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The Acidities of Substituted α-Phenylsulfinylacetophenones

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Synopsis. The acidities of eleven *meta*- and *para*-substituted α-phenylsulfinylacetophenones (**1**) were determined potentiometrically in a 50% ethanol solution. pK_a values (10.22—12.01) which can be nicely correlated with Hammett's σ-values were obtained.

In recent years, many chemists have examined β-keto sulfoxides as key synthetic intermediates. During the course of our research concerned with the reactions of β-keto sulfoxides and their derivatives at the α-carbon atom with electrophiles in the presence of a base,[1] we became interested in the acidities of β-keto sulfoxides, synthesized eleven substituted α-phenylsulfinylacetophenones (**1**), and determined their acidities, which may shed light on the problem of their reactivity.

The β-keto sulfoxides (**1**) were prepared by treating *meta*- or *para*-substituted ethyl benzoates with α-sulfinylcarbanions derived from the corresponding *meta*- or *para*-substituted methyl phenyl sulfoxides;[2] their pK_a values were measured potentiometrically with 0.1 M potassium hydroxide in a 50% ethanol solution. The pK_a values thus obtained are listed in Table 1. The data reveal that the β-keto sulfoxides possess rather strong acidities.

Recently, Amel and Marek[3] determined the acidities of substituted phenyl phenacyl sulfones in a 95% ethanol solution, and gave pK_a values which can be correlated with Hammett's σ-values. Furthermore, the basicities of phenacyl-substituted phosphonium,[4,9a] sulfonium,[5,9a] and pyridinium[6] ylides have been determined in order to confirm the stability and reactivity of these ylides in terms of the substituent effect.

The pK_a values of the phenacyl-substituted active methylene compounds hitherto reported are summarized in Table 2, together with our results for comparison. One finds in Table 2 that the β-keto sulfoxides(**1**) are less acidic than the other active methylene compounds. This fact is compatible with the relatively weak electron-withdrawing character of sulfinyl group in comparison with those of the sulfonyl, sulfonium, and ammonium groups.[7]

When the pK_a values for the β-keto sulfoxides (**1**) thus obtained were plotted against Hammett's σ-values, a good straight line was obtained. For the substituents (X) on the phenylsulfinyl aromatic ring, $\rho=1.32$, and for the substituents (Y) on the phenacyl aromatic ring, $\rho=2.68$. The electron-withdrawing substituents on both the aromatic rings increase the acidity of **1**. As is revealed in Table 2, the magnitude of the ρ-value for the phenacyl substituents, Y, closely resembles those of phenacyl sulfones(**2**), arylmethylphenacylsulfonium salts(**3**), dimethylphenacylsulfonium

TABLE 1. α-PHENYLSULFINYLACETOPHENONES (**1**) (X-C_6H_4-SO-CH_2-CO-C_6H_4-Y)

X	Y	pK_a[a]	Mp (°C)	NMR chemical shifts ($CDCl_3$), δ(multiplicity)[b]	Anal. Found, % C	Found, % H	Calcd, % C	Calcd, % H
H	*m*-Cl	10.22	101—103	4.45 (q, J=13.8 Hz, 2H, -CH_2-) 7.20—8.10 (m, 9H)	60.81	3.84	60.32	3.98
H	*p*-Cl	10.55	119—120	4.42 (q, J=14 Hz, 2H, -CH_2-), 7.25—8.05 (m, 9H)	60.32	3.77	60.32	3.98
H	*m*-CH_3	11.13	70— 72	4.40 (q, J=13.7 Hz, 2H, -CH_2-), 7.20—8.00 (m, 9H), 2.42 (s, 3H, CH_3)	69.98	5.32	69.74	5.46
H	*p*-CH_3	11.59	92— 93	4.45 (q, J=14 Hz, 2H, -CH_2-), 7.10—8.00 (m, 9H), 2.42 (s, 3H, CH_3)	69.39	5.42	69.74	5.46
H	*p*-OCH_3	12.01	95— 96	4.43 (q, J=14 Hz, 2H, -CH_2-), 6.75—8.15 (m, 9H), 3.90 (s, 3H, OCH_3)	65.45	4.96	65.67	5.14
H	H	11.06	70— 71	4.47 (q, J=14 Hz, 2H, -CH_2-), 7.20—8.15 (m, 10H)	68.65	4.97	68.83	4.95
p-OCH_3	H	11.37	79— 80	4.48 (q, J=14 Hz, 2H, -CH_2-), 6.90—8.20 (m, 9H), 3.87 (s, 3H, OCH_3)	65.19	4.92	65.67	5.14
p-CH_3	H	11.25	82— 85	4.48 (q, J=14 Hz, 2H, -CH_2-), 7.10—8.25 (m, 9H), 2.43 (s, 3H, CH_3)	69.99	5.41	69.74	5.46
m-CH_3	H	11.14	65— 66	4.44 (q, J=13.8 Hz, 2H, -CH_2-), 6.97—8.10 (m, 9H), 2.41 (s, 3H, CH_3)	69.23	5.62	69.74	5.46
p-Cl	H[c]	10.63	99—101	4.47 (q, J=14 Hz, 2H, -CH_2-), 7.15—8.25 (m, 9H)				
m-Cl	H[c]	10.61	94.5—95	4.49 (q, J=14 Hz, 2H, -CH_2-), 7.17—8.09 (m, 9H)				

