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Kinetic Study of Synthesizing 1-(3-Phenylpropyl)pyrrolidine-2,5-dione under Solid−Liquid Phase-Transfer Catalytic Conditions Assisted by Ultrasonic Irradiation

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Abstract:

The synthesis of 1-(3-phenylpropyl)pyrrolidine-2,5-dione (SUC-R) (1) was successfully carried out by reacting succinimide (SUC-H) (2) with 1-bromo-3-phenylpropane (RBr) (3) in a small amount of KOH and organic solvent solid−liquid phase medium under phase-transfer catalysis (PTC) and almost anhydrous conditions assisted by ultrasonic irradiation. The main purpose of this work was to obtain the kinetic behavior, activation energy, and the related parameters in the solid−liquid PTC reaction combined with the ultrasonic irradiation. Based on the experimental data, a rational mechanism for the reaction is proposed. The reaction followed a pseudo-first-order rate law. A rate expression was developed to describe the kinetic behaviors from which the apparent rate constant (k_{app}) of the organic-phase solution was obtained via experimental data. Kinetics of the reaction, including the effects of agitation speed, ultrasonic energy, amount of water, amount of potassium hydroxide, temperature, amount of tetrabutylammonium bromide (TBAB), volume of cyclohexanone, amount of SUC-H, quarternary ammonium salts, and organic solvents on the conversion of RBr and the apparent rate constant (k_{app}) were investigated in detail. Rational explanations to account for the resulting phenomena were provided.

1. Introduction

Phase-transfer catalysis (PTC), a technique to bring the reactants together to react in two mutually insoluble phases by adding a phase transfer agent, is useful for the synthesis of organic chemicals and is widely applied in a variety of industries.[1−3] Although examples of PTC can be found in the early literature, the technique has only been significantly developed since the middle of the 1960s. In comparison with traditional methods, PTC has the advantages of no need for expensive aprotic solvents, a simpler workup, shorter reaction time and lower reaction temperatures.[4]

Ultrasound irradiation has increasingly been used in organic synthesis over the past three decades. A large number of organic reactions can be carried out in higher yield in a shorter reaction time and milder condition with ultrasonic irradiation.[5−7] A natural combination would be ultrasonication and PTC, and such applications have been reported recently.[8−11]

Imide derivatives are organic compounds with numerous applications in biology,[12,13] as well as synthetic[14] and polymer[15] chemistry. In recent years, the synthesis of these derivative compounds were also reported in the literature.[16−20] However, there are only a few papers[21,22] discussing the synthesis of imide derivatives under solid−liquid PTC (SL-PTC). The main advantage in using such a solid−liquid process to carry out the reaction is to decrease the reaction rate due to hydration in the presence of water in the reaction solution.

In a recent paper, 1-(3-phenylpropyl)pyrrolidine-2,5-dione (SUC-R) (**3**) was synthesized,[22] as shown in Scheme 1. In this article, we report an efficient method for the synthesis of **3** catalyzed by tetrabutylammonium bromide (TBAB) in the presence of potassium hydroxide under ultrasound irradiation and nearly anhydrous conditions. The reaction is greatly

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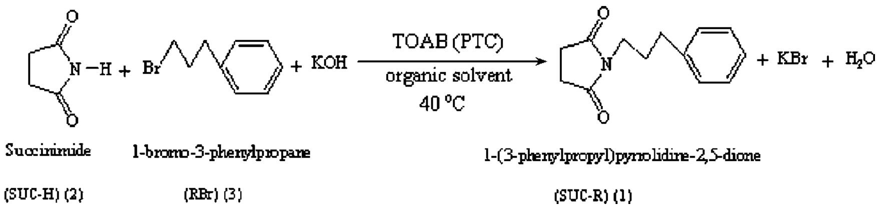
Scheme 1



enhanced by adding a small quantity of PTC and KOH during ultrasonication. Studies on the kinetics were investigated in detail, and a mechanism is proposed.

2. Experimental Section

The ultrasonic bath, model 3210, was specially designed and constructed by Branson Instruments Co. Ltd., U.S.A. The internal dimensions of the ultrasonic cleaner tank were 25 cm ×25 cm ×38 cm with a liquid (water) holding capacity of 24 L. The external tank size was 52 cm ×42 cm ×55 cm. Two types of ultrasound frequencies were used in these experiments, 40 kHz and 120 kHz with 300 W of output power. Both frequencies were separately produced through a flat transducer mounted at the bottom of the tank. In this ultrasonic instrument there was a provision for a drain as well as an outlet at the top. An additional heater with a temperature controller has also been provided so as to facilitate some high- and low-temperature reactions. This reaction vessel was suspended at the center of the ultrasonic cleaning bath 8 cm above the position of the transducer to obtain the maximum ultrasound energy.

2.1. Kinetics of the Solid−Liquid Phase Reaction. The reactor was a 150 mL three-necked round-bottomed Pyrex flask, fitted with an agitator, a thermometer, a sample port, and a feed port. Known quantities of succinimide (6.0×10^{-2} mol, as excess reagent, SUC-H), potassium hydroxide (1 g), TBAB (0.25 g, QBr), and 30 mL of cyclohexanone were put into the reactor and stirred at 800 rpm for about 30 min to form the tetrabutylammonium succinimide (SUC-Q) in an organic-phase solution, which was immersed in a water bath with well-controlled temperature (stability within ±0.1 °C). Measured quantities of 1-bromo-3-phenylpropane (6.0×10^{-3} mol, as limiting reagent, RBr) and naphthalene (0.3 g, internal standard) were then dissolved in 30 mL of cyclohexanone to form the organic solution. The organic solution was added to the reactor and agitated to start the reaction. The reaction mixture was stirred at 800 rpm; simultaneously the ultrasonic waves 40 kHz (300 W) were passed through the reactor.

An aliquot sample (0.2 mL) was withdrawn from the reaction solution and quenched in 6 mL of methanol at each time interval. The sample for analysis was withdrawn from the organic solution after the separation of the solid−liquid phases and then was analyzed quantitatively by HPLC using the internal standard method. The conditions for the HPLC analysis (Shimadzu LC-10A, Japan) were system controller: SCL-10AVP; UV−vis detector: SPD-10AVP; liquid chromatograph: LC-10ATVP; column: C-18 (25 cm ×4.6 mm, 5 μm, applied Supelco Co.); eluent: acetonitrile/deionized water (DI) = 65/35; flow rate = 1.2 mL/min; wavelength = 210 nm with retention time: succinimide = 2.72 min; 1-bromo-3-phenylpropane = 9.55 min; naphthalene = 7.35 min; 1-(3-phenylpropyl)pyrrolidine-2,5-dione = 3.84 min.

