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Preparation of a novel soluble multi-site phase transfer catalyst and the kinetic study for the C-alkylation of α-pinene☆

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Abstract

Novel soluble "multi-site" phase transfer catalyst viz.1,3,5-tris(4-(2,2′-bis(*N*-triethylammoniummethylene chloride)eth-1-ene)phenoxymethyl)benzene (TBTEAPB) was synthesized and characterized by different spectral techniques such as FT-IR, ^{1}H NMR, ^{13}C NMR, MALDI-TOF mass and chloride ion analysis. The catalytic potential of this new multi-site TBTEAPB phase transfer catalyst was demonstrated by the C-alkylation of α-pinene with epichlorohydrin using low concentration of base (20% NaOH) at 40 °C. The pseudo-first order rate constants were calculated by following the disappearance of α-pinene through gas liquid chromatography. The efficiency of TBTEAPB catalyst was also studied by comparing the rate constants of reaction facilitated by single and di-site PTCs in a similar catalytic environment. The observed rate constants were found to be ≅6 and 3 times higher for the TBTEAPB multi-site PTC than for the single and di-site PTCs. Thorough kinetics of the reaction was also studied by varying the experimental parameters such as stirring speed, [catalyst], [substrate], [NaOH] and temperature. Thermodynamic parameters of the reaction were also evaluated from the Arrhenius plot and the values are as follows; 7.12, −33.66, 13.46 and 0.41 kcal mol^{-1} for E_a, $\Delta S^{\#}$, $\Delta G^{\#}$ and $\Delta H^{\#}$, respectively. Based on the kinetic and thermodynamic parameters, we have proposed an hydroxide ion extraction mechanism.

Keywords: Multi-site phase transfer catalyst; C-alkylation; Extraction mechanism

1. Introduction

Phase transfer catalysis (PTC) has been considered as a fascinating area of current research interest especially for synthetic organic chemists. It is a well recognized and more versatile technique applicable to a number of organic biphase reactions. The significant applications of PTC technique include the preparation of compounds from an unreactive starting material, dramatic enhancement in yields and product selectivity. The first soluble single-site phase transfer catalyst has come into limelight during 1960s [1] and then a variety of quaternary ammonium [2–4] and phosphonium salts [5], crown ethers [6], cryptands [7], etc., had been reported and used to carry out reactions particularly *O*-alkylation [8–11], C-alkylation [12–14], *N*-alkylation [15–17], dichlorocarbene addition to olefinic double bonds [18,19], oxidation [20], reduction [21,22], etc.

Directly or indirectly most of the alkylated products have pharmaceutical significance and hence attention should be paid to the optimization of the reaction conditions for the efficient synthesis of alkylated product. In order to increase the yield of alkylated product, chemists frequently used strong bases in the presence of inert solvents which in turn are environmentally polluting. The pollution, i.e., the problem of using highly concentrated base for alkylation reaction, has been alleviated by employing the PTC with mild NaOH (concentration). Several reports appeared for alkylation under mild aqueous basic conditions [23,24]. Methylation of phenylacetone has been performed using methyl iodide, but

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this requires an equimolar amount of phase transfer catalysts [25]. Makosza et al. [26] reported higher amount of monoalkylated product from benzyl and allyl halides as substrate using single-site triethylbenzylammonium chloride as a PTC.

In order to get the maximum desired product in a short duration of reaction time, the catalyst should be more efficient. The important considerations in the selection of the catalysts are economy of scale and efficiency of the phase transfer catalyst specifically in the industrial scale preparations of organic compounds. In order to satisfy these needs, novel "multi-site phase transfer catalysts" (MPTC) have been developed which contain more than one catalytic site per molecule. The first report published on MPTC was by Idoux et al. [27] and they have synthesized soluble and insoluble phosphonium as quaternary onium ions containing three active sites per molecule. Balakrishnan et al. [28] and Wang and Hsieh [29] have also reported soluble ammonium quaternary onium ions having two active sites and the efficiency of the di-site PTC were also examined through simple S_N2 reactions and some weak nucleophilic SnAr reactions. Recently, dimeric [30,31] and trimeric [32] chiral quaternary ammonium catalysts were synthesized from *o*-, *m*- or *p*-xylene dibromide, bis(bromomethyl)naphthalenes and mesitylene tribromide respectively. These CPTCs have been employed for C-alkylation of *N*-(diphenylmethylene)glycine *tert*-butyl ester and have been found to be good in terms of yields and ee's.

Systematic literature survey reveals that so far only very few reports are available in "MPTC" synthesis. Further, the catalytic abilities of those catalysts were studied using higher amount of aqueous base to carry out various organic reactions; such reaction conditions are not environmentally acceptable owing to heavy base pollution. It may be expected that the increased number of catalytic active site present in a molecule should enhance its catalytic efficiency and the reaction yield and hence the economy of the reaction process. Considering all the early studies, we have proposed to synthesize a novel soluble multi-site phase transfer catalyst (TBTEAPB) containing as many as six possible active sites per molecule. The catalytic ability of the TBTEAPB was tested for the C-alkylation of α-pinene with epichlorohydrin under pseudo-first order condition with low concentrations of the base (Schemes 1 and 2). Further, the catalytic efficiency of the new MPTC was compared with that of single-site and di-site PTCs with a similar catalytic moiety. Thorough kinetic studies were also performed by varying the different experimental parameters, and based on the results a mechanism is also proposed.

