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5-Amino-4-(4-diethylaminophenyl)-2-(4-hydroxyphenyl)-7-(pyrrolidin-1-yl)-1,6-naphthyridine-8-carbonitrile

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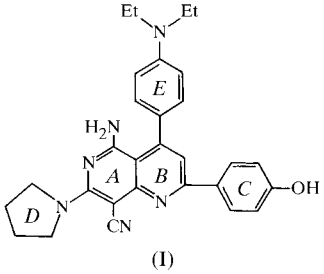
In the title compound, $C_{29}H_{30}N_6O$, the naphthyridine moiety is planar with a dihedral angle between the fused rings of 1.9 (1)°. The phenol ring is nearly coplanar, while the diethylaminophenyl substituent is orthogonal to the central naphthyridine ring and the pyrrolidine ring makes an angle of 11.2 (1)° with it. The O atom of the hydroxy substituent is coplanar with the phenyl ring to which it is attached. The molecular structure is stabilized by a C—H···N-type intramolecular hydrogen bond and the packing is stabilized by intermolecular C—H···π, O—H···N and N—H···O hydrogen bonds.

Comment

Naphthyridine derivatives constitute an important class of compounds possessing diverse types of biological properties. They have been reported as potential drugs for the treatment of bladder function disorders (Natsugari *et al.*, 1999). They also possess antitumor (el-Subbah *et al.*, 1999), antibacterial (Domagala *et al.*, 1993), tuberculostatic (Ferrarini *et al.*, 1998), cardiotonic (Mohan & Mishra, 1997), anticonvulsant and insecticidal (Damon & Nadelson, 1981) properties. 1,6-Naphthyridine derivatives have been tested pharmacologically as potent antagonists at adrenoreceptors (Brown *et al.*, 1993), they are also used as novel potent adenosine 3′,5′-cyclic phosphate phosphodiesterase III inhibitors (Singh *et al.*, 1995). As a continuation of studies on 1,6-naphthyridine derivatives (Sankaranarayanan *et al.*, 1999) and to achieve a better understanding of the influence of structural and conformational changes on its biological activity, the X-ray crystal structure analysis of the title compound, (I) (Fig. 1), has been carried out.



(I)

The five rings of the molecule are identified as *A* (C5/N6/C7–C10), *B* (N1/C2–C4/C10/C9), *C* (C19–C24), *D* (N14/C15–C18) and *E* (C25–C30). The N—C and other bond distances are comparable with the related structures studied previously (Sankaranarayanan *et al.*, 1999; Thirumurugan *et al.*, 1999; Govindasamy *et al.*, 2000). The bond distance C5—N11 is shorter than the typical C—N single-bond distance (1.47 Å) indicating conjugation of the amino group with the aromatic system of naphthyridine. The naphthyridine ring is planar with a dihedral angle between the fused pyridine rings (rings *A* and *B*) of 1.9 (1)°.

The least-squares planes through the phenyl rings make dihedral angles of 1.9 (1) (ring *C*) and 89.5 (1)° (ring *E*) with ring *B*, to which they are attached, indicating the perpendicular orientation of ring *E*. The best plane through the pyrrolidine ring makes a dihedral angle of 11.3 (1)° with the pyridine ring (*A*). The sum of the bond angles around N14 and N31 are 359.6 (3) and 358.2 (3)°, respectively, indicating sp^2 hybridization. The cyano bond distance C12≡N13 agrees well with the literature value of 1.138 (7) Å (Allen *et al.*, 1987). The orientation of the diethyl substituent with respect to the phenyl ring (*E*) can be described by the torsion angles C28—N31—C32—C33 of −122.5 (3)° and C28—N31—C34—C35 of 82.0 (3)°. Atom O36 is coplanar [C20—C21—C22—O36 = 177.3 (2)°] with the phenyl ring (*C*) to which it is attached. Due to steric interactions, bond angles C4—C10—C5 [127.3 (2)°] and C8—C7—N14 [125.1 (2)°] are widened and bond angles N1—C9—C8 [116.7 (2)°] and N1—C2—C19

