PHYSICO-CHEMICAL INVESTIGATIONS

of

SUBSTITUTED HYDROXYPYRIDINES

A Thesis

submitted for the

Degree of Doctor of Philosophy

in the

Australian National University

by

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June 1962

The work described in this thesis was carried out by the candidate at the Australian National University. Where the work of others was used, appropriate references have been given.

J.C.B. White

I thank Dr E. Spinner for supervision throughout this work, and Professor A. Albert, Dr D.J. Brown and Dr D.D. Perrin for helpful advice and discussions.

Grateful acknowledgement is also made to the Australian National University for the award of a Scholarship.

CONTENTS

PREFACE.

Two tautomeric forms may be written for the mono-aza-heterocyclic hydroxy-compound, 2-hydroxy-pyridine. Such tautomerism is possible for all compounds containing the group R-CO-NHR', the amides, ureas and heterocyclic hydroxy-compounds (amides), and it is now well established[1-6] that all of these substances exist in the neutral state as the "keto" forms (Nos. 1, 5 and 9, in the diagrams on pages iii, iv). A similar tautomerism is possible for their cations, the two forms of which are derived by proton addition to the nitrogen (N-protonation) or oxygen (O-protonation) atoms. The question of which of these forms predominates is still the subject of debate. In the anions formed by these substances, the mobile hydrogen atom has been removed, and the corresponding structures are canonical forms of resonance hybrids.

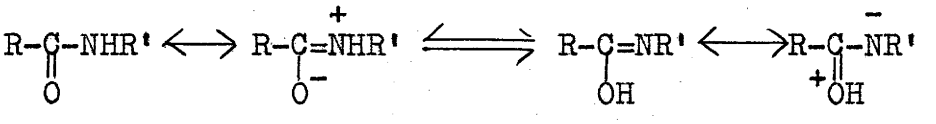
In this thesis, the ultra-violet spectra, vibration spectra and ionization constants of some substituted 2-hydroxypyridines are studied, and it is shown that all the substances exist as pyridones in the neutral form. Particular attention is given to the cations; the vibration spectra clearly indicate

that certain of these have the O-protonated structures, and the spectra of the other cations are consistent with their having such structures also.

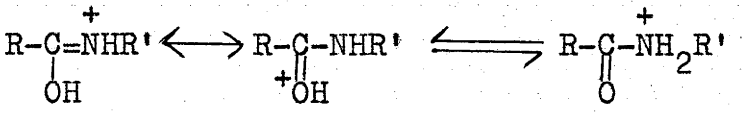
The infra-red spectra of certain of the 2-hydroxy-pyridine anions suggest that they are most closely represented by the canonical form in which the negative charge resides on the oxygen atom (13a, page iv), and the data for the other anions examined are interpreted in similar terms.

TAUTOMERIC EQUILIBRIA AND RESONANCE FORMS.

A. Amides.

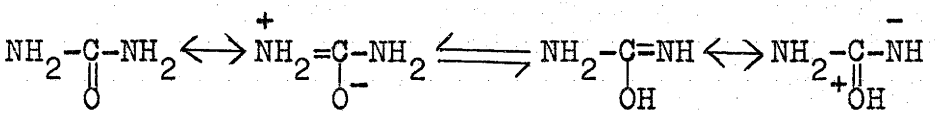


1a 1b 2a 2b



3a 3b 4

B. Urea.



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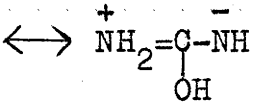

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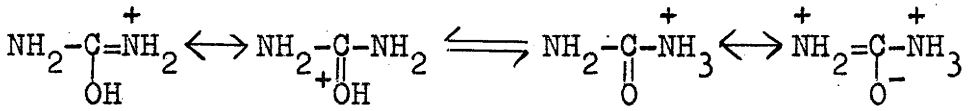

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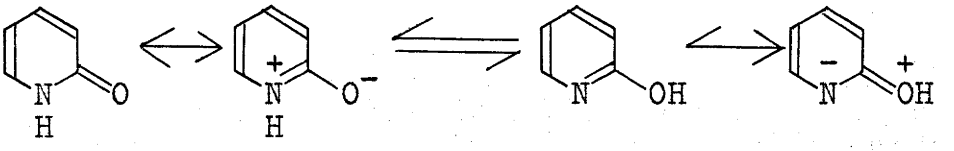
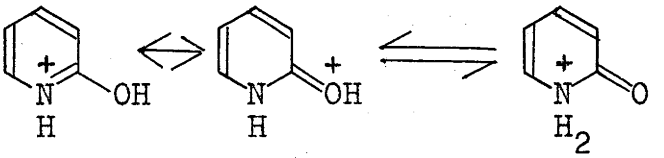
TAUTOMERIC EQUILIBRIA AND RESONANCE FORMS.

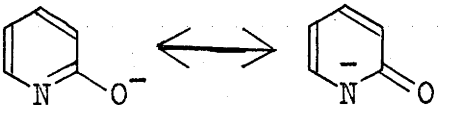
C. Pyridones.



9a 9b 10a 10b



11a 11b 12



13a 13b

CHAPTER 1.

INTRODUCTION.

A. Tautomeric Equilibria.

The word "tautomerism" was suggested in 1885 by Laar[7], who discussed the properties of isatin, ethyl acetoacetate, p-nitrosophenol and 4-phenylazo-1-naphthol. He showed that these substances behaved as though they contained two isomers, which differed only in the position of a single hydrogen atom, and proposed that this "mobile" hydrogen atom occupied a mean position between the two possible sites. The dual character of the substances was thought to arise as the hydrogen atom oscillated to one side or the other of this mean position. This view was effectively disproved, however, when certain tautomeric substances were isolated in two different solid forms, and it was shown that the tautomers had individual existence[8]. The individuality of the tautomers has been demonstrated even for substances such as 1-phenylazo-2-naphthol[9], in which the mobile hydrogen atom lies in a hydrogen bond linking the two possible sites.

Some examples of tautomeric equilibria are:

(1) Three-carbon system $\quad R-\underset{H}{C}-C=C-R' \quad R-C=C-\underset{H}{C}-R'$

(2) Azomethine system $\quad R-\underset{H}{C}-C=N-R' \quad R-C=C-\underset{H}{N}-R'$

(3) Keto-enol system $\quad R-\underset{H}{C}-C=O \quad R-C=C-\underset{H}{O}$

(4) Amido-imidol system $R-\underset{H}{N}-C=O$ $R-N=C-\underset{H}{O}$

(2), (3) and (4) (and others) may be regarded as being derived from the three-carbon system by the substitution of hetero-atoms for carbon atoms, and vinylogues[10] are possible.

The interconversion of tautomers in the three-carbon system is considered to proceed through the anion

$$R-C=C=C-R'$$

as intermediate[11]. The interconversion of keto-enol tautomers is catalysed by acids and (very strongly) by bases[12], so that both anionic and cationic intermediates (14 and 15) may be postulated.

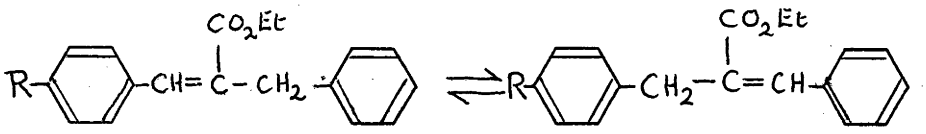
$R-C=C=O$ (H, H) — 14 $\qquad$ $R-C=C=O$ — 15

In aza-hydroxy tautomeric systems, such as arylazonaphthols, nitrosophenols and amides, both of the possible sites for the proton are capable of partaking in rapid acid-base equilibria, so that both anionic and cationic intermediates may be important under different conditions of acidity or alkalinity. A diagram showing the various equilibria possible for a lactam-lactim system (2-hydroxypyridine) is given on page 75.

The effect of substituents on the equilibrium ratio

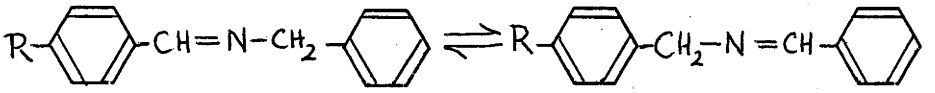
of tautomers has been investigated for several systems. Figures obtained for the ratios

K_1 = [16] / [17] in the α,γ-diphenylpropene equilibrium[13],



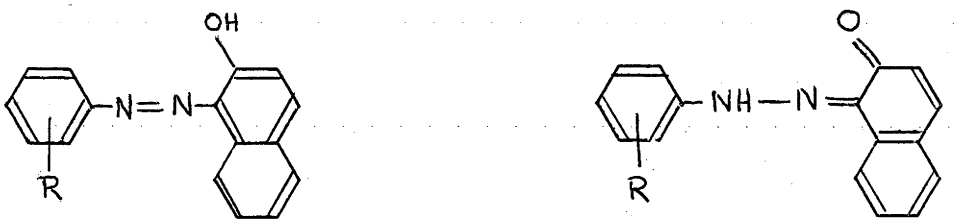
16 17

K_2 = [18] / [19] in the azomethine equilibrium[14],



18 19

and K_3 = [20] / [21] in the 1-phenylazo-2-naphthol equilibrium[15],



20 21

can be correlated qualitatively with the Hammett σ constant for the substituent R, the relative stabilities of the forms 17, 19, and 21 being increased by electron-attracting substituents and decreased by electron-donating substituents.

In some cases the equilibrium ratio of tautomers

is markedly affected by the solvent used. For instance, 2- and 4- hydroxyacridine exist predominantly as enols in non-polar solvents, and as lactams in polar solvents[16], and a similar solvent-dependent equilibrium has been reported for 2-hydroxyphenazine[17]. In the case of the hydroxyacridines, Albert and Short[16] suggest that the more polar[18] lactam form is stabilized relative to the lactim form in a polar solvent. In the phenylazonaphthol system[15] already referred to (20 ⇌ 21), the proportion of the phenylhydrazone tautomer 21 increases as the polarity of the solvent is increased, and a similar phenomenon is observed in the equilibrium of the isomeric 4-phenylazo-1-naphthol system[19]. The importance of hydrogen bonding has been pointed out in connection with the phenylazonaphthol equilibria[19]; where hydrogen bonding between solute and solvent is possible, that tautomer which can form the strongest bonds will be stabilized relative to the other. The ultra-violet spectra of certain nitrosophenols (quinone oximes) suggest that a solvent-dependent equilibrium exists in these, also[20].

The reversible interconversion of tautomers generally proceeds only in the liquid phase, and may be very slow in the absence of catalysts. However, Cairns-Smith[21] has prepared compounds in which the interconversion of tautomers in the solid state would be facilitated, and has interpreted their thermochromism in terms of temperature-dependent tautomeric equilibria

(or temperature-dependent disordering of protons in hydrogen bonds) in the solid state. Hadzi[22] suggested from infra-red spectral data that certain phenylazonaphthols exist as mixtures of tautomers in the solid state, but pointed out that no good precedent has been reported to support such an interpretation.

A wide variety of methods has been used in determining the structures or equilibrium ratios of tautomers. When the interconversion of tautomers proceeds only slowly, chemical methods have proved successful[23]. Other techniques that have been used include measurements of refractive index[24], optical rotation[25], ultra-violet spectra[26, 6a], ionization constants[6b], infra-red spectra[27, 19], and X-ray crystallography[2-4, 28].

Not all of these methods are feasible for the investigation of tautomerism in ionic species. Some of the methods which lend themselves readily to this particular problem will be discussed briefly in the next section.

B. Some Methods for Structural Determination.

Diffraction Methods. X-ray or neutron diffraction procedures usually furnish the complete answer to a structural problem, provided the compound

can be obtained in the form of single crystals of suitable size. The regular, periodic structure of the crystal is used as a diffraction grating, and the intensities of the large number of beams which comprise the diffraction pattern are determined. A variety of mathematical procedures are available with which to attempt the evaluation of the unknown phases, and from these a trial structure is deduced. The diffraction pattern which would be given by such a structure is calculated, and the intensities compared with those observed. The positions of the atoms in the trial structure are adjusted through a series of successive approximations until satisfactory agreement is obtained between the two sets of intensities.

Diffraction methods of structural determination suffer from two main disadvantages: (1) the necessary calculations are tedious and very time-consuming, although modern digital computers have done much to minimise this: (2) in X-ray studies, the positions of the lightest atoms are determined with the least accuracy, so that in general, the positions of hydrogen atoms are not found. Neutron diffraction methods do not suffer from this latter defect, but facilities for such work are restricted.

Although X-ray methods seem unlikely to determine

the position of the added hydrogen atom in an amide cation, in certain cases an unambiguous result could be obtained. In the O-protonated form of N,N-disubstituted amide cations, the arrangement of bonds about the nitrogen atom is trigonal, while in the N-protonated form this arrangement is tetrahedral, and since the carbon atoms could be located with certainty, the structure would be established beyond doubt. In other cases, it is possible that hydrogen bonds, which can often be identified with certainty, could show the position of the added hydrogen atom.

Spectroscopic Methods. When a molecule absorbs a quantum of light energy, its energy is increased by an amount:

$$\triangle E = h\nu = hc/\lambda \quad .$$

($\triangle E$ is the energy increment, h is Planck's constant, and ν is the frequency, λ the wavelength, and c the velocity of the radiation.) The increased energy may appear as an increase in the rotational, vibrational, or electronic energy of the molecule. The spacings between the rotational and vibrational energy levels are relatively small, and the transitions between them are excited by infra-red radiation, in the far- and near-infra-red regions respectively. The energy difference between the electronic levels is larger, and transitions

between these are excited by ultra-violet or visible light.

In Raman spectroscopy it is not an absorption spectrum which is measured, but the spectrum scattered by a sample irradiated by a strong source of monochromatic light. When a beam of light of frequency c strikes a sample, most of the incident radiation is scattered without change of frequency, but part of the incident radiation is scattered with frequencies $c \pm \Delta c_i$, Δc_i being vibration (or rotation) frequencies of the molecules comprising the sample.

For both infra-red and ultra-violet spectra, the transition probability is proportional to the square of the "dipole moment of transition", or "transition moment"[29], and when this quantity is zero, the transition is described as "forbidden". For infra-red spectra, it can be shown[30] that absorption will not occur, (i.e. the transition will be forbidden), unless there is a change in the dipole moment of the molecule during the vibration concerned. For Raman spectra, the corresponding requirement is that the polarizability of the molecule change during the vibration[30].

In the case of molecules having a centre of symmetry, (and in the absence of extra-molecular perturbing forces), these requirements prohibit a band from appearing in both the Raman and infra-red spectra[31].

If the centro-symmetrical character of the molecule is destroyed (e.g. by substitution), such prohibitions no longer apply, but often the new bands in each spectrum will appear only weakly.

Ultra-violet spectra are usually obtained using dilute solutions of the sample in a suitable solvent, but spectra can also be determined using solid[32] or gaseous samples. For solutions, a convenient concentration in most cases is about 10^{-4}M, so that a spectrum can be obtained using less than 1 mg of sample. Infra-red spectra can be obtained for solids, liquids or vapours. Solids may be examined as mulls, as solid films deposited on a plate surface, or in pressed alkali halide discs, and liquids are examined as films of 0.01 to 0.1 mm thickness. Solutions in suitable solvents are also readily examined, a typical concentration being about 0.2M[33]. The amount of sample required for an infra-red spectrum varies from 1 to 30 mg, depending on the technique used.

The conditions necessary for obtaining a Raman spectrum are much more restrictive. Although Raman spectra have been obtained for solids and gases, most instruments are designed for liquid samples only, and

in all but the most elaborate apparatus, sample volumes of 5 ml or more are needed. If solutions are used, satisfactory spectra can be obtained only if the concentration is at least 10%, and preferably much more. Samples must be free of suspended impurities and must be non-fluorescent.

Ultra-violet Spectra. The absorption of ultra-violet or visible light by an organic molecule almost always involves the excitation of the valency electrons, and for the present work only the excitation or electrons in multiple bonds (π electrons), and unshared electron pairs (p electrons), need be considered. The isolated C=C bond in ethylene exhibits a strong absorption at 1620 Å [34a], due to the excitation of an electron from a bonding π orbital to an anti-bonding π orbital ($\pi \rightarrow \pi^*$ transition). Isolated unshared electron pairs can give rise to absorptions near 2000 Å also; trimethylamine, for instance, absorbs at 2273 Å, due to the excitation of an electron from the "lone pair" orbital to an anti-bonding σ orbital, ($n \longrightarrow \sigma^*$ transition)[34b]. If the atom bearing the unshared electron pairs is also multiply bound, a further type of transition is possible. The carbonyl group, for instance, exhibits absorptions due to both the transitions already described, and a

further band near 2800 Å, due to an $n \rightarrow \pi^*$ transition. (E.g. acetone[35].)

When two or more such absorbing groups are conjugated (separated by single σ bonds), marked effects on the absorption spectrum are observed. In general, the effect of increasing conjugation is to increase the wavelengths of the absorption maxima, and for compounds containing such conjugated groupings, the ultra-violet spectrum can be a powerful tool for the elucidation of the structure. One such conjugated group which is of some importance in later discussion is the benzene chromophore.

In the ultra-violet spectra of aromatic compounds three main bands are recognised, the α, p, and β bands. In benzene, the β band is found at 1840 Å, and is of high intensity, the p band, of moderate intensity, lies at 2020 Å, while the α band at 2550 Å is of low intensity[37].

Substituents in the benzene ring shift these bands to longer wavelengths (bathochromic shift); their positions for some monosubstituted benzenes are given in Table I. The effect of disubstitution depends on the nature and relative positions of the two substituents, and it is convenient to classify the groups as m- or o,p-directing, according to their orienting influence in chemical substitution. The bathochromic displacements of the bands (from their positions in benzene itself)

Table I Ultra-violet Absorption Maxima[37], (Å).

	λ_{max}
Benzene	2540; 2035
Toluene	2610; 2065
Phenol	2700; 2105
Anisole	2690; 2170
Chlorobenzene	2635; 2095
Bromobenzene	2610; 2100
Nitrobenzene	3300; 2685
Aniline	2800; 2300

Table II Ultra-violet Absorption Maxima, (Å).

	Substituent Position.					
	1		2		3	
Pyridine[39b]	2560					
Picoline[39c]	2630		2625		2530	
Methoxypyridine[41]	2690		2760;	2160	2350*;	2220
Chloropyridine[39d]	2640		2675			
Bromopyridine[39d]	2655		2680			
Nitropyridine[39e]	2690			2420	2820	
Aminopyridine[41]	2870;	2290	2880;	2310	2650*;	2410

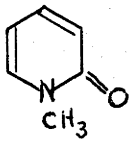
* Shoulder.

are considerable if the substituents are of opposite types, especially for p-disubstituted compounds, but if the substituents are of the same type, the displacements are much less[38]. For example, the p band in nitrobenzene (2685 Å) is shifted to a slightly shorter wavelength (2660 Å) by a p-nitro substituent, but in the p-nitrophenolate ion this band lies at 4020 Å[37].

The spectra of the N-heteroaromatic systems (containing only 6-membered rings) show three regions of absorption which may be related to the α, p, and β bands of the "parent" aromatic hydrocarbons[39]. A reasonable approximation is to regard the heterocyclic molecule as absorbing at the same wavelengths as the corresponding hydrocarbon[40].

Table II shows the ultra-violet absorption maxima of several substituted pyridines, and it will be seen that the spectra of the 2- and 3- substituted pyridines are similar to those of corresponding benzene derivatives, the long-wavelength bands for the pyridines having appreciably greater intensities than for the benzenes. Marked differences in wavelengths and intensities are observed when the substituent is in the 4 position, but Mason[41] has shown that the spectra of the amino-, methoxy-, hydroxy-, methylthio-, and mercapto- pyridines (including the 4-substituted isomers) can be satisfactorily explained on the basis of an L.C.A.O. carbanion model.

Structural interpretations of ultra-violet spectra have a largely empirical basis[42], and an example is the determination of the preferred tautomer of 2-hydroxy-pyridine[6a]. The reference compounds in this case are the compounds 22, and 23, in which the mobile hydrogen atom has been replaced by the immobile methyl group, thus "fixing" the bond arrangement of each tautomer.



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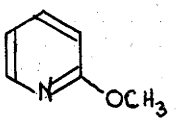

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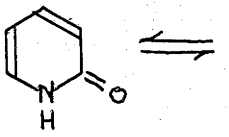


24a 24b

That the methyl group alone has little effect on the ultra-violet spectrum is evident from the comparison of the absorption maxima of phenol and anisole (Table I). Table III shows the ultra-violet absorption maxima for 2-hydroxypyridine, and the two reference compounds, N-methyl-2-pyridone and 2-methoxypyridine, and it is clear that the pyridone tautomer predominates, as the spectra of 24 and 22 are almost identical, and very different from that of 23.

TABLE III.

ULTRA-VIOLET SPECTRA.[6a]

Compound	Wavelength (Å)	Log
2-Hydroxypyridine, 24	2970, 2260	3.77, 3.86
N-Methyl-2-pyridone, 22	2930, 2240	3.75, 3.78
2-Methoxypyridine, 23	2690	3.51

Vibration Spectra.

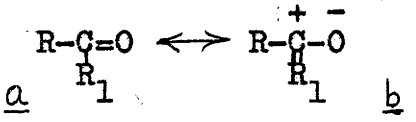
A very useful concept in the application of vibration spectra to the elucidation of structures is that of "group frequencies". Certain groups of atoms (e.g. C-H, N-H, C=O, etc.) give rise to characteristic absorption bands in the same spectral region in all compounds, and the presence or absence of such bands can often be conclusive evidence of the presence or absence of the groups in the substance being investigated. The exact position of the bands can also give an indication of the environment of the group.

The concept of localised group frequencies vibrations is, of course, an over-simplification. The vibration frequency of a group is determined primarily by the elasticity of the bond involved, and the masses of the vibrating atoms, but it is modified by both intra- and inter- molecular forces, and by mechanical coupling with other vibrating groups. Examples of these effects will arise in later sections.

In the present work, the behaviour of bands due to the stretching vibrations of carbonyl groups, and the vibrations of aromatic rings are of special interest; these will therefore be discussed briefly here.

The Carbonyl Group. This group gives rise to a very strong absorption band in the infra-red spectrum and a weaker band in the Raman spectrum. Some typical carbonyl frequencies are listed in Table IV.

The frequency in aldehydes and ketones is that of a carbonyl group in the absence of strong inductive or mesomeric effects. The frequency is raised when a substituent having an electron-withdrawing inductive effect is attached to the carbon atom, and this increase has been explained as follows[43]. In the absence of external electrical effects, the electrons in the carbonyl π bond are distributed so that the greatest density of electrons is near the oxygen atom, due to the greater attraction for electrons of the oxygen atom than the carbon atom. This corresponds to a significant contribution by the form b in the resonance



a b

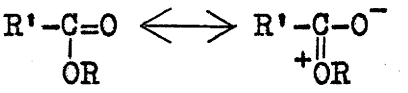
of the molecule. The replacement of R by an electron-withdrawing substituent reduces the contribution of this resonance form, so that the bond order, and hence the vibration frequency, rise. The order in which the substituents R raise the C=O stretching frequency is Cl > OH > OR. The inductive effects of the OH and OR

Table IV Carbonyl Stretching Frequencies[1], (cm^{-1}).

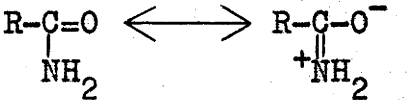
	vap.	liq.
Acetaldehyde	1752	1729
Propionaldehyde	1757	1735
Methyl ethyl ketone	1742	1721
Diethyl ketone	1738	1718
Acetyl chloride	1822	1808
Chloroacetyl chloride	1820	
Acetic acid	1785	
Chloroacetic acid	1794	
Methyl acetate	1774	1747
Ethyl acetate	1765	
Methyl phenyl ketone	1707	1687
Benzaldehyde	1725	1705
Acraldehyde	1723	
Methyl benzoate	1754	1727
Methyl acrylate	1758	1732
Phenyl acetate	1793	1766
Diethylformamide	1710	1670
Diethylacetamide		1645
N-Ethylacetamide[43c]	1715	
N-Methylacetamide[43d]	1720	1656

(1) Except where indicated, values are taken from Ref. 43b.

groups outweigh the resonance effects, such as



which, by reducing the bond order in the C=O bond, would lower its vibration frequency. In amides, the inductive effect of the nitrogen atom would also raise the C=O frequency, but this effect is overshadowed by the resonance



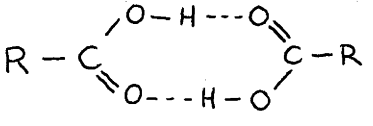
which, as described above, acts to reduce the frequency.

A description of the characteristic amide bands in terms of localised bond vibrations does not adequately explain the effects of N-substitution or of deuteration on the spectra[44, 45], and it is very likely that the individual bond movements are coupled to some extent. Calculations by Yamaguchi and Mizushima[46] indicate that the C=O stretching and NH_2 scissoring vibrations in urea are coupled to some extent and similar coupling is likely in primary amides. Frazer and Price[47] suggested that the "Amide I" band near 1650 cm^{-1} is to be regarded as an asymmetric N-C-O stretching vibration rather than a simple carbonyl stretching vibration. Mizushima et al[48] have interpreted the spectra of several amides and their N-deuterated

derivatives in these terms, but suggest that the vibration responsible for the Amide I band is largely confined to the C=O bond.

Conjugation with other double bonds reduces the carbonyl stretching frequency; the participation of the π electrons of the C=O bond in a delocalised molecular orbital reduces its bond order (and raises the bond order in the adjacent single bond), and hence the vibration frequency is reduced.

The substitution of a halogen atom adjacent (α) to the carbonyl group produces a significant increase in its vibration frequency, of the order of 20 cm^{-1}. Jones and Sandorfy[52] give reasons for ascribing this effect to a field effect operating across space, rather than an inductive effect operating along bonds. Association in the liquid state or in solution reduces the carbonyl stretching frequencies of aldehydes, ketones and esters by 20-30 cm^{-1} compared with the vapour state (Table IV). For carboxylic acids the reduction is much greater, and this is attributed to the strong hydrogen bonding in the carboxylic acid dimer[49, 50].



For amides also, the carbonyl stretching frequency is much lower in the liquid or solid state than in the vapour state; since this applies to primary, secondary

and tertiary amides, hydrogen bonding cannot be the only effect involved, and strong dipolar association effects must play some part[51].

Aromatic Compounds. The vibration spectra of benzene, the various deutero-benzenes, and substituted benzenes have been very closely studied. (See Herzberg[53], and references cited therein, also Mair and Hornig[54a]. The vibrational assignments for benzene are shown in Table V, and the normal modes of vibration in Diagram I. (In this diagram the degenerate modes of vibration are depicted separately). In the following brief discussion some features of the spectra of benzene derivatives which can provide useful structural information will be considered.

The out-of-plane C-H bending vibrations of benzene and substituted benzenes give rise to characteristic, strong infra-red bands in the region 650-900 cm^{-1}, the frequencies of which are determined more by the positions of substitution than the nature of the substituents[55, 56]. The strong Raman bands in this region do not usually occur at the same frequencies as the strong infra-red bands, but tentative correlations for them have been suggested by Jones and Sandorfy[57].

Substituted benzenes exhibit two characteristic infra-red bands in the 1300-1600 cm^{-1} region. The

Table V Vibrational Assignments, (cm^{-1}).

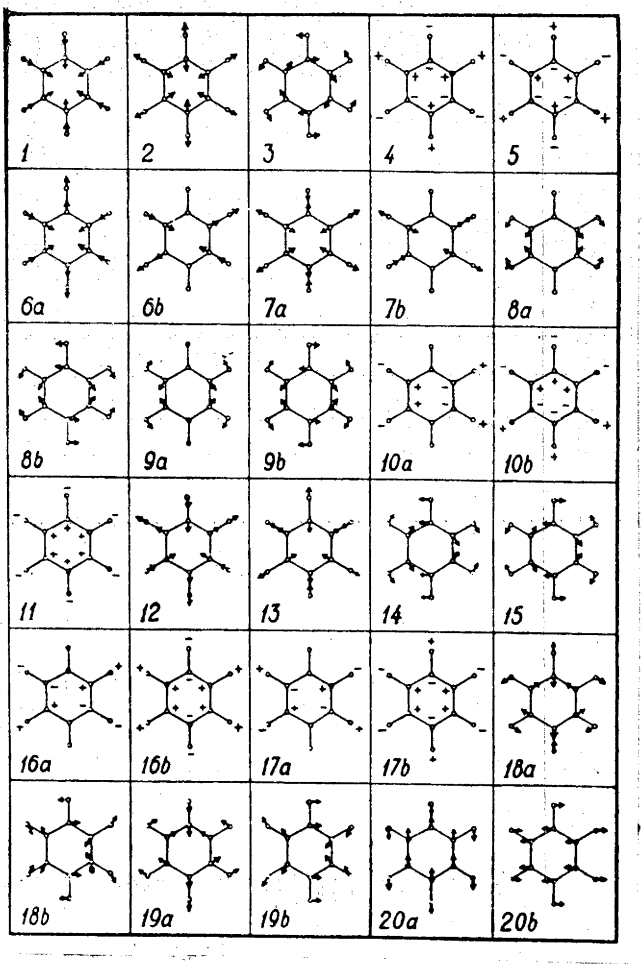
No.[a]	Benzene[54a]	Pyridine[54b]	No.	Benzene	Pyridine
1	992	992	11	675	700
2	3062	3054	12	1010	1030
3	1340	1218	13	3071	3056
4	703	749	14	1310	1375
5	995	942	15	1150	1148
6a	606	605	16a	405	374
6b	606	652	16b	405	405
7a	3047	(A)	17a	975	981
7b	3047	3036	17b	975	(A)
8a	1596	1583	18a	1038	1068
8b	1596	1572	18b	1038	1085
9a	1178	1218	19a	1478	1482
9b	1178	(A)	19b	1478	1439
10a	849	886	20a	3063	3036
10b	849	886	20b	3063	3083

(a) Numbering of vibrations according to Diagram I, and Ref. 54c.

(A) These three vibrations have been arbitrarily chosen as the three vibrations lost in passing from the twelve-atomic molecule, benzene, to the eleven-atomic molecule, pyridine.

DIAGRAM I

Vibrations of the benzene molecule (schematic).
(Taken from Ref. 54c.)



first of these, at about 1585 cm^{-1}, corresponds to the strong Raman band at 1585 cm^{-1} in benzene itself, and the lower symmetry of the substituted benzenes enables it to appear in the infra-red spectrum. The second band, at about 1485 cm^{-1}, is an infra-red active fundamental in benzene, and is retained in the substituted benzenes. A third band, at about 1610 cm^{-1}, is observed in a number of benzene derivatives, and Bellamy[58] has included it in his list of characteristic frequencies. In benzene itself, combination bands are observed at about this frequency in both the infra-red and Raman spectra.

In the 1650-2000 cm^{-1} region, benzene derivatives show a pattern of weaker overtone and combination bands whose appearance is determined by the number and relative positions of the substituents rather than their nature[59, 60].

The most prominent feature of the Raman spectrum of benzene is the very strong band at 992 cm^{-1}, due to the symmetric ring-breathing vibration, ν_1. In mono- and m-di- substituted benzenes the strongest Raman band below 2000 cm^{-1} is normally found near this frequency, but for many o- and p- disubstituted benzenes no band in this region is reported[61].

There is a close resemblance between the vibration

frequencies of benzene and pyridine. The introduction of the hetero-atom lowers the symmetry of the benzene molecule, so that the selection rules become less restrictive; the degeneracy of 10 of the vibrations is removed, and all the fundamental modes of vibration have been observed. The assignment of vibrations for pyridine is given in Table V.

