show physiological properties resembling slight oestrogenic activity[13] when tested according to the method of Dodds and co-workers.[14] (Ia) Two g. of 1,3,3-trimethyl-6-hydroxyindane was dropped in small portions into 25 cc. of concentrated nitric acid at room temperature. A very vigorous reaction took place. Upon standing overnight yellow needles separated out which were dried on porous tile and recrystallized from 75% alcohol. (Ib) Prepared by the addition of bromine water to an aqueous solution of 1,3,3-trimethyl-6-hydroxyindane. (Ic) The methyl ether was prepared by refluxing 2 g. of the sodium salt of 1,3,3-trimethyl-6-hydroxyindane and the calculated amount of methyl iodide for six hours in absolute ethyl alcohol. The methyl ether was obtained as an oil and treated with bromine in carbon tetrachloride. The crystals obtained were recrystallized from 75% alcohol.

Summary

Recent investigation as to the formation of indene and hydrindene (indane) compounds have been extended to include the formation of such compounds by the condensation of β-hydroxy ketones and α- and β-glycols with phenols.

NEW YORK, N. Y. RECEIVED JANUARY 3, 1936

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[13] Wm. F. Hart, Ph.D. Thesis, New York University, April 1, 1936.

[14] Allan, Dickens and Dodds, *J. Physiol.*, **68**, 348 (1930).

[CONTRIBUTION NO. 579 FROM THE KODAK RESEARCH LABORATORIES]

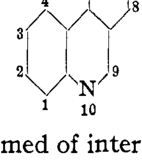
Studies in the Cyanine Dye Series. V. Dyes Derived from 9-Methylphenanthridine

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

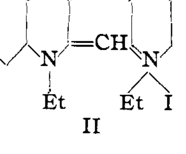
Many cyanines derived from quinoline are good photographic sensitizers, but it was found by one of us that certain cyanine dyes containing the isoquinoline nucleus, such as that obtained by condensing isoquinoline ethiodide with quinaldine ethiodide, were weak in their sensitizing action, and this observation has found confirmation and extension in the independent work of Fisher and Hamer,[1] who have devised a much improved method for the synthesis of isoquinoline dyes of this type.

In view of the fact that phenanthridine (I) may be considered as a derivative of quinoline and also of isoquinoline it seemed of interest to investigate the properties of cyanine dyes derived from this base.

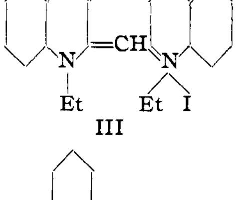
I



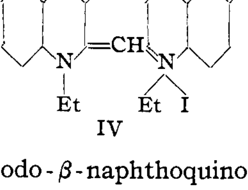
For the synthesis of these dyes 9-methylphenanthridine proved to be a convenient starting point. This base was originally prepared by Pictet and Hubert[2] and their method has been improved by Morgan and Walls.[3] The ethiodide of the base, which has not been described hitherto, was prepared by heating the base with ethyl *p*-toluenesulfonate, followed by conversion of the quaternary *p*-toluenesulfonate into the iodide. When treated with 2-iodoquinoline ethiodide in the presence of triethylamine,[4] the ethiodide readily yielded 1,1′-diethyl-3,4-benzo-2,2′-cyanine iodide (III), whilst condensation of the etho-*p*-toluenesulfonate with 2-iodopyridine ethiodide and with 2-iodo-β-naphthoquinoline ethiodide furnished 1,1′-diethyl-3′,4′-benzo-2-pyrido-2′-cyanine iodide (II) and 1,1′-diethyl-3,4,5′,6′-dibenzo-2,2′-cyanine iodide (IV), respectively. (For the sake of uniformity the phenanthridine nucleus in each formula is shown as containing the ternary nitrogen atom.)



II



III



IV

If the dyes II, III and IV are compared with the simpler dyes 1,1′-diethyl-2-pyrido-2′-cyanine iodide (V),[4,5] 1,1′-diethyl-2,2′-cyanine iodide

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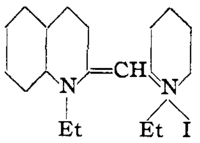
[1] Fisher and Hamer, *J. Chem. Soc.*, 1905 (1934).

