SYNTHESIS AND ACID–BASE AND THERMOCHROMIC PROPERTIES OF 5-(2-THIAZOLYL)-SUBSTITUTED FORMAZANS

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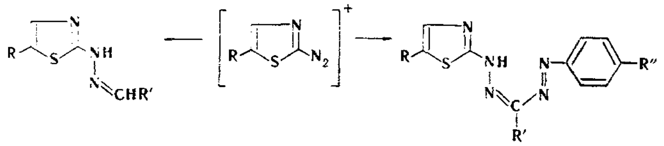
As compared with benzothiazolylformazans, the thiazole ring of synthesized 5-substituted thiazolylformazans weakens their acidic properties and decreases their tendency to form intramolecular hydrogen bonds. The thiazolylformazans have positive red-blue thermochromism. Their IR and UV spectra are presented.

The structures and properties of compounds in the benzazolylformazan series are determined primarily by the character of the heteroring [1]. No comparison has previously been made of benzazolylformazans and the analogous analylformazans. In the present communication we present the synthesis and examine the structures of thiazolylformazans as compared with benzothiazolylformazans, among which compounds with clearly expressed thermochromic properties have been found [2]. The individual 1(5)-(2-thiazolyl)formazans were obtained by Beyer [3, 4] by coupling of diazo compounds with 2-thiazolylhydrazones, the synthesis of which involves many steps and does not make it possible to obtain hydrazones that contain substituents in the 5 position of the thiazole ring.

2-Aminothiazole served as the starting material for the synthesis of formazans I-IX (Table 1). An attempt to obtain 2-hydrazinothiazoles through the 2-halo or 2-mercapto derivatives did not give the desired results. Hydrazinolysis does not occur under mild conditions, and hydrolysis of the starting compounds is observed when 2-halothiazoles are refluxed with aqueous hydrazine hydrate. The bromine atom in 2-bromo-5-nitrothiazole is very labile, but even when the reaction mixture is cooled the resulting 2-hydrazino-5-nitrothiazole resinifies almost instantaneously. 2-Hydrazinothiazole was obtained by reduction of the diazonium salt obtained from 2-aminothiazole and was isolated in the form of the hydrazones of benzaldehyde and isobutyraldehyde, which were subsequently used for the synthesis of formazans IV and V. The remaining formazans were synthesized by coupling of the diazonium salts obtained from 5-substituted 2-aminothiazoles with aromatic hydrazones.



I-IX

A distinct band of stretching vibrations of an NH group is observed in the IR spectra of phenylformazans I and VIII, i.e., these compounds, like 1(5)-benzothiazolyl-3-methyl-5(1)-(p-nitrophenyl)formazan, exists in the tautomeric amine form in solution. In contrast to 1(5)-benzothiazolyl-3-phenyl-5(1)-(p-nitrophenyl)formazan, nitrophenylformazan IV does not contain an intramolecular hydrogen bond, and an intense band of the amine form (3330 cm^{-1}) and a low-intensity band of the imine form (3425 cm^{-1}) are observed in the IR spectrum.

A study of the acid–base properties of formazans I-IX in comparison with the properties of benzothiazolylformazans showed that thiazolylformazans are weaker acids (the pK_a values are ~ 1-1.5 units higher than the pK_a values of the corresponding benzo analogs). The reason for this is probably the higher basicity of the thiazole ring as compared with the basicity of the benzothiazole ring. As in the case of benzothiazolylformazans, the pK_a values of the thiazolylformazans change in the order (R' in parentheses) III (H) < II (CH_3) < IV

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TABLE 1. Physicochemical Characteristics of 1(5)-(2-Thiazolyl)-Substituted Formazans

Compound	R	R′	R″	ν_{NH}*, cm^{-1}	λ_{max}, nm					pK_a †
					CCl$_4$	benzene	acetone	ethanol	alcoholic NaOH	
I	H	CH_3	H	3354	455	425	442	455	526	10,34
II	H	CH_3	p-NO_2		520	500	450	462	660	9,64
III	H	H	p-NO_2		420	454	462	466	606	9,00
IV	H	C_6H_5	p-NO_2	3330 3425	540—580	520—590	470, 560	500—570	620	9,91
V	H	$CH(CH_3)_2$	p-NO_2		530	520	470	474	638	10,19
VI	Br	CH_3	p-NO_2		540	460, 548	460	478	622	8,88
VII	Br	H	p-NO_2		485	478	480	485	612	8,15
VIII	NO_2	CH_3	p-NO_2	3340	440	438	440, 640	434, 615	610	4,76
IX	NO_2	H	p-NO_2		440—490	490, 554	480	484, 608	606	8,16

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*Formazans I-IX have low solubilities in CCl_4, $CHCl_3$, etc.

