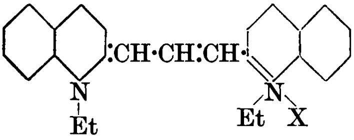
# CCCLXXIV.—*A General Method for the Preparation of Carbocyanine Dyes.*

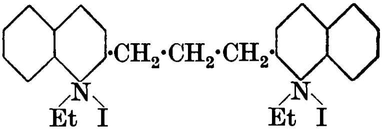
By Frances Mary Hamer.

Since 1920, when the term "carbocyanine" was first applied to pinacyanol and similar dyes (Mills and Pope, *Phot. J.*, 1920, **44**, 253), other types of compounds have been discovered which, from their structure and properties, should be included under the same name. Before describing the present general method of preparing carbocyanines, it seems desirable to summarise these various types and the methods which have hitherto been employed in making them.

The most important carbocyanine dye is 1 : 1′-diethyl-2 : 2′-carbocyanine halide (I), which, under the trade name of pinacyanol, is a well-known photographic sensitiser. Hitherto the best way of preparing it has consisted in adding formaldehyde and then alkali to a boiling alcoholic solution of a quinaldinium salt in the presence of a quinolinium salt, but the yield of pure dye is at most only 21% of that theoretically possible. The part played by formaldehyde may be taken by a trihalogenomethane (D.R.-P., 200,207/1908), or the methenyl residue may be provided by di-*o*-formylethylaminodiphenyl disulphide, reacting with quinaldine ethonitrate in pyridine solution (Mills and Braunholtz, J., 1923, **123**, 2804). König obtained pinacyanol by the condensation of quinaldine ethiodide with ethyl orthoformate in the presence of acetic anhydride (*Ber.*, 1922, **55**, 3293), but his claim to a 50% yield could not be confirmed (Hamer, J., 1925, **127**, 211). Finally, the dye has been derived from methylenediquinaldine diethiodide (II) by the action of alkali in the presence of a quinolinium salt (Hamer, J., 1923, **123**, 246).

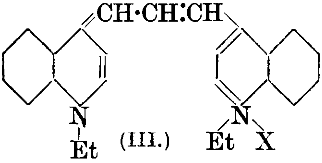


(I.)



(II.)

The establishment of the constitution of pinacyanol (Mills and Hamer, J., 1920, **117**, 1550) led to the prediction of two similar groups of carbocyanines, possessing respectively a 4 : 4′- and a 2 : 4′-linking (III and IV) in place of the original 2 : 2′-linking. Mills and Braunholtz (*loc. cit.*) prepared a dye of the first type (III) from lepidine ethonitrate by the action of the disulphide and pyridine, and showed the corresponding iodide, obtainable in 15% yield, to be identical with "kryptocyanine," which had previously been prepared, in 9% yield, by treating an alcoholic solution of lepidine ethiodide with alkali and formaldehyde or chloroform (Adams and Haller, *J. Amer. Chem. Soc.*, 1920, **42**, 2661). Mills



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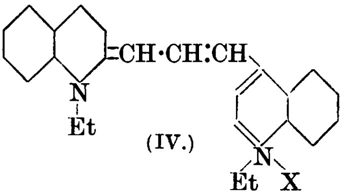
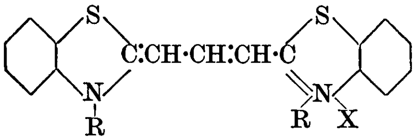


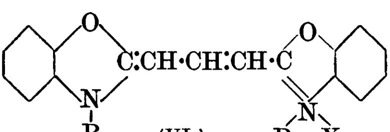
(IV.)

and Odams similarly synthesised the 2 : 4′-isomeride (IV) by the action of the disulphide on the ethonitrates of quinaldine and lepidine, and proved "dicyanine" to be a dye of this kind (J., 1924, **125**, 1913).

