what more acid soluble than II and tends to precipitate more slowly. These observations were not, however, strictly reproducible and there was considerable variation in the amount and composition of the mixtures from run to run even under apparently "identical" conditions. The figures given in Table I represent the average of several runs.

A brief investigation was also made of the effect on product distribution of varying the amount of I used for coupling. It was found that above the stoichiometric amount there was essentially no variation in the yields of II, III, and IV, but that the rate of coupling appeared to be more rapid with excess I present.

In analogy to the preparation of II by neutralization of an acid solution of V, neutralization of the diazonium solution prepared from equivalent amounts of I and sodium nitrate also gave II.

Experimental[5]

1,3-Bis[3-(5-amino-1,2,4-triazolyl)]triazene (III).—A mixture of 2.0 g. (0.016 mole) of V and 50 ml. of concentrated hydrochloric acid was stirred 1 hr. at 25°. The chilled solution was then added to a cold solution of 1.6 g. (0.016 mole) of I in 50 ml. of water. After 1 hr., the precipitate was filtered, dried, and recrystallized from methanol to give 2.1 g. (46.5%) of bright yellow needles, m.p. 187° dec. (explosive). This material was the dihydrochloride of III[6] (IIIa).

Anal. Calcd. for $C_4H_7N_{11}\cdot 2HCl$: C, 17.0; H, 3.2; Cl, 25.2; N, 54.6. Found: C, 16.7; H, 3.5; Cl, 24.8; N, 54.5.

Infrared (Nujol mull): 3290 (m), 3210 (m), 3175 (s), 2700 (s), 2550 (m), 1690 (s), 1650 (s), 1485 (m), 1260 (s), 1115 (m), 1055 (m), 920 (s), 800 (m), 715 (s).

3,5-Bis{[3-(5-amino-1,2,4-triazolyl)]triazenyl}-1,2,4-triazole (IV).—A solution of 0.69 g. (0.01 mole) of sodium nitrite in 10 ml. of water at 5° was slowly added to a cold slurry of 2.8 g. (0.01 mole) of IIIa in 100 ml. of 10% hydrochloric acid. A clear solution was rapidly obtained. To this solution was added 1.0 g. (0.01 mole) of I in 20 ml. of water. The resulting precipitate was filtered and washed thoroughly with boiling water to give 1.8 g. (56%) of IV, an orange-red solid, m.p. >300°. A recrystallization solvent could not be found and microanalysis[7] was performed on the crude, washed material.

Anal. Calcd. for $C_6H_9N_{17}$: C, 22.6; H, 2.8; N, 74.6. Found: C, 22.7; H, 2.8; N, 74.6.

Infrared (Nujol mull): 3320 (m), 3160 (s), 1640 (s), 1560 (m), 1330 (m), 1210 (m), 1080 (m), 925 (m), 720 (m).

Poly(3-diazoamino-1,2,4-triazole) (II). A. From V.—A mixture of 2.0 g. (0.016 mole) of V and 50 ml. of concentrated hydrochloric acid was stirred 1 hr. at 25°, then chilled to 10° and neutralized with 5 *N* sodium hydroxide. The resulting precipitate was filtered, washed with boiling water, and dried to give 0.78 g. (45%) of II, a dark red, amorphous solid, m.p. >300°.

B. From IIIa.—A solution of 1.73 g. (0.025 mole) of sodium nitrite in 20 ml. of water at 5° was slowly added to a cold slurry of 2.8 g. (0.01 mole) of IIIa in 100 ml. of 10% hydrochloric acid. A cold solution of 1.0 g. (0.01 mole) of I in 20 ml. of water was then added to this solution. The precipitate was washed with boiling water to give 1.0 g. (31%) of II.

The infrared spectra of the products from A and B above were identical. They were also identical with that of IV except for a broadening and loss of sharpness of the various bands.

Microanalyses of II varied with the molecular weight (see below) of the polymer but were in a range.

Anal. Calcd. for $C_2H_2N_6$: C, 21.8; H, 1.8; N, 76.4. Found: C, 21.5–22.5; H, 2.0–2.5; N, 75–76.

