Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

Phthaloyl amlodipine

Hemmige S. Yathirajan,[a] Basavegowda Nagaraj[a] and Michael Bolte[b]*

[a]Department of Studies in Chemistry, University of Mysore, Manasagangotri, Mysore 570 006, India, and [b]Institut für Anorganische Chemie, J. W. Goethe-Universität Frankfurt, Marie-Curie-Straße 11, 60439 Frankfurt/Main, Germany

Correspondence e-mail: bolte@chemie.uni-frankfurt.de

Key indicators

Single-crystal X-ray study
T = 173 K
Mean σ(C–C) = 0.002 Å
R factor = 0.034
wR factor = 0.087
Data-to-parameter ratio = 13.9

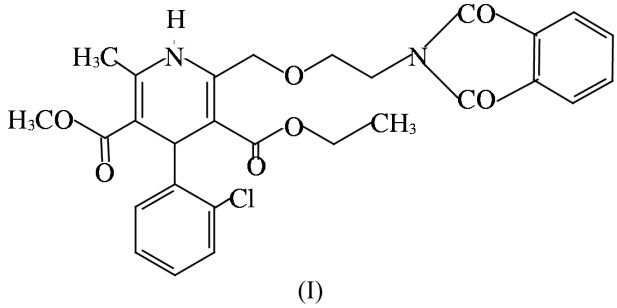
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 14 December 2004
Accepted 16 December 2004
Online 24 December 2004

The title compound [alternatively called 3-ethyl 5-methyl 4-(2-chlorophenyl)-2-(2-phthalmidoethoxymethyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate or ethyl methyl (4*RS*)-4-(2-chlorophenyl)-2-({[2-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)ethyl]oxy}methyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate], $C_{28}H_{27}ClN_2O_7$, is a calcium channel blocker and belongs to the family of anti-anginal and antihypertensive reagents. The dihydropyridine ring adopts an envelope conformation. The molecular conformation is stabilized by an intramolecular N—H···O hydrogen bond.

Comment

The title compound, (I), is a derivative of amlodipine, the latter being anti-anginal and antihypertensive. Amlodipine itself is a calcium channel blocker used for heart medication in the treatment of hypertension (Murdoch & Heel, 1991). In view of the importance of (I), the crystal structure is reported. The dihydropyridine ring exists in an envelope conformation with atoms N1, C2, C3, C5 and C6 in a common plane (r.m.s. deviation = 0.043 Å), whereas atom C4 deviates by 0.372 (2) Å from this plane. The non-H atoms of the ethoxycarbonyl and methoxycarbonyl groups are also almost in the plane of the dihydropyridine ring. The molecular conformation is stabilized by an intramolecular N—H···O hydrogen bond.



(I)

The crystal structures of other derivatives of amlodipine have been published by Goldmann *et al.* (1992) and Mereiter & Rollinger (2002).

Experimental

The title compound was obtained as a gift sample from CIPLA Company, Mumbai, India, and was used without further purification. Recrystallization from acetonitrile yielded yellow block-shaped crystals.

Crystal data

$C_{28}H_{27}ClN_2O_7$
M_r = 538.97
Triclinic, $P\overline{1}$
a = 8.0458 (9) Å
b = 10.5193 (11) Å
c = 15.7386 (17) Å
α = 98.073 (9)°
β = 90.542 (9)°
γ = 103.744 (8)°
V = 1279.8 (2) Å^3
Z = 2
D_x = 1.399 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 19123 reflections
θ = 3.6–25.7°
μ = 0.20 mm^{-1}
T = 173 (2) K
Block, light yellow
0.32 × 0.28 × 0.17 mm

Data collection

Stoe IPDS-II two-circle diffractometer
ω scans
Absorption correction: multi-scan (*MULABS*; Spek, 2003; Blessing, 1995)
T_{min} = 0.919, T_{max} = 0.967
23348 measured reflections
4849 independent reflections
3663 reflections with $I > 2\sigma(I)$
R_{int} = 0.052
θ_{max} = 25.8°
$h = -9 \rightarrow 9$
$k = -12 \rightarrow 12$
$l = -19 \rightarrow 19$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.034
$wR(F^2)$ = 0.088
S = 0.95
4849 reflections
349 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0563P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.27 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O99	0.87 (2)	2.22 (2)	3.0207 (17)	152.1 (17)

