Synthesis, Characterization and Applications of Ionic Liquid-tagged Schiff Base Complexes of Pd, Cu and Zn

THESIS

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by

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Under the supervision of

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Dedicated to

My Daughter Sanwi

(Peehu)

BIRLA INSTITUTE OF TECHNOLOGY AND SCIENCE
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CERTIFICATE

This is to certify that the thesis entitled **"Synthesis, Characterization and Applications of Ionic Liquid-tagged Schiff Base Complexes of Pd, Cu and Zn"** submitted by **Ms Pankaj Nehra** ID. No. **2011PHXF020P** for the award of Ph. D. Degree of the Institute symbolizes the original work done by her under our supervision.

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Abstract

The ionic liquid-tagged metal complexes have been known to have a tremendous potential in multidisciplinary fields in chemistry. The thesis entitled "**Synthesis, Characterization and Applications of Ionic Liquid-tagged Schiff Base Complexes of Pd, Cu and Zn**" deals with the synthesis of some selected Schiff base ligands and metal complexes with ionic liquid tag. The thesis is divided into five chapters.

The first chapter of the thesis describes the brief literature overview on current progress in the synthesis and applications of ionic liquids and Schiff bases. The catalytic, biological activities and photophysical properties of the ionic liquids and Schiff base metal complexes have been discussed in detail throughout the chapter.

The second chapter of the thesis describes about the details of materials, method used during the research work and also about the synthesis and characterization of the ionic liquid-tagged Schiff base ligands.

The third chapter of the thesis describes the synthesis, characterization and catalytic applications of imidazolium ionic liquid-tagged Schiff base complexes of palladium, copper and zinc. The synthesized palladium complex has been screened for its catalytic applications in Heck, Suzuki and Sonogashira cross coupling reaction in aqueous medium. The copper complex has been screened for its catalytic applications for the synthesis of 1, 4-disubstituted 1,2,3-triazoles under aqueous conditions and for the formation of disulfides from thiols under sonication. The zinc has been explored for its catalytic activity in the synthesis of bis(indolyl)methanes. All the three complexes are found highly efficient catalysts for the above mentioned reactions in aqueous medium.

The fourth chapter of the thesis describes about the biological activity of the ionic liquid-tagged Schiff base ligands and their Cu and Zn complexes. The ligands exhibited significant antimicrobial activity against both bacteria and fungi. The copper and zinc complexes showed good antimicrobial activity against both the bacterial and fungal strains. The DNA cleavage activity of the complexes was also deliberated and these were found highly efficient DNA cleaving agents.

The fifth chapter summarizes the overall thesis work. The future scope of the research work has also been described in the same chapter.

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Abbreviation/Symbol	Description
α	Alpha
β	Beta
Δ	Delta
°C	Degree centigrade
Å	Angstrom
θ	Theta
μL	Microliters
μg	Micrograms
ACN	Acetonitrile
μL	Microliters
μg	Micrograms
ACN	Acetonitrile
AIEE	Aggregation-induced emission enhancement
API–ILs	Active Pharmaceutical Ingredient Ionic Liquids
[Bmim][Br]	1-Butyl-3-methylimidazolium bromide
[Bmim][BF_4]	1-Butyl-3-methylimidazolium tetrafluoroborate
[bdmim][PF_6]	Butyl-dimethylimidazolium hexafluorophosphate
[Bmim][PF_6]	1-Butyl-3-methylimidazolium hexafluorophosphate
Calcd.	Calculated
^{13}C	Carbon-13
Cat.	Catalyst
CAN	Ceric ammonium nitrate
$CDCl_3$	Deuterated chloroform
CPPs	Cell-penetrating peptides
d	Doublet

dd	Doublet of doublet
DSC	Differential Scanning Calorimetry
DCM	Dichloromethane
DMF	*N*,*N*-Dimethylformamide
DMSO-d_6	Deuterated dimethylsulfoxide
ESI	Electron Spray Ionization (MS)
EtOAc	Ethyl acetate
Et	Ethyl
Equiv	Equivalent
FILs	Functionalized ionic liquids
G	Gram
h	Hours
HRMS	High Resolution Mass Spectra
Hz	Hertz
IR	Infra-red
IED	Inverse electron demand
J	Coupling constant
Lit.	Literature
MCR	Multi component reaction
Me	Methyl
MS	Mass spectrometry
M.P	Melting point
MCPBA	Meta chloro perbenzoic acid
mg	Milligram
MHz	Mega hertz

min	Minutes
MIC	Minimum inhibitory concentration
mL	Milliliter
mmol	Millimole
MW	Microwave
N_2	Nitrogen gas
NMR	Nuclear Magnetic Resonance
PEG	Polyethylene glycol
PPh_3	Triphenylphosphine
POPs	Porous organic polymers
Ph	Phenyl
ppm	Parts per million
PS	Polymer supported
%	Percentage
Psi	Per square inch
R	Hydrocarbon
rt	Room temperature
s	Singlet
SCF	Supercritical fluid technology
SSZ	Sulphasalazine
SILP	Supported ionic liquid phase
TAE	Tris-acetate-EDTA buffer
TGA	Thermogravimetric analysis
THF	Tetrahydrofuran
TLC	Thin layer chromatography

TMS	Tetramethylsilane
Δ	Parts per million
UV	Ultra violet
W	Watt
WGS	Water-gas shift
ZIF-90	Zeolitic imidazolate framework-90

Chapter 1

Introduction

A Brief Overview on the Chemistry of Ionic Liquids, Schiff Bases and Ionic Liquid-tagged Materials

1.1 Ionic liquids

Ionic liquids (ILs) are ascribed as molten salts with ionic nature, comprising of both cationic and anionic species and having a melting point below 100 °C.[1] The history of ILs dates back when Walden synthesized the first ionic liquid [$EtNH_3$][NO_3] (m.p. 12 °C) in 1914.[2] In 1951 Hurley and Wier developed low melting salts with chloroaluminate ions for low-temperature electroplating of aluminum.[3] However, these chloroaluminate salts did not attract much interest for applications due to their moisture sensitivity. In 1992, another leap forward was made by Wilkes group by synthesizing air and water stable 1-ethyl-3-methylimidazolium based ionic liquids incorporating different anions.[4] Thereafter, the applications of ionic liquids were extended as unique media for chemical reactions and the term "room temperature ionic liquids" (RTILs) was assigned to them.[5, 6] ILs are generally composed of bulky asymmetric organic cations, such as imidazolium, pyridinium, pyrrolidinium, quaternary ammonium or tetraalkylphosphonium, with weak intermolecular interactions and low charge densities.[7, 8] These cations hinder the regular packing in a crystal lattice making the solid crystalline state energetically less favorable, leading to low melting points.[9] Furthermore, this effect can been enhanced by implementation of anions with a delocalized charge.[10] A selection of typical cations and anions of ILs is given in **Figure 1.1**.

