N-{(1E)-Amino[3-methyl-5-(4-methyl-phenyl)-4,5-dihydro-1H-pyrazol-1-yl]-methylene}-1H-imidazole-1-carbox-amide

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In the title compound, $C_{16}H_{18}N_6O$, an N-carbonylimidazole derivative of pyrazoline-1-carboximidamide, the π-electron density of the N atom in the 1-position on the pyrazoline ring is delocalized through the amidine moiety and the adjacent carbonyl group. The imidazole ring, though coplanar with the rest of the molecule, is deconjugated. The pyrazoline ring adopts a flat-envelope conformation, having the substituted phenyl ring oriented perpendicular to the mean plane of the heterocycle. Both of the two potential hydrogen-bond donors are involved in intramolecular hydrogen-bonding interactions.

Comment

Recently, as part of a program aimed at developing potent inhibitor(s) of nitric oxide synthase based on heterocyclic derivatives of aminoguanidine (Griffith & Gross, 1996), we reported a study of the ring-closure reactions of 4,5-dihydro-3-methyl-5-(2-hydroxyphenyl)-1H-pyrazole-1-carboximidamide, (Ia), with $C_1–C_3$ reagents (Světlik & Liptaj, 2002). We have found that cyclocondensation of (Ia) with 1,1'-carbonyldiimidazole, (II), afforded a highly strained tetracyclic molecule, (III). Formation of the novel 5,11-methano[1,2,4]triazolo[1,2-c][1,2,4]benzoxadiazepine, (III), a prototype of a new bridged heterocyclic family, can be envisaged by the intermediacy of two transient structures, (IV) and (V) (Světlik & Liptaj, 2002). Since the inertness of the phenol hydroxy group in (Ia) towards (II) seemed striking, we were interested in verifying the postulated reaction mechanism. For this purpose, we chose a related tolyl derivative, (Ib), as a vehicle for better insight into the heterocyclization mentioned above. Thus, under similar conditions, condensation of (Ib) gave rise to a compound whose spectral properties are compatible with the first type of the two assumed intermediates, i.e. the imidazole-1-carboxamide (VI). To confirm

this and, at the same time, to establish the spatial distribution of the functional groups for subsequent molecular-modeling studies, we selected compound (VI) for X-ray structural analysis.
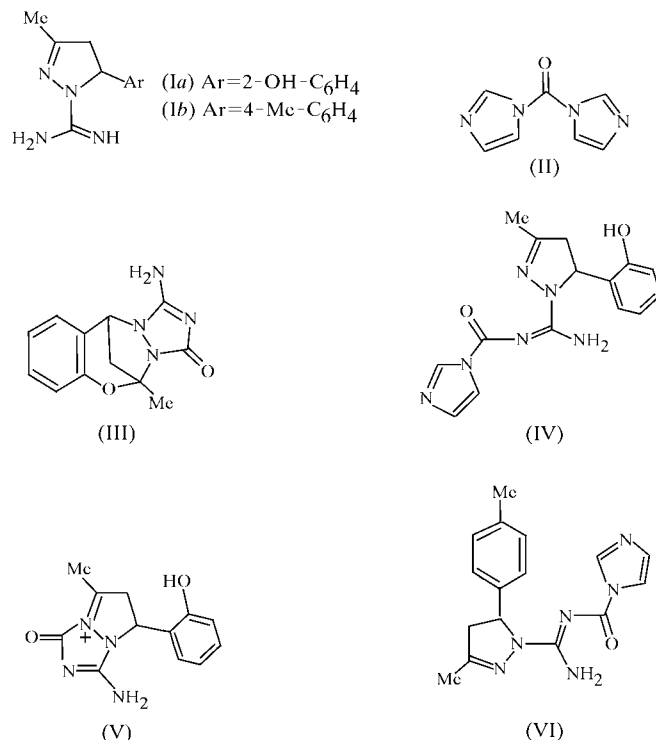
The molecular structure and the atom-numbering scheme of (VI) are shown in Fig. 1. As can be seen, (VI) is indeed the tolyl derivative of the transient intermediate (IV), i.e. (VI) consists of a substituted pyrazoline ring and a carbonyl-imidazole function attached to the amidine N atom. The overall 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 flat-envelope conformation, with atom C5 as the flap; the deviation of the out-of-plane atom from the mean plane of the remaining four atoms [r.m.s. deviation = 0.006 (2) Å] is 0.307 (3) Å. The tolyl group occupies a pseudo-axial position and, as a result, is approximately perpendicular to the mean plane of the pyrazoline ring [dihedral angle = 77.9 (1)°]. The aryl ring is situated about the exocyclic C5—C6 bond in such a manner that the ring does not bisect the heterocyclic ring but is rotated towards atom N1 [N1—C5—C6—C7 = −20.3 (2)°].

