The Metal Chelates of p-(3-Formyl-4-hydroxyphenylazo)benzene Sulfonic Acid and Its Derivatives

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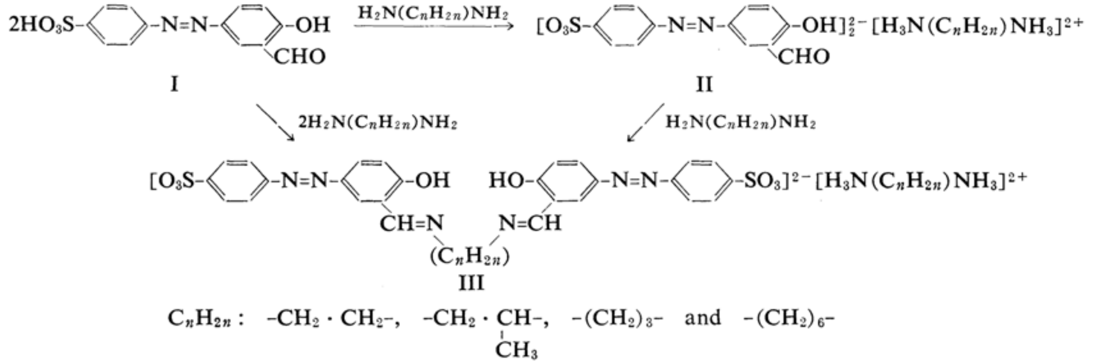
Several syntheses of *p*-aminosalicylaldehyde have been attempted in the hope that the physiological activity of *p*-aminosalicylic acid in the treatment of tuberculosis would be improved by changing the lipophobic carboxyl group into a lipophillic aldehyde group. These attempts, however, have resulted in the formation of a resinous product of a high molecular weight because of the spontaneous condensation of the amino group of one molecule with the aldehyde group of the other. Derivatives of *p*-aminosalicylaldehyde in which the amino group is protected by an acyl group, thus preventing condensation or polymerisation, have been synthesized.

The present work is a preliminary study to approach the synthesis of *p*-aminosalicylaldehyde derivatives retaining a free amino group formed by the reductive cleavage of azo linkage in an azo compound derived from salicylaldehyde. As the aromatic amino component to be used for the diazotization and for the subsequent coupling to salicylaldehyde sulfanilic acid was adopted, since it was expected both to enhance the solubility of the resultant azo compound and to ease in the isolation of the *p*-aminosalicylaldehyde derivative from the amino component formed on reduction. We tried to suppress the chemical activity of the aldehyde group by coordinating the oxygen atom of the aldehyde group with a metal atom and by allowing the aldehyde group to react with a diamine. In this way, the reaction products of *p*-(3-formyl-4-hydroxyphenylazo)-benzene sulfonic acid or 5-(*p*-sulfophenylazo)-salicylaldehyde (I) with several alkylenediamines and their metal chelates were synthesized.

A number of complex salts of hydroxyazo-compounds whose azo group participates in the complex formation are known[1], but there



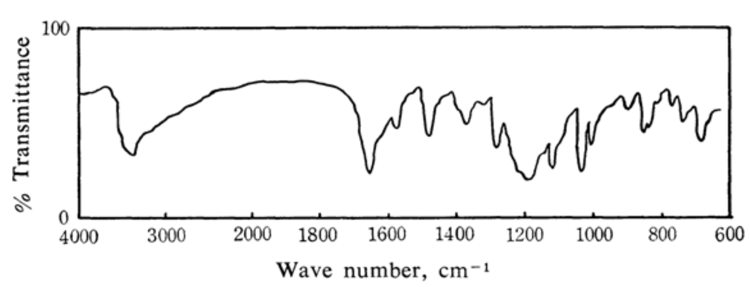


Fig. 1. Infrared spectrum of the *p*-(3-formyl-4-hydroxyphenylazo)benzene sulfonic acid.

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[1] For instance, A. H. Knight, *J. Soc. Dyecs Colourists*, **66**, 34 (1950); N. M. Mackenzie, H. E. Millson and B. L. West, *Ind. Eng. Chem.*, **44**, 1017 (1952); H. Pfitzner, *Angew. Chem.*, **62**, 242 (1950).

are a few instances[2] in which the nitrogen atoms of the azo-groups do not coordinate with central metal ions. The metal chelates in the present paper belong to the latter group.

