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5-Amino-1-[2-(diethylamino)ethyl]-1*H*-imidazole-4-carboxamide

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Key indicators

Single-crystal X-ray study
T = 173 K
Mean σ(C–C) = 0.003 Å
R factor = 0.046
wR factor = 0.121
Data-to-parameter ratio = 12.1

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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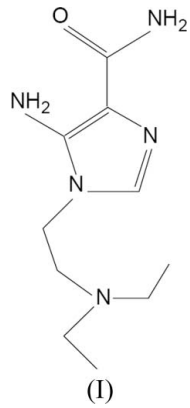
Intramolecular hydrogen bonds influence the molecular conformation of the title compound, $C_{10}H_{19}N_5O$, resulting in an extended planar hydrogen-bonded heterocyclic ring structure. The bulky diethylaminoethyl group adopts a butterfly conformation. The stabilization of the crystal structure is supported by an extensive network of intermolecular hydrogen bonds.

Comment

Studies of structure–activity relationships have observed that most of the molecules claimed to have bronchodilating activity possess a planar heterocyclic structure (Lunt, 1982). Preferably, they contain a carbonyl group and a substituent of a basic, neutral or weakly acidic character. Intramolecular hydrogen bonds form an extended planar heterocyclic structure in some potent anti-allergenics (Lunt, 1982; Ford *et al.*, 1986). These hydrogen-bonded planar structures have also been observed in the structures of 5-amino-imidazole-4-carboxamides (Banerjee, Roychowdhury, Chattopadhyay *et al.*, 1991; Banerjee, Roychowdhury, Yamane *et al.*, 1991; Banerjee *et al.*, 1999).

The butterfly conformation of bulky groups such as diphenylmethyl and similar two-ring systems in well known anti-allergenics, such as chloropheniramine, bromopheniramine and promethazine, indicates that this conformation may play a vital role in the interaction of the compound at the receptor site. The effect of various substituents at different positions of the imidazole ring on the conformation of molecules and their crystal structures has been studied (Adamiak & Saenger, 1979; Simon *et al.*, 1980; Banerjee, Roychowdhury, Chattopadhyay *et al.*, 1991; Banerjee, Roychowdhury, Yamane *et al.*, 1991; Banerjee *et al.*, 1999). Against this background, we report here the crystal structure of the title compound, (I).



(I)

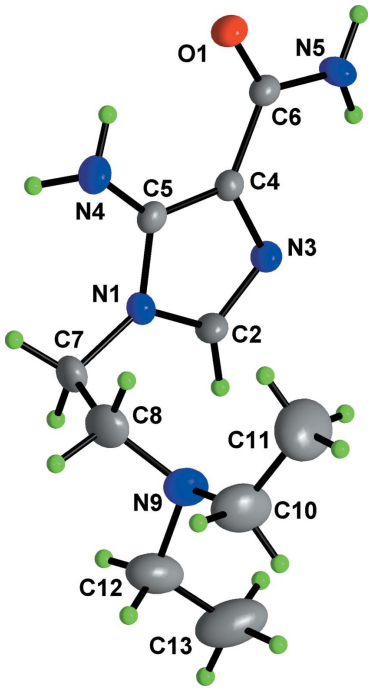


Figure 1
The molecular structure of (I), showing the atom-numbering scheme and with displacement ellipsoids drawn at the 50% probability level.

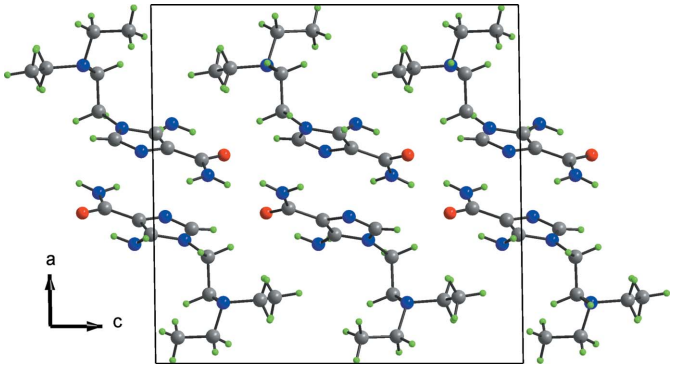


Figure 2
The molecular packing of (I), viewed along the *b* axis.

