65)–C(66)	119·9 (4)
C(26)–C(27)–C(28)	120·1 (5)	C(65)–C(66)–C(67)	120·8 (5)
C(27)–C(28)–C(29)	120·3 (5)	C(66)–C(67)–C(68)	118·9 (5)
C(28)–C(29)–C(30)	120·3 (5)	C(67)–C(68)–C(69)	121·1 (4)
C(25)–C(30)–C(29)	119·6 (4)	C(64)–C(69)–C(68)	119·7 (4)
O(31)–C(33)–O(32)	123·7 (4)	O(70)–C(72)–O(71)	126·2 (6)
O(32)–C(33)–C(34)	115·7 (3)	O(71)–C(72)–C(73)	117·6 (6)

Table 2 (*cont.*)

System *A*		System *B*	
O(31)–C(33)–C(34)	120·6 (3)	O(70)–C(72)–C(73)	116·2 (6)
C(33)–C(34)–C(39)	122·0 (3)	C(72)–C(73)–C(78)	121·7 (5)
C(33)–C(34)–C(35)	119·1 (3)	C(72)–C(73)–C(74)	118·1 (5)
C(35)–C(34)–C(39)	118·9 (4)	C(74) C(73) C(78)	120·3 (5)
C(34)–C(35)–C(36)	121·3 (4)	C(73)–C(74)–C(75)	118·9 (5)
C(35)–C(36)–C(37)	119·4 (4)	C(74)–C(75)–C(76)	117·4 (7)
C(36)–C(37)–C(38)	120·2 (4)	C(75)–C(76)–C(77)	121·0 (8)
C(37)–C(38)–C(39)	120·7 (4)	C(76)–C(77)–C(78)	121·8 (8)
C(34)–C(39)–C(38)	119·5 (4)	C(73)–C(78)–C(77)	121·0 (6)

Table 3. *Hydrogen-bonding and intermolecular-contact geometry*

Donor *R*H Acceptor *R'*	*R*–H (Å)	*R*···*R'* (Å)	H···*R'* (Å)	*R*–H···*R'* (°)
N(1)–H(79)···O(22)	0·90 (3)	2·770 (4)	1·99 (3)	143 (3)
N(8)–H(83)···O(22)	0·83 (3)	2·792 (4)	2·05 (4)	148 (3)
O(32)–H(103)···O(23)	0·90 (3)	2·488 (3)	1·59 (3)	175 (4)
N(9)–H(85)···O(61)	0·86 (4)	2·784 (3)	2·05 (4)	142 (3)
N(40)–H(109)···O(62)	0·92 (4)	2·774 (4)	1·86 (3)	167 (3)
N(47)–H(114)···O(70)	0·91 (4)	3·032 (7)	2·14 (4)	167 (3)
O(62)–H(133)···O(70)	1·02 (3)	2·722 (5)	1·73 (3)	163 (3)
N(8)–H(84)···O(61^{ii})	0·91 (4)	2·897 (3)	2·01 (4)	165 (3)
N(9)–H(86)···N(3^{ii})	1·03 (4)	2·942 (4)	1·91 (4)	176 (3)
N(47)–H(113)···O(31^{i})	0·93 (4)	3·054 (5)	2·13 (3)	172 (3)
N(48)–H(115)···O(31^{iii})	0·84 (4)	2·855 (3)	2·09 (4)	151 (3)
N(48)–H(116)···N(42^{iv})	0·99 (3)	3·042 (4)	2·07 (3)	168 (3)
C(39)–H(108)···O(32^{i})	1·01 (4)	3·478 (5)	2·56 (4)	152 (3)
C(69)–H(132)···O(62^{iii})	0·98 (4)	3·499 (5)	2·54 (4)	166 (3)

Symmetry code: none: x, y, z; (i): $-x+1, -y, -z$; (ii): $-x+2, -y, -z$; (iii): $x, y+1, z$; (iv): $-x+1, -y+1, -z$.

describing the relative orientation of the pyrimidine and trimethoxyphenyl rings of this polymorph are reported in Table 4, together with the same parameters for the low-melting crystal form (Bettinetti *et al.*, 1985) for ease of comparison. TMP adopts a twist conformation in form I (system *A*) and in form II, with a difference of about 15° between the pertinent torsion angles. This conformation is the most frequently encountered in TMP crystal structures and occurs, for instance, in the chicken liver dihydrofolate reductase complex (Matthews *et al.*, 1985). In system *B* of form I TMP shows a 'perpendicular conformation' (Cody, 1984). This minimum-energy conformation, as calculated for 2,4-diamino-5-(substituted-benzyl)pyrimidines (Ghose & Crippen, 1985), has not yet to our knowledge been found in TMP crystal structures. Thus the system exhibits conformational polymorphism, *i.e.* different conformations in different crystal forms (Byrn, 1982). Studies on the factors that control and influence the crystalline conformation of a drug (Bar & Bernstein, 1985) are relevant when the solid and solution conformations are compared (Byrn, Wier Graber & Midland, 1976), and are of particular interest with conformationally flexible drug molecules showing high activity and selectivity such as TMP (Koetzle & Williams, 1976; Hopfinger, 1983; Birdsall, Roberts, Feeney, Dann & Burgen, 1983; Kuyper *et al.*, 1985).

