Ethyl 4-(furan-2-yl)-6-methyl-2-oxo-1,2,3,4-tetra-hydropyrimidine-5-carboxylate: a triclinic polymorph

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The title compound, $C_{12}H_{14}N_2O_4$, crystallizes in the triclinic space group $P\bar{1}$. The previously reported polymorph occurs in the monoclinic space group $P2_1/c$, and has two independent molecules in the asymmetric unit [Wang (2010). *Acta Cryst.* E**66**, o2822]. The dihydropyrimidine ring adopts a screw-boat conformation. The furan ring is positioned axially and makes a dihedral angle of 85.94 (7)° with the mean plane through the pyrimidine ring. In the crystal, molecules are linked *via* pairs of N—H···O hydrogen bonds, forming inversion dimers with an $R_2^2(8)$ ring motif. The dimers are linked by N—H···O and C—H···O hydrogen bonds, forming chains propagating along the *a*-axis direction.

3D view
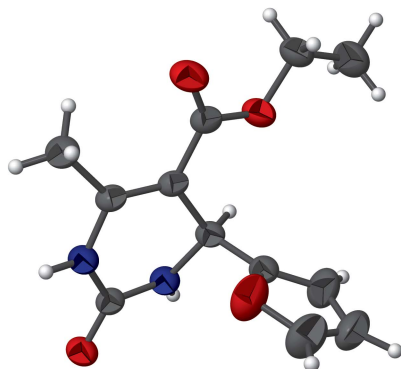
Chemical scheme
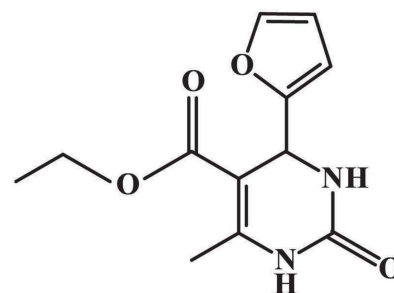
Structure description

In recent years, dihydropyrimidines (DHPMs, 'Biginelli compounds') and their derivatives have attracted considerable attention in synthetic organic chemistry because of their wide range of biological activities, such as antiviral, antitumor, antibacterial and anti-inflammatory properties (Kappe 2000; Kulkarni *et al.*, 2009; Patil *et al.*, 2011). The Biginelli reaction is a well-known multi-component reaction involving a one-pot cyclo-condensation of an aldehyde, β-ketoester and urea/thiourea. Multi-component reactions (MCRs) have recently gained tremendous importance in organic and medicinal chemistry (Kulkarni *et al.*, 2009). They are also very potent calcium channel modulators (Kappe 1998; Jauk *et al.*, 2000). Furthermore, apart from synthetic DHPM derivatives, several marine natural products with interesting biological activities containing the di-
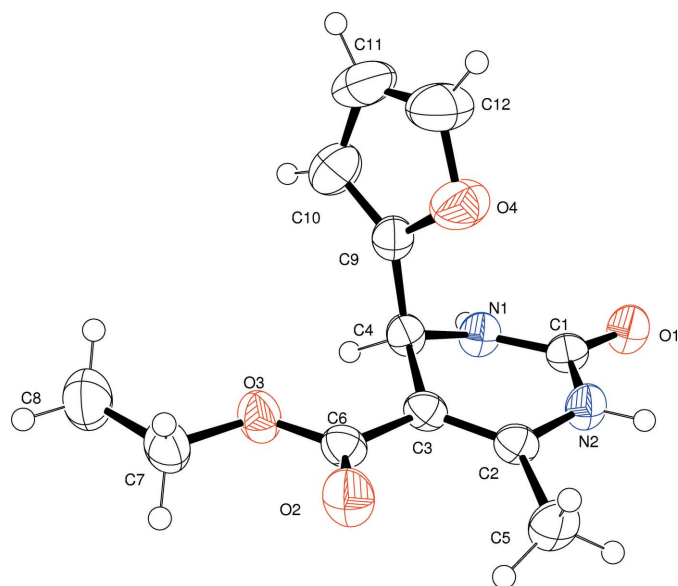
Figure 1
The molecular structure of the title compound, showing the atom labelling. Displacement ellipsoids are drawn at the 50% probability level.

