($\bar{I}$)] agree with a more enhanced two-dimensional coupling [particularly between (I) and ($\bar{I} + a$) molecules]. Such a conclusion is reinforced by the existence of short S···S contacts (3·97–4·46 Å) between these latter molecules. These structural features have been recently confirmed by calculations of transfer integrals, the results of which are largely discussed in terms of electronic structure in Vaca, Coulon, Ducasse, Fritsch, Granier & Gallois (1989).

Anion–cation interactions. As a general trend F···C (O···C) contacts are greater than the sum of the van der Waals radii, 3·10 Å (3·30 Å), of the corresponding atoms except in the ClO_4 β-phase structure where distances between O1 and C17 [($\bar{I} + c$)], O2 and C4 [($I + a$)] are 3·31 and 3·38 Å respectively, which is close to 3·30 Å.

The authors are grateful to P. Vaca and C. Coulon for fruitful discussions on structure–physical properties correlations in these compounds.

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Acta Cryst. (1989). C**45**, 1381–1384

Structure of a New Crystalline Form of Famotidine

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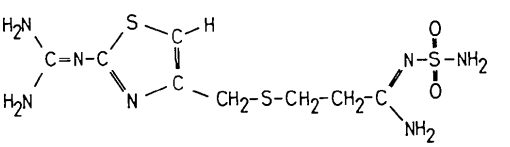
(*Received* 1 *December* 1988; *accepted* 17 *January* 1989)

Abstract. 3-{[2-(Diaminomethyleneamino)-1,3-thiazol-4-yl]methylthio}-N^2-sulfamoylpropionamidine, $C_8H_{15}N_7O_2S_3$, $M_r = 337{\cdot}44$, monoclinic, $P2_1/c$, $a = 11{\cdot}986$ (1), $b = 7{\cdot}200$ (1), $c = 16{\cdot}818$ (1) Å, $\beta = 99{\cdot}82$ (1)°, $V = 1430{\cdot}1$ (5) Å^3, $Z = 4$, $D_x = 1{\cdot}567$ g cm^{-3}, Mo $K\alpha$ radiation, $\lambda = 0{\cdot}71069$ Å, $\mu = 5{\cdot}095$ cm^{-1}, $F(000) = 704$, $T = 293$ (2) K, final $R = 0{\cdot}027$ and $wR = 0{\cdot}026$ for 3211 contributing reflections. The structure of a new crystalline form of famotidine containing only one intramolecular hydrogen bond of 2·691 (2) Å is presented.

Introduction. Famotidine is a representative of the third generation of stress-ulceration inhibitors. As a specific competitive histamine H_2-receptor antagonist, it inhibits the secretion of histamine-stimulated gastric acid. It differs from the previously described H_2-antagonists in possessing a sulfamoyl amidine function. Like cimetidine it has various crystalline forms (polymorphism) depending on the conditions of the crystallization (Kojić-Prodić, Kajfež, Belin, Toso & Sunjić, 1979). Here we present the crystal and molecular structure of the title compound (I) in a crystalline form different from those already published (Furuya, 1988; Ishida, In, Shibata, Doi, Inoue & Yanagisawa, 1987; Kálmán, 1988).



(I) Famotidine

Experimental. Synthesis of famotidine carried out by KRKA – Chemical and Pharmaceutical Works. Crystals of famotidine obtained by slow evaporation from DMF/H_2O solution. Crystal size: 0·51 × 0·50 × 0·62 mm. Unit-cell parameters and intensity data obtained on an Enraf–Nonius CAD-4 diffractometer with graphite-monochromated Mo $K\alpha$. Cell dimen-

