Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

4,5-Dihydro-3-methyl-5-(4-methylphenyl)-1*H*-pyrazole-1-carboxamidinium acetate acetone hemisolvate

Viktor Kettmann* and Jan Světlík

Faculty of Pharmacy, Comenius University, Odbojarov 10, Bratislava, Slovak Republic 83232
Correspondence e-mail: kettmann@fpharm.uniba.sk

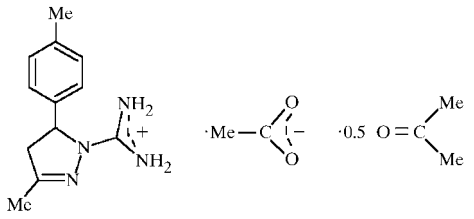
Received 2 May 2002
Accepted 23 May 2002
Online 20 June 2002

The X-ray structure analysis of the unexpected product of the reaction between 4-(4-methylphenyl)but-3-en-2-one and aminoguanidine revealed the title compound, $C_{12}H_{17}N_4^+ \cdot C_2H_3O_2^- \cdot 0.5C_3H_6O$, consisting of a protonated amidine moiety joined to a substituted pyrazoline ring at the N1 atom. The amidine group is protonated and the positive charge is delocalized over the three C—N bonds in a similar manner to that found in guanidinium salts. The amidinium moiety of the cation is linked to the acetate anions through four N—H···O hydrogen bonds, with N···O distances of 2.749 (4), 2.848 (4), 2.904 (4) and 2.911 (4) Å. The pyrazoline ring adopts a flattened envelope conformation and the substituted phenyl ring is oriented perpendicular to the attached heterocycle. The acetone solvate molecule lies across a twofold rotation axis.

Comment

Recently, aminoguanidine has been reported to be a potent inhibitor of nitric oxide synthase (Griffith & Gross, 1996). The remarkable biological activity of this simple nitrogen base prompted us to direct our research interest towards its derivatives, particularly heterocyclic congeners. For this purpose, we re-examined the literature data on the cyclocondensation of aminoguanidine with some α,β-unsaturated ketones, (1). However, under neutral conditions, the compounds obtained by us showed certain spectral dissimilarities when compared with the expected 1,2,4-triazines, (2) (Neunhoeffer, 1984). We had, therefore, to take into account three other possible candidates, of which pyrazole-1-carboximidamide, (3), was deduced as the most probable reaction product (Světlík & Sallai, 2002). To support our structural assignment, based predominantly on mass spectral behaviour, and, at the same time, to obtain detailed structural data for a subsequent structure–activity relationship study, we selected one of the unexpectedly formed heterocycles, *viz.* the title compound, (3*b*), for an X-ray structure analysis.

The asymmetric unit of (3*b*) contains a protonated amidinium molecule, one acetate anion and half an acetone molecule (Fig. 1). The latter molecule occupies a site of C_2 symmetry, with the C=O bond lying on the twofold axis along



(3*b*)

$(0,y,\frac{1}{4})$. The anomalous product of the aforementioned reaction has the structure (3), *i.e.* it consists of a substituted pyrazoline ring and a protonated amidine function attached to atom N1. The overall conformation of the molecule can also be inferred from Fig. 1. Calculation of the least-squares plane has shown that the pyrazoline ring adopts a flattened envelope conformation, with atom C5 on the flap; the deviation of the out-of-plane atom from the mean plane of the remaining four atoms [r.m.s. deviation = 0.001 (2) Å] is 0.209 (6) Å. The 4-methylphenyl group occupies a pseudo-axial position and, as a result, is approximately perpendicular to the mean plane of the pyrazoline ring [dihedral angle = 87.4 (2)°]. The phenyl ring is rotated about the exocyclic C5—C6 bond in such a manner that the ring nearly bisects the heterocyclic ring [torsion angle C4—C5—C6—C7 −62.9 (5)°]. Selected bond lengths and angles in the cation are listed in Table 1.

