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Chemistry at Hydrocarbon-Water Phase Boundaries. Biphase Hydrolysis of Organic Halides[1)]

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The kinetics of the biphase hydrolysis of 1-bromoadamantane and 1-phenylethyl chloride in toluene–water and decane–water systems have been investigated. Evidence has been obtained for the first examples of rate-limiting S_N1 reactions occurring at a hydrocarbon–water phase boundary, based on (1) the influence of temperature, mild stirring, interfacial area, reaction volume, and pH on the observed first-order rate constants, (2) comparison of absolute rates and activation energies with analogous homogeneous hydrolysis reactions, (3) the temperature dependence of the initial rate of diffusion of tritiated 1-methoxyadamantane from toluene into water, and (4) the initial rate of diffusion of ^3H_2O into toluene.

Hydrocarbon–water interfaces are found in many important bioorganic and synthetic organic systems.[3–6)] Despite this fact, their precise structure and overall chemical significance have not been well characterized.[7–9)] Several years ago, Menger reported a detailed study of the biphase hydrolysis of *p*-nitrophenyl laurate catalyzed by imidazole in a heptane–water system.[3–10)] Compelling evidence was presented which supported an interfacial reaction. Based on a very low apparent activation energy, it was also concluded that mass transport of the reactants to the interface makes a significant contribution to the observed kinetics. Remarkably few studies have since appeared which consider organic reactions at liquid–liquid interfaces.[11,12)]

In the present paper we report the results of a kinetic study of the biphase hydrolysis of 1-bromoadamantane and 1-phenylethyl chloride carried out in toluene–water and decane–water systems.[13)] Our data provide strong evidence for what we believe are the first examples of rate-limiting S_N1 reactions at a hydrocarbon–water liquid–liquid phase boundary. As such, they represent the simplest interfacial organic reactions investigated to date.

Results

Kinetics of the Hydrolysis. Biphase hydrolysis of 1-bromoadamantane and 1-phenylethyl chloride were carried out using culture tubes as reaction vessels. Rates were monitored by following the disappearance of the organic halide from the organic phase. For 1-bromoadamantane, hydrolysis rates were identical to those determined by following the appearance of 1-hydroxyadamantane in the organic phase (material balance was >95%). Partitioning of 1-phenylethyl alcohol into water was too high to permit the simultaneous analysis of reactant and product. In all cases, clean first-order kinetics was maintained over at least three half-lives. A typical first-order plot is shown in Fig. 1.

Table 1 shows the influence of mild stirring on observed first-order rate constants, k_{obsd}. For both organic halides, stirred reactions were similar in rate to unstirred processes. 1-Phenylethyl chloride hydrolized more than one order of magnititude faster than 1-bromoadamantane, and was carried out under mild stirring conditions in all subsequent experiments.

In order to evaluate the dependence of k_{obsd} on the hydrocarbon–water interfacial area, S, as well as the volumes of the aqueous (V_{aq}) and organic (V_{org}) phases used, biphase hydrolyses were carried out in culture tubes of varying dimensions. Results for 1-phenylethyl chloride, reported in Table 2, show that a normalized rate constant, k_0 (where $k_0=k_{obsd}\ V_{org}/S$), is constant over a wide range of experimental

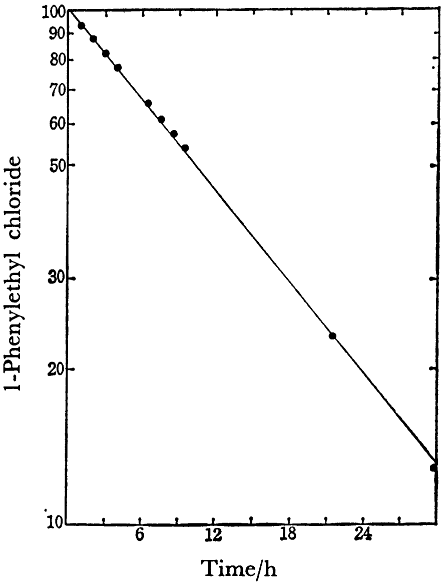

Fig. 1. Plot of percent of 1-phenylethyl chloride in the organic phase as a function of time for reaction of 4 ml of 0.01 M 1-phenylethyl chloride in toluene with 10 ml of 0.1 M aqueous sodium hydroxide at 90 °C, carried out as a mildly stirred process ($S\approx4.16$ cm^2).

