On the Correlation between Ionization Potentials and ^{13}C- and ^{15}N-Chemical Shifts in Substituted Pyridines

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A theory which predicts an approximately linear correlation between first ionization potentials and chemical shift is briefly presented. The theory is used to explain the correlation between the observed δ_C values for positions five and six and the ionization potentials for 2- and 3-substituted pyridines. Similarly, correlation of the nitrogen-15 chemical shifts with the ionization potentials for 4-substituted pyridines is discussed. The solvent-induced changes in nitrogen-15 chemical shifts can be correlated with the solvent-dependent HOMO energy for pyridine in solvents with different dielectric constants using a solvent cavity model. A correlation between the nitrogen-15 chemical shift and solvent-dependent net atomic charge on nitrogen in pyridine is also observed. The relationship with the paramagnetic shielding of the nucleus is also discussed.

The chemical shifts observed for nuclei in magnetic resonance experiments, particularly for aromatic compounds, have often been correlated with measured or calculated parameters for this class of compound. Much attention has been devoted to the relationship between the carbon-13 chemical shift and the total charge density (calculated by different quantum chemical procedures) at the *para* position of monosubstituted benzenes, and similarly for other aromatic compounds.[1]

The total nuclear shielding parameter, σ_{tot}, may be represented as:[2]

$$\sigma_{\text{tot}} = \sigma^{\text{d}}_{\text{loc}} + \sigma^{\text{p}}_{\text{loc}} + \sigma_{\text{other}} \qquad (1)$$

In this equation, $\sigma^{\text{d}}_{\text{loc}}$ is the local diamagnetic shielding of the nucleus and describes the isotropic circulation of local electrons around the nucleus. The term $\sigma^{\text{p}}_{\text{loc}}$ is the local paramagnetic term and is a measure of the deviation from spherical symmetry of the electronic distribution around the nucleus. The quantity σ_{other} includes all contributions to the shielding, from sources other than those at the nucleus: anisotropy, field effects, solvent, and so on. Usually, σ_{other} is negligible. Calculations of various types suggest that while both $\sigma^{\text{d}}_{\text{loc}}$ and $\sigma^{\text{p}}_{\text{loc}}$ for carbon and nitrogen may be relatively large, the former term remains fairly constant for a given class of compounds,[3] and that the changes in the chemical shift as a function of structure may be attributed to changes in $\sigma^{\text{p}}_{\text{loc}}$.

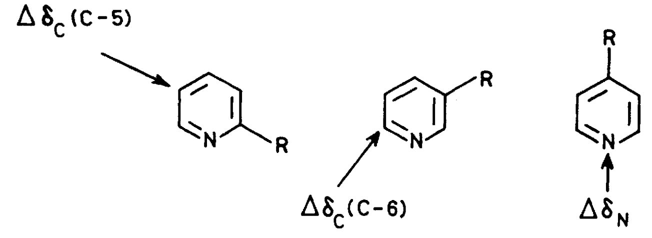
According to Karplus and Pople[3] the local paramagnetic contribution, $\sigma^{\text{p}}_{\text{loc}}$, to the shielding may be viewed in terms of four contributions:

$$\sigma^{\text{p}}_{\text{loc}} = -(\mu_0 e^{-}\hbar^2/8\pi \text{M}^2 \Delta E)\langle r^{-3}\rangle_{\text{N}}(\text{Q}_{\text{NN}} + \sum_{\text{B}\neq\text{N}} \text{Q}_{\text{BN}}) \qquad (2)$$

where ΔE is the effective electronic excitation energy; $\langle r^{-3}\rangle$ denotes the inverse cube of the orbital radius describing the influence of electrons on the chemical shift; Q_{NN} and Q_{BN} are the charge and the bond order respectively, in the MO picture. Thus, equation (2) has often been used to correlate chemical shift and charge density.[1]

It has recently been found that an approximately linear correlation exists between the carbon-13 chemical shift at the *para* position in monosubstituted benzenes and the corresponding first ionization potential.[4] As equation (2) does not provide any 'explanation' for this relationship, a simple model for the electronic structure of these systems based on the idea of scaling[5] and second quantization[6] was later presented as a tentative theoretical clue to this experimental fact.