Extreme insolubility of II made accurate determinations of molecular weight impossible, but estimates of 1000–2000 were obtained by nonaqueous titration.

Diazotization and Coupling of I.—Data on this reaction is summarized in Table I. A typical experiment was run as follows. A finely powdered, dry mixture of 5.0 g. (0.05 mole) of I and 10.4 g. (0.15 mole) of sodium nitrite was flooded with 100 ml. of concentrated hydrochloric acid. The mixture was stirred several minutes, chilled for 0.5 hr., and filtered. The cold filtrate was added, with vigorous stirring, to 7.5 g. (0.075 mole) of I in 100 ml. of water. The precipitate was filtered, dried, and extracted with three 200-ml. portions of boiling water. The water-insoluble material was II. Concentration and chilling of the aqueous extracts gave a precipitate of IIIa.

The reaction filtrate on standing overnight deposited additional solid. This material was filtered, dried, and extracted with two 25-ml. portions of boiling water. The insoluble material was IV. Concentration and chilling of the extracts gave more of IIIa.

Preparation of II from a Diazonium Solution.—A mixture of 2.0 g. (0.02 mole) of I and 1.4 g. (0.02 mole) of sodium nitrite was flooded with 50 ml. of concentrated hydrochloric acid. The mixture was chilled 0.5 hr. and filtered. The chilled filtrate was then carefully neutralized with 5 *N* sodium hydroxide. The precipitate was filtered and washed with boiling water to give 0.77 g. (35%) of II.

Acknowledgment.—The author is indebted to Miss Oksana Logush for technical assistance and to the Research Service Department, Stamford Laboratories, for microanalyses and aid in the interpretation of infrared spectra.

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[5] Melting points were taken on a calibrated Fisher-Johns apparatus. Infrared spectra were taken on a Perkin-Elmer Infracord spectrophotometer.

[6] Compound IIIa was often obtained as a hemihydrate; note the following analysis: Calcd. for $C_4H_7N_{11}\cdot 2HCl\cdot 0.5H_2O$: C, 16.5; H, 3.4; Cl, 24.4; N, 52.9; neut. equiv., 291. Found: C, 16.4; H, 3.3; Cl, 23.9; N, 52.7; *neut. equiv., 293. Drying at 130° (1 mm.) was required for complete* dehydration.

[7] Compound IV was often obtained as a hydrate: Calcd. for $C_6H_9N_{17}\cdot H_2O$: C, 21.4; H, 3.3; N, 70.6. Found: C, 21.6; H, 3.2; N, 70.1. Drying at 130° (1 mm.) was required for dehydration.

Some Merocyanines with Chelating Properties

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Received June 8, 1964

We have prepared several merocyanines in which the oxygen-containing ring of the merocyanine function is also a chelating center (of the 8-quinolinol type) for metals, a class of compounds believed to be novel solvatochromic reagents for metal ions.

Solvatochromic compounds are substances that change color in solution as a function of solvent polarity; large effects, shifts of absorption maxima of 50–100 mμ or more in going from aqueous to nonpolar solvents, are shown by merocyanines[1] as well as several other kinds of compounds.[2] In our previous studies of solvatochromic chelating agents we have examined reagents in which the solvatochromism was (in principle) not affected by the chelation and others in which solvatochromism was impaired to some extent by chelation.[3,4] Here we consider reagents in which the solvatochromism is supplied by a merocyanine function that is eliminated through employment of its phenolic oxygen in the chelation; thus the reagents may be solvatochromic but not the chelates.

5-[β-(N-Methyl-5-ethyl-2-pyridyl)vinyl]-8-hydroxyquinoline iodide (I) and related compounds (see Table I) were prepared in 65–85% yields by piperidine-catalyzed condensations of 5-formyl-8-quinolinols with

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[1] J. P. Phillips and J. T. Leach, *J. Org. Chem.*, **27**, 3309 (1962).

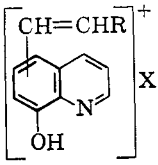
[2] J. P. Saxena, W. H. Stafford, and W. L. Stafford, *J. Chem. Soc.*, 1579 (1959); S. Hünig and O. Rosenthal, *Ann.*, **582**, 161 (1955).

