Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

2-Benzylamino-6-benzyloxypyrimidin-4(3*H*)-one: hydrogen-bonded chains of rings linked into sheets by a π–π-stacking interaction

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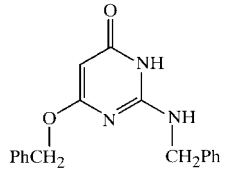
Received 2 May 2003
Accepted 19 May 2003
Online 30 June 2003

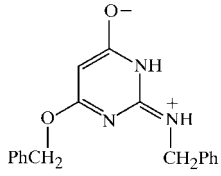
The title compound, $C_{18}H_{17}N_3O_2$, crystallizes with $Z' = 2$ in space group $P2_1/c$, and the two independent molecules are approximate, but not exact, mirror images. The molecular–electronic structure is strongly polarized, and the molecules are linked by paired N—H···O hydrogen bonds [H···O = 2.00–2.23 Å, N···O = 2.798 (3)–2.992 (3) Å and N—H···O = 145–151°] into two independent $C(4)C(6)[R_2^1(6)]$ chains of rings, which are linked into sheets by a single aromatic π–π-stacking interaction.

Comment

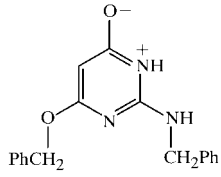
Selective monobenzylation of heterocyclic primary amines has been achieved under non-classical conditions, consisting of treatment with a large excess of sodium benzylate at temperatures above 403 K, by Koyama *et al.* (1996). Although these authors proposed a mechanism for this transformation, this mechanism proved to be inconsistent with some experimental observations, including the failure of this procedure to effect *N*-benzylation of aniline. These anomalies, together with the evident synthetic potential of such a selective procedure, led us to reinvestigate this reaction. We report here the structure of 2-benzylamino-6-benzyloxypyrimidin-4(3*H*)-one, (I), which has been prepared from 2-amino-6-chloropyrimidin-4(3*H*)-one. This is the first time that this unusual benzylation procedure has been applied to a pyrimidine derivative containing a tautomerizable oxo substituent. Compounds such as (I) are valuable synthetic intermediates for the synthesis of new biologically active products. We have reported previously the structures of several fully aromatic substituted pyrimidines obtained using this benzylation procedure (Low *et al.*, 2002; Glidewell *et al.*, 2003).



(I)



(I*a*)



(I*b*)

The corresponding bond distances (Table 1) in the two independent molecules of (I) are very similar, and several of these distances provide evidence of a strongly polarized molecular–electronic structure. Thus, within each molecule, the N*n*2—C*n*2, C*n*2—N*n*3 and N*n*3—C*n*4 distances (n = 1 or 2) are similar to one another, and certainly do not permit the assignment implied by the classically localized structure, (I), in which C*n*2—N*n*3 is a double bond and both N*n*2—C*n*2 and N*n*3—C*n*4 are single bonds. Similarly, the C*n*4—C*n*5 and C*n*5—C*n*6 distances both lie in the range of expected values (Allen *et al.*, 1987) for single and double bonds connecting two three-coordinated C atoms (mean 1.458 and 1.317 Å, respectively). Finally, the C*n*6—O*n*6 distances are significantly longer than the mean value, 1.231 Å, found in substituted carboxamides. These observations, taken together, point to the importance of the polarized form (I*a*) as a contributor to the overall molecular–electronic structure. On the other hand, the N*n*1—C*n*6 bonds are significantly longer than the upper-quartile value, 1.343 Å, for such bonds in simple amides, thus effectively ruling out the alternative polarized form (I*b*).

The two independent molecules of (I) adopt conformations that are almost mirror images of one another (Fig. 1); however, a detailed examination of the key torsion angles (Table 1) shows that this apparent equivalence is only approximate. In addition, the ADDSYM facility in *PLATON* (Spek, 2003) confirmed the absence of any additional symmetry.

