

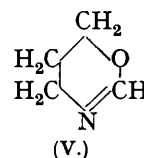
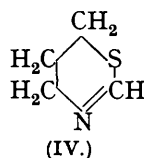
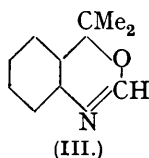
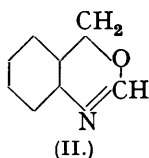
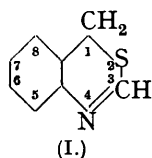
19. Thiazinocyanines. Part I. Carbocyanines containing the 2:4-Benzthiazine Nucleus.

By BERNARD BEILENSEN and FRANCES M. HAMER.

Cyanines containing a six-membered heterocyclic ring have been prepared for the first time. 3-Methyl-2:4-benzthiazine was condensed with quaternary salts containing a substituted β -aminovinyl group to give five new carbocyanine bases. Two of these were converted into their ethiodides, the carbocyanines themselves. Both 3-amino-2:4-benzthiazine ethiodide and also the base were condensed with a salt containing a substituted β -aminovinyl group, to give a γ -azatrimethincyanine and its base, respectively. Absorption maxima of the various dyes have been compared. The effect of replacing the benzthiazole by the 2:4-benzthiazine nucleus in carbocyanines is to produce a hypsochromic shift.

THE nomenclature adopted in this paper for the parent base, 2:4-benzthiazine (I), follows that of Richter's "Lexikon." Once the positions of the sulphur and the nitrogen atom in the ring are thus defined by the numbers, there can be no ambiguity as to that of the methylene group. The above name is therefore preferred to the 2:4:1-benzothiazine of *Chemical Abstracts* (*Decennial Index* for 1917—1926).

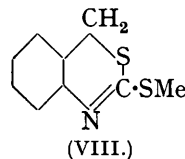
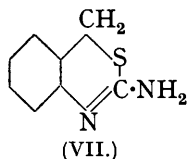
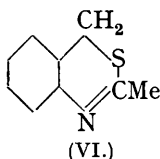
The following record of the nomenclature which has been used in the literature may be useful. Paal and Bodewig applied the name "Cumazon" to the 2:4-benzoxazine (II) (*Ber.*, 1892, **25**, 2961), although Widmann had originally proposed this name for its dimethyl derivative (III) (*Ber.*, 1883, **16**, 2576), both of them being unknown; Paal and Vanvolxem called (I) "Cumothiazon" (*Ber.*, 1894, **27**, 2413).



Gabriel and Posner, in pointing out the anomaly between Widmann's nomenclature and Paal's, suggested calling (I) and (II) "Phenpentiazol" and "Phenpentoxazol," respectively (*Ber.*, 1894, **27**, 3509).

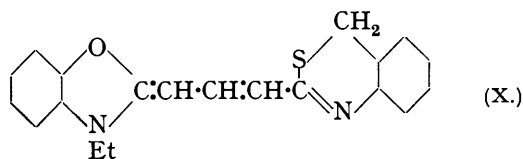
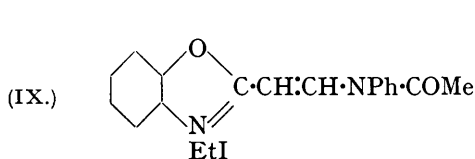
These terms are connected with those of "Penthiazolol" for (IV) (Gabriel and Lauer, *Ber.*, 1890, **23**, 87) and "Pentoxazolol" for (V) (Gabriel and Elfeldt, *Ber.*, 1891, **24**, 3213).

Our object was to introduce the 2:4-benzthiazine nucleus into cyanine dyes. Possible intermediates were 3-methyl-2:4-benzthiazine (VI) (Gabriel and Posner, *Ber.*, 1894, **27**, 3509), 3-amino-2:4-benzthiazine (VII) (*idem, ibid.*, 1895, **28**, 1029), and 3-methylthio-2:4-benzthiazine (VIII) (Paal and Commerell, *Ber.*, 1894, **27**, 2427), which we hoped would give reactive quaternary salts.

