with decolorizing charcoal at 65° and refiltered. The filtrate is cooled to 5°, the nitrosoguanidine is separated on a Büchner funnel and dried *in vacuo*. The yield varies from 36 to 62% (3.2–5.5 g.). Typical preparations are summarized in Table I.

TABLE I

TYPICAL DATA REGARDING THE CATALYTIC HYDROGENATION OF NITROGUANIDINE[1c]

H_2 press. atm.	Time of redn.	Rate ml. H_2/min.	Nitrosoguanidine yield, %	Purity of nitrosoguanidine, %
Adams Platinum Oxide Catalyst				
1	108	20.6	55.7	93.5
1	109	20.6	59.2	94.3
4	45	45.2	58.5	98.3
Raney Nickel Catalyst				
1	139	16.6	43.4	96.3
1	137	16.8	39.8	99.5
4	110	18.5	44.3	100.3
4	99	20.5	36.6	100.0

Discussion

Water, methanol, ethanol, dioxane and benzene were used as reaction media and water was found to be the most suitable for the Adams catalyst and satisfactory for the Raney catalyst. Methanol gave somewhat higher adsorption rates with Raney nickel (23 ml. of hydrogen per minute) and yields of 45% were obtained consistently. Higher pressures gave increased adsorption rates for the Adams catalyst but were without much effect for the Raney catalyst. The yields of nitrosoguanidine were not affected markedly. The optimum temperature is 25–35° and a decrease or increase of 10° resulted in a lowering of the rate of hydrogen adsorption of 40–70%. The yields of nitrosoguanidine were not affected with the Adams catalyst but with the Raney nickel the yields were materially decreased.

With the Raney nickel catalyst it was found that the optimum ratio of catalyst mass to nitroguanidine was 0.5 g. of catalyst per gram of nitroguanidine. A smaller ratio decreases the rate of adsorption of hydrogen while a ratio of 1 gives a maximum rate but at the same time the yields of nitrosoguanidine are very greatly lowered.

A more comprehensive study of the catalytic hydrogenation of nitroguanidine, now in progress, will include the further reduction to aminoguanidine, the effect of other catalysts and the reduction of nitroaminoguanidine, alkylnitroguanidines and nitrourea.

Summary

Nitroguanidine can be reduced by catalytic hydrogenation using either the Adams platinum oxide catalyst or the Raney nickel catalyst to give a satisfactory yield of nitrosoguanidine.

BROOKLYN, NEW YORK RECEIVED OCTOBER 4, 1935

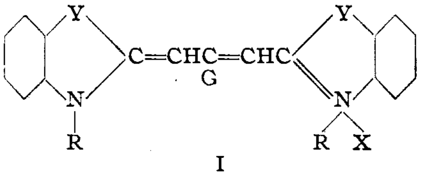
[COMMUNICATION NO. 562 FROM THE KODAK RESEARCH LABORATORIES]

Studies in the Cyanine Dye Series. II. Carbocyanines with Substituents in the Three-Carbon Chain

BY L. G. S. BROOKER AND FRANK L. WHITE

Ethyl orthoformate was employed for the preparation of dyes of the thiacarbocyanine series by König and Meier[1] and by Hamer.[2] The latter, using ethyl orthoacetate, prepared thiacarbocyanines containing an 8-methyl group.[3]

It is now found that ortho esters of higher aliphatic, of substituted aliphatic and of aromatic acids may be employed for the preparation of new thiacarbocyanines (I, Y = S) where G represents a higher alkyl, a substituted alkyl or an aryl group, according to the ortho ester used.[4]



I

Ortho esters of propionic, *n*-butyric, *n*-valeric, *n*- and isocaproic, phenylacetic, phenoxyacetic and benzoic acids have been made and used in the course of this work, and of these the majority are new. The general method used in the preparation of these ortho esters consists in allowing an alcohol to act upon an imino-ester hydrochloride (preferable to "imino-ether hydrochloride"), prepared in turn from a nitrile. This

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[1] König and Meier, *J. prakt. Chem.*, **109**, 324 (1925).

[2] Hamer, *J. Chem. Soc.*, 2796 (1927).

[3] Hamer, *ibid.*, 3160 (1928).

[4] Brooker, U. S. Patents 1,934,657, 1,934,658, 1,934,659, Kodak Ltd., British Patent 394,692.

method was first applied to the preparation of ethyl orthoformate by Pinner,[5] and to that of ethyl orthoacetate and ethyl orthopropionate by Reitter and Hess.[6] Improved methods for the preparation of these two last ortho esters have since appeared,[7,8] whilst ethyl orthophenylacetate was prepared by Staudinger and Rathsam[9] and later by Sah, Ma and Kao.[10] Ethyl orthobenzoate has been obtained by the interaction of sodium ethylate and benzotrichloride,[11] but in the present work it, too, was prepared by the general method.

In the case of 2,2′,8-triethylthiacarbocyanine iodide (I, G = R = Et), a good yield of dye was obtained when 1-methylbenzothiazole ethiodide (2 mols) and ethyl orthopropionate (3 mols, *i. e.*, 200% excess) were allowed to react together in boiling pyridine solution, but the yield was much poorer if methyl orthopropionate (3 mols) was used, the product, furthermore, being otherwise unsatisfactory for the reason given below. If, however, 1-methylbenzothiazole etho-*p*-toluenesulfonate was employed, the dye being subsequently converted into the iodide, good yields were obtained using both the methyl and ethyl orthopropionates, the former in fact giving the somewhat higher yield. Similar results were obtained in the preparation of 8-ethyl-2,2′-dimethyl- and of 2,2′-diallyl-8-ethylthiacarbocyanine iodide. The yields are given in Table I.

