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SYNTHESIS AND CRYSTAL STRUCTURES DERIVATIVES OF N'-(ALKYLSULFANYL) CARBONYL) BENZOHYDROZIDE

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ABSTRACT

Alkylation of 5-aryl-1,3,4-oxadiazole-2-thiones with alkyl halides was carried out, where instead of the expected 2-alkylthio-5-aryl-1,3,4-oxadiazoles obtained N'-((alkylsulfanyl) carbonyl)benzohydrazides having a linear structure without an oxadiazole ring. By slow evaporation of solvents at room temperature were obtained crystals of N'-((ethylsulfanyl)carbonyl)-2-oxymethylbenzohydrazide **7** from ethanol, N'-((propylsulfanyl)carbonyl)benzohydrazide **8** from ethanol, N'-((pentylsulfanyl)carbonyl)benzohydrazide **9** from methanol:chloroform and N'-((hexylsulfanyl)carbonyl)benzohydrazide **10** from acetonitrile.

Keywords – Five-membered heterocycles, Oxadiazoles, N'-((alkylsulfanyl)carbonyl) benzohydrazides, X-ray analysis, Crystal structure.

1. INTRODUCTION

5-Substituted-1,3,4-oxadiazol-2-thiones interesting representatives of one five-membered heterocycles. Numerous compounds of this class show practical interest for researchers having a broad spectrum of biological activity, such as pesticide, antibiotic, anticancer, antihypertensive, antidepressant, analgesic, anti-inflammatory and others ¹⁻⁴. The presence in its molecule ambifunctional thioamide NH-C=S and other functional groups gives oxadiazolthiones to exhibit multiple reactivity whereby depending on the reaction conditions and the nature of the reagents can be prepared isomeric (S-, N-) products.

The 1,3,4-oxadiazole-2-thiones, which have a dual reactivity, belong to a very interesting group of five-membered heterocyclic compounds. Depending on the nature of the reacting compounds and the reaction conditions, the anions of these compounds can form two series of derivatives in interactions with electrophilic reagents. This ability of these compounds to react by two reaction centers is associated with the presence of the so-called "ambident" system, which forms a single conjugated system - in oxadiazole-2-thiones, this is the thioamide group NH-C=S ⁵.

Continuing the studies on the effect of the nature of the alkylating agent, the interaction conditions, and with the aim of expanding the series of alkyl derivatives of 5-aryl-1,3,4-oxadiazole-2-thiones, we carried out the alkylation of 5-phenyl- and 5-(2-

methoxyphenyl)-1,3,4-oxadiazole-2-thione 1,2 with alkyl halides (alkyl = ethyl, propyl, amyl, hexyl) under the conditions of the other oxadiazolinthions previously studied by us ^{6,7}, prove their structure and study crystal structures (Fig. 1.).

2. MATERIALS AND METHODS

The IR spectra of the synthesized compounds were taken on an IR System-2000 Fourier Transform spectrometer (Perkin-Elmer) in KBr tablets.

The unit cell parameters of the crystals are determined and refined with CCD Xcalibur Ruby diffractometer (Oxford Diffraction) using CuK α -radiation, graphite monochromator (T=293 K). The three-dimensional set of reflections received at the appropriate diffractometer.

3. RESULTS

3.1 Synthesis

3.1.1 Alkylation of 5-phenyl- and 5-(2-methoxyphenyl)-1,3,4-oxadiazole-2-thionones with 1,2-alkyl halides (General procedure):

A mixture of oxadiazolthione (1,2), haloalkyl and K₂CO₃ with 5 mmol each is boiled in 15 ml of dry acetone for 4-5 hours. The solvent is then removed from the mixture, the residue is dissolved in chloroform and washed with water, with a 10% solution of NaOH to remove thion residues, further washed with water until a neutral reaction. After evaporation, reaction products are obtained on a porcelain cup.

3.1.2 Crystal growth

By slow evaporation of solvents at room temperature were obtained crystals of N'-((ethylsulfanyl)carbonyl)-2-oxymethylbenzohydrazide **7** from ethanol, N'-((propylsulfanyl)carbonyl)benzohydrazide **8** from ethanol, N'-((pentylsulfanyl)carbonyl)benzohydrazide **9** from methanol:chloroform and N'-((hexylsulfanyl)carbonyl)benzohydrazide **10** from acetonitrile.

