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Spectroscopic and structural investigation of interaction of 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thione potassium salt with molecular iodine

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Abstract

The interest in the study of heteroaromatic thioamides which are known to exhibit antithyroid activity is stimulated by the variety and an unusual structure their complexes with molecular iodine.

The directions of dithiones investigation are diversity enough, however a few works are devoted to the study them as the potential thyreostatics. The ability of 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thion potassium salt to form the outer-sphere charge-transfer complex in dilute chloroform solution, coordinating 2 iodine molecules has been studied by UV-vis spectroscopy (lgβ=7.91). The compound of the 5,5'-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione) - product of irreversible oxidation of 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thione potassium salthas been isolated and characterized by X-ray diffraction. Intermolecular interactions between sulfur atoms are observed with very short interatomic distance, shorter than sum of van der Waals radii. The contact between heterocyclic sulfur and heterocyclic nitrogen is also slightly short – 3.169 Å (0.053 Å less than vdW radii sum).

This investigation constitutes a starting point for study of novel antithyroid drugs in future.

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Keywords: 5-Mercapto-3-phenyl-1,3,4-thiadiazole-2-thione potassium salt; 5,5'-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione);X-ray diffraction;HRMS; NMR; UV-vis; Raman; FT-IR study.

1. Introduction

The interest in the study of structure-activity relationship of thioamides against molecular iodine is stimulated by the interest in the molecular compounds formed between antithyroid drugs and diiodine, [1-10]since thioamides are known to exhibit antithyroid activity [10].

It should be noted that the molecular interactions of antithyroid drugs with iodine have been subjected to many investigations because these drugs may inhibit thyroid hormone synthesis by forming donor-acceptor complexes with iodine[11].

Reactions of diiodine with heterocycles compounds such as ketones, thiones [12-16] or selones [17-20] are known to produce various types of iodine compounds, including charge transfer complexes [21-23], with "spoke structures" ($D–I_2$; D = donor), "extended spoke structures" ($D–I_2–I_2$) [24-26], iodonium salts [27], monocationic disulfides and dicationic disulfides or diselenides [28-30, 31-35].Synthesis, spectroscopicand structuralcharacterizationofnovelinteractionproduct of pirrolidine-2-thione withmoleculariodineformed in the resultof oxidative desulfurizationhasbeenreported [36].

Challenges related to characterization of the halogen-bonding diversity (Desirajuet al., 2013) and iodine–iodine non-covalent interactions in crystalsarethefocusofattentionofmanyresearchersworking in crystalengineering [37].

Recently, much attention has been paid to investigation the properties of heterocyclic thioamides with an oxygen, nitrogen, sulfur containing moiety for which the σ and π-donor properties were estimated [38, 39].

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Heteroaromatic compounds azole derivatives are a versatile group of compounds with a wide range of application. Among them, thiadiazole andits derivatives areessentiallybiologicalactivecompounds. Theyrevealactions in antihypertensive [40]andcardioprotectivetreatment [41, 42]. Theyhave a potential activity as G-protein coupledreceptors [43]. Thiadiazoleenzymeswithactivecysteineresidues [44] (e.g. bacterialenzymes [45]) andtheyareconstituentsof non-steroidal anti-inflammatoryagents [46].

Whenstudyingthereactions of thiadiazole-2-thione derivatives withmolecular iodine it was established that the species of forming products depend on the iodine concentration, the nature of reaction medium and the type of substitute group. In chloroform medium thereactionbetween 5-methyl-1,3,4-thiadiazole-2-thione and iodine producedthecorrespondingcharge-transfer complex 5-methylthiadiazole-2-thione-I_2andadditionofthreemolecules of iodineto two thione molecules produced a novelcationiccomplexhaving an almost linear S-I^+-S moietyand I_5 counteranion [47,48]. When 5-methyl-1,3,4-thiadiazole-2-thione was treated with I_2 in water, thereactionproducedthem monocationcontaining a disulfidebond as a majorproduct.It is suggested that the high reactivityofthione toward I_2 andtherelativelylow IC_{50}value in the LPO-catalyzediodinationreaction, is stipulated [49]bystrong antithyroidactivity.

Currently, chemistry has expanded from molecular to dynamic combinatorial chemistry (DCC) which is one of the often used methods to generate complex supramolecular systems and allow one to identify biologically active compounds, design host-guest systems and study noncovalent interactions. Organic compounds with two thionic groups, such as dithiones, are reported in dynamic combinatorial chemistry. S. Otto and others [50, 51] have recently adapted disulfide chemistry for the generation of dynamic combinatorial library (DCLs) in water using dithiol building blocks of very different chemical nature to construct the structures aiming at molecular recognition. B. M. Matysiak and others [52] combined thiol-disulfide [53,54,55-61] and thio-Michael exchange [62-66] to design antiparallel chemistries. Furthermore, the use of dithiones as the potential drugs with a various range of properties has been widespread in industrial application. Oltipraz, 4-methyl-5-

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pyrazinyl-3H-1,2-dithiole-3-thione (OPZ), which was originally developed as an antischistosomal agent, is a synthetic derivative of the naturally occurring dithiolthiones and it is currently being evaluated in clinical studies as a chemopreventive agent for hepatocarcinogenesis [67]. In addition to cancer chemopreventive activity, OPZ possesses potent antiangiogenic activity [67].

The directions of dithiones investigation are diversity enough. For 2,4-dithiouracil (DTU), a close pyrimidine analogue of the title compound, the double-proton-transfer reactions leading to 2,4-pirimidinedithiol form [68]and for 2,6-dithiopurine, a possible chemopreventive agent, the phototautomeric reactions isolated in Ar and N_2 matrix were observed by matrix isolation infrared spectroscopy.

The aim of the present research was to study the reaction of dithione, 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thion potassium salt, with molecular iodine in chloroform and ethanol solutions by UV-vis spectroscopy, Raman spectroscopy and X-ray diffraction analysis method. To give a comparative evaluation of the solvent influence on the reactivity and chemical structure of the interaction product of the k-salt of a potential thyreostatic with molecular iodine.

2. Experimental section

5-Mercapto-3-phenyl-1,3,4-thiadiazole-2-thione potassium salt (AlfaAesar) was used without additional purification. The solvents were purified according to known procedures [69].

5,5’-Disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione) was synthesized by mixing of 0.0264 g of 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thione in 1 ml ethanol solution and 0.0127 g of molecular iodine in 7.6 ml of chloroform solution (molar ratio 1:0.5) followed by slow evaporation of the solvent in air to obtain light-yellow rectangular plate-like crystals. The yield of product was 71 %. The compound mp (123ºC).

^{1}H NMR (250 MHz, CDCl3, δ /ppm, J/Hz): δ 7.43-7.53 (m 6H), δ 7.65-7.71 (m 4H).

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^{13}C (62.9 MHz, CDCl3, δ /ppm): δ 125.6; 129.17; 129.55.

HRMS spectra of 5,5'-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione) was measured in CH_3CN 100 %. The source type was ESI in positive ion polarity.

