organic compounds

2-Amino-4-(4-pyridyl)pyrimidine and the 1:1 adduct with 4-aminobenzoic acid

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The structure of the title compound, $C_9H_8N_4$, comprises non-planar molecules that associate via pyrimidine N—H···N dimer $R_2^2(8)$ hydrogen-bonding associations [N···N 3.1870 (17) Å] and form linear hydrogen-bonded chains via a pyrimidine N—H···N(pyridyl) interaction [N···N 3.0295 (19) Å]. The dihedral angle between the two rings is 24.57 (5)°. The structure of the 1:1 adduct with 4-amino-benzoic acid, $C_9H_8N_4 \cdot C_7H_7NO_2$, exhibits a hydrogen-bonding network involving COOH···N(pyridyl) [O···N 2.6406 (17) Å], pyrimidine N—H···N [N···N 3.0737 (19) and 3.1755 (18) Å] and acid N—H···O interactions [N···O 3.0609 (17) and 2.981 (2) Å]. The dihedral angle between the two linked rings of the base is 38.49 (6)° and the carboxylic acid group binds to the stronger base group in contrast to the (less basic) complementary hydrogen-bonding site.

Comment

The design of multi-dimensional organic crystal lattices requires the use of molecules with several interactive substituents. Ideally, the association of these substituents can be predicted and their specific position used to construct the desired array (Desiraju, 1995). For a number of years, the principal author has studied the association between carboxylic acids and either pyridines or 2-aminopyridine-type molecules with the additional amine group used to lock the COOH and the heterocyclic ring in essentially the same plane (Fig. 1). If the secondary substituents on the carboxylic acid molecule do not have the hydrogen-bonding donor strength of the acid itself, then association between the acid and the Lewis base can be expected (Lynch *et al.*, 2000). However, competition between these two types of bases (in one molecule) has never been investigated by X-ray crystallography and the authors postulated as to which of the two groups a carboxylic acid would preferentially bind. Etter (1991) inversely showed that the same pyridine base, when placed in a mixed carboxylic acid solution, selectively cocrystallized the acid with the lower pK_a value. Our purpose for this study was to investigate

whether the same pK_a difference would be important when two different bases were in competition for the same acid.

The principal author has always assumed that the 2-amino-pyridine site is more stable for binding with COOH groups than pyridine itself, because the resultant synthon mimics acid
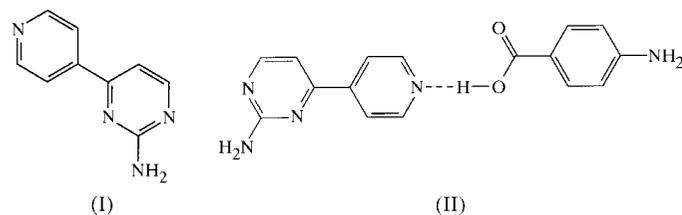
dimer formation. Therefore, a simple molecule containing both a pyridine nitrogen and a 2-aminopyridine site has been produced to test whether a COOH group is preferentially
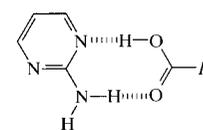
attracted to either the stronger base or the more stable binding site. The hydrogen-bonding pattern for a 2-amino-pyrimidine–carboxylic acid interaction is shown above. One of a series of simple molecules which contain both types of bases is 2-amino-4-(4-pyridyl)pyrimidine, (I). This molecule subsequently exhibited a large difference in the pK_a values of the
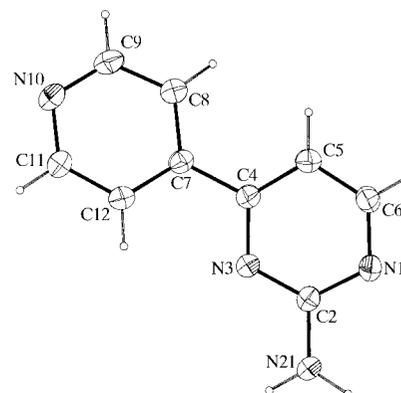

Figure 1
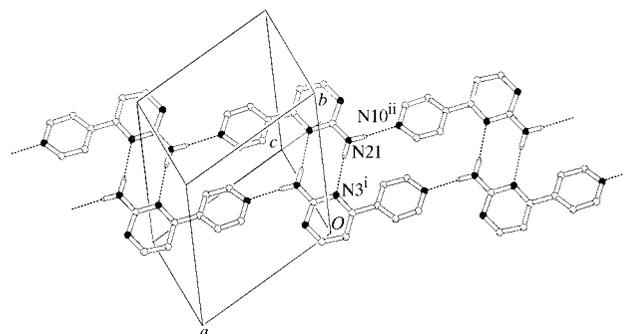The molecular configuration and atom-numbering scheme for (I), showing 50% probability ellipsoids.

