The Additivity of Substituent Effects in One-bond ^{13}C–^{1}H Coupling Constants in Polysubstituted Pyridines

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The additivity of substituent effects upon one-bond ^{13}C–^{1}H coupling constants in polysubstituted pyridines is described. The substituent effects on $^{1}J(^{13}CH)$ in monosubstituted pyridines account very well for $^{1}J(^{13}CH)$ in a variety of polysubstituted pyridines. The additivity relation has some diagnostic value in the assignment of ^{13}C resonances where the chemical shift difference is extremely small.

THE additivity of substituent effects upon ^{1}H–^{1}H coupling constants in polysubstituted aromatic and heteroaromatic compounds has frequently been described.[1] In the light of the well established relation between $J(HH)$ and $J(^{13}CH)$ for geometrically equivalent systems,[2] much the same additivity relation is expected for $J(^{13}CH)$. Although the additive nature of substituent effects on $^{1}J(^{13}CH)$ of molecules of the type CHXYZ has been known since the advent of n.m.r. spectroscopy,[3] additivity for $^{1}J(^{13}CH)$ for aromatic systems is little documented. To the best of our knowledge additivity for $^{1}J(^{13}CH)$ in halogenobenzenes[4] is the only example hitherto reported. In the course of our systematic investigation of ^{13}C–^{1}H coupling constants in pyridine derivatives,[5-8] we have found additivity of substituent effects upon $^{1}J(^{13}CH)$ for a wide range of polysubstituted pyridines.

A substituent coupling constant (SCC) for substituent X in pyridine [X-SCC(m,n)] is defined as the change that occurs in the value of $^{1}J(^{13}CH)$ at C-n(n = 2—6) upon substitution of a pyridine ring proton at C-m (m = 2—6, $m \neq n$) by a substituent X; *i.e.*, X-SCC = $\Delta^{1}J$ = ^{1}J(X-pyridine) − ^{1}J(pyridine) for the corresponding position. In Table 1, $^{1}J(^{13}CH)$ of various monosubstituted pyridines and in Table 2, the SCC for substituents NH_2, OH, Me, and Cl on pyridine are summarised. In Table 3, the $^{1}J(^{13}CH)$ values observed for various di- and tri-substituted pyridines (1)—(19) are compared with the values calculated from equation (1).

$$^{1}J[\text{X,Y,(Z)-pyridine}] = {}^{1}J(\text{pyridine}) + \Sigma(\text{X-SCC}) \quad (1)$$

TABLE 1

One-bond ^{13}C–^{1}H coupling constants for monosubstituted pyridines

	$^{1}J(^{13}CH)$/Hz				
	C-2	C-3	C-4	C-5	C-6
None [a]	178	163	162	163	178
2-NH_2 [b]		164	161	166	175
2-Me [c]		161	163	163	177
2-Cl [d]		172	167	166	182
3-NH_2 [b]	175		160	161	178
3-OH [b]	178		162	162	181
3-Me [c]	175		160 [e]	164	178
3-Cl [d]	185		168	166	181
4-NH_2 [b]	171	160		160	171
4-Me [c]	175	160		160	175

[a] Data from H. Hansen and H. J. Jakobsen, *J. Magnetic Resonance*, 1973, **10**, 74. [b] Data from ref. 7. [c] Data from ref. 6. [d] This investigation. [e] An accidental overlap of the C-3 and the upper half of the C-4 peaks under the single resonance condition makes the accurate determination of $^{1}J(^{13}CH)$ for C-4 difficult. A careful reinvestigation of the spectrum led us to revise the value from 163 to 160 Hz.

TABLE 2

Substituent coupling constant [X-SCC(m,n)] for pyridines (Hz)

Substituent	(2,3)	(2,4)	(2,5)	(2,6)	(3,2)	(3,4)	(3,5)	(3,6)	(4,2)	(4,3)
NH_2 [a]	+1	−1	+3	−3	−3	−2	−2	0	−7	−3
OH [a]					0	0	−1	+3		
Me [b]	−2	+1	0	−1	−3	−2	+1	0	−3	−3
Cl [c]	+9	+5	+3	+4	+7	+6	+3	+3		

[a] Data from ref. 7. [b] Data from ref. 6. [c] This investigation.

