^{13}C-NMR SHIFT INCREMENTS FOR 3-SUBSTITUTED PYRIDINES

Roger Dommisse, Eddy Freyne, Eddy Esmans, Josef Lepoivre,
and Frank Alderweireldt
University of Antwerpen (R.U.C.A.), Laboratory for Organic Chemistry,
Groenenborgerlaan, 171, B-2020 Antwerpen, Belgium

Abstract - The ^{13}C-NMR spectra of some 3-substituted and 3,5-disubstituted pyridines are examined. It appears that the shift increments for the 3-acetyl group previously published in the literature were based on a wrong assignment of the spectra. A new set of shift increments for 3- or 5-substituents are derived from the spectra of such compounds, most of which were not described before.

Recent publications[1,2] only mention a small set of increments $A_{ik}(R_i)$ to determine the ^{13}C-chemical shifts of 3-substituted pyridines. According to this formalism the shift of any of the pyridine carbon atoms is given by:

$$\delta C_{(k)} = C_k + \sum_i A_{ik}(R_i),$$

C_k being the shift of the corresponding carbon atom in the unsubstituted pyridine and A_{ik} being the shift increment predicted for carbon k upon introduction of substituent R_i at carbon i.

The chemical shifts of our compounds are summarized in Table 1.

The ^{13}C-NMR spectra of nicotinic acid 6, its alkyl esters[4], alkylamides[4] and 3-acetylpyridine 1 have already been described before[4]. This is also the case for the 3-substituted methyl pyridines[3]. In the case of 3-acetylpyridine however the assignment of shift values for carbon atoms C_2 and C_6 has been made in contradictory ways[4]. Our set of 5-alkylsubstituted 3-acetylpyridine derivatives enables us to clear up this matter by recording proton-coupled ^{13}C-NMR spectra. The coupled spectrum of 3-acetyl-5-isopropylpyridine is given as an example (see Figure 1).

TABLE 1: ^{13}C-N M R chemical shifts of 3-substituted and 3,5-disubstituted pyridines in $CDCl_3$.

	Substituent	C_2	C_3	C_4	C_5	C_6	Other C-atoms
1	R_3= $COCH_3$	149.86	132.19	135.35	123.58	153.43	-$COCH_3$: 196.57, 26.63
2	R_3= $COCH_3$	147.12	131.83	135.50	133.23	153.90	-$COCH_3$: 196.57, 26.6
	R_5= CH_3						-CH_3: 18.2
3	R_3= $COCH_3$	147.43	132.02	134.32	139.3.	153.38	-$COCH_3$: 196.75, 26.69
	R_5= CH_2CH_3						-CH_2CH_3: 25.90, 15.05
4	R_3= $COCH_3$	147.49	132.02	134.81	137.72	153.68	-$COCH_3$: 196.57, 26.63
	R_5= $CH_2CH_2CH_3$						-$CH_2CH_2CH_3$: 34.76, 24.09, 13.59
5	R_3= $COCH_3$	147.67	132.14	132.81	143.85	152.58	-$COCH_3$: 196.82, 26.75
	R_5= $CH(CH_3)_2$						-$CH(CH_3)_2$: 31.67, 23.54
6	R_3= COOH ¶	150.16	126.56	136.99	123.70	153.13	-COOH: 166.24
7	R_3= COOH ¶	147.43	126.07	136.99	133.17	153.55	-COOH: 166.30
	R_5= CH_3						-CH_3: 17.65
8	R_3= COOH	146.40	128.44	138.81	140.39	149.91	-COOH: 167.63
	R_5= CH_2CH_3						-CH_2CH_3: 25.91, 14.92

¶ N.M.R. spectra recorded in DMSO-d_6 solution

TABLE 1 (continued): ^{13}C-N M R chemical shifts of 3-substituted and 3,5-disubstituted pyridines in $CDCl_3$.

