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ISSN 2414-3146

Diethyl 4-(1*H*-imidazol-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate

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Received 10 January 2020
Accepted 13 January 2020

Edited by M. Bolte, Goethe-Universität Frankfurt, Germany

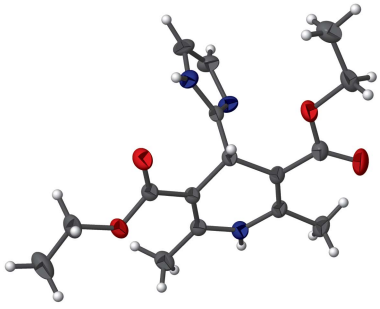
Keywords: crystal structure; 1,4-dihydropyridine; N—H···O hydrogen bonds; N—H···N hydrogen bonds.

CCDC reference: 1977288

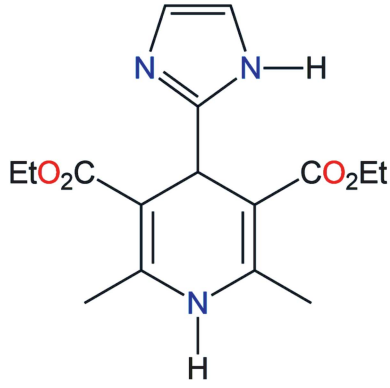
Structural data: full structural data are available from iucrdata.iucr.org

In the title compound, $C_{16}H_{21}N_3O_4$, the 1,4-dihydropyridine ring adopts a flattened boat conformation, with the imidazole substituent in an axial orientation [dihedral angle between ring planes = 82.9 (6)°]. In the crystal structure, pairs of N—H···O and N—H···N hydrogen bonds with graph-set notation $R_2^2(14)$ connect the molecules into chains running along the *c*-axis direction.

3D view



Chemical scheme



Structure description

Hantzsch 1,4-dihydropyridines (1,4-DHPs) have shown broad biological activities which include calcium channel blocker (Schaller *et al.*, 2018), antimycobacterial (Lentz *et al.*, 2016), anticonvulsant (Prasanthi *et al.*, 2014) and anti-tubercular (Khoshneviszadeh *et al.*, 2009) activities. According to our recent report, they show anti-cancer activities in HCT116 human colon cancer cell lines (Ahn *et al.*, 2018). We report herein the synthesis and crystal structure of the title compound (Fig. 1).

In the title compound, the 1,4-dihydropyridine (C1–C5/N1) ring is twisted slightly from planarity, with a maximum deviation of 0.178 (1) Å at C3 (r.m.s. deviation = 0.113 Å). The dihedral angle formed between the plane of the 1,4-dihydropyridine (C1–C5/N1) and imidazole (C10–C12/N2–N3) rings is 82.9 (6)°. One of the carbonyl groups (C13═O3) lies on the same side as the methyl group at C16 with the other carbonyl group (C7═O1) on the opposite side. In the crystal, pairs of N—H···O and N—H···N hydrogen bonds with graph-set notation $R_2^2(14)$ connect the molecules into chains running along the *c*-axis direction (Table 1, Fig. 2).

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···N3^{i}	0.87	2.05	2.913 (3)	175
N2—H2···O1^{ii}	0.87	2.18	2.979 (3)	152

Symmetry codes: (i) $-x, -y+1, -z+1$; (ii) $-x, -y+1, -z$.

Synthesis and crystallization

Methyl acetoacetate (20 mmol) and 1*H*-imidazole-2-carbaldehyde (10 mmol) were dissolved in 30 ml of ethanol to give a clear solution. To the mixture, ammonium acetate (10 mmol) was added and the reaction mixture was heated at 365 K for 5 h. After completion of the reaction (monitored by TLC), the mixture was cooled to room temperature to produce a solid product. This solid was recrystallized from ethanol solution to obtain single-crystal of the title compound in 61% yield.

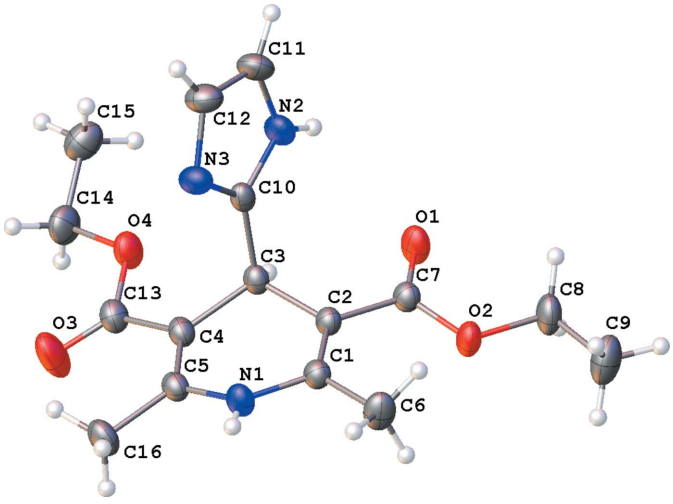


Figure 1
The molecular structure of the title compound, showing the atom-labelling scheme with displacement ellipsoids drawn at the 30% probability level.