The starting material, *p*-(3-formyl-4-hydroxyphenylazo) benzene sulfonic acid (I), was prepared by a modified Tummely[3] method; the barium salt of the sulfonic acid was used in place of sodium salt for the isolation of the free acid with a satisfactory purity and in a better yielde.

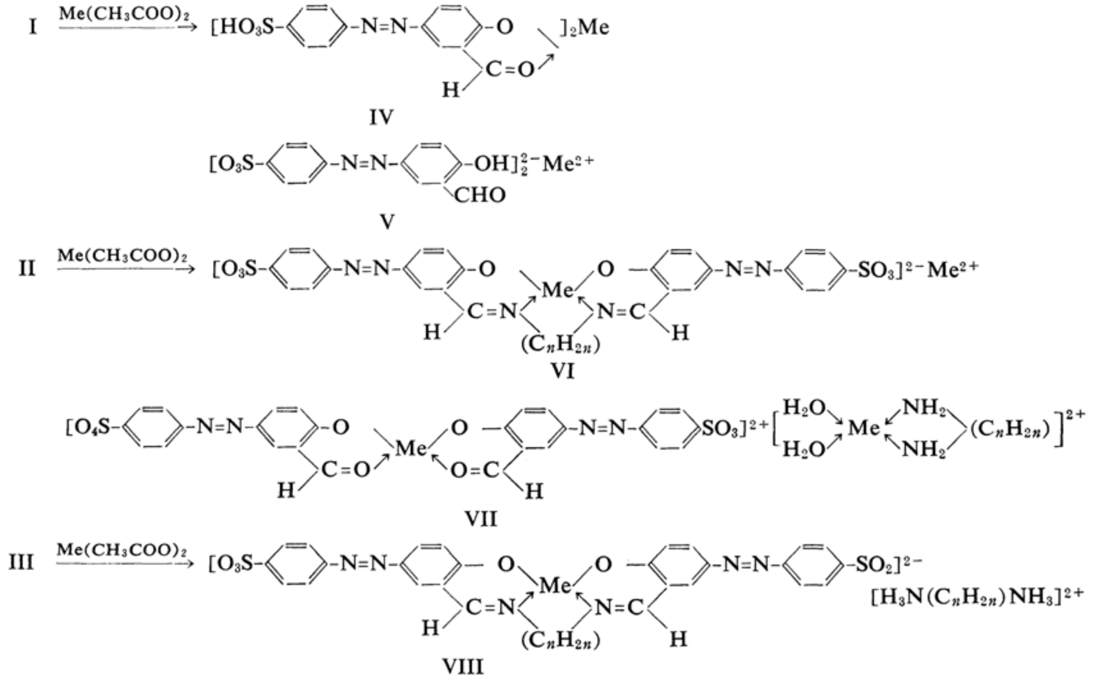
When two moles of the sulfonic acid (I) was treated with one mole of alkylene diamine, alkylene diammonium salts (II) of sulfonic acid invariably formed; those were confirmed by their infrared spectra. No formation of Schiff's base between aldehyde and diamines could be observed. As the alkylene diamine components, ethylene diamine, propylene diamine, trimethylene diamine and hexamethylene diamine were used. Figures 1 and 2 show the infrared spectra of the sulfonic acid and its ethylene diammonium salt respectively. The band in the 3200~3000 cm^{-1} region in Fig. 2 indicates the presence of a $-NH_3^+$ vibration.

On the the other hand, when the sulfonic acid was mixed with each of the above alkylene diamines in a molar ratio of 1 : 1, the Schiff's base represented by formula III was formed. Of course, the base could also be obtained from alkylene diammonium salt (II) by the action of 0.5 mol. of alkylene diamine. The infrared spectrum of one of the bases is given in Fig. 3. The band at 1625 cm^{-1} can be assigned to the –CH=N– vibration, which has already been discussed by Murase.[4]

The metal compounds of the sulfonic acid could be obtained easily when the latter was treated with metal acetates in an aqueous ethanolic medium. These metal compounds cannot be considered to be ionic metal sulfonates (V) on the basis of their infrared spectra (Fig. 4); they must be genuine chelate compounds as represented by formula IV.

It is generally accepted that, in the case of such a sulfonic acid, the formation of simple metal salts does not cause any appreciable change in their infrared spectra.

