Chem. Pharm. Bull.
26(8)2582—2585(1978)

UDC 546.723' 547.442.3.08 : 543.422.5.06

Spectrophotometric Studies on Fe(III) Complexes of Some Aryl β-Ketoimines[1]

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(Received February 28, 1978)

Spectrophotometric studies on the complex formation between Fe^{3+} ion and three kinds of aryl β-ketoimines derived from 2,4-pentanedione and anilin were reported. Spectra of these Fe(III)-ketoimine complexes revealed similar features to that of tris(2,4-pentanedionato)iron(III) in 80% EtOH. The composition, equilibrium constant and stability constant were also determined for the complexes.

Keywords——spectrophotometry; iron; complex; aryl β-ketoimine; stability constant

Schiff-base bonding is considered as a key intermediate one which is involved in biochemically significant reactions such as transamination,[3] and decarboxylation.[4] In connection with these reactions, interactions of metal ions with various Schiff-base compounds have attracted much attention,[5] but very few studies have been reported on the metal complexes of β-ketoimines derived from β-diketones and amines. The only quantitative study has been reported by D.F. Martin *et al.*,[6] and they have measured potentiometrically stability constants of aryl β-ketoimine complexes with bivalent metal ions in dioxane–H_2O. However, no investigation has been carried out spectrophotometrically on the interaction of Fe^{3+} with aryl β-ketoimines. Therefore, the present study is undertaken to investigate the complex formation of Fe^{3+} and some aryl β-ketoimines which are derived from 2,4-pentanedione and aniline derivatives.

Experimental

Materials——Three aryl β-ketoimines were synthesized by the method[6], 4-anilino-3-pentene-2-one I, mp 48—49° (petroleum ether) (lit.[6,7] mp 45°, 47°) *Anal.* Calcd. for $C_{11}H_{13}NO$: C, 75.40; H, 7.49; N, 8.00. Found: C, 75.48; H, 7.44; N, 8.12. UV $\lambda_{max}^{80\% EtOH}$ (nm, log ε): 326 (4.32), 4-(*p*-chlorophenylimino)-3-pentene-2-one II, mp 58—59° (petroleum ether) (lit.[6,8] mp 61—62°, 60—61°) *Anal.* Calcd. for $C_{11}H_{12}ClNO$: C, 63.01; H, 5.78; N, 6.68. Found: C, 63.11; H, 5.75; N, 6.90. UV $\lambda_{max}^{80\% EtOH}$ (nm, log ε): 328.5 (4.33), and 4-(*p*-methylphenylimino)-3-pentene-2-one III, mp 68—69° (benzene–petroleum ether) (lit.[6,8] mp 67—68°, 68—69°) *Anal.* Calcd. for $C_{12}H_{15}NO$: C, 76.16; H, 8. 01; N, 7.40. Found: C, 76.12; H, 7.85; N, 7.58. UV $\lambda_{max}^{80\% EtOH}$ (nm, log ε): 324.5 (4.29).

Reagents——2,4-Pentanedione IV was of analytical grade, and was distilled to collect a fraction of 137—140° before use. $FeCl_3 \cdot 6H_2O$, HCl, CH_3COOH, NaOH, KOH and CH_3COONa were of analytical grade, and the organic solvents used here were purified in the usual way and twice-distilled water was used.

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[1] A part of this work was presented at 44th Meeting of Hokuriku Branch of Pharmaceutical Society of Japan at Toyama, June 1977.

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Apparatus——Melting points were measured on a Yanagimoto Micro Melting Point Apparatus and were uncorrected. A Hitachi-Horiba Model 7 pH meter was used for measurement of pH. Spectra were measured with a Hitachi Model 323 and a Shimadzu-Bausch-Lomb Spectronic 70 UV spectrophotometers.