Molecules of each type (Fig. 1) are linked into chains of rings by means of N—H···O hydrogen bonds, but there are no hydrogen bonds between molecules of different types. In the chain formed by the type 1 molecules, atoms N11 and N12 in the molecule at (x, y, z) both act as hydrogen-bond donors to atom O16 in the molecule at ($-x$, $-\frac{1}{2}+y$, $\frac{1}{2}-z$), so producing a $C(4)C(6)[R_2^1(6)]$ chain of rings (Bernstein *et al.*, 1995) running parallel to the [010] direction and generated by the 2_1 screw axis along (0, y, $\frac{1}{4}$) (Fig. 2). An antiparallel chain of type 1 molecules is generated by the screw axis along (0, $-y$, $\frac{3}{4}$). Atoms N21 and N22 in the type 2 molecule at (x, y, z) likewise act as hydrogen-bond donors to atom O26 at (1 − x, $\frac{1}{2}+y$,

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  DOI: 10.1107/S0108270103011132

$\frac{1}{2} - z$), so producing a similar chain of rings generated by the screw axis along ($\frac{1}{2}$, y, $\frac{1}{4}$) (Fig. 3), with an antiparallel chain of type 2 molecules along ($\frac{1}{2}$, $-y$, $\frac{3}{4}$). The dimensions of the hydrogen bonds in the two chains (Table 2) preclude any additional symmetry. The distinction between the two molecular types is emphasized by the existence of a weak C—H$\cdots\pi$(arene) interactions in the type 2 chain, whereas there is no interaction of this type in the type 1 chain. The fact that atoms O*n*6 act as double acceptors of hydrogen bonds while atoms O*n*4 do not act as acceptors at all is consistent with the contribution of form (I*a*).

The two types of chain are linked weakly into sheets by a single aromatic π–π-stacking interaction. The C121–C126 and C241–C246 rings in the molecules at (x, y, z) and ($-1 + x$, $-1 + y$, z), respectively, are nearly parallel, the dihedral angle between their planes being only 1.8 (2)°. Their centroid separation is 3.812 (2) Å, and the interplanar spacing is ~3.46 Å, corresponding to a centroid offset of ~1.65 Å. These two molecules lie, respectively, in the chains generated by the screw axes along (0, y, $\frac{1}{4}$) and ($-\frac{1}{2}$, y, $\frac{1}{4}$), and propagation of the π–π interaction thus generates a (001) sheet containing the screw axes at $z = \frac{1}{4}$. A second sheet, containing the screw axes at $z = \frac{3}{4}$, is related to the first by inversion, but there are no direction-specific interactions between adjacent sheets.

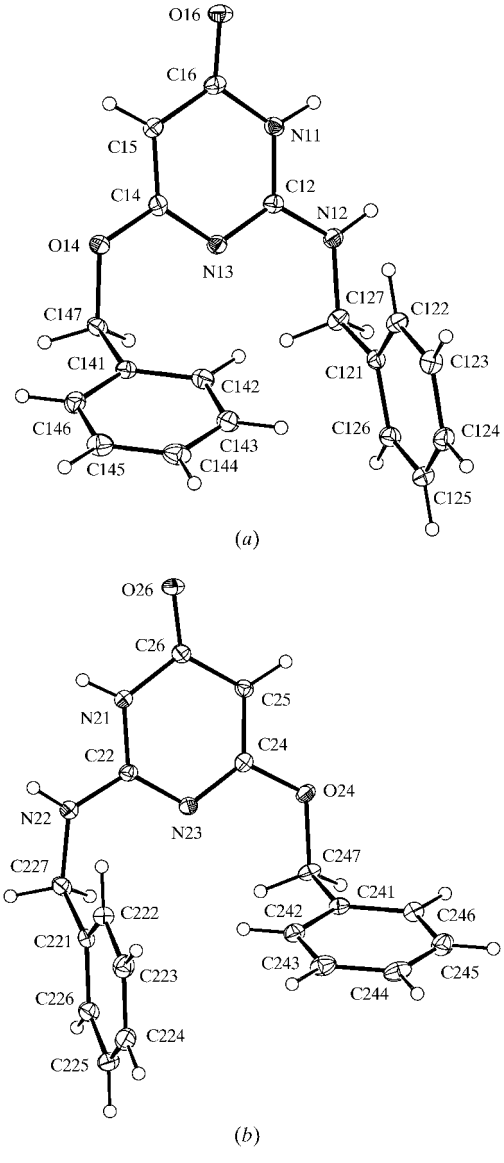

Figure 1
The two independent molecules of (I), showing the atom-labelling schemes for (*a*) the type 1 molecule and (*b*) the type 2 molecule. Displacement ellipsoids are shown at the 30% probability level.

