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REACTIONS OF 1,3,5-TRIAZINYL-NITROFORMALDOXIMES. 1. INTERACTION OF 1,3,5-TRIAZINYLNITROFORMALDOXIMES WITH DICARBONYL COMPOUNDS

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Addition of enolates of dicarbonyl compounds to 1,3,5-triazinylnitrile oxides, prepared in situ from 2-R-4-R[1]-1,3,5-triazin-6-ylnitroformaldoximes, led to the formation of 3,4,5-trisubstituted isoxazoles. The X-ray crystal structure of 4-ethoxycarbonyl-3-(2'-methoxy-5-methyl-4'-pyrrolidinyl-1,3,5-triazin-6'-yl)-5-isoxazole is described.

Keywords: enolates of dicarbonyl compounds, 1,3,5-triazinylnitroformaldoximes, 1,3,5-triazinylnitrile oxides, 3,4,5-trisubstituted isoxazoles.

Nitroformaldoximes (nitrolic acids) can be the sources of highly reactive nitrile oxides. Two routes are used for the generation nitrile oxides: elimination of nitrous acid on heating nitroformaldoximes or deprotonation in the presence of strong bases with subsequent elimination of a nitrite ion. Nitrile oxides formed *in situ* may dimerize to furoxanes [1], undergo 1,3-dipolar cycloaddition with various dipolarophiles [2-4], and add to various reagents (amines, alcohols) [5, 6]. The unique example of the reaction of nitrile oxides with the enolates of acetyl- and benzoylacetone is described elsewhere [1].

We have studied the reactions of 2-R-4-R[1]-1,3,5-triazin-6-ylnitroformaldoximes **1a-f** with acetylacetone and ethyl acetoacetate in the presence of a base.

The reaction occurred in an aqueous medium in the presence of 2 mol of sodium hydroxide and finished with the formation of 4-acetyl-5-methyl-3-(2-R-4-R[1]-1,3,5-triazin-6-yl)isoxazoles **2a-f** and 4-ethoxycarbonyl-5-methyl-3-(2-R-4-R[1]-1,3,5-triazin-6-yl)isoxazoles **3a-e** with yields of 55-75%. The 1,3,5-Triazinylnitrile oxides are formed by deprotonation of the nitroformaldoximes starting materials with subsequent loss of a nitrite anion. In accordance with the attack of the carbanion of the dicarbonyl compound on the carbon atom of the nitrile oxide and the oxygen atom of the nitrile oxide on the carbon atom of the acetyl group ring closure to

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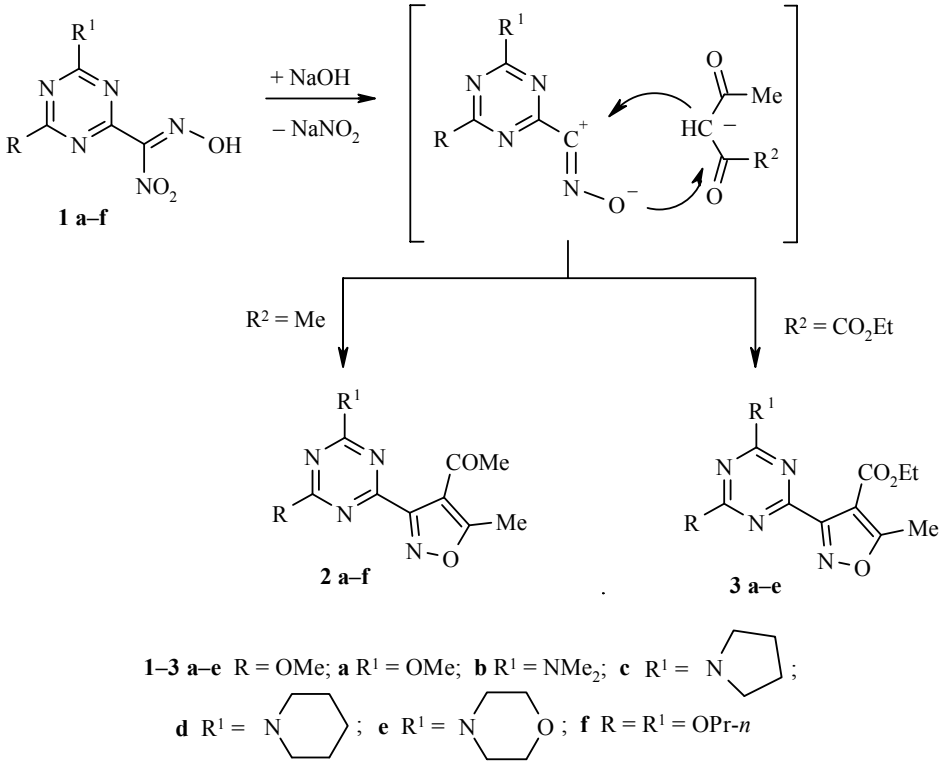
the 3,4,5-trisubstituted isoxazole occurred by [3+2] cycloaddition. In the ^{1}H NMR spectra of the isoxazoles **2a-f** and **3a-e** the signal of the methyl group in position 5 of the isoxazole appears as singlet in the 2.64-2.74 ppm range. The range of the absorptions of the carbonyl group in the isoxazoles **2a-f** is found in the range 1677-1693 cm^{-1} and in the isoxazoles **3a-e** in the 1720-1730 cm^{-1} interval.