a) The average experimental error was ±0.04 pK_a unit. b) Tetramethylsilane was used as an internal reference.
c) These compounds are very unstable.

Table 2. The pK_a values of phenacyl-substituted active methylenes ($Z-CH_2-CO-C_6H_4-Y$) and their σ-correlations

Z	pK_a[a]	ρ(X)	ρ(Y)	Ref.
$X-C_6H_4-SO-$ (**1**)	11.06[b]	1.32	2.68	This work
$X-C_6H_4-SO_2-$ (**2**)	10.97[c]	2.01	2.35	3
$X-C_6H_4S^+(CH_3)-$ (**3**)	7.06[c]	1.13—1.23	2.63—2.68	5a
	6.66[c]			9a
$(CH_3)_2S^+-$ (**4**)	8.0[c]		2.1	5b
	7.68[c]			9a
$(C_6H_5)_3P^+-$ (**5**)	5.60[d]		2.3	4
	5.60[c]			9a
$X-C_5H_5N^+-$ (**6**)	9.7[c]	2.6 —3.1	2.2 —2.3	6

a) This column shows the pK_a values of unsubstituted compounds (X=Y=H). The pK_a value was determined in ethanol-water mixture: b) in 50% ethanol, c) in 95—100% ethanol, d) in 80% ethanol.

salts(**4**), triphenylphenacylphosphonium salts(**5**), and phenacyl pyridinium salts(**6**), suggesting that the carbanions generated from these compounds, 1—6, are stabilized by a p_π–p_π delocalization system with a carbonyl group (such as: $-CH{=}\overset{\ominus}{C}-\overset{\|}{C}(=O)-C_6H_4-Y$) with the same tendency. On the other hand, the magnitude of ρ-values for the phenylsulfinyl substituents, X, is considerably small in comparison with that for phenacyl sulfones(**2**) and is comparable with that for phenacylsulfonium salts(**3**). The σ-correlation for X suggests that the demand for the resonance effect of the substituent would be negligible; hence, the inductive effect of X can cause a change in electronegativity only at the sulfinyl sulfur. In addition, since the sulfur atom can expand its valence shell beyond an octet using 3d orbitals,[8] perhaps a substantial p_π–d_π interaction may operate between the sulfinyl sulfur and the carbanion carbon to stabilize the carbanion of **1**, in a fashion analogous to the cases of phosphonium and sulfonium ylides and sulfones.[3,5,6,9] Of course, this interaction should result in a large inductive effect of the substituent, together with an increase in the acidity. However, the smaller ρ-value for **1**, as well as the higher pK_a values, seems to suggest that the p_π–d_π interaction in the β-keto sulfoxide system stabilizes the carbanion to a less extent than in the phenacyl sulfone system(**2**).

Experimental

Preparation of α-Phenylsulfinylacetophenones (1). The β-keto sulfoxides (**1**) were prepared according to a method analogous to that developed by Russell *et al.* and by Corey *et al.*[2]

A *meta-* or *para*-substituted ethyl benzoate was treated with 2 equiv of an α-sulfinylcarbanion, derived from the corresponding *meta-* or *para*-substituted methyl phenyl sulfoxide and lithium diethylamide(prepared from 0.1 g/ml solution of butyl lithium in hexane and diethylamine in tetrahydrofuran), at 0 °C. The reaction mixture was then stirred for 1 hr. After the addition of water, the solution was acidified with 10% hydrochloric acid (*ca.* pH 3) and extracted with chloroform. The concentration of the chloroform layer, followed by the crystallization of the residue from carbon tetrachloride or ether, yielded the β-keto sulfoxide in sufficient yields. Satisfactory IR, NMR, and elemental analyses were obtained for all the β-keto sulfoxides described here. Table 1 summarizes their melting points and NMR data.

Measurement of pK_a. The pK_a value of the β-keto sulfoxides(**1**) in a 50% ethanol solution was determined potentiometrically by the titration of 0.100 M potassium hydroxide in 50% ethanol at 25 °C, according to the usual method.[10]

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