Phase-Transfer Catalytic Reaction of 4,4′-Bis(Chloromethyl)-1,1′-biphenyl and 1-Butanol in a Two-Phase Medium

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Abstract:

The phase-transfer catalyzed etherification of 4,4′-bis(chloromethyl)-1,1′-biphenyl was investigated in an alkaline aqueous solution/organic solvent two-phase medium. During or after completion of the reaction, the monosubstituted product (4,4′-(butoxymethyl chloromethyl)-1,1′-biphenyl) and disubstituted product (4,4′-bis(butoxymethyl)-1,1′-biphenyl) were both produced. The reaction was enhanced by adding a small quantity of quaternary ammonium salt. A generalized model, which included the aqueous- and organic-phase reactions, the mass transfer of regenerated catalyst and active catalyst, and the phase equilibria of the regenerated catalyst and the active catalyst between two phases, was built up to describe the system performance. The purpose of this work is to examine effects of agitation, amount of organic solvent, quaternary ammonium salts, amount of tetrabutylammonium bromide, amount of potassium hydroxide, amount of water, organic solvents, and temperature on the conversion of the reactant. The kinetics are well described by a pseudo-first-order rate law. A rational explanation of the results was made. Products of high purity were also obtained using pressurized column chromatography.

Introduction

Ethers are one of the high added-value chemicals extensively used in various industries for the additives of petroleum chemicals and extractants.[1,2] The conventional method to synthesize ethers is the so-called Williamson synthesis. However, the reaction is conventionally carried out under anhydrous conditions in which sodium alkoxide is produced from the reaction of sodium hydride and alcohols. The other method to synthesize ethers is the reaction of olefins and alcohol in the presence of $NaBH_4$ reductant and mercuric trifluoroacetate. Both of these reactions are carried out under extreme conditions which are difficult to handle. Waste compounds are also generated which can create environmental problems. For these reasons, the applications of these two methods are limited.

Phase transfer catalysis (PTC), which employs quaternary ammonium salts as catalyst, is an important technology and a practical tool in synthetic organic chemistry.[3–6] Its origin goes back to the early 1950s when Jarrousse reported the substitution of 1-chlorooctane with sodium cyanide in a two-phase system in the presence of quaternary ammonium salts.[7] Reviews on the synthesis of organic chemicals using phase-transfer catalysts have been published.[3,5,6,8–11] The two immiscible reactants, which are lipophilic and hydrophilic, respectively, stay in the organic and aqueous phases, respectively. The two-phase reaction takes place in the presence of a phase-transfer catalyst. Generally, the accepted mechanism is that the catalysts transfer between the two phases. At present, tetraalkylammonium halides or tetraalkylphosphonium halides are mostly used as phase-transfer catalysts.[3,12] The major advantages of using the PTC technique to synthesize organic compounds are enhancing the reaction rate, carrying out the reaction under mild conditions, obtaining high selectivity and high conversion of reactant.[3,4,9,11]

In the present work, a monoether and diether were synthesized from the reaction of 4,4′-bis(chloromethyl)-1,1′-biphenyl and 1-butanol by PTC in an alkaline aqueous solution/organic solvent two-phase medium. Two sequential substitutions of chlorides from 4,4′-bis(chloromethyl)-1,1′-biphenyl were carried out in the organic phase. Both 4,4′-(butoxymethylchloromethyl)-1,1′-biphenyl and 4,4′-bis(butoxymethyl)-1,1′-biphenyl were obtained during or after reaction. High-purity monosubstituted and disubstituted products were obtained using pressurized column chroma-

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tography.[13] A kinetic model, which considers the reactions in the aqueous- and organic phases, mass transfer of the generated catalyst and the active catalyst, and the phase equilibria of the regenerated catalyst and the active catalyst to describe the experimental results, was set. The effects of the reaction conditions on the conversion were investigated in detail. Rational explanations of the results were made.

Experimental Section

Materials. 4,4′-Bis(chloromethyl)-1,1′-biphenyl, 1-butanol, biphenyl, and chlorobenzene, toluene, dibutyl ether, acetonitrile, benzene, o-xylene, m-xylene were obtained from Aldrich Chemical Co., Inc. and Mallinckrodt Co., respectively. Tetrabutylammonium bromide (TBAB), tetrabutylammonium chloride (TBAC), tetrabutylammonium iodide (TBAI), tetrabutylammonium hydrogensulfate (TBAHS), tetrabutylammonium hydroxide (TBAOH), tetraoctylammonium bromide (TOAB), tetraethylammonium bromide (TEAB), hexadecyltrimethylammonium bromide (HTMAB), benzyltributylammonium bromide (BTBAB), benzyltriethylammonium bromide (BTEAB), hexadecyltrimethylammonium bromide (HdTMAB), phenyltrimethylammonium bromide (PhTMAB), poly(ethylene glycol)-300 (PEG-300), poly(ethylene glycol)-600 (PEG-600), 18-crown 6-ether, and potassium hydroxide were purchased from Fluka Chemical Corp. Tricaprylmethylammonium bromide (Aliquat 336) was obtained from Lancaster Co., Inc. Octyl dimethyl propylammonium sulfonic (SB-8) was purchased from HOPAX Co., Inc. (Taiwan). Polyoxyethylene-20-sorbitan monooleate (Tween 80) was brought from Fisher Biotech Co., Inc. The silica gel and aluminium oxide are the products of MN Co., Inc.

Procedures. *(a) Synthesis of 4,4′-(Butoxymethyl chloromethyl)-1,1′-biphenyl and 4,4′-Bis(butoxymethyl)-1,1′-biphenyl and Their Separation.* The reactor was a 150-mL three-necked Pyrex flask set up for feeding the reactants, taking samples, and agitating the solution. The reactor was submerged in a constant-temperature water bath in which the temperature was controlled to within ±0.1 °C. Measured quantities of 4,4′-bis(chloromethyl)-1,1′-biphenyl (20 mmol for synthesizing products, 4 mmol for studying kinetics), 1-butanol (150 mmol), potassium hydroxide (20 g) and TBAB (0.5 mmol) were dissolved in a mixture of 50 mL of chlorobenzene and 20 mL of water at 45 ± 0.1 °C. The mixed solution was stirred continuously using a mechanical mixer equipped with a PTFE (poly(tetrafluoroethylene)) stirring blade rotating at 800 rpm. After 3 h of reaction, the two-phase solution was separated, and the portion of the organic solution was washed five times with an alkaline solution to remove TBAB catalyst. The organic solvent was evaporated in a vacuum evaporator.