Table 1. Effect of stirring on K_{obsd}[a)]

Organic halides	Stirring speed / rpm	Interfacial area / cm^2	$10^5 k_{obsd}$ / s^{-1}
1-Phenylethyl chloride	0	4.16	1.50
	70	≈4.16	1.90
1-Bromoadamantane	0	4.16	0.10
	70	≈4.16	0.16

a) Reaction of 4.0 ml of 0.01 M organic halide in toluene with 10 ml of 0.1 M aqueous sodium hydroxide in a 50 ml culture tube at 90 °C.

conditions and is independent of the volume of the aqueous phase.[14] Exactly analogous results have been obtained for 1-bromoadamantane.[13]

Data presented in Table 3 show the influence of temperature, hydroxide ion concentration, added sodium bromide and the nature of the hydrocarbon solvent on the biphase hydrolysis of 1-bromoadamantane. The apparent activation energy E_a for toluene–water and decane–water systems was 23.1 and 19.2 kcal mol^{-1} respectively. These values lie in the range found for comparable homogeneous hydrolysis (Table 4).[15] Values of k_0 at 100 °C using pure water, 0.1 M NaOH, or 1.0 M NaBr as the aqueous phase were very similar. When decane was used as the organic solvent in place of toluene, higher rates were observed. Similar results have been obtained for 1-phenylethyl chloride (Tables 4 and 5).

Diffusion of ^3H_2O into Toluene. The initial rate of diffusion of tritiated water from 0.1 M aqueous sodium hydroxide into dry toluene was measured at 70 °C and found to be 1.3×10^{-6} M s^{-1}; V_{org} and S used in this experiment were 4 ml and 1.26 cm^2, respectively.

TABLE 2. INFLUENCE OF V_{org}, V_{aq}, AND S ON k_0 FOR 1-PHENYLETHYL CHLORIDE[a]

V_{org}	V_{aq}	S	$10^3 k_0$
cm^3	cm^3	cm^2	min^{-1} cm
1	2	1.26	1.1
2	5	2.83	1.2
4[b]	10	4.16	1.1
10	40	9.08	1.2

a) Reaction of 0.05 M 1-phenylethyl chloride in toluene with 0.1 M aqueous sodium hydroxide at 90°C, using mild stirring; $k_0=k_{obsd}V_{org}/S$. b) Organic halide concentration used was 0.01 M.

Discussion

Two fundamental questions which are central to this investigation are (1) what is the rate-controlling process and (2) where does reaction occur. In principle the rate-limiting step could be (a) diffusion of the organic halide through the bulk organic phase or through the aqueous–organic phase boundary, (b) diffusion of water into the bulk organic phase, (c) chemical reaction, or (d) a combination of (a)—(c). Based on the hydrolysis data, several lines of evidence point to chemical reaction as being the rate-determining step. First, the apparent activation energy observed for both organic halides is high and is similar to that measured for comparable homogeneous reactions. These values contrast sharply with activation energies found for diffusion in most liquids (3—5 kcal mol^{-1}).[16] Furthermore, the rate of diffusion of tritiated 1-methoxyadamantane from toluene into 0.1 M aqueous sodium hydroxide has previously been shown to be only slightly sensitive to temperature ($E_a \leq 3.5$ kcal mol^{-1}).[13] This shows that the diffusional resistance for organic substrates, similar to those investigated in the present work, through the interface is low, as expected. Second, mild stirring has a relatively small effect on the biphase hydrolysis rates. This result further argues against diffusion as being an important contributor to the observed kinetics. Third, if water transport were rate limiting, the observed hydrolyses should obey zero order kinetics; also the rate for both organic halides would be equal to the diffusion rate of water into toluene. Experimentally, however, clean first-order kinetics are followed and the initial diffusion rate of water into toluene (70 °C) and the initial reaction velocity for 1-phenylethyl chloride (70 °C) and 1-bromoadamantane

TABLE 3. BIPHASE HYDROLYSIS OF 1-BROMOADAMANTANE

Organic solvent	Aqueous solution	V_{org}	V_{aq}	S	Temp	$10^7 k_0$[b]	E_a
		cm^3	cm^3	cm^2	°C	s^{-1} cm	kcal mol^{-1}
Toluene	0.1 M NaOH	1	1	1.26	75	2.03	23.07
		1	1	1.26	80	3.08	
		1	1	1.26	85	6.42	
		1	2	1.26	90	8.25	
		1	1	1.26	95	9.76	
		1	2	1.26	100	22.78	
		1	1	1.26	105	26.98	
		1	1	1.26	110	36.75	
		1	2	1.26	120	106.03	
Toluene	pure water	1	2	1.26	100	21.27	
Toluene	1.0 M NaBr	1	2	1.26	100	18.89	
Decane	0.1 M NaOH	1	10	4.16	70	4.18[c]	19.24
		1	10	4.16	80	9.09[c]	
		1	10	4.16	90	18.12[c]	
		1	1	1.26	100	42.06	
		1	1	1.26	110	77.06	
		1	1	1.26	120	144.70	

a) When the volume of the aqueous phase was >1 ml, material balance was >95%. b) $k_0=k_{obsd}V_{org}/S$. c) Mild stirring was used.

