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Technology Reports

Novelties of Solid−Liquid Phase Transfer Catalysed Synthesis of α-Isopropyl-*p*-chlorophenyl Acetonitrile from *p*-Chlorophenyl Acetonitrile

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Abstract:

C-Alkylation is an important class of synthetic reaction employed in the fine chemical industry. Although a number of C-alkylation reactions are reported under liquid−liquid (L−L) phase transfer catalysis (PTC) leading to intensification of reaction rates, there is a dearth of information on similar reactions under the solid−liquid (S−L) PTC including kinetics and mechanism. S−L PTC offers higher rates of reaction and better selectivities to the desired product vis-à-vis L−L PTC. This contribution reports the novelties of S−L PTC for C-alkylation of *p*-chlorophenyl acetonitrile to α-isopropyl-*p*-chlorophenyl acetonitrile which is an important intermediate in the synthesis of a pyrethroid insecticide named fenvalerate. *p*-Chlorophenyl acetonitrile can be mono- or dialkylated, depending on the reaction conditions, and it is a versatile synthetic intermediate in the sense that the nitrile function can be hydrolysed, reduced, or added to by organometallics after an alkylation has been carried out. It is found that the S−L PTC process is more intensified and selective. The mechanistic details of C-alkylation under basic conditions and the unexpected side reaction of oxidative decyanation are studied. The production of water as a byproduct in the reaction to form the omega (ω) phase and the mechanism in reference to the S−L−ω-phase system is described. A numerical model is composed to calculate the values of various pseudo rate constants and validate the simulated profiles against experimental data. The finer aspects of selectivity in C-alkylation reaction are analysed.

Introduction

Alkylation reactions, particularly C-alkylations, are among the most useful synthetic transformations in organic chemistry, typically performed under alkaline conditions with or without a phase transfer catalyst.[1] Although a number of C-alkylation reactions under liquid−liquid (L−L) phase transfer catalysis (PTC) leading to intensification of reaction rates are reported, there is a dearth of information on similar reactions under the solid−liquid (S−L) PTC including kinetics and mechanism. In general, S−L PTC offers higher rates of reaction in comparison with the L−L PTC. An added advantage of carrying out reactions in the presence of a base in S−L biphasic systems is that it suppresses alkaline hydrolysis of halogenated reactant leading to higher yield of the C-alkylated product.

This work is concerned with S−L PTC of C-alkylation of *p*-chlorophenyl acetonitrile to α-isopropyl-*p*-chlorophenyl acetonitrile which is an important intermediate in the synthesis of a pyrethroid insecticide named fenvalerate. Approximately 4000 tonnes of fenvalerate are used annually worldwide. India alone produces about 2300 tonnes/year. It is used primarily in agriculture but also in homes and gardens for insect control, and on cattle, alone or in combination with other insecticides.

Apart form its commercial value, *p*-chlorophenyl acetonitrile is a good substrate for study because it is reasonably acidic, but not alkylated by aqueous metal hydroxide in the absence of a catalyst at any synthetically useful rate. Another advantage is that it can be mono or dialkylated depending on the reaction conditions. It is a versatile synthetic intermediate in the sense that the nitrile function can be hydrolysed, reduced, or added to by organometallics after an alkylation has been carried out. The C-alkylation of *p*-chlorophenyl acetonitrile has reportedly been done under L−L PTC conditions using various phase transfer catalysts such as tetramethylammonium bromide, PEG, tetrabutylammonium hydrogen sulphate, benzyltriethylammonium chloride, and tetrabutylammonium chloride.[2−8] A few of these reports deal with the mechanistic details of the process.

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Synthesis under S−L PTC conditions is not reported. The current work brings out the novelties of the S−L PTC synthesis including mechanism and kinetics of this reaction.

Experimental Section

Chemicals and Catalysts. *p*-Chlorophenyl acetonitrile and isopropyl bromide were gift samples from Rallis India Ltd., Mumbai, India. Potassium hydroxide (solid pellets, 15% water content) and toluene of AR grade were obtained from M/s S.D. Fine Chem. Pvt. Ltd., Mumbai, India.

Tetrabutylammonium bromide (TBAB) of pure grade was obtained as a gift sample from M/s. Dishman Pharmaceuticals and Chemicals Ltd., Ahmedabad, India. These were used as such without further purification.

Setup and Reaction Procedure. The reactions were studied in a 5.4 cm i.d. fully baffled mechanically agitated contactor of 150 cm^3 total capacity, which was equipped with a six-blade turbine-impeller and a reflux condenser. The reactor height was 8.7 cm and the clearance of the stirrer blade from the baffles was 1.8 cm. The reactor was kept in an isothermal bath whose temperature could be maintained at a desired value by using a temperature indicator controller.

The control experiment was conducted with 0.02 mol of *p*-chlorophenyl acetonitrile and 0.04 mol isopropyl bromide dissolved in toluene to make 25 cm^3 volume of organic phase. A known quantity of tetrabutylammonium bromide (TBAB) was added. Solid potassium hydroxide (KOH) pellets (0.02 mol) were added to the reaction mixture and the reaction temperature was maintained at 60 °C.

Method of Analysis. Samples of the organic phase were withdrawn periodically and analysed by gas chromatography [Chemito model 8510]. A 2.0 m × 3.2 mm i.d. stainless steel column packed with Chromosorb WHP, which was impregnated with 10% OV-17 was used for analysis in conjunction with a FID. Rates of reaction were calculated on the basis of the disappearance of *p*-chlorophenyl acetonitrile. Quantification of data was done through calibration by using synthetic mixtures.

The reaction products were confirmed by GC−MS analysis. The GC−MS data showed that the C-alkylation under S−L PTC conditions was highly selective towards the monoalkylated product, α-isopropyl-*p*-chlorophenyl acetonitrile. The other two minor products were identified as α,α′-diisopropyl-*p*-chlorophenyl acetonitrile and *p*-chlorobenzoic acid methylethyl ester. Neither isopropyl alcohol nor diisopropyl ether was detected in the reaction mixture.

Reaction Scheme. Scheme 1 depicts the products formed in the reaction under S−L PTC conditions, namely, α-isopropyl-*p*-chlorophenyl acetonitrile, α,α′-diisopropyl-*p*-chlorophenyl acetonitrile and *p*-chlorobenzoic acid methylethyl ester. In general, for C-alkylations under L−L conditions, the dialkylated product is formed in significant amounts and also hydrolysis of *p*-chlorophenyl acetonitrile occurs to give the corresponding amide or acid. However, in the current work on S−L PTC under controlled conditions the monoalkylated α-isopropyl-*p*-chlorophenyl acetonitrile was obtained as the major product and the dialkylated product was totally suppressed. Formation of *p*-chlorobenzoic acid methylethyl ester was observed unanticipatedly. For the control reaction,

Scheme 1. **Reaction scheme of solid−liquid phase transfer catalysed C-alkylation of *p*-chlorophenyl acetonitrile with isopropyl bromide under alkaline conditions**

