979. *The Reactivity of the Alkylthio-group in Nitrogen Ring Compounds. Part IV.* Quaternary Salts of 4-Substituted Quinazolines.*†

By D. J. Fry, J. D. Kendall, and A. J. Morgan.

The quaternisation of 4-methylquinazoline and of 4-alkylthioquinazolines at the $N_{(1)}$ atom has been proved, and the salts obtained have been used in the preparation of typical cyanine and merocyanine dyes. The evidence for the quaternisation of quinazoline at $N_{(3)}$ has been examined and confirmed.

THE preparation of cyanine dyes from quaternary salts of 4-methyl- (I; R = Me) and 4-methylthio-quinazoline (I; R = SMe) was first described by Kendall,[1] who formulated the salts as either (II or III; R = Me or SMe).

Gabriel and Colman [2] concluded that in quinazoline (I; R = H) $N_{(3)}$ is the quaternary

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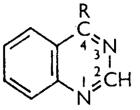
* Part III, Ficken and Kendall, *J.*, 1960, 1537.

† Part of this work was presented to the Fine Chemicals Group of the Society of Chemical Industry at a meeting at King's College, London, in February, 1956 (see *Chem. and Ind.*, 1956, 339).

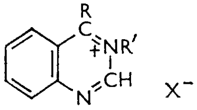
[1] Kendall, B.P. 425,609.

[2] Gabriel and Colman, *Ber.*, 1904, **37**, 3643.

centre, whilst Morley and Simpson [3,4] have shown that the basic centre is the $N_{(1)}$ atom in 4-phenoxyquinazoline and in 6- and 7-nitro-4-anilino- and -4-acetamido-quinazoline. It therefore seemed desirable to establish unequivocally which is the quaternary nitrogen atom in the salts of the 4-substituted quinazolines (I; R = Me or SMe).



(I)



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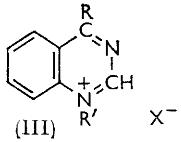
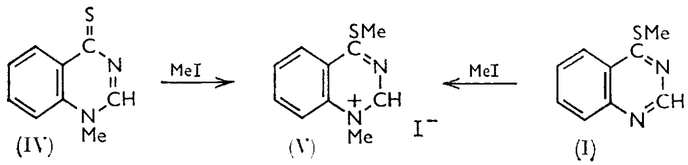


(III)

Fry and Kendall [5] showed that identical methiodides are obtained by reaction of methyl iodide with either a heterocyclic thione such as 1,2-dihydro-1-methyl-2-thiobenzothiazole or an alkylthio-derivative such as 2-methylthiobenzothiazole. The quaternary centre of 4-methylthioquinazoline should therefore be ascertainable by comparison of its quaternary salt with those from 1,4-dihydro-1-methyl- and 3,4-dihydro-3-methyl-4-thioquinazoline.

1-Methyl-4-quinazolone [6] (unambiguously synthesised from *o*-methylaminobenzoic acid and formamide) was converted by phosphorus pentasulphide into 1,4-dihydro-1-methyl-4-thioquinazoline (IV). This, with methyl iodide, gave 1-methyl-4-methylthioquinazolinium iodide (V) which was identical with the product from 4-methylthioquinazoline (I; R = SMe) and methyl iodide. Hence, in the base (I; R = SMe), $N_{(1)}$ is the quaternary centre. The identity was confirmed by using the methiodide prepared by each method to form a typical cyanine and merocyanine dye; in both dye syntheses the same dye was obtained irrespective of the origin of the methiodide. Thus reaction between the salt (V) and 2-methylbenzothiazole methiodide produced 1,3′-dimethyl-4,2′-quinazolinethiacyanine iodide and between the same salt (V) and 3-ethylrhodanine produced 3-ethyl-5-(1,4-dihydro-1-methylquinazolin-4-ylidene)rhodanine. Likewise, 2-methylbenzothiazole when heated with methyl toluene-*p*-sulphonate and either the methylthio- (I; R = SMe) or the thio-derivative (IV) gave 1,3′-dimethyl-4,2′-quinazathiacyanine toluene-*p*-sulphonate.



The quaternisation at $N_{(1)}$ in the methiodide of 4-methylthioquinazoline was further confirmed by conversion by aqueous sodium sulphide [7] or boiling pyridine [8] into the base (IV) and hydrolysis with an excess of aqueous sodium hydroxide to *o*-methylaminobenzoic acid. With one equivalent of sodium hydroxide the methiodide (V) (or, more conveniently, the corresponding methotoluene-*p*-sulphonate) gave, not the expected 1-methyl-4-quinazolone (cf. the behaviour of 2-methylthiobenzothiazole methiodide [7]), but a non-basic isomer. This substance on alkaline hydrolysis gave ammonia, *o*-methylaminobenzoic acid, and a steam-volatile reducing acid (presumably formic). These properties, together with the empirical formula, suggested that it was *o*-(*N*-methylformamido)benzonitrile. This structure was confirmed by its synthesis from formic acid and *o*-methylaminobenzonitrile,[9] although difficulty was experienced in conducting the formylation without hydrolysis of the nitrile to the amide.

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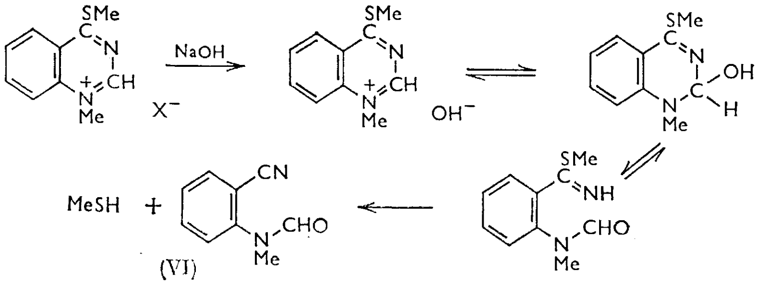
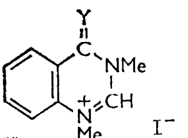
[3] Morley and Simpson, *J.*, 1949, 1354.
[4] Morley and Simpson, *J.*, 1948, 360.
[5] Fry and Kendall, *J.*, 1951, 1716.
[6] Leonard and Ruyle, *J. Org. Chem.*, 1948, **13**, 903.
[7] Sexton, *J.*, 1939, 470.
[8] Kendall, B.P. 475,647.
[9] Grammaticakis, *Bull. Soc. chim. France*, 1953, **20**, 207.

