"HIGH RESOLUTION NUCLEAR MAGNETIC RESONANCE AND ULTRAVIOLET SPECTRA STUDIES OF SOME HETEROCYCLIC COMPOUNDS"

A THESIS

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SUMMARY

This thesis reports a quantitative assessment of the various factors that contribute to the proton chemical shifts in 2,2'-, 3,3'-, and 4,4'-bipyridyl and their mono- and di-cations. The effects of the neighbouring ring current, nitrogen anisotropy and the nitrogen lone-pair on the chemical shifts of the ring protons have been calculated as a function of the dihedral angle between the planes of the two rings.

On the basis of these calculations, the experimental data suggested a planar, trans conformation of 2,2'-bipyridyl in inert solvents, but large angles of twist for the 3,3'-, and 4,4'-bipyridyls. The interaction of the methyl groups in 3,3'-dimethyl-2,2'-bipyridyl was found to twist the molecule approximately 55°. The stereochemistry of these molecules was found to be only slightly solvent dependent. Hydrogen-donor solvents, including strong acids, caused only small increases in the dihedral angle. A study of the ultraviolet spectra of these compounds was also carried out and the results were found to be in agreement with the stereochemistry suggested by the n.m.r. data.

Further studies were made on the stereochemistry of bridged biquaternary salts of 2,2'-bipyridyl. The interplanar angles in compounds of varying bridge lengths were calculated from chemical shift data and the results compared with estimated dihedral angles in singly bridged biphenyls. Evidence for mobile and frozen conformations is also presented. Ultraviolet spectra studies of these salts provided further support for the values of the dihedral angles obtained from the n.m.r. study.

The solvent dependence of the n.m.r. spectra of the pyridine system in hydrogen-donor solvents has been investigated and the anomolous variation in solvent shifts among the different ring protons interpreted in terms of a relaxation of the nitrogen lone-pair effect. The importance of the nitrogen anisotropy and lone-pair effects were also studied in oxazoles, thiazoles, isoxazoles and isothiazoles. The magnitude of both of these terms was found to be much smaller than in pyridine; the reduction of the lone-pair dipole effect being attributed to the lower basicity of the nitrogen atoms in these systems. Solvation and protonation studies further suggested a correlation between the magnitude of the solvent shifts and the basicity of the nitrogen atom.

Finally, the proton shifts in the boron trihalide complexes of alkyl-substituted pyridines were studied and rationalised in terms of the effects operating in the corresponding cations. In acetone solution interesting solvation phenomena were detected which suggested the formation of moderately stable 'acetone complexes'. Evidence regarding the conformation of 2-ethyl and 2-benzylpyridine complexes was also obtained from the n.m.r. spectra. Chemical shift data of these complexes showed no correlation with the relative acceptor strengths of the different boron halides, but a correlation of ^{11}B-H coupling constants with the strength of the donor-acceptor bond is presented.

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STATEMENT

The work described in this thesis incorporates no material previously submitted for a degree in any University, and to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference is made in the text.

Christian I. Tanzer.

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INTRODUCTION

High resolution nuclear magnetic resonance (n.m.r.) spectroscopy provides two basic parameters as probes of molecular structure, the chemical shift and the spin-spin coupling constant. Both of these quantities have been treated from quantum mechanical considerations in order to obtain usable expressions in terms of atomic electron orbitals. The chemical shift parameter is directly related to the magnetic screening constant σ.[1] This arises from secondary magnetic fields experienced by a nucleus under the influence of an external magnetic field which induces inter- and intra-atomic electron currents, thus:

$$H^A = Ho\ (1-\sigma^A)$$

where H^A is the total field at nucleus A, H_o the applied external field and σ^A the magnetic screening constant. The Lamb formula[2] describes diamagnetic contributions to the screening constant arising from spherical electron distributions whereas the calculations of Ramsay[3] include paramagnetic terms arising from non-spherical electron clouds, but neither are really usable expressions. Saika and Slichter[4] developed a theory of chemical shifts in terms of an atomic breakdown of diamagnetic currents. Pople[5] later obtained similar results, and expressed the screening constant σ^A, for an atom A as:

$$\sigma^A = \sigma_d^{AA} - \sigma_p^{AA} - \sum_{B(\neq A)} \sigma^{AB} - \sigma^A_{ring}$$

σ_d^{AA} represents the local diamagnetic currents, which turns out to be similar to the Lamb formula. σ_p^{AA} is the local paramagnetic term for which Pople[6] has derived an expression in terms of the paramagnetic susceptibility of atom A in the molecule for first-row elements. $\sum_{b(\neq a)} \sigma^{AB}$ refers to shielding effects from inter-atomic electron currents. If a dipole approximation is adopted, σ^{AB} depends on the magnetic anisotropy of neighbouring atoms or bonds:[7]

$$\sigma_{AB} = \frac{1}{3\,\overrightarrow{R_{AB}}\,N} \sum_{i=1,2,3} \chi_B^i (1 - 3\cos^2 \gamma_i)$$

Here $\overrightarrow{R_{AB}}$ is the vector joining A and B and χ_B the molar magnetic susceptibility of atom B in the molecule which has three principal components ($i=1,2,3$). γ is the angle between the direction of χ_B and $\overrightarrow{R_{AB}}$ and N is Avogrado's number.

The ring current term σ^A_{ring} was added to describe inter-atomic ring currents in aromatic compounds. Various approaches have been made on the basis of the ability of a cyclic π-electron system to sustain a superconducting ring current. The more common methods either equate the effect of the current with a magnetic dipole at the centre of the ring[8] or divide the π-electron current into two loops, above and below the plane of the ring.[9,10] Musher[11] on the other hand disclaims any deshielding of ring protons due to ring currents and showed that the magnetic susceptibility due to a ring current exactly equals the sum of the susceptibilities of electrons localised in segments of the ring. His calculations however involve the empirically estimated Pascal constants for aromatic carbon atoms which would tend to make his argument circular since any effects due to ring currents are naturally included in these constants. Dailey and co-workers[12] have calculated the chemical shifts for a number of polycyclic aromatic hydrocarbons and heterocyclic compounds using the Johnson and Bovey ring current approximation[10] and found that the predicted chemical shifts for ring protons were invariably too small, while the predicted figure for the diamagnetic anisotropy of benzene gave chemical shifts approximately 60% greater than those observed. It was suggested that the experimental anisotropy be reduced by a factor of 0.6 to accommodate these difficulties.[13] Recent calculations by Pople[13] have shown that almost 30% of the diamagnetic anisotropy in aromatic systems can be ascribed to local paramagnetic terms on the carbon atoms due only to their sp^2 hybridisation.

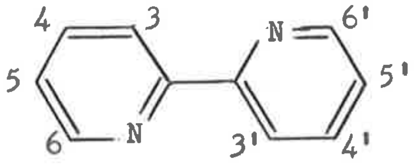
In aromatic molecules it has been accepted for some time that the proton resonance shifts of the ring protons tend to reflect the π-electron density on the carbon atom to which the proton is bonded.[14-21] Thus in substituted benzenes, a strong electron-withdrawing substituent decreases the shielding of ring protons, whereas electron-releasing groups cause increased shielding.[22] Simple linear correlations were adopted to relate the chemical shift σ, with the local 'excess' electron charge Δp (located on the carbon atoms), thus:[14,23]

$$\sigma = k\Delta p$$

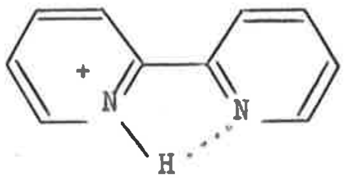
The empirically determined constant k, was found to have the value of 8-10 parts per million (p.p.m.) per electron.[15,14,24] A further study into the quantitative nature of this empirical linear correlation was made by

Schaeffer and Schneider,[16] who pointed out the failure of this equation in the pyridine molecule. Baldeschwieler and Randall[25] had earlier demonstrated that the nitrogen atom in pyridine gives rise to a magnetic anisotropy which strongly contributes to the screening constant of the nitrogen atom and ring protons. They suggested that this large paramagnetic contribution to the magnetic susceptibility was due to the low-lying $n \rightarrow \pi^*$ transition.[26] This point was later further considered by Gil and Murrell[27] who made a semi-quantitative estimate of the importance of this effect and further calculated the effect on the proton chemical shift due to the change in the electric field which arises when a C-H group is replaced by a nitrogen lone-electron pair. Gawer and Dailey[28] later published similar calculations except that in their method they failed to calculate the magnitude of the nitrogen anisotropy term as a difference between the magnetic susceptibility tensors of the carbon and nitrogen atoms, i.e. the effect on the chemical shifts on replacing a ring carbon by a nitrogen atom.

Because of the unique detail n.m.r. spectra can provide in the determination of molecular structure, this technique has been widely used in the elucidation of stereochemical problems. In particular, extended conjugated systems constrained to non-planar conformations by steric factors have attracted attention. Here both ^{13}C and proton resonance spectroscopy have been used to investigate such steric inhibition of conjugation. ^{13}C chemical shifts have been used in compounds containing a carbonyl group,[29] and proton shifts have been correlated with interplanar angles in benzoylthiophenes,[30] biphenyls,[31] 1-phenylcyclohexenes,[32] _o_-nitroanilines,[33] 3-phenylpyridazine,[34] tetraphenylnaphthalene,[35] formanilides,[36] stilbenes,[37] azabiphenyls[38] and 1-phenylpyrroles.[39] In the first section of this work, the theory of Gil and Murrell has been used to obtain information regarding the stereochemistry of various bipyridyls. Of particular interest was the 2,2'-bipyridyl molecule (I) and some of its dimethyl derivatives.

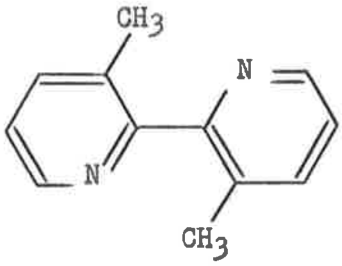


(I)



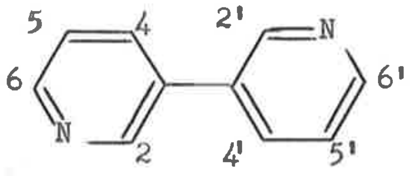
(II)

(I) is known to prefer a near planar configuration with the nitrogen atoms trans to each other.[40-43] The mono-protonated cation (II) on the other hand is claimed to exist predominantly in the cis form,[44] which is thought to be due to hydrogen-bonding as shown above. A full analysis of the variation of the chemical shift of the 3,3'-protons relative to the 5,5'-protons due to the nitrogen effects and ring current of the adjacent ring, as a function of the dihedral angle between the two rings is presented in this work. These results were then compared with the observed chemical shifts in various solvents and approximate values of the dihedral angle thus obtained. Calculations were also performed on the mono- and di-protonated bases and their stereochemistry estimated. These calculations were repeated for the methyl protons in 3,3'-dimethyl-2,2'-bipyridyl (III). The effect of the bulky methyl groups on the planarity of the system was thus determined.



(III)

Further comparisons were made by a study of the n.m.r. spectra of the two other bipyridyl isomers, namely 3,3'-bipyridyl (IV) and 4,4'-bipyridyl (V).



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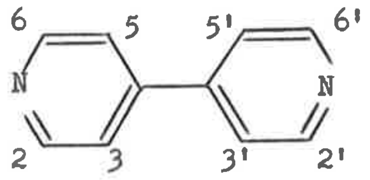


(V)

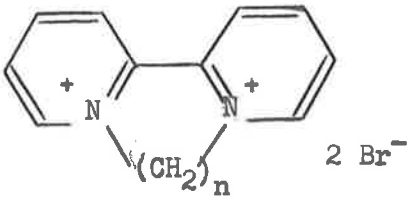
In these two compounds the effect of the nitrogen atom on the proton shifts in the adjacent ring can be neglected.

The n.m.r. spectra of 2,2'-bipyridyl and other azabiphenyls have recently been reported by several workers,[38,45-48] and a quantitative calculation of the various effects responsible for the low-field shift of the 3,3'-protons has been attempted. These reports appeared during the completion of this work but differ significantly from the calculations presented here. A general comparison between these approaches will be made in the discussion. In the calculations of the protonated bipyridyl systems, both the nitrogen anisotropy and lone-pair dipole terms are removed, but the effect of the positive charge in the neighbouring ring must be calculated instead. Both Buckingham[49] and Musher[50] have obtained semi-empirical expressions which relate the electric field E, associated with a positive charge, with a change in the screening constant:

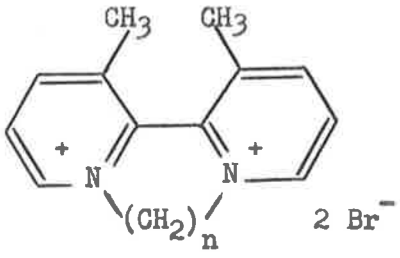
$$\sigma = -A E_z - B E^2$$

In Buckingham's formula, $A = 2 \times 10^{-12}$ and $B = 10^{-18}$ and in Musher's, $A = 2.9 \times 10^{-12}$ and $B = 7.38 \times 10^{-19}$. In this work Musher's expression has been used to calculate the effect of the positive charge in one ring, on the 3 and 5 protons in the adjacent ring. A correlation of these calculations with the observed chemical shifts in the cations thus enabled the stereochemistry of these compounds to be determined.

These calculations proved also useful in the elucidation of the stereochemistry of some bridged biquaternary salts of 2,2'-bipyridyl (VI) and those of the dimethyl derivatives, in particular the 3,3'-dimethyl isomer (VII)



(VI)



(VII)

Systems with bridge lengths from two to four carbons have been studied. These salts were first prepared by Homer and Tomlinson[51] who later investigated the stereochemistry of these compounds from an examination of their ultraviolet spectra and reduction potentials.[52] The bridged bipyridyls are more suitable for n.m.r. analysis than the analogous bridged biphenyl compounds. The presence of the electronegative nitrogen atom in the aromatic ring produces relatively large chemical shift differences between the ring protons so that the spectra can be satisfactorily analysed.

Some attention has also been given in this work to the ultraviolet spectra of the various bipyridyl compounds mentioned, with particular reference to the stereochemical problems involved. In a conjugated system of type R-S, changes in steric conformations about the single bond joining R and S are claimed to give rise to changes in the wavelength of the absorption, its intensity or both.[53] Suzuki has formulated an empirical approach from the ultraviolet spectra data to estimate the degree of non-planarity in such systems,[54] but in general the main difficulties in a quantitative evaluation lie in the lack of detailed knowledge about the origin and precise location of the various absorption bands that make up the total spectral pattern observed. For this reason an attempt has been made to resolve the long-wavelength band system into separate components by the method of Jaffe.[55] Wavelength and intensity changes were then discussed in terms of the stereochemical features and compared with the results obtained from the n.m.r. spectra.

The n.m.r. studies on heterocyclic compounds were further pursued along two lines. Firstly, in chapter III, a brief qualitative analysis is made of the chemical shifts of protons in some 5-membered heteroaromatic compounds containing a pyridine-type nitrogen. Oxazoles, thiazoles, isoxazoles and isothiazoles were studied. (Fig. 1).

oxazole thiazole isoxazole isothiazole

Fig. 1

There is already considerable n.m.r. data available in the literature on these compounds, but no serious interpretation of the chemical shifts has yet been attempted. As is the case with pyridine, π-electron densities alone do not account for the observed chemical shift differences between the ring protons. This is also the case with furan and thiophen which bear an obvious relation to the compounds studied here. In this work, the accent has been placed on the effect of the nitrogen atom on the chemical shifts of the ring protons. The Gil and Murrell concepts have again been invoked and the apparent observed deviations explained qualitatively. Solvent shifts in the n.m.r. spectra of nitrogen heterocyclic compounds have been investigated, and the shifts in hydrogen-donor solvents explained. A series of phenyl substituted thiazoles, isothiazoles and isoxazoles were also studied during the course of this work. The n.m.r. data of these compounds provided valuable information as to the degree of co-planarity of the two rings, and a survey of these results including the conclusions reached earlier from the bipyridyls systems suggested an important factor in the general problem of co-planarity in bi-aryl systems.

In the final chapter, the study of protonation effects in nitrogen-heteroaromatic systems was extended by an examination of the n.m.r. spectra of some Lewis acid complexes. The boron trihalides are powerful Lewis acids and are known to form stable addition compounds with nitrogen bases.[56] A number of such complexes with alkyl-substituted pyridines, thiazole and isothiazoles were prepared and studied. Numerous n.m.r. studies have been reported for complexes of boron halides with organic bases, but invariably they have been concerned with establishing some correlation between chemical shift data and the order of accepting power in the boron halide series. This order is known from heats of formation studies and is generally accepted as being:[57-60]

$$BBr_3 > BCl_3 > BF_3$$

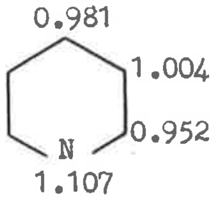
It was the purpose of this study to compare protonation effects with those found in these complexes, and to determine whether n.m.r. data provided any guide as to the relative ability of the different boron trihalides to form such compounds.

CHAPTER I

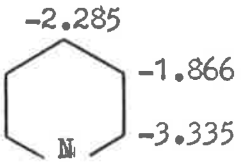
The n.m.r. spectra and stereochemistry of bipyridyls.

1.1 The interpretation of the n.m.r. spectra of pyridine and the pyridinium cation.

Gil and Murrell in 1964 described for the first time in detail the various factors underlying the anomalous chemical shifts in the pyridine molecule.[27] It had earlier been realised that the chemical shifts of the ring protons in pyridine cannot be directly correlated with π-electron densities on the ring carbon atoms.[16] This is evident from the π-electron densities obtained by Brown and Heffernan[61] from a self-consistent field calculation (I); and the observed chemical shifts in CCl_4 solution (II):[18]



(I)



p.p.m. from internal

CH_2CCl_2

(II)

In order to account for this discrepancy, Gil and Murrell considered two other factors to influence the chemical shifts in the pyridine molecule. The first is the large paramagnetic contribution to the magnetic susceptibility due to the low-lying $n \rightarrow \pi^*$ transition.[25] This is known to give rise to an absorption band at 4.5 eV.[26] The second is the effect of the electric field associated with the nitrogen lone-electron pair.

The effect of the paramagnetic contribution to the magnetic susceptibility was determined by first calculating the molar magnetic susceptibility components of both the nitrogen atom in pyridine and aromatic carbon atoms in benzene. Using Pople's equation,[6] the following results were obtained (in p.p.m.):

Pyridine: $(\chi_N^P)_{xx} = 10.85$ Benzene: $(\chi_C^P)_{xx} = 7.89$

$(\chi_N^P)_{yy} = 10.76$ $(\chi_C^P)_{yy} = 10.76$

$(\chi_N^P)_{zz} = 6.46$ $(\chi_C^P)_{zz} = 6.46$

The effect on the proton shifts was then calculated by using these values in the general McConnell's equation:[7]

$$\sigma_{AB} = \frac{1}{3\,\overrightarrow{R_{AB}}\,N} \sum_{i=1,2,3} \chi_B^i (1 - 3\cos^2\gamma)$$

$\overrightarrow{R_{AB}}$ is the vector joining A and B; χ_B the molar magnetic susceptibility of atom B in the molecule (due to electrons around B) which has three principal components. γ is the angle between the direction of χ_B and $\overrightarrow{R_{AB}}$, and N is Avogrado's number. The following results (in p.p.m.) were found:

Pyridine: $\sigma_{H\alpha}{}^N = -0.25$ Benzene: $\sigma_{H\alpha}{}^C = 0.08$

$\sigma_{H\beta}{}^N = -0.06$ $\sigma_{H\beta}{}^C = -0.05$

$\sigma_{H\gamma}{}^N = -0.04$ $\sigma_{H\gamma}{}^C = -0.07$

Analogous calculations were performed on the pyridinium system. The magnetic susceptibility tensors were found to be (in p.p.m.):

$$(\chi^{p}_{N^+})_{xx} = 7.54 \; ; \; (\chi^{p}_{N^+})_{yy} = 9.69 \; ; \; (\chi^{p}_{N^+})_{zz} = 6.46$$

and the resultant effect on the proton shifts:

$$\sigma_{H\alpha}^{N^+} = 0.05 \; ; \; \sigma_{H\beta}^{N^+} = -0.04 \; ; \; \sigma_{H\gamma}^{N^+} = -0.05$$

These values show that the α-proton signal in pyridine is shifted to low-field 0.33 p.p.m. and the γ-proton to high-field 0.03 p.p.m. relative to benzene. Hence the α-proton is shifted 0.36 p.p.m. to low-field relative to the γ-proton and the results of the pyridinium ion show that this difference is practically removed on protonation.

The effect of the electric field due to the nitrogen lone-pair was calculated from Buckingham's[49] expression relating magnetic screening constants to electric fields:

$$\sigma^{E} = -A\,E_z - B\,E^2$$

where E_z is the component of the electric field along the C-H bond, and E the total electric field at the hydrogen nucleus. Values of $A = 2 \times 10^{-12}$ and $B = 10^{-18}$ were suggested by Buckingham, whereas Musher[50] obtained $A = 2.9 \times 10^{-12}$ and $B = 7.38 \times 10^{-19}$.

The electric field E is obtained from the expression:

$$E = \frac{u}{r^3}\left[3\cos\theta\ [\vec{DP}] - [\vec{u}]\right]$$

Where: u is the dipole moment (in Debyes)

r the distance of the nucleus from the dipole centre.

$[\vec{u}]$ the unit vector along the dipole.

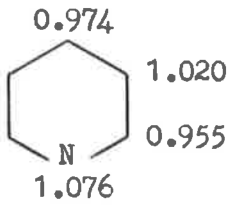
$[\vec{DP}]$ the unit vector along the line joining the dipole centre and the proton nucleus.

Using a value of 1.63 D for the dipole moment of the lone-pair and Musher's constants, the following shifts were found for the ring protons:

$$\sigma_{\alpha}^{E} = -0.42 \text{ p.p.m.} \; ; \; \sigma_{\beta}^{E} = -0.19 \text{ p.p.m.} \; ; \; \sigma_{\gamma}^{E} = -0.14 \text{ p.p.m.}$$

There appears to be an error in the original paper. The correct value of $\sigma_{\alpha}^{E} = -0.42$ and not -0.52 as stated.

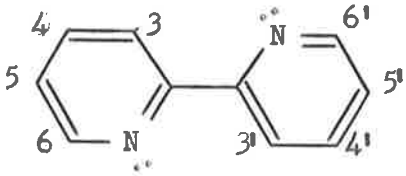
Correlation of the chemical shifts with π-electron densities after allowing for these two effects then give the following π-electron distribution:



which is in good agreement with the theoretical values obtained by Brown and Heffernan quoted earlier.

1.2 Calculations of shielding parameters in the 2,2'-bipyridyl system.

In order to determine the stereochemistry of 2,2'-bipyridyl (III) from the observed chemical shifts, it is first necessary to calculate as a function of the dihedral angle (ψ), the effect that each pyridine ring exerts on the 3- and 5-protons in the adjacent ring.



(III)

These effects can be summarised as follows:

1. The ring current effect of the adjacent ring.
2. The magnetic anisotropy of the nitrogen atom in the adjacent ring.
3. The effect of the electric field from the nitrogen lone-pair in the adjacent ring.

Each of these terms, which are assumed to be additive, have been calculated as a function of the dihedral angle. Castellano, Gunther and Ebersole[45] published similar calculations during the completion of this work. Their method and conclusions however differ significantly from that presented in this thesis. In particular, these authors assumed that Van der Waal's dispersion forces[62-64] between the 3-proton and the lone-pair in the adjacent ring significantly deshield that proton. They estimated this effect to be as large as -.21 to -.29 p.p.m. In view of the results obtained here, this figure appeared too large and in order to test the validity of the use of a Van der Waal deshielding term, the Gil and Murrell calculations were performed for the methyl protons in 2- and 4-picoline. The result of these calculations are summarised in Table 1.1.

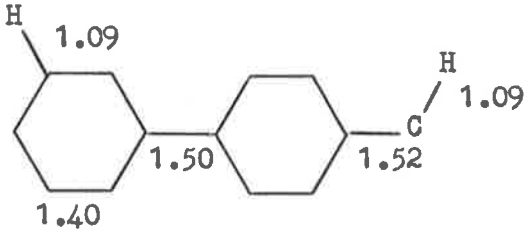
TABLE 1.1

Deshielding of the methyl protons in 2- and 4-picoline due to the nitrogen atom.

	2-picoline		4-picoline
N-anisotropy:	-0.200 p.p.m.	...	-0.000 p.p.m.
N-dipole terms:	-0.127 p.p.m.	...	-0.072 p.p.m.
Total effect:	-0.327 p.p.m.		-0.072 p.p.m.

These calculations show that the 2-methyl protons are deshielded -0.255 p.p.m. relative to the 4-methyl protons due to the effect of the nitrogen atom, whereas the observed difference was found to be -0.217 p.p.m. (CCl_4 solution). The close agreement between these two sets of results suggests that Van der Waal's dispersion forces between protons and lone-electron pairs do not appear to have a major effect on the chemical shift of those protons. Castellano's calculations are thus already open to serious criticism.

The following parameters are used in the calculations performed in this work. In the absence of experimental figures for the diamagnetic susceptibility of the pyridine ring this was assumed to be equal to that of benzene for which the experimental figure of 59.7×10^{-6} was used.[65] The values for the magnetic susceptibility tensors of the aromatic nitrogen and carbon atoms are those of Gil and Murrell listed earlier. For the electric field effect, Musher's coefficients were chosen and the value of the lone-pair dipole moment taken as 1.63 D placed 0.4A^{o} out from the nitrogen atom. (Gil's figures). In all calculations, the pyridine rings in bipyridyl were assumed to be regular hexagons with the following bond distances (in A^{o}) obtained from Sutton's table:[66]



The results of these calculations are graphically displayed as a function of the dihedral angle ψ in figure 1.1. More detailed tables of all calculations in this work are listed in the Appendix.

It is interesting to note that the nitrogen anisotropy effect (σ_N) produces a negligible contribution to the shielding at proton 3, whereas the dipole term is very significant for planar or near planar trans-conformations, falling to a negligible value above $\psi = 60^{o}$. The ring current function is obviously symmetrical about $\psi = 90^{o}$, and dominates the total deshielding experienced at proton 3.

Castellano and co-workers obtained the following values for the deshielding of proton 3 in a trans-planar conformation (in p.p.m.):

Fig. 1.1

Variation in the chemical shift of H-3 with dihedral angle in 2,2'-bipyridyl.

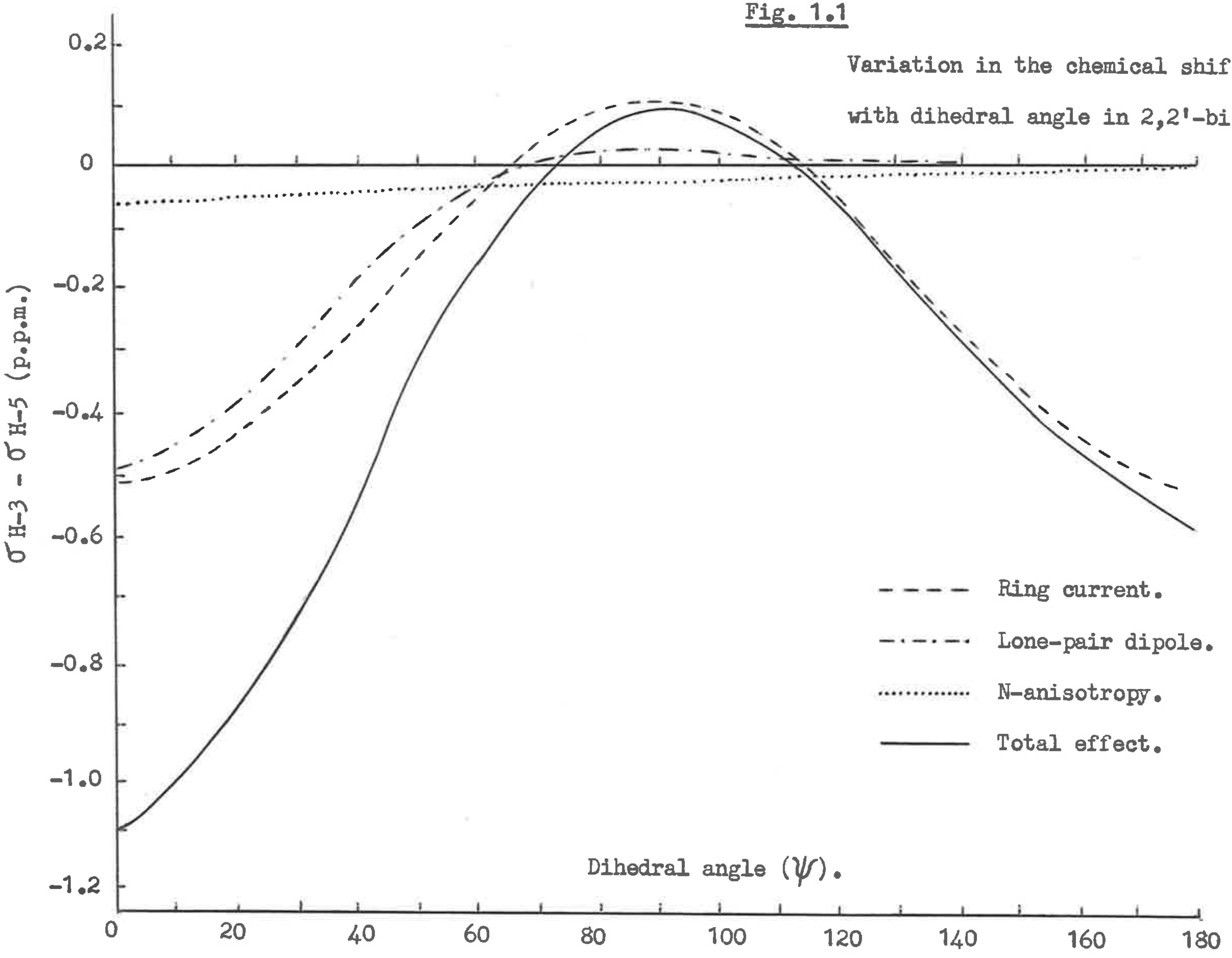
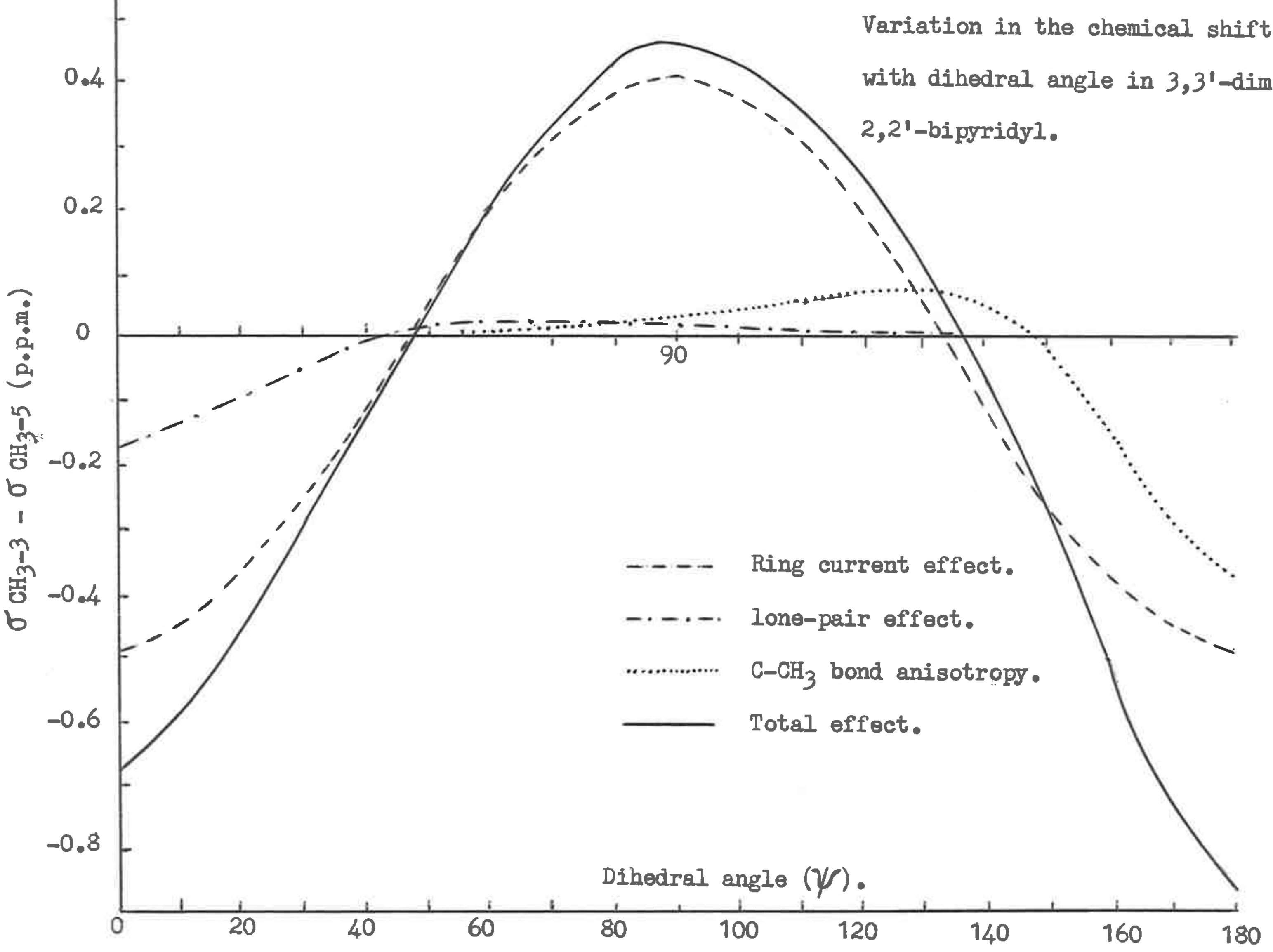


Fig. 1.2

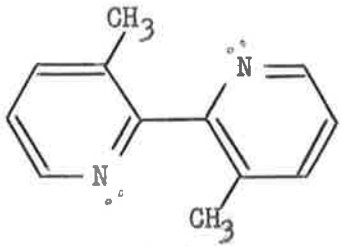
Variation in the chemical shift of CH_3-3 with dihedral angle in 3,3'-dimethyl-2,2'-bipyridyl.



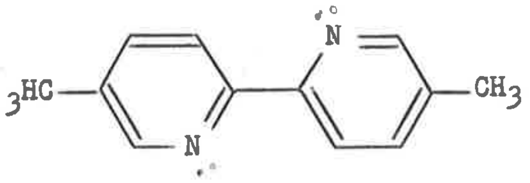
		B	M
Anisotropy of ring	σ_r	-0.49	-0.49
Anisotropy of N	σ_N	-0.16	-0.16
Dipole effect	σ_E	-0.25	-0.33
Van der Waal's forces	σ_w	-0.29	-0.21
Total deshielding	σ_T	-1.19	-1.19

The figures listed under B and M refer to the use of Buckingham's or Musher's coefficients in the calculation of the electric field term. Their smaller value of σ_r, is a consequence of the use of Johnson and Bovey's tables[10] for ring current effects, but the value for σ_N is certainly too large. This is due to the use of an average value of χ_N^p for the nitrogen atom, whereas a value of only 0.06 p.p.m. results if the calculations are performed using the three components of χ_N^p along the x, y, and z axis. In the calculation of the dipole term, Castellano placed the dipole on the nitrogen atom and used the dipole moment of the pyridine molecule, which as Gil pointed out, is erroneous since part of this is due to the polarisation of the π-electrons and part to the σ-electrons. This results in the much smaller value for σ_E obtained. If it is further considered that their Van der Waal's deshielding factor is invalid, then no reliance can be placed on their final conclusions.