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sions refined by least-squares fitting of 100 centered reflections monitored in the range $10 < \theta < 18°$ using Mo $K\alpha_1$ wavelength (0·70930 Å). Data collection parameters: max. scan time 40 s, scan width = (0·7 + 0·3tgθ)°, aperture = (2·4 + 0·9tgθ) mm. 15 357 reflections measured to $[(\sin\theta/\lambda]_{max} = 0{\cdot}6812$ Å^{-1}, $-16 \le h \le 16$, $-9 \le k \le 9$, $-12 \le l \le 22$. Orientation control monitored after each 400 reflections, standard reflections measured every 10 000 s of scanning time ($43\bar{6}$, $15\bar{2}$, $\bar{4}3\bar{1}$) did not show any significant change in intensity (−0·54%). Among 3783 unique reflections 3046 considered as observed [$I > 3{\cdot}0\sigma(I)$], R_{int} after merging for $P2_1/c$ space group 0·023. The structure was solved with the *MULTAN*80 system of computer programs (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980). An E map computed with the phases from the set with the highest combined figure of merit revealed all non-H atoms, H atoms located from difference Fourier map. Least-squares refinement on F with anisotropic displacement parameters for all non-H atoms and with isotropic thermal parameters for H atoms using *XRAY*76 package of crystallographic programs (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976). Inspection of F_o and F_c values indicated a correction for secondary extinction [$g = 3{\cdot}9\ (3) \times 10^{-3}$]. Empirical weighting function $w = 15 \times W_f \times W_s$, where: $W_f(|F_o| < 7{\cdot}00) = (|F_o|/7{\cdot}0)^{1.5}$, $W_f(|F_o| > 11{\cdot}0) = (11{\cdot}00/|F_o|)^{0.7}$, $W_f(7{\cdot}00 \le |F_o| \le 11{\cdot}00) = 1{\cdot}0$, $W_s(\sin\theta < 0{\cdot}39) = (\sin\theta/0{\cdot}39)^{4.0}$, $W_s(\sin\theta > 0{\cdot}46) = (0{\cdot}46/\sin\theta)^{2.0}$, $W_s(0{\cdot}39 \le \sin\theta \le 0{\cdot}46) = 1{\cdot}0$ applied to keep $\sum w(\Delta F)^2$ uniform over ranges of $(\sin\theta)/\lambda$ and $|F_o|$. Refinement converged to $R = 0{\cdot}027$ and $wR = 0{\cdot}026$ for 242 parameters and 3211 contributing reflections including observed and less-thans for which $|F_c| > |F_o|$; $(\text{shift/e.s.d.})_{max} = 0{\cdot}30$, $(\text{shift/e.s.d.})_{av} = 0{\cdot}002$, $S = 0{\cdot}918$, excursions in final difference Fourier map within 0·34 and −0·75 e Å^{-3}.

Atomic scattering factors for H atoms were taken from Stewart, Davidson & Simpson (1965), and for other neutral atoms from Cromer & Mann (1968), and dispersion corrections from Cromer & Liberman (1970). All calculations were performed on the DEC-10 computer at RCU-Ljubljana.

Discussion. The final positional and equivalent isotropic thermal parameters of the non-H atoms (Hamilton, 1959), along with their standard deviations, are listed in Table 1.* Principal bond angles and distances are listed in Table 2. A perspective view of the molecule, including the atom-numbering scheme, is given in Fig. 1. Fig. 2 shows molecular packing and the hydrogen-bonding scheme as viewed along the [010] axis.

Table 1. *Atomic coordinates* ($\times 10^4$) *for non-*H *atoms and* ($\times 10^3$) *for* H *atoms, and equivalent isotropic temperature factors (Hamilton,* 1959) (Å$^2 \times 10^4$) *for non-*H *atoms and* (Å$^2 \times 10^3$) *for* H *atoms, with their e.s.d.'s in parentheses*

