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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**) ($X\text{-}C_6H_4\text{-}SO\text{-}CH_2\text{-}CO\text{-}C_6H_4\text{-}Y$)

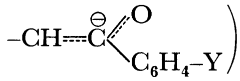
X	Y	pK_a[a]	Mp (°C)	NMR chemical shifts ($CDCl_3$), δ(multiplicity)[b]	Anal. Found, % C	Anal. Found, % H	Anal. Calcd, % C	Anal. Calcd, % H
H	*m*-Cl	10.22	101—103	4.45 (q, J=13.8 Hz, 2H, $-CH_2-$) 7.20—8.10 (m, 9H)	60.81	3.84	60.32	3.98
H	*p*-Cl	10.55	119—120	4.42 (q, J=14 Hz, 2H, $-CH_2-$), 7.25—8.05 (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	p$K_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$^{c)}$ 6.66$^{c)}$	1.13—1.23	2.63—2.68	5 a 9 a
$(CH_3)_2S^+-$ (**4**)	8.0$^{c)}$ 7.68$^{c)}$		2.1	5 b 9 a
$(C_6H_5)_3P^+-$ (**5**)	5.60$^{d)}$ 5.60$^{c)}$		2.3	4 9 a
$X-C_5H_5N^+-$ (**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 pπ–pπ delocalization system with a carbonyl group (such as:  $-\mathrm{CH}\overset{\ominus}{=}\mathrm{C}\begin{matrix}\mathrm{O}\\ \mathrm{C_6H_4{-}Y}\end{matrix}$) 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 pπ–dπ 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 pπ–dπ 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]

References

1) N. Kunieda, J. Nokami, and M. Kinoshita, *Tetrahedron Lett.*, **1974**, 3997; J. Nokami, N. Kunieda, and M. Kinoshita, *ibid.*, **1975**, 2179; N. Kunieda, J. Nokami, and M. Kinoshita, *Chem. Lett.*, **1974**, 369.

2) H. -D. Becker, G. J. Mikol, and G. A. Russell, *J. Amer. Chem. Soc.*, **85**, 3410 (1963); E. J. Corey and M. Chaykovsky, *ibid.*, **86**, 1639 (1964); E. J. Corey and M. Chaykovsky, *ibid.*, **87**, 1345 (1965).

3) R. T. Amel and P. J. Marek, *J. Org. Chem.*, **38**, 3513 (1973).

4) S. Fliszar, R. F. Hudson, and G. Salvadori, *Helv. Chim. Acta*, **46**, 1580 (1963).

5) a) K. W. Ratts, *J. Org. Chem.*, **37**, 848 (1972); b) K. W. Ratts and A. N. Yao, *ibid.*, **31**, 1185 (1966).

6) W. G. Phillips and K. W. Ratts, *ibid.*, **35**, 3144 (1970).

7) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, New York, N. Y. (1963), p. 173; H. H. Szmant and G. Suld, *J. Amer. Chem. Soc.*, **78**, 3400 (1956); F. G. Bordwell and P. J. Boutan, *ibid.*, **78**, 87 (1956); S. Oae and C. C. Price, *ibid.*, **80**, 3425 (1958). So far as our knowledge, the σ-value for the phosphonium group has never been determined.

8) C. C. Price and S. Oae, "Sulfur Bonding," Chapter 4, Ronald Press Co., New York, N. Y. (1962), and references cited therein; S. Oae, M. Yoshihara, and W. Tagaki, This Bulletin, **40**, 951 (1967).

9) a) A. W. Johnson and R. T. Amel, *Can. J. Chem.*, **46**, 461 (1968); b) A. W. Johnson, S. Y. Lee, R. A. Swor, and L. D. Royer, *J. Amer. Chem. Soc.*, **88**, 1953 (1966).

10) A. Albert and E. P. Serjeant, "Inoization Constants of Acids and Bases," Methuen & Co. London (1962), p. 16.