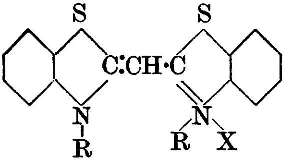
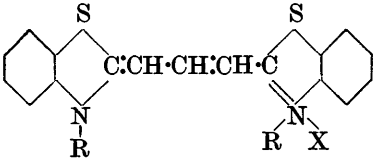
CCCXXXI.—*A General Method for the Preparation of Thiocyanine Dyes. Some Simple Thiocarbocyanines.*

By Nellie Ivy Fisher and Frances Mary Hamer.

From his observation of the similarity between quinoline and benzthiazole, Hofmann was led to attempt the preparation of cyanine dyes containing benzthiazole nuclei. He was successful in isolating a carmine-red dye by the action of ammonia on an aqueous solution of benzthiazole amyliodide and 1-methylbenzthiazole amyliodide, and it is not surprising that he regarded it as cyanine in which the quinoline nuclei are replaced by benzthiazole nuclei (*Ber.*, 1887, **20**, 2251). Mills, working with the corresponding ethiodides, effected a great improvement in yield by using pyridine, and discovered that the purple ethiodide, which corresponds with the amyliodide prepared by Hofmann, is accompanied by a yellow compound. He came to the very striking conclusion that the purple dye is not, as Hofmann supposed, the cyanine of the benzthiazole series (I), but is the corresponding carbocyanine (II), whilst the yellow substance is the cyanine (I). For this new class of yellow compound, represented by formula (I), Mills proposed the name

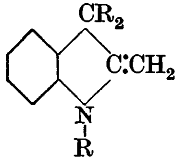

(I.)

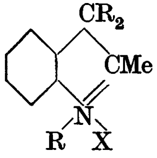

(II.)

thiocyanine, and he definitely established the constitution by synthesising thiocyanines from *o*-aminophenyl mercaptan (J., 1922, **121**, 455). His deduction, that the purple thiocarbocyanines are represented by formula (II) has been amply confirmed by syntheses, in which 1-methylbenzthiazole quaternary salts are condensed with ethyl orthoformate (König and Meier, *J. pr. Chem.*, 1925, **109**, 324; Hamer, J., 1927, 2796). Mills and Amies showed that a mixture of thiocyanine and thiocarbocyanine may also be obtained by the reaction of a 1-methylbenzthiazole quaternary salt with di-*o*-formylethylaminodiphenyl disulphide in pyridine solution (Mills and Braunholtz, J., 1923, **123**, 2804).

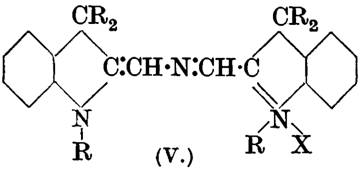
In Mills's original method of preparing 2 : 2′-diethylthiocyanine iodide, the yield of crude product amounted to 16—21% (*loc. cit.*), whilst the yield of pure 2 : 2′-diethyl-5-methylthiocyanine iodide, analogously prepared from 5-methylbenzthiazole ethiodide and 1-methylbenzthiazole ethiodide, was only 5% (Mills and Braunholtz, J., 1922, **121**, 1489); in the disulphide method, the yield of 2 : 2′-diethylthiocyanine iodide was 11% (Mills and Braunholtz, J., 1923, **123**, 2804). Both methods suffer from the disadvantage that the thiocyanine has to be separated from the accompanying thiocarbocyanine. In the present new method, however, thiocyanine is the only dye formed; the method is a general one, and simple to operate, and the yields of crude thiocyanines vary from 35 to 48%, being 18—33% after recrystallisation.

The method was discovered as the result of an examination of a method of preparing new dyes, recently patented by the I. G. Farbenindustrie A.-G. (D.R.-P. 459,616, 4.5.26; B.P. 291,888, 11.3.27). According to these patents, when 2-methylene-1 : 3 : 3-trialkylindoline (III) or the corresponding indoleninium salt (IV)

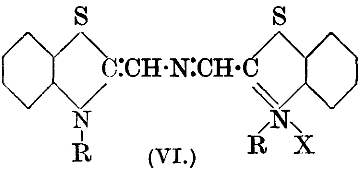
(III.)



