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# $^{13}$C-NMR QUATERNISATION SHIFT INCREMENTS FOR 3-SUBSTITUTED PYRIDINES IN N-BENZYL- AND N-2,4-DINITROPHENYL-PYRIDINIUM SALTS

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Abstract - The $^{13}$C-NMR spectra of a series of 3-substituted and 3,5-disubstituted pyridinium salts are examined. It appears that quaternisation shift increments have to be used with care because of their dependence on the pyridine substituents present, the N-alkyl- or N-aryl group and the experimental conditions (e.g. solvent, concentration, counter ion ...).

Recent publications describe only a limited number of $^{13}$C-NMR spectra of pyridinium salts[1-6], mostly halogenohydrates or N-methyl derivatives of symmetrical pyridines. A set of N-benzyl- and N-(2,4-dinitrophenyl)pyridinium salts were needed in the course of our work on the synthesis and reactivity of pyridines and pyridine nucleosides. Their $^{13}$C-NMR spectral behaviour is discussed here.

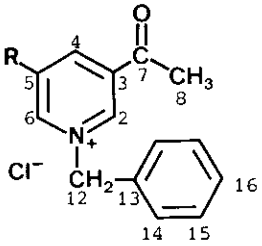
### 3-Acetyl-5-alkyl-1-benzylpyridinium salts (1-5).

The $^{13}$C-NMR chemical shifts of the 3-acetyl-5-alkylpyridine derivatives used for our syntheses have been published recently[7]. The $^{13}$C-NMR chemical shifts of the corresponding N-benzylpyridinium salts are gathered in Table 1.

The peaks of 3-acetyl-N-benzylpyridinium chloride 1 can be assigned using chemical shift rules ($C_7$,$C_8$,$C_{12}$), the singlet character in the off-resonance decoupled spectrum ($C_3$,$C_{13}$) and selective decoupling experiments (other carbon atoms).

TABLE 1

$^{13}$C-NMR chemical shifts of 3-acetyl-5-alkyl-1-benzylpyridinium chlorides[a]



1 R= H-

2 R= $\underset{9}{CH}_3$-

3 R= $\underset{10}{CH}_3$-$\underset{9}{CH}_2$-

4 R= $\underset{11}{CH}_3$-$\underset{12}{CH}_2$-$\underset{13}{CH}_2$-

5 R= $(\underset{10}{CH}_3)_2\underset{9}{CH}$-

| Atom[b] | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| C-2 | 144.64 | 141.78 | 141.97 | 142.09 | 142.15 |
| C-3 | 135.90 | 135.35 | 135.54 | 135.66 | 135.84 |
| C-4 | 144.90 | 145.43 | 144.40 | 144.82 | 143.12 |
| C-5 | 128.92 | 140.94 | 146.46 | 145.12 | 150.76 |
| C-6 | 147.00 | 146.46 | 145.91 | 146.22 | 145.22 |
| C-7 | 196.15 | 196.51 | 196.45 | 196.51 | 196.45 |
| C-8 | 26.69 | 26.75 | 26.75 | 26.82 | 26.75 |
| C-9 |  | 17.84 | 25.54 | 33.91 | 31.73 |
| C-10 |  |  | 13.71 | 22.99 | 22.08 |
| C-11 |  |  |  | 12.62 |  |
| C-12 | 64.98 | 64.80 | 64.73 | 64.80 | 64.80 |
| C-13 | 132.32 | 132.50 | 132.63 | 132.68 | 132.63 |
| C-14,15 | 129.65 | 129.53 | 129.53 | 129.59 | 129.53 |
|  | 129.23 | 129.04 | 128.99 | 128.99 | 128.92 |
| C-16 | 130.08 | 129.96 | 129.84 | 129.89 | 129.84 |

[a] All the shifts are in ppm-values measured for 1M $D_2O$ solutions with 1,4-dioxane as an internal standard and converted to the TMS scale using $\delta_{diox} = 67.4$ ppm.

