Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Three sterically hindered 6-amino-5-cyano-2-methyl-4-(1-naphthyl)-4*H*-pyran-3-carboxylate derivatives

Vladimir N. Nesterov,* David J. Wiedenfeld, Svitlana V. Nesterova and Lucas F. Hastings

Department of Natural Sciences, New Mexico Highlands University, Las Vegas, NM 87701, USA
Correspondence e-mail: vnesterov@nmhu.edu

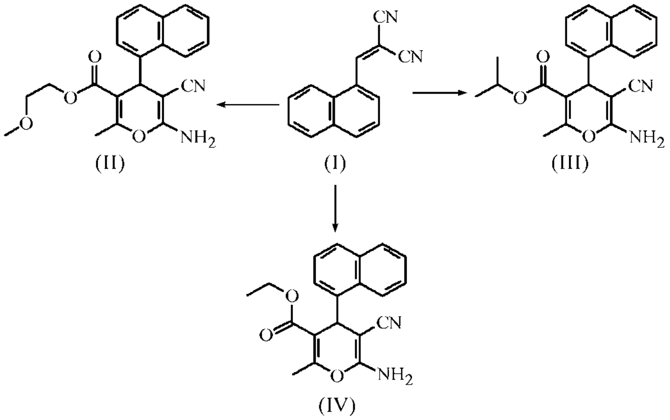
Received 29 August 2007
Accepted 5 October 2007
Online 14 November 2007

In the title compounds, 2-methoxyethyl 6-amino-5-cyano-2-methyl-4-(1-naphthyl)-4*H*-pyran-3-carboxylate, $C_{21}H_{20}N_2O_4$, (II), isopropyl 6-amino-5-cyano-2-methyl-4-(1-naphthyl)-4*H*-pyran-3-carboxylate, $C_{21}H_{20}N_2O_3$, (III), and ethyl 6-amino-5-cyano-2-methyl-4-(1-naphthyl)-4*H*-pyran-3-carboxylate, $C_{20}H_{18}N_2O_3$, (IV), the heterocyclic pyran ring adopts a flattened boat conformation. In (II) and (III), the carbonyl group and a double bond of the heterocyclic ring are mutually *anti*, but in (IV) they are mutually *syn*. The ester O atoms in (II) and (III) and the carbonyl O atom in (IV) participate in intramolecular C—H⋯O contacts to form six-membered rings. The dihedral angles between the naphthalene substituent and the closest four atoms of the heterocyclic ring are 73.3 (1), 71.0 (1) and 74.3 (1)° for (II)–(IV), respectively. In all three structures, only one H atom of the NH_2 group takes part in N—H⋯O [in (II) and (III)] or N—H⋯N [in (IV)] intermolecular hydrogen bonds, and chains [in (II) and (III)] or dimers [in (IV)] are formed. In (II), weak intermolecular C—H⋯O and C—H⋯N hydrogen bonds, and in (III) intermolecular C—H⋯O hydrogen bonds link the chains into ladders along the *a* axis.

Comment

The present investigation is a continuation of our work on the synthesis and structural study of sterically hindered heterocyclic compounds, such as 4*H*-pyran derivatives (Nesterov *et al.*, 2004, 2005), that can be obtained starting from different unsaturated nitriles (Nesterov *et al.*, 2001*a*,*b*). Some 4*H*-pyran derivatives are potential bioactive compounds, such as calcium antagonists (Suarez *et al.*, 2002) or potent apoptosis inducers (Kemnitzer *et al.*, 2004; Zhang *et al.*, 2005).

Syntheses and X-ray structural investigations have been carried out for compounds (II)–(IV) (Figs. 1–3), which were synthesized by the reaction of (1-naphthylmethylene)-malononitrile, (I), with different *β*-ketoesters. Most of the geometric parameters in the molecules (Tables 2, 4 and 6) are very similar to standard values (Allen *et al.*, 1987) and are very close to our previous data for sterically hindered 4*H*-pyran derivatives (Nesterov *et al.*, 2004, 2005, and literature values cited therein).



