

Synthesis of 1-(Isopentyloxy)-4-Nitrobenzene Under Ultrasound Assisted Liquid-Liquid Phase-Transfer Catalysis

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ABSTRACT

In this paper, we report the reaction of isoamyl alcohol with 1-chloro-4-nitrobenzene that was carried out in a batch reactor in aqueous-organic biphasic condition using the techniques like phase transfer catalysis and ultrasound irradiation. Tetrabutylammonium bromide (TBAB) was employed as the phase transfer catalyst. The reaction is greatly enhanced by adding a small quantity of phase-transfer catalyst under ultrasound (28 kHz, 300W). Kinetics of the etherification was investigated in detail. The rate constants were determined by varying the concentration of the catalyst, stirring speed, the concentration of alcohols, temperature, different solvents, and concentration of sodium hydroxide, different inorganic salts and different phase transfer catalysts. From the detailed kinetic study, the optimum reaction condition to produce higher yield of 1-(isopentyloxy)-4-nitrobenzene was obtained. The experimental data were well described by the pseudo-first-order equation. The individual experiment was carried without ultrasound; the obtained k_{app} value is 0.0094 1/min. The combination of ultrasound and stirring resulted the k_{app} value of 0.0178 1/min. From the observed results, the k_{app} value for ultrasonically promoted reaction is almost two-fold higher than the normal reaction.

1. Introduction

Preparation of organic compounds in aqueous-organic two-phase system has encountered several problems due to the difficulty of contact of the two immiscible reactants in two different phases. This problem was overcome by adding a small catalytic quantity of a quaternary ammonium salt.

The use of quaternary salt as a phase transfer catalyst in the two-phase reaction to synthesize specialty chemicals was thus extensively studied [1,2]. Phase transfer catalysts, such as quaternary ammonium and phosphonium salts, crown ethers, polyethylene glycols and cryptands have been used to carry out reaction between

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two reactants, which exist in the same or different phase(s) [3,4]. Recently, the synthesis of ethers in a two-phase reaction involving quaternary salts as phase transfer catalyst has become of interest in this area of research.

Generally, phase-transfer catalyst assisted reactions are classified as follows: (i) the nature and the solubility of the catalyst; and (ii) the number and type of the phases involved in the reacting systems. Most recognizable types are liquid-liquid PTC (LLPTC) and solid-liquid PTC (SLPTC) reactions. The advances during recent years have made a remarkable impact in organic syntheses and are frequently employed in a multitude of organic transformations. The major advantages of PTC are the higher reaction rate and better yield, lower reaction temperature, and fewer by-products, as well as enhanced selectivity.

In recent years, the application of ultrasound irradiation in organic synthesis has been broadly extended. It enhances the reaction rates, yield and selectivity of product rather significantly [5]. 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 and several hundred bars. The reaction rate is thus enhanced. Recently, the combination of ultrasound or microwave activation with phase-transfer catalysis has attracted considerable interest [6]. The effect of ultrasonic wave on the Cannizzaro reaction catalyzed by a phase-transfer catalyst showed that an ultrasonic wave of 20 kHz dramatically accelerated the reaction [7]. For the use of

ultrasound irradiation on the liquid-liquid phase-transfer catalyzed epoxidation and dichlorocyclopropanation of 1,7-octadiene, the reaction rates were greatly enhanced either in epoxidation by using Aliquat 336/phosphotungstic acid or in dichlorocyclopropanation by using benzyltriethylammonium chloride as the catalyst [8,9]. The reaction of oximes and dichloromethane catalyzed by ultrasound-assisted PTC provided 95% of product yield in 3.5 h, but the time needed to get 92% in the silent condition was 16 h [10].

In this paper, an efficient method to synthesize 1-(isopentyloxy)-4-nitrobenzene under liquid-liquid phase-transfer catalysis and ultrasound irradiation is reported. The various kinetic parameters have been studied to maximize the yield of 1-(isopentyloxy)-4-nitrobenzene.

2. Experimental section

2.1. Materials and instruments

The following chemicals, isoamyl alcohol, 1-chloro-4-nitrobenzene, sodium hydroxide, toluene, biphenyl, sodium chloride, ammonium chloride, tetrabutylammonium bromide (TBAB), tetrabutylammonium chloride (TBAC), tetrahexylammonium bromide (THAB), tetraoctylammonium bromide (TOAB) and other reagents are all reagent-grade chemicals from Fluka, Merck, Aldrich and SRL. These were used as received without any further purification. All other chemicals were of analytical grade.

