Anisoyl peroxide with 90% ^{13}C in the carbonyl groups was made from the labeled acid and ethereal H_2O_2 by the dicyclohexylcarbodiimide method:[10] mp 123.5–124 °C (lit.[10] mp 124.5–125 °C).

Anisoyl Anisyl Carbonate (CIN). To 3.20 g (0.0176 mol) of diphosgene was added dropwise with stirring 8.8 mL of 0.2 M aqueous sodium *p*-methoxyphenolate during 30 min. At this point 10 mL of ether was added and the stirring continued for 10 min. After adding a further 15 mL of ether and 10 mL of H_2O and shaking, the water layer was removed and discarded. Then 1.8 g of triethylamine in 10 mL of CH_2Cl_2 was added dropwise with stirring during 10 min to a mixture consisting of the ether solution, 2.70 g of anisic acid, and 25 mL of CH_2Cl_2. After more water and ether were added, the mixture was shaken and the organic layer was washed with water and twice with aqueous Na_2CO_3 and dried over Na_2SO_4. The ether was then removed by rotary evaporation and the residue crystallized from benzene: yield, 1.8 g (34%); mp 92–94 °C dec (gas evolution); IR 1810 cm^{-1} (s), 1740 cm^{-1} (m).

Dianisyl Carbonate. A 12-mL sample of 0.2 M sodium *p*-methoxyphenolate was stirred with 1.62 g of diphosgene for 30 min. Water and CH_2Cl_2 were added and the precipitate that had formed dissolved in the CH_2Cl_2. This solution was washed twice with water and dried over Na_2SO_4, and the solvent was removed by rotary evaporation. The residue was crystallized from benzene/pentane: yield 0.5 g; mp 85–89 °C, main GLC peak 99 area %; IR (CH_2Cl_2) 1800 cm^{-1} (shldr), 1770 cm^{-1} (s).

Product Analysis. Slurries for product runs were allowed to stand in the dark for at least 24 h. The products were recovered from the supernatant liquid and from the silica by extraction with ether. Identification was by GLC retention times, spiking of the GLC mixtures with authentic samples, GC/mass spectrometry, ^{13}C NMR, IR, or isolation. Yields were obtained by GLC runs using internal standards.

Silica. The silica S157 is the same as that called P_0H_1 in an earlier paper.[12]

Slurry Preparation and Titration. In preparing a slurry it is important to avoid the effect of adsorption exotherms by adding solvent to the silica before adding the solution of the reagent. The following is a typical procedure: 2.2 g of silica gel is slurried with 20 mL of solvent. Then 10.0 mL of a solution containing 20 mg of the peroxide is pipetted into the slurry while stirring. For titrimetric rate measurements, after an elapsed time measured from the mid-point of the addition of the peroxide, 2 mL of saturated aqueous KI and 30 mL of carbonated glacial acetic acid are added together. The flask is stoppered again and stirring continued for another 3 min. Then 80 mL of carbonated water is added and the iodine titrated with thiosulfate.

Registry No. AP, 849-83-2; CIN, 98634-05-0; *p*-anisoyl chloride, 100-07-2; diphosgene, 503-38-8; sodium *p*-methoxyphenolate, 1122-95-8; *p*-anisic acid, 100-09-4; silica, 7631-86-9; *p*-methoxyphenol, 150-76-5; anisyl anisate, 60127-34-6; dianisyl carbonate, 5676-71-1; anisoyl peroxide-$^{13}C_2$-*carbonyl*, 98612-59-0; anisic acid-^{13}C-*carboxy*, 69838-89-7.

(12) Leffler, J. E.; Zupancic, J. J. *J. Am. Chem. Soc.* **1980**, *102*, 259.

^{33}S NMR Spectra of Sulfonic Acids and Sulfonate Salts

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The field of ^{33}S NMR has expanded rapidly since Faure's[1a] report, but the emphasis has been on sulfones,[1] sulfides,[2] and other derivatives.[2,3] The problems associated with natural abundance work on the quadrupolar ^{33}S nucleus have been discussed[1-3] and will not be repeated here. An approximate magnetic shielding scale has also been proposed.[4] Sulfonic acids are very strong acids[5] which are used in many reagents and ion exchange resins and are produced in degradative oxidation reactions during structural studies on coal.[6] Faure reported spectra of several acids, but nothing further has appeared. Table I is a summary of our initial results[7] on a series of sulfonic acids and sulfonic acid salts run in water at 6.104 MHz on a Varian FT-80 spectrometer (see Experimental Section).