X-ray analysis shows that the title molecules have similar structures, with the pyran ring adopting a flattened boat conformation (Table 1). The dihedral angles between the bulky pseudo-axial naphthalene substituent and the closest four atoms (C2/C3/C5/C6) of the pyran ring are 73.3 (1), 71.0 (1) and 74.3 (1)° in (II), (III) and (IV), respectively. The mutual orientation of these fragments and the flatness of the heterocyclic rings lead to intramolecular H⋯H steric interactions: H4*A*⋯H15*A* = 2.08, 2.09 and 2.00 Å in (II)–(IV), respectively (Figs. 1–3). These contacts are shorter than the sum of the van der Waals radii of H atoms (2.2 Å; Rowland & Taylor, 1996). As in related compounds (Nesterov *et al.*, 2004, 2005), such steric hindrance causes elongation of the C4—C7 bond to 1.536 (2), 1.541 (2) and 1.531 (3) Å, respectively, in comparison with neighbouring Csp^3—Csp^2 distances. The latter are only slightly longer than or are equal to the standard value (1.507 Å; Allen *et al.*, 1987).

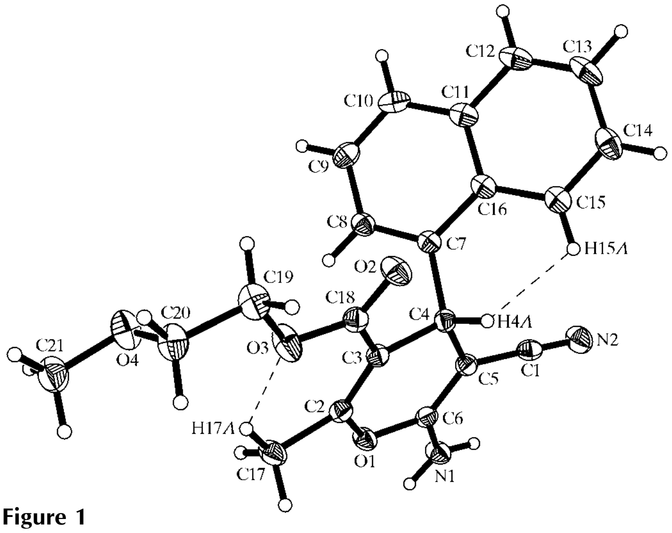


Figure 1
A view of compound (II), showing the atom numbering used. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. Dashed lines represent short intramolecular (C)H⋯O and H⋯H contacts, both of 2.08 Å.

DOI: 10.1107/S0108270107049001

In (II) and (III), the C═O group adopts an *anti* orientation relative to the C2═C3 double bond [C2—C3—C18—O2 = 172.0 (2) and 157.7 (2)°, respectively]. However, in (IV) it has a *syn* orientation [C2—C3—C18—O2 = 26.1 (3)°]. As seen in Figs. 1–3, in (II) and (III) the O3 atoms of the ester groups and in (IV) atom O2 of the carbonyl group have favourable orientations for the formation of short steric intramolecular contacts with the methyl groups of the heterocyclic ring (O3/O2···H17*A* = 2.08, 2.24 and 2.27 Å, respectively). According to literature data (Desiraju & Steiner, 1999), these contacts can be considered weak hydrogen bonds. However, in these cases it can be difficult to distinguish between a weak intramolecular hydrogen bond and a contact which is enforced by the rigid molecular framework (Desiraju & Steiner, 1999). In each case, the contact connects the atoms into a six-membered ring. As in related compounds (Nesterov & Viltchinskaia, 2001; Nesterov *et al.*, 2004), in all three title molecules there is conjugation between the donor NH_2 and acceptor CN groups *via* the C5═C6 double bond. Thus, in all three molecules, the C6—N1 bonds are shorter than the average conjugated C—N single-bond length (1.370 Å; Allen, 2002), but variations in the other distances in these flat fragments are less distinct.

