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Reactions of Substituted Pyridinium Salts with Cyanide; Formation and Metal Complexes of 2,2'bis (hydroxymethyl)-4,-4'bipyridine

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This is to certify that the dissertation prepared by DOROTHY NWANYINNA ESEONU entitled:

PART I - "REACTIONS OF SUBSTITUTED PYRIDINIUM SALTS WITH CYANIDE"

PART II - "FORMATION AND METAL COMPLEXES OF 2,2' BIS(HYDROXYMETHYL)-4,4'-BIPYRIDINE"

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Part I - "Reactions of Substituted Pyridinium Salts with Cyanide"

Part II - "Formation and Metal Complexes of 2,2'-Bis(Hydroxymethyl)-4,4'-Bipyridine"

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University

By

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TABLE OF CONTENTS

LIST OF FIGURES

Figure **Page**

Figure **Page**

Figure **Page**

Figure **Page**

LIST OF ABBREVIATIONS

α	Alpha
β	Beta
B. M.	Bohr Magneton
^0C	Degrees Celsius
$CDCl_3$	Deuterated Chloroform
cm^{-1}	Wavenumber
^{13}C NMR	Carbon-13 Nuclear Magnetic Resonance
DMF	Dimethylformamide
DMSO-d_6	Deuterated Dimethylsulfoxide
DSS	3-(Trimethylsilyl)-Propanesulfonic Acid, Sodium salt
Dq	Crystal Field parameter
B	Interelectronic repulsion parameter
ESR	Electron spin Resonance
GC/MS	Gas Chromotography/Mass Spectra

g	Gram
^{1}H NMR	Proton Nuclear Magnetic Resonance
HP	Hematoporphyrin
IR	Infrared
mL	Milliliter
mol	Mole
nm	Nanometer
NAD	Nicotinamide adenine dinucleotide
NADP	Triphosphopyridine nucleotide
NHE	Normal Hydrogen Electrode
NIR	Near Infrared
Ph	Phenyl
$PhCH_2$	Benzyl
ppm	Parts Per Million
TMS	Tetramethylsilane
UV-VS	Ultraviolet-Visible Spectroscopy
V	Volts

VK_3	Vitamin K_3
λ	Wavelength
ZnTppS33-	Mesotetraphenylporphinetrisulfonate

ABSTRACT

PART 1 - "REACTIONS OF SUBSTITUTED PYRIDINIUM SALTS WITH CYANIDE"

PART II - "FORMATION AND METAL COMPLEXES OF 2,2'-BIS(HYDROXYMETHYL)-4,4'-BIPYRIDINE"

Dorothy Nwanyinna Eseonu

Virginia Commonwealth University

Director: Dr. Lawrence J. Winters

The unique combination of properties of bipyridinium salts and their use in biological systems, chemical reactions, and as herbicides in agriculture have made them a discovery of major international importance. The controversy about the position of attack of the cyanide ion on the pyridine ring and the discovery of the formation of unsubstituted bipyridinium salts from the reaction of pyridinium salt with cyanide ion opened a new area of research.

The current work involved a study of reactions of substituted pyridinium salts with cyanide ion. The substituted pyridinium salts were prepared by the literature methods. The 2-and 3-cyanopyridinium salts reacted with cyanide ion to form 4-cyano-1,4-dihydropyridines. The 3,4-dicyano-1,4-dihydropyridines were very stable; therefore, they were isolated and characterized. An unusual product, 1-methyl-2-oxo-1,2-dihydro-4-pyridine carbonitrile, was isolated from the reaction of 1-methyl-2-cyanopyridinium iodide with cyanide ion.

The reaction of 1-benzyl-2-(acylamino)pyridinium bromide with cyanide ion did not form a 1,4-dihydropyridine; rather, hydrogen bromide was lost when the reaction mixture was heated to a boil and

1-benzylpyridinium-2-acylimide was formed. The reaction of the 1-benzyl-2-acetylpyridinium salt, the 1-benzyl-2-bromopyridinium salt, and the 1-benzyl-2-ethylpyridinium salt with cyanide ion formed complicated products that were not characterized.

The reactions of 1-benzyl-2-methylpyridinium bromide, 1-benzyl-2-(hydroxymethyl)pyridinium bromide and 1-benzyl-2,6-dimethylpyridinium bromide with cyanide ion in water, acetone, acetone-water or 95% ethanol solutions formed dark blue or green solutions. Electron spin resonance spectroscopy showed the presence of a radical in these dark-blue or green solutions. A dark solid formed from the solutions. Oxidation of the solid with an acetone and ethanolic iodine solution or acidic ethanol solution resulted in the formation of the corresponding new, 1,1'-dibenzyl-2,2'-bis(hydroxymethyl)-4-4'-bipyridinium dibromide **75**, and the known 1,1'- dibenzyl-2,2' - dimethyl -4,4'-bipyridinium dibromide, and 1,1' -dibenzyl- 2,2', 6,6'-tetramethyl- 4,4' - bipyridinium dibromide dimers.

The new dimer **75** was reduced in aqueous solution at potential (E^{o}) of about -0.34V vs NHE. It was also debenzylated with triphenylphosphine in refluxing DMF to give 2,2'-bis(hydroxymethyl)-4,4'-bipyridine **89**. 1,1'-Dibenzyl-2,2'-dimethyl-4,4'-bipyridinium dibromide was also debenzylated to give 2,2'-dimethyl-4,4'-bipyridine, which was acidified with hydrogen chloride gas, and the salt 2',2'-dimethyl-4,4'-bipyridyl dihydrochloride was formed. These were the first report on debenzylation of bipyridinium dimers. The reaction of **89** with cobalt thiocyanate formed a new 2,2'-bis(hydroxymethyl)-4,4'-bipyridine cobalt thiocyanate octahedral complex. The reaction of 2-(hydroxymethyl)pyridine and 2-(2-hydroxyethyl)pyridine with cobalt thiocyanate gave the corresponding octahedral complexes.

INTRODUCTION

The unending research on synthesis and characteristics of substituted and unsubstituted bipyridinium salts arises from their uses as redox indicators and electron carriers in biological systems [1], in chemical reactions [2], and as herbicides in agriculture [3]. Dialkyl-4,4'-bipyridinium dihalides belong to a unique class of materials which can be reduced at potentials between 0.0 and -1.0v to form stable cation radicals. These radicals are purple in color, hence their trivial name viologens. In addition, viologens have been used as the main component of electrochemical display cells [4], because the parent dication is water soluble, whereas the reduced material precipitates and imparts memory capabilities to the system (Figure 1).

It is known that alkylated pyridinium salts are unstable in the presence of nucleophiles [5]. In the presence of a nucleophile, scrambling of the alkyl groups is likely to occur in systems in which unsymmetrical pyridinium salts are used [6] (Figure 2).

A compound containing 1,1'-disubstituted-2,2'-dialkyl-4,4'-bipyridinium dihalide has been used as a herbicide [7], although it has been shown that when the 2,2'-substituent groups are electron withdrawing (eg. CN), the compound is inactive as a herbicide [8]. 1,1'-Disubstituted-2,2'-dialkyl-4,4'-bipyridinium dihalides have also been recently used as electron relays [9], and as electron-transfer agents [10, 11, 12]. Addition of a surface active 4,4'-bipyridinium dichloride in a liquid membrane containing vitamin K_3 (VK_3) has been shown to enhance the rate of electron transport from $S_2O_4^{2-}$ to $Fe(CN)_6^{3-}$ [13]. The structure-activity correlations of amines inhibiting active uptake of 4,4'-bipyridinium dihalides into rat lung slices has also been studied [14].

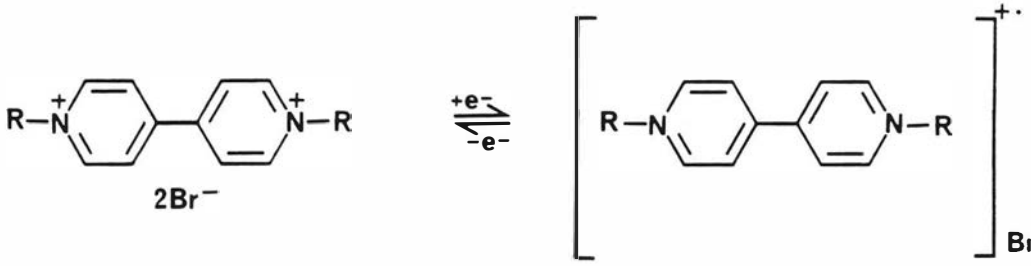
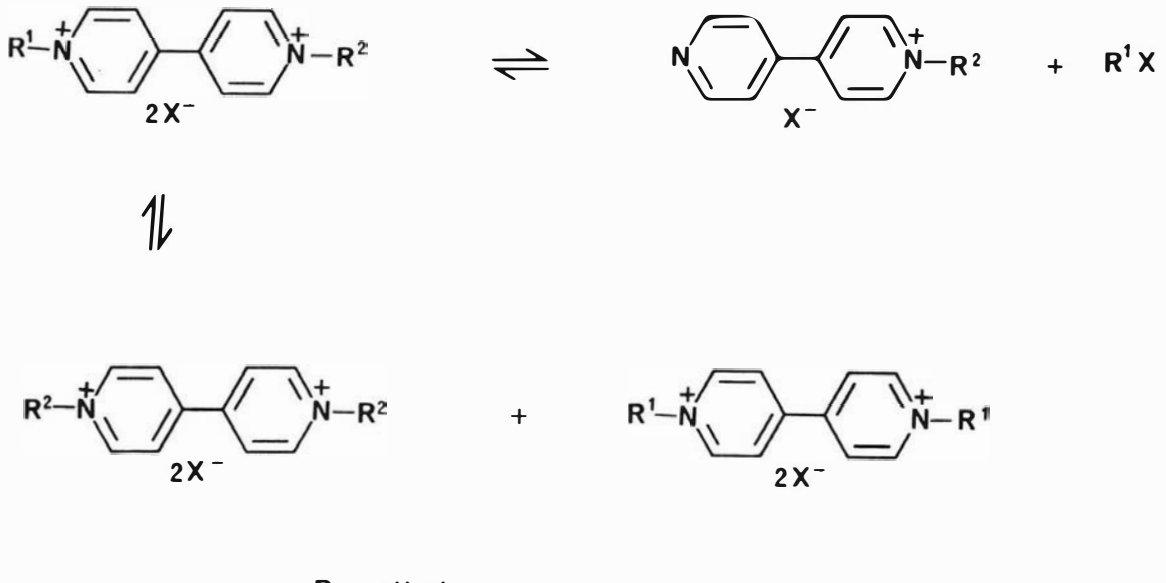


Figure 1. Reversible Reactions Between Bipyridinium Dication and Cation Radical.



R = alkyl group

Figure 2. Scrambling of the Alkyl Groups in Unsymmetrical Viologens.

There have been many reports on the reactions of 1-alkyl or aryl-substituted pyridinium salts with cyanide ion [14-23] and several different opinions have been expressed about the position of attack. At first, it was believed that the attack was at the 2- or 6-positions [24, 25], yielding a 1,2 or 1.6-dihydropyridines, **1** and **2** (Figure 3); but later, it was shown to involve the 4-position [26], yielding a 1-substituted-4-cyano-1,4-dihydropyridine as the product. There was a substituent effect when a large substituent was attached to the nitrogen [27, 28]. Electron withdrawing groups in the 3- and 5-positions were believed to be needed for the reaction to occur and to stabilize the product once it was formed [29].

The first dimerization of 1-substituted pyridinium salts with sodium or potassium cyanide was reported in 1967 by L.J. Winters and coworkers [30]. Under anaerobic conditions, unsubstituted 1-alkyl or 1-aryl pyridinium salts, **3**, reacted with sodium cyanide to form a dark solid identified as cation radical **4** . Oxidation of the radical with an alcoholic iodine solution, or with air in an acidic solution yielded the corresponding 1,1'-disubstituted-4,4'-bipyridinium dication, **5**, (Figure 4). The exploration of the uses of pyridinium and 4,4'-bipyridinium salts has continued in the 1980s. Fuhrhop et al [31] reported that pyridinium and 4,4'-bipyridinium ylides of long chain malonic esters (synthesized from distearyl bromomalonate and nitrogen heterocycles) were vesiculating pH indicators. Yamamura and coworkers in 1987, reported a novel electric stimulus-response system in which liquid crystalline bipyridinium salts, inserted between two NESA [In_2O_3 - SnO_2] electrodes, caused remarkable enhancement of the electric conductivity when a DC voltage stimulus of 1-30v was applied [32].

Recently, Chen and coworkers [33] investigated the photochromic behavior of pyridinium salts and polypyridinium salts using poly(1-vinylpyrrolidone) and poly(vinyl alcohol) as matrixes.

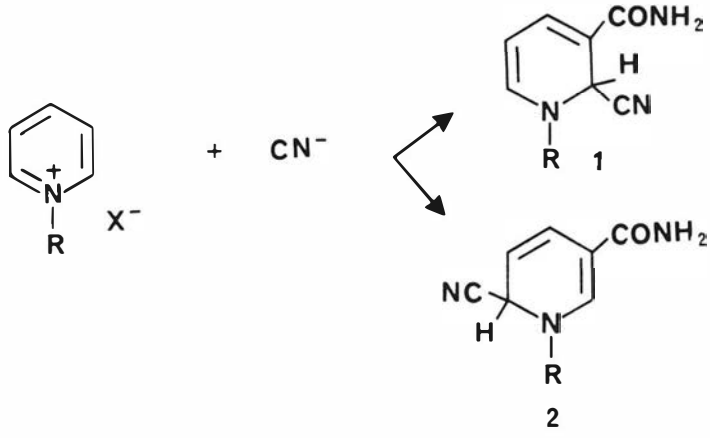


Figure 3. Formation of 1,2 or 1,6-Dihydropyridines.

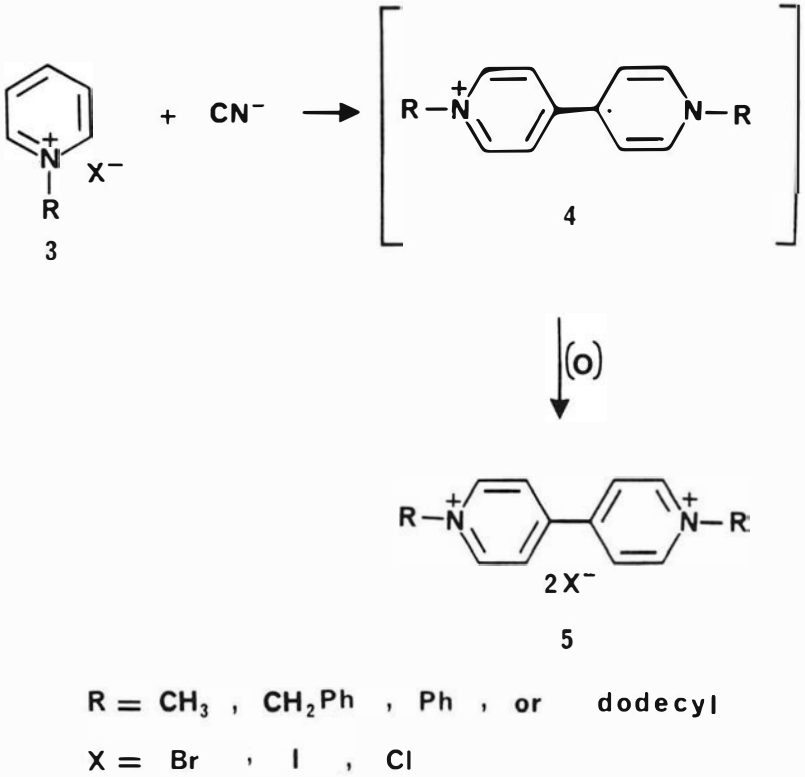


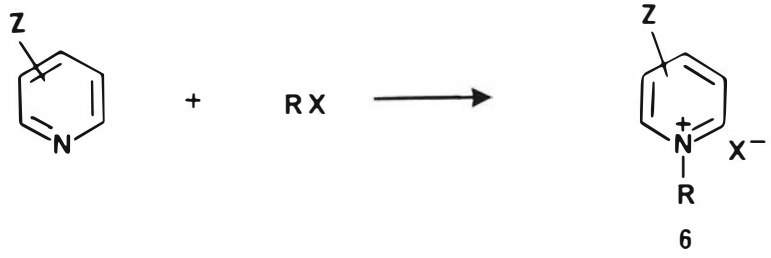
Figure 4. Dimerization of Unsubstituted Pyridinium Salts 3, with Cyanide, by Winters et al.

RESEARCH AIM

The aim of the research presented in this dissertation was to form substituted pyridinium salts **6**, (Figure 5), and to react the salts with cyanide ion to determine whether they dimerize to form the corresponding dimers **8** as reported for the reaction of the unsubstituted pyridinium salts with cyanide ion [21] (Figure 6). The focus was primarily on 2-substituted pyridinium salts, mainly because they have been least investigated by other workers. In the case where the dimers had not formed, the product of the reaction was to be isolated when possible. For many years, substituted pyridinium salts have been known to undergo reactions with cyanide ion. The position of attack was first believed to be at the 2- or 6-position [23], but later it was shown to involve the 4-position yielding disubstituted 4-cyano-1,4-dihydropyridine **9**, as the product [24, 34] (Figure 7).

The position of attack of the cyanide ion on the substituted pyridinium salts to be used in this research was to be investigated. The characteristics (electron donating or electron attracting) and the position of the substituent Z on the formation and stability of the adduct **9** was also to be investigated. If dimer formed, the reaction would constitute a short synthetic route for the preparation of such dimers. It was also a way of preparing some dimers that would not have been possible through other synthetic routes. The dimers formed could be useful in the preparations of other interesting materials such as polymers or metal complexes.

In 1970, Winters, et. al. reported the formation of a radical cation from the reaction of unsubstituted pyridinium salts with cyanide ion [35]. But in 1977, Carey and coworkers reported dimerization of unsubstituted pyridinium salts with phosphite and phosphinite ions [36] without any mention of the formation of a radical cation. Another goal



R = CH_3 or CH_2Ph

X = Br or I

Z = $-\overset{\overset{O}{\|}}{C}-CH_3$, Br , CN , CH_3 , $NH\overset{\overset{O}{\|}}{C}-CH_3$,

$-CH_2CH_3$, $-CH_2CH_2OH$, or $-CH_2OH$.

Figure 5. General Preparation of Pyridinium Salts 6.

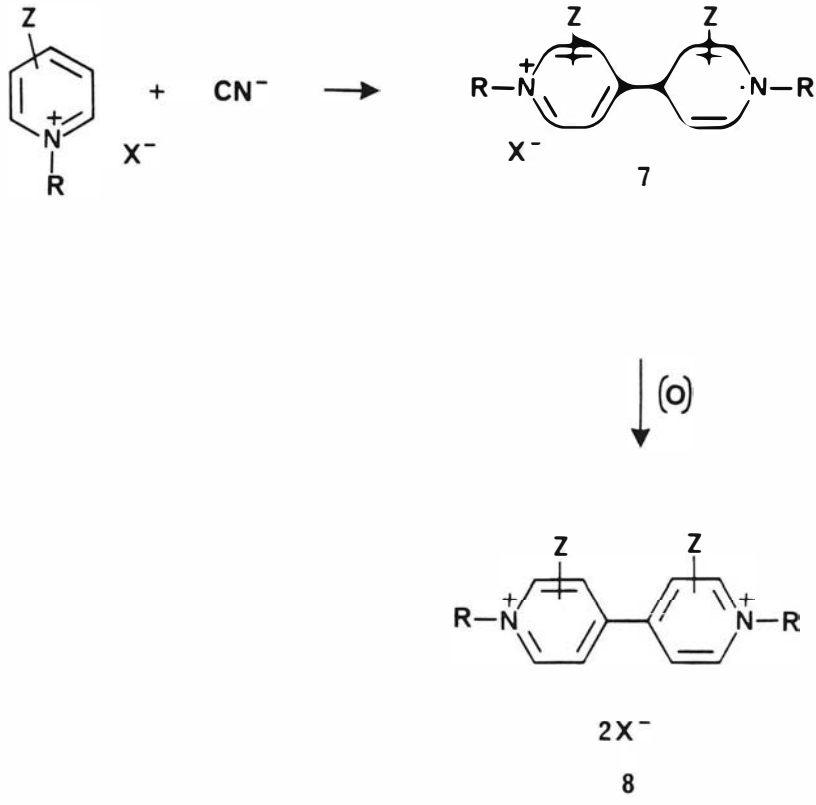


Figure 6. General Dimerization of Substituted Pyridinium Salt with Cyanide.

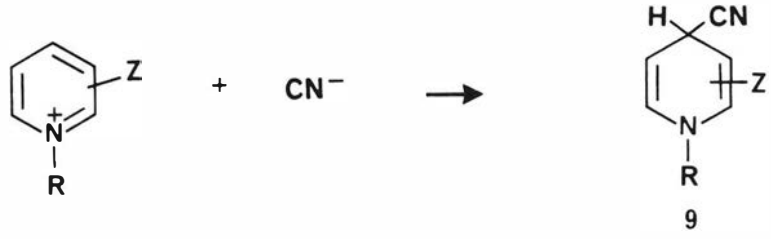


Figure 7. Formation of 4-Cyano-1,4-Dhydropyridine 9.

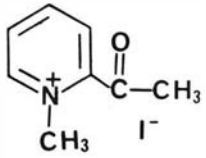
of the proposed research was to discover if radical cation **7** formed from the reaction of substituted pyridinium salts with cyanide ion.

The general approach was to study the reaction of the substituted pyridinium salt **6** with sodium or potassium cyanide (Figure 7), followed by the oxidation of the product radical cation **7** when formed.

The oxidation was to be done either with an alcoholic iodine solution or with air in an acidic solution to form the corresponding substituted bipyridinium salt, **8**.

The substituted pyridinium salts to be used are:

1. 1-methyl-2-acetylpyridinium iodide, **10**
2. 1-methyl-2-bromopyridinium iodide, **11**
3. 1-methyl-2-cyanopyridinium iodide, **12**
4. 1-methyl-3-cyanopyridinium iodide, **13**
5. 1-methyl-4-cyanopyridinium iodide, **14**
6. 1-methyl-2,4-dicyanopyridinium iodide, **15**
7. 1-methyl-2,6-dimethylpyridinium iodide, **16**
8. 1-benzyl-2-(acylamino)pyridinium bromide, **17**
9. 1-benzyl-2-bromopyridinium bromide, **18**
10. 1-benzyl-2-cyanopyridinium bromide, **19**
11. 1-benzyl-3-cyanopyridinium bromide, **20**
12. 1-benzyl-4-cyanopyridinium bromide, **21**
13. 1-benzyl-2-ethylpyridinium bromide, **22**.
14. 1-benzyl-2-(2-hydroxyethyl)pyridinium bromide, **23**
15. 1-benzyl-2-(hydroxymethyl)pyridinium bromide, **24**
16. 1-benzyl-2-methylpyridinium bromide, **25**
17. 1-benzyl-3-methylpyridinium bromide, **26**



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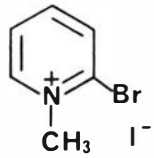

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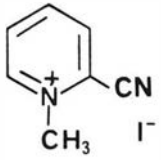

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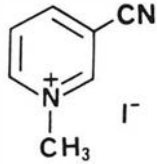

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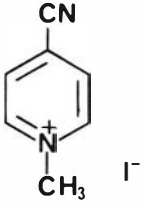

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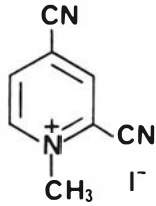

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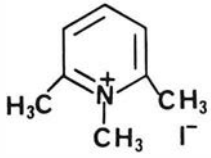
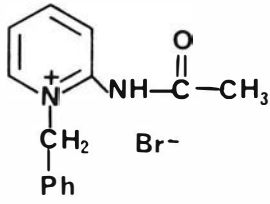
Figure 8. Subtituted 1-Methylpyridinium Iodides.



16



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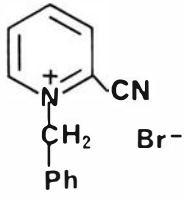

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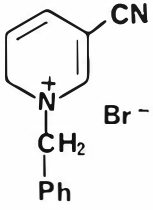

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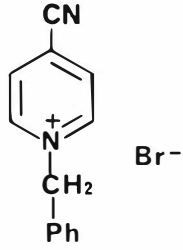
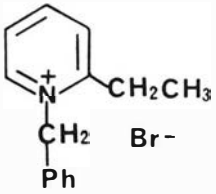


21

Figure 9. Substituted Pyridinium Salts.



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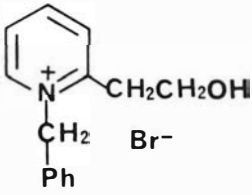

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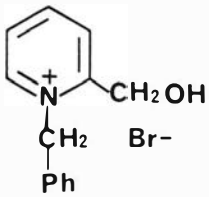

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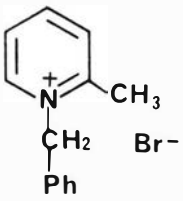

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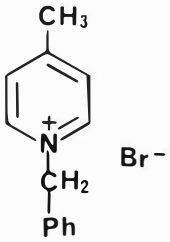

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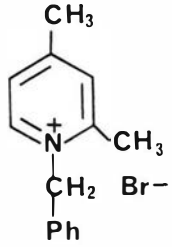
Figure 10. Substituted 1-Benzylpyridinium Bromides.



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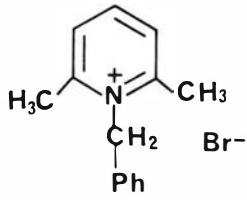


29

Figure 11. Substituted 1-Benzylpridimium Bromides.

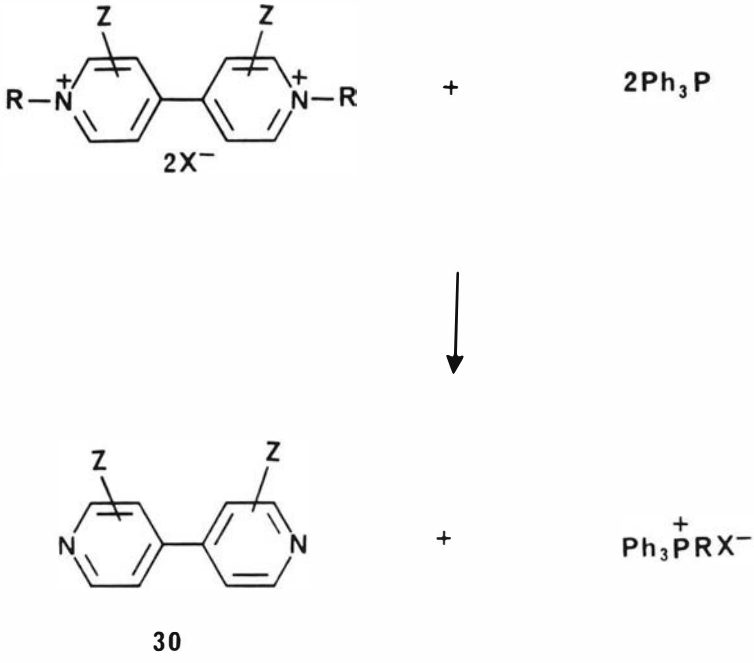
18. 1-benzyl-4-methylpyridinium bromide, **27**

19. 1-benzyl-2,4-dimethylpyridinium bromide, **28**

20. 1-benzyl-2,6-dimethylpyridinium bromide, **29**

The methods of preparation of some of these salts have been reported; however, since the salts are not available commercially, they had to be made by the reported methods. Because of the sensitivity of the intermediate radical cation to oxygen, all the reactions were to be run under a nitrogen atmosphere. The resulting products after oxidation were to be passed through an ion-exchange resin to exchange any unwanted anions for bromide.

As a result of the discovery of the herbicidal activity of bipyridinium salts by Brian and coworkers in 1958 [37] and its extension to the substituted bipyridinium salts [38, 39, 40], many investigators have been interested in the synthesis of new bipyridinium salts that have herbicidal activity. Substituted and unsubstituted bipyridinium salts that were capable of being reduced in aqueous solutions at potentials (E^{o}) of approximately -0.35 to -0.45v, have been found to be active as a herbicide [41, 42]. Therefore, when any new dimer was made, its reduction potential was to be determined to see if it was potentially active as a herbicide. Finally, the dimers when made, could be dequaternized with triphenylphosphine to form bipyridines (Figure 12). The bipyridine **30** could be polymerized or complexed with a metal depending on the substituent Z.



30

Figure 12. General Preparation of Bipyridine 30.

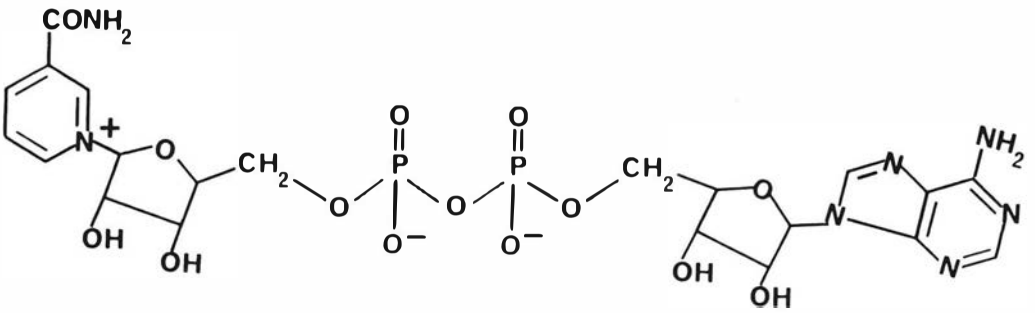
BACKGROUND

The reactions of substituted pyridinium salts with cyanide ion have been extensively investigated [15-19, 20, 21, 23-29, 43-45]. The chemistry of these salts has received considerable attention in a review article [46], and books [44, 47, 48]. The interest in these salts arose from the physiological activity of nicotinamide adenine dinucleotide **31**, (Figure 13), and triphosphopyridine nucleotide, NAD and NADP respectively.

These dinucleotides also exist in reduced forms, NADH and NADPH. They are coenzymes, and they function biologically in a large number of enzymatic oxidations and reductions [48]. There has been an establishment of the structure of NADH as a derivative of 1,4-dihydropyridine **33** [17-19, 43, 49-53] (Figure 14), eq. 1.

The reaction of pyridinium salts with cyanide ion or other related nucleophiles was usually related to the NAD-NADH system. In 1938, it was reported that NAD reacted with cyanide ion to form complexes with ultraviolet absorption spectra resembling those of NADH. Therefore, it was suggested that the addition of the cyanide ion to the substituted pyridinium ring occurred according to the reaction in equation 2 of Figure 14 [25].

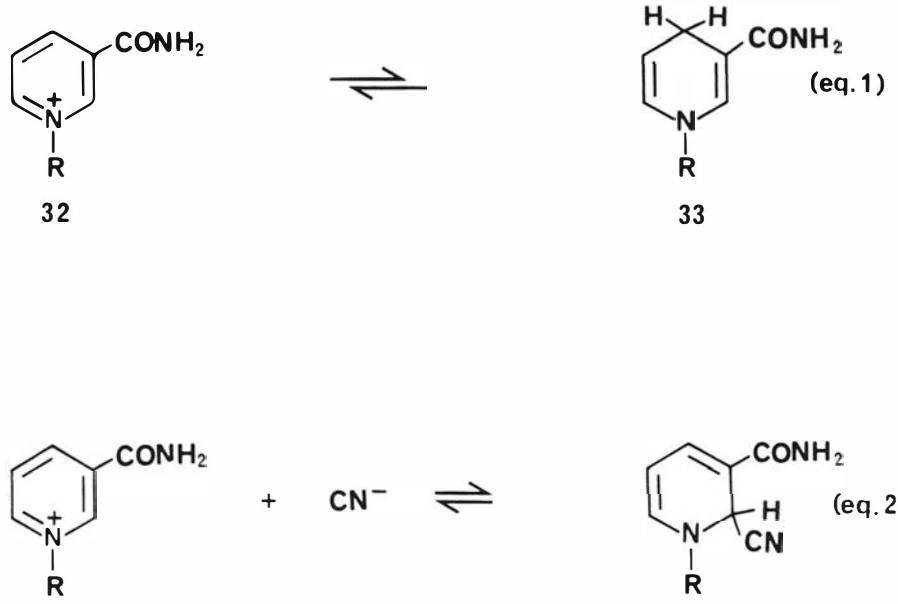
Karrer and coworkers [51, 52] investigated the nature of the products obtained upon chemical reaction of 1-methylnicotinamide with nucleophiles. They concluded that the compounds isolated were the 1,2- and 1,6-dihydro isomers by comparing their chemical and physical properties to the known 1,2-, and 1,6-, and 1,4-dihydro compounds. However, they did not answer the question of whether the 2- or 6-position was involved. Knox and Grossman [54] suggested that Karrer's reduced compounds for the 1-methyl derivatives were the



NAD

31

Figure 13. Nicotinamide Adenine Dinucleotide (NAD) 31.



Fiugre 14. Oxidized (32) and Reduced (33)
Forms of the Pyridinium Rings of NAD (eq 1)
Reaction of NAD 32 with Cyanide (eq 2).

1,6-dihydro nicotinamide. It was later established that the 4-position of the nicotinamide ring was actually the site of reduction [53].

Proton nuclear magnetic resonance spectroscopy confirmed the structure of the 1,4-dihydropyridine **33**. By reducing nicotinamide methiodide with dithionite in deuterium oxide and comparing its spectrum with that of the 2- and 6-deuterated 1-methyl-1,4-dihydronicotinamides, compound **33** ($R = CH_3$) was established as the 1,4-dihydro structure. The spectrum of 1-methyl-4-deutero-1,4-dihydronicotinamide and the spectrum of 1-methyl-1,4-dihydronicotinamide were compared and found to be different.

It was found, in 1951, that the ability of 1-substituted nicotinamide compounds **32** to form a complex with cyanide ion was a general property. Cyanide ion altered the ultraviolet absorption spectrum of these compounds in two ways: i. It was found to lower the peak at 260 nm by abolishing the contribution of the pyridinium ring at this wavelength. ii. It was found to cause the appearance of a new peak at 325 nm. Addition of cyanide ion resulted in a spectrum which resembled that of NADH and showed diminished absorption at 260 nm and a new peak at 340 nm, when compared to NAD. Because the spectra of nicotinamide, 1-methylnicotinic acid, and the reduced NAD were not affected by cyanide ion , it was concluded that both the amide and the quaternary nitrogen in the ring were essential for the reaction with cyanide ion [26].

It has been believed for many years that the addition of cyanide ion to NAD occurred at the 2- or 6-position on the basis of the indirect evidence of Karrer et al [52], who claimed that the reduction of NAD occurred at one of these two sites. After Pullman and coworkers [53] reported that the reduction of NAD occurred at the 4-position of the nicotinamide moiety, it became very interesting to find the site of cyanide ion addition to NAD. A procedure analogous to that of Pullman for the investigation of the structure of NADH was used to determine that the attack of cyanide ion was at the 4-position of the pyridinium salt [27]. In a study of the effect of pH and cyanide ion concentration on the rate and extent of reaction of cyanide ion with NAD [26], it was found that when the pH was increased, the rate at

which the complex formed and the amount of complex formed also increased. The NAD-CN complex was unstable and dissociated rapidly when the cyanide ion concentration was lowered and was destroyed by acid at room temperature. No attempt was made to isolate the complex because of its instability.

Pietro [27] isolated 2- and 6-pyridones containing equal amounts of deuterium from the reaction of NAD with cyanide ion in deuterium oxide (Figure 15). Since this indicated that the 2-or 6-positions did not contain the deuterium; therefore, the deuterium must be located at the 4- or 5-positions. But the 5-position was an extremely unlikely site for cyanide ion addition because of electronic considerations. There was a transfer of deuterium in an enzymatic oxidation reduction process by a deuterium labelled NAD 34, obtained from the NAD-CN complex after exchange in heavy water (Figure 15). Because it was known that the site of reversible oxidation was the 4-position of the nicotinamide moiety of NAD [52], the deuterium must be present at this position. Based on these findings, it was concluded that cyanide ion most probably added to NAD at the 4-position of the nicotinamide moiety.

There was also a study on the action of base on NAD in deuterium oxide in the absence of cyanide ion [27]. The results showed that a deuterium atom was present in the 2-position. The presence of deuterium at this position was also supported by the fact that deuterium exchange did occur at this position under the action of alkali in other pyridine derivatives. This property was explained by the electron-attracting properties of the CN linkage in the pyridine ring and was increased further in the quatenary salts. Since mild alkaline conditions were used with NAD, it was likely that only the hydrogen at the 2-position was sufficiently activated to undergo exchange, because it was α to the ring nitrogen and ß to the carboxamide group. Studies by Kosower on the results of the addition of nucleophiles to pyridinium rings revealed "that nucleophiles which form charge-transfer complexes easily or which might be expected to do so, add to the 4-position, while those nucleophiles which probably

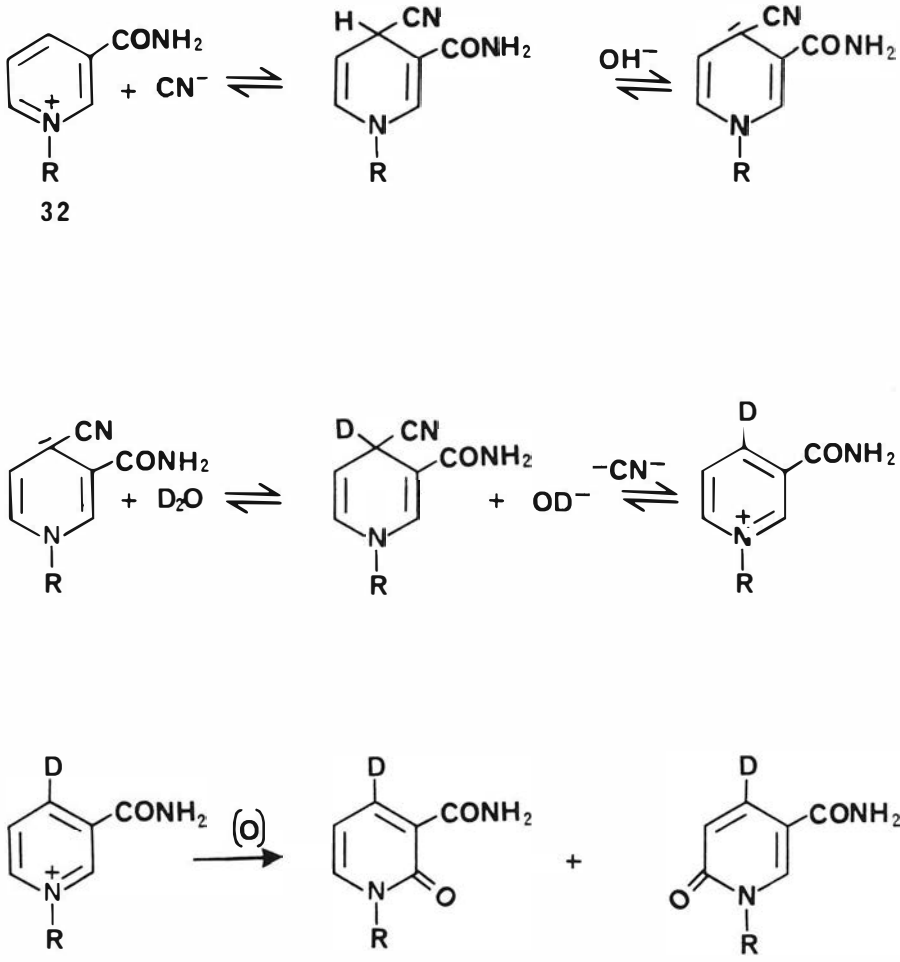


Figure 15. Oxidation-reduction Process of a Deuterium Labelled NAD 34.

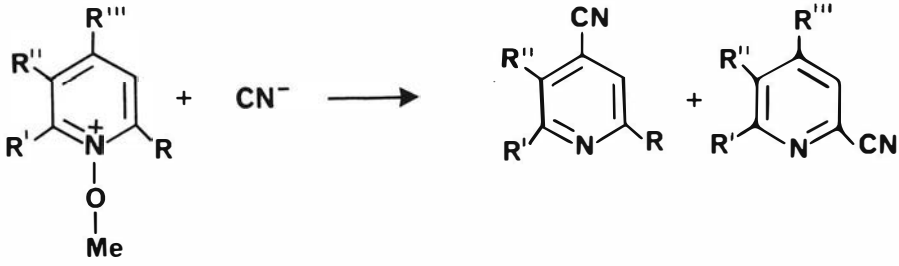
do not form complexes, or do so only to a very limited extent, add at the 2-position" [44, 55]. The ability of a nucleophile to release electronic charge determines its ability to form a charge transfer complex. The electrode potential (E^o) for the reaction

$$2X: \rightleftharpoons X_2 + 2e^-$$

could be used as a measure of the ability to donate a charge and was therefore an estimate of the ability of a nucleophile to form a charge-transfer complex [55]. Based upon the results of Hawthorne, et. al, cyanide ion was assigned an electode potential (E^o) value of -0.56v [56]. The groups which release charge almost as well as iodine ion [E^o = -0.53] was expected to form a complex. Therefore, cyanide ion was expected to form a complex and add to pyridinium ion exclusively at the 4-position. However, a mixture of an aqueous solution of 1-alkoxy-pyridinium salt with potassium cyanide solution produced a mixture of products [28, 29]. Comparison of the structure of the products with authentic samples of 2- and 4-cyanopyridines determined their structures [28] (Figure 16).

A careful ultraviolet spectroscopic investigation of the reaction of 1-methoxy-3-carboethoxypyridinium methosulfate **36** with cyanide ion in water was investigated [20]. An absorption peak due to the formation of 1,4- and 1,6-dihydro type structures **37** and **37a** appeared at 382 nm upon addition of the potassium cyanide solution; this peak disappeared slowly with the formation of the spectrum of the products **38** and **39** respectively [20] (Figure 17). The previously proposed mechanism [29], in which the initial dihydro compounds **37** and **37a** irreversibly decomposed to form the 4- and 6-cyanopyridines, was supported by these results. A 60° increase in temperature and an increase in polarity of the solvent increased the ratio of 4-/2-products.

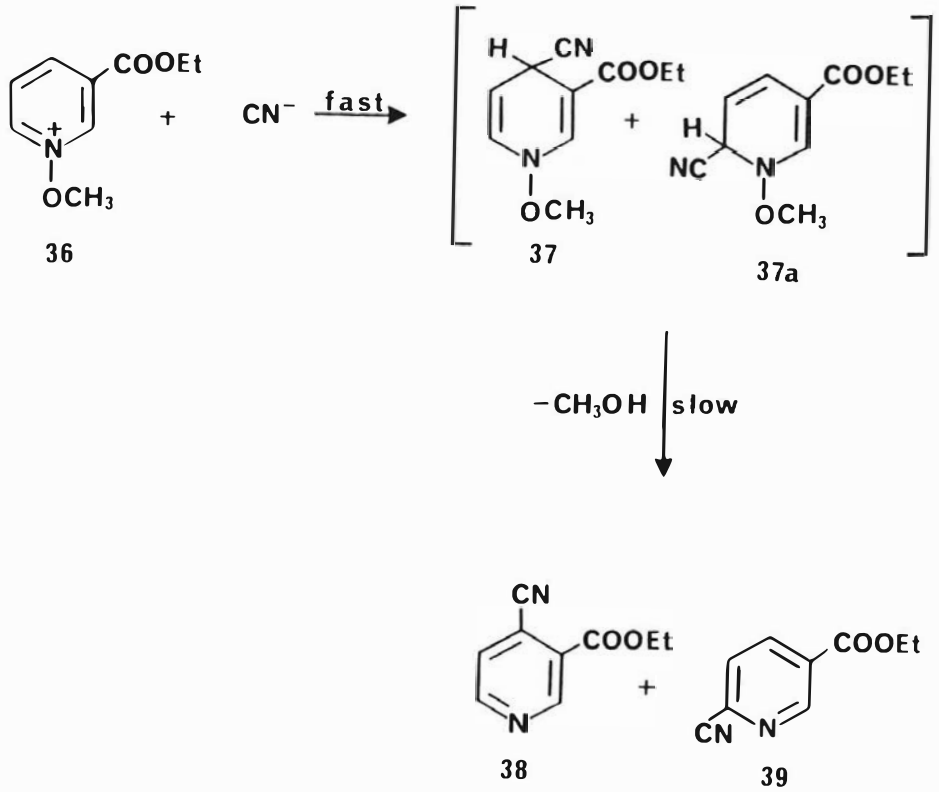
Reaction of 1-Methoxypyridinium Derivatives with Potassium Cyanide (in 70% dioxane at 23°)



Substituent	% Yield	
	4	2
a. R = R' = R'' = R''' = H	29	48
b. R = R'' = R''' = H; R' = CH_3-	18	45
c. R = R' = R'' = H; R''' = CH_3-	15	30
d. R = R' = R''' = H; R'' = CH_3-	0	30
e*. R''' = R'' = H; R = R' = CH_3-	13	0

* 33% of 6-cyanomethyl-2-picoline was also isolated.

Figure 16: Reaction of 1-Methoxypyridinium Derivatives with Cyanide.



36 37 37a 38 39

Figure 17. Reaction of 1-Methoxy-3-Carboethoxypridimium ion with Cyanide.

There was also an increase in this ratio as the size of the substituent group on the nitrogen increased from methoxy to ethoxy to butoxy

Group	Ratio of 4-/2-
1-Methoxy-	0.23
1-Ethoxy-	2.17
1-Butoxy-	2.84

This latter increase was explained to be a result of steric inhibition of a large group to the attack of cyanide ion at the 2-position [29].

A study of the reaction of 1-aminopyridinium derivatives with cyanide ion was also investigated [20]. Although the mechanism proposed was similar to that for the reaction of the 1-alkoxypyridinium derivative, however, the 1-aminopyridinium derivatives showed greater reactivity at the 4-position with cyanide ion, possibly due to the steric factor of the 1-amino group on the 2-carbon atom. Reaction of 3-substituted pyridinium salts with cyanide ion in methanol was reported by Lyle and Gauthier in 1965 [23]. They observed a change of the ultraviolet absorption spectrum with time for the initially formed products. The peak at 260-280 nm band was lost as the solutions were allowed to stand. Also, there was a shift in an absorption band from 320 nm to 340 nm respectively. The interpretation of these results was that the initially formed 1,6-dihydropyridines (260-280 nm) was undergoing a conversion to the 1,4-dihydropyridines (340 nm). The observation of a clean isosbestic point in the spectra made it evident that simple equilibria were involved [23]. Reversibility was the only difference between these reactions and those which led largely to the 1,2- or 1,6-dihydropyridines. It appeared that because of the reversibility, the kinetically favored 1,6-product was converted to the 1,4-product due to the thermodyanamic stability of the latter under most reaction conditions [23] (Figure 18).

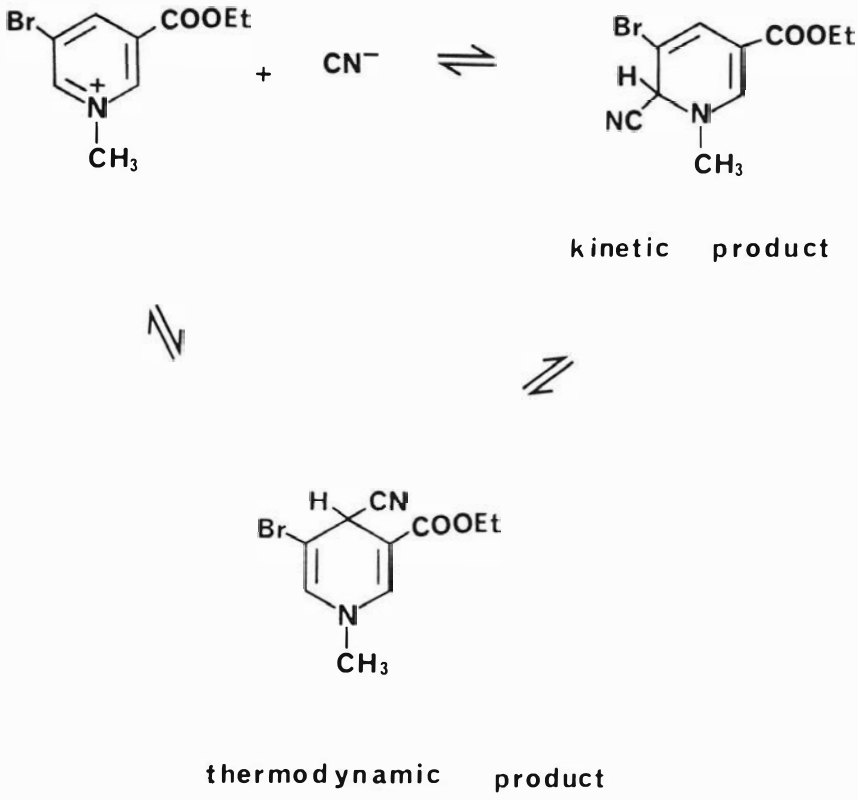


Figure 18. Preparation of 1,6-Dihydropyridine and its Conversion to the 1,4-Dihydropyridine

Linquist and Cordes [21] as well as many others [15, 16] reported that the ultraviolet, proton magnetic resonance, and mass spectra suggested that the initial site of attack of cyanide ion on the 1-substituted nicotinamide ion in water was at the 4-position. Foster and Fyfe [24] did a study of the addition of cyanide ion to various pyridinium ions in dimethyl sulfoxide solution using nuclear magnetic resonance spectroscopy. They found the addition to occur mainly at the 4-position. It has been also reported that 1-methyl-3,5-dicyanopyridinium salt reacted with cyanide ion to form the 2-adduct which rearranged to the 4-adduct upon heating [19].

A study of the reaction of cyanide ion with a number of pyridinium salts that did not have electron-withdrawing substituents in the 3-position was reported by Gauthier [23]. He found that reaction of cyanide ion with 1,2- and 1,4-dimethylpyridinium iodide, 1-methyl-4-carbomethoxypyridinium iodide, 1-methyl-3,5-diphenylpyridinium iodide, and 1-methyl-2-benzoylpyridinium iodide in methanol did not occur even in the presence of a tenfold excess of cyanide ion. The lack of reactivity of these salts with cyanide ion was not explained on steric grounds but as a result of the relatively low reactivity of these compounds compared with pyridinium salts having strong electron withdrawing group at the 3-position. For a very long period of time, it seemed that all the reports in the literature implied that, for successful addition of cyanide ion, the pyridinium ions must be made strongly electrophilic by a substituent capable of electron withdrawal, and the electron withdrawing group must be located on the pyridinium salt in a position (3 or 5) such that the dihydropyridine would stabilize once it was formed.

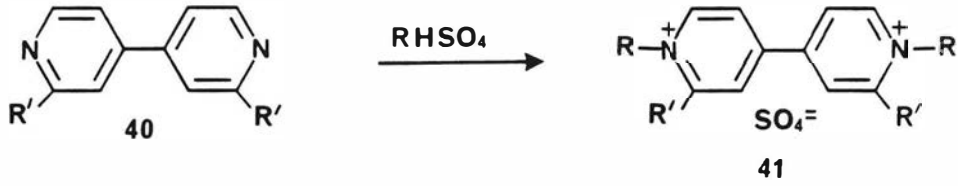
Hermolin and coworkers in 1981 [57] reduced 1-alkyl-2-(carbomethoxy)pyridinium iodide to its dihydro form in acetonitrile with sodium amalgam in the absence of oxygen at 0°C. There have been recent reports for use of pyridinium salts. In 1988, Schroth, et. al. added a pyridinium salt to a deposited nickle-iron alloy electrolyte at 45-70°C and pH 3.0-3.8 and obtained corrosion-resistant layers [58]. Also, Igarashi and coworkers in 1988 found that 1-alkylpyridinium salts could be added to a gasoline-methanol-water emulsion used in

breaking of lower 95% ethanol-crude oil or gasoline-water emulsions [59]. Much of the interest in the 4,4'-bipyridyls arose when methyl viologen **5**,($R = CH_3$) was discovered to have phytotoxic properties [60, 85]; it also was developed as the herbicide Paraquat. (1,1'-dimethyl-4,4'-bipyridinium dichloride).

In 1973, J.R. Case and coworkers [61] synthesized 1,1'-dialkyl-2,2'-dimethyl-4,4'-bipyridinium salts, **41**, by the reaction of 4,4'-bipyridines, **40**, with $ROSO_2OH$ (R = Me or Et) or their sodium salts respectively (Figure 19).

R. Fielden and L.A. Summers [8] in 1974 synthesized 1,1'-dimethyl-2,2'-dicyano-4,4'-bipyridinium dication, **43**, by the reaction of 4,4'-bipyridyl-1,1'-dioxide, **42**, dimethyl sulfate, and potassium cyanide (Figure 20). This compound, **43**, was found to have much higher redox potential than **5**, ($\mathbf{R = CH_3}$). The high redox potential of **43** compared with methyl viologen **5**,($R = CH_3$) was reported to be due to the presence of the electron withdrawing cyano group. This salt, **43**, was also found to be inactive as a herbicide when tested at 8 lbs/acre. This lack of herbicide activity was attributed to its high reduction potential [62, 63].

In 1979, R.D. Balanson and coworkers [6] synthesized 1,1'-dibutyl-2,2'-dialkyl-4,4'-bipyridinium dibromide, **46**, by dimerizing 4-bromo-2-alkyl pyridine, **44**, (via 2,2'-dialkyl-4, 4'-bipyridines, **45**), followed by addition of butyl bromide (Figure 21). Asahi Chemical Industry Co., Ltd. [7] found in 1982 that a compound containing 1,1'-dimethyl-2,2'-dimethyl-4,4'-bipyridinium dichloride was a herbicide. Duerr and coworkers [9] in 1983 showed the same compound to be an electron relay which was faster and more efficient than the classical system with $Ru(byP)_3^{3+}$. N.A. McAskill [64] in 1984 did a pulse radiolysis study of the reactions of hydrogen atoms with dimethyl-,tetramethyl-, and hexamethyl-substituted viologens. In 1985, H. Kamogawa and M. Sugiyama studied the photochromism of benzylviologens containing methyl groups on pyridinium rings and embedded in solid poly(1-vinyl-2-pyrrolidone) matrix [65].