It has been reported (Krishna *et al.*, 1999) that the N—N bond length in the pyrazoline ring varies in the wide range 1.385 (4)–1.234 (8) Å, depending on the substituents bonded to the N atoms; accordingly, the lengths of the adjacent C=N bonds range from 1.288 (4) to 1.461 (8) Å. This is caused by a varying degree of conjugation within the π-electron portion of the pyrazoline ring, which is sensitively affected by the nature

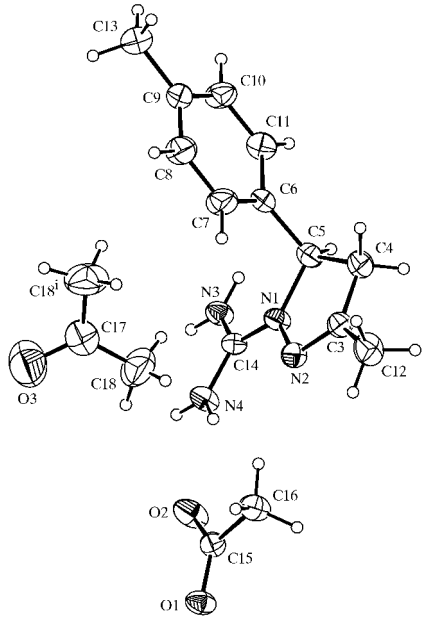


Figure 1
A view of the cation of (3*b*) with the atom-numbering scheme. Displacement ellipsoids are shown at the 35% probability level. H atoms are shown as circles of arbitrary radii. [Symmetry code: (i) $-x, y, \frac{1}{2}-z$.]

 DOI: 10.1107/S010827010200937X

of the substituent(s) bonded to the atoms of the π system. The N1—N2 bond length of 1.391 (4) Å found in (3*b*) further extends this range, approximating a pure single bond (1.41 Å; Burke-Laing & Laing, 1976). Similarly, the corresponding N2═C3 bond [1.274 (4) Å] has pure double-bond character (1.27 Å). That the lone-pair electrons on atom N1 are delocalized through conjugation with the amidine group rather than the N2═C3 double bond is also seen in the N1—C14 bond length [1.324 (5) Å], which is intermediate between a single and double bond, and equivalent to the two C—N bonds in the amidine moiety. Similar C—N bond distances have also been found in a number of inorganic salts containing the guanidinium cation (see, for example, Katrusiak & Szafrański, 1994). The bond distances and angles in the remaining parts of the molecule are normal. The positive charge of the protonated molecule is neutralized by the acetate anion. All four potential hydrogen-bond donors are involved in hydrogen bonding with the acetate anions (Table 2), and, as a result, the acetone solvate molecule is rather loosely packed by van der Waals interactions.

Experimental

The title compound, (3*b*), was synthesized by cyclocondensation of 4-(4-methylphenyl)but-3-en-2-one with aminoguanidine hydrogencarbonate, as described elsewhere (Světlík & Sallai, 2002). Briefly, a suspension of both reactants (10 mmol each) in *n*-butanol (30 ml) was refluxed with stirring for 3 h. The resulting solution was concentrated on a vacuum rotary evaporator. The syrupy residue obtained was dissolved in ethyl acetate (10 ml) and then left to stand at room temperature. After isolation of a by-product, the required amidine precipitated from the mother liquor (0.42 g, 20% yield, m.p. 493–494 K). Single crystals were obtained by recrystallization from an ethyl acetate–acetone (1:1) solution.

Crystal data

$C_{12}H_{17}N_4^+\cdot C_2H_3O_2^-\cdot 0.5C_3H_6O$
M_r = 305.38
Monoclinic, *C*2/*c*
a = 27.679 (11) Å
b = 8.126 (4) Å
c = 18.776 (9) Å
β = 129.15 (6)°
V = 3275 (3) Å^3
Z = 8
D_x = 1.239 Mg m^{-3}
D_m = 1.24 (1) Mg m^{-3}
D_m measured by flotation in bromoform/*c*-hexane
Mo $K\alpha$ radiation
Cell parameters from 15 reflections
θ = 9–20°
μ = 0.09 mm^{-1}
T = 293 (2) K
Prism, colourless
0.35 × 0.30 × 0.25 mm

