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Crystal structure of (*E*)-2-(4-ethoxycarbonyl-3,5-dimethyl-2-(pyrrole-2-ylmethyleneamino)-3',6'-dihydroxylspiro[isoindoline-1,9'-xanthen]-3-one-methanol (1/1), C₃₁H₂₉N₃O₇

Table 1: Data collection and handling.

Crystal:	Colorless plate
Size:	0.20 × 0.16 × 0.08 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.09 mm ⁻¹
Diffractometer, scan mode:	φ and ω
$\theta_{\max}$, completeness:	25.0°, >99 %
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	14248, 4998, 0.038
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 3243
$N(\text{param})_{\text{refined}}$:	372
Programs:	Bruker [1], SHELX [2, 3]

Source of material

Fluorescein hydrazide was condensed with equimolar ethyl 2,4-dimethyl-5-formylpyrrole-3-carboxylate in boiling methanol and refluxed for 4 h, during which a white powder appeared, which was filtered off, washed with methanol/water (1:1, v/v) to produce the title compound. Yield: ca. 84%. Single crystals of the title compound were obtained by slow evaporation of a methanol solution at room temperature.

Experimental details

The structure was solved by direct methods and refined with the SHELX software package [3]. All hydrogen atoms were placed at calculated positions and refined as riding atoms with isotropic displacement parameters.

Comment

Fluorescein has been widely employed as fluorescent signal reporter of chemosensors because of its excellent photophysical properties [4]. In addition, some fluorescein hydrazones from substituted benzaldehyde have exhibited considerable biological activity as non-intercalative topoisomerase catalytic inhibitors [5]. In

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Abstract

C₃₁H₂₉N₃O₇, monoclinic, $P2_1/c$ (no. 14), $a = 13.6280(14)$ Å, $b = 14.4801(15)$ Å, $c = 14.4962(15)$ Å, $\beta = 97.586(2)^\circ$, $V = 2835.6(5)$ Å³, $Z = 4$, $R_{\text{gt}}(F) = 0.0532$, $wR_{\text{ref}}(F^2) = 0.1569$, $T = 296$ K.

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The molecular structure is shown in the Figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