R = Me or Et

R′ = H or Me

Figure 19. Preparation of Substituted Bipyridinium Salt 41 by Case and coworkers.

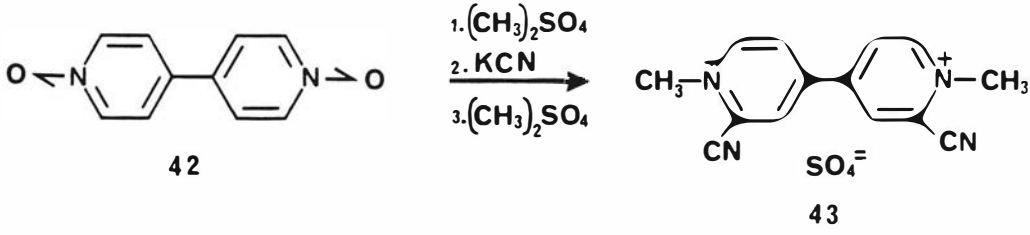


Figure 20. Preparation of 1,1'-Dimethyl-2,2'-Dicyano-4,4'-Bipyridinium Sulfate 43.

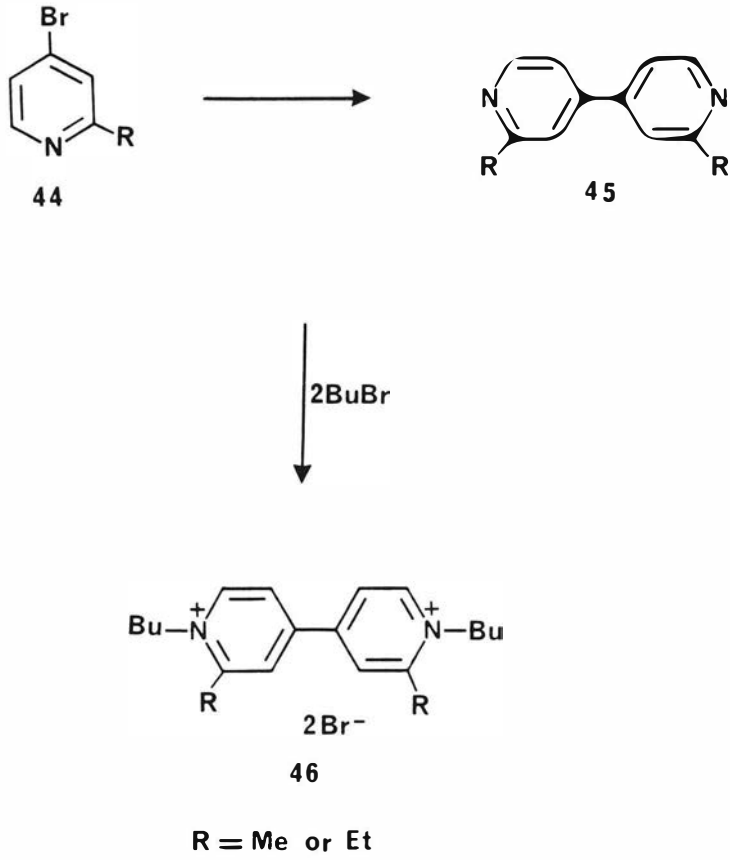


Figure 21. Preparation of Substituted Bipyridinium Salt 46, by Balanson and coworkers.

Interest in dimerization of pyridinium salts by cyanide ion arose when L.J. Winters and N.G. Smith [35] in 1970 synthesized 1,1'-disubstituted-4,4'-bipyridinium dihalides **5**,(R = CH_3, Ph, dodecyl), by the reaction of pyridinium salts, **3**, with sodium or potassium cyanide (Figure 4). Since then, much work has been done on dimerization of pyridinium salts. In 1972, J.G. Carey [66] prepared 1,1'-disubstituted-4,4'-bipyridinium salts by heating 1-substituted pyridinium salts with HCN under basic conditions (NH_3, piperidine, etc.), followed by oxidation of the intermediate. R.H. Reuss and L.J. Winters [67] in 1973 dimerized 1-(4-pyridyl) pyridinium chloride, **47**, with sodium cyanide, and oxidized the intermediate, **48**, to the corresponding 4,4'-bipyridinium salt, **49**, (Figure 22). J.G. Carey and J.R. Case [68] in 1977 synthesized methyl viologen **5**,(R = CH_3) by dimerizing 1-methylpyridinium ion **3**,(R = CH_3) with diphenylphosphinite, diphenylthiophosphinite, and diethyl or diphenyl phosphite anions in a variety of solvents (Figure 24). Also in 1977, J.G. Carey and J.R. Case [68] dimerized 1-methylpyridinium-4-carboxylate, **50**, with cyanide ion in dipolar aprotic solvents (Figure 23). Three possible mechanisms for the dimerization have been proposed [124]. They are, benzoin type reactions, hydride transfer reactions, and free radical reactions.

Of these three, only the benzoin type mechanism has been supported [68]. In the benzoin type mechanism (Figure 24), the nucleophilic attack of the cyanide ion at the 2-and 4- position has been demonstrated [21, 23, 24]. The loss of a proton from **9** to form the carbanion **51** should be facile in the basic cyanide ion solution [27].

The resulting carbanion could attack another pyridinium ion to form the 1,1',4,4'-tetrahydro-4,4'-bipyridine, **52**. Which can undergo base catalysed elimination of hydrogen cyanide to form the 1,1'-disubstituted-2,2'-disubstituted-1,1'-dihydro-4,4'-bipyridine, **53**. Oxidation of **53**, by oxygen, as reported [69], can form the cation radical, **7**.

Since N.G. Smith proposed the above mentioned possible mechanisms for dimerization, other researchers have focused on

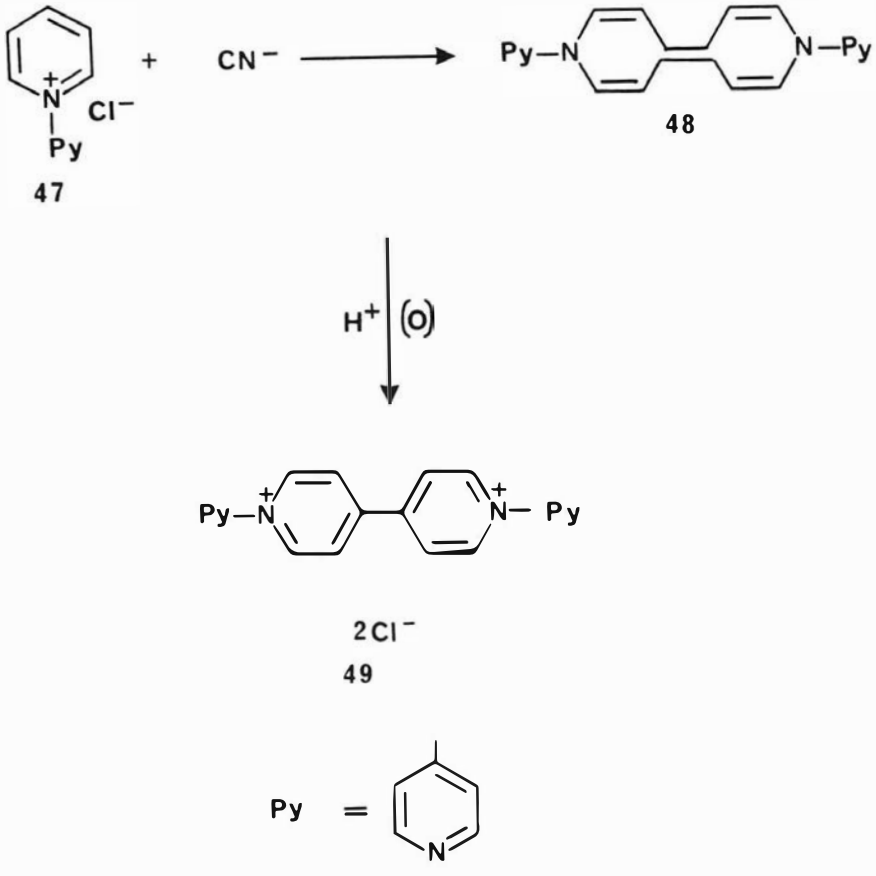


Figure 22. Dimerization of 1-(4-Pyridyl) Pyridinium Chloride 47, by Reuss and Winters.

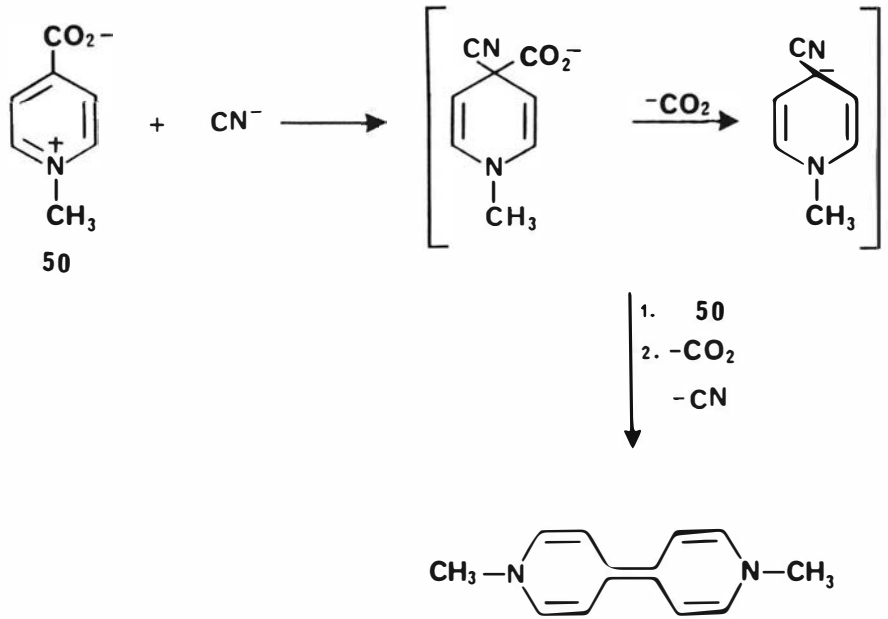


Figure 23. Mechanism for the Dimerization of 1-Methypyridimium-4-Carboxylate,50 by Carey and Case.

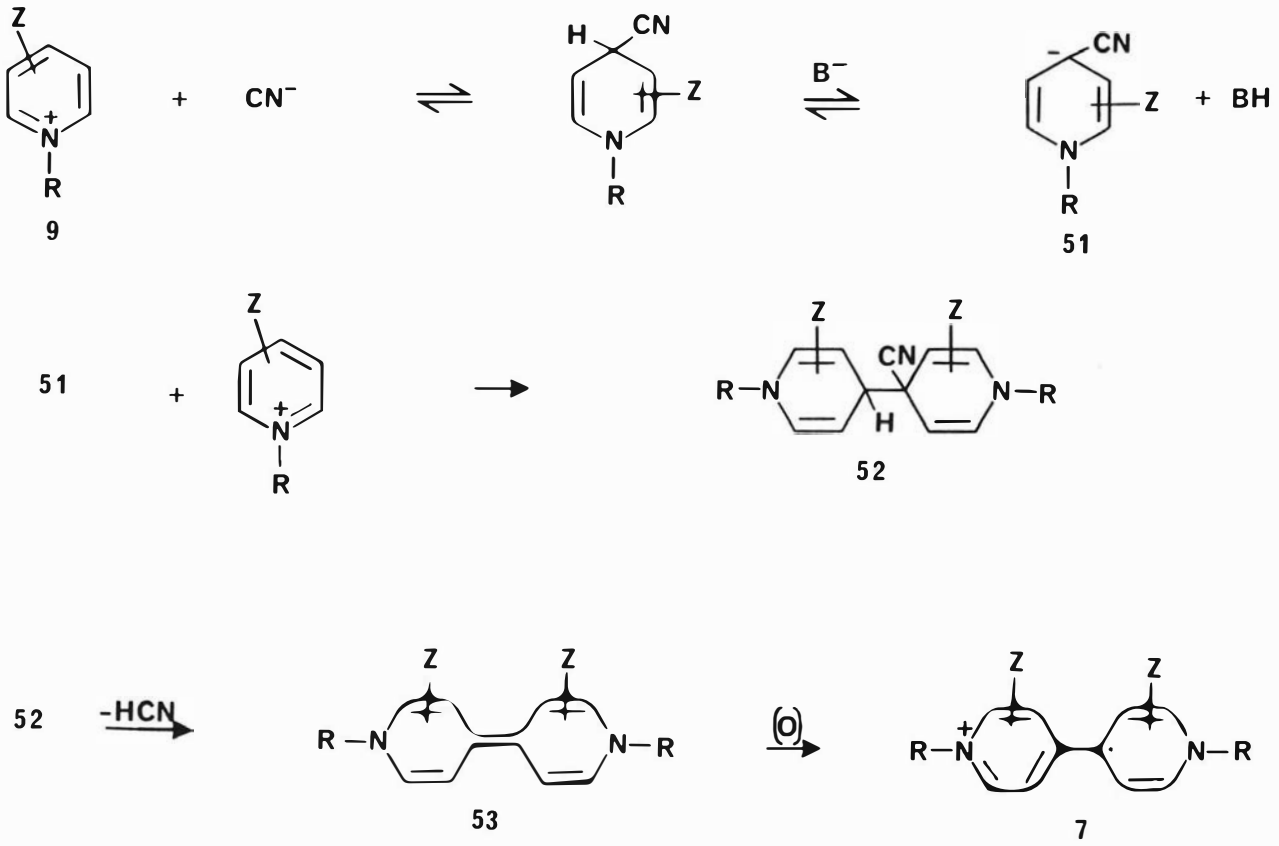


Figure 24. Benzoin Type Reaction Mechanism.

determining the actual mechanisms for these reactions. For example, J.G. Carey and J.R. Case [68] in 1977 proposed the benzoin type reaction mechanism for the dimerization of 1-methylpyridinium ion **3**, ($R = CH_3$) with phosphinite ions (Figure 25). They also proposed the same benzoin type mechanism for the dimerization of 1-methyl-pyridinium-4-carboxylate, **50** with cyanide ion [68], (Figure 23). In these benzoin type reaction mechanisms proposed for the dimerization of both compounds, **3** and **50**, the formation of the intermediates, **54** and **55** (Figure 25) were confirmed by the use of ultraviolet (UV) and proton nuclear magnetic resonance (^1H NMR) spectroscopy. Therefore, among the three possible mechanisms proposed by N.G. Smith in 1970, only the benzoin type reaction mechanism (Figure 24) has been supported to date.

Aono and coworkers in 1986 studied the photoreductive properties of viologens with NADPH as a reversible electron donor, using Zn II mesotetraphenylporphinetrisulfonate ($ZnTppS_3^{3-}$), and hematoporphyrin (Hp) as photosensitizers of the reaction [70]. Dzaraeua et al [71] prepared polyviologens **58** and **59** (Figure 26), by treating 4,4'-bipyridine with p-xylylene dichloride or by exchange reaction of 2,2',6,6'-tetraphenyl-4,4'-bipyridinium diperchlorate with $H_2N(CH_2)_6NH_2$. They found that both **58** and **59** participated in redox reactions characteristic for viologens.

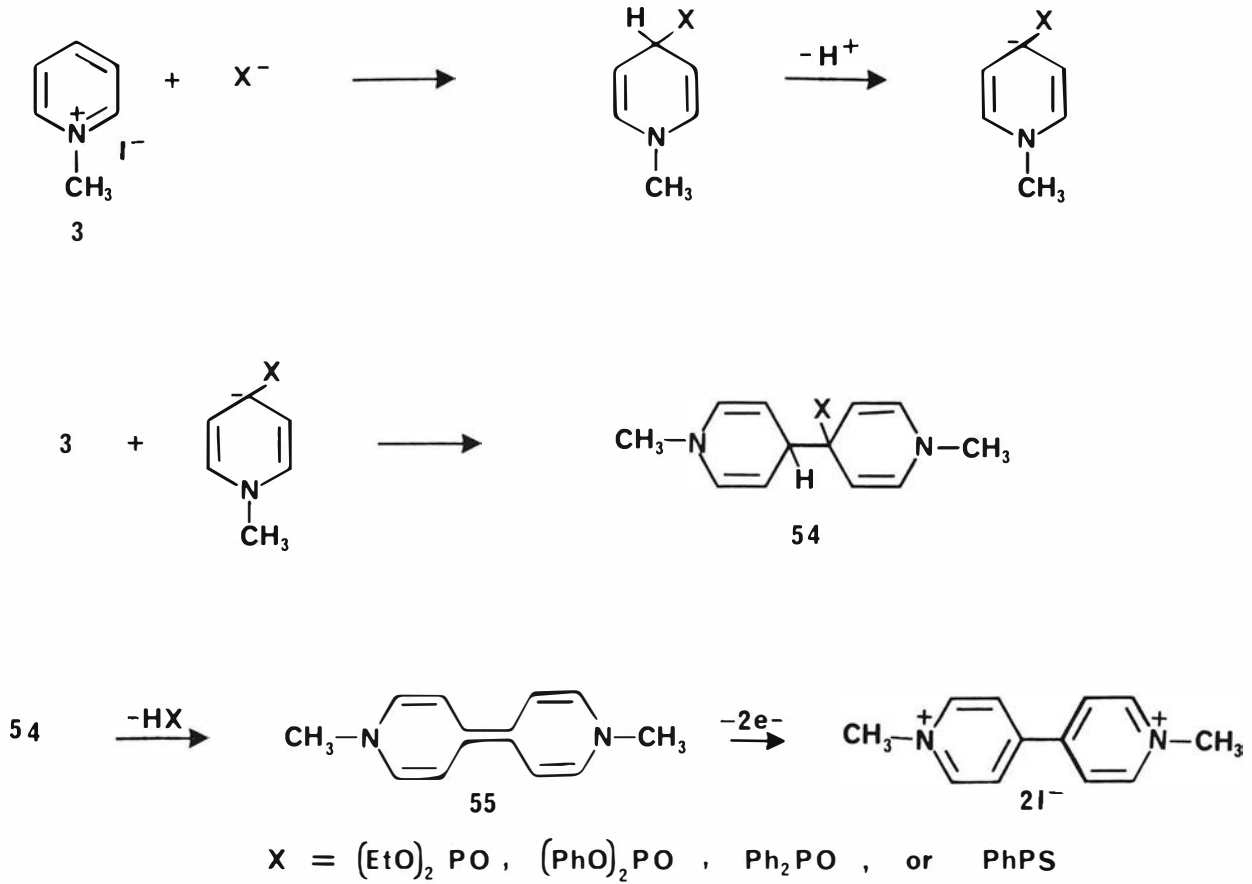
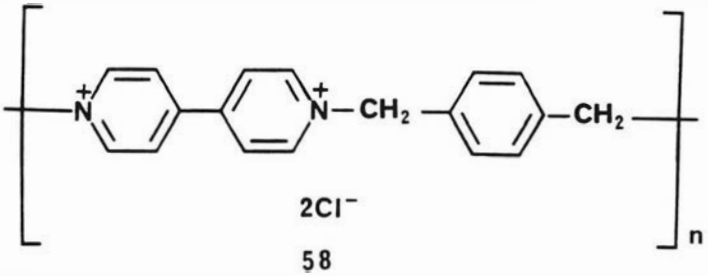


Figure 25. Carey Case Mechanism for the Dimerization of 1-Methylpyridimium ion with Phosphinite ions.



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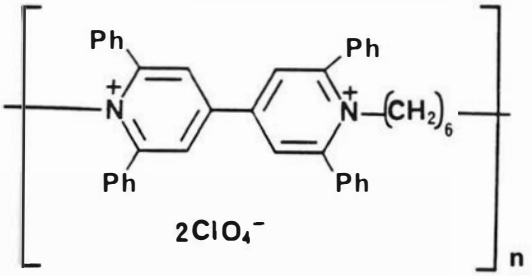


59

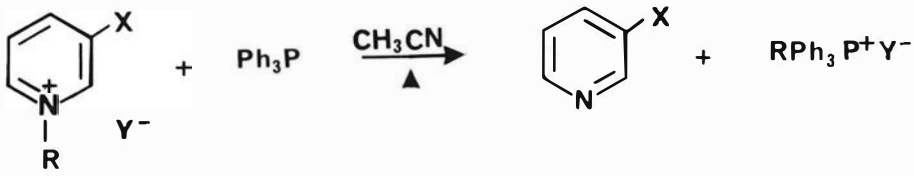
Figure 26. Polyviologens, Prepared by Dzaraeua et al.

Dequaternization of Pyridinium Salts

Many workers have focused on the quaternization and dequaternization of pyridinium salts. In 1973, Aumann and Deadly dequaternized some 1-methylpyridinium salts by heating them in dimethylformamide solution under reflux. The reaction was monitored directly by ^1H NMR spectroscopy and the disappearance of the 1-methyl peak plus the upfield shift of the aromatic proton signals in the dequaternized species indicated the completion of the reaction.

Kutney and Greenhouse [5] treated 1-alkyl-3-substituted pyridinium halide with 1:1 equivalents of triphenylphosphine in acetonitrile at 130 - 140^o for one hour and isolated 3-substituted pyridines (Figure 27). An electron withdrawing group on the pyridine ring was found to greatly accelerate the rate of dequaternization. It was also shown that benzyl groups were more easily removed than the methyl groups (Figure 27). The relative rate constant of demethylation of 1-methylpyridinium salts were determined by ^1H NMR with competition technique. Again, it was confirmed that the reaction was accelerated with electron-withdrawing substituents on the pyridine ring.

There was a report that the reactivity of ortho-substituted pyridines was decreased in quaternization reactions and increased in dequaternization reactions [73]. Alsaidi, et. al. studied the dequaternizations of 1-methyl and 1-benzylpyridinium salts with triphenylphosphine at ambient pressure in dimethylformamide under reflux. It was confirmed that the rate of demethylation was slower than the rate of debenzylation. It seems that all the dequaternization reactions reported so far in the literature have been on the pyridinium salts, with no report on the bipyridinium salts.



R	X	Y	T°C	Time(hr)	%Yields[a] Pyridine[b]	RPhP + Y-
PhCh2	CN	Br	135	1	90	98
CH_3	CN	I	135	3	89	97
$PhCH_2$	C_2H_5	Br	135	22	86	92
CH_3	C_2H_5	I	135	40	67	[c]
CH_3	C_2H_5	I	150	46	76	98
$PhCH_2$	$COCH_3$	Br	135	1.5	93	96

a. Isolated yields. b. Pyridines isolated as their crystalline hyrochloride salts, identified by comparison (nmr, tlc) to authentic samples. c. Phosphonium salt and unreacted pyridinium salt were not separated in this particular case.

Figure 27. Dequaternization of 1-Alkyl-Substituted Pyridinium Halides, by Kutney and Greenhouse.

Formation of Complexes between Transition Metals and the Thiocyanate ion.

There have been many reports of complex formation between transition metals and the thiocyanate ion (SCN-) [69, 74-83]. Since the thiocyanate ion could coordinate to a metal through either one of the end atoms, a variety of true linkage isomers involving NCS group have been prepared. Clark and Williams [83] measured the infrared spectra of some tetrahedral, monomeric octahedral and polymeric octahedral complexes of class A transition metal ions and studied the relationship between their spectra and stereochemistry. It was found that the v(CS) were higher by 40-50 cm^{-1} for tetrahedral than for octahedral complexes of the same metal, although the v(CN) were very similar for both.

Most studies on the coordination of the thiocyanate ion to transition metals have been done by infrared spectroscopy. The cis and trans isomers of some cobalt II-isothiocyanate complexes have been distinguished by infrared spectra in the v(CN) region. The v(CN) for the trans isomer was at 2136 cm^{-1} while the v(CN) for the cis isomer was at 2122 and 2110 cm^{-1} respectively [84]. Turco and Pecile reported that the presence of other ligands in a complex influences the mode of the N-C-S bonding [76]. Many linkage isomers involving the NCS group have been prepared since 1963. Epps and Marzilli [85] isolated three linkage isomers of $AsPh_4[(Co_9DMG)_2(NCS)_2]$ (Figure 28). It was found that these isomers exhibited v(CN) at 2110 cm^{-1} but with differences in the intensity of the v(CN) band. The (NCS, NCS) isomer was the strongest, the (SCN, SCN) cobalt isomer was the weakest, and the (NCS, SCN) isomer was inbetween.

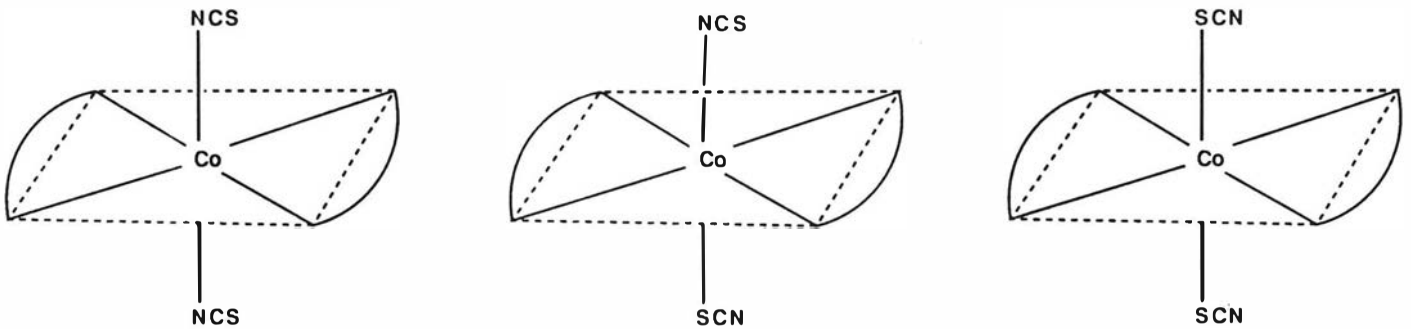


Figure 28. Linkage Isomers of $AsPh_4[(Co9DMG)_2\ (NCS)_2]$.

RESULTS AND DISCUSSION

1. Preparation of Substituted Pyridinium Salts

A. 1-Methyl-Substituted Pyridinium Iodides.

The 2,3, and 4-cyano 1-methylpyridinium iodides were prepared by the reaction of methyl iodide with the corresponding cyanopyridine in dry acetone followed by recrystallization from 95% ethanol-ethyl ether (Figure 29). These reactions proceeded smoothly in 80-95% overall yield to give 1-methyl-2-cyanopyridinium iodide **12**, 1-methyl-3-cyanopyridinium iodide **13**, and 1-methyl-4-cyanopyridinium iodide **14** respectively. The preparation of the salts **12** [86], **13** [87], and **14** [88] have been reported, but in different solvents. The use of acetone as the solvent in this case made the work-up of these compounds easier. In acetone, the salts precipitated from the solution even at reflux. The IR spectra of these compounds (**12**, **13**, and **14**) showed absorptions characteristic of aromatic C-H stretch near 3040 cm^{-1} aliphatic C-H stretch near 2960-2980 cm^{-1}, CN near 2220-2240 cm^{-1}, C-C, and C-N ring stretching near 1610-1630 cm^{-1}, and a C-H ring bending near 760-830 cm^{-1}. The ^1H NMR spectrum of compound **12** in D_2O showed a doublet at δ 9.2–9.3 (1H, carbon 6 proton), a multiplet at δ 8.8-8.9 (1H, carbon 4 proton) a doublet at δ 8.7-8.8 (1H, carbon 3 proton), a multiplet at δ 8.5-8.6 (1H, carbon 5 proton), and a singlet at d 4.6 (3H, 1-methyl protons). The ^{13}C NMR spectrum of **12** exhibited resonances at 151.4 ppm (C-6), 148.7 ppm (C-4), 136.3 ppm (C-3), 134.0 ppm (C-5), 112.5 ppm (CN); 51.3 ppm (C of 1-CH_3).

The ^1H NMR spectrum of compound **13** in DMSO-d_6 showed a singlet at δ 9.8 (1H, carbon 2-proton), a doublet at δ 9.2-9.3 (1H, carbon 6 proton), a doublet at δ 9.0-9.1 (1H, carbon 4 proton), a multiplet at δ 8.2-8.4 (1H, carbon 5 proton) and a singlet at δ 4.4

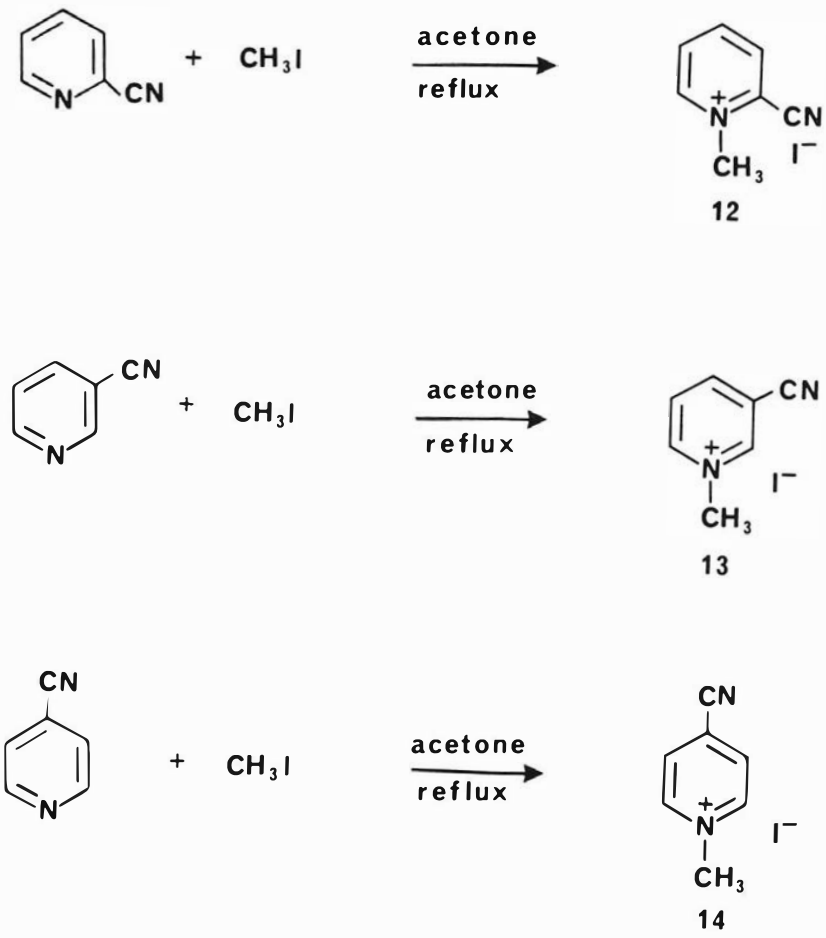


Figure 29. Reactions of 2,3, and 4-Cyanopyridines with Methyl Iodide.

(3H, 1-methyl protons). The ^{13}C NMR spectrum of **13** showed resonances at 149.5 ppm (C-2), 148.9 ppm (C-6), 148.0 ppm (C-4), 127.8 ppm (C-5), 113.6 ppm (C-3), 112.0 ppm (CN), 48.6 ppm (C of 1-CH_3). The ^1H NMR spectrum of compound **14** in DMSO-d_6 showed a doublet at δ 9.3-9.4 (2H, carbon 6 and 2 protons), a doublet at δ 8.7-8.8 (2H, carbon 5 and 3 protons), and a singlet at d 4.5 (3H, 1-methyl protons). The ^{13}C NMR spectrum of 14 showed resonances at 146.7 ppm (C-6, C-2), 130.2 ppm (C-5, C-3), 126.1 ppm (C-4), 114.5 ppm (CN), and 49.9 ppm (C of 1-CH_3) respectively.

The 1-methyl-2,4-dicyanopyridinium iodide **15** was prepared by a slightly different synthetic route (Figure 30). It was prepared in 65% yield by a neat reaction of methyl iodide with 2,4- dicyanopyridine. The IR spectrum showed absorptions characteristic of aromatic C-H stretch near 3080 cm^{-1}, aliphatic C-H stretch near 2990 cm^{-1}, -CN near 2240 and 2220 cm^{-1}, C-C and C-N ring stretching near 1660 cm^{-1}, and a C-H ring bending near 850 cm^{-1}. It should be noted that the cyano group at carbon 2 of all the 1-methyl-2-cyanopyridinium iodides have extremely weak absorption intensity. In the case of compound **15**, the cyano peaks at 2240 cm^{-1} (CN at C-4) and 2220 cm^{-1} (CN at C-2) are almost not observable. The ^1H NMR spectrum of compound **15** in DMSO-d_6 showed a doublet at δ 9.6-9.7 (1H, carbon 6 proton), a singlet at δ 9.5 (1H, carbon 3 proton), a doublet at δ 9.1 (1H, carbon 5 proton), and a singlet at δ 4.6 (3H, 1- methyl protons). The ^{13}C NMR spectrum of **15** showed resonances at 149.2 ppm (C-6), 133.6 ppm (C-3), 128.8 ppm (C-5), 112.0 ppm (CN at C-4), 109.0 ppm (CN at C-2) and 48.6 ppm (C of 1-CH_3). Since only a similar compound (1-methyl-2,4-dicyanopyridinium tosylate) has been reported [89], compound **15** was further characterized by elemental analysis and was found to give satisfactory results. Compound **15** decomposed when dissolved in DMSO-d_6 and allowed to sit for more than two hours.

The 1-methyl-2-acetyl,**10**, 1-methyl-2-bromo,**11**, and 1-methyl-2,6-dimethylpyridinium iodide,**16** were prepared in a synthetic route similar to that of compounds **12**, **13** and **14**. The corresponding 2-substituted pyridine was reacted with methyl iodide in refluxing dry acetone, and was

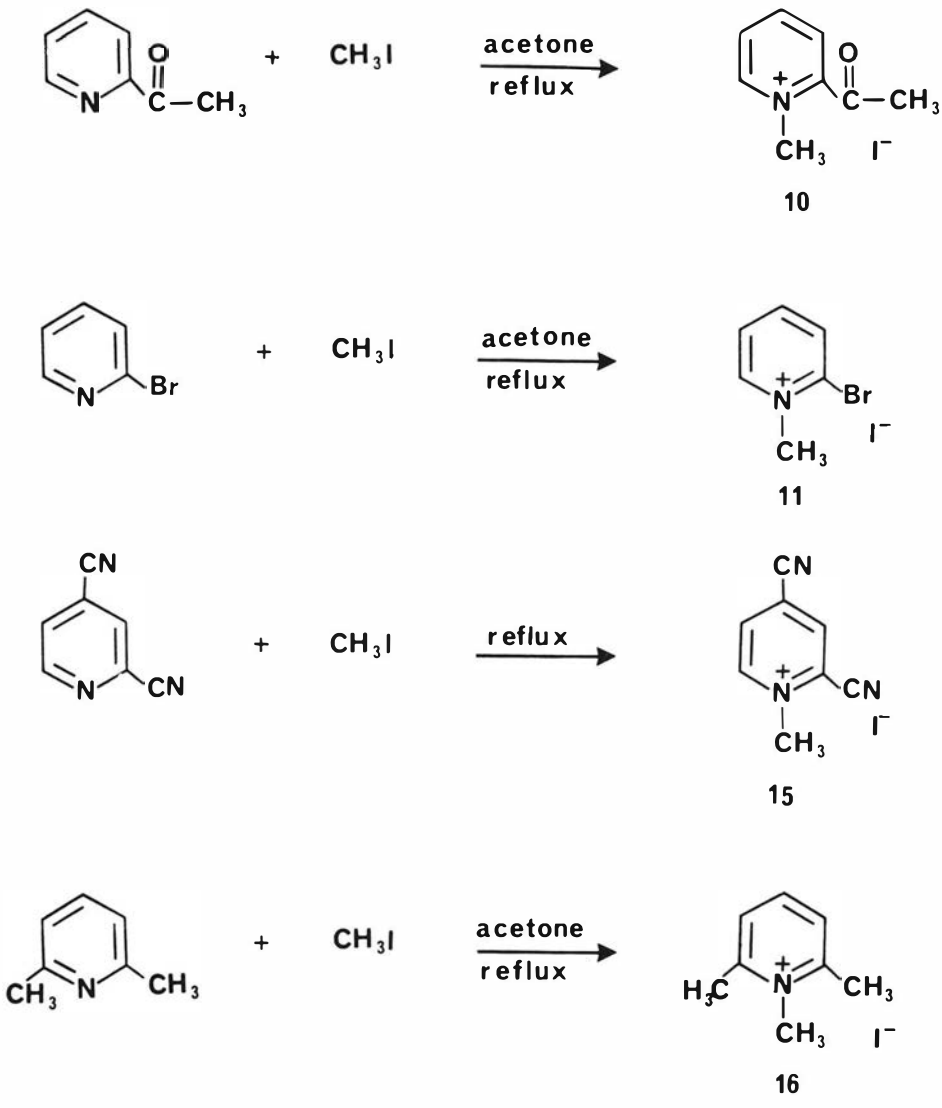


Figure 30. Preparation of the Salts 10, 11, 15 and 16.

recrystallized from 95% ethanol-ethyl ether (Figure 30). The reactions refluxed for longer time to reach completion due to steric hinderance of the pyridine nitrogen especially for the formation of the 2,6-trimethylpyridinium salt, and also due to the electron withdrawing ability of the acetyl group and to some extent, the bromine atom [90]. The lower yields of 45-75% could also be a result of the steric effect. The preparations of the salts **10** [91], **11** [92], and **16** [93] have been reported. The IR spectra of these salts (**10**, **11** and **16**), showed absorptions characteristic of aromatic C-H stretch near 2948-2990 cm^{-1}, C-C and C-N ring stretching near 1614-1630 cm-1, and a C-H ring bending near 760-790 cm^{-1} .

The ^{1}H NMR spectrum of compound **10** in DMSO-d_6 showed a doublet at δ 9.2-9.3 (1H, carbon 6 proton), a multiplet at δ 8.6-8.8 (2H, carbon 4 and 3 protons), a multiplet at δ 8.2-8.4 (1H, carbon 5 proton), a singlet at δ 4.4 (3H, 1-CH_3 protons), and a second singlet at δ 2.9 (3H, C-CH_3 protons). The ^{13}C NMR spectrum of **10** showed resonances at 194.4 ppm (C=O), 148.7 ppm (C-2), 147.8 ppm (C-6), 146.6 ppm (C-4), 129.3 ppm (C-5), 128.1 ppm (C-3), 41.5 ppm (C of 1-CH_3), and 30.3 ppm (C-CH_3).

The ^{1}H NMR spectrum of compound **11** also in DMSO-d_6 showed a doublet at δ 9.4-9.5 (1H, carbon 6 proton), a doublet at δ 8.4-8.5 (1H, carbon 3 proton), a multiplet at δ 8.00-8.3 (2H, carbon 5 and 4 protons), and a singlet at δ 4.5 (3H, 1-methyl protons). It was very difficult to obtain ^{13}C NMR spectrum of compound **11** because unexpected peaks formed after a few minutes of dissolving the compound in DMSO-d_6. These unexpected new peaks could be due to an exchange of the halogens (bromide for iodide and vice versa). A behavior of this type has been observed and reported by Alsaidi et al [93]. The ^{1}H NMR spectrum of compound **16** in DMSO-d_6 showed a multiplet at δ 8.3-8.5 (1H, carbon 4 proton), a doublet at δ 7.8-7.9 (2H, carbons 5 and 3 protons), a singlet at δ 4.1 (3H, 1-methyl protons, and a singlet at δ 2.8 (6H, methyl protons at carbon 6 and 2). The ^{13}C NMR spectrum of **16** showed resonances at 155.7 ppm (C-6, C-2), 143.7 ppm (C-4), 126.7 (C-5, C-3), and 21.4 ppm (C of CH_3 at 6 and 2).

B. 1-Benzyl-Substituted Pyridinium Bromides

Preparations of compounds **19**, **20**, and **21** were accomplished by refluxing benzyl bromide with the corresponding commercially available cyanopyridine in anhydrous acetone followed by recrystallization from 95% ethanol-ethyl ether (Figure 31). The acetone was purified and dried by distilling it from a mixture of potassium carbonate and potassium permanganate, and storing it over potassium carbonate. The potassium carbonate served as a drying agent, while the potassium permanganate served as an oxidizing agent. It oxidized any of the acetone that may have been reduced to the alcohol, back to the acetone. It was very important for the acetone to be dry because any water in the reaction mixture produced hydrogen bromide which reacted with the substituted pyridine to form the corresponding substituted pyridylhydrobromide rather than the desired substituted benzylpyridinium bromide (Figure 32). The reaction proceeded smoothly in 50-95% overall yield. The low yield of compound **19** could be due to steric hindrance and the electron withdrawing ability of the cyano group. The farther the cyano group was from the reaction center (nitrogen), the higher the yield and the faster the reaction reached completion. The preparations of the salts **19**, **20**, and **21** have been reported [94]. The IR spectra of these compounds showed absorptions characteristic of aromatic C-H stretch near 3040-3069 cm^{-1}, aliphatic C-H stretch near 2960-2983 cm^{-1}, CN near 2234-2240 cm^{-1}, C-C, and C-N ring stretching near 720-813 cm^{-1} respectively. The (CN) of compound **19** is again almost unobservable. The ^{1}H NMR spectrum of compound **19** in D_2O showed a doublet at δ 9.2-9.3 (1H, carbon 6 proton), a multiplet at δ 8.7-8.8 (2H, carbon 4 and 3 protons), a multiplet at δ 8.4-8.5 (1H, carbon 5 proton) a singlet at δ 7.6 (5H, aromatic protons), and a second singlet at δ 6.2 (2H, 1-CH_2 protons). The ^{13}C NMR spectrum of **19** showed resonances at 150.9 ppm (C-6), 149.8 ppm (C-4), 137.7 ppm (C-2), 134.9 ppm (C-3), 131.9-133.3 ppm (C-5 and aromatic C's), 113.1 ppm (CN), 67.5 ppm (C of 1-CH_2). The difficulty in observing the cyano peak of compound **19** in its IR spectrum led to further characterization of **19** by elemental analysis.

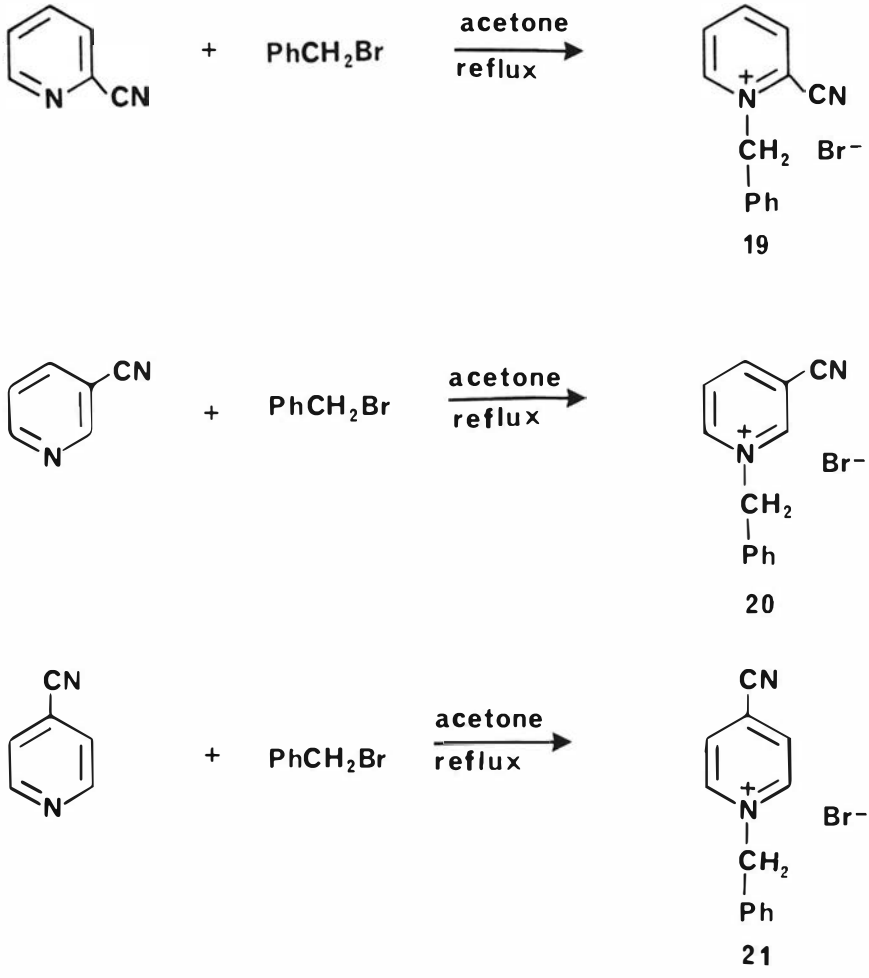
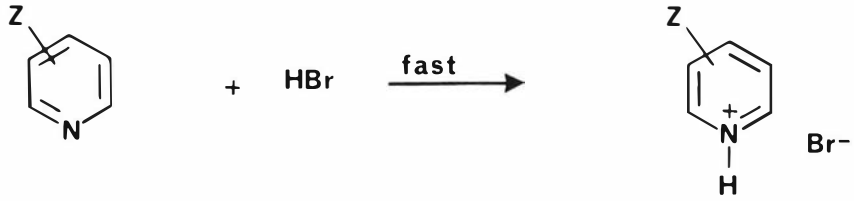


Figure 31. Reactions of 2,3, and 4-Cyanopyridines with Benzyl Bromide.



Z = Br , CN , CH_3 , $C(=O)-CH_3$, CH_2CH_3 , CH_2OH , or CH_2CH_2OH .

Figure 32. Formation of Pyridinium Hydrobromide Salts.

The ^{1}H NMR spectrum for compound **20** in DMSO-d6 showed a singlet at δ 10.5 (1H, carbon 2 proton), a doublet at δ 9.7-9.8 (1H, carbon 6 proton), a second doublet at δ 9.2- 9.3 (1H, carbon 4 proton), a multiplet at δ 8.3-8.6 (1H, carbon 5 proton), a multiplet at δ 7.3-7.9 (5H, aromatic protons), and a singlet at δ 6.1 (2H, 1-CH_2 protons). The ^{13}C NMR spectrum of **20** showed resonances at 148.9 ppm (C-2), 147.9 ppm (C-6), 133.3 ppm (C-4), 128.7-129.2 ppm (C-5 and aromatic C's), 113.6 ppm (CN), 112.9 ppm (C-3), and 63.6 ppm (C of 1-CH_2). The ^{1}H NMR spectrum of compound **21** in DMSO-d_6 showed a doublet at δ 9.7-9.8 (2H, carbon 6 and 2 protons), a doublet at δ 8.7-8.8 (2H, carbon 5 and 3 protons), a multiplet at δ 7.1-7.7 (5H, aromatic protons), and a singlet at δ 6.2 (2H, 1-CH_2 protons). The ^{13}C NMR spectrum of **21** showed resonances at 146.0 ppm (C-6, and C-2), 133.5 ppm (C-5 and C-3), 127.2-131.2 ppm (C-4 and aromatic C's), 114.6 ppm (CN), and 63.6 ppm (C of 1-CH_2).

Formation of compounds **22**, **25**, **26**, **27**, **28** and **29** was accomplished by reacting benzyl bromide with the corresponding methyl pyridines in dry acetone. The reaction of compound **25** with benzyl bromide formed oils, which after cooling in the refrigerator, crystallized to a white solid. The solid was dried in an oven and stored in a desicator because it was hygroscopic. The reaction of compounds **22** and **26** with benzyl bromide also formed an oil (Figure 33), which crystallized on cooling to a white solid that was not hygroscopic. Both **22**, **25** and **26** were recrystallized from acetonitrile. Reaction of compounds **27**, **28**, and **29** with benzyl bromide directly formed white solid which were recrystallized from 95% ethanol-ethyl ether (Figure 34). **27** and **28** were found not to be hygroscopic, while **29** was hygroscopic. These reactions proceeded smoothly in 45-90% overall yield: **22** (75%), **25** (80%), **26** (85%), **27** (90%), **28** (75%), and **29** (45%) respectively. The very low yield of compound **29** could again be explained by steric hinderance of the pyridine nitrogen by the two methyl groups at carbon two and six. Steric effects were very important in these reactions as could be seen in the case of compound **27**, which had an unhindered nitrogen and gave the highest yield (90%).

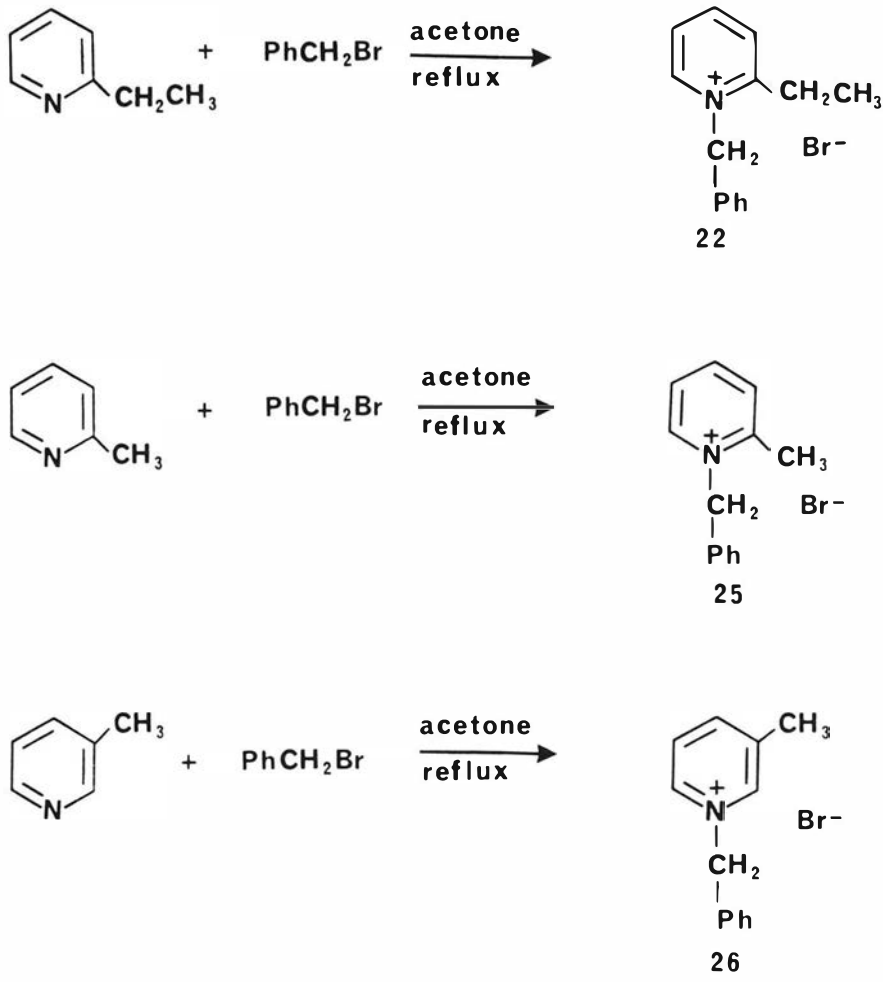


Figure 33. Preparation of 1-Benzylpyridinium Salts, 22, 25, and 26.

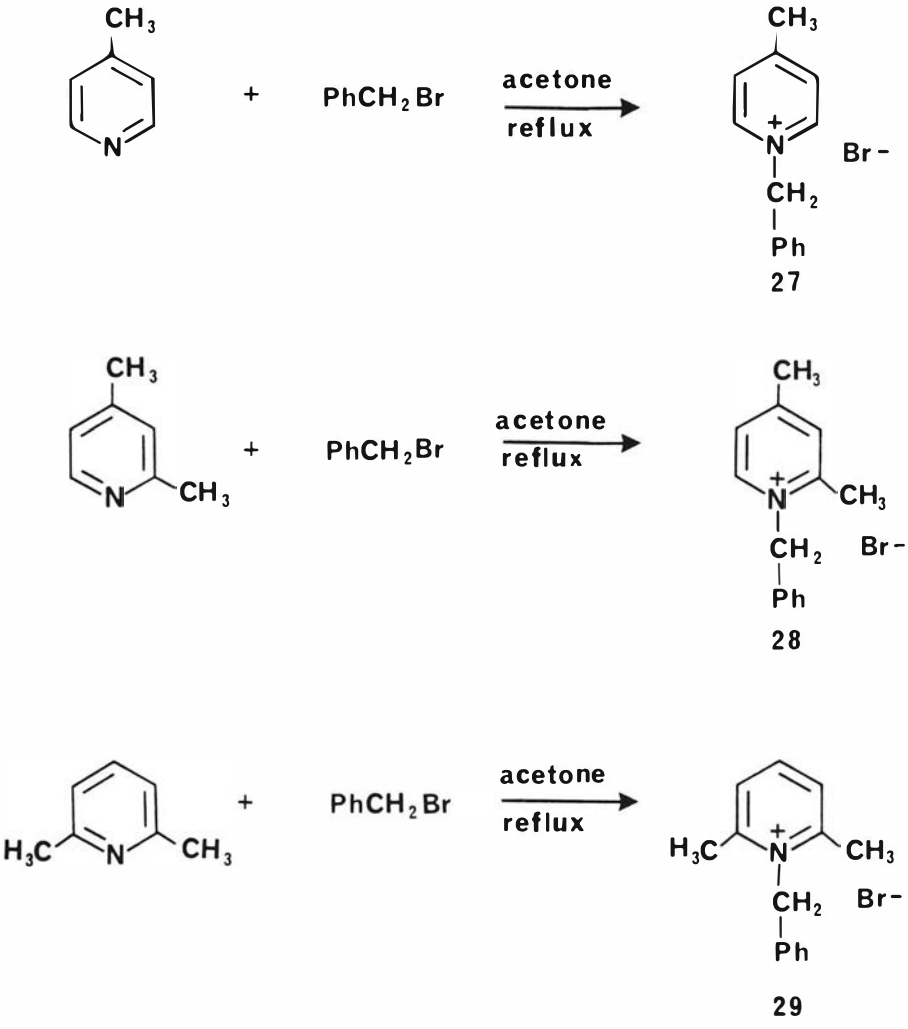


Figure 34. Preparation of 1-Benzylpyridinium Salts, 27, 28, and 29.