Thus 1,3,5-triazinylnitroformaldoximes, present as their synthetic equivalents the 1,3,5-triazinylnitrile oxides, can be starting materials for the synthesis 3,4,5-trisubstituted isoxazoles with a 1,3,5-triazine ring at position 3.

The structure of isoxazole **3c** was confirmed by X-ray crystallography. The asymmetric part of the unit cell of the crystal of compound **3c** contains two independent molecules **3cA** and **3cB** (Fig. 1).

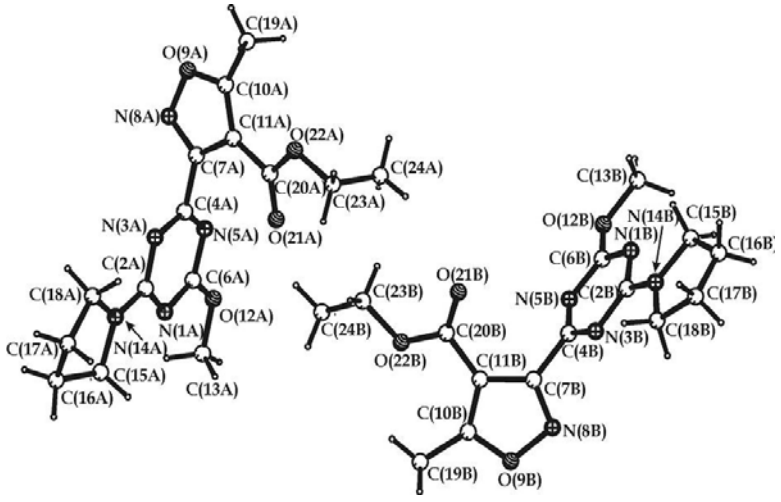


Fig. 1. Geometry of the Molecules of Compound **3c** in the Crystal.

Table 1. Bond Lengths (*d*) in Compound **3c**

Bond	*d*, Å	Bond	*d*, Å
O(21A)–C(20A)	1.198(5)	N(5B)–C(4B)	1.329(4)
O(22A)–C(20A)	1.332(5)	N(5B)–C(6B)	1.346(4)
O(22A)–C(23A)	1.509(6)	N(3B)–C(4B)	1.326(4)
C(23A)–C(24A)	1.411(8)	N(3B)–C(2B)	1.352(4)
C(2A)–N(14A)	1.325(4)	N(1B)–C(6B)	1.310(4)
C(2A)–N(3A)	1.353(4)	N(1B)–C(2B)	1.356(4)
C(2A)–N(1A)	1.354(4)	C(4B)–C(7B)	1.490(4)
C(4A)–N(3A)	1.321(4)	C(6B)–O(12B)	1.331(4)
C(4A)–N(5A)	1.321(4)	C(2B)–N(14B)	1.329(4)
C(4A)–C(7A)	1.499(4)	C(7B)–N(8B)	1.305(4)
C(6A)–N(1A)	1.316(4)	C(7B)–C(11B)	1.420(4)
C(6A)–O(12A)	1.332(4)	C(10B)–O(9B)	1.344(4)
C(6A)–N(5A)	1.342(4)	C(10B)–C(11B)	1.365(4)
O(12A)–C(13A)	1.439(4)	C(10B)–C(19B)	1.485(4)
C(7A)–N(8A)	1.293(5)	C(11B)–C(20B)	1.469(5)
C(7A)–C(11A)	1.417(5)	O(9B)–N(8B)	1.404(4)
C(11A)–C(10A)	1.357(5)	C(20B)–O(21B)	1.204(4)
C(11A)–C(20A)	1.464(5)	C(20B)–O(22B)	1.324(4)
C(10A)–O(9A)	1.334(5)	O(22B)–C(23B)	1.460(6)
C(10A)–C(19A)	1.485(5)	C(23B)–C(24B)	1.436(7)
O(9A)–N(8A)	1.419(4)	C(13B)–O(12B)	1.437(4)
N(14A)–C(15A)	1.463(4)	C(15B)–N(14B)	1.457(4)
N(14A)–C(18A)	1.465(4)	C(15B)–C(16B)	1.466(7)
C(15A)–C(16A)	1.517(6)	C(18B)–N(14B)	1.471(5)
C(18A)–C(17A)	1.499(6)	C(18B)–C(17B)	1.495(6)
C(16A)–C(17A)	1.514(7)	C(16B)–C(17B)	1.396(8)

The geometric parameters of molecules **3cA** and **3cB** differ very slightly: the bond lengths by 0.01-0.1 Å (Table 1) and the valence angles by -0.1 to 2° (Table 2). The greatest differences are observed in the geometry of the ethoxycarbonyl units at C(11A) and C(11B) of the isoxazole ring, especially for the torsion angles C(10)–C(11)–C(20)–O(21) and C(20)–O(22)–C(23)–C(24) (Table 3). Yet another difference between molecules **3cA** and **3cB** is connected with the conformation of the pyrrolidine ring. In molecule **3cA** a *twist* conformation is formed (atoms C(16) and C(17) are displaced by -0.361(5) and 0.202(5) Å respectively from the planar unit N(14)–C(15)–C(18)) while molecule **3cB** has a C-*envelope* conformation (fragment N(14)–C(15)–C(17)–C(18) is planar within limits of 0.005(4) Å, while atom C(16) is displaced from the plane by -0.158(9) Å).

