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Synergetic effect of tetrabutylammonium bromide and polyethylene glycol as phase transfer catalysts in third liquid phase for benzyl-*n*-butyl ether synthesis

Gong Jin[1], Cuifang Zhang[2], Tadaatsu Ido,[3] and Shigeo Goto[3]

[1]*The Dow Chemical Company (Shanghai), Suite 1101, Shui On Plaza, 333 Huai Hai Zhong Road, Shanghai 200021, China*
[2]*Japan Shin Shin Computer System (Shanghai), Co. Ltd., Building 61, 421 Plaza, Hong Cao Road, Shanghai 200233, China*
[3]*Department of Chemical Engineering, Nagoya University, Chikusa, Nagoya 464-8603, Japan*

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This study intends to clarify the forming characteristics of third liquid phase in phase transfer catalytic system in the presence of *n*-butanol and potassium hydroxide when tetrabutylammonium bromide, polyethylene glycol and their mixture serve as phase transfer catalyst, respectively. At 323 K, the three catalytic systems were applied to yield benzyl-*n*-butyl ether from benzyl chloride and *n*-butanol, and they performed distinct reaction activity. Among them, a combination of two kinds of catalyst results in a synergetic effect in reaction activity.

KEY WORDS: chemical reaction; phase transfer catalyst; third liquid phase.

1. Introduction

As the chemical industry strives to improve process efficiency, safety and reduce environmental impact, phase transfer catalysis (PTC) has found it way to be recognized as a strong weapon to achieve these goals.

The PTC methodology involves a substrate (which is soluble in the organic bulk) and a reagent (which is dissolved in the aqueous bulk). The substrate and the regent are then brought together by a catalyst, which transports the regent into the organic phase where reaction can take place with the substrate.

There are several advantages of the PTC system over single-phase systems, such as:an increased reaction rate, a lower reaction temperature, avoiding the need for expensive anhydrous or aprotic solvents, the use of water together with an organic solvent as reaction medium [1].

However, one of the primary drawbacks of a traditional liquid–liquid PTC is that the separation and recovery of the catalyst from the products and organic are hardly achieved [2]. One strategy to remove this obstacle is to build up a catalyst-rich third phase which could be attained under certain conditions. The third phase usually contains a high concentration of catalyst, accompanied by some water and organic solvent. This is not only improves the chances for recovery of the PTC but also, as a welcome consequence, owing to the high concentration of the catalyst and reactants in the third phase, the observed overall reaction rate increases dramatically once the third liquid is formed. [3–6].

Normally, quaternary ammonium salts with their unique capability to dissolve in both aqueous and organic liquids are the catalysts of choice for most phase transfer applications. Other phase transfer catalysts include phosphonium salts, crown ethers and polyethylene glycols (PEGs). Among them, PEG and their many derivates have been attracting attentions as they are inexpensive, thermally stable in presence of strong bases, and usually easy to remove and recover, nontoxic, easily biodegradable, and universal available [1].

A few examples in the literature investigating halogen exchange, dehydrohalogenation, alkoxylation, asymmetric- and symmetric-ether synthesis reactions by means of third liquid technique [4–9]. Almost all the efforts focused on applying one kind of PTC. However, in two phase system, some attentions have been given to dual-PTC technique in order to enhance reaction rates, to improve selectivity or to decrease the need for excess salts in the aqueous phase [1]. In three liquid phase system, we had firstly come up with a mixture of PTC in term of quaternary ammonium and PEGs, which bring in a synergetic effect when catalyzing a reaction of dehydrohalogenation of 2-bromooctane. Surely, that system was relatively simple as no *n*-butanol involved [6].

The present research devotes particular attention on a one step Williamson synthesis by means of PTC technique at 323 K. We attempted to clarify the forming characteristics of third liquid phase in PTC system in the presence of *n*-butanol and potassium hydroxide when tetrabutylammonium bromide, PEG and their mixture serve as phase transfer catalyst, respectively. Then, the

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*To whom correspondence should be addressed.

three catalytic systems were applied to yield benzyl-*n*-butyl ether from benzyl chloride and *n*-butanol in order to evaluate their catalytic activity.

