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Ethyl 1*H*-indole-2-carboxylate

Will E. Lynch,* Christine R. Whitlock and Clifford W. Padgett

Georgia Southern University, Department of Chemistry and Biochemistry, Box 8064, Statesboro, GA 30460, USA.
*Correspondence e-mail: wlynch@georgiasouthern.edu

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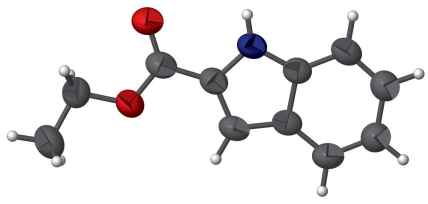
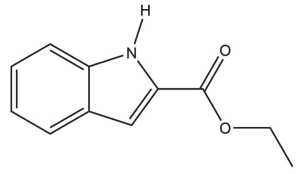
Our work in the area of synthesis of tris indole compounds as a potential chelator led to the synthesis and crystallization of ethyl 1*H*-indole-2-carboxylate, $C_{11}H_{11}NO_2$, an indole that was synthesized by the thionyl chloride reaction of 1*H*-indole-2-carboxylic acid, followed by dissolution in ethanol. The molecular packing exhibits a herringbone pattern with the zigzag running along the *b*-axis direction; the compound crystallizes as a hydrogen-bonded dimer resulting from O···H—N hydrogen bonds, between the indole N—H group and the keto oxygen atom, which build centrosymmetric $R_2^2(10)$ ring motifs in the crystal.

3D view



Chemical scheme



Structure description

Indole esters can easily be prepared from 1*H*-indole-2-carboxylic acid *via* an isolated acyl chloride intermediate followed by dissolving the residue in the appropriate alcohol solvent. These indole-type compounds are of interest because of their prevalence in nature (Stempel & Gaich, 2016). Derivatives of this type of compound have also been implicated in a number of biological roles including antifungal (Kipp *et al.*, 1999), anti-tumor (Lu *et al.*, 2016) and anti-inflammatory (Liu *et al.*, 2016) agents. These types of compounds have also been reported as potential cellular inhibitors of kinase (Jobson *et al.*, 2009) as well as an antagonist for glycine-binding sites (Ohtani *et al.*, 2002). Previous reports include the structures of indole-2-carboxylic acid (Morzyk-Ociepa *et al.*, 2004) and methyl 1*H*-indole-2-carboxylate (Almutairi *et al.*, 2017).

Herein we report the crystal structure of ethyl 1*H*-indole-2-carboxylate (Fig. 1), which forms a hydrogen-bonded dimer. The hydrogen bonding occurs between N atoms of the indole ring and the keto oxygen atoms with an $R(10)$ synthon. The hydrogen bond between N1 and O2^{i} is characterized by an N···O separation of 2.877 (3) Å [symmetry code: (i) $-x+2, -y+1, -z+1$; Table 1], and the ring motifs, $R_2^2(10)$, are placed on inversion centres in the space group $P2_1/c$ (Fig. 2). The crystal structure exhibits a classic

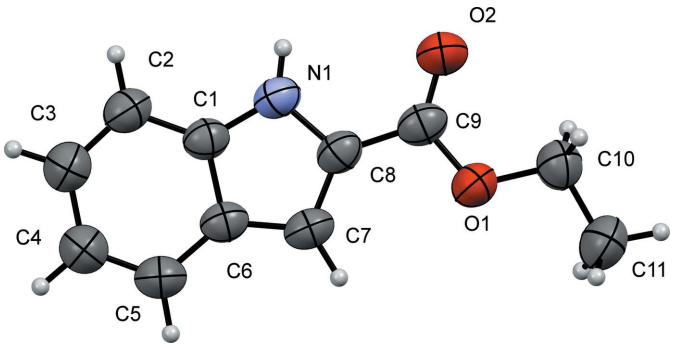


Figure 1
A view of the molecular structure of the title compound, with the atom labelling. Displacement ellipsoids are drawn at the 50% probability level.

herringbone pattern (Fig. 2) with the blocks consisting of the hydrogen-bonded dimers, with the zigzag running along the *b*-axis direction. The molecule is nearly planar, with a r.m.s.d. of 0.028 Å for the non-hydrogen atoms. There are no other short contacts or π–π interactions observed in the crystal.

