PART - I

ANALYTICAL STUDIES WITH THIOPHENE-2-ALDEHYDE GUANYLHYDRAZONE

CHAPTER - I

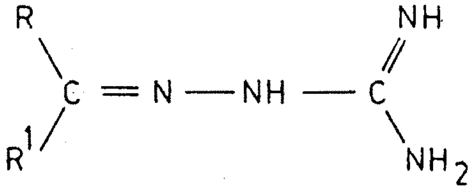
SYNTHESIS AND CHARACTERISATION OF THIOPHENE-2-ALDEHYDE GUANYLHYDRAZONE

1.1 INTRODUCTION

Spectrophotometric method is often preferred for the determination of trace amounts of metal ions. Atomic emission, flame photometry, potentiometry, polarography, radiochemical techniques etc. are also commonly used. To remove the impurities of other metal ions suitable methods can be developed for the analysis of metal ions at trace level. The rapid development both in science and technology also stresses the need for the production of pure materials. Hence new techniques are desirable for the determination of trace impurities in highly pure materials. New analytical methods are based on instrumental techniques.

The organic reagents find extensive applications in spectrophotometry. Photometric determination of inorganic metal ions with organic reagents are based on the reactions which yield products absorbing or emitting radiation. The absorption of UV and visible radiation is thus measured in spectrophotometric applications of organic reagents. These reagents are useful for the development of highly sensitive, selective and rapid methods for the analysis of variety of materials.

Metal complexes of Schiff's bases have occupied a central role in the development of coordination chemistry. As analytical reagents, schiff's bases have more importance in analytical chemistry. Thiosemicarbazones, oximes, ketones and hydrazones have been most widely studied, but guanylhydrazones have not been previously studied as analytical reagents. Aldehydes and ketones give easily crystallizable guanylhydrazone derivatives and this property is used for the identification of the compounds with C = O function. Guanylhydrazones react as chelating ligands and form complexes with transition metal ions. Guanylhydrazones were first synthesized by Thiele and Dralle.[1] Their importance is due to their pharmacological properties. Their general structure is

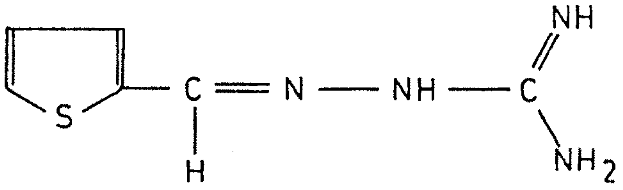


where R and R^1 are H or any organic radical. The analytical properties of the guanylhydrazone depend on the structural features of both R and R^1.

Guanylhydrazones have a similar structure to thiosemicarbazones. The great affinity to sulphur for coordination of metal ions poses a serious hindrance in the use of thiosemicarbazones as analytical reagents, and hence it makes selective methods difficult to establish. The replacement of the sulphur atom of the thiosemicarbazones by the imine group of the guanylhydrazones can increase the selectivity and sensitivity.

The reactivity of schiff's bases is also dependent on the structural characteristics of the aldehyde or ketone which is condensed with the amine. Thiophene-2-aldehyde has been used extensively.

The structure of thiophene-2-aldehyde guanylhydrazone (TAG) is



Guanylhydrazone compounds are cardioactive substances[2,3] and are used as new pharmaceuticals.[4] Several such compounds are useful as bactericides and insecticides[5-7] in treating heart insufficiency and hypersensitivity[8] in normal leukemia bearing mice as growth inhibitors. Some of these compounds have extremely high bacterial activity and are suitable as internal, external and oral disinfectants[9] and are used as antiseptics for foods.[10]

Several guanylhydrazone complexes have antifungal activity[11] and act as anticancer and antiflammatory agents.[12] Some compounds possess antileukemic activity, antihistamine activity,[13] antiviral activity[14] and also antimalarial activity.

