

137. *Preparation of Symmetrical and Unsymmetrical Neocyanines :
Structure of the Neocyanines.*

By J. D. KENDALL and J. R. MAJER.

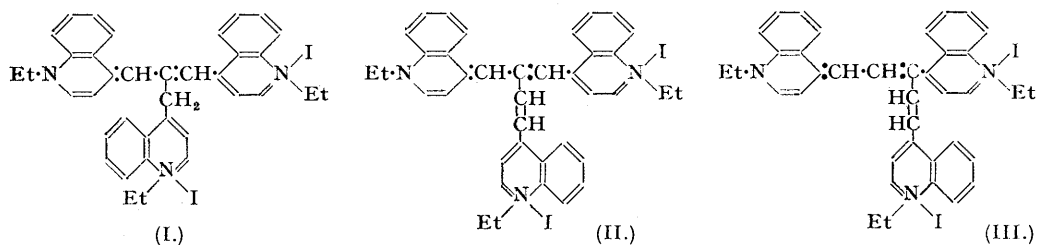
Carbocyanine dyes have been condensed with heterocyclic quaternary salts containing reactive methyl groups and esters of trithio-orthoformic acid in acetic anhydride solution to yield trinuclear dyes of the neocyanine type. By this method, unsymmetrical neocyanines containing two and three different heterocyclic rings have been prepared. The experimental evidence obtained supports the formula for neocyanines originally suggested by König.

THREE different formulæ have been proposed for the neocyanines. Hamer (*J.*, 1928, 1472) assigned to the neocyanine obtained from lepidine ethiodide the formula (I).

Later, Brooker, Hamer, and Mees replaced this by formula (II) in which the three heterocyclic nuclei were connected by a conjugated chain passing through the *meso*-carbon atom of the trimethin chain (*J. Opt. Soc. Amer.*, 1933, 23, 216).

König (*Z. wiss. Phot.*, 1935, 34, 15), without giving any reasons, suggested a third formula (III) in which the heterocyclic nuclei are connected by a conjugated chain passing through one of the terminal carbon atoms of the trimethin chain. The dye in this case may be regarded as a

substituted carbocyanine or a dicarbocyanine in which the following formula represents one of the extremes of the resonance hybrids.



This formula received immediate support from Kendall (*Proc. Ninth Int. Congress of Phot., Paris, 1935, 248*), mainly from considerations of the photographic properties of the neocyanines, and from Hamer (*Chem. and Ind., 1935, 13, 640*) as a "formula, according to which a reasonable picture of the mechanism of formation of the dye is obvious".

Theoretical considerations of the chemistry of the neocyanines likewise favour the König formula. If as is possible, the dinuclear carbocyanine is intermediate in the formation of the trinuclear neocyanine, a dye of structure (II) must arise by a reaction involving the hydrogen atom on the *meso*-carbon atom of the trimethin chain. In the quinoline series, however, only hydrogen atoms linked to carbon atoms directly attached to the carbon in the α -position, or the vinylogous γ -position, to the nitrogen atom are readily reactive. The position of the *meso*-methin group of the trimethin chain corresponds vinylogously to that of a β -methyl group, and the hydrogen atoms of β -methylquinolines are notably unreactive. The terminal methin groups on the other hand correspond to the methyl groups of lepidine and therefore possess hydrogen atoms known to be reactive. Any reaction on a hydrogen atom of a carbocyanine dye may therefore be expected to involve one of the terminal methin groups rather than the *meso*-methin. Experimental evidence detailed below supports both the formation of the neocyanine type of dye *via* the carbocyanine, and the König formula opposed to formula (II).

Since the reactants required for the synthesis of both the carbocyanine and a neocyanine are a quaternary salt containing a reactive methyl group and a formic acid derivative such as ethyl orthoformate, iodoform, or ethyl trithio-orthoformate, it would appear that, provided the carbocyanine is intermediate in the formation of the neocyanine, the latter should be obtainable from the former by further condensation with the original reactants under appropriate conditions. Consideration of the analytical figures shows that the molecule of a neocyanine contains two acid radicals, whilst a molecule of a carbocyanine contains only one. In the conversion of a carbocyanine into a neocyanine it would therefore appear preferable that the additional heterocyclic nucleus should be in the form of a quaternary salt. Conditions which favour the formation of an *N*-alkylmethylene base would be expected to be unfavourable to neocyanine formation. This explains the superiority of Kimura's method in which acetic anhydride is used as a solvent rather than pyridine, since the presence of a basic solvent would tend to favour conversion of the quaternary salt into the methylene base. It explains likewise why Hamer found that improved yields of neocyanine, as compared with those of kryptocyanine, are obtained by reducing the quantities of pyridine employed for solvent purposes.

