Molecular Crystals and Liquid Crystals
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gmcl20

Synthesis and Molecular Crystal Structure of 4-(4,5-Dimethoxy-2-nitrophenyl)-2,6-dimethyl-3,5-dicarbmethoxy-1,4-dihydropyridine ($C_{19}H_{22}N_2O_8$)

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Published online: 02 Apr 2013.

To cite this article: Minaxi S. Maru & Manish K. Shah (2013): Synthesis and Molecular Crystal Structure of 4-(4,5-Dimethoxy-2-nitrophenyl)-2,6-dimethyl-3,5-dicarbmethoxy-1,4-dihydropyridine ($C_{19}H_{22}N_2O_8$), Molecular Crystals and Liquid Crystals, 574:1, 117-128

To link to this article: http://dx.doi.org/10.1080/15421406.2012.752308

Mol. Cryst. Liq. Cryst., Vol. 574: pp. 117–128, 2013

ISSN: 1542-1406 print/1563-5287 online
DOI: 10.1080/15421406.2012.752308

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Synthesis and Molecular Crystal Structure of 4-(4,5-Dimethoxy-2-nitrophenyl)-2,6-dimethyl-3,5-dicarbmethoxy-1,4-dihydropyridine ($C_{19}H_{22}N_2O_8$)

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A novel three-component one-pot synthesis of 4-(4,5-dimethoxy-2-nitrophenyl)-2,6-dimethyl-3,5-dicarbmethoxy-1,4-dihydropyridine from methyl 3-oxobutanoate, ammonium carbonate, and 4,5-dimethoxy-2-nitrobenzaldehyde has been carried out by typical Hantzsch synthesis. The single crystal was obtained by crystallization from methanol in 0.30 × 0.20 × 0.20 mm dimensional of 4-(4,5-dimethoxy-2-nitrophenyl)-2,6-dimethyl-3,5-dicarbmethoxy-1,4-dihydropyridine ($C_{19}H_{22}N_2O_8$), which was investigated by X-ray diffraction. The compound crystallizes in the monoclinic $P2_1/c$ space group with unit cell dimensions $a = 14.4830(3)$ Å, $b = 8.66000(10)$ Å, $c = 15.1036(3)$ Å, $\alpha = 90^\circ$, $\beta = 90.0870(10)^\circ$, $\gamma = 90^\circ$. ^1H NMR (hydrogen-1 nuclear magnetic resonance), mass, and IR (infrared) spectroscopic methods of the compound are also described.

Keywords Crystal structure; Hantzsch synthesis; symmetric 1,4-DHP; X-ray diffraction study

Introduction

1,4-Dihydropyridines (DHPs) are one of the most interesting and extensively investigated molecules by chemists worldwide because of their large existence in biological and medicinal area [1–3]. 1,4-DHP drugs having substitution of *o*/*m*-nitrophenyl at C(9) position are generally used for the treatment of cardiovascular disorder as calcium channel antagonists (i.e., nifedipine, nimodipine, manidipine, nicardipine, etc.) together with cardiac arrhythmias, hypertension, angina, etc. [4]. Some new research exposes several other more medicinal applications of 1,4-DHPs, including as a cerebral anti-ischemic agent in the treatment of Alzheimer's disease [5a], platelet antiaggregratory activity [5b], and neuroprotectant [6] and as a chemosensitizer in tumor therapy [7].

The symmetric and asymmetric structures with respect to the C(10) and C(13) positions of 1,4-DHP drugs are well known [8]. The structure activity relationship studies reveal that substitutions present at the C(10), C(9), and C(13) atoms of the nifedipine vary the tissue selectivity and activity [9,10]. The selectivity and activity of 1,4-DHP derivatives is depending on the design of DHP-calcium channel modulators. Because of the selectivity and activity study, it is proved that 1,4-DHPs are the most potent molecules as calcium channel transformers and has impelled the studies for the investigation of geometrical and

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Table 1. Crystal data and structure refinement for $C_{19}H_{22}N_2O_8$

Identification code	Shelxl
Empirical formula	$C_{19}H_{22}N_2O_8$
Formula weight	406.39 gm · mole^{-1}
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	$a = 14.4830(3)$ Å $\alpha = 90^\circ$ $b = 8.66000(10)$ Å $\beta = 90.0870(10)^\circ$ $C = 15.1036(3)$ Å $\gamma = 90^\circ$
Volume	1894.33(6) A^3
Z	4
Calculated density	1.425 mg · m^{-3}
Absorption coefficient	0.112 mm^{-1}
$F(000)$	856
Crystal size	0.30 × 0.20 × 0.20 mm
Theta range for data collection	2.70° to 25.00°
Limiting indices	$-17 \le h \le 12$ $-10 \le k \le 9$ $-17 \le l \le 17$
Reflections collected/unique	16674/3335 [R(int) = 0.0290]
Completeness to theta = 25.00	100.0%
Absorption correction	Semiempirical from equivalents
Max. and min. transmission	0.9836 and 0.9325
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	3335/0/272
Goodness-of-fit on F^2	1.034
Final R indices [$I > 2$ sigma(I)]	$R_1 = 0.0374$, $wR_2 = 0.0973$
R indices (all data)	$R_1 = 0.0492$, $wR_2 = 0.1060$
Extinction coefficient	0.0090(9)
Largest diff. peak and hole	0.226 e · Å^{-3} and −0.166 e · Å^{-3}