Before the pressurized column chromatography was performed, TLC analyses were carried out on silica gel and aluminum oxide plate. Then, the mixture was separated by pressurized column chromatography in which the pressurized, controlled flow rate enhances the separation effect.[14] A glass

chromatography column 100 cm in length and 3 cm in diameter was used as the separation column. The collected sample in each test tube was analyzed by HPLC. When the silica gel was used as adsorbent and dichloromethane as eluent, the monosubstituted product was obtained first. Conversely, the disubstituted product was obtained first if aluminum oxide was used as adsorbent and methanol/pentane (1/1) as eluent. The monosubstituted product and the disubstituted product in the eluent were concentrated by vacuum evaporation.

The products were identified by mass spectrometry for molecular weight and NMR spectroscopy (^{1}H NMR and ^{13}C NMR) for functional groups. The monosubstituted product (4,4′-(butoxymethylchloromethyl)-1,1′-biphenyl) and disubstituted product (4,4′-bis(butoxymethyl)-1,1′-biphenyl) were obtained in 98% purity. High performance liquid chromatography (HPLC) was carried out by using a Shimadzu SPD-10AVP with analyzed software glass vp 5.0 with UV wavelength 269 nm. The RP-18e (5 μm) column (Applied Merck Co.) was used to separate the components and to analyze them experimentally.

(b) Kinetics of the Experimental Runs. The reactor was a 150-mL three-necked Pyrex flask. Known quantities of 4,4′-bis(chloromethyl)-1,1′-biphenyl, 1-butanol, potassium hydroxide, biphenyl (as internal standard), organic solvent, water, and phase-transfer catalyst were introduced into the reactor. The reactor was controlled at a desired temperature and agitation rate. For a kinetic run, a sample (approximately 0.3 mL) was withdrawn from the reaction solution at a chosen time. The sample was immediately added to 5 mL of methanol to quench the reaction and then analyzed for the contents in the organic phase quantitatively by HPLC using the internal standard method.

Reaction Mechanism and Kinetic Model

A total reaction for the present system is
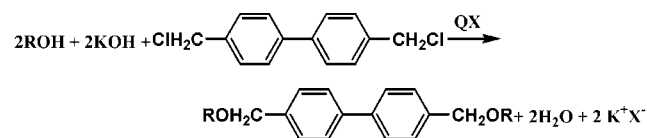
For that, a rational mechanism is proposed as follows:
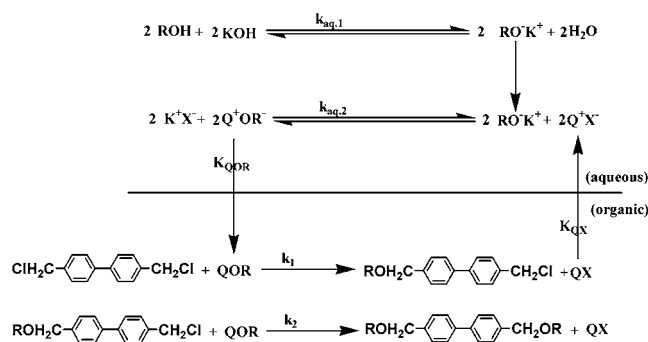
The mechanism was formulated on the basis of Starks' extraction model.[3,6] An active catalyst QOR, which is an organic-soluble compound, was produced from the aqueous solution by reacting catalyst QX and potassium alkoxide

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(ROK). Then, QOR, which transfers to the organic phase, reacts with 4,4′-bis(chloromethyl)-1,1′-biphenyl to produce 4,4′-(butoxymethylchloromethyl)-1,1′-biphenyl and 4,4′-bis-(butoxymethyl)-1,1′-biphenyl. QX transfers from the organic phase and is regenerated into QOR in the aqueous phase. In this study, $[QOR]_o$ and $[QX]_o$ are kept at a constant value by using a large excess of 1-butanol. On the basis of the experimental data, no byproducts were observed. The ion exchanges in the aqueous phase were all rapid. Therefore, the etherification in the organic phase is the rate-determining step for the whole reaction system. Material balances for the regenerated catalyst QX and the active catalyst in the organic and aqueous phases are:

$$\frac{d[QOR]_o}{dt} = K_{QOR}A\left([QOR]_a - \frac{[QOR]_o}{M_{QOR}}\right) - $$
$$k_1[C_{12}H_8(CH_2Cl)_2]_o[QOR]_o - $$
$$k_2[C_{12}H_8(CH_2Cl)(CH_2OR)]_o[QOR]_o \quad (1)$$

$$\frac{d[QOR]_a}{dt} = k_{aq,2}[ROK]_a[QX]_a - $$
$$K_{QOR}Af\left([QOR]_a - \frac{[QOR]_o}{M_{QOR}}\right) \quad (2)$$

$$\frac{d[QX]_o}{dt} = k_1[C_{12}H_8(CH_2Cl)_2]_o[QOR]_o + $$
$$k_2[C_{12}H_8(CH_2Cl)(CH_2OR)]_o[QOR]_o - $$
$$K_{QX}A([QX]_o - M_{QX}[QX]_a) \quad (3)$$

$$\frac{d[QX]_a}{dt} = K_{QX}Af([QX]_o - M_{QX}[QX]_a) - $$
$$k_{aq,2}[ROK]_a[QX]_a \quad (4)$$

$$Q_0 = V_o([QOR]_o + [QX]_o) + V_a([QOR]_a + [QX]_a) \quad (5)$$

where f is the ratio of the volume of organic solution (V_o) to the volume of aqueous solution (V_a). The subscript "o" and "a" denote the characteristics of the species in the organic and aqueous phase, respectively. k_1 and k_2 are the intrinsic rate constants of the two sequential reactions in the organic phase. $k_{aq,1}$ and $k_{aq,2}$ are the intrinsic rate constants of the two ionic reactions in the aqueous phase. A is the interfacial area between two phases. Q_0 is the total catalyst. K_{QX} and K_{QOR} are the mass transfer coefficients of QX and QOR between two phases. M_{QX} and M_{QOR} are the distribution coefficients of QX and QOR between two phases, respectively, i.e.

