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Effect of Cationic Micelles on the pK_a Values of Disulfones

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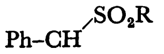
The acid dissociation constants of carbon acids activated by two sulfonyl groups were determined spectrophotometrically in aqueous solution with and without CTAB micelles. The results indicate that a cationic micelle causes larger pK_a decrease for more hydrophobic disulfones. Hydrophobic properties of cyclic and acyclic disulfones are discussed.

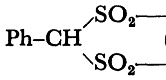
Cationic micelles stabilize carbanions,[1] this becoming more pronounced for more delocalized carbanions. In the H-D exchange reaction of micelle-forming sulfonium salts, micellar rate enhancement for the allyl-methylene group is much larger than that for the methyl group.[2] Similar phenomena were observed in the micellar effects on the acid dissociation constants of α-substituted *p*-nitrophenylacetonitrile,[3] the mechanism of hydrolysis of some activated carboxylic acid esters,[4] and the transition state of E2 elimination reaction of phenethyl bromide.[5] The carbanions are delocalized through conjugation with carbon-carbon or carbon-oxygen double bond. It is of interest to alter the behavior of carbanions by attaching other conjugative groups such as sulfonyl group.

We have examined the micellar effect on pK_a values of cyclic and acyclic disulfones, **1**—**3** and **4**—**7**, respectively, and also of β-diketone, **8**. The compounds were chosen because (a) their carbanions except for those of **4**, are stable, (b) the carbanions show suitable absorption for pK_a determination in UV region, and (c) possible variation of micellar effects with respect to cyclic and acyclic structures can be examined.



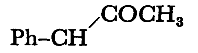
$\text{Ph-CH}(\text{SO}_2\text{R})_2$

1: $R=C_2H_5$
2: $R=C_4H_9$
3: $R=C_6H_{13}$



$\text{Ph-CH}<(\text{SO}_2)_2>(\text{CH}_2)_n$

4: $n=2$
5: $n=3$
6: $n=4$
7: $n=5$



$\text{Ph-CH}(\text{COCH}_3)_2$

8

Results and Discussion

Stability of Carbanions. The carbanions of all the compounds except **4** were confirmed to be stable in alkaline solution (2 M NaOH) under a nitrogen atmosphere. While the five-membered disulfone (**4**) decomposes in an alkaline solution,[6] the spectra of sulfonyl carbanions (λ_{max} 270—286 nm) can be reproduced quantitatively by neutralization followed by addition of excess alkali. In a 0.01 M NaOH solution, **4** shows absorption at λ_{max} 253 nm ($\varepsilon=6000\ M^{-1}\ cm^{-1}$), unchanged by acidification, the original spectrum of undissociated disulfone (λ_{max} 265 nm, $\varepsilon=510\ M^{-1}\ cm^{-1}$) not being restored (1 M=1 mol dm^{-3}).

Determination of Acid Dissociation Constants (pK_a). Acid dissociation constants were determined spectrophotometrically by means of the following equations.[7]

$$pK_a = pH + \log\frac{OD_{S^-} - OD_{obsd}}{OD_{obsd} - OD_{SH}} \qquad (1)$$

$$\varepsilon_{app} = \varepsilon_{S^-} - \frac{K_w\varepsilon_{app}}{K_a[OH^-]} \qquad (2)$$

$$OD^- \quad \varepsilon_{app} = \varepsilon_{S^-} - \frac{1}{K_a}(h_- \varepsilon_{app}), \qquad (3)$$

where OD_{S}^-, OD_{SH}, and OD_{obsd} denote optical densities of carbanion, undissociated disulfone and observed optical density, respectively, ε_{app} and ε_{S}- apparent extinction coefficient and extinction coefficient of a carbanion, respectively, and h_- denotes acidity function in concentrated NaOH solutions. Equation 1 is applicable when the carbanion is generated in buffer solutions, at a given pH and a λ_{max}. Equation 2 is applicable when the carbanion is generated in a solution of concentration below 0.1 M NaOH. It is necessary to use h_- instead of $[OH^-]$ (Eq. 3) when the concentration of NaOH is 0.1—4 M.[8]

Optical densities at 290 nm except for **8** (310 nm) were recorded at various alkaline concentrations. The spectra of **2** and the plots of ε_{app} *vs.* $\varepsilon_{app}/[OH^-]$ are shown in Figs. 1 and 2, respectively. The K_a values were then calculated from the slopes by the least squares method.