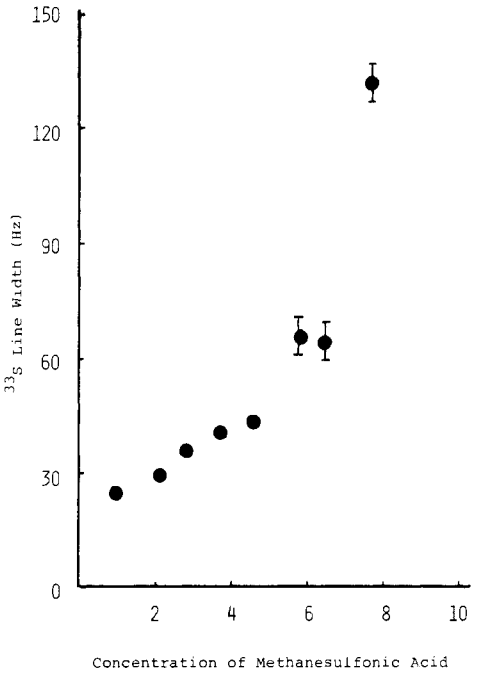

Figure 1. Concentration dependence of ^{33}S line width.

Aromatic sulfonic acids are clearly more shielded than aliphatic sulfonic acids; a similar result was observed for sulfones,[1a] and a similar result was observed for the C-13 chemical shifts of the carbonyl carbon of carboxylic acids and carboxylic acid derivatives.[8] Clearly the greater polarizability of the aromatic π system shields the adjacent carbon or sulfur better than an aliphatic system can shield an adjacent carbon or sulfur. Another interesting result is the increased shielding and increased line width of 1,2-benzenedisulfonate in comparison to either the 1,3-disulfonate or benzenesulfonic acid. Apparently the ubiquitous γ effect[9] is also present in ^{33}S NMR. Preliminary results showed that higher temperatures narrowed the line width of benzenesulfonic acid from 52 Hz at 32 °C to 27 Hz at 41 °C, so most of the spectra were run at approximately 40 °C.

It mattered little whether one started with the acid or with a salt of the acid, because the chemical shift and line

(1) (a) Faure, R.; Vincent, E. J.; Ruiz, J. M.; Lena, L. *Org. Magn. Reson.* **1981**, *15*, 401. (b) Harris, D. L.; Evans, S. A. *J. Org. Chem.* **1982**, *47*, 3355. (c) Cassidei, L.; Fiandanese, V.; Marchese, G.; Sciacovelli, O. *Org. Magn. Reson.* **1984**, *22*, 487.

(2) (a) Retcofsky, H. L.; Friedel, R. A. *J. Am. Chem. Soc.* **1972**, *94*, 6579. (b) Annunziata, R.; Barbarella, G. *Org. Magn. Reson.* **1984**, *22*, 250.

(3) Farrar, T. C.; Trost, B. M.; Tang, S. L.; Springer-Wilson, S. E. *J. Am. Chem. Soc.* **1985**, *107*, 262.

(4) Wasylishen, R. E.; Connor, C.; Freidrich, J. O. *Can. J. Chem.* **1984**, *62*, 981.

(5) Modro, T. A.; Yates, K.; Janata, J. *J. Am. Chem. Soc.* **1975**, *97*, 1492.

(6) Private communication from L. Stock, University of Chicago.

(7) Gillece-Castro, B.; Crumrine, D. S. Abstracts of Joint Great Lakes and Central Regional Meeting of the American Chemical Society, Kalamazoo, MI, May 23–25, 1984, Abst No. 404.

(8) Levy, G. C.; Nelson, G. L. "Carbon 13 Nuclear Magnetic Resonance for Organic Chemists"; Wiley Interscience: New York; 1972; p 117.

(9) Eliel, E. L. et al. *J. Am. Chem. Soc.* **1975**, *97*, 322 and references therein.