hydropyrimidine-5-carboxylate core have also been isolated. Most notable among these are the batzelladine alkaloids A and B, which inhibit the binding of HIV envelope protein gp-120 to human CD4 cells and, therefore, are potential leads for AIDS therapy (Kappe, 2000). As part of our studies in this area, we have determined the crystal structure of the title
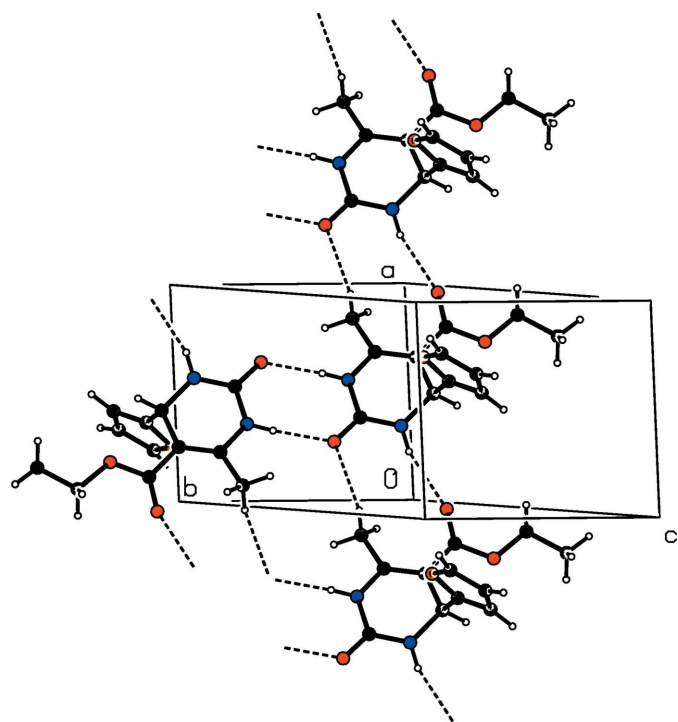

Figure 2
The crystal packing of the title compound, showing the $R_2^2(8)$ ring motif, viewed normal to the bc plane. Hydrogen bonds are shown as dashed lines (see Table 1).

Table 1
Hydrogen-bond geometry (Å, °).

$D—H\cdots A$	$D—H$	$H\cdots A$	$D\cdots A$	$D—H\cdots A$
N2—H2$\cdots$O1^i	0.86	2.00	2.855 (2)	176
N1—H1$\cdots$O2^{ii}	0.86	2.34	3.142 (2)	156
C5—H5A$\cdots$O1^{iii}	0.96	2.52	3.141 (2)	122

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

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{12}H_{14}N_2O_4$
M_r	250.25
Crystal system, space group	Triclinic, $P\bar{1}$
Temperature (K)	296
a, b, c (Å)	7.4670 (2), 8.8307 (3), 10.5426 (3)
α, β, γ (°)	106.833 (2), 108.557 (2), 99.420 (2)
V (Å^3)	605.20 (3)
Z	2
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.10
Crystal size (mm)	0.19 × 0.16 × 0.13
Data collection	
Diffractometer	Bruker Kappa APEXII CCD
Absorption correction	Multi-scan (*SADABS*; Bruker, 2008)
T_{min}, T_{max}	0.980, 0.987
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	9061, 2458, 2116
R_{int}	0.022
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.624
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.042, 0.123, 1.08
No. of reflections	2458
No. of parameters	166
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}, \Delta\rho_{min}$ (e Å^{-3})	0.31, −0.36

Computer programs: *APEX2*, *SAINT* and *XPREP* (Bruker, 2008), *SIR92* (Altomare *et al.*, 1993), *SHELXL97* (Sheldrick, 2008), *ORTEP-3 for Windows* (Farrugia, 2012) and *PLATON* (Spek, 2009).

compound presented herein. It is one of the analogues of our previously reported DHPM structures (Suresh *et al.*, 2015*a,b*; Novina *et al.*, 2015).

In the title compound, Fig. 1, the furan ring at the chiral carbon atom C4 is positioned axially and bisects the pyrimidine ring with a dihedral angle of 85.94 (7)°. The pyrimidine ring adopts a screw-boat conformation with atoms N1 and C4 displaced by −0.1674 (10) and 0.1603 (9) Å, respectively, from the mean plane of the other atoms (C1/N2/C2/C3). The puckering parameters are $q2$ = 0.2446 (16) Å, $q3$ = 0.1048 (16) Å, Q = 0.2661 (16) Å, θ = 66.8 (3)° and φ = 327.6 (4)°. The ethyl acetate group attached to the pyrimidine ring shows an extended conformation [C3—C6—O3—C7 = −179.29 (12)°].

In the crystal, molecules are linked *via* pairs of N—H$\cdots$O hydrogen bonds, forming inversion dimers with an $R_2^2(8)$ ring motif (Fig. 2 and Table 1). The dimers are linked by N—H$\cdots$O and C—H$\cdots$O hydrogen bonds, forming chains propagating along the a–axis direction (Fig. 2 and Table 1).