Dodecane is used as an organic solvent, and tetrabutylammonium bromide ((Bu)4NBr) and PEG (with molecular weight of 3000) serve as PTC, while the polar phase was made up of water with a varying potassium hydroxide.

The PTC reaction is represented by the reaction

$$C_6H_5CH_2Cl + C_4H_9OH \xrightarrow[\text{PTC with } OH^-]{} C_6H_5CH_2\text{–}O\text{–}C_4H_9 + HCl \qquad (1)$$

2. Experimental

2.1. Catalysts and reagents

Tetrabutylammonium bromide ((Bu)4NBr) and PEG with the molecular weight of 3000 (abbreviated as PEG3000) were utilized as phase transfer catalysts. All chemicals with GR grade were commercially available ((Bu)4NBr purchased from Aldrich Chemical Company, Inc and other reagents from Wako Pure Chemical Industries, Ltd) and used without any purification

2.2. Determination of third-phase volume

These experiments were conducted as the same way as the previous study [5].

2.3. Kinetic measurements

A stirred tank batch reactor at a constant temperature of 323.15 K was used as described elsewhere [5], except for adding *n*-decane as an internal standard. The initial volume of both organic and aqueous bulks was 50 cm^3.

3. Results and discussion

3.1. Formation and volume feature of the third liquid phase in three systems

In all systems involved in this study, dodecane served as the organic solvent in the presence of *n*-butanol, which varied in range of 0–1000 mol/m^3-org. Meanwhile, the polar phase was made up of water with a varying concentration of potassium hydroxide (KOH) in range of 0–1.76 × 10^4 mol-KOH/m^3-aq. KOH concentration was converted to a dimensionless expression for convenience (ξ_{KOH}), it equals to unity when the aqueous bulk is saturated with KOH (1.76 × 10^4 mol-KOH/m^3-aq).

Forming and volume varying characteristics of the third liquid phase associated with three systems in terms of (Bu)4NBr alone, PEG3000 alone, as well as a mixture of the above two species were investigated, respectively.

3.1.1. In (Bu)4NBr alone system

Previous studies [4–8] indicated for fixed non-polar organic solvent, temperature, catalyst and its concentration, another of the most critical factor affecting formation of third liquid phase would be inorganic salt concentration in the aqueous bulk. This could be understood in the following way if we take (Bu)4NBr as an example. (Bu)4NBr dissolves in water originally, but segregated from aqueous phase in the form of (Bu)4NBr or (Bu)4N-OH when KOH amount exceeds a certain value for the sake of weak hydrophilic nature of (Bu)4NBr comparing to that of KOH. However, the segregated species are insoluble in non-polar organic bulk of dodecane. Consequently, it has no way to go but staying at somewhere of the system. Due to its intermediate in density, it builds up at the interface between aqueous and organic bulk. Apparently, in order to create a third phase, the solubility of PTC must be sufficiently low in both of the polar and the organic bulk.

In the current study, however, the scenario becomes much more complicated owing to coexisting of *n*-butanol, dislike the performance of 2-bromooctane in previous study [5,6], beyond being a reactant, this species affecting the nature of organic- and third phase. Figure 1 depicts the attributes in term of the formation and volume of third liquid phase as a function of ξ_{KOH} at different level of *n*-butanol concentration (0–1000 mol/m^3-org) for (Bu)4NBr alone system.