3. Reaction Mechanism and Kinetic Model

For synthesizing the imide compound, the overall reaction of succinimide (SUC-H) and 1-bromo-3-phenylpropane (RBr), which was catalyzed by TBAB (QBr) in the low-alkaline KOH/organic solvent solid−liquid phase medium and 40 kHz ultrasonic waves (300 W), can be expressed as depicted in Scheme 1.

In this work, no dialkyl ether was produced during or after the reaction. Therefore, a rational solid−liquid phase reaction mechanism is proposed as

$$SUC - H_{(s)} + KOH_{(s)} \xrightarrow{\substack{organic \\ solvent}} SUC - K_{(org)} + H_2O \tag{1}$$

$$SUC - K_{(org)} + QBr_{(org)} \overset{K_1}{\longleftrightarrow} SUC - Q_{(org)} + KBr_{(org)} \tag{2}$$

$$KBr_{(org)} \overset{K_2}{\longleftrightarrow} KBr_{(s)} \tag{3}$$

$$SUC - Q_{(org)} + RBr_{(org)} \xrightarrow{k_{\text{int}}} SUC - R_{(org)} + QBr_{(org)} \tag{4}$$

where the species are: KBr, potassium bromide; QBr, tetrabutylammonium bromide (TBAB); RBr, 1-bromo-3-phenylpropane (**3**); SUC-H, succinimide (**2**); SUC-K, potassium salt of succinimide; SUC-R, 1-(3-phenylpropyl)pyrrolidine-2,5-dione (**1**); SUC-Q, (tetrabutylammonium)succinimide. The subscripts "s", "org", "0" represent the characteristics of the species in the solid-phase, organic-phase, and the initial concentration of the species at time zero, respectively.

The reaction mechanism indicates that the active catalyst SUC-Q is produced from the reaction of succinimide (SUC-H), potassium hydroxide, and catalyst QBr in the organic-phase solution. Although no water was added, a trace amount of water was produced during the reaction. The inorganic salt KBr precipitated as a solid from the organic-phase solution. Then, the active catalyst SUC-Q reacted with the organic-phase reactant RBr to produce the desired product, SUC-R, in the organic-phase solution.

In general, the pseudo-first-order rate law can be used to describe the experimental data when a straight line is obtained by plotting $-\ln([RBr]_{org}/[RBr]_{org,0})$ vs time. Therefore, the rate equation of the intrinsic reaction for eq 4 is given by

$$-\frac{d[RBr]_{org}}{dt} = \frac{d[SUC-R]_{org}}{dt} = k_{int}[SUC-Q]_{org}[RBr]_{org} \quad (5)$$

As shown in eq 2, the reaction is fast and reaches equilibrium in a short time.

Thus, the equilibrium constant K_1 is defined as

$$K_1 = \frac{[SUC-Q]_{org}[KBr]_{org}}{[SUC-K]_{org}[QBr]_{org}} \quad (6)$$

As stated, the inorganic salt KBr precipitates from the organic solution, and the equilibrium constant K_2 is defined as

$$K_2 = \frac{[KBr]_s}{[KBr]_{org}} \quad (7)$$

The total initial concentration of catalyst Q_0 in the organic phase is written as

$$Q_0 = [SUC-Q]_{org} + [QBr]_{org} \quad (8)$$

The initial conditions of the species are

$$\begin{aligned} &t = 0, [\mathrm{QBr}]_{\mathrm{org},0} = [\mathrm{SUC\text{-}Q}]_{\mathrm{org},0} = [\mathrm{SUC\text{-}K}]_{\mathrm{org},0} = 0 \\ &[\mathrm{QBr}]_{\mathrm{org},0} = Q_0 \\ &[\mathrm{RBr}]_{\mathrm{org}} = [\mathrm{RBr}]_{\mathrm{org},0} \\ &[\mathrm{SUC\text{-}R}]_{\mathrm{org},0} = 0 \end{aligned} \quad (9)$$

Solving eqs 6−9, the concentration of SUC-Q in the organic phase is obtained as

$$[\mathrm{SUC\text{-}Q}]_{\mathrm{org}} = Q_0 f_c \quad (10)$$

where f_c is defined as

$$f_c = \frac{1}{1 + \frac{1}{K_1 K_2}\frac{[KBr]_s}{[SUC-K]_{org}}} \quad (11)$$

assuming that $[\mathrm{KBr}]_s$ and $[\mathrm{SUC\text{-}K}]_{\mathrm{org}}$ are kept at constant values after the induction period of the reaction. Therefore, as shown in eq 10, $[\mathrm{SUC\text{-}Q}]_{\mathrm{org}}$ stays at a constant value. For this statement, eq 5 can be expressed as

$$-\frac{d[RBr]_{org}}{dt} = \frac{d[SUC-R]_{org}}{dt} = k_{app}[RBr]_{org} \quad (12)$$

where k_{app} is the apparent rate constant and is given as

$$k_{app} = k_{int}[\mathrm{SUC\text{-}Q}]_{org} = k_{int} Q_0 f_c \quad (13)$$

By using eq 9, eq 12 is integrated to yield

$$-\ln(1 - X) = k_{app} t \quad (14)$$

where X is the conversion of RBr, i.e.,

$$X = 1 - \frac{[RBr]_{org}}{[RBr]_{org,0}} \quad (15)$$

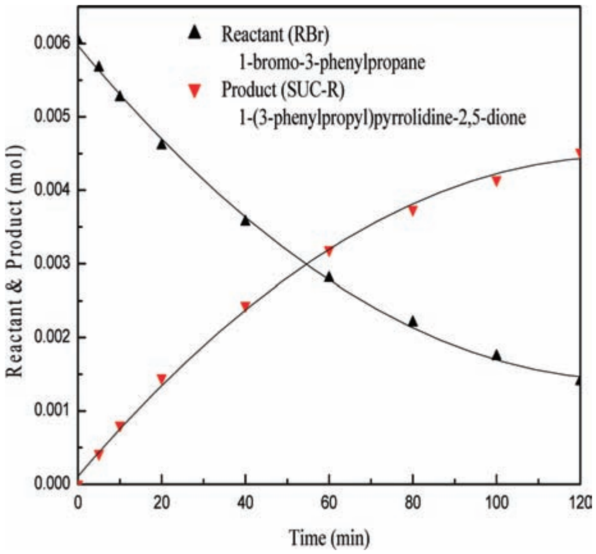


Figure 1. **Distribution of reactant and product during the reaction period; 6.0 × 10^{-2} mol of succinimide, 6.0 × 10^{-3} mol of 1-bromo-3-phenylpropane, 1 g of KOH, 60 mL of cyclohexanone, 0.3 g of internal standard (naphthalene), 0.25 g of TBAB, 45 °C, 800 rpm, 40 kHz (300 W).**

By plotting $-\ln(1 - X)$ versus t, the apparent rate constant k_{app} of the pseudo-first-order rate law from the slope of the straight line is obtained experimentally.