$$M_{QOR} = \frac{[QOR]_{o,s}}{[QOR]_{a,s}} \quad (6)$$

$$M_{QX} = \frac{[QX]_{o,s}}{[QX]_{a,s}} \quad (7)$$

On the basis of the experimental observation, the concentration of QOR and QX in the organic and aqueous phase reach a constant value at the beginning of the reaction.

Therefore, a pseudo-steady-state hypothesis (PSSH) is applied, i.e.

$$\frac{d[QOR]_o}{dt} = 0, \quad \frac{d[QOR]_a}{dt} = 0, \quad \frac{d[QX]_o}{dt} = 0, \quad \frac{d[QX]_a}{dt} = 0 \quad (8)$$

Combining eqs 1−5 and 8, we obtain

$$[QOR]_o = \frac{Q_0}{V_o}\left\{\left(1 + \frac{1}{fM_{QOR}}\right) + (1 + fM_{QX}) \times\right.$$
$$\frac{k_1[C_{12}H_8(CH_2Cl)_2]_o + k_2[C_{12}H_8(CH_2Cl)(CH_2OR)]_o}{k_{aq,2}[ROK]_a} + $$
$$\left(\frac{1}{K_{QX}A} + \frac{1}{fK_{QOR}A}\right)(k_1[C_{12}H_8(CH_2Cl)_2]_o + $$
$$\left. k_2[C_{12}H_8(CH_2Cl)(CH_2OR)]_o)\right\}^{-1} \quad (9)$$

The following Damkohler numbers, $Da_{QX,1}$, $Da_{QX,2}$, $Da_{QOR,1}$, $Da_{QOR,2}$ are defined as

$$Da_{QX,1} = \frac{k_1[C_{12}H_8(CH_2Cl)_2]_o}{K_{QX}A}$$

$$Da_{QX,2} = \frac{k_2[C_{12}H_8(CH_2Cl)(CH_2OR)]_o}{K_{QX}A}$$

$$Da_{QOR,1} = \frac{k_1[C_{12}H_8(CH_2Cl)_2]_o}{K_{QOR}A}$$

$$Da_{QOR,2} = \frac{k_2[C_{12}H_8(CH_2Cl)(CH_2OR)]_o}{K_{QOR}A} \quad (10)$$

R_1 and R_2 are defined as the ratio of the organic-phase reaction rate to the aqueous-phase reaction rate, i.e.

$$R_1 = \frac{k_1[C_{12}H_8(CH_2Cl)_2]_o}{k_{aq,2}[ROK]_a}$$

$$R_2 = \frac{k_2[C_{12}H_8(CH_2Cl)(CH_2OR)]_o}{k_{aq,2}[ROK]_a} \quad (11)$$

Thus, eq 9 can be written in a dimensionless form,

$$[QOR]_o = \frac{Q_0}{V_o}\left\{\left(1 + \frac{1}{fM_{QOR}}\right) + (1 + fM_{QX})(R_1 + R_2) + \right.$$
$$\left. (Da_{QX,1} + Da_{QX,2}) + \frac{(Da_{QOR,1} + Da_{QOR,2})}{f}\right\}^{-1} \quad (12)$$

Several experiments were carried out to measure the QOR concentration in the aqueous and organic phases. It was found that the transfer of QOR from aqueous phase to organic phase is rapid. The equilibrium state of QOR between two phases is built up fast within one minute. This result indicates that the mass transfer of QOR or QCl are rapid compared to the organic-phase reaction. On the basis of the experimental evidence, both the Damkohler numbers and R_1 and R_2 are small. Therefore, eq 12 is reduced to

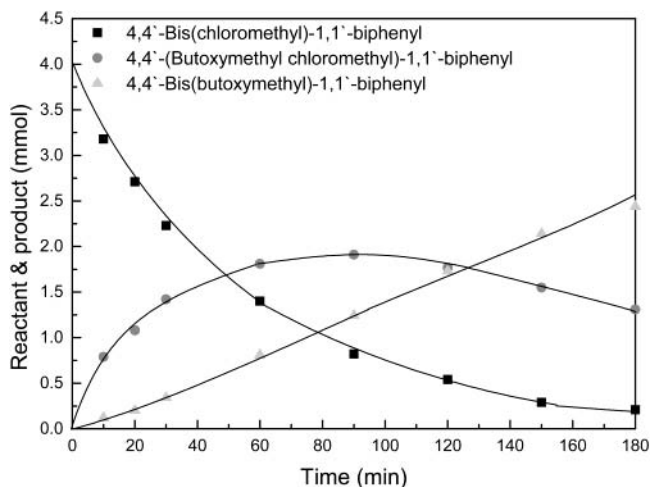$$[QOR]_o = \frac{fM_{QOR}}{1 + fM_{QOR}}\frac{Q_0}{V_o} \quad (13)$$

Figure 1. Plot of consumption of 4,4′-bis(chloromethyl)-1,1′-biphenyl and generation of monosubstituted and disubstituted product vs time.

From eq 13, it is obvious that $[QOR]_o$ is kept at a constant value. Therefore, a pseudo-first-order rate law can be applied to describe the reaction.