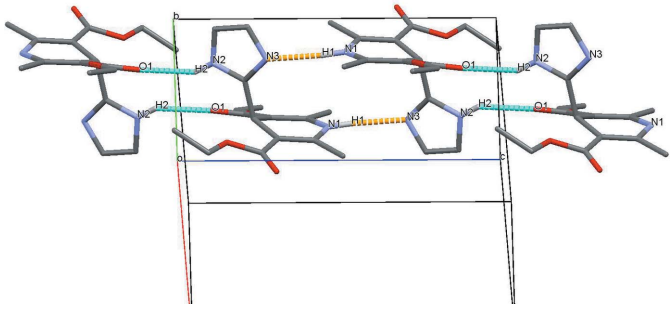


Figure 2
Part of the crystal structure with two intermolecular hydrogen bonds (blue and yellow dashed lines) are shown. For clarity, only those H atoms involved in hydrogen bonding are shown.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{16}H_{21}N_3O_4$
M_r	319.36
Crystal system, space group	Triclinic, $P\overline{1}$
Temperature (K)	223
a, b, c (Å)	8.127 (7), 8.411 (9), 12.536 (10)
α, β, γ (°)	105.36 (4), 96.52 (2), 94.77 (3)
V (Å^3)	815.1 (13)
Z	2
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.10
Crystal size (mm)	0.28 × 0.21 × 0.14
Data collection	
Diffractometer	PHOTON 100 CMOS
Absorption correction	Multi-scan (*SADABS*; Bruker, 2012)
T_{min}, T_{max}	0.974, 0.987
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	33431, 3920, 3144
R_{int}	0.041
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.667
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.049, 0.142, 1.06
No. of reflections	3920
No. of parameters	212
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.32, −0.23

Computer programs: *APEX2* and *SAINT* (Bruker, 2012), *SHELXS97* (Sheldrick, 2008), *SHELXL2014* (Sheldrick, 2015), *SHELXTL* (Sheldrick, 2008) and *publCIF* (Westrip, 2010).

Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2.

Funding information

The authors acknowledge financial support from the Basic Science Research Program (award No. NRF-2019R1F1A1058747).

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full crystallographic data

IUCrData (2020). **5**, x200034 [https://doi.org/10.1107/S2414314620000346]

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Crystal data

$C_{16}H_{21}N_3O_4$
M_r = 319.36
Triclinic, $P\overline{1}$
a = 8.127 (7) Å
b = 8.411 (9) Å
c = 12.536 (10) Å
α = 105.36 (4)°
β = 96.52 (2)°
γ = 94.77 (3)°
V = 815.1 (13) Å^3
Z = 2
$F(000)$ = 340
D_x = 1.301 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 9982 reflections
θ = 2.5–28.3°
μ = 0.10 mm^{-1}
T = 223 K
Block, colourless
0.28 × 0.21 × 0.14 mm

Data collection

PHOTON 100 CMOS diffractometer
φ and ω scans
Absorption correction: multi-scan (SADABS; Bruker, 2012)
T_{min} = 0.974, T_{max} = 0.987
33431 measured reflections
3920 independent reflections
3144 reflections with $I > 2\sigma(I)$
R_{int} = 0.041
θ_{max} = 28.3°, θ_{min} = 2.5°
h = −10→10
k = −11→11
l = −16→16

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.049
$wR(F^2)$ = 0.142
S = 1.06
3920 reflections
212 parameters
0 restraints
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0734P)^2 + 0.2436P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.32 e Å^{-3}
$\Delta\rho_{min}$ = −0.23 e Å^{-3}