The triazine and isoxazole rings in molecules **3cA** and **3cB** are planar (triazine in **3cA** within limits of 0.010(3), the triazine in **3cB** within limits of 0.006(4), the isoxazole in **3cA** within limits of 0.003(3), and the isoxazole in **3cB** within limits of 0.003(3) Å).The atoms of the methoxy group O(12)C(13) and the methyl atom C(19) lie practically in the plane of the corresponding heterocycles. The bonds C(2A)–N(14A), C(2B)–N(14B), C(6A)–O(12A), and C(6B)–O(12B) are strongly shortened (1.325-1.335 Å) which is a consequence of conjugation of the unshared electron pairs of the heteroatoms with the π-system of the 1,3,5-triazine. The dihedral angle between the planes of the triazine and isoxazole rings for molecules **3cA** is 84.0(2)° and for molecules **3cB** is 64.1(2)°.

It should be noted that formation of classical hydrogen bonds is not possible, but there are interactions of the type C-H···O both within and between molecules (parameters given in Table 4). Their aggregation leads to the combination of **3c** molecules into ribbons along the ($11\bar{1}$) direction of the crystal (Fig. 2).

Table 2. Valence Angles (ω) in Compound **3c**

Angle	ω, deg	Angle	ω, deg
C(20A)–O(22A)–C(23A)	117.2(3)	C(15A)–N(14A)–C(18A)	112.4(3)
C(24A)–C(23A)–O(22A)	106.9(5)	N(14A)–C(15A)–C(16A)	102.2(3)
N(14A)–C(2A)–N(3A)	117.6(3)	N(14A)–C(18A)–C(17A)	104.2(3)
N(14A)–C(2A)–N(1A)	118.2(3)	C(17A)–C(16A)–C(15A)	104.8(3)
N(3A)–C(2A)–N(1A)	124.2(3)	C(18A)–C(17A)–C(16A)	103.8(3)
N(3A)–C(4A)–N(5A)	128.4(3)	C(4B)–N(5B)–C(6B)	112.6(3)
N(3A)–C(4A)–C(7A)	113.8(3)	C(4B)–N(3B)–C(2B)	113.3(3)
N(5A)–C(4A)–C(7A)	117.8(3)	C(6B)–N(1B)–C(2B)	114.3(3)
N(1A)–C(6A)–O(12A)	119.3(3)	N(3B)–C(4B)–N(5B)	127.9(3)
N(1A)–C(6A)–N(5A)	127.2(3)	N(3B)–C(4B)–C(7B)	117.0(3)
O(12A)–C(6A)–N(5A)	113.5(3)	N(5B)–C(4B)–C(7B)	115.1(3)
C(4A)–N(5A)–C(6A)	112.3(3)	N(1B)–C(6B)–O(12B)	119.6(3)
C(6A)–N(1A)–C(2A)	114.3(3)	N(1B)–C(6B)–N(5B)	127.1(3)
C(4A)–N(3A)–C(2A)	113.6(3)	O(12B)–C(6B)–N(5B)	113.2(3)
C(6A)–O(12A)–C(13A)	117.5(3)	N(14B)–C(2B)–N(3B)	118.5(3)
N(8A)–C(7A)–C(11A)	112.3(3)	N(14B)–C(2B)–N(1B)	116.7(3)
N(8A)–C(7A)–C(4A)	119.8(3)	N(3B)–C(2B)–N(1B)	124.8(3)
C(11A)–C(7A)–C(4A)	127.7(3)	N(8B)–C(7B)–C(11B)	112.2(3)
C(10A)–C(11A)–C(7A)	104.3(3)	N(8B)–C(7B)–C(4B)	119.1(3)
C(10A)–C(11A)–C(20A)	131.4(3)	C(11B)–C(7B)–C(4B)	128.5(3)
C(7A)–C(11A)–C(20A)	124.3(3)	O(9B)–C(10B)–C(11B)	109.4(3)
O(9A)–C(10A)–C(11A)	109.3(3)	O(9B)–C(10B)–C(19B)	115.7(3)
O(9A)–C(10A)–C(19A)	115.5(4)	C(11B)–C(10B)–C(19B)	134.8(3)
C(11A)–C(10A)–C(19A)	135.1(4)	C(10B)–C(11B)–C(7B)	103.8(3)
C(10A)–O(9A)–N(8A)	109.3(3)	C(10B)–C(11B)–C(20B)	129.2(3)
C(7A)–N(8A)–O(9A)	104.8(3)	C(7B)–C(11B)–C(20B)	126.8(3)
O(21A)–C(20A)–O(22A)	122.8(4)	C(10B)–O(9B)–N(8B)	109.3(2)
O(21A)–C(20A)–C(11A)	123.9(4)	C(7B)–N(8B)–O(9B)	105.3(3)
O(22A)–C(20A)–C(11A)	113.2(3)	O(21B)–C(20B)–O(22B)	124.7(3)
C(2A)–N(14A)–C(15A)	124.4(3)	O(21B)–C(20B)–C(11B)	123.7(3)
C(2A)–N(14A)–C(18A)	123.3(3)	O(22B)–C(20B)–C(11B)	111.6(3)
C(20B)–O(22B)–C(23B)	117.4(3)	C(16B)–C(17B)–C(18B)	109.8(4)
C(24B)–C(23B)–O(22B)	108.6(4)	C(2B)–N(14B)–C(15B)	123.9(3)
N(14B)–C(15B)–C(16B)	103.5(3)	C(2B)–N(14B)–C(18B)	123.7(3)
N(14B)–C(18B)–C(17B)	102.5(3)	C(15B)–N(14B)–C(18B)	112.4(3)
C(17B)–C(16B)–C(15B)	110.5(4)	C(6B)–O(12B)–C(13B)	118.2(3)

