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# 3-Benzotriazol-1-yl 5-methyl 2,6-dimethyl-4-(*p*-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate

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**Key indicators**

Single-crystal X-ray study
*T* = 293 K
Mean σ(C–C) = 0.004 Å
Disorder in main residue
*R* factor = 0.058
*wR* factor = 0.147
Data-to-parameter ratio = 11.5

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



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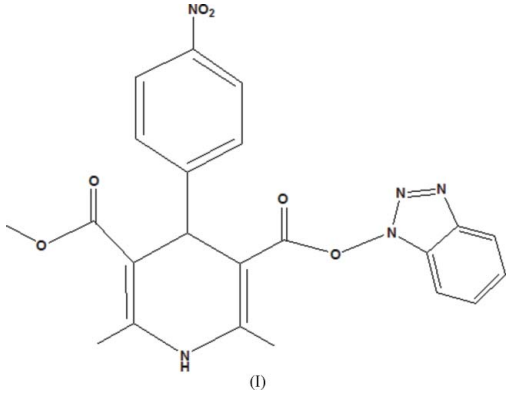
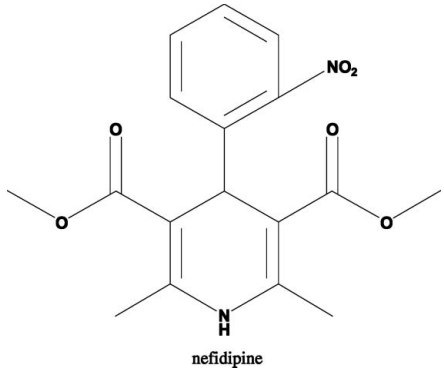
The title compound, $C_{22}H_{19}N_5O_6$, is an important intermediate in the synthesis of analogs of the dihydropyridine calcium channel blocker nefidipine. The crystal packing is stabilized by intermolecular N—H···N and C—H···O hydrogen bonds.

## Comment

4-Aryl-1,4-dihydropyridine-3,5-dicarboxylic diesters of the nefidipine type have become almost indispensable for the treatment of cardiovascular diseases since they first appeared on the market in 1975 (Yiu & Knaus, 1999; Goldmann & Stoltefuss, 1991).




(I)




nefidipine

The title compound, (I), is a key intermediate for preparing nefidipine analogs. In (I) (Fig. 1), the dihydropyridine ring has a flattened boat conformation, which compares well with the structure of a nefidipine analog reported earlier and with nefidipine itself (Sun *et al.*, 2006; Hofmann & Cimiraglia, 1990). The crystal packing is stabilized by intermolecular N—H···N and C—H···O hydrogen bonds (Table 1), which link the molecules into chains running parallel to the *a* axis.

## Experimental

The title compound was prepared by dissolving 2,6-dimethyl-4-(*p*-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylic acid monomethyl ester (332 mg, 1 mmol) and benzotriazol-1-ol (135 mg, 1 mmol) in $CH_2Cl_2$ (25 ml). Dicyclohexylcarbodiimide (206 mg, 1 mmol) in $CH_2Cl_2$ (10 ml) was added dropwise to this solution at 278 K. The reaction mixture was stirred at 276–279 K for a further 5 h. The solvent, $CH_2Cl_2$, was removed by vacuum evaporation at 293 K. The desired compound, obtained in almost quantitative yield, was purified by chromatography on a silica gel column (eluted by ethyl acetate and petroleum, 1:6) at room temperature. Suitable crystals were obtained by slow evaporation of a solution in ethyl acetate.

*Crystal data*

$C_{22}H_{19}N_5O_6$
$M_r$ = 449.42
Triclinic, $P\overline{1}$
$a$ = 10.318 (2) Å
$b$ = 10.751 (2) Å
$c$ = 11.491 (2) Å
$\alpha$ = 64.37 (3)°
$\beta$ = 76.09 (3)°
$\gamma$ = 68.77 (3)°
$V$ = 1065.9 (4) Å$^3$
$Z$ = 2
$D_x$ = 1.400 Mg m$^{-3}$
Mo $K\alpha$ radiation
$\mu$ = 0.11 mm$^{-1}$
$T$ = 293 (2) K
Block, yellow
0.10 × 0.08 × 0.06 mm