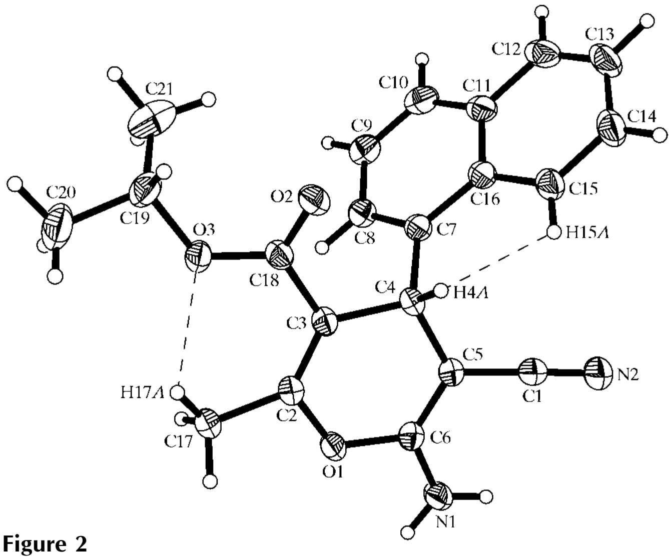


Figure 2
A view of compound (III), showing the atom numbering used. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. Dashed lines represent short intramolecular (C)H···O and H···H contacts of 2.24 and 2.09 Å, respectively.

In all three compounds, only one H atom of the NH_2 group is involved in an N—H···O [(II) and (III)] or N—H···N [(IV)] intermolecular hydrogen bond (Tables 3, 5 and 7) and chains along the *a* axis are formed in (II) and (III) (Figs. 4 and 5). In (IV), the *syn* orientation of the C═O group and its participation in the intramolecular steric contacts with the H atoms of the CH_3 and CH_2 groups (O2···H19*A* = 2.31 Å), and the different crystal packing, are reasons for the N—H···N hydrogen bonds forming centrosymmetric dimers in the crystal structure (Fig. 6). In addition, (II) exhibits weak C4—H4*A*··· O2 and C17—H17*B*···N2 interactions and in (III), C4—H4*A*··· O2 intermolecular hydrogen bonds link the chains along the *a* axis into ladders (Figs. 4 and 5; Tables 3 and 5).

Analysis of the crystal packing of the title compounds shows that in (II) and (III) there are short intermolecular steric contacts [C2···C2(1 − *x*, 1 − *y*, 1 − *z*) = 3.302 (3) Å and C10···C10(2 − *x*, −*y*, 1 − *z*) = 3.377 (3) Å in (II), and

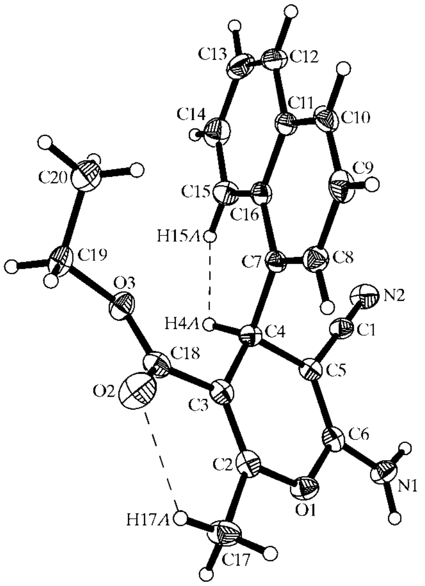


Figure 3
A view of compound (IV) showing the atom numbering used. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. Dashed lines represent short intramolecular (C)H···O and H···H contacts of 2.27 and 2.00 Å, respectively.