[2] Pictet and Hubert, *Ber.*, **29**, 1182 (1896).

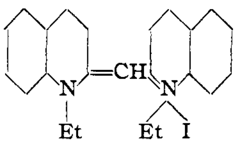
[3] Morgan and Walls, *J. Chem. Soc.*, 2447 (1931).

[4] Brooker and Keyes, THIS JOURNAL, **57**, 2488 (1935).

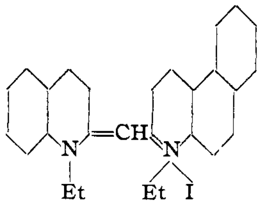
[5] Hamer and Kelly, *J. Chem. Soc.*, 777 (1931).



V



VI



VII

(VI)[4,6] and 1,1′-diethyl-5,6-benzo-2,2′-cyanine iodide (VII),[6] respectively, from which they may be considered to be derived by the attachment of an additional benzene residue, the effect of introducing the latter can be observed in the three cases.

The absorption curves of the six dyes are shown in Fig. 1.

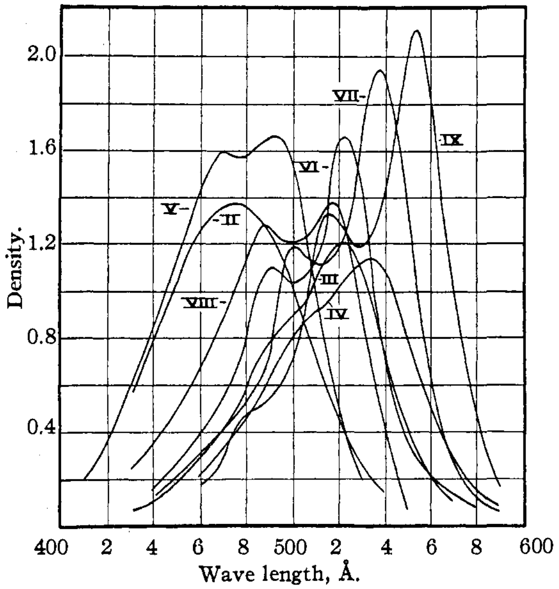
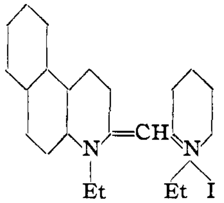


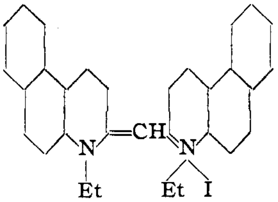
Fig. 1.—Adsorption curves of: 1,1′-diethyl-3′,4′-benzo-2-pyrido-2′-cyanine iodide (II), 1 : 40,000; 1,1′-diethyl-3,4-benzo-2,2′-cyanine iodide (III), 1 : 75,000; 1,1′-diethyl-3,4,5′,6′-dibenzo-2,2′-cyanine iodide (IV), 1 : 75,000; 1,1′-diethyl-2-pyrido-2′-cyanine iodide (V), 1 : 60,000; 1,1′-diethyl-2, 2′-cyanine iodide (VI), 1 : 100,000; 1,1′-diethyl-5,6-benzo-2,2′-cyanine iodide (VII), 1:75,000.

The absorption curves of V, VI and VII all show well marked secondary maxima in addition to the principal maxima, whereas, of the absorption curves of the dyes containing a phenanthridine nucleus, that of II shows no secondary maximum, although those of III and IV have weak secondary bands. The curves show that weighting V with a benzene residue so as to give II does not bring about a shift of the maximum in the direction of longer wave length, but a shift of 175 Å. in the opposite direction (from 4925 to 4750 Å.). However, attachment of a benzene residue to VI, giving III, does not bring about a shift in either direction (both maxima are at 5225 Å.), but attachment of a benzene residue to VII, giving IV, causes a slight shift toward the blue of 50 Å. (from 5375 to 5325 Å.). In no case, therefore, does weighting one of the simpler dyes V, VI and VII by attachment of a benzene residue so as to produce a phenanthridine nucleus, bring about a shift of the absorption maximum in the direction of longer wave length.