Data collection

Syntex $P2_1$ diffractometer
$\theta/2\theta$ scans
2972 measured reflections
2883 independent reflections
1600 reflections with $I > 2\sigma(I)$
R_{int} = 0.043
θ_{max} = 25.1°
$h = -24 \rightarrow 32$
$k = 0 \rightarrow 9$
$l = -21 \rightarrow 0$
2 standard reflections
every 98 reflections
intensity decay: 2%

Refinement

Refinement on F^2
$R(F)$ = 0.073
$wR(F^2)$ = 0.229
S = 1.00
2883 reflections
204 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1372P)^2 + 0.7484P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.27 e Å^{-3}
$\Delta\rho_{min}$ = −0.39 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

N1—C14	1.324 (4)	N2—C3	1.274 (4)
N1—N2	1.391 (4)	C14—N4	1.319 (4)
N1—C5	1.485 (4)	C14—N3	1.326 (4)
C14—N1—N2	118.9 (3)	N1—C5—C6	112.3 (3)
C14—N1—C5	128.0 (3)	N1—C5—C4	99.9 (3)
N2—N1—C5	113.0 (3)	N4—C14—N1	120.1 (3)
C3—N2—N1	107.3 (3)	N4—C14—N3	118.9 (3)
N2—C3—C4	114.7 (3)	N1—C14—N3	121.0 (3)
N2—C3—C12	121.4 (3)		
C5—N1—N2—C3	−8.6 (4)	N2—N1—C5—C4	12.9 (4)
N1—N2—C3—C4	−0.3 (4)	C3—C4—C5—N1	−11.7 (4)
N2—C3—C4—C5	8.3 (4)	N2—N1—C14—N4	4.7 (5)

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N3—H3*A*···O1^{i}	0.86	2.05	2.903 (4)	176
N3—N3*B*···O1	0.86	2.14	2.912 (5)	149
N4—H4*C*···O1^{ii}	0.86	2.16	2.848 (4)	136
N4—H4*D*···O1^{i}	0.86	1.90	2.748 (4)	169

Symmetry codes: (i) $\frac{1}{2}-x, \frac{1}{2}+y, \frac{3}{2}-z$; (ii) $1-x, -y, z-\frac{1}{2}$.

All H atoms, except for those of the acetone molecule, were located from difference maps, and were subsequently treated as riding atoms, with C—H distances in the range 0.93–0.97 Å and N—H distances of 0.86 Å.

Data collection: *Syntex Software* (Syntex, 1973); cell refinement: *Syntex Software*; data reduction: *XP*21 (Pavelčík, 1987); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976).

The present work was supported by the Grant Agency of the Slovak Republic (project Nos. 1/8216/01 and 1/8215/01).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GD1208). Services for accessing these data are described at the back of the journal.

References

Burke-Laing, M. & Laing, M. (1976). *Acta Cryst.* B**32**, 3216–3224.
Griffith, O. W. & Gross, S. S. (1996). *Methods in Nitric Oxide Research*, edited by M. Feelish & J. S. Stamler, pp. 187–208. Chichester: John Wiley.
Johnson, C. K. (1976). *ORTEP*II. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.
Katrusiak, A. & Szafrański, M. (1994). *Acta Cryst.* C**50**, 1161–1163.
Krishna, R., Velmurugan, D., Murugesan, R., Shanmuga Sundaram, M. & Raghunathan, R. (1999). *Acta Cryst.* C**55**, 1676–1677.
Neunhoeffer, H. (1984). *Comprehensive Heterocyclic Chemistry*, Vol. 3, Part 2B, edited by A. R. Katritzky & C. N. Rees, pp. 432–435. Oxford: Pergamon Press.
Pavelčík, F. (1987). *XP*21. Comenius University, Slovakia.
Sheldrick, G. M. (1997). *SHELXS*97 and *SHELXL*97. University of Göttingen, Germany.
Světlík, J. & Sallai, L. (2002). *J. Heterocycl. Chem.* **39**, 363–366.
Syntex (1973). *Syntex Software*. Syntex Analytical Instruments, Cupertino, California, USA.