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Synthesis and crystal structure of ($\pm$)-Ethyl 5'-(difluoromethyl)-2-oxo-4', 5'-dihydrospiro[indoline-3,3'-pyrazole]-4'-carboxylate, $C_{14}H_{13}F_2N_3O_3$

The molecular structure is shown in the figure. Tables 1 and 2 contain details on crystal structure and measurement conditions and a list of the atoms including atomic coordinates and displacement parameters.

Table 1: Data collection and handling.

Crystal:	Colorless block
Size:	0.22 × 0.16 × 0.12 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.12 mm ⁻¹
Diffractometer, scan mode:	Bruker APEX-II, φ and ω
$\theta_{\max}$, completeness:	26.5°, >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	12806, 5941, 0.032
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 4624
$N(\text{param})_{\text{refined}}$:	400
Programs:	SHELX [1], Bruker [2]

Source of material

The mixture of $CF_2HCH_2NH_2$ (1.0 mmol), $tBuONO$ (1.2 mmol), AcOH (0.15 mmol) and DCM (dichloromethane; 20 mL) was stirred at 70 °C for about 10 min. The mixture was placed at room temperature, then was added (*E*)-ethyl 2-(2-oxoindolin-3-ylidene)acetate (0.3 mmol). The reaction was monitored by thin-layer chromatography (TLC), which showed the disappearance of (*E*)-ethyl 2-(2-oxoindolin-3-ylidene)acetate that was indicative of the reaction being complete. After DCM was removed under reduced pressure, the residue was purified by column chromatography on silica gel column using petroleum ether/ethyl acetate (6:1, v/v) to give the corresponding pure title compound. Crystals were obtained at room temperature from the mother liquor.

Experimental details

All hydrogen atoms were identified in difference Fourier syntheses and placed in geometrically idealized positions. The U_{iso} values of the hydrogen atoms of methyl groups were set to 1. $U_{\text{eq}}(C)$ and the U_{iso} values of all other hydrogen atoms were set to 1. $U_{\text{eq}}(C)$.

Comment

1*H*-Indole-2,3-dione (isatin) and its derivatives exhibit an extraordinary biological activity. It is well known that

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Abstract

$C_{14}H_{13}F_2N_3O_3$, triclinic, $P\bar{1}$ (no. 2), $a = 9.4486(7)$ Å, $b = 12.4694(8)$ Å, $c = 13.8690(8)$ Å, $\alpha = 65.734(6)^\circ$, $\beta = 74.523(5)^\circ$, $\gamma = 83.726(6)^\circ$, $V = 1435.63(18)$ Å³, $Z = 4$, $R_{\text{gt}}(F) = 0.0495$, $wR_{\text{ref}}(F^2) = 0.1249$, $T = 293(2)$ K.

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Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
C1	−0.0749(2)	0.23340(15)	0.76413(14)	0.0160(4)
C2	−0.0381(2)	0.12764(16)	0.86157(14)	0.0168(4)
C3	−0.0693(2)	0.28591(16)	0.90792(14)	0.0167(4)
C4	−0.0994(2)	0.33038(16)	0.80553(14)	0.0161(4)
C5	−0.1429(2)	0.44558(16)	0.75910(15)	0.0200(4)
H5	−0.1646(11)	0.475114	0.691235	0.024*
C6	−0.1538(2)	0.51690(17)	0.81634(15)	0.0232(4)
H6	−0.1825(30)	0.595018	0.786437	0.028*
C7	−0.1218(2)	0.47161(17)	0.91758(16)	0.0234(4)
H7	−0.1292(10)	0.520375	0.954533	0.028*
C8	−0.0788(2)	0.35484(16)	0.96565(15)	0.0202(4)
H8	−0.0574(26)	0.324871	1.033647	0.024*
C9	0.0407(2)	0.25558(16)	0.65561(14)	0.0161(4)
H9	0.0950(63)	0.182755	0.660253	0.019*
C10	−0.0564(2)	0.28369(17)	0.57617(14)	0.0194(4)
H10	−0.0650(46)	0.369289	0.539961	0.023*
C11	−0.0060(2)	0.23396(19)	0.49080(16)	0.0272(5)
H11	−0.0763(30)	0.252359	0.445485	0.033*
C12	0.1470(2)	0.35188(16)	0.62703(15)	0.0188(4)
C13	0.3302(2)	0.40651(18)	0.68647(18)	0.0295(5)
H13A	0.2764(93)	0.470396	0.702670	0.035*
H13B	0.3903(71)	0.438623	0.612279	0.035*
C14	0.4238(3)	0.3456(2)	0.7644(2)	0.0431(6)
H14A	0.4774(84)	0.283434	0.746739	0.065*
H14B	0.3628(82)	0.313247	0.837282	0.065*
H14C	0.4915(21)	0.400861	0.759354	0.065*
O1	−0.0176(2(15))	0.02754(11)	0.86557(10)	0.0219(3)
O2	0.1559(2(16))	0.44614(12)	0.55093(11)	0.0300(4)
O3	0.2283(2(14))	0.31851(11)	0.69918(10)	0.0215(3)
N1	−0.2027(0(17))	0.23436(14)	0.64525(12)	0.0202(4)
N2	−0.2135(3(17))	0.20732(13)	0.74359(12)	0.0190(4)
N3	−0.0313(6(17))	0.16603(13)	0.93806(12)	0.0174(3)
H3	−0.0069(10)	0.122705	0.997856	0.021*
F1	0.0144(8(15))	0.11520(11)	0.53827(10)	0.0388(3)
F2	0.1288(3(13))	0.27960(11)	0.42869(9)	0.0346(3)
C1A	0.5974(2)	0.26070(16)	0.21774(14)	0.0176(4)
C2A	0.5569(2)	0.37141(16)	0.12584(14)	0.0186(4)
C3A	0.5867(2)	0.22169(16)	0.06779(14)	0.0183(4)
C4A	0.6213(2)	0.17050(16)	0.16873(14)	0.0181(4)
C5A	0.6638(2)	0.05416(17)	0.20900(15)	0.0227(4)
H5A	0.6880(88)	0.019998	0.276017	0.027*
C6A	0.6696(2)	−0.01105(18)	0.14691(17)	0.0266(5)
H6A	0.6973(50)	−0.089734	0.172746	0.032*
C7A	0.6343(2)	0.04077(18)	0.04745(17)	0.0266(5)
H7A	0.6388(76)	−0.003984	0.007101	0.032*
C8A	0.5918(2)	0.15860(17)	0.00542(16)	0.0232(4)
H8A	0.5679(97)	0.192965	−0.061761	0.028*
C9A	0.4808(2)	0.23099(16)	0.32695(14)	0.0177(4)
H9A	0.4282(62)	0.302693	0.328618	0.021*
C10A	0.5771(2)	0.19000(17)	0.40784(14)	0.0198(4)
H10A	0.5857(27)	0.104123	0.435413	0.024*
C11A	0.5269(2)	0.22515(18)	0.50298(16)	0.0265(5)
H11A	0.5957(83)	0.196859	0.550001	0.032*
C12A	0.3732(2)	0.14108(16)	0.34273(14)	0.0184(4)
C13A	0.1915(2)	0.10870(17)	0.26876(18)	0.0292(5)

