N,N′-Bis(2-chlorophenyl)-4-(4-chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxamide

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In the title compound, $C_{27}H_{22}Cl_3N_3O_2$, the dihydropyridine ring has a boat conformation. The molecules are linked by N—H⋯O, N—H⋯Cl, C—H⋯N and C—H⋯O hydrogen bonds.

Comment

1,4-Dihydropyridines are known for their pronounced drug activity, such as calcium channel antagonists (Janis & Triggle, 1983) and antihypertensive agents (Fossheim et al., 1982). Recently, symmetrical 1,4-dihydropyridines (1,4-DHP) having 3,5-dicarbamoyl substituents (Desai et al., 2001) opened up a fresh approach to the synthesis of new molecules having better pharmacokinetic properties (Triggle, 2003). Our group has synthesized and studied antitubercular activity by applying two- and three-dimensional quantitative structure–activity relationships (QSAR) to a series of 3,5-dicarbamoyl functionalities in 1,4-dihydropyridine (Desai et al., 2001; Kharkar et al., 2002). It was assumed that the presence of a group such as Cl or CH_3 at position 2 of the substituted phenylcarbamoyl group decreased the solvent-accessible surface area around the amide bond and hence decreased the antitubercular activity. However, when an electron-withdrawing group is present at position 2 of the phenylcarbamoyl group it results in higher activity (Kharkar et al., 2002). Against this background, the title compound, (I) (Fig. 1), was synthesized and its crystal structure is reported here.

(I)
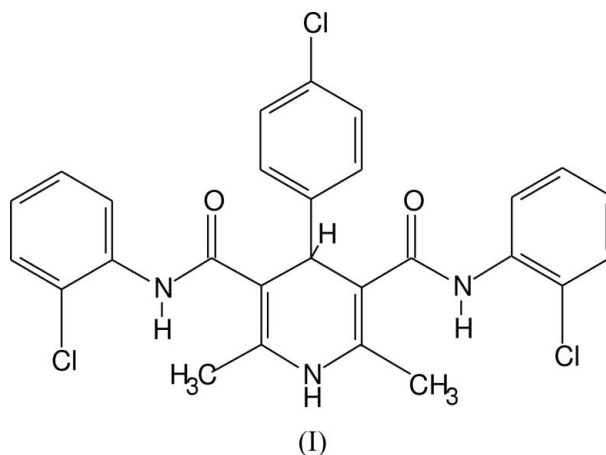
Most of the bond lengths and angles have normal values and are comparable with those reported for similar structures (Sagar et al., 1999; Mahendra et al., 2004). The 1,4-DHP ring has a boat conformation, with atoms N1 and C4 displaced by 0.126 (3) and 0.271 (3) Å, respectively, from the mean plane
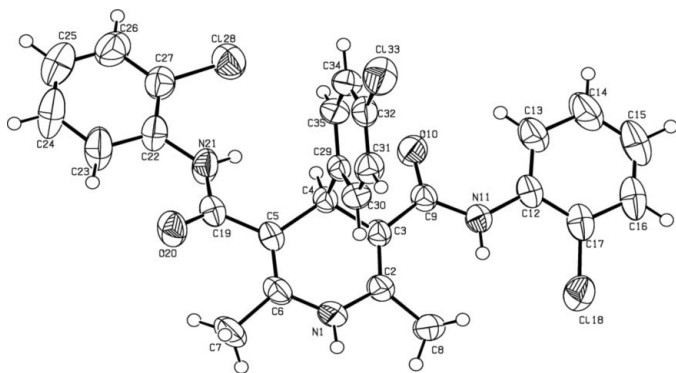
Figure 1
View of (I), shown with 50% probability displacement ellipsoids.

Figure 2
The crystal packing in (I), viewed down the *b* axis. Dashed lines indicate hydrogen bonds.

through the other four C atoms. The other structural characteristics are the conformations of the 2-chlorophenyl-carbamoyl groups on the dihydropyridine ring. Each carbonyl group of 2-chlorophenylcarbamoyl can be oriented in a synperiplanar (*cis*) or antiperiplanar (*trans*) conformation with respect to the adjacent C=C double bond of the dihdropyridine ring. The observed torsion angles are C2—C3—C9—O10 [168.5 (3)°] and C6—C5—C19—O20 [28.8 (5)°], indicating *trans* and *cis* conformations, respectively.

The structure exhibits both intra- and intermolecular hydrogen bonds (Table 2 and Fig. 2), which help to stabilize the crystal structure. The intermolecular hydrogen bonds N1—H1···O20^i and C34—H34···O10^{ii} (symmetry codes as in Table 2) link the molecules into infinite one-dimensional chains (Fig. 2).

