

introduced between the nitrofuryl and the end group of the side chain, as shown in Chart 1, the half-wave reduction potential drops and at the same time the antibacterial activity increases.

On the other hand it is known that the potentials of a series of the compounds are linearly related to the heights of the lowest vacant π -electronic energy levels of these compounds calculated by the LCAO-MO method.¹⁴⁾ From the above fact it seems that the coefficient λ_{iv} of the lowest vacant π -electronic energy level indicated in Table II lends some support to the experimental results obtained by Sasaki. Namely IV or X is lower in the lowest vacant energy level and higher in antibacterial activity than in case of II or XII. However, as it is readily seen in Table II, the compound which is low in the lowest vacant π -electronic energy level, namely may be reduced more easily, is not always presented to be strong in an antibacterial activity. From the above stated consideration, it seems reasonably to be concluded that there is no striking relation between the nature of nitro radical and the antibacterial activity.

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- 14) Fueno, *et al.*: Nippon Kagaku Zasshi, **79**, 116 (1958); Bull. Chem. Soc. Japan, **32**, 1003 (1959).

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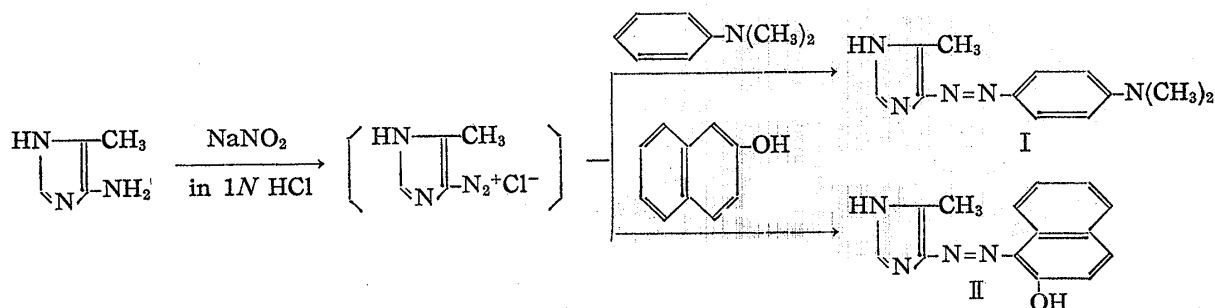
Imidazolylazo Compounds as Metallochromic Indicators

Although imidazole derivatives are expected to form complexes with various metal ions, the investigations of their complexing properties are mostly confined to imidazole itself, histidine and histamine, and no analytical applications of imidazole derivatives in general have been reported.

In the course of the systematic studies on chelating abilities and analytical applications of imidazole derivatives, it was found that some azo derivatives react with various metal ions to give intense colors and that they can be applied to analytical determinations. On the other hand, a number of *ortho*-hydroxyazo compounds, of which 1-(2-pyridylazo)-2-naphthol (PAN) and Eriochrome Black T are typical, are frequently used as indicators in complexometric titrations because of their marked color changes resulting from the reactions with metal ions. Since the successful introduction of PAN into complexometric analysis, many studies have been made on the properties of analogous compounds, such as those with thiazole nucleus in place of pyridine nucleus¹⁻⁴⁾ and those with modified phenol components.^{5,6)}

- 1) G. Nakagawa, H. Wada: Nippon Kagaku Zasshi, **83**, 1185 (1962).
- 2) A. Kawase: Bunseki Kagaku, **12**, 709 (1963).
- 3) *Idem*: *Ibid.*, **12**, 810 (1963).
- 4) *Idem*: *Ibid.*, **12**, 817 (1963).
- 5) A. Corsini, I. Mai-Ling Yih, Q. Fernando, H. Freiser: Anal. Chem., **34**, 1090 (1962).
- 6) G. Nakagawa, H. Wada: Nippon Kagaku Zasshi, **83**, 1190 (1962).

The imidazolylazo compounds were prepared by the procedure shown in Chart 1: 4(5)-Amino-5(4)-methylimidazole⁷⁾ was diazotized and coupled with *N,N*-dimethylaniline and 2-naphthol to give 4(5)-methyl-5(4)-(*p*-dimethylaminophenylazo)imidazole (I) as brown black needles, m.p. 222~224° (decomp.) (*Anal.* Calcd. for $C_{12}H_{15}N_5$: C, 62.85; H, 6.59; N, 30.55. Found: C, 62.77; H, 6.77; N, 30.49) and 1-[4(5)-methyl-5(4)-imidazolylazo]-2-naphthol (II) as reddish brown needles, m.p. 226~227° (decomp.) (*Anal.* Calcd. for $C_{14}H_{12}ON_4$: C, 66.65; H, 4.79; N, 22.21. Found: C, 66.93; H, 5.08; N, 22.04), respectively.



The compound (I) is soluble in methanol, ethanol and chloroform and insoluble in water. Its solution shows slight color change with pH, that is, yellow (acid), orange yellow (neutral) and yellow (alkaline). Spot tests at pH 3.6 revealed that it reacts with various metal ions, such as Fe (III) (reddish brown), Co (II) (deep red), Ni (II) (red), Cu (II) (deep red), Pd (II) (brown black), Pt (IV) (brown) and Au (III) (brown black). The color of the copper chelate is red near pH 2 and deepens with the increase of pH. Satisfactory results were obtained in the complexometric titration of copper (II) (1 mg./10 mL.) with EDTA in the pH range 3 to 5, a 0.1% solution of I in ethanol being used as an indicator. Under the conditions employed, the solubilities in water of I and the chelate were greater than those of PAN and its chelate, and, in addition, its color change at the end point took place instantly without heating.

The compound (II) is soluble in methanol, ethanol, chloroform, and benzene and insoluble in water. The color of the solution is yellow (acid), orange yellow (neutral) and orange red (alkaline). It was found to react with Fe (III) (deep red), Co (II) (reddish brown), Cu (II) (wine red), Pd (II) (brown), Pb (II) (red), Au (III) (brown) and UO_2 (II) (red).

These two compounds are very stable in methanol and ethanol, but in purified dioxane they gradually lose the ability to react with copper (II). They form chloroform-soluble chelates in a wide range of pH. This suggests the possibility that they may be used as extractants in the solvent extraction of metals.

Details of the reactions with metal ions, structures of chelates and analytical applications which are being investigated will be reported later.

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7) R. Weidenhagen, R. Herrmann: *Ber.*, **68**, 2207 (1935).