Dimethyl 4-[4-(benzoyloxy)phenyl]-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate

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In the title compound, $C_{24}H_{23}NO_6$, the substituted 1,4-dihydropyridine (1,4-DHP) ring has a flat-boat conformation. The carbonyl groups of the ester groups, at positions 3 and 5 of the 1,4-DHP ring, have *cis,cis* conformations with respect to the double bonds in the 1,4-DHP ring. In the solid state, the molecules are linked by intermolecular N—H···O and weak intermolecular C—H···O interactions.

Comment

1,4-Dihydropyridine (1,4-DHP) systems are useful as calcium antagonists (Triggle *et al.*, 1989) and as antihypertensive agents (Fossheim *et al.*, 1982) and are emerging as one of the most important classes of drugs for the treatment of cardiovascular diseases (Baltork *et al.*, 2000). The present study is a part of the structural investigation of a series of 1,4-DHP derivatives to study the conformational changes due to different substituents at the 3, 4 and 5 positions.
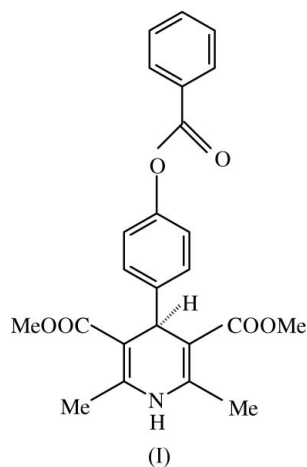

(I)

Fig. 1 shows the molecular structure of (I) with the atomic numbering scheme. The bond lengths and angles of the 1,4-DHP ring (Table 1) are comparable with those reported for similar structures (Hempel & Gupta, 1978; Mahendra *et al.*, 2005; Quesada *et al.*, 2006; Vrábel *et al.*, 2005). The substituted 1,4-DHP ring has a flat-boat conformation [puckering parameters (Cremer & Pople, 1975) $Q = 0.167$ (2) Å, $q_2 = 0.160$ (2) Å, $q_3 = 0.050$ (2) Å, $\theta = 72.8$ (7)° and $\varphi = 180.6$ (8)° for the atom sequence N1—C2—C3—C4—C5—C6], with atoms N1 and C4 deviating by 0.079 (3) and 0.204 (3) Å, respectively, from the base of the boat. The mean plane of the base of the 1,4-DHP ring, defined by atoms C2, C3, C5 and C6, makes angles of 13.7 (1) and 7.1 (3)° with the C3/C4/C5 and C2/N1/C6 planes, respectively. A similar observation has been reported for 4-(5-cyano-2-furyl)-2,6-dimethyl-l,4-dihydro-
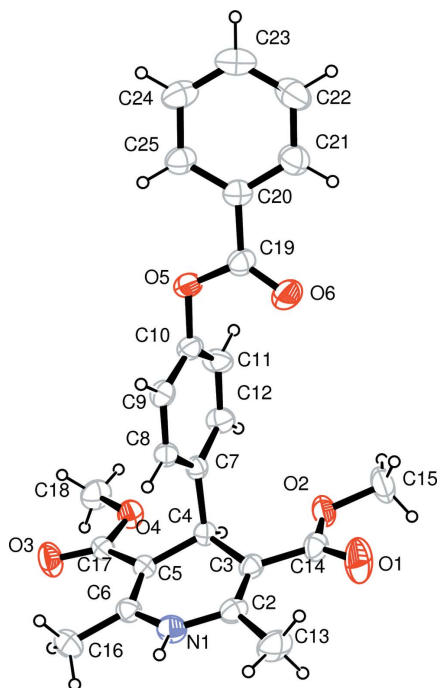
Figure 1
The molecular structure of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown by circles of arbitrary radii.
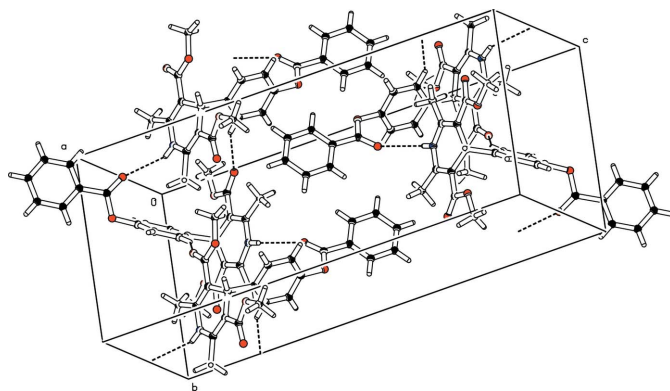
Figure 2
The crystal packing of (I). Dashed lines indicate hydrogen bonds.

