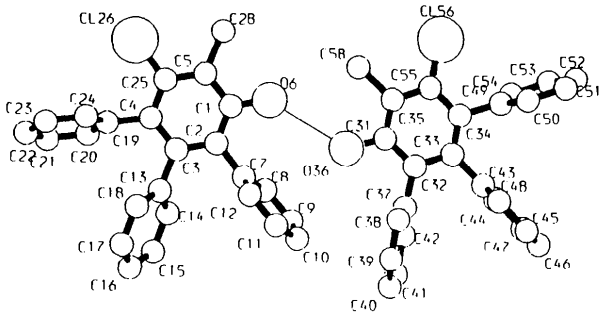


Fig. 2. View of (II) perpendicular to plane C(1)–C(5), showing hydrogen bond between crystallographically independent molecules.

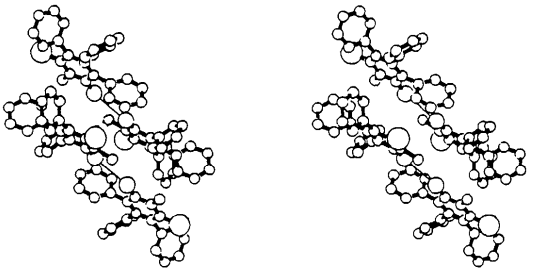


Fig. 3. Stereoview of (II) along the orthogonal axis *XO* showing the relationship between pairs of independent molecules related across the centre of inversion.

close contacts between the *XY* pair. The angle between the normals to planes *AX* and *AY* is 13·4 (5)°. These rings are approximately coplanar; the average deviation of an atom of *AY* from the mean plane of *AX* is 0·081 Å. This bimolecular fragment is close to a centre of inversion, giving a four-molecule cluster in the **c** direction (Fig. 3) in which O(36)···O(36′) is 3·88 (1) Å. There are no other short contacts between *XY* and *XY*′; molecule *X* partially overlays *Y*′ in the **c** direction with the average separation of the planes *AX* and *AY* 4·8 Å. There is no π overlap between these molecules. The rings closest to *AX* and *AY* are *CY*′ and *BX*′ respectively, with intermolecular angles between normals to planes 91·3 (5) and 64·7 (5)°.

References

AIKAWA, S., MARUYAMA, Y., OHASHI, Y. & SASADA, Y. (1978). *Acta Cryst.* B**34**, 2901–2904.

ANDERSON, D. T. & HORSPOOL, W. M. (1971). *J. Chem. Soc. Chem. Commun.* p. 615.

BARNES, J. C., HORSPOOL, W. M. & MACKIE, F. I. (1991). *Acta Cryst.* C**47**, 164–168.

HORSPOOL, W. M. (1971). *J. Chem. Soc. C*, pp. 400–404.

HORSPOOL, W. M. (1984). *J. Photochem.* **24**, 122–123.

MALLORY, F. B. & MALLORY, C. W. (1984). *Org. Reactions*, **30**, 1–456.

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

PADWA, A. (1967). *Org. Photochem.* **1**, 91–126.

ROBERTS, P. & SHELDRICK, G. M. (1975). *XANADU*. Program for crystallographic calculations. Univ. of Cambridge, England.

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

Acta Cryst. (1991). C**47**, 1885–1888

Structure of 4-[(1-Amidiniohydrazono)ethyl]-5-methyl-1-pyrazolecarboxamidium Dichloride Monohydrate

BY ALAIN COUSSON

Institut Curie, Section de Physique et Chimie, UA CNRS 448, 11 *rue Pierre et Marie Curie*, 75231 *Paris CEDEX* 05, *France*

BERNARD BACHET

Laboratoire de Minéralogie et Cristallographie, LA CNRS 09, *Université Pierre et Marie Curie*, 4 *Place Jussieu*, 75230 *Paris CEDEX* 05, *France*

AND BRUNO KOKEL AND MICHEL HUBERT-HABART

Institut Curie, Section de Physique et Chimie, Chercheurs INSERM, 11 *rue Pierre et Marie Curie*, 75231 *Paris CEDEX* 05, *France*

