Carbon Acidity. 97. Cesium Ion Pair Acidity of Some Sulfones in Cyclohexylamine

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ABSTRACT

The ion pair acidities of several sulfones were measured on the cesium-cyclohexylamine scale. Cyclopropyl phenyl sulfone is less acidic than isopropyl phenyl sulfone in agreement with earlier results in dimethyl sulfoxide. The acidities of a series of substituted phenyl methyl sulfones show that the sulfone group is an effective insulator; there is no significant delocalization of carbanion charge across the sulfone group into the phenyl ring. © 1997 John Wiley & Sons, Inc. Heteroatom Chem **8**:533–537, 1997

INTRODUCTION

A variety of sulfur-containing functional groups find use in synthetic organic chemistry as activating agents for C–H bonds and for stabilizing the resultant carbanions. Sulfides are only weakly acidifying, so that dithioketals, with two sulfide linkages, are usually employed, as in the case of the dithianes and other Corey-type reagents [1]. Sulfonium salts allow facile preparation of their associated ylides [2]. The sulfinyl group is more strongly activating than the thio group and has a variety of synthetic uses, partly because several different methods exist for subsequent transformations of sulfoxides. Sulfonyl groups

are among the most strongly activating of the sulfur-containing substituents.

The mechanism of stabilization of a carbanion by a sulfonyl group has been the subject of theoretical studies [3] and of X-ray structural studies of their lithium salts [4]. This subject of carbanion stabilization by adjacent sulfur functions has recently been extensively reviewed [5]. The stabilization by a sulfonyl group appears to be largely inductive, and, in particular, d-orbitals play no significant role [6,7]. The present work is concerned with an experimental determination of the effect of a sulfonyl group on equilibrium ion pair acidities and on the effectiveness of transition of substituent effects through a sulfonyl group.

Simple sulfones are too weakly acidic to measure in water. The pKs of several disulfones have been determined in aqueous media [8–10]. The pKs of a number of substituted phenyl phenacyl sulfones, $ArSO_2CH_2COAr$, have been reported in aqueous ethanol solution [11]. Good Hammett-type correlations were found with ρ for the phenyl sulfonyl substituents slightly smaller than that for the phenacyl functions. This work still raises the question of the nature of the substituent effects for sulfones without the stabilizing effect of an adjacent carbonyl group.

The most extensive study of acidities of monofunctional sulfones is that of the Bordwell group in dimethyl sulfoxide (DMSO) [12]. The work of this group includes a study of substituent effects on the benzylic ring of benzyl phenyl sulfone [13]. The results give a normal Hammett-type plot with $\rho = 4.8$ and, as expected, conjugating groups, such as p-nitro, require enhanced σ values of the σ^- type.
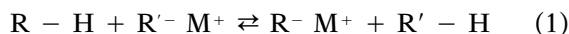
Ion pair acidities have been determined for a

number of compounds as their cesium salts in cyclo-hexylamine (CHA) [14] and in tetrahydrofuran (THF) [15]. The "ion pair" acidities are defined by the transmetallation equilibrium:

$$R - H + R'^- \, M^+ \rightleftarrows R^- \, M^+ + R' - H \quad (1)$$

in which R'H is generally some indicator whose relative acidity is known and M is an appropriate metal. In much of our work, we have used cesium as the counterion because cesium salts are known to be contact ion pairs in CHA and THF even for highly delocalized carbanions. The equilibrium constants for Equation 1 give only the acidity differences between various compounds. To put the acidities on a quantitative scale, we assigned to 9-phenylfluorene a pK of 18.49 for the cesium scale in CHA, a value obtained from studies in aqueous media and that gives for many compounds numerical pK values comparable to the ionic pKs measured in DMSO [14].

In many of the ion pair acidity studies, both the substrate salt and the indicator have useful spectra in the visible or near-UV region. In such cases, the spectra of solutions are readily analyzed to give the amounts of both carbanion salts in the equilibrium mixture. In other cases, such as those of the sulfones in the present study, the substrate salt has no useful spectrum. In these cases, the decrease in the absorption of the indicator salt on addition of a known amount of substrate is used to determine the amount converted to the invisible substrate salt. This procedure, the "single-indicator method," has been shown to give accurate results when due precaution is paid to purity of reagents and by working under an inert atmosphere.