(IV.)

is treated with an ester or salt of nitrous acid, in the presence of an acid anhydride, there result yellow to orange dyes, to which is assigned the formula (V).



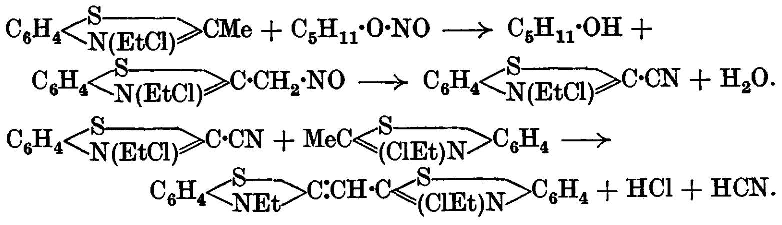
(V.)



(VI.)

Now, instead of using an indoleninium salt, the effect of amyl nitrite, in the presence of acetic anhydride, was tried on a benzthiazolinium salt containing a reactive methyl group. The ethochloride of 1-methylbenzthiazole was selected for trial, because chlorine is not liberated from chlorides by the action of nitrous acid. Reaction readily occurred on warming, with the production of a yellow chloride; the best yields were obtained by heating 2 mols. of 1-methylbenzthiazole ethochloride, 1·5 mols. of amyl nitrite, and acetic anhydride on the water-bath for 15 minutes. The yellow chloride was converted into the corresponding bromide and iodide, by means of sodium bromide and potassium iodide, respectively. But the analytical data showed no concordance with those required by a compound (VI), analogous to the new compounds of the German patents. On the other hand, the halogen contents of the chloride, bromide, and iodide closely approximated to the values required for 2 : *2′-diethylthiocyanine chloride* (I), *bromide*, and iodide, respectively. The iodide which had been made by the reaction of 1-methylbenzthiazole ethochloride and amyl nitrite, followed by treatment with potassium iodide, was carefully compared with a specimen of 2 : 2′-diethylthiocyanine iodide, which had been prepared by the method of Mills. They were found to be similar in appearance and solubility, identical in optical and photographic properties, and with the same melting point and mixed melting point. Similarly a chloride was prepared by the action of amyl nitrite, in the presence of acetic anhydride, on 1-methylbenzthiazole methochloride, and it was converted into the corresponding *bromide* and iodide; this was identical with 2 : 2′-dimethylthiocyanine iodide prepared by Mills's method.

There is no doubt that the action of amyl nitrite in the presence of acetic anhydride on a benzthiazolinium salt containing a reactive methyl group is an excellent general method for the preparation of thiocyanines, but it is a surprising reaction. The formation of thiocyanine is dependent upon the addition of amyl nitrite, yet no part of the amyl nitrite molecule is present in the thiocyanine molecule. The reaction may be tentatively represented as occurring in the following three stages:



$$\mathrm{C_6H_4}{<}\begin{matrix}\mathrm{S}\\\mathrm{N(EtCl)}\end{matrix}{>}\mathrm{CMe} + \mathrm{C_5H_{11}{\cdot}O{\cdot}NO} \longrightarrow \mathrm{C_5H_{11}{\cdot}OH} +$$

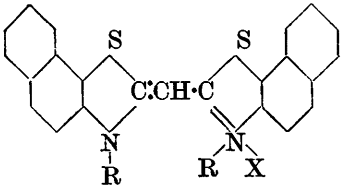
$$\mathrm{C_6H_4}{<}\begin{matrix}\mathrm{S}\\\mathrm{N(EtCl)}\end{matrix}{>}\mathrm{C{\cdot}CH_2{\cdot}NO} \longrightarrow \mathrm{C_6H_4}{<}\begin{matrix}\mathrm{S}\\\mathrm{N(EtCl)}\end{matrix}{>}\mathrm{C{\cdot}CN} + \mathrm{H_2O}.$$

$$\mathrm{C_6H_4}{<}\begin{matrix}\mathrm{S}\\\mathrm{N(EtCl)}\end{matrix}{>}\mathrm{C{\cdot}CN} + \mathrm{MeC}{<}\begin{matrix}\mathrm{S}\\\mathrm{(ClEt)N}\end{matrix}{>}\mathrm{C_6H_4} \longrightarrow$$

