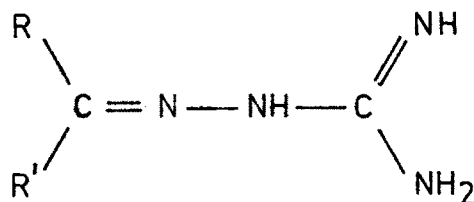


CHAPTER - I

SYNTHESIS AND CHARACTERISATION OF  
2 -BENZOYL PYRIDINE GUANYLHYDRAZONE

### 1.1 INTRODUCTION :

Schiff's bases are interesting as analytical reagents. Oximes, hydrazones and thiosemicarbazones have been the most widely studied; but guanylhydrazones have not previously been 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.<sup>1</sup> Their importance is due to their pharmacological properties. Their general structure is



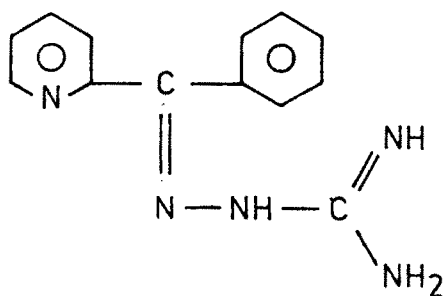
where R and R' are H or any organic radical. The analytical properties of the guanylhydrazone depend on the structural features of both R and R'.

Guanylhydrazones have a structure similar to thiosemicarbazones. The great affinity to sulphur for coordination of metal ions poses a serious hindrance in the

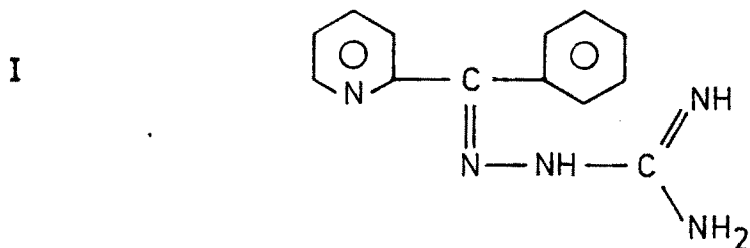
use of thiosemicarbazones as analytical reagents, and hence it makes selective methods difficult to establish. The replacement of the sulphur atom of the thiosemicarbazones by the imine group of the guanylhydrazones can increase the selectivity.

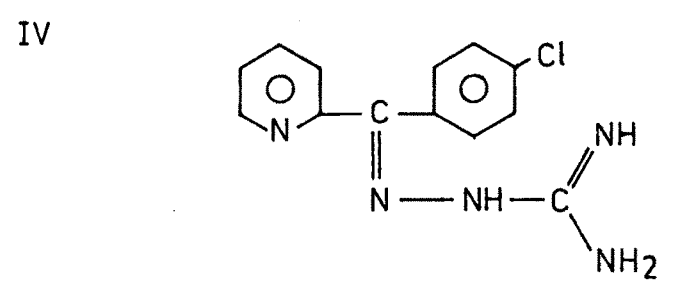
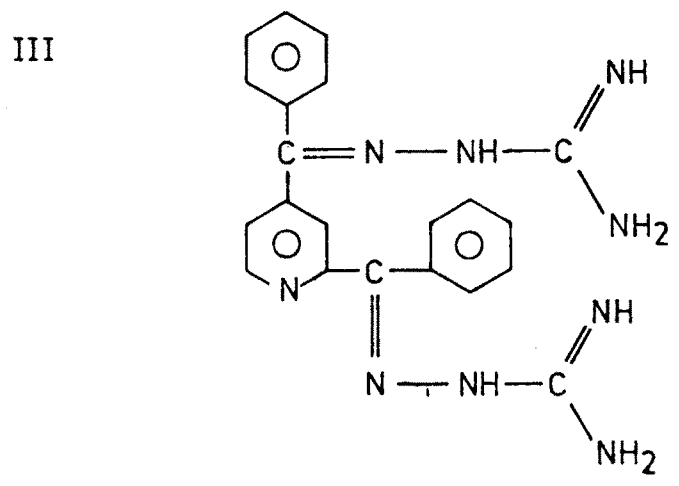
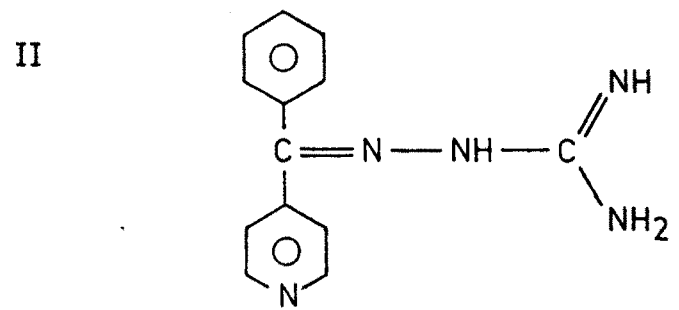
The reactivity of Schiff's bases is also dependent on the structural characteristics of the aldehyde or ketone which is condensed with the amine. 2-Benzoyl pyridine has been used extensively.

