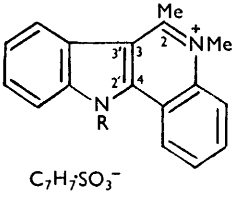
269. *Cyanine Dyes derived from 2-Methylindolo(3′ : 2′-3 : 4)quinoline.*

By Frederick G. Mann and A. F. Prior.

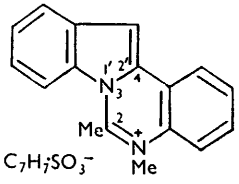
The above indoloquinoline and its 1′ : 2-dimethyl homologue readily give quaternary salts in which the reactive 2-methyl group will condense with suitable heterocyclic systems to give cyanine and azadimethincyanine salts. The properties of certain of these salts, as photographic sensitisers or desensitisers, have been investigated.

In an earlier paper,[1] we described the synthesis of 2-methylindolo(3′ : 2′-3 : 4)quinoline and the isomeric 2-methylindolo(1′ : 2′-3 : 4)quinazoline. These compounds undergo ready quaternisation with methyl toluene-*p*-sulphonate to give 1 : 2-dimethylindolo-(3′ : 2′-3 : 4)quinolinium and 1 : 2-dimethylindolo(1′ : 2′-3 : 4)quinazolinium toluene-*p*-sulphonate, (I; R = H) and (II) respectively. The corresponding 1 : 1′ : 2-trimethyl derivative (I; R = Me) has also been prepared.

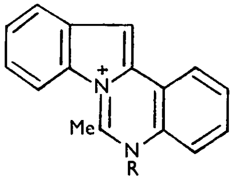
Two noteworthy points arise concerning these series of compounds. First, the quinoline and quinazoline bases corresponding to (I) and (II) are colourless and very pale yellow respectively: the salts of the quinoline base, obtained by neutralisation with acids or by quaternisation (as I) are also colourless, but the corresponding salts of the quinazoline base (as II) are bright yellow. This indicates that the quinazolinium cation receives a considerable contribution from the form (II*A*; R = H or alkyl), whereas the quinolinium cation apparently receives a very small contribution from the form analogous to (II*A*).



(I)



(II)



(II*A*)

Secondly, the 2-methyl group in the quinoline salt (I) should have high reactivity and thus with suitable reagents should form cyanine dyes: on the other hand, the 2-methyl group in quaternised pyrimidines and quinazolines very seldom shows this type of activity. We have prepared a number of cyanine dyes from the salts of type (I) but, as expected,

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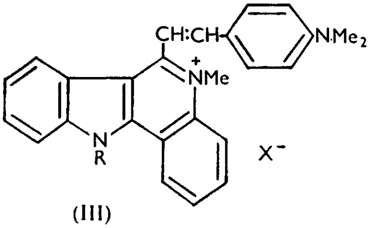
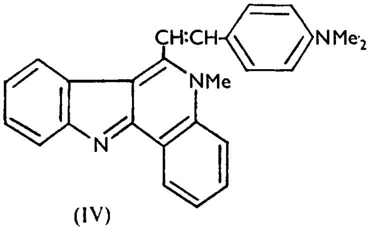
[1] Kiang, Mann, Prior, and Topham, preceding paper.

have failed with the salt (II). Furthermore, the 1 : 2-dimethylindolo(3′ : 2′-3 : 4)-quinolinium cation in (I) is, apart from other substituents, isomeric with the 1 : 2-dimethylindolo(3′ : 2′-3 : 4)*iso*quinolinium cation,* from which Huang-Hsinmin and Mann[2] prepared several cyanine dyes : comparison of the two series is of particular interest, because in the *iso*quinoline series cyanine salt formation was sometimes followed by loss of the 1-methyl group, *i.e.*, by " dequaternisation," to give a covalent compound.

