deoxynucleosides to be reported. The N^6-labeled derivative requires five steps, while the N^1-labeled compound requires eight steps. Moreover, the lowest yield reactions are all carried out before introduction of ^{15}N. Each of the reactions carried out after introduction of the ^{15}N label proceed in high yield. The reactions themselves, and the purification steps, are all straightforward and amenable to synthesis of adequate amounts of material for subsequent incorporation into synthetic oligonucleotides where the ^{15}N label can be used as a ^{15}N NMR probe.[15]

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Supplementary Material Available: Experimental section for **6c**, **4a**, **2b**, and **9b** and comparison ^{1}H NMR spectra of **1a** with **4a** and **9a** (6 pages). Ordering information is given on any current masthead page.

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Inverse Phase-Transfer Catalysis: Probing Its Mechanism with Competitive Transacylation

Wilmer K. Fife* and Yue Xin[1]

Department of Chemistry
Indiana University-Purdue University at Indianapolis
Indianapolis, Indiana 46223

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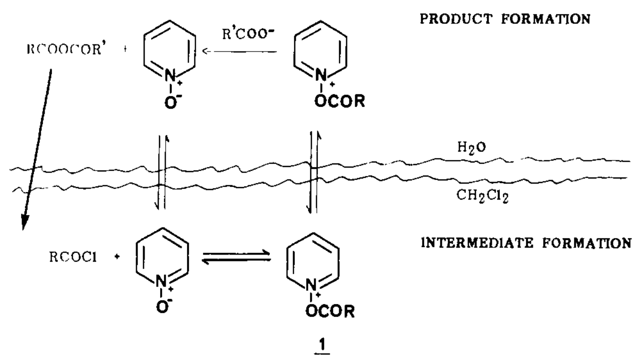
The utility of two-phase water–organic solvent media for organic synthesis is widely recognized. Nearly all reported examples of this methodology involve transport of a reactant from the water phase into the organic phase where it encounters a second reactant to effect reaction. This process commonly known as phase-transfer catalysis (PTC) is the subject of numerous reports and reviews.[2-5] The literature includes a few examples of a complementary synthetic procedure in which an organic solvent soluble reagent is activated by conversion to an ionic intermediate and transported to the aqueous phase for reaction.[6-9] The recent report by Mathias and Vaidya describes a new example of this virtually unexplored methodology, which they have named inverse phase-transfer catalysis (IPTC).[9]

We report here some preliminary results from our continuing investigation[10,11] of multiple-phase systems as media for organic reactions which provide significant new insight into the IPTC process. The reaction in Scheme I requires a nucleophilic phase-transfer agent/catalyst, and results indicate that pyridine 1-oxide (PNO) is a highly effective catalyst in this process. This anhydride-forming procedure provides a powerful, yet simple probe for investigating the nature of inverse phase-transfer catalysis. The presumed intermediate is the 1-(acyloxy)pyridinium ion, **1**. This ion and the related 1-acyl-4-(dimethylamino)pyridinium ion, **2**, form readily in the organic phase by reaction between acid chlorides and PNO[6,8] or 4-(dimethylamino)pyridine (DMAP),[12,13] eq 1. These ions are highly water soluble and sufficiently stable

Scheme I



Scheme II

$$\text{PhCOCl (org)} \xrightarrow[-2\,\text{NHEt}_3^+\ \ -\text{Cl}^-]{\text{H}_2\text{O, NEt}_3} \text{PhCOO}^-\text{ (org)} \xrightarrow[-\text{Cl}^-]{\text{PhCOCl}} \text{PhCOOCOPh (org)}$$

$$\text{Me}_2\text{CHCOO}^-\text{(aq)} \not\rightleftharpoons \text{Me}_2\text{CHCOO}^-\text{ (org or interphase)}$$

$$\text{4-MePhCOO}^-\text{(aq)} \rightleftharpoons \text{4-MePhCOO}^-\text{ (org or interphase)}$$

$$\text{PhCOCl (org)} + \text{4-MePhCOO}^-\text{ (org or interphase)} \longrightarrow \text{4MePhCOOCOPh (org)}$$