2. Experimental

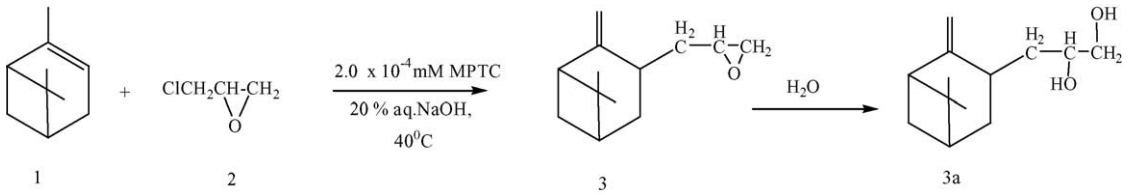
2.1. Synthesis of 1-(p-hydroxyphenyl)-2,4,8,10-tetraoxaspiro[5,5]undecane (5)

A three-necked round bottomed flask (500 ml) was fitted with a mercury seal and the flask was charged with *p*-hydroxyacetophenone (**4**) (40 mM), formaldehyde (37–41%) with 120 mM in excess and water (150 ml). The mixture was stirred sufficiently well till the formation of a homogeneous phase. Calcium oxide (8 g) dissolved in water (40 ml) was added in small portions to this mixture and the reaction was carried out at 60 °C for 10 h using an oil bath. The cold reaction mixture prepared from 50% H_2SO_4 (ice-cold) was added to the filtered sample until precipitation occurred; subsequently it was reduced to one third in volume by steam distillation. The solid product was extracted with DMF and dried over anhydrous $MgSO_4$, yield 84%, mp 54 °C.

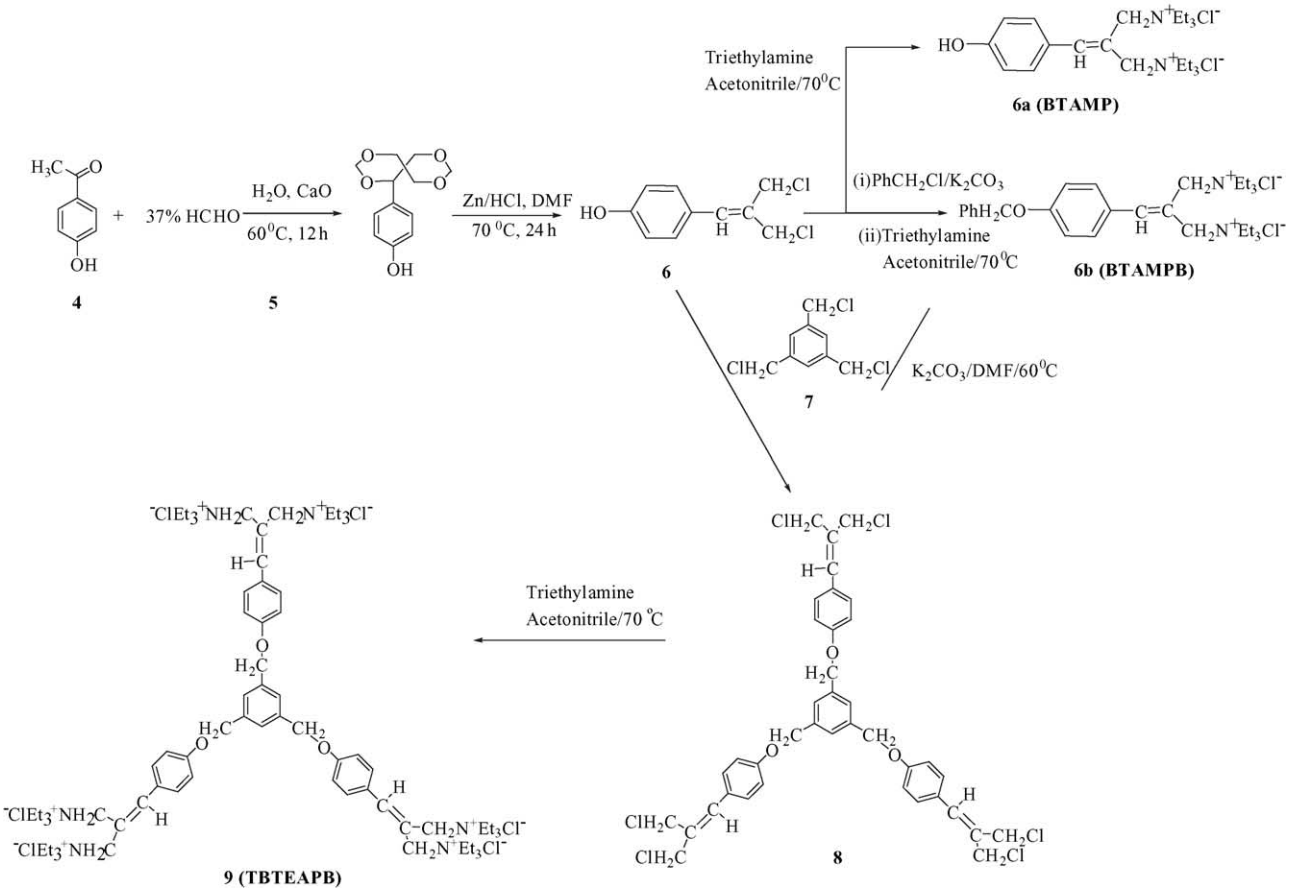
FT-IR (KBr), cm^{-1}: 1967 (aromatic C–H), 1078 (C–O–C), 3446 (O–H) ^{1}H NMR: δ (200 MHz): 1.2(s, 1H, hydroxyl), 4.29 (s, 4H,-methylene), 4.7(m, 9H,-methylene), 6.4–6.5(d, 2H, J = 8.1 Hz, aromatic), 7.39–7.42 (2H, d, J = 7.5 Hz, aromatic).

2.2. Synthesis of 1,1-bis(chloromethyl-p-hydroxy phenyl)-2-hydroxyethane (6)

A 1.45 g (6.25 mM) of 1-(*p*-hydroxyphenyl)-2,4,8,10-tetraoxaspiro[5,5]undecane was placed in a 150 cm^3 single-necked RB flask containing aqueous HCl (45 cm^3, 35% solution) and a catalytic amount (0.070 g) of anhydrous zinc chloride was added to it. The reaction mixture was gently refluxed overnight and the contents were extracted with chloroform. The crude product was found to be homogeneous and was purified using silica gel column chromatography. A low melting light brown solid was obtained in 92% yield.



Scheme 1. C-alkylation of α-pinene with epichlorohydrin under MPTC condition.



Scheme 2. Various steps involved in the synthesis of multi-site phase transfercatalyst (TBTEAPB).