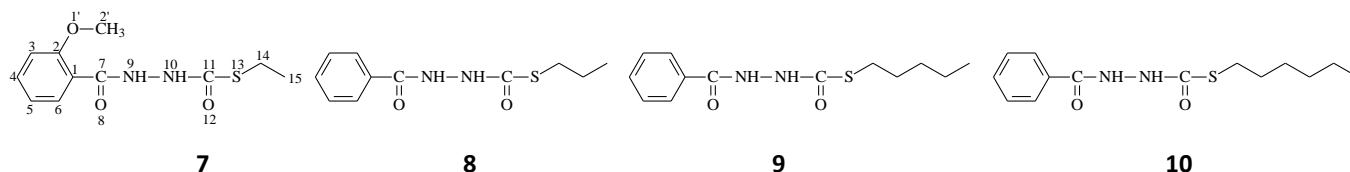


Fig. 1: Schematic formula and numbering of the atoms in the structures 7, 8, 9 and 10.

3.2 X-ray Structure Determination

The unit cell parameters of the crystals were determined and refined with CCD Xcalibur Ruby diffractometer (Oxford Diffraction) using CuK α -radiation, graphite monochromator (T=293 K). The three-dimensional set of reflections received at the appropriate diffractometer. The amendment was introduced to the absorption by Multi-scan ⁸. Table 1 shows the main parameters of the X-ray diffraction experiments and refinement calculations of the structures 7-10.

The structures were solved by direct methods using SHELXS-2014 and refined using SHELXL-2014 programs ⁹. All non-hydrogen atoms were refined by anisotropic full-matrix least-squares methods (over F²). Positions of H atoms were found geometrically and refined with fixed isotropic thermal parameters U_{iso} = nU_{eq}, where n = 1.5 for methyl hydrogens and 1.2 for others and U_{eq} is the equivalent isotropic thermal parameter of the corresponding C atoms.

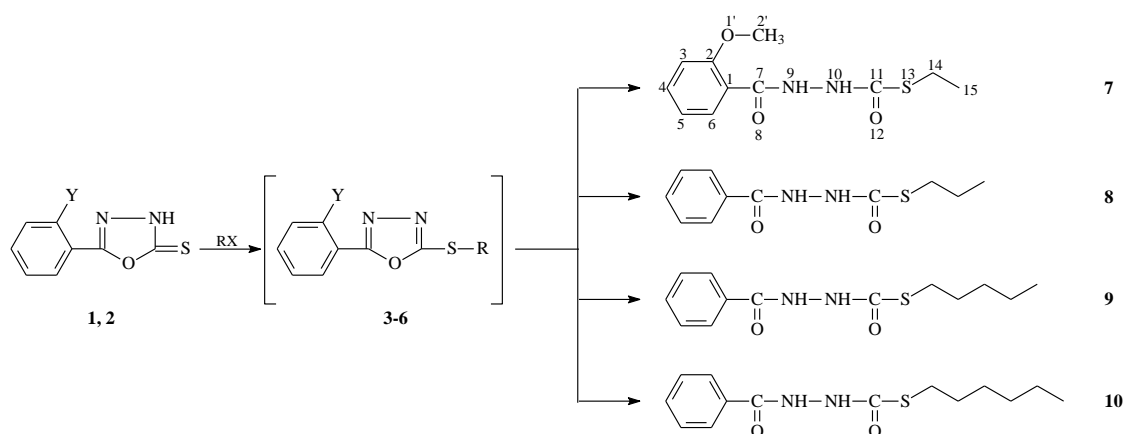
Materials X-ray diffraction as a CIF file deposited at the Cambridge center of crystal data (CCDC), from which can be obtained free on request at the following link: www.ccdc.cam.ac.uk/data_request/cif.

Table-1: Basic crystallographic parameters and characteristics of the X-ray diffraction for structures 7-10.

