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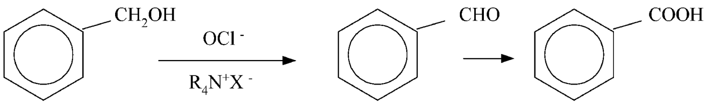

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Kinetics of Synthesizing Polymer-Supported Quaternary Ammonium Catalysts

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This study attempted to synthesize the optimum quaterary ammonium poly(styrene-*co*-methylstyrene) catalyst using the combinatorial chemistry method. The catalyst was synthesized by a mix−split method. A phase-transfer catalyst library with 25 kinds of polystyrene-supported quaternary ammonium salt catalyst was the the result of the reaction of five kinds of chloromethylated crosslinked polystyrene with five *tert*-amines. The allylation of phenol and the oxidation of benzyl alcohol were used as the probing reaction to screen out the most active catalyst for the reaction using the iterative deconvolution method. The screening conditions included teritary amine and organic solvent. The structure of the most active catalyst in the allylation of phenol shows 20 mol % ring substitution and 0.177−0.25-mm pellet size activated with trihexylamine. For oxidation of benzyl alcohol, the reaction conditions of the most active catalyst included a resin of 20% ring substitution and pellet size of 0.177−0.25 mm, activated with triethylamine reacting in an organic solvent of *n*-hexane.

Introduction

Phase-transfer catalysis (PTC) has been widely applied in the manufacturing processes of specialty chemicals, such as pharmaceuticals, dyes, perfumes, additives for lubricants, pesticides, and monomers for polymer synthesis.[1−3] However, processes using a two-phase, phase-transfer catalytic reaction always encounter the separation problem of purifying the final product from the catalyst. Regen[4] first used a solid-phase catalyst (triphase catalyst or polymer-support catalyst), in which the tertiary amine was immobilized on a polymer support, in the reaction of an organic reactant and an aqueous reactant. From the industrial application point of view, the supported catalyst can be easily separated from the final product and the unreacted reactants simply by filtration or centrifugation.

Most synthetic methods of quaternary ammonium poly(styrene-*co*-methylstyrene) resin used for triphase catalysis are studied in Regen et al.[4−7] and Tomoi et al.[8−12] Another advantage of triphase catalysis is that it can be easily adapted to continuous processes.[13−18] Therefore, triphase catalysis possessed high potential in industrial scale applications for synthesizing organic chemicals from two immiscible reactants. Poly(styrene-*co*-methylstyrene) crosslinked with divinylbenzene, which is immobilized with quaternary ammonium salts, was also investigated to synthesize the fine chemicals in our previous work.[19−21] The microenvironment of the polymer support played a crucial role in enhancing the reaction rate. More information about characterization of the polymer structure; the interaction among the organic solvent, resin, and aqueous solution; and the reuse of the catalyst are required to encourage application. However, the synthetic procedure for obtaining an optimum resin was rarely discussed and set up because the liquid−solid−liquid triphase (or phase-transfer catalytic) reaction is complicated.

Combinatorial synthesis as a high-throughput method enables the rapid production of hundreds to thousands more compounds than conventional serial organic synthesis. This in conjunction with high-throughput screening and the increasing number of new organic targets is expected to accelerate the process for discovering new and improved candidates.[22−31] Xu et al.[32] first reported that a phase-transfer catalyst library with 50 kinds of polystyrene-supported quaternary ammonium salt catalyst was synthesized by the reaction of 10 kinds of chloromethylated crosslinked polystyrene with 5 tertiary amines using a portioning−mixing method in the liquid−solid−liquid phase-transfer catalysis. However, the types of quaternary ammonium poly(styrene-*co*-methylstyrene) resins synthesized by Xu et al.[32] were almost all hydrophilic resin, and have not been involved in a phase-transfer catalytic reaction, so that the catalyst was considered the balance of lipophile−hydrophile in the microenvironment of active site. This study aims to screen the structure of the resin and tertiary amines to obtain the optimum structure of the resin in a liquid−solid−liquid phase-transfer catalytic reaction.

Experimental Section

Materials. Allyl bromide (RBr, Fluka, 99.5%), phenol (RDH, 99%), chloromethylstyrene (Aldrich, 97%), styrene (RDH, 99%), divinylbenzene (Aldrich, 80%), benzyl alcohol (RDH, 98%), and other reagents are all expanded chemicals.

Preparation of Quaternary Ammonium Poly(styrene-*co*-methylstyrene) Resin (CL, 4 mol %; RS, 20−60 mol %). Five kinds of poly(styrene-*co*-chloromethylstyrene) crosslinked with divinylbenzene were synthesized using

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Table 1. Properties of Various Polystyrene Resins[a]

resin code	degree of ring substitution (%)	particle size mesh	av diameter (mm)
1	20	35−45	0.427
2	20	45−60	0.302
3	20	60−80	0.213
4	40	45−60	0.302
5	60	45−60	0.302

[a] The degree of crosslinkage of all resins was 4 mol %.

suspension copolymerization. A solution of boric acid (0.016 mol, 1 g), gelatine (1 g), sodium hydroxide (25 wt %), calcium carbonate (0.0029 mol, 2.9 g), benzoyl peroxide (1 g), and water (500 cm^3) was introduced into the reactor. The reaction temperature was 87 °C with an agitation rate of 600 rpm. After reaction for 30 min, styrene (0.58 mol, 60.5 g), chloromethylstyrene (0.156 mol, 23.8 g, RS: 20 mol %), and divinylbenzene (0.0058 mol, 4.92 g) were introduced into the reactor. The reaction was stopped after 5 h. Polystyrene-supported resin was separated from the solution by filtration and then washed alternately with sodium hydroxide (1 kmol/m^3) and HCl (1 kmol/m^3). The resin was dried in an oven at 60 °C. The properties of three degrees of ring substitution (RS: 20, 40, 60 mol %) and three pellet sizes (30−45, 45−60, 60−80 mesh) of quaternary ammonium poly(styrene-*co*-methylstyrene) resin are listed in Table 1.

