CONDENSED HETEROCYCLES WITH THE THIAZOLE NUCLEUS.

17.* THIAZOLO[4,3-a]-ISOQUINOLINIUM COMPOUNDS

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3-Methyl-l-phenylthiazolo[4,3-a]isoquinolinium perchlorate, obtained from α -chlorobenzylisoquinoline and thioacetamide, has been used to prepare some symmetrical and unsymmetrical cyanine dyes.

We have previously [1, 2] demonstrated the potential value of condensed heterocycles with a nodal nitrogen atom, such as thiazolo[3,4-a]pyridinium compounds, as deeply colored polymethine dyes. It was therefore of interest to examine the effects of benzannelation in cyanines of this type. The method used to prepare thiazolo[3,4-a]pyridinium salts [1] was used to react chlorobenzylisoquinoline (II) with thioacetamide, to give the thiazolo[4,3-a]isoquinolinium perchlorate (II).



The PMR spectrum of (II) shows two doublets for the protons of the isoquinoline moiety in positions 5 and 6, with chemical shifts of 8.52 and 7.87 ppm (J = 8 Hz), respectively, a muiltiplet for the aromatic protons at 7.58-8.05 ppm, and a signal for the protons of the methyl group in the thiazole ring at 3.29 ppm. The absence of a signal for the methine proton in the starting isoquinoline (I), together with the shift of the signals for the methyl group and the 5-proton towards lower field, indicate the formation of a condensed system in which the positive charge is localized on the nitrogen atom.

It should be pointed out that the known methods for the preparation of thiazolo[4,3-a]isoquinolines [3, 4] only afford compounds with hydrogenated or non-quaternized nitrogen.



3-Methyl-1-phenylthiazoloisoquinoline perchlorate (II), like other condensed, methylated thiazoloazinium salts [1, 5], undergoes condensation at the methyl group. For example, reaction with p-dimethylaminobenzaldehyde in acetic anhydride gave the styril (III), and with 3-ethyl-2-ethylthiobenzothiazolium toluene-p-sulfonate, the monomethinecyanine (IVa). The unsymmetrical thiacarbocyanine (IVb) was obtained from (II) and 2-(2-acetanilidovinyl)-3-ethylbenzothiazolium perchlorate. Similarly, condensation of the salt (II) with diphenylformamide afforded the symmetrical carbocyanine (Vb). The dicarbocyanines (IVc) and (Vc) were formed

*For Communication 16, see [1].

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TABLE 1. Characteristics of Compounds Obtained

Com- pound	Empirical formula	mp, °C	λ_{max} , nm (log ε)	Yield, %
I II IVa IVb IVc Vb Vc VI	$\begin{array}{c} C_{17}H_{15}Cl_2N\\ C_{18}H_{14}ClNO_4S\\ C_{27}H_{23}ClN_2O_4S\\ C_{27}H_{21}ClN_2O_4S\\ C_{29}H_{21}ClN_2O_4S_2\\ C_{39}H_{23}ClN_2O_4S_2\\ C_{31}H_{25}ClN_2O_4S_2\\ C_{37}H_{25}ClN_2O_4S_2\\ C_{39}H_{27}ClN_2O_4S_2\\ C_{29}H_{23}ClN_2O_5S \end{array}$	122123 >200(decomp.) 289290 323324 236237 185187 268269 207208 >150(decomp.)	$\begin{array}{c} 333 & (3,79) \\ 540 & (4,55) \\ 380 & (3,88), \ 481 & (4,67) \\ 617 & (4,96) \\ 400 & (3,69), \ 712 & (5,18) \\ 402 & (4,00), \ 678 & (5,03) \\ 428 & (3,74), \ 775 & (5,23) \end{array}$	89 52 52 34 15 43 39 90

*Compounds (II), (IVb), and (IVc) were crystallized from mixtures of alcohol and nitromethane (2:1, 1:3, and 3:1, respectively), (III) and (IVa) from mixtures of acetic acid and nitrothane (10:1 and 5:1, respectively), and (Vb, c) from nitromethane.

on condensation of (II) and 2-methyl-3-ethylbenzothiazolium perchlorate, respectively, with the previously-prepared salt (VI).