† The pK_a values were determined with an accuracy of ± 0.04.

TABLE 2. Characteristics of 1(5)-(2-Thiazolyl)-Substituted Formazans

Compound	mp, °C*	Found, %			Empirical formula	Calc., %		
		C	H	S		C	H	S
I	124—125	54,2	4,5	13,2	$C_{11}H_{11}N_5S$	53,9	4,5	13,1
III	233	43,3	3,0	11,9	$C_{10}H_8N_6O_2S$	43,5	2,9	11,6
IV	155	53,2	3,3	8,7	$C_{16}H_{12}N_6O_2S \cdot 0{,}5H_2O$	53,5	3,6	8,9
V	192	47,6	4,0	—	$C_{13}H_{14}N_6O_2S \cdot 0{,}5H_2O$	47,7	4,5	—
VII	258	34,3	2,2	8,8	$C_{10}H_7N_6O_2SBr$	33,8	2,0	9,0
VIII	216—217	39,7	3,1	9,6	$C_{11}H_9N_7O_4S$	39,4	2,7	9,6
IX	235—236	35,2	2,5	9,2	$C_{10}H_7N_7O_4S \cdot H_2O$	35,4	2,4	9,5

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* Compound I was recrystallized from dimethylformamide (DMF)–water; III, V, and VII were recrystallized from nitromethane; IV was recrystallized from aqueous alcohol; IX was recrystallized from aqueous dioxane; and VIII was recrystallized from DMF.

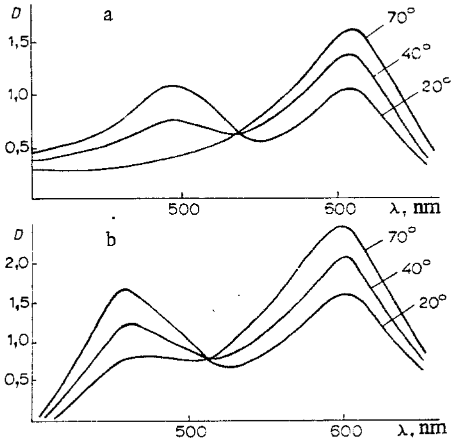
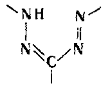
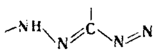


Fig. 1. Temperature variations in the electronic spectra: a) aqueous ethanol solution of VII ($c_{H_2O} \sim 30\%$); b) buffered ethanol solution of II (pH ~ 9.03).

(C_6H_5) < V [$CH(CH_3)_2$]. The increase in the pK_a values for 3-phenyl- and 3-isopropylformazans as compared with the pK_a values of 3-methyl- and 3-unsubstituted formazans can be explained by steric factors. We made this assumption by comparison of the data from the molecular diagrams of 1(5)-benzothiazolyl-3-methyl-5(1)-(p-nitrophenyl)formazan in the "syn–trans" and "anti–trans" configurations. Both the phenyl and the isopropyl residues attached to the $C_{(3)}$ atom promote the formation of the "syn–trans" configuration of formazans, in which the electron density on the nitrogen atom of the NH group is considerably higher, i.e., the acid properies of the compounds are less pronounced.


syn-trans


anti-trans

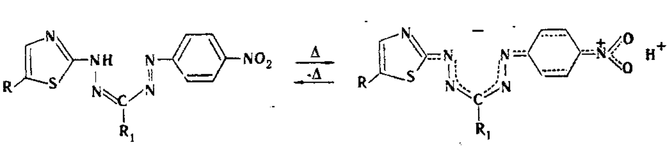
The introduction of a bromine atom or a nitro group in the 5 position of the thiazole ring considerably intensifies the acid properties of formazans (the pK_a values of VI and VII are lowered by approximately one unit, and the decrease is even greater for VIII and IX). An anomalously low pK_a value was obtained for 1(5)-(5-nitro-2-thiazolyl)-3-methyl-5(1)-(p-nitrophenyl)formazan (4.76).

Formazans I-IX can be arbitrarily divided into two groups with respect to the effect of solvents on the position of the absorption maximum in the electronic spectra. The absorption maxima of the compounds of the first group (I, III, and VII-IX) are shifted hypsochromically in nonpolar solvents as compared with the remaining formazans. Compounds II and IV-VI have negative solvatochromism, while the formazans of the first group are not subject to the solvating effects of solvents (Table 2).

