Kinetic Investigation of Nitroarylation of Pyrrole with 1-Chloro-4-Nitrobenzene Using a New Multi-Site Phase-Transfer Catalyst under Ultrasonic Condition

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Abstract
In the present research work, the solid-liquid reaction was successfully carried out in the new synthesized multi-site phase-transfer catalyst, namely, 1,3,5-tribenzyl-1,3,5-triethyl-1,3,5-triazinane-1,3,5-trium trichloride(MPTC), and sonication (40 kHz, 300 W) to produce the desired product namely 1-(4-nitrophenyl) pyrrole from pyrrole and 4-nitrochlorobenzene. The selectivity of N-arylation product was obtained under sonication and MPTC. The combination of ultrasound and MPTC resulted in better efficacy as compared to the individual operations. The apparent reaction rate is greatly enhanced and observed to obey the pseudo-first order kinetics. The kapp value increases with increasing kinetic parameters that is the amount of [MPTC], [substrate], ultrasonication, stirring speed, temperature, etc.

Keywords: Sonochemistry; Pyrrole; Interfacial reaction; Kinetics; MPTC; 1-Chloro-4-Nitrobenzene

Introduction
As the chemical reactants reside in immiscible phases, phase-transfer catalysts have the ability to carry out the heterogeneous reactions by one of the reactants penetrating from its normal phase (generally aqueous phase) to the organic phase where the reaction takes place, which gives a high conversion and selectivity for the desired product under mild reaction conditions [1]. The quaternary ammonium salts as an effective catalysts for enhancing the two-phase reaction, this methodology occupies an unique niche in organic synthesis and it is a commercially matured discipline with over six hundred applications [2-7] covering a wide spectrum of industries such as pharmaceuticals, agrochemicals, dyes, perfumes, flavours, specialty polymers, pollution control, etc. As the application of phase-transfer catalysts (PTC) grow, much effort was placed on the development of phase - transfer catalysts with higher catalytic efficiency. To this end, researchers have developed “multi-site” phase-transfer catalysts (MPTC) for much higher activity than normal phase-transfer catalysts. Recently, the catalytic behaviour of multi-site phase-transfer catalysts have been attracted much attention, due to the fact that multiple molecules of the aqueous reactant can be carried into the organic phase once a reaction cycle, thus the catalytic efficiency is enhanced [8-12].

Currently, anew analytical and process experimental techniques which are environmental benign techniques viz., ultrasound and microwave irradiation have become immensely popular in promoting various organic reactions [13-17]. Ultrasound irradiation is a transmission of a sound wave through a medium and is regarded as a form of energy enhances the rate of the reaction due to mass transfer and effective mixing [18-20].

The effect of ultrasonic energies in organic syntheses (homogeneous and heterogeneous reactions) has been boosted in recent years [21-27]. Sonication of multiphase systems accelerates the reaction by ensuring a better contact between the different phases [28,29]. Further, ultrasound irradiations also increase the reaction rate and avoid the use of high reaction temperatures [30]. These days this environmental benign technology is combined with phase-transfer catalysts (PTC) with primary objective of optimizing reaction conditions [31-33].

Our interest was entered on first time evaluating the influence of ultrasound in association with multi-site phase-transfer catalyst (MPTC) on the synthesis of 1-(4-nitrophenyl) pyrrole from pyrrole with 1-chloro-4-nitrobenzene (CNB) under heterogeneous condition. Since, the kinetic study of nitroarylation of pyrrole using 1-chloro-4-nitrobenzene under controlled MPTC reaction conditions will be interesting and challenging, we followed the kinetic studying a newly synthesized multi-site phase-transfer catalyst (MPTC) viz., 1,3,5-tribenzyl-1,3,5-triethyl-1,3,5-triazinane-1,3,5-trium trichloride, as a catalyst under ultrasonic condition (40 kHz; 300 W). Further,

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to the best of our knowledge, there is no literature reports’ regarding nitroarylation of pyrrole under MPTC-ultrasonic irradiation condition.

**Experimental**

**Chemicals**

The reagents pyrrole, 1-chloro-4-nitrobenzene (CNB), sodium hydride, benzene, toluene, chlorobenzene, biphenyl and other reagents are synthesis guaranteed grade (GR) chemicals and were used without further treatments.

**Instrumentation**

FT-IR Spectra were recorded on a Brucker-Tensor 27 FT-IR spectrophotometer. 1H NMR and 13C spectra were recorded on a Bruker 300 MHz and 75 MHz respectively using TMS as an internal standard. Gas chromatography was carried out using a GC-Varian 3700 model Ultrasonic water bath, Equitron, Media Instrument Manufacturing Company, Chennai, India. The ultrasonic generator was a thermostatic bath equipped with dual frequencies (28/40 kHz) and anedelectric power 300 W with 0.0126 W/mL of power density.

