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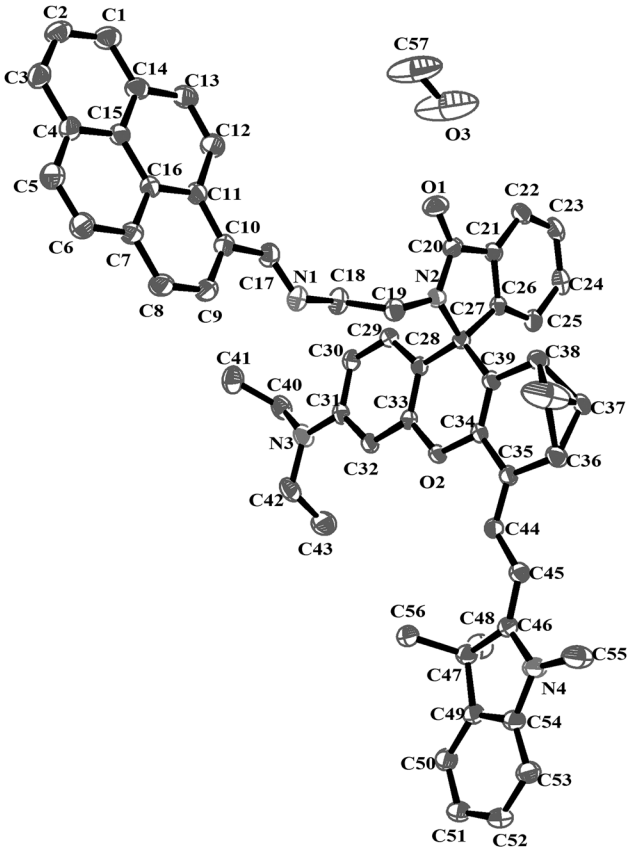
Crystal structure of [(E)-6′-(diethylamino)-2-(2-(((E)-pyren-1-ylmethylene)amino)ethyl)-4′-(2-((E)-1,3,3-trimethylindolin-2-ylidene)ethylidene)-1′,2′,3′,4′-tetrahydrospiro[isoindoline-1,9′-xanthen]-3-one]-methanol, solvate $C_{57}H_{56}N_4O_3$



Abstract

$C_{57}H_{56}N_4O_3$, monoclinic, $P2_1/c$ (no. 14), a = 10.1943(2) Å, b = 25.1257(4) Å, c = 18.6057(3) Å, β = 105.462(2)°, Z = 4, V = 4593.16(14) Å^3 R_{gt}(F) = 0.0603, $wR_{ref}(F^2)$ = 0.1869, T = 173(10) K.

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The molecular structure is shown in the figure. Table 1 contains the crystallographic data. The list of the atoms including atomic coordinates and displacement parameters can be found in the cif-file attached to this article.

1 Source of materials

All reagents were used without further purification. The title compound was synthesized via a four-step process as described in the literature.[5–7]

Synthesis of intermediate 1: Under ice-bath conditions, cyclohexanone (0.99 mL, 4.8 mmol) was carefully dripped into concentrated sulfuric acid (10.0 mL). Subsequently, 4-diethylaminolevulinic acid (1.50 g, 4.8 mmol) was slowly added under vigorous stirring. After addition, the mixture was heated to 363 K and maintained about 4 h to promote the reaction. Then, the reaction mixture was cooled and poured

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Table 1: Data collection and handling.

Crystal:	Clear light yellow block
Size:	0.20 × 0.15 × 0.10 mm
Wavelength:	Cu $K\alpha$ radiation (1.54184 Å)
μ:	0.59 mm^{-1}
Diffractometer, scan mode:	Rigaku SuperNova, ω scan
θ_{max}, completeness:	65.1°, 99 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	29090, 7712, 0.029
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 6,280
$N(param)_{refined}$:	593
Programs:	Rigaku,[1] Olex2,[2] SHELX[3,4]

into crushed ice (100.0 g). When perchloric acid (1.5 mL, 70 %) was added, a red precipitate appeared immediately, which was filtered, washed with cold water for three times and air-dried to yield a red solid, yielding 80 %, named intermediate 1. Intermediate 1 was used without further purification.

