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Inverse Phase Transfer Catalysis. Kinetics and Mechanism of the Pyridine 1-Oxide-Catalyzed Substitution Reaction of Benzoyl Chloride and Benzoate Ion in a Two-Phase Water/Dichloromethane Medium

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The two-phase reaction of benzoyl chloride (PhCOCl) and benzoate ion with pyridine 1-oxide (PNO) as the inverse phase transfer catalyst yields both the substitution product (benzoic anhydride) and the hydrolysis product (benzoic acid). A high yield (>95%) of benzoic anhydride can be obtained if a polar organic solvent like dichloromethane is used. Under appropriate conditions, this reaction follows the rate law $-d[\mathrm{PhCOCl}]_{\mathrm{org}}/dt = (k_h + k_c[\mathrm{PNO}]_{\mathrm{iaq}})[\mathrm{PhCOCl}]_{\mathrm{org}}$. The effects of agitation rate, organic solvent, ionic strength, temperature, and the concentrations of reactants and catalyst on the reaction rate were investigated. A mechanism to rationalize the kinetic results is also given.

Introduction

The phase transfer catalysis (PTC) technique has attracted tremendous attention in the past two decades and is widely recognized as a versatile and important technique in organic synthesis utilizing two-phase water/organic solvent media.[1-6] In the normal PTC system,[1,3,4] the main principle of catalysis involves the continuous formation of a lipophilic ion pair of an anionic reactant with a lipophilic cation such as tetraalkylammonium ion and the transport of the anionic reactant from the water phase into the organic phase where it effectively reacts with a second reactant. In reversed PTC, a cationic reactant in the water phase is continuously transported into the organic phase in the form of lipophilic ion pair with a lipophilic nonnucleophilic anion and reacts with the second reactant.[7-9] A complementary methodology named by Mathias and Vaidya[10] as "inverse phase transfer catalysis (IPTC)" involves the conversion of reactant in organic phase to an ionic intermediate which is transported into the water phase for reaction. Fife and Xin[11] probed the mechanism with competitive transacylation for the IPTC process in the reaction of acid chloride (RCOCl) with carboxylate ions ($R'CO_2^-$) catalyzed by pyridine 1-oxide (PNO) as shown in reactions R1 and R2.

$$\mathrm{RCOCl} + \mathrm{PNO} \xrightarrow[\mathrm{CH_2Cl_2}]{} \mathrm{RCOONP^+Cl^-} \qquad \text{(R1)}$$

$$\mathrm{RCOONP^+} + \mathrm{R'CO_2^-} \xrightarrow[\mathrm{H_2O}]{} \mathrm{RCOOCOR'} + \mathrm{PNO} \qquad \text{(R2)}$$

The presumed intermediate 1-(acyloxy)pyridinium chloride ($RCOONP^+Cl^-$) formed in the organic phase (R1) is highly water soluble and sufficiently stable that it transports into the water phase and reacts with carboxylate ion to produce acid anhydride (R2). Carboxylic acid anhydrides, being less reactive than acyl chlorides, are very important intermediates for the synthesis of esters, amides, and peptides. The PTC technique[11-13] provides one of the most attractive methods[11-17] for the preparation of acid anhydrides. In this paper, we study the kinetics of the reaction of benzoyl chloride with benzoate ion in a two-phase medium catalyzed by pyridine 1-oxide. The results provide significant insight into the detailed mechanism of this IPTC system.

Experimental Section

Materials. Benzoic anhydride ($(PhCO)_2O$, analyze, ACS), pyridine 1-oxide (PNO, C_5H_5NO, 95%), naphthalene ($C_{10}H_8$, 99%) (Merck), benzoyl chloride (PhCOCl, extra pure), dichloromethane (CH_2Cl_2, AR 99%) (Ferak), benzoic acid ($PhCO_2H$, extra pure) (Hanawa), and sodium benzoate ($PhCO_2Na$, extra pure) (Ishizu) were used. Other chemicals used were of the highest reagent grade commercially available. Deionized water was obtained from the Millipore Milli-RO 20 reverse osmosis.

Due to the hygroscopic property of PNO, $(PNO)H^+Cl^-$ crystals (mp 179–181 °C) were used instead. These crystals were prepared by adding dropwise 4 mL of concentrated HCl to 20 mL of aqueous solution containing 10 g of PNO. Anal. Calcd for C_5H_6ClNO: C, 45.60; H, 4.56; N, 10.64; Cl, 26.99. Found: C, 45.64; H, 4.58; N, 10.65; Cl, 27.00.

1-(Benzyloxy)pyridinium chloride ($PhCOONP^+Cl^-$) was prepared by adding dropwise and under stirring 20 mL of an anhydrous CH_3CN solution of PNO (2.0 g) to 10 mL of an anhydrous CH_3CN solution of PhCOCl (2.9 g). The white precipitate (hygroscopic) formed was then quickly filtered off and dried in vacuum. Dissolving this compound in 0.500 M aqueous solution of $PhCO_2Na$ gave benzoic anhydride and benzoic acid.