Synthesis of Triphase Catalyst Library. Five kinds of chloromethylated crosslinked polystyrene resins synthesized for different degrees of ring substitution and crosslinkage were named as **1**, **2**, **3**, **4**, and **5** and then were uniformly mixed with every resin. The mixture was then divided into five portions, as shown in the first step in Figure 1. Five portions of the resins were individually activated with triethylamine, tripropylamine, tributylamine, trihexylamine, and triethanolamine. Thus, a polymer-supported quaternary ammonium catalyst library with five sublibraries was obtained. The codes of the five amine groups of trimethylamine, triethylamine, tripropylamine, tributylamine, trihexylamine and triethanolamine were named as A, B, C, D, and E, respectively. Immobilization reaction conditions were performed as follows: methanol (100 cm^3) and amine (1 kmol/m^3) and a mixture of chloromethylated polystyrene resins (5 g) were introduced into a three-necked, round-bottom flask. These reactions were then thermostated at 50 °C for 3 days at an agitation of 150 rpm. After reaction, the resin was washed alternately with water and methanol and then dried under vacuum at 60 °C.

Screening Triphase Catalyst for Allylation of Phenol. The allylation of phenol and the oxidation of benzyl alcohol were employed as the probing reaction to screen the active catalyst from the library. Solvent, kind of *tert*-amine, and structure of the catalyst were investigated to obtain the optimum reaction conditions. The screening triphase catalyst for allylation of phenol is presented in the following.

1. Screening Solvent from the Most Active Sublibrary. The solvents (chloroform, 1,2-dichloroethane, hexane, chlorobenzene, or toluene) were introduced into each of five 250-cm^3, three-necked flasks with a mixture of polymer-supported quaternary ammonium catalyst (0.5 mmol) added for each sublibrary. The codes of the five solvents of chloroform, 1, 2-dichloroethane, hexane, chlorobenzene, and toluene were named as a, b, c, d, and e, respectively. The reaction procedure was chosen as follows. A solvent (50 cm^3) with allylbromide (0.0075 mol) and diphenyl ether (0.000 84 mol,

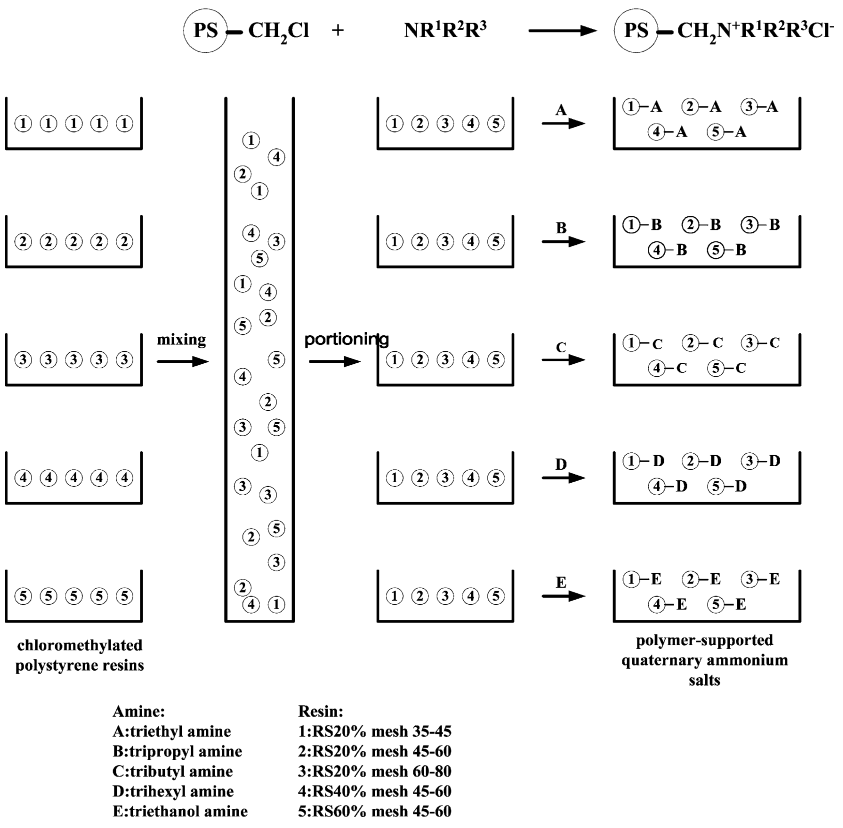


Figure 1. Scheme of the mix−split synthesis of catalyst library.

internal standard for HPLC) were introduced into each three-necked flask. After 30 min, allowing the catalyst to swell, phenol (0.009 mol) and sodium hydroxide (0.0102 mol) with water (50 cm^3) were introduced into each flask. The reaction was performed at 35 °C and an agitation rate of 500 rpm. Samples were withdrawn at selected time intervals. The yield of allyl phenyl ether was determined by liquid chromatography or gas chromatography with an internal standard method for different solvents. The reaction was stopped after 2 h. The corresponding sublibrary for the solvents that was of the highest yield was chosen as the best solvent for the allylation of sodium phenolate.

2. Screening the Most Active Amine Sublibrary. According to the result obtained in part 1, a solvent suitable for the allylation of phenol was selected. The screening procedures of the most active sublibraries of different tertiary amines were identical to those of part 1. Samples were withdrawn to determine the yield of allyl phenyl ether. The corresponding sublibrary for the amines with the highest yield of allyl phenyl ether was chosen as the most active sublibrary.

