UDC 547.79 + 547.78 + 543.422 + 542.95

THIAZOLOBENZO-1, 2, 3-THIADIAZOLES AND DERIVED CYANINE DYES

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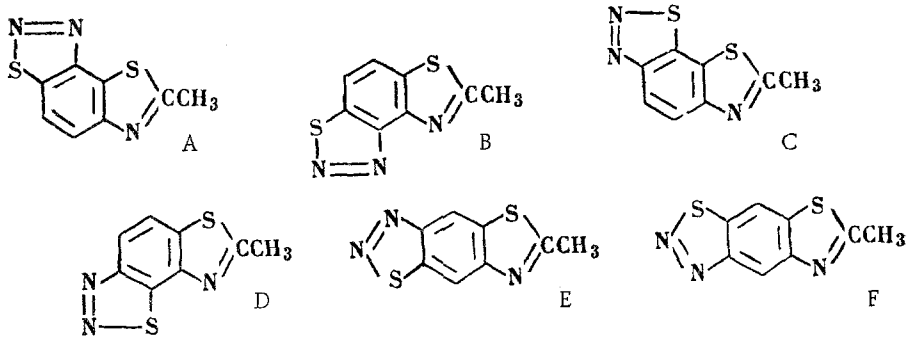
The following tricyclic heterocyclic compounds are synthesized: 2-methylthiazolo(5,4-e)benzo-1',2',3'-thiadiazole, 2-methylthiazolo(4,5-e)benzo-1',2',3'-thiadiazole, 2-methylthiazolo(4,5-g)benzo-1',2',3'-thiadiazole, and 2-methylthiazolo(5,4-g)benzo-1',2',3'-thiadiazole. The quaternary salts of these bases are used to prepare symmetrical and unsymmetrical trimethinecyanines and dimethinemercocyanines containing N-ethylrhodanine residues. The absorption maxima of these dyes are shifted toward the long-wave region as compared with the corresponding thiacyanines.

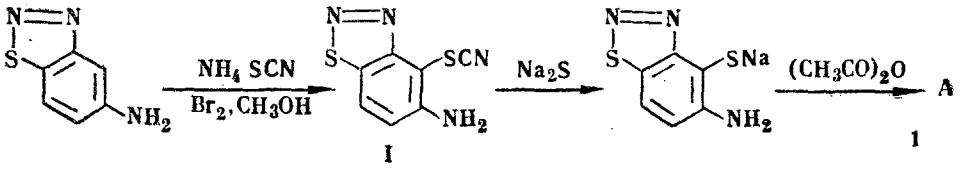
A preceding paper [1] described the synthesis of thiazolobenzo-2,1,3-thiadazoles. The work described in the present paper aimed to prepare isomeric thiazolobenzo-1,2,3-thiadiazoles and synthesize dyes containing those heterocyclic systems.

There are six theoretically possible isomeric 2-methylbenzo-1',2',3'-thiadazoles

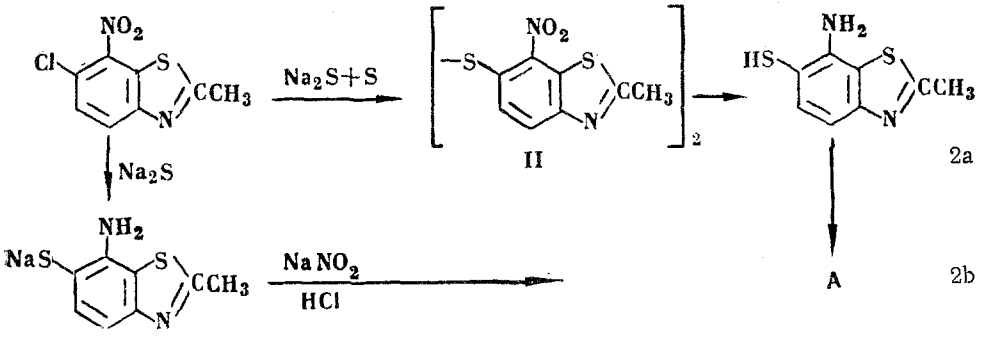


It proved possible to prepare the isomers A, B, C, D, but attempts to prepare E and F failed.