*Data collection*

Bruker SMART CCD area detector diffractometer
$\omega$ scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
$T_{min}$ = 0.990, $T_{max}$ = 0.994
6615 measured reflections
3740 independent reflections
2226 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.051
$\theta_{max}$ = 25.0°

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)]$ = 0.058
$wR(F^2)$ = 0.147
$S$ = 0.99
3740 reflections
324 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0742P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.28 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.22 e Å$^{-3}$
Extinction correction: *SHELXL97*
Extinction coefficient: 0.041 (5)

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

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| N1—H1···N5$^{i}$ | 0.86 (3) | 2.35 (3) | 3.156 (3) | 155 (2) |
| C15—H15···O2$^{ii}$ | 0.93 | 2.45 | 3.184 (4) | 136 |
| C18—H18···O3′$^{iii}$ | 0.93 | 2.42 | 3.333 (8) | 167 |
| C21—H21···O4′$^{iv}$ | 0.93 | 2.60 | 3.230 (9) | 126 |

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

The H atom bonded to N1 was located in a difference map and its positional parameters were refined freely [$U_{iso}$(H) = 1.2$U_{eq}$(N)]. All other H atoms were positioned geometrically and refined using a riding model, with C—H = 0.93–0.98 Å and $U_{iso}$(H) = 1.2$U_{eq}$(C) or 1.5$U_{eq}$(C). The nitro group is disordered; each O atom was refined on two alternative sites with equal occupancy, and restraints were applied for geometrical similarity, planarity and approximately isotropic displacement parameters.

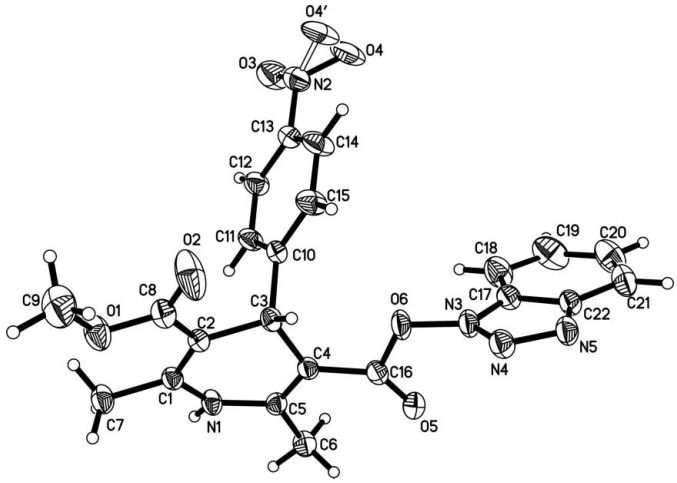



**Figure 1**
The molecular structure of (I). Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii. The nitro group is disordered with each O atom refined on two alternative sites with equal occupancy.

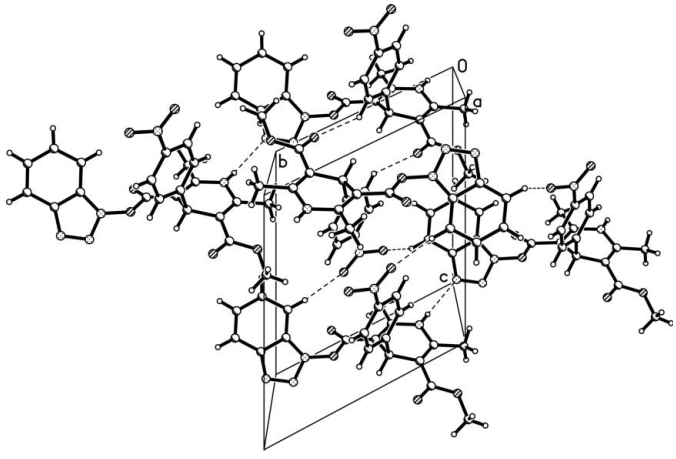



**Figure 2**
A packing diagram of (I). Dashed lines indicate hydrogen bonds.

Data collection: *CrystalClear* (Rigaku, 2005); cell refinement: *CrystalClear*; data reduction: *CrystalClear*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 1997); software used to prepare material for publication: *SHELXTL*.

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