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Ultrasound-assisted third-liquid phase-transfer catalyzed esterification of potassium 4-methoxyphenylacetate by dual-site phase-transfer catalyst

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ABSTRACT

The catalytic esterification of potassium 4-methoxyphenylacetate to synthesize 4-methoxyphenylacetic acid butyl ester (an ether–ester compound) by ultrasound-assisted third-liquid phase-transfer catalysis (U-TLPTC) using the prepared dual-site phase transfer catalyst 1,4-bis(tributylammoniomethyl)benzene dibromide (BTBAMBB) was investigated. The catalyst BTBAMBB was synthesized from p-xylylene dibromide and tributylamine, and the catalytic intermediate was also synthesized to verify the reaction mechanism. The third-liquid phase containing more than 50% of the added catalyst was formed by introducing BTBAMBB, potassium 4-methoxyphenylacetate and a critical amount of NaCl in the aqueous phase. Without using catalyst, the reaction system was liquid–liquid type and the product was not observed. With BTBAMBB in liquid–liquid system the product yield was only 39.3% at 70 °C in 4 h of reaction even under sonication (28 kHz/300 W), but was increased to 94.2% by forming the third-liquid phase with NaCl at the same reaction conditions. The green process to synthesize ether–ester by U-TLPTC was developed with good catalytic efficiency of dual-site phase-transfer catalyst.

1. Introduction

The reactions between mutually insoluble reactants can be effectively conducted by phase-transfer catalysis (PTC) which has been widely applied in the synthesis of pharmaceuticals, agricultural chemicals, flavorants, dyes, perfumes, environmental applications, *etc.* [1] The high conversion and good product selectivity using PTC at mild reaction conditions are usually obtained. For further enhancing the efficiency of phase-transfer catalyst, several methods about the reactor assembly were developed and showed good performance in liquid–liquid PTC system, such as membrane reactor [2] and micro-channel reactor [3]. Recently, third-liquid phase-transfer catalysis (TLPTC) has attracted much attention since TLPTC behaves the characteristics of a green technology. A TLPTC system is with the catalyst highly concentrated in a small volume of viscous layer locating between the aqueous phase and a low-polar or non-polar organic phase. This viscous layer is called the "third-liquid phase". The intrinsic reaction conducted in the third-liquid phase or in the interface can be greatly promoted [4–8]. Due to the high reaction rate, high product selectivity, with green solvent, mild reaction conditions, and easy reuse of catalysts, TLPTC is an environmentally benign technology and has the potential to be used in process implementation.

In TLPTC system, the key component in the third-liquid phase is the catalytic intermediate, which is produced from the ionic exchange reaction of the aqueous reactant and phase-transfer catalyst in the aqueous phase [9,10]. When the solubility of the catalytic intermediate in the aqueous phase is limited by introducing excess inorganic salts into the system, the catalytic intermediate would be salted to form the third-liquid phase. Several factors are important to prepare the third-liquid phase, including the catalyst type, the amount of inorganic salts, polarity of the organic solvent, and structure of the aqueous reactant. Since the catalyst is highly concentrated in the third-liquid phase, the intrinsic reaction will be enhanced. Phase-transfer catalysts which can be used to form the liquid–liquid–liquid system include quaternary 'onium type and polyethylene glycol, showing good enhancement in reaction rate [11–13].

The quaternary 'onium phase-transfer catalyst QX generally contains an active center, that carries one molecule of reactant MY in the form of catalytic intermediate QY once a reaction cycle, then QY transferring from the aqueous phase into the third-liquid phase. When more than one active center contained in a catalyst molecule, more than one molecule of MY can be carried to react in a reaction cycle [14]. Multi-site phase-transfer catalyst presents a significant enhancement in the catalytic efficiency. In addition, ultrasound irradiation has been broadly applied in organic synthesis, and shows a good improvement in the reaction rate. When the ultrasonic waves propagate in a liquid solution, the alternate compression and depression are produced to form cavities, within which temperature and pressure can reach 5000 K

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and several hundred bars, and the reaction rate is thus enhanced [15].

Apparently, the combination of ultrasound irradiation with phase-transfer catalysis might give a synergy effect in promoting the reaction [16]. The Cannizzaro reaction catalyzed by a phase-transfer catalyst under ultrasonic condition showed that an ultrasonic wave of 20 kHz dramatically accelerated the reaction [17]. The liquid–liquid phase-transfer catalyzed dichlorocyclopropanation of 1,7-octadiene was reported using benzyltriethylammonium chloride as the catalyst assisted by ultrasound irradiation, giving the reaction rate greatly accelerated [18]. The reaction of oximes and dichloromethane by PTC assisted by ultrasound got 95% of product yield in 3.5 h, but the time needed to reach 92% in the silence condition was 16 h [19]. Ultrasound irradiation combined with liquid–liquid phase-transfer catalysis reveals a significant improvement in the reaction rate [20–22].

In the present study, using dual-site phase-transfer catalyst in TLPTC under ultrasound irradiation, we developed the green method for synthesizing 4-methoxyphenylacetic acid butyl ester which is easily hydrolyzed in acidic or basic condition. With the prepared dual-site phase-transfer catalyst to form a system of tri-liquid phases, the hydrolysis side-reaction can be prevented. The formation of the third-liquid phase and variation of the catalytic intermediate in esterification assisted by ultrasound were explored. A kinetic model was proposed to describe the U-TLPTC system successfully.