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
N1	0.18302 (15)	0.47356 (14)	0.46454 (9)	0.0280 (3)
H1	0.1979	0.5159	0.5367	0.034*
C1	0.21728 (16)	0.57673 (16)	0.39890 (11)	0.0251 (3)
C2	0.16729 (15)	0.52079 (16)	0.28644 (10)	0.0232 (3)
C3	0.04796 (16)	0.36033 (15)	0.23758 (10)	0.0229 (3)
H3	0.0781	0.3040	0.1637	0.028*
C4	0.06773 (16)	0.24414 (16)	0.31144 (11)	0.0253 (3)
C5	0.12622 (16)	0.30616 (17)	0.42189 (11)	0.0261 (3)
C6	0.3103 (2)	0.74263 (19)	0.46493 (12)	0.0374 (4)
H6A	0.4280	0.7424	0.4580	0.056*
H6B	0.2959	0.7626	0.5430	0.056*
H6C	0.2669	0.8296	0.4363	0.056*
C7	0.21403 (16)	0.60658 (17)	0.20487 (11)	0.0258 (3)
O1	0.15784 (14)	0.55990 (13)	0.10544 (8)	0.0368 (3)
O2	0.32952 (13)	0.73897 (13)	0.24786 (8)	0.0333 (3)
C8	0.3728 (2)	0.83898 (19)	0.17506 (13)	0.0387 (4)
H8A	0.2719	0.8672	0.1369	0.046*
H8B	0.4361	0.7785	0.1186	0.046*
C9	0.4771 (3)	0.9939 (2)	0.24842 (16)	0.0521 (5)
H9A	0.4123	1.0534	0.3030	0.078*
H9B	0.5110	1.0643	0.2028	0.078*
H9C	0.5754	0.9640	0.2867	0.078*
C10	−0.13059 (16)	0.39732 (15)	0.21997 (10)	0.0231 (3)
N2	−0.20049 (15)	0.42932 (16)	0.12553 (10)	0.0315 (3)
H2	−0.1525	0.4293	0.0669	0.038*
C11	−0.36104 (19)	0.4617 (2)	0.13918 (13)	0.0384 (4)
H11	−0.4397	0.4889	0.0878	0.046*
C12	−0.38247 (19)	0.4467 (2)	0.24119 (13)	0.0373 (3)
H12	−0.4814	0.4613	0.2730	0.045*
N3	−0.23804 (14)	0.40668 (16)	0.29244 (9)	0.0302 (3)
C13	0.00797 (18)	0.06611 (17)	0.26232 (12)	0.0308 (3)
O3	0.02408 (19)	−0.04606 (14)	0.30548 (11)	0.0556 (4)
O4	−0.07121 (14)	0.03801 (12)	0.15720 (9)	0.0360 (3)
C14	−0.1454 (2)	−0.13100 (19)	0.10123 (14)	0.0406 (4)
H14A	−0.2060	−0.1768	0.1517	0.049*
H14B	−0.0586	−0.2015	0.0776	0.049*
C15	−0.2623 (2)	−0.1240 (2)	0.00188 (14)	0.0441 (4)
H15A	−0.3471	−0.0535	0.0264	0.066*
H15B	−0.3149	−0.2350	−0.0377	0.066*
H15C	−0.2006	−0.0790	−0.0475	0.066*
C16	0.1393 (2)	0.2112 (2)	0.50829 (13)	0.0372 (4)
H16A	0.0529	0.1174	0.4870	0.056*
H16B	0.1256	0.2835	0.5803	0.056*
H16C	0.2479	0.1716	0.5132	0.056*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.0361 (6)	0.0299 (6)	0.0185 (5)	0.0004 (5)	0.0041 (4)	0.0086 (4)
C1	0.0256 (6)	0.0272 (6)	0.0237 (6)	0.0016 (5)	0.0050 (5)	0.0090 (5)
C2	0.0240 (6)	0.0247 (6)	0.0222 (6)	0.0008 (5)	0.0045 (5)	0.0088 (5)
C3	0.0280 (6)	0.0228 (6)	0.0186 (6)	0.0010 (5)	0.0044 (5)	0.0068 (4)
C4	0.0273 (6)	0.0246 (6)	0.0269 (6)	0.0043 (5)	0.0060 (5)	0.0111 (5)
C5	0.0268 (6)	0.0288 (7)	0.0265 (6)	0.0045 (5)	0.0061 (5)	0.0130 (5)
C6	0.0467 (9)	0.0365 (8)	0.0239 (7)	−0.0088 (7)	0.0006 (6)	0.0055 (6)
C7	0.0272 (6)	0.0277 (6)	0.0236 (6)	0.0010 (5)	0.0049 (5)	0.0092 (5)
O1	0.0488 (6)	0.0388 (6)	0.0221 (5)	−0.0082 (5)	0.0029 (4)	0.0124 (4)
O2	0.0368 (6)	0.0343 (5)	0.0292 (5)	−0.0092 (4)	0.0029 (4)	0.0144 (4)
C8	0.0481 (9)	0.0347 (8)	0.0352 (8)	−0.0084 (7)	0.0090 (7)	0.0158 (6)
C9	0.0616 (12)	0.0394 (9)	0.0509 (10)	−0.0158 (8)	0.0143 (9)	0.0092 (8)
C10	0.0296 (6)	0.0211 (6)	0.0170 (6)	−0.0020 (5)	0.0001 (5)	0.0055 (4)
N2	0.0356 (6)	0.0397 (7)	0.0216 (6)	0.0011 (5)	0.0005 (4)	0.0147 (5)
C11	0.0332 (8)	0.0492 (9)	0.0336 (8)	0.0043 (7)	−0.0072 (6)	0.0180 (7)
C12	0.0272 (7)	0.0506 (9)	0.0353 (8)	0.0071 (6)	0.0013 (6)	0.0144 (7)
N3	0.0274 (6)	0.0424 (7)	0.0228 (6)	0.0058 (5)	0.0034 (4)	0.0119 (5)
C13	0.0350 (7)	0.0270 (7)	0.0325 (7)	0.0034 (5)	0.0064 (6)	0.0113 (5)
O3	0.0870 (10)	0.0298 (6)	0.0494 (7)	−0.0010 (6)	−0.0086 (7)	0.0200 (5)
O4	0.0481 (6)	0.0242 (5)	0.0332 (6)	−0.0033 (4)	0.0001 (5)	0.0083 (4)
C14	0.0466 (9)	0.0245 (7)	0.0461 (9)	−0.0043 (6)	0.0013 (7)	0.0065 (6)
C15	0.0401 (9)	0.0456 (9)	0.0402 (9)	−0.0039 (7)	0.0046 (7)	0.0040 (7)
C16	0.0491 (9)	0.0376 (8)	0.0299 (7)	0.0046 (7)	0.0038 (6)	0.0187 (6)