Procedures. The kinetic experiments were run in a 250-mL smooth-wall three-necked flask fitted with a flat-bladed stirring paddle. The stirrer was driven by a laboratory stirrer (Heidolph RZR o/4, Germany). The agitation rate was measured by a Hard tachometer TM-2011 Line Seilci (Japan). The kinetic run was started by adding 40 mL of aqueous solution (containing a known amount of PNO and $PhCO_2Na$) to 40 mL of organic phase solution (containing a known amount of PhCOCl and $C_{10}H_8$) in the flask. Both solutions were thermostated at the desired temperature for

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Table I. Pseudo-First-Order Rate Constant for the Two-Phase Reaction of Benzoyl Chloride and Benzoate Ion Catalyzed by Pyridine 1-Oxide[a]

entry no.	$[NaNO_3]_{iaq}$/ M	$[PhCO_2Na]_{iaq}$/ M	$[PNO]_{iaq}$/ 10^{-4} M	$[PhCOCl]_{iorg}$/ 10^{-2} M	k_{obs}/ 10^{-3} s^{-1}	$(PhCO)_2O$ yield %
1	0.170	0.0300	6.00	1.00	1.93	85.5
2	0.100	0.100	6.00	1.00	2.38	90.6
3	0	0.200	6.00	1.00	2.62	91.8
4	0.100	0.200	6.00	1.00	2.50	91.0
5	0.200	0.200	6.00	1.00	2.43	89.7
6	0.300	0.200	6.00	1.00	2.41	89.2
7	0.100	0.400	6.00	1.00	2.50	89.5
8	0	0.500	6.00	1.00	2.50	88.0
9	0	0.500	6.00	1.00	0.417[b]	~14
10	0	0.500	6.00	1.00	2.25[c]	~11
11	0	0.500	6.00	0.500	2.57	
12	0	0.500	6.00	1.50	2.50	
13	0	0.500	6.00	2.00	2.47	
14	0	0.500	4.00	1.00	1.82	
15	0	0.500	2.00	1.00	1.03 (0.743)[e]	81.8
16	0.200	0.300	2.00	1.00	1.03	
17	0.300	0.200	2.00	1.00	1.04 (0.712)[e]	77.5
18	0.400	0.100	2.00	1.00	0.977 (0.600)[e]	76.6
19	0.490	0.0100	2.00	1.00	0.617	61.9
20[d]	0	0.100	4.00	0.500	1.72	74.0
21[d]	0	0.100	4.00	1.00	1.72	86.5
22[d]	0	0.100	4.00	1.50	1.75	87.1
23[d]	0	0.100	4.00	2.00	1.75	88.9
24[d]	0	0.100	8.00	1.00	3.35	90.0

[a] 40 mL of H_2O/40 mL of CH_2Cl_2, 1200 rpm, 22 °C. [b] 40 mL of C_6H_6/40 mL of H_2O. [c] 40 mL of n-C_6H_{14}/40 mL of H_2O. [d] 25 mL of H_2O/25 mL of CH_2Cl_2. [e] Values in parentheses are obtained from the plot of $\ln([PhCOCl]_{iorg} - [(PhCO)_2O])$ vs time.

at least 20 min. The reactor was submerged into a constant temperature water bath in which the temperature was controlled within ±0.2 °C. At a chosen time interval, 0.2 mL of solution was withdrawn and put into the extraction sample bottle which contained 0.2 mL of n-C_6H_{14}/0.5 mL of H_2O. The extraction bottle was shaked vigorously for 1 min and then allowed to stand for a few min to allow the two phases to separate. The organic phase was then analyzed by HPLC (Hitachi L6300 series) using the internal standard method. HPLC analysis conditions: column, Lichrospher 100 RP18 (5 μm); eluent, CH_3CN/H_2O = 62/38 by volume; flow rate, 1.5 mL/min; wavelength, 254 nm (UV detector); elution time (min), $PhCO_2H$ (0.9), PhCOCl (4.90), $(PhCO)_2O$ (5.60), $C_{10}H_8$ (6.40). The response factor f was calibrated using $C_r/C_{is} = f(S_r/S_{is})$ (C, concentration; S, peak area; is, internal standard; r, unknown compound). The values of f measured were 0.172 ± 0.004 and 0.300 ± 0.003 for $(PhCO)_2O$ (0.002–0.01 M) and PhCOCl (0.002–0.01 M), respectively, with $[C_{10}H_8]$ = 0.0200 M. The pseudo-first-order rate constant was determined by the linear-least-squares fit of the plot of ln [PhCOCl] vs time.