FT-IR: (KBr, cm^{-1}): 706 (C–Cl), 1636 (C=C), 3429 (b, O=H); ^{1}H NMR: δ (300 MHz, $CDCl_3$): 4.07 (s, 4H, methylene), 5.25 (s, 1H, hydroxy), 6.12 (s, 1H, vinylic), 7.25–7.29 (d, 2H, J = 12.0 Hz, adjacent to phenolic aromatic), 7.79–7.83 (d, 2H, J = 12.0 Hz, adjacent to vinylic aromatic); ^{13}C NMR (75 MHz, $CDCl_3$): 43.2, 115.6, 124.8, 127.6, 128.7, 135.8, 156.2; $m/z = M^+$ 216.98.

*2.3. Synthesis of 4-[2,2′-bis(N-triethylammoniummethylene chloride)-eth-1-ene]phenol (BTAMP, **6a**)*

1,1-Bis(chloromethyl-*p*-hydroxyphenyl)-2-hydroxyethane (**6**) (1.5 g, 6.91 mM), excess of triethylamine (15 ml) and acetonitrile (25 ml) were taken in an RB flask. The solution was refluxed in inert atmosphere for about 6 h at 70 °C. After the reaction the solvent was removed by distillation and the crude product was washed twice with chloroform (2× 10 ml). The resulting low melting solid 4-[bis(*N*,*N*′-triethylammoniummethylene chloride)-eth-1-ene]phenol was dried and characterized by FT-IR and NMR techniques.

FT-IR (cm^{-1}): 1056 (C–N), 1646 (C=C), 1960.5 (aromatic C–H), 3475.0 (O–H); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.97–1.01 (t, 18H, J = 4.0 Hz, -methyl), 1.86–1.92 (q, 12H, J = 8.2 Hz, -methylene), 3.45 (s, 4H, methylene), 4.5 (bs, 1H, -OH), 5.02 (s, 1H, vinylic), 6.35–6.52 (m, 4H, aromatic); ^{13}C NMR (50 MHz, $CDCl_3$): 7.9, 54.6, 60.5, 115.7, 121.1, 127.2, 127.8, 131.2, 156.6.

*2.4. Synthesis of 4-(2,2'-bis(N-triethylammoniummethylene chloride)eth-1-ene) phenoxymethyl]benzene (BTAMPB, **6b**)*

1,1-Bis(chloromethyl-*p*-hydroxyphenyl)-2-hydroxyethane (**6**) (1.0 g, 4.61 mM) was allowed to react with benzyl chloride in the presence of K_2CO_3 and methylene chloride for about 3 h at 60 °C. After completion of the reaction the solvent was removed by evaporation and then it is quaternized with excess of triethylamine using acetonitrile as a solvent for 6 h at 50 °C [33–37]. Then the solvent was removed by distillation and the final solid crude product was recrystallised from ethanol; the structure of the pure di-site catalyst **6b** was confirmed through FT-IR and ^{1}H NMR spectra.

FT-IR (cm^{-1}): 1640.5 (C=C), 1165.5 (C–N), 1045.0 (C–O); ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.02–1.05 (t,

18H, $J = 3$ Hz, -methyl), 1.92–1.98 (q, 12H, $J = 8.2$ Hz, -methylene), 2.45 (s, 2H, methylene), 5.45 (s, 1H, vinylic), 6.20–6.78 (m, 9H, aromatic); ^{13}C NMR (50 MHz, $CDCl_3$): 12.4, 49.8, 59.2, 77.3, 114.3, 120.5, 127.3, 127.7, 128.2, 128.6, 129.2, 131.2, 161.6; *m*/*e*: $M^{2+} = 438.32$.

2.5. Synthesis of 1,3,5-tris(4-(2,2′-bis(N-triethylammoniummethylene chloride)eth-1-ene)-phenoxymethyl)benzene (9)

The title compound, i.e. TBTEAPB **9**, was prepared by the treatment of 1,3,5-tricholoromethylenebenzene with 1,1-bis(chloromethyl-*p*-hydroxyphenyl)-2-hydroxy ethane (**6**) (4.37 g, 6.91 mM) in the presence of potassium carbonate (1 g, 10 mM) and dimethylformamide (25 ml) in a 250 ml RB flask. The reaction mixture was refluxed at 70 °C in an oil bath for 18 h. After completion of the reaction, the solvent was removed by distillation and the final viscous reaction product was brown in colour. Further, the resulting compound 8 (1.5 g, 6.71 mM) was quaternized by following the usual procedure [33,35]. The final pale yellowish crystal was repeatedly washed with methanol and acetone and then dried; the yield is 87%. The estimation of chloride concentration was also carried out by the Volhard method [33–37].

FT-IR (cm^{-1}): 1172.88 (C–N), 1035.87 (C–O); ^{1}H NMR (300MHz, $CDCl_3$): 1.75–2.2 (m, 36H, -methyl), 4.75–5.00 (broad, 54H,-*N*-ethyl), 5.15 (s, 6H,-methylene), 7.25–7.86 (m, 15H, aromatic), 8.20 (s, 3H, olefinic); ^{13}C NMR (75 MHz, $CDCl_3$): 9.2, 10.4, 42.5, 76.5, 77.0, 77.4, 114.5, 123.7, 126.3, 128.9, 129.3, 132.8, 133.8, 138.3, 141.3, 161.3; MALDI TOF: Calc. Value for $C_{75}H_{126}N_6O_3^{6+}$: 1159.59; Found: 1159.36; [Chloride ion]: Calculated value 15.2 mequiv. g^{-1}, Found 15.15 mequiv. g^{-1}