functional requirements at the DHP binding site [11]. Namely, the activity of 1,4-DHP calcium channel antagonists is highly dependent on the nature, size, and position of the C(9) phenyl ring substitutions, which were key of voltage-dependent calcium channel antagonist activity [12,13]. The substitutions, such as ester, acyl, sulphonyl, or nitrile groups, present at C(10) and C(13) positions of 1,4-DHP ring have established to be a vital necessities for the pharmacological activity [14,15]. Earlier crystallographic studies of several 2,6-dimethyl-3,5-dicarbmethoxy-1,4-dihydropyridines show that substitution present on the phenyl ring confine the free rotation of the phenyl ring due to the repulsion effect of the carbmethoxy groups at the C(10) and C(13) positions and also could influence the possibility of puckering of the 1,4-DHP ring, which cause a more suitable conformation for drug receptor interaction [16,17].

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters (Å^2 $\times 10^3$) for $C_{19}H_{22}N_2O_8$

No.	Atom	*x*	*y*	*z*	*U*(eq)
1	C(1)	8116(1)	1729(2)	5236(1)	33(1)
2	C(2)	8978(1)	1939(2)	5634(1)	37(1)
3	C(3)	9432(1)	718(2)	6002(1)	37(1)
4	C(4)	9041(1)	−761(2)	5936(1)	36(1)
5	C(5)	8192(1)	−935(2)	5539(1)	34(1)
6	C(6)	7692(1)	298(2)	5184(1)	30(1)
7	C(7)	10641(1)	2296(2)	6541(1)	53(1)
8	C(8)	9264(2)	−3461(2)	6153(2)	56(1)
9	C(9)	6767(1)	−81(2)	4738(1)	30(1)
10	C(10)	6925(1)	−981(2)	3884(1)	33(1)
11	C(11)	6798(1)	−2524(2)	3848(1)	36(1)
12	C(12)	6046(1)	−2528(2)	5285(1)	37(1)
13	C(13)	6144(1)	−983(2)	5364(1)	32(1)
14	C(14)	5693(1)	−168(2)	6093(1)	35(1)
15	C(15)	5608(2)	2199(2)	6858(1)	55(1)
16	C(16)	7267(1)	−147(2)	3110(1)	39(1)
17	C(17)	7997(2)	2147(3)	2639(2)	65(1)
18	C(18)	5536(2)	−3589(2)	5894(1)	52(1)
19	C(19)	6971(1)	−3593(2)	3090(1)	49(1)
20	N(1)	7715(1)	3142(2)	4875(1)	40(1)
21	N(2)	6442(1)	−3269(2)	4575(1)	42(1)
22	O(1)	8248(1)	4149(2)	4614(1)	66(1)
23	O(2)	6879(1)	3302(1)	4838(1)	52(1)
24	O(3)	10253(1)	810(2)	6439(1)	53(1)
25	O(4)	9559(1)	−1914(2)	6281(1)	51(1)
26	O(5)	7360(1)	−641(2)	2369(1)	64(1)
27	O(6)	7512(1)	1308(2)	3314(1)	48(1)
28	O(7)	5122(1)	−682(2)	6593(1)	54(1)
29	O(8)	6003(1)	1284(2)	6163(1)	48(1)

U(eq) = 1/3 of the trace of the orthogonalized *Uij* tensor.

With a view of the wide pharmacological importance of 1,4-DHPs, a novel symmetric 4-(4,5-dimethoxy-2-nitrophenyl)-2,6-dimethyl-3,5-dicarbmethoxy-1,4-dihydropyridine ($C_{19}H_{22}N_2O_8$) compound has been synthesized by the Hantzsch synthetic method and characterized by single crystal X-ray diffraction crystallography, ^{1}H NMR (hydrogen-1 nuclear magnetic resonance), mass, and IR (infrared) spectroscopy.

Experimental

General Methods

All the chemicals and solvents were commercially available and used as purchased without further purification. Analytical thin layer chromatography (TLC) was performed on silica gel-G, using ethyl acetate:hexane (1:4) solvent system. Melting point was determined in open capillaries on a melting point apparatus purchased from Jain Scientific Glass

Table 3. Bond lengths [Å] and angles [°]

