DESIGN OF FUNCTIONALIZED IONIC LIQUIDS FOR APPLICATION IN DEHYDRATION REACTIONS

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DESIGN OF FUNCTIONALIZED IONIC LIQUIDS FOR APPLICATION IN DEHYDRATION REACTIONS

by

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CERTIFICATE

This is to certify that the thesis titled **"DESIGN OF FUNCTIONALIZED IONIC LIQUIDS FOR APPLICATION IN DEHYDRATION REACTIONS"** being submitted by **Mr**. **Tanmoy Patra** to the Indian Institute of Technology, Delhi, for the award of degree of **Doctor of Philosophy** is a record of bonafide research work carried out by him. **Mr. Tanmoy Patra** has worked under my guidance and supervision and has fulfilled the requirements for the submission of this thesis, which to my knowledge has reached the requisite standard.

The results contained in this thesis are original and have not been submitted, in part or full, to any other University or Institute for the award of any other degree or diploma.

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Dedicated to my beloved sister

Sudha

Without whom this journey would have been incomplete

"There are 2 possible outcomes: If the result confirms the hypothesis, then you've made a measurement. If the result is contrary to the hypothesis, then you've made a discovery."

***- Enrico Fermi*.**

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ABSTRACT

Functionalized ILs are an important class of compounds considered as green substitutes for a vast number of industrially important catalysts as well as solvents. The present work is based on designing novel class of such ILs for dehydration reactions like alkylation of phenolic compounds with alcohols and polypeptide synthesis. Task specific Bronsted, Lewis and Bronsted-Lewis acidic ILs were synthesized in the laboratory and characterized using spectroscopic techniques. Density functional theory (DFT) was used to investigate the structure-activity relationship of these ILs to correlate their acidic properties and their relative effect on the reactant conversion and desired product selectivity. These acidic ILs were tested for their catalytic activity in the alkylation of phenolic compounds with aliphatic alcohols. Design of Experiments (DOE) using Response Surface Methodology (RSM) was used for the statistical optimization of the process variables affecting the alkylation reactions in these ILs. The kinetics of these alkylation reactions were then investigated in an experimental batch reactor and kinetic models were developed based on the product distribution. Using these phenomenological models, the activation energies and the frequency factors for the alkylation of phenolic compounds with aliphatic alcohols were estimated and they show good agreement with the experimental data.

Furthermore, a new class of hydrophilic as well as hydrophobic ILs were synthesized in the laboratory and characterized using spectroscopic techniques. Their activity was investigated in the synthesis of homogeneous phase di- and oligopeptides. The ILs showed promising results in the peptide synthesis with high product yields and purity of commercially important dipeptide, aspartame, as well as biologically active pentapeptide, Leu-enkephalin without any racemization issues. A new class of polystyrene resin bound ILs was also prepared and characterized using FTIR, elemental data, SEM images. These also showed improved yield and purity of Leu^5-enkephalin without any racemization problems. The combined use of ILs as heterogeneous phase support as well as solvents was further demonstrated by kinetics of amino acid loading. Overall, a novel methodology using functionalized ILs as homogeneous as well as heterogeneous

phase supports and solvent was developed for the synthesis of di, oligo and polypeptides.

PERMISSIONS

Permissions have been taken from the respective journals for the publications related to work presented in this thesis.

List of Publications Related to Work Presented in this Thesis as on Date of Submission of Thesis

PATENTS

1. Upadhyayula, S.; **Patra, T.**; Kondamudi, K. Ionic liquid catalyst and a process for preparation thereof, and improved tertiary butylation of phenol/phenolic compounds for higher conversion of phenol and phenolic compounds, Indian Patent Application no: 1290/DEL/2012, Publication date: 31/08/2016.
2. Upadhyayula, S.; **Patra, T.**; Paul, S. Ionic liquid based support for manufacture of peptides, Indian Patent Application no: 201611044691, Date of filing: 28/12/2016.
3. Upadhyayula, S.; **Patra, T.**; Paul, S. A process for preparation of a peptide, Indian Patent Application no: 201611044692, Date of filing: 28/12/2016.

PEER-REVIEWED JOURNAL PUBLICATIONS

1. **Patra, T.**; Ahmad, S.; Upadhyayula, S. Highly efficient alkylation of phenol with *tert*-butyl alcohol using environmentally benign Bronsted acidic ionic liquids, *Appl. Catal. A Gen*. **2015**, *506*, 228-236.
2. **Patra, T.**; Parveen, F.; Upadhyayula, S. Mechanistic insights into solvent induced alkylation of *p*-cresol with *tert*-butyl alcohol using Brönsted acidic ionic liquids, *Mol. Catal.* **2017**, *433*, 175-184.
3. **Patra, T.**; Karmakar, S.; Upadhyayula, S. Multifunctional ionic liquid-bound polystyrene resin with high loading capacity as support in solid-phase peptide synthesis, *Tetrahedron Lett.* **2017**, *58*, 1531-1534.

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List of Abbreviations and Acronyms

IL	Ionic Liquid
RTIL	Room temperature IL
SPPS	Solid phase peptide synthesis
FPPS	Fluorous-phase peptide synthesis
PEPSIL	Peptide synthesis in ILs
ILSPS	IL supported peptide synthesis
SILBPS	Supported IL based peptide synthesis
2-TBP	2-*tert*-butyl phenol
4-TBP	4-*tert*-butyl phenol
2, 4-DTBP	2, 4-di-*tert*-butyl phenol
2, 6-DTBP	2, 6-di-*tert*-butyl phenol
TBPE	*tert*-butyl phenol ether
IL-HSO_4	1-(4-sulfonic acid) triethylammonium hydrogen sulfate
IL-CF_3SO_3	1-(4-sulfonic acid) triethylammonium trifluoromethane sulfonate
IL-PTS	N,N,N-triethyl-4-sulfobutan-1-aminium-4-methylbenzenesulfonate
IL-CH_3SO_3	N-(4-sulfonic acid) butyl triethylammonium methane sulfonate
TBA	*tert*-butyl alcohol
2-TBC	2-*tert*-butyl-*p*-cresol
TBCE	*tert*-butyl-*p*-cresol ether
2, 6-DTBC	2, 6-di-*tert*-butyl-*p*-cresol
H_o	Hammett function
T	temperature, °C
IPMCE	*iso*-propyl *m*-cresol ether

DCM Dichloromethane

DMF N, N′-dimethylformamide

NMP N-methyl-2-pyrrolidone

TFA Trifluoroacetic acid

HBTU 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate

PSIL Polystyrene resin-bound IL