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The Solvent Effects of Water-Dimethyl Sulfoxide Mixtures on the Keto-Enol Tautomerization Rate of Di-*n*-alkyl β-Diketones

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Synopsis. The kinetic solvent effects of water–dimethyl sulfoxide (DMSO) mixtures on the ketonization and the enolization rate constants of eight di-*n*-alkyl β-diketones were analyzed in terms of the group-transfer free energy from water to the mixed solvents. The transfer free energy of the transition state, as calculated from the rate constant and the partition coefficient of the keto or enol form, is found to be divided into three contributions: the two group-transfer free energies of the "transition state skeleton" and the methylene group, and the transfer free energy change due to the inductive effect of the *n*-alkyl group.

In the course of our study aimed at elucidating the kinetic behavior of β-diketones in a liquid-liquid partition system, it was found that the partition rate is controlled by the keto-enol tautomerization in the aqueous phase[1] and the important kinetic influence of aqueous solvent on the reaction was demonstrated.[2] Although it is well recognized that a kinetic solvent effect results from the difference in solvent effects on the reactant state and on the transition state, there have been only a few studies aimed at assessing the solvent effect on the two states individually. Previously, we ourselves demonstrated that a kinetic solvent effect can be experimentally assessed in terms of the free energies of transfer for a reactant and a transition state from a standard solvent to others, as calculated from the liquid-liquid partition coefficient and the rate constant.[2,3]

The purpose of this study is to elucidate the solvent effect and the substituent effect in the keto-enol tautomerization of di-*n*-alkyl β-diketones in a water–DMSO mixed solvent in terms of the transfer free energy.

Experimental

Chemicals. The acetylacetone and eight β-diketones were obtained from the same sources described elsewhere.[1] The solvents used were purified by the ordinary method. The mixed solvents were prepared by weight at the desired mole fraction of DMSO within ±0.0005.

Measurement of the Tautomerization Rate. The tautomerization rate constants were obtained from the absorption decreases of the enol form in 3 ml of a solution contained in quartz cell thermostated at 25±0.1 °C. The tautomerization reaction was initiated by the vapor injection method[2] for 2,3-hexanedione as well as for acetylacetone. For the other β-diketones, a minute quantity of pure liquid of β-diketone was quickly dissolved into a mixed solvent by means of a Teflon spatula designed to mix the solution effectively. Since the enol fraction in the pure liquid state of β-diketone is about 0.8, an enol-rich solution which shows an intense absorbance at 273 nm is produced by the dissolution procedure. First-order analysis of the absorbance change gave the tautomerization rate constant, $k_{\mathrm{obsd}}(\mathrm{s}^{-1})$. Measurements were repeated from two to five times.

TABLE 1. TAUTOMERIZATION RATE CONSTANTS OF DI-*n*-ALKYL β-DIKETONES IN WATER–DMSO MIXED SOLVENTS AT 25 °C

No.	β-Diketone	$k_{\mathrm{obsd}} \times 10^2/\mathrm{s}^{-1}$					
		$x_s=0.000$	0.100	0.200	0.300	0.400	0.500
1	2,4-Pentanedione	9.93	7.42	5.45	3.17	1.92	1.08
2	2,4-Hexanedione	7.72	5.00	3.45	1.93	1.03	0.467
3	3,5-Heptanedione	5.72	3.23	1.98	1.04	0.532	0.233
4	2,4-Heptanedione	7.35	4.73	3.08	1.83	0.888	0.415
5	3,5-Octanedione	5.02	2.85	1.82	0.945	0.475	0.202
6	2,4-Octanedione	6.87	4.82	3.12	1.70	0.972	0.412
7	4,6-Nonanedione	4.92	2.80	1.67	0.867	0.443	0.188
8	2,4-Nonanedione	7.17	4.42	3.08	1.75	0.892	0.415

Results

The observed rate constants are listed in Table 1. The ketonization and enolization rate constants, k_{k} and k_{e}, were calculated from the following equations:

$$k_{\mathrm{k}} = (1-f)k_{\mathrm{obsd}}, \quad k_{\mathrm{e}} = fk_{\mathrm{obsd}}, \tag{1}$$

where f is the enol fraction in the mixed solvent determined previously.[4]

The transfer free energies (kcal mol^{-1}) of the keto form, the enol form, and the transition state from water to mixed solvents were calculated by means of following equations,[3]

$$\begin{aligned} \delta\Delta G_{\mathrm{K}} &= 0.592 \ln \left(\frac{P}{P_{\circ}} \frac{1-f_{\circ}}{1-f} \right), \\ \delta\Delta G_{\mathrm{E}} &= 0.592 \ln \left(\frac{P}{P_{\circ}} \frac{f_{\circ}}{f} \right), \\ \delta\Delta G_{\mathrm{x}} &= 0.592 \ln \left(\frac{P}{P_{\circ}} \frac{1-f_{\circ}}{1-f} \frac{f_{\circ}}{f} \frac{k_{\mathrm{obsd},\circ}}{k_{\mathrm{obsd}}} \right), \end{aligned} \tag{2}$$

where P is the apparent partition coefficient of β-diketone in the heptane/water–DMSO system and where the subscript ○ refers to water as the standard solvent. The data of the partition coefficient were reported previously.[4] The calculated results are listed in Table 2, where the partition coefficient for 2,4-nonanedione was assumed to be equal to that of 4,6-nonanedione. The error in the calculation is less than 0.05 kcal mol^{-1}.

