New 'multi-site' phase transfer catalyst for the addition of dichlorocarbene to styrene

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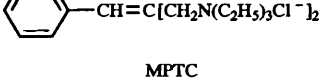
The kinetics of dichlorocarbene addition to styrene has been studied under phase transfer catalytic conditions using aqueous sodium hydroxide as the base and 2-benzylidine-*N*,*N*,*N*,*N*′,*N*′,*N*′-hexaethylpropane-1,3-diammonium dichloride as a new 'multi-site' phase transfer catalyst. The reaction was carried out at 40 °C under pseudo-first order conditions by keeping aqueous sodium hydroxide and chloroform in excess and was monitored by GC. The effect of various experimental parameters on the rate of the reaction has been studied and based on the results obtained, a suitable mechanism is proposed.

Introduction

Phase transfer catalysis is one of the most attractive new techniques in organic synthesis.[1,2] The method has a very broad scope of application. Chemically, the possibilities include the preparation 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 soluble 'single-site' phase transfer catalysts (PTCs) 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 PTC specifically on the industrial scale. In order to satisfy these needs more effectively, novel 'multi-site' phase transfer catalysts have been developed. Idoux *et al.*[3] synthesised 'multi-site' phosphonium PTCs as soluble and polymer-supported catalysts. The efficacy of the catalytic abilities of these 'multi-site' PTCs towards simple Sn2 reactions and some weak nucleophile–electrophile SnAr reactions were reported. In general, 'multi-site' PTCs offer the potential of providing greater PTC activity and to effect a particular synthetic transformation under mild conditions.

Dihalocyclopropanes are very useful compounds that can be reduced to cyclopropane derivatives, treated with magnesium or sodium to give allenes and can be converted to a number of other products.[4] Literature reports of the generation and reaction of dichlorocarbene stress the necessity of operating under strictly anhydrous conditions, because of the ready and rapid hydrolysis of dichlorocarbene. Many of these difficulties are eliminated when the reactions are carried out in biphase systems of concentrated sodium hydroxide in the presence of 'single-site' PTCs; quaternary ammonium 'multi-site' PTCs are more effective. Similar studies employing PTCs for the generation of dichlorocarbene have been reported earlier by several authors.[5–8]

The synthesis of 'multi-site' PTCs of the ammonium type have not been explored in contrast to the 'single-site' PTCs. We have synthesised and characterised a novel 'multi-site' PTC, *viz.*, 2-benzylidine-*N*,*N*,*N*,*N*′,*N*′,*N*′-hexaethylpropane-1,3-diammonium dichloride (MPTC) and studied its utility in some hydroxide ion initiated reactions.

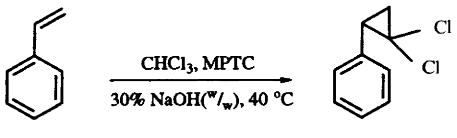

$C_6H_5CH{=}C[CH_2\overset{+}{N}(C_2H_5)_3Cl^-]_2$

MPTC

Improved yields of products were observed using the new MPTC as compared to those catalysed by a 'single-site' PTC (namely triethylbenzylammonium chloride) under identical conditions. In this paper, we report a kinetic study of dichlorocarbene addition to styrene (double bond) using the new water soluble MPTC and also propose a suitable mechanism.

Results and discussion

The kinetic experiments (followed by GC) of the dichlorocarbene addition to styrene were carried out under pseudo-first order conditions, taking chloroform and 30% aq. NaOH in excess, at 40 °C (Scheme 1).