Material balances for the compounds in the reaction solution are:

$$- \frac{[C_{12}H_8(CH_2Cl)_2]_o}{dt} = k_{app,1}[C_{12}H_8(CH_2Cl)_2]_o \qquad (14)$$

$$\frac{[C_{12}H_8(CH_2Cl)(CH_2OR)]_o}{dt} = k_{app,1}[C_{12}H_8(CH_2Cl)_2]_o -$$
$$k_{app,2}[C_{12}H_8(CH_2Cl)(CH_2OR)]_o \quad (15)$$

$$\frac{[C_{12}H_8(CH_2OR)_2]_o}{dt} = k_{app,2}[C_{12}H_8(CH_2OR)_2]_o \qquad (16)$$

where $C_{12}H_8(CH_2Cl)_2$, $C_{12}H_8(CH_2Cl)(CH_2OR)$, and $C_{12}H_8(CH_2OR)_2$ are 4,4′-bis(chloromethyl)-1,1′-biphenyl, 4,4-(butoxy-methylchloromethyl)-1,1-biphenyl (monosubstituted product), and 4,4-bis(butoxymethyl)-1,1-biphenyl (disubstituted product), respectively. As shown in Figure 1, the distribution of reactants and products is typical of a series reaction in an organic phase. The monosubstituted product increases first and then decreases. The disubstituted product increases throughout the reaction period. The concentration of QOR in the organic phase is at a constant value immediately after starting the reaction. $k_{app,1}$ and $k_{app,2}$ are the two apparent rate constants of the two sequential reactions in the organic phase and are defined as

$$k_{app,1} = k_1[QOR]_o \qquad (17)$$

$$k_{app,2} = k_2[QOR]_o \qquad (18)$$

The data obtained from the kinetic runs were analyzed using the integral method of rate data analysis. A pseudo-first-order rate expression was tried first for all the kinetic runs and was found to be sufficient for rate data analysis.

Integrating eq 14 yields

$$[C_{12}H_8(CH_2Cl)_2]_o/[C_{12}H_8(CH_2Cl)_2]_{o,i} = \exp(-k_{app,1}t) \quad (19)$$

The subscript "i" represents the initial concentration of the species. Equation 19 is rewritten as

$$-ln(1 - X) = k_{app,1}t \qquad (20)$$

where X is defined as the conversion of $C_{12}H_8(CH_2Cl)_2$, i.e.

$$X = 1 - \frac{[C_{12}H_8(CH_2Cl)_2]_o}{[C_{12}H_8(CH_2Cl)_2]_{o,i}} \qquad (21)$$

in which $[C_{12}H_8(CH_2Cl)_2]_{o,i}$ denotes the initial concentration of 4,4′-bis(chloromethyl)-1,1′-biphenyl (reactant) in the organic phase. Thus, the value of $k_{app,1}$ can be obtained from experimental data in conjunction with eq 20.

Substituting eq 21 into eq 15, we obtain

$$\frac{[C_{12}H_8(CH_2Cl)(CH_2OR)]_o}{[C_{12}H_8(CH_2Cl)_2]_{o,i}} = \frac{k_{app,1}}{k_{app,2} - k_{app,1}} \times$$
$$[\exp(-k_{app,1}t) - \exp(-k_{app,2}t)] \quad (22)$$

On the basis of the experimental data for $[C_{12}H_8(CH_2Cl)-(CH_2OR)]_o$, the value of $k_{app,2}$ can be obtained from eq 22 with the previous knowledge of $k_{app,1}$. The kinetic parameters of the equation were obtained using a computer program (software Fortran 90).

Results and Discussion

In the present work, the products of 4,4′-(butoxymethyl-chloromethyl)-1,1′-biphenyl and 4,4′-bis(butoxymethyl)-1,1′-biphenyl produced from reaction solution were successfully separated and purified by pressurized column chromatography. The content of each product was identified by HPLC analysis. The optimum conditions for separating these two products were to set a 90-cm height of silica gel or aluminum oxide at the flow rate of 15−20 mL/min eluent. By this method, the purity of each product can reach 98% based on HPLC analysis. As shown in Figure 1, a material balance for the reactant, monosubstituted product, and disubstituted product is satisfactorily made. The effects of the operating conditions on the yield of the monoether and diether are discussed in the following.

(i) Effect of the Agitation Speed. Usually, the mass transfer of components (e.g., active catalyst QOC_4H_9 or the regeneration catalyst QCl) between two phases is an important factor in affecting the conversion in a heterogeneous reaction. As shown in Figure 2, no improvement in the reaction rate is observed when the agitation rate exceeds 200 rpm. Below 200 rpm, the conversion is highly dependent on the agitation speed because the reaction is under mass transfer and chemical reaction control. When the agitation speed is increased over 200 rpm, mass transfer effects are, to all intents and purposes, removed. The results indicate that the reaction rate is relatively slow compared to the mass transfer rate in the present system. The chemical reaction is obviously a rate-determining step; therefore, the agitation rate was set at 800 rpm in the following experimental runs to eliminate the mass transfer effect.

The apparent rate constants, $k_{app,1}$ and $k_{app,2}$ are shown in Figure 3. The value of $k_{app,1}$ is larger than that of $k_{app,2}$. This
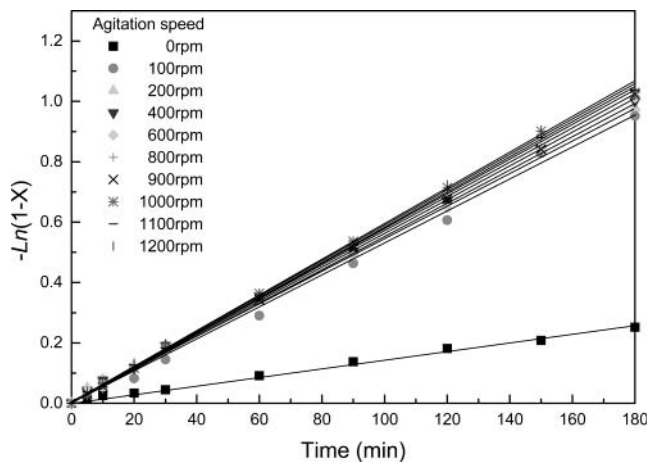
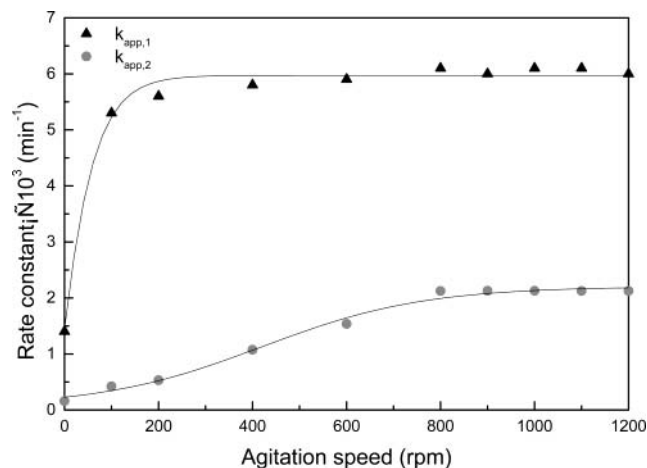**Figure 2.** Effect of the agitation speed on the conversion of 4,4′-bis(chloromethyl)-1,1′-biphenyl.

