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Study of the Reaction of Benzoyl Chloride and Sodium Dicarboxylate under Inverse Phase Transfer Catalysis

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The reaction of benzoyl chloride (PhCOCl) and sodium dicarboxylate ($R(COONa)_2$) catalyzed by an inverse-phase-transfer catalyst (IPTC) in the two-phase medium H_2O/CH_2Cl_2 was investigated. Pyridine 1-oxide (PNO) was used as the inverse-phase-transfer catalyst. Ten dicarboxylates, namely oxalate, malonate, maleate, succinate, adipate, nonanedioate, fumarate, phthalate, isophthalate, and terephthalate, were selected for study. In general, the observed mixed products included mono- and bis(benzoyloxycarbonyl) compounds, benzoic anhydride and benzoic acid, depending on the molecular structure of the dicarboxylate ion. Dicarboxylates of four types were classified according to distribution of products. The reaction rate is strongly affected by PhCOCl and $R(COONa)_2$ due to their influence on the distribution of PNO in the organic phase. A mechanistic interpretation of the experimental data is presented.

Phase-transfer catalysis (PTC) is an effective tool for synthesis of organic chemicals from two immiscible reactants.[1—3] Inexpensive quaternary salts are commonly used as the phase-transfer catalyst[4,5] for transport of a reactant from an aqueous phase into an organic phase to enhance the rate of reaction. In the recent literature, few techniques were reported[6—11] in which an organic reactant is activated by conversion to an ionic intermediate and then transported to the aqueous phase for reaction. Mathias and Vaidya[12] reported one such technique called inverse-phase-transfer catalysis (IPTC). Pyridine 1-oxide (PNO) and 4-dimethylaminopyridine (DMAP) were commonly used as inverse-phase-transfer catalyst for reaction of benzoyl chloride and carboxylate ion to produce acid anhydride.[12—14] The IPTC method was also employed to produce ketones from oxidation of alcohols.[15]

Anhydride is an important reagent in organic synthesis. Conventionally, anhydride is synthesized in anhydrous conditions.[16] At present, phase transfer catalysis (PTC)[12—14,17] and similar techniques[9,10] are customarily applied to synthesize both symmetric and mixed anhydrides. However, only scant work has been done on synthesis of acid dianhydride. The reaction of di acyl chloride and carboxylic acid in a homogeneous solution to synthesize dianhydride was reported.[18] In this work, we investigated the PNO-catalyzed reaction of PhCOCl and $R(COONa)_2$ in the two-phase medium H_2O/CH_2Cl_2 to synthesize their mono- and bis(mixed anhydride)s. The feasibility, the kinetics, and mechanism of the reaction are presented.

Experimental

Materials. Pyridine 1-oxide (PNO, C_5H_5O, 95%), naphthalene ($C_{10}H_8$, 99%), disodium succinate ($C_2H_4(COONa)_2$), disodium fumarate (*trans*-$C_2H_2(COONa)_2$) (Merck), benzoyl chloride (PhCOCl, extra pure), malonic acid ($CH_2(COOH)_2$, extra pure) (FERAK), sodium oxalate ($Na_2C_2O_4$), nonanedioic acid ($(CH_2)_7(COOH)_2$) (TCI), phthalic acid (*o*-$C_6H_4(COOH)_2$), dichloromethane (CH_2Cl_2, extra pure) (WAKO), isophthalic acid (*m*-$C_6H_4(COOH)_2$), terephthalic acid (*p*-$C_6H_4(COOH)_2$) (Hayashi), maleic acid (*cis*-$C_2H_2(COOH)_2$) (Santoku) were used. Other chemicals used were of the highest reagent grade commercially available. Deionized water was obtained from reverse osmosis (Millipore Milli-RO 20). As PNO is hygroscopic, crystals of $PNOH^+Cl^-$ were used instead, which were prepared by adding dropwise concentrated HCl (3 M, 4 mL, 1 M=1 mol dm^{-3}) to an aqueous solution (20 mL) containing PNO (10 g).[14]

Procedures. (A) Synthesis and Characterization of Mono- and Bis(mixed anhydride)s. A CH_2Cl_2 solution (50 mL) containing PhCOCl (0.25 M) and aqueous solution (50 mL) containing $R(COONa)_2$ (0.2 M) and PNO (0.005 M) were poured into a 250-mL three-necked Pyrex flask (250 mL). The reaction was carried out under agitation at 1200 rpm. After the reaction was complete, the CH_2Cl_2 solution was separated and immediately washed with diluted alkaline solution to remove organic acid. Then it was washed twice with deionized water and dehydrated by adding magnesium sulfate. A white precipitate was obtained after concentrating the CH_2Cl_2 solution with a rotary evaporator.

Elemental Analysis: Calcd for $C_{22}H_{14}O_6$ (*m*-$C_6H_4(COOCOPh)_2$): C, 70.60; H, 3.74%. Found: C, 70.63;

H, 3.74%. Calcd for $C_{22}H_{14}O_6$ (p-$C_6H_4(COOCOPh)_2$): C, 70.6; H, 3.74%. Found: C, 70.55; H, 3.72%. Calcd for $C_{20}H_{18}O_6$ ($(CH_2)_4(COOCOPh)_2$): C, 67.80; H, 5.08%. Found: C, 67.87; H, 5.11%. Calcd for $C_{23}H_{24}O_6$ ($(CH_2)_7(COOCOPh)_2$): C, 69.70; H, 6.06%. Found: C, 69.69; H, 6.10%. Calcd for $C_{18}H_{12}O_6$ (*trans*-$C_2H_2(COOCOPh)_2$): C, 66.67; H, 3.70%. Found: C, 66.85; H, 3.74%. Calcd for $C_{15}H_{10}O$ (o-$C_6H_4(COOCOPh)$): C, 66.67; H, 3.70%. Found: C, 66.67; H, 3.67%.

(B) Characteristics of Spectra of PNO and $PNOH^+$ Ion. The spectrum of PNO in CH_2Cl_2 exhibits an absorption maximum at 275 nm and its molar absorption coefficients measured are $(1.43\pm0.01)\times10^4$ at 275 nm and $(3.16\pm0.06)\times10^3$ M^{-1} cm^{-1} at 254 nm, respectively. The spectrum of $PNOH^+Cl^-$ in glacial acetic acid exhibits an absorption maximum at 254 nm and its molar absorption coefficients measured are $(2.24\pm0.01)\times10^3$ at 275 nm and $(1.03\pm0.01)\times10^4$ M^{-1} cm^{-1} at 254 nm, respectively.