Katritzky[62] has examined the infra-red spectra of a number of mono-substituted pyridines, and indicated some general correlations between the frequencies and intensities of the characteristic bands and the nature of the substituents. In the present work, the spectra of poly-substituted pyridines are of greater interest, but little data is available for substituents other than alkyl groups. Shindo and Ikekawa[63] have shown that bands in the 650-900 cm^{-1} region in the spectra of alkylpyridines are characteristic of the positions of substitution, bands for each type of substitution falling within quite small frequency ranges. (See also Cook and Church[64], and Podall[65].) These ranges must be extended considerably, however, if data for other substituents are to be included[66]. Nearly all substituted pyridines exhibit a pattern of four bands between 1600 and 1350 cm^{-1}, the intensities of which are rather variable, even for the alkylpyridines[63-66].

The frequencies, especially those of the two bands near 1600 cm^{-1} show less variation.

Nuclear Magnetic Resonance Spectra[67].

In nuclear magnetic resonance spectroscopy, the degenerate energy levels which arise from the orientations in space of the nuclear magnetic moments are split into sub-levels of differing energy by an applied magnetic field. Transitions between these levels are excited by electromagnetic radiation in the radio-frequency region (wavelengths of the order of 1 metre), and the resulting absorption pattern forms the n.m.r. spectrum.

The greatest application of these effects has been in the study of proton magnetic resonance (p.m.r.) spectra, i.e. the spectra given by the hydrogen atoms of a molecule. The p.m.r. spectrum is useful because the electronic environment of the hydrogen atom affords to it a measure of diamagnetic shielding, so that hydrogen atoms with different environment give signals in different parts of the spectrum. This constitutes the "chemical shift". A further effect is spin-spin coupling, which is illustrated in the p.m.r. spectrum of ethanol[68]. (See diagram II). Under low resolution, three peaks are observed, of intensity 1, 2 and 3,

DIAGRAM II

N.m.r. spectra of ethanol. (Taken from Ref. 67.)

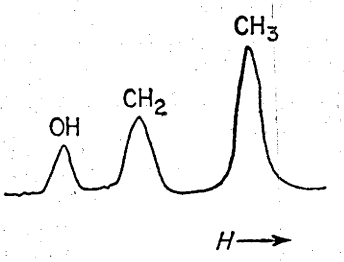


FIG. 1-3. Proton resonance spectrum of liquid ethyl alcohol under low resolution showing distinct signals for methyl, methylene, and hydroxyl protons.

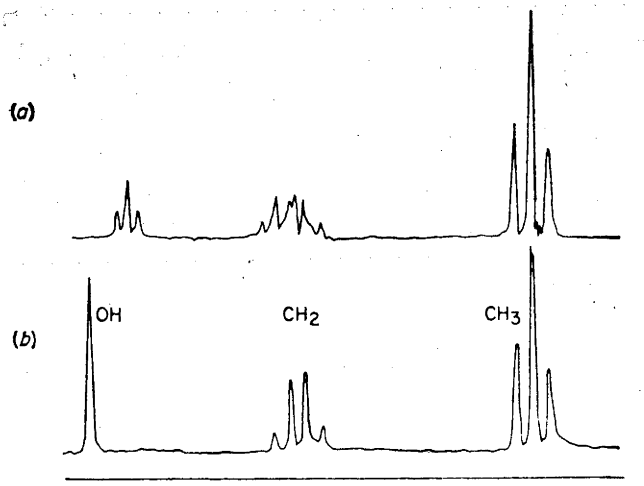


FIG. 5-7. The proton resonance spectrum of ethyl alcohol. (*a*) Pure dry alcohol. (*b*) Alcohol to which a small amount of hydrochloric acid has been added. (Arnold.[20])

corresponding to the protons of the OH, CH_2 and CH_3 groups respectively. Under higher resolution, the peaks are seen to be split, as shown in the second spectrum, the methyl protons giving rise to a triplet, and the CH_2 protons giving rise to a quartet. This is because (in the latter case) the magnetic field experienced by the CH_2 protons is modified according to the orientations of the magnetic moments of the protons in the adjacent CH_3 group, and since there are four possible combinations of these orientations, the signal appears as a quartet. The splitting of the signal due to the protons of the methyl group is split in a similar way, due to the three possible combinations of the orientations of the magnetic moments of the CH_2 protons.

When the sample of ethanol is pure and dry, further splitting can be observed, (see third spectrum) and this is due to the effect of the OH proton in further splitting the CH_2 absorption pattern. The signal for the OH proton is also split into a triplet, indicating normal spin-spin interaction with the CH_2 group. Impurities, especially acids, prevent these interactions from being observed, and this is explained through an exchange effect. The impurities increase the rate of exchange of the hydroxyl proton, and the mean life-time of a proton on

this group becomes less than the time required for a nuclear transition, so that only an "averaged" signal is seen, and the spin-spin interactions are no longer observed.

In recent years, considerable use has been made of n.m.r. (and especially p.m.r.) spectra in structural determinations, and several important p.m.r. investigations of the structure of amide cations will be discussed in Section C of this chapter.

Ionization Constants.

The equilibrium constant for the ionization of an acid or base is defined as :

$$K_a = \frac{[H]^+ [A]}{[HA]}$$

where $[H^+]$ is the hydrogen ion concentration, [A] is the concentration of the anion (or neutral base), and [HA] is the concentration of the acid (or protonated base). K_a (usually expressed as its negative logarithm, pK_a) is therefore a measure of the free energy of the reaction (in aqueous solution):

$$HA + H_2O \rightleftharpoons A^- + H_3O^+.$$

A change in the structure of A will normally affect the free energies of HA and A to different extents, and hence affect the pK_a value. Thus, a substituent which stabilizes the ion relative to the

neutral acid or base will favour ionization, and if it has the reverse effect, ionization will be inhibited. Estimation of substituent effects in this way is difficult, however, and the simpler but less satisfactory electrostatic approach is almost invariably used. If the substituent lowers the electron density in the vicinity of the A-H bond, in an acid, removal of the proton is facilitated, and ionization is favoured. For a base, lowering the electron density at the proton-accepting site by an electron-withdrawing substituent inhibits ionization.

An example of the use of ionization constants in structural determination is the determination of the dominant tautomer of 2-hydroxypyridine in aqueous solution[5]. The pK_a value for 2-hydroxypyridine (0.75), is similar to that for N-methyl-2-pyridone (0.32), and very different from that for 2-methozypyridine (3.28). That the methyl group alone cannot have a very large effect on the pK_a value is evident from the comparison of the pK_a values of o-, m-, and p-methoxyaniline (4.49, 4.20, and 5.29 respectively) with those of o-, m-, and p-hydroxyaniline (4.72, 4.17 and 5.50 respectively).[69] Hence 2-hydroxypyridine exists predominantly as the pyridone in aqueous solution.

Conclusion.

Of the techniques described for the elucidation of structures, only diffraction (and possibly p.m.r.) methods do not require comparisons with reference compounds. Most other methods are comparative. The applications of ultra-violet spectra and ionization constants already described relied on comparisons with suitable reference compounds, and the use of group frequencies in infra-red spectroscopy is similarly, essentially a comparative method. In p.m.r. spectroscopy, deductions based on the magnitudes of chemical shifts are also comparative, but diagnoses based on the number and relative intensities of the observed signals, or on spin-spin interactions are not.

C. Historical.

1. Amide and Urea Cations. 2-Hydroxypyridine is a cyclic amide, and an investigation of its ions must take account of the related work on the ions of amides and ureas. In the neutral form, all these tautomeric substances exist in the "keto" forms (1, 5 and 9 in the diagrams on pages iii, iv)[1-6]. Although the question of the structures of the cations has been much studied in recent years, it is still a matter for

debate, and in this section, some published investigations into the structures of the amide and urea cations will be discussed. In a recent review, Katritzky and Jones[1] concluded that the preferred structures (in all three cases) were the O-protonated cations (3, 7 and 11), that all the evidence was compatible with this view, and that some of the evidence suggested it very strongly.

Nuclear Magnetic Resonance Studies (Amides). Katritzky and Jones[1] consider that p.m.r. spectra provide the strongest evidence for the O-protonated cation structure. The resonance signals due to the N-H protons are seldom observed, either because of rapid exchange of these protons, or because of the effect of the quadrupole moment of the N^{14} nucleus, and only in one instance has an O-H proton signal been observed. Because of this, most workers have studied mono- and di-N-methylated amides.

N-Methylacetamide[70]. In neutral solution, the signal due to the N-methyl protons in N-methylacetamide is a doublet, arising from spin-spin interaction with the single proton attached to the nitrogen atom.

(See Diagram III). The doublet collapsed to a single peak below pH 1, due to rapid exchange of this single proton, and kinetic studies indicate that the exchange occurs mainly through the reaction

$$CH_3.CO.NHCH_3 + H_3O^+ \rightleftharpoons CH_3.CO.\overset{+}{N}H_2CH_3 + H_2O.$$

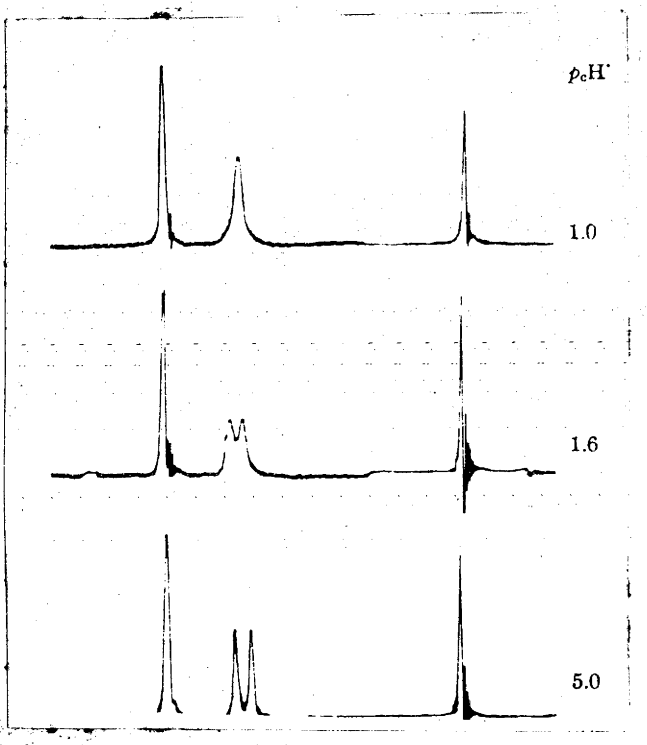
In conc. H_2SO_4 the doublet re-appears, and since the splitting has been shown to be field-independent[71], it must arise from spin-spin interaction between the N-methyl protons and a single proton attached to the nitrogen atom. For the N-protonated cation, a triplet methyl resonance should be observed (cf. the splitting by the CH_2 group in ethanol, page 26), and the doublet constitutes strong evidence for the predominance of the O-protonated species. The cation $CH_3.CO.\overset{+}{N}H_2CH_3$, which is the intermediate in the exchange reaction, must therefore be a minor component of the system at equilibrium.

An alternative explanation of the doublet N-methyl resonance in acid solution is that the exchange of <u>two</u> protons attached to the nitrogen atom is of such a rate that only one, and not both, of them exchange in the time required for a nuclear transition. This seems unlikely, as in all cases where the collapse of multiplet structures has been studied, the multiplet has collapsed as a whole, without the intermediate

DIAGRAM III

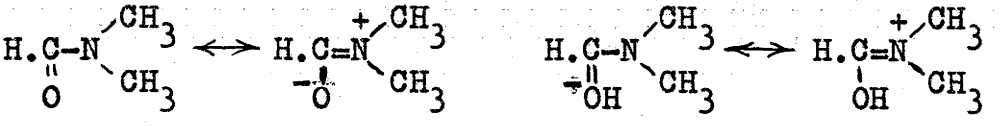
N.m.r. spectra of N-methylacetamide

(Taken from Ref. 70.)



formation of a triplet from a quartet, or a doublet from a triplet. (E.g. the studies on methylammonium ions[72]).

Dimethylformamide[73]. The p.m.r. spectrum of dimethylformamide is shown in diagram IV. Two peaks of equal area are observed for the N-methyl proton signals, showing that the two methyl groups are non-equivalent. If rotation about the C-N bond were free, these two signals would merge, and the fact that they do not indicates that there is an energy barrier to such rotation. Such an energy barrier is to be expected for a C-N bond possessing partial double-bond character (25a↔25b).



25a 25b 26a 26b

The doublet N-methyl resonance is also observed in strong acid solution, the energy barrier to rotation being greater in this case than for the neutral molecule. This is to be expected for the cation 26, in which the contribution of the canonical form 26b is likely to be greater than the contribution of the corresponding form (25b) in the resonance of the neutral molecule. In the cation $H.CO-\overset{+}{N}H(CH_3)_2$, however, the loss of the partial double bond

DIAGRAM IV

N.m.r. spectra of dimethylformamide (N-methyl proton resonances only). (Taken from Ref. 73.)

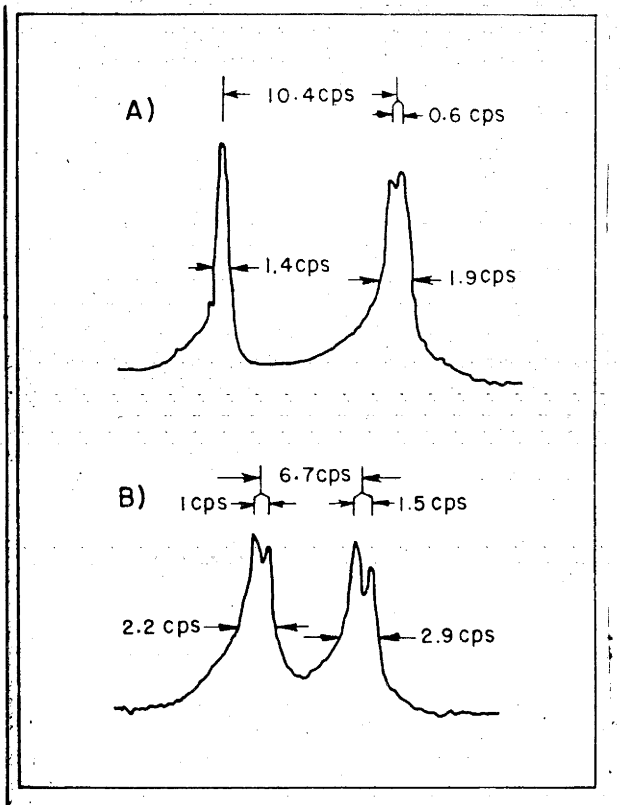


Fig. 1.—N.m.r. spectra of N-methyl protons in DMF, 60 Mc., 29°: A, DMF pure; B, 0.4 *M* DMF in 100% H_2SO_4. The magnetic field increases from left to right.

character in the C-N bond would be expected to leave the rotation less restricted than in the neutral molecule.

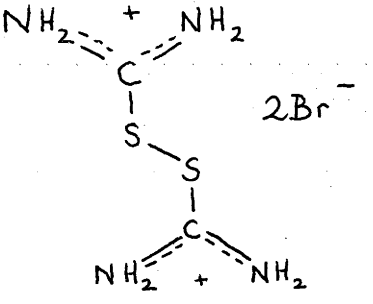
ε-Caprolactam. The p.m.r. spectrum of ε-caprolactam hydrochloride in chloroform solution has been described by Ottenheym and co-workers[74]. It proves unambiguously that the cation formed by this substance is protonated at the oxygen atom, since separate resonances are observed for protons attached to the nitrogen and oxygen atoms. (For further references to the caprolactam cation, see pages 47, 49).

Thus, the p.m.r. spectrum of this compound has proved conclusively that the cation has the O-protonated structure, and the spectra of the other two amide cations discussed are most readily interpreted in terms of O-protonated structures, the spectrum of the N-methylacetamide cation in particular being difficult to account for in terms of an N-protonated structure. Other p.m.r. investigations of amide cations have led to similar conclusions[75].

X-ray Diffraction Studies, (Ureas).

The only X-ray diffraction analyses which bear on the problem of the structures of amide cations are studies of salts and metal complexes of urea and thiourea.

In Table VIare listed the bond lengths in a number of compounds structurally related to the O-protonated urea cation. The metal complexes (which all form through oxygen- or sulphur-to-metal bonds) probably reproduce only approximately the effect which an oxygen- or sulphur-to-hydrogen bond would have on the rest of the molecule, and the S-S single bond in formamidine disulphide dibromide (27) is probably a nearer approach to a bond with hydrogen.



27

Although the accuracy with which these bond lengths were determined was limited, it does appear that the lengths in the urea or thiourea moieties are not greatly different from those in the neutral molecules (also quoted in the Table).

Table VI Bond Lengths, (Å).

Compound	C-O(C-S)	C-N[1]	C-N[2]	Ref.
$(Methylurea)_2.CdCl_2$	1.27	1.36	1.39	76
$(Urea)_2.\ CdCl_2$	1.23	1.34	1.38	77
Urea phosphate	1.29	1.32	1.34	78
Methylurea nitrate	1.28	1.29	1.30	79
Urea	1.26	1.335	1.335	2a
$(Thiourea)_2.CdCl_2$	1.64	1.32	1.32	80
$(Thiourea)_2.Ni(SCN)_2$	1.77	1.31	1.31	81
Compound 27	1.78	1.33	1.33	82
Thiourea	1.71	1.33	1.335	83

The (more accurately determined) bond lengths in the urea moieties of the two salts, urea phosphate and methylurea nitrate are again similar to those in the neutral urea molecule, and the following discussion of the hydrogen bonding in these salts suggests strongly that they also form through bonding to the oxygen atom.

In urea phosphate the system of hydrogen bonding is extensive and complex; nine close inter-molecular approaches are found for seven possible hydrogen bonds, so that the positions of the hydrogen atoms cannot be deduced on this basis alone. However, there are only three very close O...O approaches, two between oxygen atoms of the $H_2PO^-_4$ anions, which undoubtedly correspond to the two hydrogen bonds formed by the unionized phosphate hydrogens, and one between urea and phosphate oxygens. If this approach is indeed a hydrogen bond, it indicates that the cation has formed by protonation at the oxygen atom.

The crystal structure of methylurea nitrate is more conclusive. The symmetry of the lattice requires that the molecule (including the nitrate group) lie in a plane of symmetry, and the distance between planes is 3.18 Å. Although there is some

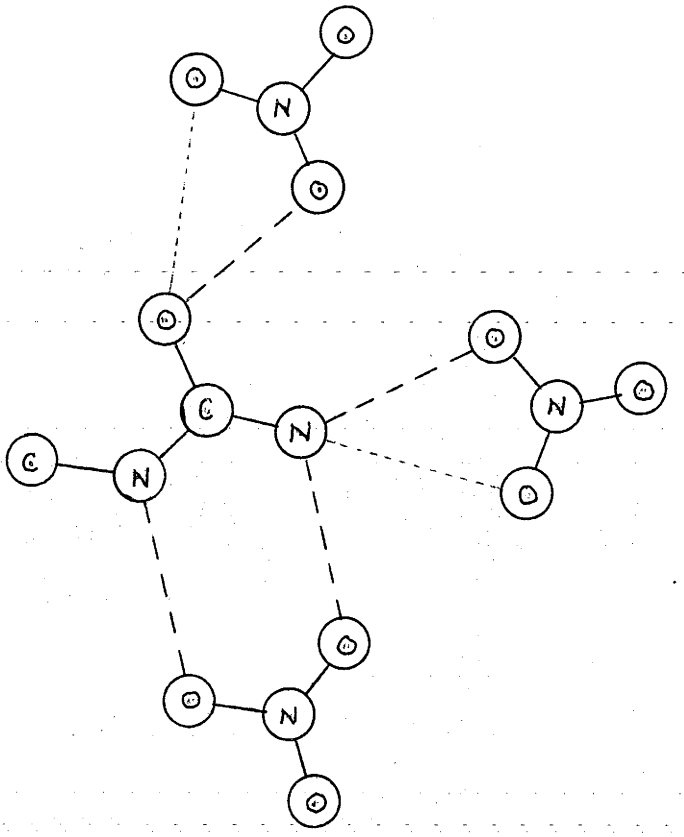


DIAGRAM V

Inter-molecular environment, N-methylurea nitrate.

Hydrogen bonds — — — — —

Other close inter-molecular approaches - - - - - - - - - -

fairly close packing of nitrate ions above and below the urea oxygen, there are no out-of-plane approaches short enough to be attributed to hydrogen bonds, and there are no in-plane approaches between methylurea moieties. It remains, therefore, to allocate the hydrogen atoms to the close in-plane anion-to-cation approaches, (see Diagram VI), and it is most unlikely that the tetrahedral nitrogen atom in an N-protonated cation could form three in-plane hydrogen bonds. The hydrogen atoms must therefore be im positions corresponding to the O-protonated cation structure, one on the urea oxygen, (presumably in the direction of the very close contact, 2.59 Å), one on the methylated nitrogen atom, and two on the remaining nitrogen atom, (presumably in the two directions not in the line of the C-N bond). The final electron density contour gives some evidence for the presence of hydrogen atoms in these positions.

This structure can only be interpreted in terms of an O-protonated cation structure, and constitutes proof that for methylurea, and very probably for most ureas, proton addition occurs at the oxygen, and not the nitrogen atom.

It is desirable in the spectroscopic studies to know

what types of hydrogen bonds are to be expected in amide cations. In particular, it would be useful to know whether the carbonyl oxygen atom in an N-protonated amide or urea is likely to be involved in hydrogen bonding, i.e. whether cation-to-cation hydrogen bonds are likely. Structures containing such bonds are rare. A fairly complete survey of the literature has revealed only two such structures, the hydrated hydrochlorides of adenine and guanine[84,85]. In the amino-acid hydrochlorides, where the cations contain both NH_3^+ and C=O groups, only anion-to-cation hydrogen bonds are formed[86]. More complex cations containing groups such as $NH_3^+..COO^-..NH^+$, do form inter-cation hydrogen bonds[87], but these compounds are not comparable with those discussed in the present work.

Summary: The results of X-ray diffraction studies show that for methylurea and hence probably for most ureas, the preferred site for proton addition is the oxygen atom, and that the bond lengths in the cation thus formed are very similar to those in the neutral molecule. Further, it is shown that in ionic structures of this type, only cation-to-anion hydrogen bonds are to be expected.

Vibration Spectroscopic Studies.

Although in the search for structural evidence the whole vibration spectrum must be considered, the most important single feature in the spectra of amide cations is undoubtedly the presence or absence of a band which may be assigned to the carbonyl stretching vibration. It was shown in Section B (page 18) that the frequency of this vibration in amides is lower than the "normal" value due to the contribution of the dipolar form 1b (page iii) to the resonance of the molecule, and that the frequency is also considerably reduced by hydrogen bonding. In O-protonated cations, the C-O link would be expected to lose much of its double-bond character, and this band should no longer be observed. In N-protonated cations, however, the frequency of this band should be raised very considerably. The loss of the normal amide resonance, and the strongly electron-withdrawing effect of the positively-charged nitrogen atom should, in the absence of intra-molecular forces, raise the frequency to 1800 cm^{-1} or more. (This is the value for acid chlorides, and the NH_3^+ group must have a stronger electron-withdrawing effect than the chlorine atom). Since hydrogen bonding to the carbonyl oxygen atom is unlikely (page 42), the only effect tending to lower the frequency would be the normal polar

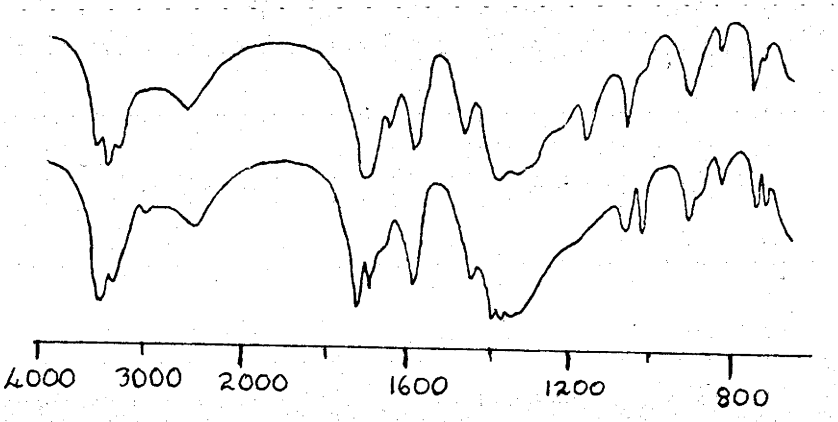
association forces in the solid state

(a) Ureas. As shown in the previous section, methylurea nitrate is known to contain the O-protonated cation, and the spectra of urea salts will therefore be considered first. Diagram VIshows the infra-red spectra of both methylurea and urea[88] nitrates. The spectra are very similar, and in particular, all the bands taken to be structurally significant by other authors[88-90] are to be found in both spectra. There can be no doubt that the same cationic species is present in both salts, i.e. that urea nitrate, and hence probably urea salts in general, are formed by proton addition at the oxygen atom.

The most important feature, which is not easily predicted, is the strong band at 1700±10 cm^{-1}. This has been assigned by some workers[88,90] to the carbonyl stretching vibration of an N-protonated cation, but it must now be re-assigned. A confirmation that it is not due to a carbonyl vibration is provided by the work of Stewart and Muenster[91]. They showed that the corresponding band in N,N'-dicyclohexylurea hydrochloride is unaffected by the substitution of O^{18} for O^{16}, whereas a true carbonyl band is shifted to lower frequencies by at least 10 cm^{-1} by such substitution

DIAGRAM VI

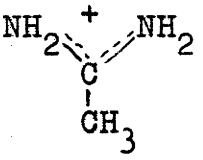
Infra-red Spectra (schematic).



Lower curve: urea nitrate[89].

Upper curve: N-methylurea nitrate.

The acetamidinium cation[92] (28) has a strong



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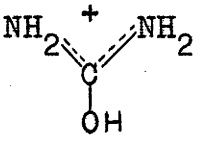


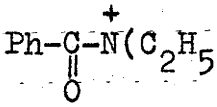
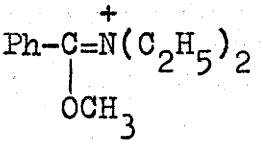
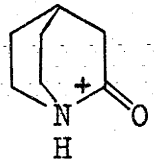
29

absorption band at 1960 ± 3 cm^{-1}, assigned to the N-C-N asymmetric stretching vibration[92], possibly coupled with an NH_2 deformation vibration[93]. The O-protonated urea cation (29) could well absorb near 1700 cm^{-1}, therefore.

Bands in the region of 2500 cm^{-1} in the spectra of urea salts have been assigned[88, 90] to the N-H stretching vibrations of an $\overset{+}{N}H_3$ group in an N-protonated cation. However, Kutzelnigg and Mecke[89] assigned them to the O-H stretching frequency of a hydroxyl group involved in very strong hydrogen bonding, and predicted an O...O distance of 2.55 Å in urea nitrate. This is very close to the value of 2.59 Å observed in the structure of methylurea nitrate[83].

(b) Amides. No crystal structure studies are available for amide salts. However, in one case, benzamide, actual model compounds are available for both the possible cation structures[94]. These are shown in Table VII The frequency of the carbonyl band in compound 30 (see Table) confirms the rough predictions given earlier, and it is clear that the

Table VII. High-frequency Skeletal Bands.

Compound		ν (cm^{-1})	$\nu_{C=O}$ parent molecule	Ref.
30	 ClO_4^-	1783 1724		94
	$SbCl_6^-$	1771 1714		
31	 ClO_4^-	1640		"
Benzamidium perchlorate		1654	1656	"
N-Ethylbenzamidium perchlorate		1677	1633	"
32	 Cl^-	1800	1733	98
Hydrochlorides				
Acetamide		1718	1684	90
N-Ethylacetamide		1718	1686	95
Propionamide		1706	1660	96
Di-N-methylacetamide		1660	1645(1)	97
-Caprolactam		1645	1660	74

(1) Value for di-N-ethylacetamide, from Ref. 43b

benzamide salts resemble compound 31, the model for an O-protonated cation, rather than 30.

In the spectra of unconjugated amide cations, strong bands are found at higher frequencies than those of benzamide cations, and some examples are included in Table VII. Similarly, the carbonyl band for the unconjugated compound 32 (which is generally agreed to be N-protonated[1,98]) is higher than that for the benzamide derivative 30.

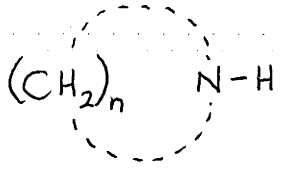
In the case of propionamide hydrochloride, it has been shown[96] that the 1706 cm^{-1} band is unaffected by the isotopic substitution of O^{18} for O^{16}, confirming that this band, and hence the corresponding bands in the other compounds listed, are not due to carbonyl stretching vibrations. The assignment of these bands to $C{=}\overset{+}{N}$ stretching vibrations is reasonable in view of Leonard's finding[99] that the $C{=}\overset{+}{N}$ group absorbs in the range 1685-1700 cm^{-1}.

In their review, Katritzky and Jones[1] stated that the chief evidence in support of N-protonation of amides comes from vibration spectra, an essential feature of this evidence being the assignment of certain bands to carbonyl stretching vibrations. It

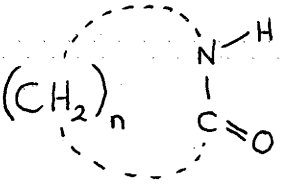
will be seen from the foregoing discussion, however, that reasonable assignments of these bands are possible for O-protonated cations, and that there is some evidence to indicate that the assignment of the bands to carbonyl stretching vibrations is incorrect.

Other Investigations.

Huisgen and Brade have shown that N-substituents affect the Ionization constants of amides less than those of similarly N-substituted amines, suggesting that the site of proton addition in amides is further away from the N-substituent than in amines[100]. The dependence of the ionization constant on ring size for the imines (30) and the lactams (31) has been interpreted in terms of O-protonation in the lactams, also.



30

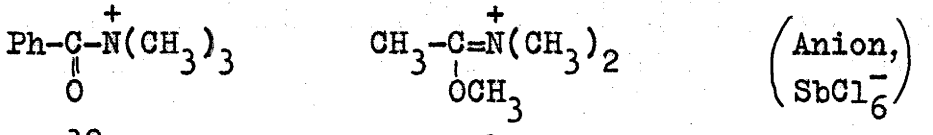


31

The pK_a values for the imines are lowest when n is approximately 12, and this is thought to indicate crowding at the nitrogen atom, inhibiting the addition of a further proton. No such minimum is observed in the pK_a values of the lactams, suggesting[101] that the proton in this case adds to the exocyclic oxygen atom, and not the (ring) nitrogen atom. The validity of

this comparison between a ring composed entirely of tetrahedral atoms and a ring containing a trigonal carbon atom has not been proved, however, and the conclusion cannot be considered to be firmly based.

Klages and Zange[102] prepared the salts 32 and 33, and showed that the former is very unstable, and more readily hydrolysed than the latter. Since the acid hydrolysis of amides



32 33

is considered to proceed through the N-protonated cation (the hydrogen analogue of 32) as intermediate, the fact that this hydrolysis is relatively slow led them to suggest that the N-protonated species is only a minor component of the equilibrium in acid solution.

The application of the Hammett equation to the ionization constants of some substituted benzamides led Stewart et al[104] to deduce that the benzamide cation had the N-protonated structure. Katritzky and Jones[1] have given an alternative explanation of their results.

Conclusion.