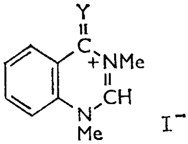
The annexed reaction sequence is suggested for the formation of the nitrile. The tautomerism of pseudo-bases with decyclised amino-aldehydes is well known,[10] as is the ready conversion of ethylthiobenzimidoate into benzonitrile.[11]


(VI)

The formyl derivative (VI) when heated with one equivalent of aqueous sodium hydroxide or, less effectively, with dilute mineral acid was converted into 1-methyl-4-quinazolone, which was also formed if a 4-methylthioquinazoline quaternary salt was heated with two equivalents of aqueous sodium hydroxide. As an incidental observation bearing on the behaviour of alkylthio-substituted heterocyclic quaternary salt with alkali, we were unable to repeat the experiment in which O. Fischer[12] obtained 1,2-dihydro-1-methyl-2-thioquinoline from its methiodide with potassium hydroxide: in our hands, 2-methylthioquinoline methiodide with one equivalent of sodium hydroxide gave the expected 1-methyl-2-quinolone.

3-Methyl-4-quinazolone[13] (prepared from anthranilic acid and *N*-methylformamide) with phosphorus pentasulphide produced 3,4-dihydro-3-methyl-4-thioquinazoline. This, with methyl iodide, formed a methiodide which did not undergo the reactions to be expected for a compound with the structure 3-methyl-4-methylthioquinazolinium iodide. No dye was formed when the salt was heated in a basic medium with 2-methylbenzothiazole or 3-ethylrhodanine, and the salt was recovered from boiling pyridine solution. It was shown to be dihydro-1,3-dimethyl-4-thioquinazolinium iodide (VII or VIIa; Y = S) by its identity with material obtained by the thiation of the quinazolone (VII or VIIa; Y = O) which Bogert and Geiger[14] prepared by the action of methyl iodide on 4-methoxyquinazoline, 3-methyl-4-quinazolone, or 4-quinazolone.


(VII)


(VIIa)

Morley and Simpson[3] treated the quaternary salt (VII or VIIa; Y = O) with 2N-sodium hydroxide and obtained an oil which was assumed to be isomeric with the expected pseudo-base (VIII) since its picrate was different from the picrate of the salt (VII or VIIa; Y = O). It seemed to us that the compound obtained by Morley and Simpson might, by ring-chain tautomerism, be *N*-methyl-*o*-(*N*-methylformamido)benzamide (IX). However, Morley and Simpson's analyses were in better agreement with the deformylated product

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[10] Ingold, "Structure and Mechanism in Organic Chemistry," London, G. Bell and Sons, Ltd., 1953, p. 578.

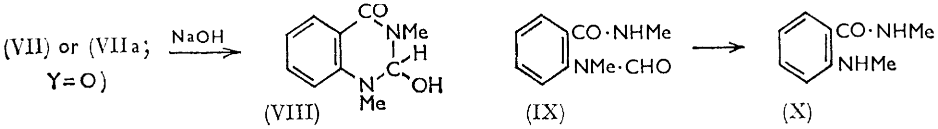
[11] Bernthsen, *Annalen*, 1879, **197**, 350.

[12] Fischer, *Ber.*, 1902, **35**, 3677.

[13] Knape, *J. prakt. Chem.*, 1890, **43**, 209; Bogert and Geiger, *J. Amer. Chem. Soc.*, 1912 **34**, 524.

[14] Bogert and Geiger, *J. Amer. Chem. Soc.*, 1912, **34**, 683.

(X): this structure was confirmed by its synthesis from *N*-methylisatoic anhydride [15] and methylamine. Its picrate was identical (m. p. and infrared absorption) with the picrate obtained from the oil produced by the action of sodium hydroxide on the quinazolone (VII or VIIa; Y = O).



(VIII) (IX) (X)

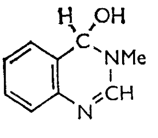
4-Ethylthioquinazoline (I; R = SEt) with methyl iodide formed a single quaternary salt which was identical with the product from ethyl iodide and 1,4-dihydro-1-methyl-4-thioquinazoline and was therefore 4-ethylthio-1-methylquinazolinium iodide. Likewise, 1-ethyl-4-methylthioquinazolinium iodide was prepared by interaction of either 4-methylthioquinazoline and ethyl iodide or 1-ethyl-1,4-dihydro-4-thioquinazoline and methyl iodide. There was no anomalous quaternisation such as has been observed in the quinoline,[16] benzothiazole,[16] and thiazine [17] series.

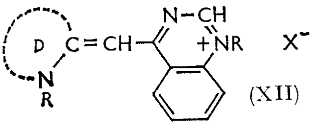
4-Methylquinazoline with methyl iodide formed a methiodide which could not be purified but could be used to provide cyanine dyes. With 2-methylthiobenzothiazole methiodide it gave a dye identical with that described above from 1-methyl-4-methylthioquinazolinium iodide and 2-methylbenzothiazole methiodide; and hence in 4-methylquinazoline methiodide, $N_{(1)}$ is again the quaternary centre. Likewise, fusion of 4-methylquinazoline with 2-methylthiobenzothiazole and methyl toluene-*p*-sulphonate gave 1,3′-dimethyl-4,2′-quinazolinethiacyanine toluene-*p*-sulphonate. 1,4-Dihydro-1-methyl-4-[2-methyl-2-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-ylidene)ethylidene]quinazoline was obtained by reaction either between 4-isopropylidene-3-methyl-1-phenylpyrazol-5-one and 1-methyl-4-methylthioquinazolinium toluene-*p*-sulphonate or between 4-methylquinazoline methotoluene-*p*-sulphonate, ethyl orthoacetate, and 3-methyl-1-phenylpyrazol-5-one.

Because the above work added two further examples to the number of quinazoline derivatives in which $N_{(1)}$ is the basic centre, attention was directed to Gabriel and Colman's evidence [2] for $N_{(3)}$ as the basic centre in quinazoline (I; R = H).

Quinazoline methiodide (which Gabriel *et al.*[2] could obtain crystalline only as the methanol solvate) was obtained analytically pure as a very deliquescent yellow solid by interaction of pure quinazoline and pure methyl iodide. With alkali it gave the stable solid, sparingly soluble in water to give a weakly basic solution, which Gabriel *et al.* considered to be the corresponding quaternary hydroxide. The same substance was synthesised by Schöpf and Oechler,[18] who formulated it as the pseudo-base (XI), which structure seems in better agreement with the physical properties. They did not, however, make a direct comparison with a sample obtained from quinazoline.

