Research Article

Synthesis of Diethyl 2,2’-(1,3-phenylenebis(oxy))diacetate Under a Multi-site Phase-transfer Catalyst and Ultrasound Irradiation in Solid-liquid Condition

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Abstract
The multi-site phase-transfer catalyst viz., 1,4-dibenzyl-1,4-diazoniabicyclo[2.2.2] octanium dibromide (MPTC) was reported for the reaction of ethyl bromoacetate (EBA) with 1,3-di-hydroxybenzene using mild base potassium carbonate under ultrasonic irradiation (40 kHz, 300W) in a solid–liquid bi-phase condition. The little amount of water is added to the reaction system to avoid the hydration of sodium salt of 1,3-di-hydroxybenzene, the active intermediate and extraction of water to the organic phase. The addition of trace amount of water to solid-liquid (SL–PTC) reactions, it increases the availability of base that resulted in the generation of much more anions. The overall reaction greatly enhanced with ultrasound irradiation and catalyzed by a multi-site phase-transfer catalyst than the individual operations. The reaction mechanism is proposed and verified by examining the experimental evidence. A kinetic model is proposed in which a pseudo first-order rate law is sufficient to describe all the results. All the kinetic experiments are carried out using the catalyst MPTC. The catalytic activity of MPTC was compared with commercially available PTCs. There is high selectivity for bis-derivative of the product under sonication and MPTC condition.

Keywords: Multi-site phase-transfer catalyst; sonochemistry; solid-liquid reaction; 1,3-di-hydroxybenzene; ethyl bromoacetate

Introduction

The reaction between the hydrophilic reactant dissolved in aqueous phase and lipophilic substrate dissolved in organic phase was not take place due to poor collision and both reactants were placed in different phases. This problem was overcome by use of phase-transfer catalyst, it transfer the anion from the aqueous phase to organic phase where the reaction take place with other reactant [1]. PTC technique was being used in pharmaceuticals, agrochemicals, perfumes, flavors, dyes, specialty polymers, pollution control, etc [1-3]. The process has several advantages from economical and environmental point of view such as short reaction time, high yield and mild conditions etc. The number of reactions carried out under the liquid-liquid phase-transfer catalysis (L–L PTC) leading to intensification of reaction rates are reported. In general, solid-liquid phase-transfer catalysis (S-L PTC) offers higher rate of reaction compared with the liquid-liquid phase-transfer catalysis (L–L PTC). An added advantage of carrying out the reactions in the presence of a base in S-L PTC biphasic system is suppresses the water promoted reactions and which leading to high yield of the desired product.
The small quantity of water play an important role in the catalytic processes i.e. increases in the apparent rate constant or the conversion [4, 5]. The S-LPTC provides the advantages of easy separation of products, selection of organic solvents and prevention of unfavorable side reactions [4, 5]. The S-LPTC is inherently faster due to greater mass transfer rates provided by fine solid particles than liquid droplets [6-9]. Among the phase-transfer catalyst, quaternary ammonium salt has the unique properties that, it dissolves in both aqueous and organic solvents, which is the choice of catalyst and can transport back and forth from one of the phase to the other.

Aromatic ethers used in a variety of industries, are produced by PTC routes [10-12]. Ether–ester compounds have the applications as anticholesteremics, antilipemics, hypocholesteremic agents and hypolipemics for medical compounds [12].

Nowadays, in the heterogeneous phase-transfer catalysis, some attentions have been given to multi-site phase-transfer catalysis technique in order to enhance the reaction rates, to improve the selectivity, minimize the need of single-site PT catalyst in large amount and time consumption [13-17]. The merit of MPTC is, it transfers more number of anionic species from aqueous or solid phase to organic phase per cycle in contrast with single-site phase-transfer catalyst which transports single anionic species per cycle.

Ultrasound is a wave of frequency 2 x 10^4–10^9 Hz. When ultrasonic wave passes through a liquid medium, a large number of micro bubbles form, grow and collapse in a very short time about a few microseconds, which is called ultrasonic cavitations [18]. The cavitations can generate local temperatures and local pressures. Ultrasound leads to an increase in the reaction rate or to improvement in many reactions such as organic and inorganic reactions, polymerization and so on [19]. Ultrasonic irradiation in biphasic reaction can increase interfacial area coupled with local hot-spot generation, and has been demonstrated to promote high reaction rate in organic synthesis [20-23]. The anionic salt present in the solid phase and PT Catalyst form the catalytic intermediate and leads to organic bulk phase where the intrinsic reaction takes place. Sometime the diminution of reaction rate observed by S-LPTC was commonly due to the side product, salt deposited on the surface of solid reactant particles, that reduces the formation of the catalytic intermediate [24, 25]. The surface-deposited side-product was removed by ultrasound, by creating the liquid jet and increasing the formation of the catalytic intermediate.