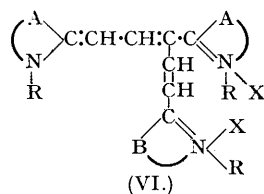
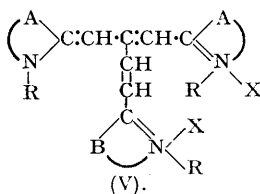
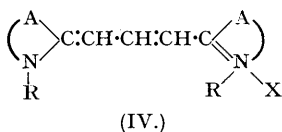
On the basis of these assumptions an attempt was first made to prepare the neocyanines by interaction of the quaternary salts of α - ω -ethylthiovinyl heterocyclic bases with carbocyanines in acetic anhydride, but the reactions failed to give the required dyes. This appeared inexplicable unless the formation of the neocyanine proceeded *via* a primary condensation product of the trithio-orthoformate and the carbocyanine. A solution of 3:3-diethylthiacarbocyanine iodide in acetic anhydride was therefore refluxed with ethyl trithio-orthoformate and 2-methylbenzthiazole methiodide; the colour deepened gradually from magenta to blue, whilst a green dye separated from solution. Analysis and the properties of this dye showed it to be the anticipated neocyanine. A neocyanine dye was obtained similarly by using *p*-toluquinaldine methiodide instead of 2-methylbenzthiazole methiodide. Reactions with 2:3:3-trimethylindolenine methiodide and 2:3:3:6-tetramethylindolenine methiodide were also attempted, but these were found to be much less reactive than the thiazole quaternary salts and the resulting neocyanines were more soluble and difficult to isolate.

The ability to give neocyanines did not appear to be limited to the quaternary iodides of the carbocyanines, and 3:3'-diethylthiacarbocyanine *p*-toluenesulphonate was condensed with

ethyl trithio-orthoformate and both 2-methylbenzthiazole etho-*p*-toluenesulphonate and 2-methylbenzelenazole metho-*p*-toluenesulphonate, the resulting dyes being converted into the di-iodides with potassium iodide solution. 1 : 3 : 3 : 1' : 3' : 3'-Hexamethylindocarbocyanine iodide was very unreactive and only appeared to condense to a slight extent with very insoluble quaternary salts, but 3 : 3'-diethylselenacarbocyanine iodide appeared to be as reactive as its sulphur analogue. 3 : 3'-Diethyloxacarbocyanine iodide readily gave the symmetrical neocyanine on being heated with 2-methylbenzoxazole ethiodide and ethyl trithio-orthoformate in acetic anhydride.

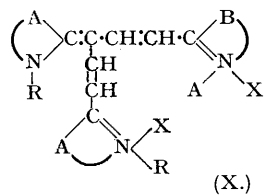
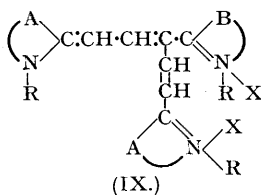
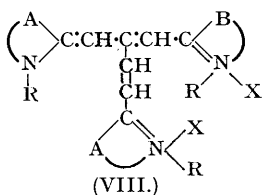
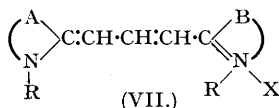
The neocyanines derived from a symmetrical carbocyanine and the quaternary salts of a different ring system contain two dissimilar nuclei. By the use of unsymmetrical carbocyanines, however, neocyanines which contained two or three different nuclei could be prepared. Attempts at formulation of these neocyanines indicated that a study of a simple series of unsymmetrical dyes might serve to demonstrate the correctness or otherwise of the König formula. If, for example, a symmetrical carbocyanine (IV) is converted into a neocyanine with a quaternary salt $\begin{matrix} \text{B} \\ \diagup \\ \text{C} \\ \diagdown \\ \text{N} \\ | \\ \text{R} \quad \text{X} \end{matrix}$ (A and B being the remainder of dissimilar heterocyclic nuclei) the resulting

neocyanine may be formulated as either (V) or (VI) (resonance extremes), depending whether reaction occurs at the *meso* or terminal methin group.