The dyes obtained (Table 1) showed in the visible region of the absorption spectrum a single narrow, high-intensity band. In contrast to the analogous thiazolopyridinium compounds, the short-wavelength (heterocyclic) absorption, corresponding to the π - π * transition was much less intense, was in most cases present in the UV region, and was less dependent on the structure of the dye. These findings show that annelation of the benzene and thiazolopyridinium moieties results in a reduction in electron transition interactions localized at the atoms of the polymethine chain and the terminal hetero-residue respectively [2].

Important features of the heterocycle in dyes are its effective length (L) and its electron-donor capacity (Φ_0) [6], found experimentally by the deviation method [7]. It has been found that the calculated deviation value for the styril (III) (99 nm) is considerably less than in the corresponding thiazolopyridinium compound (117 nm), and the heterocycle obtained is similar in its electron-donor capacity to benzo[f]quinoline [8].

To judge from the absorption maximum of the carbocyanine (Vb), the effective length of the thiazoloquinolinium residue (5.78), expressed in dyes as the equivalent number of vinylene groups [6], is also less than the analogous value for the thiazolopyridinium nucleus (6.28). This is a somewhat unusual finding, since it is known that benzannelation results in a bathochromic shift of the absorption maximum of dye solutions. For instance, in the carbocyanines, changing from the pyridine to the quinoline analogs is accompanied by a deepening of color by 46 nm [9]. However, it has been reported [1] that changing from thiazolopyridinium dyes [1] to their thiazoloisoquinolinium analogs (V) results in a hypsochromic shift of 50 nm.

One reason for the decreased value of L for the thiazoloisoquinololinium nucleus could be a change in the angle of rotation of the phenyl group in the 1-position in cyanines (Vb) and (Vc). In fact, the color of compounds of this type is highly sensitive to the nature of the substituents. For example, in a series of 6-methylthio-2,3-diphenylthiazolo[3,4-b]-1,2,4triazinium salts [10], replacement of the phenyl group in the 8-position (corresponding to the l-position in thiazolo[4,3-a]isoquinolinium compounds) by hydrogen actually results in a hypsochromic shift. However, according to quantum chemical calculations [2], there is an insignificant change in charge in the carbocyanine from the thiazolopyridinium to the corresponding carbon atoms of the terminal nuclei in the dye molecule in the first excited state. In addition, examination of the projection formulae of model thiazolopyridinium (a) and thiazoisoquinolinium (b) cations (Fig. 1), constructed taking into account the bond lengths, valence angles, and the steric radii of the atoms [11], shows that in both instances there is considerable steric hindrance to the planar arrangement of the phenyl groups. Consequently, rotation of the phenyl substituents relative to the molecular plane will, despite a slight difference in the angles, have the same, small effect on the positions of the absorption maxima of the dyes.

Consequently, the hypsochromic shift of the absorption in thiazolo[4,3-a]-isoquinolinium compounds could be due to benzannelation, resulting in a reduction in the contributions of resonance structures with localization of the negative charge on terminal nuclei. Indeed, in the



Fig. 1. Projection formulae of model thiazolo[3,4-a]pyridinium (a) and thiazolo[4,3-a]isoquinolinium (b) cations.

case of the thiazolopyridinium dyes, structures (VIII-X) may be regarded as approximately equivalent.



In the case of thiazoloisoquinolinium compounds, a substantial contribution is made by structure (XI) only, since disturbance of the aromaticity of the annelated ring in other structures results in the excited state being of higher energy, and consequently to a hypsochromic shift of the absorption maximum.



EXPERIMENTAL

UV and visible spectra were obtained on an SF-8 spectrophotometer, in acetonitrile, and PMR spectra on a VP-100 spectrometer (100 MHz, internal standard TMS) in DMSO-D₆. The characteristics of the products are given in Table 1. The elemental analyses for Cl and S were in agreement with the calculated values.

<u>l-(α -Chlorobenzyl)isoquinoline Hydrochloride (I)</u>. To a solution of 2.3 g (10 mmole) of l-(α -hydroxybenzyl)isoquinoline [12] in 10 ml of benzene was added 2 g (15 mmole) of thionyl chloride. The mixture was boiled for 10 min, the benzene removed under reduced pressure. The oily residue crystallized on trituration with ether. Yield 2.7 g.