Table 4. Rate constants and activation energy for hydrolysis of organic halides in aqueous dioxane

Organic halide	Solvent, Dioxane in water(V/V)	Temp °C	$10^6 k_{\mathrm{obsd}}$ s^{-1}	E_a kcal mol^{-1}
1-Phenylethyl[a] chloride	90	70	0.31	19.94
		80	0.81	
		90	1.54	
	80	70	4.57	25.32
		75	7.72	
		80	13.00	
	70	65	20.44	22.94
		75	55.47	
		80	86.05	
1-Bromo-adamantane	92[b]	100	0.128	23.39
		110	0.292	
		120	0.635	
	88[b]	100	0.96	22.72
		110	2.24	
		120	4.54	
	80[c]	25	0.007	21.28
		75	1.22	
		100	9.75	

a) Reactions were carried out in 8-ml culture tubes using 4 ml of 0.01 M 1-phenylethyl chloride in aqueous dioxane. b) Taken from Ref. 13. c) Taken from D. J. Raber, R. C. Bingham, J. L. Fry, and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **92**, 5977 (1970).

Table 5. Biphase hydrolysis of 1-phenylethyl chloride[a]

Organic solvent	Aqueous solution	Temp °C	$10^5 k_{\mathrm{obsd}}$ s^{-1}	E_a kcal mol^{-1}
Toluene	pure water	70	1.39	17.60
		80	2.74	
		90	5.74	
	0.1 M NaOH	70	1.56	17.26
		80	3.43	
		90	6.26	
	0.5 M NaOH	70	1.24	17.20
		80	2.40	
		90	4.96	
Decane	0.1 M NaOH	70	6.83	13.33
		80	12.78	
		90	19.94	

a) Reaction of 1.0 ml of 0.01 M 1-phenylethyl chloride with 10 ml of 0.1 M aqueous sodium hydroxide using mild stirring ($S \approx 4.16$ cm^2).

(75 °C) are 1.3×10^{-6}, 1.6×10^{-7}, and 6.9×10^{-9} M s^{-1}, respectively (S=4.16 cm^2; V_{org}=1 ml; [organic halide]=0.01 M). Taken together, these data provide very strong evidence that diffusion plays a minor role in the apparent kinetics and that chemical reaction dominates.

For a rate-limiting chemical reaction, the constancy of k_0 over a wide range of V_{org}, V_{aq}, and S can be rationalized only in terms of an interfacial process. If reaction were occurring in the bulk water phase, the rate should increase with increasing V_{aq}, due to an increase in the molar amount of water soluble organic halide. Experimentally, the observed rate was independent of V_{aq}. That reaction is not occurring in the bulk organic phase is further demonstrated by a comparison of observed first-order rate constants for hydrolysis in toluene–water (two phase) *vs.* dioxane–water (one phase) systems. At 100 °C, k_{obsd} found for reaction of 1 ml of 0.01 M 1-bromoadamantane with 2 ml of 0.1 M aqueous sodium hydroxide (S=1.26 cm^2) was 2.87×10^{-6} s^{-1}. In contrast, k_{obsd} for the hydrolysis of 2.0 ml of 0.01 M 1-bromoadamantane in homogeneous 92% (v/v) dioxane–water was 1.28×10^{-6} s^{-1}. Similarly, at 90 °C, k_{obsd} for the biphase hydrolysis of 1.0 ml of 0.01 M 1-phenylethyl chloride with 10 ml of 0.1 M aqueous sodium hydroxide (S=4.16 cm^2) was 6.26×10^{-5} s^{-1}. The k_{obsd} for homogeneous hydrolysis of 4 ml of 0.01 M 1-phenylethyl chloride in 90% (v/v) dioxane–water was 1.54×10^{-5} s^{-1}. Thus, the observed first-order rate constants for homogeneous reactions which contained substantial amounts of water were *lower* than those found for comparable biphase reactions. Finally, the higher biphase hydrolysis rates observed with decane–water *vs.* toluene–water, while difficult to rationalize in terms of chemical reaction occurring in the organic phase (water is more soluble in toluene than in decane), is easily accounted for as an interfacial process; *i.e.*, partitioning of the relatively polar organic halide into the phase boundary should be greater when a less polar solvent (decane) is used.