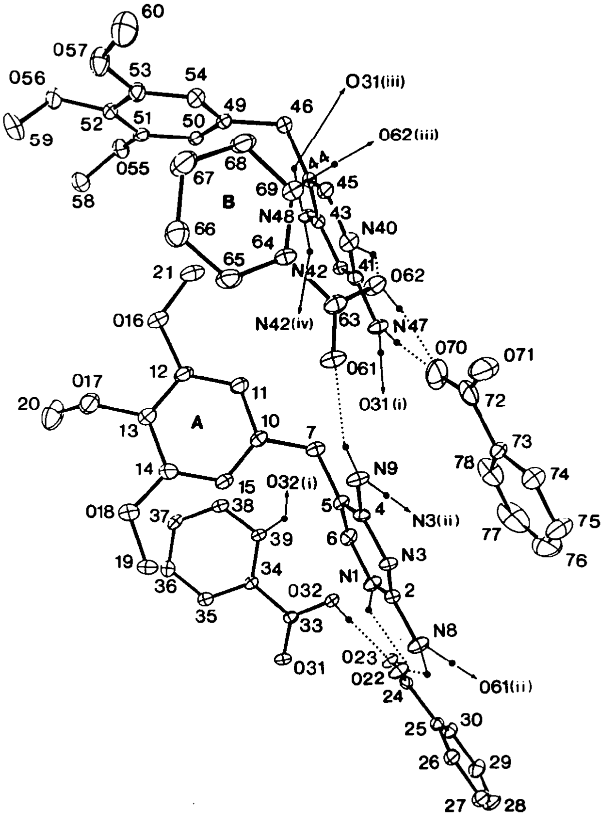

Fig. 1. *ORTEP* drawing of the *A* and *B* systems in the asymmetric unit of the high-melting polymorph, form I. Only the hydrogen atoms involved in intra-(···) and intermolecular bonds and contacts (→: see Table 3 for symmetry code) are drawn (●). The numbers of non-carbon atoms are preceded by the symbol of the atom.

Table 4. *Conformational parameters of forms* I *and* II

Crystal form	Torsion angles (°) τ_1	τ_2	Angles (°) between TMP rings
Form I, system *A*	C(4)–C(5)–C(7)–C(10) –74·4 (5)	C(5)–C(7)–C(10)–C(11) 157·0 (4)	87·2 (1)
Form I, system *B*	C(43)–C(44)–C(46)–C(49) 92·7 (5)	C(44)–C(46)–C(49)–C(54) 90·9 (5)	63·1 (1)
Form II	C(4)–C(5)–C(7)–C(1*a*) –90·5 (2)	C(5)–C(7)–C(1*a*)–C(2*a*) 171·0 (2)	101·2 (1)

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Structure of *N*,*N*'-Diacetylparabanic Acid*

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Abstract. $C_7H_6N_2O_5$, $M_r = 198{\cdot}14$, orthorhombic, $Pnma$, $a = 8{\cdot}130\,(3)$, $b = 19{\cdot}120\,(9)$, $c = 5{\cdot}243\,(2)$ Å, $V = 815{\cdot}0$ Å^3, $Z = 4$, D_m (displacement of benzene) $= 1{\cdot}59$, $D_x = 1{\cdot}614$ Mg m^{-3}, $\lambda(\text{Mo }K\alpha) = 0{\cdot}71069$ Å, $\mu = 0{\cdot}131$ mm^{-1}, $F(000) = 408$, room temperature, final $R = 0{\cdot}067$ for 304 unique observed reflections; crystal selected from synthetic material. The structure contains almost planar molecules which lie perpendicular to crystallographic mirror planes and are closely packed in layers parallel to them.

Introduction. In the course of study of the title compound it was found that the compound underwent hydrolysis in two stages, first to *N*-acetylparabanic acid and then by ring opening to *N*-acetyloxaluric acid. The crystal structure determination was undertaken in an attempt to discover why this should be so.

Experimental. The compound was synthesized by acetylation of the disodium salt of parabanic acid (Murray, 1963) with acetyl chloride and recrystallization from a chloroform/acetone mixture provided crystals suitable for further study (m.p. 433–435 K).

Colourless triangular crystal fragment of 0·15 mm side and 0·08 mm thickness; Nicolet $P3$ diffractometer with Mo$K\alpha$ radiation and $\omega/2\theta$ scan method with $\Delta 2\theta$ 2·40–2·66° and scan rate 5·33 ($I < 150$) to 58·6° 2θ min^{-1} ($I > 2500$); cell refined from 071, 002 and 311 reflections with $15 < 2\theta < 18°$; no correction for absorption or extinction; $(\sin\theta)/\lambda \le 0{\cdot}4813$ Å^{-1}; $0 \le h \le 7$, $0 \le k \le 15$, $0 \le l \le 5$; no significant variation in the intensities of the standard reflections 071 and 311; 342 unique reflections including 38 with $I < 3\sigma(I)$ which were excluded from further calculations. Structure solved in the space group $Pn2_1a$ using *MULTAN*80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980) but results clearly compatible with the space group $Pnma$, consistent with E-value statistics. Refinement of all non-H atoms vibrating anisotropically in $Pnma$ minimizing $\sum w(|F_o| - |F_c|)^2$ with $w = \{1 + [(|F_o| - 16)/9]^2\}^{-1/2}$ gave $R = 0{\cdot}093$, $wR = 0{\cdot}113$. Further refinement including H from a difference map vibrating isotropically gave final $R = 0{\cdot}067$, $wR = 0{\cdot}074$ and $S = 0{\cdot}844$ for 80 refined

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* Parabanic acid is imidazolidinetrione.

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