Recrystallization from MeOH afforded **3** as yellow needles; mp 183.5 °C: ^{1}H NMR δ 8.67 (dd, H_{12}, $J_{11,12}$ = 9.3 Hz, $J_{10F,12}$ = 5.4 Hz), 8.37 (d, H_1, $J_{1,2}$ = 7.1 Hz), 8.04 (d, H_6, $J_{7,8}$ = 8.4 Hz), 7.98 (d, H_6, $J_{5,6}$ = 6.8 Hz), 7.88 (d, H_4, $J_{4,5}$ = 8.3 Hz), 7.86 (d, H_3, $J_{2,3}$ = 8.2 Hz), 7.77 (d, H_7), 7.74-7.60 (m, $H_{2,5}$), 7.53 (dd, H_9, $J_{9,10F}$ = 9.9 Hz, $J_{9,11}$ = 2.6 Hz), 7.38 (m, H_{11}); ^{13}C NMR δ 160.77 (d, J = 245.4 Hz), 137.94, 137.59, 137.54, 137.47, 135.52, 135.34, 132.35, 130.16, 128.64, 128.46, 128.03, 127.90, 127.74, 127.04 (d, J = 8.7 Hz), 124.59, 121.42, 121.37, 117.65 (d, J = 25.0 Hz), 112.75 (d, J = 20.2 Hz); high resolution mass spectrum, exact mass calcd for

$C_{20}H_{11}F$ 270.084530, obsd 270.084475.

Improved Correlation of ^{33}S Chemical Shifts with pK_a's of Arenesulfonic Acids: Use of ^{33}S NMR for pK_a Determination

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Reported here is an improved linear correlation between ^{33}S chemical shifts and the pK_a's of arenesulfonic acids **1**, **2**, and **8-10**, previously determined by UV spectroscopy. Using that linear correlation, we determined the following previously unreported pK_a's ($\pm$0.04) from ^{33}S chemical shifts: *p*-aminobenzenesulfonic (-6.47), *p*-(dimethylamino)benzenesulfonic (-6.43), *p*-(dimethylammonio)benzenesulfonic (-7.18), *p*-chlorobenzenesulfonic (-6.88), *p*-acetylbenzenesulfonic (-6.96), *p*-nitrobenzenesulfonic (-7.23), *m*-(trifluoromethyl)benzenesulfonic (-7.04), and *m*-nitrobenzenesulfonic (-7.25) acids. Also, ^{33}S NMR provides an improved value for the second pK_a of *m*-benzenedisulfonic acid (-7.00); the second pK_a of *p*-benzenedisulfonic acid (-6.99) is, within experimental error, identical with that of the meta compound.

Introduction

Previous studies of substituent effects on the acidities of arenesulfonic acids, including **1**, **2**, and **8-10**, and the first pK_a's of **3** and **13**, have been conducted by measuring their degrees of ionization in solutions of varying Hammett acidity (H_0) with UV or ^{1}H NMR methods.[1] It has been necessary to carry out these pK_a determinations in concentrated sulfuric acid solution, where significant amounts of the free sulfonic acid and its conjugate base are both present. Experimental difficulties limited these methods to sulfonic acids showing an isolated B band in the UV and to the determination of first ionizations of disulfonic acids only. Therefore, the pK_a's of **4**, **5**, **15**, and 3,5-bis(trifluoromethyl)benzenesulfonic acid have previously been calculated from a Hammett plot of pK_a vs σ, with use of the experimentally determined pK_a's of **1**, **2**, **8**, **10**, and the first ionization of **3**.[2]

The field of ^{33}S NMR has grown rapidly, and a good review of the subject has appeared.[3] Hinton found a linear relationship between the ^{33}S chemical shifts of arenesulfonic acids **1**, **8**, **11**, and **15** and Hammett σ constants.[4] Crumrine et al. reported a linear correlation between the ^{33}S NMR chemical shifts of sulfonic acids **1**, **2**, **4**, **5**, **8**, **10**, **15**, and their pK_a's.[5] The ^{33}S NMR spectra in both of these studies were recorded on low-field spectrometers, with aqueous solutions of rather high concentration.

