MESOIONIC COMPOUNDS WITH A BRIDGED NITROGEN ATOM.

16.* THIAZOLOTHIAZOLOPYRIMIDINES

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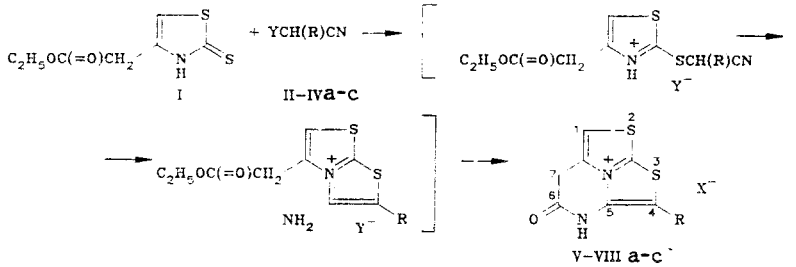
Derivatives of a new heterocyclic system were obtained in the reaction of 2-mercapto-4-ethoxycarbonylmethylthiazole with α-haloacetonitriles. Cyanine dyes were synthesized on the basis of these products, and their absorption spectra were studied.

Condensed heterocycles with a nodal nitrogen atom that contain a thiazole ring have found diverse applications. For example, thiazolo[2,3-b]thiazole derivatives display physiological activity [2]. In this connection the synthesis of new condensed heterocyclic systems that include the indicated structural fragments and an investigation of their chemical reactions seem of interest.

With this end in mind we investigated the reaction of 2-mercapto-4-ethoxycarbonylmethylthiazole I with α-haloacetonitriles IIa, IIIa, α-bromopropionitrile IIIb, and α-cyanobenzyl benzenesulfonate IVc.

Since it is known that alkylating agents such as α-substituted nitriles II-IV react with thioamides to give, usually, 4-aminothiazole derivatives [3, 4], one might have expected that building of yet another thiazole ring onto the I molecule would also occur in our case.



II Y=X=Cl, III Y=X=Br, IV Y=X=$C_6H_5SO_2$; V X=Cl, VI X=Br, VII X=$C_6H_5SO_3$, VIII X=ClO_4; V—VIII a R=H, b R=CH_3, c R=C_6H_5

It was found that this reaction actually occurs when the starting reagents are fused. However, the process does not stop at this stage, and the resulting intermediate substances, as a result of intramolecular condensation during the synthesis, are converted to cycloazines V-VIII.

The compositions and structures of the synthesized compounds are confirmed by the results of elementary analysis and the IR and PMR spectra. In fact, absorption bands corresponding to the stretching vibrations of an amide C=O group (1680-1690 cm^{-1}) are observed in the IR spectra of the synthesized compounds, and absorption bands of an ethoxycarbonyl group (1740 cm^{-1}) and a cyano group (2000-2220 cm^{-1}) of the starting I-IV are absent. The corresponding signals of the R substituent, a singlet of a proton in the 1 position (7.3-7.4 ppm), and a singlet of protons of a methylene group (4.00 ppm) are observed in the PMR spectra of V-VII, but signals of the protons of the ethoxy group of the starting ethoxycarbonylmethylthiazole I [0.90 t (3H), 3.93 ppm, q (2H), J = 8 Hz)] are absent. It must be noted that the signals of the protons of the methylene group and the proton in the 1

*See [1] for Communication 15.

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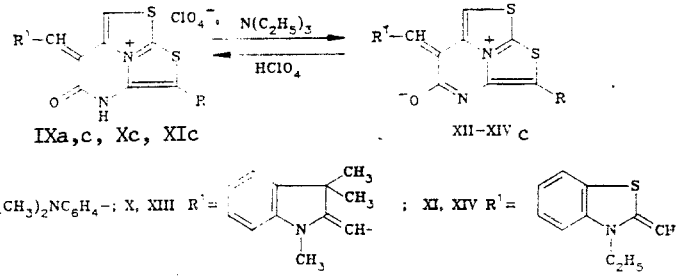
TABLE 1. Characteristics of the Synthesized Compounds

