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Synthesis and characterization of novel multi-site phase transfer catalyst and its catalytic efficiency for dichlorocarbene addition to citral

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Abstract

Novel soluble multi-site phase transfer catalyst was synthesized from low cost starting materials and its catalytic efficiency is assessed by observing the kinetics of dichlorocarbene addition to citral in the absence of solvents. This new synthesized phase transfer catalyst viz., 1,3,5-tris[4-{2,3-bis(triethylammoniummethylene chloride)}-phenoxymethyl]benzene possesses six active centers. This novel catalyst has higher activity than the commercially available single-site phase transfer catalysts. The dichlorocarbene addition to citral reaction was carried out at low temperature (40 °C) under pseudo-first order conditions by keeping low concentration of aqueous sodium hydroxide and excess of chloroform and the disappearance of citral were monitored by gas chromatography. The effect of various experimental parameters such as [substrate], [catalyst], [aqueous NaOH], stirring speed and temperature on the rate of the reaction has been studied, and based on the kinetic results obtained, a plausible mechanism is proposed.

Keywords: Phase transfer catalyst; Dichlorocarbene; Citral; Multi-site; Interfacial mechanism; Dihalocyclopropane

1. Introduction

Phase transfer catalysis (PTC) is now recognized as a general and versatile technique applicable to a variety of organic reactions [1,2]. PTC was little more than a curiosity in the late 1960s when Makosza first published his biphase method for the generation of dichlorocarbene [3]. PTC method has a very broad scope of application. Chemically, the possibilities include the separation of compounds from an unreactive or unstable starting material and more generally the increase of yields or selectivities in a large number of syntheses. The "single-site" PTCs viz., quaternary phosphonium and ammonium salts, crown ethers, cryptands, etc., are immensely popular due to their availability and easy reaction work-up. The important considerations in the selection of the catalyst are economy of scale and efficiency of the PTC, specifically on the industrial-scale preparation of organic compounds. In order to cater to these needs, "multi-site" phase transfer catalysts (MPTC) have been developed. In general, MPTCs have more potential of offering greater PTC activity and to effect a particular synthetic transformation under mild reaction conditions. Idoux et al. [4] first reported the soluble and insoluble phosphonium ion containing MPTCs, which have only three active sites. Recently, Balakrishnan and Jeyachandran [5] also reported a quaternary ammonium ion containing two active sites. Benaglia et al. [6] have reported poly(ethylene glycol) supported quaternary ammonium catalyst recyclable in nature. The efficiency of the catalytic abilities of these MPTCs towards simple S_N2 reactions and some weak nucleophilic–electrophilic S_NAr reactions were reported. Wang and Hsieh [7] have reported the dihalocyclopropanation of 4-vinyl-1-cyclohexene in the presence of a novel soluble two-site PTC catalyst. Recently, dimeric [8–11], trimeric [12] and dendritic [13] chiral quaternary ammonium catalysts were synthesized from *o*-, *m*- or *p*-xylene dibromide, bis(bromomethyl)naphthalenes, 9,10-di(chloromethyl)anthracene, mesitylene tribromide

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and 3,5-dihydroxabenzylbromide, respectively. These CPTCs have been employed for C-alkylation of *N*-(diphenylmethylene)glycine *tert*-butyl ester to result in higher chemical yields and ee's.

Dihalocyclopropanation was previously a difficult reaction to conduct, and so the ease and economy of the new method attracted a broad interest in the organic chemical community. Dihalocyclopropanes are intermediate compounds for the synthesis of cyclopropane derivatives and other pharmaceutically valuable products [14]. Normally, halocarbene undergoes hydrolysis easily in the presence of water; hence, vigorous anhydrous conditions are required for its synthesis. These difficulties are eliminated when the synthesis of cyclopropane reactions are carried out in biphasic systems of concentrated sodium hydroxide in the presence of single-site PTCs and quaternary ammonium MPTCs that are more effective. There are numerous reports for the dichlorocarbene addition to various olefins using single-site PTCs [15–19].

By considering all the above-mentioned points, we have decided to synthesize a novel multi-site phase transfer catalyst containing the maximum number of possible active sites equaling six. For the first time, we have synthesized a new "1,3,5-tris[4-(2,3-bis(triethylammoniummethylene chloride)-phenoxymethyl)benzene" (TEAMCPB) as MPTC by a simple synthetic method using inexpensive starting materials. The product obtained at each step has been characterized by FT-IR, ^{1}H NMR, ^{13}C NMR and mass analysis. Furthermore, the amount of chloride ion present in the MPT catalyst was estimated by the Volhard method [20]. The efficiency of the TEAMCPB catalyst was elucidated by the addition of dichlorocarbene to citral under pseudo-first order condition. The kinetics of this reaction was studied and based on the obtained kinetic results a plausible mechanism has been proposed and also the catalytic efficiencies of the MPTC is compared with the commercially available single-site PTCs.

2. Experimental section

2.1. Synthesis of 1,3,5-tribromomesitylene (*2*)

Mesitylene (10 ml, 72.0 mmol), 2.5 equivalent of *N*-bromosuccinamide (44.8 g, 252 mmol) and catalytic amount of benzoyl peroxide (8.75 g, 36.0 mmol) and CCl_4 (100 ml) were taken in a 150 ml RB flask. The reaction mixture was refluxed for 6 h at 70 °C. After completion reaction time, the formation of imide was removed by filtration and the solvent was eliminated from the filtrate by distillation to give the pale yellow solid of 1,3,5-tribromomesitylene. Yield is 96%.

FT-IR (KBr) cm^{-1}: 584 (C–Br), 1618 (C=C); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 4.34 (s, 6H, methylene), 6.78 (s, 3H, aromatic); *m*/*e* [M^+] 353.45 (100%), 261.9 (22%), 169.25 (18%), 77.67 (36%).