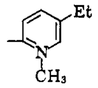
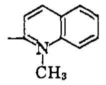
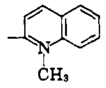
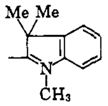
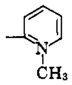
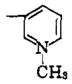
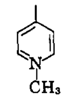
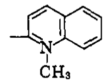
[3] A. Mueller, J. T. Leach, and J. P. Phillips, *Talanta*, **10**, 1087 (1963).

[4] J. W. Faller and J. P. Phillips, *ibid.*, **11**, 641 (1964).

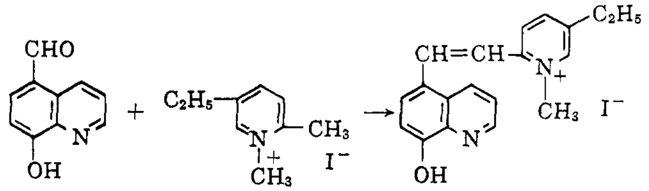
TABLE I

MEROCYANINE-TYPE SOLVATOCHROMIC CHELATING AGENTS

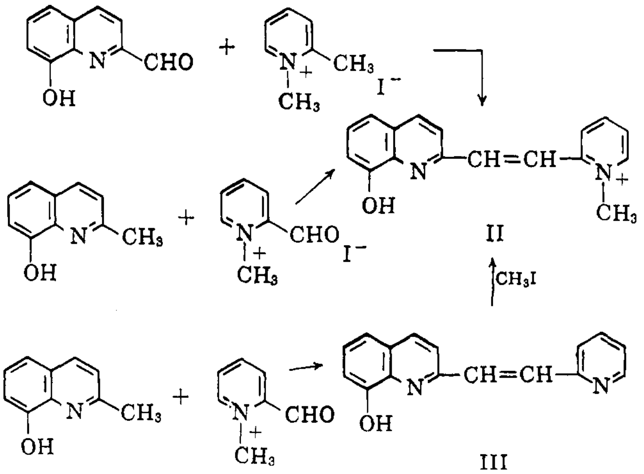


No.	—CH=CHR position	R	X	Formula	M.p., °C.[a]	Nitrogen, % Calcd.	Found
I	5		I	$C_{19}H_{19}IN_2O$	247	6.70[b]	6.43
Ia	5		I	$C_{21}H_{17}IN_2O \cdot H_2O$	220	6.13[c]	6.66
Ib[d]	5		Cl	$C_{22}H_{19}ClN_2O \cdot HCl \cdot H_2O$	255	6.71	6.56
Ic	5		Cl	$C_{22}H_{21}ClN_2O \cdot 3H_2O$	256	6.69[e]	6.47
II	2		Cl	$C_{17}H_{15}ClN_2O \cdot H_2O$ hydrochloride	236 248	8.84 7.94	9.27 8.00
IIa	2[f]		Cl	$C_{17}H_{15}ClN_2O \cdot H_2O$	226–231	8.84	8.77
IIb	2[g]		Cl	$C_{17}H_{15}ClN_2O \cdot H_2O$ hydrochloride	240 240	8.84 7.94	8.77 7.88
IIc	2		Cl	$C_{21}H_{17}ClN_2O \cdot H_2O$	199	7.62	7.94

[a] All melting points were accompanied by decomposition and varied somewhat with manner of heating. Values given here are for capillaries heated gradually in melting point bath. [b] Also analyzed for C–H. Calcd.: C, 54.55; H, 4.58. Found: C, 54.47; H, 4.94. [c] Also analyzed for C–H. Calcd.: C, 55.00; H, 4.17. Found: C, 55.14; H, 4.43. [d] A 2-methyl group is also present in the 8-quinolinol ring. [e] Also analyzed for C–H. Calcd.: C, 63.0; H, 6.48. Found: C, 62.3; H, 6.50. [f] The purple betaine of this compound melts with decomposition at 324°. [g] The purple betaine of this compound melts with decomposition at 262°.



I



II

III

the N-methyl derivatives of appropriate heterocyclic bases having an active methyl group.