The preparations of the salts **22**, **25**, **26**, **27**, **28**, and **29** have been reported [95, 96]. The IR spectra of these compounds showed absorptions characteristic of aromatic C-H stretch near 3060-3100 cm^{-1}, aliphatic C-H stretch near 2879-2965 cm^{-1}, a C-C, and C-N ring stretching near 1600-1635 cm^{-1}, and a C-H ring bending near 720-800 cm^{-1}. The ^1H NMR spectrum of compound **22** showed a doublet at δ 9.5-9.6 (1H, carbon 6 proton), a second doublet at δ 8.4-8.5 (1H, carbon 3 proton), a multiplet at δ 8.2-8.3 (2H, carbon 5 and 4 protons), a singlet at δ 7.4 (5H, aromatic protons), a second singlet at δ 6.1 (2H, 1-CH_2 protons), a quartet at δ 3.11-3.2 (2H, CH_2 of ethyl), and a triplet at δ 1.1-1.3 (3H, CH_3 of ethyl). The ^{13}C NMR spectrum of **22** showed resonances at 159.6 ppm (C-2), 146.2 ppm (C-6), 145.9 ppm (C-4), 125.7 ppm (C-5, C-3 and aromatic C's), and 59.7 ppm (C of 1-CH_2), 25.4 ppm (CH_2 of ethyl) and 11.9 ppm (C of CH_3 of ethyl).

The ^1H NMR spectrum of compound **25** in $CDCl_3$ showed a doublet at δ 9.5-9.6 (1H, carbon 6 proton) a doublet at δ 8.4-8.6 (1H, carbon 3 proton), a multiplet at δ 7.9-8.1 (2H, carbon 5 and 4 protons), a singlet at δ 7.3 (5H,aromatic protons), a singlet at δ 6.2 (2H, 1-CH_2 protons), and a third singlet at δ 2.9 (3H, carbon 2 methyl protons). The ^1H NMR spectrum of compound **26** in DMSO-d_6 showed a singlet at δ 9.5 (1H, carbon 2 proton), a doublet at δ 9.3-9.4 (1H, carbon 6 proton), a second doublet at δ 8.5-8.6 (1H, carbon 4 proton), a multiplet at δ 8.0-8.3 (1H, carbon 5 proton), a singlet at δ 7.3-7.9 (5H, aromatic protons), a singlet at δ 6.00 (2H, 1-CH_2 protons), and a third singlet at δ 2.5 (3H, carbon 3 methyl protons). The ^1H NMR spectrum of compound **27** in DMSO-d_6 showed a doublet at δ 9.2-9.3 (2H, carbon 6 and 2 protons) a second doublet at δ 8.0-8.1 (2H, carbon 5 and 3 protons), a multiplet at δ 7.4-7.6 (5H, aromatic protons), a singlet at δ 6.0 (2H, 1-CH_2 protons) and second singlet at δ 2.6 (3H, carbon 4 methyl protons). The ^1H NMR spectrum of compound **28** also in DMSO-d_6 showed a doublet at δ 9.2-9.3 (1H, carbon 6 proton), a singlet at δ 8.1 (1H, carbon 3 proton), a multiplet at δ 7.9-8.0 (1H, carbon 5 proton) a second multiplet at δ 7.3-7.5 (5H, aromatic protons), a singlet at δ 6.0 (2H, 1-CH_2 protons), a singlet at δ 2.8 (3H, carbon 2 methyl protons), and a third singlet at δ 2.6 (3H,

carbon 4 methyl protons). The ^{13}C NMR spectrum of **28** showed resonances at 158.8 ppm (C-2), 154.0 ppm (C-6), 144.9 ppm (C-4), 133.2 ppm (C-3), 126.3-130.4 ppm (C-5 and aromatic C's), 59.2 ppm (C of 1-CH_2), 21.1 ppm (C of CH_3 at C-2), and 19.8 ppm (C of CH_3 at C-4).

The ^1H NMR spectrum of compound **29** again in DMSO-d_6 showed a multiplet at δ 8.5-8.6 (1H, carbon 4 proton), a doublet at δ 8.0-8.1 (2H, carbon 5 and 3 protons), a multiplet at δ 7.4-7.5 (5H, aromatic protons), a singlet at δ 6.0 (2H, 1-CH_2 protons), and a second singlet at δ 2.8 (6H, CH_3 protons at carbon 6 and 2). The ^{13}C NMR spectrum of **29** showed resonances at 156.1 ppm (C-6 and C-2), 145.1 ppm (C-4), 132.3 ppm (C-3), 125.5 ppm (C-5 and aromatic C's), 55.5 ppm (C of 1-CH_2), and 21.0 ppm (C of CH_3 at C-6 and C-2).

Compounds **23** and **24** were prepared in 80% yield from the reaction of benzyl bromide with the corresponding substituted pyridine in dry acetone, followed by recrystallization from 95% ethanol-ethyl ether(Figure 35). Reaction of compound **23** with benzyl bromide formed a viscous oil, which crystallized after one hour of continuous stirring. 2-(Hydroxymethyl) pyridine with benzyl bromide formed a white solid directly in refluxing. It was necessary to use excess solvent (acetone) for this reaction because **24** swelled when formed in the absence of excess solvent. Compound **23** has not been reported in the literature to date, but **24** has been reported [93]. The IR spectra of **23** and **24** showed absorptions characteristic of O-H near 3260 cm^{-1}, aromatic C-H stretch near 3000-3080 cm^{-1}, aliphatic C-H stretch near 2880 cm-1, C-C and C-N ring stretching near 1630-1640 cm^{-1}, and a C-H ring bending near 730-760 cm^{-1} respectively. The ^1H NMR spectrum of compound **23** in DMSO-d_6 showed a doublet at δ 9.1-9.2 (1H, carbon 6 proton), a triplet at δ 8.6-8.7 (1H, carbon 4 proton), a multiplet at δ 8.0-8.2 (2H, carbon 5 and 3 protons), a second multiplet at δ 7.2-7.4 (5H, aromatic protons), a singlet at δ 6.0 (2H, 1-CH_2 protons), a broad peak at δ 4.8-5.6 (1H, O-H proton), a triplet at δ 3.7-3.9 (2H, CH_2CH_2OH),

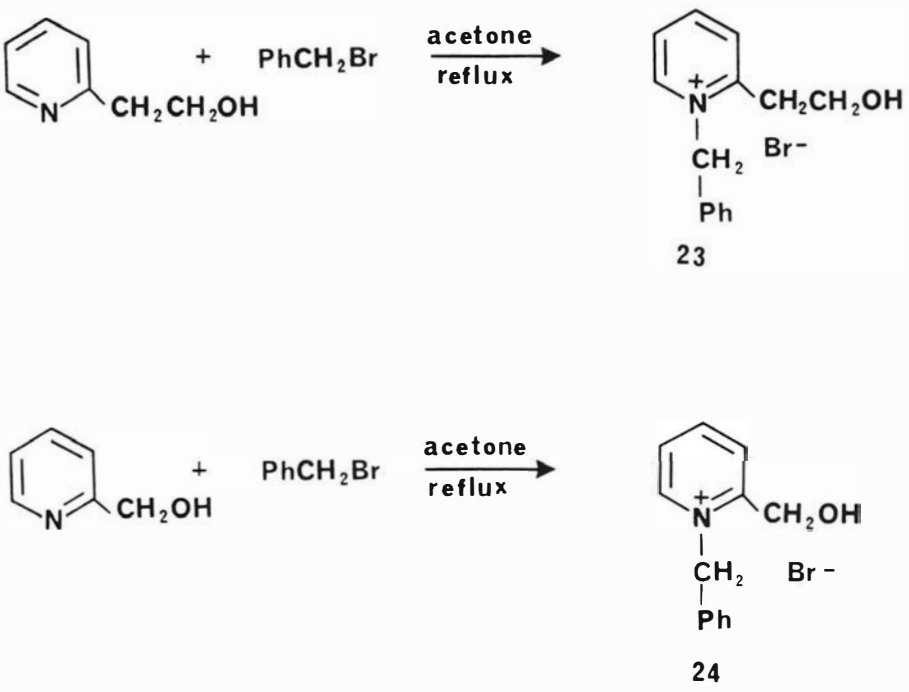


Figure 35. Preparations of 1-Benzylpyridinium Salts, 23 and 24.

and a second triplet at δ 3.2-3.3 (2H, CH_2CH_2OH). The ^{13}C NMR spectrum of **23** showed resonances at 157.1 ppm (C-2), 146.2 ppm (C-6), 145.5 ppm (C-4), 133.7 ppm (C-3), 126.0-129.2 ppm (C-5, and aromatic C's), 60.0 ppm (C of 1-CH_2), and 58.9 ppm (C of CH_2CH_2OH), 35.1 ppm (C of CH_2CH_2OH). The ^1H NMR spectrum of **24** also in DMSO-d_6 showed a doublet at δ 9.1-9.2 (1H, carbon 6 proton), a triplet at δ 8.6-8.8 (1H, carbon 4 proton), a multiplet at δ 8.0-8.3 (2H, carbon 5 and 3 protons), a second multiplet at δ 7.2-7.4 (5H, aromatic protons), a broad peak at δ 6.3-6.8 (1H, O-H proton), a singlet at δ 5.9 (2H, 1-CH_2 protons), and a second singlet at δ 4.9 (2H, CH_2OH). The ^{13}C NMR spectrum of **24** showed resonances at 158.1 ppm (C-2), 146.1 ppm (C-6), 132.9 ppm (C-4), 126.3-129.2 ppm (C-3, C-5, and aromatic C's), 59.2 ppm (C of 1-CH_2), 58.8 ppm (C of CH_2OH). Compounds **23** and **24** were further characterized by elemental analysis and were found to give satisfactory results.

Compound **18** was prepared by the reaction of benzyl bromide with 2-bromopyridine in dry acetone. The white solid of **18**, which formed during reflux, was recrystallized from 95% ethanol-ethyl ether (Figure 36). The low yield of 60% obtained could be due to the electron withdrawing ability of bromine, and the steric hindrance of the pyridine nitrogen by bromine. Compound **18** has been reported in the literature [97]. The IR absorption spectrum of **18** showed characteristic peaks at aromatic C-H stretch near 3100, aliphatic C-H stretch near 2990 cm^{-1}, a C-C and C-N ring stretching near 1630 cm^{-1} and a C-H ring bending near 760 cm-1. The ^1H NMR spectrum in DMSO-d_6 showed a doublet at δ (ppm) 9.5-9.6 (1H, carbon 6 proton), a second doublet at δ 8.7-8.8 (1H, carbon 3 proton), a multiplet at δ 8.2-8.5 (2H, carbon 5 and 4 protons), a singlet at δ 7.4 (5H, aromatic protons), and a second singlet at δ 6.1 (2H, 1-CH_2 protons). The ^1H NMR spectrum of compound **18** in DMSO-d_6 developed new unexpected peaks when the sample remained in the tube for more than one hour. The explanation to this could be that the bromine atoms were exchanging, and adding to different positions on the pyridine ring.

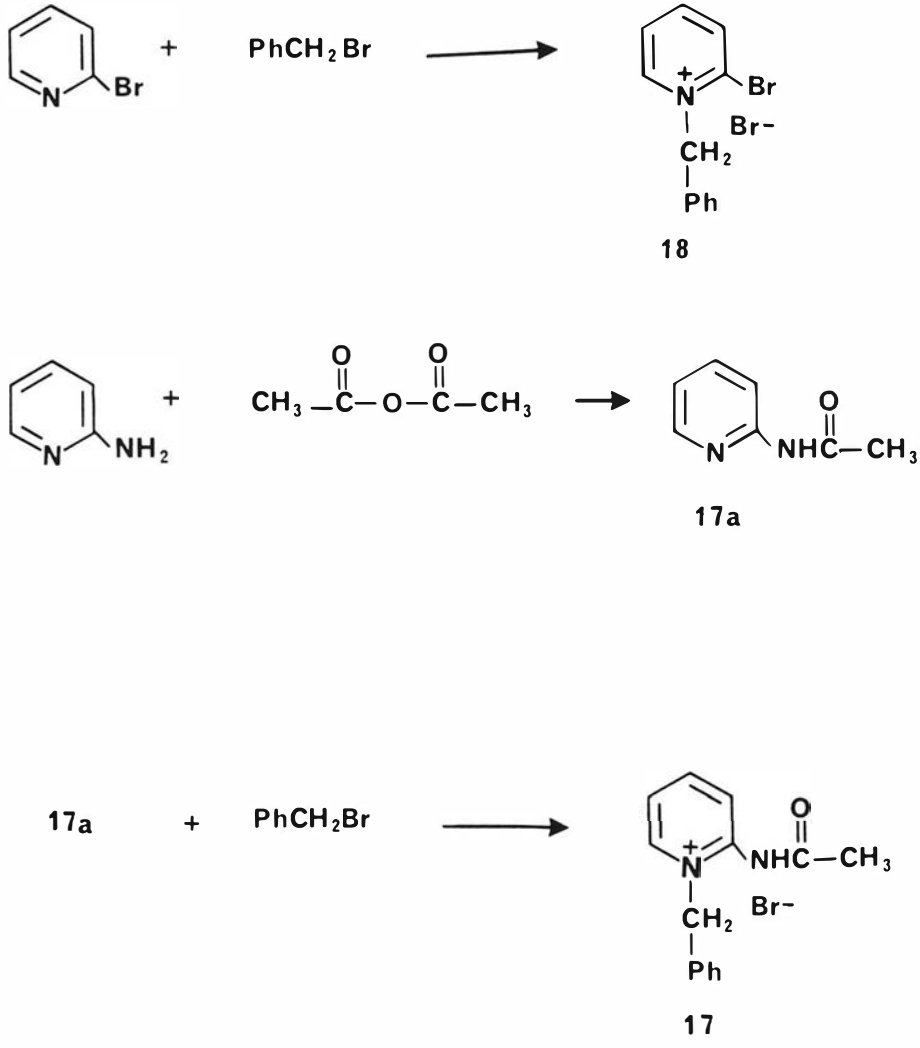


Figure 36. Preparation of 1-Benzylpyridinium Salts 17 and 18.

The 2-(acylamino)pyridine, **17a**, was prepared in 85 percent yield by the reaction of commercially available 2-aminopyridine with acetic anhydride (Figure 36). The white solid of **17a** was recrystallized from benzene-petroleum ether. Compound **17a** has been reported in the literature [98]. Its IR spectrum showed absorptions for N-H near 3284 cm^{-1}, aliphatic C-H stretch near 2974 cm^{-1}, C = 0 near 1682 cm^{-1}, and a C-H ring bending near 761 cm^{-1}. The ^{1}H NMR spectrum of **17a** in $CDCl_3$ showed a singlet at δ 9.6 (1H, N-H proton), a multiplet at δ 8.2-8.3 (2H, carbon 6 and 3 protons), a multiplet at δ 7.6-7.8 (1H, carbon 4 proton), a third multiplet at δ 7.0-7.1 (1H, carbon 5 proton), and a singlet at δ 2.2 (3H, CH_3 protons). The ^{13}C NMR spectrum of **17a** showed resonances at 169.1 ppm (C = 0), 152.0 ppm (C-2), 147.8 ppm (C-6), 137.8 ppm (C-4), 119.1 ppm (C-5), 113.5 ppm (C-3), and 23.8 ppm (C of CH_3).

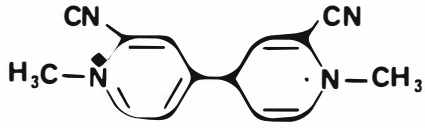
1-Benzyl-2-(acylamino)pyridinium bromide **17** was prepared by the reaction of benzyl bromide with 2-(acylamino)pyridine **17a** in dry acetone (Figure 36). The benzyl bromide-acetone solution turned cloudy as **17a** was added. **17** precipitated as a white solid from the acetone solution during the refluxing. Compound **17** which has been reported in the literature [99] was recrystallized from 95% ethanol-ethyl ether in 65% yield. The low yield could be due to steric and resonance effects. The IR spectrum of **17** showed characteristic absorptions for N-H near 3438 cm^{-1}, C = O near 1713 cm^{-1}, C-C and C-N ring stretching near 1639 cm^{-1} and C-H ring bending near 779 cm^{-1}. The ^{1}H NMR spectrum of **17** in DMSO-d_6 showed a singlet at δ 11.3 (1H, N-H proton), a doublet at δ 9.1-9.2 (1H, carbon 6 proton), a triplet at δ 8.5-8.6 (1H, carbon 4 proton), a doublet at δ 8.1 - 8.2 (1H, carbon 3 proton)a multiplet at δ 7.9-8.1 (1H, carbon 5 proton), a singlet at δ 7.4 (5H, aromatic protons), a singlet at δ 6.1 (2H, 1-CH_2 protons), and a third singlet at δ 2.2 (3H, C-CH_3 protons). The ^{13}C NMR spectrum of **17** showed resonances at 169.1 ppm (C = 0), 146.8 ppm (C-2), 146.3 ppm (C-6), 144.8 ppm (C-4), 127.8-132.9 ppm (aromatic C's), 124.4 ppm (C-5), 123.2 ppm (C-3), 59.0 ppm (C of 1-CH_2), and 23.5 ppm (C of CH_3). Characterization of compound **17** by elemental analysis gave satisfactory results.

2. Reactions of Cyanide ion with the Substituted Pyridinium Salts

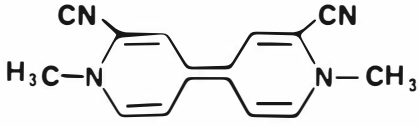
A. Reaction of cyanide ion with 1-methyl-2-cyanopyridinium iodide 12

1-Methyl-2-cyanopyridinium iodide was reacted with potassium cyanide in water to give a dark solid. Since it has been reported that unsubstituted pyridinium salts react with cyanide ion to form a cation radical [100] or 1,1'-dihydro-4,4'-dipyridyls [35, 68], the dark solid was expected to be either the 1,1'-dimethyl-2,2'-dicyano-4,4'-bipyridinium cation radical **60** or the 1,1'-dimethyl-2,2'-dicyano-1',1'-dihydro-4,4'-bipyridine **61** (Figure 37); therefore, it was immediately oxidized with iodine in ethanol-acetone solution (Figure 38). The acetone was needed to completely dissolve the iodine. The iodine solution was passed through a column of ion exchange resin which had previously been saturated with bromide ion. The ion-exchanged solution was evaporated to dryness. The dark brown solid which resulted partially dissolved in water. The water solution was washed several times with methylene chloride; evaporation of the methylene chloride produced a yellow solid of 1-methyl-2-oxo-1,2-dihydro-4-pyridine carbonitrile **62**, in 20% overall yield. Compound **62** was used in the literature by Tomisawa and coworkers in 1979 [101] as a dienophile in Diels-Alder reactions for the formation of isoquinolones. Their unpublished route requires five-steps for the synthesis of **62** (125) (Figure 38a). This work requires only two steps starting from 1-methyl-2-cyanopyridinium iodide.

The IR spectrum of **62** showed absorptions characteristic of CN at 2240 cm^{-1}, C = 0 near 1650-1770 cm^{-1} and a C-H ring bending near 780 cm^{-1}. The 1H NMR spectrum of 62 in CDCl3 showed a doublet at δ 7.4-7.5 (1H, carbon 6 proton), a singlet at δ 6.9 (1H, carbon 3 proton), a doublet at δ 6.3 (1H, carbon 5 proton), and a singlet at δ 3.6 (3H, 1-CH_3 protons). The ^{13}C NMR spectrum of **62** showed resonances at 160.9 ppm (C = 0), 140.3 ppm (C-6), 126.2 ppm (C-4), 123.8 ppm (C-3), 115 ppm (CN), 105.0 ppm (C-5), and 38.0 ppm (C of 1-CH_3). The mass spectrum of compound **62** showed a parent ion at m/z 134 ($C_7H_6N_2O$ = 134), followed by a loss of C = 0



60



61

Figure 37. 1,1'-Dimethyl-2,2'-Dicyano-4,4'-Bipyridimium cation Radical 60, and 1,1'-Dimethyl-2,2'-Dicyano-1,1'-Dihydro-4,4'-Bipyridine 61.

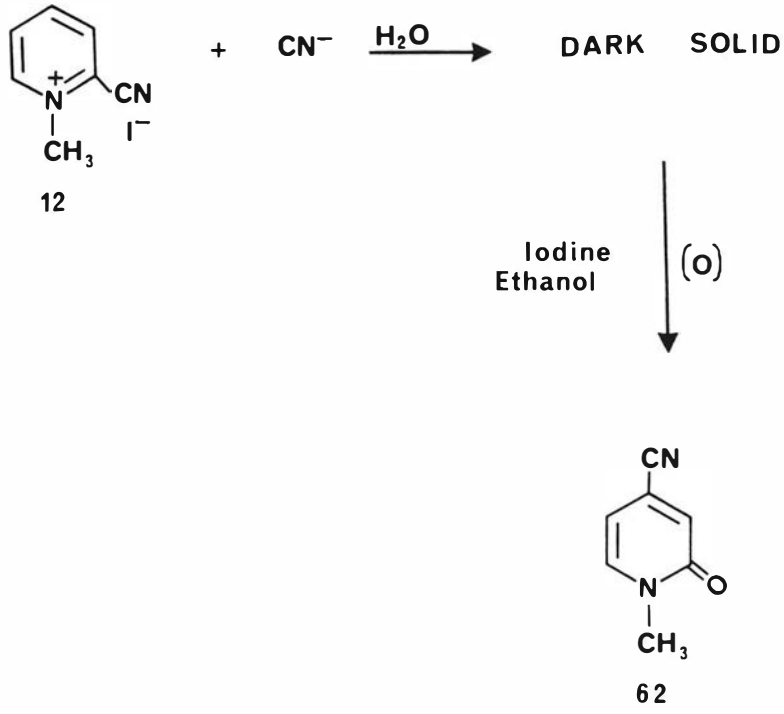


Figure 38. Preparation of 1-Methyl-2-Oxo-1,2-Dihydro-4-Pyridine Carbonitrile.

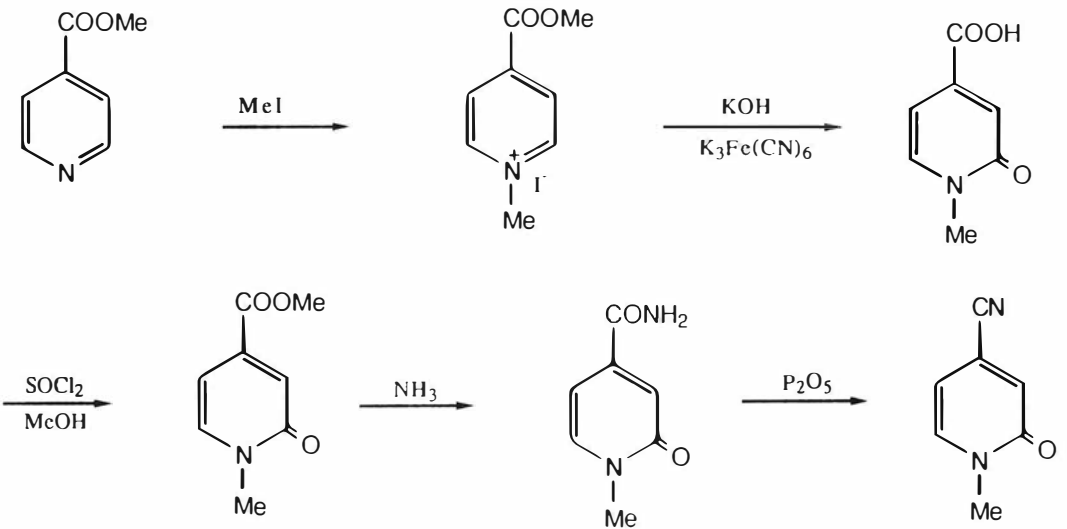


Figure 38a. Synthesis of 1-Methyl-2-Oxo-1,2-Dihydro-4-Pyridine Carbonitrile, by Tomisawa and coworkers (unpublished).

($C_6H_6N_2$ = 106), a loss of CN (C_5H_6N = 80), a loss of C-H (C_3H_2N = 52) respectively. Characterization of compound **62** by elemental analysis gave satisfactory results.

Electron spin resonance spectroscopic analysis of the resulting reaction mixture of compound **12** and cyanide ion, showed presence of a radical. Therefore, there were many attempts to determine the nature of the dark solid. Exposure of this dark solid to the atmosphere had no noticeable effect, indicating a possible absence of a radical in the solid. The IR spectrum showed two cyano peaks at 2240 and 2220 cm-1 characteristic of cyano groups at 4 and 2-carbons of pyridinium salts. Sodium fusion was performed following the procedure of Pavia, Lampman and Kriz [102]. A positive test was obtained for nitrogen while the test for iodine was negative.

The mechanism of the formation of compound **62** seemed unclear. It has been reported that 1-methyl-2-cyanopyridinium iodide hydrolyzed to 1-methyl-2-pyridone at pH 8 or higher [103]; therefore, since the reaction of **12** with cyanide ion had to be at pH 8 or above, perhaps 1-methyl-2-pyridone was formed in the reaction. Then, it may have reacted with the cyanide ion in the solution to form compound **62**. Therefore, commercially available 1-methyl-2-pyridone was reacted with potassium cyanide in different solvents (water-acetone, acetone, acetone-ethanol, and ethanol), no reaction occurred. The reactants (potassium cyanide and 1-methyl-2-pyridone) were recovered in almost 100% yield.

In 1966, Kosower and Patton studied the kinetics of hydrolysis of 1-methyl-2-cyano, 3-cyano, and 4-cyanopyridinium ions by aqueous base [88]. They found that the 2- and 4-cyano compounds yielded the corresponding pyridones at different rates. The 2-cyanopyridinium ion hydrolyzed faster than the 4-cyanopyridinium ion. The cyanide ion could add to the 4-position of the pyridinium salt first to form 1-methyl-2,4-dicyanopyridinium iodide. Then, the 2-cyano quickly hydrolyzed to the pyridone to form compound **62**. To test for this product, commercially available 2,4-dicyanopyridine was heated with refluxing methyl iodide to form **15** (Figure 30). Compound **15** was dissolved in aqueous base and warmed in a hot water bath to give **62**

in 65% yield (Figure 39, eq. 2). This result did not answer the question of what the mechanism for the formation of **62** was, but it accounts for the two cyano absorptions in the IR spectrum. The dark solid was a mixture as proved by its partial solubility in water and methylene chloride. But, it must have contained a compound that had two cyano groups possibly at the 2- and 4- positions. The oxidation and the work-up of the 2,4-dicyano adduct could have formed compound **62**. This was proved by the failure to isolate **62** from the unoxidized dark solid.

B. Reaction of cyanide ion with 1-methyl-3-cyanopyridinium iodide **13**

Compound **13** reacted with sodium cyanide to give a yellow solid which was recrystallized from chloroform to give 1-methyl-3,4-dicyano-1,4-dihydropyridine **63** in 90% yield (Figure 40). The reaction of **13** with cyanide ion to form **63** has been followed by ultraviolet absorption spectroscopy [23], and proton nuclear magnetic resonance spectroscopy [24], but the isolation and characterization of the solid has not been reported in the literature. This yellow solid **63** decomposed before it melted and darkened in color when exposed to the atmosphere for more than twenty-four hours, but it maintained the same structure.

The IR spectrum of **63** showed absorptions characteristic of aliphatic C-H stretch near 2960 cm^{-1}, CN at C-3 near 2220 cm-1 CN at C-4 near 2180 cm^{-1}, C-C and C-N ring stretching near 1680 cm^{-1}, characteristic of 1,4-dihydropyridine [124] and a C-H ring bending near 720 cm^{-1} . The ^1H NMR spectrum of **63** in $CDCl_3$ showed a singlet at δ 6.7 (1H, carbon 2 proton), a doublet at δ 5.9-6.0 (1H, carbon 6 proton), a multiplet at δ 4.8-4.9 (1H, carbon 5 proton), a doublet at δ 4.4-4.5 (1H, carbon 4 proton) and a singlet at δ 3.1 (3H, 1-CH_3 protons). Further characterization of **63** by elemental analysis gave convincing results.

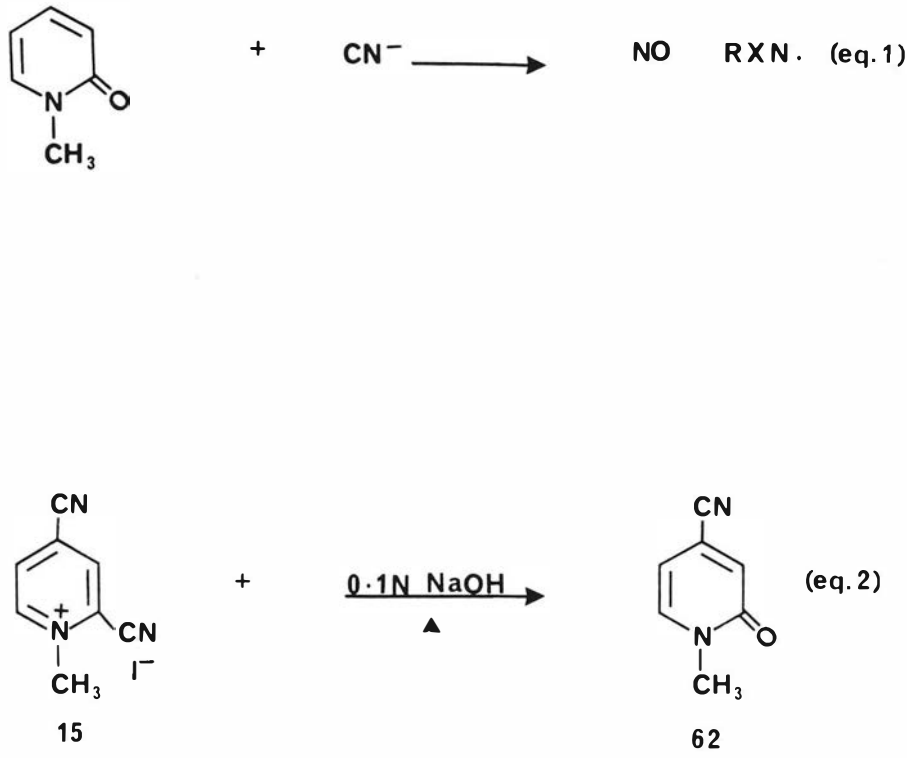


Figure 39. Reaction of 1-Methyl-2-Pyridone with Cyanide Ion and Preparation of 62 from 15 in Basic Solution.

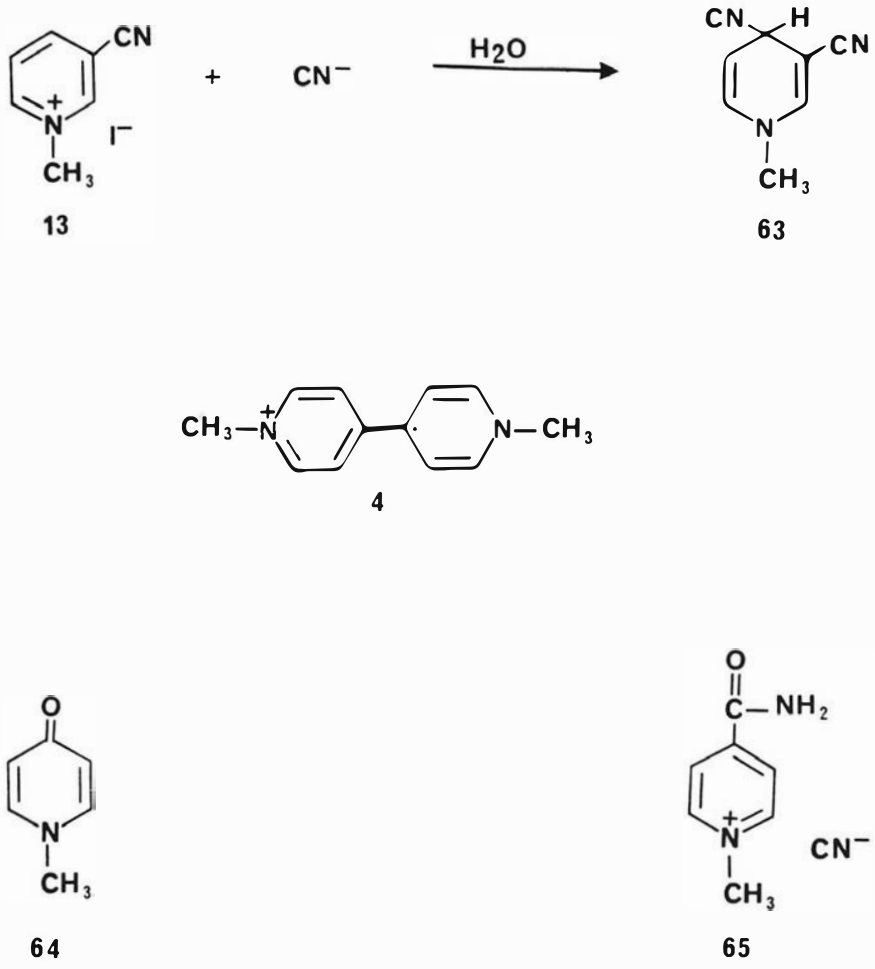


Figure 40. Preparation of 1-Methyl-3,4-Dicyano-1,4-Dihydropyridine 63.

C. Reaction of cyanide ion with 1-methyl-4-cyanopyridinium iodide **14**

1-Methyl-4-cyanopyridinium iodide was reacted with sodium cyanide in water to give a dark brown solution from which a dark solid precipitated. Because the dark solid could have been the expected cation radical **4** [104], the solid was immediately oxidized with alcoholic iodine solution, and the solution was past through an ion-exchange resin. Evaporation of the solvent produced a brown solid. All attempts to characterize the brown solid by spectroscopic methods failed. The IR spectrum of the dark solid from the reaction of **14** with cyanide ion showed an absorption characteristic of CN near 2240 cm^{-1} and a second CN near 2220 cm^{-1}. Further characterization of the dark solid failed. It also failed to give IR absorptions characteristic of the products of hydrolysis of compound **14**, **64** and **65** [88] (Figure 40),respectively.

D (i). Reaction of cyanide ion with 1-benzyl-2-(acylamino)pyridinium bromide **17**

Compound **17** with sodium cyanide in water-acetone solution did not show any observable changes at room temperature. When half of this solution was evaporated to dryness, the reactants (**17** and sodium cyanide) were recovered in 100% yield. When the other half was heated to the boiling point on a hot plate, an oil formed. The oil was dissolved in methylene chloride, dried, and the methylene chloride was removed using rotary evaporator. Spectroscopic characterization of the oil showed it was 1-benzylpyridinium-2-acylimide **66**. On standing for six to eight hours, the oil solidified.

Compound **66** was a product of the elimination of hydrogen bromide from **17** by heating (Figure 41). The solid **66** was more soluble in water in the solid state than in oily state. Similar behavior was also observed by Inokuma and coworkers in 1979 [99], for compound **68**. They synthesized **68** by the alkali treatment of 1-methyl-2-(acylamino)pyridinium iodide **67** (Figure 41a).

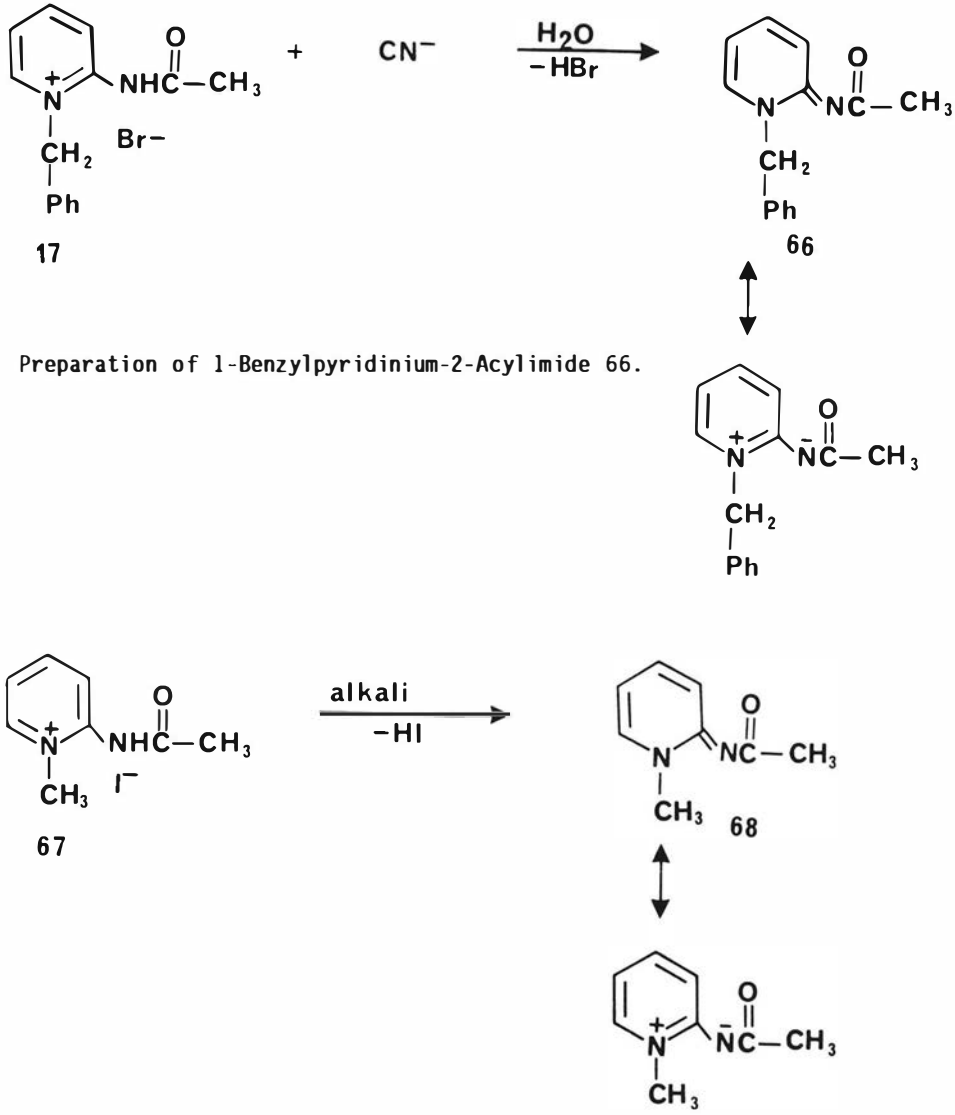


Figure 41. Preparation of 1-Benzylpyridinium-2-Acylimide 66.

Figure 41a. Preparation of 1-Methylpyridinium-2-Acylimide 68, by Inokuma and coworkers.

The reason compound **66** changed from liquid to solid is probably due to its existence as a zwitterionic compound (Figure 41). Similar behavior was also observed by Inokuma and coworkers.

The IR spectrum of **66** showed absorptions characteristic of aromatic C-H stretch near 3063 cm^{-1}, C=0 near 1636 cm^{-1}, and a C-C ring bending near 750 cm^{-1}. The ^{1}H NMR spectrum in DMSO-d_6 showed a multiplet at δ 7.9-8.2 (2H, carbon 6 and 3 protons), a multiplet at δ 7.2-7.7 (6H, carbon 4, and aromatic protons) a third multiplet at δ 6.5-6.9 (1H, carbon 5 proton), a singlet at δ 5.5 (2H, 1-CH_2 protons), and a second singlet at δ 2.3 (3H, CH_3 protons). The ^{13}C NMR spectrum of **66** showed resonances at 178.5 ppm (C=0), 157.0 ppm (C-2), 139.3 ppm (C-6), 136.5 ppm (C-4), 127.5-128.3 ppm (aromatic C's), 119.5 ppm (C-5), and 110.3 ppm (C-3). The mass spectrum of compound **66** showed a parent ion at m/z 226 ($C_{14}H_{14}N_2O$ = 226), followed by a loss of CH_3 ($C_{13}H_{11}N_2O$ = 211), a loss of C=0 ($C_{12}H_{11}N_2$ = 183), and a peak for $C_6H_5CH_2$ (C_7H_7 = 91).

It should be noted that the characteristic IR absorbance of the carbonyl group in **66** was shifted to lower frequencies than those of **17a** and **17**. Also, the chemical shifts of the methylene protons attached to the nitrogen of the pyridine ring in **66**, appeared at a lower field than that in **17**. The solubility of **66** in water was higher than that of **17a**.

ii. Reaction of **66** with Hydrogen Bromide

To confirm the formation of compound **66**, it was dissolved in water and made acidic to litmus paper with hydrogen bromide. Compound **66** was not very soluble in water, but dissolved as soon as the reaction mixture was made acidic. The water solution was evaporated to give a white solid in 95% yield. The melting point and spectroscopic analysis of this solid was identical to **17** (Figure 42).

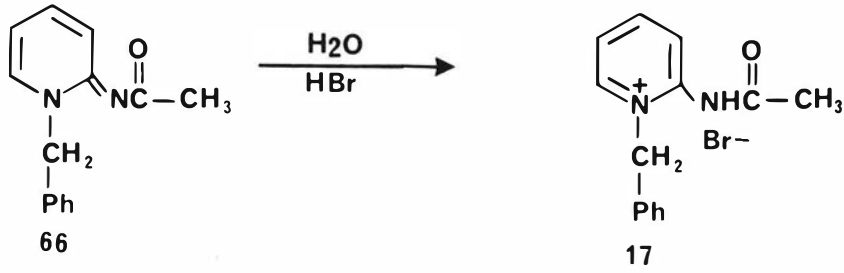


Figure 42. Reaction of 1-Benzylpyridinium-2-Acylimide 66, with Hydrogen Bromide.

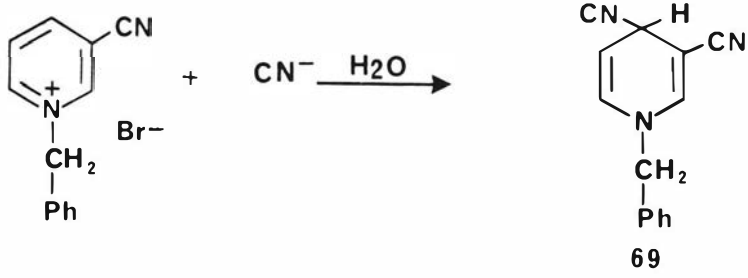


Figure 43. Preparation of 1-Benzyl-3,4-Dicyano-1,4-Dihydropyridine 69.

E. Reaction of cyanide ion with 1-benzyl-2-cyanopyridinium bromide **19**

The reaction of **19** with sodium cyanide in water or water-acetone at room temperature gave a dark brown solution. Attempts to isolate any compound from the dark brown solution failed. No report exists to date in the literature on the reaction of **19** with cyanide ion.

F. Reaction of cyanide ion with 1-benzyl-3-cyanopyridinium bromide **20**

Compound **20** reacted with sodium cyanide in water at room temperature to form an oily liquid. The oil was dissolved in methylene chloride, dried, and the methylene chloride was evaporated. The dry yellow oil was obtained in 85% yield, and proved to be 1-benzyl-3,4-dicyano-1,4-dihydropyridine **69** by spectroscopic analysis (Figure 43). **69** was not affected by exposure to the atmosphere. The formation of **69** from the reaction of **20** and cyanide ion was followed by ultraviolet absorption spectroscopy in alcoholic solutions by Lyle and Gauthier [23]. The IR spectrum of this oily liquid showed absorptions characteristic of aromatic C-H stretch near 3060 cm^{-1}, aliphatic C-H stretch near 2940 cm^{-1}, CN at C-3 near 2240 cm^{-1}, CN at C-4 near 2200 cm^{-1}, and a C-C and C-N ring stretching near 1690 cm^{-1}. The ^{1}H NMR spectrum of **69** in DMSO-d_6 showed a singlet at δ 7.5 (1H, carbon 2 proton), a second singlet at δ 7.4 (5H, aromatic protons), a doublet at δ 6.3-6.4 (1H, carbon 6 proton), a multiplet at δ 4.7-4.8 (1H, carbon 5 proton), a second doublet at δ 4.6-4.7 (1H, carbon 4-proton), and a singlet at δ 4.5 (2H, 1-CH_2 protons). The ^{13}C NMR spectrum of **69** showed resonances at 145.2 ppm (C-2), 136.9 ppm (C-6),30.9 ppm (C-4), 127.4-128.7 ppm (aromatic C's), 119.2 ppm (CN at C-3), 96.0 ppm (C-5), 72.8 ppm (CN at C-4), and 56.3 ppm (C of 1-CH_2).

G. Reaction of cyanide ion with 1-benzyl-2-(hydroxymethyl)pyridinium bromide **24**

1-Benzyl-2-(hydroxymethyl)pyridinium bromide was dissolved in water-acetone solution and flushed with oxygen-free nitrogen. The nitrogen was made oxygen-free by bubbling it through an alkaline pyrogallol solution. This water-acetone solution was frozen with liquid nitrogen while passing the oxygen-free nitrogen through it. Potas-

sium cyanide dissolved in water was also flushed with the oxygen-free nitrogen, and was poured into the frozen solution of **24**. The reaction mixture was , frozen completely, and was allowed to stand in the nitrogen atmosphere for forty-eight hours at room temperature. The colorless solution first turned green, then, blue-green, and a dark solid formed. The solid was filtered and immediately oxidized with 4.00g of iodine in 50mL of 95% ethanol-acetone solution. This dark solid decomposed to a sticky gum when allowed to stand in air, suggesting the presence of a cation radical **74** or a dihydro compound **73.** The blue-green solution that formed,was decolorized to a yellow solution when allowed to stand in the air, again strongly suggesting the presence of a radical. The blue-green solution showed the presence of a radical by electron spin resonance spectroscopic analysis. These observations were consistent with the benzoin type reaction mechanism for the dimerization of unsubstituted pyridinium salts by cyanide ion [35] (Figure 44). In the mechanism (Figure 44), the nucleophilic attack of the cyanide ion at the 2- and 4- position has been demonstrated (21, 23, 24). The loss of a proton from **70** to form the carbanion **71** should be facile in the basic cyanide solution [105]. The resulting carbanion could attack another pyridinium ion to form 1,1' ,4,4'-tetrahydro-2,2'-bis(hydroxymethyl)-4,4'-bipyridine **72,** which could undergo base catalyzed elimination of hydrogen cyanide to form the 1,1'-dihydro-4,4'-bipyridine **73**. Oxidation of **73** by oxygen, as reported [106], formed the dication **74**. Compound **73** could also be a strong reducing agent [107].

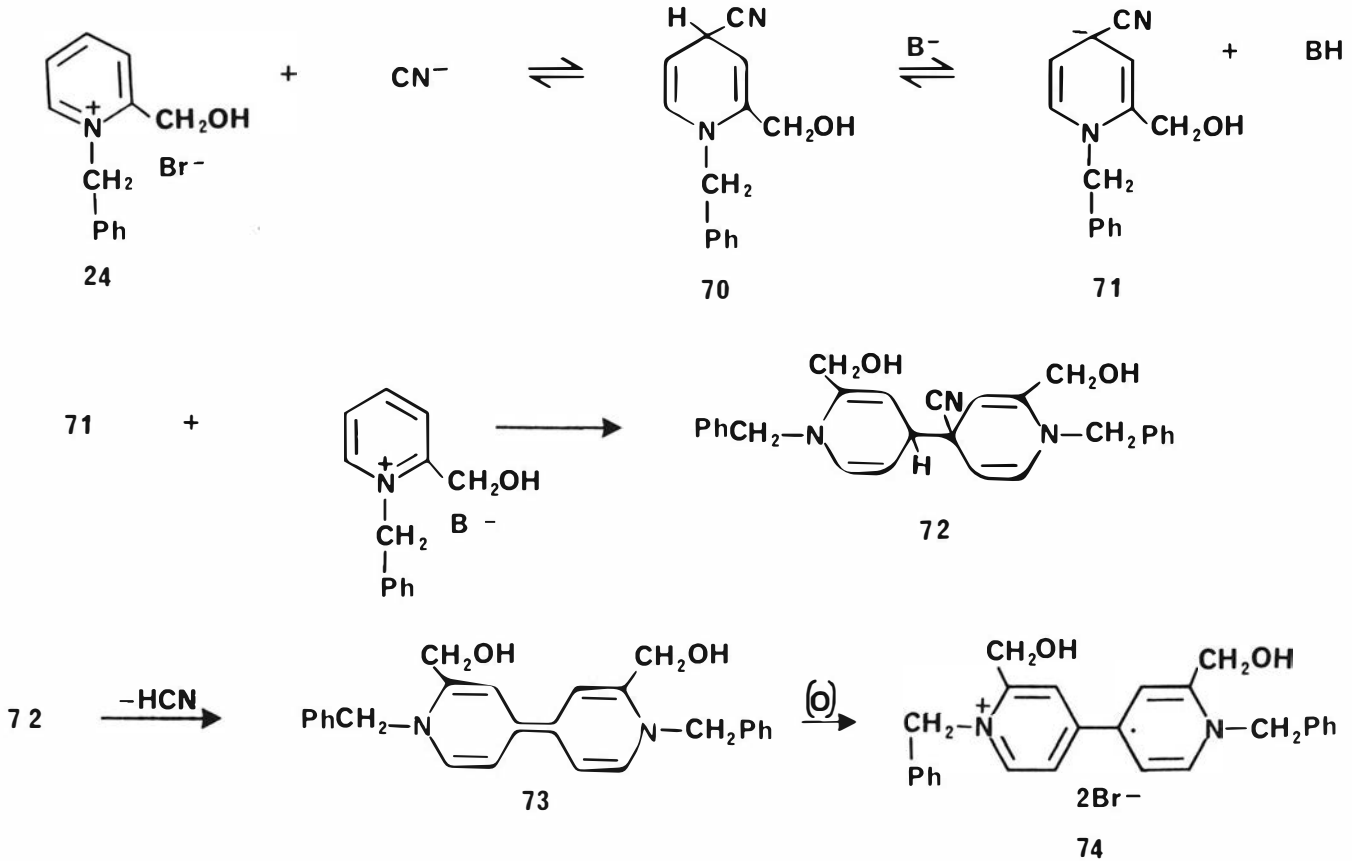


Figure 44. Proposed Mechanism for the Formation of the Cation Radical 74.

This benzoin type reaction mechanism was proposed [35] and has now been accepted by other researchers [36] for the dimerization of pyridinium salts by either cyanide ion [35] or other ambifunctional nucleophilic ions [36].

The oxidized iodine solution was passed through an ion-exchange resin which had been previously saturated with bromide ion to exchange bromide for cyanide or triiodide that may be present in the solution. Evaporation of the ion-exchanged solution produced a dark yellow solid which was washed with water. The water solution was evaporated and the resultant yellow solid was recrystallized from ethanol-ethyl acetate to give **75** in 60% yield. Spectroscopic analysis of the solid showed it was the expected dimer, 1,1'-dibenzyl-2-2'-bis(hydroxymethyl)-4,4'-bipyridinium dibromide **75** (Figure 45). **75** has not been reported in the literature to date. It decomposed at temperatures above 190°C.

The IR spectrum of **75** showed absorptions characteristic of O-H stretch near 3360 cm^{-1}, aromatic C-H stretch near 3100 cm^{-1} C-C and C-N ring stretch near 1640 cm^{-1} and a C-H ring bending near 730 cm^{-1}. The ^1H NMR spectrum of **75** in DMSO-d_6 showed a broad peak at δ 9.4-9.5 (2H, carbon 6, 6' protons), a second broad peak at δ 8.8-8.9 (4H, carbon 5, 5', and 3, 3'- protons), a singlet at δ 7.4 (12H, Ar, Ar', and OH, OH' protons), a singlet at δ 6.1 (4H, 1-CH_2 and 1-CH_2' protons), and a third singlet at δ 5.0 (4H, CH_2OH, CH_2OH' protons). The ^{13}C NMR spectrum of **75** showed resonances at 159.2 ppm (C-2, C-2'), 146.9 ppm (C-6, C-6'), 132.7-133.7 ppm (C-4, C-4'), 125.2 ppm (C-3, C-3', C-5, C-5' and aromatic C's), 59.3 ppm (C of 1-CH_2 and C of CH_2OH). Further characterization of **75** by elemental analysis gave satisfactory results.

An aqueous solution of **75** exhibited a strong absorption band at 280nm (log e = 3.3). When **75** was reduced in aqueous solution with sodium dithionite, a dark blue solution containing the radical cation was formed (Figure 46). The radical cation strongly absorbed near 340nm (log e = 4.0). This radical cation also exhibited a less intense broad absorption in the visible region near 600nm (log e = 7.0). These observations are

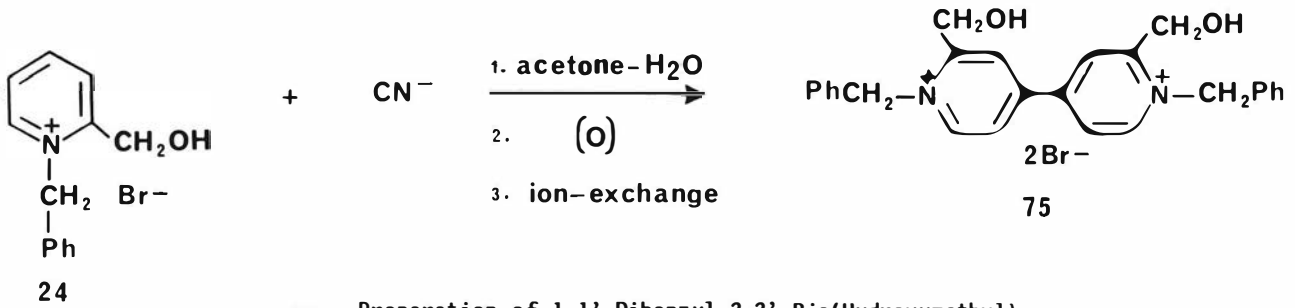


Figure 45. Preparation of 1,1'-Dibenzyl-2,2'-Bis(Hydroxymethyl)-4,4'-Bipyridinium Dibromide 75.