It is of interest to compare these results with those produced when the quinoline nuclei of V, VI and VII are weighted with benzene residues so as to give β-naphthoquinoline nuclei. Dye VII may be considered to be derived from VI by such a change, and in this case the weighting is accompanied by a shift in the position of the maximum of 150 Å. toward the red.



VIII



IX

By condensing α-picoline ethiodide with 2-iodo-β-naphthoquinoline ethiodide in the presence of N-methylpiperidine, 1,1′-diethyl-5′,6′-benzo-2-pyrido-2′-cyanine iodide (VIII) was readily obtained, but the alternative method which utilizes 2-iodopyridine ethiodide and β-naphthoquinaldine ethiodide gave a lower yield and the product was difficult to purify. This dye is the β-naphthoquinoline derivative corresponding to V, and weighting in this case brings about a shift in the absorption maximum of 250 Å. toward the red (from 4925 to 5175 Å.). Like V, VIII has a pronounced secondary maximum, the figures being 4700 and 4875 Å. for the two dyes, respectively.

Finally, the 1,1′-diethyl-5,6,5′,6′-dibenzo-2,2′-cyanine iodide (IX)[5] has its maximum absorption at 5525 Å., which is 150 Å. nearer the red than that of the corresponding quinoline derivative

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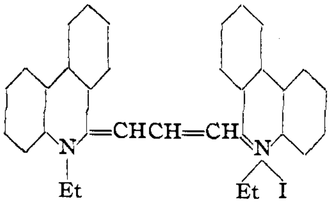
(6) Hamer, *J. Chem. Soc.*, 206 (1928).

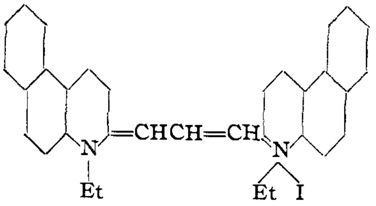
VII. In all three cases, therefore, replacement of a quinoline ring by a β-naphthoquinoline ring is accompanied by a shift in the position of maximum absorption toward the red, whereas replacement of the quinoline ring by a phenanthridine ring in the three cases mentioned either produces no shift at all or else a shift toward the blue.

There is thus a striking contrast between these β-naphthoquinoline and phenanthridine dyes. Furthermore, the latter showed no signs of photographic sensitizing action whatever, even when given twenty times the normal amount of exposure in a wedge spectrograph, but, on the other hand, dyes V, VI, VII and IX are sensitizers,[4,5,6] as is also VIII. This produces its maximum effect at about 5350 Å.

By treating 9-methylphenanthridine etho-p-toluenesulfonate with ethyl orthoformate in the presence of pyridine,[7] followed by conversion of the resulting dye to the iodide, there was obtained 1,1′-diethyl-3,4,3′,4′-dibenzo-2,2′-carbocyanine iodide (X).



X



XI

The absorption curve of this dye (Fig. 2, A) has its maximum at 6125 Å. which is 75 Å. nearer to the red than the absorption maximum of 1,1′-diethyl-2,2′-carbocyanine iodide (pinacyanol) (Fig. 2, B), whereas the absorption maximum of the isomeric 1,1′-diethyl-5,6,5′,6′-dibenzo-2,2′-carbocyanine iodide (XI)[8] is at 6350 Å. (Fig. 2, C), *i. e.*, 300 Å. nearer to the red than that of pinacyanol. Whereas XI, also, is a photographic sensitizer,[8] X showed no sensitizing action at all.

The absorption curves were all determined for methyl alcoholic solutions.

Experimental

The dyes described in this section were all recrystallized from methyl alcohol. In every case the yield of crude product is given and is followed in most instances by the yield of purified material in brackets, together with the amount of solvent required.