We have previously concluded that the basicity of the heteroring has the primary effect on the deepening of the color in the open formazan series. In our case the thiazolylformazans are more deeply colored than their benzo analogs. For example, in CCl_4, λ_{max} of II is found at 520 nm, as compared with λ_{max} 458 nm for 1(5)-benzothiazolyl-3-methyl-5(1)-(p-nitrophenyl)formazan. Thus the principal effect of the thiazole ring is weakening of the acid properties of the formazans and reducing their tendency to form intramolecular hydrogen bonds.

Formazans I-IX form Na salts when NaOH is added to alcohol solutions, and the compounds that contain a nitro group are characterized in this case by a large bathochromic shift. Formazans I-IX react readily with metals of the 3d series to give deeply colored complexes.

The thermochromic properties of thiazolylformazans with a CH_3 group or hydrogen attached to the $C_{(3)}$ atom were studied, since it has been shown [2] that formazans with precisely these substituents most distinctly display thermochromic properties in the benzothiazolylformazan series. Aqueous alcohol solutions (20–30% water) of the compounds, the pK_a values of which range from 8 to 9 (III, VI, VII, and IX), have positive thermochromism (See Fig. 1). A decrease in the absorption of solutions of the compounds is observed at 460–480 nm in the electronic spectra, after which this absorption vanishes completely, and there is a simultaneous increase in the intensity of the absorption at 600–620 nm when the solutions are heated. The process is reversed when the solutions are cooled. Buffered ethanol solutions of formazans with $pH \approx pK_a$ are also thermochromic. The maximum bathochromic shift ($\Delta\lambda_t$) is observed for 1(5)-(2-thiazolyl)-3-methyl-5(1)-(p-nitrophenyl)formazan (~200 nm); $\Delta\lambda_t \sim 100$–140 nm for the other compounds. As in the case of 1(5)-benzothiazolylformazans, the position of the long-wave absorption band of the thermally induced form coincides with the absorption of alcoholic alkali solutions of the formazans, i.e., the reason for the thermochromic transitions of the thiazolylformazans also consists in a shift in the A ⇌ B equilibrium when the solutions are heated:


A

B

EXPERIMENTAL

The IR spectra of saturated solutions of the formazans in CCl_4 were obtained with a UR-20 spectrometer. The electronic spectra of $1 \cdot 10^{-4}$–$1 \cdot 10^{-5}$ mole/liter solutions of the compounds were obtained with an SF-10 spectrophotometer. The acid ionization constants were determined by the method presented in [5].

Synthesis of the Formazans. The diazotization of 2-aminothiazole was accomplished by the method in [5], 2-amino-5-bromothiazole was diazotized by the method in [6], and 2-amino-5-nitrothiazole was diazotizedbythe method in [5]. Diazo coupling was accomplished by the following method. A solution of the diazonium salt was added gradually with cooling to an alcohol solution of acet(form)aldehyde p-nitrophenyl-hydrazone along with sodium acetate, and the suspension was made alkaline to pH 8-9 and allowed to stand for 1 h. It was then acidified with HCl (1:1), and the formazans were isolated at pH 4-5. Equimolar ratios of the reactants were used in the case of coupling with acetaldehyde hydrazone. Insufficient diazonium salt was used in the case of coupling with formaldehyde hydrazone (2:1), since reaction at the labile hydrogen atom in the meso position of the formazan ring to give 1,3-dihetarylformazans is possible. The characteristics of formazans I-IX are presented in Table 2.

Benzaldehyde 2-Thiazolylhydrazone. A solution of the diazonium salt of 2-aminothiazole (0.046 mole) was added slowly to a cooled solution of 0.063 mole of stannous chloride in 25 ml of concentrated HCl, and the mixture was allowed to stand at 0° for 3 h and at room temperature for 1 h. The suspension was then cooled and made alkaline to pH 8-9 with 30% NaOH solution. A 1.5-fold excess (by volume) of alcohol was added to the suspension, and the precipitate was removed by filtration. A 0.01-mole sample of benzaldehyde was added to the filtrate, and the solution was heated to the boiling point. The hydrazone, with mp 173° [mp 172-173° (benzene)], was isolated by the addition of ice to the solution. Isobutyraldehyde 2-thiazolylhydrazone, with mp 100-102° [alcohol–water (2:1)], was similarly obtained. Found: C 49.9; H 6.9; S 19.1%. $C_7H_{11}N_3S$. Calculated: C 49.7; H 6.5; S 18.9%.

1(5)-Thiazolyl-3-phenyl(isopropyl)-5(1)-(p-nitrophenyl)formazans were obtained by coupling with a p-nitrobenzenediazonium salt. The characteristics are presented in Table 2. The synthesis of formazans II and VI is presented in [7].

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