Many works were reported in the heterogeneous reaction condition, whether it is liquid-liquid or solid-liquid, the reaction rate or conversion is tremendously increased by the use of PTC combined with ultrasonic irradiation [26-28]. But few works only were reported in solid-liquid reaction condition catalyzed by multi-site phase-transfer catalyst under ultrasound irradiation [29]. This is prompt us to do the reaction that, the reaction between 1,3-dihydroxybenzene and ethyl bromoacetate (EBA) was proceeded in the SL–PTC system involving solid K$_2$CO$_3$ as the mild base under the combined effect of MPTC (1,4-dibenzyl-1,4-diazoniabicyclo[2.2.2] octane dibromide) and ultrasound irradiation (40 kHz, 300W). The factors affecting the reaction rate i.e., various stirring speed, amount of MPTC, different ultrasonic frequencies, amount of potassium carbonate, various ethyl bromoacetate concentration, MPTC and different PTCs, various temperature, kind of organic solvents, volume of chlorobenzene, volume of water were investigated in detail under pseudo first-order reaction conditions and a reasonable mechanism is proposed.

**Experimental**

**Catalysts, chemicals and solvents**

All the reagents, including, 1,3-dihydroxybenzene, Ethyl bromoacetate, DABCO (1,4-diazabicyclo[2.2.2]octane), benzyl bromide, biphenyl, tetrabutylammonium bromide (TBAB), tetrahexyl ammonium bromide (THAB), tetroctyl ammonium bromide (TOAB) potassium carbonate, n-hexane, toluene, chlorobenzene, anisole, ethanol, diethyl ether and other reagents for synthesis were guaranteed grade (GR) chemicals and were used without further purification.

**Instrumentation**

Gas chromatography was carried out using a GC-Varian 3700 model. Ultrasonic water bath, Equitron, Media Instrument Manufacturing Company, Chennai, India-600 004. The ultrasonic generator was a thermostatic bath equipped with dual frequencies (28/40 kHz) and electric power 300W with 0.0126 W/mL of power density. $^1$H NMR was recorded on a Bruker 300 MHz and 400 MHz and $^{13}$C spectra were recorded on 75 MHz and 100 MHz respectively using TMS as an internal standard.
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 liters. Two types of frequencies of ultrasound were used in these experiments, which are 28 kHz and 40 kHz with each output as 300W. Both ultrasounds 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 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 300W.

synthesis of 1,4-dibenzyl-1,4-diaza[2.2.2]octan dibromide, (MPTC)
A mixture of 1,4-diaza[2.2.2]octane (DABCO, 5 g, 44.58 mmol), benzyl bromide (16.78 g, 98.13 mmol) and 70 mL of ethanol was placed in a 250 mL three-necked round bottomed Pyrex flask. The reaction was carried out at 60°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., 1,4-dibenzyl-1,4-diaza[2.2.2]octan dibromide, (MPTC) was washed with n-hexane (4 x 25 mL). The colorless solid was stored in CaCl₂ desiccators, Yield: 90% (Scheme 1).

Scheme 1 Preparation of MPTC

Synthesis of diethyl 2,2'-(1,3-phenylenebis(oxy))diacetate
To the 10g of potassium carbonate in 3 mL water, the 1,3-dihydroxybenzene (3g, 27.25 mmol) was added under overhead stirring for few minutes to generate the resorcinol anion. Then ethyl bromoacetate (3.3g, 19.75 mmol) and the newly synthesized MPTC (3 mol %) in chlorobenzene (40 mL) were added slowly. The reaction mixture was heated at 315 K for one hour with vigorous stirring. The product formed was evidenced by thin layer chromatography (TLC). The organic layer is collected separately and the solvent chlorobenzene is stripped off under vacuum. The crude sample is dissolved in ethyl acetate and work up process continued with potassium carbonate solution and deionized water to remove the excess catalyst and base respectively for several times. The organic layer was collected and the solvent was evaporated under reduced pressure. The crude product was subjected to chromatography (SiO₂) employing hexane: ethyl acetate (9:8:0.2) as an eluent to obtain the pure product (Scheme 2) in the form of colorless liquid having the fruity smell of esters. The identity of the product (diethyl 2,2'-(1,3-phenylenebis(oxy))diacetate) was confirmed by ¹H NMR and ¹³C NMR spectra and elemental analysis.
$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 1.254-1.301 (6H, t, -CH$_3$), 4.208-4.277 (4H, q, -O-CH$_2$-CH$_3$), 4.574 (4H, s, -O-CH$_2$-C=O), 6.204 (1H, s, Ar-H), 6.509-6.534 (2H, d, Ar-H), 7.139-7.189 (1H, t, Ar-H).