TABLE I

PERCENTAGE YIELDS OF 8-ETHYLTHIACARBOCYANINE DYES

	Quaternary iodide orthopropionate		Quaternary *p*-toluenesulfonate orthopropionate	
Dye	Methyl	Ethyl	Methyl	Ethyl
8-Ethyl-2,2′-dimethylthiacarbocyanine iodide	13 (—)	67 (56)	69 (56)	50 (41)
2,2′,8-Triethylthiacarbocyanine iodide	29 (—)	52 (41)	51 (42)	45 (38)
2,2′-Diallyl-8-ethylthiacarbocyanine iodide	9 (—)	47 (30)		

In each column the yield of crude dye is given, followed in parentheses (except in the first column) by the recrystallized yield. In each of the three cases in the first column the product was found to consist of a mixture of two dyes. In the attempted preparation of 2,2′,8-triethylthiacarbocyanine iodide which resulted in the 29% yield, the product was resolved by fractional crystallization into two fractions, the more soluble of which was proved to be true 2,2′,8-triethylthiacarbocyanine iodide, the less soluble fraction being identical with 2,2′-diethyl-8-methylthiacarbocyanine iodide (I, G = Me, R = Et). This latter fact was established using the means already detailed,[12] when it was shown that 2,2′-diethyl-8-methylthiacarbocyanine iodide is produced when 1-methylbenzothiazole ethiodide is heated alone in pyridine, the =CMe— group at the center of the dye molecule being provided by a breakdown of a portion of the quaternary salt used. There is no doubt that this dye is so produced in the present instance and it is significant that it was not encountered in the three preparations of the 2,2′,8-triethyl dye in which high yields of product were obtained, but only in that in which the yield of crude dye was relatively low. An explanation of these facts is that in the three cases, the reaction between ortho ester and quaternary salt is more rapid than that in which 8-methyl dye is formed from the quaternary salt alone, but in the remaining case, the ortho ester is slow to react with the salt and the latter is available to undergo the reaction which gives the 8-methyl dye.

In the preparation of 8-ethyl-2,2′-dimethylthiacarbocyanine iodide from the quaternary iodide using methyl orthopropionate the dye appeared to be largely that sought for, with some contamination with the related 8-methyl dye, but in the attempted corresponding preparation of 2,2′-diallyl-8-ethylthiacarbocyanine iodide the product, after one recrystallization, appeared to consist almost entirely of the 2,2′-diallyl-8-methyl dye. No attempts were made to isolate the individual components of the mixtures in these two cases.

In the preparation of dyes containing higher alkyl groups (I, G = *n*-Pr, *n*-Bu, *n*- and *i*-Am), 1-methylbenzothiazole alkyl *p*-toluenesulfonates were used in conjunction with the appropriate methyl ortho esters, it being convenient to use these latter, since the methyl imino-ester hydrochlorides from which they are prepared are easier

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(5) Pinner, *Ber.*, **16**, 1644 (1883).

(6) Reitter and Hess, *ibid.*, **40**, 3020 (1907).

(7) Sah, THIS JOURNAL, **50**, 516 (1928).

(8) Sigmund and Herschdörfer, *Monatsh.*, **58**, 280 (1931).

(9) Staudinger and Rathsam, *Helv. Chim. Acta*, **5**, 645 (1922).

(10) Sah, Ma and Kao, *J. Chem. Soc.*, 305 (1931).

(11) Limpricht, *Ann.*, **135**, 87 (1865); see also Sah, THIS JOURNAL, **53**, 1836 (1931).

(12) Brooker and White, *ibid.*, **57**, 547 (1935).

to isolate than the corresponding ethyl compounds.[13]

In the preparation of thiacarbocyanines containing substituted aliphatic groups (I, G = $C_6H_5CH_2$, $C_6H_5OCH_2$), or an aromatic group (I, G = C_6H_5) in the 8-position, the corresponding ethyl ortho esters gave satisfactory results when used with 1-methylbenzothiazole alkyl *p*-toluenesulfonates.

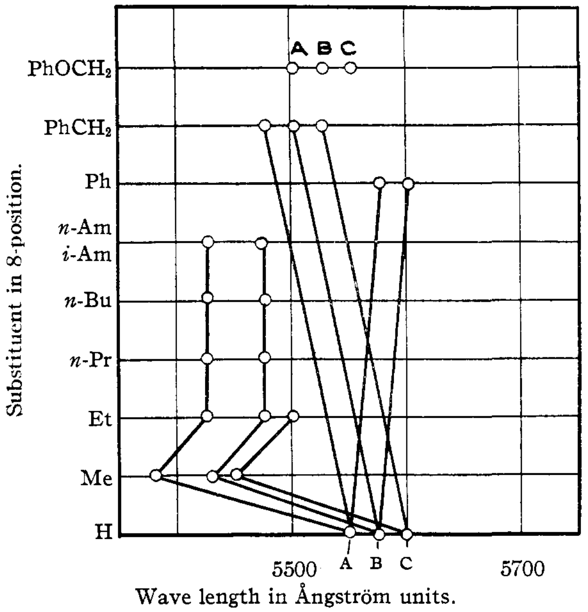

Fig. 1.—Absorption maxima of thiacarbocyanines (I, Y = S): A, 2,2′-dimethyl series; B, 2,2′-diethyl series; C, 2,2′-diallyl series.

The absorption curves of the new dyes showed a well-defined principal band in every case, with, as is often met in cyanine dyes, evidence of a weaker and usually ill-defined secondary band nearer the blue. The positions of the absorption maxima of the main absorption bands are given in Table II, and for comparison there are added the corresponding figures for the related unsubstituted and 8-methyl substituted dyes.

TABLE II

ABSORPTION MAXIMA OF THIACARBOCYANINES IN Å. (I, Y = S)

G.	R Me	 Et	 *n*-Pr	 *n*-Bu	 Al
H	5550	5575	5575	5575	5600
Me	5380	5430	5450	5450	5450
Et	5425	5475	5500	5475	5500
n-Pr	5425	5475			
n-Bu	5425	5475			
n-Am	5425	5475			
i-Am	5425	5475			
$PhCH_2$	5475	5500			5525
$PhOCH_2$	5500	5525			5550
Ph	5575	5600			

In Fig. 1 the positions of maximum absorption have been plotted for the 2,2′-dimethyl, 2,2′-diethyl and 2,2′-diallyl series against the groups in the 8-position, these groups being arranged in the order of increasing complexity. There are striking regularities in these curves.

It has already been noted that replacement of 8-hydrogen in 2,2′-dimethylthiacarbocyanine iodide by methyl, results in a shift of 170 Å. of the absorption maximum toward the blue.[12] We now find that replacement of 8-methyl by 8-ethyl shifts the maximum back toward the red by about 45 Å., but replacement of 8-ethyl by higher aliphatic groups brings about no further shift. Introduction of 8-benzyl and 8-phenoxymethyl into 2,2′-dimethylthiacarbocyanine causes shifts toward the blue of 75 and 50 Å., respectively. The 8-phenyl group, on the other hand, causes a shift toward the red of 25 Å. Very similar relationships have been found in the 2,2′-diethyl series, but these dyes invariably have their absorption maxima somewhat nearer the red than those of the corresponding 2,2′-dimethyl dyes, the amount of the difference varying from 25 to 50 Å. In order to ascertain whether members of the 2,2′-di-*n*-propyl and 2,2′-di-*n*-butyl series would have absorption maxima still further toward the red, three members of each series were prepared, these dyes having in the 8-position, hydrogen, methyl and ethyl, respectively. The two dyes with unsubstituted trimethenyl chains, however, had absorption maxima identical in position with that of 2,2′-diethylthiacarbocyanine iodide, but dyes of the 2,2′-di-*n*-propyl and 2,2′-di-*n*-butyl series containing 8-methyl and 8-ethyl groups had their absorption maxima, as a rule, somewhat nearer the red than the corresponding dyes of the 2,2′-diethyl series.