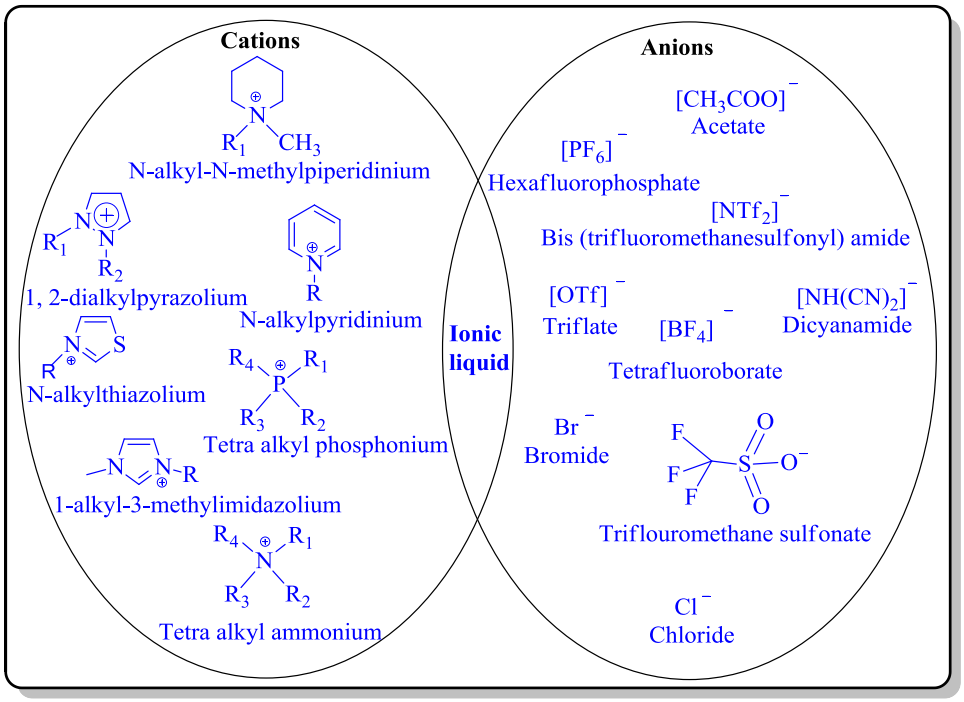


Figure 1.1 Commonly used cations and anions in ionic liquids

In 1998, a new class of ionic liquids called "functionalized ionic liquids (FILS)" based on cations derived from the antifungal drug miconazole were prepared by Davis and co-workers.[11] This introduced the idea that ionic liquids could incorporate functional groups such as amine, amide, ether, alcohol, acid, urea etc. covalently tethered to the anion or cation or both.[12, 13] The functionalized ionic liquids (FILS), when modified and used as a particular task are known as task specific ionic liquids.[14] Promising diverse applications of ILs are due to their unusual physical and chemical properties like high thermal stability, lack of inflammability, low volatility, chemical stability and excellent solubility with many organic compounds.[15] Moreover, these properties can be tailored by varying the combination of cations and anions. Due to high possibility for synthetic variations, ILs are referred as designer fluids.[16] Although ionic liquids were initially introduced for electrochemical applications and as alternative reaction media but today they have marched far beyond this border and are being used for a myriad of applications as shown in **Figure 1.2**.[17-22]

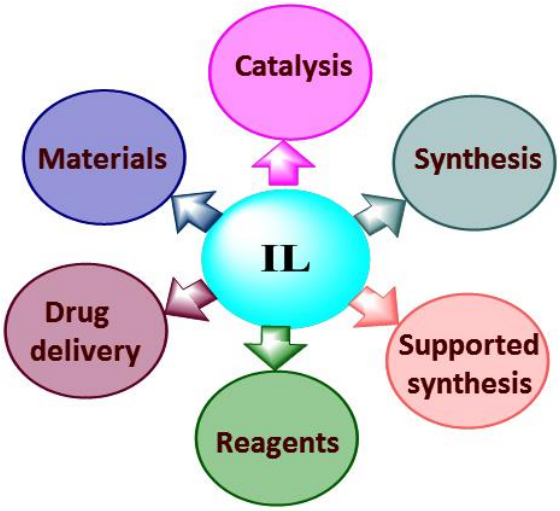


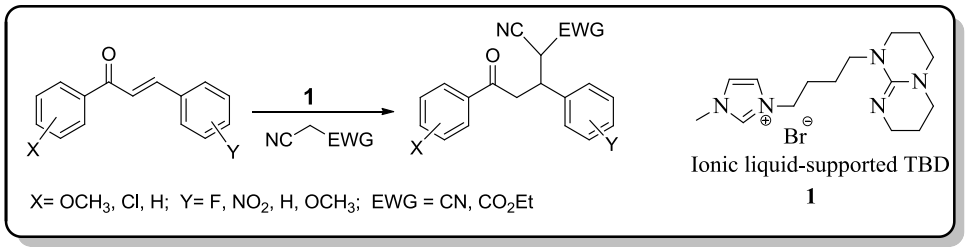
Figure 1.2 Applications of ionic liquids

1.2 Catalytic applications of ionic liquids

The stringent demands for greener and sustainable technologies have focused attention on the development of cost-effective and environmentally benign catalytic systems for chemical synthesis.[23, 24] However, efficient recycling and subsequent reuse of homogeneous catalysts can be achieved by heterogenizing a homogeneous catalyst.[25] Catalyst immobilization is a well-established strategy to achieve recycling and ionic liquid-tagged ligands are readily used for immobilization of transition-metal-based catalysts. Ionic liquid-tagged catalysts have appeared as useful alternatives to classical catalysts showing enhanced catalytic activities

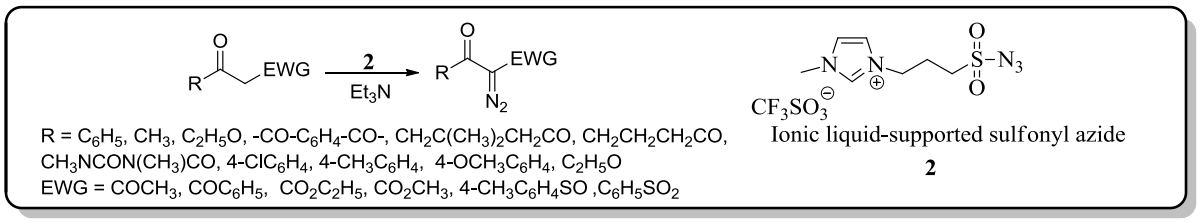
with additional benefit of simplified product isolation and catalyst reuse.[26-31] The catalytic activity of these catalysts can be tuned substantially by varying cation/anion or both the tags. Majority of the reports are based on the use of imidazolium or pyridinium as cationic tags and sulfonic or phosphonic acids as anionic tags.[32-37] Ionic liquid-tagged compounds have been synthesized and employed as solvents, catalysts, alternatively supported tools and reagents in various chemical reactions.

Ionic-liquid-tagged 1,5,7-triazabicyclo [4.4.0] dec-5-ene (**1**) was used as an efficient and recyclable organocatalyst for Michael addition reaction (**Scheme 1.1**).[38]



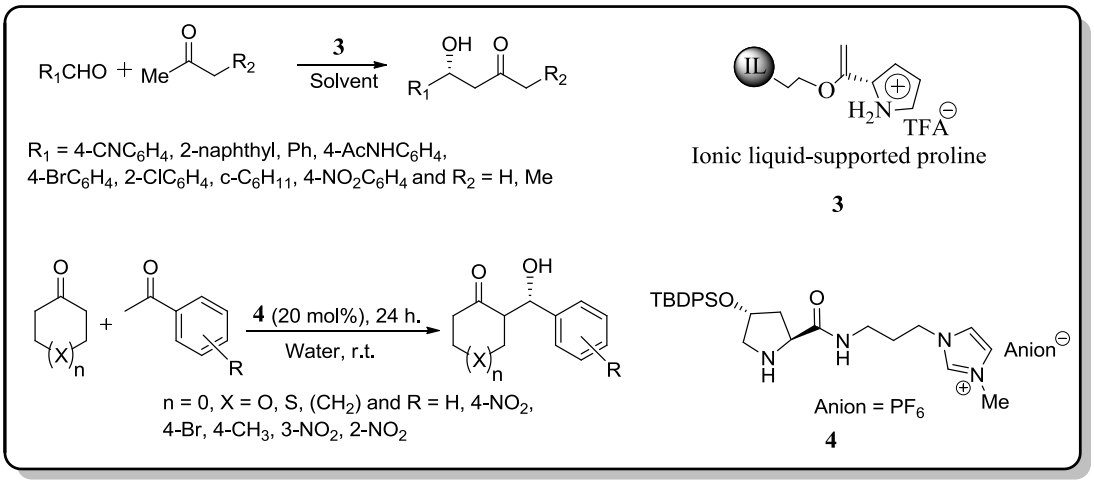
Scheme 1.1 Ionic liquid-tagged TBD catalyzed Michael addition reaction

Ionic liquid-tagged sulfonyl azide (**2**) was synthesized and investigated for diazotransfer reaction under solvent free conditions (**Scheme 1.2**). Excellent yields with high purity of the diazo compounds were isolated and the method offered better separation of product and reagent. The described method is experimentally simple, mild and requires very short reaction time.[39]