$^{13}$C NMR (75 MHz, CDCl$_3$): Aliphatic carbons; $\delta$ 14.06 (-CH$_3$), 62.16 (-O-CH$_2$-CH$_3$), 65.38 (-CH$_2$ Carbon in between ether and keto group), 168.64 (Ketone Carbon).
Aliphatic carbons: δ 14.06 (-CH₃), 62.16 (-O-CH₂-CH₃), 65.38 (-CH₂ Carbon in between ether and keto group), 168.64 (Ketone Carbon).
Aromatic carbons: δ102.23, 108.15, 130.02, 159.06.

Elemental analysis:
Calculated: C, 60.01%; H, 6.45%; O, 34.04% and Found: C, 59.57%; H, 6.43%; O, 34.01% .

Reaction mechanism and kinetic model
To overcome the small amount of product was obtained when the reaction was carried out in a liquid –liquid heterogeneous reaction due to hydration [30, 31], the reaction between 1,3-dihydroxybenzene and ethyl bromoacetate was carried out in a solid-liquid condition and catalyzed by multi-site phase-transfer catalyst under ultrasound irradiation (40 kHz, 300W). Trace amount of water added to the reaction system in order to minimize the loss of reactant due to hydration and to enhance the formation of sodium salt of 1,3-dihydroxybenzene.

The solid–liquid reaction mechanisms are classified into two categories. First one is the non-soluble system (heterogeneous solubilization) introduced by Doraisamy and Naik [30] and other is soluble system (homogeneous solubilization) introduced by Yadav and Sharma [31], which depend on the solubility of the inorganic salt of anion in the organic solvent. In this work, sodium salt of 1,3-dihydroxybenzene is sparingly soluble in organic solvent (chlorobenzene). First, potassium salt of 1,3-dihydroxybenzene dissolved in the organic solvent with the addition of quaternary ammonium salt, i.e. Ph(O-K⁺)₂ dissolved in the organic solvent with the addition of quaternary ammonium salt to form an active intermediate[Ph(O)₂ Q²⁺]. The inorganic salt KX precipitated as a solid form in the organic solution and then it is transported to the aqueous or solid phase. In a similar way, Vander and Hartner [32] and Yoel and Zahalka [33] proved that quaternary ammonium salt can be used to dissolve the solid reactant. The active [Ph(O)₂ Q²⁺] (org) then react with ethyl bromoacetate (EBA) to produce the desired product (diethyl 2,2’-(1,3-phenylenebis(oxy))diacetate, Scheme 3) and the catalyst is regenerated, transferred to the inter-face and the above said process taking place continuously up to the disappearance of ethyl bromoacetate in the bulk organic phase.

Definition
The conversion (X) of ethyl bromoacetate (EBA) is defines as follows:

\[ X = 1 - \frac{[EBA]_0}{[EBA]_{o,i}} \]  \hspace{1cm} (1)

where [EBA]₀ and [EBA]ᵦᵢ represent the concentration of ethyl bromoacetate at time (t) t=0 and t>0, respectively.

Rate expression
The rate expression for this reaction may be expressed as:

\[ -r_{EBA} = k_{app} [EBA]_o \]  \hspace{1cm} (2)

Where \( k_{app} \) is the apparent reaction rate constant.

This reaction is carried out in a batch reactor, so the diminution rate of EBA with time (t) can we expressed as

\[ -d[EBA]_0 / dt = -r_{EBA} = k_{app} [EBA]_o \]  \hspace{1cm} (3)

on integrating the Eq. (3) yields:

\[ -\ln\left(\frac{[EBA]_0}{[EBA]_{o,i}}\right) = -\ln(1-X) = k_{app} \times t \]  \hspace{1cm} (4)

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

The reactor was a 250 ml three-necked Pyrex flask, serving the purposes of agitating the solution, inserting the condenser to recover the solvent and reactant and taking samples, feeding the feed etc. This reaction vessel was supported at the centre of the sonicator. Known quantities of chlorobenzene (40 mL, solvent), well powdered potassium carbonate (10 g in 3 mL water) and 0.2 g biphenyl (IS-internal standard) were introduced into the reactor.

Then, 3 g of 1,3-dihydroxybenzene (27.25 mmol) and 3.3 g of ethyl bromoacetate (19.75 mmol), 3 mol % of the synthesized MPTC were introduced to the reactor to start the reaction. The reaction mixture was stirred at 500 rpm.

