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Crystal structure of methyl (*E*)-*N*²-((3-methylquinolin-8-yl)sulfonyl)-*N*^{ω'}-nitro-*L*-argininate - ethanol (1/1), C₁₉H₂₈N₆O₇S

Table 1: Data collection and handling.

Crystal:	Block, colorless
Size:	0.31 × 0.25 × 0.22 mm
Wavelength:	Cu Kα radiation (1.54184 Å)
μ:	1.69 mm ⁻¹
Diffractometer, scan mode:	XtaLAB Synergy R, ω-scans
θ _{max} , completeness:	75.5°, >99%
<i>N</i> (<i>hkl</i>) _{measured} , <i>N</i> (<i>hkl</i>) _{unique} , <i>R</i> _{int} :	21113, 4394, 0.019
Criterion for <i>I</i> _{obs} , <i>N</i> (<i>hkl</i>) _{gt} :	<i>I</i> _{obs} > 2 σ(<i>I</i> _{obs}), 4350
<i>N</i> (<i>param</i>) _{refined} :	302
Programs:	CrysAlis ^{PRO} [1], SHELX [2, 3], DIAMOND [4]

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Abstract

C₁₉H₂₈N₆O₇S, monoclinic, *P*₂₁ (no. 4), *a* = 8.1573(1) Å, *b* = 17.4823(1) Å, *c* = 9.1162(1) Å, β = 116.432(1)°, *V* = 1164.14(2) Å³, *Z* = 2, *R*_{gt}(*F*) = 0.0273, *wR*_{ref}(*F*²) = 0.0732, *T* = 170(2) K.

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The crystal 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.

Source of materials

Procedures for preparation of methyl (*E*)-*N*²-((3-methylquinolin-8-yl)sulfonyl)-*N*^{ω'}-nitro-*L*-argininate was adapted from the reported paper [5, 6]. Sodium carbonate (3.64 g, 34.3 mmol) was added to a solution of methyl *N*^{ω'}-nitro-*L*-argininate (4.00 g, 17.15 mmol) in water (40 mL) under stirring. The mixture was stirred for 1 hour at 0 °C. Then a solution of 3-methylquinoline-8-sulfonyl chloride

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}
S1	0.85986(6)	0.37651(3)	0.28561(5)	0.01876(12)
O1	−0.3533(3)	0.65911(14)	0.2025(3)	0.0560(6)
O2	−0.1375(3)	0.71613(14)	0.4088(3)	0.0587(6)
O3	0.4740(3)	0.50527(11)	−0.0885(2)	0.0422(5)
O4	0.4055(2)	0.38181(11)	−0.09722(18)	0.0349(4)
O5	0.7888(2)	0.31740(9)	0.3507(2)	0.0295(4)
O6	1.0424(2)	0.40402(9)	0.38129(17)	0.0259(3)
N1	−0.1905(3)	0.66482(12)	0.3028(3)	0.0348(5)
N2	−0.0780(3)	0.61244(11)	0.2883(3)	0.0285(4)
N3	0.1913(3)	0.66470(11)	0.5140(2)	0.0260(4)
H3A	0.310183	0.660562	0.574524	0.031*
H3B	0.130377	0.702112	0.532039	0.031*
N4	0.1968(2)	0.55826(11)	0.3690(2)	0.0260(4)
H4	0.136362	0.526289	0.288289	0.031*
N5	0.7264(2)	0.45014(10)	0.2511(2)	0.0177(3)
H5	0.772961	0.495832	0.285517	0.021*
N6	0.9252(2)	0.46816(11)	0.0431(2)	0.0210(4)
C1	0.1039(3)	0.61466(13)	0.3957(3)	0.0222(4)
C2	0.3924(3)	0.54635(15)	0.4655(3)	0.0282(5)
H2A	0.418771	0.533680	0.579716	0.034*
H2B	0.458811	0.594000	0.467202	0.034*
C3	0.4586(3)	0.48193(14)	0.3938(3)	0.0254(5)
H3C	0.392153	0.434450	0.393306	0.030*
H3D	0.590448	0.473106	0.464781	0.030*
C4	0.4304(3)	0.49857(14)	0.2203(3)	0.0245(4)
H4A	0.478211	0.550216	0.216572	0.029*
H4B	0.297741	0.498226	0.145188	0.029*

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Table 2 (continued)