2.2. Preparation of 1,3,5-tris[4-(2,3-dimethyl-phenoxymethyl)]benzene (*3*)

1,3,5-Tribromomesitylene **2** (5 g, 14.0 mmol), 3,5-dimethylphenol (5.13 g, 42.0 mmol), methanol (50 ml) and NaOH (0.5 g, 42.0 mmol) were taken in a 150 ml round bottom flask. The reaction mixture was refluxed in an oil bath at 70 °C for 12 h. Then the solvent was removed from the reaction mixture by vacuum distillation. The crude product of 1,3,5-tris[4-(2,3-dimethylphenoxymethyl)]benzene **3**. The crude product of **3** was purified silica gel column chromatography using benzene:ethyl acetate (80:20, v/v). The yield is 92%, mp 134–135 °C.

FT-IR: KBr (cm^{-1}): 1218 (C–O), 1623 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.3 (s, 18H, methyl), 5.23 (s, 6H, phenoxy methylene), 6.38 (s, 6H, phenoxy aromatic), 6.44 (s, 3H, phenoxy aromatic), 7.07 (s, 3H, mesityl aromatic); ^{13}C NMR (75 MHz): 21.4, 78.5, 111.7, 122.4, 125.6, 138.7, 142.2, 164.3; *m*/*e* EI-S [M^+] = 480.34.

2.3. Synthesis of 1,3,5-tris[4-(2,3-bis-chloromethyl) phenoxymethyl]benzene (*4*)

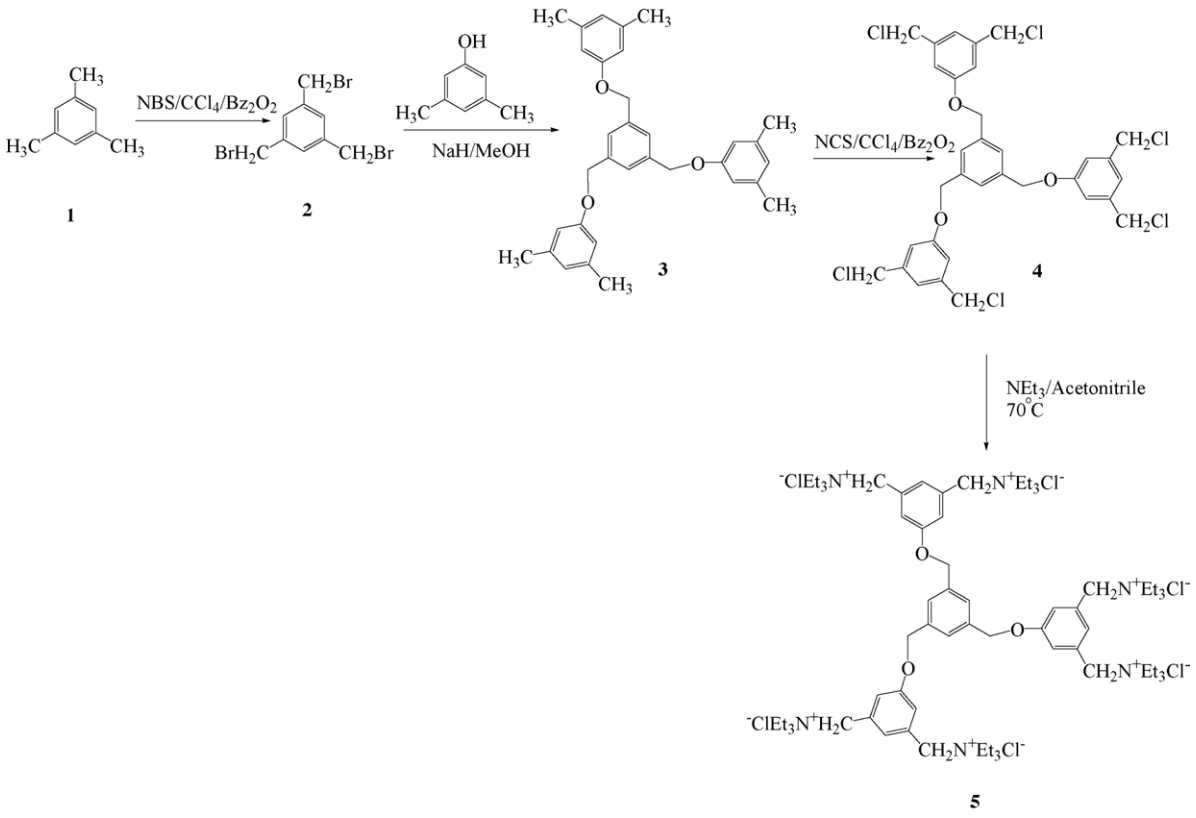
1,3,5-Tris[4-(2,3-dimethylphenoxymethyl)]benzene **3** (3.50 g, 7.28 mmol), *N*-chlorosuccinamide (7.12 g, 47.3 mmol), benzoyl peroxide (8.13 g, 33.5 mmol) and CCl_4 (60 ml) were taken in a 150 ml round bottom flask. The reaction mixture was refluxed for 6 h at 70 °C. After completion of reaction time, the formation of imide from the reaction mixture was removed by filtration and the filtrate containing CCl_4 solvent was eliminated by vacuum distillation. The yellow coloured chlorinated compound **4** was obtained in 87% yield, mp 47–148 °C.

FT-IR (KBr pellet) (cm^{-1}): 722 (C–Cl), 1027 (C–O), 1620 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.34 (s, 12H, methylene), 5.27 (s, 6H, phenoxy methylene), 6.57 (s, 6H, phenoxy aromatic), 6.68 (s, 3H, phenoxy aromatic), 7.33 (s, 3H, mesitylene aromatic); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 54.4, 72.2, 110.3, 121.1, 124.0, 138.4, 145.2, 162.7; *m*/*e* EI-MS [M^+] 680.24.