Packing of the molecules in the crystals of compound **3c** is also stabilized by π-π interactions between the triazine rings of molecule **3cA** (parameters: distances between the centers of the rings d_c 3.68Å, angles between the rings α 0°, shortest distance between the planes of the angles $d\perp$ 3.39Å, symmetry operation 1-*x*, 2-*y*, -*z*), and the triazine rings of molecule **3cB** (parameters: d_c 3.52 Å, α 0°, $d\perp$ 3.33 Å, 1- *x*, -*y,* 1-*z*).

EXPERIMENTAL

IR spectra of KBr tablets were recorded on an Avatar 360ESP spectrometer. ^{1}H NMR spectra were recorded on Bruker AM-300 (300 MHz) and Bruker AC-200 (200 MHz) instruments in $CDCl_3$ (compounds **2a,b, e, f** and **3a-e**) and DMSO-d_6 solutions (compounds **2c,d**) with TMS as internal standard.

Table 3. Torsion Angles (θ) in Compound **3c**

Angle	θ, deg.	Angle	θ, deg.
C(20A)–O(22A)–C(23A)–C(24A)	92.8(6)	C(6B)–N(1B)–C(2B)–N(14B)	179.5(3)
N(3A)–C(4A)–N(5A)–C(6A)	-1.5(5)	C(6B)–N(1B)–C(2B)–N(3B)	-0.8(5)
C(7A)–C(4A)–N(5A)–C(6A)	177.9(3)	N(3B)–C(4B)–C(7B)–N(8B)	-65.3(4)
N(1A)–C(6A)–N(5A)–C(4A)	0.4(5)	N(5B)–C(4B)–C(7B)–N(8B)	113.8(4)
O(12A)–C(6A)–N(5A)–C(4A)	-179.3(3)	N(3B)–C(4B)–C(7B)–C(11B)	119.2(4)
O(12A)–C(6A)–N(1A)–C(2A)	-179.1(3)	N(5B)–C(4B)–C(7B)–C(11B)	-61.7(4)
N(5A)–C(6A)–N(1A)–C(2A)	1.3(5)	O(9B)–C(10B)–C(11B)–C(7B)	-0.4(3)
N(14A)–C(2A)–N(1A)–C(6A)	177.9(3)	C(19B)–C(10B)–C(11B)–C(7B)	177.8(4)
N(3A)–C(2A)–N(1A)–C(6A)	-2.1(4)	O(9B)–C(10B)–C(11B)–C(20B)	-175.2(3)
N(5A)–C(4A)–N(3A)–C(2A)	0.7(5)	C(19B)–C(10B)–C(11B)–C(20B)	3.0(6)
C(7A)–C(4A)–N(3A)–C(2A)	-178.7(3)	N(8B)–C(7B)–C(11B)–C(10B)	0.5(4)
N(14A)–C(2A)–N(3A)–C(4A)	-178.8(3)	C(4B)–C(7B)–C(11B)–C(10B)	176.2(3)
N(1A)–C(2A)–N(3A)–C(4A)	1.3(4)	N(8B)–C(7B)–C(11B)–C(20B)	175.5(3)
N(1A)–C(6A)–O(12A)–C(13A)	0.2(5)	C(4B)–C(7B)–C(11B)–C(20B)	-8.8(5)
N(5A)–C(6A)–O(12A)–C(13A)	179.9(3)	C(11B)–C(10B)–O(9B)–N(8B)	0.3(4)
N(3A)–C(4A)–C(7A)–N(8A)	-94.2(4)	C(19B)–C(10B)–O(9B)–N(8B)	-178.3(3)
N(5A)–C(4A)–C(7A)–N(8A)	86.4(4)	C(11B)–C(7B)–N(8B)–O(9B)	-0.3(4)
N(3A)–C(4A)–C(7A)–C(11A)	80.9(4)	C(4B)–C(7B)–N(8B)–O(9B)	-176.5(3)
N(5A)–C(4A)–C(7A)–C(11A)	-98.6(4)	C(10B)–O(9B)–N(8B)–C(7B)	0.0(4)