Compound	Empirical formula	mp, °C*	λ_{max}, nm (log ε), in CH_3OH	Yield, %
V a	$C_7H_5ClN_2OS_2$	298...300	250 (4,12), 320 (3,66)	87
VI a	$C_7H_5BrN_2OS_2$	300	250 (4,13), 320 (3,66)	76
VI b	$C_8H_7BrN_2OS_2$	300	249 (4,18), 320 (3,65)	69
VII c	$C_{19}H_{14}N_2O_4S_3$	300	240 (4,27), 322 (4,18), 380 (3,71)	65
VIII c	$C_{13}H_9ClN_2O_5S_2$	283...285	240 (4,27), 322 (4,13), 380 (3,61)	83
IX a	$C_{16}H_{14}ClN_3O_5S_2$	300	488 (4,23)	61
IX c	$C_{22}H_{18}ClN_3O_5S_2$	300	490 (4,45)	81
X c	$C_{26}H_{22}ClN_3O_5S_2$	300	505 (4,89)	90
XI c	$C_{24}H_{18}ClN_3O_5S_3$	300	519 (4,89)	58
XII c	$C_{22}H_{17}N_3OS_2$	248...250	436 (4,50)	86
XIII c	$C_{26}H_{21}N_3OS_2$	251...252	486 (4,64)	80
XIV c	$C_{24}H_{17}N_3OS_3$	241...242	518 (4,73)	71

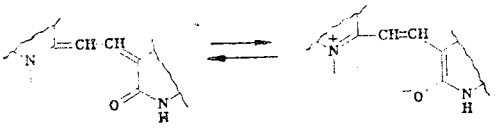
*The compounds were crystallized: Va from alcohol–water (1:1), VIIc and VIIIc from alcohol, IXc from acetic acid, Xc from alcohol–formic acid (2:1), and XIIc-XIVc from alcohol–triethylamine.

position of salts V-VIII are shifted to weak field (by 0.4 and 0.3 ppm, respectively) as compared with the analogous protons of starting thiazole I [3.60 s (2H), 7.03 ppm, s (1H)]. This can evidently be explained by a decrease in the electron density on the nodal nitrogen atom as compared with the corresponding protonated nitrogen atom of a solution of starting thiazole I as a result of the formation of a condensed system.

Further investigations showed that the methylene group in the molecules of the synthesized cyclazines proved to be rather active in cyanine condensations. For example, salts Va and VIIIc react readily with the electrophilic intermediates used to obtain polymethine dyes. Thus 2-(2-acetanilidovinyl)-3-ethylbenzothiazolium tosylate and 1,3,3-trimethyl-2-formylmethyleneindoline reacts with p-dimethylaminobenzaldehyde to give the corresponding cyanines IX-XI, the spectral characteristics of which are presented in Table 1.

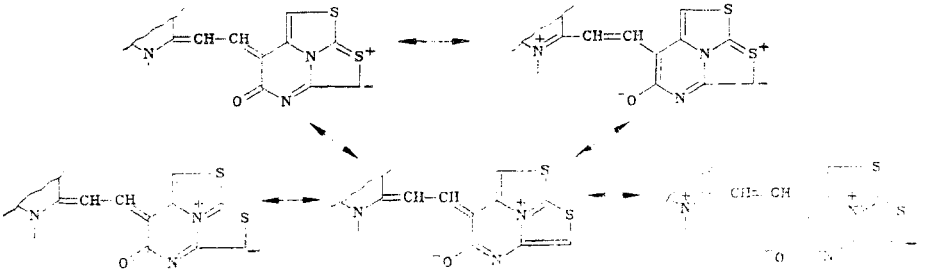


The colors of the synthesized compound are due to the chromophore system that is typical for merocyanine dyes; however, in contrast to the latter, which are uncharged intraionoid compounds, the cation is responsible for the color in the IX-XI dye molecules. When one compares the absorption maxima of these compounds with the analogous data for ordinary dimethinemerocyanines [5], it is apparent that, with respect to the effect to light absorption, the thiazolothiazolopyrimidinone ring is equivalent to the 2-thioxo-3-ethyl-4-thiazolidinone residue.