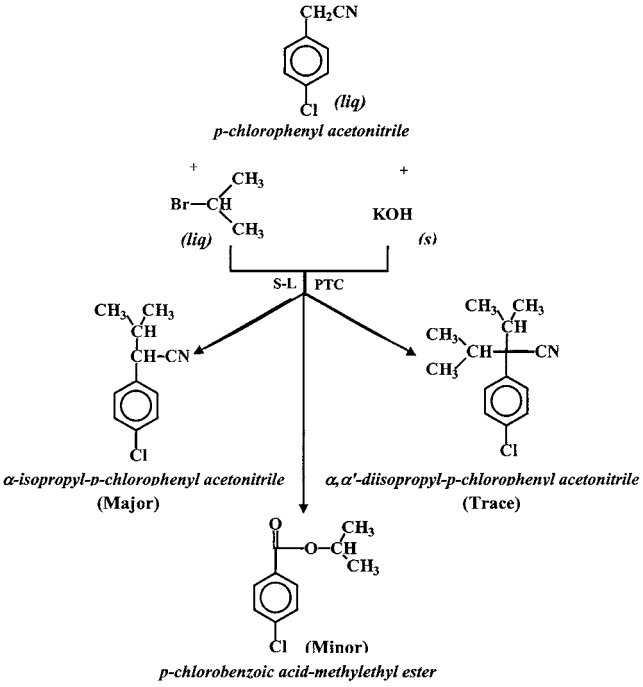

Table 1. **Control reaction**

Reaction Conditions	
p-chlorophenyl acetonitrile	0.02 mol
isopropyl bromide	0.04 mol
potassium hydroxide	0.02 mol
tetrabutylammonium bromide	0.002 mol
toluene	25 cm^3
temperature	60 °C
time	2 h
speed of agitation	1000 rpm

	Selectivity, %		
conversion %	monoalkylated	dialkylated	ester
45	84	−	16

as given in Table 1, at the end of 4 h, the monoalkylated product was detected in 84% selectivity and the residual 16% was the ester whereas there was no dialkylated product. Consequently, it is beneficial to conduct the C-alkylation under S−L PTC if the desired product is the monoalkylated α-isopropyl-*p*-chlorophenyl acetonitrile.

Confirmation of Formation of *p*-Chlorobenzoic Acid Methylethyl Ester. In the presence of atmospheric oxygen and under alkaline conditions, oxidative decyanation of *p*-chlorophenyl acetonitrile leads to the formation of the ester. This was confirmed by GC−MS. This was further established through independent experiments in which the reactions were conducted separately under oxygen and nitrogen blankets. Bubbling pure oxygen gas through the reaction mixture increased the formation of the ester (31% in 4 h). Conversely, when the reaction was conducted in an autoclave under nitrogen atmosphere, the ester was not at all detected in the reaction mixture. Thus, the formation of the ester indicates the necessity of rigorously excluding oxygen from the

reaction mixture, when other desired reactions are sought. However, since formation of the ester was a novel observation, it was decided to conduct the experiments under normal atmospheric conditions and observe the effect of varying parameters on the formation of the ester. A plausible mechanism is provided in what follows.

Reaction Mechanism

Although a wide variety of PTC reactions are conducted in the presence of a base, the mechanism of these reactions under S−L PTC conditions is obscure. PTC systems operate via different mechanisms in the presence of bases.[1] In L−L PTC reactions involving strong bases, it is believed that the mechanism involves extraction of hydroxide ion pair into the organic phase followed by deprotonation and alkylation of the substrate. However, the extraction of hydroxide is difficult because of its limited solubility and partitioning in the organic phase. Alkylation reactions have been proposed to be mediated through $[Q^+OH^-]$ intermediate and probably involve reaction between $[Q^+OH^-]$ and the organic substrate at the liquid−liquid interface in the case of L−L PTC and in the bulk organic phase after formation of $[Q^+OH^-]$ at the solid−liquid interface in the case of S−L PTC.

Presently, there is relatively little information available on alkylation by the S−L phase transfer method. S−L PTC reactions can follow two mechanisms based on the solubility of the solid in the organic phase and the location of the ion-exchange reaction, namely, *homogeneous* and *heterogeneous* solubilisation.[9]

One of the important aspects of S−L PTC systems is the role of trace quantities of water and its effect on the mechanism and kinetics of the PTC cycle. In most solid−liquid PTC/OH systems, water is always formed, and thus the formation a thin film aqueous phase, called the "omega (ω)-phase" is almost certain. In the present system, water is a byproduct of the reaction and it has to be deliberated in reference to the formation of ω-phase. Here the maximum quantity of water (15% w/w water content in solid KOH taken initially plus water generated in situ during the reaction considering maximum conversion of 45%) in the reaction mixture will be 0.65 cm^3. Considering the following calculations, it can be seen that a ω-phase of 0.4 mm thickness surrounds the KOH particle. Typical calculations are given below:

For solid KOH,

$$r_p = \text{average pellet radius} = 0.27 \text{ cm}$$

N = average number of pellets in 1.12 g KOH loading = 13. (The particles are not broken and remain as such during the course of reaction and shrink as the reaction proceeds. Hence the number of particles remain constant.)

Volume of water available for ω-phase = 0.65 cm^3.

$$4/3\ \pi\ N(r_{p+\omega}^3 - r_p^3) = 0.65$$

where $r_{p+\omega}$ = radius of particle + ω-phase. Therefore, $r_{p+\omega}$ = 0.31 cm. Hence, r_ω = 0.4 mm. This means that a ω-phase thickness of 0.4 mm is available, which shows that the reaction is indeed a solid−liquid PTC reaction with ω-phase.

Different observations have led to different theories, which explain the role of ω-phase in S−L system. A few papers have reported the increase in rates of the S−L PTC reaction with increasing amounts of water in the system.[10−11] A comprehensive discussion of the ω-phase theory in accordance with the S−(ω)−L PTC cyanide displacement of *p*-chlorobenzyl chloride has been published recently by us.[12] According to the ω-phase theory, trace quantities of water aid dissolution of the solid salt by forming a thin aqueous film (known as the ω-phase) around the solid particle. In S−L PTC, only minute quantities of the PT catalyst are present in the organic phase while most of it is translocated on the surface of the inorganic nucleophilic salt. Trace quantities of water facilitate interaction between the quat and the salt by breaking down the crystal lattice structure and thus augment the ion-exchange reaction which in turn enhances the reaction rates. On the basis of the ω-phase theory, a general mechanism for the S−(ω)−L reaction can be represented as shown in Scheme 2, which involves the dissolution of solid OH^- into the ω-phase followed by the anion-exchange reaction with the catalyst to form the active ion-pair Q^+OH^- which is then transferred to the organic phase where it can abstract a proton from the nitrile to form the active species $[RCH^-CNQ^+]$ which reacts with isopropyl bromide to give the monoalkylated product. Abstraction of another proton from the monoalkylated product and subsequent reaction with isopropyl halide leads to the formation of the dialkylated product. This is depicted in Scheme 3.