Compound	7	8	9	10
Molecular formula	C ₁₁ H ₁₄ N ₂ O ₃ S	C ₁₁ H ₁₄ N ₂ O ₂ S	C ₁₃ H ₁₈ N ₂ O ₂ S	C ₁₄ H ₂₀ N ₂ O ₂ S
Mr	254.30	238.30	266.35	280.38
Crystal symmetry	Monoclinic	Orthorhombic	Monoclinic	Monoclinic
Space group	P2 ₁ /c	Pbca	P2 ₁ /c	P2 ₁ /c
Z	4	8	8	4
a, Å	12.7777(14)	11.8572(10)	13.3174(19)	13.6078(10)
b, Å	4.7384(5)	9.7801(8)	11.6046(10)	11.8731(5)
c, Å	21.215(2)	21.938(4)	19.101(2)	9.8109(7)
α, °	90	90	90	90
β, °	105.428(11)	90	91.406(14)	91.827(7)
γ, °	90	90	90	90
V, Å ³	1238.2(2)	2544.0(6)	2951.0(6)	1584.31(18)
ρ, g/cm ³	1.364	1.244	1.199	1.175
Crystal dimension (mm)	0.35x0.48x0.55	0.35x0.45x0.50	0.40x0.45x0.55	0.30x0.35x0.35
Range scanned, 2θ°	3.588≤θ≤76.135°	4.030≤θ≤76.648°	3.320≤θ≤77.131°	3.249≤θ≤76.278°
μ _{exp} (cm ⁻¹)	2.334	2.177	1.926	1.817
No. reflection collected	2471	2636	6078	3259
No. reflection with I>2σ(I)	1528	1149	2800	2136
R ₁ (I>2σ(I) and total)	0.0641 (0.0965)	0.0995 (0.1710)	0.0779 (0.1556)	0.0793 (0.1026)
wR ₂	0.1616 (0.1886)	0.2992 (0.3539)	0.2025 (0.2656)	0.2478 (0.2864)
GOOF	0.948	1.060	1.031	1.043
Largest diff. peak and hole (e Å ⁻³)	0.417 and -0.334	0.356 and -0.273	0.631 and -0.425	0.446 and -0.384

4. DISCUSSION

The experiments were carried out, respectively, by boiling in the acetone of equimolar amounts of oxadiazolthiones, haloalkyls and K₂CO₃. The reaction was monitored by TLC. After the removal of acetone from the reaction mixture, the residue was dissolved in chloroform and it was washed with water, a 10% solution of alkali to remove the unreacting thion, then with water until neutral. After this, the chloroform was removed by evaporating on a porcelain cup. At the same time crystals formed on the bottom of the cup. X-ray diffraction analysis of these crystals gave an unexpected result, namely, instead of the expected products of 2-alkylthio-5-aryl-1,3,4-oxadiazoles **3-6**, substances without an oxadiazole ring were obtained and they had a linear form with the following structures **7-10**:



1 Y=OCH₃; 2 Y=H; 3 Y=OCH₃, R=C₂H₅; 4 Y=H, R=C₃H₇; 5 Y=H, R=C₅H₁₁; 6 Y=H, R=C₆H₁₃.

The IR spectra also confirm structure of the crystals obtained, so there are signals corresponding to C=O and -C=O-NH-NH- groups in the region 1668-1692 and 3178-3291 cm⁻¹, respectively, which are absent in the spectra of the original thions.

In the independent part of crystal structures **7**, **8**, **10** consist of one molecule, but in crystal structure **9** consist of two molecules, which difference with values of the torsion angle C11-S13-C14-C15 (-104.53 and 94.94° for **9a** and **9b**, respectively). Six membered ring in molecular structures **7**, **8**, **9a**, **9b** and **10** comprise a flat (within ± 0.003 , ± 0.003 , ± 0.005 , ± 0.002 and ± 0.009 Å respectively). The location of phenyl ring relative to alkylsulfanyl group characterizing with location of bicarbohydrazide fragment -CO-NH-NH-CO- (value of torsion angle C7-N9-N10-C11 71.86 , -106.16 , 91.15 , -86.76 and -101.70° for **7**, **8**, **9a**, **9b** and **10**, respectively) (Fig.2.).