However, when the curves in Fig. 4 are compared with the curve of the original sulfonic acid (Fig. 1), a considerable change is observed. For instance, the carbonyl band of the free acid at 1650 cm^{-1} shifts towards the 1600 cm^{-1} region in the copper compound (Fig. 4, curve Cu), indicating the presence of a strong chelation; the magnitude of the shift is comparable to that between salicylaldehyde and its copper chelate.[5] The nickel, cobalt or



Me : Cu(II), Ni(II), Co(II) or Mn(II)

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[2] H. Ohta, K. Nawata, C. Soejima and T. Tsumaki, *Memoirs of the Faculty of Science, Kyushu University, Series C, Chemistry*, Vol. 5, No. 1. 1. (1962).

[3] E. Tummely, *Ann.*, **251**, 180.

[4] I. Murase, This Bulletin, **32**, 828 (1959).

[5] L. J. Bellamy and R. F. Branch, *J. Chem. Soc.*, **1954**, 4491.

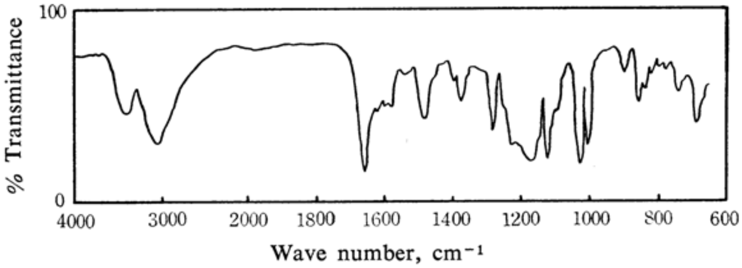

Fig. 2. Infrared spectrum of the ethylene diammonium *p*-(3-formyl-4-hydroxyphenylazo)-benzene sulfonate.

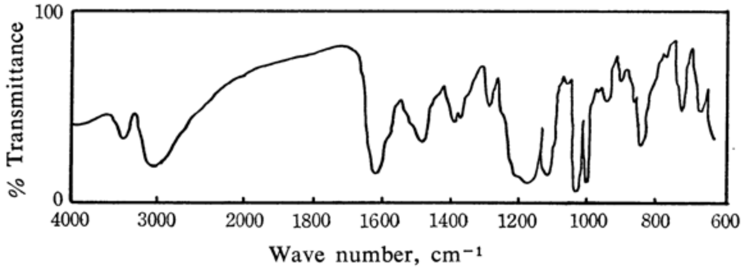

Fig. 3. Infrared spectrum of the ethylene diammonium salt of *N*, *N'*-bis[5-(*p*-sulfophenylazo)salicylidene]ethylene diamine.

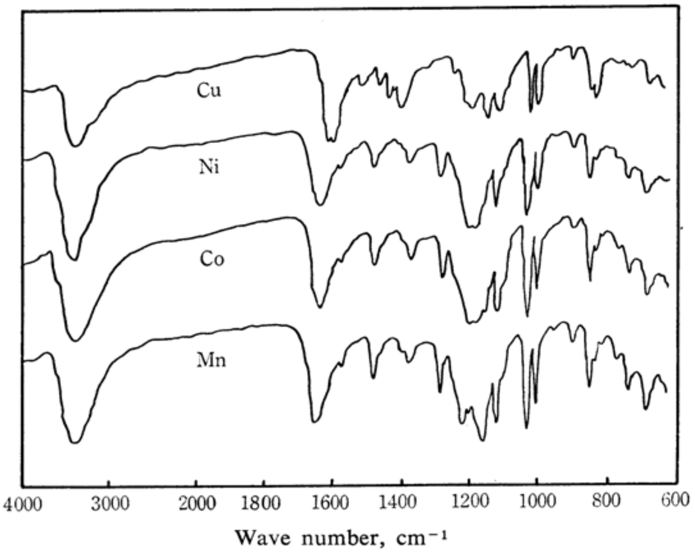

Fig. 4. Infrared spectra of the bis[5-(*p*-sulfophenylazo)salicylaldehyde]metal chelates.

manganese compound also shows a definite shift, though its magnitude is not as large.