Figure 3. Effect of the agitation speed on the two apparent rate constants, $k_{app,1}$ and $k_{app,2}$.

Figure 4. Effect of the volume of chlorobenzene on the two apparent rate constants, $k_{app,1}$ and $k_{app,2}$.

result indicates that the first substitution reaction is faster than the second one in the organic solution. The agitation speed for reaching constant values for the apparent rate constants are 400 and 800 rpm for $k_{app,1}$ and $k_{app,2}$, respectively. This evidence verifies that the sequential reactions are taking place in the organic solution. Also, the organic-phase reactant has two chlorine atoms to be substituted by alkoxide (RO^-). Therefore, the probability of collision of alkoxide with any one of the two chlorine atoms of the organic-phase reactant to produce monosubstituted product is greater than that of collision of alkoxide with only one chlorine atom of the monosubstituted product to produce disubstituted product. In principle, the agitation speed is an index of the probability of collision of two molecules in the solution. Therefore, it naturally takes less agitation speed to synthesize monosubstituted product than that to synthesize disubstituted product.

(ii) Effect of the Volume of the Organic Solvent. Both the apparent rate constants, $k_{app,1}$ and $k_{app,2}$, are increased with a decrease in the amount of chlorobenzene. The results are shown in Figure 4. It is obvious that a greater concentration of the active catalyst is obtained in the organic phase using less chlorobenzene; hence, the reaction rate (or the conversion) is increased by decreasing the amount of organic
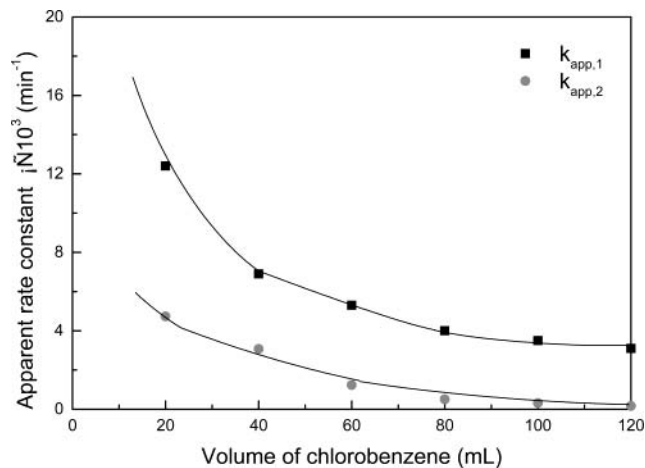
solvent. However, less organic solvent will lead to a smaller organic−aqueous interfacial area which then reduces the mass transfer between the two phases. The effect of the concentration on the reaction rate (or conversion) is still greater than that of the interfacial area on the reaction rate. Hence, the reaction rate is decreased with an increased amount of organic solvent. However, a small amount of chlorobenzene will not be sufficient to dissolve 4,4′-bis-(chloromethyl)-1,1′-biphenyl reactant completely.

(iii) Effect of the Catalysts. Quaternary ammonium salts are extensively used as the phase-transfer catalysts in synthesizing speciality chemicals. However, there is not a universal rule to guide chemists in selecting an appropriate catalyst to use in PTC. The choice is highly dependent on the characteristics of the chemical reaction system and the physical properties of the reactants. Different reactions require different catalysts to enhance the reaction rate and to maximize the yield of product. The primary condition for the reaction rate enhancement is that the interfacial tension between two phases is decreased by adding quaternary ammonium salt. Therefore, the transfer of species across the interfacial boundary in contacting two phases is facilitated. Furthermore, both the solubility of the organic-phase reactant in the aqueous-phase solution and the solubility of the aqueous phase reactant in the organic-phase solution are both increased by the addition of quaternary ammonium salt. Hence, the reaction rate is increased with increased amounts of quaternary ammonium salt.

As shown in Table 1, both cation and anion affect the reactivities of quaternary ammonium salts under PTC. Comparing the results for TBAB, TBAC, TBAI, TBAHS, and TBAOH for the same cation (tetrabutylammonium cation), the order of the reactivity of these anions is OH^- > HSO_4^- = Br^- > Cl^- = I^-. Furthermore, different alkyl groups in the quaternary ammonium cation with the same anion (bromide), such as TEAB, TBAB, and TOAB, exhibit different reactivities under the same experimental conditions. A higher total carbon number in the alkyl groups gives higher reaction rates. The reason for this is due to the fact that a higher total carbon number confers increased hydrophobic properties on the PTC. TEAB, which is very water soluble,

