The Partition Mechanism of Thenoylacetone and Thenoyltrifluoroacetone in Water/Alcohol Systems

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The apparent partition coefficients of thenoylacetone (TA) in ten alcohol/water systems and the enol fractions of TA in both phases were determined. Comparing the results with those of thenoyltrifluoroacetone (TTA), the substituent effect of methyl and trifluoromethyl groups on the partition behavior of the β-diketones in the alcoholic partition systems was examined. The experimental results showed that the apparent partition coefficient of TA is larger than that of TTA, while the partition coefficient of the enol form of TA is smaller than that of TTA. This was related to the differences in the partitioning species of TA and TTA; that is, TA is in keto and enol forms, while TTA is in enol, hydrate, and hemiacetal forms. The partition coefficient of each species was discussed in terms of the solubility parameter of alcohol.

The two-phase system composed of alcohol and water is known to be effective for the extraction of a neutral metal complex which is co-ordinatively unsaturated. For example, the Co(II)–TTA complex can be extracted more effectively by butanol than by benzene.[1] In such extraction studies, TTA has frequently been used as an extractant. However, our information about the partition behavior of TTA in alcohol/water systems is limited. The purpose of our present study is to elucidate the partition mechanism of TTA. In a previous study,[2] the chemical species of TTA in wet higher alcohols are identified as of the enol, hydrate, and hemiacetal forms, and the high reactivity of TTA with hydroxylic solvents was interpreted in terms of the electron-withdrawing effect of the trifluoromethyl group. Such a characteristic property of TTA is expected to affect its partition behavior. In this study, we obtain the partition equilibrium data for TA in alcohol/water systems and examine the substituent effect of the trifluoromethyl group by comparing the partition data of TA with those of TTA.[3]

Experimental

Materials. The TA was synthesized by the Claisen acylation of acetylthiophene.[4] The crude product was purified by the copper salt method[5] and by subsequent vacuum sublimation. The elemental analysis of the purified reagent showed: C: 57.24% and H: 4.79% (calcd for C: 57.11%, H: 4.80%), while the mp is 33.7—34.5 °C. The alcohols were purified by the method described previously.[2] The β-naphthol was purified by recrystalization from ethanol and by vacuum sublimation. The other reagents were used as purchased in the reagent-grade.

Partition Experiment. Five ml of a water-saturated alcohol solution of TA (0.002 M) and an equal volume of the alcohol-saturated aqueous phase ($I=0.1$ by $NaClO_4$, pH=3.5) were agitated for over 3 h at 25±0.5 °C. After centrifugation, an aliquot of the aqueous phase was pipetted out into a quartz cell and the concentration of TA was determined photometrically (295 nm, $\varepsilon=7.94\times10^3$). The concentration in the aqueous phase and the initial concentration allowed the calculation of the apparent partition coefficient of TA. The experiment was repeated six times for each partition system. On the other hand, the apparent partition coefficients of TTA were reported previously by one of the authors for most alcohols except for heptanol,[3] for which we determined the partition coefficient by a procedure similar to that described above.

Bromination. The enol fractions and the enolization rate constants of TA in several water-saturated alcohols were determined by Meyer's bromination method.[6] The procedure was as follows. A 0.01 M solution of TA in water ($I=0.1$, pH=3)-saturated alcohol was prepared. After the solution has stood for over 6 h, 5 ml of the solution was mixed with an equal volume of a 0.1 M alcoholic solution of bromine. After a certain interval, the bromination reaction was stopped by adding a 0.05 M ethanol solution of β-naphthol. Subsequently, after 50 ml of ethanol and 10 ml of the aqueous solution of potassium iodide has been added, and after the mixture had stood for 30 min, the iodine was titrated with a sodium thiosulfate solution. The end point was determined from the vanishing of the color of iodine. The sodium thiosulfate solution used in the titration was standardized by potassium iodate. By this procedure, the enol concentration at a certain time after the initiation of bromination was determined. Hence, the enol fraction at equilibrium was obtained from the enol concentration at reaction time zero, and the enolization rate constant from the slope of the plot of the logarithmic enol concentration against the time.