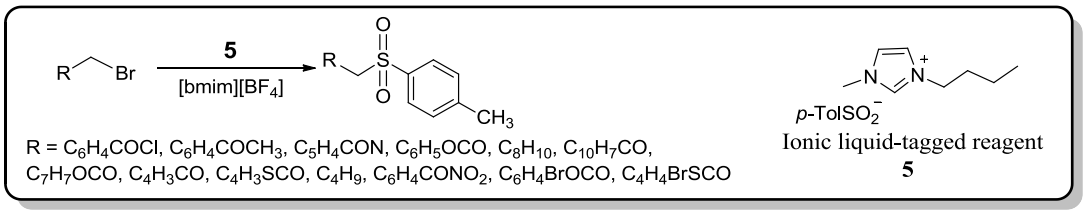
Scheme 1.2 liquid-Ionic liquid-tagged sulfonyl azide catalyzed diazotransfer reaction

An ionic liquid-tagged (*2S, 4R*)-4-hydroxy-proline and an imidazolium ion tagged prolinamide organocatalysts (**3**, **4**) were synthesized and used as recyclable catalysts for direct asymmetric aldol reactions (**Scheme 1.3**).[40, 41]



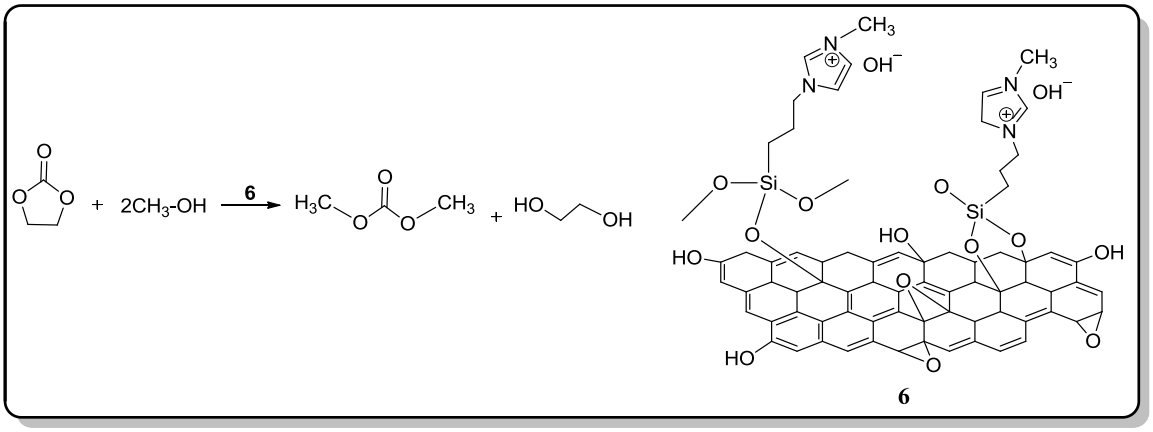
Scheme 1.3 Proline based ionic liquid-tagged organo catalysts for asymmetric aldol reaction

1-butyl-3-methylimidazolium *p*-toluenesulfinate, [bmim][*p*-TolSO$_2$] (**5**) was synthesized (**Scheme 1.4**) and used as a nucleophile for the reaction with alkyl bromides and phenacyl bromides to synthesize sulfones and *β*-ketosulfones in [bmim][BF$_4$].[42]



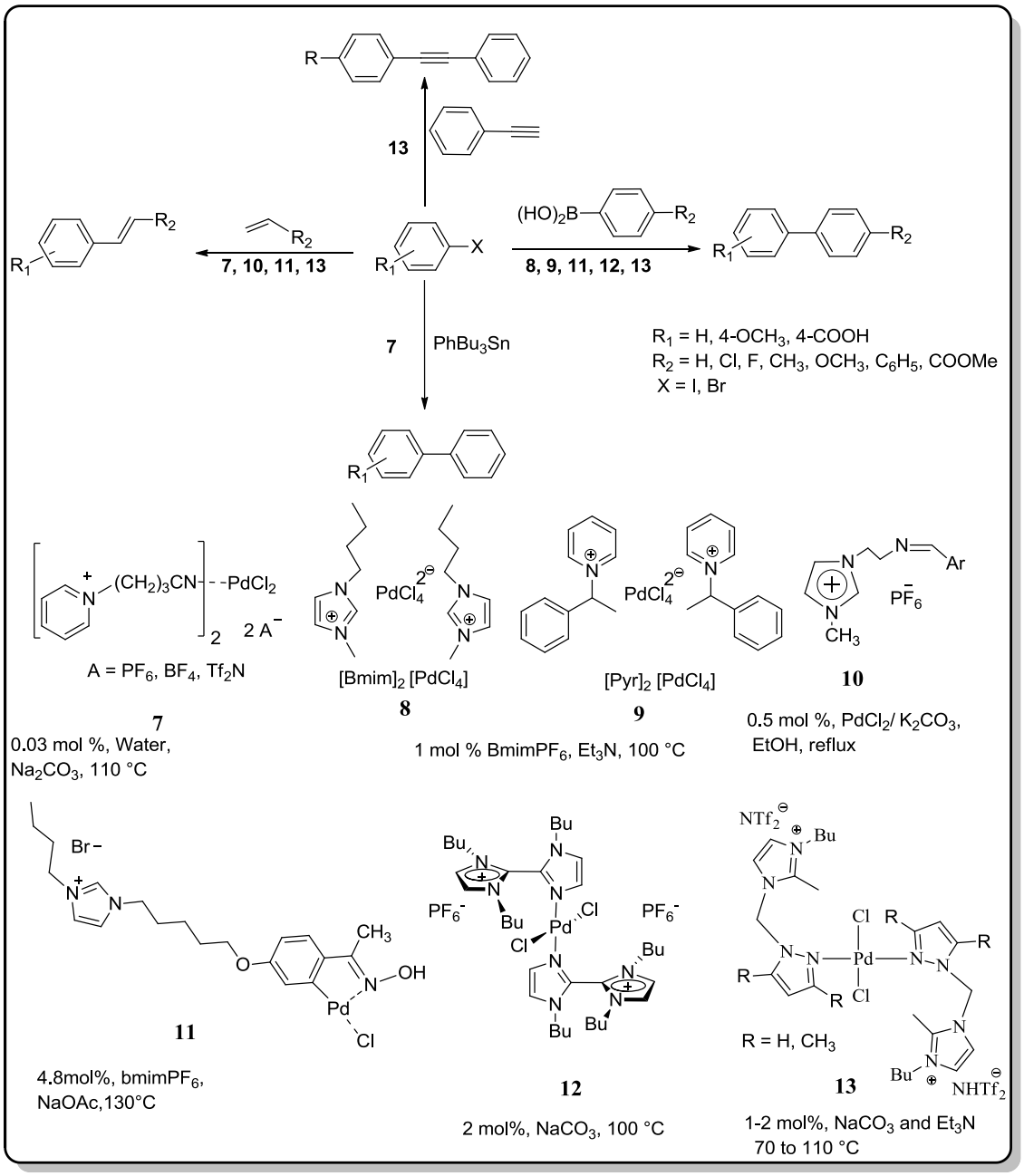
Scheme 1.4 Ionic liquid-tagged [bmim][*p*-TolSO$_2$] for the synthesis of sulfones and *β*-ketosulfones

Li and co-workers reported catalytic activity of immobilized 1-(trimethoxysilyl)propyl-3-methylimidazolium hydroxide (**6**) on the surface of graphene oxide (GO) for trans esterification reactions (**Scheme 1.5**).[43]