Infrared spectra in the region 7800-375 cm^{-1} were obtained in vaseline oil, with Varian 660 FT-IR spectrophotometer.

The UV-vis absorption spectra of chloroform solutions containing thione and molecular iodine in different ratios were measured on a Cary 100 (Varian) UV-vis spectrophotometer in a quartz cell with a 1.0 cm light path in the 250-800 nm range at 22.0 °C. 1.0×10^{-3} mol/L concentration of thione and the iodine in chloroform were used as the stock solutions. The precise value of the molar absorption coefficient of iodine (ε_{510}) was determined from the calibration curve ($\varepsilon = 899.83$ L × mol^{-1}× cm^{-1}). The concentration of molecular iodine was varied from zero to a 24-fold excess, the concentration of thione remained constant (2×10^{-5} mol/L).

X-ray crystallographydiffraction study. Crystal data $C_{16}H_{10}N_4S_6$ are shown in Table 1 [70]. Atomic coordinates, bond lengths, bond angles and termal parameters of 5,5'-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione) have been deposited at the Cambridge Crystallographic Data Centre (CCDC) 1575843.

$C_{16}H_{10}N_4S_6$ are triclinic, space group *P*-1:a=8.8166(5)Å, b=13.2398(7)Å, c=16.1522(8)Å, α=97.1090(10)°,β=90.1590(10)°, γ=93.6000(10)°, V = 1867.2(2) Å^3, Z = 4, M = 450.64, d_{calc} = 1.603 g·cm^{-3}, μ= 0.121 mm^{-1}. 46366 reflections were collected at SMART APEX II CCD difractometer (λ(Mo-Kα)=0.71073 Å, graphite monochromator, ω-scans, 2θ<58.66°) at 120K. The structure was solved by the direct methods and refined by the full-matrix least-squares procedure in anisotropic approximation. 10198 independent reflections [R_{int} = 0.0422] were used in the refinement procedure that was converged to wR_2 = 0.0795 calculated on F^2_{hkl} (*GOF* = 1.056, R_1 = 0.0348 calculated on F_{hkl} using 8499 reflections with I>2σ(I)). These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif. All calculations were carried out on an IBM PC AT with the use of the SHELXTL

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program package [71]. The experimental data had been corrected for absorption effects with SADABS procedure [72].

PLATON [73] and Mercury v.2.3 software [74] were used to prepare material for publication.

Raman spectra of the 5,5'-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione) were obtained in the frequency range of 50-1800 cm^{-1}.

The Raman spectra were excited by polarized radiation from an argon laser (λ=514.5 nm)with output power 25 mW and recorded on a single-beam Renshaw unit equipped with a (NExT) Near-Excitation Tuneable filter to analyze the low frequency spectral region. The exciting radiation beam focused onto the sampleusing a Leica optical microscope; the diameter of the focused beam on the sample was 5 µm.

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Table 1

Crystal data and structure refinement for 5,5’-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione).

Identification code	tdak
Empirical formula	$C16\ H10\ N4\ S6$
Formula weight	450.64
Temperature	120(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	a = 8.8166(5) Å α= 97.1090(10)°
	b = 13.2398(7) Å β= 90.1590(10)°
	c = 16.1522(8) Å γ = 93.6000(10)°
Volume	1867.15(17) Å^3
Z	4
Density (calculated)	1.603 Mg/m^3
Absorption coefficient	0.741 mm^{-1}
F(000)	920
Crystal size	0.14 x 0.12 x 0.03 mm^3
Theta range for data collection	1.88 to 29.33°.
Index ranges	$-12\leq h\leq 12$, $-18\leq k\leq 18$, $-22\leq l\leq 22$
Reflections collected	46366
Independent reflections	10198 [R(int) = 0.0422]
Completeness to theta = 29.33°	99.5 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2

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Data / restraints / parameters	10198 / 0 / 469
Goodness-of-fit on F^2	1.056
Final R indices [for 8499 rfln with $I>2\sigma(I)$]	R1 = 0.0348, wR2 = 0.0726
R indices (all data)	R1 = 0.0470, wR2 = 0.0795
Largest diff. peak and hole	0.441 and -0.318 e.Å^{-3}

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3. Results and discussion

Since the good correlation between the antithyroid activity of heteroaromatic thioamides *in vivo* and the charge transfer complex constants with the iodine [75] has been revealed, it was interesting to evaluate the stability of outer-sphere complex of 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thione potassium salt with the molecular iodine. Electronic absorption spectra of chloroform solutions containing 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thione potassium salt, molecular iodine, forming molecular adduct and the product of irreversible oxidation of 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thione potassium salt (5,5'-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione)) are presented in Fig. 2. When each solution having been prepared the spectra were registered after 5 sec. The concentration of molecular iodine was varied from its absence to 24-fold excess while the concentration of thioamide remained constant.When the iodine solutions were added to the chloroform thioamide solutions, the solutions became peach-colored. The 326 nm absorption band has characterized the 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thione potassium salt(Fig. 2. curve (1)), the 510 nm absorption band (Fig. 2. curves 2-8) has characterized the molecular iodine and the 335 nm (Fig. 2. curve (9)) has characterized5,5'-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione), which wasdiscussed above.

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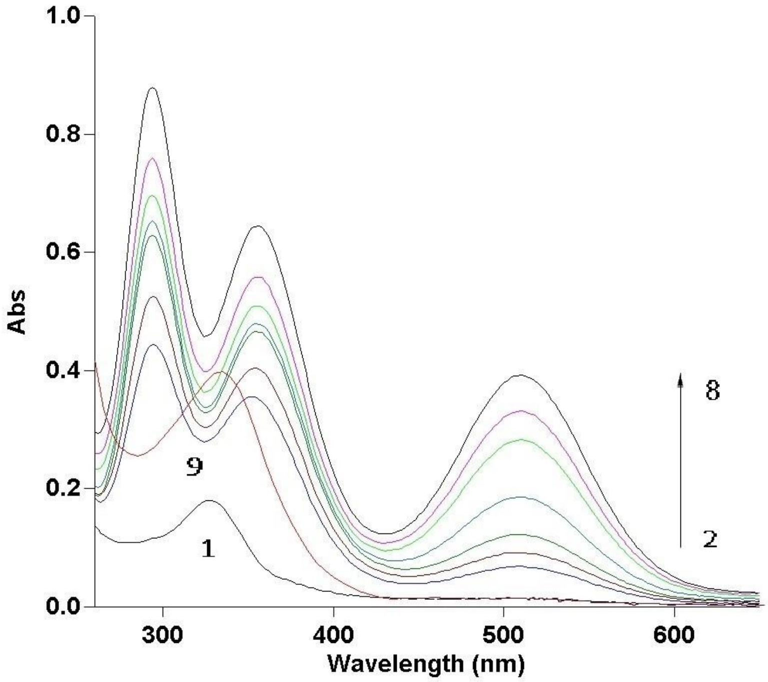

Fig. 2. Electronic absorption spectra of chloroform solutions containing thione 2×10^{-5}mol/L and molecular iodine at the concentration: 0 (1), 8.0×10^{-5} (2), 1.2×10^{-4} (3), 1.6×10^{-4} (4), 2.4×10^{-4} (5), 3.6×10^{-4} (6), 4.0×10^{-4} (7), 4.8×10^{-4} (8)mol/L in chloroform,ε (I_2) = 899.83 L × $mol^{-1}\times cm^{-1}$, (9) 2×10^{-5}mol/L5,5'-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione), *l*=1.0cm.