3. Screening the Most Active Structure of Catalyst in the Library. The corresponding tertiary amine of the most active catalyst sublibrary was reacted with three degrees of ring substitution (RS 20, 40, 60%) for 45-60 mesh and three pellet sizes (35−45, 45−60, 60−80 mesh) for RS 20% polystyrenes. The codes of the polystyrenes are listed in Table 1. These synthesizing procedures were identical to those for synthesizing the most active sublibrary, as mentioned in part 1. The ion exchange capacity of each catalyst was determined using the Volhard method. The most active catalyst with the highest yield of allyl phenyl ether was obtained for selecting the best active sublibrary.

4. Screening for Oxidation of Benzyl Alcohol. The procedure of screening triphase catalyst for oxidaiton of benzyl alcohol was indentical to that for allylation of phenol as mentioned above.

Ion-Exchange Capacity of Quaternary Ammonium Poly(styrene-*co*-methylstyrene) Catalyst. The ion-exchange capacity of the catalyst was determined using the Volhard method. The determining procedure is presented in the following. The catalyst (0.5 g) and methanol (5 cm^3) were added to the flask. After allowing 30 min for the catalyst to swell, HNO_3 (0.2 cm^3, 0.05 kmol/m^3) was added to the flask. After 2 h, the catalyst was filtered and washed using deionized water (50 cm^3). Then, ammonium iron (III) solution (2 cm^3, 0.015 kmol/m^3) was added to the solution, which turned yellow. KSCN (0.2 cm^3, 0.02 kmol/m^3) was added to the solution, which became orange. The solution was titrated with $AgNO_3$ (0.015 N) until the solution was clear, and $AgNO_3$ was then added in excess (the solution turned green-yellow). The white solid was separated by filtration. The solution was heated until suspended substances were formed. It was then cooled and titrated with KSCN (0.02 kmol/cm^3) until the solution changed from yellow to orange.

Results and Discussion

The resin was synthesized with a poly(styrene-*co*-chloromethylstyrene) crosslinked with divinylbenzene activated with tertiary amine. In this study, the synthesis of the resin was performed by the mix−split method. This method has the best efficiency in solid-phase synthesis in combinatorial chemistry. Two reactions, the allylation of phenol and oxidation of benzyl alcohol, were chosen as the probing reactions. Detection was performed by the iterative deconvolution method. The reactivity of the resin was influenced by the particle size, degree of ring substitution, degree of crosslinkage, type of pore size (macro or gel), structure of the active site, and so on, in a liquid−solid−liquid phase-transfer catalytic reaction.[1−3] Because the degree of crosslinkage and the type of pore size for the reactivity of the catalyst were obvious in a liquid−solid−liquid PTC reaction, they were not needed in the study of optimum synthesis of polymer-supported resin in a phase-transfer catalytic reaction, which was reported in our previous works.[19−21] Hence, this combinatorial library was made from three degrees of ring substitution (20, 40 and 60 mol %), three particle sizes (35−45, 45−60, 60−80 mesh), and five kinds of *tert*-amines (trimethylamine, tripropylamine, tributylamine, trihexylamine, and triethanolamine). Figure 1 shows the scheme of the mix−split synthesis of the catalyst library. The five resins for different degrees of ring substitution and particle sizes (**1**, RS 20%, 35−45 mesh; **2**, RS 20%, 45−60 mesh; **3**, RS 20%, 60−80 mesh; **4**, RS 40%, 45−60 mesh; **5**, RS 60%, 45−60 mesh) were prepared and then uniformly mixed and split into five portions. Each portion was reacted with each of the five *tert*-amines to obtain five five-member sublibraries, that is, 25 kinds of the catalysts.

The chloride densities of five sublibraries activated with triethylamine (A), tripropylamine (B), tributylamine (C), trihexylamine (D), and triethanolamine (E) determined by the Volhard method were 1.2, 1.15, 1.02, 0.41, and 0.9 mmol/g, respectively. The immobilization solvent was methanol, except for triethanol in dimethylformaldehyde, because the density of the active site when methanol was used as an immobilized solvent was low. A good immobilization solvent increases the swelling degree of the resin and, furthermore, increases the density of active sites formed in the resin. The chloride densities of the resin activated with triethanolamine when methanol and dimethylformaldehyde were used as the solvent, were 0.37 and 0.9 mmol/g, respectively. However, the chloride densities for the other four catalysts when using methanol as the immobilization solvent were larger than those when using dimethylformaldehyde. Hence, the catalysts adapted were of higher chloride density of the catalyst for each sublibrary in the following discussion. Moreover, the chloride density of the former four catalysts decreased with increasing carbon number of the alkyl group in the *tert*-amine when the immobilization time was 24 h. The experimental result revealed that because of steric effects, the diffusion resistance of *tert*-amine was also increased with increasing carbon number of the alkyl group in the *tert*-amine during the immobilization reaction.