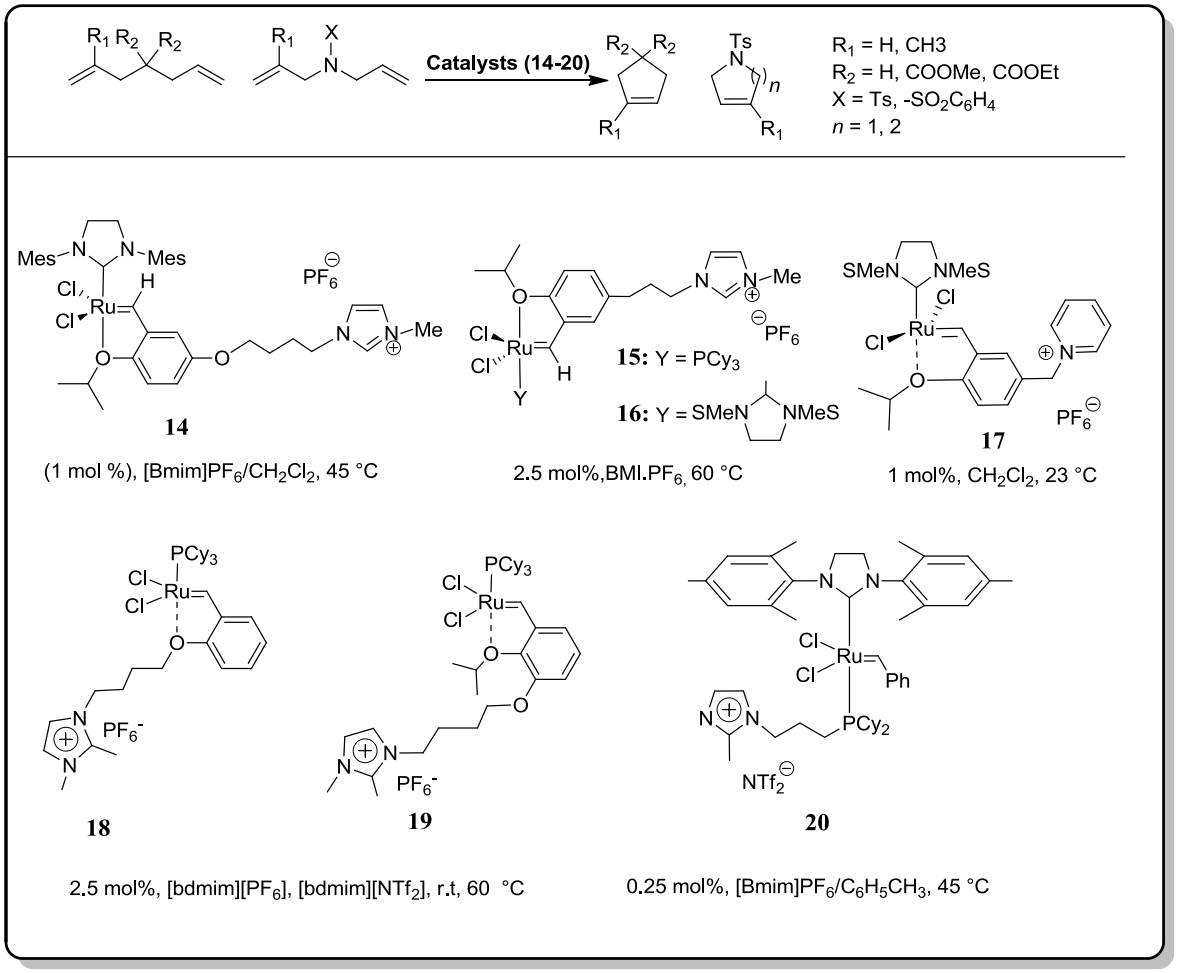
Scheme 1.5 Ionic liquid-supported graphene oxide for transesterification reaction

The use of ionic liquid based palladium systems **7-13** (**Scheme 1.6**) in the cross-coupling reactions allows effective recovery and reuse of the catalyst. Ionic liquids based on the *N*-butyronitrile pyridinium cation $[C_3CNpy]^+$ reacted with palladium chloride to form $[C_3CNpy]_2[PdCl_4]$ when the anion is Cl^- and complexes of the formula $[PdCl_2(C_3CNpy)_2][anion]_2$ when the anion is PF_6^-, BF_4^-, or $N(SO_2CF_3)_2^-$. The complexes following immobilization in *N*-butylpyridinium and nitrile-functionalized ionic liquids (**7**) showed good catalytic activity for the Suzuki and Stille coupling reactions. The recycling and reuse of the catalyst was more efficient in the nitrile-functionalized ionic liquid. The presence of the coordinating nitrile moiety in the ionic liquid led to a considerable decrease in palladium leaching relative to simple *N*-alkylpyridinium ionic liquids.[44] Imidazolium salt and pyridinium chiral salt, $[Bmim]_2[PdCl_4]$ (**8**) and $[Pyr]_2[PdCl_4]$ (**9**) were employed as catalyst for the Heck reaction in ionic liquid.[45] An ionic liquid-supported Schiff base prepared from the condensation of aromatic aldehydes with the ionic liquid 1-(2-aminoethyl)-3-methylimidazolium hexafluorophosphate (**10**) along with $PdCl_2$ was used as a catalyst for Suzuki-Miyaura coupling reaction under air in ethanol solution. Good to excellent yields of the products were achieved and the catalytic system could be reused at least 5 times without losing the activity.[46] An oxime carbapalladacycle (**11**) with an imidazolium group covalently attached through a chain at the complex was synthesized. The catalytic activity of this complex for the Heck and Suzuki reaction increased by supporting it on high surface area Al/MCM-41 aluminosilicate.[47] An ionic liquid synthesized by the reaction of 2, 2′-biimidazole with iodobutane worked as solvent as well as ligand. The coordinated palladium complex (**12**) of this ionic liquid showed good catalytic activity for the Heck reaction with good recyclability up to ten cycles.[48] Palladium complexes of 2-methylimidazolium-based ionic salts containing pyrazolyl and 3,5-dimethylpyrazolyl-functional groups (**13**) were employed as catalyst precursors for the Heck, Suzuki and Sonogashira cross-coupling reactions in corresponding ionic liquids.[49]



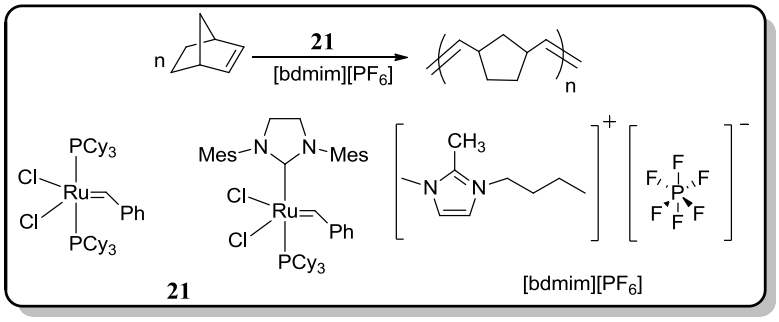
Scheme 1.6 Imidazolium and pyridinium based IL-tagged palladium catalysts for cross-coupling reactions

Ionic liquid tagged ruthenium complexes were widely employed as catalyst for the olefin metathesis and the ionic liquid tag plays a crucial role in the recyclability of the catalyst systems. A series of the second generation Hoveyda-Grubbs ruthenium catalysts with IL-tags (**14-20**) were prepared and used as effective catalytic systems for the ring-closing metathesis (**Scheme 1.7**).[50-54]



Scheme 1.7 Ionic liquid-tagged Hoveyda-Grubbs ruthenium catalysts for the ring-closing metathesis

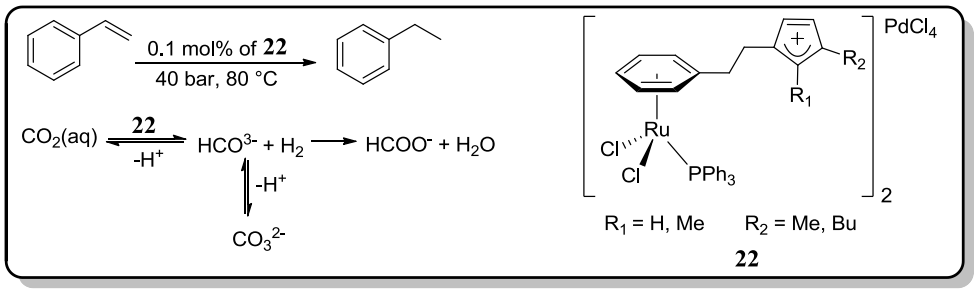
Ring-opening metathesis polymerization of norbornene was carried out in a biphasic medium comprising of an ionic liquid [bdmim][PF_6] and toluene (**Scheme 1.8**) with a cationic ruthenium allenylidene precatalyst (**21**).[55]



Scheme 1.8 Ruthenium catalyzed ring-opening metathesis polymerization of norbornene