4. Results and Discussion

From the experimental observation, no byproducts (e.g., dialkyl ether) were observed during or after the reaction, indicating that only 1-(3-phenylpropyl)pyrrolidine-2,5-dione (**1**) was produced from the reactant 1-bromo-3-phenylpropane (**3**) by PTC and ultrasound (sonication) conditions, as shown in Figure 1. Therefore, the consumption of the reactant equals the production of the product. The effects of the reaction conditions on the conversion (X) of the limited reactant (**3**) and the apparent rate constant (k_{app}) are discussed below.

4.1. Effect of the Agitation Speed. For a solid−liquid phase reaction, stirring agitation increases the rate of solid−liquid mass transfer of the reaction system and tends to speedup the reaction until a limiting value is reached. After this, the reaction rate is not affected by further increases in the stirring rates. Thus, the effect of the agitation speed on the conversion and the reaction rate was studied in the range of 0−1200 rpm and the ultrasonic energy at 40 kHz (300 W) throughout the reaction. The particle size of KOH is chosen as 5 mm in this system. As shown in Figure 2, the experimental data of the reaction kinetics follows the pseudo-first-order rate law and passes the origin point of a straight line for each experimental run. On the basis of experimental observation, the reaction is still enhanced by ultrasonic irradiation even when the reaction is not agitated by the stirrer. Torok et al.[23] reported that the ultrasonic wave also enhanced the reaction rate due to an increase in the collision rate between the organic−aqueous phase. It is believed that the interfacial area between two phases is affected both by the agitation speed and the use of ultrasound. Therefore, the

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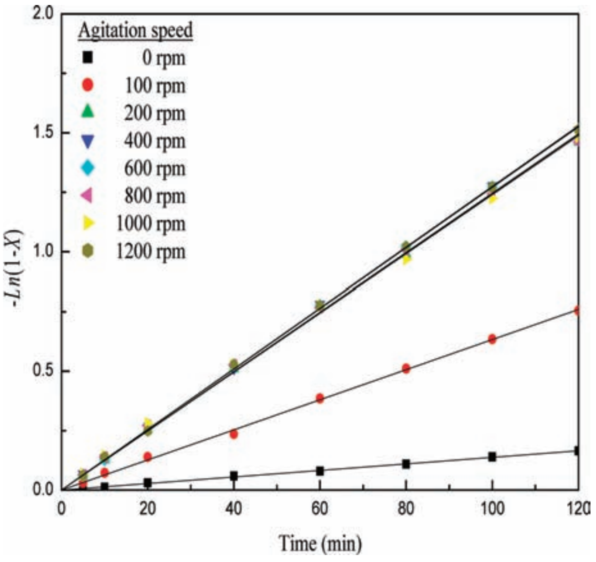

Figure 2. **Plot of $-\ln(1 - X)$ of 1-bromo-3-phenylpropane versus time with various agitation speeds; 6.0×10^{-2} mol of succinimide, 6.0×10^{-3} mol of 1-bromo-3-phenyl-propane, 1 g of KOH, 60 mL of cyclohexanone, 0.3 g of internal standard (naphthalene), 0.25 g of TBAB, 45 °C, 40 kHz (300 W).**

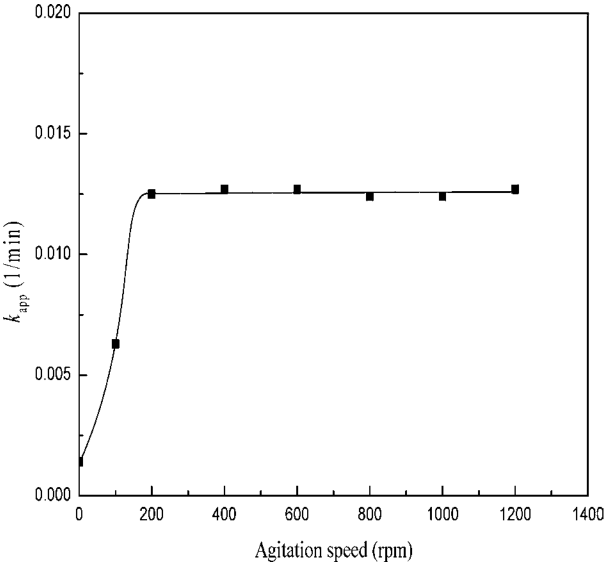

Figure 3. **Plot of the apparent rate constants versus various agitation speeds; 0.09 mol of succinimide, 0.006 mol of 1-bromo-3-phenylpropane, 1 g of KOH, 60 mL of cyclohexanone, 0.3 g of internal standard (naphthalene), 0.25 g of TBAB, 45 °C, 40 kHz (300 W).**

agitation and the ultrasonic irradiation are synergistic in enhancing the reaction. The apparent rate constants (k_{app}) were obtained from the slopes of the straight lines. As shown in Figure 3, there was a significant increase in the apparent rate constant (k_{app}) from 0 to 200 rpm, but it remained constant from 200 to 1200 rpm. This phenomenon indicates that the influence of the external mass transfer resistance on the reaction beyond 200 rpm is less. Thus, the organic-phase reaction was obviously a rate-determining step at 200−1200 rpm. All subsequent reactions were set at 800 rpm to asses the effect of various factors on the rate of reaction.