It was found that mesoionic dyes XIIc-XIVc are formed by the action of bases on solutions of salts IXc-XIc. The presence of a less intense second maximum or inflection of the curve is characteristic for the spectra of these compounds; this indicates the existence in their molecules of several electron transitions that differ in energy. However, the maxima of the bands are shifted to the short-wave part of the spectrum as compared with

the analogous characteristics of the salt analogs; this can be explained by a decrease in the degree of conjugation of the terminal residue in the dyes with a carbonyl group. The hypsochromic shift is proportional to the electron-donor character of the terminal grouping. Thus on passing from the low-basicity p-dimethylaminophenyl residue (benzylidene derivative XIIc) to the moderately basic (2-benzothiazolylidene)methyl residue (dimethinecyanine XIVc) $\Delta\lambda$ decreases from 54 to 1 nm; this is evidently associated with the attendant increase in the contribution to the color of cyanines with mesomeric structures with a smaller separation of charges in the mesoionic fragment of the dye molecules.



Thus we have developed a simple method for obtaining derivatives of a new heterocyclic system with a nodal nitrogen atom of a number of cycloazines that can be used to obtain cyanine dyes.

EXPERIMENTAL

The electronic spectra were obtained with an SF-8 spectrophotometer. The PMR spectra of solutions in CF_3COOH were obtained with a BS 467 spectrometer [60 MHz, hexamethyldisiloxane (HMDS) as the internal standard]. The IR spectra of KBr pellets were obtained with a UR-10 spectrometer. The characteristics of the synthesized compounds are presented in Table 1. The results of elementary analysis for Hal, N, and S were in agreement with the calculated values.

6,7-Dihydro-6-oxo-5H-thiazolo[4,3,2-d,e]thiazolo[3,4-*a*]pyrimidinium Chloride (Va). A mixture of 0.2 g (1 mmole) of thiazole I [6] and 0.12 g (1.5 mmole) of α-chloroacetonitrile was heated for 1 h at 80°C, after which the melt was triturated with acetone, and the precipitate was removed by filtration, washed with ether, and crystallized to give 0.20 g of product. PMR spectrum (R = H), δ: 4.00 ($-CH_2-$), 6.87 (R, s, 1H), 7.37 ppm [$C_{(1)}-H$)].

6,7-Dihydro-6-oxo-5H-thiazolo[4,3,2-d,e]thiazolo[3,4-*a*]pyrimidinium Bromide (VIa). A mixture of 0.2 g (1 mmole) of thiazole I and 0.18 g (1.5 mmole) of bromoacetonitrile was heated for 30 min at 75°C. The product was isolated as in the preceding experiment.

6,7-Dihydro-4-methyl-6-oxo-5H-thiazolo[4,3,2-d,e]thiazolo[3,4-*a*]pyrimidinium Bromide (VIb). A mixture of 0.2 g (1 mmole) of thiazole I and 0.15 g (7.1 mmole) of bromopropionitrile was heated for 1 h at 85-90°C, after which the product was isolated as in the preceding experiment. The yield was 0.2 g. PMR spectrum (R = CH_3), δ: 4.00 ($-CH_2-$), 2.17 (R, s, 3H), 7.33 ppm [$C_{(1)}-H$].

6,7-Dihydro-6-oxo-4-phenyl-5H-thiazolo[4,3,2-d,e]thiazolo[3,4-*a*]pyrimidinium Benzenesulfonate (VII). A mixture of 0.2 g (1 mmole) of thiazole I, 0.27 g (1 mmole) of α-cyanobenzyl benzenesulfonate [7] was heated for 1 h at 95-100°C. The melt was triturated with acetone, and the substance was removed by filtration. The yield was 0.36 g.