The new intensive absorption bands corresponded to the interaction product of molecular iodine and thione have been observed in the electronic spectrum at 289 nm and 354 nm, respectively. The number of iodine molecules coordinated to thione and the stability constant of molecular adduct were evaluated with the use of average iodine number$\overline{n}_{I_2}$ function which was proposed in our previous works[76-78]. The equilibrium concentration of iodine ([I_2]) was calculated from the absorbance of the individual absorption band at λ (510±5) nm of elemental iodine accordingto the equation $[I_2]=A/l\varepsilon_{I_2}$. For each equilibrium concentration of iodine, the corresponding value of $\overline{n}_{I_2}$was calculated according to the Eq. 1:

$$\overline{n}_{I_2} = (C_{I_2}-[I_2])/C_{Het}, \qquad (1)$$

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where C_{Het} and C_{I_2} are the analytical concentrations of 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thione potassium salt and molecular iodine, respectively. The experimental data reflect the high coordination saturation of complex ($\bar{n}_{I_2} \geq 1.9$).

The stability constants $\beta 1$ and $\beta 2$ were calculated by the least squares method according to Eq.2:

$$\frac{\bar{n}_{I_2}}{(1-\bar{n}_{I_2})[I_2]} = \beta_1 + \beta_2 \frac{(2-\bar{n}_{I_2})[I_2]}{(1-\bar{n}_{I_2})} \quad (2)$$

lgβ_2=7.91, lg β_1=5.07(ρ =0.999).

The comparative assessment of coordinating ability of the 5-methyl-1,3,4-thiadiazoline-2-thione [48], shows that the thione coordinates one iodine molecule, the stability constant of the molecular adduct with iodine in dilute chloroform solutions (lgβ=2.9±0.1, (ρ =0.993)) is lower than molecular adduct constant stability of 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thion potassium salt with molecular iodine.Apparently, it can be explained by the presence of two thione groups in the molecule of heterocycle, that enhances thyreostatic activity of this compound. Therefore, 5-methyl-1,3,4-thiadiazoline-2-thione will be able to show pharmacological activity close to the activity of thiouracil *in vivo* which inhibit the activity of iodothyroninedeiodinase (ID-SeH), an enzyme responsible for the monodeiodination of the T4 prohormone to the T3 hormone [16].

The interaction of 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thione potassium salt with iodine molecule in 1:0.5 ratio in mixing of ethanol and chloroform solution gave 5,5’-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione) according to the equation:

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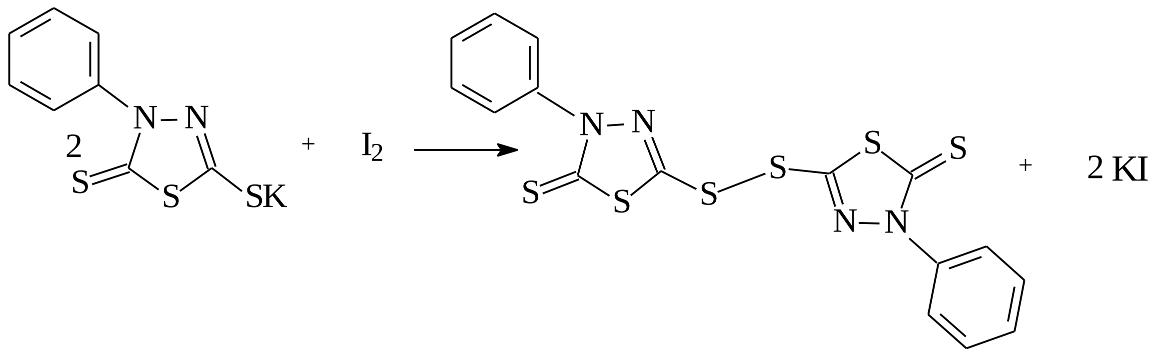

The crystal structure of reaction product of 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thione potassium salt with molecular iodine is disulfide of 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thion potassium salt Fig.1. The bonds and angles for the crystal structure of reaction product 5,5'-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione) with molecular iodine are presented: distances S(4)-C(9) 1.760 Å (1), S(3)-C(8) 1.7692 Å (2). The S(3)-S(4) bond length 2.0577(6)Å (3), torsion angles C(8)-S(3)-S(4)-C(9) is 86.15 (8)°.

ORTEP-diagram 5,5'-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione) is presented in Fig. 1.

Fig. 1. ORTEP-diagram $C_{16}H_{10}N_4S_6$. The thermal ellipsoid at the 50% probability level.

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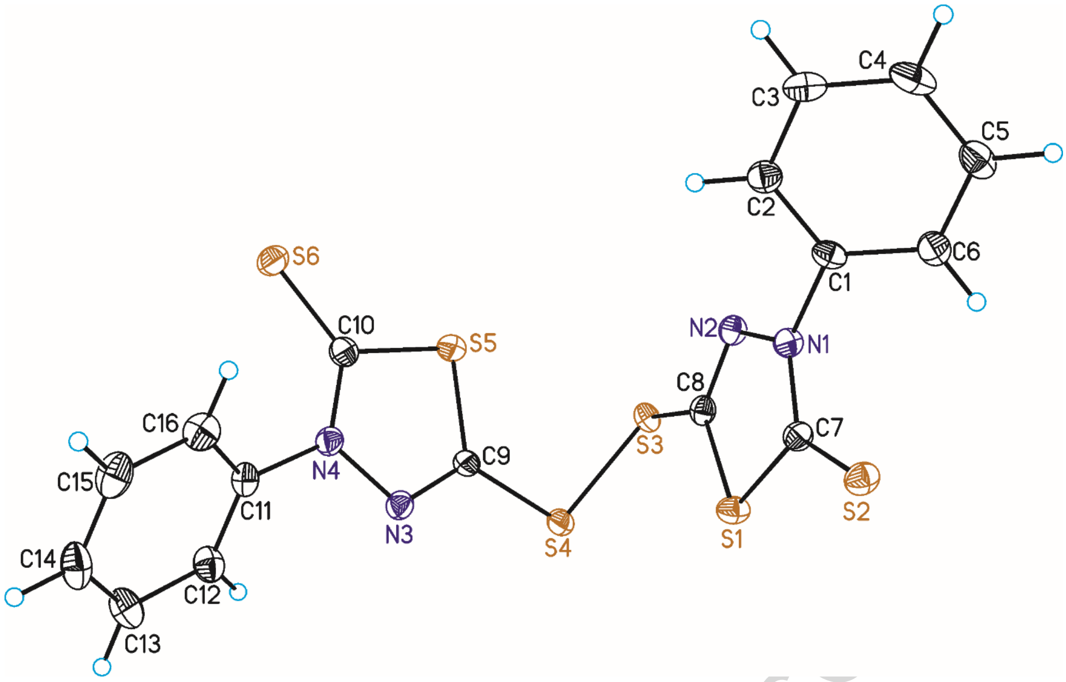

Mixing ethanol solution of 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thion potassium salt and chloroform solution of iodine resulted in irreversible oxidation of the thione with formation of disulfide 5,5’-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione), for which molecular and crystal structure was studied by X-ray diffraction data.