The phase separation was immediate when stopping the agitation process. Samples were taken from the organic layer at regular time intervals and put it into the 10 mL vials and then 0.5 mL of chlorobenzene was added to vials to dilute the solution. The kinetics was followed by estimating the amount of ethyl bromoacetate (limiting reagent) 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.

Effects of speed of agitation

The theory of mass-transfer in the phase-transfer catalyzed heterogeneous reactions is discussed in many papers by many researchers [34-42]. This theory is also applicable to this S-L PTC reaction of 1,3-dihydroxybenzene and ethyl bromoacetate (EBA) under a multi-site phase-transfer catalyst viz., 1,4-dibenzyl-1,4-diaziobiocyclo[2.2.2]octane dibromide (MPTC) along with ultrasound irradiation (40 kHz, 300W). To ascertain the influence of external mass-transfer resistance on the transfer of the reactant to the reaction phase, the speed of agitation was varied in the range of 0-600 rpm. As seen from Table 1, the conversion or the reaction rate increases with an increase in speed of agitation from 0 to 400 rpm. This is due to the dissolving rate of Ph(O*K*)2 in chlorobenzene is highly influenced by
the agitation speed. In general, a high concentration of Ph(O K⁺)₂ dissolving in organic solvent is obtained at a high agitation speed up to 400 rpm. In principle, Ph(O K⁺)₂ first dissolves gradually in chlorobenzene in the presence of MPTC to forming (Ph(O)₂ Q²⁺) at the inter-phase. Then, the formed intermediate (Ph(O)₂ Q²⁺) reacted with ethyl bromoacetate to produce diethyl 2,2′-(1,3-phenylenebis(oxy))diacetate in the organic phase. However, when the speed of agitation was increased from 400 to 600 rpm the increase in conversion was marginal which suggests elimination of external resistance to mass transfer. Therefore all further experiments were conducted at 500 rpm.

When the reaction was carried out in ultrasound irradiation only, the k<sub>app</sub> is to be 6.40 x 10<sup>-3</sup>, min<sup>-1</sup>. The same reaction was carried out without ultrasound (having stirring speed 500 rpm only) that is, conventional method, the observed k<sub>app</sub> value (k<sub>app</sub> = 10.41 x 10<sup>-3</sup>, min<sup>-1</sup>) is almost 3.5 times lesser than in the presence of sonication (40 kHz, 300W) and stirring (k<sub>app</sub> = 36.45 x 10<sup>-3</sup>, min<sup>-1</sup>). The increased k<sub>app</sub> values 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, especially in solid-liquid systems, high erosion of the solid particles occurs and the surface area is increased [43] and ultrasound decreases the surface area between the two layers [44, 45].

**Table 1 Effect of stirring speed.**

<table>
<thead>
<tr>
<th>Stirring rate (rpm)</th>
<th>k&lt;sub&gt;app&lt;/sub&gt; x 10&lt;sup&gt;-3&lt;/sup&gt;, min&lt;sup&gt;-1&lt;/sup&gt; (40 kHz, 300W)</th>
<th>k&lt;sub&gt;app&lt;/sub&gt; x 10&lt;sup&gt;-3&lt;/sup&gt;, min&lt;sup&gt;-1&lt;/sup&gt; (without ultrasound)</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>6.4</td>
<td>1.83</td>
</tr>
<tr>
<td>100</td>
<td>12.12</td>
<td>3.46</td>
</tr>
<tr>
<td>200</td>
<td>19.16</td>
<td>5.47</td>
</tr>
<tr>
<td>300</td>
<td>28.2</td>
<td>8.06</td>
</tr>
<tr>
<td>400</td>
<td>36.41</td>
<td>10.41</td>
</tr>
<tr>
<td>500</td>
<td>36.45</td>
<td>10.44</td>
</tr>
<tr>
<td>600</td>
<td>36.7</td>
<td>10.56</td>
</tr>
</tbody>
</table>

Effect of stirring speeds on the apparent rate constant: 10 g of K₂CO₃, 3 mL H₂O, 0.2 g of biphenyl (internal standard), 27.25 mmol of 1,3-dihydroxybenzene, 19.75 mmol of ethyl bromoacetate, 3 mol% of MPTC, 40 mL of chlorobenzene, 318 K, ultrasound condition (40 kHz, 300W).