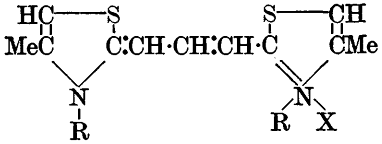
$$\mathrm{C_6H_4}{<}\begin{matrix}\mathrm{S}\\\mathrm{NEt}\end{matrix}{>}\mathrm{C{:}CH{\cdot}C}{<}\begin{matrix}\mathrm{S}\\\mathrm{(ClEt)N}\end{matrix}{>}\mathrm{C_6H_4} + \mathrm{HCl} + \mathrm{HCN}.$$

It is, however, questionable whether the hypothetical product of the second stage, 1-cyanobenzthiazole ethochloride, would react with 1-methylbenzthiazole ethochloride to form the thiocyanine.

The application of the new method to the methylnaphthathiazoles was tried. From 1-methyl-α-naphthathiazole ethochloride and methochloride, two new thiocyanines were obtained (VII), and each of these was converted into the corresponding bromide and iodide. There were, on the other hand, only negative results when the starting point was 2-methyl-β-naphthathiazole ethochloride or methochloride. This falls into line with a previous observation, that thiocarbocyanines containing the chain :CH·CMe:CH· can only be prepared from quaternary salts of 1-methyl-α-naphthathiazole and not from those of 2-methyl-β-naphthathiazole (Hamer, J., 1929, 2598).



(VII.)

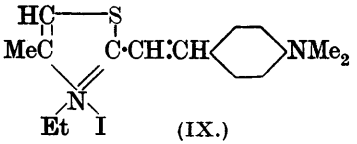


(VIII.)

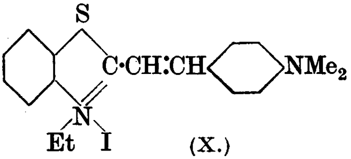
Thus four sets of thiocyanines were actually prepared, each set consisting of chloride, bromide, and iodide: namely, 2 : 2′-diethylthiocyanine halide, 2 : 2′-dimethylthiocyanine halide, 2 : *2′-diethyl-*5 : 6 : *5′ : 6′-dibenzthiocyanine halide*, and 2 : *2′-dimethyl-*5 : 6 : 5′ : *6′-dibenzthiocyanine halide*; of these twelve compounds, only the iodides of the first two groups and the chloride of the second group had previously been prepared. In all four groups the solubility decreases in the series chloride, bromide, iodide, and the melting point rises. The first two sets of dyes are pale yellow, crystalline solids, and the latter two sets are powders of deeper colour. In the case of the latter two sets, the absorption maxima of the spirit solutions lie 150—200 Å. further into the less refrangible region of the spectrum than do those of the former two sets. Mr. O. F. Bloch has found that all the thiocyanines confer extra-sensitivity on silver chloride emulsions bathed in their solutions; in the case of those containing two naphthathiazole nuclei, the sensitising maxima lie 250—300 Å. nearer to the red region than do those of the thiocyanines containing two benzthiazole nuclei. The fact that the thiocyanines are adsorbed by silver halide is sufficient to characterise them as dyes.

Attempts to prepare thiocyanines by the new method from the methochloride and the (previously unknown) ethochloride of 2 : 4-dimethylthiazole proved unsuccessful. This is not surprising, for it is recognised that the simplest cyanines are difficult to prepare: for instance, the ethyl orthoformate and pyridine method of preparing carbocyanines fails completely in the case of the pyridocarbocyanines (Hamer, J., 1927, 2796), so that these, the simplest of all 2 : 2′-carbocyanines, have only recently been prepared, by a special method devised by Rosenhauer and Barlet (*Ber.*, 1929, **62**, 2724). It is in this connexion noteworthy that the ethyl orthoformate and pyridine method, which has been described as being at its best in the case of the thiocarbocyanines (Hamer, *loc. cit.*), does not fail in the case of the simpler thiocarbocyanines (VIII) derived from the ethiodide and methiodide of 2 : 4-dimethylthiazole. But the difficulty of preparing simple cyanines is again illustrated by the fact that the yields of these new dyes, after recrystallisation, are only 27% and 14%, respectively, whereas, normally, thiocarbocyanines are obtainable in 79—83% of the theoretical yield.