The agreement between the observed and calculated values is excellent with a deviation of <2 Hz except for one entry [C-4 of (14)]. Since the SCC values for Me, NH_2, and OH are generally small, and occasionally cancel each other in polysubstituted systems, one can attribute the agreement observed for polymethylpyridines (1)—(8), aminomethylpyridines (12)—(14), and methylpyridinol (18) to a mere coincidence. The excellent agreement observed for dichloropyridines (9)—(11), aminochloropyridines (15)—(17), and chloropyridinol (19), where the SCC values are large and the sum of the SCCs amounts to 12 Hz in not a few cases, clearly demonstrates the existence of an additivity relation.

The observed additivity has some diagnostic value in the assignment of ^{13}C resonances. Thus, two nearby peaks at δ 123.7 (^{1}J 169 Hz) and 123.9 (^{1}J 163 Hz) for C-3 and -4 of 5-amino-2-chloropyridine (17) are hard to assign if based solely on the chemical shift. There is, however, a difference of 5 Hz in the calculated ^{1}J(170 for C-3 and 165 Hz for C-4), which is sufficient to differentiate between the two peaks; the peak at higher field which splits more under the single resonance condition was unequivocally assigned to C-3. Another, less unambiguous example is the assignment of two peaks due to C-4 and -5 of (19). The chemical shift difference is again 0.2 p.p.m. The calculated ^1J is 167 for C-4 and 165 Hz for C-5. Thus, the peak at higher field which splits by 1.5 Hz more than the one at lower field is tentatively assigned to C-4.

TABLE 3

One-bond $^{13}C-^{1}H$ coupling constants in polysubstituted pyridines

Compound	Substituent	C-2	C-3	C-4	C-5	C-6
(1)	2,3-Me_2 [b]			159 (161)	163 (164)	176 (177)
(2)	2,4-Me_2 [b]		157 (158)		159 (160)	175 (174)
(3)	2,5-Me_3 [b]		161 (161)	159 (161)		174 (174)
(4)	2,6-Me_2 [b]		162 (161)	162 (164)	162 (161)	
(5)	3,4-Me_2 [b]	175 (172)			160 (161)	177 (175)
(6)	3,5-Me_2 [b]	175 (175)		157 (158)		175 (175)
(7)	2,3,6-Me_3 [b]			159 (161)	160 (162)	
(8)	2,4,6,-Me_3 [c]		159 (158)		159 (158)	
(9)	2,3-Cl_2 [c]			172 (173)	170 (169)	186 (185)
(10)	2,6-Cl_2 [c]		175 (175)	170 (172)	175 (175)	
(11)	3,5-Cl_2 [c]	189 (188)		175 (174)		189 (188)
(12)	2-NH_2-3-Me [b]			158 (159)	165 (167)	175 (175)
(13)	2-NH_2-4-Me [c]		160 (161)		163 (163)	173 (172)
(14)	2-NH_2-6-Me [c]		162 (164)	159 (162)	163 (164)	
(15)	2-NH_2-5-Cl [c]		165 (167)	165 (167)		181 (182)
(16)	3-NH_2-2-Cl [c]			163 (164)	164 (165)	183 (182)
(17)	5-NH_2-2-Cl [c]		169 (170)	163 (165)		179 (179)
(18)	3-OH-6-Me [d]	175 (177)		161 (163)	162 (160)	
(19)	3-OH-2-Cl [d]			165.5 (167)	164 (165	184 (185)

[a] Values in parentheses are the calculated based on the additivity relation. [b] Data from ref. 6. [c] This investigation. [d] Data from ref. 8.

It must be emphasised that the assignment based on the fine splitting pattern due to long-range $^{13}C-^{1}H$ couplings observed under the single resonance condition [5-8] failed in the latter case because the pattern is nearly identical for the two nuclei. It is worth noting that the resolution required to permit observation of the fine splitting is more difficult to attain compared with that necessary for a rough estimation of $^1J(^{13}CH)$. Further examples of the additivity of $^1J(^{13}CH)$ together with carbon-13 n.m.r. parameters of the compounds (9)—(18) will be described elsewhere.

EXPERIMENTAL

Carbon-13 n.m.r. spectra were determined on Varian XL-100FT or Varian CFT-20 spectrometers. All samples were contained in precision ground 10 mm o.d. tubes as [$^2H_6$]DMSO solutions (1 : 1 v/v or saturated). In a typical measurement under the single resonance condition, on average 8 or 14 μs pulses were employed. The delay between pulses was 2 or 3 s for an average spectral width of 1 000 Hz. The number of acquisitions was on average 1 000, over 8 K data points.

All the compounds are commercially available and were used without further purification.

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