The calculations were repeated for the methyl protons in both 3,3'-(IV) and 5,5'-dimethyl-2,2'-bipyridyl (V).



(IV)



(V)

Included in these calculations is an estimate of the effect of the C–CH$_3$ bond anisotropy as suggested by Garbisch.[32] The results are shown in Fig. 1.2. The N anisotropy term σ_N is not included since it was found to be negligible.

1.3 Application of experimental data with theory.

The stereochemistry of 2,2'-bipyridyls.

In order to avoid complications arising out of solvent interactions, only the results of spectra obtained in CCl$_4$ solution are considered at this stage. The n.m.r. parameters of 2,2'-bipyridyl and the dimethyl derivatives are given in Table 1.2. The spectra were satisfactorily analysed as either ABMX or ABX spin systems[67] and the results agree well with those obtained by other workers. The spectra of 2,2'-bipyridyl is shown in Fig. 1.3 and that of the 3,3'-dimethyl isomer in Fig. 1.4. The spectra of the methyl compounds are interesting because of large spin-spin coupling between ring and methyl protons (0.7–1.0 c/s). This is clearly illustrated in Fig. 1.4 at the 4-proton.

TABLE 1.2

Chemical shifts of 2,2'-bipyridyls in CCl_4

(in cycles/sec. from TMS at 60 Mc/sec.)

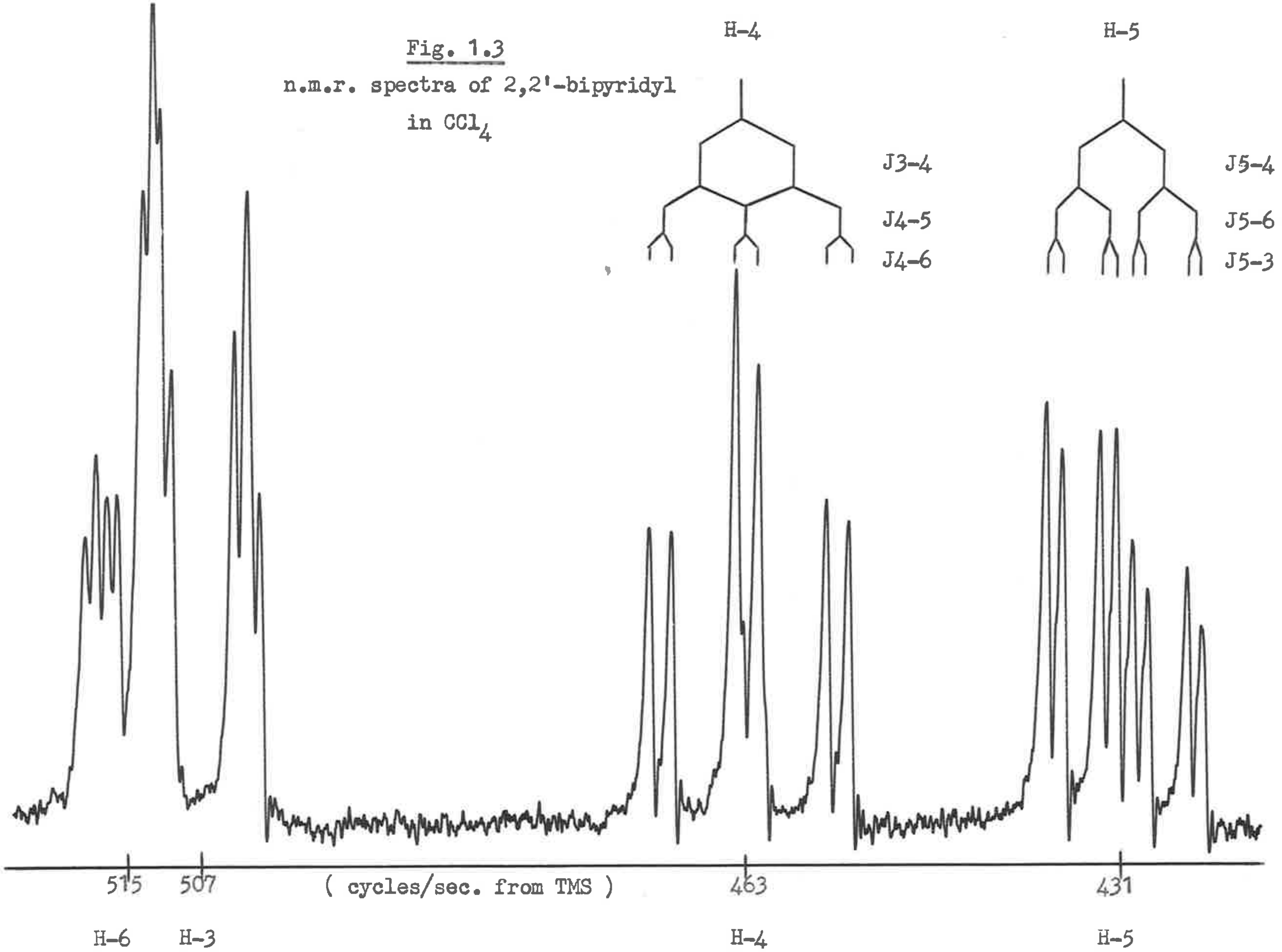
Bipyridyl	H-3	H-4	H-5	H-6	3.5
2,2'-bipyridyl:	507.2	463.1	430.5	514.7	76.7
3,3'-dimethyl- :	129.7	451.4	426.0	503.2	-
4,4'-dimethyl- :	497.1	145.6	420.3	504.7	76.8
5,5'-dimethyl- :	496.8	448.3	138.9	501.5	-

Coupling constants (in Cycles/sec.)

Bipyridyl:	J3-4	J4-5	J5-6	J3-5	J4-6	J3-6
2,2'-bipyridyl:	7.68	7.56	4.77	1.40	1.86	0.93
3,3'-dimethyl- :	-	7.60	5.00	-	2.00	-
4,4'-dimethyl- :	-	-	5.01	1.40	-	0.80
5,5'-dimethyl- :	8.20	-	-	-	2.40	0.70

Fig. 1.3

n.m.r. spectra of 2,2'-bipyridyl in CCl_4



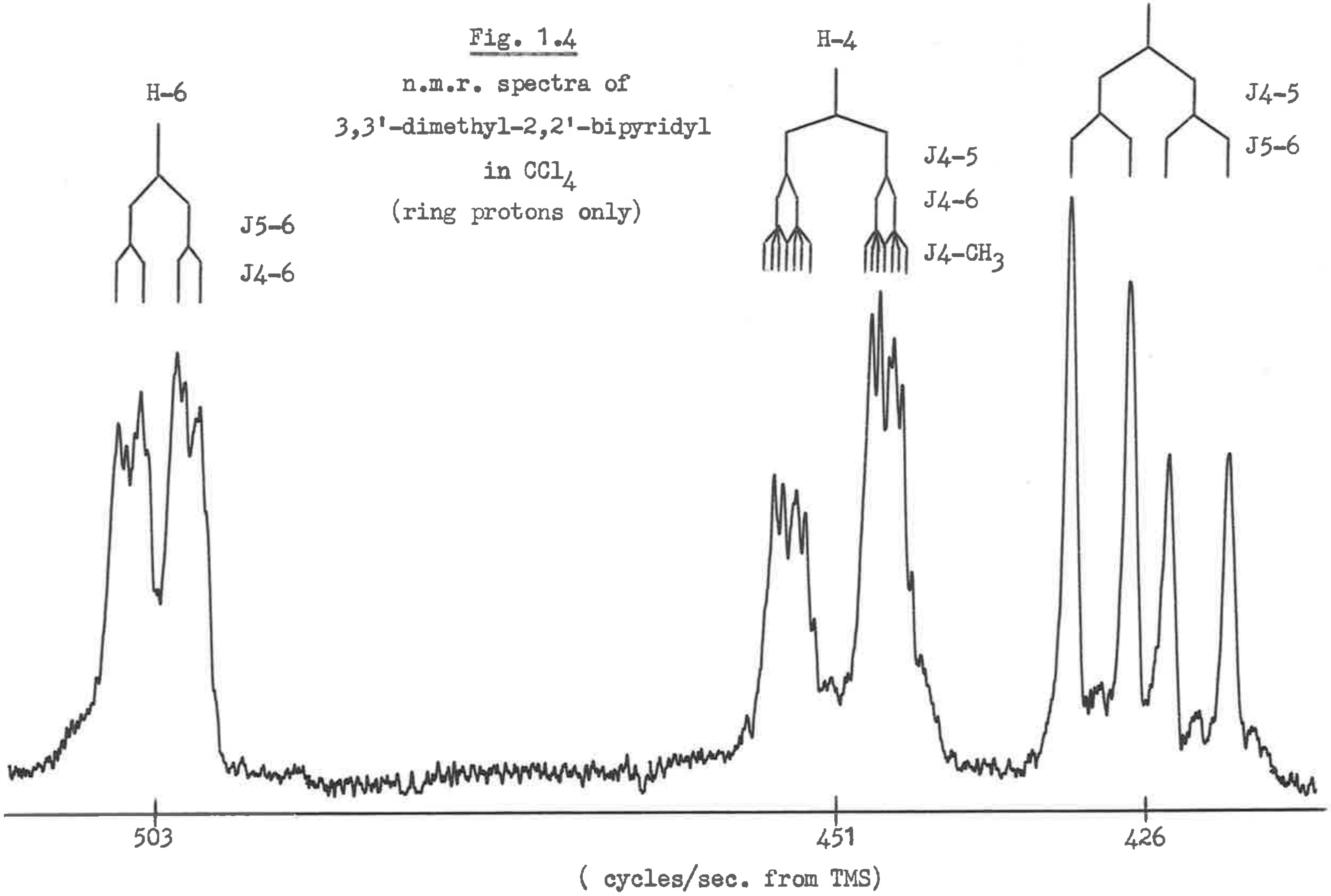


Fig. 1.4
n.m.r. spectra of
3,3'-dimethyl-2,2'-bipyridyl
in CCl_4
(ring protons only)

To obtain an estimate of the deshielding effect on proton 3 caused by the various factors outlined in the previous section, it is necessary to compare the chemical shift of this proton with that of the 5-proton, since the latter is also situated β-relative to the nitrogen atom, as well as being along the axis of rotation. Rotation about this axis should have little effect on the chemical shift of proton 5. In dilute CCl_4 solution P-3 lies 76.7 c/s or 1.278 p.p.m. to low-field of P-5, this value being beyond the maximum calculated (-1.058 p.p.m. at $\psi = 0^\circ$). It is realised however that the calculations involve considerable approximations not the least of which is the precise location of the lone-pair dipole. For instance, with the dipole located 0.6 A° out from the nitrogen atom instead of 0.4 A°, a value of 1.267 p.p.m. is obtained at $\psi = 0^\circ$. As it is felt that the ring current calculations, which involve experimental anisotropy data are probably fairly reliable, it would appear that the lone-pair dipole term has been underestimated by approximately 0.2 p.p.m.

What appears certain from these figures however is that 2,2'-bipyridyl prefers a trans, near planar conformation in an inert solvent, which is in agreement with observations made from other physical data.[40-43] It is interesting to note that biphenyl on the other hand is considered to be highly twisted or possibly freely rotating.[3e,g] It follows therefore that the nitrogen atoms exert significant forces that maintain a co-planar conformation, a point which is further considered in Chapter III.

The case of 3,3'-dimethyl-2,2'-bipyridyl is important because the steric interaction of the bulky methyl groups is expected to force the two rings out of plane. An intra-molecular comparison of chemical shifts is not possible in this system, but a reasonable estimate of the deshielding of the 3-methyl protons can be made by a comparison with the chemical shift of the methyl protons in the 5,5'-isomer. It is then found that the 3,3'-methyl protons are in fact shielded by 9.2 c/s (0.153 p.p.m.). Reference to the calculated curve (Figure 1.2) then yield two possible solutions, 65° cis or trans. This arises because of the symmetry of the curve near $\psi = 90^\circ$. The high degree of steric interference caused by the methyl groups is thus clearly illustrated and is in accordance with results obtained for o,o-bisubstituted biphenyls.[54,68] The results for the 4,4'- and 5,5'-dimethyl compounds are identical with that of 2,2'-bipyridyl itself as expected. Although it is realised that no great importance can be attached to the absolute values of the dihedral angles obtained, the general features of the stereochemistry of these systems are quite clear and in accordance with previous conclusions by other workers.

1.4. Solvent shifts in the n.m.r. spectra of heterocyclic compounds.

During the study of the n.m.r. spectra of the bipyridyls in different solvents, interesting solvent shifts were observed in strong hydrogen-donor solvents which prompted an examination of the general problem of such effects in nitrogen heterocyclic compounds. This was considered essential before the stereochemistry of the bipyridyls is determined in these media. To examine these effects the n.m.r. spectra of 2, 3, and 4-picoline were studied in a number of solvents. The results are shown in Table 1.3. All spectra were calibrated relative to internal tetramethylsilane (TMS) except those in D_2O solution which were measured relative to an internal dioxan reference. In a separate experiment the dioxane signal in water was found to have a τ-value of 6.17, and not 6.30 as suggested by Jones and co-workers.[69]

The chemical shifts in Table 1.3 show trends which are not satisfactorily explained by the reaction field theory of Buckingham,[49] especially those for the α-protons. According to this theory, chemical shifts in such polar molecules should be markedly dependent on the dielectric constants of the media which is not observed for the α-protons and only very irregularly for the other protons. In D_2O solution fairly large downfield shifts (approx. 16 c/s) are observed for the β- and γ-protons, whereas the α-protons are little affected (approx. -2 c/s). The internal separations between the α-protons and the β- and γ-protons (also listed in Table 1.3) are thus markedly reduced in water, and their absolute values very similar to those in methanol solution.

This phenomenon is reminiscent of the protonation shifts in these compounds also included in the above table. It appears therefore that the explanation of these solvent shifts may be found along the same lines as the theory outlined by Gil and Murrell to explain the protonation shifts. This will be discussed in detail in a later section of this chapter, but the basic factors may be summarised as follows:

1. The change in the N-magnetic anisotropy on protonation.
2. The removal of the deshielding due to the lone-pair dipole.
3. Effects due to the positive charge in the molecule.

TABLE 1.3

Chemical shifts of 2-, 3-, and 4-picolines

(in cycles/sec. from TMS.)

2-picoline	$CDCl_3$	Acetone	MeOH	D_2O	CF_3COOD
H-3	427.4	431.0	436.3	437.5	478.3
H-4	452.7	456.8	464.2	465.9	512.6
H-5	424.4	427.7	432.6	433.5	474.9
H-6	508.7	506.1	504.5	504.9	517.5
Δ 4,6	56.0	49.3	40.3	39.0	4.9
3-picoline					
H-2	506.9	504.5	502.0	500.2	517.9
H-4	447.7	452.6	459.8	459.2	512.0
H-5	429.6	432.3	437.1	439.0	482.2
H-6	504.4	502.3	499.6	500.2	517.9
Δ 4,6	56.7	49.7	39.8	41.0	5.9
Δ 5,6	74.8	70.0	62.5	61.2	35.7
4-picoline					
H-2,6	506.9	504.5	503.0	506.3	517.9
H-3,5	425.1	429.2	433.5	439.4	476.6
Δ 5,6	81.8	75.3	70.0	66.9	41.3

The effects of the first two factors are experienced most intensely at the α-protons, so that the overall downfield shift on protonation is quite small compared to the β- and γ-protons. It is here suggested that solvation of the nitrogen lone-pair by strong hydrogen donor solvents such as methanol and water, partly or wholly remove the dipole term due to this lone-pair and probably influence the N-anisotropy term as well. The normal downfield shifts are thus opposed by the upfield shifts arising from the removal of the dipole terms. These upfield shifts are greatest at the α-protons, which thus account for the small solvent shifts of this proton compared to the other ring protons. It is interesting to note that changes in the ultraviolet spectra of pyridine in water compared to inert solvents are also very similar to those produced on protonation,[70] and that the dipole moment of pyridine in water is considerably reduced.[71] This solvent shift theory was further studied and verified in a number of other nitrogen heterocyclic compounds discussed in chapter III. An interesting correlation of these shifts with the base strength of the nitrogen atom was found.

1.5 Solvent effects in the 2,2'-bipyridyl system.

The n.m.r. spectra of 2,2'-bipyridyl was further studied in a number of different solvents to determine whether the <u>trans</u>-coplanar conformation is retained in such polar solvents as methanol and water. The chemical shift data in a range of seven solvents is shown in Table 1.4. It is immediately obvious from these figures that proton 3 undergoes unusually large upfield shifts in both methanol and water. These were also

TABLE 1.4.

Chemical shifts of 2,2'-bipyridyl in different solvents (cycles/sec. from TMS).

Proton	CCl_4	$CDCl_3$	CH_2Cl_2	CH_3I	Acetone	CH_3OH	D_2O
H-3	507.2	504.4	505.4	505.0	509.5	497.7	479.3
H-4	463.1	467.9	468.0	468.6	474.5	475.0	475.5
H-5	430.5	436.9	437.3	437.0	443.7	444.9	448.0
H-6	514.7	520.5	518.5	517.5	520.2	518.4	515.3
Δ 5,6	84.2	83.6	81.2	80.5	76.5	73.5	73.0
Δ 3,5	76.7	67.5	68.1	68.0	65.8	52.8	31.3
Δ 4,6	51.6	52.6	50.5	48.9	45.7	43.4	39.8

observed by other workers[45,38] who attributed them to large increases in the angle of twist in these solvents. The spectrum in D_2O, in which bipyridyl is only sparingly soluble is shown in Fig. 1.5. If the shift differences between protons 3 and 5 are directly applied to fig. 1.1, then indeed large increases in ψ are evident, but this approach is invalid considering the solvent effects outlined in the previous section. There it was shown that the lone-pair deshielding term is practically removed in strong hydrogen-donor solvents, and proof that this effect also operates in bipyridyl is illustrated by the negligible shift of P-6 compared to P-5 in both methanol and water. The curve in Fig. 1.1 is therefore not valid for the system in methanol or water since the dipole term must be removed from the calculations. Such a curve is shown in Fig. 1.6, and applying the observed chemical shift difference between protons 3 and 5 (52.8 c/s in methanol and 31.3 c/s in water) to this curve it is found that this molecule still prefers a co-planar conformation in these solvents with only a slight twist (20°) in water. Because of the symmetry of the curve no firm conclusion can be reached whether a cis- or trans-conformation is preferred. To investigate this problem the spectra were recorded in various D_2O-acetone solvent mixtures. The results are shown graphically in Fig. 1.7 which also includes the results for an identical study of 4-picoline as a reference system. In no case line broadening was observed, which could be interpreted as a slow stereochemical inversion from cis to trans, but the shifts in fact show a gradual trend, with P-5 moving to low-field on increasing the water concentration and P-3 to high-field due to the gradual relaxation of the dipole-effect. It can be concluded therefore

Fig. 1.5

n.m.r. spectra of 2,2'-bipyridyl in D_2O

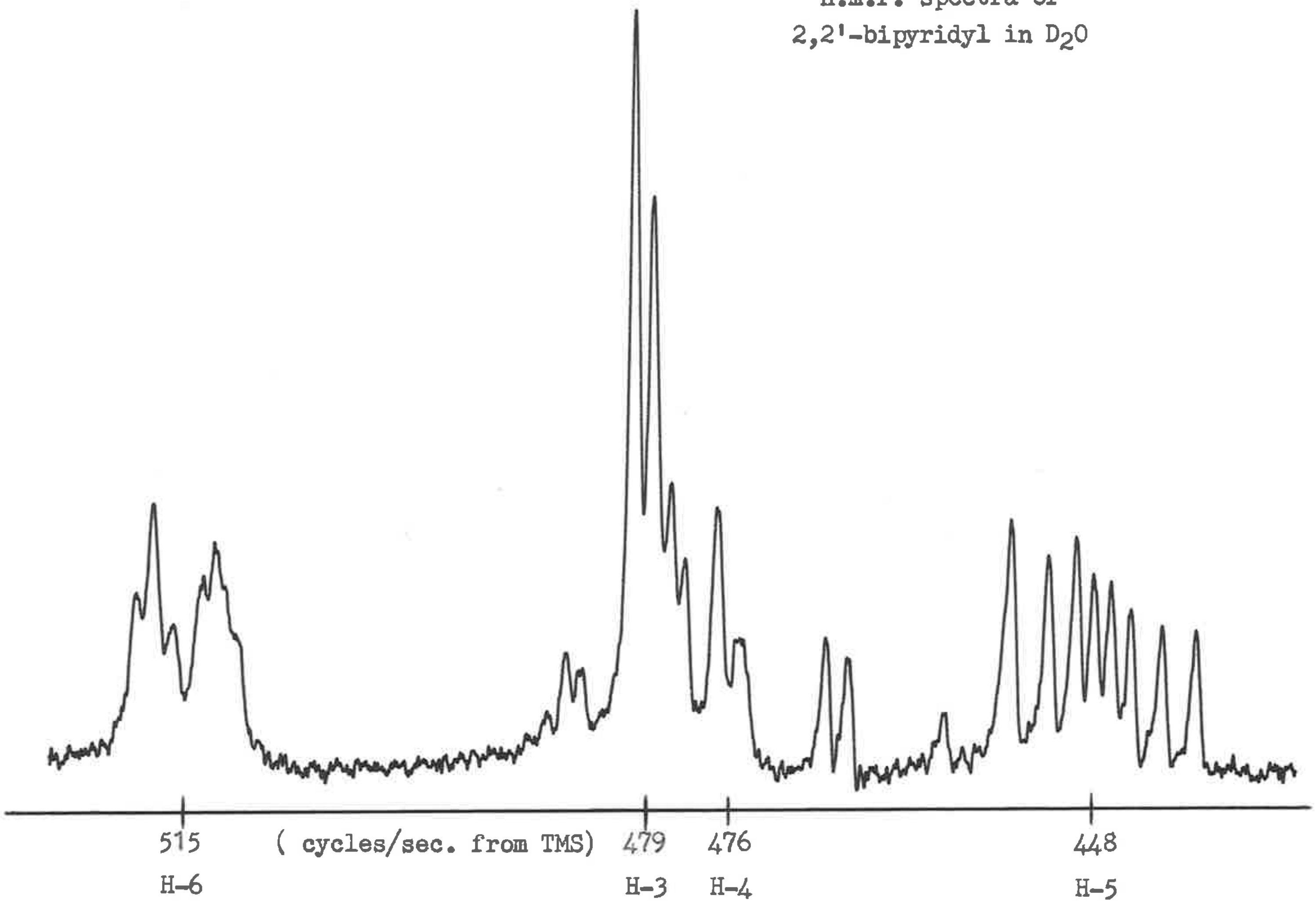


Fig. 1.6

Variation in the chemical shift of H-3 with dihedral angle in 2,2'-bipyridyl -: strong H-donor solvents.

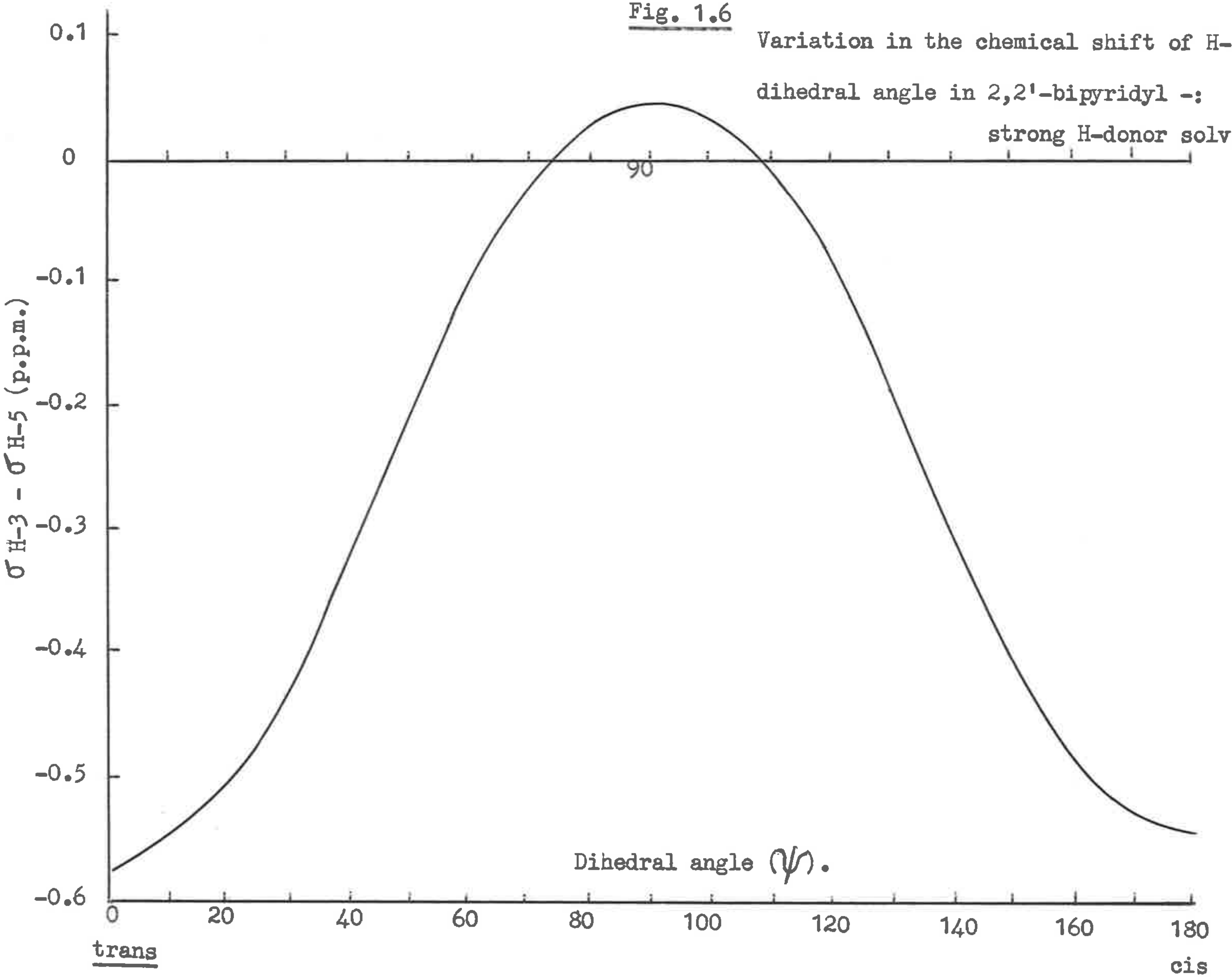
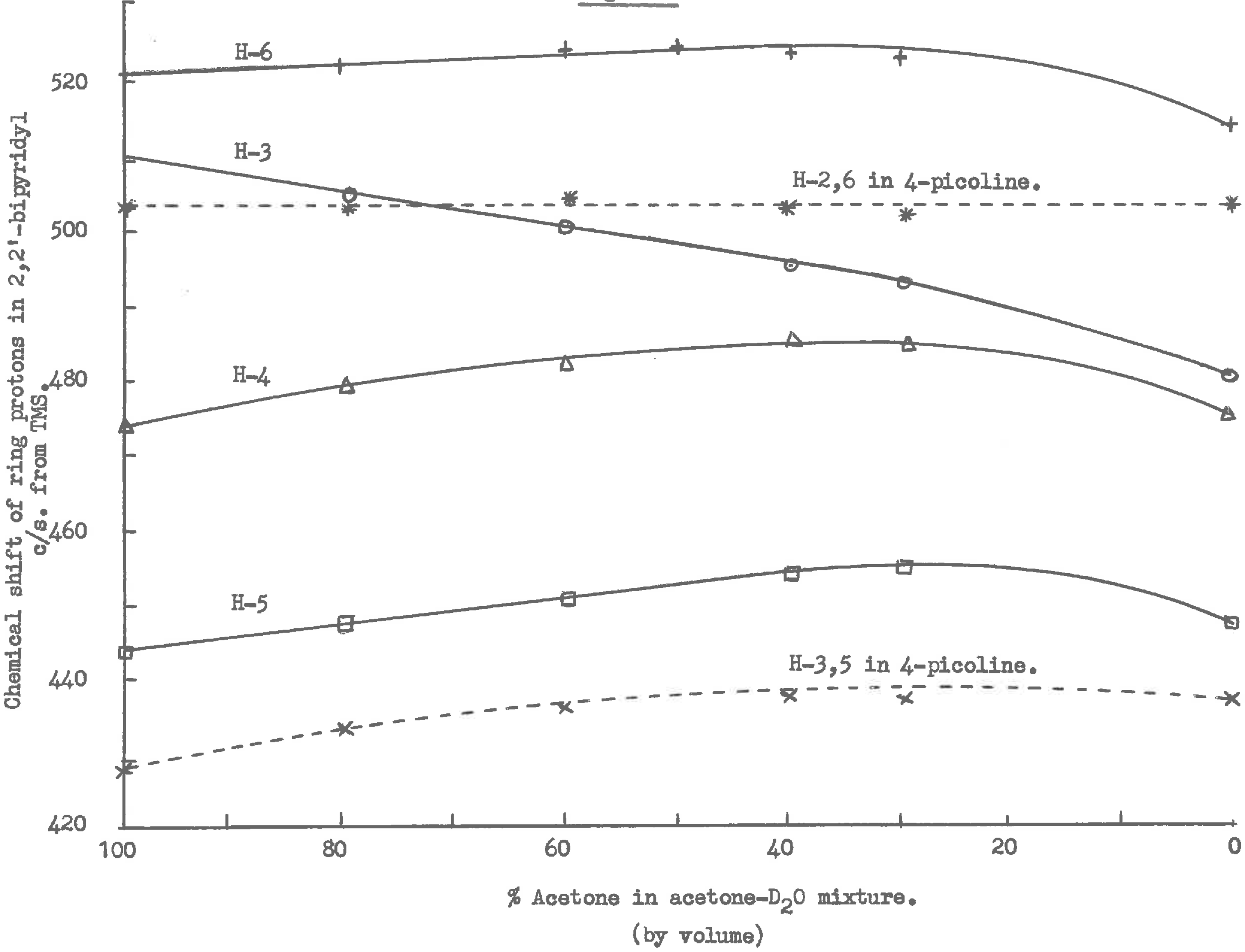


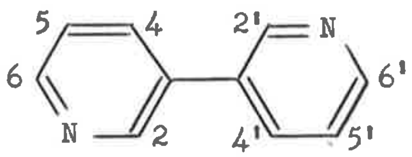
Fig. 1.7


H-6
H-3
H-2,6 in 4-picoline.
H-4
H-5
H-3,5 in 4-picoline.
520
500
480
460
440
420
100
80
60
40
20
0
Chemical shift of ring protons in 2,2'-bipyridyl c/s. from TMS.
% Acetone in acetone-D2O mixture.
(by volume)

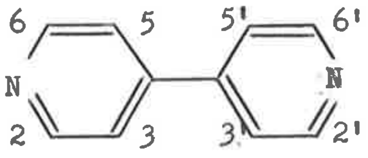
that the conformation of 2,2'-bipyridyl in water remains predominantly cis. These conclusions are at variance with those of Castellano, but additional evidence from ultraviolet spectra studies outlined in a later section suggest the results presented here to be correct. The chemical shifts in the other solvents used give no clear indication as to any change in stereochemistry. It would be unrealistic to relate the small changes observed with variations in the dihedral angle of the molecule.

1.6 N.m.r. spectra and stereochemistry of 3,3'- and 4,4'-bipyridyl.

It was considered useful to supplement the n.m.r. studies of the 2,2'-bipyridyl system with an analysis of the spectra of the other two isomeric compounds, namely 3,3'-bipyridyl (VI) and 4,4'-bipyridyl (VII).



(VI)



(VII)

In both these systems the effect of the nitrogen atom on the chemical shifts of protons in the other ring can be considered to be small, so that only ring current terms need to be considered in estimating the stereochemistry. The n.m.r. spectra of (VI) appeared as a well separated ABMX spin system (Fig. 1.8) and that of (VII) as a clear A_2X_2 case (Fig. 1.9.) The chemical shift of the ring protons in various solvents are shown in

Table 1.5. The most reliable information for an estimation of the dihedral angle in (VI) is the chemical shift difference between P-2 and P-6 since both are α-protons. In CCl_4 solution P-2 is found 12.7 c/s to low-field of P-6 and if this difference is wholly attributed to a ring current effect, an approximate value of 55° is obtained for the dihedral angle. It is thus apparent that considerably more rotational freedom exists in (VI) compared to the 2,2'-isomer. As will be shown later, this conclusion is further substantiated by a study of the ultraviolet spectra of these molecules.

In D_2O solution the resonance lines of P-2 and P-6 overlap which implies that P-2 is now little affected by the neighbouring ring current. This thus suggests a further easing of the rotational freedom in D_2O, which is further confirmed by the slight up-field shift of P-4 from its value in CCl_4 solution (rather than the down-field shift usually observed). The solvent shifts in the other solvents do not justify any serious consideration in terms of stereochemistry.

In (VII), there is no way in which intra-molecular shift differences can be used directly. It was considered best to compare the chemical shift of the 5- and 6-protons in (VII) with those in 2,2'-bipyridyl, since at least they are similarly located with respect to the nitrogen atom. In 2,2'-bipyridyl, the difference between the chemical shifts of P-6 and P-5 in CCl_4 solution is 72.6 c/s, whereas in (VII) this is 84.2 c/s. Approximately therefore, P-5 in (VII) is deshielded only 11.6 c/s by the neighbouring ring current. This value is close to that found in (VI) so that in this case too, considerable rotational freedom exists, a conclusion again backed

TABLE 1.5.

Chemical shifts of 3,3'-bipyridyl (cycles/sec. from TMS).

