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Dimethyl 2-[(*E*)-(hydroxyimino)methyl]-6-methyl-4-(2-thienyl)-1,4-dihydropyridine-3,5-dicarboxylate

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Key indicators

Single-crystal X-ray study
T = 295 K
Mean σ(C–C) = 0.002 Å
Disorder in main residue
R factor = 0.034
wR factor = 0.085
Data-to-parameter ratio = 16.1

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

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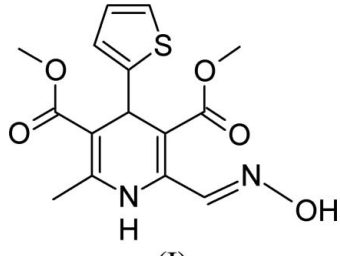
In the title compound, $C_{15}H_{16}N_2O_5S$, the substituted 1,4-dihydropyridine (1,4-DHP) ring has a flattened boat conformation. The 2-thiophene ring is disordered over two essentially equally occupied sites and is approximately perpendicular to the 1,4-DHP ring. The carbonyl groups of the ester groups at positions 3 and 5 of the 1,4-DHP ring have *cis–cis* configurations with respect to the double bonds in the 1,4-DHP ring. The crystal packing is stabilized by intramolecular N—H···N and C—H···O, and intermolecular N—H···O and O—H···O, hydrogen bonds.

Comment

A wide range of chemical substances influence the flow of Ca^{2+} ions through the channels found in cell membranes. While some compounds, the calcium agonists, activate this flow, other compounds, the calcium antagonists, selectively inhibit the flow of Ca^{2+} ions through the Ca^{2+}-conducting channels (Nayler, 1988). 1,4-DHP derivatives constitute a major class of calcium agonists or antagonists and have been a target of structure–activity relationship studies (Langs & Triggle, 1985; Langs *et al.*, 1987; Rose, 1989, 1990). Nifedipine is the prototype of this group and both nifedipine and its structural analogues are used as antihypertensive and anti-anginal drugs. These compounds inhibit the normal excitation–contraction coupling in muscle tissue by blocking the flow of Ca^{2+} ions through plasma membrane channels into the muscle cell (Janis & Triggle, 1983; Triggle *et al.*, 1989). Our interest is in the structure and calcium antagonistic behaviour of condensed derivatives of 1,4-DHP. The crystal structures of some of these derivatives have already been reported (Vrábel *et al.*, 2001, 2003, 2005, 2006). The title compound, (I), has been prepared as a further potentially active 1,4-DHP derivative.



(I)

We have studied the crystal structure of (I) and present its structure here (Fig. 1). The 1,4-DHP ring adopts a flattened boat conformation with atoms C4 and N1 deviating by 0.392 (3) and 0.197 (2) Å, respectively, from the base of the boat. The nearly planar 2-thiophene ring, which is approxi-

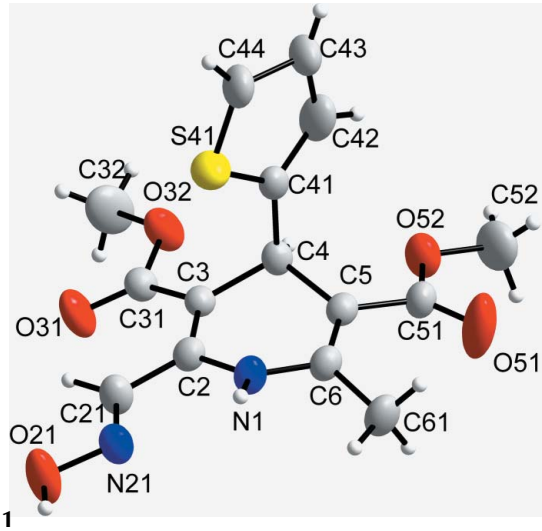


Figure 1
The molecular structure of (I) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level. The minor disorder component of the thiophene ring has been omitted. The thiophene ring shows orientational disorder and the site occupancy factors of atoms S41 and C42–C44 are 0.504 (2). The other orientation of the thiophene has been omitted for clarity.