[b] This C-atom numbering, although non strictly IUPAC, is consistently used for simplicity.

### 3-Alkylaminocarbonyl-1-(2,4-dinitrophenyl)pyridinium chlorides (7 - 9).

The spectrum of 1-(2,4-dinitrophenyl)-3-aminocarbonylpyridinium chloride 7 is given as an example in the following figure

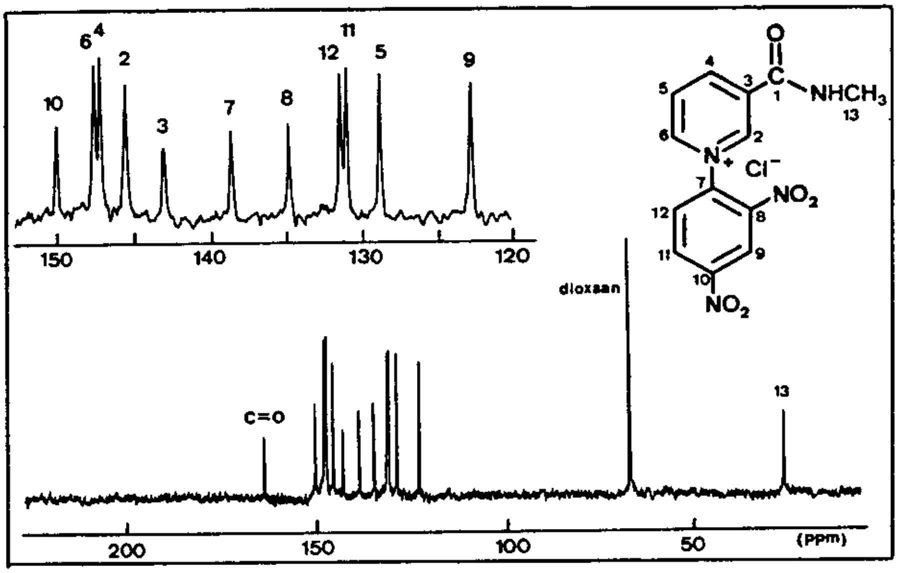


Figure 1: Noise decoupled $^{13}$C-NMR spectrum of 1-(2,4-dinitrophenyl)-3-aminocarbonylpyridinium chloride 7.

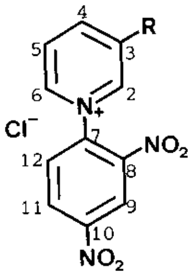
The chemical shifts measured for these compounds and for the unsubstituted pyridine analogue 6 are summarized in Table 2. The assignment of the phenyl carbon atoms of 6 is possible using increment values for nitro- and pyridinium groups on the aromatic ring recently published by Ewing[9]. Peak intensities can be used for the identification of pyridine signals C-2 + C-6 and C-3 + C-5. The peaks in the other compounds can be assigned by comparing with product 6 and by selective proton decoupling experiments.

### 3-Acetyl-5-alkyl-1-(2,4-dinitrophenyl)pyridinium p-toluenesulphonates (11 - 13).

The carbon-13 chemical shifts of this series of compounds are summarized in Table 3. The assignments of all the signals is only possible by comparing the spectrum of 1-(2,4-dinitrophenyl)pyridinium p-toluenesulphonate 10 with the spectra of the substituted pyridinium salts (11 -13). The signals of 10 can be identified by the same methods as described for 6.