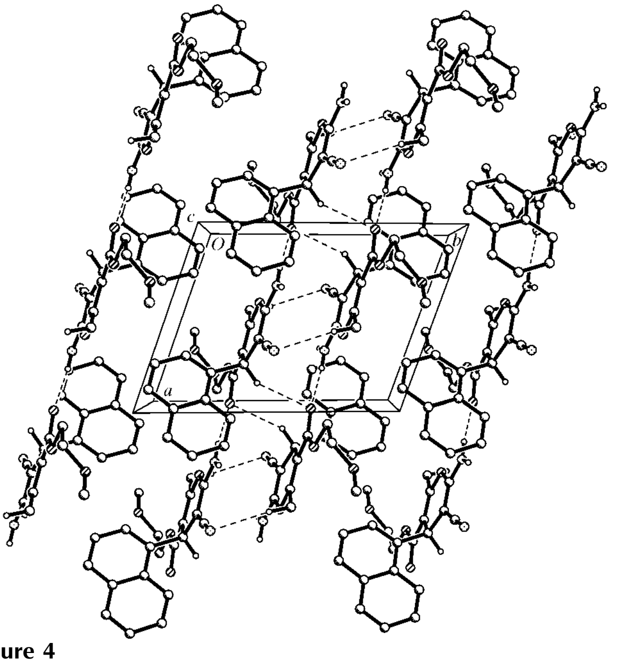


Figure 4
A projection of the crystal packing of (II) along the *c* axis. Dashed lines represent intermolecular N—H···O and weak C—H···O and C—H···N hydrogen bonds. H atoms not involved in these interactions have been omitted for clarity.

C8···C9(1 − *x*, 1 − *y*, −*x*) = 3.345 (3) Å in (III)] between atoms of the heterocycle or naphthalene fragments of neighbouring molecules which are below the sum of the van der Waals radii of C (3.40 Å; Rowland & Taylor, 1996). In (IV), similar contacts are comparable with or slightly exceed the sum of the van der Waals radii of C. Such steric intermolecular contacts can play a role in determining the orientation of the bulky naphthalene substituents in the molecules and can be considered as *π*–*π* interactions between them in the crystal structures (Figs. 4 and 5). The other geometric parameters in compounds (II)–(IV) do not differ significantly from standard values (Allen *et al.*, 1987).

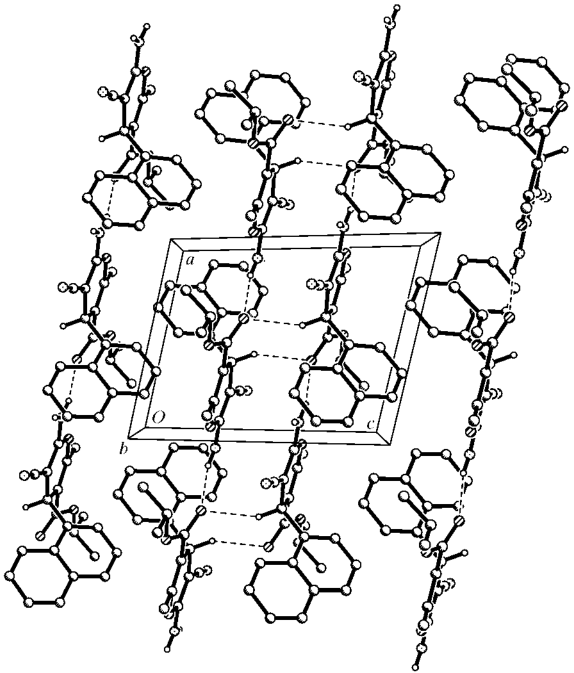


Figure 5
A projection of the crystal packing of (III) along the *b* axis. Dashed lines represent intermolecular N—H···O and weak C—H···O hydrogen bonds. H atoms not involved in these interactions have been omitted for clarity.