0022-3263/85/1950-4408$01.50/0

Table I. ^{33}S NMR of Sulfonic Acids and Sulfonic Acid Salts

compound	mol/L	δ^a	$w_{1/2}$, Hz	T, °C	pH[b]
methanesulfonic acid	2.2	−4.8	30 ± 1	37	14
methanesulfonic acid	2.2	−5.2	22	37	14[c]
methanesulfonic acid	2.2	−5.6	30	37	1
methanesulfonic acid			90		*d*
sodium 2-hydrazinoethanesulfonate	3.0	0	33	37	14
sodium 2-bromoethanesulfonate	2.4	−6.0	33	42	14
sodium 2-bromoethanesulfonate	2.4	−6.3	38	42	1
sodium 2-bromoethanesulfonate	2.3	very very broad		42	<0[e]
sodium 2-propene-1-sulfonate	2.6	−0.4	74	37	1
d-camphor-10-sulfonic acid	1.6	−0.3	113	37	<1
benzenesulfonic acid	4.5	−12.1	27	41	14
benzenesulfonic acid	2.7	−11.8	24	35	1
benzenesulfonic acid	2.7	−11.7	19	38	1[c]
benzenesulfonic acid	3.0	−12.2	31	41	1
benzenesulfonic acid	3.3	−11.1 ± 1	410 ± 30	41	<0[e]
4-toluenesulfonic acid		−10	90		*d*
4-toluenesulfonic acid	1.4	−10.9	35	38	1
mesitylenesulfonic acid	1.6	−16	38	37	1
α-naphthalenesulfonic acid	1.7	−11	46	37	1
4-aminotoluene-2-sulfonic acid	2.1	−14	27	37	1
sulfosalicylic acid	1.9	−10	80	37	1
sodium 2-formylbenzenesulfonate	1.8	−18	99	37	1
disodium *m*-benzenedisulfonate	1.3	−14	51	37	1
dipotassium *o*-benzenedisulfonate	1.1	−19	240	37	1

[a] Measured against external 4 M $(NH_4)_2SO_4$. [b] Measured with pH paper ● 1 unit. [c] The decoupler was on. [d] Reference 1a. [e] Concentrated HCl used as the solvent.

width were nearly the same at the same temperature, concentration, and pH. Additionally, for individual sulfonates within the normal pH range from 1 to 14, there was little variation in the line widths or chemical shifts, but when concentrated hydrochloric acid was used as the solvent, the line widths increased dramatically. Figure 1 gives the concentration dependence of the line width for methanesulfonic acid. There is a clear break at about 5 M with narrow line widths at lower concentrations.

Although there is coupling between the protons on the α carbon and the sulfonate group, most of the spectra were run without the decoupler. However, when the decoupler was turned on, the methanesulfonate line width decreased from 31 to 22 Hz at 2.2 M, and the benzenesulfonate line width decreased from 24 to 19 Hz at 2.7 M. It is interesting that the decoupled line width for a sulfonate was greater than that for dimethyl sulfone where the decoupled line width was reported[3] to be 6 Hz with a J_{S-H} coupling constant of 3 Hz. We did not see a signal for trifluoromethanesulfonic acid, probably because of a multiplet caused by the larger sulfur–fluorine coupling.[10] The ^{19}F spectrum showed only a singlet because of the rapid sulfur relaxation.

Spectra were also run in several other solvents. The line width of benzenesulfonic acid increased from 25 Hz in water to 59 Hz in formamide and 200 Hz in methanol, but no signal was visible in dimethyl sulfoxide, dimethylformamide, acetonitrile, ethylene glycol, or formic acid. In a similar manner the line width for ammonium sulfate increased from 6 Hz in water to 10 Hz in 1 to 1 formamide/water, but interestingly enough, the line width for 2-bromoethanesulfonate changed little on going from water (33 Hz) to formamide (30 Hz). The change of line width for benzenesulfonate does not correlate with the viscosity, dielectric constant, or donor number of the solvent, but there was a correlation with Winstein's Y values (r = −0.88) and Dimroth's E_t values (r = −0.74). In a series of experiments where the benzenesulfonate concentration was held at 3 M and the temperature was held at 42 °C, the benzenesulfonate line width increased with increasing

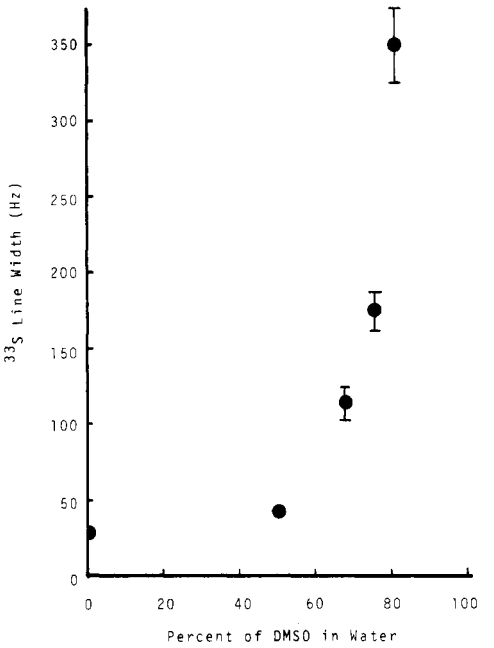

Figure 2. Benzenesulfonate ^{33}S line width in Me_2SO:water mixtures.

concentration of Me_2SO in water as shown in Figure 2. Although there was only a 50% increase in 1 to 1 Me_2SO/water, the line width increased dramatically thereafter. This all suggested that the degree of ionization is a major factor in determining the line width. Formamide or 50% Me_2SO in water appear to be reasonable solvent alternatives.

