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OXYGEN-17 NMR SPECTROSCOPY: σ_I DEPENDENCE FOR THE SUBSTITUENT CHEMICAL SHIFTS OF 3-SUBSTITUTED PYRIDINE 1-OXIDES

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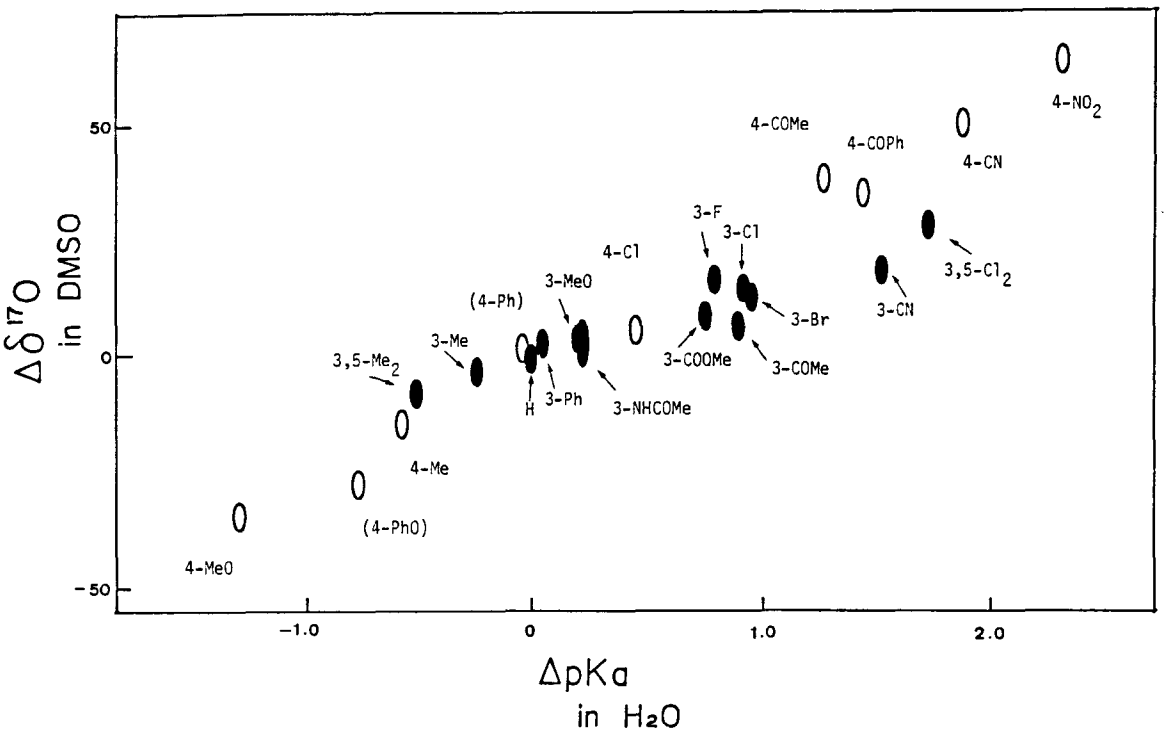
Abstract: ^{17}O NMR spectra were measured at natural abundance in DMSO for a series of 3-substituted pyridine 1-oxides and their substituent chemical shifts were found to be correlated with σ_I substituent constants and not with ΔpK_a values.

Oxygen-17 NMR chemical shifts have been extensively used as an electronic probe of substituent effects on aromatic or heteroaromatic compounds.[1-3] Relatively large ^{17}O-NMR chemical shift changes with substituents are one of the most attractive characteristics. Recently, Boykin et al.[4] and we[5] reported that the change of substituent from OMe to NO_2 in the 4-position of pyridine 1-oxide gives ca. 100 ppm down-field shift in ^{17}O NMR spectra and their resulted substituent chemical shifts(SCS) depend strongly on both inductive and pi-electronic substituent effects, providing a good linear relationship with the acidities of the conjugate acids of pyridine 1-oxides (ΔpK_a). We now report a series of the relevant ^{17}O SCS values at the 3-position and the important finding that there exists no single relationship between ^{17}O SCS and ΔpK_a in the system of pyridine 1-oxides covering both 3- and 4-substituents.

Natural abundance ^{17}O NMR spectra were measured in DMSO at 80°C (concentration of ca. 15 W/V%) and treated as described in the earlier paper.[5] The obtained SCS values are summarized in Table 1 with an estimated error of ±2 ppm. Fig. 1 shows a plot of ^{17}O SCS against ΔpK_a values,[6] which consist of observed and calculated ones. As roughly reflected in Fig. 1, two sets of 3- and 4-substituents make approximately two different linear relations. In a more precise expression, the present ^{17}O NMR SCSs of 3-substituents are described in terms of σ_I scale of substituent constants[7] rather than σ_m.

$$\Delta\delta\,^{17}O = 35.5\ \sigma_I - 2.1 \qquad (r=0.983,\ s=\pm1.9,\ n=12)^{8)}$$



Fluorine-19 NMR SCSs of meta substituted fluorobenzenes are well-known to show σ_I dependence.[7] The obvious σ_I dependence on SCS may be the first observation other than the case of ^{19}F SCS. Combined with 3- and 4-substituents, ^{17}O SCS in pyridine 1-oxides gives us another good chance to investigate critically general expressions of electronic substitent effects. Further study under this line is in progress.

Table 1. Oxygen-17 NMR SCS Values (ppm)

Subst	$\Delta\delta^{17}O$	Subst	$\Delta\delta^{17}O$	Subst	$\Delta\delta^{17}O$	Subst	$\Delta\delta^{17}O$
3,5-Cl_2	29	3-CN	19	3-F	17	3-Cl	15
3-Br	14	3-COOMe	9	3-COMe	7	3-MeO	4
3-Ph	3	3-NHCOMe	(3)	H	0[a]	3-Me	-3
3,5-Me_2	-8						

a) 336 ppm from $DMS^{17}O$

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(7) σ_I scales are taken from S. Ehrenson, R. T. C. Brownlee, R. W. Taft, Prog. Phys. Org. Chem., 1973, 10, 1.
(8) NHAc is excluded because of uncertainty.

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