Results and Discussion

Kinetics of Reaction between Benzoyl Chloride and Benzoate Ion Catalyzed by Pyridine 1-Oxide. Preliminary study of the title reaction in a two-phase water/organic solvent medium showed that the rates of reaction depended on the amounts of reactants and catalyst, the organic solvent, the ionic strength of aqueous solution, the interfacial area, the agitation rate, and the temperature. The title reaction produced both the substitution product (benzoic anhydride) and the hydrolysis product (benzoic acid).

Effect of Agitation. Without agitation, the reaction rate was slow. For $[PhCOCl]_{iorg}$ = 0.0100 M, $[PhCO_2^-]_{iaq}$ = 0.0200 M, $[PNO]_{iaq}$ = 0.001 00 M in 25 mL of H_2O/25 mL of CH_2Cl_2, at 22 °C and 0 rpm, the observed pseudo-first-order rate constants (k_{obs}) were 9.72×10^{-5} s^{-1}, 1.36×10^{-4} s^{-1}, and 2.03×10^{-4} s^{-1} for the approximate interfacial area 19, 45, and 58 cm^2, respectively. For $[PhCOCl]_{iorg}$ = 0.0100 M, $[PhCO_2^-]_{iaq}$ = 0.500 M, $[PNO]_{iaq}$ = 6.00×10^{-4} M in 40 mL of H_2O/40 mL of CH_2Cl_2, the values of k_{obs} at 22 °C were 2.02×10^{-3} s^{-1}, 2.22×10^{-3} s^{-1}, 2.50×10^{-3} s^{-1}, and 2.50×10^{-3} s^{-1} at the agitation rates of 700, 900, 1100, and 1200 rpm, respectively. When the agitation rate was greater than 1100 rpm, it appeared that the two phases exhibited uniform mixing; i.e., the reaction rate was independent of the agitation rate. Therefore, most of the experiments were run at 1200 rpm. The value of k_{obs} was determined by the linear-least-squares (LLS) fit of the plot of ln [PhCOCl] vs time. Typical results were shown in Figures 1 and 2 (see supplementary material) and Table I. The values of k_{obs} obtained from the plots of ln $([PhCOCl]_{iorg} - [(PhCO)_2O])$ vs time are always smaller than those from the plots of ln [PhCOCl] vs time (Table I, entries 15, 17, and 18).

Solvent Effect. Dichloromethane, benzene, and n-hexane were chosen for studying the solvent effect. Under similar conditions, the order of the relative reaction rate in different solvent media was $H_2O/CH_2Cl_2 > n\text{-}C_6H_{14}/H_2O > C_6H_6/H_2O$ (Table I, entries 8–10). The yield of $(PhCO)_2O$ was about 90% in H_2O/CH_2Cl_2, which was considerably higher than those of ~14% in C_6H_6/H_2O and ~10% in n-C_6H_{14}/H_2O. The low yield of $(PhCO)_2O$ in C_6H_6/H_2O and n-C_6H_{14}/H_2O media was due to the hydrolysis of PhCOCl and $(PhCO)_2O$ itself, which produced $PhCO_2H$.

Rate Law. As shown in Figure 1 (supplementary material) and Table I (entries 8, 11–13, 20–23) this reaction is first order with respect to PhCOCl. Keeping $[PhCO_2Na]$ constant while varying the ionic strength of aqueous solution, we observed that the value of k_{obs} and the yield of $(PhCO)_2O$ decreased slightly with increasing ionic strength (Table I, entries 3–6). The yields of $(PhCO)_2O$ were 91.8, 91.0, 89.7, and 89.2% for entries 3–6 (Table I), respectively. In contrast, if both $[PhCO_2Na]$ and the ionic strength were not constant, the value of k_{obs} first increased with increasing $[PhCO_2Na]$ up to about 0.2 M and then decreased with further increase in $[PhCO_2Na]$ (Figure 2, supplementary material). This result can be rationalized by the fact that $PhCO_2^-$ ion plays the roles of both reactant and ionic strength adjustor. Thus, it is very important to keep the ionic strength constant in order to study the kinetics of this reaction. Keeping the ionic strength constant, we observed that the value of k_{obs} increased asymptotically with $[PhCO_2Na]$ to a limit value (Table I, entries 6–8 and 15–19). For $[PhCO_2Na]_{iaq} = 0.500$ M, $[PhCOCl]_{iorg} = 0.0100$ M, at 22 °C, the plot of k_{obs} vs $[PNO]_i$ is linear, implying that this reaction is also first order with respect to PNO with $k_{obs} = 2.54 \times 10^{-4}\ s^{-1}$ at the intercept, which is consistent with $k_h = 2.17 \times 10^{-4}\ s^{-1}$ of the uncatalyzed reaction between PhCOCl and $PhCO_2^-$ ion (shown in the next section). Therefore, the rate law of this reaction can be expressed as

$$-d[PhCOCl]_{org}/dt = k_{obs}[PhCOCl]_{org} = (k_h + k_c[PNO]_{iaq})[PhCOCl]_{org} \quad (1)$$