Several steroid guanylhydrazones were prepared.[15,16] Inhibitory effect of these compounds are shown on invitro growth of some dermatophytes. They are also useful in waste water purification, precipitation of organic anions especially dyes from waste water.

Some aminoguanidine derivatives are used in photographic materials and for paper treatment,[17] useful as cationic agents for retention of dyes and pigments on cellulose fibres and provides dry and wet strength in paper.

These studies have been very much useful in the chemistry of guanylhydrazone complexes. In the solid state most of the chemical research have been made towards the structure and bonding in metal complexes. No significant investigation is made about the properties of complexes and the reactions of the ligands and complexes. Therefore, the present authors have chosen this topic.

Thiophene-2-aldehyde guanylhydrazone (TAG) can be used for the determination of palladium and iron.

1.2 EXPERIMENTAL

1.2.1 Apparatus :

The absorbance measurements were done on a spectronic-20-Bausch and Lomb equipped with matched pair of glass test-tubes.

For pH measurements, Digital pH meter ELICO, Model L1-120 having glass-calomel combination electrode was used. The pH meter was standardized by using 0.05 M potassium hydrogen phthalate (pH = 4.01) and 0.01 M borax (pH = 9.18) buffers.

All the measurements were done at room temperature $\sim$ 25 to 30°C.

1.2.2 Reagents :

All solvents and reagents were of analytical reagent grade.

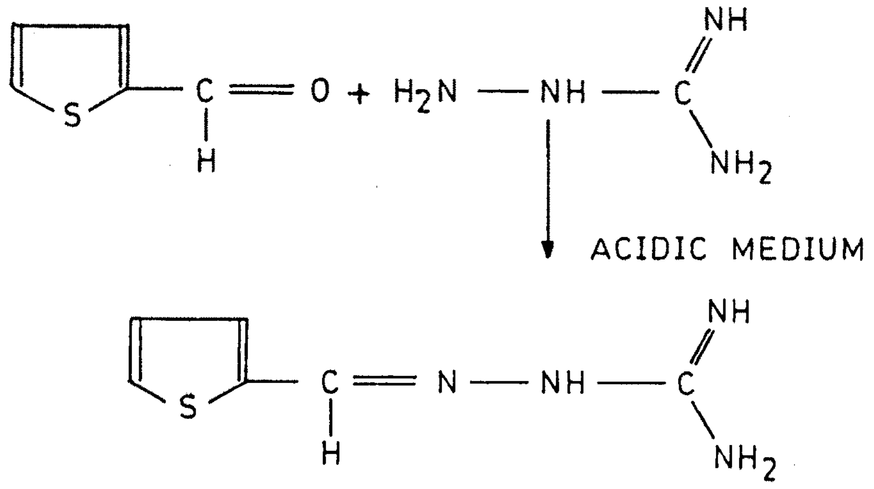
Glass distilled conductivity water was used throughout the work.

1.2.3 Synthesis of TAG :

For the synthesis of thiophene-2-aldehyde guanylhydrazone (TAG), aminoguanidine bicarbonate was used instead of aminoguinidine dihydrochloride, which simplified the synthesis and gave much better yield.

2.0 g. of aminoguanidine bicarbonate was completely dissolved in 60 % nitric acid (till evolution of carbon dioxide was completely stopped). 2.0 ml of thiophene-2-aldehyde was diluted to 10.0 ml with ethanol and the two solutions were mixed together. The mixture was kept as such for about 24 hours. The white coloured product was formed which was filtered and crystallised from ethanol to give shining white crystals of thiophene-2-aldehyde guanylhydrazone (~0.7 g). M.P. = 170°C ± 1°C. The compound is quite stable for months.

The reaction is



1.2.4 Solubility :

The reagent is soluble in ethanol, methanol and acetone but insoluble in water, chloroform, carbon tetrachloride and benzene.

The solution of the reagent in ethanol was stable for months without any deterioration.