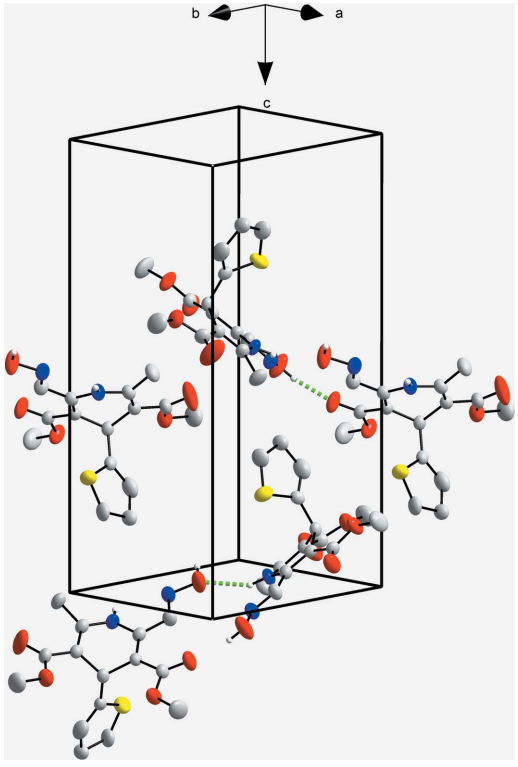


Figure 2
Part of the packing of (I), showing N1—H1···O21 hydrogen-bonded helices. Hydrogen bonds are shown as dashed lines, and C-bound H atoms have been omitted.

mately perpendicular to the 1,4-DHP ring [dihedral angle 89.7 (3)°], is disordered over two positions of essentially half occupancy [occupancy factors are 0.504 (2) and 0.496 (3)]. The ester groups at position 3 and 5, which both have synper-iplanar (*sp*) conformation, are slightly rotated out of the plane defined by C2, C3, C5 and C6 [torsion angles C2—C3—C31—O31 = 13.0 (2)° and C6—C5—C51—O51 = −0.8 (3)°]. Intermolecular N—H···O and O—H···O hydrogen bonds lead to the formation of infinite helices of molecules (Fig. 2 and Table 1).

Experimental

The title compound was prepared by a condensation reaction of 2-formyl-1,4-dihydropyridine with hydroxylamine. To a stirred solution of dimethyl 2-formyl-6-methyl-4-(2-thienyl)-1,4-dihydropyridine-3,5-dicarboxylate (321 mg, 1 mmol) in acetic acid (10 ml), hydroxylamine hydrochloride (73 mg, 1.05 mmol) and then potassium acetate (118 mg, 1.2 mmol) were added. The mixture was stirred at room temperature for 2 h and poured into ice-cold water (150 ml). After vigorous stirring for 15 min, the solid material was filtered off, washed thoroughly with water and ice-cold ethanol and crystallized from a mixture of ethanol–water (1:1); yield 295 mg (88%) of oxime, m.p. 481–483 K (yellow crystals).

Crystal data

$C_{15}H_{16}N_2O_5S$
M_r = 336.36
Orthorhombic, $P2_12_12_1$
a = 8.3272 (2) Å
b = 10.0252 (2) Å
c = 19.1730 (4) Å
V = 1600.60 (6) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.23 mm^{-1}
T = 295 K
0.4 × 0.3 × 0.3 mm

Data collection

Oxford Diffraction Gemini R CCD diffractometer
Absorption correction: analytical (Clark & Reid, 1995)
T_{min} = 0.929, T_{max} = 0.934
31461 measured reflections
3981 independent reflections
2676 reflections with $F^2 > 2\sigma(F^2)$
R_{int} = 0.026

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.034
$wR(F^2)$ = 0.085
S = 1.00
3981 reflections
248 parameters
10 restraints
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}
Absolute structure: Flack (1983), 1646 Friedel pairs
Flack parameter: 0.03 (8)

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O21^{i}	0.86	2.19	2.956 (2)	148
O21—H21···O31^{i}	0.82	1.92	2.732 (2)	168

Symmetry code: (i) $x-\frac{1}{2}, -y+\frac{3}{2}, -z+1$.

Compound (I) has a disordered 2-thiophene ring in which C42, C43, C44 and S41 have the alternative positions S42, C73, C74 and C72; the occupancy factors are 0.504 (2) and 0.496 (3), respectively. All atoms of the thiophene ring were subject to geometrical and displacement parameter restraints. All H atoms were positioned geometrically and treated as riding atoms (N—H = 0.86 Å; O—H = 0.82 Å; C—H = 0.93-0.98 Å), with U_{iso} set at 1.2U_{eq} (1.5U_{eq} for methyl and O—H) of the parent atom.

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2006); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2006); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SHELXS97*

(Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *DIAMOND* (Brandenburg, 2002); software used to prepare material for publication: *SHELXL97*.

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