N(8A)–C(7A)–C(11A)–C(10A)	0.7(4)	C(10B)–C(11B)–C(20B)–O(21B)	157.1(4)
C(4A)–C(7A)–C(11A)–C(10A)	-174.7(3)	C(7B)–C(11B)–C(20B)–O(21B)	-16.6(5)
N(8A)–C(7A)–C(11A)–C(20A)	-179.2(4)	C(10B)–C(11B)–C(20B)–O(22B)	-22.3(5)
C(4A)–C(7A)–C(11A)–C(20A)	5.4(6)	C(7B)–C(11B)–C(20B)–O(22B)	164.0(3)
C(7A)–C(11A)–C(10A)–O(9A)	-0.6(4)	O(21B)–C(20B)–O(22B)–C(23B)	-3.1(6)
C(20A)–C(11A)–C(10A)–O(9A)	179.3(4)	C(11B)–C(20B)–O(22B)–C(23B)	176.2(4)
C(7A)–C(11A)–C(10A)–C(19A)	175.5(5)	C(20B)–O(22B)–C(23B)–C(24B)	165.4(5)
C(20A)–C(11A)–C(10A)–C(19A)	-4.6(8)	N(14B)–C(15B)–C(16B)–C(17B)	-10.6(9)
C(11A)–C(10A)–O(9A)–N(8A)	0.3(5)	C(15B)–C(16B)–C(17B)–C(18B)	11.7(10)
C(19A)–C(10A)–O(9A)–N(8A)	-176.6(4)	N(14B)–C(18B)–C(17B)–C(16B)	-7.6(8)
C(11A)–C(7A)–N(8A)–O(9A)	-0.5(5)	N(3B)–C(2B)–N(14B)–C(15B)	179.5(3)
C(4A)–C(7A)–N(8A)–O(9A)	175.3(3)	N(1B)–C(2B)–N(14B)–C(15B)	-0.8(5)
C(10A)–O(9A)–N(8A)–C(7A)	0.1(5)	N(3B)–C(2B)–N(14B)–C(18B)	2.6(5)
C(23A)–O(22A)–C(20A)–O(21A)	1.1(7)	N(1B)–C(2B)–N(14B)–C(18B)	-177.7(3)
C(23A)–O(22A)–C(20A)–C(11A)	178.7(4)	C(16B)–C(15B)–N(14B)–C(2B)	-171.6(5)
C(10A)–C(11A)–C(20A)–O(21A)	-171.3(4)	C(16B)–C(15B)–N(14B)–C(18B)	5.6(6)
C(7A)–C(11A)–C(20A)–O(21A)	8.6(7)	C(17B)–C(18B)–N(14B)–C(2B)	178.1(4)
C(10A)–C(11A)–C(20A)–O(22A)	11.2(7)	C(17B)–C(18B)–N(14B)–C(15B)	0.9(5)
C(7A)–C(11A)–C(20A)–O(22A)	-168.9(4)	N(1B)–C(6B)–O(12B)–C(13B)	1.9(5)
N(3A)–C(2A)–N(14A)–C(15A)	178.8(3)	N(5B)–C(6B)–O(12B)–C(13B)	-178.9(3)
N(1A)–C(2A)–N(14A)–C(15A)	-1.2(5)	C(2B)–N(3B)–C(4B)–N(5B)	0.5(5)
N(3A)–C(2A)–N(14A)–C(18A)	-0.2(5)	C(2B)–N(3B)–C(4B)–C(7B)	179.4(3)
N(1A)–C(2A)–N(14A)–C(18A)	179.7(3)	C(6B)–N(5B)–C(4B)–N(3B)	-0.1(5)
C(2A)–N(14A)–C(15A)–C(16A)	-165.1(3)	C(6B)–N(5B)–C(4B)–C(7B)	-179.0(3)
C(18A)–N(14A)–C(15A)–C(16A)	14.1(4)	C(2B)–N(1B)–C(6B)–O(12B)	-179.7(3)
C(2A)–N(14A)–C(18A)–C(17A)	-172.9(3)	C(2B)–N(1B)–C(6B)–N(5B)	1.3(5)
C(15A)–N(14A)–C(18A)–C(17A)	8.0(4)	C(4B)–N(5B)–C(6B)–N(1B)	-0.9(5)
N(14A)–C(15A)–C(16A)–C(17A)	-30.5(4)	C(4B)–N(5B)–C(6B)–O(12B)	-180.0(3)
N(14A)–C(18A)–C(17A)–C(16A)	-26.8(5)	C(4B)–N(3B)–C(2B)–N(14B)	179.7(3)
C(15A)–C(16A)–C(17A)–C(18A)	36.1(5)	C(4B)–N(3B)–C(2B)–N(1B)	0.0(5)