The molecular structure of compound (I) is shown in Fig. 1. The imidazole ring is planar (χ^2 = 0.6). The carboxamide group is oriented in such a manner that it participates in two intramolecular hydrogen bonds, thus stabilizing the molecular conformation. The carbonyl atom O1 of the carboxamide group accepts a hydrogen bond from the amino group at the 5-position of the imidazole ring (for geometric details, see Table 1) and forms a six-membered (O1/C6/C4/C5/N4/H41) hydrogen-bonded chelate ring, almost coplanar with the imidazole ring; the dihedral angle is 1.89 (3)°. The imidazole atom N3 accepts an intramolecular hydrogen bond from the amino N atom of the carboxamide group, forming a five-membered chelate ring (N3/C4/C6/N5/H52), nearly coplanar with the imidazole ring; the dihedral angle is 4.22 (3)°. The actual substituents in the imidazole ring make the molecular conformation quite rigid, producing an extended planar

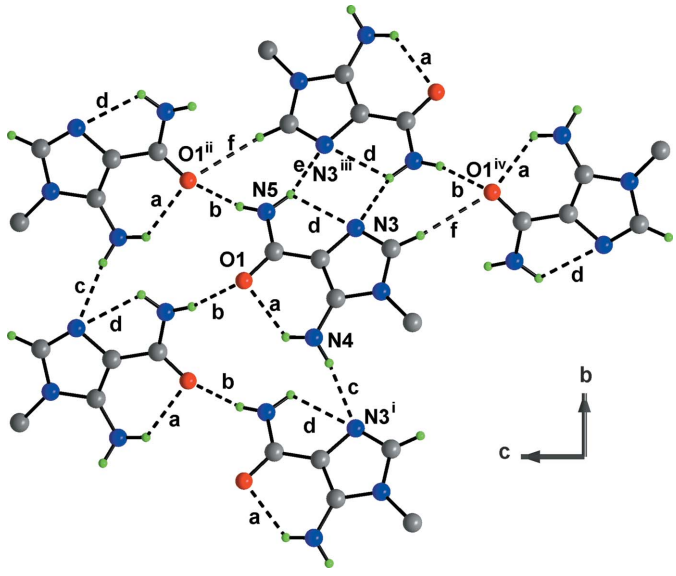


Figure 3
The hydrogen-bonding scheme (dashed lines). Hydrogen bond labels *a–f* and symmetry codes are as defined in Table 1.

hydrogen-bonded ring structure, an important structural requirement for antihistaminic and anti-asthmatic activity. It has been found that an intramolecular hydrogen bond is more difficult to break than a comparable intermolecular bond formed between similar donors and acceptors (Etter, 1990).

The C5—N4 bond distance of 1.378 (2) Å indicates that the lone pairs of electrons on the amino group are highly conjugated with the imidazole ring, and it is close to the distance found in the structure of 5-amino-1-(2-hydroxyethyl)imidazole-4-carboxamide [1.370 (4) Å; Banerjee *et al.*, 1999]. The geometry of the carboxamide group agrees well with values reported in the literature (Adamiak & Saenger, 1979; Banerjee, Roychowdhury, Chattopadhyay *et al.*, 1991). The lengthening of the C6═O1 bond, together with the concomitant shortening of the C6—N5 bond, suggests conjugation of the carboxamide group with the imidazole ring. This conjugation favours the coplanarity of the carboxamide group with the imidazole ring and, as a result, facilitates the formation of the intramolecular hydrogen bonds. Systematic studies of substituted 5-amino-imidazole-4-carboxamides and 1,2,3-triazole-4-carboxamide (Banerjee *et al.*, 1999; Afshar *et al.*, 1987) have shown that the orientation of the 4-carboxamide group facilitates the formation of an intramolecular hydrogen bond between the vicinal 5-amino group and the 4-carboxamide group. Angular asymmetry in the exocyclic angles at C5, as observed in other amino-substituted imidazoles (Banerjee *et al.*, 1999; Afshar *et al.*, 1987; Adamiak *et al.*,1979), has also been found in this structure.

The deviation of the N1—C7—C8 angle [111.74 (15)°] from the ideal tetrahedral value relieves the steric strain due to the bulky diethylaminoethyl substitution at C7. The N1—C7—C8—N9 torsion angle is −65.6 (2)°.