If instead of the symmetrical carbocyanine, the unsymmetrical carbocyanine (VII) is converted into a neocyanine with the quaternary salt $\begin{matrix} \text{A} \\ \diagup \\ \text{C} \\ \diagdown \\ \text{N} \\ | \\ \text{R} \quad \text{X} \end{matrix}$ the resulting dye may be

represented as either (VIII), (IX), or (X) (resonance extremes) :

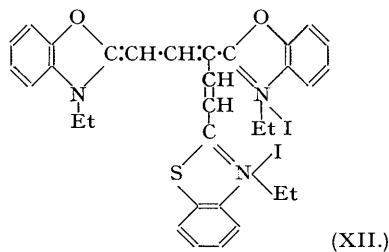
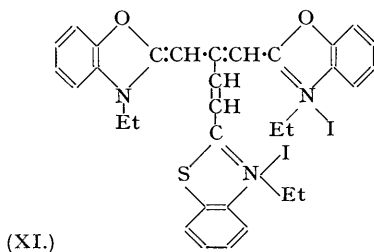


Isomers on König formulation.

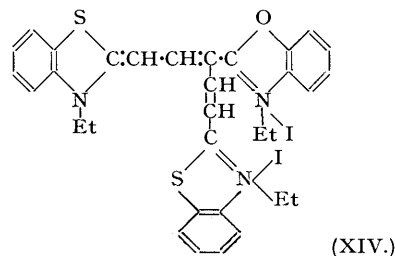
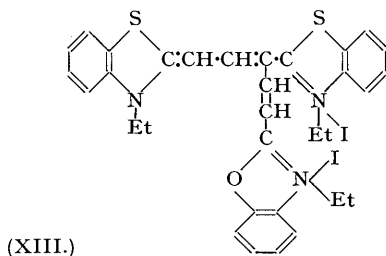
From these it is obvious that under no conditions can the neocyanines obtained be identical on the basis of formulæ (V) and (VIII), whilst formula (VI) is identical with (X) (two extremes of the resonance hybrid). In the event, therefore, of the dyes prepared by the two different methods being identical, the formula representing a neocyanine as a carbocyanine substituted in the *meso*-methin group must be incorrect.

When 3 : 3'-diethyloxathiacarbocyanine iodide was heated in acetic anhydride with 2-methylbenzoxazole ethiodide and ethyl trithio-orthoformate, only one product was obtained which was identical in all respects with the neocyanine produced from 3 : 3'-diethyloxacarbocyanine iodide and 2-methylbenzthiazole ethiodide. It follows, therefore, that the formula of the

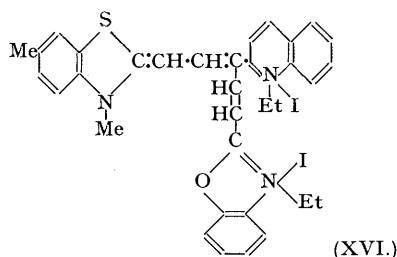
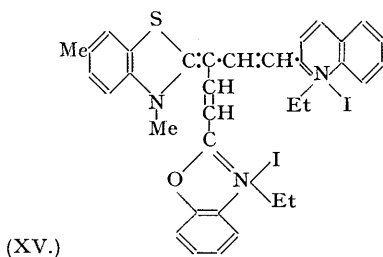
compound produced cannot be (XI) but may be a hybrid of which (XII) represents one of the resonance extremes.



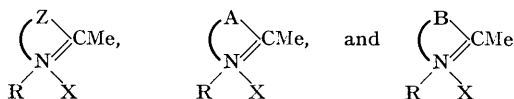
The condensation of 3:3'-diethylxathiacarbocyanine iodide and 2-methylbenzthiazole ethioidide also gave only one neocyanine, but this was different from that obtained from 3:3'-diethylthiacarbocyanine iodide and 2-methylbenzoxazole ethioidide. It is suggested, therefore, that whilst the structure of the latter may be represented as (XIII) that of the former is (XIV).