The structure of 2-benzoyl pyridine guanylhydrazone (BPG) is



Four compounds<sup>2</sup> and the hydrochloride salts of benzoyl pyridine guanylhydrazones were prepared. They are useful as prolonged acting antihypertensive drugs.





Several compounds were prepared with guanylhydrazones and are useful as bactericides and insecticides,<sup>3-5</sup> in treating heart insufficiency and hypersensitivity,<sup>6</sup> in normal leukemia bearing mice as growth inhibitors.

Some Such compounds have extremely high bacterial activity and are suitable as internal, external and oral disinfectants,<sup>7</sup> and are used as antiseptics for foods.<sup>8</sup>

Several guanyldrazone complexes have antifungal activity<sup>9</sup> and act as anticancer and antiinflammatory agents.<sup>10</sup>

Some compounds possess antileukemic activity, antihistamine activity,<sup>11</sup> antiviral activity<sup>12</sup> and also antimalarial activity.

Several steroid guanyldrazones were prepared.<sup>13,14</sup> 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 waters.

Some aminoguanidine derivatives are used in photographic materials and for paper treatment,<sup>15</sup> useful as cationic agents for retention of dyes and pigments on cellulose fibres and provide dry and wet strength in paper.

Guanyldrazone compounds are cardioactive substances<sup>16,17</sup> and also used as new pharmaceuticals.<sup>18</sup>

These studies have created an increased interest in the chemistry of complexes of guanyldrazones. Because of the several applications of guanyldrazone to pharmacology there has been almost a unidirectional growth in the field of

physiological activity of the ligands and their ability to form chelates with trace metals. Most of the chemical research is directed towards the structure and bonding in complexes in the solid state. No significant investigation is made about the properties of complexes in solutions and virtually nothing is known of the reactions of the ligands and complexes. It is with this view that the present authors have chosen the topic.

2-Benzoyl pyridine guanylhyazone (BPG) can be used for the determination of cobalt, Nickel, Iron, Copper and Silver. The reagent is useful for the determination of single elements.

## 1.2 EXPERIMENTAL :

### 1.2.1 Apparatus :

Preliminary colorimetric work is done on a Carl Zeiss grating spectrophotometer, Spekol equipped with ZV booster amplifier and EGS and EG photocells. A matched pair of glass cuvettes ( 10.01 mm) was used.

The absorbance measurements over ultraviolet and visible regions are made on a Beckman Model DU 2 ultraviolet spectrophotometer ( Sr. No. 109200 ) equipped with tungsten lamp, red-sensitive phototube and photomultiplier. Standard 10 mm path length rectangular cells were used.



For the measurement of the pH values of the solutions, Philips pH meter PR. 9405 L was used with Philips PV 9014 combination electrode. The pH meter was standardized by using phthalate ( pH 4.0 ) and borax ( 9.15 ) buffers.

The measurements were done at room temperature  $\sim 30^{\circ}\text{C}$

#### 1.2.2 Reagents :

All solvents and reagents were of analytical reagent grade.

Glass distilled conductivity water was used throughout the work.

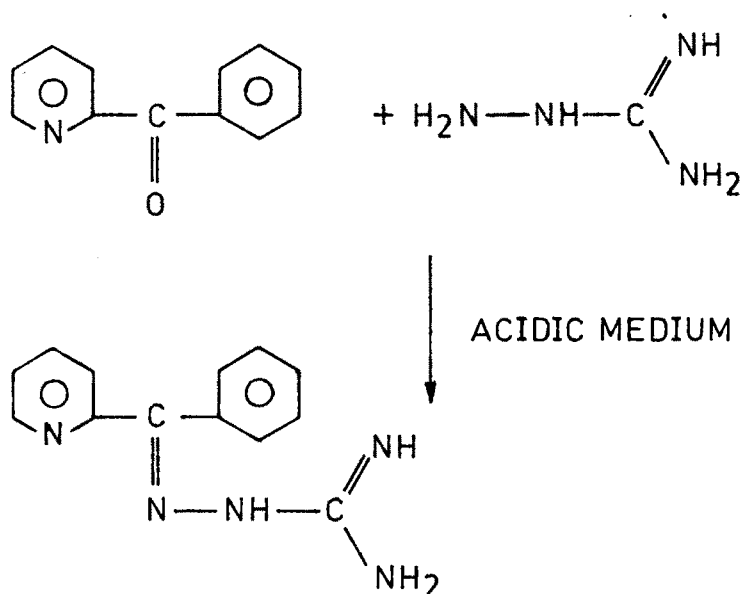
#### 1.2.3 Synthesis of BPG :