The molecular structure of 5,5’-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione) with the atom-numbering scheme is shown in Fig. 2 and selected geometric parameters are given in Table 1.

Connected in such «head-tail» manner molecules of disulfide form infinite chains. The structure is shown in Fig.3.

The S3-S4 bond length (2.0577(6) Å) is rather short for acyclic disulfide bridge connecting five-membered heterocycles (common range is 2.013-2.141 Å)[79].

The crystal structure of the interaction product 5-methyl-1,3,4-thiadiazoline-2-thione with the iodine was formed by the iodonium cations $(C_3H_4N_2S_2)_2I^+$ and I_5 counter anions interconnected by intermolecular hydrogen bonds. 5-Methyl-1,3,4-thiadiazoline-2-thione forming n-σ complex with the molecular iodine initiates complete charge transfer in the molecule and generates iodonium salt with 3-center-10-electron molecular orbital [48].

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Itisshown [80, 81] themechanismofthethiomidesinteractionwiththeiodine (formation disulfide or iodonium salt) depends upon electrodonor properties of heterocycle and a number of thiol groups in molecule.

Fig. 3. Packing arrangement of 5,5'-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione) in crystal structure.

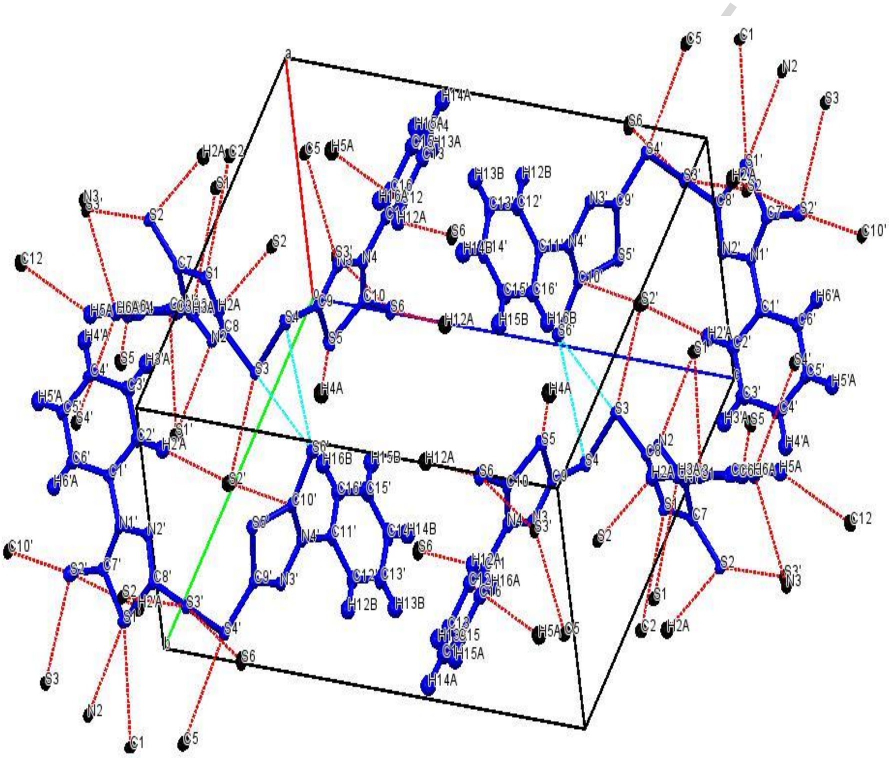

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Table 2. Selected geometric parameters (Å, °)

Parameter	Value
Bond lengths (Å)	
S(3)-C(8)	1.7692(18)
S(3)-S(4)	2.0577(6)
S(4)-C(9)	1.7601(18)
S(3')-S(4')	2.0583(6)
S(4')-C(9')	1.7554(18)

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S(3')-C(8')	1.7683(18)
Bond angles (°)	
C(8)-S(3)-S(4)	100.00(6)
C(9)-S(4)-S(3)	99.46(6)
Torsion angles (°)	
C(8)-S(3)-S(4)-C(9)	86.15(8)

An asymmetric unit cell of 5,5’-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione contains two molecules (Z'=2) denoted by unprimed (A) and primed (A') labels. In Figure 1, general view of the first independent molecule (A) is depicted. In both molecules, benzene and neighbouring thiadiazole rings are not coplanar (corresponding C-C-N-N torsion angles vary in the range of 37 to 54°). Two independent molecules adopt somewhat different conformations that is reflected in different values of the N3-C9-S4-S3 and C2-C1-N1-N2 torsion angles being equal to -161.0(2) and 54.1(2) ° for the first independent molecule, and -175.7(2) and 37.7(2) for the second one. The crystal packing is stabilized by close intermolecular S…S contacts in the range of 3.2 – 3.5 Å and by van-der-Waals interactions (Table 1S). It is interesting to note that the close contacts are observed between symmetrically independent molecules (A…A') which are somewhat strongly bound to each other than molecules of the same symmetrical type (A…A or A'…A', connected by ordinary van-der-Waals interactions). Similar observations were made earlier for co-crystals, solvates and crystals with Z'≥2 [82-84]. It can be suggested that the stronger intermolecular interaction in A…A' molecular pairs is responsible for appearance of two symmetrically independent molecules.Intermolecular contacts between S(2)...S(3') atoms 3.201 Å and also S(3)…S(2') atoms 3.445 Å are observed with very short interatomic distance. There are 0.33 Å and 0.085, respectively, shorter than sum of van der Waals radii. Intermolecular contacts between S(3)...S(6') atoms 3.267 Å and S(4)...S(6') atoms 3.587 of another molecule of thione are shorter than sum of

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van der Waals radii, respectively. The contact between heterocyclic sulfur S(1') and heterocyclic nitrogen N(2) is also slightly short – 3.169 Å (0.053 Å less than vdW radii sum).

Raman Spectroscopy is a powerful tool for the structural identification compounds. One band can be seen in the Raman spectrum of the product of irreversible oxidation of 5,5'-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione. The Raman spectrum of 5,5'-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione in the ν (S-S) region shows intense peaks at 505 cm^{-1}.

The FT-IR spectra of 5,5'-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione shown prominent peaks at the range 1300-1400 cm^{-1}, 900-1300 cm^{-1}, 1590-1700 cm^{-1} (for C=S, C-N, C=N bond vibrations, respectively).

HR-Mass spectra of 5,5'-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione) isotope claster are characterized by ESI: m/z, I_r (%) M+nH [$C_{16}H_{10}N_4S_6$]: 450.9293 (100), 451.9313 (25), 452.9261 (30), 453.9274 (5), 454.9226 (1.5).
The theoretical calculations are characterized m/z, I_r (%) M+nH [$C_{16}H_{10}N_4S_6$]: 450.9302 (100), 451.9334 (23), 452.9262 (30), 453.9294 (5), 454.9219 (1).

