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Heterocyclic Azomethine Compounds and Their Reduction Products as Analytical Reagents. I. Syntheses and Acid Dissociation Constants of Picolinaldehyde 2-Hydroxyanil and Its Derivatives and Their Reactions with Metal Ions

Makoto Otomo and Kazunobu Kodama

Department of Synthetic Chemistry, Nagoya Institute of Technology, Showa-ku, Nagoya 466

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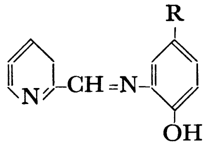
Picolinaldehyde 2-hydroxyanil and its methyl, chloro and nitro derivatives at the 5-position of benzene nucleus were synthesized for the purpose of investigating their applicability as an analytical reagent. The acid dissociation constants were determined by means of potentiometric titration in aqueous dioxane of various concentrations. It was found that the basicity of donor atoms of the parent compound increases with the introduction of a methyl group and decreases with that of a chloro or nitro group. The three compounds other than the nitro derivative are light-colored and react with many divalent metal ions in slightly basic media to form strongly colored chelates, which can be extracted into organic solvents such as partially halogenated hydrocarbons. The distribution coefficients of the three compounds between chloroform and water were also determined spectrophotometrically, that of the chloro derivative being the largest.

The analytical use of heterocyclic azo compounds in color forming reactions with metal ions is very familiar. 2-Pyridylazo compounds, which are strongly colored and have a hydroxy group in *ortho*-position to the azo group, have been proved to be very useful as spectrophotometric reagents and also as metal indicators. However, in spite of the easiness of preparation, only a limited number of azomethine analogs have been used analytically. It is important to note that the stability constants of some metal chelates with picolinaldehyde 2-hydroxyanil are of the same order of magnitudes as those of 4-(2-pyridylazo)-resorcinol.[1] Both compounds have three donor groups capable of coordinating to metals and act as a terdentate ligand. 2-(2-pyridylazo)phenyl (*o*-PAP) also reacts with many metal ions over a wide range of pH to form strongly colored chelates.[2] A series of azomethines represented by the general formula(1) have been synthesized and their applicability to the spectrophotometric determination of copper(II) examined.[3] However, no attempt seems to have been made so far to elucidate the stability of the chelates formed. Picolinaldehyde 2-mercaptoanil, a thio analog of picolinaldehyde 2-hydroxyanil, shows a marked selectivity towards metals which form brightly colored insoluble sulfides.[4] Some azomethine derivatives of 8-hydroxyquinoline have also been synthesized.[5]



$R = H, CH_3, Cl, C_6H_5$

(1)

We have synthesized four azomethine compounds, picolinaldehyde 2-hydroxyanil (I), -2-hydroxy-5-methylanil(II), -2-hydroxy-5-chloroanil(III) and -2-hydroxy-5-nitroanil(IV), in order to study quantitatively the effects of substituents at the 5-position of the benzene nucleus on the acid dissociation constants and the stability of metal chelates, and to obtain information on their applicability as an analytical reagent. It is found that the basicity of the imino and pyridine nitrogens, as well as of the phenolic oxygen, is greatly affected by the introduction of an electron-releasing or -withdrawing group into the ring. These compounds except for (IV) may be conveniently used as an extractive spectrophotometric reagent for some divalent metal ions.

Experimental

Preparations. Compound (I) is prepared as follows: To a solution of 10 g of *o*-aminophenol (purified by sublimation) in 80 ml ethanol is added a solution of 11 g of freshly distilled picolinaldehyde in 20 ml ethanol. The mixture is kept at 60—70 °C for 2 hr, and the ethanol is evaporated under reduced pressure. The resulting brown residue is recrystallized from ligroin to give 10 g of pale yellow-orange needle-like crystals.

The other azomethine compounds are prepared similarly from substituted *o*-aminophenols. The melting points and analytical data of the synthesized compounds together with the IR data are given in Table 1.

Sodium perchlorate is prepared by neutralization of a sodium carbonate solution with perchloric acid, followed by shaking with 1-(2-pyridylazo)-2-naphthol (PAN) in benzene to remove heavy metals which may be present and concentrating the aqueous phase until bulk of sodium perchlorate has crystallized out. The crystals are collected and recrystallized from water.

