CXCIV.—*Neocyanine.*

By Frances Mary Hamer.

Almost all the important photographic sensitisers belong to the cyanine group of dyes and no fewer than sixteen types of cyanines have been described, for fifteen of which the constitution is known : ψ-cyanine, *iso*cyanine, cyanine, 2 : 2′-carbocyanine (pinacyanol), 2 : 4′-carbocyanine (dicyanine), 4 : 4′-carbocyanine (kryptocyanine), thiocyanine, thiocarbocyanine, thio-ψ-cyanine, thio*iso*cyanine, oxacarbocyanine, indocarbocyanine, indo-ψ-cyanine, xanthoapocyanine, and erythroapocyanine (compare Bloch and Hamer, *Phot. J.*, 1928, **68**, 21). Neocyanine is the sixteenth.

Neocyanine is the name given to a dye which Dundon, Schoen, and Briggs isolated as a less soluble by-product in the preparation of kryptocyanine (*J. Opt. Soc. Amer.*, 1926, **12**, 397). They describe in detail its optical and photographic properties, which are particularly interesting, and state that it sensitises more powerfully beyond 8000 Å. than any dye previously reported; since the publication of their paper, it has been recorded that a substance called " prozyanol," of which neither the origin nor the constitution is mentioned, possesses a sensitising maximum still further in the infra-red (Blunck, *Astr. Nachr.*, 1928, **231**, 338). Since Dundon, Schoen, and Briggs have given no details for the preparation of neocyanine, and since no suggestion has been made as to its constitution, it seems desirable to publish what further information is elsewhere available.

1 : 1′-Diethyl-4 : 4′-carbocyanine iodide, or " kryptocyanine," was originally prepared in 9% yield by treatment of an alcoholic solution of lepidine ethiodide with alkali and formaldehyde or chloroform (Adams and Haller, *J. Amer. Chem. Soc.*, 1920, **42**, 2661), and it was presumably according to this method that neocyanine was originally obtained. The constitution of kryptocyanine was

established by Mills and Braunholtz, who synthesised it from lepidine ethonitrate by the action of di-*o*-formylethylaminodiphenyl disulphide, and obtained a 15% yield of pure iodide (J., 1923, **123**, 2804). A general method for the preparation of carbocyanine dyes, by the action of ethyl orthoformate in the presence of pyridine on quaternary salts containing reactive methyl groups, has recently been described; it was applied to the preparation of three 4 : 4′-carbocyanines and, as the yields varied from 36 to 43% of those theoretically possible, its success was regarded as especially striking in this case (Hamer, J., 1927, 2796). It is recorded that in addition to a 42% yield of recrystallised 1 : 1′-diethyl-4 : 4′-carbocyanine iodide, there was also obtained about half its weight of neocyanine, which was identified by its optical and photographic properties.

Three dyes of the neocyanine type have now been prepared by this general method. Since the neocyanine is in each instance less soluble than the corresponding kryptocyanine, it may readily be obtained pure by boiling the mixture of dyes with successive quantities of spirit insufficient for complete solution and, so soon as the colour of the filtrate shows the absence of kryptocyanine, recrystallising the undissolved residue of neocyanine. By the action of pyridine and ethyl orthoformate on lepidine ethiodide, the yield of recrystallised 1 : 1′-diethyl-4 : 4′-carbocyanine iodide obtained was 42%, and that of *neocyanine ethiodide* was 17%. But by carrying out the condensation with lepidine etho-*p*-toluenesulphonate, under slightly modified conditions, the yield of 1 : 1′-diethyl-4 : 4′-carbocyanine iodide was only 7%, whereas that of neocyanine ethiodide was 26% of that theoretically possible. By treatment of the reaction mixture with sodium bromide instead of potassium iodide, *neocyanine ethobromide* was isolated, and this was found more convenient to deal with on account of its greater solubility; in this case the yield of recrystallised 1 : 1′-diethyl-4 : 4′-carbocyanine bromide was 5%, and a 37% yield of neocyanine ethobromide was obtained. When lepidine methiodide is condensed with ethyl orthoformate in pyridine solution, the sole product is 1 : 1′-dimethyl-4 : 4′-carbocyanine iodide (Hamer, *loc. cit.*). By carrying out the condensation with lepidine metho-*p*-toluenesulphonate, isolating the resulting sulphonates, and converting them into bromides, there were obtained a 14% yield of 1 : 1′-dimethyl-4 : 4′-carbocyanine bromide and a 41% yield of *neocyanine methobromide*. From condensations carried out with lepidine etho-*p*-toluenesulphonate, it appears that in the presence of much pyridine there is a tendency to the formation of kryptocyanine rather than of neocyanine, but that with a small amount of pyridine the reverse is the case.

