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THE STRUCTURE OF 2-PHENYLAZO-5-(TRICHLORO-1,4-BENZOQUINONYL)-THIAZOLE*

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X-ray diffraction crystallographic analysis was used to determine the structure of 2-phenylazo-5-(trichloro-1,4-benzoquinonyl)thiazole and these results were used to establish that 2-phenylazo-5-(2,5-dihydroxy-3,4,6-trichlorophenyl)thiazole is formed in the reaction of 3,4,6,7-tetrachloro-2,5-dihydroxy-3 2,3-dihydro-benzo[b]furan with 1-phenylthiosemicarbazide.

Keywords: 1,4-benzoquinone, 2,3-dihydrobenzo[*b*]furan, thiazole.

Heterocyclic derivatives of 1,4-benzoquinones have generated considerable interest due to the presence of both an electron-withdrawing fragment (quinone) and electron-donor fragment (heterocycle) in a single molecule. Many derivatives of 1,4-benzoquinones and 1,4-naphthoquinones have pharmacological activity. The methods and properties of these compounds have been reviewed by Spyroudis [1] and in our previous work [2].

In the present communication, we present refined data on the structure of the product of the reaction of 3,4,6,7-tetrachloro-2,5-dihydroxy-2,3-dihydrobenzo[*b*]furan (**1**) with 1-phenylthiosemicarbazide. Dihydrobenzofuran **1** is the cyclic form of the *o*-hydroxyphenyl derivative of α-chloroacetaldehyde [3, 4]. The major products of the reactions between 1-substituted thiosemicarbazides and α-halocarbonyl compounds are derivatives of 4H-1,3,4-thiadiazine [5].

In previous work [6, 7], we showed that two compounds are formed in the reaction of dihydrobenzofuran **1** with 1-phenylthiosemicarbazide, namely, 2-amino-4-phenyl-6-(3,4,6-trichloro-2,5-dihydroxyphenyl)-4H-1,3,4-thiadia-zine (**2**) and 2-amino-5-(3,4,6-trichloro-2,5-dihydroxyphenyl)thiazole (**3**). The structure of **2** was assigned using data derived from elemental analysis and ^{1}H NMR (90 MHz), IR, and UV spectroscopy. However, a study of subsequent transformations of compound **2** cast some doubt on the correctness of this assignment and we decided to carry out a further investigation. The data of the ^{1}H NMR spectrum at 200 MHz and ^{13}C NMR spectrum at 100 MHz permitted us to refine the structure of compound **2** and assign the structure of 2-phenylazo-5-(3,4,6-trichloro-2,5-dihydroxyphenyl)- thiazole (**5**). The ^{1}H NMR spectrum clearly shows two signals for different OH groups at 10.13 and 9.94 ppm but lacks signals for an NH_2

* Dedicated to Professor Andris Strakovs on the occasion of his seventy-fifth jubilee.