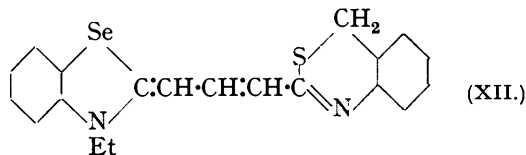
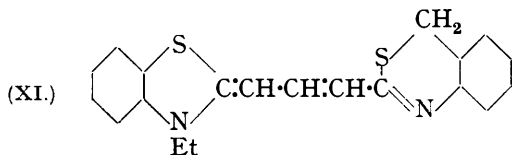


Anthranilic acid, which is the starting point in the synthesis of (VI), was reduced electrolytically to *o*-aminobenzyl alcohol (Mettler, *Ber.*, 1905, **38**, 1745); by a modification of Gabriel and Posner's method, this was converted into *o*-aminobenzyl chloride hydrochloride, which was condensed with thioacetamide, according to their method (*loc. cit.*), to give (VI). Attempts to prepare the methiodide and metho-*p*-toluenesulphonate gave unattractive products which could not be condensed with ethyl orthoformate in the presence of pyridine. Since quaternary salts of (VI) would have the structure with which Mills and Smith found reactivity of the methyl group to be correlated (J., 1922, **121**, 2724), we conclude that we were unsuccessful in obtaining the desired quaternary salts. However, having failed here, we developed the following line of attack through the base (VI) itself.

Unsymmetrical carbocyanines were prepared by I.C.I. Ltd., Piggott and Rodd by condensing two quaternary, heterocyclic ammonium salts, one containing a reactive methyl, the other a reactive sub-



stituted β -aminovinyl group (B.P. 454,898/1930), which latter intermediates, *e.g.* (IX), they had described (B.P. 344,409/1929). Kendall found that a quinoline base, containing a reactive methyl group, could be condensed with a salt containing a substituted β -aminovinyl group (B.P. 456,362/1935), resulting in a base, the quaternary salt of which would be a carbocyanine. Preparative details were given by Barent and Kendall (B.P. 477,483/1936), and two such carbocyanine bases were described. We have now prepared five carbocyanine bases of a new type, by condensing 3-methyl-2:4-benzthiazine (VI) with intermediates containing a substituted β -aminovinyl group. Thus (VI) and (IX) gave the trimethincyanine base (X); bases (XI) and (XII) containing the benzthiazole and benzselenazole in

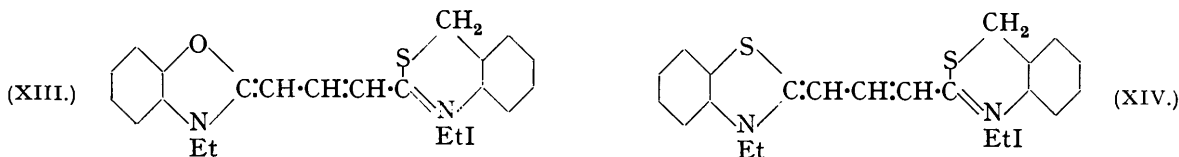


place of the benzoxazole nucleus were also prepared, besides one containing a 6:7-benzbenzoxazole and one a 4:5-benzbenzthiazole nucleus.

Absorption spectra of methyl-alcoholic solutions of the dyes were obtained by use of a wedge spectrograph. When the benzoxazole nucleus is replaced by the benzthiazole and the benzselenazole nucleus, respectively, the maximum shifts 200 \AA . towards the region of longer wave-length. The introduction of a benz-group causes, in the two instances, shifts of 250 and 150 \AA . With all five bases, addition of sulphuric acid to the methyl-alcoholic solution has a bathochromic effect, the shifts of maximum varying from 600—800 \AA . Thus the yellow solution of (X) becomes orange, the orange of (XI) becomes pink, and the red of its 4:5-benz-derivative becomes purple. The absorption curves of the bases are rounded, but those of the acid salts are narrower, with more sharply defined maxima. This group of substances comprises some powerful sensitizers for gelatino silver bromide emulsions.

Unsymmetrical carbocyanines (XIII) and (XIV) containing the 2:4-benzthiazine nucleus, were prepared by heating the bases (X) and (XI), respectively, with excess of ethyl *p*-toluenesulphonate,

followed by treatment with potassium iodide. These carbocyanines possess sharp absorption bands. Replacement of the benzoxazole by the benzthiazole nucleus, in passing from (XIII) to (XIV), causes



the usual bathochromic shift, its value being 300 Å. It is particularly interesting to compare the unsymmetrical oxathiocarbocyanine (Beilenson, Fisher, and Hamer, *Proc. Roy. Soc.*, 1937, *A*, **163**, 138) with (XIII) and the symmetrical thiocarbocyanine (Fisher and Hamer, *ibid.*, 1936, *A*, **154**, 703) with (XIV): the effect of replacing the five-membered benzthiazole by the six-membered 2:4-benzthiazine nucleus, in these two instances, is to shift the absorption maximum 200 and 270 Å, respectively, towards the blue. The absorption maxima of the new ethiodides (XIII) and (XIV) lie 550 and 650 Å, respectively, nearer to the red than the absorption maxima of the corresponding bases; they approximate in position to those of acid solutions of the corresponding bases, lying, in each instance, 50 Å. nearer to the blue. The ethiodides are good sensitizers, but, surprisingly, their action closely resembles that of the bases.