that reaction with carboxylate ions can be carried out in water. In fact, reaction mixtures may include the reactive acylating ion and two or more carboxylate ions, eq 2. If reaction between these

$$\text{RCOCl} + \text{Nu} \xrightarrow[\text{CH}_2\text{Cl}_2]{} \text{RCO}\overset{+}{\text{Nu}}\ \text{Cl}^- \qquad (1)$$

$$\begin{matrix} \textbf{1},\ \text{Nu} = \text{PNO} \\ \textbf{2},\ \text{Nu} = \text{DMAP} \end{matrix}$$

$$\underset{\textbf{1}}{\text{RCO}\overset{+}{\text{Nu}}} + \begin{matrix} \text{4-MePhCOO}^- \\ \text{Me}_2\text{CHCOO}^- \end{matrix} \xrightarrow[\text{H}_2\text{O}]{} \begin{matrix} \text{4-MePhCOOCOR} \\ \text{Me}_2\text{CHCOOCOR} \end{matrix} + \text{Nu} \qquad (2)$$

oppositely charged ions is occurring exclusively in the aqueous phase, product formation is expected to be statistically controlled.[14,15] Thus, the composition of product mixtures should reflect the relative concentrations of the carboxylate ions. This prediction has been verified by treating preformed acylating agent, **1** (R = phenyl), with varying proportions of sodium *p*-toluate and

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(11) Two-phase experiments were carried out in either a separatory funnel or a round-bottomed flask with Teflon-coated spin bar and magnetic stirrer. Reaction mixtures containing 2.58 mmol of benzoyl chloride, 1.0 equiv. each of sodium *p*-toluate, sodium isobutyrate, and catalyst/phase-transfer agent in 15 mL of water–15 mL of dichloromethane were mixed vigorously for 1.0 min at ~22 C. Reaction mixtures containing 0.10 equiv of catalyst were stirred vigorously for 10 min. Products were isolated by separating the dichloromethane layer followed by washing with 2.0 M hydrochloric acid and then 10% aqueous potassium carbonate, drying over anhydrous magnesium sulfate, and evaporating to constant weight.

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Table I. Effect of Catalyst and Reaction Medium on Benzoylation of *p*-Toluate Ion-Isobutyrate Ion Mixtures[a]

equivalent of catalyst	reaction medium	anhydride[b] total yield, %	products, mole fraction[c]		
			p-MePhCOOCOPh	$Me_2CHCOOCOPh$	PhCOOCOPh
		Catalysis by PNO[d]			
1.0	H_2O	79	0.50	0.50	0.00
1.0[e]	H_2O	73	0.66	0.34	0.00
1.0[f]	H_2O	81	0.33	0.67	0.00
0.1	H_2O/CH_2Cl_2	69	0.68	0.32	0.00
1.0	H_2O/CH_2Cl_2	84	0.58	0.42	0.00
		Catalysis by DMAP[d]			
1.0	H_2O	52	0.85	0.15	0.00
0.1	H_2O/CH_2Cl_2	64	0.92	0.08	0.00
1.0	H_2O/CH_2Cl_2	35	1.00	0.00	0.00
1.0[g]	H_2O/CH_2Cl_2	50	0.88	0.12	0.00
		Catalysts by TEA[d]			
1.0	H_2O	60	0.52	0.00	0.48
0.1	H_2O/CH_2Cl_2	65	0.67	0.00	0.33
1.0	H_2O/CH_2Cl_2	69	0.63	0.00	0.37

[a] Reaction conditions and workup procedure are described in ref 11 and 16. [b] Reaction mixtures also contained mixtures of carboxylic acids (excess reactants and hydrolysis products). [c] Composition of product mixtures was estimated by integration of ^1H NMR spectra of isolated materials. Signals used for anslysis: δ 2.4, s (Me-Ph); 1.3, d (Me_2CH-). Repeatability based on three or more experiments: ±2%. [d] PNO = pyridine 1-oxide; DMAP = 4-(dimethylamino)pyridine; TEA = triethylamine. [e] Reactants included 2.0 equiv of sodium *p*-toluate and 1.0 equiv of sodium isobutyrate. [f] Reactants included 1.0 equiv of sodium *p*-toluate and 2.0 equiv of sodium isobutyrate. [g] Reaction time was 10 s.

sodium isobutyrate in aqueous solution.[16] The results summarized in Table I show that product ratios correspond closely to ratios of reactant carboxylate ion concentrations.