Most of the reports on phase transfer catalysed oxidative decyanation are in reference to the transformation of α-secondary nitriles to ketones and involve the use of strong bases and is proposed to proceed via formation of the 1-cyanoalkyl peroxide anion intermediate.[13−14] The mechanism of formation of *p*-chlorobenzoic acid methylethyl ester involves the abstraction of the proton from the nitrile followed by the oxidation of the resulting active species by molecular oxygen. The unstable peroxy species thus formed rapidly dissociates to *p*-chlorobenzoic acid and $[Q^+CN^-]$. The acid instantaneously reacts with isopropyl bromide to give *p*-chlorobenzoic acid methylethyl ester and HBr which reacts instantaneously with $[Q^+OH^-]$ to give $[Q^+OBr^-]$ and water. To support the proposed mechanism, a control reaction with *p*-chlorobenzoic acid and isopropyl bromide in the presence of an alkali under the reaction conditions was performed, and it was observed that the reaction does yield the ester quantitatively and that no other product was formed. Further, esterification of phenylacetic acid and derivatives under S−L PTC conditions using triethylbenzylammonium chloride and solid KOH is reported,[15−16] and these reports describe PTC esterification of carboxylic acid, C-alkylation,

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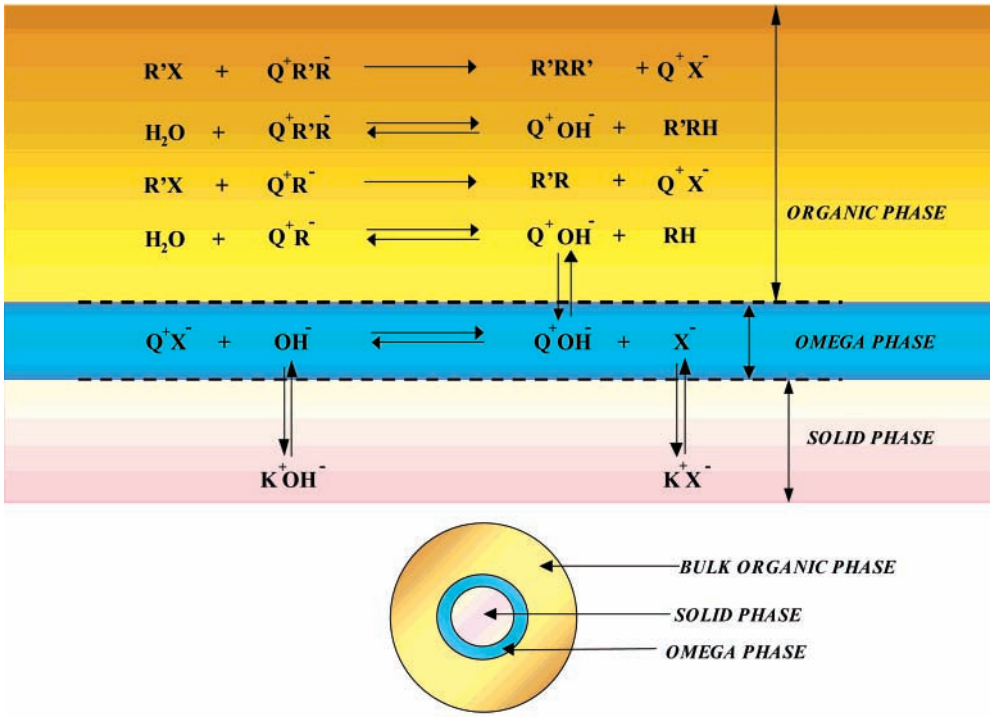
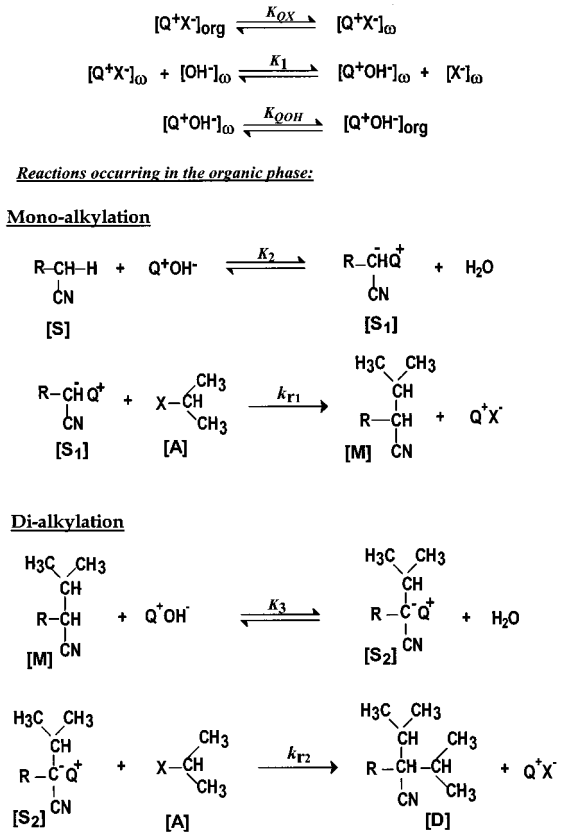
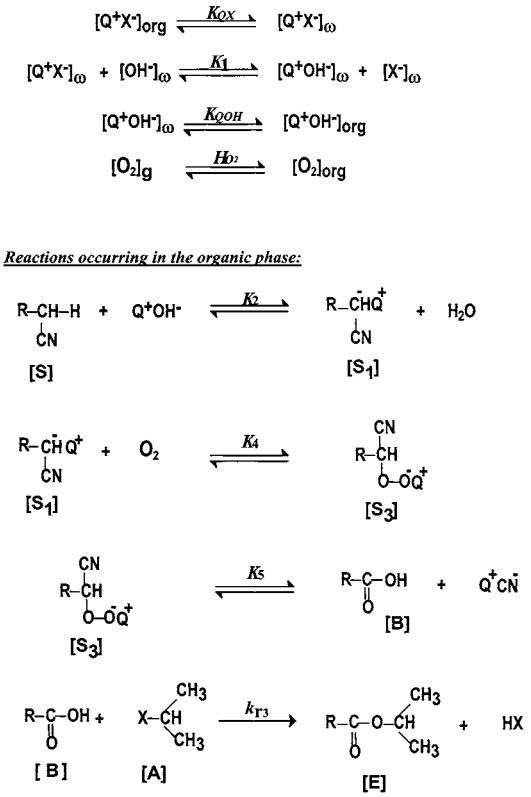
Scheme 2. **Mechanism of S−(*ω*)−L PTC C-alkylation of *p*-chlorophenyl acetonitrile**



Scheme 3. **Mechanism of solid−liquid phase transfer catalysed C-alkylation of *p*-chlorophenyl acetonitrile with isopropyl bromide**



Scheme 4. **Mechanism of solid−liquid phase transfer catalysed oxidative decyanation of *p*-chlorophenyl acetonitrile under alkaline conditions**



and hydrolysis all under S−L PTC conditions by using solid KOH. On the basis of the experimental observations and reported literature, the mechanism for oxidative decyanation of *p*-chlorophenyl acetonitrile under alkaline conditions is proposed and represented in Scheme 4.

