CORRELATION OF ^{15}N NMR CHEMICAL SHIFTS WITH CALCULATED PARTIAL CHARGES IN PYRIDINE *N*-OXIDES

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Abstract - *p*-Substituted pyridine *N*-oxides have been found very good linear correlations between the ^{15}N NMR chemical shifts and the partial charges, obtained by semiempirical molecular orbital methods.

Pyridine *N*-oxides are of great synthetic utility due to the reactivity-modifying influence of the oxygen atom on the ring system. This influence often leads to complex and unexpected differences between the properties of pyridines and their *N*-oxides.[1] The presence of the oxygen atom can have, depending on the reagent used in any particular transformation, either an electron-withdrawing or an electron-donating effect. The effect reflects an important contribution of the canonical structures (**1b**) and (**1c**) to the resonance hybrid of pyridine *N*-oxide.[1]

^{15}N NMR spectroscopy can in principle have a chemical application as the identification of structure of nitrogen compounds, since their chemical shifts are intimately related to the electronic environment of the given nucleus.[2] We reported the substituent effects on the ^{15}N NMR chemical shifts of the ylidic nitrogens in pyridinium bis(methoxycarbonyl)methylids[3] and dicyanomethylids,[4] whereas other workers

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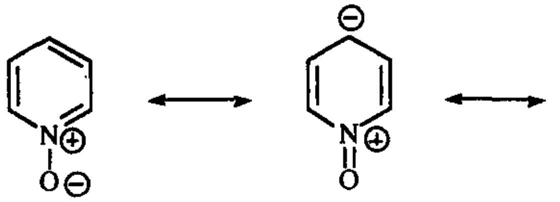
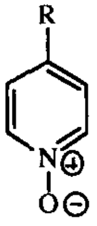
Dedicated to the memory of Professor Shunichi Yamada, Professor Emeritus Tokyo University.



1a **1b** **1c**



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have reported ^{14}N and ^{15}N NMR spectra[5,6] for some pyridine *N*-oxides. We report herein that there are good correlations between the ^{15}N NMR chemical shifts and the calculated partial charges of pyridine *N*-oxides which are derived from semiempirical molecular orbital (MO) methods.

In order to observe the nitrogen nucleus of pyridine *N*-oxides (**1**~**11**), we have attempted the natural-abundance ^{15}N NMR spectroscopy. The sensitivity is limited by the low solubility of several substrates and by the natural line width of the ^{15}N resonances. To obtain the signals accurately in the ^{15}N resonances at high signal/noise ratios, we have performed the spectroscopy at the highest achievable resolution in dimethyl sulfoxide-d_6 with and without $Cr(acac)_3$ at 68 °C, respectively.[2]

Table 1 shows the chemical shifts obtained as above and the partial charges computed with four MO (AM1, PM3, INDO, and ETH) methods.[7] As it can be seen in Table 1, the ^{15}N chemical shifts of pyridine *N*-oxides are sensitive to the nature of substituents at the 4-position on the pyridine ring. When the ring has a strong electron-withdrawing substituent (NO_2, CN, PhCO, $MeCO_2$, or MeCO) on the ring, the contribution of resonance structures analogous to **1b** becomes predominant. Thus, the nitrogen-oxygen bonds in the pyridine *N*-oxides tend to possess a substantial double-bond character. Accordingly, the ^{15}N nuclei of the *N*-oxides (**7**~**11**) resonate at downfields relative to the parent pyridine *N*-oxide (**1**). In contrast, when the ring has an electron-donating substituent (Me, Et, *i*-Pr, *t*-Bu, or Ph) at the 4-position, the ^{15}N nuclei of the *N*-oxides (**2**~**6**) resonate at upfield as compared with that of **1**.

Hence, we may expect good correlations between the ^{15}N NMR chemical shifts and the calculated partial charges.[7] Figures 1~4 exhibit the correlations between the chemical shifts and the partial charges. These demonstrate explicitly that there are very good linear correlations (correlation coefficients, r^2=0.976~0.905) in all four cases, particularly when AM1 method was used (correlation coefficient: r^2=0.976) and even when ETH was used (correlation coefficient: r^2=0.951).

In summary, we have found linear correlations between the ^{15}N chemical shifts and partial charges of the nitrogen nucleus in pyridine *N*-oxides. Therefore, semiempirical molecular orbital calculations such as AM1, PM3, INDO, and ETH methods which are readily and commercially available have proven useful to predict the ^{15}N chemical shifts of aromatic *N*-oxides.

Table 1. ^{15}N Chemical Shifts and Partial Charges (Obtained with Semiempirical MO Methods) of Pyridine *N*-Oxides (**1**-**11**).