Determination of PNO and $PNOH^+$ Ion in CH_2Cl_2: Aqueous solution (25 mL) containing known amounts of $R(COONa)_2$ and $PNOH^+Cl^-$ was mixed with CH_2Cl_2 solution (25 mL). The mixed solution was agitated at 1200 rpm and thermostatted for 3 h. An aliquot sample was then withdrawn from CH_2Cl_2 and its absorbance at 275 and 254 nm were measured. The concentration of PNO and $PNOH^+$ ion in CH_2Cl_2 were calculated by solving Eqs. 1 and 2.

$$A_{275} = \varepsilon_{11}[PNO]_{org} + \varepsilon_{12}[PNOH^+]_{org}, \quad (1)$$

$$A_{254} = \varepsilon_{21}[PNO]_{org} + \varepsilon_{22}[PNOH^+]_{org}, \quad (2)$$

in which A_{275} and A_{254} are the total absorbances of solution measured at 275 and 254 nm, respectively and (ε_{11}, ε_{12}) and (ε_{21}, ε_{22}) are the molar absorption coefficients measured at (275 and 254 nm) for (PNO, $PNOH^+$), respectively.

(C) Kinetic Run. The reactor was a three-necked Pyrex flask (250 mL), fitted with a flat-bladed stirring paddle. The reactor was submerged into a water bath at a temperature controlled within ±0.1 °C. A kinetic run was started by adding aqueous solution (50 mL) containing known amounts of $PNOH^+Cl^-$, $R(COOH)_2$, and NaOH or $R(COONa)_2$ to an organic solution (50 mL) containing known amounts of PhCOCl and $C_{10}H_8$ in the flask. Both solutions were thermostatted at the desired temperature at least 20 min. During the reaction, an aliquot (0.2 mL) was withdrawn at a chosen time and was immediately extracted with CH_2Cl_2 (0.8 mL) and HCl aqueous solution (0.6 M, 0.3 mL), which was shaken vigorously for 30 s. After separation of the two phases, the organic phase was further diluted with dichloromethane and analyzed with a HPLC using the internal standard method.

The HPLC was a Shimadzu model LC-9A (Japan). The analytic conditions were: column, Shim-pack CLC-ODS (M); eluent, $CH_3CN/H_2O=65/35$ by volume, flow rate, 1.2 mL min^{-1}; wavelength, 254 nm (UV detector); elution time/min, PhCOCl (7.00), $(PhCO)_2O$ (8.10), $C_{10}H_8$ (8.70), o-$C_6H_4(COOCOPh)_2(COOH)$ (3.50), *trans*- $C_2H_2(COOCOPh)_2$ (9.50), $(CH_2)_4(COOCOPh)_2$ (9.72), m-$C_6H_4(COOCOPh)_2$ (14.1), p-$C_6H_4(COOCOPh)_2$ (16.10). The response factor f was calibrated using $C_r/C_{is}=f(S_r/S_{is})$ (C, concentration; S, area of signal; is, internal standard; r, unknown compound). The values of f measured were 0.310 ± 0.003 for PhCOCl, 0.618 ± 0.001 for $(PhCO)_2O$, 0.202 ± 0.005 for *trans*-$C_2H_2(COOCOPh)_2$, 0.282 ± 0.004 for $(CH_2)_4(COOCOPh)_2$, 0.113 ± 0.001 for m-$C_6H_4(COOCOPh)_2$, 0.0683 ± 0.0012 for p-$C_6H_4(COOCOPh)_2$ and 0.645 ± 0.022 for o-$C_6H_4(COOH)(COOCOPh)$ with $[C_{10}H_8]=0.02$ M and [analyzed compound]=(0.002—0.02) M. The pseudo-first-order rate coefficient (k_{obsd}) was determined from a linear-least-squares fit of the plot of $\ln[PhCOCl]_{org}$ vs. time.

Other HPLC conditions were: eluent, CH_3CN/H_2O (5% propanoic acid)=65/35 by volume; wavelength 240 nm (UV detector); elution time/min, PhCOOH (2.95), $PhCOOCO(CH_2)_4COOH$ (3.35), $PhCOOCO(CH_2)_7COOH$ (4.80), PhCOCl (6.50), $(PhCO)_2O$ (7.50), $C_{10}H_8$ (8.05), $(CH_2)_4(COOCOPh)_2$ (8.85), $(CH_2)_7(COOCOPh)_2$ (18.0); the other conditions were described above. The values of f measured were 0.0667 ± 0.0013 for PhCOOH, 0.266 ± 0.006 for $(PhCO)_2O$, and 0.0667 ± 0.0001 for $(CH_2)_7(COOCOPh)_2$.

Results and Discussion

I. Classification of Dicarboxylate Salts. The main product of the pyridine 1-oxide-catalyzed reaction of benzoyl chloride (PhCOCl) and carboxylate ion ($RCOO^-$) is the mixed anhydride (PhCOOCOR).[19] However, products such as PhCOOH, $(PhCO)_2O$, PhCOOCORCOOH (mono(mixed anhydride)) and $R(COOCOPh)_2$ (bis(mixed anhydride)) were obtained from the reaction of PhCOCl and dicarboxylate ($(RCOO^-)_2$) ion catalyzed by PNO in a two-phase medium H_2O/CH_2Cl_2. The composition of products depended strongly on the properties of the dicarboxylate. Typical results are presented in Table 1 and Figs. 1, 2, 3, and 4. According to the distribution of the products, dicarboxylate salts were classified into four groups, i.e.

Type 1: The main product is PhCOOH (70—80% yield) and the minor product is $(PhCO)_2O$. Neither mono- nor bis(mixed anhydride)s were detected. Some dicarboxylate salts of Type 1 are $(COONa)_2$, $CH_2(COONa)_2$, *cis*-$C_2H_2(COONa)$, and $C_2H_4(COONa)_2$.

Type 2: The main products are the mono(benzoyloxycarbonyl) compound, $(PhCO)_2O$, and the minor product is PhCOOH. No bis(mixed anhydride) was detected. o-$C_6H_4(COONa)_2$ belongs to Type 2 of dicarboxylate salts.

Type 3: The main product is the bis(mixed anhydride). Trace amounts of PhCOOH and $(PhCO)_2O$ were also produced. The mono(mixed anhydride) was not detected. Dicarboxylates of Type 3 are *trans*-$C_2H_2(COONa)_2$, m- and p-$C_6H_4(COONa)_2$.

Type 4: Dicarboxylates of Type 4 are $(CH_2)_4(COONa)_2$ and $(CH_2)_7(COONa)_2$. The products are PhCOOH, $(PhCO)_2O$, mono- and bis(mixed anhydride)s.

