Chapter VI

Summary
SUMMARY

The present study entitled “Synthesis, characterization of achiral and chiral multi-site phase-transfer catalysts and their applications to various organic reactions” is broadly divided into six chapters.

The first chapter viz., “Introduction” describes the principles of “Phase-transfer catalysis”, historical account of soluble and insoluble PTCs, mechanisms and their applications. Further, this chapter also highlights the necessity for the attention to be paid for the synthesis of both achiral and chiral MPTC’s and literature starting with their existence period until now. The history of chiral sources particularly, “Cinchona alkaloids” and its role in synthesizing different CMPTCs has been described. Much emphasis has been given to document the catalytic applications of achiral and chiral MPTC’s in the selective organic reactions like C-alkylations, additions to olefins, condensations and synthesis of optically active a-amino acids and N-arylaziridines. The kinetic criteria and mechanism operative in PTC system have been extensively discussed.

The second chapter deals with the scope and objectives of the present investigation. This chapter critically discusses the exploration of the recent developments in soluble and insoluble forms of achiral and chiral single-site and MPTC’s and also their applications to different organic reactions. Further, the total plan of the work has been presented point-by-point to explain the whole study without any ambiguity.

The types and nature of the chemicals employed in these studies and their corresponding purification techniques are given in detail in the third chapter viz., “Experimental methods”. The experimental strategies adopted for synthesis of various achiral and chiral MPTC’s are discussed and presented, The analytical
instruments used in the study for the characterization of various ACMPTC’s and CMPTC’s have been described. The kinetic procedures followed in conducting the selected organic reactions using different ACMPTC’s and the procedure for the CMPTC’s catalysed reactions such as asymmetric alkylation of ketimine & aldime and aziridination are described in this chapter.

In the IV Chapter, the obtained experimental results in the form of tables, graphs and spectra are given coherently.

Chapter V presents a thorough discussion towards rationalization of various results. This chapter is divided into two parts viz., Part-I and Part-II. Part-I describes the synthesis, characterization, structural elucidation and significance of various soluble and insoluble ACMPTC’s. Especially, the spectroscopic data for the each ACMPTC’s and their corresponding interpretations are well discussed, It also covers the discussion of the comparative efficacy study of all the ACMPTC’s in four different organic reactions followed by thorough kinetics and mechanistic aspects of three different organic reactions using superior ACMPTC’s. The catalytic function of each ACMPTC in each reaction are logically explained from the pseudo-first order rate constants. The following conclusion may be arrived from Part I of the present investigation.

1. For the first time, we have successfully synthesized 12 different ACMPTCs such as two soluble di-site like DSPTC I, DSPTC II, one soluble tri-site TTEAMCB, two insoluble six-site viz., PTBTEAPMB & PTBTEAPB and also three soluble forms of six-site HTAMCM, TBTEAPMB, TBTEAPB and soluble forms of each one of 10-site, 16-site, 24-site and 32-site.

2. The structures of the each ACMOPTC’s was confirmed through various spectral techniques viz., FT-IR, ‘H-NMR, 13C-NMR, MALDI-TOF, FAB-MS, HRMS (ESI) mass spectral analyses.
3. For the first time in the literature, we have examined the comparative catalytic efficiencies of all the ACMPTC’s through different new organic reactions such as C-alkylation of a-pinene with epichlorohydrin, dichlorocarbene addition to (R)-limonene, Darzen’s condensation to 1,6-dibromohexan-2-one with 4-nonalolide and Michael addition to cyclopentadiene with methylmethacrylate under identical pseudo-first order conditions.

4. The superiority of the ACMPTC’s was ascertained based on the pseudo-first order rate constants of four different organic reactions and found the following order. 32-site > 24-site > 16-site > 10-site > six-site PTBTEAPB (insoluble) > six-site PTBTEAPMB (insoluble) > six-site (HTAMCM) > six-site (TBTEAPMB) > six-site (TBTEAPB) > tri-site (TTEAMCB) > DSPTC II > DSPTC I > PSPTC > TEAC for C-alkylation of a-pinene. Unless it is mentioned, all the ACMPTCs are only soluble in nature. The orders of efficiency for other three reactions are similar but different from the alkylation of a-pinene, i.e., 32-site > 24-site > 16-site > 10-site > six-site PTBTEAPMB (insoluble) > six-site PTBTEAPB (insoluble) > six-site TBTEAPB > six-site HTAMCM > six-site TBTEAPMB > tri-site TTEAMCB > DSPTC II > DSPTC I > PSPTC > TEAC.

5. We have also found that irrespective of the nature and structure of the insoluble ACMPTC’s, they catalysed the reactions with more efficiency than their corresponding soluble analogs. This is because, the increased lipophilicity of these insoluble polymer-supported phase transfer catalysts would facilitate easily the transportation of the reactant from aqueous to organic phase, thereby increasing the reaction rate as compared to their
respective soluble analogs in all the four different organic reactions. This observation indicates that the polymer-supported ACMPTCs can no longer be a constraint to use very often quoting their lower efficiency in the early studies.

6. It is concluded from the studies that though we prepared different types of ACMPTC’s ranging from di-site to 32 site but the enhancement of rate constant observed in higher numbered active site of ACMPTC’s such as 32-, 24-, 16-, and tri-site do not exactly promote the reaction rate in proportion to the number of active sites present in each ACMPTC’s (per molecule) as compared with the single-site PTCs. However, it is shown that there must always be a larger increase in the rate constants irrespective of the ACMPTC’s as compared with their corresponding lower numbered active-site catalysts.