(XI)





(XII)

With picric acid quinazoline methiodide gave the picrate which we have found to be identical with the picrate synthesised by Schöpf and Oechler's method. The picrate melted at 180°, whereas Schöpf *et al.* record 145—146°. This may be the temperature at which ethanol of crystallisation is lost, since a sample placed in a bath preheated to

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[15] Heilbron, Kitchen, Parkes, and Sutton, *J.*, 1925, **127**, 2171.

[16] Beilenson and Hamer, *J.*, 1939, 143; Sexton, *J.*, 1939, 470; Fry and Kendall, *J.*, 1951, 1716.

[17] Beilenson, Hamer, and Rathbone, *J.*, 1945, 222; Hamer and Rathbone, *J.*, 1945, 243.

[18] Schöpf and Oechler, *Annalen*, 1936, **523**, 1.

145° melted but quickly resolidified, to remelt at 180°. Schofield[19] has also observed 3-methylquinazolinium picrate to melt at 176—178°. After completion of our work, Osborn and Schofield[20] independently confirmed that the pseudo-base (XI) from quinazoline methiodide was identical with the substance unambiguously synthesised by the method of Schöpf *et al.* As an additional confirmation, we have oxidised the pseudo-base (XI) (from quinazoline methiodide) to 3-methyl-4-quinazolone, isolated as the picrate.

There is therefore now ample confirmatory evidence of the correctness of the assignment of $N_{(3)}$ as the quaternary centre in quinazoline methiodide.

The stability of the pseudo-base (XI) recalls the stability of 3,4-dihydroquinazoline[21] and is another illustration of the marked tendency for position 3,4 in quinazoline to acquire the dihydro-structure.[22]

The crude ethotoluene-*p*-sulphonate of 4-methylquinazoline gave, with ethyl orthoformate in pyridine, the symmetrical trimethinquinazoline cyanine dye, isolated as the iodide. The Table records the preparation of a number of monomethine cyanine dyes (XII) containing the quinazoline nucleus.

EXPERIMENTAL

Light-absorption measurements were determined on a Unicam S.P. 500 spectrophotometer for ethanol solutions; values in parentheses are log ε. Infrared absorptions were measured for Nujol suspensions with a Perkin–Elmer model 137 spectrophotometer.

4-*Mercaptoquinazoline* (I; R = SH).—(*a*) Hydrogen sulphide was passed into a solution of potassium hydroxide (15 g.) in dry ethanol (100 c.c.) until a gain in weight of 8—9 g. was shown. To this solution was added 4-chloroquinazoline (22 g.); some reaction occurred with the production of a yellow precipitate. After 1 hour's heating on a water-bath the precipitate was filtered off (m. p. 300°). The filtrate on acidification gave a further crop of the same material. The total weight was 19·7 g. (92%). The thiol formed yellow needles (from acetic acid), m. p. 312° [lit.,[23] 312° or 324—325° (corr.)] (Found: S, 19·6. Calc. for $C_8H_6N_2S$: S, 19·75%).

(*b*) 4-Quinazolone (110 g.) and phosphorus pentasulphide (179 g.) were mixed and dry pyridine (770 c.c.) was added. The mixture was boiled under reflux for 3 hr., then poured into warm water (1200 c.c.) with stirring to decompose the excess of phosphorus pentasulphide. A yellow solid separated, which was collected when cold and washed with water. It was purified by dissolving it in 10% aqueous sodium hydroxide (400 c.c.), filtering from a little insoluble material, and acidifying the filtrate with hydrochloric acid (*d* 1·16), to precipitate the yellow product (114 g., 93%), m. p. 320—322°.

4-*Methylthioquinazoline* (I; R = SMe).—4-Mercaptoquinazoline (114 g.) was dissolved in 10% aqueous sodium hydroxide (270 c.c.), and methyl iodide (40 c.c.) added. The mixture was shaken for 1 hr., during which the temperature rose to 40° and an oil separated. This solidified and was distilled (b. p. 172°/18 mm.). 4-Methylthioquinazoline (104 g., 84%) was obtained and after two crystallisations from light petroleum (b. p. 60—80°) formed pale yellow needles, m. p. 64—65° (lit.,[1] m. p. 68°) (Found: C, 61·4; H, 4·6; N, 15·9; S, 18·05. Calc. for $C_9H_8N_2S$: C, 61·35; H, 4·6; N, 15·9; S, 18·2%), $\lambda_{max.}$ 279 (3·84), 288 (3·84), 320 (3·96), 330 (3·94), 305 (sh) (3·82), 315 (sh) (3·95), 340 mμ (sh) (3·74), $\lambda_{min.}$ 255 (3·47), 285 (3·81), 295 (3·70), 325 mμ (3·91). The *methotoluene*-p-*sulphonate* crystallised from acetone–ethanol–ether as a cream-coloured slightly hygroscopic solid, m. p. 147—150° (Found: C, 56·5; H, 5·2; N, 7·9; S, 17·2. $C_{17}H_{18}N_2O_3S_2$ requires C, 56·35; H, 5·0; N, 7·75; S, 17·7%).

1,4-*Dihydro*-1-*methyl*-4-*thioquinazoline* (IV).—(*a*) 1-Methyl-4-quinazolone[6] (1·2 g.), phosphorus pentasulphide (1·8 g.), and pyridine (8·0 c.c.) were heated under reflux for 2 hr. at 150° and the dark brown liquid poured into hot water (15 ml.). An orange-brown solid separated which was filtered off, washed, and dried. 1,4-*Dihydro*-1-*methyl*-4-*thioquinazoline* crystallised from ethanol (1 in 50) as orange-yellow needles (0·6 g.), m. p. 192—194° (Found: C, 60·95; H, 4·7; N, 15·75; S, 18·4. $C_9H_8N_2S$ requires C, 61·35; H, 4·6; N, 15·9; S, 18·2%), $\lambda_{max.}$ 244 (3·86), 266 (3·68), 380 mμ (4·23), $\lambda_{min.}$ 230 (3·76), 255 (3·65), 325 mμ (3·21).

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[19] Schofield, personal communication.
[20] Osborn and Schofield, *J.*, 1957, 4191.
[21] Gabriel, *Ber.*, 1903, **36**, 808.
[22] Dewar, *J.*, 1944, 621.
[23] Leonard and Curtin, *J. Org. Chem.*, 1946, **11**, 349.

(*b*) 4-Methylthioquinazoline methiodide (6·36 g.), sodium sulphide nonahydrate (4·8 g.), and water (20 c.c.) were mixed and left at room temperature for 20 hr. A pale yellow flocculent solid (3·7 g.) separated and was collected (m. p. 155—177°). This crystallised from ethanol (1 g. in 50 ml.) to give an orange-yellow solid (1·8 g.), m. p. 191—194°, not depressed on admixture with material obtained as above.

