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A ^{17}O NMR STUDY. SUBSTITUENT CHEMICAL SHIFTS OF 4-SUBSTITUTED PYRIDINE 1-OXIDES IN DMSO : IMPORTANCE OF DUAL ENHANCED RESONANCE CONTRIBUTIONS WITH PI-DONOR AND PI-ACCEPTOR SUBSTITUENTS

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Abstract: ^{17}O NMR spectra of some 4-substituted pyridine 1-oxides were measured at natural abundance in DMSO and the obtained substituent chemical shifts were correlated with σ^0, $\Delta\bar{\sigma}_R^+$, $\Delta\bar{\sigma}_R^-$ substituent constants. The result could visualize the qualitatively accepted concept for the dual (pi-donor and pi-acceptor) resonance contributions of the substituted N-oxide system.

Studies of pyridine 1-oxides have occupied an important position in heterocyclic chemistry.[1-4] Ample evidence suggests that the N-O moiety of pyridine 1-oxide possesses a unique functionality which can act effectively in both directions as a pi-electron donor and a pi-electron acceptor function. Until recently, substituent effects on reactivities and physical properties of substituted pyridine 1-oxides or the related compounds have appeared in the literature: the examples are N-O stretching frequencies,[5,6] $E_{1/2}$ of polarographic reductions,[7] ^{13}C NMR,[8] and ^{14}N NQR data[9], etc. However, there are very few where the substantial dual N-oxide functionality has been apparently expressed in a quantitatively treated equation on the basis of a systematic change of substituents: the one is the Jaffe's work of basicities in water[10] and the other is the Katritzky's of IR intensities in CCl_4.[11] We have been continuingly much interested in how one can describe the dual resonance contributions in a general fashion.[12]

NMR substituent chemical shifts (SCS) reflect changes in electron density on probe-nuclei.[13,14] Since substituent-induced electronic effects at oxygen have been known to be sensitive (∿2000 ppm/e),[15-18] we attempted to apply

^{17}O NMR spectrometry to this interesting system of pyridine 1-oxides to detect such a dual functionality. Just recently, Boykin et al. communicated the corresponding SCS data in acetonitrile.[19] Here, the ^{17}O NMR SCS of pyridine 1-oxides in DMSO will be reported and discussed on the important view point of the dual resonance contributions of the system.

Natural abundance ^{17}O NMR spectra were measured on a Bruker AM-360 instrument at 48.82 MHz for 10-mm sample tubes containing each pyridine 1-oxide(ca 5-20 W/V %) in DMSO(total 3.5-4.0 mL): DMSO-d_6(0.5 mL) was added for field frequency locking. Typical spectral parameters include a pulse width of 30 μs, 1 K data points, a 25 kHz spectral width, acquisition time of 20.5 ms, and delay time of 25 μs. For data processing, 8 K data points(by zero filling), an exponential weighting function to FID(50 Hz line broadening), and a left-shifting of FID(50-100 μs) were used. A reasonable quality spectrum was obtained in 100000-500000 scans. Chemical shifts ($\delta^{17}O$) were directly determined with the solvent DMSO-^{17}O signal as an internal reference. The resulting substituent chemical shifts ($\Delta\delta^{17}O$) are summarized in Table 1.

Table 1. Natural Abundance ^{17}O **NMR** Data in DMSO[a]

Subst.	W/V %	Temp °C	No.Scan	$W_{1/2}$ Hz	$\delta^{17}O$[b] ppm	$\Delta\delta^{17}O$ ppm	$\Delta\delta^{17}O_{ave}$[c] ppm	Others[b] $\delta^{17}O(W_{1/2};Hz)$
4-NO_2	5	50	96000	830	400	66		
	20(26)	80	233000	550	401(400)	65(64)	65±1	558(480)
4-CN	5	50	168000	1400	383	49		
	10	80	183000	380	390,387	54,51	51±3	
4-$COCH_3$	5	50	244000		---			
	20	80	242000	570	375,374	39,38	39±1	537(440)
4-COC_6H_5	30	80	261000	650	372	36	36	532(430)
4-Cl	5	50	316000	920	343	9		
	14(11)	80	150000	430	340(340)	4(4)	6±3	
H	5	50	300000	550	333			
	13	50	100000	550	334	0		
	13	80	109000	260	336,336	0	0	
4-CH_3	7	50	62000	920	321	-13		
	21	80	140000	380	322,323	-14,-13	-14±1	
4-CH_3O	5	50	485000	830	298	-39		
	16(11)	80	288000	710	303(305)	-33(-31)	-34±4	40(280)
4-$N(CH_3)_2$	10	50	893000		---			
	14(12)	80	677000		---			
	3	30	2200000		---			