The effects of the reaction conditions on the product distribution are presented in Tables 2, 3, and 4. For Type-3 dicarboxylates, favorable conditions for produc-

Table 1. Distribution of the Products for the Reaction of Benzoyl Chloride and Dicarboxylate Salts Catalyzed by PNO in a Two-Phase H_2O/CH_2Cl_2 Medium[a)]

$R(COONa)_2$		Yield/%			
Type		PhCOOCORCOOH	$R(COOCOPh)_2$[d)]	PhCOOH	$(PhCO)_2O$[c)]
—	$NaNO_3$	0	0	93	7
1	$(COONa)_2$[b)]	nD	nD	62	38
1	$CH_2(COONa)_2$	nD	nD	87	13
1	$(CH_2)_2(COONa)_2$	nD	nD	79	19
1	*cis*-$C_2H_2(COONa)_2$	nD	nD	88	12
2	*o*-$C_6H_4(COONa)_2$	77	nD	17	6
3	*trans*-$C_2H_2(COONa)_2$	nD	71	23	6
3	*m*-$C_6H_4(COONa)_2$	nD	83	16	1
3	*p*-$C_6H_4(COONa)_2$	nD	88	11	1
4	$(CH_2)_4(COONa)_2$	5	34	55	16
4	$(CH_2)_7(COONa)_2$	9	80	8	3

a) $[R(COONa)_2]_{i,aq}=0.500$ M, $[PNO]_{i,aq}=6.00\times10^{-4}$ M, $[PhCOCl]_{i,org}=0.0100$ M, 18 °C. b) $[(COONa)_2]_{i,aq}=0.100$ M, $[NaNO_3]_{i,aq}=0.400$ M. c) Yield of $(PhCO)_2O=(2\times[(PhCO)_2O]_{org}/[PhCOCl]_{i,org})\times100\%$. d) Yield of $R(COOCOPh)_2=(2\times[R(COOCOPh)_2]_{org}/[PhCOCl]_{i,org})\times100\%$.

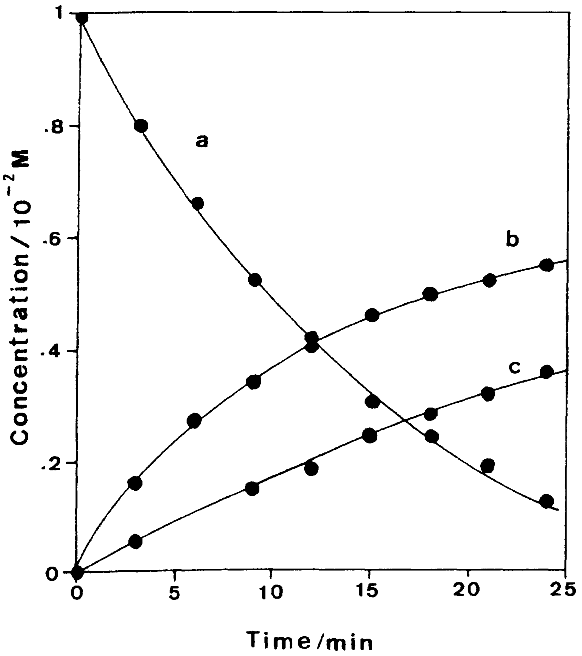

Fig. 1. Concentration vs. time curve for the PNO-catalyzed two-phase reaction of PhCOCl and $(COONa)_2$ (Type 1); $[(COONa)_2]_{i,aq}=0.100$ M, $[NaNO_3]_{i,aq}=0.400$ M, $[PNO]_{i,aq}=6.00\times10^{-4}$ M, $[PhCOCl]_{i,org}=0.0100$ M, 18 °C. a: PhCOCl, b: PhCOOH, c: $(PhCO)_2O$ (corrected). ($[(PhCO)_2O]_{corrected}=2\times[(PhCO)_2O]_{org}$).

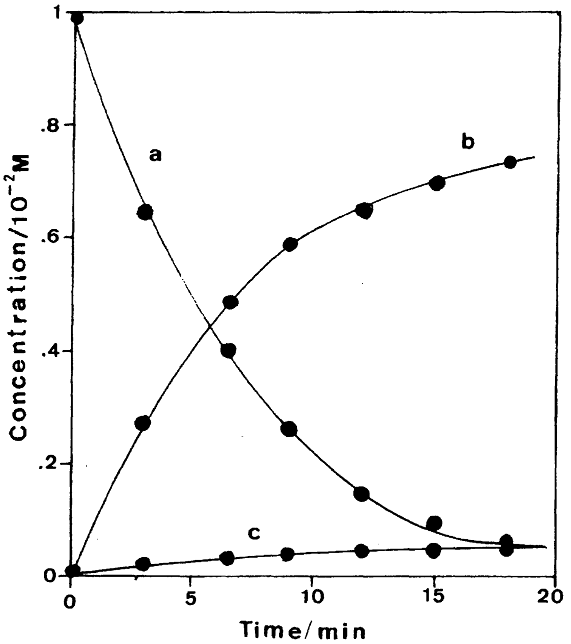

Fig. 2. Concentration vs. time curve for the PNO-catalyzed two-phase reaction of PhCOCl and *o*-$C_6H_4(COONa)_2$ (Type 2); $[o\text{-}C_6H_4(COONa)_2]_{i,aq}=0.500$ M, $[PNO]_{i,aq}=6.00\times10^{-4}$ M, $[PhCOCl]_{i,org}=0.0100$ M, 18 °C. a: PhCOCl, b: *o*-C_6H_4-(COOCOPh)(COOH), c: $(PhCO)_2O$ (corrected). ($[(PhCO)_2O]_{corrected}=2\times[(PhCO)_2O]_{org}$).

ing bis(mixed anhydride)s are to run the reaction at low temperature and with relatively higher concentrations of PhCOCl and PNO. For $[R(COONa)_2]_{i,aq}=0.500$ M, $[PhCOCl]_{i,org}=0.0500$ M, $[PNO]_{i,aq}=6.00\times10^{-4}$ M, 18 °C, the yields of bis(mixed anhydride)s are greater than 90% for *trans*-$C_2H_2(COONa)_2$, *m*- and *p*-$C_6H_4(COONa)_2$ cases. In contrast, for Type-2 dicarboxylates a large yield of the mono(mixed anhydride) was obtained at low temperature and with PNO at high concentration for the *o*-$C_6H_4(COONa)_2$ case. Increasing the concentration of PhCOCl raises the yield of $(PhCO)_2O$ whereas it decreased the yield of mono(mixed anhydride). An effective IPTC catalyst, DMAP (4-dimethylaminopyridine)[11] is unfavorable for synthesis of mono(mixed anhydride).