For the synthesis of 2-benzoyl pyridine guanyldrazone (BPG), aminoguanidine bicarbonate was used instead of aminoguanidine 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 ). 2.68 g of 2-Benzoyl pyridine was dissolved in methyl alcohol and the two solutions were mixed together. The pH of the solution was adjusted to 2 to 3 with dilute hydrochloric acid. The mixture was kept as such for about 24 hours.

To this mixture, then aqueous concentrated ammonia solution was added to adjust <sup>the</sup> pH of the solution to 8 to 9. The yellowish coloured product was formed which was filtered and crystallised from ethanol-water mixture twice to give yellow needles of benzoyl pyridine guanyldrazone ( $\sim 3.5$  g). M.P. =  $148^\circ - 150^\circ\text{C}$ . The compound is quite stable for months.

The reaction is



#### 1.2.4 Solubility :

The Reagent is sparingly soluble in cold water. It is soluble in methanol and ethanol. It is also soluble in acetone, n- butanol, n-propanol and methyl ethyl ketone, but insoluble in chloroform and carbon tetrachloride.



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

#### 1.2.5 Characterization of BPG :

BPG 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  $C_{13}H_{13}N_5$ . Calculated percentage of elements are C = 65.27%, H = 5.44% and N = 29.29%. Experimentally found percentage of elements are C = 64.80%, H = 5.40% and N = 29.80%.

#### 1.2.6 Ultraviolet Spectra :

Figure 1.1 shows the absorption spectrum of the reagent (BPG) in ethanol ( $1.255 \times 10^{-5}M$ ).