4. Conclusions

Therefore, the reaction product of 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thione potassium salt is presented disulfide with intermolecular interactions between sulfur atoms and very short interatomic distances, shorter than sum of van der Waals radii. The contact between heterocyclic sulfur and heterocyclic nitrogen is also slightly short – 3.169 Å (0.053 Å less than vdW radii sum). Connected in such «head-tail» manner molecules of disulfide form infinite chains. The method of UV-vis a

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spectroscopy found that 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thion potassium salt in dilute chloroform solutions forms the charge transfer complex of a high stability (lgβ=7.91) with molecular iodine.

Hence, it was shown, that the formation of 5,5’-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione), the interaction product of the thioamide with iodine in 1mixed of ethanol and chloroform solution, depends on nature of the heteroaromatic moiety and presence of two thione groups.

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References

[1] V. Daga, S.K. Hadjikakou, N. Hadjiliadis, M. Kubicki, J.H.Z. dos Santos, I.S. Butler, Interaction of Thioamides, Selenoamides and Amides with Di-iodine: A Study of the Mechanism of Action of Anti-thyroid Drugs, *Eur. J. Inorg. Chem* (2002) 1718-1728.

[2] J.H.Z. dos Santos, I.S. Butler, V. Daga, S.K. Hadjikakou, N. Hadjiliadis, Interaction of Thioamides, Selenoamides and Amides with Di-iodine: A Study of the Mechanism of Action of Anti-thyroid Drugs,*Spectrochim. Acta Part A*. 58 (2002)

ACCEPTED MANUSCRIPT

2725-2735.

[3] C.D. Antoniadis, G. Corban, S.K. Hadjikakou, N. Hadjiliadis, M. Kubicki, S. Warner, I.S. Butler, Synthesis and Characterization of (PTU)I_2 (PTU = 6-*n*-propyl-2-thiouracil) and (CMBZT)I_2 (CMBZT = 5-chloro-2-mercaptobenzothiazole) and Possible Implications for the Mechanism of Action of Anti-Thyroid Drugs, *Eur. J. Inorg Chem*. 2003 (2003) 1635-1640.

[4] C.D. Antoniadis, S.K. Hadjikakou, N. Hadjiliadis, M. Kubicki, I.S. Butler, Synthesis, X-ray Characterisation and Studies of the New Ionic Complex [Bis(pyridin-2-yl) disulfide] Triiodide, Obtained by Oxidation of 2-Mercaptopyridine with I_2 − Implications in the Mechanism of Action of Antithyroid Drugs,*Eur. J. Inorg Chem*. 2004 (2004) 4324-4329.

[5] D.R. Morris, L.P. Hager, Chloroperoxidase. 1. Isolation and properties of the crystalline glycoprotein, *J. Biol. Chem*. 241 (1966) 3582-3589.

[6] A. Nagasaka, H. Hidaka, Effect of antithyroid agents 6-propyl-2-thiouracil and 1-mehtyl-2-mercaptoimidazole on human thyroid iodine peroxidase, *J. Clin. Endocrinol. Metab*. 43 (1976) 152-158.

[7] W.W. du Mont, G. Mugesh, C. Wismach, P.G Jones, Biomimetic studies on the iodothyronine deiodinase intermediates: Modeling the reduction of selenenyl iodide by thiols, *Angew. Chem*., Int. Ed. 40 (2001) 2486-2489.

[8] M.J. Berry, J.D. Kieffer, J.W. Harney, P.R. Larsen, Selenocysteine confers the biochemical properties characteristic of the type I iodothyronine deiodinase, *J. Biol. Chem.* 266 (1991) 14155-14158.

[9] M.J. Berry, L. Banu, P.R. Larsen, Type I iodothyronine deiodinase is a selenocysteine-containing enzyme, *Nature*. 349 (1991) 438-440.

[10] J.E.F. Reynolds, A.B. Prasad, Martindale: The Extra Pharmacopoeia, The Pharmaceutical Press, 28th ed., London, UK, 1982, 268-271.

[11] A. Tamilselvi, G. Mugesh,Inhibition of Peroxidase-Catalyzed Iodination by Cephalosporins: Metallo-β-Lactamase-Induced Antithyroid Activity of Antibiotics,*ChemMedChem*. 4 (2009) 481.

[12] P.H. Svensson and L. Kloo,Synthesis, Structure, and Bonding in Polyiodide and

ACCEPTED MANUSCRIPT

ACCEPTED MANUSCRIPT

Metal Iodide−Iodine Systems,*Chem. Rev.*103 (2003) 1649–1684.

[13] P. Deplano, F.A. Devillanova, J.R. Ferraro, F. Isaia, V. Lippolis and M.L. Mercuri, FT-Raman Study on Charge-Transfer Polyiodide Complexes and Comparison with Resonance Raman Results,*Appl. Spectrosc.*46 (1992) 1625.

[14] D.R. Morris and L.P Hager, Mechanism of the Inhibition of Enzymatic Halogenation by Antithyroid Agents, *J. Biol. Chem.*241 (1966) 3582–3589.

[15] T. Nakashima, A. Taurog, Rapid conversion of Carbimazole to methimazole in serum: evidence for an enzymatic mechanism, *Endocrinology*. 10 (1979) 637-648.

[16] J.W. Harney and P.R. Larsen and D.D. Moore, Sequences required for cell-type specific thyroid hormone regulation of rat growth hormone promoter activity, *J. Biol. Chem.* 261 (1986) 14373.

[17] V. Daga, S.K. Hadjikakou, N. Hadjiliadis, M. Kubicki, J.H.Z. dos Santos and I.S. Butler, Interaction of Thioamides, Selenoamides and Amides with Di-iodine: A Study of the Mechanism of Action of Anti-thyroid Drugs, *Eur. J. Inorg. Chem.*2002(2002) 1718–1728.

[18] C.D. Antoniadis, G. Corban, S.K. Hadjikakou, N. Hadjiliadis, M. Kubicki, S. Warner and I.S. Butler, Synthesis and Characterization of (PTU)I_2 (PTU = 6-*n*-propyl-2-thiouracil) and (CMBZT)I_2 (CMBZT = 5-chloro-2-mercaptobenzothiazole) and Possible Implications for the Mechanism of Action of Anti-Thyroid Drugs,*Eur. J. Inorg. Chem*. 2003 (2003) 1635–1640.

[19] F. Bigoli, P. Deplano, M.L. Mercuri, et al., Evaluation of thermodynamic parameters for highly correlated chemical systems: a spectrophotometric study of the 1:1 and 2:1 equilibria between I2 and 1,1’-methylenebis(3-methyl-4imidazoline-2-thione)(mbit) and 1,1’-ethylenebis(3-methyl-4-imidazoline-2-thione)(ebit).Crystal and molecular structures of mbit. 2I2 and ebit.2I2, *J. Chem. Soc., Dal. Trans*. 17 (1996) 3583–3589.