II. Kinetic Tests. A. Comparison of Reac-

Table 2. Effects of Concentrations of PhCOCl and PNO on the Yields of the Bis(mixed anhydride)s[a)]

$R(COONa)_2$	$[PhCOCl]_{i,org}$	$[PNO]_{i,aq}$	$R(COOCOPh)_2$[d)]	$(PhCO)_2O$[e)]
	10^{-2} M	10^{-4} M	%	%
trans-$C_2H_2(COONa)_2$	0.5	6	62	5
	2.0	6	87	7
	5.0	6	90	10
	1.0	4	72	7
	1.0	3	66	8
	1.0	2	61	10
	1.0[b)]	2	66	9
	1.0[c)]	2	42	11
$(CH_2)_4(COONa)_2$	0.5	6	26	—
	2.0	6	49	2.2
	5.0	6	55	—
	1.0	4	29	1.9
	1.0	3	28	2
	1.0	2	23	2.4
	1.0[b)]	2	31	2.2
	1.0[c)]	2	16	2.6

a) $[R(COONa)_2]_{i,aq}=0.50$ M, 18 °C. b) 10 °C. c) 25 °C. d) Yield of $R(COOCOPh)_2=(2\times[R(COOCOPh)_2]_{org}/[PhCOCl]_{i,org})\times100\%$. e) Yield of $(PhCO)_2O=(2\times[(PhCO)_2O]_{org}/[PhCOCl]_{i,org})\times100\%$.

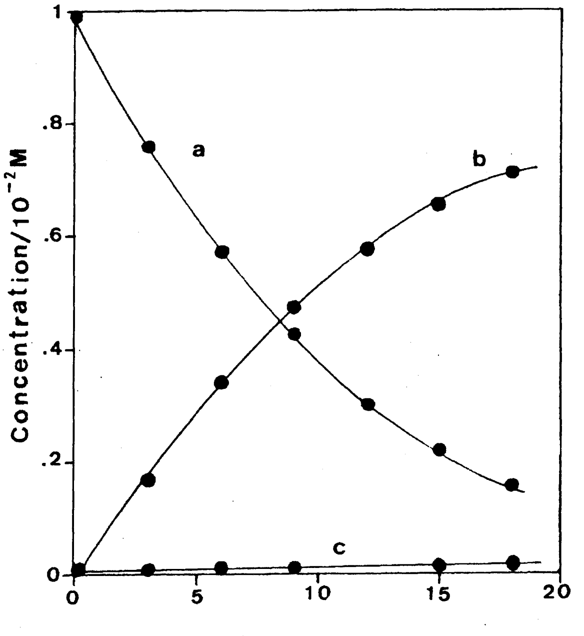

Fig. 3. Concentration vs. time curve for the PNO-catalyzed two-phase reaction of PhCOCl and m-$C_6H_4(COONa)_2$ (Type 3); $[m\text{-}C_6H_4(COONa)_2]_{i,aq}=0.500$ M, $[PNO]_{i,aq}=6.00\times10^{-4}$ M, $[PhCOCl]_{i,org}=0.0100$ M, 18 °C. a: PhCOCl, b: m-$C_6H_4(COOCOPh)_2$ (corrected), c: $(PhCO)_2O$ (corrected), $[m\text{-}C_6H_4(COOCOPh)_2]_{corrected}=2\times[m\text{-}C_6H_4(COOCOPh)_2]_{org}$, $[(PhCO)_2O]_{corrected}=2\times[(PhCO)_2O]_{org}$.

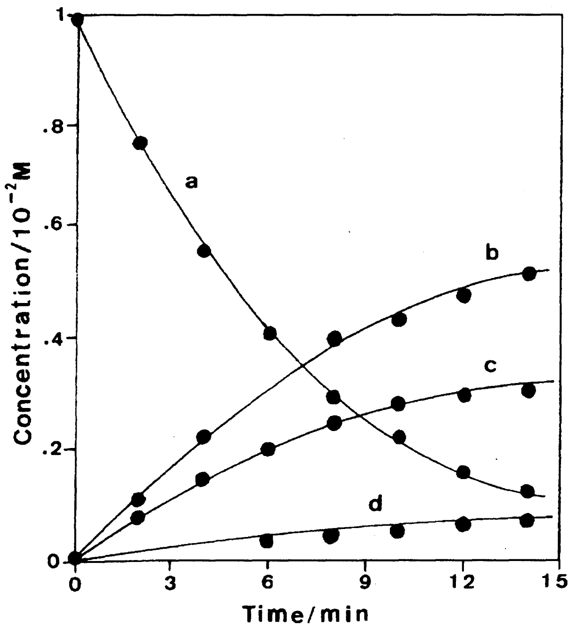

Fig. 4. Concentration vs. time curve for the PNO-catalyzed two-phase reaction of PhCOCl and m-$C_6H_4(COONa)_2$ (Type 4); $[(CH_2)_4(COONa)_2]_{i,aq}=0.500$ M, $[PNO]_{i,aq}=6.00\times10^{-4}$ M, $[PhCOCl]_{i,org}=0.0100$ M, 18 °C. a: PhCOCl, b: PhCOOH, c: $(CH_2)_4(COOCOPh)_2$(corrected), d: $(PhCO)_2O$ (corrected). $[(CH_2)_4(COOCOPh)_2]_{corrected}=2\times[(CH_2)_4(COOCOPh)_2]_{org}$, $[(PhCO)_2O]_{corrected}=2\times[(PhCO)_2O]_{org}$.

tivities of Dicarboxylate Salts. Based on the kinetic data,[14,19)] the reaction of PhCOCl with $PhCOO^-$ and CH_3COO^- ions catalyzed by PNO in a two-phase medium is the rate-determining step. Under appropriate reaction conditions, the rate equation is expressed as Eq. 3

$$-\frac{d[PhCOCl]_{org}}{dt}=k_{obsd}[PhCOCl]_{org} \qquad (3)$$

Table 3. Effects of Concentrations of PhCOCl and PNO on the Yields of the Bis(mixed anhydride)s a)

$R(COONa)_2$	$[PhCOCl]_{i,org}$	$[PNO]_{i,aq}$	$R(COOCOPh)_2$ d)	$(PhCO)_2O$ e)
	10^{-2} M	10^{-4}	%	%
m-$C_6H_4(COONa)_2$	0.5	6	78	—
	2.0	6	86	1.6
	5.0	6	90	2.7
	1.0	8	84	1.2
	1.0	4	81	1.4
	1.0	2	75	2.5
	1.0 b)	2	81	2.5
	1.0 c)	2	71	2.0
p-$C_6H_4(COONa)_2$	1.0	8	91	1.3
	1.0	4	87	1.7
	1.0	2	79	1.0
	1.0 b)	2	90	1.0
	1.0 c)	2	70	2.6
	5.0	6	96	3.2

a) $[R(COONa)_2]_{i,aq}$=0.50 M, 18 °C. b) 10 °C. c) 25 °C. d) Yield of $R(COOCOPh)_2=(2\times[R(COOCOPh)_2]_{org}/[PhCOCl]_{i,org})\times 100\%$. e) Yield of $(PhCO)_2O=(2\times[(PhCO)_2O]_{org}/[PhCOCl]_{i,org})\times 100\%$.

