Appendix A

Descriptors

Descriptors for Torsion Angles and ring substituents

Table A.0.1: Descriptors for Torsion Angles

Torsion Angle Range, (Å)	Full Descriptor	Short Descriptor
0 to 30	+ Syn-Periplanar	+ sp
30 to 90	+ Syn-Clinal	+ sc
90 to 150	+ Anti-Clinal	+ ac
150 to 180	+ Anti-Periplanar	+ ap
0 to −30	− Syn-Periplanar	− sp
−30 to −90	− Syn-Clinal	− sc
−90 to −150	− Anti-Clinal	− ac
−150 to −180	− Anti-Periplanar	− ap

Table A.0.2: Descriptors for Ring Substituents

Angle Range of Substitution	Full Descriptor	Short Descriptor
0 to 30	Axial	ax
30 to 60	Bisectional	bi
60 to 90	Equatorial	eq

Colophon

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The details of software packages used are as follows:

Text editing	Vim `http://vim.sourceforge.net`
Type setting	LaTeX
Coverpage	*front*-Gdis `http://freshmeat.net/projects/gdis` back-XdisplayF Z. Otwinowski et al[†].
Schematic diagrams	Chemtool `http://freshmeat.net/projects/chemtool`
Molecular diagrams	PLATON A. L. Spek [‡]
Graph	Gnuplot `http://gnuplot.sourceforge.net`

[†]Z. Otwinowski and W. Minor, "Processing of X-ray Diffraction Data Collected in Oscillation Mode", Methods in Enzymology, Volume 276: Macromolecular Crystallography, part A, p.307-326, 1997,C.W. Carter, Jr. & R.M. Sweet, Eds., Academic Press.

[‡]A. L. Spek, J. Appl. Cryst., **36**, 7-13, 2003.

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Publications

Pertaining to the research work

1. Crystal and Molecular Structure of 3,5-Dicarbethoxy-2, 6-dimethyl-4-(4-methoxy)phenyl-1,4-dihydropyridine: Lakshmi Srinivasan, Sridhar M. Anandalwar, Javaregowda S. Prasad, Dinesh Manvar, Alpesh Parecha, Gautam Patel, Anamik Shah, *J. Anal. Sci.*, **21**, 93–94, 2005.

2. Synthesis and Molecular Structure Analysis of Venlafaxine Intermediate and its Analog, Kavitha C. V., Lakshmi Srinivasan, Basappa, Rangappa Kanchugarakoppal Subbegowda, Mantelingu K., Sridhar M. Anandalwar, Shashidhara Prasad J.: *Jour. of Chem. Cryst.*, (*accepted*), Manuscript No. JOCC207R1.

Communicated/to be communicated

1. Crystal and Molecular Structure of 2,6-dimethyl-3, 5-di-N- (2′-chlorophenyl) carbamoyl-4-(4″-hydroxy phenyl)-1,4-dihydropyridine: Lakshmi Srinivasan, Sridhar M. Anandalwar, J. Shashidhara Prasad, Dinesh Manvar, Rajesh Loriya, Gautam Patel, Anamik Shah. *(Communicated to J. Anal. Sci.)*, 2005.

2. Crystal structure of 2,6-dimethyl-3,5-di-N-phenylcarbamoyl-4(3′- nitro phenyl)-1,4-dihydropyridine:Lakshmi Srinivasan, Sridhar M. Anandalwar, J. Shashidhara Prasad, Chintan Dholakia, Dinesh Manvar, Vishal Narodia, Anamik Shah.

3. Crystal structure of 2-amino-4(3′-Chloro Phenyl)-3-ethoxycarbonyl-4H-pyrano-[3,2-c]-chromene-5-one:Lakshmi Srinivasan Sridhar M. Anandalwar, Shashidhara Prasad J., Dinesh Manvar, Alpesh Parecha, Gautam Patel, Jignesh Patel, Anamik Shah.