Scheme 1 Dichlorocarbene addition to styrene under phase transfer catalytic conditions

Effect of varying stirring speed

The effect of varying the stirring speed on the rate of dichlorocarbene addition to styrene reaction using MPTC was studied in the range of 0–700 rpm. The rate of the reaction increases on increasing the stirring speed. The effect of varying the stirring speed is well documented[1,6,9] for interfacial mechanisms which are transfer rate limited (the rate constant increases with stirring) below a given stirring speed (600–800 rpm) and intrinsic reaction rate limited (the rate constant is nearly a constant) above this stirring speed. Similar behaviour is displayed by reactions with a real 'phase transfer' (Starks' extraction mechanism) but with a much smaller limit of stirring speed between physical and chemical control (100–300 rpm). Thus the observed rate constants are strongly mass transfer dependent and the kinetics of the reaction is independent of the mass transfer-limited domain. The rate constants of the reaction increase as stirring speed increases and levels off to a constant value above the optimum stirring speed (500 rpm). Therefore Fig. 1 is indicative of an interfacial mechanism not of a real 'phase transfer' mechanism. In a generally accepted phase transfer catalysis, irrespective of the mechanism (interfacial or real 'phase transfer'), the reaction rate constant becomes dependent on the stirring speed only below a given limit of stirring speed, the value of which depends on the nature of the mechanism.