This paper intends to show that such a correlation between ionization potential and chemical shift is more general and is obtained in other aromatic systems *e.g.* pyridine. Pyridine is particularly interesting because a greater variation is possible: substitution in positions two, three, or four in pyridine can cause changes in the chemical shift in positions five, six, or one respectively. Furthermore, it is possible to study the effect on different nuclei. The procedure cannot be applied to the carbon or nitrogen which is substituted, or to '*ortho*' chemical shifts, because integrals involving substituent orbitals become important. As an example, a change in the substitution pattern in position two at the pyridine ring (**1**) will cause changes in the carbon-13 chemical shift for C-5, whereas a change of substitution at position four will affect the nitrogen-15 chemical shift for the nitrogen in the pyridine ring (**3**). It will also be shown that the model can be used to explain the solvent-induced change in ^{15}N chemical shift of pyridine.



(**1**) (**2**) (**3**)

The major part of the data used is available from the literature, and *ab initio* calculations[7] were performed when necessary.

Theory.—The theory for the correlation between the observed first ionization potential and chemical shift has been described recently and will be presented briefly only here. The first ionization potential of different monosubstituted pyridines corresponds to an emission of an electron from an orbital of the same type in the different pyridines. In a simple independent-particle model of the ionization process it was assumed that the orbital for the leaving electron has the asymptotic form:

$$\varphi \sim \text{f}(\vec{r}) \exp[-(2\text{m}I)^{\frac{1}{2}}\, \vec{r}/\hbar] \qquad (3)$$

By comparing the electronic structure of closely related systems exhibiting different ionization potentials a scaling parameter[4,5] was introduced:

$$\mu_k = (I_k/I_1)^{\frac{1}{2}} \qquad (4)$$

where I_k is the first ionization potential of the kth system and I_1 is the ionization potential of a reference system, *i.e.* pyridine.

The scaled shielding tensor for the kth system can then be expressed as a sum of three terms:[4] a shielding tensor inert to the scaling, σ_0, and the dia- and para-magnetic tensor which depends on the scaling, σ_d and σ_p. This leads to an expression for the chemical shift for the kth system of the following form:[4]

$$\delta_k = \sigma_{ref} - \sigma_0 - \sigma_d\mu_k - \sigma_p\mu_k^3 \qquad (5)$$

The paramagnetic contribution causes deshielding ($\sigma_p < 0$) and $|\sigma_p| \gg |\sigma_d|$.[8]

The local minimum for the curve described by equation (5) with respect to μ_k occurs at $(-\sigma_d/3\sigma_p)^{\frac{1}{2}}$ which is much less than one. The scaling data for pyridine, as we will see later, approximate to one and the curve is here predicted by equation (5) to be almost a straight line:

$$\delta_k \approx \delta_1 + [(-3\sigma_p - \sigma_d)/2I_1](I_k - I_1) \qquad (6)$$

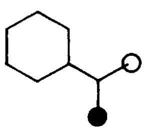
To study the solvent-induced changes in nitrogen-15 chemical shift in pyridine, the molecule in a solvent cavity model introduced by Kirkwood will be used.[9] The quantum chemical treatment of this model has recently been described,[10] and here the solvent-induced changes on the calculated HOMO energy and net atomic charge will be used.[11]

Results and Discussion

Table 1 gives the first ionization energy,[12] the *ab initio* calculated HOMO energy,* and the carbon-13 chemical shifts for positions five and six for some 2- and 3-substituted pyridines, respectively. The entries 1—10 refer to 2-substituted pyridines and 11—17 to 3-substituted pyridines. Figure 1 shows a plot of the first ionization potential *versus* the change in carbon-13 chemical shift for the 2-substituted pyridines.