2. Experimental

The reagents p-xylylene dibromide (97%, from ALFA), 4-methoxyphenylacetic acid (98%, from Aldrich), and butyl bromide (98%, from ALFA) were used without further treatment. Other reagents are all reagent-grade chemicals from SHOWA, ACROS, TEDIA, Mallinckvodt, and TCI. The ultrasonic generator was a thermostatic bath equipped with dual frequencies (28/50 kHz or 40/80 kHz) and variable electric powers (max. 300 W).

2.1. Synthesis of 1,4-bis(tributylammoniomethyl)benzene dibromide (BTBAMBB)

The dual-site phase-transfer catalyst BTBAMBB was synthesized from the reaction of 0.005 mol of p-xylylene dibromide and 0.1 mol of tributylamine in 12 cm^3 of acetonitrile at 70 °C and 150 rpm for 22 h. After completing the reaction, white precipitates were separated by centrifugation and re-dissolved in 5 cm^3 of propanol at 70 °C. Subsequently 150 cm^3 of acetone was slowly instilled into the foregoing solution and sonicated (40 kHz, 200 W) to re-precipitate the catalyst for at least 1 h. The precipitates were then separated and washed with acetone. The re-dissolved and re-precipitated steps were performed repeatedly at least three times. The final solids were dried at 70 °C for 1 h to get the dual-site phase-transfer catalyst 1,4-bis(tributylammoniomethyl)benzene dibromide (BTBAMBB). The prepared catalyst was identified with ^1H NMR, ^{13}C NMR and EA. The amount of 1,4-bis(tributylammoniomethyl)benzene cation (denoted as Q^{2+}) was determined by the titration method in water-dichloromethane system using sodium tetraphenyl borate (0.05 N of Na^+TBP^-) as the titrant and bromophenol blue (0.2% in ethanol) as the indicator. When the end point is reached, the color of dichloromethane phase would change from blue to colorless.

2.2. Synthesis of the product 4-methoxyphenylacetic acid butyl ester

The product 4-methoxyphenylacetic acid butyl ester was synthesized from potassium 4-methoxyphenylacetate (ArCOOK) in the aqueous phase reacting with butyl bromide (RBr) in the organic phase in the presence of tetra-n-butylammonium bromide. An excess quantities of 4-methoxyphenylacetic acid was added in 30 cm^3 of aqueous KOH solution in a 150-cm^3 flask and stirred for 1 h, definite amounts of tetra-n-butylammonium bromide and n-butyl bromide dissolved in dichloromethane were poured into the flask to react with potassium 4-methoxyphenylacetate at 60 °C and 150 rpm for 24 h. The organic phase was then separated from the mixture and subsequently extracted with de-ionized water for several times to remove the catalyst remained in dichloromethane phase. After that, dichloromethane was removed from the organic solution by vacuum evaporation to get a yellow liquid, that was further purified with column chromatography to obtain the product 4-methoxyphenylacetic butyl ester. The product was identified by ^1H NMR and ^{13}C NMR.

2.3. Analysis of the catalytic intermediate $Q(ArCOO)_2$

The catalytic intermediate 1,4-bis(tributylammoniomethyl)-benzene di-4-methoxyphenylacetate ($Q(ArCOO)_2$) was synthesized from the reaction of ArCOOK and BTBAMBB (QBr_2). An excess amount of ArCOOK in 30 cm^3 of water was prepared to react with QBr_2 at 60 °C and 250 rpm of stirring speed for at least 1 h to produce $Q(ArCOO)_2$, which was then extracted into 5 cm^3 of dichloromethane for at least ten times and collected together. Dichloromethane was then removed from the collected solution by vacuum evaporation to obtain a viscous liquid of $Q(ArCOO)_2$, and that was identified with ^1H NMR. To determine the content of $Q(ArCOO)_2$ in the third-liquid phase, a solution of 30 cm^3 of dichloromethane containing a definite quantity of diphenyl methane (as the internal standard in HPLC analysis) was added into the separate third-liquid phase to dissolve the catalytic intermediate. The un-reacted ArCOOK and other inorganic salts were precipitated and removed by filtration. A sample (0.2 cm^3) of the dichloromethane phase was withdrawn and diluted with 4 cm^3 of methanol to determine the amount of $Q(ArCOO)_2$ with HPLC.

2.4. Kinetic measurements

In a batch run, definite amounts of ArCOOK, BTBAMBB, water, and organic solvent were stirred for 15 min in a 150-cm^3 three-necked reactor, which was set in a constant-temperature water bath equipped with ultrasound irradiation. The third-liquid phase was formed prior to the substitution reaction by introducing extra inorganic salt into the aqueous and organic phase. When the set temperature was reached, definite quantities of RBr and diphenylmethane (internal standard) were introduced, and the sonicator was activated to start the reactions. During the reaction, an organic sample (0.2 cm^3) was withdrawn at the chosen time and diluted into 4 cm^3 of methanol for analysis using HPLC with C_{18} (5-μm) column and variable-wavelength UV detector at 254 nm. The flow rate of eluent was 1.0 cm^3/min in a volume ratio of acetonitrile/methanol/water to be 37/37/26.

3. The kinetic model

In this TLPTC system, the reaction of ArCOOK in the aqueous phase and RBr in the organic phase to produce the product ArCOOR is catalyzed by the dual-site phase-transfer catalyst QBr_2 forming the third-liquid phase under ultrasonic irradiation (denoted as "))))") in a batch reactor. The reaction mechanism for the intrinsic reactions conducting at the interface of organic and third-liquid phases is shown below.