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Ethyl 6-amino-2-methoxypyridine-3-carboxylate, interplay of molecular and supramolecular structure

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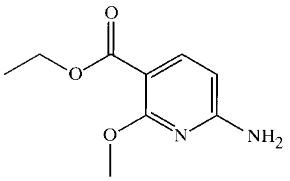
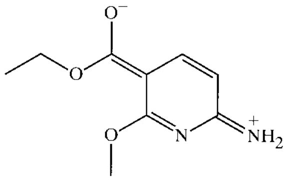
The title compound, $C_9H_{12}N_2O_3$, crystallizes with two molecules in the asymmetric unit. There is extensive hydrogen bonding which results in the formation of a two-dimensional corrugated sheet. This supramolecular structure is determined by the formation of hydrogen-bonded chains resulting from the presence of a 6-amino group and an ethoxycarbonyl group as substituents on a pyridine ring in relative *para* positions which constitute a π-electron 'push–pull' system.

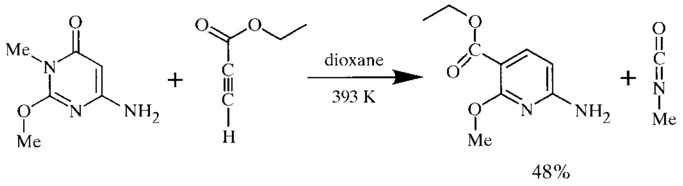
Comment

The title compound, (I), was obtained through a hetero-Diels–Alder/retro-Diels–Alder transformation of 4-amino-2-methoxy-3-methylpyrimidin-4(3*H*)-one (acting as 2-azadiene) and ethyl propiolate (acting as dienophile) (see reaction scheme below), and the presence of a 6-amino group and an ethoxycarbonyl group as substituents on a pyridine ring in relative *para* positions constitutes a clear π-electron 'push–pull' system which explains the main structural features found in the crystal structure.


(I)


(I*a*)

The two unique molecules in the asymmetric unit were chosen to give a dimer formed by the three-centred $R_1^2(6)$ (Bernstein *et al.*, 1995) hydrogen bond between the amino H atom attached to N21 in molecule 1, and O25 and O26 in molecule 2 (Fig. 1); the sum of the angles at the H atom is 353°. The former of these two hydrogen bonds is the shorter (Table 2) and is hence the stronger. The two molecules have similar bond lengths and angles.



The pyridine rings, while are essentially planar, show deviations from regular hexagonal geometry (Table 1). In both molecules, the C—NH$_2$ groups lie in the plane of the pyridine ring. The N atoms have predominantly sp^2-character, as is shown by the C—N bond lengths [N12—C12 1.3449 (16) Å and N22—C22 1.3406 (17) Å], which are shorter than the mean value (1.360 Å) reported for planar amino groups bonded to aromatic systems (Allen *et al.*, 1987). It is also noteworthy that the C151—O15 [1.2115 (15) Å] and C251—O25 bonds [1.2162 (15) Å] are long compared with the mean (1.202 Å; Schweizer & Dunitz, 1982) for other carbonyl groups in aromatic carboxylic esters.

The compensation by the 6-amino lone pair for the π-electron deficiency of the 3-carboxylate group produces an increase in the acidity of the amino H atoms, as well as an enhancement of the electron density of the carbonyl O atom. The partial charges thus developed favour the formation of N—H···O═C hydrogen bonds, which was confirmed by an analysis of the hydrogen bonding. This indicates the great contribution of canonical form (I*a*) (see scheme opposite) and hence this can be considered as an example of resonance-assisted hydrogen bonding (Gilli *et al.*, 1989).