Table 1. Effect of the catalysts on the two apparent rate constants[a]

catalyst	$k_{app,1}$ (10^3 min^{-1})	$k_{app,2}$ (10^3 min^{-1})	catalyst	$k_{app,1}$ (10^3 min^{-1})	$k_{app,2}$ (10^3 min^{-1})
TBAB	6.09	2.13	BTEAB	3.22	1.18
TBAC	5.68	2.10	BTBAB	5.24	1.86
TBAI	5.60	1.96	PhTMAB	2.05	0.80
TBAHS	6.16	2.13	Aliquat336	2.61	0.98
TBAOH	6.42	2.14	SB-8	1.71	0.60
TEAB	2.91	1.05	PEG-300	1.45	0.48
TOAB	6.67	2.35	PEG-600	2.76	0.97
HTMAB	1.94	0.67	Tween80	3.21	1.18
HdTMAB	1.97	0.68	18-crown 6-ether	14.99	5.22

[a] Reaction conditions: 4 mmol 4,4′-bis(chloromethyl)-1,1′-biphenyl, 150 mmol 1-butanol, 3 mmol internal standard (biphenyl), 50 mL of chlorobenzene, 20 g of KOH, 20 mL of water, 800 rpm, 45 °C.

provides less reactivity, whilst TOAB catalyst, which possesses 32 carbon atoms, is extremely hydrophobic and gives the highest reaction rate of any phase-transfer catalyst tested.

The different structural groups, such as HdTMAB, PhTMAB, HTMAB, BTEAB, and BTBAB, also affect the catalytic reactivity. Catalysts, which have aromatic groups, possess higher catalytic reactivity than a straight long chain alkyl group. This effect is due to the fact that the electron density of N$^+$ for an aromatic group in the quaternary ammonium cation is larger than that of N$^+$ for a long chain alkyl group. It is thus unfavorable to form QOR using a quaternary ammonium cation of a long chain alkyl group. On the basis of the principle of like dissolving like, the solubility of quaternary ammonium salt with aromatic group is larger than that of the quaternary ammonium salt with a long chain alkyl group. Therefore, a high reaction rate is obtained using a quaternary ammonium salt with aromatic group.[8,15] Phosphonium salts were not used as phase-transfer catalysts in this reaction system because they decompose rapidly under base conditions (half-lives of minutes) via an Ylide mechanism yielding phosphine oxides and a hydrocarbon.[16]

$$R_4P^+OH^- \rightarrow PR_3{=}O + RH$$
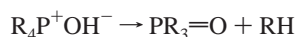
Several other phase-transfer catalysts were used to examine the reactivity in the etherification reaction. 18-Crown-6 ether exhibits the highest reactivity of all catalysts tested. Tween 80 possesses a certain catalytic effect; however, SB-8 (QSO$_3$) does not show high reactivity in this reaction system although it has excellent reactivity for the dichlorocarbene system.[17]

(iv) Effect of the Amount of Tetrabutylammonium Bromide (TBAB). Normally, the consumption of the reactant 4,4′-bis(chloromethyl)-1,1′-biphenyl is less than 10% after 3 h in the absence of catalyst. The effect of TBAB catalyst on the two apparent rate constants is shown in Figure 5. It is obvious that the catalyst enhances the reaction rate up to 50 mol % loading. It may be that there is no increase in rate above 50 mol % because the concentration of the catalyst is
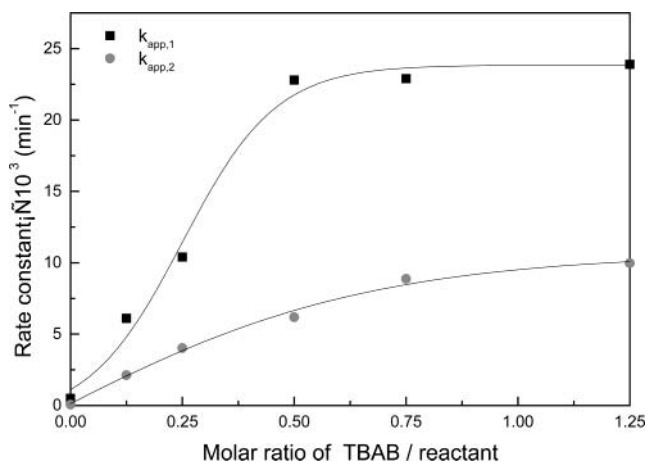
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Figure 5. Effect of the amount of TBAB catalyst on the two apparent rate constants, $k_{app,1}$ and $k_{app,2}$.
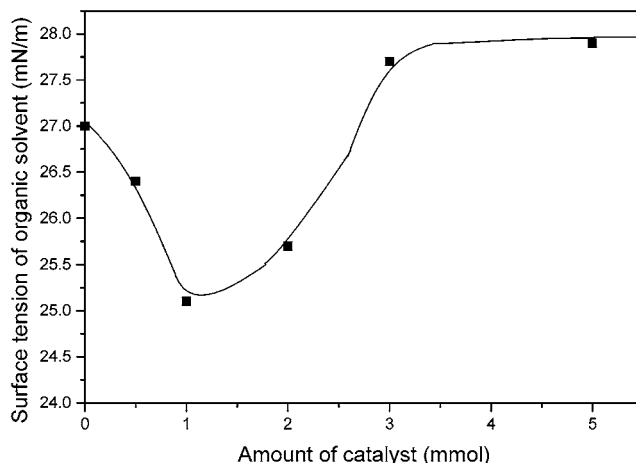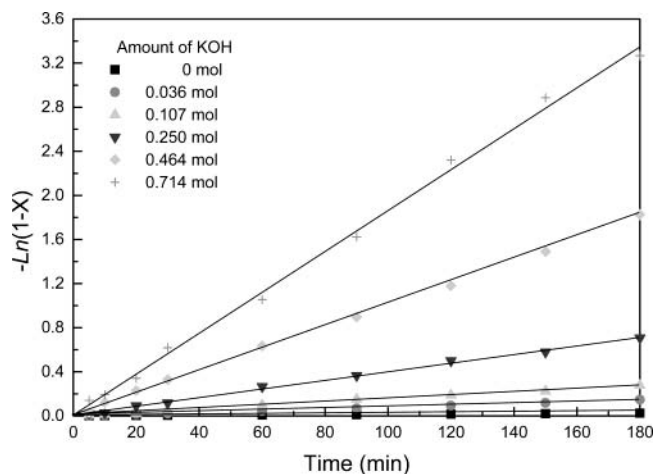