A case of the absence of *n*-butanol (refer to as the base curve) was also included for comparison. For this curve, in the range of $0 < \xi_{KOH} < 0.2$, as all of the (Bu)4NBr dissolved in aqueous bulk, the system appears as dual-phases. In $0.2 < \xi_{KOH} < 0.4$, as KOH condensed, resulted in salted out effect of (Bu)4NBr, then the system turns to three-phases. In $0.4 < \xi_{KOH} < 0.57$, the third phase volume keeps constant, this implies nearly all amount of (Bu)4NBr in the system containing in the third phase already from $\xi_{KOH} = 0.4$, therefore, the

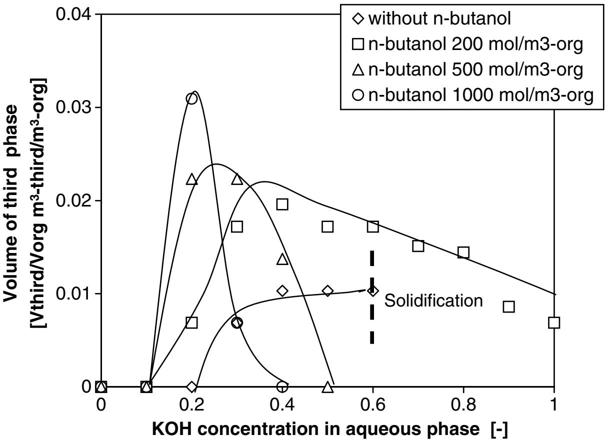

Figure 1. Volume of third phase as a function of KOH concentration in aqueous phase at different *n*-butanol level $(Bu)_4NBr$: 30 mol/m^3-org.

volume varied in a fairly small range which is hardly measured. Nevertheless, further increase in ξ_{KOH} will result in an unique phenomenon, the place of third liquid phase substituted by a solid one. The solidification phenomena were also observed by Mason *et al.* and ourselves previously [5,8,10]. The answer to this puzzle lies in the composition of the third phase. If the base becomes very concentrated, it dehydrates the catalyst phase (third phase), causing its destabilization and precipitation of catalyst. Our studies validated this explanation by determining the water concentration in the third phase [8].

In figure 1, the other three curves indicate third phase volume varies significantly if *n*-butanol exists. In all the three cases, the third phase are observed from $\xi_{KOH} > 0.1$, but proceeded in distinct trend.

In case of 200 mol/m^3-org of *n*-butanol, once the third phase formed, it runs through the whole range until to $\xi_{KOH} = 1.0$. However, on passing from 500 to 1000, the third phase vanished in case $\xi_{KOH} > 0.5$ and $\xi_{KOH} > 0.4$, respectively.

Note the maximum of third phase volume keeps on going up with the amount of the *n*-butanol. Meanwhile, no solidification was observed if *n*-butanol exists within the investigated range. The two facts suggest the third phase containing *n*-butanol, and which take the role of water in the third phase in despite of dehydration happened in higher ξ_{KOH}. For the same reason, the maximum volume associated with third liquid phase increase with the amount of *n*-butanol added to the system.

In contrary to the volume, with the amount of *n*-butanol added, vanishing point in term of ξ_{KOH} decreased. It could be explained as following. Generally, *n*-butanol disperses among aqueous, third liquid and organic phase. Solubility of *n*-butanol in water is less than 7.8% by weight, and this value should be limited largely due to KOH existence in water. With the added amount increasing, fraction of *n*-butanol existing in both organic and third phase goes up. The addition of *n*-butanol increase the solubility of (Bu)4NBr in the organic phase. A similar study carried out by Holger *et al.* illustrated that in addition of hexanol or octanol increased the solubility of benzyltributylammonium chloride in organic solvent, which was virtually no solubility original [11]. We consider it is the fact indeed the case here, with addition of *n*-butanol, the third phase dissolved in organic bulk and the third phase disappeared thoroughly.

3.1.2. In PEG3000 alone system

The volume of third phase as a function of ξ_{KOH} is depicted in figure 2. The lower curve present the case in the absent of *n*-butanol, which shaped in the same way as did of (Bu)4NBr, the solidification occurred in range of $\xi_{KOH} > 0.55$. Unlike (Bu)4NBr, no solidification was observed and the volume increases with the amount of *n*-butanol. This implies the mechanism associated with (Bu)4NBr and PEG is distinct from each other. This is in fact indeed the case. PEG as phase transfer catalyst has rings such as crown ether [12] while the ammonium salt does not have this structure. The crown-like rings do dissolve in neither dodecane nor dodecane with *n*-butanol, keeping the third phase in its original form.