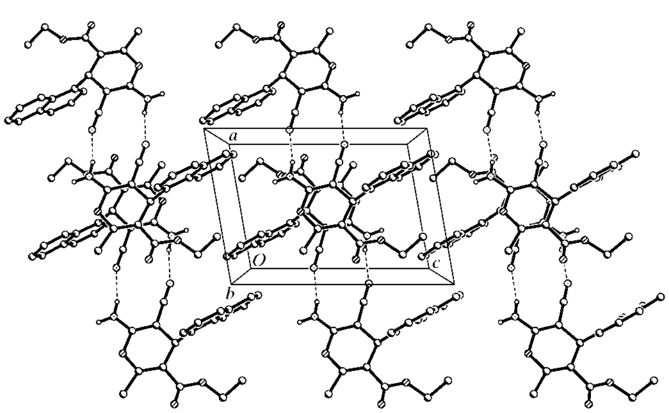


Figure 6
A projection of part of the crystal packing of (IV) along the *b* axis. Dashed lines represent intermolecular N—H···N hydrogen bonds. H atoms not involved in these interactions have been omitted for clarity.

Experimental

The title compounds, (II)–(IV), were obtained by the reaction of (1-naphthylmethylene)malononitrile, (I), with 2-methoxyethyl acetoacetate, isopropyl acetoacetate and ethyl acetoacetate, respectively, according to a literature procedure (Nesterov & Viltchinskaia, 2001; Nesterov *et al.*, 2004). The resulting precipitates were isolated and recrystallized from acetonitrile [m.p. 437 K and yield 75% for (II); m.p. 451 K and yield 79% for (III); m.p. 417 K and yield 77% for (IV)]. Crystals of the compounds were grown by slow isothermic evaporation from absolute ethanol solutions. All compounds were characterized by ^{1}H and ^{13}C NMR spectroscopy.

Compound (II)

Crystal data

$C_{21}H_{20}N_2O_4$	$\gamma = 107.349\ (7)^\circ$
$M_r = 364.39$	$V = 910.9\ (4)$ Å^3
Triclinic, $P\overline{1}$	$Z = 2$
$a = 8.245\ (2)$ Å	Mo $K\alpha$ radiation
$b = 10.962\ (3)$ Å	$\mu = 0.09$ mm^{-1}
$c = 11.008\ (3)$ Å	$T = 100\ (2)$ K
$\alpha = 98.391\ (7)^\circ$	0.22 × 0.17 × 0.14 mm
$\beta = 100.819\ (8)^\circ$	

Data collection

Bruker SMART APEXII CCD area-detector diffractometer	7926 measured reflections
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)	3594 independent reflections
$T_{\min} = 0.902$, $T_{\max} = 0.987$	2533 reflections with $I > 2\sigma(I)$
	$R_{\rm int} = 0.029$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.043$	246 parameters
$wR(F^2) = 0.111$	H-atom parameters constrained
$S = 1.00$	$\Delta\rho_{\max} = 0.27$ e Å^{-3}
3594 reflections	$\Delta\rho_{\min} = -0.26$ e Å^{-3}

Table 1
Geometric parameters (Å, °) for the heterocyclic rings in compounds (II)–(IV).

Δ(C2/C3/C5/C6) is the r.m.s. deviation of the atoms from the least-squares mean plane through the four atoms specified.

Plane/Compound	(II)	(III)	(IV)
Δ(C2/C3/C5/C6)	0.004 (1)	0.017 (1)	0.001 (1)
Displacement of atom O1 from the plane	−0.054 (1)	−0.046 (1)	0.026 (1)
Displacement of atom C4 from the plane	−0.115 (1)	−0.066 (1)	0.028 (1)
Hinge angle			
O1—C4	7.8 (1)	5.3 (1)	2.5 (1)
C2—C6	4.6 (1)	3.9 (1)	2.1 (1)
C3—C5	7.5 (1)	4.4 (1)	1.8 (1)

Table 2
Selected geometric parameters (Å, °) for (II).

O2—C18	1.215 (2)	C3—C18	1.481 (2)
O3—C18	1.330 (2)	C4—C7	1.536 (2)
N1—C6	1.340 (2)	C5—C6	1.353 (2)
C2—C3	1.347 (2)		
C2—C3—C18—O2	171.95 (17)	C2—C3—C18—O3	−7.9 (2)

Table 3
Hydrogen-bond geometry (Å, °) for (II).

