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

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Key indicators

Single-crystal X-ray study
T = 294 K
Mean σ(C–C) = 0.004 Å
Disorder in main residue
R factor = 0.052
wR factor = 0.146
Data-to-parameter ratio = 13.4

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

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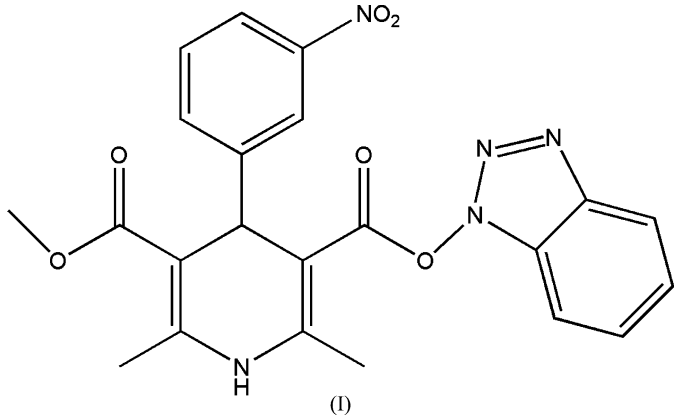
The title compound, $C_{22}H_{19}N_5O_6$, is an important intermediate in the synthesis of nefidipine-type pharmaceuticals. The dihydropyridine ring has a flattened boat conformation. Molecules are linked by N—H···N hydrogen bonds.

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). The title compound is a key intermediate for their preparation. Fig.1 shows its molecular structure. The dihydropyridine ring has a flattened boat conformation. This compares well with the structure of 3-benzotriazol-1-yl-5-*tert*-butyl-2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate and nefidipine (Liu *et al.*, 2006; Hofmann & Cimiraglia, 1990; Ramusino & Varì, 1999). The nitro group is found to be disordered.



(I)

Intermolecular hydrogen bonds link the molecules in a chain (Table 1 and Fig. 2); the acceptor is a triazole N atom.

Experimental

2,6-Dimethyl-4-(*m*-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylic acid monomethyl ester (332 mg, 1 mmol) was dissolved in 25 ml CH_2Cl_2, and a solution of dicyclohexylcarbodiimide (206 mg, 1 mmol) and benzotriazol-1-ol (135 mg, 1 mmol) in 10 ml CH_2Cl_2 was added dropwise at 278 K. The reaction mixture was stirred at 276–279 K for 8 h. The solvent was removed by vacuum evaporation at 293 K. The product was purified by chromatography on a silica gel column (eluted with ethyl acetate and petroleum ether, 1:5) at room temperature (yield 450 mg). Crystals were obtained by slow evaporation of the solution.

Crystal data

$C_{22}H_{19}N_5O_6$
M_r = 449.42
Monoclinic, $P2_1/c$
a = 8.113 (3) Å
b = 17.934 (5) Å
c = 14.723 (4) Å
β = 98.008 (6)°
V = 2121.2 (11) Å^3
Z = 4
D_x = 1.407 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 2365 reflections
θ = 2.5–22.6°
μ = 0.11 mm^{-1}
T = 294 (2) K
Block, colourless
0.26 × 0.22 × 0.20 mm

Data collection

Bruker SMART CCD area detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.973, T_{max} = 0.979
11847 measured reflections
4343 independent reflections
2397 reflections with $I > 2\sigma(I)$
R_{int} = 0.046
θ_{max} = 26.5°
$h = -9 \rightarrow 10$
$k = -20 \rightarrow 22$
$l = -14 \rightarrow 18$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.052
$wR(F^2)$ = 0.146
S = 1.00
4343 reflections
324 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.063P)^2 + 0.4855P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.46 e Å^{-3}
$\Delta\rho_{min}$ = −0.33 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N4—H4A···N1^{i}	0.83 (2)	2.28 (3)	3.079 (3)	163 (2)

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

The H atom bonded to N4 was located in a difference map and refined freely. All other H atoms were positioned geometrically and refined using a riding model, with C—H = 0.97 Å and U_{iso}(H) = 1.2U_{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.

Data collection: *SMART* (Bruker, 1997); cell refinement: *SAINT* (Bruker, 1997); data reduction: *SAINT*; 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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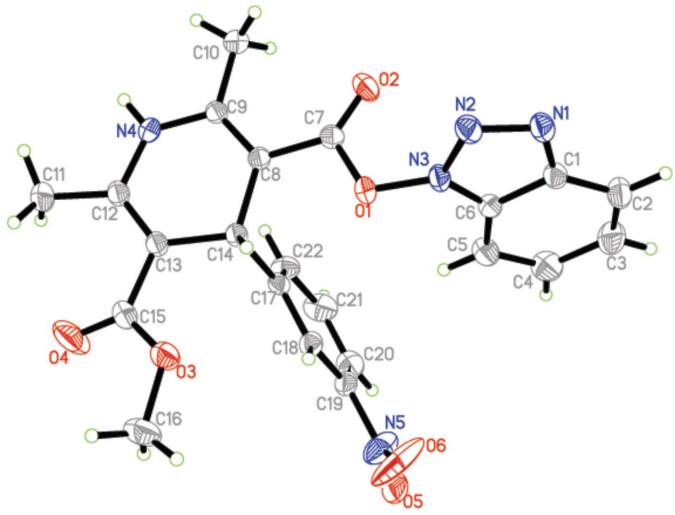

Figure 1
Molecular structure of the title compound. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

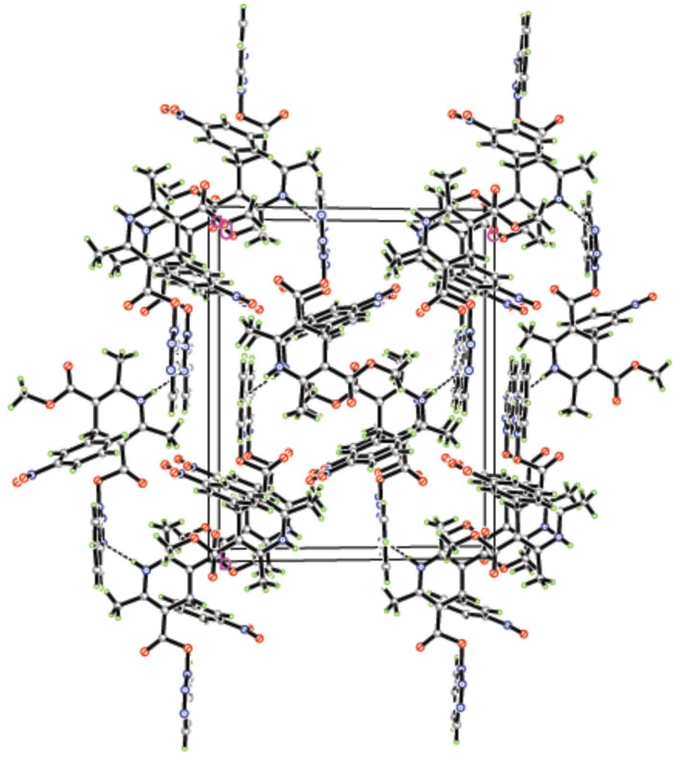

Figure 2
A packing diagram of (I). Dashed lines indicate hydrogen bonds.

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