The temperature dependence of k_{obs} is shown in Table III (supplementary material). The apparent activation energy (E_a) was obtained by the LLS fit of the Arrhenius plot (ln k_{obs} vs $1/T$). The yield of $(PhCO)_2O$ increased with decreasing temperature. For example, the yield of $(PhCO)_2O$ was 88%, 90%, 92%, and 96% at 22, 16, 10, and 0 °C, respectively, when $[PhCO_2Na]_{iaq} = 0.500$ M, $[PhCOCl]_{iorg} = 0.0100$ M, and $[PNO]_{iaq} = 6.00 \times 10^{-4}$ M.

Kinetics of the Uncatalyzed Reaction between Benzoyl Chloride and Benzoate Ion. In the absence of a phase-transfer catalyst, PhCOCl and $PhCO_2^-$ ion in a two-phase water/organic solvent medium undergo slow reaction to produce $PhCO_2H$ and $(PhCO)_2O$, with $PhCO_2H$ being the major product. The observed pseudo-first-order rate constant (k_h) was determined by the LLS fit of the plot of ln [PhCOCl] vs time. Typical results were shown in Table II (see supplementary material). The relative rate of hydrolysis of PhCOCl in different solvent media was $n\text{-}C_6H_{14}/H_2O > C_6H_6/H_2O \geq H_2O/CH_2Cl_2$ (Table II, entries 1, 5, and 9, supplementary material). The rate of reaction depended on the ionic strength in aqueous phase. With the ionic strength being kept constant, we observed that in H_2O/CH_2Cl_2 medium the value of k_h also increased asymptotically with $[PhCO_2Na]$ to a limit value (Table II, entries 11–14, supplementary material). The presence of PNO in the aqueous phase increased the value of k_h for H_2O/CH_2Cl_2 and C_6H_6/H_2O media (Table II, entries 7 and 10, supplementary material), whereas it did not show significant effect on the rate of hydrolysis in $n\text{-}C_6H_{14}/H_2O$ medium (Table II, entry 3, supplementary material).

The temperature dependence of k_h was shown in Table III (see supplementary material). The apparent activation energies (E_a) obtained by the LLS fit of the plot of ln k_h vs $1/T$ were 69.8 and 57.6 kJ/mol with the presence of $[NaNO_3]_{iaq} = 0.500$ M and $[PhCO_2Na]_{iaq} = 0.500$ M, respectively.

Therefore, the activation energy of the uncatalyzed reaction between PhCOCl and benzoate ion is considerably higher than that of the corresponding PNO-catalyzed reaction (~35 kJ/mol). The larger temperature dependence of k_h than that of k_{obs} causes the yield of $(PhCO)_2O$ to decrease with increasing temperature as mentioned above.

Partition Equilibrium. The partition coefficients ($K_p = [X]_{aq}/[X]_{org}$) for X = PhCOCl, $PhCO_2H$, $(PhCO)_2O$, and $C_{10}H_8$ were measured in H_2O/CH_2Cl_2, C_6H_6/H_2O, and $n\text{-}C_6H_{14}/H_2O$ media. The partition coefficient of PhCOCl was hard to measure due to its hydrolysis in the water phase. Since PhCOCl, $C_{10}H_8$, and $(PhCO)_2O$ are practically insoluble in the water phase, their concentrations can then be determined by analyzing them in the organic phase. The values of K_p for them are nearly zero. The values of K_p at 22 and 36 °C for $PhCO_2H$ are 0.200 and 0.220, 1.43 and 2.22, and 0.310 and 0.340 in H_2O/CH_2Cl_2, $n\text{-}C_6H_{14}/H_2O$, and C_6H_6/H_2O media, respectively. Since it was also observed that the presence of $PhCO_2H$ in the organic phase did not affect the reaction rate significantly, it was not crucial to determine the exact concentration of $PhCO_2H$. Due to its highly polar property, PNO (4.24*D*)[18,19] is soluble in water and some organic solvents such as CH_2Cl_2, THF, and CH_3CN whereas it is only sparingly soluble in nonpolar organic solvents such as $n\text{-}C_6H_{14}$ and C_6H_6. The measurement of the partition coefficient confirms this argument. The values of K_p for PNO in $n\text{-}C_6H_{14}/H_2O$ and C_6H_6/H_2O media are about 10^3 and are quite independent of temperature and the ionic strength in the aqueous phase. The values of K_p for PNO in H_2O/CH_2Cl_2 medium are 23.8 and 18.9 at 22 and 36 °C, respectively ($[PhCO_2Na] = 0$ M) and are 44.4, 35.8, 31.4, and 28.9 at 10, 15, 22, and 36 °C, respectively ($[PhCO_2Na] = 0.500$ M). The very low partitioning of PNO in nonpolar organic solvents makes it a less effective inverse phase transfer catalyst for systems that include those solvents. The partitioning of PNO in CH_2Cl_2 increases significantly with increasing temperature, which makes PNO a more efficient catalyst at high temperatures.