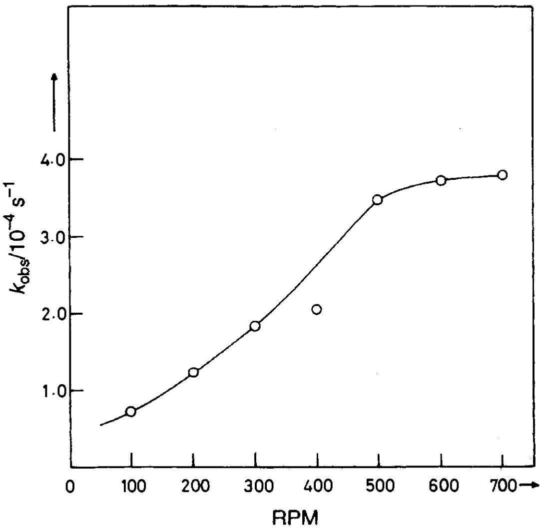


Fig. 1 Effect of variation of stirring speed

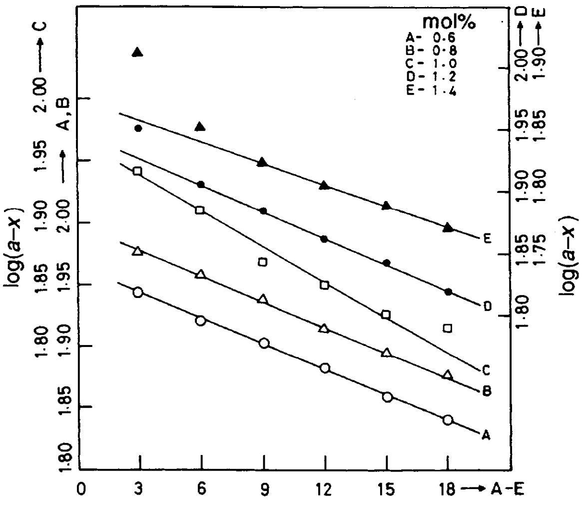


Fig. 2 Effect of variation of catalyst amount

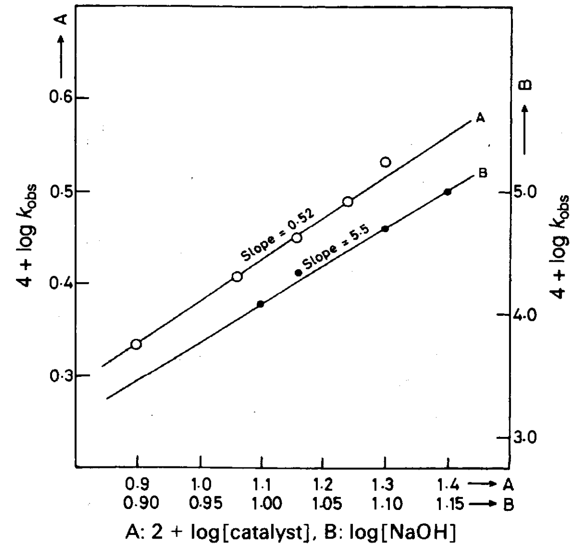


Fig. 3 Effect of catalyst amount and [NaOH] on the observed rate constant

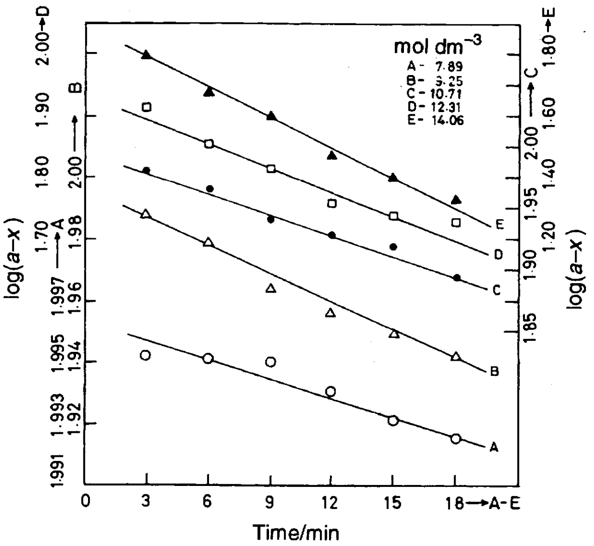


Fig. 4 Effect of variation of [NaOH]

Effect of varying catalyst amount

The effect of catalyst amount on the rate of dichlorocarbene addition reaction to styrene was studied in the range 0.6–1.4 mol% of the catalyst (based on the substrate amount). The rate constant of the reaction is proportional to the amount of catalyst added (Fig. 2). Control experiments were carried out and there is absolutely no reaction even after three hours of stirring. The linear dependence of reaction rate constants on catalyst concentration shows that the reaction is believed to proceed through the extraction mechanism. A bilogarithmic plot of the reaction rate *versus* the concentration of the catalyst gives a straight line over a wide range of concentration. The slope of 0.5 for dichlorocarbene addition to styrene (Fig. 3) was found to be identical with the slope of the same reaction reported by Balakrishnan *et al.*[10] in the presence of a 'single-site' PTC (triethylbenzylammonium chloride). This suggests that the chemical reaction between the ion-pair and the organic substrate is not the sole rate-determining step.

The foregiven observations enable us to predict that the carbanions formed cannot leave the phase boundary to go into the organic phase since their counter ions Na^+ are strongly solvated in the aqueous phase and poorly in the organic phase. In this state, the carbanions are very unreactive being able to react only with strong electrophiles. The 'multi-site' quaternary ammonium cations serve as a source of organic cations to form the organic phase-soluble ion pairs with carbanions, thus transferring them into the organic phase for further transformation. The remarkable increase in yield of the dichlorocarbene adduct reflects the ability of the quaternary salt to cause $:CCl_2$ to be generated in or transferred to the organic phase, where its reaction rate with substrate is much greater than with water as reported by Starks in the study of dichlorocarbene addition to cyclohexene using tridecylmethylammonium chloride.[11]

Effect of varying substrate amount

Kinetic experiments were performed by varying the substrate amount ranging from 6.52 to 21.75 mmol, maintaining other reactants such as chloroform and 30% w/w NaOH in excess. Pseudo-first order rate constants are obtained from the linear plots of log ($a - x$) *versus* time. The observed rate constants decrease as the [substrate] increase. It is clear from Table 1 that the molar ratio of substrate to catalyst increases considerably for small increments in substrate amount. The decrease in rate

Table 1 Effect of variation of substrate amount

Entry	Substrate amount/mmol	Substrate : Catalyst	$k_{obs}/10^{-4}$ s^{-1}
A	6.5	74.97	11.13
B	8.7	100.03	3.49
C	13.1	150.05	3.08
D	17.4	200.07	2.91
E	21.8	250.66	2.73

Table 2 Effect of variation of [NaOH]

Entry	[NaOH]/mol dm^{-3}	$k_{obs}/10^{-4}$ s^{-1}
A	7.89	0.07
B	9.25	1.16
C	10.71	2.10
D	12.31	4.91
E	14.06	11.78

constants may be attributed to the decrease in the ratio of the number of active sites of the catalyst to the corresponding amount of substrate present.

