

Long Range ^{13}C — ^1H Coupling Constants

III†—Methylpyridines

Yoshito Takeuchi

Department of Chemistry, College of General Education, University of Tokyo, Komaba, Meguro-ku, Tokyo, Japan

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Abstract—Proton coupled carbon-13 NMR spectra of eleven mono-, di- and trimethylpyridines were analysed on a first order basis. The long range ^{13}C — ^1H coupling constants are similar to those observed for pyridine and cyanopyridines.

RECENT advances in the CW and FT carbon-13 NMR technique have made it possible to determine ^{13}C — ^1H coupling constants, including long range ones (i.e. through more than two bonds) directly from the natural abundance spectra.^{1–7} In a previous communication⁷ we compiled a few simple rules for long range ring-carbon-ring-proton coupling constants for cyanopyridines. Thus: (i) 2J : 1 to 4 Hz except for $^2J(\text{H}_\alpha)$ associated with the α -proton (8 to 9 Hz); (ii) 3J : 5 to 8 Hz except for $^3J(\text{N})$, i.e. through nitrogen (12 to 13 Hz) and $^3J(\text{C}_x)$, i.e. through the substituted carbon (3 to 5 Hz); (iii) 4J : less than 2 Hz and often unresolved.

The purpose of this study is to see whether methyl substitution will affect these J values and to estimate ring-carbon—methyl-proton or methyl-carbon—ring-proton coupling constants. This paper describes proton coupled carbon-13 NMR spectra of 2-, 3- and 4-methylpyridines (2-MP, etc.), 2,3-, 2,4-, 2,5-, 2,6-, 3,4- and 3,5-dimethylpyridines (2,3-DMP, etc.), and 2,3,6- and 2,4,6-trimethylpyridines (2,3,6-TMP, etc.).

EXPERIMENTAL

Natural abundance carbon-13 NMR spectra of eleven methylpyridines were determined at 25.2 MHz on a Varian XL-100-FT spectrometer with and without proton noise decoupling. Samples

were examined as solutions in dimethylsulphoxide- d_6 (methylpyridine 2.5 ml + solvent 1 ml). Chemical shifts are given in δ (ppm relative to TMS).

Conditions of Measurements

Decoupled spectra: spectral width 5000 Hz with 4096 memory points; acquisition time 0.4 s; pulse width 25 μsec ; No. of pulses accumulated 100 to 400. Coupled spectra: spectral width 2500 Hz with 4096 memory points; acquisition time 0.8 s; pulse width 0.8 μsec ; No. of pulses accumulated 6000 to 14000.

RESULTS AND DISCUSSION

δ and 1J Values

δ values for these methylpyridines are well documented^{8–10} except for 2,3,6-TMP. Previously, assignments were made based on the additivity relationship of methyl substituent parameters (SCS). In this study the assignment was made based on the fine splitting pattern caused by long range couplings, as well as on 1J values. δ values thus obtained, together with 1J values, are listed in Table 1. The agreement with the previous values confirms the additivity relationships, as expected.

Long Range Coupling Constants

The analysis of the fine splitting observed for methylpyridines is more difficult because of the additional couplings with methyl protons. On the other hand, this additional splitting can be used as a diagnostic

† For Part II, see Ref. 1.

TABLE 1. CHEMICAL SHIFTS (δ) AND ONE BOND COUPLING CONSTANTS (1J) FOR METHYLPYRIDINES^a

	C_2	C_3	C_4	C_5	C_6	C_2'	C_3'	C_4'	C_5'	C_6'
2-MP	158.5	123.5 (161)	136.4 (163)	121.1 (163)	149.5 (177)	24.7 (127)				
3-MP	150.6 (175)	133.4	136.8 (163)	123.7 (164)	147.3 (178)		18.5 (127)			
4-MP	150.0 (175)	125.0 (160)	147.0	125.0 (160)	150.0 (175)			20.9 (127)		
2,3-DMP	157.9	132.6	137.6 (159)	122.2 (163)	147.5 (176)	23.0 (126)	19.0 (126)			
2,4-DMP	158.9	124.8 (157)	147.7	122.7 (159)	149.9 (175)	24.6 (128)		21.1 (128)		
2,5-DMP	156.1	123.5 (161)	137.6 (159)	130.6	150.5 (174)	24.4 (128)			21.1 (127)	
2,6-DMP	158.3	120.9 (162)	137.3 (162)	120.9 (162)	158.3	24.8 (126)				24.8 (126)
3,4-DMP	151.1 (175)	133.0	146.1	125.0 (160)	148.4 (177)		16.4 (126)	19.1 (128)		
3,5-DMP	148.5 (175)	133.2	137.6 (157)	133.2	148.5 (175)		18.4 (127)		18.4 (127)	
2,3,6-TMP	158.1	128.0	138.0 (159)	121.1 (160)	155.4	22.9 (126)	18.8 (126)			24.4 (126)
2,4,6-TMP	158.1	121.8 (159)	148.0	121.8 (159)	158.1	24.6 (126)		21.0 (126)		24.6 (126)