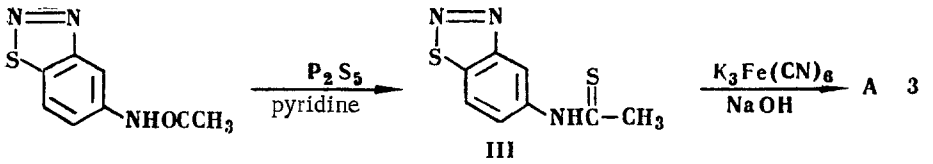
The isomer A is obtained in good yield (60%), by thiocyanating 5-aminobenzo-1,2,3-thiadiazole, reducing the reaction product I with sodium sulfide, and condensing the resultant aminomercaptan with acetic anhydride



Though the above reaction would be expected to give precisely isomer A, the product structure was checked by alternative syntheses from 2-methyl-6-chloro-7-nitrobenzothiazole (2a, 2b) and 5-acetylamino-1,2,3-thiadiazole by the Jacobsen method (3) via the thioacetyl derivative III



In neither case does the yield of A exceed 10%.

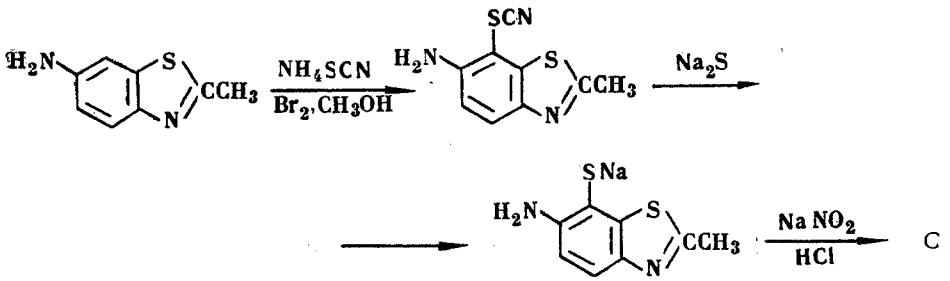


III

The yield of A obtained by method (3) does not exceed 20%, based on the thioacetyl derivative.

Analogous to A, isomer B was prepared by reactions (2b), starting from 2-methyl-5-chloro-4-nitrobenzothiazole. The yield did not exceed 10%.

Isomer C is synthesized by thiocyanating 6-aminobenzo-1, 2, 3-thiadiazole, in accordance with 1 above. It is also obtained in good yield by thiocyanating 2-methyl-6-aminobenzothiazole:



Under the same conditions thiocyanating 2-methyl-5-aminobenzothiazole gives isomer D in very good yield.

This reaction might also be expected to result in formation of isomer F, if the thiocyano group entered at position 6 of the benzothiazole ring. However, in the present work it has been shown that thiocyanation takes place only at position 4, giving compound IV, since reduction of the thiocyano derivative and condensation of the product with acetic anhydride gives the known [2, 3] 2, 5-dimethylthiazolo (5, 4-g) benzothiazole (V).

IV V

Attempts to prepare isomer E by boiling 2-methyl-5-chloro-6-nitrobenzothiazole with sodium sulfide in aqueous solution, followed by diazotization, analogous to the scheme used for isomer A (2b), did not give the desired result. While the nitro group is reduced to amino in the heating with sodium sulfide, the chlorine atom is not replaced by a mercapto group. This serves to confirm the results in the literature, that with bicyclic hetrocyclic compounds, benzimidazole, benzothiazole, benzothiadiazole, the bonding between carbon atoms five and six is mainly a single bond [4], with the result that the nitro group does not exert an activating effect on the neighboring chlorine atom [5].

The UV absorption spectra of alcohol solutions of the thiazolo-benzothiadiazoles were investigated. The Figure gives the absorption plot for isomer A, and for comparison the absorption plots for 2-methylbenzothiazole [6], and benzo-1, 2, 3-thiadiazole. It can be seen that the absorption curve for isomer A is closer to that for benzo-1, 2, 3-thiadiazole than to that for the benzothiazole. The absorption plots for isomers B, C, D are more or less close to that for isomer A.

With the exception of isomer D, which forms a quaternary salt only with dimethylsulfate, the thiazolobenzo, 1, 2, 3-thiadiazoles undergo quaternary salt formation at the thiazole ring when heated with ethyl tosylate. Cyanine dyes were prepared from the quaternary salts by the usual methods. The dyes prepared from the quaternary salts of the isomers A and B are readily purified by recrystallizing from alcohol. Dyes were also prepared from quaternary salts of isomers C and D, but only a few could be isolated pure.

The dyes prepared are given in the table. The tabulated data show that the absorption maxima for dyes with thiazolobenzothiadiazole rings lie in a longer wavelength part of the spectrum than dyes with an unsubstituted benzothiazole ring. The dyes prepared from isomer B are somewhat deeper than those obtained from isomer A.

