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.

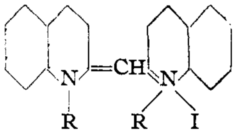
4. Somewhat similar relationships to those summarized above can be traced in the 3,4,3',4'- and 5,6,5',6'-dibenzothiacarbocyanine series and in the selenacarbocyanines. The oxacarbocyanines are exceptional.

ROCHESTER, NEW YORK RECEIVED SEPTEMBER 5, 1935

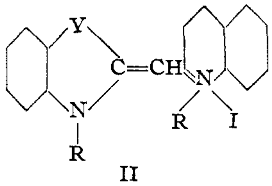
[CONTRIBUTION NO. 563 FROM THE KODAK RESEARCH LABORATORIES]

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

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



I



II

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)$_2$).

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).

product is only 3% and is not improved by substituting sodium ethylate for potassium hydroxide. If, however, the quaternary salts are heated together in dimethylaniline or especially diethylaniline, the yield of dye is enormously increased, being 89% with the latter.[4]

If used for effecting other 2′-cyanine condensations, however, the dialkylanilines are not so satisfactory, but triethylamine has been found to be a good general condensing agent, being markedly superior to potassium hydroxide and giving better yields in every case studied.[5] The following yields of purified dyes are those obtained using triethylamine, the figures in parentheses being the corresponding yields using potassium hydroxide: 1,1′-diethyl-2,2′-cyanine iodide, 87% (72%); 1′,2-diethylthia-2′-cyanine iodide, 88% (72%); 1′,2-diethyloxa-2′-cyanine iodide, 43% (3%); 1′,2-diethylselena-2′-cyanine iodide (II, Y = Se), 72% (55%); 1,1′-diethyl-2,4′-cyanine iodide, 92.5% (73.5%). In the experiments which gave these yields, the crude dyes were recrystallized and the purity of the first crops established by analysis. The mother liquors were then concentrated and second, in some cases third, crops obtained, the purity of which was established by melting point determinations, carried out side by side with specimens of the analyzed materials. In no case did a second or third crop melt lower than four degrees below the corresponding first crop.

The preparation of 1′,2-diethylselena-2′-cyanine iodide has been described by the I. G. Farbenindustrie A.-G.[6] and the preparation of the 2,4′ (or iso)-cyanine using 2-iodoquinoline ethiodide has been described by Hamer.[3]

The absorption of 1′,2-diethyloxa-2′-cyanine iodide has been determined as well as the absorptions of the 1′,2-diethylthia- and 1′,2-diethylselena-2′-cyanine iodides, dyes containing ethyl groups being chosen for comparison here as well as in the rest of this paper for the sake of uniformity, and the three curves are shown in Fig. 1.

It is now well known that replacement of sulfur in a cyanine dye by selenium produces but a slight shift in the position of the absorption maximum,[7,8] and this is further illustrated in the present instance, the maximum for the thia-2′-cyanine being at 4850 Å.,[9] while that for the selena-2′-cyanine is at 4875 Å. In each case there is indication of a less well-defined secondary band nearer the blue. The absorption curve of the oxa-2′-cyanine likewise reveals the presence of two overlapping bands, but in this case it is the band nearer the blue end of the spectrum which is the more pronounced, and this has its maximum at 4350 Å. The positions of the maxima are indicated by the arrows in Fig. 1. It will be noted that the difference between the maximum of the oxa-2′-cyanine and that of the thia-2′-cyanine, amounting to 500 Å., is enormously greater than that between the latter and that of the selena-2′-cyanine.