Effect of varying the sodium hydroxide concentration

The reaction rates were measured in the range 7.89–14.06 mol dm^{-3}. The rate constants of dichlorocarbene addition strongly depend on the concentration of sodium hydroxide.[12] The rate constants were found to increase with an increase in sodium hydroxide concentration (Table 2 and Fig. 4). A bilogarithmic plot of the reaction rate against sodium hydroxide concentrations gives a straight line having a slope of 5.5 (Fig. 3). This may be attributed to the fact that hydroxide ions are less solvated by water molecules and thereby the activity of hydroxide ion increases. In the reaction dichlorocarbene addition to styrene using triethylbenzylammonium chloride and 40% NaOH was employed whereas 30% NaOH is the optimum concentration used in the present study. A lower amount of NaOH is of specific interest in industry as there is a scope of easy reaction workup and durability of the reaction vessels.

Effect of temperature variation

The effect of varying temperature on the rate of dichlorocarbene addition reaction to styrene was studied in the temperature range 20–40 °C. The kinetic profile of the reaction is obtained by plotting log $(a - x)$ *versus* time. The rate constants increase with the increase in temperature. The energy of activation is calculated from an Arrhenius plot, $E_a = 15.07$ kcal mol^{-1} (Fig. 5). The other thermodynamic parameters, $\Delta S^\ddagger$, $\Delta G^\ddagger$ and $\Delta H^\ddagger$, were evaluated from an Eyring plot as -25.11 cal K^{-1} mol^{-1}, 21.99 kcal mol^{-1} and 14. 47 kcal mol^{-1} respectively.

The activation energy of intraparticle diffusion of anion exchange resins in aqueous solutions is of the order of 5–10 kcal mol^{-1}.[13] The activation energy for the dehydrobromination of (2-bromoethyl)benzene in the presence of tetraoctylammonium bromide was reported to be 8 kcal mol^{-1} and for this an extraction mechanism was proposed.[14]

A higher E_a value and a less negative $\Delta S^\ddagger$ suggest that a contribution of intrinsic reactivity limitations is more than that of intraparticle diffusion limitations. A higher E_a value has been reported[15] for the polystyrene bound trimethylammonium ion catalysed reaction, which was controlled by strict intrinsic reactivity under triphase conditions. The activation energy for the heterogenous ethylation of phenylacetonitrile was reported to be 20 kcal mol^{-1} and for this an interfacial mechanism was proposed.[16] The observed energy of activation for dichlorocarbene addition to styrene is 15.07 kcal mol^{-1} and hence we conclude, since the intraparticle diffusion is minimised at 500 rpm, that intrinsic reactivity is the rate limiting step.

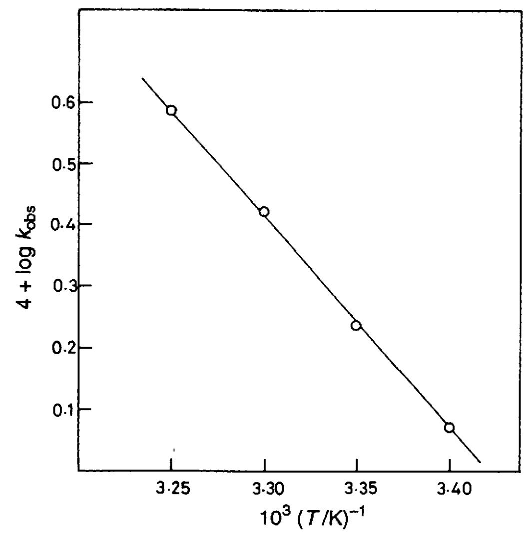


Fig. 5 Arrhenius activation energy

Comparison of reaction rate constants

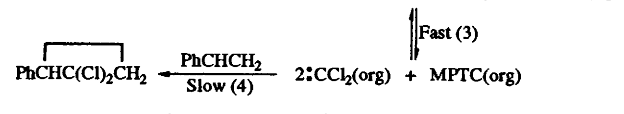
The reaction, dichlorocarbene addition to styrene, has been chosen to investigate the comparitive reactivities of three different catalysts, *viz.*, 'multi-site' PTC (MPTC), soluble 'single-site' PTC [triethylbenzylammonium chloride (TEBA)] and polymer-bound 'single-site' [triethylbenzylammonium chloride (2% cross-linked, 200 mesh, 18–20% ring substitution)].[17]