Three dyes of the 2,2′-diallylthiacarbocyanine series were also examined, these being the unsubstituted dye and the 8-methyl and 8-ethyl derivatives. Within this series, the same general relations held as were found to apply in the 2,2′-dimethyl and 2,2′-diethyl series, but the 2,2′-diallyl derivatives had their absorption maxima consistently nearer the red than the corresponding 2,2′-diethyl compounds.

The new dyes described act as photographic sensitizers for the green and yellow portions, and,

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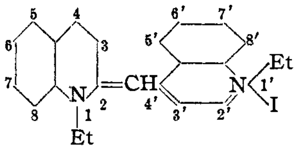
[13] Compare Hill and Rabinowitz, THIS JOURNAL, **48**, 732 (1926).

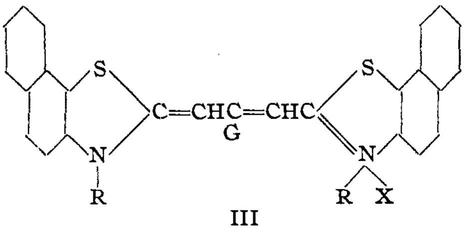
to a varying extent, the red portion of the spectrum.[14]

It was pointed out by Mills and Pope[15] that substitution of a methyl, phenyl or cyano grouping in the 2′-position of 1,1′-diethyl-2,4′-cyanine iodide (II) gave dyes with greatly reduced sensitizing power, the depressant effect of the three groups increasing in the order given. They suggested that this was due to the loading effect of the substituent on the ethylenic chain joining the two nitrogen atoms, the ability of the molecule to interact with light waves being inhibited. From this it might have been expected that loading the ethylenic chain in 2,2′-diethylthiacarbocyanine iodide by the introduction of substituents in the 8-position would materially depress the sensitizing action, but this is not the case.

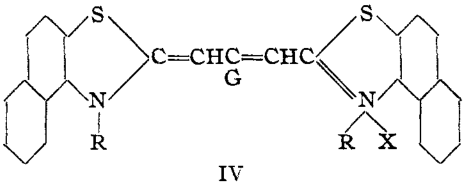
II



8-Methylthiacarbocyanine dyes derived from the methyl-α- and β-naphthothiazoles have previously been described.[12,16] Using ortho esters of propionic and of benzoic acids in conjunction with the alkyl *p*-toluenesulfonates of the two bases, eight more dyes have now been prepared, these being the 8-ethyl and 8-phenyl-5,6,5′,6′-dibenzothiacarbocyanines (III) and the 8-ethyl and 8-phenyl-3,4,3′,4′-dibenzothiacarbocyanines (IV), the 2,2′-dimethyl and 2,2′-diethyl derivatives being prepared of each of the four types.[17]



III



IV

On account of the insolubility of the iodides of these dyes, the bromides were prepared except in the case of 2,2′,8-triethyl-5,6,5′,6′-dibenzothiacarbocyanine iodide, which was sufficiently soluble.

In Table III are given the positions of the maximum absorption of these dyes together with similar data on related unsubstituted and 8-methyl substituted dyes.

TABLE III

ABSORPTION MAXIMA OF DIBENZOTHIACARBOCYANINES (III AND IV) IN Å.

(a) 5,6,5′,6′-dibenzothiacarbocyanines

G (III)	R (III) Me	Et
H	5900	5925
Me	5660	5725
Et	5675	5750
Ph	5920	5925

(b) 3,4,3′,4′-dibenzothiacarbocyanines

G (IV)	R (IV) Me	Et
H	5925	5950
Me	5700	5750
Et	5750	5775
Ph	5950	5925

If these values are plotted against the groups occupying the 8-positions of the dyes, curves are obtained which, in their general characteristics, are very similar to those given in Fig. 1. Figure 2 deals with the 5,6,5′,6′-dibenzothiacarbocyanines and Fig. 3 with the 3,4,3′,4′-dibenzothiacarbocyanines.

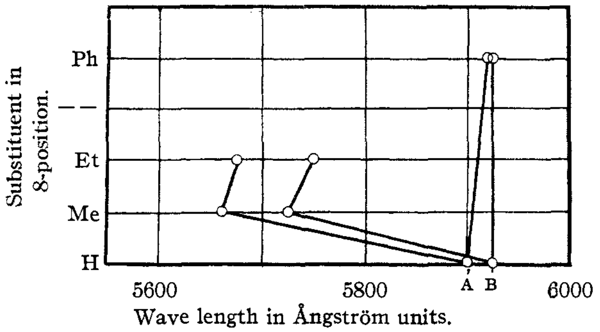


Fig. 2.—Absorption maxima of 5,6,5′,6′-dibenzothiacarbocyanines (III): A, 2,2′-dimethyl series; B, 2,2′-diethyl series.

From these curves it is seen that, as in the simple thiacarbocyanines, introduction of an 8-methyl group into a dibenzothiacarbocyanine brings about a marked shift of the absorption maximum toward the blue. This shift is partially canceled if the 8-methyl group is replaced by an 8-ethyl group. The 8-phenyl dyes have

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[14] Brooker, U. S. Patents 1,846,302, 1,846,303, 1,846,304, Kodak Ltd., British Patent 394,691.

[15] Mills and Pope, *Phot. J.*, **60**, 183 (1920).

[16] Hamer, *J. Chem. Soc.*, 2598 (1929).

[17] Brooker, U. S. Patents 1,969,444, 1,969,447; Kodak Ltd., British Patent 378,870.

maxima either identical with or very close to those of the related unsubstituted dyes, but in the 3,4,3′,4′-dibenzo series the usual relative positions of the 2,2′-dimethyl and 2,2′-diethyl dyes are reversed. In every case except this, a 2,2′-dimethyl dye has its absorption maximum nearer the blue than the corresponding 2,2′-diethyl dye. In every case but one, also, a 3,4,3′,4′-dibenzothiacarbocyanine has its absorption maximum somewhat nearer the red than the corresponding 5,6,5′,6′-dibenzothiacarbocyanine.