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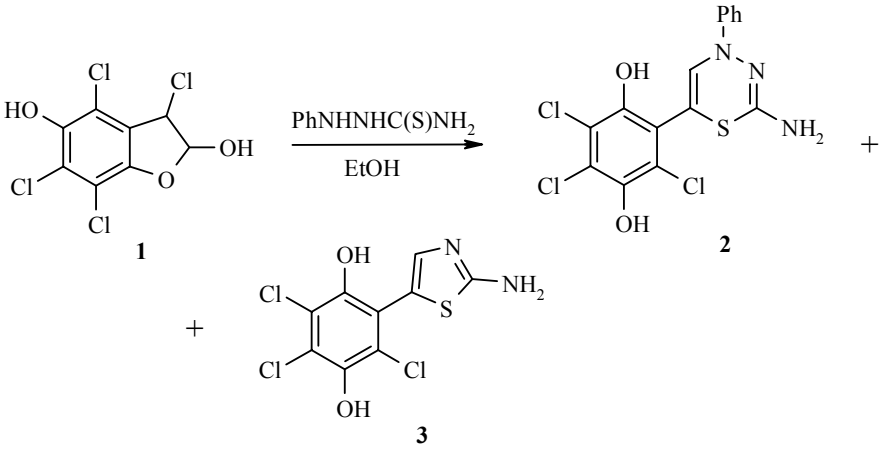
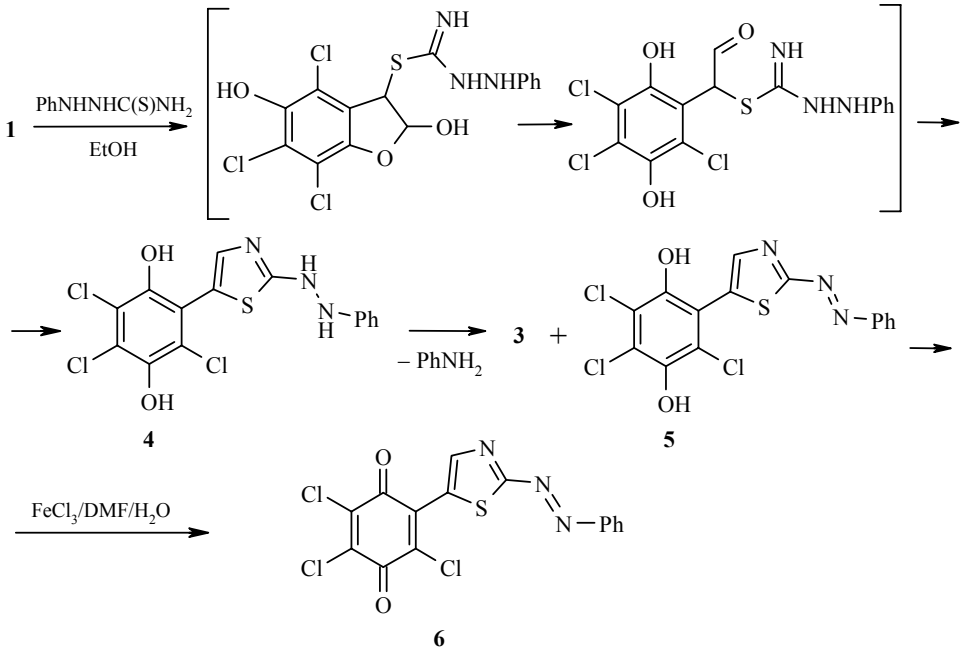
group. The downfield shift of the signals of the *ortho* protons of the benzene ring indicate their proximity to an electron-withdrawing substituent and correspond to the position of the signals of azobenzene protons [8].



In previous work [3], we showed that the synthesis of 4H-1,3,4-thidiazines is often complicated by the formation of cyclization sideproducts though we were unable to correlate the formation of any of these products with the structure of the starting compounds.

In our present case, in all likelihood, formation of the thiazole ring initially involves replacement of the chlorine atom at C(3) of dihydrobenzofuran **1** followed by opening of the dihydrobenzofuran ring and formation of the thiazole N(3)–C(4) bond. The structure of compound **2** presupposes formation of a bond with the N(1) atom of 1-phenylthiosemicarbazide. The structure of product **5** indicates that the cyclization proceeds at the N(4) atom of the thiosemicarbazide. Disproportionation of the 1,2-disubstituted hydrazine leads to hydroquinone **5** and accounts for the appearance of compound **3**.



The oxidation of hydroquinone **5** gives 2-phenylazo-5-(trichloro-1,4-benzoquinonyl)thiazole (**6**). Suitable monocrystals may be grown from methylene chloride and the structure of this compound was definitively solved by X-ray diffraction crystallographic analysis.

Figure 1 shows the molecular structure of azothiazole **6** with thermal vibration ellipsoids and the designation of the atoms. The major bond lengths and valence angles are given in Table 1. This molecule has a planar conformation. All the atoms lie in a single plane within the margin of error the substituents at the azogroup are in *trans* position. This structure of azothiazole **6** is very tentative: the conjugation system encompasses the entire molecule. Thus, there are no pure double bonds or pure single bonds in this structure. The mean bond length of the chlorine atoms with the corresponding carbon atoms in the benzoquinone fragment (1.711(9) Å) indicates that the conjugation system in this molecule also extends to the chlorine atoms.