2.6. Typical kinetic procedure for the alkylation of α-pinene

The kinetic experiments were performed in a 150 ml two-necked flask fitted with flat-bladed stirring paddles and the reaction was carried out by reverse addition methods, i.e. taking excess of epichlorohydrin first in the reaction flask followed by the addition of α-pinene in the presence of multi-site PTC viz., TBTEAPB catalyst. The alkylating agent epichlorohydrin (20 ml), aqueous NaOH 20% w/w (25 ml), hexadecane (1 ml) and TBTEAPB catalyst (3.0×10^{-4} mM) were taken initially in the flask and stirred at 200 rpm for 5 min at 50 °C to condition the catalyst. Then the stirring speed was increased to 500 rpm and 2 mM of α-pinene was added to the reaction mixture to start the reaction. Samples were collected from the organic layer of the mixture (by stopping the stirring for 10–15 s each time) at regular intervals. The kinetics of the reaction was followed by estimating the amount of α-pinene that disappeared using gas chromatography. The column (5% SE-30 chrom WHP 80/100, 3 m × 1/8 in. stainless steel packed column) was maintained at 200 °C. For every sample 0.5 μl of the reaction mixture was injected into the column and the product was analysed. The observed values of the retention time are 2.37 min for epichlorohydrin, 4.27 min for α-pinene and 2.82 min for the epoxide product. The pseudo-first order rate constants were evaluated from the plots of $\log(a - x)$ versus time. In a similar manner, studies on the C-alkylation of α-pinene were also performed using the same catalytic environmental moiety of single and di-site PTCs. Four different single-site PTCs viz., triethylbenzylammonium chloride (TEBAC), triethylbenzylammonium bromide (TEBAB), tetrabutylammonium bromide (TBAB), tetrabutylammonium chloride (TBAC) and two different di-site PTCs viz., 4-[2,2′-bis(*N*-triethylammoniummethylene chloride)eth-1-ene]phenol (BTAMP) and 4-(2,2′-bis(*N*-triethylammoniummethylene chloride)eth-1-ene)phenoxymethyl)benzene (BTAMPB) were used for the reaction under identical experimental conditions.

In order to isolate the product for confirmation, after 1 h of the reaction period, the reaction mixture was allowed to cool and to the cold reaction mixture, 50 ml of ether was added and the ether layer was decanted by a separating funnel. The compound was purified using silica gel column chromatography. The product was analyzed by different techniques and the obtained spectral data confirmed the formation of epoxide product **3** (2-(6,6-dimethyl-2-methylene bicyclo[3.1.1]hept-3-ylmethyl)oxirane). We have also obtained the diol viz., 3-(6,6-dimethyl-2-methylene-bicyclo[3.1.1]hept-3-yl)propane-1,2-diol as a product **3a**. The ratio between epoxide and diol product was found to be 20:80 within 1 h of reaction time. The diol product was formed due to the hydrolysis of epoxide.

2.6.1. 2-(6,6-Dimethyl-2-methylene bicyclo[3.1.1] hept-3-ylmethyl)oxirane (3)

FT-IR: $cm^{-1} = 3085$ (C=C–H), 1240 (C–O), 1456 (methylene C–H bend). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.11$ (s, 6H, -methyl). 1.25–1.28 (d, 2H, $J = 9.0$ Hz, -methylene), 1.40–1.42 (d, 2H, $J = 6$ Hz, -methylene), 1.90–1.94 (m, 3H, -methylene), 2.50–2.53 (m, 3H, -methyne and -methylene), 2.14-2.16 (m, 2H, -methyne), 2.62-2.65 (t, 1H, $J = 3.2$ Hz, -methyne), 4.75-4.78 (dd, 2H, $J = 2.8$ Hz, and $J = 3.1$ Hz, -methylene); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 24.8$, 30.1, 35.7, 36.2, 36.7, 41.2, 45.9, 47.3, 48.1, 52.5, 105.5, 157.8. *m*/*e*: 192.15.

2.6.2. 3-(6,6-Dimethyl-2-methylenebicyclo[3.1.1] hept-3-yl)propane-1,2-diol (3a)

FT-IR (KBr) cm^{-1}: 3458 (–OH), 3025 (C=C–H), 1235 (C–O), 1486 (methylene C–H bend). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.20$ (s, 6H, -methyl). 1.22–1.28 (d, 2H, $J = 18$ Hz, -methylene), 1.42–1.45 (t, 2H, $J = 4.5$ Hz, methylene), 1.92–1.96 (m, 2H, -methylene), 2.01–2.07 (m, 1H, methyne), 2.16-2.20 (m, 1H, methyne), 2.50–2.53 (m, 1H, methyne), 3.30–2.35 (m, 1H, methyne), 3.68–3.71 (d, 2H, $J = 9.0$ Hz, methylene), 4.72–4.74 (d, 2H, $J = 6$ Hz, -

vinylic); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.7, 30.1, 34.9, 36.1, 36.6, 41.5, 45.3, 45.9, 52.6, 71.4, 105.5, 157.8. *m*/*e*: 211.07.

3. Results and discussion

The objective of this study was to generate more than one catalytic ammonium site per molecule of catalyst. *p*-Hydroxyacetophenone is taken as a starting material due to its –OH functionality which in turn served as an easy blocking agent when its resulting compound **6** condensed with 1,3,5-trichloromethylenebenzene (**7**). Early studies [28] of MPTC shows that only two catalytic quaternary onium sites could be obtained using acetophenone as a starting material. The chlorinated compound **6** acted as building block for synthesis of new multi-site TBTEAPB **9** catalyst; the compound **8** was prepared by condensation of **6** with **7** in the presence of K_2CO_3. The condensation was confirmed by the formation of C-O bond (1100 cm^{-1}) in FT-IR spectra (Fig. 1a). The compound **8** was treated for quaternization in the presence of triethylamine and acetonitrile to get the TBTEAPB multi-site catalyst **9**.