Figure 6. Plot of surface tension of organic solvent with different amounts of phase-transfer catalysts at 45 °C; same conditions as given in Figure 2.

over the critical micelle concentration (CMC). The effect of the amount of catalyst on the surface tension of the organic solvent is shown in Figure 6. At a concentration of phase-transfer catalyst higher than the critical micelle concentration, the shielded effect is significant. Groups (or aggregates) that contain many catalyst molecules are formed in the organic solution. The hydrophilic ending groups (i.e., nucleophilic reagent) of the catalysts are located inside the micelle group where the hydrophobic ending groups of the catalysts are

Figure 7. Effect of the amount of KOH on the conversion of reactant (4,4′-bis(chloromethyl)-1,1′-biphenyl).
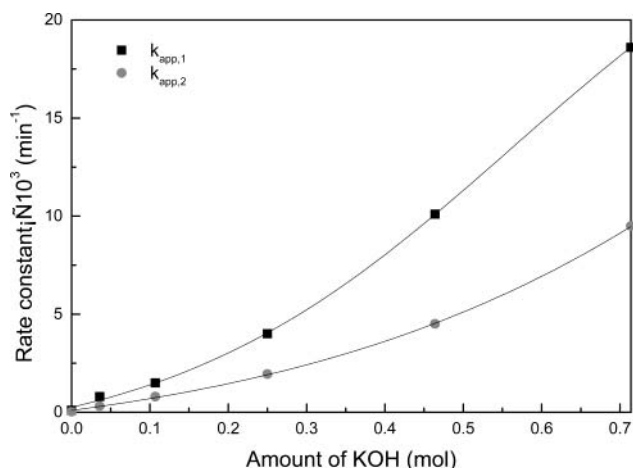

Figure 8. Effect of the amount of KOH on the two apparent rate constants, $k_{app,1}$ and $k_{app,2}$.

facing outward intimating with the organic solvent. For this, the nucleophilic reaction is retarded.[18−21]

(v) Effect of the Amount of KOH. KOH can reduce the amount of water available for anion hydration and force the catalyst from the aqueous phase to the organic phase.[16,22] KOH affects the distribution of the active catalyst QOR between the two phases and the hydration number of QOR. Increased KOH concentration also enhances the production of RO⁻. Hence, the concentration of QOR in the organic phase is increased by increasing the concentration of KOH in the aqueous phase. As shown in Figure 7, the conversion is increased with the increase in the amount of KOH. The corresponding apparent rate constants, $k_{app,1}$ and $k_{app,2}$ are given in Figure 8. Both the apparent rate constants are increased with the increase in the amount of KOH. Although quaternary ammonium salt also decomposes to tertiary amine and alcohol at high alkaline concentrations, the half-lives of quaternary ammonium salts are longer than these of quater-
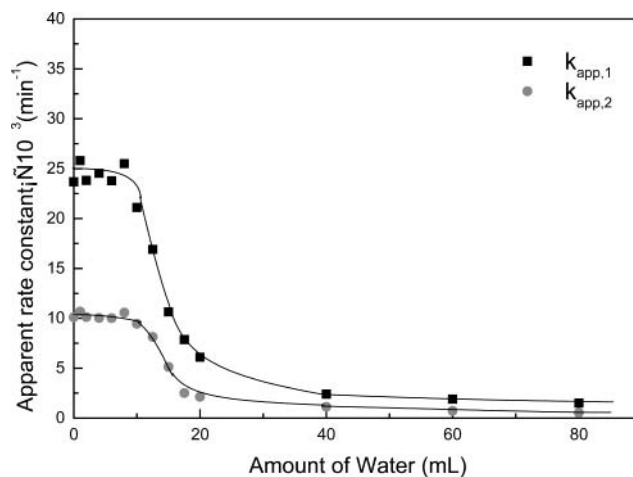
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Figure 9. Effect of the amount of water on the two apparent rate constants, $k_{app,1}$ and $k_{app,2}$.

nary phosphonium salts Thus, quaternary ammonium salts are the phase-transfer catalyst of choice in a hydroxide-initiated phase-transfer catalytic reaction.[23]

(vi) Effect of the Amount of Water. As stated in part (i), the mass transfer resistance was kept at a constant value when the agitation speed was controlled at 800 rpm. Hence, any increase in the reaction rate caused by changing other reaction conditions was not due to the increase of the contact of the interfacial area. For a constant quantity of organic solvent (e.g., chlorobenzene), changing the amount of water affects the concentration of the active catalyst and the nucleophilic reagent in organic and aqueous phases. Also, the concentration of KOH is decreased with the increase in the amount of water used. The concentration of the active catalyst in the organic phase is increased, and the concentration of the active catalyst in the aqueous phase is decreased by decreasing the amount of water used. Therefore, the distribution of the active catalyst QOR between the organic and aqueous phases is affected by the concentration of KOH. In addition, hydration effects are increased by increasing the amount of water. Solvation effects are also affected significantly as the concentration of KOH is increased by decreasing the amount of water. As expected, as shown in Figure 9, the reaction rate is decreased with the increase in the amount of water.