1.2.5 Characterisation of TAG :

TAG is stable in air. There is no action of light on the reagent. So, no special care is required to protect it from light.

The microelemental analysis of the chromatographically purified reagent confirmed the formula to be $C_6H_8N_4S$. Calculated percentage of elements are C = 42.85 %, H = 4.77 %, N = 33.34 % and S = 19.04 %. Experimentally found percentage of elements are C = 42.56 %, H = 4.83 %, N = 33.91 % and S = 18.70 %.

1.2.6 Ultraviolet spectra of the reagent (TAG) :

Fig. 1.1 shows the ultraviolet absorption spectra of the reagent (TAG) in ethanol (1.0×10^{-4}M) at different pH values.

Absorption maxima and molar extinction coefficients of the reagent at different pH values are given in table 1.1

Table 1.1 : Spectral characteristics of the reagent (TAG)

pH	Absorbances at λ		Molar extinction coefficients, ϵ l $mole^{-1}$ cm^{-1} at λ	
	307 nm	325 nm	307 nm	325 nm
3.0	1.48	0.62	1.48×10^4	0.62×10^4
5.0	1.35	0.65	1.35×10^4	0.65×10^4
7.0	1.20	0.70	1.20×10^4	0.70×10^4
8.0	1.05	0.75	1.05×10^4	0.75×10^4
9.0	0.96	0.84	0.96×10^4	0.84×10^4
10.0	0.90	1.04	0.90×10^4	1.04×10^4
11.0	0.84	1.26	0.84×10^4	1.26×10^4
12.0	0.78	1.44	0.78×10^4	1.44×10^4
13.0	0.75	1.50	0.75×10^4	1.50×10^4