The supramolecular structure of (I) consists of corrugated two-dimensional sheets formed by linked hydrogen-bonded antiparallel chains formed by hydrogen bonding the dimers, described above, together in a head-to-tail fashion. These sheets lie in the (010) plane. Individual sheets are not linked to neighbouring sheets. The dimers are connected by an N22—

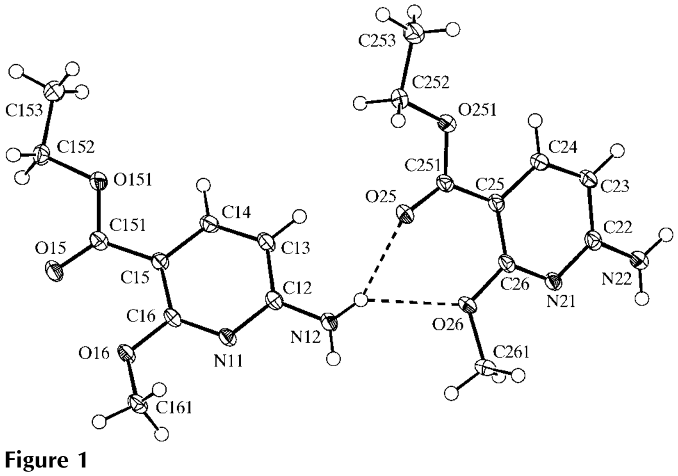


Figure 1
A view of (I) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 30% probability level. The dimer selected as the asymmetric unit is shown with the three-centred hydrogen bond between N12—H12*B*···O26 and N12—H12*B*···O25 forming an $R_1^2(6)$ ring motif.

H22*B*···O15(−1 + *x*, *y*, −1 + *z*) hydrogen bond, producing *via* the N12—H12*B*···O25 bond, a $C_2^2(16)$ chain which runs parallel to [101]. The $C_2^2(14)$ chain *via* O26 is shorter but, as mentioned above, the N12—H12*B*···O25 bond is the stronger of the pair. Crystallographic symmetry produces an alternating pattern of antiparallel chains which are linked to neighbouring chains in two distinct ways. The first linkage is produced by an N22—H22*A*···N11(−1 − *x*, −*y*, −*z*) hydrogen bond, which produces a ribbon with alternating centrosymmetric $R_4^4(20)$ and $R_4^4(16)$ rings (Bernstein *et al.*, 1995) centred on the inversion centres at $(-\frac{1}{2},0,0)$ and $(0,0,\frac{1}{2})$, respectively (Fig. 2). The second linkage is produced by an N12—H12*A*···O25(−*x*, −*y*, −*z*) hydrogen bond, the ribbon so produced being made up of alternating centrosymmetric $R_4^2(8)$ and $R_4^4(32)$ rings (Bernstein *et al.*, 1995) centred on the centres of inversion at (0,0,0) and $(\frac{1}{2},0,\frac{1}{2})$, respectively (Fig. 3).

The following related compounds were retrieved from the Cambridge Structural Database (CSD; Allen & Kennard, 1993): SAVZEU, ethyl 2-*N*-(6-amino-5-cyano-3-ethoxycarbonylpyridin-2-yl)aminobenzoate, $C_{18}H_{18}N_4O_4$ (Deady *et al.*, 1989); ZIVHAN, 2-amino-6-methoxy-4,5-bis(methoxycarbonyl)pyridine, $C_{10}H_{12}N_2O_5$ (Low *et al.*, 1996); ZIVHER, 2-amino-4,5-bis(methoxycarbonyl)-6-(methylthio)pyridine, $C_{10}H_{12}N_2O_4S$ (Low *et al.*, 1996). These are the only pyridine compounds with a 2-amino group *para* to a 5-carboxylate group (6-amino and 3-carboxylate in the numbering of the title compound) and they all crystallize in space group $P\overline{1}$, like compound (I). These are all push–pull systems similar to (I) and, in all cases, formation of N—H···O═C hydrogen bonds is observed. These hydrogen bonds form *C*(8) chains in ZIVHAN and ZIVHER, which have only one molecule in the asymmetric unit. Antiparallel chains link together to form a ribbon consisting of alternating $R_2^2(14)$ and $R_4^2(18)$ rings. In SAVZEU, in which the asymmetric unit, like that of (I), contains two molecules, the chain is of the $C_2^2(16)$ type, as in (I), and antiparallel chains are linked to form a ribbon consisting of alternating $R_4^4(36)$ and $R_4^2(8)$ rings. Thus, although ribbons are formed in all these structures, only in (I) do they combine to form a sheet structure.