With higher applied magnetic field strength, the receptivity of the nucleus and spectral resolution are both enhanced. Recently, we reported that, in a given solvent, line widths were narrowest at low concentration where ion-ion contributions to nuclear relaxation were minimized.[6] It is well-known that narrower spectral lines are obtained at higher temperatures than at lower ones.[7] By these principles, more accurate ^{33}S chemical shifts were

obtained in this investigation. Also, it was possible to record the ^{33}S spectra of several compounds with limited solubility. Subsequently, we found ^{33}S NMR to be an accurate and facile experimental method for determining the pK_a's of arenesulfonic acids, which circumvented the experimental difficulties of earlier methods.

The ^{33}S NMR spectra of arenesulfonates ($ZC_6H_4SO_3^-$ Cat^+) **1-15** were recorded in 0.046-0.13 M aqueous solutions, where the sulfonates are almost completely ionized.[8] Consequently, the ^{33}S chemical shifts were not affected by the counterion.[9]
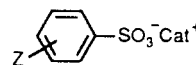
1, Z = H	**6**, Z = *p*-N(CH$_3$)$_2$	**11**, Z = *p*-Cl
2, Z = *m*-CH$_3$	**7**, Z = *p*-NH$_2$	**12**, Z = *p*-COCH$_3$
3, Z = *m*-SO$_3^-$	**8**, Z = *p*-CH$_3$	**13**, Z = *p*-SO$_3^-$
4, Z = *m*-CF$_3$	**9**, Z = *p*-NH$_3^+$	**14**, Z = *p*-NH(CH$_3$)$_2^+$
5, Z = *m*-NO$_2$	**10**, Z = *p*-Br	**15**, Z = *p*-NO$_2$

Results and Discussion

Table I shows the ^{33}S chemical shifts and line widths of the arenesulfonates ($ZC_6H_4SO_3^-Cat^+$) at 20 and 39 °C. Errors in the chemical shift values are ca. $\pm$0.3 ppm for

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Table I. ^{33}S Chemical Shifts and Line Widths of Arenesulfonic Acids and Arenesulfonate Salts (ZC$_6$H$_4$SO$_3^-$Cat$^+$) in Aqueous Solution at 20 and 39 °C

Z	Cat$^+$	temp, °C	pH (20 °C)	δ	$\Delta\nu_{1/2}$, Hz
H	H$^+$	20	2	-11.3	8.8
m-CH$_3$	H$^+$	20	2	-10.9	18.8
m-SO$_3^-$	2 Na$^+$	20	4	-13.9	21.5
m-CF$_3$	H$^+$	20	2	-14.2	19.5
m-NO$_2$	H$^+$	20	2	-15.9	49.0
p-N(CH$_3$)$_2$	Na$^+$	20	8	-9.6	75.6
p-NH$_2$	K$^+$	20	11	-9.8	51.5
p-CH$_3$	H$^+$	20	2	-10.6	21.2
p-NH$_3^+$	K$^+$	20	1	-14.2	18.1
p-Br	H$^+$	20	2	-12.8	9.0
p-Cl	H$^+$	20	2	-13.0	9.0
p-COCH$_3$	Na$^+$	20	4	-13.6	13.8
p-SO$_3^-$	2 K$^+$	20	8	-13.8	18.8
p-NH(CH$_3$)$_2^+$	Na$^+$	20	2	-15.3	55.0
p-NO$_2$	Na$^+$	20	5	-15.7	58.8
H	H$^+$	39	2	-11.7	6.5
m-CH$_3$	H$^+$	39	2	-11.2	8.8
m-SO$_3^-$	2 Na$^+$	39	4	-14.2	16.0
m-CF$_3$	H$^+$	39	2	-14.4	18.2
m-NO$_2$	Na$^+$	39	2	-16.2	42.5
p-N(CH$_3$)$_2$	Na$^+$	39	8	-9.6	45.0
p-NH$_2$	K$^+$	39	11	-10.0	23.8
p-CH$_3$	H$^+$	39	2	-11.1	11.5
p-NH$_3^+$	K$^+$	39	1	-14.4	15.6
p-Br	H$^+$	39	2	-13.2	7.5
p-Cl	H$^+$	39	2	-13.3	6.2
p-COCH$_3$	Na$^+$	39	4	-13.9	12.5
p-SO$_3^-$	2 K$^+$	39	8	-14.1	14.2
p-NH(CH$_3$)$_2^+$	Na$^+$	39	2	-15.2	34.5
p-NO$_2$	Na$^+$	39	5	-15.7	47.5

narrow lines and ±0.5 ppm for broad lines. The temperature effect on the ^{33}S chemical shifts of these compounds is negligible. The ^{33}S chemical shifts for m-nitrobenzenesulfonic acid (**5**) and sodium p-nitrobenzenesulfonate (**15**) are substantially different from those previously recorded at 6.104 MHz (1.879 T) and 39 °C in ca. 2 M aqueous solution.[5] Since the respective line widths for acids **5** and **15** were 91 and 125 Hz, there was considerable error in the earlier chemical shift measurements.