**Different ultrasound frequencies**

When ultrasonic wave passes through a liquid medium, a large number of micro bubbles form, grow and collapse in a very short time about a few microseconds, which is called ultrasonic cavitations [46, 47]. Ultrasonic cavitations creates a very extreme environment, i.e. extremely high local temperature and pressure [48-51], as well as heating and cooling rates for chemical reaction [52]. Sonication is increased the chemical reactivity due to enhancement in mass-transfer in heterogeneous reaction. In solid-liquid system, ultrasonic frequency affects the surface morphology of the particulate phase from the impact of liquid-jet and hot-spot generated by ultrasonic wave. From the literature, it is clear that the ultrasonically promoted (having stirring) reaction proceeded somewhat faster than the ‘‘silent’’ reaction condition [28, 44]. The effect of two different ultrasound frequencies having same output power of 300W is studied. Ultrasonic frequencies 28 kHz and 40 kHz are used to test their effect on the reaction rate or conversion in the solid-liquid biphasic reaction catalyzed by multi-site phase-transfer catalyst. When we use higher frequency (40 kHz, 300W), it gives the higher ultrasonic energy entering the system and a consequent increase in the sonochemical effect that resulted in effective mixing of phases and, collision between the molecule increases and that resulted in the increased conversion or the apparent reaction rate. The reaction also conducted in silent method as well to compare the rate of the reaction. The rate constants, 10.44 x 10<sup>-3</sup> min<sup>-1</sup>, 25.12 x 10<sup>-3</sup> min<sup>-1</sup>, 36.45 x 10<sup>-3</sup> min<sup>-1</sup> are related to 0 kHz, 28 kHz, 40 kHz respectively has shown in Table 2. Hence, the overall k<sub>app</sub> value was increased by increasing the ultrasonic frequency in the order of 0 kHz (silent method) < 28 kHz (300W) < 40 kHz (300W) for our system (Table 2). Similar trend was observed by Entezari et al [53, 54].
Table 2 Effect of ultrasonic frequency.

<table>
<thead>
<tr>
<th>Ultrasonic frequency (kHz, 300W)</th>
<th>$k_{\text{app}} \times 10^3$, min$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (silent)</td>
<td>10.44</td>
</tr>
<tr>
<td>28</td>
<td>25.12</td>
</tr>
<tr>
<td>40</td>
<td>36.45</td>
</tr>
</tbody>
</table>

Influence of ultrasonic frequencies on the apparent rate constant: 10 g of $\text{K}_2\text{CO}_3$, 3 mL $\text{H}_2\text{O}$, 0.2 g of biphenyl (internal standard), 27.25 mmol of 1,3-dihydroxybenzene, 19.75 mmol of ethyl bromoacetate, 3 mol% of MPTC, 40 mL of chlorobenzene, 500 rpm, 318 K.

Effect of MPTC concentration

The reaction of potassium salt of 1,3-dihydroxybenzene and ethyl bromoacetate was carried out in a homogeneous chlorobenzene solution. The potassium salt of 1,3-dihydroxybenzene in solid form first dissolves in chlorobenzene in the presence of a MPTC (viz., 1,4-dibenzyl-1,4-diazeniabicyclo[2.2.2]octanium dibromide). To find the influence of MPTC catalyst on the rate of the reaction, the catalyst is varied from 1 mol% to 5 mol% under otherwise similar reaction conditions. The conversion of ethyl bromoacetate is increased with the increase in the amount of catalyst. The conversion is low in the absence of any catalyst, although the reaction is greatly enhanced by adding a small amount of catalyst. As stated above, potassium salt of 1,3-dihydroxybenzene is insoluble in organic solvent however, it is only soluble in chlorobenzene in the presence MPTC. Figure 1 shows the effects of the amount of MPTC on the $k_{\text{app}}$ value, which increases with the increase in the amount of MPTC along with ultrasound irradiation (40 kHz, 300W). The increase in the $k_{\text{app}}$ value is attributed to the synergic effect of ultrasound, i.e. induce the surface area, change the size, and morphology of phase-transfer catalyst (MPTC) [55, 56]. The $k_{\text{app}}$ value is linearly proportional to the amount of the MPTC catalyst up to 3 mol%. However, the result does not follow the linear relation between $k_{\text{app}}$ value and the amount of the MPTC catalyst by using large amount of MPTC catalyst. This phenomenon is the same as that result by Yadav and Sharma [31], and Yoel and Zahalka [33]. In addition, Yoel and Zahalka [33] attributed this phenomenon by the salting out effect. It could bring mass transfer resistance in picture at higher catalyst concentration. Therefore, all the further experiments were done at 3 mol% of catalyst concentration.

![Figure 1 Effect of amount of MPTC.](image-url)
**Effect of the amount of MPTC on the conversion:** 10g of K$_2$CO$_3$, 3 mL H$_2$O, 0.2 g of biphenyl (internal standard), 27.25 mmol of 1,3-dihydroxybenzene, 19.75 mmol of ethyl bromoacetate, 40 mL of chlorobenzene, 500 rpm, 318 K; ultrasound condition (40 kHz, 300W).