Proton	CCl_4	$CDCl_3$	Acetone	MeOH	D_2O
H-2	526.0	530.9	534.1	531.1	514.0
H-4	468.9	437.8	485.9	489.5	474.5
H-5	438.6	444.5	449.6	453.9	448.9
H-6	513.3	519.3	518.2	516.1	(513)
Δ 5,6	74.7	74.8	68.6	62.2	65.1
Δ 2,6	12.7	11.6	15.9	15.0	2.0
Δ 4,6	44.4	45.5	32.3	26.6	28.5

Chemical shifts of 4,4'-bipyridyl:

Proton	CCl_4	$CDCl_3$	Acetone	MeOH	D_2O
H-3,5	447.2	452.4	465.2	468.7	471.9
H-2,6	520.1	524.4	523.4	521.5	525.0
Δ 5,6	72.9	72.0	58.2	52.8	53.1

Fig. 1.8

n.m.r. spectra of 3,3'-bipyridyl in CCl_4

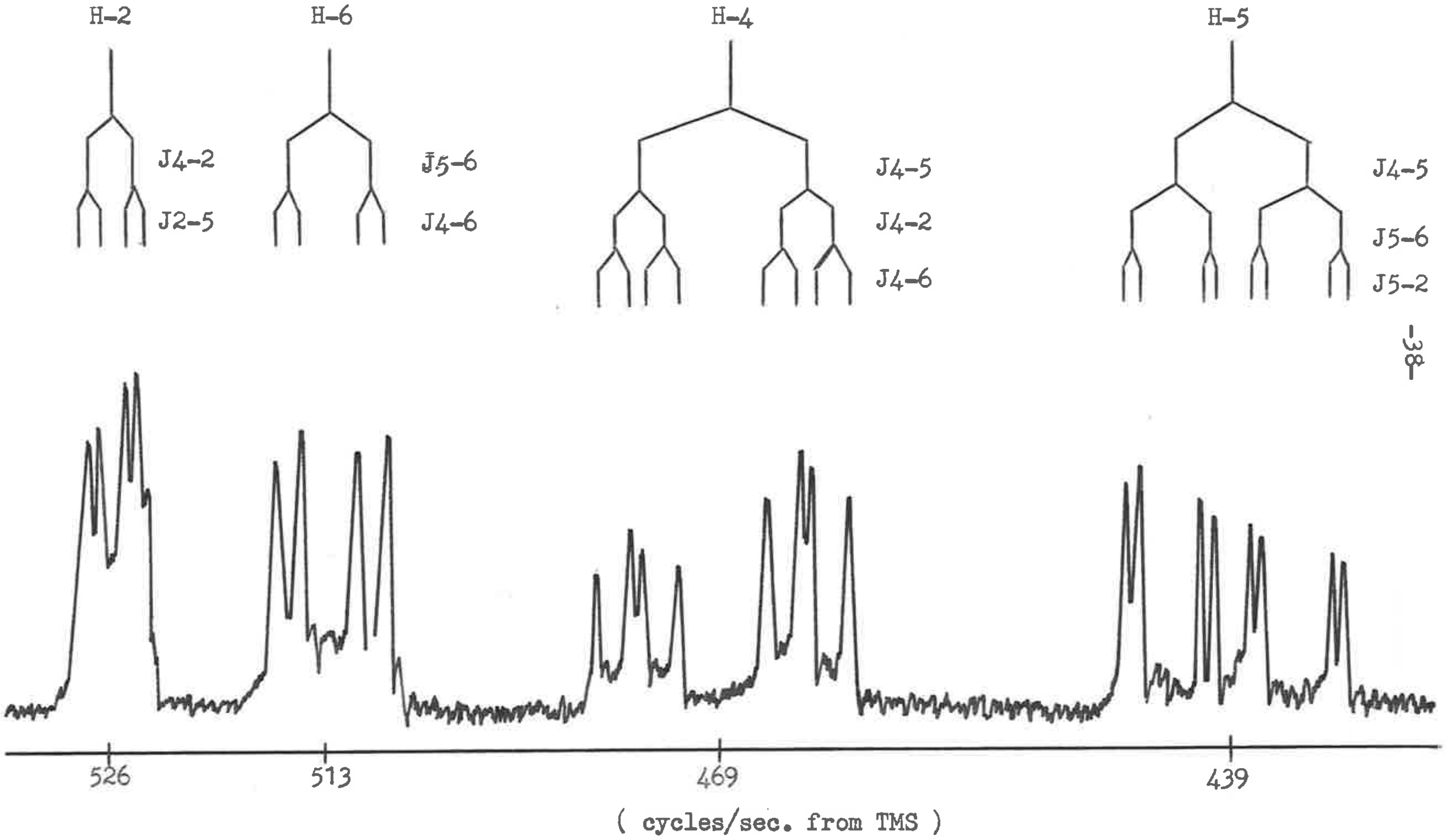
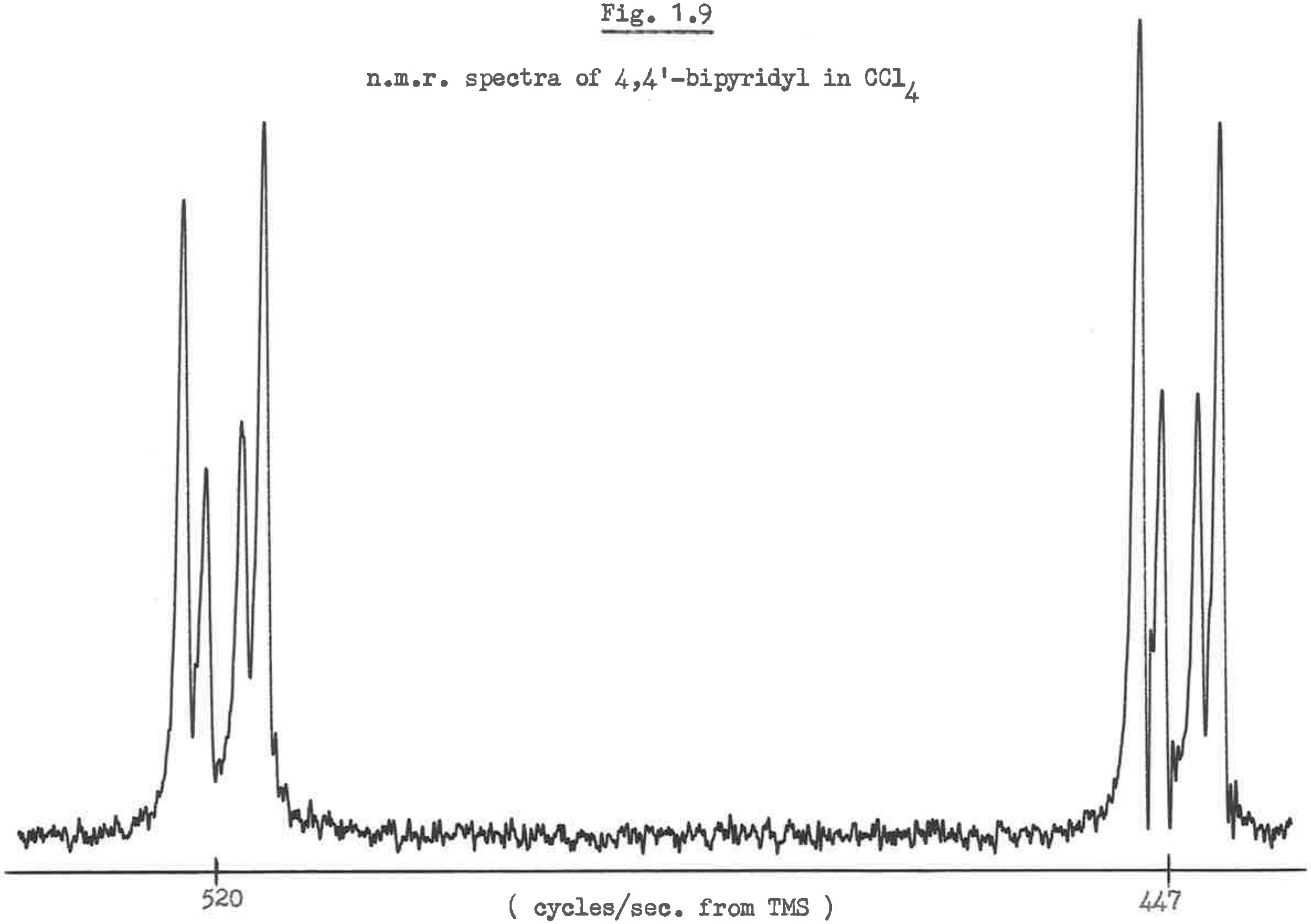


Fig. 1.9

n.m.r. spectra of 4,4'-bipyridyl in CCl_4



by ultraviolet spectra data. The solvent shifts in D_2O are very similar to those observed in 4-picoline, which suggests little change in the stereochemistry of this already highly twisted molecule.

In conclusion therefore, the n.m.r. studies indicate a planar conformation only in the case of 2,2'-bipyridyl. Both 3,3'- and 4,4'-bipyridyl are more analogous to the biphenyl system in that they possess considerable freedom of rotation. The effect of strong hydrogen-donor solvents such as water only marginally affect the dihedral angle, causing a small increase in each case.

1.7 Ultraviolet spectra studies of bipyridyls.

It was considered useful to supplement the n.m.r. studies of the bipyridyls with an investigation of their ultraviolet spectra. Ultraviolet spectroscopy has been extensively used in the past in the study of steric effects in conjugated systems.[72] Braude and Sondheimer first claimed that a reduction in ε_{max} with little or no hypsochromic shift of λ_{max} is associated with minor deviations from planarity; and if both hypsochromic and hypochromic shifts are observed then appreciable interference from co-planarity is assumed. In those cases in which ε_{max} is reduced without a concurrent hypsochromic shift (less than 5mμ), the following equation was derived:

$$\frac{\varepsilon^{\phi}}{\varepsilon^{\circ}} = \cos^2 \theta$$

ε° here refers to a planar reference compound. The oscillator strenghts of absorption lines in the spectra of some ortho-substituted dimethylanilines have been found to follow such a relationship. Suzuki[54] obtained an expression in terms of changes in λ_{max}, but his equation contains many empirical terms,most of which are difficult if not impossible to determine with any accuracy. Murrell* predicts the direction of the steric shifts from a consideration of the molecular orbitals that involve the bond being twisted. According to this theory,if the value of the resonance integral across the bond being twisted is reduced, than those orbitals which have a node across this bond will be decreased in energy,whereas those that have no nodes across this bond will increase in energy. The energy of an orbital will thus be decreased if the noded bonds are twisted,and increased if the non-noded bonds are twisted. The direction of the shift is thus predictable provided the absorption bands involved are clearly resolved and assignable to calculated transition frequencies .

Unfortunately it is very difficult to obtain reliable information from the complex spectra of the compounds studied here. The spectra are shown in Figs.1.10 to 1.12 . An attempt was made at resolving the broad complex long-wavelenght tail of the spectra. The resolutions were done using Jaffe's method[55],commencing from the long-wavelenght side assumed symmetric and unperturbed by other transitions. The resolutions are also shown on the diagrams,and the data is tabulated in tables 1.6 to 1.8.

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* J.N.Murrell, 'The theory of the electronic spectra of organic molecules',(John Wiley and Sons: New York) P.238

Fig.1.10

2,2'-bipyridyl (cyclohexane)

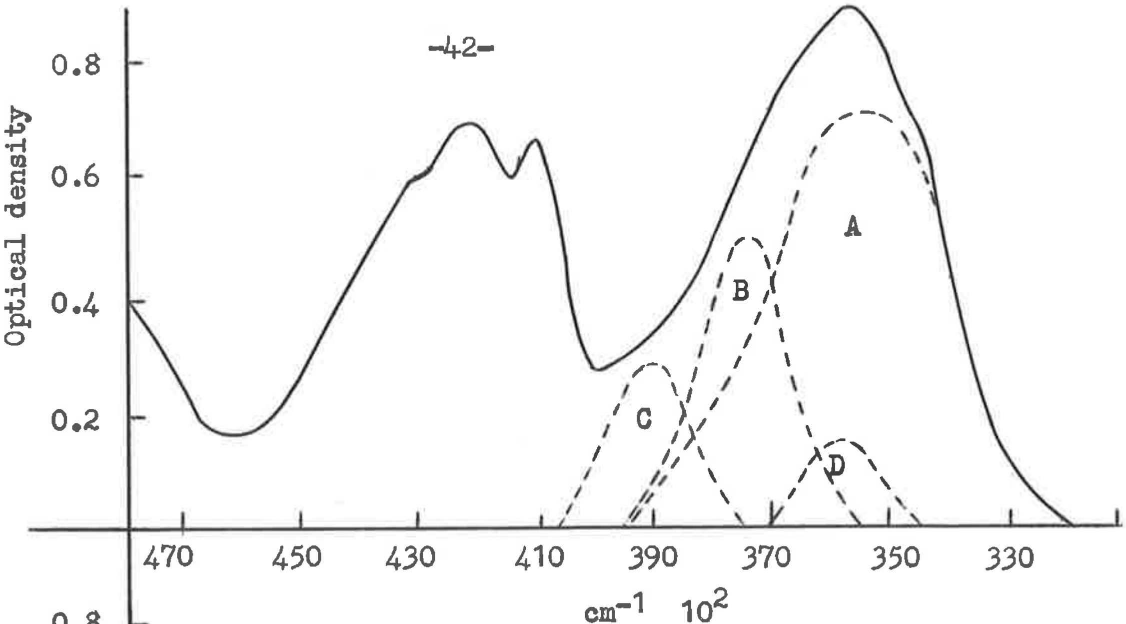


Fig.1.11

3,3'-bipyridyl (cyclohexane)

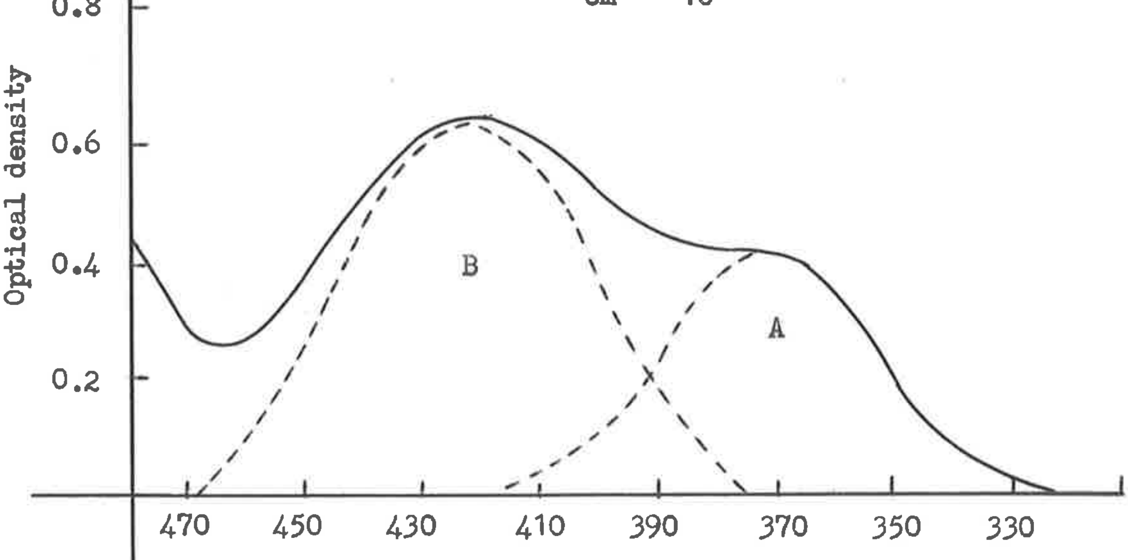
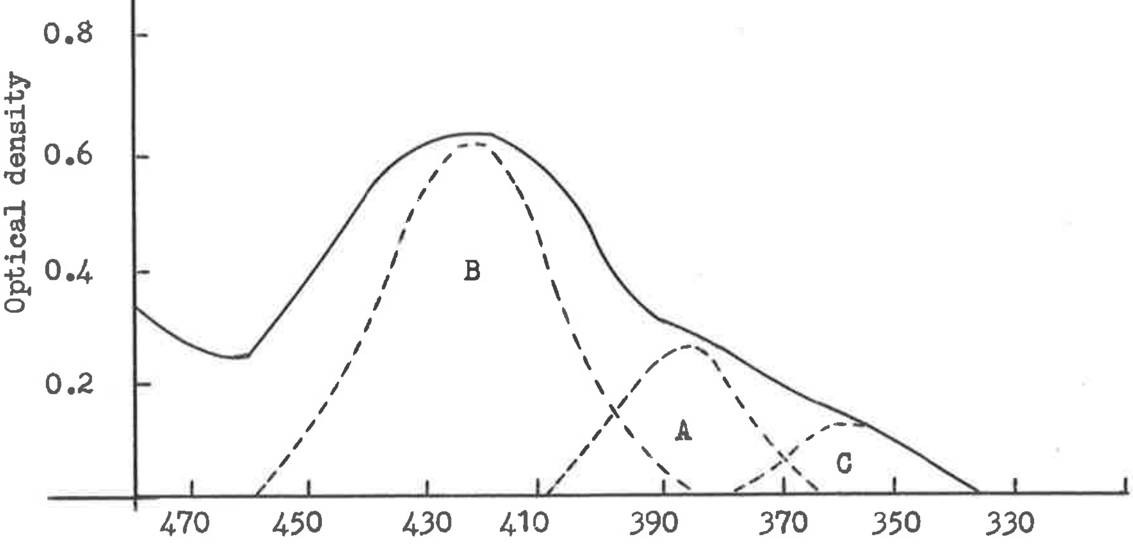


Fig.1.12

4,4'-bipyridyl (cyclohexane)



The oscillator strenght f was calculated from the expression:[78]

$$f = 4.315 \times 10^{-9} \int \varepsilon \, d\nu$$

where $\int \varepsilon \, d\nu$ is the integrated band area which for symmetrical curves approximates to $\varepsilon_{max} \Delta \nu$, $\Delta \nu$, being the width of the band at $\frac{1}{2} \varepsilon_{max}$.

In the process of resolving the bands it was assumed that the long-wavelenght tail is unperturbed by other transitions. This assumption has really little validity and the uncertainties involved in the process renders little significance to the results, except that it helps to locate some of the maxima in the spectra.

It is tempting to associate the long-wavelenght band-envelope with a $\pi \rightarrow \pi^*$ transition along the long-axis of the molecules, and then predict deviations from planarity in the case of 3,3'-and 4,4'-bipyridyl from the wavelenght of band A compared to that in 2,2'-bipyridyl. However, this approach must be rejected for the following reasons:

1) The long-wavelenght band is complex, and any accurate assignment to a particular band is thus extremely difficult and ambigous.

2) There is as yet no accurate information available on any particular assignment in the spectrum of the bipyridyls. i.e. positive identifications of observed lines with calculated transitions.

3) Comparisons of the three spectra is further complicated by the fact that the three compounds have in fact quite different symmetry properties. Thus this factor alone may account for some of the wavelenght and intensity shifts.

TABLE 1.6

Ultraviolet spectra analysis of 2,2'-bipyridyl

I Cyclohexane solution.

Band	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	f
A	283.3	12,700	0.238
B	267.4	8,560	0.074
C	257.9	5,300	0.053
D	280.0	2,800	0.033

II Methanol solution.

Band	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	f
A	283.1	12,900	0.218
B	266.9	9,000	0.096
C	254.8	5,500	0.056
D	280.0	3,360	0.043

III Water solution.

Band	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	f
A	285.4	9,100	0.157
B	266.5	5,800	0.077
C	250.7	5,000	0.064
D	281.7	2,000	0.017
E	305.5	3,000	0.041

TABLE 1.7

Ultraviolet spectra analysis of 3,3'-bipyridyl

I Cyclohexane solution.

Band	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	f
A	268.9	7,900	0.218
B	238.0	11,500	0.329

II Methanol solution.

Band	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	f
A	268.9	8,100	0.174
B	238.7	11,260	0.312

III Water solution.

Band	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	f
A	269.5	9,400	0.200
B	236.8	12,130	0.380

TABLE 1.8

Ultraviolet spectra analysis of 4,4'-bipyridyl

I Cyclohexane solution.

Band	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	f
A	259.9	5,700	0.118
B	236.9	13,560	0.334
C	280.7	2,500	0.040

II Methanol solution.

Band	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	f
A	264.9	6,130	0.159
B	238.4	14,080	0.351

III Water solution.

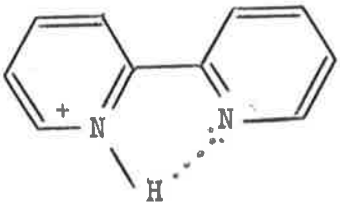
Band	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	f
A	261.6	9,310	0.257
B	238.9	11,800	0.277

Gondo[76] has calculated excitation energies and intensities associated with transitions from the ground state in 2,2'-bipyridyl, but his results for the absorption above 250mμ appear inadequate and do not satisfactorally explain the observed spectra. Little can further be deduced from the solvent shifts in the spectra,particularly with regard to intensity changes. Pyridine itself for instance,shows very large intensity changes in water compared to cyclohexane solution.

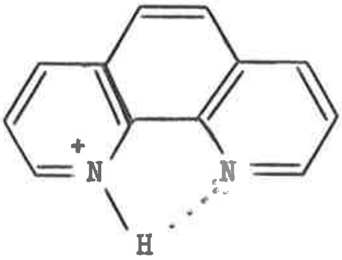
In conclusion therefore,it seems that insufficient information is as yet available to draw any reliable conclusion from the ultraviolet spectra. The data however may prove to be useful when more is known about the assignment of the bands in relation to calculated spectral absorption frequencies.

1.8 The stereochemistry of the bipyridyl cations.

2,2'-bipyridyl, being dibasic, can give rise to a mono- and di-cation, so that both systems must be considered here. It is well known that the diprotonated base is not easily formed, very strong acids being necessary for diprotonation to occur. Krumholz[74] has in fact shown that the ratio of the two ionisation constants K_1/K_2 is of the order of 10^5. Baxendale and George[44] regarded the effect of hydrogen bonding in a cis conformation (VIII) to stabilise the mono-cation and Beattie and Webster[44c] reached similar conclusions from hydration studies of (VIII) and the 1,10-phenanthroline cation (IX).



(VIII)



(IX)

In this work n.m.r. spectroscopy is again used to deduce the stereochemistry of these systems. The effect on the chemical shift of proton 3 due to protonation of the adjacent ring was first calculated theoretically, and these results then compared with the experimental data. As mentioned in section 1.4, the basic terms arising in these calculations are:

1. The change in the N magnetic anisotropy.
2. The removal of the electric field associated with the nitrogen lone-pair.
3. The effect of the positive charge.

In the Gil and Murrell calculations the values of the magnetic susceptibility tensors for a protonated pyridine nitrogen are:

$$(\chi^{P}_{N^+})_{xx} = 7.54; \quad (\chi^{P}_{N^+})_{yy} = 9.69 ; \quad (\chi^{P}_{N^+})_{zz} = 6.46$$

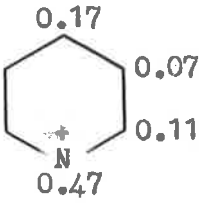
These values are very similar to those for an aromatic carbon atom.

Changes in magnetic shielding due to the replacement of a $>\!C$ function by an $>\!N^{+}\!-\!H$ group can therefore be regarded as small and unimportant. The lone-pair effect can also be omitted from the calculations since the lone-pair is removed on protonation. Only the effect of the positive charge in the adjacent ring need therefore be considered. This was calculated from the electric field associated with a positive charge, given by:[20]

$$E^{+} = 4.803 \times 10^{-10} \frac{\Delta q \cos \phi}{R_i^2}$$

Where R_i is the distance of the proton from the charge Δq, and ϕ the angle between the line joining the charge with the proton and the C-H bond. The location and value of the charge Δq were taken from the π-electron densities in the pyridinium cation as calculated by Brown and Heffernan (X):[61]

Excess positive charge



(X)

The effect of the positive charge delocalised in the ring was considered as a resultant dipole, a value of 2.29 D located in the centre of the ring, being obtained by taking moments of the excess positive charges in the α, β, and γ-positions about the centre. This dipole effect on P-5 in the adjacent ring was found to be negligible, but the deshielding due to the E^+ term (σ_5^+) is considerable; a constant -.165 p.p.m. for all values of ψ. From results obtained in Chapter III in which bridged bi-quaternary salts are considered, it appears that σ_5^+ is in fact not completely independent of ψ, but that the full value is only realized at large angles of twist. Admittedly, this term is small and quantities of this nature could well be accounted for by the inherent approximations involved in this approach, but in order to comply with the observed facts found in the next Chapter, a linear variation of σ_5^+ was used in the calculation (from 0.000 p.p.m. at $\psi = 0°$, to -0.165 p.p.m. at $\psi = 90°$). Although the final conclusions are not altered by this approximation, the resultant calculations better accommodate the magnitude of the chemical shift differences observed. The final curve of Δ 3,5 versus ψ is shown in Figure 1.13 but is only valid for the diprotonated molecule; for the monoprotonated system in aqueous sulphuric acid, the positive charge calculations must be averaged between the deshielding in water and that in the di-cation. The results are also shown in Fig. 1.13, and those of identical calculations for the methyl protons in 3,3'-dimethyl-2,2'-bipyridyl in Fig. 1.14.

Experimental.

The chemical shifts of the protons in 4,4'-dimethyl-2,2'-bipyridyl in various concentrations of aqueous sulphuric acid are shown in Fig. 1.15. This compound was studied rather than 2,2'-bipyridyl itself in order to facilitate the spectra analysis. Spectra were recorded for solutions of constant concentration with respect to base and calibrated relative to an external dioxan reference. As only shift differences between protons were

Fig. 1.13

Variation in the chemical shift of H-3 with dihedral angle in protonated 2,2'-bipyridyl.

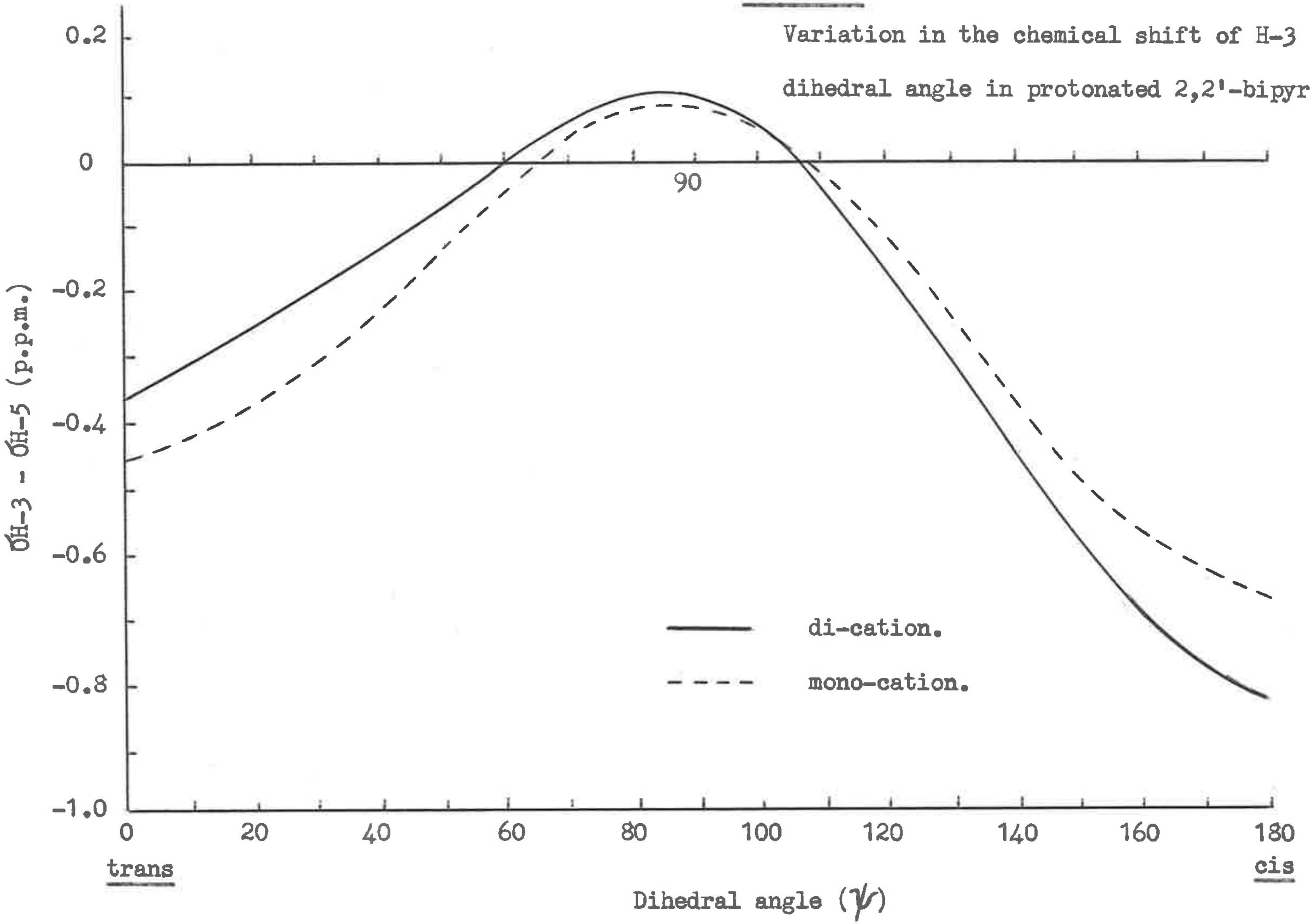


Fig. 1.14

Variation in the chemical shift of CH_3-3 with dihedral angle in protonated 3,3'-dimethyl-2,2'-bipyridyl.

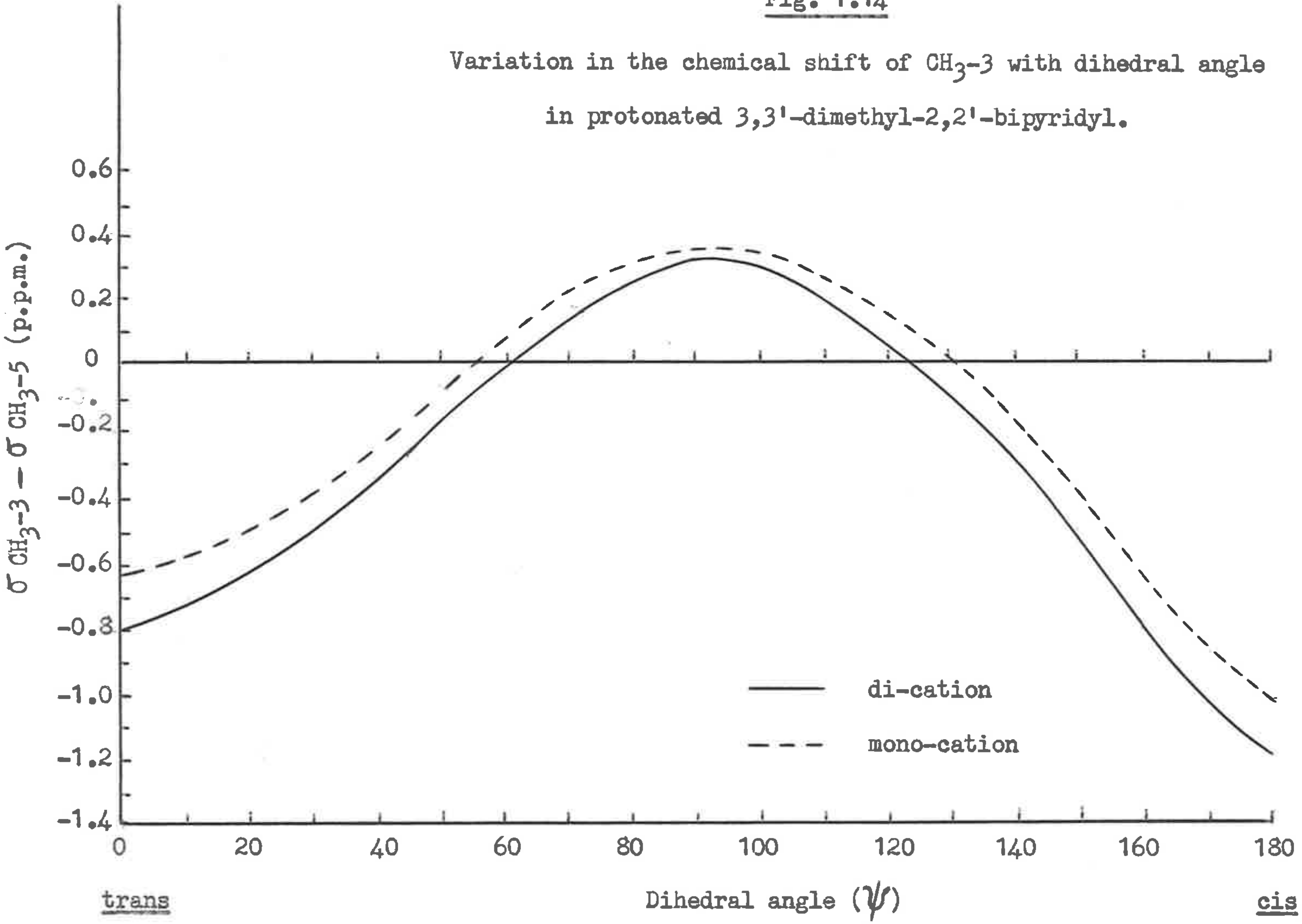
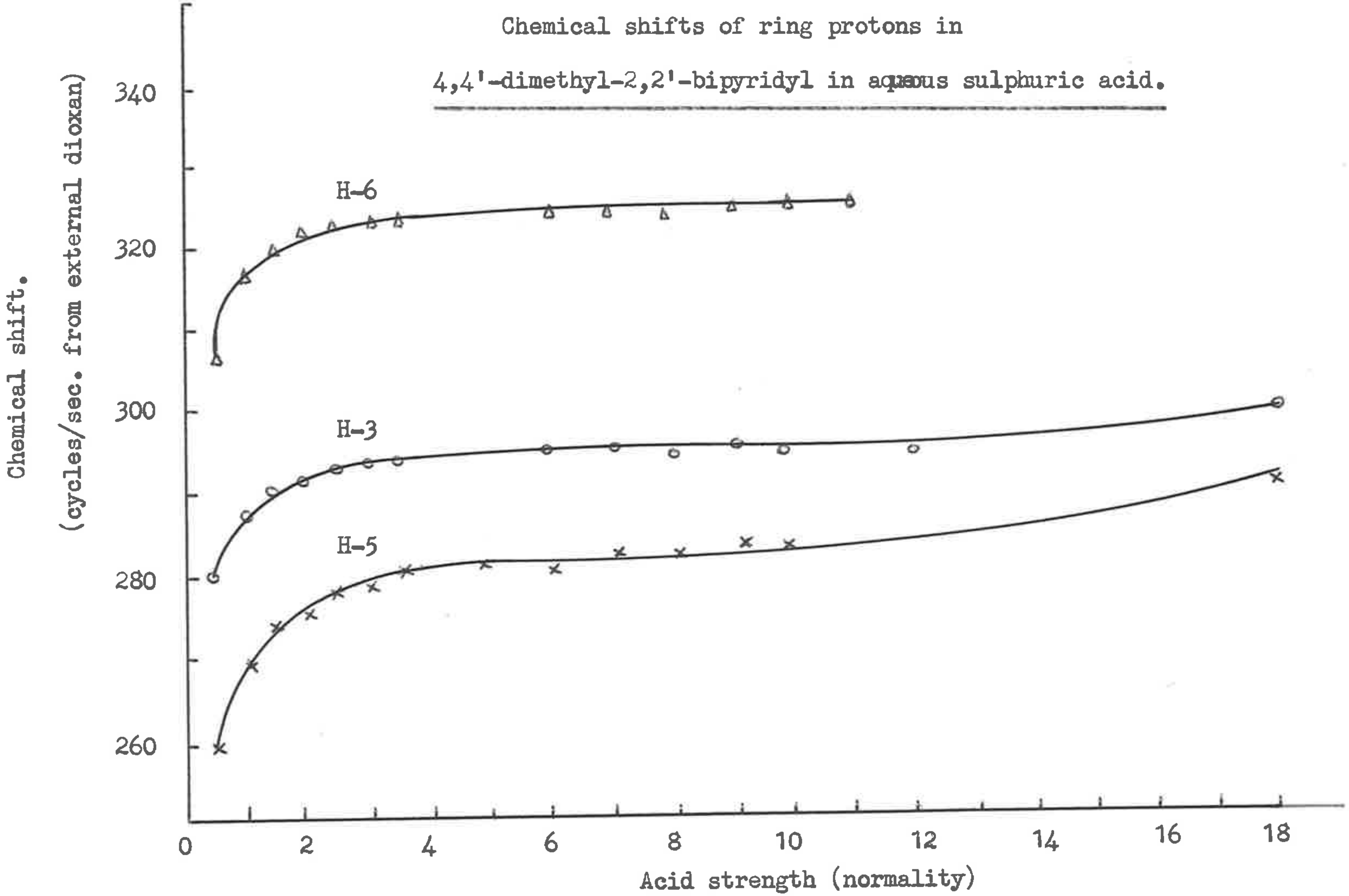


Fig. 1.15

Chemical shifts of ring protons in 4,4'-dimethyl-2,2'-bipyridyl in aqueous sulphuric acid.