Apparatus. A model HM-6A pH meter (Toa Dempa Co., Ltd.) equipped with a combination electrode, type GC-125, is calibrated at pH 6.88 and 4.01 with standard buffer solutions (Toa Dempa Co., Ltd.). The pH meter readings are corrected according to the method described by van Uitert and Haas.[6] A Hitachi model 181 spectrophotometer

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[1] W. J. Geary, G. Nickless and F. H. Pollard, *Anal. Chim. Acta*, **26**, 575 (1962); *ibid.*, **27**, 71 (1962).

[2] F. H. Pollard, G. Nickless and R. G. Anderson, *Talanta*, **13**, 725 (1966).

[3] K. Isagai and K. Isagai, *Nippon Kagaku Zasshi*, **88**, 1292 (1967); *Bunseki Kagaku*, **17**, 171 (1968).

[4] R. G. Anderson and G. Nickless, *Proc. Soc. Anal. Chem.*, **3**, 149 (1966).

[5] T. Hata and T. Uno, This Bulletin, **45**, 477 (1972).

[6] L. G. van Uitert and C. G. Haas, *J. Amer. Chem. Soc.*, **75**, 451 (1953).

Table 1. Azomethine compounds synthesized

Compound	Mp (°C)[a]	Formula	Analysis (%)			IR(CH=N) band (cm^{-1})
				Found	Calcd	
I	108	$C_{12}H_{10}ON_2$	C	72.68	72.71	1627
			H	5.01	5.09	
			N	14.21	14.13	
II	104	$C_{13}H_{12}ON_2$	C	73.56	73.57	1623
			H	5.72	5.70	
			N	13.20	13.20	
III	138	$C_{12}H_9ON_2Cl$	C	62.15	61.95	1627
			H	4.05	3.90	
			N	12.05	12.04	
IV	200	$C_{12}H_9O_3N_3$	C	59.14	59.25	1621
			H	3.63	3.73	
			N	17.14	17.28	

a) Although all the melting points are uncorrected, the reported values for I, II, and III in Refs. 1 and 3 seem to be too low.

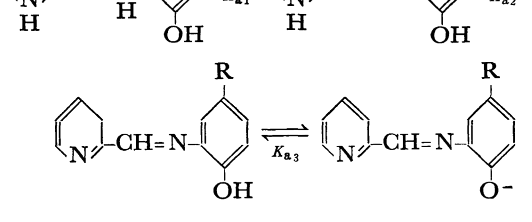
and a Hitachi model 124 double-beam spectrophotometer are used for measurement of absorbance in quartz cells of 10 mm pathlength.

Determination of Acid Dissociation Constants. Since all the azomethine compounds synthesized are almost insoluble in water, potentiometric titration is carried out in aqueous dioxane of various concentrations. A solution containing the sodium salt of each ligand (5×10^{-3} M) and sodium perchlorate (0.1 M) is titrated with 0.2 M perchloric acid at 25±0.1 °C under CO_2-free nitrogen atmosphere.

Determination of Distribution Coefficients. The distribution coefficients of the three compounds other than (IV) are determined spectrophotometrically. Extraction is carried out in a 50 ml centrifuging tube fitted with a glass stopper. A 10 ml portion of 0.1 M sodium perchlorate solution containing appropriate amounts of sodium hydroxide is vigorously shaken with 10 ml each of 1×10^{-3} M reagent in chloroform for 10 min at 25±0.5 °C. After equilibration, the pH of the aqueous phase is determined, and the absorbance of the organic phase is then measured at the absorption maximum, 358 nm for (I), 370 nm for (II), or 367 nm for (III).

Results and Discussion

Acid Dissociation Constants. The acid dissociation constants of the four compounds are determined in aqueous dioxane of various concentrations. The potentiometric titration curves in 50 v/v% aqueous dioxane are shown in Fig. 1. Each titration curve exhibits only one pH inflection at $a=1$. This shows that the dissociation of proton from the phenolic oxygen occurs independently in the alkaline region, whereas the dissociation of protons from the pyridine and azomethine nitrogens overlaps in the acidic region:



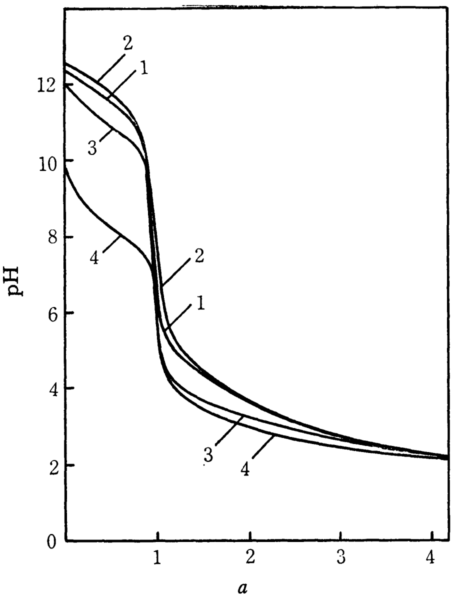


Fig. 1. Potentiometric titration curves of the azomethine compounds in 50 v/v% aqueous dioxane solution, $\mu=0.1$, 25 °C; abscissa a represents mol of acid added per mol of ligand (sodium salt).