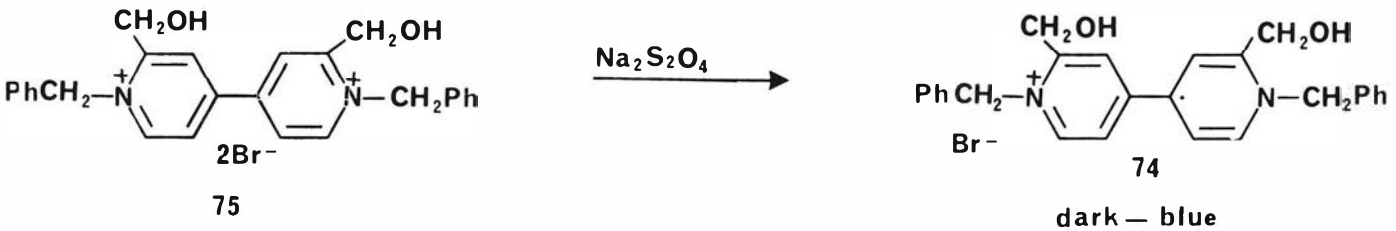


Figure 46. Formation of the Cation Radical 74, by the Reaction of 75 with Sodium Dithionite.

characteristic of bipyridinium cations [8, 108, 109]. The absorption bands in the visible region were attributed to charge transfer between the anion and the bipyridinium dication.

It has long been known that 1,1'-dimethyl-4,4'-bipyridinium dichloride (Paraquat) was a herbicide [110, 111]. Its herbicide activity was due to its ability to be reduced in aqueous solution at a potential (E^o) of about -0.45V to a stable radical cation by a one-electron transfer that is rapidly and quantitatively reversed by oxygen. On the other hand, 1,1'-dibenzyl-4,4'-bipyridinium dichloride (benzyl viologen) was reduced in aqueous solution at a potential (E^o) of about -0.35v to a stable radical cation by a one-electron transfer. As can be seen, benzyl viologen was more easily reduced with higher potentials. The high potential of benzyl viologen was suggested to be due to the effect of the electron attracting phenyl substituent in the benzyl quaternizing group [110]. Electron-releasing substituents on the bipyridine nitrogens have been suggested to lower the reduction potential, while electron-attracting substituents raised it [112].

Most bipyridimium salts containing substitutents on the bipyridinium ring have been found to be inactive as herbicides, For example, 1,1'-dimethyl-2,2'-dicyanopyridiniuum dibromide was found to be reduced in aqueous solution at a potential (E^o) of about +0.09v. This very high reduction potential was attributed to the effect of the electron attracting cyano group [8]. In view of the results obtained with many compounds, it has been suggested that large sized compounds have higher reduction potentials and lower herbicide activity [110]. The large size presumably hinders the movement of the salts to the biochemically important site of herbicidal action in plants. It may also hinder the salts from positioning themselves close enough to the photosynthetic electron donor molecules, such as the porphyrins of chlorophyll for electron transfer to occur to the salts.

Compound 75 was reduced in aqueous solution at a potential (E^o) of about -0.34v vs NHE. This potential could be considered good for this compound to be active as a herbicide. It has been suggested [41, 42] that for high herbicidal activity of the bipyridinium salt, the salt must be capable of being reduced in aqueous solution at a potential

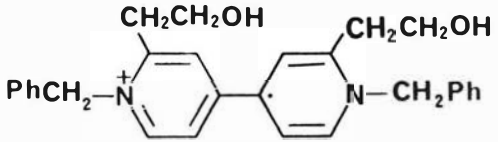
(E^{o}) of about -0.35 to -0.45v to a stable radical cation by a one-electron transfer that was rapidly and quantitatively reversed by oxygen.

H. Reaction of cyanide ion with 1-benzyl-2-(2-hydroxyethyl)pyridinium bromide **23**

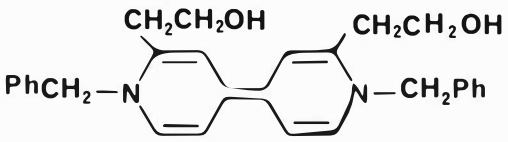
A solution of **23** in water-acetone flushed with oxygen-free nitrogen was reacted with a solution of potassium cyanide in water also flushed with nitrogen. The reaction mixture was frozen with liquid nitrogen. When defrosted, a blue-green solution formed, and a dark solid precipitated from the solution. The dark solid decomposed to a sticky gum when exposed to the air, and the green solution turned yellow when allowed to stand open in air at room temperature. These behaviors were characteristics of a cation radical **76** or a dihydro compound **77** (Figure 47). The blue-green solution showed the presence of a radical by electron spin resonance spectroscopy.

The dark solid was immediately oxidized with iodine in 95% ethanol-acetone solution. The mixture was warmed gently on a hot plate to dissolve all the dark solid, yet not all dissolved. The undissolved solids were removed by decanting the solution. The oxidized solution was passed through an ion-exchange resin and was evaporated to dryness. A dark yellow solid which remained was dissolved in 95% ethanol-ethyl acetate; the precipitate that formed decomposed when filtered. Trials to filter the solid in an inert atmosphere also failed.

An aqueous solution of the yellow solid exhibited a strong absorption band near 280nm. When the yellow solid was reduced in an aqueous solution with sodium dithionite, a dark blue radical cation was formed. The radical cation strongly absorbed near 340nm. This radical cation also exhibited a less intense broad absorption in the visible region near 600nm. This observed behavior of the yellow solid

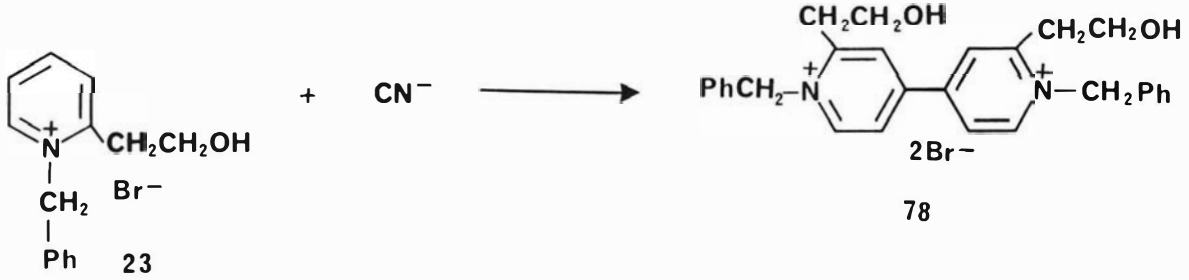


76



77

Figure 47. 1,1'-Dibenzyl-2,2'-Bis(2-Hydroxyethyl)-4,4'-Bipyridinium Cation Radical 76, and 1,1'-Dibenzyl-1,1'-Dihydro-2,2'-Bis(2-Hydroxyethyl)-4,4'-Bipyridine 77.



23

78

Figure 48. Reaction of 23 with Cyanide Ion.

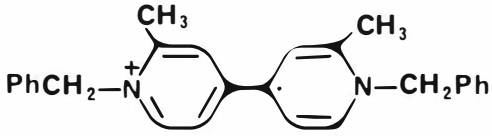
was characteristic of pyridinium dication **78** (Figure 48), but why it was not stable when filtered could not be explained.

I. Reaction of cyanide ion with 1-benzyl-2-methylpyridinium bromide 25

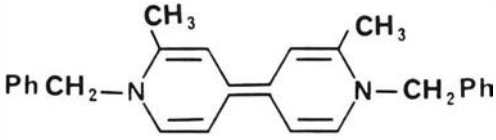
1-Benzyl-2-methylpyridinium bromide was dissolved in water-acetone solution, flushed with oxygen free nitrogen, and frozen with liquid nitrogen. Sodium cyanide was also dissolved in water, flushed with nitrogen, and added to the solution of **25**. The reaction mixture was frozen completely while flushing it with nitrogen. The flask containing the frozen mixture was sealed with a torch. The frozen mixrute was allowed to defrost at room temperature in the sealed flask. The sealed flask with the content was allowed to stand at room temperature for six days. The solution first turned green, then dark-blue, and a dark solid formed. The dark-blue solution showed presence of a radical by electron spin resonance spectroscopy. The dark solid was filtered and oxidized with oxygen in hydrogen bromide ethanol solution. This solid decomposed to a sticky gum when exposed to air. The dark blue solution turned yellow when exposed to the air. This behavior indicated the presence of a cation radical **79**, or a dihydro compound **80** respectively (Figure 49).

The solution was passed through an ion-exchange resin and the solvent was evaporated. A dark sticky solid which formed was washed several times with water. Evaporation of the water solution produced a dark yellow solid which was dissolved in 95% ethanol. Addition of ethyl ether to the 95% ethanol solution precipitated a yellow solid in 30% yield identified as the expected dimer, 1,1'-dibenzyl-2,2'-dimethyl-4,4'-bipyridinium dibromide **81**, (Figure 50). A similar preparation has been reported in the literature [35] but with the 1-methylpyridinium salt as shown in Figure 51. This is the first dimerization of **25** with cyanide ion to give the dimer **81**. This compound decomposed at temperatures above 238°C.

The IR spectrum of **81** showed absorptions characteristic of aromatic C-H stretch near 3060 cm^{-1}, aliphatic C-H stretch near 2980 cm^{-1}, C-C and C-N ring stretching near 1640 cm^{-1} and a C-H ring



79



80

Figure 49. 1,1'-Dibenzyl-2,2'-Dimethyl-4,4'-Bipyridinium Cation Radical 79, and 1,1'-Dibenzyl-1,1'-Dihydro-2,2'-Dimethyl-4,4'-Bipyridine 80.

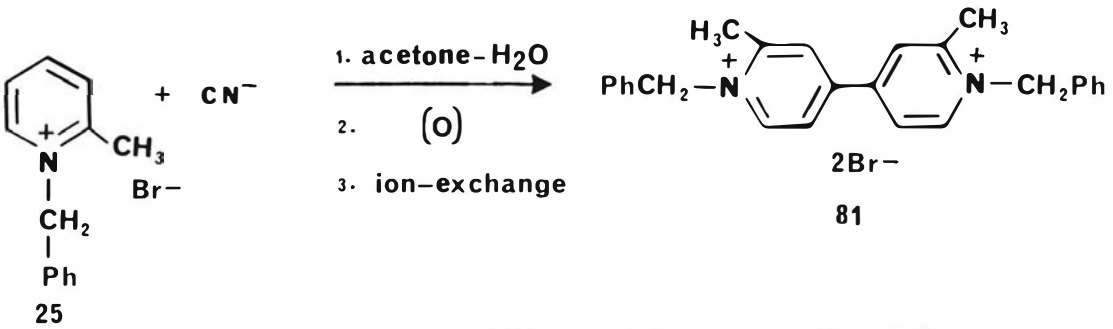


Figure 50. Preparation of 1,1'-Dibenzyl-2,2'-Dimethyl-4,4'-Bipyridimium Dibromide 81.

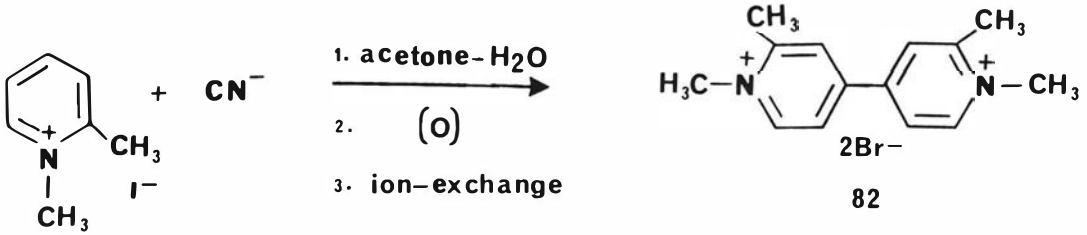


Figure 51. Preparation of 1,1',2,2'-Tetramethyl-4,4'-Bipyridinium Dibromide 82, by Winters et. al.

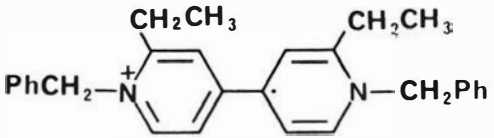
bending near 730 cm^{-1}. The ^{1}H NMR spectrum of **81** showed a doublet at δ 9.0-9.1 (1H, carbon 6, 6'-protons),a singlet at δ 8.5 (2H, carbon 3,3') a doublet at δ 8.4-8.5 (4H, carbon 5, 5' and 3, 3'-protons), a multiplet at δ 7.4-7.5 (5H, Ar and Ar' protons), a singlet at δ 6.0 (4H, 1-CH_2 and 1-CH_2' protons), and a second singlet at δ 3.0 (6H, CH_3, CH_3' protons at C-2 and C-2'). The ^{13}C NMR spectrum of **81** showed resonances at 160.0 ppm (C-2, C-2'), 152.5 ppm (C-6, C-6'), 148.9 ppm (C-4, C-4'), 134..3 ppm (C-3, C-3'), 130.7-132.2 ppm (aromatic C's), 126.9 ppm (C-5, C-5'), 63.9 ppm (C of 1-CH_2 and 1-CH_2'). 22.9 ppm (C of CH_3 and CH_3). Further charcterization by elemental analysis gave satisfactory results. An aqueous solution of **81** was reduced by sodium dithionite to a dark blue solution which indicated presence of a radical cation.

J. Reaction of cyanide ion with 1-benzyl-2-ethylpyridinium bromide 22

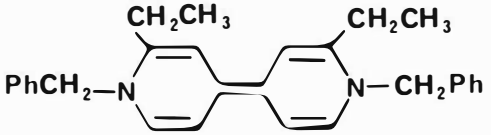
A water-acetone solution of **22** flushed with nitrogen, reacted with solution of potassium cyanide in water at room temperature to give a dark blue solution. The solution was allowed to stand at room temperature for five days in a sealed flask. Electron spin resonance spectroscopic analysis of the blue solution showed the presence of a radical. The dark solid which formed from the blue solution decomposed to a sticky gum when exposed to the air. Also, the blue solution turned yellow when allowed to stand in the air. These properties were indications of the presence of cation radical **83** or the dihydro compound **84** (Figure 52). The dark solid was oxidized with iodine in 95% ehthanol and was passed through an ion-exchange resin and the solvent was evaporated to give a dark solid which did not show the characteristic behavior of the expected dimer.

K. Reaction of cyanide ion with 1-benzyl-2,6-dimethylpyridinium bromide **29**

Compound **29** reacted with sodium cyanide in acetone-water while flushing with nitrogen to give a dark blue solution which showed the presence of a radical **85** by electron spin resonance spectroscopy.

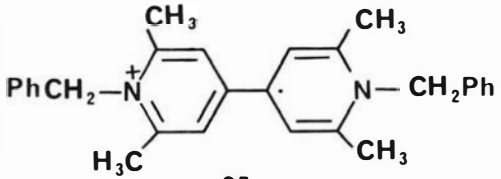


83

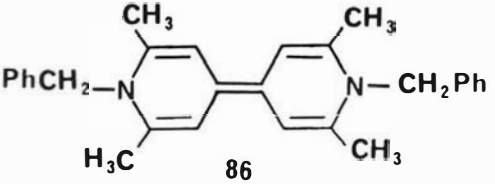


84

Figure 52. 1,1'-Dibenzyl-2,2'-Diethyl-4,4'-Bipyridinium Cation Radical 83, and 1,1'-Dibenzyl-1,1'-Dihydro-2,2'-Diethyl-4,4'-Bipyridine 84.



85



86

Figure 53. 1,1'-Dibenzyl-2,2',6,6'-Tetramethyl-4,4'-Bipyridinium Cation Radical 85, and 1,1'-Dibenzyl-1,1'-Dihydro-2,2',6,6'-Tetramethyl-4,4'-Bipyridine 86.

A dark solid formed from the blue solution. The solid decomposed to a sticky gum when exposed to the air, and the blue solution turned yellow when allowed to stand open in the atmosphere, indicating the presence of **85** or the dihydro compound **86** (Figure 53). The dark solid was oxidized with oxygen in hydrogen bromide- 95% ethanol solution, passed through an ion-exchange resin and the solution was evaporated to give a dark yellow compound. This compound was washed several times with water. Evaporation of the water gave a solid which was recrystallized from 95% ethanol-ethyl ether to give 1,1'-dibenzyl-2,2',6,6'-tetramethyl-4,4'- bipyridinium dibromide **87** in 20% overall yield (Figure 54). Compound **87** decomposed above 245°C. This was the first synthesis of this dimer by the reaction of **29** with cyanide ion. The IR spectrum of **87** showed absorptions characteristic of aromatic C-H stretch near 3233 cm^{-1}, aliphatic C-H stretch near 2793 cm^{-1}, C-C and C-N ring stretching near 1657 cm^{-1}. The ^1H NMR spectrum of **87** in D_2O showed a singlet at δ 8.3 (4H, carbon 5, 5' and 3, 3' protons), a multiplet at δ 7.1-7.5 (10H, Ar, Ar' protons), a singlet at δ 6.0 (4H, 1-CH_2, 1-CH_2' protons), and a second singlet at δ 3.0 (12H, CH_3 protons at 6, 6' and 2, 2' carbons). An aqueous solution of compound **87** also was reduced by sodium dithionite to a dark blue radical cation. Characterization of **87** by elemental analysis gave satisfactory results.

3. Formation of 2,2'-bis(hydroxymethyl)-4,4'-bipyridine **89** by debenzylation of compound 75

Compound 75 was debenzylated with triphenyphosphine in refluxing dimethylformamide (DMF). On cooling, a white solid formed; the solid was identified to be benzyltriphenylphosphonium bromide **88**. The ^1H NMR and IR spectroscopic analysis of this compound showed that it was identical with an authentic sample commercially available.

The remaining DMF solution was evaporated to dryness. An off-white solid obtained was washed four times with ethyl ether to remove any unreacted triphenylphosphine and compound **89**. White solid formed from the ether solution on cooling. Spectroscopic analysis of the solid indicated that it was the expected debenzylation product

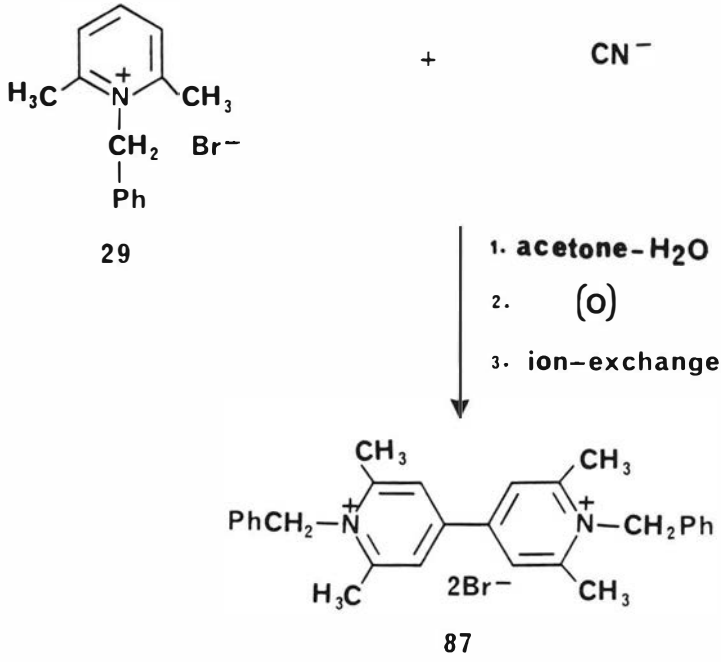


Figure 54. Preparation of 1,1'-Dibenzyl-2,2',6,6'-Tetramethyl-4,4'-Bipyridinium Dibromide 87.

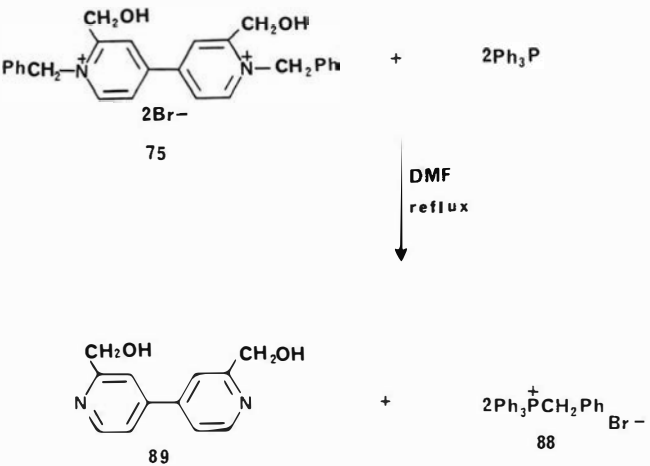


Figure 55. Preparation of 2,2'-Bis(Hydroxymethyl)-4,4'-Bipyridine 89.

2,2'-bis(hydroxymethyl)-4,4'-bipyridine **89** (Figure 55). Compound **89** melted at 149-150°C.

This was the first synthesis of **89** reported to date. The IR spectrum of **89** showed absorptions characteristic of O-H near 3260 cm^{-1}, aromatic C-H stretch near 3060 cm^{-1}, a C-C and C-N ring stretching near 1610 cm^{-1}, and a C-H ring bonding near 810 cm^{-1}. The ^1H NMR spectrum of **89** in $CDCl_3$ showed a broad peak at δ 8.6 (2H, carbon 6, 6'-protons), a singlet at δ 7.9 (2H, carbon 3, 3' protons), a doublet at δ 7.6-7.7 (2H, carbon 5, 5', protons), a broad peak at δ 4.9-5.2 (2H, OH and OH' protons), and a singlet at δ 4.7 (4H, CH_2OH and CH_2OH'). The ^{13}C NMR spectrum of **89** showed resonances at 162.9 ppm (C-2, C-2'), 149.4 ppm (C-6, C-6'), 145.2 ppm (C-4, C-4'), 119.3 ppm (C-5, C-5'), 117.3 ppm (C-3, C-3'), 64.1 ppm (C of CH_2OH and CH_2OH'). Characterization by elemental analysis gave satisfactory results.

4. Formation of 2, 2'-dimethyl-4,4'-bipyridyl dihydrochloride **91**

1,1'-Dibenzyl-2,2'-dimethyl-4,4'-bipyridinium dibromide and triphenylphosphine were heated in refluxing dimethylformamide (DMF). On cooling the solution, white solid appeared, which was identified to be benzyltriphenyl phosphonium bromide **88**. The spectroscopic analysis of **88** was identical with an authentic sample of benzyltriphenyl phosphonium bromide commercially available. The dimethylformamide solution was evaporated to dryness, and the remaining solid was dissolved in 95% ethanol. The ethanol solution contained the unreacted triphenylphosphine, and the expected 2,2'-dimethyl-4,4'-bipyridine **90**. It may be very difficult to separate these two compounds; therefore, it was necessary to acidify the ethanol solution with hydrochloric acid so that the bipyridine would form a dihydrochloride salt and precipitate from the solution. Therefore, the ethanol solution was acidified with dry hydrogen chloride gas. As soon as the ethanol solution became acidic, a white solid formed. The solid gradually dissolved back into the solution, but precipitated again on cooling in an ice bath. The white solid was identified as 2,2'-dimethyl-4,4'-bipyridyl dihydrochloride **91** (Figure

56). Compound **91** has been reported in the literature, but from a different synthetic route. This is the first report on debenzylation of compound **81**. The ^{1}H NMR spectrum of **91** in D_2O showed a doublet at δ 8.8-8.9 (2H, carbon 6, 6'-protons), a singlet at δ 8.4 (2H, carbon 3, 3'-protons), a doublet at δ 8.2-8.3 (2H, carbon 5, 5' protons), and a singlet at δ 2.9 (6H, CH_3, CH_3' protons at 2,2' carbons).

5. Cobalt Thiocyanate Complexes of:

A. 2-(Hydroxymethyl)pyridine **92**

Compound **92** contained nitrogen and oxygen suitable for metal complexing. Cobalt thiocyanate was dissolved in absolute ethanol to form a blue solution. When **92** was added to the blue solution, the solution immediately turned purple and a purple solid appeared. Recrystallization of the solid from methanol furnished pure crystals of 2-(hydroxymethyl)pyridine cobalt thiocyanate complex **93** (Figure 57). This metal complex decomposed before it melted. There has been a report on the polarographic study of complex **92** with cobalt ion [113].

Since cobalt II is paramagnetic, it was not possible to obtain the nuclear magnetic resonance spectrum of this complex. However, the IR spectrum showed absorptions characteristic of O-H near 3258 cm^{-1}, CN near 2096 cm^{-1}, C-S near 810 cm^{-1}, NCS near 460 cm^{-1} and a M-N near 310 cm^{-1}. Characterization by elemental analysis gave satisfactory results.

Thiocyanate ion (SCN^-) is called a pseudohalide ion because it resembles halide ions in its chemical properties. This ion can coordinate to a metal through either of the end atoms, to form either the sulfur linkage (M-SCN), called the thiocyanate linkage, or the nitrogen linkage (M-NCS), called the isothiocyanate linkage, or

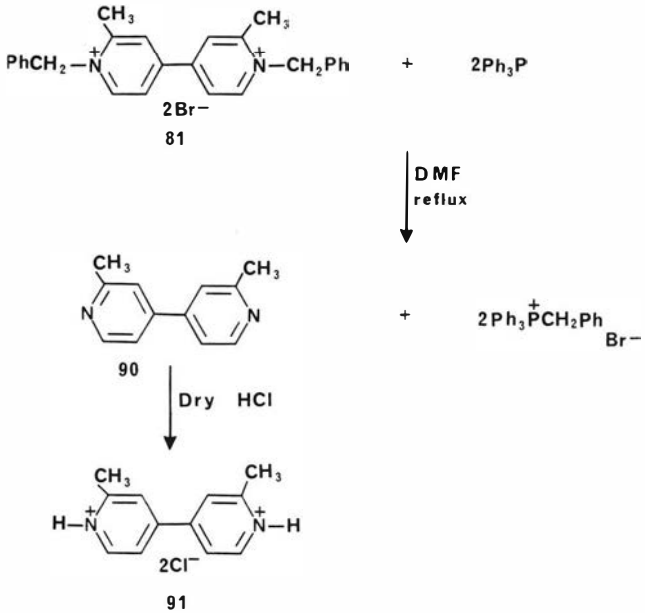


Figure 56. Preparation of 2,2'-Dimethyl-4,4'-Bipyridyl Dihydrochloride 91.

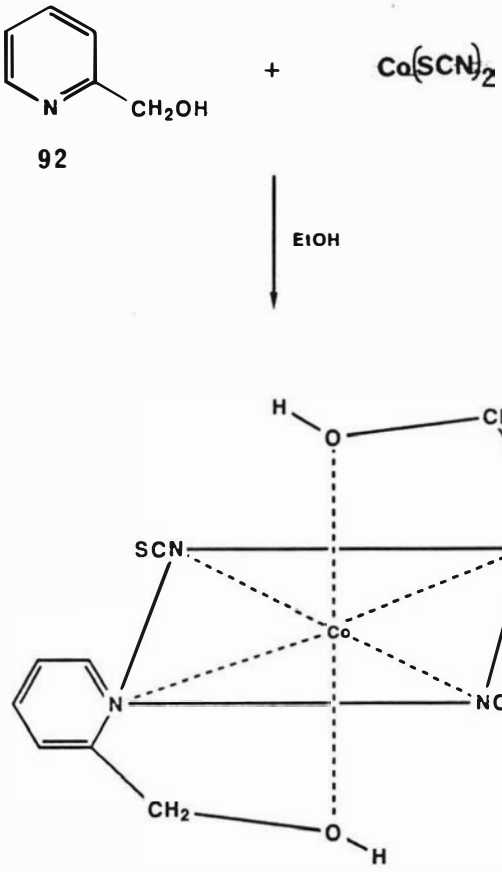


Figure 57. Preparation of 2-(Hydroxymethyl)pyridine Cobalt Thiocyanate Complex 93.

through both the sulfur and the nitrogen linkages (M-NCS-M'). These structures are called linkage isomers.

Cobalt is a class A metal (first transition series). It is known to form metal-nitrogen (M-N) bonded complexes, as opposed to either the metal-sulfur (M-S) bonded complexes or the bridging (M-NCS-M') complexes [74]. Several workers have developed empirical criteria to determine the bonding type of NCS or SCN groups in metal complexes. For the work presented in this dissertation, the IR frequencies for the complexes were assigned by comparing the IR spectrum of the metal-ligand complex with the IR spectrum of the corresponding ligand.

The CN stretching frequencies were known to be broad and lower in N-bonded complexes (near 2050 and 2065 cm^{-1}) than in S-bonded complexes (near 2100 cm^{-1}) [75, 114]. Compound **93** had a broad CN stretching frequency at 2096 cm^{-1}. The C-S frequency was considered to absorb near 860-780 cm^{-1} for N-bonded and near 720-690 cm^{-1} for S-bonded complexes [69,76,77]. Compound **93** had C-S absorption at 810 cm^{-1}. It was suggested [69, 77] that the N-bonded complex exhibited a single sharp (NCS) absorption near 480 cm^{-1}, whereas the S-bonded complex showed several bands of low intensity near 420 cm^{-1},**93** had a sharp single absorption at 460 cm^{-1}. Some workers have also used the absorption of (M-N) and (M-S) in the far-infrared region [69, 78] to distinguish between the absorptions of (M-N) and (M-S). They proposed that (M-N) has higher absorption. A combination of these four criteria would provide reliable structural diagnosis of a particular complex.

Udovenko and Pilipenko used infrared spectoscopic studies made in the 3700-400 cm^{-1} range to conclude that a coordination bond was formed between a transition metal and the nitrogen atom of the 2-(hydroxymethyl)pyridine, and between the metal and the nitrogen atom of the thiocyanate group [115].

Following their argument, the broad intense peak at 3258 cm^{-1} and the intense peak at 1039 cm^{-1} confirmed the presence of an unsubstituted OH group in the complex of **93** with cobalt II [116, 117]. The valence vibration band of the OH group that was near 3500 cm^{-1} was

replaced by a 3258 cm^{-1} peak due to the formation of a coordination bond between the OH group and the cobalt (II) atom, or due to the presence of a hydrogen bond in the complex **93** [117].

The C-C and C-N bond valence vibration frequencies of 2-(hydroxymethyl)pyridine at 1598 and 1572 cm^{-1} were shifted towards higher frequencies in complex **93** to 1600 and 1579 cm^{-1}. With these changes, a conclusion could be made that the 2-(hydroxymethyl)pyridine in complex **93** was coordinated through the nitrogen atom [118-121] respectively.

The appearance of the CN valence vibration frequency of complex **93** at 2096 cm^{-1} indicated an isothiocyanate structure for the thiocyanate group. Also, the strong band at 810 cm^{-1} in the infrared spectrum of complex 93 could be due to the valence vibrations of the thiocyanate group coordinated through the nitrogen atom.

Therefore,base on these informations, the complex of **93** could be coordinated to the cobalt through the nitrogen atom of the 2-(hydroxymethyl)pyridine ring and through the nitrogen atom of the thiocyanate group forming an isothiocyanate linkage as shown in figure 57.

In addition to the importance of the visible region spectral properties of transition metal complexes, their paramagnetism which arose from the presence of unpaired electrons was considered important. If a metal is paramagnetic, it forms complexes that have significant magnetic moment. Cobalt II is paramagnetic, therefore; the complex **93** was found to have magnetic moment of 5.50 Bohr magneton (B.M.). This property in the case of cobalt II should depend on the strength of the metal-ligand bonding [122, 123]. The reflectance spectra of **93** gave absorptions that fitted the Tanabe-Sugano octahedral diagram for $Dq/B = 0.93$. The fitting was best for a distorted octahedral diagram, meaning that the complex **93** was a little distorted. Since a five membered chelate ring was formed, the distortion could be due to its non planarity.

B. 2,2'-Bis(Hydroxymethyl)-4,4'-Bipyridine **89**

Compound **89** was dissolved in absolute ethanol, and added to an ethanol solution of cobalt thiocyanate. A solid formed on mixing the two solutions. The ethanol solution was decanted, and the solid was dissolved in fresh absolute ethanol. The purple solid that formed was recrystallized from methanol to give 2,2'- bis(hydroxymethyl)-4,4'-bipyridine cobalt thiocyanate complex **94** (Figure 58). This complex decomposed before it melted.

This was the first report of this complex in the literature. The IR spectrum of **94** showed absorptions characteristic of O-H near 3350 cm^{-1} CN near 2079 cm^{-1}, a C-S near 813 cm^{-1}, an NCS near 468 cm^{-1}, and a M-N near 310 cm^{-1}. These IR absorptions of **94** correspond to the characteristic absorptions of a metal nitrogen bonded complex as explained in the case of **93**. Again, the broad intense peak at 3350 cm^{-1} and the intense peak at 1035 cm^{-1} confirmed the presence of an unsubstituted OH group in the complex **94**. The valence vibration band of the OH group that was near 3500 cm^{-1} was replaced by a 3164 cm^{-1} peak due to the formation of a coordination bond between the OH group and the cobalt (II) atom or due to the presence of a hydrogen in the complex **94**.

The C-C and C-N bond valence vibration frequencies in 2-(hydroxymethyl)pyridine at 1598 and 1572 cm^{-1} were shifted to higher frequencies in the complex **94**, to 1605 and 1576 cm^{-1} respectively. With these changes, a conclusion could be made that the 2,2'-bis(hydroxymethyl)-4,4'-bipyridine in complex **94** was coordinated through the nitrogen atom.

The appearance of (CN) valence-vibration frequency of complex **94** at 2079 cm^{-1} indicated an isothiocyanate structure for the thiocyanate group. Also, the strong band at 813 cm^{-1} in the infrared spectrum of complex **94** could be due to the valence vibrations of the thiocyanate group coordinated through the nitrogen atom.

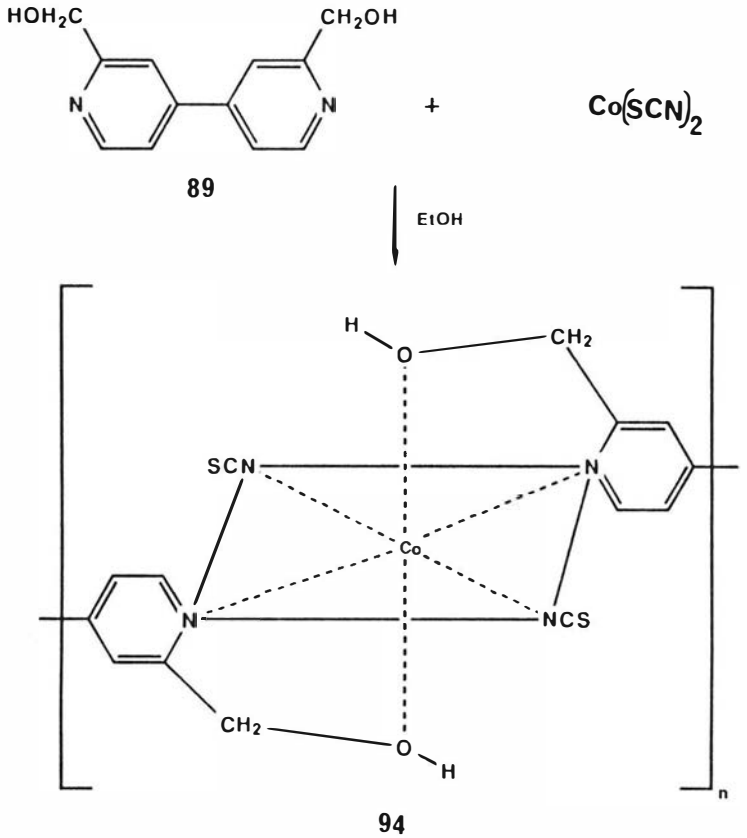


Figure 58. Preparation of 2,2'-Bis(hydroxymethyl)-4,4'-Bipyridine Cobalt Thiocyanate Complex 94.

Therefore, based on these criteria, the complex **94** could be coordinated to the cobalt through the nitrogen atom of the 2,2'-bis(hydroxymethyl)-4,4'-bipyridine ring, and through the nitrogen atom of the thiocyanate group as shown in figure 58. Characterization of **94** by elemental analysis gave satisfactory results. The complex **94** had magnetic moment of 4.66 B.M.. Again, this property depends on the strength of the metal ligand bonding. Like **93** above, the reflectance spectra of **94** gave absorptions that fitted the Tanabe-Sugano octahedral diagram for Dq/B = 0.93. Again, the fit was best for a distorted octahedral diagram. The distortion might be due to the same reason as explained for the case of **93**.

C. 2-(2-Hydroxyethyl)pyridine **95**

Addition of **95** to a blue solution of cobalt thiocyanate in absolute ethanol changed the blue solution to pink, and an orange-pink solid formed. The solid could be recrystallized from hot methanol to give an orange-pink complex of 2-(2-hydroxyethyl) pyridine cobalt thiocyanate **96** (Figure 59). This complex decomposed before it melted. The IR spectrum of **96** showed absorptions characteristic of O-H near 3207 cm^{-1}, CN near 2087 cm^{-1}, a C-S near 850 cm^{-1}, NCS near 417 cm^{-1}, and M-N near 320 cm^{-1}. The absorptions were consistent with the characteristic absorptions of nitrogen-bonded metal complexes.

Again, the peak at 3207 and 1049 cm^{-1} confirmed the presence of an unsubstituted OH group. The vibration band of OH group was shifted from 3520 to 3207 cm^{-1} due to the formation of a coordination bond between the OH group and the cobalt (II) atom or due to the presence of a hydrogen bond in the complex **96**. The C-C and C-N bond valence vibration frequencies in 2-(2-hydroxyethyl)pyridine 95 at 1605 and 1580 cm^{-1} were replaced by band at 1613 and 1585 cm^{-1}. Combining these criteria, the complex **96** could be coordinated to the cobalt through the nitrogen atom of **95**, and through the nitrogen atom of the thiocyanate group, (Figure 59). Elemental analysis of the complex **96** gave satisfactory results.

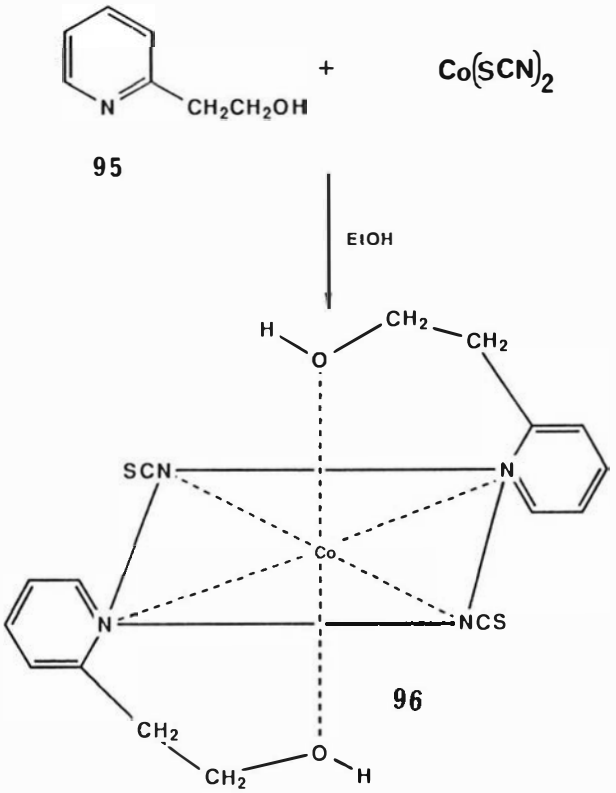


Figure 59. Preparation of 2-(2-hydroxyethyl) Pryridine Cobalt Thiocyanate Complex 96.

Its magnetic moment was found to be 5.05 B.M. The reflectance spectra of **96** gave absorptions that fitted the Tanabe-Sugano octahedral diagram for Dq/B = 0.95. The fit was almost perfect for a perfect octahedral diagram, meaning that the complex **96** was not distorted. Since a six membered chelate ring was formed, there should not be strain in the complex.

SUMMARY

The reactions of substituted pyridines with methyl iodide or benzyl bromide in dry acetone formed their corresponding salts as expected. Reactions of the substituted pyridinium salts with potassium or sodium cyanide in water, acetone, acetone-water, or ethanol solutions formed dark blue or green solutions in most cases. Electron spin resonance spectroscopy showed the presence of a radical in those dark blue or green solutions. A dark solid formed from the solutions; oxidation of the solid with ethanolic iodine acetone solution or acidic ethanol solution resulted in the formation of the corresponding dimers in some cases, and in other cases, other products were isolated.

It was obvious that a substituent [eg, 2-(acylamino) group] on the pyridinium salt did not allow reaction of such salts with cyanide ion. For example, 1-benzyl-2-(acylamino)pyridinium bromide, **17** did not react with cyanide ion as expected but rather hydrogen bromide was eliminated when the slolution was heated to a boil, and 1-benzyl-pyridinium-2-acylimide,66 was formed.

There was one key to the reactions of all the substituted pyridinium salts presented in this dissertation. All the substituted pyridinium salts reacted with cyanide ion to form a cyano adduct of the form shown in Figure 7. The attack of the cyanide ion was at the 4-position of the substituted pyridinium salts, except when the 4-position was blocked.

In the cases where the substituent Z was CH_3, CH_2OH, or CH_2CH_2OH, and at the 2-positions of the pyridinium salts, the adduct **9** dimerized. In the cases where Z was CN and also at the 2-position of the pyridinium salt, the adduct **9** formed complicated products due to the hydrolysis, oxidation, and other reactions of the 2-CN groups in basic solutions [86, 88]. Finally, in the cases where Z was CN and at the 3-position of the pyridinium salts, the adduct **9** was stable enough

to be isolated. The dimer **75** was reduced in aqueous solution at potential (E^{o}) of about -0.34v. This potential could be considered good for this salt to be active as a herbicide.

Since this was the first synthesis of 1,1'-dibenzyl-2,2'-bis(hydroxymethyl)-4,4'-bipyridinium dibromide, it was of interest to determine whether or not it could form a complex with a metal since it had the appropriate nitrogen and oxygen needed for metal complexing. To do this, **75** had to be debenzylated. Debenzylation was accomplished by heating it with triphenylphosphine in refluxing DMF to give 2,2'-bis(hydroxymethyl)-4,4'-bipyridine. 1,1'-Dibenzyl-2,2'-dimethyl-4,4'-bipyridinium dibromide was also debenzylated to give 2,2'-dimethyl-4,4'-bipyridine, which was acidified and the salt 2,2'-dimethyl-4,4'-bipyridyl dihydrochloride **91** was formed. This was the first debenzylation of bipyridinium salts. If this is the first synthesis of the dimer **75**, it is also the first synthesis of 2,2'-bis(hydroxymethyl)-4,4'-bipyridine **89**. Reaction of **89** with cobalt thiocyanate formed 2,2'-bis(hydroxymethyl)-4,4'-bipyridine cobalt thiocyanate complex. Also, reaction of 2-(hydroxymethyl)pyridine and 2-(2-hydroxyethyl)pyridine with cobalt thiocyanate formed the corresponding complexes.

EXPERIMENTAL

Melting points were determined on a Fisher-Johns melting point apparatus and were uncorrected. Infrared (IR) spectra were obtained on a Perkin Elmer 283 spectrophotometer and on a Nicolet 740 FT-IR instrument. Ultraviolet (UV) spectra were measured on a Hewlett Packard 8452 A Diode Array spectrophotometer. Elemental analysis were performed by Atlantic Microlab, Inc., Atlanta Georgia. Proton and carbon 13 nuclear magnetic resonance (^{1}H and ^{13}C NMR) spectra were obtained using deuterochloroform, deuterium oxide and deuterodimethyl sulfoxide as solvents and tetramethylsilane and 3-(trimethylsilyl)-propane sulfonic acid, sodium salt as internal standards. ^{1}H NMR spectra were recorded on a Varian EM360A MHz NMR spectrometer or on a JEOL FX90 90 MHz NMR spectrophotometer located in the Chemistry Department at Virginia Commonwealth University. ^{13}C-NMR spectra were recorded on a JEOL FX90 NMR spectrometer. Electron spin resonance (E.S.R.) spectra were recorded on a Varian E-9 E.S.R spectrometer. Gas Chromotography/Mass Spectra (GC/MS) were recorded on a Hewlett Packard RTE 5890 GC/MS spectrometer located in the Pharmacology Department at Virginia Commonwealth University. Magnetic moment was determined with a Cahn electrobalance TRL Faraday Magnetic susceptibility. Reflectance spectra were recorded on a Varian Cary 2390 UV-VIS NIR spectrophotometer located in the Chemistry Department at Hampton University, Hampton, Virgina. Ion-exchange were performed using a 3 cm x 40 cm column of Amberlite IRA-400, from Polyscience, Inc. Warrington Pa. Reduction potential was determined on a Princeton Applied Research Polarographic Analyzer Model 174 located in the Chemistry Department at Virginia Commonwealth University. Parafilm "M" used was obtained from Greenwhich, Division of American Can Company. Most reagents were purchased from Aldrich and Lancaster Chemical Co. and were used without fur-

ther purification. Acetone was purified by distillation from potassium carbonate and potassium permanganate and stored over potassium carbonate.

B. Preparation of Pyridinium Salts

1. 1-Methyl-2-acetylpyridinium iodide **10** (2-acetylpyridine methiodide)

A solution of 22.00g (0.18 mole) of 2-acetylpyridine and 38.75g (0.27 mole) of methyl iodide dissolved in 180 mL of dry acetone was heated under reflux for 4 days (96 hours). A double condenser was used to prevent excessive evaporation of the methyl iodide. A dark yellow solid started appearing after 24 hours of refluxing. The heating was stopped when the size of the solid remained constant. Filtration and recrystallization of the solid from 95% ethanol-ethyl ether yielded 14.88g (45%) of 1-methyl-2-acetylpyridinium iodide **10**, mp 161-162°C, reported 162-163°C [48]. IR (KBr): 3040, 1710, 1620, 760 cm^{-1}. ^1H NMR (DMSO-d_6): δ 9.18-9.25 (d, 1H, 6-H), 8.61-8.84 (m, 2H, 3-H, 4-H), 8.22-8.40 (m, 1H, 5-H), 4.38 (S, 3H, 1-CH_3 protons), 2.85 (S, 3H, C-CH_3 protons). ^{13}C NMR (DMSO-d_6): ppm 194.4 (C = 0), 148.7 (C-6) 147.8 (C-2), 146.6 (C-4), 129.3 (C-5), 128.1 (C-3), 41.5 (C of 1-CH_3), 30.3 (C of C-CH_3).

2. 1-Methyl-2-bromopyridinium iodide **11** (2-bromopyridine methiodide)

Into a round bottom flask was placed 15.00g (0.09 mole) of 2-bromopyridine, dissolved in 20 mL of dry acetone. 13.48g (0.09 mole) of methyl iodide dissolved in 30 mL of dry acetone was added and the reaction mixture was heated to reflux. After thirty minutes, white solid appeared. After ten hours of heating, refluxing was stopped. The reaction mixture was cooled in an ice bath. The solid was filtered and washed with dry acetone. Recrystallization from 95% ethanol-ethyl ether gave 1-methyl-2-bromopyridinium iodide **11**, as a white solid 18.10g (75%) mp 207-208°C (dec), reported 208-209°C (dec), [92]. IR (KBr): 3069, 1614, 770 cm^{-1}. ^1H NMR (DSMO-d_6): δ 9.4-9.5 (d, 1H, 6-H), 8.4-8.5 (d, 1H, 3-H), 8.3-8.00 (m, 2H, 5-H, 4-H), 4.5 (S, 3H, 1-CH_3 protons).

3. 1-methyl-2-cyanopyridinium iodide **12** (2-cyanopyridine methiodide)

Following the procedure reported by Ellin [86], a solution of 15.10g (0.14 mole) of 2-cyanopyridine, and 20.50g (0.14 mole) of methyl iodide was dissolved in 80 mL of dry acetone. The reaction mixture was heated under reflux for twelve hours. Yellow solid continued forming from the solution throughout the refluxing period. At the end of the reaction, the reaction mixture was cooled, and the solution was filtered and the solid was collected and recrystallized from 95% ethanol-ethyl ether to give 28.50g (80%) of 1-methyl-2-cyanopyridinium iodide, mp 184-185°C, reported 183-184°C [86]. IR (KBr): 3040, 2980, 2220, 1610, 760 cm^{-1}. ^1H NMR (D_2O): δ 9.19-9.25 (d, 1H, 6-H), 8.83-8.92 (m, 1H, 4-H), 8.72-8.75 (m, 1H, 3-H), 8.52-8.66 (m, 1H, 5-H), 4.63 (S, 3H, 1-CH_3 protons). ^{13}C NMR (D_2O): ppm 151.4 (C-6), 148.7 (C-4), 136.3 (C-3), 134.0(C-5), 112.5 (CN), 51.3 (C of 1-CH_3).

4. 1-Methyl-3-cyanopyridinium iodide **13** (3-cyanopyridine methiodide)

Using the same procedure as in the preparation of 1-methyl-2-cyanopyridinium iodide, 20.00g (0.19 mole) of 3-cyanopyridine and 27.00g (0.19 mole) of methyl iodide were dissolved in 150 mL of dry acetone. This mixture was heated at reflux for eight hours. The reaction mixture was filtered and a yellow solid was collected and recrystallized from 95% ethanol- ethyl ether to give 40.20g (85%) of 1-methyl-3-cyanopyridinium iodide **13**, mp 196-197°C, reported 194.5-196.1°C [87] IR (KBr): 3060, 2960, 2240, 1630, 780 cm^{-1}. ^1H NMR (DMSO-d_6): δ 9.8 (S, 1H, 2-H), 9.2-9.3 (d, 1H, 6-H), 9.0-9.1 (d, 1H, 4-H), 8.2-8.4 (m, 1H, 5-H), 4.44 (S, 3H, 1-CH_3 protons). ^{13}C NMR (DMSO-d_6): ppm 149.5 (C-2), 148.9 (C-6), 148.0 (C-4) 127.8 (C-5), 113.6 (C-3), 112.0 (CN), 48.6 (C of 1-CH_3).

5. 1-Methyl-4-cyanopyridinium iodide **14** (4-cyanopyridine methiodide)

Using the same procedure for the preparation of 1-methyl-2-cyanopyridinium iodide, 30.00g (0.28 mole) of 4-cyanopyridine, and 40.90g (0.28 mole) of methyl iodide dissolved in 200 mL of dry acetone was heated at reflux for five hours. The dark yellow solid

precipitated from the acetone solution as soon as the reaction mixture became warm. At the end of the reaction, the flask with content was cooled in an ice bath. The yellow solid collected was recrystallized as above to give 67.30g (95%) of 1-methyl-4-cyanopyridinium iodide **14**, mp 197.5-198.5°C reported 198.5-199.5°C [88]. IR (KBr): 3020, 2240, 1630, 830 cm^{-1} ^1H NMR(DMSO-d_6): δ 9.33-9.39 (d, 2H, 6-H, 2-H), 8.71-8.77 (d, 2H, 5-H, 3-H), 4.48 (S, 3H, 1-CH_3 protons). ^{13}C NMR (DMSO-d_6): ppm 146.7 (C-6, C-2), 130.2 (C-5, C-3) 126.1 (C-4), 114.5 (CN), 49.9 (C of 1-CH_3).

6. 1-Methyl-2,4-dicyanopyridinium iodide **15** (2,4-dicyanopyridine methiodide)

5.00g (0.04 mole) of 2,4-dicyanopyridine, and 22.80g (0.11 mole) of methyl iodide was refluxed for seventy-two hours. A double condenser was used to prevent excessive evaporation of the methyl iodide. The hot reaction mixture was vacuum filtered. The dark red solid obtained was washed with two 5mL portions of anhydrous ethyl ether, to remove the unreacted 2,4-dicyanopyridine. The resulting dark red solid was dried and recrystallized from 95% ethanol-ethyl ether to give 3.30g (65%) of 1-methyl-2,4-dicyanopyridinium iodide **15**, mp 186-187°C, IR (KBr): 3080, 2990, 2240, 2220, 1660, 850 cm^{-1}. ^1H NMR (DMSO-d_6): δ 9.67-9.72 (d, 1H,6-H), 9.49 (S, 1H, 3-H), 9.09 (d, 1H, 5-H), 4.60 (S, 3H, 1-CH3 protons). ^{13}C NMR (DMSO-d_6): ppm 149.2 (C-6), 133.6 (C-3), 128.8 (C-5), 112 (CN at C-4), 109 (CN at C-2), 48.6 (C of 1-CH_3).

Anal. calcd. for $C_8H_6N_3I$; C, 35.53; H, 2.25; N, 15.40. Found: C, 35.44; H, 2.24; N, 15.51.

7. 1-Methyl-2,6-dimethylpyridinium iodide **16** (2,6-dimethylpyridine methiodide)

Into a round bottom flask was placed 15.00g (0.14 mole) of 2,6-dimethylpyridine (2,6-lutidine) (Aldrich), dissolved in 50 mL of dry acetone to which 22.00g (0.15 mole) of methyl iodide was added. As described for the preparation of 1-methyl-2-cyanopyridinium iodide, a double condenser was used to prevent evaporation of the methyl iodide. The flask with contents was heated under reflux for seventy-two hours. White solid precipitated from the reaction mixture three

hours after start of heating. The reaction was assumed to have been completed when precipitation of the white solid stopped. The reaction mixture with the solid was cooled, filtered, and the product was washed with acetone. Recrystallization from 95% ethanol-ethyl ether yielded 23.00g (65%) of 1-methyl-2,6-dimethylpyridinium iodide. IR (KBr): 3020, 1630, 790 cm^{-1}. ^1H NMR (DMSO-d_6): δ 8.27-8.45 (m, 1H, 4-H), 7.87-7.96 (d, 2H, 5-H, 3-H), 4.09 (S, 3H, 1-CH_3 protons), 2.83 (S, 6H, CH_3 at C-6, C-2). ^{13}C NMR (DMSO-d_6): ppm 155.7 (C-6, C-2); 143.7 (C-4) 126.7 (C-5, C-3); 21.4 (C of CH_3 at 6,2).

8. 1-Benzyl-2-(acylamino)pyridinium bromide **17**

The following solutions were prepared:

a. 25.00g (0.14 mole) of benzyl bromide in 50 mL of anhydrous acetone.

b. 20.00g (0.14 mole) of 2-(acylamino) pyridine dissolved in 250 mL of anhydrous acetone.