This abnormality in sensitizing action might lie either with the ethiodide or with the base. It is attributed to the latter, for the reason that with the carbocyanines, (XIII) and (XIV), the shifts on passing from absorption maximum to sensitizing maximum are 300 and 200 Å, respectively, which may be regarded as normal (cf. Bloch and Hamer, *Phot. J.*, 1928, **68**, 21), whereas with the bases (X) and (XI) the corresponding shifts are exceptionally high, being 850 and 750 Å, respectively. The sensitizing action of the base is then what might be expected from an acid salt of the base. At first this seemed fully accounted for by the fact that the photographic emulsion used for the tests was on the acid side, p_H 6.5. On carrying them out, however, with a definitely alkaline emulsion, p_H 7.5, we found that the sensitizing action of the base was unaltered.

In assigning chemical names to the cyanines described in this paper, systematic nomenclature is used. The bases are given the simplified names which were suggested by Dr. J. T. Hewitt, F.R.S., and have been applied to similar dye bases (Hamer, J., 1940, 799).

Two interesting dyes containing the chain $:CH:CH:N\cdot$ (or $\cdot CH:CH:N:$) have been synthesised. For this, 3-amino-2:4-benzthiazine (VII) was prepared from *o*-aminobenzyl chloride hydrochloride and thiocarbamide, by the method of Gabriel and Posner (*Ber.*, 1895, **28**, 1029). Although we could not make quaternary salts of 3-methyl-2:4-benzthiazine, we made 3-amino-2:4-benzthiazine ethiodide. Kendall has recorded the condensation in pyridine of 2-aminobenzthiazole and an intermediate containing a substituted β -aminovinyl group (B.P. 447,038/1934). By condensing 3-amino-2:4-benzthiazine with an intermediate of this type, we obtained the dye base (XV). Moreover, by condensing 3-amino-2:4-benzthiazine ethiodide with the same intermediate, we prepared the azatrimethincyanine (XVI), which is the ethiodide of (XV).



The substances (XV) and (XVI) bear a close structural relationship to (XI) and (XIV), respectively, the one difference being that the nuclei in (XV) and (XVI) are linked by the chain $:CH:CH:N\cdot$, instead of by $:CH:CH:CH\cdot$. On passing from the trimethincyanine (XIV) to the azatrimethincyanine (XVI), the absorption maximum undergoes a hypsochromic shift of 900 Å.; here it is interesting to note the rather smaller hypsochromic shift which Fisher and Hamer found on passing from certain trimethincyanines to $\alpha\beta$ (or $\beta\gamma$)-diazatrimethincyanines and the much greater one on passing to an $\alpha\gamma$ -diazatrimethincyanine (J., 1937, 907). On passing from the trimethincyanine base (XI) to the azatrimethincyanine base (XV), the small shift, 50 Å., is bathochromic. The new base (XV) has a broad absorption band, and its ethiodide (XVI) a more sharply defined band. One difference between this base and the five trimethincyanine bases is that it shows no deepening of colour on addition of sulphuric acid. Another striking difference is that the absorption maximum, on passing from base (XV) to ethiodide (XVI), shifts 300 Å. towards the region of shorter wave-length, whereas in the trimethincyanine series the shift

is in the opposite direction. The azatrimethincyanine sensitised a gelatino silver chloride emulsion, but the base did not sensitise it.

