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Dedicated to the memory of Professor Nicholas Alexandrou

The electronic absorption and emission spectra of some symmetrical heterocyclic disulfides are investigated. The reversible disulfide - thione transformation in water is discussed in view of the complex equilibrium processes present. UV irradiation and pH influence on the above transformation is also studied. The emission properties at room and low temperature are related to the computed molecular geometries of the ground and low excited states of the compounds.

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Introduction.

The biological importance and activity of disulfide (RS-SR) and thiol (RSH) groups in cells, enzymes and proteins is well documented [1]. Thiols are probably the most active compounds in living cells and oxidize, in general reversibly, to their corresponding disulfides [2] thus forming a redox system which is used in the reaction known as "disulfide interchange" [3].

In a previous study [4] significant changes were observed on standing in the absorption spectra of tautomeric heterocyclic thiones, leading, almost quantitatively, to their transformation to the corresponding symmetrical disulfides. The spectral uv-visible characteristics of the corresponding thiols and disulfides are expected to be very similar due to the common parent chromophore and the non-planar structure of disulfides [5,6]. The aim of the present work is to study

Scheme 1

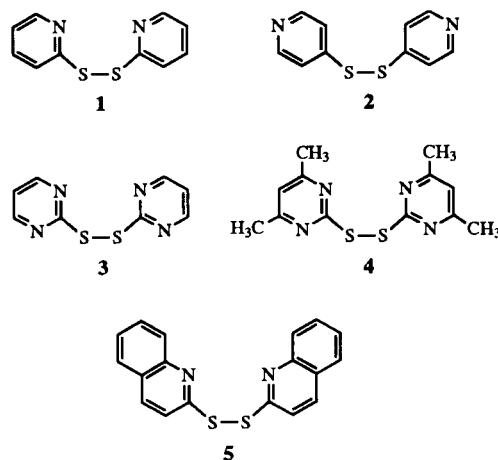


Table 1

UV-Visible Spectral Data of the Investigated Symmetrical Disulfides 1-5 in Different Solvents. Absorption Maxima Reported in nm

Solvent Compound	H ₂ O		CH ₃ CN		EtOH		cyclohexane	
	λ_{\max}	ϵ_{\max}	λ_{\max}	ϵ_{\max}	λ_{\max}	ϵ_{\max}	λ_{\max}	ϵ_{\max}
1	243	22100	236	17100	237	16800	240	18600
	282	14300	282	9900	283	10700	284	10200
2	248	15400	245	15800	248	17600	244	16200
	238	23100	238	21600	240	22600	244	23900
3	278 sh	5800	275 sh	4400	280 sh	5300	280	4900
	240	22300	241	21200	242	20800	247	22400
4	271 sh	8100	275 sh	6800	278 sh	6600	280 sh	7700
	[a]		211	73800	211	71600	212	77200
5			252	52800	254	54700	255	55900
			320	11500	322	13700	322	13400
			333	14800	335	17200	336	17200

[a] Insoluble.

the spectral properties of symmetrical disulfides 1-5 and discuss them in view of some computational results with respect to their structure. This feature may be pertinent to important aspects of thiol and disulfide groups in biological action. In this respect the extensive use of 1 and 2 for the modification and estimation of proteine thiol groups [7] should be noted.

Results and Discussion.

Spectral data of the investigated symmetrical disulfides 1-5 in water, acetonitrile, ethanol, and cyclohexane are collected in Table 1.

The absorption spectra of 1-5 in organic solvents indicate their stability, while in the most polar solvent water the observed spectral changes (Figure 1a) are accounted for by the reduction of the initial disulfide to the corresponding