Effect of a Cationic Micelle. The concentrations of hexadecyltrimethylammonium bromide (CTAB) were

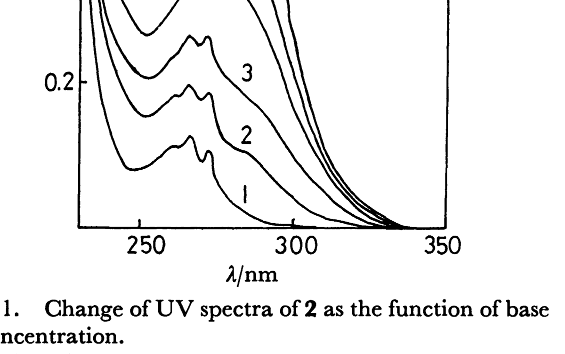


Fig. 1. Change of UV spectra of **2** as the function of base concentration.
1: ([NaOH]=0), 2: (0.005), 3: (0.01), 4: (0.025), 5: (0.05), 6: (0.1).

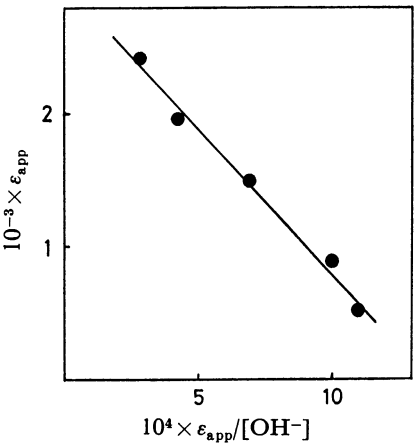


Fig. 2. Plots of ε_{app} *vs.* $\varepsilon_{app}/[OH^-]$ for **2** (see Eq. 2 and Fig. 1): $K_w/K_a=2.11\times10^{-2}$, $K_a=4.74\times10^{-13}$, $pK_a=12.33$.

TABLE 1. EFFECT OF CTAB CONCENTRATION ON pK_a

$10^3\times$[CTAB]/M	pK_a **1**	pK_a **2**	pK_a **8**[a)]
0	12.09[b)]	12.33[b)]	9.08
0.4	—	11.90[b)]	9.08
0.6	11.86[b)]	—	—
1.0	11.26[c)]	10.63[d)]	—
2.0	11.11[c)]	10.47[d)]	8.94
4.0	11.06[c)]	10.41[d)]	8.61
8.0	11.12[c)]	10.57[d)]	8.62
12.0	—	—	8.61
20.0	—	—	8.61

a) Eq. 1 used (pH 6.62—10.2, 8 or 9 points). b) Eq. 2 used (0.004—0.1 M NaOH, 6 points). c) Eq. 1 used (pH 10.00—11.92, 7 points). d) Eq. 1 used (pH 10.00—11.60, 8 points).

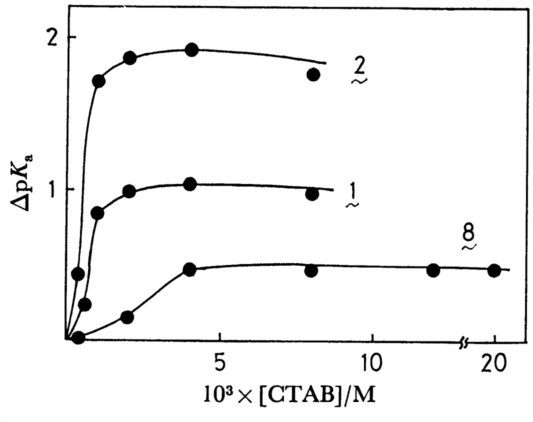


Fig. 3. Plots of ΔpK_a [$pK_a(H_2O)-pK_a$(CTAB)] *vs.* CTAB concentration (see Table 1).

varied as usual for **1**, **2**, and **8**. The results are given in Table 1. The plots of $\Delta pK_a[pK_a(H_2O)-pK_a(CTAB)]$ against CTAB concentration gave saturation curves (Fig. 3), indicating the incorporation of substrates into the micelle. Larger ΔpK_a values were observed for more hydrophobic substrates (**2**>**1**>**8**).