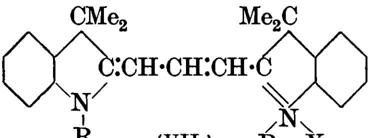
Besides these three closely related classes of carbocyanines, analogous dyes are obtained when the quinoline nuclei are replaced by other basic nuclei. Mills has shown that the dyes formed by the action of ammonia on the quaternary salts of 1-methylbenzthiazole and benzthiazole (Hofmann, *Ber.*, 1887, **20**, 2262) result in better yield (19%) when the salts are heated in pyridine solution, and has proved that they have formula (V) (J., 1922, **121**, 455). Substances of the same class were prepared by König and Meier, by condensation of 1-methylbenzthiazole methohalide with ethyl orthoformate, or anhydrous sodium formate, in nitrobenzene solution; they mention that the reaction proceeds equally well in acetic anhydride or pyridine solution (*J. pr. Chem.*, 1925, **109**, 324). Repetition of the preparation of the methobromide in nitrobenzene solution, or of the methiodide in acetic anhydride solution, has been found to give unsatisfactory results. By heating 1-methylbenzoxazole methiodide with ethyl orthoformate in the presence of nitrobenzene or acetic anhydride, König and Meier prepared a dye of a new type (VI) (*loc. cit.*), whilst König prepared another class of carbocyanine (VII) by treatment of a 2 : 3 : 3-trimethylindoleninium salt with ethyl orthoformate and acetic anhydride (*Ber.*, 1924, **55**, 3293).

(V.)





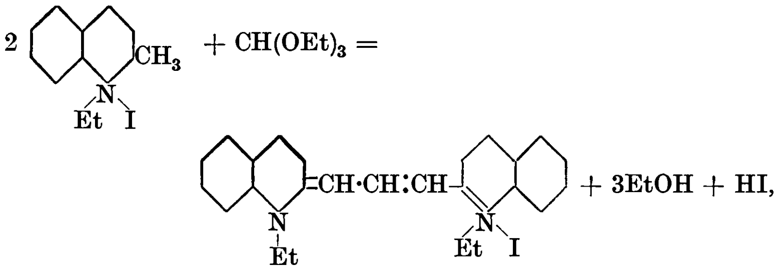
(VI.)



(VII.)

As regards the nomenclature of these last three groups of carbocyanine dyes, the term *thiocarbocyanine* is preferred to the name carbothiocyanine (Mills, *loc. cit.*), as being more consistent with the terms thio*iso*cyanine (Braunholtz and Mills, J., 1922, **121**, 2004), thio*pseudo*cyanine (Mills and Braunholtz, *loc. cit.*), and pyridocarbocyanine (*ibid.*). It is proposed that the dyes (VI) and (VII), derived from benzoxazole and indolenine, be named *oxacarbocyanines* and *indocarbocyanines* respectively.

Now the equation representing the reaction of quinaldine ethiodide with ethyl orthoformate suggests that the pinacyanol condensation would be favoured by the use of a basic solvent. Boiling pyridine proved in fact to serve excellently, and to its use is attributable the whole success of the present method. The only precaution necessary is that of drying the solvent, whilst about four times the calculated quantity of ester should be taken. Three 2 : 2′-carbocyanines have been prepared by the pyridine method, the yields of pure product varying from 70 to 79%, and the method was subsequently applied to the preparation of carbocyanines of the other five classes. With the 2 : 4′-carbocyanines, the yield of crude material is higher and the labour involved is less than in any other published method of preparing dicyanines; their separation, by fractional crystallisation, from the 2 : 2′- and 4 : 4′-isomerides was not, however, carried out. The success of the method is especially striking in the case of the 4 : 4′-carbocyanines, the yields being 36 to 43% of the theoretical. In the preparation of 1 : 1′-diethyl-4 : 4′-carbocyanine iodide, there is formed in addition about half its amount of another dye, which may readily be isolated by virtue of its slight solubility. Its properties show it to be identical with " neocyanine," which has been described as a by-product in the preparation of kryptocyanine by the formaldehyde method, and which is a powerful sensitiser for the deep red and infra-red (Dundon, Schoen, and Briggs, *J. Opt. Soc. Amer.*, 1926, **12**, 397). The pyridine method is at its best in the case of the thiocarbocyanines, giving between 79 and 83% yields of pure dyes; with the oxacarbocyanines the yields are about 40% and with the indocarbocyanines about 70% of those theoretically obtainable.