The chelate compounds corresponding to formula VI were obtained when one mole of the alkylene diammonium salts (II) was mixed with 2 mol. of metal acetates. Figs. 5a and 5b give the infrared spectra of the copper and the nickel compounds (formula VI); the presence of the $-CH=N-$ vibration band at 1600 cm^{-1} excludes formula VII for the nickel compound, for formula VII would require the chelated carbonyl absorption to be present at a greater wave number (ordinarily at 1640 cm^{-1}), as can be seen, for example, in the case of bis(salicylaldehyde)-nickel⁵⁾ or the nickel chelate of the sulfonic acid mentioned above (Fig. 4, curve Ni). Moreover, the band in the 3200∼3000 cm^{-1} region of the $-NH_3^+$ vibration in Fig. 2 apparently has disappeared in the infrared spectra shown in Figs. 5a and 5b. Therefore, it can be concluded that, during the reaction, alkylene diamine is replaced by

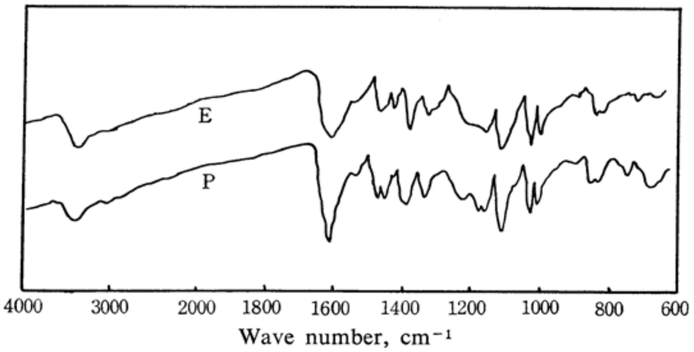

Fig. 5a. Infrared spectra of the copper(II) salt of *N*, *N*-bis[5-(*p*-sulfophenylazo)salicylidene]-alkylene diamine-copper(II).
E : Ethylene diamine, P : Propylene diamine.

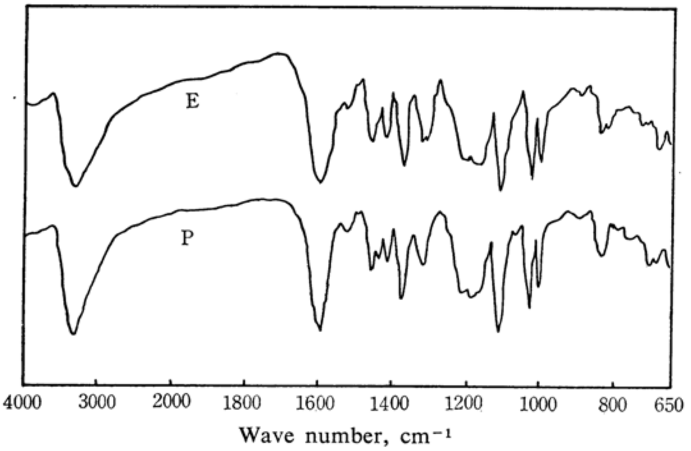

Fig. 5b. Infrared spectra of the nickel(II) salt of *N*, *N'*-bis[5-(*p*-sulfophenylazo)salicylidene]-alkylene diamine-nickel(II).
E : Ethylene diamine, P : Propylene diamine.

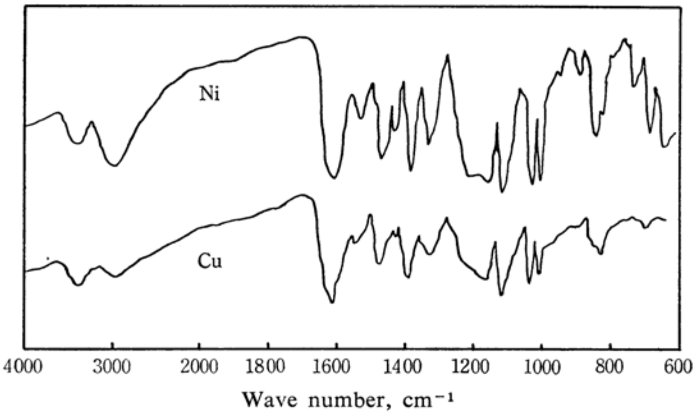

Fig. 6. Infrared spectra of the alkylene diammonium salt of *N*, *N'*-bis[5-(*p*-sulfophenylazo)-salicylidene]alkylene diamine-metal chelate.
Ni : Ethylene diamine, Cu : Trimethylene diamine

a bivalent metal ion and that the diamine molecule enters into condensation with the aldehyde group to form a Schiff's base. In the case of the copper or cobalt compound, the data indicate the same conclusion.