(vii) Effect of the Organic Solvents. In this study, the Starks' extraction mechanism is employed to explain the reaction characteristics. Chlorobenzene, dibutyl ether, benzene, toluene, o-xylene, and m-xylene were chosen to investigate the effect of dielectric constants on the reaction, and the results are shown in Table 2 and Figure 10. Larger apparent rate constants were obtained when using a higher-polarity organic solvent (e.g., chlorobenzene). The apparent rate constants are increased with the increase in the polarity of the organic solvent except for dibutyl ether. The reactant and the monosubstituted product possess the dipole moment of a chloromethylene group. The formation of dipole−dipole force from a polar solvent and chloromethylene groups is favorable to stay in the polar organic solvent. Hence, the activation energy E_a is reduced for the S_N2 nucleophilic

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Table 2. Effect of the organic solvents on the two organic-phase apparent rate constants[a]

organic solvent	E_T^N	$k_{app,1}$ (10^3 min^{-1})	$k_{app,2}$ (10^3 min^{-1})
chlorobenzene ($\epsilon = 5.6$)	0.19	6.09	2.13
dibutyl ether ($\epsilon = 2.8$)	0.07	3.77	1.34
benzene ($\epsilon = 2.3$)	0.11	4.46	1.57
toluene ($\epsilon = 2.4$)	0.10	4.22	1.51
o-xylene ($\epsilon = 2.3$)	0.09	4.12	1.43
m-xylene ($\epsilon = 2.2$)	–	3.81	1.36

[a] Reaction conditions: 4 mmol 4,4′-bis(chloromethyl)-1,1′-biphenyl, 150 mmol 1-butanol, 3 mmol internal standard (biphenyl), 0.5 mmol TBAB, 20 g of KOH, 20 mL of water, 800 rpm, 45 °C.
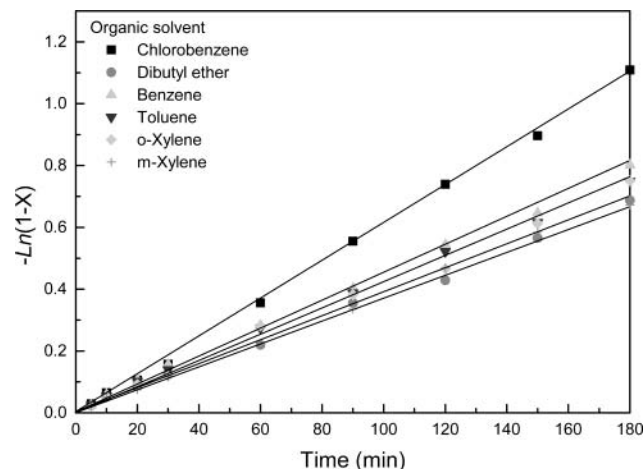

Figure 10. Effect of the organic solvents on the conversion of 4,4′-bis(chloromethyl)-1,1′-biphenyl.

substitution in more polar solvents. The oxygen in dibutyl ether possesses an electron lone pair which affects the reactivity. The electron lone pair hinders RO$^-$ from displacing the chloride atom so less reactivity is expected. However, as shown in Table 2, the apparent rate constants are not well correlated with the dielectric constants of the organic solvents. A better way to explain this difference is to use Recihardt's solvatochromatic scale E_T^N.[24−26]

(viii) Effect of Temperature. Effect of the temperature on the conversion of 4,4′-bis(chloromethyl)-1,1′-biphenyl is shown in Figure 11. A higher temperature enhances the reaction rate which is a type of endothermic. A pseudo-first-order rate law is sufficient to describe the reaction characteristics. The first apparent rate constant $k_{app,1}$ and the second apparent rate constant $k_{app,2}$ are listed in Table 3. The two activation energies (E_{a1} and E_{a2}) obtained, were 16 and 20 kcal/mol, by plotting $\ln(k_{app})$ vs $1/T$ from the Arrhenius equation.

Conclusions

In the present work, the substitution of 4,4′-bis(chloromethyl)-1,1′-biphenyl with 1-butanol is successfully carried out in an alkaline aqueous solution of KOH/organic solvent
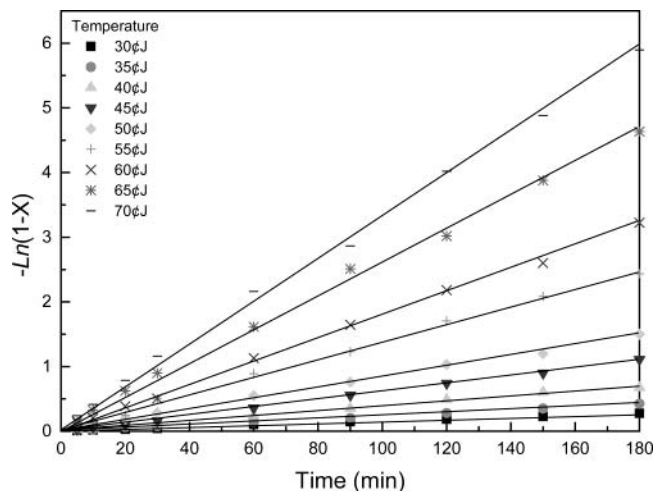
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Figure 11. Plot of $-ln(1 - X)$ of 4,4′-bis(chloromethyl)-1,1′-biphenyl vs time with various reaction temperatures.

Table 3. Effect of temperature on the two organic-phase apparent rate constants[a]

temperature (°C)	$k_{app,1}$ (10^{-3} min^{-1})	$k_{app,2}$ (10^{-3} min^{-1})
30	1.55	0.52
35	2.35	0.80
40	3.90	1.44
45	6.09	2.13
50	8.35	4.25
55	13.84	7.16
60	17.87	10.78
65	26.02	14.26
70	32.99	23.75

[a] Reaction conditions: 4 mmol 4,4′-bis(chloromethyl)-1,1′-biphenyl, 150 mmol 1-butanol, 3 mmol internal standard (biphenyl), 50 mL of chlorobenzene, 0.5 mmol TBAB, 20 g of KOH, 20 mL of water, 800 rpm.

two-phase medium under phase-transfer catalysis. Furthermore, the monosubstituted and disubstituted products are separated successfully by the effective method of pressurized column chromatography.

Among the catalysts, crown ether exhibits the highest reactivity. Among the quaternary ammonium salts, a quaternary ammonium salt having a large number of total carbons such as TOAB offers the highest reaction rate. The anion of quaternary ammonium salt does not significantly affect the conversion or the reaction rate. The reaction rate is increased by decreasing the amount of water and the amount of organic solvent. Nevertheless, the reaction rate is greatly increased with the increase in the amount of KOH. On the basis of the experimental results, the reaction is controlled by both chemical kinetics and mass transfer. The effect of the reaction conditions on the apparent rate constants, $k_{app,1}$ and $k_{app,2}$, and the conversion was obtained.