The evidence discussed in this section can all be interpreted in terms of O-protonated urea and

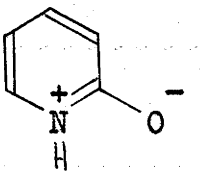
amide cation structures, that provided by p.m.r. spectroscopic and X-ray crystallographic investigations being particularly strong. The principal evidence which has been advanced in support of N-protonated structures comes from vibration spectra, but the results of several investigations in this field suggest that such interpretations are incorrect.

2. Pyridones and their Ions.

The pyridone structure of the tautomeric substance 2-hydroxypyridine was recognised as likely, long before the development of quantitative physico-chemical techniques enabled it to be reliably confirmed. As early as 1885, Haitinger and Lieben[105] suggested that certain properties of 4-hydroxypyridine resembled those of N-methyl-2-pyridone rather than of 4-methoxy-pyridine. In 1907, Baker and Baly[106] examined the ultra-violet spectra of 2-, 3-, and 4-hydroxypyridine in neutral, acid and alkaline solution, and showed that while the 3-isomer appeared to be attrue pyridine, and also resembled a phenol, the other two isomers had very different spectroscopic properties. Further, 2-hydroxy-pyridine and N-methyl-2-pyridone had very similar spectra, and they deduced that both 2- and 4-hydroxypyridine existed as pyridones. Other quantitative studies were

published in 1930 by von Auwers[107], who showed that the results of refractivity measurements made on a number of 2-hydroxypyridines resembled those obtained for the N- rather than the O-methyl derivatives.

Since then the 2- and 4-pyridone structures have been confirmed many times, using ultra-violet[108, 6a] and infra-red[109, 9] spectra, ionization constants[5], and (for 2-hydroxypyridine) X-ray crystallographic investigation[4]. Dipole moment studies by Leis and Curran[110], and Albert and Phillips[5] show that the dipolar canonical forms such as

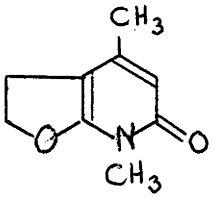


contribute significantly to the resonance of the molecules, as had been suggested earlier by Arndt and Kalischek[111] and von Auwers[107].

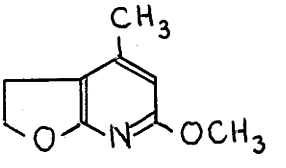
Several substituted 2-hydroxypyridines have been examined. The infra-red spectra of the 5-bromo, 5-iodo, 3, 5-dibromo, and 4, 6 dimethyl derivatives of 2-hydroxy-pyridine have been published, together with the spectra of two reference compounds, 2-ethoxypyridine and 5-bromo-2-methoxypyridine[112]. The authors concluded that all the substituted 2-hydroxypyridines examined, like 2-hydroxypyridine itself, are pyridones. Den Hertog and Buurman[113] have shown from the ultra-violet spectra of

2, 4-dihydroxypyridine and all its N- and O-methyl derivatives that this compound exists as 4-hydroxy-2-pyridone. Den Hertog[114] has also published the spectra of all the possible dihydroxy- and diethoxypyridines but since the ionization constants of these compounds were not determined, some of the spectra could be those of ionic species. (In the present work it is shown that his spectrum for 2, 6-dihydroxypyridine is in fact the spectrum of the mono-anion of this substance).

In two instances, the isolation of both tautomers of substituted 2-hydroxypyridines has been claimed, the substances being 2,3-(2'x3'-dihydrofurano)-4-methyl-6-hydroxypyridine[115], and 2-hydroxy-5-arsenilic acid[116]. The evidence for the former is much more complete, but Ritchie[117], who re-examined the question, was unable to obtain the second isomer, or to observe the establishment of an equilibrium mixture under the conditions which the earlier workers had described. He examined the ultra-violet spectra of the compound, and of two methylation productions which he considered to be the N- and O-methyl derivatives, 34 and 35, and he concluded that the



34



35

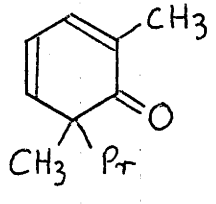
hydroxy-tautomer, corresponding to 35, preponderates in solution. This is at present the only instance of a 2-hydroxypyridine derivative for which the genuine hydroxypyridine structure, as distinct from the pyridone structure, has been proposed, that has remained unchallenged.

The salts of 2-hydroxypyridine have attracted little attention in the past, and indeed, almost all the studies of them have been made in the past decade. Baker and Baly[106] recorded the ultra-violet spectra of the anions and cations of 2-, 3-, and 4-hydroxypyridine, but a reliable re-examination of these results was not published until 1955, when Bliznyukov and Reznikov examined the ultra-violet spectra of the cations of 2- and 4-hydroxypyridine, 2-ethoxypyridine, 4-methoxypyridine, and N-methyl-2- and 4-pyridone[108b]. They deduced that the cations of the hydroxypyridines had O-protonated structures such as 36 (R=R'=H), and that the anions of the hydroxypyridines, which they also examined, resembled the canonical forms such as 13a (see diagrams on page iv) rather than 13b. These spectra were also examined by Mason[41].

The relevant spectral data are listed in Table VIII The cations of 2-hydroxy- and 2-methoxypyridine and N-methyl-2-pyridone have practically identical spectra, and this suggests that they all have the structure 36,

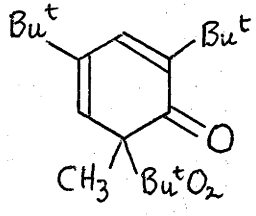
Table VIII. Ultra-violet Spectra.

	λ_{Max} (Å)	ε	λ_{Max} (Å)	ε	Ref.
2-Hydroxypyridine	2930; 2240	5890; 7230	2770; 2090	6950; 3500	41
2-Methoxypyridine	2690;	3230	2790; 2100	6920; 3550	"
N-Methyl-2-pyridone	2970; 2260	5700; 6100	2790; 2100	6250; 3500	"



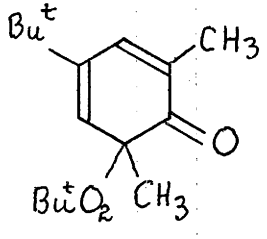
λ 3120; 2420
ε 3020; 4470

Ref. 119



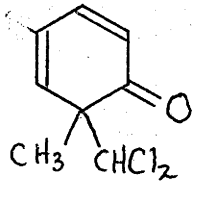
λ 3100
ε 3600

Ref. 120



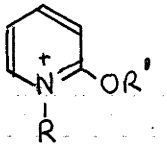
λ 3100; 2200
ε 4500;

120

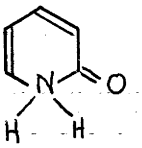


λ 2950
ε 5000

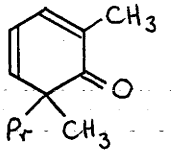
(R,R' = CH_3 or H). However, in the absence of spectroscopic data



36



37



38

for the alternative cation, 37, this is not final proof. Since in this latter cation, there has been a loss of conjugation compared with the neutral hydroxypyridine, (2-pyridone), the absorption bands could be at shorter wavelengths than in the neutral molecule, and could coincide with those of the O-protonated (or O-methylated) cation. Katritzky and Jones[1] have suggested that the compound 38 is a suitable model for the ion 37, since the effect of the $\overset{+}{N}H_2$ group should be small[118b]. The absorption maxima for this compound are at higher wavelengths than those of neutral 2-hydroxypyridine, and thus suggest that the cation structure 37 is incorrect. The spectra of some similar molecules are listed in Table VIII

Sensi and Gallo[109a] examined the spectra of all the hydroxypyridine hydrochlorides, and considered that the spectra of the 2- and 4-hydroxypyridine cations resembled those of the neutral 2- and 4-pyridone, rather than those of the neutral 2- and 4-methoxypyridines. In particular,

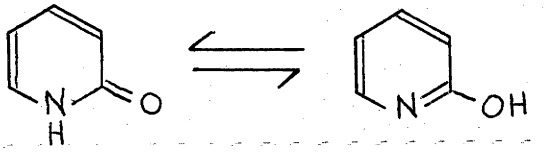
they considered that strong bands near 1650 cm^{-1} in the spectra of the hydroxypyridine cations were carbonyl bands, and deduced that the cations had N-protonated structures. Spinner[118] examined the infra-red and Raman spectra of the hydrochlorides and sodium salts of the hydroxypyridines, and he, too, concluded that 2- and 4-hydroxypyridine formed salts by proton addition to the nitrogen atom. He further deduced (from the Raman spectra) that the anion of 2-hydroxypyridine resembled the canonical form 13b rather than the form 13a. (See diagrams, page iv). Scheinker and Pomerantsev[118c] examined the infra-red spectra of a number of metallic salts of 2-hydroxypyridine, and reached the opposite conclusion regarding the nature of the anion.

No p.m.r. spectra of 2-hydroxypyridine cations have been reported yet, but the p.m.r. spectra of 4-hydroxypyridine hydrochloride and a number of reference compounds were examined by Katritzky and Jones[121]. Of the two proton signals expected for protons not attached to carbon atoms (two N-H, or one N-H and one O-H), only one was observed, and this was considered to be due to an O-H proton, as it was present in the spectra of the 4-hydroxypyridine and N-methyl-2-pyridone cations, but absent from the spectrum of the 4-methoxypyridine cation. Thus, the p.m.r. spectra indicate an O-protonated structure for the 4-hydroxypyridine cation.

CHAPTER II.

DISCUSSION OF EXPERIMENTAL RESULTS.

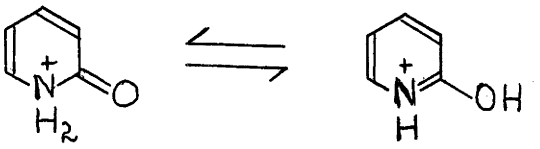
The object of this study of substituted 2-hydroxypyridines and their ions was to obtain information about the structures of the various species, and to find out whether the tautomeric equilibrium positions are markedly influenced by the substituents. Thus, 2-hydroxypyridine exists predominantly as the lactam or pyridone form 39, (see page 52),



39 40

but the introduction of substituents offered the possibility of obtaining a preponderance of the genuine hydroxypyridine form 40. For example, electron-withdrawing substituents, by reducing the electron density at the ring nitrogen atom, could possibly render the tautomer in which the mobile hydrogen atom bonds to the exocyclic oxygen atom more stable, while hydroxy or nitro groups in the 3 position could stabilize this tautomer through internal hydrogen bonding. Similarly, the tautomeric equilibrium

for the cation,



could be markedly affected by a substituent. Furthermore, the presence of a substituent could possibly permit an unambiguous structure determination, even where the results for the unsubstituted cation leave room for ambiguity.

The properties examined in this work, i.e. ultra-violet spectra, ionization constants and vibration spectra, will be discussed separately, and, as far as this is practicable, independently of one another.

A. Ultra-violet spectra.

The ultra-violet spectra of the substituted 2-hydroxypyridines studied are listed in Table IX, together with those of some similarly substituted 2-methoxypyridines. Five 2-methoxypyridines have been examined, and the differences between their spectra and those of their 2-hydroxypyridine counterparts prove that the latter are not genuine hydroxy compounds. The similarities among the spectra of the methyl-substituted 2-hydroxypyridine (2260±10;

Table IX Ultra-Violet Spectra of Substituted Pyridines.

Pyridine	pH solvent	λ_{max} (Å)		ε	
2-OH	5	2940;	2240	5,670;	7,050
2-OCH_3	7	2690;		3,380;	
2-OH, 3-CH_3	7	2940;	2265	6,800;	5,650
2-OH, 4-CH_3	7	2890;	2260	5,800;	4,900
2-OH, 5-CH_3	7	3020;	2270	5,750	8,200
2-OCH_3, 5-CH_3	7	2795;	2165	3,670;	7,000
2-OH, 6-CH_3	7	3010;	2250	7,770;	7,150
2-OH, 3-Cl	5	3035;	2295	6,930;	5,230
2-OCH_3, 3-Cl	5	2775;	2195	4,940;	6,550
2-OH, 3-Br	5	3060;	2305	7,340;	4,550
2-OCH_3, 3-Br	5	2795;	2195	5,170;	5,960
2-OH, 5-Cl	5	3100;	2330	4,970;	10,000
2-OCH_3, 5-Cl	5	2835;	2225	3,510;	10,000

TABLE IX (Continued)

Pyridine	pH solvent	λ_{max} (Å)			ε		
2-OH, 5-Br	5	3100;	2330		4,600;	9,600	
2-OCH_3, 5-Br	5	2840;	2220		3,480;	10,120	
2-OH, 5-I	5	3160;	2355		4,300;	17,500	
2-OH, 3,5-Cl_2	5	3200;	2380		6,250;	6,780	
2-OCH_3, 3,5-Cl_2	Methanol	2920;	2285		4,850;	8,850	
2-OH, 3,5-Br_2	5	3230;	2360*;	2160	6,300;	6,300;	18,500
2-OCH_3, 3,5-Br_2	Methanol	2940;	2270		5,330;	9,500	
2-OH, 3,5-I_2	5	3320;	2360		-	-	
2,3-$(OH)_2$	5	2970;	2345		7,430;	4,120	
2-OCH_3, 3-OH	5	2800;	2210		5,730;	5,800	
2,6-$(OH)_2$	2.8	3065;	2250		7,700	6,800	
2-OH, 3-NO_2	5	3620;	2570		7,050;	2,520	
2-OH, 5-NO_2	5	2800;	2210		5,730;	5,800	

Table IX Ultra-Violet Spectra of Substituted Pyridines
(Taken from the literature)

Pyridine	pH solvent	λ_{max} (Å)		ε		Ref.
2,3-$(OC_2H_5)_2$	H_2O	2794;	2234	5,000;	6,300	122
2,6-$(OC_2H_5)_2$	H_2O	2765;	2165	5,000;	5,000	122
2-OC_2H_5, 6-CH_3	H_2O	2730;		6,400;		123
N-Ethyl-2-Pyridines:						
3-CH_3	H_2O	2960;		6,000;		124
5-CH_3	H_2O	3050;		5,500;		124
3-Br	H_2O	3100;		7,700;		124
5-Br	H_2O	3130;	2350	4,450;	8,100;	124

2950±60 Å) are sufficient to establish that all have similar structures, and by the same reasoning, all of the halogen derivatives have similar structures. Furthermore, the similarities between the published spectra of the N-ethyl-2-pyridones listed at the end of Table IX, and those of the similarly substituted 2-hydroxypyridines prove that the latter, and hence all of the methyl and halogen derivatives of 2-hydroxypyridine, are pyridones. The predominance of pyridone forms for the two dihydroxypyridines examined may be deduced from the differences between their spectra and those of the corresponding diethoxypyridines[122], and (for 2,3-dihydroxypyridine) the spectrum of 2-methoxy-3-hydroxypyridine .

The ultra-violet spectra do not establish the structures of 2-hydroxy-3-nitropyridine and 2-hydroxy-5-nitropyridine, the 2-methoxypyridine counterparts of which were not prepared. (See, however, infra-red evidence, page 98).

It is of interest to compare the spectra of the methoxypyridines (acting as reference compounds for the inaccessible hydroxy-tautomers) which those of similarly substituted phenols, and a table of such comparisons is given on page 64. It will be seen that the

Table X Ultra-Violet Spectra

2-Methoxy-pyridine	λ_{max} (Å)		ε		Phenol	λ_{max} (Å)		ε		Ref.
5-CH_3	2795;	2165	3,670;	7,000	4-CH_3	2802;		2,100		125
5-Cl	2835;	2225	3,510;	10,000	4-Cl	2800;	2220	1,600;	8,900	126
5-Br	2840;	2220	3,480;	10,120	4-Br	2845;		1,650;		125
3-Cl	2775;	2195	4,940;	6,550	2-Cl	2745;	2100	2,100;		126
3-Br	2795;	2195	5,170	5,960	2-Br	2789		2,800;		125
3-OH	2800;	2210	5,730;	5,800	2-OH	2755;	2140*	2,300;	6,300	38
3,5-Cl_2	2920;	2285	4,850;	8,850	2,4-Cl_2	2850;		2,000		127

introduction of the hetero-atom shifts the absorption maxima to longer wavelengths, the shift of the long-wavelength band being fairly small. The bathochromic shifts given by substituents in 2-methoxypyridine are generally similar to those for substituents in 2-hydroxypyridine. For 2-hydroxypyridines the position of the long-wavelength band is affected much more by substituents than that of the short-wavelength band, 2,3-dihydroxypyridine being exceptional in this regard.

The Spectra of the cations. (Table XI) The cations of the 2-methoxypyridines absorb at slightly longer wavelengths than the neutral molecules. The spectra of the cations of substituted 2-hydroxy- and 2-methoxypyridines are very similar, and such similarities are essential if (as in the present work) the hydroxypyridine (pyridone) cations are considered to form by proton addition to the oxygen atom. However, they provide no further evidence for the correctness of such cation structures. If the N- and O-protonated cations are thought to have identical spectra, their substituted derivatives could well have similar spectra also, since substituents have almost the same effects on the spectra of the neutral methoxy- and hydroxy-pyridines.

For 2-hydroxypyridines, the "ionization shifts", i.e. the changes in the positions of the bands on protonation, are altered only by small amounts through the effect of substituents other than nitro groups.

Table XI Ultra-Violet Spectra of Substituted Pyridine Cations.

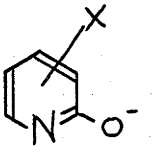
Pyridine	pH or solvent	λ_{max} (Å)		ε	
2-OH	20N-H_2SO_4	2770;	2095	6,590;	3,260
2-OCH_3	10N-HCl	2790;		7,140;	
2-OH, 3-CH_3	"	2795;	2150	7,380;	3,000
2-OH, 4-CH_3	"	2720;	2120	6,600;	2,400
2-OH, 5-CH_3	"	2850;	2150	7,300;	5,000
2-OCH_3, 5-CH_3	"	2900;	2150	6,820;	4,800
2-OH, 6-CH_3	"	2840;	2140	9,100;	3,960
2-OH, 3-Cl	28N-H_2SO_4	2870;	2200	7,960;	3,070
2-OCH_3, 3-Cl	Methanolic HCl	2885;	2235	7,210;	4,950
2-OH, 3-Br	28N-H_2SO_4	2900;	2265	8,000;	2,920
2-OCH_3, 3-Br	Methanolic HCl	2900;	-	7,600;	-
2-OH, 5-Cl	10N-HCl	2940;	2230	6,260;	6,800
2-OCH_3, 5-Cl	"	2980;	2210	6,500;	7,770

Table XI (Continued)

Pyridine	pH or solvent	λ_{max} (Å)			ε		
2-OH, 5-Br	10N-HCl	2965;	2250*		5,600;	7,300	
2-OCH_3, 5-Br	"	3005;	2250*		6,000;	8,600	
2-OH, 5-I	"	3050;	2305		4,300;	12,300	
2-OH, 3,5-Cl_2	28N-H_2SO_4	3100;	2350		6,030;	5,580	
2-OH, 3,5-Br_2	"	3130;	2350*;	2160	6,200;	6,000;	17,000
2-OH, 3,5-I_2	"	3250;	2330;	2130	6,500;	13,800;	8,600
2,3-$(OH)_2$	"	2900;	2225		8,310;	2,850	
2-OCH_3, 3-OH	5N-HCl	2925;	2295		8,520;	4,020	
2,6-$(OH)_2$	"	2925;	2170		11,130;	4,790	
2-OH, 3-NO_2	35N-H_2SO_4	3030;	2400		7,370;	3,500	
2-OH, 5-NO_2	28N-H_2SO_4	2875;	2180		10,050;	7,200	

The shifts of the long-wavelength bands are less affected than those of the short-wavelength bands. The change in the position of the long-wavelength band of 2-hydroxy-3-nitropyridine, however, is extremely large, while the corresponding change for the 5-substituted isomer is actually in the opposite direction from that for all of the other compounds.

The Spectra of the anions. (Table XII) The only spectra with which the spectra of substituted 2-hydroxypyridine anions may be compared are those of similarly substituted phenols. If the anions are most closely represented by the canonical forms



their spectra should be related, at least approximately, to those of the corresponding phenolate ions, in the same way as the spectra of the neutral 2-methoxypyridines were related to those of the phenols. (See page 64). Table XIII lists the absorption maxima for substituted 2-hydroxypyridine anions and the corresponding phenolate ions. The positions of the long-wavelength bands differ by slightly more than was the case in comparisons between the neutral methoxypyridines and phenols, while for the short-wavelength bands, the phenolate ions absorb at longer wavelengths than do the hydroxypyridine anions.

Table XII Ultra-Violet Spectra of Substituted Hydroxypyridine Anions.

Pyridine	pH or solvent	λ_{max} (Å)			ε		
2-OH	6.5N-NaOH	2920;	2280		4,650;	9,900	
2-OH, 3-CH_3	10N-NaOH	2935;	2295		5,850;	8,830	
2-OH, 4-CH_3	"	2890;	2310		4,700;	9,000	
2-OH, 5-CH_3	"	3020;	2320		4,850;	10,150	
2-OH, 6-CH_3	"	2950;	2300		6,160;	9,050	
2-OH, 3-Cl	0.16N-NaOH	3015;	2310		6,090;	8,510	
2-OH, 3-Br	"	3030;	2310		6,420;	8,480	
2-OH, 5-Cl	13	3050;	2380		4,320;	12,400	
2-OH, 5-Br	13	3065;	2370		4,150;	12,400	
2-OH, 5-I	13	3090;	2415		3,800;	17,400	
2-OH, 3,5-Cl_2	12	3150;	2400		5,550;	9,750	
2-OH, 3,5-Br2	12	3180;	2400		4,400;	9,100	
2-OH, 3,5-I_2	13	3250;	2440*;	2280	5,800;	12,000;	12,600

Table XII (Continued)

Pyridine	pH or solvent	λ_{max} (Å)			ε		
2,3-$(OH)_2$	12	3100;	2550		9,100;	6,450	
2-OCH_3, 3-OH	12	2960;	2415		6,700;	8,900	
2,6-$(OH)_2$ mono-anion	7	3220;	2345		14,950	8,430	
2,6-$(OH)_2$ di-anion (1)	16N-NaOH	3085;	2420		8,430;	7,650	
2-OH, 3-NO_2	12	3920;	2600*;	2165	6,610;	3,400;	17,000
2-OH, 5-NO_2	12	3650;	2960;	2175	14,700;	3,410;	7,050

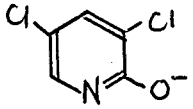
(1) See "Experimental", page 164.

Table XIII Ultra-Violet Spectra - Anions.

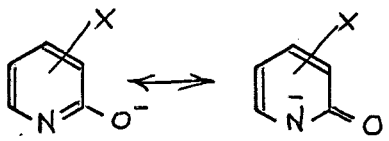
2-Hydroxy-pyridine	λ_{max} (Å)			ε			Phenol	λ_{max} (Å)			ε			Ref.
5-Cl	3050;	2380		4,320;	12,400		4-Cl	2980;	2440		2,600;	11,700		126
3-Cl	3015;	2310		6,090;	8,510		2-Cl	2940;	2365		3,780;	8,300		126
3,5-Cl_2	3150;	2400		5,550;	9,750		2,4-Cl_2	3040;	2440		3,400;	9,500		127
3-NO_2	3920;	2600*;	2165	6,610;	3,400;	17,000	2-NO_2	4160;	2820;	2275	4,800;	4,300;	14,500	38
5-NO_2	3650;	2960;	2175	14,700;	3,410;	7,050	4-NO_2	4020;		2260	19,200;		6,500	37

(Cf. the comparison between these bands for the neutral phenols and methoxypyridines, page).

It will be shown (page 135) that the vibration spectrum of the anion of 3,5-dichloro-2-hydroxypyridine corresponds to a structure best represented by the canonical form 43.



43



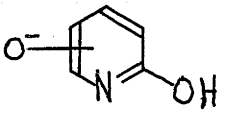
44a 44b

The general similarity of the comparisons between the hydroxypyridine anions and the phenolate ions, including the comparison for the abovementioned ion, combined with the knowledge of the essential nature of this ion, is consistent with the view that the canonical form 44 plays only a minor part in the resonance of the 2-hydroxypyridine anions.

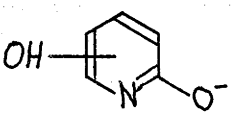
The spectra of the anions of 2-hydroxy-3- and 5-nitropyridine also bear some resemblance to those of the o- and p-phenolate ions, and are consistent with the predominance of the canonical form 44 in the resonance of the ions.

The changes in the spectra of the dihydroxypyridines as a result of the first acidic ionization differ from

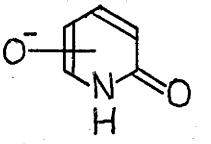
those shown by the other substituted hydroxypyridines. Thus, whereas 2-hydroxypyridines normally exhibit a small hypsochromic ionization shift in the long-wavelength band, and a small bathochromic ionization shift in the short-wavelength band, the dihydroxypyridines exhibit marked bathochromic ionization shifts in both bands. The mono-anions of the dihydroxypyridines can have structures 45, 46 or 47,



45



46



47

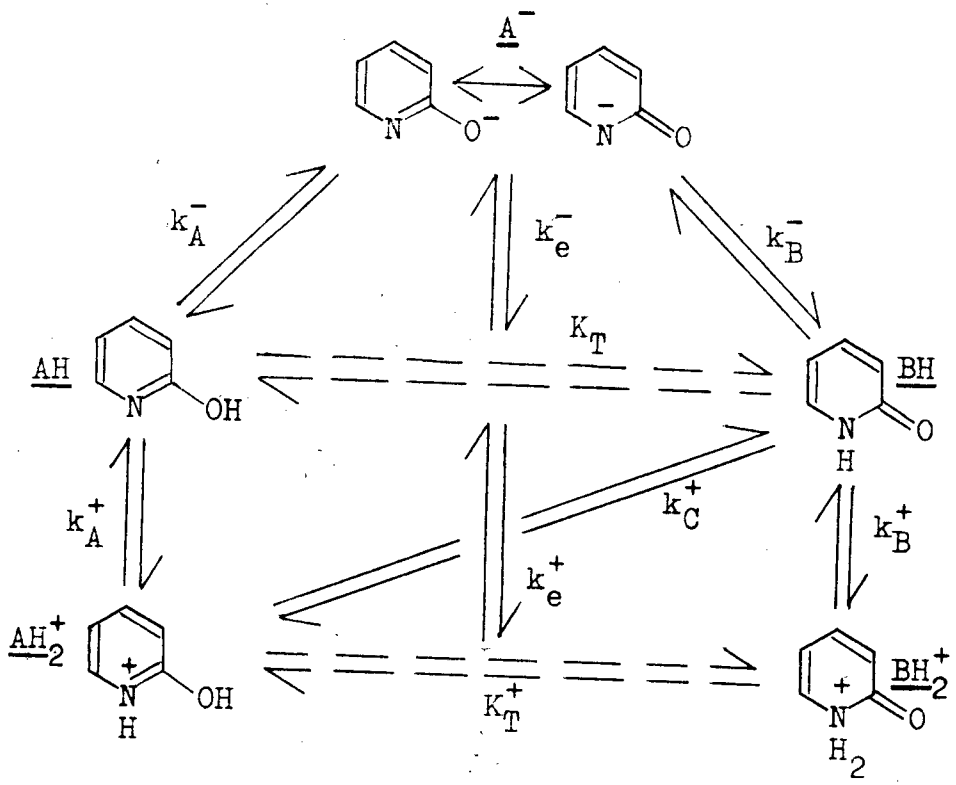
and the unusual ionization shifts suggest that the ions do not exist in the form 46, as this is derived from the neutral molecules by the normal acid dissociation of 2-hydroxypyridines. For 2,6-dihydroxypyridine, structures 45 and 46 are identical, while for the anion of 2,3-dihydroxypyridine, structure 45 is excluded by the difference between its spectrum and that of the anion of 3-hydroxy-2-methoxypyridine. Thus, the ultra-violet spectra indicate that the mono-anions of the dihydroxypyridines exist in the form 47, derived from the neutral molecules by removal of the hydroxyl proton.

B. Ionization Constants.

The complete diagram for the tautomeric and ionization equilibria of 2-hydroxypyridine is shown on page 75, together with the equations defining the various equilibrium constants. The measured ionization constants are k_e^+ and k_e^-, representing the equilibria between the total neutral species (AH +BH), and the total ionized species, (AH_2^+ + BH_2^+) or (A^- + B^-). Some of the relationships that exist between the various equilibrium constants are shown below the diagram.

The ionization constant of 2-methoxypyridine provides an estimate of k_A^+ (see page 29), and, if, as is commonly assumed[5, 6b], $K_T^+ \ll 1$, this estimate enables approximate values to be calculated for k_A^-, k_B^-, k_C^+ and K_T. The value of K_T which is obtained in this way is approximately 230, i.e. the equilibrium proportion of the true hydroxy-tautomer would be 0.43%. If K_T^+ is greater than one, (predominance of the N-protonated cation), K_T must be greater than 230 (from equation 4, page 75).

Since K_T is large, $k_e^+ \backsimeq k_{NMe}$, the ionization constant of the N-methyl derivative, (from equation 6), and hence further increases in K_T cannot significantly affect the equilibrium ionization constant k_e.



$$k_A^+ = \frac{[AH][H^+]}{[AH_2^+]} \qquad k_B^+ = \frac{[BH][H^+]}{[BH_2^+]} \qquad k_C^+ = \frac{[BH][H^+]}{[AH_2^+]}$$

$$k_A^- = \frac{[A^-][H^+]}{[AH]} \qquad k_B^- = \frac{[A^-][H^+]}{[BH]} \qquad K_T = \frac{[BH]}{[AH]}$$

$$k_e^+ = \frac{[AH+BH][H^+]}{[AH_2^+ + BH_2^+]} \qquad k_e^- = \frac{[A^-][H^+]}{[AH+BH]} \qquad K_T^+ = \frac{[BH_2^+]}{[AH_2^+]}$$

$$k^*_{NMe} = \frac{[BH][H^+]}{[AH_2^+ + BH_2^+]}$$

1/ $K_T = \frac{k_A^-}{k_B^-}$ 2/ $\frac{K_T^+}{K_T} = \frac{k_A^+}{k_B^+}$ 3/ $K_T^+ = \frac{k_C^+}{k_B^+}$

4/ $\frac{k_A^+}{k_e^+} = \frac{K_T^+ + 1}{K_T + 1}$ 5/ $\frac{k_{NMe}}{k_B^+} = \frac{K_T^+}{K_T^+ + 1}$ 6/ $\frac{k_e^+}{k_{NMe}} = 1 + \frac{1}{K_T}$

7/ $k_e^+(K_T^+ + 1) = k_C^+ = k_B^+ . K_T^+$ if K_T is large.

* Ionization constant of the N-methyl derivative

Table XIV.

Ionization Constants of Substituted 2-hydroxypyridines.

Substituent(s)	pK_a (acidic)	pK_a (basic)
---	11.70±0.03	0.77±0.02
3-CH_3	12.59±0.03	0.20±0.02
4-CH_3	12.23±0.04	1.14±0.02
5-CH_3	12.01±0.03	1.13±0.02
6-CH_3	12.45±0.03	1.12±0.03
3-Cl	10.40±0.02	-2.03±0.15
3-Br	10.42±0.01	-2.15±0.15
5-Cl	9.87±0.02	-0.07±0.02
5-Br	10.03±0.03	-0.06±0.02
5-I	9.93±0.02	0.00±0.02
3,5-Cl_2	8.52±0.02	-2.54±0.15
3,5-Br_2	8.43±0.03	-2.45±0.13
3-NO_2	8.52±0.03	-4.00±0.15
5-NO_2	7.97±0.03	-2.45±0.15
3-OH	9.00±0.01	--- (1)
6-OH	4.52±0.01	1.00±0.03
2-methoxy-3-hydroxypyridine	8.65±0.01	2.10±0.01

All basic pK_a values were obtained spectrophotometrically, as were the acidic pK_a values for the methyl derivatives. The remainder were determined by potentiometric titration.

