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Base-Catalyzed Ester Hydrolysis in a Toluene-Water System

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Abstract: Hydrolysis reactions of aromatic esters in a toluene phase with sodium hydroxide in an aqueous phase have been studied in a stationary system. Relative reactivities of various esters are remarkably different from those obtained in a homogeneous system. For example, the hydrolysis rates for three isomers of dimethyl phthalates are in the order of ortho > para > meta isomer, whereas in 56% aqueous acetone the order is para > meta > ortho isomer. The diffusion rate of esters through the bulk liquid was found to be the most important factor which controlled the heterogeneous reaction rate of the present system. The effects of the following variables were also determined: interfacial area, reaction volume, temperature, degree of stirring, and presence of surface active agent.

Because of slow reaction velocities, organic reactions between two substances located in different phases of a mixture have not been investigated extensively. Recently, however, two interesting developments have been made in this field. One of them is a micelle catalyzed reaction system,¹ and the other one involves reactions with so-called phase-transfer catalysts.² Except for these systems, only a few studies have been reported. Bell³ investigated the oxidation of benzoyl-*o*-toluidine in benzene with a neutral aqueous solution of potassium permanganate. Several decades after this pioneer work, Menger⁴ successfully established a methodology of interfacial reactions. He examined an imidazole-catalyzed hydrolysis of *p*-nitrophenyl laurate at a heptane-water boundary. He found that the reaction is an interfacial one and that the reaction profile is different from that of a homogeneous reaction. Judging from the very low activation energy (nearly 0), he concluded that the migration of reactants to the interface must be at least partially rate determining. Thus, in order to clarify the property of the binary phase reaction system, it is desirable to accumulate data with respect to the mass transfer phenomena. Although there are several studies on this subject from a chemical engineering point of view,⁵⁻⁷ no diffusion study with simultaneous organic reaction has been reported. The present study was undertaken to clarify the contribution of diffusion process to the reaction rate in a binary phase system. Base-catalyzed hydrolysis reactions of various aromatic esters were utilized for this purpose. Corresponding homogeneous reactions have been already investigated intensively in this connection.⁸⁻¹⁰ In addition, this system has the advantage that a variety of esters are readily available. In the present study, three structural isomers of dimethyl phthalates, three phthalates with different alkyl groups, and several benzoates with

different substituents have been used as reactants in a toluene-water system.

Experimental Section

Materials. Most of the starting materials were guaranteed reagents and used without a further purification. Methyl *p*-anisate was not standardized, and it was used after recrystallizations. Guaranteed reagent toluene and distilled water were used as solvents for ester and NaOH, respectively.

Hydrolysis Reaction. The reaction was carried out under the following conditions unless otherwise stated. An aqueous solution of NaOH (0.186 N, 20 mL) was placed in a cylindrical vessel of 20 cm² in cross section and of 120 mL in capacity. Then a toluene solution of ester (0.050 M, 20 mL) was added carefully. The vessel was placed in a thermostated bath. Hydrolysis was usually carried out without stirring. After a required time, the content of remaining hydroxide ion in an aqueous phase was determined by titrating with a standard HCl solution. The ester content in toluene was determined by using GLPC with a 2-m PEGS column. The rate of ester disappearance agreed well with that of NaOH consumption in water. In cases of the hydrolysis of dialkyl phthalate, no half-ester and acid were found at all in toluene. The initial hydrolysis product, the half-ester, might be extracted into the basic water where fast homogeneous hydrolysis takes place.

Diffusion of Ester. The diffusion rate of ester from a toluene phase to an aqueous phase was determined in the absence of NaOH. A toluene solution of ester (0.050 M, 20 mL) was placed over pure water (20 mL). The concentration of ester transferred into water was determined spectrophotometrically after different intervals of time, ranging from 5 min to 90 h. Spectral measurements were made by using 1-cm silica cells in a Cary 14 spectrophotometer. The absorption coefficients for most esters have not been reported yet, and we determined them in 50% aqueous ethyl alcohol. The maximum wavelengths are listed below, together with log ϵ in parentheses: DMP, 283 (3.1), 276 (3.2), 228 (4.0); DMIP, 289 (3.0), 282 (3.0), 230 (4.1);