(*c*) A solution of 4-methylthioquinazoline methiodide (4·5 g.) in pyridine (45 c.c.) was boiled for 2 hr. About 30 c.c. of the solvent were removed by distillation *in vacuo* and the residue was cooled in ice and diluted with water. A brown solid separated (1·0 g.) which crystallised from ethanol in needles, m. p. and mixed m. p. 192—193° (Found: C, 61·05; H, 4·4; N, 15·4; S, 18·35%).

3,4-*Dihydro*-3-*methyl*-4-*thioquinazoline*.—(*a*) 3-Methyl-4-quinazolone [11] (16·0 g.) was ground with phosphorus pentasulphide (22·2 g.), heated with pyridine (150 c.c.) at 150° for 2 hr., and then poured into hot water (1250 c.c.). After cooling in ice-water, 3,4-*dihydro*-3-*methyl*-4-*thioquinazoline* (11·1 g.) was collected. Crystallisation from dry benzene gave pale yellow crystals, m. p. 144—147° (Found: N, 16·45; S, 18·05%), $\lambda_{max.}$ 282 (3·80), 352 (4·12), 365 (sh) mμ (3·97), $\lambda_{min.}$ 245 (3·40), 305 (3·51), 335 (sh) mμ (3·96).

Dihydro-1,3-*dimethyl*-4-*thioquinazolinium Iodide* (VII; Y = S).—(*a*) 3,4-Dihydro-3-methyl-4-thioquinazoline (2·9 g.) and dry methyl iodide (2·9 c.c.) were heated in benzene (20 c.c.) for 20 hr. When cold, the solid (2·5 g.) product was filtered off, washed with dry benzene, and dried (m. p. 142—235°). Some unchanged thione was removed by grinding with dry benzene and then refiltering. The residual quaternary *iodide* (1·6 g.), after crystallisation from ethanol (1 g. in 60 ml.) formed orange-yellow needles, m. p. 230—231·5° (decomp.) (Found: C, 38·1; H, 3·9; N, 8·9; S, 9·9; I, 39·95. $C_{10}H_{11}IN_2S$ requires C, 37·75; H, 3·5; N, 8·8; S, 10·1; I, 39·9%), $\lambda_{max.}$ 283 (4·12), 285 (4·12), 295 (sh) (4·07), 350 (sh) (4·05), 355 (4·06), 365 (sh) mμ (4·02), $\lambda_{min.}$ 260 (3·86), 284 (4·11), 320 mμ (3·73).

(*b*) Dihydro-1,3-dimethyl-4-oxoquinazolinium iodide [3,14] (VII; Y = O) (4·7 g.) and phosphorus pentasulphide (3·5 g.) were fused for 6 hr. at 145°. The brownish-orange mass was extracted with chloroform, and the extracts were evaporated to dryness. The residue crystallised from ethanol (1 g. in 60 ml.) as a pale yellow solid, m. p. and mixed m. p. 221·5—224°. The ultraviolet and infrared absorption data were also correct.

4-*Methylquinazoline Methiodide* (III; R = R′ = Me).—Redistilled 4-methylquinazoline [1,24] (1·44 g.) and dried, redistilled methyl iodide (1·42 g.) were mixed and left overnight in a sealed tube. The mixture solidified to a brownish-orange glass (2·75 g.) which was powdered and dried over phosphorus pentoxide in a vacuum-desiccator; the quaternary *salt* had m. p. 101—108° (decomp.) but was very deliquescent and it was not possible to crystallise it (Found: C, 42·95; H, 4·05; N, 10·2; I, 42·55. $C_{10}H_{11}IN_2$ requires C, 41·95; H, 3·9; N, 9·8; I, 44·35%), $\lambda_{max.}$ 266 (3·75), 341 (2·85), 490 mμ (2·45), $\lambda_{min.}$ 245 (3·47), 333 (2·80), 420 mμ (2·40).

1-*Methyl*-4-*methylthioquinazolinium Iodide* (III; R = Me, R′ = Me).—(*a*) 4-Methylthioquinazoline (17·6 g.) and dry methyl iodide (17·6 c.c.) were mixed and heated under reflux on a water-bath for 4 hr. The orange-yellow 1-*methyl*-4-*methylthioquinazolinium iodide* (28·8 g.) separated rapidly as a hard mass. It was ground with dry ether and dry acetone and recrystallised from ethanol (1 g. in 50 ml.), m. p. 217—219° (decomp.) (Found: S, 10·15· N, 8·95; I, 39·5. $C_{10}H_{11}IN_2S$ requires S, 10·1; N, 8·8; I, 39·9%), $\lambda_{max.}$ 295 (sh) (3·65), 306 (3·70), 315 (3·71), 345 (3·94), 355 mμ (3·92), $\lambda_{min.}$ 267 (3·42), 310 (3·70), 323 (3·70), 352 mμ (3·91).

(*b*) 1,4-Dihydro-1-methyl-4-thioquinazoline (0·5 g.), dry methyl iodide (2·0 c.c.), and dry benzene (50 c.c.) were heated together for 6 hr. The orange-yellow product (0·6 g.) was filtered off from the hot solution, washed with dry benzene, and dried (m. p. 206·5—209·5°). After two crystallisations from ethanol the methiodide had m. p. 219—220° (decomp.) and gave no depression in m. p. when mixed with the product prepared by method (*a*). The ultraviolet and infrared absorption data also were identical.

1,3′-*Dimethyl*-4,2′-*quinazathiacyanine Toluene*-p-*sulphonate*.—(*a*) 1,4-Dihydro-1-methyl-4-thioquinazoline (0·88 g.), 2-methylbenzothiazole (0·75 g.), and methyl toluene-*p*-sulphonate (1·86 g.) were fused together for 3 hr. at 140°, giving an orange-yellow solid. This was heated in warm ethanol (30 c.c.) with triethylamine (0·7 c.c.) for 30 min. on the water-bath. The *dye* (1·5 g.) that separated from the hot solution was collected after cooling, and washed with a little ethanol and ether (m. p. 297—305°). Two crystallisations from methanol (1 g. in 30 ml.)