2.4. 1,3,5-Tris[4-{2,3-bis(triethylammoniummethylene chloride)}- phenoxymethyl]benzene(TEAMCPB)(*5*)

1,3,5-Tris[4-(2,3-bis-chloromethyl)phenoxymethyl]benzene **4** (2.50 g, 3.63 mmol) was quaternised in an inert atmosphere (N_2) with excess of triethylamine (25 ml) in the presence of acetonitrile (50 ml) for 12 h at 70 °C. Then the solvent was removed from the reaction mixture by vacuum distillation and the crude product of quaternised compound **5** was washed with *n*-hexane (3 × 10 ml). Further it was purified by silica gel column chromatography using benzene:methanol (70:30, v/v) as an eluent. The obtained yield is 86%. (Scheme 1).

FT-IR (KBr pellet) (cm^{-1}): 1015 (C–O), 1020 (C–N), 1110 (N^+CH_2), 1620 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$)



Scheme 1. A schematic diagram for the synthesis of MPT catalyst.

δ: 1.25–1.28(t, 54H, J = 4.8 Hz, $-N^+CH_2$-methyl), 3.28–3.34 (q, 36H, N^+-methylene), 3.91–3.94 (s, 12H, methylene-N^+-), 5.22 (s, 6H, phenoxy methylene), 6.13 (s, 6H, phenoxy aromatic) 6.30 (s, 3H, phenoxy aromatic), 7.54 (s, 3H, mesitylene aromatic); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 7.3, 52.3, 60.5, 85.6, 115.8, 120.5, 126.4, 137.8, 140.1, 164.3; $C_{69}H_{1201}Cl_6N_6O_3$; HRMS (EI) [M^{6+}]1078.2, Anal. Calc. C 64.02, H 9.34, N 6.49; found: C 63.12, H 8.85, N 5.89; [Cl^-] = 14.55% (Volhard method).

2.5. Typical kinetic measurements

The kinetic experiments were performed in a 150 ml two-necked flask fitted with flat-bladed stirring paddle and the reaction viz., addition of dichlorocarbene to citral was carried out by the reverse addition methods (i.e. late addition of citral) using TEAMCPB as MPTC. The substrate citral (2 ml), aqueous NaOH 15% (w/w) (20 ml), hexadecane (1 ml) and catalyst (3.0×10^{-4} mmol) were taken and stirred at 200 rpm for 5 min at 40 °C to stabilize the catalyst and substrate. Then the stirring speed was increased to 800 rpm and 20 ml of chloroform was added to the reaction mixture at zero time. Samples were collected from the organic layer of the mixture (by stopping the stirring for 10–15 s in each time) at regular intervals. The kinetics of the reaction was studied by determining the amount of citral consumed using a gas chromatograph. The column (5% SE-30 chrom WHP 80/100, 3 m × 1/8 in. stainless steel packed column) was maintained at 190 °C. For every sample 0.5 μl of reaction mixture was injected to the column and the products were analysed; the retention time was monitored at [citral (3.56 min), chloroform (0.71 min), mono dihalocyclopropane product (2.37 min) and bis addition of dihalocyclopropane derivative (3.12 min)]. The pseudo-first order rate constants were evaluated from the plots of $\log(a - x)$ versus time. In order to isolate the product from the cold reaction mixture, 50 ml of ether was added to it, the ethereal layer was decanted using a separating funnel, and the compound was further purified using silica gel column chromatography using benzene and ethylacetate (20:80, v/v) as a solvent. The spectral data for all the dihalo derivatives were collected by FT-IR, ^{1}H NMR and ^{13}C NMR and mass spectral analyses.

2.5.1. 2,2-Dichloro-3-methyl-3-(4-methyl-pent-3-enyl) cyclopropanecarbaldehyde (7)

FT-IR (KBr pellet) (cm^{-1}): 725 (C–Cl), 1697 (C=O), 3080 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.14 (s, 3H, methyl), 1.25–1.28 (t, 2H, J = 7.6 Hz, methylene), 1.71–1.74 (m, 6H, methyl), 1.96–1.98(q, 2H, methylene), 5.20–5.24 (m, 1H, methyne), 9.56 (s, 1H, −aldehyde); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16, 19.3, 25.3, 20.2, 32.1, 32.7, 53.7, 70.3, 125.6, 133.6, 203.2; EI-MS [M^+] = 234.06

*2.5.2. 2,2-Dichloro-3-[2-(2,2-dichloro-3,3-dimethylcyclopropyl)-ethyl]-3-methyl-cyclopropanecarbaldehyde (**8**)*

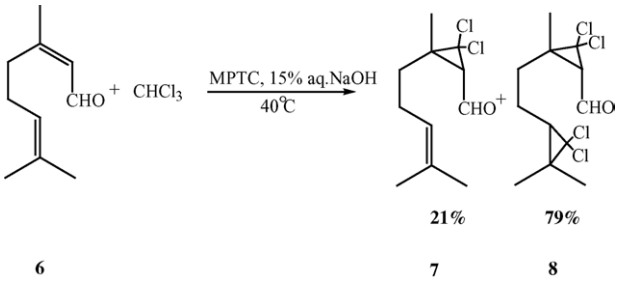
FT-IR (KBr pellet) (cm^{-1}): 727 (C–Cl), 1680 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.12(s, 6H, methyl), 1.19 (s, 3H, –methyl), 1.21–1.27 (t, 2H, J = 7.2 Hz, methylene), 1.29–1.36 (m, 2H, methylene), 1.66–1.73(m, 1H, vinyl), 9.76 (s, 1H, aldehyde); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.2, 17.8, 19.5, 26.6, 29.2, 32.3, 40.7, 53.8, 70.8, 203.3; EI-MS [M^+] = 316.01.

3. Results and discussion

The kinetic experiment of dichlorocarbene addition to citral **6** was conducted under pseudo-first order conditions with excess of 15% (w/w) aqueous sodium hydroxide and chloroform (Scheme 2). The reaction was studied at a stirring speed of 800 rpm, at 40 °C.