	x	y	z	U_{eq}
N(1)	5616 (1)	2726 (2)	56 (1)	563 (7)
N(2)	5249 (1)	848 (2)	1076 (1)	473 (5)
C(1)	5081 (1)	2459 (2)	683 (1)	369 (5)
N(3)	4419 (1)	3828 (1)	868 (1)	381 (4)
C(2)	3868 (1)	3647 (1)	1504 (1)	325 (4)
N(4)	3768 (1)	2199 (1)	1965 (1)	368 (4)
C(3)	3144 (1)	2632 (2)	2562 (1)	353 (5)
C(4)	2735 (1)	4391 (2)	2548 (1)	409 (5)
S(1)	3162·3 (3)	5629·8 (4)	1773·9 (2)	417 (1)
C(5)	2993 (1)	1171 (2)	3161 (1)	428 (6)
S(2)	1894·1 (3)	−529·8 (4)	2777·9 (2)	452 (2)
C(6)	614 (1)	800 (2)	2769 (1)	364 (5)
C(7)	123 (1)	713 (2)	3553 (1)	390 (5)
C(8)	869 (1)	1700 (1)	4235 (1)	302 (4)
N(5)	802 (1)	3534 (1)	4216 (1)	295 (4)
S(3)	1659·4 (2)	4784·3 (3)	4839·2 (1)	294 (1)
O(1)	1288 (1)	6665 (1)	4666 (1)	501 (5)
O(2)	2829 (1)	4361 (1)	4805 (1)	458 (4)
N(6)	1471 (1)	4159 (2)	5737 (1)	397 (5)
N(7)	1528 (1)	665 (1)	4760 (1)	449 (5)
H(11)	559 (2)	373 (4)	−18 (1)	50 (5)
H(12)	603 (2)	191 (4)	−5(2)	55 (5)
H(21)	491 (2)	64 (3)	145 (1)	48 (5)
H(22)	569 (2)	10 (4)	94 (1)	52 (5)
H(4)	231 (2)	497 (3)	292 (1)	49 (5)
H(51)	282 (2)	175 (3)	366 (1)	47 (5)
H(52)	368 (2)	49 (4)	331 (2)	61 (6)
H(61)	9 (2)	31 (4)	236 (2)	54 (5)
H(62)	76 (2)	200 (3)	264 (1)	42 (4)
H(71)	−59 (2)	132 (3)	347 (1)	49 (5)
H(72)	6 (2)	−59 (4)	371 (1)	51 (5)
H(81)	205 (2)	437 (3)	609 (2)	52 (5)
H(82)	86 (2)	461 (4)	587 (2)	56 (5)
H(91)	197 (3)	113 (5)	512 (2)	67 (7)
H(92)	150 (2)	−53 (4)	472 (1)	54 (5)

Bond distances and angles in the structure have expected values. The C(1) atom of the guanidino group and the C(8) atom of the amidino group are sp^2 hybridized as shown by the sums of the bond angles around C(1) and C(8) which are 360·0 (3) and 360·0 (3)°. The thiazole ring is essentially planar, with bond distances and angles in good agreement with the thiazole molecule (Nygaard, Asmussen, Hoeg, Maheshwari, Nielsen, Petersen, Rastrup-Andersen & Soerensen, 1971). The sulfamoyl group with the amidino N atom is in the form of a slightly distorted tetrahedron. The O—S—O angle of 117·3 (1)° deviates from the ideal tetrahedral value, as has been observed in other sulfamoyl-group-containing compounds (Sabesan & Venkatesan, 1971; Dupont & Dideberg, 1972; Eliopoulos, Sheldrick & Hamodrakas, 1983). For the purpose of geometric analysis of our compound it would be interesting to consider which atoms participate in binding to the histamine H_2 receptor. Although the structure of the receptor is not known, conformational studies of histamine and its analogues suggest

* Lists of structure factors, anisotropic thermal parameters, least-squares-planes equations and torsion angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51881 (16 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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

N(1)—C(1)	1·339 (2)	C(5)—S(2)	1·832 (1)
N(2)—C(1)	1·333 (2)	S(2)—C(6)	1·806 (1)
C(1)—N(3)	1·335 (2)	C(6)—C(7)	1·535 (2)
N(3)—C(2)	1·356 (2)	C(7)—C(8)	1·506 (1)
C(2)—N(4)	1·317 (1)	C(8)—N(5)	1·323 (1)
C(2)—S(1)	1·758 (1)	C(8)—N(7)	1·312 (1)
N(4)—C(3)	1·386 (2)	N(5)—S(3)	1·612 (1)
C(3)—C(4)	1·357 (2)	S(3)—O(1)	1·440 (1)
C(3)—C(5)	1·489 (2)	S(3)—O(2)	1·445 (1)
C(4)—S(1)	1·726 (1)	S(3)—N(6)	1·628 (1)