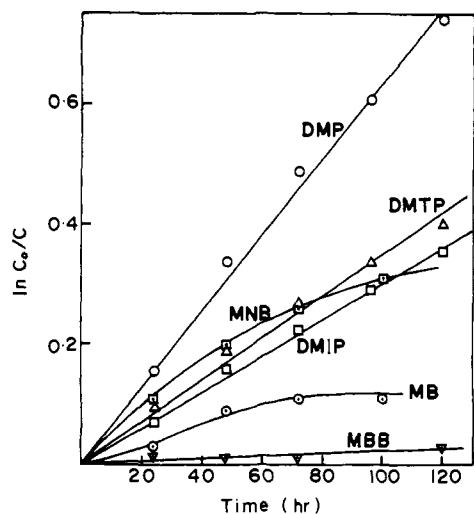


Figure 1. Pseudo-first-order rate plots for the base hydrolysis in a binary phase system. Reaction conditions are as follows: NaOH in water, 0.186 N, 20 mL; ester in toluene, 0.050 M, 20 mL; interfacial area, 20 cm²; temperature, 25 °C.

Table I. Hydrolysis Rate Constants at 25 °C

Ester	Category	10 ⁶ k, ^a s ⁻¹	10 ³ k _{homo} , M ⁻¹ s ⁻¹
Dimethyl phthalate (DMP)	A	1.77	12.6 ^b
Dimethyl isophthalate (DMIP)	A	0.85	50 ^b
Dimethyl terephthalate (DMTP)	A	0.99	112 ^b
Diethyl phthalate (DEP)	A	0.12	
Di- <i>n</i> -butyl phthalate (DBP)	C	<0.03	
Methyl benzoate (MB)	B	0.28	9.0 ^c
Ethyl benzoate (EB)	C	<0.03	2.9 ^d
<i>n</i> -Propyl benzoate (PB)	C	<0.03	1.9 ^d
Methyl <i>p</i> -nitrobenzoate (MNB)	B	1.24	626 ^c
Methyl <i>p</i> -methylbenzoate (MMB)	B	0.08	3.1 ^b
Methyl <i>p</i> -anisate (MA)	B	0.24	2.2 ^c
Methyl <i>p</i> -bromobenzoate (MBB)	C	<0.03	27.7 ^e

^a The rate constants for ester of category B and C were estimated from the rate in the initial stage. ^b Data from reference 10. ^c Data from reference 8. ^d Data from reference 9. ^e Estimated by the Hammett relationship; ρ and σ values from reference 11.

DMTP, 295 (3.2), 285 (3.3), 240 (4.3); DEP, 283 (3.1), 276 (3.1), 228 (3.9); DBP, 283 (3.1), 276 (3.2), 228 (4.0); MB, 282 (2.9), 274 (3.1), 231 (4.1); MNB, 261 (4.1); MMB, 282 (2.8), 272 (3.0), 241 (4.2); MA, 258 nm (4.2). The full names for the above abbreviations are listed in Table I. These values were used for analyses of ester in 100% water without any corrections for solvent effect.

Solubility of Ester in Water. The solubility of ester in pure water was roughly determined at 25 °C without a toluene phase in order to check the affinity of ester with water. A large excess of ester was put in water, and the concentrations of ester dissolved in water were analyzed spectrometrically after 3, 13, and 65 days. It was found that an aqueous solution became saturated with ester at least after 13 days.

Surface Excess Quantities. In order to estimate a surface excess quantity of ester, an interfacial tension between a toluene solution of ester and pure water was measured immediately after the contact at 25 °C according to the Wilhelmy method. Measurements were made for the ester concentration from 0.030 to 0.200 M. An adsorption concentration, Γ mol cm⁻², was determined at $C = 0.050$ M by Gibbs' equation

$$\Gamma = (-1/RT)(d\gamma/d \ln C)$$

where γ is an interfacial tension, erg cm⁻², and R is the gas constant. From the value of Γ , we can calculate the surface area covered by ester, assuming the cross section for the ester molecule.

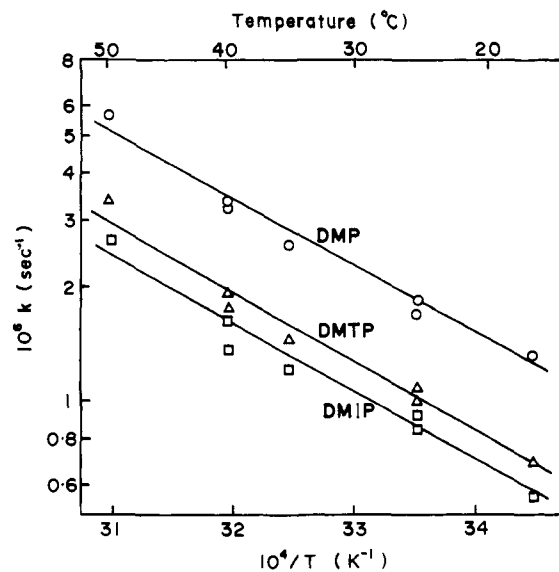


Figure 2. Arrhenius plots for the base hydrolysis of dimethyl phthalates in a binary system. Reaction conditions are the same as in Figure 1 except the temperature.