TABLE 2. pK_a AND λ_{max} OF CARBANIONS WITH AND WITHOUT CTAB (8×10^{-3} M)

Compd	pK_a (λ_{max}/nm) CTAB=0	pK_a (λ_{max}/nm) CTAB=8×10^{-3} M	ΔpK_a	$\Delta\lambda$/nm
1	12.09[a)] (274)	11.12 (284)	0.97	10
2	12.33 (274)	10.48 (286)	1.85	12
3	12.37[b)] (274)	10.14[c)] (286)	2.23	12
5	14.24[d)] (270)	13.35[d)] (280)	0.89	10
6	14.24[d)] (274)	11.17[c)] (283)	1.12	9
7	12.24[b)] (274)	10.69[c)] (284)	1.55	10
8	9.08 (305)	8.61 (305)	0.47	0

a) Reported value 12.12. b) Eq. 2 used for NaOH in the range 0.004—0.1 M. c) Eq. 1 used in the pH range 10.36—11.61. d) Eq. 3 used for NaOH in the range 0.1—2 M.

The pK_a and λ_{max} of carbanions in the micellar phase and in the absence of CTAB are summarized in Table 2. The absorption spectra (λ_{max}) of the carbanions of disulfones shift to longer wave length ($\Delta\lambda$=9—12 nm) in the presence of CTAB (8×10^{-3} M), the λ_{max} of diketone (**8**) remaining unchanged irrespective of the presence of CTAB. The ΔpK_a of **8** is also small. In the case of disulfone, both equilibrium (ΔpK_a) and delocalization ($\Delta\lambda_{max}$) of carbanion are favored to a greater extent in a cationic micellar phase than in aqueous phase. In the case of diketone, the carbanion might assume the enolate form preferentially which is stablized by hydration. No change in λ_{max} and the small ΔpK_a value in **8** suggest that such hydration is little affected by incorporation into a cationic micelle.

Hydrophobic Nature of Carbanion. A certain relation holds between pK_a and the hydrophobic nature of substrates. The plots of ΔpK_a against the number of methylene group of the disulfones are shown in Fig. 4. If a single least squares line is drawn for the six points, the slope gives 200 cal/mol as the standard free energy change associated with pK_a decrease per methylene group. However, if two lines are drawn separately for the acyclic and cyclic derivatives, they give 210 and 450 cal/mol, respectively. The choice of

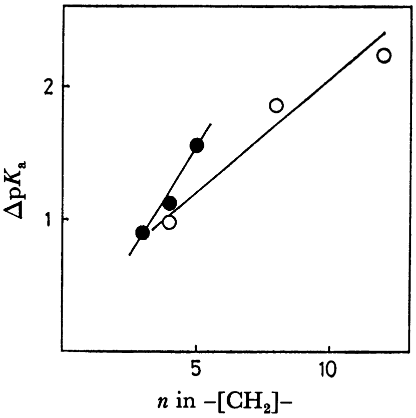


Fig. 4. Plots of ΔpK_a *vs.* methylene number of alkyl chains:
○: Acylic disulfones, ●: cyclic disulfones (see Table 2).

value is difficult due to insufficiency of data. The value of 450 cal/mol for cyclic disulfones seems to be normal as compared to the values (350—900 cal/mol) suggested for hydrophobic interactions.[9] A micellar effect associated with the change of methylene number might be larger for more rigid molecules than for flexible ones, since conformational changes such as curling up of long alkyl chain in aqueous phase are much more easy for acyclic than for cyclic compounds which reduce the free energy change (micellar effect) between aqueous and micellar phase.

The unusually high pK_a of six membered disulfone **5**, is puzzling although ΔpK_a is normal.

Experimental

Melting points are uncorrected. NMR spectra were recorded on a Varian A-60 spectrometer, the chemical shifts being given downfield from tetramethylsilane, and UV spectra on a Shimadzu UV 200 spectrophotometer. pH was measured with a Hitachi-Horiba F-7DE pH meter. Water used for pK_a measurement was purified by distillation of deionized water.