(1) See page 163.

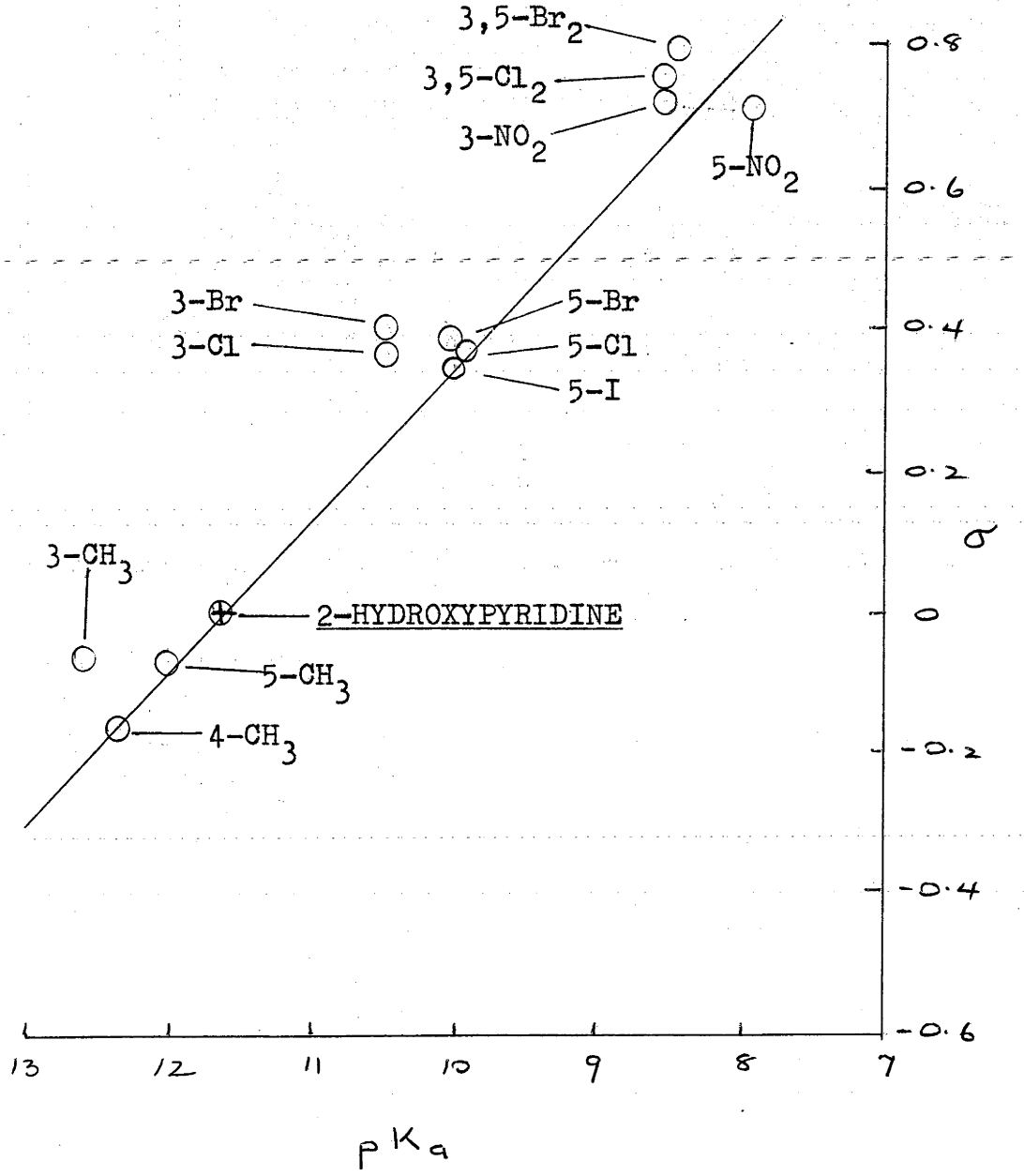
Decreases in K_T would be base-strengthening. If K_T^+ is large, further increases in its value would not significantly affect k_e^+, and if K_T^+ is small, decreases in its value would not affect k_e^+ significantly (from equation 7). Changes in K_T^+ tending to reverse the equilibrium between AH_2^+ and BH_2^+ (i.e. increases in K_T^+ if it is small, or decreases if it is large) would involve changes in k_B^+ and k_C^+ (equation 3), and could appear as base-weakening or base-strengthening effects (equation 7).

Acid Dissociations. 2-Hydroxypyridine is a weak acid, its pK_a value of 11.62 being 2.67 units greater than that for phenol[128]. Electron-donating (methyl) and electron-withdrawing (halogen, nitro) substituents have the expected acid-weakening and acid-strengthening effects respectively. (See page 29).

In Diagram VII is shown the plot of pK_a for the acid dissociations against σ, the Hammett substituent constant. Since the reaction site is the nitrogen atom, position 1, positions 3 and 5 are considered to be meta, and the 4 position para. The σ constants are derived from studies of substitution effects in aromatic systems, so that a close correlation between pK_a and for the non-aromatic pyridone system would not be

DIAGRAM VII

pK_a (acidic) plotted against Hammett σ.



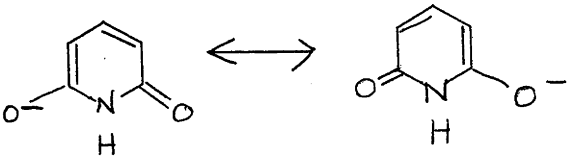
expected; nevertheless, the points lie quite close to a straight line, and if the 3-substituted compounds (see below) are omitted from the plot, this straight-line relationship is improved. The value of ρ, the reaction constant, obtained from this plot is 5.0, which is of the same order as values of ρ for reactions involving nuclear hydrogen atoms in aromatic systems[129].

Since the 2-hydroxypyridine molecule is not symmetrical, substituents in the two meta positions, 3 and 5, could have quantitatively different effects on the ionization constant, and this is found to be so. However, the 3-substituted compounds are all less acidic than their 5-substituted counterparts, and since this applies to both electron-donating and electron-withdrawing substituents, it cannot be ascribed to inductive or mesomeric effects. A possible explanation of these differences is that substituents in the 3 position offer steric inhibition to solvation.

The dihydroxypyridines (acid dissociations). Three structures are possible for the mono-anion of 2,3-dihydroxypyridine, and two for the mono-anion of 2,6-dihydroxypyridine. (See page 73). The pK_a value for 2,3-dihydroxypyridine, (9.00), is similar to those for 3-hydroxypyridine[6b] (8.72), and 2,5-dihydroxypyridine[120] (8.51). This is what one would expect if the anion has

structure 47 (page 73), because Albert[120] has shown that the ionization constants of substituent groups in 5-substituted 2-hydroxypyridines are similar to the constants for the ionization of these groups in pyridine itself. (E.g. nicotinic acid, pK_a = 3.82; 6-hydroxy-nicotinic acid, pK_a = 3.75[120]).

The pK_a value for 2,6-dihydroxypyridine (4.52) is 7 pK units lower than the pK_a value for 2-hydroxypyridine itself. The introduction of a hydroxy group adjacent to the NH group is most unlikely to have so great an effect on the ionization of the NH proton, and it may be deduced that it is the OH proton which is removed. The value 4.52 is 4 pK units less than Mason's[6b] estimate of the ionization constant for the enolic form of 2-hydroxypyridine, i.e. than the estimated pK_a value for a hydroxyl group in position 2. Stabliization of the anion by the resonance between two equivalent canonical forms



could explain this difference. (Alternatively, if K_T^+ (page 75) is taken to be 10^4, the estimate of pk_A^- thus obtained is approximately 4.5).

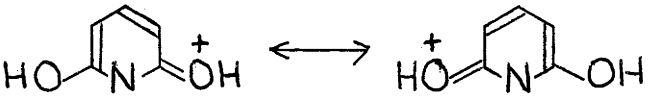
2,3-dihydroxypyridine exists as its mono-anion even in 16N alkali, and no estimate of its second ionization

constant could be made. 2,6-dihydroxypyridine appears from ultra-violet spectra to exist as the mono-anion in 1N alkali, and largely as the di-anion in 16N alkali; its second pK_a probably lies between 14.5 and 14.8 (stoichiometric value).

Basic ionization. The compounds examined are all quite weak bases, the pK_a values ranging from 1.15 to -4.0. No general correlation was found between the basic pK_a values and the Hammett σ constants. The 5 position could be regarded as meta or para, depending on whether proton addition is considered to occur at the oxygen or nitrogen atoms, and Diagrams VIII and IX show the plots obtained for each of these alternatives.

A satisfactory determination of the basic ionization constant for 2,3-dihydroxypyridine was not achieved (see "Experimental", page 163).

If proton addition to 2,6-dihydroxypyridine occurs at the oxygen atom, the resonance between two equivalent canonical forms



would be expected to stabilize the ion, with a consequent increase in basic strength. This is not observed, the

DIAGRAM VIII

pK_a (basic) for substituted 2-Hydroxypyridines plotted against Hammett σ.

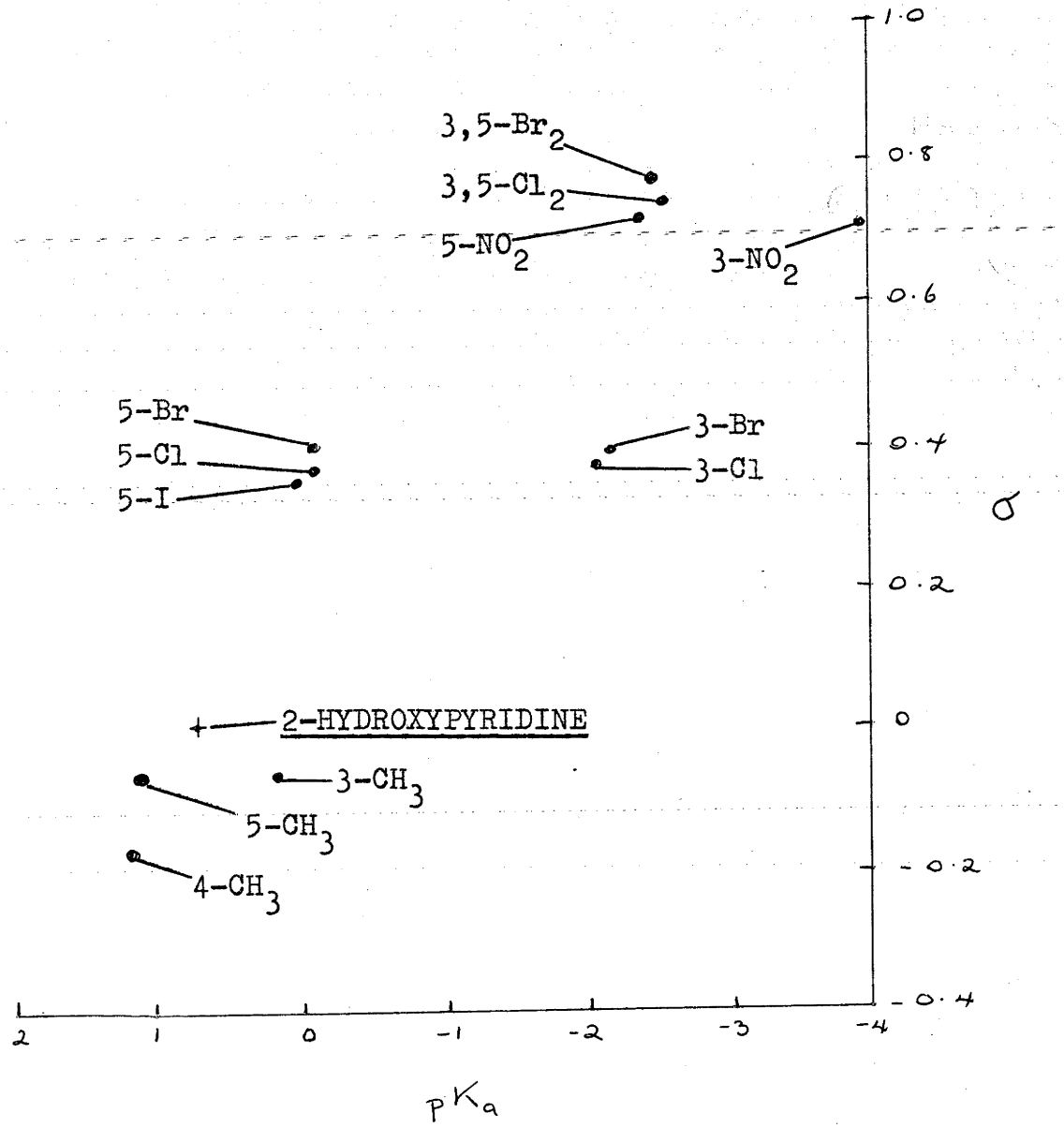
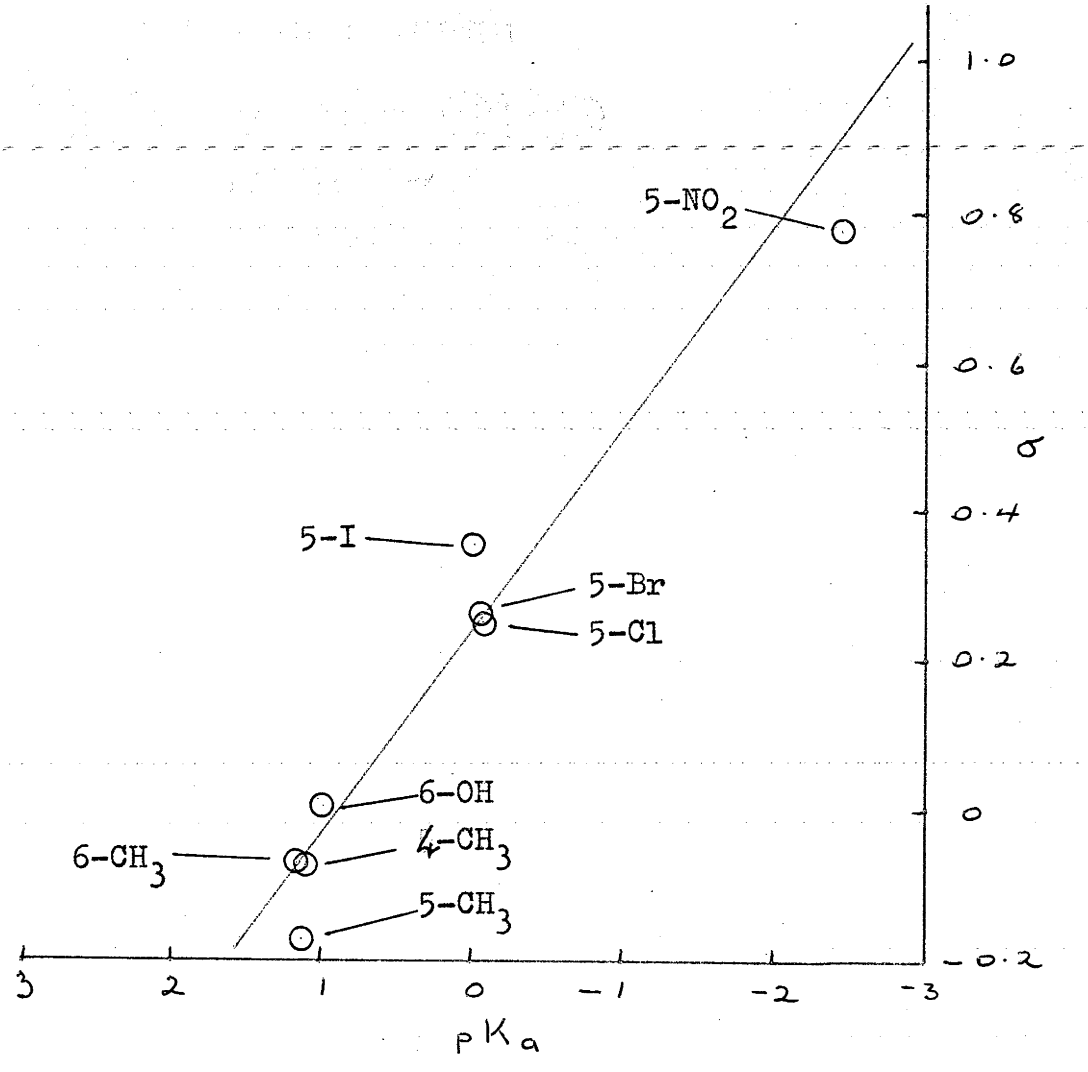


DIAGRAM IX

pK_a (basic) for substituted 2-hydroxypyridines plotted against Hammett σ.



pK_a value of 1.00 being only slightly higher than that for the unsubstituted 2-hydroxypyridine.

In this series of ionization constants, the 3-substituted compounds are very sharply distinguished from their 5-substituted counterparts, the former being the weaker bases. This unusual effect is most clearly illustrated in the case of methyl substitution; a methyl group in the 5 position has the expected base-strengthening effect, while in the 3 position it has an anomalous base-weakening effect. Similarly, a chlorine atom in the 3 position is more base-weakening (apparently more electron-withdrawing) than in the 5 position. (Cf. the effects of such substitution on the acidic ionizations, page 79). The anomaly cannot be ascribed to any unusual combination of electrical effects, since it is observed for substituents having electron-withdrawing and electron-donating inductive and mesomeric effects. Since the 3-substituted compounds have unusually low basicities, the anomaly cannot be due to a change in K_T (see page 74). It was shown on page 77 that a change in the preferred structure of the cation could be accompanied by a reduction in basicity, but the reversal of the tautomeric equilibrium between the two forms of the cation by such diverse substituents is difficult to justify. (See also the vibration spectra of

3- and 5-chloro-2-hydroxypyridine cations).

Some kind of steric interaction may therefore be involved; direct steric interference with the ionization process seems unlikely, but steric inhibition of solvation is a possibility. Solvent-to-solute hydrogen bonds would be an important part of this solvation. Such bonds would be expected to be stronger for ions than for neutral species, so that inhibition of them would tend to inhibit ionization, as is observed for both the basic and acidic ionizations. Direct steric interference with hydrogen bonding for the cations is possible (but not necessarily inevitable) only if they have the O-protonated structure, since the ability of the carbonyl oxygen atom of an N-protonated cation to participate in hydrogen bonding would be slight.

C. Vibration spectra.

The main object in the discussion of vibration spectra is to discover those features of the spectra which distinguish the non-aromatic 2-pyridones from the aromatic 2-methoxypyridines (which are taken as reference compounds for the inaccessible hydroxy tautomers), and to examine the spectra of their cations for evidence of distinguishing features which might

indicate a similar structural difference. (see diagrams on page (v). Finally, the spectra of the sodium salts will be discussed in the light of any structural criteria thus obtained.

An indication of the extent to which methoxypyridines and their cations reproduce the vibrational features of hydroxypyridines and their cations is provided by the comparisons between the spectra of 3-hydroxy- and 3-methoxy-pyridine and their cations. These comparisons, however, are strictly applicable only to hydroxy- and methoxy- groups in positions not conjugated with the ring nitrogen atom, and slightly different relationships could exist between 2- and 4-methoxy- and (genuine) hydroxy-pyridines. To this end, the hitherto unknown vibration spectra of the hydrochlorides of 2- and 3-methoxypyridine have been determined, and, for the sake of completeness, the corresponding data for 4-methoxypyridine. The infrared spectra of the neutral methoxypyridines have been published previously[62, 109a], but the Raman spectra reported here are new.

Strictly, in the study of vibration spectra, Raman spectra should be obtained for all species examined, but a number of factors prevented this ideal from being

realized, or even approached, in the present work. As a result, some of the band assignments are less certain than they otherwise might have been. Large amounts of sample were required in order to obtain Raman spectra using the equipment available, and it was therefore decided that spectra should be attempted for a representative selection of the compounds only. Of the substituted 2-hydroxypyridines examined, only three were sufficiently soluble to enable Raman spectra to be obtained, and one of these compounds, the 5-methyl derivative, exhibited a strong fluorescence which obscured all but one of the Raman bands. Solubility was less restrictive for the ionic species, but fluorescence or photo-decomposition prevented satisfactory spectra from being obtained in some cases.

The Methoxypyridines. (Appendix, pages 190, 191.) The vibration spectra of the methoxypyridines are typical of substituted pyridines[62], and comparison with the spectra and vibrational assignments for benzene[54a], pyridine[54b] and toluene[131] suggests a number of assignments which are listed in Table XV. These will be discussed mainly with reference to 2-methoxypyridine. (See Diagram I, page 22, which shows the modes of vibration for benzene.)

Table XV Vibrational Assignments[1], (cm^{-1}), Methoxypyridines.

Vibration No.	2-Methoxy-pyridine	3-Methoxy-pyridine	4-Methoxy-pyridine
8a	1575	1588	1597
8b	1606	1578	1574
19a	1484	1482	1507
19b	1422	1427	1423
3	1314 ?		1333 ?
9a	1144	1193	1215 ?
9b	1150 ?		
15	1099	1111	1089
12	1046	1018	1051
1	988	1052	990
10b ?	812	799	802
C-O-C asym. str.	1292	1284	1289
C-O-C sym. str.	1022		1029

(1) Numbering of vibrations as in Ref. 54c.
See also Diagram I on page 22.

Skeletal Stretching vibrations. Vibrations 8a, 8b, 19a, and 19b in the region between 1400 and 1600 cm^{-1} can be assigned with some certainty, since they correspond fairly well with similarly assigned bands showing similar frequencies and Raman and infra-red intensities in the spectra of pyridine and toluene. Vibration 12 has been assigned on a similar basis, while the symmetrical "ring-breathing" mode, vibration 1, is clearly correctly placed at 988 cm^{-1}.

C-H Bending modes. The prominent Raman band at 1308 cm^{-1} in the spectrum of 2-methoxypyridine is attributed to ν_3, which has been assigned to bands at 1210 and 1313 cm^{-1} in the spectra of pyridine[54b] and toluene[131] respectively. Similar considerations have led to the assignments of vibrations 9a, and with less certainty, 9b. The strong band near 800 cm^{-1} (Raman and infra-red) is found also in the spectra of the picolines[63b] and toluene, and in terms of Green's[131] assignments for the latter, the choice appears to be between modes 12 and 10b. The former assignment is rather far removed from the corresponding assignment in the spectrum of pyridine, and 10b has been chosen here. Another possibility, vibration 5, while somewhat further removed in frequency, could also be proposed.

Bands due to C-O-C symmetric and asymmetric stretching vibrations are probably located near 1000 and 1290 cm^{-1} respectively, bands in these positions having no counterparts in the spectra of the methylthiopyridines[132]. (See, however, the comparison between the spectra of 3-hydroxy- and 3-methoxypyridine.) The methyl group can be expected to absorb near 1460 and 1375 cm^{-1}, and for comparisons with the hydroxypyridines, bands in these two positions must be treated with caution.

In the spectra of substituted 2-methoxypyridines, (see Table XVI), the bands 8a and 8b (1576, 1606 cm^{-1}) move to higher frequencies in the 5-methyl compound, and to lower frequencies in the other compounds examined, the lowest values being 1550, 1571 cm^{-1} in the spectrum of 2-hydroxy-3,5-dibromopyridine. 8a, which is fairly prominent in the Raman spectra, becomes quite weak in the infra-red spectra of the substituted compounds, appearing only as a shoulder in the spectrum of the dibromo derivative. The frequency of the band 19a appears to change quite markedly on substitution, the band being at 1406 ± 1 cm^{-1} in the 3-chloro and 3-bromo derivatives, and 1373 ± 5 cm^{-1} in the spectra of the two 5-substituted compounds. The Raman spectra of the 3-chloro and 3-bromo derivatives also suggest this

Table XVI Infra-red Spectra, Substituted 2-Methoxypyridines.

2-Methoxy-pyridine	-5-CH_3	-5-Br	-3-Cl	-3-Br	-3-OH	-3,5-Br_2
3000)m 2940)	2940 m	2980)m 2950)	2980)m 2950)	2950	2570	2910
	1650 *	1656 w	1654	1640	1655 ?	
1606 s	1614 m	1586 s	1586 vs	1583 vs	1604 m	1571 m
1576 s	1574 m	1564 w	1563 w	1560 *	1575 m	1550 *
1484 vs	1494 vs	1481 vs	1471 vs	1470 vs	1501 s	1572 vs
1447 m	1445 *	1430 w	1444 s	1444 s	1451 s	1442 w
1422 s	1378 m	1368 s	1407 vs	1405 vs	1376 vs	1410 s 1373 s
1314 m	1305 vw	1302 w	1317)s 1302)	1300 s	1287 s	1305 s
1292 s	1288 vs	1284 vs	1258 s	1256 s	1245 m	1255 s
1144 m	1127 m	1122 m	1128 s	1120 m	1102 s	1110 w
1045 m		1047 *	1073 vs	1071 vs	1065)w	
1022 m	1028 s	1022 s	1046 s	1035 vs	1055)	1056 s
988 m	990 vw	1002 w	1012 s	1010 s	1014 s	
812 m	823 m	826 m				
781 s			785 s	785 s	776 m	
	740 m	757 m	751 s	751 s	751 m	742 m

large frequency shift. The two prominent Raman bands near 1300 cm^{-1} in the spectrum of 2-methoxypyridine, which have been assigned to ν_3 (1308 cm^{-1}) and the C-O-C asymmetric stretching mode (1286 cm^{-1}), appear at lower frequencies in the spectra of the two 3-halogeno derivatives, 1301±1 cm^{-1} and 1245±1 cm^{-1}. The assignment of infra-red bands in the other substituted 2-methoxypyridines are made accordingly, giving a range of 1314-1300 cm^{-1} for ν_3, and 1292-1245 cm^{-1} for the C-O-C vibration.

There are three strong infra-red bands near 1025 cm^{-1} in the spectra of the 3-chloro and 3-bromo compounds, while only one band appears in the spectra of the 5-substituted derivatives. Cook and Church[64] have suggested that in 2,5-disubstituted pyridines, as in 3-substituted pyridines, ν_1 occurs between 1021 and 1034 cm^{-1}, so that the single band in the 5-substituted 2-methoxypyridines may be due to a coincidence between ν_1, ν_{12} and the asymmetric C-O-C mode.

In the region between 650 and 1000 cm^{-1}, 3-substituted compounds absorb near 750 and 780 cm^{-1}, while 5-substituted compounds absorb near 750 and 820 cm^{-1}. Similar correlations for 2,3- and 2,5-disubstituted pyridines have been noted by Podall[65] and Shindo and Ikekawa[63a]. All the halogen-substituted compounds

absorb between 650 and 700 cm^{-1}.

In the comparison between the spectra of 3-hydroxy-[109c] and 3-methoxypyridine, the following points may be noted. (See Table XVII.)

a/ Bands due to vibrations 8a, 8b and 19a are little affected by the substitution of hydroxy for methoxy groups.

b/ ν_{19b} either appears only weakly in the spectrum of the hydroxy compound (at 1440 cm^{-1}) or shifts markedly to 1377 cm^{-1}, the latter band having no counterpart in the spectrum of the methoxy compound otherwise.

c/ The 1313 cm^{-1} band in the spectrum of 3-hydroxypyridine has no counterpart in the spectrum of the methoxy compound.

d/ Bands between 1240 and 1300 cm^{-1} appear in the infra-red spectra of both compounds, rendering the assignment of the C-O-C asymmetric stretching vibration less certain, but the hydroxy compound shows fewer Raman bands in this region than does the methoxypyridine.

e/ For the methoxy compound, strong bands are found at 798 cm^{-1} in both the Raman and infra-red spectra. For the hydroxy compound, only the infra-red spectrum shows a strong band near this frequency, and it is the

Table XVII Vibration Spectra, 3-Hydroxy- and 3-Methoxy-Pyridine [109c]

3-Methoxy-pyridine	Raman	3-Hydroxy-pyridine	Raman
3015), 2950) m		2908 s	
1588)* 1578) s	1588) 5 1579) 2	1581) 1569) s	1570w
1482 s		1484 s	
1427 s	1426 1	1440 vw	
		1377 s	
		1313 ms	
1284 vs	1282 2	1290) 1279) s	
1269 m	1271 3		
1234 s	1233 1	1240 s	
1193 m	1191 2	1218 *	
1179 *	1179 2	1180 ms	1180 ?
1130 w		1127 mw	
1111 m	1111 1	1105 ms	1107 ?
1052 m	1051 10	1050 m	1045 m
1018 s	1014 7	1020 m	
		915 m	
897 vw		895 ms	
		849), 843) ms	846 mw
		830 mw	
799 s	798 9	806), 800) s	798 vw
706 s		705 ms	703 ?

band at 846 cm^{-1} which is strong in both the Raman and infra-red spectra. The infra-red band near 895 cm^{-1} is much stronger in the spectrum of the hydroxy compound than in that of the methoxy compound. f/ A source of difference between the spectra of the compounds is the hydrogen bonding, which is strong for the hydroxy-compound, and non-existent for the methoxy compound.

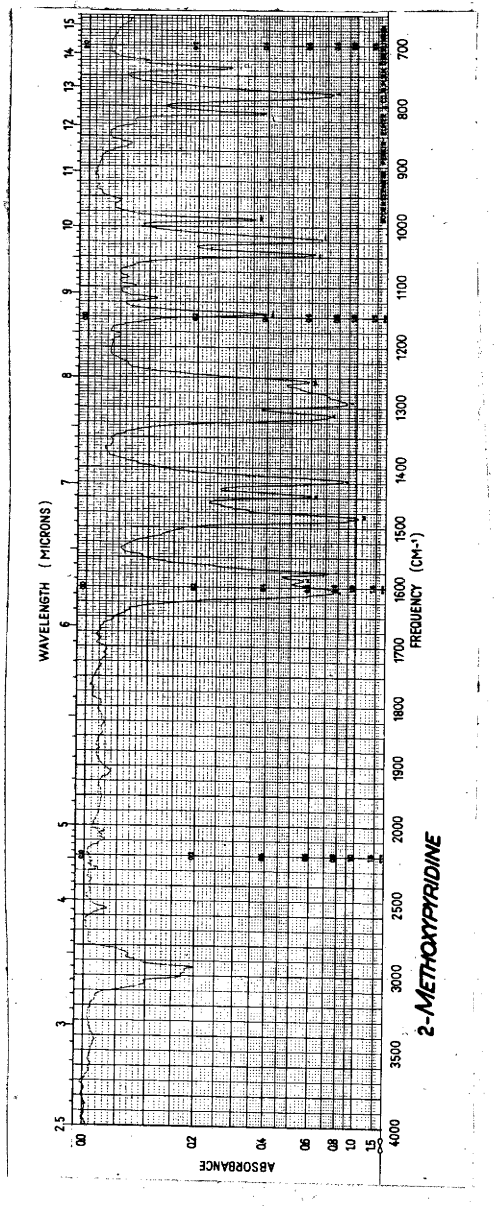
2-Hydroxypyridines. 2-Hydroxypyridine exists in the pyridone form, and Table XVIII gives a comparison between its vibration spectrum and that of 2-methoxy-pyridine, (the reference compound for the inaccessible hydroxy tautomer). (See also Diagram X.) The most striking differences between these spectra are the 1645 cm^{-1} band in the infra-red spectrum of 2-hydroxy-pyridine, which can be assigned to the carbonyl stretching vibration, and which has no counterpart in the spectrum of the methoxypyridine, and the strong band at 985 cm^{-1} in the Raman spectrum of the methoxy compound, assigned to the symmetrical ring-breathing mode, which has no counterpart in the spectrum of the hydroxy compound. Further, the 1484 cm^{-1} band in the spectrum of the methoxypyridine appears only weakly in the spectrum of the hydroxypyridine, while the 1314 cm^{-1} band of the former spectrum does not appear at all in the

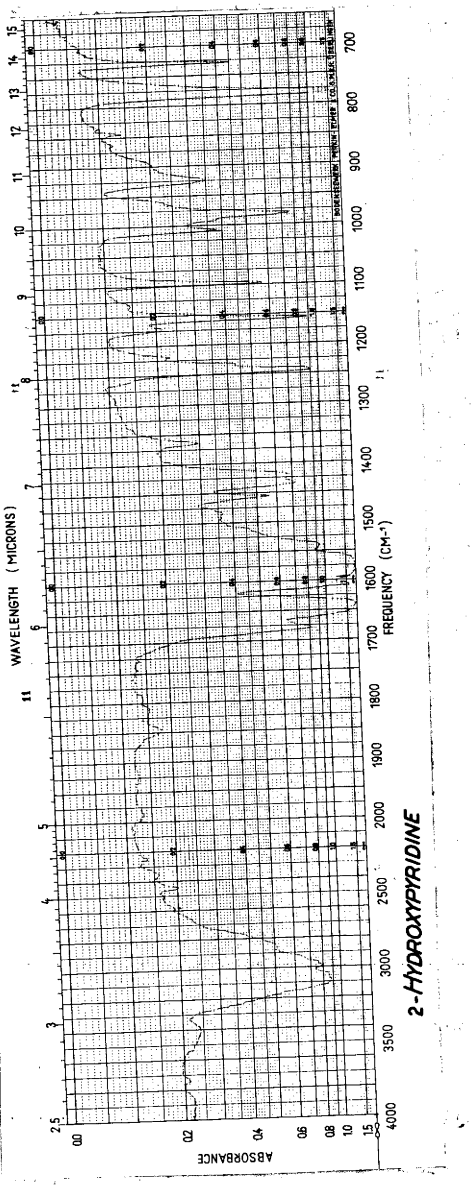
Table XVIII Vibration Spectra, 2-Methoxy- and 2-Hydroxy-pyridine.

