Synthesis and Structure of (*E*)-1-(3-Methylsulfanyl-1,2,4-triazin-5-yl)-ethanone *O*-Acryloyl Oxime[†]

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The title compound, C₉H₁₀N₄O₂S, crystallizes in the triclinic system, space group *P* $\bar{1}$, with cell constants *a* = 7.5330(2) Å, *b* = 7.9138(3) Å, *c* = 10.2635(3) Å, α = 109.313(1)°, β = 101.626(1)°, γ = 90.405(1)° and *Z* = 2. The oxime group adopts a *trans* conformation, while the acryloyl group is in a *cis* conformation. The molecular packing is influenced by the C–H...N intermolecular hydrogen bonds and π – π interactions.

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The reaction of 1,2,4-triazines with alkyl nitronate anions has shown considerable synthetic utility, and allows a highly efficient entry into oximes of alkyl (1,2,4-triazin-5-yl) ketones.¹ The latter may serve as common intermediates in the construction of pyrazolo[4,3-*e*][1,2,4]triazines,² 2-acylpyridines and 3-acyl-5,6,7,8-tetrahydroisoquinolines, valuable precursors for the synthesis of sempervirine, and its analogues,³ possessing interesting pharmacological activity. In view of the wide application of the 1,2,4-triazine oximes in organic synthesis, unequivocal assignments of their stereochemistry became indispensable. The configuration of alkyl-1,2,4-triazin-5-yl ketooximes was determined previously by means of ¹H-NMR, ¹³C-NMR, and homonuclear NOE-difference spectroscopy.⁴ Oximes resulting from reaction of 1,2,4-triazines with nitronate anions were found to be either pure *E*-isomers or *E/Z*-mixture with the amount of *E*-isomer greatly predominating. Here, we have extended this study to a single-crystal X-ray diffraction structure of 1-(3-methylsulfanyl)-1,2,4-triazin-5-yl)ethanone *O*-acryloyl oxime, simply obtained by the reaction of 3-bromopropanoyl chloride with oxime of 5-acetyl-3-methylsulfanyl-1,2,4-triazine in the presence of triethylamine. Attempts to obtain mono crystals of the oximes of alkyl (1,2,4-triazin-5-yl)ketones suitable for X-ray analysis, failed.

5-Acetyl-3-methylsulfanyl-1,2,4-triazine was prepared as a reference.⁴ (*E*)-1-(3-Methylsulfanyl)-1,2,4-triazin-5-yl)-ethanone *O*-acryloyl oxime was synthesized according to the

following procedure: to a solution of oxime of 5-acyl-3-methylsulfanyl-1,2,4-triazine (1.5 mmol) and triethylamine (4.5 mmol) in dry CH₂Cl₂ (5 mL) at –40°C was added the acid chloride (1.5 mmol) in CH₂Cl₂ (2 mL), dropwise. The reaction mixture was allowed to warm to room temperature and stirred for 12 h. It was then washed with water (2 × 10 mL), saturated aqueous sodium bicarbonate (3 × 10 mL), brine (1 × 10 mL) and dried over MgSO₄. Removal of the solvent yielded a crude product, which was then purified by column chromatography on silica gel using CH₂Cl₂/hexane mixture (2:1) as an eluent. Yield, 81%; m.p., 99–100°C. ¹H NMR (CDCl₃) δ : 2.48 (s,

Table 1 Crystal and experimental data

Formula: C ₉ H ₁₀ N ₄ O ₂ S
Formula weight = 238.27
Crystal size (mm): 0.50 × 0.20 × 0.20
Crystal system: triclinic
Space group: <i>P</i> $\bar{1}$ <i>Z</i> = 2
<i>a</i> = 7.5330(2) Å α = 109.313(1)°
<i>b</i> = 7.9138(3) Å β = 101.626(1)°
<i>c</i> = 10.2635(3) Å γ = 90.405(1)°
<i>V</i> = 563.78(3) Å ³
<i>D</i> _x = 1.404 g/cm ³
Radiation: Mo <i>K</i> _α
No. of reflections measured = 12926
No. of reflections used = 2623
No. of parameters = 145
<i>R</i> = 0.0363
($\Delta\rho$) _{max} = 0.000
($\Delta\rho$) _{max} = 0.287 e Å ^{–3}
($\Delta\rho$) _{max} = –0.237 e Å ^{–3}
Measurement: Bruker SMART APEX II CCD
Program system: Bruker SMART
Structure determination: direct methods (SIR92)
Refinement: full matrix least-squares (SHELXL97)

CCDC 653814 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Fig. 1 Structural chemical diagram.

[†] Part 39 in a series “1,2,4-Triazines in Organic Synthesis”. For part 38, see M. Mojzych and A. Rykowski, *Heterocycles*, **2007**, *71*, 2449.