Gas chromatography was carried out using a GC-Varian 3700 model. Ultrasonic water bath, Equitron, Media Instrument Manufacturing Company, Chennai, India-600

004 was also used. The ultrasonic generator was a thermostatic bath equipped with dual frequencies (28/40 kHz) and electric power 300 W with 0.0126 W/mL of power density. Details of ultrasonic equipment were discussed in our previous report [11], in which we used 28 kHz for the entire kinetic study.

2.2. Kinetics of the liquid-liquid bi-phase reaction

The reaction was conducted on a 250 mL three-necked Pyrex round-bottom flask, this permits agitating the solution, inserting the water condenser to recover organic reactant and taking samples and feeding the reactants. This reaction vessel was supported at the centre of the sonicator. Known quantities of toluene (40 mL, solvent), 10 g sodium hydroxide in 10 mL water and 0.2 g biphenyl (IS-internal standard) were introduced into the reactor. Then, 5 mL of isoamyl alcohol and 1 g of 1-chloro-4-nitrobenzene, 0.2 g of TBAB were introduced to the reactor to start the reaction. The reaction mixture was stirred at 400 rpm. The phase separation was almost immediate on arresting the stirring process. Samples were collected from the organic layer at regular time intervals. A pinch of anhydrous sodium sulphate was placed in the sample vials to absorb any moisture present in the organic layer and 0.5mL of toluene was added to vials to dilute the solution. The filtrate solution was subjected to GC analysis. The kinetics was followed by estimating the amount of 1-chloro-4-nitrobenzene that disappeared, and measured by a gas Chromatography (GC-Varian 3700 model). The analyzing conditions were as follows: Column, 30 m x 0.525 mm i.d. capillary

column containing 100% poly(dimethyl siloxanen); injection temperature, 250°C; FID detector (300°C). Yields were determined from standard curve using biphenyl as an internal standard.

3. Result and discussion

Kinetic experiments at different experimental parameters were performed under pseudo-first order to investigate the rate of etherification in this biphasic phase transfer reaction. Under appropriate conditions, a high yield of the product was obtained. From experimental data, no by-products were observed during the reaction. This indicates that only 1-(isopentyloxy)-4-nitrobenzene was produced from the etherification under PTC conditions. Therefore, the consumption of the reactant equals the production of the product. In the following subsections, the effects of the reaction conditions on the conversion (X) of organic-phase reactant and the apparent rate constant (k_{app}) are discussed. The k_{app} values are obtained from the plot of $-\ln(1-X)$ vs time.

3.1. Effect of stirring speed

For any kinetic study, elimination of mass-transfer resistance during the reaction is very important to obtain true reaction kinetics. To determine the role of mass-transfer resistance the effect of stirring speed on the conversion of 1-chloro-4-nitrobenzene was studied in the range 0–400 rpm under otherwise identical experimental conditions in the presence of PTC and ultrasound as shown in Fig. 1. The rate constants were evaluated from the plots of $-\ln(1-X)$ vs time. As it is evident from the Fig. 1, the variation of conversion of 1-chloro-4-