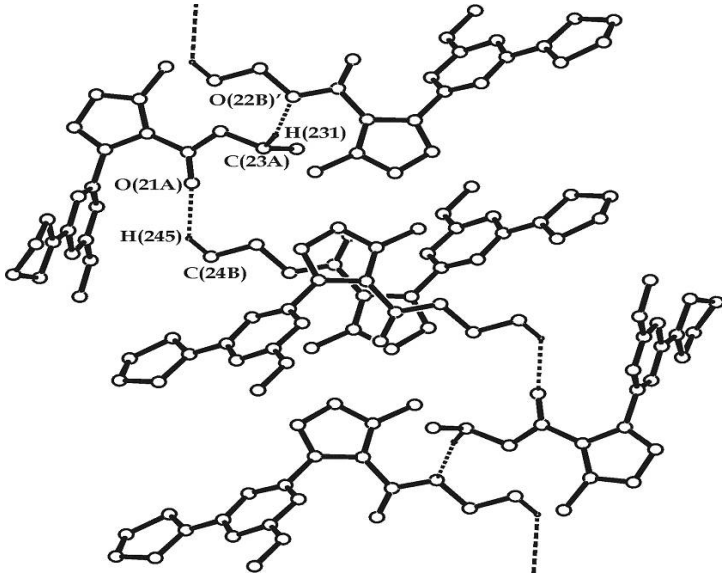


Fig. 2. Ribbons of molecules **3c** in the crystal, formed by C-H···O interactions. In the diagram only those hydrogen atoms taking part directly in this interaction are shown.

Table 4. Interaction Parameters in the Crystal of Compound **3c**

D–H···A	D–H, Å	H···A, Å	D···A, Å	DHA, deg.	Symmetry operation
C(23A)–H(231)···O(22B)	0.97	2.59	3.551(6)	170.7	1 + *x*, *y*, *z*
C(24B)–H(245)···O(21A)	0.96	2.57	3.290(8)	131.9	—
C(19B)–H(196)···O(22B)	0.96	2.44	3.035(5)	120.1	—

X-ray Crystallographic Analysis of Crystals of Compound 3c were carried out on a Bruker Smart APEX II CCD automatic diffractometer: graphite monochromator; λMoKα = 0.71073 Å; temperature 293 K; absorption corrections were carried semiempirically on equivalent reflexions using the SADABS program [8]. Treatment of the initial mass of experimental intensity data was carried out with the SAINT Plus program [10]. The structure was solved by direct methods and refined by full-matrix least-squares analysis in F^2 in the anisotropic approximation for non-hydrogen atoms. All calculations were carried out using the SHELXTL PLUS suite of programs [10]. Hydrogen atoms were placed in geometrically calculated positions and included in the refinement in the "riding" model. All diagrams and analysis of intermolecular interactions were carried out with the PLATON programs [11]. Atomic coordinates and structural parameters of compound **3c** have been deposited in the Cambridge Center for Crystal Structure Data (deposit no. CCDC 677330).

Crystals of compound **3c** grown from acetone were colorless transparent prisms, triclinic, $C_{15}H_{19}N_5O_4$, M 333.35, a = 8.6299(6), b = 11.9384(8), c = 16.774(1) Å, α = 89.504(1), β = 85.945(1), γ = 74.057(1)°, V = 1657.4(2) Å^3, d_{calc} = 1.34 g/cm^3, Z = 4, space group P-1. Scanning angle 2.1 < θ< 26.0°. 6389 Independent reflections were measured, 5122 with $I > 2\sigma(I)$. Calculations of absorptions were not carried out because they were so small, (μ(Mo) = 1.0 cm^{-1}). Final values of the divergence factors were R_{ob} = 0.089 and R_{wob} = 0.254 for 5122 reflexions.

Investigations of a monocrystal of compound **3c** were carried out in the X-ray Structural Section of the Collective Analitical Center of the Physicochemical Investigation of the Structure, Properties, and Composition of substances and Materials based on the A. E. Arbuzov Laboratory of Diffraction Methods of Investigation of Institute of Organic and Physical Chemistry, Kazan Scientific Center of the Russian Academy of Sciences.

Compounds 1a-f were synthesized by method [12].

4-Acetyl-3-(4,6-dimethoxy-1,3,5-triazin-2-yl)-5-methylisoxazole (2a). Acetylacetone (2.05 ml, 2 mmol) was added with stirring to a solution of sodium hydroxide (1.6 g, 4 mmol) in water (20 ml) at 20-25°C, and then compound **1a** (2.46 g, 1 mmol) was added. The reaction mixture was kept at 20-25°C with stirring until compound **1a** had disappeared (TLC, 1-1.5 h). At the end of the reaction, the precipitate of compound **2a** was filtered off, washed with water (5 ml) and dried in the air. Yield 1.90 g (72%); mp 152-153°C. IR spectrum, ν, cm^{-1}: 3026, 2966, 1681, 1560, 1525, 1475, 1440, 1396, 1371, 1267, 1224, 1199, 1109, 1082, 1016, 1002, 975, 931, 860, 825, 769. ^{1}H NMR spectrum, δ, ppm: 2.41 (3H, s, $COCH_3$); 2.69 (3H, s, CH_3); 4.11 (3H, s, OCH_3). Found, %: C 50.21; H 4.50; N 21.09. $C_{11}H_{12}N_4O_4$. Calculated, %: C 50.00; H 4.58; N 21.20.