^a Chemical shifts are in δ (ppm from TMS). Values in parentheses are 1J in Hz.

means. It was assumed that the rules (i) to (iii) found for cyanopyridines are also applicable to methylpyridines, which was confirmed as described below.

J associated with α -carbon. When coupled, the C_6 signal of 3,4-DMP [Fig. 1(a)] is a doublet of doublets (dd) (11 Hz and 2 Hz)[†] and the C_6 signal of 2,3-DMP [Fig. 1(b)] is also dd (7 Hz and 2 Hz). The smaller coupling constants can then be ascribed to $^2J(C_6-H_5)$. This assignment is confirmed by a doublet (d) (3 Hz) observed for C_6 of 2,4-DMP [Fig. 1(c)]. $^3J(N)(C_6-H_2)$ is again large (11 Hz) while $^3J(C_6-H_4)$ (7 Hz) remains in the normal range for 3J . This suggests that the pattern observed for pyridine⁵ and cyanopyridines⁷ is also applicable to methylpyridines. Thus, a quintet (qui) observed for C_6 of 2,5-DMP [Fig. 1(d)] is due to four couplings of the same magnitude (5 Hz), i.e. couplings with three protons of the 5-methyl group [$^3J(C_6-H_5)$][§] and with H_4 [$^3J(C_x)(C_6-H_4)$]. $^2J(C_2-H_2)$ can be estimated from the $C_{2,6}$ signal of 2,4,6-TMP, which is essentially a quartet (qua) (6 Hz) with fine structure [$^2J(C_2-H_3) = c. 2$ Hz] [Fig. 1(e)].

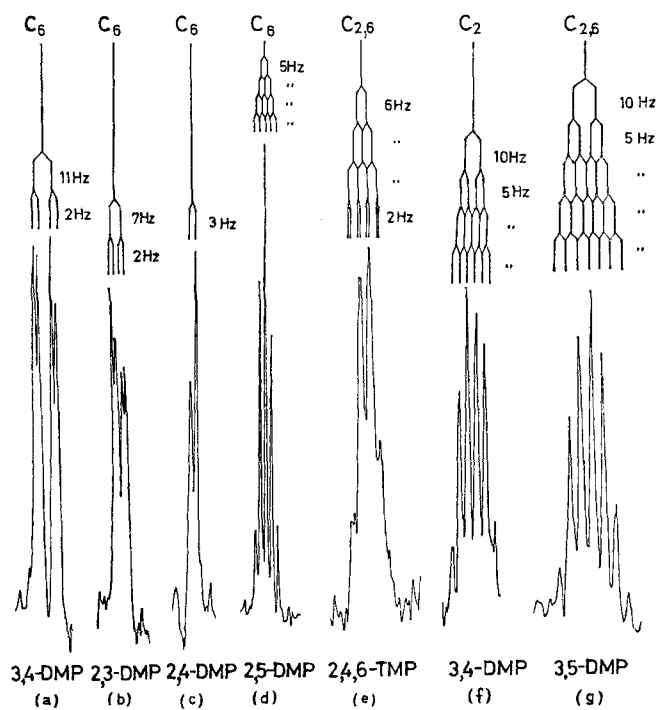


FIG. 1. Fine splittings observed for α -carbons (C_2 and C_6) of methylpyridines.

The validity of these interpretations is further confirmed by the successful analysis of a few more complicated splittings observed for other compounds. Thus, a sextet (sex) [Fig. 1(f)] observed for C_2 of 3,4-DMP can be rationalised so as to involve $^3J(N)(C_2-H_6)$ (10 Hz) and three $^3J(C_2-H_3)$ (5 Hz). A septet (sep) observed for C_2 of 3-MP or 3,5-DMP [Fig. 1(g)] again involves $^3J(N)(C_2-H_6)$ (10 Hz), $^3J(C_x)(C_2-H_4)$ (5 Hz) and three $^3J(C_2-H_3)$ (5 Hz). These results are summarised in Table 2.