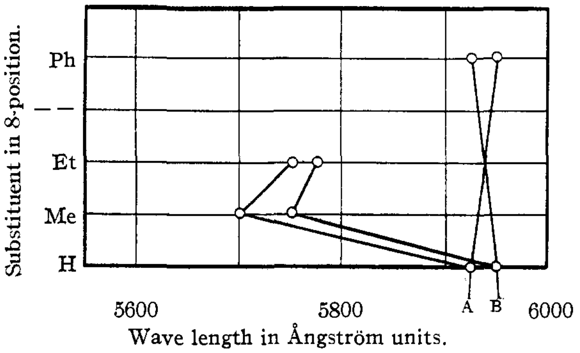

Fig. 3.—Absorption maxima of 3,4,3′,4′-dibenzothiacarbocyanines (IV): A, 2,2′-dimethyl series: B, 2,2′-diethyl series.

All the new dyes derived from the methylnaphthothiazoles act as photographic sensitizers, some of them being exceedingly powerful.[18] They sensitize further in the direction of longer wave length than the corresponding dyes derived from 1-methylbenzothiazole. It is a striking generalization that every one of the eight carbocyanine dyes derived from 2-methyl-β-naphthothiazole is a stronger sensitizer than the related isomeric dye derived from 1-methyl-α-naphthothiazole.

An 8-methylselenacarbocyanine dye (I, R = Et, G = Me, Y = Se, X = I) has recently been described,[12] and the 8-ethyl-2,2′-dimethyl- and 2,2′,8-triethylselenacarbocyanine iodides and the two corresponding 8-phenylselenacarbocyanines have now been prepared.[19] In these syntheses 1-methylbenzoselenazole alkyl *p*-toluenesulfonates were employed. The absorption maxima of these dyes as well as those of the related unsubstituted[20] and 8-methyl substituted dyes are given in Table IV.

Made up into Fig. 4, these values give curves very similar in general appearance to those already obtained. The same sharp recession toward the blue is noticeable upon introducing an 8-methyl group as was found in the previous instances, and on proceeding to the 8-ethyl compounds the absorption maxima advance again toward the red. Introduction of an 8-phenyl group brings about a shift in the absorption maximum toward the red by an amount greater than has been encountered hitherto. It is also worthy of note that in this series the unsubstituted 2,2′-dimethyl- and 2,2′-diethyl dyes both have their maximum absorption at the same wave length.

Table IV

Absorption Maxima of Selenacarbocyanines in Å. (I, Y = Se)

G (I)	R (I) Me	R (I) Et
H	5675	5675
Me	5485	5525
Et	5525	5575
Ph	5725	5740

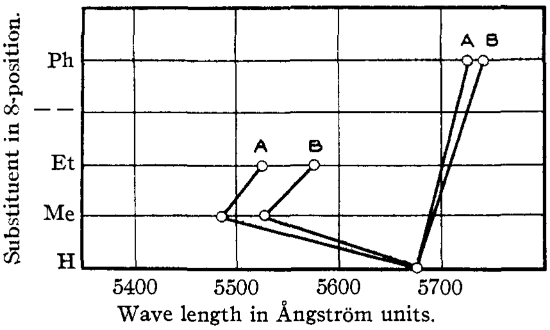

Fig. 4.—Absorption maxima of selenacarbocyanines (I, Y = Se): A, 2,2′-dimethyl series: B, 2,2′-diethyl series.

The new selenacarbocyanines are photographic sensitizers, their sensitizing bands extending somewhat further into the red than those of the corresponding thiacarbocyanines.[21]

In the oxacarbocyanine series an 8-methyl derivative (I, G = Me, R = Et, Y = O, X = I) has been obtained,[12] triethylamine being used in addition to pyridine in its preparation. Using this same device the 8-ethyl-2,2′-dimethyl- and 2,2′,8-triethyloxacarbocyanine iodides have now been prepared. The absorption maxima of these dyes, as well as those of the unsubstituted oxacarbocyanines, are given in Table V and Fig. 5 is based on these values.

The curves in Fig. 5 differ markedly from those preceding it in that introduction of an 8-methyl group into an unsubstituted oxacarbocyanine pro-

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(18) Brooker, U. S. Patent 1,846,301; Kodak Ltd., British Patent 378,885.

(19) White, U. S. Patent 1,990,681.

(20) Clark, *J. Chem. Soc.*, 2313 (1928); 216 (1933).

(21) White, U. S. Patent 1,990,507; Kodak Ltd., British Patent 390,406.

TABLE V

ABSORPTION MAXIMA OF THE OXACARBOCYANINES IN Å. (I, Y = O)

G (I)	R (I) Me	R (I) Et
H	4820	4825
Me	4875	4885
Et	4900	4900

duces a shift toward the red. This advance is continued on introducing an 8-ethyl group. The differences between the positions of the maxima of corresponding members of the 2,2′-dimethyl and 2,2′-diethyl series are very slight and, indeed, the values for the two 8-ethyl dyes are identical.

The new oxacarbocyanines are photographic sensitizers for the blue-green and green.[22]

All the absorption curves used in the present paper were determined for methyl alcoholic solutions using the means already detailed.[12]

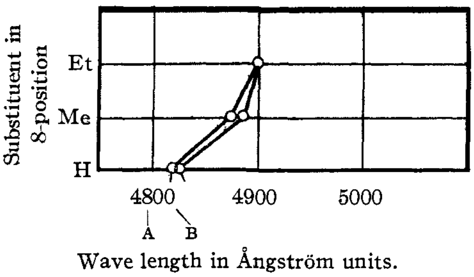

Fig. 5.—Absorption maxima of oxacarbocyanines (I, Y = O): A, 2,2′-dimethyl series; B, 2,2′-diethyl series.