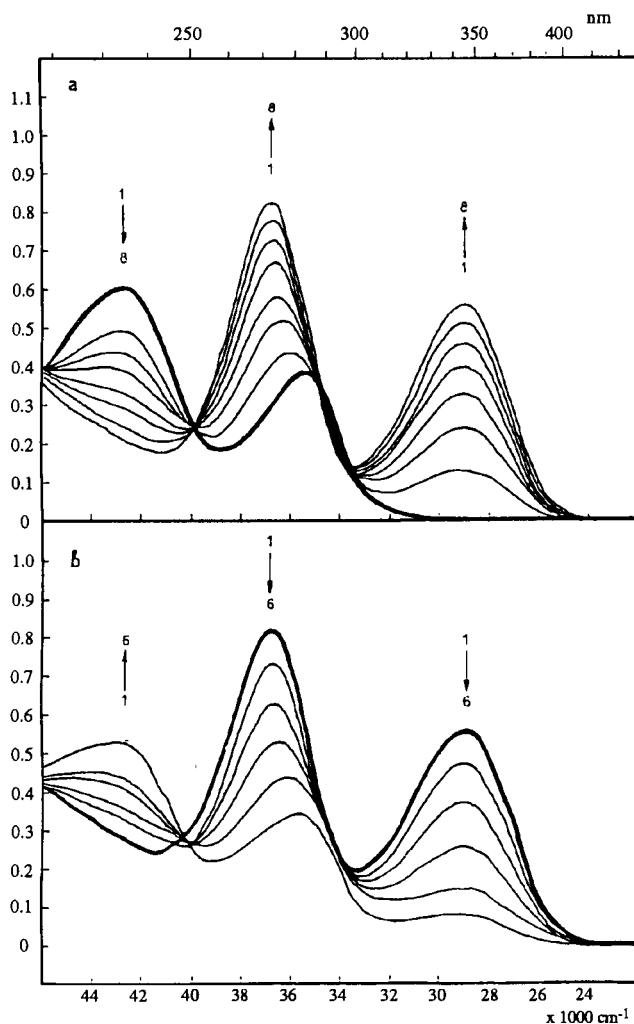
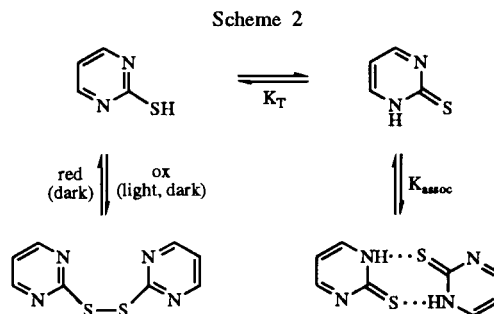


Figure 1. a: Absorption spectra of 1 in water; $c = 1.36 \cdot 10^{-5} M$, $l = 2$ cm, recorded in the dark with time: 1-initial solution; 8-after 25 days; b: absorption spectra of 2-pyridinethione in water; $c = 7.65 \cdot 10^{-5} M$, $l = 1$ cm, exposed to indirect sunlight and recorded with time: 1- initial solution; 6- after 30 days.

thione. This process is reverse of the initial thiones oxidation [4,9] in the same solvent, exposed at indirect sunlight (Figure 1b). The reversible disulfide-thione transformation in water could be represented with the Scheme 2 [9].



The thione-disulfide interchange is a complex one and may be regarded as composed of the following equilibria processes:

- thione monomer-dimer equilibrium
- thione-thiol tautomeric equilibrium
- reversible thiol-disulfide chemical transformation

Various factors, including the nature of solvent, relative stability, temperature, concentration and uv-irradiation, influence these equilibria [4,9,10].

Thione self-association [11] is essential for the interpretation of the thione-disulfide oxidation. Upon dilution, the monomer-dimer equilibrium (Scheme 2) is shifted towards the monomer species, where both tautomeric forms are possible. The process of thiol-disulfide transformation is related to the existence of the dissolved oxygen, whose concentration in water is approximately $10^{-3} M$ [12] and may be summarized as follows:



In the case of disulfide-thione reduction in water, the rate of reduction has a tendency to increase, following the mass action law [9].

Due to the great reactivity of the thiol SH group [1,2] and the very fast thione-thiol tautomeric transition [13] the absorption spectra in water (Figure 1) are dominated by the bands of the relatively stable final forms, which are the thiones and the corresponding disulfides respectively. Depending on relative rates of thione-to-disulfide oxidation and, conversely, disulfide-to-thione reduction as well as on the effects of molecular environment and relative stability of the tautomeric thiol form it is possible to account for the observed spectral features accompanying the reversible disulfide-thione transformation. The acidity and basicity constants pK_a' and pK_b for the symmetrical disulfides 1-5 and their corresponding thiones are also essential in this respect. In all cases in alkaline medium the corresponding ionized thiones are formed immediately. In acidic medium

disulfides 3-5 are converted immediately to the corresponding protonated thiones, as is evident from the comparison of their absorption spectra. Apparently the observed disulfide-thione reduction in water involves the cleavage of the S-S bond carried out in basic[14] and in specific cases acidic species:

a) In water (neutral medium):



Since the OH^- concentration is low, process (3) is, most probably, the rate determining step. It should be noted at this point, that due to the difference in polarity of the two tautomeric forms appearing in tautomeric equilibrium (5) this is shifted almost completely to the right. The estimated rate constants K_{obs} for 1-3 are presented in Table 2, along with corresponding values for thione-disulfide oxidation and pK_a ' of both final species.