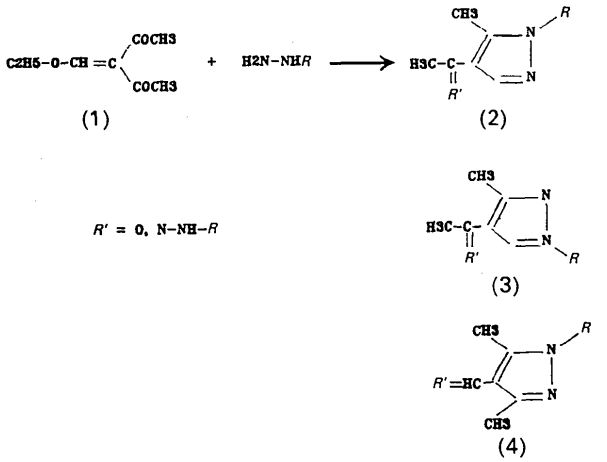
(*Received* 15 *November* 1990; *accepted* 25 *January* 1991)

Abstract. $[C_8H_{16}N_8]^{2+}.2Cl^-.H_2O$, $M_r = 313{\cdot}19$, triclinic, $P\bar{1}$, $a = 9{\cdot}069$ (3), $b = 10{\cdot}781$ (4), $c = 7{\cdot}810$ (4) Å, $\alpha = 108{\cdot}68$ (3), $\beta = 100{\cdot}68$ (3), $\gamma = 86{\cdot}68$ (4)°, $V = 711$ (6) Å^3, $Z = 2$, $D_x = 1{\cdot}463$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 0{\cdot}43$ mm^{-1}, $F(000) = 328$, $T = 293$ K. The structure

0108-2701/91/091885-04$03.00

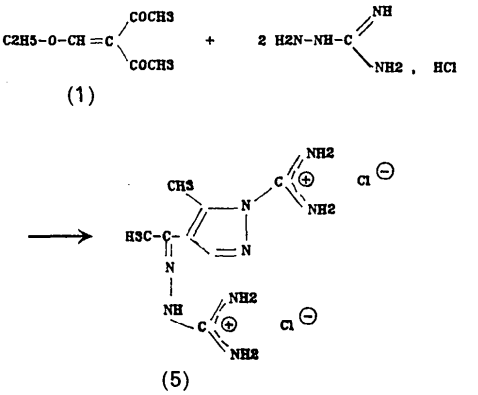
was solved by direct methods and refined to $R = 0{\cdot}047$ and $wR = 0{\cdot}048$ for 2385 independent reflections. The structural comparison between 4-acetyl-1-amidino-5-methylpyrazole amidinohydrazone dihydrochloride monohydrate and its isomer, 4-acetyl-1-amidino-3-methylpyrazole amidinohydrazone dihydrochloride monohydrate, allows definite discernment of these two closely related pyrazole isomers and confirmation of their mechanisms of formation.

Introduction. The reaction of 3-ethoxymethylenepentane-2,4-dione (1) and monosubstituted hydrazines can *a priori* lead to three 4-carbonylpyrazole isomers or their corresponding hydrazones.