3.1. Effect of stirring speed

The effect of stirring speed on the reaction using MPTC was studied in the range of 100–1200 rpm. The rate of the reaction was increased on increasing the stirring speed. The effect of varying stirring speed is well documented [1,19,21]; interfacial mechanisms are proposed, which are transfer rate limited (the rate constant increase with increasing stirring speed from 100 to 700 rpm) and there is a sharp increase in rate constant at 700–800 rpm. Furthermore, there is no significant influence in the rate of the dichlorocarbene addition reaction with increase in stirring speed above 800–1200 rpm (Fig. 1). Starks et al. [2] reported similar behavior displayed by reactions with a real 'phase transfer' (Stark's extraction mechanism); there is much smaller limit of stirring speed between physical and chemical control (100–400 rpm). We have observed that rate constants are strongly dependent on mass transfer and the kinetics of the reaction dependent of the stirring speed. Similar observation was reported by Landini et al. [22], Starks and Owens [23], Herriott and Picker [24] and Freedman and Dubois [25], which reflects kinetic control by mass transfer of the chemical reaction when [Q^+X^-] is at a steady state concentration. In a systematic kinetic study [26]



Scheme 2. Dichlorocarbene addition to citral under MPTC conditions.

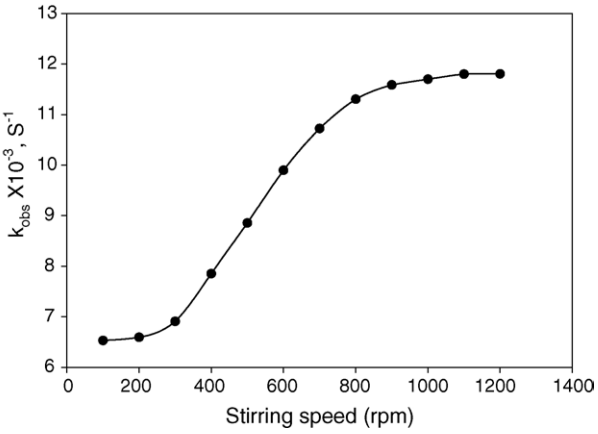


Fig. 1. Effect of variation of stirring speed on observed reaction rates.

of dichlorocarbene addition under solid/liquid phase transfer catalysts in the presence of *t*-BuOK, a sharp increase in the rate constant was observed between 400 and 500 rpm. Hence the dependence of the reaction rate constants on the stirring speed above 800 rpm in the present study is indicative of an interfacial mechanism. Balakrishnan and Jayachandran observed a similar trend in dichlorocarbene addition to styrene [27] and C-alkylation of phenyl acetone using ethyl iodide [27].

3.2. Effect of substrate amount

Kinetic experiments were studied by varying the substrate (citral) amount ranging from 6.17 to 21.6 mmol with the concentrations of other reactants such as chloroform and aqueous NaOH constant. Pseudo-first order rate constants were evaluated from the linear plots of $\log(a - x)$ versus time. The observed reaction rate constant increases as the amount of substrate increases (Fig. 2). The increase in the rate may be attributed to the proportionate increase in the number of catalytic active sites available in the MPT catalyst. A similar trend was observed by Balakrishnan et al. [28] in the study

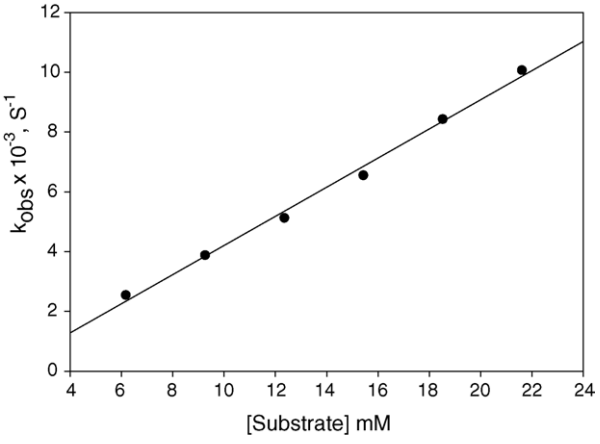


Fig. 2. Effect of variation of substrate amount on observed rate constant.

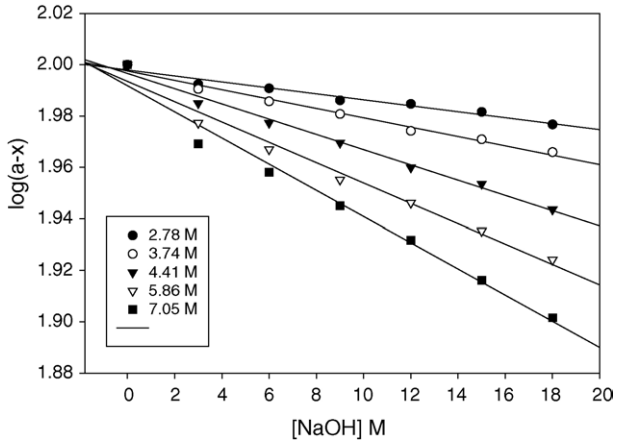


Fig. 3. Effect of variation of [NaOH].

of C-alkylation of phenylacetone with *n*-bromobutane and triethylbenzyl ammonium chloride as a PTC.