Spectral Measurements——Both Fe^{3+} and the ketoimine stock solutions were prepared by dissolving known amounts of the materials in 80% EtOH, respectively and the complex formations of Fe^{3+} with the ketoimines were examined by continuous variation method. Further studies on the equilibria between Fe^{3+} and the ketoimines were performed by the method of McConnel–Davidson[9] on Fe^{3+} to the ketoimine at a ratio of 1 to 1, and the equilibrium constants for the complexes were obtained, respectively. The pK_a of the ketoimines were determined graphically by using spectral data of the ketoimines measured at various pH.

Calculations of the Equilibrium Constant, log K_1 of Fe(III)-ketoimine Complex and pK_a of the Ketoimines——The equilibrium constant of Fe(III)-ketoimine (1: 1) complex defined below is calculated according to the McConnel-Davidson's equation (1). $a/A = 1/E_c + (1/E_c k)^{1/2}([H^+]/A)^{1/2}$—(1) where, a: initial concentration of Fe^{3+}, A: absorbancy of the solution at definite λ, E_c: molar extinction coefficient of the complex formed, k: equilibrium constant of the complex ML, defined as $M + HL = ML + H^+$, $k = [ML][H^+]/[M][HL]$. When pK_a of the ketoimine is known, stability constant of the complex, $\log K_1$ can be derived according to the equation (2). $\log K_1 = \log k + pK_a$—(2) The pK_a of the ketoimine is calculated from the equation (3). $pH = pK_a + \log (As_1 - As)/(As - As_2)$—(3) where, As: absorbancy of the intermediate form of the ketoimine (HL+L), As_1: absorbancy of the undissociated form of the ketoimine (HL), As_2: absorbancy of the dissociated form of the ketoimine (L). By plotting $\log (As_1 - As)/(As - As_2)$ against pH, pK_a of the ketoimine is obtained as the pH value where $\log(As_1 - As)/(As - As_2)$ is zero.

Results and Discussion

Stability of Ketoimines in Solutions

It is generally known that compounds having a Schiff-base bonding are affected by hydrogen ion in solutions and decomposition of the bonding will occur at low pH region. Therefore, stability of I, II, and III was examined by measuring their spectra at various pH in preceding to study the complex formations. All of the ketoimines showed the same spectral features. A typical spectra of I and IV are shown in Fig. 1.

As are seen in Fig. 1, I was found stable within the pH region from 4.8 to 14. By comparing the spectra of I with those of aniline which are also given in Fig. 1, the spectral behavior might be clearly explained. When the decomposition of the ketoimine occurred, absorbancy near 275 nm increased and it was deduced that the increase of the absorbancy

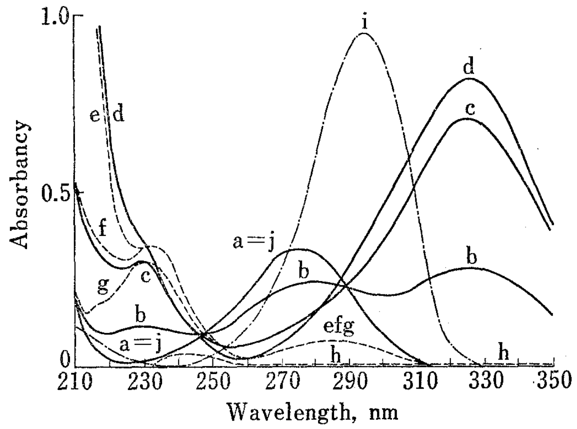

Fig. 1. UV Spectra of 4-Anilino-3-pentane-2-one I, Aniline and 2,4-Pentanedione IV at Various pH

Concentration: I, 4.0×10^{-5} M [pH a) 2.0, b) 3.1, c) 4.8, d) 14] aniline, 4.0×10^{-5} M [pH e) 14, f) 8.6, g) 5.5, h) 3.2] IV, 4.0×10^{-5} M [pH i) 12.1, j) 1.5. Spectra of a and j were superdisposable each other.