2-Methoxy-pyridine		2-Hydroxy-pyridine	
3000)m 2940)		3095) 3055)vs 2980)	
		1681 m	Raman
	Raman	1645 vs	1640 vw
1606 s	1600 1	1608 s	1599 w
1576 s	1570 5	1576 vs	
	1539 w	1542 m	
1484 vs		1485 w	
1447 m	1443 2	1456 m	1463 m
1422 s	1417 *	1435) 1420)s	
		1364 w	1371 m
1314 m	1308 6		
1292 s	1286 3		
1256 w	1256 *	1244 s	1260 s
		1156 s	
1144 m	1140 1	1132 w	
1099 w	1095 2	1098 m	
1045 m	1041 3		
1022 m	1019 1	1008 m	1010 ?
989 m	985 10	981 s	
		925 m	
862 w		845 w	850 ms
812 m	807 5		812 ms
781 s	781 1	780 vs	778 w
737)m)		729 m	742 w
725 w			

DIAGRAM X

INFRA-RED SPECTRA.





latter spectrum. (Bands at 1292 and 1045 cm^{-1} in the spectrum of 2-methoxypyridine must be excluded from the comparison, since they have been assigned to vibrations of the C-O-C group.) In the low frequency region, differences between the two spectra are paralleled to some extent by similar differences between the spectra of 3-hydroxy- and 3-methoxy-pyridine.

All of the substituted 2-hydroxypyridines examined exhibit strong bands of frequency greater than 1640 cm^{-1}, which can only be due to carbonyl stretching vibrations, and which prove that all exist as pyridones. Of considerable interest is the effect of the substituents on the carbonyl stretching frequency, and this is tabulated in Table XIX.

Increases in the carbonyl stretching frequency are expected when electron-withdrawing substituents are present. (See page 16.) For this reason, it was thought that the spectra of 2-hydroxypyridines containing such substituents, and particularly the spectra of their cations, should be informative. In fact, most substituents raise the frequency, a nitro group in the 3 position having the greatest effect. No marked rise in the frequency is observed when a halogen atom is substituted in the 3 position, the 3-methyl and 3-chloro

Table XIX.

Carbonyl stretching frequencies.

2-Hydroxypyridine	$\nu_{C=O}(cm^{-1})$
----	1645
3-CH_3, 4-CH_3, 5-CH_3,	1652-1657
3-Cl, 3-Br, 3-OH	1658)
5-Cl	1641)
5-Br	1641
5-I	1639
5-NO_2	1674
3-NO_2	1694
3,5-Cl_2	1697
3,5-Br_2	1692
3,5-I_2	1634
6-OH	1640
6-CH_3	1672

derivatives absorbing at 1652 and 1653 cm^{-1} respectively. (Cf page 19.) However, for the 3,5-dichloro and 3,5-dibromo derivatives, the carbonyl band falls at 1694 ± 3 cm^{-1}, which is a much greater increase over the frequency in 2-hydroxypyridine itself than would be predicted from the effects of 3- and 5-halogeno substituents separately.

Kabachnik, Ioffe and Sheinker[112], who examined the infra-red spectrum of the 3,5-dibromo compound, suggested that the steric effect of the bromine atom in the 3 position inhibits hydrogen bonding to the carbonyl oxygen atom, thereby raising the carbonyl stretching frequency. The principal bands in the X-H stretching region are at higher frequencies for this compound (and the dichloro compound) than for most of the other substituted 2-hydroxypyridines examined in the present work, in accordance with this view. However, the carbonyl and X-H stretching frequencies in the spectra of the 3-chloro, 3-bromo, and 3,5-diiodo derivatives of 2-hydroxypyridine are lower than would be expected if such an explanation were correct, and it is more likely that the combined inductive effects of the halogen atoms in positions 3 and 5 are the major causes of the high frequencies. These inductive effects could, by lowering the electron

density at the carbonyl oxygen atom, raise the carbonyl stretching frequency (see page 16), and at the same time, weaken the electron donor properties of the oxygen atom, thereby weakening the hydrogen bonding to it.

Another unusually high carbonyl stretching frequency is seen in the spectrum of the 6-methyl derivative, in which the band falls at 1673 cm^{-1}, 15 cm^{-1} higher than for any other single substituent except the nitro group. (The same rise in frequency is not seen, however, in the spectrum of 2-hydroxy-4,6-dimethylpyridine[112], in which the band is found at 1650 cm^{-1}.)

A lowering of the frequency is observed in the 5-bromo, 5-iodo and 6-hydroxy derivatives, and a further lowering in the 3,5-diiodo derivative. The carbonyl stretching frequency for this compound, 1634 cm^{-1}, is the lowest in the series of compounds examined, contrasting sharply with the frequencies for the dichloro and dibromo derivatives.

The spectra of the substituted 2-hydroxypyridines are very different from those of the corresponding 2-methoxypyridines, confirming the pyridone structures for the former compounds. Table XX, which lists the main bands in the infra-red spectra of the 5-bromo- and 3-chloro derivatives of 2-hydroxy- and 2-methoxy-pyridine, shows that the differences between these pairs of spectra

Table XX Main infra-red bands

5-Bromo-		5-Chloro-	
2-Methoxy-pyridine	2-Hydroxy-pyridine	2-Methoxy-pyridine	2-Hydroxy-pyridine
2980), 2950) m	3005), 2925) vs, 2810), 2740)	2980), 2950) m	2780 vs
1656 w	1641 vs	1654 w	1657 vs
	1604 vs		1612 s
1586 s		1586 vs	
1548 *	1538 s		1546 m
1481 vs	1475 w	1471 vs	1472 m
1466 *	1458 s	1444 s	1435 *
1430 w	1424 m	1407 vs	
1368 s		1317), 1302) s	1325 m
	1340 m	1258 s	1246 m
1284 vs		1128 s	1123 m
1247 m	1226 m	1073 vs	1066 *
1156 w	1143 m	1046 vs	1046 m
1122 m		1012 s	
1090 m	1079 m		982 m
1022 s		963 w	944 m
1002 w	991 m	891 w	876 m
	965 m	785 s	774 m
915) w, 890) *	908) m, 897) w	751 s	756 m
826 m	844), 833) m	698 s	671 m
757 m			

are greater than those between the spectra of the unsubstituted compounds (Table XVIII). In particular, strong bands near 1605 cm^{-1} and 1575 cm^{-1} appear in the spectra of both 2-hydroxy- and 2-methoxy-pyridine, but in the spectra of their substituted derivatives, no such parallels can be drawn.

Methoxypyridine cations. The vibration spectra of the methoxypyridine cations, discussed here mainly with reference to the 2-methoxypyridine cation, show a general similarity with the spectra of the neutral molecules, although significant differences are to be seen in a few bands. The greatest changes in frequency are those of ν_{8a} and ν_{19a}, both of which increase by approximately 50 cm^{-1} in the case of 2-methoxypyridine. ν_{8b} apparently increases only slightly in frequency. Of significance for later comparisons is the change in the relative intensity of the Raman band at 985 cm^{-1}, ν_1, which is almost twice as intense as any other band in the Raman spectrum below 2000 cm^{-1} for the neutral molecule, but which is not the strongest band in the Raman spectrum of the cation. Its intensity is approximately equal to that of ν_3, (1326 cm^{-1}), and slightly less than that of the band at 809 cm^{-1}, both of these bands being due to C-H motions. Suggested assignments for some of the bands in the spectra of the methoxypyridine cations are listed in Table XXI.

Table XXI Vibrational Assignments(1), (cm^{-1}), Methoxypyridine Hydrochlorides.

Vibration No.	2-Methoxy-pyridine	3-Methoxy-pyridine	4-Methoxy-pyridine
8a	1631	1620	1635
8b	1613	1612	1600
19a	1540	1552	1524
19b	1462 ($+CH_3$ bend?)	1461 ($+CH_3$ bend?)	1512 ?
3	1321	1323	1322
9a	1175	1191	1192
15 ?	1102	1109	1099
12	1037	1012	1044
1	981	1050	991
10b ?	810	796	803

(1) Numbering of vibrations as in Ref. 54C. See also Diagram I.

In the solid (or, for Raman spectra, solvated) cations, strong hydrogen bonding is to be expected, and the low frequencies of the N-H stretching vibrations in the hydrochlorides show that this expectation is realized. If the methoxypyridine cations are to be used as reference compounds for the O-protonated pyridone cations, it is desirable to obtain spectra under conditions which minimize this difference (hydrogen bonding) between methoxy and hydroxy groups. No such conditions can be applied to the Raman spectra of the ions in solution, but for the infra-red spectra of the solid salts, substitution of the simple chloride ion by complex anions such as trichloromercurate, hexachloroantimonate, etc., will achieve this result[89,92]. Therefore, the spectra of the methoxypyridinium trichloromercurates or octachlorotrimercurates were obtained, and are given in the Appendix.

The N-H stretching frequency, at 2510 cm^{-1} in the spectrum of 2-methoxypyridine hydrochloride, undergoes a very large shift to higher frequencies when the strengths of the hydrogen bonds are reduced, appearing at 3090 cm^{-1} in the spectrum of the trichloromercurate, and at 3290 cm^{-1} in the spectrum of the hexachloroantimonate. Another marked shift is that of the band at 939 cm^{-1},

which appears at 884 cm^{-1} in the spectrum of the trichloromercurate, and at 868 cm^{-1} in that of the hexachloroantimonate. This band can therefore reasonably be assigned to the $\overset{+}{N}$-H out-of-plane bending mode. The remaining bands are less affected by the substitution of complex anions for the chloride ion, frequency shifts of less than 15 cm^{-1} being observed.

For the substituted 2-methoxypyridine cations, only infra-red spectra have been obtained; those compounds which were prepared in quantities sufficient for Raman spectroscopy proved to be too fluorescent in the ionized form to allow Raman bands to be observed. Table XXII shows the positions in some of the strong bands between 980 and 1650 cm^{-1}. Bands assigned to the C-O-C asymmetric stretching vibration fall between 1254 and 1296 cm^{-1}. The band at 1037 cm^{-1} in the spectrum of 2-methoxypyridine cation, ν_{12}, does not appear in the spectra of the 5-chloro or 5-bromo derivatives, while a band which could be due to vibration 1 or the C-O-C symmetric stretching vibration appears between 981 and 1004 cm^{-1}.

Finally, it is necessary to consider to what extent the methoxypyridine cations reproduce the vibrational characteristics of the hydroxypyridine cations. The spectra of 3-hydroxy- and 3-methoxy-

Table XXII Main Infra-red Bands, 2-Methoxypyridine Cations.

2-Methoxy-pyridine	-5-CH_3	-5-Cl	-5-Br	-3-Cl	-3-Br	-3-OH	-3,5-Cl_2	-3,5-Br_2
1631 s	1611 s	1630 m	1621 m	1623 m	1623 s	1630) 1620) m	1601 s	1601 m
1613 vs		1606 vs	1604 vs	1596 vs	1591 vs	1572 vs		
1539 s	1552 s	1535 vs	1531 vs	1528 vs	1515 vs	1540 *	1521 s	1513 s
1462 m	P		1475) 1463) w	1478 m	1486 s	1489 w	P	P
1425 w	1434 w	1432 s	1429 s	1432 m	1441 m 1424 m	1454 m	1428 w	1428 w
1321 s	1355 m 1320 m	1335 vs	1334 vs	1357 m 1326 s	1356 s 1332 s	1304 m	1319 s	1309 s
1296 vs	1290 s	1292) 1284) s	1291) 1286) s	1260 m	1254 m	1286 vs	1254 s	1256 m
1235 m	1235 w	1233 m	1232 m	1214 m	1221 s		1212 m	1212 m
1174 m	1190 m	1198 w	1197 w	1181 w	1190 m	1205) 1186) m	1179 w	1174 w
1130 vw	1157 m	1141 m	1151) 1141) m	1125 m	1124 m	1112 m	1137 m	
1037 m	1058 w			1054 m	1043 m	1053 m		
1012 m								

Table XXII (Continued)

2-Methoxy-pyridine	-5-CH_3	-5-Cl	-5-Br	-3-Cl	-3-Br	-3-OH	-3,5-Cl_2	-3,5-Br_2
981 s	1000 s	1004 s	1007) 1003)m	990 s	996 vs	1004 s	987 s	987 s
					960 m		963) 946)m	
939 m				902 m	892 m			
	849 m	872) 866)m	865 m			857 m	866) 848)s	852 s
810 m		837) 826)m	835) 826)m	801 vs				
774 vs				779 m	783 vs	777 s		
723 m	735) 725)s				726 m	731 m	722 s	726 m
				690 s	665 s		661) 654)m	686 m

pyridine hydrochlorides are compared in Table XXIII. There is a fairly close correspondence between the frequencies (and, to a lesser extent, the intensities) of many of the bands, but several significant differences are observed. The band at 1492 cm^{-1} in the spectrum of the hydroxy compound has no counterparts in the spectrum of the methoxy compound nearer than the two bands at 1441, 1461 cm^{-1}, one of which may be due to a vibration of the methyl group. There is a difference of 40 cm^{-1} between corresponding bands near 1375 cm^{-1}, while the band at 1240 cm^{-1} in the spectrum of the hydroxy compound has no counterpart in the spectrum of the methoxy compound. 3-Methoxypyridine hydrochloride exhibits four prominent infra-red bands between 980 and 1050 cm^{-1}, while the hydroxy compound exhibits only three weak bands. However, the intense Raman band near 1050 cm^{-1}, ascribed to vibration 1, is seen in both spectra. The strong Raman and infra-red band at 800 cm^{-1} in the spectrum of the methoxy compound appears at 839 cm^{-1} in the spectrum of the hydroxy compound; a similar difference between the spectra of the neutral molecules has already been noted (page 93). The corresponding bands near 850 cm^{-1} differ in frequency by 35 cm^{-1}.

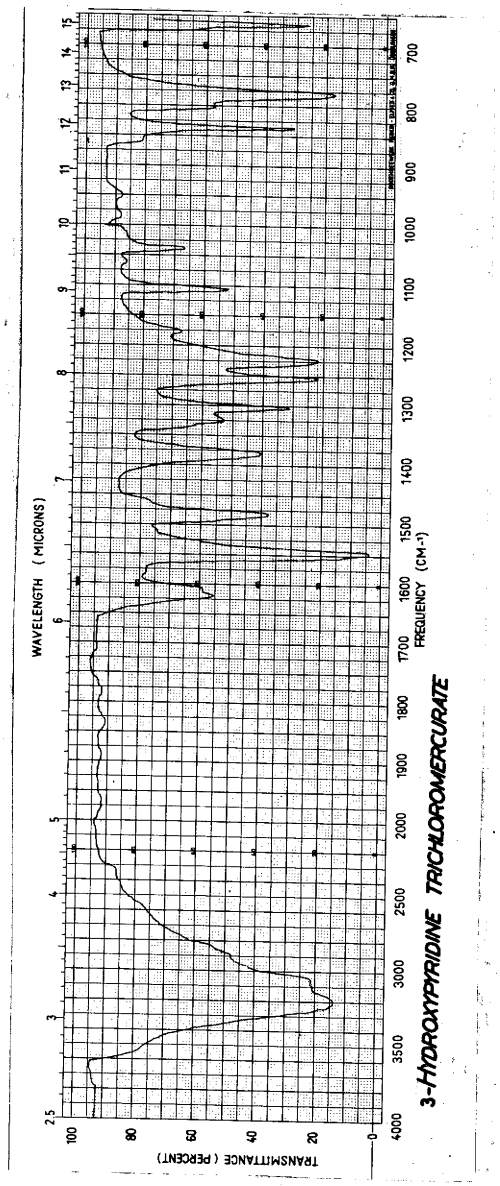
Since some of these differences may be due to the

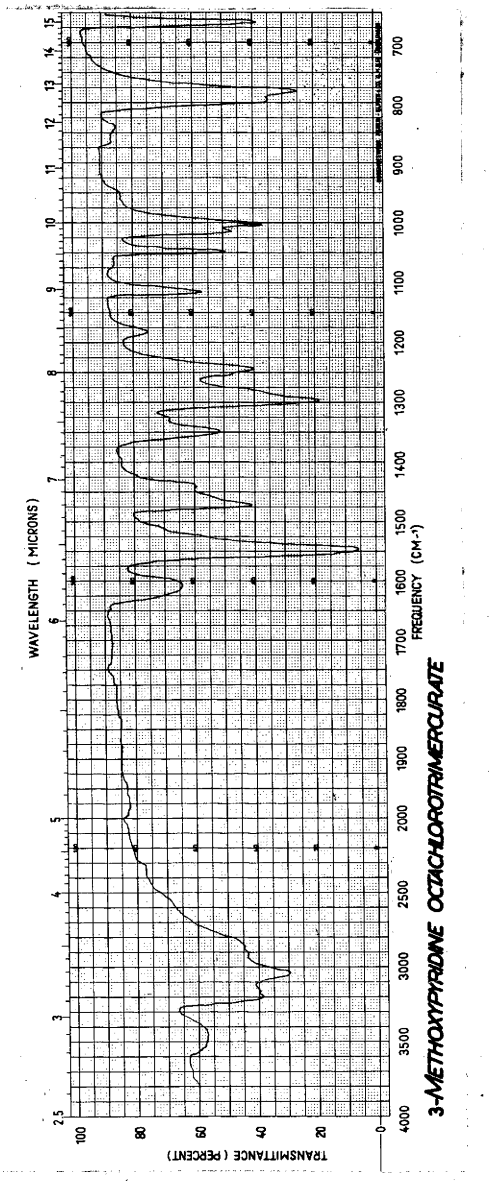
Table XXIII Vibration Spectra, 3-Methoxy- and 3-Hydroxy- Pyridine Cations.

Hydrochlorides				Mercurichlorides	
3-Methoxy-pyridine		3-Hydroxy-pyridine[118a]		3-Methoxy-pyridine	3-Hydroxy-pyridine
2650 vs		3008 s, 2807 ms		3090 s	3250 s
	Raman		Raman		
1620, 1612 m	1636 *, 1628 4	1627	1625 4	1612 m	1622 m, 1612 *
1552 vs	1561 1	1554 s	1553 3	1548 s	1550 vs
		1492 m			
1461, 1441 m	1461 1			1473 m	1483 w
	1382 2	1398 ms			1380 m
1356 vs				1349 m	
			1332 2		
1323 m	1324 *	1315 m	1305 2		
1279 vs	1282 3	1268 ms		1296 s	1302 m
		1240 m	1240 1b	1243 m	1253 s
1191 m	1182 2	1176 w	1174 2		1224 s
1109 m	1116 1	1109 w	1107 2	1115 m	1106 m
1050 m	1051 10	1042 w	1042 10	1048 m	1038 w
1023 m					
1012 s	1006 6	1014 w	1014 4	1014 w	1013 *
998 s	998 *	988 vw		1002 m	983 vw
874 m				860 w	
		839 m	838 9	840	835 m
807, 796 s	800 7	805 ms		780 s	779 s
673 s		677 m		666 s	664 s

DIAGRAM Xa

INFRA-RED SPECTRA





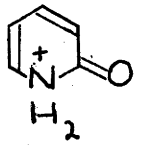
differences in hydrogen bonding inevitable in the use of a methoxy group as a model for a hydroxy group, and in fact, when the strength of the hydrogen bonds are reduced by replacing the chloride ion by the trichloromercurate (or octachlorotrimercurate) ion, the agreement between the infra-red spectra is much closer, as can be seen in the second part of Table XXIII. The band at 1380 cm^{-1} in the spectrum of the hydroxy compound has no counterpart nearer than 1349 cm^{-1}, while that at 1224 cm^{-1} is absent from the spectrum of the methoxy compound. At frequencies less than 1050 cm^{-1}, intensities rather than frequencies are different.

It appears from this comparison, (at present the only one available) that the methoxypyridine cations should be satisfactory models for the hydroxypyridine cations; most, but not all of the bands should be at similar frequencies in the vibration spectra of both compounds.

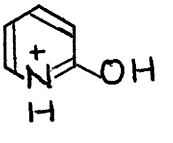
Hydroxypyridine cations. It is now possible to discuss the most important single problem which this thesis concerns, the structures of the cations of 2-hydroxy-pyridine and its substituted derivatives. The study of the substituted compounds has provided several useful reference compounds, the spectra of which add

valuable support to the interpretations given here of the spectrum of the 2-hydroxypyridine cation.

The following features of the spectrum of the hydrochloride of 2-hydroxypyridine have been considered to indicate that the cation has the N-protonated (non-aromatic) structure 48, and not the O-protonated (aromatic) structure 49.



48



49

1/ The strong band near 1640 cm^{-1}, attributable to a carbonyl stretching vibration[109a, 118a].

2/ The absence of certain infra-red bands characteristic of the (neutral) methoxypyridines[109a], or of pyridine and 3-hydroxypyridine hydrochlorides[118a].

3/ The absence of a strong Raman band near 1000 cm^{-1}, such as is known to occur in the spectra of simple aromatic compounds, pyridines, and pyridine and 3-hydroxy-pyridine hydrochlorides[118a].

It was pointed out in connection with the vibration spectra of the cations of amides and ureas, that the frequency of the carbonyl band should rise considerably when an N-protonated cation is formed, and that for these compounds, although strong bands were observed in the spectra of the cations, at higher frequencies than the

carbonyl bands of the neutral molecules, they were at much lower frequencies than those of available models for the N-protonated cations, and close to the values which have been observed for $C{=}\overset{+}{N}$ stretching vibrations. In the spectrum of the hydrochloride of 2-hydroxypyridine, the band which has been considered[109, 118a] to be a carbonyl band is actually at practically the same frequency as in the neutral molecule, and the frequency is considerably lower than those of the known carbonyl bands in the 2- and 4-hydroxypyrimidine cations[118a]. (The additional electron-withdrawing effect of the second ring nitrogen atom could be responsible for this difference, but the change in the carbonyl stretching frequency on cation formation in these compounds is still quite marked.)

If the band at 1641 cm^{-1} in the spectrum of the hydrochloride of 2-hydroxypyridine hydrochlorides is a carbonyl band, it could be argued that the low frequency is due to strong hydrogen bonding to the carbonyl oxygen atom, but the new data now obtained show that such is not the case. The frequency of the 1641 cm^{-1} band actually falls significantly when the strongly hydrogen bonding chloride ion is replaced by weakly hydrogen bonding complex anions. (See Table XXV.)

Comparison of the spectra of 2-hydroxy- and 2-methoxy-pyridine hydrochlorides (Table XXIV and Diagram XI) shows that the infra-red spectra are related in much the same way as were the spectra of the 3-substituted isomers. (Table XXIII.) The greatest point of difference, for which no counterpart exists in the comparison of the spectra of the 3-substituted compounds, is in the region above 1600 cm^{-1}; the methoxy compound exhibits two close peaks, at 1613 and 1631 cm^{-1}, while the hydroxy compound exhibits a poorly resolved pair of bands of greater relative intensity, of frequency 1632 and 1640 cm^{-1}. (See Diagram XI.) The latter compound could, on this basis alone, and despite the foregoing discussion, be considered to contain a carbonyl group, i.e. to have the N-protonated structure. However, the lack of confirming evidence in the form of marked differences in the remainder of the infra-red spectra suggest that this is not the case. The differences between the infra-red spectra of methoxy- and hydroxy-pyridine cations are actually less marked for the 2-substituted than for the 3-substituted compounds in the vicinity of 1475, 1375, and 1240 cm^{-1}, but generally correspond elsewhere.

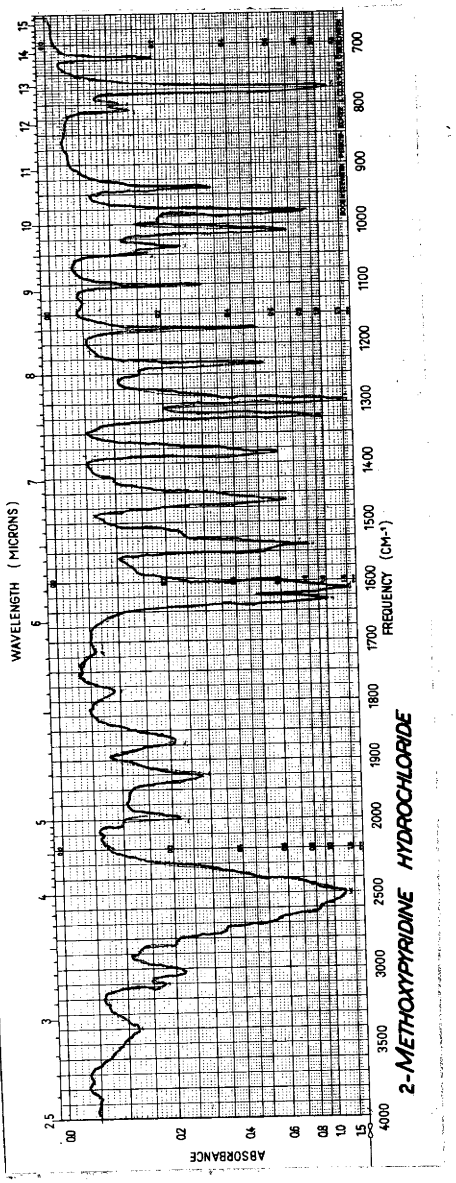
Greater differences are seen between the Raman spectra of 2-hydroxy- and 2-methoxy-pyridine than

Table XXIV Vibration Spectra Hydrochlorides of 2-Methoxy- and 2-Hydroxy-pyridine

2-Methoxy-pyridine		2-Hydroxy-pyridine	
2510 s	Raman	2620 vs	Raman
1631 s	1630 2	1641) vs 1632)	1643 2
1613 vs			
1540 s	1545 4	1543 s	1505 2
1462 m	1461 2	1483 w	
1426 w		1420 w	
		1406 w	
		1395 w	
1384 m			
		1369 m	1363 2
1321 s	1326 8	1335 vs	
1297 vs	1295 4		
			1267 3
1249) vw 1235) m	1240 1	1244) m 1224) w	
1175 m	1186) 1 1167) 1	1165 m	
1102 m	1105 1	1098 m	1095 1
1049) * 1037) m	1046 6		1037 1
1012 m		1003 m	1005 4
993 vs	986 9		984 2
		963 w	
939 m			
		906 m	
		850 m	852 10
810 m	809 10		
774 vs		777 vs	
723 m		724 vw	

DIAGRAM XI

INFRA-RED SPECTRA



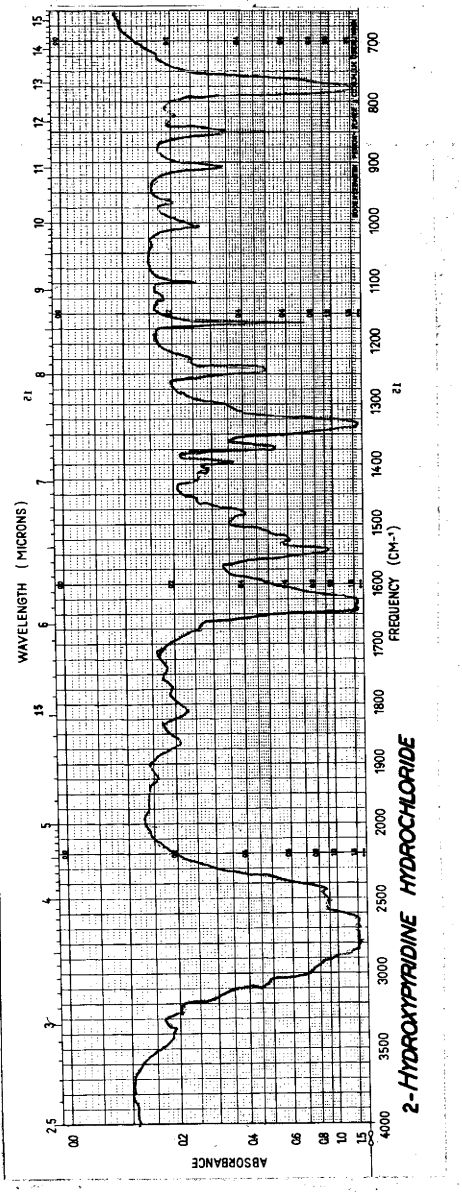
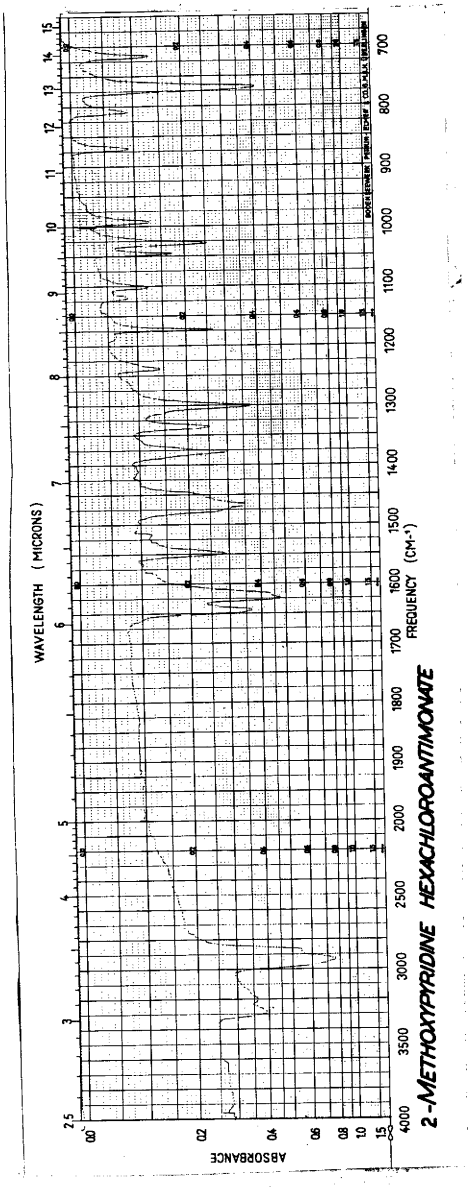
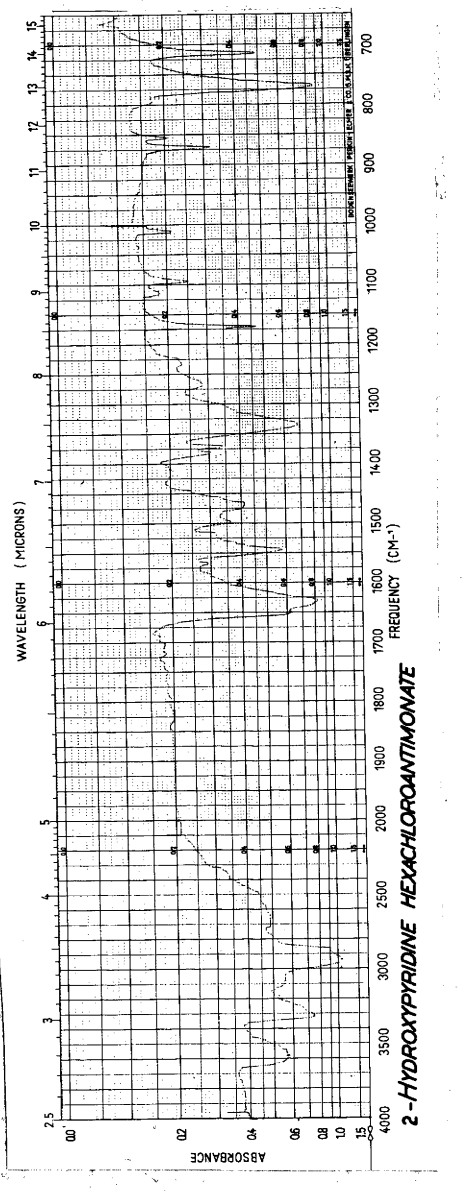


DIAGRAM XII

INFRA-RED SPECTRA





between those of the 3-substituted isomers. The strong band at 1326 cm^{-1} in the spectrum of the methoxy compound has no counterpart in the spectrum of the hydroxy compound while the strongest Raman band near 1000 cm^{-1} in the spectrum of the latter compound is of lower relative intensity than its counterpart in the spectrum of the methoxy-compound. The band at 1005 cm^{-1} in the spectrum of the 2-hydroxy-pyridine cation is still, however, the second strongest band in the Raman spectrum (0-1700 cm^{-1}), as is the band at 986 cm^{-1} in the spectrum of the methoxypyridine cation, and the lowered relative intensity of the former is not necessarily conclusive evidence that the two ions have fundamentally different structures.