The same reactions of 2-formyl-8-quinolinol in place of the 5-formyl compound could be used to obtain II and similar products, but these proved more easily prepared by condensing the appropriate N-methylheterocyclic aldehyde with 8-hydroxyquinaldine in acetic anhydride at room temperature. In the preparation of 2-[β-(N-methyl-2-pyridyl)vinyl]-8-hydroxyquinolinium chloride (II) both methods were tried, and the compound was also obtained by condensing 8-hydroxyquinaldine with 2-pyridinecarboxaldehyde followed by methylation.

Apparent ionization constants in the pH range 1–13 were obtained for some of the new compounds by the usual spectrophotometric methods, with K_1 identified with the protonated quinoline nitrogen and K_2 with the phenolic hydroxyl; as shown in the following equation

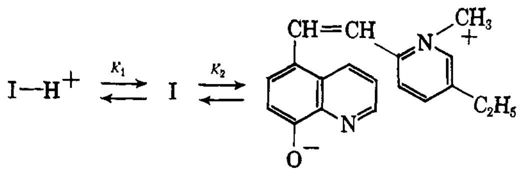


TABLE II
APPARENT DISSOCIATION CONSTANTS OF 8-QUINOLINOL MEROCYANINES

Compd.	pK_1	pK_2
8-Quinolinol	5.1	9.9
I	3.8	7.9
II	2.7	9.1
IIa	3.5	9.7
IIb	2.7	9.2

Loss of the phenolic hydrogen forms the merocyanine structure which is much more strongly colored than the cationic species. By comparison with 8-quinolinol (Table II) both ionizations of I and II are larger, a result probably to be expected from the greater ease of removal of protons from cations than from neutral species in general.

The solvatochromism of compounds of type I was more pronounced than that of type II compounds, as anticipated from the more directly conjugated path from positive to negative ends of the merocyanine function in I. Indeed, solvatochromism in IIa was almost negligible, and that in II and IIb a decrease in maximum wave length of only about 50 mμ in passing from the relatively nonpolar chloroform to aqueous base as solvent.

Most of these reagents did not form precipitates with metal ions but did give color changes indicative of complex formation in some cases. Thus, I gave a yellow complex with cupric ion even in acid solution (pH 2), and at pH 9 yellow extracts of copper and cobalt into benzyl alcohol were obtained (reagent blank red). Evidence of reaction with cupric ion was observed for all compounds, and II and IIb gave distinctive red colors with nickel at pH 9, as well, when extracted with benzyl alcohol. The reaction of IIc with zinc at pH 9 gave a solution that darkened in color with time, becoming red-violet in a few minutes. Further investigation of these effects is planned, but the present results suggest the possibility of using these reagents as extractive colorimetric systems for copper and nickel.

All compounds were submitted to the Cancer Chemotherapy National Service Center. Several passed the cell culture screening procedure but were only toxic at reasonable dosages in tests on animals.

Experimental

Preparation of Compounds.—5-Formyl-8-quinolinol was obtained by the Reimer–Tiemann reaction of 8-quinolinol and chloroform,[5] 5-formyl-8-hydroxyquinaldine by oxidation of 5-hydroxymethyl-8-hydroxyquinaldine,[6] and 2-formyl-8-quinolinol through selenium dioxide oxidation of 8-benzyloxyquinaldine and removal of the benzyl group.[7] Formylpyridine methiodides were obtained by the action of methyl iodide on the appropriate pyridinecarboxaldehydes.[8]

5-[β-(N-Methyl-5-ethyl-2-pyridyl)vinyl]-8-hydroxyquinolinium iodide (I) was prepared by refluxing 0.01 *M* amounts of 5-formyl-8-quinolinol and aldehydine methiodide for 4 hr. in propanol containing a few drops of piperidine as catalyst. On cooling, the product precipitated and was filtered, washed several times with ether, and recrystallized from 80% ethanol as golden needles decomposing at 247° (65% yield).

Essentially the same procedure was used to obtain Ia, Ib, Ic, II, and IIc from the appropriate formyl-8-quinolinol and N,2-dimethyl heterocyclic salt. (No piperidine was used in the preparation of Ic because 1,3,3-trimethyl-2-methyleneindoline has sufficient catalytic action itself to produce the desired reaction.)