It can be seen from Figure 1 that there is an approximately linear correlation between the carbon-13 chemical shift for C-5 and the first ionization potential in 2-substituted pyridines. Systems with a low ionization potential such as 2-aminopyridine (entry 5) and 2-methoxypyridine (entry 4) have a relatively low δ_C value for position five, whereas systems with a higher ionization potential it is higher. This corresponds to a relatively more shielded C-5 for systems with low ionization potentials compared with systems of higher ionization potential. The slope in Figure 1 was calculated to be 6.95 ± 0.85 p.p.m. eV^{-1} (correlation coefficient = 0.95).

2-Nitropyridine (entry 10) has an ionization potential and ^{13}C-chemical shift (for C-5) 10.2 eV and +6.6 p.p.m. [relative to δ_C (C-5) in pyridine] respectively, which do not correlate with the results shown in Figure 1. This is a consequence of the HOMO being mainly (98%) located on the oxygens in the nitro group, (4), whereas the second HOMO, (5), has the same symmetry as the HOMO in the other 2-substituted pyridines.



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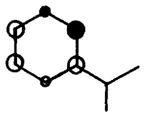

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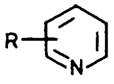
Table 1. First ionization potential,[12] *ab initio* calculated HOMO energy, and ^{13}C-chemical shift for positions five and six for some 2- and 3-substituted pyridines[13]



	R	IP[12]	$-\varepsilon_{HOMO}$[7b]	$\Delta\delta_C5$[13]	μ^a	μ^b
1	H	9.60	8.09	0	1.000	1.000
2	CH_3	9.29	7.85	−3.4	0.984	0.985
3	OH	9.28	7.08	−3.1	0.983	0.935
4	OCH_3	8.96	7.00	−7.5	0.966	0.930
5	NH_2	8.5	6.57	−10.6	0.941	0.901
6	CN	10.5	8.53	3.6	1.046	1.027
7	F	9.7	7.88	−2.7	1.005	0.987
8	Cl	9.91	8.16	−1.2	1.016	1.004
9	Br	9.65		−0.5	1.003	
10	NO_2		9.07[c]	6.6		1.059
11	H	9.60	8.09	0	1.000	1.000
12	CH_3	9.40	7.89	−2.3	0.990	0.988
13	OH	9.55	7.08	−8.6	0.997	0.936
14	NH_2	8.7	6.60	−10.8	0.952	0.903
15	CN	10.4	8.67	4.2	1.041	1.035
16	Cl	9.5	8.20	−1.4	0.995	1.007
17	Br	9.75		−0.9	1.008	

[a] See equation (4). [b] $\mu = (\varepsilon_k/\varepsilon_1)^{\frac{1}{2}}$, where ε_k is the HOMO energy for the kth system and ε_1 is the HOMO energy for pyridine. [c] See Discussion.

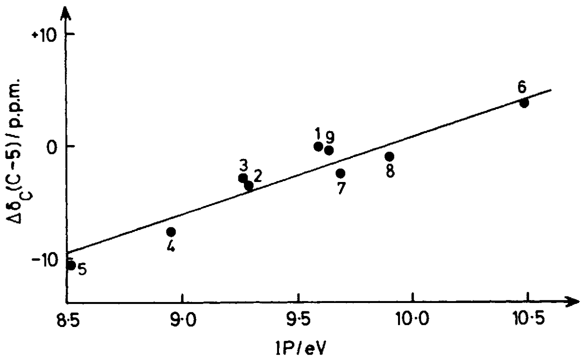


Figure 1. Carbon-13 chemical shifts for position five as a function of the ionization potential of 2-substituted pyridines. For numbers see Table 1

Using the second HOMO energy for 2-nitropyridine, the calculated HOMO energies for the remaining 2-substituted pyridines and the changes in ^{13}C-chemical shifts given in Table 1, a similar correlation to the one shown in Figure 1, now including 2-nitropyridine, is found. The slope for the change in δ_C as a function of the calculated HOMO energies is 6.26 ± 0.76 (correlation coefficient = 0.95; it should furthermore be noted that there is a linear correlation between the first ionization potentials and calculated HOMO energies with a slope of 1.04), and is thus in good agreement with the slope found for the double experimental values in Figure 1.