The spectra of the trichloromercurates of the 2-hydroxy- and 2-methoxy-pyridine, as was the case in comparing the 3-substituted isomers, agree more closely than the spectra of the hydrochlorides. (Table XXV.) With the exception of those regions for which the 3-substituted compounds exhibit spectral differences, the agreement between spectra is so close as to justify attempts to interpret them in terms of similar ionic structures. The spectra of the hexachloroantimonates are also closely similar.

Thus, the comparison between the spectra of the 2-hydroxy- and 2-methoxy-pyridine cations suggests that

Table XXV Infra-Red Spectra of Complex Salts of 2-Hydroxy- and 2-Methoxy-pyridine.

Trichloromercurates		Hexachloroantimonates	
2-Methoxy-pyridine	2-Hydroxy-Pyridine	2-Methoxy-pyridine	2-Hydroxy-pyridine
3090	3090	3290	3300
1630)* 1617)s	1628 vs 1591 w	1640 m 1620 s	1627 s
1543 m	1536 s	1542 m	1538 m
1522 *	1512 *	1512 *	1514 *
1468) 1460)m	1481 w	P	P
1437 w			1410 w
1376 m	1363 w	P	P
1326 m	1311 s	1330 m	1329 s
1296 s		1295 m	
1230 m	1220 m	1233 w	1227 vw
1166 m	1160 m	1169 m	1166 m
1120 w		1115 w	1110 w
1100 m	1090 m	1096 w	1090 w
1041 m	1050 w	1042 m	
1024 s		1025 m	
989 m	1000 m	989 m	1007 w
884 m	873 m	868 m	873 m
853 w	850 ?		850 vw
806 w		808 m	
771 s	768 vs	766 s	768 vs
716 w	714 m	714 m	714 m

they arise from essentially similar ionic structures. However, some differences, which could be indications of an N-protonated structure for the hydroxypyridine (pyridone) cation, remain. Of these, the most important is seen in the vicinity of the carbonyl stretching frequency of the neutral hydroxypyridine. The question of whether the single strong band shown by the hydroxypyridine cation can reasonably be related to the two medium to strong bands in the spectrum of the methoxypyridine cation will be considered in relation to the substituted derivatives.

The Substituted 2-hydroxypyridine cations. It was shown in discussing the spectra of the neutral 2-hydroxypyridine, the carbonyl band is subject to considerable changes in frequency as substituents are introduced into the parent molecule, the highest value being that in the 3,5-dichloro derivative, 1697 cm^{-1}. Even if no increase in the carbonyl stretching frequency occurred when this compound formed an N-protonated cation, the band would still be sufficiently removed from the upper limit of aromatic skeletal vibrations to make the assignment of the band, and hence of the cation structure, unambiguous.

The spectra of the hexachloroantimonates of 3,5-Dibromo-2-hydroxy- and 2-methoxy-pyridine, and of the corresponding 3,5-dichloro derivatives, are listed in TableXXVI, while the spectra of the

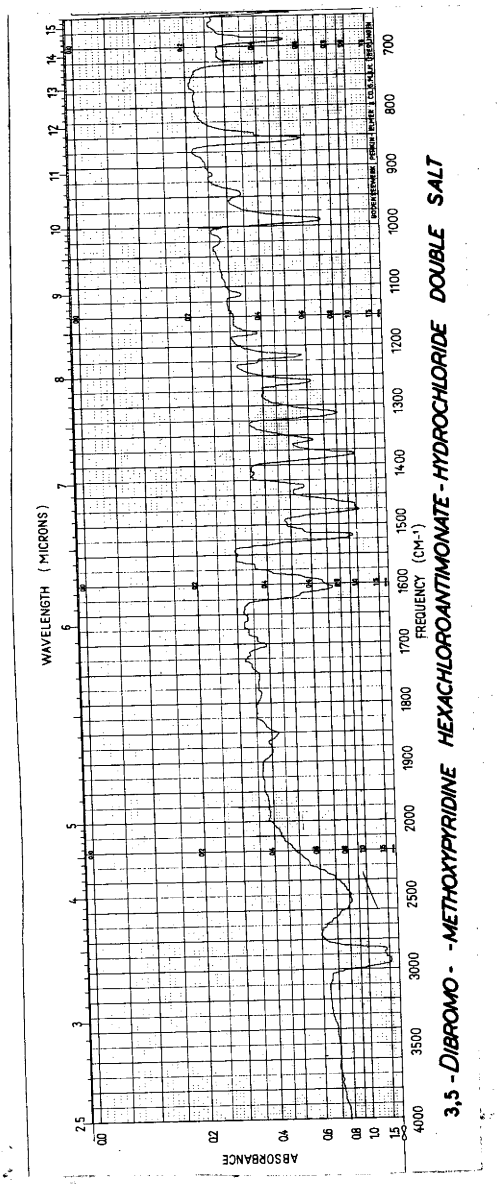
Table XXVI Infra-Red Spectra, Hexachloroantimonates[1].

3,5-Dibromo-		3,5-Dichloro-	
2-Methoxy-pyridine	2-Hydroxy-pyridine	2-Methoxy-pyridine	2-Hydroxy-pyridine
1616 *	1621 s	1620 w	1623 m
1601 m	1610 *	1601 s	
1513 s	1520 s	1521 s	1534 s
1503 *	1502 *		1510 *
1428 w	1418 w	1428 w	1425 *
1309 s	1299 s	1319 s	1308 s
1256 m	1281 m	1254 s	1282 m
1212 m	1216 m	1212 m	1223 w
1174 w	1153), 1141) mb	1179 w	
1109 w	1111 *	1137 m	1150 *
	1061 w	1072 w	1100), 1073) mb
1009 w		1016 vw	1021 w
987 s		987 s	
943 w	932 w	963), 942) m	
911 w	880 w	922 *	897 m
852 s		866), 848) s	867 m
794 *	800 m		
726 m		722 s	743), 721) m
686 m	696 w	661), 694) m	

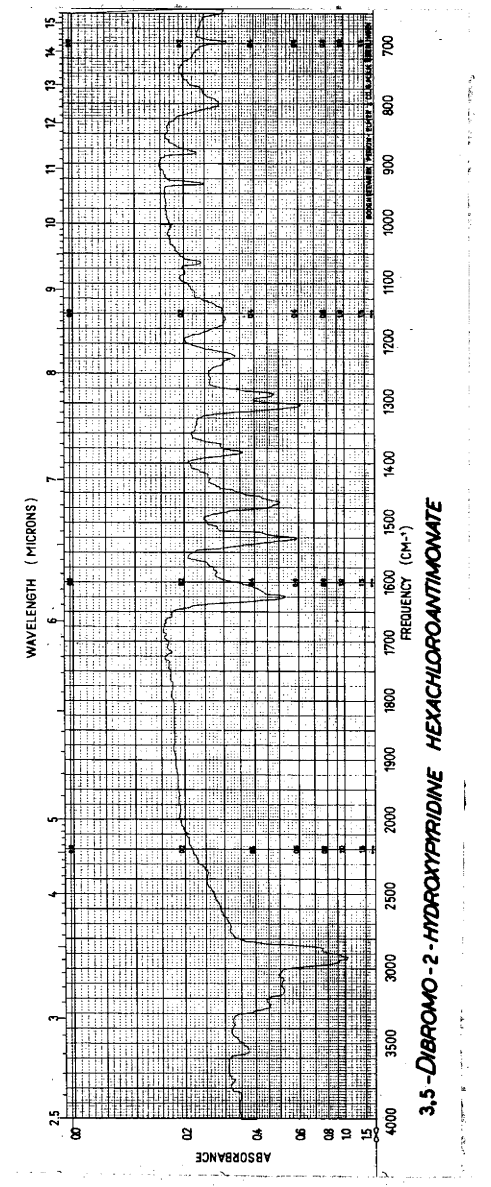
(1) See text for compositions of salts.

DIAGRAM XIII

INFRA-RED SPECTRA



3,5 - DIBROMO - -METHOXYPYRIDINE HEXACHLOROANTIMONATE - HYDROCHLORIDE DOUBLE SALT



3,5 - DIBROMO - 2 - HYDROXYPYRIDINE HEXACHLOROANTIMONATE

dibromo compounds are given in Diagram XIII. The spectra of the two hydroxy compounds immediately establish that the cations do not have the N-protonated structures, as there are no strong bands between 1630 and 2000 cm^{-1}. (In fact, these compounds were prepared in the expectation that their structures could be established beyond doubt.)

The only salts which could be prepared from the two compounds, 3,5-dichloro- and 3,5-dibromo-2-methoxypyridine were mixed hexachloroantimonate-hydrochlorides, of composition $(BH^+)_2.SbCl_6^-.Cl^-$, and the spectra show that the cations in these salts form strong (presumably $\overset{+}{N}-H...Cl^-$) hydrogen bonds. The spectra which must be compared are therefore those of hydroxypyridinium ions forming weak hydrogen bonds and methoxypyridinium ions forming strong hydrogen bonds.

Differences between the spectra between 800 and 1300 cm^{-1} are those expected from the comparison of the spectra of 3-methoxy- and 3-hydroxy-pyridine cations, and the only other significant difference is observed near 1620 cm^{-1}. The methoxy compounds exhibit a strong to medium intensity band at 1601 cm^{-1} with a weaker band or shoulder near 1620 cm^{-1}. The genuine hydroxy compounds, however, exhibit strong bands at $1622\pm$ cm^{-1}.

The spectra of the hexachloroantimonates of 3-chloro-

2-hydroxy- and 2-methoxy-pyridine are compared in Table XXVII. [redacted]. The carbonyl band in the spectrum of neutral 3-chloro-2-hydroxypyridine occurs at 1652 cm^{-1}, but the spectrum of the cation shows no strong band of frequency greater than 1621 cm^{-1}. The methoxypyridine cation exhibits two bands near this frequency, at 1623 and 1595 cm^{-1}, the latter being the more intense. A very similar relationship between the bands in this region in the spectra of the di-halogeno derivatives of 2-hydroxy- and 2-methoxy-pyridinium ions has been noted (page 124), so that no structural difference can be deduced from it. With the exception of certain bands near 1250, 1000 and 780 cm^{-1}, the spectra are similar, and the exceptions are those which might be expected from the previous comparisons of methoxypyridinium and (genuine) hydroxy-pyridinium ions. It may therefore be deduced that the cation of 3-chloro-2-hydroxypyridine, like the cations of the 3,5-dichloro- and 3,5-dibromo-2-hydroxy-pyridine, forms through proton addition to the oxygen atom.

The spectra of the hydrochlorides of 5-chloro-2-methoxy- and 2-hydroxypyridine are compared in Table XXVIII and Diagram XIV. The case for assigning the high-frequency skeletal band in the spectrum of the

Table XXVII Infra-Red Spectra, (1)
Hexachloroantimonates

2-Methoxy-pyridine	3-Chloro-2-Hydroxy-pyridine
2510 m	3260 w
1623 m	1621 s
1595 s	
1521 s	1538 m
1359 s	
1325 s	1319 s
	1290 w
1260 m	1266 vw
1214 w	1239 w
1183 w	1193 w
	1156 w
1136 m	1141 w
1074 vw	1076 w
1050 m	1048 m
1020 w	1018 w
989 s	
923) 905) w 888)	944 vw 880 vw
797 s	783 *
	761 s
734 m	733 *
686 s	

(1) See page 124,161 for composition of salts.

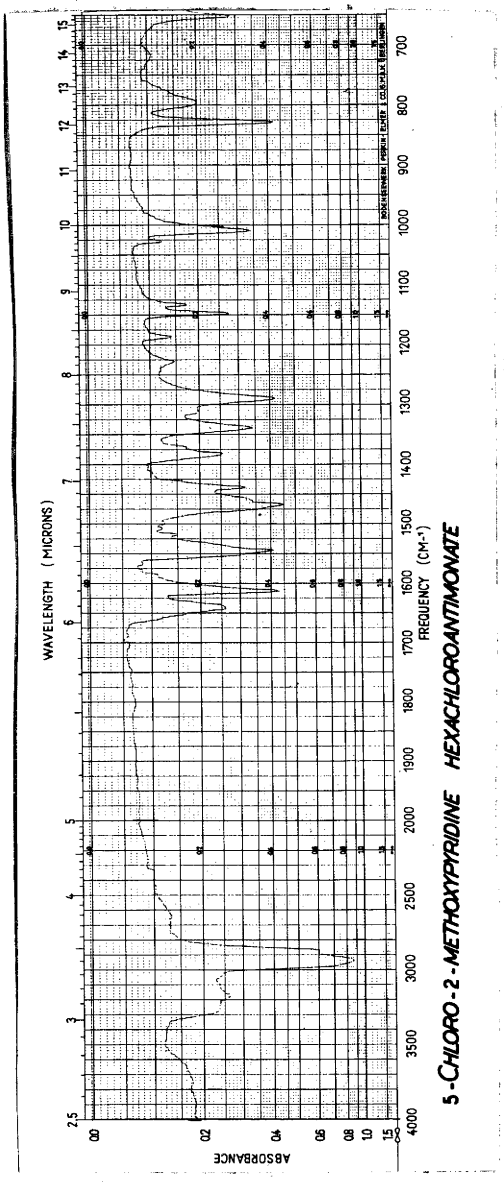
hydroxy compound to a carbonyl stretching vibration is stronger than for the cation of 2-hydroxypyridine itself, as the band appears at 1653 cm^{-1} (in potassium bromide) or 1640 cm^{-1} (in paraffin mull), with a second peak at 1612 cm^{-1} (mull), while the methoxy analogue shows a strong band at 1606 cm^{-1}, and a weaker band at 1630 cm^{-1}. Thus, there is some justification for assigning the 1640-1650 cm^{-1} band to a carbonyl stretching vibration. However, in the spectra of the hexachloroantimonates, these differences are considerably reduced, peaks appearing at 1640 and 1621 cm^{-1} in the spectrum of the hydroxy compound, and at 1637 and 1608 cm^{-1} in the spectrum of the methoxy compound. (See Diagram XIV.) In all other respects, the spectra of the methoxy- and hydroxy-pyridine hexachloroantimonates are very similar indeed, the only major point of difference, the strong band at 1006 cm^{-1} in the spectrum of the methoxy compound, being reasonably attributable to a C-O-C symmetric stretching vibration. (Cf. the similar differences between methoxy- and hydroxy-pyridinium ions, Tables XXIII, XXVI, and XXVII.) It is extremely unlikely that two fundamentally different ionic species could exhibit such very

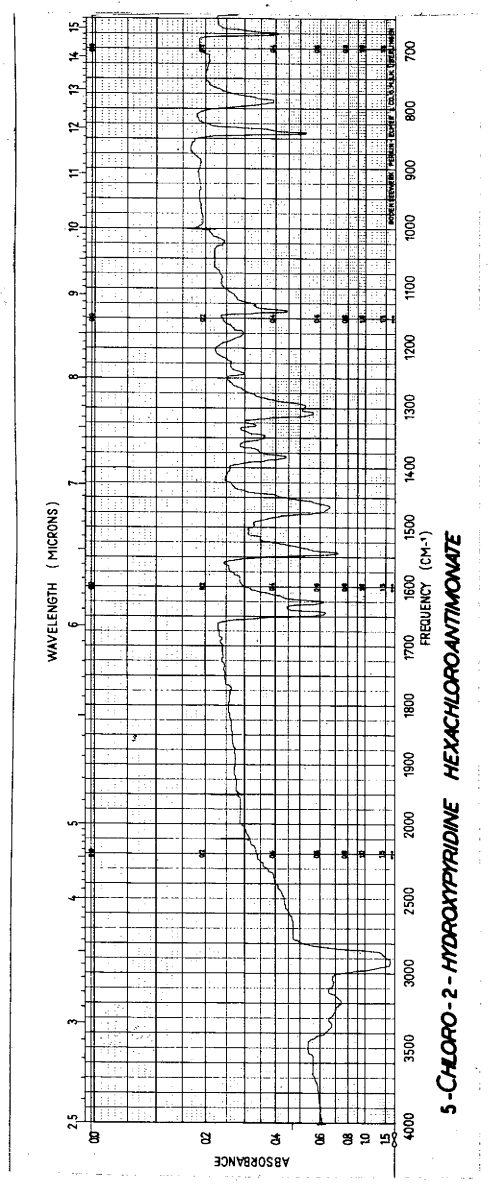
Table XXVIII Infra-red Spectra.

Hydrochlorides			Hexachloroantimonates.	
	5-Chloro-			5-Chloro-
2-Methoxy-pyridine	2-Hydroxy-pyridine		2-Methoxy-pyridine	2-Hydroxy-pyridine
(KBr)	(Mull)	(KBr)		
2510 vs	3200 s 2670 s		3060 m	3190 m
1630 m	1640 s	1653 s	1637 m	1640 s
1606 vs	1612 m	1626 m 1600 m	1608 s	1621 s
1535 vs	1533 s		1538 s	1538 s
1478 w	P	1460 w	1512 vw	1513 *
1432 w	1421 m		1432 w	
	P	1365 w		
				1343 w
1335 vs	1320 *	1325 s	1334 m	1324 vw
1292) 1284)s	1264 m		1305)* 1286)s	1304) 1292)s
1233 m	1231 m		1224 w	1238 w
			1182 w	1171 w
1152 w 1141 w	1135 m		1144 m	1134 m
	1052 w		1024 vw	1017 w
1004 s	1006 w		1006 s	
	992 w			
960 w	960 m			
872) 866) m	867 m			
			827 s	839 m
			793 m	785 m
			715 w	715 m
	667 m		c650	673 m

DIAGRAM XIV

INFRA-RED SPECTRA





close spectral similarities, and it must be concluded that 5-chloro-2-hydroxypyridine also forms a cation through proton addition to the oxygen atom.

For all of the hydroxypyridine cations so far discussed, the strongest band (or strongest of two) near 1600 cm^{-1} in the infra-red spectrum lies between 20 and 40 cm^{-1} to higher frequencies than the strongest band in this region in the spectrum of the methoxy-pyridine analogue. This feature therefore cannot be taken as evidence of a fundamental difference in structure in comparing the spectra of 2-methoxy- and 2-hydroxy-pyridine cations, and may well be a normal, though hitherto unexpected, point of difference in such spectral comparisons.

The spectra of the hexachloroantimonates of 5-bromo-2-methoxy- and 2-hydroxypyridine differ rather more than those of the 5-chloro compounds. (Table XXIX.) The only point of difference which is not accountable for in terms of known differences between methoxy- and (genuine) hydroxy-pyridine cation spectra is that near 1427 cm^{-1}. (The spectra of the hydrochlorides, but not the complex salts of 3-hydroxy- and 3-methoxy-pyridine differ in this region.) It may be deduced, though with rather less certainty, that the cation of 5-bromo-2-hydroxypyridine also has the O-protonated

Table XXIX Infra-Red Spectra.

Hexachloroantimonates		Hydrochlorides	
5-Bromo-		5-Methyl-	
2-Methoxy-pyridine	2-Hydroxy-pyridine	2-Methoxy-pyridine	2-Hydroxy-pyridine
3270) m 3170)	3280) m 3200)		2750) vs 2660)
		2400 sb	
1632 m	1638 s	1639 mw	1650 s
1606 s	1618 mb	1611 s	1631 s
1535 s	1537 s	1552 s	1556 s
1427 m		1513 *	1510 vw
	1339 s	P	1481 m
1317 *	1321 w	1434 w	1433 m
1284 s		P	1389 m
	1265 w	1355) m 1320) m	1329 vs
1234 w	1247 w	1290 s	1271 w
1182 w		1250 w	1252 w
1141 m	1136 m	1235 w	1221 w
1102 w	1094 w	1190 m	
1022 w		1157 ms	1143 s
1003 m		1058 w	1047 vw
883 vw	870 vw		1023 vw
876 s		1000 s	992 w
	834 m		927 m
788 m	785 m	861 *	864 m
713 vw	713 w	849 m	841 s
			763 m
		735) s 725)	721 m

structure. Similarly, from the spectra of the hydrochlorides of 2-methoxy- and 2-hydroxy-5-methyl-pyridine, it may be deduced that the hydroxypyridine has the O-protonated structure. (Table XXIX.)

In discussing the spectra of the cations of other substituted 2-hydroxypyridines, the possibility must be considered that some of them, unlike the cations discussed above, have the N-protonated structure. If so, they might be expected to exhibit carbonyl bands at higher frequencies than the bands in the spectra of the genuine hydroxy-pyridine cations. No such bands are observed, however. Table XXX lists the bands between 1500 and 1660 cm^{-1} in the spectra of the substituted 2-hydroxypyridine cations, and shows that the band of highest frequency falls within the narrow range 1618-1653 cm^{-1}, the highest frequency observed being that in the spectrum of the 5-chloro derivative, which, as shown above, is most unlikely to have the N-protonated structure.

The general similarity of the spectra of the hydrochlorides of 5-chloro-, bromo-, and iodo-2-hydroxy-pyridine (Appendix, pages 181, 182), provides good reason for assigning the same cationic structures to

Table XXX Infra-Red Bands, 1500-1660 cm^{-1}, 2-Hydroxypyridine Cations.

2-Hydroxy-pyridine	Frequency (cm^{-1}).			Anion
----	1641 vs	1632 vs	1543 s	Cl^-
3-Methyl	1651 vs	1613 s	1546 mw	"
4-Methyl	1636 vs		1525 s	"
5-Methyl	1650 s	1631 s	1556 s	"
6-Methyl	1638 vs		1550 m	"
5-Chloro (KBr)	1653 vs	1626)m 1600)m	1534 s	"
(Mull)	1640 s	1612 m	1533 s	"
5-Bromo	1645 vs	1599 s	1537 m	"
5-Iodo (KBr)	1641)w 1627)s		1522 s	"
(Mull)	1618+1610 vs		1524 s	"
3-Chloro	1621 s		1538 m	$SbCl_6^-$
3,5-Dichloro	1623 m		1534 s	"
3,5-Dibromo	1621 s	1610 *	1520 s	"
6-Hydroxy	1641 vs	1617 *	1549 m	Cl^-

all of them. For many bands, the frequencies decrease in the order chloro, bromo, iodo substituents. (A similar trend is seen in the spectra of the neutral molecules, and, for chloro and bromo compounds only, in the spectra of the methoxypyridine cations.)

The spectra of the four methyl-substituted 2-hydroxypyridine cations are listed together in the Appendix, and while, as might be expected for compounds bearing similar substituents in different positions, they differ to some extent, they are at least compatible with the view that all have similar cation structures. However, in the absence of data for all the methoxy analogues, this conclusion is not firmly based.

Sodium Salts. No reference compounds are possible in any attempt to determine the nature of an ion which may resemble one or other of its contributing canonical forms more or less closely. However, the structural criteria which have emerged from the study of the hydroxy- and methoxy-pyridine cations can be usefully applied to the spectra of the anions. In particular, the criterion of uniformity of major spectral features among the various substituted compounds is of some value.

The spectra of the 3,5-dichloro, 3,5-dibromo, and 5-nitro derivatives give a clear indication of the nature of the anions in these three cases, for the

highest frequency (below 2000 cm^{-1}) at which strong absorption occurs is below 1605 cm^{-1}, and this is far too low to represent a carbonyl band in compounds whose carbonyl bands in the neutral form lie between 1670 and 1700 cm^{-1}. Thus, the predominance of the canonical form 50 in the resonance of these three anions is well established.

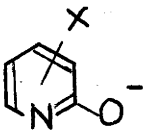


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Table XXXI lists the main bands in the infra-red spectra of the 2-hydroxypyridine anions examined. The relationship between the spectra suggests that the structures are probably reasonably uniform throughout the series. The Raman spectra (not included in the Table) provide further evidence for this conclusion. Such a relationship is consistent with (although it does not prove) the view that the canonical form 50 plays the major part in the resonance of all of the ions.

The main evidence which has been considered[118b] to indicate a predominance of the form 51 is the absence of a strong band near 1000 cm^{-1} in the Raman spectrum. However, the discussion of the spectra of the 2-hydroxypyridine cations has shown that this criterion is almost certainly not a reliable indication of their

Table XXXI Infra-red Spectra, 2-Hydroxypyridines, Sodium Salts.

2-Hydroxy-pyridine	1605 vs	1546 s	1474 vs	1432 vs	1340 s	1290 m	1149 m
4-CH_3	1615 vs	1532 m	1483 vs	1445) 1439) vs	1321 s	1289 m	
5-CH_3	1635 s	1542 s	1490 vs	1416 s	1329 vw	1289 m	1137 m
5-Cl	1600 s	1531 m	1482 vs	1402 s	1325 w	1278 m	1126 m
5-Br	1608 s	1525 w	1490) 1470) vs	1403 m	1330 w	1281 m	1134 m
5-I	1603 s	1523 m	1498 vs 1470 vs	1401 s	1333 w	1286 m	1139 m
3,5-Cl_2	1588 s	1515 w	1488 s	1400 w	1314 w	1248 m	1118 m
3,5-Br_2	1576 s	1525 vw 1503 vw	1481 s	1388 w	1318 w	1254 w	1109 w
3,5-I_2	1561 s		1461 s	1375 m	1324 w	1250 w	
5-NO_2	1602 vs	1533 vs	1477 m	1437 s		1302 vs	1111 m

Table XXXI (Continued)

2-Hydroxy-pyridine	1100 w	989 s	860 s			787 s	
4-CH_3	1106 vw	985 m	866 m			791 s	
5-CH_3		1016 s	889 m, 878m, 865 m		827 s		
5-Cl	1100 m	998 m	890 w, 878 w, 862 w		834 s		
5-Br	1089 m	994 m	891 w, 880w, 859 w		826 s		
5-I	1075 w	989 m	890 w, 857w,		827 s		
3,5-Cl_2	1051 s		898 m, 886s, 865 w			770 s	755 s
3,5-Br_2	1026 m			885 m		766 m	706 m
3,5-I_2	1012 m		898 m			766 m	676 m
5-NO_2					843 m	771 m	728 s

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structure, and its validity in the case of the anions is therefore suspect.

Summary.

The deductions which have been made from the physico-chemical data are not necessarily the only deductions possible, but for the most part, they represent the simplest interpretations of the data, and are consistent throughout the various sections.

All of the 2-hydroxypyridines examined, like 2-hydroxypyridine itself, exist as pyridones in the neutral form, as shown by ultra-violet and vibration spectra. The substituents range from strongly electron-withdrawing (nitro) to strongly electron-donating (hydroxyl anion).

The infra-red spectra establish that the cations of certain 2-hydroxypyridines have the O-protonated structures, and for other 2-hydroxypyridine cations, comparisons between their spectra and those of their 2-methoxypyridine analogues suggests very strongly that they also have the O-protonated structures. The spectra of these cations set the pattern to be expected for the spectra of true hydroxypyridinium ions,

and none of the spectra of the hydroxypyridine cations examined depart sufficiently from this pattern to justify the assignment of an N-protonated structure. In particular, the band near 1640 cm^{-1} in the infra-red spectrum of the parent 2-hydroxypyridine cation, which could conceivably be due to the carbonyl stretching vibration of the N-protonated form, and which represents the most important evidence in favour of such a form, is adequately accounted for.

Such a cation structure could possibly account for the unusual effects of substituents in the 3 position on the basic ionization constants of the 2-hydroxypyridines, since steric inhibition of hydrogen bonding between the ion and the solvent is possible (although not necessarily inevitable), for this structure.

The infra-red spectra of the anions of the substituted 2-hydroxypyridines are shown to be consistent with a single ionic type, represented most closely by the canonical form in which the negative charge resides on the oxygen atom. The ultra-violet spectra of these ions are also consistent with such an interpretation.

CHAPTER III.

EXPERIMENTAL

Microanalyses were carried out by Dr. J.E. Fildes and her staff in the Department of Medical Chemistry, Australian National University, Canberra.

All melting points were recorded in soda-glass capillaries, and are uncorrected.

A. Preparation of substituted 2-hydroxypyridines.

2-Hydroxy-3-, 4-, 5- and 6-methylpyridines.

These compounds were prepared by diazotisation of the commercially available 2-amino-3, 4-, 5- and 6-methylpyridines, using the method described by Seide[133] for the preparation of the 4-methyl isomer. The melting points were as follows :

2-Hydroxy-pyridine	m.p.	Lit. m.p.	Ref.
3-methyl	138-139°	140°	133
4-methyl	129-130°	130°	133
5-methyl	180.5-181.5°	182-183°	134
6-methyl	156-158°	159°	135

5-Chloro-2-Hydroxypyridine.

This was prepared by chlorination of 2-amino-pyridine[136] to give 2-amino-5-chloropyridine, followed by diozotisation[137] (overall yield 20%), and by direct chlorination of 2-hydroxypyridine. Chlorine was passed

through a solution of 2-hydroxypyridine (5 g, 0.052 mol) in chloroform (20 ml). The white precipitate formed was dissolved in water, and the solution was neutralized with sodium carbonate, and evaporated to small volume. The mixture of 5-chloro- and 3,5-dichloro-2-hydroxypyridine which separated out of the solution was extracted with ethanol, and the solid obtained after evaporation of the ethanol was recrystallized from benzene, giving 5-chloro-2-hydroxypyridine (4.7 g, 70% yield), m.p. 162-163°. (Lit. m.p. 163° [137].) This method is based on one that is briefly described in a patent by Dohrn [138].