Table II. The Effect of Reactor Size and Interfacial Area at 40 °C

V , cm ³	S , cm ²	10 ⁶ kV/S, cm s ⁻¹		
		DMP	DMIP	DMTP
20	20	3.2	1.4	1.9
40	20	3.4	1.7	2.1
20	28	3.4	1.5	1.9

^a $V = V(\text{toluene}) = V(\text{water})$.

Results

Hydrolysis Rate. First-order rate plots for hydrolyses of several esters are illustrated in Figure 1. Plots for three dimethyl phthalates give straight lines, showing the pseudo-first-order nature with respect to the ester concentration, C . The initial concentration of ester is expressed as C_0 . The linear portion of the plots extended up to a conversion of 80%. We term these esters as belonging to group A. On the other hand, the slope of plots decreases with time in the case of methyl benzoate or methyl *p*-nitrobenzoate. Most esters of substituted benzoic acids belong to this category B. The hydrolysis of methyl *p*-bromobenzoate is very slow and the conversion is less than 5% even after 5 days. The accurate rate constant cannot be obtained in this case. Ethyl benzoate, *n*-propyl benzoate, and di-*n*-butyl phthalate also fall into this group C. We can divide all esters into these three groups. The rate constants are summarized in Table I together with corresponding homogeneous rate constants reported in literatures. The heterogeneous rate constants for categories B and C are estimated from the rate in the very initial stage.

The hydrolysis rates for three dimethyl phthalates were determined in detail as a function of several reaction variables. The apparent rate constant k is nearly independent of the initial concentration of hydroxide ion in the range from 0.12 to 0.23 N. The effect of the volume of both solution V and the interfacial area S are summarized in Table II. The value of kV/S remains constant in every case.

Figure 2 shows the temperature dependences of the observed rate constants. Apparent activation energies are nearly equal for three esters, and they are about ~ 8 to ~ 9 kcal/mol.

Table III shows the effect of stirring on the observed rate. Stirring was accomplished in two different manners. One series of reactions was carried out with mild stirring, which maintained a constant apparent area (20 cm²). Two stirrers agitated

Table III. The Acceleration Effect by Stirring at 25 °C

Stirring condition	$10^6 k, s^{-1}$		
	DMP	DMIP	DMTP
No ($S = 20 \text{ cm}^2$)	1.77	0.85	0.99
Mild ($S \approx 20 \text{ cm}^2$)	3.7	2.0	2.4
Rigorous ($S \gg 20 \text{ cm}^2$)	62	30	44

Table IV. The Effect of Surface Active Agent at 25 °C

NaDodSO ₄ /ester	Conversion after 48 h, %		
	DMP	DMIP	DMTP
0	29	15	17
0.0066	28	15	15
0.0132	25	14	15

Table V. Diffusion of Ester into Water at 25 °C

Ester	Initial diffusion rate, $10^6 \text{ mM s}^{-1} \text{ cm}^{-2}$	Distribution coefficient, $C_{\text{H}_2\text{O}}/C_{\text{C}_7\text{H}_8}$	Solubility in water, mM
DMP	4.2	0.0060	23.3
DMIP	1.3	0.0015	1.5
DMTP	0.6	0.0010	0.17
DEP	0.4	0.0006	4.6
DBP	0.05	0.0002	0.09
MB	1.0	0.0020	16.0
EB			5.0
PB			1.5
MNB	9.8	0.0179	2.3
MMB	0.39	0.0011	8.6
MA	2.0	0.0085	5.4