3:6-Dimethyl-1'-ethyl-2:2'-thiaquinocarbocyanine iodide on conversion into the neocyanine with 2-methylbenzoxazole ethioidide likewise gave only one product which may be represented as either (XV) or (XVI). The predominant formation of only one neocyanine from an unsymmetrical carbocyanine is remarkable. It is explicable, however, if the electronic displacements in the unsymmetrical molecule under conditions of reaction are such as to induce a high reactivity on only one of the terminal methin groups. If this is correct the type of neocyanine formed is always determined by the carbocyanine employed and not by the quaternary salt with the reactive methyl group.



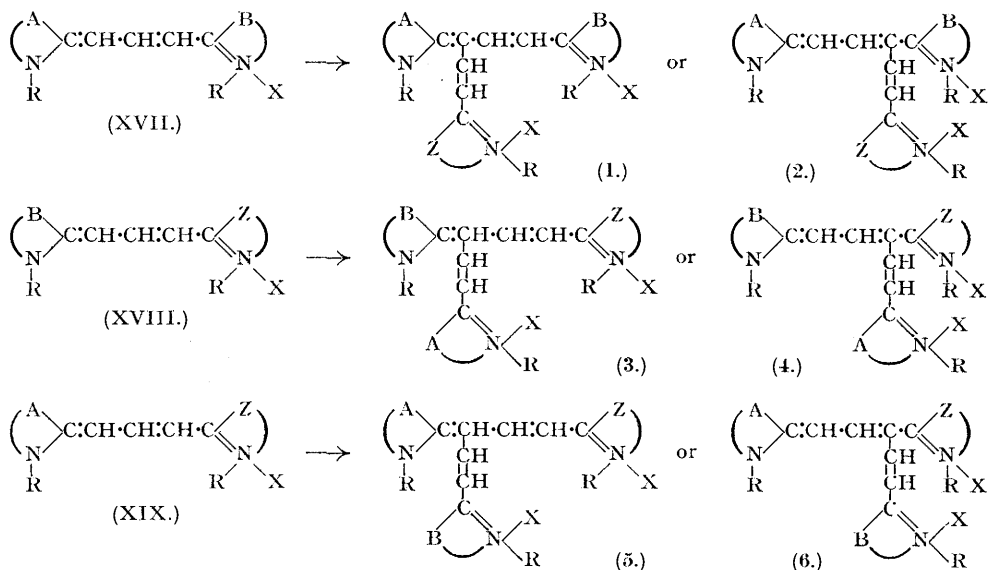
The precise formulation of a neocyanine with three different heterocyclic nuclei may be possible, however, by a simple permutation of the nuclei in the reactants. If three different unsymmetrical carbocyanines (XVII), (XVIII), and (XIX) are converted into neocyanines



containing three dissimilar heterocyclic nuclei by condensation with quaternary salts of the three heterocyclic bases respectively (where Z, A, and B represent the remainder of heterocyclic

694 *Preparation of Symmetrical and Unsymmetrical Neocyanines.*

rings), the resulting dyes should have structures corresponding to the following formulæ (1) or (2), (3) or (4), and (5) or (6).



In these formulæ, however, the pairs (1) and (5), (2) and (3), and (4) and (6) are identical. If, therefore, the product from the first of these reactions is identical with that from the second, the neocyanine must be of the type of formula (2). Similarly, if the product from the reaction is identical with that from the third reaction its formula would be (1). Again, if the products of the second and third reactions are identical the formula would be (4). Only in the event of all three reaction products being different would it not be possible to decide the structure by this method. It is hoped later to communicate the results of investigations on a series of unsymmetrical neocyanines prepared according to this scheme.

Attempts to convert other cyanine dyes, for example, monomethin cyanines, pinaflavols, and tricarboyanines, into trinuclear dyes appeared to be unsuccessful. There were indications, however, that dicarboyanines might be converted to trinuclear dyes by the method used for the preparation of neocyanines from carbocyanines.

EXPERIMENTAL.