Synthesis and crystallization

A mixture of ethylacetoacetate (1.3 ml, 0.01 mol), furfural (1 ml, 0.01 mol), and urea (1.8 g, 0.03 mol) in ethanol (5 ml) was heated under reflux in the presence of CeCl$_3$·7H$_2$O (25 mol %) for 8 h (monitored by TLC). The reaction mixture, after being cooled to room temperature, was poured onto crushed ice and stirred for 5–10 min. The precipitate was then washed with water, filtered, dried and again washed with petroleum ether (40–60%) and dried in a vacuum. The compound was recrystallized from absolute ethanol giving colourless block-like crystals [m.p. 435–438 K, yield 88%].

Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2.

Acknowledgements

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full crystallographic data

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Ethyl 4-(furan-2-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate

Crystal data

$C_{12}H_{14}N_2O_4$	$Z = 2$
$M_r = 250.25$	$F(000) = 264$
Triclinic, $P\bar{1}$	$D_x = 1.373$ Mg m^{-3}
Hall symbol: -P 1	Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
$a = 7.4670$ (2) Å	Cell parameters from 2458 reflections
$b = 8.8307$ (3) Å	$\theta = 2.2$–26.3°
$c = 10.5426$ (3) Å	$\mu = 0.10$ mm^{-1}
$\alpha = 106.833$ (2)°	$T = 296$ K
$\beta = 108.557$ (2)°	Block, colourless
$\gamma = 99.420$ (2)°	0.19 × 0.16 × 0.13 mm
$V = 605.20$ (3) Å^3	

Data collection

Bruker Kappa APEXII CCD diffractometer	9061 measured reflections
Radiation source: fine-focus sealed tube	2458 independent reflections
Graphite monochromator	2116 reflections with $I > 2\sigma(I)$
ω and φ scan	$R_{int} = 0.022$
Absorption correction: multi-scan (SADABS; Bruker, 2008)	$\theta_{max} = 26.3°$, $\theta_{min} = 2.2°$
$T_{min} = 0.980$, $T_{max} = 0.987$	$h = -9 \rightarrow 9$
	$k = -10 \rightarrow 10$
	$l = -13 \rightarrow 12$

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)] = 0.042$	$w = 1/[\sigma^2(F_o^2) + (0.0596P)^2 + 0.1739P]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.123$	
$S = 1.08$	$(\Delta/\sigma)_{max} < 0.001$
2458 reflections	$\Delta\rho_{max} = 0.31$ e Å^{-3}
166 parameters	$\Delta\rho_{min} = -0.36$ e Å^{-3}
0 restraints	Extinction correction: SHELXL97 (Sheldrick, 2008), Fc*=kFc[1+0.001xFc$^2\lambda^3$/sin(2θ)]$^{-1/4}$
Primary atom site location: structure-invariant direct methods	Extinction coefficient: 0.010 (5)
Secondary atom site location: difference Fourier map	