Effect of Different Parameters

To validate the proposed mechanism, effects of various parameters on the rate of reaction were studied, and

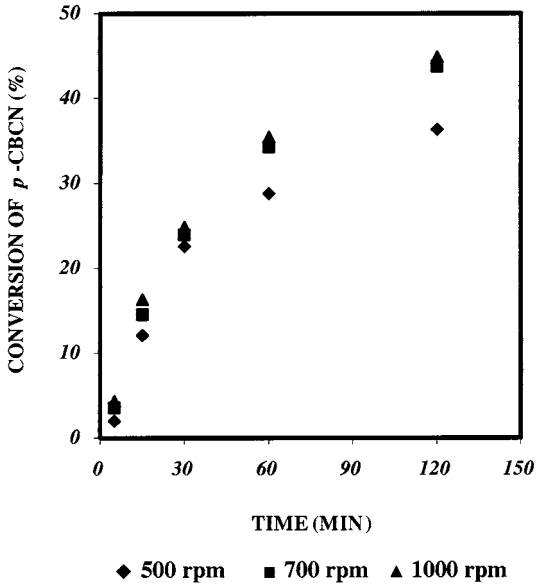


Figure 1. **Effect of speed of agitation.**

Table 2. **Effect of speed of agitation on selectivity[a]**

	Selectivity, %			
speed of agitation, rpm	conversion %	monoalkylated	dialkylated	ester
500	36	89	–	11
700	44	85	–	15
1000	45	84	–	16

[a] *p*-CBCN: 0.02 mol, IPB: 0.04 mol, KOH: 0.02 mol, TBAB: 0.002 mol, toluene: 25 cm^3, temperature: 60 °C.

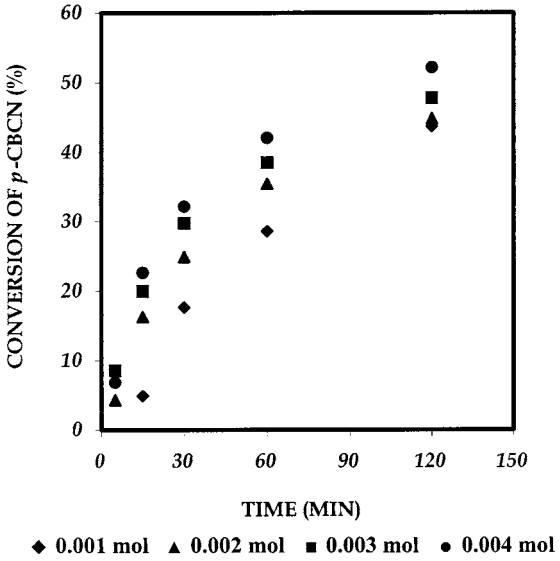


Figure 2. **Effect of catalyst concentration.**

Table 3. **Effect of catalyst concentration on selectivity[a]**

	Selectivity, %			
[TBAB] mol	conversion %	monoalkylated	dialkylated	ester
0.001	43	86	–	14
0.002	45	84	–	16
0.003	48	81	2	17
0.004	52	80	2	18

[a] *p*-CBCN: 0.02 mol, IPB: 0.04 mol, KOH: 0.02 mol, toluene: 25 cm^3, temperature: 60 °C, speed of agitation: 1000 rpm.

selectivity towards each product was calculated from the moles of product formed to the moles of reactant converted at the end of the reaction. All the reactions were conducted for a period of 120 min. A standard reaction was performed for 5 h, but it was observed that under standard reaction conditions, the reaction slowed considerably after 3 h. Also the standard reaction was a part of a more extensive research on cascade-engineered PTC reaction systems and hence was studied under the mentioned conditions with the formation of the ester being explored as an interesting outcome.

(a) Effect of Speed of Agitation. The theory of mass transfer with reaction for phase transfer catalysed reactions is discussed in our earlier paper on L−L PTC oxidation of benzyl chloride.[17] This theory is also applicable to S−L reactions. To ascertain the influence of external mass transfer resistance on the transfer of the reactants to the reaction phase, the speed of agitation was varied in the range of 500−1000 rev/min. As is seen from Figure 1, the conversion increases with an increase in speed of agitation from 500 to 700 rev/min. However, when the speed of agitation was increased from 700 to 1000 rev/min, the increase in conversion was marginal which suggests elimination of external resistance to mass transfer. All further experiments were conducted at 1000 rpm. The selectivity of various products at the end of 2 h of reaction is given in Table 2. It is obvious that the solid−(ω)−liquid mass transfer is very fast vis-à-vis the reaction in the organic phase.

(b) Effect of Catalyst Concentration. There was no reaction in the absence of PTC. The concentration of catalyst (TBAB) was varied from 0.001 to 0.004 mol, maintaining all other experimental conditions constant. Figure 2 shows the effect of catalyst loading on the conversion of *p*-chlorophenyl acetonitrile. As is typical for all PTC reactions, the conversion is found to increase with increasing catalyst loading but the increase is marginal. The selectivity towards C-alkylated product decreases and the formation of the ester increases with increasing catalyst concentration. The dialkylated product is formed in small amounts at higher concentrations of the PTC (Table 3).

(c) Effect of *p*-Chlorophenyl Acetonitrile Concentration. The concentration of *p*-chlorophenyl acetonitrile was varied from 4×10^{-4} to 1.2×10^{-3} mol/cm^3 organic phase at 60 °C. The conversion of *p*-chlorophenyl acetonitrile is plotted against time in Figure 3. The selectivity values at the end of 2 h of reaction shows that the C-alkylated product formation is favoured with increasing *p*-chlorophenyl acetonitrile concentration (Table 4).

(d) Effect of Solid Potassium Hydroxide Loading. Figure 4 shows the effect of increase in solid KOH loading on the conversion of *p*-chlorophenyl acetonitrile. The study was conducted over a range of 0.01−0.03 mol loading of solid KOH pellets. As the loading of solid alkali is increased, conversion increases drastically. This is because more and

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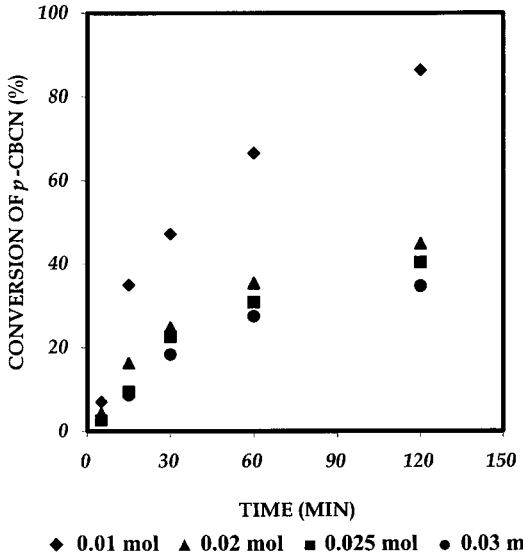

Figure 3. **Effect of *p*-CBCN concentration.**

Table 4. **Effect of *p*-CBCN on selectivity[a]**

[*p*-CBCN] mol	conversion %	Selectivity, % monoalkylated	dialkylated	ester
0.01	86	82	–	18
0.02	45	84	–	16
0.025	40	85	–	15
0.03	35	88	–	12

[a] IPB: 0.04 mol, KOH: 0.02 mol, TBAB: 0.002 mol, toluene: 25 cm^3, temperature: 60 °C, speed of agitation: 1000 rpm.

