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Carbon-13 Magnetic Resonance Spectral Studies of Some Bipyridine Derivatives

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Assignments of ^{13}C chemical shifts and ^{13}C—^{1}H coupling constants are presented for six bipyridine derivatives. Some earlier spectral assignments have been corrected. The spectral parameters of the bipyridines are generally very similar to those of the appropriate simple substituted pyridines. Long range inter-ring coupling constants in these compounds have been discussed.

(Keywords: ^{13}C *NMR spectroscopy;* ^{13}C—^{1}H *Coupling constants; Bipyridines)*

^{13}C-*NMR einiger Bipyridine*

Es werden die Zuordnungen der ^{13}C-Verschiebungen und der ^{13}C—^{1}H-Kopplungskonstanten für sechs Bipyridinderivate präsentiert. Dabei wurden einige früher getroffene Zuordnungen korrigiert. Das NMR-Verhalten der Bipyridine ist dem der analog substituierten Pyridine generell sehr ähnlich. Die Long-Range-Kopplungen zwischen den Ringen werden diskutiert.

Introduction

Carbon-13 Nuclear Magnetic Resonance spectral studies of bipyridines have already attracted some interest [1–7]. However, certain chemical shift assignments have been subject to repeated revision [2–5], whilst others would appear to be in need of correction [5]. Although detailed analyses of the ^{13}C—^{1}H coupling interactions in pyridine derivatives have been presented [8–12], no such studies have yet been reported for the bipyridines.

The well known chelating agent 2,2′-bipyridine **1** (see Table 1) has naturally attracted most interest. The spectrum was first determined on a saturated solution in CS_2 by *Retcofsky* and *Friedel* [1] in 1968. The C-2, C-4 and C-6 carbons were readily assigned by comparison with their respective shieldings in pyridine, however, since C-3 and C-5 differed by only 2.7 ppm unambiguous assignments were not considered possible. The

Table 1. *List of Compounds*

1	2,2′-Bipyridine
2	3,3′-Bipyridine
3	4,4′-Bipyridine
4	2,3′-Bipyridine
5	3,3′-Dimethyl-2,2′-bipyridine
6	5,5′-Dimethyl-2,2′-bipyridine
7	4,4′-Dimethyl-2,2′-bipyridine
8	4,4′-Dichloro-2,2′-bipyridine

compound was then examined by *Breitmaier* and co-workers in *DMSO-d_6* solution. In their first report [2] the β-carbons were not specifically assigned, but in the second paper [3] C-3 was assigned as the upfield signal from "the appearance of the geminal ^{13}C—^1H multiplets of the off-resonance spectrum". However, in their third report a few years later in an Atlas of C-13 NMR data [4] the assignments of C-3 and C-5 were reversed, such that C-5 was then considered as the most upfield signal.

Mal'tseva et al. [5] presented a ^{13}C NMR study of several bipyridine derivatives (**1**–**4**) and also of 2,2′,2″-terpyridine, in order to examine the ring interactions. Assignments of the methine carbons were performed by off-resonance decoupling, and of quaternary carbons by calculation of symmetries. No reference to any earlier work was given, but for **1** C-5 was placed upfield of C-3 in accordance with the later revised assignment of *Breitmaier* et al. [4].

Another extensive study of 2,2′-bipyridine derivatives in $CDCl_3$ solution was reported in 1978 by *Marker* et al. [6]. The resonances for C-3 and C-5 of **1** were assigned on the basis of methyl Substituent Chemical Shift (S.C.S.) effects obtained from the spectra of **5** and **6**. Since the quaternary C-3 carbon in **5** was upfield of the quaternary C-5 carbon in **6**, and taking other S.C.S. effects into consideration, C-3 was accordingly assigned as the most upfield signal in contradistinction to the later revised assignment by *Breitmaier* et al. [4] and the work of *Mal'tseva* et al. [5].

Later *Cook* et al. [7] examined the ^{13}C NMR spectra of several 2,2′-bipyridine derivatives, including **1**, **7** and **8**, and of their ruthenium(II) tris complexes. The signal patterns for the complexes were similar to those for the free ligands and in each case C-3 was shielded relative to C-5, as proposed by *Marker* et al. [6]. The assignments were made on the basis of the splitting pattern in the proton coupled spectrum, such that C-3 appeared as a doublet of doublets, whilst C-5 was a doublet of triplets.