4. Crystal structure confirmation and comparison of pyrano-[3,2-c]-chromene derivatives: Lakshmi S., Sridhar M. A., Shashidhara Prasad J.,Dinesh Manvar, Alpesh Parecha, Jignesh Patel, Anamik Shah.

Others

1. Structural Analysis of 4, 4′-Methoxy Bis Hydrazone: S. Lakshmi, M.A. Sridhar, J. Shashidhara Prasad, J. Indira, Prakash P. Karat, B. Veerendra, B. Shivarama Holla. *Mol. Cryst. Liq. Cryst.*, **381**, pp 59–68, 2002.

2. Synthesis and Structural Analysis of Tetrathioureacopper(I) Chloride: Lakshmi S., Sridhar M.A., Shashidhara Prasad J., Srinivasan V., Kandhaswamy M. A., Dhandapani M., *J. Anal. Sci.*, **19**, 19–20, 2003.

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4. Growth, characterization and crystal structure analysis of 1-(4-chlorophenyl)-3-(4-chlorophenyl)-2-propen-1-one: Vincent Crasta, V. Ravindrachary, S. Lakshmi, S. N. Pramod, M. A. Shridar and J. Shashidhara Prasad, *Journal of Crystal Growth*, **275**, e329–e335, 2005.

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X-ray Structure Analysis Online

Crystal and Molecular Structure of 3,5-Dicarbethoxy-2,6-dimethyl-4-(4′-methoxy)phenyl-1,4-dihydropyridine

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1,4-Dihydropyridines (DHP)are known for their action as calcium channel blockers and are used for treatment of various cardiovascular diseases. The title compound was synthesised following the classical Hantzsch synthesis. The compound crystallises in monoclinic crystal class in the space group $P2_1/n$ with cell parameters $a = 9.744(3)$Å, $b = 7.460(2)$Å $c = 26.662(5)$Å, $\beta = 98.34(2)^\circ$, $Z = 2$. The structure adopts a flat boat conformation.

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1,4-Dihydropyridines are known for their action as calcium channel blockers and are used for treating various cardiovascular diseases. Most of the 1,4-dihydropyridine compounds possess different functional groups on the C4 phenyl ring.[1] 1,4-Dihydropyridine compounds are widely prescribed for the treatment of hypertension and heart deliberation. The activity is believed to arise from binding with a receptor site located in the α_1 subunit of the L-type voltage gated channels present in skeletal and cardiac muscle.[2] For DHP molecules, structure-activity relationship studies[3] have indicated specific conformational details which correlate with high binding efficiency.[4]

X-raycrystallographic studies of molecules of dihydropyridine have established the fact that a majority of 1,4-dihydropyridine rings have a boat type conformation with varying degrees of puckering at C4 position.[5] Modifications to the C4 part of 1,4-dihydropyridine moiety have been carried out. The title compound was prepared by Hantzsch (Dihydro) pyridine synthesis. A schematic diagram of the molecule is shown in Fig. 1.

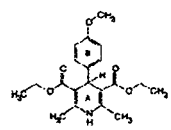

Fig. 1 Schematic diagram of the molecule.

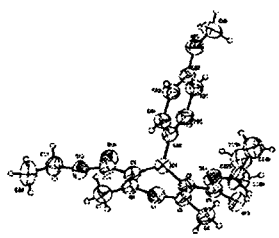

Fig. 2 ORTEP of the molecule at 30% probability.