	Substituent	C_2	C_3	C_4	C_5	C_6	Other C-atoms
9	R_3= COOH R_5= $CH_2CH_2CH_3$	146.03	128.68	139.66	139.12	149.86	-COOH: 167.38 $-CH_2CH_2CH_3$: 34.70, 23.90, 13.53
10	R_3= COOH R_5= $CH(CH_3)_2$	146.46	128.80	137.48	144.94	148.94	-COOH: 167.33 $-CH(CH_3)_2$: 31.79, 23.48
11	R_3= $COOCH_3$	150.87	126.01	136.93	123.28	153.38	$-COOCH_3$: 165.68, 52.36
12	R_3= $COOCH_3$ R_5= CH_3	148.09	125.59	137.24	132.99	153.92	$-COOCH_3$: 165.93, 52.30 $-CH_3$: 18.26
13	R_3= $COOCH_3$ R_5= CH_2CH_3	148.28	125.71	136.02	138.99	153.25	$-COOCH_3$: 165.81, 52.18 $-CH_2CH_3$: 25.84, 15.05
14	R_3= $COOCH_3$ R_5= $CH_2CH_2CH_3$	148.34	125.65	136.63	137.54	153.62	$-COOCH_3$: 165.87, 52.24 $-CH_2CH_2CH_3$: 34.70, 24.09, 13.53
15	R_3= $COOCH_3$ R_5= $CH(CH_3)_2$	148.46	125.77	134.50	143.48	152.40	$-COOCH_3$: 165.87, 52.24 $-CH(CH_3)_2$: 31.67, 23.54
16	R_3= $CONH_2$ R_5= $CH(CH_3)_2$	145.67	129.17	133.60	144.03	151.25	$-CONH_2$: 168.30 $-CH(CH_3)_2$: 31.67, 23.45

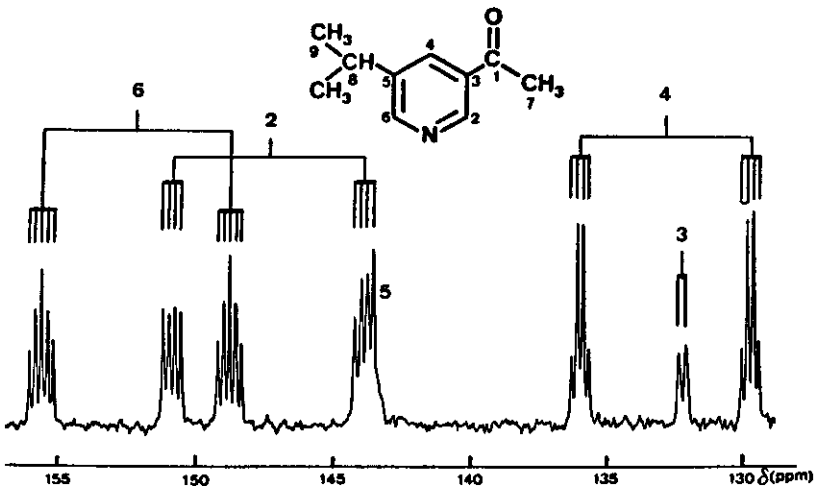

Figure 1: Proton-coupled ^{13}C-NMR spectrum of the pyridine C-atoms of 3-acetyl-5-isopropylpyridine (5) in $CDCl_3$.

The carbon atoms C_2, C_4 and C_6 exhibit a large $^1J_{CH}$ coupling of 182, 161 and 176 Hz respectively and also two $^3J_{CH}$ couplings to the protons of the carbon atoms situated in meta-position. Carbon C_6 however shows an additional $^3J_{CH}$ coupling to the proton of the alkyl substituent in α-position to the ring. This observation allows an unambiguous assignment of C_2 and C_6 for all our 5-substituted derivatives, but also for 3-acetylpyridine. This is done by substracting the known methyl shift increments from our experimental results for compound 2. A set of increments A_{3k} for several 3-substituents was derived from our experimental results and gathered in Table 2. The values for the 3-acetyl group have been included in this series. The corresponding values published in different reference works must be replaced by these new values since they are based on an erroneous assignment for C_2 and C_6.

TABLE 2.

R_3	A_{32}	A_{33}	A_{34}	A_{35}	A_{36}
$-COCH_3$	-0.3	+8	-0.8	-0.6	+3.8
$-CH_2CH_2CH_3$	0.2	+14.2	-0.4	-0.3	-2.5
$-CH(CH_3)_2$	-0.9	+20.2	-2.5	-0.2	-2.3
-COOH ¶	-0.8	+4.7	+3.9	0.8	-0.1
$-COOCH_3$	0.9	+1.9	+1.0	-0.3	+3.5

¶ The values for the -COOH group are based on the chemical shifts of $CDCl_3$ soluble acids.

Acknowledgements

We thank the N.F.W.O. for financial support and Mr. J. Schrooten for technical assistance.

References

1. E. Pretsch, T. Clerc, J. Seibl, and W. Simon, "Tabellen zur Strukturaufklärung Organischer Verbindungen", Springer Verlag, Berlin, 1976.
2. F.W. Wehrli, and T.W. Wirthlin, "Interpretation of Carbon-13 NMR spectra", Heyden, London, 1976.
3. F.J. Weigert, J. Husai, and J.D. Roberts, J. Org. Chem., 1973, 38, 1313.
4. For a review of 3-substituted pyridines: W. Bremser, L. Ernst, and B. Franke, "Carbon-13 NMR spectral data", Verlag Chemie, Weinheim, 1979.

Received, 23rd June, 1981