5-Bromo-2-hydroxypyridine.

This compound was prepared by bromination of 2-aminopyridine in 20% sulphuric acid [124], followed by diazotisation [124] of the 2-amino-5-bromopyridine so obtained; it had m.p. 176.5-178°. (Lit. m.p. 162-166° [124], 172-176° [122], 177-178° [139].)

2-Hydroxy-5-iodopyridine.

2-Amino-5-iodopyridine, prepared according to Caldwell, Tyson and Lauer [140], was diazotised to give 2-hydroxy-5-iodopyridine [141] (overall yield 18%). It had m.p. 188-189°. (Lit. m.p. 183-189° [141], 191-193° [142].)

3-Chloro-2-hydroxypyridine.

This compound was prepared by the hydrolysis of 3-chloro-2-methoxypyridine (see page [148]) in concentrated

hydrochloric acid[143], and had m.p. 169-170°. (Lit. m.p. 169-170°[143].)

3-Bromo-2-hydroxypyridine.

This compound was prepared by the hydrolysis of 3-bromo-2-methoxypyridine (see page 149), according to the method used by Schickh, Binz and Schulz[143] for the 3-chloro compound (above), and had m.p. 181-182.5°. (Lit. m.p. 183-184°[144].)

3,5-Dichloro-2-hydroxypyridine.

Chlorine was passed through a solution of 2-hydroxypyridine (5 g, 0.053 mol) in water (40 ml) until 7.2 g (0.101 mol) had been absorbed. The white precipitate obtained was recrystallized from water, giving 3,5-dichloro-2-hydroxypyridine (4.1 g, 48% yield), m.p. 177-177.5°. (Lit. m.p. 178-179°[135].)

This compound was also obtained as a by-product in the preparation of 5-chloro-2-hydroxypyridine (page), and by diazotisation[137] of 2-amino-3,5-dichloropyridine (obtained as a by-product in the preparation of 2-amino-5-chloropyridine, page 140.)

3,5-Dibromo-2-hydroxypyridine.

This compound was prepared by bromination of 2-hydroxypyridine in water, as described by Koenigs and Geigy[145], and by diazotisation[139] of 2-amino-3,5-dibromopyridine (a by-product in the preparation of 2-amino-5-bromopyridine, page 141). It had m.p. 206-207°. (Lit. m.p. 206-207°[145].)

3,5-Diiodo-2-hydroxypyridine.

This compound was prepared by the iodination of 2-hydroxypyridine [140], and had m.p. 265° dec. (The melting and decomposition temperature is dependent on the rate at which that temperature is reached, and values in the literature range from 257° [146] to 270° [140].)

2,3-Dihydroxypyridine.

This compound was prepared by the hydrolysis of 3-hydroxy-2-methoxypyridine (see page 150) in concentrated hydrochloric acid, according to Schickh, Binz and Schulz [143], and had m.p. 245-247°. (Lit. m.p. 248° [143].)

2,3-Dihydroxypyridine was also prepared by the hydrolysis of 3-hydroxy-2-iodopyridine (sse page 150), as follows. 3-Hydroxy-2-iodopyridine (2 g) was heated on a steam-bath with a 2-fold excess of 10N-sodium hydroxide for 1 hour. The solution was acidified, and the precipitate which formed was recrystallized from water, giving 2,3-dihydroxypyridine (0.85 g, 85% yield), m.p. 245-247°.

2,6-Dihydroxypyridine.

Dicyanoglutaconic acid diethyl ester, prepared from ethyl cyanoacetate and chloroform [147],

$$2CH_2CN\text{-}CO_2C_2H_5 + CHCl_3 + 3NaOH \longrightarrow C_2H_5O_2C\text{-}\underset{\underset{CN}{|}}{C}\text{=}CH\text{-}\underset{\underset{CN}{|}}{CH}\text{-}CO_2C_2H_5 + 3NaCl + 3H_2O$$

was converted to 3,5-dicarbethoxy-2,6-dihydroxypyridine

as described by Ruhemann and Browning[147]. The latter compound had m.p. 199-201°. (Lit. m.p. 202°[147].) Removal of the carbethoxy groups[148] gave 2,6-dihydroxypyridine, m.p. 186-188°. (Lit. m.p. 183°[148].)

2-Hydroxy-5-nitropyridine.

2-Amino-5-nitropyridine, prepared by nitration of 2-aminopyridine according to Caldwell, Tyson and Lauer[140], was diazotised[140] to give the 2-hydroxy compound, m.p. 179.5-181°. Lit. m.p. 186°[149], 192°[150].)

2-Hydroxy-3-nitropyridine.

This compound was prepared from 2-amino-3-nitropyridine (removed as an impurity from the commercially available 2-amino-5-nitrooyridine, or obtained as a by-product in its preparation) by the same method as for the 5-nitro isomer, and had m.p. 222-223°. (Lit. m.p. 224°[139].)

Preparation of salts of 2-hydroxypyridines.

Hydroxypyridines bearing the substituents listed below were converted to their hydrochlorides by recrystallization from concentrated hydrochloric acid. The salts were dried at 70-100°/0105 mm.

Substituents: 3-, 4-, 5- and 6-methyl, 5-chloro, 5-bromo, 5-iodo, and t-hydroxy.

Hydrochlorides could not be prepared for the 3- and 5-nitro, 3,5-dichloro-, 3,5-dibromo-, 3,5-diiodo-, 3-chloro-, 3-bromo-, and 3-hydroxy-2-hydroxypyridines,

recrystallization from concentrated hydrochloric acid giving the neutral species in each case.
Perchlorates of several of these compounds were obtained by cautious recrystallization from 72% perchloric acid, and drying the moist crystals so obtained at 40-50° / 0.05 mm. Most of the perchlorates thus obtained were unsatisfactory for infra-red spectroscopic examination (see page 165) and analysis showed that the perchlorate of 3,5-dichloro-2-hydroxypyridine had the composition $BH^+.ClO_4^- + HClO_4$. (See page 162).

Hexachloroantimonates were prepared by dissolving the bases in concentrated hydrochloric acid and adding equivalent amounts of 1M-hexachloroantimonic acid in concentrated hydrochloric acid. (This reagant was prepared by dissolving antimony pentachloride (2.99 g) in concentrated hydrochloric acid (10 ml).) The salts were recrystallized from concentrated hydrochloric acid, large volumes usually being required. (e.g. 0.9 g of 2-hydroxypyridinium hexachloroantimonate was recrystallized from 150 ml of concentrated hydrochloric acid). They were dried over concentrated sulphuric acid in an atmosphere of hydrogen chloride.

The sodium salts were prepared by dissolving the compounds in equivalent amounts of 10N-sodium hydroxide

(with addition of water if necessary), and the salts which crystallized out on cooling were recrystallized from iso-propyl alcohol (methyl and mono-halogeno derivatives). The two dihydroxypyridines oxidise very readily in alkaline solution, even when a reducing agent is present, and satisfactory preparations of their sodium salts were not achieved. Attempts to recrystallise the salts from water failed, as considerable decomposition occurred within a few minutes at 60-80°. A white solid, rapidly turning bluish-black even under vacuum, was obtained by quickly adding a large volume of acetone to an alkaline solution of 2,6-dihydroxypyridine, and, although the analysis of this salt is not satisfactory, and some di-sodium salt may have been present, the infra-red spectrum is given in the Appendix.

B. Preparation of methoxypyridines and substituted 2-methoxypyridines.

2-Methoxypyridine.

This compound was prepared from 2-chloropyridine according to Grave[151], and distilled at 138-140° / 728 mm. (Lit. b.p. 142.4°/ 760 mm[151].) (Yield 60%).

3-Methoxypyridine.

This compound was prepared by the action of diazomethane on 3-hydroxypyridine at -40°, as described

by Prins[152], and distilled at 178-180°/ 721 mm. (Yield 20%).

4-Methoxypyridine.

This compound was prepared by the action of sodium methoxide on 4-chloropyridine. Since Haitinger and Lieben[105], who previously used the method, gave few experimental details, the procedure followed will be described in full.

4-Chloropyridine (Fluka, 98%, 104 g, 0.91 mol) was added to a stirred solution of sodium methoxide in methanol (25.5 g, 1.11 mol of sodium in 190 ml of methanol). Over a period of 20 minutes the temperature of the mixture rose gradually to 65°, and then rose sharply. Ice-cooling was applied until the vigorous reaction had subsided, after which refluxing was continued for a further 5 hours. The sodium chloride formed (in quantitative yield) was removed by filtering the hot mixture into an ice-cooled Buchner flask. The excess alkali was then neutralized with methanolic hydrogen chloride, and the sodium chloride formed was removed as before, after which the solution was distilled through a 10 inch column until the temperature of the vapour rose sharply to 140°. Distillation under reduced pressure gave 4-methoxypyridine (51.3 g,

52% yield), b.p. 106-108°/ 50 mm., m.p. 3.7-4.3°.

A solid residue (32 g) in the distallation flask proved to be crude N-methyl-4-pyridone. The Plantinichloride (prepared by dissolving a portion of the solid in methanol, adding an approximately equivalent amount of chloroplatinic acid in methanol, and recrystallizing the solid thus formed from ethanol-water) had m.p. 186.5-187.5°, alone and mixed with an authentic sample of N-methyl-4-pyridone chloroplatinate. (Lit. m.p. 188° [153]).

3-Chloro-2-methoxypyridine.

3-Amino-2-chloropyridine, prepared from 3-aminopyridine according to Schickh, Binz and Schulz [143], (10 g, 0.078 mol), was dissolved in 8.5N-hydrochloric acid (140 ml). Sodium nitrate (7.4 g, 0.107 mol) was added slowly, the temperature being kept below 0°. The resulting diazonium salt solution was added slowly to a hot solution of cuprous chloride (10 g) in concentrated hydrochloric acid (50 ml). The solution was then refluxed for 1 hour. The acid was neutralized with 5N-sodium hydroxide, and the mixture was subjected to steam distillation. The product solidified in the receiver, and was filtered off. 2,3-Dichloropyridine (8.6 g, 75% yield) had m.p. 68-70°. (Lit. m.p. 66-67° [154]).

2,3-Dichloropyridine (25 g, 0.17 mol) in methanol (40 ml) was added to a sodium methoxide solution prepared from sodium (12g, 0.52 mol) and anhydrous methanol (100 ml). The temperature rose until the mixture was refluxing. After the reaction had moderated, the mixture was refluxed for a further 5 hours. The excess sodium methoxide was neutralized with methanolic hydrogen chloride, the sodium chloride filtered off, and the solution distilled to remove most of the methanol. Water was then added, and the resulting mixture was extracted with ether. The dried ether extract gave on distillation 3-chloro-2-methoxypyridine (12 g, 50% yield) b.p. 107-109°/ 52 mm. Analysis: Found: C, 50.37; H, 4.10; N, 9.57; Cl, 25.18%. C_6H_6ClNO requires C, 50.2; H, 4.21; N, 9.77; Cl, 24.75%. (For analyses of the hydrochloride and the hexachloroantimonate-hydrochloride double salt, see pages 159, 161).

The compound is slowly hydrolysed to 3-chloro-2-hydroxypyridine by dilute hydrochloric acid at room temperature.

3-Bromo-2-methoxypyridine.

3-Bromo-2-chloropyridine was prepared in the same manner as 2,3-dichloropyridine (page 148), by the action of cuprous bromide on 2-chloropyridine-3-diazonium bromide, the yield being 85%. M.p. 51-53°. (Lit. m.p.

55-56° [155]). It was converted to 3-bromo-2-methoxypyridine by the method used for the 3-chloro compound (page 149) in 63% yield. The compound distilled at 98.5-100°/ 26 mm.

Analysis: Found: C, 38.58; H, 3.10; N, 7.39; Br, 44.01%. C_6H_6BrNO requires C, 38.35; H, 3.22; N, 7.45; Br, 42.5%.

The compound is slowly hydrolysed to 3-bromo-2-hydroxypyridine by dilute hydrochloric acid at room temperature. It darkens fairly quickly on exposure to air, but may be kept for short periods in stoppered containers, and for longer periods in sealed ampoules.

3-Hydroxy-2-methoxypyridine.

3-Hydroxy-2-iodopyridine was prepared from 3-hydroxypyridine and converted to 3-hydroxy-2-methoxypyridine according to Schickh, Binz and Schulz [143], the latter compound having m.p. 67.5-68°. (Lit. m.p. 67-68° [143]).

5-Bromo-2-methoxypyridine.

Kabachnik, Ioffe and Scheinker [112] have published the infra-red spectrum of this compound, but did not state how it was obtained. Attempts to prepare it by reacting 5-bromo-2-chloropyridine with sodium methoxide having been unsuccessful in the present work, direct bromination of 2-methoxypyridine was used. (Cf. the direct bromination of 2-ethoxypyridine [122]).

Bromine (1.68 g, 0.0105 mol) in glacial acetic acid (2 ml) was added dropwise to a refluxing solution of 2-methoxypyridine (1.09 g, 0.010 mol) and sodium acetate (0.82 g, 0.010 mol) in glacial acetic acid (3 ml). When the addition was complete, the reaction mixture was allowed to stand for 1 hour, after which water (10 ml) was added, and the solution was made alkaline with 5N-sodium hydroxide, and extracted with ether. The dried ether extract was saturated with dry hydrogen chloride, and the resulting precipitate was recrystallized from methanolic hydrogen chloride-ether, giving 5-bromo-2-methoxypyridine hydrochloride (1.1 g, 49% yield), m.p. 125-126° eff.

Analysis: Found: C, 31.94; H, 2.98; Br, 35.35; Cl, 16.18; N, 5.98%. $C_6H_7BrClNO$ requires C, 32.05; H, 3.14; Br, 35,60; Cl, 15.80; N, 6.28%. (For the analysis of the hexachloroantimonate see page 161).

Entry of the halogen atom into the 5 position in this reaction is proved by the hydrolysis of the product to 5-bromo-2-hydroxypyridine. 5-Bromo-2-methoxypyridine hydrochloride (5 mg) was refluxed with 60% hydrobromic acid (1 ml) for 4 hours, and the solution was evaporated to dryness. The resulting solid was treated with a few drops of 3N-ammonia solution, washed with a few drops of water, and crystallized from a small volume of water, giving 5-bromo-2-hydroxypyridine. The latter was identified by its m.p.

(175-177°, alone and mixed with an authentic specimen), and by paper chromatography (ascending, on Whatman No. 4 paper, with 3% aqueous ammonium chloride solution, and with n-butanol-5N-acetic acid, (7:3).).

A sample of the neutral 5-bromo-2-methoxypyridine for infra-red spectroscopy was obtained by dissolving the hydrochloride (400 mg) in water, treating with an excess of 1N-sodium hydroxide, and extracting with ether. The dried ether extract was distilled, giving a few drops of liquid boiling at approximately 180°. The spectrum of this liquid is essentially the same as that published by Sheinker et al.[112].

5-Chloro-2-methoxypyridine.

A solution of 2-methoxypyridine (2.18 g, 0.02 mol) and sodium acetate (1.64 g, 0.02 mol) in glacial acetic acid (6 ml) was heated to 100°, and chlorine was passed through until the required weight (1.42 g, 0.02 mol) had been absorbed. Water was added to the solution, which was then made alkaline with 5N-sodium hydroxide and extracted with ether. The dried ether extract was distilled, and the fraction distilling between 167 and 180° was again taken up into ether. The ethereal solution was saturated with hydrogen chloride, and the resulting precipitate was recrystal-

lized from methanolic hydrogen chloride, giving 5-chloro-2-methoxypyridine hydrochloride (150 mg), m.p. 121° eff.

Analysis: Found: C, 40.14; H, 403; Cl, 41.52%. $C_6H_7Cl_2NO$ requires C, 40.05; H, 3.92; Cl, 39.4%.

2-Methoxy-5-methylpyridine.

$$ROH + PCl_5 = RCl + HCl + POCl_3$$

$$RCl + NaOCH_3 = ROCH_3 + NaCl$$

An intimate mixture of 2-hydroxy-5-methylpyridine (43 g, 0.39 mol) and phosphorus pentachloride (100 g, 0.48 mol) was heated by occasional immersion in a bath at 200°. After the first vigorous reaction had subsided, the mixture was refluxed for 3 hours. The phosphorus oxychloride formed during the reaction was removed by distillation under reduced pressure, and the residue was poured on to ice. The resulting mixture was made alkaline with sodium carbonate, and extracted with ether. Distillation of the ether extract gave 2-chloro-5-methylpyridine (10 g, 20% yield), and much tarry residue.

2-Chloro-5-methylpyridine (10 g, 0.079 mol) was added to a solution of sodium methoxide in methanol (2.35 g, 0.105 mol of sodium in 18 ml of methanol) and the mixture was refluxed for 10 hours. The excess alkali was neutralized with methanolic hydrogen

chloride, and the sodium chloride filtered off. The methanol was distilled off at atmospheric pressure, and the residue distilled between 173 and 190°/ 26 mm., (8 g). Thin film chromatography showed that the product contained much starting material, and attempts at separation were unsuccessful. 4 g of the liquid was therefore reacted for a further 12 hours with sodium methoxide (3 g of sodium in 18 ml of methanol). After neutralization, filtration, and distillation as before, 2-methoxy-5-methylpyridine (1.1 g, 23% yield) was obtained, b.p. 163-165°/ 722 mm. A thin-film chromatogram showed only one spot (not due to the starting material). 0.4 g of this liquid was dissolved in anhydrous ether and dry hydrogen chloride was passed through the solution to precipitate the hydrochloride, which was then recrystallized from methanol-ether.

Analysis: Found: C, 52.79; H, 6.29; Cl, 21.60; N, 8.80%. $C_7H_{10}ClNO$ requires C, 52.75; H, 6.31; Cl, 22.25; N, 8.78%.

The hydrochloride is extremely hygroscopic.

3,5-Dibromo-2-methoxypyridine.

This was prepared by the same route as 2-methoxy-5-methylpyridine (page 153). An intimate mixture of

3,5-dibromo-2-hydroxypyridine (14 g, 0.055 mol) and phosphorus pentachloride (12.7 g, 0.061 mol) was heated in a reflux apparatus to approximately 150°, and after the initial reaction had subsided, refluxing was continued for 4 hours. The phosphorus oxychloride formed was distilled off under reduced pressure, the residue was poured on to ice, and the solid which formed was recrystallized from alcohol, giving 2-chloro-3,5-dibromopyridine (12 g, 85% yield), m.p. 42-43°. (Lit. m.p. 43° [156]).

2-Chloro-3,5-dibromopyridine (1 g, 0.0037 mol) in anhydrous methanol (4 ml) was added to a solution of sodium methoxide in methanol (0.3, 0.013 mol) of sodium in 3 ml of methanol). The reaction mixture was refluxed for 30 minutes, after which the excess sodium methoxide was neutralized with methanolic hydrogen chloride. Water was added, and the white precipitate obtained was recrystallized from equeous ethanol, giving 3,5-dibromo-2-methoxypyridine (0.75 g, 75% yield), m.p. 48.5-49°.

Analysis: Found: C, 26.84; H, 1.84; Br, 59.27; N, 5.21%. $C_6H_5Br_2NO$ requires C, 26.60; H, 1.89; Br, 59.8; N, 5.24%.

The compound is rapidly hydrolysed to 3,5-dibromo-

2-hydroxypyridine by the action of dilute hydrochloric acid at room temperature.

3,5-Dichloro-2-methoxypyridine.

This was prepared by the same route as the 3,5-dibromo compound (above), in an overall yield of 50%. M.p. of 2,3,5-trichloropyridine, 48-49°. (Lit. m.p. 49-50°.)[158] M.p. of 3,5-dichloro-2-methoxypyridine, 38.5-40°. An analysis of the hexachloroantimonate-hydrochloride double salt is given on page .

Jones, Jenkins and Christian[157] claimed to have prepared 3,5-dichloro-2-methoxypyridine by the action of diazomethane on 3,5-dichloro-2-hydroxypyridine, but the m.p. of their product, 137-140°, is almost the same as that of 3,5-dichloro-N-methyl-2-pyridone (141°[159]) and different from that of the compound prepared here by an unambiguous method.

Preparation of salts of methoxypyridines.

Hydrochlorides. All of the methoxypyridine hydrochlorides were prepared by dissolving the neutral bases in anhydrous ether and passing in dry hydrogen chloride to precipitate the salts.

Hexachloroantimonates. Hydrochlorides could not be obtained for the two compounds, 3,5-dibromo- and 3,5-dichloro-2-methoxypyridine, and salts of these were prepared by adding to solutions of them in

methanolic hydrogen chloride, a solution of hexachloroantimonic acid in methanolic hydrogen chloride. (This reagant was prepared by adding 1 g of antimony pentachloride to 10 ml of approximately 8N-methanolic hydrogen chloride). Analysis showed that the solids obtained in this way were mixed salts having the composition $(BH^+)_2.SbCl_6^-.Cl^-$. (See page 162). Pyridine itself forms a salt having this composition[160]. Hexachloroantimonates of 5-chloro- and 5-bromo-2-methoxypyridine were prepared by the method used for preparing the hexachloroantimonates of the hydroxypyridines (page 145).

Trichloromercurates. (Including hydroxypyridine salts). In the first attempts to prepare the trichloromercurates of 2-, 3- and 4-hydroxy- and methoxy-pyridines, equimolar quantities of base, mercuric chloride and concentrated hydrochloric acid were dissolved in hot water, and the solids which crystallized out on cooling were recrystallized from water. The salts of 3- and 4-methoxypyridine and 4-hydroxypyridine obtained in this way had the composition $(BH^+)_2.Hg_3Cl_8^=$, and could be recrystallized from concentrated hydrochloric acid without change of composition. Salts of 3-hydroxy- and 2-methoxy-pyridine had the composition $BH^+.HgCl_3^-$, while the solid obtained from 2-hydroxypyridine had the

composition $B.HgCl_2$. A salt of 2-hydroxypyridine having the composition $BH^+.HgCl_3^-$ was prepared by dissolving equimolar amounts of base and mercuric chloride in concentrated hydrochloric acid, and recrystallizing the solid which separated out on cooling from concentrated hydrochloric acid.

(See table of analyses on page 160)

The complex salts of the methoxypyridines were dried at room temperature, in an atmosphere of hydrogen chloride.

Table of Salts Analysed.

Hydrochlorides.

2-Hydroxypyridinium hydrochloride. Found: C, 45.67; H, 4.62; N, 10.52; Cl, 27.02%. C_5H_6ClNO requires C, 45.65; H, 4.60; N, 10.65; Cl, 26.95%.

2-Hydroxy-4-methylpyridinium hydrochloride. Found: C, 49.27; H, 5.63; N, 9.63; Cl, 24.87%. C_6H_8ClNO requires C, 49.5; H, 5.55; N, 9.63; Cl, 24.1%.

5-Chloro-2-hydroxypyridinium hydrochloride. Found: C, 36.44; H, 3.10; N, 8.36; Cl, 42.52%. $C_5H_5Cl_2NO$ requires C, 36.2; H, 3.35; N, 8.44; Cl, 42.7%

2-Hydroxy-5-iodopyridinium hydrochloride. Found: C, 22.75; H, 1.86; N, 5.32; Cl, 13.28; I, 48.77%. C_5H_5ClINO requires C, 23.35; H, 1.96; N, 5.44; Cl,13.8; I, 49.4%.

4-Methoxypyridinium hydrochloride. Found: C, 49.99; H, 5.38; N, 9.55; Cl, 23.73%. C_6H_8ClNO requires C, 49.5; H, 5.55; N, 9.63; Cl, 24.4%

3-Chloro-2-methoxypyridinium hydrochloride. Found: C, 40.3; H, 3.79; N, 7.61; Cl, 39.83%. $C_6H_7Cl_2NO$ requires C, 40.4; H, 3.92; N, 7.78; Cl, 39.4%.

3-Hydroxy-2-methoxypyridinium hydrochloride. Found: C, 44.48; H, 4.86; N, 8.60; Cl, 21.72%. $C_6H_8ClNO_2$ requires C, 44.6; H, 6.00; N, 8.67; Cl, 21.95%.

Other analyses of hydrochlorides have already been given on pages 151, 153, 154.

Complex salts containing mercury.

3-Methoxypyridinium octachlorotrimercurate. Found: C, 13.01; H, 1.37; N, 2.53; Cl, 25.85; Hg, 54.88%. $C_{12}H_{16}Cl_8Hg_3N_2O_2$ requires C, 13.15; H, 1.47; N, 2.56; Cl, 24.9; Hg, 54.9%.

4-Methoxypyridinium octachlorotrimercurate. Found: C, 13.05; H, 1.40; N, 2.56; Cl, 25.08%. $C_{12}H_{16}Cl_8Hg_3N_2O_2$ - see above.

4-Hydroxypyridinium octachlorotrimercurate. Found: C, 10.79; H, 1.07; N, 2.31; Cl, 26.10; Hg, 56.48%. $C_{10}H_{12}Cl_8Hg_3N_2O_2$ requires C, 11.25; H, 1.13; N, 2.62; Cl, 25.6; Hg, 56.5%.

2-Methoxypyridinium trichloromercurate. Found: C, 16.69; H, 1.94; N, 3.26; Cl, 24.55; Hg, 48.92%. $C_6H_8Cl_3HgNO$ requires C, 17.25; H, 1.93; N, 3.36; Cl, 25.5; Hg, 47.9%.

3-Hydroxypyridinium trichloromercurate. Found: C, 14.42; H, 1.33; N, 3.35; Cl, 24.67%. $C_5H_6Cl_3HgNO$ requires C, 14.9; H, 1.50; N, 3.47; Cl, 26.4%.

2-Hydroxypyridinium trichloromercurate. Found: C, 14.66; H, 1.52; N, 3.45; Cl, 26.54%. $C_5H_6Cl_3HgNO$ - see above.

Complex salts containing antimony.

2-Hydroxypyridinium hexachloroantimonate. Found: C, 13.95; H, 1.65; N, 3.16; Cl, 49.3%. $C_5H_6Cl_6NOSb$ requires C, 13.95; H, 1.41; N, 3.25; Cl, 49.45%.

5-Bromo-2-hydroxypyridinium hexachloroantimonate. Found: C, 11.72; H, 1.07; N, 2.71; Br, 15.77; Cl, 42.69%. $C_5H_5BrCl_6NOSb$ requires C, 11.80; H, 0.99; N, 2.75; Br, 15.72; Cl, 41.8%.

5-Choro-2-hydroxypyridinium hexachloroantimonate. Found: C, 12.67; H, 1.04; N, 2.89%. $C_5H_5Cl_7NOSb$ requires C, 12.9; H, 1.08; N, 3.01%.

3,5-Dibromo-2-hydroxypyridinium hexachloroantimonate. Found: C, 10.12; H, 1.04; N, 2.38% $C_5H_4Br_2Cl_6NOSb$ requires C, 10.22; H, 0.168; N, 2.38%.

3,5-Dichloro-2-hydroxypyridinium hexachloroantimonate. Found: C, 11.90: H, 1.08: Cl, 55.48%. $C_5H_4Cl_8NOSb$ requires C, 12.01; H, 0.80; Cl, 56.6%.

2-Methoxypyridinium hexachloroantimonate. Found: C, 16.28; H, 1.89; N, 3.07; Cl, 47.76%. $C_6H_8Cl_6NOSb$ requires C, 16.20; H, 1.82; N, 3.15; Cl, 47.9%.

5-Bromo-2-methoxypyridinium hexachloroantimonate. Found: C, 13.86; H, 1.51; N, 2.72; Br, 15.29; Cl, 40.35%. $C_6H_7BrCl_6NOSb$ requires C, 13.79; H, 1.35; N, 2.68; Br, 15.28; Cl, 40.6%.

3-Chloro-2-methoxypyridinium hexachloroantimonate: hydrochloride double salt. Found: C, 21.50; H, 2.12; Cl, 47.23%. $C_{12}H_{14}Cl_9N_2O_2Sb$ requires C, 21.85; H, 2.14; Cl, 48.5%.

3,5-Dichloro-2-methoxypyridinium hexachloroantimonate: hydrochloride double salt. Found: C, 19.53; H, 1.64; N, 3.76; Cl, 49.87% $C_{12}H_{12}Cl_{11}N_2O_2Sb$ requires C, 19.80; H, 1.66; N, 3.86; Cl, 53.6%.

Perchlorate:

3,5-Dichloro-2-hydroxypyridinium perchlorate: perchloric acid double salt. Found: C, 19.23; H, 1.86; N, 4.47; Cl, 39.78%. $C_5H_5Cl_4NO_9$ requires C, 19.07; H, 1.43; N, 4.44; Cl, 39.4%.

Sodium Salts.

Sodium salt of 2-hydroxy-5-iodopyridine. Found: C, 24.68; H, 1.33; I, 51.6; N, 5.69%. C_5H_3INONa requires C, 24.7; H, 1.24; N, 5.76; I, 52.2%.

Sodium salt of 3,5-dibromo-2-hydroxypyridine. Found: C, 21.23; H, 0.81; Br, 57.46; N, 5.07%. $C_5H_2Br_2NONa$ requires C, 21.85; H, 0.73; Br, 58.1; N, 5.10%.

Sodium salt of 2-hydroxy-5-nitropyridine. Found: C, 37.20; H, 1.99; N, 16.73%. $C_5H_3N_2O_3Na$ requires C, 37.05; H, 1.86; N, 17.30%.

Mono-sodium salt of 2,6-dihydroxypyridine. Found: C, 42.43; H, 2.98; N, 9.48%. $C_5H_4NO_2Na$ requires C, 45.1; H, 3.02; N, 10.53%.

Physico-Chemical Measurements.

Ionization constants. Where possible, these were determined by potentiometric titration, as described by Albert and Phillips[5]. If the pKa value was greater than 11 or less than 3, however, the spectrophotometric method[5] was employed.

Ionization constants could not be determined for 3-bromo-, 3-chloro-, 3,5-dibromo- and 3,5-dichloro-2-methoxypyridines, as these compounds hydrolyse readily in dilute aqueous acid, nor for 3,5-diiodo-2-hydroxypyridine, which is not sufficiently soluble in water. A pKa value could not be obtained for the basic ionization of 2,3-dihydroxypyridine. The spectrum of this compound changed gradually as the pH of the solvent was changed from 1.5 to -2, and attempts to determine pKa values in the usual way gave results varying from 0.7 to -1.2. The spectrum changed most rapidly with changing pH of the solvent near pH 0.7, and this may be an approximation to the pKa value for the ionization. However, it was not possible to obtain a hydrochloride of 2,3-dihydroxypyridine (Schickh, Binz and Schulz[143] obtained the substance in the neutral form by evaporation of a solution in concentrated hydrochloric acid), and this is characteristic of compounds having much lower pKa

values, (e.g. 3-chloro-2-hydroxypyridine, with pKa value of -2.03).

Ultra-violet spectra. These were recorded using a Perkin-Elmer "Spectracord" 4000A, and the extinction coefficients at the wavelengths of maximum absorption were checked using a manually operated single-beam instrument, either a Hilger "Uvispek" H.700.305 or an Optica Cf.4.

Compounds were dissolved in buffer solutions of pH at least 2 units different from a pK_a value of the substance, to ensure that the spectrum recorded was that of at least a 99% pure species. This was not possible, however, for 2,6-dihydroxypyridine in the neutral form (2% of cationic and 2% of anionic species present), or for the di-anion of 2,6-dihycroxypyridine (possibly as much as % of the mono-anionic species present).