<u>3-Methyl-1-phenylthiazolo[4,3-a]isoquinolinium Perchlorate (II)</u>. A mixture of 0.3 g (1 mmole) of the hydrochoride (I) and 0.75 g (1 mmole) of thioacetamide was heated for 20 min at 125°C. The cooled melt was dissolved in 20 ml of 2-propanol, the ammonium chloride filtered off, and the filtrate treated with a solution of 0.1 g (1 mmole) of sodium perchlorate in 1 ml of water. The solid which separated was filtered off. Yield 0.2 g.

<u>3-(p-Dimethylaminostyryl)-1-phenylthiazolo[4,3-a]isoquinolinium Perchlorate (III)</u>. A mixture of 0.38 g (1 mmole) of the perchlorate (II), 0.15 g (1 mmole) of p-dimethylaminobenzaldehyde, and 10 ml of acetic anhydride was boiled for 10 min, cooled to room temperature, and treated with 15 ml of 2-propanol. The dye was filtered off and crystallized. Yield 0.26 g.

<u>1-Phenyl-3-[(3-ethyl-2(3H)-benzothiazolylidene)methyl]thiazolo[4,3-a]-isoquinolinium</u> <u>Perchlorate (IVa)</u>. A mixture of 0.38 g (1 mmole) of the perchlorate (II), 0.44 g (1 mmole) of 2-methyl-3-ethylbenzothiazolium toluene-p-sulfonate, and 25 ml of alcohol was heated to the boil, and treated with 0.1 g (1 mmole) of triethylamine. After cooling, the dye was filtered off and crystallized. Yield 0.29 g. <u>l-Phenyl-3-[3-(3-ethyl-2(3H)-benzothiazolylidene)-l-propenyl]thiazolo-[4,3-a]-isoquino-</u> <u>linium Perchlorate (IVb)</u>. A mixture of 0.38 g (1 mmole) of the perchlorate (II), 0.44 g (1 mmole) of 2-(2-acetanilidovinyl)-3-ethylbenzothiazolium perchlorate, and 5 ml of acetic anhydride was heated to the boil, 0.1 g (1 mmole) of triethylamine added, and the mixture cooled rapidly to room temperature. The dye was filtered off and crystallized. Yield 0.19 g.

<u>1-Phenyl-3-[3-(1-phenyl-3(3H)-thiazolo[4,3-a]isoquinolylidene)-1-propenyl]-thiazolo[4,</u> <u>3-a]isoquinolinium Perchlorate (Vb)</u>. A mixture of 0.76 g (2 mmole) of the perchlorate (II), 0.20 g (1 mmole) of diphenylformamidine, and 20 ml of acetic anhydride was heated to the boil, and treated with 0.1 g (1 mmole) of triethylamine. After cooling, the dye was filtered off and crystallized. Yield 0.28 g.

<u>l-Phenyl-3-(4-acetanilido-1,2-butadienyl)thiazolo[4,3-a]isoquinolinium Perchlorate (VI).</u> A mixture of 0.38 g (1 mmole) of the perchlorate (II) and 0.26 g (1 mmole) of malonaldehyde dianil hydrochloride was boiled for 10 min in 5 ml of acetic anhydride. After cooling, the product was filtered off and washed with alcohol. Yield 0.49 g.

<u>l-Phenyl-3-[5-(3-ethyl-2(3H)-benzothiazolylidene)-1,3-pentadienyl]-thiazolo[4,3-a]iso-quinolinium Perchlorate (IVc)</u>. A mixture of 0.55 g (1 mmole) of the perchlorate (VI) and 0.35 g (1 mmole) of 2-methyl-3-ethylbenzothiazolium toluene-p-sulfonate in 50 ml of alcohol was brought to the boil, and 0.09 g (1 mmole) of sodium acetate added. After boiling, the dye was filtered off and crystallized. Yield 0.09 g.

<u>l-Phenyl-3-[5-(l-phenyl-3(3H)-thiazolo[4,3-a]isoquinolinylidene)-1,3-pentadienyl]thiazolo[4,3-a]isoquinolinium Perchlorate (Vc)</u>. A mixture of 0.38 g (l mmole) of the perchlorate (II) and 0.55 g (l mmole) of the perchlorate (VI) in 5 ml of nitromethane was heated to the boil, and 0.1 g (l mmole) of triethylamine added. The dye was filtered off and crystallized. Yield 0.27 g.

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