Screening in Allylation of Phenol. The iterative deconvolution method is usually used to screen out the most active catalysts from combinatorial libraries. Figure 2 shows the scheme of screening the library using the iteration deconvolution method. The probing reaction system chosen for study was first the reaction of allyl bromide and phenol, with polymer-supported quaternary ammonium salt as a triphase

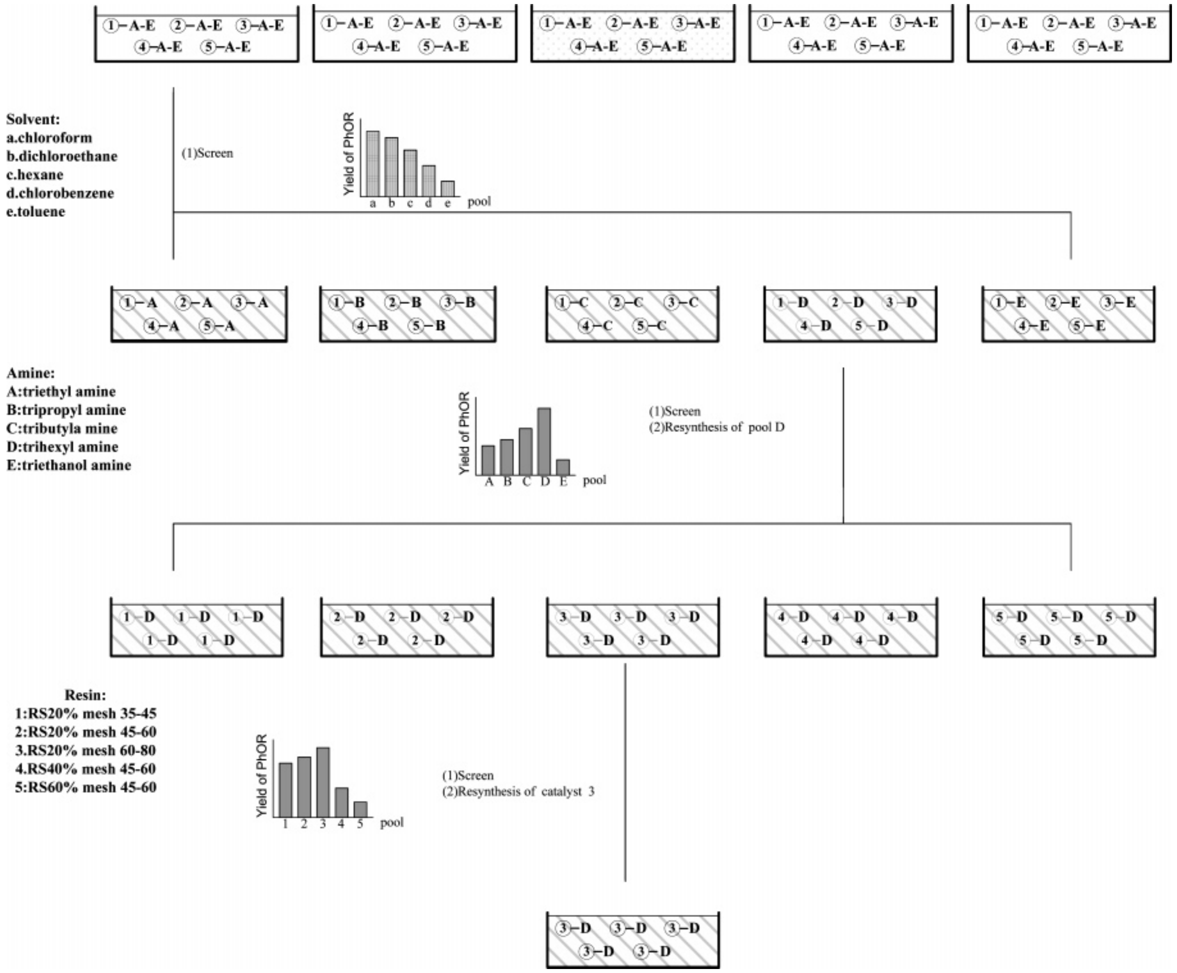


Figure 2. The iteration deconvolution method applied to screen the library.

catalyst in an organic solvent/alkaline solution. The reaction was given as

$$C_3H_5Br + C_6H_5OH + NaOH \xrightarrow{\text{triphase catalyst}} C_3H_5OC_6H_5 + NaBr + H_2O \quad (1)$$

In previous works,[33−35] the formation kinetics of allyl phenyl ether using tetra-*n*-butyl ammonium bromide (TBAB) as a liquid−liquid-phase transfer catalyst has been studied and obtained higher reactivity. The screening factors of the catalysts in the allylation of phenol using a combinatorial chemistry method included the kinds of solvents and *tert*-amines and the structures of the resins.

1. Screening of Solvent. First, 25 kinds of catalysts, as mentioned above, were divided into five five-membered sublibraries. Each sublibrary as the catalyst was examined using different organic solvents (chloroform (a), dichloroethane (b), hexane (c), chlorobenzene (d), and toluene (e)) in the allylation of phenol. The five organic solvents were chosen because they were employed in a PTC reaction, and their boiling point was higher than 50 °C; i.e., the range of operating temperatures was broad. In general, the solvent influences the reactivity of the active site, the diffusivity of the reactant in the resin, the solubility of the reactant in two phases, the distribution of the reactant between both phases, the swelling degree of the resin, and so on. The experimental result for the solvent effect is displayed in Figure 3. The yields of PhOR for solvents were in the following descending order: chloroform > dichloroethane > hexane > chlorobenzene > toluene. Hence, chloroform was chosen as the solvent in the following screening procedure.