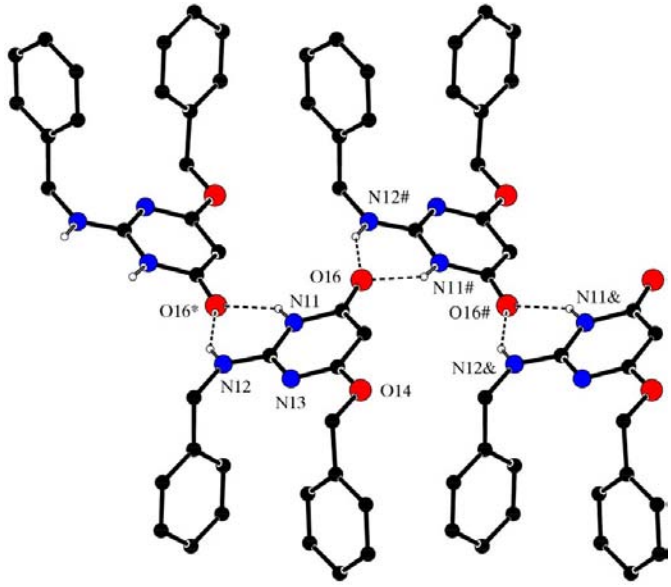

Figure 2
Part of the crystal structure of (I), showing the formation of the type 1 chain of rings. For clarity, H atoms bonded to C atoms and the unit-cell box have been omitted. Atoms marked with an asterisk (*), a hash (#) or an ampersand (&) are at the symmetry positions ($-x$, $-\frac{1}{2} + y$, $\frac{1}{2} - z$), ($-x$, $\frac{1}{2} + y$, $\frac{1}{2} - z$) and (x, $1 + y$, z), respectively.

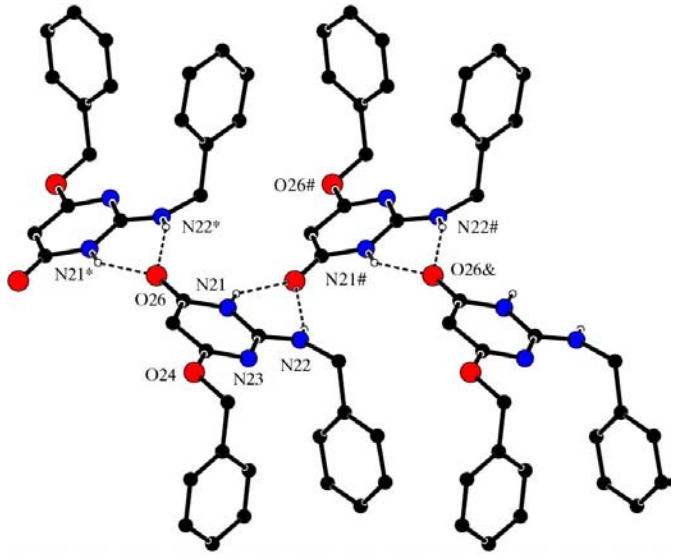

Figure 3
Part of the crystal structure of (I), showing the formation of the type 2 chain of rings. For clarity, H atoms bonded to C atoms and the unit-cell box have been omitted. Atoms marked with an asterisk (*), a hash (#) or an ampersand (&) are at the symmetry positions ($1 - x$, $-\frac{1}{2} + y$, $\frac{1}{2} - z$), ($1 - x$, $\frac{1}{2} + y$, $\frac{1}{2} - z$) and (x, $1 + y$, z), respectively.