**Effect of ethyl bromoacetate concentration**

To investigate the influence of ethyl bromoacetate (EBA) on the conversion, the amount of ethyl bromoacetate (EBA) was varied from 13.75 mmol to 25.75 mmol under standard reaction conditions. The results are shown in **Table 3**. The data clearly indicates that the $k_{app}$ value increases with increase in the amount of ethyl bromoacetate (EBA). This observation due to presence of more number of active sites in the MPTC and higher concentration of substrate (EBA) had co-operatively influence the reaction and thus enhance the more number of contacts between active intermediate and substrate (EBA), and hence it is reflected in enhanced $K_{app}$ values. In addition ultrasound enhance the rate of the reaction, it may be due to reduces the surface area between the solid and organic phase, and hence more reactants collide to each other simultaneously we get higher $k_{app}$ value [57, 58].

<table>
<thead>
<tr>
<th>Ethyl bromoacetate (EBA), Mmol</th>
<th>$k_{app} \times 10^3$, min$^{-1}$ (40 kHz, 300W)</th>
<th>$k_{app} \times 10^3$, min$^{-1}$ (without ultrasound)</th>
</tr>
</thead>
<tbody>
<tr>
<td>13.75</td>
<td>26.68</td>
<td>7.62</td>
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<td>16.75</td>
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<td>19.75</td>
<td>36.45</td>
<td>10.44</td>
</tr>
<tr>
<td>22.75</td>
<td>40.3</td>
<td>11.51</td>
</tr>
<tr>
<td>25.75</td>
<td>43.78</td>
<td>12.51</td>
</tr>
</tbody>
</table>

*Effect of amount of ethyl bromoacetate (EBA) on the apparent rate constant:* 10 g of K$_2$CO$_3$, 3 mL H$_2$O, 0.2 g of biphenyl (internal standard), 27.25 mmol of 1,3-dihydroxybenzene, 3 mol% of MPTC, 40 mL of chlorobenzene, 500 rpm, 318 K, ultrasound condition (40 kHz, 300W).

**Effect of various temperatures**

![Figure 2 Effect of temperature](image-url)
**Effect of temperature on the conversion:** 10 g of K₂CO₃, 3 mL H₂O, 0.2 g of biphenyl (internal standard), 27.25 mmol of 1,3-dihydroxybenzene, 19.75 mmol of ethyl bromoacetate, 3 mol% of MPTC, 500 rpm, ultrasound condition (40 kHz, 300W).

The effect of temperature on the reaction rate was studied in the range of 308 K to 348 K (Figure 2). The conversion of ethyl bromoacetate is increased with an increase in the temperature along with ultrasonic effect [44, 59]. This is due to the number of reactant molecules which possess higher activated energy at higher temperature and thus the ultrasonic wave easily passes through the reactor [44]. The increase in the conversion is almost linear when the temperature is increased from 308 K to 338 K. For reaction temperature beyond 338 K, there was marginal difference in the final conversions (Figure 2). The use of ultrasound reduces the need of high temperature for the reaction system. Arrhenius plots were made of $\ln k_{app}$ against $T^{-1}$ to get activation energy of 48.44 kJ.mol$^{-1}$ (Figure 3). This higher activation energy demonstrates that this ultrasound assisted solid-liquid reaction under multi-site phase-transfer catalyst (MPTC) was kinetically controlled and the mass-transfer resistance between phases was unimportant. The higher activation energy value is an indicative of the interfacial mechanism [44, 60].

![Arrhenious plot for 1,3-dihydroxybenzene](image)

**Figure 3** Arrhenius plot for 1,3-dihydroxybenzene

**Arrhenious plot:** 10 g of K₂CO₃, 3 mL H₂O, 0.2g of biphenyl (internal standard), 27.25 mmol of 1,3-dihydroxybenzene, 19.75 mmol of ethyl bromoacetate, 3 mol% of MPTC, 40 mL of chlorobenzene, 318 K, 500 rpm, ultrasound condition (40 kHz, 300W).