J associated with β -carbon. The C_5 signal of both 3-MP and 2,3-DMP is a wide d (8 Hz) [Fig. 2(a)]

[†] When long range couplings are discussed, splitting due to the one bond coupling is not quoted.

[§] Carbons and protons numbered with (') are associated with the methyl group.

TABLE 2. LONG RANGE ^{13}C - 1H COUPLING CONSTANTS FOR METHYLPYRIDINES (Hz)^a

	3J	2J	
C_2	$^3J(C_2-H_4)$	7	$^2J(C_2-H_3)$
	$^3J(C_x)(C_2-H_4)$	5	$^2J(C_2-H_2')$
	$^3J(N)(C_2-H_6)$	10-11	
	$^3J(C_2-H_3')$	5	
C_3	$^3J(C_3-H_6)$	6-7	$^2J(H_{\alpha})(C_3-H_3)$
	$^3J(C_x)(C_3-H_3)$	5	$^2J(C_x)(C_3-H_2)$
	$^3J(C_3-H_2')$	4	$^2J(C_3-H_3')$
	$^3J(C_3-H_4')$	4	
C_4	$^3J(C_4-H_2)$	6	$^2J(C_4-H_4')$
	$^3J(C_x)(C_4-H_2)$	5	
	$^3J(C_4-H_3')$	5	
C_2'	$^3J(C_2'-H_3)$	2	
etc.	$^3J(C_3'-H_2)$	3	
	$^3J(C_3'-H_4)$	5	
	$^3J(C_4'-H_3)$	5	

^a Carbons and protons numbered with (') are associated with the methyl group.

while the C_5 signal of 2-MP is dd (8 Hz and 6 Hz) [Fig. 2(b)]. As is the case with pyridine and cyanopyridines,⁷ 2J involving an α -proton is again enhanced [$^2J(H_{\alpha})(C_5-H_6) = 8$ Hz] while $^3J(C_5-H_3)$ remains normal (6 Hz). The $C_{3,5}$ signal of 4-MP is sep with fine structure [Fig. 2(c)]; since $^2J(C_{\alpha})(C_3-H_2)$ is 8 Hz, the rest of the splitting is due to $^3J(C_x)(C_3-H_5)$ (5 Hz) and three $^3J(C_3-H_4')$ (4 Hz). The C_3 signal of 2,5-DMP is qua (Fig. 2(e)); hence $^3J(C_3-H_2')$ is 4 Hz. The $C_{3,5}$ signal of 3,5-DMP is qui [Fig. 2(f)], indicating that both $^2J(C_3-H_3')$ and $^2J(C_x)$ observed for other compounds is less remarkable here, perhaps due to the methyl substitution. The results are listed in Table 2.

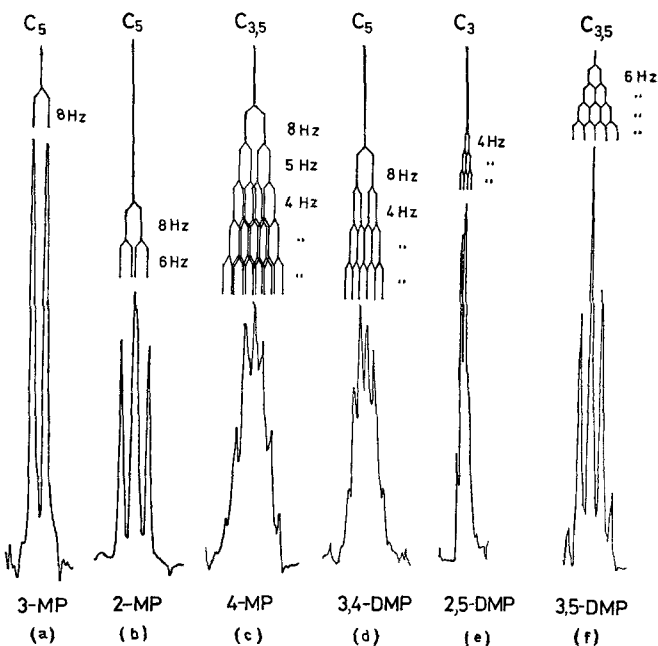


FIG. 2. Fine splittings observed for β -carbons (C_3 and C_5) of methylpyridines.