UV Absorption Measurement. The UV spectra of alcoholic solutions of TA show two absorption maxima, at 264 and 320 nm. The maximum at the longer wavelength is thought to be due to the enol form.[7] The absorption coefficient at the wavelength was determined for each water-saturated alcohol and for each alcohol-saturated aqueous solution. In order to estimate the enol fraction of TA in an aqueous solution, the following measurements were carried out. An alkaline (pH=11.6) solution of TA(2×10^{-5} M) in which TA ($pK_a=8.1$) dissociates entirely and diluted perchloric acid were rapidly mixed by means of a sample-mixing device (Union Co. Type MX-7), and the subsequent increase in the transmittance at 340 nm was recorded on a Hitachi 356 spectrophotometer. At the time of mixing, TA is thought to be in the enol form completely.[8,9] Hence, the ratio of the absorbances at time zero and at equilibrium refers to the enol fraction. Furthermore, from the absorption change, the tautomerization rate constant of TA in an aqueous solution was obtained.

Results

Apparent Partition Coefficients. The observed partition coefficients of TA are shown in Table 1, together with those of TTA. The value for TA is larger than that for TTA in every alcohol–water pair.

Enol Fractions and Tautomerization Rate Constants. The enol fractions and the enolization rate constants of TA, which were determined by bromination tech-

Table 1. The apparent partition coefficients of TA and TTA at 25±0.5 °C

Solvent	P(TA)[a]	P(TTA)[b]
1-Butanol	32.1	30.9
1-Pentanol	52.4	43.7
1-Hexanol	55.6	38.9
1-Heptanol	55.0	37.4[a]
1-Octanol	49.6	28.8
2-Ethyl-1-hexanol	44.8	29.5
2-Octanol	51.4	22.9
3-Methyl-1-butanol	43.3	38.0
Cyclohexanol	48.4	33.9
2-Methyl-1-propanol	28.2	26.9
Benzyl alcohol	—	56.2

a) This work. b) Ref. 3.

Table 2. The enol fractions and the enolization rate constants of TA in water-saturated alcohols and the enol fractions in alcohol-saturated water[c] at 25 °C

No.	Solvent	Enol fraction	Enolization rate constant ($\times 10^{-2}$ s^{-1})
1	1-Butanol[a]	0.812 (0.184)	2.46
2	1-Pentanol[a]	0.878 (0.150)	2.77
3	1-Octanol[a]	0.899 (0.136)	2.87
4	3-Methyl-1-butanol[a]	0.834 (0.150)	2.27
5	1-Hexanol[b]	0.879 (0.141)	
6	1-Heptanol[b]	0.885 (0.136)	
7	2-Ethyl-1-hexanol[b]	0.894 (0.137)	
8	2-Octanol[b]	0.887 (0.137)	
9	Cyclohexanol[b]	0.823 (0.156)	
10	2-Methyl-1-propanol[b]	0.829 (0.182)	

a) Bromination. b) Enol fraction$=0.566\varepsilon_{\max}$.
c) Shown in parentheses.

nique, are listed in Table 2 for four alcohols. In the other alcohols, reproducible results were not obtained; therefore, the following convenient method was adopted. A simple correlation between the enol fraction of TA in the four alcohols and the absorption coefficients at the absorption maximum, $\varepsilon_{\max}$, was obtained:

$$\text{Enol fraction} = 0.566\varepsilon_{\max}. \tag{1}$$

The enol fractions for the other alcohols were calculated from Eq. 1; they are listed in Table 2. The enol fraction in an aqueous solution was obtained as 0.13_4 from the kinetic experiment. From the experiment, the enolization rate constant, 1.62×10^{-2} s^{-1}; the ketonization rate constant, 1.19×10^{-1} s^{-1}, and the absorption coefficient of the enol form at 340 nm, $\varepsilon_e=1.78\times10^4$, were also obtained. The enol fractions of TA in alcohol-saturated water were estimated by the ratio of the apparent absorption coefficient to ε_e, they are shown in Table 2.