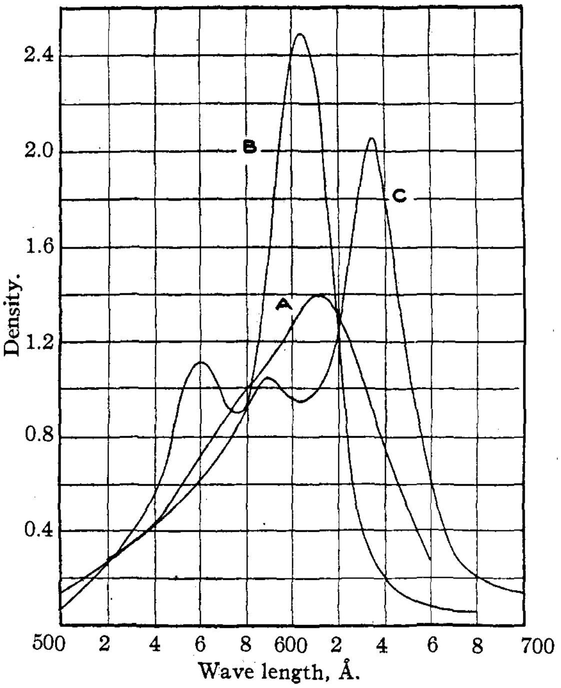


Fig. 2.—Absorption curves of: A = 1,1′-diethyl-3,4,3′,4′-dibenzo-2,2′-carbocyanine iodide (X), 1:100,000; B = 1,1′-diethyl-2,2′-carbocyanine iodide, 1:150,000; C = 1,1′-diethyl-5,6,5′,6′-dibenzo-2,2′-carbocyanine iodide (XI), 1:100,000.

9-Methylphenanthridine Ethiodide.—The base (3 g., 1 mol) and ethyl p-toluenesulfonate (3.2 g., 1 mol) were heated at 100° for three days. The viscous product was dissolved in hot methyl alcohol (20 cc.) and treated with a hot solution of potassium iodide (3.6 g., 1.5 mols) in water (5 cc.). The solid which separated was washed and dried; yield 4.8 g. (89%). After several recrystallizations from methyl alcohol (12 cc. per g.) the greenish yellow powder had m. p. 237–239° (dec.).

Anal. Calcd. for $C_{16}H_{18}IN$: I, 36.37. Found: I, 36.23.

1,1′ - Diethyl - 3′,4′ - benzo - 2 - pyrido - 2′ - cyanine iodide (II).—9-Methylphenanthridine (0.95 g., 1 mol) and ethyl p-toluenesulfonate (1 g., 1 mol) were condensed together as above and the product dissolved in n-propyl alcohol[4] (13 cc.) and heated at 100° for forty minutes with 2-iodopyridine ethiodide (1.8 g., 1 mol) and triethylamine (1.1 g., 2.1 mols). The dye was precipitated by the addition of ether. The tarry residue became crystalline on stirring with a little acetone and was filtered off and washed with a little water; yield 27% (16%, 8 cc. per g.). The dye formed brownish aggregates with a green reflex and had m. p. 221–224° (dec.).

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(7) Hamer, *J. Chem. Soc.*, 2796 (1927).

(8) Mees and Gutekunst, *J. Ind. Eng. Chem.*, **14**, 1060 (1922).

Anal. Calcd. for $C_{23}H_{23}IN_2$: I, 27.95. Found: I, 27.60.

1,1′-Diethyl-3,4-benzo-2,2′-cyanine Iodide (III).—9-Methylphenanthridine ethiodide (1 g., 1 mol) was condensed with 2-iodoquinoline ethiodide (1.1 g., 1 mol) by refluxing with triethylamine (0.6 g., 2.1 mols) and ethyl alcohol (13 cc.) for twenty minutes; yield 46% (32%, 100 cc. per g.). After a further recrystallization (yield 23%) the dye formed garnet prisms with a greenish reflex and had m. p. 259–262° (dec.).

Anal. Calcd. for $C_{27}H_{25}IN_2$: I, 25.18. Found: I, 25.15.

1,1′-Diethyl-3,4,5′,6′-dibenzo-2,2′-cyanine Iodide (IV).—Crude 9-methylphenanthridine etho-*p*-toluenesulfonate (1.95 g., 1 mol) was condensed with 2-iodo-β-naphthoquinoline ethiodide (2.3 g., 1 mol) using triethylamine (1.05 g., 2.1 mols); yield 50% (22% after two recrystallizations; 100 cc. per g.). The minute greenish-bronze crystals had m. p. 250–251° (dec.).

Anal. Calcd. for $C_{31}H_{27}IN_2$: I, 22.91. Found: I, 22.93.

