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REACTION OF 2, 6-DIMETHYLTHIAPYRONE WITH COMPOUNDS CONTAINING ACTIVE METHYL OR METHYLENE GROUPS

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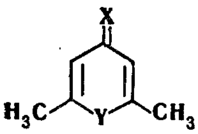
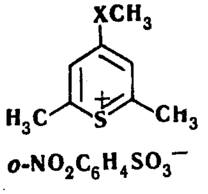
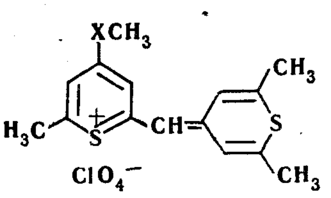
The reaction of 2, 6-dimethylthiapyrone with compounds containing active methyl or methylene groups is investigated. Position 4 in the thiapyrone ring is found to react. If the components with active methylene groups are malonodinitrile or cyclic diketomethylene compounds, the methylene groups in the resultant 2, 6-dimethylthiapyrane compounds are still reactive towards electrophilic reagents, a property which is utilized for synthesis of nonionic polymethylene dyes containing thiapyrane rings.

2, 6-Dimethylpyrone (I) is the most accessible γ-pyrone derivative, and hence that most investigated. Its condensations with compounds containing active methyl or methylene groups have been described [1–5]. Unlike I, the reactions of 2, 6-dimethylthiapyrane (II) are practically unexplored. The present work aimed to study the condensation of II with compounds containing active methyl or methylene groups.

II can be synthesized by decomposing the sodio complex of 2, 6-dimethylthiathiopyrone (III) with mercuric chloride [7], though the yield does not then exceed 10%. Our attempt to prepare the thiapyrone II by hydrolysis of 2, 6-dimethyl-4-methylmercaptothiopyrylium perchlorate (V) did not give the desired result; treatment of an aqueous solution of this salt with sodium carbonate gave the monomethinecyanine VII, formed by self-condensation.







I X=Y=O; II X=O, Y=S; III X=Y=S;

IV X=O; V X=S;

VI X=O, λ_{max} 557 mμ* VII X=S, λ_{max} 587 mμ.

In 1954 there was published a communication, stating that II can be obtained in high yield by heating dimethylpropynylketone at 100° for 1 hr with a saturated ethanolic solution of hydrogen sulfide [8]. A check on the method showed that using pure ketone, the yield of the desired product under the given conditions does not exceed 5%. We showed that hydrogen sulfide readily adds to dipropynylketone in alcohol in the presence of basic catalysts (e.g., triethylamine). Heat is evolved, and a high yield of II obtained.

Our MO-LCAO calculations show**, in agreement with the results in the literature [9], that at position 4 in γ-thiapyrone the electron density is less than at the same position in the γ-pyrone, so that γ-thiapyrone derivatives should react more readily with nucleophilic reagents than γ-pyrone ones, and experiment confirms this. I and II were reacted with malonodinitrile under identical conditions, when the yield of condensation product VIIIa was much higher than that of its oxygen analog VIIIb. Apart from VIIIa, monomethinecyanine (IX) and nonmethinemercocyanines (X-XV) were synthesized by condensing II with compounds containing active methyl or methylene groups. Reaction was carried out in acetic anhydride at 135°. A number of identical compounds can be synthesized by using 2, 6-dimethylthiathiopyrone (III) in the reaction instead of II, though the yields of condensation products are then considerably less. It is possible that the basic reason for that lies in the comparative instability of III, which when heated in acetic anhydride at 130° for 30 min is completely decomposed. Due to their facile self-condensation to dyes VI and VII, it is practically impossible to use the thionium salts IV and V for synthesizing monomethinceyanines and nonmethinemerocyanines containing a thiapyranylidene group.