Discussion

Solvent Composition Dependence of Transfer Free Energies. In Table 2, $\delta\Delta G_{\mathrm{E}}$ is a negative value in all systems, while $\delta\Delta G_{\mathrm{x}}$ is positive for the smaller β-diketone and slightly negative for the larger β-diketone. $\delta\Delta G_{\mathrm{K}}$ takes medium values between $\delta\Delta G_{\mathrm{E}}$ and $\delta\Delta G_{\mathrm{x}}$. When we recall that the activation energy changes are represented by $\delta\Delta G_{\mathrm{x}}-\delta\Delta G_{\mathrm{K}}$ or $\delta\Delta G_{\mathrm{x}}-\delta\Delta G_{\mathrm{E}}$, the variation in the tautomerization rate with the solvent composition is found to be primarily governed by those in $\delta\Delta G_{\mathrm{K}}$ and $\delta\Delta G_{\mathrm{E}}$, because the variation in $\delta\Delta G_{\mathrm{x}}$ is smaller than the two others.

Recently, we proposed a new solvent parameter for a mixed solvent, $-(P_{\mathrm{i}}/\alpha T)$ (v^{E}/v), where P_{i}, α, v^{E}, and v correspond to the internal pressure, the coefficient of

TABLE 2. TRANSFER FREE ENERGIES (kcal mol^{-1}) FROM WATER TO WATER–DMSO MIXED SOLVENTS AT 25 °C

No.[a]	State	X_s 0.100	0.200	0.300	0.400	0.500
1	$\delta\Delta G_K$	0.11	0.19	0.15	0.03	−0.13
	$\delta\Delta G_E$	−0.11	−0.25	−0.50	−0.77	−1.04
	$\delta\Delta G_X$	0.11	0.21	0.36	0.44	0.56
2	$\delta\Delta G_K$	0.03	0.08	−0.07	−0.16	−0.34
	$\delta\Delta G_E$	−0.25	−0.41	−0.75	−1.02	−1.30
	$\delta\Delta G_X$	0.05	0.14	0.21	0.37	0.44
3	$\delta\Delta G_K$	−0.05	−0.10	−0.25	−0.51	−0.75
	$\delta\Delta G_E$	−0.32	−0.58	−0.93	−1.31	−1.69
	$\delta\Delta G_X$	0.04	0.11	0.22	0.24	0.32
4	$\delta\Delta G_K$	−0.06	−0.09	−0.25	−0.53	−0.81
	$\delta\Delta G_E$	−0.30	−0.56	−0.91	−1.32	−1.71
	$\delta\Delta G_X$	0.01	0.07	0.10	0.16	0.29
5	$\delta\Delta G_K$	−0.16	−0.26	−0.51	−0.89	−1.15
	$\delta\Delta G_E$	−0.42	−0.76	−1.22	−1.68	−2.11
	$\delta\Delta G_X$	−0.05	−0.06	−0.07	−0.08	0.04
6	$\delta\Delta G_K$	−0.14	−0.25	−0.49	−0.79	−1.17
	$\delta\Delta G_E$	−0.39	−0.74	−1.16	−1.63	−2.09
	$\delta\Delta G_X$	−0.13	−0.15	−0.15	−0.22	−0.13
7	$\delta\Delta G_K$	−0.20	−0.37	−0.71	−1.10	−1.50
	$\delta\Delta G_E$	−0.53	−0.96	−1.48	−2.03	−2.52
	$\delta\Delta G_X$	−0.13	−0.18	−0.24	−0.32	−0.26
8	$\delta\Delta G_K$	−0.19	−0.37	−0.71	−1.10	−1.51
	$\delta\Delta G_E$	−0.44	−0.83	−1.37	−1.91	−2.40
	$\delta\Delta G_X$	−0.10	−0.22	−0.35	−0.43	−0.43

a) The numbers correspond to those in Table 1.

the thermal expansion, the excess molar volume, and the mean molar volume of the mixed solvent respectively.[5)] For the transfer free energy, we can derive the following relation:

$$\delta\Delta G - \phi_s\delta\Delta G_l = -q(r)\frac{P_i}{\alpha T}\left(\frac{v^E}{v}\right), \qquad (3)$$

where $\delta\Delta G_l$ is the transfer free energy from water to DMSO and where $q(r)$ is a correction factor depending on the molar volumes of the solute and the solvent.[4)] The plot of $\delta\Delta G - \phi_s\delta\Delta G_l$ against the pressure factor gave a linear relationship for $\delta\Delta G_K$ and $\delta\Delta G_E$ (the figure is not shown). This suggests that the variation in the solvent-solvent interaction energy in a water–DMSO mixture is an important factor govering the solvent-composition dependence of the tautomerization rate.