1,1′-Diethyl-5,6-benzo-2,2′-cyanine iodide (VII).—A higher yield of this dye than that previously recorded[6] was obtained as follows: β-naphthoquinaldine (0.97 g., 1 mol) was condensed with ethyl *p*-toluenesulfonate (1 g., 1 mol) by heating at 120–125° for six days. The solution of the product in ethyl alcohol (7 cc.) was boiled for twenty minutes with 2-iodoquinoline ethiodide (2.05 g., 1 mol) and triethylamine (1.05 g., 2.1 mols); yield 78% (63%, 200 cc. per g.).

1,1′-Diethyl-5′,6′-benzo-2-pyrido-2′-cyanine Iodide (VIII).—α-Picoline ethiodide (5 g., 2 mols, *i. e.*, 100% excess), 2-iodo-β-naphthoquinoline ethiodide (4.6 g., 1 mol), N-methylpiperidine (3 g., 3 mols) and *n*-propyl alcohol (20 cc.) were heated at 100° for one and one-half hours; yield 51%. The dye was dissolved in hot methyl alcohol (200 cc.) and refluxed for one-half hour with one-twentieth of its weight of Norite. The crystals which separated from the filtrate were again recrystallized (yield 33%) and formed beautiful reddish-brown tablets with green reflex and had m. p. 268–270° (dec.).

Anal. Calcd. for $C_{23}H_{23}IN_2$: I, 27.95. Found: I, 27.90.

1,1′-Diethyl-5,6,5′,6′-dibenzo-2,2′-cyanine iodide[6] **(IX)** was obtained in a yield of 78% (51%; 1230 cc. per g.) using triethylamine to effect the condensation.

1,1′-Diethyl-3,4,3′,4′-dibenzo-2,2′-carbocyanine iodide (X) was prepared by refluxing crude 9-methylphenanthridine etho-*p*-toluenesulfonate (3.9 g.; 2 mols) with ethyl orthoformate (3.3 cc., 4 mols) and pyridine (20 cc.) for one and one-half hours. The dye was isolated as the iodide; yield 34% after recrystallization. After a further recrystallization (230 cc. per g.) the dark greenish crystals had m. p. 234–235° (dec.).

Anal. Calcd. for $C_{33}H_{29}IN_2$: I, 21.88. Found: I, 21.85.

Summary

1. Four cyanine dyes containing the phenanthridine nucleus have been prepared.

2. In every case the absorption maximum of a dye containing a phenanthridine nucleus lies nearer the blue than that of the isomeric dye which contains a β-naphthoquinoline nucleus in place of phenanthridine.

3. In all four cases the new dyes show no signs of photographic sensitizing action.

Rochester, New York Received February 10, 1936

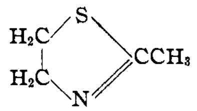
[Contribution No. 580 from the Kodak Research Laboratories]

Studies in the Cyanine Dye Series. VI. Dyes Derived from 2-Methylthiazoline

By L. G. S. Brooker

Up to the present only derivatives of completely unsaturated heterocyclic bases, such as those of the pyridine, quinoline, thiazole and benzothiazole series, have been used for the preparation of cyanine dyes. It was therefore of interest to examine the reactivity of the methyl group in quaternary salts of 2-methylthiazoline (I), since the nucleus of this base is partly saturated.

I



That this methyl group was indeed very reactive was demonstrated by the fact that the quaternary salts underwent the commoner cyanine dye condensations.[1,2] Thus, 2-methylthiazoline ethiodide when treated with 2-iodoquinoline ethiodide in the presence of triethylamine gave 1′,3-diethylthiazolino-2′-cyanine iodide (III) in excellent yield, and similar treatment with 2-iodopyridine ethiodide and with 2-iodo-β-naphthoquinoline ethiodide gave 1′,3-diethylthiazolino-2′-pyridocyanine iodide (II) and 1′,3-diethyl-5′,6′-benzo-thiazolino-2′-cyanine iodide (IV), respectively.

Alcoholic solutions of these dyes range in color from pale yellow (II) to orange-yellow (IV). The

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[1] Brooker, U. S. Patent 1,950,876; British Patent 385,320.

[2] *Cf.* Fisher and Hamer, *J. Chem. Soc.*, 189 (1933).