Each of the three neocyanines exhibits a higher melting and decomposition point than does the corresponding 4 : 4′-carbocyanine. This fact, in conjunction with the slight solubility of the neocyanines as compared with the 4 : 4′-carbocyanines, indicates that the neocyanines are compounds of greater molecular weight. The crests of the absorption and sensitising bands of the neocyanines lie nearly 1000 Å. further into the red than those of the 4 : 4′-carbocyanines, from which it may be concluded, either that neocyanine possesses a longer carbon chain connecting the nitrogen atoms than does kryptocyanine, or that it is a substance of greater complexity of structure and higher molecular weight.

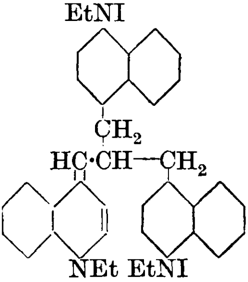
After the three neocyanines had been dried in a vacuum at 100—120° until of constant weight, analyses were made, and the empirical formulæ were calculated. The ratio of halogen atoms to nitrogen atoms was in each case 2 : 3. The molecule is very large, so that it is not possible to determine the number of carbon atoms with absolute certainty from the analytical results. With the ethiodide and ethobromide the mean values found for the number of carbon atoms are 37·8 and 36·9 respectively, and with the methobromide the mean is 34·7. It is clear that the neocyanine molecule is formed from three molecules of lepidine alkyl halide, with elimination of one halogen atom, presumably in the form of hydrogen halide, which would combine with the pyridine, and the analyses indicate two possibilities : that either one or two additional carbon atoms may enter into the new molecule. It has not been found possible to formulate the course of the reaction on the second hypothesis. On the other hand, it seems extremely probable that three molecules of lepidine alkyl halide would, through their reactive methyl groups, condense with one molecule of ethyl orthoformate, the process simply consisting in the production of three molecules of ethyl alcohol and being accompanied by removal of hydrogen halide. But formula (I) is not regarded as representing the constitution of neocyanine, for it is only reasonable to suppose that the colour and sensitising properties of neocyanine are attributable to causes similar to those obtaining in kryptocyanine, and that the dyes must in fact bear a very close structural relationship to each other. Now in certain cyanine condensations, two atoms of hydrogen are eliminated per mol. of dye formed. For instance, the preparation of an *iso*cyanine, by the action of sodium ethoxide on an alcoholic solution of quinoline ethiodide and quinaldine ethiodide, is represented by the equation :

$$C_9H_6N(EtI)\cdot CH_3 + C_9H_7N(EtI) = C_9H_6NEt{:}CH\cdot C_9H_6N(EtI) + HI + H_2.$$

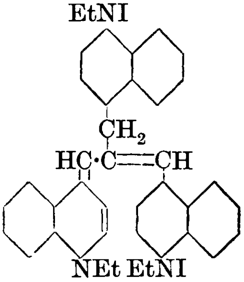
Similarly the preparation of pinacyanol by the action of alkali on an alcoholic solution of quinaldine ethiodide and formaldehyde, in the presence of quinoline ethiodide, is accompanied by the loss of two hydrogen atoms :

$$2C_9H_6N(EtI)\cdot CH_3 + CH_2O = C_9H_6NEt{:}CH\cdot CH{:}CH\cdot C_9H_6N(EtI) + H_2O + HI + H_2.$$

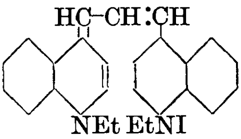
It is therefore probable that the same phenomenon takes place in the formation of neocyanine, and that the trilepidylmethane derivative (I) loses two hydrogen atoms, so that neocyanine ethiodide may be represented by formula (II). According to this, it is very simply related to 1 : 1′-diethyl-4 : 4′-carbocyanine iodide (III), since it is derived from it merely by substitution of a lepidyl ethiodide group for the hydrogen atom attached to the central carbon atom of the three-carbon chain. This formula, which is proposed for neocyanine, accords with the method of synthesis of the compound, and accounts for its optical and photographic properties, and also explains the slight solubility and high melting point of the neocyanines. It shows reasonable agreement with the analytical results. The question of the presence or absence of the two hydrogen atoms is of course not one that can be decided by analytical data in the case of compounds of such high molecular weight. Although formula (II) has a high degree of probability, it is greatly to be desired that its validity should be further tested by the synthesis of neocyanine or by experiments on its breakdown.