A similar correlation is found between the first ionization potential and δ_C (C-6) for 3-substituted pyridines (Table 1; entries 11—17). The change in chemical shift as a function of ionization potential has here been calculated as 8.67 ± 2.48 p.p.m. eV^{-1} (correlation coefficient 0.86), and as a function of the

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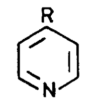
* We have used the STO-3G basis set for the calculations as we are interested in relative changes in HOMO energies. Calculations with an extended basis set (4-31G) give almost the same relative changes, but take much longer.

Table 2. First ionization potential,[12] *ab initio* calculated HOMO energy,[7] and $\Delta\delta_N$ in some 4-substituted pyridines[14]



	R	IP[12]	$-\varepsilon_{HOMO}$	$\Delta\delta_N$[14]	μ^a	μ^b
1	H	9.60	8.09	0	1.000	1.000
2	NH_2	8.97	6.69	−45.8	0.967	0.909
3	CN	10.3	8.67	10.6	1.036	1.035
4	CH_3	9.5	7.96	−8.0	0.995	0.992
5	CHO		8.36	15.2		1.017
6	F		7.99	−17.9		0.994
7	Cl		8.30	−4.9		1.013
8	$CH=CH_2$		7.99	−2.1		0.994
9	OCH_3		7.09	−23.1		0.936

[a,b] See Table 1.

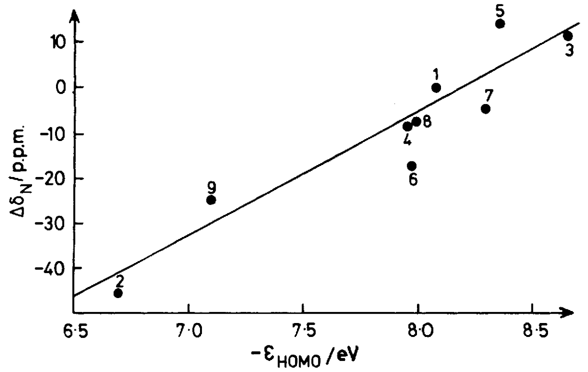


Figure 2. Nitrogen-15 chemical shifts as a function of the ionization potential for 4-substituted pyridines. For numbers see Table 2

calculated HOMO energies as 7.17 ± 0.67 p.p.m. eV^{-1} (correlation coefficient 0.99; the slope for the correlation between ionization potentials and HOMO energies is 1.18). It appears that the agreement between the experimental and calculated results here is not as good as for the 2-substituted pyridines. The 3-substituted pyridines exhibit the same features as the 2-substituted: 3-aminopyridine (entry 14), which has a relatively low ionization potential, has a relatively low δ_C (C-6) value, and systems in which there is higher ionization potential exhibit higher δ-values, indicating that the nucleus is more deshielded.

Before a comparison is made of the different systems, it is worth considering some 4-substituted pyridines, which according to the theory will experience changes in the ^{15}N chemical shift. Table 2 gives the first ionization potential,[12] the *ab initio* calculated HOMO energy,* and the nitrogen-15 chemical shifts for some 4-substituted pyridines.[14] As there are only relatively few ionization potentials available for 4-substituted pyridines, the change in δ_N is here plotted as a function of the calculated HOMO energies (Figure 2), since a reasonable agreement between experimental ionization potentials and calculated HOMO energies is obtained.

From Figure 2 it again appears that systems with low ionization potentials such as 4-amino- and 4-methoxy-pyridine (Table 2; entries 2 and 9) have relatively low δ_N values, whereas systems of high ionization potential *e.g.* 4-cyano- and 4-formylpyridine (Table 2; entries 3 and 5) have relatively high nitrogen-15 chemical shifts. The slope for the change in δ_N as a function the HOMO energy, shown in Figure 2, has been calculated as 27.2 ± 4.4 p.p.m. eV^{-1} (correlation coefficient 0.92).