2-[β-(N-Methyl-2-pyridyl)vinyl]-8-hydroxyquinolinium chloride (II) was also obtained by stirring 0.05 *M* amounts of 8-hydroxyquinaldine and 2-formyl-1-methylpyridinium iodide in 100 ml. of acetic anhydride for 40 hr. The resulting acetate (80% yield, m.p. 212°) was collected by filtration, washed with ether, and hydrolyzed by standing with 100 ml. of 10% sodium hydroxide for 1 hr. in the dark. The resulting purple crystals (m.p. 203°) were washed with very small amounts of water and dried. A solution in methanol was treated with hydrogen chloride and the chloride hydrochloride of II was precipitated by addition of ether. Recrystallization from ethanol gave the chloride (see Table I); addition of a few drops of hydrochloric acid during the recrystallization gave the hydrochloride instead. This same procedure was also used to obtain IIa and IIb.

A third method for the preparation of II was the condensation of 0.1 *M* amounts of 8-hydroxyquinaldine and pyridine-2-carboxaldehyde in 25 ml. of acetic anhydride by standing at room temperature for 24 hr. The acetate was hydrolyzed by 20% sodium hydroxide and neutralization of the solution gave the crude free base, which was converted to the dihydrochloride by addition of hydrochloric acid to a concentrated solution in ethanol. After two recrystallizations from ethanol containing hydrochloric acid, a 60% yield of *2[β-(8-hydroxy-2-quinolyl)vinyl]pyridine (III)* was obtained as the orange-red dihydrochloride, m.p. 219–222°.

Anal. Calcd. for $C_{16}H_{12}N_2O \cdot 2HCl \cdot 3H_2O$: C, 51.21; H, 5.37; N, 7.47. Found: C, 51.45; H, 5.17; N, 7.50.

The free base was liberated by neutralization of an alcohol solution with sodium bicarbonate and purified by recrystallization from ethanol to give a yellow product, m.p. 118–119°.

Anal. Calcd. for $C_{16}H_{12}N_2O$: N, 11.28. Found: N, 11.41.

This product (III, 0.5 g.) was heated with 2 ml. of methyl iodide and 10 ml. of anhydrous acetone in a sealed tube at 65° for 72 hr. Addition of ether precipitated 0.6 g. of the red methiodide, m.p. 237–238°. This was converted to the chloride hydrochloride (II) by evaporating a solution in methanol containing 2 ml. of concentrated hydrochloric acid to dryness. Recrystallization from 80% ethanol containing a few drops of hydrochloric acid gave a pure product, m.p. 248°; mixture melting point with the second preparation of II was undepressed. (The infrared spectrum of II by the first of the three methods given above did not have a band at 745 $cm.^{-1}$ that the other two preparations did possess; since the compound can have geometric isomers, we suppose this is the source of the difference. All other bands were the same.)

Apparent Ionization Constants and Spectra.—Spectra as a function of pH for over twenty different pH values from 1 to 13 were recorded with a Beckman DK-2 spectrophotometer for most of the reagents and apparent p*K* values were computed from the results. Principal maxima for I were at 346 in acid, 380 in neutral solutions, and 465 mμ in base. Comparable maxima for II, IIa, and IIb in basic solution were 467, 434, and 475 mμ, respectively, and none of these three could be extracted out of aqueous base into chloroform, differing in this respect from the merocyanines previously described.[3,4]

Spot Tests with Metal Ions. Bivalent ions of copper, iron, cobalt, nickel, zinc, cadmium, manganese, calcium, and magnesium and trivalent ions of aluminum, chromium, and iron were tested with all reagents in buffers of pH 2, 5, and 9. Extractions of the solutions with benzyl or amyl alcohol were also made, with blanks for all reagents and solvents. Few positive color changes were noted, and most of these have been mentioned in the discussion section. At pH 5 compound Ia gave red to violet colors with Co, Ni, Cu, Zn, and Cd and extraction with amyl alcohol gave blue solutions for cobalt and nickel only, the other three ions not being extracted.

Acknowledgment.—This work was supported by grants from the Public Heath Service (CA-07403) and the National Science Foundation (NSF G18559).

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