Experimental

A mixture of 2-chloroacetoacetanilide (4.22 g, 0.02 mol) and 4-chlorobenzaldehyde (1.40 g, 0.01 mol) was heated continuously at reflux for 15 min, with stirring, using 30 ml methanol as solvent. Ammonia (4 ml) was added to the reaction mixture after 3 h. A light-yellow product separated in the flask; this was filtered off, washed twice with methanol and finally dried in a hot-air oven. Recrystallization from dimethylformamide gave a yield of 53–54% (m.p. 472 K). Analysis calculated: C 64.37, H 4.82, Cl13.57, N 8.04, O 9.19%. 3 g was taken up in 30 ml of methanol/dimethylformamide (8:2). Charcoal (3 g) was added and the solution heated for 5 min. It was then filtered while hot through a Whatman 42 filter paper. The solution was kept for 30 d in a conical flask with the stopper left slightly open, and pale-yellow crystals grew by evaporation.

Crystal data

$C_{27}H_{22}Cl_3N_3O_2$	$D_x = 1.440$ Mg m^{-3}
$M_r = 526.83$	Mo $K\alpha$ radiation
Monoclinic, $C2/c$	Cell parameters from 8244
$a = 20.566$ (2) Å	reflections
$b = 10.698$ (1) Å	$\theta = 2.2$–27.9°
$c = 22.789$ (2) Å	$\mu = 0.41$ mm^{-1}
$\beta = 104.300$ (2)°	$T = 295$ (2) K
$V = 4858.6$ (6) Å^3	Block, pale yellow
$Z = 8$	$0.25 \times 0.2 \times 0.2$ mm

Data collection

MacScience DIPLabo 32001	3458 reflections with $I > 2\sigma(I)$
diffractometer	$R_{int} = 0.017$
ω scans	$\theta_{max} = 27.9°$
Absorption correction: none	$h = -23 \rightarrow 24$
8244 measured reflections	$k = -10 \rightarrow 11$
4452 independent reflections	$l = -29 \rightarrow 29$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0987P)^2$
$R[F^2 > 2\sigma(F^2)] = 0.051$	$+ 5.2071P]$
$wR(F^2) = 0.181$	where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.06$	$(\Delta/\sigma)_{max} = 0.001$
4452 reflections	$\Delta\rho_{max} = 0.57$ e Å^{-3}
318 parameters	$\Delta\rho_{min} = -0.54$ e Å^{-3}
H-atom parameters constrained	

Table 1
Selected geometric parameters (Å, °).

Cl18—C17	1.740 (3)	N1—C6	1.376 (4)
Cl28—C27	1.735 (4)	N11—C9	1.357 (4)
Cl33—C32	1.739 (3)	N11—C12	1.404 (4)
O10—C9	1.213 (4)	N21—C19	1.353 (4)
O20—C19	1.227 (3)	N21—C22	1.410 (5)
N1—C2	1.382 (4)		
C2—N1—C6	124.0 (2)	Cl18—C17—C12	120.0 (3)
C9—N11—C12	129.0 (2)	Cl18—C17—C16	118.1 (3)
C19—N21—C22	128.8 (3)	O20—C19—N21	120.7 (3)
N1—C2—C3	119.1 (3)	O20—C19—C5	123.5 (3)
N1—C2—C8	112.0 (2)	N21—C19—C5	115.8 (2)
N1—C6—C5	119.5 (3)	N21—C22—C23	124.0 (3)
N1—C6—C7	112.9 (3)	N21—C22—C27	118.5 (3)
O10—C9—N11	120.8 (2)	Cl28—C27—C22	119.8 (3)
O10—C9—C3	120.2 (3)	Cl28—C27—C26	118.1 (3)
N11—C9—C3	119.1 (3)	Cl33—C32—C31	119.8 (2)
N11—C12—C17	118.3 (3)	Cl33—C32—C34	119.5 (2)
N11—C12—C13	124.2 (3)		

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

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
N1—H1$\cdots$O20^i	0.86	2.05	2.891 (3)	167
N11—H11$\cdots$Cl18	0.86	2.46	2.943 (3)	116
N21—H21$\cdots$Cl28	0.86	2.48	2.935 (3)	114
C4—H4$\cdots$N21	0.98	2.54	2.905 (4)	102
C7—H7$C\cdots$O20	0.96	2.36	2.838 (4)	110
C8—H8$B\cdots$O20^i	0.96	2.56	3.423 (4)	149
C13—H13$\cdots$O10	0.93	2.24	2.833 (5)	121
C23—H23$\cdots$O20	0.93	2.28	2.842 (5)	119
C34—H34$\cdots$O10^{ii}	0.93	2.49	3.227 (4)	136

Symmetry codes: (i) $-x+\frac{1}{2}, +y-\frac{1}{2}, -z-\frac{1}{2}$; (ii) $-x+\frac{1}{2}, -y+\frac{5}{2}, -z$.

H atoms were placed at idealized positions and allowed to ride on their parent atoms, with C—H distances in the range 0.93–0.98 Å and N—H = 0.86 Å; U_{iso}(H) values were set equal to xU_{eq}(carrier atom), where x = 1.5 for methyl H atoms and 1.2 for all other H atoms.

Data collection: *XPRESS* (MacScience, 2002); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *SCALEPACK* and *DENZO* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003) and *ORTEPII* (Johnson, 1976); software used to prepare material for publication: *SHELXL97*.

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