Synthesis and crystallization

The title compound was synthesized by modification of an early method laid out by Terent'ev *et al.* (1969). Indole-2-carboxylic acid (0.50 g, 3.1 mmol) was dissolved in $SOCl_2$ (19 ml) at 0°C. After stirring for 1 h, the solution was rotary evaporated and to the resulting oil was added absolute ethanol (17 ml) at room temperature. After stirring overnight, the solution was vacuum filtered to yield ethyl 1*H*-indole-2-carboxylate as a beige solid, which was recrystallized from methanol to yield 0.54 g (2.9 mmol, 93%) of the product. Further recrystallization by slow evaporation from methanol solution resulted in X-ray quality crystals.

Refinement

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

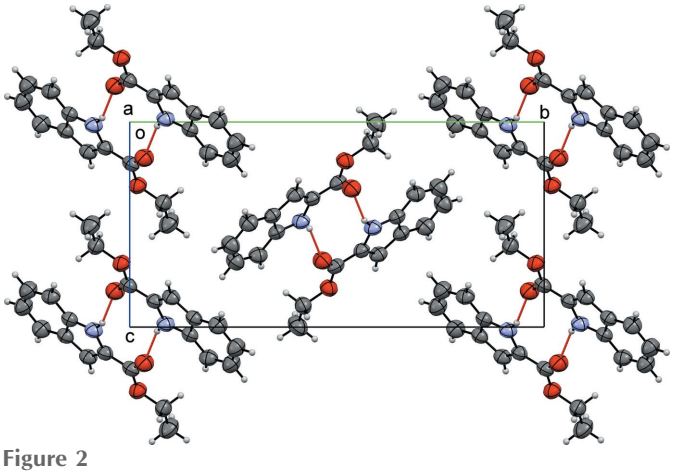


Figure 2
Crystal packing diagram of title compound viewed along [100]. Hydrogen bonds are coloured red.

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O2^{i}	0.84 (3)	2.08 (3)	2.877 (3)	158 (3)

Symmetry code: (i) $-x+2, -y+1, -z+1$.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{11}H_{11}NO_2$
M_r	189.21
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	170
a, b, c (Å)	5.5622 (7), 18.891 (2), 9.6524 (13)
β (°)	104.454 (13)
V (Å^3)	982.1 (2)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.09
Crystal size (mm)	0.4 × 0.05 × 0.05
Data collection	
Diffractometer	Rigaku XtaLAB mini
Absorption correction	Multi-scan (*CrysAlis PRO*; Rigaku OD, 2018)
T_{min}, T_{max}	0.998, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	5586, 1804, 991
R_{int}	0.047
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.602
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.049, 0.144, 1.01
No. of reflections	1804
No. of parameters	132
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.28, −0.16

Computer programs: *CrysAlis PRO* (Rigaku OD, 2018), *SHELXT* (Sheldrick, 2015*a*), *SHELXL* (Sheldrick, 2015*b*) and *OLEX2* (Dolomanov *et al.*, 2009).

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full crystallographic data

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Ethyl 1*H*-indole-2-carboxylate

Crystal data

$C_{11}H_{11}NO_2$
$M_r = 189.21$
Monoclinic, $P2_1/c$
$a = 5.5622$ (7) Å
$b = 18.891$ (2) Å
$c = 9.6524$ (13) Å
$\beta = 104.454$ (13)°
$V = 982.1$ (2) Å^3
$Z = 4$
$F(000) = 400$
$D_x = 1.280$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 611 reflections
$\theta = 2.4$–$21.1°$
$\mu = 0.09$ mm^{-1}
$T = 170$ K
Needle, colourless
0.4 × 0.05 × 0.05 mm