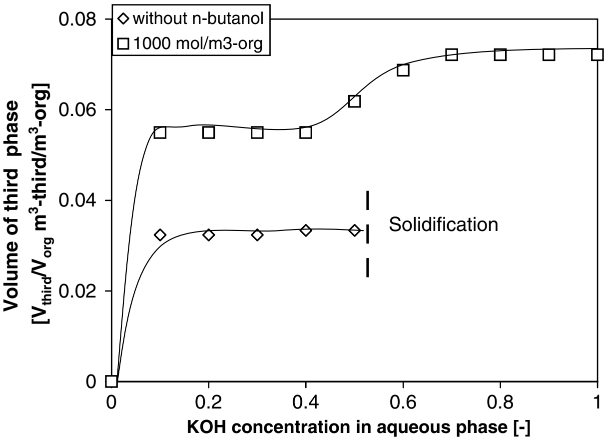

Figure 2. Volume of third phase as a function of KOH concentration in aqueous phase at different *n*-butanol lever for PEG 3000 PEG3000 : 10 mol/m^3-org.

3.1.3. In (Bu)4NBr and PEG3000 combination system

Figure 3 shows the effect of ξ_{KOH} on the volume of the third phase with the presence of *n*-butanol in the combination of (Bu)4NBr and PEG3000.

In this case, the volumes of the third phase increase with the amount of *n*-butanol. The volume in the combination is larger than that of either (Bu)4NBr or PEG3000 alone. These results suggest that the third phase contains (Bu)4NBr, which is not extracted to the organic phase but dissolved in the third phase when the

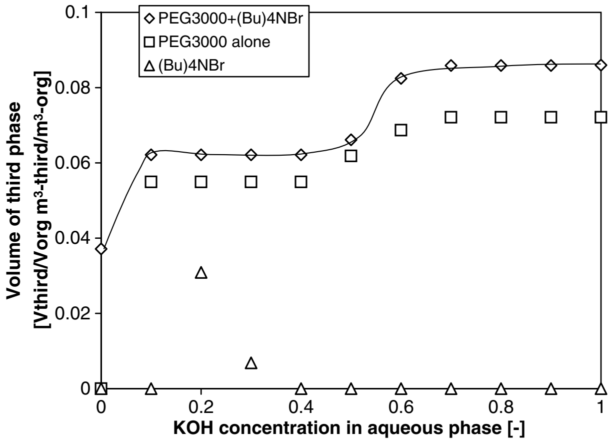

Figure 3. Volume of third phase as a function of KOH concentration in aqueous phase at different *n*-butanol lever for combination of (Bu)$_4$NBr and PEG 3000 PEG3000 : 10 mol/m^3-org, (Bu)$_4$NBr : 30 mol/m^3-org.

third phase of PEG3000 is present. This could be explained as affinity between PEG and (Bu)4NBr is stronger enough, no matter how the concentration of *n*-butanol in the organic phase.

3.2. Reaction characteristics in three systems

Catalytic activity associated with the above three systems was determined by putting the synthesis reaction from benzyl chloride and *n*-butanol into operation. We will first consider the cases where the reaction are promoted by (Bu)4NBr alone in a two phase system, followed by PEG3000 alone in a three phase system, then compare these results to a combination effect of the two species.

3.2.1. Reaction in (Bu)4NBr alone system

The reaction was carried out by (Bu)4NBr at $\xi_{\mathrm{KOH}} = 1.0$. Equal concentrations of benzyl chloride and *n*-butanol were added to the batch reactor and the concentration of benzyl chloride, *n*-butanol and the ether were determined versus time. Figure 4 shows their concentration in the organic bulk as a function of time. We note, however, the system perform as dual-phase as one could easily find it refer to figure 1.

