# THIAPYRYLOCYANINES

## I. Thiaflavylocyanines

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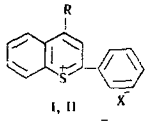
Khimiya Geterotsiklicheskikh Soedinenii, Vol. 5, No. 5, pp. 804–808, 1969

UDC 547.818+547.979

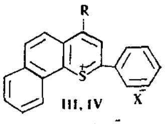
The reaction of thiaflavones with methylmagnesium iodide has yielded 4-methylthiaflavylium salts, from which a number of symmetrical and unsymmetrical polymethine dyes have been obtained. The thiaflavylocyanines have considerably deeper colors than the flavylocyanines. The thiaflavylium styryl dyes, like the flavylium analogs, have negative deviations. It follows from the results on the deviations that in the polymethine dyes the thiaflavylium nucleus behaves as less basic than the flavylium nucleus.

In contrast to the pyrylocyanines, which are described in a number of papers [1–6], there are only isolated items of information on the thiapyrylocyanines [2, 7–10], although systematic information on their coloration should be of interest for the theory of color in its relation to structure.

The present paper describes the synthesis and spectral properties of a definite group of dyes of this type—the thiaflavylocyanines. The dyes were synthesized from 4-methyl- and 4-methoxythiaflavylium salts (I, II) and also from the 7, 8-benzo derivatives (III, IV). Compounds I and III were obtained by the reaction of thiaflavone and 7, 8-benzothiaflavone with methylmagnesium iodide, and compounds II and IV by the addition to the same bases of methyl o-nitrobenzenesulfonate.

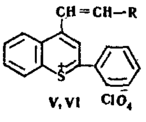


I R = $CH_3$, X = $ClO_4^-$;
II R = $OCH_3$, X = o-$NO_2C_6H_4SO_3^-$



III R = $CH_3$, X = $ClO_4^-$;
IV R = $OCH_3$, X = o-$NO_2C_6H_4SO_3^-$

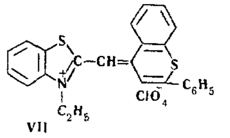
In the thiaflavylium salts, as in flavylium salts [3, 11], methyl groups are active with respect to electrophilic agents and methoxy groups are readily replaced by nucleophilic reagents. Thus, the reaction of 4-methylthiaflavylium perchlorate (I) with p-dimethylaminobenzaldehyde in acetic anhydride gives the styryl V, while fusing I with diphenylformamidine gives the hemicyanine VI.

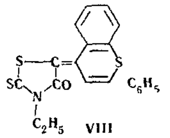


V R=$C_6H_4N(CH_3)_2$—p, $\lambda_{max}$ 725 nm*;

VI R=$NHC_6H_5$, $\lambda_{max}$ 530 nm (492)**.

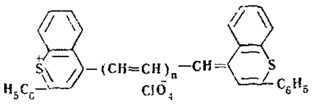
In the reaction of II with a quaternary salt of 2-methylbenzothiazole or with N-ethylrhodanine the monomethinecyanine VII and the zeromethinemerocyanine VIII were obtained. The condensation of the 4-methylthiaflavylium salts I and III





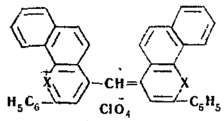
VIII $\lambda_{max}$ 483 nm VII $\lambda_{max}$ 514 nm (482)

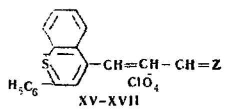
with the methoxythiaflavylium salts II and IV give the symmetrical thiaflavylomonomethinecyanines IX and XIII, while when the oxygen analogs of salts III and IV are used the dye XIV is obtained. When I is heated in glacial acetic acid



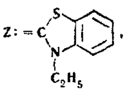
IX $n=0$, $\lambda_{max}$ 695 nm (600), $\varepsilon=6.56\cdot10^4$
X $n=1$, $\lambda_{max}$ 792 nm (703), $\varepsilon=1.76\cdot10^5$
XI $n=2$, $\lambda_{max}$ 900 nm (812).
XII $n=3$, $\lambda_{max}$ 1007nm (920).