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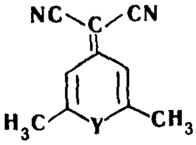
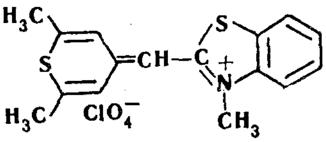
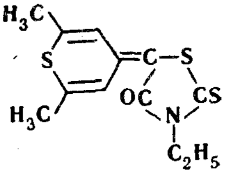
* Here and subsequently λ_{max} is for alcohol solutions.

** Results to be published separately.

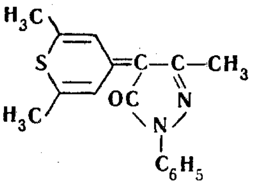
Compound No.	Properties of Compounds Prepared	Decomp. temp., °C	Formula	Found, %	Calculated, %	Yield, %
XX	2-Methyl-4-(dicyanomethylene)-6-[3"-(3'-ethylbenzothiazolinylidene-2")-propenylidene-1'] thiapyran	262	$C_{21}H_{17}N_3S_2$	S 16.80 16.85	S 17.09	48
XXI	2-Methyl-4-(dicyanomethylene)-6-[3'-(5"-methoxy-3"-ethylbenzothiazolinylidene-2")propenylidene-1']thiapyran	255	$C_{22}H_{19}N_3OS_2$	S 15.80 15.76	S 15.80	47
XXII	2-Methyl-4-(dicyanomethylene)-6-[3'-(1" ethyl-1", 1"-dihydroquinolinylidene-2") propenylidene-1'] thiapyran	240	$C_{23}H_{19}N_3S$	S 8.56 8.67	S 8.67	8
XXIII	2-Methyl-4-(1", 3"-diphenyl-2", 4", 6"-triketohexahydropyrimidinylidene-5")-6-[3'-(3'''-ethylbenzothiazolinylidene-2''') propenylidene-1'] thiapyran	277	$C_{34}H_{27}N_3O_3S_2$	S 10.46 10.50	S 10.87	53
XXIV	2-Methyl-4-(1", 3"-diphenyl-2", 4", 6"-triketohexahydropyrimidinylidene-5")-6-[3'-(5"-methoxy-3'''-ethylbenzothiazolinidene-2''') propenylidene-1']-thiapyran	303	$C_{35}H_{29}N_3O_4S_2$	S 10.33 10.27	S 10.34	53
XXV	2-Methyl-4-(1", 3"-diethyl-2", 4", 6"-triketohexahydropyrimidinylidene-5")-6-[3'-(3'''-ethylbenzothiazolinylidene-2''') propenylidene-1'] thiapyran	195	$C_{26}H_{27}N_3O_3S_2$	S 12.96 13.19	S 12.98	43
XXVI	2-Methyl-4-(1", 3"-diethyl-2", 4", 6"-triketohexahydropyridinylidene-5")-6-[3'-(5'''-methoxy-3'''-ethylbenzothiazolinylidene-2''') propenylidene-1']thiapyran	212	$C_{27}H_{29}N_3O_4S_2$	S 11.94 11.80	S 12.24	42
XXVII	2-Methyl-4-(1", 3"-diethyl-2"-thio-4", 6"-diketohexahydropyrimidinylidene-5")-6-[3'-(3'''-ethylbenzothiazolinidene-2''') propenylidene-1']-thiapyran	175	$C_{26}H_{27}N_3O_2S_3$	S 18.51 18.46	S 18.86	34
XXVIII	2-Methyl-4-(1", 3"-diethyl-2"-thio-4", 6"-diketohexahydropyrimidinylidene-5")-6-[3'-(5'''-methoxy-3'''-ethylbenzothiazolinylidene-2''')-propenylidene-1'] thiapyran	170	$C_{27}H_{29}N_3O_3S_3$	S 17.66 17.54	S 17.81	48
XXIX	2-(p-Dimethylaminostyryl)-4-(dicyanomethylene)-6-methylene) thiapyran	257	$C_{19}H_{17}N_3S$	N 13.07 13.26	N 13.17	38
XXX	2, 6-di(p-Dimethylaminostyryl)-4-(dicyanomethylene) thiapyran	290	$C_{28}H_{26}N_4S$	N 12.16 12.12	N 12.44	27