Discussion

The Tautomerization of TA in Aqueous and Alcoholic Phases. As is shown in Table 2, the enol fractions of TA in water-saturated alcohols seem to increase with a decrease in the solvent polarity. This tendency was also noted in the case of TTA, as was reported in a previous paper,[2] in which the solvent effect was discussed in terms of electrostatic theory and the regular solution theory. The electrostatic theory proposes that an equilibrium constant depends on the dielectric constant, ε, of the solvent through the terms of $(\varepsilon-1)/V_0(2\varepsilon+1)$, in which V_0 is the molar volume of the solvent.[10] On the other hand, the regular solution theory relates an equilibrium constant to the solubility parameter of the solvent.[11] The dependencies of the keto-enol equilibrium constant on the dielectric factor

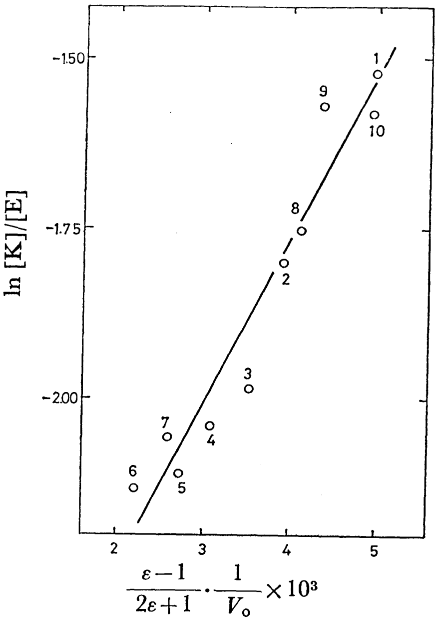

Fig. 1. Correlation between the keto-enol equilibrium constant and the solvent quantity $(\varepsilon-1)/V_0(2\varepsilon+1)$. The numbers correspond to those in Table 2.

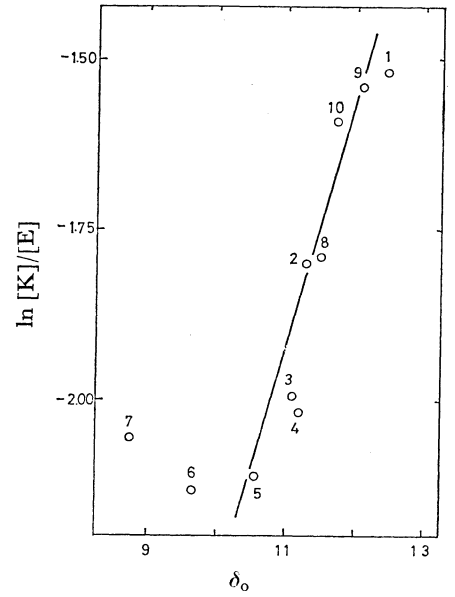

Fig. 2. Correlation between the keto-enol equilibrium constant and the solubility parameter of alcohol. The numbers correspond to those in Table 2.