Cyanine Dyes Containing Thiazolobenzo-1, 2, 3-thiadiazole Rings

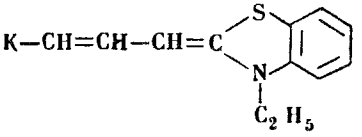
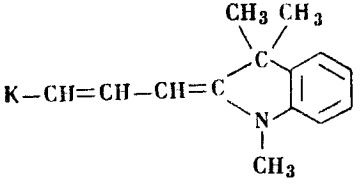
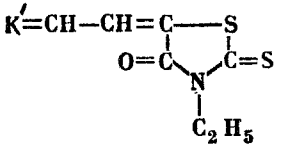
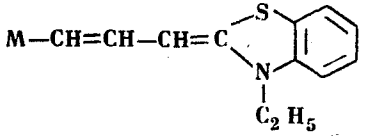
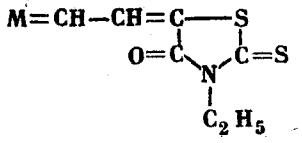
Dye name and structure*	Mp, °C	λ_{max}, mμ	Formula	S, % Found	S, % Calculated	Yield, %
K—CH=CH—CH=K′ Bis [3-ethylthiazolo(5, 4-e) benzo-1', 2', 3'-thiadiazole-2] trimethinecyanine iodide	215—216	570	$C_{21}H_{17}JN_5S_4$	20.91; 20.92	20.88	15
 [3-Ethylthiazolo(5, 4-e) benzo-1', 2', 3'-thiadiazole-2]-[3-ethylbenzothiazole-2] trimethinecyanine iodide	275 (разл.)	568	$C_{21}H_{19}JN_4S_2$	17.29; 17.19	17.45	22
 3-Ethylthiazolo(5, 4-e) benzo-1', 2', 3)-thiadiazole-2]-[1, 3, 3-trimethylindolenine-2] trimethinecyanine iodide	231	558	$C_{23}H_{23}JN_4S_2$	11.84; 11.69	11.72	40
 3-Ethyl-5 [3-ethylthiazolo(5, 4-e) benzo-1', 2', 3'-thiadiazole-2-ethylidene] thiazolidinethione-2-one-4	269	526	$C_{16}H_{14}ON_4S_4$	31.02; 31.19	31.52	41

Table (continued)

Dye name and structure*	Mp, °C	λ_{max}, mμ	Formula	S, % Found	S, % Calculated	Yield, %
M–CH=CH–CH=M′ Bis [3-ethylthiazolo(4, 5-e) benzo-1′, 2′, 3′-thiadiazole-2] trimethinecyanine iodide	197—198	592	$C_{21}H_{28}JN_6S_4$	20.72; 20.86	20.88	28
 [3-Ethylthiazolo (4, 5-e) benzo-1′, 2′, 3′-thiadiazole-2]-[3-ethylbenzothiazole-2] trimethinecyanine iodide	242	576	$C_{21}H_{19}JN_4S_3$	17.41; 17.55	17.45	27
 3-Ethyl-5 [3-ethylthiazolo (4, 5-e) benzo-1′, 2′, 3′-thiadiazole-2-ethylidene] thiazolidinethione-2-one-4	257	538	$C_{16}H_{14}ON_4S_4$	31.52; 31.55	31.52	35

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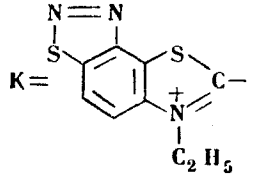
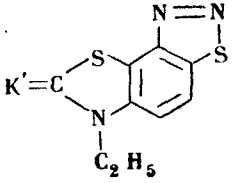
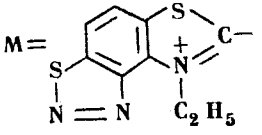