The only study reported to date concerning bipyridine derivatives other than **1** is that by *Mal'tseva* et al. [5]. However, since their assignments of C-3 and C-5 in **1** have been shown to be in need of revision

[6, 7], then their assignments for C-2 and C-6 in **2**, which are subject to similar problems, must also now be questioned. Moreover, since the assignments made for the unsymmetric compound **4** were based on the symmetric compounds **1** and **2**, then these too would appear to be in need of clarification. In particular in the central spectral region (130–140 δ) of **4**, there should be three signals present (C-4, C-4′ and C-3′), however, only two were reported [5].

As far as the present author is aware no detailed analyses of the ^{13}C—^{1}H spin-spin coupling constants for the bipyridine series have been presented. However, it would appear that the interactions are similar to those already experienced with simple pyridine derivatives [8–12] as demonstrated by *Cook* et al. [7].

In the present work the ^{13}C chemical shifts and ^{13}C—^{1}H coupling constants are reported for a series of bipyridine derivatives.

Results and Discussion

The ^{13}C chemical shifts are reported in Tables 2 and 3 and ^{13}C—^{1}H coupling constants in Tables 4 and 5.

The assignments of C-2, C-4 and C-6 in **1** were readily made by comparison with reported spectral data for pyridine [8] and were found to be in accordance with the earlier work [6, 7]. Differentiation between C-3 and C-5 was achieved by reference to the fully coupled spectra. *Cook* et al. [7] reported C-3 as a doublet of doublets and C-5 as a doublet of triplets. In the present work with a 1 000 Hz sweep width (digital resolution = 0.24 Hz), C-3 (121.26 δ) was a wide doublet (J_{33}) of broadened doublets (J_{35}) whilst C-5 (123.90 δ) appeared as a wide doublet (J_{55}) of doublets ($J_{56} = 9.0$ Hz) of doublets ($J_{53} = 6.6$ Hz) which confirmed the assignment of C-3 as the upfield signal in accordance with the earlier work [6, 7]. All of the coupling constants were very similar to those previously observed at the β-carbons in pyridine [8]. At the higher digital resolutions used in the present work, the broadened C-3 signal was further split into very poorly resolved triplets ascribed to additional weak $^{2}J_{34}$ and $^{4}J_{36}$

Table 2. ^{13}C *NMR chemical shifts (δ, ppm) for symmetrical bipyridines*

	1	**2**	**3**	**7**	**8**
C-2	156.49	147.99	151.00	156.41	156.74
C-3	121.26	133.22	121.66	122.23	122.07
C-4	137.04	134.11	145.79	148.27	145.67
C-5	123.90	123.53	121.66	124.24	124.67
C-6	149.45	149.13	151.00	149.21	150.34
CH_3				21.16	

Table 3. ^{13}C *NMR chemical shifts (δ, ppm) for asymmetric bipyridine* **4**

	Chemical shift	Chemical shift variation Δ, ppm (a)
C-2	154.70	− 1.79
C-3	120.52	− 0.74
C-4	137.04	0.0
C-5	122.96	− 0.94
C-6	150.10	+ 0.65
C-2′	148.48	+ 0.49
C-3′	134.80	+ 1.58
C-4′	134.19	+ 0.08
C-5′	123.61	+ 0.08
C-6′	150.10	+ 0.97

(a) $\Delta = \delta_C$ (**4**) $- \delta_C$ (**1**) for C-2 to C-6 or δ_C (**4**) $- \delta_C$ (**2**) for C-2′ to C-6′