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[24] Elderfield and Serlin, *J. Org. Chem.*, 1951, **16**, 1669.

gave orange-yellow needles, m. p. 304—304·5° (Found: C, 62·6; H, 4·9; N, 8·65; S, 13·45. $C_{25}H_{23}N_3O_3S_2$ requires C, 62·85; H, 4·85; N, 8·8; S, 13·45%), $\lambda_{max.}$ 296 (3·91), 430 (sh) (4·45), 453 (4·74), 480 mμ (4·82), $\lambda_{min.}$ 265 (3·52), 360 (2·98), 465 mμ (4·64). Incorporated in a gelatine-silver iodo-bromide photographic emulsion the spectral sensitivity was extended to 540 with a max. at 500 mμ.

(*b*) 4-Methylquinazoline (0·72 g.), 2-methylthiobenzothiazole (0·91 g.), and methyl toluene-*p*-sulphonate (1·86 g.) were heated together as in (*a*). The orange-yellow dye (0·8 g.), m. p. 306·5—308° (after two crystallisations from methanol), was obtained as orange-yellow crystals (0·4 g.), m. p. and mixed m. p. 310° (Found: N, 8·65; S, 13·6%). The ultraviolet, visible, and infrared absorptions and the photographic sensitising data were identical.

(*c*) 4-Methylthioquinazoline (0·88 g.), 2-methylbenzothiazole (0·75 g.), and methyl toluene-*p*-sulphonate (1·86 g.) were caused to react as above. The product (1·7 g.), twice crystallised from methanol, gave needles (0·8 g.), m.p. and mixed m. p. 304·5—305° (absorption identical) (Found: N, 8·45; S, 13·6%).

1,3′-*Dimethyl*-4,2′-*quinazathiacyanine Iodide*.—(*a*) To 4-methylquinazoline methiodide (1·43 g.) and 2-methylthiobenzothiazole methotoluene-*p*-sulphonate (1·84 g.) in warm ethanol (40 c.c.), triethylamine (0·7 c.c.) was added; dye began to separate immediately. After 15 min. the mixture was cooled and the *dye* [1·2 g., m. p. 288—290° (decomp.)] filtered off. After crystallisation from methanol (1 g. in 200 ml.) and pyridine (1 g. in 150 ml.) it had m. p. 294—295° (decomp.) (Found: C, 49·55; H, 4·2; S, 7·5; I, 29·1. $C_{18}H_{16}IN_3S$ requires C, 49·9; H, 3·7; S, 7·4; I, 29·3%), $\lambda_{max.}$ 295 (3·81), 425 (sh) (4·42), 453 (4·75), 479 mμ (4·85), $\lambda_{min.}$ 260 (2·63), 360 (2·63), 465 mμ (4·65).

(*b*) 1-Methyl-4-methylthioquinazolinium iodide (from 1,4-dihydro-1-methyl-4-thioquinazoline) (0·4 g.), 2-methylbenzothiazole methiodide (0·4 g.), and triethylamine (0·15 c.c.) in ethanol (5 c.c.) were treated as in (*a*). The orange crystals (0·5 g.), after crystallisation from ethanol, had m. p. 294—295° (decomp.), not depressed when admixed with the product from (*a*). The ultraviolet, visible, and infrared absorption data were identical.

(*c*) 1-Methyl-4-methylthioquinazolinium iodide (from 4-methylthioquinazoline) (1·59 g.) and 2-methylbenzothiazole methiodide (1·46 g.) in ethanol (50 c.c.) were treated with triethylamine (0·7 c.c.) as in (*a*). The product (2·5 g.; m. p. 288—295°) was crystallised twice from methanol (1 g. in 200 ml.) and then from ethanol (1 g. in 200 ml.), to give orange crystals, m. p. and mixed m. p. 293—295° (decomp.) (Found: S, 7·55; I, 29·15%) (absorption identical).

Other Dyes.—Other *dyes* prepared are recorded in the annexed Table.

4-(3-*Ethyl*-4-*oxo*-2-*thiothiazolidin*-5-*ylidene*)-1,4-*dihydro*-1-*methylquinazoline*.—(*a*) 1-Methyl-4-methylthioquinazolinium iodide (from 1,4-dihydro-1-methyl-4-thioquinazoline) (1·6 g.) and 3-ethylrhodanine (0·81 g.) were boiled in pyridine (15 c.c.) for 30 min. When cold, the *dye* (1·3 g.; m. p. 301—306°) was collected, washed with ethanol and ether, and extracted with boiling chloroform (100 c.c.), which raised the m. p. to 306—308° (Found: C, 55·15; H, 4·45; N, 13·35; S, 21·25. $C_{14}H_{13}N_3OS_2$ requires C, 55·45; H, 4·3; N, 13·85; S, 21·15%), $\lambda_{max.}$ 285 (3·68), 310 (3·84), 340 (sh) (3·40), 458 (sh) (4·58), 463 (4·59), 485 (sh) mμ (4·56), $\lambda_{min.}$ 280 (3·65), 290 (3·65), 360 mμ (2·50).

(*b*) 1-Methyl-4-methylthioquinazolinium iodide (from 4-methylthioquinazoline) (1·6 g.) was treated with 3-ethylrhodanine in pyridine as above. The product (1·0 g.) had m. p. and mixed m. p. 306—308° (Found: N, 13·8; S, 21·15%) (infrared absorptions identical).

1,4-*Dihydro*-1-*methyl*-4-[2-*methyl*-2-(3-*methyl*-5-*oxo*-1-*phenyl*-2-*pyrazolin*-4-*ylidene*)*ethylidene*]-*quinazoline*.—(*a*) 1-Methyl-4-methylthioquinazolinium methotoluene-*p*-sulphonate (7·2 g.) and 4-isopropylidene-3-methyl-1-phenylpyrazol-5-one (4·28 g.) were treated in warm ethanol (30 c.c.) with triethylamine (2·8 c.c.) and, after 30 minutes' heating, the mixture was cooled and the *dye* (3·0 g.; m. p. 216—219°) filtered off. It was washed with ethanol and ether and, twice crystallised from benzene (1 g. in 200 ml.), formed dark brown crystals with a bronze reflex, m. p. 223—224° (decomp.) (Found: C, 73·95; H, 5·8. $C_{22}H_{20}N_4O$ requires C, 74·15; H, 5·65%), $\lambda_{max.}$ 232 (4·43), 320 (3·63), 535 (4·62), 440 (sh) mμ (4·13), $\lambda_{min.}$ 220 (4·23), 307 (3·56), 357 mμ (3·00).