pyridine-3,5-dicarbonitrile (Kozísek *et al.*, 1993). The base of the 1,4-DHP ring is almost perpendicular to the benzene ring substituted at C4, with a dihedral angle of 88.6 (1)°. The dihedral angle between this base and the benzene ring attached to the carbonyloxy group is 61.1 (1)° and that between the two benzene rings is 64.1 (1)°. Langs & Triggle (1985) have observed that the majority of 1,4-DHP analogues have one of the ester groups at positions 3 and 5 in the *cis* conformaton and the other in the *trans* conformation. A small number of very active antagonists are found to have *cis,cis* geometry. The present compound also has *cis,cis* geometry and is moderately active as a calcium channel blocker. Nimodipine, a very active antagonist, also possesses *cis,cis* geometry

(Wang *et al.*, 1989). The carbonyl groups of the carboxylate groups attached at the 3 and 5 positions are oriented in a synperiplanar (*cis*) conformation with respect to the adjacent C=C double bond of the 1,4-DHP ring (Table 1).

In the solid state, the molecules are linked by N—H···O and weak intermolecular C—H···O interactions (Table 2), which help to stabilize the crystal structure. Imine atom N1 acts as a donor to carbonyl atom O6 of a neighbouring molecule (Fig. 2).

Experimental

Benzoyl chloride (1 ml, 8.65 mmol) was added to a stirred and refluxing solution of dimethyl 4-(4-hydroxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1.0 g, 3.15 mmol) in ethyl methyl ketone (50 ml) in the presence of anhydrous potassium carbonate (1.0 g). The reaction mixture was further refluxed with continuous stirring for 6 h. The resultant slurry was filtered and the solvent was removed under reduced pressure to obtain a solid residue, which was crystallized from methanol to afford (I) (yield: 0.47 g, 35.6%; m.p. 466–468 K).

Crystal data

$C_{24}H_{23}NO_6$	$Z = 4$
$M_r = 421.43$	$D_x = 1.299$ Mg m^{-3}
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation
$a = 7.8943$ (6) Å	$\mu = 0.09$ mm^{-1}
$b = 10.6426$ (8) Å	$T = 273$ (2) K
$c = 25.7386$ (18) Å	Block, brown
$\beta = 94.642$ (1)°	$0.09 \times 0.08 \times 0.04$ mm
$V = 2155.4$ (3) Å^3	

Data collection

Bruker SMART CCD area-detector diffractometer	3799 independent reflections
	2786 reflections with $I > 2\sigma(I)$
ω scans	$R_{int} = 0.032$
Absorption correction: none	$\theta_{max} = 25.0°$
20310 measured reflections	

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0645P)^2$
$R[F^2 > 2\sigma(F^2)] = 0.050$	$\quad + 0.4502P]$
$wR(F^2) = 0.134$	$\quad$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.03$	$(\Delta/\sigma)_{max} < 0.001$
3799 reflections	$\Delta\rho_{max} = 0.20$ e Å^{-3}
288 parameters	$\Delta\rho_{min} = -0.13$ e Å^{-3}
H atoms treated by a mixture of independent and constrained refinement	

Table 1
Selected geometric parameters (Å, °).

C2—C3	1.344 (3)	C4—C5	1.519 (3)
C2—N1	1.378 (3)	C5—C6	1.347 (3)
C3—C4	1.522 (2)	C6—N1	1.375 (3)
C3—C2—N1	119.33 (19)	C6—C5—C4	121.59 (17)
C2—C3—C4	121.31 (18)	C5—C6—N1	119.05 (19)
C5—C4—C3	111.58 (15)	C6—N1—C2	124.50 (19)
C2—C3—C14—O1	−8.1 (4)	C6—C5—C17—O3	11.3 (3)

Table 2
Hydrogen-bond geometry (Å, °).

$D-\text{H}\cdots A$	$D-\text{H}$	$\text{H}\cdots A$	$D\cdots A$	$D-\text{H}\cdots A$
N1—H1⋯O6[i]	0.81 (2)	2.53 (2)	3.233 (3)	146 (2)
C8—H8⋯O1[i]	0.93	2.45	3.249 (3)	144
C16—H16C⋯O3	0.96	2.32	2.854 (3)	115
C13—H13C⋯O1	0.96	2.50	2.830 (4)	100

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

The methyl H atoms were constrained to an ideal geometry (C—H = 0.96 Å), with $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C})$, but were allowed to rotate freely about the C—C bonds. All remaining H atoms, except H1, were placed in geometrically idealized positions (C—H = 0.93–0.98 Å), with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$ and were constrained to ride on their parent atoms. Atom H1 attached to N1 was located in a difference map and refined isotropically [N—H = 0.81 (2) Å].

Data collection: *SMART* (Bruker, 2000); cell refinement: *SAINT* (Bruker, 2000); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1997) and *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97* and *PARST* (Nardelli, 1995).

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