No.	Atoms	Lengths [Å]	No.	Atoms	Lengths [Å]
1	C(1)–C(6)	1.386(2)	27	C(11)–C(19)	1.493(2)
2	C(1)–C(2)	1.396(2)	28	C(12)–C(13)	1.351(2)
3	C(1)–N(1)	1.460(2)	29	C(12)–N(2)	1.375(2)
4	C(2)–C(3)	1.363(2)	30	C(12)–C(18)	1.496(3)
5	C(2)–H(2)	0.9300	31	C(13)–C(14)	1.463(2)
6	C(3)–O(3)	1.362(2)	32	C(14)–O(7)	1.206(2)
7	C(3)–C(4)	1.404(2)	33	C(14)–O(8)	1.339(2)
8	C(4)–O(4)	1.354(2)	34	C(15)–O(8)	1.434(2)
9	C(4)–C(5)	1.375(2)	35	C(15)–H(15A)	0.9600
10	C(5)–C(6)	1.396(2)	36	C(15)–H(15B)	0.9600
11	C(5)–H(5)	0.9300	37	C(15)–H(15C)	0.9600
12	C(6)–C(9)	1.534(2)	38	C(16)–O(5)	1.207(2)
13	C(7)–O(3)	1.412(2)	39	C(16)–O(6)	1.344(2)
14	C(7)–H(7A)	0.9600	40	C(17)–O(6)	1.436(2)
15	C(7)–H(7B)	0.9600	41	C(17)–H(17A)	0.9600
16	C(7)–H(7C)	0.9600	42	C(17)–H(17B)	0.9600
17	C(8)–O(4)	1.419(2)	43	C(17)–H(17C)	0.9600
18	C(8)–H(8A)	0.9600	44	C(18)–H(18A)	0.9600
19	C(8)–H(8B)	0.9600	45	C(18)–H(18B)	0.9600
20	C(8)–H(8C)	0.9600	46	C(18)–H(18C)	0.9600
21	C(9)–C(13)	1.523(2)	47	C(19)–H(19A)	0.9600
22	C(9)–C(10)	1.524(2)	48	C(19)–H(19B)	0.9600
23	C(9)–H(9)	0.927(17)	49	C(19)–H(19C)	0.9600
24	C(10)–C(11)	1.350(2)	50	N(1)–O(2)	1.2193(19)
25	C(10)–C(16)	1.461(2)	51	N(1)–O(1)	1.2298(19)
26	C(11)–N(2)	1.375(2)	52	N(2)–H(2A)	0.88(2)
No.	Atoms	Angle [°]	No.	Atoms	Angle [°]
1	C(6)–C(1)–C(2)	122.52(15)	45	N(2)–C(12)–C(18)	113.52(16)
2	C(6)–C(1)–N(1)	123.47(14)	46	C(12)–C(13)–C(14)	119.82(15)
3	C(2)–C(1)–N(1)	114.00(14)	47	C(12)–C(13)–C(9)	121.01(15)
4	C(3)–C(2)–C(1)	120.25(16)	48	C(14)–C(13)–C(9)	119.07(14)
5	C(3)–C(2)–H(2)	119.9	49	O(7)–C(14)–O(8)	121.81(16)
6	C(1)–C(2)–H(2)	119.9	50	O(7)–C(14)–C(13)	126.93(17)
7	O(3)–C(3)–C(2)	124.90(16)	51	O(8)–C(14)–C(13)	111.26(14)
8	O(3)–C(3)–C(4)	116.12(15)	52	O(8)–C(15)–H(15A)	109.5
9	C(2)–C(3)–C(4)	118.98(15)	53	O(8)–C(15)–H(15B)	109.5
10	O(4)–C(4)–C(5)	125.59(16)	54	H(15A)–C(15)–H(15B)	109.5
11	O(4)–C(4)–C(3)	114.94(15)	55	O(8)–C(15)–H(15C)	109.5
12	C(5)–C(4)–C(3)	119.46(15)	56	H(15A)-C(15)-H(15C)	109.5
13	C(4)–C(5)–C(6)	123.08(15)	57	H(15B)–C(15)–H(15C)	109.5
14	C(4)–C(5)–H(5)	118.5	58	O(5)–C(16)–O(6)	120.95(17)
15	C(6)–C(5)–H(5)	118.5	59	O(5)–C(16)–C(10)	127.29(18)
16	C(1)–C(6)–C(5)	115.62(14)	60	O(6)–C(16)–C(10)	111.73(15)
17	C(1)–C(6)–C(9)	127.11(14)	61	O(6)–C(17)–H(17A)	109.5
18	C(5)–C(6)–C(9)	117.19(14)	62	O(6)–C(17)–H(17B)	109.5
19	O(3)–C(7)–H(7A)	109.5	63	H(17A)–C(17)–H(17B)	109.5
20	O(3)–C(7)–H(7B)	109.5	64	O(6)–C(17)–H(17C)	109.5
21	H(7A)–C(7)–H(7B)	109.5	65	H(17A)–C(17)–H(17C)	109.5
22	O(3)–C(7)–H(7C)	109.5	66	H(17B)–C(17)–H(17C)	109.5

(Continued on next page)

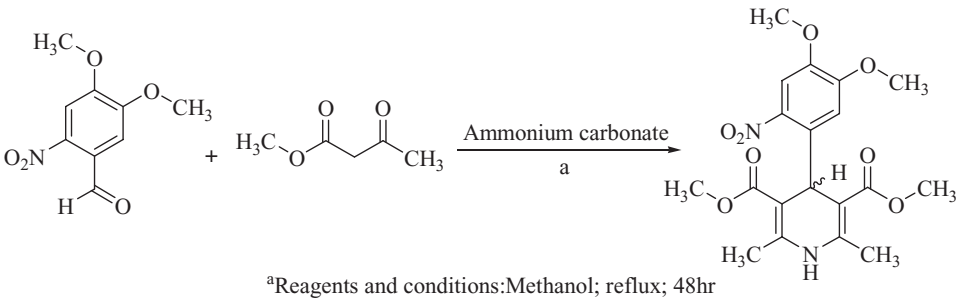
Table 3. Bond lengths [Å] and angles [°] *(Continued)*

