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# Dimethyl 4-(4-isopropylcarbonyloxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate

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**Key indicators**

Single-crystal X-ray study
$T$ = 273 K
Mean $\sigma$(C–C) = 0.002 Å
Disorder in main residue
$R$ factor = 0.049
$wR$ factor = 0.141
Data-to-parameter ratio = 13.1

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



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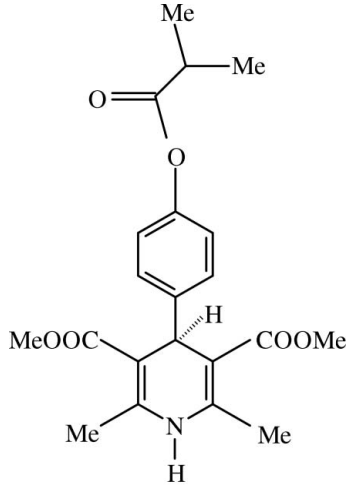
In the molecule of the title compound, $C_{21}H_{25}NO_6$, the substituted 1,4-dihydropyridine (1,4-DHP) ring has a flattened boat conformation. The carbonyl groups of the ester groups at positions 3 and 5 of the 1,4-DHP ring have *cis* configurations with respect to the double bonds in the 1,4-DHP ring. In the solid state, the molecules are linked by intermolecular N—H···O hydrogen bonds. Weak intramolecular C—H···O interactions stabilize the molecular structure.

## Comment

1,4-Dihydropyridine (1,4-DHP) systems exhibit calcium antagonistic activity and are prescribed as drugs in the treatment of a variety of cardiovascular diseases, such as angina and hypertension (Triggle *et al.*, 1989). 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 effected at the 3, 4 and 5 positions (Sundar *et al.*, 2006).




(I)

Fig. 1 shows the molecular structure of (I) with the atomic numbering scheme. Atom C20 is disordered over two sites with a site-occupation factor of 0.842 (7) for the major conformer (C20*A*). The bond lengths and angles of the 1,4-DHP ring (Table 1) are comparable to those reported for similar structures (Sundar *et al.*, 2006, and references therein). The substituted 1,4-DHP ring has a flattened boat conformation [puckering parameters (Cremer & Pople, 1975) $Q$ = 0.328 (2) Å, $q_2$ = 0.316 (2) Å, $q_3$ = 0.088 (2) Å, $\theta$ = 74.6 (3)° and $\varphi$ = 181.2 (3)° for the atom sequence N1—C2—C3—C4—C5—C6], with atoms N1 and C4 deviating by 0.169 (2) and

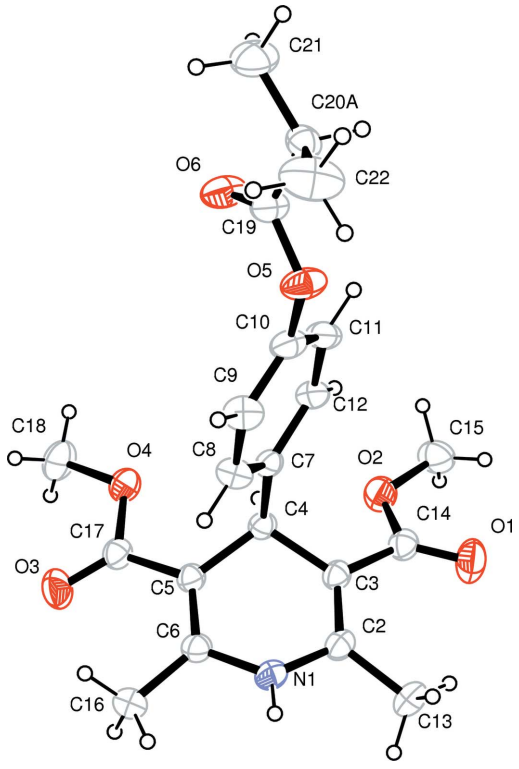



**Figure 1**
A view of the molecular structure of (I), with the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as circles of arbitrary radii.

0.387 (3) Å, respectively, from the base of the boat. The mean plane of the 1,4-DHP ring, defined by atoms C2, C3, C5 and C6, makes angles of 26.4 (2) and 15.4 (2)° with the C3/C4/C5 and C2/N1/C6 planes. A similar observation has been reported for dimethyl 4-[4-(benzoyloxy)phenyl]-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (Sundar *et al.*, 2006). The sum of the absolute values of the internal torsion angles of the 1,4-DHP ring is a measure of the planarity. In the literature, increased planarity (sum value close to zero) is correlated with higher activity of the compound (Rowan & Holt, 1996*a*). In (I), this value is 19.32 (9)°, indicating moderate activity. The mean plane of the 1,4-DHP ring, is almost perpendicular to the benzene ring, substituted at C4, with a dihedral angle of 85.3 (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* configuration and the other in the *trans* configuration. It is also suggested that *o*-phenyl-substituted derivatives of 1,4-DHPs have a preferance for *cis*,*cis* geometry, whereas the non-*o*-substituted derivatives prefer *cis*,*trans* geometry. (Rowan & Holt, 1996*b*). The title compound, (I), a *para*-substituted 1,4-DHP derivative has *-sp*,*-sp* geometry, contrary to the supposition. This is evident from the orientation of the the carbonyl groups of ester groups attached at the 3 and 5 positions. The observed torsion angles [C2—C3—C14—O1 = −22.0 (3)° and C6—C5—C17—O3 = −1.6 (3)°], indicate a *cis*, *cis* configuration.