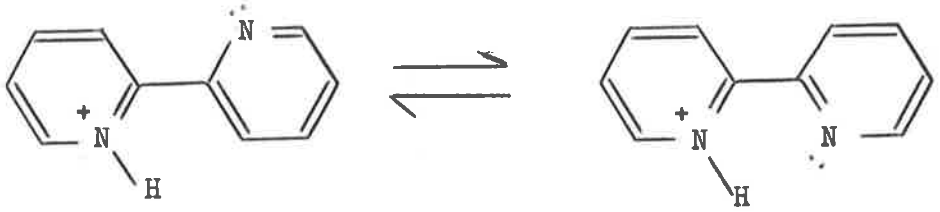
required this was considered adequate. An interesting phenomenon occurred in the spectra for a 0.5 N solution, which was not observed for any of the other isomeric bipyridyls nor for the spectra of the 3,3'-dimethyl derivative. The spectra at this concentration appeared as a broad unresolved band covering a region of nearly 100 c/s. (Fig. 1.16). This is in contrast to the much sharper peaks obtained in higher acid strengths. The relevance of this phenomenon will be treated in the following discussion.

Discussion.

The experimental data required to determine the stereochemistry of the mono- and di-cations are the differences in chemical shifts between the 3-proton and 5-proton (Δ 3,5). For the mono-cation this difference was obtained from a plot of Δ 3,5 versus acid strength, as shown in Fig. 1.17. The central, level portion of the curve was taken as the required value for the mono-cation. Applying this value (-12.5 c/s) to Fig. 1.13 then results in two solutions of the dihedral angle:

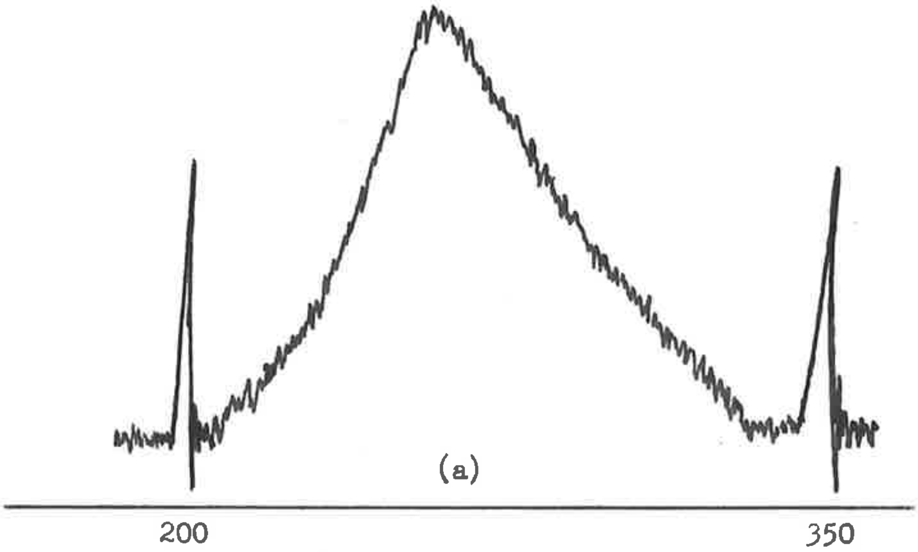
a) $\psi = 38^\circ$ <u>trans</u> b) $\psi = 53^\circ$ <u>cis</u>

Both these values are considerably smaller than the values suggested by Castellano (80-100°), but an examination of the ultraviolet spectra data of Krumholz[74] shows that the mono-cation absorbs as far as 300 mμ which is in better agreement with the smaller angles obtained here. Chemical shift data cannot differentiate between the two solutions obtained from Fig. 1.13, but the problem may possibly be resolved from the broadening effect observed earlier in 0.5 N acid. It was suggested that this phenomenon was due to a slow stereochemical inversion under these conditions, as shown below:



This suggestion was confirmed by cooling the solution to near freezing. It was then found that the spectrum sharpened up considerably as shown in Fig. 1.16. If it is assumed that the conformation of the free base in water is trans, then these arguments imply a cis-conformation of the mono-cation in aqueous acid in agreement with the original conclusions of Baxendale and George.[44] It may be argued that the broadening effect observed is due to slow proton exchange between the two rings, but this appears unlikely since this effect was not observed in the other bipyridyl isomers in acid strengths down to 0.25 N, nor was it observed in 3,3'-dimethyl-2,2'-bipyridyl.

In 18 N sulphuric acid the value of $\Delta 3,5$ is only 9.1 c/s. Both rings are expected to be protonated in this solvent and reference to Fig. 1.13 suggests angle of twists of 40° trans or 62° cis. The trans value appears more attractive because of the strong electrostatic repulsions between the two positive charges in a cis-conformation. Because of the approximations involved in these calculations, the dihedral angles obtained



(a) room temperature

(b) near freezing point

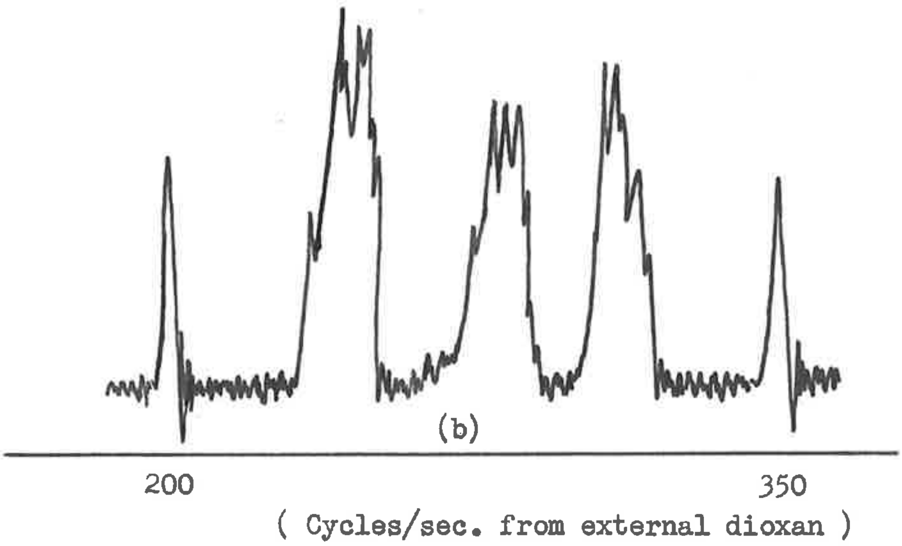


Fig. 1.16

n.m.r. spectra of 4,4'-dimethyl-2,2'-bipyridyl in 0.5 N H_2SO_4

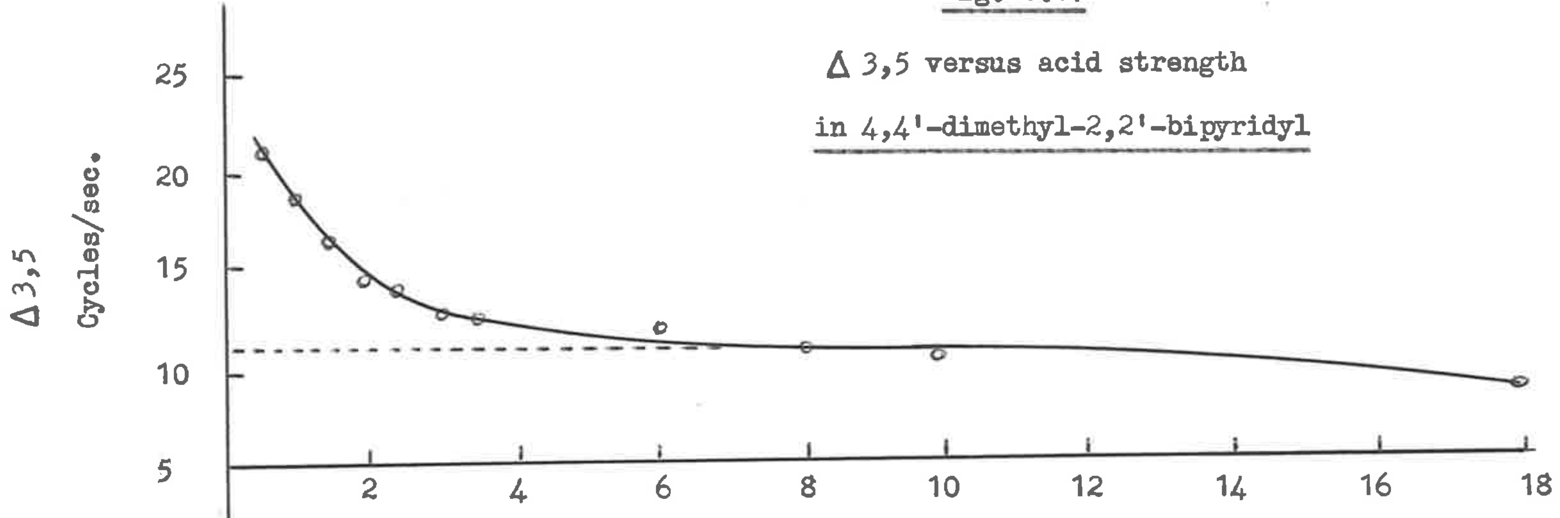


Fig. 1.17

Δ 3,5 versus acid strength

in 4,4'-dimethyl-2,2'-bipyridyl

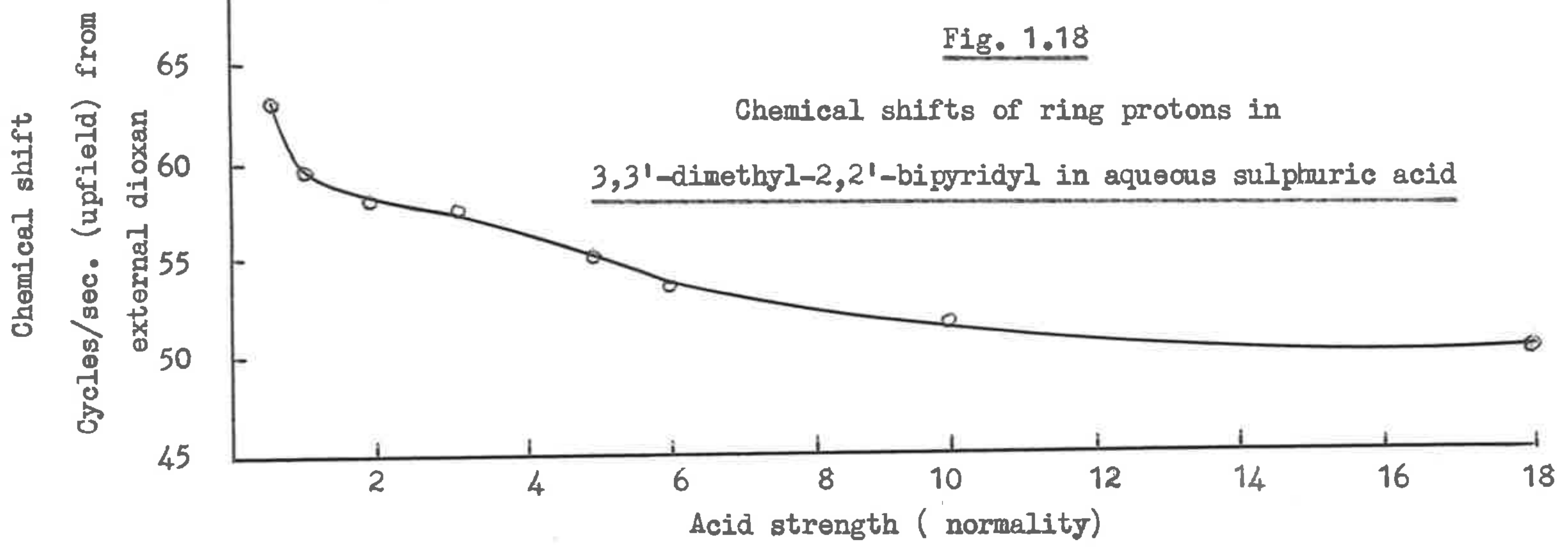


Fig. 1.18

Chemical shifts of ring protons in

3,3'-dimethyl-2,2'-bipyridyl in aqueous sulphuric acid are indicative rather than conclusive. The results tend to show that protonation of 2,2'-bipyridyl causes some relaxation of the forces that constrain the free base to a co-planar conformation and further suggest a twisted cis-conformation for the mono-protonated base.

The chemical shift variation of the methyl protons of 3,3'-dimethyl-2,2'-bipyridyl in different acid strengths is shown in Fig. 1.18. The molecule appears to be mono-protonated in 4 N acid and a comparison with the methyl frequency of the 5,5'-dimethyl compound in 4 N acid shows the former to be at higher field by 23 c/s.. This according to Fig. 1.14 implies a near right angle between the two rings in the mono-cation of the 3,3'-dimethyl isomer.

The stereochemistry does not appear to be altered in the di-cation. The shift difference between the 3- and 5-methyl protons in 18 N acid is still 21 c/s which according to Fig. 1.14 again suggests a value of about 90° for the di-cation. Both these results are consistent with the general pattern of conclusions reached in this work. As was shown earlier, the 3,3'-dimethyl compound is already highly twisted in the free base so that a further relaxation of co-planarity produces the large dihedral angles found here.

Protonation effects in 3,3'- and 4,4'-Bipyridyl.

Both 3,3'- (VI) and 4,4'-bipyridyl (VII) are stronger bases than the 2,2'-isomer, in particular with regards to the second protonation step as Krumholz's experimental[74] figures indicate. (Table 1.9.) The di-cations in these bipyridyls are thus easily formed and will only be

TABLE 1.9

Acid dissociation constants of bi-pyridinium cations in water.

	K_1	K_2
2,2'-bipyridyl	3.6×10^{-5}	-
3,3'-bipyridyl	2.5×10^{-5}	1×10^{-3}
4,4'-bipyridyl	1.5×10^{-5}	6.8×10^{-4}

discussed here. The chemical shifts in CF_3COOD solutions are shown in Table 1.10.

TABLE 1.10

Chemical shifts of 3,3'- and 4,4'-bipyridyl in CF_3COOD solution. (Cycles/sec. from TMS).

	H-2	H-3	H-4	H-5	H-6
3,3'-bipyridyl	564.4	-	546.4	504.3	546.4
4,4'-bipyridyl	550.6	515.7	-	515.7	550.6

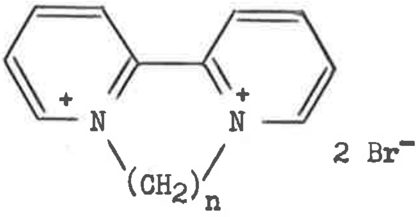
In (VI), P-2 is 18 c/s downfield from P-6, but calculations showed that as much as 15.5 c/s of this amount can be attributed to the effect of the positive charge in the adjacent ring on P-2 for $\psi = 90°$. This leaves only a small ring current contribution to the deshielding at P-2 which from the previous ring current calculations implies a very large dihedral angle for the di-cation of (VI). The same conclusion can be drawn for the protonated form of (VII). The protonation shifts here were found to be almost identical with those in γ-picoline (Table 1.3) which implies no major change in stereochemistry on protonation. In conclusion therefore the di-cations of both (VI) and (VII), like the free bases themselves enjoy considerable rotational freedom about the long axis of the molecules. It is interesting that the ultraviolet spectra data of Krumholz show no abnormally large wavelength shifts on protonation, in good agreement with the conclusions reached here.

CHAPTER II

THE STEREOCHEMISTRY OF THE BRIDGED BIQUATERNARY SALTS OF 2,2'-BIPYRIDYL

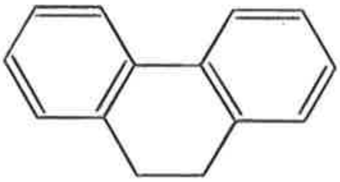
2.1 Introduction.

A set of compounds which are of particular relevance to the calculations performed in Chapter I, are the bridged biquaternary salts of 2,2'-bipyridyl (XI). These salts were first described by Homer and Tomlinson[51] in 1958, and the stereochemistry of these compounds, i.e. the dihedral angles between the planes of the two rings, was later investigated by these authors from a study of their ultraviolet spectra and reduction potentials.[52] The analogous bridged biphenyl compounds have been studied both by ultraviolet[54,79] and n.m.r.[31c,d,f,g,] spectroscopy, but the difficulty of analysing the complex n.m.r. spectra of the phenyl ring protons precluded quantitative correlations with interplanar angles. This is not the case with the bridged biquaternary salts studied here, since the presence of the electronegative nitrogen atom in the aromatic ring produces relatively large chemical shift differences between the ring protons. The spectra can thus be satisfactorily analysed as ABMX spin systems to give precise values for the chemical shifts and coupling constants.

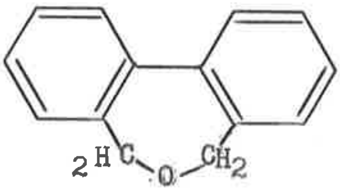


(XI)

The stereochemical problem in these salts is more clearly defined than in the compounds studied in Chapter I, since the bridging group locks the molecule in a cis conformation with a dihedral angle which is expected to increase with the length of this bridge. A further point of interest is the amount of freedom for the enantiomeric conformations to suffer interconversion. Such conformational stability has been extensively studied in the bridged biphenyl compounds where a number of singly bridged molecules with bulky ortho groupings have been resolved into their optical isomers.[31c] No singly bridged biphenyl unsubstituted in the aromatic ring has been resolved, and the magnetic equivalence of the bridge protons in 9,10-dihydrophenanthrene (XII), the oxepin (XIII) and the ketone (XIV) indicate a rapid conformational inversion.[31c,d.]



(XII)



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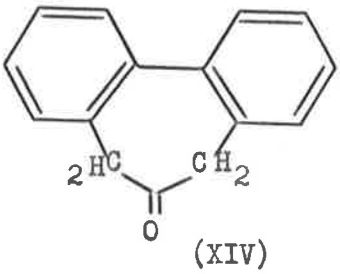
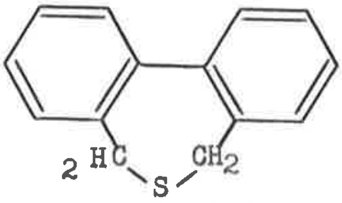


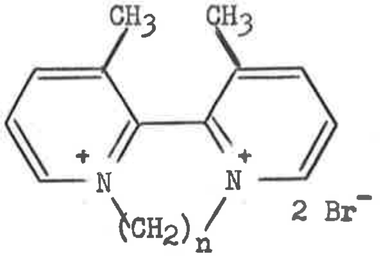
(XIV)



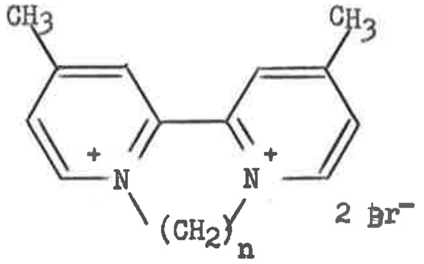
(XV)

Little is known about the conformational stability of systems with bridge lengths greater than 2 atoms, but a preliminary report of yet unpublished work indicates that the oxepin (XIII) shows magnetic non-equivalence of the methylene protons at low temperature, the energy barrier for the inversion being approximately 9.6 kcal/mole.[80] A poorly resolved AB quartet was also obtained for the bridge protons in the thiepin (XV).[31c] Magnetic non-equivalence of the methylene protons in the bridging group is good evidence of conformational stability, since in a locked conformation these protons subtend different angles at the aromatic rings.

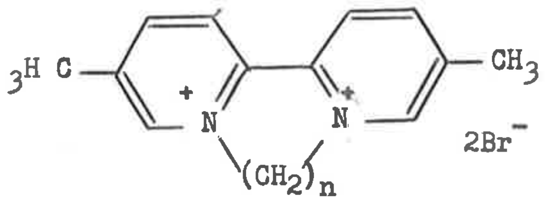
In this work the conformational stability of these systems was also investigated. As well as (XI), with n=2,3 and 4, the bridged salts of the 3,3'-dimethyl- (XVI), 4,4'-dimethyl- (XVII) and 5,5'-dimethyl-2,2'-bipyridyl (XVIII) were prepared and studied. In addition, through the kind assistance of Dr. Calder,[81] compounds (XIX, XX) and the oxepin (XXI) were also available.



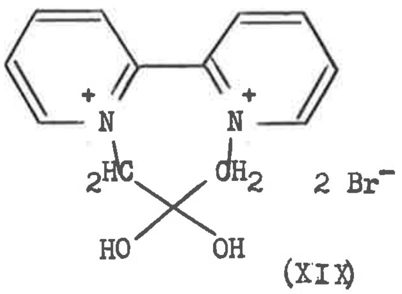
(XVI)



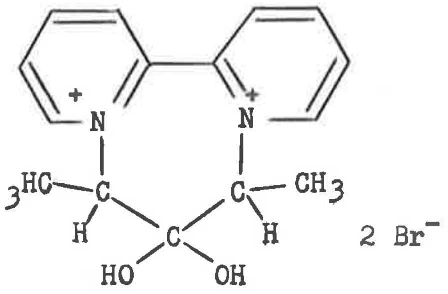
(XVII)



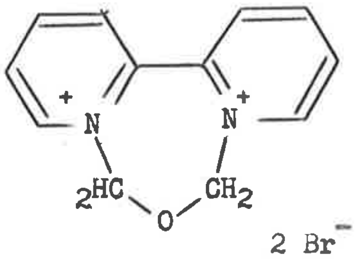
(XVIII)



(XIX)



(XX)



(XXI)

2.2 Analysis of n.m.r. spectra.

The assignments and analysis of the n.m.r. spectra of all the compounds studied were straightforward, and marked changes in the appearance of the spectra on increasing the chain length of the bridging-group from two to four carbon atoms are apparent. This is illustrated in the spectra of (XVII) with n= 2,3, and 4, shown in Figures 2.1 to 2.3. The spectra were satisfactorily analysed as ABMX spin systems for the unsubstituted bipyridyls, and as ABX systems for the methyl substituted compounds. The n.m.r. data is summarised in Table 2.1. Spectra were recorded in D_2O solution at approximately constant molar concentration (0.1M), but dilution shifts were found to be negligible. Magnetic non-equivalence for methylene protons in the bridging group was observed in (XIX) where the signal due to these protons appeared as a clear AB quartet (Fig. 2.5) and also in (XVI) n=2 which appeared as an A_2B_2 pattern (Fig. 2.4). Such multiplicity was also observed for the bridge protons in (XI, XVI, XVII, XVIII) with n=3 and 4, but these patterns could not be fully analysed because of their complexity and the superposition of the HOD signal on the multiplet assigned to the methylene protons α to the pyridinium nitrogen.

2.3 Discussion.

The theory relating the chemical shift difference between the 3 and the 5 proton (Δ 3,5) as a function of the dihedral angle ψ, has been fully treated in Chapter I and will therefore not be expanded here. The calculations applicable in these systems are of course those for the di-protonated bases as illustrated in Fig. 1.13. The dibromide salts studied here behave as typical ionic compounds and are almost completely dissociated in water. It has been shown that in the pyridinium hydrohalides, the nature of the counter ion produces small variations in the chemical shifts of the ring protons in solvents of varying dielectric constant,[82] but these effects are probably of importance only for intimate ion-pairs, and not for the dissociated salts. Polarization of solvent molecules by the charged biquaternary bipyridyl will produce an electric field at the heterocyclic ring protons,[49] but since it is difficult to estimate its magnitude or direction, it is assumed in the present series of compounds that the effect on proton 3 is the same as that on proton 5 and that any change in the magnitude of this effect with increasing dihedral angle will be cancelled by internal comparison of the shifts of these protons.

The calculations carried out previously should fully account for the range of values of Δ 3,5 found in these compounds. In this regard some comments are required in retrospect to the theory outlined earlier. The data in Table 2.1 shows that values of Δ 3,5 range between -40 c/s and

Fig. 2.1

n.m.r. spectra of XVII n=2

(in D_2O)

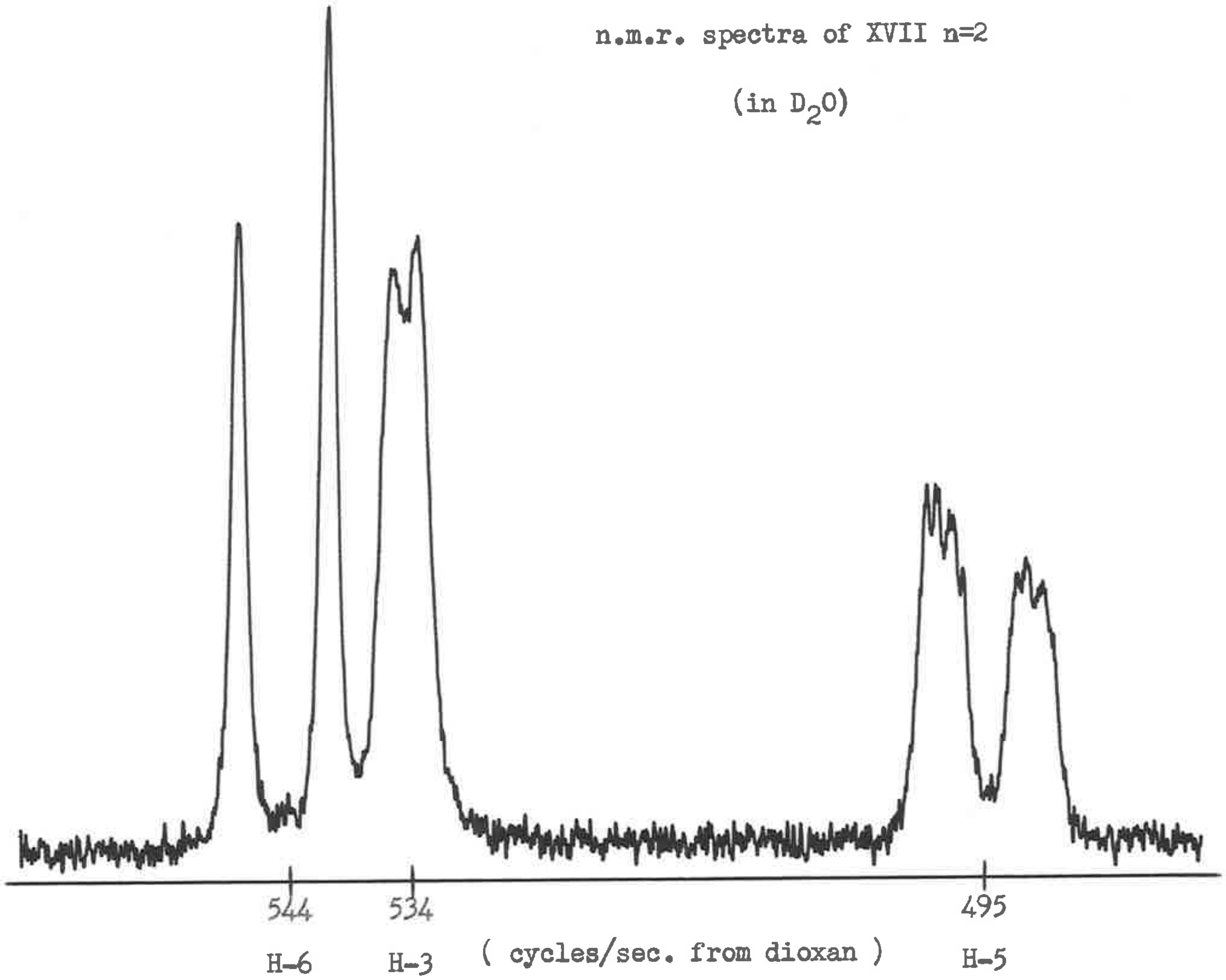


Fig. 2.2

n.m.r. spectra of XVII n=3

(in D_2O)

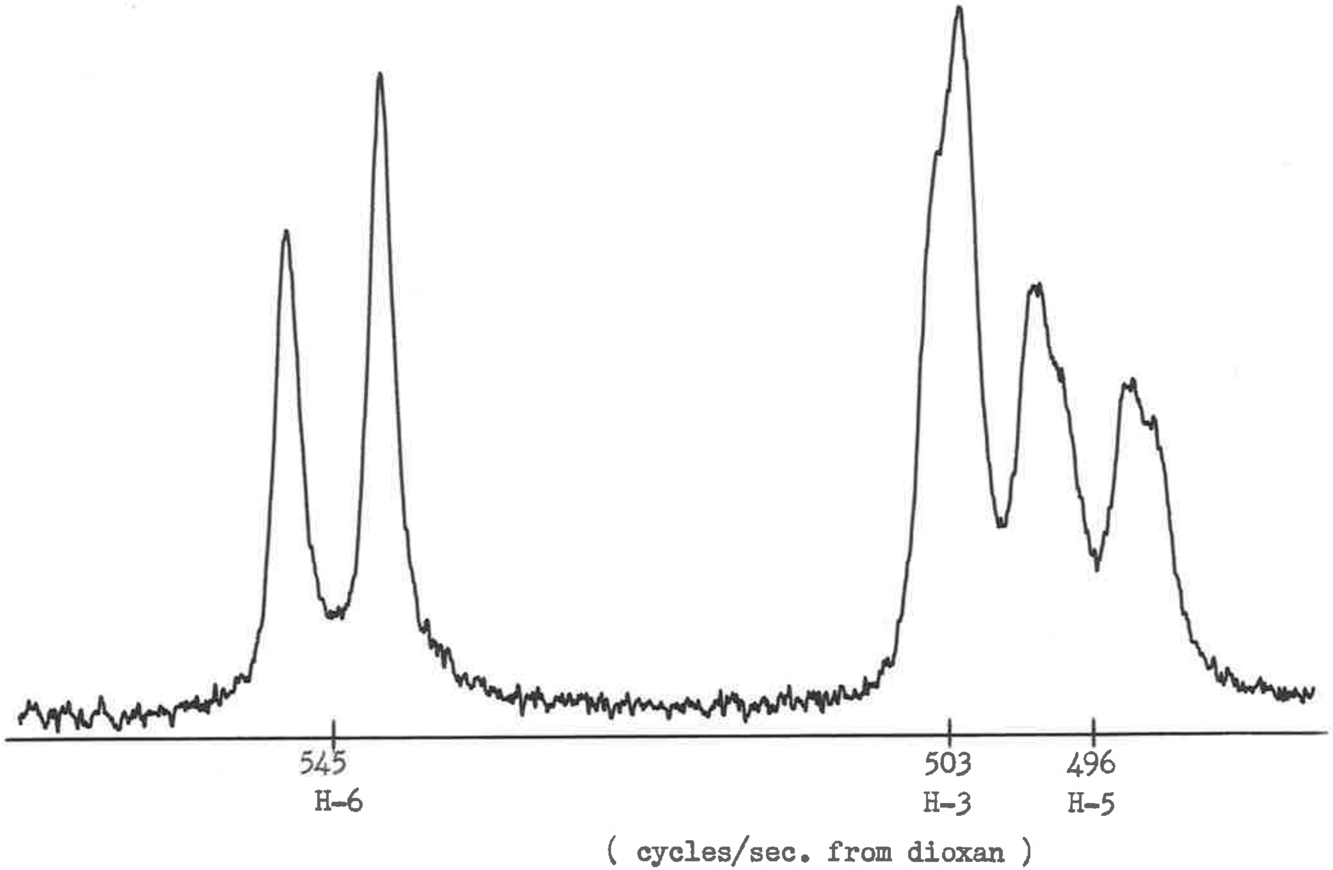
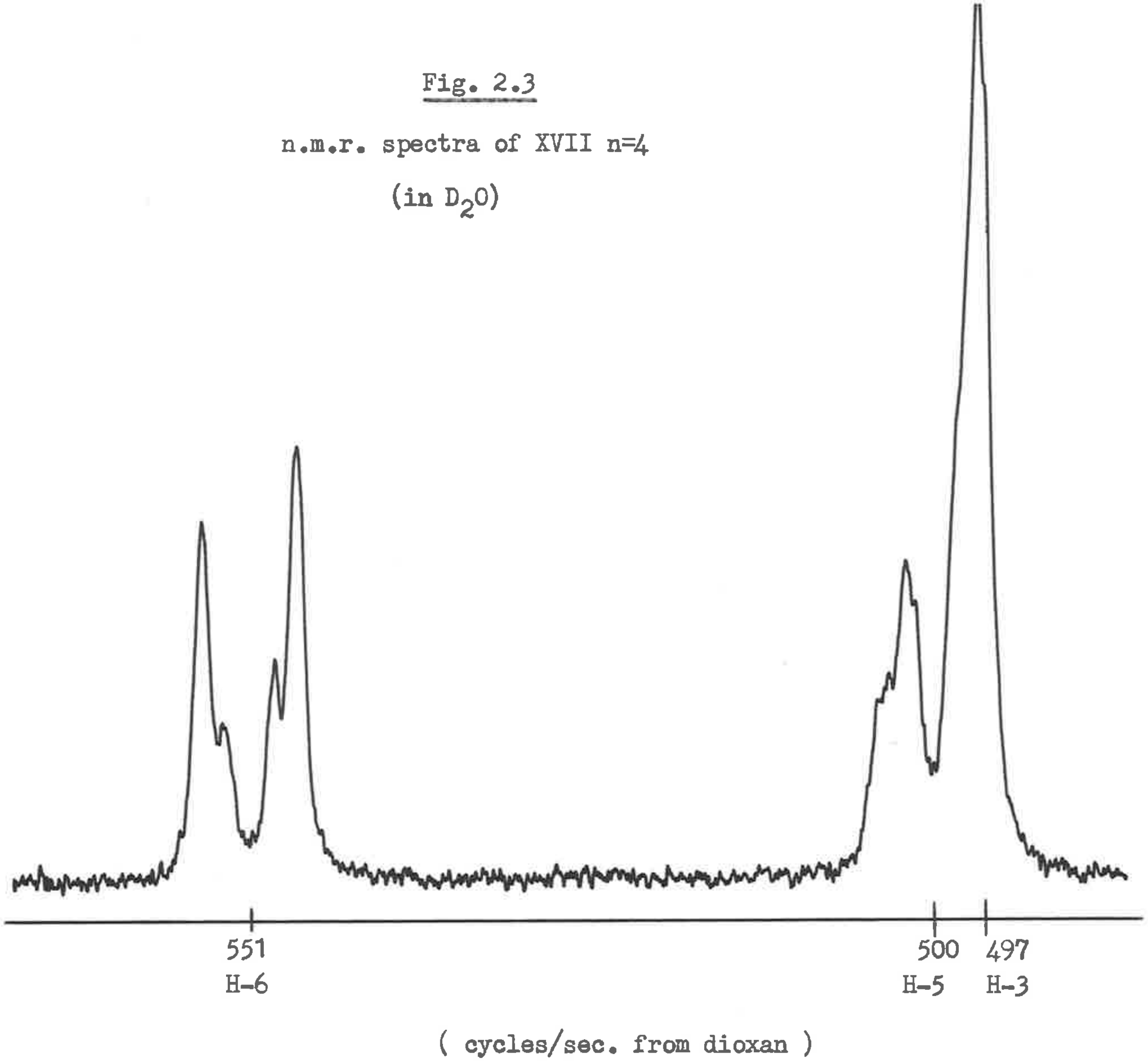


Fig. 2.3

n.m.r. spectra of XVII n=4

(in D_2O)



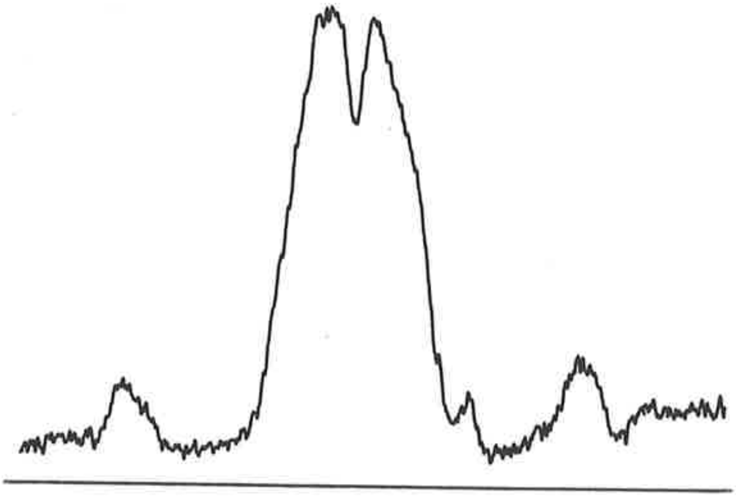


Fig. 2.4

n.m.r. spectra of methylene protons in XVI n=2

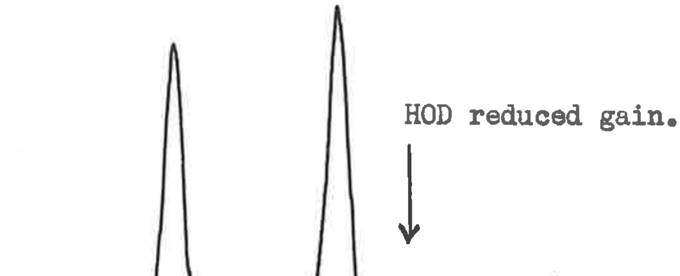


Fig. 2.5

n.m.r. spectra of methylene protons in XIX.