EXPERIMENTAL.

o-Aminobenzyl Alcohol.—Mettler's method of electrolytic reduction of anthranilic acid was applied, but whereas he started with 5 g. (*Ber.*, 1905, **38**, 1745), the present scale was much larger. Anthranilic acid (100 g.), partially dissolved in 15% sulphuric acid (2000 c.c.), was placed in a 4-l. beaker as cathode chamber. Inside that was the anode chamber, a porous pot containing 15% sulphuric acid. Both anode and cathode were pure lead strip, and 200 sq. cm. of cathode were immersed. Mettler kept the temperature below 30° by water-cooling, but here it was kept at 15—20° by cooling with ice. Mechanical stirring proved advantageous, as did a reduction time (12 hours at an amperage of 13·5) which was twice that calculated. The solution was made just alkaline with ammonia, instead of with ammonium carbonate, but filtration, saturation with ammonium sulphate, and extraction with ether (200 c.c. × 3) were as described by Mettler. Nine such batches gave 454 g., with an average yield of 56%, as against his 69%. After recrystallisation from benzene (50 c.c. for 30 g.), the yield dropped to 46% and the m. p. was 84°, as recorded by him.

o-Aminobenzyl Chloride Hydrochloride.—The scale was four times that of Gabriel and Posner (*Ber.*, 1894, **27**, 3509). The time of heating together crude *o*-aminobenzyl alcohol (20 g.; 1 mol.) and hydrochloric acid (*d* 1·195; 100 c.c.; 6 mols.), in a pressure bottle at 100°, was only 12 minutes, instead of 30. The hydrochloride was filtered off when cold, washed with ether, and dried at about 40°. The yield from eight such preparations was 84% (194 g.) as against their 76% yield (5·5 g.).

3-Methyl-2:4-benzthiazine (VI).—*o*-Aminobenzyl chloride hydrochloride (14 g.; 1 mol.) and thioacetamide (7 g.; 1·2 mols.) were ground together and heated on the water-bath for 15 minutes, and the mixture was made just alkaline with sodium hydroxide and steam-distilled, according to the method of Gabriel and Posner (*loc. cit.*). Whereas they on their smaller scale obtained a 78% yield (0·5 g.), the present yields of solid varied unaccountably from 19 to 63% (8 g.).

3-Amino-2:4-benzthiazine (VII).—*o*-Aminobenzyl chloride hydrochloride (20 g.) was ground with thio-carbamide (40 g.), and the mixture heated at 140° for 10 minutes and at 160—170° for 5 minutes, whereas Gabriel and Posner (*Ber.*, 1895, **28**, 1029) heated at 140—150° for 15 minutes. After alkali treatment, they by ether extraction obtained a 54% yield on their half scale. In the present preparation, after alkali treatment the solid was filtered off and purified by solution in dilute hydrochloric acid and reprecipitation with alkali, being thus obtained in 52% yield. After recrystallisation from spirit (2 c.c. per g.), the yield dropped to 40% and the m. p. was 135°, whereas Gabriel and Posner record 136—137° (Found after drying in a vacuum at 55—60°: N, 17·0. Calc. for C₈H₈N₂S: N, 17·1%).

3-Amino-2:4-benzthiazine Ethiodide.—3-Amino-2:4-benzthiazine (6·56 g.; 1 mol.) and ethyl iodide (9·6 c.c.; 3 mols.) were refluxed on the water-bath for 2 days. The gummy product, after being stirred with absolute alcohol (20 c.c.; 3·87 g. obtained), separated from absolute alcohol (40 c.c.) in 23% yield in cream-coloured crystals. It was dried to constant weight in a vacuum at 60—80° and analysed by the method of Carius; these methods of drying and analysis were employed throughout this work, except where otherwise stated (Found: I, 39·6. C₁₀H₁₃N₂IS requires I, 39·65%). M. p. 220° (decomp.).

Trimethin[2-(3-ethylidihydrobenzoxazole)][3-(2:4-benzthiazine)] (X).—2-β-Acetanilidovinylbenzoxazole ethiodide (IX) (4·34 g.; 1 mol.), 3-methyl-2:4-benzthiazine (VI) (1·63 g.; 1 mol.) and pyridine (10 c.c.) were refluxed for 5 minutes. The product was poured into a mixture of aqueous ammonia (20 c.c., *d* 0·880) and spirit (20 c.c.). More aqueous ammonia (40 c.c.), diluted with water (40 c.c.), was added. When cold, the aqueous layer was decanted from the dark oil, which was washed with water. On stirring with acetone (10 c.c.) it crystallised (1·46 g.). After recrystallisation from ethyl acetate (12 c.c.), the yield was 37% (1·22 g.) (Found: S, 9·4. C₂₀H₁₈ON₂S requires S, 9·6%). M. p. 138°. It formed bright orange crystals with a purple reflex. Their methyl-alcoholic solution had a rounded absorption curve with maximum at 4450 Å. With addition of sulphuric acid (5 g. per 100 c.c.) the absorption curve had two maxima, at 4800 and 5050. The dye is a strong sensitiser for the green with a maximum at 5300 Å., but the sensitising action is almost uniform up to 5400, extending to 5800 for moderate exposures.