with orthoformic ester in the presence of anhydrous sodium acetate, the carbocyanine X is formed, while the reaction of the same salt with the hydrochlorides of the dianils of malondialdehyde and glutaconic dialdehyde in acetic anhydride gives the dicarbo- and tricarbocyanines XI and XII. In addition to the symmetrical thiaflavylocyanines, the unsymmetrical trimethinecyanines XV–XVII have been synthesized by the condensation of I with the ethyl tosylate derivative of 2-(ω-anilinovinyl)benzothiazole, with 2-formylmethylene-1, 3, 3-trimethylindoline, and with 4-(ω-anilinovinyl)flavylium perchlorate.





XV Z:



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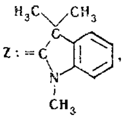
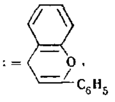
*Here and below, $\lambda_{max}$ is given for solutions in nitromethane.

** The $\gamma_{max}$ values of the analogous flavylocyanines are given in brackets.

XVI Z :

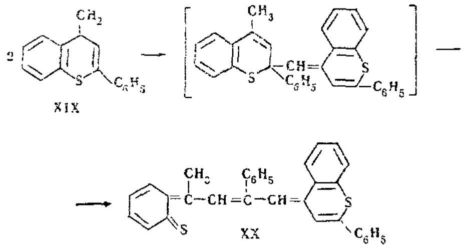


XVII Z :



XIII X=S, $\lambda_{max}$ 700 nm;
XIV X=0, $\lambda_{max}$ 602 nm;
XV (–) $\lambda_{max}$ 586 nm (586)*, $\varepsilon = 4.3 \cdot 10^4$;
XVI $\lambda_{max}$ 618 nm $\varepsilon = 5.4 \cdot 10^4$;
XVII $\lambda_{max}$ 750 nm $\varepsilon = 6.3 \cdot 10^4$.

4-Methylthiaflavylium salts are characterized by a high reactivity, as a result of which the preparation of the thiaflavylocyanines is accompanied by side reactions. Thus, when a solution of I in acetic anhydride is allowed to stand at room temperature, the monomethinecyanine IX is gradually formed, and when the same salt is heated in acetic anhydride with diphenylformamidine the main reaction product is not the hemicyanine VI but a dye with $\gamma_{max}$ 788 nm (in formic acid)—probably the mesomethylthiaflavylotrimethinecyanine XVIII. When I is heated in dimethylformamide or in glacial acetic acid in the presence of bases (sodium acetate or triethylamine), the nonsalt dye XX with $\gamma_{max}$ 496 nm (in benzene) is formed, probably as a result of the dimerization of the 4-methylene-2-phenylbenzothiapyran (XIX) formed initially. In order to suppress side reactions



in the synthesis of the thiaflavylocyanines X–XII it is appropriate to use a two- to six-fold excess of the second component. Alcoholic solutions of the symmetrical thiaflavylocyanines are unstable but solutions of these dyes in nitromethane, glacial acetic acid, and nitrobenzene are relatively stable.