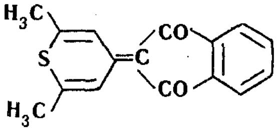


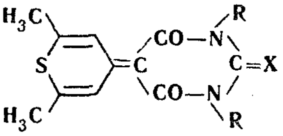




VIII
a Y=S, λ_{max} 386, 409 mμ; IX λ_{max} 476, 504 mμ; X λ_{max} 460; 482 mμ
b Y=O



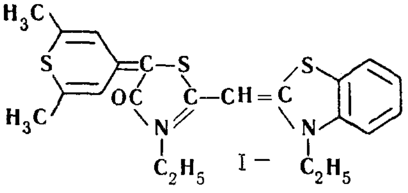


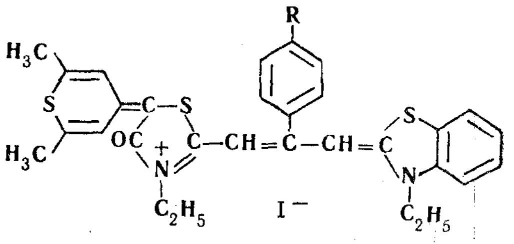


XI λ_{max} 392; 450 mμ; XII λ_{max} 449 mμ; XIII R=C_6H_5, X=O, λ_{max} 430 mμ;
XIV R=C_2H_5, X=O, λ_{max} 432 mμ;
XV R=C_2H_5, X=S, λ_{max} 453 mμ.

It follows from the stated values for the absorption maxima that a solution of the monomethinecyanine IX is red, while solutions of the nonmethinemerocyanines X-XV are yellow or orange. For example, the absorption maxima of solutions of these dyes were 40 mμ further towards the long wavelengths than those of the similar compounds containing 2, 6-dimethylpyranylidene groups [4, 6].

The condensation products prepared from II can be used to synthesize more complex dyes. Thus rhodacyanines can easily be synthesized from X, and we have prepared 3 such compounds (XVI-XVIII). Hitherto dyes of this kind with pyran or thiapyran rings have not been described. It is of interest to note that the absorption maxima of dyes XVII and XVIII are the same. Hence the aryl rings in these dyes are perpendicular to the plane of the dye molecule, as obtains, too, in 9-aryl-substituted thiacarbocyanines [10].

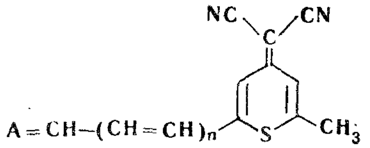


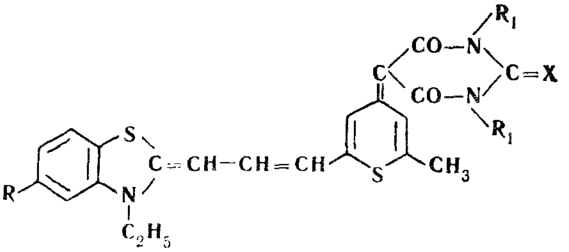


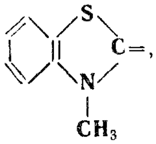
XVI λ_{max} 542 mμ; XVII R=H, λ_{max} 652 mμ; XVIII R=OCH_3, λ_{max} 652 mμ.