A mixture of 4-methoxybenzaldehyde (1.2 g, 0.01 mol) and ethylacetoacetate (3.18 g, 0.025 mol) in methanol (40 ml) was stirred and refluxed for 5 to 10 min. Then ammonia solution (4 ml) was added to it. It was stirred for 15 to 16 more h. The resulting solid product was separated out and filtered. The yield was 58%. The purity of the compound was checked by TLC (acetone:benzene = 4:6). The compound was recrystallized

Table 1 Crystal data and structure refinement table

Empirical formula	$C_{25}H_{29}NO_5$
Formula weight	359.41
λ(Mo K_α)	0.71073 Å
Crystal system	monoclinic
Space group	$P2_1/n$ $Z = 4$
Cell dimensions	$a = 9.744(3)$Å
	$b = 7.460(2)$Å
	$c = 26.662(5)$Å
	$\beta = 98.34(2)^\circ$
Volume	1917.6(9)Å^3
D_c	1.245 Mg/m^3
θ_{max}	28.28°
R	0.0975
$(\Delta/\sigma)_{max}$	0.000
$(\Delta\rho)_{max}$	0.248 eÅ^{-3}
$(\Delta\rho)_{min}$	-0.265 eÅ^{-3}
Refinement method	full-matrix least-squares on F^2
Measurement	DIPLabo Kappa
Program system	Denzo
Structure determination	SHELXS-97[6]
Refinement	full-matrix: SHELXL-97[6]

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Table 2 Atomic coordinates and equivalent thermal parameters of the non-hydrogen atoms

Atom	x	y	z	U_{eq}
N1	0.1637(3)	-0.1455(4)	-0.0388(1)	0.0602(9)
C2	0.2471(4)	-0.1151(6)	-0.0736(2)	0.0460(9)
C3	0.3199(3)	0.0484(5)	-0.0829(1)	0.0354(9)
C4	0.2988(3)	0.1950(5)	-0.0589(1)	0.0295(8)
C5	0.3158(3)	0.1622(5)	-0.0301(2)	0.0466(9)
C6	0.2383(4)	-0.0688(5)	-0.0131(2)	0.0487(11)
C7	0.1563(4)	-0.0764(6)	0.0322(2)	0.0856(1)
C8	-0.0374(4)	-0.2844(6)	-0.0655(2)	0.1007(1)
C9	-0.1006(4)	0.0843(7)	-0.1285(2)	0.0892(1)
O10	-0.1907(3)	-0.0257(5)	-0.1466(1)	0.1186(1)
O11	-0.1218(3)	0.2096(5)	-0.1397(1)	0.1080(1)
C12A*	-0.267(2)	0.309(4)	-0.1835(8)	0.156(6)
C13A*	-0.228(2)	0.489(4)	-0.2017(7)	0.155(1)
C12B†	-0.2224(2)	0.211(3)	-0.1743(7)	0.134(6)
C13B†	-0.1770(2)	0.336(4)	-0.2280(6)	0.192(1)
C14	0.2754(4)	0.3211(5)	-0.0604(3)	0.0832(1)
O15	0.3715(3)	0.2917(4)	0.0050(1)	0.0980(8)
O16	0.2186(3)	0.4235(5)	-0.0310(12)	0.1055(9)
C17	0.4224(5)	0.4454(5)	0.0697(2)	0.1105(1)
C18	0.5114(6)	0.3703(9)	0.1110(3)	0.153(2)
C19	0.3180(3)	0.3088(5)	-0.1220(2)	0.0621(1)
C20	0.1815(4)	0.3204(6)	-0.1636(2)	0.0953(1)
C21	0.2540(4)	0.3171(5)	-0.2019(2)	0.0948(1)
C22	0.3874(3)	0.2972(6)	-0.2008(1)	0.0959(1)
C23	0.4606(4)	0.1101(6)	-0.1658(2)	0.0895(1)
C24	0.3319(3)	0.1036(5)	-0.1254(2)	0.0853(1)
O25	0.5175(3)	0.2229(5)	-0.2440(1)	0.1020(9)
C26	0.4058(6)	0.3200(9)	-0.2858(2)	0.1571(2)

$[U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij}(a_i^* a_j^*)(a_i . a_j)]$
*Occupancy factor is 0.35(3).
†Occupancy factor is 0.65(3).