J associated with γ -carbon. The C_4 signal of 2-MP is a sharp d [Fig. 3(a)], indicating that $^3J(C_4-H_6)$ is normal (6 Hz). The C_4 signal of 2,3,6-TMP is qua [Fig. 3(b)] to give $^3J(C_4-H_3)$ (5 Hz). This assignment is confirmed by qui [Fig. 3(c)] of the C_4 signal for 2,5-DMP where $^3J(C_x)(C_4-H_6)$ (5 Hz) is involved in addition to three $^3J(C_4-H_5')$ (5 Hz). The C_4 signal

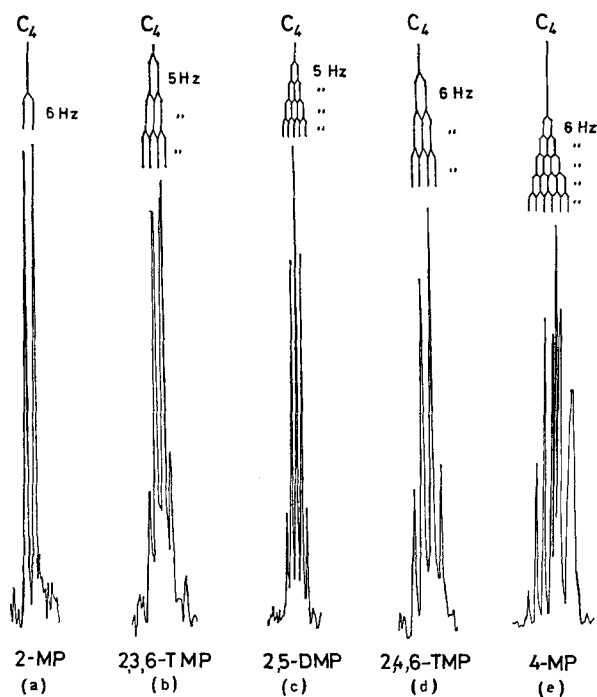


FIG. 3. Fine splittings observed for γ -carbons (C_4) of methylpyridines.

of 2,4,6-TMP is qua [Fig. 3(d)]; hence $^2J(\text{C}_4\text{—H}_4)$ is 6 Hz. Thus C_4 of 4-MP should give a sex [$^3J(\text{C}_4\text{—H}_2)$, $^3J(\text{C}_4\text{—H}_6)$ and three $^3J(\text{C}_4\text{—H}_4')$, all 6 Hz] as is in fact observed [Fig. 3(e)]. A part of the peaks is masked here by the other signal. The results are listed in Table 2.

J associated with methyl carbon. When coupled, each methyl carbon gives qua ($^1J = c. 127$ Hz). Each of the four peaks is further split through the coupling with ring proton(s), (if any) *ortho* to the methyl group as shown by the C_2' signal for 2-MP, 2,4-DMP, etc. d (2 Hz) [Fig. 4(a)]. The magnitude of the long range splitting seems to depend on the nature of the proton involved. Thus, the C_3' signal of 3-MP is dd (5 Hz and 3 Hz) [Fig. 4(b)]. The smaller one (3 Hz) is likely to be the one involving the α -proton [$^3J(\text{C}_3'\text{—H}_2)$]. Interestingly,

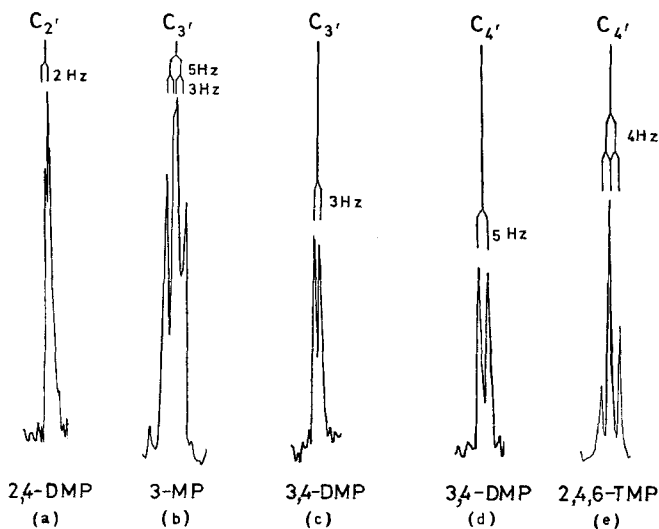


FIG. 4. Fine splittings observed for methyl carbons of methylpyridines.

the effect of the α -proton is reversed here as compared with that on $^2J(\text{C}_3\text{—H}_2)$.