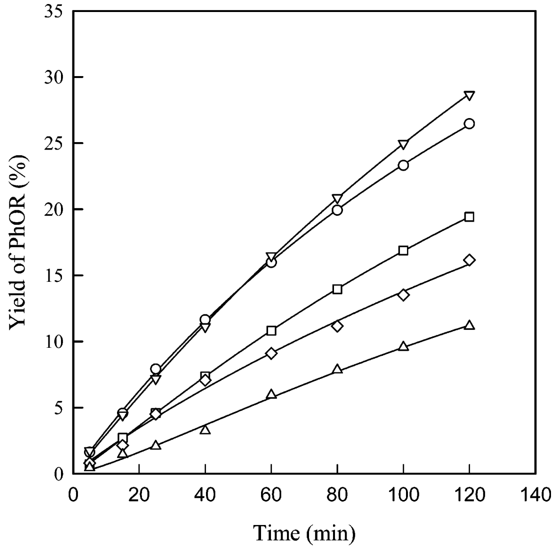


Figure 3. Yield of allyl phenyl ether vs reaction time using various organic solvents: (▽) chloroform, (○) dichloroethane, (□) hexane, (◇) chlorobenzene, and (△) toluene. Conditions: 35 °C, 500 rpm; aqueous phase, 50 cm^3; oil phase, 50 cm^3; C_3H_5Br, 0.0075 mol; PhONa, 0.01125 mol; NaOH, 0.0135 mol; mixture of catalyst (equal mole), 0.0005 mol.

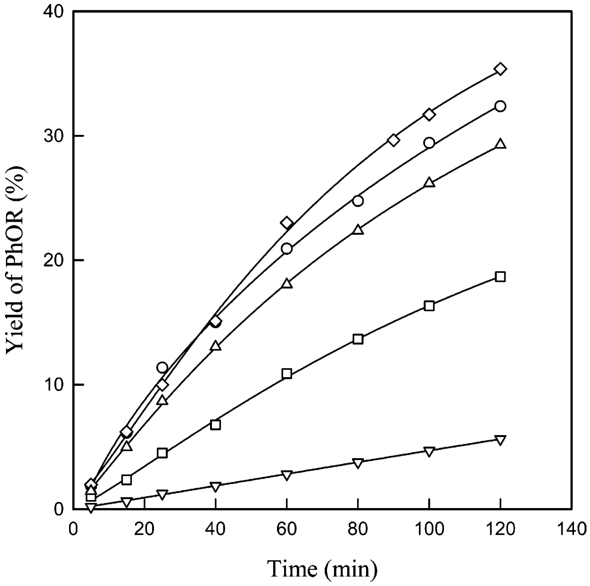


Figure 4. Yield of allyl phenyl ether vs reaction time with various *tert*-amines: (▽) triethanolamine, (○) tributylamine, (□) triethylamine, (◇) trihexylamine, and (△) tripropylamine. Conditions: 35 °C, 500 rpm; aqueous phase, 50 cm^3; oil phase, 50 cm^3; C_3H_5Br, 0.0075 mol; PhONa, 0.01125 mol; NaOH, 0.0135 mol; mixture of catalyst (equal mole), 0.0005 mol.

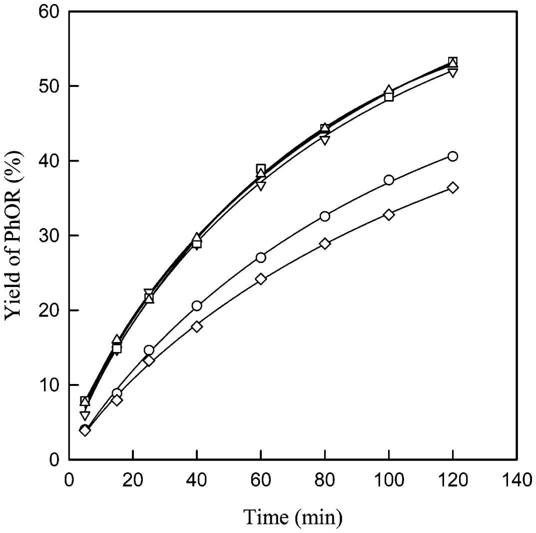


Figure 5. Yield of allyl phenyl ether vs time with various polymer-support catalysts: (▽) RS 20%, mesh 35−45; (○) RS 20%, mesh 45−60; (□) RS 20%, mesh 60−80; (◇) RS 60%, mesh 45−60; and (△) RS 20%, mesh 45−60. Conditions: 35 °C, 500 rpm; aqueous phase, 50 cm^3; oil phase, 50 cm^3; C_3H_5Br, 0.0075 mol; PhONa, 0.01125 mol; NaOH, 0.0135 mol; mixture of catalyst (equal mole), 0.0005 mol.

2. Screening of *tert*-Amine. The second screen was the screening of *tert*-amine in Figure 2. Five kinds of amine—triethylamine (A), tripropylamine (B), tributylamine (C), trihexylamine (D), and triethanolamine (E)—were chosen as the screening tertiary amine. The diffusion resistance in the resin and the lipophilicity of the active site was increased with increasing carbon number of the alkyl group of the *tert*-amine immobilized in the resin. The methyl and ethyl groups in *tert*-amine used in the resin were usually examined in an ion-exchange aqueous reaction. They were almost incorrectly examined in a phase-transfer catalyzed reaction because of higher hydrophilicity, except that the rate-determining step was in the aqueous phase. Hence, the resin activating with tributylamine was employed in a phase-transfer catalyzed reaction, 1−3. Figure 4 shows the relationships between yield of PhOR and reaction time using different catalysts. The yields of PhOR for the resin activated with *tert*-amine were ranked in the following descending order: trihexylamine > tributylamine > tripropylamine > triethylamine > triethanolamine. This finding reveals a novel result that the resin activated with trihexylamine was never employed in a phase-transfer catalyzed reaction to obtain high reactivity of the reaction. Previously, Wu and Lee[21] reported that the reaction rate of the resin activated with trioctylamine was slow because the density of the active sites was too low. However, when the resin immobilized with trihexylamine was employed as the catalyst in a liquid−solid−liquid phase-transfer catalyzed reaction, its reactivity was larger than that of the resin activated with tributylamine. The performance of the resin immobilized with trihexylamine may be studied in the future. Hence, trihexylamine was chosen as the solvent in the following screening procedure.