3.3. Effect of sodium hydroxide concentration

The rate of dichlorocarbene addition to citral strongly depends on the strength of the sodium hydroxide [29]. Kinetic experiments were measured in the range of 2.78–10.7 M aqueous sodium hydroxide. Pseudo-first order rate constants are evaluated from the plots of $\log(a-x)$ versus time (Fig. 3). The reaction rate constants are strongly influenced by the concentrations of aqueous NaOH. The observed rate constants tremendously increased with increase in basicity of hydroxide ion concentration (Table 2). A bilogarithmic plot of the reaction rate constants against sodium hydroxide concentration gives a straight line having a slope value of 0.25 (Fig. 4, plot A). This may be attributed to the fact that hydroxide ions are less solvated by water molecules and thereby the activity of hydroxide ions increases. In the reaction of dichlorocarbene addition to citral using MPTC, 30% NaOH was employed, whereas 15% NaOH is the optimum concentration for the present study since the catalyst decomposition was observed at higher concentration of aqueous base (i.e. more than 30%). This process is environmentally acceptable due to easy reaction workup and durability of the reaction vessels. In the case of LL-PTC conditions, anions are transferred into the organic phase with certain number of molecules of water, which noticeably reduce their reactivity. Highly concentrated alkaline solutions have low water activity and effectively act as desiccants for the organic phase. Furthermore, the application of highly concentrated alkaline aqueous solution was sometimes subject to partial catalyst decomposition when quaternary onium salts are used as PTC agents, especially when heated. However, onium salt degradation reactions mainly proceed in the organic phase viz., extraction of OH^-. The interfacial phenomenon is less important and they are strongly or completely inhibited if the extractability of OH^- is minimized. This can be avoided by reducing the water activity with high concentrated aqueous solutions of inorganic salts, in particular 30% aqueous NaOH. A similar trend was observed in a kinetic study of the dichlorocarbene addition to hexene [30] under phase transfer catalyzed conditions, where potassium hydroxide is used as a base rather than sodium hydroxide, as it enhances the reaction rate. In this case, the reaction rate initially increases and then decreases gradually when the concentration of KOH increases due to the catalytic decomposition at higher KOH concentration.

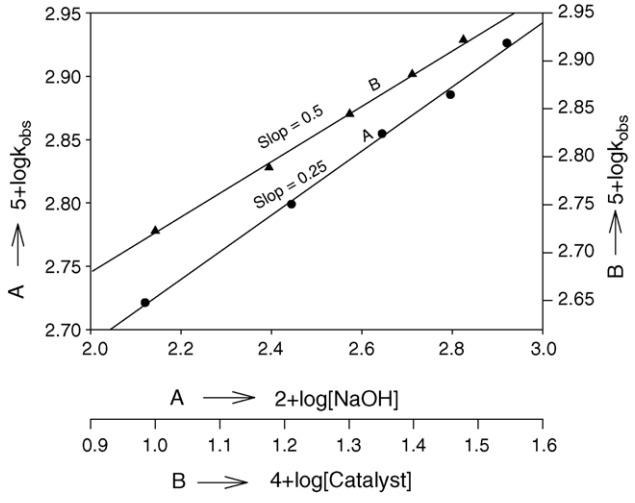


Fig. 4. Effect of variation of NaOH and catalyst amount on the observed rate constant.

3.4. Effect of catalyst amount

The amount of catalyst was varied from 2.0×10^{-4} to 3.0×10^{-4} mmol (based on the substrate amount) and other reactants are kept constant. The rate constants were plotted against the amount of added catalyst (mmol). Pseudo-first order rate constants are evaluated from the plots of $\log(a-x)$ versus time (Fig. 5). The rate constants were linearly depen-

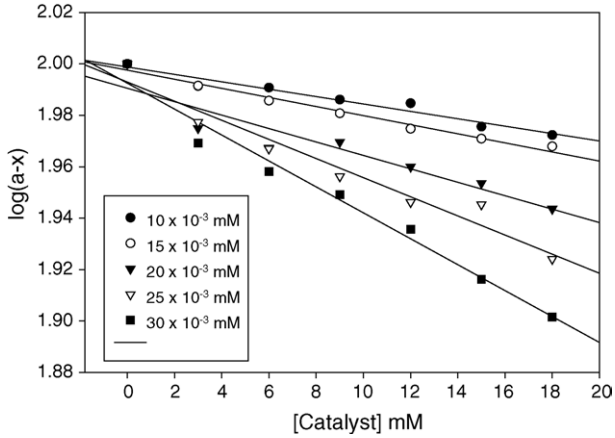


Fig. 5. Effect of variation of catalyst amount.

dent on the amount of the catalyst used in each reaction. The increased rate constants are attributed to the increase in the number of catalytic active sites. In the absence of the catalyst, no product was detected even after 5 h of the reaction. Only a small catalytic amount (1.50×10^{-3} mmol based on the substrate) is required in order to obtain good yields of the dihalochlorinated product. The linear dependence of the reaction rate constants on the catalyst concentration shows that the reaction is believed to proceed through the interfacial mechanism. In the present study, bi-logarithmic plot of the reaction rate constants versus the concentrations of the catalyst gave a straight line having a slope value of 0.5 (Fig. 4, plot B). In the study of dehydrobromination of phenethyl bromide [29] in the presence of tetraoctylammonium bromide, zero order kinetics with respect to the catalyst amount was observed. This observation suggests that the chemical reaction between the ion pair and the organic substrate is not the sole rate-determining step. From the observed results, it can be concluded that the carbanions cannot leave from the phase boundary into the organic phase, since the counter ion Na^+ are strongly solvated in the aqueous phase and poorly in the organic phase. In this case, the carbanions are unreactive being able to react only with strong electrophiles. The MPTC quaternary ammonium cations serve as a source of organic cation to form the organic phase soluble ion pairs with carbanions, hence transferring them into the organic phase for further transformation. The remarkable increase in the yield of dichlorocarbene adducts reflects the ability of the quaternary ammonium salt to affect the $:CCl_2$ to be generated/transferred to the organic phase, which was more reactive with the organic substrates than the water molecule. Starks reported similar observation in the study of dichlorocarbene addition to cyclohexene using tridecylmethylammonium chloride as a PTC [31].

3.5. Effect of temperature variation

The effect of varying temperature on rate of dichlorocarbene addition to citral was studied in the temperature range from 30 to 50 °C with other parameters such as [substrate], [catalysts], [aqueous base] kept constant. The kinetic profile of the reaction is obtained by plotting $\log(a-x)$ versus time. The rate constants increase with increase in temperature. The energy of activation is calculated from Arrhenius plot (Fig. 6) $E_a = 17.3$ kcal mol^{-1}. The other thermodynamic parameters such as $\Delta S^{\#}$, $\Delta G^{\#}$ and $\Delta H^{\#}$ for dichlorocarbene addition to citral was found to be −31.7, 98.89 and −20.4 kcal mol^{-1}, respectively. Many PTC/OH reactions have energy of activation up to 15 kcal mol^{-1}; these particular reactions may be carried out successfully without significant catalyst decomposition, if performed at low temperature.