50 mL of the benzyl bromide solution was placed in a 500 mL round bottom flask which was equipped with a Claisen adapter. To one joint of the adapter was attached a condenser and to the other a pressure equalizing addition funnel. Each of these was stoppered with an anhydrous calcium chloride drying tube. The 250 mL 2-(acylamino) pyridine solution was added dropwise to the benzyl bromide solution while it was heated under reflux. The addition took place for approximately one and one-half hours. After addition of the 2-(acylamino) pyridine, the reaction mixture was refluxed an additional eight hours.

The solution became cloudy as the 2-(acylamino) pyridine was added; after about thirty minutes, the cloudiness disappeared and a white solid began precipitating from the solution. When precipitation of the solid stopped, the heating was stopped. The acetone solution with the white solid was cooled in an ice bath. The solution was filtered, and the solid the washed with cold acetone, and recrystallized from 95% ethanol-ethyl ether to give 27.80g (65%) of 1-benzyl-2-(acylamino)pyridinium bromide **17**, mp 194-195°C. IR (KBr): 3438, 2882, 1713, 1639, 779 cm^{-1}. ^1H NMR (DMSO-d_6): δ 11.37 (broad, 1H,

N-H), 9.09-9.17 (d, 1H, 6-H), 8.50-8.66 (t, 1H, 3-H), 7.98-8.20 (m, 2H, 5-H, 4-H), 7.37 (S, 5H, Ar-H), 6.09 (S, 2H, 1-CH_2 protons), 2.17 (S, 3H, C-CH_3 protons). ^{13}C NMR (DMSO-d_6): ppm 169.1 (C=0), 146.8 (C-2), 146.3 (C-6), 144.8 (C-4), 132.9 (C-3), 127.8-132.9 (aromatic C's), 124.4 (C-5), 123.2 (C-3), 59.0 (C of 1-CH_2), 23.5 (C of CH_3).

Anal. calcd. for $C_{14}H_{15}N_2O$ Br: C, 54.73; H, 4.93; N, 9.12. Found: C, 54.62; H, 4.97; N, 9.11.

9. 1-Benzyl-2-bromopyridinium bromide **18**

Using the same apparatus as described for the preparation of compound **17** above, 18.96g (0.12 mole) of 2-bromopyridine (Lancaster) dissolved in 45mL of anhydrous acetone was added dropwise to solution of 20.52g (0.12 mole) of benzyl bromide dissolved in 150 mL of anhydrous acetone. The addition took 15 minutes and heated under reflux for seventy-two hours. A white solid precipitated from the acetone solution after forty-eight hours. Like above, the flask with content was cooled, the solution was filtered and the solid collected was washed with acetone. Recrystallization from 95% ethanol-ethyl ether yielded a pure white 23.70g (60%) of 1-benzyl-2-bromopyridinium bromide **18**, mp 155-156°C, reported 156-157°C [97]. IR (KBr): 3100, 3000, 1630, 760 cm^{-1}. ^1H NMR (DMSO-d_6): δ 9.5-9.6 (d, 1H, 6-H), 8.7-8.8 (d, 1H, 3-H), 8.2-8.5 (m, 2H, 5-H, 4-H), 7.4 (S, 5H, Ar-H), 6.1 (S, 2H, 1-CH_2 protons.)

10. 1-Benzyl-2-cyanopyridinium bromide **19**

To 35.95g (0.21 mole) of benzyl bromide dissolved in 70 mL of anhydrous acetone was added dropwise 10.93g (0.10 mole) of 2-cyanopyridine dissolved in 100 mL of anhydrous acetone. The light yellow acetone solution turned cloudy as the 2-cyanopyridine solution was added. The addition took approximately thirty-five minutes while refluxing. Six hours from the start of refluxing, a very light yellow solid appeared from the solution. The reaction mixture was allowed to reflux for a total of seventy-eight hours. Filteration of the solution and recrystallization of the light yellow solid collected from 95% ethanol-ethyl ether yielded 14.45g (50%) of 1-benzyl-2-

cyanopyridinium bromide **19**. mp 185-186°C. IR (KBr): 3040, 2960, 1620, 730 cm^{-1}. ^1H NMR (D_2O): δ 9.20-9.28 (d, 1H, 6-H), 8.74-8.77 (m, 2H, 4-H, 3-H), 8.40-8.50 (m, 1H, 5-H), 7.55 (S, 5H, Ar-H), 6.15 (S, 2H, 1-CH_2 protons). ^{13}C NMR (D_2O): ppm 150.9 (C-6), 149.8 (C-4), 137.7 (C-2), 134.9 (C-3), 131.9-133.3 (C-5, aromatic C's), 113.1 (CN), 67.5 (C-1-CH_2).

Anal. cald for $C_{13}H_{11}N_2Br$: C, 56.74; H, 4.04; N, 10.18. Found: C, 56.75; H, 4.07; N, 10.17.

11. 1-Benzyl-3-cyanopyridinium bromide **20**

A solution of 3-cyanopyridine (14.59g, 0.14 mole) in 40 mL of dry acetone was added dropwise for twenty minutes to a 23.97g (0.14 mole) of benzyl bromide in 145 mL of dry acetone. The mixture was heated under reflux over five hours. A solid first formed in thirty minutes from the start of refluxing period. The flask with content was cooled as usual, and the solution was filtered and the solid collected and recrystallized from 95% ethanol-ethyl ether to give 30.82g (80%) of 1-benzyl-3-cyanopyridinium bromide as an off-white solid, mp 150°C, reported 149°C [94]. IR (KBr): 3069, 3034, 2983, 2234, 1622, 813 cm^{-1}. ^1H NMR (DMSO-d_6): δ 10.5 (S, 1H, 2-H) 9.8-9.7 (d, 1H, 6-H), 9.2-9.3 (d, 1H, 4-H) 8.3-8.6 (m, 1H, 5-H), 7.3-7.9 (m, 5H, Ar-H), 6.1 (S, 2H, 1-CH_2 protons). ^{13}C NMR (DMSO-d_6): ppm 148.9 (C-2); 147.9 (C-6); 133.3 (C-4); 128.7-129.2 (aromatic C's) 113.7 (CN); 112.9 (C-3); 63.5 (C of 1-CH_2).

12. 1-Benzyl-4-cyanopyridinium bromide **21**

A solution of 4-cyanopyridine (15.00g, 0.14 mole) in 90 mL of anhydrous acetone was added dropwise over fifteen minutes to a refluxing solution of benzyl bromide (24.00g, 0.14 mole), dissolved in 50 mL of anhydrous acetone. A bright yellow solid formed almost instantly on addition of the 4-cyanopyridine solution to the refluxing benzyl bromide solution. The reaction mixture was heated under reflux for one hour. The flask with content was cooled in an ice bath, the solution was filtered and the solid was collected and washed with acetone. It was recrystallized from 95% ethanol-ethyl ether to give a

bright yellow 1-benzyl-4-cyanopyridinium bromide **21** (37.60g, 95%), mp 207-208°C. IR (KBr): 3020, 2980, 2240, 1650, 720 cm^{-1}. ^1H NMR (DMSO-d_6): δ 9.7-9.8 (d, 2H, 6-H, 2-H), 8.7-8.8 (d, 2H, 5-H, 3-H), 7.1-7.7 (m, 5H, Ar-H), 6.15 (S, 2H, 1-CH_2 protons). ^{13}C NMR (DMSO-d_6): ppm 146.0 (C-6, C-2) 133.5 (C-5, C-3), 127.2-131.2 (C-4 and aromatic C's), 114.6 (CN), 63.6 (C of 1-CH_2).

13. 1-Benzyl-2-ethylpyridinium bromide **22**

To 30.00g (0.28 mole) of 2-ethylpyridine, dissolved in 70 mL of anhydrous acetone, was added dropwise 47.88g (0.28 mole) of benzyl bromide dissolved in 250 mL of anhydrous acetone at reflux using the apparatus described for the preparation of **17.** In approximately one hour, an oil began to collect at the bottom of the flask. When the formation of the oil stopped, the reaction was terminated by cooling the reaction mixture in an ice bath. The colorless oily liquid solidified to a white solid on cooling. The solution was filtered, and the solid washed with anhydrous acetone, and recrystallized from acetonitrile to yield 58.30g (75%) of 1-benzyl-2-ethylpyridinium bromide **22**, mp 108-109°C. IR (KBr): 3034, 2965, 2879, 1622, 727 cm^{-1}. ^1H NMR (DMSO-d_6): δ 9.50-9.6 (d, 1H, 6-H), 8.4-8.5 (t, 1H, 3-H), 8.3-8.2 (m, 2H, 5-H, 4-H), 7.38 (S, 5H, Ar-H), 6.1(S, 2H, 1-CH_2 protons), 3.11-3.25 (q, 2H, CH_2 of ethyl), 1.12-1.26 (t, 3H, CH_3 of ethyl). ^{13}C NMR (DMSO-d_6): ppm 159.6 (C-2), 146.2 (C-6), 145.9 (C-4), 125.7 (C-5, C-3, aromatic C's), 5.97 (C of 1-CH_2) 25.4 (C of CH_2CH_3), 11.9 (C of CH_2CH_3).

14. 1-Benzyl-2-(2-hydroxyethyl)pyridinium bromide **23**

A solution 16.67g (0.13 mole) of 2-(2-hydroxyethyl)pyridine in 40 mL of dry acetone was added dropwise over fifteen minutes to a refluxing solution of 23.14g (0.13 mole) of benzyl bromide in 130 mL of dry acetone. Upon completion of the addition of the pyridine solution, the reaction mixture was refluxed for an additional twelve hours.

The solution became cloudy as the 2-(2-hydroxyethyl)pyridine was being added. After approximately twenty minutes, the cloudiness dis-

appeared, and a second layer formed. The flask with its content was cooled in an ice bath and the acetone solution was decanted.

The gummy oil still in the flask was allowed to stay in the refrigerator for two weeks but it did not crystallize. The viscous oil was poured in a beaker and was stirred continuously. After one hour of constant stirring, the yellow oil turned white and appeared crystalline. This solid was washed three times with acetone, and was dissolved in hot 95% ethanol. Ethyl ether was added to the 95% ethanol solution. The flask with content was cooled in the refrigerator for three days after which a pure white crystalline solid appeared. The solution was filtered and the solid was dried to give 31.80g (80%) of 1-benzyl-2(2-hydroxyethyl)pyridinium bromide **23**, mp 116- 117°C. IR (KBr): 3260, 3000, 2880, 1630, 730 cm^{-1}. ^1H NMR (DMSO-d_6): δ 9.17-9.23 (d, 1H, 6-H), 8.56-8.70 (t, 1H, 3-H), 8.03-8.21 (m, 2H, 5-H, 3-H), 7.23-7.47 (m, 5H, Ar-H), 6.07 (S, 2H, 1-CH_2 protons), 5.61-4.80 (broad, 1H, OH), 3.72-3.85 (t, 2H, CH_2CH_2OH), 3.18-3.31 (t, 2H, CH_2CH_2OH) ^{13}C NMR (DMSO-d_6): ppm 157.1 (C-2), 146.2 (C-6), 145.5 (C-4), 133.7 (C-3), 126.0-129.2 (C-5, aromatic C's), 60-0 (C of 1-CH_2), 58.9 (C of CH_2CH_2OH), 35.1 (C of CH_2CH_2OH).

Anal. calcd. for $C_{14}H_{16}NOBr$, C, 57.15; H, 5.49; N, 4.76. Found: C, 57.12; H, 5.49; N, 4.72.

15. 1-Benzyl-2-(hydroxymethyl)pyridinium bromide **24**

In a 500 mL round bottom flask was placed 16.97g (0.15 mole) of 2-(hydroxymethyl)pyridine. 26.15g (0.15 mole) of benzyl bromide dissolved in 200 mL of dry acetone was added. The flask was equipped with a calcium chloride drying tube and the reaction mixture was heated under reflux.

Fifteen minutes from the start of refluxing, a white solid precipitated from the refluxing acetone solution. After one hour, the reaction was completed, the solution was cooled, filtered and the solid was washed with dry acetone. It was recrystallized twice from 95% ethanol ethyl ether to give 35.00g (80%) of 1-benzyl-2-(hydroxymethyl) pyridinium bromide **24**, mp 159-160°C. IR (KBr): 3260, 3080, 1640, 760 cm^{-1}. ^1H NMR (DMSO-d_6): δ 9.11-9.18 (d, 1H,

6-H), 8.61-8.78 (t, 1H, 3-H), 8.04-8.29 (m, 2H, 5-H, 4-H), 7.23-7.45 (m, 5H, Ar-H), 6.35-6.81 (broad, 1H, OH), 5.92 (S, 2H, 1-CH_2 protons), 4.87 (S, 2H, CH_2OH). ^{13}C NMR (DMSO-d_6): ppm 158.1 (C-2), 146.1 (C-6), 132.9 (C-4), 126.3-129.2 (C-3, C-5, aromatic C's), 59.2 (C of 1-CH_2), 58.8 (C of CH_2OH).

Anal. calcd. for $C_{13}H_{14}NOBr$; C, 55.72; H, 5.05; N, 5.00. Found: C, 55.83; H, 5.05; N, 4.98.

16. 1-Benzyl-2-methylpyridinium bromide **25**

Using the same apparatus described for the preparation of **17**, 16.33g (0.17 mole) of 2-methylpyridine dissolved in 50 mL of anhydrous acetone was added dropwise over forty-five minutes to a refluxing solution of 30.00g (0.17 mole) of benzyl bromide in 130 mL of anhydrous acetone. The reaction mixture was refluxed for a total of eight hours.

The solution became cloudy as 2-methylpyridine solution was added and after approximately forty-five minutes, the cloudiness disappeared and an oil layer formed. The acetone solution was placed in the ice bath. On cooling, the oil crystallized to a white solid. The acetone was decanted and enough acetonitrile to dissolve the solid was added to the flask. The mixture was heated until all the solid dissolved. The reaction mixture was put in the refrigerator overnight. The white solid that formed was collected, washed with acetone, and immediately dried in the oven at 50°C. Spectroscopic analysis of the compound showed it was 1-benzyl-2-methylpyridinium bromide **25** (32.36g, 70%). ^1H NMR ($CDCl_3$): δ 9.57-9.64 (d, 1H, 6-H), 8.40-8.57 (d, 1H, 3-H), 7.90-8.09 (m, 2H, 5-H, 4-H), 7.32 (S, 5H, Ar-H), 6.23 (S, 2H, 1-CH_2 protons), 2.93 (S, 3H, CH_3 protons).

17. 1-Benzyl-3-methylpyridinium bromide **26**

Using the same apparatus as described for the preparation of **17**, 20.00g (0.21 mole) of 3-methylpyridine, dissolved in 50 mL of dry acetone, was added dropwise to a solution of 36.80g (0.21 mole) of benzyl bromide in 150 mL dry acetone.. During addition of 3-methylpyridine solution, an oil formed. The solution was cooled for twenty-

four hours. A white solid crystallized out of the solution. Filteration of the solution and recrystallization of the white solid from acetonitrile-ethyl ether gave 45.40g (80%) of 1-benzyl-3-methylpyridinium bromide **26**, mp 122-123°C. IR (KBr): 3100, 1635, 720 cm^{-1}. ^1H NMR (DMSO-d_6): δ 9.5 (S, 1H, 2-H), 9.3-9.4 (d, 1H, 6-H), 8.5-8.6 (d, 1H, 4-H), 8.30-8.00 (m, 1H, 5-H), 7.3-7.9 (S,5H, Ar-H), 6.00 (S, 2H, 1-CH_2 protons, 2.5 (S, 3H, CH_3 protons).

18. 1-Benzyl-4-methylpyridinium bromide **27**

A solution of 15.00g (0.16 mole) of 4-methylpyridine, in 50 mL of anhydrous acetone, was added dropwise to a solution of 27.50g (0.16 mole) of benzyl bromide in 100 mL of anhydrous acetone which was heating under reflux as described in the preparation of **17**. A white solid formed instantly on addition of the acetone solution. After the reaction mixture was allowed to reflux for an additional hour, the flask with content was cooled and the solution was filtered, the solid was washed with acetone, and recrystallized from 95% ethanol-ethyl ether to give 38.30g (90%) of 1-benzyl-4-methylpyridinium bromide, mp 161-162°C, reported: 159-161°C [96]. ^1H NMR (DMSO-d_6): δ 9.25-9.33 (d, 2H, 6-H, 2-H), 8.04-8.11 (d, 2H, 5-H, 3-H), 7.40-7.66 (m, 5H, Ar-H), 5.99 (S, 2H, 1-CH_2 protons), 2.63 (S, 3H, CH_3 protons).

19. 1-Benzyl-2,4-dimethylpyridinium bromide **28**

To 15.91g (0.09 mole) of a refluxing benzyl bromide in 35 mL of dry acetone was added dropwise 10.00g (0.09 mole) of 2,4-dimethylpyridine. Ten minutes after the complete addition of the 2,4-dimethylpyridine, a white solid precipitated from the acetone solution. The reaction mixture was allowed to reflux for ten hours. At the end of the reaction, the flask with content was cooled in the refrigerator. The white solid was collected and recrystallized from 95% ethanol-ethyl ether to yield 19.40g (75%) of 1-benzyl-2,4-dimethylpyridinium bromide **28**, mp 168-170°C. IR (KBr): 3060, 1600, 800 cm^{-1}. ^1H NMR (DMSO-d_6): δ 9.19-9.25 (d, 1H, 6-H), 8.07 (S, 1H, 3-H), 7.94-8.02 (m, 1H, 5-H), 7.31-7.45 (m, 5H, Ar-H), 6.03 (S, 2H, 1-CH_2 protons), 2.76 (S, 3H, CH_3 protons at C-2), 2.60 (S, 3H, CH_3 protons at C-4). ^{13}C

NMR (DMSO-d_6): ppm 158.8 (C-2), 154.0 (C-6), 144.9 (C-4), 133.2 (C-3), 126.3-130.4 (C-5 and aromatic C's), 59.2 (C of 1-CH_2), 21.1 (C of CH_3 at C-2), 19.8 (C of CH_3 at C-4).

20. 1-Benzyl-2,6-dimethylpyridinium bromide **29**

Using the apparatus for the preparation of **17**, 38.60g (0.36 mole) of 2,6-dimethylpyridine, dissolved in 70 mL of anhydrous acetone, was added dropwise to 61.10g (0.36 mole) of benzyl bromide dissolved in 150 mL of anhydrous acetone. The addition took approximately fifty minutes. The reaction mixture was refluxed for one week. White solid began to precipitate after twenty-four hours of refluxing, and continued during the reaction period. Collection and recrystallization of the white solid from acetonitrile afforded 45.00g (45%) of 1-benzyl-2,6-dimethylpyridinium bromide as a hygroscopic salt. This compound was stored in a desicator. mp 186-187°C, reported 185-187°C [95], ^{1}H NMR (DMSO-d_6): δ 8.46-8.64 (m, 1H, 4-H), 8.05-8.14 (d, 2H, 5-H, 3-H),7.38-7.46 (m, 5H, Ar-H), 6.01 (S, 2H, 1-CH_2 protons), 2.82 (S, 6H, CH_3 protons at C-6, C-2). ^{13}C NMR (DMSO-d_6): ppm 156.1 (C-6, C-2), 145.1 (C-4), 132.3 (C-3), 125.5 (C-5, aromatics C's), 55.5 (C of 1-CH_2), 21 (C of CH_3 at C-6 and C-2).

C. Preparation of 2-(acylamino)pyridine **17a**

To 2-Aminopyridine (4.00g, 0.04 mole) in a 100 mL Erlenmeyer flask was added 4.39g (0.04 mole) of acetic anhydride with stirring. The resulting light yellow solution was warmed gently on a hot plate. On cooling in an ice bath, a white solid formed. The solid was collected and recrystallized from a minimum amount of benzene-petroleum ether, to give 5.00g (85%) of 2-(acylamino)pyridine **17a**, mp 71-72°C reported 71°C [98]. IR (KBr): 3284, 2974, 1682, 761 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 9.65 (s, 1H, N-H), 8.21-8.24 (m, 2H, 6-H, 3-H), 7.62-7.81 (m, 1H, 4-H), 7.04-7.11 (m, 1H, 5-H), 2.21 (S, 3H, CH_3 protons). ^{13}C NMR ($CDCl_3$): ppm 169.1 (C=0), 152 (C-2), 147.8 (C-6), 137.8 (C-4), 119.1 (C-5), 113.5(C-3), 23.8 (C of CH_3).

D. Reactions of cyanide ion with substituted pyridinium salts

1. Reaction of cyanide ion with 1-methyl-2-cyanopyridinium iodide **12**

1-Methyl-2-cyanopyridinium iodide (4.00g, 0.01 mole) prepared above was dissolved in 30 mL of water. While flushing the water solution with oxygen free nitrogen, 2.00g (0.04 mole) of potassium cyanide dissolved in 10 mL of water was added. The reaction mixture still being flushed with nitrogen immediately turned dark brown and a dark solid precipitated. The flask with content was allowed to stand at room temperature for three more hours. At the end of the reaction, the dark solution was filtered and the solid weighed (3.00g). It was dissolved in 30 mL of ethanolic iodine-acetone solution. 2.00g of iodine was used. The 95% ethanol-acetone solution was allowed to stand at room temperature for 24 hours, after which it was passed through a column of ion-exchange resin. Evaporation of the resulting solution left a dark brown solid (2.00g) which partially dissolved in water. The water solution was washed four times with methylene chloride. Evaporation of the methylene chloride gave 0.45g (20%) of a yellow solid of 1-methyl-2-oxo-1,2-dihydro-4-pyridine carbonitrile **62**. It was recrystallized from aqueous 95% ethanol, mp 147-149°C. IR (KBr): 3060, 3020, 2240, 165-1770, 780 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.42-7.50 (d, 1H, 6-H), 6.90 (S, 1H, 3-H), 6.34 (d, 1H, 5-H), 3.58 (S, 3H, 1-CH_3 protons). ^{13}C NMR ($CDCl_3$): ppm 160.9 (C=0), 140.3 (C-6), 126.2 (C-4), 123.8 (C-3), 115 (CN), 105 (C-5), 38.0 (C of 1-CH_3). Mass Spectra (MS), (calculated values in parentheses): m/z 134, $C_7H_6N_2O$ (134); 106, $C_6H_6N_2$ (106); 80, C_5H_6N (80); 64, C_4H_3N (65); 52, C_3H_2N (52).

Anal. calcd. for $C_7H_6N_2O$: C, 62.71; H, 4.57; N, 2.82; Found: C, 62.67; H, 4.52; N, 2.89.

2. Reaction of cyanide ion with 1-methyl-3-cyanopyridinium iodide **13**

8.00g (0.03 mole) of 1-methyl-3-cyanopyridinium iodide was dissolved in 30 mL of water and 10 mL of acetone. To this was added 4.00g (0.08 mole) of sodium cyanide dissolved in 10 mL of water. The reaction mixture turned dark yellow ten minutes after addition of the salt solution. In approximately twenty minutes, a solid began to ap-

pear. The flask with content was allowed to stand at room temperature for twenty-four hours. Recrystallized from chloroform gave a pure yellow solid 4.31g (90%) of 1-methyl-3,4-dicyano-1,4-dihydropyridine **63**. IR (KBr): 2960, 2220, 2180, 1680, 1600, 720 cm^{-1}. ^1H NMR ($CDCl_3$): δ 6.70 (S, 1H, 2-H), 5.89-6.0 (d, 1H, 6-H), 4.8-4.9 (m, 1H, 5-H), 4.4-4.5 (d, 1H, 4-H), 3.1 (S, 3H, 1-CH_3 protons).

Anal. cacld. for $C_8H_7N_3$: C, 66.18; H, 4.87; N, 28.95. Found: C, 66.24; H, 4.89; N, 28.86.

3. Reaction of cyanide ion with 1-methyl-4-cyanopyridinium iodide **14**

A solution of 10.00g (0.04 mole) of 1-methyl-4-cyanopyridinium iodide in 40 mL of water was flushed with oxygen-free nitrogen. 4.50g (0.09 mole) of sodium cyanide dissolved in 10 mL of water (also flushed with nitrogen) was added. The reaction mixture was flushed with nitrogen throughout the addition. As the cyanide solution was added, the reaction mixture turned dark brown. A dark solid precipitated from the dark brown solution approximately ten minutes after completion of the cyanide addition. The solution was filtered, and a dark solid collected was washed with water and dried. Efforts to analyze the dark solid failed. Oxidation and ion-exchange of the dark solid also failed to give any analyzable product. The only information about the dark solid was that it gave two peaks with infrared spectra, at 2240 and 2220 cm^{-1}.

4a. Reaction of cyanide ion with 1-benzyl-2-(acylamino)pyridinium bromide **17**

8.00g (0.02 mole) of 1-benzyl-2-(acylamino)pyridinium bromide was placed in a long necked pyrex 100 mL round bottom flask. 10 mL of water and 30 mL of acetone was added to dissolve the salt. The colorless solution was flushed with nitrogen for twenty-five minutes. The solution was frozen with liquid nitrogen and was flushed for five more minutes. 4.00g (0.08 mole) of sodium cyanide dissolved in 10 mL of water was flushed with nitrogen for fifteen minutes and was poured into the frozen liquid. The reaction mixture was further flushed with nitrogen for ten minutes until the solution was completely frozen. The flask was sealed with a torch under vacuum.

As the frozen solution was defrosting , no color change was observed. The flask with content was allowed to stand at room temperature for three days. The flask was opened; still no observable change occurred to the reaction mixture. Therefore, it was divided into two halves; one half was evaporated to dryness and was found to contain one hundred percent of the starting materials (pyridinium salt **17** and sodium cyanide). The other half was heated to a boil on a hot plate. As the solution boiled, oil formed at the bottom of the flask. This oil was dissolved in methylene chloride and was washed several times with water. The methylene chloride solution was dried with magnesium sulfate filtered and was evaporated with a rotary evaporator. The oil which remained in the flask solidified on standing at room temperature. It was found to be 1-benzylpyridinium-2-acylimide **66** mp 62-63°C. IR (Neat): 3063, 1636, 750 cm^{-1}. ^1H NMR (DMSO-d_6): δ 7.9-8.2 (m, 2H, 6-H, 3-H), 7.2-7.77 (m, 6H, 4-H, Ar-H), 6.5-6.9 (m, 1H, 5-H), 5.5 (S, 2H, 1-CH_2 protons), 2.3 (S, 3H, CH_3 protons), ^{13}C NMR (DMSO-d_6): ppm 178.5 (C=0), 157.0 (C-2), 139.3 (C-6), 136.5 (C-4), 127.5-128.3 (aromataic C's), 119.5 (C-5), 110.3 (C-3). Gas Chromotography/Mass Spectra (GS/MS), (calculated values in parenthesis): m/z 226, $C_{14}H_{14}N_2O$ (226); 211, $C_{13}H_{11}N_2O$ (211); 183, $C_{12}H_{11}N_2$ (183); 91, C_7H_7 (91).

4b. Reaction of 1-benzylpyridinium-2-acylimide **66** with hydrogen bromide

To confirm the formation of compound **66** above, 2.00g (0.01 mole) of **66** was dissolved in 10 mL of water. The water solution was made acidic to litmus paper with aqueous hydrogen bromide. Compound **66** was not very soluble in water, but dissolved immediately when the water solution became acidic. Evaporation of the water gave a white solid in the flask. The solid was recrystallized from 95% ethanol ethyl ether to give the salt, 1-benzyl-2-(acylamino)pyridinium bromide, **17**, 2.36g (90%). Melting point, infrared, and NMR spectroscopic analysis of this compound were identical with those of compound **17**, prepared by the reaction of **17a** with benzyl bromide.

5. Reaction of cyanide ion with 1-benzyl-2-cyanopyridinium bromide **19**

15.00g (0.05 mole) of 1-benzyl-2-cyanopyridinium bromide dissolved in 30 mL of water was placed in a flask and frozen while flushing with nitrogen as described for the reaction of cyanide ion with compound **17**. 17. 50g (0.10 mole) of sodium cyanide dissolved in 7 mL of water was added. The colorless solution was frozen with liquid nitrogen while flushing it with oxygen free nitrogen. The flask was corked and sealed with parafilm "M" . The frozen solution was allowed to defrost at room temperature. On defrosting, the solution became brown. The flask with content was allowed to stand at room temperature for twenty-four hours. When the flask was opened, only a dark brown solution was found, no solid formed. The dark brown solution was not further analyzed.

6. Reaction of cyanide ion with 1-benzyl-3-cyanopyridinium bromide **20**

Following the method described for reaction of cyanide ion with compound **17**, 10.00g (0.03 mole) of 1-benzyl-3-cyanopyridinium bromide in 5 mL of acetone and 30 mL of water was placed in a flask. 4.00g (0.08 mole) of sodium cyanide dissolved in 5 mL of water was added. The flask with the colorless solution was corked, wrapped with parafilm "M" and allowed to stand at room temperature for ten minutes, when an oil layer formed. The flask was opened and the water-acetone solution was decanted. The oil was dissolved in methylene chloride and dried with potassium carbonate, and methylene chloride was evaporated. The remaining oil weighed (6.96g, 85%). Spectroscopic analysis of the oil showed 1-benzyl-3,4-dicyano-1,4-dihydropyridine **69**. IR (Neat): 3060, 2940, 2240, 2200, 1690, 1600 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 7.43-7.49 (S, 1H, 2-H), 7.35 (S, 5H, Ar-H), 6.29-6.37 (d, 1H, 6-H), 4.73-4.78 (m, 1H, 5-H), 4.65-4.70 (d, 1H, 4-H), 4.50 (S, 2H, 1-CH_2 protons). ^{13}C NMR (DMSO-d_6): ppm 145.2 (C-6), 136.9 (C-4), 130.9 (C-2), 127.4-128.7 (C-5 and aromatic C's), 119.2 (CN at C-4), 96.0 (C-3), 72.8 (CN, at C-3), 56.3 (C of 1-CH_2).

7. Reaction of cyanide ion with 1-benzyl-2-ethylpyridinium bromide 22

A 250 mL long neck flask containing 10.00g (0.03 mole) of 1-benzyl-2-ethylpyridinium bromide dissolved in 30 mL of water and 15 mL of acetone was flushed with nitrogen for thirty minutes and frozen with liquid nitrogen. To the frozen solution, was added 4.00g (0.06 mole) of potassium cyanide dissolved in 5 mL of water which had been flushed with nitrogen. The flask with the frozen solution was stoppered with a cork, wrapped with parafilm "M", and was permitted to stand at room temperature for three days. On defrosting the colorless solution turned blue.

The third day, the flask was opened and the dark solid that had formed was filtered, washed quickly with water and was placed in a 95% ethanol-acetone-iodine solution which had been flushed with nitrogen. The flask with the iodine solution was allowed to stand at room temperature for twenty-four hours. It was passed through an ion-exchange resin as described above. The resulting solution was evaporated, and a dark solid was left in the flask. All trials to isolate the expected, 1,1'-dibenzyl-2,2'-diethyl-4,4'-bipyridinium dibromide failed. In some trials, the 95% ethanol-water solution of the dark solid turned blue in the presence of sodium dithionite. Also, a radical was found to be present in the water-acetone solution of the reaction of 1-benzyl-2-ethylpyridinium bromide with cyanide ion by electron spin resonance spectroscopy.

8. Reaction of cyanide ion with 1-benzyl-2-(hydroxymethyl)pyridinium bromide 24

In a long-necked pyrex flask was placed 12.00g (0.04 mole) of 1-benzyl-2-(hydroxymethyl) pyridinium bromide dissolved in 40 mL of water and 15 mL of acetone. The colorless resulting solution was flushed with oxygen free nitrogen for thirty minutes and was frozen with liquid nitrogen. The frozen solution was flushed for ten more minutes and 5.00g (0.07 mole) of potassium cyanide ion dissolved in 10 mL of water was flushed with nitrogen and added slowly. The reaction mixture was frozen completely while flushing with nitrogen. The flask with the frozen solution was stoppered with a cork, wrapped with parafilm "M" and allowed to stand at room temperature for 48 hours.

The dark solid that formed was filtered, washed with water, and immediately placed in a solution of 5.00g (0.03 mole) of iodine in 50 mL of 95% ethanol and 50 mL of acetone which had been flushed by bubbling nitrogen through it. The Buchner funnel was washed with acetone to assure the removal of all the solid. The flask containing the iodine solution was stoppered with a cork, wrapped with parafilm and allowed to stand at room temperature for 48 hours.

The iodine solution was passed through a column of ion exchange resin, which had previously been saturated with bromide ion. To ensure complete exchange of anions (bromide for cyanide, chloride, etc.), the solution was passed through the ion-exchange column twice. To dissolve all the dark solid, the 95% ethanol-acetone solution was warmed gently on a hot plate.

The ion-exchanged solution was rotary evaporated to dryness. The dark yellow solid obtained after evaporation of the solvents was washed several times with distilled water. The water solution was decolorized with charcoal and evaporated leaving a yellow solid that was dissolved in a minimum amount of absolute ethanol. Addition of anhydrous ethyl ether precipitated a yellow solid that was recrystallized from 95% ethanol-ethyl acetate to give 14.41g (60%) of 1,1'-dibenzyl-2,2'-bis (hydroxymethyl)-4,4'-bipyridinium dibromide **75**, mp 190°C (Dec). It should be noted that potassium bromide was also isolated from the ion-exchanged solution. IR (KBr): 3360, 3100, 1640, 730 cm^{-1}. ^1H NMR (DMSO-d_6): δ 9.44-9.49 (broad, 2H, 6, 6'-H's), 8.78-8.95 (broad, 4H, 5, 5'-Hs, 3, 3'-Hs), 7.44 (S, 12H, Ar, Ar'-Hs, OH, OH'), 6.07 (S, 4H, 1-CH_2, 1-CH_2' protons), 5.00 (S, 4H, CH_2OH, CH_2OH' protons). Anal. calcd: for $C_{26}H_{26}N_2O_2Br_2$: C, 55.92; H, 4.70; N, 5.02. Found: C, 56.03; H, 4.72; N, 5.02. Electron spin resonance (ESR) spectroscopic analysis of the ethanol-acetone solution of the reaction of 1-benzyl-2-(hydroxymethyl) pyridinium bromide with cyanide ion showed the presence of a radical.

9. Reaction of cyanide ion with 2-(2-hydroxyethyl)pyridinium bromide 23

Into a 250 mL long neck flask was placed 12.00g (0.04 mole) of 1-benzyl-2-(2-hydroxyethyl)pyridinium bromide, 45 mL of water, and 25 mL of acetone. The flask was flushed with oxygen-free nitrogen for thirty minutes and was frozen with liquid nitrogen, 5.00g (0.07 mole) of potassium cyanide was dissolved in 7 mL of water and was added to the frozen salt solution. The nitrogen was permitted to blow on the frozen solution for fifteen more minutes. The flask was then stoppered with a cork, wrapped several times with parafilm "M" and allowed to stand at room temperature for three days. On defrosting, the colorless solution turned green and became darker green at the end of the reaction. The dark solid formed was suction filtered, washed with water, and immediately placed in a solution of 5.00g (0.03 mole) of iodine in 50 mL of 95% ethanol and 50 mL of acetone while flushing nitrogen through it. The Buchner funnel was washed with 95% ethanol to assure the removal of all the solid. The iodine solution was warmed on a hot plate, however; it was very difficult to completely dissolve all the dark solid.

The flask with the reaction mixture was stoppered with a cork, wrapped with parafilm "M", and allowed to stand at room temperature for twenty-four hours. The iodine solution was then passed through a column of ion-exchange resin as described for the reaction of cyanide ion with 1-benzyl-2-(hydroxymethyl) pyridinium bromide.

Evaporation of the solution gave a dark yellow solid that was washed four times with water. The water solution was evaporated and the yellow solid that remained in the flask was not stable when filtered. Efforts to isolate the expected,1,1'-dibenzyl-2,2'-bis(2-hydroxyethyl)-4,4'-bipyridinium dibromide failed. It should be noted that the solution of this yellow solid in 95% ethanol-water turns blue in the presence of sodium dithionite. Also, electron spin resonance (ESR) spectroscopy showed the presence of a radical in the 95% ethanol-acetone solution of 1-benzyl-2-(2-hydroxyethyl)pyridinium bromide with cyanide ion.

10. Reaction of cyanide ion with 1-benzyl-2-methylpyridinium bromide **25**

10.00g (0.03 mole) of 1-benzyl-2-methylpyridinium bromide **25**, 20 mL of acetone and 35 mL of water was placed into a long necked flask. The flask with content was flushed with nitrogen and frozen as described above. A solution of 4.00g (0.08 mole) of sodium cyanide was dissolved in 10 mL of water, flushed with nitrogen, and added to the frozen salt solution. The flask was sealed with a torch under vacuum while in the liquid nitrogen. The sealed flask with the contents was allowed to defrost at room temperature. The solution was colorless at first, turned blue-green after twenty-five minutes and turned completely dark blue after four hours. The flask with the dark blue solution was allowed to sit at room temperature for one week. A dark solid appeared after twenty-four hours. At the end of the reaction, the flask was opened and the dark solid was filtered and quickly dissolved in acidic ethanol solution (95% ethanol made acidic with HCl). The acidic ethanol was heated to completely dissolve all the solid. Oxygen gas was then flushed through the solution for four hours. The solution was allowed to stand in air at room temperature for twenty-four hours.

The solution was then passed through a column of ion exchange resin as described for the reaction of cyanide ion with 1-benzyl-2-(hydroxymethyl) pyridinium bromide. Again to ensure complete exchange of ions, the solution was passed through the column more than one time. Evaporation of the ion-exchanged solution gave a dark yellow sticky product that was washed several times with water. Decolorization and evaporation of the water gave a yellow solid that dissolved in absolute ethanol to give a white solid identified as sodium bromide, or sodium chloride. The addition of an anhydrous ethyl ether to the yellow ethanol solution precipitated a yellow solid when cooled in the refrigerator for three days. Recrystallization of the yellow solid with 95% ethanol-ethyl ether gave 6.00g (30%) of 1,1'-dibenzyl-2,2'-dimethyl-4,4'-bipyridinium dibromide **81**, mp 238°C (Dec). IR (KBr): 3060, 2980, 1640, 730 cm^{-1}. ^1H NMR (D_2O): δ 9.01-9.08 (d, 1H, 6, 6'-Hs), 8.36-8.48 (m, 4H, 5, 5'-Hs, 3, 3'-Hs), 7.42-7.49 (m, 5H, Ar, Ar'-Hs), 5.95 (S, 4H, 1-CH_2, 1-CH_2' protons),

2.96 (S, 6H, CH_3, CH_3' at C-2, C-2'). ^{13}C NMR (D_2O): ppm 160.0 (C-2, C-2'), 152.5 (C-6, C-6'), 148.9 (C-4, C-4'), 134.3 (C-3, C-3'), 130.7-132.2 (aromatic Cs), 126.9 (C-5, C-5'), 56.99 (C of CH_3, CH_3'). Electron spin resonance (ESR) spectoscopic investigation of the 95% ethanol-acetone solution of 1-benzyl-2-methylpyridinium bromide with cyanide ion showed the presence of a radical.

Anal. calcd. for $C_{26}H_{26}N_2Br_2$: C, 59.33; H, 4.99; N, 5.32. Found: C, 59.13; H, 5.06; N, 5.26.

11. Reaction of cyanide ion with 1-benzyl-4-methylpyridinium bromide **27**

A solution of 5.00g (0.02 mole) of 1-benzyl-4-methylpyridinium bromide , **27** in 15 mL of water and 5 mL of acetone was flushed with nitrogen and frozen as described above. A solution of 2.00g (0.04 mole) of sodium cyanide dissolved in 5 mL of water was also flushed with nitrogen and added to the frozen salt solution. As described for the reaction of compound **24** with cyanide ion, the flask with the reaction mixture was sealed with a torch and allowed to defrost at room temperature. On defrosting, the solution turned green and remained green for seventy-two hours. After this time, the flask was opened and no solid formed. It was observed that the presence of oxygen did not affect the color of this solution. Also, the green color disappeared when the solution was left open for the acetone to evaporate. Further investigation of this green solution showed that the solution turned green only when acetone was present. In the absence of acetone, the colorless solution remained colorless, and the starting materials were recovered in almost one hundred precent. Electron spin resonance (ESR) spectroscopic investigation of the green solution confirmed the absence of a radical. The green color could be caused by condensation of compound **27** with acetone.

12. Reaction of cyanide ion with 1-benzyl-2,6-dimethylpyridinium bromide **29**

Following the procedure used for the reaction of cyanide ion with 1-benzyl-2-(acylamino)pyridinium bromide, 20.00g (0.01 mole) of 1-benzyl-2,6-dimethylpyridinium bromide was dissolved in 25 mL of acetone and 40 mL of water. A solution of 6.00g (0.12 mole) of

sodium cyanide dissolved in 10 mL of water was added. A dark solid appeared after three days, but the reaction was allowed to stand for seven days. The flask was opened and the solid was quickly suction filtered, oxidized with acidic ethanol solution as described for the reaction of cyanide ion with compound **25.** Oxygen was bubbled through the solution for four hours, and the solution was left open in the air at room temperature for two days.

The 95% ethanol solution was ion-exchanged as described earlier. Evaporation of the water gave 8.00g (20%) of 1,1'-dibenzyl-2,2',6,6'-tetramethyl-4,4'-bipyridinium dibromide **87** as a yellow solid. It was recrystallized from 95% ethanol ethyl ether, mp 245°C (dec). IR (KBr): 3233, 2793, 1687 cm^{-1}. ^1H NMR (D_2O): δ 8.34 (S, 4H, 5, 5'-Hs, 3, 3'-Hs), 7.11-7.48 (m, 10H, Ar, Ar'-Hs), 5.98 (S, 4H, 1-CH_2, 1-CH_2' protons), 2.91 (S, 12H, CH_3, CH_3' at C-6, 6', C-2, 2'). It should be noted that electron spin resonance (ESR) spectroscopic investigation of the ethanol-acetone solution of the reaction of 1-benzyl-2,6-dimethylpyridinium bromide with cyanide ion showed the presence of a radical.

Anal. calcd. for $C_{28}H_{30}N_2Br_2$: C, 60.66; H, 5.46; N, 5.05. Found: C, 60.55; H, 5.59; N, 4.94.

E. Debenzylation of the Dimers **75** and **81**

1. Formation of 2,2'-bis(hydroxymethyl)-4,4'-bipyridine **89**

2.00g (0.16 mole) of compound **75** was put in a flask; 1.89g (0.01 mole) of triphenylphosphine was added. 10 mL of dimethylformamide (DMF) was dried with potassium carbonate and was heated under reflux for ten hours. Triphenylphosphine dissolved completely in DMF at room temperature, and compound **75** dissolved partially at room temperature but dissolved completely when heated. At the end of the reaction, the flask with content was cooled in a refrigerator for twenty-four hours.

A white solid precipitated from the DMF solution. This solid was washed twice with ethyl acetate and was recrystallized from 95% ethanol-ethyl ether to give a 2.60g (83%) of benzyltriphenylphosphonium bromide **88** as a white solid. Comparison of the nuclear magnetic resonance (NMR) and infrared spectrum of compound **88** with an authentic commercially available sample showed they were identical.

The DMF-ethyl acetate solution was evaporated to dryness using a rotary evaporator. The crude solid left in the flask was washed three times with ethyl ether. The washing was to remove all the unreacted triphenylphosphine. The ether wash was cooled in the refrigerator for three days, and a white solid precipitated. Spectroscopic and elemental analysis of the solid showed 0.70g (85%) of 2,2'-bis(hydroxymethyl)-4,4-bipyridine **89**, mp 149-150°C (KBr): 3260, 3060, 2860, 1610, 810 cm^{-1}. ^1H NMR ($CDCl_3$): δ 8.62 (broad, 2H, 6, 6'-Hs), 7.86 (S, 2H, 3, 3'-Hs), 7.67-7.71 (d, 2H, 5, 5'-Hs), 4.73-5.20 (broad, 2H, OH, OH'), 4.67 (S, 4H, CH_2OH, CH_2OH'), ^{13}C NMR ($CDCl_3$), ppm 162.9 (C-2, C-2'), 149.4 (C-6, C-6'), 145.2 (C-4, C-4'), 119.3 (C-5, C-5'), 117.3 (C-3, C-3'), 64.1 (C of CH_2OH and C of CH_2OH').

Anal. calcd. for $C_{12}H_{12}N_2O_2$, C, 66.64; H, 5.60; N, 12.96. Found: C, 66.11; H, 5.66; N, 12.36.

2. Formation of 2,2'-dimethyl-4,4'-bipyridyl dihydrochloride **91**

2.00g (0.01 mole) of compound **81** was placed in a flask. 2.00g (0.01 mole) of triphenylphosphine was added to the flask and 12 mL of N,N-dimethylformamide (DMF) was added. The flask was equipped with condenser and a calcium chloride drying tube. The solution was heated under reflux for ten hours. The flask with content was cooled in the refrigerator for eighteen hours. Benzyltriphenylphosphonium bromide **88** was removed by filtration and washed with ethyl ether. Cold ethyl ether was added to the DMF solution to precipitate the remaining phosphonium salt. The DMF-ethyl ether solution was evaporated with rotary evaporator, and the solid that remained in the flask was dissolved in 95% ethanol (dried with potassium carbonate), and was acidified with dry hydrogen chloride gas. As soon as the 95% ethanol solution became acidic, a white solid formed from the solution but the solid gradually redissolved into the acidic ethanol solution. Addition of a small amount of anhydrous ethyl-ether to the acidic ethanol solution and cooling of the solution in an ice bath precipitated 0.82g (80%) of 2,2'-dimethyl-4,4'-bipyridyl dihydrochloride **91**, as a white solid. ^{1}H NMR (D_2O): δ 8.84-8.90 (d, 2H, 6-6'-Hs), 8.39 (S, 2H, 3, 3'-Hs), 8.28-8.36 (d, 2H, 5, 5'-Hs), 2.87 (S, 6H, CH_3, CH_3' protons).

Complexes of 2-Substituted Pyridines and Bipyridine with Cobalt Thiocyanate

1. Formation of 2-(hydroxymethyl)pyridine cobalt thiocyanate complex **93**

Into a 250 mL Erlenmeyer flask was placed 1.00g of cobalt thiocyanate $Co(SCN)_2$. 20 mL of absolute ethanol was added while warming the solution on a hot plate, a blue solution formed. On addition of 1.10g (0.01 mole) of 2-(hydroxymethyl) pyridine, the solution immediately turned purple, and a purple solid precipitated. The flask with content was warmed gently on a hot plate, and then cooled in an ice bath for two hours. The solution was filtered, the solid collected was washed with cold absolute ethanol, and was recrystallized from

hot methanol to yield 0.90g of 2-(hydroxymethyl) pyridine cobalt thiocyanate complex **93**. IR (KBr): 3258, 2096, 1596, 1398, 1028, 761 cm^{-1}.

Anal. calcd. for $C_{14}H_{14}N_4O_2S_2Co$: C, 42.74; H, 3.59; N, 14.25. Found: C, 42.76; H, 3.62; N, 14.20.

2. Formation of 2,2'-Bis(hydroxymethyl)-4,4'-bipyridine cobalt thiocyanate complex **94**

To 1.00g (0.01 mole) of compound **89** dissoolved in 10 mL of absolute ethanol was added dropwise. 1.00g of cobalt thiocyanate dissolved in 15 mL of absolute ethanol. Solution of compound **89** in absolute ethonal was added dropwise with shaking to the blue solution of cobalt thiocyanate while warming the flask gently on a hot plate. The blue solution turned purple, and a purple solid precipitated instantly. The ethanol solution was immediately decanted and the solid was redissolved in a fresh absolute ethanol. The reaction mixture was cooled in an ice bath for two hours; the solution was filtered, and the solid was washed with cold 95% ethanol, and recrystallized from hot methanol to give 0.80g of 2,2'-bis(hydroxymethyl)-4,4'-bipyridine cobalt thiocyanate complex **94**. IR (KBr): 3164, 2079, 1605, 1028, 813 cm^{-1}.

Anal. cacld. for $(C_{14}H_{12}N_4O_2S_2C_o)n$ C, 42.96; H, 3.1; N, 14.32; Found: C, 42.56; H, 3.59; N, 13.53.

3. Formation of 2-(2-hydroxyethyl)pyridine cobalt thiocyanate complex **96**

Following the procedure used for the complexation of 2-(hydroxymethyl)pyridine **92** with cobalt thiocyanate, 15 mL of absolute ethanol was placed in a flask, 1.00g cobalt thiocyanate was added. The mixture was warmed gently on a hot plate to completely dissolve the cobalt thiocyanate. To this blue solution was added 3.30g (0.02 mole) of 2-(2-hydroxyethyl) pyridine **95**. The solution turned pink in two minutes and upon warming, an orange-pink solid precipitated in approximately one minute after addition of the pyridine. The flask with content was cooled in an ice bath, the solu-

tion was filtered and the solid was recrystallized from methanol to give 2.00g of 2-(2-hydroxyethyl)pyridine cobalt thiocyanate complex **96**. IR (KBr): 3207, 2087, 1499, 1019, 417 cm^{-1}.

Anal. calcd. for $C_{16}H_{18}N_4O_2S_2C_0$, C, 45.60; H, 4.31; N, 13.30; Found: C, 45.68; H, 4.33; N, 13.25.

G. Complexes of 2-(hydroxyethyl)pyridine with nickel thiocyanate

The following solutions were prepared:

(a). A saturated solution of nickel thiocyanate in absolute ethanol which was stirred for five days and was allowed to stand for twenty-four hours at room temperature. (b) 1mL of 2-(hydroxymethyl)pyridine dissolved in 5 mL of absolute ethanol. The 2-(hydroxymethyl)pyridine solution was poured in a flask containing the light green nickle thiocyanate solution. Upon addition, the light green solution turned dark green and blue solid precipitated instantly. The flask with content was cooled in an ice bath, and the blue solid was filtered, washed twice with cold absolute ethanol. Trials to recrystallize the blue solid failed, but the infrared spectrum and the elemental analysis showed that the blue solid was pure. IR (KBr): 3176, 2105, 1605, 1266, 1027, 759 cm^{-1}.

Anal. cald. for $C_{14}H_{14}N_4O_2S_2Ni$, 42.77; H, 3.60; N, 14.25. Found: C, 42.88; H, 3.68; N, 14.12.

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APPENDIX

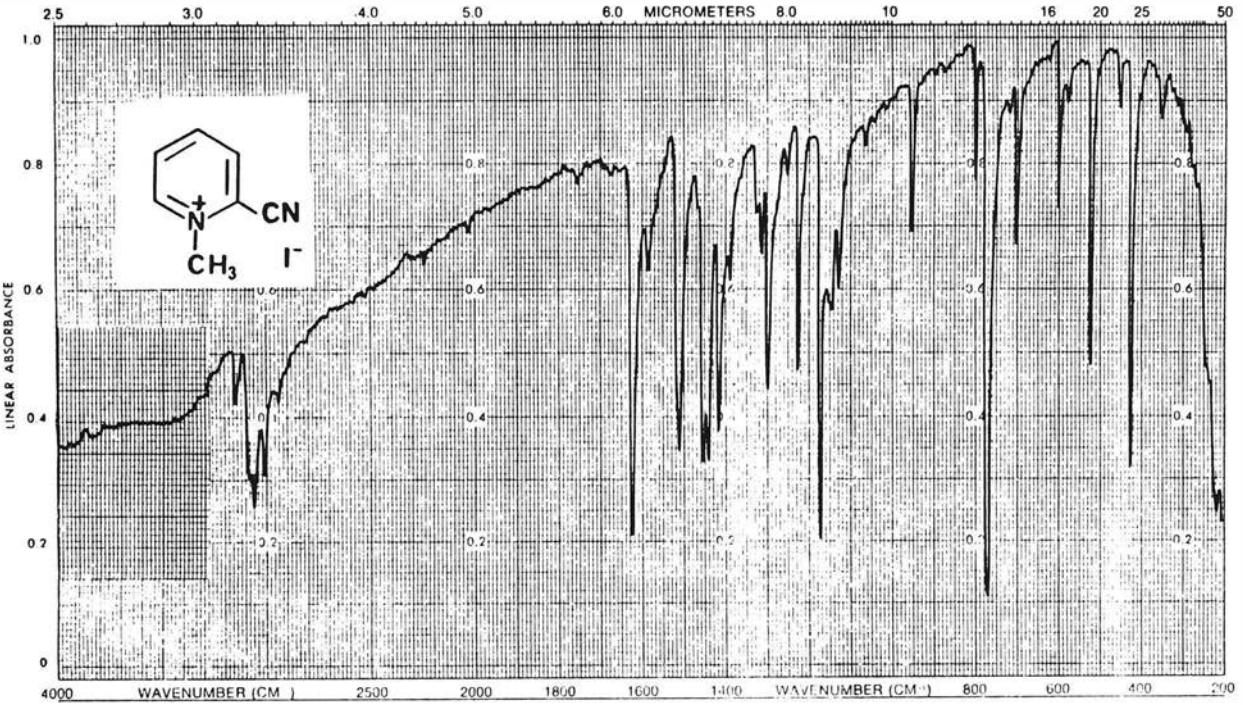


Figure 60. IR Spectrum (KBr) of 1-Methyl-2-Cyanopyridinium Iodide 12.