[*Bis*-2-(3-ethylbenzthiazole)][γ -2'-(3-ethylbenzthiazole)]*pentamethincyanine Di-iodide*.^{*}—A mixture of 2-methylbenzthiazole (0.4 g.) and ethyl *p*-toluenesulphonate (0.55 g.) was heated at 140–150° for 4 hours, and the product dissolved in acetic anhydride (50 c.c.) containing ethyl trithio-orthoformate (0.5 g.) and 3 : 3'-diethylthiacarbocyanine *p*-toluenesulphonate (1.45 g.). The mixture was heated under reflux for 1 hour and the deep blue solution poured, with stirring, into hot aqueous potassium iodide. A green dye was precipitated, collected, and crystallised from methanol to yield bronze green crystals (0.6 g.), m. p. 241° (decomp.) (Found : S, 12.01. Calc. for C₃₂H₃₁N₃S₃: S, 11.9%). Kimura (*loc. cit.*) gives the decomposition point of this neocyanine as 260–261°, but repeated crystallisation failed to raise the decomposition point of the dye obtained above.

[*Bis*-2-(3-ethylbenzoxazole)][γ -2'-(3-ethylbenzoxazole)]*pentamethincyanine Di-iodide*.—3 : 3'-Diethyl-oxacarbocyanine iodide (0.88 g.) and 2-methylbenzoxazole ethiodide (0.64 g.) were dissolved by heating in acetic anhydride (30 c.c.) containing ethyl trithio-orthoformate (0.4 c.c.), and the mixture boiled under reflux for 30 minutes. The solution, which was originally orange, became deep red, and on cooling small green crystals separated. The dye was collected and crystallised from methanol to yield minute green crystals with a golden reflex (0.48 g.), m. p. 233° (decomp.). Kimura (*loc. cit.*) gives m. p. 225° (decomp.) (Found : I, 33.7. Calc. for C₃₂H₃₁O₃N₃I₂: I, 33.46%).

[2-(3-Ethylbenzthiazole)][2'-(3-methylbenzthiazole)][γ -2'-(3-ethylbenzthiazole)]*pentamethincyanin Di-iodide*.—3 : 3'-Diethylthiacarbocyanine iodide (2 g.) and 2-methylbenzthiazole methiodide (1.2 g.) were dissolved in acetic anhydride (100 c.c.) containing ethyl trithio-orthoformate (0.8 g.) and refluxed for 1 hour. The solution gradually changed colour from magenta to deep blue, and a green powder separated. This was collected and crystallised from methanol to yield the dye as vivid green crystals (2.3 g.), m. p. 220° (decomp.) (Found : I, 31.75. C₃₁H₂₉N₃I₂S₃ requires I, 32.0%).

^{*} Hamer, Rathbone, and Winton (*J.*, 1947, 1434) named the neocyanines as derivatives of trimethincyanine. The present authors prefer to consider them as substituted pentamethincyanines.

[2-(3-Ethylbenzthiazole)][2'-(1:6-dimethylquinoline)][γ -2''-3-ethylbenzthiazole]pentamethincyanine Di-iodide.—3:3'-Diethylthiacarbocyanine iodide (2.5 g.) and *p*-toluquinaldine methiodide (1.5 g.) were dissolved in acetic anhydride (100 c.c.) containing ethyl trithio-orthoformate (0.8 g.) and the solution refluxed for 2 hours; it had then become deep blue. The green powder which separated was collected and extracted with 5×10 c.c. portions of methanol. The dye crystallising from the methanol was collected and the process repeated. The fractions were finally bulked and recrystallised to yield dark green crystals with a bronze lustre (2.5 g.), m. p. 221° (Found: I, 31.7. $C_{34}H_{33}N_3I_2S_2$ requires I, 31.6%).

[2-(3-Ethylbenzselenazole)][2'-(1-ethylquinoline)][γ -2''-(3-ethylbenzselenazole)]pentamethincyanine Di-iodide.—3:3'-Diethylselenacarbocyanine iodide (1.5 g.) and quinaldine ethiodide (1 g.) were dissolved in acetic anhydride (50 c.c.) containing ethyl trithio-orthoformate (0.6 g.) and refluxed for 2 hours. The dye which separated from the blue solution on cooling was collected and crystallised from methanol to yield metallic green needles (0.5 g.), m. p. 218° (Found: N, 4.9; I, 28.2. $C_{33}H_{33}N_3I_2Se_2$ requires N, 5.2; I, 28.4%).