**Ultrasonic process equipment**

Ultrasonic energy is transmitted to the process vessel through the liquid medium, usually water in the tank. For safety purpose, the sonochemical reactor consisted of two layers stainless steel body. The sonochemical reactor configuration used in the present work is basically an ultrasonic bath. The internal dimension of the ultrasonic cleaner tank is 48 cm x 28 cm x 20 cm with liquid holding capacity of 5 litres. Two types of frequencies of ultrasound were used in these experiments, which are 28 kHz and 40 kHz with each output as 300 W. Both ultrasound separately produces through a flat transducer mounted at the bottom of the sonicator. The reactor was a 250 mL three-necked Pyrex round-bottom flask. This reaction vessel was mounted at the bottom of the sonicator. The reactor was a 250 mL three-necked Pyrex round-bottom flask. This reaction vessel was supported at the centre of the ultrasonic cleaning bath 2 cm above from the position of the transducer to get the maximum ultrasound energy. All the experimental parameters were done at 40 kHz with output power of 300 W.

**Synthesis of 1,3,5-triethyl-1,3,5-triazinane**

A mixture of 83 g of ethylamine, 40 g of Para paraldehyde and 25 mL of benzyl chloride, and 75 mL of ethanol was placed in a 250 mL three-necked round bottomed Pyrex flask. The reaction was carried out at 30°C for 4 hours and was gently refluxed in the nitrogen atmosphere. The solvent was then completely removed under vacuum at 40°C. The reagents pyrrole, 1-chloro-4-nitrobenzene (CNB), sodium hydride, benzene, toluene, chlorobenzene, biphenyl and other reagents are synthesis guaranteed grade (GR) chemicals and were used without further treatments.

**Synthesis of 1,3,5-triethyl-1,3,5-triazinane**

A mixture of 8.7 g (50.7 mmol) of 1,3,5-triethyl-1,3,5-triazane, 25 mL of benzyl chloride, and 75 mL of ethanol was placed in a 250 mL three-necked round bottomed Pyrex flask. The reaction was carried out at 40°C for 24 hours and was gently refluxed in the nitrogen atmosphere. The solvent was then completely removed under vacuum and onium salt, i.e., 1,3,5-tribenzyl-1,3,5-triethyl-1,3,5-triazinane-1,3,5-triium trichloride, (MPTC, Scheme 2) was washed with n-hexane (3 x 20 mL). The white solid MPTC was stored in CaCl₂ desiccators.

**Reaction mechanism and kinetic model**

For synthesising 1-(4-nitrophenyl) pyrrole compound, the overall reaction of pyrrole and 1-chloro-4-nitrobenzene (CNB) was catalyzed by the newly prepared MPTC (QCl) in the aqueous alkaline (NaOH) medium under ultrasonic irradiation condition.
bi-phase medium and is represented in Scheme 2. The reaction is carried out under MPTC assisted ultrasonic irradiation condition (40 kHz, 300 W) under pseudo first-order condition. In the current investigation the kinetics was followed in the presence of an excess amount of pyrrole and by fixing 1-chloro-4-nitrobenzene as limiting agent. The main reason for investigating this reaction is, the effect of low frequency ultrasound irradiation (40 kHz, 300 W) along with agitation speed (300 rpm) to find out the effect of change of $k_{\text{app}}$ value of this system.

Definition

The conversion (X) of 1-chloro-4-nitrobenzene (CNB) is defined as follows:

$$X = 1 - \left( \frac{[\text{CNB}]_0}{[\text{CNB}]_{\text{app}}} \right)$$

Where $[\text{CNB}]_0$ and $[\text{CNB}]_{\text{app}}$ represent the concentration of 1-chloro-4-nitrobenzene at time (t) $t=0$ and $t>0$, respectively.

Rate expression

The rate expression for this reaction may be expressed as;

$$-\frac{d[\text{CNB}]_0}{dt} = k_{\text{app}} [\text{CNB}]_0$$

Where $k_{\text{app}}$ is the apparent reaction rate constant. This reaction is carried out in a batch reactor, so the diminution rate of CNB with time (t) can be expressed as

$$-\frac{d[\text{CNB}]_0}{dt} = -r_{\text{CNB}} = k_{\text{app}} [\text{CNB}]_0$$

on integrating the Eq. (3) yields:

$$\ln \left( \frac{[\text{CNB}]_0}{[\text{CNB}]_{\text{app}}} \right) = -\ln (1 - X) = k_{\text{app}} t$$

Using Eq. (4), we can get the $k_{\text{app}}$ value experimentally by plotting $\ln (1 - X)$ against time, (t).