No.	Atoms	Lengths [Å]	No.	Atoms	Lengths [Å]
23	H(7A)–C(7)–H(7C)	109.5	67	C(12)–C(18)–H(18A)	109.5
24	H(7B)–C(7)–H(7C)	109.5	68	C(12)–C(18)–H(18B)	109.5
25	O(4)–C(8)–H(8A)	109.5	69	H(18A)–C(18)–H(18B)	109.5
26	O(4)–C(8)–H(8B)	109.5	70	C(12)–C(18)–H(18C)	109.5
27	H(8A)–C(8)–H(8B)	109.5	71	H(18A)–C(18)–H(18C)	109.5
28	O(4)–C(8)–H(8C)	109.5	72	H(18B)–C(18)–H(18C)	109.5
29	H(8A)–C(8)–H(8C)	109.5	73	C(11)–C(19)–H(19A)	109.5
30	H(8B)–C(8)–H(8C)	109.5	74	C(11)–C(19)–H(19B)	109.5
31	C(13)–C(9)–C(10)	110.69(13)	75	H(19A)–C(19)–H(19B)	109.5
32	C(13)–C(9)–C(6)	110.79(13)	76	C(11)–C(19)–H(19C)	109.5
33	C(10)–C(9)–C(6)	110.36(13)	77	H(19A)–C(19)–H(19C)	109.5
34	C(13)–C(9)–H(9)	107.3(10)	78	H(19B)–C(19)–H(19C)	109.5
35	C(10)–C(9)–H(9)	109.6(10)	79	O(2)–N(1)–O(1)	121.88(15)
36	C(6)–C(9)–H(9)	108.0(10)	80	O(2)–N(1)–C(1)	120.46(14)
37	C(11)–C(10)–C(16)	120.21(16)	81	O(1)–N(1)–C(1)	117.65(15)
38	C(11)–C(10)–C(9)	121.30(15)	82	C(12)–N(2)–C(11)	124.12(15)
39	C(16)–C(10)–C(9)	118.41(15)	83	C(12)–N(2)–H(2A)	116.9(13)
40	C(10)–C(11)–N(2)	118.89(16)	84	C(11)–N(2)–H(2A)	118.9(13)
41	C(10)–C(11)–C(19)	128.45(17)	85	C(3)–O(3)–C(7)	116.94(14)
42	N(2)–C(11)–C(19)	112.64(16)	86	C(4)–O(4)–C(8)	118.51(14)
43	C(13)–C(12)–N(2)	119.18(16)	87	C(16)–O(6)–C(17)	116.18(15)
44	C(13)–C(12)–C(18)	127.30(17)	88	C(14)–O(8)–C(15)	116.26(15)

Works, Ambala Cantt, Haryana, India and is uncorrected. The IR spectra were recorded on Shimadzu FT-IR 8400 spectrophotometer, using KBr discs. The mass spectra were recorded on the Shimadzu GC-MS QP-2010 gas chromatograph. ^{1}H NMR spectra were recorded in dimethyl sulfoxide-d6 (DMSO-d6) on a Bruker AV 400 spectrophotometer. The chemical shifts are reported in parts per million (ppm) on the δ scale, using the Tetramethylsilane (TMS) peak as a reference value. The single crystal X-ray diffraction analyzed on Enraf Nonius CAD4-MV_{31} diffractometer.

Synthesis of 4-(4,5-Dimethoxy-2-nitrophenyl)-2,6-dimethyl-3,5-dicarbmethoxy-1,4-dihydropyridine

A mixture of methyl 3-oxobutanoate (0.025 mole) and 4,5-dimethoxy-2-nitrobenzaldehyde (0.01 mole) was dissolve in 30 mL of methanol and then ammonium carbonate (0.015 mole) was added to the mixture and allowed to refluxed on water bath for 48 hours. The progress of reaction was monitored by TLC. After completion of reaction, the resulting reaction mixture was poured into the crushed ice, filtered, and then dried over suction to get yellow colored compound by several washes of water (Scheme 1). Melting point 180°C–183°C, yield 95%. Elemental analysis: Calcd. for $C_{19}H_{22}N_2O_8$: C, 56.15; H, 5.46; N, 6.89; O, 31.50. Found: C, 56.10; H, 5.40; N, 6.83; O, 31.44. Mass: $m/z = 406$, IR (KBr, ν cm^{-1}): 3367 (N–H stretching), 3088 and 3010 (C–H stretching of aromatic), 2982 and 2926 (C–H asymmetric stretching of $-CH_3$), 2872 and 2845 (C–H symmetric stretching of $-CH_3$), 1735 and 1693 (C = O stretching of ester). ^{1}H NMR (δ ppm, DMSO-d_6 + 400 MHz): 2.25 (s, 6H, $-CH_3$), 3.45 (s, 6H, $-OCH_3$ of 1,4-DHP ring), 3.71 and 3.78 (2s, 6H, $-OCH_3$ of phenyl ring), 5.57 (s, 1H, –CH), 6.85 (s, 1H, Ar–H), 7.29 (s, 1H, Ar–H), and 8.95 (s, 1H, –NH).