TABLE 2

$^{13}$C-NMR chemical shifts of 1-(2,4-dinitrophenyl)pyridinium chloride 6 and three 3-alkylaminocarbonyl-1-(2,4-dinitrophenyl)pyridinium chlorides 7 - 9



6 R= H-

7 R= $\underset{13}{CH_3}NH\underset{15}{C}O-$

8 R= $\underset{14}{CH_3}-\underset{13}{CH_2}NH\underset{15}{C}O-$

9 R= $(\underset{14}{CH_3}-\underset{13}{CH_2})_2N\underset{15}{C}O-$

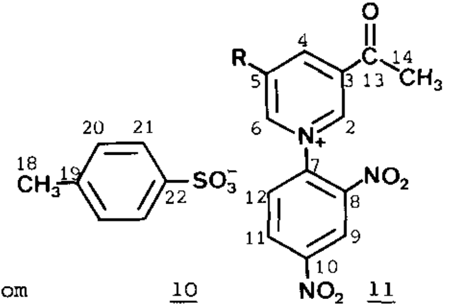
| Atom | 6 | 7 | 8 | 9 |
|---|---|---|---|---|
| C-2 | 146.24 | 146.03 | 146.03 | 144.25 |
| C-3 | 129.35 | 135.47 | 135.66 | 137.26 |
| C-4 | 150.07 | 147.73 | 147.73 | 147.26 |
| C-5 | 129.35 | 129.47 | 129.41 | 130.12 |
| C-6 | 146.24 | 148.09 | 148.04 | 147.50 |
| C-7[a] | 143.61 (146.6)[b] | 143.55 | 143.48 | 143.56 |
| C-8[a] | 139.54 (147.2) | 139.18 | 139.12 | 139.06 |
| C-9 | 123.43 (122.0) | 123.58 | 123.53 | 123.57 |
| C-10 | 150.32 (153.9) | 150.58 | 150.58 | 150.60 |
| C-11 | 131.58 (133.9) | 131.66 | 131.59 | 131.68 |
| C-12 | 132.21 (129.3) | 132.02 | 132.02 | 131.96 |
| C-13 | | 27.60 | 36.46 | 41.74 and 45.43 |
| C-14 | | | 14.13 | 12.72 and 14.03 |
| C-15 | | 164.17 | 163.38 | 165.27 |

[a] The assignment of C-7 and C-8 may be reversed because the multiplets obtained in proton coupled spectra are not completely resolved.

[b] Chemical shifts calculated according to the increments published by D.F. Ewing[9].

TABLE 3

$^{13}$C-NMR chemical shifts[a] of 1-(2,4-dinitrophenyl)pyridinium p-toluenesulphonate 10 and a series of 3-acetyl-5-alkyl-1-(2,4-dinitrophenyl)pyridinium p-toluenesulphonates (11 - 13)



10 R= H-

11 R= $\underset{15}{C}H_3$-

12 R= $\underset{15}{C}H_3$-$\underset{16}{C}H_2$-

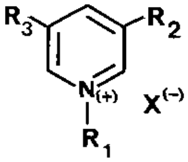
13 R= $\underset{15}{C}H_3$-$\underset{16}{C}H_2$-$\underset{17}{C}H_2$-

| Atom | 10 | 11 | 12 | 13 |
|---|---|---|---|---|
| C-2 | 146.00 | 144.14 | 144.58 | 144.52 |
| C-3 | 127.94 | 134.26 | 134.81 | 134.63 |
| C-4 | 148.86 | 147.31 | 145.00 | 146.58 |
| C-5 | 127.94 | 138.94 | 148.52 | 142.87 |
| C-6 | 146.00 | 148.04 | 147.12 | 147.97 |
| C-7 | 142.89 | 142.70 | 142.76 | 142.76 |
| C-8 | 138.67 | 138.39 | 138.51 | 138.45 |
| C-9 | 121.29 | 121.16 | 121.04 | 121.09 |
| C-10 | 148.86 | 148.94 | 148.82 | 148.76 |
| C-11 | 130.02 | 129.96 | 129.89 | 129.89 |
| C-12 | 131.77 | 132.02 | 132.14 | 132.08 |
| C-13 |  | 193.72 | 193.78 | 193.78 |
| C-14 |  | 27.24 | 27.36 | 27.36 |
| C-15 |  | 17.84 | 31.49 | 33.49 |
| C-16 |  |  | 22.38 | 22.87 |
| C-17 |  |  |  | 13.04 |
| C-18 | 20.72 | 20.69 | 20.75 | 20.68 |
| C-19 | 145.42 | 145.36 | 145.12 | 145.06 |
| C-20 | 125.32 | 125.28 | 125.35 | 125.28 |
| C-21 | 127.94 | 127.95 | 128.01 | 127.95 |
| C-22 | 137.60 | 137.60 | 137.78 | 137.78 |