Results and Discussion

The reaction was conducted on a 250 mL three-necked Pyrex round-bottom flask which 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. A known quantity of chlorobenzene (30 mL, solvent), sodium hydroxide (20 g wt%), 0.2 g biphenyl IS,(internal standard) were introduced into the reactor. Then, 1.0 g of pyrrole (0.0152 mol) and 2.0 g of 1-chloro-4-nitrophenol (0.0127 mol), 0.3 g of the newly synthesized MPTC (with respect to 1-chloro-4-nitrophenol, limiting reagent) were introduced to the reactor to start the reaction. The reaction mixture was stirred at 300 rpm. The phase separation was almost immediate on arresting the stirring process. Samples were collected from the organic layer of the mixture (by stopping the stirring for 20-30 seconds each time) at regular time intervals. A pinch of anhydrous CaCl$_2$ was placed in the sample vials to absorb any moisture present in the organic layer. Each run consisted of six samples taken over the period ranging from 5 to 30 minutes. The kinetics was followed by estimating the amount of 1-chloro-4-nitrobenzene (limiting reagent) that disappeared using a gas Chromatography (GC-Varian 3700 model). The analyzing conditions were as follows; Column, 30 m × 0.525 mm i.d. capillary column containing 100% poly(dimethyl siloxane); injection temperature, 250°C; FID detector (300°C). Yields were determined from standard curve using biphenyl as an internal standard.

Combined effect of ultrasound and mechanical stirring on the reaction

To ascertain the influence of agitation speed on the rate of nitroarylation of pyrrole, the speed of agitation was varied in the range of 50-500 rpm along with ultrasound irradiation (40 kHz, 300 W) using 1,3,5-tribenzy1-1,3,5-triethyl-1,3,5-triazinane-1,3,5-trium trichloride(MPTC). The result indicates that the rate of the reaction increases linearly as the agitation speed increases from 50 to 300 rpm (Figure 1). However, on further increasing the agitation speed from 300 to 500 rpm, there is no significant improvement in the reaction rate constant. This is because the interfacial area per unit volume of dispersion increased linearly with increasing the stirring speed till 300 rpm is reached, where there is no significant increase in the interfacial area per unit volume of dispersion with the corresponding increase in the speed. Therefore, the agitation speed was set at 500 rpm for studying the reaction phenomena from which the resistance of mass transfer stays at a constant value [34-42]. The $k_{\text{app}}$ values are evaluated from the linear plot of $-\ln (1-X)$ versus time. The results indicate that the mechanical effects brought up by the use of low frequency ultrasounds are responsible for the enhancement of the kinetics by harsh mixing, enhancement of mass transfer and so on further, when the same reaction was carried out in the absence of ultrasound, the observed $k_{\text{app}}$ value (0 kHz, silent condition: $k_{\text{app}}=7.98 \times 10^{-3}$, min$^{-1}$) almost five fold lesser than in the presence of ultrasonication (40 kHz, 300 W $k_{\text{app}}=27.92 \times 10^{-3}$, min$^{-1}$).

Effect of the amount of newly prepared MPTC

Experiments were conducted by varying the amount of the newly synthesized MPTC viz., 1,3,5-tribenzy1-1,3,5-triethyl-1,3,5-triazinane-1,3,5-trium trichlorideby keeping other experimental parameters are kept constant. The influence of the amount of MPTC on the nitroarylation of pyrrole has been studied by varying amount of MPTC from 0.1 g to 0.5 g with respect to 1-chloro-4-nitrobenzene under ultrasound irradiation (40 kHz, 300 W). Apparent rate constants were evaluated from the plot of $-\ln (1-X)$ versus time. As shown in Figure 2, the rate of the reaction increased with increasing in the amount of MPTC along with ultrasound irradiation (40 kHz, 300 W). The $k_{\text{app}}$ values are linearly dependent on the amount of multi-site phase-transfer catalyst. The increasing the $k_{\text{app}}$ value is attributed to the synergic effect of ultrasound might be enlarged [34,43].

Effect of the concentration of 1-chloro-4-nitrobenzene

To investigate the influence of 1-chloro-4-nitrobenzene (CNB) on the kinetics of synthesis of 1-(4-nitrophenyl) pyrrole under ultrasonic

![Figure 1: Effect of stirring speed. Plot of the apparent rate constant versus various stirring speeds. 1 g of pyrrole 20 g of NaOH, 15 mL of H2O, 0.2 g of internal standard (biphenyl), 2.0 g of 1-chloro-4-nitrobenzene, 0.3 g of MPTC, 30 mL of chlorobenzene, 300 rpm, 60°C; ultrasound conditions (40 kHz, 300 W).](image-url)
collide to each other simultaneously we get higher k between the aqueous and organic phases, and hence more reactants substrate with active-site of the catalyst and ultrasound enhanced the nitrobenzene concentration increased, the probability of finding the increases with increasing the amount of CNB. When the 1-chloro-4-nitrobenzene (CNB), g

Table 1: Effect of the amount of 1-chloro-4-nitrobenzene on the apparent rate from 1.0 g to 3.0 g. In the presence and absence of ultrasound results irradiation condition (40 kHz, 300 W). The other point is that the collision of the reactants at higher temperature is also increased. Hence, the apparent rate constant is increased at higher temperature. Arrhenius plots were made in Figure 3 of –ln kapp against 1/1000104 to get activation energy of 52.16 kJ.mol⁻¹.