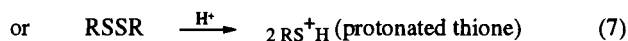
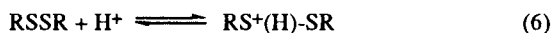
Table 2

K_{obs} ($\times 10^{-7}$) for Thione-to-disulfide and the Reverse Process in the Dark and pK_a ' Values of the Corresponding Thiones and Disulfides (Measurements were carried out in the concentrations ($\times 10^{-5}$) reported)

Compound	C [M]	Thione \rightarrow Disulfide K_{obs} [s^{-1}]	Disulfide \rightarrow Thione K_{obs} [s^{-1}]	Protonation pK_a '
2-pyridinethione	2.23	3.67 ± 0.5		-1.07 ± 0.02
1	1.36		4.66 ± 0.02	2.46 ± 0.03
4-pyridinethione	1.14	3.90 ± 0.8		1.50 ± 0.05
2	3.45		4.37 ± 0.10	4.40 ± 0.04
2-pyrimidinethione	1.11	5.82 ± 0.8		1.31 ± 0.02
3	3.33		3.69 ± 0.02	

b) In alkaline medium the ionized mesomeric thione RS^- is formed immediately (equation 3) and the overall rate of reduction is very fast.

c) In acidic medium the process may be described as:



For 1 and 2 the protonated disulfides produced from (6) are relatively stable and process (7) does not appear to proceed within a period of 10 days. For compounds 3-5, however, process (7) is the rate determining in highly acidic solutions.

Ultraviolet-irradiation with polychromatic light of symmetrical disulfides 1-5 in proton donor solvents (water and ethanol) leads to the cleavage of the S-S bond and the observed spectral changes (Figure 2) reveal formation of

the corresponding thione. This process proceeds, in the beginning, to the formation of about 30% and 50% of the theoretically estimated thione in water and ethanol respectively. Further uv-irradiation leads to photochemical degradation of the resulting thione, therefore complicating the overall picture.

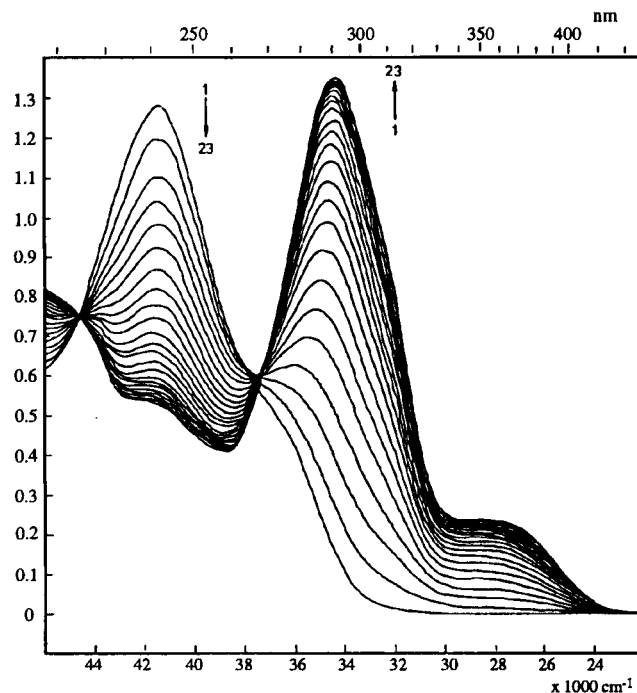


Figure 2. Absorption spectra of 4 in ethanol recorded after uv-irradiation with polychromatic light: 1-initial solution (time of irradiation 10 seconds).

Partial recovery of the initial disulfide is observed if the final irradiated ethanolic solution is kept in dark for 48-72 hours. Most probably the free radicals formed during the irradiation and the dissolved oxygen are the reasons for this back transformation.

In the case of 1 and 2 uv-irradiation in dichloroethane (Figure 3) leads to the corresponding protonated disulfides due to the well known ability of chlorinated solvents to produce photoreactive chloride radicals, and consequently hydrogen chloride, upon uv-irradiation [15] leading finally to relatively stable products. When the irradiated solution is neutralized the initial disulfide is recovered.

The uv-irradiation of 2- and 4-pyridine thiones in dichloroethane leads to almost identical absorption spectra, suggesting the formation of protonated disulfides 1 and 2 respectively.

There are no literature data about the luminescence properties of the symmetrical disulfides investigated. According to our experimental results at room temperature only 2,2'-dipyridil disulfide exhibits weak fluorescence