[20] W.W. du Mont, G. Mugesh, C. Wismach and P.G. Jones, Reactions of organoselenenyl iodides with thiouracil drugs: an enzyme mimetic study on the inhibition of iodothyronine deiodinase,*Angew. Chem., Int. Ed.*40 (2001) 2486–2489.

[21] C.D. Antoniadis, S.K. Hadjikakou, N. Hadjiliadis, M. Kubicki and I.S. Butler,

ACCEPTED MANUSCRIPT

ACCEPTED MANUSCRIPT

Synthesis, X-ray Characterisation and Studies of the New Ionic Complex [Bis(pyridin-2-yl) disulfide] Triiodide, Obtained by Oxidation of 2-Mercaptopyridine with I_2 − Implications in the Mechanism of Action of Antithyroid Drugs,*Eur. J. Inorg. Chem.* 2004 (2004) 4324-4329.

[22] G.J. Corban, S.K. Hadjikakou, N. Hadjiliadis et al., Synthesis, structural characterization, and computational studies of novel diiodine adducts with the heterocyclic thioamides N-methylbenzothiazole-2-thione and benzimidazole-2-thione: implications with the mechanism of action of antithyroid drugs, *J. Inorg. Chem.* 44 (2005) 8617–8627.

[23] F. Freeman, J.W. Ziller, H.N. Poand, M.C. Keindl, Reactions of Imidazole-2-thiones with Molecular Iodine and the Structures of Two Crystalline Modifications of the 1:1 1,3-Dimethylimidazole-2-thione-Diiodine Charge-Transfer Complex (C5H8I2N2S),*J. Am. Chem. Soc.*110 (1988) 2586–2591.

[24] M. Esseffar, W. Bouab, A. Lamsabhi, J.L.M. Abboud, R. Notario and M. Yanez, An experimental and theoretical study on some thiocarbonyl-I-2 molecular complexes, *J. Am. Chem. Soc.*122 (2000) 2300–2308.

[25] F. Bigoli, P. Deplano, A. Ienco, C. Mealli, M.L. Mercuri, M.A. Pellinghelli, G. Pintus, G. Saba and E.F. Trogu, Structure and Bonding of Diiodine Adducts of the Sulfur-Rich Donors 1,3-Dithiacyclohexane-2-thione (ptc) and 4,5-Ethylenedithio-1,3-dithiole-2-thione,*Inorg. Chem.*38 (1999)4626–4636.

[26] P. Deplano, J.R. Ferraro, M.L. Mercuri, E.F. Trogu, Structural and Raman spectroscopic studies as complementary tools in elucidating the nature of the bonding in polyiodides and in donor-I2 adducts, *Coord. Chem. Rev*. 188 (1999) 71-95.

[27] C.D. Antoniadis, S.K. Hadjikakou, N. Hadjiliadis, M. Kubicki, and I.S. Butler,Synthesis, X-ray characterization and study of new ionic complexes of 2-pyridone, obtained by oxidation with I2, *New J. Chem*. 29 (2005) 714–720.

[28] C.D. Antoniadis, S.K. Hadjikakou, N. Hadjiliadis, A. Papakyriakou, M. Baril, and I.S. Butler, Synthesis and structures of Se analogues of the antithyroid drug 6-n-propyl-2-thiouracil and its alkyl derivatives: Formation of dimeric Se-Se compounds and deselenation reactions of charge-transfer adducts of diiodine, *Chemistry - A Eur.*

ACCEPTED MANUSCRIPT

ACCEPTED MANUSCRIPT

J. 12 (2006) 6888–6897.

[29] S.K. Hadjikakou and N. Hadjiliadis, Interaction of thioamides, selenoamides, and amides with diiodine,*Bioinorg. Chem. Appl.* 2006 (2006) 60291.

[30] J.H.Z. dos Santos, I.S. Butler, V. Daga, S.K. Hadjikakou, N. Hadjiliadis, Interaction of Thioamides, Selenoamides and Amides with Di-iodine: A Study of the Mechanism of Action of Anti-thyroid Drugs, *Spectrochim. Acta Part A*. 58 (2002) 2725-2735.

[31] D. Atzei, P. Deplano, E.F. Trogu, F. Bigoli, M.A. Pellinghelli, and A. Vacca, Interaction of diiodine with some tetrasubstituted dithiooxamides. Crystal and molecular structure of bis(morpholinothiocarbonyl)bis(diiodine), *Can. J. Chem*. 66 (1988) 1483–1489.

[32] F. Cristiani, F.A. Devillanova, A. Diaz and G. Verani, Molecular Adducts between Iodine and Some Benzazole-2-thione and -2-selone Derivatives, *J. Chem. Soc.2* (1984) 1383–1386.

[33] F.A. Devillanova and G. Verani, Charge Transfer Complexes Between I2 And Selenoamido Entity Contained In Some Pentaatomic Rings, *Tetrahedron*. 37 (1981) 1803–1808.

[34] M.C. Aragoni, M. Arca, F. Demartin, et al., Anti-thyroid drug methimazole: X-ray characterization of two novel ionic disulfides obtained from its chemical oxidation by I2, *J. Am. Chem. Soc*. 124 (2002) 4538– 4539.

[35] P.D. Boyle, W.I. Cross, S.M. Godfrey, C.A. McAuliffe, R.G. Pritchard and S.J. Teat, Reaction of dimethylselenourea and selenourea with dibromine to produce selenourea-dibromine, the ‘T’-shaped 1:1 molecular adduct N, N-dimethyl-2-selenourea-dibromine, its solvent of crystallisation-containing analogue and the unusual ionic compound, *J. Chem. Soc., Dalton Trans*. 16 (1999) 2845– 2852.

[36] T.S. Kolesnikova, M.S. Chernov’yants, Charge Transfer Complexes Formed by Heterocyclic Thioamides and Tetracyanoethlene: Experimental and Theoretical Study, *J. Phys. Chem. Part A.* 121 (2017) 7000-7008.

[37] E. Bartashevich,a*, I. Yushina, K. Kropotina, S. Muhitdinova and V. Tsirelsonb, Testing the tools for revealing and characterizing the iodine – iodine halogen bond in

ACCEPTED MANUSCRIPT

ACCEPTED MANUSCRIPT

crystals,*Acta Cryst.*73 (2017) 217–226.

[38] M.S. Chernov’yants, E.V. Khohlov, J.I. Bondarenko, I.V. Burykin, Estimation of σ and π-donor properties of heterocyclic thioamides by Spectroscopic and Magnetic Resonance Methods, *SpectroChimActa Part A.* 81 (2011) 640-644.

[39] M.S Chernov’yants, I.V. Burykin, Z.A. Starikova, A.Y. Tereznikov, T.S. Kolesnikova, Spectroscopic and Structural Study of Novel Interaction Product of Pyrrolidine-2-thione with Molecular Iodine. Presumable mechanisms of oxidation, *J. Mol. Struct.* 1047 (2013) 204-208.

