Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

5-Acetyl-2-amino-6-methyl-4-(3-nitrophenyl)-4*H*-pyran-3-carbonitrile and 2-amino-5-ethoxycarbonyl-6-methyl-4-(3-nitrophenyl)-4*H*-pyrano-3-carbonitrile

Vladimir N. Nesterov[a,b]* and Elena A. Viltchinskaia[a]

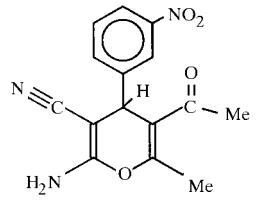
[a]Department of Physical Sciences, New Mexico Highlands University, Las Vegas, NM 87701, USA, and [b]Institute of Organoelement Compounds, Russian Academy of Sciences, 28 Vavilov Street, Moscow, Russian Federation
Correspondence e-mail: vlad@kremlin.nmhu.edu

Received 10 November 2000
Accepted 7 February 2001

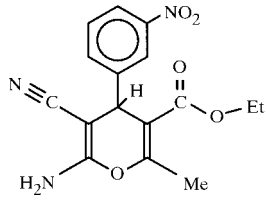
The structures of the title compounds, $C_{15}H_{13}N_3O_4$, (I), and $C_{16}H_{15}N_3O_5$ [IUPAC name: ethyl 6-amino-5-cyano-2-methyl-4-(3-nitrophenyl)-4*H*-pyrano-3-carboxylate], (II), are very similar, with the heterocyclic rings adopting boat conformations. The pseudo-axial *m*-nitrophenyl substituents are rotated by 84.0 (1) and 98.7 (1)° in (I) and (II), respectively, with respect to the four coplanar atoms of the boat. The dihedral angles between the phenyl rings and nitro groups are 12.1 (2) and 8.4 (2)° in (I) and (II), respectively. The two compounds have similar patterns of intermolecular N—H···O and N—H···N hydrogen bonding, which link molecules into infinite tapes along **b**.

Comment

The synthesis of hydrogenated compounds has been extensively studied due to interest in their biological properties. For example, derivatives of 1,4-dihydropyridine exhibit high biological activities as calcium channel blockers (Bossert *et al.*, 1981) and as calcium agonists or antagonists (Triggle *et al.*, 1980; Kokubun & Reuter, 1984; Bossert & Vater, 1989; Wang *et al.*, 1989; Alajarin *et al.*, 1995). 4*H*-Pyran derivatives have structures similar to those of 1,4-dihydropyridine and elicit the interest of organic chemists as well as of crystallographers. Many different methods have been proposed for the synthesis of 4*H*-pyran derivatives, for example, by Junek & Aigner (1970) and Rappoport & Ladkani (1974). Structural studies of some derivatives of 4*H*-pyrans by X-ray analysis have been published (Florencio & Garcia-Blanco, 1987; Bellanato *et al.*, 1987, 1988; Lokaj *et al.*, 1990; Marco *et al.*, 1993). The present study represents a continuation of our investigations of the structures of 4*H*-pyran derivatives (Sharanina *et al.*, 1986; Klokol *et al.*, 1987; Shestopalov *et al.*, 1991; Samet *et al.*, 1996; Kisliyi *et al.*, 1999*a*,*b*). The crystal structures of 5-acetyl-2-amino-6-methyl-4-(3-nitrophenyl)-4*H*-pyran-3-carbonitrile, (I), and 2-amino-5-ethoxycarbonyl-6-methyl-4-(3-nitrophenyl)-4*H*-pyrano-3-carbonitrile, (II), are presented herein.