It is concluded that the introduction of pyridine as solvent converts the synthesis of carbocyanines, by condensation of ethyl orthoformate with quaternary salts containing reactive methyl groups, into an excellent practical and general method of preparation; this is not only the simplest method to apply, but gives, in any and every instance, the best yield obtainable. The following carbocyanines are now described for the first time: 6 : 6′-*dimethyl-1 : 1′-diallyl-2 : 2′-carbocyanine iodide* and *bromide*, 1 : 1′-*dimethyl-4 : 4′-carbocyanine iodide*, 1 : 1′-*diallyl-4 : 4′-carbocyanine iodide*, 2 : 2′-*diallylthiocarbocyanine bromide*, 2 : 2′-*diethyloxacarbocyanine iodide*, and 3 : 3 : 3′ : 3′-*tetramethyl-1 : 1′-diethylindocarbocyanine iodide*.

Mr. O. F. Bloch has examined the absorption spectra of all the dyes in alcoholic solution and tested their sensitising action, both by bathing plates in a solution and by adding the dye to the emulsion before coating. He has found that the indocarbocyanines and oxacarbocyanines are, like other cyanine dyes, photographic sensitisers, and it seems remarkable that their photographic properties have not previously been recorded. In the experimental section of this paper the photographic action is described only in those instances where this has not previously been done.

So far no carbocyanine containing two pyridine nuclei has been isolated, though Mills and Braunholtz (*loc. cit.*) attributed to a 2 : 2′-carbocyanine of this type absorption bands which they detected in the pyridine reaction mixture of 2-methylpyridine ethonitrate and di-*o*-formylethylaminodiphenyl disulphide. It is now found that a 2 : 2′-pyridocarbocyanine is not formed by condensation of 2-methylpyridine ethiodide with ethyl orthoformate in the presence of boiling pyridine, a negative result which is curious in view of the readiness with which 2-methylpyridine quaternary salts condense with *p*-nitrosodimethylaniline (Kaufmann and Vallette, *Ber.*, 1912, **45**, 1736) and with *p*-dimethylaminobenzaldehyde (Mills and Pope, J., 1922, **121**, 946).

## EXPERIMENTAL.

1 : 1′-*Diethyl-2 : 2′-carbocyanine Iodide*.—Quinaldine ethiodide (5 g.; 2 mols.), ethyl orthoformate (5·5 c.c.; 4 mols.), and pyridine (20 c.c.), which had been dried by being left over barium oxide and subsequent decantation, were boiled under reflux for 3 hours; crystals then separated (yield 78%). After recrystallisation from dilute spirit, the yield was 70%. The dye was dried under reduced pressure at 100—120° and an iodine determination was made by the method of Carius; these methods of drying and analysis were used in all cases, except where otherwise stated (Found: I, 26·2. Calc. for $C_{25}H_{25}N_2I$: I, 26·4%).

6 : 6′-*Dimethyl-1 : 1′-diallyl-2 : 2′-carbocyanine Iodide*.—By heating 2 : 6-dimethylquinoline (5 g.; 1 mol.) and allyl iodide (3·4 c.c.; 1·2 mols.) in a sealed tube at 100° for 48 hours, extracting the product with ether, and recrystallising the residue from spirit, a 72% yield of 2 : 6-*dimethylquinoline alliodide* was obtained, in yellow crystals,

m. p. 198—199° (decomp.) (Found : I, 39·2. $C_{14}H_{16}NI$ requires I, 39·05%). The condensation of the alliodide (5 g.) with ethyl orthoformate was carried out as in the previous preparation and the product was washed with ether (yield 82%) and recrystallised from methyl alcohol (yield, 71%). It melts with decomposition at 280—281° (Found : I, 23·5. $C_{29}H_{29}N_2I$ requires I, 23·85%). In spirit solution there are absorption maxima at λ 5700 Å. and λ 6200, of which the latter is the stronger. When the dye is added to the emulsion the sensitising maxima lie at λ 5800 and λ 6450 and there is considerable fog. The fog is less when the plate is bathed in a solution of the dye, and the sensitising action is considerably greater, the principal band now extending from λ 6200 to λ 7300.