In addition to the synthesis of rhodacyanines, a number of 2, 6-dimethylthiapyrone condensation products can be utilized to prepare dyes of a different structure. Those containing groups derived from malonodinitrile or cyclic diketomethylene compounds (IVa, VII-XV), can be condensed at the methyl groups with electrophilic reagents. 2-Mercapto- and 2-ω-acetanilidovinyl- or 2-ω-anilinovinyl derivatives of quaternary salts of nitrogen heterocyclic rings, and p-dimethylaminobenzaldehyde were used in this latter capacity. Reaction is effected in pyridine in the presence of triethylamine. This method was used to synthesize dyes XIX-XXIX. If for 1 mole of the thiapyrane derivative with active methyl groups, 2 moles of the second component are taken, or if the product formed from condensation at 1 methyl group is treated with a further 1 mole of electrophilic reagent, condensation products involving the 2 methyl groups of the thiapyrane ring can be obtained. Compounds XXX and XXXI were prepared by this method. The methyl groups in the nonmethinemerocyanines X and XI are not reactive enough to react with the above-mentioned electrophilic reagents. Further, it is not always possible to effect such condensation with compounds VIIIa, XII-XV. For example, an attempt to effect reaction between VIIIa and 2-ω-anilinovinyl-4, 5-benzobenzothiazole ethyltosylate led to isolation of a sym. 5, 6-benzothiacarbocyanine, instead of the expected product.

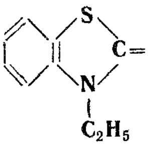
In addition to the formulas of the dyes prepared, there are given the absorption maxima of alcohol solutions of them, and also, in certain cases (parentheses) the absorption maxima values for carbon tetrachloride solutions. Comparison of absorption maxima of compounds XIX and XX shows that the vinyl shift for such dyes is about 90 mμ. Comparison of absorption maxima in ethanol and carbon tetrachloride shows that the dyes are solvatochroic. Their color increases on changing to the less polar solvent, i.e., the II type is solvatochroic [11]. When dilute hydrochloric acid is added to alcohol solutions of the dyes, the colors of the solutions change to yellow, and this is due to salt formation. The nature of the spectrum of the dye XXXI is well explained by A. I. Kiprianov and L. K. Mushkalo's recently developed idea about the spectra of dyes containing two chromophoric groups [12]. The dye XXXI contains two identical chromophoric systems, identical too with the one in the dye XXVI. Furthermore, because of interaction of energy levels in compound XXXI, instead of the absorption bands in the 684 mμ region with dye XXVI, there are two bands, one in the shorter wavelength region (at 603 mμ), the other in the longer wavelength one (at 734 mμ).



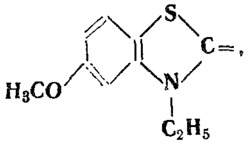


XIX A=  , n=0,

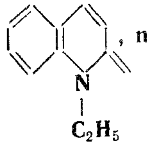
$\lambda_{max}=517(484,510)$ mμ;

XX A=  , n=1,

$\lambda_{max}=606(542,575)$ mμ;

XXI A=  , n=1,

$\lambda_{max}=616(550,584)$ mμ;

XXII A=  , n=1,

$\lambda_{max}=607(544,580)$ mμ;

XXIII R=H, $R_1=C_6H_5$, X=0,
$\lambda_{max}=676$ mμ;

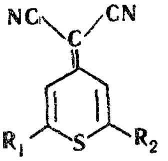
XXIV $R=OCH_3$, $R_1=C_6H_5$,
X=0, $\lambda_{max}=688$ mμ;

XXV R=H, $R_1=C_2H_5$, X=O.
$\lambda_{max}=672$ mμ (606 mμ);

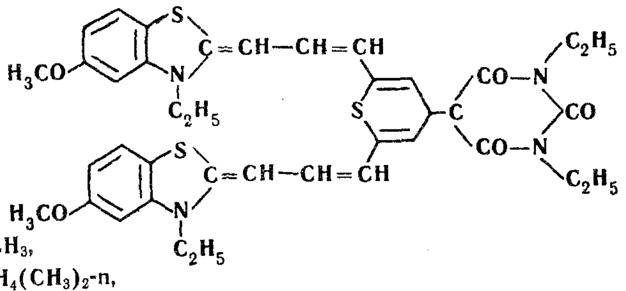
XXVI $R=OCH_3$, $R_1=C_2H_5$, X=0,
$\lambda_{max}=684$ mμ;

XXVII R=H, $R_1=C_2H_5$, X=S,
$\lambda_{max}=690(636)$ mμ;

XXVIII $R=OCH_3$, $R_1=C_2H_5$, X=S,
$\lambda_{max}=702(644)$ mμ;



XXIX $R_1=CH_3$,
$R_2= -CH=CH-C_6H_4(CH_3)_2$-n,
$\lambda_{max}=506$ mμ (440,486,510 mμ);
XXX $R_1=R_2= -CH=CH-C_6H_4N(CH_3)_2$-n,
$\lambda_{max}=524$ mμ (495,526 mμ);



XXXI λ_{max} 603, 734 mμ.