H atoms were located in a difference map. Those bonded to carbon were positioned geometrically and refined with fixed individual displacement parameters [U_{iso}(H) = 1.2U_{eq}(C) or 1.5 U_{eq}(C_{methyl})] using a riding model, with C—H = 1.00, 0.99, 0.98 and 0.95 Å for tertiary CH, secondary CH, methyl CH and aromatic CH groups, respectively. In addition, the methyl groups bonded to the heterocycle and to oxygen were allowed to rotate but not to tip. The H atom bonded to nitrogen was refined isotropically.

Data collection: *X-AREA* (Stoe & Cie, 2001); cell refinement: *X-AREA*; data reduction: *X-AREA*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *XP* in *SHELXTL-Plus* (Sheldrick, 1991); software used to prepare material for publication: *SHELXL*97 and *PLATON* (Spek, 2003).

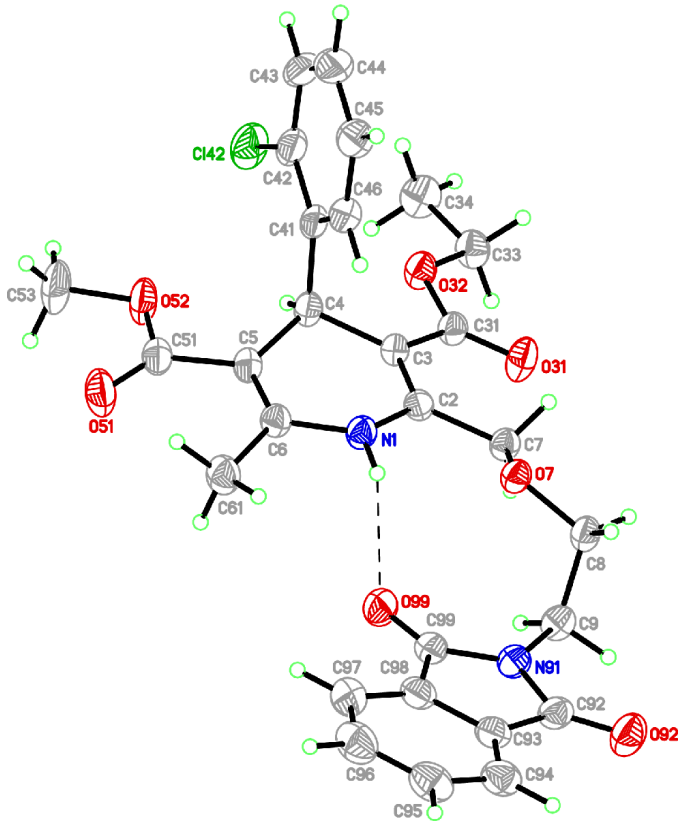


Figure 1
Perspective view of the title compound, with the atom numbering; displacement ellipsoids are drawn at the 50% probability level. The intramolecular hydrogen bond is shown as a dashed line.

One of the authors (HSY) thanks the CIPLA Company, Mumbai, for a gift sample of phthaloyl amlodipine.

References

Blessing, R. H. (1995). *Acta Cryst.* A**51**, 33–38.
Goldmann, S., Stoltefuss, J. & Born, L. (1992). *J. Med. Chem.* **35**, 3341–3344.
Mereiter, K. & Rollinger, J. (2002). Private communication to the Cambridge Structural Database, refcode XOZRUZ. Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, England.
Murdoch, D. & Heel, R. C. (1991). *Drugs*, **41**, 478–505.
Sheldrick, G. M. (1990). *Acta Cryst.* A**46**, 467–473.
Sheldrick, G. M. (1991). *SHELXTL-Plus.* Release 4.1. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Stoe & Cie (2001). *X-AREA*. Stoe & Cie, Darmstadt, Germany.