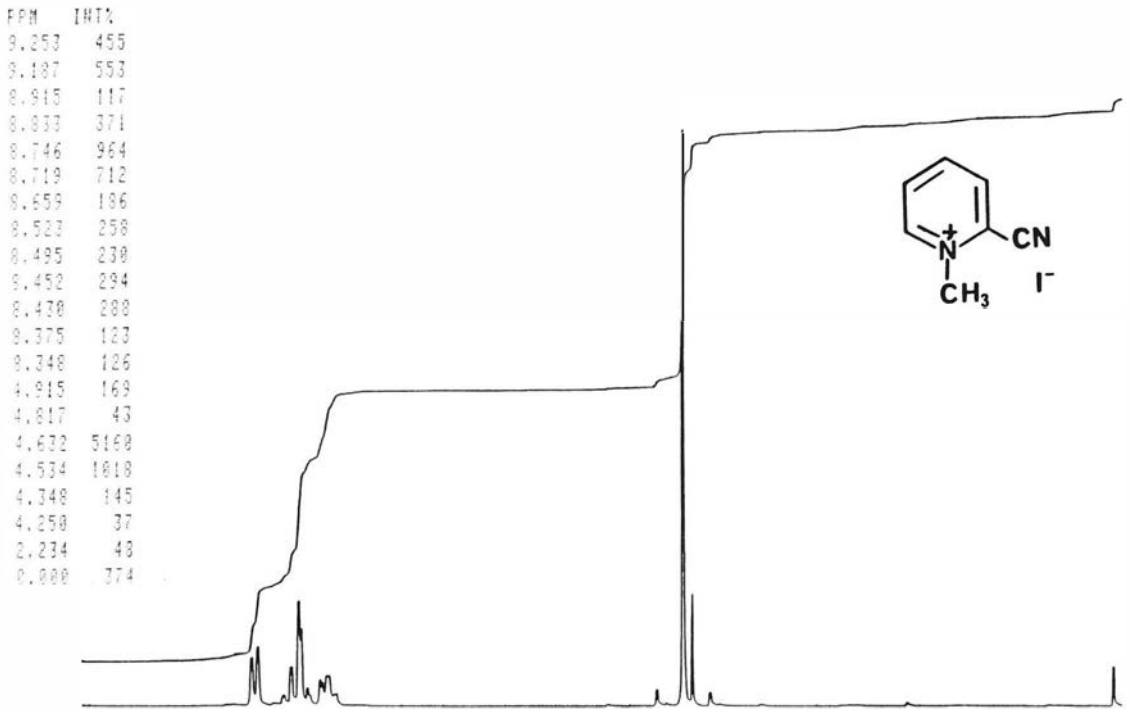


Figure 61. ^{1}H-NMR Spectrum (90MHz) of 1-Methyl-2-Cyanopyridinium Iodide 12.

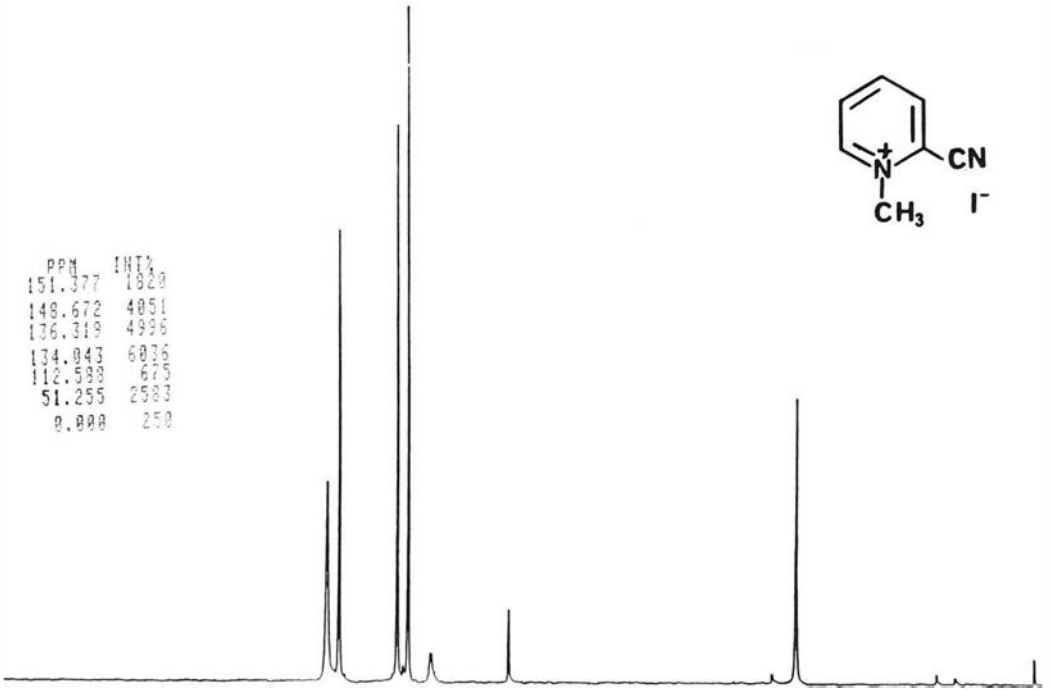


Figure 62. ^{13}C-NMR Spectrum of 1-Methyl-2-Cyanopyridinium Iodide 12.

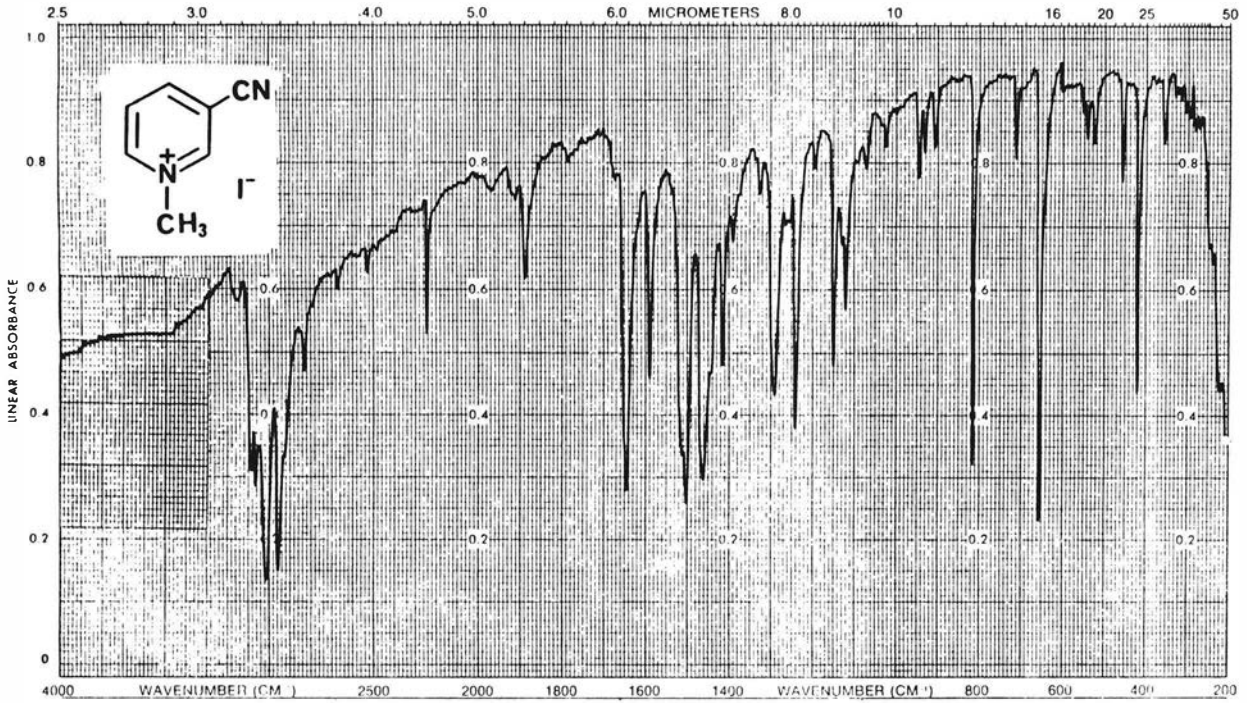


Figure 63. IR Spectrum (KBr) of 1-Methyl-3-Cyanopyridinium Iodide 13.

Figure 64. ^{1}H-NMR Spectrum (90MHz) of 1-Methyl-3-Cyanopyridinium Iodide 13.

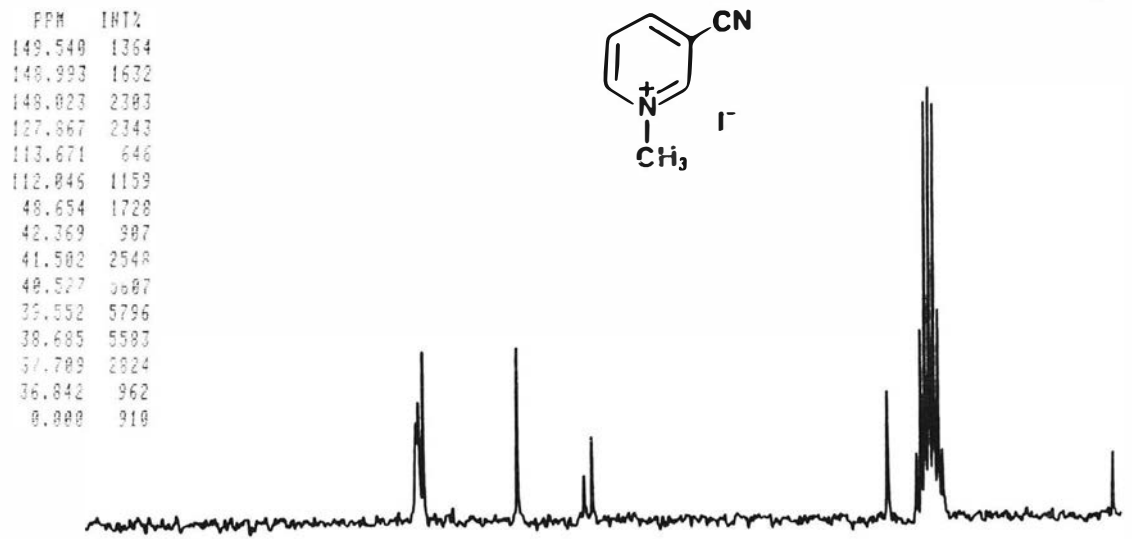


Figure 65. ^{13}C-NMR Spectrum of 1-Methyl-3-Cyanopyridinium Iodide 13.

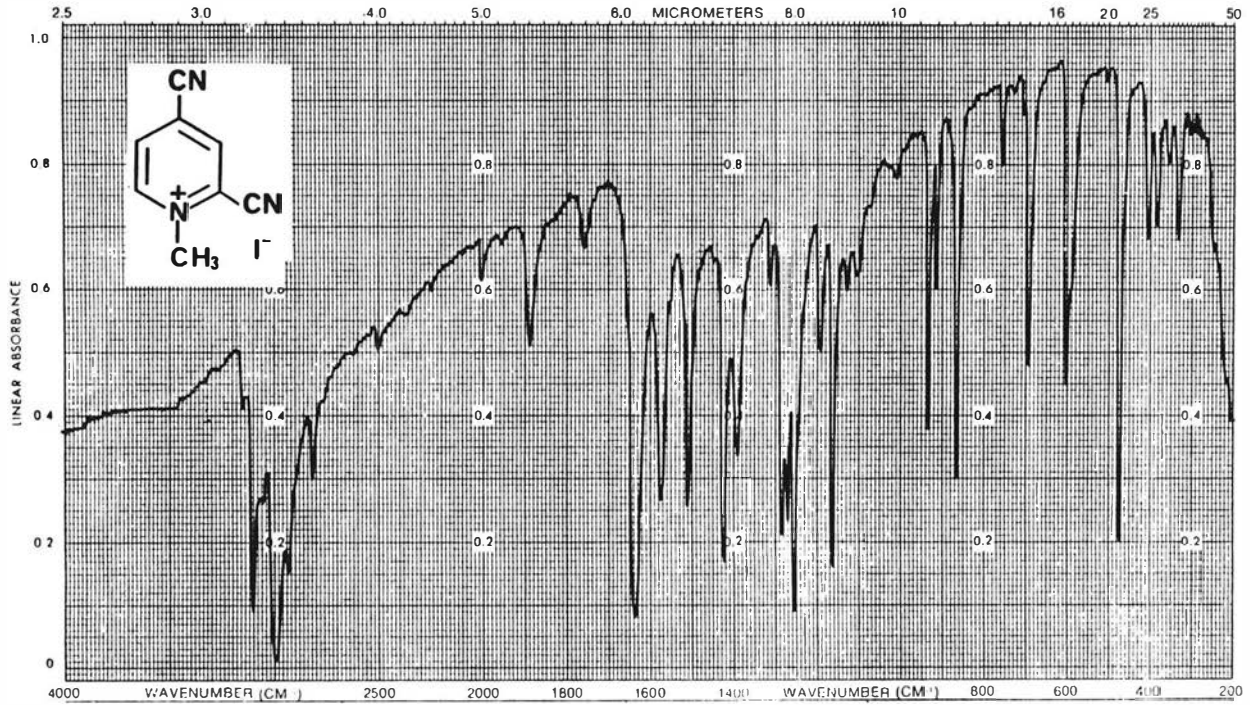


Figure 66. IR Spectrum (KBr) of 1-Methyl-2,4-Dicyanopyridinium Iodide 15.

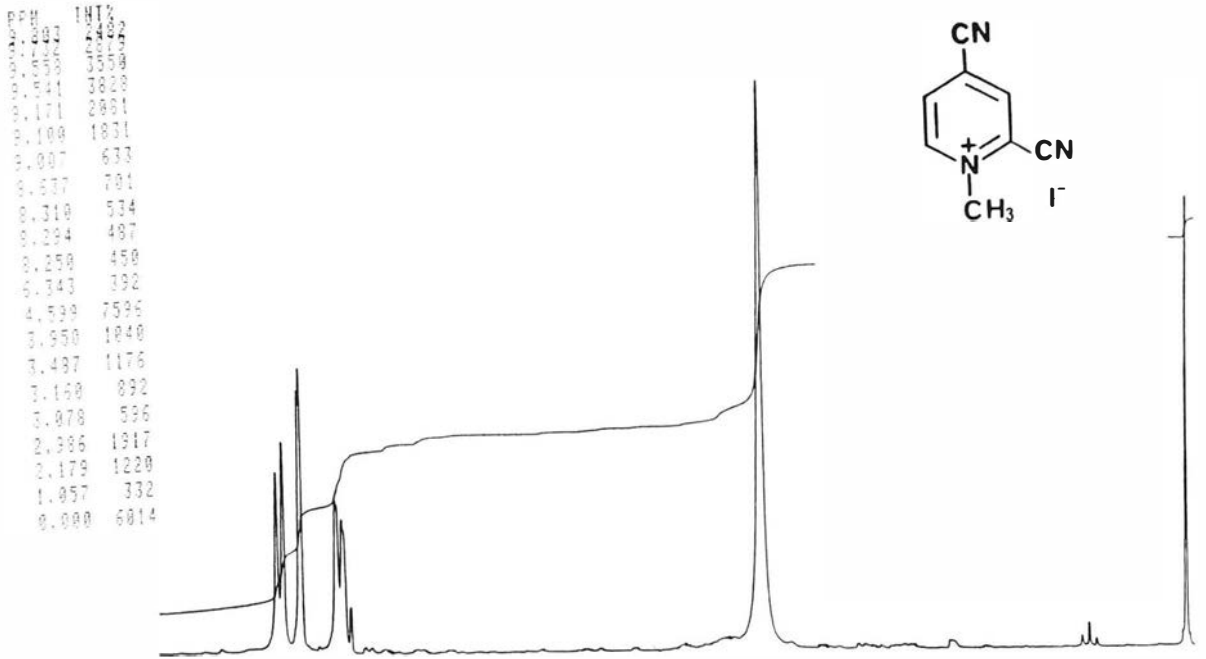


Figure 67. ^{1}H-NMR Spectrum (90MHz) of 1-Methyl-2,4-Dicyanopyridinium Iodide 15.

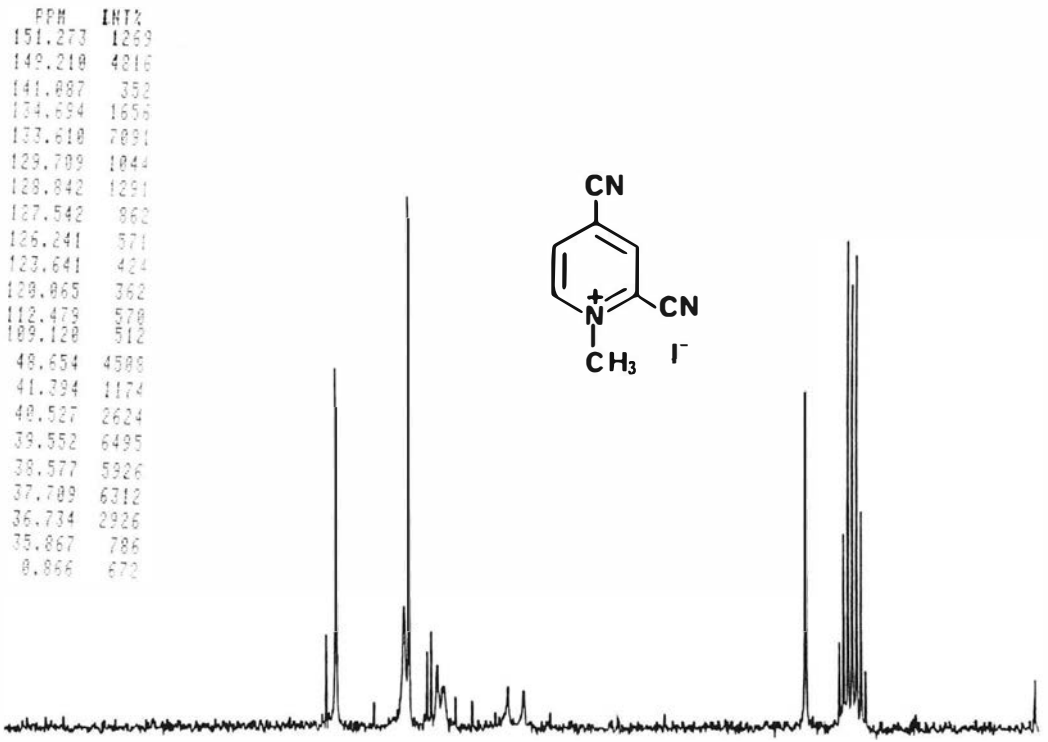


Figure 68. ^{13}C-NMR Spectrum of 1-Methyl-2,4-Dicyanopyridinium Iodide 15.

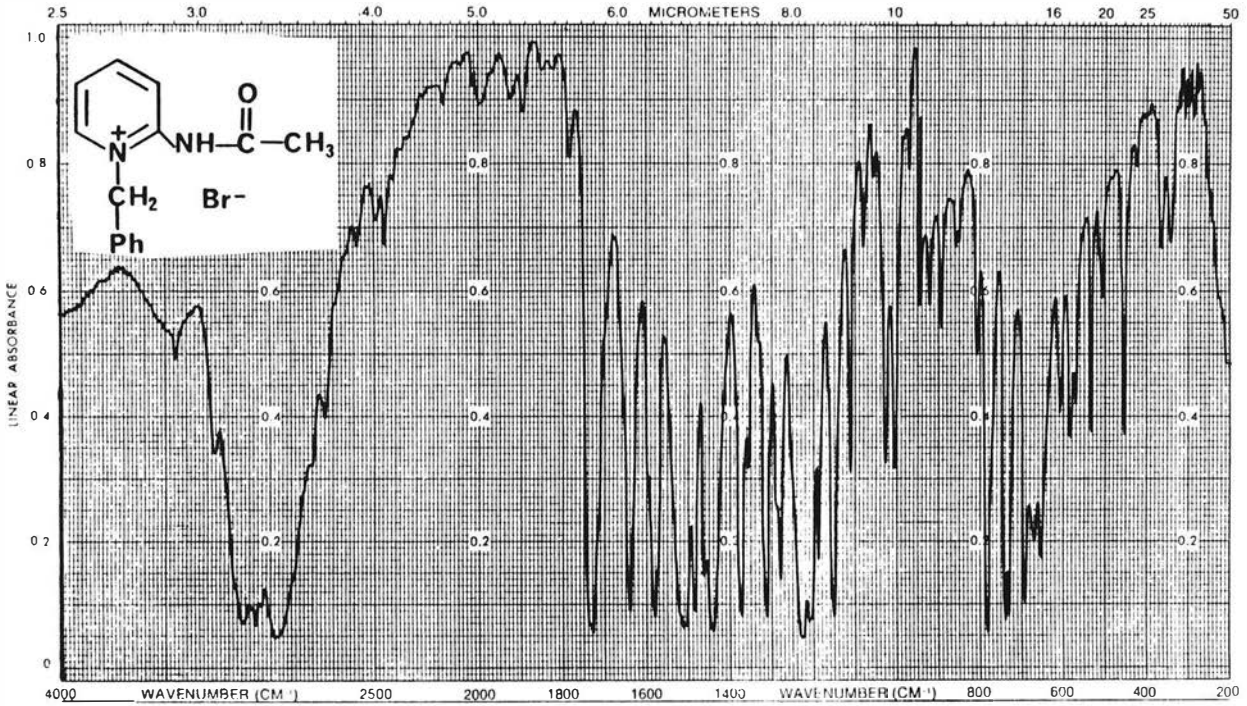


Figure 69. IR Spectrum (KBr) of 1-Benzyl-2-(Acylamino)pyridinium Bromide 17.

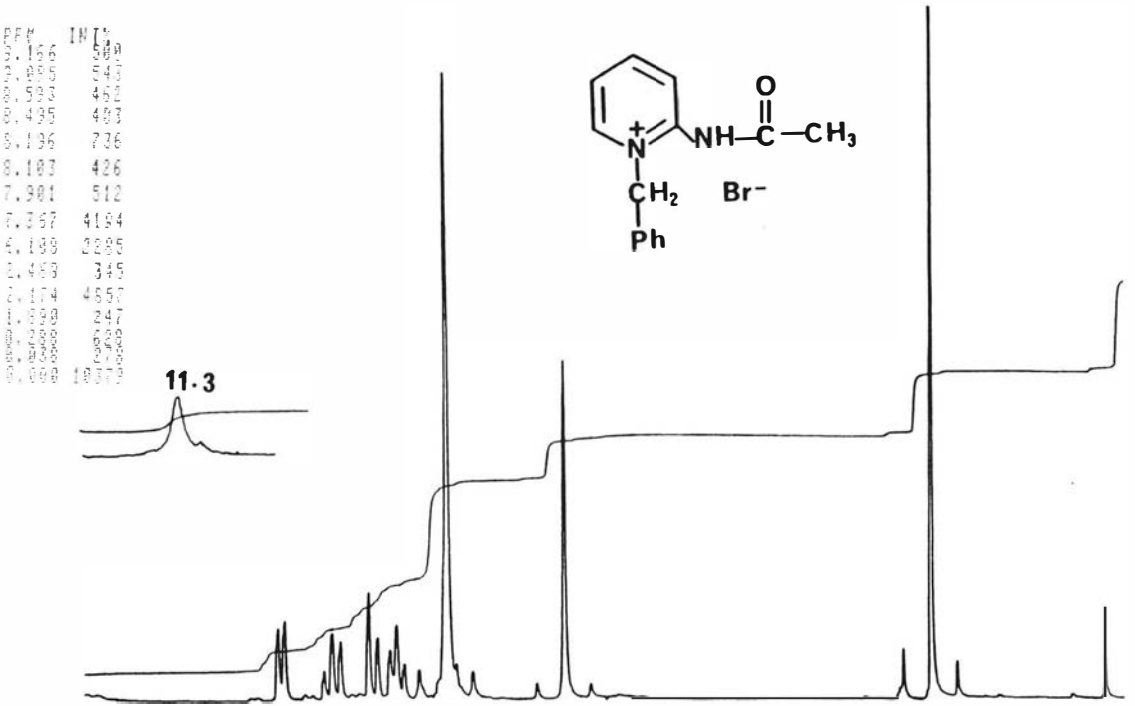


Figure 70. ^{1}H-NMR Spectrum (90MHz) of 1-Benzyl-2-(Acylamino)pyridinium Bromide 17.

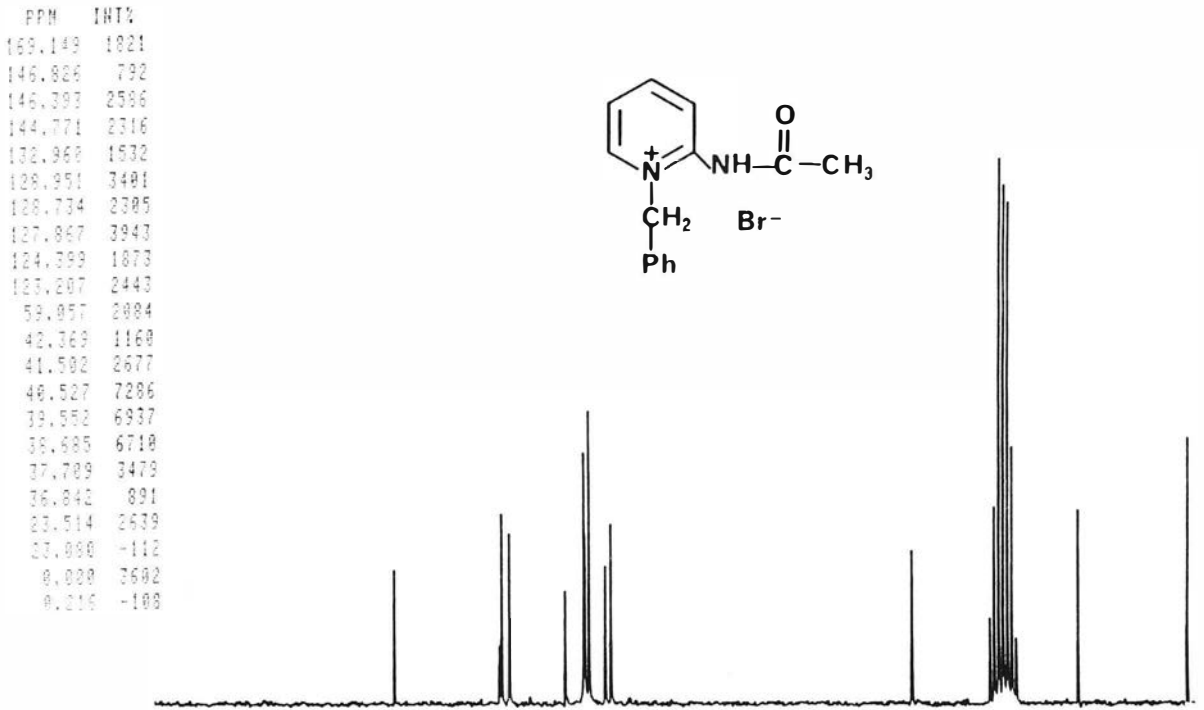


Figure 71. ^{13}C-NMR Spectrum of 1-Benzyl-2-(Acylamino)pyridinium Bromide 17.

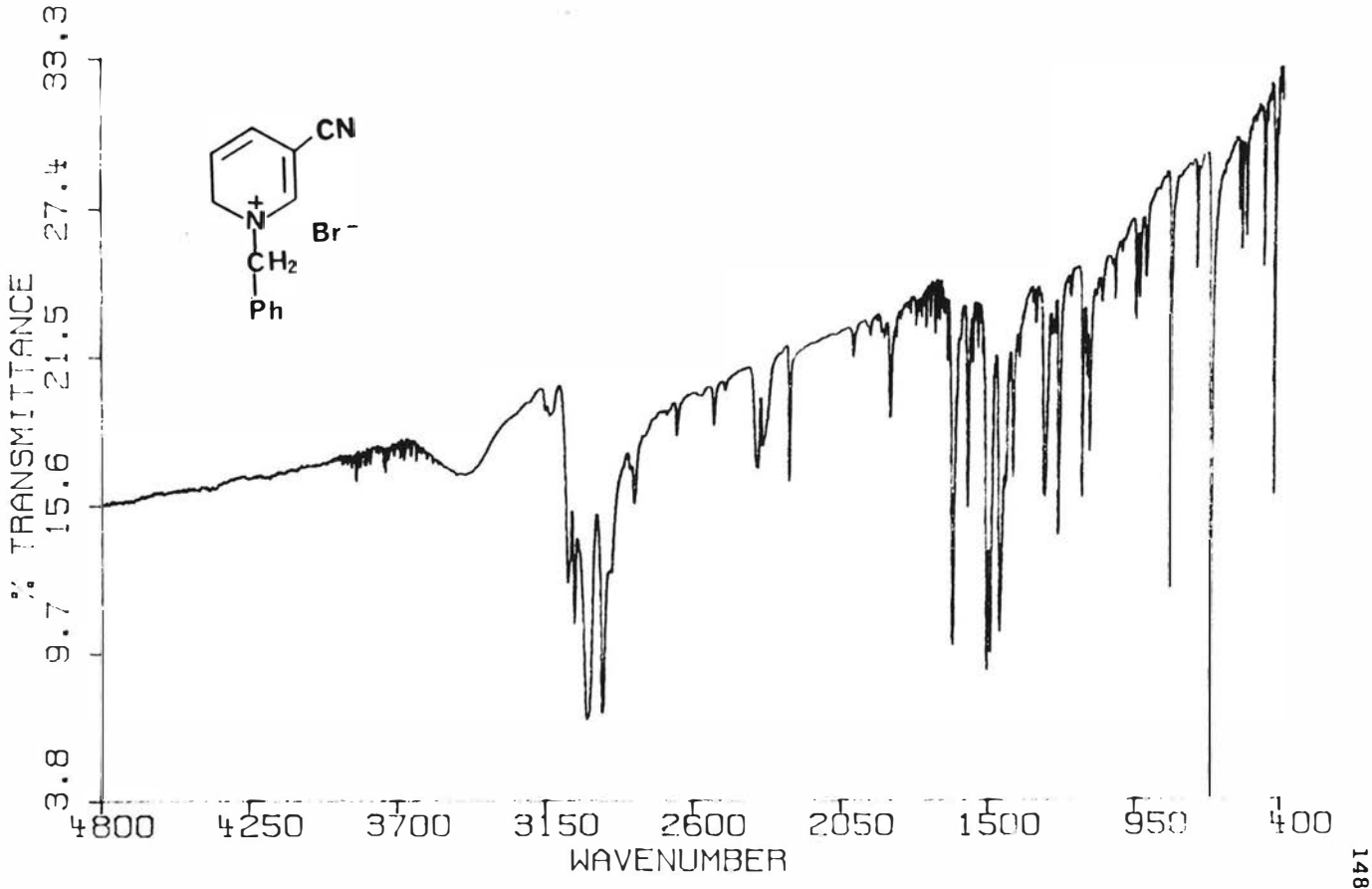


Figure 72. IR Spectrum (KBr) of 1-Benzyl-3-Cyanopyridinium Bromide 20.

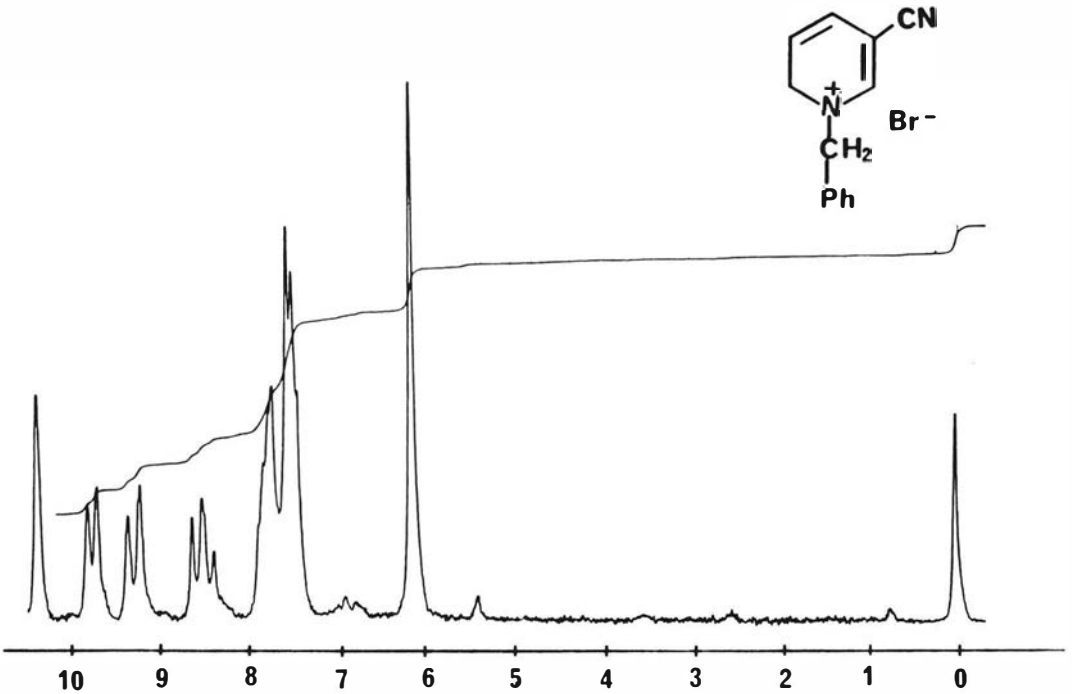


Figure 73. ^{1}H-NMR Spectrum (60MHz) of 1-Benzyl-3-Cyanopyridinium Bromide 20.

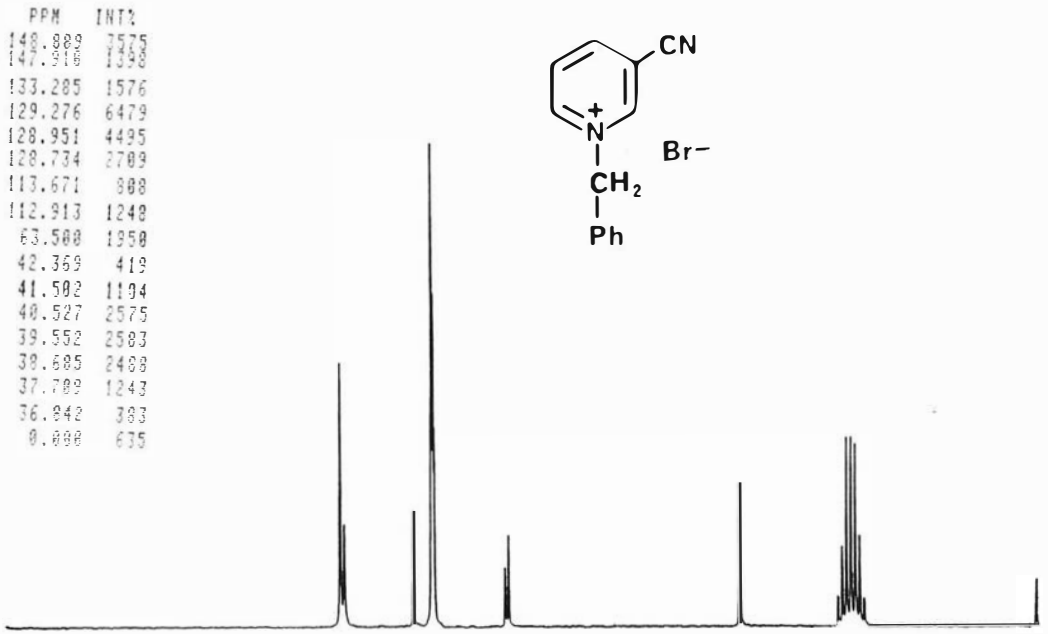


Figure 74. ^{13}C-NMR Spectrum of 1-Benzyl-3-Cyanopyridinium Bromide 20.

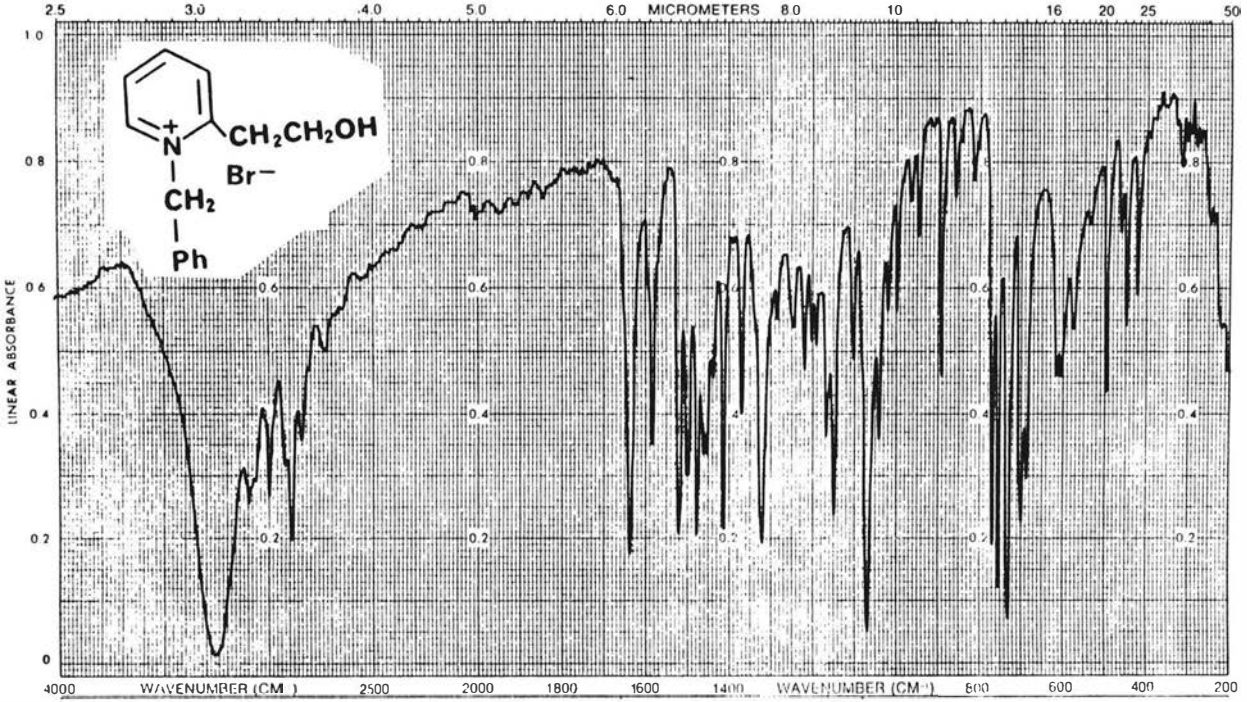


Figure 75. IR Spectrum (KBr) of 1-Benzyl-2-(2-Hydroxyethyl)pyridinium Bromide 23.

PPM	INT%
9.231	1854
9.166	1853
8.730	698
8.642	1718
8.555	1293
8.207	2598
8.185	1731
8.119	2742
8.032	802
7.465	2810
7.400	7012
7.313	3864
7.269	2594
7.226	1623
6.070	7874
3.847	1647
3.781	4117
3.716	2827
3.313	2633
3.247	3691
3.182	1558
2.517	332
0.000	8929

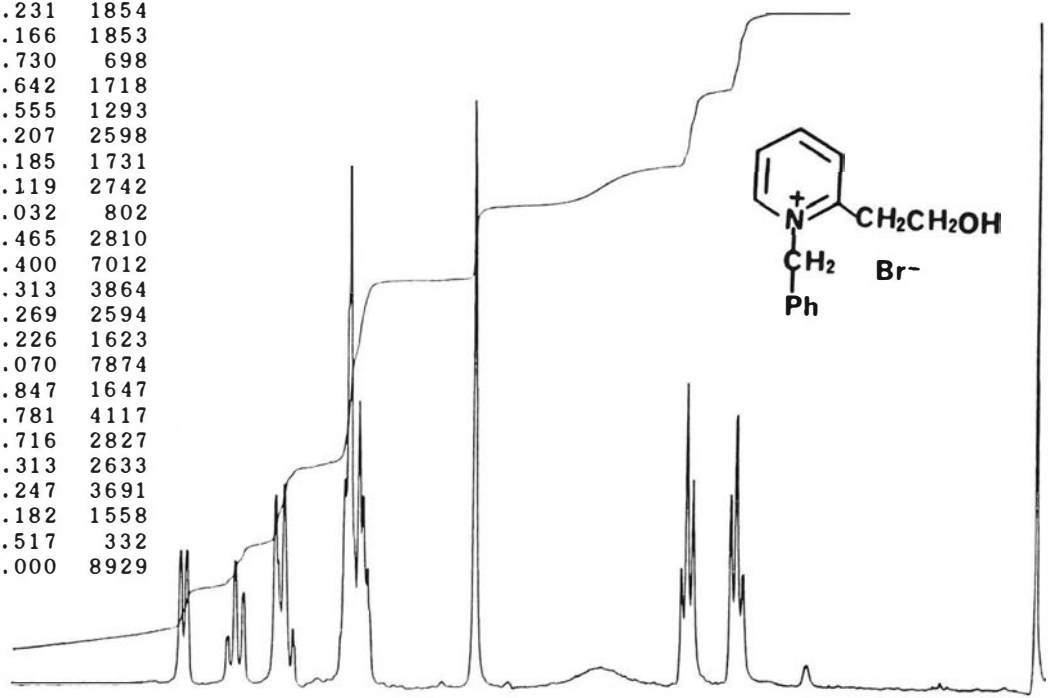


Figure 76. ^{1}H-NMR Spectrum (90MHz) of 1-Benzyl-2-(2-Hydroxyethyl)pyridinium Bromide 23.

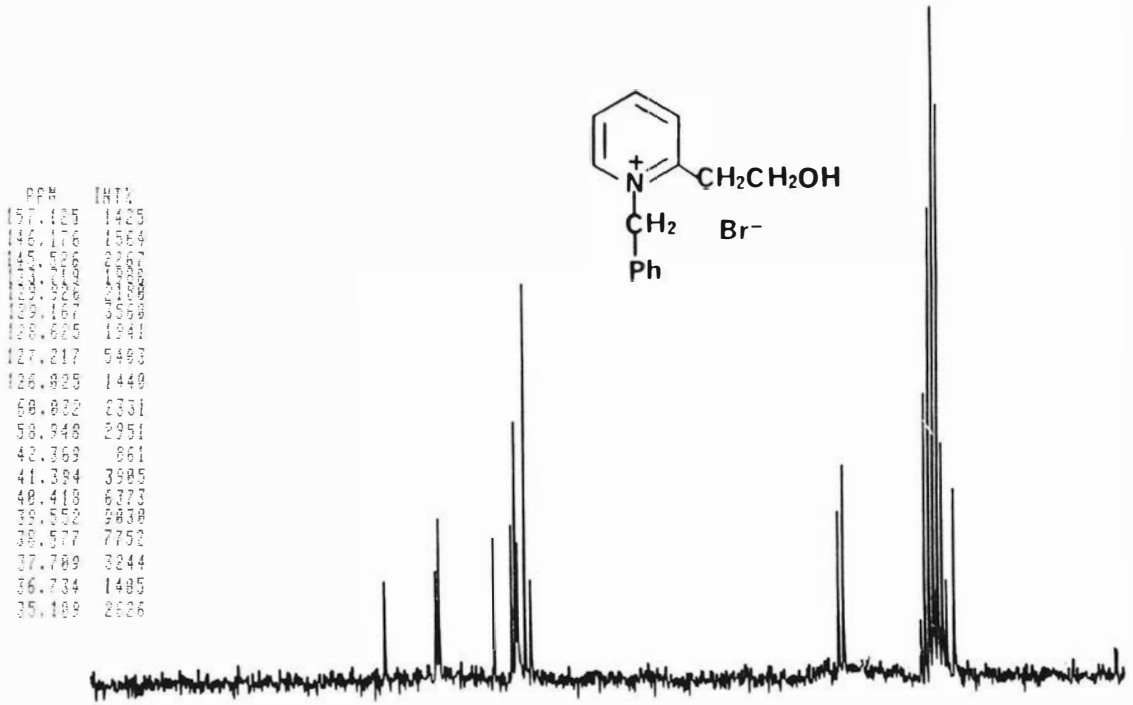


Figure 77. ^{13}C-NMR Spectrum of 1-Benzyl-2-(2-Hydroxyethyl)pyridinium Bromide 23.

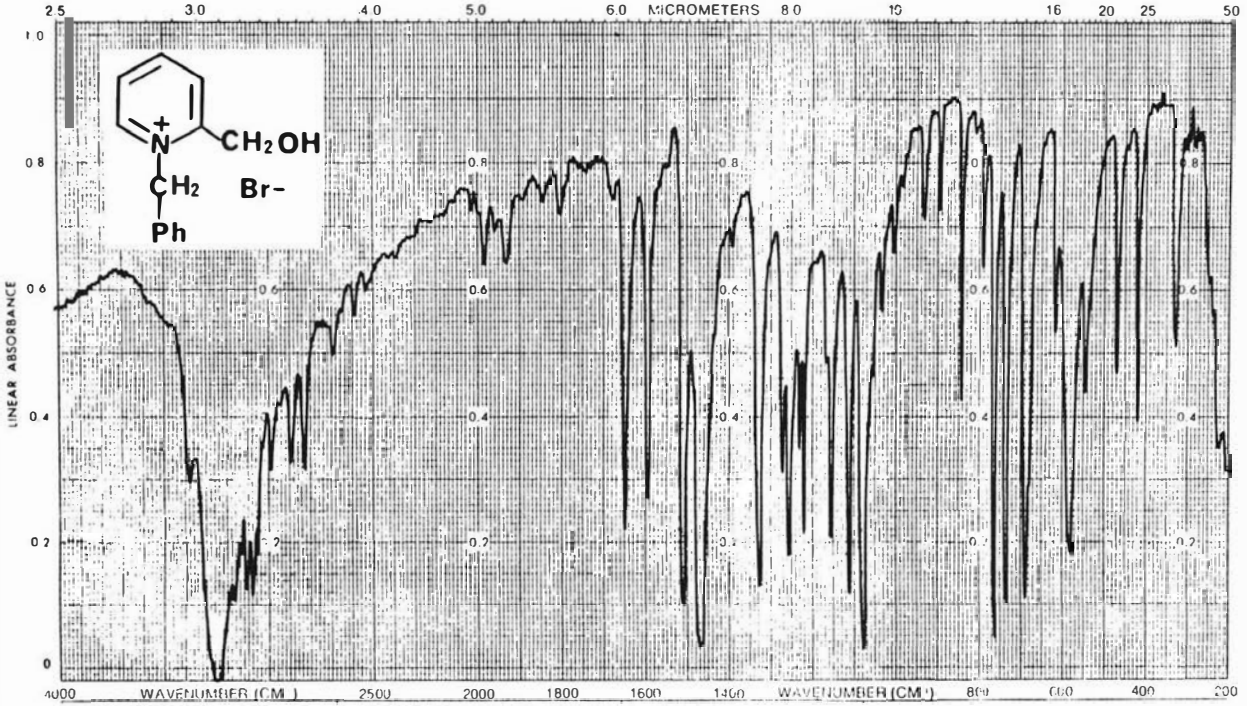


Figure 78. IR Spectrum (KBr) of 1-Benzyl-2-(Hydroxymethyl)pyridinium Bromide 24.

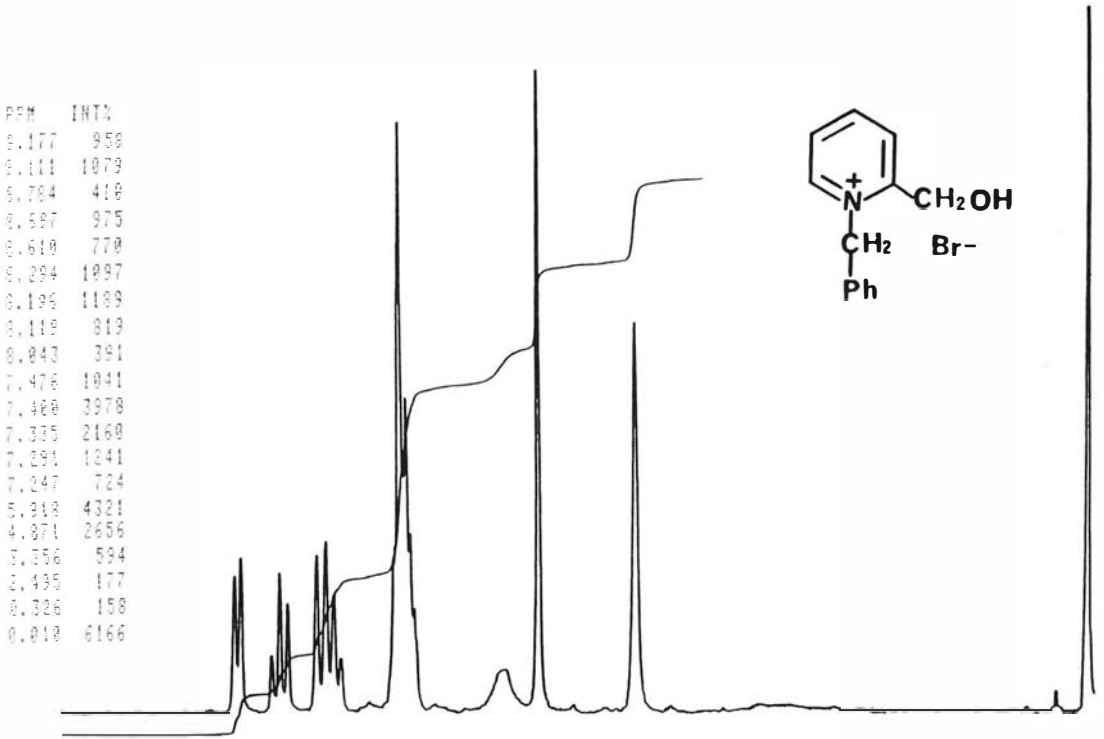


Figure 79. ^{1}H-NMR Spectrum (90Mhz) of 1-Benzyl-2-(Hydroxymethyl)pyridinium Bromide 24.

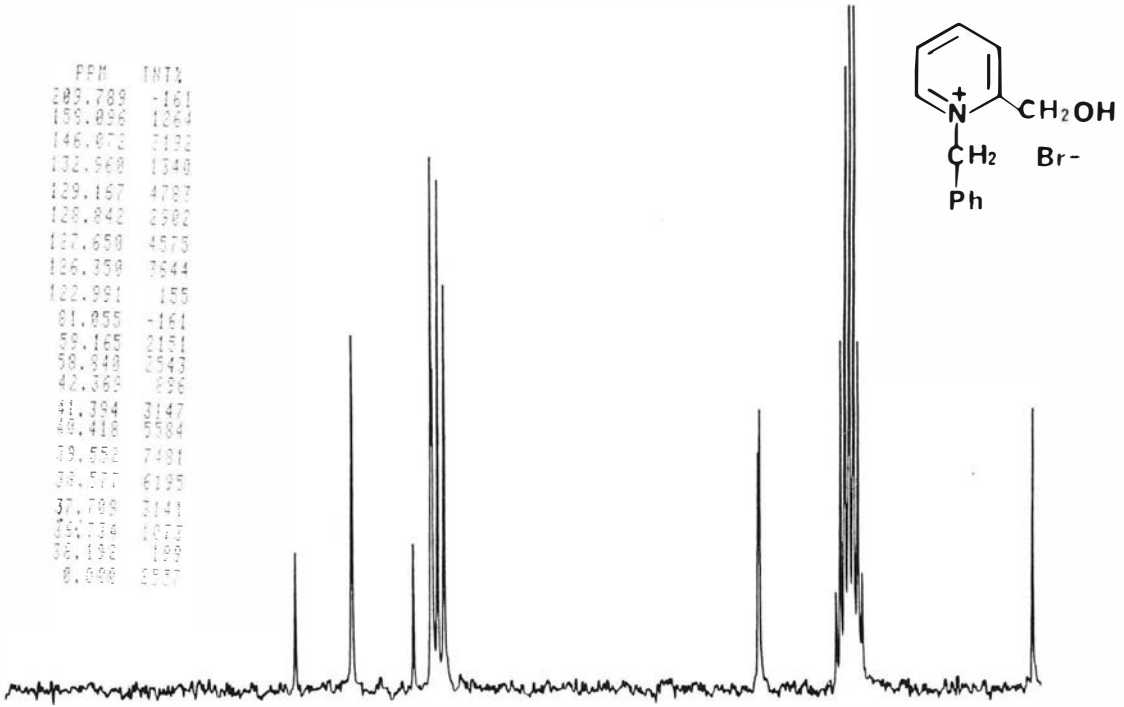


Figure 80 ^{13}C-NMR Spectrum of 1-Benzyl-2-(Hydroxymethyl)pyridinium Bromide 24.

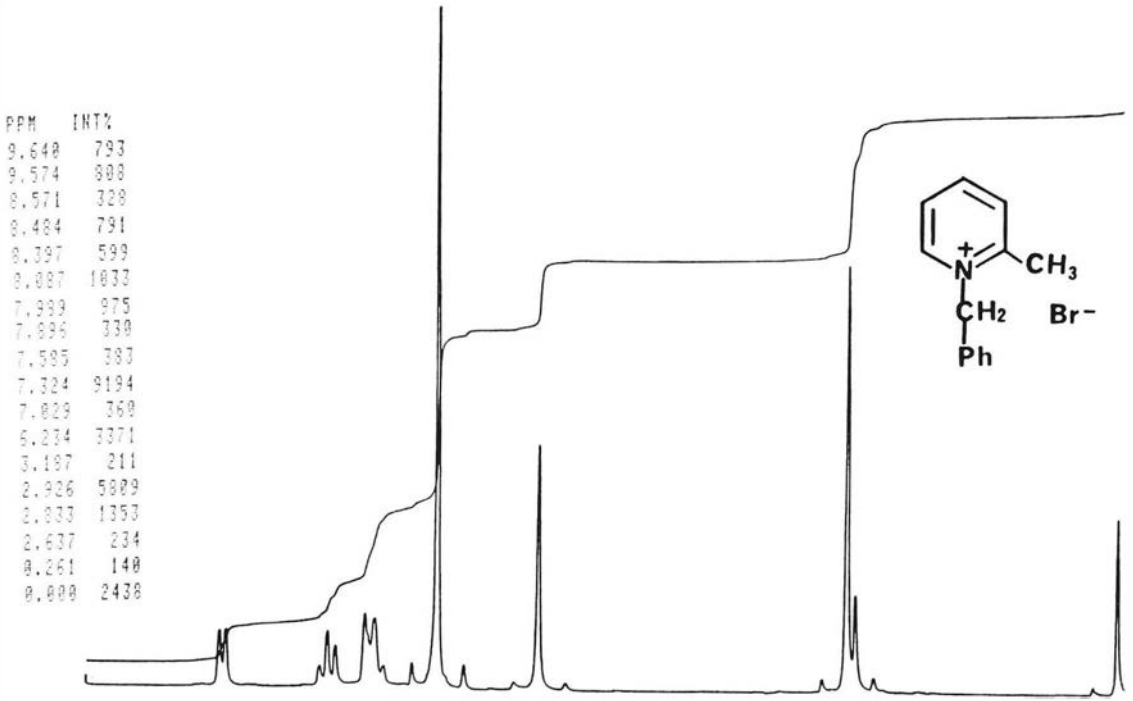


Figure 81. ^{1}H-NMR Spectrum (90MHz) of 1-Benzyl-2-Methylpyridinium Bromide 25.