Experimental

2, 6-Dimethylthiapyrone (II). 0.5 ml 4% ethanolic solution of triethylamine was added to a solution of 5.3 g dipropynylketone [13] in 30 ml dry EtOH, and dry H_2S passed in at such a rate that the temperature did not rise above 60°. The EtOH was distilled off, and the product recrystallized from water, using active charcoal. After removing water of crystallization in a vacuum at 100°, yield 4.7 g (62%), mp 104° (literature 104° [8]).

2, 6-Dimethyl-4-methylmercaptothiapyrylium o-nitrobenzenesulfonate (V). 0.62 g 2, 6-dimethylthiathiopyrone [7, 14] (prepared from 2, 6-dimethyl-4-thiopyrone [15]) and 0.86 g methyl o-nitrobenzenesulfonate [16] in 10 ml CH_2Cl_2 were left together at room temperature for 2 days. The salt which separated was filtered off and washed with CH_2Cl_2, then with ether. Yield 0.6 g (80%), mp 140–142°. The material was slightly blue, due to the presence of VII as impurity. The salt was converted to the perchlorate, identical with that previously [17] described.

2-[(2', 4'-Dimethylthiapyranylidene-4') methyl]-6-methyl-4-methoxythiapyrylium perchlorate (VI). 0.56 g thiapyrone II and 0.86 g methyl o-nitrobenzenesulfonate were heated together in 4 ml toluene for 15 min at 100°. The toluene was poured off, 0.16 g fused NaOAc added to the solid residue, then 4 ml MeOH, and the mixture refluxed for 15 min. Addition of 0.5 ml 30% $HClO_4$ converted the dye to perchlorate. Recrystallization from nitromethane gave 0.24 g (32%) dye. Green crystals, with a metallic reflex, decomp 305°. Found: Cl 9.22, 9.11%. Calculated for $C_{15}H_{17}ClO_5S_2$: Cl 9.43%.

2-[(2', 4'-Dimethylthiapyranylidene-4') methyl]-6-methyl-4-methylmercaptothiapyrylium perchlorate (VII). Prepared by heating the thionium salt V in methanol, in the presence of NaOAc, similarly to the above. Green crystals with a metallic reflex. Yield 71%, decomp 298°. Found: Cl 8.68, 8.69%. Calculated for $C_{15}H_{17}O_4S_3$: Cl 9.04%.

2, 6-Dimethyl-4-dicyanomethylenethiapyran (VIIIa). 0.7 g dimethylthiapyrone II and 0.4 g malonodinitrile were heated together in 5 ml Ac_2O, at 135° for 20 min. The product was fitered off, washed with Ac_2O, and then with ether, yield 0.75 g (80%), mp 285°. After recrystallizing from nitromethane, it formed red prisms, mp unaltered. Found: S 17.19, 17.03%. Calculated for $C_{10}H_8N_2S$: S 17.02%.

An experiment was carried out to prepare compound VIIIa by heating the same starting materials together in Ac_2O for 2 hr at 100°. After filtering off the product, what remained in the mother liquor was separated by diluting with water; this material was then purified by chromatography on Al_2O_3, and added to the bulk of the product VIIIa. Yield 60%. Condensing II with malonodinitrile under similar conditions gave a 35% yield of VIIIa [4].

Compound VIIIa was also obtained in 53% yield by heating 0.614 g III and 0.28 g malonodinitrile in 4 ml Ac_2O for 1 hr at 100°.