In almost all cases, more rapid condensation and higher yields were obtained from the salt (I; R = Me) than from (I; R = H). Thus the salt (I; R = H) condensed with *p*-dimethylaminobenzaldehyde in acetic anhydride–triethylamine[3] to give [1-methylindolo(3′ : 2′-3 : 4)-2-quinoline][*p*-dimethylaminobenzene]dimethincyanine toluene-*p*-sulphonate (III; R = H, X = $C_7H_7{\cdot}SO_3$) but only in very low yield. Condensation by prolonged boiling in methanol–piperidine gave yellow needles of a stable monomethanol solvate of composition $C_{25}H_{21}N_3,CH_4O$ or $C_{26}H_{23}N_3,CH_4O$, formed by the loss of methyl or hydrogen toluene-*p*-sulphonate respectively from (III; R = H, X = $C_7H_7{\cdot}SO_3$). The structure of this compound is uncertain but, by analogy with the azadimethin analogue (VII) discussed below, it is probably the ψ-indolo-derivative (IV) formed by loss of toluene-*p*-sulphonic acid; alternatively, it may be the base (III; R = Me, X = OH), formed in turn by the union of methanol with (IV), which would account for its great stability. The use of the salt (I; R = Me) in ethanol–piperidine readily gave the brick-red cyanine (III; R = Me, X = $C_7H_7{\cdot}SO_3$) in 88% yield.

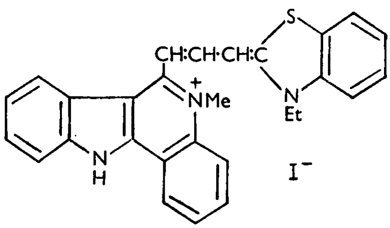


(III)



(IV)

(V)



The salt (I; R = H) condensed speedily with 2-2′-acetanilidovinylbenzothiazole ethiodide[4] to give the dark green [1-methylindolo(3′ : 2′-3 : 4)-2-quinoline][3-ethyl-2-benzothiazole]trimethincyanine iodide (V) in 38% yield : exceptionally, no satisfactory product could be isolated when the salt (I; R = Me) was used in this condensation.

The use of suitable nitroso-compounds similarly gave rise to azadimethincyanine salts. Thus the salt (I; R = H) condensed with dimethyl-*p*-nitrosoaniline in methanol–piperidine to give the crimson crystalline salt (VI; R = H, X = $C_7H_7{\cdot}SO_3$). Increasing the proportion of piperidine in this experiment gave dark-red crystals of composition $C_{24}H_{20}N_4$ or $C_{25}H_{22}N_4$, which being solvent-free could be investigated spectroscopically. Loss of methyl toluene-*p*-sulphonate from the above salt would give the base (VII*A*), whilst loss of toluene-*p*-sulphonic acid would give the methylated compound (VII*B*). The infrared spectrum of this product, in a Nujol and a hexachlorobutadiene mull, showed no indication of an :NH band in the 2·9 μ region, and the compound is therefore (VII*B*). This conclusion

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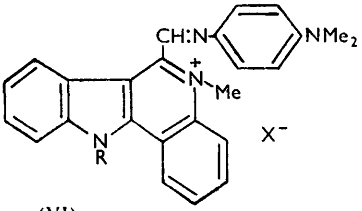
* It is noteworthy that this cation is also yellow (although the parent base is colourless) and thus resembles the cation in the salt (II) and not that in (I).

[2] Huang-Hsinmin and Mann, *J.*, 1949, 2911.

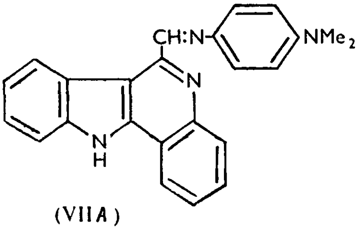
[3] Hamer, Rathbone, and Winton, *J.*, 1949, 21.

[4] Brooker, White, Keyes, Smyth, and Oesper, *J. Amer. Chem. Soc.*, 1941, **63**, 3201.