7. It is confirmed that multi-active site present in each ACMPTCs (a molecule) should always enhance its catalytic efficiency (yield) to the larger extent as compared with single-site PTCs and hence the new MPTC’s may definitely reduced the economy of the reaction process.

8. Thorough kinetics for the selected three different organic reactions were also carried out in presence of four different superior six-site ACMPTC’s by maintaining the identical pseudo first order reaction conditions and varying the experimental parameters such as stirring speed, [substrate], [NaOH], [ACMPTC’s] and temperature.

9. Each of the experimental parameters directly influence the rate of the reaction.

10. For the first time in the literature the $E_a$ value and other thermodynamic parameters such as $AS^*$, $AG^*$ and $AH^*$ for all the three reaction are
calculated and presented. Based on these kinetic results, for the first time we have proposed an extraction mechanism for C-alkylation of ot-pinene and intei facial mechanism for other two reactions such as dichlorocarbene addition to (R)-limonene and Michael addition to cyclopentadiene.

Similarly, Chapter V also contains Part-II discussion and is divided into Section-A and Section-B. Section-A explains the spectral characterization of 28 types of CMPTC's. In Section-B the presence of number of active-sites in each CMPTC’s has been further ascertained based on their comparative reaction yields in C-alkylation of ketimine. It also discussed the reason for selection of superior CMPTC’s followed by their catalytic optimization study for the same reaction. Further, this section also describes the dialkylation of aldimine by changing the different substrate and alkylating agents using superior CMPTC’s. Similarly, the discussion related to aziridination reaction yield and ee using selected CMPTC’s and optimization of the same reaction using the best CMPTC viz., 61b are also explained. However, taking into consideration all the observed results we have proposed following conclusion from Section B.

1. For the first time in the literature, we have synthesised 28 types of different CMPTCs using optically pure Cinchonine and Cinchonidine as a chiral source materials. It is also concluded that the synthetic procedure of each CMPTC’s may allow further ways and means for the preparation of a variety of chiral related quaternary ammonium chloride/bromides with desired steric and electronic properties.

2. We have successfully synthesised

   (i) Natural and synthetic a-amino acids using C-alkylation of different Schiff bases like ketimine and aldimine
(ii) Enantioselective synthesis of N-arylaziridine derivatives

3. The number of active-sites present in each CMPTCs and their respective chirality were ascertained based on their spectral results such as FT-IR, NMR, HRMS, HPLC and Autopol experiment respectively.

4. For the first time, we have reported C\textsubscript{9} (O) protected (by tosylation) single-site PTCs which remarkably enhanced the yield and ee of the C-alkylations of ketimine and aldimine reactions as well as the aziridination reaction. In feet, the C\textsubscript{9} (O)-tosylated CPTCs are superior to those reported in literature in catalyzing the C-alkylation of Schiff base.

5. It is found that irrespective of CMPTC’s the C\textsubscript{9} (O) protected (by allylation) catalysts are found to be superior and hence produced a higher chemical yield and ee’s than their corresponding CMPTC’s containing C\textsubscript{g}free -OH in catalyzing the alkylation of ketimine, aldimine and also in aziridination reaction.

6. The reactivity and selectivity of these CMPTC’s have been evaluated for the asymmetric alkylation of ketimine and found that the reactivity and ee are parallely increased in the order w-xylene based di-site (61b, 62b) > tetra-site (with spacer chain) (81b, 82b) > p-xylene derived di-site (67b, 68b) > tri-site (71b, 72b) > 4,4’-bipyridyl based di-site (55b, 56b) > tetra-site with out spacer (77b, 78 b) > single site (46, 49),

7. However, from the observed results, the w-xylene derived C\textsubscript{9} (0) protected CMPTC’s viz., 61b and 62b is established as a best CMPTC for the synthesis of enantioselective a-amino acids and N-arylaziridines than the other CMPTC’s. This is because, irrespective of the substrate the anions are appropriately fixed between the asymmetric environment of chiral centre
R₄N site of CMPTC's by an effective dipole-dipole attraction, as a result of which, two cationic moieties are simultaneously activated and cooperatively influence the reaction more effectively hence the maximum conversion/formation of yield and ee’s has been observed.

The enantioselective synthesis of α-amino acids and N-aryiaziridination reaction is affected by several factors that in turn influence the chemical yields and e.e’s. From the study, we observed that

(i) *i tert*-Butyl present in Schiff bases as well as hydroxamic acids gave higher chemical yield and ee’s for the synthesis of amino acids and aziridination reaction respectively.

(ii) In both the reactions, higher yield and ee’s are noticed in the presence of electron donating substituents (-Me, -OMe, -OEt, and -OiPr) of alkyl halide and hydroxamic acids.

(iii) Both the electronic and steric factors are simultaneously involved in the C-alkylation of Schiff bases and as well as aziridination of hydroxamic acids that in turn influenced the ee and the chemical yield.

(iv) Mixture of solvents like toluene: CH₂Cl₂ (8:2 v/v) is found to be good for the synthesis of α-amino acids and also toluene is the best solvent for the aziridination reaction.

(v) Both the reactions have produced higher yield and ee’s with aqueous NaOH at lower concentrations than for the other bases. Further, at higher concentration of base the catalyst decomposition takes place easily.
The observed results show that iS'-enantiomers were more predominant than the i?-enantiomers with cinchonidine as CMPTCs; whereas the i?-enantiomers were more predominant in the case of cinchonine based CMPTCs.

We have proposed a new interfacial mechanism for mono and di-alkylation of ketimine and aldimine respectively. Similarly, we proposed extraction mechanism for the aziridination reaction.