The absorption maxima of the symmetrical thiaflavylocyanines are displaced by approximately 90 nm in the long-wave direction as compared with the absorption maxima of the flavylocyanines. The vinylene shift in the series of thiaflavylocyanines IX–XII on passing from n = 0 to n = 1 is 97 nm, and on passing from n = 1 to n = 2 it is 108 nm, while in the xanthylocyanines the corresponding vinylene shifts are 57 and 87 nm [8]. This difference is due to the smaller influence of steric hindrance on the color of the thiaflavylocyanines and flavylocyanines as compared with the xanthylocyanines. A comparison of the absorption maxima of the thiaflavylocyanines and flavylomonomethinecyanines with the absorption maxima of their 7,8-benzo homologs (XIII, XIV) shows that the fusion of a benzo ring in the 7,8 position of the thiaflavylium or the flavylium ring has little influence on the color of the dyes. Of the results on the color of the unsymmetrical dyes, the fact deserves attention that the absorption maximum of the styryl dye V is displaced by 24 nm in the long-wave direction from the arithmetic mean of the wavelength of the absorption bands of the mother dyes, i.e., in contrast to the overwhelming majority of unsymmetrical dyes [12, 13], there is a negative deviation. It was found that the styryl containing a flavylium nucleus also has a negative deviation of 27 nm [14]. Cases of negative deviation have been observed rarely and are of theoretical interest [15]. The unsymmetrical trimethinecyanines XV and XVI possess larger deviations (90 and 51.5 nm, respectively), while for the flavylothiaflavylocarbocyanine XVII the deviation is small (3 nm). The latter result indicates that the flavylium and thiaflavylium nuclei have comparatively close basicities. It is interesting that for the thiaflavylothiacarbocyanine XV the deviation is greater (90 nm) than for the flavylothiacarbocyanine (63.5 nm). In the case of the thiaflavylothiamonomethinecyanine VII the deviation is again greater (47 nm) than that observed for the flavylothiamonomethinecyanine II (29.5 nm). Consequently, judging from the deviations, in the polymethine dyes the thiaflavylium nucleus behaves as less basic than the flavylium nucleus, while it is known that benzothiapyrylium salts are converted into the anhydrobases with greater difficulty than the benzopyrylium salts [16] and thiachromone derivatives are more basic than chromone derivatives [17].

## EXPERIMENTAL

**4-Methylthiaflavylium perchlorate (II).** With mechanical stirring, a solution of 2.85 g (0.012 mole) of thiaflavone [18] in 65 ml of dry tetrahydrofuran was added over 20 min to a solution of the Grignard reagent obtained from 0.5 g (0.02 mole) of magnesium and 2.9 g (0.02 mole) of ethyl iodide in 25 ml of ether. The mixture was kept at 35–40° C for 30 min, the bulk of the solvent was distilled off, and 200 ml of 20% perchloric acid was added to the cooled mixture. After crystallization from glacial acetic acid, yellow crystals with mp 166° C were obtained; yield 3.4 g (87%). Found, %: S 9.39, 9.24. Calculated for $C_{16}H_{13}ClO_4S$, %: S 9.51.

**4-Methoxythiaflavylium o-nitrobenzenesulfonate (II).** A mixture of 2 g (0.008 mole) of thiaflavone and 1.8 g (0.008 mole) of methyl o-nitrobenzenesulfonate [19] was heated at 100° C for 2 hr. The melt was ground in a mortar with dry benzene, and the solid matter was filtered off and washed with ether. Yield 3.4 g (74%). After crystallization from acetic anhydride, yellow crystals with mp 187–188° C. Found, %: S 14.26, 14.17. Calculated for $C_{22}H_{17}NO_6S$, %: S 14.07.

**4-Methyl-7, 8-benzothiaflavylium perchlorate (III).** α-Thionaphthol [20] was obtained in 80% yield by the reduction of naphthalene-α-sulfonyl chloride [21]. 7, 8-Benzothiaflavone was obtained in a similar manner to thiaflavone [18] in 77% yield, mp 182° C [22]. The salt III was obtained in a similar manner to I, yield 83%. It was crystallized in portions from glacial acetic acid. Dark yellow crystals with mp 218° C. Found, %: Cl 8.87, 8.86. Calculated for $C_{20}H_{15}ClO_4S$, %: Cl 9.17.

**The salt IV** was synthesized in a similar manner to **II.**

**4-(p-Dimethylaminostyryl)thiaflavylium perchlorate (V)** was obtained by heating 0.224 g (0.0006 mole) of I and 0.098 g (0.0006 mole) of p-dimethylaminobenzaldehyde in 6 ml of acetic anhydride at 100°C

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*The flavylothiocarbocyanine XVa was obtained in the present work.

for 10 min. Yield 0.248 g (80%). After crystallization from nitromethane, green crystals with a metallic luster, decomp. p. 245° C. Found, %: Cl 7.61, 7.53. Calculated for $C_{25}H_{22}ClNO_4$, %: Cl 7.58.