Table 2.1

A Chemical shifts of ring protons in bridged biquaternary 2,2'-bipyridyls; ABMX analysis (Cycles/sec. from TMS.)

Compound	Bridge	Chemical shifts;				
		H-3	H-4	H-5	H-6	3.5
(XI)	$-(CH_2)2-$	546.8	541.7	509.2	559.6	37.6
(XI)	$-(CH_2)_3-$	518.9	541.7	511.7	563.2	7.2
(XI)	$-(CH_2)_4-$	512.7	539.1	516.0	568.0	-3.3
(XVI)	$-(CH_2)_2-$	165.9	531.8	500.1	554.4	-
(XVI)	$-(CH_2)_3-$	155.1	535.5	503.3	553.1	-
(XVI)	$-(CH_2)_4-$	147.9	531.5	507.1	560.5	-
(XVII)	$-(CH_2)_2-$	533.5	176.0	494.5	543.5	39.0
(XVII)	$-(CH_2)_3-$	503.4	174.7	496.0	545.1	7.4
(XVII)	$-(CH_2)_4-$	496.5	173.6	500.0	551.2	-3.5
(XVIII)	$-(CH_2)_2-$	534.7	524.2	166.5	547.0	-
(XVIII)	$-(CH_2)_3-$	505.8	527.7	166.5	550.8	-
(XVIII)	$-(CH_2)_4-$	499.2	525.4	167.8	557.8	-
(XIX)	$-(CH_2C(OD)_2CH_2)-$	527.1	547.1	515.7	565.5	11.4
(XX)	$-(CHCH_3C(OD)_2CH_3CH)-$	523.5	544.3	516.5	562.1	7.0
(XXI)	$-(CH_2OCH_2)-$	534.1	553.3	522.3	575.7	11.8

Table 2.1
(contd)

B Coupling constants for ring protons (Cycles/sec) ABMX or ABX analysis.

Compound	Bridge	J3,4	J4,5	J5,6	J3,5	J4,6	J3,6
(XI)	$-(CH_2)_2-$	8.2	7.5	6.0	1.9	1.5	0.9
(XI)	$-(CH_2)_3-$	8.1	7.7	5.9	1.8	1.4	0.7
(XI)	$-(CH_2)_4-$	8.1	7.7	5.9	1.8	1.5	0.6
(XVI)	$-(CH_2)_2-$	-	8.0	5.7	-	1.2	-
(XVI)	$-(CH_2)_3-$	-	8.4	5.7	-	1.5	-
(XVI)	$-(CH_2)_4-$	-	8.3	5.8	-	(1.4)	-
(XVII)	$-(CH_2)_2-$	-	-	6.3	1.5	-	(0.8)
(XVII)	$-(CH_2)_3-$	-	-	6.1	1.6	-	(0.8)
(XVII)	$-(CH_2)_4-$	-	-	6.3	1.8	-	(1.1)
(XVIII)	$-(CH_2)_2-$	8.6	-	-	-	1.4	0.9
(XVIII)	$-(CH_2)_3-$	8.2	-	-	-	1.6	(0.7)
(XVIII)	$-(CH_2)_4-$	8.3	-	-	-	(2.0)	(0.8)
(XIX)	$-(CH_2C(OH)_2CH_2)-$	7.8	7.6	5.8	1.9	1.4	-
(XX)	$-(CHCH_3C(OH)_2CH_3CH)-$	7.8	7.9	5.8	1.5	1.4	-
(XXI)	$-(CH_2OCH_2)-$	7.8	7.8	5.9	1.7	1.5	0.7

+3.5 c/s (or -0.667 and +0.058 p.p.m.), but this range must be accommodated between approximately 20 and 90°, since from molecular models the two-membered bridge compounds are twisted at least 20°. If the deshielding effect due to the positive charge on P-5 in the adjacent ring (σ^+_5) is treated normally, then the theoretical curve does not satisfactorily accommodate the experimental range of $\Delta 3,5$. It is here suggested that in a planar conformation σ^+_5 is sharply attenuated, since in this conformation the 5 proton is in fact well shielded from the positive charge by the intervening ring structure. At larger values of Ψ, the nitrogen atom is lifted above the plane of the adjacent ring and a more direct contact with P-5 is possible. The only experimental evidence that might be accounted for by this hypothesis is the gradual down-field shift of P-5 in a given series (which is not accounted for in the calculations since σ^+_5 is constant for all Ψ). The actual value of this shift is about 7 c/s between n=2 and n=4, which compares well with the calculated value of σ^+_5 (10 c/s). In order to allow for the observed shift of P-5 in the calculations, a linear variation is assumed for the value of σ^+_5 between $\Psi = 0^\circ$ ($\sigma^+_5 = 0$) and $\Psi = 90^\circ$ ($\sigma^+_5 =$ -10 c/s). This approximation does not alter the final conclusions to any extent, but the calculations then account better for the range of $\Delta 3,5$ found and also gives reasonable values of the dihedral angle in the two-membered bridge compounds from a direct application of $\Delta 3,5$ to Figure 1.13.

Actual values of the dihedral angle Ψ, in these compounds are thus obtained by applying the experimental value of $\Delta 3,5$ to Figure 1.13, and for compounds (XVI) to Figure 1.14. In (XVIII) $\Delta 3,5$ is not obtainable from an intra-molecular difference, but here the chemical shift of P-3 was compared with the shift of P-5 in (XVII). The values of ψ so obtained still agree remarkably well with those obtained in the other cases. The final results are shown in Table 2.2. Estimated dihedral angles in a number of bridged biphenyls obtained by a number of workers are shown in Table 2.3 for comparison.

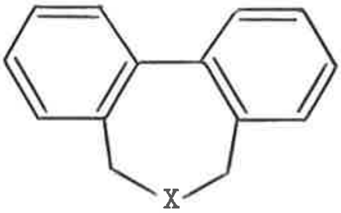
Table 2.2

Estimated dihedral angles in bridged biquaternary salts of 2,2'-bipyridyl.

Compound	Number of bridge atoms		
	n=2	n=3	n=4
(XI)	26°	64°	82°
(XVI)	55	68	90
(XVII)	23	64	82
(XVIII)	21	61	77
(XIX)	-	60	-
(XX)	-	65	-
(XXI)	-	58	-

Table 2.3.

Estimated dihedral angles in biphenyl derivatives.



References	Interplanar angle						
X=	-	O	NMe	CH_2	CO	S	$(CH_2)_2$
31c	15.3°	44.1°	45.8°	50.6°	52.4°	56.6°	-
83	20	50	-	50	-	-	60°
84	20	-	-	46	-	-	60
85	18	21	-	-	-	-	-

The interesting and encouraging aspect of the results obtained in this work is the remarkable agreement between compounds with similar bridge lengths, and also the general agreement with dihedral angles obtained in the biphenyl system.

It is interesting to note however that in every case the values obtained here are somewhat greater than those estimated in the biphenyls. This is not unreasonable if it is considered that the electrostatic repulsion between the positive charges on the nitrogen atoms would exert additional forces and slightly twist the two rings further out of plane.

The value of 58° in the oxepin (XXI) is smaller than the average value for the three-membered carbon bridge compounds which is consistent with the smaller size of an oxygen atom compared to a carbon atom. The results for (XVI) are particularly interesting because it clearly illustrates the steric crowding caused by the two methyl groups in the 3-position. In (XVI) n=2, this steric interference increases the dihedral angle to 55°, but for the compounds with n=3 and n=4 the values of ψ are only slightly greater than those in the compounds unsubstituted in the 3-position. The large twist already caused by the bridging group must release the interaction between the two methyl groups thus allowing ψ to assume a normal value.

As mentioned earlier, some evidence was obtained regarding the conformational stability of these salts. This was obtained from an examination of the n.m.r. spectra of the bridge protons in these compounds, and is best illustrated by the appearance of the n.m.r. signal of the methylene protons in (XVI),n=2, as shown in Fig. 2.4, and those in (XIX) as shown in Fig. 2.5. It is obvious in the case of (XVI) that the methyl groups are responsible for the locked conformation since the analogous compounds unsubstituted in the 3-position show only a single sharp peak due to rapid interconversion between the two equivalent conformations.

The appearance of the methylene protons signals in the three- and four-membered bridged compounds also suggests that they prefer a frozen conformation, but the complexity of the patterns and the superposition of the HOD signal on the multiplet assigned to the methylene protons α to the pyridinium nitrogen made further analysis imposible. Those spectra which showed magnetic non-equivalence for the bridge protons were further run at temperatures up to

90°, which is about the limit for aqueous solutions. Up to this temperature however, no change in the appearance of the spectra could be detected, which implies reasonable rigidity for the structure of those compounds.

2.4 The ultraviolet spectra of the bridged biquaternary salts of 2,2'-bipyridyl.

The ultraviolet spectra of the bridged biquaternary salts were also examined in this work, and a band resolution carried out as in section 1.7. As explained earlier, no theoretical significance can be assigned to them. The spectra are shown on Figs. 2.6 to 2.8, and the data is summarised in table 2.4.

It is immediately clear from table 2.4 that changes in the wavelenght of the absorption bands dominate the effect on the electronic spectra with an increase in bridge lenght, although there also appears to be a slight attenuation of the intensity of the long-wavelenght band envelope. However, even though symmetry problems are largely eliminated in these systems, one can only still speculate that the hypsochromic shift observed is directly a consequence of the increase in the dihedral angle with increase in bridge lenght. In order to determine whether an empirical relationship exists between the ultraviolet spectra and the n.m.r. results, the wavelenght of absorption band A in these systems was plotted against the dihedral angles calculated from the n.m.r. studies. The results are shown in Figs. 2.9 and 2.10. Reasonable straight lines are observed in any given series which is particularly interesting particularly if we consider the agreement of compounds XIX, XX and XXI in Fig. 2.9 and also the line obtained for the series of the 3,3'-dimethyl derivative. There is thus interesting information, which may prove to be useful in future theoretical considerations of the ultraviolet spectra of such systems.

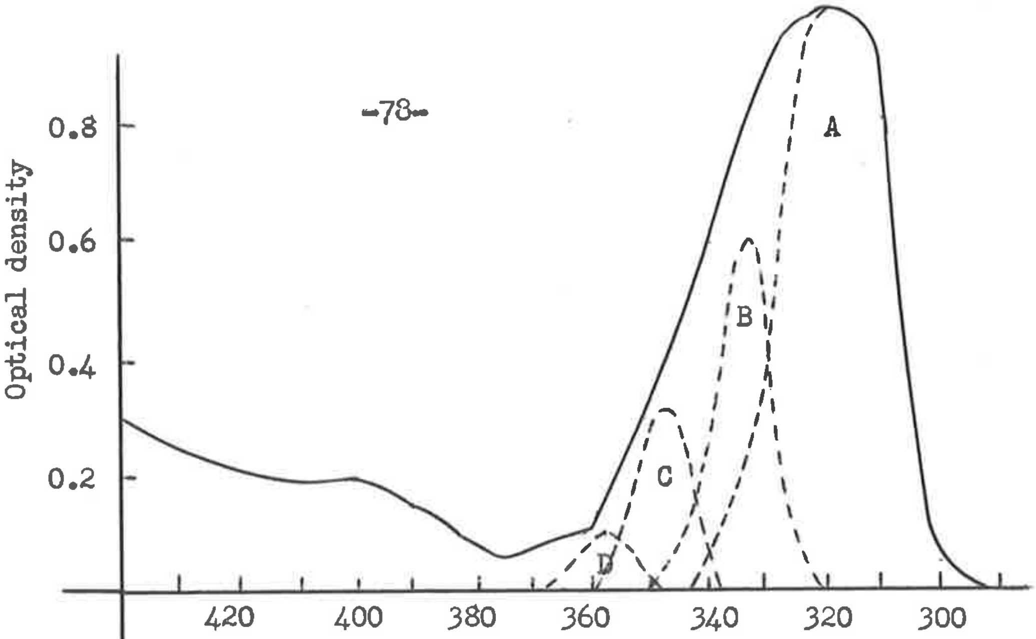


Fig.2.6

(XI) n=2

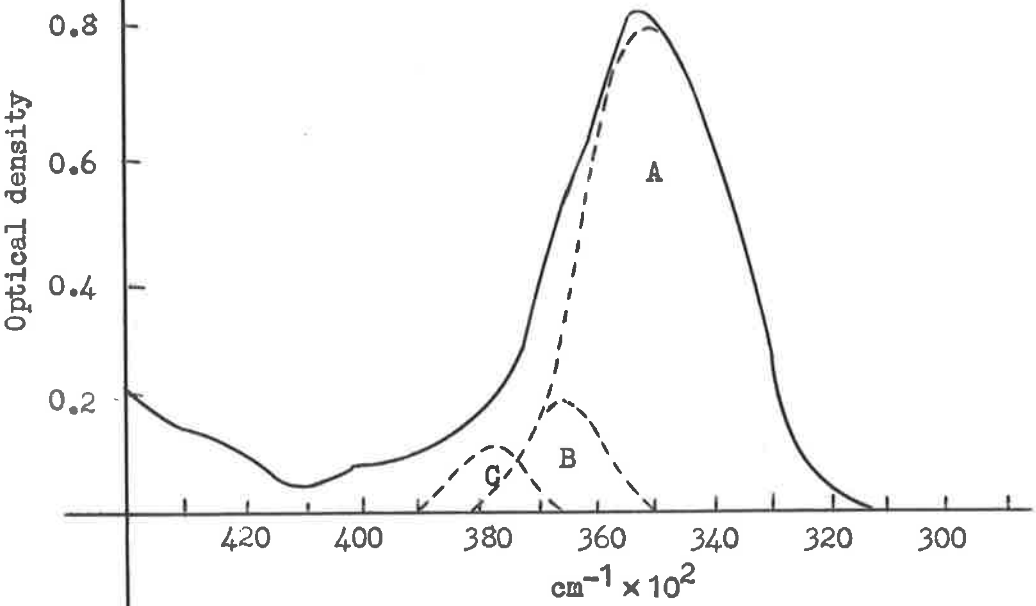


Fig. 2.7

(XI) n=3

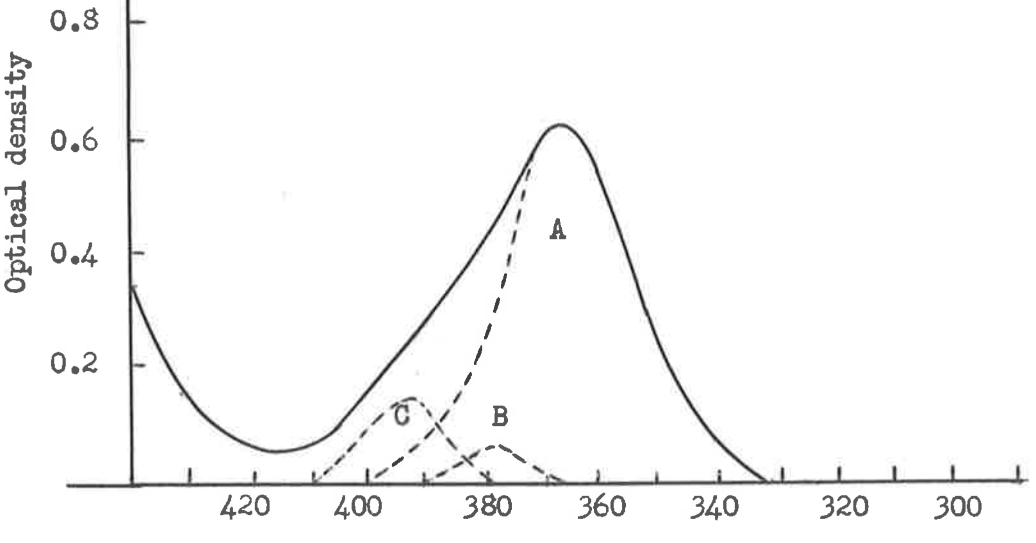


Fig. 2.8

(XI) n=4

Table 2.4

Ultraviolet spectra data of the bridged biquaternary salts of 2,2'-bipyridyl

	Band	λ max. (mμ)	ε max.	f
(XI) n=2	A	314.1	17,710	0.18
	B	298.1	10,770	0.06
	C	288.7	4,520	0.024
	D	279.8	2,260	0.010
(XI) n=3	A	287.9	15,460	0.190
	B	273.7	3,390	0.023
	C	264.6	2,070	0.013
(XI) n=4	A	274.4	13,070	0.169
	B	263.9	1,250	0.006
	C	255.5	2,910	0.023
		***		
(XVI) n=2	A	30.9.0	15,950	0.199
	B	290.6	5,390	0.031
	C	281.5	3,050	0.014
(XVI) n=3	A	298.0	14,800	0.163
	B	271.0	4,580	0.047
	C	257	2,600	0.018

Table 2.4 (contd.)

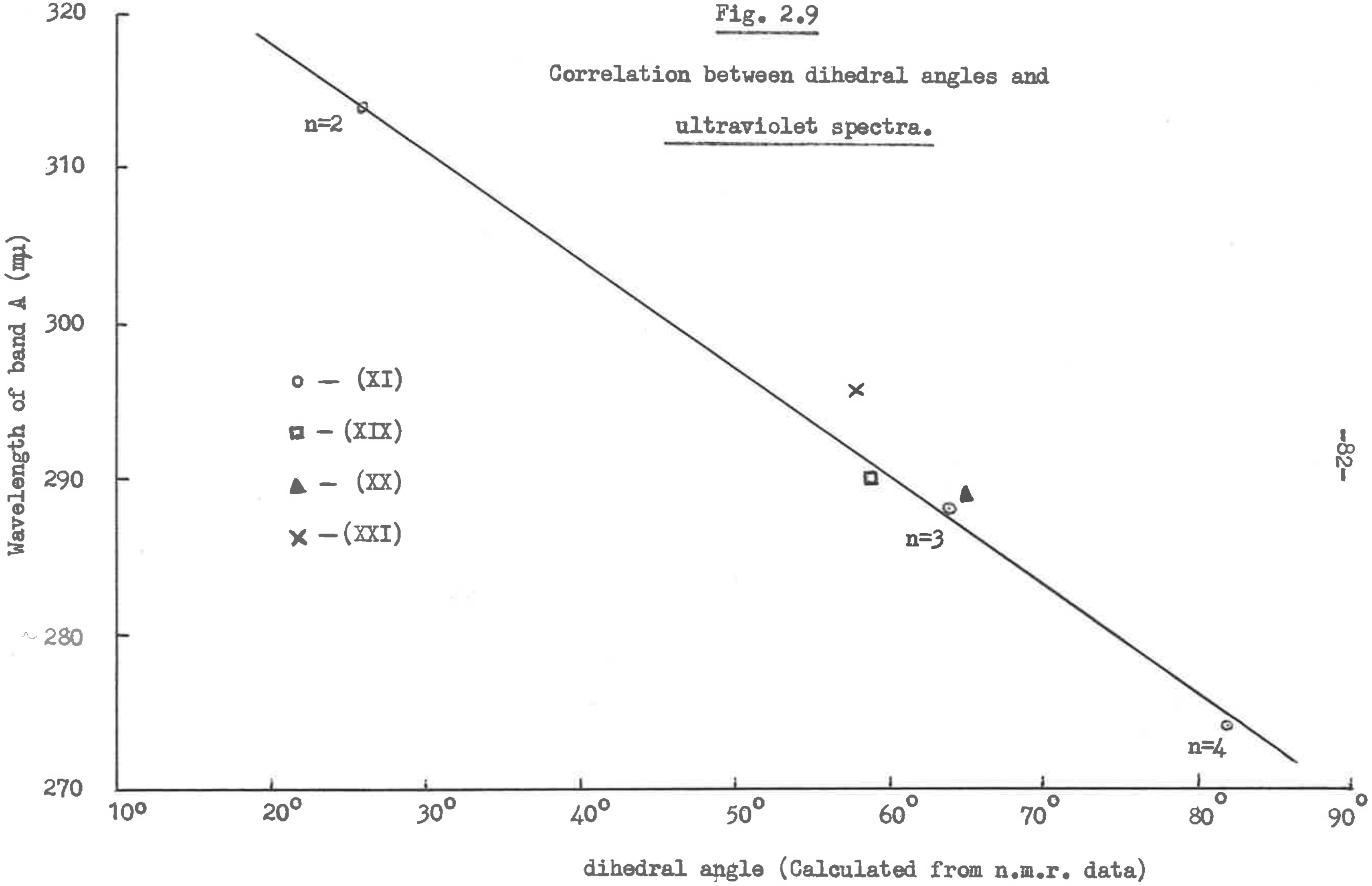
	Band	λ max.(mμ)	ε max.	f
(XVI) n=4	A	279	14,180	0.141
	B	267.5	5,560	0.045
	C	257.5	4,580	0.024
		***		
(XVII) n=2	A	311.5	19,380	0.159
	B	297.2	15,630	0.088
	C	286.5	8,150	0.044
(XVII) n=3	A	283.7	14,770	0.182
	B	266.0	3,580	0.030
(XVII) n=4	A	270.6	12,330	0.160
	B	252.5	4,000	0.038
		***		
(XVIII) n=2	A	325.7	20,190	0.174
	B	309.6	13,750	0.113
	C	295.4	5,550	0.026
(XVIII) n=3	A	296.7	10,270	0.137
	B	278.2	2,260	0.018
	C	267.0	2,760	0.017

Table 2.4 (contd.)

	Band	λ max. (mμ)	ε max.	*f*
(XVIII) n=4	A	281.7	11,190	0.164
	B	259.4	3,380	0.043
		***		
(XIX)	A	289.9	15,650	0.203
	B	270.3	4,090	0.041
		***		
(XX)	A	288.8	14,460	0.203
	B	268.2	4,410	0.045
	C	251.4	8,090	0.082
		***		
(XXI)	A	295.6	15,530	0.208
	B	276.4	3,690	0.030
	C	265.4	2,460	0.011
	D	257.6	2,380	0.012
		***		

Fig. 2.9

Correlation between dihedral angles and ultraviolet spectra.



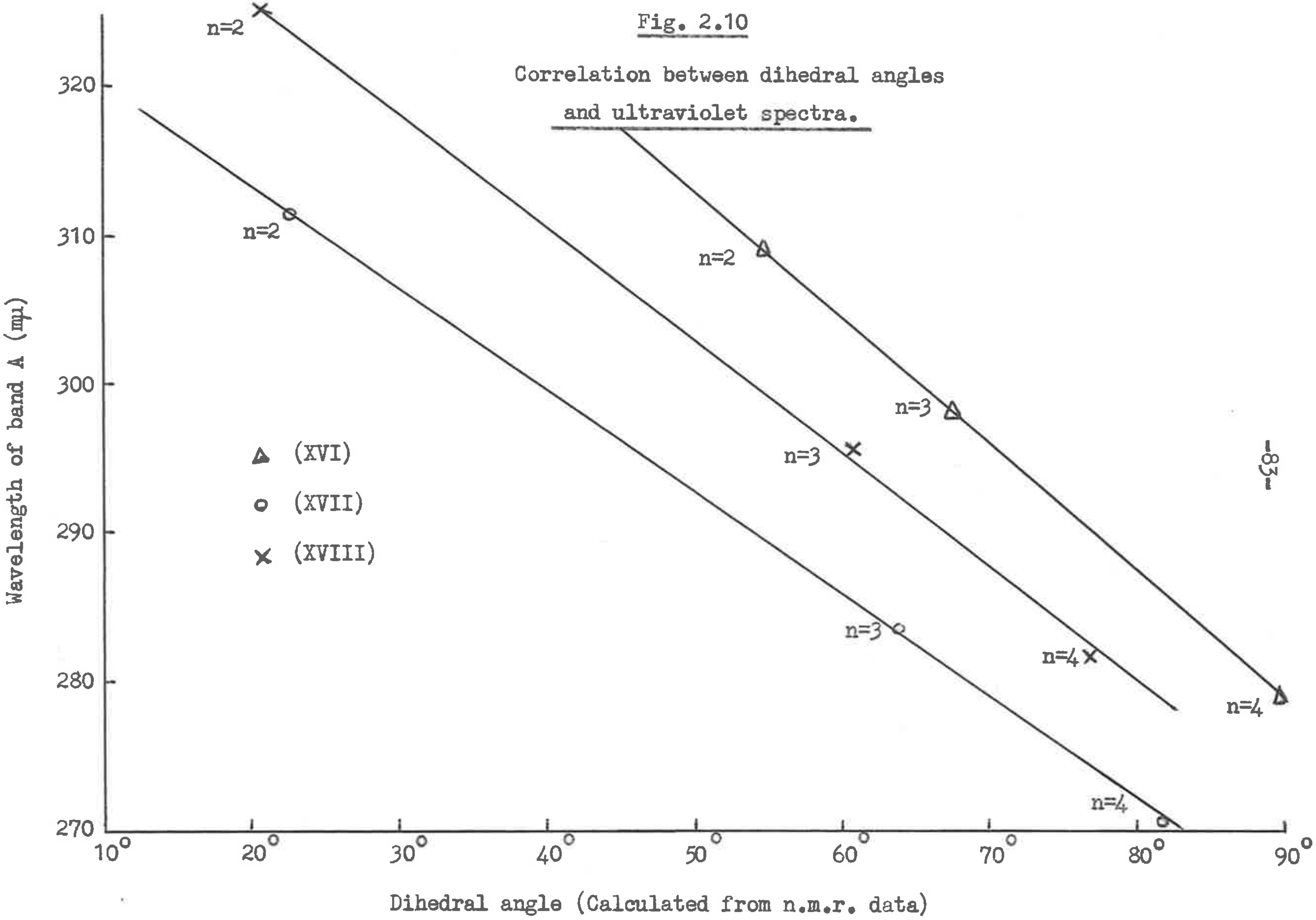


Fig. 2.10

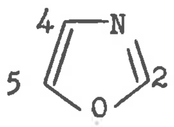
Correlation between dihedral angles and ultraviolet spectra.

CHAPTER III

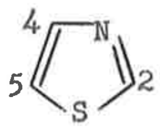
The n.m.r. spectra of some five-membered heterocyclic compounds.

3.1 Introduction.

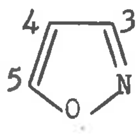
With the underlying factors determining the proton resonance spectra of pyridine now well established, it is surprising that the general concept has not yet been extended to other heterocyclic systems containing a pyridine-type nitrogen atom. It is disconcerting in fact that in many cases crude correlations of proton shifts with local π-electron densities are still attempted without reference to the basic theory already available.[86,87,88] It was for this reason that an investigation was commenced on a number of such nitrogen heterocyclic compounds, even though extensive n.m.r. data for some of these compounds have been, and still are being, published. The compounds chosen form a group of five-membered heterocyclic aromatic compounds containing two different heteroatoms, namely oxazoles (XXII), thiazoles (XXIII), isoxazoles (XXIV) and isothiazoles(XXV). The parent members of this group are shown below with the numbering of the ring systems included.



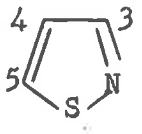
(XXII)



(XXIII)



(XXIV)



(XXV)

The study reported here, is confined to the effects of the nitrogen atom on the chemical shifts of the ring protons in terms of the theory of Gil and Murrell. Since the effects of the oxygen and sulphur atoms are not as yet fully understood in furan and thiophen, no attempt is made to evaluate the contribution to the chemical shifts by these atoms in the compounds studied here.

The n.m.r. spectra of oxazoles and thiazoles have been reported by Bak and coworkers,[89] Haake and Miller,[90] Staab and coworkers[91,92] and Clarke and Williams.[93] Comprehensive data is already available on the recently synthesised isothiazole ring system[94], e.g. the work by Staab and Mannschreck,[95] Anderson[96], and Olofsen,[97] but no systematic studies have been reported for isoxazoles.

In this work a number of unsubstituted and methyl-substituted members of this set of compounds have been synthesised and their n.m.r. spectra re-examined, in particular with regards to solvent and protonation effects.

3.2 Results of n.m.r. spectra.

The compounds studied together with the resonance frequencies of the various protons are listed in Table 3.1, and the n.m.r. spectra of the unsubstituted compounds shown in Figs. 3.1 to 3.4. The oxazole spectra shown is taken from the work by Staab and coworkers.[92] Interpretation and analysis of the spectra was straightforward in all cases and the assignments of the ring protons confirmed by the spectra of the methyl compounds. Spectra recorded in CF_3COOD solution tended to be broad, thus reducing the accuracy of the chemical shifts to ± 1 c/s. Although dilution shifts were found to be negligible (less than 0.5 c/s), the spectra were all recorded at the same concentration. Coupling constants are shown in Table 3.2.