4.2. Effect of the Ultrasound. In our experiments, an ultrasonic bath filled with water, model 3210, was used as described in the Experimental Section. The reaction rates at 40 kHz and 120 kHz were compared with same output power of 300 W. The results are shown in Figure 4. The effect of the ultrasonic frequency on the apparent rate constant (k_{app}) is shown in Table 1. At 120 min, without ultrasonic irradiation the conversion is only 62% ($k_{app} = 8 \times 10^{-3}$ min^{-1}), but in the presence of ultrasound the conversion is 76% ($k_{app} = 12.4 \times 10^{-3}$ min^{-1}) and 90% ($k_{app} = 19.3 \times 10^{-3}$ min^{-1}) for 40 and 120 kHz, respectively. From this observed result ultrasonic-assisted phase-transfer catalysis significantly increased the reaction rate. The same trend is also observed.[8−11] The application of ultrasound in organic synthesis is one of the popular areas in sonochemistry. In addition, the ultrasonic effect enhances the rate 1.55 times with respect to the conventional method (agitation speed at 800 rpm only). Thus, all the experimental parameters were done at 40 kHz with an output power of 300 W.

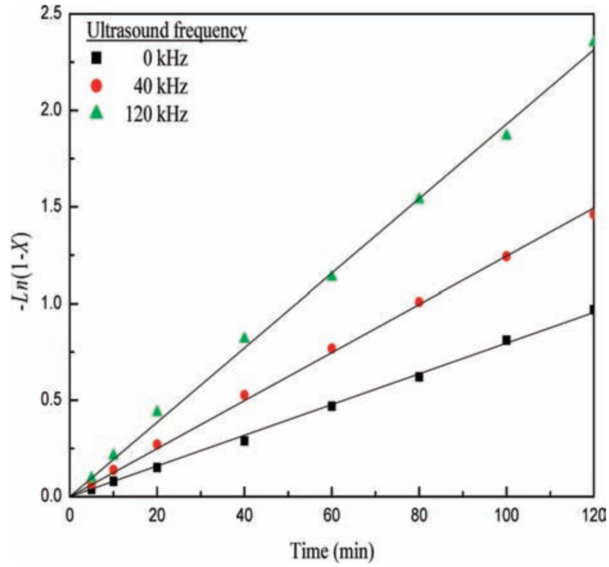

Figure 4. **Plot of $-\ln(1 - X)$ of 1-bromo-3-phenylpropane versus time with various ultrasound frequency; 6.0×10^{-2} mol of succinimide, 6.0×10^{-3} mol of bromo-3-phenylpropane, 1 g of KOH, 60 mL of cyclohexanone, 0.3 g of internal standard (naphthalene), 0.25 g of TBAB, 45 °C, 800 rpm.**

Table 1. **Effect of the ultrasound frequencies on the apparent rate constants (k_{app})[a]**

ultrasound frequency (kHz)	apparent rate constant k_{app} ($\times 10^{-3}$ min^{-1})
0	8
40	12.4
120	19.3

[a] Reaction conditions: 6.0×10^{-2} mol of succinimide, 6.0×10^{-3} mol of 1-bromo-3-phenylpropane, 1 g of KOH, 60 mL of cyclohexanone, 0.3 g of internal standard (naphthalene), 0.25 g of TBAB, 45 °C, 800 rpm.

4.3. Effect of the Amount of Water. Generally, there is no water added to the SL-PTC reaction. However, in this work, <1 mL was added in order to examine how the reaction rate and the conversion were affected by water. The water content of the reactants which was obtained by Karl Fisher analysis at the beginning of the reaction is few, e.g., <0.1% for succimmide, <0.5% for 1-bromo-3-phenylpropane, <0.5% for KOH, <0.1% for TBAB catalyst, and <0.1% for cyclohexanone. The effect

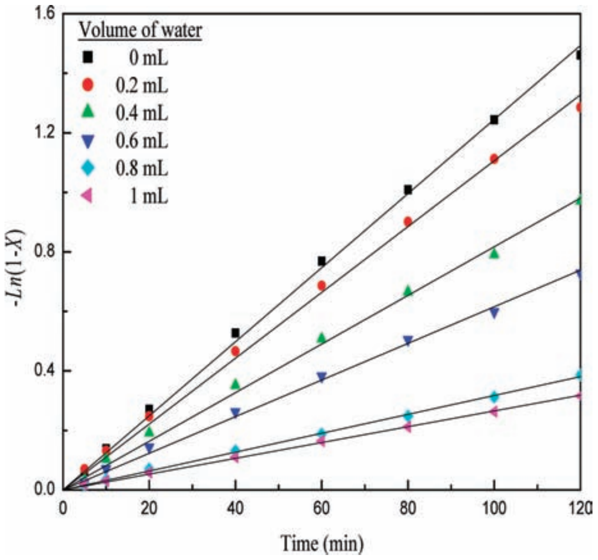

Figure 5. Plot of $-\ln(1 - X)$ of 1-bromo-3-phenylpropane versus time with various volumes of water; 6.0×10^{-2} mol of succinimide, 6.0×10^{-3} mol of 1-bromo-3-phenylpropane, 1 g of KOH, 60 mL of cyclohexanone, 0.3 g of internal standard (naphthalene), 0.25 g of TBAB, 45 °C, 800 rpm, 40 kHz (300 W).

Table 2. Effect of the volumes of water on the apparent rate constants (k_{app}) and hydration number of the active catalyst[a]

volume of water (mL)	apparent rate constant k_{app} ($\times 10^{-3}$ min^{-1})	$[QOR]org/[QBr]_{add}$ % w/w	hydration number
0	12.4	99.1	0.001
0.2	11.1	88.3	0.008
0.4	8.2	68.6	0.017
0.6	6.2	53.2	0.029
0.8	3.2	41.3	0.040
1	2.7	30.1	0.051

[a] Reaction conditions: 6.0×10^{-2} mol of succinimide, 6.0×10^{-3} mol of 1-bromo-3-phenylpropane, 1 g of KOH, 60 mL of cyclohexanone, 0.3 g of internal standard (naphthalene), 0.25 g of TBAB, 45 °C, 800 rpm, 40 kHz (300 W).