The best explanation for the narrow lines of sulfonic acids and sulfonate salts is derived from the idea that sulfonic acids are almost completely ionized at 1–3 M concentrations in water.[5] As the sulfonate group ionizes, it approaches tetrahedral symmetry where the NMR line is narrower because the interaction with the quadrupole moment is minimized. Ion pairing or proton transfer rates could also contribute significantly to line widths. In nonaqueous solvents, one might expect the degree of ioni-

(10) Inglefield, P. T.; Reeves, W. T. *J. Chem. Phys.* **1964**, *40*, 2425.

zation and the rate of proton transfer to decrease and the amount of ion pairing to increase. All of these could contribute to the observed increase in line width. In concentrated aqueous hydrochloric acid, however, proton transfer rates would still be high because of the high proton concentration, but the same high proton concentration would cause the sulfonic acid to ionize less, and the ^{33}S line width would increase. Thus, the degree of ionization appears to be the most important factor in determining the ^{33}S line widths of sulfonic acids. Clearly, ^{33}S NMR is a novel way to study the solution properties of sulfonic acids, and we are continuing our studies in this area.

Experimental Section

Instrumental. All spectra were run on a standard Varian 24K FT-80 spectrometer equipped with a 10-mm broad-band probe. During the course of this work the signal to noise ratio was significantly improved by the addition of a new preamplifier and quarter wavelength filter from Varian. Most of the spectra were acquired with an 8-kHz window, but, to avoid possible folding of spectra, preliminary work was done with a 20-kHz window using an Ithaco 4302 audio filter in the low pass mode and the program WIDESW obtained from Steve Patt. The standard conditions for 8-kHz spectra were the following: a 70-μs pulse (90°); a 0.05-s acquisition time; a 1500-μs α delay between pulse and acquisition; no proton decoupling; 40 000 to 1×10^6 transients; and external lock. The choice of 1500 μs for the α delay is a compromise between signal to noise ratio and base-line roll.[11] It should be noted that apparent line width is limited by acquisition time: a very narrow line such as ammonium sulfate requires a longer acquisition time. All chemical shift values are reported with reference to external 4 M ammonium sulfate[1a,12] since the broader line of carbon disulfide[2,3] afforded less precision in the measurements. We also discovered that spinning the sample made little difference with line widths of over 10 Hz. In preliminary studies, there was a decrease of line width with increased temperature, so we ran most spectra at temperatures around 40 °C. The temperature of the probe varied with the temperature of the cooling water, so temperatures were measured with a mercury thermometer positioned against the probe.

Compounds. Samples were commercially available from Aldrich, Eastman, or Mallinckrodt or have been prepared by previously reported procedures. Physical properties such as IR spectra and melting points were consistent with those previously reported. Spectroscopic samples were prepared by dissolving approximately 1.0 g of compound in sufficient deionized water or other specified solvent to make a 2.0 mL volume. If the solution was not complete, solvent was added as necessary to effect solution. Actual concentrations are listed in Table I. A number of compounds could not be run because of solubility problems. When no signal was seen, a C-13 spectrum was generally run to check the sample. The pH values were measured with pHydrion paper.

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Registry No. $MeSO_3H$, 75-75-2; $NH_2NH(CH_2)_2SO_3^-\cdot Na^+$, 62716-44-3; $Br(CH_2)_2SO_3^-\cdot Na^+$, 4263-52-9; $CH_2{=}CHCH_2SO_3^-\cdot Na^+$, 2495-39-8; $PhSO_3H$, 98-11-3; p-$MeC_6H_4SO_3H$, 104-15-4; d-camphor-10-sulfonic acid, 3144-16-9; mesitylenesulfonic acid, 3453-83-6; α-naphthalenesulfonic acid, 85-47-2; 4-aminotoluene-2-sulfonic acid, 118-88-7; sulfosalicylic acid, 97-05-2; sodium 2-benzaldehydesulfonate, 1008-72-6; disodium m-benzenedisulfonate, 831-59-4; dipotassium o-benzenedisulfonate, 5710-54-3.

(11) Canet, D.; Goulon-Ginet, C.; Marchal, J. P. *J. Magn. Reson.* **1976**, *22*, 537, and erratum **1977**, *25*, 397.
(12) Lutz, O.; Nolle, A.; Schwenk, A.; *Z. Naturforsch. A: Phys., Phys. Chem., Kosmoph.* **1973**, *28*, 1370.