Trimethin[2-(3-ethylidihydro-6:7-benzbenzoxazole)][3-(2:4-benzthiazine)].—This was prepared in a similar manner from 2-β-acetanilidovinyl-6:7-benzbenzoxazole ethiodide (4·84 g.), 3-methyl-2:4-benzthiazine, and pyridine, followed by aqueous ammonia, spirit, and water. After decantation of the cold aqueous layer, the residual pasty mass solidified on treatment with acetone (1·04 g. obtained). It separated from ethyl acetate (30 c.c.) in 21% yield (0·80 g.) in brown crystals with a blue reflex (Found: S, 8·2. C₂₄H₂₀ON₂S requires S, 8·3%). M. p. 163°. The absorption maximum was at 4700 Å. With addition of sulphuric acid (5 g. per 100 c.c.), there were two maxima at 4850 and 5200. The broad sensitising band has its maximum at 5400 Å. and sensitivity extends beyond 6000.

Trimethin[2-(3-ethylidihydrobenzthiazole)][3-(2:4-benzthiazine)] (XI).—This was prepared from 2-β-acetanilidovinylbenzthiazole ethiodide (4·5 g.), 3-methyl-2:4-benzthiazine, and pyridine, boiling being continued for 30 minutes. The oily precipitate, obtained by treatment with spirit and aqueous ammonia, hardened on cooling and was filtered off and washed with water. It was extracted three times with hot benzene (60 c.c. × 3);

on considerable concentration, the base crystallised (0.86 g.). The product from two such experiments was first boiled out with methyl alcohol (40 c.c.) and then boiled with enough to dissolve it (850 c.c.). It was only on great concentration (to 25 c.c.) that crystallisation occurred. The yield was 14% (0.98 g.) (Found: S, 18.1. $C_{20}H_{18}N_2S_2$ requires S, 18.3%). M. p. 199—200°. A pyridine or methyl-alcoholic solution of the dull red crystals showed a broad absorption band with maximum at 4650 Å. On addition of sulphuric acid (5 g. per 100 c.c.) to the latter, the maximum shifted to 5400 and was a sharper peak. The dye confers strong and almost uniform extra-sensitising from 5000—5700 Å., with a maximum at about 5400; the sensitising extends to 6200, but there is considerable depression of blue sensitivity.

Trimethin[2-(3-ethylidihydro-4 : 5-benzbenzthiazole)][3-(2 : 4-benzthiazine)].—2-β-Acetanilidovinyl-4 : 5-benzthiazole ethiodide (5 g.), 3-methyl-2 : 4-benzthiazine, and pyridine were refluxed for 7 minutes, and the reaction mixture treated as in other instances. The viscous product was filtered off and ground with acetone. The dark residue (2.8 g.) was boiled out with benzene (40 c.c.) and there crystallised a 23% yield (0.94 g.) of maroon-coloured needles, with a blue reflex (Found: S, 16.0. $C_{24}H_{20}N_2S_2$ requires S, 16.0%). M. p. 196°. Their methyl-alcoholic solution, or pyridine solution, had a broad indefinite absorption band, with its principal maximum at about 4800 Å. On addition of sulphuric acid (5 g. per 100 c.c.), the band became well defined and had its maximum at 5500. The base gives weak sensitising, with a flat maximum at about 5800, but it also causes general desensitisation and fog.

Trimethin[2-(3-ethylidihydrobenzelenazole)][3-(2 : 4-benzthiazine)] (XII).—2-β-Acetanilidovinylbenzelenazole ethiodide (4.97 g.), 3-methyl-2 : 4-benzthiazine, and pyridine were heated together for 5 minutes, and the reaction mixture treated as before. When cold, the precipitate was ground with water (3.59 g. obtained). It was boiled out three times with benzene (20 c.c. × 3). The benzene extracts gave a 22% yield (0.86 g.) of dull orange crystals (Found: N, 7.2. $C_{20}H_{18}N_2S_2Se$ requires N, 7.05%). M. p. 212°, with previous shrinking. The absorption maximum was at 4650 Å. in methyl alcohol or pyridine and shifted to 5450 on addition of sulphuric acid (5 g. per 100 c.c.) to the methyl alcohol. Although the substance depresses the blue sensitivity of a photographic emulsion, it is a fairly good sensitiser, with a maximum at 5200 Å., and sensitisation extends to 6400.