Table 3. The partition coefficients of the enol (P_E) and the keto (P_K) forms of TA and those of the enol (P_E) and the hydrate (P_H) forms of TTA at 25 °C

No.	Solvent	TA P_E	TA P_K	TTA P_E	TTA P_H
1	1-Butanol	143	7.06	961	19.4
2	1-Pentanol	300	8.75	1820	23.8
3	1-Hexanol	347	7.83	1860	19.1
4	1-Heptanol	357	7.32	1870	17.4
5	1-Octanol	325	6.19	1640	11.7
6	2-Ethyl-1-hexanol	293	5.49	1420	8.5
7	2-Octanol	333	6.74	1780	13.6
8	3-Methyl-1-butanol	246	7.50	1480	19.7
9	Cyclohexanol	256	10.11	1160	27.4
10	2-Methyl-1-propanol	128	5.88	812	16.3
11	Benzyl alcohol	—	—	1950	36.3

$(\varepsilon-1)/V_o(2\varepsilon+1)$ and on the solubility parameter of alcoholic phase are shown in Figs. 1 and 2 respectively. In both figures, satisfactory relationships are obtained. The positive sign of the slopes of the figures seems to be related to the more dipolar character of the keto form than the enol form. The enolization rate constant of TA is about $2.5\times10^{-2}\,s^{-1}$ for most alcohols, and no significant solvent dependency is observed, different from the enolization rate of the hemiacetal form of TTA.[2]

The Partition Coefficient of Each Species of TA and TTA. The TTA in the alcohol phase is in the enol, the hydrate and the hemiacetal forms, while in the aqueous phase, it is in the enol and hydrate forms. On the other hand, TA is thought to be in the enol and the keto forms in both phases. Consequently, the partition schemes of the two diketones are considerably different and can be drawn as follows:

$$\begin{array}{lcclcl} \text{TA;} & K\rightleftharpoons E & \quad \text{TTA;} & H\rightleftharpoons E\rightleftharpoons A & \quad \text{org.} & \\ & \upharpoonleft\!\downharpoonright \;\; \upharpoonleft\!\downharpoonright & & \upharpoonleft\!\downharpoonright \;\; \upharpoonleft\!\downharpoonright & & (2) \\ & K\rightleftharpoons E & & H\rightleftharpoons E & \quad \text{aq} & \end{array}$$

Here E, K, H, and A refer to the enol, keto, hydrate, and hemiacetal forms respectively. On the basis of the above schemes, the partition coefficients of the enol (P_E), keto (P_K), and hydrate (P_H) forms can be represented by

$$P_E = \frac{f_o}{f}P,\quad P_K = \frac{1-f_o}{1-f}P,\quad P_H = \frac{g_o}{1-f}P, \tag{3}$$

where f, f_o, and g_o refer to the enol fraction in the aqueous phase, the enol fraction in the organic phase, and the hydrate fraction in the organic phase respectively, and where P refers to the apparent partition coefficient. The values of P_E and P_K for TA and those of P_E and P_H for TTA are shown in Table 3. The order of the magnitude of the partition coefficient is: $P_E(\text{TTA}) > P_E(\text{TA}) > P_H(\text{TTA}) > P_K(\text{TA})$.

For the solvent effect of alcohol on the partition coefficients, it is difficult to draw out any regularity instantaneously. In an earlier work, one of the present authors demonstrated the utility of the regular solution theory for an interpretation of the solvent effect in alcohol/water systems.[3] Hence, we employed this treatment for the partition coefficient of each species of TA and TTA. On a certain species, i, the following equation is derived from the regular solution approximation for the present partition system:[3]

$$\frac{\ln P_i}{\delta_a-\delta_o} = \frac{V_i}{RT}\left\{\delta_o+\delta_a-2\delta_i+\frac{RT}{\delta_a-\delta_o}\left(\frac{1}{V_o}-\frac{1}{V_a}\right)\right\}, \tag{4}$$