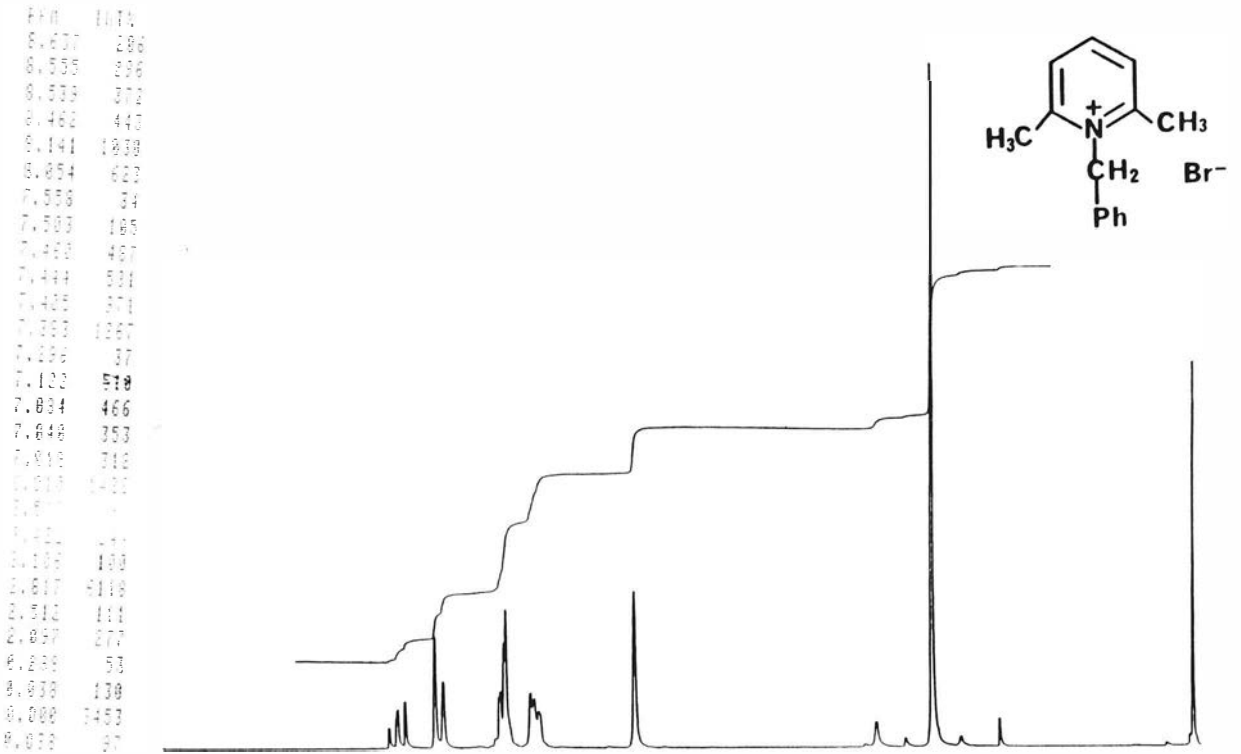


Figure 82. ^{1}H-NMR Spectrum (90MHz) of 1-Benzyl-2,6-Dimethylpyridinium Bromide 29.

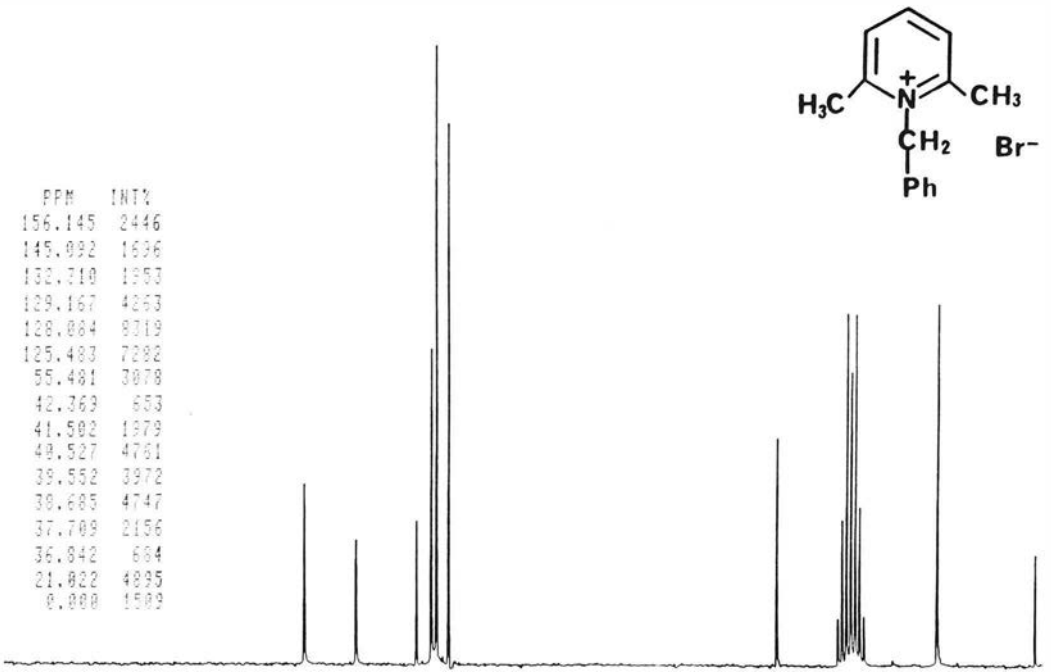


Figure 83. ^{13}C-NMR Spectrum of 1-Benzyl-2,6-Dimethylpyridinium Bromide 29.

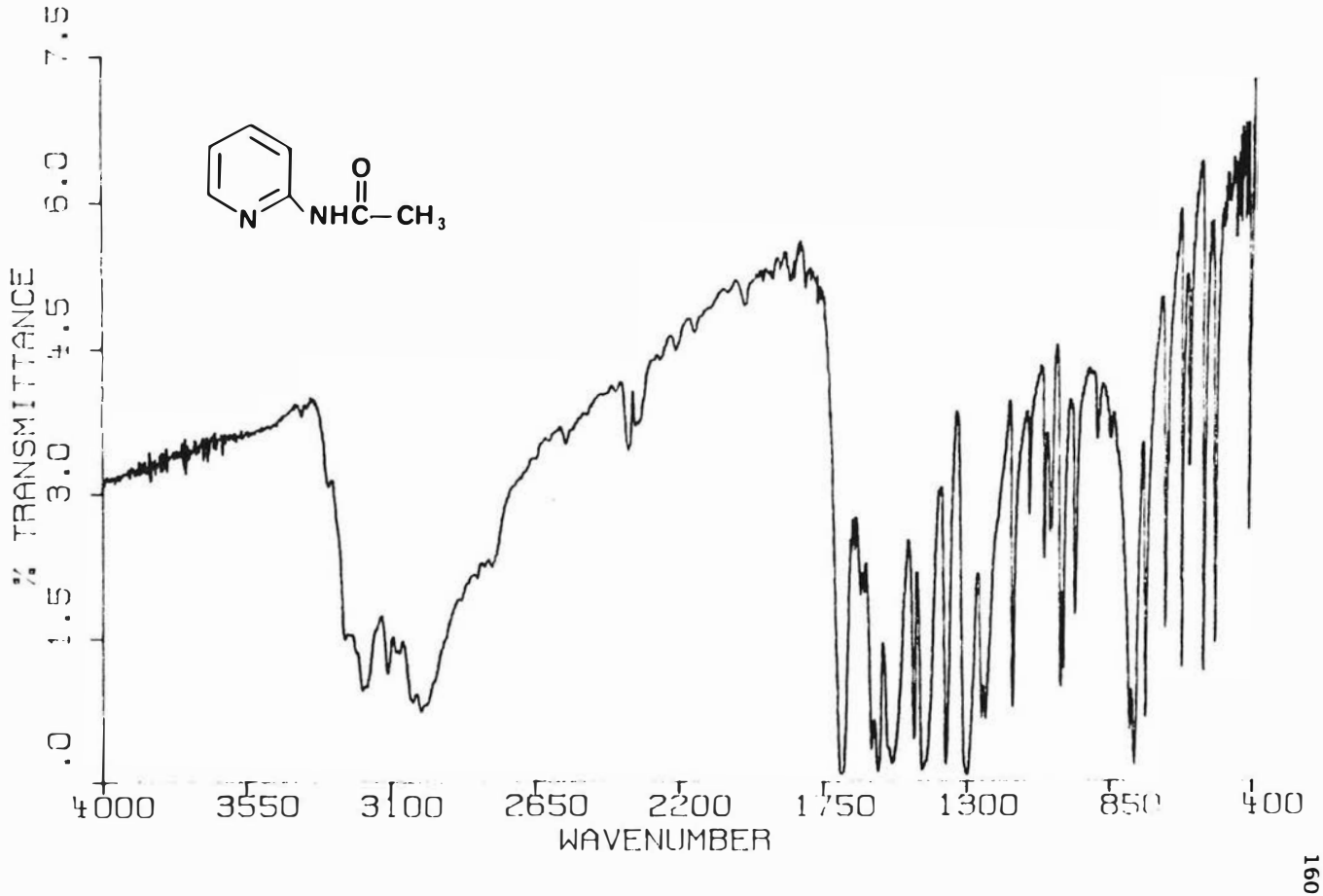


Figure 84. IR Spectrum (KBr) of 2-(Acylamino)pyridine 17a.

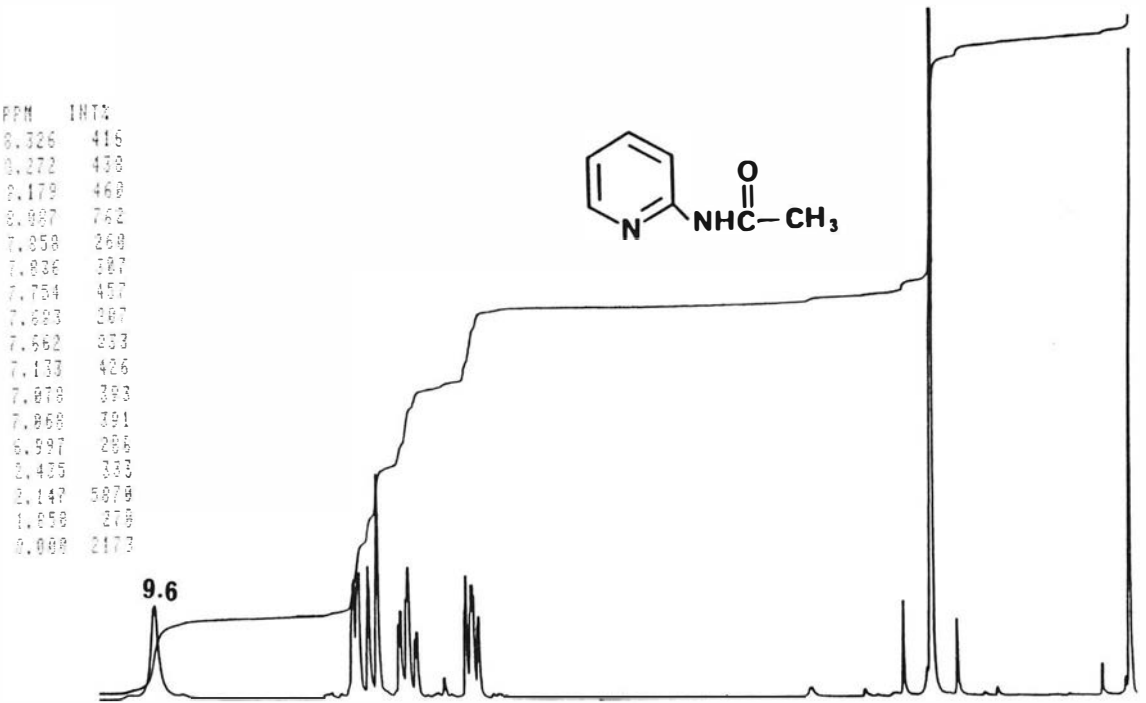


Figure 85. ^{1}H-NMR Spectrum (90MHz) of 2-(Acylamino)pyridine 17a.

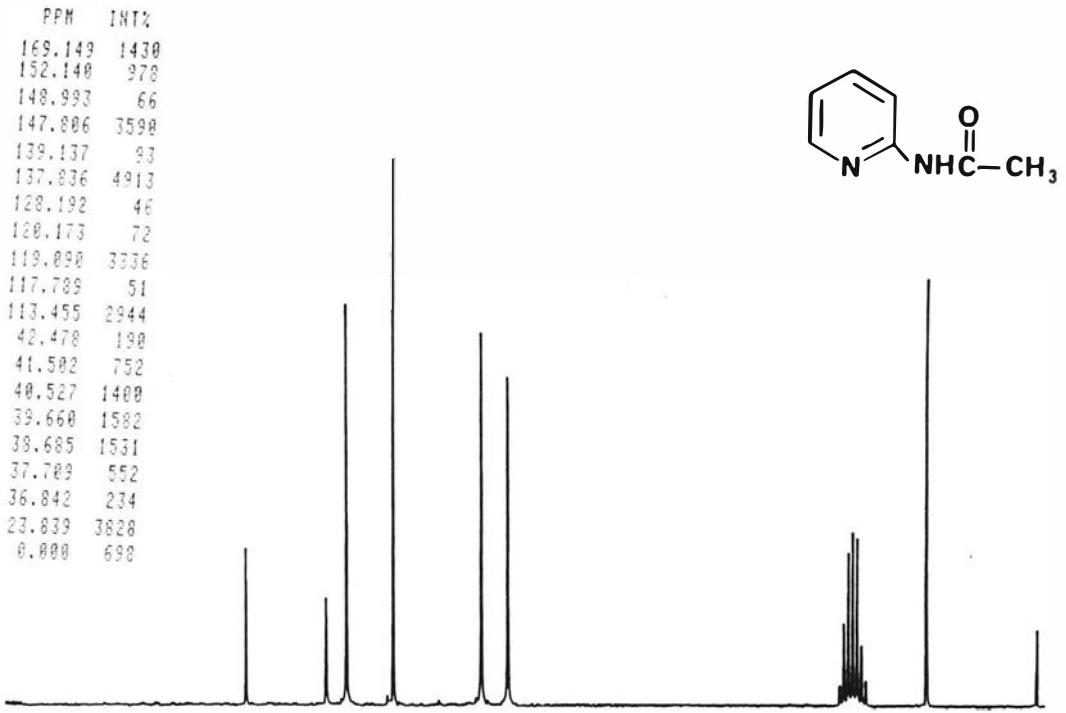


Figure 86. ^{13}C-NMR Spectrum (90MHz) of 2-(Acylamino)pyridine 17a.

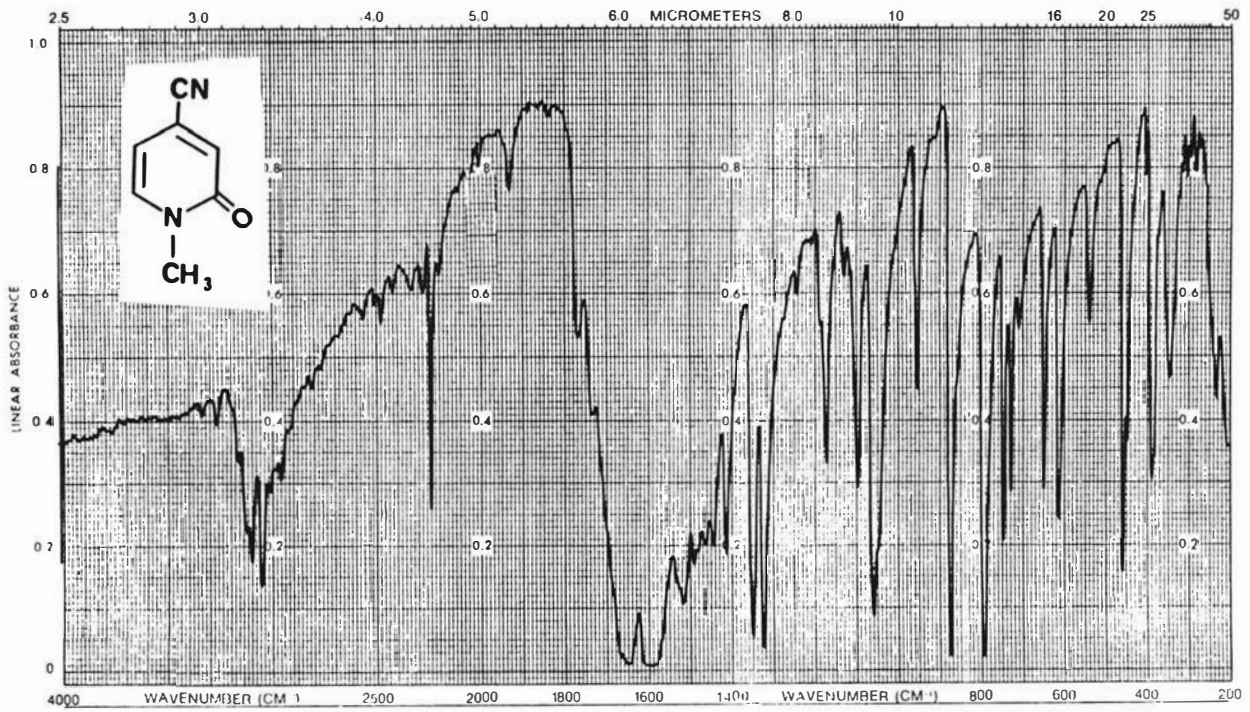


Figure 87. IR Spectrum of 1-Methyl-2-Oxo-1,2-Dihydro-4-Pyridine Carbonitrile 62.

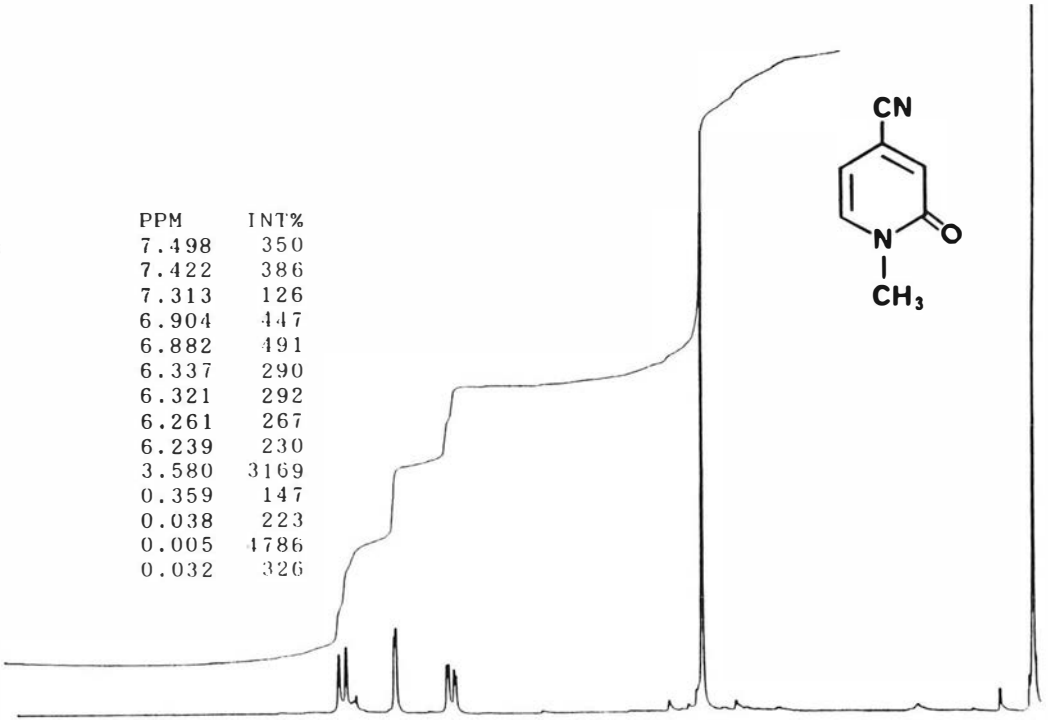


Figure 88. ^{1}H-NMR Spectrum Spectrum (90MHz) of 1-Methyl-2-Oxo-1,2-Dihydro-4-Pyridine Carbonitrile 62

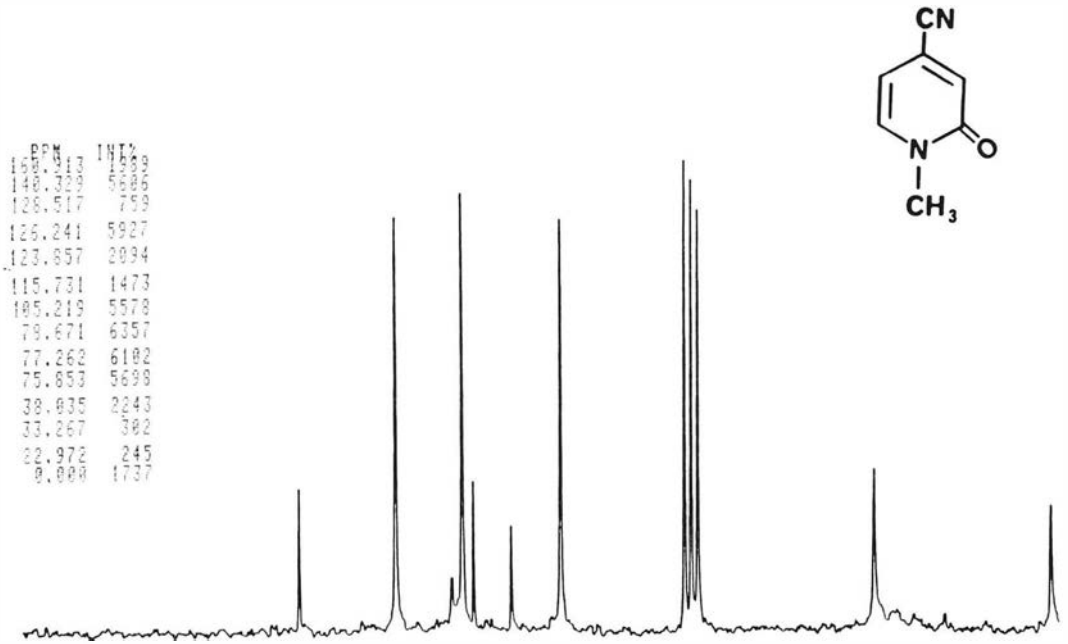
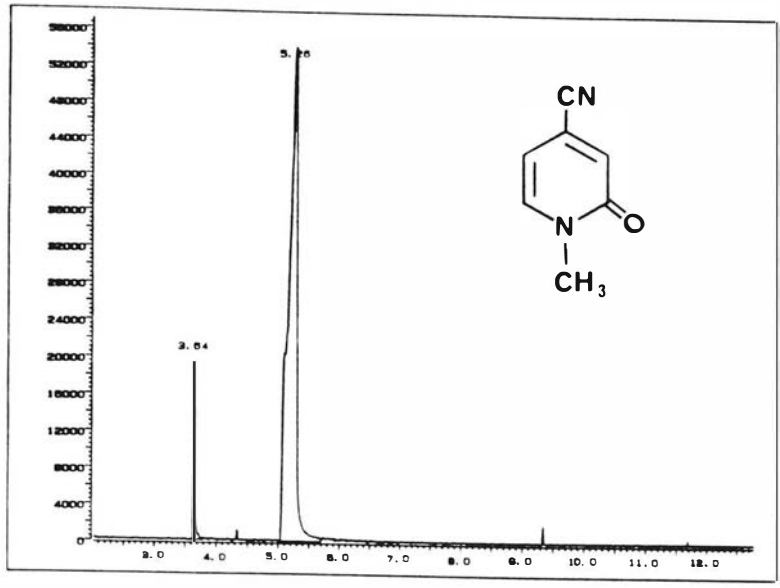


Figure 89. ^{13}C-NMR Spectrum of 1-Methyl-2-Oxo-1,2-Dihydro-4-Pyridine Carbonitrile 62.



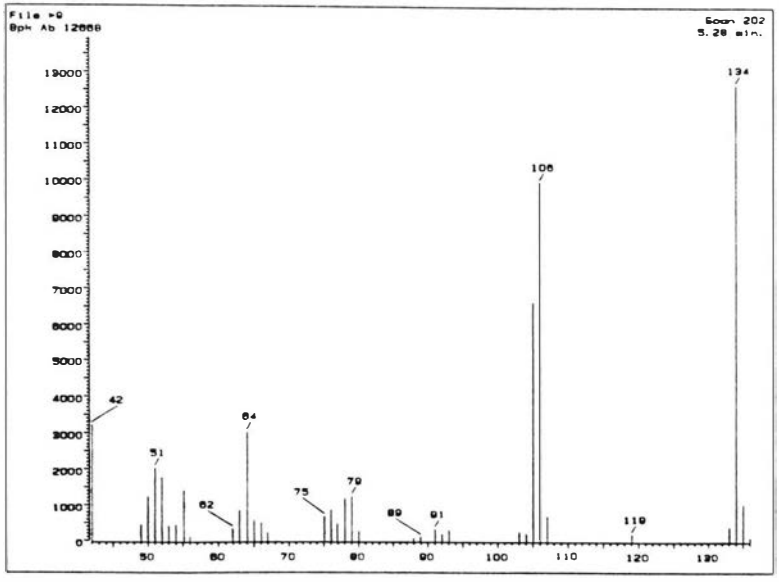


Figure 90. GC/Mass Spectrum of Compound 62.

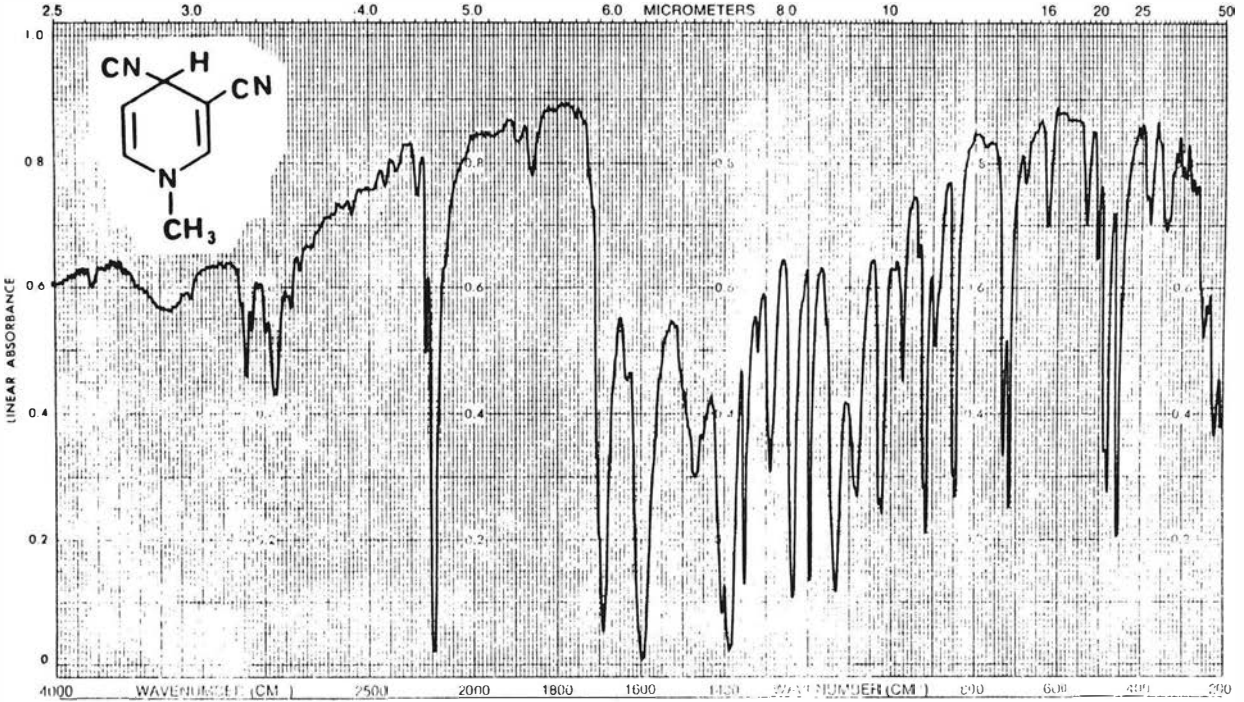


Figure 91. IR Spectrum (KBr) of 1-Methyl-3,4-Dicyano-1,4-Dihydropyridine 63.

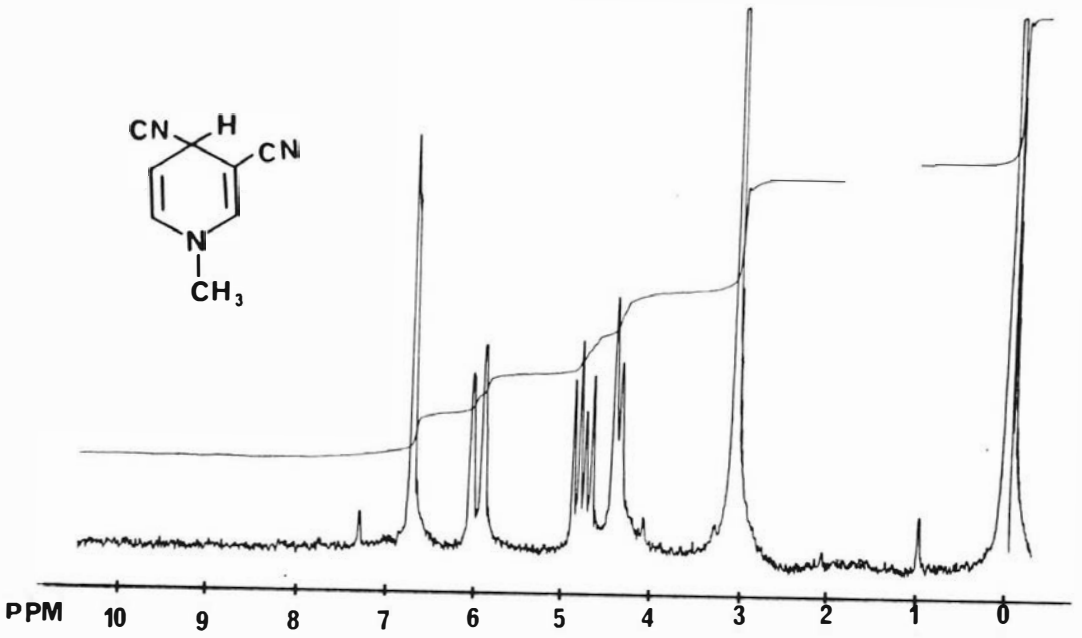


Figure 92. ^{1}H-NMR Spectrum (60MHz) of 1-Methyl-3,4-Dicyano-1,4-Dihydropyridine 63.

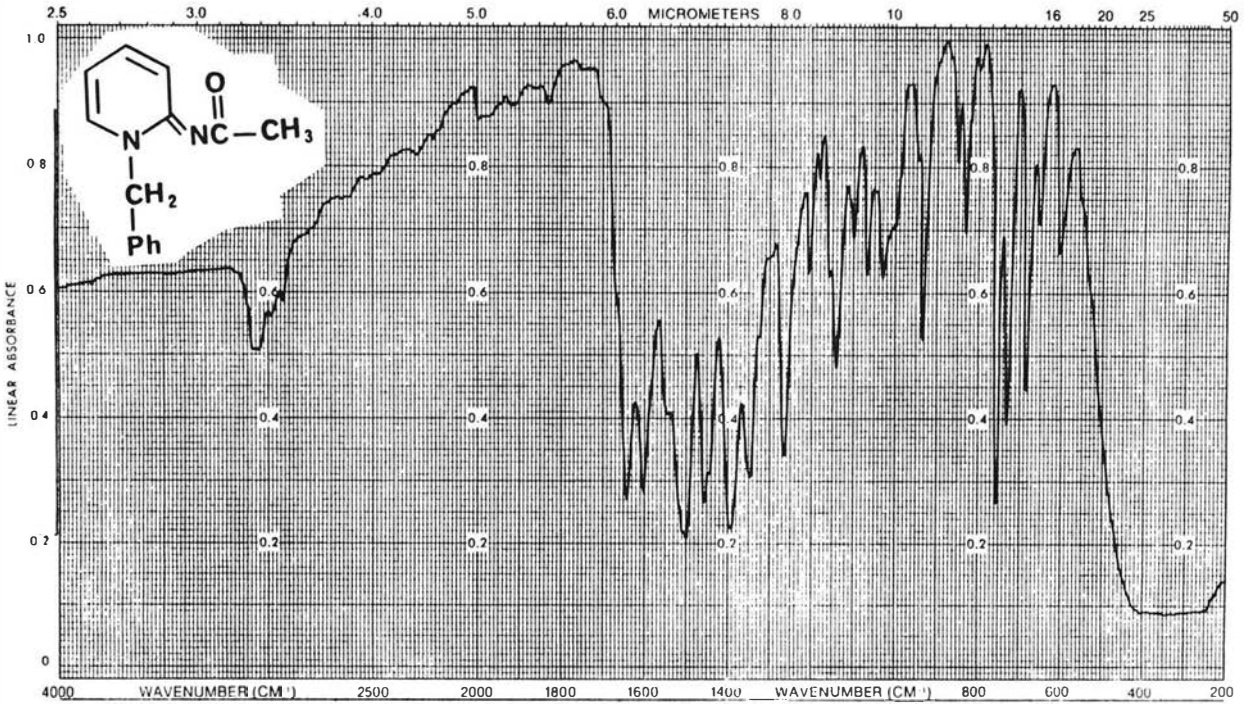


Figure 93. IR Spectrum (Neat) of 1-Benzylpyridinium-2-Acylimide 66.

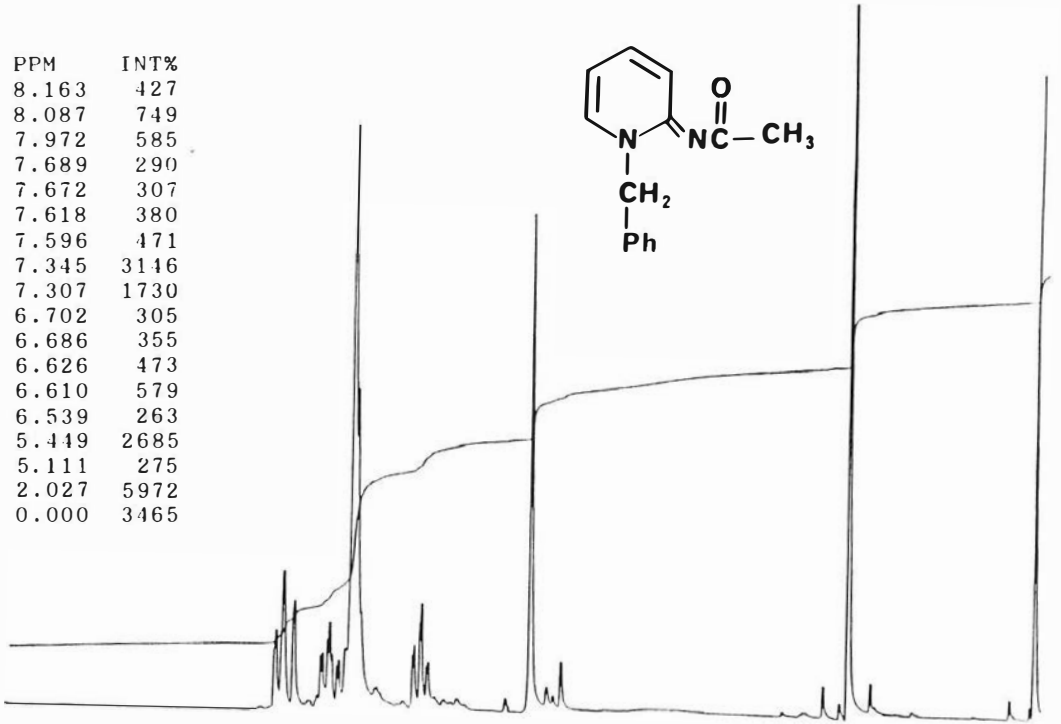


Figure 94. ^{1}H-NMR Spectrum (90MHz) of 1-Benzylpyridinium-2-Acylimide 66.

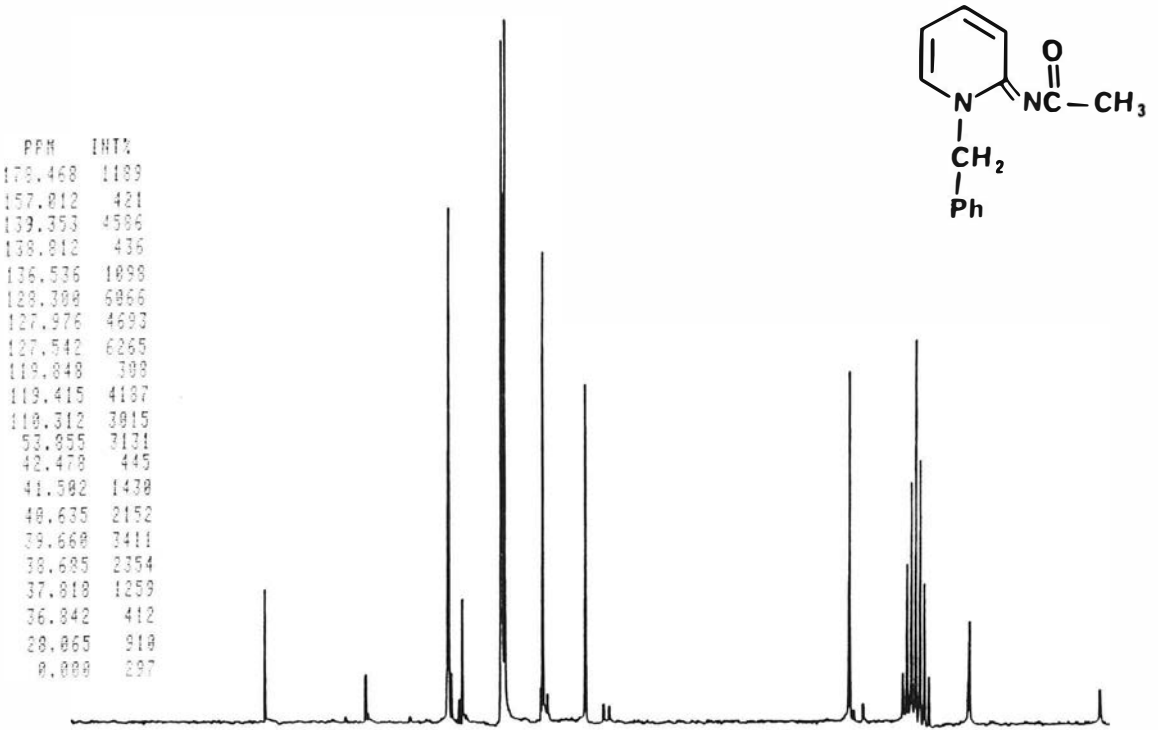
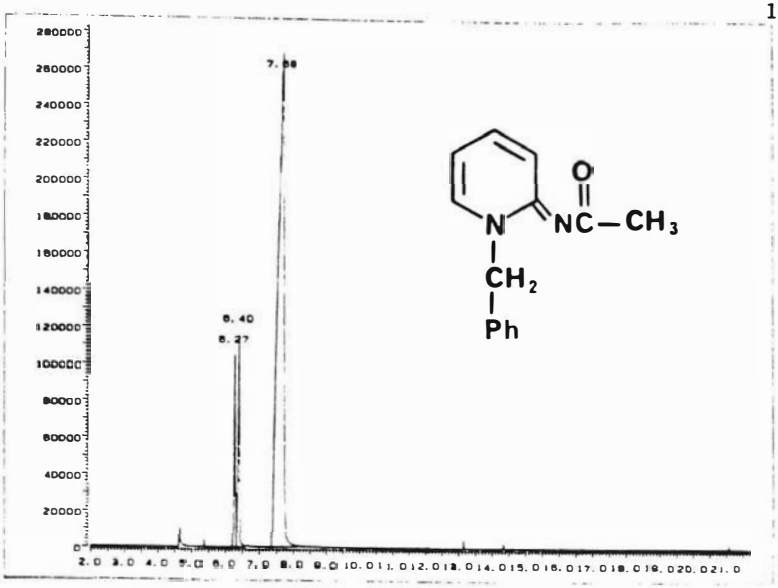


Figure 95. ^{13}C-NMR Spectrum of 1-Benzylpyridinium-2-Acylimide 66.



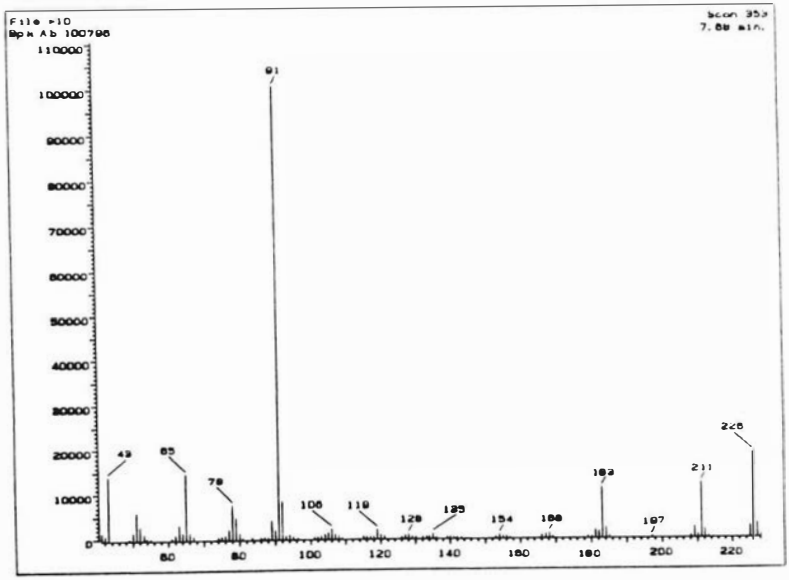


Figure 96. GC/Mass Spectrum of Compound 66.

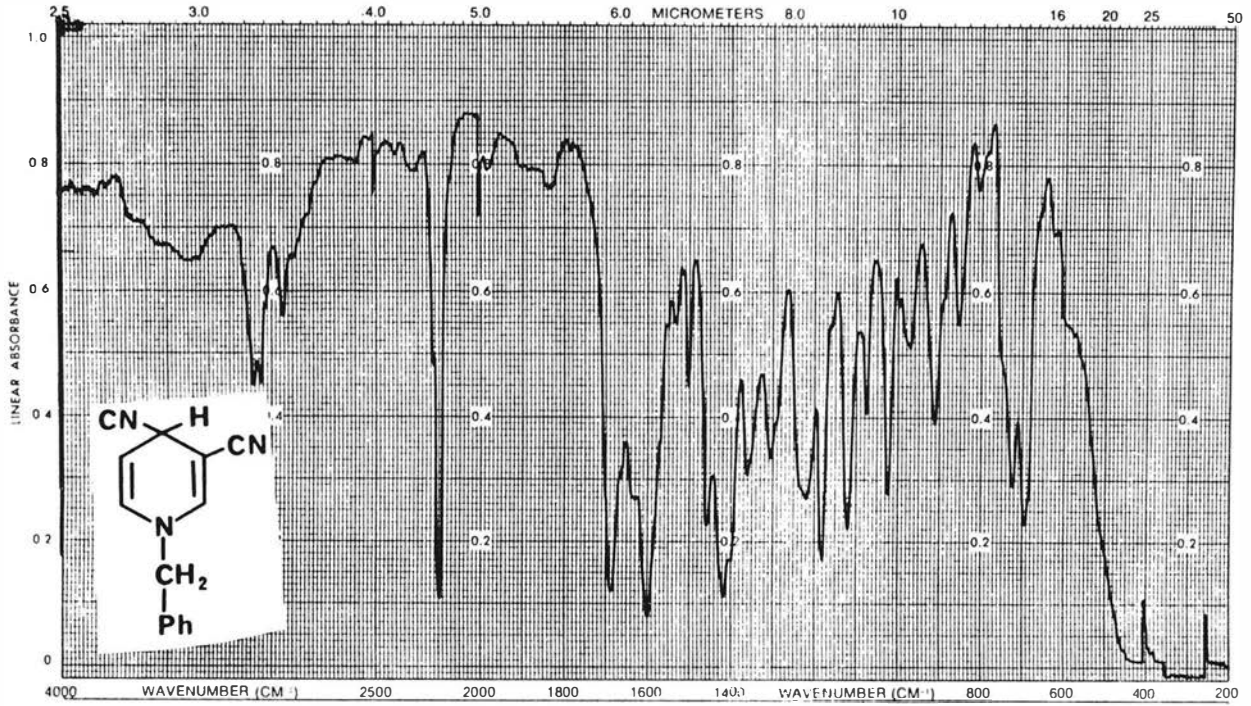


Figure 97. IR Spectrum (Neat) of 1-Benzyl-3,4-Dicyano-1,4-Dihydropyridine 69.

PPM	INT%
9.040	81
7.781	26
7.612	52
7.492	1015
7.482	1036
7.433	245
7.351	3598
7.242	291
7.078	83
6.375	405
6.359	415
6.294	475
6.234	53
5.727	25
5.133	129
4.915	302
4.871	551
4.839	139
4.779	1406
4.730	403
4.495	2247
4.234	49
4.174	21
3.356	191
2.517	38
2.495	44
0.659	34
0.266	45
0.038	308
0.000	6613

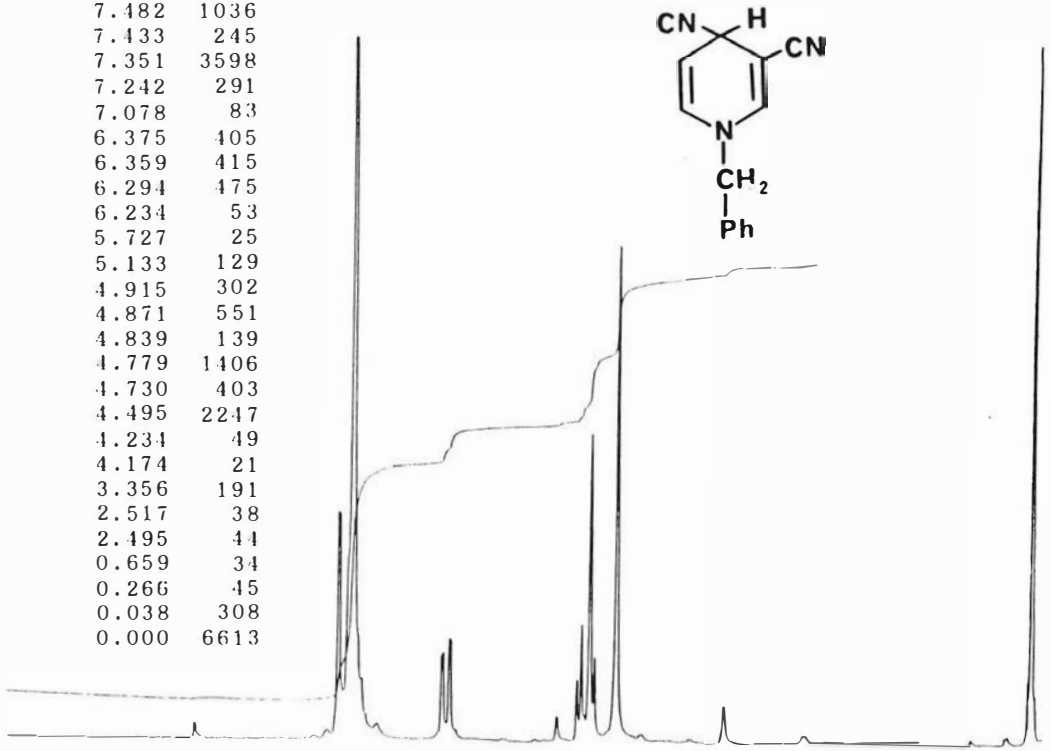


Figure 98. ^{1}H-NMR Spectrum (90Hmz) of 1-Benzyl-3,4-Dicyano-1,4-Dihydropyridine 69.

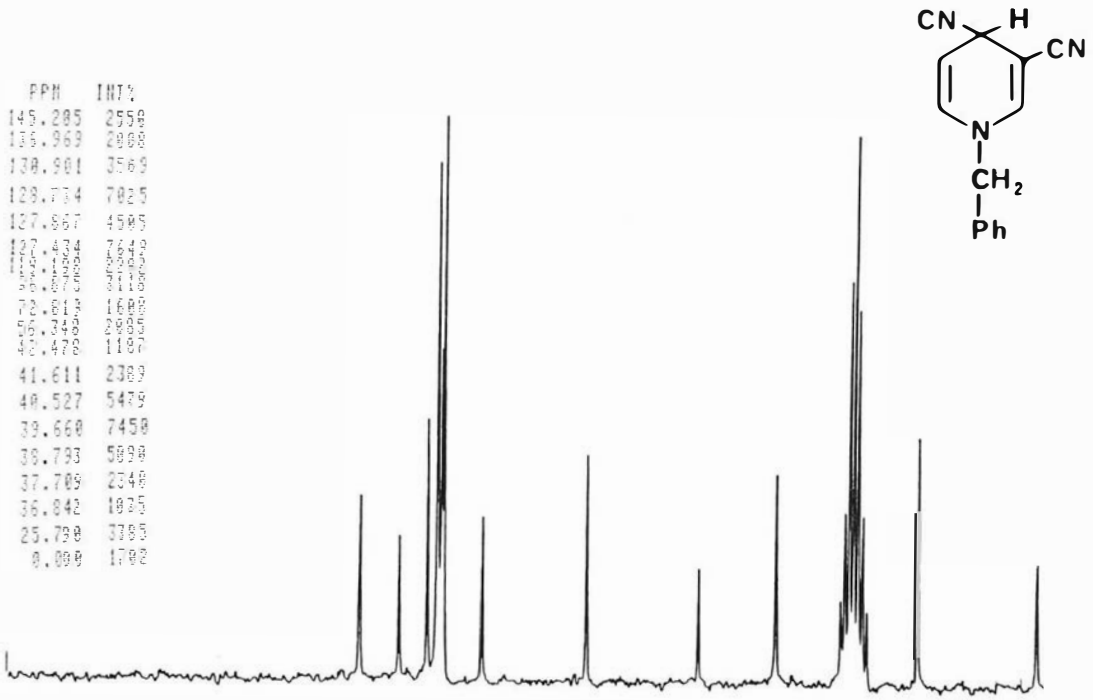


Figure 99. ^{13}C-NMR Spectrum of Compound 69.

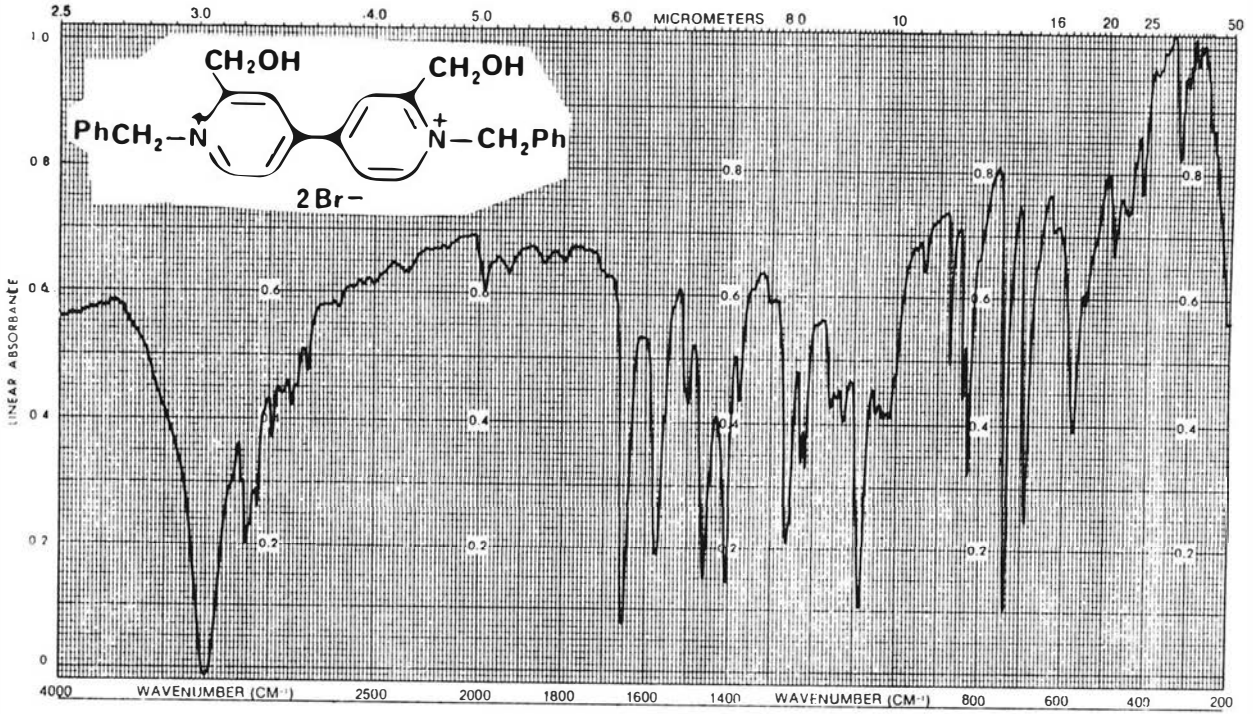


Figure 100. IR Spectrum (KBr) of 1,1'-Dibenzyl-2,2'-Bis(Hydroxymethyl)-4,4'-Bipyridinium Dibromide 75.