(I.)



(II.)



(III.)

EXPERIMENTAL.

Neocyanine Ethiodide.—Lepidine ethiodide (5 g.; 2 mols.), dry pyridine (20 c.c.), and ethyl orthoformate (5·5 g.; 4 mols.) were boiled together for 3 hours, during which crystals separated. These were collected when cold (0·89 g.; 21% yield) and recrystallised from spirit (1000 c.c.); the yield of neocyanine ethiodide (0·72 g.) was 17%. To isolate 1 : 1′-diethyl-4 : 4′-carbocyanine iodide, the pyridine mother-liquor was poured into boiling water, cooled, and filtered. The solid obtained (2·23 g.; 56% yield) was recrystallised from spirit (150 c.c.) and resulted in 42% yield (1·67 g.). It was dried in a vacuum at 100—120° and analysed by the method of Carius, which methods of drying and analysis were used throughout this work (Found : I, 26·4. Calc. for $C_{25}H_{25}N_2I$: I, 26·4%).

According to the second method of preparing neocyanine ethiodide, lepidine (5·6 g.; 2 mols.) and ethyl *p*-toluenesulphonate (7·83 g.; 2 mols.) were heated at 140—150° for 3 hours, and the quaternary salt so formed was boiled with pyridine (30 c.c.) and ethyl orthoformate (13 c.c.; 4 mols.) for 3 hours. The hot reaction liquid, which was free from solid, was poured into an excess of boiling aqueous potassium iodide. The iodide obtained (5·9 g.) was boiled with successive quantities of spirit (50 c.c. × 6) until the filtrate was pure green, and the residue was then recrystallised from spirit (3000 c.c.) : a 26% yield of neocyanine ethiodide (2·62 g.) resulted. The first two spirit solutions gave a 9% yield of crude 1 : 1′-diethyl-4 : 4′-carbocyanine iodide, which on recrystallisation from spirit (25 c.c.) gave a 7% yield (0·65 g.) (Found : I, 26·6%); the next four spirit solutions gave only a small amount of solid (0·03 g.), which was a mixture of the two dyes. That the neocyanine was completely freed from kryptocyanine was evident.

The large proportion of neocyanine ethiodide, as compared with 1 : 1′-diethyl-4 : 4′-carbocyanine iodide, afforded by the second method can hardly be attributable to the difference in the lepidine quaternary salt, and the separation of neocyanine ethiodide during the first reaction might be expected to favour its formation. In the following two comparative experiments, volumes of pyridine in the ratio 1 : 50 were taken : the dyes (1·08 g. and 0·81 g., respectively) obtained by the reaction of the quaternary salt from lepidine (1 c.c.; 2 mols.) and ethyl *p*-toluenesulphonate (1·50 g.; 2 mols.) with ethyl orthoformate (2·5 c.c.; 4 mols.) and pyridine (2 c.c. and 100 c.c., respectively) were boiled with successive quantities of spirit (each of 20 c.c.) and, when a green filtrate was obtained, the residue was recrystallised from spirit. In the case of the dye prepared in the solution of small volume the yield of recrystallised kryptocyanine was small compared with that of neocyanine (0·02 g. : 0·31 g.), whereas with more pyridine, the yield of kryptocyanine was large compared with that of neocyanine (0·30 g. : 0·08 g.).

When heated, 1 : 1′-diethyl-4 : 4′-carbocyanine iodide gives rise at about 205° to a tar of metallic appearance; sudden and violent decomposition occurs at about 260°, the exact point depending upon the rate of heating. Mills and Braunholtz (*loc. cit.*) give m. p. 253—254°.

Neocyanine ethiodide, unlike 1 : 1′-diethyl-4 : 4′-carbocyanine iodide, only forms minute crystals, which show a coppery lustre, and it is also obtained in the form of a dull green powder. It is only very slightly soluble in spirit. It melts with decomposition at about 284° (Found : C, 57·25, 57·0; H, 5·1, 4·9; N, 5·1, 5·2; I, 32·2, 32·0. $C_{37}H_{37}N_3I_2$ requires C, 57·1; H, 4·8; N, 5·4; I, 32·7%).