Table 4. Effects of Concentrations of PhCOCl, o-$C_6H_4(COONa)_2$ and PNO on the Yields of the Mono(benzoyloxycarbonyl)carboxylic Acid a)

$[PhCOCl]_{i,org}$	$[PNO]_{i,aq}$	$[o\text{-}C_6H_4(COONa)_2]_{i,aq}$	o-$C_6H_4(COOCOPh)COOH$	$(PhCO)_2O$ g)
10^{-2} M	10^{-4} M	M	%	%
0.2	6	0.5	82	4
0.5	6	0.5	83	8
1.0	6	0.5	77	10
2.0	6	0.5	74	20
3.0	6	0.5	70	30
1.0 b)	6	0.5	79	6
1.0 c)	12	0.5	82	5
1.0	12	0.5	79	6
1.0	2	0.5	69	20
1.0 d)	2	0.5	60	9
1.0 c)	2	0.5	73	9
1.0	2	0.1	49	22
1.0	4	0.1	55	19
1.0	6	0.1	61	22
0.5	2	0.5	76	12
2.0	2	0.5	65	24
5.0	2	0.5	53	46
10	2	0.5	40	60
20	2	0.5	32	68
50	2	0.5	20	80
1.0 e)	0	0.5	38	62
1.0 f)	0	0.5	34	66

a) 18 °C. b) 10 °C. c) 5 °C. d) 25 °C. e) $[DMAP]_{i,aq}=4.00\times10^{-5}$ M. f) $[DMAP]_{i,aq}=2.00\times10^{-4}$ M. g) Yield of $(PhCO)_2O=(2\times[(PhCO)_2O]_{org}/[PhCOCl]_{i,org})\times 100\%$.

in which $[PhCOCl]_{org}$ is the concentration of PhCOCl in the organic phase and k_{obsd} is a linear function of the initial concentration of PNO in the aqueous phase, i.e.

$$k_{obsd} = k_h + k_c[PNO]_{i,aq} \tag{4}$$

$[PNO]_{i,aq}$ is the initial concentration of PNO in the aqueous phase and k_h and k_c are uncatalyzed and catalyzed rate coefficients, respectively. The values of k_{obsd} and k_c (calculated from the linear plot of k_{obsd} vs. $[PNO]_{i,aq}$ (Fig. 5)) are presented in Table 5. The rate of the reaction of PhCOCl and $R(COO^-)_2$ ion catalyzed by PNO is always first-order with respect to either PhCOCl or PNO.

Table 5. Effects of Dicarboxylate Salts on Rate Constants of the PNO-Catalyzed Reaction of PhCOCl and $R(COONa)_2$ in a Two-Phase H_2O/CH_2Cl_2 Medium[m)]

$R(COONa)_2$	$k_{obsd}/10^{-3}$ min^{-1}					k_c
	$[PNO]_{i,aq}/10^{-4}$ M					M^{-1} min^{-1}
	2.00	3.00	4.00	6.00	8.00	
$(COONa)_2$	$(36.0)^{a)}$	—	$(68.1)^{a)}$	$(99.8)^{a)}$	—	$(160\pm1)^{a)}$
	$(27.9)^{b)}$	—	$(52.5)^{b)}$	$(70.7)^{b)}$	$(92.4)^{b)}$	$(106\pm4)^{b)}$
$CH_2(COONa)_2$	52.7	81.9	106	152	—	246±9
$(CH_2)_2(COONa)_2$	55.1	76.4	98.7	151	—	241±9
	$(40.6)^{c)}$	—	$(77.9)^{c)}$	$(109)^{c)}$	$(143)^{c)}$	$(169\pm4)^{c)}$
cis-$C_2H_2(COONa)_2$	59.0	82.3	107	151	—	230±4
trans-$C_2H_2(COONa)_2$	51.6	67.5	85.7	124	—	182±5
$(CH_2)_4(COONa)_2$	58.9	80.3	109	160	—	256±7
$(CH_2)_7(COONa)_2$	60.1	—	107	158	—	245±6
o-$C_6H_4(COONa)_2$	56.7	77.6	105	147	—	228±8
	$(41.3)^{c)}$	—	$(80.5)^{c)}$	$(112)^{c)}$	$(149)^{c)}$	$(177\pm5)^{c)}$
m-$C_6H_4(COONa)_2$	40.0	—	76.5	105	140	164±5
p-$C_6H_4(COONa)_2$	38.6	—	73.4	102	138	163±5

m) $[R(COONa)_2]_{i,aq} = 0.500$ M, $[PhCOCl]_{i,org} = 0.0100$ M, 18 °C. a) $[(COONa)_2]_{i,aq}=0.200$ M, $[NaNO_3]_{i,aq}=0.300$ M. b) $[(COONa)_2]_{i,aq}=0.100$ M. c) $[R(COONa)_2]_{i,aq}=0.100$ M, $[NaNO_3]_{i,aq}=0.400$ M.

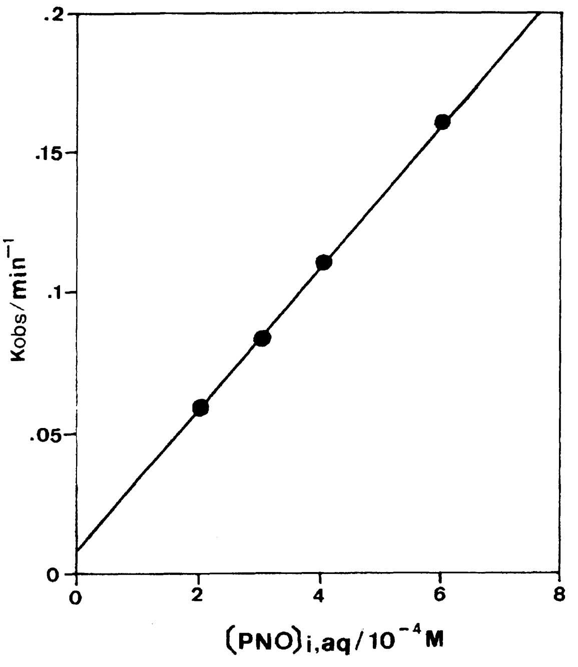

Fig. 5. Effect of PNO on the rate constant of the PNO-catalyzed two-phase reaction of PhCOCl and *cis*-$C_2H_2(COONa)_2$;$[PhCOCl]_{i,org}=0.0100$ M, [*cis*-$C_2H_2(COONa)_2]_{i,aq}=0.500$ M, 18 °C.