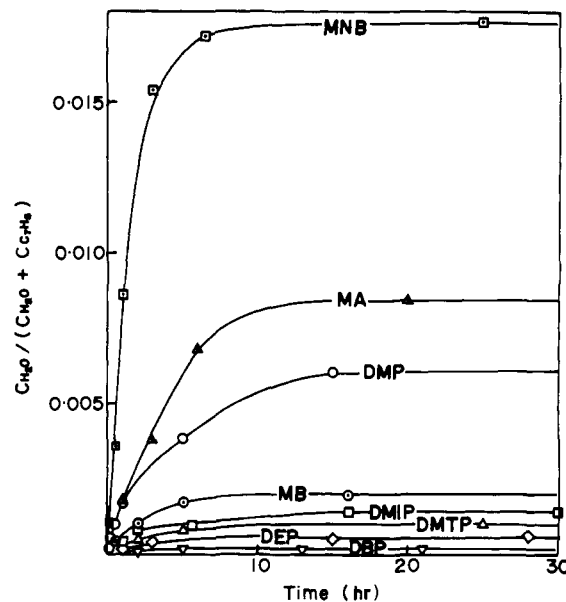
the two phases independently. Another method of stirring was so rigorous that the system formed an emulsion. The interfacial area increased greatly in this case. In proportion to the degree of agitation, the apparent rate constant increases remarkably. It should be noted that the relative reactivities among three isomers are not different from that observed in an immovable system (DMP:DMIP:DMTP \approx 1:0.5:0.6).

Addition of a small amount of a surface active agent sometimes influences interfacial phenomena remarkably.^{2,4} In the present case, the addition of sodium dodecyl sulfate (NaDodSO₄) hardly retarded the hydrolysis. Table IV indicates the small decrease of conversion after 48 h.

Diffusion Rate. Figure 3 shows the diffusion rate profile for esters from a toluene phase to an aqueous phase in the absence of NaOH. The concentration in water, $C_{\text{H}_2\text{O}}$, increases with time and finally reaches the equilibrium value. The distribution equilibrium is attained at around 10 h in most cases. Generally speaking, the larger the final concentration in water, the larger the initial diffusion rate. As will be discussed later, the initial diffusion rate is important in order to check the correlation between hydrolysis rate and diffusion rate. These properties are listed in Table V together with the solubility of ester in water. There is no direct relationship between the solubility and the diffusion rate nor distribution coefficient. The diffusion of hydroxide ion from water to toluene was undetectable.

Discussion

The difference between the homogeneous hydrolysis and the heterogeneous hydrolysis will be discussed in this section. First, the overall rates for both cases are roughly compared with each other. The half-life period observed for DMP at 25 °C may be used as an indication of reactivity. It is about 0.2, 3, and 100 h for the homogeneous, heterogeneous with rigorous stirring, and heterogeneous hydrolysis without stirring, respectively. From a practical point of view, the low heterogeneous rate is disadvantageous. The above data, however, indicate that the

**Figure 3.** Diffusion of ester from toluene to water. Diffusion conditions are as follows: ester in toluene, 0.050 M, 20 mL; water, 20 mL; interfacial area, 20 cm²; temperature, 25 °C.

difference can be minimized to a factor of about $1/10$ if a sufficient agitation is provided. The system with stirring still shows the characteristic property for the heterogeneous hydrolysis as indicated in Table III.

The heterogeneous rate constant, k , is compared with the homogeneous one, k_{homo} , in Table I. The relative reactivity among a certain homologous series is quite different in the two systems. For example, the ratio of reactivity among ortho, meta, and para isomers of dimethyl phthalate is 1:4.0:9.3 in a homogeneous system, whereas the ratio in a heterogeneous system is 1:0.48:0.56. The effect of the length of alkyl group, R, may be compared in *o*-C₆H₄(COOR)₂ and C₆H₅COOR series. The relative ratio in a homogeneous system is as follows; CH₃:C₂H₅:*n*-C₃H₇:*n*-C₄H₉ = 1:0.32:0.21:0.19. The heterogeneous rate constant decreases more rapidly with an increase in the length of the alkyl group. In the case of *p*-XC₆H₄COOCH₃, the reactivity ratio is also completely different in the two systems, where X is the substituent group in a benzene ring. It is noteworthy that nitro and bromo groups do not have such a large enhancing effect as observed in a homogeneous system. Thus, it can be concluded that the heterogeneous reaction mechanism is quite different from the homogeneous one.