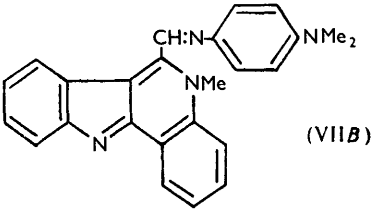
is confirmed by the fact that this compound readily combined with toluene-*p*-sulphonic acid to re-form the salt (VI; R = H, X = $C_7H_7{\cdot}SO_3$).*



(VI)



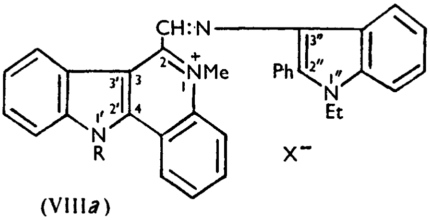
(VII*A*)



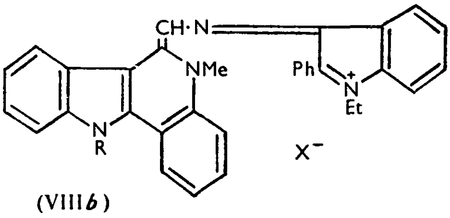
(VII*B*)

It is of interest that charge separation could occur in the compound (VII*A*) by either the :NH or the ·NMe_2 group's becoming positively charged, the quinoline-nitrogen atom in each case taking the negative charge, and in (VII*B*) by the ·NMe_2 or the :NMe group's becoming positively charged, the pyrrole-nitrogen now becoming in each case negatively charged. Both compounds are thus of the general *mero*cyanine type.

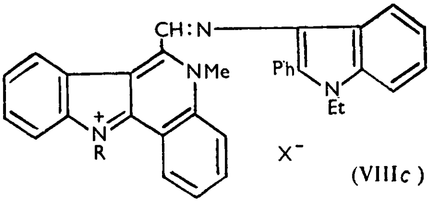
The salt (I; R = Me) reacted with dimethyl-*p*-nitrosoaniline, to give solely the 1 : 1′-dimethylcyanine salt (VI; R = Me, X = $C_7H_7{\cdot}SO_3$) in 62% yield.



(VIII*a*)



(VIII*b*)



(VIII*c*)

Particular interest attaches to the cyanine salts obtained by condensation with 3-nitrosoindoles. The salt (I; R = H) reacted very readily with 1-ethyl-3-nitroso-2-phenylindole [5] in acetic anhydride–triethylamine to form the scarlet cyanine toluene-*p*-sulphonate (VIII; R = H, X = $C_7H_7{\cdot}SO_3$) in 62% yield: the salt (I; R = Me) gave the corresponding 1 : 1′-dimethyl derivative (VIII; R = Me, X = $C_7H_7{\cdot}SO_3$). These salts, like the analogous compounds recorded by Huang-Hsinmin and Mann,[2] differ from most cyanine salts, inasmuch as the positive charge can now be carried by the three nitrogen atoms (as in VIII*a*, *b*, and *c*) instead of the usual two atoms.

The salt (I; R = H) did not apparently condense with the above nitrosoindole when a methanol–piperidine solution was boiled for 24 hr. Condensation occurred however when

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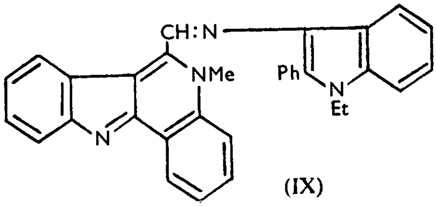
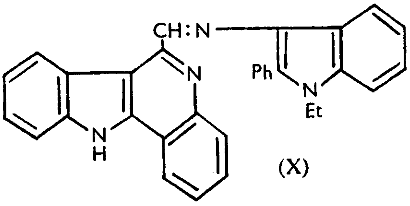
* For other examples of polycyclic *ψ*-indoles, and their reaction with acids and alkyl halides, see Mann, *J.*, 1949, 2816; Almond and Mann, *J.*, 1952, 1870; Braunholtz and Mann, *J.*, 1955, 381.