[a] All the spectra were recorded for equally concentrated DMSO-$d_6$ solutions, taking the solvent signal as an internal reference ($\delta$= 39.5 ppm).

## TABLE 4

Chemical shift increments of pyridine carbon atoms upon protonation or quaternisation



$$\Delta\delta = \delta^{13}C^{salt} - \delta^{13}C^{pyridine}$$

| Comp. | $R_1$ | $R_2$ | $R_3$ | X | solv. | $C_2$ | $C_3$ | $C_4$ | $C_5$ | $C_6$ | Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 14a | -H | -H | -H | $CF_3COO^-$ | TFA | -10.2 | 5.5 | 8.7 | | | 1 |
| 14b | -H | -H | -H | $Cl^-$ | $D_2O$ | -7.2 | 4.8 | 12.1 | | | 3 |
| | -H | -H | -H | $Cl^-$ | $D_2O$ | -7.0 | 3.7 | 10.2 | | | 8 |
| 15 | -H | $-CONH_2$ | -H | $Cl^-$ | $D_2O$ | -6.0 | 3.9 | 9.6 | 4.3 | -3.8 | 8 |
| 16 | $-CH_3$ | $-CONH_2$ | -H | $Cl^-$ | $D_2O$ | -2.0 | 4.8 | 8.2 | 4.8 | -3.7 | 8 |
| 17 | $-CH_3$ | -H | -H | $I^-$ | TFA | -2.8 | 5.4 | 10.3 | | | 1 |
| 18 | $-CH_3$ | $-COCH_3$ | -H | $I^-$ | TFA | -2.2 | 4.8 | 10.8 | 6.5 | -3.7 | 1 |
| 1 | $-CH_2$Ø | $-COCH_3$ | -H | $Cl^-$ | $D_2O$ | -5.2 | 3.7 | 9.5 | 5.3 | -6.4 | this work |
| 2 | $-CH_2$Ø | $-COCH_3$ | $-CH_3$ | $Cl^-$ | $D_2O$ | -5.3 | 3.5 | 9.9 | 7.7 | -7.4 | " |
| 3 | $-CH_2$Ø | $-COCH_3$ | $-C_2H_5$ | $Cl^-$ | $D_2O$ | -5.5 | 3.5 | 10.1 | 7.2 | -7.5 | " |
| 4 | $-CH_2$Ø | $-COCH_3$ | $-C_3H_7$ | $Cl^-$ | $D_2O$ | -5.4 | 3.6 | 10.0 | 7.4 | -7.5 | " |
| 5 | $-CH_2$Ø | $-COCH_3$ | $-CH(CH_3)_2$ | $Cl^-$ | $D_2O$ | -5.5 | 3.7 | 10.3 | 6.9 | -7.3 | " |
| 6 | $2,4-(NO_2)_2$Ø | -H | -H | $Cl^-$ | $D_2O$ | -3.4 | 5.1 | 13.9 | 5.1 | -3.4 | " |
| 7 | $2,4-(NO_2)_2$Ø | $-CONHCH_3$ | -H | $Cl^-$ | $D_2O$ | -1.8 | 5.6 | 13.2 | 6.6 | -3.0 | " |
| 8 | $2,4-(NO_2)_2$Ø | $-CONHC_2H_5$ | -H | $Cl^-$ | $D_2O$ | -1.8 | 5.4 | 13.0 | 6.4 | -3.8 | " |
| 9 | $2,4-(NO_2)_2$Ø | $-CON(C_2H_5)_2$ | -H | $Cl^-$ | $D_2O$ | -2.9 | 4.2 | 13.2 | 6.8 | -2.7 | " |
| | | | | | | -5.8 | 4.1 | 13.3 | 6.8 | +0.2 | 6 |
| | | | | | | (-3.1) | | | | (-2.6)[a] | |
| 10 | $2,4-(NO_2)_2$Ø | $-COCH_3$ | -H | $CH_3$Ø$SO_3^-$ | DMSO | -3.6 | 3.7 | 12.7 | | | |
| 11 | $2,4-(NO_2)_2$Ø | $-COCH_3$ | $-CH_3$ | $CH_3$Ø$SO_3^-$ | DMSO | -3.0 | 2.4 | 11.8 | 5.7 | -5.9 | this work |
| 12 | $2,4-(NO_2)_2$Ø | $-COCH_3$ | $-C_2H_5$ | $CH_3$Ø$SO_3^-$ | DMSO | -2.8 | 2.8 | 10.7 | 9.2 | -6.3 | " |
| 13 | $2,4-(NO_2)_2$Ø | $-COCH_3$ | $-C_3H_7$ | $CH_3$Ø$SO_3^-$ | DMSO | -3.0 | 2.6 | 11.7 | 5.2 | -5.7 | " |