For sodium salts of ten dicarboxylic acids tested, the values of k_{obsd} and k_c were similar except for $(COONa)_2$, *trans*-$C_2H_2(COONa)_2$, *m*- and *p*-$C_6H_4(COONa)_2$. This observation does not support our prediction that the value of k_c is expected to be independent of the dicarboxylate ion in the aqueous phase if the rate-determining step takes place in the organic phase.

To explain this discrepancy, we measued the distribution of PNO between two phases. The results appear in Table 6. As shown in Tables 5 and 6, a good correlation between k_c and $[PNO]_{org}$ was obtained (Fig. 6); the k_c-value increased with increasing concentration of PNO in the organic phase. A large deviation from the trend was observed for the $(CH_2)_7(COONa)_2$ system due to the emulsion of the reaction solution.

B. Effect of Benzoyl Chloride. The effect of benzoyl chloride on the reaction is presented in Tables 7 and 8. The k_{obsd}-value decreased with increasing concentration of PhCOCl in the organic phase. Benzoyl chloride shows a significant inhibitive effect on its PNO-catalyzed hydrolysis reaction in the medium H_2O/CH_2Cl_2. For example, for $[NaNO_3]_{i,aq}=0.500$ M and $[PNO]_{i,aq}=6.00\times10^{-4}$ M, the k_{obsd}-values at 18 °C are 0.0288, 0.0195, and 0.00952 min^{-1} for $[PhCOCl]_{i,org}=0.0100$, 0.0200, and 0.100 M, respectively. In contrast, the effect of PhCOCl on its uncatalyzed hydrolysis reaction in a H_2O/CH_2Cl_2 medium is insignificant. For example, for $[PhCOO^-]_{i,aq}=0.500$ M, the k_{obsd}-values at 18 °C are 7.28×10^{-3} and 7.48×10^{-3} min^{-1} for $[PhCOCl]_{i,org}=0.0100$ and 0.100 M, respectively. This result indicates that the concentration of PNO in the organic phase decreased in the presence of PhCOCl.

III. Reaction Mechanism. Based on the above results, the mechanism of PNO-catalyzed reaction of PhCOCl and sodium dicarboxylate in a two-phase H_2O/CH_2Cl_2 medium appears in Scheme 1. The evidence of inverse phase transfer catalysis is that the intermediate produced by PhCOCl and PNO can be isolated as $(PhCOONP^+Cl^-)$, which can react with $PhCOO^-$ ion to produce the anhydride $(PhCO)_2O$. The reaction of PhCOCl and PNO in the organic phase

Table 6. Effects of Dicarboxylate Salts on the Distribution of PNO Species[a)]

$[PNO]_{i,aq}$ 10^{-4} M	10.0		4.0	
$R(COONa)_2$	$[PNO]_{org}$	$[PNOH^+]_{org}$	$[PNO]_{org}$	$[PNOH^+]_{org}$
	10^{-5} M	10^{-7} M	10^{-5} M	10^{-7} M
$(COONa)_2$	(4.43)[b)]	(0.889)[b)]	(1.73)[b)]	(0.340)[b)]
	(4.38)[c)]	(2.72)[c)]	(1.77)[c)]	(1.25)[c)]
$CH_2(COONa)_2$	5.83	3.93	2.33	0.486
$(CH_2)_2(COONa)_2$	5.84	6.02	2.40	9.41
	(4.46)[b)]	(0.772)[b)]	(1.80)[b)]	(0.123)[b)]
	(4.37)[c)]	(0.913)[c)]	(1.81)[c)]	(1.93)[c)]
cis-$C_2H_2(COONa)_2$	5.79	3.25	2.44	1.79
trans-$C_2H_2(COONa)_2$	5.20	5.88	2.09	9.70
$(CH_2)_4(COONa)_2$	5.73	2.60	2.31	0.190
$(CH_2)_7(COONa)_2$	4.98	1.16	2.01	4.37
o-$C_6H_4(COONa)_2$	5.32	3.07	2.20	5.03
	(4.29)[b)]	(3.62)[b)]	(1.75)[b)]	(2.72)[b)]
	(4.31)[c)]	(6.79)[c)]	(1.70)[c)]	(2.26)[c)]
m-$C_6H_4(COONa)_2$	3.96	4.02	1.61	1.12
	(4.06)[b)]	(5.73)[b)]	(1.64)[b)]	(3.04)[b)]
	(4.15)[c)]	(7.67)[c)]	(1.69)[c)]	(7.35)[c)]
p-$C_6H_4(COONa)_2$	3.79	1.16	2.01	4.37

a) $[R(COONa)_2]_{i,aq}$=0.500 M, 25 mL H_2O, 25 mL of CH_2Cl_2, 18 °C. b) $[R(COONa)_2]_{i,aq}$=0.100 M. c) $[R(COONa)_2]_{i,aq}$=0.100 M, $[NaNO_3]_{i,aq}$=0.400 M.

Table 7. Effects of PhCOCl and $R(COONa)_2$ on the PNO-Catalyzed Reaction of PhCOCl and $R(COONa)_2$ in a Two-Phase H_2O/CH_2Cl_2 Medium[m)]

	$k_{obsd}/10^{-3}$ min^{-1}				
$R(COONa)_2$	$[PhCOCl]_{org}/10^{-2}$ M				
	0.200	0.50	1.00	2.00	3.00
$(COONa)_2$	—	(112)[a)]	(99.8)[a)]	(85.9)[a)]	—
$CH_2(COONa)_2$	—	174	160	151	—
$(CH_2)_2(COONa)_2$	—	182	160	151	—
cis-$C_2H_2(COONa)_2$	—	167	151	142	—
trans-$C_2H_2(COONa)_2$	—	142	124	114	—
$(CH_2)_4(COONa)_2$	—	171	151	142	—
$(CH_2)_7(COONa)_2$	—	173	158	141	—
o-$C_6H_4(COONa)_2$	164	161	147	135	125
m-$C_6H_4(COONa)_2$	128	124	105	102	—
p-$C_6H_4(COONa)_2$	—	117	102	85.0	—

m) $[R(COONa)_2]_{i,aq}$=0.500 M, $[PNO]_{i,aq}$=6.00×10^{-4} M, 18 °C. a) $[(COONa)_2]_{i,aq}$ = 0.200 M, $[NaNO_3]_{i,aq}$=0.300 M.