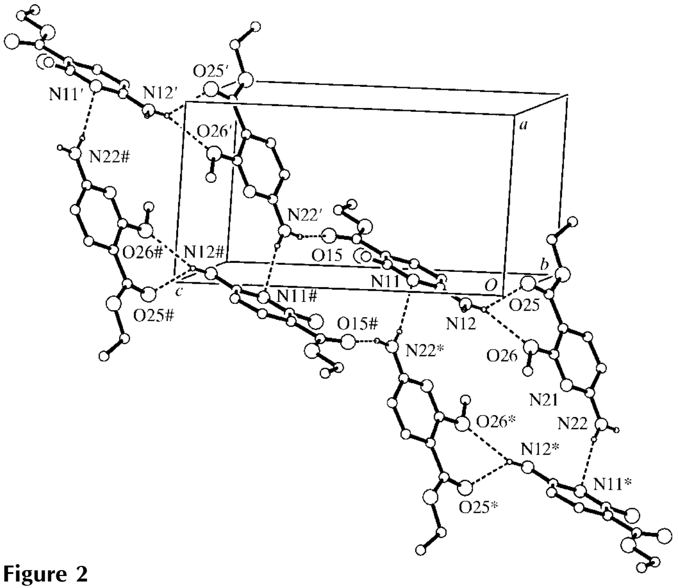


Figure 2
The molecular ribbon produced by the linking of antiparallel $C_2^2(14)$ chains *via* the N22—H22*A*···N11* hydrogen bond, showing the alternating centrosymmetric $R_4^4(20)$ and $R_4^4(16)$ rings. Atoms labelled with primes (′), asterisks (*) and hashes (#) are at (1 + *x*, *y*, 1 + *z*), (−1 − *x*, −*y*, −*z*) and (−*x*, −*y*, 1 − *z*), respectively.

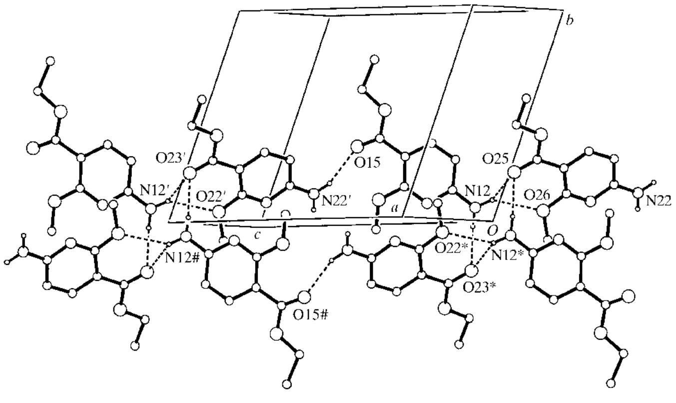


Figure 3
The molecular ribbon produced by the linking of antiparallel $C_2^2(14)$ chains *via* the N12—H22*A*···O25* hydrogen bond, showing the alternating centrosymmetric $R_4^2(8)$ and $R_4^4(32)$ rings. Atoms labelled with primes (′), asterisks (*) and hashes (#) are at (1 + *x*, *y*, 1 + *z*), (−*x*, −*y*, −*z*) and (1 − *x*, −*y*, 1 − *z*), respectively.

Experimental

Ethyl propiolate (0.95 g, 9.5 mmol) was added to a suspension of 6-amino-2-methoxypyrimidin-4(3*H*)-one (0.50 g, 3.2 mmol) in dry dioxane (3 ml) and the reaction mixture was stirred at 393 K for 62 h. The resulting dark solution was evaporated *in vacuo* to dryness and the title compound was isolated and purified by flash-column chromatography on silica gel using dichloromethane/acetone mixtures in an acetone gradient as eluent. Recrystallization from acetone produced colourless crystals (yield: 48%, m.p. 396–397 K). Analysis calculated for $C_9H_{12}N_2O_3$: C 55.1, H 6.2, N 14.3%; found: C 54.8, H 6.0, N 14.1%.