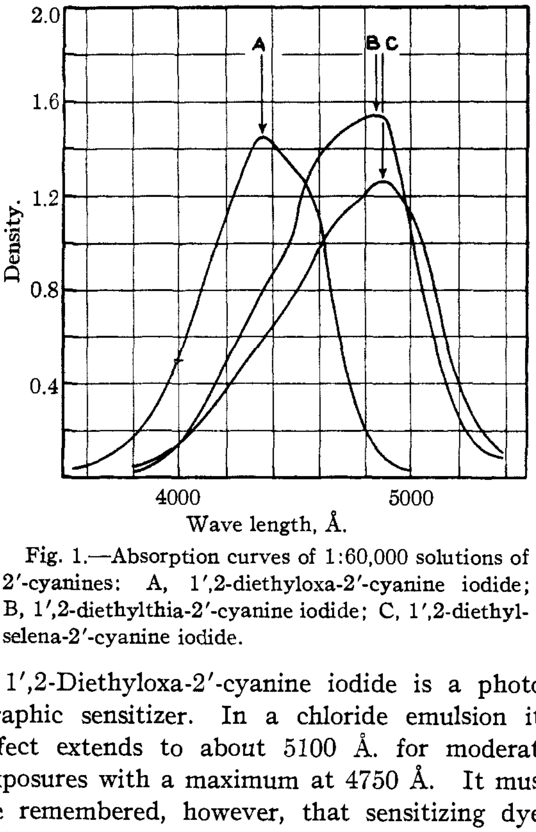

Fig. 1.—Absorption curves of 1:60,000 solutions of 2′-cyanines: A, 1′,2-diethyloxa-2′-cyanine iodide; B, 1′,2-diethylthia-2′-cyanine iodide; C, 1′,2-diethylselena-2′-cyanine iodide.

1′,2-Diethyloxa-2′-cyanine iodide is a photographic sensitizer. In a chloride emulsion its effect extends to about 5100 Å. for moderate exposures with a maximum at 4750 Å. It must be remembered, however, that sensitizing dyes behave very differently with different photographic emulsions, and that general statements as to sensitizing power must be considered in the light of this qualification.

Dyes related to the 2′-cyanines but containing pyridine and β-naphthoquinoline nuclei have been described by Hamer and Kelly,[10] who employed

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[4] Brooker, U. S. Patent 1,969,448.

[5] Kodak Ltd., British Patent 408,571.

[6] I. G. Farbenindustrie A.-G., British Patent 386,791; see also ref. 5.

[7] Fisher and Hamer, *J. Chem. Soc.*, 189 (1933); *ibid.*, 1905 (1934).

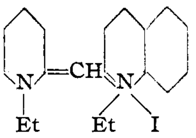
[8] Brooker and White, Part II of this series,

[9] Two absorption curves of 1′,2-diethylthia-2′-cyanine iodide have previously been published [Bloch and Hamer, *Phot. J.*, **68**, 21 (1928); *ibid.*, **70**, 374 (1930)] but differ from one another.

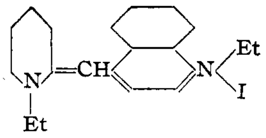
[10] Hamer and Kelly, *J. Chem. Soc.*, 777 (1931).

2-iodopyridine alkyl iodides and 2-iodo-β-naphthoquinoline alkyl iodides, respectively, in their preparation. The general name of 2′-pyridocyanine is now suggested for dyes derived from 2-iodopyridine alkyl iodides.

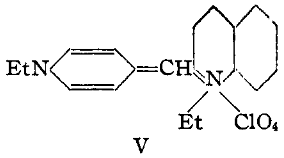
The use of triethylamine results in higher yields of the dye III, for which the name 1,1′-diethyl-2-pyrido-2′-cyanine iodide is proposed. As was pointed out by Hamer and Kelly, this dye is theoretically obtainable by two methods, that which consists in condensing α-picoline ethiodide with 2-iodoquinoline ethiodide being found by them to be fruitless when potassium hydroxide was used. Using triethylamine, however, this method gives a 35% yield of pure dye. The second method, in which 2-iodopyridine ethiodide and quinaldine ethiodide are condensed together, was found by Hamer and Kelly to give a yield of 10% after recrystallization, but optical and photographic tests revealed the presence of impurity. Using triethylamine we have obtained a 41% yield of the pure dye by this method. The specimens obtained by both methods were identical in their appearance, solubility, melting point, absorption and sensitizing effects, thus affording additional evidence of the virtual tautomerism of the cyanine dyes.[3,11]



III



IV



V

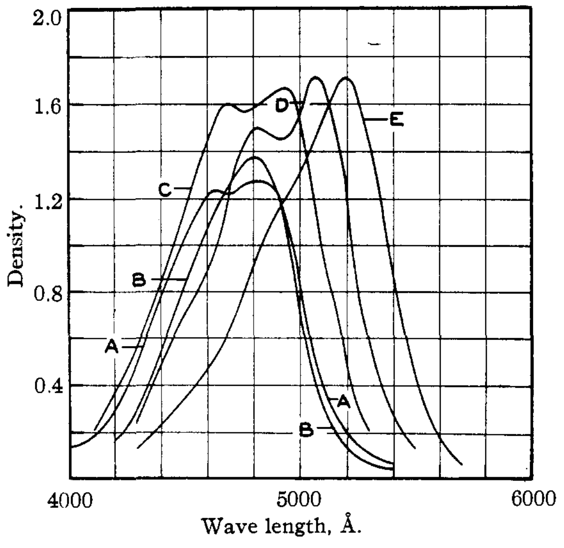
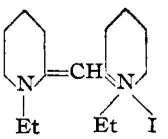