3. Screening of Resin Structure. Figure 2 shows the screening of the catalyst structure. Five structures of the resin (1−5) were individually activated with trihexylamine in methanol for 4 days. The chloride densities of the five catalysts determined by the Volhard method were 0.187, 0.27, 0.326, 0.44, and 0.58 mmol/g, respectively. Figure 5 shows the relationships between the yield of PhOR and the reaction at different structures of the catalysts. The experimental result reveals that the yield of PhOR obtained was higher when the degree of ring substitution was 20% in the allylation of phenol. Furthermore, the effect of particle size of the resin was not obvious under this reaction condition (35 °C). Therefore, the optimum catalyst was used in chloroform, and the degree of crosslinkage of 4 mol % and ring substitution of 20 mol %, and the resin activated with trihexylamine in this allylation of phenol (35 °C, 500 rpm; H_2O, 50 cm^3; organic phase, 55 cm^3; 0.0075 mol of C_3H_5Br; 0.01125 mol of PhOH; 0.0135 mol of NaOH).

The optimum reaction condition was obtained by combinatorial chemistry; however, it may not be the real optimum reaction condition. Figure 6 displays the yield of PhOR and the reaction time under nine reaction conditions by the traditional synthesis method. These conditions were chosen with the better organic solvents and *tert*-amines. The results in Figure 6 correspond with those obtained using the combinatorial chemistry method, thus verifying the optimum reaction condition. Figure 7 shows the comparison of the number synthesizing of experiments between the classic and combinatorial chemistry methods. The optimum reaction was easily obtained by means of the combinatorial chemistry method in this reaction. Experiments performed using the traditional method needed 125 runs, whereas those performed using the combinatorial chemistry method needed 25 runs. The number of synthesizing experiments was reduced to 100 runs. Therefore, the combinatorial chemistry method is a proper method for achieving an optimum catalyst in a liquid−solid−liquid phase-transfer-catalyzed reaction.

Kinetics of Allylation of Phenol Using Polymer-Supported Resin Reacting with Trihexyl Amine. The resin

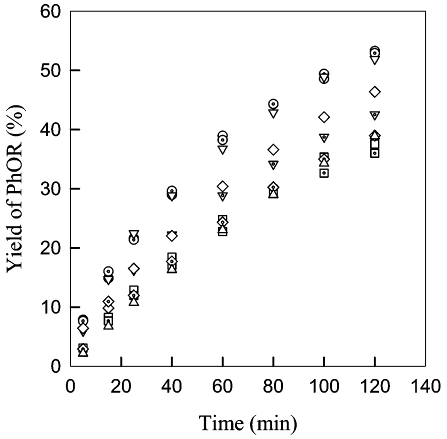


Figure 6. Yield of allyl phenyl ether vs time using various reaction conditions: (○) mesh 60−80, (chloroform) trihexylamine; (⊙) mesh 45−60, (chloroform) trihexylamine; (triangle with dot) mesh 60−80, (chloroform) tributylamine; (▽) mesh 35−45, (chloroform) trihexylamine; (□) mesh 45−60, (chloroform) tributylamine; (⊡) mesh 35−45, (chloroform) tributylamine; (◇) mesh 60−80, (dichloroethane) trihexylamine; (diamond with dot) mesh 45−60, (dichloroethane) trihexylamine; (△) mesh 35−45 (dichloroethane) trihexylamine; 35 °C, 500 rpm; aqueous phase, 50 cm^3; oli phase, 50 cm^3; 0.0075 mol of C_3H_5Br; 0.01125 mol of PhONa; NaOH 0.0135 mol; catalyst: 0.0005 mol.

activated with trihexylamine was the best catalyst in the allylation of phenol. However, its chloride density was low in the resin. Errede[25] suggested that the swelling degree of this resin was good when the solubility parameter was in the range of 8.6 and 9.7 (cal/cm^3)$^{0.5}$. Five solvents (methanol (14.3 (cal/cm^3)$^{0.5}$), acetone (9.6 (cal/cm^3)$^{0.5}$), DMF (12.1 (cal/cm^3)$^{0.5}$), toluene (8.9 (cal/cm^3)$^{0.5}$) and chloroform (9.6 (cal/cm^3)$^{0.5}$)) were used to immobilize trihexylamine in the resin, whose chloride densities were 0.15, 5.95×10^{-3}, 0.15, 0.02, and 0.06, respectively. This finding demonstrates that the solvent influences not only the swelling degree of the resin but also the reactivity between the chloromethylstyrene group and trihexylamine. Hence, methanol was chosen as an immobilization solvent in this study. When the immobilization durations were 24 h, 72 h, 120 h, 168 h ,and 2 weeks, the chloride densities of the resin were 0.00986, 0.0759, 0.104, 0.287, and 0.33 mmol/g, respectively. The chloride density of the resin increased with increasing immobilization time. It is demonstrated that the reaction rate of the chloromethyl group reacting with trihexylamine was slow. Hence, if the immobilization method is improved, the utility of this resin increases.