(I)



(II)

The pyran rings in both molecules have boat conformations, with atoms O1 and C4 out of the C2/C3/C5/C6 plane by −0.179 (1) and −0.341 (1) Å, respectively, in (I), and by 0.151 (2) and 0.306 (2) Å, respectively, in (II). The C2/C3/C5/C6 plane is planar to within 0.005 (1) Å for (I) and 0.026 (1) Å for (II). The bending of the ring along O1···C4, C2···C6 and C3···C5 equals 24.0 (1), 15.1 (1) and 22.8 (2)°, respectively, in (I), and 21.2 (1), 12.7 (1) and 20.3 (2)°, respectively, in (II). The heterocycles in (I) and (II), in pyrans with comparable structures, and in derivatives of 1,4-dihydropyridine, for example, nifedipine (Triggle *et al.*, 1980), nimodipine (Wang *et al.*, 1989) and furnidipine (Alajarin *et al.*, 1995), have similar conformations.

The dihedral angle between the pseudo-axial aryl substituent and the C2/C3/C5/C6 plane of the boat of the heterocycle is 84.0 (1)° in (I) and 98.7 (1)° in (II), minimizing possible intramolecular steric contacts in both molecules. Similar orientations of sterically demanding substituents were found in all previously determined derivatives of 4*H*-pyrans (Sharanina *et al.*, 1986; Klokol *et al.*, 1987; Shestopalov *et al.*, 1991; Samet *et al.*, 1996; Kisliyi *et al.*, 1999*a*,*b*; Florencio & Garcia-Blanco, 1987; Bellanato *et al.*, 1988; Lokaj *et al.*, 1990; Marco *et al.*, 1993). The value of the angle is close to 90° in practically all known 4*H*-pyran derivatives containing sterically demanding substituents in the 4-position of the heterocycle.

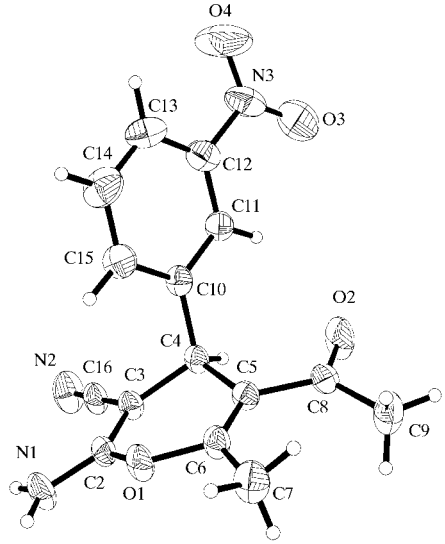


Figure 1
A view of (I) with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

The nitro groups are slightly rotated from the plane of the phenyl ring of the aryl substituent, by 12.1 (2)° in (I) and 8.4 (2)° in (II). As shown in Figs. 1 and 2, the substituents at C5 of the heterocycle have *trans* orientations with respect to the C5═C6 double bond. The C6—C5—C8—O2 torsion angle is −179.3 (2)° in (I) and −157.2 (2)° in (II). It is interesting to note that the acetyl substituent has a *cis* geometry in the 1,4-dihydropyridine derivative described by Nesterov *et al.* (1985), and ester groups have *cis* geometry in substituted 4*H*-pyrans and form intramolecular hydrogen bonds with amino groups (Sharanina *et al.*, 1986; Klokol *et al.*, 1987; Shestopalov *et al.*, 1991).

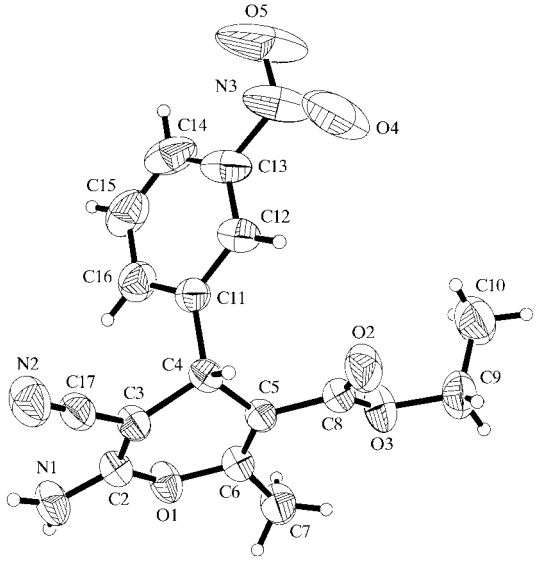


Figure 2
A view of (II) with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