[5] Crowther, Mann, and Purdie, *J.*, 1943, 58; Mann and Haworth, *J.*, 1944, 670.

a solution of the reagents in methanol containing sodium methoxide was boiled for 50 hr., giving two products of almost identical composition, corresponding to the formula $C_{32}H_{24}N_4$ or $C_{33}H_{26}N_4$. The minor component, orange crystals, m. p. 295—297°, was almost insoluble in boiling methanol but readily recrystallised from dimethylformamide, and its infrared spectrum showed no band in the 2·9 μ region corresponding to an :NH group : it almost certainly has the *ψ*-indolo-structure (IX), having been formed by loss of toluene-*p*-sulphonic acid from the salt (VIII; R = H, X = $C_7H_7{\cdot}SO_3$). The second component, yellow crystals, m. p. 261—264°, readily recrystallised from methanol, and the infrared spectrum of the thoroughly dried material showed a band at 2·95 μ, in both Nujol and hexachlorobutadiene mull, characteristic of an :NH group. There is little doubt that this compound has the structure (X), and represents the only authenticated example of true " dequaternisation," due to loss of methyl toluene-*p*-sulphonate, encountered in the present series.



(IX)



(X)

Using 1 : 2-dimethyl-1′-phenylindolo(3′ : 2′-3 : 4)*iso*quinolinium iodide, Huang-Hsinmin and Mann [2] found that dequaternisation with loss of methyl iodide accompanied the condensation with dimethyl-*p*-nitrosoaniline and 3-nitroso-1 : 2-diphenylindole, but not that with *p*-dimethylaminobenzaldehyde and 1-ethyl-3-nitroso-2-phenylindole. Clearly, in these condensations, the presence of the 1′-phenyl group in the indolo*iso*quinoline salt would prevent any reaction comparable with the loss of toluene-*p*-sulphonic acid encountered in the present series.

The absorption and sensitising properties of some of the above compounds have been kindly investigated by Imperial Chemical Industries Limited, Dyestuffs Division. The cyanine salt (V; R = H) in particular ranks as a good sensitiser in positive and negative emulsions, comparable in action to the better known [1-*n*-butyl-2-quinoline][3-ethyl-2-benzothiazole]trimethincyanine iodide, but it does not sensitise in photographically useful regions. All the azamethin compounds tested proved to be desensitisers : this was expected, for in these compounds the nitrogen atom in the chain is separated from the heterocyclic nitrogen atoms by an even number of carbon atoms.[6] For details, see p. 1336.

EXPERIMENTAL

The cyanine derivatives described below were heated at 70—80°/0·2 mm. before analysis, but certain members retained solvent of crystallisation. This firm adherence of solvent occurs in many types of cyanine salts.

Quaternisation.—(1) A mixture of 2-methylindolo(3′ : 2′-3 : 4)quinoline (2·1 g.) and methyl toluene-*p*-sulphonate (2·1 g., 1·2 mols.) was immersed in an oil-bath and stirred with a thermometer : at 125° a vigorous reaction occurred with effervescence, the temperature rose to 150° and the melt solidified. A mixture of the cold pulverised melt and ethanol (20 c.c.) was boiled to extract much gummy impurity, and the insoluble *quinolinium* salt (I; R = H) was collected, washed with hot ethanol, and dried (yield, 2·0 g., 53%). Recrystallisation from much methanol gave the pure salt, as needles, m. p. 298—300° (decomp.) (Found : C, 69·3; H, 5·4; N, 6·6. $C_{24}H_{22}O_3N_2S$ requires C, 68·9; H, 5·3; N, 6·7%) : solutions in methanol and in water had a blue fluorescence.

(2) The 1′ : 2-dimethylindoloquinoline, similarly treated, also gave a melt which solidified, and when triturated with ether to remove unchanged sulphonate yielded the crude *quinolinium* salt (I; R = Me) in theoretical yield. Recrystallisation from ethanol gave prisms, m. p. 243—244°, also giving a blue fluorescence in ethanol and in water (Found : C, 68·75; H, 5·5; N, 6·3. $C_{25}H_{25}O_3N_2S$ requires C, 69·6; H, 6·0; N, 6·45%).

(3) A similar mixture of 2-methylindolo(1′ : 2′-3 : 4)quinazoline, heated as before, melted at

[6] Kendall, *J. Soc. Dyers and Colourists*, 1936, **52**, 13.

100—110° and underwent a vigorous reaction, the temperature rising to 140° and the bright yellow melt solidifying. The melt was extracted with ether as in (2), and the residue, when recrystallised from ethanol, afforded the pure *quinazolinium* salt (II), large lemon-coloured prisms (68%), m. p. 258—260°, readily soluble in cold water giving a non-fluorescent bright yellow solution (Found : C, 69·0; H, 5·15. $C_{24}H_{22}O_3N_2S$ requires C, 68·9; H, 5·3%).