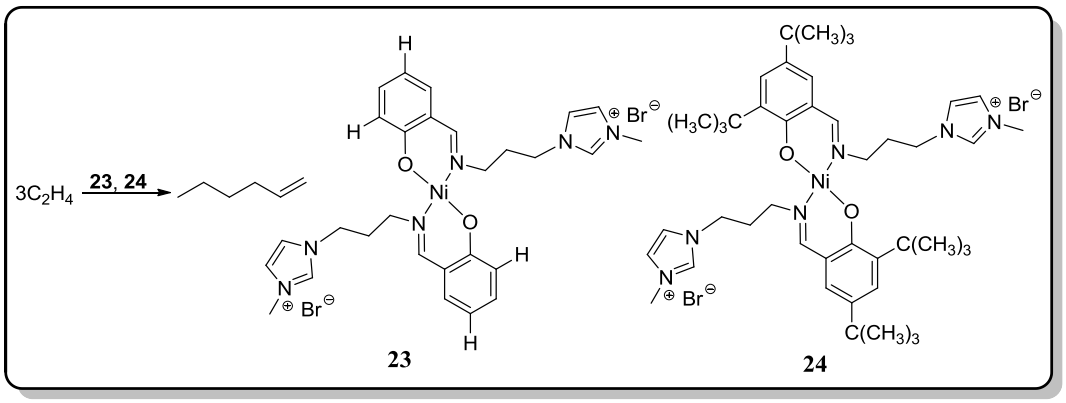
Ruthenium complexes (**22**) of imidazolium functionalized η^6-arene ligands were utilized in the biphasic ionic liquids and aqueous catalysis for the hydrogenation of styrene and CO_2

(**Scheme 1.9**). An imidazolium tag gave high water solubility even in the presence of a lipophilic ligand such as tricyclohexyl phosphine is present.[56]



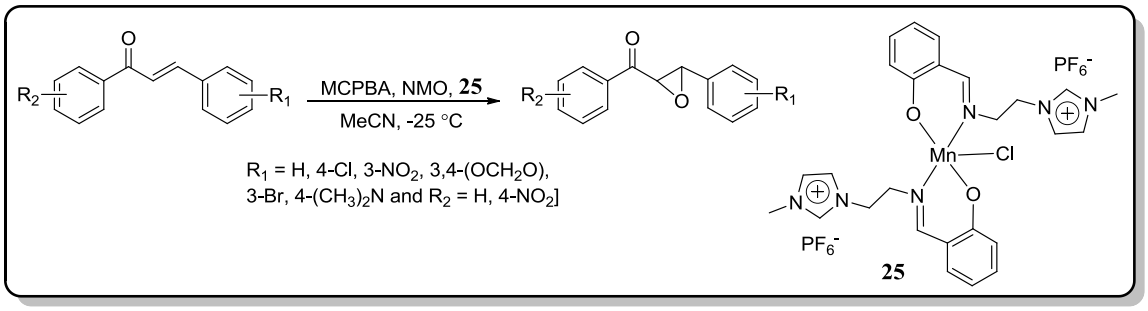
Scheme 1.9 Imidazolium functionalized η^6-arene ligands based ruthenium complexes for hydrogenation of styrene and CO_2

Gao group synthesized two ionic liquid-supported bis-(salicylaldimine) nickle(II) complexes (**23, 24**) and used them as catalyst for the ethylene oligomerization reactions in biphasic solvent systems consisting of chloro aluminate ionic liquid and toluene or *n*-heptane (**Scheme 1.10**). The IL-supported complexes showed much better stability and recyclability for ethylene oligomerization as compared with unsupported complexes.[57]



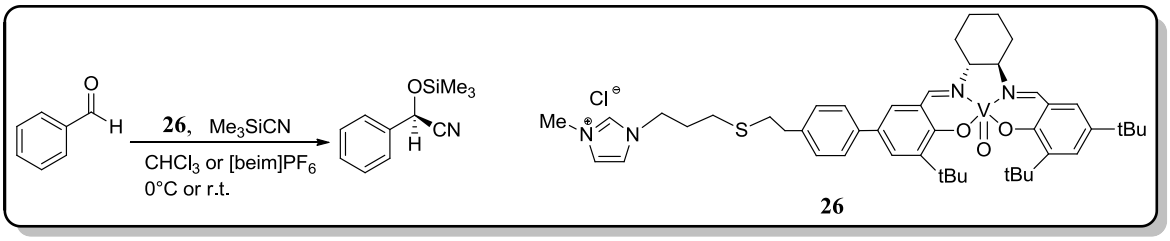
Scheme 1.10 IL-tagged Ni(II) complexes for ethylene oligomerization

A Mn(III)-Schiff base complex with imidazolium phase tag (**25**) was synthesized and employed as an efficient and recyclable catalyst for the epoxidation of chalcones with MCPBA/NMO (**Scheme 1.11**). It could be recovered and reused at least five times without any loss of activity. Unlike solid-supported catalysts extensive mechanical degradation of the catalyst after operating at the high stirring rates was not observed.[58]



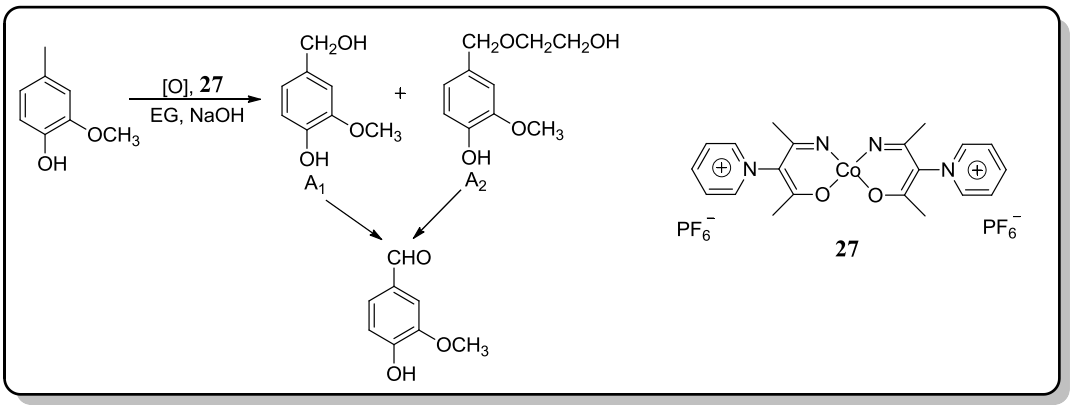
Scheme 1.11 An imidazolium phase tag Mn(III)-catalyst for the epoxidation of chalcones

The chiral vanadyl salen complex tagged to an imidazolium ion (**26**) showed enhanced catalytic activity than that of the unmodified catalyst as well as catalyst anchored on silica, activated carbon and single wall carbon nanotubes for the asymmetric cyanosilylation of benzaldehyde in [bmim]PF_6 (**Scheme 1.12**).[59]



Scheme 1.12 Imidazolium ion-tagged vanadyl complex catalyzed cyanosilylation

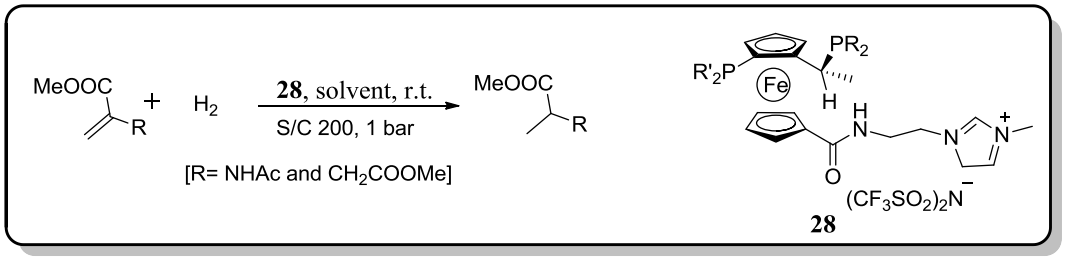
Li and co-workers developed an ionic liquid-tagged cobalt Schiff base catalyst (**27**). The complex showed excellent catalytic performance for the oxidation of 4-methyl guaiacol to vanillin (**Scheme 1.13**).[60]



Scheme 1.13 IL-tagged cobalt catalyst for the oxidation of 4-methyl guaiacol to vanillin

Pugin and co-workers developed an imidazolium ionic-tagged Josiphos ligand (**28**). Introduction of an imidazolium group at the lower *Cp* ring of the ferrocene backbone varied the ligand properties towards its catalytic activity (**Scheme 1.14**). Ligands bearing an