2-[(2', 6'-dimethylthiapyranylidene-4') methyl] benzothiazole (IX). 0.56 g II, 1.3 g 2-methylbenzothiazole methylmethosulfate, and 8 ml Ac_2O were heated together for 2 hr at 135°, the products cooled and diluted with ether. The dye was extracted with hot water, and separated by adding $NaClO_4$ to the aqueous solution. Recrystallized from nitromethane, yield 0.6 g (39%). Reddish-orange needles, mp 330°. Found: Cl 9.40, 9.41%. Calculated for $C_{16}H_{16}ClNO_4S_2$: Cl 9.21%.

3-Ethyl-2-thio-4-oxo-5-(2', 6'-dimethylthiapyranylidene-4') thiazoline (X). This was prepared by heating together for 1 hr at 135°, 0.56 g II, 0.72 g N-ethylrhodanine, and 4 ml Ac_2O. After chromatographing, using $CHCl_3$ as a solvent, on Al_2O_3, and recrystallizing from nitromethane, yield 0.3 g (53%). Reddish-brown needles, mp 190°. Found: S 33.67, 33.73%. Calculated for $C_{12}H_{18}NOS_3$: S 33.92%.

1-Phenyl-3-methyl-4-(2', 6'-dimethylthiapyranylidene-4') pyrazol-5-one (XI). Prepared similarly to the above, from 0.56 g II, and 0.84 g 1-phenyl-3-methylpyrazol-5-one. Oblong red prisms mp 220° (ex EtOH). Yield 0.36 g (60%). Found: S 11.10, 11.11%. Calculated for $C_{17}H_{16}N_2OS$: S 10.81%.

A 54% yield of the same compound was obtained by heating 0.78 g III with 0.84 g 1-phenyl-3-methylpyrazol-5-one in 2.5 ml Ac_2O for 30 min at 100°.

2-(2', 6'-Dimethylthiapyranylidene-4') indan-1, 3-dione. 0.56 g II, 0.64 g indan-1, 3-dione, and 4 ml Ac_2O were heated together at 135° for 30 min. Reddish-brown needles, mp 219° (ex EtOH). Yield 0.632 g (59%). Found: S 11.74, 11.84%. Calculated for $C_{16}H_{12}O_2S$: S 11.94%.

5-(2', 6'-Dimethylthiapyranylidene-4')-1, 3-diphenylbarbituric acid (XIII). Prepared similarly to the above, from 0.56 g II and 1.12 g 1, 3-diphenylbarbituric acid. Minute yellow crystals, decomp 315° (ex pyridine + EtOH). Yield 1.4 g (87%). Found: S 7.91, 7.85%. Calculated for $C_{23}H_{18}N_2O_3S$: S 7.96%.

The same reaction product, but in 62% yield, was obtained when the thiathiopyrone III was used instead of the thiapyrone II.

Nonmethinemerocyanines XIV and XV. These were prepared, under similar conditions, from II or III and 1, 3-diethyl- or 1, 3-diethyl-2-thiobarbituric acid. The dye XIV was purified by chromatographing on Al_2O_3, solvent $CHCl_3$. Minute brown crystals, mp 190°. Found: S 10.62, 10.72%. Calculated for $C_{15}H_{18}N_2O_3S$: S 10.46%. The dye XV was purified by repeated recrystallization from EtOH. Orange needles, mp 181°. Found: S 19.57, 19.79%. Calculated for $C_{15}H_{18}N_2O_2S_2$: S 19.87%.

3, 3'-Diethyl-4-keto-5-(2", 6"-dimethylthiapyranylidene-4") thiazolinothiacyanine iodide (XVI). 0.414 g merocyanine X was heated with excess Me_2SO_4 at 100° for 20 min. The salt formed was washed with toluene, and along with 0.526 g 2-methylbenzothiazole ethyltosylate dissolved in 9 ml Ac_2O, 1 ml pyridine added, and the whole heated at 100° for 10 min. The dye was filtered off, and converted to iodide by dissolving it in MeOH, and adding a solution of NaI in the same solvent. Brown needles with a metallic glance, decomp 300° (ex nitromethane). Yield 0.456 g (55%). Found: S 17.33, 17.20%. Calculated for $C_{22}H_{23}IN_2OS_3$: S 17.33%.

