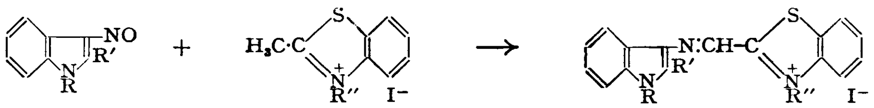
765. *The Preparation and Properties of Certain Diazadimethin Cyanine Salts.*

By R. H. Glauert, Frederick G. Mann, and A. J. Tetlow.

Several substituted [3-indole][2-benzothiazole]diazadimethincyanine salts have been prepared: all prove to be powerful desensitisers. A brief discussion of their absorption spectra and of those of the analogous monoazadimethin compounds is added.

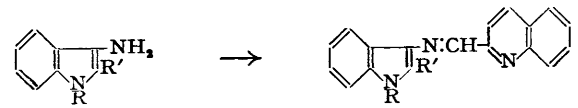
It has been shown by Mann and Haworth (*J.*, 1944, 670) that 1 : 2-disubstituted 3-nitrosoindoles (I) readily condense with the quaternary salts of many heterocyclic nitrogen compounds having appropriate reactive methyl groups to give the corresponding α-azadimethincyanine salts. For example, 1-ethyl-3-nitroso-2-phenylindole (I; R = Et, R′ = Ph) condenses with 2-methylbenzothiazole ethiodide (II; R″ = Et) to give [1-ethyl-2-phenyl-3-indole][3-ethyl-2-benzothiazole]-α-azadimethincyanine iodide (III; R = R″ = Et, R′ = Ph). Similar compounds were obtained by using the quaternary salts of 2- and 4-picoline, quinaldine, lepidine, tetrahydrobenzothiazole, benzoselenazole, etc.



(I) (II) (III)

An alternative but less convenient synthesis of certain members of this series was later developed by Huang-Hsinmin and Mann (*J.*, 1949, 2903), who condensed 3-amino-1-ethyl-2-phenylindole (IV; R = Et, R′ = Ph) and its 1 : 2-diphenyl analogue with quinoline-2-aldehyde to give the Schiff's base (V), which when quaternised gave the same α-azadimethincyanine salts as were prepared in this series by the earlier method.

All the above azadimethincyanines proved to be photographic desensitisers, and thus conform with Kendall's empirical rule (*J. Soc. Dyers and Col.*, 1936, **52**, 13) that when the nitrogen atom in a polymethin chain of a cyanine is separated from both the heterocyclic nitrogen atoms by an odd number of carbon atoms, the cyanine will be a sensitiser, but when separated from either of these nitrogen atoms by an even number of carbon atoms, the cyanine will be a desensitiser.

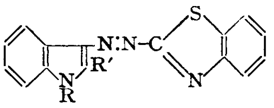
(IV)


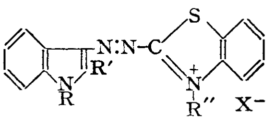
(V)

It was therefore of considerable interest to investigate the diazadimethincyanine salts corresponding to certain of the above monoazadimethin compounds, although for synthetic reasons the range of our compounds was now much more restricted. In early experiments, we attempted to diazotise the methyl methosulphate of 2-aminobenzothiazole in order to couple the product with a 1 : 2-disubstituted indole in the 3-position, but this diazotisation proved uniformly unsatisfactory, in spite of the use of a variety of conditions.

A solution of 2-aminobenzothiazole in 75% sulphuric acid underwent satisfactory diazotisation, however, since the subsequent addition of an ethanolic solution of the 1 : 2-disubstituted indole followed by neutralisation precipitated the deep orange or red azo-compounds (VI). In this way the 1 : 2-dimethyl, 1-methyl-2-phenyl, 2-*p*-chlorophenyl-1-ethyl, and the 1 : 2-diphenyl members were prepared, these compounds being selected to give a reasonable range of alkyl and aryl substituents.