A substantial change in the ^{33}S chemical shift was observed for both potassium p-aminobenzenesulfonate (**7**) and sodium p-(dimethylamino)benzenesulfonate (**6**) upon HCl titration to the pH values in Table I, thereby furnishing ^{33}S chemical shifts for the corresponding zwitterions (**9** and **14**).[10] The ^{33}S chemical shifts of these compounds fit the previously observed trend that ^{33}S resonances of benzenesulfonates with electron-withdrawing substituents are found upfield from those of benzenesulfonates with electron-donating substituents.[8]

Previously Crumrine et al. reported a linear relationship between the ^{33}S chemical shifts of compounds **1, 2, 4, 5, 8, 10,** and **15** and respective Taft substituent constants.[5] The data reported here yielded improved Taft dual-substituent plots of $\delta(^{33}$S) vs σ_I and σ_R following the relationships in eqs 1–4; the substituent constants used and

$$\delta(^{33}\text{S}) = -6.38\sigma_I - 6.69\sigma_R - 11.69 \quad \text{meta at 20 °C} \quad (1)$$

$$\delta(^{33}\text{S}) = -6.57\sigma_I - 5.32\sigma_R - 11.42 \quad \text{para at 20 °C} \quad (2)$$

$$\delta(^{33}\text{S}) = -6.31\sigma_I - 6.40\sigma_R - 11.99 \quad \text{meta at 39 °C} \quad (3)$$

$$\delta(^{33}\text{S}) = -6.10\sigma_I - 5.47\sigma_R - 11.81 \quad \text{para at 39 °C} \quad (4)$$

calculated ^{33}S chemical shifts appear in Table II.[11] The

Table II. Taft Substituent Constants Used and Calculated ^{33}S Chemical Shifts of Arenesulfonates (ZC$_6$H$_4$SO$_3^-$) in Aqueous Solution at 20 and 39 °C

Z	σ_I	σ_R	$\delta(^{33}$S) calcd 20 °C	39 °C
H	0.00	0.00	-11.7	-12.0
m-CH$_3$	-0.01	-0.13	-10.8	-11.1
m-SO$_3^-$	0.23	0.07	-13.6	-13.9
m-CF$_3$	0.40	0.00	-14.2	-14.5
m-NO$_2$	0.67	0.00	-16.0	-16.2
H	0.00	0.00	-11.4	-11.8
p-N(CH$_3$)$_2$	0.17	-0.53	-9.7	-10.0
p-NH$_2$	0.17	-0.51	-9.8	-10.1
p-CH$_3$	-0.01	-0.13	-10.7	-11.0
p-NH$_3^+$	0.60	-0.18	-14.4	-14.5
p-Br	0.47	-0.33	-12.8	-12.9
p-Cl	0.47	-0.35	-12.6	-12.8
p-COCH$_3$	0.30	0.09	-13.9	-14.1
p-SO$_3^-$	0.23	0.07	-13.3	-13.6
p-NH(CH$_3$)$_2^+$	0.70	-0.14	-15.3	-15.3
p-NO$_2$	0.67	0.00	-15.8	-15.9

Table III. pK_a's of Arenesulfonic Acids (ZC$_6$H$_4$SO$_3$H) Determined by Three Methods