Mechanism. The elucidation of the mechanism of this two-phase reaction between benzoyl chloride and benzoate ion was based on the present kinetic results and on some important and relevant literature results. Wamser and Yates[20] studied the kinetics and mechanisms for the two-phase reaction between aqueous aniline and benzoyl chloride in $CHCl_3$, with and without pyridine catalysis. They found that this reaction could take place in either phase, depending on the conditions, in particular in the presence of pyridine as a phase transfer catalyst. However, the uncatalyzed reaction occured in the organic phase to form benzanilide whereas the catalyzed reaction occurred in the aqueous phase to give predominantly hydrolysis to benzoic acid. In contrast, our results indicate that for the reaction of benzoyl chloride and benzoate ion in H_2O/CH_2Cl_2 medium, the PNO-catalyzed reaction produces predominantly benzoic anhydride whereas the uncatalyzed reaction produces predominantly benzoic acid. Wamser's results as well as some reported by Fife et al.[11] and Plusquellec et al.[13] strongly suggest that acyl transfer occurs in both the aqueous and organic phases. They also described conditions by which the symmetrical anhydride derived from an acid chloride was produced in the presence of competing carboxylate ions added in the aqueous phase. This observation is most easily explained by locating formation of symmetrical anhydride in the organic phase. In addition, Fife's results indicate that for competitive anhydride formation carried out in H_2O/CH_2Cl_2 and catalyzed by PNO, the more lipophilic toluate ion is more favored over the more hydrophilic isobutyrate ion. Apparently, the transacylation process includes an ion-pair extraction component as described by Bränström[3] to account for reaction in the organic phase between an anionic reactant originally in the aqueous phase and a lipophilic cation.

A schematic diagram of this two-phase reaction between benzoyl chloride and benzoate ion is shown in Scheme I and the abbreviated mechanistic steps are outlined in Scheme II. For the uncatalyzed reaction the hydrolysis

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part in Scheme I describes its reaction pathways whereas for the PNO-catalyzed reaction the pathways in both hydrolysis and IPTC parts are involved.

According to Scheme II, the following rate expressions can be written:

$$-\mathrm{d}[\mathrm{B}]/\mathrm{d}t = k_1[\mathrm{W_o}][\mathrm{B_o}] + (k_2[\mathrm{W_w}] + k_3[\mathrm{A_w}^-])[\mathrm{B_w}] + (k_7[\mathrm{W_w}] + k_8[\mathrm{A_w}^-])[\mathrm{I_w}] + k_6[\mathrm{W_o}][\mathrm{I_o}] \quad (2)$$

$$\mathrm{d}[\mathrm{B_w}]/\mathrm{d}t = k_\mathrm{m}[\mathrm{B_o}] - (k_{-m} + k_2[\mathrm{W_w}] + k_3[\mathrm{A_w}^-] + k_5[\mathrm{N_w}])[\mathrm{B_w}] \quad (3)$$

$$\mathrm{d}[\mathrm{I_o}]/\mathrm{d}t = \mathrm{k}_4[\mathrm{B_o}][\mathrm{N_o}] - (k_{-4} + k_n + k_6[\mathrm{W_o}] + k_9[\mathrm{A_o}^-])[\mathrm{I_o}] + k_{-n}[\mathrm{I_w}] \quad (4)$$

$$\mathrm{d}[\mathrm{I_w}]/\mathrm{d}t = k_5[\mathrm{B_w}][\mathrm{N_w}] - (k_{-n} + k_7[\mathrm{W_w}] + \mathrm{k}_8[\mathrm{A_w}^-])[\mathrm{I_w}] + k_n[\mathrm{I_o}] \quad (5)$$

Applying the steady-state approximation to $\mathrm{B_w}$, $\mathrm{I_o}$, and $\mathrm{I_w}$, we derived the steady-state concentrations of these species (eqs 6–8).

$$[\mathrm{I_o}]_\mathrm{s} = [k_4(k_{-n} + k_7[\mathrm{W_w}] + k_8[\mathrm{A_w}^-])[\mathrm{N_o}][\mathrm{B_o}] + k_{-n}k_5[\mathrm{N_w}][\mathrm{B_w}]]/D \quad (6)$$

$$[\mathrm{I_w}]_\mathrm{s} = [k_4k_n[\mathrm{N_o}][\mathrm{B_o}] + k_5(k_{-4} + k_n + k_6[\mathrm{W_o}] + k_9[\mathrm{A_o}^-])[\mathrm{N_w}][\mathrm{B_w}]]/D \quad (7)$$