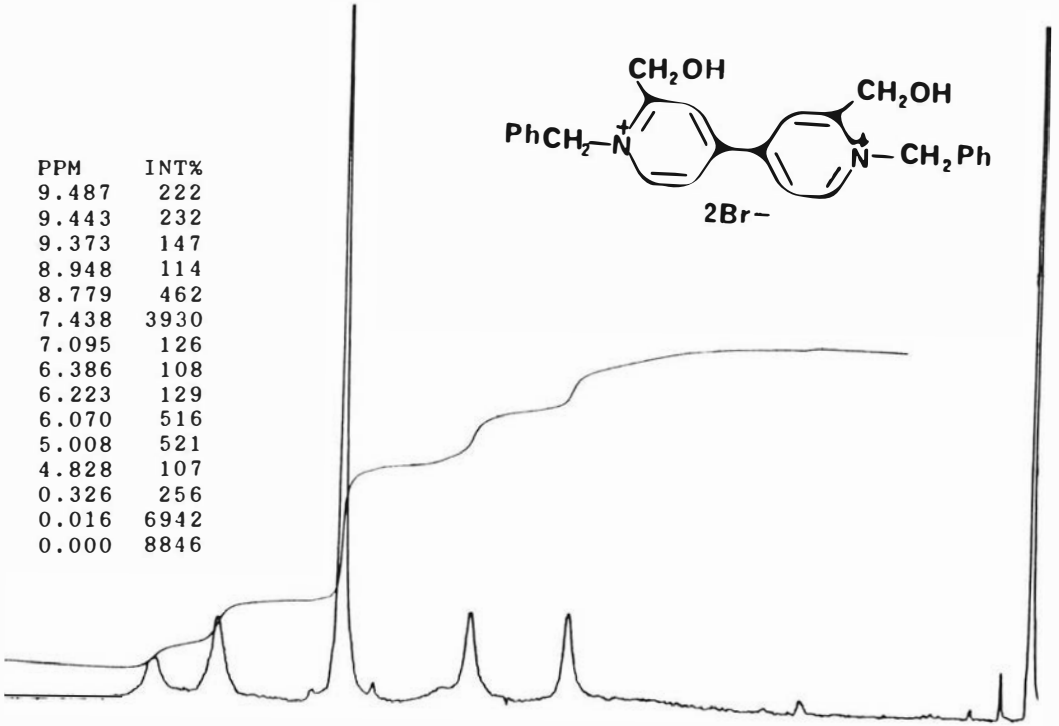


Figure 101. ^{1}H-NMR Spectrum (90MHz) of Compound 75.

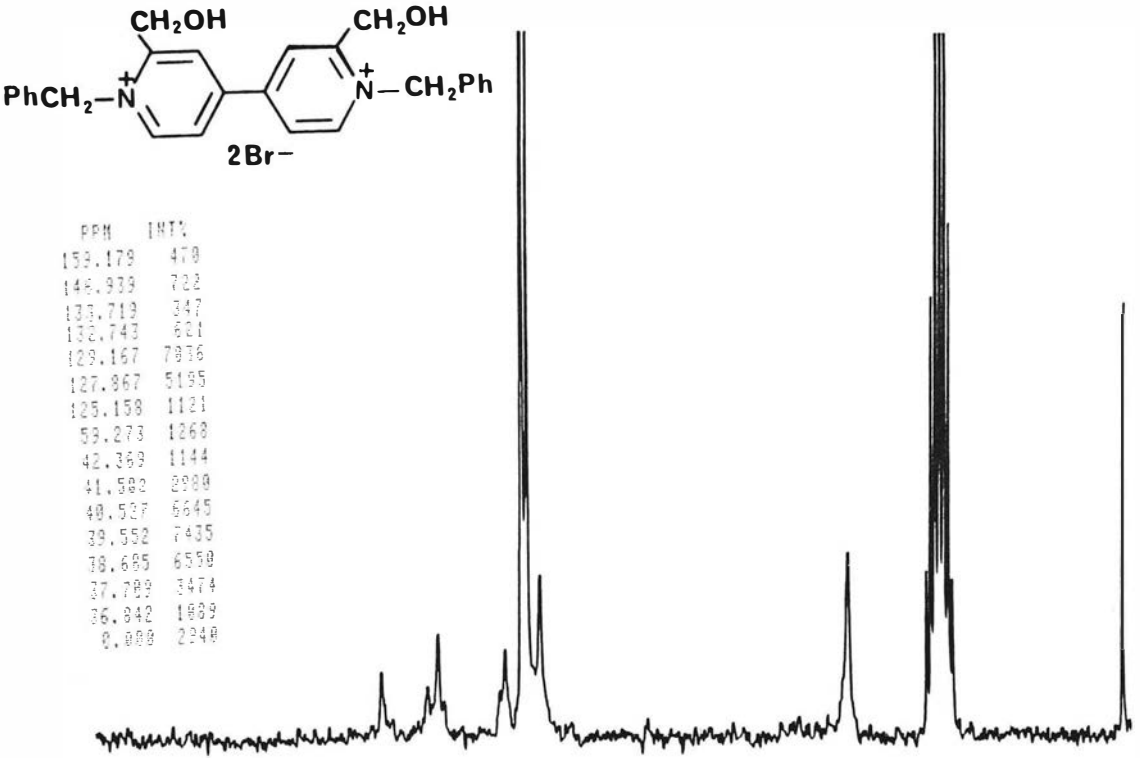


Figure 102. ^{13}C-NMR Spectrum of Compound 75.

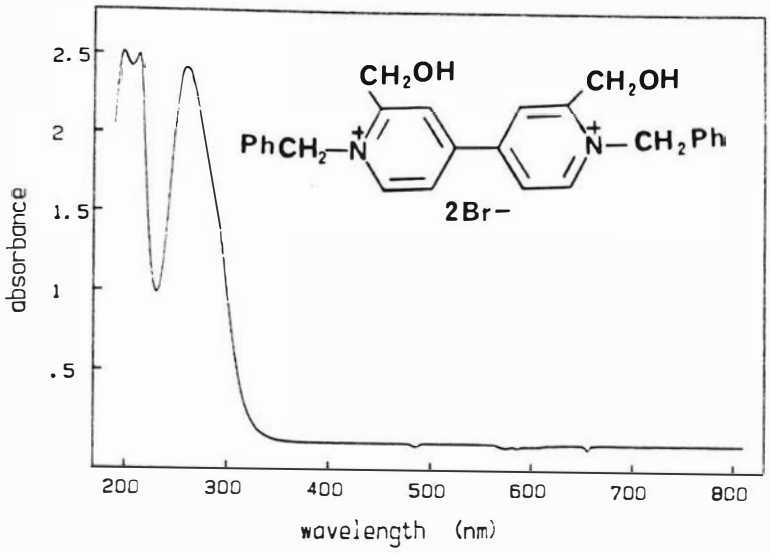


Figure 103. Absorption Spectrum of Compound 75 in Water.

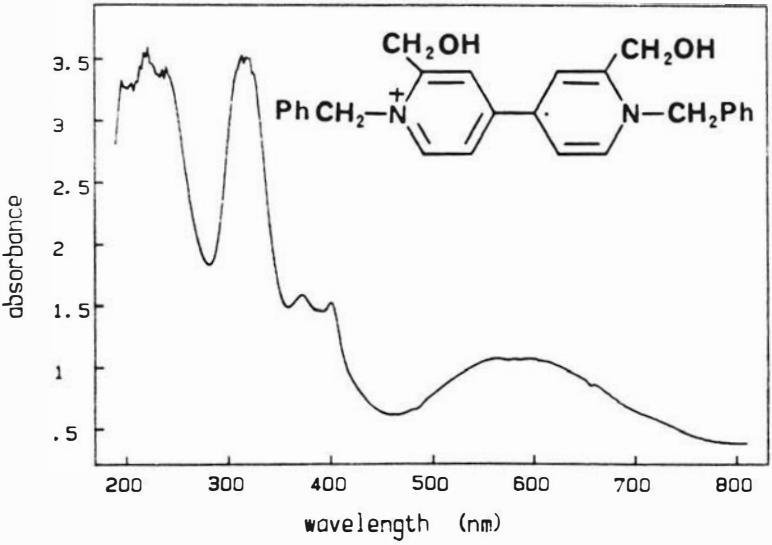


Figure 104. Absorption Spectrum of Bipyridinium Cation Radical 74 in Water.

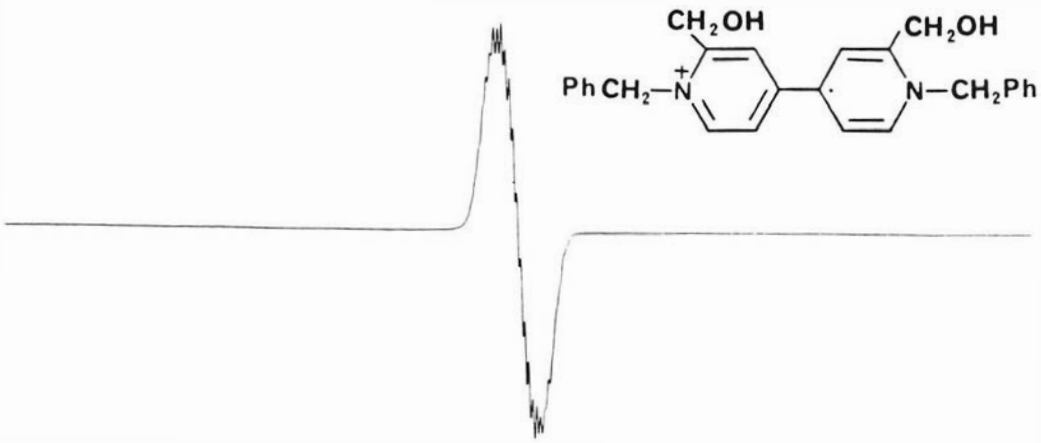


Figure 105. Electron Spin Resonance Spectrum of Compound 74.

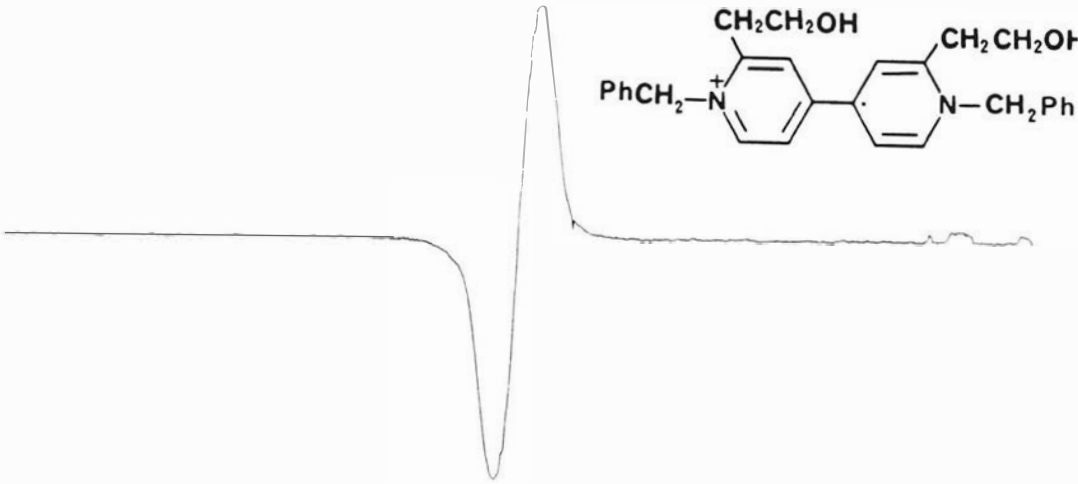


Figure 106. Electron Spin Resonance Spectrum of Bipyridinium Cation Radical 76.

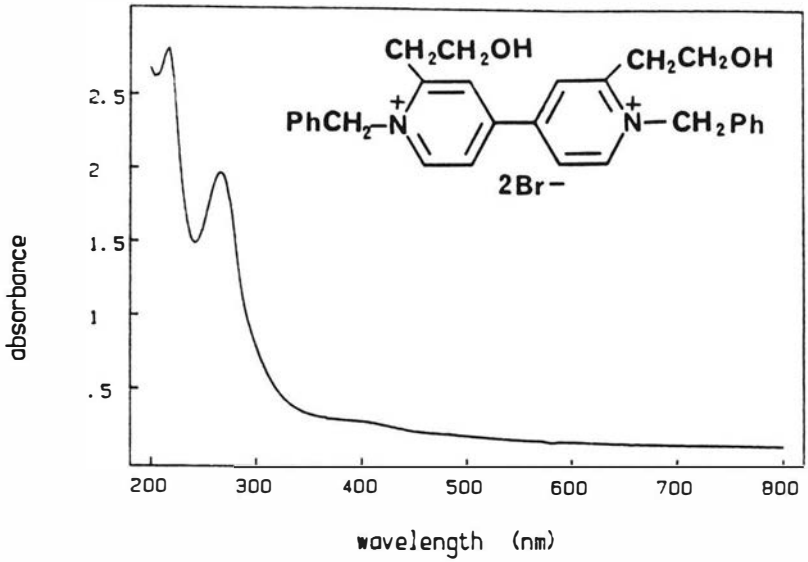


Figure 107. Absorption Spectrum of Bipyridinium Dication 78.

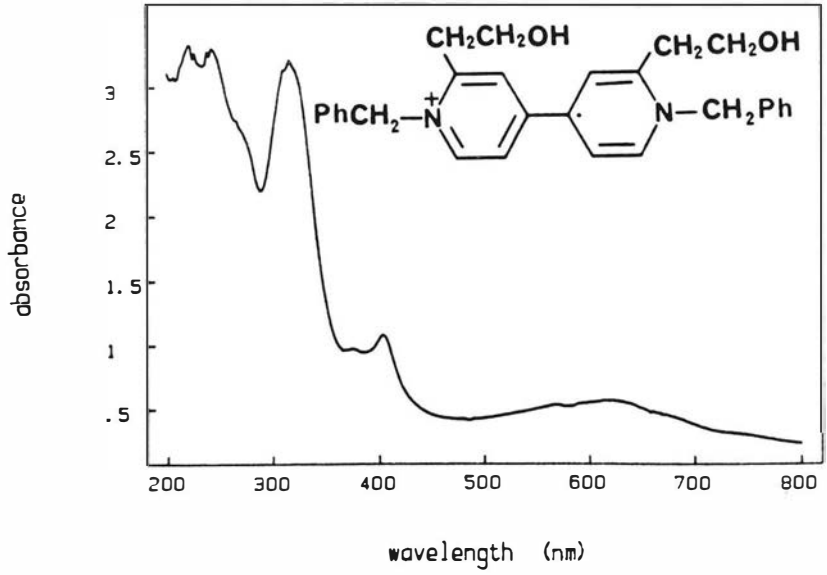


Figure 108. Absorption Spectrum of Compound 76.

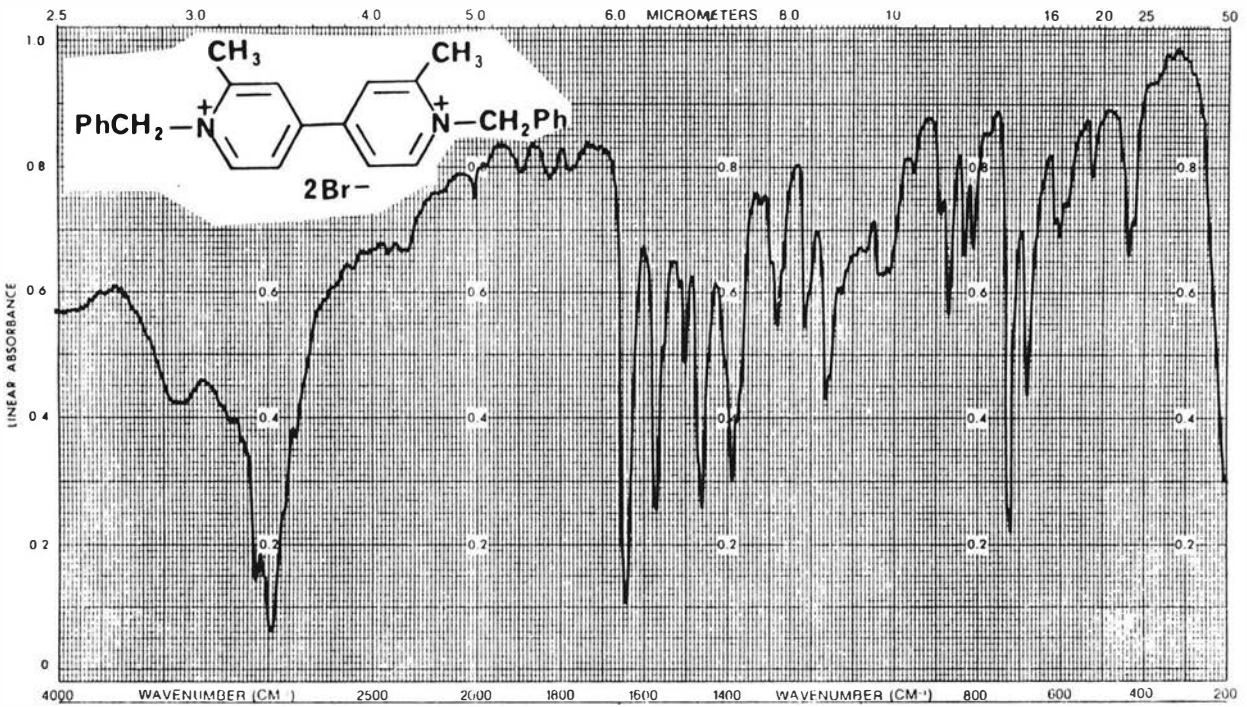


Figure 109. IR Spectrum (KBr) of 1,1'-Dibenzyl-2,2'-Dimethyl-4,4'-Bipyridinium Dibromide 81.

PPM	INT%
9.078	271
9.007	327
8.484	397
8.135	250
8.359	194
7.590	336
7.547	667
7.511	1027
7.422	455
5.950	1028
5.073	334
4.790	7358
4.501	303
3.716	73
3.640	64
3.247	63
2.964	1810
2.681	77
1.286	75
1.204	156
1.122	66
0.000	248

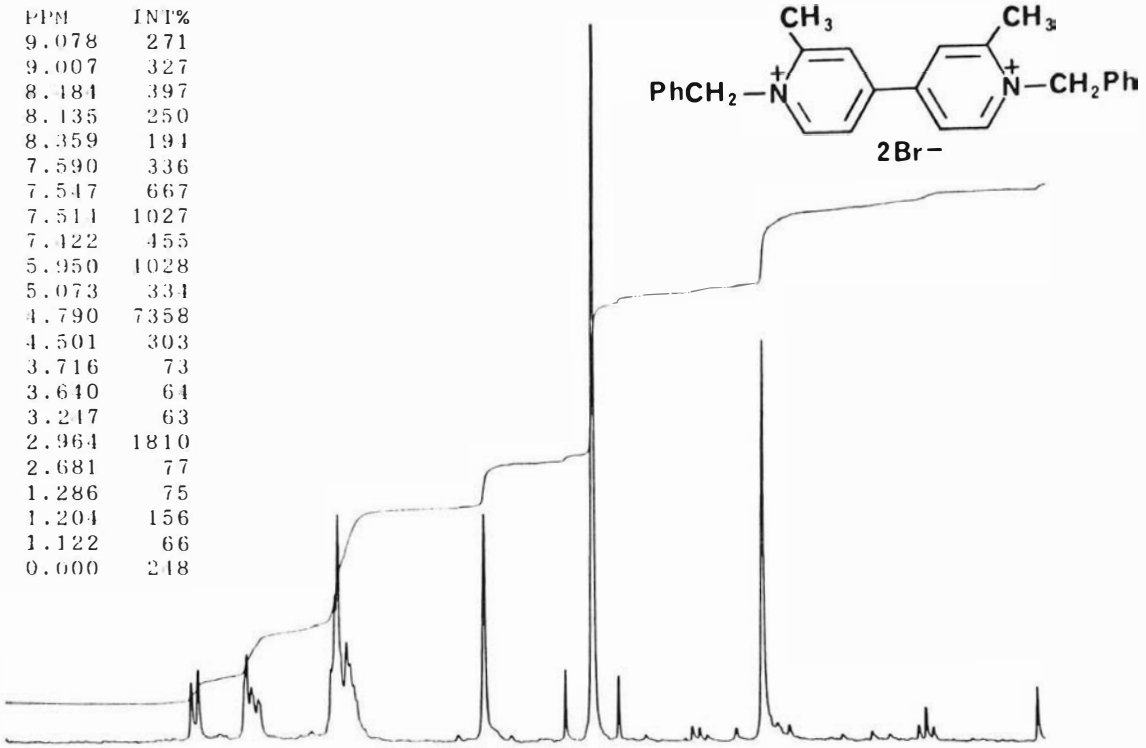


Figure 110. ^{1}H-NMR Spectrum (90MHz) of Compound 81.

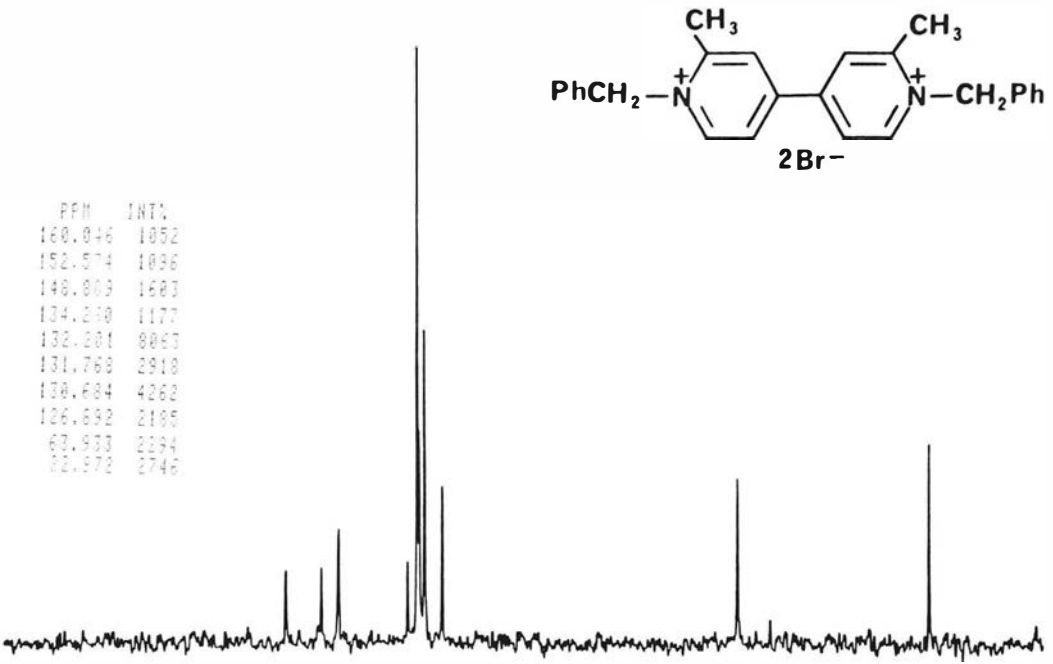


Figure 111. ^{13}C-NMR Spectrum of Compound 81.

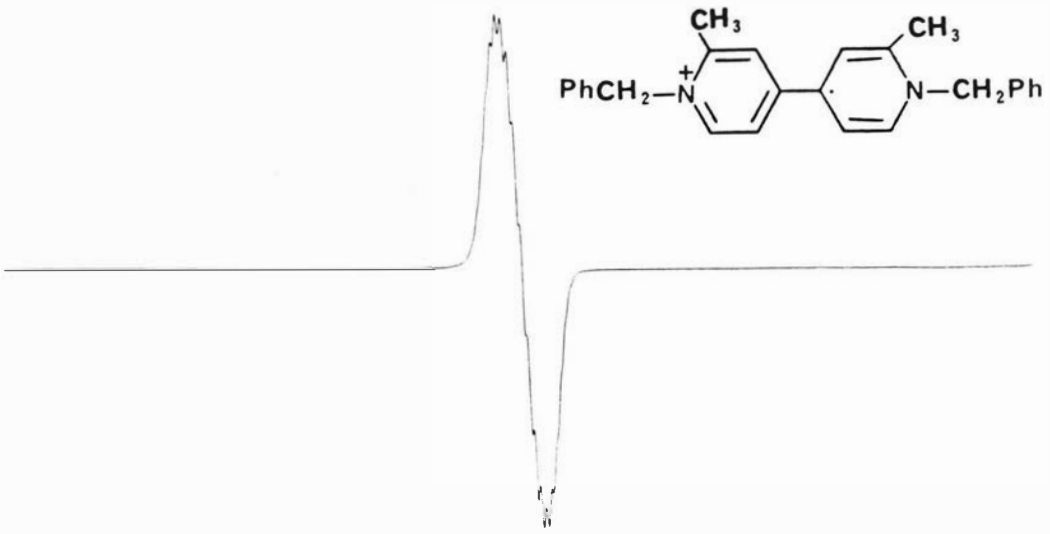


Figure 112. Electron Spin Resonance Spectrum of Bipyridinium Cation Radical 79.

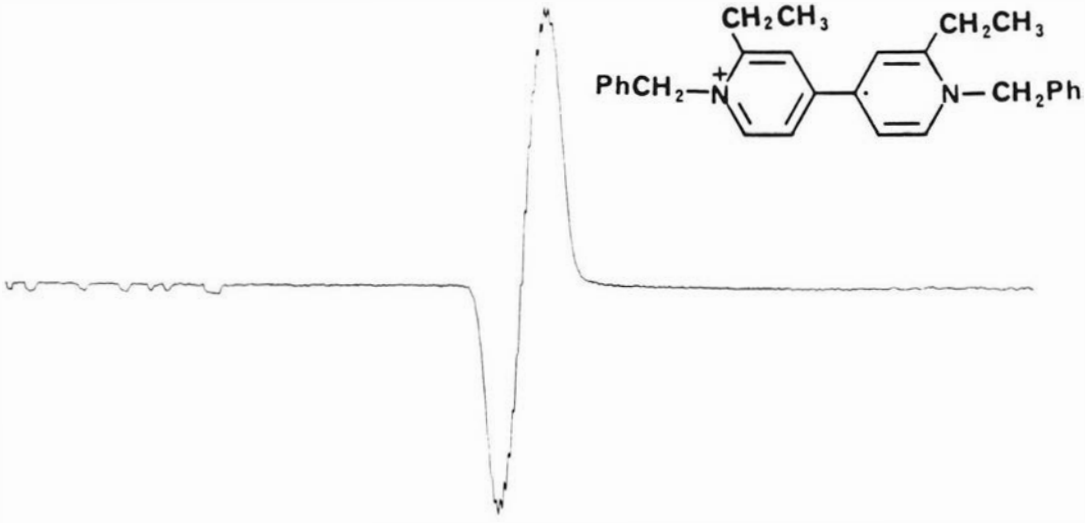


Figure 113. Electron Spin Resonance Spectrum of Bipyridinium Cation Radical 83.

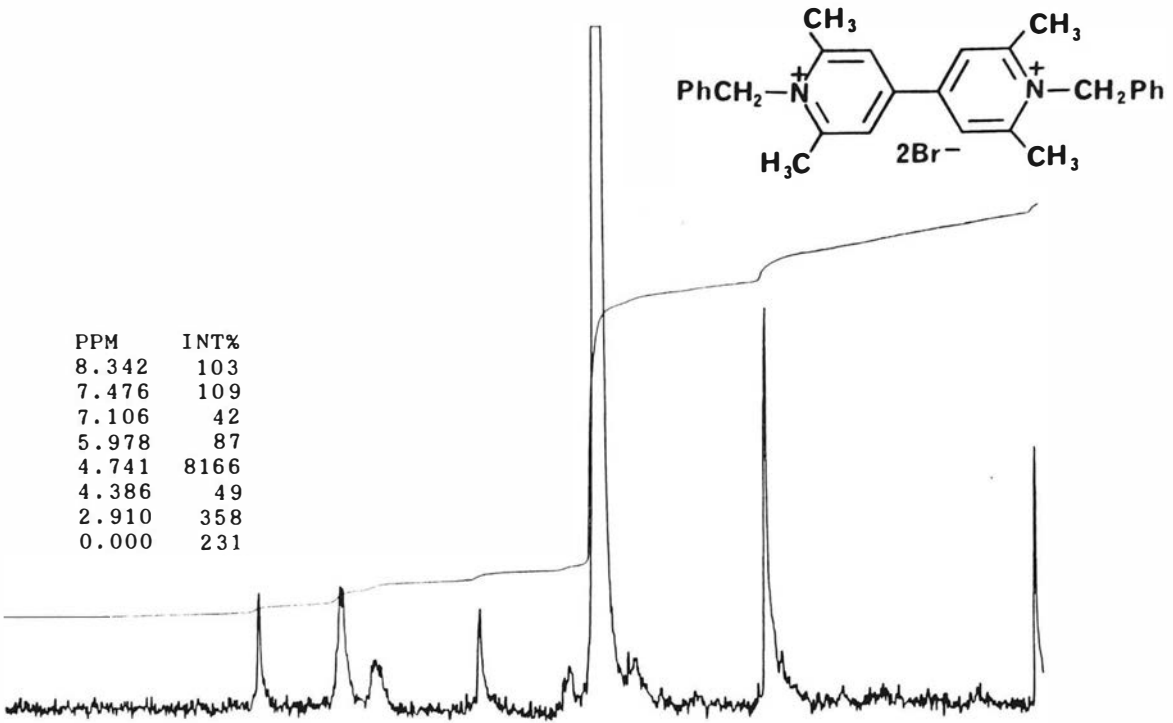


Figure 114. ^{1}H-NMR Spectrum (90MHz) of Compound 87.

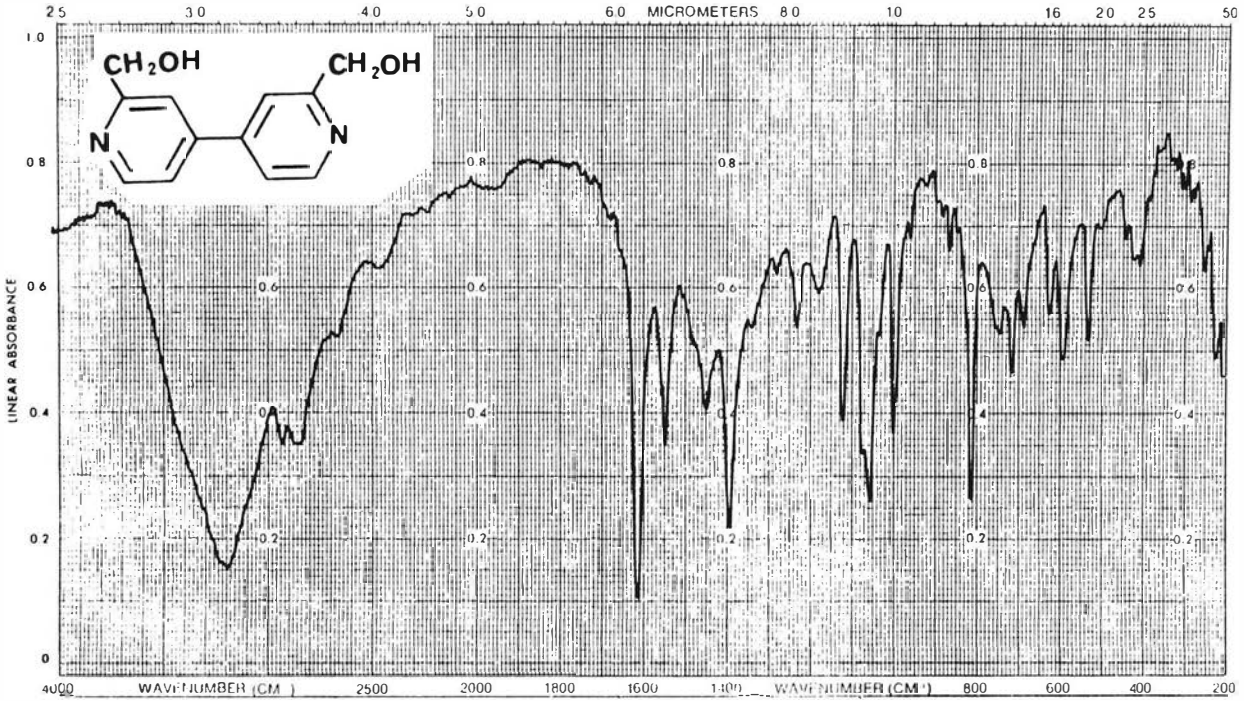


Figure 115. IR Spectrum (KBr) of 2,2'-Bis (Hydroxymethyl)-4.4'-Bipyridine 89.

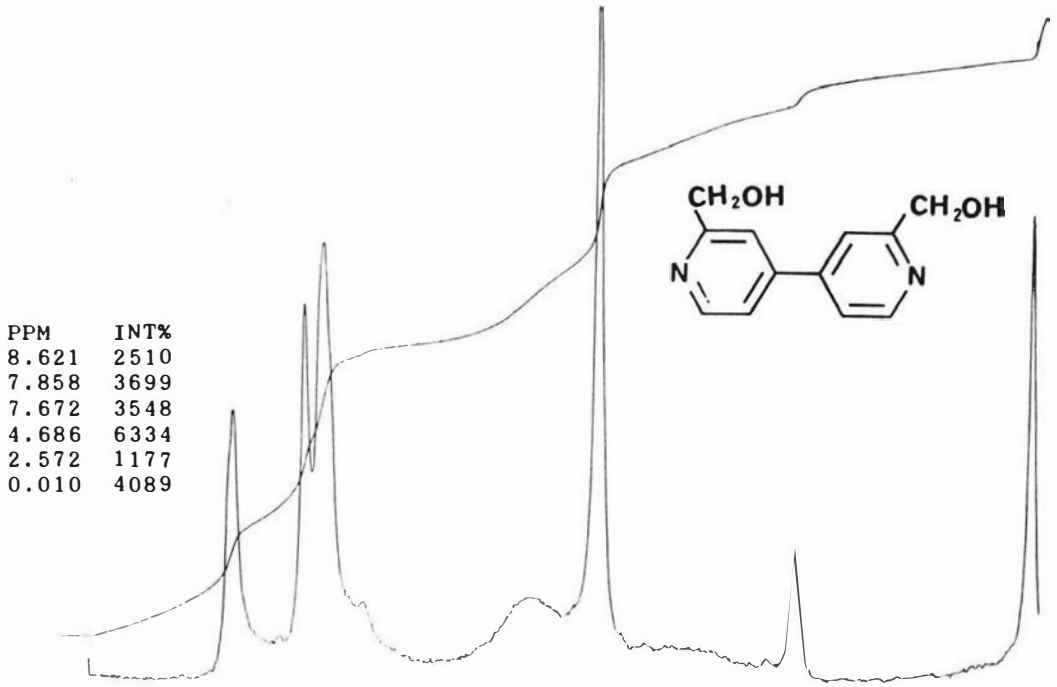


Figure 116. ^{1}H-NMR Spectrum (90MHz) of Compound 89.

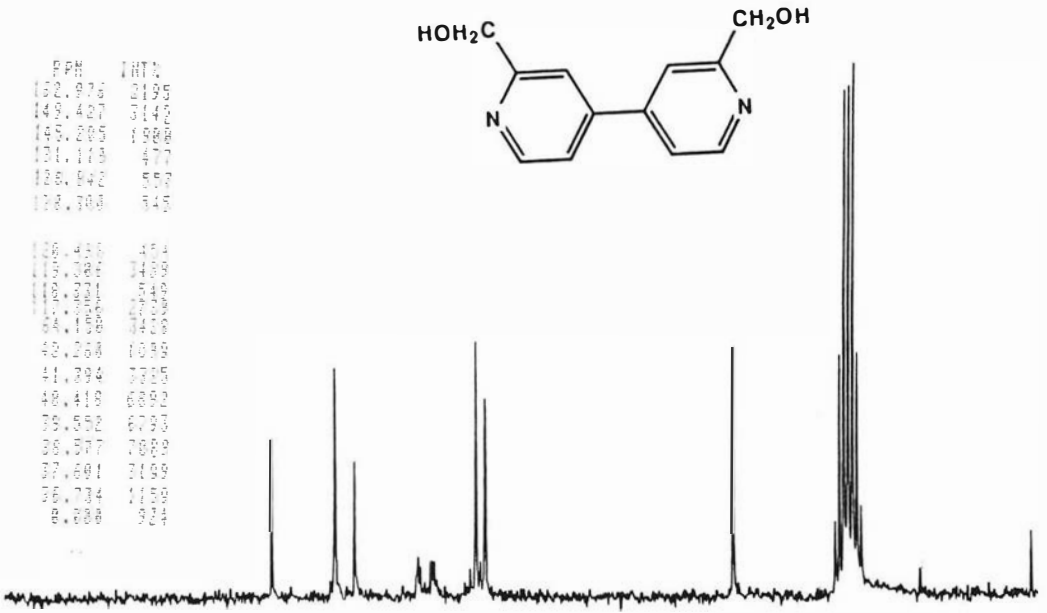


Figure 117. ^{13}C-NMR Spectrum of Compound 89.

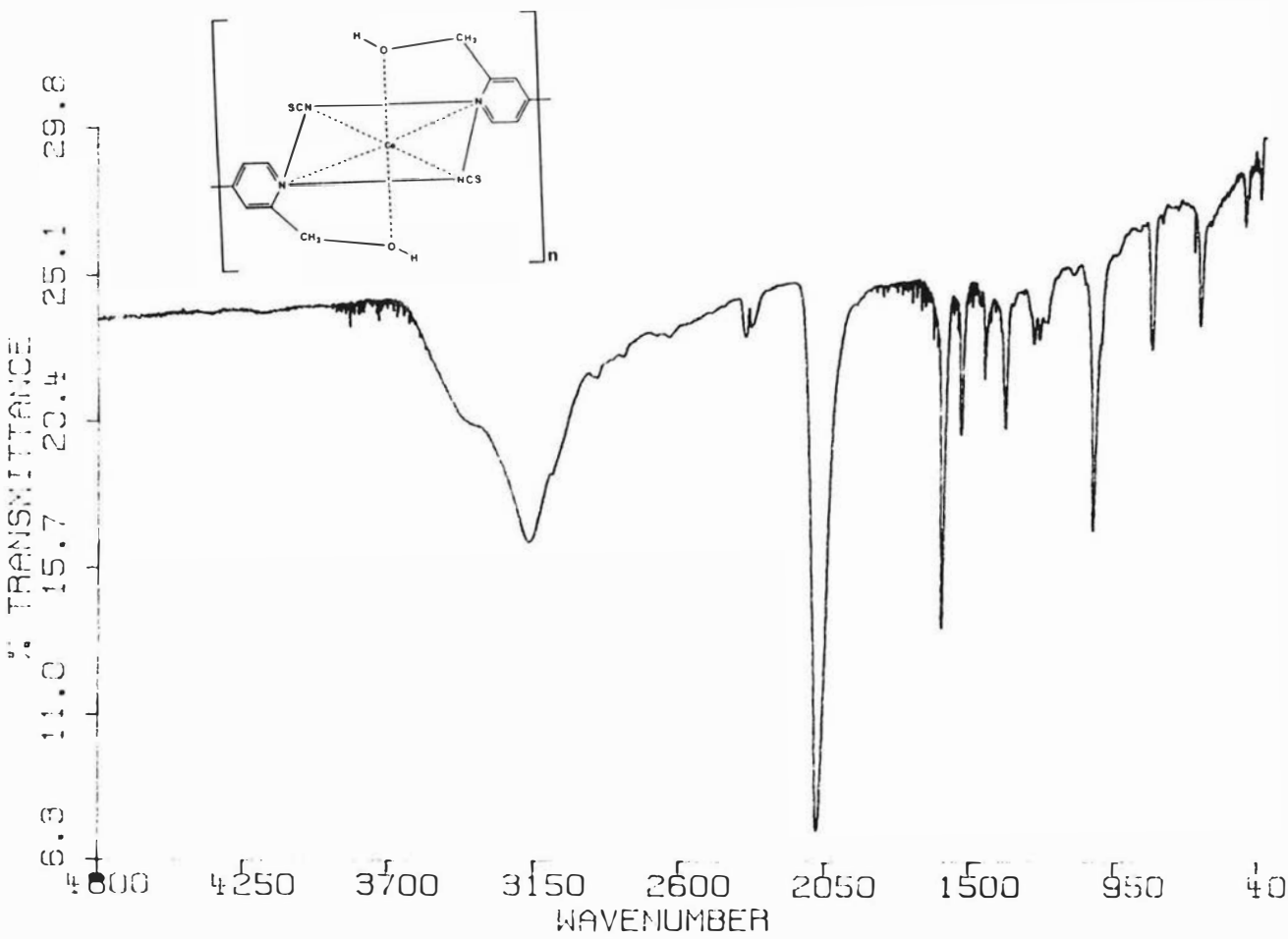


Figure 118. IR Spectrum (KBr) of 2,2'-Bis(Hydroxymethyl)-4,4'-Bipyridine Cobalt Thiocyanate Complex 94.

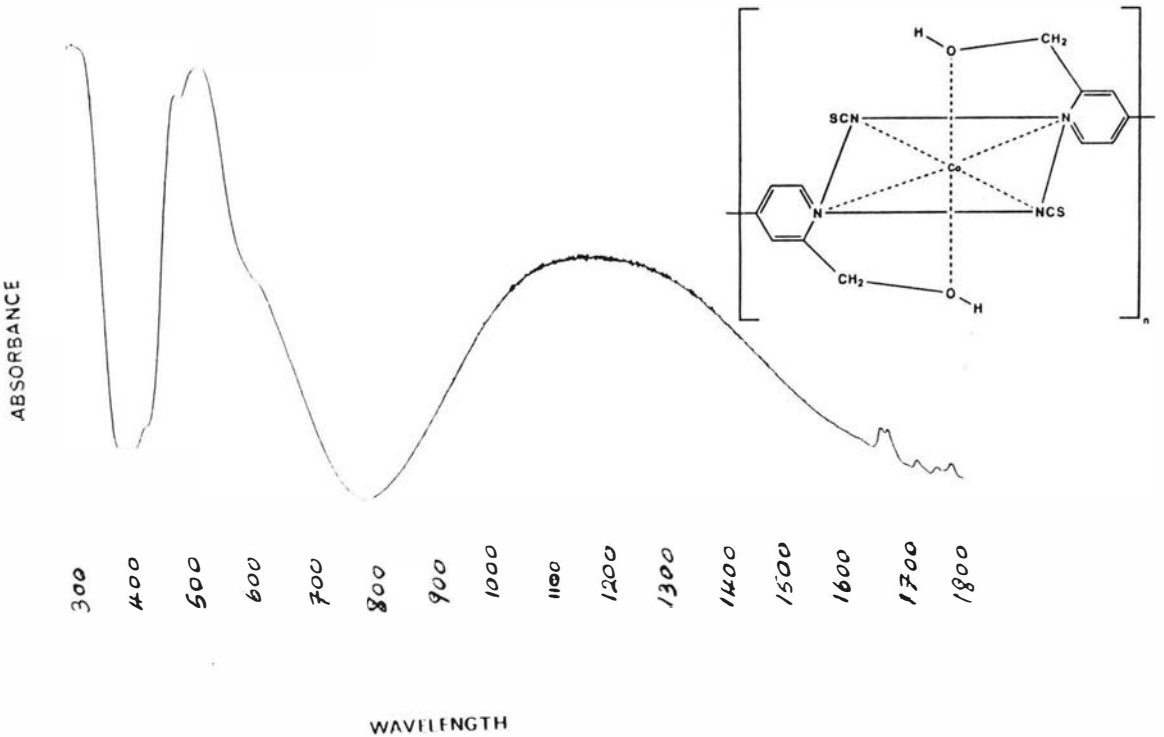


Figure 119. Reflectance Spectrum of Compound 94.

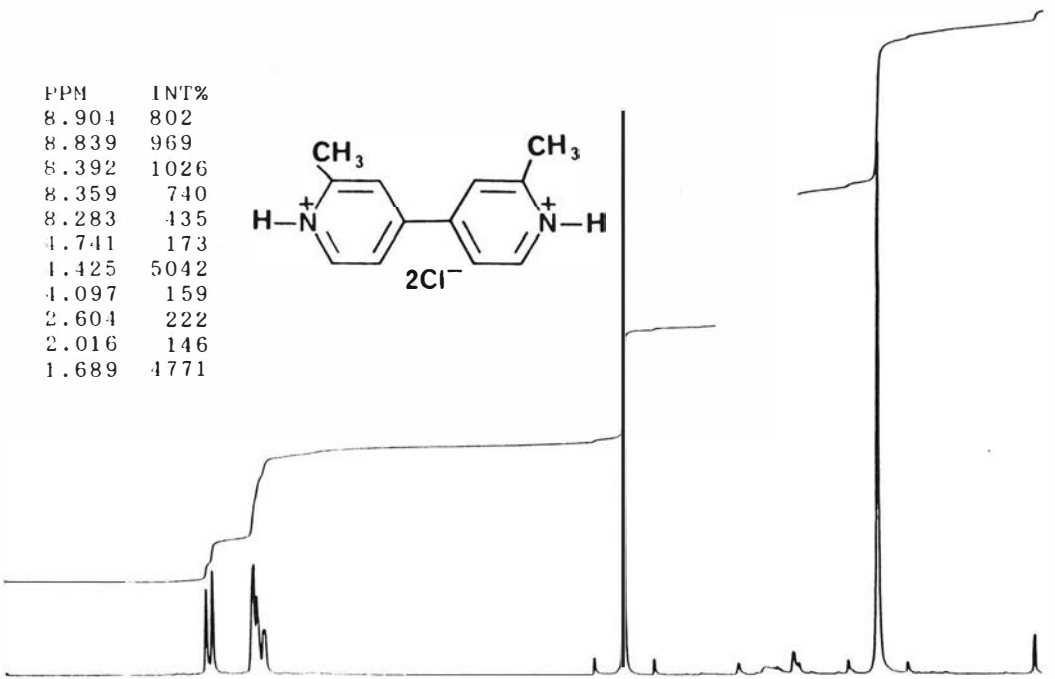


Figure 120. ^{1}H-NMR Spectrum (90MHz) of 2,2'-Dimethyl-4,4'-Bipyridyl Dihydrochloride 91.

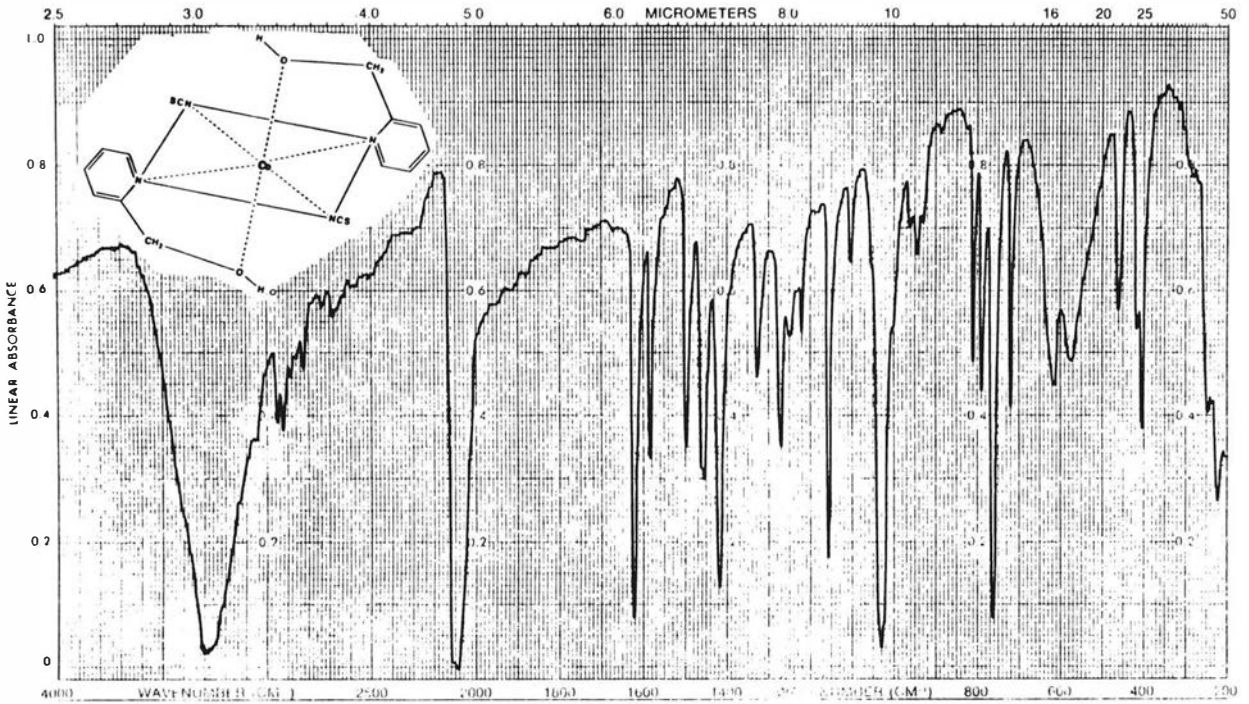


Figure 121. IR Spectrum (KBr) of 2-(Hydroxymethyl)pyridine Cobalt Thiocyanate Complex 93.

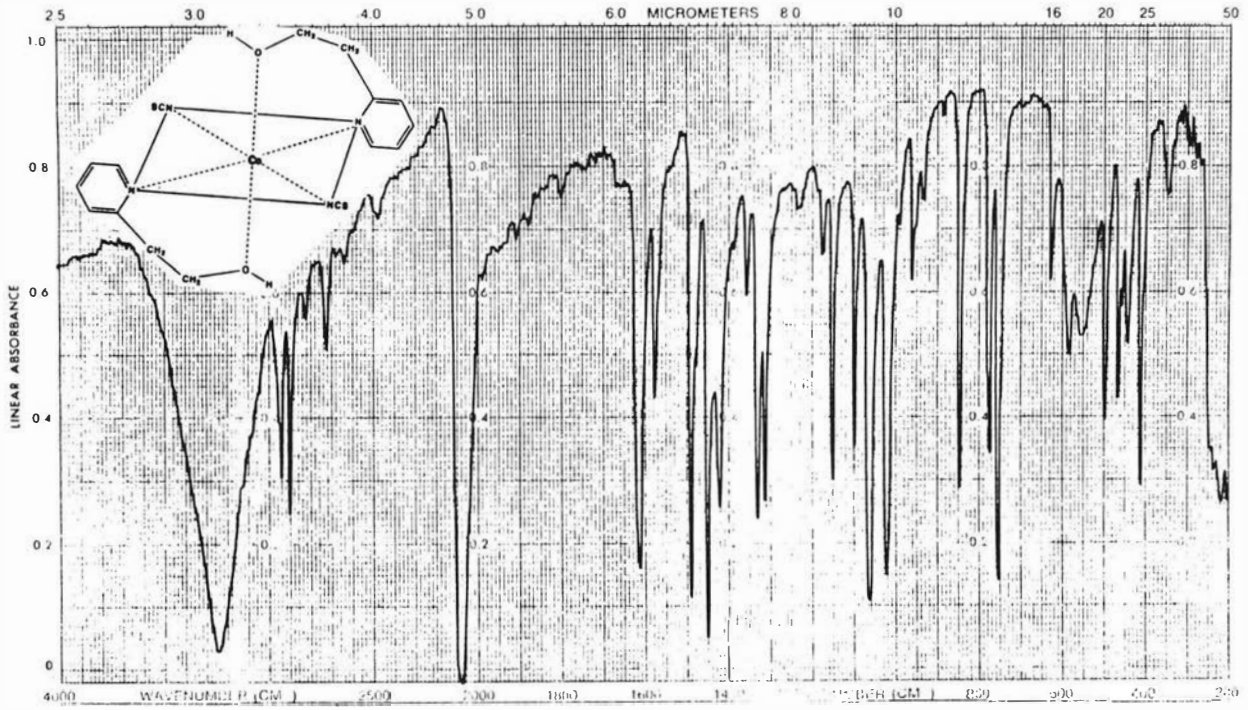


Figure 122. IR Spectrum (KBr) of 2-(2-Hydroxyethyl)pyridine Cobalt Thiocyanate Complex 96.

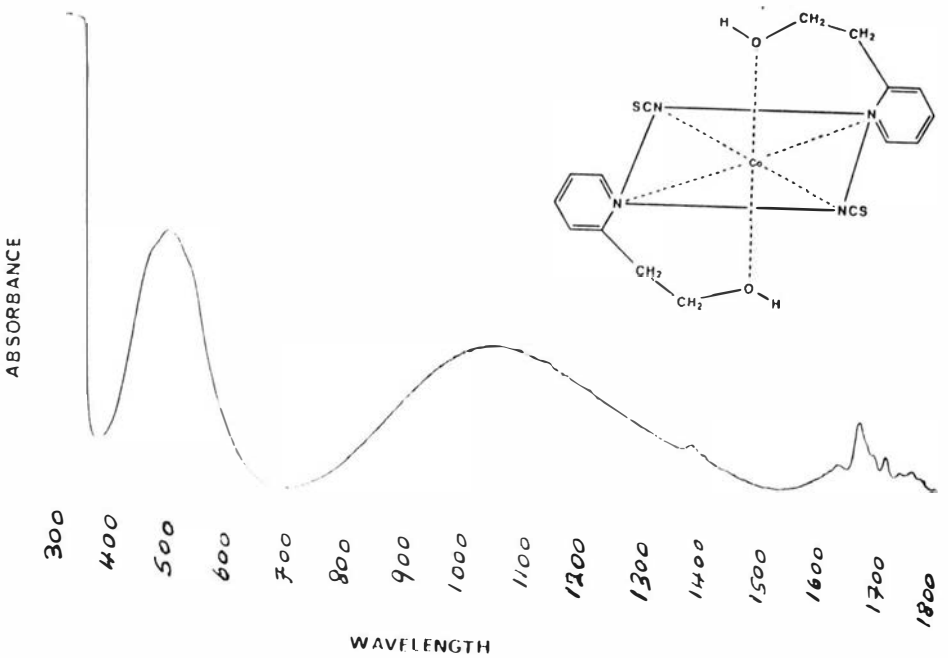


Figure 123. Reflectance Spectrum of Compound 96.