**Effect of different organic solvents**

The influence of various organic solvents on the rate of ether-esterification of 1,3-dihydroxybenzene was followed under otherwise standard reaction conditions. The polarity of organic solvent affects the dissolution of solid reactant anion (i.e., potassium salt of 1,3-dihydroxybenzene) in organic solvent. With adding 3 mL of water, the more polar solvent induced the higher activity of phase-transfer catalyst, because a higher content of (Ph(O)$_2$Q$^+$) was acquired. From the plot of $-\ln (1-X)$ against time, the $k_{app}$ values are obtained. It is clear from the Table 4; chlorobenzene possesses a higher $k_{app}$ value among the five organic solvents used.
### Table 4 Effect of organic solvents

<table>
<thead>
<tr>
<th>Solvent, dielectric constant (ε&lt;sup&gt;a&lt;/sup&gt;)</th>
<th>k&lt;sub&gt;app&lt;/sub&gt; x 10&lt;sup&gt;3&lt;/sup&gt;, min&lt;sup&gt;-1&lt;/sup&gt; (with ultrasound, 40 kHz, 300W)</th>
<th>k&lt;sub&gt;app&lt;/sub&gt; x 10&lt;sup&gt;3&lt;/sup&gt;, min&lt;sup&gt;-1&lt;/sup&gt; (without ultrasound)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorobenzene (5.6)</td>
<td>36.45</td>
<td>10.44</td>
</tr>
<tr>
<td>Anisole (4.3)</td>
<td>32.21</td>
<td>9.2</td>
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<tr>
<td>Toluene (2.4)</td>
<td>27.59</td>
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<td>Hexane (2.2)</td>
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<td>12.5</td>
</tr>
<tr>
<td>Cyclohexane (2.0)</td>
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</tbody>
</table>

Influence of various organic solvents on the apparent rate constant: 10 g of K<sub>2</sub>CO<sub>3</sub>, 3 mL H<sub>2</sub>O, 0.2 g of biphenyl (internal standard), 27.25 mmol of 1,3-dihydroxybenzene, 19.75 mmol of ethyl bromoacetate, 3 mol% of MPTC, 40 mL of solvents, 500 rpm, 318 K, ultrasound condition (40 kHz, 300W).

**Effect of different volume of chlorobenzene**

The conversion or the reaction rate is directly proportional to the concentration of the reactants in 60 minutes of reaction. A dilute concentration of the reactant is obtained using a large amount of organic solvent. The conversion of ethyl bromoacetate is increased with the decrease in the volume of chlorobenzene. **Figure 4** shows the dependence of the % conversion on the volume of chlorobenzene. The k<sub>app</sub> value is inversely proportional to the volume of chlorobenzene, as we expected.

**Figure 4** Effect of volume of chlorobenzene.

**Effect of volume of chlorobenzene on the conversion:** 10 g of K<sub>2</sub>CO<sub>3</sub>, 3 mL H<sub>2</sub>O, 0.2 g of biphenyl (internal standard), 27.25 mmol of 1,3-dihydroxybenzene, 19.75 mmol of ethyl bromoacetate, 3 mol% of MPTC, 318 K, 500 rpm, ultrasound condition (40 kHz, 300W).

**Effect of MPTC and single-site phase-transfer catalyst**

In this study, the MPTC and three single-site phase-transfer catalysts were used to check their efficacies for the ether-
esterification reaction of 1,3-dihydroxybenzene with ethyl bromoacetate (EBA) keeping the other reaction conditions are constant under sonication (40 kHz, 300W). The Phase-transfer catalysts are tetrabutylammonium bromide (TBAB), tetrahexyl ammonium bromide (THAB) and tetraoctyl ammonium bromide (TOAB) and the MPTC is 1,4-dibenzyl-1,4-diazoniabicyclo[2.2.2]octanium dibromide. Figure 5 depicts the conversion for these four catalysts. Unexpectedly, the reaction rate constant estimated for the reaction in the absence of PTCs is about one-tenth of that with MPTC. It is attributed to interfacial solid–liquid reaction. In other words, the anion is generated at the surface of solid base and the intrinsic reaction occurs at the solid–liquid interface [61]. However, the potassium salt of 1,3-dihydroxybenzene cannot be dissolved in chlorobenzene and contacts between molecules at the solid–liquid interface are difficult. Hence, the reaction rate is relatively low. However, the reaction rate is enhanced dramatically even with adding a small quantity of PTC or MPTC. It is attributed that the anion can be easily transferred into the bulk organic phase and the mechanism is changed. This is because, the expansion of catalytic active site of catalyst. The results suggest that the chemical reaction between the active intermediate and the ethyl bromoacetate be the sole rate-determining step. From Figure 5, it is clear that the order of catalytic reactivity of PTCs and MPTC are MPTC >TOAB >THAB > TBAB. This order reveals that the lipophilic character of the phase-transfer catalysts and the MPTC [44, 60, 62].