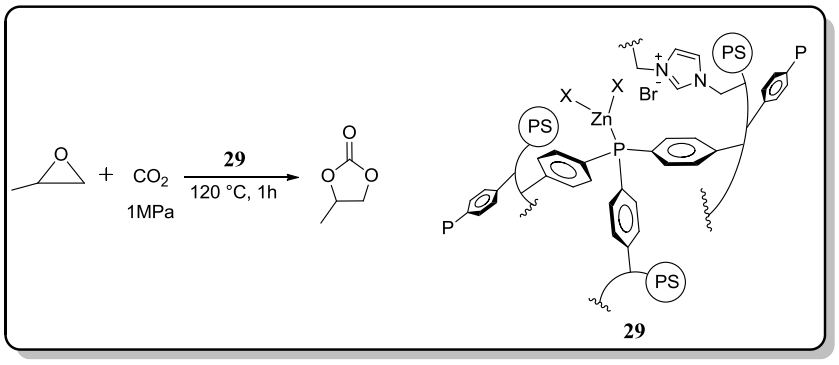
imidazolium moiety showed high efficiency and reusability for the rhodium-catalyzed enantioselective hydrogenation of methyl acetamidoacrylate and dimethyl itaconate in biphasic solvent/ionic liquid combinations. The ionic tag contained ligands showed better results in comparison to the unmodified simple ligands.[61]



Scheme 1.14 Imidazolium ionic liquid-tagged Josiphos ligands in hydrogenation reaction

Ru/IL@SiO_2 catalysts for the water-gas shift (WGS) reaction were synthesized using a sol-gel method with five different 1-butyl-2, 3-dimethylimidazolium ionic liquids (ILs) with BF_4^-, NO_3^-, Cl^-, OTf^-, and NTf_2^- as anions. The performance of the catalysts was affected by hydrogen bond formation capability and size of the anion of ILs. The catalysts showed high activity and stability at atmospheric pressure and low reaction temperatures.[62]

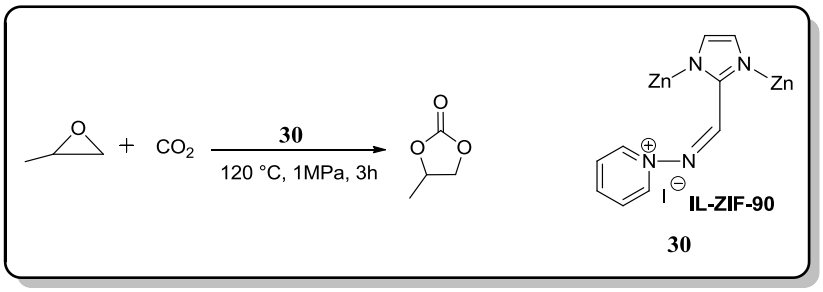
Yan *et al*. reported a series of ionic liquid (IL), zinc halide (ZnX_2), and triphenylphosphine (PPh_3) integrated porous organic polymers (POPs) as heterogeneous catalyst (**29**) for the conversion of CO_2 to cyclic carbonates (**Scheme 1.15**). Due to the cooperative effect of ionic liquid and homogeneously distributed Zn-PPh_3, catalyst exhibited high CO_2 capture and conversion performance.[63]



Scheme 1.15 IL/Zn-PPh_3 integrated POP for the conversion of CO_2 to cyclic carbonates

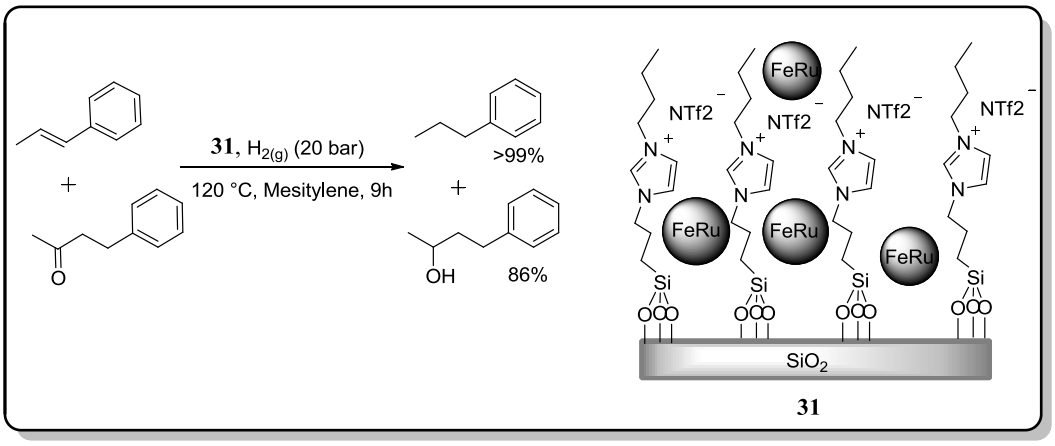
Park and co-workers synthesized IL-tagged ZIF-90 (IL-ZIF-90) catalyst (**30**) by the functionalization of zeolitic imidazolate framework-90 with a pyridinium base ionic liquid. The synthesized catalyst was employed for the solvent less cycloaddition of epoxides and CO_2 to give cyclic carbonates (**Scheme 1.16**). The reaction mechanism was proposed on the basis of density functional theory calculations. The mechanism suggested involvement of

Lewis acidic center (Zn) activating epoxide, a halide ion making a nucleophilic attack to give a ring open intermediate which on ring closure gave a cyclic carbonate.[64]



Scheme 1.16 (IL-ZIF-90) catalyst for the cycloaddition reaction

Leitner *et al.* used an organometallic synthetic approach to synthesize bimetallic iron-ruthenium nanoparticles immobilized on a supported ionic liquid phase (SILP) (**31**). The system showed high catalytic activity and selectivity for the reduction of a variety of unsaturated moieties without saturation of the aromatic ring due to the partial replacement of iron for ruthenium (**Scheme 1.17**).[65]

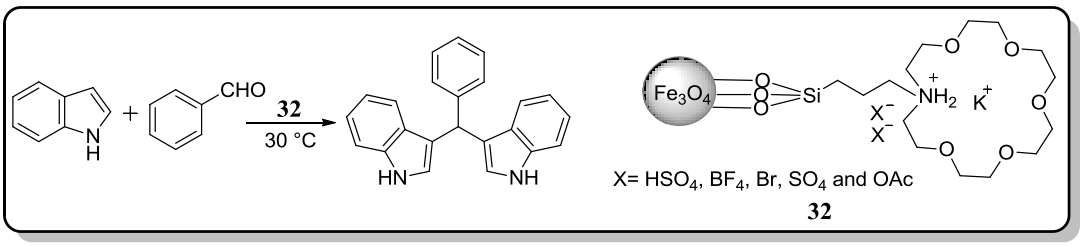


Scheme 1.17 SILP ruthenium catalyst for reduction reaction

Bifunctional copper(II) substituted polyoxometalate-based ionic liquids were synthesized and used as catalysts for the carboxylative cyclization of propargylic amines with CO_2. This protocol for the fixation of CO_2 worked smoothly at atmospheric pressure under solvent-free conditions. Various propargylic amines could react easily to afford 2-oxazolidinones as the target products in good to excellent yields.[66]

Chen *et al.* prepared a series of aza-crown ether ionic liquids supported on magnetic Fe_3O_4@SiO_2 core-shell particles (**32**) and utilized them as acidic catalysts in Friedel-Crafts alkylation and Hantzsch reactions (**Scheme 1.18**). The heterogeneous catalysts were found

highly active in both of the reactions and good yields were achieved under convenient reaction conditions. Furthermore, these magnetic particles supported IL catalysts could be easily recovered by an external magnet and reused five times without much loss of activity.[67]



Scheme 1.18 Fe_3O_4@SiO_2 supported IL aza-crown ether complex for Friedel–Crafts alkylation reaction