Fig. 3.1

n.m.r. spectra of oxazole

in CCl_4

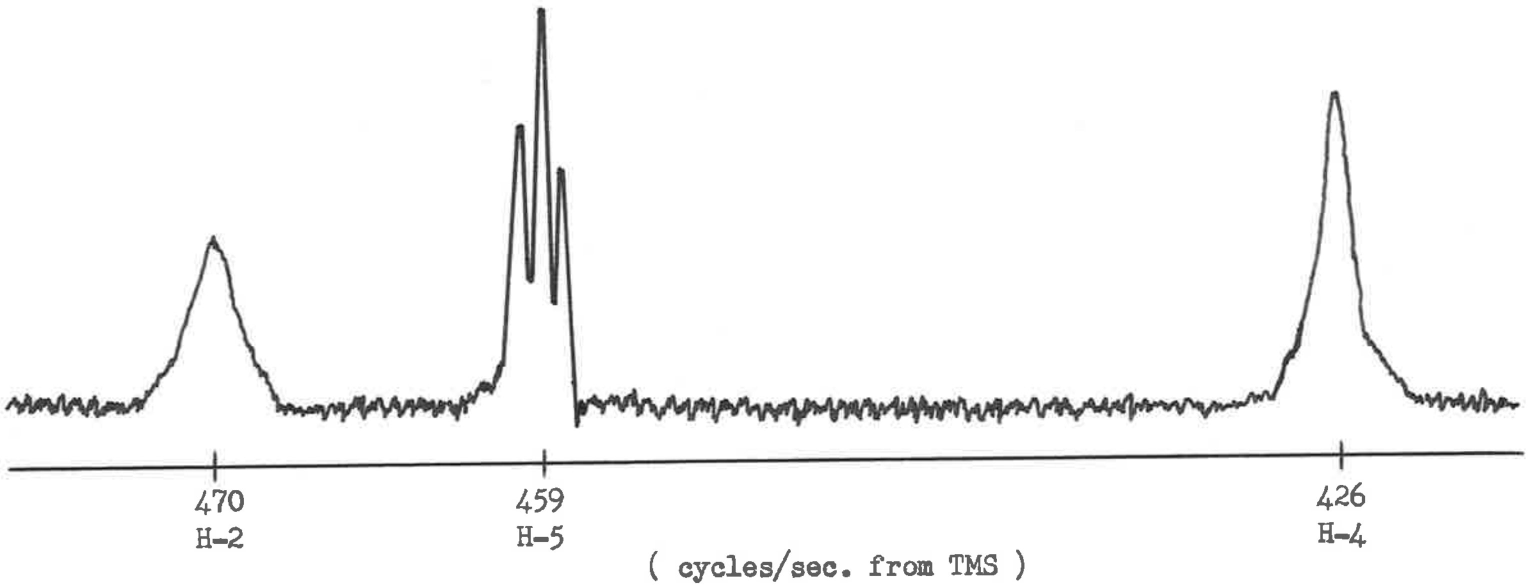


Fig. 3.2

n.m.r. spectra of Thiazole

in CCl_4

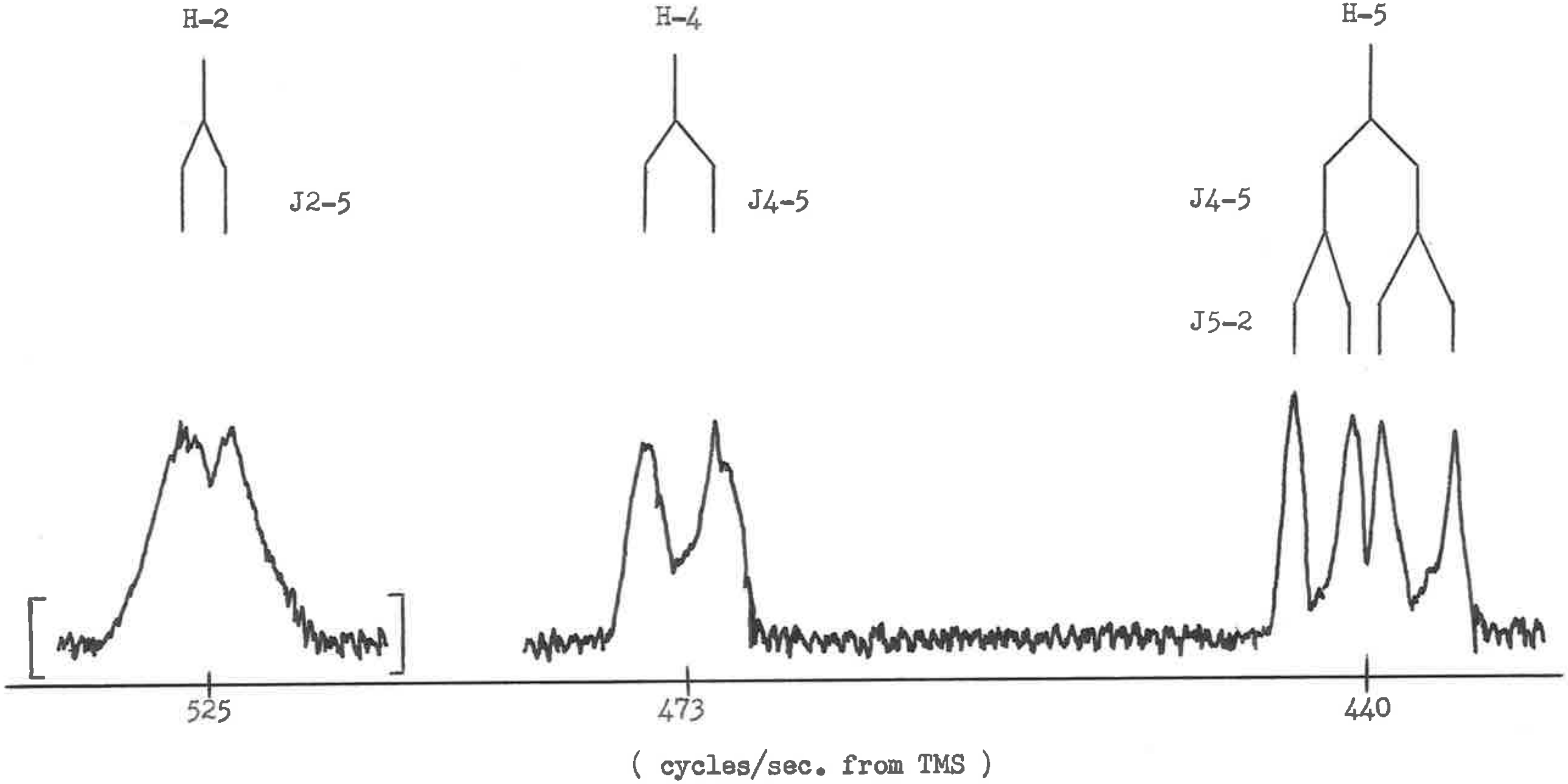


Fig. 3.3

n.m.r spectra of isoxazole

in CCl_4

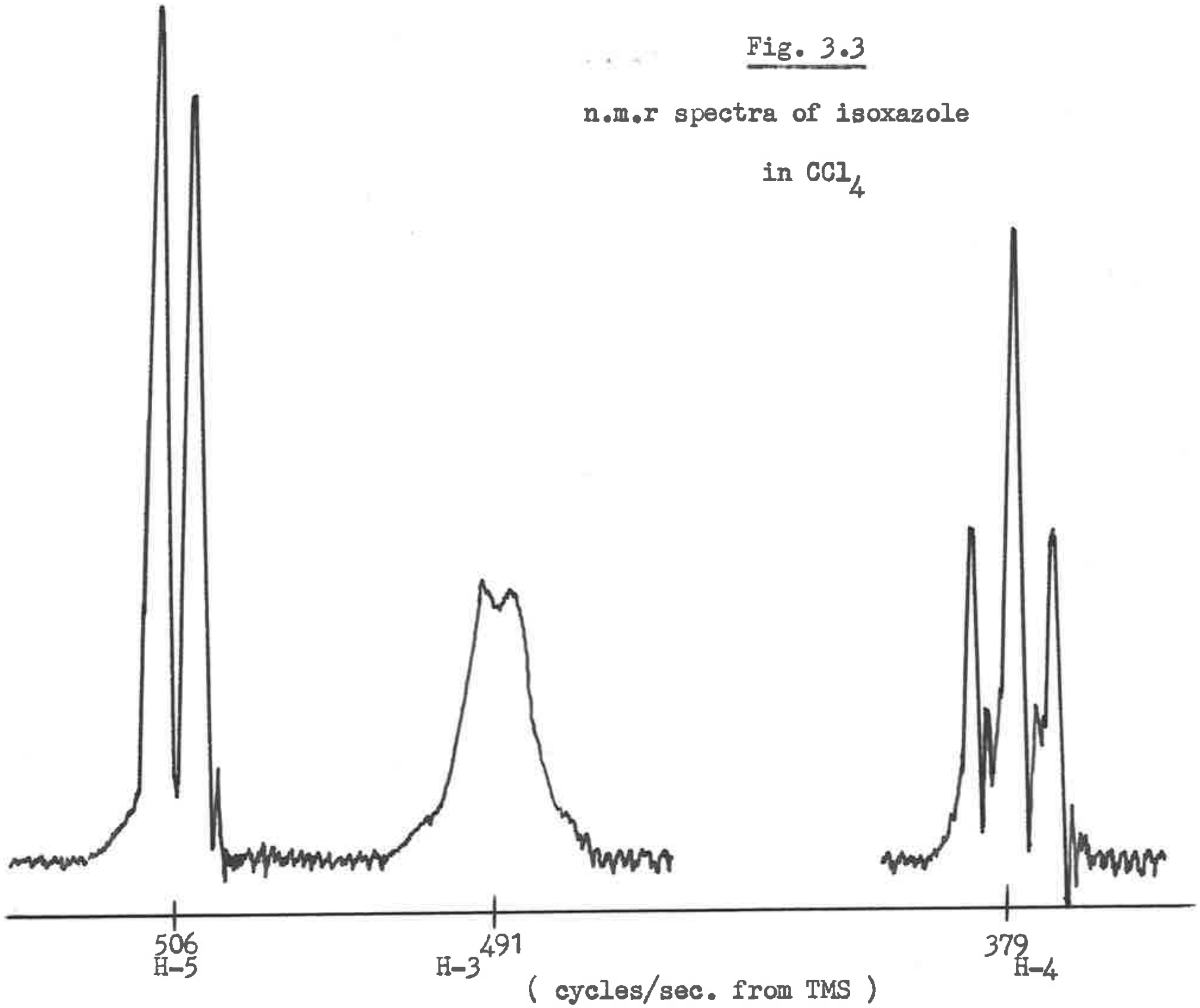
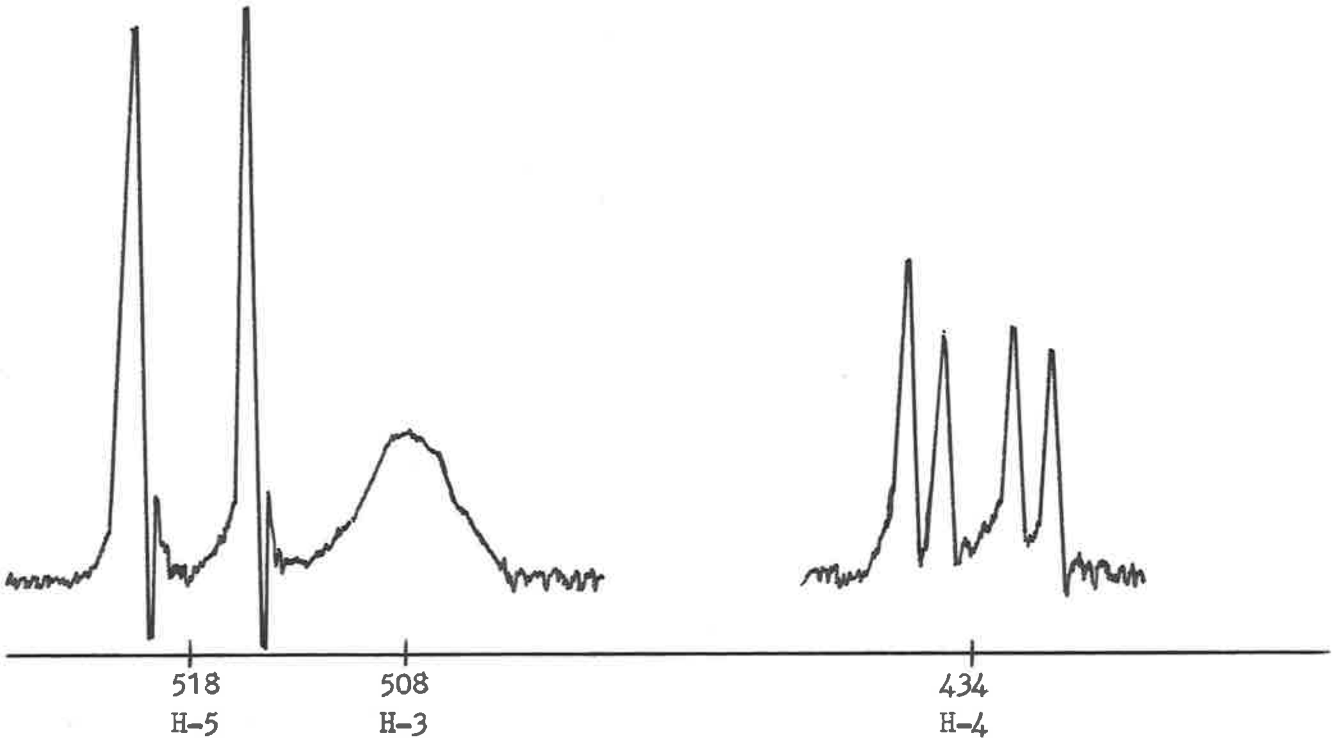


Fig. 3.4

n.m.r. spectra of isothiazole

in CCl_4



(cycles/sec. from TMS)

Table 3.1

Chemical shift data of oxazoles, thiazoles, isoxazoles, and isothiazoles (Cycles/sec. from TMS)

Compound	Solvent	H-2	H-3	H-4	H-5
2-methyloxazole	CCl_4	144.8	-	412.0	447.2
	D_2O	150.6	-	426.8	468.6
	CF_3COOD	176.1	-	461.7	489.0
4-methyloxazole	CCl_4	461.9	-	130.7	439.5
	D_2O	489.1	-	133.8	461.7
	CF_3COOD	567.4	-	150.0	481.8
thiazole	CCl_4	525.2	-	473.0	439.5
	CF_3COOD	599	-	507	493
2-methylthiazole	CCl_4	161.5	-	451.5	423.0
	D_2O	166.0	-	462.6	447.6
	CF_3COOD	187.1	-	484.4	474.2
4-methylthiazole	CCl_4	515.5	-	148.0	408.9
	D_2O	536.4	-	150.6	432.9
	CF_3COOD	585.5	-	163.4	463.1
5-methylthiazole	CCl_4	508.5	-	447.3	149.9
	D_2O	530.7	-	461.6	152.6
	CF_3COOD	582.2	-	482.6	164.7

Table 3.1 (contd).

Compound	Solvent	H-2	H-3	H-4	H-5
isoxazole	CCl_4	-	491.4	379.3	506.0
	D_2O	-	514.6	398.2	526.2
	CF_3COOD	-	507.9	393.3	513.8
3-methylisoxazole	CCl_4	-	136.9	366.4	494.9
	D_2O	-	144.6	388.4	514.6
	CF_3COOD	-	148.1	390.1	507.9
isothiazole	CCl_4	-	508.0	433.8	517.8
	D_2O	-	520.8	450.6	542.5
	CF_3COOD	-	548.7	468.8	574.6
3-methylisothiazole	CCl_4	-	152.5	421.5	512.7
	D_2O	-	153.8	434.5	531.7
	CF_3COOD	-	173.8	450.7	561.5
4-methylisothiazole	CCl_4	-	491.5	140.4	488.3
	D_2O	-	506.3	153.7	514.7
	CF_3COOD	-	532.8	154.6	548.3

***

Table 3.2.

Coupling constants in oxazoles, thiazoles, isoxazoles, and isothiazoles (Cycles/sec.)

(n.obs. = Coupling not observed)

Compound	Solvent	J2,4	J2,5	J3,4	J3,5	J4,5
2-methyloxazole	CCl_4	n.obs.	n.obs.	-	-	0.8
	D_2O	n.obs.	n.obs.	-	-	0.9
	CF_3COOD	n.obs.	n.obs.	-	-	1.3
4-methyloxazole	CCl_4	(0.5)	2.4	-	-	1.2
	D_2O	(0.6)	2.4	-	-	1.4
	C_FCOOD	n.obs.	2.4	-	-	1.4
thiazole	CCl_4	0.5	1.8	-	-	3.1
	CF_3COOD	0.9	2.2	-	-	3.6
2-methylthiazole	CCl_4	n.obs.	n.obs.	-	-	3.4
	D_2O	n.obs.	n.obs.	-	-	3.5
	CF_3COOD	n.obs.	n.obs.	-	-	4.1
4-methylthiazole	CCl_4	(0.4)	1.9	-	-	1.0
	D_2O	(0.4)	2.1	-	-	1.0
	CF_3COOD	n.obs.	2.5	-	-	0.9

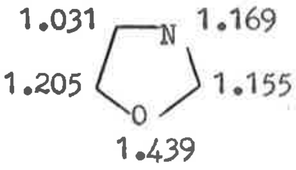
Table 3.2 (contd.)

Compound	Solvent	J2,4	J2,5	J3,4	J3,5	J4,5
5-methylthiazole	CCl_4	0.6	n.obs.	-	-	1.2
	D_2O	0.6	n.obs.	-	-	1.2
	CF_3COOD	1.1	n.obs.	-	-	1.2
		J3,4	J3,5	J4,5		
isoxazole	CCl_4	1.5	n.obs.	1.6		
	D_2O	2.0	n.obs.	1.8		
	CF_3COOD	2.0	n.obs.	1.8		
3-methylisoxazole	CCl_4	0.5	(0.3)	1.7		
	D_2O	(0.5)	0.6	1.7		
	CF_3COOD	spectrum very broad				
Isothiazole	CCl_4	1.7	n.obs.	5.0		
	D_2O	1.8	n.obs.	4.8		
	CF_3COOD	2.6	n.obs.	5.5		
3-methylisothiazole	CCl_4	n.obs.	0.4	4.4		
	D_2O	n.obs.	0.4	4.6		
	D_2O	n.obs.	n.obs.	5.5		
4-methylisothiazole	CCl_4	(0.4)	n.obs.	1.0		
	D_2O	(0.4)	n.obs.	(1.0)		
	CF_3COOD	n.obs.	n.obs.	(1.0)		

***

Table 3.3.

A. π-electron densities in oxazole, thiazole, isoxazole and isothiazole.



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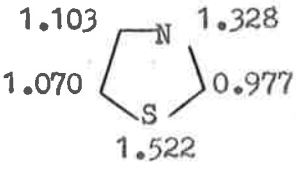

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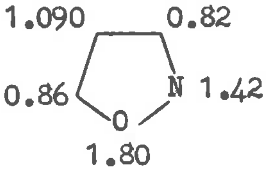

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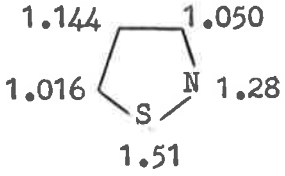

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B. Chemical shift separations between ring protons due to differences in π-electron densities. (using 10 p.p.m. per electron).

		Δ calculated	Δ found	δ
<u>Oxazole</u>	Δ 2,4	- 74 c/s	+ 44 c/s	- 118 c/s
	Δ 2,5	+ 30 c/s	+ 12 c/s	+ 18 c/s
<u>Thiazole</u>	Δ 2,4	+ 76 c/s	+ 53 c/s	+ 23 c/s
	Δ 2,5	+ 56 c/s	+ 86 c/s	- 30 c/s
<u>Isoxazole</u>	Δ 3,4	+ 162 c/s	+ 112 c/s	+ 50 c/s
	Δ 3,5	+ 24	- 15 c/s	+ 39 c/s
<u>Isothiazole</u>	Δ 3,4	+ 56 c/s	+ 75 c/s	- 19 c/s
	Δ 3,5	- 21 c/s	- 10 c/s	- 11 c/s

***

3.3 Discussion.

The observed chemical shifts shown in Table 3.1 are clearly not satisfactorily explained by variations in local π-electron densities alone, as is evident from the data and calculations listed in Table 3.3. Because of the large discrepancies between chemical shifts and π-electron densities and the unknown effects of the oxygen and sulphur atoms, the only real estimate of the effectiveness of the nitrogen anisotropy (σ_N) and lone-pair dipole (σ_D) terms can be made from changes in resonance frequencies on protonation or solvation in strong hydrogen-bonding solvents such as water. As was shown in Chapter I, protonation of the nitrogen atom removes the paramagnetic shift of both of these effects; the protons α to the nitrogen are most affected and changes in the chemical shift of these protons on protonation are thus considerably smaller than those for the other ring protons. The magnitude of the σ_N and σ_D terms can thus be estimated from the relative changes in chemical shifts of the various ring protons on protonation. The main difficulty involved in this approach however is that possible changes in π-electron distributions can seriously affect the relative shifts. It seems more profitable therefore to examine first the solvent shifts in aqueous media, as it was shown earlier in this work that hydrogen-bonding of solvent with the nitrogen lone-pair also causes a relaxation of the dipole deshielding term. The total shift in resonance frequency of each proton on protonation (ΔH^+) and on solvation in water (ΔH_2O) are shown in Table 3.4 and 3.5. For comparison, the data for the picolines are included in these tables.

A comparison of the ΔH_2O values with those of the picolines show that the solvent shifts in the five-membered heterocyclic series are consistently greater than those observed in the picolines in particular for protons adjacent to a nitrogen atom. The ΔH^+ values follow a similar pattern, with large values of ΔH^+ for protons adjacent to a nitrogen atom compared with those observed in the pyridine system. The unusually small values of ΔH^+ for the isoxazoles seem to indicate that they are in fact not protonated in CF_3COOD and these values are therefore of no use in any comparison.

The above observations suggest that the σ_N and σ_D terms are much less effective in these compounds than in pyridine, a conclusion which is not in conflict with the theory proposed by Gil and Murrell, since they can be explained qualitatively as follows:

1) σ_N:- The magnitude of σ_N in pyridine is a consequence of the low-lying $n \rightarrow \pi^*$ transition found at 4.5 eV[26] (or 276 mμ). The ultraviolet spectra of the compounds studied here have been studied by a number of workers and is summarised in Table 3.6. This shows that the position of the $n \rightarrow \pi^*$ transition must be much higher than 4.5 eV since in no case is there absorption above 240 mμ. This must therefore imply a reduction in the σ_N term relative to pyridine.

2) σ_D:- The magnitude of this effect should correlate with the donating property of the lone-pair, i.e., with the basicity of the nitrogen atom. From the available pKa data in

Table 3.4

ΔH^+ values, calculated from CF_3COOD and CCl_4 solution data (Cycles/sec.)

(figures marked * are for protons α to a nitrogen atom)

Compound	H-2	H-3	H-4	H-5	CH_3
2-methyloxazole	-	-	49.7*	41.8	31.3*
4-methyloxazole	105.5*	-	-	42.3	19.3*
thiazole	74*	-	34*	54	-
2-methylthiazole	-	-	32.9*	51.2	25.6*
4-methylthiazole	70.0*	-	-	54.2	15.4*
5-methylthiazole	73.7*	-	35.3*	-	14.8
isothiazole	-	40.7*	35.0	56.8	-
3-methylisothiazole	-	-	29.2	48.8	21.3*
4-methylisothiazole	-	41.3*	-	60.0	14.2
isoxazole	-	16.5*	14.0	7.8	-
3-methylisoxazole	-	-	23.7	13.0	11.2*
	H-2	H-3	H-4	H-5	H-6
2-picoline	-	50.9	59.9	50.5	8.8*
3-picoline	11.0*	-	64.3	52.6	13.5*
4-picoline	11.0*	51.5	-	51.5	11.0*

****

Table 3.5

Δ H_2O values, calculated from D_2O and CCl_4 solution data (Cycles/sec.)
(figures marked* are for protons α to a nitrogen atom).

Compound	H-2	H-3	H-4	H-5	CH_3
2-methyloxazole	-	-	14.8*	21.4	5.8*
4-methyloxazole	27.2*	-	-	22.2	3.1*
2-methylthiazole	-	-	11.1*	24.6	4.5*
4-methylthiazole	20.9*	-	-	24.0	2.6*
5-methylthiazole	22.2*	-	14.3*	-	2.7
isothiazole	-	12.8*	16.8	24.7	-
3-methylisothiazole	-	-	13.0	19.0	1.3*
4-methylisothiazole	-	14.8*	-	26.4	3.3
isoxazole	-	23.2*	18.9	20.2	-
3-methylisoxazole	-	-	22.0	19.7	7.7*

	H-2	H-3	H-4	H-5	H-6
2-picoline	-	17.3	18.4	16.5	1.7*
3-picoline	-0.3*	-	16.2	15.6	1.7*
4-picoline	5.1*	20.7	-	20.7	5.1*

***

Table 3.6

Ultraviolet spectra data for oxazole, thiazole, isoxazole and isothiazole.

Compound	U.V. absorption bands. $\lambda_{max.}$ in mμ.			
	A	B	Solvent	Reference
Oxazole	Little or no absorption above 220 mμ			101
Thiazole	231.5	209	n-hexane	102
Isoxazole	absent	211 (ε = 3981)	ethanol	103
Isothiazole	241.5 (ε = 6577)	not reported	-	99

Table 3.7

pKa data of pyridine, thiazole and isoxazole in aqueous solution.[104]

	pKa	Temperature
Pyridine	5.25	25°
Thiazole	2.44	20°
Isoxazole	1.3	25°

***

aqueous solution (shown in Table 3.7) it is obvious that these compounds are much weaker bases than pyridine. If it is assumed that reduced basicity implies a lower dipole moment for the lone-pair, then it follows that the σ_D term in these compounds is much smaller than the value in pyridine.

From this last argument an important point follows, since ΔH_2O values, and possibly ΔH^+ values, should then reflect the basicity of the nitrogen atom in these compounds; the smaller the value of ΔH_2O, for protons α to the nitrogen atom, the greater the basicity of the nitrogen atom. Inspection of Table 3.5 gives the following order of ΔH_2O values (discounting the values for H-2 in oxazole and thiazole):

isoxazole > oxazole > isothiazole > thiazole > pyridine

and Table 3.4 gives the following order of ΔH^+ values:

oxazole > isothiazole > thiazole > pyridine

The order of basicity in these compounds as suggested by the above argument then is:

pyridine > thiazole > isothiazole > oxazole > isoxazole

From the known basicity of pyridine, thiazole and isoxazole (Table 3.7) and the fact that isoxazole is obviously a weaker base than either oxazole or isothiazole since it failed to protonate in CF_3COOD, the known order of basicity can be written as:

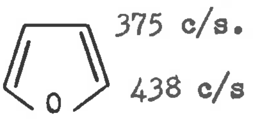
pyridine > thiazole > isothiazole > oxazole > isoxazole

The order suggested by both ΔH_2O and ΔH^+ is thus in excellent agreement with the known experimental data.

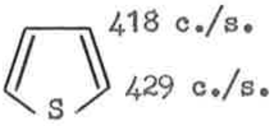
In conclusion it can be said therefore that the effect of the nitrogen atom on the chemical shift of the ring protons in these five-membered heterocyclic compounds are still satisfactorily explained by the theory of Gil and Murrell. The smaller magnitude of the σ_N and σ_D terms in these compounds is a reflection of the smaller basicity of the nitrogen atoms in these ring systems compared to pyridine. More extensive studies of the phenomenon may therefore prove it to be valuable in the estimation of pKa data.

It is not possible at this stage to obtain quantitative estimates of the σ_N and σ_D values in these compounds because of the many other factors that contribute to the chemical shifts. The very large dipole moment of isoxazole (3.01 D in dioxan[105]) for instance may well partly account for the anomalous low-field chemical shift of both H-3 and H-5 in this compound and this effect probably also operates in isothiazole as well. Ring current contributions are also difficult to estimate, but from the fact that the chemical shifts of H-5 in oxazole and thiazole, and H-4 in isoxazole and isothiazole are not very different from those in similar positions in furan[106] (XXVI) and thiophen[107] (XXVII), it can be concluded that ring currents in these molecules are probably not very different than the corresponding furan or thiophen.

Chemical shifts of ring protons.



(XXVI)



(XXVII)

C/s. from TMS.

3.4 N.m.r. spectra and stereochemistry of phenylthiazoles, isothiazoles and isoxazoles.

During the n.m.r. study of the five-membered heterocyclic compounds described in the last section, a number of readily accessible phenyl derivatives of thiazole and isoxazole were also prepared and studied. As a result of this study interesting evidence was obtained regarding the co-planarity of the two rings in these compounds which was further investigated using the results of phenylisothiazoles published recently by Olofson and co-workers.[97] From this study, and from the conclusions reached earlier regarding the stereochemistry of various bipyridyls, an important factor was established in the general problem of the stereochemistry of aryl-substituted nitrogen heteroaromatic compounds.

The chemical shifts and coupling constants of the 2-, 4-, and 5-phenyl thiazoles, 3-phenylisoxazole and 4,4'-bithiazole studied here, together with the data obtained by Olofson are shown in Table 3.8. The spectra in general were complicated by the wide spread of the signals due to the phenyl protons, but the heterocyclic ring protons could be assigned without difficulty.

Because of the complexity of the spectra in CF_3COOD, and the insolubility of the phenyl compounds in water, no useful information could be obtained about the anisotropy of the nitrogen atom. However, important evidence regarding the planarity of the two rings was obtained from two independent observations. The first of these was a comparison of the chemical shifts of protons ortho to the phenyl group with those in the unsubstituted molecule. In a co-planar conformation of the two rings, these protons in the phenyl compounds will be considerably deshielded by the ring current of the phenyl group, whereas in non-planar conformations they will be less affected.

Table 3.8

N.m.r. spectra data for phenyl substituted thiazoles, isoxazoles, and isothiazoles. (CCl_4 solution)

A Chemical shifts. (cycles/sec. from TMS)

Compounds	H-2	H-3	H-4	H-5	Phenyl (average)	Phenyl (spread)
2-phenylthiazole	-	-	465.9	432.0	458	50
4-phenylthiazole	523.7	-	-	468.8	458	50
5-phenylthiazole	516.6	-	478.0	-	443.4	24
5-phenylisoxazole	-	488.2	384.9	-	448	25
4,4'-bithiazole	523.3	-	-	471.0	-	-

Table 3.8 (contd.)

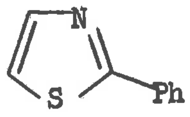
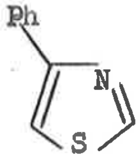
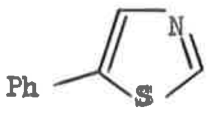
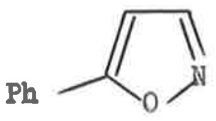
Compound	H-2	H-3	H-4	H-5	Phenyl (average)	Phenyl (spread)
Olofson's data: (in $CDCl_3$)						
3-phenylisothiazole	-	-	464	528	471	57
4-phenylisothiazole	-	506	-	516	440	40
5-phenylisothiazole	-	509	?	-	449	30

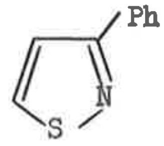
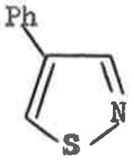
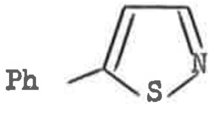
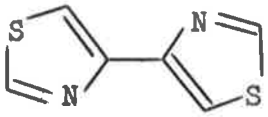
B. Coupling constants (Cycles/sec.)

Compound	J3,4	J4,5	J2,5
2-phenylthiazole	-	3.3	-
4-phenylthiazole	-	-	1.9
5-phenylthiazole	-	-	-
5-phenylisoxazole	1.8	-	-
3-phenylisothiazole	5.0	-	-
4-phenylisothiazole	-	-	-
5-phenylisothiazole	2.0	-	-
4,4'-bithiazole	-	-	2.0

***

Secondly, a similar phenomenon must be expected for the ortho protons in the phenyl ring due to contributions from the heterocyclic ring. The estimated stereochemistry of each compound can be summarised as follows:

COMPOUND	Conformation	Evidence
	near-planar	a) very large spread of phenyl protons (50 c/s)
	near-planar	a) H-5 shifted -29 c/s relative to thiazole. b) Very large spread of phenyl protons (50 c/s)
	non-planar	a) H-4 shifted only -5 c/s. relative to thiazole. b) Spread of phenyl protons only 24 c/s.
	non-planar	a) H-4 shifted only -5 c/s. relative to isoxazole. b) Spread of phenyl protons only 25 c/s.

COMPOUND	Conformation	Evidence
	near-planar	a) H-4 shifted -26 c/s relative to isothiazole. b) Spread of phenyl protons as much as 57 c/s.
	non-planar	a) H-3 shifted only -8 c/s, and H-5 only -6 c/s relative to isothiazole. b) Smaller spread of phenyl protons (40 c/s) compared to 3-phenyl isomer.
	non-planar	a) Phenyl protons spread only 30 c/s. b) H-4 overlapped by phenyl protons. Upper limit of shift 26 c/s.
	near-planar (assume trans)	a) H-5 shifted -32 c/s relative to thiazole. b) H-2 not shifted.

Ultraviolet spectra of such systems are also markedly dependent on the degree of planarity as was found in Chapters I and II. Such data is available in the literature and is shown in Table 3.9.

Table 3.9

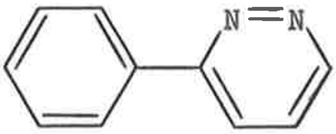
Ultraviolet spectra of phenyl-substituted thiazoles, isoxazoles, and isothiazoles. (only the long-wavelength band is listed)

Compound	λ max.	log ε	References
4-phenylthiazole	252 mμ	4.14	108
5-phenylthiazole	275 mμ	4.11	108
3-phenylisoxazole	240 mμ	4.09	109
4-phenylisoxazole	236 mμ	4.08	109
5-phenylisoxazole	260 mμ	4.26	109
3-phenylisothiazole	291 mμ	3.81	97
	283 mμ	3.99 (shoulder)	
	270 mμ	4.18	
4-phenylisothiazole	266 mμ	4.14	97
5-phenylisothiazole	266 mμ	3.90	97

***

An inspection of this table shows that only in the isothiazole series does the ultraviolet absorption data appear to agree with the n.m.r. conclusions, but it is possible that other factors may play a role in determining the position of the long-wavelength band.

The important conclusion that can be reached from the results of the n.m.r. study is that only in those compounds where the phenyl group (or heterocyclic ring) is substituted α to the ring nitrogen atom are the two rings held in a planar or near-planar conformation. This conclusion is in accordance with the results of the bipyridyls studied in Chapter I, where it was found that only 2,2'-bipyridyl preferred a planar conformation with the 3,3'- and 4,4'-isomers both enjoying a considerable amount of rotational freedom. 3-Phenylpyridazine (XXVIII) has also been assigned a planar conformation by Crossland,[34] a result in agreement with the above hypotheses.



(XXVIII)

It appears evident therefore that a heterocyclic nitrogen atom, probably through the influence of its lone-pair is possible to hold any aromatic ring <u>ortho</u> to it in a co-planar conformation. Substitution at other positions immediately results in greater rotational freedom.

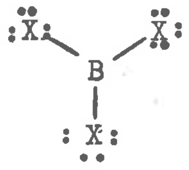
This hypothesis may prove to be useful in the prediction of the stereochemistry of such compounds, and also in the interpretation of their n.m.r. and ultraviolet spectra. A much wider application of this concept, both experimentally and theoretically, is needed at this stage in order to gain a full insight into the entire problem.

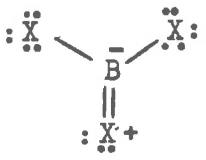
CHAPTER IV

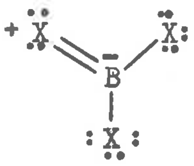
The nuclear magnetic resonance spectra of pyridine-boron trihalide complexes

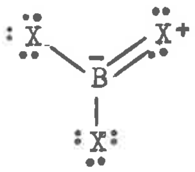
4.1 Introduction.

In the previous chapters it has been shown that important information regarding the interpretation of chemical shifts in nitrogen heterocyclic compounds can be obtained from the relative changes in chemical shifts of the ring protons on protonation. It was regarded of interest to examine in this light the chemical shift changes in the formation of some pyridine complexes, where the H^+ function is replaced by a powerful Lewis acid such as a boron trihalide. The acidity of boron trihalides can be regarded as being due to the possession of the boron atom of an unfilled low-lying orbital, and to some formal positive charge which the atom bears because of the polarity of the B - X bonds. Pauling[110] suggested that besides the more conventional structure (A) of the boron halides, other structures involving polar contributions (B, C, and D) could be expected to contribute to the resonance structure.


(A)


(B)


(C)


(D)

This is due to the fact that boron possesses a fourth stable orbital which can be used for bond formation.

As a result of this, the boron halides are powerful complexing agents with organic molecules, in particular amines, carbonyls, nitriles, and ethers.[111-114] Of particular interest has been the relative acceptor power of the boron halides towards organic bases. It was originally thought on electronegativity grounds that boron trifluoride (BF_3) was the strongest Lewis acid of the group,[113] but more recently, thermodynamic data of the formation of such complexes suggested a reverse of this order.[115] The now accepted order of acidity in the boron halide series is:

$$BBr_3 > BCl_3 > BF_3$$

Brown and Holmes[115] postulated that structures involving back co-ordination (e.g. Structures B, C, and D) explain the observed order. They reasoned that back co-ordination is more favourable with BF_3 than in the other halides as suggested by the much shorter B - F bond length,[110] and that this results in a reduction of the net positive charge on the boron atom as well as saturating the spare orbital. Cotton and Leto[116] have calculated the reoganization energies for the boron halide molecules on changing from sp^2 to sp^3 hybridisation. These were found to be:

BF_3	BCl_3	BBr_3
48.3 kcal/mole	30.3 kcal/mole	26.1 kcal/mole

They thus concluded that unless the reorganised BF_3 molecule forms a complex with the release of 18 kcal/mole more energy than is released when reorganised BCl_3 forms a bond to the same donor, it will be the weaker Lewis acid. A number of experimental techniques have been employed to substantiate the relative acceptor strengths[117-119] and in particular, changes in the chemical shift parameter of protons on the ligand group on complex formation have been correlated with acceptor strengths.[120-123] The validity of this approach is questionable, since the underlying theory of such a correlation has never been established. It is also clearly erroneous to interpret chemical shift data of the complexes in terms of properties of the unbonded boron halides. Arguments relating such data with the nature of the donor-acceptor bond are more meaningful, but no such specific correlation has as yet been presented.