4-Acetyl-3-(6-dimethylamino-4-methoxy-1,3,5-triazin-2-yl)-5-methylisoxazole (2b) was prepared analogously from compound **1b** (2.42 g, 1 mmol).Yield 1.80 g (65%); mp 101-102°C. IR spectrum, ν, cm^{-1}: 3029, 2960, 2933, 2875, 1679, 1598, 1571, 1533, 1500, 1475, 1444, 1369, 1259, 1241, 1199, 1079, 1054, 1004, 950, 887, 817, 617. ^{1}H NMR spectrum, δ, ppm: 2.35 (3H, s, $COCH_3$); 2.67 (3H, s, CH_3); 3.15 and 3.19 (6H, two s, NCH_3); 3.94 (3H, s, OCH_3). Found, %: C 52.05; H 5.59; N 25.16. $C_{12}H_{15}N_5O_3$. Calculated, %: C 51.98; H 5.45; N 25.26.

4-Acetyl-3-(4-methoxy-6-pyrrolidinyl-1,3,5-triazin-2-yl)-5-methylisoxazole (2c) was prepared analogously from compound **1c** (2.68 g, 1 mmol). Yield 2.06 g (68%); mp 113-115°C. IR spectrum, ν, cm^{-1}: 3012, 2993, 2946, 2883, 1681, 1585, 1568, 1529, 1460, 1444, 1371, 1342, 1259, 1220, 1178, 1157, 1080, 1035, 1010, 966, 950, 891, 854, 819, 761, 619. ^{1}H NMR spectrum, δ, ppm: 1.96 (6H, m, CH_2); 2.37 (3H, s, $COCH_3$); 2.64 (3H, s, CH_3); 3.53 (4H, m, NCH_2); 3.93 (3H, s, OCH_3). Found, %: C 55.32; H 5.74; N 23.02. $C_{14}H_{17}N_5O_3$. Calculated, %: C 55.44; H 5.65; N 23.09.

4-Acetyl-3-(4-methoxy-6-piperidino-1,3,5-triazin-2-yl)-5-methylisoxazole (2d) was prepared analogously from compound **1d** (2.82 g, 1 mmol). Yield 1.97 g (62%); mp 73-75°C. IR spectrum, ν, cm^{-1}: 3012, 2995, 2958, 2921, 2862, 1679, 1577, 1529, 1463, 1442, 1369, 1294, 1259, 1238, 1215, 1124, 1087, 1024, 993, 950, 885, 817, 619. ^{1}H NMR spectrum, δ, ppm: 1.59 (6H, m, CH_2); 2.35 (3H, s, $COCH_3$); 2.67 (3H, s, CH_3); 3.70 (4H, m, NCH_2); 3.92 (3H, s, OCH_3). Found, %: C 56.85; H 6.12; N 22.15. $C_{15}H_{19}N_5O_3$. Calculated, %: C 56.77; H 6.03; N 22.07.

4-Acetyl-3-(4-methoxy-6-morpholino-1,3,5-triazin-2-yl)-5-methylisoxazole (2e) was obtained analogously from compound **1e** (2.84 g, 1 mmol). Yield 2.39 g (75%); mp 120-122°C. IR spectrum, ν, cm^{-1}: 3018, 2983, 2962, 2923, 2869, 1693, 1581, 1560, 1527, 1467, 1438, 1367, 1305, 1272, 1228, 1110, 1087, 1068, 1026, 989, 921, 889, 852, 817, 765, 630, 538. ^{1}H NMR spectrum, δ, ppm: 2.34 (3H, $COCH_3$); 2.66 (3H, s, CH_3); 3.68 and 3.80 (8H, m, NCH_2CH_2O); 3.92 (3H, s, OCH_3). Found, %: C 52.53; H 5.48; N 21.79. $C_{14}H_{17}N_5O_4$. Calculated, %: C 52.66; H 5.37; N 21.93.

4-Acetyl-5-methyl-3-(4,6-di-*n*-propoxy-1,3,5-triazin-2-yl)isoxazole (2f) was prepared analogously from compound **1f** (2.85 g, 1 mmol). Yield 1.86 g (58%); mp 65-66°C. IR spectrum, ν, cm^{-1}: 2971, 2929, 2881, 1677, 1670, 1560, 1521, 1485, 1452, 1419, 1380, 1359, 1332, 1299, 1245, 1211, 1139, 1110, 1089, 1066, 999, 952, 931, 879, 827, 765, 622, 534. ^{1}H NMR spectrum, δ, ppm, (*J*, Hz): 1.03 (6H, t, J = 7.2, CH_3); 1.84 (4H, m, CH_2); 2.40 (3H, s, $COCH_3$); 2.69 (3H, s, CH_3); 4.44 (4H, m, OCH_2). Found, %: C 56.38; H 6.41; N 17.40. $C_{15}H_{20}N_4O_4$. Calculated, %: C 56.24; H 6.29; N 17.49.