a) Distilled and stored over molecular sieves. b) Values are taken from the DMSO-^{17}O signal as the internal standard. To convert the value to the usual scale from external H_2O, 17 ppm must be added.[15] c) Values are used for statistical analyses.

Under our experimental conditions, their half-height line widths were roughly around 500 Hz. Changes in temperature (50-80 °C) and concentration (5-20 W/V %) seemed to provide no significant effect on the SCS values. Reproducibility of the SCS was less than ±5 ppm from 2 or 3 runs including different conditions. We tried to get a ^{17}O signal of 4-NMe$_2$ derivative, but failed probably because of extreme signal broadening due to the association between the two molecules of 4-NMe$_2$-PYNO in a solution.

The ^{17}O SCS values vary with substituents covering a range of 100 ppm. The present SCS data in DMSO are correlated well with the reported data in acetonitrile (Eq. 1),[19] indicating that the SCS values in the two solvents are generally equivalent. As seen in a good correlation with basicity data of ΔpKa (Eq. 2), the SCS values obviously depend on both inductive and resonance parameters. The DSP treatment provides Eq. 3. Only from the finding that the σ_R^0 scale is preferred, it is very difficult to think simply about enhanced resonance interactions with pi-donor and acceptor substituents. The LArSR treatment, on the other hand, gives Eq. 4. Although the analysis is carried out with a very limited data set, it is noteworthy that the enhanced resonance interactions with both types of substituents, pi-donor and pi-acceptor ones, are just reflected on the values of $r^+(\simeq 0.8)$ and $r^-(\simeq 0.8)$, respectively. Compared with the C-O bond in anisoles $(\rho \simeq 20)$,[18] the larger $\rho(\simeq 53)$ value must reflect the larger substituent effect on the ^{17}O atom of the N^+-O^- bond in pyridine 1-oxides. Thus, in the ^{17}O NMR substituent chemical shift values, the dual functionality of the pyridine 1-oxide system is recognized as an important aspect. Further studies are in progress.

Table 2. Correlation Parameters of ^{17}O NMR Substituent Chemical Shifts

Eq. No.	Expression	R	±SD	n
1	$\Delta\delta^{17}O_{DMSO} = 0.96\Delta\delta^{17}O_{AN} + 0.7$	0.999	1.9	7[a)]
2	$\Delta\delta^{17}O_{DMSO} = 27.9\Delta pKa_{H_2O} + 0.1$	0.995	3.7	7[c)]
3	$\Delta\delta^{17}O_{DMSO} = 68.9\sigma_I + 117.3\sigma_R^o + 0.7$	0.999	1.7	7
4	$\Delta\delta^{17}O_{DMSO} = (52.6\pm8.4)\sigma^o + (46.2\pm6.5)\Delta\bar{\sigma}_R^+ + (42.2\pm14.6)\Delta\bar{\sigma}_R^- + (0.2\pm2.7)$			
	$\simeq 53(\sigma^o + 0.8\Delta\bar{\sigma}_R^+ + 0.8\Delta\bar{\sigma}_R^-)$	0.994	3.8	10[b)]
5	$\Delta pKa_{H_2O} = 2.60(\sigma^o + 0.59\Delta\bar{\sigma}_R^+ + 0.22\Delta\bar{\sigma}_R^-)$	0.997		20[c)]

a) Data taken from Ref. 19. b) $\Delta\delta^{17}O_{DMSO}$ values for 4-ph(2) and for 4-phO(-27) are interpolated from Eq. 1 and used for this analysis. c) Ref. 12.

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