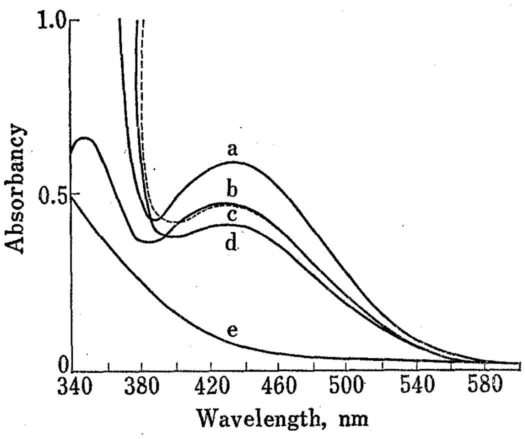

Fig. 2. Spectra of Fe (III) Complexes of Aryl β-ketoimines I, II, and III, and 2,4-Pentanedione IV

Concentration: Fe^{3+}, 5.0×10^{-3} M; ligand, 7.5×10^{-3} M a) Fe^{3+}+II, b) Fe^{3+}+IV, c) Fe^{3+}+III, d) Fe^{3+}+I, e) Fe^{3+}

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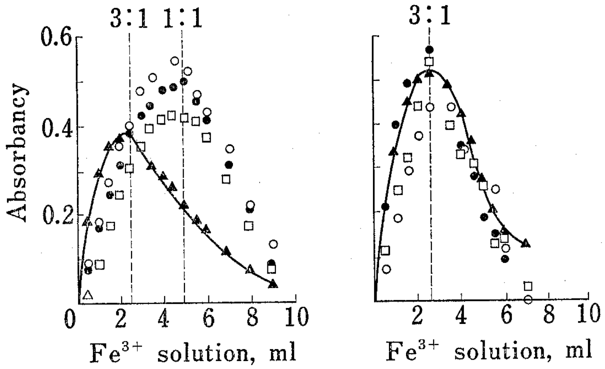
would arise from IV produced by the decomposition of the ketoimine at lower pH. The examination of the ketoimines here used showed that these would be stable between pH 4 and 13.

Consequently, the complex formations of Fe^{3+} with the ketoimines were investigated at this pH region.

Composition of Fe(III)-Ketoimine Complexes

The absorption spectra of Fe(III)-ketoimine complexes are shown in Fig. 2.

As are seen in Fig. 2, these complexes showed maximum absorption between 430 nm and 440 nm, and the spectral features were similar to that of tris(2,4-pentanedionato) iron (III). The continuous variation method clearly indicated definite compositions of these complexes as are given in Fig. 3. In both Fe(III)-ketoimine and tris(2,4-pentanedionato)-iron (III), stepwise complex formations would be anticipated to occur according to gradual increase of pH of the solutions. In fact, composition ratios of Fe^{3+} to the ketoimine ranging from 1:1 to 1:3 were obtained for the complexes, while this was not the case in tris(2,4-pentanedionato) iron (III). Accordingly, the stepwise complex formations could be more clearly observed in the complexes than in tris(2,4-pentanedionato) iron (III). The above finding suggested that the stepwise complex formations would be strongly affected by the steric effect which had been brought by a bulky substitution at nitrogen atom in the ketoimine molecule.



a) at pH4.5

b) at pH6.5

Fig. 3. Continuous Variation Method

○: Fe^{3+}+I, a) at λ 440 nm, b) at λ 430 nm.
●: Fe^{3+}+II, a) at λ 460 nm, b) at λ 460 nm.
□: Fe^{3+}+III, a) at λ 450 nm, b) at λ 450 nm.
▲: Fe^{3+}+IV, a) at λ 450 nm, b) at λ 430 nm.
The total concentration of Fe^{3+} plus the ligand was kept at 2.0×10^{-3}M.