Experimental

2-Amino-6-chloropyrimidin-4(3*H*)-one (10.33 mmol) was added to a stirred solution of sodium benzylate (61.83 mmol) in toluene (50 ml), and the resulting mixture was heated under reflux, with stirring, for 56 h. The mixture was then cooled, and diethyl ether (60 ml), toluene (30 ml) and a solution of ammonium chloride (75.5 mmol) in water (15 ml) were added successively. The mixture was stirred for 1 h and then filtered through a silica-gel bed (silica gel 60 for flash chromatography). The silica gel was washed with toluene (3 × 40 ml) and diethyl ether (3 × 40 ml), and the filtrate and the mother liquors were pooled together. The solvent was evaporated under reduced pressure, yielding the desired product, (I), as a white solid (yield 70%, m.p. 432 K). NMR ($CDCl_3$): δ(H) 4.47 (2H, *s*, CH_2), 4.47 (*s*, 1H, NH), 4.84 (2H, *s*, CH_2), 7.20 (10H, *m*, 2 × Ph), 11.41 (*s*, 1H, NH); δ(C) 44.8, 68.2, 81.3, 127.5, 127.5, 127.8, 127.9, 128.5, 128.6, 136.7, 138.0, 154.3, 166.7, 171.9. Crystals suitable for single-crystal X-ray diffraction were obtained by slow evaporation of a solution in ethyl acetate.

Crystal data

$C_{18}H_{17}N_3O_2$
M_r = 307.35
Monoclinic, $P2_1/c$
a = 10.7611 (4) Å
b = 8.0306 (3) Å
c = 34.9826 (17) Å
β = 98.5740 (15)°
V = 2989.3 (2) Å^3
Z = 8
D_x = 1.366 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 5946 reflections
θ = 3.1–27.4°
μ = 0.09 mm^{-1}
T = 120 (2) K
Needle, colourless
0.40 × 0.25 × 0.02 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} = 0.953, T_{max} = 0.998
21 880 measured reflections
5946 independent reflections
3917 reflections with $I > 2\sigma(I)$
R_{int} = 0.087
θ_{max} = 27.4°
$h = -13 \rightarrow 13$
$k = -10 \rightarrow 10$
$l = -45 \rightarrow 40$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.062
$wR(F^2)$ = 0.146
S = 1.03
5946 reflections
415 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0429P)^2 + 2.0855P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.28 e Å^{-3}

Crystals of (I) are monoclinic and the space group $P2_1/c$ was uniquely assigned from the systematic absences. H atoms were treated as riding, with C—H distances of 0.95 (aromatic) and 0.99 Å (CH_2), and N—H distances of 0.88 Å.

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: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL*97 (Sheldrick, 1997) and *PRPKAPPA* (Ferguson, 1999).

Table 1
Selected geometric parameters (Å, °).

N11—C12	1.367 (3)	N21—C22	1.374 (3)
C12—N13	1.328 (3)	C22—N23	1.330 (3)
N13—C14	1.345 (3)	N23—C24	1.346 (3)
C14—C15	1.379 (3)	C24—C25	1.374 (3)
C15—C16	1.405 (3)	C25—C26	1.411 (3)
C16—N11	1.389 (3)	C26—N21	1.392 (3)
C12—N12	1.337 (3)	C22—N22	1.336 (3)
C14—O14	1.352 (3)	C24—O24	1.353 (3)
C16—O16	1.262 (3)	C26—O26	1.265 (3)
N11—C12—N12—C127	−179.1 (2)	N21—C22—N22—C227	167.9 (2)
C12—N12—C127—C121	−90.9 (3)	C22—N22—C227—C221	91.5 (3)
N12—C127—C121—C122	6.5 (4)	N22—C227—C221—C222	10.1 (3)
C15—C14—O14—C147	172.1 (2)	C25—C24—O24—C247	−179.7 (2)
C14—O14—C147—C141	98.8 (2)	C24—O24—C247—C241	−93.5 (2)
O14—C147—C141—C142	−80.6 (3)	O24—C247—C241—C242	95.8 (3)

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

*Cg*1 is the centroid of the C241–C246 ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N11—H11···O16^{i}	0.88	2.07	2.852 (3)	148
N12—H12···O16^{i}	0.88	2.03	2.826 (3)	150
N21—H21···O26^{ii}	0.88	2.23	2.992 (3)	145
N22—H22···O26^{ii}	0.88	2.00	2.798 (3)	151
C225—H225···*Cg*1^{iii}	0.95	3.00	3.858 (3)	151

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

X-ray data were collected at the EPSRC X-ray Crystallographic Service, University of Southampton, England; the authors thank the staff for all their help and advice. JNL thanks NCR Self-Service, Dundee, for grants that have provided computing facilities for this work.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG1169). Services for accessing these data are described at the back of the journal.

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