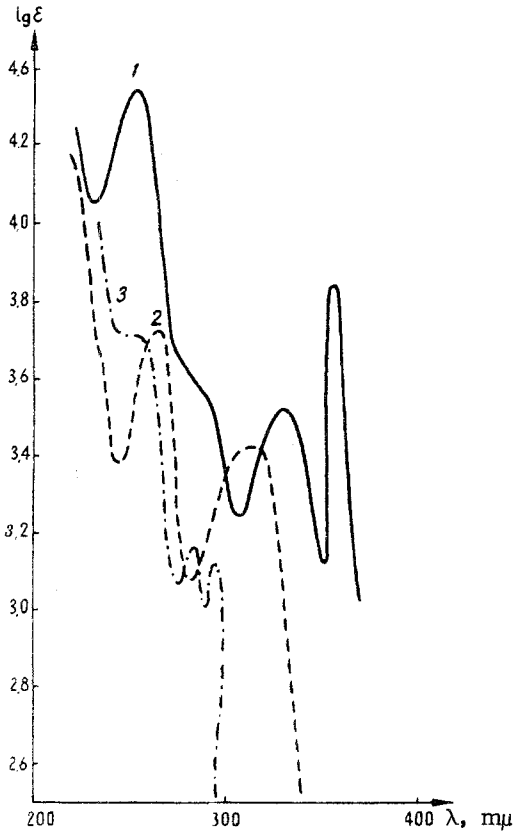
Experimental

5-Amino-4-thiocyano-1,2,3-thiadazole (I). 6 g (0.04 mole) 5-amino-benzo-1,2,3-thiadiazole [7] and 9.6 g (0.126 mole) ammonium thiocyanate were dissolved in 120 ml methanol. A solution of 2.4 ml (0.04 mole) bromine in 75 ml methanol saturated with ammonium bromide was, over 1 hr, dropped into the above solution while the latter was stirred and held at −5°to −10°. Stirring was continued for 2 hr after completion of addition, with the temperature held the same, the thiocyano derivative was filtered off, washed with water and alcohol, and then dried in a vacuum desiccator. Yield 5.8 g (72%) yellow needles mp 186° (from dioxane). After melting the compound resolidified, and remelted at 240°* (decomp). Found: S 30.90, 30.78%. Calculated for $C_7H_4N_4S_2$: S 30.76%.

2-Methylthiazolo (5,4-e) benzo-1',2',3'-thiadiazole (A).

Method (1). 4 g (0.02 mole) 5-amino-4-thiacyanobenzo-1,2,3-thiadazole was added in small portions to a stirred solution of 9.6 g (0.04 mole) sodium sulfide in 15 ml water heated to 60°. The resultant solution was filtered, cooled and 30 ml acetic anhydride added. The mixture was refluxed for 3 hr, then, with cooling, neutralized with sodium carbonate. The precipitate was recrystallized from alcohol. Yield 1.8 g (60%), colorless needles mp 164°. Found: N 20.36, 20.20; S 30.75, 30.63%. Calculated for $C_8H_5N_3S_2$: N 20.28; S 30.92%.

Method (2a). 2-Methyl-6-chloro-7-nitrobenzothiazole was prepared by the method of [8,9], 2-methyl-5-chloro-6-nitrobenzothiazole and 2-methyl-5-chloro-4-nitrobenzothiazole by that of [10], but with certain modifications. 20 g 2-methyl-5-chlorobenzothiazole was dissolved in 75 ml concentrated sulfuric acid, the solution held at 0° while a mixture of 40 ml nitric acid (d 1.5) and 40 ml concentrated sulfuric acid was added dropwise over 30 min, after which the temperature was slowly allowed to rise to room temperature, and the reaction products poured onto 1 kg ice. The precipitate formed was filtered off, washed with water, and air-dried. The crude nitro compound weighed 23 g. To separate the isomers, the nitration product was dissolved in 1.5 *l* boiling methanol, and the solution filtered to remove the small quantity of insoluble impurity. After cooling, 2-methyl-5-chloro-6-nitrobenzothiazole mp 171° crystallized out as colorless needles, yield 9.92 g. After removing the crystals, the filtrate was distilled to remove solvent, the residue boiled with 100 ml dilute hydrochloric acid (1 : 1), the insoluble residue filtered off, boiled twice with about 50 ml of the dilute acid, washed with water, and then recrystallized from methanol. Yield 4.46 g 2-methyl-5-chloro-4-nitrobenzothiazole mp 161-162°. Dilution of the hydrochloric acid solution with water precipitated 2-methyl-5-chloro-6-nitrobenzothiazole, yield after a single recrystallization from alcohol 3.1 g mp 171°. Thus 23 g mixed isomers gave 4.46 g (19%) 2-methyl-5-chloro-4-nitrobenzothiazole, and 13.02 g (56%) 2-methyl-5-chloro-6-nitrobenzothiazole.



Absorption spectra of alcohol solutions: 1) 2-methylthiazolo (5,4-e) benzol 1',2',3'-thiadazole (A); 2) benzo-1, 2, 3-thiadazole; 3) 2-methylbenzothiazole.