Atom	x	y	z	U_{iso}^*/U_{eq}
C5	0.5270(3)	0.43976(12)	0.1620(2)	0.0204(4)
H5A	0.495451	0.387321	0.185175	0.024*
C6	0.4652(3)	0.44737(12)	−0.0218(2)	0.0224(4)
C7	0.3542(5)	0.3810(2)	−0.2722(3)	0.0489(7)
H7A	0.250333	0.415568	−0.329160	0.073*
H7B	0.319561	0.328988	−0.314719	0.073*
H7C	0.458239	0.398010	−0.290296	0.073*
C8	0.8428(3)	0.34286(12)	0.0965(2)	0.0208(4)
C9	0.7882(3)	0.26874(14)	0.0494(3)	0.0320(5)
H9	0.758353	0.235960	0.117108	0.038*
C10	0.7769(4)	0.24199(17)	−0.1011(4)	0.0435(6)
H10	0.740243	0.190735	−0.134014	0.052*
C11	0.8181(4)	0.28883(17)	−0.1994(3)	0.0405(6)
H11	0.812147	0.269419	−0.298963	0.049*
C12	0.8694(3)	0.36586(14)	−0.1558(3)	0.0277(5)
C13	0.9044(3)	0.41828(17)	−0.2564(3)	0.0331(5)
H13	0.901724	0.401232	−0.356423	0.040*
C14	0.9418(3)	0.49288(16)	−0.2117(3)	0.0321(5)
C15	0.9493(3)	0.51471(14)	−0.0593(3)	0.0262(5)
H15	0.973543	0.566946	−0.028566	0.031*
C16	0.8826(3)	0.39381(12)	−0.0049(2)	0.0203(4)
C17	0.9782(4)	0.5516(2)	−0.3143(3)	0.0499(8)
H17A	1.106181	0.568157	−0.257881	0.075*
H17B	0.897657	0.595800	−0.331460	0.075*
H17C	0.954292	0.529222	−0.420509	0.075*
O7	0.5473(3)	0.65204(13)	0.8022(2)	0.0552(6)
H7	0.547795	0.625940	0.879771	0.083*
C18	0.6725(5)	0.7570(2)	0.7241(5)	0.0571(9)
H18A	0.549594	0.775887	0.651662	0.086*
H18B	0.713903	0.722315	0.662988	0.086*
H18C	0.757169	0.800328	0.765271	0.086*
C19	0.6675(4)	0.71484(18)	0.8660(4)	0.0485(7)
H19A	0.791700	0.696663	0.941559	0.058*
H19B	0.623675	0.749152	0.927502	0.058*

(746 g, 30.87 mmol) in tetrahydrofuran (40 mL) was added and the mixture was warmed up to room temperature and stirred for 4 hours.

The crude residue was purified by flash column chromatography with an appropriate eluting solvent system. Off-white, **Yield**, 85%. **¹H NMR** (400 MHz, DMSO) δ 8.86 (d, J = 2.2 Hz, 1H), 8.27 (s, 1H), 8.21 (dd, J = 7.3, 1.3 Hz, 1H), 8.17 (dd, J = 8.3, 1.2 Hz, 1H), 7.90 (d, J = 8.5 Hz, 1H), 7.72–7.64 (m, 1H), 4.36–4.26 (m, 1H), 3.18 (s, 3H), 3.11–2.99 (m, 2H), 2.53 (s, 3H), 1.72–1.33 (m, 5H), 1.23 (s, 2H). **¹³C NMR** (101 MHz, CDCl₃): δ 171.34, 159.25, 153.11, 141.17, 135.66, 135.52, 133.08, 132.36, 129.51, 128.66, 125.52, 55.71, 52.13, 40.35, 30.19, 24.33, 18.74. **HR-MS**(ESI⁺) m/z calcd. for C₁₇H₂₃N₆O₆S [M + H]⁺: 439.1400, Found: 439.1422 (M + H); **IR** (cm^{−1}): 3408(w), 3295(w), 3250(w), 1737(s), 1623(s), 1596(s), 1538(w), 1418(m), 1331(m), 1253(s), 1221(m), 1160(s), 1138(m), 1008(w), 937(w), 886(w), 770(m), 679(m), 582(s), 536(m), 489(w).

The ethanol solvate was synthesized by the following procedure. An amount of 1 mmol methyl(*E*)-N²-((3-methylquinolin-8-yl)sulfonyl)-N^ω'-nitro-*L*-argininate was dissolved in a mixed solvent of 5 mL absolute ethanol and 1 mL dichloromethane, then the solution was stayed in room temperature for slow evaporation. Colorless crystals were formed after three days. **Yield**: 80%.

Experimental details

The structure was solved with the ShelXT [2] structure solution program and refined with the XL [3] refinement package. The positions of the hydrogen atoms were generated geometrically. The figure was drawn by Diamond 4.0 [4].

Comment

The title compound is an important intermediate for the thrombin inhibitor argatroban. Argatroban was synthesized in 1970 [7]. The crystal structure of this intermediate is benefit to understand the reaction mechanism. Two related structures were found in the CSD: One is Nη-nitro-*L*-arginine methyl ester hydrochloride, and the other is *L*-nitroargininium picrate [8, 9].

The asymmetric unit contains one title molecule and one ethanol. The bond lengths and angles within these moieties are in the expected ranges. The S1–N5 distance is 1.6237(17) Å. The C5–N5 distance is 1.470(3) Å. Viewing nitroguanidine part closer. For C–N bond, the distance of C1–N2, C1–N3, C1–N4 is 1.367(3) Å, 1.324(3) Å and 1.330(3) Å, respectively. For N–N bond, the distance of N1–N2 is 1.344(3) Å.

There are four intermolecular hydrogen bonds: N3–H3A···O7 (dN···O = 2.932(1) Å; ∠NHO = 153°, " = 1 − x; +¹/₂ + y; 1 − z), N4–H4···N6 (dN···N = 3.218(1) Å; ∠NHN = 165°, " = −1 + x; y; z), N5–H5···N2 (dN···N = 3.198(1) Å; ∠NHN = 157°, " = 1 + x; y; z) and O7–H7···O3 (dO···O = 2.909(1) Å; ∠OHO = 136°, " = 1 − x; −¹/₂ + y; −z). Intermolecular hydrogen bonds extend the structure to a three dimensional framework.

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