The activation energy for the ethylation of pyrrolidin-2-one under PTC condition was reported to be 12.4 kcal mol^{-1} and for this an interfacial mechanism was proposed [21]. In a comprehensive study for the dichlorocarbene addition to isobutylene, it has been observed that the formation of 1,1-dichloro-2,2-dimethyl cyclopropane increases with increase in temperature and the E_a value was found to be 12.3 kcal mol^{-1}. Do and Chou [32] observed a favorable effect on the extraction of tetrabutylammonium hypochlorite ion-pair from the aqueous phase into the organic phase on increasing the temperature in the study of the oxidation of benzyl alcohol by hypochlorite ion under PTC conditions.

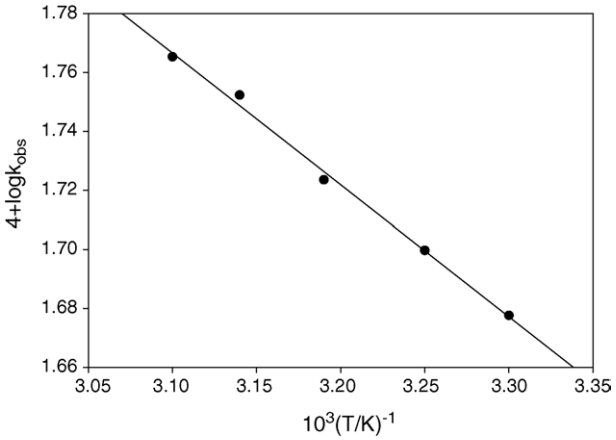


Fig. 6. Arrhenius plot.

A higher E_a value has been reported [33] for the polystyrene bound triethylammonium ion catalyzed reaction, which was controlled by strict intrinsic reactivity under triphase reactions. The observed energy of activation higher for the dichlorocarbene addition to citral is 17.3 kcal mol^{-1} and hence interfacial mechanism was proposed for the reaction study, which is governed by diffusion control.

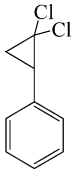
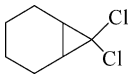
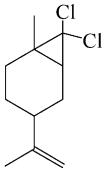
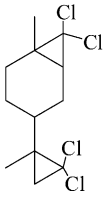
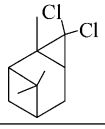
3.6. Comparison of reaction rate constant with various single-site PTC and MPTCs

Dichlorocarbene addition to citral has been chosen to investigate the comparative relativities of various commercially available soluble single-site PTC such as triethylbenzylammonium chloride (TEBAC), triethylbenzylammonium bromide (TEBAB), tetrabutylammonium bromide (TBAB) and tetrabutylammonium chloride (TBAC) with TEAMCPB 5; all the reactions were carried out under identical reaction conditions. TEAMCPB 5 has almost 10-fold more active than the commercially available single-site PTCs (Table 1). This observation proves that in MPTC all the catalytic sites

Table 1
Comparison of reaction rate using different phase transfer catalysts

Catalysts	[Catalyst] $\times 10^{-4}$ mM	$k_{obs} \times 10^{-3}$ s^{-1} [N$^+$]
None	4.00	Nil
TEBAC	4.00	1.2245
TEBAB	4.00	1.0535
TBAC	4.00	1.3565
TBAB	4.00	1.1893
TEAMCPB	4.00	11.9097

Table 2
Dichlorocarbene addition to various olefins under MPTC and SPTC conditions

Entry	Olefins	Name of the catalyst	Product	Yield (%)	Spectral data
1	Styrene	TEBAC TEBAB TEAMCPB		35 42 97	FT-IR (KBr) cm^{-1}: 715 (C—Cl); ^1H NMR (200 MHz, $CDCl_3$) δ: 0.99 (d, 2H, $J = 5.7$ Hz, —CH_2), 2.25 (t, 1H, $J = 4.3$ Hz, —CH), 7.10–7.34 (m, 5H, aromatic); *m/e*: 187.23
2	Cyclohexene	TEBAC TEBAB TEAMCPB		47 38 95	FT-IR (KBr) cm^{-1}: 706 (C—Cl); ^1H NMR (200 MHz, $CDCl_3$) δ: 1.28 (q, 4H, —CH_2), 1.48 (t, 4H, $J = 3$ Hz, —CH_2), 2.25 (m, 2H, —CH)
3	(*R*)-Limonene	TEBAC		25:06	Mono dihalocyclo product: FT-IR (KBr) cm^{-1}: 724 (C—Cl); ^1H NMR (200 MHz, $CDCl_3$) δ: 1.14 (s, 3H, —CH_3), 1.46 (m, 6H, —CH_2), 1.85 (s, 3H, —CH_3), 2.04 (t, 1H, $J = 3.4$ Hz, —CH), 2.23 (p, 1H, —CH), 4.96 (m, 2H, vinyl); *m/e* [M^+]: 219.13.
		TEBAB		21:11	bis-Dihalocyclo product: FT-IR (KBr) cm^{-1}: 728 (C—Cl); ^1H NMR (200 MHz, $CDCl_3$) δ: 0.87 (s, 2H, —CH_2), 1.05 (s, 3H, —CH_3), 1.15 (s, 3H, —CH_3), 1.36–1.52 (m, 6H, —CH_2), 1.61 (m, 1H, —CH), 2.25 (m, 1H, —CH); *m/e* [M^+]: 303.55
		TEAMCPB		10:87	
4	α-Pinene	TEBAC TEBAB TEAMCPB		39 32 84	FT-IR (KBr) cm^{-1}: 719 (C—Cl); ^1H NMR (200 MHz, $CDCl_3$) δ: 1.12 (s, 6H, —CH_3), 1.22 (s, 3H, —CH_3), 1.35 (m, 4H, —CH_2), 1.40 (m, 2H, —CH), 2.25 (t, 1H, $J = 5.0$ Hz, —CH); *m/e* [M^+]: 219.02

Olefin + $CHCl_3$ $\xrightarrow[15\%\text{aq. NaOH}]{\text{PTC}(20\times10^{-3}\text{ mM})}$ mono/bis-dihalocyclopropane.
40 °C, 1 h

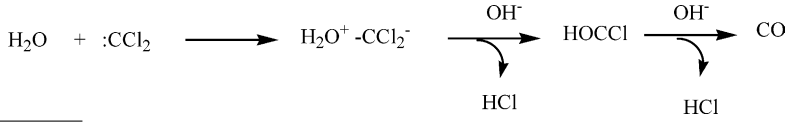
appear to be co-operatively involved in the dichlorocarbene addition reaction. Furthermore, the efficacy of the TEAMCPB with various single-site PTCs were studied by the dichlorocarbene addition to various olefins under identical reaction conditions (Table 2). The observed results from the Table 2, TEAMCPB is superior to the other single-site catalysts.