6 : *6′-Dimethyl-*1 : *1′-diallyl-*2 : *2′-carbocyanine Bromide.*—A 76% yield of 2 : *6-dimethylquinoline allobromide* is obtained by heating 2 : 6-dimethylquinoline (7 g.; 1 mol.) and allyl bromide (6·2 c.c.; 1·2 mols.) in a sealed tube at 100° for 48 hours and recrystallising the product from absolute alcohol. It is a colourless solid, m. p. 214—215° (decomp.) (Found : Br, 28·9. $C_{14}H_{16}NBr$ requires Br, 28·7%). Its condensation with ethyl orthoformate in the presence of pyridine gave an 84% yield of carbocyanine (14·6 g.) and on recrystallisation from methyl alcohol a 79% yield of pure dye. This forms green and gold crystals, m. p. 281—282° (decomp.) (Found : Br, 16·5. $C_{29}H_{29}N_2Br$ requires Br, 16·5%).

1 : *1′-Dimethyl-*4 : *4′-carbocyanine Iodide.*—This compound is mentioned in the literature (Adams and Haller, *loc. cit.*), but none of its properties has been recorded. After condensation of lepidine methiodide (1 g.) with ethyl orthoformate in the presence of pyridine, the reaction mixture was poured into water; a 71% yield of crude product then resulted. From methyl alcohol it separated in minute, bright green crystals (yield 38%), m. p. 290—295° (decomp.) (Found : I, 28·0. $C_{23}H_{21}N_2I$ requires I, 28·1%). The dye shows an absorption maximum at λ 7150. The sensitising action towards plates on bathing is poor and is accompanied by veil; the single sensitising band has its maximum at λ 7500. When the dye is added to the emulsion, the sensitising action is less but the fog greater.

1 : *1′-Diethyl-*4 : *4′-carbocyanine Iodide* (*Kryptocyanine*).—After the condensation of lepidine ethiodide with ethyl orthoformate in the usual way, the reaction mixture was cooled and filtered (0·89 g. removed); on addition of water to the filtrate, the kryptocyanine was precipitated (2·23 g., *i.e.*, 56% of the theoretical yield). The kryptocyanine was recrystallised from spirit (150 c.c.); the yield (1·67 g.) was then 42% (Found : I, 26·4. Calc. for $C_{25}H_{25}N_2I$ : I, 26·4%). The less soluble neocyanine iodide also was recrystallised

from spirit (1000 c.c.; 0·72 g. obtained). When heated, it melts with decomposition at 286°.

1 : 1′-*Diallyl*-4 : 4′-*carbocyanine Iodide*.—Lepidine (3·9 c.c.; 1 mol.) and allyl iodide (3·2 c.c.; 1·2 mols.) were heated in a sealed tube at 100° for 2 days. The *lepidine alliodide* was recrystallised twice from dry spirit, charcoal being used once (Found: I, 40·8. $C_{13}H_{14}NI$ requires I, 40·8%). The condensation product from lepidine alliodide (1 g.) and ethyl orthoformate was precipitated as a tar on the addition of ether to the pyridine reaction liquid. Rapid crystallisation from a little methyl alcohol gave a 43% yield of green crystals, but the carbocyanine was unstable and decomposed on prolonged boiling with the solvent. When heated, decomposition began at about 150° (Found: I, 25·6. $C_{27}H_{25}N_2I$ requires I, 25·2%). The maximum absorption in spirit solution is at λ 7150. On a bathed plate, the dye confers a strong sensitisation band with its maximum at λ 7550. The band occupies the same position when the dye is added to the emulsion, but is in this case much weaker.