nitrobenzene (CNB) with speed of agitation is

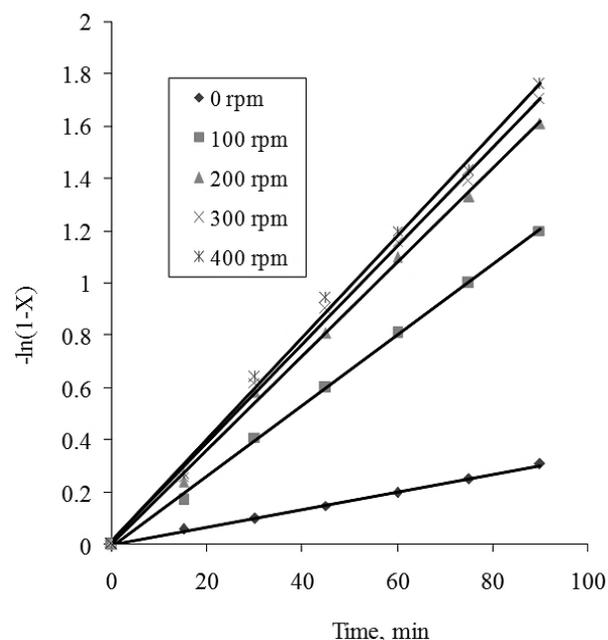


Figure 1. Effect of various stirring speeds on the conversion: 10 g of NaOH in 10 mL H₂O, 0.2 g of biphenyl (internal standard), 5 mL of isoamyl alcohol, 1 g of 1-chloro-4-nitrobenzene, 40 mL of toluene, 0.2 g of TBAB, 50°C, 28 kHz, 300 W.

increased from 0 to 200 rpm in the range studied, after that there is no significant difference in the conversion. This indicates that there is no mass transfer resistance in the range of 200 rpm to 400 rpm. All the other experiments were performed at 400 rpm with negligible effect of mass-transfer resistance on the reaction kinetics. The individual experiment was performed without ultrasound; the obtained k_{app} value is 0.0094 1/min. By combination of ultrasound and stirring; the k_{app} value is 0.0178 1/min. From the observed results, the k_{app} value for ultrasonically promoted reaction is almost two-fold higher than the normal reaction [11].

3.2. Effect of the amount of catalyst

The effect of varying catalyst amounts on the rate of the etherification was studied in the

range of 0.1–0.4 g of the PT catalyst. The conversion is low for 0.1 g of TBAB (Table 1). However, the reaction is greatly enhanced by adding a small quantity of the TBAB catalyst. The concentration of quaternary ammonium cation (Q^+), which affects the concentration of the active catalyst $RO^- Q^+$, increases in the organic phase with the increased amount of TBAB catalyst. The apparent rate constant (k_{app}) is linearly dependent on the amount of TBAB catalyst [12,13]. So, the k_{app} value increases under sonication along with phase-transfer catalyst, which may be due to inducing the change in size, and morphology of phase-transfer catalyst.

3.3. Effect of the volume of isoamyl alcohol

The effect of the volume of isoamyl alcohol on the apparent rate constant (k_{app}) was investigated under standard reaction condition. The results are shown in Fig. 2. The reaction rate is decreased with an increase in the volume of ethanol (5–20 mL). The reason is that the concentration of the anion is reduced using a larger volume of isoamyl alcohol. Hence, the k_{app} value decreases with increase in the amount of isoamyl alcohol.

3.4. Influence of temperature variation

The effect of temperature on the rate of

Table 1.

Effect of various amounts of TBAB on the rate of reaction: 10 g of NaOH in 10 mL H₂O, 0.2 g of biphenyl (internal standard), 5 mL of isoamyl alcohol, 1 g of 1-chloro-4-nitrobenzene, 40 mL of toluene, 600 rpm, 50°C, 28 kHz, 300 W.

Amount of TBAB (g)	0.1	0.2	0.3	0.4

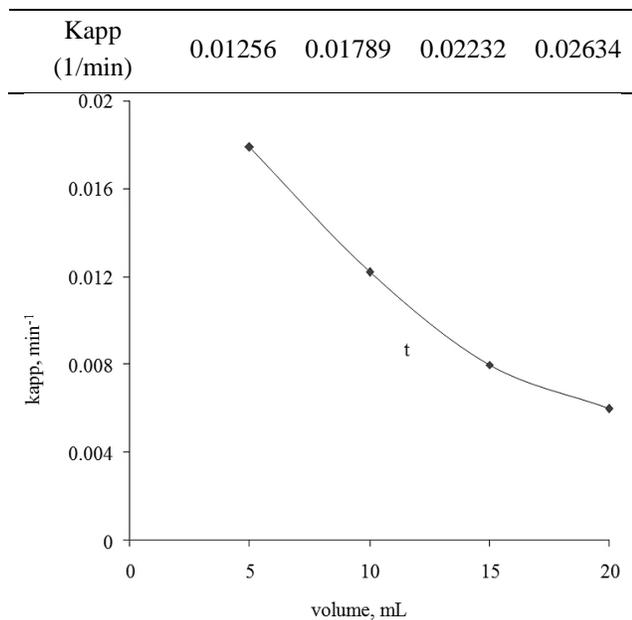


Figure 2. Effect of various volume of isoamyl alcohol on the rate of reaction: 10 g of NaOH in 10 mL H₂O, 0.2 g of biphenyl (internal standard), 1 g of 1-chloro-4-nitrobenzene, 40 mL of toluene, 0.2 g of TBAB, 600 rpm, 50°C, 28 kHz, 300 W.