Z	UV spectroscopy[a]	Hammett plot[b] σ	pK_a	^{33}S NMR chemical shift[c] 20 °C	39 °C
H	-6.65 ± 0.05	0.0	-6.66	-6.66	-6.66
m-CH$_3$	-6.56 ± 0.05	-0.06	-6.62	-6.61	-6.60
m-SO$_3^-$	<-5.1; >-7	0.05	-6.69	-7.00	-7.01
m-CF$_3$		0.46	-6.96	-7.04	-7.04
m-NO$_2$		0.71	-7.12	-7.25	-7.28
p-N(CH$_3$)$_2$		-0.32	-6.45	-6.43	-6.37
p-NH$_2$		-0.30	-6.47	-6.47	-6.42
p-CH$_3$	-6.62 ± 0.05	-0.14	-6.57	-6.57	-6.57
p-NH$_3^+$	-7.04 ± 0.05	0.60	-7.05	-7.03	-7.03
p-Br	-6.86 ± 0.05	0.26	-6.83	-6.86	-6.87
p-Cl		0.24	-6.82	-6.88	-6.88
p-COCH$_3$		0.47	-6.96	-6.96	-6.97
p-SO$_3^-$		0.09	-6.72	-6.99	-6.99
p-NH(CH$_3$)$_2^+$				-7.18	-7.14
p-NO$_2$		0.81	-7.18	-7.23	-7.21

[a] Values taken from ref 1. [b] All pK_a values are ±0.05. [c] All pK_a values are ±0.04.

correlation coefficients for experiments carried out at both temperatures are good ($r = 0.993$ for meta and $r = 0.994$ for para at 20 °C; $r = 0.994$ for meta and $r = 0.990$ for para at 39 °C), and all calculated ^{33}S chemical shifts are within experimental error of the measured values (Table I). When experimental versus calculated chemical shifts are plotted, all slopes obtained are within experimental error of the theoretical value of 1.00.

The pK_a's of arenesulfonic acids **1, 2,** and **8–10** previously determined by UV techniques[1] (Table III) were employed to calculate pK_a's of arenesulfonic acids **1–15**. Linear regression analysis of pK_a vs $\delta(^{33}$S) yielded the relationships in eqs 5 and 6, and results appear in Table III.

$$\text{p}K_a = 0.130\delta(^{33}\text{S}) - 5.19 \quad r = 0.982 \quad 20 \text{ °C} \quad (5)$$

$$\text{p}K_a = 0.139\delta(^{33}\text{S}) - 5.03 \quad r = 0.988 \quad 39 \text{ °C} \quad (6)$$

The pK_a for the second ionization of m-benzenedisulfonic acid (**3**) was previously estimated to lie between

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(10) March, J. *Advanced Organic Chemistry*, 3rd ed.; Wiley: New York, 1985; p 221.

(11) (a) σ values for **1, 2, 4, 5–8, 10–12,** and **15** taken from: Exner, O. *Correlation Analysis of Chemical Data*; Plenum Press: New York, 1988; p 143. (b) σ values for **3, 9, 13,** and **14** taken from: Exner, O. *Correlation Analysis In Chemistry – Recent Advances*; Chapman, N. B., Shorter, J., Eds.; Plenum Press: New York, 1978; p 439.
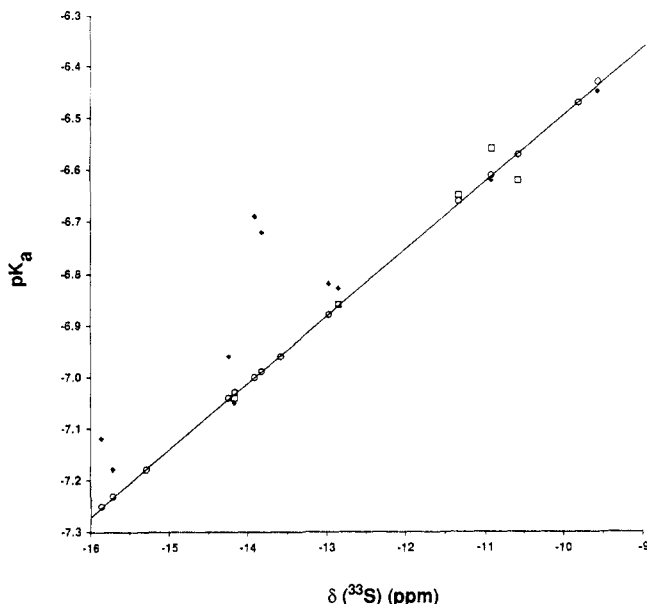
Figure 1. pK_a's of arenesulfonic acids determined by three methods vs [33]S chemical shifts of arenesulfonates in aqueous solution recorded at 20 °C: □, UV spectroscopy; ◊, Hammett plot; ○, [33]S chemical shifts.