The optical properties of the simple thiocarbocyanines (VIII) derived from 2 : 4-dimethylthiazole are remarkable, in that the absorption band of the spirit solution lies only 100 Å. nearer to the blue end of the spectrum than does that of 2 : 2′-diethylthiocarbocyanine iodide (II), which is derived from 1-methylbenzthiazole; corresponding with this, their sensitising spectra are very like that of 2 : 2′-diethylthiocarbocyanine iodide. It is a general rule that, in a given series of compounds, decrease in molecular weight occasions a shift of the absorption towards the blue end of the spectrum, but exceptions to this rule have been recorded in the cyanine series (Hamer, this vol., p. 995; Bloch and Hamer, *Phot. J.*, 1930, **70**, 374). In the present instance, the shift is indeed in the expected direction, but it is not so great as had been anticipated from the recently recorded observation (Bloch and Hamer, *loc. cit.*) that the absorption maximum of 2-*p*-dimethylaminostyryl-4-methylthiazole ethiodide (IX), which is derived from 2 : 4-dimethylthiazole, lies as much as 600 Å. nearer to the blue end of the spectrum than does that of 1-*p*-dimethylaminostyrylbenzthiazole ethiodide (X), which is derived from 1-methylbenzthiazole.



(IX.)



(X.)

EXPERIMENTAL.

Methylbenzthiazolinium Chlorides.—These chlorides were prepared from the corresponding iodides by boiling the latter in spirit solution with an excess of freshly precipitated silver chloride. If the lumps of halide are broken up at intervals, and the boiling is prolonged so as to decompose the double halide which is at first produced, there is no difficulty in obtaining uniformly excellent yields of the methylbenzthiazolinium chlorides on evaporation of the filtrate and washings to dryness. The solid was in every case thoroughly dried in a vacuum desiccator and, before the subsequent condensation was carried out, the complete absence of iodide was confirmed.

2 : 2′-*Diethylthiocyanine Chloride.*—1-Methylbenzthiazole ethochloride (5 g.; 2 mols.) was treated with acetic anhydride (75 c.c.), freshly distilled amyl nitrite (2·4 c.c.; 1·5 mols.) was added, and the mixture was heated under reflux on the water-bath for 15 minutes, moisture being excluded by means of a calcium chloride guard-tube. When cold, the yellow chloride was filtered off, washed with a little ether, and dried in the air (2·10 g.; 48% yield). It was recrystallised from spirit (12 c.c. per g.) and the yield so obtained was 29%. The dye was dried in a vacuum at 100—110° until of constant weight and was analysed by the method of Carius. This method of drying and of analysis was employed throughout the present work (Found: Cl, 9·5. After a second recrystallisation, found: Cl, 9·6; S, 16·9. $C_{19}H_{19}N_2ClS_2$ requires Cl, 9·5; S, 17·1%). M. p. 255° (decomp.).

2 : 2′-*Diethylthiocyanine Bromide.*—Crude 2 : 2′-diethylthiocyanine chloride (2 g.) was dissolved in spirit, and the solution filtered hot into a hot solution of sodium bromide (4 g.) in water (24 c.c.). The solid, which immediately began to separate, was filtered off when cold (1·76 g.; 79% yield) and recrystallised from spirit (40 c.c.). The yield was 56% (1·25 g.) (Found: Br, 19·2. $C_{19}H_{19}N_2BrS_2$ requires Br, 19·1%). M. p. 298° (decomp.).

2 : 2′-*Diethylthiocyanine Iodide.*—When solutions of crude 2 : 2′-diethylthiocyanine chloride (1·15 g.) in hot spirit (15 c.c.) and of potass-

ium iodide (2·3 g.) in hot water (15 c.c.) were mixed, a precipitate formed instantaneously; it was filtered off when cold (0·95 g.; 67% yield) and recrystallised from hot spirit (400 c.c.), the yield then being 0·66 g. (Found: I, 27·2; N, 5·9. Calc. for $C_{19}H_{19}N_2IS_2$: I, 27·2; N, 6·0%). When heated, the iodide melted at 312° (decomp.), simultaneously with a specimen prepared by the method of Mills (*loc. cit.*), and with their mixture. Both specimens showed the same absorption and gave the same sensitisation towards chloride plates on bathing, properties which have already been described by Mills.