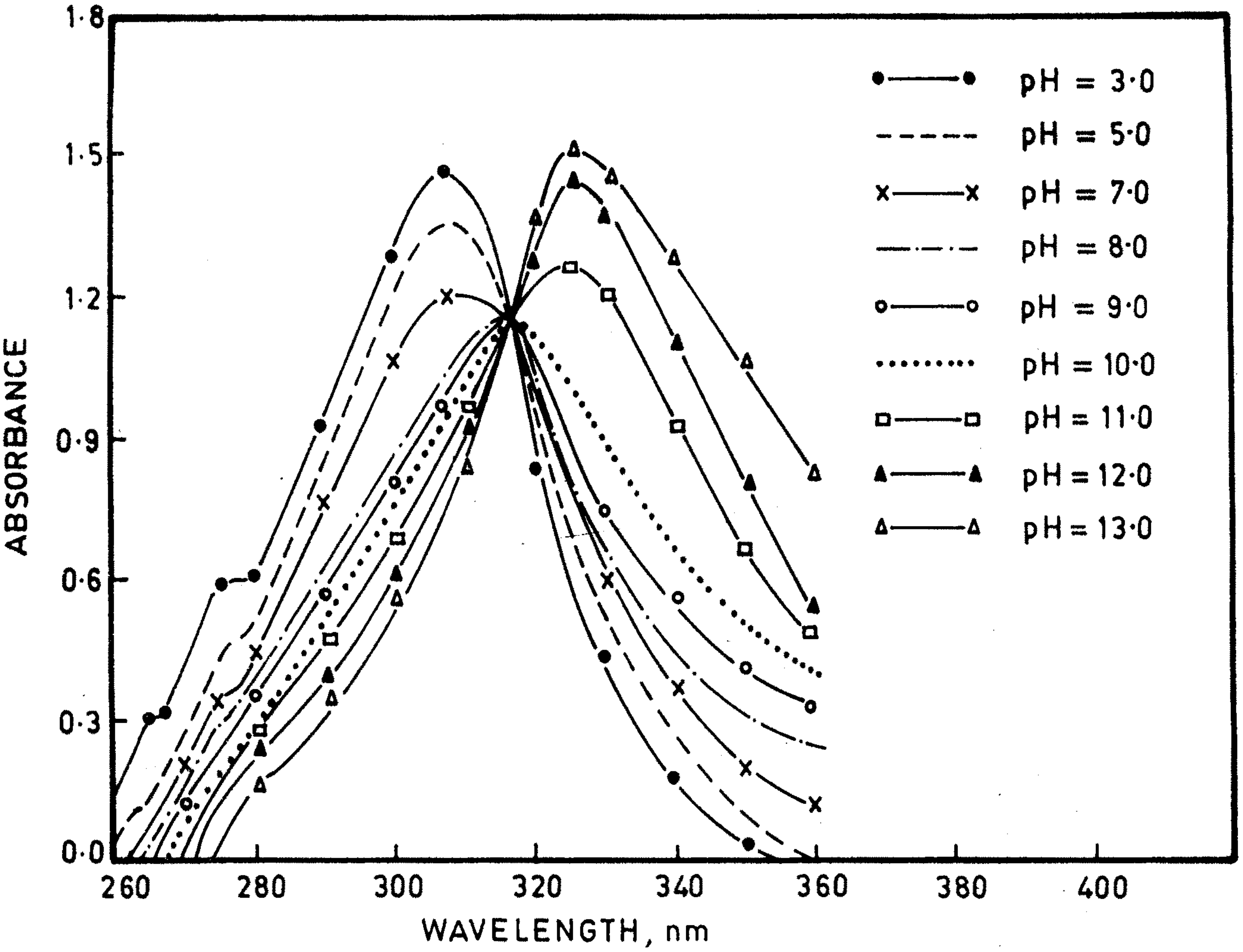


FIG. 1·1 — ULTRAVIOLET SPECTRA OF REAGENT (TAG).

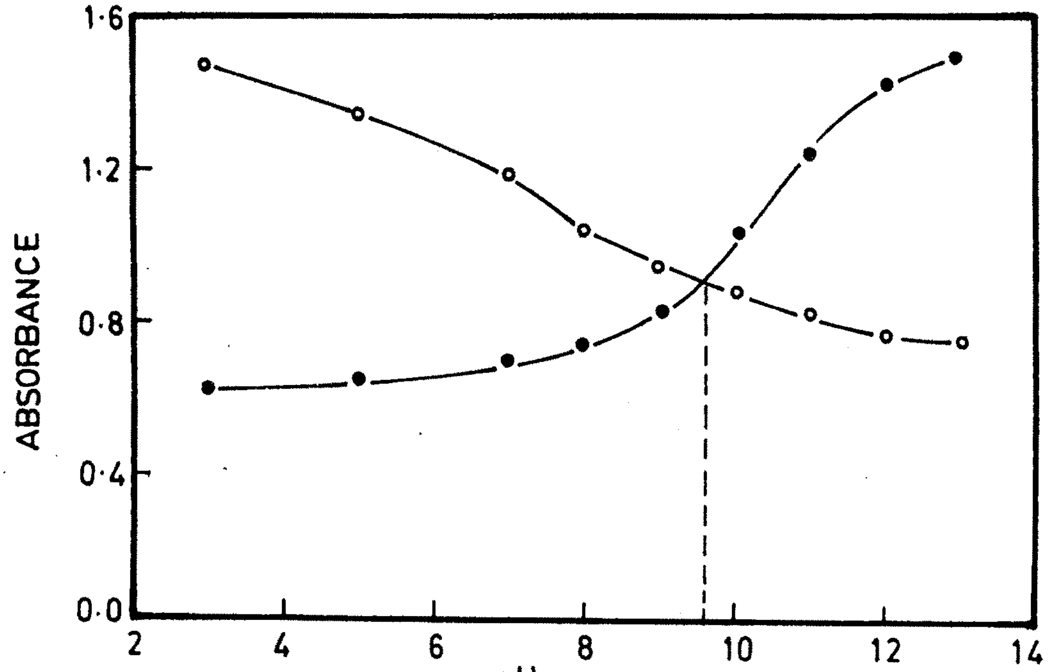


FIG. 1·2 — DETERMINATION OF pK.
○——○ 307 nm, ●——● 325 nm.