According to the experimental result, the rate of allyl bromide reacting with phenol remained constant when the agitation rate was larger 200 rpm. In general, the reaction was only influenced by the reaction-kinetic control. The reaction rate increased only when the temperature increased. The apparent activity energy calculated by the Arrhenius law using a pseudo-first-order hypothesis was 39.1 kJ/mol and was smaller than that previously reported, which were 58−66 and 77 J/mol in the liquid−liquid and the liquid−solid−liquid PTC reactions, respectively.[34−37] The apparent turnover number (s^{-1}) of the resin activated with tertiary amine was defined as the initial reaction rate (mol/s) per mole of chloride ion at 35 °C; H_2O, 50 cm^3; organic phase, 55 cm^3; 0.0075 mol of C_3H_5Br; 0.01125 mol of PhOH; 0.0135 mol of NaOH, 8.6×10^{-3} s^{-1} and larger than that (1.2×10^{-3} s^{-1} at 30 °C) of the resin activated with tributylamine[35] and the result (1.53×10^{-3} s^{-1} at 65 °C) of the membrane with a pyridinium group.[37]

1. Screening of Oxidation of Benzyl Alcohol. Oxidation is a common reaction in an organic synthesis. The reaction type is almost a homogeneous and dramatic operating condition. In the literature,[1−3] oxidation using phase-transfer catalysis could obtain a blended operating condition and take place in the heterogeneous reaction (liquid−liquid or liquid−solid−liquid). Hence, this work tries to screen the polymer-supported quaternary ammonium resins as mentioned above

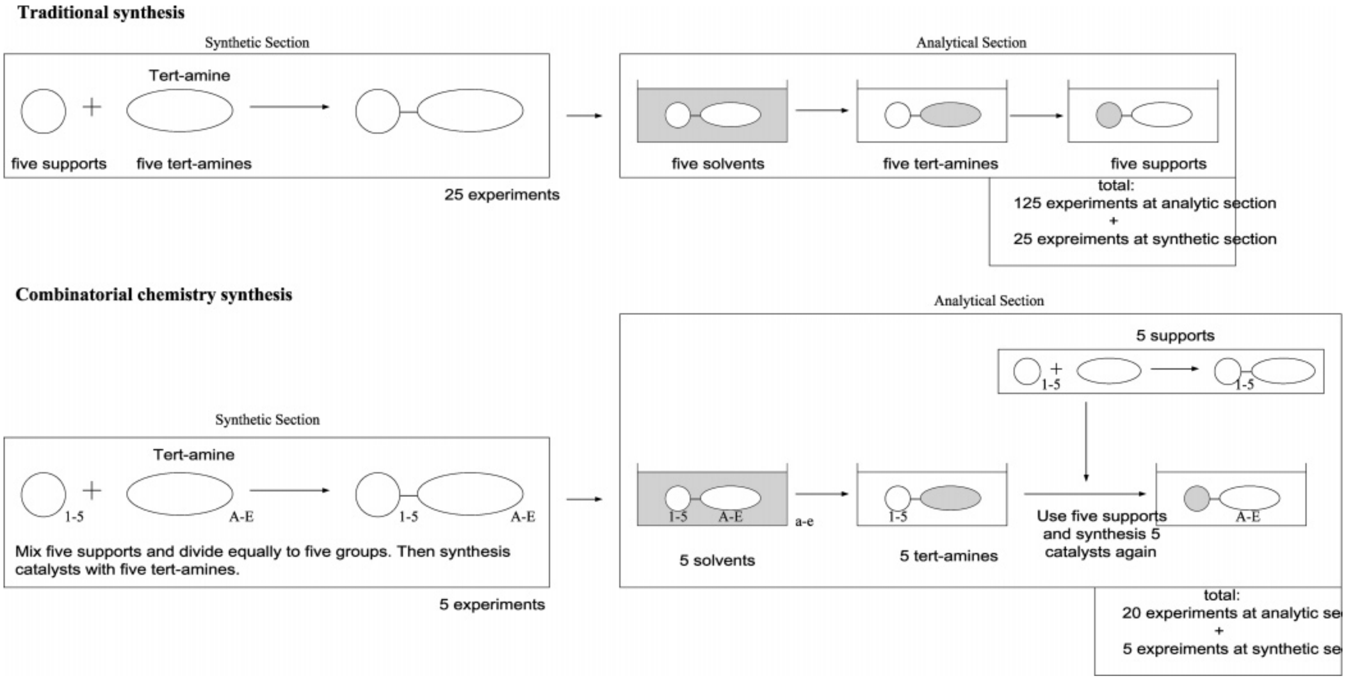


Figure 7. Comparison of experiments between traditional and combinatorial methods.

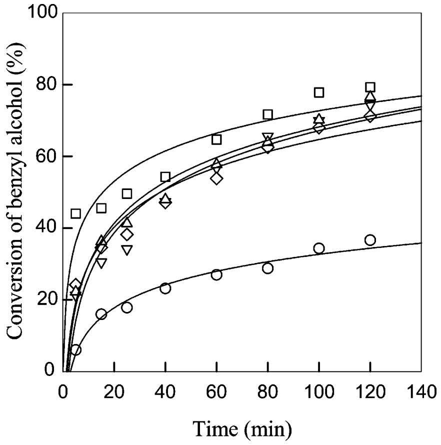
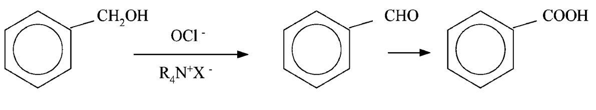


Figure 8. Conversion of benzyl alcohol vs time using various solvents: (▽) dichloroethane; (○) chloroform, (□) hexane, (◇)-toluene, and (△) chlorobenzene. Conditions: 40 °C, 500 rpm; aqueous phase, 50 cm^3; oil phase, 50 cm^3; 0.009 mol of $C_6H_5CH_2$-OH; 0.006 mol of $NaHCO_3$; NaOCl, 0.03 mol; mixture of catalyst (equal mole): 0.0005 mol.

in the oxidation of benzyl alcohol as a probing reaction. The reaction is given as



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In previous works,[38] the oxidation of benzyl alcohol using different quaternary ammonium or phosphonium salts as a liquid–solid–liquid phase transfer catalyst has been studied, and higher reactivity has been obtained. The screening procedure was identical to that in the allylation of phenol. The catalyst was synthesized by the mix–split method. The screening of oxidation was analyzed by the iterative deconvolution method. Five-member sublibraries were synthesized. Each sublibrary as the catalyst was examined using different organic solvents (chloroform (a), 1,2-dichloroethane (b), hexane (c), chlorobenzene (d), and toluene (e)) in the oxidation of benzyl alcohol. Figure 8 shows the relationships between conversion of benzyl alcohol and reaction time using different organic solvents. The conversions of benzyl alcohol for solvents were ranked in the following descending order:

hexane > dichloroethane ≒ chlorobenzene ≒ toluene > chloroform

Hence, hexane was chosen as the solvent in the following screening procedure.