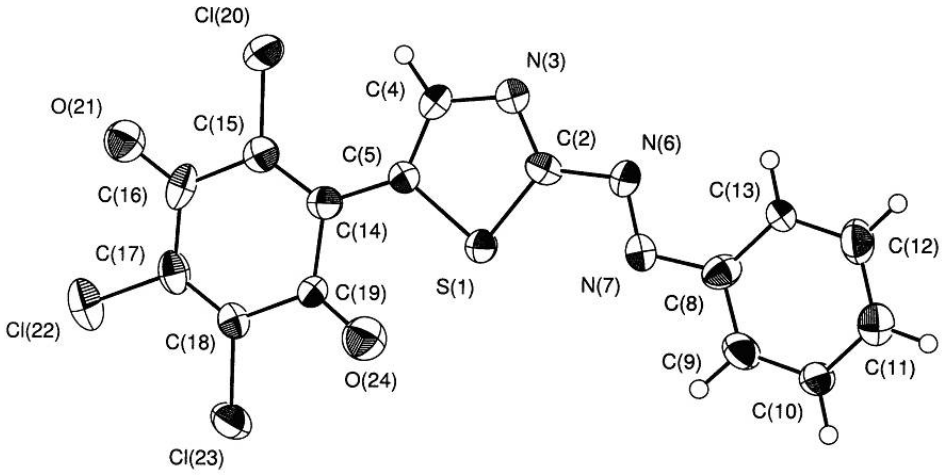


Fig. 1. Three-dimensional model of azothiazole **6** according to X-ray diffraction crystallographic data.

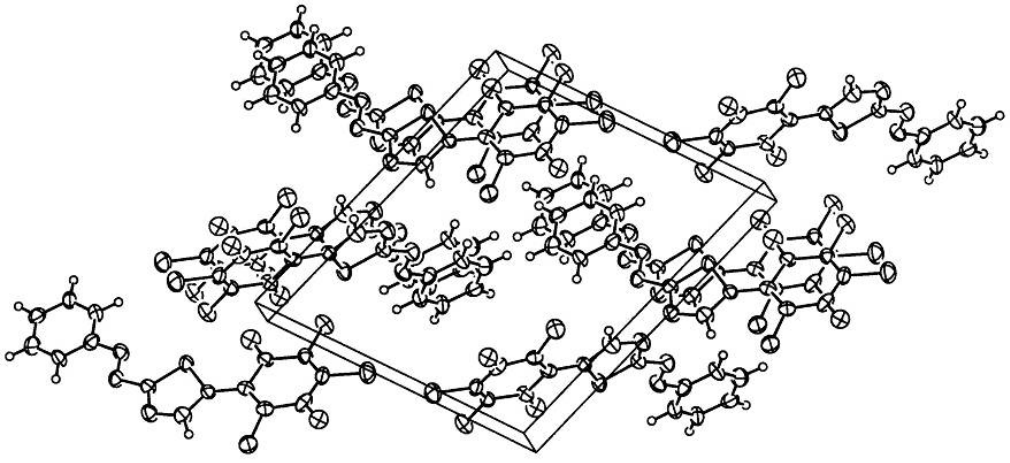


Fig. 2. Fragment of the crystal structure of azothiazole **6**.

Figure 2 shows a fragment of the packing of molecules of azothiazole **6** in the crystal lattice. An intermolecular π-π stacking interaction is observed between the molecules in the crystal structure leading to the formation of stacks of molecules along the crystallographic *y*-axis. The shortest contact in the molecular stacks

TABLE 1. Main Bond Lengths (*l*) and Valence Angles (ω) of **6**.

Bond	*l*, Å	Angle	ω, deg
S(1)–C(2)	1.706(9)	C(2)–S(1)–C(5)	89.6(5)
S(1)–C(5)	1.754(9)	S(1)–C(2)–N(3)	116.4(7)
C(2)–N(3)	1.324(12)	N(3)–C(4)–C(5)	118.8(9)
C(4)–C(5)	1.384(13)	C(4)–C(5)–S(1)	106.6(7)
C(2)–N(6)	1.414(12)	C(2)–N(6)–N(7)	108.6(8)
N(6)–N(7)	1.263(11)	N(6)–N(7)–C(8)	115.0(8)
N(7)–C(8)	1.411(12)	C(4)–C(5)–C(14)	131.6(9)
C(5)–C(14)	1.457(13)	C(5)–C(14)–C(15)	126.0(8)
C(14)–C(15)	1.356(13)	C(14)–C(15)–C(16)	122.3(9)
C(15)–C(16)	1.505(13)	C(15)–C(16)–O(21)	119.4(10)