RESULTS AND DISCUSSION

Cyclopropane is more acidic than alkanes, an effect usually attributed to the greater **s**-character of the cyclopropyl-hydrogen bond [16]. For conjugated carbanions, as in enolate ions that require the carbanion carbon to be planar, the cyclopropyl anions have lower stabilities than simple alkyl anions [17]. The crystal structure of a phenylsulfonylcyclopro-pyllithium shows a highly pyramidal carbanionic carbon [18]; yet the equilibrium acidity studies of Bordwell's group in DMSO show that cyclopropyl sulfones are generally less acidic than the corresponding methyl or isopropyl sulfones [19,20]. This result contrasts with kinetic acidity studies in which cyclopropyl sulfones undergo base-catalyzed hydrogen isotope exchange faster than the isopropyl analogs [21,22].

Our results are summarized in Table 1 and com-

TABLE 1 Cesium Ion Pair Acidities of Some Phenyl Alkyl Sulfones (PhSO$_2$R) in Cyclohexylamine (CsCHA) at 25°C

Alkyl Group	pK (CsCHA)[a,b]	pK (DMSO)[b,c]
Methyl	27.2	29.5
Ethyl	28.9	31.3
Isopropyl	29.3	>32
Cyclopropyl	30.9	>32
Benzyl	22.6	23.7

[a]Based pn pK of 9-phenylfluorene = 18.49.
[b]Statistically corrected; e.g., the uncorrected value for ethyl is lower by 0.3 (= log 2).
[c]Ref. [19].

pared with those of Bordwell. Some other values are known. A pK of 24 ± 2 was reported for benzyl phenyl sulfone in dimethylformide by a polarographic method [23]. Its cesium ion pair acidity in THF, 23.0 [24], agrees well with the CHA value. The CHA values, however, are significantly lower than those in DMSO. The pK values of >32 recorded for the isopropyl and cyclopropyl sulfones result because these compounds are less acidic than the solvent and are therefore subject to the solvent leveling effect. CHA has a much lower acidity and permits measurement of higher pKs. The DMSO value for ethyl is close to the limit possible in DMSO, but the ΔpK with CHA, 2.4 units, is close to the 2.3 ΔpK unit difference found for methyl. It seems likely, therefore, that the DMSO pKs for isopropyl and cyclopropyl should be about 31.7 and 33.3, respectively. Most importantly, the CHA ion pair acidities confirm the DMSO results that cyclopropyl sulfones are significantly less acidic than the isopropyl analogues.

Cesium ion pair acidities in CHA generally are rather close numerically to the DMSO results, especially for delocalized carbanions, even though those in DMSO refer to free ions in the dilute DMSO solution standard state. This fortunate accident of nature has been explained on the basis that structural change results in interaction changes of delocalized anions with the large cesium cation that are comparable to the interaction changes of the anions with DMSO solvent molecules [14]. The changes are larger for the sulfones probably because the cation is associated more closely to the negative sulfone oxygens. Crystal structures of several lithium salts of sulfones show association of lithium with the sulfone oxygens within dimer structures and no coordination of lithium with the carbanion carbon [4,25,26]. Thus, the cesium cation may be expected to coordinate more closely to these sulfone anions than to the delocalized indicator anions resulting in a somewhat lower observed pK. Note that the difference for the benzyl sulfone, ΔpK = 1.1 units, in

which the carbanion is undoubtedly more delocalized, is less than for the other compounds.

To study the effect of aryl substituents in a sulfone without other stabilizing groups, we prepared and measured the pKs of a number of substituted phenyl methyl sulfones. The results are summarized in Table 2. The substituent effect is found to be rather small—the total change in pK is only 0.8 units.

