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Ethyl 6-methyl-4-(3-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate

Noor Shahina Begum* and D. E. Vasundhara

Department of Studies in Chemistry, Bangalore University, Bangalore 560 001, India

Correspondence e-mail: noorsb@rediffmail.com

Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.002 Å
R factor = 0.040
wR factor = 0.113
Data-to-parameter ratio = 14.4

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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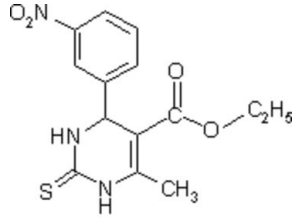
In the title compound, $C_{14}H_{15}N_3O_4S$, the tetrahydropyrimidine ring adopts a half-boat form. There are intermolecular N—H···O hydrogen bonds and π–π stacking interactions.

Comment

The Biginelli reaction is a three-component condensation of ethyl acetoacetate, benzaldehyde and urea for the synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones (abbreviated as DHPMs). DHPMs have recently emerged as important target molecules because of their therapeutic and pharmacological properties (Kappe, 2000*a*), such as antiviral (Hurst *et al.*, 1961), antimitotic (Mayer *et al.*, 1999), anticarcinogenic (Kato, 1984) and antihypertensive (Atwal *et al.*, 1991). They are also noteworthy as calcium channel modulators (Kappe, 1998; Jauk *et al.*, 2000). Additionally, their particular structure has been found in the natural marine alkaloids batzelladine A and B, which are the first low-molecular-weight natural products reported in the literature to inhibit the binding of HIV gp-120 to CD4 cells, so opening up a new area in the development of AIDS therapy (Patil *et al.*, 1995). Also, because of the close relationship between the structure of DHPMs with that of the known dihydropyridine calcium channel modulators of the Hantzsch-type, intensive research has been devoted to the synthesis of the dihydropyrimidinone nucleus; this subject was recently reviewed (Kappe, 1993, 2000*b*, 2003). Since knowledge of the molecular geometry and the probable bioactive structure of a compound is a prerequisite for any understanding of its attractive pharmacological properties, we report here the structure of the title compound, (I), which is a calcium antagonist.



(I)

In (I), the benzene ring (atoms C1–C6) has an orientation such as to bisect the half-boat form of the tetrahydropyrimidine ring (Fig. 1). DHPMs of this type are known to show conformational flexibility whereby the aryl ring and the ester group can rotate and the conformation of the tetrahydropyrimidine ring can change (Kappe *et al.*, 1997; Shishkin *et al.*, 1997). In the crystal structure, there is an intermolecular

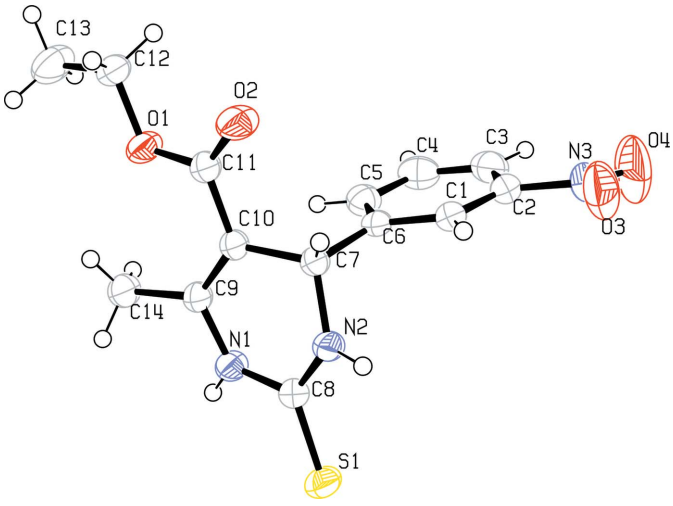


Figure 1
The molecular structure of (I), showing 50% probability displacement ellipsoids.