Data collection

Rigaku XtaLAB mini diffractometer
Radiation source: fine-focus sealed X-ray tube, Rigaku (Mo) X-ray Source
Graphite monochromator
ω scans
Absorption correction: multi-scan (CrysAlisPro; Rigaku OD, 2018)
$T_{min} = 0.998$, $T_{max} = 1.000$
5586 measured reflections
1804 independent reflections
991 reflections with $I > 2\sigma(I)$
$R_{int} = 0.047$
$\theta_{max} = 25.3°$, $\theta_{min} = 2.2°$
$h = -6\rightarrow6$
$k = -22\rightarrow22$
$l = -6\rightarrow11$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.049$
$wR(F^2) = 0.144$
$S = 1.01$
1804 reflections
132 parameters
0 restraints
Primary atom site location: dual
Secondary atom site location: difference Fourier map
Hydrogen site location: mixed
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0611P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.28$ e Å^{-3}
$\Delta\rho_{min} = -0.16$ e Å^{-3}

Special details

Refinement. All carbon-bound H atoms were positioned geometrically and refined as riding, with C—H = 0.95, 0.98 or 0.99 Å and $U_{iso}(H) = 1.2U_{eq}(C)$ or $U_{iso}(H) = 1.5U_{eq}(C)$ for C(H) and CH_3 groups, respectively. Hydrogen atom of the N—H group was refined freely.

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

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	0.4202 (3)	0.51968 (8)	0.18977 (19)	0.0674 (5)
O2	0.8074 (3)	0.53509 (10)	0.32447 (19)	0.0769 (6)
N1	0.7445 (4)	0.41313 (12)	0.4844 (2)	0.0618 (6)
C1	0.6528 (4)	0.35476 (13)	0.5376 (2)	0.0546 (6)
C6	0.4072 (4)	0.34466 (13)	0.4568 (2)	0.0561 (6)
C9	0.6121 (5)	0.50269 (13)	0.2963 (3)	0.0603 (7)
C8	0.5633 (4)	0.44041 (13)	0.3735 (3)	0.0559 (6)
C7	0.3542 (4)	0.39987 (13)	0.3545 (3)	0.0604 (7)
H7	0.201542	0.407332	0.285492	0.072*
C2	0.7649 (5)	0.30983 (14)	0.6497 (3)	0.0667 (7)
H2	0.931108	0.317126	0.703333	0.080*
C10	0.4457 (5)	0.58135 (13)	0.1043 (3)	0.0713 (8)
H10A	0.570546	0.572318	0.049089	0.086*
H10B	0.499351	0.622958	0.166698	0.086*
C5	0.2734 (5)	0.28695 (15)	0.4909 (3)	0.0713 (8)
H5	0.107754	0.278384	0.437693	0.086*
C3	0.6258 (5)	0.25482 (14)	0.6791 (3)	0.0745 (8)
H3	0.696946	0.223507	0.755363	0.089*
C4	0.3833 (5)	0.24349 (15)	0.6006 (3)	0.0760 (8)
H4	0.292584	0.204613	0.624028	0.091*
C11	0.1971 (5)	0.59444 (16)	0.0056 (3)	0.0935 (10)
H11A	0.149807	0.553780	−0.058508	0.140*
H11B	0.204101	0.637068	−0.051138	0.140*
H11C	0.073960	0.601063	0.061479	0.140*
H1	0.879 (5)	0.4339 (15)	0.520 (3)	0.087 (10)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0631 (11)	0.0688 (12)	0.0625 (11)	−0.0022 (9)	0.0009 (9)	0.0064 (9)
O2	0.0672 (13)	0.0828 (13)	0.0715 (13)	−0.0150 (10)	0.0001 (10)	0.0024 (10)
N1	0.0537 (14)	0.0712 (15)	0.0544 (13)	−0.0052 (12)	0.0021 (12)	−0.0023 (12)
C1	0.0522 (15)	0.0606 (16)	0.0496 (14)	−0.0010 (12)	0.0101 (12)	−0.0062 (13)
C6	0.0500 (15)	0.0628 (15)	0.0530 (14)	0.0000 (12)	0.0082 (12)	−0.0084 (13)
C9	0.0573 (17)	0.0670 (17)	0.0524 (15)	0.0007 (14)	0.0054 (14)	−0.0125 (14)
C8	0.0564 (16)	0.0586 (15)	0.0486 (14)	0.0021 (12)	0.0054 (12)	−0.0056 (13)
C7	0.0487 (15)	0.0709 (17)	0.0557 (15)	0.0014 (13)	0.0021 (12)	−0.0063 (14)
C2	0.0571 (16)	0.0769 (18)	0.0607 (17)	0.0033 (14)	0.0046 (13)	0.0009 (15)
C10	0.0766 (19)	0.0626 (17)	0.0715 (18)	−0.0028 (14)	0.0127 (15)	0.0068 (14)
C5	0.0549 (16)	0.0793 (18)	0.0742 (19)	−0.0090 (14)	0.0056 (14)	−0.0001 (16)
C3	0.0708 (19)	0.0766 (19)	0.0727 (19)	0.0011 (15)	0.0115 (16)	0.0111 (15)
C4	0.0697 (19)	0.0777 (19)	0.078 (2)	−0.0072 (14)	0.0136 (16)	0.0097 (16)
C11	0.088 (2)	0.089 (2)	0.091 (2)	0.0041 (17)	−0.0015 (18)	0.0239 (18)