$$[\mathrm{B_w}]_\mathrm{s} = k_\mathrm{m}[\mathrm{B_o}]/E \quad (8)$$

in which

$$D = [(k_\mathrm{n} + k_6[\mathrm{W_o}] + k_9[\mathrm{A_o}^-])(k_7[\mathrm{W_w}] + k_8[\mathrm{A_w}^-]) + k_{-\mathrm{n}}k_6[\mathrm{W_o}]] + k_{-4}(k_{-n} + k_7[\mathrm{W_w}] + k_8[\mathrm{A_w}^-])$$

$$E = k_{-m} + k_2[\mathrm{W_w}] + k_3[\mathrm{A_w}^-] + k_5[\mathrm{N}]_\mathrm{t}/(1 + K)$$

$$[\mathrm{N}]_t = [\mathrm{N_o}] + [\mathrm{N_w}],\ [\mathrm{N_w}]/[\mathrm{N_o}] = K \gg 1$$

$$[\mathrm{A_w}^-]/[\mathrm{A_o}^-] = K' \gg 1,\ [\mathrm{W_w}]/[\mathrm{W_o}] = K'' \gg 1$$

Substituting eqs 6–8 into eq 2, we derived eq 9.

$$\begin{aligned} -\mathrm{d}[\mathrm{PhCOCl}]_\mathrm{org}/\mathrm{d}t &\approx -\mathrm{d}[\mathrm{B}]/\mathrm{d}t \\ &= (k_\mathrm{h}' + k_\mathrm{c}[\mathrm{N}]_\mathrm{t})[\mathrm{B_o}] \\ &= k_\mathrm{obs}[\mathrm{PhCOCl}]_\mathrm{org} \end{aligned} \quad (9)$$

in which

$$k_\mathrm{obs} = k_\mathrm{h}' + k_\mathrm{c}[\mathrm{N}]_t = k_\mathrm{h}' + k_\mathrm{c}[\mathrm{PNO}]_\mathrm{iaq} \quad (10)$$

$$k_\mathrm{h}' = k_1[\mathrm{W_o}] + k_m(k_2[\mathrm{W_w}] + k_3[\mathrm{A_w}^-])/E \quad (11)$$

$$k_\mathrm{c} = [(k_4 + q_1) - [k_{-4}(q_2 + q_3)/D]]/(1 + K) \quad (12)$$

$$q_1 = k_5Kk_m/E \quad (13)$$

$$q_2 = k_4(k_{-n} + k_7[\mathrm{W_w}] + k_8[\mathrm{A_w}^-]) \quad (14)$$

$$q_3 = k_mk_5k_{-n}K/E \quad (15)$$

When $[\mathrm{N}]_t = [\mathrm{PNO}]_\mathrm{iaq} = 0$ M and $[\mathrm{A_w}^-] \approx [\mathrm{PhCO_2}^-]_\mathrm{iaq}$, k_h' reduces to k_h (eq 16).

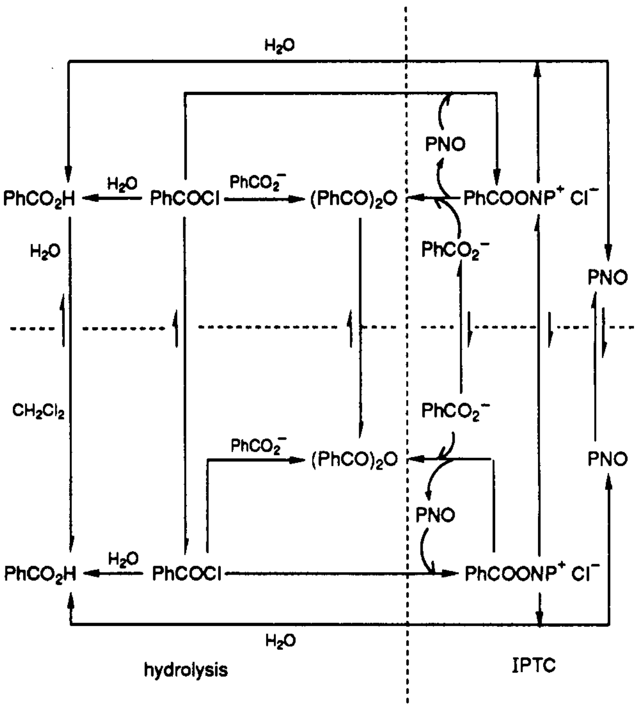
$$k_\mathrm{h} = k_1[\mathrm{H_2O}]_\mathrm{org} + k_m(k_2[\mathrm{H_2O}]_\mathrm{aq} + k_3[\mathrm{PhCO_2}^-]_\mathrm{iaq})/E' \quad (16)$$

$$E' = k_{-m} + k_2[\mathrm{H_2O}]_\mathrm{aq} + k_3[\mathrm{PhCO_2}^-]_\mathrm{iaq}$$