Crystal data

$C_9H_{12}N_2O_3$
$M_r = 196.21$
Triclinic, $P\overline{1}$
$a = 7.4906$ (2) Å
$b = 10.2409$ (2) Å
$c = 13.1449$ (3) Å
$\alpha = 104.9607$ (9)°
$\beta = 90.7398$ (9)°
$\gamma = 101.2452$ (9)°
$V = 953.34$ (4) Å^3

$Z = 4$
$D_x = 1.367$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 4295 reflections
$\theta = 3.0$–27.5°
$\mu = 0.10$ mm^{-1}
$T = 150$ (1) K
Block, colourless
0.40 × 0.25 × 0.15 mm

Data collection

Nonius KappaCCD diffractometer
φ scans, and ω scans with κ offsets
Absorption correction: multi-scan (*DENZO-SMN*; Otwinowski & Minor, 1997)
$T_{\min} = 0.960$, $T_{\max} = 0.985$
14 744 measured reflections
4295 independent reflections

3541 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.061$
$\theta_{\max} = 27.5°$
$h = -9 \rightarrow 9$
$k = -13 \rightarrow 12$
$l = -16 \rightarrow 17$
Intensity decay: negligible

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.051$
$wR(F^2) = 0.142$
$S = 1.05$
4295 reflections
258 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0940P)^2 + 0.1054P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.37$ e Å^{-3}
$\Delta\rho_{\min} = -0.42$ e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.155 (12)

Table 1
Selected geometric parameters (Å, °).

N11—C16	1.3311 (16)	N21—C26	1.3268 (17)
N11—C12	1.3525 (15)	N21—C22	1.3500 (16)
C12—N12	1.3449 (16)	C22—N22	1.3406 (17)
C12—C13	1.4086 (18)	C22—C23	1.4159 (19)
C13—C14	1.3681 (18)	C23—C24	1.3607 (18)
C14—C15	1.4084 (17)	C24—C25	1.4045 (17)
C15—C16	1.4034 (18)	C25—C26	1.4113 (18)
C15—C151	1.4725 (17)	C25—C251	1.4660 (18)
C151—O15	1.2115 (15)	C251—O25	1.2162 (15)
C16—N11—C12	118.41 (11)	C26—N21—C22	118.90 (11)
N12—C12—C13	121.18 (11)	N21—C22—C23	121.81 (12)
C14—C13—C12	118.24 (11)	C24—C23—C22	117.74 (11)
C13—C14—C15	121.18 (12)	C23—C24—C25	122.07 (12)
C16—C15—C14	115.92 (11)	C24—C25—C26	115.54 (12)
N11—C16—C15	124.21 (11)	N21—C26—C25	123.89 (11)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N12—H12*A*···O25^{i}	0.88	2.23	3.0543 (15)	156
N12—H12*B*···O26	0.88	2.41	3.1574 (14)	143
N12—H12*B*···O25	0.88	2.30	3.0250 (14)	139
N22—H22*A*···N11^{ii}	0.88	2.37	3.2167 (17)	162
N22—H22*B*···O15^{iii}	0.88	2.14	2.9791 (16)	160

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

H atoms were treated as riding atoms with C—H distances in the range 0.95–0.99 Å and N—H distances of 0.88 Å. The positions of the methyl and amino H atoms were confirmed by a difference map.

Data collection: *KappaCCD Server Software* (Nonius, 1997); cell refinement: *DENZO–SMN* (Otwinowski & Minor, 1997); data reduction: *DENZO–SMN*; 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) and *PLATON* (Spek, 2000); software used to prepare material for publication: *SHELXL*97 and *WordPerfect* macro *PRPKAPPA* (Ferguson, 1999).

X-ray data were collected at the EPSRC, X-ray Crystallographic Service, University of Southampton, using an Enraf–Nonius KappaCCD diffractometer. The authors thank the staff for all their help and advice.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GD1162). Services for accessing these data are described at the back of the journal.

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