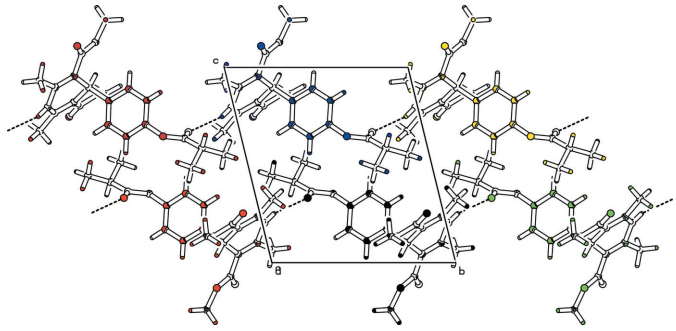


**Figure 2**
The packing of (I), viewed down the *a* axis. Dashed lines indicate hydrogen bonds.

In the solid state, the molecules are linked by intermolecular N—H···O hydrogen bonds and weak intramolecular C—H···O interactions (Table 2), which help to stabilize the crystal structure. The ring atom N1 acts as a donor to carbonyl atom O6 of a neighbouring molecule. The molecules are hydrogen bonded into an infinite one-dimensional chain, which runs parallel to the *b* axis, with a graph-set motif *C*(12) (Bernstein *et al.*, 1995) (Fig. 2).

## Experimental

Isobutyryl chloride (1 ml, 9.46 mmol) was added to a stirred and refluxing suspension 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 solvent was removed under reduced pressure to obtain a solid residue, which was crystallized from methanol to afford the title compound (yield: 0.69 g, 56.6%; m.p. 489–493 K).

*Crystal data*

$C_{21}H_{25}NO_6$
$M_r$ = 387.42
Triclinic, $P\overline{1}$
$a$ = 8.4488 (4) Å
$b$ = 10.5809 (5) Å
$c$ = 11.5520 (6) Å
$\alpha$ = 103.020 (1)°
$\beta$ = 95.971 (1)°
$\gamma$ = 95.506 (1)°
$V$ = 993.07 (8) Å$^3$
$Z$ = 2
$D_x$ = 1.296 Mg m$^{-3}$
Mo $K\alpha$ radiation
$\mu$ = 0.10 mm$^{-1}$
$T$ = 273 (2) K
Block, brown
0.10 × 0.07 × 0.04 mm

*Data collection*

Bruker SMART CCD area-detector diffractometer
$\omega$ scans
Absorption correction: none
9621 measured reflections
3487 independent reflections
3155 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.016
$\theta_{max}$ = 25.0°

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)]$ = 0.049
$wR(F^2)$ = 0.141
$S$ = 1.07
3487 reflections
267 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.073P)^2 + 0.3133P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.25 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.25 e Å$^{-3}$

**Table 1**
Selected geometric parameters (Å, °).

| | | | |
|---|---|---|---|
| N1—C6 | 1.377 (2) | C3—C4 | 1.528 (2) |
| N1—C2 | 1.379 (2) | C4—C5 | 1.514 (2) |
| C2—C3 | 1.347 (2) | C5—C6 | 1.352 (2) |
| | | | |
| C6—N1—C2 | 123.25 (14) | C5—C4—C3 | 110.06 (13) |
| C3—C2—N1 | 118.79 (15) | C6—C5—C4 | 119.53 (14) |
| C2—C3—C4 | 119.48 (15) | C5—C6—N1 | 118.76 (15) |

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

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| N1—H1···O6$^{i}$ | 0.86 | 2.22 | 3.030 (2) | 158 |
| C4—H4···O2 | 0.98 | 2.31 | 2.738 (2) | 105 |
| C4—H4···O4 | 0.98 | 2.35 | 2.7132 (19) | 101 |
| C13—H13*B*···O1 | 0.96 | 2.25 | 2.917 (3) | 126 |
| C15—H15*B*···O1 | 0.96 | 2.29 | 2.669 (3) | 103 |
| C16—H16*C*···O3 | 0.96 | 2.47 | 2.826 (3) | 102 |
| C22—H22*A*···O5 | 0.96 | 2.39 | 2.743 (3) | 101 |

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

Atom C20 is disordered over two sites with a site-occupation factor of 0.842 (7) for the major conformer (C20*A*). Two sets of positions were refined by applying a distance restraint of 1.55 (1) Å for the C—C bonds involving the disordered atoms. The H atoms of the methyl groups C21 and C22 were refined using a split model. The methyl H atoms of atoms C13 and C16 were constrained to an ideal geometry (C—H = 0.96 Å), with $U_{iso}(H) = 1.5U_{eq}(C)$, but were allowed to rotate freely about the C—C bonds. All other H atoms were placed in idealized positions (C—H = 0.93–0.98 Å and N—H = 0.86 Å) and were constrained to ride on their parent atoms, with $U_{iso}(H) = 1.2U_{eq}(C,N)$.

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2001); 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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