Ethyl 3-(4,6-dimethoxy-1,3,5-triazin-2-yl)-5-methylisoxazol-4-ylcarboxylate (3a). Ethyl aceto-acetate (2.53 ml, 2 mmol) was added with stirring at 20-25°C to a solution of sodium hydroxide (1.6 g, 4 mmol) in water (20 ml) and then compound **1a** (2.46 g, 1 mmol) was added. The reaction mixture was kept at 20-25°C with stirring until the initial compound **1a** had disappeared (TLC, 1-1.5 h). At the end of the reaction, the precipitate of compound **3a** was filtered off, washed with water (5 ml) an dried in the air. Yield 1.62 g (55%); mp 91-95°C. IR spectrum, ν, cm^{-1}: 3035, 2985, 2964, 2883, 1727, 1554, 1529, 1492, 1467, 1450, 1400, 1355, 1346, 1267, 1240, 1217, 1193, 1107, 1068, 1020, 1006, 977, 939, 914, 860, 825, 788, 752, 692, 536, 478. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.20 (3H, t, J = 6.9, CH_3); 2.74 (3H, s, CH_3); 4.10 (3H, s, OCH_3); 4.23 (3H, q, J = 6.9, OCH_3). Found, %: C 48.93; H 4.95; N 19.12. $C_{12}H_{14}N_4O_5$. Calculated, %: C 48.98; H 4.80; N 19.04.

Ethyl 3-(4-methoxy-6-dimethylamino-1,3,5-triazin-2-yl)-5-methylisoxazol-4-ylcarboxylate (3b) was prepared analogously from compound **1b** (2.42 g, 1 mmol). Yield 2.30 g (75%); mp 111-113°C. IR spectrum, ν, cm^{-1}: 3031, 2995, 2964, 2929, 2877, 2806, 1730, 1591, 1498, 1473, 1457, 1415, 1363, 1268, 1244, 1201, 1130, 1109, 1080, 1055, 1024, 997, 917, 896, 840, 821, 790, 715, 675, 644, 540. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.21 (3H, t, *J* = 6.8, CH_3); 2.71 (3H, s, CH_3); 3.22 (6H, s, NCH_3); 3.99 (3H, s, OCH_3); 4.24 (3H, q, *J* = 6.8, OCH_2). Found, %: C 50.69; H 5.70; N 22.83. $C_{13}H_{17}N_5O_4$. Calculated, %: C 50.81; H 5.58; N 22.79.

Ethyl 3-(4-methoxy-6-pyrrolidino-1,3,5-triazin-2-yl)-5-methylisoxazol-4-ylcarboxylate (3c) was obtained analogously from compound **1c** (2.68 g, 1 mmol). Yield 2.30 g (69%); mp 121-123°C. IR spectrum, ν, cm^{-1}: 2975, 2877, 1729, 1596, 1583, 1568, 1527, 1498, 1452, 1365, 1342, 1269, 1247, 1224, 1187, 1168, 1112, 1076, 1020, 999, 966, 914, 817, 790, 675. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.21 (3H, t, *J* = 6.9, CH_3); 1.98 (4H, m, CH_2); 2.71 ((3H, s, CH_3); 3.64 (4H, t, *J* = 7.2, NCH_2); 3.99 (3H, s, OCH_3); 4.23 (3H, q, *J* = 6.9, OCH_2). Found, %: C 53.94; H 5.70; N 21.13. $C_{15}H_{19}N_5O_4$. Calculated, %: C 54.05; H 5.75; N 21.01.

Ethyl 3-(4-methoxy-6-piperidino-1,3,5-triazin-2-yl)-5-methylisoxazol-4-ylcarboxylate (3d) was prepared analogously from compound **1d** (2.82 g, 1 mmol). Yield 2.28 g (61%); mp 83-85°C. IR spectrum, ν, cm^{-1}: 3137, 2987, 2946, 2923, 2856, 1726, 1585, 1525, 1496, 1471, 1454, 1375, 1348, 1296, 1269, 1244, 1217, 1155, 1130, 1110, 1087, 1074, 1026, 987, 906, 881, 850, 817, 790, 742, 717, 684, 538, 497. ^{1}H NMR spectrum, δ, ppm *(J*, Hz): 1.21 (3H, t, *J* = 7.0, CH_3), 1.65 (6H, m, CH_2); 2.70 (3H, s, CH_3); 3.83 (4H, t, *J* = 6.0, NCH_2); 3.98 (3H, s, OCH_3); 4.22 (3H, q, *J* = 7.0, OCH_2). Found, %: C 55.47; H 6.20; N 20.00. $C_{16}H_{21}N_5O_4$. Calculated, %: C 55.32; H 6.09; N 20.16.

Ethyl 3-(4-methoxy-6-morpholino-1,3,5-triazin-2-yl)-5-methylisoxazol-4-ylcarboxylate (3e) was prepared analogously from compound **1e** (2.84 g, 1 mmol). Yield 2.31 g (66%); mp 94-96°C. IR spectrum, ν, cm^{-1}: 3002, 2979, 2958, 2927, 2869, 2846, 1720, 1579, 1535, 1504, 1469, 1448, 1375, 1350, 1303, 1278, 1244, 1224, 1132, 1112, 1080, 1028, 993, 885, 850, 839, 817, 792, 738, 677, 632, 540. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.23 (3H, t, *J* = 7.0, CH_3); 2.70 (3H, s, CH_3); 3.72 and 3.91 (8H, m, NCH_2CH_2O); 4.00 (3H, s, OCH_3); 4.23 (3H, q, *J* = 7.0, OCH_2). Found, %: C 51.66; H 5.42; N 20.18. $C_{15}H_{19}N_5O_5$. Calculated, %: C 51.57; H 5.48; N 20.05.

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