Based on the observed rate constants, it is evident that the MPTC is 37% and 95% more active than the 'single-site' TEBA and polymer-bound TEBA respectively (Table 3). The much lower rate constants obtained on using polymer-bound catalyst were attributed to the diffusional limitations of the rates under triphase conditions.[18]

Mechanism

Haloform treated with concentrated aq. sodium hydroxide and a quaternary ammonium salt, Q^+X^- (as a PTC) generates trihalomethyl anion which further splits into dichlorocarbene.[19] The selectivities of dichloro- and dibromo-carbenes (generated under PTC conditions) towards alkenes are independent of the structure of catalysts. This indicates that free $:CX_2$ is involved in all cases inspite of the fact that there is a strong catalyst influence on the reaction path starting from $CX_3^- \rightleftharpoons :CX_2$.[20]

The generation and reaction of carbene with styrene may be represented as Scheme 2.



Scheme 2 Mechanism for the dichlorocarbene addition to styrene under PTC conditions

According to Starks' extraction mechanism, it was thought that the hydroxide ion may be extracted from an aqueous

Table 3 Comparison of k_{obs} using different phase transfer catalysts[a]

Entry	Catalyst	Amount (mol%)	$k_{obs}/10^{-4}$ s^{-1}
A	None	None	Nil[b]
B	MPTC	1.0	4.013
C	TEBA	1.0	2.509
D	Polymer-bound TEBA	1.0	0.207

[a] The reaction conditions employed are 30% w/w aq. sodium hydroxide, 500 rpm stirring speed and 1.5 cm^3 styrene. All the reactions were carried out at 40 °C. [b] No conversion after 3 h.

reservoir into an organic phase with the help of quaternary onium cations. Makosza and Bialecka proposed[21] an alternative mechanism for dichlorocarbene addition reactions in which deprotonation of the organic substrate by the hydroxide ion occurs at the interface. According to this mechanism, the role of catalyst is to remove the resulting organic anion from the interface into the bulk organic phase for subsequent reaction. Several studies[16,22] have provided support for various aspects of Makosza's mechanism.

It has been established by Makosza and Fedorynski[23] that the slowest reaction is the addition of :CCl$_2$ to alkenes, considering the other steps as fast equilibrium processes. In our study, a fractional order with respect to catalyst concentration suggests that the step (2) is not the sole rate-determining one and that of the chemical reaction in the organic phase is also rate-determining. The effects of other experimental results such as stirring speed, sodium hydroxide concentration and temperature over the observed rate of the reaction support the interfacial mechanism proposed by Makosza for the PTC/OH$^-$ systems rather than Starks' extraction mechanism.

Experimental

General

^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a JEOL-GSX-400 NB FT-NMR spectrometer with Me$_4$Si as internal standard. Mass spectra and HRMS were obtained on a Finnigan mat 8230 mass spectrometer. Elemental analysis was carried out on a Heraeus-CHN-Rapid Analyser and IR spectra were measured on a Perkin-Elmer model 983 IR spectrophotometer.