Equation 16 is consistent with the kinetic results of the uncatalyzed two-phase reaction between PhCOCl and $\mathrm{PhCO_2}^-$ ion in that the value of k_h increases asymptotically with $[\mathrm{PhCO_2}^-]$ to a limit value. If $[\mathrm{PNO}]_\mathrm{iaq}$ is sufficiently low, k_h is approximately equal to k_h' and k_c can then be determined by eq 17.

$$k_\mathrm{obs} = k_\mathrm{h} + k_\mathrm{c}[\mathrm{PNO}]_\mathrm{iaq} \quad (17)$$

Scheme I



Scheme II

$$\mathrm{B_o} \underset{k_{-m}}{\overset{k_m}{\rightleftharpoons}} \mathrm{B_w} \quad \text{(E1)}$$

$$\mathrm{B_o} + \mathrm{W_o} \xrightarrow{k_1} \mathrm{A_o} + (\mathrm{H^+Cl^-})_\mathrm{o} \quad \text{(M1)}$$

$$\mathrm{B_w} + \mathrm{W_w} \xrightarrow{k_2} \mathrm{A_w} + (\mathrm{H^+Cl^-})_\mathrm{w} \quad \text{(M2)}$$

$$\mathrm{B_w} + \mathrm{A_w}^- \xrightarrow{k_3} \mathrm{P_w} + \mathrm{Cl^-}_\mathrm{w} \quad \text{(M3)}$$

$$\mathrm{N_o} \overset{K}{\rightleftharpoons} \mathrm{N_w} \quad \text{(E2)}$$

$$\mathrm{B_o} + \mathrm{N_o} \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} \mathrm{I_o} \quad \text{(M4)}$$

$$\mathrm{B_w} + \mathrm{N_w} \xrightarrow{k_5} \mathrm{I_w} \quad \text{(M5)}$$

$$\mathrm{I_o} \underset{k_{-n}}{\overset{k_n}{\rightleftharpoons}} \mathrm{I_w} \quad \text{(E3)}$$

$$\mathrm{I_o} + \mathrm{W_o} \xrightarrow{k_6} \mathrm{A_o} + \mathrm{N_o} + (\mathrm{H^+Cl^-})_\mathrm{o} \quad \text{(M6)}$$

$$\mathrm{I_w} + \mathrm{W_w} \xrightarrow{k_7} \mathrm{A_w} + \mathrm{N_w} + (\mathrm{H^+Cl^-})_\mathrm{w} \quad \text{(M7)}$$

$$\mathrm{I_w} + \mathrm{A_w}^- \xrightarrow{k_8} \mathrm{P_w} + \mathrm{N_w} \quad \text{(M8)}$$

$$\mathrm{I_o} + \mathrm{A_o}^- \xrightarrow{k_9} \mathrm{P_o} + \mathrm{N_o} \quad \text{(M9)}$$

$$\mathrm{A_o}^- \overset{K'}{\rightleftharpoons} \mathrm{A_w}^- \quad \text{(E4)}$$

$$\mathrm{W_o} \overset{K''}{\rightleftharpoons} \mathrm{W_w} \quad \text{(E5)}$$

$$\mathrm{P_o} \rightleftharpoons \mathrm{P_w} \quad \text{(E6)}$$

$$\mathrm{A_o} \rightleftharpoons \mathrm{A_w} \quad \text{(E7)}$$

Equation 12 can also rationalize the kinetic results of this IPTC system in that the value of k_obs increases asymptotically with $[\mathrm{PhCO_2}^-]$ to a limit value. If $[\mathrm{PhCO_2}^-]$ is sufficiently high, the reverse reaction of step M4 and the term $k_{-4}(q_2 + q_3)/D$ in k_c become negligible. This argument is supported by the result in Table I (entries 6–8). Furthermore, since the term q_1 in k_c is contributed by the reaction of PhCOCl in the aqueous phase and is expected to be negligible, at the limit eq 12 will reduce to eq 18.

$$k_c = k_4/(1 + K) \qquad (18)$$

Therefore, the second-order rate constant (k_4) of the reaction between PhCOCl and PNO in the organic phase can then be estimated by eq 18. The calculated values of k_4 obtained with $[\mathrm{PNO}]_{\mathrm{iaq}} = 2.00 \times 10^{-4}$ and 6.00×10^{-4} M (Table III, supplementary material) are 64.6 and 63.8, 99.9 and 101, 111 and 110, and 135 and 123 s^{-1} at 0, 10, 16, and 22 °C, respectively. The corresponding thermodynamic parameters ($\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$) obtained by the LLS fit of the Eyring plot ($\ln k_4/T$ vs $1/T$) are 19.6 ± 2.2 kJ/mol and −137 ± 8 J/mol·K and 17.6 ± 3.5 kJ/mol and −145 ± 13 J/mol·K for reactions with $[\mathrm{PNO}]_{\mathrm{iaq}} = 2.00 \times 10^{-4}$ M and 6.00×10^{-4} M (Table III, supplementary material), respectively. The above argument can therefore be justified by these consistent results. The negative value of entropy can be rationalized by considering that the transition state formed during the reaction between PhCOCl and PNO is much more polar than both reactant molecules. Thus, this reaction is more favorable to take place in polar solvent like CH_2Cl_2 and unfavorable in nonpolar solvents like C_6H_6 and n-C_6H_{14} as observed in the present system.