Materials. Commercial 3-phenyl-2,4-pentanedione (**8**) was used after recrystallization from benzene–hexane, mp 57—58 °C (lit,[10] 58—60 °C).

Disulfones were prepared by oxidation of the corresponding thioacetals with 30% hydrogen peroxide in acetic acid containing acetic anhydride.[11],.

1: Yield 56%, mp 133 °C (EtOH–H_2O) (lit,[11] mp 133—134 °C). NMR (DMSO-d_6): δ 1.22 (6H, t), 3.31 (4H, q), 6.56 (1H, s), 7.37—7.84 (5H, m).

2: Yield 56%, mp 90—91 °C (EtOH–H_2O) (lit,[12] mp 86 °C). Found: C, 54.36; H, 7.10; S, 19.5%. Calcd for $C_{15}H_{24}O_4S_2$: C, 54.18; H, 7.29; S, 19.28%.

3: Yield 47%. 78.5—80.5 °C (MeOH). NMR (DMSO-d_6): δ 0.84 (6H, t), 1.10—1.40 (16H, br. s), 3.25 (4H, t), 6.53 (1H, s), 7.35—7.75 (5H, m). Found: C, 59.00; H, 8.34; S 17.0%. Calcd for $C_{19}H_{32}O_4S_2$: C, 58.72; H, 8.32; S, 16.50%.

4: Yield 43%, mp 243—245 °C (benzene). NMR (DMSO-d_6): δ 4.20 (4H, s), 6.27 (1H, s), 7.50—7.70 (5H, m). Found: C, 43.90; H, 4.13; S, 26.2%. Calcd for $C_9H_{10}O_4S_2$: C, 43.88, H, 4.10; S, 26.03%.

5: Yield 49%, mp 259—262 °C (EtOH) (lit,[13] 264—265 °C). NMR (DNSO-d_6): δ 2.30—2.60 (2H, m), 3.45—3.77 (4H, m), 6.53 (1H, s), 7.45—7.75 (5H, m). Found: C, 46.13; H, 4.51; S, 24.1%. Calcd for $C_{10}H_{12}O_4S_2$: C, 46.13; H, 4.66; S, 24.63%.

6: Yield 55%, mp 249—251 °C (EtOH). NMR (DMSO-d_6): δ 2.00—2.33 (6H, m), 3.60—3.97 (4H, m), 6.63 (1H, s), 7.45—7.62 (5H, m). Found: C, 48.47; H, 5.23; S, 23.4%. Calcd for $C_{11}H_{14}O_4S_2$: C, 48.16; H, 5.14; S, 23.37%.

7: Yield 40%, mp 258—260 °C (EtOH). NMR (DMSO-d_6); δ 1.42—2.08 (6H, m), 3.14—3.62 (4H, m), 6.35 (1H, s) 7.38—7.78 (5H, m). Found: C, 49.89; H, 5.51; S, 22.3%. Calcd for $C_{12}H_{16}O_4S_2$: C, 50.00; H, 5.59; S, 22.20%.

pK_a Measurement. The pK_a values were determined by the spectrophotometric method.[7] The stock solutions (4×10^{-2} M) were prepared in EtOH for **1**, **2**, **3**, and **8**, and in CH_3CN for **4**, **5**, **6**, and **7**. Aqueous alkaline solution in a septum-rubber capped volumetric flask (5 ml) was bubbled with nitrogen for 15 min. The CTAB solution was added with a microsyringe, the solution being equilibrated at 25 °C. The substrate solution (25 µl) was added with a microsyringe, *ca.* 3 ml of the solution being put into the rubber-capped UV cell with a syringe. Optical densities at 290 nm except for **8** (310 nm) were recorded at various alkaline concentrations with a Shimadzu 200 UV instrument. Typical spectra are shown in Fig. 1. The pK_a of **3** in water (CTAB=0) could not be determined because of solubility. Thus, pK_a in H_2O was estimated from the pK_a values in 40, 60, and 80% EtOH. The pK_a values in these solvents (12.29, 12.14, and 11.81) were plotted against reciprocal of H_2O %, giving a straight line and allowing extrapolation to give pK_a=12.37 (Table 2).

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