Selected bond lengths and angles in the molecule are listed in Table 1. It has been reported (Krishna et al., 1999) that the N—N bond length in the pyrazoline ring lies in a wide range, from 1.385 (4) to 1.234 (8) Å, depending on the substituents bonded to the N atoms; accordingly, the length of the adjacent C=N bond ranges from 1.288 (4) to 1.461 (8) Å. This variation is caused by the varying degrees of conjugation within the π-electron portion of the pyrazoline ring, which is sensitively affected by the nature of the substituent(s) bonded to the atoms of the π system. The N1—N2 bond length [1.401 (2) Å] found in the present derivative further extends this range,

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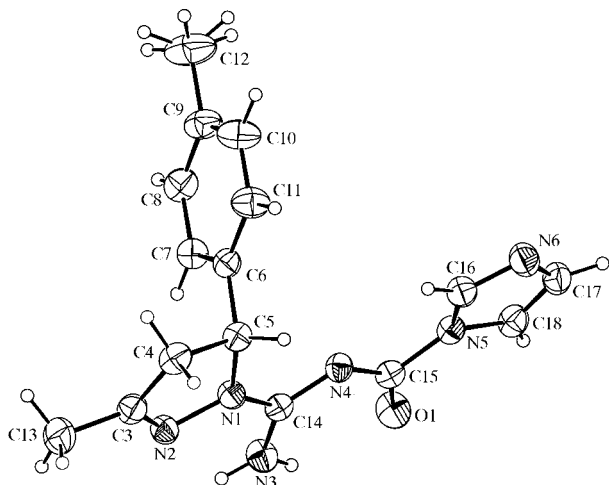
organic compounds

Figure 1
A view of the title compound, (VI), with the atom-numbering scheme. Displacement ellipsoids are shown at the 35% probability level and H atoms are shown as circles of arbitrary radii.

approximating to a purely single bond (1.41 Å; Burke-Laing & Laing, 1976). Similarly, the corresponding N2=C3 bond [1.280 (2) Å] has pure double-bond character (1.28 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 [1.342 (2) Å], which is intermediate between a single and double bond and equivalent to the two C—N bonds in the amidine moiety. The conjugation is further extended to the N4—C15—O1 moiety, as reflected in its molecular dimensions (Table 1), which are comparable to those typically found in amides (Benedetti *et al.*, 1983). In contrast, the imidazole ring is deconjugated (though coplanar) with the adjacent π system, as indicated by (i) the N5—C15 bond distance [1.435 (2) Å], which is slightly longer than the value [1.425 (3) Å] reported for a pure Nsp^2—Csp^2 single bond (Adler *et al.*, 1976) and (ii) the pattern of bond lengths and angles within the imidazole ring, which is identical to that found in unsubstituted imidazole or its derivatives containing substituents not involved in conjugation with the aromatic system (*e.g.* Perry *et al.*, 1980; Moriuchi *et al.*, 2001), as revealed by a search of the Cambridge Structural Database (Allen, 2002). Other bond distances and angles are close to those generally expected.

The molecule is stabilized by two intramolecular hydrogen bonds, between atom N3 as a double hydrogen-bond donor, and atoms O1 and N2 as acceptors (Table 2). Besides these hydrogen bonds, there is also a short intramolecular C16—H···N4 contact, which, on the basis of its H···N distance (Table 2), can be regarded as a weak hydrogen-bonding interaction (Taylor & Kennard, 1982) and may contribute to the planarity of the imidazolecarboxamide moiety. An analysis of the intermolecular contacts reveals two weak intermolecular C—H···π(aryl) interactions [H8···Cg1 = 3.01 Å and H13C···Cg2 = 3.08 Å, where Cg1 and Cg2 are the centroids of the phenyl rings of the molecules at ($x - y, x, -z$) and ($y, -x + y, -z$), respectively] and a number of van der Waals interactions.