Table 8. Effects of PhCOCl and Temperature on the PNO-Catalyzed Reaction of PhCOCl and *o*-$C_6H_4(COONa)_2$ in a Two-Phase H_2O/CH_2Cl_2 Medium[a)]

$[PhCOCl]_{i,org}$	$k_{obsd}/10^{-3}$ min^{-1}		
10^{-2} M	5 °C	18 °C	25 °C
0.500	29.8	60.7	77.0
1.00	28.4	56.7	74.4
2.00	27.1	54.6	73.9
3.00	26.6	—	66.0
4.00	25.4	—	65.5

a) $[o\text{-}C_6H_4(COONa)_2]_{i,aq}$=0.500 M, $[PNO]_{i,aq}$=2.00×10^{-4} M.

(reaction (O1)) is a rate-determining step for all reaction systems. Various reactions take place at the interface or in the aqueous phase for the various reaction systems.

For Type-1 dicarboxylates ($(COONa)_2$, $CH_2(COONa)_2$, $C_2H_4(COONa)_2$, and *cis*-$C_2H_2(COONa)_2$), the distance between two carboxylato groups is small and these dicarboxylates are soluble in water. If the main product (PhCOOH) came directly from the hydrolysis of $PhCOONP^+Cl^-$, the reaction rate is expected to be independent of the aqueous-phase reactant. However, a considerably larger reaction rate is observed when dicarboxylate salts are present in the aqueous phase. For example, for $[PNO]_{i,aq}$ = 6.00×10^{-4} M, $[PhCOCl]_{i,org}$ = 0.0100 M, the k_{obsd}-values at 18 °C are 0.152 and 0.0288 min^{-1} for $[CH_2(COONa)_2]_{i,aq}$=0.500 M, and $[NaNO_3]_{i,aq}$=0.500 M, respectively. Thus, sodium dicarboxylate enhances the hydrolysis of $PhCOONP^+Cl^-$ considerably. The reaction of $PhCOONP^+Cl^-$ and sodium dicarboxylate produces the mono(benzoyloxycarbonyl) compound $PhCOOCORCOO^-$ (reactions (A1)). For type-1 systems, $PhCOOCORCOO^-$ ion is very soluble in water

Organic-phase reactions

$$PhCOCl + PNO \rightleftharpoons PhCOONP^+Cl^- \tag{O1}$$

$$PhCOONP^+Cl^- + R(COOH)_2 \rightarrow PhCOOCORCOOH + PNOH^+Cl^- \tag{O2}$$

$$PhCOONP^+Cl^- + PhCOOCORCOOH \rightarrow R(COOCOPh)_2 + PNOH^+Cl^- \tag{O3}$$

$$PhCOONP^+Cl^- + PhCOOH \rightarrow (PhCO)_2O + PNOH^+Cl^- \tag{O4}$$

$$PhCOCl + R(COOH)_2 \rightleftharpoons PhCOOCORCOOH + HCl \tag{O5}$$

$$PhCOCl + PhCOOCORCOOH \rightleftharpoons R(COOCOPh)_2 + HCl \tag{O6}$$

Interface reactions

$$PhCOONP^+Cl^-_{(org)} + R(COO^-)_{2(aq)} \rightarrow PhCOOCORCOO^-_{(aq)} + PNO_{(aq)} + Cl^-_{(aq)} \tag{I1}$$

$$2PhCOONP^+Cl^-_{(org)} + R(COO^-)_{2(aq)} \rightarrow R(COOCOPh)_{2(org)} + 2PNO_{(aq)} + 2Cl^-_{(aq)} \tag{I2}$$

$$PhCOONP^+Cl^-_{(org)} \rightleftharpoons PhCOONP^+Cl^-_{(aq)} \tag{I3}$$

$$PhCOOCORCOOH_{(org)} \rightleftharpoons PhCOOCORCOOH_{(aq)} \tag{I4}$$

$$R(COOCOPh)_{2(org)} \rightleftharpoons R(COOCOPh)_{2(aq)} \tag{I5}$$

$$(PhCO)_2O_{(org)} \rightleftharpoons (PhCO)_2O_{(aq)} \tag{I6}$$

$$PhCOOH_{(org)} \rightleftharpoons PhCOOH_{(aq)} \tag{I7}$$

$$R(COOH)_{2(org)} \rightleftharpoons R(COOH)_{2(aq)} \tag{I8}$$

Aqueous-phase reactions

$$PhCOONP^+ + R(COO^-)_2 \rightarrow PhCOOCORCOO^- + PNO \tag{A1}$$

$$PhCOONP^+ + PhCOOCORCOO^- \rightarrow R(COOCOPh)_2 + PNO \tag{A2}$$

$$PhCOONP^+ + R(COO^-)_2 \rightarrow PhCOO^- + {}^-OOCRCOONP^+ \tag{A3}$$

$$PhCOOCORCOO^- + H_2O \rightarrow PhCOOH + HOOCRCOO^- \tag{A4}$$

$$PhCOONP^+ + H_2O \rightarrow PhCOOH + PNOH^+ \tag{A5}$$

$$2PhCOONP^+ + R(COO^-)_2 + H_2O \rightarrow (PhCO)_2O + R(COOH)_2 + 2PNO \tag{A6}$$

$$PhCOONP^+ + PhCOO^- \rightarrow (PhCO)_2O + PNO \tag{A7}$$

$$PhCOOH + OH^- \rightleftharpoons PhCOO^- + H_2O \tag{A8}$$

$$R(COOH)_2 + OH^- \rightleftharpoons HOOCRCOO^- + H_2O \tag{A9}$$

$$HOOCRCOO^- + OH^- \rightleftharpoons R(COO^-)_2 + H_2O \tag{A10}$$

$$PhCOOCORCOO^- + H_2O \rightleftharpoons PhCOOCORCOOH + OH^- \tag{A11}$$

Scheme 1.