Attempted quaternisation of the thiazole-nitrogen with boiling methyl iodide gave only impure products. When, however, the azo-compounds (VI) were heated with methyl toluene-*p*-sulphonate, the crystalline [1 : 2-disubstituted 3-indole][3-methyl-2-benzothiazole]diazadimethincyanine toluene-*p*-sulphonates (VII; R'' = Me, X = $C_7H_7{\cdot}SO_3$) were usually readily isolated and on treatment with sodium iodide solution gave the brownish-black crystalline cyanine iodides (VII; R'' = Me, X = I).

(VI)


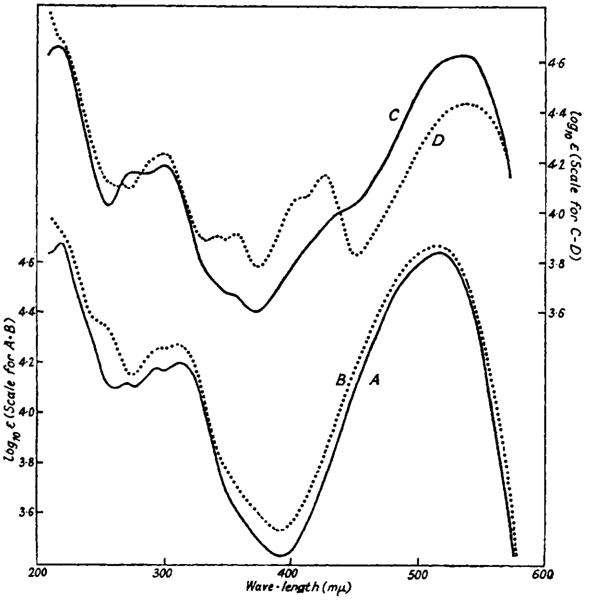


(VII)

The optical properties of these four diazadimethincyanine salts (sulphonates or iodides) have been investigated by Imperial Chemical Industries Limited, Dyestuffs Division, who find that the salts when incorporated in a chlorobromide emulsion exert a strong desensitising action. These compounds provide a particularly interesting example of Kendall's rule, since of the two nitrogen atoms of the diazadimethin chain in compounds of type (VII), the first is separated by an even, and the second by an odd, number of atoms from both the two heterocyclic nitrogen atoms. The position of the second nitrogen atom might therefore be expected to entail sensitising action; one of these compounds does in fact show slight sensitisation at 570—600 mμ at great dilution, and it is possible that the other three have similar properties, although this has not been rigorously tested. The desensitising action determined by the position of the first nitrogen atom, however, clearly heavily predominates over this weak sensitising property.

In view of the fact that our compounds of type (VII) apparently represent the first recorded series of diazadimethincyanine salts, a comparison of their absorption spectra with those of the corresponding monoazadimethin salts of type (III) should prove of interest. Certain practical difficulties have, however, limited the scope of this comparison. In the annexed Figure, *A* and *B* represent the absorption spectra of [2-*p*-chlorophenyl-1-ethyl-3-indole]- and [1 : 2-diphenyl-3-indole]-[3-methyl-2-benzothiazole]-α-azadimethincyanine iodide (as III) in 1·5 and 1·8 × 10^{-5}M ethanolic solution respectively. These solutions were stable throughout the determination, and the spectra were reproducible without change. It is noteworthy that the nature of the indole substituents has remarkably little effect on the spectra.