The second screen was the screening of *tert*-amine. The five *tert*-amines—triethylamine, tripropylamine, tributylamine, trihexylamine, and triethanolamine—were chosen as the screening *tert*-amine. Figure 9 shows the relationships between the conversion of benzyl alcohol and the reaction time using different *tert*-amines. The conversion of benzyl alcohol for the catalyst immobilized with *tert*-amine was ranked in the following descending order: triethylamine > tributylamine > trihexylamine > tripropylamine > triethanolamine. This finding reveals that the conversion of benzyl alcohol was not related to the carbon number of the alkyl group of the *tert*-amine.

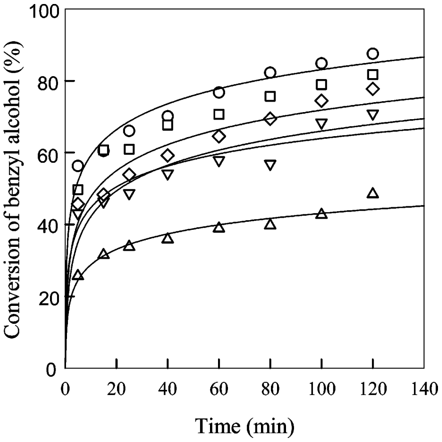

Figure 9. Conversion of benzyl alcohol vs time at various *tert*-amines: (▽) tripropylamine, (○) triethylamine, (□) tributylamine, (◇) trihexylamine, and (△) triethanolamine. Conditions: 40 °C, 500 rpm; aqueous phase, 50 cm^3; oil phase, 50 cm^3; 0.009 mol of $C_6H_5CH_2OH$; 0.006 mol of $NaHCO_3$; NaOCl 0.03 mol; mixture of catalyst (equal mole): 0.0005 mol.

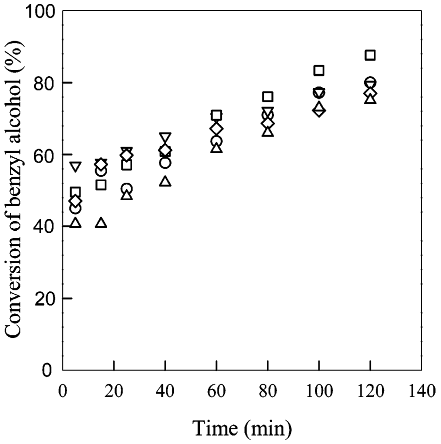

Figure 10. Conversion of benzyl alcohol vs time at various structures of the catalyst: (▽) RS 20%, mesh 45–60; (○) RS 20%, mesh 35–45; (□) RS 20%, mesh 60–80; (◇) RS 40%, mesh 45–60; and (△) RS 60% mesh 45–60. Conditions: 40 °C, 500 rpm; aqueous phase, 50 cm^3; oil phase, 50 cm^3; 0.009 mol of $C_6H_5CH_2$-OH; 0.006 mol of $NaHCO_3$; NaOCl 0.03 mol; mixture of catalyst (equal mole): 0.0005 mol.

The third screen was the screening of the resin structure. Five resin structures (**1**–**5**) were individually activated with triethylamine in methanol for 4 days. The chloride densities of the five resins determined by the Volhard method were 0.19, 0.27, 0.33, 0.44, and 0.58 mmol/g, respectively. Figure 10 shows the relationships between the conversion of benzyl alcohol and the reaction time at different structures of the resins. The conversion of benzyl alcohol increased with decreasing particle size or degree of ring substitution. Therefore, the optimum catalyst in the oxidation of benzyl alcohol was obtained from operating in hexane, and the degree of crosslinkage of 4 mol % and ring substitution of 20 mol % of the resin was activated with triethylamine in this allylation of phenol (40 °C, 500 rpm; H_2O, 25 cm^3; organic phase, 40 cm^3; 0.00925 mol of benzyl alcohol; 5.95 × 10^{-3}mol of $NaHCO_3$; 10 wt % of NaOCl; 0.005 mol of catalyst).

Conclusions

A phase-transfer catalyst library with 25 kinds of quaternary ammonium poly(styrene-*co*-methylstyrene) catalyst was synthesized by reacting five kinds of poly(styrene-*co*-methylstyrene) salt with five tertiary amines using a mix−split method. Combinatorial chemistry was verified as an effective tool for obtaining the best catalyst in a liquid−solid−liquid PTC reaction. The optimum reaction condition corresponded to the result for liquid−liquid PTC reaction in a replacement reaction. It may be studied in the future that the resin immobilized with trihexylamine was employed in a liquid−solid−liquid phase-transfer catalyzed reaction. However, the optimum conditions for the oxidation of benzyl alcohol in a liquid−solid−liquid reaction were not a clear trend. This field could be worthwhile to investigate in the future.

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Notation

CL = degree of crosslinkage (mol %)
PHOR = allyl phenyl ether
RS = degree of ring substitution (mol %)

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