Cyanines.—[1-*Methylindolo*(3′ : 2′-3 : 4)-2-*quinoline*][p-*dimethylaminobenzene*]*dimethincyanine toluene*-p-*sulphonate* (III; R = H, X = $C_7H_7\cdot SO_3$). A mixture of the salt (I; R = H) (0·21 g.), *p*-dimethylaminobenzaldehyde (0·1 g., 1·5 mols.), acetic anhydride (10 c.c.), and triethylamine (0·2 c.c., *ca.* 2 mols.) was boiled under reflux for 1 hr. : after 10 min. a clear brownish-red solution was obtained. The solution was poured into water (50 c.c.), the crude cyanine, m. p. 305° (decomp.), being precipitated in very low yield. Many variations in conditions of reaction and isolation gave no better yield : the united product from these experiments, when recrystallised from methanol, afforded the *cyanine* (III; R = H, X = $C_7H_7\cdot SO_3$), orange-red needles, m. p. 307—308° (decomp.) (Found : C, 71·3; H, 5·5. $C_{33}H_{31}O_3N_3S$ requires C, 71·8; H, 5·6%).

A solution of the salt (I; R = H) (0·85 g.) and the aldehyde (0·45 g., 1·5 mols.) in methanol (40 c.c.) and piperidine (0·15 c.c.) was boiled under reflux for 24 hr., concentrated to half-bulk, and set aside overnight at 0°. The crude crystalline deposit, when recrystallised from methanol, gave yellow needles, m. p. 263—265° to a bright red liquid, presumably *dimethin*-2-[1-*methyl*-ψ-*indolo*(3′ : 2′-3 : 4)*quinoline*][p-*dimethylaminobenzene*] *monomethanol solvate* (IV) [alternatively named as solvate of 2-p-*dimethylstyryl*-1-*methyl*-ψ-*indolo*(3′ : 2′-3 : 4)*quinoline*] (Found : C, 79·2; H, 5·9; N, 10·8. $C_{26}H_{23}N_3,CH_4O$ requires C, 79·2; H, 6·6; N, 10·3. $C_{25}H_{21}N_3,CH_4O$ requires C, 79·0; H, 6·4; N, 10·6%). The presence or absence of an :NH group could not be determined with certainty by infrared spectroscopy, owing to the hydroxyl band of the methanol; the name given above applies to the C_{26} compound.

The 1 : 1′-*dimethylcyanine sulphonate* (III; R = Me, X = $C_7H_7\cdot SO_3$). A mixture of the salt (I; R = Me) (0·87 g.) and *p*-dimethylaminobenzaldehyde (0·45 g., 1·5 mols.) in ethanol (40 c.c.) and piperidine (0·25 c.c.), when boiled for 30 hr., concentrated, and cooled to 0°, slowly deposited the *cyanine monoethanol solvate* (III; R = Me, X = $C_7H_7\cdot SO_3$), bright red prisms with a yellow reflex, m. p. 266—267° after recrystallisation from ethanol (Found: C, 71·3; H, 6·3; N, 7·0. $C_{34}H_{33}O_3N_3S,C_2H_6O$ requires C, 71·3; H, 6·4; N, 6·9%). One much smaller preparation gave the *monohydrate*, of identical m. p. (Found : C, 72·9; H, 6·45. $C_{34}H_{33}O_3N_3S,H_2O$ requires C, 72·5; H, 6·45%).

[1-*Methylindolo*(3′ : 2′-3 : 4)-2-*quinoline*][2-*ethyl*-2-*benzothiazole*]*trimethincyanine iodide* (V). A mixture of the salt (I; R = H) (0·21 g.), 2-2′-acetanilidovinylbenzothiazole ethiodide (0·25 g., 1 mol.), ethanol (12 c.c.), and triethylamine (0·2 c.c.) was boiled for 1 hr. and cooled. The crude deposit (0·25 g., 38%), when collected and recrystallised from methanol–pyridine (4 : 1 by vol.), gave the pure *iodide monohydrate*, dark green tablets, m. p. 264° (decomp.) (Found : C, 58·5; H, 4·7; N, 7·7. $C_{28}H_{24}N_3IS,H_2O$ requires C, 58·3; H, 4·5; N, 7·3%). The salt gives permanganate-coloured solutions; that in pyridine has a green fluorescence.