etherification was investigated by varying the temperature from 40 to 70°C. Kinetic results were obtained from the plot of $-\ln(1-X)$ vs time, which indicates increased reactivity with increase in the temperature occurs along with sonication (Fig. 3). This is due to the increase in the number of collisions between reactant molecules at higher temperature and the number of reactant molecules, which possess larger activated energy at a higher temperature and thus the ultrasonic wave easily passes through the reactor. Thus the conversion is increased. The plot of $-\ln k_{app}$ versus $1/T$ was made in Fig. 4 to obtain the activation energy. The apparent activation energy was calculated from the slope of the best fitted straight line as 51.79 kJ/mol. The observed apparent activation energy confirms that the reaction is kinetically controlled [14].

3.5. Different phase transfer catalysts effect

For liquid-liquid two-phase reactions, the overall rate of reaction is governed by rate of transportation of anions from aqueous phase to organic phase. In the presence of PTC, the

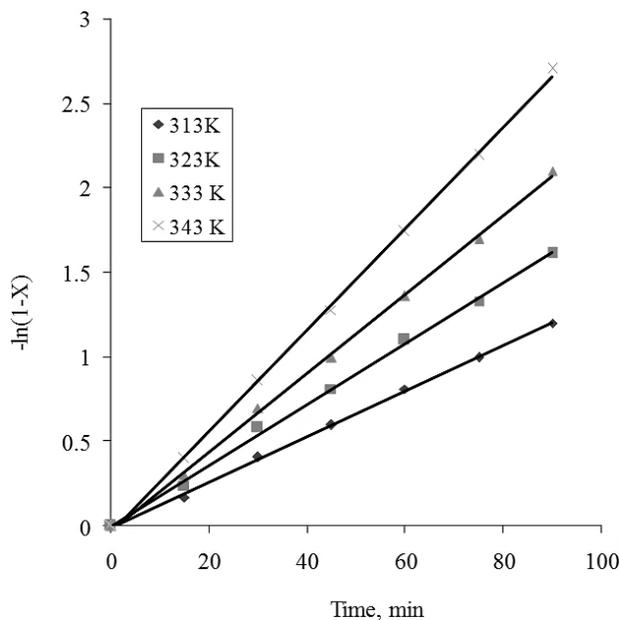


Figure 3. Effect of various temperature on the conversion: 10 g of NaOH in 10 mL H₂O, 0.2 g of biphenyl (internal standard), 5 mL of isoamyl alcohol, 1 g of 1-chloro-4-nitrobenzene, 40 mL of toluene, 600 rpm, 0.2 g of TBAB, 28 kHz, 300 W.

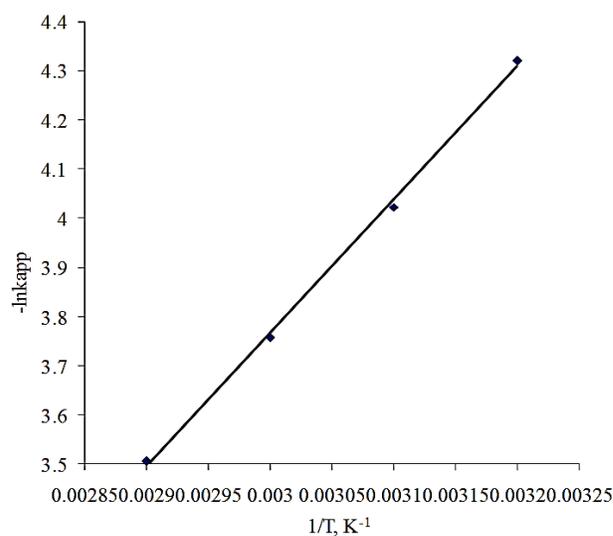


Figure 4. Arrhenius plot: 10 g of NaOH in 10 mL H₂O, 0.2 g of biphenyl (internal standard), 5 mL of

isoamyl alcohol, 1 g of 1-chloro-4-nitrobenzene, 40 mL of toluene, 600 rpm, 0.2 g of TBAB, 28 kHz, 300 W.