2 : 2′-*Dimethylthiocyanine Chloride.*—By the reaction of 1-methylbenzthiazole methochloride (5 g.) with amyl nitrite in the presence of acetic anhydride, there was obtained a 40% yield of the thiocyanine chloride (1·7 g.), and after recrystallisation from spirit (40 c.c. per g.), the yield was 33% (Found: Cl, 10·2. Calc. for $C_{17}H_{15}N_2ClS_2$: Cl, 10·2%). M. p. 261° (decomp.). Mills prepared this dye from the corresponding thiocyanine iodide and gives its melting point as 269° (decomp.) (*loc. cit.*).

2 : 2′-*Dimethylthiocyanine Bromide.*—This was prepared from the thiocyanine chloride, as in the case of the corresponding diethyl compound, and the yield was 91%. After recrystallisation from spirit (115 c.c. per g.), the yield was 72% (Found: Br, 20·4. $C_{17}H_{15}N_2BrS_2$ requires Br, 20·5%). M. p. 287° (decomp.).

2 : 2′-*Dimethylthiocyanine Iodide.*—The iodide was obtained from the crude thiocyanine chloride in 74% yield and, after recrystallisation from spirit (315 c.c. per g.), the yield was 55% (Found: I, 28·9. Calc. for $C_{17}H_{15}N_2IS_2$: I, 29·0%). This specimen of iodide, one prepared by Mills's method, and their mixture, all melted simultaneously at 290—292° (decomp.); Mills gives m. p. 279—280°. Spirit solutions of both specimens had the same absorption spectrum, with the maximum at λ 4150 Å. Both specimens also produced exactly the same sensitising effect on chloride plates on bathing, the maximum being at λ 4500 Å., and the sensitisation extending to λ 4900 Å. for moderate exposures.

2 : 2′-*Diethyl*-5 : 6 : 5′ : 6′-*dibenzthiocyanine Chloride.*—The yield of crude *thiocyanine* obtained from 1-methyl-α-naphthathiazole ethochloride (5 g.) was 26% (1·16 g.) and, after recrystallisation from spirit (100 c.c. per g.), the yield was 20% (Found: Cl, 7·3. $C_{27}H_{23}N_2ClS_2$ requires Cl, 7·5%). M. p. 264° (decomp.). Its spirit solution shows an absorption band with its maximum at λ 4450 Å. With chloride plates the well-marked band of extra-sensitivity extends to λ 5300 Å. and has a maximum at λ 4800 Å.; the plates were stained yellow.

2 : 2′-*Diethyl*-5 : 6 : 5′ : 6′-*dibenzthiocyanine bromide* was obtained

from the crude thiocyanine chloride in 81% yield, and after recrystallisation from spirit (310 c.c. per g.) the yield was 51% (Found: Br, 15·45. $C_{27}H_{23}N_2BrS_2$ requires Br, 15·4%). M. p. 286° (decomp.).

2 : 2′-*Diethyl*-5 : 6 : 5′ : 6′-*dibenzthiocyanine iodide*, prepared from the corresponding thiocyanine chloride, was so sparingly soluble that its recrystallisation was not attempted; it was washed with water and obtained in 70% yield (Found: I, 22·3. $C_{27}H_{23}N_2IS_2$ requires I, 22·4%). M. p. 297° (decomp.).

2 : 2′-*Dimethyl*-5 : 6 : 5′ : 6′-*dibenzthiocyanine Chloride*.—From 1-methyl-α-naphthathiazole methochloride (5 g.), the *thiocyanine* was prepared in 35% yield (1·59 g.). After recrystallisation from spirit (250 c.c. per g.), the yield was 18% (Found: Cl, 7·9. $C_{25}H_{19}N_2ClS_2$ requires Cl, 7·9%). M. p. 275° (decomp.).