of the amount of water added on the apparent rate constant (k_{app}) was studied in the range of 0−1 mL with 1 g of KOH and the ultrasonic energy at 40 kHz (300 W) throughout the reaction. As shown in Figure 5, the reaction rate and the conversion of RBr decreased upon increasing amount of water. In Table 2, the apparent rate constant (k_{app}) is dramatically decreased with the increase in the amount of water by Karl Fischer analysis. This phenomenon indicates that the concentration of KOH is decreased upon increasing the amount of water. Thus, the concentration of active catalyst SUC-$Q_{(org)}$ is also decreased with the increase in the amount of water, which is unfavorable for the reaction. In addition, the hydration effect of active catalyst SUC-$Q_{(org)}$ is increased by increasing the amount of water, which is unfavorable for the reaction. As shown in Table 2, the apparent rate constant is drammatically decreased with the increase in the amount of water. This phenomenon indicates that the hydration number of the active catalyst SUC-$Q_{(org)}$ is clearly increased by increasing the amount of water, which is unfavorable for the reaction. Therefore, the highest reactivity was found with no added water. In the meantime, the kinetics of the alkylation of succinimide in the presence of various bases namely dry NaOH and desiccant K_2CO_3 were also analyzed. The results are presented in Table 3; the apparent rate constant in the following order: K_2CO_3 > KOH > NaOH. Comparing the results for KOH and NaOH, it can clearly be seen that the water is formed by the deprotonation by KOH and NaOH. The order of bascities of these two bases are: KOH > NaOH. Therefore, the apparent rate constant of KOH is faster than that of NaOH. Comparing the experimental results for K_2CO_3 and KOH, we believe that H_2CO_3 instead of K_2CO_3 is formed in the presence of K_2CO_3. Therefore, the apparent rate constant for using K_2CO_3 is larger than that of KOH or NaOH. In order to increase the apparent rate constant (k_{app}), it is favorable for the reaction to use less water or be in an anhydrous condition although water is produced from reaction. Thus, that is the reason why the reaction was carried out in a solid−liquid solution in this work.[22]

Table 3. Effect of the alkaline compounds on the apparent rate constants (k_{app})[a]

alkaline compound	apparent rate constant k_{app} ($\times 10^{3}$ min^{-1})
K_2CO_3	24
KOH	12.4
NaOH	1.2

[a] Reaction conditions: 6.0×10^{-2} mol of succinimide, 6.0 × 10-3 mol of 1-bromo-3-phenylpropane, 1.78 × 10-2 mol of alkaline compound, 60 mL of cyclohexanone, 0.3 g of internal standard (naphthalene), 0.25 g of TBAB catalyst, 45 °C, 800 rpm, 40 kHz (300 W).

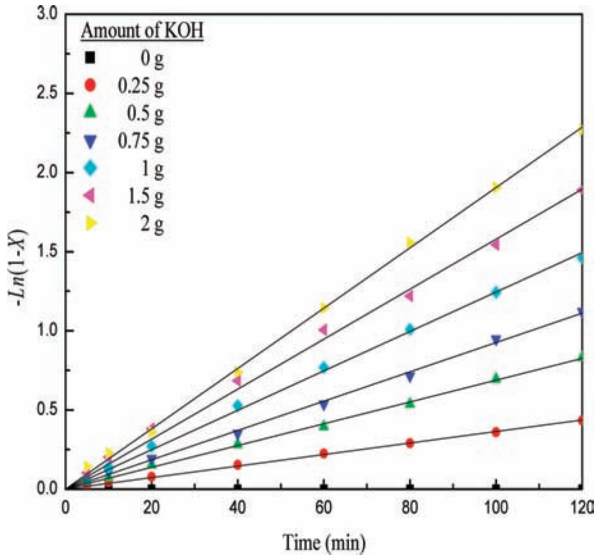

Figure 6. Plot of $-\ln(1 - X)$ of 1-bromo-3-phenylpropane versus time with various amounts of KOH; 6.0×10^{-2} mol of succinimide, 6.0×10^{-3} mol of 1-bromo-3-phenylpropane, 60 mL of cyclohexanone, 0.3 g of internal standard (naphthalene), 0.25 g of TBAB, 45 °C, 800 rpm, 40 kHz (300 W).

4.4. Effect of the Amount of KOH. The effect of the amount of KOH on the apparent rate constant (k_{app}) was studied in the range of 0−2 g under anhydrous condition and the ultrasonic energy of 40 kHz (300 W). As shown in Figure 6, the reaction rate was increased with the increase in the amount of KOH. In Table 4, the apparent rate constant (k_{app}) was dramatically increased upon increasing amount of KOH. In the absence of KOH, no reaction was observed after 2 h of reaction. Nevertheless, the conversion was dramatically increased to

Table 4. **Effect of the amounts of KOH on the apparent rate constants (k_{app})[a]**

amount of KOH (g)	apparent rate constant k_{app} ($\times 10^{-3}$ min^{-1})
0	0
0.25	3.6
0.5	6.9
0.75	9.3
1	12.4
1.5	15.8
2	19.1

Reaction conditions: 6.0×10^{-2} mol of succinimide, 6.0×10^{-3} mol of 1-bromo-3-phenylpropane, 60 mL of cyclohexanone, 0.3 g of internal standard (naphthalene), 0.25 g of TBAB, 45 °C, 800 rpm, 40 kHz (300 W).

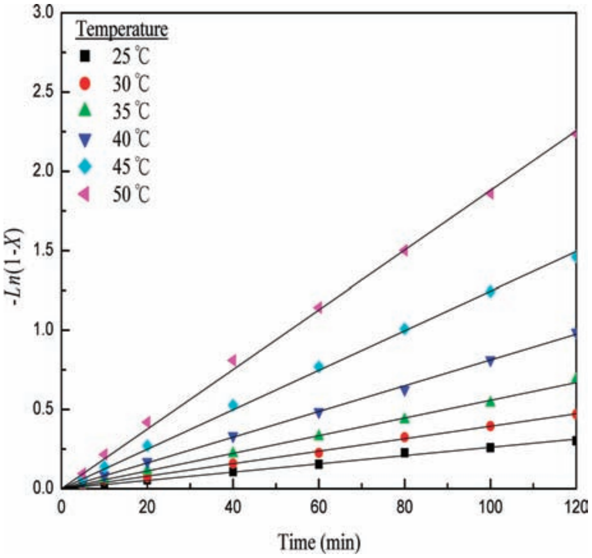

Figure 7. **Plot of $-\ln(1 - X)$ of 1-bromo-3-phenylpropane versus time with various temperatures; 6.0×10^{-2} mol of succinimide, 6.0×10^{-3} mol of 1-bromo-3-phenylpropane, 1 g of KOH, 60 mL of cyclohexanone, 0.3 g of internalstandard (naphthalene), 0.25 g of TBAB, 800 rpm, 40 kHz (300 W).**

35.16% after 2 h of reaction when a small quantity of KOH (0.25 g) is added to the reaction solution. This phenomenon indicates that increased KOH concentration enhances the production of the active species. $H_2CC(O)N^-C(O)CH_2$ Thus, the concentration of active catalyst SUC-$Q_{(org)}$ is increased by increasing the amount of KOH, which is favorable for the reaction.