Geometric parameters (Å, º)

N1—C1	1.3777 (19)	C9—H9B	0.9700
N1—C5	1.385 (2)	C9—H9C	0.9700
N1—H1	0.8700	C10—N3	1.3221 (19)
C1—C2	1.364 (2)	C10—N2	1.3558 (19)
C1—C6	1.508 (2)	N2—C11	1.375 (2)
C2—C7	1.464 (2)	N2—H2	0.8700
C2—C3	1.532 (2)	C11—C12	1.347 (2)
C3—C10	1.513 (2)	C11—H11	0.9400
C3—C4	1.520 (2)	C12—N3	1.383 (2)
C3—H3	0.9900	C12—H12	0.9400
C4—C5	1.357 (2)	C13—O3	1.214 (2)
C4—C13	1.476 (2)	C13—O4	1.350 (2)
C5—C16	1.506 (2)	O4—C14	1.452 (2)
C6—H6A	0.9700	C14—C15	1.496 (3)
C6—H6B	0.9700	C14—H14A	0.9800
C6—H6C	0.9700	C14—H14B	0.9800
C7—O1	1.2239 (19)	C15—H15A	0.9700
C7—O2	1.3434 (19)	C15—H15B	0.9700
O2—C8	1.4473 (19)	C15—H15C	0.9700