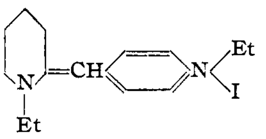
Fig. 2.—Absorption curves: A, 1,1′-diethyl-2,2′-pyridocyanine iodide (1:70,000); B, 1,1′-diethyl-2,4′-pyridocyanine iodide (1:100,000); C, 1,1′-diethyl-2-pyrido-2′-cyanine iodide (1:60,000); D, 1,1′-diethyl-4-pyrido-2′-cyanine perchlorate (1:100,000); E, 1,1′-diethyl-2-pyrido-4′-cyanine iodide (1:75,000).

By condensing 2-iodopyridine ethiodide with lepidine ethiodide, 1,1′-diethyl-2-pyrido-4′-cyanine iodide (IV) was similarly obtained, while an isomeric dye was prepared by condensing γ-picoline etho-*p*-toluenesulfonate with 2-iodoquinoline ethiodide. The dye was, however, easier to purify as the perchlorate (V) and was isolated as such.

Hamer and Kelly were unable to prepare the dye VI by the condensation of α-picoline ethiodide and 2-iodopyridine ethiodide using potassium hydroxide, but it is readily obtainable using triethylamine, it being advantageous to use *n*-propyl alcohol as a solvent here and in a number of the other condensations. This dye, for which the name 1,1′-diethyl-2,2′-pyridocyanine iodide is proposed, may be regarded as the simplest cyanine. The corresponding 1,1′-dimethyl compound was similarly prepared.[12]



VI



VII

Condensation was also effected between 2-iodopyridine ethiodide and γ-picoline etho-*p*-toluenesulfonate giving 1,1′-diethyl-2,4′-pyridocyanine iodide (VII).

The absorption curve of VI (Fig. 2, A) consists of two overlapping bands, that nearer the red with its head at 4825 Å. being only slightly stronger than the second band with its head at 4650 Å. The absorption curve of the corresponding 1,1′-dimethyl compound is very similar in general shape, there being two bands of almost equal strength but situated nearer the blue, the maxima being at 4775 and 4550 Å. The curve of VII differs in shape from that of VI and apparently consists of but a single band with its head at 4800 Å. (Fig. 2, B). It is remarkable that the maximum absorption of VII should be nearer the blue

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[11] Mills and Braunholtz, *J. Chem. Soc.*, **121**, 1489 (1922).

[12] *Cf.* Moir, *ibid.*, **127**, 2338 (1925).

than that of VI, since in the related dyes of the quinoline series the maximum absorption of 1,1′-diethyl-2,4′-cyanine iodide is 350 Å. nearer the red than that of 1,1′-diethyl-2,2′-cyanine iodide.

The absorption curve of III (Fig. 2, C) is very similar in shape to that of VI, there being two overlapping bands of almost equal strength, that nearer the red being the stronger; the maxima are at 4925 and 4700 Å. The absorption curve of V (Fig. 2, D) shows well-marked heads at 4825 and 5075 Å., the latter being the stronger. The maximum of IV (Fig. 2, E) is at 5200 Å., but there is evidence of a less well defined secondary band nearer the blue. Both IV and V may be considered as derived from VII by attachment of a benzene residue to one or the other of the pyridine nuclei of VII. The curves show that the deepening of color brought about by attaching the benzene residue to that pyridine nucleus of VII which is linked through its 4-position, giving IV, is greater than that produced by attaching a benzene residue to the other pyridine nucleus of VII, giving V. All of dyes III to VII show photographic sensitizing action.

Experimental

The condensations are summarized in Table I. In every case a mixture of one mol of each of the quaternary salts, suspended in absolute ethyl or *n*-propyl alcohol, was treated with 2.1 mols (5% excess) of triethylamine and the whole refluxed with constant shaking where ethyl alcohol was used or heated at 100° where *n*-propyl alcohol was used, the time of reaction varying from ten to forty minutes. Dye (D1–9), usually separated during the reaction or on cooling. The yield of crude washed (acetone, water) dye is given in each case followed by the yield after recrystallization, the volume of solvent required for this being indicated. In every case the dye melted with decomposition. The absorptions were measured in methyl alcoholic solutions.

