

BENZAZOLES AND NAPHTHAZOLES
 XXXIX.* SYNTHESIS OF 1,5-DIHETARYLFORMAZANS
 ON THE BASIS OF AUTOOXIDATION
 OF THIAZOLO[4,5-b]-2-PYRIDYL-
 AND 2-BENZOTHAZOLYLHYDRAZINES

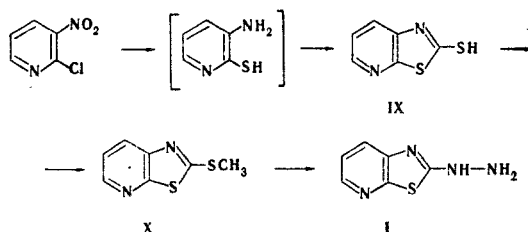
N. P. Bednyagina, N. N. Gulemina,
 G. N. Lipunova, and L. V. Saloutina

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Thiazolo[4,5-b]-2-pyridylhydrazine, which like 2-benzothiazolylhydrazine, undergoes auto-oxidation in ethanol solution to give a symmetrical 1,5-bis(thiazolo[4,5-b]-2-pyridyl)-3-methylformazan, was synthesized. Asymmetrical 1,5-dihetarylformazans were obtained by autooxidative coupling of 2-hydrazinobenzothiazole with acetaldehyde thiazolo[4,5-b]-2-pyridylhydrazone and 5-nitro-2-pyridyl hydrazone. Formazans containing a thiazolopyridine ring have more acidic character than benzothiazolylformazans.

Of the heterocyclic hydrazines investigated up to now, only 2-hydrazinobenz(naphth)azoles have the ability to undergo autooxidation to give 1,5-dihetarylformazans [2-5]. It seems to us that the search for new autooxidizing hydrazines is most promising in bisheterocyclic systems containing a 2-hydrazinoazole grouping.

In the present research we investigated the autooxidizing capacity of thiazolo[4,5-b]-2-pyridylhydrazine (I) which was newly synthesized via the following scheme:

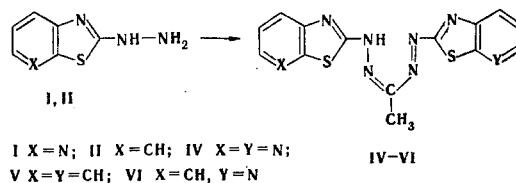


The color of a solution of hydrazine I in ethanol changes from pale-rose to deep-blue on standing in air for several days, and a crystalline precipitate, which was found to be 1,5-bis(thiazolo[4,5-b]-2-pyridyl)-3-methylformazan (IV), is formed. Compound IV was also obtained by the method in [6] by autooxidative coupling of hydrazine I with acetaldehyde thiazolo[4,5-b]-2-pyridylhydrazone (III). Catalytic amounts of sodium acetate accelerate the autooxidation of thiazolo[4,5-b]-2-pyridylhydrazine and 2-benzothiazolylhydrazine (II).

Using the autooxidative coupling method [6], we obtained both symmetrical and asymmetrical 1,5-dihetaryl formazans IV, VI, and VIII from hydrazines I and II. Thus the autooxidative coupling of hydrazine II with hydrazone III gave 1-benzothiazolyl-5-(thiazolo[4,5-b]-2-pyridyl)-3-methylformazan (VI), whereas formazan VIII was synthesized by coupling of II with acetaldehyde 5-nitro-2-pyridylhydrazone (VII).

*See [1] for communication XXXVIII.

S. M. Kirov Ural Polytechnic Institute, Sverdlovsk. Translated from *Khimiya Geterotsiklicheskikh Soedinenii*, No. 7, pp. 925-927, July, 1975. Original article submitted June 26, 1974.



The electronic spectra and acid-base properties of formazans IV-VI and VIII were studied (Table 1). A rather large hypsochromic shift in alcohol solutions of HCl (pH ~ 1) as compared with alcohol solutions of NaOH (pH ~ 12) is observed for all of the compounds. In contrast to IV-VI, the previously described [7] symmetrical 1,5-dibenzimidazolylformazans had approximately identical absorption spectra to these pH values, and this was explained by their amphoteric properties. Thus IV-VI can be considered to be only weak acids that do not form hydrochlorides with cyanine structures, inasmuch as their absorption spectra in alcoholic HCl are close to the absorption spectra in CCl_4 , in which only the nonionized form is present.

The acidic ionization constants were determined by a spectrophotometric method. All of the formazans have pK_a values ranging from 5 to 8, and they are therefore already partially ionized in alcohol solutions, as a consequence of which their alcohol solutions are deeply colored, and their spectra have diffuse character. Replacement of the benzothiazole residue by a thiazolo[4,5-b]pyridine residue at the nitrogen atom of the formazan chain leads to an increase in the acid properties of the formazan. The pK_a values increase in the order $\text{V} > \text{VI} > \text{IV}$.

EXPERIMENTAL

The ionization constants in 50% alcohol-buffer solutions of the formazans (alkaline borate buffer) were measured by the method in [8] at the wavelength of alcoholic alkali.

2-Amino-3-nitro-, 2-Amino-5-nitro-, 2-Hydroxy-3-nitro-, and 2-Hydroxy-5-nitropyridines. These compounds were obtained by the method in [9-11], respectively.