By the reaction of metal acetates with the alkylene diammonium salts of *N, N'*-bis[5-(*p*-sulfophenylazo)salicylaldehyde] alkylene diamine (III) or by the reaction of the metal acetates with the sulfonic acid (I) and alkylene diamines, the chelates represented by formula VIII were obtained; they are supported by the analytical data and infrared spectra (Fig. 6).

Experimental

The Infrared Spectra.—Those in Figs. 1, 2, 3, 4, 5a and 6 were measured with an Hitachi I. R. spectrophotometer, model EPI-2, and that in Fig. 5b, with an Hitachi I. R. spectrophotometer, model EPI-S2.

Chelating Agent. — *p-(3-Formyl-4-hydroxyphenylazo)benzene Sulfonic Acid (I).*—The sodium salt of the sulfonic acid was prepared by Tummely's method.[3] For the isolation of free sulfonic acid, the sodium salt was dissolved in water, and then, by the addition of an aqueous barium chloride solution, it was converted into barium salt, which was obtained as a yellowish brown precipitate. It was then decomposed with a theoretical amount of dilute sulfuric acid in an aqueous solution. The barium sulfate was removed, and the filtrate was concentrated in a vacuum desiccator. The sulfonic acid crystallized out as red or yellowish red prisms.

Alkylene Diammonium p-(3-Formyl-4-hydroxyphenylazo)benzene Sulfonate (II).—As the diamine components, ethylene diamine, propylene diamine, trimethylene diamine and hexamethylene diamine were used. One thousandth mol. of alkylene diamine was added slowly to a warm aqueous or ethanolic solution of 0.002 mol. of sulfonic acid (I). The sulfonate, which immediately separated out, was filtered and recrystallized from hot water, forming yellow needles or prisms. The analytical data are given in Table I.

TABLE I. ALKYLENE DIAMMONIUM *p*-(3-FORMYL-4-HYDROXYPHENYLAZO)BENZENE SULFONATE (Formula II).

Alkylene diamine component	Appearance	Analysis (%) Found C	H	N	Calcd. for II C	H	N
Ethylene diamine[a)]	Yellow needles	49.20	4.35	11.93	49.33	4.29	12.33
Propylene diamine[b)]	Yellow needles	48.21	4.71	11.51	48.19	4.74	11.63
Trimethylene diamine[c)]	Yellow needles	49.14	4.60	11.34	49.43	4.58	11.93
Hexamethylene diamine[d)]	Yellow needles	52.39	5.11	11.17	52.09	5.05	11.39

Percentage were calculated according to the Formulae a) $C_{28}H_{28}O_{10}N_6S_2 \cdot 0.5H_2O$, b) $C_{29}H_{30}O_{10}N_6S_2 \cdot 2H_2O$, c) $C_{29}H_{30}O_{10}N_6S_2 \cdot H_2O$ and d) $C_{32}H_{36}O_{10}N_6S_2 \cdot 0.5H_2O$.

TABLE II. ALKYLENE DIAMMONIUM SALT OF *N, N'*-BIS[5-(*p*-SULFOPHENYLAZO)-SALICYLIDENE]-ALKYLENEDIAMINE (Formula III).

Alkylene diamine component	Appearance	Analysis (%) Found C	H	N	Calcd. for III C	H	N
Ethylene diamine[a)]	Orange yellow needles	51.53	4.77	15.88	51.71	4.63	16.08
Propylene diamine[b)]	Yellowish orange crystalline powder	52.34	4.97	15.06	52.38	5.08	15.27
Trimethylene diamine[c)]	Yellowish orange needles	52.28	5.05	15.18	52.38	5.08	15.27
Hexamethylene diamine[d)]	Orange crystalline powder	55.98	5.97	13.49	55.80	6.04	13.70

Percentage were calculated according to the Formulae a) $C_{30}H_{32}O_8N_8S_2$, b) $C_{32}H_{36}O_8N_8S_2 \cdot 0.5H_2O$, c) $C_{32}H_{36}C_8N_8S_2 \cdot 0.5H_2O$ and d) $C_{38}H_{48}O_8N_8S_2 \cdot 0.5H_2O$.

TABLE III. BIS[5-(*p*-SULFOPHENYLAZO)SALICYLALDEHYDE]METAL CHELATE (Formula IV).