Geometric parameters (Å, º)

O1—C9	1.324 (3)	C2—H2	0.9500
O1—C10	1.455 (3)	C2—C3	1.367 (3)
O2—C9	1.217 (3)	C10—H10A	0.9900
N1—C1	1.368 (3)	C10—H10B	0.9900
N1—C8	1.374 (3)	C10—C11	1.491 (3)
N1—H1	0.84 (3)	C5—H5	0.9500
C1—C6	1.406 (3)	C5—C4	1.359 (4)
C1—C2	1.394 (3)	C3—H3	0.9500
C6—C7	1.416 (3)	C3—C4	1.389 (4)
C6—C5	1.404 (3)	C4—H4	0.9500
C9—C8	1.454 (3)	C11—H11A	0.9800
C8—C7	1.366 (3)	C11—H11B	0.9800
C7—H7	0.9500	C11—H11C	0.9800
C9—O1—C10	117.45 (19)	O1—C10—H10A	110.4
C1—N1—C8	108.9 (2)	O1—C10—H10B	110.4
C1—N1—H1	127 (2)	O1—C10—C11	106.8 (2)
C8—N1—H1	123 (2)	H10A—C10—H10B	108.6
N1—C1—C6	107.6 (2)	C11—C10—H10A	110.4
N1—C1—C2	130.2 (2)	C11—C10—H10B	110.4
C2—C1—C6	122.2 (2)	C6—C5—H5	120.3
C1—C6—C7	106.9 (2)	C4—C5—C6	119.3 (2)
C5—C6—C1	118.3 (2)	C4—C5—H5	120.3
C5—C6—C7	134.8 (2)	C2—C3—H3	119.1
O1—C9—C8	112.1 (2)	C2—C3—C4	121.8 (3)
O2—C9—O1	123.6 (2)	C4—C3—H3	119.1
O2—C9—C8	124.3 (2)	C5—C4—C3	121.3 (3)
N1—C8—C9	120.5 (2)	C5—C4—H4	119.4
C7—C8—N1	109.2 (2)	C3—C4—H4	119.4
C7—C8—C9	130.3 (2)	C10—C11—H11A	109.5
C6—C7—H7	126.4	C10—C11—H11B	109.5
C8—C7—C6	107.3 (2)	C10—C11—H11C	109.5
C8—C7—H7	126.4	H11A—C11—H11B	109.5
C1—C2—H2	121.4	H11A—C11—H11C	109.5
C3—C2—C1	117.2 (2)	H11B—C11—H11C	109.5
C3—C2—H2	121.4		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···O2^{i}	0.84 (3)	2.08 (3)	2.877 (3)	158 (3)

Symmetry code: (i) −*x*+2, −*y*+1, −*z*+1.