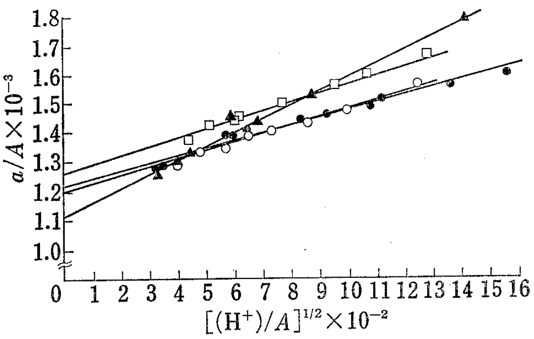


Fig. 4. McConnel-Davidson's Plots

○: Fe^{3+}: I=1: 1 ●: Fe^{3+}: II=1: 1
□: Fe^{3+}: III=1: 1 ▲: Fe^{3+}: IV=1: 1
Both concentrations of Fe^{3+} and the ligand were the same (1.0×10^{-3} M).

Equilibrium Constant and Stability Constant of Fe(III)-Ketoimine Complexes

From the spectral data of the ketoimines and 2,4-pentanedione, pK_a values were obtained for I (8.5), II (5.5), III (7.5) and IV (9.6), respectively. These values showed considerable decrease of basicity of IV by forming β-ketoimine with aniline and its derivatives, and further substitution at *p*-position of aniline moiety with a chlor or a methyl group yielded diversity in basicity of the ketoimine. The treatments of the spectral data by McConnel–Davidson's method are shown in Fig. 4. Equilibrium constant (k) values were calculated for I (2.1×10^2), II (2.2×10^2), III (2.0×10^2) and IV (1.8×10), respectively. Using k and pK_a of the ketoimine, stability constant, log K_1 values were obtained for the complexes (Fe(III)–I, 10.8; Fe(III)–II, 7.8; and Fe(III)–III, 9.8). Log K_1 of tris(2,4-pentanedionato) iron (III) was calculated to be 10.8 by this method. The substitution effect may also be valid for explaining the differences in stability constants of the complexes and here also an electron-donating or -withdrawing group at *p*-position of aniline seems to influence substantially the complex formation between Fe^{3+} and aryl β-ketoimines.

Aknowledgement The authors thank to Mr. M. Hojo for his helpful contribution to this study and to Mr. Y. Itatani and Miss. Y. Arano of this Faculty for elemental analyses.

[Chem. Pharm. Bull.
26(8)2585—2588(1978)]

UDC 547.775.09 : 615.451.011.4.015.14

Effect of Pyrazolone Derivatives on the Critical Micelle Concentration of Ionic Surfactants

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(Received April 4, 1978)

Effect of pyrazolone derivatives on the critical micelle concentration (cmc) of surfactants was investigated by using ionic surfactants which were sodium dodecyl sulfate (SDS) and dodecyl N-dimethylethylammonium bromide (DDAB). It is shown that antipyrine and 4-aminoantipyrine which are very water soluble is in breaking up micelles of SDS and DDAB. However, addition of phenylbutazone which is very slightly soluble in water results in increase in stability of the micelles. It is presumed from these results that the affinity of these additive for water plays an important role in stability of the micelles.

Keywords——hydrophobic interaction; critical micelle concentration; micelle stability; ionic surfactant; pyrazolone derivertives

The preferential association of non-polar groups with each other rather than with the surrounding water molecules is generally referred to as hydrophobic interactions or, less precisely, as hydrophobic or lyophobic bonding.[2] Hydrophobic interactions are responsible to a large degree for stabilization of the secondary and tertiary structures of proteins in aqueous solutions, and protein denaturation is a consequence, at least in part, of the weakening of the hydrophobic interactions of the native proteins by denaturing agents such as urea and guanidium salts.[3] Generally denaturing agents are very water soluble and their efficacy has been ascribed to the breaking of protein-protein hydrogen bonds and preferential formation of protein-denaturants hydrogen bonds. And also it was suggested that the urea-induced increase of the drug-protein binding may be related to a disorganization of the protein structures probably caused by a reduction of the intramolecular hydrophobic force.[3a,4]

However, although the drug-protein binding have been widely investigated,[5] attempts to analyze how the intramolecular hydrophobic forces are influenced by various drugs have

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