Metal	Appearance	Analysis (%) Found C	H	N	Me	Calcd. for IV C	H	N	Me
Cu[a)]	Yellowish green needles	37.94	4.43	6.77	7.38	37.75	4.26	6.77	7.68
Ni[b)]	Yellow needles	38.58	4.27	6.65	7.26	38.82	4.14	6.97	7.30
Co[c)]	Yellow needles	40.23	4.16	7.23	7.48	40.16	3.89	7.21	7.58
Mn[d)]	Yellow needles	38.94	4.24	6.94	7.02	39.01	4.15	7.00	6.86

Percentages were calculated according to the Formulae a) $C_{26}H_{18}O_{10}N_4S_2Cu \cdot 8.5H_2O$, b) $C_{26}H_{18}O_{10}N_4S_2Ni \cdot 7.5H_2O$, c) $C_{26}H_{18}O_{10}N_4S_2Co \cdot 6H_2O$ and d) $C_{26}H_{18}O_{10}N_4S_2Mn \cdot 7.5H_2O$.

TABLE IV. METAL SALT OF *N*, *N'*-BIS[5-(*p*-SULFOPHENYLAZO)SALICYLIDENE]ALKYLENE DIAMINE METAL CHELATE (Formula VI).

Alkylene diamine component	Metal	Appearance	Analysis (%) Found C	H	N	Me	Calcd. for VI C	H	N	Me
Ethylene diamine	Cu hydrate[a)]	Green powder	38.73	3.87	9.92	14.47	38.75	3.72	9.68	14.64
	Cu pyridinate[b)]	Dark green needles	51.93	4.43	12.42	10.80	51.84	3.99	12.59	11.43
	Ni hydrate[c)]	Orange red needles	39.34	3.84	9.62	13.73	39.19	3.76	9.79	13.68
	Ni pyridinate[d)]	Orange red needles	48.29	4.56	11.73	9.77	48.34	4.56	11.75	9.85
Propylene diamine	Cu pyridinate[e)]	Green needles	49.41	4.61	11.80	11.08	49.12	4.54	11.69	10.61
	Ni hydrate[f)]	Orange red needles	39.22	3.84	9.54	13.39	39.13	4.08	9.44	13.19
	Ni pyridinate[g)]	Reddish orange needles	53.47	4.67	12.58	9.04	53.33	4.70	12.65	8.84
Trimethylene diamine	Cu pyridinate[h)]	Dark green prisms	50.25	4.72	11.65	10.82	50.25	4.39	11.96	10.85
	Ni hydrate[i)]	Reddish orange crystals	39.91	4.08	9.53	13.81	39.94	3.93	9.64	13.46
	Ni pyridinate[j)]	Red needles	49.47	4.67	11.49	9.93	49.52	4.58	11.78	9.88
Hexamethylene diamine	Cu pyridinate[k)]	Dark green powder	49.65	5.00	11.18	10.41	49.63	4.97	11.13	10.10

Percentages were calculated according to the Formulae a) $C_{28}H_{20}O_8N_6S_2Cu_2 \cdot 6H_2O$, b) $C_{28}H_{20}O_8N_6S_2Cu_2 \cdot 4C_5H_5N \cdot 2H_2O$, c) $C_{28}H_{20}O_8N_6S_2Ni_2 \cdot 6H_2O$, d) $C_{28}H_{20}O_8N_6S_2Ni_2 \cdot 4C_5H_5N \cdot 7H_2O$, e) $C_{29}H_{22}O_8N_6S_2Cu_2 \cdot 4C_5H_5N \cdot 6H_2O$, f) $C_{29}H_{22}O_8N_6S_2Ni_2 \cdot 7H_2O$, g) $C_{29}H_{22}O_8N_6S_2Ni_2 \cdot 6C_5H_5N \cdot 5H_2O$, h) $C_{29}H_{22}O_8N_6S_2Cu_2 \cdot 4C_5H_5N \cdot 4.5H_2O$, i) $C_{29}H_{22}O_8N_6S_2Ni_2 \cdot 6H_2O$ j) $C_{29}H_{22}O_8S_2N_6S_2Ni_2 \cdot 4C_5H_5N \cdot 6H_2O$ and k) $C_{32}H_{28}O_8N_6S_2Cu_2 \cdot 4C_5H_5N \cdot 7H_2O$.