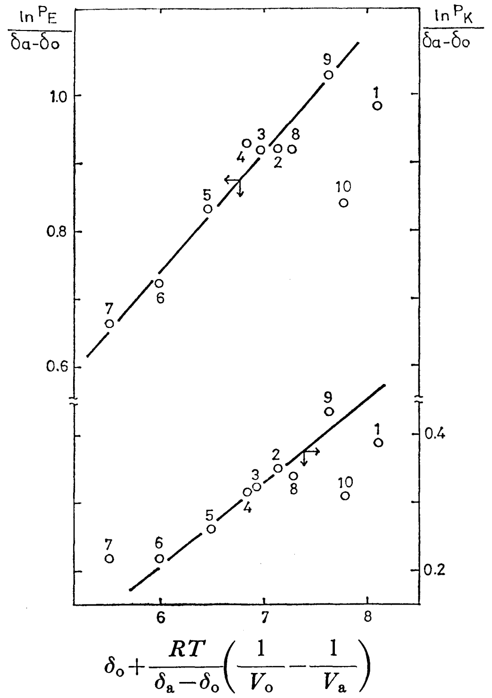

Fig. 3. Correlation between the partition coefficients of the keto (P_K) and the enol (P_E) forms of TA and the solubility parameter of alcoholic phase. The numbers correspond to those in Table 3.

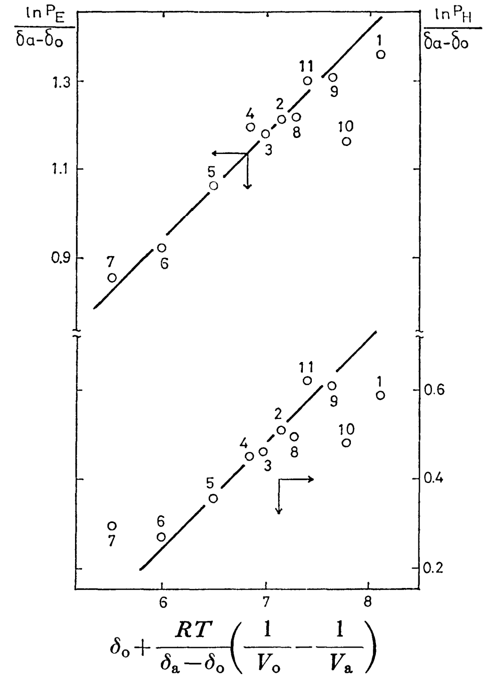

Fig. 4. Correlations between the partition coefficients of the enol (P_E) and the hydrate (P_H) forms of TTA and the solubility parameter of alcoholic phase. The numbers correspond to those in Table 3.

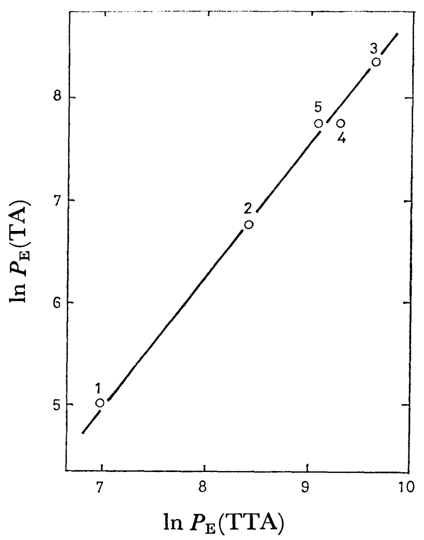

Fig. 5. Correlation between ln P_E(TA) and ln P_E(TTA). The numbers correspond to those in Table 3.

where P is the partition coefficient; V, the molar volume and δ, solubility parameter, and where the subscripts i, and o refer to the solute i, the aqueous phase, and the organic phase respectively. Figures 3 and 4 show the plots based on the above relation. A satisfactory correlation is obtained in each case.