Experimental

The title compound, (VI), was synthesized by reaction of 3-methyl-5-(4-methylphenyl)-4,5-dihydro-1*H*-pyrazole-1-carboximidamide acetate, prepared previously (Světlik & Sallai, 2002), with 1,1′-carbonyldiimidazole according to the method of Světlik & Liptaj (2002). A solution of the pyrazole derivative (0.5 mmol) and 1,1′-carbonyldiimidazole (5 ml) was heated at 373 K for 1 h. The reaction mixture was concentrated *in vacuo* and the residue was dissolved in dichloromethane (10 ml). After washing with 5% HCl (2 × 5 ml) and water (1 × 5 ml), the organic layer was dried (MgSO$_4$) and concentrated. The resulting oil was dissolved in ethyl acetate (5 ml) and left to stand at room temperature. The crystalline material was collected and recrystallized from acetone (yield: 0.040 g, 26%; m.p. 446–448 K). IR (KBr, cm^{-1}): 3470 (NH$_2$), 3330 (NH$_2$ assoc.), 1663 (C=O + C=N), 1596 (C=N), 1562 (C=C); ^{1}H NMR (CDCl$_3$): δ 2.17 (3H, *s*, Me), 2.31 (3H, *s*, Me tolyl), 2.78 (1H, *dd*, *J* = 18.3 and 5.4 Hz, 4-H$_a$ pyrazole), 3.46 (1H, *dd*, *J* = 18.3 and 11.7 Hz, 4-H$_b$ pyrazole), 5.48 (1H, *dd*, *J* = 11.7 and 5.4 Hz, 5-H pyrazole), 6.56 (1H, *brs*, NH), 6.89 (1H, *s*, 4-H imidazole), 7.07 (2H, *d*, H-3′ and H-5′), 7.16 (2H, *d*, H-2′ and H-6′), 7.30 (1H, *s*, 5-H imidazole), 7.90 (1H, *s*, 2-H imidazole), 8.72 (1H, *brs*, NH assoc.); ^{13}C NMR (CDCl$_3$): δ 16.2 (Me), 21.0 (Me tolyl), 47.4 (CH$_2$), 60.9 (CH), 116.8 (CH-5 imidazole), 124.8 (CH-2′ + CH-6′), 129.1 (CH-4 imidazole), 129.8 (CH-3′ + CH-5′), 137.3 (CH-2 imidazole), 137.6 (C-4′), 139.4 (C-1′), 157.2, 157.3 (CON, N—C=N), 158.1 (C-3 pyrazole).

Crystal data

C$_{16}$H$_{18}$N$_6$O	Mo $K\alpha$ radiation
M_r = 310.36	Cell parameters from 25
Trigonal, $R\bar{3}$	reflections
a = 32.322 (5) Å	θ = 9–20°
c = 8.084 (2) Å	μ = 0.09 mm^{-1}
V = 7314 (2) Å^3	T = 293 (2) K
Z = 18	Prism, colourless
D_x = 1.267 Mg m^{-3}	0.35 × 0.30 × 0.25 mm

Data collection

Siemens P4 diffractometer	$h = -38 \rightarrow 38$
$\omega/2\theta$ scans	$k = -38 \rightarrow 38$
3678 measured reflections	$l = -1 \rightarrow 9$
2872 independent reflections	3 standard reflections
2061 reflections with $I > 2\sigma(I)$	every 97 reflections
R_{int} = 0.040	intensity decay: 2%
θ_{max} = 25.1°	

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0531P)^2$
$R[F^2 > 2\sigma(F^2)]$ = 0.040	$+ 2.798P]$
$wR(F^2)$ = 0.108	where $P = (F_o^2 + 2F_c^2)/3$
S = 1.01	$(\Delta/\sigma)_{max}$ = 0.001
2872 reflections	$\Delta\rho_{max}$ = 0.14 e Å^{-3}
218 parameters	$\Delta\rho_{min}$ = -0.16 e Å^{-3}
H atoms treated by a mixture of independent and constrained refinement	

The parameters of the two H atoms bonded to atom N3 were refined isotropically; other H atoms were refined with fixed geometry, riding on their carrier atoms, with U_{iso}(H) set at 1.2 (1.5 for the methyl H atoms) times U_{eq} of the parent atom. The C12 methyl H atoms were treated using a twofold disorder model. Reflection $\bar{1}20$, affected by secondary extinction, was omitted from the refinement.

Data collection: *XSCANS* (Siemens, 1991); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics:

PLUTON (Spek, 1992); software used to prepare material for publication: *SHELXL*97.

Table 1
Selected geometric parameters (Å, °).

N1—C14	1.342 (2)	C14—N3	1.327 (2)
N1—N2	1.401 (2)	C14—N4	1.331 (2)
N1—C5	1.471 (2)	N4—C15	1.332 (2)
N2—C3	1.280 (2)	C15—O1	1.2224 (19)
C3—C4	1.493 (3)	C15—N5	1.435 (2)
C4—C5	1.536 (2)		
C14—N1—N2	121.07 (13)	N4—C14—N1	114.34 (14)
C14—N1—C5	125.26 (14)	C14—N4—C15	120.31 (14)
N2—N1—C5	112.77 (12)	O1—C15—N4	132.00 (16)
N3—C14—N4	127.73 (16)	O1—C15—N5	117.94 (14)
N3—C14—N1	117.93 (16)	N4—C15—N5	110.06 (14)
N1—C5—C6—C7	−20.3 (2)	C14—N4—C15—O1	−3.6 (3)
N2—N1—C14—N3	3.3 (2)	N4—C15—N5—C16	−6.9 (2)

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

D—H⋯A	D—H	H⋯A	D⋯A	D—H⋯A
N3—H3A⋯O1	0.87 (2)	2.15 (2)	2.754 (2)	126 (2)
N3—H3B⋯N2	0.92 (2)	2.26 (2)	2.688 (2)	108 (2)
C16—H16⋯N4	0.93	2.52	2.728 (2)	93

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