Substrate	^{15}N Chemical Shift [a]	Partial Charge [b]			
		AM1 [c]	PM3 [d]	INDO [e]	ETH [f]
1 (R = H)	84.0	0.354	1.073	0.237	0.518
2 (R = Me)	90.1	0.351	1.067	0.226	0.500
3 (R = Et)	88.4	0.351	1.067	0.227	0.499
4 (R = i-Pr)	88.4	0.351	1.070	0.226	0.494
5 (R = t-Bu)	88.8	0.351	1.070	0.226	0.493
6 (R = Ph)	85.9	0.354	1.070	0.232	0.495
7 (R = MeCO)	74.8	0.369	1.093	0.242	0.550
8 (R = $MeCO_2$)	74.4	0.371	1.096	0.246	0.544
9 (R = PhCO)	75.4	0.368	1.092	0.242	0.544
10 (R = CN)	74.9	0.366	1.087	0.239	0.539
11 (R = NO_2)	70.5	0.376	1.114	0.247	0.555

[a] Chemical shifts are reported in ppm scale from the external standard, nitromethane. [b] Partial charges in the nitrogens are described in au unit. [c] Correlation coefficient: r^2=0.976. [d] r^2=0.905. [e] r^2=0.933. [f] r^2=0.951

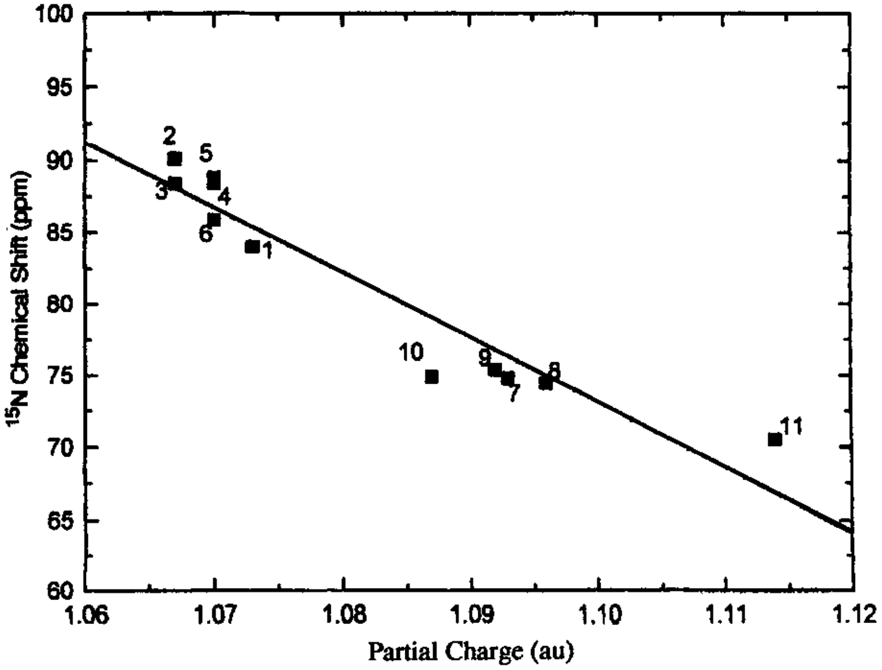

Figure 1. Correlation of ^{15}N Chemical Shifts versus Partial Charges Calculated with AM1 Method.

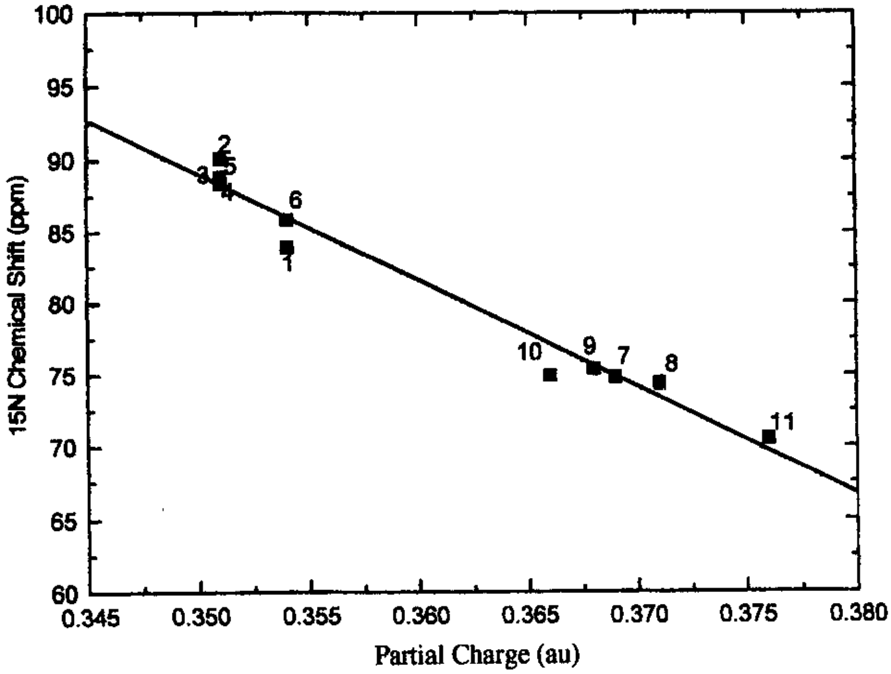

Figure 2. Correlation of ^{15}N Chemical Shifts versus Partial Charges Calculated with PM3 Method.