This interpretation is confirmed by d for C_3' (3 Hz) and d for C_4' (5 Hz) of 3,4-DMP [Fig. 4(c) and 4(d)]. $^3J(\text{C}_4'\text{—H}_6)$ is evidently larger than $^3J(\text{C}_3'\text{—H}_2)$ since C_4' of 2,4,6-TMP gives t (6 Hz) [Fig. 4(e)]. The results are listed in Table 2.

Assignment Based on the Fine Splitting

In principle, the differentiation between C_2 and C_6 (or C_2' and C_6') or between C_3 and C_5 (or C_3' and C_5') signals of unsymmetrically substituted pyridines is not trivial if the assignment is based on δ values alone. Assignment based on J values (1J and long range ones) is, on the contrary, unambiguous as will be seen in the following examples:

(a) C_2 and C_6 signals of 3-MP. C_2 should give sep similar to the one observed for $\text{C}_{2,6}$ of 3,5-DMP while C_6 should exhibit eight lines due to three different couplings [$^3J(\text{N})(\text{C}_6\text{—H}_2) = 11$ Hz, $^3J(\text{C}_6\text{—H}_4) = 7$ Hz, and $^2J(\text{C}_6\text{—H}_5) = 2$ Hz] which is the case [Fig. 5(a)].

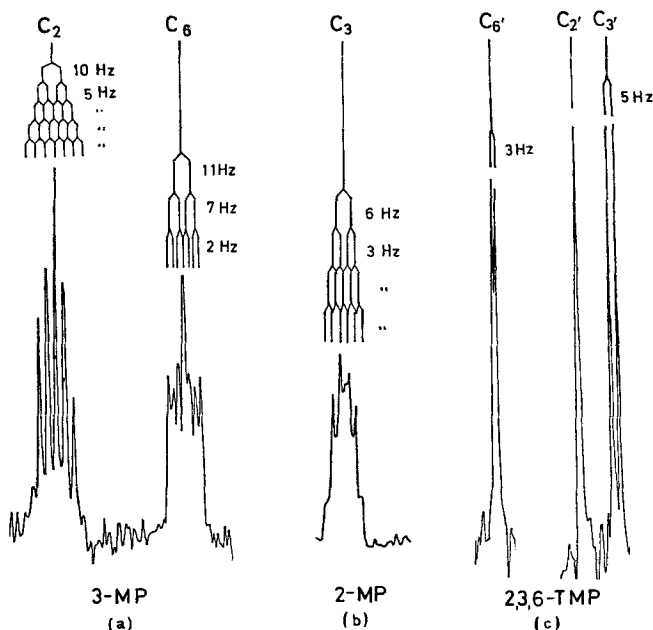


FIG. 5. Differentiations of two α -, β - and α' -carbon resonances based on the fine splittings.

(b) C_2 and C_6 signals of 3,4-DMP. C_2 gives sex [Fig. 1(f)] while C_6 is dd [Fig. 1(a)].

(c) C_3 and C_5 signals of 2-MP. C_3 signal should be sex [$^3J(\text{C}_3\text{—H}_5) = 6$ Hz and three $^3J(\text{C}_3\text{—H}_2) = 3$ Hz] while C_5 is expected to give dd [Figs. 5(b) and 2(b)].

(d) C_3 and C_5 signals of 2,4-DMP. C_3 should give a complex multiplet similar to the one observed for C_3 of 2,4,6-TMP while the C_5 signal should be a multiplet similar to the $\text{C}_{3,5}$ signal of 4-MP.

(e) C_2' and C_6' signals of 2,3,6-TMP. For the C_2' signal no fine splitting is observed, while C_6' gives d which can easily be differentiated from the C_3' signal because of the narrower splitting for the former [Fig. 5(c)].

CONCLUSION

It has been found that the long range coupling constants in methylpyridines followed the general

pattern observed for pyridine and cyanopyridines. The fine splitting pattern caused by long range couplings is very characteristic and can be used as a type of fingerprint for the assignment.

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