TABLE 2. Main Crystallographic Data for Azothiazole **6** and Refinement Characteristics for the Crystal Structure

Empirical formula	$C_{15}H_6Cl_3N_3O_2S$
Molecular mass	398.655
Crystal form	Needle
Crystal size, mm	0.01 × 0.03 × 0.37
Symmetry	Monoclinic
Unit cell parameters:	
a, Å	11.427(1)
b, Å	5.3467(5)
c, Å	13.179(2)
β, deg.	106.991(4)
Unit cell volume, *V*, Å^3	770.0(1)
Space group	$P2_1$
Number of molecules in unit cell, *Z*	2
F(000)	400
Density, ρ_{calc}, g/cm^3	1.719
Maximum angle, $2\theta_{max}$, град.	55.0
Miller index ranges	$-14 \le h \le 14$
	$-6 \le k \le 5$
	$-17 \le l \le 16$
Absorption coefficient, μ, mm^{-1}	0.744
Total number of reflections	5467
Number of independent reflections	3287
Number of reflections with $I > 2\sigma(I)$	2055
R-Factor	0.0534
R-indices over all reflections (R_1, wR_2)	0.1033, 0.2213
Number of refined parameters	207
GOOF	0.974
$(\Delta/\sigma)_{max}$	0.001

(3.202(11) Å) is found between C(18) and O(21) of adjacent molecules. Features of the crystal structure account for the deep color of crystals of azothiazole **6**. We should note that although there are no asymmetric atoms in the structure of azothiazole **6** and the molecules completely coincide with their mirror antipodes by virtue of the planar conformation, the crystal structure is nevertheless chiral; the space group is $P2_1$. This circumstance should determine the physical properties of crystals of azothiazole **6** characterized by third-order

tensors since all the components of these tensors should be nonzero due to the indicated symmetry. In particular, non-zero components should be found for the nonlinear optical susceptibility tensor, which should give rise to the optical properties of the crystals of azothiazole **6**, for example, the generation of a second harmonic.

EXPERIMENTAL

The ^{1}H NMR spectra were taken on a Varian Mercury BB 200 spectrometer at 200 MHz, while the ^{13}C NMR spectra were taken on a Varian Mercury BB 400 spectrometer at 100 MHz using TMS as the internal standard. The melting points of **3, 5,** and **6** correspond to previously reported values [6].

A diffraction pattern for the X-ray diffraction crystallographic analysis was obtained for the monocrystals on a Bruker-Nonius KappaCCD automatic diffractometer at room temperature. The crystal structure was solved by a method developed at the Latvian Institute of Organic Synthesis [9]. The initial *R*-factor of the model of the structure after the solution was 30%. Further refinement was carried out by the full-matrix method of least squares anisotropically for the non-hydrogen atoms using the AREN program package [10]. The positions of the hydrogen atoms were localized in the Fourier electron density difference map and refined using the "rider" model. The crystallographic data for azothiazole **6** and refinement parameters for the structure are given in Table 2. The complete crystallographic data set and diffraction data for crystals of azothiazole **6** were deposited in the Cambridge Crystallographic Data Center (CCDC No. 725676).

2-Phenylazo-5-(3,4,6-trichloro-2,5-dihydroxyphenyl)thiazole (5). Mp >250°C (dec.) [6]. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 7.66 (3H, m, H-3, H-4, H-5 C_6H_5); 7.96 (2H, m, H-2, H-6 C_6H_5); 8.18 (1H, s, H-4 thiazole); 9.94 (1H, s, OH); 10.13 (1H, s, OH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 118.69, 120.95, 122.28, 123.69, 123.94, 130.37, 132.54, 134.03, 144.37, 146.16, 146.23, 151.52, 176.52.

2-Phenylazo-5-(trichloro-1,4-benzoquinonyl)thiazole (6). Mp 166°C (dec.) [6]. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 7.57 (3H, m, H-3, H-4, H-5 C_6H_5); 8.08 (2H, m, H-2, H-6 C_6H_5); 8.80 (1H, s, H-4 thiazole).

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