[a]Reagents and conditions:Methanol; reflux; 48hr

Scheme 1. Reaction scheme for the synthesis of $C_{19}H_{22}N_2O_8$.

Method for Single Crystal Development

The dried pure product of 1 g of quantity was taken in a small beaker with sufficient amount of methanol and heated on hot plate to dissolve the solid product and then 1 g of charcoal was added to it and filtered the hot solution in 50-mL stopper flask through Whatman 42 filter paper. The collected filtrate was allowed to stand at room temperature for few weeks to obtained yellow colored crystals. Figure 1 shows a prospective view of a molecule with an atomic number scheme.

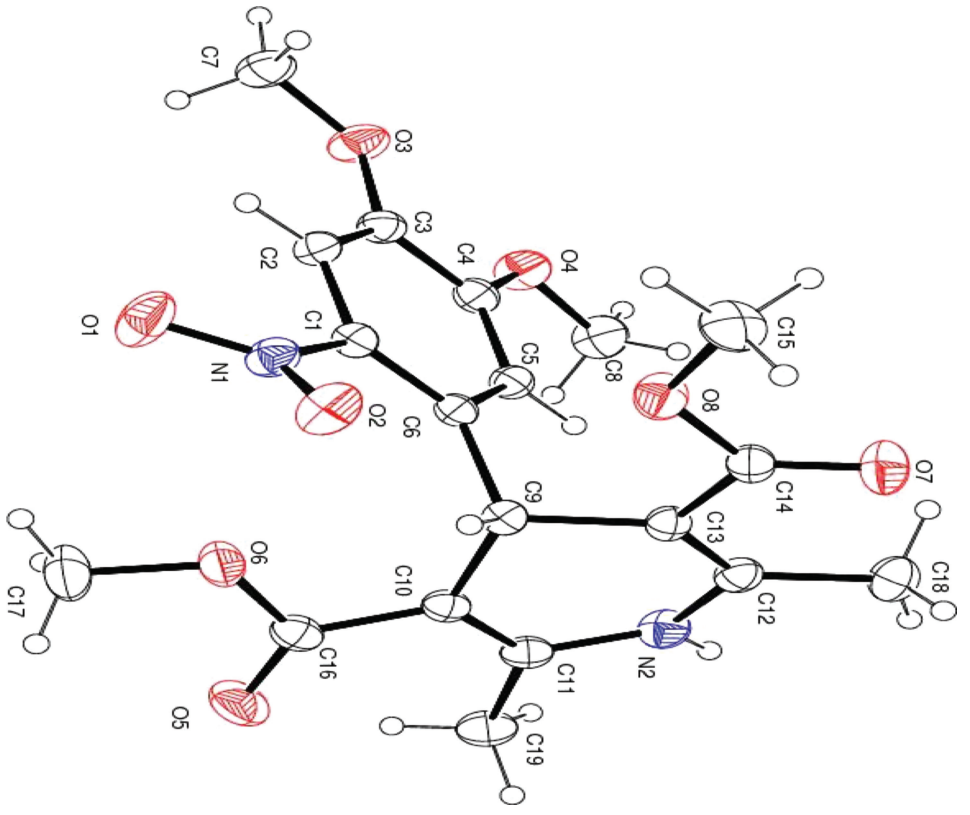


Figure 1. The molecular structure of the title compound showing the atom-labeling scheme (ORTEP).

Results and Discussion

The crystal data of the title compound was collected at 293(2) K. Intensity data were collected in the ω-2θ scan mode, using graphite monochromated Mo Kα radiation (0.71073 Å). The title compound crystallizes in the monoclinic $P2_1/c$ space group with unit cell dimensions $a = 14.4830(3)$ Å, $b = 8.66000(10)$ Å, $c = 15.1036(3)$ Å, $\alpha = 90^\circ$, $\beta = 90.0870(10)^\circ$, $\gamma = 90^\circ$. The crystal data solved by direct method and resolve by full-matrix least-squares on F^2 with program system SHELXS-97 [18] and SHELXL-97 [19], respectively. The crystal data and structure refinement parameters of the title compound are summarized in Table 1.

The atomic coordinates and equivalent isotropic displacement parameters for title compound ($C_{19}H_{22}N_2O_8$) are listed in Table 2. The list of bond lengths and bond angles

Table 4. Anisotropic displacement parameters (Å$^2 \times 10^3$) for $C_{19}H_{22}N_2O_8$