Regiospecific α-Alkylation of 4-Chloro(bromo)pyridine

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Halopyridines have been widely used as intermediates in synthetic sequences. The 4-halopyridines are particularly useful as they undergo a wide variety of substitution reactions. Nucleophilic substitution of 4-halopyridines is an important method for the introduction of a wide range of oxygen, sulfur, nitrogen, and carbon substituents.[1] This approach to 4-substituted pyridines is limited, however, by the availability of substituted 4-halopyridines. Generally, the 4-halopyridines are prepared from 4-pyridone or 4-aminopyridine precursors, which frequently require multistep synthesis.[2] Since 4-chloro- and 4-bromopyridine are commercially available as their hydrochloride salts, it seemed desirable to explore ring α-alkylation of these compounds as a short and convenient route to α-substituted 4-halopyridines.

The Grignard addition to 1-acylpyridinium salts has proven to be a convenient method for the synthesis of substituted dihydropyridines and pyridines.[3] We chose to examine the reaction of Grignard reagents with the 1-phenoxycarbonyl salt of 4-chloropyridine. Initially we were concerned that displacement of halogen from the 1-(phenoxycarbonyl)-4-chloropyridinium ion **1** might occur instead of α-addition, since methoxide ion reacts faster with *N*-methyl-4-chloropyridinium ion than with 4-chloropyridine by roughly a factor of 10^{10}.[4] However, substitution of the halogen was not a problem as the Grignard reagent added to the α-position in high yield to give dihydropyridines **2**. Aromatization of crude **2** with o-chloranil in toluene/acetic acid gave the desired 2-alkyl-4-chloropyridines **3** in moderate overall yield as shown in Table I.

The analogous sequence using 1-(phenoxycarbonyl)-4-bromopyridinium chloride provides 2-substituted 4-bromopyridines. The free base of 4-bromopyridine hydrochloride is rather unstable at room temperature, however, so the first step is best carried out by neutralizing the hydrochloride salt in situ with Grignard reagent. We found it most convenient to add 2 equiv of the Grignard reagent to a slurry of 4-bromopyridine hydrochloride (**4**) in THF at −78 °C, followed by the dropwise addition of phenyl chloroformate. The resulting dihydropyridine can

(1) Boulton, A. J.; McKillop, A. "Comprehensive Heterocyclic Chemistry"; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press Ltd: Oxford, 1984; Vol. 2, p 29.
(2) Mertel, H. E. "Pyridine and its Derivatives"; Klingsberg, E., Ed.; Interscience: London, 1961; Vol. 14, Part 2, p 299.
(3) Fraenkel, G.; Cooper, J. W.; Fink, C. M. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 523. Lyle, R. E.; Comins, D. L. *J. Org. Chem.* **1976**, *41*, 3250. Lyle, R. E.; Marshall, J. L.; Comins, D. L. *Tetrahedron Lett.* **1977**, 1015. Comins, D. L.; Abdullah, A. H. *J. Org. Chem.* **1982**, *47*, 4315. Yamaguchi, R.; Nakazono, Y.; Kawanisi, M. *Tetrahedron Lett.* **1983**, *24*, 1801. Comins, D. L.; Mantlo, N. B. *J. Heterocycl. Chem.* **1983**, *20*, 1239. Comins, D. L.; Abdullah, A. H.; Smith, R. K. *Tetrahedron Lett.* **1983**, *24*, 2711. Comins, D. L.; Stroud, E. D.; Herrick, J. *Heterocycles* **1984**, *22*, 151. Comins, D. L.; Abdullah, A. H.; Mantlo, N. B. *Tetrahedron Lett.* **1984**, *25*, 4867. Courtois, G.; Al-arnaout, A.; Miginiac, L. *Tetrahedron Lett.* **1985**, *26*, 1027. Comins, D. L.; Abdullah, A. H. *Tetrahedron Lett.* **1985**, *26*, 43.
(4) Liveris, M.; Miller, J. *J. Chem. Soc.* **1963**, 3486.
(5) Weber, H. *Arch. Pharm. (Weinheim, Ger.)* **1975**, *308*, 637; *Chem. Abstr.* **1975**, *93*, 193028k.
(6) Kucherova, N. F.; Khomutov, R. M.; Budovskii, E. I.; Evadakov, J. P.; Kochetkov, N. K. *Magy. Kem. Lapia* **1959**, *29*, 915; *Chem. Abstr.* **1960**, *54*, 1515f.

0022-3263/85/1950-4410$01.50/0