Table 4. $^{13}C—^{1}H$ *coupling constants (Hz) for symmetrical bipyridines*

	1		**2**		**3**		**7**		**8**	
C-2	J_{24}	6.8	J_{22}	178.0	J_{22}	179.5	J_{26}	11.0	J_{26}	10.3
	J_{26}	10.0	J_{24}	5.6	J_{23}	2.4				
			J_{26}	11.5	J_{26}	11.3				
C-3	J_{33}	166.3	J_{32}	~ 6.5	J_{33}	162.4	J_{33}	162.8	J_{33}	171.9
	J_{34}	1.2[a]	J_{35}	~ 6.5	J_{32}	8.7	J_{35}	5.9	J_{35}	4.4
	J_{35}	6.6			J_{35}	5.5	J_{36}	1.5[a]	J_{36}	1.5[a]
	J_{36}	1.2[a]			J_{36}	1.7[a]	$J_{3.Me}$	4.9		
C-4	J_{44}	163.6	J_{44}	161.9	J_{42}	6.5	J_{46}	6.6	J_{46}	9.8
	J_{46}	6.1	J_{42}	5.1	J_{43}	1.2	$J_{4.Me}$	6.1	J_{43}	3.7[a]
			J_{46}	6.6	$J_{4.3'}$	4.0			J_{45}	3.7[a]
C-5	J_{55}	163.4	J_{55}	165.5	J_{55}	162.4	J_{55}	160.2	J_{55}	170.6
	J_{53}	6.6	J_{54}	m	J_{52}	1.7[a]	J_{53}	5.6	J_{53}	4.4
	J_{56}	9.0	J_{56}	m	J_{53}	5.5	J_{56}	8.8	J_{56}	8.1
					J_{56}	8.7	$J_{5.Me}$	4.9		
C-6	[b]		J_{66}	180.2	J_{66}	179.5	J[c]	180.2	J[c]	184.1
			J_{62}	11.0	J_{62}	11.3				
			J_{64}	6.6	J_{65}	2.4				
			J_{65}	2.7						
CH_3							J_{CH}	127.2		
							$J_{Me.3}$	4.3		
							$J_{Me.5}$	4.3		

[a] By comparison with the literature [11, 12] sign expected to be negative

[b] C-6 partially obscured X component of second order ABCX system, not analysed

[c] $J_{66} + J_{65}$ (X component of second order ABX system), see also Table 6

m multiplet (not analysed)

Table 5. $^{13}C—^{1}H$ *coupling constants (Hz) for asymmetric bipyridine* **4**

C-2		[a]	C-2′	$J_{2'2'}$	179.2
				$J_{2'3}$	0.7
				$J_{2'4'}$	5.4
				$J_{2'6'}$	11.2
C-3	J_{33}	162.2	C-3′	$J_{3'2'}$	6.4
	J_{35}	6.6		$J_{3'5'}$	6.4
C-4	J_{44}	163.8	C-4′	$J_{4'4'}$	163.8
	J_{46}	6.3		$J_{4'2'}$	5.2
				$J_{4'6'}$	6.3
C-5	J_{55}	164.5	C-5′	$J_{5'5'}$	165.5
	J_{53}	6.6		$J_{5'6'}$	m
	J_{56}	8.8			
C-6		[b]	C-6′	$J_{6'6'}$	179.9
				$J_{6'2'}$	11.5
				$J_{6'4'}$	7.1
				$J_{6'5'}$	2.4

[a] Signal obscured

[b] C-6 partially obscured X component of second order ABCX system, not analysed

m multiplet (not analysed)

couplings. In the spectra of **7** (with the methyl protons selectively decoupled) [13] and of **8** C-3 was a well resolved wide doublet of doublets of doublets (J_{36} = 1.5 Hz) which suggests that the coupling allocations made in **1** are correct. In accordance with the work of *Denisov* et al. [11] J_{36} should be given a negative sign.

The quaternary C-2 in **1** was a doublet of doublets only (J_{24} = 6.8 Hz, J_{26} = 10.0 Hz) and in **7** and **8** was a doublet only (J_{26} = 11.0, 10.3 Hz respectively) indicating no strong coupling to H-3 in contradistinction to the situation in pyridine and its simple derivatives (e.g. J_{23} = 3.1 Hz) [8]. In each case the C-2 peak was noticeably broadened suggesting that either some weak J_{23} or inter-ring coupling ($^{3}J_{2.3'}$) could be present. The broadening may also result from the adjacent quadrupolar ^{14}N nucleus.