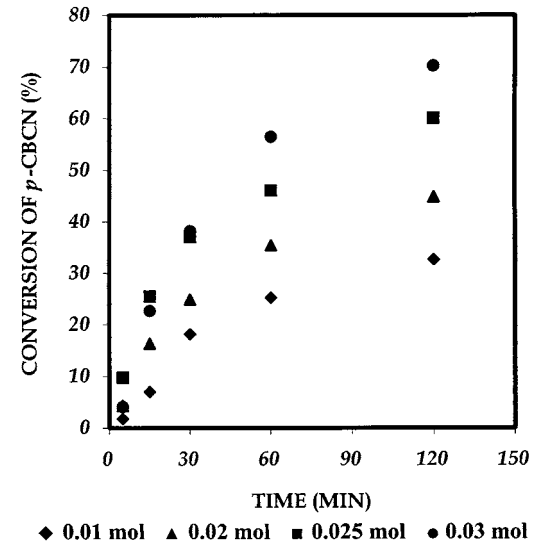

Figure 4. **Effect of solid KOH loading.**

more nucleophile in the [Q^+OH^-] form is available for proton abstraction. The selectivity of various products is not altered much except that the formation of dialkylated product is observed at higher alkali concentrations (Table 5).

(e) Effect of Isopropyl Bromide Concentration. The effect on conversion of increasing the concentration of isopropyl bromide is represented in Figure 5. There is a marginal increase in conversion from 41 to 54% as the moles of IPB are increased from 0.02 to 0.06 mol. Even though the quantity of IPB available for the reaction has become

Table 5. **Effect of solid KOH loading on selectivity[a]**

[KOH] mol	conversion %	Selectivity, % monoalkylated	dialkylated	ester
0.01	33	88	–	12
0.02	45	84	–	16
0.025	60	84	3	13
0.03	70	84	3	13

[a] *p*-CBCN: 0.02 mol, IPB: 0.04 mol, TBAB: 0.002 mol, toluene: 25 cm^3, temperature: 60 °C, speed of agitation: 1000 rpm.

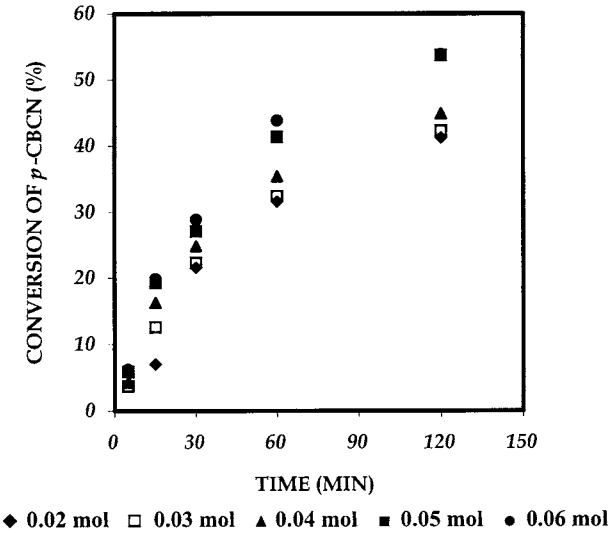

Figure 5. **Effect of Isopropyl bromide concentration.**

Table 6. **Effect of IPB concentration on selectivity[a]**

[IPB] mol	conversion %	Selectivity, % monoalkylated	dialkylated	ester
0.02	41	85	–	15
0.03	42	84	–	16
0.04	45	84	–	16
0.05	54	84	2	14
0.06	54	81	7	12

[a] *p*-CBCN: 0.02 mol, KOH: 0.02 mol, TBAB: 0.002 mol, toluene: 25 cm^3, temperature: 60 °C, speed of agitation: 1000 rpm.

greater, there is no corresponding increase in the amount of caustic available for deprotonation; hence, the increase in conversion is insignificant. For better conversion values, both the IPB and KOH concentrations have to be increased simultaneously. At higher IPB concentrations of 0.05 and 0.06 mol some of the monoalkylated product is further converted to dialkylated product. However, the change in selectivity is not very significant (Table 6).

(f) Effect of Increasing IPB and Solid KOH Concentration. Since increasing the strength of IPB and solid alkali individually did not have a substantial effect on conversion, it was decided to increase their loading simultaneously. Therefore, both IPB and KOH at equimolar concentrations were varied at 0.02, 0.03, 0.04, and 0.06 mol. As seen from Figure 6, it was observed that almost complete conversion could be achieved when the loading of IPB and KOH was in triple molar excess to *p*-chlorophenyl acetonitrile. The selectivity towards monoalkylated product, however, suffered

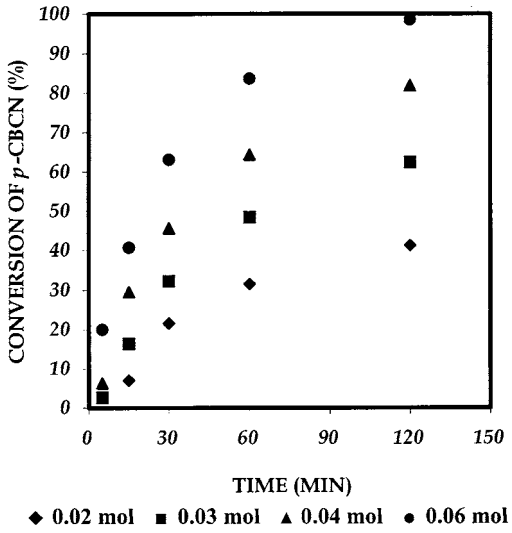

Figure 6. **Effect of varying IPB and KOH concentration.**

Table 7. **Effect of varying IPB and KOH concentration on selectivity[a]**

[IPB] and [KOH] mol	conversion %	Selectivity, % monoalkylated	dialkylated	ester
0.02	41	85	–	15
0.03	62	84	2	14
0.04	82	83	5	12
0.06	98	79	11	9

[a] *p*-CBCN: 0.02 mol, TBAB: 0.002 mol, toluene: 25 cm^3, temperature: 60 °C, speed of agitation: 1000 rpm.

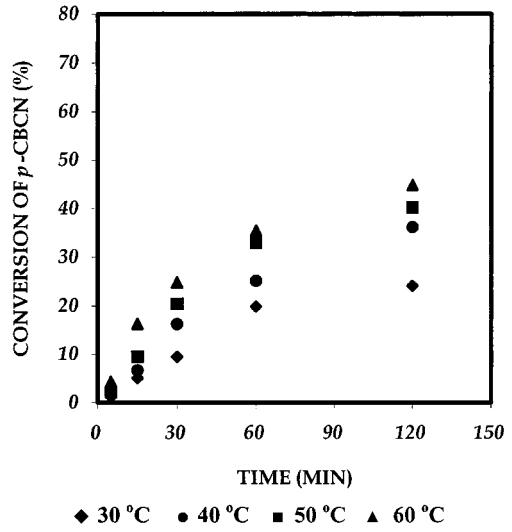

Figure 7. **Effect of temperature.**

at higher concentration of IPB and KOH. Table 7 depicts the selectivity of various products.