N(2)—C(1)—N(1)	117·6 (1)	N(3)—C(1)—N(1)	117·5 (1)
N(3)—C(1)—N(2)	124·9 (1)	C(2)—N(3)—C(1)	120·1 (1)
N(4)—C(2)—N(3)	130·2 (1)	S(1)—C(2)—N(3)	116·5 (1)
S(1)—C(2)—N(4)	113·3 (1)	C(3)—N(4)—C(2)	111·3 (1)
C(4)—S(1)—C(2)	89·6 (1)	C(4)—C(3)—N(4)	115·8 (1)
C(5)—C(3)—N(4)	118·3 (1)	C(5)—C(3)—C(4)	125·9 (1)
S(1)—C(4)—C(3)	110·1 (1)	S(2)—C(5)—C(3)	113·4 (1)
C(6)—S(2)—C(5)	101·9 (1)	C(7)—C(6)—S(2)	114·9 (1)
C(8)—C(7)—C(6)	111·8 (1)	N(5)—C(8)—C(7)	115·3 (1)
N(7)—C(8)—C(7)	117·1 (1)	N(7)—C(8)—N(5)	127·6 (1)
S(3)—N(5)—C(8)	120·8 (1)	O(1)—S(3)—N(5)	104·7 (1)
O(2)—S(3)—N(5)	111·8 (1)	N(6)—S(3)—N(5)	106·0 (1)
O(2)—S(3)—O(1)	117·3 (1)	N(6)—S(3)—O(1)	111·1 (1)
N(6)—S(3)—O(2)	105·5 (1)		

H(11)—N(1)	0·82 (3)	H(61)—C(6)	0·92 (2)
H(12)—N(1)	0·81 (3)	H(62)—C(6)	0·92 (2)
H(21)—N(2)	0·81 (3)	H(71)—C(7)	0·95 (2)
H(22)—N(2)	0·81 (3)	H(72)—C(7)	0·99 (3)
H(42)—C(4)	0·97 (2)	H(81)—N(6)	0·85 (2)
H(51)—C(5)	0·99 (2)	H(82)—N(6)	0·87 (3)
H(52)—C(5)	0·96 (3)	H(91)—N(7)	0·80 (3)
		H(92)—N(7)	0·86 (3)

H(12)—N(1)—H(11)	120·6 (25)
H(22)—N(2)—H(21)	121·7 (25)
H(52)—C(5)—H(51)	107·3 (21)
H(62)—C(6)—H(61)	108·5 (21)
H(72)—C(7)—H(71)	111·1 (21)
H(82)—N(6)—H(81)	112·3 (25)
H(92)—N(7)—H(91)	119·6 (29)

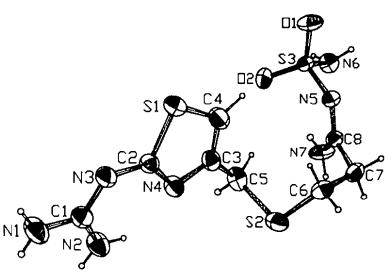

Fig. 1. *ORTEP* plot (Johnson, 1965) of the famotidine molecule. The anisotropic ellipsoids are at 50% probability.

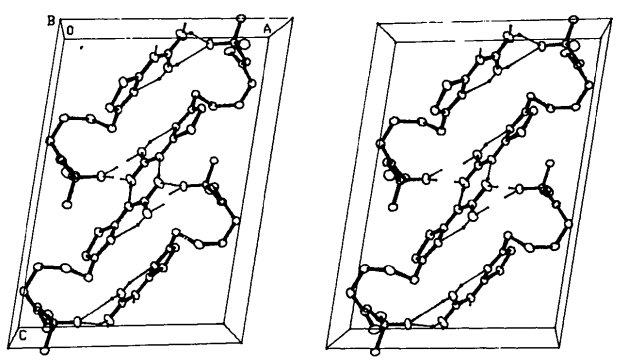

Fig. 2. Stereoscopic view of the crystal packing as seen along **b** showing intermolecular hydrogen bonds N1···N3, O2···N2, O2···N1 and intramolecular hydrogen bond N2···N4.

that the thiazole N as an electron acceptor, and the amidinil group as an electron donor could participate in hydrogen bonding to the receptor (Kier, 1968). In the structure of famotidine determined by Furuya (1988) the molecule is in a folded conformation stabilized by two intramolecular hydrogen bonds: between the guanidino N atom and the sulfamoyl N atom, and between the guanidino N atom and the thiazole N atom. This type of folded conformation was observed among other H_2-receptor antagonists (Haedicke, Frickel & Franke, 1978; Kojić-Prodić, Ružić-Toroš & Toso, 1982), although it might not represent the actual conformation when bound to the H_2 receptor (Lumma, Baldwin, Bikcing, Bolhofer, Hoffman, Philips, Robb, Torchiana, Schlegel, Smith, Hirshfield, Snyder & Splinger, 1984).