4.5. Effect of Temperature. The effect of temperature on the apparent rate constant (k_{app}) was studied in the range 25−50 with the same ultrasonic energy of 40 kHz (300 W). The results are shown in Figure 7. It is clear that the reaction rate and the conversion were both increased upon increasing temperature along with ultrasonic effect. This phenomenon indicated that the number of reactant molecules, which possessed larger activated energy at a higher temperature made the ultrasonic waves easily pass through the reactor. Thus, the conversion was increased. Furthermore, the collision of the reactants at higher temperatures was also increased. Hence, the reaction rate increased with the increased temperature. As shown in Table 5, the apparent rate constant (k_{app}) is increased with the increase in temperature, and the apparent activation energy (E_a) is 15.01 kcal/mol from the slope of the Arrhenius plot of $-\ln(k_{app})$ versus 1/*T*. The value of apparent activation energy (E_a) shows that the solid−liquid reaction is under organic-phase reaction control with agitation speed under 800 rpm agitation speed and ultrasonic energy 300 W (40 kHz).

Table 5. **Effect of the temperature on the apparent rate constants (k_{app})[a]**

temperature (°C)	apparent rate constant k_{app} ($\times 10^{-3}$ min^{-1})	activation energy kcal/mol
25	2.6	15.01
30	3.9	
35	5.6	
40	8.1	
45	12.4	
50	18.8	

[a] Reaction conditions: 6.0×10^{-2} mol of succinimide, 6.0×10^{-3} mol of 1-bromo-3-phenylpropane, 1 g of KOH, 60 mL of cyclohexanone, 0.3 g of internal standard (naphthalene), 0.25 g of TBAB, 800 rpm, 40 kHz (300 W).

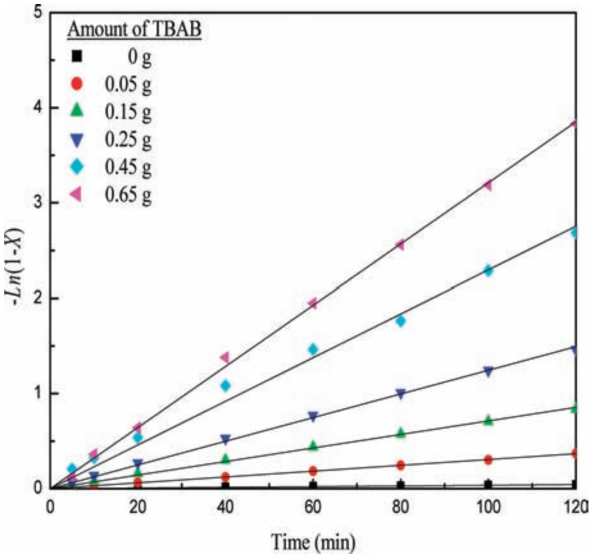

Figure 8. **Plot of $-\ln(1 - X)$ of 1-bromo-3-phenylpropane versus time with various amounts of TBAB; 6.0×10^{-2} mol of succinimide, 6.0×10^{-3} mol of 1-bromo-3-phenylpropane, 1 g of KOH, 60 mL of cyclohexanone, 0.3 g of internal standard (naphthalene), 45 °C, 800 rpm, 40 kHz (300 W).**

4.6. Effect of the Amount of TBAB Catalyst. The effect of the amount of TBAB catalyst on the apparent rate constant (k_{app}) was studied in range 0.0−0.65 g with the ultrasonic energy set at 40 kHz (300 W) throughout the reaction. As shown in Figure 8, the apparent rate constant (k_{app}) was increased linearly with the increase in the amount of TBAB catalyst. In the absence of TBAB catalyst, a conversion of 3.99% was observed after 2 h of reaction.

However, the conversion was dramatically increased to 30.97% after 2 h of reaction when a small quantity of TBAB catalyst (0.05 g) was added to the reaction solution. The concentration of quaternary ammonium cation (Q^+) in organic-phase solution, which affected the concentration of the active catalyst SUC-$Q_{(org)}$, was increased with the increased amount of TBAB catalyst. Thus, as shown in Table 6, the apparent rate constant (k_{app}) was highly dependent on the amount of TBAB catalyst. The k_{app} values were increased with the increase in

Table 6. **Effect of the amount of TBAB catalyst on the apparent rate constants (k_{app})[a]**

amounts of TBAB (g)	apparent rate constant k_{app} ($\times 10^{-3}$ min^{-1})
0	0.4
0.05	3.1
0.15	7.1
0.25	12.4
0.45	23
0.65	32.1

[a] Reaction conditions: 6.0×10^{-2} mol of succinimide, 6.0×10^{-3} mol of 1-bromo-3-phenylpropane, 1 g of KOH, 60 mL of cyclohexanone, 0.3 g of internal standard (naphthalene), 45 °C, 800 rpm, 40 kHz, (300 W).

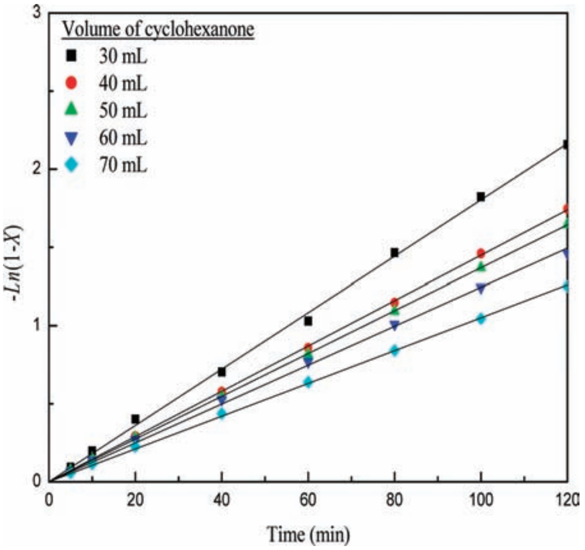

Figure 9. **Plot of $-\ln(1 - X)$ of 1-bromo-3-phenylpropane versus time with various volumes of cyclohexanone; 6.0×10^{-2} mol of succinimide, 6.0×10^{-3} mol of 1-bromo-3-phenylpropane, 1 g of KOH, 0.3 g of internal standard (naphthalene), 0.4 g of TBAB, 45 °C, 800 rpm, 40 kHz (300 W).**

the amount of TBAB catalyst. In addition, the experimental results were consistent with the theoretical derivation give by eq 14.