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
O4	0.7408 (2)	0.90463 (16)	0.92870 (14)	0.0670 (4)
C10	0.5796 (3)	0.7209 (3)	0.9849 (2)	0.0647 (5)
H10	0.5005	0.6241	0.9791	0.078*
C11	0.6772 (3)	0.8695 (3)	1.1090 (2)	0.0699 (6)
H11	0.6753	0.8875	1.1999	0.084*
C12	0.7690 (3)	0.9745 (3)	1.0699 (2)	0.0725 (6)
H12	0.8433	1.0821	1.1296	0.087*
O1	0.32040 (15)	0.90923 (14)	0.55610 (13)	0.0463 (3)
N2	0.60593 (17)	0.84873 (15)	0.56522 (14)	0.0391 (3)
H2	0.6340	0.9242	0.5326	0.047*
O2	1.01790 (16)	0.58238 (15)	0.69053 (14)	0.0529 (3)
C3	0.71862 (19)	0.65870 (17)	0.66569 (15)	0.0346 (3)
O3	0.79382 (16)	0.45399 (13)	0.75180 (13)	0.0474 (3)
C6	0.8590 (2)	0.56456 (18)	0.70103 (16)	0.0378 (3)
N1	0.39886 (17)	0.70961 (15)	0.64088 (13)	0.0384 (3)
H1	0.2789	0.6658	0.6263	0.046*
C1	0.4345 (2)	0.82776 (18)	0.58816 (15)	0.0354 (3)
C2	0.73651 (19)	0.75677 (17)	0.59092 (15)	0.0350 (3)
C4	0.5541 (2)	0.65133 (17)	0.72213 (16)	0.0354 (3)
H4	0.4969	0.5358	0.7054	0.042*
C9	0.6239 (2)	0.74810 (18)	0.87951 (16)	0.0388 (3)
C7	0.9206 (3)	0.3533 (2)	0.7928 (2)	0.0510 (4)
H7A	1.0495	0.4230	0.8629	0.061*
H7B	0.9365	0.2840	0.7093	0.061*
C5	0.8859 (2)	0.7784 (2)	0.52603 (19)	0.0501 (4)
H5A	1.0055	0.8581	0.5979	0.075*
H5B	0.8361	0.8162	0.4486	0.075*
H5C	0.9118	0.6749	0.4900	0.075*
C8	0.8261 (4)	0.2502 (3)	0.8552 (3)	0.0700 (6)
H8A	0.8160	0.3200	0.9399	0.105*
H8B	0.9041	0.1790	0.8801	0.105*
H8C	0.6969	0.1848	0.7861	0.105*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O4	0.0817 (9)	0.0548 (8)	0.0514 (7)	−0.0049 (7)	0.0300 (7)	0.0097 (6)
C10	0.0792 (13)	0.0694 (12)	0.0645 (12)	0.0188 (10)	0.0445 (11)	0.0339 (10)
C11	0.0797 (14)	0.0946 (16)	0.0453 (10)	0.0336 (12)	0.0338 (10)	0.0241 (10)
C12	0.0817 (14)	0.0704 (13)	0.0480 (10)	0.0099 (11)	0.0246 (10)	0.0043 (9)
O1	0.0360 (6)	0.0589 (7)	0.0635 (7)	0.0228 (5)	0.0282 (5)	0.0348 (6)
N2	0.0326 (6)	0.0449 (7)	0.0532 (7)	0.0143 (5)	0.0248 (5)	0.0260 (6)
O2	0.0403 (6)	0.0607 (7)	0.0782 (8)	0.0246 (5)	0.0336 (6)	0.0363 (6)
C3	0.0303 (7)	0.0343 (7)	0.0405 (7)	0.0091 (5)	0.0179 (6)	0.0110 (6)
O3	0.0455 (6)	0.0469 (6)	0.0666 (7)	0.0214 (5)	0.0303 (5)	0.0300 (6)
C6	0.0362 (7)	0.0360 (7)	0.0431 (8)	0.0109 (6)	0.0196 (6)	0.0121 (6)
N1	0.0261 (6)	0.0458 (7)	0.0495 (7)	0.0094 (5)	0.0190 (5)	0.0215 (6)
C1	0.0292 (6)	0.0404 (7)	0.0383 (7)	0.0100 (6)	0.0157 (5)	0.0138 (6)
C2	0.0292 (7)	0.0371 (7)	0.0399 (7)	0.0091 (6)	0.0171 (6)	0.0116 (6)
C4	0.0320 (7)	0.0342 (7)	0.0470 (8)	0.0105 (5)	0.0211 (6)	0.0177 (6)
C9	0.0370 (7)	0.0426 (8)	0.0473 (8)	0.0155 (6)	0.0229 (6)	0.0214 (6)
C7	0.0530 (9)	0.0506 (9)	0.0620 (10)	0.0262 (8)	0.0265 (8)	0.0274 (8)
C5	0.0438 (9)	0.0659 (11)	0.0649 (10)	0.0250 (8)	0.0362 (8)	0.0357 (9)
C8	0.0852 (15)	0.0629 (12)	0.0862 (14)	0.0319 (11)	0.0446 (12)	0.0428 (11)

Geometric parameters (Å, º)

O4—C9	1.3575 (19)	O3—C7	1.4528 (19)
O4—C12	1.366 (2)	N1—C1	1.3444 (19)
C10—C9	1.328 (2)	N1—C4	1.4702 (18)
C10—C11	1.432 (3)	N1—H1	0.8600
C10—H10	0.9300	C2—C5	1.4967 (19)
C11—C12	1.301 (3)	C4—C9	1.496 (2)
C11—H11	0.9300	C4—H4	0.9800
C12—H12	0.9300	C7—C8	1.481 (3)
O1—C1	1.2312 (17)	C7—H7A	0.9700
N2—C1	1.3700 (17)	C7—H7B	0.9700
N2—C2	1.3791 (18)	C5—H5A	0.9600
N2—H2	0.8600	C5—H5B	0.9600
O2—C6	1.2152 (18)	C5—H5C	0.9600
C3—C2	1.347 (2)	C8—H8A	0.9600
C3—C6	1.465 (2)	C8—H8B	0.9600
C3—C4	1.5258 (18)	C8—H8C	0.9600
O3—C6	1.3378 (18)		
C9—O4—C12	106.82 (15)	N2—C2—C5	112.94 (12)
C9—C10—C11	106.66 (18)	N1—C4—C9	109.89 (11)
C9—C10—H10	126.7	N1—C4—C3	109.59 (11)
C11—C10—H10	126.7	C9—C4—C3	113.30 (11)
C12—C11—C10	106.67 (17)	N1—C4—H4	108.0
C12—C11—H11	126.7	C9—C4—H4	108.0