D—H$\cdots$*A*	*D*—H	H$\cdots$*A*	*D*$\cdots$*A*	*D*—H$\cdots$*A*
N1—H1*B*$\cdots$O2^{i}	0.88	2.05	2.931 (2)	175
C4—H4*A*$\cdots$O2^{ii}	1.00	2.56	3.463 (3)	150
C17—H17*B*$\cdots$N2^{iii}	0.98	2.61	3.552 (2)	161

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

Compound (III)

Crystal data

$C_{21}H_{20}N_2O_3$
$M_r = 348.39$
Triclinic, $P\overline{1}$
$a = 8.248$ (3) Å
$b = 11.184$ (4) Å
$c = 11.394$ (4) Å
$\alpha = 63.646$ (7)°
$\beta = 73.836$ (8)°
$\gamma = 79.069$ (7)°
$V = 901.9$ (6) Å^3
$Z = 2$
Mo $K\alpha$ radiation
$\mu = 0.09$ mm^{-1}
$T = 100$ (2) K
$0.20 \times 0.16 \times 0.01$ mm

Data collection

Bruker SMART APEXII CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{min} = 0.913$, $T_{max} = 0.999$
7635 measured reflections
3528 independent reflections
2682 reflections with $I > 2\sigma(I)$
$R_{int} = 0.030$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.053$
$wR(F^2) = 0.148$
$S = 1.01$
3528 reflections
238 parameters
H-atom parameters constrained
$\Delta\rho_{max} = 0.38$ e Å^{-3}
$\Delta\rho_{min} = -0.23$ e Å^{-3}

Table 4
Selected geometric parameters (Å, °) for (III).

O2—C18	1.219 (2)	C3—C18	1.482 (3)
O3—C18	1.338 (2)	C4—C7	1.541 (2)
N1—C6	1.343 (2)	C5—C6	1.359 (3)
C2—C3	1.345 (3)		
C2—C3—C18—O2	157.71 (17)	C2—C3—C18—O3	−23.8 (2)

Table 5
Hydrogen-bond geometry (Å, °) for (III).

D—H$\cdots$*A*	*D*—H	H$\cdots$*A*	*D*$\cdots$*A*	*D*—H$\cdots$*A*
N1—H1*B*$\cdots$O2^{i}	0.88	2.12	2.989 (2)	168
C4—H4*A*$\cdots$O2^{ii}	1.00	2.40	3.325 (3)	154

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

Compound (IV)

Crystal data

$C_{20}H_{18}N_2O_3$
$M_r = 334.36$
Monoclinic, $P2_1/c$
$a = 7.8638$ (7) Å
$b = 19.4628$ (18) Å
$c = 11.0823$ (10) Å
$\beta = 99.963$ (2)°
$V = 1670.6$ (3) Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 0.09$ mm^{-1}
$T = 100$ (2) K
$0.20 \times 0.16 \times 0.14$ mm

Data collection

Bruker SMART APEXII CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{min} = 0.918$, $T_{max} = 0.987$
14847 measured reflections
3413 independent reflections
2184 reflections with $I > 2\sigma(I)$
$R_{int} = 0.078$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.047$
$wR(F^2) = 0.111$
$S = 1.00$
3413 reflections
228 parameters
H-atom parameters constrained
$\Delta\rho_{max} = 0.27$ e Å^{-3}
$\Delta\rho_{min} = -0.22$ e Å^{-3}

Table 6
Selected geometric parameters (Å, °) for (IV).

O2—C18	1.209 (2)	C3—C18	1.490 (3)
O3—C18	1.334 (2)	C4—C7	1.531 (3)
N1—C6	1.346 (2)	C5—C6	1.351 (3)
C2—C3	1.336 (3)		
C2—C3—C18—O2	26.1 (3)	C2—C3—C18—O3	−155.87 (18)

Table 7
Hydrogen-bond geometry (Å, °) for (IV).

D—H$\cdots$*A*	*D*—H	H$\cdots$*A*	*D*$\cdots$*A*	*D*—H$\cdots$*A*
N1—H1*A*$\cdots$N2^{i}	0.88	2.14	2.999 (2)	165

Symmetry code: (i) $-x, -y+1, -z+1$.