The results presented in this paper provide strong evidence that chemistry at hydrocarbon–water phase boundaries can play an important role in liquid–liquid biphase ractions.[3,11,12] Further studies aimed at establishing the generality and chemical significance of interfacial organic chemistry are in progress.

Experimental

General Methods. 1-Bromo- and 1-hydroxyadamantane (Aldrich Chem. Co.) were purified by sublimation at 90 °C (1 mm), and 120 °C (1 mm) respectively. 1-Phenylethyl chloride was prepared from 1-phenylethyl alcohol using established procedures. Toluene and decane (Aldrich Chem. Co., spectrophotometric grade) were used as obtained. Deionized water was purified by distillation from $KMnO_4/Ba(OH)_2$. The temperature of the oil bath used for the kinetic experiments was controlled (±0.5 °C) with the aid of a "Therm-O-Watch" electronic controller Model L6-1000 (I^{2}R Co., Cheltenhan, Pa), attached to a thermometer. All kinetic experiments were conducted in culture tubes equipped with a Teflon-lined screw cap. Reaction mixtures were analyzed by GLC on a Hewlett-Packard Model 5830A flame ionization instrument (2 ft. × 0.125 in UCW-982 on Chromosorb W column). Culture tubes (interfacial area) used were the following: Corning No. 9826, 13 × 100 mm (1.26 cm^2); Corning No. 9825, 20 × 125 mm (2.83 cm^2); Corning No. 9825, 25 × 150 mm (4.16 cm^2); Kimax No. 45066, 38 × 200 mm (9.08 cm^2). Radioactivity was measured using a Packard Tri-Carb Model 3330 scintillation spectrometer.

Kinetic Methods. All biphase hydrolysis reactions were studied between 70 and 120 °C. In a typical experiment, 1 ml of a solution of 1-phenylethyl chloride (0.01 M) in toluene containing a known quantity of undecane (internal standard) and 10 ml of (0.1 M) sodium hydroxide were introduced *via* pipet into a 50-ml culture tube (Corning No. 9826, 25 × 150 mm) containing a Teflon-coated magnetic stirring bar (1/2 × 5/16 in octagonal bar with pivot ring).

The tube was sealed with a Teflon-lined screw cap and was placed in an oil bath maintained at the desired temperature. The reaction was followed by withdrawing 1-μl samples of the organic phase at different times (no less than 30 min intervals) and monitoring the disappearance of the reactant by GLC. For sampling, the tube was removed from the oil bath, quickly cooled to nearly room temperature, opened, resealed, and returned to the bath (the overall process took less than 1 min). In all cases, clean first-order kinetics was observed over at least 3 half-lives. First-order rate constants were calculated with a least-squares program. The reproducibility of the observed rate constants was good (±10%). For biphase hydrolysis of 1-bromoadamantane, reactions were conducted in 8-ml culture tubes as unstirred processes using procedures previously described.[13] Apparent activation energies were derived from Arrhenius plots made by plotting k_0 as a function of $1/T$.

Diffusion of ^3H_2O *into Toluene.* An 8-ml culture tube was charged with 4.0 ml of dry toluene (distilled from sodium benzophenone ketyl) and sealed with a Teflon-lined screw cap. The tube was placed in an oil bath maintained at 70 °C. After thermal equilibration (15 min), 0.5 ml of 0.1 M NaOH in ^3H_2O (preequilibrated at 70 °C) was injected into the bottom of the toluene phase. The appearance of tritium in the organic layer was then monitored as a function of time by withdrawing 10 μl aliquots. The aliquots were blended with 2 ml of a scintillation liquid (dioxane solution of Omnifluor (New England Nuclear)) and the concentration of ^3H_2O in toluene computed using a standard curve.

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15) In our preliminary report, ΔH^*, ΔS^*, and ΔG^* were computed from observed first-order rate constants and compared with analogous homogeneous reactions. Unfortunately, since hydrocarbon–water liquid–liquid interfaces have not been unequivocally defined (three dimensional *vs.* two dimensional), absolute values of rate constants and corresponding ΔS^* and ΔG^* values cannot be meaningfully compared with homogeneous systems.

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