-5.1 and -7 by UV.[1a] When the pK_a's of *m*-benzenedisulfonic acid (3) and *p*-benzenedisulfonic acid (13) were previously determined by ^{1}H NMR, only pK_a's for the first ionization could be obtained because the solvent was sulfuric acid.[1c] The [33]S NMR method produced pK_a -7.00 ± 0.04 (Table III). Thus, [33]S NMR provides a method of determining the second ionizations of 3 and 13. Noteworthy also, [33]S NMR furnishes pK_a's for *m*-nitrobenzenesulfonic acid (5) and *p*-nitrobenzenesulfonic acid (15), which cannot be determined by UV techniques due to unresolved B bands and which were not determined by ^{1}H NMR in sulfuric acid.[1]

A Hammett plot of pK_a vs σ with UV-determined pK_a's of arenesulfonic acids 1, 2, and 8-10 gave ρ = -0.646 (r = 0.976).[12] Linear regression analysis produced the calculated pK_a's shown in Table III for comparison with experimental values. The pK_a for 14 could not be calculated from the Hammett plot because σ for this compound was unavailable. Good agreement is demonstrated btween the pK_a's determined by all three methods. The pK_a's determined by [33]S NMR are plotted in Figure 1, as well as those determined by UV and calculated values from the Hammett plot shown for comparison. Therefore, we concluded that [33]S NMR is an accurate and facile method for determining pK_a's of arenesulfonic acids, which is free of the experimental difficulties of previous methods.

Experimental Section

Sulfonic acids 1, 2, 8, and 11 and sodium sulfonates 3, 12, and 6 were obtained from commercial sources and were used without

further purification. Sulfonic acids 4, 5, and 10 were prepared previously and completely identified.[5] Dipotassium *p*-benzenedisulfonate (13) was prepared and identified by literature methods.[13] Sodium *p*-nitrobenzenesulfonate (15) was prepared by dissolving *p*-nitrobenzenesulfonic acid[5] in deionized water and adding 1 equiv of NaOH.

Potassium *p*-aminobenzenesulfonate (7) was prepared by stirring a suspension of *p*-aminobenzenesulfonic acid (Fisher) in deionized water and adding 1 equiv of KOH. Complete dissolution of the potassium salt was achieved by continued stirring and gentle heating. The resulting solution was frozen and water removed in vacuo.

Potassium *p*-ammoniobenzenesulfonate (9) and sodium *p*-(dimethylammonio)benzenesulfonate (14) were prepared by incremental acidification of aqueous solutions of 7 and 6 with a minimum amount of 12 M HCl, with subsequent [33]S chemical shift determinations. No further changes in the [33]S spectra were observed when the pH values given in Table I were reached.

The natural-abundance [33]S spectra were recorded unlocked at 23.008 MHz (7.047 T) on a Varian VXR-300 NMR spectrometer, operating in the Fourier transform mode, using a high-resolution, broad-band probe and 10-mm-o.d. sample tubes. The concentrations of the aqueous arenesulfonates were 0.046-0.13 M. In all cases, [33]S chemical shifts were referenced to 0.12 M aqueous ammonium sulfate contained in a coaxial 5-mm-o.d. NMR sample tube. Broad-band (square wave modulated) proton decoupling was employed throughout.

The [33]S spectral width was 10 000 Hz, acquisition times were 0.147 s (2944 data points) for spectra recorded at 20 ± 1 °C and 0.198 s (3968 data points) for those recorded at 39 ± 1 °C, and FID's were transformed in 32K data points. In most cases, acquisition of transients was continued until a signal to noise ratio of at least 20 was attained. In order to minimize "base-line roll" resulting from acquisition of ultrasonic acoustic ringing in the probe, a receiver dead time (Varian VXR parameter ROF2) of 50 μs was employed.[14]

For spectra recorded at 39 ± 1 °C, the probe temperature was calibrated by recording the ^{1}H NMR of degassed ethylene glycol (Aldrich, 99+% spectrophotometric grade) contained in a sealed 10-mm-o.d. NMR sample tube.[15] The ^{1}H NMR spectra were recorded without field frequency lock, and the magnetic field was shimmed on the FID. All samples for spectra recorded at 39 ± 1 °C were thermostated for at least 30 min prior to insertion into the probe, and the sample temperature was allowed to equilibrate with the probe for approximately 30 min prior to acquisition of transients.

(12) σ values taken from ref 11a, p 61.

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(15) Varian VXR Program TEMCAL(E).