These five substituents provide the opportunity to observe a variety of effects. For the meta substituents, phenyl is inductively electron withdrawing, and methyl is donating. In the para position, phenyl should stabilize anionic charge in the ring by delocalization, while methyl should destabilize it as a pi donor. The fluoro substituent is a powerful electron-withdrawing group. Unfortunately, several other informative substituents could not be employed. The halogen substituents are prone to decomposition through benzyne formation, and nitro groups are sensitive to one-electron transfer leading to reduction. The para fluoro was judged to be the heteroatomic substituent most likely to remain intact during the course of an acidity measurement.

One is immediately struck by two facets of these results. The substituents used lead to a pK range of only 0.8 pK units. This small number suggests that very little charge is delocalized through the sulfonyl group into the aromatic ring. Further, the para phenyl substituent has a pK almost equal to that of the unsubstituted compound. This suggests that very little pi delocalization is available to enhance the weak inductive electron withdrawal of the phenyl group.

The dependence of pK on the substituents is shown better by a Hammett-type linear free-energy treatment. Of the many possible choices of various sigma values now available [27], we chose a set of σ^0 values [28] in order to remove the effects of conjugation. Figure 1 shows an excellent linear correlation ($r = 0.994$) with a relatively small ρ of -2.55. This magnitude is consistent with a normal through-space interaction between the carbanion charge and a ring substituent.

TABLE 2   Cesium Ion Pair Acidities in Cyclohexylamine of Substituted Phenyl Methyl Sulfones, $ArSO_2CH_3$, at 25°C

Substitutent	pK
H	27.19
p-Phenyl	27.16
m-Phenyl	27.04
p-Methyl	27.56
m-Methyl	27.40
p-Fluoro	26.77

Although the number of substituents is relatively small, they were chosen to point up significant effects. The acidifying nature of the p-F group requires a rather positive sigma value; the typical Hammett value of 0.06 [29] is much too small. Moreover, the p-phenyl group fits exactly for an inductive effect. If through-conjugation of the carbanion charge into the aromatic ring were significant, the p-phenyl group would be expected to show an enhanced effect. The absence of such an effect confirms that the sulfonyl group is an effective insulator for charge conjugation.

CONCLUSION

The α-hydrogens of cyclopropyl sulfones are less acidic than those of isopropyl analogs. The sulfonyl group is an effective insulator for electronic effects and is not a conduit for charge effects to an attached aromatic ring.

EXPERIMENTAL

Compounds.   The sulfones are all known compounds [30–35]. Purity was checked by elemental analysis and TLC.

Single-Indicator Acidity Measurements.   The density of cyclohexylamine was determined by equilibrating it at four temperatures in 50 mL volumetric
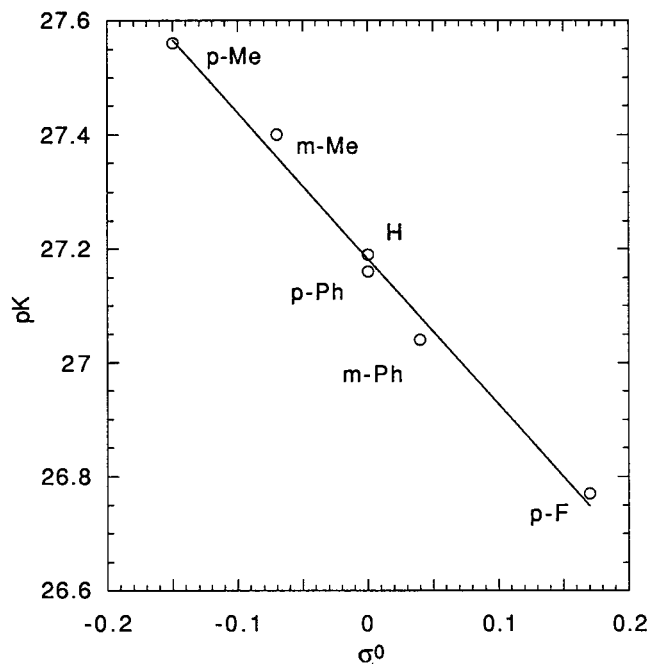
FIGURE 1   pKs of substituted phenyl methyl sulfones on the CsCHA scale compared to σ^0 values. The least-squares line shown is pK = 27.18 − 2.55 σ^0 (R = 0.994).