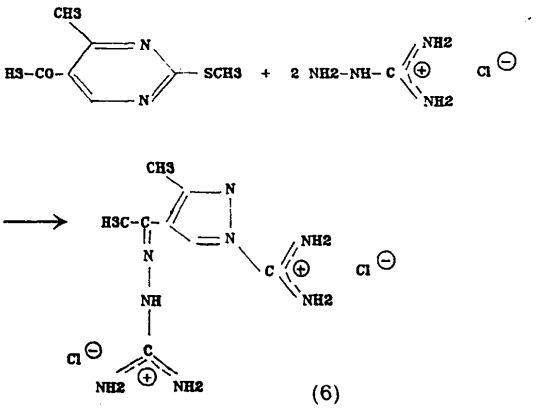


However, owing to the more electrophilic character of the ethoxy substituted methylene carbone of molecule (1), only the isomers (2) and (3) should be expected and are in fact isolated when such reactions are carried out. The relative proportion of formation of these two isomers depends on the type of monosubstituted hydrazine used, as well as on the conditions of the reaction (Menichi, Naciri, Kokel & Hubert-Habart, 1984; Menichi, Boutar, Kokel, Takagi & Hubert-Habart, 1986; Nagarajan, Arya & Shanoy, 1986). Thus, the formation of the 4-acetylpyrazole derivative or its corresponding hydrazone obviously depends on the quantity of hydrazine used and on the nature of this hydrazine (Menichi, Boutar, Kokel, Takagi & Hubert-Habart, 1986).

Operating at room temperature in methanolic solution and, using two equivalents of amidinohydrazine hydrochloride with a slight excess of hydrochloric acid and (1), we obtained exclusively 4-acetyl-1-amidino-5-methylpyrazole amidinohydrazone dihydrochloride (5), of type (2) (Menichi, Naciri, Kokel & Hubert-Habart, 1984).



In order to synthetize 4-acetyl-1-amidino-3-methylpyrazole amidinohydrazone dihydrochloride (6), an isomer of pyrazole (5) and of type (3), we started from 5-acetyl-4-methyl-2-methylthiopyrimidine which, under action of two equivalents of amidinohydrazine hydrochloride in boiling methanol made acidic by adding a small amount of hydrochloric acid, is unequivocally transformed into pyrazole (6) (Menichi, Naciri, Kokel & Hubert-Habart, 1984).



The structures of pyrazoles (5) and (6) were first established on the basis of their elemental analysis, mass and NMR spectra, and chemical behaviour (Menichi, Naciri, Kokel & Hubert-Habart, 1984). But the definite proof of the structure of pyrazole (6) was recently presented by establishing its crystal structure using X-ray diffraction (Cousson, Robert & Hubert-Habart, 1990), therefore giving more strength to the previous arguments used to discriminate between isomers (5) and (6), and more generally between isomers of types (2) and (3).

The pyrazole isomer (5), like pyrazole (6), shows a structural analogy with mitoguazone [methylglyoxal bis(guanylhydrazone), or MGBG], an anticancer drug. The accurate definition of common structural features pertaining to these molecules should help in

understanding better the structure–activity relationship among this family of compounds, and possibly facilitate the design of new anticancer drugs.

We wish now to report the crystal structure of isomer (5), and therefore complete the distinction between these two isomers.

Experimental. The preparation and description of (5) and (6) have already been reported (Menichi, Naciri, Kokel & Hubert-Habart, 1984; Menichi, Boutar, Kokel, Takagi & Hubert-Habart, 1986). (5) has been prepared according to the published procedure. 0·5 g of (5) was dissolved in 20 ml of boiling methanol and left to stand at room temperature for 9 d. Large crystals were thus formed. Single crystal 0·20 × 0·30 × 0·30 mm was selected for data collection. Unit-cell dimensions (from 25 reflections, $26 < \theta < 30°$) and reflection intensities were measured with a Philips PW 1100 four-circle diffractometer, graphite-monochromatized radiation [λ(Cu $K\alpha$) = 1·5418 Å], scan type: flying step-scan, scan range 1·65°θ, scan speed 0·03°θ s^{-1}, θ limits: 1–67°, $-10 \le h \le 10$, $-12 \le k \le 12$, $0 \le l \le 9$, 2559 data collected, 2385 unique, R_{int} = 0·032. Three standard reflections ($\bar{2}\bar{2}2$, 004 and 222), decomposition less than 0·01, absorption correction by *DIFABS* (Walker & Stuart, 1983), max. and min. transmission 0·98 and 0·84. Structure solved using direct methods [*SHELXS*86, from Sheldrick (1986) and *CRYSTALS* from Watkin, Carruthers & Betteridge (1985)]. Final R = 0·047 and wR = 0·048 for 2385 independent reflections such that $I \ge 3\sigma(I)$,* w = 1·0. Form factors from *International Tables for X-ray Crystallography* (1974, Vol. IV, pp. 99–101). On the last difference Fourier map ρ_{max} = 0·2 and ρ_{min} = −0·5 e Å^{-3}. Computer used: VAX 6313.