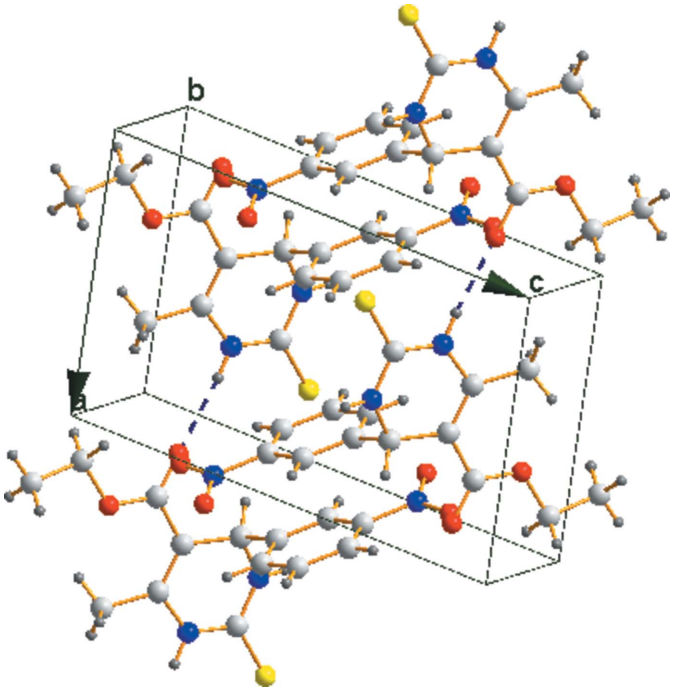


Figure 2
The crystal structure of (I). Dashed lines indicate hydrogen bonds.

N—H···O hydrogen bond (Table 1 and Fig. 2). The molecular packing is further stabilized by π–π stacking interactions between the benzene rings. The C4···C5($1-x, 1-y, 1-z$) distance is 3.412 (3) Å.

Experimental

A mixture of ethyl acetoacetate (3.12 g, 25 mmol), 3-nitrobenzaldehyde (3.02 g, 20 mmol) and thiourea (1.83 g, 24 mmol) in acetonitrile (25 ml) was heated under reflux for 5 h. After cooling, the reaction mixture was poured on to crushed ice. Stirring was continued for several minutes. The solid product, (I), was filtered, washed with cold water, dried and recrystallized from ethanol (yield 85%; m.p. 485 K). Single crystals of (I) were grown from a chloroform solution by slow evaporation at room temperature.

Crystal data

$C_{14}H_{15}N_3O_4S$
M_r = 321.35
Triclinic, $P\overline{1}$
a = 7.4275 (14) Å
b = 9.3536 (18) Å
c = 11.290 (2) Å
α = 74.260 (3)°
β = 75.418 (3)°
γ = 82.888 (3)°
V = 729.3 (2) Å^3
Z = 2
D_x = 1.463 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.24 mm^{-1}
T = 293 (2) K
Prism, yellow
0.3 × 0.2 × 0.15 mm

Data collection

Bruker SMART CCD area-detector diffractometer
φ and ω scans
Absorption correction: none
5725 measured reflections
2897 independent reflections
2556 reflections with $I > 2\sigma(I)$
R_{int} = 0.015
θ_{max} = 27.3°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.040
$wR(F^2)$ = 0.113
S = 1.02
2897 reflections
201 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0591P)^2 + 0.3089P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.32 e Å^{-3}
$\Delta\rho_{min}$ = −0.21 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1A···O2^{i}	0.86	2.14	3.003 (2)	173

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

All H atoms were positioned geometrically and refined as riding, with C—H = 0.93–0.97 Å and N—H = 0.86 Å, and with U_{iso}(H) = 1.2U_{eq}(C,N).

Data collection: *SMART* (Bruker, 1998); cell refinement: *SAINT-Plus* (Bruker, 1998); data reduction: *SAINT-Plus*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *SHELXL97*.

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