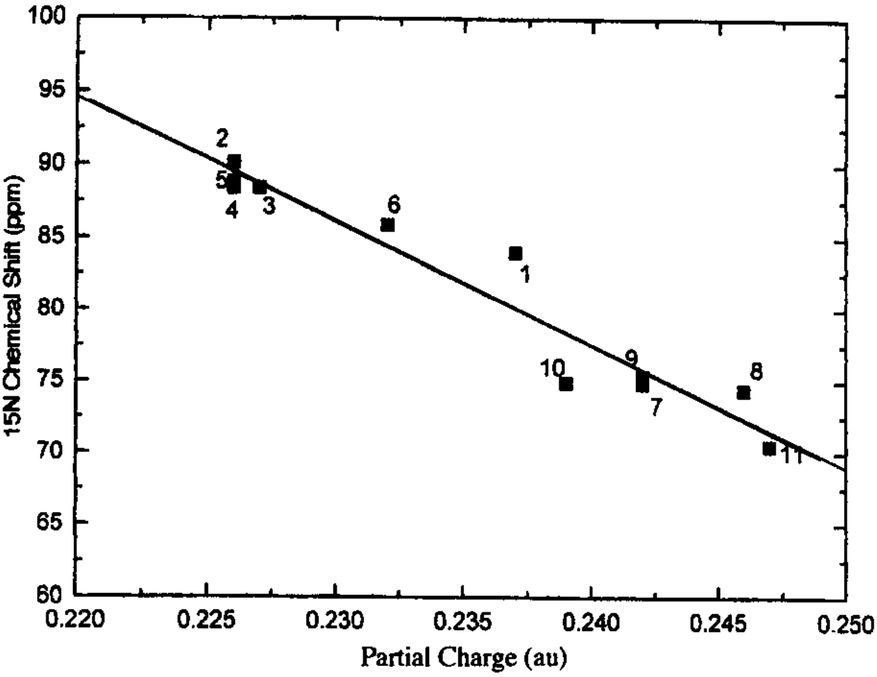

Figure 3. Correlation of ^{15}N Chemical Shifts versus Partial Charges Calculated with INDO Method.

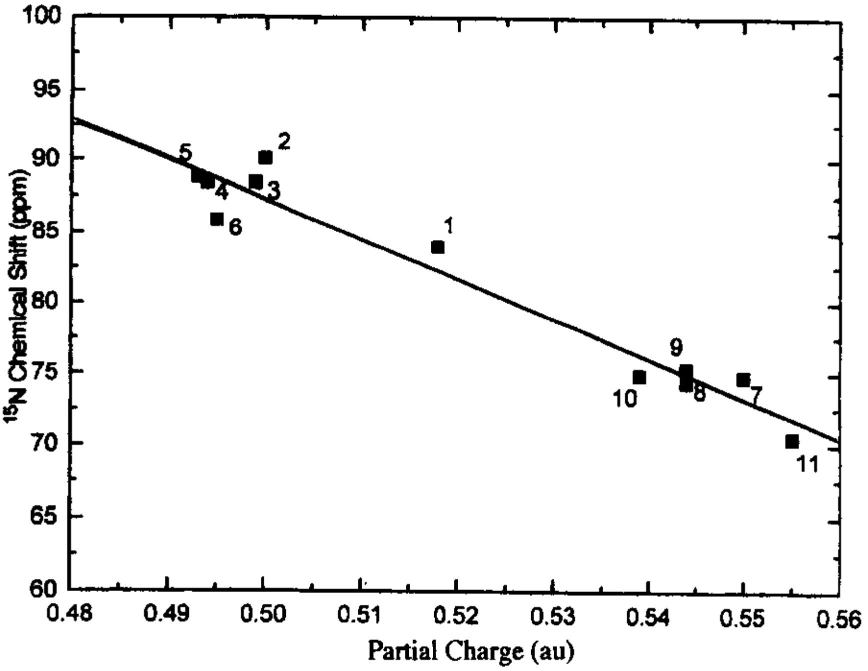

Figure 4. Correlation of ^{15}N Chemical Shifts versus Partial Charges Calculated with ETH Method.

EXPERIMENTAL

Pyridine *N*-oxides (**1**~**11**) were prepared according to the method of Ochiai et al.[8] The NMR spectra were recorded in DMSO-d_6 on a JEOL FX 90Q FT NMR spectrometer. Chemical shifts are reported in ppm upfield from nitromethane as the external standard.

ACKNOWLEDGEMENT

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