The structure of the MPTC catalyst was confirmed by FT-IR, ^{1}H NMR, ^{13}C NMR and MALDI TOF mass techniques along with chloride ion estimation. The disappearance of C–Cl stretching vibration at 700–750 cm^{-1} and formation of C–N stretching vibration at 1173 cm^{-1} (Fig. 1b) proved the generation of quaternised active sites. This is further confirmed by the appearance of methyl proton of the triethylamine unit of compound **9** as a multiplet at 1.72–2.22 ppm, not found with compound **8**. In the case of ^{13}C NMR, the presence of *N*-ethyl group appeared at 9.2 and 10.4 ppm. The compound **9** was further con-

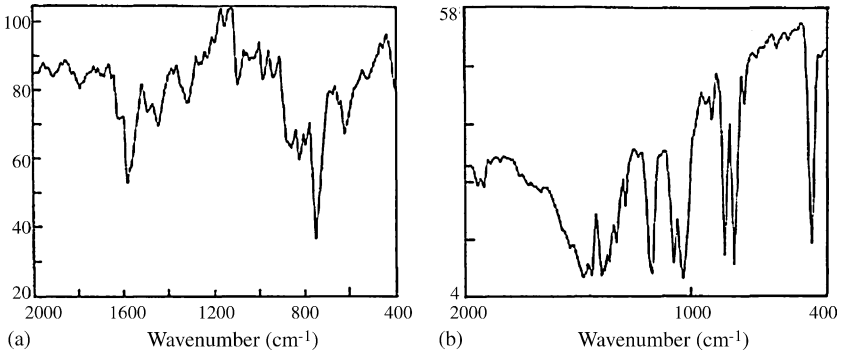


Fig. 1. FT-IR spectra of (a) unquaternised compound 8 and (b) quaternised compound 9 (MPTC).

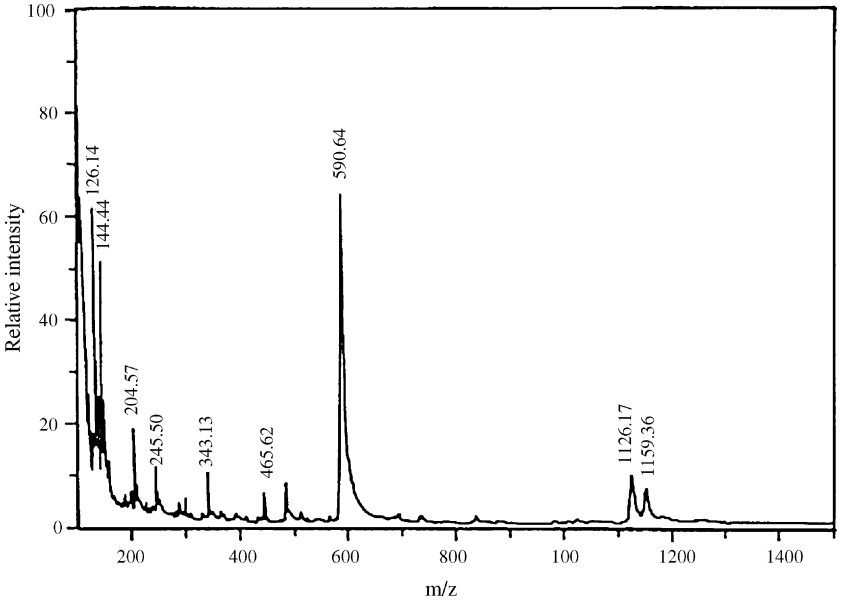


Fig. 2. MALDI TOF mass spectrum of TBTEAPB catalyst.

firmed by MALDI TOF mass for $[C_{75}H_{126}N_6O_3]^{6+}$ ion; the obtained experimental value is 1159.36 and the calculated theoretical value is 1159.59 (Fig. 2). Finally, the formation of six quaternised ammonium cation sites was confirmed by the chloride ion analysis by the Volhard method showing 15.15 mequiv. g^{-1}, the expected value being 15.20 mequiv. g^{-1}.

In order to inspect the catalytic behavior of the new six-site MPTC viz., TBTEAPB catalyst, the alkylation of α-pinene with epichlorohydrin was carried out and the pseudo-first order rate constant was calculated by measuring the disappearance of α-pinene through gas chromatography. The formation of monoalkylated product viz., 2-(6,6-dimethyl-2-methylene-bicyclo[3.1.1]hept-3-ylmethyl)oxirane as well as diol 3-(6,6-dimethyl-2-methylene-bicyclo[3.1.1]hept-3yl)propane-1,2-diol product was confirmed by isolating the products. The effect of various experimental parameters such as stirring speed, [catalyst], [substrate], [sodium hydroxide] and temperature, on the reaction rate constant was studied and, the results are discussed.

3.1. Effect of varying stirring speeds

The effect of varying the stirring speed on the rate of C-alkylation of α-pinene with epichlorohydrin was studied in the range 100–700 rpm. The observed rate constant reveals that the rate of the reaction increases on increasing the stirring speed and becomes saturated at higher rpm. That is, to start with, the observed rate constant gradually increased from 100 to 300 rpm and then there is a sharp increase at 400–500 rpm (Fig. 3). Further increase in speed does not alter the reaction rate. This type of observation on stirring speed is well documented in early studies [38–41] and an interfacial mechanism was proposed. Similar observation was also reported by Starks and Owens [42] in PTC facilitated cyanide displacement reaction on 1-chlorooctane and strongly proved that the reaction proceed by the extraction mechanism. The sharp increase in rate constant at 400–500 rpm must be the contribution of effective mass transformation of Q^+OH^- ion pair. The rate constant is dependent on the stirring speed up to 500 rpm and becomes constant beyond 500 rpm, proving that further increase in rpm does not increase the transformation of Q^+OH^- ions to organic phase. It has been shown that the activity of the ammonium catalyst depends on the degree of exchange of Q^+Cl^- into Q^+OH^- in the aqueous phase and simultaneously abstraction of proton from α-pinene. Similar observations are already reported in literature [43]. Starks [43], Herriott and Picker [44] and Freedman and Dubois [45] also reported analogous effects using quaternary ammonium and phosphonium/ammonium ions respectively. Particularly, Herriott et al. observed that increasing the stirring speed from 200 to 2200 rpm had no effect on the reaction rates, and that at a lower speed (<50 rpm) negligible amount of product was noted and hence they have simply carried out the reaction by fixing the optimum speed in the range of 1000–1500 rpm. Freedmann et al. observed that the rate constants were increased with increasing stirring speed and maximized at 800 rpm. Further increase in stirring speed does not enhance the rate constant. In contrast, the present TBTEAPB catalyst could facilitate the alkylation to saturation even at 500 rpm providing the strong evidence for the confirmation of multi-active sites.