No.	Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
1	C(1)	35(1)	31(1)	32(1)	0(1)	0(1)	2(1)
2	C(2)	37(1)	35(1)	37(1)	−3(1)	−1(1)	−5(1)
3	C(3)	32(1)	45(1)	35(1)	−2(1)	−3(1)	0(1)
4	C(4)	37(1)	38(1)	33(1)	2(1)	−1(1)	5(1)
5	C(5)	37(1)	31(1)	34(1)	−1(1)	−1(1)	−1(1)
6	C(6)	32(1)	32(1)	26(1)	−2(1)	2(1)	2(1)
7	C(7)	40(1)	61(1)	59(1)	−4(1)	−13(1)	−9(1)
8	C(8)	62(1)	39(1)	66(1)	9(1)	−8(1)	6(1)
9	C(9)	31(1)	27(1)	34(1)	1(1)	−1(1)	3(1)
10	C(10)	29(1)	36(1)	32(1)	−2(1)	−3(1)	4(1)
11	C(11)	31(1)	38(1)	39(1)	−5(1)	−6(1)	5(1)
12	C(12)	33(1)	37(1)	40(1)	2(1)	−5(1)	−1(1)
13	C(13)	29(1)	34(1)	35(1)	2(1)	−1(1)	1(1)
14	C(14)	31(1)	39(1)	36(1)	5(1)	−2(1)	2(1)
15	C(15)	60(1)	52(1)	52(1)	−13(1)	12(1)	11(1)
16	C(16)	37(1)	45(1)	35(1)	−1(1)	−2(1)	7(1)
17	C(17)	78(2)	63(1)	54(1)	13(1)	23(1)	−9(1)
18	C(18)	60(1)	40(1)	58(1)	7(1)	3(1)	−11(1)
19	C(19)	53(1)	44(1)	51(1)	−15(1)	−6(1)	3(1)
20	N(1)	43(1)	31(1)	47(1)	1(1)	−6(1)	−2(1)
21	N(2)	50(1)	28(1)	48(1)	−2(1)	−2(1)	0(1)
22	O(1)	58(1)	45(1)	96(1)	27(1)	−15(1)	−14(1)
23	O(2)	41(1)	35(1)	80(1)	3(1)	−3(1)	7(1)
24	O(3)	42(1)	53(1)	65(1)	1(1)	−20(1)	−3(1)
25	O(4)	49(1)	43(1)	62(1)	9(1)	−16(1)	5(1)
26	O(5)	89(1)	68(1)	34(1)	−8(1)	8(1)	−2(1)
27	O(6)	63(1)	44(1)	39(1)	4(1)	11(1)	−6(1)
28	O(7)	52(1)	55(1)	56(1)	5(1)	21(1)	−2(1)
29	O(8)	54(1)	41(1)	49(1)	−10(1)	17(1)	−4(1)

The anisotropic displacement factor exponent takes the form: $-2\pi^2\,[h^2a^{*2}U11 + \cdots + 2\,hk\,a^*b^*U12]$.

between the atoms of title compound are given in Table 3. The atoms rather than hydrogen were defined by anisotropic displacement parameters as shown in Table 4, and the hydrogen atoms were refined riding on their bonded atoms with a global isotropic temperature factor (Table 5). The torsion angles between anisotropic atoms are given in Table 6, and the hydrogen bonding geometry summarized in Table 7. The bond angles and bond lengths are in good agreement with the previously reported symmetric 1,4-DHP crystal structures [20].

The N(1) atom show an sp^2 hybridization [21], which can be seen from the observed values of the bond angles of the title compound about at 120°, O(2)–N(1)–O(1) at 121.88(15)°, O(2)–N(1)–C(1) at 120.46(14)°, and O(1)–N(1)–C(1) at 117.65(15)°. The same trend is observed for the N(2) atom in the pyridyl ring C(12)–N(2)–C(11) at 124.12(15)° (Table 3). The C(11)–C(10)–C(16)–O(5) and C(9)–C(13)–C(14)–O(7) torsion angles are 9.6(3)° and 10.8(3)°, respectively, showing that both carbonyl groups are *sp/cis* (*synperiplanar*) to the respective endocyclic double bonds of the 1,4-DHP ring [22]. It was stated in past literature that the carbonyl groups, which are not involved in the hydrogen bonding, exist in *sp/cis* (*synperiplanar*) conformation, and if the carbonyl groups are involved in hydrogen bonding, it would be considered as an *ap/trans* (*antiperiplanar*) conformation [23,24]. The degree of distortions N(2) and C(9) is directly reflected in the magnitude of the torsion angles originating from these two atoms. The torsion angle value of C(10)–C(9)–C(13)–C(12) is higher, showing 21.3(2)° angle in DHP ring, which indicates the puckering is grater at C(9) than at N(2) (Table 6).

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters (Å$^2 \times 10^3$)

No.	Atom	*x*	*Y*	*z*	*U*(eq)
1	H(2)	9245	2917	5646	44
2	H(5)	7939	−1921	5505	41
3	H(7A)	11215	2217	6856	80
4	H(7B)	10222	2939	6867	80
5	H(7C)	10749	2741	5968	80
6	H(8A)	9694	−4152	6431	83
7	H(8B)	9234	−3681	5531	83
8	H(8C)	8664	−3597	6412	83
9	H(15A)	5877	3212	6850	82
10	H(15B)	5729	1718	7419	82
11	H(15C)	4953	2279	6770	82
12	H(17A)	8138	3165	2850	98
13	H(17B)	7617	2218	2119	98
14	H(17C)	8560	1616	2497	98
15	H(18A)	5578	−4628	5676	79
16	H(18B)	4899	−3285	5921	79
17	H(18C)	5803	−3534	6475	79
18	H(19A)	6398	−3811	2794	74
19	H(19B)	7234	−4538	3307	74
20	H(19C)	7391	−3118	2682	74
21	H(9)	6471(11)	840(20)	4611(10)	26(4)
22	H(2A)	6439(13)	−4280(30)	4585(13)	53(6)