TABLE VI

PREPARATION OF IMINO-ESTER HYDROCHLORIDES

Imino-ester hydrochloride	Nitrile	Alcohol	Days A	Days B	Yield, %
Me iminopropionate	C_2H_5CN	MeOH	2	3	88
Me imino-*n*-butyrate	*n*-C_3H_7CN	MeOH	3	3	67
Me imino-*n*-valerate	*n*-C_4H_9CN	MeOH	2	3	63
Me imino-*n*-caproate	*n*-$C_5H_{11}CN$	MeOH	4	2	75
Me iminoisocaproate	*i*-$C_5H_{11}CN$	MeOH	3	3	71
Et iminophenoxyacetate	$C_6H_5OCH_2CN$	EtOH	2	2	82
Et iminobenzoate	C_6H_5CN	EtOH	20	8	90

TABLE VII

PREPARATION OF ORTHO ESTERS

Ortho ester	Stood, days	Yield, %	B. p., °C.	Formula	Analyses, % Calcd. C	Analyses, % Calcd. H	Analyses, % Found C	Analyses, % Found H
OE3 Me *o*-propionate	6	69	126–128	$C_6H_{14}O_3$	53.68	10.52	53.90	10.60
OE5 Me *o*-*n*-butyrate	28	13	145–147	$C_7H_{16}O_3$	56.70	10.88	56.75	10.86
OE6 Me *o*-*n*-valerate	28	12	167–170	$C_8H_{18}O_3$	59.21	11.19	59.45	11.10
OE7 Me *o*-*n*-caproate	5	40	187–190	$C_9H_{20}O_3$	61.31	11.45	61.30	11.36
OE8 Me *o*-isocaproate	35	9	178–181	$C_9H_{20}O_3$	61.31	11.45	61.35	11.34
OE9 Et *o*-phenoxyacetate[a]	28	30	99–100 (1.5 mm.)	$C_{14}H_{22}O_4$	66.10	8.72	66.30	8.34
OE10 Et *o*-benzoate	42	20	239.5–240.5	$C_{13}H_{20}O_3$	69.60	8.99	69.65	8.74

[a] The crude ortho ester fraction, b. p. 130–140° (8.5 mm.), was well washed with water to remove amide, Benzene was added, the solution again washed with water and the benzene layer dried with anhydrous sodium sulfate and fractionated.

Experimental

Ortho Esters.—For the preparation of the imino-ester hydrochlorides, the method of Hill and Rabinowitz[13] and of Sah[7] was used, a mixture of the nitrile (1 mol) and the alcohol (1 mol) in ether being treated at 5–10° with hydrochloric acid gas (1.05–1.1 mols), it being of the utmost importance that the materials should be as free from water as possible. The imino-ester hydrochlorides (listed in Table VI) usually set to a cake of crystals after standing for some days at 0° (Table VI, Days A) and this was well crushed, washed with absolute ether, and the excess of hydrochloric acid removed by standing in a vacuum over powdered potassium hydroxide, a separate dish of phosphorus pentoxide being also included. This treatment was continued until a small quantity of the salt, dissolved in absolute alcohol no longer affected moistened Congo red paper (Table VI, Days B). The hydrochlorides so obtained formed colorless crystals which had no true melting points but decomposed with gas evolution after shrinking.

The imino-ester hydrochlorides are unstable compounds and were converted directly into the corresponding ortho esters by treatment at room temperature, with occasional shaking, with the appropriate alcohols for periods which varied from a few days to a few weeks. The solid which separated (largely ammonium chloride) was removed by filtration. The filtrate was distilled from the steam-bath under reduced pressure, a residue of amide usually remaining. The distillate was then repeatedly fractionated, it being necessary in some cases to remove accompanying

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(22) Brooker, U. S. Patent 1,962,124.

normal ester. By this procedure all the ortho esters were obtained analytically pure, and those not previously described are given in Table VII. For convenience they are numbered as shown.

Ortho esters used in addition to the above are ethyl orthoformate, OE1; ethyl orthoacetate, OE2; ethyl orthopropionate,[6,8] OE4; ethyl orthophenylacetate,[9,10] OE11.

Quaternary Salts.—The quaternary salts used are numbered for convenience as follows:

QS1	1-Methylbenzothiazole methiodide
QS2	1-Methylbenzothiazole ethiodide
QS3	1-Methylbenzothiazole *n*-propiodide
QS4	1-Methylbenzothiazole *n*-butiodide
QS5	1-Methylbenzothiazole alliodide
QS6	1-Methylbenzothiazole metho-*p*-toluenesulfonate
QS7	1-Methylbenzothiazole etho-*p*-toluenesulfonate
QS8	1-Methyl-α-naphthothiazole metho-*p*-toluenesulfonate
QS9	1-Methyl-α-naphthothiazole etho-*p*-toluenesulfonate
QS10	2-Methyl-β-naphthothiazole metho-*p*-toluenesulfonate
QS11	2-Methyl-β-naphthothiazole etho-*p*-toluenesulfonate
QS12	1-Methylbenzoselenazole metho-*p*-toluenesulfonate
QS13	1-Methylbenzoselenazole etho-*p*-toluenesulfonate
QS14	1-Methylbenzoxazole metho-*p*-toluenesulfonate
QS15	1-Methylbenzoxazole ethiodide

QS12 and 14 were prepared by heating equimolecular proportions of base and methyl-*p*-toluenesulfonate at 100° for several hours. QS13 was similarly prepared, the mixture being heated for three days. These salts were used without purification. Other new quaternary salts are given in Table VIII, the normal methods of preparation being used.[12] In all cases the crude products were ground with acetone and washed with this solvent and were then sufficiently pure for dye formation. The yields given correspond to this stage. For analysis and melting point determinations those salts which were iodides were recrystallized from methyl alcohol. The *p*-toluenesulfonates were dissolved in hot methyl alcohol and precipitated by adding acetone. The salts were all colorless or almost colorless solids.

Dyes.—The quaternary salts were condensed with the ortho esters in boiling anhydrous pyridine solution, the period of heating varying from ten to ninety minutes. In general, a 200% excess of orthoester was used except that a 100% excess was used of OE5, 6, 7 and 8. When the quaternary salt was an iodide, separation of the dye from

TABLE VIII

PREPARATION OF QUATERNARY SALTS

Salt	Reactants heated, hrs.	Yield, %	M. p., °C.	Formula	Analyses, % Calcd.	Analyses, % Found
QS3	72[a]	82	173 –175	$C_{11}H_{14}INS$	I, 39.77	39.88
QS4	72[a]	63	186 –187	$C_{12}H_{16}INS$	I, 38.11	38.10
QS5	20[a]	88	192 –193	$C_{11}H_{12}INS$	I, 40.03	39.95
QS6[a]	3[b]	90	183.5–184.5	$C_{16}H_{17}NO_3S_2$	N, 4.16	4.22
QS8	48[c]	88	232 –233	$C_{20}H_{19}NO_3S_2$	C, 62.29	61.98
					H, 4.97	4.83
QS10	–[d]	94	189 –190	$C_{20}H_{19}NO_3S_2$	C, 62.29	62.10
					H, 4.97	4.90

[a] Heated on steam-bath under reflux. [b] Heated at 100°. [c] Heated at 105–110°. [d] Heated for three hours at 130–140° and for three days at 100°.