3.2. Effect of varying substrate concentration

Kinetic experiments were performed by varying the substrate concentration [4.71–20.42 mM] and keeping other parameters such as [MPTC], [epichlorohydrin] [NaOH] and temperature (40 °C) constant. The pseudo-first order rate constants were evaluated from the linear plots of $\log(a-x)$ versus time. The observed rate constants increase with increasing [substrate] (Fig. 4). The increase in the rate con-

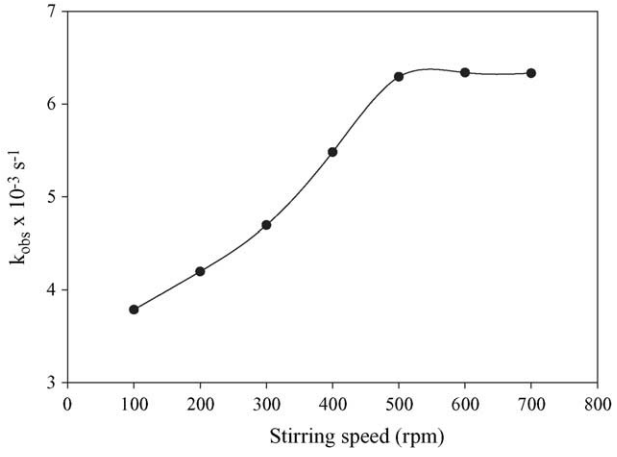


Fig. 3. Effect of stirring speed.

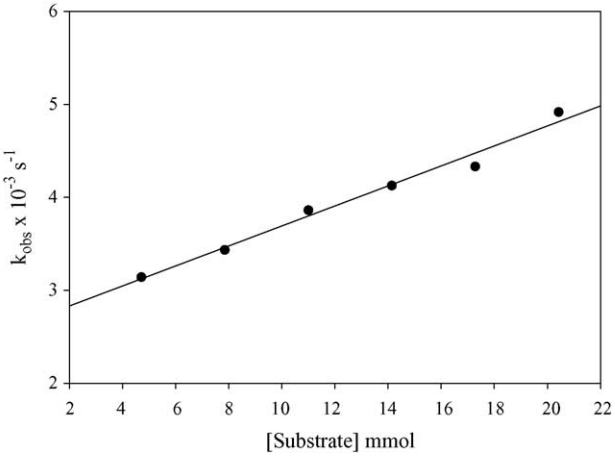


Fig. 4. Effect of substrate amount on the observed rate constant.

stant even at higher concentrations of substrate may be attributed to the proportionate increase in the number of catalytic active sites available in the MPTC catalyst. Though the rates of the concentration of substrate (4.71–20.42 mM) and catalyst (3.00×10^{-4} mM) was fixed with wide difference, the rate constant was found to increase remarkably even with respect to low [MPTC], explaining the presence and participation of multi-catalytic site. Balakrishnan et al. [46] reported a similar trend with lower rate constants in the study of C-alkylation of phenylacetone with *n*-bromobutane using triethylbenzylammonium chloride as a PTC.

3.3. Effect of varying catalyst concentration

The pseudo-first order constant for the alkylation of α-pinene has been determined by varying the MPTC concentration in the range 2.0×10^{-4} to 4.0×10^{-4} mM with the other parameters constant. The observed rate constants were found to be proportional to [catalyst]. The rate constant is found to increase with increasing [MPTC] (Fig. 5). The increase in rate constants should be due to the presence of a large number of active sites on MPTC.

Control experiments were also performed and no product was found even after 1 h of reaction. The minimum catalyst concentration required in order to obtain total conversion of reactant into product **3** is estimated to be 2.0×10^{-4} mM for 4.71 mM of α-pinene. Molinari et al. [47] observed a similar dependence of pseudo-first order rate constant using phosphonium ion as PTC for Br-I exchange reaction of 1-bromooctane. A bilogerthmic plot of the rate constants versus the concentration of the catalyst gave a straight line with a slope value of 0.5 (Fig. 5). Halpern et al. [48] reported a similar observation for dehydrobromination of phenethyl bromide in the presence of tetraoctylammonium bromide as a PTC under zero order kinetics. Analogous studies reported in the literature reveals that the rapid increase in the rate of the reaction even at very low concentrations of catalyst may be due to the cooperative influence of two-cationic ammonium active sites on the catalyst [49].

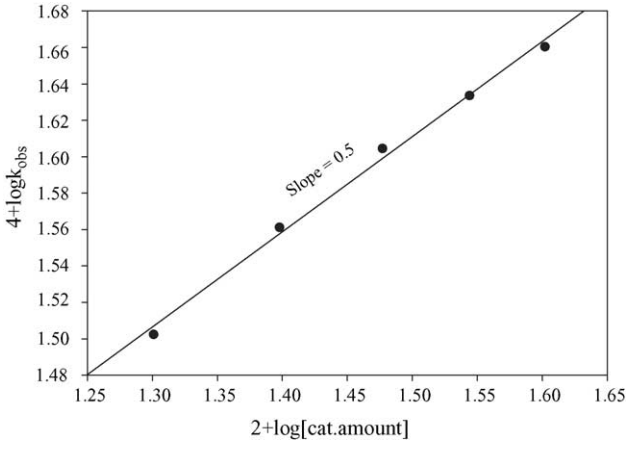


Fig. 5. Effect of catalyst concentration on the observed rate constant.