The bond lengths in the planar fragment N1—C2═C3—C16/C17≡N2 in both structures are different from typical literature values (Allen *et al.*, 1987). This bond-length distribution was observed in all derivatives of 4*H*-pyrans that we investigated and has also been noted in the literature (Samet *et al.*, 1996; Bellanato *et al.*, 1987; Lokaj *et al.*, 1990; Marco *et al.*, 1993). This regularity can be explained by the conjugation of bonds in the fragment. However, in the C6═C5—C8═O2 fragment, located on the opposite side of the pyran ring in both compounds, the bond lengths agree with standard values (Allen *et al.*, 1987) and this confirms the absence of conjugation in this fragment of both molecules. The mutual orientation of substituents of the pyran ring in both molecules gives rise to an intramolecular O2···H4*A* non-bonded interaction. The length of this interaction is 2.38 Å in (I) and 2.43 Å in (II), less than the sum of the relevant van der Waals radii (Rowlend & Taylor, 1996). The rest of the geometrical parameters in (I) and (II) have standard values (Allen *et al.*, 1987).

The structures of (I) and (II) both exhibit intermolecular N1—H1*B*···O2($x, y-1, z$) and N1—H1*A*···N2($2-x, 1-y, 1-z$) hydrogen bonds, which connect the molecules into infinite tapes along the *b* axis.

Experimental

Compounds (I) and (II) were prepared by the reaction of *m*-nitrobenzaldehyde (0.01 mol) with acetylacetone (0.01 mol) and ethyl acetoacetate (0.01 mol), respectively, in the presence of a catalytic amount of morpholine in ethanol (20 ml) under reflux (Sharanina *et al.*, 1986). The precipitates were isolated and recrystallized from ethanol [m.p.: 492 K for (I) and 457 K for (II); yield: 90% for (I) and 86% for (II)]. Colourless crystals of (I) and (II) suitable for X-ray analysis were obtained by isothermal evaporation from ethanolic solutions.

Compound (I)

Crystal data

$C_{15}H_{13}N_3O_4$
$M_r = 299.28$
Triclinic, $P\overline{1}$
$a = 8.1470$ (16) Å
$b = 8.4120$ (17) Å
$c = 11.149$ (2) Å
$\alpha = 98.46$ (3)°
$\beta = 108.69$ (3)°
$\gamma = 96.93$ (3)°
$V = 704.3$ (2) Å^3
$Z = 2$
$D_x = 1.411$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 24 reflections
$\theta = 11$–12°
$\mu = 0.11$ mm^{-1}
$T = 298$ (2) K
Parallelepiped prism, colourless
0.50 × 0.40 × 0.25 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\theta/2\theta$ scans
3277 measured reflections
3019 independent reflections
1896 reflections with $I > 2\sigma(I)$
$R_{int} = 0.017$
$\theta_{max} = 27°$
$h = 0 \rightarrow 10$
$k = -10 \rightarrow 10$
$l = -14 \rightarrow 13$
3 standard reflections
every 97 reflections
intensity decay: 3%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.055$
$wR(F^2) = 0.169$
$S = 1.02$
3019 reflections
201 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1084P)^2 + 0.037P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.003$
$\Delta\rho_{max} = 0.22$ e Å^{-3}
$\Delta\rho_{min} = -0.20$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °) for (I).

O2—C8	1.215 (3)	C3—C16	1.408 (3)
N1—C2	1.333 (3)	C5—C6	1.342 (3)
N2—C16	1.147 (3)	C5—C8	1.483 (3)
C2—C3	1.356 (3)		
N1—C2—C3	127.8 (2)	C6—C5—C4	120.45 (18)
N1—C2—O1	111.45 (17)	C8—C5—C4	114.67 (16)
C3—C2—O1	120.70 (18)	C5—C6—O1	120.62 (19)
C2—C3—C16	119.32 (19)	C5—C6—C7	132.0 (2)
C2—C3—C4	120.76 (18)	O1—C6—C7	107.31 (17)
C16—C3—C4	119.79 (17)	N2—C16—C3	178.8 (3)
C6—C5—C8	124.87 (19)		
O1—C2—C3—C4	−5.6 (3)	C4—C5—C6—O1	7.3 (3)
C2—C3—C4—C10	−97.7 (2)	C6—C5—C8—O2	−179.3 (2)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1*B*···O2^{i}	0.86	2.02	2.860 (3)	166
N1—H1*A*···N2^{ii}	0.86	2.27	3.048 (3)	151

