Crystal Structure of 3,5-diethylcarboxylate-2,6-dimethyl-4-(3-bromophenyl)-1,4-dihydropyridine

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The compound 3,5-diethylcarboxylate-2,6-dimethyl-4-(3-bromophenyl)-1,4-dihydropyridine crystallizes in the orthorhombic space group *Pbca* with cell parameters $a = 13.9570(14)\text{\AA}$, $b = 16.3850(9)\text{\AA}$, $c = 16.6910(16)\text{\AA}$ and $Z = 8$. The 1,4-dihydropyridine (1,4-DHP) ring has a flat boat conformation. The molecules are linked into chains by N-H...O bonds.

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The nucleus of 1,4-dihydropyridine is an important scaffold for calcium channel antagonism and other cardiovascular activities.¹ The structural requirement for such antihypertensive and antianginal properties has the envisaged importance of electron-withdrawing groups at a *meta* substituted phenyl ring attached to the C4 of 1,4-dihydropyridine rings. Most of the known DHP drugs have symmetric as well as unsymmetrical structures with respect to the C3 and C5 positions.² The *m*-NO₂ phenyl 1,4-DHPs were well-explored to obtain Nimodipine, Nitrendipine, Cilnidipine, Manidipine, Barnidipine and Efonidipine. The bromo substituent has not been well-explored in such DHP systems. Thus, in continuation of our earlier work^{3,4} on an XRD study of 1,4-dihydropyridine systems, a DHP having *m*-bromophenyl at C4 of symmetrical 1,4-dihydropyridine was synthesized by Hantzsch synthesis,⁵ and a single crystal of the title compound was obtained. A schematic diagram of the molecule is shown in Fig. 1.

A single crystal (C₁₉H₂₂O₄NBr) having dimensions of 0.2 × 0.3 × 0.25 mm was chosen for X-ray diffraction studies. The measurements were performed on a DIPLabo image plate diffractometer system with graphite-monochromated radiation (Mo K α). The crystal and experimental data are given in Table 1. Lorentz and polarisation corrections were applied. The structure was solved by direct methods and refined by full-matrix least-squares methods. Soft restraints (SIMU and SADI/SAME) were applied to the ethoxy group to handle the

disorder structure. There are two conformations in the ethoxy group; the atoms represented are O11A, C12A and C13A and O11B, C12B and C13B, respectively. The bond lengths and angles as well as the *U*-values of the two conformations are consistent. The final positional coordinates with equivalent isotropic temperature factors of all non-hydrogen atoms are given in Table 2. Table 3 gives the selected bond distances and angles of non-hydrogen atoms. Most of the bond lengths and angles agree with the standard values. Figure 2 represents the ORTEP⁶ diagram of the molecule with thermal ellipsoids at 50% probability.

The 3-bromophenyl substituent is in the pseudo axial *syn*-periplanar orientation with respect to the 1,4-DHP ring plane. The 1,4-DHP ring has a flat boat conformation, with N1 and C4 at a distance of 0.143(3) $\text{\AA}$ and 0.345(3) $\text{\AA}$, respectively, from the mean plane through the four carbon atoms (C2, C3, C5 & C6), which define the base of the boat. The deviations of the latter four carbon atoms are -0.006(3) $\text{\AA}$, 0.006(3) $\text{\AA}$, -0.006(3) $\text{\AA}$ and

Fig. 1 Schematic diagram of the molecule.

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Table 1 Crystal and experimental data.

Formula: C ₁₉ H ₂₂ O ₄ NBr
Formula weight = 408.29
Crystal system: orthorhombic
Space group: <i>Pbca</i> $Z = 8$
$a = 13.9570(14)\text{\AA}$
$b = 16.3850(9)\text{\AA}$
$c = 16.6910(16)\text{\AA}$
$V = 3817.0(6)\text{\AA}^3$
$D_x = 1.421\text{ Mg/cm}^3$
$2\theta_{\text{max}} = 50.04^\circ$ with Mo K α
No. of reflections used = 2131 [$I > 2\sigma(I)$]
$R = 0.0560$
$(\Delta\sigma)_{\text{max}} = 0.000$
$(\Delta\rho)_{\text{max}} = 0.540\text{ e}\text{\AA}^{-3}$
$(\Delta\rho)_{\text{min}} = -0.582\text{ e}\text{\AA}^{-3}$
Measurement: DIPLabo (IP)
Program system: Denzo
Structure determination: SHELXS-97 (Sheldrick, 1990)
Refinement: SHELXL-97 (Sheldrick, 1997)
H atoms: geometrically fixed