Although the reactants are added in equal amounts, the decrease in *n*-butanol is greater than that in benzyl chloride. This could be understood when we review the traditional Williamson ether synthesis. Williamson ether synthesis mechanism had been proposed by several authors [13]. Three steps reaction involved as below when PTC serve as catalyst in a two phase system.

$$\mathrm{ROH} + \mathrm{KOH} \leftrightarrow \mathrm{KOR} + \mathrm{H_2O} \quad \text{(aqueous phase)} \quad (2)$$

$$\mathrm{KOR} + \mathrm{Q^+Cl^-} \leftrightarrow \mathrm{Q^+OR^-} + \mathrm{KCl} \quad \text{(aqueous phase)} \quad (3)$$

$$\mathrm{R'Cl} + \mathrm{Q^+OR^-} \leftrightarrow \mathrm{ROR'} + \mathrm{Q^+Cl^-} \quad \text{(organic phase)} \quad (4)$$

Alkoxide is created by equation (2) in the aqueous phase, then, the alkoxide combined with catalyst to form ion-pair $\mathrm{Q^+OR^-}$ by equation (3), followed by the extraction of ion-pair from aqueous phase into the organic bulk. Finally, the ion-pair reacts with RX' to yield ether by equation (4). Comparing all amount of benzyl chloride stores in organic phase, some amount of *n*-butanol dissolves in aqueous in form of ROH or KOR according to equation (2). Consequently, the fraction determined in organic bulk is less than benzyl chloride.

We note, however, there exists a reaction present in the absence of PTC, which was indicated as dash-dotted line in figure 4. Since the solubility of benzyl chloride in water is negligible, this baseline reaction should take place at the interface between the organic and aqueous phase. This would be follow the traditional Williamson ether synthesis mechanism as below [7].

The first step : potassium alkoxide creates from alcohol and KOH as equation (2) indicates.

The second step:ether yield from potassium alkoxide and alkyl halide

$$\mathrm{R'Cl} + \mathrm{KOR} \leftrightarrow \mathrm{ROR'} + \mathrm{KCl} \quad \text{(organic-aqueous interface)} \quad (5)$$

3.2.2. Reaction in PEG3000 alone system

The reaction was carried out by PEG3000 at $\xi_{\mathrm{KOH}} = 1.0$ in the same condition as (Bu)4NBr. Figure 5 shows reactants and product concentration in the

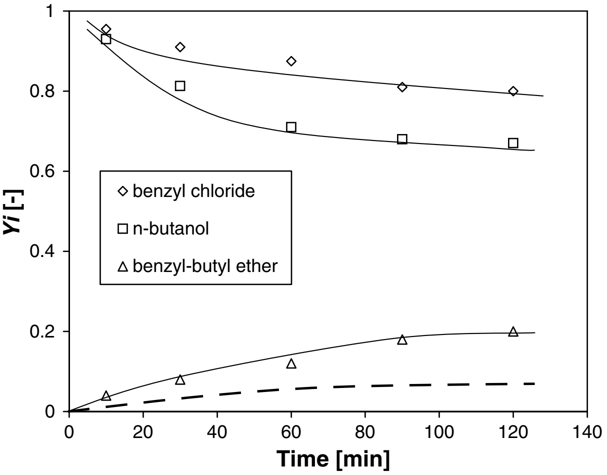

Figure 4. Concentration of benzyl chloride, *n*-butanol and benzyl–butyl ether in the organic bulk as a function of reaction time with $(\mathrm{Bu})_4\mathrm{NBr}$ as a phase transfer catalyst. Aqueous phase : KOH satuated. Reactant : 1000 mol/m^3-org benzyl chloride and 1000 mol/m^3-org *n*-butanol. $(\mathrm{Bu})_4\mathrm{NBr}$: 5 mol/m^3-org.