1.3 Biological applications of ionic liquids

The commonly employed classes of ionic liquids exhibit toxicity towards both prokaryotic and eukaryotic organisms.[68, 69] 1,3-Dialkylimidazoliums exhibit toxicity towards the few species of algae, crustaceans, phytoplanktons and nematodes.[70-72] There are many reports illustrating the antimicrobial activity of various classes of ionic liquids against both environmental and clinically important microorganisms.[73-76] An appropriate design of ionic liquids having antimicrobial activity may result in significant benefits in infection control and can also lead to the improvement in the quality of disinfectants, biocides and antiseptics.[77-79] 3-alkoxymethyl-1-methylimidazolium salts of $[Cl]^-$, $[BF_4]^-$, $[PF_6]^-$, choline-like quaternary ammonium chlorides (**33),** and chiral ammonium-based ionic liquids containing (1R,2S,5R)-(-)-menthyl group (**Figure 1.3**) were evaluated for their antimicrobial activities.[80] Quaternary ammonium chlorides derivatives of deanol esters exhibited strong and wide spectrum antibacterial activity.[81] 1-Alkylquinolinium ionic liquid (**34**) showed excellent broad spectrum antimicrobial activity against microorganisms grown in both the planktonic and sessile, or biofilm mode of growth (**Figure 1.3**). The compounds were potent against Gram positive and Gram negative bacteria, as well as fungi, and the activity depends on length of the alkyl substituent. The compounds containing twelve and fourteen carbons in the alkyl group exhibited highest antimicrobial and antibiofilm activities.[82, 83] The change in cationic and anionic component in ionic liquids can alter their antimicrobial properties. Imidazolium and pyridinium ionic liquids with varying alkyl chain lengths (**35**, **36**), were investigated for their microbial activities and both were found highly active towards the microbes (**Figure 1.3**).[84]

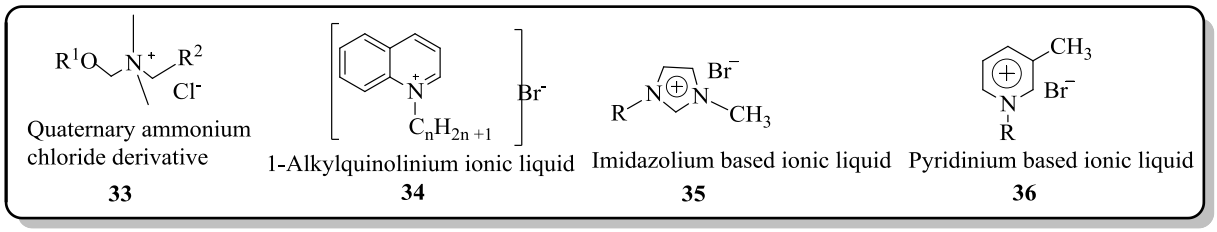


Figure 1.3 Some biologically active ionic liquids

A series of ampicillin based Active Pharmaceutical Ingredient Ionic Liquids (API–ILs) was synthesized and examined for antibacterial activities. It was suggested that ILs based on ampicillin can reverse the resistance in some clinical strains. These studies showed that the ion-pair effect is crucial for the action and the selection of hydrophobic ampicillin counter-ions.[69] Silva and co-workers developed porous chitin-based materials by combining the processing of chitin using ionic liquids together with the use of supercritical fluid technology (SCF). The prepared materials were used as potential aspirants for biomedical applications.[85] Iwai *et al.* reported antibacterial activity of imidazolium, pyrrolidinium and piperidinium salts with both propargyl group and alkyl and/or silylalkyl chains of different lengths. (3-pentyl)propargyl group was effective for the activity as compared to benzyl group, and silylalkyl group was responsible for the antibacterial activity of imidazole salts.[86] Whitney and collaborators reported ionic liquids as active pharmaceutical ingredients and explained the biological activities of anionic and cationic counter parts (**Figure 1.4**).[87]

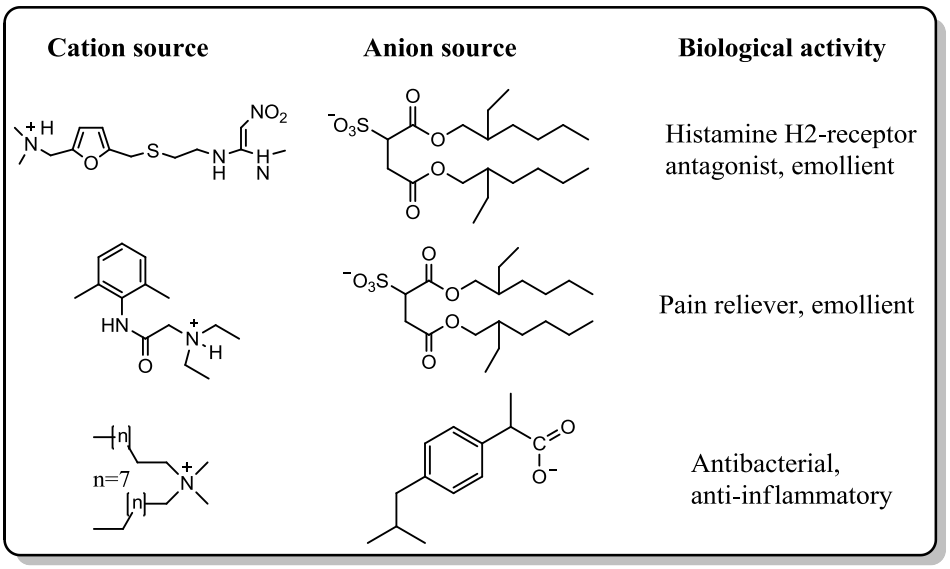


Figure 1.4 Biological activities of some ionic liquids

Kumar *et al.* synthesized quinoline based dicationic benzimidazolophanes and imidazolophanes (**37**) by incorporating various spacer units in them. The selected number of

quinolinophanes exhibited good antibacterial activity against most of the human pathogenic bacteria in tested concentrations (**Figure 1.5**).[88]

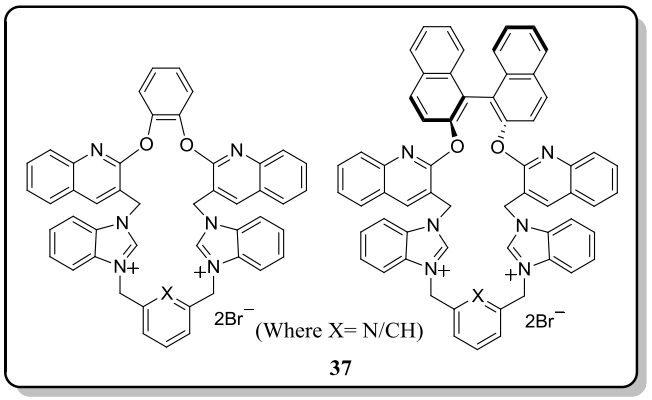


Figure 1.5 Antibacterial benzimidazole-based dicationic quinolinophanes ionic liquids

Elshaarawy *et al.* prepared a series of biopolymeric chitosan Schiff bases bearing salicylidene ionic liquid brushes and their Ag(I)/M(II) complexes (where M = Co, Pd) (**38**). These designed constructions were pharmacologically evaluated for *in vitro* antimicrobial activities against common bacteria, fungi and anticancer activities against human colon carcinoma (HCT-116) cell line. Functionalization of chitosan with IL-Sal brushes coupled with metalation synergistically enhances the antimicrobial and antitumor properties (**Figure 1.6**).[89]

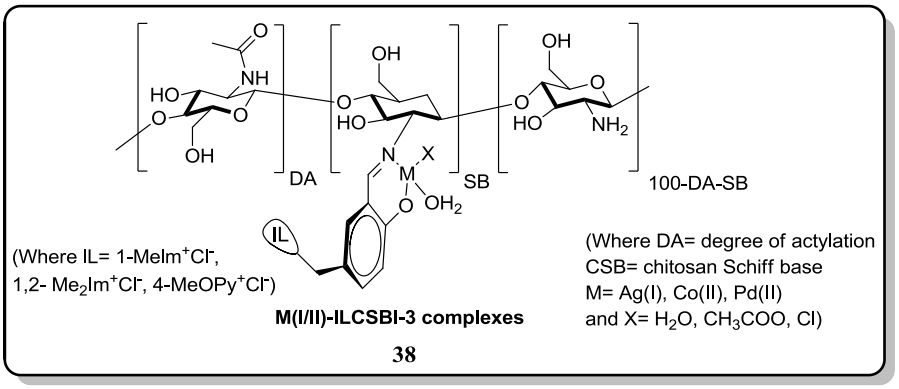


Figure 1.6 Biologically active metal complexes of chitosan Schiff bases bearing IL brushes