Figure 2
The molecular packing for (I). Hydrogen-bonding associations are shown as dotted lines. [Symmetry codes: (i) $-x, 2-y, -1-z$; (ii) $x-1, y, z-1$.]
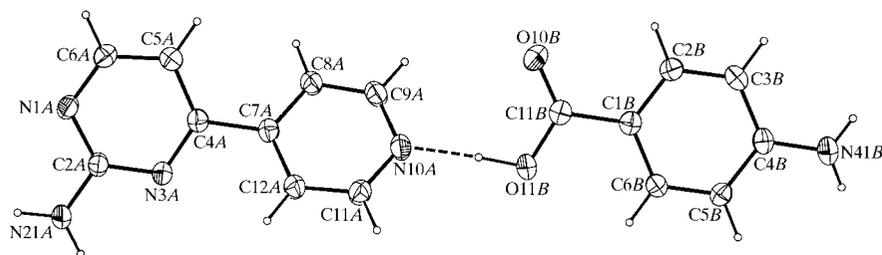
Figure 3
The molecular configuration and atom-numbering scheme for (II), showing 50% probability ellipsoids.
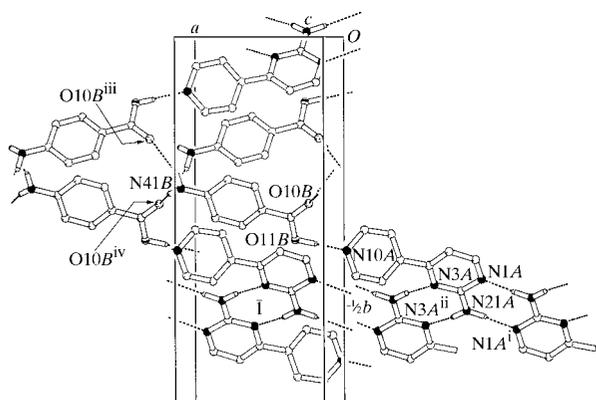

Figure 4
The molecular packing for (II). Hydrogen-bonding associations are shown as dotted lines. [Symmetry codes: (i) $-2 - x, 1 - y, -1 - z$; (ii) $-1 - x, 1 - y, -1 - z$; (iii) $1 + x, \frac{1}{2} - y, \frac{1}{2} + z$; (iv) $1 + x, y, z$.]

two bases ($pK_a = 5.58$ and 1.83 for the pyridine and the pyrimidine, respectively). The chosen acid was 4-aminobenzoic acid, which has proven to be a very useful crystallization aid for a number of functional multi-substituted molecules (Smith *et al.*, 1997). The amine group, with the lesser inherent acid strength ($pK_a = 5.05$), was not expected to directly compete with the COOH ($pK_a = 2.38$) for binding to the stronger base, yet additional hydrogen-bonding donors were required to satisfy the remaining hydrogen-bonding acceptors (after the COOH has bound). We report here the single-crystal structures of 2-amino-4-(4-pyridyl)pyrimidine, (I), and its 1:1 adduct with 4-aminobenzoic acid, (II).

The structure of (I) comprises non-planar molecules (Fig. 1) that, similar to other analogous compounds, form $R_2^2(8)$ hydrogen-bonded dimers across one of the pyrimidine N/NH$_2$ sites. The second amine H atom, instead of forming another dimer, interacts with the pyridyl N atom, thus creating a linear hydrogen-bonded polymer chain (Fig. 2); the hydrogen-bonding geometry is listed in Table 1. In (I), the dihedral angle between the two rings is 24.57 (5)°. The structure of (II) (Fig. 3) comprises twisted 2-aminopyrimidine derivatives associating *via* continuous $R_2^2(8)$ hydrogen-bonded dimers with the inclusion of the acid molecules bound to the 4-pyridyl group (Fig. 4). The two 4-amino H atoms are also involved in the hydrogen-bonding network with three-centre associations to the carbonyl O atom; the hydrogen-bonding geometry is

listed in Table 2. The dihedral angle between the two linked rings of the base in the structure of (II) is 38.49 (6)°.

4-Aminobenzoic acid is a relatively strong organic acid with a pK_a value of 2.38, thus when adducted with 2-amino-4-(4-pyridyl)pyrimidine the carboxylic acid group could have bound to a complementary acidic pyrimidine N/NH$_2$ site ($pK_a = 1.83$), but instead was found to prefer the more basic pyridyl N atom ($pK_a = 5.58$). The pK_a difference between the COOH and the pyridyl group is < 3.75 (Johnson & Rumon, 1965) so no proton transfer (and hence an organic salt) results. The pyrimidine N/NH$_2$ sites then form dimers with themselves and leave the 4-amino H atoms to associate with the only other available hydrogen-bonding acceptor atom, the carbonyl O atom (although a few cases exist where the 4-amino N atoms have also been hydrogen-bond acceptors). The results of this study may have been affected by the fact that the carboxylic acid group has a higher pK_a value than the pyrimidine N/NH$_2$ site. However, to use an organic acid with a $pK_a < 1.83$ would have led to a pK_a difference between the COOH group and the pyridyl N atom being > 3.75, above which proton transfer to the pyridyl group could have occurred (Johnson & Rumon, 1965), assuring binding to the pyridyl N atom. The acidity of the pyrimidine group was also affected by the direct substitution of an electron-accepting group, thus attempts are underway to synthesize a molecule which contains these two heterocyclic bases but between which is an alkyl spacer (preferably hexacyclic such that the conformation can be controlled). In such a molecule, the pK_a value of the pyrimidine ring should be closer to the pK_a value of 2-aminopyrimidine itself ($pK_a = 2.40$). A lowering of the inherent acid strength of this group thus increases the potential for COOH binding to the pyrimidine as opposed to the pyridine.