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

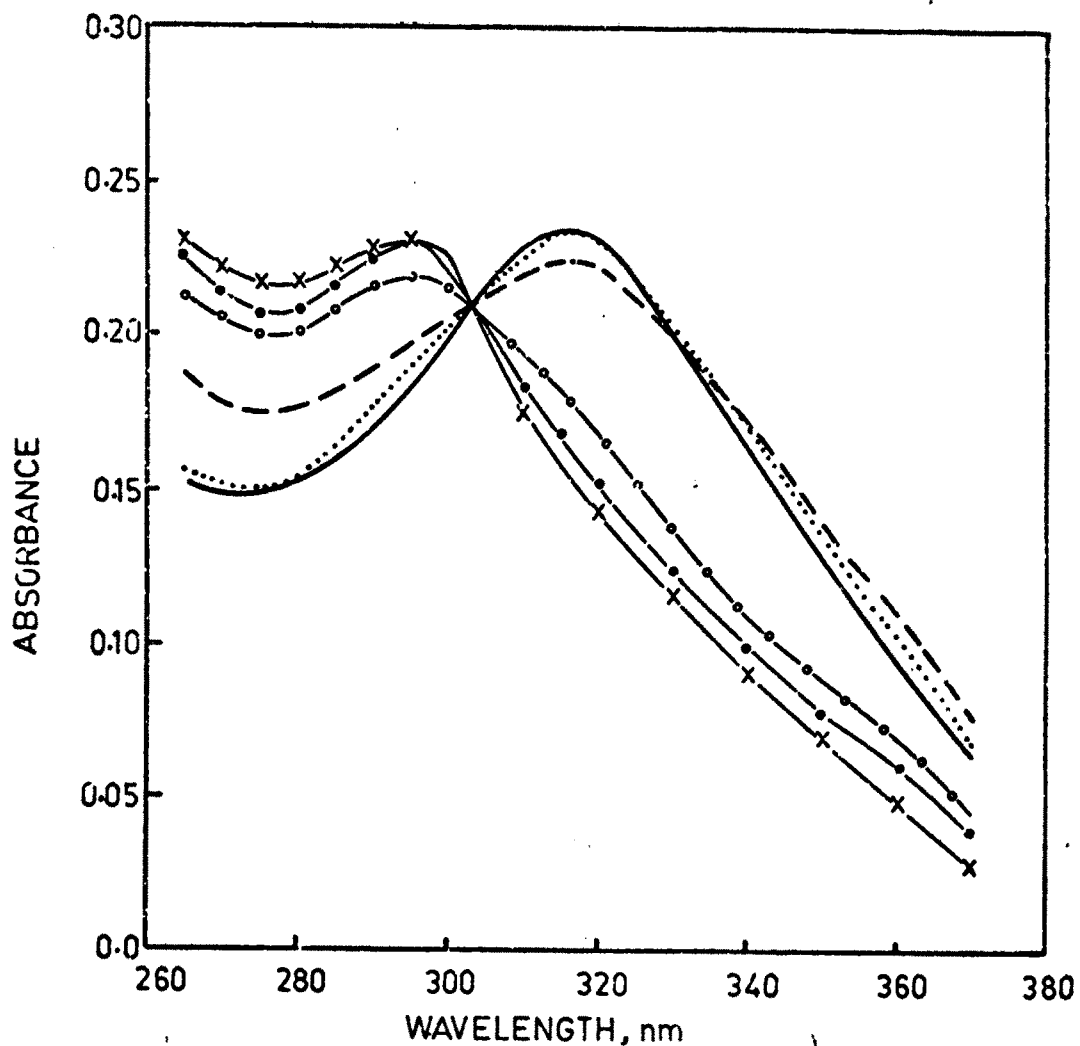


FIG.1.1 ULTRAVIOLET SPECTRA OF REAGENT (BPG).

x—x—x pH = 7.5  
 ●—●—● pH = 8.0  
 ●—●—● pH = 9.0  
 - - - - - pH = 10.0  
 ..... pH = 11.0  
 ——— pH = 12.0

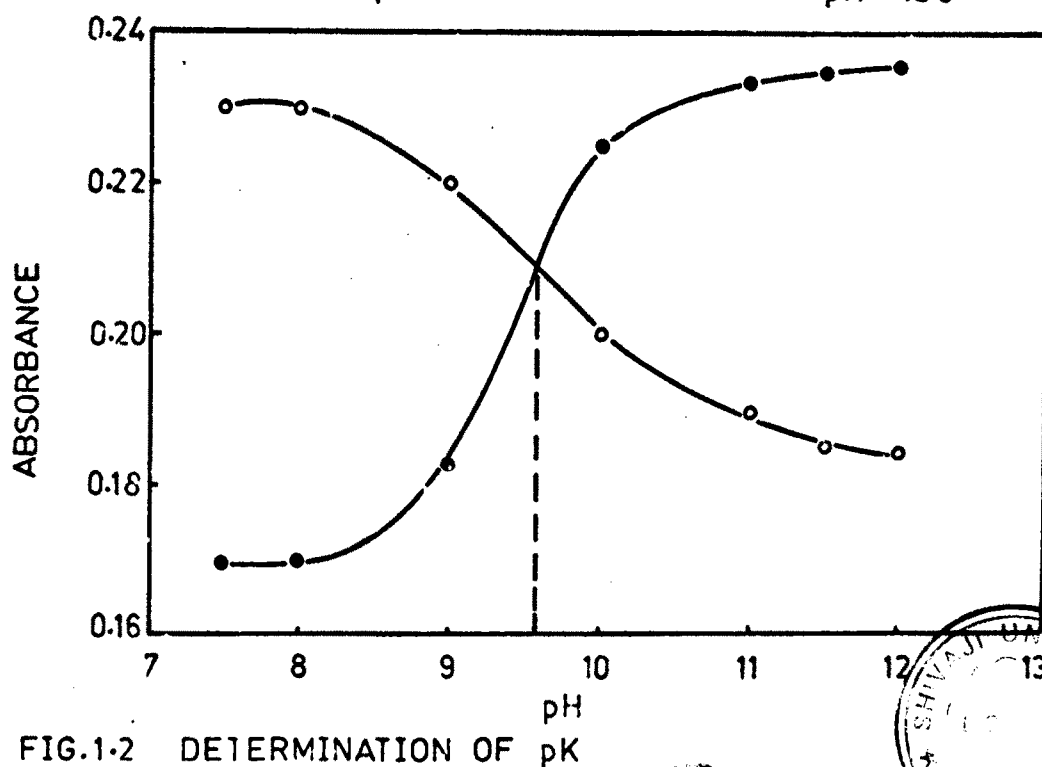


FIG.1.2 DETERMINATION OF pK

○—○—○ 295 nm ; ●—●—● 315 nm

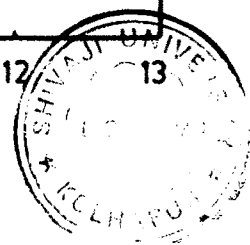


Table 1.1 : Spectral characteristics of the reagent in  
Ultraviolet region.

