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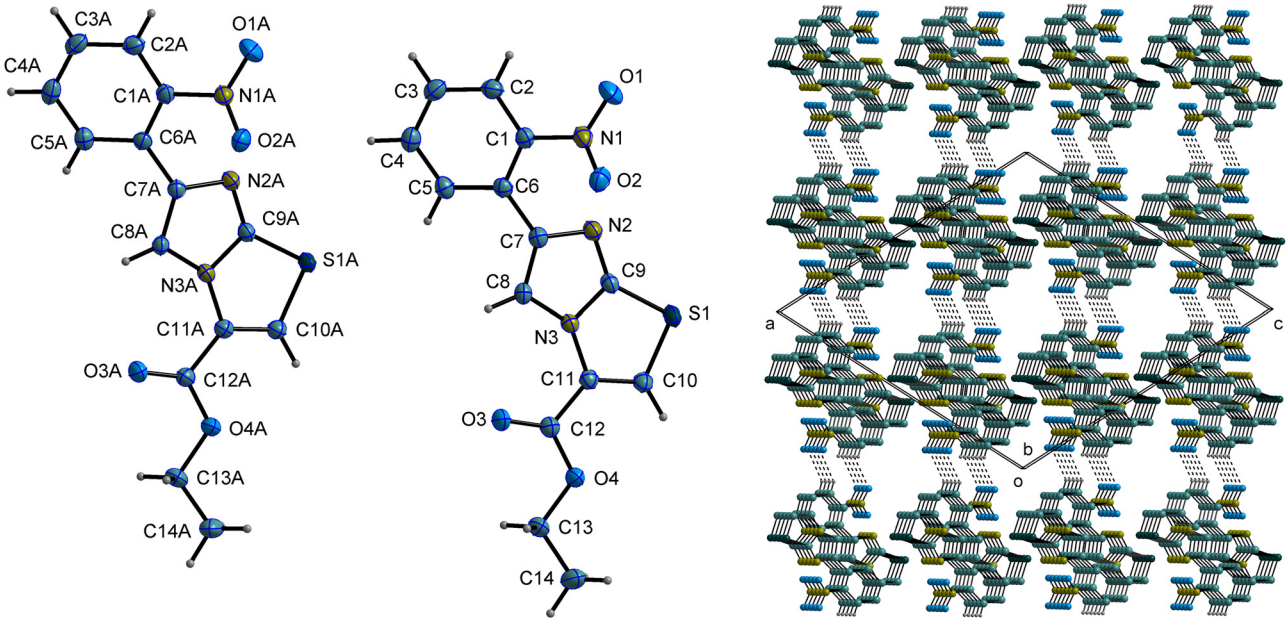
The crystal structure of ethyl 6-(2-nitrophenyl) imidazo[2,1-*b*]thiazole-3-carboxylate, $C_{14}H_{11}N_3O_4S$



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Abstract

$C_{14}H_{11}N_3O_4S$, monoclinic, $P2_1/n$ (no. 14), a = 20.6433(8) Å, b = 6.9795(3) Å, c = 20.9482(8) Å, β = 112.440(1)°, V = 2789.67(19) Å^3, Z = 8, $R_{gt}(F)$ = 0.0344, $wR_{ref}(F^2)$ = 0.0972, T = 170 K.

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Table 1: Data collection and handling.

Crystal:	yellow block
Size:	0.48 × 0.26 × 0.19 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.26 mm^{-1}
Diffractometer, scan mode:	Bruker D8 Venture, φ and ω scans
θ_{max}, completeness:	27.1°, 100 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	45938, 6145, 0.036
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 5,351
$N(param)_{refined}$:	399
Programs:	Bruker,[1] Olex2,[2] SHELX.[3,4]

1 Source of materials

A representative purification of the crude title compound was performed as follows: Ethyl 6-(2-nitrophenyl)imidazo-[2,1-*b*]thiazole-3-carboxylate (0.3 g, 1 mmol) was dissolved in dichloromethane and washed with water under stirring for 10 min. After phase separation, the organic layer was treated with activated charcoal and filtered through a sand core funnel. Following an additional phase separation, the organic layer was concentrated under reduced pressure until precipitation occurred. The resulting viscous solid was dissolved in n-hexane and filtered in an ice-water bath,

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yielding a yellow solid upon evaporation that was suitable for single crystal growth (Table 1).