C8—C9	1.506 (2)	C16—H16A	0.9700
C8—H8A	0.9800	C16—H16B	0.9700
C8—H8B	0.9800	C16—H16C	0.9700
C9—H9A	0.9700		

C1—N1—C5	123.55 (12)	H9A—C9—H9B	109.5
C1—N1—H1	118.2	C8—C9—H9C	109.5
C5—N1—H1	118.2	H9A—C9—H9C	109.5
C2—C1—N1	118.86 (13)	H9B—C9—H9C	109.5
C2—C1—C6	128.14 (12)	N3—C10—N2	110.72 (13)
N1—C1—C6	113.00 (13)	N3—C10—C3	126.17 (12)
C1—C2—C7	124.90 (13)	N2—C10—C3	123.10 (12)
C1—C2—C3	120.01 (11)	C10—N2—C11	107.57 (12)
C7—C2—C3	115.05 (12)	C10—N2—H2	126.2
C10—C3—C4	111.44 (10)	C11—N2—H2	126.2
C10—C3—C2	111.01 (12)	C12—C11—N2	105.92 (13)
C4—C3—C2	110.65 (12)	C12—C11—H11	127.0
C10—C3—H3	107.9	N2—C11—H11	127.0
C4—C3—H3	107.9	C11—C12—N3	110.26 (14)
C2—C3—H3	107.9	C11—C12—H12	124.9
C5—C4—C13	121.28 (13)	N3—C12—H12	124.9
C5—C4—C3	120.13 (13)	C10—N3—C12	105.53 (13)
C13—C4—C3	118.36 (13)	O3—C13—O4	121.56 (14)
C4—C5—N1	119.54 (12)	O3—C13—C4	127.60 (15)
C4—C5—C16	126.95 (14)	O4—C13—C4	110.84 (12)
N1—C5—C16	113.51 (13)	C13—O4—C14	116.62 (12)
C1—C6—H6A	109.5	O4—C14—C15	106.98 (14)
C1—C6—H6B	109.5	O4—C14—H14A	110.3
H6A—C6—H6B	109.5	C15—C14—H14A	110.3
C1—C6—H6C	109.5	O4—C14—H14B	110.3
H6A—C6—H6C	109.5	C15—C14—H14B	110.3
H6B—C6—H6C	109.5	H14A—C14—H14B	108.6
O1—C7—O2	122.36 (12)	C14—C15—H15A	109.5
O1—C7—C2	123.54 (13)	C14—C15—H15B	109.5
O2—C7—C2	114.06 (12)	H15A—C15—H15B	109.5
C7—O2—C8	117.63 (12)	C14—C15—H15C	109.5
O2—C8—C9	106.51 (14)	H15A—C15—H15C	109.5
O2—C8—H8A	110.4	H15B—C15—H15C	109.5
C9—C8—H8A	110.4	C5—C16—H16A	109.5
O2—C8—H8B	110.4	C5—C16—H16B	109.5
C9—C8—H8B	110.4	H16A—C16—H16B	109.5
H8A—C8—H8B	108.6	C5—C16—H16C	109.5
C8—C9—H9A	109.5	H16A—C16—H16C	109.5
C8—C9—H9B	109.5	H16B—C16—H16C	109.5

C5—N1—C1—C2	11.5 (2)	C3—C2—C7—O2	−174.61 (11)
C5—N1—C1—C6	−168.01 (13)	O1—C7—O2—C8	7.2 (2)
N1—C1—C2—C7	−171.32 (12)	C2—C7—O2—C8	−175.03 (12)

C6—C1—C2—C7	8.1 (2)	C7—O2—C8—C9	169.35 (14)
N1—C1—C2—C3	11.18 (19)	C4—C3—C10—N3	32.28 (17)
C6—C1—C2—C3	−169.38 (13)	C2—C3—C10—N3	−91.54 (16)
C1—C2—C3—C10	96.34 (14)	C4—C3—C10—N2	−149.20 (12)
C7—C2—C3—C10	−81.40 (14)	C2—C3—C10—N2	86.98 (15)
C1—C2—C3—C4	−27.93 (17)	N3—C10—N2—C11	0.37 (16)
C7—C2—C3—C4	154.33 (11)	C3—C10—N2—C11	−178.36 (12)
C10—C3—C4—C5	−98.67 (15)	C10—N2—C11—C12	−0.51 (17)
C2—C3—C4—C5	25.35 (17)	N2—C11—C12—N3	0.48 (19)
C10—C3—C4—C13	75.95 (15)	N2—C10—N3—C12	−0.07 (16)
C2—C3—C4—C13	−160.02 (12)	C3—C10—N3—C12	178.60 (12)
C13—C4—C5—N1	179.24 (12)	C11—C12—N3—C10	−0.26 (18)
C3—C4—C5—N1	−6.29 (19)	C5—C4—C13—O3	−11.3 (2)
C13—C4—C5—C16	−0.2 (2)	C3—C4—C13—O3	174.13 (16)
C3—C4—C5—C16	174.29 (13)	C5—C4—C13—O4	169.00 (12)
C1—N1—C5—C4	−14.2 (2)	C3—C4—C13—O4	−5.56 (17)
C1—N1—C5—C16	165.30 (13)	O3—C13—O4—C14	3.9 (2)
C1—C2—C7—O1	−174.51 (14)	C4—C13—O4—C14	−176.41 (12)
C3—C2—C7—O1	3.1 (2)	C13—O4—C14—C15	165.03 (13)
C1—C2—C7—O2	7.8 (2)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···N3^{i}	0.87	2.05	2.913 (3)	175
N2—H2···O1^{ii}	0.87	2.18	2.979 (3)	152

Symmetry codes: (i) −*x*, −*y*+1, −*z*+1; (ii) −*x*, −*y*+1, −*z*.