4.7. Effect of the Volume of Cyclohexanone (Organic Solvent). The effect of the volume of cyclohexanone on the apparent rate constant (k_{app}) was studied in the range 30−70 mL and at the same ultrasonic power 40 kHz (300 W). As shown in Figure 9, the conversion of RBr decreased with the increase in the volume of cyclohexanone. In Table 7, the apparent rate constant (k_{app}) decreased with the increase in the volume of cyclohexanone. This phenomenon indicated that a low concentration of the reactants and active catalyst SUC-$Q_{(org)}$ decreased with the increase in the volume of cyclohexanone. Hence, the probability of collision between the active catalyst SUC-$Q_{(org)}$ and the reactant at larger volume of cyclohexanone was not significant. In order to enhance the apparent rate constant, decreasing the volume of cyclohexanone was favorable for the reaction.

Table 7. **Effect of the volume of cyclohexanone on the apparent rate constants (k_{app})[a]**

volumes of cyclohexanone (mL)	apparent rate constant k_{app} ($\times 10^{-3}$ min^{-1})
30	18
40	14.5
50	13.7
60	12.4
70	10.5

[a] Reaction conditions: 6.0×10^{-2} mol of succinimide, 6.0×10^{-3} mol of 1-bromo-3-phenylpropane, 1 g of KOH, 0.3 g of internal standard (naphthalene), 0.4 g of TBAB, 45 °C, 800 rpm, 40 kHz (300 W).

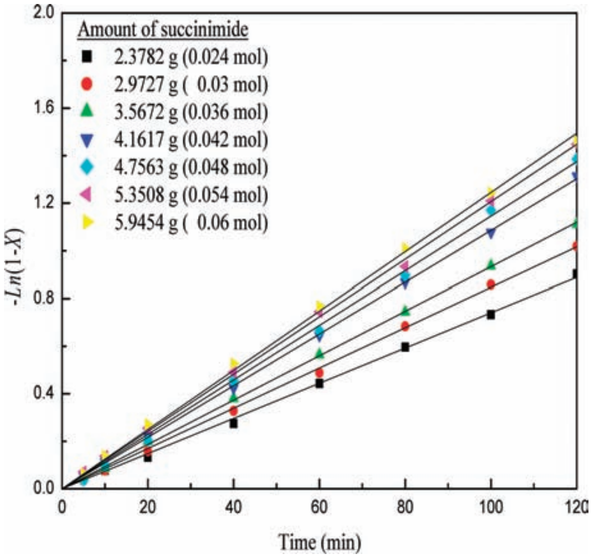

Figure 10. **Plot of $-\ln(1 - X)$ of 1-bromo-3-phenylpropane versus time with various amounts of succinimide; 6.0×10^{-3} mol of 1-bromo-3-phenylpropane, 1 g of KOH, 60 mL of cyclohexanone, 0.3 g of internal standard (naphthalene), 0.25 g of TBAB, 45 °C, 800 rpm, 40 kHz (300 W).**

Table 8. **Effect of the amount of succinimide on the apparent rate constants (k_{app})[a]**

amount of succinimide (g)	apparent rate constant k_{app} ($\times 10^{-3}$ min^{-1})
2.3782	7.4
2.9727	8.5
3.5672	9.3
4.1617	10.9
4.7563	11.5
5.3805	12.1
5.9454	12.4

[a] Reaction conditions: 6.0×10^{-3} mol of 1-bromo-3-phenylpropane, 1 g of KOH, 60 mL of cyclohexanone, 0.3 g of internal standard (naphthalene), 0.25 g of TBAB, 45 °C, 800 rpm, 40 kHz (300 W).

4.8. Effect of the Amount of Succinimide. The effect of the amount of succinimide on the apparent rate constant (k_{app}) was studied in the range 2.3782−5.9454 g and at the same ultrasonic energy 40 kHz (300 W). The results are shown in Figure 10. It is seen that the conversion of RBr is increased with the increase in the amount of succinimide (**2**). As shown in Table 8, the apparent rate constant was increased with the increase in the amount of succinimide. This phenomenon indicates that the production of SUC-K and active catalyst SUC-$Q_{(org)}$ are increased with the increase in the amount of succinimide by Le Chatelier's principle. Thus, the concentration of active catalyst SUC-$Q_{(org)}$ and the production of SUC-K were increased by increasing the amount of KOH, which was favorable for the reaction.

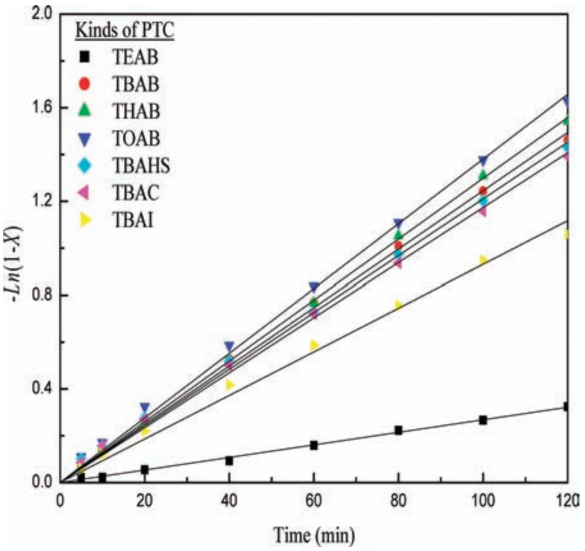

Figure 11. **Plot of $-\ln(1 - X)$ of 1-bromo-3-phenylpropane versus time with various phase-transfer catalysts; 6.0×10^{-2} mol of succinimide, 6.0×10^{-3} mol of 1-bromo-3-phenylpropane, 1 g of KOH, 60 mL of cyclohexanone, 0.3 g of internal standard (naphthalene), 7.75×10^{-4} mol of PTCs, 45 °C, 800 rpm, 40 kHz (300 W).**

Table 9. **Effect of phase transfer catalysts on the apparent rate constants (k_{app})[a]**

kinds of phase transfer catalyst	carbon number	q	apparent rate constant k_{app} ($\times 10^{-3}$ min^{-1})
TEAB	8	1	2.7
TBAB	16	1	12.4
THAB	24	1	13
TOAB	32	1	13.8
TBAHS	16	–	12.1
TBAC	16	–	11.7
TBAI	16	–	9.3

[a] Reaction conditions: 6.0×10^{-2} mol of succinimide, 6.0×10^{-3} mol of 1-bromo-3-phenylpropane, 1 g of KOH, 60 mL of cyclohexanone, 0.3 g of internal standard (naphthalene), 7.75×10^{-4} mol of PTCs, 45 °C, 800 rpm, 40 kHz (300 W).