[40] Y. Kohara, K. Kubo, E. Imamiya, T. Wada, Y. Inada, T. Naka, Synthesis and Angiotensin II Receptor Antagonistic Activities of Benzimidazole Derivatives Bearing Acidic Heterocycles as Novel Tetrazole Bioisosteres, *J. Med. Chem*. 39 (1996) 5228-5235.

[41] U.K.M. Decking, M. Hartmann, Cardioprotective actions of KC 12291 I. Inhibition of voltage-gated Na+ channels in ischemia delays myocardial Na+ overload, *J. Naunyn-Schmiedeberg’s Arch. Pharm*. 358 (1998) 547-553.

[42] M. Hartmann, U.K.M. Decking, Cardioprotective actions of KC 12291 II. Delaying Na+ overload in ischemia improves cardiac function and energy status in reperfusion, *J. Naunyn-Schmiedeberg’s Arch. Pharm*. 358 (1998) 554-560.

[43] A. Lanzafame, A. Christopoulos, Effects of anandamide on the binding and signaling properties of M 1 muscarinic acetylcholine receptors, *J. Pharmacol. Exp. Ther.* 308 (2004) 830-837.

[44] T.F. Tam, R. Leung-Toung, W. Li, M. Spino, K. Karimian, Medicinal chemistry and properties of 1, 2, 4-thiadiazoles, MiniRev. *Med. Chem*. 5 (2005) 367.

[45] J. Marcinkieviciene, M.J. Rogers, L. Kopcho, W. Jiang, K. Wang, D.J. Murphy, J. Lippy, S. Link, T.D.Y. Chung, F. Hobbs, T. Haque, G.L. Trainor, A. Slee, A.M. Stern, R. Copeland, Selective inhibition of bacterial dihydroorotate dehydrogenases by thiadiazolidinediones, *Biochem. Pharmacol*. 60 (2000) 339-342.

ACCEPTED MANUSCRIPT

[46] Y. Song, D.T. Connor, A.D. Sercel, R.J. Sorenson, R. Doubleday, P.C. Unangst, B.D. Roth, V.G. Beylin, R.B. Gilbersten. K. Chan, D.J. Schrier, A. Guglietta, D.A. Bornemeier, Synthesis, structure-activity relationships, and *in vivo* evaluations of substituted di-*tert*-butylphenols as a novel class of potent, selective, and orally active cyclooxygenase-2 inhibitors. 2. 1,3,4- and 1,2,4-thiadiazole series, *J. Med. Chem*. 42 (1999) 1161-1169.

[47] A. Tamilselvi, G. Mugesh, Interaction of heterocyclic thiols/thiones eliminated from cephalosporins with iodine and its biological implications,*Bioorg. Med. Chem. Lett*. 20 (2010) 3692-3697.

[48] M.S. Chernov'yants, N.V. Aleshina, Z. A. Starikova and E.N. Sul'zhenko, Reaction of 5-methyl-1,3,4-thiadiazoline-2-thione with molecular iodine, *Russ. Chem. Bull, International Edit*. 59 (2010) 1.

[49] A. Tamilselvi, G. Mugesh, Inhibition of Peroxidase-Catalyzed Iodination by Cephalosporins: Metallo-β-Lactamase-Induced Antithyroid Activity of Antibiotics,*ChemMedChem*. 4 (2009) 512.

[50] S. Otto, R.L.E. Furlan, J.K.M. Sanders, Dynamic combinatorial libraries of macrocyclic disulfides in water, *J. Am. Chem. Soc*. 122 (2000) 12063.

[51] O. Ramström, J.M. Lehn, In Situ Generation and Screening of a Dynamic Combinatorial Carbohydrate Library against Concanavalin A, *Chembiochem*. 1 (2000) 41-48.

[52] B.M. Matysiak, P. Nowak, I. Cvrtila, C. Pappas, B. Liu, D. Komaromy, S. Otto, Antiparallel Dynamic Covalent Chemistries, *J. Am.Chem.Soc.* 139 (2017) 6744-6751.

[53] L.O. Ofori, J. Hoskins, M. Nakamori, C.A. Thornton, B.L. Miller, From dynamic combinatorial 'hit' to lead: in vitro and in vivo activity of compounds targeting the pathogenic RNAs that cause myotonic dystrophy, *Nucleic Acids Res*. 40 (2012) 6380-6390.

ACCEPTED MANUSCRIPT

ACCEPTED MANUSCRIPT

[54] S. Otto, R.L.E. Furlan, J.K.M. Sanders, Selection and amplification of hosts from dynamic combinatorial libraries of macrocyclic disulfides, *Science.* 297 (2002) 590-593.

[55] L. J. P. Nowak, S. Otto, An Allosteric Receptor by Simultaneous “Casting” and “Molding” in a Dynamic Combinatorial Library, *Angew.Chem.Int.Ed*. 54 (2015) 833-837.

[56] F. Ulatowski, A. Sadowska-Kuziola, J. Jurczak, Choose-a-Size” approach in dynamic combinatorial chemistry: a single substrate dynamic combinatorial library of oligomacrocycles that adapts to the size and shape of carboxylates, *J.Org. Chem*. 79 (2014) 9762-9770.

[57] S.P. Black, J.K.M. Sanders, A.R. Stefankiewicz, Diverse topologies in dynamic combinatorial libraries from tri- and mono-thiols in water: sensitivity to weak supramolecular interactions, *Chem. Soc. Rev*. 43 (2014) 1861-1872.

[58] J. Atcher, A. Moure, I. Alfonso, The emergence of halophilic evolutionary patterns from a dynamic combinatorial library of macrocyclic pseudopeptides, *Chem. Commun.* 49 (2013) 487-489.

[59] L.I. James, J.E. Beaver, N.W. Rice, M.L. Waters, A Synthetic Receptor for Asymmetric Dimethyl Arginine, *J. Am. Chem. Soc*. 135 (2013) 6450-6455.

[60] N. Ponnuswamy, F.B.L. Cougnon, J.M. Clough, G.D. Pantos, J.K.M. Sanders, Discovery of an Organic Trefoil Knot, *Science*. 338 (2012) 783-785.

[61] S. Otto, R.L.E. Furlan, J.K.M. Sanders, Dynamic combinatorial libraries of macrocyclic disulfides in water, *J. Am. Chem. Soc*. 122 (2000) 12063-12064.

[62] Y. Zhong, Y. Xu, E.V. Anslyn, Studies of Reversible Conjugate Additions, Eur. *J. Org.Chem*.2013 (2013) 5017-5021.

[63] G. Joshi, E.V. Anslyn, Dynamic Thiol Exchange with ß-Sulfido-α, ß-Unsaturated Carbonyl Compounds and Dithianes, *Org.Lett*. 14 (2012) 4714-4717.

ACCEPTED MANUSCRIPT

ACCEPTED MANUSCRIPT

[64] G.L. Khatik, R. Kumar, A.K. Chakraborti, Catalyst-Free Conjugated Addition of Thiols to α,β-Unsaturated Carbonyl Compounds in Water, *Org. Lett.* 8 (2006) 2433-2436.