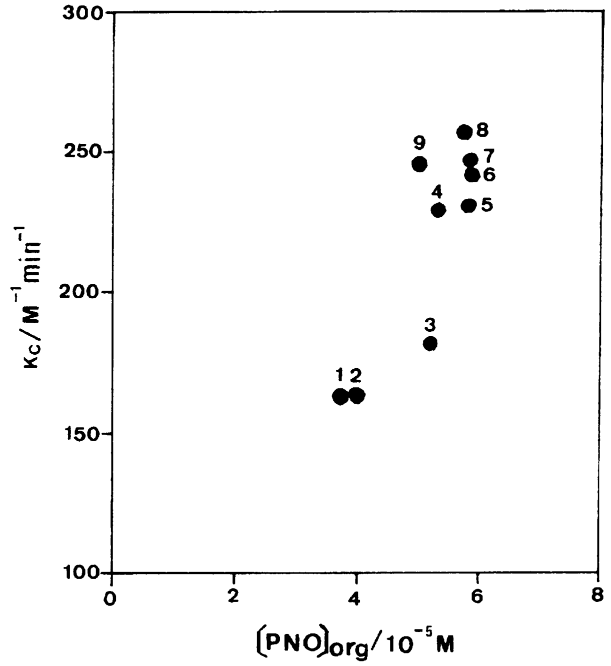

Fig. 6. Correlation between k_c and $[PNO]_{org}$ for the PNO-catalyzed two-phase reaction of PhCOCl and $R(COONa)_2$. For k_c measurement: $[PhCOCl]_{i,org} = 0.0100$ M, $[PNO]_{i,aq} = (2—8)\times10^{-4}$ M, $[R(COONa)_2]_{i,aq} = 0.500$ M, 18 °C. For $[PNO]_{org}$ measurement: $[PNO]_{i,aq} = 1.00\times10^{-3}$ M, $[R(COONa)_2]_{i,aq} = 0.500$ M, 18 °C. 1. *p*-$C_6H_4(COONa)_2$; 2. *m*-$C_6H_4(COONa)_2$; 3. *trans*-$C_2H_2(COONa)_2$; 4. *o*-$C_6H_4(COONa)_2$; 5. *cis*-$C_2H_2(COONa)_2$; 6. $(CH_2)_2(COONa)_2$; 7. $CH_2(COONa)_2$; 8. $(CH_2)_4(COONa)_2$; 9. $(CH_2)_7(COONa)_2$.

and distributes mainly in the aqueous phase. In general, the unsymmetric acid anhydride is relatively unstable and decomposes rapidly by acid or base catalyst.[20,21] Thus, for Type 1 systems, PhCOOH can be generated by reactions (A3), (A4), and (A5).

Because bis(mixed anhydride) was not observed, reaction (A2) is negligible for Type-1 systems. However, the amount of $(PhCO)_2O$ produced exceeded that of the blank reaction system without sodium dicarboxylate in the aqueous phase. As shown in Fig. 1, $(PhCO)_2O$ gradually accumulated during the reaction. Reactions that produced $(PhCO)_2O$ include reactions (O4), (A6), and (A7). Ion-pair formation and rearrangement reactions are considered to be operating in reaction (A6).

For a Type-2 dicarboxylate system such as *o*-$C_6H_4(COONa)_2$, a large steric effect is expected and it is difficult to produce a bis(mixed anhydride). The main product *o*-$C_6H_4(COOCOPh)(COOH)$ in the organic phase is produced in reactions (A1), (A11), and (I4) because its solubility in the organic phase is greater than that of PhCOOCORCOOH of Type-1 system. Another main product $(PhCO)_2O$ is generated in reactions (O4), (A6), and (A7). The minor product PhCOOH is produced in reactions (A3), (A4), and (A5). As presented in Table 4, the yields of o-$C_6H_4(COOCOPh)(COOH)$ and $(PhCO)_2O$ depend greatly on the concentrations of PhCOCl and PNO. The yield of o-$C_6H_4(COOCOPh)(COOH)$ is favored on decreasing the PhCOCl concentration and increasing the PNO concentration. In contrast with o-$C_6H_4(COOCOPh)(COOH)$, PhCOCl, and PNO show opposite effects on the yield of $(PhCO)_2O$.

For Type-3 dicarboxylate systems (*trans*-$C_2H_2(COONa)_2$, *m*- and *p*-$(C_6H_4(COONa)_2)$), the main product was the bis(benzoyloxycarbonyl) compound $R(COOCOPh)_2$. No induction period was observed for the appearance of $R(COOCOPh)_2$. Possible reactions to generate $R(COOCOPh)_2$ include reactions (O3), (A2), and (I2). Because of the small concentration of PhCOOCORCOOH, reaction (O3) is negligible. As the concentration of $R(COO^-)_2$ ion (0.5 M) in the aqueous phase was much greater than that of $PhCOOCORCOO^-$ ion, the probability of forming $R(COOCOPh)_2$ through reaction (A2) is minute. The possibility of transfer of PhCOOCORCOOH from aqueous phase to organic phase to react with PhCOCl via reaction (O6) is also negligible beacuse of the small reactivity of PhCOCl with RCOOH. The fact that $R(COOCOPh)_2$ appears at an early stage of the reaction strongly indicates that interface reaction (I2) plays an important role to produce $R(COOCOPh)_2$ for a Type-3 dicarboxylate system. For these dicarboxylates, the distance between two carboxylate groups is relatively large and their structures are rigid due to the presence of a C=C double bond or benzene ring. The solubility of $R(COONa)_2$ in water is also small. Therefore, it is easier to arrange the $R(COO^-)_2$ ion in an ordered array at the interface, which is suitable for reaction (I2) to take place.

In the past, most research on uncatalyzed two-phase reactions emphasized interface reactions.[22,23] Makosza[24] first proposed the interface reaction in a PTC reaction, but it was not proved by experiment. In this work, we observed that the bis(mixed anhydride) appeared at an early stage of the reaction for the Type-3 dicarboxylate systems. This experimental evidence strongly indicates that the reaction takes place at the interface.

A wide distribution of products was found for Type-4 dicarboxylate systems ($(CH_2)_4(COONa)_2$ and $(CH_2)_7(COONa)_2$). The carbon chain of $(CH_2)_7(COONa)_2$ is long and the solubility in water is small. It behaves like a surfactant at the interface. Therefore, the reaction takes place mainly at the interface (reaction (I2)) with the 1,7-bis(benzoyloxycarbonyl)heptane ($(CH_2)_7(COOCOPh)_2$) as the main product. The observed minor products were $(CH_2)_7(COOCOPh)(COOH)$, PhCOOH and $(PhCO)_2O$. The carbon chain of $(CH_2)_4(COONa)_2$ is intermediate between those of $(CH_2)_2(COONa)_2$ (Type 1) and $(CH_2)_7(COONa)_2$. Therefore $(CH_2)_4(COOCOPh)_2$, PhCOOH, and $(PhCO)_2O$ were the main products. A minor amount of $(CH_2)_4(COOCOPh)(COOH)$ was also produced.

Conclusion

The reaction of benzoyl chloride (PhCOCl) and dicarboxylate salts ($R(COONa)_2$) in a two-phase medium H_2O/CH_2Cl_2 using pyridine 1-oxide (PNO) as inverse phase transfer catalyst (IPTC) was investigated. The intermediate 1-(benzoyloxy)pyridinium chloride may react with $R(COONa)_2$ either at the interface or in the aqueous bulk phase to produce the mono- or bis(mixed anhydride), $(PhCO)_2O$, PhCOOH, depending on the molecular structure of the dicarboxylate ion. Dicarboxylates of four types were classified according to the distribution of products. The reaction rate was strongly affected by PhCOCl and $R(COONa)_2$ because of their influence on the distribution of PNO in the organic phase.

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