Similar experiments[11] carried out in two-phase mixtures of dichloromethane-water furnished contrasting and especially revealing results, Table I. Reaction mixtures containing equimolar quantities of benzoyl chloride, sodium *p*-toluate, and sodium isobutyrate gave anhydride mixtures that contained somewhat more benzoic *p*-toluic anhydride than benzoic isobutyric anhydride when PNO was used as catalyst. Product composition was found to depend on catalyst concentration. A catalytic amount of PNO (0.10 equiv) gave a higher ratio of benzoic p-toluic anhydride to benzoic isobutyric anhydride than a stoichiometric amount of catalyst.[17] Similar reactions catalyzed by DMAP gave somewhat smaller yields of benzoic *p*-toluic anhydride but little or no benzoic isobutyric anhydride. Surprisingly, catalysis by triethylamine (TEA) led to product mixtures that included benzoic anhydride as well as the expected benzoic *p*-toluic anhydride. However, the second expected product, benzoic isobutyric anhydride, could not be detected.

The results obtained under two-phase conditions are consistent with reaction between either **1** or **2** and carboxylate ion both in the bulk aqueous phase and at the water-organic solvent interface where concentrations of the more lipophilic *p*-toluate ion are expected to be greater than those of the smaller, more hydrophilic isobutyrate ion. DMAP appears to function in much the same fashion as PNO, except **2** is either much more selective with carboxylate ions than **1** or anhydride products, particularly benzoic isobutyric anhydride, are unstable in the reaction mixtures that contain DMAP. In control experiments, DMAP has been shown to catalyze rapid hydrolysis of benzoic isobutyric anhydride, but hydrolysis of benzoic *p*-toluic anhydride occurs much more slowly.[18] Reactions catalyzed by TEA appear to be more typical of PTC processes with reaction occurring in the organic phase. TEA is believed to function as a general base to accelerate hydrolysis of benzoyl chloride, and the benzoate ion so formed remains in the organic phase to produce symmetrical anhydride by reaction with benzoyl chloride, Scheme II.[19,20] The mixed anhydride, benzoic *p*-toluic anhydride, is believed to form at the interface or in the organic layer after phase transfer of the more lipophilic *p*-toluate ion. Apparently, the more hydrophilic isobutyrate ion remains isolated in the aqueous layer.

From the above results, we conclude that inverse phase-transfer catalysis like phase-transfer catalysis includes an interphase component as evidenced by selective transport of the more lipophilic p-toluate ion at the dichloromethane-water interface. The results from more extensive studies currently in progress will be reported fully in due course.

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(16) Reactive intermediates, **1** and **2**, were produced with PNO or DMAP and 1.0 equiv of benzoyl chloride in dichloromethane. For reactions run in water, the dichloromethane was removed by evaporation, and the residues were treated, unless otherwise noted, with aqueous solutions containing 1.0 equiv of sodium *p*-toluate and 1.0 equiv of sodium isobutyrate for 1.0 min at ~22.0 °C.

(17) The experiments that used 1.0 equiv of catalyst (Table I) represent an extreme case scenario in which formation of 1.0 equiv of acylating ion, **1** or **2**, is expected to maximize the possibility for reaction in the bulk aqueous phase.

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Unexpected Diversity in the Coordination Chemistry of Tartrate Esters with Titanium(IV)

Steven F. Pedersen,[1a] John C. Dewan,[1a]
Richard R. Eckman,[1b] and K. Barry Sharpless*[1a]

Department of Chemistry, Massachusetts Institute of
Technology, Cambridge, Massachusetts 02139
Exxon Chemical Company, Baytown, Texas 77520

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Our interest in the structural[2] and mechanistic[3] aspects of the titanium-catalyzed asymmetric epoxidation reaction has led us to undertake a more general investigation of the solution and solid-state properties of titanium tartrate ester complexes. One of the most intriguing features of titanium tartrate reaction chemistry, beyond the standard asymmetric epoxidation system, is the number of other asymmetric oxidation reactions that have

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