(g) Effect of Temperature. The effect of temperature on the rate of the reaction was studied in the range of 30−60 °C. The conversion of *p*-chlorophenyl acetonitrile was observed to increase with an increase in the reaction temperature (Figure 7). There was no significant change in selectivity of various products with increase in reaction temperature (Table 8). The energy of activation from the Arrhenius plot was calculated to be 6.82 kcal/mol (Figure 8). It is well-known that heterogeneous reactions with activation energy values lower than 4 kcal/mol are mass-transfer limited and systems above 6 kcal/mol are kinetically controlled. The current system is thus kinetically controlled.

Table 8. **Effect of temperature on selectivity[a]**

temperature °C	conversion %	Selectivity, % monoalkylated	dialkylated	ester
30	24	88	–	12
40	36	88	–	12
50	40	88	–	12
60	45	84	–	16

[a] *p*-CBCN: 0.02 mol, IPB: 0.04 mol, KOH: 0.02 mol, TBAB: 0.002 mol, toluene: 25 cm^3, speed of agitation: 1000 rpm.

Mathematical Modeling

The various steps involved in C-alkylation and oxidative decyanation of *p*-chlorophenyl acetonitrile can be represented as:

$$[Q^+X^-]_{org} \overset{K_{QX}}{\rightleftharpoons} [Q^+X^-]_\omega \quad (1)$$

$$[Q^+X^-]_\omega + [OH^-]_\omega \overset{K_1}{\rightleftharpoons} [Q^+OH^-]_\omega + [X^-]_\omega \quad (2)$$

$$[Q^+OH^-]_\omega \overset{K_{QOH}}{\rightleftharpoons} [Q^+OH^-]_{org} \quad (3)$$

$$O_{2(g)} \overset{H_{O_2}}{\rightleftharpoons} O_{2(org)} \quad (4)$$

In the above equation, $[O_2]_{org}$ is the solubility of oxygen in the organic phase. $[O_2]_{org}$ is approximately taken as 8.47×10^{-5} mol/cm^3 toluene at 90 °C which is a constant.[18] H_{O_2} is the Henry's law solubility constant for O_2.

Reactions Occurring in the Organic Phase:

$$S + QOH \overset{K_2}{\rightleftharpoons} S_1 + H_2O \quad (5)$$

$$S_1 + A \xrightarrow{k_{r_1}} M + QX \quad (6)$$

$$M + QOH \overset{K_3}{\rightleftharpoons} S_2 + H_2O \quad (7)$$

$$S_2 + A \xrightarrow{k_{r_2}} D + QX \quad (8)$$

$$S_1 + O_2 \overset{K_4}{\rightleftharpoons} S_3 \quad (9)$$

$$S_3 \xrightarrow{K_5} B + QCN \quad (10)$$

$$B + A \xrightarrow{k_{r_3}} E + HX \quad (11)$$

$$HX + [Q^+OH^-]_{org} \rightarrow [Q^+X^-]_{org} + H_2O \quad (11a)$$

$$[Q^+CN^-]_{org} \overset{K_{QCN}}{\rightleftharpoons} [Q^+CN^-]_\omega \quad (12)$$

$$[Q^+CN^-]_\omega + [OH^-]_\omega \xrightarrow{K_6} [Q^+OH^-]_\omega + [CN^-]_\omega \quad (13)$$

Derivation of the Rate Equation

On the basis of the proposed mechanism, the rate equation for the S−L PTC C-alkylation reaction can be derived.

(18) Green, D. W.; Maloney J. O. *Perry's Chemical Engineers' Handbook*; McGraw-Hill: New York, 1997

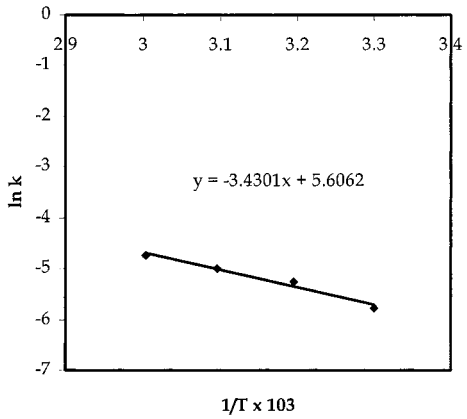

Figure 8. **Arrhenius plot.**

Rate of Formation of the Monoalkylated Product [M]:

$$r_M = \frac{d[M]_{org}}{dt} = k_{r_1}[S_1]_{org}[A]_{org} \quad (14)$$

From eq 5,

$$K_2 = \frac{[S_1]_{org}[H_2O]_{org}}{[S]_{org}[QOH]_{org}} \quad (15)$$

$$[S_1]_{org} = K_2\frac{[S]_{org}[QOH]_{org}}{[H_2O]_{org}} \quad (16)$$

Substituting in eq 14, we get

$$\frac{d[M]_{org}}{dt} = k_{r_1}K_2\frac{[A]_{org}[S]_{org}[QOH]_{org}}{[H_2O]_{org}} \quad (17)$$

From eq 2,

$$K_1 = \frac{[QOH]_\omega[X^-]_\omega}{[QX]_\omega[OH^-]_\omega} \quad (18)$$

$$[QOH]_\omega = K_1\frac{[QX]_\omega[OH^-]_\omega}{[X^-]_\omega} \quad (19)$$

from eq 3,

$$[QOH]_\omega = \frac{[QOH]_{org}}{K_{QOH}} \quad (20)$$

from eq 1,

$$[QX]_\omega = K_{QX}[QX]_{org} \quad (21)$$

By substituting eqs 20 and 21 in eq 19, the following is obtained

$$[QOH]_{org} = K_1K_{QOH}K_{QX}\frac{[QX]_{org}[OH^-]_\omega}{[X^-]_\omega} \quad (22)$$

Substituting for $[QOH]_{org}$ in eq 17, we get

$$r_M = \frac{d[M]_{org}}{dt} = k_{r_1}K_1K_2K_{QOH}K_{QX}\frac{[A]_{org}[S]_{org}[QX]_{org}[OH^-]_\omega}{[X^-]_\omega[H_2O]_{org}} \quad (23)$$

Thus, the final rate equation for the monoalkylated product, α-isopropyl-*p*-chlorophenyl acetonitrile [M] can be given as:

$$r_M = \frac{d[M]_{org}}{dt} = k_M\frac{[A]_{org}[S]_{org}[QX]_{org}[OH^-]_\omega}{[X^-]_\omega[H_2O]_{org}} \quad (24)$$

where $k_M = k_{r_1}K_1K_2K_{QOH}K_{QX}$, pseudorate constant. Similarly, for the dialkylated product, α,α′-diisopropyl-*p*-chlorophenyl acetonitrile [D], the rate equation can be given as:

$$r_D = \frac{d[D]_{org}}{dt} = k_{r_2}K_1K_3K_{QOH}K_{QX}\frac{[A]_{org}[M]_{org}[QX]_{org}[OH^-]_\omega}{[X^-]_\omega[H_2O]_{org}} \quad (25)$$

$$r_D = \frac{d[D]_{org}}{dt} = k_D\frac{[A]_{org}[M]_{org}[QX]_{org}[OH^-]_\omega}{[X^-]_\omega[H_2O]_{org}} \quad (26)$$

where $k_D = k_{r_2}K_1K_3K_{QOH}K_{QX}$, pseudorate constant.