transportation of anion (RO^-) is facilitated and the reaction becomes organic-phase limited. Etherification reaction has been chosen in the study of the comparative reactivities of four different phase-transfer catalysts, namely TBAB, TBAC and THAB and TOAB. Apparent rate constants are evaluated from the linear plot of $-\ln(1-X)$ vs time. Table 2 shows the effects of different phase-transfer catalysts on the reaction reactivity at 50°C under ultrasound irradiation. From the Table 2, the order of the catalysts are $TOAB > THAB > TBAB$ merely equal to TBAC [15]. This is because the catalyst degenerated in the organic phase is TBAC.

3.6. Effect of different solvents

In the study of solvent effects the reaction was carried out under the same reacting conditions as in the following: 40 mL of solvent, 1g of 1-chloro-4-nitrobenzene (CNB), 5mL of isoamyl alcohol, 400 rpm agitation rate, 28 kHz, 300W and 50°C . Typical results for conversion vs time are shown in Fig. 5. It is obvious that a higher conversion rate is obtained in o-dichlorobenzene. The order of relative activities of solvents is o-dichlorobenzene > chlorobenzene > toluene. As expected, it was clearly found that the apparent rate constant or

Table 2.

Effect of various PTC's on the rate of reaction: 10g of NaOH in 10 mL H_2O , 0.2 g of biphenyl (internal standard), 5 mL of isoamyl alcohol, 1 g of 1-chloro-4-nitrobenzene, 0.2 g of PTC, 40 mL of toluene, 600 rpm, 50°C , 28 kHz, 300 W.

Kind of PTC	TBAB	TBAC	THAB	TOAB
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Kapp, 1/min	0.01789	0.01767	0.02021	0.02234
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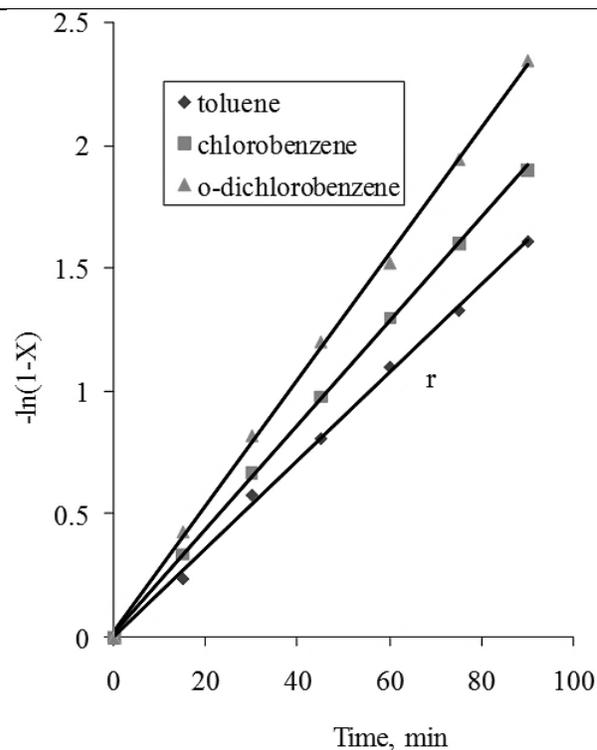


Figure 5. Effect of various solvents on the conversion: 10 g of NaOH in 10 mL H_2O , 0.2 g of biphenyl (internal standard), 5 mL of isoamyl alcohol, 1 g of 1-chloro-4-nitrobenzene, 40 mL of solvents, 600 rpm, 0.2 g of TBAB, 28 kHz, 300 W.

conversion 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 is favorable for the reaction. In addition, the degradation of any organic solvent was not observed during or after the reaction.