C10—C11—H11	126.7	C3—C4—H4	108.0
C11—C12—O4	110.45 (19)	C10—C9—O4	109.38 (15)
C11—C12—H12	124.8	C10—C9—C4	133.32 (16)
O4—C12—H12	124.8	O4—C9—C4	116.85 (12)
C1—N2—C2	124.35 (12)	O3—C7—C8	107.47 (15)
C1—N2—H2	117.8	O3—C7—H7A	110.2
C2—N2—H2	117.8	C8—C7—H7A	110.2
C2—C3—C6	121.82 (12)	O3—C7—H7B	110.2
C2—C3—C4	119.48 (12)	C8—C7—H7B	110.2
C6—C3—C4	118.62 (12)	H7A—C7—H7B	108.5
C6—O3—C7	117.05 (12)	C2—C5—H5A	109.5
O2—C6—O3	122.08 (14)	C2—C5—H5B	109.5
O2—C6—C3	126.50 (14)	H5A—C5—H5B	109.5
O3—C6—C3	111.41 (12)	C2—C5—H5C	109.5
C1—N1—C4	123.44 (11)	H5A—C5—H5C	109.5
C1—N1—H1	118.3	H5B—C5—H5C	109.5
C4—N1—H1	118.3	C7—C8—H8A	109.5
O1—C1—N1	123.84 (12)	C7—C8—H8B	109.5
O1—C1—N2	120.65 (13)	H8A—C8—H8B	109.5
N1—C1—N2	115.45 (12)	C7—C8—H8C	109.5
C3—C2—N2	119.95 (12)	H8A—C8—H8C	109.5
C3—C2—C5	127.10 (13)	H8B—C8—H8C	109.5
C9—C10—C11—C12	1.0 (3)	C1—N2—C2—C3	−12.1 (2)
C10—C11—C12—O4	−0.8 (3)	C1—N2—C2—C5	166.89 (14)
C9—O4—C12—C11	0.3 (3)	C1—N1—C4—C9	91.93 (16)
C7—O3—C6—O2	−0.7 (2)	C1—N1—C4—C3	−33.18 (18)
C7—O3—C6—C3	−179.29 (12)	C2—C3—C4—N1	20.23 (18)
C2—C3—C6—O2	12.9 (2)	C6—C3—C4—N1	−162.82 (12)
C4—C3—C6—O2	−163.98 (15)	C2—C3—C4—C9	−102.90 (15)
C2—C3—C6—O3	−168.65 (13)	C6—C3—C4—C9	74.05 (16)
C4—C3—C6—O3	14.48 (18)	C11—C10—C9—O4	−0.8 (2)
C4—N1—C1—O1	−159.14 (14)	C11—C10—C9—C4	−172.63 (17)
C4—N1—C1—N2	23.7 (2)	C12—O4—C9—C10	0.3 (2)
C2—N2—C1—O1	−176.44 (13)	C12—O4—C9—C4	173.67 (15)
C2—N2—C1—N1	0.8 (2)	N1—C4—C9—C10	96.8 (2)
C6—C3—C2—N2	−177.23 (12)	C3—C4—C9—C10	−140.24 (19)
C4—C3—C2—N2	−0.4 (2)	N1—C4—C9—O4	−74.56 (16)
C6—C3—C2—C5	4.0 (2)	C3—C4—C9—O4	48.40 (18)
C4—C3—C2—C5	−179.20 (14)	C6—O3—C7—C8	175.87 (15)

Hydrogen-bond geometry (Å, °)

D—H⋯A	D—H	H⋯A	D⋯A	D—H⋯A
N2—H2⋯O1[i]	0.86	2.00	2.855 (2)	176

| N1—H1···O2[ii] | 0.86 | 2.34 | 3.142 (2) | 156 |
| C5—H5*A*···O1[iii] | 0.96 | 2.52 | 3.141 (2) | 122 |

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