(*b*) 4-Methylquinazoline (1·8 g.) and methyl toluene-*p*-sulphonate (2·4 g.) were heated together on a water-bath for 2 hr. To the crude metho-toluene-*p*-sulphonate in hot ethanol (40 c.c.) were added 3-methyl-1-phenylpyrazol-5-one (2·3 g.), ethyl orthoacetate (4·0 c.c.), and triethylamine (3·6 c.c.). The mixture was boiled under reflux for 2 hr., and then cooled. The dye (0·5 g.) was collected, washed with ethanol and ether, and crystallised twice from benzene

Monomethine dyes (XII) *prepared by fusion together of* 4-*methylthioquinazoline, methyl-substituted heterocyclic bases, and alkyl toluene*-p-*sulphonates.*

No.	Residue D	R	X	Yield (%)	Colour [a]	M. p.
1	Benzothiazole	Et	I	40	Orange	295
2	Benzoxazole	Et	I	33	Orange	285
3	4-Quinoline	Et	I	24	Crimson	278
4	2-Quinoline	Me	I	41	Red	262
5	Benzoxazole	Me	I	27	Yellow	285
6	Naphtho[1,2-*d*]-oxazole	Me	I	5	Red	258
7 [c]	,, ,,	Et	I	8·5	Red-brown	265
8	Naphtho[2,1-*d*]-thiazole	Me	I	37	Red-orange	>300
9 [c]	,, ,,	Et	I	45	Red-orange	>300
10	Benzoselenazole	Me	Br	22	Orange	>300
11	4-Quinazoline	Et	I	7	Golden-brown	258

	Required (%)				Found (%)			$\lambda_{max.}$	
No.	I	N	S	Formula	I	N	S	(mμ)	log ε
1	27·6	—	—	$C_{20}H_{20}IN_3S$	27·8	—	—	453 480	4·67 4·68
2	28·6	—	—	$C_{20}H_{20}IN_3O$	28·7	—	—	442 465	4·55 4·59
3	27·95	—	—	$C_{22}H_{22}IN_3$	27·9	—	—	505 530	4·71 5·01
4	29·7	9·85	—	$C_{20}H_{18}IN_3$	29·85	9·85	—	478 510	4·60 4·81
5	29·3	9·65	—	$C_{18}H_{16}IN_3O,H_2O$ [b]	29·15	9·75	—	440 466	4·65 4·68
6	27·2	—	—	$C_{22}H_{18}IN_3O$	27·5	—	—	460 485	4·54 4·44
7	25·65	—	—	$C_{24}H_{22}IN_3O$	25·75	—	—	460 485	4·61 4·47
8	—	—	6·7	$C_{22}H_{18}IN_3S$	—	—	7·0	471 501	4·65 4·64
9	—	—	6·3	$C_{24}H_{22}IN_3S$	—	—	6·6	470 500	4·74 4·70
10	—	—	—	$C_{18}H_{17}BrN_3Se$ [d]	—	—	—	457 484	4·67 4·91
11	27·8	—	—	$C_{21}H_{21}IN_4$	27·95	—	—	459 489	4·57 4·69

[a] Needles from EtOH. [b] Found: C, 50·05; H, 4·4. Required: C, 49·7; H, 4·1%. [c] From 4-ethylthioquinazoline. [d] Found: Br, 18·3. Required: Br, 18·4%.

to give dark brown crystals, m. p. and mixed m. p. 224° (decomp.) (Found: C, 74·2; H, 5·75%) (infrared absorption identical with the above material).

Action of Sodium Hydroxide on 1-*Methyl*-4-*methylthioquinazolinium Salts.*—(*a*) 1-Methyl-4-methylthioquinazolinium iodide (6·36 g.) was boiled in aqueous 0·99N-sodium hydroxide (20·3 c.c.) for 2 hr. An oil appeared soon but gradually dissolved, and methanethiol was evolved. A yellow oil which separated from the cooled solution later crystallised and was collected (2·0 g.) and washed with a little ether. After crystallisation from benzene–light petroleum the o-N-*methylformamidobenzonitrile* (VI) had m. p. 69—70° and sublimed at 90°/1 mm. (Found: C, 67·5; H, 5·15; N, 17·35%; *M*, 151. $C_9H_8N_2O$ requires C, 67·5; H, 5·05; N, 17·5%; *M*, 160). It did not depress the m. p. of the authentic material (see below) and had identical infrared absorption curves, and $\lambda_{max.}$ 284 (3·20), 235 (sh) (3·80), 310 (sh) mμ (2·28), $\lambda_{min.}$ 265 mμ (2·91) (cf. data for *o-N*-methylacetamidobenzonitrile [9]).

(*b*) The methiodide (4 g.) was boiled with 10% aqueous sodium hydroxide (10 c.c.) for 6 hr., by which time the oil which first separated had redissolved. The cold solution was acidified with dilute hydrochloric acid, and the precipitate washed and ground with water to remove inorganic material. After crystallisation from ethanol *o*-methylaminobenzoic acid (0·3 g.), m. p. and mixed m. p. 177—182° (decomp.), was obtained.

(*c*) 1-Methyl-4-methylthioquinazolinium methotoluene-*p*-sulphonate (3·62 g.) was set aside in 1·04N-aqueous sodium hydroxide (9·6 c.c.) for 16 hr. The solid dissolved rapidly and methanethiol was evolved. The mixture was then extracted with ether, and the solvent removed to leave a yellow oil (1·5 g.) which solidified. Crystallisation from benzene–light petroleum gave a solid (0·8 g.), m. p. 67—69° alone or mixed with material obtained as in (*a*).

Hydrolysis of o-N-*Methylformamidobenzonitrile.*—(*a*) The amide (0·5 g.) (from methiodide) in

10% aqueous sodium hydroxide (10 c.c.) was boiled for 3 hr. and the evolved gases were aspirated through 3% alcoholic picric acid: a yellow solid separated. The alkaline solution was cooled and acidified with dilute sulphuric acid to precipitate *o*-methylaminobenzoic acid, m. p. and mixed m. p. 178—181·5° (decomp.). The filtrate was steam-distilled. The aqueous distillate had pH 4 and reduced cold aqueous alkaline potassium permanganate. Filtration of the picric acid gave ammonium picrate (0·6 g.), m. p. and mixed m. p. 280—282° (decomp.) (from ethanol).

(*b*) The nitrile (0·8 g.) in N-sodium hydroxide (10 c.c.) was boiled for 2½ hr. The solid (0·4 g.) which crystallised after cooling was collected and recrystallised from hot water to give *o*-methylaminobenzamide, m. p. and mixed m. p. 158—160° (Found: C, 65·4; H, 6·7; N, 18·55. Calc. for $C_8H_{10}N_2O$: C, 64·0; H, 6·7; N, 18·65%). [*Picrate*, leaflets (from ethanol), m. p. 208—210° (decomp.) (Found: C, 44·8; H, 3·85; N, 18·35. $C_{14}H_{13}N_5O_8$ requires C, 44·35; H, 3·45; N, 18·45%].