Curve 1. Picolinaldehyde 2-hydroxyanil
2. Picolinaldehyde 2-hydroxy-5-methylanil
3. Picolinaldehyde 2-hydroxy-5-chloroanil
4. Picolinaldehyde 2-hydroxy-5-nitroanil

The acid dissociation constants are calculated as follows. For dissociation of a tribasic ligand acid, we have the relation[7]

$$R[H^+]^3+(R-1)K_{a1}[H^+]^2+(R-2)K_{a1}K_{a2}[H^+]+(R-3)K_{a1}K_{a2}K_{a3}=0 \qquad (1)$$

where $R=\{(3-a)C_L+[H^+]-[OH^-]\}/C_L$, C_L is the concentration of the ligand, and a the degree of neutralization. Since pK_{a1} and pK_{a2} are obviously close in magnitude whereas pK_{a3} is much larger, values for the first two dissociation constants are obtained conveniently by transforming Eq. (1) into the linear forms

$$\frac{(1-R)[H^+]}{R-2}=\frac{R[H^+]^2}{R-2}\cdot\frac{1}{K_{a1}}+K_{a2} \qquad (2)$$

and

$$\frac{2-R}{R[H^+]^2}=\frac{R-1}{R[H^+]}\cdot\frac{1}{K_{a2}}+\frac{1}{K_{a1}K_{a2}} \qquad (3)$$

and solving them to obtain K_{a1} and K_{a2} as the reciprocals of the calculated slopes. The value of K_{a3} is calculated from the approximate equation, $K_{a3}=(R-2)[H^+]/(3-R)$.

The plots of pK_{a1}, pK_{a2}, or pK_{a3} thus obtained *vs.* the mole fraction of dioxane, n_2, are linear in every case. The values of pK_{a1} and pK_{a2} decrease and that of pK_{a3} increases with increasing mole fraction of dioxane. These are summarized in Table 2. The value of pK_{a1} for (II) can not be estimated since hydrolysis takes place below pH 4. The acid dissociation constants of (I) in 50 v/v% aqueous dioxane agree well with the values reported by Geary, Nickless and Pollard (pK_{a1}=3.05, pK_{a2}=4.45 and pK_{a3}=11.80[1]).

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[7] H. Irving and J. J. R. F. da Silva, *J. Chem. Soc.*, **1963**, 448.

Table 2. Acid dissociation constants of the azomethine compounds
At 25 °C, $\mu=0.1$

Compound	pK_{a1}	pK_{a2}	pK_{a3}
(I)	$3.69-3.62n_2$	$4.80-2.47n_2$	$9.99+8.68n_2$
(II)	—	$5.03-2.82n_2$	$10.31+8.22n_2$
(III)	$3.43-3.56n_2$	$4.08-3.33n_2$	$9.52+8.05n_2$
(IV)	$2.81-4.37n_2$	$3.98-3.97n_2$	$7.12+6.49n_2$

It can be seen from Table 2 that the basicity of the donor atoms of the parent compound (I) is increased by the introduction of an electron-releasing group into the benzene ring and *vice versa* by the introduction of an electron-withdrawing group. As may be expected, the basicity of (II) is the highest. A good linear relationship holds between the pK_{a3} values for these compounds and the Hammett σ_p values for the benzene series.[8] The value of pK_{a2} may be ascribed to the dissociation of the -NH= group of pyridine nucleus.[9] The pK_{a2} and pK_{a3} values for (I) and (II) are higher than those of the corresponding azo compounds, *o*-PAP[4] and 2-(2-pyridylazo)-4-methylphenol (PAC),[10] respectively. This means that one would expect metal complexes of (I) and (II) to be more stable than those of *o*-PAP and PAC, respectively. The pK_{a2} and pK_{a3} values for (II) are also higher than those of 2-(2-thiazolylazo)-4-methylphenol (TAC).[11]

Distribution Coefficients. In the range of pH investigated (9.90—11.80), the following equation might hold for reagent extraction.

$$\log D_L = \log K_{DL} - \log(K_{a3}/[H^+]+1) \qquad (4)$$

where D_L is the distribution ratio. The value of the distribution coefficient K_{DL} for a given compounds is obtained from Eq. (4). The results are given in Table 3. It is apparent that the log K_{DL} value varies with the substituent in the order $Cl>CH_3>H$ ($\gg NO_2$). These compounds show weak fluorescence in chloroform.