1.2.7 Infrared spectrum of the reagent (TAG) :

Infrared absorption spectrum in the range 4000 to 200 cm^{-1} was run on Perkin Elmer 221 IR spectrophotometer in Nujol mull. (Fig. 1.3). The characteristic absorption bands were observed as follows :

3460 cm^{-1}	NH stretch
3200 - 3100 cm^{-1} (broad)	NH$_2$ stretching
2920 cm^{-1}	= N-Vibrations
2720 cm^{-1}	Overtone pattern
2200 cm^{-1}	
1950 cm^{-1}	
1890 cm^{-1}	
1820 cm^{-1}	
1760 cm^{-1}	
1680 - 1600 cm^{-1}	NH$_2$ deformation, complicated pattern
1670 - 1500 cm^{-1}	$N_2C = N$ absorption due to guanidines and due to NH deformation and CN stretching vibrations.
1460 cm^{-1}	Nujol scissoring band H - C - H
1370 cm^{-1}	Nujol symmetric deformation
1145, 1050, 820 cm^{-1}	Ortho substitution pattern
770, 725, 710 cm^{-1}	3 adjacent H wag
719 cm^{-1}	Nujol band
700 - 600 cm^{-1}	C - S - C linkage

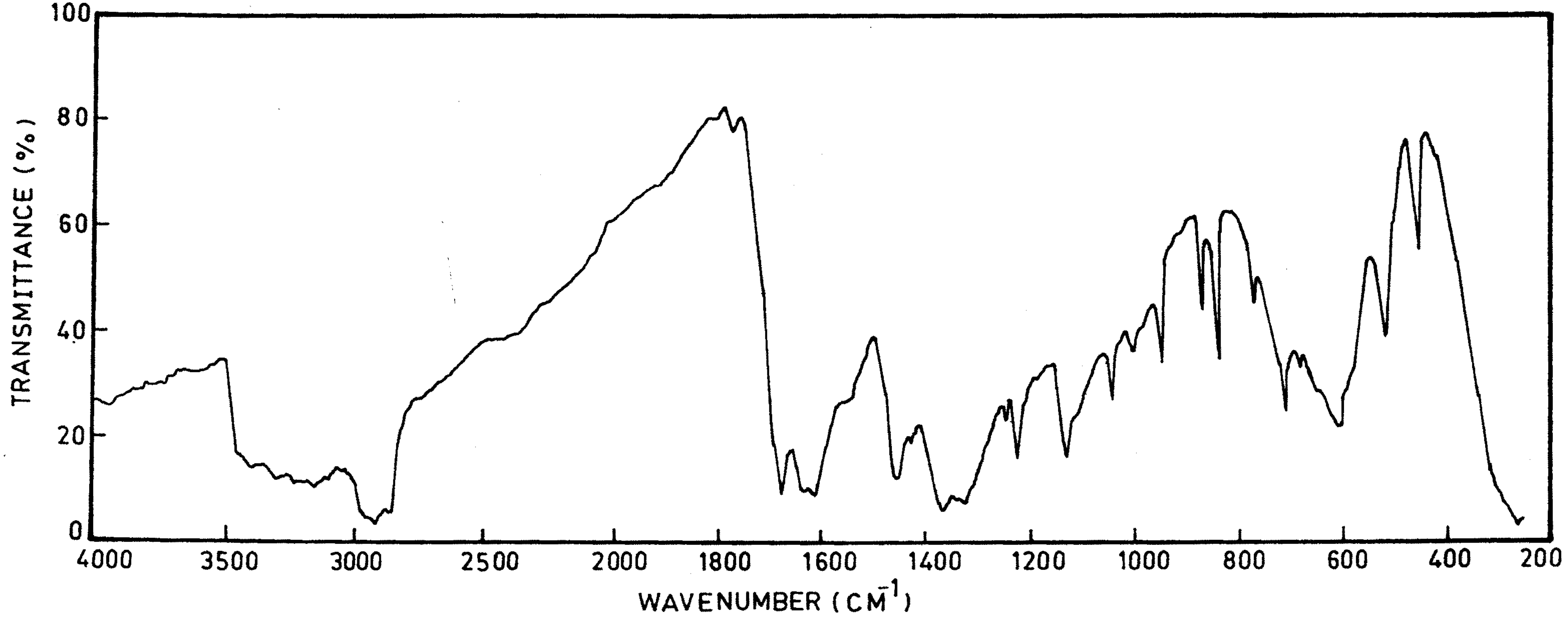


FIG. 1·3 – INFRARED SPECTRUM OF REAGENT (TAG).

1.2.8 Determination of ionization constant of TAG :

The ionization constant of the reagent (TAG) was obtained both by spectrophotometric method and by pH - metric method.

a) By Spectrophotometric Method :

The ultraviolet spectra of the reagent are shown in fig. 1.1. At pH 3.0, the reagent shows the absorption band with λ_{max} at 307 nm, which lowers in intensity as pH increases. With increasing value of pH, the absorbance at longer wavelength increases, and at pH 13.0, highest intensity band with λ_{max} at 325 nm appears. All the spectral curves pass through the isosbestic point at 317 nm, thereby indicating a dynamic equilibrium between ligand and its deprotonated species, assuming that at pH 3.0, the molecular form of the ligand is exclusively present and the deprotonated species is absent and that at pH 13.0, the deprotonated species is present exclusively and the molecular form is absent. By using Henderson equation and also from the half height[18] of the sigmoid curve (Fig. 1.2), the pk value for the deprotonation of the ligand is found to be 9.56.