Table 3. Calculated solvent-dependent HOMO energy and net atomic charge on nitrogen in pyridine for a series of solvents with the dielectric constant ε,[10,11] and the solvent-induced changes in δ_N[15]

	Solvent	ε[16]	$-\varepsilon_{HOMO}$ (eV)	q_N	$\Delta\delta_N$[15]
1	Gas phase	0.0	8.093	−0.229	0
2	C_6H_{12}	2.023	8.056	−0.237	−4.8
3	C_6H_6	2.284	8.051	−0.238	−7.7
4	$CHCl_3$	4.806	8.028	−0.242	−14.6
5	CH_2Cl_2	9.08	8.017	−0.245	−11.7
6	CH_3OH	32.63	8.006	−0.247	−24.5
7	H_2O	78.54	8.003	−0.248	−27.5

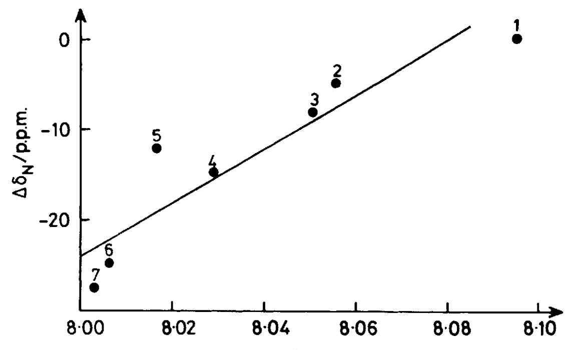


Figure 3. The solvent-induced nitrogen-15 chemical shifts as a function of the solvent-dependent HOMO energy for pyridine. For numbers see Table 3

Comparison of the slopes of the three substitution patterns indicates that C-6 (which corresponds to 3-substituted pyridines) is less sensitive to changes in substituent, whereas the nitrogen (which corresponds to 4-substituted pyridines) is *ca.* 3—4 times as sensitive as carbon. The change in δ_C as a function of ionization potential for the substituted pyridines corresponds well with change in δ_C (*para*) in monosubstituted benzenes,[4] which has been calculated as 8.24 ± 0.75 p.p.m. eV^{-1} (correlation coefficient 0.97). An explanation for the slope differences between C-5 and -6 might be that the π-electron density for the HOMO of C-6 is affected less as a function of the ionization potential for 3-substituted pyridines than that for C-5 in 2-substituted pyridines (0.0192 relative to 0.0209). A similar explanation might also be used to account for the observed difference in slope between δ_C and δ_N as a function of the ionization potentials: nitrogen has a lone pair of electrons extra compared with carbon, which are very easily perturbed when the substituent in position four is changed.

Recently, δ_N (pyridine) has been measured in the gas phase and in a variety of solvents.[15] Attempts were made to relate the solvent-induced nitrogen-15 chemical shift with both the solvent dielectric constant, ε, and the function (ε − 1)/(2ε + 2.5), but no correlation was found.[15] However, a linear correlation with the Kosower *Z* values was found,[15] indicating that the solvent shifts are dependent upon the contribution of the $n \longrightarrow \pi^*$ transition to the secondary paramagnetic shift term. According to the molecule-in-solvent-cavity model a change in the dielectric constant of the solvent will cause changes in the electronic structure of the molecule,[10] and here the solvent-induced changes in the HOMO energy and net atomic charge on the pyridine nitrogen will be applied. Table 3 gives the calculated HOMO energy and the net atomic charge on

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* See footnote on p. 886.