TABLE 3 Experimental Results for Ion Pair Acidity Measurements

Substate	Indicator[a]	ΔpK[b]	Average pK[b]
Phenyl methyl sulfone	BDDA	$-0.84, -1.07, -0.99, -0.95$	27.23
		$-1.40, -1.00, -1.45, -1.37,$	
	PDDA	-1.26	27.19
	9-PX	$-1.87, 1.79, -1.90$	27.11
Phenyl ethyl sulfone	BDDA	0.91, 0.96	28.96
	PDDA	0.71, 0.65, 0.48	28.92
	9-PX	0.04, 0.16. 0.24	28.94
Phenyl isopropyl sulfone	BDDA	1.00, 2.14	29.29
	PDDA	0.96, 1.46, 2.25, 1.53	29.56
	9-PX	0.41, 0.71, 0.61	29.07
Phenyl cyclopropyl sulfone	TPM	$-0.58, -0.64, -0.49$	30.88
	DCH	0.01	30.91
Phenyl benzyl sulfone	45MP	$-0.34, -0.33, -0.32, -0.31$	22.60
	9TBF	-1.90	22.65
	9MF	$-0.06, -0.05, -0.11$	22.56
p-Tolyl methyl sulfone	BDDA	$-0.58, -0.56$	27.63
	PDDA	-1.07	27.41
	9PX	$-1.41, -1.41, -1.39$	27.56
m-Tolyl methyl sulfone	BDDA	$-0.75, -0.81$	27.42
	9PX	-1.61	27.36
p-Biphenylyl methyl sulfone	BDDA	$-1.05, -1.03, -1.03$	27.16
m-Biphenylyl methyl sulfone	BDDA	$-1.16, -1.16$	27.04
	9PX	-1.93	27.03
	PDDA	-1.44	27.05
p-Fluorophenyl methyl sulfone	9TBF	2.12	26.85
	BDDA	$-1.49, -1.43$	26.74

[a]Indicators and pKs with CsCHA: BDDA, 10-p-biphenylyl-9-9-dimethyl-9,10-dihydroanthracene, 27.72; PDDA, 10-p-phenyl-9,9-dimethyl-9,10-dihydroanthracene, 28.01; 9PX, 9-phenylxanthene, 28.49; TPM, triphenylmethane, 31.45; DCH, dibenzocyclohepta-1,4-diene, 30.83; 45MP, 4,5-methylenephenanthrene, 22.93; 9TBF, 9-t-butylfluorene, 24.25; 9MF, 9-methylfluorene, 22.33 [14].
[b]Statistically corrected.

flasks. The density obtained from the weight shows good linearity with temperature;

$$d(t) = 0.88459 - 0.00091t \ (t \text{ in } °C), \qquad (2)$$

with a correlation coefficient (r^2) of 0.994.

A weighed amount of an appropriate indicator hydrocarbon was placed in a tube to which a 1 mm and 1 cm spectrometer cell were attached, and a known weight of CHA was added in the glove box. The volume of CHA was determined from the weight. Stock base solution of CsCHA was added through a microliter syringe until a stable coloration of the indicator anion was achieved. In most cases, a maximum absorbance of about 1.0 was desirable. The visible spectrum was determined and checked for stability. If the spectrum decreased with time, or decreased more than a few percent of the total absorbance before stabilizing, the run was abandoned. A weighed amount of the substrate compound was added, and the spectrum was redetermined. The decrease in absorbance upon adding the substrate gives the concentration of substrate anion, and the remaining absorbance gives the indicator anion concentration. The concentrations of the protonated species were determined by difference. In some cases, the substrate anion was unstable and the spectrum decayed. In these cases, the spectrum was monitored as a function of time, and the absorbance was extrapolated back to the time of addition.

At least two indicators were used for most determinations. The results of these experiments are summarized in Table 3. The results generally show good consistency with precision generally ± 0.1 or better even with different indicators.

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