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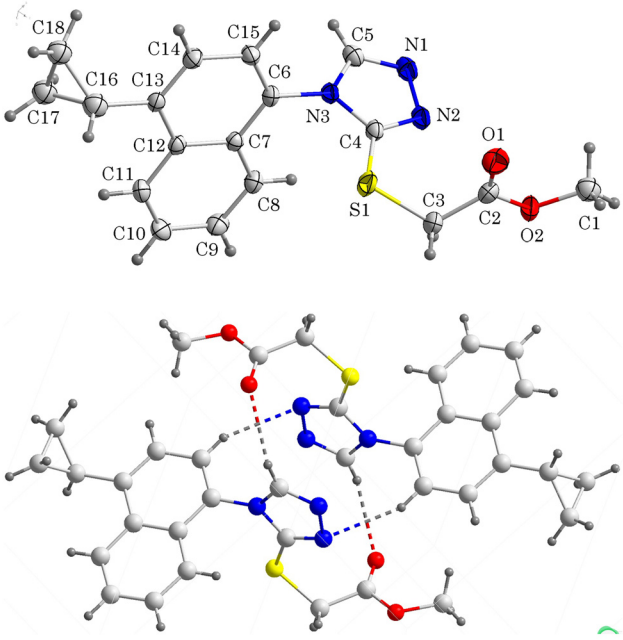
Synthesis and crystal structure of methyl 2-{[4-(4-cyclopropyl-1-naphthyl)-4*H*-1,2,4-triazole-3-yl]thio} acetate, $C_{18}H_{17}N_3O_2S$



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Abstract

$C_{18}H_{17}N_3O_2S$, monoclinic, $P2_1/c$ (no. 14), a = 10.9713(5) Å, b = 15.4445(8) Å, c = 9.8221(4) Å, β = 98.275(4)°, V = 1646.99(13) Å^3, Z = 4, $R_{gt}(F)$ = 0.0401, $wR_{ref}(F^2)$ = 0.0990, T = 296(2) K.

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Table 1: Data collection and handling.

Crystal:	Yellow block
Size:	0.23 × 0.17 × 0.14 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.21 mm^{-1}
Diffractometer, scan mode:	D8/APEX2, φ and ω
θ_{max}, completeness:	25.0°, >99 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	9313, 2906, 0.019
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 2430
$N(param)_{refined}$:	226
Programs:	Bruker [1], SHELX [2, 3], Diamond [4]

Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

1 Source of materials

Intermediate 4-(4-cyclopropylnaphthalen-1-yl)-2,4-dihydro-3H-1,2,4-triazole-3-thione (45.0 g, 0.169 mol) and triethylamine (18.7 g, 0.183 mol) of were added into absolute ethanol (400 mL) at room temperature. Cooling to 0 °C, dropping 150 mL of absolute ethanol solution of ethyl bromoacetate (29.6 g, 0.18 mol), and controlling the temperature to 0 °C for 1 h after dropping. Most of the solvent was evaporated under reduced pressure, and the reaction solution was poured into 250 mL of water, extracted with dichloromethane (100 mL × 3), and the organic layers were combined. Wash with 200 mL water and 200 mL saturated sodium chloride solution, and dry the organic layer with anhydrous sodium sulfate. 52.4 g yellow oil product was obtained with a yield of 88.2 %.

2 Experimental details

All H atoms were included in calculated positions and refined as riding atoms, with C–H = 0.90–0.97 Å with U_{iso}(H) = 1.5 U_{eq}(C) for methyl H atoms and 1.2 U_{eq}(C) for all other H atoms.

