THIAZOLOCYANINES

XV.* N-HETARYLTHIAZOLIUM SALTS WITH AN ACTIVE METHYL GROUP AND CYANINE DYES FROM THEM

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A method was developed for the preparation of 2-methyl-N-(2-thiazolyl)-, 2-methyl-N-(2-pyridyl)-, and 2-methyl-N-(2-benzothiazolyl)thiazolium salts. Cyanine dyes were synthesized from these salts. A comparison of the absorption spectra of dyes with various substituents (ethyl, phenyl, and 2-hetaryl) attached to the nitrogen atoms of the thiazole rings of the dyes demonstrated that the color deepens as the electronegativity of these substituents increases.

The effect of electronegative substituents attached to the carbon atoms of nitrogen heterocyclic rings and the polymethine chain on the color of cyanine dyes is well-known and has been studied in detail. However, the literature contains no studies pertaining to the investigation of the absorption spectra of cyanine dyes and dyes of other classes with electronegative substituents attached to the nitrogen atoms of the heterocyclic rings or pertaining to the synthesis of the starting materials for them – the corresponding quaternary salts. This is explained to a certain degree by the fact that attempts to synthesize and isolate the quaternary salts of nitrogen heterocyclic bases with negative substituents attached to the nitrogen atom have, as a rule, been unsuccessful. One such attempt – the synthesis of N-cyanopyridinium bromide – led to a very valuable preparative method [2]. N-Cyanopyridinium bromide proved to be so unstable that its formation was immediately accompanied by cleavage of the pyridine ring. The ability of the pyridine ring to undergo cleavage in this compound and in N-dinitrophenylpyridinium chloride has been used extensively in the chemistry of cyanine dyes to form the polymethine chain of tricarbocyanines.

We set out to obtain stable quaternary salts with an active methyl group, in which the nitrogen atoms of the heterocyclic rings would be bonded to a C=N group that is a part of another heterocyclic ring, for example, N-(2-thiazolyl)- or N-(2-pyridyl)thiazolium salts. We also set out to synthesize cyanine dyes from them and to investigate the absorption spectra of the latter. We reckoned that salts in which the nitrogen atom is connected to the CN group included in the ring will be quite stable and that the joining of this ring with the α position would ensure the manifestation of its electronegativity. We synthesized such salts with an active methyl group from thiazole derivatives. They actually proved to be stable compounds and served as starting materials for the preparation of a large number of cyanine dyes. It should be mentioned that separate notes concerning salts that are similar in structure to the type that we developed – three of them regarding pyridine derivatives [3-5] and one concerning a benzimidazole derivative [6] – have appeared in the literature.

The basis for the synthesis of quaternary thiazolium salts with 3-hetaryl residues and an active methyl group was the reaction between N-(2-hetaryl)thioacetamide and α-halo ketones. However, the reaction between halo ketones and N-hetarylthioacetamides can also proceed in another direction. It has been shown that chloroacetone and α-bromoacetophenone react with 2-acetamidothiazole [7] and 2-acetamidopyridine [8] to give quaternary salts of the latter (IV). Moreover, the salt (IV) contains an active methylene

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*See [1] for communication XIV.

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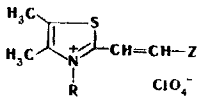
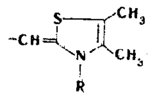
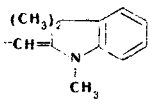
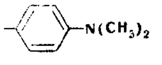
TABLE 1. Thiazolocyanines



Comp.	R	Z	Preparative method*	mp, °C	Empirical formula	S, %		λ max, nm (ε · 10^{-4})	Deviation, nm
						found	calc.		
1	Ethyl		Refluxing in pyridine for 2 h	267[11]	$C_{17}H_{25}N_2S_2I$†	N 6,3	6,2	563 (6,9)	—
2	Phenyl		A (45)	125	$C_{25}H_{25}ClN_2O_4S_2 \cdot H_2O$	11,7	12,0	572 (8,5)	—
3	2-Pyridyl		B (2—3)	113	$C_{23}H_{23}ClN_4O_4S_2 \cdot 2H_2O$	11,3	11,5	576 (7,8)	—
4	2-Thiazolyl		B (90)	221	$C_{19}H_{19}ClN_4O_4S_4 \cdot 1{,}5H_2O$	22,9	23,0	585 (9,4)	—
5	2-Benzothiazolyl		B (45)	140	$C_{27}H_{23}ClN_4O_4S_4 \cdot H_2O$	19,9	19,7	591 (9,8)	—
6	Ethyl		B (45)	214	$C_{21}H_{27}ClN_2O_4S$	7,4	7,4	516 (7,5)	39
7	Phenyl		A (60)	136	$C_{25}H_{37}ClN_2O_4S$	6,5	6,6	535 (7,44)	24
8	2-Pyridyl		B (50)	206	$C_{24}H_{26}ClN_3O_4S$	N 8,7	N 8,6	542 (9,75)	19
9	2-Thiazolyl		A (50)	209	$C_{22}H_{27}ClN_3O_4S_2$	12,9	13,0	556 (9,8)	9
10	Ethyl		B (45)	248	$C_{17}H_{23}IN_2S$†	I 30,7	I 30,7	480 (2,4)	106
11	Phenyl		B (90)	169	$C_{21}H_{23}ClN_2O_4S$	7,2	7,4	502 (3,2)	89
12	2-Pyridyl		B (45)	243	$C_{20}H_{22}ClN_3O_4S$	7,5	7,4	510 (5,0)	83
13	2-Thiazolyl		B (45)	Does not melt at 300°	$C_{18}H_{20}ClN_3O_4S_2 \cdot H_2O$	13,9	13,9	532 (2,5)	65