Table 3 Selected Bond Lengths (Å) and Angles (°)

Atoms	Length	Atoms	Length
N1-C2	1.372(5)	O25-C26	1.422(5)
N1-C6	1.378(5)	C12A-C13A	1.34(4)
C4-C19	1.524(5)	C12B-C13B	1.56(3)
C5-C14	1.445(5)	C14-O16	1.217(5)
C6-O16	1.215(5)	C14-O15	1.338(5)
C8-O11	1.392(5)	O15-C17	1.452(5)
O11-C12A	1.305(5)	C17-C18	1.45(7)
	Angle		Angle
C2-N1-C6	119.4(3)	O10-C9-C8	126.8(4)
C3-C2-N1	122.5(4)	O11-C9-C8	112.8(4)
N1-C2-C8	113.2(4)	C12B-O11-C9	119.9(1)
C2-C3-C9	121.0(4)	C9-O11-C12A	114.4(4)
C2-C3-C4	118.9(3)	C13A-C12A-O11	106.1(2)
C9-C3-C4	119.9(4)	O11-C12B-C13B	113.1(9)
C5-C4-C19	112.6(3)	O16-C14-O15	120.4(4)
C5-C4-C3	110.8(3)	O16-C14-C5	123.3(4)
C19-C4-C3	110.0(3)	O15-C14-C5	115.7(4)
C6-C5-C4	125.1(4)	C14-O15-C17	117.7(3)
C8-C5-C4	119.8(3)	O15-C17-C18	106.9(4)
C14-C5-C4	115.4(3)	C24-C19-C4	121.8(3)
C5-C6-N1	118.7(4)	C20-C19-C4	121.2(3)
C5-C6-C7	126.6(4)	C23-C22-C21	120.6(4)
N1-C8-C7	112.7(4)	O25-C22-C23	115.7(3)
O10-C9-O11	121.1(4)	C22-O25-C26	117.1(3)

from dimethylformamide (DMF) and methanol, m. p. 116°C. [Required C (66.85%) H (6.96%) N (3.89%)] [Found C (66.82%) H (6.94%) N (3.85%)].

A 2.0 g amount of compound was taken in 15 ml of DMF. Charcoal (1.5 g) was added and the solution was heated for 2 min. The solution was filtered while hot through Whatmann 42 filter paper. The solution was kept in a slightly opened stopper conical flask for 25 days. Light yellow crystals were grown by thin film evaporation technique.

A single crystal of the title compound with dimensions 0.2 × 0.3 × 0.3 mm was chosen for X-ray diffraction studies. The data were collected on a DIPLabo Image Plate system with graphite monochromated radiation (Mo K_α). Thirty six frames of data were collected in oscillation mode with an oscillation range of 5° and processed using Denzo.[7] The reflections were merged with Scalepack.[8] Figure 2 shows the ORTEP of the molecule at 30% probability. The crystal and experimental details are given in Table 1.

Table 2 gives the atomic coordinates and equivalent thermal parameters of the non-hydrogen atoms. The hydrogen atoms were fixed at chemically acceptable positions and were refined with isotropic temperature factors. Tables 3 and 4 give the bond lengths and angles of non-hydrogen atoms. The carbon atoms C12 and C13 of the dicarbethoxy group at C5 exhibit positional disorder. However, atoms of dicarbethoxy group at C3 do not show any disorder.

The pyridine ring (N1, C2, C3, C4, C5, C6) conforms to a flattened boat configuration with the deviation of N1 and C4 being 0.144(3)Å and 0.200(3)Å respectively indicating higher binding efficiency.[4] The phenyl ring is planar. The torsion angle about C4-C5-C14-O15 is −168.7(3)° and that about C4-C3-C9-O11 is −11.2(5)°, showing that the dicarbethoxy group at C3 and C5 do not conform symmetrically about the pyridine ring. The torsion angles C6-C5-C14-O16 and C2-C3-C9-O10 are −170.31(4)° and −5.95(7)° respectively. These are comparable with the torsion angles reported for the methoxy-substituted diethyl 4-phenyl-2, 6-dimethyl-1, 4-dihydropyridine-3, 5-dicarboxylate compounds.[4]

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