A solution of 2.4 g (0.01 mole) sodium sulfide and 0.32 g (0.01 g.at.) sulfur in 20 ml alcohol was added dropwise over 1 hr to a refluxing solution of 4.57 g (0.02 mole) 2-methyl-6-chloro-7-nitrobenzothiazole in 85 ml alcohol. The mixture was refluxed for 5 hr, and the precipitate of disulfide which formed after cooling filtered off, washed with alcohol, and then with water. Yield of 2, 2'-dimethyl-7,7'-dinitro-6, 6'-dibenzothiazolyl disulfide, 3.16 g (70%), II, forming pale yellow plates, mp 274° (from acetic acid). Found: S 28.15, 28.17%. Calculated for $C_{16}H_{10}N_4O_4S_4$: S 28.44%.

6 g (0.013 mole) II was suspended in 100 acetic acid heated on a boiling water bath, and the whole stirred, while 16 g zinc dust and 30 ml concentrated hydrochloric acid were added in small portions over 45 min. The mixture was refluxed for 15 min longer, and filtered. A saturated sodium acetate solution was added to the hot filtrate till it was no longer acid to congo red, and the solution left overnight. The precipitate of zinc salt of 2-methyl-7-amino-6-mercaptobenzothiazole was washed with water, and dried. Yield 4.4 g (70%).

*Temperatures uncorrected.

1.2 g (0.0026 mole) of the zinc salt was dissolved in 10 ml concentrated hydrochloric acid, the solution diluted with 50 ml water, cooled to 0°, and a solution of 0.3 g (0.0054 mole) sodium nitrite in 5 ml water, added dropwise over 10 min. After 2 hr the precipitate formed was filtered off, washed with water, and after drying, extracted with hot toluene. The residue left after distilling off the solvent was tiwce recyrstallized from alcohol, using active charcoal. Yield of A, 0.1 g (9%), colorless needles, mp 164°, undepressed mixed mp with a specimen of A prepared by the route (1).

Method (2b). A mixture of 4.6 g (0.02 mole) 2-methyl-6-chloro-7-nitrobenzothiazole, 12 g (0.05 mole) sodium sulfide, and 50 ml water was refluxed for 6 hr, the hot red solution filtered, 1.4 g (0.02 mole) sodium nitrite added to the filtrate, the solution then cooled to 0°, and added dropwise, with stirring, to 50 ml dilute hydrochloric acid, cooled to −5°. The resultant precipitate was dissolved in boiling dilute hydrochloric acid, filtered to remove the insoluble impurity, and then neutralized with ammonia. After recrystallizing from alcohol, 0.3 g (7.5%) product mp 164° was obtained.

Method (3). A well-ground mixture of 6.4 g (0.033 mole) 5-acetylaminobenzo-1,2,3-thiadiazole [7] and 7.7 g (0.034 mole) phosphorus pentasulfide in 20 ml dry pyridine was refluxed for 40 min, cooled, and poured into 300 ml water. After some time the oily dark product separated and solidified. The solid was filtered off, washed with water, dissolved in 10% sodium hydroxide solution, filtered, and precipitated with acetic acid. Yield of 5-thioacetylaminobenzothiadiazole III, after recrystallizing from alcohol, was 2.88 g (43%), yellow prisms, mp 156-157°. Found: S 30.57, 30.38%. Calculated for $C_8H_7N_3S_2$: S 30.62%.

3.6 g (0.017 mole) 5-thioacetylaminobenzo-1,2,3-thiadiazole was dissolved in 75 ml 5% sodium hydroxide solution, the solution stirred, and at room temperature a solution of 11.5 g potassium ferricyanide in 30 ml water added over 15 min. After an hour the precipitate of A was filtered off, washed with water, and recrystallized a few times from alcohol. Yield of A 41%, mp 164°.

2-Methylthiazolo (4,5-e) benzo-1',2',3'-thiadiazole (B). This was prepared, in a way similar to A, using method (2b) starting from 2,-methyl-4-nitro-5-chlorobenzothiazole. Yield 10%, pale yellow needles mp 205° (decomp) (from alcohol). Found: S 30.65, 30.75%. Calculated for $C_8N_9N_3S_2$: S 30.92%.

6-Acetylaminobenzo-1,2,3-thiadiazole. Prepared by boiling 6-amino-benzo-1,2,3-thiadiazole [11] with acetic anhydride, mp 162° (from dilute acetic acid). Found: N 21.50, 21.62%. Calculated for $C_8H_9N_3OS$: N 21.76%.