3.7. Effect of concentration of sodium hydroxide

The reaction rate is known to be greatly affected by a concentration of the alkaline compound. The rate of arylation of amyl

alcohol strongly depends on the strength of the sodium hydroxide. The pseudo first-order kinetic experiments were carried out, employing 5–20 g of NaOH under similar reaction conditions. The Kinetic profile of the reaction is obtained by $-\ln(1-X)$ against time. The kapp values significantly increased with increase in basicity of hydroxide ion (Table 3). This suggests that the hydroxide ions are less solvated by water molecules at higher concentration of NaOH and therefore the activity of the hydroxide ion increases. In the kinetic study of C-alkylation of benzyl cyanide with n-bromopropane under PTC condition [16,17] the observed rate constant tremendously increased with increase in basicity of hydroxide ion. In the present case, extraction of isoamyl alcohol is more effective when the reaction is carried out in the presence of ultrasound irradiation along with higher concentration of sodium hydroxide.

3.8. Effect of addition of inorganic salts

Previous reports indicate that adding extra inorganic salt affects not only the reaction environment but also the effective concentration of catalytic intermediate. To investigate the effect of the inorganic salts added on the etherification system, sodium chloride and ammonium chloride were used as inorganic salts in this reaction system. Fig. 6 indicates the effect of reaction rate

Table 3.

Effect of various amounts of NaOH on the rate of reaction: 10 mL H₂O, 0.2 g of biphenyl (internal standard), 5 mL of isoamyl alcohol, 1 g of 1-chloro-4-nitrobenzene, 0.2 g of PTC, 40 mL of toluene, 600 rpm, 50°C, 28 kHz, 300 W.

Amount of NaOH (g)	5	10	15	20
Kapp, 1/min	0.01023	0.01789	0.02361	0.02654

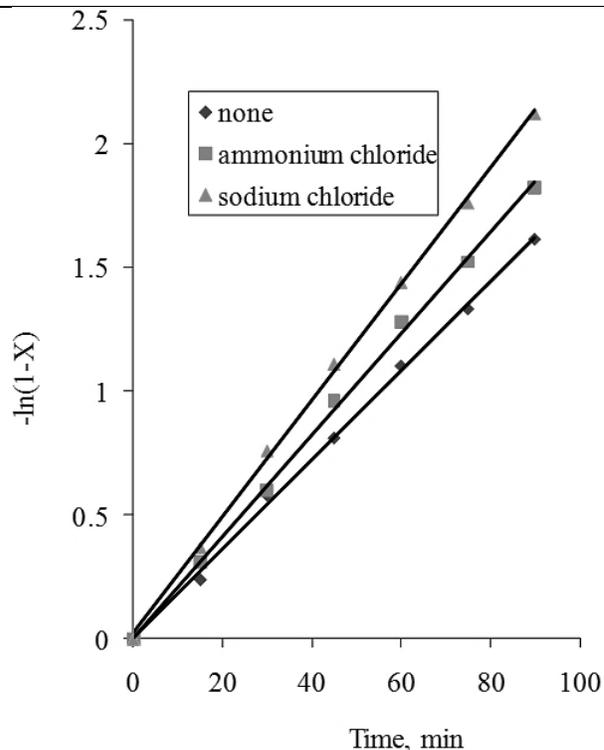


Figure 6. Effect of inorganic salts on the conversion: 10 g of NaOH in 10 mL H₂O, 0.2 g of biphenyl (internal standard), 5 mL of isoamyl alcohol, 1 g of 1-chloro-4-nitrobenzene, 40 mL of toluene, 1 g of inorganic salts, 600 rpm, 0.2 g of TBAB, 28 kHz, 300 W.

influenced by the addition of extra salts, and it is evident that the rate of reaction in the absence of inorganic salt is slower than in its presence. The order of reactivity of salts is as follows: sodium chloride > ammonium chloride. From the aforementioned reactivity, it is clear that addition of extra inorganic salt affects not only the reaction environment but also the effective concentration of catalytic intermediate [12].

4. Conclusions

In conclusion, the reaction rate of 1-chloro-4-nitrobenzene with isoamyl alcohol catalyzed by phase-transfer catalyst combined with ultrasonic irradiation was investigated. The various process parameters (stirring speed, catalyst concentration, base concentration, different catalysts, different solvents, volume of isoamyl alcohol, inorganic salts and temperature) have been optimized. The apparent reaction rates were observed to obey the pseudo-first order kinetics with respect to the 1-chloro-4-nitrobenzene. The reaction rate increased with increase in temperature, catalyst amount, base concentration and inorganic salts. From the Arrhenius plot, the activation energy (51.79 kJ/mol) was obtained. From the experimental evidence, this etherification reaction proceeds through interfacial mechanism.

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