The curves *C* and *D* represent the spectra of the analogous diazadimethincyanine iodides (as VII) in 6·9 and 5·2 × 10^{-5}M ethanolic solution respectively (the scale of $\log_{10} \varepsilon$ values for *C* and *D* having been raised above that of *A* and *B* to avoid superposition). It is noteworthy that *C* is similar in general type to *A* and *B*, whereas *D* shows a marked minimum at 450 mμ which is absent in *A*, *B*, and *C*. When the concentration of the 1 : 2-diphenyl-3-indole derivative (as VII) was reduced from 5·2 to 1·6 × 10^{-5}M, a spectrum almost identical with the original *D* was obtained, and these spectra at both concentrations were also reproducible without change. When, however, the concentration of the 2-*p*-chlorophenyl-1-ethyl-3-indole derivative (as VII) was reduced from 6·9 to 1·4 × 10^{-5}M, the absorption underwent a steady and general decrease (with the transient appearance of a minimum at 455 mμ) during its determination, and no reliable and constant results could therefore be obtained. The 1-methyl-2-phenyl-3-indole analogue (as VII) behaved similarly. It is possibly significant that the spectrum of the 2-*p*-chlorophenyl-1-ethyl-3-indole compound was almost unaffected by 10 hours' exposure to normal electric light or by 1 hour's exposure to ultra-violet light from a mercury lamp. The change thus appeared to be caused by exposure to the light of the tungsten lamp in the spectrometer, for this exposure caused the bright red colour of the dilute solution of the 2-*p*-chlorophenyl-1-ethyl-3-indole compound to fade to a very pale brown. These factors render difficult a reliable interpretation of the marked difference between *C* and *D*, particularly in view of the close similarity of *A* and *B*. Moreover, an intensive investigation would be required to determine whether, when the transient minimum at 455 mμ developed in the modified curve *C*, the temporary similarity of this curve and *D* was co-incidental or not.



Absorption spectra of:
A, [2-p-*Chlorophenyl-1-ethyl-3-indole*][3-*methyl-2-benzothiazole*]-α-*azadimethincyanine iodide in* 1·5 × 10^{-5}M-*solution.*
B, *The* [1 : 2-*diphenyl-3-indole*] *analogue, in* 1·8 × 10^{-5}M-*solution.*
C, [2-p-*Chlorophenyl-1-ethyl-3-indole*][3-*methyl-2-benzothiazole*]*diazadimethincyanine iodide in* 6·9 × 10^{-5}M-*solution.*
D, *The* [1 : 2-*diphenyl-3-indole*] *analogue, in* 5·2 × 10^{-5}M-*solution.*

It should be added that [1 : 2-dimethyl-3-indole][3-ethyl-2-benzothiazole]dimethincyanine iodide has been prepared by Brooker, Sprague, Smyth, and Lewis (*J. Amer. Chem. Soc.*, 1940, **62**, 1116) : its spectra in pyridine and in nitromethane differ markedly from those described above.

EXPERIMENTAL

Consistent and reasonably sharp m. p.s could be obtained for the cyanine salts (III and VII) only if they were immersed in a heating-bath just below their m. p. : this temperature of immersion is stated in parentheses after the m. p.

3-(2-*Benzothiazolylazo*)-(1 : 2-*disubstituted indoles*) (VI).—A solution of 2-aminobenzothiazole (1·5 g.) in sulphuric acid (18 c.c.) previously diluted with water (10 c.c.) was cooled to 5°, and a solution of sodium nitrite (0·8 g., 1·1 mols.) in water (8 c.c.) was slowly added with stirring. The yellow diazonium solution was set aside for 30 min. at 10°, and a solution of the indole (0·5 mol.) in ethanol (25 c.c.) then added dropwise with stirring, the temperature being kept below 20°. After a further 30 min., the deep maroon-coloured solution was poured on ice and neutralised with 20% aqueous potassium hydroxide. The azo-compound was collected, extracted wth hot water (2 × 100 c.c.) to remove potassium sulphate, dried, and recrystallised from acetic acid.

3-(2-*Benzothiazolylazo*)-1 : 2-*dimethylindole* (VI; R = R′ = Me) formed orange-red needles, m. p. 213—214° (Found: C, 66·6; H, 5·0; N, 18·0. $C_{17}H_{14}N_4S$ requires C, 66·6; H, 4·6; N, 18·3%) : 44%.