Rate of Consumption of Isopropyl Bromide [A]:

$$-r_A = -\frac{d[A]_{org}}{dt} = [A]_{org}\{k_{r_1}[S_1]_{org} + k_{r_2}[S_2]_{org} + k_{r_3}[B]_{org}\} \quad (27)$$

From eq 5,

$$[S_1]_{org} = K_2\frac{[S]_{org}[QOH]_{org}}{[H_2O]_{org}}$$

From eq 7,

$$[S_2]_{org} = K_3\frac{[M]_{org}[QOH]_{org}}{[H_2O]_{org}}$$

Substituting for $[S_1]_{org}$ and $[S_2]_{org}$ in eq 27,

$$-r_A = -\frac{d[A]_{org}}{dt} = [A]_{org}[QOH]_{org}\left\{k_{r_1}K_2\frac{[S]_{org}}{[H_2O]_{org}} + k_{r_2}K_3\frac{[M]_{org}}{[H_2O]_{org}} + k_{r_3}\frac{[B]_{org}}{[QOH]_{org}}\right\} \quad (28)$$

Substituting for $[QOH]_{org}$ from eq 22, eq 28 leads to the following:

$$-r_A = -\frac{d[A]_{org}}{dt}$$

$$= K_1K_{QOH}K_{QX}\frac{[A]_{org}[QX]_{org}[OH^-]_\omega}{[X^-]_\omega}\left\{k_{r_1}K_2\frac{[S]_{org}}{[H_2O]_{org}} + k_{r_2}K_3\frac{[M]_{org}}{[H_2O]_{org}} + K_1K_{QOH}K_{QX}k_{r_3}\frac{[B]_{org}[X^-]_\omega}{[QX]_{org}[OH^-]_\omega}\right\} \quad (29)$$

$$-r_A = -\frac{d[A]_{org}}{dt} = K_a\frac{[A]_{org}[QX]_{org}[OH^-]_\omega}{[X^-]_\omega}\left\{K_b\frac{[S]_{org}}{[H_2O]_{org}} + K_c\frac{[M]_{org}}{[H_2O]_{org}} + K_d\frac{[B]_{org}[X^-]_\omega}{[QX]_{org}[OH^-]_\omega}\right\} \quad (30)$$

where $K_a = K_1K_{QOH}K_{QX}$, $K_b = k_{r_1}K_2$, $K_c = k_{r_2}K_3$ and $K_d = K_1K_{QOH}K_{QX}k_{r_3}$.

Table 9. **Rate equations used for numerical solution for C-alkylation**

equation	equation no.
rate of formation of monoalkylated product [M]:	
$$r_M = \frac{d[M]_{org}}{dt} = k_M \frac{[A]_{org}[S]_{org}[QX]_{org}[OH^-]_\omega}{[X^-]_\omega[H_2O]_{org}}$$	24
rate of formation of dialkylated product [D]:	
$$r_D = \frac{d[D]_{org}}{dt} = k_D \frac{[A]_{org}[M]_{org}[QX]_{org}[OH^-]_\omega}{[X^-]_\omega[H_2O]_{org}}$$	26
rate of consumption of isopropyl bromide [A]:	
$$-r_A = -\frac{d[A]_{org}}{dt} = K_a \frac{[A]_{org}[QX]_{org}[OH^-]_\omega}{[X^-]_\omega}\left\{K_b\frac{[S]_{org}}{[H_2O]_{org}} + K_c\frac{[M]_{org}}{[H_2O]_{org}} + K_d\frac{[B]_{org}[X^-]_\omega}{[QX]_{org}[OH^-]_\omega}\right\}$$	30
rate of formation of *p*-chlorobenzoic acid methylethyl ester [E]:	
$$r_E = \frac{d[E]_{org}}{dt} = k_E \frac{[A]_{org}[O_2]_{org}[S]_{org}[QX]_{org}[OH^-]_\omega}{[H_2O]_{org}[X^-]_\omega\,[QCN]_{org}}$$	35
rate of consumption of *p*-chlorophenyl acetonitrile [S]:	
$$-\frac{d[S]_{org}}{dt} = K_2[S]_{org}[QOH]_{org}$$	36

Rate of Formation of *p*-Chlorobenzoic Acid Methylethyl Ester [E]:

$$r_E = \frac{d[E]_{org}}{dt} = k_{r_3}[B]_{org}[A]_{org} \tag{31}$$

From eq 10,

$$K_5 = \frac{[B]_{org}[QCN]_{org}}{[S_3]_{org}}$$

$$[B]_{org} = K_5\frac{[S_3]_{org}}{[QCN]_{org}} \tag{32}$$

From eq 9,

$$K_4 = \frac{[S_3]_{org}}{[S_1]_{org}[O_2]_{org}}$$

$$[S_3]_{org} = K_4\,[S_1]_{org}[O_2]_{org}$$

Substituting in eq 32, we get

$$[B]_{org} = K_4\,K_5\frac{[S_1]_{org}[O_2]_{org}}{[QCN]_{org}} \tag{33}$$

$$K_2 = \frac{[S_1]_{org}[H_2O]_{org}}{[S]_{org}[QOH]_{org}}$$

$$[S_1]_{org} = K_2\frac{[S]_{org}[QOH]_{org}}{[H_2O]_{org}}$$

Again,

$$[QOH]_{org} = K_1K_{QOH}K_{QX}\frac{[QX]_{org}[OH^-]_\omega}{[X^-]_\omega}$$

$$[S_1]_{org} = K_1K_2K_{QOH}K_{QX}\frac{[S]_{org}[QX]_{org}[OH^-]_\omega}{[H_2O]_{org}[X^-]_\omega}$$

Substituting the above in eq 33, the following is obtained:

$$[B]_{org} = K_1K_2K_{QOH}K_{QX}K_4K_5\frac{[O_2]_{org}[S]_{org}[QX]_{org}[OH^-]_\omega}{[H_2O]_{org}[X^-]_\omega[QCN]_{org}}$$

$$[B]_{org} = K_C\frac{[O_2]_{org}[S]_{org}[QX]_{org}[OH^-]_\omega}{[H_2O]_{org}[X^-]_\omega[QCN]_{org}} \tag{34}$$

where $K_C = K_1K_2K_{QOH}K_{QX}K_4K_5$.

Substituting the above in eq 31 leads to

$$r_E = \frac{d[E]_{org}}{dt} = k_{r_3}K_C\frac{[A]_{org}[O_2]_{org}[S]_{org}[QX]_{org}[OH^-]_\omega}{[H_2O]_{org}[X^-]_\omega[QCN]_{org}}$$

$$r_E = \frac{d[E]_{org}}{dt} = k_E\frac{[A]_{org}[O_2]_{org}[S]_{org}[QX]_{org}[OH^-]_\omega}{[H_2O]_{org}[X^-]_\omega[QCN]_{org}} \tag{35}$$

where $k_E = k_{r3}K_C$ = pseudorate constant.

Rate of Consumption of *p*-Chlorophenyl Acetonitrile [S]:

$$-\frac{d[S]_{org}}{dt} = K_2\,[S]_{org}[QOH]_{org} \tag{36}$$

Now, the various equations as given in Table 9 can be solved to get the concentration profiles of individual species. The profiles of A, M, D, E, and S are interrelated, and the pertinent equations can be solved simultaneously. Owing to their complex nature, these equations cannot be analytically solved; hence, a numerical method was employed.