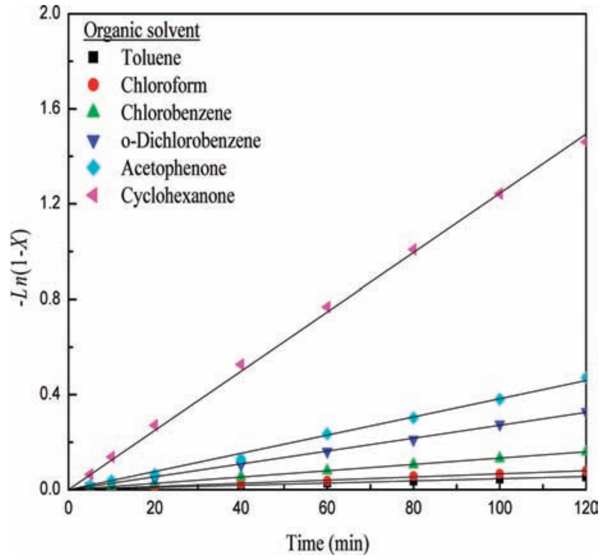

Figure 12. **Plot of $-\ln(1 - X)$ of 1-bromo-3-phenylpropane versus time with various organic solvents; 6.0×10^{-2} mol of succinimide, 6.0×10^{-3} mol of 1-bromo-3-phenylpropane, 1 g of KOH, 60 mL of organic solvent, 0.3 g of internal standard (naphthalene), 0.25 g of TBAB, 45 °C, 800 rpm, 40 kHz (300 W).**

Table 10. **Effect of the organic solvents on the apparent rate constants (k_{app})[a]**

kinds of organic solvent	dielectric constant ε	polarity	apparent rate constant k_{app} ($\times 10^{-3}$ min^{-1})
toluene	2.4	2.4	0.5
chloroform	4.8	4.1	0.7
chlorobenzene	5.6	2.7	1.3
o-dichlorobenzene	9.93	–	2.7
acetophenone	17.4	4.8	3.8
cyclohexanone	18.3	4.7	12.4

[a] Reaction conditions: 6.0×10^{-2} mol of succinimide, 6.0×10^{-3} mol of 1-bromo-3-phenylpropane, 1 g of KOH, 60 mL of organic solvent, 0.3 g of internal standard (naphthalene), 0.25 g of TBAB, 45 °C, 800 rpm, 40 kHz (300 W).

4.9. Effect of the Quaternary Ammonium Salts. In this work, seven quaternary ammonium salts were selected for the solid–liquid reaction at 40 and 1200 rpm along with the ultrasonic energy 40 kHz (300 W). As shown in Figure 11, and Table 9, the order of the reactivities of these seven catalysts are: TOAB > THAB > TBAB > TBAHS > TBAC > TBAI > TEAB. Comparing the experimental results for TOAB, THAB, TBAB, and TEAB, it can clearly be seen that the reactivity of quaternary salt increases with the increase in the total carbon number of the alkyl group of the cation. This phenomenon indicates that a large total carbon number increases the hydrophobic properties of the S-L PTC and aids ultrasonication. As shown in Figure 11 and Table 9, it is favorable for the reaction in choosing quaternary ammonium salts of larger carbon numbers. The reason is that the lipophilicity is strong using the quaternary ammonium salts of larger carbon number. The reaction rate is increased with the increase in the carbon number of quaternary ammonium salts. However, this increase is not further sensitive to the total carbon number of larger than 32, The reason is that the lipophilicities of the quaternary ammonium salts that have a total carbon number larger than 32 are almost the same. Furthermore, Table 1 depicts the apparent rate constant for these seven catalysts in which TOAB contributes high reactivity. Furthermore, the Halpern number[3] (q) is an indication of the activity of the quaternary ammonium salts. The Halpern number approaching 1 indicates that the activity of the catalyst is high. Table 9 also shows the Halpern number of the quaternary ammonium salts

4.10. Effect of the Organic Solvents. According to solid–liquid PTC reaction systems, intrinsic reactions including the rate constants and the rate are highly affected by the organic solvents. Various solvents have different reaction rates. In this work, five organic solvents were applied to investigate the effect of their polarities and dielectric constants (ε) on the S-L PTC and ultrasonication system. As shown in Figure 12 and Table 10, the order of reactivities of these six solvents are: cyclohexanone > acetophenone > *o*-dichlorobenzene > chlorobenzene > chloroform > toluene. It was clearly found that the apparent rate constant increased with the dielectric constant of the solvents but did not increase with the polarity. In order to enhance the apparent rate constant, using a high dielectric constant solvent (cyclohexanone) is favorable for the reaction. In addition, the degradation of any organic solvent was not observed during or after the reaction. The results are also shown in Table 10. It was clearly found that the apparent rate constant increases with the dielectric constant of the solvents but does not increase with the polarity. Although toluene is so common in industry and academic PTC studies, using a solvent with a low dielectric constant is unfavorable to the reaction. As a result of the low dielectric constant of toluene, its apparent rate constant is low.

5. Conclusions

On the basis of the results of this work, the synthesis of 1-(3-phenylpropyl)pyrrolidine-2,5-dione (**1**), a biologically and industrially useful imide derivative, was successfully carried out by the reaction of succinimide (**2**) with 1-bromo-3-phenylpropane (**3**) in a small amount of KOH and organic solvent under solid−liquid phase-transfer catalysis almost water-free conditions in combination with ultrasonic irradiation. The reaction mechanism and apparent rate constants were obtained from the experimental results. When the agitation speed exceeds 200 rpm, the mass transfer resistance at the solid−liquid interface could be ignored. The overall reaction could be described by pseudo-first-order kinetics, and the apparent activation energy in cyclohexanone is 15.01 kcal/mol.

The reaction rate is increased by increasing the amount of ultrasound energy, KOH, TBAB, and SUC-H. Nevertheless, the reaction rate is decreased by increasing the volume of water and cyclohexanone. An organic solvent with a high dielectric constant, such as cyclohexanone, enhances the reaction to obtain a high conversion of RBr. A high reactivity of a PTC, such as that of TOAB, enhances the reaction to obtain a high conversion of RBr.

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