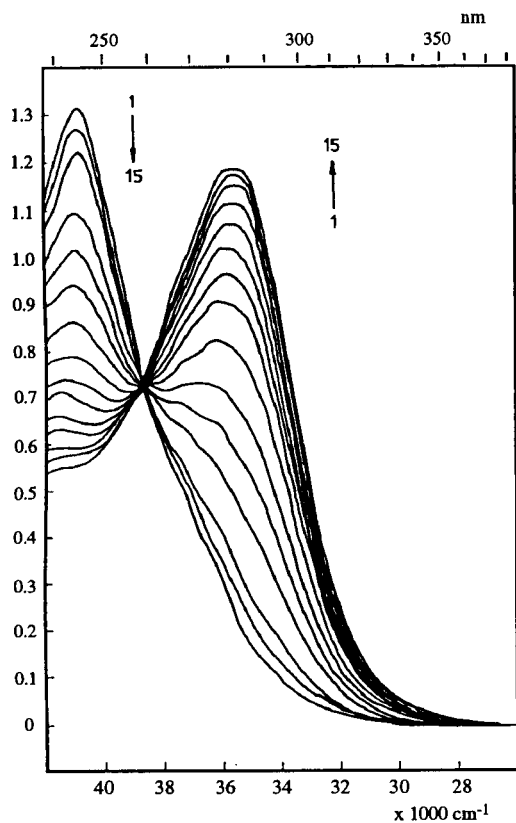


Figure 3. Absorption spectra of **2** in dichloroethane recorded after uv-irradiation with polychromatic light: 1-initial solution (time of irradiation 60 seconds).

with a maximum at about 400 nm in water and acetonitrile. In frozen ethanol matrix at 77 K a weak emission band in the same region is also observed for compounds **1**, **2** and **4**.

A possible interpretation of the observed variable emission behavior may lie in the geometric differences between the ground and the first singlet excited state of the investigated compounds. Some relevant structural data about these states, obtained from AM1 computations, are presented in Table 3. The ground state geometries are compared with structural information present in the literature.

From the data in Table 3 it is apparent that the ground state of the studied disulfides adopts a configuration with a CSSC torsion angle of approximately 90° in accordance with experimental observations [16-18]. This situation is not retained in the excited states with the exception of **5**, a fact that may support its lack of emission. The most marked difference in the excited state torsion angle, and consequently in the lone pair interaction within the disulfide bond, is observed in **1** and **4** where the compounds appear to be almost planar. The ring torsion angles relative to the corresponding CSS planes, are generally small but indicative, in the case of **5**, of the crowding effect of the system. The expected similarity of **3** and **4**, as far as the ground state is concerned is also confirmed.

Table 3

AM1 Derived Structural Parameters for the Disulfides in the Ground (S_0) and First Singlet (S_1) and Triplet (T_1) States. Bond Lengths are in Å, Angles and Torsion Angles (in absolute values) in $^\circ$. NCSSC Denotes the Torsion Angle of the Heterocyclic Ring with Respect to the Corresponding CSS Plane. The Two Values Reported Correspond to the Two Heterocyclic Rings

Compound	State	S-S	S-C	SSC	CSSC	NCSS
1	S_0	2.110	1.689	110.9	86.7	8.0 4.0
		2.016	1.785	105.7	87.1	172 [16]
	S_1	2.032	1.728	109.5	169.5	20.0 25.0
2	S_0	2.140	1.694	105.9	105.0	12.0 50.0
		2.112	1.697	108.0	94.2	5.0 4.0
	S_1	2.016	1.692	110.5	140.2	27.0 26.0
3	S_0	1.894	1.702	123.2	120.3	20.0 23.0
		2.098	1.728	108.5	82.6	6.0 4.0
	S_1	2.019	1.782	105.1	84.6	3.5 [17]
4	S_0	2.016	1.781	104.8	82.5	3.9 [18]
		1.906	1.742	118.4	137.4	5.0 10.0
	T_1	1.954	1.739	113.1	118.9	4.0 8.0
5	S_0	2.096	1.734	108.5	83.6	6.0 5.0
		1.906	1.736	112.9	169.4	8.0 14.0
	T_1	1.940	1.753	114.3	135.5	7.0 10.0
5	S_0	2.050	1.755	116.7	90.5	43.0 91.0
		2.043	1.745	120.3	85.7	20.0 104.0
	T_1	1.960	1.757	123.7	143.6	10.0 103.0

EXPERIMENTAL

The disulfides **1-5** were obtained from the corresponding tautomeric heterocyclic thiones (Scheme 1) by oxidation with equimolar amount of hydrogen peroxide [4]. The absorption spectra were measured at constant temperature (20°) on a Specord UV-Vis and PE Lambda 17 spectrophotometers with cells in the range 0.1 to 5 cm. The corrected fluorescence and excitation spectra were recorded on a Perkin-Elmer MPF-44 B spectrofluorimeter. Spectral grade solvents were used as received in the measurements. The computations utilized the AM1 hamiltonian as implemented in MOPAC93 program [8]. The convergence criterion was set to 10^{-8} and the gradient norm threshold at 0.01. Symmetry conditions were applied only to the internal parameters related to the non-hydrogen atoms. The ground, first singlet and first triplet excited states were optimized within a configuration interaction scheme involving the two highest occupied and the two lowest virtual molecular energy levels.

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