2 : 2′-*Dimethylthiocarbocyanine Iodide*.—Repetition of the preparation using ethyl orthoformate and acetic anhydride gave only 17% and 9% yields of crude and recrystallised dye respectively. By the new method, 1-methylbenzthiazole methiodide (4 g.; 2 mols.), pyridine (40 c.c.), and ethyl orthoformate (4·6 c.c.; 4 mols.) were boiled for an hour. The thiocarbocyanine (yield, 95%) was recrystallised from dilute spirit and obtained in 74% yield. Melting with decomposition occurs at about 280°; König and Meier (*loc. cit.*) give m. p. 254° (Found: I, 27·1. Calc. for $C_{19}H_{17}N_2IS_2$: I, 27·3%).

2 : 2′-*Diethylthiocarbocyanine Iodide*.—This dye was similarly prepared from 1-methylbenzthiazole ethiodide (2 g.), and recrystallised from methyl alcohol (yield, 82%); m. p. 264—265° (decomp.); Mills (*loc. cit.*) gives m. p. 269° (decomp.) (Found: I, 25·6. Calc. for $C_{21}H_{21}N_2IS_2$: I, 25·8%).

2 : 2′-*Diallylthiocarbocyanine Bromide*.—By heating 1-methylbenzthiazole (6·3 g.; 1 mol.) with allyl bromide (3·5 c.c.; 1·2 mols.) in a sealed tube at 100° for 48 hours and recrystallising the product from spirit, 1-*methylbenzthiazole allobromide* was obtained in almost colourless crystals (yield, 68%), m. p. 202° (decomp.) (Found: Br, 29·8. $C_{11}H_{12}NBrS$ requires Br, 29·6%). The crude dye (yield, 95%), obtained on condensation of 1-methylbenzthiazole allobromide (2 g.) with ethyl orthoformate, was recrystallised from methyl alcohol; the pure thiocarbocyanine (yield, 79%) forms purple crystals, m. p. about 260° (decomp.) (Found: Br, 17·0. $C_{23}H_{21}N_2BrS_2$ requires Br, 17·0%). In spirit solution, the stronger absorption band has its maximum at λ 5600 and the weaker at λ 5220. As used in the emulsion, the dye is a powerful sensitiser;

there is a strong band with its maximum at λ 6000 and a weaker one with a maximum at λ 5450. It acts as an excellent sensitiser when plates are bathed in its solution, the sensitisation being almost uniform up to λ 6200 and decreasing to zero at λ 6800; there is a slight gap at λ 4900.

2 : 2′ - *Dimethyloxacarbocyanine Iodide.* — 1 - Methylbenzoxazole could not be obtained by interaction of *o*-aminophenol and ethyl acetate (Niementowski, *Ber.*, 1897, **30**, 3062), but was prepared by Ladenburg's method (*Ber.*, 1876, **9**, 1524). The methiodide, after being washed with dry ether as described by Clark (J., 1926, 232), was rapidly recrystallised from absolute alcohol; the colourless crystals obtained were washed with ether and dried in a vacuum desiccator before analysis (Found: I, 46·1. Calc. for $C_9H_{10}ONI$: I, 46·15%). M. p. 196° (decomp.) as recorded by Clark; König and Meier (*loc. cit.*) give m. p. 200°. 1-Methylbenzoxazole methiodide (2 g.; 2 mols.), ethyl orthoformate (3·0 c.c.; 4 mols.), and pyridine (20 c.c.) were boiled for an hour. The dye (yield, 57%) was recrystallised from absolute alcohol (yield, 40%). The yield is about half as great when acetic anhydride is used as solvent in the condensation. The oxacarbocyanine has m. p. 275—277° (decomp.); König and Meier give m. p. 259° (Found: I, 29·2. Calc. for $C_{19}H_{17}O_2N_2I$: I, 29·4%). The absorption maxima in spirit solution lie at λ 4850 and λ 4600, of which the former is the stronger. When added to the emulsion, the dye confers a region of extra sensitivity with a maximum at λ 5100. Both in this case and with the bathed plate the sensitisation curve is very uniform, reaching to λ 5700 for moderate exposures.