TABLE I

	Dye	Quaternary		NEt_3	Solvent, cc.	Heated, min.	Yield, %	Solvent, cc./g.	M. p., °C., dec.	Formula	Analyses, %	
		Salt	g.								Calcd.	Found
D1	1′,2-DiEt-oxa-2′-cyanine iodide[a]	QS4 QS1	2.9 4.1	2.1	EtOH 20	10	56; 43	MeOH 30	290– 292	$C_{21}H_{21}IN_2O$	I, 28.58	28.45
D2	1′,2-DiEt-selena-2′-cyanine iodide[b]	QS5 QS1	3.5 4.1	2.1	EtOH 25	20	87; 72[c]	MeOH 80	280– 282	$C_{21}H_{21}IN_2Se$	I, 25.01	24.81
D3	1,1′-DiEt-2-pyrido-2′-cyanine iodide[d]	QS9 QS1	2.5 4.1	2.1	*n*-PrOH 20	40	45; 35	H_2O 40	237– 239	$C_{19}H_{21}IN_2$	I, 31.41	31.37
		QS6 QS3	3 3.6	2.1	*n*-PrOH 20	40	74; 41[e]					31.35
D4	1,1′-DiEt-2-pyrido-4′-cyanine iodide[f]	QS7 QS3	3 3.6	2.1	*n*-PrOH 15	40	30; 22	MeOH 9	194– 196	$C_{19}H_{21}IN_2$	I, 31.41	31.64
D5	1,1′-DiEt-4-pyrido-2′-cyanine perchlorate[g]	QS11 QS1	5.8 8.2	4.2	EtOH 13	30	25;[h] 12[e]	H_2O 220	211– 214	$C_{19}H_{21}ClN_2O_4$	C, 60.53 H, 5.62	60.35 5.59
D6	1,1′-DiMe-2,2′-pyridocyanine iodide[i]	QS8 QS2	4.8 7	4.2	*n*-PrOH 20	40	20;[j] 14	H_2O 80	315– 317	$C_{13}H_{15}IN_2$	C, 47.85 H, 4.64 I, 38.93	47.98 4.51 38.93
D7	1,1′-DiEt-2,2′-pyridocyanine iodide[k]	QS9 QS3	5 7.2	4.2	*n*-PrOH 10	40	28; 12[l]	H_2O 12	237– 239	$C_{15}H_{19}IN_2$	I, 35.84	35.88
D8	1,1′-DiMe-2,4′-pyridocyanine iodide[m]	QS10 QS2	6.9 8.7	5.5	*n*-PrOH 10	40	15; 10	H_2O 7	214– 217	$C_{13}H_{15}IN_2$	I, 38.93	38.95
D9	1,1′-DiEt-2,4′-pyridocyanine iodide[n]	QS11 QS3	7.3 9	5.5	*n*-PrOH 10	40	19; 13	H_2O 12	163– 166	$C_{15}H_{19}IN_2$	I, 35.84	35.97

[a] This dye was also obtained when the finely pulverized salts were heated with freshly distilled diethylaniline at 100° with frequent shaking for two and one-half hours; the yield after washing was 89% (71% after purification). With dimethylaniline the corresponding yields were 75% (51%), with quinoline 63% (47%). The dye formed orange-yellow needles. [b] Red needles with a blue reflex; the dye acts as a green sensitizer. [c] Two crops. [d] Reddish-brown crystals with green reflex. [e] After two recrystallizations. [f] Reddish-brown tablets, some faces with a green reflex. [g] Beautiful dark red crystals with a double blue and green reflex. [h] The dye iodide was precipitated from the reaction mixture by adding ether and the residue was dissolved in hot water and precipitated as the perchlorate by adding excess of hot aqueous potassium perchlorate (3 g.). [i] Light orange-brown crystals with pale-green reflex. Moir[12] stated that the compound he obtained corresponding to this dye gave absorption maxima at 4280 and 4050 Å. (in, presumably, aqueous solution). We find that in a 1:80,000 aqueous solution the absorption of our dye is similar to that in methyl alcohol except that the two maxima are less widely separated, the crests in water being at 4600 and 4725 Å., the former being now somewhat the stronger. [j] A colorless solid was removed by washing with water. [k] Crystals similar to D6. [l] After three recrystallizations. [m] Reddish-brown needles with a bluish luster. [n] Dull reddish flakes.