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	1.1379 (2)	0.1369 (2)	1.5252 (3)	0.0835 (9)
H1A	1.1233	0.1180	1.6145	0.125*
H1B	1.1824	0.0930	1.4838	0.125*
H1C	1.1853	0.1894	1.5342	0.125*
C2	1.0259 (2)	0.17954 (14)	1.3117 (2)	0.0481 (5)
C3	0.8980 (2)	0.2046 (2)	1.2460 (2)	0.0571 (6)
C4	0.85857 (17)	0.07197 (13)	1.06705 (18)	0.0389 (4)
C5	0.83748 (17)	−0.05848 (13)	0.9907 (2)	0.0430 (5)
H5	0.8198	−0.1059	0.9329	0.052*
C6	0.75820 (16)	0.05789 (12)	0.82003 (18)	0.0349 (4)
C7	0.63682 (15)	0.09122 (11)	0.81232 (17)	0.0322 (4)
C8	0.56984 (17)	0.08977 (12)	0.92520 (19)	0.0396 (5)
H8	0.6058	0.0666	1.0088	0.048*
C9	0.45342 (18)	0.12197 (14)	0.9127 (2)	0.0470 (5)
H9	0.4103	0.1200	0.9876	0.056*
C10	0.39791 (18)	0.15789 (14)	0.7888 (2)	0.0500 (5)
H10	0.3188	0.1807	0.7822	0.060*
C11	0.45914 (17)	0.15966 (13)	0.6774 (2)	0.0432 (5)
H11	0.4212	0.1838	0.5954	0.052*
C12	0.57983 (16)	0.12522 (11)	0.68472 (18)	0.0342 (4)
C13	0.64333 (16)	0.12171 (11)	0.56667 (18)	0.0349 (4)
C14	0.75834 (17)	0.08656 (13)	0.58105 (19)	0.0417 (5)
H14	0.7990	0.0834	0.5044	0.050*
C15	0.81785 (17)	0.05486 (13)	0.70790 (19)	0.0414 (5)
H15	0.8970	0.0321	0.7149	0.050*
C16	0.58272 (18)	0.15701 (13)	0.43202 (18)	0.0414 (5)
H16	0.5770	0.2203	0.4283	0.050*
C17	0.4766 (2)	0.11063 (16)	0.3497 (2)	0.0597 (6)
H17A	0.4519	0.0554	0.3840	0.072*
H17B	0.4098	0.1454	0.3029	0.072*
C18	0.5974 (2)	0.11506 (18)	0.2987 (2)	0.0682 (7)
H18A	0.6040	0.1524	0.2207	0.082*
H18B	0.6461	0.0625	0.3019	0.082*
H3A	0.834 (2)	0.1770 (16)	1.292 (2)	0.071 (8)*
H3B	0.894 (2)	0.2632 (18)	1.252 (3)	0.075 (8)*
N1	0.88388 (15)	−0.06394 (12)	1.11983 (18)	0.0506 (5)
N2	0.89793 (15)	0.02069 (12)	1.16988 (16)	0.0467 (4)
N3	0.81796 (13)	0.02530 (10)	0.95072 (15)	0.0373 (4)
O1	1.11751 (16)	0.18538 (12)	1.26099 (17)	0.0684 (5)
O2	1.02109 (14)	0.15273 (11)	1.43938 (14)	0.0606 (4)
S1	0.86185 (6)	0.18445 (4)	1.06464 (5)	0.0578 (2)

3 Comment

Lesinurad sodium is the first inhibitor of uric acid selective reabsorption transporter-1 (URAT1), which was first developed by Aread Biosciences and then continued to be developed by Astra Zeneca [5]. The chemical name of lesinurad sodium is 2-{[5-bromo-4-(4-cyclopropylnaphthalene-1-yl)-4h-1,2,4-triazol-3-yl]thio} acetic acid, which is mainly used for treating hyperuricemia related to gout in combination with xanthine oxidase inhibitors (such as allopurinol and febuxostat) [6–8]. Optimizing the synthesis process of lesinurad sodium and its derivatives has attracted the attention of researchers [9–11]. Recently, we have been focusing on the synthesis of esinurad sodium and optimizing its synthesis process. Here we reveal the synthesis and crystal structure of methyl 2-{[4-(4-cyclopropyl-1-naphthyl)-4H-1,2,4-triazole-3-yl]thio} acetate, the key intermediate of lesinurad sodium.

In the molecules of the title structure bond lengths and angles are very similar to those given in the literature [12–15]. In the title structure, the dihedral angle formed by the naphthalene ring plane, the 1,2,4-triazole-3-thione plane and the cyclopropyl group plane are 54.6°, 71.5(73)° and 86.9°, respectively. These parameters are different from the data reported before [13]. The dihedral angle between the 1,2,4-triazole-3-thione plane and the ester plane to which it is connected is 89.0(213)°. The torsion angles of N2–C4–S1–C3 and C4–S1–C3–C2 are –12.798(207)° and 69.286(186)°. Intermolecular C–H···O hydrogen bonds and C–H···N hydrogen bonds connect two adjacent compounds into a dimer.

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Conflict of interest: The authors declare no conflicts of interest regarding this article.

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