Synthesis of intermediate 2: Equimolar amounts of intermediate 1 (1.25 g, 3.33 mmol) and 2-(1,3,3–trimethylindolin-2-ylidene)acetaldehyde (0.67 g, 3.33 mmol) were successively dissolved in acetic anhydride (20.0 mL) and stirred for 30 min at room temperature. The reaction was promptly quenched by cooling it to 273 K. Then, the crude product was filtered and purified by column chromatography, ethanol-dichloromethane (CH_2Cl_2/CH_3CH_2OH = 200:1~20:1 v/v) as the gradient eluent. At last, a dark green solid was obtained, named intermediate 2, yielding 42 %.

Synthesis of intermediate 3: Intermediate 2 (1.2 g, 2.15 mmol), PyBOP (1.4 g, 2.68 mmol) and ethylenediamine (1.07 mL, 16 mmol) were successively dissolved in dichloromethane (25 mL). And then, the mixture was stirred 10 h at room temperature. Next, the mixture was distilled under reduced pressure to obtain the crude product. Purification was performed by column chromatography, using ethanol-dichloromethane (CH_2Cl_2/CH_3CH_2OH = 200:1~50:1 v/v) as the gradient eluent. A yellow powder was collected, which was identified as intermediate 3, yielding 30 %.

Synthesis of the title compound: Intermediate 3 (0.42 g, 0.734 mmol) and 1-pyrenecarboxaldehyde (0.25 g, 1.1 mmol) were dissolved in ethanol (20 mL) and refluxed for 3 h, during which a yellow precipitate formed. Then, the precipitate was filtered and washed thoroughly with cold water for three times and purified through column chromatography using a mixture of ethanol and dichloromethane (CH_2Cl_2/CH_3CH_2OH = 200:1~50:1 v/v) as the eluent. The yellow powder was collected and labeled as the title compound, yielding 32 %.

2 Experimental details

The H atoms were added using riding models. Their U_{iso} values were set to 1.2 U_{eq} of the parent atoms.

3 Comment

Pyrene-based fluorophores constitute structurally versatile systems endowed with inherent chemical stability, extended radiative lifetimes, and superior quantum efficiencies. While extensive investigations have established their prominence in visible-range sensing applications, systematic exploration of near-infrared (NIR) emissive pyrene derivatives remains limited.[8–10] Expanding the π-conjugated system drives NIR fluorophore design. Yuan et al. pioneered xanthene-hemicyanine hybrids inducing bathochromism via extended conjugation, advancing NIR dyes.[11–13] Building on this, we engineered pyrene-integrated hemicyanine-xanthene fluorophores with NIR emission.[14] However, The study found that this dye exhibits low sensitivity in metal ion binding. Prompting structural optimization through precise modulation of the xanthene-pyrene interchromophoric distance. This rational design approach yielded the title compound. Cu^{2+} homeostasis dysfunction, implicated in Alzheimer's, Parkinson's, and Wilson's diseases, drives demand for specific probes.[15] Given the potential of the title compound to bind selectively to Cu^{2+}, it may act as a valuable Cu^{2+} probe, facilitating the visualization of copper dynamics *in vivo* and offering critical insights for disease diagnosis and therapeutic intervention.

The title compound crystallizes within the monoclinic system, belonging to the space group $P2_1/c$. The asymmetric unit of the title compound comprises a title neutral molecule and a methanol molecule. The bond lengths and angles within the crystal structure are within normal ranges. The disordered treatment was applied to the C37, revealing a statistical coexistence of two conformational states with refined occupancies of 0.837(11) and 0.163(11), respectively. Notably, the dihedral angles between the xanthene and pyrene moieties in the current structure are measured at 83.0°, and the dihedral angle between the plane of the spirolactam and the pyrene plane is merely 22.3°. In contrast, angular parameters for the previously synthesized analogs were reported as 68.6° (xanthene-pyrene) and 26.3° (spirolactam-pyrene),[14] demonstrating substantial conformational modifications in the newly designed compound. This implies that the coordination of the N and O atoms on the title compound with copper ions may trigger the ring-opening of the spirolactam, thereby conferring the compound with the ability to release near-infrared fluorescence.[16] The C17=N1 bond distance, measured as 1.255(4) Å, aligns well with the C=N double bond length of Schiff bases as reported in the literature.[12,14]

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