[a] Chemical shift differences obtained by reversing the assignments of $C_2$ and $C_6$ proposed in ref. 6

## DISCUSSION

Kozerski[1] and Long[5] already pointed out that care should be taken in using quaternisation shift increments for pyridine derivatives unless solvent, concentration e.a. can be kept constant. All our spectra were therefore taken for identical concentrations within each series of compounds.
It is clear from the results in Table 4 (comp. 14) that experimental conditions can cause large differences in the chemical shifts of pyridinium compounds.
The results mentioned in Table 4 not only emphasize the expected dependence of the quaternisation shift increments on the structure of the original alkylating agent, which brings about variation possibilities of the N-substituent and also of the anion. Substituents on other sites of the pyridine ring also can considerably influence the quaternisation increments. As an example we mention the average deshielding of 3.6 and 7.4 ppm experienced respectively by the equivalent positions C-3 and C-5 on alkylation of 3-acetylpyridine derivatives to the salts 2 - 5. Comparison of the 3-alkyl-1-(2,4-dinitrophenyl)pyridinium chlorides with the corresponding p-toluenesulphonates shows the possible effect of the anion. Care should thus be taken in using quaternisation shift increments for pyridines. Careless use can result in wrong or reversed assignments as was the case for C-2 and C-6 in 3-diethylaminocarbonyl-1-(2,4-dinitrophenyl)pyridinium chloride[6] 9. It is therefore clear that these increments are nevertheless useful when used in an appropriate way within a series of analogues.

## ACKNOWLEDGEMENTS

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## REFERENCES

1.L. Kozerski, Org. Magn. Res.,1977, 9, 935.

2.J.F. Biellmann, C.G. Hirth, M.J. Jung, N. Rosenheimer and A.D. Wrixon, Eur. J. Biochem.,1974, 41, 517.

3.R.J. Pugmire and D.M. Grant, J. Am. Chem. Soc.,1968, 90, 69.

4.W. Bremser , L. Ernst and B. Francke, "Carbon-13 NMR spectral data" Verlag Chemie, Weinheim, 1981.

5. K.R. Long, J. Magn. Res., 1972, 8, 207.

6. Sadtler Standard $^{13}$C-N.M.R. Spectra (SAD 01852)

7. R. Dommisse, E. Freyne, E. Esmans, J. Lepoivre and F. Alderweireldt, Heterocycles, 1981, 16, 1893.

8. E. Freyne, Ph.D. thesis, University of Antwerpen, Belgium (1981).

9. D.F. Ewing, Org. Magn. Res., 1979, 12, 499.

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