The couplings at C-4 in **1** were very similar to those in pyridine [8], whilst those in **7** and **8** were very similar to the appropriate 4-substituted pyridines, including enhanced values for J_{43} and J_{46} in **8** as previously demonstrated for 4-chloropyridine [12].

The signal for C-6 in **1** appeared as a second order multiplet, partially obscured by C-2 at the low field end and by C-4 at the high field end. Second order $^{13}C—^{1}H$ multiplets have been found to occur [14, 15] when the condition ${}^1J_{CH}/2 = \Delta\delta$ is satisfied (where $\Delta\delta = {}^1H$ chemical shift separation between two closely coupled protons associated with the adjacent carbon atom).

From the literature for 2-methylpyridine $J_{66} = 177$ Hz [10] and $\Delta\delta = 83.6$ Hz [16] from which $0.5\,J/\Delta\delta = 1.059$. Hence C-6 represents the X component of an ABCX spin system which has not been analysed in the present work. With **7** C-6 again appeared as a second order multiplet and in this case it was the X component of an ABX spin system, with $0.5\,J/\Delta\delta = 0.96$, a similar pattern was also obtained for **8**. *Pople, Schneider* and *Bernstein* [17] have calculated the transition energies for the X part of the spectrum from which the separation of the two strongest lines in the observed multiplets gives $J_{66} + J_{65}$ directly. However, an analysis of the AB portion of the spectrum is necessary to define J_{65}, which has not been carried out in the present work. Instead, the sums of couplings obtained from the X component for both **7** and **8** have accordingly been compared with the sums of couplings calculated from the reported individual couplings for the appropriate substituted pyridine derivatives. The results are shown in Table 6, from which it is evident that the couplings in the two series are quite similar.

Table 6. ${}^{13}C$—${}^1H$ *coupling constants (Hz) at C-6 in bipyridine derivatives* **7** *and* **8**

	7	8
$J_{66} + J_{65}$ [a]	180.2	184.1
J_{66} (lit.)[b]	176.92	182.08
J_{65} (lit.)[b]	3.18	2.28
$J_{66} + J_{65}$ (calc.)	180.10	184.36

[a] From X part of ABX system

[b] Literature values [12] for 4-methylpyridine and 4-chloropyridine

For 2,2′-bipyridine **1** it may be concluded that the coupling patterns are generally very similar to those found in pyridine with the notable exception that J_{23} is considerably reduced. This may result from a substituent effect or it might be a consequence of the *trans* arrangement of the pyridine rings resulting in the nitrogen lone pair effecting the coupling constant.

The assignments of C-3 (quaternary carbon), C-4 and C-5 in 3,3′-bipyridine (**2**) were readily performed by comparison with reported spectral data for pyridine [8] and were in accordance with the earlier work of *Mal'tseva* et al. [5]. Differentiation between the closely spaced C-2 and

C-6 was achieved by reference to the coupled spectrum, since C-6 would be expected to exhibit an extra coupling. The signal at 147.99 δ was a wide doublet (J_{22}) of doublets of doublets (J_{26}, J_{24}) as expected for C-2, whilst that at 149.13 δ was a wide doublet (J_{66}) of doublets of doublets of doublets (J_{62}, J_{64}, J_{65}) and may therefore be regarded as C-6. The original assignments made by *Mal'tseva* et al. [5] therefore require reversal.

The C-4 signal was a wide doublet of doublets of doublets, with the smallest coupling designated as J_{42} since this was across the bridge, in accordance with the work of *Denisov* et al. [11] for other 3-substituted pyridines. The quaternary C-3 carbon appeared as a very broad triplet (see Fig. 1) which suggested that some unresolved long range inter-ring coupling was present (see later discussion). A second order multiplet was observed for C-5, which was partially overlapped by C-4. In general the coupling constants in **2** were very similar to those previously reported for pyridine [8]. It is interesting to note that the value of J_{32} was diminished, whilst in **1** J_{23} could not be detected.