From the literature survey, the dehydrobromination of (2-bromoethyl)benzene catalyzed by tetaoctylammonium bromide (TOAB), an extraction mechanism was proposed [45] due to lower E value (<43 kJ.mol⁻¹). In general, higher activation energy (more than 43 kJ.mol⁻¹) suggests an interfacial mechanism [44,46]. The activation energy for the heterogeneous ethylation of phenylactonitrile was reported to be 63.64 kJ.mol⁻¹ and for this an interfacial mechanism was proposed [47]. Further, in the N-alkylation of pyrroleidine-2-one, the Ea (51.35 kJ.mol⁻¹) was reported by Sasson and Bilman [48], and for this reaction they proposed an interfacial mechanism. They concluded that the deprotonation of the substrate takes place at the interphase and consequently the organic anion is extracted and reacts in the bulk of the organic phase. The rate-determining step in the process is the anion exchange at the interphase. In our study, the observed E value is 52.36 kJ.mol⁻¹. Hence, we proposed an interfacial mechanism for our present study [49-52].

Influence of amount of water

N-Nitroarylation of pyrrole with 1-chloro-4-nitrobenzene (as a limiting agent) under ultrasound condition (40 kHz, 300 W) was examined by varying the amount of water from 5 to 25 mL under standard reaction conditions. Apparent rate constants were obtained from the plot of –ln(1-X) against time. Generally, the volume of water directly affects both the concentration of sodium hydroxide in the aqueous phase and also generation of anions. Therefore, the conversion (or the reaction rate) will be affected by the volume of water. Figure 4
shows the effect of the amount of water on the rate of the reaction. On increasing the volume of water, the concentration of alkali compound in aqueous solution is decreases. This situation would dramatically reveal the hydration effect of the active catalyst \([N Q^+]\) (Scheme 3) as the volume of water changed from 30 to 50 mL. From the literature, the kinetic study of the phase-transfer catalyzed etherification of 4,4'-bis(chloromethyl)-1,1'-biphenyl with phenol in an alkaline solution of potassium hydroxide/organic solvent two-phase medium, similar decrease in rate of the reaction on corresponding increase in volume of water was reported [53].

**Effect of ultrasonic power**

Ultrasonic irradiation is defines as acoustic waves with frequencies in the 20 kHz -100 MHz range [24-30]. They create cavities generating locally high temperature and pressures [40-43] or strong electric fields [42-45]. Ultrasound is known to accelerate diverse types of organic reactions and it is established generous reactions, which are otherwise slow due to poor mass transfer are accelerated by sonication due to cavitation [41-45]. It has been reported that a combination of PTC and ultrasound is often better than either of the two techniques alone [43-47]. In such transfer of species across the interface and ultrasound merely facilitates this transfer, possibly by increasing the interfacial area across which this transfer occurs.

To ascertain the influence of various ultrasonic frequencies on the rate of nitroarylation of pyrrole with same output power of 300 W, the ultrasonic frequency was varied in the range of 28 and 40 kHz under otherwise similar conditions using MPTC as the catalyst. Also we followed the reaction under silent condition. The kinetic profile of the reaction is obtained by plotting –\(\ln(1-X)\) against time. In our experimental condition at 30 minutes, without ultrasonic irradiation (silent condition) the \(k_{app}\) values is \(7.98 \times 10^{-3}\), min\(^{-1}\) but in the presence of ultrasonic condition the \(k_{app}\) values are \(13.46 \times 10^{-3}\), min\(^{-1}\) and \(27.92 \times 10^{-3}\), min\(^{-1}\) for 28 kHz (300 W) and 40 kHz.
Effect of organic solvents

In this work, the influence of various organic solvents on the rate of nitroarylation of pyrrole was followed under otherwise standard reaction conditions. Five organic solvents employed in this study are toluene, anisole, cyclohexane, chlorobenzene, and n-hexane. From the plot of $-\ln(1-X)$ against time, the $k_{app}$ values are shown in the Table 3. From the Table 3, chlorobenzene possesses a higher $k_{app}$ value among the five organic solvents, due to its higher dielectric constant. In another view the ultrasonic irradiation can enhance the rate in the presence of more polar solvents due to passing higher ultrasonic waves to the reactor and makes fruitful collision between the reactants, and hence we get higher $k_{app}$ value for chlorobenzene solvent of this system and also this statement is not always true [48,49].
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