Table 6. Torsion angles [°]

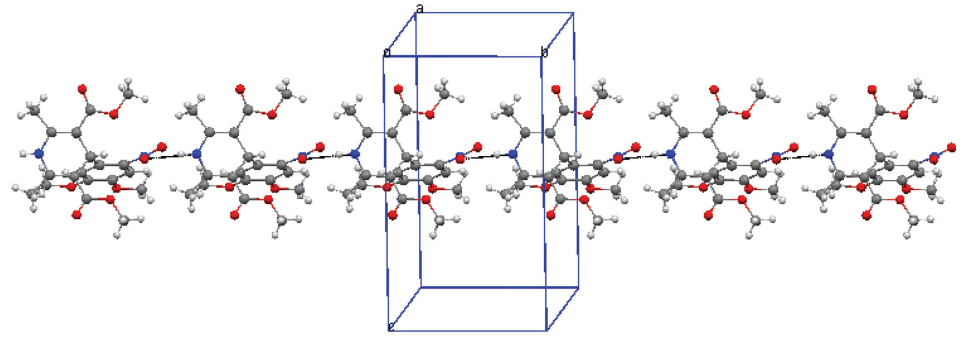
No.	Atom	Angle [°]	No.	Atom	Angle [°]
1	C(6)–C(1)–C(2)–C(3)	1.1(3)	31	N(2)–C(12)–C(13)–C(9)	6.5(2)
2	N(1)-C(1)–C(2)–C(3)	179.76(15)	32	C(18)–C(12)–C(13)–C(9)	173.80(17)
3	C(1)-C(2)–C(3)–O(3)	176.90(16)	33	C(10)–C(9)–C(13)–C(12)	21.3(2)
4	C(1)-C(2)–C(3)–C(4)	3.2(3)	34	C(6)–C(9)–C(13)–C(12)	101.47(17)
5	O(3)-C(3)–C(4)–O(4)	3.1(2)	35	C(10)–C(9)–C(13)–C(14)	162.49(14)
6	C(2)-C(3)–C(4)–O(4)	176.81(16)	36	C(6)–C(9)–C(13)–C(14)	74.75(18)
7	O(3)-C(3)–C(4)–C(5)	177.12(15)	37	C(12)–C(13)–C(14)–O(7)	10.8(3)
8	C(2)–C(3)–C(4)–C(5)	3.0(3)	38	C(9)–C(13)–C(14)–O(7)	172.94(17)
9	O(4)–C(4)–C(5)–C(6)	179.17(16)	39	C(12)–C(13)–C(14)–O(8)	168.37(15)
10	C(3)–C(4)–C(5)–C(6)	0.6(3)	40	C(9)–C(13)–C(14)–O(8)	7.9(2)
11	C(2)–C(1)–C(6)–C(5)	1.2(2)	41	C(11)–C(10)–C(16)–O(5)	9.6(3)
12	N(1)–C(1)–C(6)–C(5)	177.81(15)	42	C(9)–C(10)–C(16)–O(5)	173.58(18)
13	C(2)–C(1)–C(6)–C(9)	177.76(15)	43	C(11)–C(10)–C(16)–O(6)	168.51(15)
14	N(1)–C(1)–C(6)–C(9)	1.3(3)	44	C(9)–C(10)–C(16)–O(6)	8.3(2)
15	C(4)–C(5)–C(6)–C(1)	1.5(2)	45	C(6)–C(1)–N(1)–O(2)	30.4(2)
16	C(4)–C(5)–C(6)–C(9)	178.34(15)	46	C(2)–C(1)–N(1)–O(2)	150.47(16)
17	C(1)–C(6)–C(9)–C(13)	129.22(17)	47	C(6)–C(1)–N(1)–O(1)	149.76(17)
18	C(5)–C(6)–C(9)–C(13)	54.30(19)	48	C(2)–C(1)–N(1)–O(1)	29.4(2)
19	C(1)–C(6)–C(9)–C(10)	107.83(18)	49	C(13)–C(12)–N(2)–C(11)	12.0(3)
20	C(5)–C(6)–C(9)–C(10)	68.66(18)	50	C(18)–C(12)–N(2)–C(11)	167.69(16)
21	C(13)–C(9)–C(10)–C(11)	20.9(2)	51	C(10)–C(11)–N(2)–C(12)	12.4(3)
22	C(6)–C(9)–C(10)–C(11)	102.09(17)	52	C(19)–C(11)–N(2)–C(12)	165.95(16)
23	C(13)–C(9)–C(10)–C(16)	162.25(14)	53	C(2)–C(3)–O(3)–C(7)	2.4(3)
24	C(6)–C(9)–C(10)–C(16)	74.73(18)	54	C(4)–C(3)–O(3)–C(7)	177.77(16)
25	C(16)–C(10)–C(11)–N(2)	177.51(15)	55	C(5)–C(4)–O(4)–C(8)	6.8(3)
26	C(9)–C(10)–C(11)–N(2)	5.7(2)	56	C(3)–C(4)–O(4)–C(8)	173.05(17)
27	C(16)–C(10)–C(11)–C(19)	0.6(3)	57	O(5)–C(16)–O(6)–C(17)	8.1(3)
28	C(9)–C(10)–C(11)–C(19)	176.19(16)	58	C(10)–C(16)–O(6)–C(17)	170.08(16)
29	N(2)–C(12)–C(13)–C(14)	177.28(15)	59	O(7)–C(14)–O(8)–C(15)	0.8(2)
30	C(18)–C(12)–C(13)–C(14)	2.4(3)	60	C(13)–C(14)–O(8)–C(15)	179.96(15)