Experimental

Compound (I)

Crystal data

$C_9H_8N_4$	$D_x = 1.411$ Mg m^{-3}
$M_r = 172.19$	Mo $K\alpha$ radiation
Monoclinic, $P2_1/c$	Cell parameters from 3577
$a = 9.450$ (2) Å	reflections
$b = 13.689$ (3) Å	$\theta = 2.9$–47.8°
$c = 6.439$ (1) Å	$\mu = 0.09$ mm^{-1}
$\beta = 103.35$ (3)°	$T = 150$ (2) K
$V = 810.4$ (3) Å^3	Prism, yellow
$Z = 4$	$0.27 \times 0.12 \times 0.12$ mm

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Data collection

Nonius KappaCCD diffractometer	1417 reflections with $I > 2\sigma(I)$
φ and ω scans	$R_{int} = 0.04$
Absorption correction: multi-scan	$\theta_{max} = 27.5°$
($SORTAV$; Blessing, 1995)	$h = -11 \rightarrow 12$
$T_{min} = 0.976$, $T_{max} = 0.989$	$k = -17 \rightarrow 17$
6415 measured reflections	$l = -8 \rightarrow 8$
1841 independent reflections	

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0846P)^2$
$R[F^2 > 2\sigma(F^2)] = 0.047$	$\quad + 0.0128P]$
$wR(F^2) = 0.132$	where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.03$	$(\Delta/\sigma)_{max} < 0.001$
1841 reflections	$\Delta\rho_{max} = 0.25$ e Å^{-3}
126 parameters	$\Delta\rho_{min} = -0.25$ e Å^{-3}
H atoms treated by a mixture of independent and constrained refinement	

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

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
N21—H22···N3^i	0.917 (16)	2.303 (17)	3.1870 (17)	161.7 (13)
N21—H21···N10^{ii}	0.919 (18)	2.114 (19)	3.0295 (19)	174.1 (14)

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

Compound (II)

Crystal data

$C_9H_8N_4 \cdot C_7H_7NO_2$	$D_x = 1.386$ Mg m^{-3}
$M_r = 309.33$	Mo $K\alpha$ radiation
Monoclinic, $P2_1/c$	Cell parameters from 10 808 reflections
$a = 7.881$ (2) Å	$\theta = 1.0–27.5°$
$b = 26.354$ (5) Å	$\mu = 0.10$ mm^{-1}
$c = 7.297$ (2) Å	$T = 150$ (2) K
$\beta = 102.04$ (3)°	Prism, yellow
$V = 1482.2$ (5) Å^3	$0.55 \times 0.20 \times 0.20$ mm
$Z = 4$	

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

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
N21A—H21A···N1A^i	0.928 (18)	2.151 (18)	3.0737 (19)	172.8 (16)
N21A—H22A···N3A^{ii}	0.917 (17)	2.274 (17)	3.1755 (18)	167.5 (15)
O11B—H11B···N10A	1.01 (2)	1.63 (2)	2.6406 (17)	173 (2)
N41B—H41B···O10B^{iii}	0.85 (2)	2.25 (2)	3.0609 (19)	159.0 (17)
N41B—H42B···O10B^{iv}	0.90 (2)	2.15 (2)	2.981 (2)	153.6 (16)

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

Data collection

KappaCCD diffractometer	2349 reflections with $I > 2\sigma(I)$
φ and ω scans	$R_{int} = 0.047$
Absorption correction: multi-scan	$\theta_{max} = 27.5°$
($SORTAV$; Blessing, 1995)	$h = -9 \rightarrow 10$
$T_{min} = 0.949$, $T_{max} = 0.981$	$k = -34 \rightarrow 27$
10418 measured reflections	$l = -9 \rightarrow 9$
3303 independent reflections	

Refinement

Refinement on F^2	H atoms treated by a mixture of independent and constrained refinement
$R[F^2 > 2\sigma(F^2)] = 0.048$	
$wR(F^2) = 0.123$	
$S = 1.03$	$w = 1/[\sigma^2(F_o^2) + (0.0708P)^2]$
3303 reflections	where $P = (F_o^2 + 2F_c^2)/3$
228 parameters	$(\Delta/\sigma)_{max} < 0.001$
	$\Delta\rho_{max} = 0.28$ e Å^{-3}
	$\Delta\rho_{min} = -0.32$ e Å^{-3}

All aromatic H atoms were included in the refinement at calculated positions, as riding models with C—H set to 0.95 Å. All H atoms involved in the hydrogen-bonding associations were located in difference syntheses and both their positions and thermal parameters were subsequently refined.

For both compounds, data collection: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT* (Hooft, 1998); cell refinement: *DENZO* and *COLLECT*; data reduction: *DENZO* and *COLLECT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON*97 (Spek, 1997); software used to prepare material for publication: *SHELXL*97.

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