3, 3'-Diethyl-4-keto-5-(2", 6"-dimethylthiapyranylidene-4")-9-phenylthiazolinothiacarbocyanine iodide (XVII). Prepared from the merocyanine X and 2-(β-phenylpropenyl) benzothiazole ethiodide [18], in a way similar to the preceeding. Green crystals with a metallic glance, decomp 262° (ex EtOH), yield 51%. Found: S 14.51%, 14.55%. Calculated for $C_{30}H_{29}IN_2OS_3$: S 14.63%.

Rhodacyanine XVIII. Prepared from the merocyanine X and 2-[β-(p-methoxyphenyl) propenylbenzothiazole ethyltosylate, in a way similar to XVI. It was purified by chromatographing on Al_2O_3, solvent $CHCl_3$, then recrystallizing from EtOH. Green crystals with a metallic glance, decomp 274°, yield 31%. Found: S 13.88, 13.96%. Calculated for $C_{31}H_{31}N_2O_2S_3$: S 13.99%.

2-Methyl-4-(dicyanomethylene)-6-[(3'-methylbenzothiazolinylidene) methyl]-thiapyran (XIX). 0.956 g dinitrile VIIIa, 0.92 g 2-methylmercaptobenzothiazole methylmethosulfate, 0.3 g triethylamine, and 15 ml pyridine were refluxed together gently for 10 min. The solution was then diluted with water, the product filtered off, and chromatographed on Al_2O_3, solvent $CHCl_3$. The first forward-moving zone was unreacted VIIIa; after it came the red zone of XIX. The product obtained on evaporating the eluate of the latter zone was recrystallized from CH_2NO_2, yield 0.1 g (10%), red glistening crystals, decomp 270°. Found: S 19.02, 19.04%. Calculated for $C_{18}H_{13}N_3S_2$: S 19.10%.

Dyes XXIII-XXX. These were synthesized by the following general method. 0.002 mole of compound VIIIa, XIII, or XV, 0.002 mole 2-ω-acetanilidovinylbenzothiazole ethiodide (or 2-ω-anilinovinyl derivatives of quinoline or 5-methoxybenzothiazole ethiodides), 0.8 g Et_3N, and 10 ml pyridine, were refluxed together gently for 15 min. The material which separated (if nothing separated, the products were diluted with water) was washed with water, and chromatographed over Al_2O_3, $CHCl_3$ being the solvent. The product on the column was divided into 2 zones. Generally the lower zone was considerably bigger than the upper one, and was not so deeply colored. In general the compound in the upper zone, which was the product from condensation at both the methyl groups of the thiapyran ring, was not isolated. In the condensation of VIIIa with p-dimethylaminobenzaldehyde, of which latter 0.004 mole was employed, condensation products from condensation of 1 molecule of the aldehyde, and having structure XXIX, and from 2 molecules of the aldehyde, with structure XXX, were isolated. The dyes obtained were appropriately recrystallized from Ac_2O or $MeNO_2$. The dyes synthesized are listed in the Table.

2, 6-Di-[3'-(5'''-methoxy-3'''-ethylbenzothiazolinylidene-2''') propenylidene-1']-4-(2", 3"-diethyl-2", 4", 6"-triketohexahydropyrimidinylidene-5") thiapyran (XXXI). This was prepared by reacting the dye XXVI with 2-ω-anilinovinyl-5-methoxybenzothiazole ethyltosylate, in the way described above. The product formed dark blue crystals with a metallic glance, decomp 231°, yield 40%. Found: S 12.55, 12.64%. Calculated for $C_{39}H_{40}N_4O_5S_3$: S 12.98%.

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