The torsion angles observed for the title compound specify that the atoms C(9) and N(2) are displaced from the ring in the same direction, conflicting to that of the substituted phenyl ring orientated in a pseudoaxial confirmation, this pseudoaxial phenyl ring C(6), C(1), C(2), C(3), C(4), C(5) being perpendicular to dihydropyridine ring (Figs 2(a) and (b)). The distance between C(9) and N(2) atoms and the perpendicular orientation of phenyl ring on C(9) atom allows more quantification about a flattened boat-type conformation of the dihydropyridine ring. The perpendicular orientation of the phenyl ring with respect to

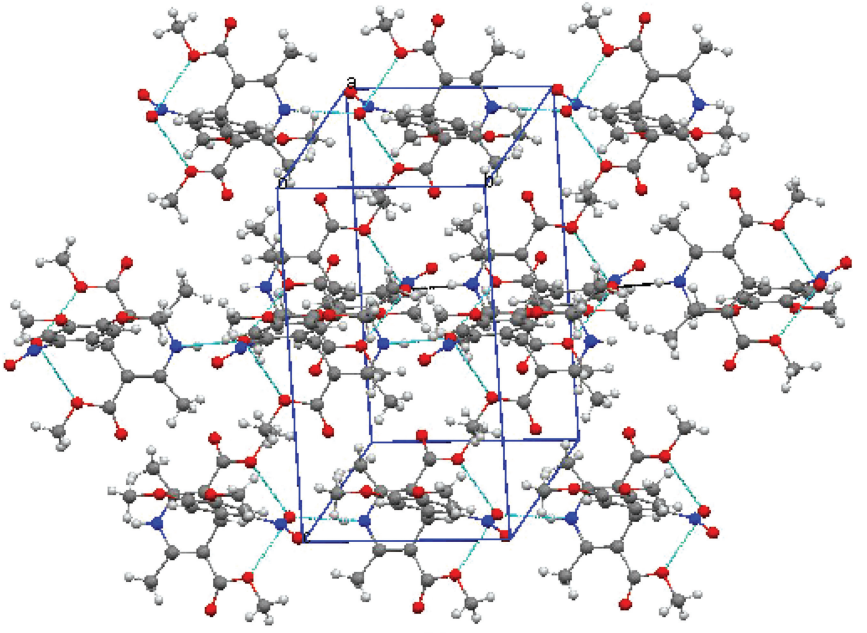
Table 7. Hydrogen bonds [Å] and [°]

D–H ... A	*d*(D–H)	*d*(H ... A)	*d*(D ... A)	<(DHA)
N(2)–H(2A) ... O(2)[a]	0.88(2)	2.22(2)	3.062(2)	160.8(18)

[a] = symmetry transformations used to generate equivalent atoms: $x, y-1, z$.



(a)



(b)

Figure 2. (a) The unit cell content of $C_{19}H_{22}N_2O_8$ showing hydrogen bonding interactions. (b) The unit cell content of $C_{19}H_{22}N_2O_8$ showing hydrogen bonding interactions.

the dihydropyridine ring and the flattened boat-type conformation of 1,4-DHP is the highly active position as well as conformation for the antagonist activity [25,26].

The carbonyl group substituted at C(10) and C(13) (*sp*) is not involved in hydrogen bonding; consequently, the structure exhibits only one intermolecular hydrogen bond involving the O(2) atom of C(1) substituted nitro group to the H(2A) atom substituted at N(2) atom of 1,4-DHP ring (Figs 2(a) and (b)). The presence of hydrogen bonding in the crystal structure shows the major role of calcium antagonist effect [27–29]. The intermolecular hydrogen bond observed in the crystal structure of title compound is the type of N(2)–H(2A) ... O(2) having (x, $y - 1$, z) symmetry code with 2.22(2) Å length and 160.8(18)° angle (Table 7).

Supplementary data

Crystallographic data for the structure reported in this paper have been deposited in the Cambridge Crystallographic Data Centre as supplementary publications no. CCDC-896984 for 4-(4,5-dimethoxy-2-nitrophenyl)-2,6-dimethyl-3,5-dicarbmethoxy-1,4-dihydropyridine. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44)1223–336-033; e-mail: deposit@ccdc.cam.ac.uk, www: http://www.ccdc.cam.ac.uk).

Supplemental materials are available for this article. Go to the publisher's online edition of Molecular Cyrstals and Liquid Crystals to view the free supplemental file.

Acknowledgments

The authors would like to thank the Department of Chemistry, Saurashtra University, Rajkot, Gujarat, India, for providing necessary facilities for this research. M.S.M. would like to express her genuine gratitude to the University Grant Commission, New Delhi, India, for financial support under Rajiv Gandhi National Fellowship Scheme.

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