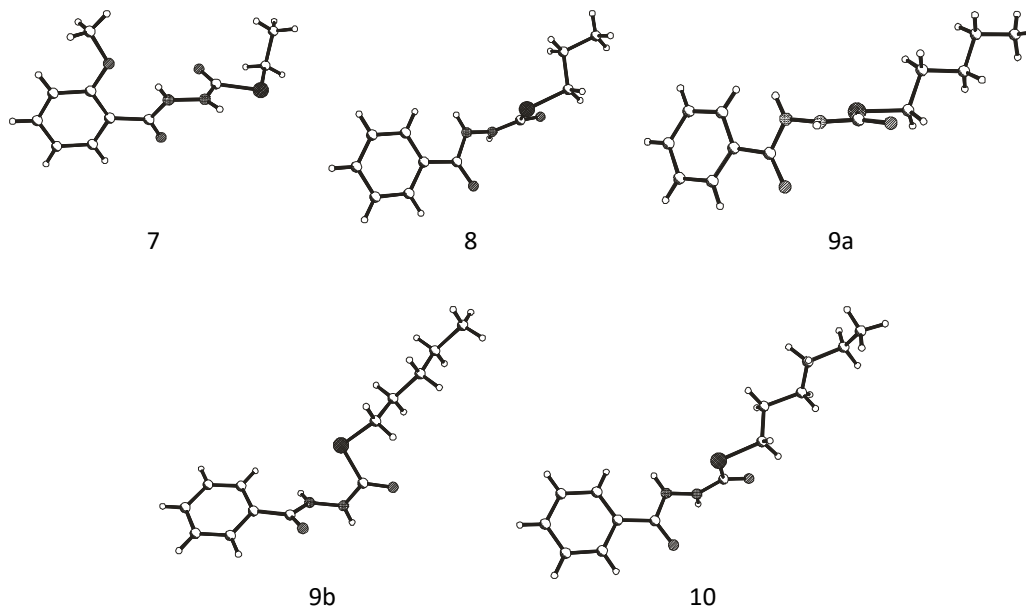


Fig.2 Crystal structures 7-10

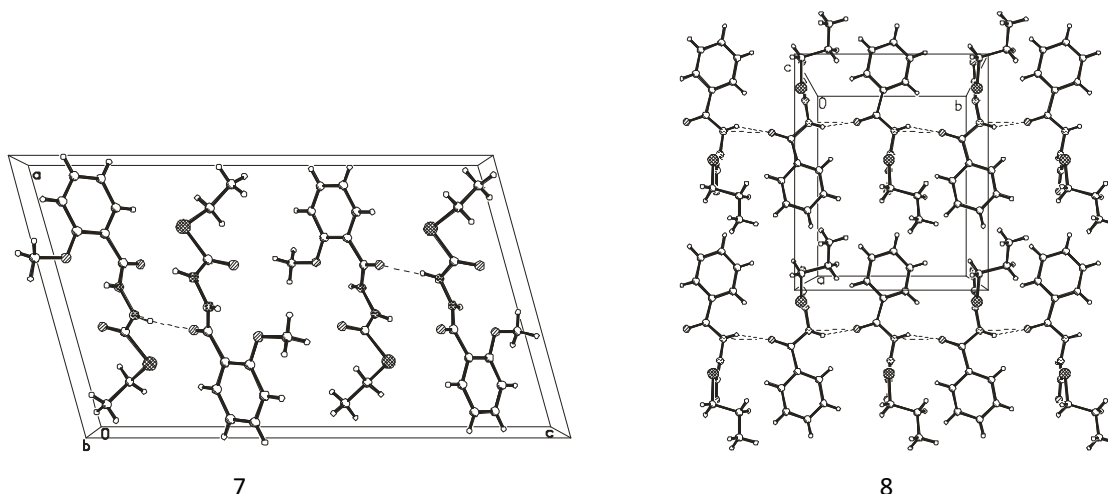
Crystal structures **7-10** form intermolecular H-bonds¹⁰ (Fig. 3).

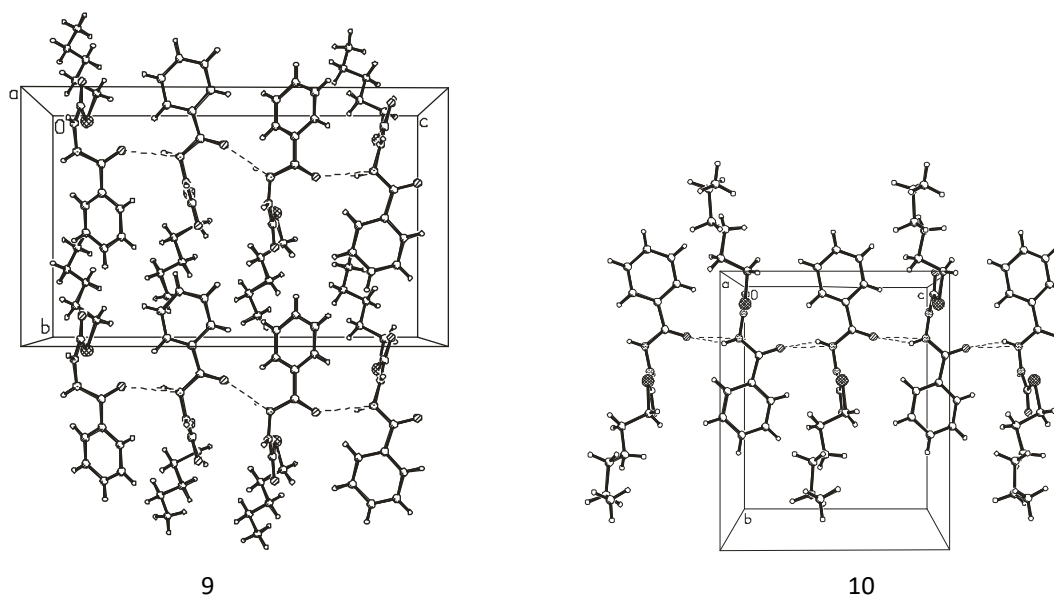
In the crystal structure of **7** C=O group and NH group form intermolecular H-bonds. In the crystal between molecules are formed N-H...O type H-bonded chains along *b* axis with graph set motifs of $C_1^2(5)$.