The 1-*methyl*-2-*phenyl* analogue (VI; R = Me, R′ = Ph) formed crimson needles, m. p. 243·5—245° (Found: C, 71·6; H, 4·3; N, 14·9. $C_{22}H_{16}N_4S$ requires C, 71·7; H, 4·4; N, 15·2%) : 62%. The 2-p-*chlorophenyl*-1-*ethyl* analogue (VI; R = Et, R′ = C_6H_4Cl) formed orange needles, m. p. 238—239° (Found: C, 66·5; H, 4·4; N, 13·5. $C_{23}H_{17}N_4ClS$ requires C, 66·3; H, 4·1; N, 13·5%) : 57%. The 1 : 2-*diphenyl* analogue (VI; R = R′ = Ph), orange-red rhombs, had m. p. 285·5—286·5° (Found: C, 75·15; H, 4·3; N, 12·7. $C_{27}H_{18}N_4S$ requires C, 75·3; H, 4·2; N, 13·0%) : 61%. All the above compounds gave orange-coloured solutions in ethanol.

After this work had been completed, the successful diazotisation of aminobenzothiazole in dilute sulphuric acid containing formic acid was reported by Colonna and Risalti (*Gazzetta*, 1952, **82**, 31).

The [1 : 2-*Disubstituted* 3-*indole*][3-*methyl*-2-*benzothiazole*]*diazadimethincyanine Salts* (VII).—All the following salts were dried at 50°/0·1 mm. for 16 hr. before analysis. (*a*) A mixture of equal weights of the azo-compound (VI; R = R′ = Me) and methyl toluene-*p*-sulphonate was heated at 80° for 5 min. The initial red melt rapidly formed an almost black solid. The latter was triturated with ether to remove unchanged sulphonate, and the residual quaternary salt extracted with hot water. The filtered cooled extract, when treated with sodium iodide solution, deposited the [1 : 2-*dimethyl*-3-*indole*]-*cyanine iodide* (VII; R = R′ = R″ = Me, X = I), which after recrystallisation from methanol formed brownish-purple needles (43%), m. p. 184—185° (180°), giving a dull orange-red ethanolic solution; drying as above gave a stable *monohydrate* (Found: C, 46·2; H, 4·3; N, 11·8. $C_{18}H_{17}N_4IS,H_2O$ requires C, 46·35; H, 4·1; N, 12·0%). The above quaternisation, unlike those recorded below, did not proceed satisfactorily in an organic solvent. (*b*) A solution of equal weights of the azo-compound (VI; R = Me, R′ = Ph) and methyl toluene-*p*-sulphonate in xylene (100 c.c./1 g. of mixture) was boiled under reflux for 5 hr.; the [1-*methyl*-2-*phenyl*-3-*indole*]-*cyanine toluene*-p-*sulphonate* (VII; R = R″ = Me, R′ = Ph, X = $C_7H_7{\cdot}SO_3$) separated as reddish-brown needles (54%). m. p. 209—211° (205°), which when collected, washed with benzene, and dried, were pure (Found: C, 64·9; H, 4·95; N, 10·3. $C_{30}H_{26}O_3N_4S_2$ requires C, 65·0; H, 4·7; N, 10·1%). Recrystallisation from methanolic ether gave the *monohydrate*, purple-brown crystals, m. p. 171° (170°) in an open tube, 167·5—168° (165°) in a sealed tube (Found: C, 62·7; H, 5·1; N, 10·1. $C_{30}H_{26}O_3N_4S_2,H_2O$ requires C, 62·9; H, 4·9; N, 9·8%). This salt, treated in methanolic solution with aqueous sodium iodide, deposited the *monohydrated iodide*, brownish-black needles having a green iridescence, m. p. 213—214° (210°), from methanol (Found: C, 52·4; H, 4·05; N, 10·6. $C_{23}H_{19}N_4IS,H_2O$ requires C, 52·3; H, 4·0; N, 10·6%). Both these salts gave red methanolic solutions. (*c*) The azo-compound (VI; R = Et, R′ = C_6H_4Cl), treated as in (*b*) but with toluene and 45 hours' boiling, gave the [2-p-*chlorophenyl*-1-*ethyl*-3-*indole*]-*cyanine toluene*-*p*-*sulphonate* (VII; R = Et, R′ = C_6H_4Cl, R″ = Me, X = $C_7H_7{\cdot}SO_3$), as pale brown crystals (81%), m. p. 159—162° (155°) (Found: N, 9·25. $C_{31}H_{27}O_3N_4ClS_2$ requires N, 9·3%). This gave the *iodide* which separated from methanol as the stable *monohydrate*, brownish-black needles having a green iridescence, m. p. 172—173·5° (165°) with resolidification and remelting at *ca.* 200° (Found: C, 50·05; H, 3·95; N, 9·9. $C_{24}H_{20}N_4ClIS,H_2O$ requires C, 49·95; H, 3·8; N, 9·7%). It formed a red ethanolic solution. (*d*) The azo-compound (VI; R = R′ = Ph), treated as in (*b*) with 8 hours' boiling, gave the [1 : 2-*diphenyl*-3-*indole*]-*cyanine toluene*-*p*-*sulphonate* (VII; R = R′ = Ph, R″ = Me, X = $C_7H_7{\cdot}SO_3$), black crystals, m. p. 266·5—267° (265°) (Found: C, 68·0; H, 4·65; N, 9·3. $C_{35}H_{28}O_3N_4S_2$ requires C, 68·2; H, 4·55; N, 9·1%) : 49%. The *iodide* separated from methanol as black needles, m. p. 225·5° (222°) (Found: C, 58·7; H, 3·7; N, 9·65. $C_{28}H_{21}N_4IS$ requires C, 58·7; H, 3·65; N, 9·8%); it formed a red ethanolic solution. The crystals of both the sulphonate and the iodide had a green iridescence. The colour of all the above salts varies with the crystalline nature of individual crops; the colour of all by normal transmitted light was yellow or orange.