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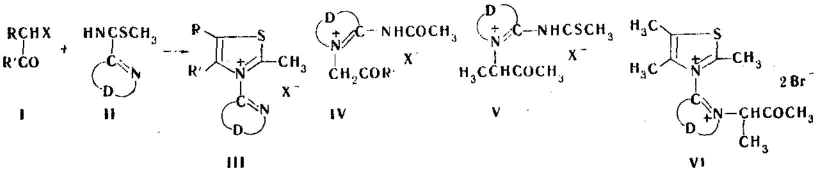
*The refluxing time of the reagents is indicated in parentheses (minutes). The yields for dyes 6, 8, and 10 were 37, 13, and 40%, respectively. The yields for the remaining dyes were less than 10%.

† Isolated and analyzed as the iodide.

group, at which various condensations, including the formation of cyanines, can occur. Considering the possibility of this sort of competitive reaction, we used 3-bromo-2-butanone (I, R = R' = CH_3), which, in the case of reaction via the second direction, ensures the absence of an active methylene group in the resulting quaternary salt, since one of the hydrogen atoms is replaced by a methyl group (V).



D is a group of atoms that close the heteroring (a is thiazole, b is pyridine, and c is benzothiazole)

Thus the direction of the reaction might have been judged according to whether the product gives cyanine dyes, since this is possible only for III and not for V. Of course, the possibility that the reaction proceeds immediately via the two directions to give VI was not excluded. Our experiments demonstrated that the reaction proceeds principally to form III, although side products of the VI type were also isolated in some cases. Quaternary salts III were converted to cyanine dyes – symmetrical and unsymmetrical carbocyanines, monomethylidynecyanines, and styryls. A comparison of their absorption spectra with the spectra of the corresponding dyes with ethyl and phenyl groups attached to the nitrogen atoms demonstrated that the color of the dyes is deeper, the more electrophilic the character of the substituent attached to the nitrogen atoms of the thiazolocarbocyanines; i.e., the bathochromic shift of the absorption band increases in a series of dyes with substituent R in the order $C_2H_5 < C_6H_5 <$ 2-pyridyl < 2-thiazolyl < 2-benzothiazolyl (Table 1). The relative degree of electronegativity of the substituents attached to the nitrogen atoms in the dyes can be judged from the deviations in the unsymmetrical dyes and styryls (Table 1). The deviations decrease as the electronegativity of the substituents increases, as should have been expected in accordance with the rule [9, 10] that in dyes with weakly basic terminal links of the dye chromophore (pyrrole, p-dimethylaminophenyl, and indolenine), the decrease in the basicity of the second terminal group induces equalization of the bonds in the chromophore and a decrease in the deviation.

EXPERIMENTAL

2-Thioacetamidothiazole (IIa). A 1.42-g (10 mmole) sample of 2-acetamidothiazole [7] was fused with 1.1 g (5 mmole) of phosphorus pentasulfide at 155-160° for 15 min, and the melt was extracted several times with 8% sodium hydroxide. The solution was diluted with a fourfold quantity of water, and carbon dioxide was passed through the mixture until precipitation had ceased. The precipitate was removed by filtration, washed with water, dried, and crystallized from benzene to give 0.56 g (35%) of IIa with mp 218.5°. Found: S 40.4%. $C_5H_6N_2S_2$. Calculated: S 40.5%.