**4-(ω-Anilinovinyl)thiaflavylium perchlorate (VI).** A mixture of 3 g (0.0006 mole) of **I** and 2 g (0.011 mole) of diphenylformamidine was heated at 150° C for 5 min. The melt was dissolved in 100 ml of boiling ethanol and the filtered solution was treated with 20 ml of 20% perchloric acid. The reaction product was filtered off, washed with water, and purified by chromatography in chloroform on a column of alumina with subsequent crystallization from glacial acetic acid. Yield 0.7 g (18%). Green needles with decomp. p. 208° C. Found, %: Cl 8.40, 8.20. Calculated for $C_{23}H_{16}ClNO_4$, %: Cl 8.07.

The ethyl perchlorate derivative of **2-(2'-phenyl-γ-benzothiapyranylidenemethyl)benzothiazole (VII)** was obtained by heating at 100° C 0.91 g (0.002 mole) of **II** and 0.7 g (0.002 mole) of the ethyl tosylate derivative of 2-methylbenzothiazole in a mixture of 2 ml of acetic anhydride, 2 ml of glacial acetic acid, and 0.2 ml of pyridine for 2 hr. The dye that precipitated when the cold solution was diluted with ether was converted into the perchlorate by precipitation with sodium perchlorate from methanolic solution. After crystallization from ethanol, lustrous green crystals, decomp. p. 257° C. Yield 0.26 g (26%). Found, %: Cl 7.08, 7.07. Calculated for $C_{25}H_{20}ClNO_4S_2$, %: Cl 7.14.

**4-(3'-Ethyl-4'-oxo-2'-thioxothiazolidin-5'-ylidene)-2-phenylbenzothiopyran (VIII)** was obtained from 0.91 g (0.002 mole) of **II** and 0.32 g (0.002 mole) of 3-ethylrhodanine in a similar manner to the preceding experiment. The dye that separated out at the end of the heating period was filtered off and washed with acetic acid and water. Yield 0.32 g (42%). Red-violet crystals with mp 163° C. Found, %: S 24.89, 25.20. Calculated for $C_{20}H_{15}NOS_3$, %: S 25.19.

**Bis(4-thiaflavylo)monomethinecyanine perchlorate (IX).** A mixture of 0.25 g (0.0007 mole) of **I** and 0.76 g (0.001 mole) of **II** was heated in 8 ml of acetic anhydride at 100° C for 15 min. The dye was filtered off, reprecipitated from hot methanol with 5 ml of 30% perchloric acid and crystallized from acetic anhydride. Yield 0.33 g (80%). Lustrous dark green crystals, decomp. p. 228° C. Found, %: Cl 6.26, 6.18. Calculated for $C_{31}H_{21}ClO_4S_2$, %: Cl 6.37.

**Bis(4-Thiaflavylo)trimethinecyanine perchlorate (X).** A mixture of 0.28 g (0.0008 mole) of **I**, 0.68 g (0.0045 mole) of o-formic ester, and 0.6 g (0.006 mole) of anhydrous sodium acetate was heated in 15 ml of glacial acetic acid at 100° C for 5 min. The dye was filtered off, washed with acetic acid, and crystallized from nitromethane. The yield was quantitative, decomp. p. 293° C. The dye is insoluble in glacial acetic acid, sparingly soluble in ethanol and more soluble in nitromethane. Found, %: Cl 5.99, 6.01. Calculated for $C_{33}H_{33}ClO_4S_2$, %: Cl 6.08.

**Bis(4-thiaflavylo)pentamethinecyanine perchlorate (XI).** A mixture of 0.37 g (0.001 mole) of **I** and 0.13 g (0.0005 mole) of the hydrochloride of the dianil of malondialdehyde in 8 ml of acetic anhydride was heated to the boil. The dye was filtered off, freed from the monomethine cyanine **IX** by washing with hot glacial acetic acid, and crystallized from nitromethane. Yield 0.062 g (22%), decomp. p. 262° C. Found, %: Cl 5.85, 6.04. Calculated for $C_{35}H_{25}ClO_4S_2$, %: Cl 5.82.