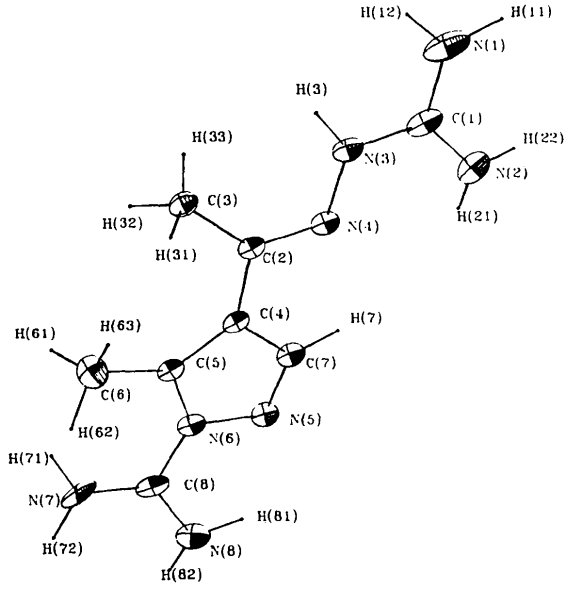


Fig. 1. Molecular structure of $[C_8N_8H_{16}]^{2+}.2Cl^-.H_2O$.

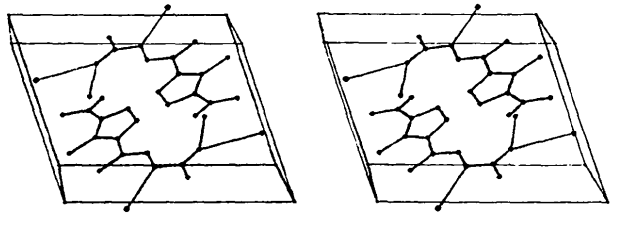


Fig. 2. Stereoscopic view of $[C_8N_8H_{16}]^{2+}.2Cl^-.H_2O$.

Table 1. *Atomic positional parameters and* U_{eq} *values for non-*H *atoms*

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

	x	y	z	U_{eq}(Å^2)
Cl(1)	0·70652 (9)	0·96596 (7)	0·3726 (1)	0·0396
Cl(2)	0·90759 (9)	0·25775 (8)	−0·0655 (1)	0·0407
C(1)	0·7034 (3)	0·5625 (3)	0·1735 (4)	0·0259
C(2)	0·4774 (3)	0·3153 (2)	0·1832 (3)	0·0192
C(3)	0·5531 (4)	0·1902 (3)	0·0957 (5)	0·0296
C(4)	0·3395 (3)	0·3151 (2)	0·2557 (3)	0·0194
C(5)	0·2470 (3)	0·2152 (3)	0·2423 (3)	0·0223
C(6)	0·2462 (5)	0·0741 (3)	0·1363 (6)	0·0403
C(7)	0·2747 (3)	0·4304 (3)	0·3609 (4)	0·0274
C(8)	0·0099 (3)	0·2221 (3)	0·3700 (4)	0·0256
N(1)	0·8320 (3)	0·5713 (3)	0·1198 (4)	0·0434
N(2)	0·6275 (3)	0·6652 (3)	0·2499 (4)	0·0333
N(3)	0·6529 (3)	0·4417 (2)	0·1433 (3)	0·0262
N(4)	0·5239 (3)	0·4304 (2)	0·2052 (3)	0·0228
N(5)	0·1528 (3)	0·4075 (2)	0·4121 (3)	0·0282
N(6)	0·1353 (3)	0·2737 (2)	0·3417 (3)	0·0237
N(7)	−0·0023 (4)	0·0968 (3)	0·3389 (5)	0·0427
N(8)	−0·0968 (3)	0·3038 (3)	0·4264 (4)	0·0349
O(1)	0·3390 (3)	0·7426 (2)	0·4007 (3)	0·0428