TABLE IX

PREPARATION OF THIACARBOCYANINE IODIDES

	Thiacarbocyanine iodide	Quaternary salt, g.		Ortho-ester, g.		C_5H_5N, cc.	Boiled, min.	Method	Yield, %		Soln. MeOH cc./g.	M. p., °C. dec.	Formula	Halogen, % Calcd.	Halogen, % Found
D1	2,2'-di-Al[a]	QS5	6.34	OE1	4.44	25	45	A	96	77	170	264–266	$C_{23}H_{21}IN_2S_2$	24.59	24.46
D2	2,2'-di-*n*-Pr	QS3	6.38	OE1	4.44	25	45	A	95	87	150	296–297	$C_{23}H_{25}IN_2S_2$	24.40	24.46
D3	2,2'-di-*n*-Bu	QS4	6.66	OE1	4.44	25	45	A	95	77	48	275–277	$C_{25}H_{29}IN_2S_2$	23.15	23.20
D4	2,2'-di-Al-8-Me	QS5	6.34	OE2	4.86	25	45	A	75	64	190	267–268	$C_{24}H_{23}IN_2S_2$	23.93	23.86
D5	8-Me-2,2'-di-*n*-Pr	QS3	6.38	OE2	4.86	25	45	A	70	64	1560	295–296	$C_{24}H_{27}IN_2S_2$	23.75	23.77
D6	2,2'-di-*n*-Bu-8-Me	QS4	6.66	OE2	4.86	25	45	A	59	53	63	236–237	$C_{26}H_{31}IN_2S_2$	22.57	22.64
D7	8-Et-2,2'-di-Me[b]	QS1	5.28	OE4	5.28	25	45	A	67	56	440	286–287	$C_{21}H_{21}IN_2S_2$	25.78	25.63
D8	2,2',8-tri-Et[c]	QS2	6.10	OE4	5.28	25	45	A	52	41	75	236–237[d]	$C_{23}H_{25}IN_2S_2$	24.40	24.32
D9	2,2'-di-Al-8-Et[e]	QS5	6.34	OE4	5.28	25	45	A	47	30	55	214–216	$C_{25}H_{25}IN_2S_2$	23.32	23.37
D10	8-Et-2,2'-di-*n*-Pr	QS3	6.38	OE4	5.28	25	45	A	38	28	110	248–250	$C_{25}H_{29}IN_2S_2$	23.15	23.17
D11	2,2'-di-*n*-Bu-8-Et	QS4	6.66	OE4	5.28	25	45	A	35	28	65	241–243	$C_{27}H_{33}IN_2S_2$	22.03	21.95
D12	2,2'-di-Me-8-*n*-Pr	QS6	6.70	OE5	2.96	25	45	C	59	50	110	268–269	$C_{22}H_{23}IN_2S_2$	25.07	24.97
D13	2,2'-di-Et-8-*n*-Pr	QS7	6.98	OE5	2.96	25	45	B	65	55	58	246–248	$C_{24}H_{27}IN_2S_2$	23.75	23.72
D14	8-*n*-Bu-2,2'-di-Me	QS6	6.70	OE6	3.24	25	45	C	55	42	68	168–169	$C_{23}H_{25}IN_2S_2$	24.40	24.41
D15	8-*n*-Bu-2,2'-di-Et	QS7	6.98	OE6	3.24	25	45	B	64	58	50	233–234	$C_{25}H_{29}IN_2S_2$	23.15	23.03
D16	8-*n*-Am-2,2'-di-Me	QS6	6.70	OE7	3.52	25	45	B	66	55	34	217–219	$C_{24}H_{27}IN_2S_2$	23.75	23.51
D17	8-*n*-Am-2,2'-di-Et	QS7	6.98	OE7	3.52	25	45	B	62	53	39	237–238	$C_{26}H_{31}IN_2S_2$	22.57	22.42
D18	8-iso-Am-2,2'-di-Me	QS6	6.70	OE8	3.52	25	45	C	61	47	80	241–242	$C_{24}H_{27}IN_2S_2$	23.75	23.65
D19	8-iso-Am-2,2'-di-Et	QS7	6.98	OE8	3.52	25	45	B	61	51	35	219–220	$C_{26}H_{31}IN_2S_2$	22.57	22.55
D20	8-PhCH₂-2,2'-di-Me	QS6	6.70	OE11	7.14	25	45	C	27	15	500	288–289	$C_{26}H_{23}IN_2S_2$	22.90	22.87
D21	8-PhCH₂-2,2'-di-Et	QS7	6.98	OE11	7.14	25	45	C	16	11	155	242–243	$C_{28}H_{27}IN_2S_2$	21.80	21.80
D22	2,2'-di-Al-8-PhCH₂	QS5	6.34	OE11	7.14	25	45	A	38	33	180	225–227	$C_{30}H_{27}IN_2S_2$	20.94	20.91
D23	2,2'-di-Me-8-PhOCH₂[f]	QS6	6.70	OE9	7.62	25	30	B	71	48	110	255–257	$C_{26}H_{23}BrN_2OS_2$	15.27	15.37
D24	2,2'-di-Et-8-PhOCH₂	QS7	3.49	OE9	3.80	10	30	B	71	39[g]	52	202–204	$C_{28}H_{27}IN_2OS_2$	21.21	21.05
D25	2,2'-di-Al-8-PhOCH₂	QS5	6.34	OE9	7.62	25	10	A	57	41[g]	80	211–213	$C_{30}H_{27}IN_2OS_2$	20.39	20.38
D26	2,2'-di-Me-8-Ph	QS6	6.70	OE10	6.72	25	45	C	75	56	210	275–277	$C_{25}H_{21}IN_2S_2$	23.49	23.51
D27	2,2'-di-Et-8-Ph	QS7	6.98	OE10	6.72	25	45	C	73	56	210	300–301	$C_{27}H_{25}IN_2S_2$	22.34	22.02

TABLE IX (*Concluded*)