**Bis(4-thiaflavylo)heptamethinecyanine perchlorate (XII).** A solution of 1.42 g (0.005 mole) of the hydrochloride of the dianil of glutaconic dialdehyde in 40 ml of acetic anhydride was added to a filtered solution of 0.674 g (0.002 mole) of **I** in 50 ml of acetic anhydride. The mixture was left to stand for a day at room temperature in the dark. The dye was filtered off and the monomethinecyanine impurity was washed out with nitromethane. Yield 0.16 g (25%). Light brown crystals, decomp. p. 178° C. Found, %: Cl 5.45, 5.60. Calculated for $C_{37}H_{27}ClO_4S_2$, %: Cl 5.58.

**Bis[4-(7,8-benzothiaflavylo)]monomethinecyanine perchlorate (XIII)** was obtained from the salts **III** and **IV** in a similar manner to **IX**. After crystallization from nitromethane, dark green crystals with decomp. p. 174° C. Yield 70%. Found, %: Cl 5.29, 5.28. Calculated for $C_{39}H_{25}ClO_4S_2$, %: Cl 5.40.

**Bis[4-(7,8-benzoflavylo)]monomethinecyanine perchlorate (XIV).** 4-Methyl-7,8-benzoflavylium perchlorate was obtained in a similar manner to **I** in 94% yield; decomp. p. 245° C. Found, %: Cl 9.49, 9.51. Calculated for $C_{20}H_{15}ClOS$, %: Cl 9.57. From this salt and 4-methoxy-7,8-benzoflavylium o-nitrobenzenesulfonate the dye **XIV** was obtained in a similar manner to **IX**. After crystallization from acetic anhydride, decomp. p. 244° C, yield 77%. Found, %: Cl 5.54, 5.74. Calculated for $H_{39}H_{25}ClO_6$, %: Cl 5.67.

**(3-Ethylthia)(4-thiaflavylo)trimethinecyanine perchlorate (XV).** A mixture of 0.219 g (0.0005 mole) of the hemicyanine **VI** and 0.137 g (0.0005 mole) of 2-methylbenzothiazole methyl methosulfate was heated in a mixture of 3.5 ml of acetic anhydride and 0.1 mole of pyridine at 130° C for 15 min. The dye was filtered off, washed with acetic anhydride and with benzene, and was reprecipitated with 20% perchloric acid from solution in nitromethane, after which it was crystallized from the same solvent. Yield 0.11 g (43%). Blue crystals with decomp. p. 242° C. Found, %: S 12.81, 12.88. Calculated for $C_{26}H_{20}ClNO_4S_2$, %: S 12.56.

**(3-Ethylthia)(4-flavylo)trimethinecyanine perchlorate (XVa)** was obtained in a similar manner to **XV** from 4-(ω-anilinovinyl)flavylium perchlorate [4]. Yield 67%. Blue crystals with decomp. p. 240° C. Found, %: Cl 7.15. Calculated for $C_{26}H_{20}ClNO_5S$, %: Cl 7.19.

**(4-Thiaflavylo)(1,3,3-trimethylindo)trimethinecyanine perchlorate (XVI).** A mixture of 0.336 g (0.001 mole) of **I** and 0.2 g (0.0005 mole) of 2-formylmethylene-1,3,3-trimethylindoline was heated in 4 ml of acetic anhydride at 135° C for 15 min. The cooled solution was treated with 5 ml of 20% perchloric acid. The dye was filtered off, chromatographed on a column of alumina from a mixture of chloroform and nitromethane (4:1), and crystallized from glacial acetic acid, decomp. p. 240° C. Yield 0.200 g (80%). Found, %: Cl 6.94, 6.93. Calculated for $C_{29}H_{26}ClNO_4S$, %: Cl 6.83.