pH	Absorbance at $\lambda$	Molar extinction coefficients, $\epsilon$
7.5	: 295 nm	: $1.833 \times 10^4 \text{ l. mole}^{-1} \text{ cm}^{-1}$
8.0	: 295 nm	: $1.833 \times 10^4 \text{ l. mole}^{-1} \text{ cm}^{-1}$
9.0	: 295 nm	: $1.753 \times 10^4 \text{ l. mole}^{-1} \text{ cm}^{-1}$
10.0	: 315 nm	: $1.793 \times 10^4 \text{ l. mole}^{-1} \text{ cm}^{-1}$
11.0	: 315 nm	: $1.873 \times 10^4 \text{ l. mole}^{-1} \text{ cm}^{-1}$
12.0	: 315 nm	: $1.873 \times 10^4 \text{ l. mole}^{-1} \text{ cm}^{-1}$

#### 1.2.7 Infrared Spectra :

Infrared absorption spectra in the range  $4000$  to  $500 \text{ cm}^{-1}$  were run on Perkin Elmer 221 IR Spectrophotometer in Nujol mull. The characteristic absorption bands were observed as follows.

3530 $\text{cm}^{-1}$	→	$\text{NH}_2$ asymmetric stretch
3460 $\text{cm}^{-1}$	→	NH stretch
3340 $\text{cm}^{-1}$	→	$\text{NH}_2$ stretch symmetric
2960 $\text{cm}^{-1}$	→	CH stretch for methyl group- Nujol band
2930 $\text{cm}^{-1}$	→	CH stretch for methylene groups- Nujol band
2720 $\text{cm}^{-1}$	→	} Overtone pattern.
2200 $\text{cm}^{-1}$	→	
1950 $\text{cm}^{-1}$	→	
1920 $\text{cm}^{-1}$	→	
1890 $\text{cm}^{-1}$	→	
1820 $\text{cm}^{-1}$	→	
1760 $\text{cm}^{-1}$	→	
1650- 1590 $\text{cm}^{-1}$	→	$\text{NH}_2$ deformation
1610 $\text{cm}^{-1}$	→	Aromatic ring frequency
1590 $\text{cm}^{-1}$	→	Guanidines - $\text{N}_2\text{C}=\text{N}$ absorption
		1500-1670 $\text{cm}^{-1}$ due to NH deformation.
1570 $\text{cm}^{-1}$	→	2-substituted pyridine ring
1520 $\text{cm}^{-1}$	→	CN-H bending of secondary aromatic amine
1490 $\text{cm}^{-1}$	→	Aromatic band
1460 $\text{cm}^{-1}$	→	Nujol scissoring bend, H-C-H
1390 $\text{cm}^{-1}$	→	Nujol symmetric deformation of terminal methyl group
1120 $\text{cm}^{-1}$	→	Aromatic band-monosubstituted benzene
780 $\text{cm}^{-1}$	→	5 adjacent H wag
740 $\text{cm}^{-1}$	→	4 adjacent H wag for pyridine ring