Table 2 Atomic coordinates and equivalent thermal parameters

Atom	x	y	z	U_{eq}
Br24	0.28405(4)	0.21771(3)	0.33267(3)	0.0865(3)
N1	0.7179(3)	0.4836(2)	0.2052(2)	0.0642(10)
C2	0.6690(3)	0.5168(2)	0.2690(2)	0.0573(10)
C3	0.5731(3)	0.5043(2)	0.2727(2)	0.0569(10)
C4	0.5245(3)	0.4447(2)	0.2165(2)	0.0507(9)
C5	0.5794(3)	0.4379(2)	0.1381(2)	0.0558(10)
C6	0.6741(3)	0.4529(2)	0.1364(3)	0.0574(10)
C7	0.7421(4)	0.4404(3)	0.0682(3)	0.0801(13)
C8	0.7315(4)	0.5615(4)	0.3258(3)	0.0800(14)
C9	0.5081(4)	0.5431(3)	0.3298(3)	0.0719(13)
O10	0.4222(2)	0.5333(2)	0.3290(2)	0.0840(10)
O11A*	0.5525(7)	0.5723(6)	0.3977(5)	0.090(3)
C12A*	0.4940(11)	0.6126(7)	0.4574(7)	0.104(3)
C13A*	0.4670(12)	0.6915(8)	0.4289(9)	0.120(3)
O11B*	0.5467(7)	0.6073(5)	0.3707(5)	0.091(3)
C12B*	0.4810(10)	0.6543(7)	0.4184(7)	0.111(3)
C13B*	0.4918(10)	0.6351(8)	0.5011(6)	0.124(3)
C14	0.5268(3)	0.4100(3)	0.0672(3)	0.0652(11)
O15	0.5572(3)	0.4031(2)	-0.00042(19)	0.0916(11)
O16	0.4356(2)	0.39210(18)	0.08598(17)	0.0706(8)
C17	0.3748(4)	0.3617(3)	0.0220(3)	0.0814(14)
C18	0.2832(4)	0.3352(5)	0.0609(4)	0.125(3)
C19	0.5096(3)	0.3623(2)	0.2566(2)	0.0512(9)
C20	0.5884(3)	0.3151(3)	0.2783(3)	0.0649(11)
C21	0.5768(3)	0.2406(3)	0.3149(3)	0.0736(13)
C22	0.4878(4)	0.2101(3)	0.3306(3)	0.0675(12)
C23	0.4090(3)	0.2568(3)	0.3096(2)	0.0572(10)
C25	0.4192(3)	0.3318(2)	0.2723(2)	0.0540(9)

$$U_{eq} = (1/3)\sum_i \sum_j U_{ij}(a_i^* a_j^*)(a_i a_j)$$

*Occupancy factors for A is 0.472(8) and B is 0.528(8).

Fig. 2 ORTEP of the molecule at 50% probability.

0.006(4)Å, respectively. The degree of ring distortions at N1 and C4 is directly reflected in the magnitude of the torsion angles emanating from these two atoms. The torsion-angle value of C2-C3-C4-C5 ($-27.3(6)^\circ$) or C3-C4-C5-C6 ($26.2(6)^\circ$) is higher in the DHP ring, which indicates that puckering is greater at C4 than at N1.

The structure has intra and intermolecular hydrogen bonds of the type C-H...O and N-H...O, which help to stabilize the crystal structure. The molecules are linked into infinite one-

Table 3 Bond Lengths (Å) and Bond Angles ($^\circ$).

Atoms	Length	Atoms	Length
Br24-C23	1.897(4)	O11A-C12A	1.448(10)
N1-C2	1.377(5)	C12A-C13A	1.427(12)
N1-C6	1.394(6)	O11B-C12B	1.437(10)
C2-C3	1.356(5)	C12B-C13B	1.423(12)
C2-C8	1.481(6)	C14-O15	1.210(5)
C9-O10	1.210(5)	C22-C23	1.386(6)
C9-O11B	1.365(7)	C9-O11A	1.377(8)
Atoms	Angle	Atoms	Angle
C2-N1-C6	124.2(4)	O11A-C9-C3	114.1(5)
C3-C2-N1	117.7(4)	C9-O11A-C12A	118.1(9)
C3-C2-C8	128.8(4)	C13A-C12A-O11A	109.4(9)
N1-C2-C8	113.5(4)	C9-O11B-C12B	116.1(8)
C2-C3-C9	125.2(4)	C13B-C12B-O11B	110.6(9)
C2-C3-C4	120.8(4)	O15-C14-O16	122.0(4)
O10-C9-O11B	119.9(6)	C25-C23-C22	121.4(4)
O10-C9-O11A	120.1(6)	C25-C23-Br24	119.1(3)

Table 4 Hydrogen bond schemes (Å, $^\circ$).

D-H...A	D-H	H-A	D-A (Å)	D-H...A($^\circ$)
N1-H1...O10 ⁱ	0.77(4)	2.26(4)	3.020(5)	169(4)
C4-H4...O10	0.98	2.42	2.770(5)	101
C7-H7B...O15	0.96	2.16	2.889(7)	132
C8-H8B...O11B	0.96	2.41	2.789(11)	103
C12B-H12D...O10	0.97	2.17	2.614(12)	106

i. 1/2 + x, y, 1/2 - z

dimensional chains by an intermolecular hydrogen bond between the amine of one molecule and the carbonyl oxygen of the neighbouring molecule. The hydrogen-bond schemes are given in Table 4.

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