Neocyanine Ethobromide.—The quaternary salt from lepidine (12·8 g.; 2 mols.) and ethyl *p*-toluenesulphonate (17·9 g.; 2 mols.) was boiled with pyridine (45 c.c.) and ethyl orthoformate (30 c.c.; 4 mols.) for 3 hours, and the reaction mixture was poured into a hot solution of sodium bromide (18·5 g. in 100 c.c. of water). The resultant bromide (11·6 g.) was boiled with successive quantities of spirit (50 c.c. × 3), and the residue was then recrystallised from spirit (1500 c.c.): the yield of neocyanine ethobromide (7·12 g.) was 35% of that theoretically possible. The first spirit solution gave a 5% yield (0·83 g.) of product which was chiefly 1 : 1′-diethyl-4 : 4′-carbocyanine bromide, m. p. about 250° (decomp.), and the second and third solutions gave a 2% yield (0·37 g.) of neocyanine.

In another experiment (2·04 g. of lepidine taken), in which 50 times the above proportion of pyridine was used, most of the solvent was distilled off after the condensation, and the residue was treated with sodium bromide. The crude bromide (2·35 g.) was boiled with spirit (20 c.c. × 2): the first spirit solution gave a 52% yield (1·62 g.) of dye which was mainly 1 : 1′-diethyl-4 : 4′-carbocyanine bromide, the second gave a 4% yield (0·12 g.) of neocyanine ethobromide, and the undissolved residue (0·05 g.) amounted to a further 1% yield of neocyanine.

Neocyanine ethobromide forms small green and gold crystals and is considerably more soluble in spirit than is the corresponding ethiodide. It melts with decomposition at about 291° (Found: C, 64·2, 64·2; H, 5·6, 5·6; N, 5·9; Br, 23·2, 23·1. $C_{37}H_{37}N_3Br_2$ requires C, 65·0; H, 5·5; N, 6·15; Br, 23·4%).

Condensation of Lepidine Methiodide with Ethyl Orthoformate.—During the boiling of lepidine methiodide (3 g.) with pyridine (30 c.c.) and ethyl orthoformate (3½ c.c.) for 3 hours, much solid separated. It was collected when cold, and the yield of green crystals (1·44—1·80 g.) was 61—76%. In one experiment, boiling with successive quantities of spirit (100—200 c.c.), insufficient to dissolve all the solid, showed this to consist of 4 : 4′-carbocyanine free from neocyanine methiodide. In another case, recrystallisation from spirit (950 c.c.) gave a 37% yield (0·89 g.) of minute green crystals of 1 : 1′-dimethyl-4 : 4′-carbocyanine iodide (Found : I, 28·0. Calc. for $C_{23}H_{21}N_2I$: I, 28·1%).

Neocyanine Methobromide.—Lepidine (5·4 g.; 2 mols.) and methyl *p*-toluenesulphonate (7·03 g.; 2 mols.) were heated at 140—150°

for 3 hours and the resulting quaternary salt was boiled with pyridine (70 c.c.) and ethyl orthoformate ($12\frac{1}{2}$ c.c.; 4 mols.) for 3 hours, during which time much solid separated. This sulphonate was filtered off when cold, dissolved in a hot mixture of spirit (100 c.c.) and water (180 c.c.), and treated with aqueous sodium bromide (10 g. in 20 c.c. of water). The resulting bromide was washed and dried (5·6 g.). It was boiled with two lots of spirit (each of 100 c.c.) and, as the second filtrate was green, the residue was recrystallised from spirit (1100 c.c.): the resulting yield of neocyanine methobromide (3·13 g.) was 39%. The solid (0·29 g.) from the second spirit extract gave a green solution, so it was again crystallised from spirit (100 c.c.), and the further amount of neocyanine methobromide obtained (0·17 g.) brought the total yield up to 41%. The crystals (1·12 g.) from the first spirit extract consisted of a 22% yield of crude 1 : 1′-dimethyl-4 : 4′-carbocyanine bromide, and after recrystallisation from spirit (50 c.c.), the yield (0·72 g.) was 14%. The difference in solubility between this 4 : 4′-carbocyanine and the corresponding neocyanine is not so marked as in other cases, so that 1 : 1′-dimethyl-4 : 4′-carbocyanine bromide was not obtained free from the latter dye (Found: Br, 20·3. $C_{23}H_{21}N_2Br$ requires Br, 19·7%). The 4 : 4′-carbocyanine begins to decompose at about 265° and melting with violent decomposition occurs at about 275°. Neocyanine methobromide forms beautiful little crystals of a bright copper colour and these melt with decomposition at about 288° (Found: C, 64·0, 64·0; H, 5·1, 5·0; N, 6·1; Br, 24·5, 24·6. $C_{34}H_{31}N_3Br_2$ requires C, 63·6; H, 4·9; N, 6·55; Br, 24·9%). All three neocyanines show a very similar sensitising action.

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