Effect of various potassium carbonate concentrations
The reaction rate is known to be greatly affected by a concentration of the alkaline potassium carbonate. The rate of the esterification of 1,3-dihydroxybenzene is strongly depends on the strength of the potassium carbonate. Kinetic experiments were carried out by employing 5 to 16 g of K₂CO₃ (keeping 3 mL water constant) under otherwise similar reaction conditions. The k_{app} value or conversion tremendously increased with increasing in the basicity (Table 5). The main reasons are that on increasing the alkaline concentration, (i) the base is less solvated by water molecule. (ii) The amount of production of anion (potassium salt 1,3-dihydroxybenzene) is increased. (iii) The distribution of active catalyst is increased. From the Table 5, the conversion is increased linearly with increase in the

Effect of MPTC and PTCs on the conversion: 10 g of K₂CO₃, 3 mL of water, 0.2 g of biphenyl (internal standard), 27.25 mmol of 1,3-dihydroxybenzene, 19.75 mmol of ethyl bromoacetate, 3 mol% of MPTC and PTCs, 40 mL of chlorobenzene, 500 rpm, 318 K; ultrasound condition (40 kHz, 300W).

**Figure 5** Effect of MPTC and PTCs.

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alkali concentration. The water has a subtle influence on the basicity and the hydration of the ion-pair [63-65].

### Table 5 Effect of amount of potassium carbonate.

<table>
<thead>
<tr>
<th>potassium carbonate, (g)</th>
<th>( k_{\text{app}} \times 10^{-3} ), \text{min}^{-1} (with ultrasound, 40 kHz, 300W)</th>
<th>( k_{\text{app}} \times 10^3 ), \text{min}^{-1} (with ultrasound)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>20.42</td>
<td>5.83</td>
</tr>
<tr>
<td>10</td>
<td>36.45</td>
<td>10.44</td>
</tr>
<tr>
<td>13</td>
<td>42.21</td>
<td>12.35</td>
</tr>
<tr>
<td>16</td>
<td>48.14</td>
<td>14.13</td>
</tr>
</tbody>
</table>

*Effect of potassium carbonate on the apparent rate constant:* 3 mL H₂O, 0.2 g of biphenyl (internal standard), 27.25 mmol of 1,3-dihydroxybenzene, 19.75 mmol of ethyl bromoacetate, 3 mol% of MPTC, 40 mL of chlorobenzene, 500 rpm, 318 K, ultrasound condition (40 kHz, 300W).

*Effect of volume of water*

In a series of experiments, the amount of water had been varied from 0 to 15mL keeping the other reaction conditions are constant. It was demonstrated from Figure 6 that the reaction rate first increased slightly, then decreased sharply and finally slowly decreased as the amount of water is increased. The reaction rate of the reaction was increased with the addition of trace water, as in the other SL–PTC reactions [66]. The reason behind is amount of the available \( \text{K}_2\text{CO}_3 \) increases, that results in the generation of much more anions (i.e., potassium salt of 1,3-dihydroxybenzene). Nevertheless, hydration will form around the carbonate anion if the amount of water further increases. Meanwhile, a little water is extracted into the organic phase and the degree of hydration of the ion-pair increases. Accordingly, the basicity of carbonate anion considerably decreases and the reactivity of the ion-pair is lowered. In fact, the solid base will become pasty and the ion-pair in the organic phase is completely hydrated as excess water is added. Therefore, the reaction rate constant is decreased when the amount of water is increased. With only 3 mL of water, the formation of \([\text{Q}^2+\text{Ph(O)}_2\text{]}\) is greatly increased and concentrated in the inter-phase and leads to the bulk organic phase where the intrinsic reaction take place [25, 29].

![Effect of volume of water](image)

*Figure 6 Effect of volume of water.*

*Effect of the volume of water on the apparent rate constant:* 10 g of \( \text{K}_2\text{CO}_3 \), 0.2 g of biphenyl (internal standard), 27.25 mmol of 1,3-dihydroxybenzene, 19.75 mmol of ethyl bromoacetate, 3 mol% of MPTC, 40 mL of chlorobenzene, 500 rpm, 318 K; ultrasound condition (40 kHz, 300W).
Conclusion

In the present research work, the solid-liquid reaction was successfully carried out in the presence of multi-site phase-transfer catalyst (MPTC) and sonication (40 kHz, 300W) to produce the desired product namely diethyl 2,2’-(1,3-phenylenebis(oxy))diacetate from 1,3-dihydroxybenzene and ethyl bromoacetate (EBA). The selectivity of bis-derivative 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 reaction mechanism and the apparent rate constants were obtained from the experimental results; Energy of activation was calculated from the Arrhenius plot. From the experimental evidence we propose the interfacial mechanism for the present reaction system.

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