TABLE V. ALKYLENE DIAMINE SALT OF *N*, *N'*-BIS[5-(*p*-SULFOPHENYLAZO)SALICYLIDENE]ALKYLENE DIAMINEMETAL CHELATE (Formula VIII)

Alkylene diamine component	Metal	Appearance	Analysis (%) Found C	H	N	Me	Calcd. for VIII C	H	N	Me
Ethylene diamine	Cu[a)]	Green needles	45.45	4.45	14.58	8.22	45.36	4.31	14.11	8.00
	Ni[b)]	Orange red needles	46.82	4.21	14.28	7.74	46.71	4.18	14.52	7.61
Propylene diamine	Cu[c)]	Green needles	45.06	5.05	12.66	7.67	44.78	4.93	13.05	7.40
	Ni[d)]	Red needles	44.18	5.02	13.08	6.83	44.10	5.08	12.86	6.74
Trimethylene diamine	Cu[e)]	Green needles	44.73	5.05	13.08	7.65	44.78	4.93	13.05	7.40
	Ni[f)]	Orange red prisms	43.53	5.54	12.83	6.65	43.21	5.21	12.60	6.60
Hexamethylene diamine	Cu[g)]	Green crystalline powder	46.97	5.97	11.85	6.65	47.07	5.93	11.56	6.55

Percentages were calculated according to the Formulae a) $C_{30}H_{30}O_8N_8S_2Cu \cdot 2H_2O$, b) $C_{30}H_{30}O_8N_8S_2Ni \cdot H_2O$, c) $C_{32}H_{34}O_8N_8S_2Cu \cdot 4H_2O$, d) $C_{32}H_{34}O_8N_8S_2Ni \cdot 5H_2O$, e) $C_{32}H_{34}O_8N_8S_2Cu \cdot 4H_2O$, f) $C_{32}H_{34}O_8N_8S_2Ni \cdot 6H_2O$ and g) $C_{38}H_{46}O_8N_8S_2Cu \cdot 5.5H_2O$.

In the case of the copper chelate of the propylene diamine analogue, it was prepared by mixing the sulfonic acid (I), propylene diamine and copper acetate in an aqueous solution.

Alkylene Diammonium Salt of N, N'-Bis[5-(p-sulfophenylazo)salicylidene]alkylene Diamine (III).—To a warm solution of 0.002 mol. of the sulfonic acid (I) in 100 ml. of water, a solution of 0.002 mol. of alkylene diamine in 10 ml. of water was added. The yellow precipitate thus obtained was recrystallized from a large quantity of water, a pyridine-water mixture, or an ethanol-water mixture. The salts are listed in Table II.

Metal Chelate. — *Bis-[5-(p-sulfophenylazo)salicylaldehyde]metal Chelate (IV).*—The copper, the nickel, the cobalt and the manganese chelates were synthesized by adding a solution of 0.0005 mol. of metal acetate in 10 ml. of water to a solution of 0.001 mol. of the sulfonic acid (I) in 50 ml. water. The mixture was heated on a water-bath for a short time and then left to cool. The precipitate was collected and recrystallized from water. The results are listed in Table III.

The Metal Salt of N, N'-Bis[5-(p-sulfophenylazo)-salicylidene]alkylene Diamine-metal Chelate (VI).—Four alkylene diammonium sulfonates of Table I were used as the ligand components, and copper and nickel acetate as the metal components. The chelates thus obtained are listed in Table IV. A solution of 0.001 mol. of copper acetate or nickel acetate in 10 ml. of water was added to a warm solution of 0.0005 mol. of the alkylene diammonium salt (III) in 200 ml. of water (50 ml. of a pyridine-water mixture was used for the preparation of copper chelates). The mixture was filtered when necessary, boiled for a short time, and concentrated on a water-bath until the precipitation of the chelate was completed. The chelates thus obtained were recrystallized from a pyridine-water mixture or from an ethanol-water mixture. All of the nickel chelates were obtained in the form of hydrates or pyridinates. They are listed in Table IV.

Alkylene Diammonium Salt of N, N'-Bis[5-(p-sulfophenylazo) - salicylidene]alkylene Diamine-metal Chelate (VIII).—These salts are listed in Table V. A solution of 0.0005 mol. of metal acetate in 20 ml. of water was added to a solution of 0.0005 mol. of the salt (III) in 100 ml. of a hot pyridine-water mixture (in the case of the ethylene diamine analogue, 800 ml. of hot water was used). The mixture was heated for a short time and concentrated on a water-bath to an adequate volume. The precipitate was then collected and recrystallized from an ethanol-water mixture or a pyridine-water mixture.

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