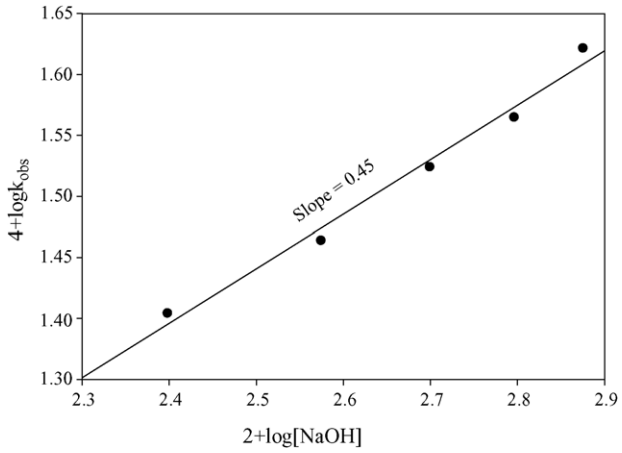


Fig. 6. Effect of [NaOH] on the rate constant.

3.4. Effect of sodium hydroxide

Kinetic experiments were performed by varying the concentration of NaOH in the range 2.78–10.71 M with the other experimental parameters kept constant. A bilogerthemic plot of the reaction rate against sodium hydroxide concentration gives a straight line with a slope of 0.45 (Fig. 6). The observed rate constants increases with increase in [OH^-]. This may be due to the very high activity of OH^- arising from the high OH^- concentration as well as a low solvation by water. This should lead to a significant proton abstraction from α-pinene, producing water molecules to easily hydrolyze the epoxide product and the diol as a secondary by product. Hence, the optimum [OH^-] for C-alkylation of α-pinene with epichlorohydrin using MPTC as a catalyst was found to be 20% NaOH (W/W). Furthermore, lower [NaOH] is always of specific interest in industry as there is a scope for easy reaction workup and durability of the reaction vessels and particularly harmless to the environment.

3.5. Thermodynamic parameters for the alkylation of α-pinene

The effect of temperature was studied in the range between 30 and 50 °C keeping other parameters constant. The observed pseudo-first order rate constants are found to increase with increase in temperature. The energy of activation (E_a) is calculated from Arrhenius plot and found to be 7.1 kcal mol^{-1} (Fig. 7). The other thermodynamic parameters viz., $\Delta S^{\#}$, $\Delta G^{\#}$ and $\Delta H^{\#}$ were also evaluated and found to be −33.7, 13.5 and 0.41 kcal mol^{-1}, respectively. Earlier studies report the activation energy for the dehydrobromination of (2-

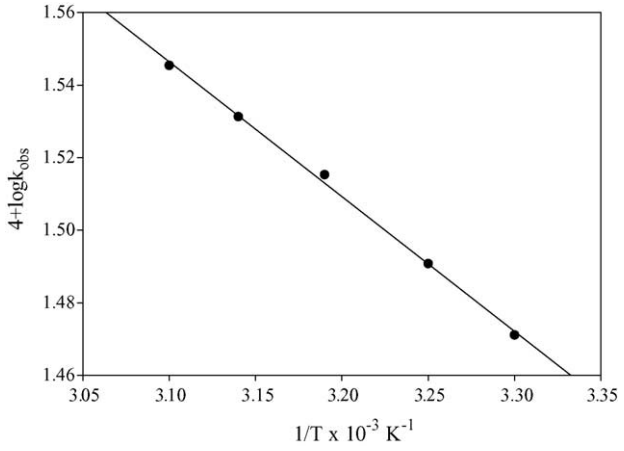


Fig. 7. Arrhenius plot.

bromoethyl)benzene using tetraoctylammonium bromide as PTC to be 8 kcal mol^{-1}; based on this E_a value, they proposed an extraction mechanism for the reaction [50]. The lower values of activation energy and negative $\Delta S^{\#}$ for the alkylation of α-pinene reaction indicate that the step (2) (i.e. chemical reaction) is not the rate determining step. The results are characteristic of mild diffusion control till 100–300 rpm and at a given temperature and at stirring speed, there should be a definite effective mass transfer between the aqueous and organic phases. Lee et al. [51] reported a similar study viz., the effect of temperature on the reaction rate for the formation of phenyl benzoate in the presence of tetrabutylammonium bisulfate ($TBAHSO_4$) as PTC and in the absence of PTC; the activation energies were reported as 3.6 kcal mol^{-1} for tetrabutylammoniumbisulfate phase transfer catalyst and 8.1 kcal mol^{-1} without PTC and confirmed that the reaction proceeded via an extraction mechanism. The observed energy of activation for the C-alkylation of α-pinene (7.1 kcal^{-1} mol^{-1}) is also in agreement with the reported values and hence reaction should proceed through the hydroxide ion extraction mechanism.

3.6. Assessment of the merits of the multi-site PTC over single and di-site PTCs

The pseudo-first order rate constants for the reaction of C-alkylation of α-pinene with epichlorohydrin have been determined to investigate the relative catalytic efficiency of various commercially available soluble single-site PTCs viz., triethylbenzylammonium chloride (TEBAC), triethylbenzylammonium bromide (TEBAB), tetrabutylammonium bromide (TBAB), tetrabutylammonium chloride (TBAC) and newly synthesized di-site PTCs such as 4-[2,2′-bis(*N*-triethylammoniummethylene chloride)eth-1-ene]phenol (BTAMP-DPTC I) and 4-(2,2′-bis(*N*-triethylammoniummethylene chloride)eth-1-ene)phenoxymethyl)benzene (BTAMPB-DPTC II)] along with MPTC. The reaction was carried out under identical experimental conditions using all these catalysts individually. It is observed that MPTC is almost three times more active than the di-site PTCs (entries 5, 6, 7, Table 1) and also six times more active than the commercially available single-site PTCs (entries 1-4, 7, Table 1) as evidenced by a three- and six-fold enhancement in rate constant for TBTEAPB over the di-site/single-site. That is, the rate of the reaction is linearly related to the each active sites (quaternary ammonium ions) present in permolecule. This observation proves that in MPTC all the catalytic sites independently influenced in the C-alklylation reaction.