3.7. Kinetic model of the dichlorocarbene addition reaction

Chloroform was first reacted with the base to form an trichloromethyl anion (CCl_3^-), which can be converted into dichlorocarbene (:CCl_2). In this case, organic olefin does not react directly with the dichlorocarbene to form a dihalocyclopropane product because of easy hydrolysis of dichlorocarbene as follows:

$$CHCl_3 + OH^- \rightleftharpoons H_2O + CCl_3^-$$

$$CCl_3^- \rightarrow : CCl_2 + Cl^-$$



Hence, the addition of phase transfer catalysts (quaternary ammonium salts, QX) to the aqueous solution to generate dichlorocarbene in the organic solution is essential. Then the intermediate ($Q^+CCl_3^-$) is formed from the reaction of trichloromethyl anion and quaternary ammonium ion at the interface of two phases. Further the intermediate was transferred to the bulk of the organic phase preparing for reaction with olefins to produce the mono and dihalocyclopropane derivatives. The reaction mechanism is thus proposed as follows:

$$6CHCl_{3(org)} + 6NaOH_{(aq)} \rightleftharpoons 6CCl_3{}^-Na^+{}_{(inter)} + 6H_2O_{(aq)} \quad (1)$$

$$6CCl_3{}^-Na^+{}_{(inter)} + MPTC[CH_2N^+Et_3Cl^-]_{6(inter)} \rightleftharpoons MPTC[CH_2N^+Et_3{}^-CCl_3]_{6(org)} + 6NaCl_{(aq)} \quad (2)$$

$$MPTC[CH_2N^+Et_3{}^-CCl_3]_{6(org)} \rightleftharpoons 6 : CCl_{2(org)} + MPTC[CH_2N^+Et_3Cl^-]_{6(aq.)} \quad (3)$$

$$C_{10}H_{16}O_{(org)} + : CCl_{2(org)} \xrightarrow{k_1} C_{11}H_{16}OCl_{2(org)} \quad (4)$$

$$C_{11}H_{16}OCl_{2(org)} + : CCl_{2(org)} \xrightarrow{k_2} C_{12}H_{16}OCl_{4(org)} \quad (5)$$

where k_1 represents the intrinsic rate constant for the reaction of dichlorocarbene (:CCl_2) and citral ($C_{10}H_{16}O$) to produce the mono-dichlorocyclopropane ($C_{11}H_{16}OCl_2$) in the organic solution and k_2 the intrinsic rate constant for the formation of bis-dichlorocyclopropane product ($C_{12}H_{16}OCl_4$) from mono-dichlorocyclopropane ($C_{11}H_{16}OCl_2$) and dichlorocarbene (:CCl_2) in the organic phase. In this case, the rate of citral consumption would be written as

$$-\frac{d[C_{10}H_{16}O]_{org}}{dt} = k_1[C_{10}H_{16}O]_{org}[: CCl_2]_{org} \quad (6)$$

Since the concentration of dichlorocarbene was kept constant throughout the reaction, the Eq. (6) can be written as

$$\frac{d[C_{10}H_{16}O]_{org}}{dt} = k_{obs,1}[C_{10}H_{16}O]_{org} \quad (7)$$

where

$$k_{obs,1} = k_1[: CCl_2]_{org} \quad (8)$$

Similarly, the rate constant of bis-dichlorocyclopropane of the dichlorocarbene addition to citral is as follows

$$k_{obs,1} = k_2[: CCl_2]_{org} \quad (9)$$

In this case, the consecutive reaction of citral and dichlorocarbene is irreversible and is expressed as,

$$C_{10}H_{16}O \xrightarrow{k_{obs,1}} C_{11}H_{16}OCl_2 \xrightarrow{k_{obs,2}} C_{12}H_{16}OCl_4 \quad (10)$$

From the Eq. (10), the change in the concentration of these three components is:

$$\frac{d[C_{10}H_{16}O]_{org}}{dt} = -k_{obs,1}[C_{10}H_{16}O]_{org} \quad (11)$$

$$\frac{d[C_{11}H_{16}OCl_2]_{org}}{dt} = -k_{obs,1}[C_{10}H_{16}O]_{org} - k_{app,2}[C_{11}H_{16}OCl_2]_{org} \quad (12)$$

$$\frac{d[C_{12}H_{16}OCl_4]_{org}}{dt} = k_{obs,2}[C_{11}H_{16}OCl_2]_{org} \quad (13)$$

Eq. (11) is integrated as

$$[C_{10}H_{16}O]_{org} = [C_{10}H_{16}O]_{org,inter} \exp(-k_{obs,1}t) \quad (14)$$

where $[C_{10}H_{16}O]_{org,inter.}$ is the initial concentration of citral. Define the conversion of citral X as

$$X = 1 - \frac{[C_{10}H_{16}O]_{org}}{[C_{10}H_{16}O]_{org,inter}} \quad (15)$$

Thus, the Eq. (15) can be expressed as,

$$-\ln(1-X) = k_{obs,1}t \quad (16)$$

The value of $k_{obs,1}$ can be obtained by plotting $-\ln(1-X)$ versus time. From Eqs. (12) and (14), we obtain the concentration of mono-dichlorocyclopropane, i.e.

$$[C_{11}H_{16}OCl_2]_{org} = [C_{10}H_{16}O]_{org,inter} \frac{k_{obs,1}}{k_{obs,2} - k_{obs,1}} \{\exp(-k_{obs,1}t) - \exp(-k_{obs,2}t)\} \quad (17)$$

$$[C_{11}H_{16}OCl_2]_{org} = K[C_{10}H_{16}O]_{org,inter}\{\exp(-k_{obs,1}t) - \exp(-k_{obs,2}t)\} \quad (18)$$

where

$$K = \frac{k_{obs,1}}{k_{obs,2} - k_{obs,1}}$$

The value of $k_{obs,2}$ can be estimated from the experimental data of mono and bis-dichlorocyclopropane and from the knowledge of $k_{obs,1}$ value given in Eq. (16) via parameter variation.