PREPARATION OF 5,6,5',6'-DIBENZOTHIACARBOCYANINE BROMIDES

5,6,5',6'-Dibenzothiacarbocyanine bromide	Quaternary salt, g.		Ortho-ester, g.		C_5H_5N, cc.	Boiled, min.	Method	Yield, %		Soln. MeOH cc./g.	M. p., °C. dec.	Formula	Halogen, %	
													Calcd.	Found
D28 2,2'-di-Me[h]	QS8	3.85	OE1	2.22	30	60	B	99	83	1350	285	$C_{27}H_{21}BrN_2S_2$	15.45	15.45
D29 2,2'-di-Et[i]	QS9	8.00	OE1	4.45	50	60	C	86	68	70	280	$C_{29}H_{27}BrN_2S_2$	14.66	14.66
D30 2,2'-8-tri-Me[h]	QS8	3.85	OE2	2.43	20	60	B	66	42	680	278–281	$C_{28}H_{23}BrN_2S_2$	15.05	14.84
D31 2,2'-di-Et-8-Me[h]	QS9	8.00	OE2	4.85	50	60	B	58	43	215	261	$C_{30}H_{27}BrN_2S_2$	14.29	14.11
D32 8-Et-2,2'-di-Me	QS8	7.70	OE3	4.02	30	60	C	70	54	265	299	$C_{29}H_{25}BrN_2S_2$	14.66	14.53
D33 2,2',8-tri-Et[j]	QS9	8.00	OE3	4.02	20	60	C	47	37	520	296	$C_{31}H_{29}IN_2S_2$	20.46	20.56
D34 2,2'-di-Me-8-Ph	QS8	7.70	OE10	6.70	30	90	C	70	47	1120	308–310	$C_{33}H_{25}BrN_2S_2$	13.47	13.31
D35 2,2'-di-Et-8-Ph	QS9	8.00	OE10	6.70	20	90	C	50	38	355	296	$C_{35}H_{29}BrN_2S_2$	12.86	12.81

PREPARATION OF 3,4,3',4'-DIBENZOTHIACARBOCYANINE BROMIDES

3,4,3',4'-Dibenzothiacarbocyanine bromide	Quaternary salt, g.		Ortho-ester, g.		C_5H_5N, cc.	Boiled, min.	Method	Yield, %		Soln. MeOH cc./g.	M. p., °C. dec.	Formula	Halogen, %	
													Calcd.	Found
D36 2,2'-di-Me[h]	QS10	3.85	OE1	2.22	30	60	C	96	73	2150	237	$C_{27}H_{21}BrN_2S_2$	15.45	15.15
D37 2,2',8-tri-Me	QS10	7.70	OE2	4.85	20	30	C	31	19[g]	150	240–241	$C_{28}H_{23}BrN_2S_2$	15.05	15.10
D38 8-Et-2,2'-di-Me	QS10	7.70	OE4	5.30	30	30	C	39	24	285	230	$C_{29}H_{25}BrN_2S_2$	14.66	14.79
D39 2,2',8-tri-Et	QS11	8.00	OE4	5.30	15	30	C	37	29	130	247	$C_{31}H_{29}BrN_2S_2$	13.94	13.81
D40 2,2'-di-Me-8-Ph	QS10	7.70	OE10	6.70	20	15	C	8	3[k]		242–244	$C_{33}H_{25}BrN_2S_2$	13.47	13.34
D41 2,2'-di-Et-8-Ph	QS11	8.00	OE10	6.70	20	30	B	6	4.5	150	252	$C_{35}H_{29}BrN_2S_2$	12.86	12.81

PREPARATION OF SELENACARBOCYANINE IODIDES

Selenacarbocyanine iodide	Quaternary salt, g.		Ortho-ester, g.		C_5H_5N, cc.	Boiled, min.	Method	Yield, %		Soln. MeOH cc./g.	M. p., °C. dec.	Formula	Halogen, %	
													Calcd.	Found
D42 2,2',8-tri-Me[f]	QS12	7.64	OE2	4.85	25	25	C	51	36	280	290–291	$C_{20}H_{19}BrN_2Se_2$	15.21	15.05
D43 8-Et-2,2'-di-Me	QS12	7.64	OE4	5.28	25	15	C	51	32	1300	271–272	$C_{21}H_{21}IN_2Se_2$	21.64	21.47
D44 2,2',8-tri-Et	QS13	7.92	OE4	5.28	25	15	C	20	16	35	146–148	$C_{23}H_{25}IN_2Se_2$	20.65	20.53
D45 2,2'-di-Me-8-Ph	QS12	7.64	OE10	6.72	25	15	C	27	18	130	271–272	$C_{25}H_{21}IN_2Se_2$	20.00	19.86
D46 2,2'-di-Et-8-Ph	QS13	7.92	OE10	6.72	25	15	C	19	13	230	280–281	$C_{27}H_{25}IN_2Se_2$	19.15	18.85

PREPARATION OF OXACARBOCYANINE IODIDES

Oxacarbocyanine iodide	Quaternary salt, g.		Ortho-ester, g.		C_5H_5N, cc.	Boiled, min.	Method	Yield, %		Soln. MeOH cc./g.	M. p., °C. dec.	Formula	Halogen, %	
													Calcd.	Found
D47 2,2',8-tri-Me	QS14	6.4	OE2	6.5	20[l]	7	C	8	6	105	290–292	$C_{20}H_{19}IN_2O_2$	28.45	28.21
D48 8-Et-2,2'-di-Me	QS14	6.4	OE4	7.05	20[l]	7	C	16	11	28	280–282	$C_{21}H_{21}IN_2O_2$	27.58	27.40
D49 2,2',8-tri-Et	QS15	2.89	OE4	2.64	15[m]	60	A	13	8	45	269–270	$C_{23}H_{25}IN_2O_2$	25.99	25.91

[a] The bromide of this dye was described by Hamer.[2] [b] When methyl orthopropionate (4.02 g.) was used in place of the ethyl ortho ester, the yield of dye was 0.65 g. (13% calculated as 8-ethyl dye). The iodine content was somewhat high (found: I, 25.91) which would correspond to a certain degree of contamination with the 2,2',8-trimethyl dye. [c] When methyl orthopropionate (4.02 g.) was used instead of the ethyl ortho ester, the method otherwise being the same, the yield of crude dye was 1.52 g. (29% calculated as 2,2',8-triethyl dye). When a solution of the product in methyl alcohol was allowed to evaporate slowly, large greenish crystals separated together with smaller coppery crystals. These were separated mechanically, and the two fractions were purified by repeated fractional crystallization. The more soluble fraction was identical in properties with the analyzed 2,2',8-triethyl compound (appearance, melting point and mixed melting point, absorption and sensitizing action) (found: I, 24.47). The less soluble fraction was similarly found to be identical with the 2,2'-diethyl-8-methyl dye (found: I, 25.11. $C_{22}H_{23}IN_2S_2$ required I, 25.07). [d] When the specimen was heated from room temperature. [e] Use of methyl orthopropionate gave a yield of only 9% (calculated as 8-ethyl dye). After one recrystallization (about 200 cc. per gram), the dye was identical with the 8-methyl dye. (Found: I, 23.89. 8-Methyl dye requires I, 23.93.) [f] Bromide. [g] After a further recrystallization. [h] Iodide of this dye was prepared by Hamer.[16] [i] Described by Hamer,[16] who gives melting point 274° (dec.). [j] Iodide. [k] After two recrystallizations from 95% EtOH and two from glacial acetic acid. [l] Plus 2.2 g. NEt_3. [m] Plus 0.5 g. NEt_3.