2 (C-3)   **4** (C-3')

Fig. 1. Triplet signals for C-3 in **2** and C-3′ in **4**

Although the chemical shift assignments in 4,4′-bipyridine (**3**) were readily performed, in the coupled spectrum at 15 MHz C-2/C-6 exhibited second order character whilst the lower portion of the C-3/C-5 doublet partially obscured C-4. The spectrum was therefore additionally examined at 50.32 MHz from which the required coupling information was obtained. The C-3 signal was then a well resolved wide doublet of doublets of doublets of doublets with couplings to each of the ring protons. The C-2/C-6 peak still showed second order character even at 50 MHz. The inner components of the wide doublet appeared as clear "doublets" whilst the outer components appeared to consist of a "doublet" and a superimposed "triplet" (see Fig. 2), rather similar to the multiplets obtained by *Denisov* et al. [12] for 4-bromopyridine. The signal

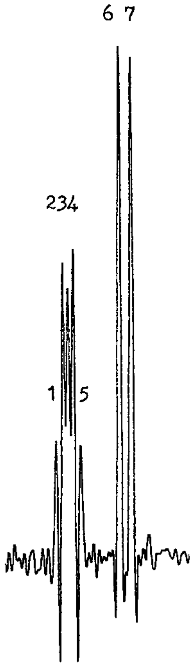


Fig. 2. Downfield portion of C-2/C-6 signal of **3** at 50.32 MHz

therefore represented the X portion of an AA'BX spin system. An attempt was made to analyse the multiplets to ascertain whether the required coupling constants could be extracted directly. This approach was then verified by reference to the 15 MHz spectrum and also by a similar analysis of the illustrated literature spectrum [12] of 4-bromopyridine. The required coupling information was obtained as follows:

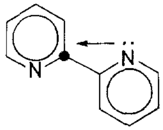
$$J_{26} = \nu_3 - \frac{(\nu_6 - \nu_7)}{2}$$

$$J_{23} = \nu_6 - \nu_7$$

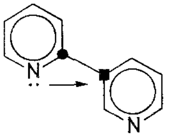
The coupling constants obtained by the above analysis were very similar to those reported by *Denisov* et al. [12] for other 4-substituted pyridines.

The signal for C-4 was a triplet of triplets of triplets suggesting three different couplings to each of two equivalent protons. The largest coupling ($J = 6.5$ Hz) was to H-2 and the smallest ($J = 1.2$ Hz) that to H-3, in accordance with earlier work [12]. Since in 4-bromopyridine C-4 was a clear triplet of triplets only [12], then the remaining splitting in **3** must therefore represent an inter-ring interaction ($^3J_{4,3'} = {}^3J_{4,5'} = 4.0$ Hz).

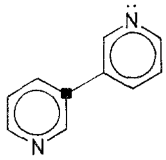
The assignments for the unsymmetric 2,3′-bipyridine (**4**) were then attempted. Initial allocations were made by direct comparison with the shieldings found for **1** and **2** and then the final assignments were deduced by reference to the proton coupled spectrum. It was found that the shifts for **4** were very similar to those of **1** and **2**. In order to assess any significant shielding differences, the chemical shift variation factors, Δ, were calculated (see Table 3). In general the variations were quite small (less than 1 ppm) except for the quaternary bridge carbons C-2 (1.79 ppm shielded) and C-3′ (1.58 ppm deshielded). These changes may be rationalised by consideration of variations in the nitrogen lone pair deshielding effects, by simple inspection to ascertain if the β-sites are occupied by carbon or nitrogen. Thus for C-2, the deshielding effect is present in **1**, but absent in **4** and accordingly an upfield shift results, whilst at C-3′ the reverse situation applies.