Table 2. *Intramolecular bond distances* (Å) *and angles* (°)

C(1)—N(1)	1·328 (4)	C(1)—N(2)	1·303 (4)
C(1)—N(3)	1·340 (4)	C(2)—C(3)	1·494 (4)
C(2)—C(4)	1·466 (4)	C(2)—N(4)	1·283 (3)
C(4)—C(5)	1·370 (4)	C(4)—C(7)	1·416 (4)
C(5)—C(6)	1·480 (4)	C(5)—N(6)	1·389 (3)
C(7)—N(5)	1·304 (4)	C(8)—N(6)	1·378 (4)
C(8)—N(7)	1·301 (4)	C(8)—N(8)	1·310 (4)
N(3)—N(4)	1·371 (3)	N(5)—N(6)	1·376 (3)

N(2)—C(1)—N(1)	122·5 (3)	N(3)—C(1)—N(1)	116·8 (3)
N(3)—C(1)—N(2)	120·7 (3)	C(4)—C(2)—C(3)	121·1 (2)
N(4)—C(2)—C(3)	125·3 (3)	N(4)—C(2)—C(4)	113·5 (2)
C(5)—C(4)—C(2)	131·5 (2)	C(7)—C(4)—C(2)	123·2 (2)
C(7)—C(4)—C(5)	105·3 (2)	C(6)—C(5)—C(4)	131·4 (3)
N(6)—C(5)—C(4)	105·6 (2)	N(6)—C(5)—C(6)	122·8 (3)
N(5)—C(7)—C(4)	112·9 (3)	N(7)—C(8)—N(6)	120·9 (3)
N(8)—C(8)—N(6)	117·3 (3)	N(8)—C(8)—N(7)	121·7 (3)
N(4)—N(3)—C(1)	117·7 (2)	N(3)—N(4)—C(2)	118·3 (2)
N(6)—N(5)—C(7)	104·4 (2)	C(8)—N(6)—C(5)	131·3 (2)
N(5)—N(6)—C(5)	111·7 (2)	N(5)—N(6)—C(8)	116·9 (2)

* Lists of structure factors, anisotropic thermal parameters and intramolecular bond distances and angles involving H atoms and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53949 (14 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Discussion. A view of the molecule showing its conformation and the numbering system is presented in Fig. 1; Fig. 2 is a stereoscopic view [figures drawn using *ORTEP* (Johnson, 1965)]. All intermolecular distances and angles were computed and evidence was found for hydrogen bonding. Crystalline cohesion seems to be due to hydrogen bonds as for MGBG, where parallel planar molecules are tied together by hydrogen bonds through water and Cl^- ions (Hamilton & La Placa, 1968). Atomic positional parameters are reported in Table 1. The intramolecular bond distances and angles are reported in Table 2.

Our study shows that in (5) and (6) the amidinohydrazone groups both have a *trans* conformation (*E*); however, these groups differ notably in their relative position on the pyrazole ring. The visualization of this difference offers a definite proof of the respective structures of these isomers and sustains the value of the chemical and NMR data hitherto put forward to characterize them.

The comparison of the three-dimensional structures of (5), (6) (Cousson, Robert & Hubert-Habart, 1990) and MGBG (Hamilton & La Placa, 1968) shows that pyrazole (6) is more closely related to MGBG than pyrazole (5). This could help to interpret the fact that the first two are good inhibitors of the enzyme *S*-adenosylmethioninedecarboxylase (SAMDC, 4.1.1. 50; *Enzyme Nomenclature*, 1978; Porter, Dave & Mihich, 1981), while the last one is much less so (Mamont, 1989). Extension of such a type of observation should help in designing analogues of MGBG with more satisfactory anticancer activity.

This work was supported by a grant (Contrat coopératif, décision 90-24) from the Institut Curie.