Summary

In the two-phase reaction of benzoyl chloride and benzoate ion, pyridine 1-oxide acts as an inverse phase transfer catalyst for the transport of benzoyl chloride (as (benzoyloxy)pyridinium chloride) into the aqueous phase, where it reacts with benzoate ion to produce benzoic anhydride or hydrolyzes to benzoic acid. A high yield (>95%) of benzoic anhydride can be obtained if a polar organic solvent like dichloromethane is used. Under appropriate conditions, the reaction of benzoyl chloride and pyridine 1-oxide in the organic phase is slow, and the study of the kinetics of this IPTC system becomes possible.

Abbreviations: PNO = pyridine 1-oxide, pyridine N-oxide, $\mathrm{PhCOONP^+Cl^-}$ = 1-(benzoyloxy)pyridinium chloride, A = $PhCO_2H$, A^- = $PhCO_2^-$, B = PhCOCl, N = PNO, I = $\mathrm{PhCOONP^+Cl^-}$, P = $(PhCO)_2O$, W = H_2O, [X] = concentration of species X, $[X]_i$ = initial concentration of species X, $[X]_s$ = steady-state concentration of species X, LLS = linear-least-squares, K = partition (equilibrium) constant, k_{obs} = observed rate constant, k_{h} = uncatalyzed rate constant, k_{c} = catalyzed rate constant, o = org = organic phase (subscript), w = aq = aqueous phase (subscript).

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Registry No. Benzoyl chloride, 98-88-4; benzoate, 766-76-7; pyridine 1-oxide, 694-59-7; benzoic anhydride, 93-97-0.

Supplementary Material Available: Figure 1 (the plot of ln [PhCOCl] vs time) and Figure 2 (the plot of k_{obs} vs $[\mathrm{PhCO_2Na}]$) for the two-phase reaction of benzoyl chloride and benzoate ion catalyzed by pyridine 1-oxide and Table II (pseudo-first-order rate constant for the uncatalyzed) and Table III (temperature dependence of the pseudo-first-order rate constant of the uncatalyzed and pyridine 1-oxide catalyzed) for the two-phase reaction of benzoyl chloride and benzoate ion (4 pages). Ordering information is given on any current masthead page.

Stereochemical Aspects of Hydration of Carbohydrates in Aqueous Solutions. 2.[1] Kinetic Medium Effects

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Rate constants for the hydrolysis of 1-benzoyl-3-phenyl-1,2,4-triazole in aqueous solutions of carbohydrates have been measured as a function of molality and nature of added mono- and disaccharides. The kinetic medium effects induced by the carbohydrates originate from hydration sphere overlap effects. The results are analyzed using the additivity principle and reveal specificity in the stereochemical aspects of hydration. The major effect determining the hydration of a monosaccharide appears to be the position of the OH(4) group in conjunction with OH(2). The position of the carbonyl function and the number of equatorial groups present in the molecule are of minor importance. The experimentally obtained G(C) values, which are representative of the interaction between the carbohydrate and the initial state and activated complex for the hydrolysis reaction, show that the hydration of the carbohydrates is mainly determined by the methine moieties. The G(CHOH,endo) values obtained for the dominant conformers in solution point to a similar conclusion. With an increase in compatibility of the carbohydrate molecule with the three-dimensional hydrogen-bond structure of water, the hydroxy groups become less important in determining carbohydrate–solute interactions. This might be important in molecular recognition, since under these conditions the carbohydrates are recognized as hydrophobic moieties. For disaccharides the medium effects are larger than expected on the basis of the medium effect of two monosaccharide subunits. We suggest that this is caused by a cooperativity effect, which makes the methine moieties even more dominant in governing the hydration characteristics. The G(C) values reveal that the type of linkage in the disaccharide molecule hardly influences the kinetic medium effect. Only when one of the monosaccharide subunits has an axial OH(4) or when there is a 1–3 type of linkage between the moieties is a significantly different G(C) found. It is suggested that the compatibility of the carbohydrates with the three-dimensional hydrogen-bond structure of water largely depends on the compatibility of the next nearest neighbor oxygens of the carbohydrate molecule with the nearest or next nearest neighbor oxygens of liquid water.

Carbohydrates play an important role in life processes. Not only do they serve as structural and protective materials and as an energy source[3] but they are also very important moieties in glycoproteins[4] and play a significant

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