1



4



2

The agreement between the chemical shifts in CDCl$_3$ solution obtained in the present work (see Fig. 3) and those in CHCl$_3$ solution reported by

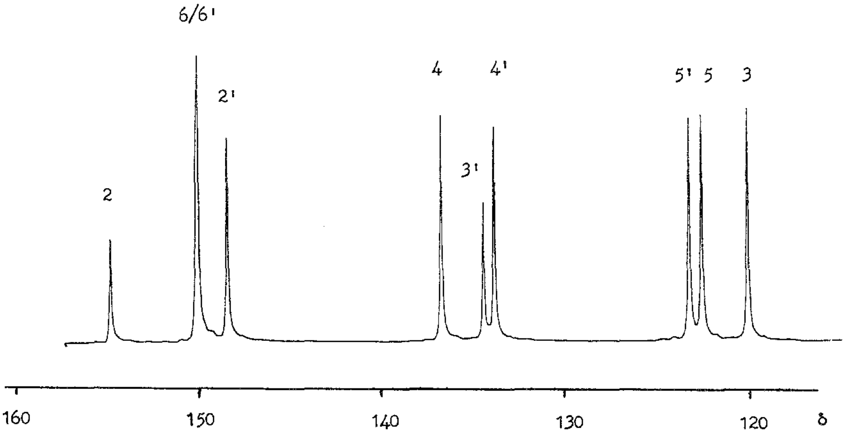
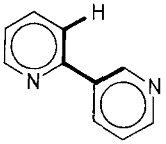


Fig. 3. Proton decoupled ^{13}C NMR spectrum of 2,3′-bipyridine

Mal'tseva et al. [5] were rather poor. In particular in the central spectral region three signals (C-4, C-4′ and C-3′) are present whilst in the earlier report only two peaks appeared. Many of the earlier literature assignments are in need of correction, and hence the present assignments are preferred.

The coupling patterns found for **4** were generally very similar to those observed in the appropriate symmetrical bipyridines, with C-6 and C-5′ both again exhibiting second order character. There were, however, two interesting differences which are worthy of discussion. In **4** C-2′ appeared as a wide doublet of doublets of doublets of doublets, the finest splitting being 0.7 Hz. This small coupling, which was not present in **2**, must be a ^4J interaction which could be either $^4J_{2'.5'}$ or $^4J_{2'.3}$. Although *Denisov* et al. [11] have reported weak $^4J_{25}$ couplings ($J = -0.85$ to -1.20 Hz) in 3-substituted pyridines, since no such splitting was detected in **2** it is therefore suggested that this fine splitting in **4** (and also the broadening seen at C-2 in **1**) represents an inter-ring interaction, which could be facilitated by a "through space" mechanism, *viz*:



4 $^4J_{2'.3} = 0.7$ Hz

The quaternary C-3′ signal was a much clearer triplet in **4** than C-3 in **2** (see Fig. 1). This would suggest that additional unresolved long range inter-ring couplings are present. In **4** only one ^3J interaction is possible ($^3J_{3'.3}$) whilst in **2** two are feasible ($^3J_{3.2'}$ and $^3J_{3.4'}$). The considerable broadening of the triplet in **2** therefore indicates that at least one inter-ring coupling must be present.

Evaluation of any potential inter-ring couplings at C-2 was unfortunately not possible since this peak was totally obscured by C-2′, C-6 and C-6′.

In the bipyridine series ^{13}C chemical shifts and ^{13}C—^{1}H spin-spin coupling constants are generally similar to those found for the appropriate substituted pyridine derivatives. Assignments for unsymmetric bipyridines may initially be made by reference to the chemical shifts of the simple bipyridines with appropriate correction for any nitrogen lone pair deshielding effects where necessary. For 3,4′-bipyridine, for example, these would be expected to be negligible.

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Experimental

^{13}C NMR spectra were generally recorded at 15 MHz (Jeol FX-60) and also at 50.32 MHz (Bruker WP200SY at University of Edinburgh) in the case of **3**. Samples were examined as dilute solutions in $CDCl_3$; for the 15 MHz spectra, the pulse width was 7 μs (45° pulse angle), pulse repetition rate 4 s, spectral width 2 500 Hz with 8 K data points. For proton coupled spectra, the "Gated-1" alternatively pulsed sequence was used and the spectral width reduced to 1 000 Hz or 500 Hz to provide better digital resolution, 4 or 8 data points per Hz, respectively; estimated error for coupling constants 0.05 Hz.

Compounds **1**, **2**, **3**, **4** and **7** were commercially available (Aldrich Chemical Co. Ltd.), compound **8** (m.p. 131–132°) was synthesised according to the general procedure of *Cook* et al. [18].

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