The following α-azadimethincyanine iodides were prepared for comparison with the corresponding diazadimethincyanine salts. (i) A solution of 2-*p*-chlorophenyl-1-ethyl-3-nitrosoindole

(0·22 g.) and 2-methylbenzothiazole methiodide (0·24 g., 1 mol.) in methanol (15 c.c.) was boiled for 4 hr., and on cooling deposited [2-p-*chlorophenyl*-1-*ethyl*-3-*indole*][3-*methyl*-2-*benzothiazole*]-α-*azadimethin iodide* (III; R = Et, R′ = C_6H_4Cl, R″ = Me) as black crystals, which crystallised from methanol as the *monohydrate*, reddish-brown crystals, m. p. 231° (225°) (Found: C, 52·3; H, 4·1; N, 7·2. $C_{25}H_{21}N_3ClIS,H_2O$ requires C, 52·15; H, 4·05; N, 7·3%). (ii) The [1 : 2-*diphenyl*-3-*indole*] analogue (III; R = R′ = Ph, R″ = Me), similarly prepared, when recrystallised from methanol formed reddish-brown crystals apparently of a *monomethanolate*, m. p. 202° (200°) (Found: C, 59·6; H, 4·4; N, 7·25. $C_{29}H_{22}N_3IS,CH_4O$ requires C, 59·7; H, 4·35; N, 6·95%).

The following report was furnished by Imperial Chemical Industries Limited, Dyestuffs Division.

" Four compounds of type (VII) were received, namely, (*a*) R = R′ = Me, R″ = Me, X = I (monohydrate); (*b*) R = Me, R′ = Ph, R″ = Me, X = $C_7H_7{\cdot}SO_3$; (*c*) R = Et, R′ = C_6H_4Cl; R″ = Me, X = I (monohydrate); (*d*) R = R′ = Ph, R″ = Me, X = $C_7H_7{\cdot}SO_3$. The compounds were dissolved in methanol (1/4000) and coated in a chlorobromide emulsion using 0·5, 1·5, and 5 mg. per 100 g. of emulsion. In each case strong desensitisation was produced, at the lowest concentration amounting to 5, 5, 5, and 6 steps respectively. Fog occurred at higher concentrations. In the case of (*d*), a trace of sensitisation was observed at 570—600 mμ at the lowest concentration. It is possible that all four compounds are both sensitisers and desensitisers, with the latter property strongly predominating."

We are greatly indebted to Imperial Chemical Industries Limited, Dyestuffs Division, both for the optical investigation recorded above and for the gift of various intermediate compounds.

University Chemical Laboratory, Cambridge. [*Received, July 2nd*, 1953.]