[2-(3-Ethylbenzthiazole)][2'-(3-methylbenzselenazole)][γ -2''-(3-ethylbenzthiazole)]pentamethincyanine Di-iodide.—2-Methylbenzselenazole (1.0 g.) and methyl *p*-toluenesulphonate (0.93 g.) were heated at 120° for 3 hours. The product was dissolved in acetic anhydride (100 c.c.) containing ethyl trithio-orthoformate (0.8 g.) and 3:3'-diethylthiacarbocyanine *p*-toluenesulphonate (2.6 g.). The solution was refluxed for 2 hours, poured into boiling aqueous potassium iodide solution, and the green dye precipitated was crystallised from ethanol to give green needles (2 g.), m. p. 225° (Found: I, 30.05. $C_{31}H_{23}N_3I_2S_2Se$ requires I, 30.2%).

[2-(3-Ethylbenzthiazole)][2'-(3-ethylbenzoxazole)][γ -2''-(3-ethylbenzthiazole)]pentamethincyanine Di-iodide.—3:3'-Diethylthiacarbocyanine iodide (2.5 g.) and 2-methylbenzoxazole ethiodide (1.5 g.) were dissolved by boiling in acetic anhydride (100 c.c.) containing ethyl trithio-orthoformate (0.8 g.). The solution was refluxed for 2 hours; the magenta colour had then changed to a deep purple, and a green solid had separated; this was crystallised from methanol to yield the dye as grass-green needles (2 g.), m. p. 222° (Found: I, 32.3. $C_{32}H_{31}ON_3I_2S_2$ requires I, 32.1%).

[Bis-2-(3-ethylbenzthiazole)][γ -2''-(3-ethylbenzoxazole)]pentamethincyanine Di-iodide.—3:3'-Diethyl-oxathiacarbocyanine iodide (2.4 g.) and 2-methylbenzthiazole ethiodide (1.5 g.) were dissolved in acetic anhydride (50 c.c.) containing ethyl trithio-orthoformate (0.8 c.c.) and the solution was refluxed for 2 hours; it had then become deep purple and had deposited a green dye. This was crystallised from methanol to yield brownish-green needles (1.4 g.), m. p. 235° (Found: I, 32.05. $C_{32}H_{31}ON_3I_2S_2$ requires I, 32.1%).

[2-(3-Ethylbenzoxazole)][2'-(3-ethylbenzthiazole)][γ -2''-(3-ethylbenzoxazole)]pentamethincyanine Di-iodide.—3:3'-Diethyl-oxathiacarbocyanine iodide (2.4 g.) and 2-methylbenzoxazole ethiodide (1.45 g.) were dissolved in acetic anhydride (15 c.c.) containing ethyl trithio-orthoformate (0.8 g.), and the solution refluxed for 30 minutes. Ethanol (15 c.c.) was added and then ether until a faint cloudiness appeared. The dye, which crystallised on cooling, was recrystallised from methanol to yield dark green octahedra (2 g.), m. p. 190° (decomp.) (Found: I, 32.7. $C_{32}H_{31}O_2N_3I_2S$ requires I, 32.75%). The dye was obtained similarly from 3:3'-diethyl-oxacarbocyanine iodide (2.5 g.) and 2-methylbenzthiazole ethiodide (1.5 g.) as dark green octahedra, m. p. 190° (decomp.) (Found: I, 32.8%). Both samples gave identical optical sensitizing in silver iodobromide emulsions, extending the normal sensitivity to ca. 6800 Å. with a shallow maximum at ca. 6400 Å. The absorption curves of both samples in ethanol were likewise identical, with sharp maxima at 6100 Å.

[2-(3-Ethylbenzoxazole)][2'-(6-methyl-1-ethylquinoline)][γ -2''-(3-methylbenzthiazole)]pentamethincyanine Di-iodide (or Isomer).—This was prepared likewise from 3:6'-dimethyl-1'-ethylthiaquinocarbocyanine iodide (1.5 g.), 2-methylbenzoxazole methiodide (0.7 g.), and ethyl trithio-orthoformate (0.4 g.). It was obtained as brown needles, m. p. 237° (decomp.) (Found: I, 33.0. $C_{33}H_{31}ON_3I_2S$ requires I, 32.9%).

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