The quaternary salts (QS1 to 11) used in the condensations are numbered as follows.

QS1	2-Iodoquinoline ethiodide	QS6	Quinaldine ethiodide
QS2	2-Iodopyridine methiodide	QS7	Lepidine ethiodide
QS3	2-Iodopyridine ethiodide	QS8	α-Picoline methiodide
QS4	1-Methylbenzoxazole ethiodide	QS9	α-Picoline ethiodide
QS5	1-Methylbenzoselenazole ethiodide	QS10	γ-Picoline metho-*p*-toluenesulfonate
		QS11	γ-Picoline etho-*p*-toluenesulfonate

QS10 was prepared by heating equimolecular proportions of γ-picoline and methyl-*p*-toluenesulfonate at 100° for fifteen minutes. QS11 was similarly prepared from ethyl-*p*-toluenesulfonate, heating at 100° for ninety minutes. Both salts were used without purification.

Summary

1. Triethylamine is superior to potassium hydroxide as a condensing agent for the preparation of 2′-cyanines. Thus, 1′,2-diethyloxa-2′-cyanine iodide is obtainable in a yield of 43% using triethylamine, whereas with potassium hydroxide the yield is only 3%. A selena-2′-cyanine has also been prepared.

2. The use of triethylamine also greatly facilitates the preparation of 1,1′-diethyl-2-pyrido-2′-cyanine iodide; a 2-pyrido-4′-cyanine and a 4-pyrido-2′-cyanine have likewise been prepared by its aid.

3. The failure of potassium hydroxide in the preparation of dyes of the 2,2′-pyridocyanine series has been recorded previously, but using triethylamine these dyes are readily available. Two 2,4′-pyridocyanines have also been prepared.

4. The absorption characteristics of the new dyes are given.

Rochester, New York Received September 5, 1935

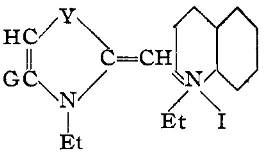
[Communication No. 564 from the Kodak Research Laboratories]

Studies in the Cyanine Dye Series. IV

By L. G. S. Brooker, G. H. Keyes and F. L. White

Up to the present no 2′-cyanine has been described in which the nucleus linked to quinoline consists of a simple 5-membered ring. In a number of instances it has been found that cyanine dyes containing single ring nuclei are difficult to prepare. For example, the thiazolocarbocyanines derived from 2,4-dimethylthiazole were obtained in very much smaller yields than the thiacarbocyanines derived from 1-methylbenzothiazole, and furthermore, whereas the latter base readily gave rise to thiacyanines, the simple thiazolocyanines could not be prepared by the same method.[1]

We have now found, however, that when an equimolecular mixture of 2-methylthiazole ethiodide and 2-iodoquinoline ethiodide is treated with triethylamine, the simplest member of a new group of cyanine dyes, the thiazolo-2′-cyanines, is produced.[2] This dye, 1′,3-diethylthiazolo-2′-cyanine iodide (I, Y = S, G = H) is formed in excellent yield, and 2,4-dimethylthiazole ethiodide and 2-methyl-4-phenylthiazole ethiodide likewise give good yields of the corresponding dyes.



I

These new thiazolo-2′-cyanines give yellowish-orange solutions. The absorption maximum of the 1′,3-diethyl compound is at 4650 Å., and there is a secondary band nearer the red (Fig. 2, B). Introduction of a 4-methyl group shifts the maximum to 4725 Å. (Fig. 1, B) and there is still a secondary band nearer to the red, but in this case it is less pronounced. Replacement of 4-methyl by 4-phenyl produces no further shift, a fact which is worthy of notice, considering that the methyl and phenyl groups have very different effects as 8-substituents in dyes of the thia- and selenacarbocyanine series.[3]

Dyes of the 2′-cyanine series containing the benzoxazole and benzoselenazole nuclei have been described[4] and we have now prepared certain related dyes containing the simple oxazole and selenazole nuclei. 2-Methyloxazole has not itself been prepared, but certain of its substituted derivatives have been known for a long time. Of

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(1) Fisher and Hamer, *J. Chem. Soc.*, 2502 (1930).

(2) Brooker, U. S. Patent 1,969,446.

(3) Brooker and White, This Journal, 57, 2480 (1935).

(4) Brooker and Keyes, *ibid.*, 57, 2488 (1935).