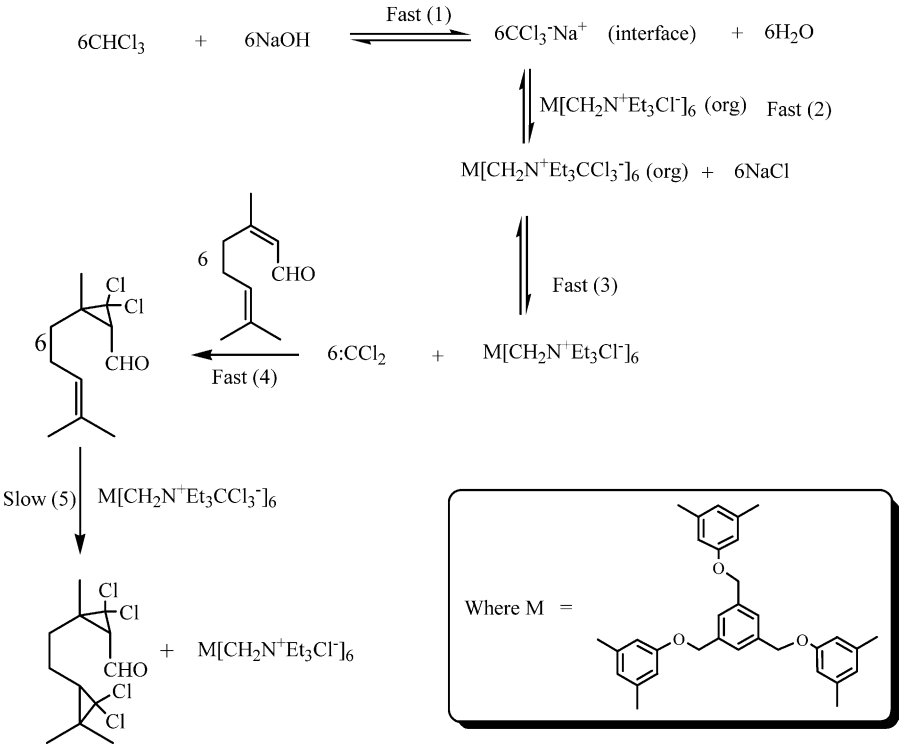
3.8. Reaction mechanism

Dichlorocarbene addition reaction may occur in two steps, base deprotonation of chloroform catalyzed by a phase transfer agent, followed by addition of electrophile. The selectivities of dichlorocarbene generated under MPTC conditions towards the alkenes are independent of the structure of the catalysts. That means that the :CCl_2 is involved in all cases whereas there is a strong influence on the reaction medium starting from trihalocarbene to dihalocarbene [14]. In the phase transfer system, two major mechanisms are believed to be operative viz., Stark's extraction mechanism [23] (characterized by increased reaction rate with increased organophilicity, independence of reaction rate on stirring speed above certain value and linear dependence of reaction rate on catalyst concentration) and Makosza's interfacial mechanism [34] (characterized by maximum reactivity with relatively hydrophilic quats, usually alkyltriethyl ammonium quats, increased reaction rate with increased speed even up to 1950 rpm and fractional order with respect to catalyst). From the observed experimental results, the dependency of kinetic data on the stirring speed up to 800 rpm, concentrations of the catalyst, aqueous hydroxide ions, temperature,

dependence on the stirring speed and higher E_a value strongly proved that this reaction proceeded via the interfacial mechanism.

In this interfacial mechanism, the hydroxide anion first reacted with the chloroform in the organic phase without the help of quaternary onium cations. Then the MPTC catalyst anion exchanged by trihalo derivative to form an active intermediate of MPTC/CCl_3^- which can react with the olefinic group containing citral to give an mono dihalocyclopropanated product. Furthermore, the concentration of catalytic site per molecule is increased from single-site to multi-site as a result that the abstraction of proton from chloroform is more effective than the single-site PTC. Since there is a higher amount of Q^+OH^- ion pair in the medium, it has a tendency to undergo addition with another olefinic double bond from the mono addition product resulting in the formation of a bis-dihalocyclopropanated product.

3.9. Interfacial mechanism



4. Conclusion

It is very clear that we have successfully synthesized and confirmed multi-site phase transfer catalyst containing the maximum number of six active sites per molecule and its catalytic abilities were thoroughly studied by dichlorocarbene addition to citral using excess of chloroform and 15% aqueous sodium hydroxide. The effect of various experimental parameters on the reaction of dichlorocarbene addition; viz., stirring speed, [substrate], [catalyst], [hydroxide ion] and temperature were found to extraordinarily influence the observed rate constant values under mild base and low MPTC conditions. This novel multi-site catalyst has higher activity than the other single-site quaternary ammonium salts. The E_a value and other thermodynamic parameters $\Delta S^{\#}$, $\Delta G^{\#}$ and $\Delta H^{\#}$ were calculated from the Arrhenius plot. The increased reaction rates with increased organophilicity or with larger symmetrical ammonium ions, dependence of reaction rate on the stirring speed above certain value, linear dependence of the reaction rate on the catalyst concentration and higher E_a value suggested that the dichloro carbene addition to citral should proceed with the interfacial mechanism.

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