The values of various rate constants and distribution coefficients were calculated with a numerical computing program that uses Euler's method.[19] The basic concept for Euler's method is to add small increments to the given functions corresponding to derivatives multiplied by step

(19) Press, W. H.; Teukolsky, S. A.; Vetterling, W. T.; Flannery, B. P. *Numerical Recipes in C*; Cambridge University Press: New York, 1992.

Table 10. **Values of pseudorate constants by Euler's method**

parameter studied	concentration mol	K_2	k_M cm^3/mol·s	K_a cm^3/mol·s	K_b	k_E cm^3/mol·s	k_D cm^3/mol·s	K_c
			p-CBCN					
	0.02	4.98×10^{-3}	27	2	38	2	–	–
	0.025	4.26×10^{-3}	25	2	35	2	–	–
	0.03	3.6×10^{-3}	23.2	2	32.5	2	–	–
			IPB					
	0.03	4.56×10^{-3}	33	2	38	2	–	–
	0.05	6.48×10^{-3}	23	2	20	2	18	23
	0.06	6.48×10^{-3}	20	2	20	1	4.8	23
average values		$\mathbf{5.058 \times 10^{-3}}$	**25.2**	**2**	**30.58**	**1.83**	**11.4**	**23**

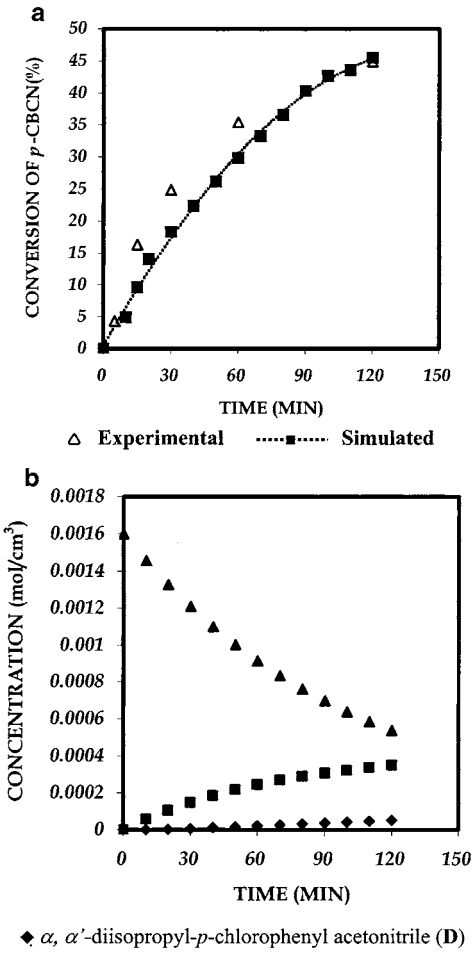

Figure 9. **(a) Conversion profile for simulated and experimental results. (b) Concentration profile resulting from numerical analysis.**

sizes. The formula for Euler's method is

$$y_{n+1} = y_n + hf(x_n,y_n) \tag{37}$$

where y_{n+1} is the increment in y_n corresponding to an increment of h in x_n.

The formula is unsymmetrical. It advances the solution through an interval h but uses derivative information only at the beginning of that interval. This means that the steps error is only one power of h smaller than the correction. This method was selected because of its simplicity and accuracy to solve simple differential equations.

The known values of initial concentrations of each species were used as input, and the above equations were defined as functions. The values of various pseudorate constants and equilibrium constants for varying *p*-CBCN and IPB concentrations were calculated independently and are summarised in Table 10. The relative error was found to be negligible. It can be seen from Figure 9a, that the simulated conversion profile of *p*-chlorophenyl acetonitrile matches with the experimental curve within the range of reasonable accuracy. The concentration profiles of each species obtained from numerical analysis are shown in Figure 9b.

Conclusions

The alkylation of *p*-chlorophenyl acetonitrile with isopropyl bromide under solid−liquid phase transfer conditions is an enticing system from the mechanistic perspective. The C-alkylation reaction is accompanied by oxidative decyanation of the nitrile, resulting in the generation of *p*-chlorobenzoic acid methylethyl ester as the byproduct. The monoalkylated compound is the major product, and the dialkylated product results only at higher concentrations of catalyst, alkali, and alkylating agent. The reaction following S−L numerical analysis was performed using Euler's method to get the values of various rate constants, equilibrium constants, and the concentration profile of each species.

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NOMENCLATURE

K_1	Equilibrium constant for anion-exchange reaction in the ω-phase, dimensionless
K_{QOH}	Distribution coefficient of Q^+OH^- between ω and organic phase, dimensionless
K_{QX}	Distribution coefficient of Q^+X^- between ω and organic phase, dimensionless
K_{QCN}	Distribution coefficient of Q^+CN^- between ω and organic phase, dimensionless

k_{r_1} Rate constant for formation of α-isopropyl-*p*-chlorophenylacetonitrile in organic phase, $cm^3/mol \cdot s$

k_{r_2} Rate constant for formation of α,α′-diisopropyl-*p*-chlorophenyl acetonitrile in organic phase, $cm^3/mol \cdot s$

k_{r_3} Rate constant for formation of *p*-chlorobenzoic acid methylethyl ester in organic phase, $cm^3/mol \cdot s$

$[OH^-]_\omega$ Concentration of OH^- in ω-phase, mol/cm^3

$[QX]_{org}$ Concentration of QX in organic phase, mol/cm^3

$[QX]_\omega$ Concentration of QX in ω-phase, mol/cm^3

$[QOH]_{org}$ Concentration of QOH in organic phase, mol/cm^3

$[QOH]_\omega$ Concentration of QOH in ω-phase, mol/cm^3

$[X^-]_\omega$ Moles of X^- in ω-phase, mol/cm^3

$[A]_{org}$ Concentration of isopropyl bromide in organic phase, mol/cm^3

$[S]_{org}$ Concentration of *p*-chlorophenylacetonitrile in organic phase, mol/cm^3

$[H_2O]_{org}$ Concentration of H_2O in organic phase, mol/cm^3 of organic phase

$[M]_{org}$ Concentration of α-isopropyl-*p*-chlorophenylacetonitrile in organic phase, mol/cm^3

$[D]_{org}$ Concentration of α,α′-diisopropyl-*p*-chlorophenylacetonitrile in organic phase, mol/cm^3

$[E]_{org}$ Concentration of *p*-chlorobenzoic acid methylethyl ester in organic phase, mol/cm^3

r_M Rate of formation of α-isopropyl-*p*-chlorophenylacetonitrile, $cm^3/mol \cdot s$

r_D Rate of formation of α,α′-diisopropyl-*p*-chlorophenylacetonitrile in organic phase, $cm^3/mol \cdot s$

r_E Rate of formation of *p*-chlorobenzoic acid methylethyl ester in organic phase, $cm^3/mol \cdot s$

r_A Rate of consumption of isopropyl bromide, $cm^3/mol \cdot s$

k_D Pseudorate constant, $cm^3/mol \cdot s$

k_M Pseudorate constant, $cm^3/mol \cdot s$

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