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

Compound (II)

Crystal data

$C_{16}H_{15}N_3O_5$
M_r = 329.31
Triclinic, $P\overline{1}$
a = 8.4550 (10) Å
b = 8.4750 (10) Å
c = 12.073 (2) Å
α = 83.05 (2)°
β = 71.33 (2)°
γ = 76.35 (2)°
V = 795.46 (19) Å^3
Z = 2
D_x = 1.375 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 24 reflections
θ = 11–12°
μ = 0.10 mm^{-1}
T = 298 (2) K
Rhombohedral prism, colourless
0.5 × 0.4 × 0.3 mm

Data collection

Siemens *P3*/*PC* diffractometer
$\theta/2\theta$ scans
4216 measured reflections
3942 independent reflections
2553 reflections with $I > 2\sigma(I)$
R_{int} = 0.027
θ_{max} = 29.1°
$h = 0 \rightarrow 11$
$k = -11 \rightarrow 11$
$l = -15 \rightarrow 16$
2 standard reflections
every 98 reflections
intensity decay: 5%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.058
$wR(F^2)$ = 0.154
S = 1.03
3942 reflections
219 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0686P)^2 + 0.1782P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.003
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}

Table 3
Selected geometric parameters (Å, °) for (II).

O2—C8	1.203 (2)	C3—C17	1.413 (3)
N1—C2	1.330 (2)	C5—C6	1.333 (2)
N2—C17	1.143 (2)	C5—C8	1.473 (2)
C2—C3	1.355 (2)		
N1—C2—C3	128.39 (17)	C6—C5—C4	121.73 (15)
N1—C2—O1	110.66 (15)	C8—C5—C4	114.09 (15)
C3—C2—O1	120.95 (15)	C5—C6—O1	120.82 (16)
C2—C3—C17	119.14 (16)	C5—C6—C7	130.77 (17)
C2—C3—C4	121.16 (16)	O1—C6—C7	108.40 (15)
C17—C3—C4	119.26 (15)	N2—C17—C3	179.2 (2)
C6—C5—C8	124.14 (17)		
O1—C2—C3—C4	11.4 (3)	C6—C5—C8—O2	−157.15 (19)
C2—C3—C4—C11	96.7 (2)	C8—O3—C9—C10	−92.6 (3)
C4—C5—C6—O1	−1.3 (3)		

Table 4
Hydrogen-bonding geometry (Å, °) for (II).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1B···O2^{i}	0.86	2.00	2.830 (2)	161
N1—H1A···N2^{ii}	0.86	2.17	2.995 (2)	160

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

H atoms were located from difference Fourier syntheses and idealized for refinement with N—H = 0.86 Å, and C—H = 0.93, 0.96 and 0.98 Å for aryl, methyl and methine H atoms, respectively, and with U_{iso}(H) = xU_{eq}(N/C), where x = 1.5 for methyl H atoms and 1.2 for all others.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989) for (I), *P*3 (Siemens, 1989) for (II); cell refinement: *CAD*-4 *Software* for (I), *P*3 for (II); for both compounds, data reduction: *SHELXTL-Plus* (Sheldrick, 1994); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL-Plus*; software used to prepare material for publication: *SHELXL*97.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM1442). Services for accessing these data are described at the back of the journal.

References

Alajarin, R., Vaquero, J. J., Alvarez-Builla, J., Pastor, M., Sunkel, C., de Casa-Juana, M. F., Priego, J., Statkow, P. R., Sanz-Aparicio, J. & Fonseca, I. (1995). *J. Med. Chem.* **38**, 2830–2841.

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.