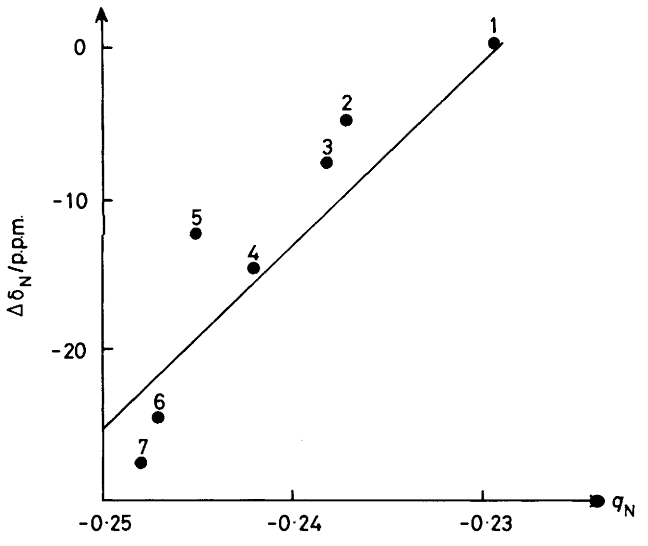

Figure 4. The solvent-induced nitrogen-15 chemical shift as a function of the solvent-dependent net atomic charge on nitrogen in pyridine. For numbers see Table 3

nitrogen in pyridine, in a series of solvents with the dielectric constant, ε. The solvent-induced changes in δ_N[15] are given as well.

It appears from Table 3 that an increase in the dielectric constant of the solvent causes an increase in the solvent-dependent HOMO energy, which is destabilized by 0.09 eV ($\simeq$ 2 kcal) on going from the gas-phase to dissolution in water. The net atomic charge on the nitrogen in pyridine decreases with increasing dielectric constant of the solvent. Figure 3 shows the change in solvent-induced δ_N as a function of the calculated solvent-dependent HOMO energy of pyridine. From the curve in Figure 3, it is seen that an approximately linear correlation is obtained (correlation coefficient 0.92). A relatively high solvent-dependent ionization potential for pyridine, which corresponds to pyridine in a solvent of high dielectric constant (*e.g.* water or methanol), causes a relatively large decrease in ^{15}N chemical shift relative to the gas-phase value, whereas a lower solvent-dependent HOMO energy, corresponding to pyridine in a solvent with a low dielectric constant (*e.g.* cyclohexane or benzene), leads to a relatively small decrease in δ_N relative to the gas-phase value. Figure 4 shows the correlation between the solvent-induced nitrogen-15 chemical shift and the solvent-dependent net atomic charge on nitrogen in pyridine (correlation coefficient 0.91).

Solvents with a high dielectric constant cause a more negative net atomic charge on nitrogen compared with solvents of small dielectric constant. According to equations (2) and (5) an increase in chemical shift should be observed with decreased net atomic charge, so it appears that the results fit well. The solvent effects probably arise from the polarization of the pyridine π-electronic system by the polar solvents.

In previous studies on solvent effects on chemical shifts, attempts were made to correlate both the solvent dielectric constant, or the function $(\varepsilon - 1)/(2\varepsilon + 2.5)$, with the observed solvent-induced changes in δ_N in pyridine.[15] Here, we have studied the effect of a given solvent on the electronic structure of pyridine, and then correlated these effects with the solvent-induced changes in δ_N in pyridine. It thus appears from Figures 3 and 4 that it is possible to obtain reasonable correlations by this method.

Only a few correlations between π-charge density on the nitrogen atom obtained by quantum chemical calculations and ^{15}N chemical shift in pyridine have been performed.[17] Table 4 gives the *ab initio* calculated net atomic charge on nitrogen in some substituted pyridines.

Table 4. Calculated net atomic charge on nitrogen in some substituted pyridines and the change in δ_N[14a]

Entry	Substituent	q_N	$\Delta\delta_N$
1	H	−0.229	0
2	2-F	−0.249	−41.6
3	3-F	−0.217	−17.9
4	2,6-F_2	−0.268	−72.1
5	2-NH_2	−0.266	−51.5
6	3-NH_2	−0.219	9.9
7	4-NH_2	−0.252	−45.8
8	2-CN	−0.207	−0.9
9	3-CN	−0.221	−0.8
10	4-CN	−0.212	10.6
11	2-CH_3	−0.229	−0.4
12	3-CH_3	−0.229	0.3
13	4-CHO	−0.233	−0.8
14	4-CHO	−0.220	15.2
15	4-COOH	−0.224	11.0
16	2-OCH_3	−0.253	−49.2

A plot of the change in nitrogen-15 chemical shift *versus* the net atomic charge gives a straight line with a correlation coefficient of 0.91 and is thus in accordance with equation (2).

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