Numerous n.m.r. studies of the boron halide complexes of various nitrogen bases are recorded in the literature. Gates and co-workers[123] studied triethylamine and some pyridine complexes, and Miller and Onyszchuk those of acetonitrile[121] and trimethylamine.[120] A number of amine complexes were studied by Coyle and Stone,[124] Heitsch,[122] and Greenwood, Hooton and Walker.[125] Heitsch concluded that ^{11}B resonance data gives a poor criterion of complex stability, whereas chemical shifts of protons on either the boron atom or on the ligand can be correlated with enthalpies of formation provided the variations in structure of the compounds are held within narrow limits. The fundamental question regarding the exact nature of such a correlation with n.m.r. data however still remains. Chemical shifts are strongly influenced by many factors such as local electron densities and the presence of local shielding or deshielding groups or bonds. It is possible that variations in any of these terms between the different compounds are responsible for the effects observed by these workers. In this work as well as making a comparative study of the chemical shifts in pyridine-boron halide complexes with those in the protonated base, an attempt is made to clarify the relationship between n.m.r. spectra and donor-acceptor bond strength.

4.2 The n.m.r. spectra of boron halide complexes of some alkyl-substituted pyridines.

The alkyl-substituted pyridines studied here were chosen rather than pyridine itself in order to simplify spectra interpretation and analysis. In addition valuable data is also available from the chemical shifts of the alkyl protons. The study at first was confined to the complexes of α, β, and γ-picoline, and the 2-ethyl and 2-benzyl-pyridines added later to investigate interesting steric and solvation effects. The chemical shifts of the various protons in the free base, the boron halide complex and in the cation are listed in Table 4.1. The spectra were analysed as either ABMX or A_2X_2 spin systems, and although the approximations involved in many cases is appreciated, the method was considered adequate because of the broad nature of the spectra. The estimated accuracy of the chemical shifts is ± 1 c/s.

The spectra of the complexes were recorded both in chloroform and acetone solution, and in a number of cases, interesting solvent effects were observed in acetone solution. This phenomenon was most marked in the 2-substituted pyridine complexes and was further investigated in detail. The data listed in Table 4.1 however is that of the true complex, recorded immediately after the preparation of the solution. The spectra of each complex was checked carefully using freshly prepared samples, but no noticeable variations were observed. Because of the solvation effects, it was decided not to recrystallise the complexes. The complexes were prepared by adding the boron halide to a solution of the base in carbon tetrachloride. The precipitated complex was then washed with excess solvent and dried under vacuum. Analysis data confirmed the presence of 1:1 complexes in all cases. The BBr_3 complex of 2-benzylpyridine were too unstable in solution and the spectra could not be interpreted. Similar difficulties were found for the BF_3 complex of 2-benzylpyridine in chloroform solution and of 3-methylpyridine in acetone.

Appreciable spin-spin coupling was found between α-protons and the ^{11}B nuclei in BCl_3 and BBr_3 complexes. Boron exists predominantly as either ^{10}B or ^{11}B, the natural abundance being approximately 1:4 respectively.[126] Both isotopes are n.m.r. active, but only coupling with the more abundant ^{11}B nuclei was clearly visible. The observed coupling constants were all found to be about 3.4 c/s, and an example of this phenomenon is shown in Fig. 4.1. Coupling could not be clearly resolved in the 3-picoline complexes due to the overlap of the H-2 and H-6 signals.

4.3 Discussion of chemical shift data.

An interpretation of the chemical shifts in the pyridine complexes must take into account the following factors:

1. Removal of the nitrogen anisotropy and lone-pair dipole effects.
2. Deshielding to any positive charge on the nitrogen atom in the complexes.
3. Shielding or deshielding contributions from the BX_3 group.

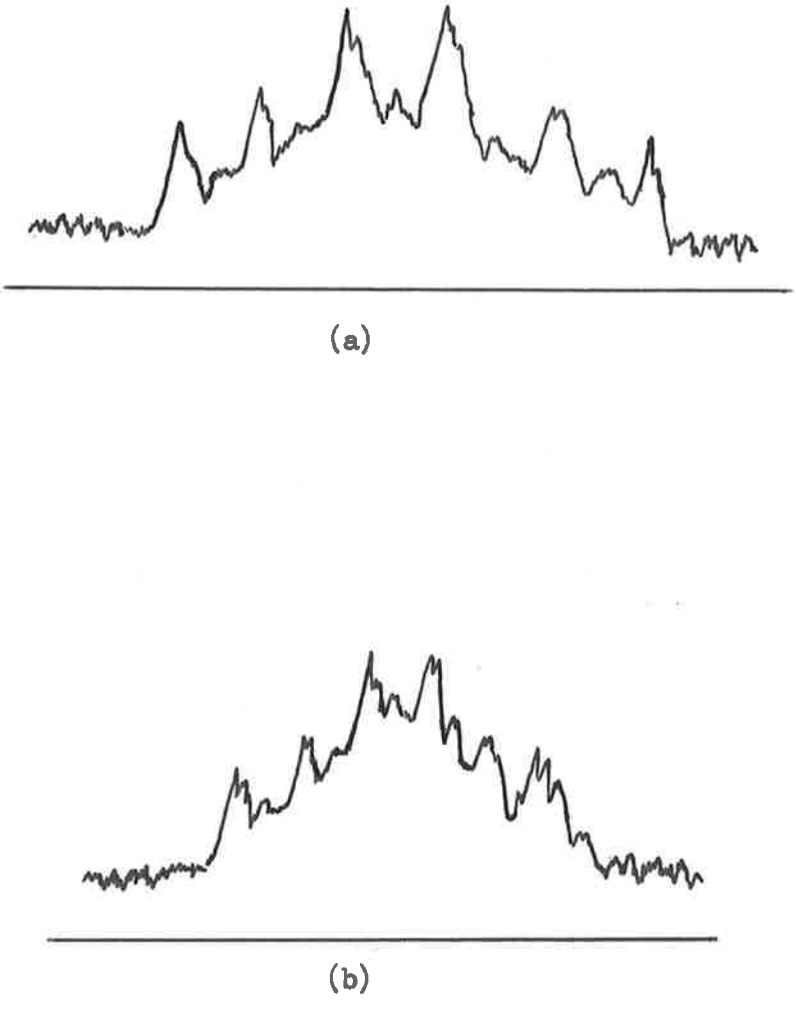


Fig. 4.1

(a) n.m.r. spectra of H-2,6 in
4-methylpyridine:BCl_3

(b) n.m.r. spectra of H-6 in
2-methylpyridine:BCl_3

Because of the many unknown parameters involved, a quantitative determination of the last two factors is not possible. It is possible however to discuss the problem qualitatively by a comparison with protonation effects in the pyridine system. In order to make such a study it is necessary to carry out a suitable breakdown of the chemical shift data in Table 4.1. Two empirical methods were here adopted. Table 4.2 shows the changes in chemical shifts of the various protons on complex formation (Δ H), using the data of both free base and complex in chloroform solution. Protonation shifts are also included and are for CF_3COOD solutions. The Δ H values for H-5 and H-6 are of special interest since they are positions common to all the compounds studied. Table 4.3 lists ratios of Δ H values between protons in the same molecule (R). These were calculated to compare relative changes in chemical shifts within a molecule on complex formation with those due to protonation. Because of the complicating factors arising from the presence of the BX_3 group, only R values between protons non-adjacent to the nitrogen atom can give a reasonable comparison. Thus the value of $R_{5,6}$ in a given complex is approximately equal for the 3- and 4-methylpyridines, but is sharply attenuated in the 2-substituted compounds. Only in the case of BF_3 complexes is $R_{5,6}$ comparable to the protonation value which implies strong deshielding contributions from the BCl_3 and BBr_3 groups since an R value between two protons non-adjacent to the nitrogen atom e.g. $R_{5,4}$, remains surprisingly constant between the different acid functions used and also between the different pyridine compounds studied, although a definite small increase of $R_{5,4}$ is apparent between protonation and complex formation with BBr_3. Basically these observations point to the fact that the electronic changes in the pyridine molecule on complex formation and on protonation are closely related.

The actual magnitude of these electronic changes appear to be much smaller in the complexes than in the cation as is evident from the Δ values. Three main points are evident from Table 4.2. Firstly, the Δ values for protonation are considerably greater than those for complex formation. Secondly, the Δ values for the different boron halides used are of the same order of magnitude, with small but definite increases between BF_3 and BBr_3, and lastly the Δ values for the 2 and 6 protons in the BCl_3 and BBr_3 complexes are unusually large, particularly in 2-substituted pyridines. Regarding the first point, it seems that this is a reflection of a difference in positive charge distribution between the cation and the complex. In the cation a full positive charge is distributed in the ring, but since the complexes are zwitterionic, the deshielding due to the positive charge is partly neutralised. The second observation shows that there are no major differences in the electronic changes of the pyridine ring on complex formation with the different boron halides, and lastly it is very clear that the BCl_3 and BBr_3 groups have large deshielding characteristics compared to the BF_3 group. This point is also evident from the unusual R values involving protons 2 or 6 in the BCl_3 and BBr_3 complexes. It is possible to estimate the magnitude of the deshielding due to the BX_3 groups at the α-protons by using the R values for protonation to calculate the theoretical value of ΔH-2 or ΔH-6. The difference between this value and the observed one then can be attributed to the BX_3 anisotropy. The results of these calculations are summarised in Table 4.4 It is encouraging to note that the anisotropy term calculated for each halide is nearly identical in each compound except at H-6 in 2-substituted pyridine complexes for which this term is considerably larger. A possible explanation of this phenomenon may be found along the lines of the "buttressing effect" postulated by Adams.[127-129] According to this theory the interaction between the 2-substituent and the BX_3 group forces the two groups slightly apart, thus pushing the BX_3 group closer to the 6 proton as shown in Fig. 4.2. The closer proximity of H-6 to the BX_3 group then accounts for the extra large ΔH-6 value in these complexes. The effect of this steric strain caused by α-substituents has also been studied by Brown and Holmes[130] from the heats of formation of these complexes. Their results show that bulky α-substituents significantly decrease the strength of the donor-acceptor bond. In the free bases this "buttressing effect" may also explain the

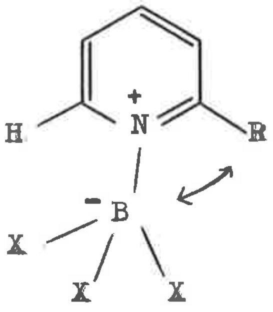


Fig. 4.2

gradual downfield shift of H-6 on increasing the size of the 2-substituent, as well as the fact that the Δ values for H-6 on protonation become progressively smaller as illustrated in Table 4.5.

Table 4.5.

Chemical shifts of H-6 in substituted pyridines and their cations. (in cycles/sec. from TMS)

	Substituent			
	4-methyl	2-methyl	2-ethyl	2-benzyl
H-6 ($CDCl_3$)	507	509	511	512
H-6 (CF_3COOD)	518	518	518	517
Δ H-6	11	9	7	5

The steric repulsion of the lone-pair from the 2-substituent increases the deshielding to these electrons at the 6-position, and since this dipole term is removed on protonation, the resonance frequencies of H-6 become nearly identical in the cations of these compounds.

From the discussion so far, the following points have thus emerged:

1. The Δ values of the pyridines on complex formation parallel those due to protonation, but are of smaller magnitude due to the zwitterionic character of the complexes.
2. The diamagnetic anisotropy of the BF_3 group is quite small, unlike that of the BCl_3 and BBr_3 groups which cause large downfield shifts of the α-protons.

3. Considerable steric interference exists between 2-substituents and the BX_3 groups which shows itself by further downfield shifts of the opposite α-proton.

It follows therefore that the chemical shifts of the boron trihalide-pyridine complexes interpreted in the light of the above mentioned points then give no indication as to the relative strengths of the donor-acceptor bonds.

4.4 Conformational aspects in the complexes of 2-ethyl and 2-benzylpyridine.

In 2-ethyl and 2-benzylpyridine considerable rotational freedom can be expected for the 2-ethyl and 2-benzyl groups in the free base, but a severe restriction of rotation about the C_2—CH_2R bond must occur in their complexes. Thus two extreme conformations can be drawn for these complexes as shown in Fig. 4.3.

Fig. 4.3.

(a) (b)

Conformation (b) is expected to be sterically more favourable, and evidence that this conformation is in fact preferred is given by the n.m.r. spectra of these complexes. In conformation (b) the methylene protons are in very close contact with the BX_3 group and should therefore experience a larger downfield shift than the methyl protons in 2-methylpyridine. Inspection of the Δ values of the BCl_3 and BBr_3 complexes in Table 4.2 shows this to be the case. In 2-ethylpyridine complexes, further information is available from the very small downfield shift of the $-CH_3$ protons (8.6 c/s and 11.0 c/s for the BCl_3 and BBr_3 complexes respectively), as much larger values would be expected for these protons in conformation (a). Very interesting information regarding the stereochemistry of 2-benzylpyridine complexes was obtained from inspections of the signal due to the phenyl protons and the resonance frequency of the 3-proton. The signal due to the phenyl protons appeared as a narrow line about 5 c/s wide and only slightly shifted from its position in the free base. Furthermore the 3-proton absorbs at much higher field than the 5-proton, which is consistent with the conformation shown in Fig. 4.4.

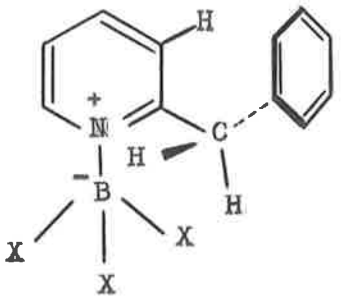


Fig. 4.4

With the phenyl ring at right angles to the pyridine ring for minimum steric interaction, proton 3 is situated in the shielding region of the phenyl ring thus accounting for the upfield shift of H-3 compared to H-5. The phenyl protons in this conformation are also removed from the influence of the BX_3 group, thus explaining the appearance and position of their n.m.r. signal. Little steric rigidity is apparent in the cations or BF_3 complexes. The chemical shifts, Δ values and R values involving H-6, H-3 and the methylene protons appear normal, and the resonance lines due to the phenyl protons in the cation are spread over about 25 c/s. The much smaller steric requirements of the proton and BF_3 groups are therefore insufficient to prevent free rotation of the 2-substituent.

4.5 Solvation effects of the complexes in acetone solution.

Strong solvation effects were observed during the recording of the spectra of the BCl_3 and BBr_3 complexes in acetone solution. The solutions on standing showed gradual changes in the n.m.r. spectra together with the formation of a white precipitate in the sample tube. The spectra of a fresh solution shows a signal due to the α-protons at very low field on which $^{11}B - H$ coupling is clearly visible. This signal on standing slowly diminished in size, re-emerging at much higher field but without the B - H coupling. The phenomenon is illustrated in Fig. 4.5. These solvation effects were most pronounced with the 2-substituted pyridine complexes and were investigated in detail in the BCl_3 complex of 2-ethylpyridine.

Fig. 4.5 (a)

n.m.r. spectra of 2-ethylpyridine:BCl_3 in acetone.

Recorded immediately after preparing solution.

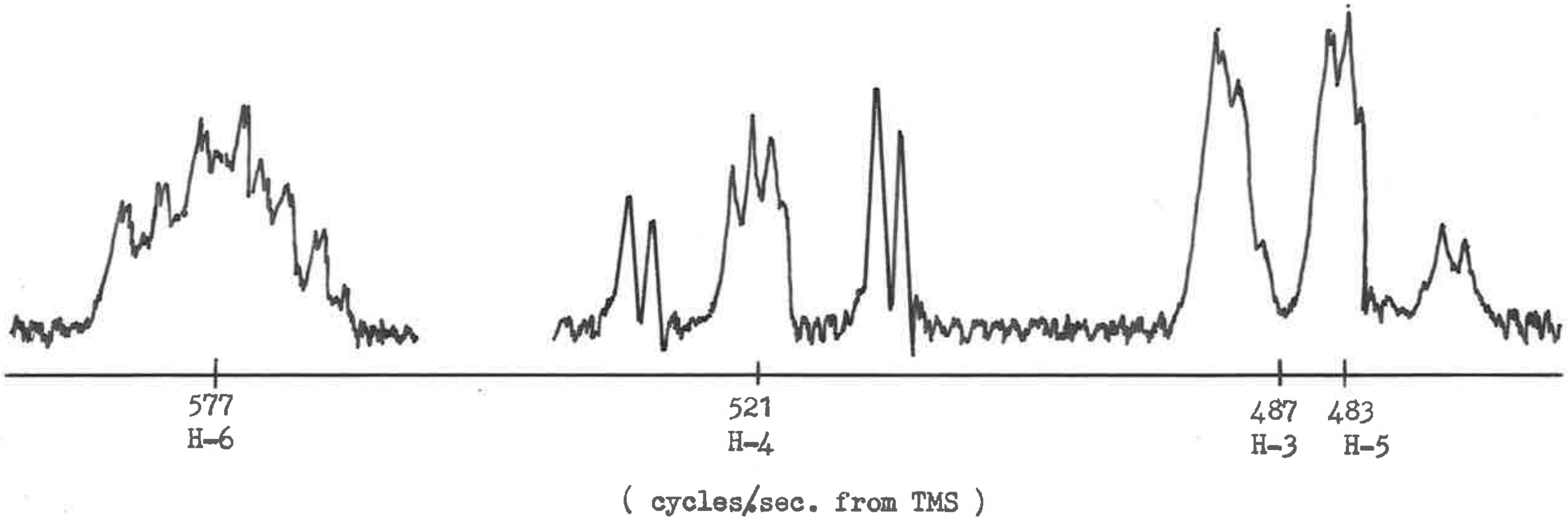
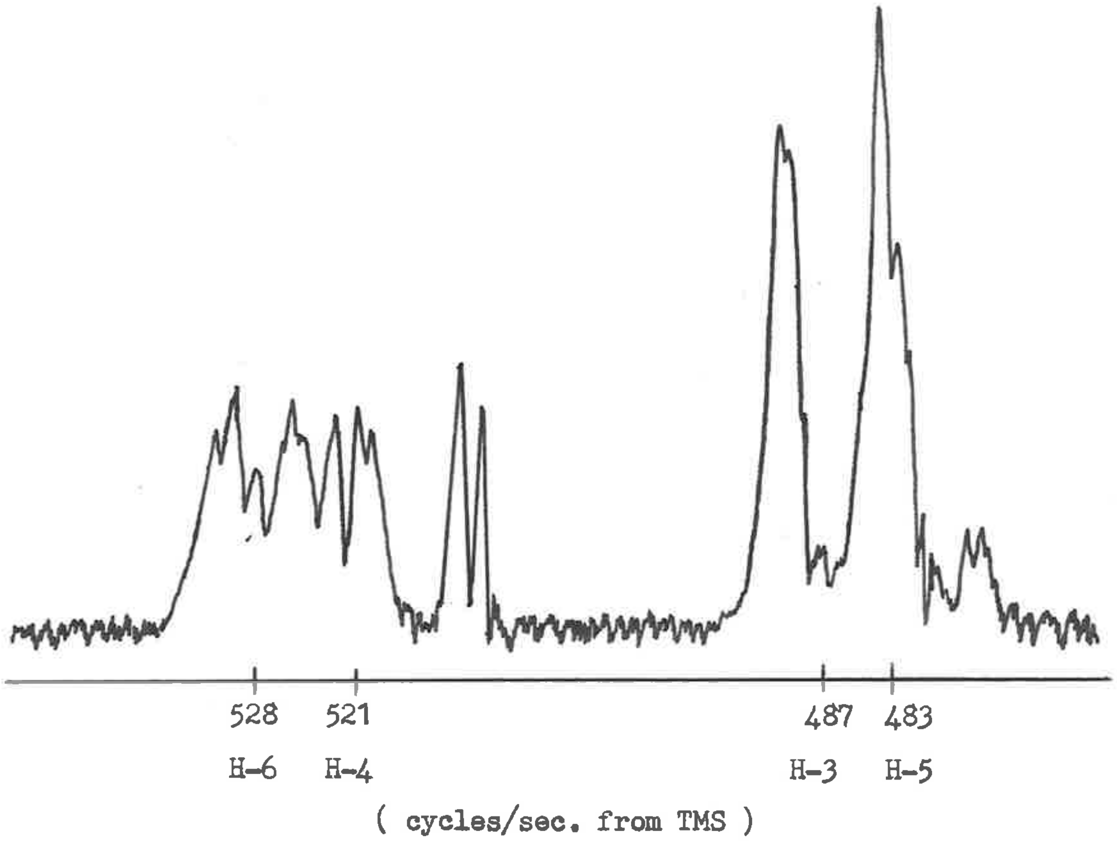


Fig. 4.5 (b)

n.m.r. spectra of 2-ethylpyridine:BCl_3 in acetone.

Recorded after 30 min. of preparing the solution.



Several gram of the 2-ethylpyridine BCl_3 complex was dissolved in acetone and the white precipitate that resulted on standing filtered and carefully dried under high vacuum at room temperature. The material, which appeared to be only moderately stable, was found to be highly insoluble in both acetone and water, but very soluble in acetone containing a small quantity (5-10%) of water. The n.m.r. spectra of such a solution made up in acetone-D_2O was identical with that shown in Fig. 4.5 (b), except that an additional signal appeared in the region 300-400 c/s from TMS, the exact location depending on the concentration of D_2O used. This signal gradually increased in size, with the final intensity proportional to the amount of D_2O used. An identical sample prepared in acetone -H_2O produced a similar signal which showed no change in intensity. It is clear from this study that this signal is due to H_2O protons, and that a fairly rapid H-D exchange between the acetone and D_2O is taking place. The precipitate itself was suspected to be a solvated acetone complex, e.g. (pyridine:BX_3):n(acetone).

No suitable solvent was available to verify the acetone moiety in this molecule, but a sample of this material was decomposed by hot D_2O in a sample tube, taking care to avoid loss of vapours. The n.m.r. spectra of the resulting solution was then recorded and showed a sharp acetone signal which slowly diminished in size, with a corresponding increase in the signal due to the water protons. Total integration of both of these signals amounted to six protons per mole of pyridine base, which shows the complex to be solvated with one mole of acetone.

The donor-acceptor bond in the solvated complex has clearly been affected since both the B-H coupling and the large BX_3 anisotropy effects are removed on solvation. Solvation of the 2-ethyl and 2-benzylpyridine complexes also have conformational consequences. The methylene protons in both cases are shifted appreciably upfield and the 3-proton in the 2-benzyl complexes assume resonance frequencies comparable to that of the 5-proton. It is thus apparent that the structure of the pyridine-BX_3 complexes are considerably affected on solvation, but the exact nature of these changes still remain obscure.

4.6 ^{11}B-H spin-spin coupling in BX_3 complexes.

As pointed out in earlier parts of the discussion, spin-spin coupling was observed between the ^{11}B nuclei and α-protons in the pyridine ring in BCl_3 and BBr_3 complexes. ^{11}B has a spin number of 3/2, so that coupling with protons causes each proton line to be split into an equal quartet. The ^{10}B nucleus is also n.m.r. active having a spin number of 3, thus splitting proton lines into seven equal lines, but such coupling is difficult to detect because of the low abundance of this isotope. Because of the broad nature of the signals, accurate values of the B-H coupling constants were not obtainable in this work, but those recorded were found to have a value of 3.4 c/s. Such coupling in BF_3 complexes was not clearly visible and if present must be quite small. The phenomenon is well documented in the literature, but considerable confusion exists at present about the presence of B-H coupling in BF_3 complexes of nitrogen bases.

Gates and co-workers[123] stated that the α-resonance signals of pyridine -BX_3 complexes were complicated by coupling to either ^{14}N, ^{11}B, or the ^{10}B nuclei, but gave no further details or illustrations of this effect. Miller and Onyszchuk[120] reported the methyl resonance of $(Me)_3N{:}BF_3$ in chloroform solution as a slightly broadened singlet, whereas Heitsch[122] described the spectra of the same compound in acetonitrile solution as an approximate 1-3-4-4-4-4-4-4-3-1 decet due to coupling of the methyl protons with both the ^{11}B, ^{10}B, and F nuclei. He also reported a similar pattern for $(C_2H_5)_3N{:}BF_3$ and further commented on the failure of previous workers to observe these splittings, suggesting that this was due to a lack of spectrometer sensitivity. On a careful inspection of the original papers of these authors however, this conclusion seems to be unfounded. On the other hand, Greenwood, Hooton and Walker[125] did find B-H coupling in a number of primary and secondary amine BF_3 complexes in aqueous solution.

The mechanism of this B-H coupling and the factors affecting it have so far remained obscure. Miller and Onyszchuk[120] have suggested that restricted rotation about the B-N bond is necessary for such coupling to be appreciable. This appears to be an unlikely explanation since primary and secondary amine BF_3 complexes clearly show coupling whereas in the sterically unfavourable tertiary amine this is disputed. It was shown in the last section that solvent interaction caused the removal of B-H coupling which suggests that the nature of the solvent used may well influence the observance of coupling with the boron atom.

Spin-spin coupling is transmitted predominantly through the σ-bond framework of molecules, and is strongly influenced by the nature of chemical bonds and the presence of strong electron withdrawing or releasing substituents. For instance in the olefinic series it has been shown that the vicinal coupling constant across the double bond is markedly decreased by electron-withdrawing groups.[131] A possible explanation of the B-H coupling effects observed here may thus lie in the nature of the B-N bonds. The stronger BCl_3 and BBr_3 complexes show B-H coupling in all cases reported both in the literature and in this work, whereas the weaker (thermodynamically) BF_3 complexes show, if at all, very much smaller coupling constants. The reported values in the $(CH_3)_3N{:}BX_3$ complexes are:

	$J\ ^{11}B\text{-}H$
$(CH_3)_3N{:}BF_3$[122]	1.54 c/s
$(CH_3)_3N{:}BCl_3$[120]	2.7 c/s
$(CH_3)_3N{:}BBr_3$[120]	2.8 c/s

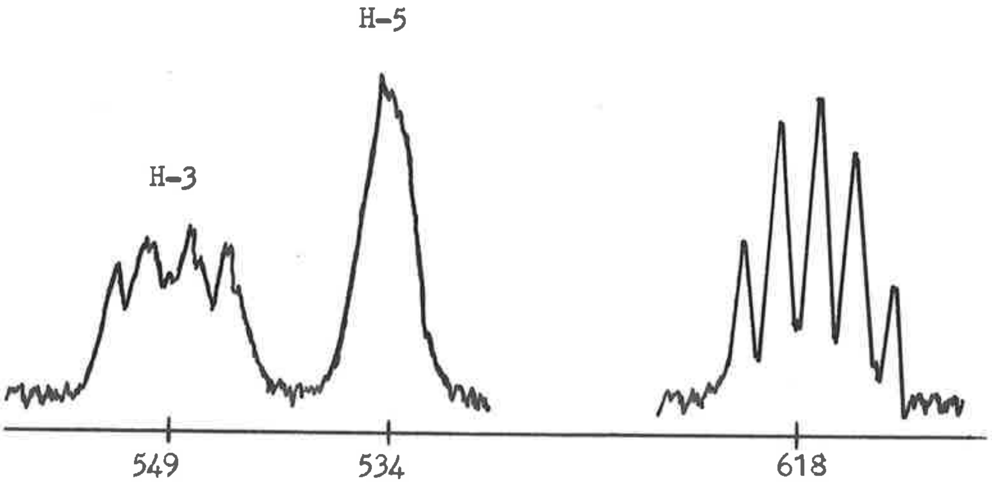
This order agrees well with the observed order of B-N bond strengths. Furthermore, the sterically more favourable methylamine and dimethylamine BF_3 complexes show coupling constants of 2.0 and 1.8 c/s respectively,[122] greater than the value for the trimethylamine complex listed above. The solvated pyridine:BX_3 complexes discussed earlier also showed no coupling, which may be due to the weakening of the B-N bond by the acetone, but since the exact structure of this system is still uncertain no reliable information can be obtained from this phenomenon.

It does appear however from the above observations, that the factors influencing the presence and magnitude of B-H coupling in these complexes include strong contributions from the amount of orbital overlap in the donor-acceptor bond, i.e., from the actual strength of this bond. This shows that coupling constants and not chemical shift data can be correlated with the heats of formation of these complexes. A more comprehensive study of this effect including the effects of solvents on the B-H coupling constants will prove valuable in the full interpretation of this phenomenon.

4.7 Boron halide complexes of thiazoles and isothiazoles.

In order to further test the conclusions reached in this chapter, the boron halide complexes of some of the heterocycles studied in Chapter III were prepared and studied. Some methyl-substituted thiazoles and isothiazoles were chosen in this study because of the inert behaviour of the sulphur atom towards the boron halides, e.g. thiophen itself showed no ability to form complexes whereas furan at room temperature reacted violently. Table 4.7 lists the chemical shifts and Tables 4.8 and 4.9 the Δ and R values respectively.

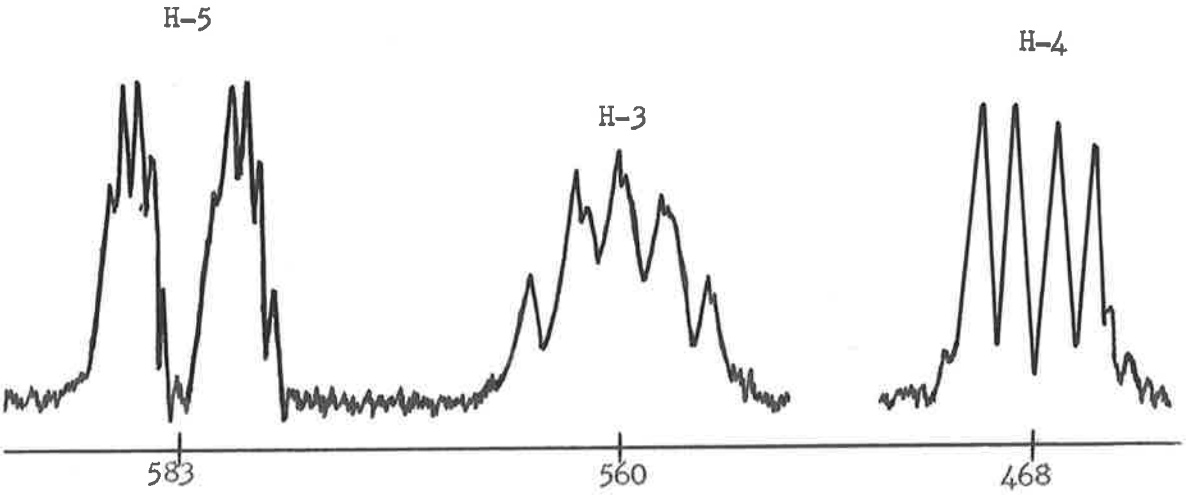
The discussion of these results follows from that developed in section 4.3. Isothiazole itself has two protons non-adjacent to the nitrogen atom and the R value for these two protons is remarkably constant in all cases, thus verifying the basic similarity between protonation and complex formation in this system. The $R_{3,4}$ values again clearly demonstrates the BX_3 anisotropy terms, but its actual magnitude, calculated by the method



Spectra of H-3 and H-5 in 4-methylisothiazole:BBr_3

Spectra of H-2 in 4-methylthiazole:BCl_3 (acetone)

Fig. 4.6



n.m.r. spectra of isothiazole:BCl_3 (acetone)

Fig. 4.7

described earlier, is smaller than that found in the pyridine system (Table 4.10). This however is reasonable considering the different geometry of a five-membered ring which allows slightly greater separation between the BX_3 group and the 3-proton.

4-Methylisothiazole complexes closely follow the pattern of isothiazole itself as expected, but the 3-methyl isomer due to the steric interaction of the methyl group is more analogous to the 2-substituted pyridine complexes. It also very clearly shows the solvation effects for the BCl_3 and BBr_3 complexes in acetone solution. The complexes of 4-methylthiazole show spectral features typical of the sterically hindered systems and do not appear to be anomalous in any way.

B-H coupling was again clearly detected in the BCl_3 and BBr_3 complexes (Fig. 4.6) but not in the BF_3 complexes. The coupling constants are listed in Table 4.11. It is interesting to note that these coupling constants are appreciably smaller than those found in the pyridine complexes, which agrees with the hypothesis put forward in the last section regarding the relationship of B-H coupling constants and the strengths of the donor-acceptor bonds since thiazoles and isothiazoles are weaker bases than pyridine. Furthermore B-H coupling constants in 4-methylthiazole are somewhat greater than those in the isothiazole complexes which correlates well with the order of basicity in these compounds. Of some interest is the long range B-H coupling observed between H-5 and ^{11}B in the BCl_3 and BBr_3 complexes of isothiazole. This is illustrated in Fig. 4.7.

In conclusion therefore the present work indicates that the behaviour of chemical shifts on complex formation in the heterocyclic compounds studied show a close similarity with the changes that occur in these systems on protonation. A full interpretation of the chemical shifts in these complexes show that they bear no relation to donor-acceptor bond strength, whereas $^{11}B - H$ coupling constants appear to correlate well with such bond strengths. A full investigation into the nature and theory of this relationship would be of considerable interest.

Table 4.1.

Chemical shifts in substituted pyridines. Free bases, cations and BX_3 complexes. (cycles/sec. from internal TMS)

Substituent.	Protons					
	H-2	H-3	H-4	H-5	H-6	$-CH_2-R$
(A) Free bases- in $CDCl_3$						
4-methyl	506.9	425.1	-	425.1	506.9	140.2
3-methyl	506.9	-	447.7	429.6	504.4	138.9
2-methyl	-	427.4	452.7	424.4	508.7	153.1
2-ethyl	-	428.2	455.0	424.8	510.9	169.8
2-benzyl	-	433.1	453.6	429.8	512.0	249.5
(B) Free bases- in Acetone						
4-methyl	504.5	429.2	-	429.2	504.5	-
3-methyl	504.5	-	452.6	432.3	502.3	-
2-methyl	-	431.0	456.8	426.7	506.1	-
2-ethyl	-	432.0	458.0	429.3	506.1	-
2-benzyl	-	431.8	458.8	428.3	508.9	246.3
(C) Cations- in CF_3COOD						
4-methyl	517.9	476.6	-	476.6	517.9	167.6
3-methyl	517.9	-	512.0	482.2	517.9	160.7
2-methyl	-	478.3	512.6	474.9	517.5	175.1
2-ethyl	-	479.6	514.8	476.0	518.2	193.3
2-benzyl	-	477.6	513.5	473.0	516.8	271.8

Table 4.1 (contd.)

Substituent.	Protons					
	H-2	H-3	H-4	H-5	H-6	$-CH_2-R$
(D) BF_3 Complexes- in $CDCl_3$						
4-methyl	513.2	453.5	-	453.5	513.2	156.0
3-methyl	511.9	-	485.6	462.0	511.9	151.5
2-methyl	-	453.9	485.5	453.9	527.2	172.1
2-ethyl	-	458.5	490.0	454.8	527.1	196.1
2-benzyl	-	Sample too unstable				
(E) BF_3 Complexes- in Acetone						
4-methyl	516.7	468.9	-	468.9	516.7	-
3-methyl	Sample too unstable					
2-methyl	-	477.0	509.1	473.0	528.5	-
2-ethyl	-	478.7	511.8	474.8	528.8	189.6
2-benzyl	-	476.0	513.9	478.0	530.9	273.0
(F) BCl_3 Complexes- in $CDCl_3$						
4-methyl	546.9	458.4	-	458.4	546.9	159.2
3-methyl	546.9	-	490.5	467.9	542.5	156.1
2-methyl	-	461.7	490.4	459.0	581.6	196.8
2-ethyl	-	454.5	493.3	463.7	579.2	225.5
2-benzyl	-	443.0	482.0	454.0	583.3	303.9

Table 4.1 (contd.)