Table 3. Distribution coefficients of the azomethine compounds
At 25 °C, $\mu=0.1$

Compound	$\log K_{DL}$
(I)	1.53 ± 0.04
(II)	2.18 ± 0.06
(III)	2.38 ± 0.04

Reaction with Metal Ions. Many metal ions react with the synthesized compounds in the neutral or slightly basic region to give orange to orange-red color. Of these only divalent metal ions form chelates extractable into organic solvent such as chloroform, 1,2-dichloroethane, and *o*-dichlorobenzene, suggesting that uncharged 1 : 2 metal-ligand chelates are extracted. It is noteworthy that the extracted metal chelates are red to reddish violet in color, fairly differing from those observed in an aqueous dioxane solution; *e.g.*, the nickel(II) chelate of (I) in 20 v/v % aqueous dioxane at pH 9.3 has an absorption maximum at about 455 nm, while the peak of the chloroform extract is located at 529 nm. Metal chelates of (IV), however, can not be extracted into any organic solvent examined, although a potentiometric titration curve of a mixture of nickel(II) and (IV) in 50 v/v % aqueous dioxane with a standard sodium hydroxide solution clearly shows a 1 : 2 metal-ligand complex being formed. The absorption maxima and the apparent molar absorptivities of the divalent-metal chelates extracted into chloroform are given in Table 4. The spectrum of each chelate shows a broad, intense band well separated from that of the reagent, the shift being larger than 100 nm. The band for a metal shifts toward longer wavelength in the order $CH_3>Cl>H$.

Cadmium(II) and zinc(II) are found to form the most strongly colored chelates with these compounds. The cobalt(II) chelates change in color from red to violet during the course of extraction with chloroform

Table 4. Spectral properties of the metal chelates extracted into chloroform
Total metal concentration: 2.0×10^{-5} M
Total ligand concentration: 2.5×10^{-4} M

Metal	(I)			(II)			(III)		
	λ_{max} (nm)	$\varepsilon_{max}\times10^{-4}$ (l/mol·cm)	pH	λ_{max} (nm)	$\varepsilon_{max}\times10^{-4}$ (l/mol·cm)	pH	λ_{max} (nm)	$\varepsilon_{max}\times10^{-4}$ (l/mol·cm)	pH
Mn(II)	500	2.2	8.9	520	1.9	9.0	512	2.3	8.8
Co(II)	493	1.7	8.9				505	2.1	8.8
Ni(II)	520	2.2	8.9	540	2.0	9.2	532	2.1	8.6
Cu(II)	515	1.3	8.9	535	1.2	9.9	530	1.4	8.7
Zn(II)	500	2.6	8.9	518	2.2	7.2	513	2.3	8.7
Cd(II)	500	2.5	8.9	518	2.1	8.7	512	2.3	8.6
Hg(II)	502	~2	8.9	521	~2	8.7	515	~2	8.6
Pb(II)	475	0.68	8.9				480	0.60	8.6
UO_2(II)	450	0.81	8.9	472	1.3	6.4			

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[8] H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953).

[9] S. J. Angyal and C. L. Angyal, *J. Chem. Soc.*, **1952**, 1461.

[10] G. Nakagawa and H. Wada, *Nippon Kagaku Zasshi*, **83**, 1098 (1962).

[11] G. Nakagawa and H. Wada, *ibid.*, **85**, 202 (1964).

in a slightly basic solution, a precipitate appearing on the boundary of the two phases even in the presence of perchlorate ion. The reaction of nickel(II) with these compounds proceeds rapidly at the pH given in Table 4 and the chelates formed can be readily extracted into chloroform. However, the rate decreases markedly with decrease in pH of the solution. The comparatively lower molar absorptivities of the copper(II) chelates give rise to structural interest. The results imply that the azomethine compounds may be useful as a reagent for extractive spectrophotometric analysis of zinc(II), cadmium(II) and mercury(II). Their behaviors which are similar to those of *o*-PAP and PAR, suggest that these compounds act as a terdentate ligand toward metals to form two five-membered chelate rings.

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