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

Atom	x	y	z	<i>U</i> _{iso} */ <i>U</i> _{eq}
O1	0.26715 (13)	0.98351 (13)	0.25689 (15)	0.0582 (6)
H1A	0.2635	1.0400	0.2579	0.087*
O2	0.58059 (13)	1.05719 (12)	0.16896 (13)	0.0490 (5)
O3	0.82119 (14)	1.16596 (14)	−0.01283 (15)	0.0655 (6)
H3A	0.8197	1.2118	0.0201	0.098*
O4	0.75502 (13)	0.66803 (12)	0.23700 (13)	0.0519 (5)
O5	0.81359 (18)	1.18234 (15)	0.59881 (14)	0.0718 (6)
O6	0.92263 (14)	1.08467 (14)	0.67519 (13)	0.0580 (5)
O7	0.87706 (19)	0.71644 (17)	0.40776 (17)	0.0868 (8)
H7	0.8352	0.7166	0.3616	0.130*
N1	0.69167 (15)	0.81353 (14)	0.20560 (14)	0.0404 (5)
N2	0.74240 (15)	0.84540 (15)	0.28790 (14)	0.0418 (5)
N3	0.84983 (15)	0.90521 (15)	0.45562 (15)	0.0467 (6)
H3B	0.8660	0.8501	0.4415	0.056*
C1	0.52975 (18)	0.89678 (17)	0.16787 (17)	0.0392 (6)
C2	0.45502 (19)	0.83537 (18)	0.18452 (18)	0.0444 (6)
H2B	0.4639	0.7726	0.1749	0.053*
C3	0.3691 (2)	0.86475 (18)	0.21461 (19)	0.0475 (7)
H3C	0.3208	0.8222	0.2256	0.057*
C4	0.35419 (19)	0.95820 (18)	0.22859 (19)	0.0450 (6)
C5	0.42640 (18)	1.02091 (18)	0.21295 (19)	0.0448 (6)
H5A	0.4173	1.0836	0.2227	0.054*
C6	0.51225 (18)	0.98938 (17)	0.18272 (17)	0.0407 (6)
C7	0.65272 (18)	1.03525 (18)	0.11317 (18)	0.0434 (6)
C8	0.70113 (19)	1.11044 (19)	0.08124 (19)	0.0492 (7)
H8A	0.6860	1.1701	0.0985	0.059*
C9	0.7723 (2)	1.0952 (2)	0.0233 (2)	0.0508 (7)
C10	0.7938 (2)	1.0065 (2)	−0.0013 (2)	0.0566 (8)
H10A	0.8407	0.9962	−0.0413	0.068*
C11	0.7462 (2)	0.9326 (2)	0.03304 (19)	0.0514 (7)
H11A	0.7624	0.8730	0.0166	0.062*
C12	0.67460 (18)	0.94551 (17)	0.09177 (18)	0.0417 (6)
C13	0.62352 (18)	0.86478 (17)	0.13207 (17)	0.0403 (6)
C14	0.60028 (18)	0.78607 (18)	0.06299 (18)	0.0422 (6)
C15	0.5398 (2)	0.7887 (2)	−0.0207 (2)	0.0591 (8)
H15A	0.5114	0.8437	−0.0442	0.071*
C16	0.5229 (2)	0.7069 (3)	−0.0687 (2)	0.0721 (10)
H16A	0.4819	0.7071	−0.1253	0.087*
C17	0.5647 (2)	0.6248 (2)	−0.0353 (2)	0.0671 (9)
H17A	0.5510	0.5708	−0.0693	0.081*
C18	0.6268 (2)	0.6219 (2)	0.0482 (2)	0.0548 (7)
H18A	0.6559	0.5670	0.0711	0.066*
C19	0.64380 (18)	0.70427 (17)	0.09634 (18)	0.0424 (6)
C20	0.70351 (18)	0.72266 (17)	0.18602 (18)	0.0410 (6)
C21	0.73122 (19)	0.92826 (18)	0.31429 (18)	0.0431 (6)
H21A	0.6889	0.9679	0.2775	0.052*
C22	0.78360 (18)	0.96064 (18)	0.40036 (18)	0.0427 (6)
C23	0.77697 (19)	1.04350 (18)	0.44577 (18)	0.0459 (7)
C24	0.84164 (19)	1.03703 (18)	0.53147 (18)	0.0445 (6)
C25	0.88558 (19)	0.94941 (19)	0.53462 (18)	0.0456 (7)
C26	0.7110 (3)	1.1225 (2)	0.4113 (2)	0.0739 (10)
H26A	0.7200	1.1722	0.4554	0.111*
H26B	0.7277	1.1432	0.3524	0.111*
H26C	0.6433	1.1026	0.4040	0.111*
C27	0.9577 (2)	0.9025 (2)	0.6054 (2)	0.0626 (8)

Table 2: (continued)

Atom	x	y	z	<i>U</i> _{iso} */ <i>U</i> _{eq}
H27A	0.9756	0.9433	0.6570	0.094*
H27B	0.9282	0.8476	0.6266	0.094*
H27C	1.0158	0.8863	0.5781	0.094*
C28	0.8566 (2)	1.1081 (2)	0.60262 (19)	0.0515 (7)
C29	0.9363 (3)	1.1472 (2)	0.7538 (2)	0.0764 (10)
H29A	0.8781	1.1467	0.7857	0.092*
H29B	0.9463	1.2096	0.7326	0.092*
C30	1.0226 (3)	1.1172 (3)	0.8167 (3)	0.1053 (14)
H30A	1.0327	1.1580	0.8693	0.158*
H30B	1.0120	1.0555	0.8377	0.158*
H30C	1.0799	1.1182	0.7847	0.158*
C31	0.9549 (3)	0.6582 (3)	0.3924 (3)	0.0990 (14)
H31A	0.9934	0.6870	0.3495	0.149*
H31B	0.9287	0.6008	0.3668	0.149*
H31C	0.9961	0.6469	0.4503	0.149*