[2-(3-Ethylbenzoxazole)][3-(4-ethyl-2 : 4-benzthiazine)]*trimethincyanine Iodide* (XIII).—Trimethin[2-(3-ethylidihydrobenzoxazole)][3-(2 : 4-benzthiazine)] (X) (1.63 g.; 1 mol.) and ethyl *p*-toluenesulphonate (4 g.; 4 mols.) were heated together at 150—155° for 1 hour. The melt was dissolved in hot spirit (12 c.c.) and treated with a hot solution of potassium iodide (5 g.) in water (7 c.c.). The water-washed product (2.26 g.) was recrystallised from methyl alcohol (30 c.c.) and thus obtained in 57% yield (1.39 g.) (Found: I, 26.0. $C_{22}H_{23}ON_2IS$ requires I, 25.9%). M. p. 237° (decomp.). It crystallised in red needles with a blue reflex. Absorption maxima were at 4700 and 5000 Å. It is a good sensitiser, with its maximum action at 5300; sensitivity extends to 5700 for moderate exposures.

[2-(3-Ethylbenzthiazole)][3-(4-ethyl-2 : 4-benzthiazine)]*trimethincyanine Iodide* (XIV).—Trimethin[2-(3-ethylidihydrobenzthiazole)][3-(2 : 4-benzthiazine)] (XI) (0.7 g.; 1 mol.) and ethyl *p*-toluenesulphonate (0.8 g.; 2 mols.) were heated together at 150° for 1 hour. The viscous product was dissolved in hot spirit and treated with a hot aqueous solution of potassium iodide. The water-washed, crystalline solid (0.98 g.) was recrystallised from methyl alcohol (33 c.c.) and thus obtained in 61% yield (0.61 g.) (Found: I, 25.2. $C_{22}H_{23}N_2IS_2$ requires I, 25.1%). The dark bluish-grey needles had m. p. 231—232° (decomp.). The absorption maximum was at 5300 Å. The broad sensitising band extended to 6400 and had its maximum at 5500 with a slight maximum at 4700.

γ-Azatrimethin[2-(3-ethylidihydrobenzthiazole)][3-(2 : 4-benzthiazine)] (XV).—2-β-Acetanilidovinylbenzthiazole ethiodide (4.5 g.; 1 mol.), 3-amino-2 : 4-benzthiazine (1.64 g.; 1 mol.), and pyridine (10 c.c.) were refluxed for 5 minutes. The hot reaction mixture was poured into aqueous ammonia (20 c.c., *d* 0.880) and spirit (20 c.c.), and further diluted with water (40 c.c.). The water-washed product (1.02 g.) was boiled out with benzene (25 c.c.), from which, on addition of light petroleum (b. p. 40—60°), it crystallised in 20% yield (0.71 g.) (Found: S, 18.1. $C_{16}H_{17}N_3S_2$ requires S, 18.25%). The brick-red crystals had m. p. 145° (decomp.). The broad absorption band had an indefinite maximum at 4700 Å. The substance did not sensitise.

[2-(3-Ethylbenzthiazole)][3-(4-ethyl-2 : 4-benzthiazine)]*γ-azatrimethincyanine Iodide* (XVI).—2-β-Acetanilidovinylbenzthiazole ethiodide (2.0 g.; 1 mol.), 3-amino-2 : 4-benzthiazine ethiodide (1.5 g.; 1 mol.), anhydrous potassium carbonate (180-mesh; 0.63 g.; 1 mol.), and absolute alcohol (10 c.c.) were stirred and heated together on the water-bath for 7 minutes. The product obtained on cooling (2.2 g.) was recrystallised from methyl alcohol (70 c.c.); yield, 74% (1.42 g.) (Found: I, 25.0. $C_{21}H_{22}N_3IS_2$ requires I, 25.0%). The dark yellowish product had m. p. 240° (decomp.). The absorption maximum was at 4400 Å. The substance sensitised a gelatino chloride photographic emulsion from 4200 to 5000 Å., with a maximum at 4700.

We are indebted to Dr. E. P. Davey for testing the sensitising action of the compounds and to Mr. E. D. Rowell for photographing the absorption spectra.