1-Phenyl-2,4,8,10-tetraoxaspiro[5.5]undecane

A 500 cm^3 capacity three-necked round bottomed flask was fitted with a mercury seal and efficient stirrer. Acetophenone (30.9 g, 0.255 mol), formaldehyde (37–41% solution) in excess and water (150 cm^3) were placed in the flask and the mixture was stirred well. Calcium oxide (8 g) dissolved in water (40 cm^3) was added in small portions. The reaction was carried out at 60 °C for 5 h. To the cold reaction mixture, 50% ice-cold H$_2$SO$_4$ was added until the filtered sample gave no precipitate. It was reduced to one-third volume by steam distillation. The viscous liquid was extracted with chloroform and dried over anhydrous MgSO$_4$. The title spiroundecane was collected at 165 °C/1.5 mmHg by vacuum distillation, yield 58%, mp 86 °C; δ_H 3.35–5.15 (m, 11 H, CH$_2$, CH) and 7.05–7.25 (m, 5 H, Ar); δ_C 36.806 (s), 66.390 (t), 69.699 (t), 71.091 (t), 82.768 (d), 94.107 (t), 94.547 (t), 127.0 (d), 128.0 (d), 128.2 (d) and 135.97 (s); ν_{max}/cm^{-1} 3010, 2880, 1580 and 960; m/z 236 (66%, M$^+$), 107 (100), 91 (37), 77 (74) and 31 (19) (Found: 236.102 87. C$_{13}$H$_{16}$O$_4$ requires 236.104 86).

1,1-Bis(chloromethyl)-2-phenylethene

1-Phenyl-2,4,8,10-tetraoxaspiro[5.5]undecane (6 g, 0.254 mol) was placed in a 150 cm^3 single-necked round-bottomed flask, 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 homogenous (TLC) (R_f 0.9, hexane) and was purified using column chromatography on silica gel. A clear colourless liquid was obtained in 48% yield; δ_H 4.30 (d, J = 4 Hz, 4 H, CH$_2$), 6.75 (t, J = 4 Hz, 1 H, –CH=) and 7.2–7.6 (m, 5 H, Ar); δ_C 40.343 (t), 47.249 (t), 128.199 (d), 128.609 (d), 133.754 (s), 134.377 (d) and 135.954 (s); ν_{max}/cm^{-1} 3040, 3000, 1648, 1491, 1443, 928 and 700; m/z 200 (30%, M$^+$), 165 (60), 129 (100), 128 (60) and 115 (30) (Found: 200.014 41. C$_{10}$H$_{10}$Cl$_2$ requires 200.015 95).

2-Benzylidine-*N*,*N*,*N*,*N*′,*N*′,*N*′-hexaethylpropane-1,3-diammonium dichloride (MPTC)

1,1-Bis(chloromethyl)-2-phenylethene (2 g, 0.01 mol) was dissolved in dry acetonitrile (10 cm^3) and transferred into a 150 cm^3 three-necked round-bottomed flask. The solution was deaerated and triethylamine (20 cm^3), dissolved in acetonitrile (10 cm^3) was added to the solution. The resultant mixture was gently refluxed for 5 h under an inert atmosphere (N$_2$). To the cold reaction mixture diethyl ether (20 cm^3) was added and a precipitate was collected after 2 h. Then the precipitated 'multi-site' quaternary ammonium salt was filtered and washed repeatedly with ether (3 times). The pure white, solid MPTC was stored in a CaCl$_2$ desiccator. It was found to be highly hygroscopic; yield, 95%, 3.9 g; δ_H 1.05–1.6 (m, 18 H, CH$_3$), 3.1–4.9 (m, 16 H, CH$_2$) and 7.4–7.9 (m, 6 H, vinylic, Ar); δ_C 8.406 (q), 8.573 (q), 45.731 (t), 53.245 (t), 53.670 (t), 56.144 (t), 118.226 (s), 128.973 (d), 129.428 (d), 129.611 (d), 134.346 (d) and 154.717 (s); ν_{max}/cm^{-1} 3000, 2960, 2880, 1630, 1450 and 1170 (Found: N, 6.93. C$_{22}$H$_{40}$Cl$_2$N$_2$ requires 6.94%).