Azadimethin Cyanines.—[1-*Methylindolo*(3′ : 2′-3 : 4)-2-*quinoline*][p-*dimethylaminobenzene*]-β-*azadimethincyanine toluene*-p-*sulphonate* (VI; R = H, X = $C_7H_7\cdot SO_3$). A mixture of the salt (I; R = H) (0·85 g.), dimethyl-*p*-nitrosoaniline (0·5 g., 1·5 mols.), methanol (30 c.c.), and piperidine (0·25 c.c.) was boiled for 10 hr., small red crystals separating from the deep red solution. After cooling to 0°, the crude *cyanine sulphonate* (0·40 g., 36%) was collected and recrystallised from much methanol, giving crimson crystals, m. p. 310—311° (decomp.; immersed at 295°) (Found : C, 69·5; H, 5·8; N, 10·1. $C_{32}H_{30}O_3N_4S$ requires C, 69·7; H, 5·5; N, 10·2%). Recrystallisation from dimethylformamide gave the salt having the same m. p. No other product could be isolated from the original mother-liquor.

Repetition of this experiment, with twice the quantity of piperidine, gave dark red needles of β-*azadimethin*-2-[1-*methyl*-ψ-*indolo*(3′ : 2′-3 : 4)*quinoline*][p-*dimethylaminobenzene*] (VII*B*) [alternatively named 2-p-*dimethylanilinomethyl*-1-*methyl*-ψ-*indolo*(3′ : 2′-3 : 4-*quinoline*)] (0·21 g., 29%), which did not crystallise from methanol, but from dimethylformamide gave crimson needles, m. p. 281—281·5° (Found : C, 79·0; H, 5·7; N, 14·8. $C_{25}H_{22}N_4$ requires C, 79·3; H, 5·9; N, 14·8%). No other crystalline compound could be isolated. A solution of this product (32 mg.) and toluene-*p*-sulphonic acid (21 mg., 1·2 mols.) in dimethylformamide (20 c.c.) was gently boiled for 10 min., and when cooled deposited deep red crystals, which after one recrystallisation from this solvent had m. p. 309° (decomp.), undepressed on admixture with the authentic salt (VI; R = H, X = $C_7H_7SO_3$) of m. p. 310—311° (decomp.), both immersed at 295°.

The 1 : 1′-*dimethylindolocyanine sulphonate monohydrate* (VI; R = Me, X = $C_7H_7\cdot SO_3$) was prepared in the same way as the sulphonate (VI; R = H), but from the salt (I; R = Me) in ethanol with 7 hours' boiling (62% yield): it separated from ethanol in scarlet prisms with a yellow reflex, m. p. 275—276° (decomp.; immersed at 265°) (Found: C, 69·1; H, 6·1; N, 9·7. $C_{33}H_{32}O_3N_4S,H_2O$ requires C, 68·6; H, 5·9; N, 9·65%).

[1-*Methylindolo*(3′ : 2′-3 : 4)-2-*quinoline*][1″-*ethyl*-2″-*phenyl*-3″-*indole*]-β-*azadimethincyanine toluene*-p-*sulphonate* (VIII*a*—*c*; R = H, X = $C_7H_7\cdot SO_3$). A solution of the salt (I; R = H) (0·21 g.) and 1-ethyl-3-nitroso-2-phenylindole (0·15 g., 1·5 mols.) in hot acetic anhydride (10 c.c.) was treated with triethylamine (0·2 c.c., 2 mols.) and boiled for 15 min. The blood-red solution, on cooling, deposited the *cyanine sulphonate monohydrate* (0·2 g., 62%), scarlet needles, m. p. 255—257° after crystallisation from dimethylformamide (Found: C, 71·8; H, 5·4. $C_{40}H_{34}O_3N_4S,H_2O$ requires C, 72·1; H, 5·4%). Increasing the scale of this experiment did not give a corresponding increase in the yield.