1-*Methyl*-4-*quinazolone*.—(*a*) To *o*-*N*-methylformamidobenzonitrile (0·5 g.) in water (5 c.c.) was added N-sodium hydroxide (3·2 c.c.). After 2 hours' boiling the solution was cooled and impure *o*-methylaminobenzamide (0·05 g.) filtered off [picrate, m. p. and mixed m. p. 208—210° (decomp.)]. Addition of picric acid to the filtrate precipitated 1-methyl-4-quinazolone picrate (0·3 g.), m. p. and mixed m. p. 244—247° (decomp.) (lit., 246—247°,[6] 249—250° [3]).

(*b*) The same amido-nitrile (0·5 g.) was boiled in water (5 c.c.) and N-hydrochloric acid (3·25 c.c.) for 2 hr.; the cooled mixture was filtered from some unchanged nitrile, then warmed and treated with picric acid (0·45 g.) in hot alcohol (15 c.c.). 1-Methyl-4-quinazolone picrate (0·2 g.) crystallised, having m. p. 243—245° (decomp.).

(*c*) 4-Methylthioquinazoline methotoluene-*p*-sulphonate (1·81 g.) in N-aqueous sodium hydroxide (10 c.c.) was kept overnight. After filtration from *o*-*N*-methylformamidobenzonitrile (0·3 g.; m. p. 68—70°) addition of picric acid (1·0 g.) in ethanol (25 c.c.) to the hot filtrate precipitated 1-methyl-4-quinazolone picrate (0·5 g.), m. p. and mixed m. p. 243—245° (decomp.).

o-*Methylaminobenzonitrile*.—Anthranilonitrile (11·8 g.) and dimethyl sulphate (16 g.) were boiled in 2N-sodium hydroxide (60 c.c.) for 1 hr. The oil (3·5 g.) which separated solidified and was twice crystallised from light petroleum, giving *o*-methylaminobenzonitrile (2·0 g.), m. p. 64—68° (lit.,[9] m. p. 70°) (Found: N, 21·0. Calc. for $C_8H_8N_2$: N, 21·2%).

o-N-*Methylformamidobenzonitrile*.—*o*-Methylaminobenzonitrile (0·5 g.) and formic acid (3·0 c.c.; *d* 1·2) were heated at 50—55° for 1 hr. The excess of formic acid was removed by evaporation at 50°/20 mm. and the oily residue extracted with light petroleum (b. p. 40—60°; 10 c.c.) to yield a yellow solid, m. p. 40—44°, which did not depress the m. p. of the starting material. A second similar extraction of the residue gave *o*-methylformamidobenzonitrile, m. p. 64—67° (a mixture with *o*-methylaminobenzonitrile melted at 35—40°). It crystallised from benzene–light petroleum as needles, m. p. 69—70° (Found: C, 67·3; H, 5·0%). The residue from the light petroleum extractions was impure *o*-*N*-methylformamidobenzamide, m. p. 85—95°.

o-N-*Methylformamidobenzamide*.—The preceding amido-nitrile (0·5 g.) and formic acid (1·0 c.c.; *d* 1·2) were boiled for 1 hr. The excess of acid was removed by evaporation *in vacuo*, the residue solidifying. After crystallisation from benzene the product had m. p. 110—113° (Knape [13] gives m. p. 113°).

Quinazoline Methiodide.—Quinazoline (1·5 g.) and methyl iodide (1·15 c.c.) were left together overnight. The very deliquescent hard yellow *methiodide*, m. p. (sealed capillary tube) 165°, was dried for analysis over phosphorus pentoxide at 80°/2 mm. (Found: N, 9·95; I, 46·25. $C_9H_9IN_2$ requires N, 10·3; I, 46·65%).

3,4-*Dihydro*-4-*hydroxy*-3-*methylquinazoline* (XI).—The methiodide (from 4·4 g. of quinazoline) in water (30 c.c.) was treated with 33% aqueous potassium hydroxide (6 c.c.), and the solid (3·7 g., 68%) was collected; it had m. p. 158° (Gabriel and Colman [2] give m. p. 162—163°; Schöpf and Oechler [18] give m. p. 164—165°). With picric acid it gave 3-methylquinazolinium picrate, also obtained from aqueous quinazoline methiodide and picric acid. The picrate separated from alcohol as yellow solvate, m. p. 180° (Found: C, 48·4; H, 4·35; N, 16·75. Calc. for $C_{15}H_{11}N_5O_7,C_2H_6O$: C, 48·7; H, 4·1; N, 16·7%). Schöpf and Oechler [18] give m. p. 145—146°. A sample prepared by their method melted at 180° and did not depress the m. p. of our sample; the infrared absorptions were identical. Both samples melted when placed in a bath preheated to 145°, then resolidified and remelted at 180°. The alcohol of crystallisation is probably lost at the first m. p.

Oxidation of 3,4-*Dihydro*-4-*hydroxy*-3-*methylquinazoline.*—To the pseudo-base (0·5 g.) (from quinazoline methiodide) in acetic acid (8 c.c.) was added at 60° during 20 min. a solution of chromium trioxide (0·42 g.) in 66% aqueous acetic acid (3 c.c.). The mixture was heated at 60° for an additional 2 hr. and poured into a solution of picric acid (1 g.) in hot water (20 c.c.). The picrate (1·2 g., 100%) of 3-methyl-4-quinazolone separated immediately; it had m. p. (from alcohol) 208°, as did a mixture with the picrate (m. p. 208°) prepared from 3-methyl-4-quinazolone (Schöpf and Oechler [18] give m. p. 209—210°; Morley and Simpson,[3] m. p. 215—216°) (Found: C, 46·4; H, 3·2; N, 17·9. Calc. for $C_{15}H_{11}N_5O_8$: C, 46·3; H, 2·9; N, 18·0%.) The infrared absorptions of the two picrates were identical.

Degradation of 3,4-*Dihydro*-4-*hydroxy*-3-*methylquinazoline.*—The compound (3·5 g.) was steam-distilled with potassium hydroxide (see Gabriel and Colman [2]), the volatile oil (1·8 g.) mixed with hydrochloric acid (4 c.c.; *d* 1·18), and the bright red dihydrochloride (1·1 g.) of *o-o'*-aminobenzylideneaminobenzaldehyde methylimide collected. The same substance (2 g.) was obtained by action of hydrochloric acid on *N*-*o*-aminobenzylidenemethylamine (3·2 g., from 3·4 g. of *o*-aminobenzaldehyde). The free bases liberated from the hydrochlorides by ammonia melted, after recrystallisation from alcohol, at 192°, as did their mixture (Gabriel and Colman [2] record m. p. 190°).