b) By pH-metric Method :

5.0 ml of 0.01 M TAG was taken in a thermostated titration vessel at 30 ± 1°C containing 20.0 ml distilled water. The solution was titrated with 0.1 M NaOH. An ELICO

Digital pH meter with pH readable to ± 0.01 was used. The pH meter was calibrated with pH 4.01 and 9.18 by phthalate and borax buffers respectively. The ionization constants were calculated from the pH values. The pk was determined by using the formula

$$pK = pH + \log \frac{[HA]}{[A^-]}$$

HA represents the reagent, TAG. The log $[H^+]$ values were read from the pH meter.

The titration was repeated until two sets of values differing within ± 0.01 pH units were obtained. The results of study are summarised in table 1.2 which show that the pk is 9.56 for thiophene-2-aldehyde guanylhydrazone (TAG).

Table 1.2 : Determination of ionisation constant of TAG at 30 ± 1°C.

[TAG] = 0.01 M; NaOH = 0.1 M.

NaOH ml	pH	Stoichiometric concentration		$\log\frac{[HA]}{[A^-]}$	pK
		HA	A^-		
0.5	7.49	0.018	0.002	0.954	8.444
1.0	8.51	0.016	0.004	0.602	9.112
1.5	9.50	0.014	0.006	0.367	9.867
2.0	9.78	0.012	0.008	0.176	9.956
2.5	9.98	0.010	0.010	0.000	9.980
3.0	10.08	0.008	0.012	-0.176	9.904
3.5	10.16	0.006	0.014	-0.367	9.793
4.0	10.27	0.004	0.016	-0.602	9.668
4.5	10.31	0.002	0.018	-0.954	9.356
				Mean pK =	9.56

1.2.9 Complex formation :

The reagent (TAG) forms complexes with Pd(II) and Fe(II). A detailed account of the complex formation with these two metals is discussed in the 2nd and 3rd chapters respectively.

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