Thiazolo[4,5-b]pyridine-2-thiol (IX). A 2-g (16 mmole) sample of 2-chloro-3-nitropyridine [11] was added gradually to a refluxing solution of 2 g (35 mmole) of NaSH in 8 ml of H_2O , and the mixture was refluxed for 30 min. A 6-g (26 mmole) sample of $\text{Na}_2\text{S} \cdot 9\text{H}_2\text{O}$ was then added in portions to the refluxing reaction mixture with simultaneous bubbling of hydrogen sulfide through the solution for 2.5 h. The mixture was then cooled, 1 g (17.5 mmole) of NaSH and 4 ml (65 mmole) of CS_2 were added, and the mixture was refluxed on a water bath for 5-6 h. The reaction solution was then cooled and neutralized to pH ~ 7 with acetic acid, and the resulting precipitate was removed by filtration. The product was purified by reprecipitation from ammonium hydroxide solution by the addition of acetic acid to give a compound with mp 294° (mp 294° [12]).

2-Methylthiothiazolo[4,5-b]pyridine (X). A 0.1-ml sample of 30% NaOH solution and 1 ml (10 mmole) of CH_3I were added to an alcohol solution of 0.6 g (4 mmole) of thiol IX, and the mixture was refluxed for 10 min. The alcohol was then removed by distillation to give a product with mp 95° (from alcohol) in 85% yield. Found: C 45.0; H 3.3; N 15.0%. $\text{C}_7\text{H}_6\text{N}_2\text{S}_2$. Calculated: C 46.1; H 3.3; N 15.4%.

Thiazolo[4,5-b]-2-pyridylhydrazine (I). A solution of 0.5 g (2.5 mmole) of X in 15 ml of isopropyl alcohol was refluxed with 1 ml (30 mmole) of hydrazine hydrate for 1 h, after which the alcohol was removed by distillation to give white crystals with mp 246° (sublimes, from 50% aqueous alcohol) in 65% yield. Found: C 43.4; H 3.8; S 19.0%. $\text{C}_6\text{H}_6\text{N}_4\text{S}$. Calculated: C 43.4; H 3.6; S 19.3%.

TABLE 1. Physicochemical Characteristics of the Dihetarylformazans

| Compound | λ_{max} , nm | | | | pK_a^* |
|----------|-----------------------------|---------|------------------|---------------|-----------------|
| | CCl_4 | alcohol | alcoholic alkali | alcoholic HCl | |
| IV | 490 | 580-610 | 598 | 490 | 4.96 |
| V | 500 | 544 | 580-614 | 526 | 6.82 |
| VI | 484 | 570-610 | 590 | 480 | 5.59 |
| VIII | 450 | 450-594 | 622 | 450 | 7.83 |

* The pK_a values were measured with an accuracy of ± 0.05 .

Acetaldehyde Thiazolo[4,5-b]-2-pyridylhydrazone (III). Acetaldehyde (3 ml) was added to a solution of 0.62 g (3.5 mmole) of hydrazine I in 30 ml of ethanol (the reaction was exothermic). After 15 min, the solution was cooled, and the alcohol was evaporated at 25–30° to give a product with mp 225° (from 50% aqueous alcohol) in 80% yield. Found: C 50.3; H 4.5; N 29.0%. $C_8H_8N_4S$. Calculated: C 50.0; H 4.2; N 29.2%.

1,5-Bis(thiazolo[4,5-b]-2-pyridyl)-3-methylformazan (IV). A) A 0.3-g sample of sodium acetate was added to a hot alcohol solution of 0.8 g (4.4 mmole) of hydrazine I. After 5–7 days, the solution was acidified with dilute acetic acid to pH ~ 6, and the resulting dark-blue precipitate was removed by filtration to give a product with mp 251° [dimethylformamide (DMF)] in 40% yield.

B) Solutions of 0.5 g (27 mmole) of hydrazine I and 0.59 g (27 mmole) of hydrazone III in pyridine were mixed, and 0.3 g of sodium acetate was added. Formazan IV, with mp 251°, was isolated and purified as described in experiment A. Found: C 47.7; H 3.2; S 17.9%. $C_{14}H_{10}N_8S_2$. Calculated: C 47.4; H 2.8; S 18.1%.

1-(Thiazolo[4,5-b]-2-pyridyl)-3-methyl-5-(2-benzothiazolyl)formazan (VI). This compound, with mp 257° [DMF–water (3:1)], was obtained in 55% yield from equivalent amounts of II and III by the method used to prepare IV. Found: C 51.8; H 3.3; N 27.8%. $C_{15}H_{11}N_7S_2$. Calculated: C 51.0; H 3.1; N 27.8%.

Acetaldehyde 5-Nitro-2-pyridylhydrazone (VII). An alcohol solution of 0.3 g (19 mmole) of 2-hydrazino-5-nitropyridine (XI) [13] and 2.2 ml (40 mmole) of acetaldehyde was heated for 10 min, after which the ethanol was evaporated to give a product with mp 265–266° (alcohol) in 82% yield. Found: C 47.4; H 4.6%. $C_7H_8N_4O_2$. Calculated: C 46.7; H 4.4%.

1-Benzothiazolyl-3-methyl-5-(5-nitro-2-pyridyl)formazan (VIII). A hot solution of 1 g (60 mmole) of hydrazine II in isopropyl alcohol (45 ml) was added to a solution of 1 g (55 mole) of hydrazone VII in isopropyl alcohol (20 ml), 0.2 g of sodium acetate was added, and the mixture was allowed to stand. After 5–7 days, the solution was acidified to pH 5–7 with dilute acetic acid to give a dark-brown precipitate. Workup gave a product with mp 237° (nitromethane) in 60% yield. Found: C 50.1; H 3.3%. $C_{14}H_{11}N_7O_2$. Calculated: C 49.7; H 3.3%.

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