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Table 2 Final atomic coordinates ($\times 10^4$) and equivalent isotropic temperature factors ($\text{\AA}^2 \times 10^3$)

Atom	x	y	z	U_{eq}^*
S(1)	1849(1)	708(1)	9178(1)	72(1)
O(13)	-2900(1)	5136(1)	4581(1)	47(1)
O(17)	-3284(2)	8093(2)	5526(1)	78(1)
N(1)	1963(2)	5757(2)	9463(1)	58(1)
N(2)	2291(2)	4245(2)	9785(1)	55(1)
N(4)	388(2)	2477(1)	7567(1)	46(1)
N(12)	-1736(1)	5330(1)	5901(1)	44(1)
C(3)	1500(2)	2710(2)	8836(1)	47(1)
C(5)	56(2)	3964(2)	7288(1)	41(1)
C(6)	872(2)	5630(2)	8263(2)	52(1)
C(11)	-1184(2)	3815(2)	5920(1)	41(1)
C(14)	-3583(2)	6733(2)	4542(1)	46(1)
C(15)	-4692(2)	6455(2)	3124(1)	50(1)
C(16)	-5375(2)	7797(2)	2773(2)	61(1)
C(18)	-1628(2)	2031(2)	4780(1)	53(1)
C(31)	3280(3)	1429(3)	10913(2)	89(1)

$$U_{\text{eq}}^* = (1/3) \sum_i \sum_j U_{ij} (a_i^* a_j^*) (a_i a_j)$$

Table 3 Selected bond distances ($\text{\AA}$), angles ($^\circ$), and torsion angles ($^\circ$)

O(13)-C(14)	1.3776(15)	C(5)-C(11)	1.4898(16)
O(13)-N(12)	1.4176(13)	C(11)-C(18)	1.4887(16)
O(17)-C(14)	1.1894(17)	C(14)-C(15)	1.4704(18)
N(12)-C(11)	1.2771(16)	C(15)-C(16)	1.307(2)
C(14)-O(13)-N(12)	112.07(9)	O(17)-C(14)-O(13)	123.57(12)
C(11)-N(12)-O(13)	110.45(10)	O(17)-C(14)-C(15)	127.29(13)
N(12)-C(11)-C(18)	128.25(12)	O(13)-C(14)-C(15)	109.14(10)
N(12)-C(11)-C(5)	112.13(10)	C(16)-C(15)-C(14)	121.36(13)
C(18)-C(11)-C(5)	119.63(11)		
C(31)-S(1)-C(3)-N(2)	1.55(15)	O(13)-N(12)-C(11)-C(5)	179.57(8)
O(17)-C(14)-C(15)-C(16)	5.5(2)		

3H), 2.72 (s, 3H), 6.07 – 6.10 (d, 1H, $J = 10.5$ Hz), 6.30 – 6.39 (dd, 1H, $J = 10.5$ Hz), 6.65 – 6.70 (d, 1H, $J = 17.5$ Hz), 9.64 (s, 1H). ^{13}C NMR (CDCl_3) δ : 11.51, 13.98, 125.60, 133.77, 141.95, 150.98, 160.80, 162.45, 173.75; HR-MS (m/z) for $\text{C}_9\text{H}_{11}\text{N}_4\text{O}_2\text{S}$: 239.0619 [$\text{M}^+ + \text{H}$]; Calcd. 239.0603. Yellowish prism crystals suitable for X-ray diffraction analysis were grown by the slow evaporation of an ethanol solution. X-ray data were collected by graphite-monochromatized Mo K_α radiation at 293 K, ω scans. The structure was solved by direct methods and refined by a full-matrix least-squares method with anisotropic temperature factors for non-H atoms. All hydrogen atoms were fixed geometrically and treated as riding on their parent C atoms, with C–H = 0.93 or 0.96 $\text{\AA}$ and with $U_{\text{iso}} = 1.5U_{\text{eq}}(\text{C})$. Details of the crystal data and a structure refinement and selected geometrical parameters are given in Tables 1, 2 and 3. A view of the molecule with numbering of the atoms is shown in Fig. 2.

Fig. 2 ORTEP III drawing of the title compound with atom labeling. The thermal ellipsoids are drawn at the 50% probability level.

The 1,2,4-triazine (A), acetyloxime (B) and acryloyl (C) groups are planar to within 0.010(1), 0.016(1) and 0.019(1) $\text{\AA}$, respectively. The dihedral angles between the mean planes of these groups are: A/B = 19.45(5) $^\circ$, A/C = 17.03(8) $^\circ$ and B/C = 5.09(7) $^\circ$. The double N12–C11 bond of 1.2771(16) $\text{\AA}$ is characteristic of an oxime group [1.281(13) $\text{\AA}$ for $\text{Csp}^2=\text{N}(2)$ in oximes⁵] and C–O bonds clearly distinguish between single and double bonds. The remaining bond lengths and angles are within the expected ranges. The title molecule has a chain-extended conformation. The oxime group adopts a *trans* conformation (*E*-configuration) with a torsion angle, O13–N12–C11–C5, of 179.57(8) $^\circ$, while the acryloyl group is in *s-cis* conformation [O17–C14–C15–C16 = 5.5(2) $^\circ$]. The methylthio substituent lies almost in the plane of the triazine ring; the torsion angle, N2–C3–S1–C31, is 1.55(15) $^\circ$.

The molecular packing in the crystal structure of the title compound is influenced by the intermolecular C16–H162 $\cdots$ N1⁽ⁱ⁾ hydrogen-bond linking molecules into molecular chains along the [101] direction; C16–H162=0.93, H162 $\cdots$ N1=2.55, C16 $\cdots$ N1 = 3.427(2) $\text{\AA}$, C16–H162 $\cdots$ N1 = 157 $^\circ$ and (i) = 1 + x, y, 1 + z. Additionally, the triazine rings belonging to inversion-related molecules partially overlap each other with a centroid-to-centroid separation of 3.6815(7) $\text{\AA}$ and a $\pi\cdots\pi$ distance of 3.340 $\text{\AA}$, comparable to a van der Waals distance about 3.4 $\text{\AA}$ for the overlapping π aromatic systems.

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