In the crystal structure of **8** C=O group and NH group form intermolecular H-bonds. In the crystal between molecules are formed N-H...O type H-bonded networks parallel to *bc* plain with graph set motifs of $R_6^6(28)$.

In the crystal structure of **9** C=O group and NH group form intermolecular H-bonds. In the crystal between molecules are formed N-H...O type H-bonded networks parallel to *bc* plain with graph set motifs of $R_4^4(20)$.

In the crystal structure of **10** C=O group and NH group form intermolecular H-bonds. In the crystal between molecules are formed N-H...O type H-bonded networks parallel to *bc* plain with graph set motifs of $R_6^6(28)$.




Fig.3: Crystal packing of molecules 7-10

Parameters of these H-bonds are shown in table 2.

In the structures **8** and **10** was observed weak $\pi \dots \pi$ interaction between the six membered aromatic rings (atoms C1, C2, C3, C4, C5, C6) of molecules related by symmetry $-x, 1-y, 1-z$; $2-x, 2-y, 1-z$ and with centroid-centroid distance of 3.803(5), 3.784(3) Å respectively ¹¹.

Table 2: The geometrical parameters of intermolecular hydrogen bonds in the crystals 7-10

(*d*: the distance, D: donor, A: acceptor)

No	D—H...A	<i>d</i> (D—H), Å	<i>d</i> (H...A), Å	<i>d</i> (D...A), Å	∠(DHA), deg.	Symmetry
7	N9-H9A...O1'	0.86	2.04	2.650(4)	127	
7	N9-H9A...O8	0.86	2.58	3.120(4)	122	$x, -1+y, z$
7	N10-H10A...O8	0.86	1.99	2.822(4)	162	$1-x, -1/2+y, 3/2-z$
7	C6-H6A...O8	0.93	2.42	2.754(5)	101	
7	C14-H14B...O12	0.97	2.42	2.869(6)	108	
8	N9-H9A...O8	0.86	2.05	2.759(5)	139	$1/2-x, 1/2+y, z$
8	N10-H10A...O12	0.86	2.04	2.871(8)	162	$1-x, 1-y, 1-z$
8	C4-H4A...O12	0.93	2.58	3.421(7)	150	$-1+x, y, z$
8	C14-H14B...O12	0.97	2.43	2.869(12)	107	
9	N9B-H9BA...O8A	0.86	2.10	2.827(5)	142	$1-x, 1-y, 1-z$
9	N9A-H9AA...O8B	0.86	2.08	2.895(5)	159	$1-x, 1/2+y, 3/2-z$
9	N10A-H10A...O12B	0.86	2.07	2.916(6)	169	
9	N10B-H10B...O12A	0.86	2.10	2.888(6)	153	
9	C6A-H6AA...O8B	0.93	2.59	3.373(6)	142	$1-x, 1/2+y, 3/2-z$
9	C14B-H14B...O12B	0.97	2.40	2.878(8)	110	
9	C14A-H14C...O12A	0.97	2.28	2.828(8)	115	
10	N9-H9A...O8	0.86	2.07	2.772(3)	138	$x, 3/2-y, 1/2+z$
10	N10-H10A...O12	0.86	2.02	2.871(4)	168	$2-x, 1-y, 1-z$
10	C4-H4A...O12	0.93	2.59	3.433(4)	151	$x, 1+y, z$
10	C14-H14B...O12	0.97	2.38	2.835(6)	108	

5. CONCLUSION

Thus, in our opinion, after the treatment the reaction mixtures of alkylation reactions with alkali solutions, the oxadiazole ring was opened. Such results were not observed in similar experiments conducted by us earlier ¹².

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