Substituent.	Protons					
	H-2	H-3	H-4	H-5	H-6	$-CH_2-R$
(G) BCl_3 complexes- in Acetone						
4-methyl	551.4	475.6	-	475.6	551.4	-
3-methyl	551.3	-	505.1	480.8	551.3	-
2-methyl	-	478.1	507.0	474.5	581.7	207.0
2-ethyl	-	487.0	521.0	483.2	577.0	222.0
* 2-benzyl	-	480.0	517.5	483.4	528.7	276.7
(H) BBr_3 Complexes- in $CDCl_3$						
4-methyl	562.0	460.5	-	460.5	562.0	160.0
3-methyl	563.9	-	487.8	466.6	563.9	157.0
2-methyl	-	461.3	491.0	461.3	601.0	203.2
2-ethyl	-	469.4	496.7	461.4	594.6	227.9
2-benzyl		Sample too unstable				
(I) BBr_3 Complexes- in Acetone						
4-methyl	564.2	476.4	-	476.4	564.2	-
3-methyl	563.5	-	506.2	481.7	563.5	-
2-methyl	-	480.0	507.7	476.5	598.4	202.1
2-ethyl	-	486.0	518.5	475.9	595.4	227.9
2-benzyl		Sample too unstable				

* Data for solvated complex- Spectrum changed too fast for unsolvated complex to be measured, except:

H-6 : 583 $-CH_2-R$: 303

Table 4.2.

Δ Values in chloroform solutions (in cycles/sec.)

$\Delta = \sigma_H \text{ (complex)} - \sigma_H \text{ (free base)}$

	Δ H-2	Δ H-3	Δ H-4	Δ H-5	Δ H-6	Δ-CH_2-R
(A) Protonation (H^+)						
4-methyl	11.0	51.5	-	51.5	11.0	27.4
3-methyl	11.0	-	64.3	52.6	13.5	21.8
2-methyl	-	50.9	59.9	50.5	8.8	22.0
2-ethyl	-	51.4	59.8	51.2	7.3	23.5
2-benzyl	-	44.5	59.9	43.2	4.8	22.3
(B) BF_3 complexes						
4-methyl	6.3	28.4	-	28.4	6.3	15.8
3-methyl	5.0	-	37.9	32.4	7.5	12.6
2-methyl	-	26.5	32.8	29.5	18.5	19.0
2-ethyl	-	30.4	35.0	30.0	16.2	26.3
2-benzyl (acetone)	-	44.2	55.1	49.7	22.0	26.7

Table 4.2 (contd.)

	Δ H-2	Δ H-3	Δ H-4	Δ H-5	Δ H-6	Δ $-CH_2-R$
(C) BCl_3 complexes						
4-methyl	40.0	33.3	-	33.3	40.0	19.0
3-methyl	40.0	-	42.8	38.3	38.1	17.2
2-methyl	-	34.3	37.7	34.6	72.9	43.7
2-ethyl	-	26.3	38.3	38.9	68.3	55.7
2-benzyl	-	9.9	28.4	24.2	71.3	54.4
(D) BBr_3 complexes						
4-methyl	55.1	35.4	-	35.4	55.1	19.8
3-methyl	57.0	-	40.1	37.0	59.5	18.1
2-methyl	-	33.9	38.3	36.9	92.4	50.1
2-ethyl	-	41.2	41.7	36.6	83.7	58.1
2-benzyl	-	-	-	-	-	-

Table 4.3.

R values of pyridines on protonation and complex formation in chloroform solutions. ($R_{x,y} = \frac{\Delta H\text{-}x}{\Delta H\text{-}y}$)

	$R_{5,6}$	$R_{5,CH_2\text{-}R}$	$R_{5,4}$
(A) Protonation			
4-methyl	4.68	1.88	-
3-methyl	3.90	2.41	0.82
2-methyl	5.74	2.29	0.84
2-ethyl	7.01	2.18	0.85
2-benzyl	9.00	1.94	0.72
(B) BF_3 complexes			
4-methyl	4.51	1.80	-
3-methyl	4.32	2.57	0.86
2-methyl	1.59	1.55	0.90
2-ethyl	0.47	1.14	0.86
2-benzyl	0.40	-	-

Table 4.3 (contd.)

	R5,6	R5,CH_2-R	R5,4
(C) BCl_3 complexes			
4-methyl	0.83	1.75	-
3-methyl	1.01	2.23	0.89
2-methyl	0.47	0.79	0.91
2-ethyl	0.57	0.70	1.01
2-benzyl	0.34	0.45	0.85
(D) BBr_3 complexes			
4-methyl	0.64	1.79	-
3-methyl	0.62	2.05	0.92
2-methyl	0.40	0.74	0.96
2-ethyl	0.44	0.63	0.88
2-benzyl	-	-	-

Table 4.4.

Calculation of the deshielding effect of the BX_3 group at the 6 protons. (in cycles/sec.)

	R5,6 protonation value	Δ H-6 calculated	Δ H-6 observed	BX_3 anisotropy
(A) BF_3 complexes				
4-methyl	4.68	6.1	6.3	0.2
3-methyl	3.90	8.3	7.5	-
2-methyl	5.74	5.1	18.5	13.4
2-ethyl	7.01	4.3	16.2	11.9
2-benzyl	9.00	5.5	22.0	16.5
(B) BCl_3 complexes				
4-methyl	4.68	7.1	40.0	32.9
3-methyl	3.90	9.8	38.1	28.3
2-methyl	5.74	6.0	72.9	66.9
2-ethyl	7.01	5.6	68.3	62.7
2-benzyl	9.00	2.7	71.3	68.6
(C) BBr_3 complexes				
4-methyl	4.68	7.6	55.1	47.5
3-methyl	3.90	9.5	59.5	50.0
2-methyl	5.74	6.4	92.4	86.0
2-ethyl	7.01	5.2	83.7	78.5
2-benzyl	9.00	-	-	-

Table 4.6.

Chemical shift data for solvated complexes. Only values for H-2, H-6, and for $-CH_2-R$ could be accurately determined. (in cycles/sec. from TMS)

	H-2	H-6	$-CH_2-R$
(A) BCl_3 complexes			
4-methyl	529.5	529.5	166
3-methyl	not clearly observable		
2-methyl	-	526.2	-
2-ethyl	-	528.2	193
2-benzyl	-	528.7	276.7
(B) BBr_3 complexes			
4-methyl	not clearly observable		
3-methyl	not clearly observable		
2-methyl	not clearly observable		
2-ethyl	-	528	193
2-benzyl	-	-	-

Table 4.7

Chemical shift data for some methyl-substituted thiazole and isothiazole boron trihalide complexes. (in cycles/sec. from TMS)

	H-2	H-3	H-4	H-5	CH_3
(A) BF_3 complexes ($CDCl_3$)					
Isothiazole	-	527.8	450.3	543.8	-
3-methylisothiazole	-	-	430.0	533.3	164.9
4-methylisothiazole	-	514.6	-	518.5	147.0
4-methylthiazole	560.4	-	-	439.9	157.9
(B) BF_3 complexes (acetone)					
isothiazole	-	539.2	462.6	569.7	-
3-methylisothiazole	-	-	449.9	558.2	166.2
4-methylisothiazole	-	525.9	-	544.3	147.5
4-methylthiazole		Sample too unstable			
(C) BCl_3 complexes (in $CDCl_3$)					
isothiazole	-	551.0	453.9	551.0	-
3-methylisothiazole	-	-	439.1	534.0	180.6
4-methylisothiazole	-	535.7	-	528.0	149.4
4-methylthiazole	602.8	-	-	448.0	176.8

Table 4.7 (contd.)

	H-2	H-3	H-4	H-5	CH_3
(D) BCl_3 complexes (in acetone)					
isothiazole	-	560.5	467.9	583.0	-
3-methylisothiazole	-	-	456.9	565.2	-
4-methylisothiazole	-	549.2	-	558.8	-
4-methylthiazole	618.4	-	-	477.4	-
(E) BBr_3 complexes (in $CDCl_3$)					
isothiazole	-	563.2	456.2	556.4	-
3-methylisothiazole	-	-	437.9	536.3	187.6
4-methylisothiazole	-	548.5	-	534.3	149.5
4-methylthiazole	620.8	-	-	449.8	133.8
(F) BBr_3 complexes (in acetone)					
isothiazole	-	571.6	471.6	589.6	-
3-methylisothiazole	-	-	462.2	566.7	186.5
4-methylisothiazole	-	560.6	-	566.5	-
4-methylthiazole	633.4	-	-	482.1	198.5

Table 4.8

Δ values of isothiazole and thiazole complexes measured in chloroform solutions (in cycles/sec.)

	Δ H-2	Δ H-3	Δ H-4	Δ H-5	Δ CH_3
(A) Protonation:					
isothiazole	-	34.9	31.0	52.8	-
3-methylisothiazole	-	-	29.2	48.8	21.3
4-methylisothiazole	-	39.3	-	49.6	14.3
4-methylthiazole	62.7	-	-	48.2	13.2
(B) BF_3 complexes:					
isothiazole	-	14.0	12.5	22.0	-
3-methylisothiazole	-	-	8.5	20.6	12.4
4-methylisothiazole	-	15.9	-	25.0	6.7
4-methylthiazole	37.6	-	-	25.1	7.7
(C) BCl_3 complexes:					
isothiazole	-	37.2	16.1	29.2	-
3-methylisothiazole	-	-	17.6	21.3	38.1
4-methylisothiazole	-	37.0	-	34.5	9.1
4-methylthiazole	80.0	-	-	33.1	26.6
(D) BBr_3 complexes:					
isothiazole	-	49.4	18.4	34.6	-
3-methylisothiazole	-	-	16.4	13.6	35.1
4-methylisothiazole	-	49.8	-	40.8	9.2
4-methylthiazole	98.0	-	-	34.9	33.6

Table 4.9

R values of isothiazole and thiazole complexes

isothiazole	R3,4	R4,5
H^+	1.13	0.59
BF_3	1.12	0.57
BCl_3	2.31	0.55
BBr_3	2.69	0.53
3-methylisothiazole	**R4,5**	**R4,CH_3**
H^+	0.60	1.37
BF_3	0.41	0.69
BCl_3	0.83	0.46
BBr_3	0.89	0.46
4-methylisothiazole	**R3,5**	**R3,CH_3**
H^+	0.79	2.75
BF_3	0.64	2.38
BCl_3	1.07	4.07
BBr_3	1.22	5.42
4-methylthiazole	**R2,5**	**R5,CH_3**
H^+	1.30	3.65
BF_3	1.50	3.26
BCl_3	2.42	1.25
BBr_3	2.81	1.04

Table 4.10

Calculation of deshielding effect of BX_3 group in isothiazole and thiazole complexes. (in cycles/sec.) (using R values for protonation)

	Proton	Δ Calculated	Δ found	BX_3 anisotropy
BF_3 complexes:				
isothiazole	H-3:	14.1	14.0	0
4-methylisothiazole	H-3:	18.4	15.9	2.5
4-methylthiazole	H-2:	32.6	37.6	5.0
BCl_3 complexes:				
isothiazole	H-3:	18.1	37.2	19.1
4-methylisothiazole	H-3:	25.0	37.0	12.0
4-methylthiazole	H-2:	43.0	80.0	37.0
BBr_3 complexes:				
isothiazole	H-3:	20.7	49.4	28.7
4-methylisothiazole	H-3:	25.3	49.8	24.5
4-methylthiazole	H-2:	45.4	98.0	56.6

Table 4.11

^{11}B - H coupling constants in isothiazole and thiazole complexes

		BCl_3 complex	BBr_3 complex
isothiazole	H-3: H-5:	2.2 c/s 0.8 c/s	2.6 c/s 0.8 c/s
4-methylisothiazole	H-3: H-5:	1.9 c/s 0.7 c/s	2.16 c/s -
4-methylthiazole	H-2:	2.5 c/s	2.8 c/s

EXPERIMENTAL

(A) Instrumentation.

N.m.r. spectra: - All n.m.r. spectra were determined on Varian DP60 and DA60-IL spectrometers operating at 60 Mc/s. Tetramethylsilane was used as internal standard for all solvents except deuterium oxide (D_2O) where dioxan ($\delta = 3.83$) was used. Calibration of spectra recorded on the DP60 spectrometer was by the usual side band technique, using a Muirhead-Wigan D-890A audio-oscillator. At least eight separate determinations with increasing and decreasing magnetic field were recorded under slow-scan conditions. Spectra obtained using the DA60-IL spectrometer were measured directly with the aid of a R.A.C.A.L. SA535 frequency counter. Chemical shifts are believed to be accurate to ± 0.005 p.p.m. unless otherwise stated, and coupling constants to at least 0.2 cycles/sec. Variable temperature studies were performed on the DP60 instrument using the special probe assembly supplied by the Varian company. All solvents used were of spectroscopic grade and carefully purified and dried before use.

Electronic spectra:- These were determined in ca. 0.5×10^{-4} M solutions on a Unicam SP700 spectrophotometer. For the curve resolutions the spectra were recorded at scan rate 2 and a chart speed of 120" per hour. Each spectra was calibrated using a holmium oxide glass filter at the wavelengths 278.5 and 286.4 mμ.

(B) Preparation of compounds.

1. Preparation of bipyridyls.

2,2'-bipyridyl and its 4,4'- and 5,5'-dimethyl derivatives were prepared by the action of degassed raney nickel catalyst (W7-J) on pyridine[132] or the appropriate picoline.[77] The three bipyridyls were obtained as colourless crystals; 2,2'-bipyridyl m.p. 69.5-70.5° (lit.[133] m.p. 69.5), 4,4'-dimethyl-2,2'-bipyridyl m.p. 170-172° (lit.[77] m.p. 170-172°), and 5,5'-dimethyl-2,2'-bipyridyl m.p. 114-115° (lit.[77] m.p. 114.5-115°).

3,3'-dimethyl-2,2'-bipyridyl was obtained by heating 2-bromo-3-methylpyridine with copper bronze.[134] The product was obtained as a colourless liquid b.p. 166-170°/18 mm (lit.[134] b.p. 293-298°).

3,3'-bipyridyl was prepared by oxidation of p-phenanthroline followed by decarboxylation of the di-carboxylic acid.[135] The product was obtained as a colourless oil b.p. 285-295° (lit.[135] b.p. 291-292°).

4,4'-bipyridyl resulted from the action of sodium on pyridine[144] and was obtained as colourless needles, m.p. 113-114.5° (lit.[133] 114°).

2. Preparation of the bridged biquaternary salts of 2,2'-bipyridyl.

The general method described by Homer and Tomlinson[52] was used for the preparation of all the biquaternary salts described below. Equimolar amounts of the appropriate 2,2'-bipyridyl or dimethyl derivative and the α,ω-dibromo-alkane were heated for 4 hours at 120-180° in o-dichlorobenzene (rather than nitrobenzene as suggested by the above authors). The precipitated salts were filtered, washed with acetone, dissolved in methanol and treated with charcoal. The filtrate was reduced to half its volume by distillation and the biquaternary salts precipitated by the addition of acetone. Several recrystallisations from methanol-acetone gave the pure salts.

Compounds (XI) n=2 (9,10-dihydro-8a,10a-diazoniaphenanthrene dibromide), m.p. 320-330° (dec.), (XI) n=3 (7,8-dihydro-6H-dipyrido[1,2-a:2',1'-c]-[1,4]diazopidiinium dibromide), m.p. 300°, and (XI) n=4 (6,7,8,9-tetrahydrodipyrido[1,2-a:2',1'-c][1,4]diazocinidiinium bromide) m.p. 264-265° have been reported by Homer and Tomlinson[52] and the data above agrees with the results obtained by these authors.

Compounds (XXI) (6,8-dihydrodipyrido[1,2-c:2',1'-e][1,3,6]oxadiazepidiinium dibromide), (XIX) (7,8-dihydro-7,7-dihydroxy-6H-dipyrido[1,2-a:2',1'-c]-[1,4]diazepidiinium dibromide), and (XX) (7,8-dihydro-7,7-dihydroxy-6,8-dimethyl-6H-dipyrido[1,2-a:2',1'-c][1,4]diazepidiinium dibromide) were prepared by Dr. I.C. Calder[81] in this department and kindly supplied for the study in this work.

(XVI) n=2 (9,10-dihydro-4,5-dimethyl-8a,10a-diazoniaphenanthrene dibromide)

Prepared from 3,3'-dimethyl-2,2'-bipyridyl and 1,2-dibromoethane. Colourless crystals, m.p. 350° (lit.[52] 380°).

(XVI) n=3 (7,8-dihydro-1,13-dimethyl-6H-dipyrido[1,2-a:2',1'-c][1,4]-diazepidiinium dibromide)

Prepared from 3,3'-dimethyl-2,2'-bipyridyl and 1,3-dibromopropane. Colourless crystals, m.p. 310-313°. (Found: C, 44.69; H, 5.02; N, 7.27; Br, 40.5. $C_{15}H_{18}N_2Br_2 \cdot \frac{1}{2}H_2O$ requires C, 44.57; H, 4.99; N, 6.93; Br, 39.6%).

(XVI) n=4 (6,7,8,9-tetrahydro-1,14-dimethyldipyrido[1,2-a:2',1'-c][1,4]-diazocinidiinium dibromide)

Prepared from 3,3'-dimethyl-2,2'-bipyridyl and 1,4-dibromobutane. Colourless hygroscopic solid which could not be recrystallised. A satisfactory sample for analysis could not be obtained.

(XVII) n=2 (9,10-dihydro-3,6-dimethyl-8a,10a-diazoniaphenanthrene dibromide)

Prepared from 4,4'-dimethyl-2,2'-bipyridyl and 1,2-dibromoethane. Light green crystals, m.p. 265-270° (lit.[52] 268-270°).

(XVII) n=3 (7,8-dihydro-2,12-dimethyl-6H-dipyrido[1,2-a:2',1'-c][1,4]-diazepidiinium dibromide)

Prepared from 4,4'-dimethyl-2,2'-bipyridyl and 1,3-dibromopropane. Colourless crystals, m.p. 335-340° (dec.) (Found: C, 45.61; H, 5.11; N, 6.74; Br, 40.7. $C_{15}H_{18}N_2Br_2 \cdot \frac{1}{2}H_2O$ requires C, 45.59; N, 4.85; N, 7.09; Br, 40.5%).

(XVII) n=4 (6,7,8,9-tetrahydro-2,13-dimethyldipyrido[1,2-a:2',1'-c][1,4]-diazocinidiinium dibromide)

Prepared from 4,4'-dimethyl-2,2'-bipyridyl and 1,4-dibromobutane. Colourless crystals m.p. 255-260° (dec.) (Found: C, 44.86; H, 5.62; N, 6.26; Br, 37.1. $C_{16}H_{20}N_2Br_2 \cdot \frac{1}{2}H_2O$ requires, C, 44.98; H, 5.42; N, 6.56; Br, 37.4%).

(XVIII) n=2 (9,10-dihydro-2,7-dimethyl-8a,10a-diazoniaphenanthrene dibromide)

Prepared from 5,5'-dimethyl-2,2'-bipyridyl and 1,2-dibromoethane. Green needles, m.p. 330-340° (dec.) (lit.[52] 330-335° (dec.)).

(XVIII) n=3 (7,8-dihydro-3,11-dimethyl-6H-dipyrido[1,2-a:1',2'-c][1,4]-diazepidiinium dibromide)

Prepared from 5,5'-dimethyl-2,2'-dipyridyl and 1,3-dibromopropane. Colourless crystals, m.p. above 300° (dec.) (Found: C, 44.66; H, 4.76; N, 6.60; Br, 39.2. $C_{15}H_{18}N_2Br_2 \cdot H_2O$ requires C, 44.57; H, 4.99; N, 6.93; Br, 39.6%).

(XVIII) n=4 (6,7,8,9-tetrahydro-3,12-dimethyldipyrido[1,2-a:2',1'-c][1,4]-diazocinidiinium dibromide)

Prepared from 5,5'-dimethyl-2,2'-bipyridyl and 1,4-dibromobutane. Colourless crystals, m.p. 300-302° (dec.) (Found: C, 47.60; H, 5.19; N, 6.63; Br, 40.0. $C_{16}H_{20}N_2Br_2$ requires C, 48.01; H, 5.03; N, 7.00; Br, 39.9%).

3. Preparation of the oxazoles, thiazoles, and isoxazoles.

The various compounds studied in this group were all prepared by established methods and their physical properties were in agreement with those recorded in the literature. They are summarised as follows:

Compound	appearance	m.p. or b.p.		References
		Found	lit.	
2-methyloxazole	colourless liquid	87-88°	87-88°	136
4-methyloxazole	colourless liquid	87-89°	87-89°	137
thiazole	colourless liquid	114-117°	116.8°	138
2-methylthiazole	colourless liquid	128-130°	129-130°	139
4-methylthiazole	colourless liquid	133.5-130°	133-134°	140
5-methylthiazole	colourless liquid	57-60°/32 mm	70-72°/41 mm	140
isoxazole	colourless liquid	95-96°	94.8°/769 mm	141
3-methylisoxazole	colourless liquid	118-119°	118°	142

Compound	appearance	m.p. or b.p.		refer-ences
		Found	lit.	
2-phenylthiazole	colourless oil	265-275°	267-269°/ 732 mm	143
4-phenylthiazole	colourless oil	52-54°	52°	138
5-phenylthiazole	colourless plates	44-46°	45-46°	143
5-phenylisoxazole	colourless oil.	241-250°	246-248°	144
4,4'-bithiazole	colourless crystals	169-171°	170-171°	145

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Isothiazole, 3-methylisothiazole and 4-methylisothiazole were kindly donated by Dr. F. Hubenett of the Hans J. Zimmer Verfahrenstechnik.

4. Preparation of the boron trihalide complexes of alkyl-substituted pyridines, thiazoles and isothiazoles.

All complexes were prepared by the direct addition of the boron trihalide to a solution of the base in carbon tetrachloride which was first carefully dried over potassium hydroxide pellets and then filtered. The BF_3 was added by bubbling the gas (Fluka) through the solution, but BCl_3

and BBr_3 were added as chloroform solutions.

The reactions are strongly exothermic and were controlled with the aid of an acetone-dry ice-bath where necessary. The complexes precipitated on standing and after several washings with carbon tetrachloride, were dried <u>in vacuo</u> at room temperature. Because of the strong solvation effects observed, they were not further purified but satisfactory analyses were obtained except for a number of BF_3 complexes which were too unstable. They are listed in the following table.

Complex.	Analysis data.
4-methylpyridine:BF_3	Found: C, 42.97; H, 4.55; F, 33.0.
	$C_6H_7N.BF_3$ requires: C, 44.77; H, 4.38; F, 35.42%.
4-methylpyridine:BCl_3	Found: C, 35.56; H, 4.19; N, 7.89; B, 5.46.
	$C_6H_7N{:}BCl_3$ requires C, 34.26; H, 3.35; N, 6.66; B, 5.14%.
4-methylpyridine:BBr_3	Found: C, 20.51; H, 2.20; N, 3.95; B, 3.30.
	$C_6H_7N{:}BBr_3$ requires C, 20.96; H, 2.05; N, 4.08; B, 3.15%.
3-methylpyridine:BF_3	Found: C, 44.00; H, 4.46; B, 5.4; F, 35.4.
	$C_6H_7N{:}BF_3$ requires C, 44.77; H, 4.38; B, 6.72; F, 35.42%.
3-methylpyridine:BCl_3	Found: C, 35.54; H, 3.92; N, 6.82; B, 5.42.
	$C_6H_7N{:}BCl_3$ requires C, 34.26; H, 3.35; N, 6.66; B, 5.14%.
3-methylpyridine:BBr_3	Found: C, 21.77; H, 2.44; B, 2.92.
	$C_6H_7N{:}BBr_3$ requires C, 20.96; H, 2.05; B, 3.15%.

Complex.	Analysis data.
2-methylpyridine:BF_3	Found: C, 39.73; H, 4.83; B, 6.1; F, 33.9. $C_6H_7N:BF_3$ requires C, 44.77; H, 4.38; B, 6.72; F, 35.42%.
2-methylpyridine:BCl_3	Found: C, 35.6; H, 3.96; B, 5.23. $C_6H_7N:BCl_3$ requires C, 34.26; H, 3.35; B, 5.14%.
2-methylpyridine:BBr_3	Found: C, 21.57; H, 3.17; B, 2.79. $C_6H_7N:BBr_3$ requires C, 20.96; H, 2.05; B, 3.15%.
2-ethylpyridine:BF_3	Found: C, 47.37; H, 5.67; B, 6.3; F, 32.9. $C_7H_9N:BF_3$ requires C, 48.05; H, 5.19; B, 6.18; F, 32.58%.
2-ethylpyridine:BCl_3	Found: C, 37.23; H, 4.48; B, 5.15; Cl, 45.5. $C_7H_9N:BCl_3$ requires C, 37.47; H, 4.04; B, 4.82; Cl, 47.41%.
2-ethylpyridine:BBr_3	Found: C, 24.69; H, 2.95; B, 3.02. $C_7H_9N:BBr_3$ requires C, 23.50; H, 2.54; B, 3.02%.
2-benzylpyridine:BF_3	No crystalline sample could be obtained for analysis.
2-benzylpyridine:BCl_3	No crystalline sample could be obtained for analysis.
Isothiazole:BF_3	Sample too unstable.
Isothiazole:BCl_3	Found: C, 18.16; H, 1.76; S, 15.45; B, 5.5. $C_3H_3NS:BCl_3$ requires C, 17.81; H, 1.49; S, 15.85; B, 5.35%.

Complex.	Analysis data.
Isothiazole:BBr_3	Found: C, 10.50; H, 0.81; N, 4.35; B, 3.50. $C_3H_3NS{:}BBr_3$ requires C, 10.73; H, 0.90; N, 4.17; B, 3.22%.
3-methylisothiazole:BF_3	Found: C, 27.77; H, 3.31; N, 7.22. $C_4H_5NS{:}BF_3$ requires C, 28.77; H, 3.02; N, 8.39%.
3-methylisothiazole:BCl_3	Found: C, 21.78; H, 2.23; S, 14.37; B, 5.5. $C_4H_5NS{:}BCl_3$ requires C, 22.21; H, 2.33; S, 14.82; B, 5.00%.
3-methylisothiazole:BBr_3	Found: C, 14.28; H, 1.50; S, 9.10; Br, 68.3. $C_4H_5NS{:}BBr_3$ requires C, 13.74; H, 1.44; S, 9.17; Br, 68.55%.
4-methylisothiazole:BF_3	Sample too unstable.
4-methylisothiazole:BCl_3	Found: C, 21.71; H, 2.39; S, 14.60; B, 5.10. $C_4H_5NS{:}BCl_3$ requires C, 22.21; H, 2.33; S, 14.82; B, 5.00%.
4-methylisothiazole:BBr_3	Found: C, 13.89; H, 1.74; S, 9.14; Br, 67.5. $C_4H_5NS{:}BBr_3$ requires C, 13.74; H, 1.44; S, 9.17; Br, 68.55%.
4-methylthiazole:BF_3	Found: C, 27.79; H, 3.48; N, 8.18; F, 33.3. $C_4H_5NS{:}BF_3$ requires C, 28.77; H, 3.02; N, 8.39; F, 34.13%.
4-methylthiazole:BCl_3	Found: C, 22.46; H, 2.71; S, 14.53; Cl, 47.5. $C_4H_5NS{:}BCl_3$ requires C, 22.21; H, 2.33; S, 14.82; Cl, 49.17%.
4-methylthiazole:BBr_3	Found: C, 14.56; H, 1.73; S, 10.05; Br, 67.3. $C_4H_5NS{:}BBr_3$ requires C, 13.74; H, 1.44; S, 9.17; Br, 68.55%.

***

APPENDIX

Appendix.

Summary of calculations outlined in Chapter I.

1) Deshielding due to point-dipoles:

$$\sigma_{AB} = \frac{1}{3\, \overrightarrow{R_{AB}}\, N} \sum_{i=1,2,3} \chi_B^i \,(1-3\cos^2\gamma)$$

$\overrightarrow{R_{AB}}$ is the vector joining A and B; χ_B the molar magnetic susceptibility of B. γ is the angle between the direction of χ_B and $\overrightarrow{R_{AB}}$, and N is Avogrado's number.

2) Deshielding due to electric fields (E):

$$\sigma^E = -2.9 \times 10^{-12}\, E_z - 7.38 \times 10^{-19}\, E^2$$

where E_z is the component of the electric field along the C-H bond, and E the total electric field at the hydrogen nucleus.

3) The electric field is obtained from the expression:

$$E = \frac{u}{r^3}\left[3\cos\phi\, [\overrightarrow{DP}] - [\vec{u}] \right]$$

where u is the dipole moment in Debyes, r the distance of the nucleus from the dipole centre, $[\vec{u}]$ the unit vector along the dipole, and $[\overrightarrow{DP}]$ the unit vector along the line joining the dipole centre and the hydrogen nucleus. ϕ is the angle between $[\overrightarrow{DP}]$ and $[\vec{u}]$.

4) The electric field due to an electronic charge is given by:

$$E = 4.803 \times 10^{-10} \; \frac{\Delta q \cos\phi}{R_i^2}$$

where R_i is the distance of the proton from the charge Δq, and ϕ the angle between the line joining the charge with the proton and the C-H bond.

Notes to Tables A-1 and A-2.

Table A-1.	The 2,2'-bipyridyl system	Fig.	Page
I	Ring current effect (H-3 - H-5).	1.1	19
II	Lone-pair dipole effect at H-3.	1.1	19
III	N-anisotropy effect at H-3.	1.1	19
IV	Total effect I + II + III. (free base)	1.1	19
V	Total effect I + III. (free base in water)	1.6	33
VI	Effect of positive charge (N^+) on H-3.		
VII	Effect of positive charge (N^+) on H-5.		
VIII	Effect of delocalised positive charge on H-3.		
IX	Total effect I + VI + VIII - VII (for di-cation)	1.13	52
X	Total effect (V + IX)/2 (for mono-cation)	1.13	52

Table A-2	The 3,3'-dimethyl-2,2'-bipyridyl system		
XI	Ring current effect (H-3 - H-5).	1.2	20
XII	Effect of $C-CH_3$ bond anisotropy on H-3.	1.2	20
XIII	Lone-pair dipole effect on H-3 .	1.2	20
XIV	Total effect XI + XII + XIII. (free base)	1.2	20
XV	Effect of positive charge (N^+) on H-3		
XVI	Effect of positive charge (N^+) on H-5		
XVII	Effect of delocalised positive charge on H-3		
XVIII	Total effect XI + XII + XV + XVII - XVI. (for di-cation)	1.14	53
XIX	Total effect (XIV - XIII + XVIII)/2 (for mono-cation)	1.14	53

Table A-1

calculations of the 2,2'-bipyridyl system (in p.p.m.)

	I	II	III	IV	V	VI	VII	VIII	IX	X
0	-0.517	-0.480	-0.060	-1.057	-0.576	+0.146	-0.000	+0.032	-0.339	-0.458
10	-0.498	-0.430	-0.058	-0.987	-0.556	+0.135	-0.019	+0.031	-0.313	-0.435
20	-0.445	-0.0397	-0.055	-0.898	-0.500	+0.114	-0.038	+0.028	-0.265	-0.382
30	-0.370	-0.290	-0.055	-0.725	-0.435	+0.080	-0.057	+0.022	-0.211	-0.324
40	-0.260	-0.183	-0.052	-0.495	-0.312	+0.040	-0.076	+0.014	-0.130	-0.220
50	-0.154	-0.085	-0.050	-0.290	-0.205	-0.020	-0.095	+0.005	-0.074	-0.138
60	-0.053	-0.055	-0.050	-0.158	-0.103	-0.040	-0.114	-0.006	+0.015	-0.043
70	+0.029	-0.008	-0.045	+0.025	-0.017	-0.060	-0.133	-0.019	+0.083	+0.033
80	+0.083	+0.028	-0.043	+0.068	+0.040	-0.090	-0.152	-0.032	+0.113	+0.077
90	+0.102	+0.028	-0.042	+0.090	+0.062	-0.112	-0.165	-0.045	+0.110	+0.085
100	+0.083	+0.022	-0.040	+0.065	+0.043	-0.126	-0.152	-0.059	+0.050	+0.047
110	+0.029	+0.025	-0.037	+0.017	-0.008	-0.136	-0.133	-0.072	-0.048	-0.028
120	-0.053	+0.022	-0.035	-0.067	-0.083	-0.146	-0.114	-0.084	-0.169	-0.128
130	-0.154	+0.020	-0.033	-0.168	-0.188	-0.151	-0.095	-0.095	-0.305	-0.247
140	-0.260	+0.020	-0.032	-0.272	-0.297	-0.156	-0.076	-0.104	-0.444	-0.367
150	-0.370	+0.020	-0.030	-0.390	-0.410	-0.159	-0.057	-0.112	-0.584	-0.496
160	-0.445	+0.020	-0.030	-0.457	-0.475	-0.161	-0.038	-0.118	-0.686	-0.580
170	-0.498	+0.018	-0.028	-0.509	-0.526	-0.162	-0.019	-0.121	-0.762	-0.643
180	-0.517	+0.001	-0.027	-0.530	-0.540	-0.162	-0.000	-0.123	-0.802	-0.674

Table A-2

Calculations of the system
3,3'-dimethyl-2,2'-bipyridyl (in p.p.m.)

	XI	XII	XIII	XIV	XV	XVI	XVII	XVIII	XIX
0	-0.482	0.000	-0.163	-0.645	-0.250	0.000	-0.047	-0.777	-0.630
10	-0.455	0.000	-0.142	-0.597	-0.250	-0.016	-0.050	-0.739	-0.596
20	-0.377	0.000	-0.095	-0.472	-0.240	-0.032	-0.053	-0.637	-0.506
30	-0.258	0.000	-0.046	-0.304	-0.240	-0.048	-0.056	-0.504	-0.380
40	-0.112	0.000	-0.010	-0.122	-0.240	-0.054	-0.059	-0.353	-0.232
50	+0.043	0.000	+0.007	+0.050	-0.240	-0.070	-0.061	-0.188	-0.072
60	+0.185	+0.010	+0.015	+0.210	-0.230	-0.086	-0.062	-0.007	+0.093
70	+0.313	+0.014	+0.015	+0.342	-0.220	-0.102	-0.062	+0.153	+0.240
80	+0.387	+0.020	+0.020	+0.427	-0.210	-0.118	-0.062	+0.260	+0.333
90	+0.413	+0.030	+0.009	+0.452	-0.210	-0.134	-0.062	+0.333	+0.388
100	+0.387	+0.040	+0.005	-0.432	-0.200	-0.118	-0.069	+0.284	+0.355
110	+0.313	+0.055	+0.002	+0.370	-0.190	-0.102	-0.076	+0.216	+0.292
120	+0.185	+0.068	-0.001	+0.252	-0.180	-0.086	-0.083	+0.067	+0.160
130	+0.043	+0.073	-0.006	+0.110	-0.180	-0.070	-0.091	-0.083	+0.017
140	-0.112	+0.055	-0.003	-0.060	-0.180	-0.054	-0.098	-0.283	-0.170
150	-0.258	-0.008	-0.006	-0.271	-0.180	-0.048	-0.102	-0.500	-0.384
160	-0.377	-0.140	-0.006	-0.523	-0.180	-0.032	-0.105	-0.767	-0.641
170	-0.455	-0.295	-0.006	-0.756	-0.180	-0.016	-0.110	-1.035	-0.893
180	-0.482	-0.375	-0.006	-0.863	-0.180	-0.000	-0.115	-1.165	-1.010

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