Compound VIIc. PMR spectrum (R = C_6H_5), δ: 4.00 ($-CH_2-$), [the $C_{(1)}-H$ signal coincides with the multiplet of aromatic protons], 6.9-7.5 ppm (Ar–H, m, 11H).

6,7-Dihydro-6-oxo-4-phenyl-5H-thiazolo[4,3,2-d,e]thiazolo[3,4-*a*]pyrimidinium Perchlorate (VIIIc). This compound was obtained by the action of sodium perchlorate or perchloric acid on an alcohol solution of benzenesulfonate VIIc.

6,7-Dihydro-7-(p-dimethylaminobenzylidene)-6-oxo-5H-thiazolo[4,3,2-d,e]thiazolo[3,4-*a*]-pyrimidinium Perchlorate (IX). A mixture of 0.23 g (1 mmole) of chloride Va, 0.15 g (1 mmole) of p-dimethylaminobenzaldehyde, 2 ml of formic acid, and 4 ml of acetic anhydride was heated to the boiling point, 0.5 ml of perchloric acid was added, the mixture was cooled, and the resulting precipitated dye was removed by filtration and washed with alcohol. The yield was 0.26 g.

6,7-Dihydro-7-(p-dimethylaminobenzylidene)-6-oxo-4-phenyl-5H-thiazolo[4,3,2-d,e]thiazolo[3,4-*a*]pyrimidinium Perchlorate (IXc). A mixture of 0.43 g of benzenesulfonate VIIc, 0.15 g (1 mmole) of p-dimethylaminobenzaldehyde, and 6 ml of acetic anhydride was refluxed for 20 min, after which 1.8 g of sodium perchlorate was added, and the precipitate was removed by filtration. The yield was 0.41 g.

6,7-Dihydro-7-[2-(1,3,3-trimethyl-2,3-dihydro-2-indolylidene)ethylidene]-6-oxo-4-phenyl-5H-thiazolo[4,3,2-d,e]thiazolo[3,4-*a*]pyrimidinium Perchlorate (Xc). A mixture of 0.43 g (1 mmole) of benzenesulfonate VIIc, 0.2 g of 1,3,3-trimethyl-2-formylmethyleneindoline, and 6 ml of acetic anhydride was refluxed for 20 min, after which 0.3 ml of perchloric acid was added. The mixture was cooled, and the precipitate was removed by filtration and crystallized. The yield was 0.5 g.

6,7-Dihydro-7-[2-(3-ethyl-2(3H)-benzothiazolylidene)ethylidene]-6-oxo-4-phenyl-5H-thiazolo[4,3,2-d,e]thiazolo[3,4-*a*]pyrimidinium Perchlorate (XIc). A mixture of 0.43 g (1 mmole) of benzenesulfonate VIIc, 0.45 g (1 mmole) of 2-(2-acetanilidovinyl)-3-ethylbenzothiazolium tosylate, and 7 ml of acetic anhydride was heated for 1 h at 120-130°C, after which 0.5 ml of perchloric acid was added, and the precipitate was removed by filtration and crystallized. The yield was 0.35 g.

7-(p-Dimethylaminobenzylidene)-4-phenyl-7H-thiazolo[4,3,2-d,e]thiazolo[3,4-*a*]pyrimidinium 6-Oxide (XIIc). This compound was obtained by the action of triethylamine on an alcohol solution of perchlorate IXc.

7-[2-(1,3,3-Trimethyl-2,3-dihydro-2-indolylidene)ethylidene]-4-phenyl-7H-thiazolo[4,3,2-d,e]thiazolo[3,4-*a*]pyrimidinium 6-Oxide (XIIIc). This compound was obtained as in the preceding experiment from perchlorate Xc.

7-[2-(3-Ethyl-2(3H)-benzothiazolylidene)ethylidene]-6-oxo-4-phenyl-7H-thiazolo[4,3,2-d,e]thiazolo[3,4-*a*]pyrimidinium 6-Oxide (XIVc). This compound was obtained as in the preceding experiment from perchlorate XIc.

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