6-Thioacetylaminobenzo-1,2,3-thiadiazole. This was prepared in a way similar to III, from 6-acetylaminobenzo-1,2,3-thiadiazole and phosphorus pentasulfide. Yield 46%, mp 167° (from aqueous alcohol). Found: S 30.70, 30.52%. Calculated for $C_8H_7N_3S_2$: S 30.62%.

2-Methylthiazolo (4,5-g) benzo-1',2',3'-thiadiazole (C). a) 6-Amino-7-thiocyano-1,2,3-thiadiazole was prepared, by a method similar to route (1), from 6-aminobenzo-1,2,3-thiadiazole. Yield 58% mp 188° (from benzene-dioxane). Found: S 30.83, 30.74%. Calculated for $C_7H_4N_4S_2$: S 30.76%. Sodium sulfide reduction of the thiocyano derivative, as described for A, following method (1), gave C in 65% yield, mp 160° (from alcohol). Found: S 30.68, 30.79%. Calculated for $C_8H_5N_3S_2$: S 30.92%.

b) 2-Methyl-6-amino-7-thiocyanobenzothiazole was similarly prepared by method (1) from 2-methyl-6-aminobenzothiazole. Yield 60%, mp 165° (from benzene). Found: S 29.07, 29.04%. Calculated for $C_9H_7N_3S_2$: S 28.96%. The thiocyano derivative prepared was reduced similarly to the thiocyanated benzo-1,2,3-thiadiazole. The solution was filtered to remove the small amount of insoluble impurity (apparently an isomerization product of the thiocyano derivative), cooled, and neutralized with 50% acetic acid. The resultant yellow precipitate of 2-methyl-6-amino-7-mercaptobenzothiazole was quickly filtered off, washed with water, and dissolved in 5% sodium hydroxide solution. Sodium nitrite was added to the solution, and over 30 min the solution was dropped into stirred dilute hydrochloric acid held at 0-2°. Stirring was then continued for an hour longer, the precipitate filtered off, washed with water, and crystallized from alcohol. Yield 60%, mp 160°. Mixed mp with a sample of C prepared as described above, undepressed.

2-Methylthiazolo (5,4-g) benzo-1,2,3-thiadiazole (D). Thiocyanation of 2-methyl-5-aminobenzothiazole was carried out similarly to the thiocyanation of 2-methyl-6-aminobenzothiazole. 3.28 g (0.02 mole) amino compound gave 2.8 g thiocyanation product (IV). Without further purification IV was reduced with sodium sulfide in aqueous solution, and the solution then diazotized as described above. Yield 1.52 g substance mp 135-137°. After chromatography of part of the product in chloroform on aluminum oxide it had mp 137°. The other part of the product was recrystallized from ligroin, to give large crystals mp 137°. On evaporation the mother liquor gave an insignificant amount of gum. Found: S 30.65, 30.59%. Calculated for $C_8H_5N_3S_2$: S 30.92%.

2,5-Dimethylthiazolo (5,4-e) benzothiazole (V). The product obtained by thiocyanating 3.28 g 2-methyl-5-aminobenzothiazole was, without further purification, reduced with 9.6 g sodium sulfide in 15 ml water at 60-70°. The resultant solution was refluxed with 30 ml acetic anhydride for 3 hr, filtered, and neutralized with ammonia. A

precipitate was formed, and it was recrystallized from alcohol. Yield 2.2 g colorless needles mp 106° (the literature [2] gives mp 106°). A further 0.39 g material, mp 105-106° was obtained from the mother liquor on concentration. Total yield 2.59 g (89%). Evaporation of the mother liquor to dryness gave 0.1 g gum.

Ethiodide of 2-methylthiazolo (5, 4-e) benzol-1', 2', 3'-thiadiazole (isomer A). This was prepared by heating the base with an equimolecular amount of ethyl tosylate at 120-130° for 3 hr. The resultant tosylate was converted to iodide in the usual way, and recrystallized from alcohol. Yield 60%, mp 246° (decomp). Found: I 34.67, 34.70%. Calculated for $C_{10}H_{10}N_3S_2$: I 34.98%. The ethiodides of isomers B and C were obtained similarly.

The dyes were prepared from the tosylates in the suual ways, and purified by recrystallizing from alcohol. Dimethinemerocyanines with an N-ethylrhodanine group were recrystallized from acetic acid. The Table lists the dyes obtained.

UV spectra were measured with a SF-4 instrument, using alcohol solutions, concentrations of the order 10^{-4} – 10^{-5} M.

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