2 : 2′-*Diethyloxacarbocyanine Iodide.*—1-*Methylbenzoxazole ethiodide* was prepared by heating 1-methylbenzoxazole (5·5 g.; 1 mol.) and ethyl iodide (4·0 c.c.; 1·2 mols.) in a sealed tube at 100° for 48 hours. After extraction with dry ether, the crude product was rapidly recrystallised from absolute alcohol, washed with ether, and dried for analysis in a vacuum desiccator (yield, 74%); the colourless crystals thus obtained had m. p. 195—197° (decomp.) (Found: I, 43·7. $C_{10}H_{12}ONI$ requires I, 43·9%). Condensation of the ethiodide (8 g.) with ethyl orthoformate gave 2 : 2′-*diethyloxacarbocyanine iodide* (yield, 57%), which crystallised from pyridine, in 38% yield, in red crystals with a blue reflex; m. p. 277—279° (decomp.) (Found: I, 27·5. $C_{21}H_{21}O_2N_2I$ requires I, 27·6%). The absorption maxima in spirit solution are at λ 4600 and λ 4850, of which the latter is the stronger. For bathing plates the dye acts as a powerful sensitiser, extending the normal sensitivity by a band which shows a maximum at λ 5150. Its action is weaker when it is added to the emulsion.

1 : 3 : 3 : 1′ : 3′ : 3′-*Hexamethylindocarbocyanine Iodide*.—In this instance the yield obtained by using acetic anhydride as solvent is equal to that which results when pyridine is employed. 2 : 3 : 3-Trimethylindolenine methiodide (2 g.; 2 mols.), pyridine (20 c.c.), and ethyl orthoformate (3·0 c.c.; 4 mols.) were boiled for an hour and the reaction mixture was poured into water. The crude product (yield, 78%) gave on recrystallisation from dilute or dry spirit, acidified with hydrogen iodide, a 66% yield of beautifully crystalline dye, but the iodine content was invariably low (*e.g.*, a specimen which had been dried in a vacuum desiccator gave C, 60·6; H, 6·5; I, 24·0. Calc. for $C_{25}H_{29}N_2I$ : C, 61·95; H, 6·0; I, 26·2%. $C_{25}H_{29}N_2I,C_2H_5{\cdot}OH$ requires C, 61·1; H, 6·65; I, 23·9%). The indocarbocyanine has m. p. about 228° (decomp.); König (*loc. cit.*) gives m. p. 229° (decomp.). The absorption maxima lie at λ 5120 and λ 5480. When added to the emulsion, the dye gives very clean plates and shows fair sensitising action; the maxima lie at λ 5320 and λ 5720. When plates are bathed in a solution of the dye, the sensitisation is very powerful, and maxima occur at λ 5300 and λ 5800.

3 : 3 : 3′ : 3′-*Tetramethyl*-1 : 1′-*diethylindocarbocyanine Iodide*.—Trimethylindolenine ethiodide has been previously prepared by the action of methyl iodide on 2-methyl-1-ethylindole (König and Müller, *Ber.*, 1924, **57**, 144), but in the present work it was obtained by heating 2 : 3 : 3-trimethylindolenine (8·2 g.; 1 mol.) and ethyl iodide (5 c.c.; 1·2 mols.) in a sealed tube at 100° for 48 hours. After recrystallisation from rectified spirit, the ethiodide (yield, 61%) had m. p. 224° (decomp.) (Found: I, 40·2. Calc. for $C_{13}H_{18}NI$ : I, 40·3%). The crude carbocyanine (yield, 86%), obtained by condensation with ethyl orthoformate, was recrystallised from dilute spirit acidified with hydrogen iodide, and was obtained in 75% yield. It forms pleochroic crystals, which are olive-green and steel-blue. If rapidly heated, it softens at 204—210°, or, if slowly heated, melts and resolidifies; it melts at 260—263° (decomp.) (Found: I, 24·8. $C_{27}H_{33}N_2I$ requires I, 24·8%). In spirit solution, the chief absorption maximum occurs at λ 5480 and there is a weaker band with its maximum at λ 5120. When added to the emulsion, the dye shows moderate sensitising action and has three maxima, at λ 5350, 5750 and 6000, respectively. In sensitising by bathing, it shows two maxima, at λ 5320 and λ 5700, and its action is more powerful.

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