Table 1
Comparative rate constants of assessment for the merits of the multi-site PTC over single and di-site PTCs

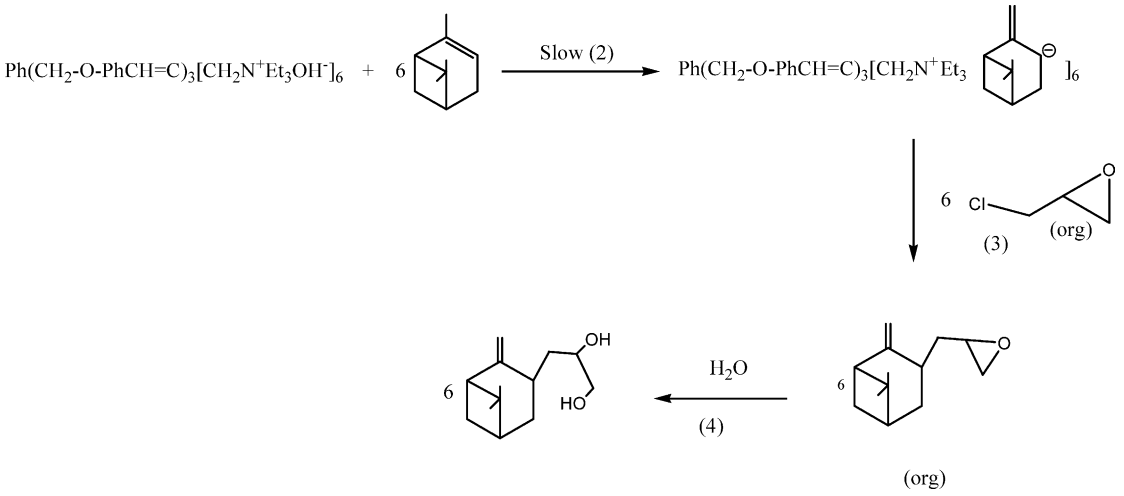
Sl. no.	Name of the catalyst	$k_{obs} \times 10^{-3}$ s^{-1}
1	TEAC	0.8639
2	TEAB	0.9878
3	TEBAC	1.0063
4	TEBAB	0.9901
5	BTAMP (DPTC I)	1.9878
6	BTAMB (DPTC II)	2.3052
7	MPTC	6.2598

3.7. Mechanism

The C-alkylation of α-pinene appears to proceed by a two-step pathway. The mode of the addition of substrate into the reaction flask appears to have a significant role. Generally, earlier studies related to the alkylation of α-pinene, explained that the anion of the substrate is first generated through abstraction of proton using Q^+OH^- species and later the addition of epichlorohydrin leads to dissociation into anions and cations and the cationic species react with the carbonanion of α-pinene to form an alkylated epoxide product.

So far, in literature two types of mechanisms have been proposed frequently for phase transfer catalyzed reactions viz., extraction mechanism [43] by Stark's and interfacial mechanism [52] by Makosza's. Increased rates with increased organophilicity or with larger symmetrical ammonium ions [53,44,54], independence of reaction rate with respect to stirring speed [53,44,54] and linear dependence of reaction rate on [catalyst] confirm that the reaction should proceed via., extraction mechanism. Interfacial mechanism is strongly dependent on stirring speed (rpm), maximum reactivity with relatively hydrophilic triethylammonium ions [55–57] and fractional order with respect to the catalyst are the parameters for confirmation of interfacial mechanism. In the present study, from the observed experimental results, i.e. dependence of the rate constant on the stirring speed beyond 500 rpm, dependence on [catalyst], [hydroxide ions], temperature and lower E_a value we conclude that the alkylation of α-pinene should proceed via., hydroxide ion extraction mechanism.

$$\underset{\text{(aq./org.)}}{\mathrm{Ph(CH_2{-}O{-}(PhCH=C)_3[CH_2N^+Et_3Cl^-]_6}} + 6\mathrm{NaOH} \overset{(1)}{\rightleftharpoons} \underset{\text{(aq./org.)}}{\mathrm{Ph(CH_2{-}O{-}PhCH=C)_3[CH_2N^+Et_3OH^-]_6}} + 6\mathrm{NaCl}$$



4. Conclusion

We have successfully synthesized the new soluble MPTC viz., 1,3,5-tris(4-(2,2′-bis(*N*-triethylammoniummethylene chloride)eth-1-ene)phenoxymethyl)benzene (TBTEAPB) containing six active sites in a molecule through a simplified five step method. The attachment of **6** with **7** through condensation reaction is the key step for the whole reaction scheme. The blocking of **6** and **7** were confirmed through the appearance of C–O bond stretching at 1100 cm^{-1} in FT-IR, the formation of methylene proton (–CH_2–O–) singlet at 5.15 ppm in ^{1}H NMR and also the peak at 46.7 ppm in ^{13}C NMR techniques. Similarly the quaternization of –CH_2Cl in compound **8** was also confirmed through the appearance of C–N bond stretching at 1173 cm^{-1} in FT-IR and chloride ion analyses. The chloride ion concentration was found to be 15.15 mequiv. g^{-1} (theoretical value 15.20 mequiv. g^{-1}) for compound **9**. Further the catalytic efficiency of the catalyst was studied by the C-alkylation of α-pinene with epichlorohydrin. Two different di-site PTCs were also synthesized with the same environment as six-site PTC. These di-site, single-site PTCs and MPTC were also employed for C-alkylation under identical reaction conditions. The trend observed by relative rate constants of all the catalysts showed that the efficiency of TBTEAPB is ≅3 times as high as the di-site PTCs and ≅6 times as high as the single-site PTCs. This observation proves the presence of six-sites in the TBTEAPB catalyst.

The observed various pseudo-first order rate constants were found to be proportional to experimental parameters such as the stirring speed, [substrate], [catalyst], [sodium hydroxide] and temperature. The reaction was facilitated even under mild base (20% w/w) and lower MPTC (2.0×10^{-4} mM) concentrations. The E_a value and other thermodynamic parameters such as $\Delta S^{\#}$, $\Delta G^{\#}$, and $\Delta H^{\#}$ were also evaluated and found to be 7.1, −33.7, 13.5 and 0.41 kcal mol^{-1}, respectively. Based on the kinetic results, an extraction mechanism is proposed for the C-alkylation of α-pinene.

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