The ultra-violet spectra of 3,5-dibromo- and 3,5-dichloro-2-methoxypyridine were recorded in methanol (purified according to Leighton, Crary and Schipp [161]), as these compounds were insufficiently soluble in water. The compounds are rapidly hydrolysed by aqueous acids, and spectra have not been obtained for their cations. For 3-bromo- and 3-chloro-2-methoxypyridine, spectra in methanolic hydrogen chloride have been obtained.

3,5-Diiodo-2-hydroxypyridine has a very low solubility in water and the usual organic solvents. A qualitative spectrum for the neutral species was obtained with a saturated solution in water (using 5 cm cells), but the solute concentration, and hence the extinction coefficients at the wavelengths of maximum absorption are not known.

Infra-red spectra. These were determined using a Perkin-Elmer model 21 double-beam recording spectrometer, fitted with a sodium chloride prism.

As far as possible, spectra were obtained using potassium bromide pellets as the sample-containing medium, the usual concentration being 1 mg of substance in 200 mg of potassium bromide. (Satisfactory spectra of the complex salts containing mercury, however, should be obtained only if the concentration was 2 to 3 times this value). Liquids were examined as thin films between sodium chloride plates.

When potassium bromide or sodium chloride pellets of the perchlorates of weak bases were examined, only the infra-red spectra of the free bases were observed, and even the spectra from silver chloride pellets or paraffin mulls were unsatisfactory.

Hexachloroantimonates were examined as paraffin mulls. Mulls were also used for the hydrochlorides of 5-chloro- and 5-iodo-2-hydroxypyridine, and of

2-methoxy-5-methylpyridine, which proved to be very difficult to grind with potassium bromide.

Many of the salts examined were hygroscopic, and samples of such compounds for infra-red analysis were ground in a dry box.

Raman spectra. These were obtained using a Hilger E612 glass spectrograph fitted with a Hilger E616 scanning attachment and a recorder. Whenever possible, spectra were recorded at a scanning speed such that the range 0 to 1700 cm^{-1} was covered in approximately 2 hours, but for some compounds, which became coloured too rapidly under the strong irradiation, this range had to be covered in approximately 8 minutes, with a resultant loss in accuracy.

The instrument is suitable for examining liquids samples only, and the amount of liquid required is approximately 5.7 ml. Solutions for Raman spectroscopy were treated with charcoal to remove coloured or fluorescent impurities, filtered through a sintered glass filter, subjected to a moderate vacuum to remove small air bubbles, and, in many cases, centrifuged before examination. Many of the compounds became coloured in the course of a 2-hour recording of the spectrum, and had to be purified again before duplicate spectra could be obtained.

Solutions for Raman spectroscopy were saturated with respect to the organic moiety at 20°. All compounds, other than pure liquids, for which Raman spectra were obtained, were examined in aqueous solution. 3-Chloro- and 3-bromo-2-methoxypyridine hydrolyse too rapidly in aqueous acids for Raman spectra to be obtained, and were found to be insufficiently soluble in methanolic hydrogen chloride for spectra to be obtained in this solvent. In dimethyl sulphoxide, their hydrochlorides exhibited a strong fluorescence which masked the Raman bands.

APPENDIX.

Vibration Spectra.

Introduction. In this appendix are given the infra-red and Raman spectra of the salts examined. It has been necessary to divide many of the spectra into two parts :

A. The region 4000 - 1000 cm^{-1}. The region 4000 - 2000 cm^{-1} proved to be of little value for structural elucidations, and the frequencies of the principal absorption maxima only are recorded. For the region 2000 - 1000 cm^{-1} the absorption spectra are given in full.

B. The region 1000 - 650 cm^{-1}. The data for this region are given in full also.

Infra-red intensities are given as "weak", "medium", "strong", etc., and Raman intensities are given on a scale of 1 to 10, 10 being the intensity assigned to the strongest band observed in each spectrum.

The following abbreviations have been used :

w.	Weak	v.	Very
m.	Medium	b.	Broad
s.	Strong	P.	Bands due to paraffin mulling agent.

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Hydroxypyridine mercurichlorides

2-Hydroxypyridine	204
3-Hydroxypyridine	"
4-Hydroxypyridine	"

2-Hydroxypyridines.

3-Methyl-		4-Methyl-		5-Methyl-	6-Methyl-
		2930		3020	
2780		2810		2950	
		2750		2830	2770
1975 vw		1963 vw			
1940 vw		1926 vw		1912 vw	
1903 vw					
1845 w		1849 w		1800 vw	1856
1751 vw		1750 vw		1698 w	1777 w
1652 vs		1656 vs	Raman	1657 vs	1672 vs
1610 vs	Raman	1615 vs	1605 1	1613 vs	1610 s
1571 m	1570 3	1560 w			
		1536 m	1533 0	1548 vs	1551 m
		1510 vw			
1482 s		1485 m	1483 2	1490 m	1469 m
	1466 1 1446 0	1454 s		1462 vs	1434 m
1423 m		1442 w		1426 s	1407 w
1375 m		1377 m	1381 2	1377 m	1371 m
1351 m	1350 9	1335 m	1340 5	1357 m	
1255 m	1260 10	1248 m	1260 10	1269 w	1250 w
1230 s		1220 vw		1236 m	
1197 vw	1205 ?			1206 m	1212 m
1165 w	1174 1	1169 s		1146 m	1168 m
1105 w	1114 2	1110 w			1080 w
1059 m	1060 1	1039 m		1045 w	1045 w
1041 vw		1021 m		1015 m	1031 w
986 m	991 2 ?	988 w	987 1	979 m	998 m

2-Hydroxypyridines.

3-Methyl-		4-Methyl-		5-Methyl-	6-Methyl-
		971 m	Raman	965 m	
940 m		941 m	935 1		935 *
914 w	Raman	923 m		908 w	922 m
885 s	891 1			897 m	870 w
		847 m		846 m	
				804 w	810 w
775 vs		777 s	763 5	759 vs	799 m
		759 m			
735 w	744 2	731 m		737 vw	733 m
	542 0		574 3		

Only one Raman band, at 860 cm^{-1}, was observed for 2-hydroxy-5-methylpyridine.

3-Chloro-	3-Bromo-	3-Hydroxy-
944 m	946 w	
920 w	929) w 921)	914 w
		899 m
876 m	868 m	842 m
774 m	772 m	778 m
756 m	754 w	749 s
671 m	650 m	690 m

2-Hydroxypyridines.

3-Chloro-	3-Bromo-	3-Hydroxy-
2780 s	2810 s	3180 s
1920 vw		1857 vw
1860 vw		1835 vw
1822 vw	1825 w	
		1656 vs
1657 vs	1653 vs	1608 vs
1612 s	1612 s	1571 m
1546 m	1542 w	1545 *
	1512 vw	1452 w
1472 m	1464 m	1440 m
1435 *	1433 vw	1404 w
1325 m	1324 m	1366 s
1306 vw	1300 w	1335 *
1246 m	1244 m	1285 s
1194 w	1186 vw	1183 s
1170 w	1160 vw	1170 *
1123 m	1114 vw	1097 w
1046 m	1032 m	1042 m
982 m	981 w	

2-Hydroxypyridines.

5-Chloro-	5-Bromo -	5-Iodo-
3010 }	3005 }	3000 }
2930 } vs	2929 } vs	2925 } vs
2820 }	2810 }	2815 }
2760 }	2740 }	2760 }
1892 vw	1886 vw	1889 vw
1844 vw	1834 vw	1831 vw
1805 vw	1791 vw	1782 vw
1735 vw		1679 w
1658 } vs	1641 vs	1639 vs
1641 }		
1605 vs	1604 vs	1603 s
1543 s	1536 s	1533 s
	1509 vw	1510 w
1478 w	1475 w	1471 w
1460 s	1458 s	1456 s
1426 m	1424 m	1422 m
1341 m	1340 m	1339 m
	1325 w	1324 w
1233 m	1226 m	1233 m
1104 m	1143 m	1146 m
		1130 w
1053 vw	1079 m	1065 w
1033 vw		
990 m	991 m	988 m

2-Hydroxypyridines.

3,5-Dichloro-	3,5-Dibromo-	3,5-Diiodo-
1048 m	1026 w	1025 m
		960 w
916 m	919 m	
	896 w	
897 m	880 w	
844 s	841 s	864 s
750), 745) m	747 w	748 w
	699 s	670 m

5-Chloro-	5-Bromo-	5-Iodo-
971 w	965 m	964 m
909 m	908) m, 897) w	905) w, 891) m
842) m, 838) w, 830) w	844) s, 833) m	847) w, 836) w, 825) w
668 s		

2-Hydroxypyridines.

3,5-Dichloro-	3,5 Dibromo-	3,5-Diiodo-
	3130	
3080	3080	
3050	3050	
		2830
		2720
		2680
1947 vw		1922 vw
1871 vw		1888 vw
1813 w	1817 w	1829 vw
	1805 vw	1802 vw
		1691 vw
1697 s	1692 s	1634 s
1658 w	1653 w	
1632 m	1626 m	
1589 vw	1583 vs	1593 m
		1559 vw
1534 m	1527 m	1525 s
1506 w	1511 vw 1500 vw	1500 w
1440 m	1440 m	1459 m
1384 w	1374 w	
1365 w		1365 m
1304 w	1301 m	1308 s
1293 w	1285 w	
1235 s	1231 s	1249 m
1179 m	1174 m	
1163 w	1151 w	1145 vw
1119 m	1100 m	1088 w

2-Hydroxypyridines.

3-Nitro-	5-Nitro-
3090 vs	3000 s 2800 vs
	1975 w
1694 s	1674 s
1658 s	1630 s
1590 s	
1550 vs	1566 m
1508 m	1505 s
1467 *	
1437 *	1432 m
1348 s	1355 vs
1296 s	
1221 vs	1251 s
1164 w	1166 vw
1139 m	1145 m
	1131) 1120) s
1064 m	
1045 m	
978 w	984 m
896 m	915) m 885) w
876 m	
826 w	835 s
796 w	
762 s	760 m
717 w	716 m

2-Hydroxypyridine Hydrochlorides.

3-Methyl-		4-Methyl-		5-Methyl-	6-Methyl-
3120 vs					
		2760 vs		2750) vs	2880) vs
		2515 m		2660)	2710)
		2435 m			2530) s
					2470)
		1928 w			
1846 w		1874 w		1854 m	
1740 vw	Raman	1818 w	Raman	1785 w	1736 vw
1651 vs	1633 2	1636 s	1644 3	1650) s	1638 vs
1613 s	1619 2			1631)	
1546 m	1565 1			1556 s	1550 m
		1525) s			
		1510)		1510 w	1499 m
1480 m	1475 1	1473 w		1481 m	1467 m
		1446 w		1433 m	1440 m
1403 s		1405 m			1395 m
1379 *	1385 3	1367 s		1389 m	1372 w
1349 w	1340 4	1343 w	1347 2	1329 vs	1345 *
		1312 s			1323 s
1273 vw				1271 w	
1254 m	1250 3	1241 m		1252 w	1258 w
1230 m		1225 w		1221 w	1230) w
					1216)
1170 w	1178 1	1186) w			1174 s
		1175) m			
				1143 s	
	1125 2	1122 w			
1105 w	1097 0				
1059 m	1069 2				
1045 *		1033 w		1047) vw	1049) m
				1023)	1040)
	1002 1	1004 w	1004 6		1006 m

2-Hydroxypyridine Hydrochlorides.

3-Methyl-		4-Methyl-		5-Methyl-	6-Methyl-
	Raman				
986 m	994 1			992 w	
975 *		966 w	Raman		
940 m		941 w	948 1	927 m	
912 vw		906 w			
885 m	885 1	890 vw			894 m
				864 m	
	851 0	853 m		841 s	864 w
					824 w
		804 s		800 *	798 s
776 s	753 10	766 w	767 9	763 m	754 m
		751 m		736 m	
	696 1	715 w		721 m	720 w
	603 1		563 4		
	539 1		520 3		

5-Chloro-		5-Bromo-		5-Iodo-
960 m				945 w
908 w		895 w		
867 m	Raman		Raman	864 w
856 w	855 10		855 10	853 w
844 m		840 *		837 m
		825 m		828 w
776 vw				783 m
669 m				720 vw
	676 1			
	640 1			
	495 0			
	466 1			
	391 2			
	322 1			

2-Hydroxypyridine Cations. (Hydrochlorides)

5-Chloro-		5-Bromo		5-Iodo-
2670 s		3110 s		2700) s 2660)
1903 m				1884 w
1816 m				1796 w
1725 m	Raman	1674 vw		1715 vw
1640 s	1640 2	1645 vs		1618 vs
1612 m		1599 s		1610 vs
1533 s	1541 1	1537 m		1524 s
1460 w		1457 w		1441 w
1421 m		1420 *		1420 vw
		1402 s		
1365 w	1385 2			
1325 m	1329 2	1339) 1323) w	Raman	1335 s
1264 m	1267 4		1269 4	1256 w
1231 m		1223 w		1205 vw
1135 m		1138 w		1139 m
1122 w	1123 2	1127 *		1115 vw
1104 vw				
1052 w		1076 w	1097 3	1075 vw
1006 w				1007 w
992 w		985 w	988 2	

2-Hydroxypyridine Hexachloroantimonates.

3-Chloro-	3,5-Dichloro-	3,5-Dibromo-
3260 w		3240 w
	3060 w	3140 w
		3070 w
1621 s	1623 m	1621 s 1610 *
1538 m	1534 s	1520 s
1520 *	1510 *	1502 *
	1425 *	1418 w
1319 s	1308 s	1299 s
1290 w	1282 m	1281 m
1266 vw		
1239 w	1223 w	1216 m
1193 w		
1156 w	1150 w	1153 1141 m
1141 w	1100 m 1073	1111*
		1061 w
1048 m		
1018 w	1021 w	
944 vw		932 vw
880 vw	897 m	880 w
	867 m	
817 vw		800 m
783 *		777 *
761 s		
733 *	743 721 m	
		696 m

2-Hydroxypyridine Hexachloroantimonates.

5-Chloro-	5-Bromo-
3350 w 3190 m	3280) 3200) m
1640 s	1638 s
1621 s	1618 mb
	1600 *
1538 s	1537 s
1513 *	1510 *
1343 w	1339 s
1324 vw 1304) 1292) s	1321 w
1238 w	1265) 1247) vw
1220 *	
1171 w	
1134 m	1136 m
1123 *	1094 w
1017 w	
	870 vw
839 m	834 m
785 m	785 m
715 vw	713 w
673 m	

2-Hydroxypyridines, Sodium Salts.

4-Methyl-		5-Methyl-	
3080 vs		3180)vs 3000)	
2440 vw		2410 m 2360 m	
1656)w 1615)vs	Raman	1662)vw 1635)s	Raman 1615 3
1532 m	1540 6	1542)s 1513)vs	1532 2
1483)vs 1445)vs 1433)s		1490)vs 1451 w 1416 s	
1371 w	1379 2		1386 5
		1345 vw	
1321 s	1323 6	1329 vw	1330 5
		1316 vw	
1289 m		1289 m	1280 5
1227 m			1234 10
	1213 10	1211 w	
1177 s	1176 2		
		1137 m	
1106 vw			
1016 w		1036)w 1016)s	
985 m	985 6		984 ?

2-Hydroxypyridine, Sodium Salts.

5-Chloro-		5-Bromo-		5-Iodo-	
				956 w	
904 w					Raman
890)w		891)w		890 w	890 3
878)w	Raman	880)w	Raman		
862 w	862 5	859 w	858 3	857 w	856 5
834)s					
826) w		826 s		827 s	
746 w		744 w		744 w	
682 s					

4-Methyl-		5-Methyl-	
	Raman		Raman
945 w	944 4		
890 vw		889)m	
		878)m	
866 m		865)m	864 10
835 w		827 s	
791 s			
771 w	771 10	771 m	770 ?
755 vw		745 w	
	528 2		

2-Hydroxypyridines, Sodium Salts.

5-Chloro-		5-Bromo-		5-Iodo-	
3150 vs, 3070 vs		3160 vs		3160 vs	
1927 vw					
1803 vw				1850 vw	
1785 vw		1789 vw		1796 w	
1718 vw		1718 vw		1720 vw	
1700 vw					
1659 w		1651 vw		1646 w	
1611 w	Raman	1608 s		1603 s	
1600 s	1591 2			1561 vw	
1531 m	1534 3	1525 w		1523 m	
1482 vs		1490 vs, 1470 vs		1498 vs, 1470 vs	
1402 s		1403		1401 s	
	1386 3	1392 vw		1391 m	
1325 w	1328 2	1330 w		1333 w	
1311 vw			Raman		
1278 m	1282 2	1281 m	1282 2	1286 m	Raman
1219 w	1217 10	1221 w	1213 10	1220 w	1213 10
1170 w					
1126 m		1134 m		1139 m	
1110 m		1089 m	1090 2	1075 w	1081 2
998 m	985 2	994 m	983 2	989 m	984 3

2-Hydroxypyridines, Sodium Salts.

3,5-Dichloro-		3,5-Dibromo-	3,5-Diiodo-
3250		3130	3160
1792 vw			
1777 vw			
1720 vw			
1643 m		1641 w	1636 w
1588 s		1576 s	1561 s
1543 vw		1525 vw	
1515 w		1503 vw	
1488 vs		1481 vs	1461 vs
1465 w			
1414 vw	Raman		
1400 w	1395	1388 w	1376 m
1314 w		1318), 1309) w	1324 w
1248 m	1246	1254) w, 1240) vw	1250 m
1178 m	1183	1168 w	1165 w
1118 m		1109 w	
1102 w		1085 w	
1051 s		1026 m	1012 m
898) m, 886) s	894	894) vw, 885) m	898 m
865 w			874 vw
770 s		766 m	766 m
755 s			
660 m		706 m	676 m

2,6-Dihydroxypyridine, Sodium Salt.

3380 m

3150 s

2610 s

1980 m

1723 w

1632 s

1608 w

1532 vs

1449), 1431) vs

1334 m

1302), 1285) s

1181 m

1105 m

1048 w

1000 m

886 s

768 m

740 w

723 vs

Methoxypyridines.

2-Methoxy-Pyridine		3-Methoxy-Pyridine		4-Methoxy-Pyridine	
3045 *					
3000) 2975) m 2940)		3015) 2950) m 2835 w		3040) 2970) m 2840 w	
2550 vw		2500 w			
2100) 2040) vw		2075) 2040) w		2100 w	
1910 vw				1926 w	
	Raman		Raman		Raman
1606 s	1601 1				
1589 w		1588 *	1588 5	1579 vs	1590 2
1575 s	1750 5	1578 m	1579 2	1574 m	1569 0
		1548 *		1548 *	
1484 vs		1482 s		1507 s	1501 0
1447 m	1443 2	1465 *	1460 1	1465 m	1460 0
				1445 m	1441 0
1422 s	1417 *	1427 s	1426 1	1423 m	1419 0
1314 m	1308 6			1358 vw 1333 vw	1332 1
1292 s	1286 3	1284) s	1282 4	1289 vs	1284 2
1257 w	1256 *	1269)	1271 3		
		1234 s	1233 1	1244 w	1240 1
1180 vw	1177 1	1193 m	1191 2	1183 *	1180 1
		1179 *	1179 2		
1144 m	1140 1	1130 w		1151 vw	1149 0
1119 w		1111 w	1111 1	1089 w	1073 0 1051 0
1099 vw 1084 vw	1095 2	1105 *			

Methoxypyridines.

2-Methoxy-pyridine		3-Methoxy-pyridine		4-Methoxy-pyridine	
	Raman		Raman		Raman
1046 m	1041 3	1052 m	1051 10		
1022 m	1019 1	1018 s	1014 7	1029 m	987 10
988 m	985 10			990 m	987 10
956 vw					
	930 1	923 w			930 0
862 w		897 vw			885 0
828 vw	826 1			818))s	
812 m	810 6			802)	801 3
781 s	781 1	799 s	798 9		
736 m					
725 vw		706 s		707 w	
	622 1		620 2		661 2
	602 1		570 1		552 0
	525 0		515 1		537 0
	456 2		442 2		442 1
					389 0
	231 1		256 1		261 0
			209 1		

2-Methoxypyridines.

3-Chloro-		3-Bromo-	
2980)m 2950)		2950 m	
1896 w		1898 w	
1745)w 1720)		1717 w	
1654 w	Raman	1640 vw	Raman (F)
1586)vs	1586 2	1583)vs	1585 1
1563)w	1563 7	1560)*	
	1507 1		1508 9
1471 vs	1467 1	1470vs	1468 1
1444 s	1443 2	1444 s	
1407 vs	1407 0	1405)vs	1403 0
	1334 *	1374)vw	
1317)	1315 *		
)s 1302)	1303 7	1300 s	1301 7
1258 s		1256 s	
1250 *	1246 5		1246 6
	1232 *		
1199 vw			
1180 w	1179 1	1180 w	1182 1
		1144 m	
1128 s	1126 2	1120 m	1121 3
1073 vs	1074 2	1070 s	1070 3
1046 vs	1046 10	1035 vs	1035 5
1012 s	1015 1	1010 s	1011 1

2-Methoxypyridines.

3-Chloro-		3-Bromo-	
	Raman		Raman
	987 1		977 1
963 w	966 0	962 w	
931 vw	945 0		
891 w		889 m	
828 w	828 2	823 w	826 4
785 s	789 0	785 s	
751 s	754 1	751 s	757 1
698 s	700 6	696 vw	
		675 m	677 5
	643 0		
	604 1		
	501 4		512 2
			493 5
	444 1		440 1
	413 4		
			324 10
	289 2		278 4

2-Methoxypyridines.

5-Methyl-	5-Bromo-	3-Hydroxy-	3,5-Dibromo-
2940	2980) m 2950)	2690) 2630) 2570)	2910 w
	2100) 2040) vs		
1935 vw	1913 vw		
1875 vw			
1848 vw	1817 vw	1815 vw	
1650 *	1656 w	1665 vw	
1614 m		1604 m	
1574 m	1586 s	1575 m	1571 m
1562 *	1564 w	1559 *	
	1548 *		1484 w
1494 vs	1481 vs	1501 s	1472 vs
1461 w	1466 *	1451 s	1442 vw
1445 *	1430 w	1419 vw	1410 s
1378 m	1368 s	1376 vs	1373 s
		1336 w	
1304 vw	1302 w	1310 w	1305 s
1284 vs	1284 vs	1287 s	1291 w
1255 m	1247 m	1255 s	1245 m
1220 w	1218 *	1230 w	1238 w
		1195 *	
1167 *	1176 vw	1177 vs	1175 w
	1156 w		
1127 m	1122 m	1102 s	1110 w

2-Methoxypyridines.

5-Methyl-	5-Bromo-	3-Hydroxy-	3,5-Dibromo-
1074 vw	1090 m		1090 w
		1065)w	
		1055)	1056 s
1028 s	1022 s	1014 s	1012 w
990 vw	1002 w		1000 w
911 w	915 w	938 vw	
890 *	890 *	870 m	896 m
848 *			839 m
823 m	826 m		
		785)*	
775 vw		776)m	
	757)m		
740 m	740)*	751 m	742 m
			694 m

2-Methoxypyridine Hydrochlorides.

5-Methyl-	5-Chloro-	5-Bromo-
	1133 *	1102 vw
1058 w		
		1007)m
1000 s	1004 s	1003)
973 *	960 w	953 w
	872)m	
861 *	866)	865 m
	837)m	835)m
849 m	826)	826)
735)s	719 vw	719 vw
725)		

2-Methoxypyridine Hydrochlorides.

5-Methyl-	5-Chloro-	5-Bromo-
2400 s	2510 s	2500 vs
	1972 w	1965 w
	1942 m	1915 m
	1830), 1816) w	1875 *, 1815 m
	1743 vw	1733 w
1639 m	1630 m	1621 m
1611 s	1606 vs	1604 vs
1552 s	1535 vs	1531 vs
1528), 1513) *	1514 *	1512 *
P	1460), 1447) vw	1475), 1463) w
1434 w	1432 s	1429 s
1355 m	1335 vs	1334 vs
1320 m		
1290 s	1292), 1284) s	1291), 1286) s
1250 w		
1235 w	1233 m	1232 m
1190 m	1198 w	1197 w
1157 m	1152) w, 1141) m	1151), 1141) m
1058 w	1033 *	1102 vw
1000 s	1004 s	1007), 1003) m
973 *	980 w	953 w
861 *	872), 866) m	865 m
849 m	837), 828) m	835), 826) m
735), 725) s	719 vw	719 vw

2-Methoxypyridine Hydrochlorides.

3-Chloro-	3-Bromo-	3-Hydroxy-
		3080 m
2550 vs	2580 vs	2930 m
		2870 m
1975 w	1950 w	
	1918 m	
1880 w		
1801 w	1778 m	
1701 ?		
1650 *	1648 w	1623 *
1626 m	1623 s	1620 m
1599 vs	1591 vs	1572 vs
1530 vs	1515 vs	1540 *
1481 m	1486 s	1489 w
1461 vw		
1435 m	1441 m	1454 m
1409 *	1424 m	1409 m
1359 s	1356 s	1374 m
1328 vs	1332 s	1304 m
		1286)vs
1263 m	1254 m	1265)*
1215 w	1221 s	1205)m
		1186)m
1182 w	1190 m	1179)*
1128 w	1124 m	1112 m
1079 w	1060 w	
1059 m	1043 m	1053 m
991 s	996 vs	1004 s

2-Methoxypyridine Hydrochlorides.

3-Chloro-	3-Bromo-	3-Hydroxy-
	960 m	
903 m	892 m	915 w
		857 m
	818 vw	832 w
801 vs	783 vs	777 s
749 m	726 m	731 m
691 s	665 s	

2-Methoxypyridine Hexachloroantimonates.

3-Chloro-	3,5-Dichloro-	3,5-Dibromo-
989 s	987 s	987 s
972 *	963), 946) m	943 w
923), 905) w, 888)	922 *	911 w
	866), 848) s	852 s
820 vw		
797) s, 788) *, 775) *		794 *
734 m	722 s	726 m
692) *, 686) s	661), 654) m	686 m

2-Methoxypyridine Hexachloroantimonates.

3-Chloro-	3,5-Dichloro-	3,5-Dibromo-
2510	2560	2520
	2360	
1960 vw	1913 vw	
1870 w	1875 vw	1877 vw
1811 w		1850 vw
	1715 w	1701 w
1623 m	1620 w	1616 *
1595 s	1601 s	1601 m
	1591 *	
	1561 *	
		1536 *
1521 s	1521 s	1513 s
1444 vw		
1427 w	1428 w	1428 w
	1411 *	
1359 m?	1359 w?	1353 w?
1325 s	1319 s	1309 s
	1292 *	
1260 m	1254 s	1256 s
		1221 *
1214 w	1212 m	1212 m
1183 m	1179 w	1174 w
1136 m	1137 m	1109 w
1074 vw	1072 w	
1050 m		
1020 vw	1016 vw	1009 w

2-Methoxypyridine Hexachloroantimonates.

5-Chloro-	5-Bromo-
3250 3060	3270 3170
1637 m	1632 m
1608 s	1606 s
1538 s	1535 s
1512 *	1512 *
1492 *	
1432 w	1427 m
1334 m 1305 *	1317 *
1286 s	1284 s
1224 w	1234 w 1221 *
1182 w	1182 w
1144 m	1141 m
1134 w	1102 w
1024 vw	1022 w
1006 s	1003 m
	883 vw
	876 s
	861 *
827 s	
793 m	788 m
715 w	713 vw

Methoxypyridine Hydrochlorides.

2-Methoxy-pyridine		3-Methoxy-pyridine		4-Methoxy-pyridine	
3040 m		3055 m		3070 m	
3100 m					
2510 vs		2660 vs		2635 vs	
2000 m		2040 m		2025 w	
1926 m		1939 w		1931 m	
1867 m		1896 w			
1784 w		1836 w		1833 w	
1720 w		1729 w		1752 m	
	Raman		Raman		Raman
1631 s	1630 2	1620)m	1628 4	1635 vs	1640 8
1613 vs		1612		1600 m	
1540 s	1545 0	1552 vs	1561 1 1542 0		
1520 *			1508 2	1529 vw	1536 1
				1512 vs	
1462 m	1461 2	1461)ms	1464 1	1459 w	1466 2
1426 *		1444)		1433 m	1442 2
1384 m				1398 m	1403 3
		1356 vs	1362 2	1362 vw	
1321 s	1326 8	1323 m	1324 *	1322 vs	1318 3
1297 vs	1295 4	1279 vs	1282 3	1304 s	
1249)vw					
1235)m	1240 2	1246 *		1259 w	1265 3
	1186 1	1191 vw	1185 2	1192 m	1200 3
1175 m					
	1167 1	1167 vw			
		1148 vw	1147 1		
1102 m	1105 1	1109 m	1116 1	1099 w	1102 1
		1079 vw	1082 1		
1049 w	1046 6	1050 m	1051 10	1044 w	1049 s
1037 m		1023 m			
1012 m		1012 s	1006 6	1012 s	1014 4

Methoxypyridine Hydrochlorides.

2-Methoxy-pyridine	Raman	3-Methoxy-pyridine	Raman	4-Methoxy-pyridine	Raman
993)vw					
981)s	986 9	998 s	998 *	991 m	994 10
				974 *	
939 m					935 0
		874 m	897 1	856 w	
				826 vs	828 5
810 m	809 10	807)vs	800 7	803 w	803 9
		)			
799 w		796 s			
774 vs					
723 m		673 s			
6	621 3		620 2		642 4
	560 2		563 1		522 1
	465 5		445 2		449 4
			407 1		
	242 1		253 1		259 1

Methoxypyridine Mercurichlorides.

2-Methoxy-pyridine	3-Methoxy-pyridine	4-Methoxy-pyridine
		802 *
806 w	790 *	770 *
771 s	780 s	753 m
716 w		720 w
	666 s	

Methoxypyridine Mercurichlorides.

2-Methoxy-pyridine	3-Methoxy-pyridine	4-Methoxy-pyridine
3250 w	3250 m	3250 s
3090 vs	3090 s	3170) 3100)m
1630 *		1634 s
1617 s	1612 m	1594 m
1543 m	1548 vs	1515 vs
1522 *	1511 *	
1468) 1460)m	1473 m	1462 vw
1437 w	1441 *	1435 m
1376 m	1349 m	1385 w
1326 m	1326 *	1355 vw
1296 s 1275 *	1296 s	1317) 1300)s
1230 m 1182 *	1243 m	1245)* 1200)m
1166 m	1181 w	
1120 w 1100 m	1115 m	1096 m
	1067 vw	
1041 m	1048 m	
1024 s	1014 w	1015 s
989 m	1002 m	994 m
966 *	950 *	
884 m	860 w	
833 w	840 w	817 w

Hydroxypyridine Mercurichlorides.

2-Hydroxy-pyridine	3-Hydroxy-pyridine	4-Hydroxy-pyridine
3090 s	3250 vs	3200 vs
1628 vs	1622 m	1632 s
1591 w	1612 *	1606 m
1536 s		1538 w
1512 *	1550 vs	1511 vs
	1483 w	
1481 w	1462 *	
1390 *	1380 m	1369 m
1363 w	1324 w	
1311 s	1302 m	1316 m
1260 *		1268 *
1238 m	1253 s	1249 m
1220 m	1224 s	1223 w
1160 m	1175 w	1188 m
1090 m	1106 m	1084 m
1050 vw	1060 vw	
	1038 w	
1000 mw	1013 *	1004 mw
	983 vw	
	950 vw	
873 m		875 w
	856 *	
	835 m	846 m
809 ?		813 w
	799 *	786) m
768 vs	779 s	780)
714 m	664 s	

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