References

COUSSON, A., ROBERT, F. & HUBERT-HABART, M. (1990). *Acta Cryst.* C**47**, 395–397.

Enzyme Nomenclature (1978). pp. 378–379. New York: Academic Press.

HAMILTON, W. C. & LA PLACA, S. J. (1968). *Acta Cryst.* B**24**, 1147–1156.

JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.

MAMONT, P. S. (1989). Personal communication.

MENICHI, G., BOUTAR, M., KOKEL, B., TAKAGI, K. & HUBERT-HABART, M. (1986). *J. Heterocycl. Chem.* **23**, 275–279.

MENICHI, G., NACIRI, J., KOKEL, B. & HUBERT-HABART, M. (1984). *Heterocycles*, **22**, 2013–2017.

NAGARAJAN, K., ARYA, V. P. & SHANOY, S. J. (1986). *J. Chem. Res.* (*S*), pp. 166–167. *J. Chem. Res.* (*M*), pp. 1401–1443.

PORTER, C. W., DAVE, C. V. & MIHICH, E. (1981). *Polyamines in Biology and Medicine*, edited by D. R. MORRIS & L. J. MARTON, pp. 407–436. New York: Marcel Dekker.

SHELDRICK, G. M. (1986). *SHELXS*86. Program for the solution of crystal structures. Univ. of Göttingen, Germany.

WALKER, N. & STUART, D. (1983). *Acta Cryst.* **139**, 158–166.

WATKIN, D. J., CARRUTHERS, J. R. & BETTERIDGE, P. W. (1985). *CRYSTALS Users Guide*. Chemical Crystallography Laboratory, Univ. of Oxford, England.

Acta Cryst. (1991). C**47**, 1888–1892

Camphoric Acid and Ammonium Hydrogen Camphorate Monohydrate

BY JOHN C. BARNES,* JOHN D. PATON AND CHRISTINE S. BLYTH

Chemistry Department, The University, Dundee DD1 4HN, Scotland

AND R. ALAN HOWIE

Department of Chemistry, University of Aberdeen, Old Aberdeen, AB9 2UE, Scotland

(*Received* 8 *October* 1990; *accepted* 1 *February* 1991)

Abstract. (I) $C_{10}H_{16}O_4$, $M_r = 200{\cdot}23$, monoclinic, $P2_1$, $a = 13{\cdot}107$ (12), $b = 11{\cdot}828$ (8), $c = 7{\cdot}740$ (6) Å, $\beta = 109{\cdot}93$ (6)°, $V = 1128{\cdot}06$ Å^3, $Z = 4$, $D_x = 1{\cdot}18$ g cm^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, $\mu = 0{\cdot}28$ cm^{-1}, $F(000) = 432$, $T = 293$ K, $R = 0{\cdot}069$ for 1283 reflexions. (II) $C_{10}H_{16}O_4$, $M_r = 200{\cdot}23$, orthorhombic, $P2_12_12_1$, $a = 16{\cdot}31$ (3), $b = 13{\cdot}372$ (4), $c = 11{\cdot}486$ (2) Å, $V = 2505{\cdot}06$ Å, $Z = 8$, $D_x = 1{\cdot}06$ g cm^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, $\mu = 0{\cdot}59$ cm^{-1}, $F(000) = 864$, $T = 293$ K, 665 reflexions, disordered structure, refinement unsatisfactory. (III) $NH_4^+.C_{10}H_{15}O_4^-.H_2O$, $M_r = 235{\cdot}28$, trigonal, $P3_2$, $a = 13{\cdot}013$ (5), $c = 6{\cdot}326$ (7) Å, $V = 927{\cdot}71$ Å^3, $Z = 3$, $D_x = 1{\cdot}26$ g cm^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, $\mu = 0{\cdot}94$ cm^{-1}, $F(000) = 384$, $T = 293$ K, $R = 0{\cdot}080$ for 960 reflexions. Several crystalline forms of camphoric

* To whom correspondence should be addressed.

0108-2701/91/091888-05$03.00