In order to clarify the mechanism of heterogeneous hydrolysis, it is essential to investigate the diffusion rate of ester in toluene, across the interface, and in water. The distribution coefficient is very small in every case. Only 6×10^{-3} mmol of DMP is present in water at equilibrium, while the rest of ester, 994×10^{-3} mmol, is in toluene. This small distribution coefficient, however, does not exclude the possibility of homogeneous reaction in an aqueous phase. The ester may diffuse into water, react homogeneously, thereby driving the distribution equilibrium toward the aqueous phase and causing more ester to diffuse into water. In other words, the toluene phase may act as a "pool" which supplies ester as it is consumed in water. Since the homogeneous hydrolysis in water might be much faster than the diffusion process, the concentration of ester in water during the hydrolysis reaction can be assumed to be negligible. Thus, it is important to determine the diffusion rate immediately after the contact of two phases (toluene with ester and water without NaOH), when there is no ester in water. Although the accuracy of the measurement at this stage is not

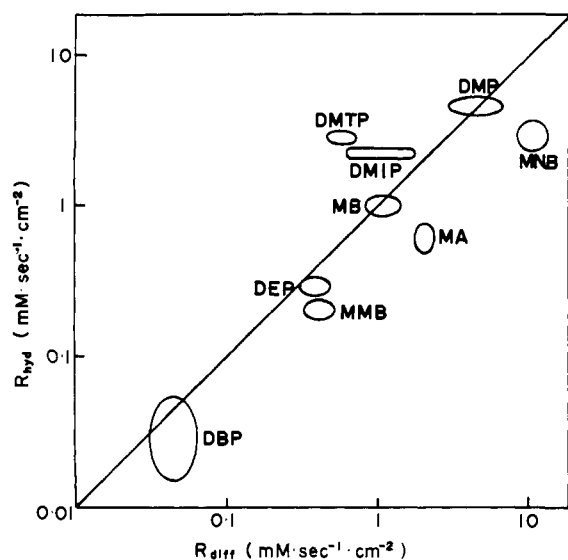


Figure 4. Relationship between hydrolysis rate, R_{hyd} , and initial diffusion rate, R_{diff} .

so good, the initial diffusion rates are determined and shown in Table V. When the hydrolysis rate is plotted against this initial diffusion rate, we can obtain a fairly good correlation like Figure 4. The numbers on both axes indicate the ester concentration hydrolyzed or diffused in a unit time across a unit interfacial area. The size of the circle expresses the range of experimental error.

The low activation energy also suggests a substantial contribution of mass transport process. The activation parameters for dimethyl phthalates have not been reported in a homogeneous system. The activation energies for the base hydrolysis of diethyl esters were known to range from 13.0 to 14.5 kcal/mol.^{12,13} Since the effect of the alkyl group on the activation energy was not so large,^{8,9} we can expect that the value for dimethyl esters may be around about 13 to ~14 kcal/mol. The observed value for the present system is smaller than this by 5 kcal/mol. This difference must be partly due to the contribution of a diffusion process.

The experiment with a mild stirring (Table III) offers an additional evidence for the importance of diffusion process. The rate increased by accelerating the mass transfer in liquid phases. In this case the interfacial area is almost the same as the case without stirring. This fact may suggest that the diffusional resistance in the liquid phase is larger than that in the interfacial region. This is in accordance with a general observation for a clean surface.⁶ A small effect of surface active

agent (Table IV) is also reported for a stationary binary phase system.⁷ The surface active agent adsorbed at the interface may increase the interfacial resistance, which is, however, still smaller than the bulk resistances.

One of the interesting properties of the binary phase reaction is reaction specificity owing to the orientation of reactant at the interface. Some of the present results can be explained by such a orientation model. For example, a longer alkyl group has a larger affinity with an organic phase, and then its ester group might orientate toward a toluene phase. Such orientation may reduce the hydrolysis rate as is observed here. However, the lower reactivity for ester with a longer alkyl group can also be explained by the lower diffusion rate as shown in Table V. Considering the low surface coverage, we conclude that the orientation effect is less important in the present case. The surface area covered by ester was calculated from the surface excess quantity. The coverage was less than 30% for all esters, even if the maximum cross section was assumed for the ester molecule. Therefore, the vertical stacking of the esters which may induce the orientation effect is not plausible.

In conclusion, we determined the hydrolysis rates of various esters in a binary phase system and revealed the remarkable difference from the homogeneous system. If one can choose a suitable system, a reaction selectivity can be dramatically changed by using such a system. Further, this system has an advantage in separating the product, if the product transfers from an original phase to another phase as observed in the present system. The rate-controlling step was found to be a diffusional process for ester through a bulk liquid. The diffusion process undoubtedly is one of the most important step in such a multiphase reaction system. However, it has been underestimated or sometimes neglected in mechanistic interpretations. The present study shows the direct evidence for the relationship between reaction rate and diffusion rate.

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