**(4-Flavylo)(4-thiaflavylo)trimethinecyanine perchlorate (XVII).** A mixture of 0.22 g (0.0005 mole) of VI and 0.168 g (0.0005 mole) of 4-methylflavylium perchlorate in a mixture of 4 ml of acetic anhydride and 0.4 ml of pyridine was heated at 100° C for 30 min. The dye was filtered off and crystallized from nitromethane. Yield 0.104 g (40%), decomp. p. 293° C. Found, %: S 5.65, 5.76. Calculated for $C_{33}H_{23}ClO_5S$, %: S 5.64.

**The dye XVIII.** A mixture of 1.6 g (0.0047 mole) of **I** and 1.7 g of diphenylformamidine in 4 ml of acetic anhydride was heated at 130° C for 15 min. The dye that separated out was filtered off and crystallized from formic acid. Yield 0.62 g (decomp. p. 284° C). Found, %: Cl 5.90, 6.13. Calculated for $C_{34}H_{25}ClO_4S_2$, %: Cl 5.94 (for 10-methylthiaflavylotrimethinecyanine perchlorate).

**The dye XX.** A mixture of 0.268 g (0.0007 mole) of **I** and 2 ml of dimethylformamide was heated at 130° C for 5 min. The product that separated in the form of dark red needles was crystallized from dimethylformamide. Calculated to a dye of structure **XX**, the yield was quantitative, decomp. p. 286° C. The substance is insoluble in ethanol and acetic acid, slightly soluble in nitromethane, and soluble in benzene and chloroform. With concentrated sulfuric acid it forms a salt which is hydrolyzed by water with the liberation of **XX**. Found, %: C 81.44, 81.12; H 4.81, 4.80; S 13.85, 13.89. Calculated for $C_{32}H_{24}S_2$, %: C 81.36; H 5.08; S 13.56.

## REFERENCES

1. I. R. Wizinger, Angew. Chem., **51**, 895, 1938.
2. R. Wizinger, Experientia, 1, 29, 1945.
3. R. Wizinger and H. Tobel, Helv. Chim. Acta., **40**, 1305, 1957.
4. R. Wizinger and W. Heldeman, Ber., **93**, 1933, 1960.
5. J. Kelemann and R. Wizinger, Helv. Chim. Acta., **45**, 1908, 1962.
6. M. Kamel and H. Shoeb, Ann., **699**, 168, 1966.
7. R. Wizinger and P. Ulrich, Helv. Chim. Acta, **39**, 217, 1956.
8. R. Wizinger and U. Arni, Ber., **92**, 2309, 1959.
9. A. Lutringhaus, M. Engelhard, and A. Kolb, Ann., **654**, 189, 1962.

10. A. I. Tolmachev and V. P. Sribnaya, ZhOKh, **33**, 3864, 1963.
11. A. I. Tolmachev, ZhOKh, **30**, 640, 1960.
12. A. I. Kiprianov and G. T. Pilyugin, Uch. zap. KhGU, **10**, 104, 1937.
13. L. Brooker, Rev. Mod. Phys., **14**, 275, 1942.
14. R. Wizinger and A. Luttinger, Helv. Chim. Acta, **36**, 526, 1953.
15. G. G. Dyadyusha, Ukr. khim. zh., **31**, 1293, 1965.
16. J. Degani, R. Fachi, and G. Spunta, Boll. scient. Fac. chim. Industr. Bologna, **23**, 243, 1965, RZhKh, 22Zh38, 1966.
17. A. I. Tolmachev, L. M. Shulezhko, and A. A. Kisilenko, ZhOKh, **37**, 367, 1967.
18. F. Bossert, Ann., **680**, 40, 1964.
19. A. I. Kiprianov and A. I. Tolmachev, ZhOKh, **29**, 2871, 1959.
20. F. Krollpfeiffer and H. Schultze, Ber., **56**, 1819, 1923.
21. R. Schuloff, R. Pollak, and E. Riesz, Ber., **62**, 1851, 1929.
22. S. Ruhemann, Ber., **47**, 123, 1914.

23 May 1967

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