particular, fluorescein hydrazones with pyrrole- and pyridine-2-aldehyde have been reported as fluorescent probes for the turn-on detection of Cu²⁺ ions [6, 7]. Herein, we report the crystal structure of the title compound derived from fluorescein hydrazide and a substituted pyrrole-2-aldehyde, namely ethyl 2,4-dimethyl-5-formylpyrrole-3-carboxylate, which is also an intermediate of the anticancer drug of Sunitinib [8].

The asymmetric unit contains a neutral hydrazone molecule in a ring-closed form and a methanol molecule. The C20=O4 bond distance is 1.236(3) Å, indicating the keto form of the amide. The bond length of C21–N2 is 1.275(3) Å, suggesting the existence of the Schiff base C=N moiety. All bond lengths are in the expected ranges and comparable with those of reported fluorescein hydrazones [7, 9–11]. The dihedral angle between the least-square plane of the benzamide and pyrrole is 11.09°.

The crystal packing features numerous O–H...O and N–H...O hydrogen bonds, generating a two-dimensional network parallel to the *bc* plane, and incorporates the crystal methanol molecule.

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References

1. Bruker. *SMART and SAINT*. Bruker AXS Inc.: Madison, Wisconsin, USA, 2007.
2. Sheldrick G. M. SHELXT—Integrated space-group and crystal-structure determination. *Acta Crystallogr.* 2015, A71, 3–8.

3. Sheldrick G. M. Crystal structure refinement with *SHELX*. *Acta Crystallogr.* 2015, *C71*, 3–8.
4. Chen X. Q., Pradhan T., Wang F., Kim J. S., Yoon J. Fluorescent chemosensors based on spiroring-opening of xanthenes and related derivatives. *Chem. Rev.* 2012, *112*, 1910–1956.
5. Rahman A. F. M. M., Park S.-E., Kadi A. A., Kwon Y. Fluorescein hydrazones as novel nonintercalative topoisomerase catalytic inhibitors with low DNA toxicity. *J. Med. Chem.* 2014, *57*, 9139–9151.
6. Bao X. F., Cao Q. S., Wu X. L., Shu H., Zhou B. J., Geng Y. L., Zhu J. Design and synthesis of a new selective fluorescent chemical sensor for based on a pyrrole moiety and a fluorescein conjugate. *Tetrahedron Lett.* 2016, *57*, 942–948.
7. Huo F.-J., Yin C.-X., Yang Y.-T., Su J., Chao J.-B., Liu D. S. Ultraviolet–visible light (UV–Vis)-reversible but fluorescence-irreversible chemosensor for copper in water and its application in living cells. *Anal. Chem.* 2012, *84*, 2219–2223.
8. Zou H. B., Zhang L., Ouyang J. F., Giulianotti M. A., Yu Y. P. Synthesis and biological evaluation of 2-indolinone derivatives as potential antitumor agents. *Eur. J. Med. Chem.* 2011, *46*, 5970–5977.
9. Ghosh A., Nandi S., Sengupta A., Chattopadhyay A., Lohar S., Das D. Single crystal X-ray structurally characterized palladium(II) selective fluorescence and colorimetric indicator for human breast cancer cell imaging. *Inorg. Chim. Acta.* 2015, *436*, 52–56.
10. Hyman L. M., Stephenson C. J., Dickens M. G., Shimizu K. D., Franz K. J. Toward the development of prochelators as fluorescent probes of copper-mediated oxidative stress. *Dalton Trans.* 2010, *39*, 568–576.
11. Yuan J., Cheng D. Crystal structure of (E)-3',6'-bis(ethylamino)-2',7'-dimethyl-2-((pyridin-2-ylmethylene)amino)spiro[isindoline-1,9'-xanthen]-3-one, $C_{32}H_{31}N_5O_2$. *Z. Kristallogr. NCS* 2019, *234*, 149–151.