Substituent Effect. The relationship between $\delta\Delta G$ and the total number of carbon atoms, n, in β-diketones is summarized as follows:

(i) $\delta\Delta G_K$ and $\delta\Delta G_E$ decrease in proportion to n, *i.e.*,

$$\delta\Delta G_K = \delta\Delta G(\text{-COCH}_2\text{CO-}) + n\delta\Delta G(\text{-CH}_2\text{-}), \qquad (4)$$
$$\delta\Delta G_E = \delta\Delta G(\text{-COCHCOH-}) + n\delta\Delta G(\text{-CH}_2\text{-}),$$

where $\delta\Delta G(\text{-COCH}_2\text{CO-})$, $\delta\Delta G(\text{-COCHCOH-})$, and $\delta\Delta G(\text{-CH}_2\text{-})$ are the transfer free energies of the diketone skeleton, the enol skeleton, and the methylene group.

(ii) $\delta\Delta G_X$ does not show a simple linear relationship with n, but it can be represented by the next equation:

$$\delta\Delta G_x = \delta\Delta G(\bar{X}) + \delta\Delta G(x) + n\delta\Delta G(\text{-CH}_2\text{-}), \qquad (5)$$

where $\delta\Delta G(\bar{X})$ is the transfer free energy of the transition-state skeleton, calculated by subtracting $2\delta\Delta G(\text{-CH}_2\text{-})$ from the $\delta\Delta G_x$ of acetylacetone, and where $\delta\Delta G(x)$ is an increment in $\delta\Delta G(\bar{X})$ induced by an alkyl group other than the methyl group. For methyl group, $\delta\Delta G(x)$ is equal to zero, from the definition. Since the charge distribution in the transition state is expected to be highly delocalized, $\delta\Delta G(x)$ may be sensitive to the electronic property of the alkyl substituent. Therefore, we tested the correlation between $\delta\Delta G(x)$ and the inductive parameter of the substituent proposed by Taft.[6)] The plot of $\delta\Delta G(x)$ calculated from Eq. 5 against the sum of Taft σ^* (*vide infra*) for two alkyl groups of R_1 and R_2, $(\sigma_1^*+\sigma_2^*)$, in R_1-$COCH_2COR_2$ showed a linear relationship. Therefore, Eq. 5 can be rewritten as:

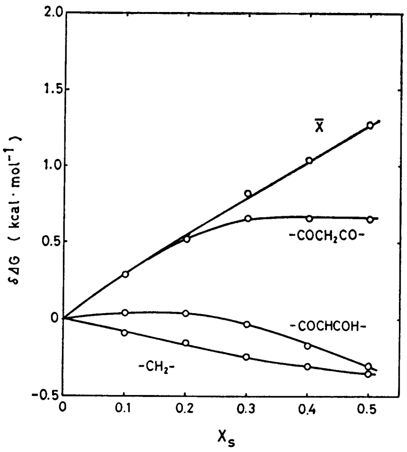

Fig. 1. Variation of the group transfer free energies with mole fraction of DMSO.

n-Alkyl group	CH_3	C_2H_5	C_3H_7	C_4H_9
Taft's σ^*	0.000	−0.100	−0.115	−0.130

$$\delta\Delta G_x = \delta\Delta G(\bar{X}) + \rho(x_s)(\sigma_1^*+\sigma_2^*) + n\delta\Delta G(\text{-CH}_2\text{-}), \qquad (6)$$

where $\rho(x_s)$ is a characteristic coefficient depending on the solvent composition. Because of the repulsive property of the interaction energy between DMSO and the anion,[7)] $\delta\Delta G(\bar{X})$ is expected to be large and positive when Taft's σ^* value of the substituent is large and negative. Hence, the apparent proportionality between the tautomerization rate constant and the number of the methyl group can be ascribed to the large difference between the Taft σ^* values of the methyl group and those of the other substituents.

The group transfer free energies obtained on the basis of Eqs. 4 and 5 are shown in Fig. 1 as a function of the mole fraction of DMSO. The decreasing order of $\delta\Delta G(\bar{X}) > \delta\Delta G(\text{-COCH}_2\text{CO-}) > \delta\Delta G(\text{-COCHCOH-}) > \delta\Delta G(\text{-CH}_2\text{-})$ may correspond to the decreasing order of the extent of charge delocalization. It is noticeable that the inductive effect has been clearly shown to be effective only in the transition state.

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