The suitable single crystals for X-ray diffraction were obtained through the slow evaporation method.

n–Hexane solvent was added dropwise to the clean crystal growth tube containing the title compound. Care was taken to achieve near saturation of the solution. The crystal growth tube was then covered with aluminum foil, which was perforated with a needle to allow for ventilation. Subsequently, the crystal growth tube was placed in a dark cabinet to facilitate the slow evaporation of the n–hexane solvent.

During this equilibration process, yellow crystalline particles of the title compound were formed within approximately one week, and a suitable crystal was selected for X-ray crystallography.

2 Experimental details

U_{iso} values of hydrogen atoms were set to $1.2U_{eq}$ of the parent atoms for all C(H) groups, C(H,H) groups, and $1.5U_{eq}$ for all C(H,H,H) groups.

Secondary hydrogen atoms, were refined using riding coordinates. The phenyl hydrogen atoms, along with the imidazo[2,1-b]thiazole hydrogen atoms, wer refined as aromatic hydrogen using riding coordinates. The methyl hydrogen atoms, C14(H14A, H14B, H14C) and C14A(H14D, H14E, H14F), were refined as a idealized rotating group.

3 Comment

The title compound, a derivative of imidazothiazoles, is a high-value pharmaceutical intermediate for the synthesis of various drugs.[5]

The synthesis method of the title compound has been reported in the literature.[6,7]

The structural determination of the title compounds containing the moiety of heterocyclic imidazothiazole has been documented in several publications.[8–10]

As part of our ongoing research interest on the structure-activity relationship about the antimicrobial agent, and understanding of hydrogen bonding schemes of related compounds,[11–14] this study presents the first successful preparation of single crystals of the title compound and provides a determination of its structure.

The asymmetric unit comprises two molecules of ethyl 6-(2-nitrophenyl)imidazo[2,1-*b*]thiazole-3-carboxylate (*cf.* left part of the figure).

The two molecules are indeed independent in the asymmetric unit.

First, the two molecules exhibit slightly different spatial conformations. The angle between the ring planes S1–C9–N3–C11–C10 and C9–N2–C7–C8–N3 is measured at 4.06(7)°, while in another molecule, the corresponding angle is 2.85(7)°. And, the angle between the eight-membered ring plane S1–N2–N3–C7–C8–C9–C10–C11 and the phenyl ring plane C1–C2–C3–C4–C5–C6 is 39.36(5)°. In contrast, in another molecule, this corresponding angle is 38.97(5)°.

Furthermore, the crystallographic independence of the two molecules in the asymmetric unit was confirmed by PLATON,[15,16] analysis. The ADDSYM routine, which searches for additional symmetry elements, found no missed or pseudo symmetry that could relate these two molecules. The analysis confirmed that the $P2_1/n$ space group is correct and complete, with no higher symmetry possible. This crystallographic evidence, combined with the distinct conformational differences between the two molecules, conclusively proves that these are indeed two crystallographically independent molecules.

In the title compound molecule, the imidazo[2,1-*b*]thiazole moiety and the 2-nitrophenyl moiety form an interesting case of atropisomerism due to restricted rotation around the single bond (C6–C7) connecting them.

Our calculation using MM2 force field method,[17] shows the rotation energy barriers of the title compound is about 22 kcal/mol. According to literature,[18,19] the interconversion half life of this atropisomers is about 0.2 h. That means this atropisomers are usually used as mixture. But in our crystal prepared, only one atropisomeric enantiomer is present, because crystal packing forces may favor one atropisomer over another in the crystal solid state.

No classic hydrogen bonds were identified. However, two C–H···O nonclassic hydrogen interactions were observed (*cf.* right part of the figure. Some hydrogen atoms and ethyl carboxylate group are omitted for clarity).

These two hydrogen bonds (C2···O1A′ = 3.3250(19) Å′ = 2-*x*, 1-*y*, 2-*z*), and(C2A···O1″ = 3.2934(19) Å″ = 2-*x*, 1-*y*, 2-*z*) connect molecules in alternation layers together.

The imidazothiazole and phenyl ring planes arrange themselves in a layered configuration along the *ac*-plane of the crystal lattice.

Simultaneously, multiple π-π weak interactions between imidazothiazole and phenyl rings form a chain-like structure that connects the molecules along the *b*-axis.

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