[65] B. Shi, R. Stevenson, D.J. Campopiano, M.F. Greaney, Discovery of Glutathione S-Transferase Inhibitors Using Dynamic Combinatorial Chemistry,*J. Am. Chem. Soc.* 128 (2006) 8459-8467.

[66] B. Shi,; M.F. Greaney, Reversible Michael addition of thiols as a new tool for dynamic combinatorial chemistry, *Chem. Commun*. (2005) 886-888.

[67] Z. Wang, H. Qi, Q. Shen, G. Lu, M. Li, K. Bao, Y. Wu, W. Zhang, 4,5-diaryl-3H-1,2-dithiole-3-thiones and related compounds as combretastatin A-4/oltiprazhybrids:Synthesis,molecular modelling and evaluation as antiprolifirative agents and inhibitors of tubulin, *Eur. J. Med. Chem*., 2016.

[68] L. Lapinski, M.J. Nowak, R. Kolos, J.S. Kwiatkowski, J. Leszczynsky, Spectroscopic identification of 2,4-pyrimidinedithiol; an experimental matrix isolation and ab initio Hartree–Fock and density functional theory study, *J. Spectrochim. Acta A*. 54 (1998) 685.

[69] A. Gordon. R. Ford, A Handbook of Practical Data, The Chemist Companion, Wiley, New York, 1971.

[70] The crystallographic structure of 5,5’-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione) in Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21 EZ, England.

[71] C. M. Sheldric Programs SHELX597 (crystal structure solution and SHELXL97 (crystal structure refinement), University of Gottinge, Germany, 1997.

[72] Bruker Programs APEX II, version 2.0-1; SAINT, version 7.23A; SADABS, version 2004/1, 2005; XPREP, version 2005/2; SHELXTL, version 6.1. Bruker AXS Inc., Madison, WI, USA, 2005.

ACCEPTED MANUSCRIPT

ACCEPTED MANUSCRIPT

[73] A.I. Spec, Single-crystal structure validation with the program *PLATON*,*J. Appl. Crystallogr*. 36 (2003) 7.

[74] C.F. Macrae, P.R. Edgington, P.E. Pidcock, G. P. Shields, R. Taylor, M. Towler, J. van de Streek, *Mercury*: visualization and analysis of crystal structures, *J. Appl. Crystallogr*. 39 (2006) 453.

[75] J. Buxeraud, A. B. Absil, J. Claude, C. Raby, G. Catazano, C. Beck, F. Claude, The steady-state kinetics of peroxidase with 2, 2′-azino-di-(3-ethyl-benzthiazoline-6-sulphonic acid) as chromogen, *Eur. J. Med. Chem.-Chem. Ther*. 20 (1985) 43.

[76]M.S. Chernov'yants, E.B. Podgornaya, A. I. Pyshchev, I.N. Shcerbakov,*Russ.J.Gen.Chem*.Engl.Transl., 68 (1998) 822.

[77] M.S. Chernov'yants, E.V. Khokhlov, Investigation of the reaction of 1-methylimidazoline-2-thione with molecular iodine,*Russ.Chem.Bull*. Inter.Edit., 57 (2008) 1239-1234.

[78] M.S. Chernov'yants, T.S. Kolesnikova, Synthesis and structure of interaction product of quinolone-2(1H)-thione with molecular iodine, *Spectrochim. Acta Mol. Biomol. Spectrosc*., 139 (2015)533-538.

[79]N. V. Aleshina, M. S. Chernov'yants, I. N. Shcherbakov, Z. A. Starikova,Solvent mediated reaction of 1-methyl-1-H-tetrazoline-5-thione with iodine, *J. Struct. Chem.* 22 (2011) 313-317.

[80] F. Hipler, M.Winter, R. A. Fisher, N–H···S hydrogen bonding in 2-mercapto-5-methyl-1,3,4-thiadiazole. Synthesis and crystal structures of mercapto functionalised 1,3,4-thiadiazoles,*J. Mol. Struct*. 658 (2003) 179.

[81] J.-L.Song, W.-B. Zhou, H.-Y.Zeng, Z.-C.Dong, 5,5'-Dimethyl-2,2'-dithiodi-1,3,4-thiadiazole, *ActaCrystallogr*. Sect. E. 58 (2002) o1045-o1047.

[82] C. B. Aakeröy, J.Desper, M. Fasulo, I. Hussain, B. Levin, N. Schultheiss, Ten years of co-crystal synthesis; the good, the bad, and the ugly, *CrystEngComm.10* (2008) 1816.

ACCEPTED MANUSCRIPT

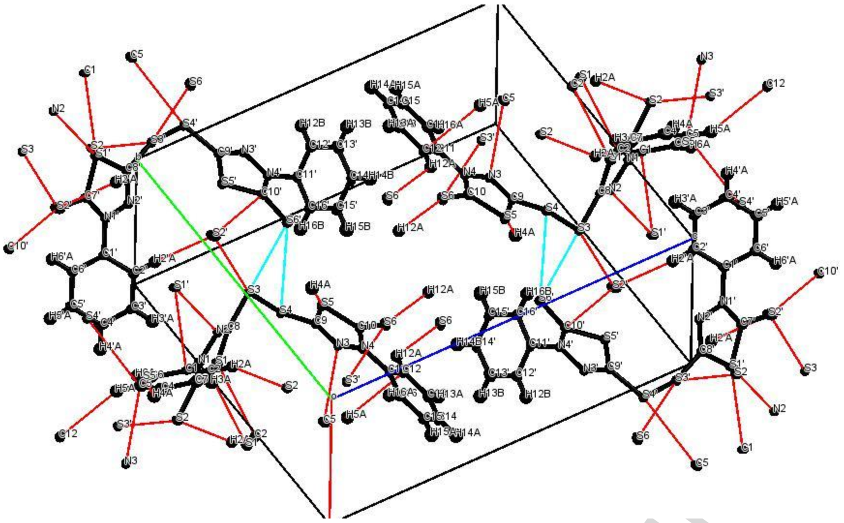
ACCEPTED MANUSCRIPT

[83] A.B. Sheremetev, N.V. Palysaeva, M.I. Struchkova, K.Yu. Suponitsky, M.Yu. Antipin, Copper-Catalyzed C-N Coupling Reactions of Nitrogen-Rich Compounds - Reaction of Iodofurazans with s-Tetrazinylamines, *Eur. J. Org. Chem.* 11 (2012) 2266-2272.

[84] A.O. Dmitrienko, V.A. Karnoukhova, A.A. Potemkin, M.I. Struchkova, I.A. Kryazhevskikh, K.Yu. Suponitsky,*Chem. Heterocycl. Compounds*. *53 (*2017) 532-539.

ACCEPTED MANUSCRIPT

ACCEPTED MANUSCRIPT



Graphical abstract

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Highlights

- The relationship between the nature of the thioamide and thyreostatic activity is revealed.
- Product of oxidation, 5,5’-disulfanediylbis(3-phenyl-1,3,4-thiadiazole-2(3H)-thione), has been characterized by molecular spectroscopic methods and X-ray diffraction.
- In crystal package intermolecular S...S contacts, shorter than sum of van der Waals radii.

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