Bellanato, J., Florencio, F., Blanco, S. G., Martin, N. & Seoane, C. (1987). *J. Mol. Struct.* **162**, 19–30.

Bellanato, J., Florencio, F., Martin, N. & Seoane, C. (1988). *J. Mol. Struct.* **172**, 63–72.

Bossert, F., Meyer, H. & Wehinger, E. (1981). *Angew. Chem. Int. Ed. Engl.* **20**, 762–764.

Bossert, F. & Vater, W. (1989). *J. Med. Res.* **9**, 291–324.

Enraf–Nonius (1989). *CAD*-4 *Software*. Version 5.0. Enraf–Nonius, Delft, The Netherlands.

Florencio, F. & Garcia-Blanco, S. (1987). *Acta Cryst.* C**43**, 1430–1432.

Junek, H. & Aigner, H. A. (1970). *Z. Naturforsch. Teil B*, **25**, 1423–1426.

Kislyi, V. P., Nesterov, V. N., Shestopalov, A. M. & Semenov, V. V. (1999*a*). *Izv. Akad. Nauk SSSR Ser. Khim.* (*Russ. Chem. Bull.* **48**), pp. 1142–1145.

Kislyi, V. P., Nesterov, V. N., Shestopalov, A. M. & Semenov, V. V. (1999*b*). *Izv. Akad. Nauk SSSR Ser. Khim.* (*Russ. Chem. Bull.* **48**), pp. 1146–1149.

Klokol, G. V., Sharanina, L. G., Nesterov, V. N., Shklover, V. E., Sharanin, Yu. A. & Struchkov, Yu. T. (1987). *Zh. Org. Khim.* **23**, 412–421.

Kokubun, S. & Reuter, H. (1984). *Proc. Natl Acad. Sci. USA*, **81**, 4824–4827.

Lokaj, J., Kettmann, V., Pavelčík, F., Ilavský, D. & Marchalín, Š. (1990). *Acta Cryst.* C**46**, 788–791.

Marco, J. L., Martin, G., Martin, N., Martinez-Grau, A., Seoane, C., Albert, A. & Cano, F. H. (1993). *Tetrahedron*, **49**, 7133–7144.

Nesterov, V. N., Shklover, V. E., Struchkov, Yu. T., Sharanin, Yu. A., Shestopalov, A. M. & Rodinovskaya, L. A. (1985). *Acta Cryst.* C**41**, 1191–1194.

Rappoport, Z. & Ladkani, D. (1974). *J. Chem. Soc. Perkin Trans.* 1, pp. 2595–2601.

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

Samet, A. V., Shestopalov, A. M., Struchkova, M. I., Nesterov, V. N., Struchkov, Yu. T. & Semenov, V. V. (1996). *Izv. Akad. Nauk SSSR Ser. Khim.* **95**, 2050–2055.

Sharanina, L. G., Nesterov, V. N., Klokol, G. V., Rodinovskaya, L. A., Shklover, V. E., Sharanin, Yu. A., Struchkov, Yu. T. & Promonenkov, V. K. (1986). *Zh. Org. Khim.* **22**, 1315–1322.

Sheldrick, G. M. (1990). *Acta Cryst.* A**46**, 467–473.

Sheldrick, G. M. (1994). *SHELXTL-Plus*. PC Version 5.02. Siemens Analytical X-ray Instruments Inc., Karlsruhe, Germany.

Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.

Shestopalov, A. M., Sharanin, Yu. A., Khikuba, M. R., Nesterov, V. N., Shklover, V. E., Struchkov, Yu. T. & Litvinov, V. P. (1991). *Khim. Geterotsikl. Soedin. SSSR*, pp. 205–211.

Siemens (1989). *P*3. Siemens Analytical X-ray Instruments Inc., Karlsruhe, Germany.

Triggle, A. M., Shefter, E. & Triggle, D. G. (1980). *J. Med. Chem.* **23**, 1442–1445.

Wang, S. D., Herbette, L. G. & Rhodes, D. G. (1989). *Acta Cryst.* C**45**, 1748–1751.