When the salt (I; R = H) (0·65 g.) and the indole (0·55 g., 1·5 mols.) were added to the product from the interaction of sodium (20 mg.) and methanol (25 c.c.), which was then boiled for 50 hr. and cooled, a mixed crop of crystals appeared. These were collected and extracted with boiling methanol. The undissolved residue (78 mg.), when crystallised from dimethylformamide, gave β-*azadimethin*-2-[1-*methyl*-ψ-*indolo*(3′ : 2′-3 : 4)*quinoline*]-3″-[1″-*ethyl*-2″-*phenylindole*] (IX) [alternatively named 2-(1-*ethyl*-2-*phenyl*-3-*indolyliminomethyl*)-1-*methyl*-ψ-*indolo*-(3′ : 2′-3 : 4)*quinoline*], orange needles, m. p. 295—297° (decomp.) (Found: C, 82·1; H, 6·0; N, 11·9. $C_{32}H_{26}N_4$ requires C, 82·7; H, 5·5; N, 11·7%). The methanolic extract, when worked up, yielded β-*azadimethin*-2-[*indolo*(3′ : 2′-3 : 4)*quinoline*]-3″-[1″-*ethyl*-2″-*phenylindole* (X) (alternatively named analogously to (IX)] (0·15 g.), yellow crystals, m. p. 261—264° to a deep red liquid, after recrystallisation from much methanol (Found: C, 82·2; H, 6·0; N, 11·8. $C_{32}H_{24}N_4$ requires C, 82·7; H, 5·2; N, 12·05%). The infrared spectrum of this compound has a band at 2·95 μ: otherwise the spectra of the bases (IX) and (X) are closely similar, and they have a strong band at 6·17 and 6·18 μ respectively, which is in the region in which a band due to the ·CH:N· group would be expected.

The 1 : 1′-*dimethylindolocyanine sulphonate* (VIII*a*—*c*; R = Me, X = $C_7H_7\cdot SO_3$) was readily obtained when a solution of the salt (I; R = Me) (0·7 g.) and the indole (0·5 g., 1·1 mols.) in ethanol (25 c.c.) and piperidine (0·25 c.c.) was boiled for 5 hr., concentrated, and cooled to 0°. The deposited sulphonate (0·65 g., 61%), when recrystallised from ethanol, formed deep red prisms with a yellow reflex, m. p. 254—255° (Found: C, 73·75; H, 5·2; N, 8·5. $C_{41}H_{36}O_3N_4S$ requires C, 74·0; H, 5·4; N, 8·5%).

Attempts to form a cyanine salt by the condensation of the salt (I; R = Me) and quinoline-2-aldehyde gave indefinite results.

The absorption and sensitising properties of certain of the above compounds are given in the Table.

Compound	$\lambda_{max.}$(mμ)	$10^{-4}\epsilon$	Sensitising max. (mμ)	Sensitising extends to (mμ)	Remarks
(III; R = Me, X = $C_7H_7\cdot SO_3$)	444	1·8	~510	615	Weak sensitiser for positive (Cl/Br) emulsions
			550 *	670 *	Rather better in negative (I/Br) emulsions.
(V)	555	8·3	585	640	Good sensitiser in positive and negative emulsions, but does not sensitise in useful region
			~580 *	665 *	
(VI; R = H, X = $C_7H_7\cdot SO_3$) ...	435	1·2	No sensitisation		Desensitiser
(VI; R = Me, X = $C_7H_7\cdot SO_3$)	462	1·45	,,		Strong desensitiser
(VII*B*)	417 *	1·45	,,		Moderately strong desensitiser
(VIII; R = H, X = $C_7H_7\cdot SO_3$)	462	2·1	,,		Desensitiser
(VIII; R = Me, X = $C_7H_7\cdot SO_3$)	450	1·6	,,		Moderately strong desensitiser

The values for $\lambda_{max.}$ were determined in methanolic solution except that for (VII*B*), which was determined in 2-ethoxyethanol. The sensitising maxima were determined in chlorobromide emulsions except those marked *, which were in iodobromide emulsions.

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