APPEARANCE OF THE DYES

D1 Bright, bronze needles.
D2 Prism reflecting green and purple.
D3 Dark purplish felt.
D4 Dark crystals with purplish reflex.
D5 Minute purplish-bronze crystals.
D6 Dark crystals reflecting blue and purple.
D7 Minute crystals with green reflex.
D8 Beautiful prisms with double blue and green reflex.
D9 Clusters of greenish crystals.
D10 Granular green crystals.
D11 Dark prisms, some faces reflecting purple, others brilliant bronze.
D12 Minute purplish crystals.
D13 Brilliant greenish-bronze prisms.
D14 Purplish needles with blue reflex.
D15 Pale bronze granular crystals.
D16 Brownish needles (transmitted light) with very brilliant blue reflex
D17 Granular greenish-bronze crystals.
D18 Purplish-brown granular crystals with green reflex.
D19 Prisms with double blue and green reflex.
D20 Small reddish - brown needles.
D21 Magnificent emerald-green prisms.
D22 Beautiful greenish - blue prisms.
D23 Felted mat of minute purplish-brown needles.
D24 Reddish-coppery crystals.
D25 Beautiful green prisms.
D26 Bronze needles.
D27 Greenish-bronze crystals.
D28 Dark purplish felted mat.
D29 Dark greenish needles.
D30 Minute emerald - green crystals.
D31 Dark greenish - bronze needles.
D32 Small purplish crystals with blue reflex.
D33 Minute greenish - bronze crystals.
D34 Dull purplish felted crystals.
D35 Minute dull purplish crystals.
D36 Greenish-bronze felt.
D37 Minute lustrous green needles.
D38 Minute greenish crystals.
D39 Minute glittering crystals with greenish-bronze reflex.
D40 Minute greenish - bronze crystals.
D41 Minute greenish crystals.
D42 Bluish-purple felt.
D43 Minute greenish crystals.

D44 Prisms with double blue and brassy-green reflex.
D45 Greenish-bronze needles.
D46 Metallic greenish prisms.
D47 Beautiful garnet - red prisms.
D48 Orange-red powder.
D49 Orange-red prisms.

the reaction mixture was facilitated by the addition of ether, the crude product being treated with hot acetone and the suspension chilled and filtered. This procedure removed tarry impurities. Any unchanged quaternary salt was removed by washing with water and the dye was finally recrystallized from methyl alcohol. This procedure is referred to as Method A. When the quaternary salt was a *p*-toluenesulfonate, one of two procedures was used. In Method B, the hot reaction mixture was treated directly with excess of hot aqueous potassium bromide or iodide, the precipitated dye washed with water, treated with acetone and then recrystallized as in Method A. In Method C, the dye was precipitated from the cooled reaction mixture as the *p*-toluenesulfonate by the addition of ether. The residue was redissolved in the minimum quantity of hot methyl alcohol and converted into the bromide or iodide by treatment with excess of an aqueous solution of the appropriate potassium salt, the further treatment being the same as in Method B.

The dye condensations are summarized in Table IX. The yield of crude product is given in each case, followed by the yield of recrystallized dye. Methyl alcohol was used as a solvent for recrystallization in all cases except one and the amount required is indicated. The melting points were determined as described in Part I.[12]

Summary

1. Thiacarbocyanines containing various groups attached to the central carbon atom of the three-carbon chain have been prepared utilizing the appropriate ortho esters for the purpose. The following are the groups so introduced: Et, *n*-Pr, *n*-Bu, *n*- and *i*-Am, PhCH$_2$-, PhOCH$_2$- and Ph. Selena- and oxacarbocyanines containing certain of these groups have also been prepared.

2. The following ortho esters are described for the first time: methyl orthopropionate, methyl ortho-*n*-butyrate, methyl ortho-*n*-valerate, methyl ortho-*n*-caproate, methyl orthoisocaproate, ethyl orthophenoxyacetate.

3. Substitution of hydrogen in the molecule of a thiacarbocyanine dye derived from 1-methylbenzothiazole by an 8-methyl group causes the absorption maximum in methyl alcohol to shift about 150 Å. toward the blue, but replacement of 8-methyl by 8-ethyl shifts the maximum about 50 Å. back toward the red. Replacement of 8-ethyl by higher aliphatic groupings up to *n*- and isoamyl causes no further shift. Replacement of hydrogen by 8-benzyl causes a shift (75 Å.) toward the blue, but replacement by 8-phenyl causes a slight shift (25 Å.) toward the red.

4. Somewhat similar relationships to those summarized above can be traced in the 3,4,3′,4′- and 5,6,5′,6′-dibenzothiacarbocyanine series and in the selenacarbocyanines. The oxacarbocyanines are exceptional.

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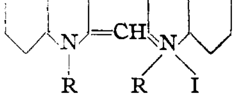
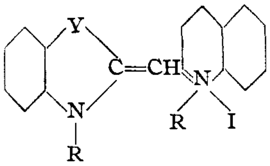
Studies in the Cyanine Dye Series. III. Improvements in the 2′-Cyanine Condensation

BY L. G. S. BROOKER AND G. H. KEYES

Kaufmann and Vonderwahl[1] were the first to observe the formation of a dye of the 2,2′(or ψ)-cyanine class (I) and Fischer and Scheibe[2] succeeded in isolating the 1,1′-dimethyl compound by the action of potassium hydroxide on a mixture of 2-iodoquinoline methiodide and quinaldine methiodide. Higher yields of dyes of this type were obtained by Hamer,[3] who showed further that the reaction was a general one in that the quinaldine alkiodide could be replaced by quaternary salts of other bases containing a reactive methyl group. Alkyl iodides of 1-methylbenzothiazole were found to yield thia-2′-cyanines (II, Y = S) and 2,3,3-trimethylindolenine alkyl iodides yielded indo-2′-cyanines (II, Y = C(Me)$_2$).



I



II

We have now found that if the method of Hamer is employed for the preparation of the hitherto unknown 1′,2-diethyloxa-2′-cyanine iodide (II, Y = O), using 1-methylbenzoxazole ethiodide and 2-iodoquinoline ethiodide, the yield of purified

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(1) Kaufmann and Vonderwahl, *Ber.*, **45**, 1417 (1912).

(2) Fischer and Scheibe, *J. prakt. Chem.*, ii, **100**, 86 (1919).

(3) Hamer, *J. Chem. Soc.*, 206 (1928).