2 : 2′-*Dimethyl*-5 : 6 : 5′ : 6′-*dibenzthiocyanine bromide* was prepared from the crude thiocyanine chloride and washed with water (yield, 43%) (Found: Br, 16·3. $C_{25}H_{19}N_2BrS_2$ requires Br, 16·3%). M. p. 309° (decomp.). The absorption maximum of its spirit solution lies at λ 4500 Å. The band of extra-sensitivity, conferred on chloride plates, reaches its maximum at λ 4750 Å. and extends to λ 5200 Å. for moderate exposures.

2 : 2′-*Dimethyl*-5 : 6 : 5′ : 6′-*dibenzthiocyanine iodide*, similarly prepared and washed, was obtained in 44% yield (Found: I, 23·6. $C_{25}H_{19}N_2IS_2$ requires I, 23·6%). M. p. 314° (decomp.).

2 : 4-*Dimethylthiazole Methiodide*.—2 : 4-Dimethylthiazole (5·05 g.; 1 mol.) and methyl iodide (3·3 c.c.; 1·2 mols.) were heated in a sealed tube at 100° for 2 days. The product was treated with water and filtered to remove periodide. The filtrate was evaporated to dryness, and the resultant solid extracted with ether. The colourless residue (10·6 g.; 93% yield) was recrystallised from dry spirit (55 c.c.) and the yield was 81% (9·2 g.) (Found: I, 49·95. Calc. for $C_6H_{10}NIS$: I, 49·7%). M. p. 260° (decomp.). Hantzsch says that slow decomposition occurs above 225° (*Annalen*, 1889, **250**, 257).

2 : 4-*Dimethylthiazole Ethiodide*.—2 : 4-Dimethylthiazole (4·25 g.; 1 mol.) and ethyl iodide (3·6 c.c.; 1·2 mols.) were heated in a sealed tube at 100° for 2 days, and the product was treated with water and benzene. The filtered aqueous solution was boiled with charcoal, filtered, and evaporated to dryness; the yield of *ethiodide* was 90% (9·06 g.), but the iodine content was higher than that calculated (Found: I, 47·7. $C_7H_{12}NIS$ requires I, 47·15%). The colourless hygroscopic ethiodide is much more soluble in dry spirit than is the corresponding methiodide.

Thiocarbocyanine prepared from 2 : 4-*Dimethylthiazole Methiodide*.—The methiodide (2 g.; 2 mols.), ethyl orthoformate (2·6 c.c.

4 mols.), and pyridine (20 c.c.) were boiled together for 4 hours. The crude product contained only a relatively small amount of dye; the other product was not ether-soluble, but could readily be removed by virtue of its greater solubility in methyl alcohol: recrystallisation from this (70 c.c.) gave a 14% yield of the *thiocarbocyanine* (0·21 g.) in steely crystals (after a second recrystallisation, found: I, 32·2. $C_{13}H_{17}N_2IS_2$ requires I, 32·4%). M. p. 255° (decomp.). The spirit solution possesses a rather broad absorption band with its maximum at λ 5500 Å. and there is an indication of another band at λ 5100 Å. A gelatino-bromide plate, bathed in it, shows practically uniform sensitivity, extending to λ 6800 Å. for moderate exposures; the maximum is at λ 5900 Å.

Thiocarbocyanine prepared from 2 : 4-*Dimethylthiazole Ethiodide.*—A *thiocarbocyanine* was similarly prepared from 2 : 4-dimethylthiazole ethiodide (2 g.), and the crude product (0·50—0·55 g.; 32—35% yield) gave, on recrystallisation from methyl alcohol (50 c.c.), a 27% yield (0·42 g.) (Found: I, 30·1. After a second recrystallisation, found: I, 29·95. $C_{15}H_{21}N_2IS_2$ requires I, 30·2%). The m. p. is sharp but depends upon the rate of rise of temperature, varying from 271° to 294°. The spectral absorption resembles that of the preceding compound. The band of extra-sensitivity is not quite so uniform, showing one maximum at λ 5900 Å. and a weaker one at λ 5350 Å.; it extends to λ 6500 Å.

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