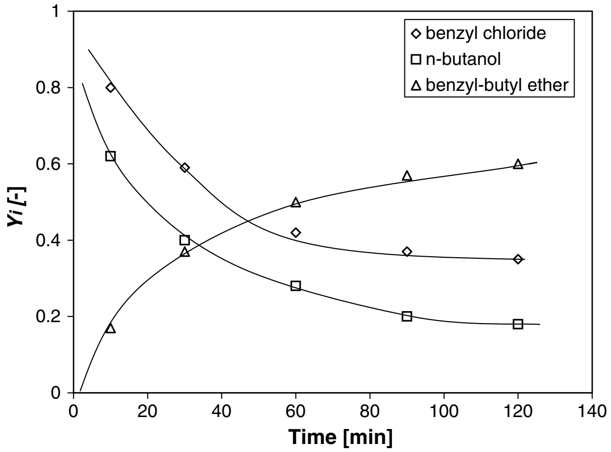

Figure 5. Concentration of benzyl chloride, *n*-butanol and benzyl–butyl ether in the organic bulk as a function of reaction time with PEG3000 as a phase transfer catalyst. Aqueous phase : KOH satuated. Reactant : 1000 mol/m^3-org benzyl chloride and 1000 mol/m^3-org *n*-butanol; PEG3000:10 mol/m^3-org.

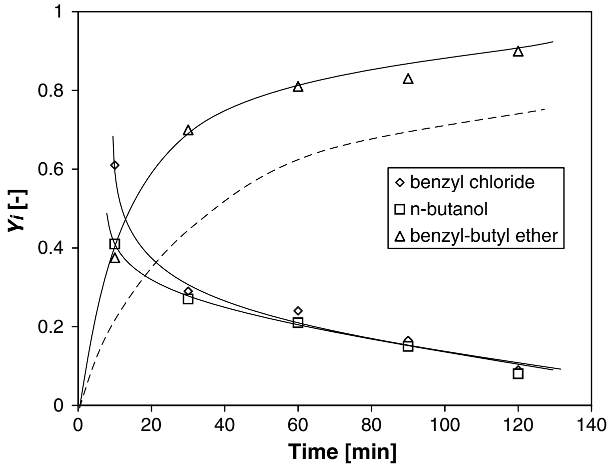

Figure 6. Concentration of benzyl chloride, *n*-butanol and benzyl–butyl ether in the organic bulk as a function of reaction time when $(Bu)_4NBr$ together with PEG3000 as phase transfer catalyst aqueous phase : KOH satuated; Reactant:1000 mol/m^3-org benzyl chloride and 1000 mol/m^3-org *n*-butanol. $(Bu)_4NBr$: 5 mol/m^3-org.; PEG3000 : 10 mol/m^3-org.

organic bulk as a function of time. Note this is a three phase system as the presence of third liquid phase.

The reaction rate by PEG3000 is higher than that by (Bu)4NBr. We had attributed these rate enhancement effect to the high reactants concentration in the third liquid phase, where being rich in catalyst as well [4–6].

3.2.3. *Reaction with the combination of (Bu)4NBr and PEG3000*

Figure 6 shows the result in combination of (Bu)4NBr and PEG3000. The ether production rate increases compared to those from figures 4 and 5. The dash-dotted line indicates a summation of ether yield of (Bu)4NBr alone and PEG3000 alone, respectively. The gap between the black circle and the dash-dotted line may present the synergetic effect.

We consider the synergetic effect is originated by (Bu)4NBr rather than PEG3000. In figure 4, (Bu)4NBr exists and the reaction takes place in the organic phase. In figure 5, PEG3000 exists consequently the reaction happens in the third phase. However, coexisting of (Bu)4NBr and PEG300 with the presence of *n*-butanol, would result in a relocation associated with (Bu)4NBr. Owing to their strong affinity, (Bu)4NBr dissolved in the third phase. Therefore, the reaction generated by (Bu)4NBr in third phase ought to raise, where existing abundant reactants. As a consequence, the observed reaction proceeded much fast than any others.

The approach open a possibility to reduce the consumption of quaternary ammonium salts, which is expensive and some toxic, just replacing by the low price and non-toxicity PEGs.

4. Conclusion

The study reveals the formation of third liquid phase depends on the kinds of PTC, *n*-butanol concentration as well as aqueous salt concentration in the investigated system. A combination of tetrabutylammonium bromide and PEG may yield a third liquid phase with a synergetic effect in reaction activity.

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