For all three title compounds, H atoms were placed in geometrically calculated positions and refined using a riding model, with C—H = 0.95 Å and U_{iso}(H) = $1.2U_{eq}$(C) for aromatic, C—H = 0.98 Å and U_{iso}(H) = $1.5U_{eq}$(C) for CH_3 (AFIX 137 in *SHELXTL*; Sheldrick, 2001), C—H = 0.99 Å and U_{iso}(H) = $1.2U_{eq}$(C) for CH_2, and C—H = 1.00 Å and U_{iso}(H) = $1.2U_{eq}$(C) for CH groups, and N—H = 0.88 Å and U_{iso}(H) = $1.2U_{eq}$(N) for the NH_2 group.

For all compounds, data collection: *APEX2* (Bruker, 2005); cell refinement: *SAINT-Plus* (Bruker, 2001); data reduction: *SAINT-Plus*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 2001); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

The authors thank the NIH (grant No. 1 P20 MD001104-01) for generous financial support, and the NSF/DMR for support (grant No. 0420863) for the acquisition of a single-crystal X-ray diffractometer.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM3039). Services for accessing these data are described at the back of the journal.

References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans. 2*, pp. S1–19.
Bruker (2001). *SAINT-Plus for Windows NT*. Version 6.2. Bruker AXS Inc., Madison, Wisconsin, USA.
Bruker (2005). *APEX2*. Version 1.27. Bruker AXS Inc., Madison, Wisconsin, USA.
Desiraju, G. R. & Steiner, T. (1999). *The Weak Hydrogen Bond*. Oxford University Press.

Kemnitzer, W., Drewe, J., Jiang, S., Zhang, H., Wang, Y., Zhao, J., Jia, S., Herich, J., Labreque, D., Storer, R., Meerovitch, K., Bouffard, D., Rej, R., Denis, R., Blais, C., Lamothe, S., Attardo, G., Gourdeau, H., Tseng, B., Kasibhatla, S. & Cai, S. X. (2004). *J. Med. Chem.* **47**, 6299–6310.

Nesterov, V. N., Kuleshova, L. N. & Antipin, M. Yu. (2001*a*). *Crystallogr. Rep.* **46**, 402–410.

Nesterov, V. N., Kuleshova, L. N. & Antipin, M. Yu. (2001*b*). *Crystallogr. Rep.* **46**, 959–965.

Nesterov, V. N., Wiedenfeld, D. J., Nesterova, S. V. & Daniels, L. M. (2005). *J. Chem. Crystallogr.* **35**, 917–922.

Nesterov, V. N., Wiedenfeld, D. J., Nesterova, S. V. & Minton, M. A. (2004). *Acta Cryst.* C**60**, o334–o337.

Nesterov, V. N. & Viltchinskaia, E. A. (2001). *Acta Cryst.* C**57**, 616–618.

Rowland, R. S. & Taylor, R. (1996). *J. Phys. Chem.* **100**, 7384–7391.

Sheldrick, G. M. (2001). *SHELXTL*. Version 6.12 for Windows NT. Bruker AXS Inc., Madison, Wisconsin, USA.

Sheldrick, G. M. (2003). *SADABS*. Version 2.03. Bruker AXS Inc., Madison, Wisconsin, USA.

Suarez, M., Salfran, E., Verdecia, Y., Ochoa, E., Alba, L., Martin, N., Martinez, R., Quinteiro, M., Seoane, C., Novoa, H., Blaton, N., Peeters, O. M. & De Ranter, C. (2002). *Tetrahedron*, **58**, 953–960.

Zhang, H.-Z., Kasibhatla, S., Kuemmerle, J., Kemnitzer, W., Ollis-Mason, K., Qiu, L., Crogan-Grundy, C., Tseng, B., Drewe, J. & Cai, S. X. (2005). *J. Med. Chem.* **48**, 5215–5223.