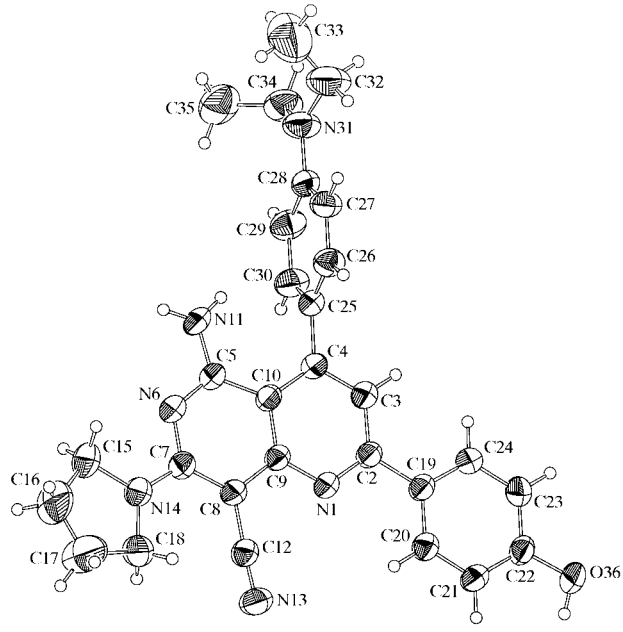


Figure 1
The molecular structure of (I) showing 50% probability displacement ellipsoids and the atom-numbering scheme.

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[116.3 (2)°] are narrowed from 120°; these observations are also noted in related structures (Chinnakali *et al.*, 1998).

Apart from normal van der Waals interactions, the molecular structure is stabilized by an intramolecular C—H···N-type hydrogen bond and the molecular packing is stabilized by intermolecular N—H···O and O—H···N hydrogen bonds and a C—H···*Cg*1 interaction (Table 2), where *Cg*1 is the centroid of ring *E*.

Experimental

A solution of 4-methoxy-4′-hydroxybenzalacetophenone (2.4 mmol), malononitrile (4.8 mmol) and pyrrolidine (4.8 mmol) in ethanol (20 ml) was refluxed for 25 h. The solvent was removed under reduced pressure. The residue was purified by column chromatography and the solid thus obtained was recrystallized from ethanol–ethyl acetate (1:1) solvent by slow evaporation.

Crystal data

$C_{29}H_{30}N_6O$
M_r = 478.59
Triclinic, $P\overline{1}$
a = 9.9502 (2) Å
b = 10.3680 (2) Å
c = 12.4995 (2) Å
α = 94.692 (1)°
β = 94.319 (1)°
γ = 98.505 (1)°
V = 1266.03 (4) Å^3
Z = 2
D_x = 1.255 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 4453 reflections
θ = 2.8–33.1°
μ = 0.08 mm^{-1}
T = 293 (2) K
Block, yellow
0.42 × 0.38 × 0.32 mm

Data collection

Siemens SMART CCD area-detector diffractometer
ω scans
6716 measured reflections
4298 independent reflections
3707 reflections with $I > 2\sigma(I)$
R_{int} = 0.020
θ_{max} = 25.0°
$h = -11 \rightarrow 10$
$k = -12 \rightarrow 12$
$l = -14 \rightarrow 14$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.055
$wR(F^2)$ = 0.170
S = 1.01
4298 reflections
329 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0900P)^2 + 0.5843P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.36 e Å^{-3}
$\Delta\rho_{min}$ = −0.36 e Å^{-3}

The coordinates of the hydroxyl H atom (H36) have been calculated with *HYDROGEN* (Nardelli, 1999). By accepting these coordinates and keeping the distance between the O36 and H36 atoms as 0.85 Å using the command *DFIX* in *SHELXL*97 (Sheldrick, 1997), the structure was further refined. All other H atoms were included in calculated positions and allowed to ride on their corresponding parent atoms.

Table 1
Selected geometric parameters (Å, °).

N1—C2	1.322 (2)	C7—N14	1.348 (3)
N1—C9	1.357 (2)	C8—C12	1.419 (3)
C3—C4	1.377 (3)	C12—N13	1.147 (3)
C5—N6	1.316 (3)	N14—C18	1.453 (3)
C5—N11	1.346 (3)	N14—C15	1.473 (3)
N6—C7	1.351 (3)		
C2—N1—C9	118.9 (2)	C28—N31—C34	120.5 (2)
C7—N14—C18	126.3 (2)	C28—N31—C32	122.0 (2)
C7—N14—C15	121.7 (2)	C34—N31—C32	115.7 (2)
C18—N14—C15	111.6 (2)		

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

*Cg*1 is the centroid of ring *E*.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C20—H20···N1	0.93	2.44	2.775 (2)	101
N11—H11*A*···O36^{i}	0.86	2.39	3.047 (2)	134
O36—H36···N13^{ii}	0.85	1.94	2.759 (3)	163
C32—H32*B*···Cg1^{iii}	0.97	2.87	3.716 (7)	146

Symmetry codes: (i) $x-1, y-1, z$; (ii) $2-x, 1-y, 1-z$; (iii) $-x, 1-y, -z$.

Data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ZORTEP* (Zsolnai, 1997); software used to prepare material for publication: *SHELXL*97 and *PARST* (Nardelli, 1995).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: NA1495). Services for accessing these data are described at the back of the journal.

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