Comparison of the Partition Coefficients of TA with Those of TTA. As is shown in Table 3, P_E(TTA) is larger than P_E(TA). In addition, a linear correlation appears between ln P_E(TTA) and ln P_E(TA), as is shown in Fig. 5. This relationship may be understood from the point of view of the linear free-energy relationship. The partition coefficient is related to a transfer free energy, ΔG, from the aqueous phase to the organic phase by the following equation:

$$-RT \ln P = \Delta G. \tag{5}$$

Assuming an additivity of group-transfer free energy,[12] the ΔG of the enol forms of TA and TTA can be represented as

$$\begin{aligned} \Delta G(\mathrm{TA}) &= \Delta G(\mathrm{CH_3}) + \Delta G(\mathrm{R}), \\ \Delta G(\mathrm{TTA}) &= \Delta G(\mathrm{CF_3}) + \Delta G(\mathrm{R}), \end{aligned} \tag{6}$$

where R refers to the group of $-\mathrm{COCHCOC_4H_3S}$. Hence, the partition coefficients are

$$\begin{aligned} \ln P(\mathrm{TA}) &= \ln P(\mathrm{CH_3}) + \ln P(\mathrm{R}), \\ \ln P(\mathrm{TTA}) &= \ln P(\mathrm{CF_3}) + \ln P(\mathrm{R}). \end{aligned} \tag{7}$$

Equation 7 provides

$$\ln P(\mathrm{TA}) - \ln P(\mathrm{TTA}) = \ln P(\mathrm{CH_3}) - \ln P(\mathrm{CF_3}). \tag{8}$$

Equation 8 and the intercept in Fig. 5 allow the estimation of $\Delta G(\mathrm{CH_3}) - \Delta G(\mathrm{CF_3})$ as 1.4 kcal/mol. Similar analysis has been performed for the previous results in apolar solvent/water systems;[13] the free energy difference was estimated as 2.1 kcal/mol. The larger value for the apolar system corresponds to a general tendency for a fluorocompound to show a high solubility in an apolar solvent.

Finally, let us discuss the effect of the solution species on the apparent partition coefficient. On the basis of the scheme of Eq. 2, the apparent partition coefficient of TA can be represented by

$$\begin{aligned} P(\mathrm{TA}) &= \frac{[\mathrm{E}]_o + [\mathrm{K}]_o}{[\mathrm{E}] + [\mathrm{K}]} = \frac{[\mathrm{E}]_o}{[\mathrm{E}] + [\mathrm{K}]} + \frac{[\mathrm{K}]_o}{[\mathrm{E}] + [\mathrm{K}]} \\ &= P'(\mathrm{E}) + P'(\mathrm{K}). \end{aligned} \tag{9}$$

Since the ratio of $P'(\mathrm{K})/P'(\mathrm{E})$, which is identical with the keto-enol equilibrium constant in the alcoholic phase, is much smaller than unity, it may be concluded that the magnitude of P_E(TA) is primarily governed by that of P'(E). On the other hand, the apparent partition coefficient of TTA can be separated into the following terms:

$$\begin{aligned} P(\mathrm{TTA}) &= \frac{[\mathrm{E}]_o}{[\mathrm{E}] + [\mathrm{H}]} + \frac{[\mathrm{H}]_o}{[\mathrm{E}] + [\mathrm{H}]} + \frac{[\mathrm{A}]_o}{[\mathrm{E}] + [\mathrm{H}]} \\ &= P'(\mathrm{E}) + P'(\mathrm{H}) + P'(\mathrm{A}). \end{aligned} \tag{10}$$

The relative magnitude among P'(E), P'(H), and P'(A) is equal to that among $[\mathrm{E}]_o$, $[\mathrm{H}]_o$, and $[\mathrm{A}]_o$ (*cf.* Table 1 in the preceding paper).[2] Hence, we found that the contribution of P'(H), or approximately $P_H = [\mathrm{H}]_o/[\mathrm{H}]$, to P(TTA) is the most important because the major species of TTA in the alcohol phase is the hydrate form in most cases. However, in 2-ethyl-1-hexanol P'(A) plays the most important role because of the high fraction (50%) of the hemiacetal form in the solvent. In conclusion, we can state that P(TA) is governed by P'(E), and P(TTA) by P_H and P'(A). Although P_E(TTA) is larger than P_E(TA), because of the small contribution of P_E(TTA) P(TA) is larger than P(TTA).

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