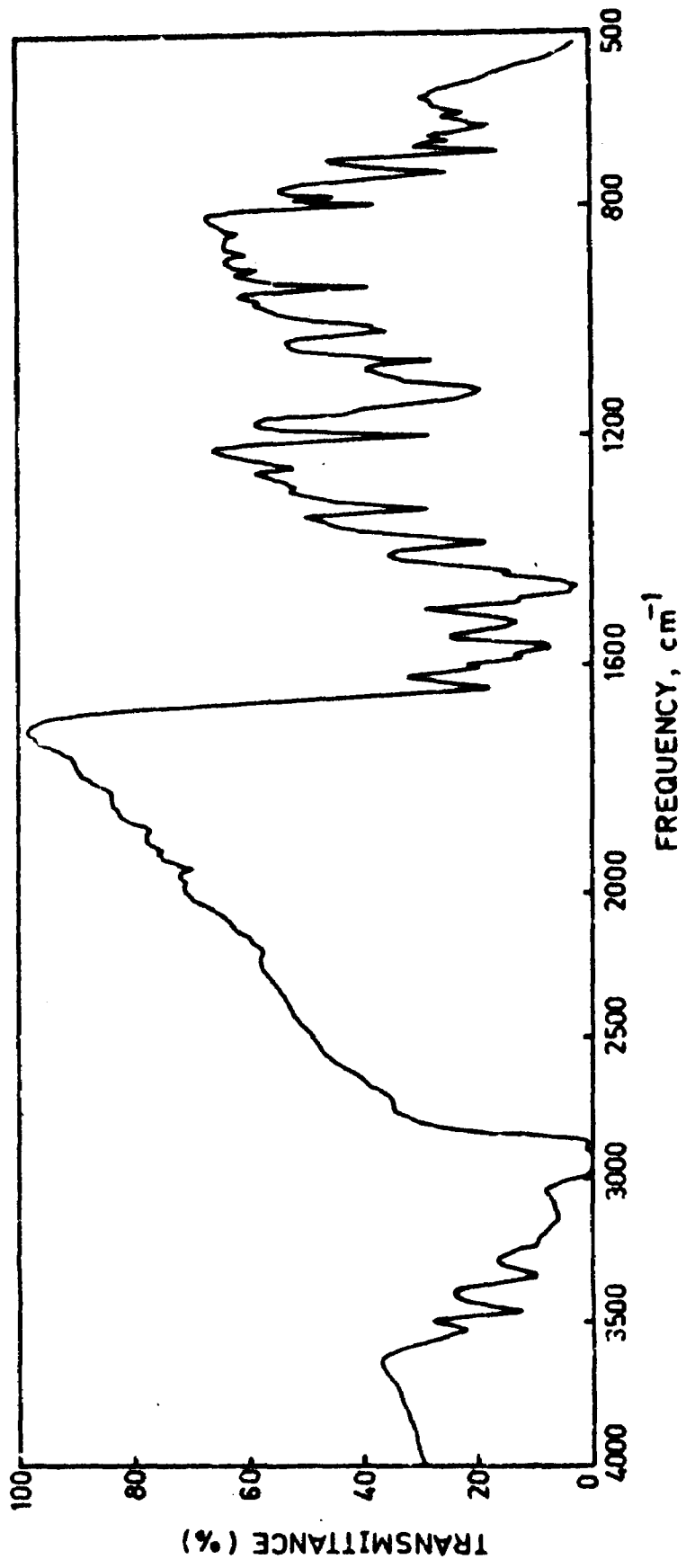


FIG. 1-3 INFRARED SPECTRUM OF REAGENT (BPG).

The infrared spectrum of the reagent (BPG) is shown in figure 1.3.

1.2.8 Determination of ionization constants of BPG :

To determine the ionization constant of the reagent, the hydrochloride salt of BPG was prepared as follows :

60 mg of the reagent (BPG) was taken in an evaporating dish. To this, 4.0 ml concentrated hydrochloric acid was added and the mixture was evaporated almost to dryness. The hydrochloride salt of 2-benzoyl pyridine guanylhydrazone (L.HCl) was thus prepared. It was then dissolved and diluted with distilled water.

The ionization constant was obtained pH metrically by the titration of 2-benzoyl pyridine guanylhydrazone- hydrochloride ( L.HCl) Vrs. 0.1 N sodium hydroxide, which gives the pK value as 6.1 for the process L.HCl to L.

Further above pH 7.0, the ligand base, L is studied spectrophotometrically, which shows the absorption band with  $\lambda_{max}$  at 295 nm, which lowers in intensity as pH increases. With increasing value of pH, the absorbance at longer wavelength increases, and at pH 12.0, highest intensity band with  $\lambda_{max}$  at 315 nm appears ( Fig.1.1). All the spectral curves pass through the isosbestic point at 303 nm, thereby indicating a

dynamic equilibrium between L and its deprotonated species, assuming that at pH 7.5, the molecular form of the ligand is exclusively present and the deprotonated species is absent, and that at pH 12.0, the deprotonated species is present exclusively and the molecular form is absent. By using Hinderson equation and also from the half height<sup>19</sup> of the sigmoid curve (Fig.1.2), the pK value for the deprotonation of the ligand is found to be 9.6.

#### 1.2.9 Complex formation :

The reagent (BPG) forms complexes with Co(II), Ni(II), Fe(II), Cu(II) and Ag(I). A detailed account of the complex formation with these five metals is discussed in the following chapters.

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