Kinetic measurements

The kinetic experiments were performed in an ordinary smooth-wall 150 cm^3 three-necked flask fitted with flat-bladed stirring paddle and reflux condenser. All ingredients, *viz.*, 20 cm^3 30% w/w NaOH (10.71 mol dm^3), 35.90 mg of the 'multi-site' phase transfer catalyst (1.0 mol% based on the substrate amount) and 10 cm^3 (124.98 mmol) chloroform (solvent) were added. The contents were conditioned for about 10 min at 40 °C before initiating the reaction. The reaction mixture was stirred very slowly by a mechanical stirrer. Styrene (1.5 cm^3) preheated to 40 °C was added to the reaction mixture. The stirring speed was adjusted to 500 rpm, by using a tachometer (Teclock, Japan). Phase separation was almost immediate after the stirring was stopped. Samples were collected from the organic layer at regular intervals of time. A pinch of anhydrous CaCl$_2$ was placed in the sample vials to absorb any moisture present in the organic layer. Samples were analysed using a GC (Varian 3700 Model), with flame ionization detector and using 5% SE-30, Chrom WHP 80/100, 2 m 1/8 in stainless steel column. The reaction was followed by estimating the disappearance of styrene. The retention time for chloroform (0.57 min), styrene (1.35 min), 1-phenyl-2,2-dichlorocyclopropane (3.91 min) were obtained by employing auto linear temperature programming (ALTP) 80 °C/01/20/180 °C/01. The pseudo-first order rate constants were evaluated from the plot of log $(a - x)$ *versus* time. The reaction was followed up to 50% conversion.

Acknowledgements

The authors are grateful to CSIR, New Delhi, for the award of Senior Research Fellowship to J. P. J.

References

1 E. V. Dehmlow and S. S. Dehmlow, in *Phase Transfer Catalysis*, Verlag, Weinheim, 1993.

2 C. M. Starks, C. L. Liotta and M. Halpern, in *Phase Transfer Catalysis*, Chapman, New York, 1994.
3 J. P. Idoux, R. Wysocki, S. Young, J. Turcot, C. Ohlman and R. Leonard, *Synth. Commun.*, 1983, **13**, 139.
4 W. Kirmse, in *Carbene Chemistry*, Academic Press, New York and London, 1971.
5 E. V. Dehmlow, *Tetrahedron Lett.*, 1976, 91.
6 M. Rabinovitz, Y. Sasson and M. Halpern, *J. Org. Chem.*, 1983, **48**, 1022.
7 A. Brandstrom and V. Junggren, *Acta Chem. Scand.*, 1969, **23**, 2204.
8 E. J. Fendler and J. H. Fendler, *Adv. Phys. Org. Chem.*, 1970, **8**, 271.
9 W. P. Reeves and R. G. Hilbrich, *Tetrahedron*, 1976, **32**, 2235.
10 T. Balakrishnan, T. K. Shabeer and K. Nellie, *Proc. Indian Acad. Sci. (Chem. Sci.)*, 1991, **103**, 785.
11 C. M. Starks, *J. Am. Chem. Soc.*, 1971, **93**, 195.
12 M. Halpern, Y. Sasson, I. Willner and M. Rabinovitz, *Tetrahedron Lett.*, 1981, 1719.
13 F. Helfferich, in *Ion Exchange*, McGraw Hill, New York, 1962.
14 M. Halpern, Y. Sasson and M. Rabinovitz, *J. Org. Chem.*, 1984, **49**, 2011.
15 M. Tomoi and W. T. Ford, *J. Am. Chem. Soc.*, 1981, **103**, 3821.
16 E. Chiellini, R. Solaro and S. D. Antone, *J. Org. Chem.*, 1980, **45**, 4179.
17 T. Balakrishnan, S. Haribabu and T. K. Shabeer, *J. Polym. Sci., Chem. Ed.*, 1993, **31**, 317.
18 W. T. Ford and M. Tomoi, *Adv. Polym. Sci.*, 1984, 51.
19 M. Fedorynski, W. Ziolkowska and A. Jonczyk, *J. Org. Chem.*, 1993, **58**, 6120.
20 E. V. Dehmlow and U. Fastabend, *J. Chem. Soc., Chem. Commun.*, 1993, **16**, 1241.
21 M. Makosza and E. Bialecka, *Tetrahedron Lett.*, 1977, 183.
22 M. Halpern, Y. Sasson and M. Rabinovitz, *Tetrahedron*, 1982, **38**, 3183.
23 M. Makosza and M. Fedorynski, *Adv. Catal.*, 1987, **35**, 375.

Paper 5/01481F
Received 10*th March* 1995
Accepted 25*th May* 1995