Fig. 2 shows the packing arrangement of the molecules, viewed down the *b* axis. The crystal structure is stabilized by an extensive network of intermolecular hydrogen bonds,

shown in Fig. 3. There are classical hydrogen bonds of type N—H···O (labelled *a* and *b* in Fig. 3) and N—H···N (*c*, *d* and *e*), and a weak hydrogen bond of type C—H···O (*f*) (Table 1). Assignment of the hydrogen-bond descriptors, based on graph-set theory (Etter, 1990; Etter *et al.*, 1990; Bernstein *et al.*, 1995; Grell *et al.*, 1999), was obtained using the program *PLUTO*, according to Motherwell *et al.* (1999). These hydrogen bonds make the following patterns at the first level of the graph-set: intramolecular strings $S(6)$ (hydrogen bond type *a*) and $S(5)$ (*d*), chains $C(4)$ (*b*), $C(5)$ (*c*) and $C(6)$ (*f*), and a ring $R_2^2(10)$ (*e*). On the second level of the graph-set, chains $C_2^2(11)$ (hydrogen bond types *b* and *c*), $C_2^2(9)$ and $C_2^2(7)$ (*b* and *e*), $C_2^2(9)$ (*c* and *f*), $C_2^2(10)$ (*c* and *f*), $C_2^2(7)$ (*e* and *f*) and $C_2^2(11)$ (*e* and *f*), and rings $R_4^4(20)$ (*b* and *f*), $R_2^4(16)$ (*b* and *f*), $R_4^4(20)$ (*c* and *e*) and $R_2^4(16)$ (*c* and *e*) are recognized.

Experimental

The title compound, (I) (m.p. 481–482 K), was synthesized by reaction of 2-diethylaminoethylamine with ethyl *N*-(carbamoylcyanomethyl)formimidate in refluxing acetonitrile, which was in turn generated by heating an equimolar mixture of 2-amino-2-cyanoacetamide and triethyl orthoformate in refluxing acetonitrile (Sen & Ray, 1976). Diffraction-quality single crystals were obtained by slow evaporation of an ethanolic solution of (I) at room temperature.

Crystal data

$C_{10}H_{19}N_5O$
M_r = 225.30
Monoclinic, $P2_1/c$
a = 14.2768 (1) Å
b = 5.9066 (1) Å
c = 14.6413 (2) Å
β = 90.778 (1)°
V = 1234.55 (3) Å^3
Z = 4
D_x = 1.212 Mg m^{-3}
D_m = 1.202 Mg m^{-3}
D_m measured by flotation in benzene–bromoform
Mo $K\alpha$ radiation
Cell parameters from 8192 reflections
θ = 2.8–25.0°
μ = 0.08 mm^{-1}
T = 173 (2) K
Plate, colourless
1.00 × 0.20 × 0.04 mm

Data collection

Bruker SMART CCD area-detector diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2002)
T_{min} = 0.921, T_{max} = 0.997
11862 measured reflections
2161 independent reflections
1866 reflections with $I > 2\sigma(I)$
R_{int} = 0.048
θ_{max} = 25.0°
$h = -16 \rightarrow 16$
$k = -7 \rightarrow 7$
$l = -17 \rightarrow 17$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.046
$wR(F^2)$ = 0.121
S = 1.03
2161 reflections
178 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0608P)^2 + 0.6313P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}

Table 1
Hydrogen-bonding geometry (Å, °).

Label	D—H···A	D—H	H···A	D···A	D—H···A
a	N4—H41···O1	0.89 (2)	2.28 (2)	2.944 (2)	132 (2)
b	N4—H42 N3^{i}	0.90 (2)	2.25 (2)	3.137 (2)	168 (2)
c	N5—H51···O1^{ii}	0.88 (2)	2.06 (2)	2.9248 (19)	165 (2)
d	N5—H52···N3	0.91 (2)	2.47 (2)	2.852 (2)	105 (2)
e	N5—H52···N3^{iii}	0.91 (2)	2.26 (2)	3.088 (2)	150 (2)
f	C2—H2···O1^{iv}	0.95	2.55	3.463 (2)	162

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

C-bound H atoms were constrained to an ideal geometry, with C—H distances of 0.95 (aromatic H), 0.99 (methylene H) and 0.98 Å (methyl H); their displacement parameters were refined isotropically. Amino H atoms were located in a difference Fourier map and refined without restraints.

Data collection: *SMART* (Siemens, 1995); cell refinement: *SAINT* (Siemens, 1995); data reduction: *SAINT* and *SADABS* (Sheldrick, 2002); program(s) used to solve structure: *SHELXTL* (Bruker, 2001); program(s) used to refine structure: *SHELXTL*; molecular graphics: *DIAMOND* (Brandenburg, 2005); software used to prepare material for publication: *SHELXTL*.

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