Table 2 (continued)

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
H13C	0.125991	0.073284	0.340668	0.035*
H13D	0.243422	0.046494	0.248719	0.035*
C14A	0.1069(3)	0.1820(2)	0.1874(2)	0.0424(6)
H14D	0.173254	0.217453	0.116994	0.064*
H14E	0.055103	0.242454	0.208846	0.064*
H14F	0.037880	0.133349	0.184082	0.064*
O1A	0.53441(15)	0.46797(11)	0.12974(10)	0.0237(3)
O2A	0.36167(16)	0.04148(12)	0.41016(11)	0.0289(3)
O3A	0.29505(14)	0.18741(11)	0.26836(10)	0.0196(3)
N1A	0.72388(18)	0.24281(14)	0.34234(12)	0.0227(4)
N2A	0.73507(17)	0.28148(13)	0.24255(12)	0.0204(4)
N3A	0.54801(17)	0.34044(13)	0.04538(12)	0.0189(4)
H3A	0.521907	0.387446	−0.012700	0.023*
F1A	0.51216(15)	0.34467(11)	0.46668(9)	0.0377(3)
F2A	0.39011(13)	0.18027(11)	0.55989(9)	0.0320(3)

isatin was found in human organism and its influence on different systems in organism has long been discussed in the literature [3–10]. The biological activity of isatin includes the impact on human brain and protection from different types of infectious diseases [7–9]. *N*-Methylisatin-3-thiosemicarbazone (methisazon) is one of the first antivirals used in clinical practice. In recent years, isatin derivatives with acylhydrazone substituents at the C(3) position of the indole cycle have been intensively studied as antituberculosis drugs [10]. *N*-Alkyl-substituted isatins can act as selective antagonists of cannabinoid receptor 2 in treating neuropathic pain [11]. On the other hand pyrazole derivatives have known to exhibit diverse biological applications such as antidiabetic [12], anaesthetic [13], antimicrobial and antioxidant [14]. According to physiological activity structure combination strategy, indolin-2-one skeleton and 4,5-dihydro-3H-pyrazole ring were joined together and the title compound was synthesized.

The molecular structure of the title structure consists of one indolin-2-one ring, a 4,5-dihydro-3H-pyrazole ring, a difluoromethyl and a ethyl formate group (*cf.* the figure). The title structure contains two crystallographically independent molecules Mole1 (C1–C14/N1–N3/O1–O3) and Mole2 (C1A–C14A/N1A–N3A/O1A–O3A), Mole1 and Mole2 are a pair of optical isomers. Furthermore the space group symmetry verifies the inverted molecules additionally. The indolin-2-one ring is essentially planar, with a mean deviation from plane of 0.0152(2) Å for Mole1 and 0.0168(2) Å for Mole2. The 4,5-dihydro-3H-pyrazole ring adopts an envelope conformation with C9 atom deviating by 0.3474(3) Å from the plane formed by C1, C10, N1 and N2 for Mole1, C9A atom deviates by 0.3816(2) Å from the plane formed by C1A, C10A, N1A and N2A

for Mole2 [15]. The bond lengths and angles of indolin-2-one and 4,5-dihydro-1*H*-pyrazole ring are similar to those found in literature [16–18]. The indolin-2-one ring and 4,5-dihydro-3*H*-pyrazole ring form spiro structural feature through their third atom (C1). Because C1 is a sp^3 hybridized carbon, the indolin-2-one ring is non-coplanar with 4,5-dihydro-3*H*-pyrazole ring, the dihedral angles between the two rings are $89.793(4)^\circ$ for Mole1 and $89.471(2)^\circ$ for Mole2. In the crystal structure of title compound, adjacent molecules are connected by classical hydrogen bonds $N3(A) \cdots H3(A) \cdots O1(A)$ and $C10(A) \cdots H10(A) \cdots O2(A)$ to form one-dimensional chain along the direction [011].

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