1-*Methyl*-2-*quinolone.*—2-Methylthioquinoline methiodide (1·59 g.) was kept in N-sodium hydroxide (5 c.c.) for 72 hr. The oily product was extracted in chloroform and the solvent removed. Crystallisation of the residue from light petroleum (b. p. 40—60°; 20 c.c.) gave 1-methyl-2-quinolone (0·3 g.), m. p. and mixed m. p. 69—70°.

N-*Methyl*-o-*methylaminobenzamide* (X).—*N*-Methylisatoic anhydride [15] (11·7 g.), water (30 c.c.), and 30% methylamine solution (15 c.c.) were heated on a water-bath for 20 min. The mixture rapidly became oily but later a clear solution was obtained. Extraction with ether gave N-*methyl*-o-*methylaminobenzamide* (10·5 g.), b. p. 199—201°/22 mm. After two crystallisations from cyclohexane this formed needles, m. p. 43—45° (Found: C, 66·5; H, 7·05; N, 16·95. $C_9H_{12}N_2O$ requires C, 65·85; H, 7·35; N, 17·05%). The *picrate* was obtained as yellow laths (from ethanol), m. p. 184—186° (decomp.) (Found: C, 46·15; H, 3·85; N, 17·45. $C_{15}H_{15}N_5O_8$ requires C, 45·8; H, 3·85; N, 17·8%). It did not depress the m. p. of the picrate (0·5 g.; m. p. 184—185°) obtained from the oil formed by treating dihydro-1,3-dimethyl-4-oxoquinazolinium iodide (VII; Y = O) (0·5 g.) with alkali according to Morley and Simpson's procedure [3] (Found: C, 46·1; H, 4·15; N, 17·75%) (Morley *et al.* give m. p. 188—189° and comparable analytical figures). The two picrates had identical infrared absorption curves.

4-*Ethylthioquinazoline* (I; R = SEt).—Quinazoline-4-thione (60 g.), 20% aqueous sodium hydroxide (60 ml.), ethanol (150 ml.), and ethyl bromide (50 ml.) were heated on a water-bath for 3 hr. After dilution with water the liquors were extracted with benzene, the extracts were dried (K_2CO_3) and evaporated, and the residue distilled (b. p. 174°/16 mm.). From light petroleum the 4-*ethylthioquinazoline* (18 g.) formed crystals, m. p. 33—35° (Found: C, 62·75; H, 5·3; S, 16·65. $C_{10}H_{10}N_2S$ requires C, 63·1; H, 5·3; S, 16·85%).

1-*Ethyl*-4-*ethylthioquinazolinium Iodide.*—4-Ethylthioquinazoline (5 g.) and ethyl iodide (5 ml.) were refluxed for 6 hr. The product was ground with dry acetone, filtered, washed with a little acetone, and dried. The *salt* (5·5 g.), crystallised three times from ethanol, formed yellow crystals (2 g.), m. p. 152—156° (Found: S, 9·25; I, 36·3. $C_{12}H_{15}IN_2S$ requires S, 9·25; I, 36·65%). With boiling 10% aqueous sodium hydroxide it gave *N*-ethylanthranilic acid, m. p. and mixed m. p. 155—158°.[25]

1-*Ethyl*-1,4-*dihydro*-4-*thioquinazoline.*—4-Ethylthioquinazoline (7·6 g.) and ethyl toluene-*p*-sulphonate (8 g.) were heated together for 6 hr. at 145—150°, allowed to cool, and treated with sodium sulphide (9·6 g.) in water (50 ml.); during 72 hr. at room temperature some orange-coloured solid separated; this was filtered off and the filtrate extracted with benzene. The benzene extracts were evaporated to dryness to give an orange solid *product* (4·7 g.), that from ethanol formed orange crystals, m. p. 146—149° (Found: N, 14·75; S, 16·9. $C_{10}H_{10}N_2S$ requires N, 14·75; S, 16·85%).

1-*Ethyl*-4-*methylthioquinazolinium Iodide.*—1-Ethyl-1,4-dihydro-4-thioquinazoline (3·8 g.) and dry methyl iodide (4 ml.) were heated for 4 hr., then cooled, ground with dry acetone, collected, washed with acetone, and dried. The orange-yellow *product* (5·5 g.), crystallised three times from ethanol, had m. p. 198—199° (1·5 g.) (Found: S, 9·2; I, 38·2. $C_{11}H_{13}IN_2S$ requires S, 9·65; I, 38·2%).

[25] Houben and Brassert, *Ber.*, 1906, **39**, 3237.

4-Methylthioquinazoline (3·5 g.) and ethyl iodide (4 ml.) yielded, as above, the same product, m. p. and mixed m. p. 198—200°.

4-*Ethylthio*-1-*methylquinazolinium Iodide*.—1,4-Dihydro-1-methyl-4-thioquinazoline (1·76 g.) was heated in warm chloroform (50 ml.) with dry ethyl iodide (2 ml.) for 16 hr., the solvent was removed *in vacuo*, and the residual solid ground with dry acetone, collected, washed with acetone, and dried. The yellow *product* (2·7 g.) had m. p. 154—155° (Found: S, 9·7. $C_{11}H_{13}IN_2$ requires S, 9·65%). On attempted crystallisation from ethanol some ethanethiol was eliminated and the solid which crystallised was less pure.

(*b*) 4-Ethylthioquinazoline (1·9 g.) and dry methyl iodide (2 ml.) gave the same iodide (3·2 g.), m. p. and mixed m. p. 156·5—157·5° (Found: S, 9·65%).

1,1′-*Diethyl*-4,4′-*quinazacarbocyanine Iodide*.—4-Methylquinazoline (3 g.) and ethyl toluene-*p*-sulphonate (4 g.) were heated together at 140° for 3 hr. The quaternary salt was then dissolved in dry pyridine (30 ml.), ethyl orthoformate (8 ml.) added, and the solution boiled for 3 hr. The deep blue solution was poured into an aqueous solution of potassium iodide (10 g.). The *dye* which separated on cooling was filtered off and from methanol formed green crystals (1·3 g.), m. p. 286°; $\lambda_{max.}$ 600 (4·80), 650 mμ (5·22) (Found: I, 26·75. $C_{23}H_{23}IN_4$ requires I, 26·3%).

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