2,4,5-Trimethyl-3-(2-thiazolyl)thiazolium Bromide (IIIa, R = R' = CH_3). A 1.58-g (0.01 mole) sample of IIa and 1.51 g (0.01 mole) of 3-bromo-2-butanone was heated at 105° for 3 h. The melt was extracted with boiling benzene, the benzene was decanted, and the residue was triturated with acetic anhydride and filtered off from the product of the addition of a second molecule of bromo ketone (VIa). The addition of absolute ether to the solution liberated IIIa as an oil. The oil was dissolved in water, and the solution was refluxed with animal charcoal, filtered, and evaporated to dryness. The residue was used to obtain the cyanine dyes. Compound IIIa was converted to the perchlorate for analysis by dissolving it in acetic anhydride and treating the solution with a few drops of 60% perchloric acid. Colorless crystals of the quaternary salt (IIIa, X = ClO_4) gradually precipitated. The process can be accelerated by adding absolute ether. It can also be purified by reprecipitation from alcohol solution by the addition of absolute ether to give a product with mp 130°. Found: Cl 11.8; S 20.4%. $C_9H_{11}ClN_2O_4S_2$. Calculated: Cl 11.4; S 20.6%.

2,4,5-Trimethyl-3-[3-(α-acetylethyl)-2-thiazolium]thiazolium Dibromide (VIa). This compound had mp 136°. Found: Br 36.5%. $C_{13}H_{18}Br_2N_2OS_2$. Calculated: Br 36.2%.

2-Thioacetamidopyridine (IIb). A 0.68-g (4 mmole) sample of 2-acetamidopyridine [8] was refluxed with 0.7 g (3 mmole) of phosphorus pentasulfide in 3 ml of absolute dioxane for 1.5 h. The dioxane solution was decanted, and the residue was again extracted with hot dioxane. The extracts were combined and evaporated to a small volume. The precipitate was chromatographed in chloroform solution on aluminum oxide. The substance was eluted from the weakly yellow zone (0.19 g) and repeatedly crystallized from hexane to give 0.08 g of IIb with mp 103-104°. Found: N 18.6; S 20.6%; $C_7H_8N_2S$. Calculated: N 18.4; S 21.0%.

2-Thioacetamidobenzothiazole (IIc). A 1.92-g (10 mmole) sample of 2-acetamidobenzothiazole and 2 g (9 mmole) of phosphorus pentasulfide were refluxed in 15 ml of absolute dioxane for 1 h. The solution was decanted, and the combined dioxane extracts were evaporated. The dry residue was dissolved in 8% sodium hydroxide solution and diluted with a fourfold quantity of water. Carbon dioxide was passed through the solution until precipitation had ceased. The precipitate was washed with water, dried, and crystallized from benzene to give 0.7 g of IIc with mp 184°. Crystallization from alcohol gave a product with mp 185-186°. Found: S 30.4%. $C_9H_8N_2S_2$. Calculated: S 30.7%.

2,4,5-Trimethyl-3-(2-pyridyl)thiazolium Bromide (IIIb) and 2,4,5-Trimethyl-3-(2-benzothiazolyl)-thiazolium Bromide (IIIc). These compounds were obtained by the method used to prepare IIIa ($R = R' = CH_3$). Both preparations were viscous masses that solidified in a desiccator over phosphorus pentoxide to vitreous masses that could not be crystallized. They were used without further purification for the preparation of dyes.

Symmetrical Carbocyanines (Table 1, Compounds 1-5). These dyes were obtained by refluxing 1 mmole of the thiazolium quaternary salt with a fourfold quantity of ethyl orthoformate in 0.5 ml of acetic anhydride with several drops of triethylamine (method A) or without it (method B). (Table 1). The dye was isolated from the reaction mixture by adding sodium perchlorate solution to it, and the product was purified by chromatography on aluminum oxide in chloroform solution containing 0.1% methanol (11), several drops of acetic acid (13), or without them. Where necessary, the chromatography was repeated. The chloroform extract of the requisite zone of the column was evaporated, the residue was triturated with ether, and the solid was removed by filtration.

Unsymmetrical Carbocyanines (Table 1, Compounds 6-9). Equimolecular amounts (1 mmole each) of the quaternary salt of 2,4,5-trimethylthiazole and 1,3,3-trimethyl-2-formylmethyleneindoline with 1 ml of acetic anhydride were refluxed with the addition of 1 mmole of triethylamine (method A) or without it (method B). The dye was isolated and purified as indicated above. In individual cases, the dye was recrystallized from isopropyl alcohol.

Styryls (Table 1, Compounds 10-13). A mixture of 1 mmole of the quaternary salt of 2,4,5-trimethylthiazole, 1 mmole of p-dimethylaminobenzaldehyde, and 2-3 ml of acetic anhydride was refluxed for 45-90 min. Several drops of sodium perchlorate solution or 20% potassium iodide solution were added to the solution, and the precipitated dye was purified by successive crystallization from ethanol and isopropyl alcohol.

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