The conformation of our compound differs from the above by having only one short intramolecular hydrogen bond, between the thiazole N(4) and the guanidino N(2) atoms, 2·691 (2) Å, while the sulfamoylamidine 'tail' is oriented in the opposite direction in space.

The famotidine molecules are connected by O(1)—N(7) hydrogen bonds of length 2·896 (1) Å in the direction parallel to the [010] axis. The guanidino N atoms N(3) and N(1) participate in intermolecular hydrogen bonds of 2·924 (2) Å forming a stable six-membered ring. The O atom O(2) of the sulfamoyl amidino group and the guanidino N atoms N(1) and N(2) are connected by intermolecular hydrogen bonds of length 3·041 (2) and 3·133 (2) Å. This system of hydrogen bonds links the molecules in a three-dimensional network.

We would like to thank Dr Furuya for sending us the complete crystallographic data on the famotidine form described by Yanagisawa, Hirata & Ishii (1987).

The financial support of KRKA – Pharmaceutical and Chemical Works is gratefully acknowledged.

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Acta Cryst. (1989). C**45**, 1384–1387

Structure of 3-[*N*-Methyl-*N*-(*S*)-α-methylbenzyl]carbamoyl-1,2,4-trimethylpyridinium Iodide

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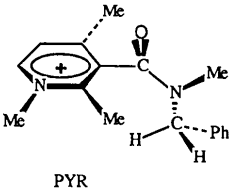
(*Received* 17 *January* 1989; *accepted* 6 *February* 1989)

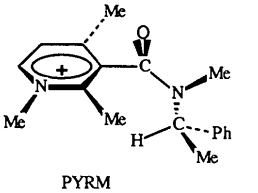
Abstract. $C_{18}H_{23}N_2O^+.I^-$, $M_r = 410{\cdot}30$, orthorhombic, $P2_12_12_1$, $a = 7{\cdot}0112\ (9)$, $b = 14{\cdot}385\ (1)$, $c = 37{\cdot}213\ (2)$ Å, $V = 3753{\cdot}2\ (6)$ Å^3, $Z = 8$, $D_x = 1{\cdot}452$ g cm^{-3}, Mo $K\alpha$, $\lambda = 0{\cdot}71073$ Å, $\mu = 16{\cdot}9$ cm^{-1}, $F(000) = 1648$, $T = 294$ K, final $R = 0{\cdot}0458$ for 3596 unique observed reflections. The two independent molecules have identical geometries. There are three planar moities, the pyridinium and phenyl rings, and the carbamoyl fragment in which the carbonyl and *N*-methyl groups are in the *anti* position. In both molecules the I^- ion has a short contact with the N atom of the pyridinium ring: 3·664 (8) [molecule (I)] and 3·590 (8) Å [molecule (II)].

Introduction. In a previous paper we described the crystal structures of 3-(*N*-methyl-*N*-benzyl)carbamoyl-1,2,4-trimethylpyridinium iodide (PYR) and of 3-[*N*-methyl-*N*-(*R*)-α-methylbenzyl]carbamoyl-1,2,4-trimethylpyridinium iodide (PYRM) (Kanters, van der Steen, Bastiaansen & de Graaf, 1986).

PYR, which crystallizes in space group $P2_12_12_1$, was found to contain a dissymmetric molecule and it was concluded that spontaneous resolution had occurred on crystallization. The chirality of PYR is caused by the two ring-methyl groups that force the carbonyl group out of the plane of the pyridinium ring, thus causing axial chirality of PYR.



PYR



PYRM

In PYRM additional chirality is introduced by the α-methyl group. In both PYR and PYRM the carbonyl group is directed to the *A* side† of the pyridine ring, and the carbonyl oxygen and *N*-methyl group are in a nearly eclipsed *syn* conformation. The *syn* rotamer is preferably formed when the quaternization is carried out at elevated temperature (373 K) in a nonpolar solvent (toluene), whereas the

† The *A* side of the pyridine ring is the side which faces the observer when the ring is viewed from a direction perpendicular to the plane of the ring and one travels around the ring in a counterclockwise direction when taking the shortest path from the ring N atom to the carboxamide group. The other side is the *B* side.

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0108-2701/89/091384-04$03.00