1.4 Photophysical properties of ionic liquids

The recent sighting in the field of ionic liquids is the wide range study on their photophysical properties. Du *et al*. studied correlation between the structural and optical properties of imidazolium amino acid based ionic liquid, 1-butyl-3-methylimidazolium glycine (**39**) with the help of molecular dynamics simulations, statistical analysis and excited-state calculations. The absorption behavior of imidazolium-based ionic liquids was sensitive towards their

locally heterogeneous environments.[90] Sadeghi and co-workers developed a selective method to determine sulphasalazine (SSZ) in aqueous solutions based on an asymmetric hydrophilic ionic liquid 1,3-butylimidazolium bromide as a fluorescence probe. In the presence of an anionic surfactant with increasing concentration of SSZ, the copper ion mediated fluorescence of the [Bbim][Br] (**40**) was significantly quenched. The method was successfully applied for monitoring low level amounts of SSZ residue in tap water, honey and milk samples (**Figure 1.7**).[91]

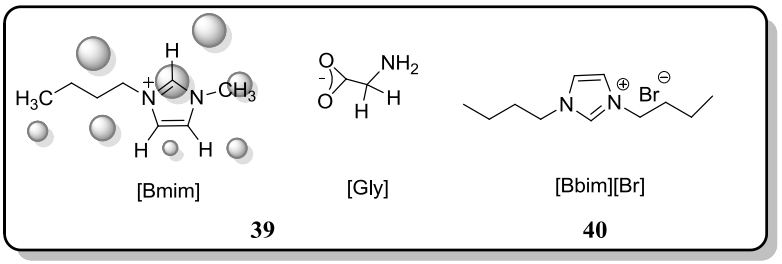


Figure 1.7 Fluorescent 1-butyl-3-methylimidazolium glycine and [Bbim][Br] ionic liquids

Circu and co-workers synthesized and studied the liquid crystalline properties of 3,4,5-tridodecyloxybenzyl pyridinium salts derived from 4-hydroxypyridine (**41**). Two columnar mesophases were recognized for bromide pyridinium salt and replacement of bromide ion with other counter ions resulted in mesophase suppression. These salts showed weak emission in dichloromethane solutions and the photo luminescent properties did not depend remarkably on the nature of counterion (**Figure 1.8**).[92] Mudring and co-workers presented the long chain imidazolium halides [$C_n$mim]Br.$x$$H_2O$ (n = 10, 12; x = 0, 1) (**42**) and characterized their structural and thermal behavior together with their photophysical properties. Short lived ($^1\pi \leftarrow {}^1\pi^*$) and long lived transitions ($^1\pi \leftarrow {}^3\pi^*$) produce intense whitish photoluminescence for all the compounds (**Figure 1.8**).[93]

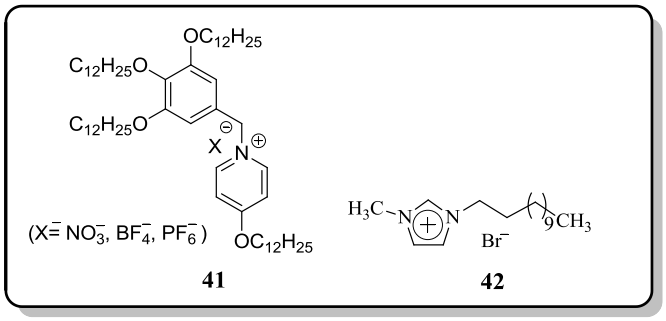


Figure 1.8 Photoluminescent imidazolium halides and pyridinium salts

Kana and colleagues studied optical absorption, fluorescence behavior and fluorescence life time of imidazolium ionic liquids (**43-46**) in the neat condition and with two types of laser

dyes (**Figure 1.9**). The emission behavior of neat ionic liquids was found to depend on the excitation wavelength, but with the dye dissolved in ionic liquids, it was independent.[94]

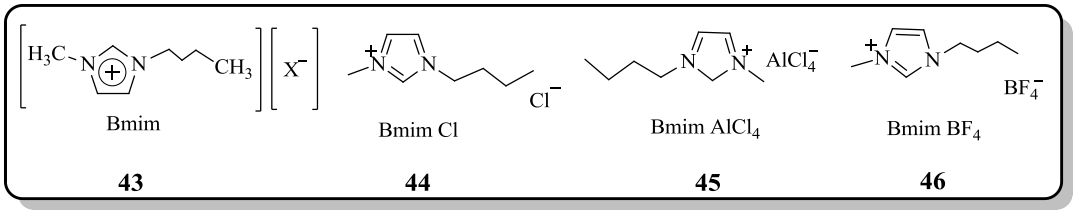


Figure 1.9 Imidazolium based photoluminescent salts

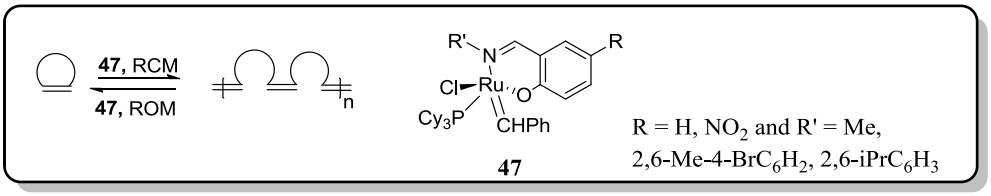
1.5 Schiff base metal complexes

Schiff bases, named after Hugo Schiff,[95] with general structural formula $R_2C=NR'$, ($R' \neq H$) are synthesized by the condensation of primary amines and aldehydes. Schiff bases are considered as privileged ligands as they are easy to prepare[96] and are able to form complexes with almost all metal ions. The suitable route of synthesis and thermal stability of Schiff base ligands have offered significant applications in catalysis as metal complexes. Study of Schiff base metal complexes has grown to occupy a central position in the field of chemistry. Research has shown significant progress of their utilization in fields as varied as catalysis, biochemistry, medicine, molecular receptors and devices.[97] The possibility of predetermining the structure, stability, and reactivity of metal complexes has been the main driving force in the development of complexes and sophisticated systems. It is the relative arrangement and nature of the functional groups as well as the structure of the ligand framework or the ligand topology that ultimately defines these characteristics. Transition metal complexes are powerful catalysts for organic reactions when Schiff base ligands are associated with the metal center, as they can offer chemoselectivity,[98] regioselectivity,[99] or stereoselectivity[100] under mild conditions. Transition metal complex catalysts tethered to organic or inorganic supports have received much attention in the past few decades because they can, in principle, combine the advantages of homogeneous and heterogeneous catalysts.[101-104] Transition metals exhibit different oxidation states and can interact with a number of negatively charged molecules. This activity of transition metals has led to the

development of metal based drugs with promising pharmacological application and may offer unique therapeutic opportunities.[101, 105-107]

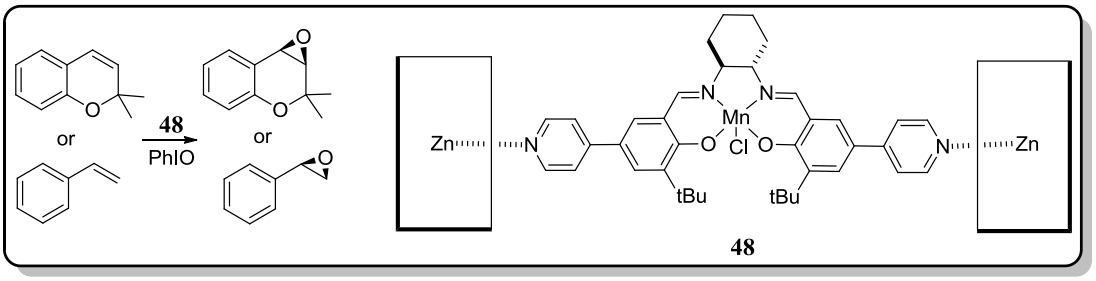
1.6 Catalytic applications of Schiff base metal complexes

Schiff base metal complexes show excellent catalytic activity in various organic reactions.[96, 108] Ruthenium based catalysts coordinated with a 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene and a Schiff base ligand (**47**) was used for ring-closing and ring-opening metathesis polymerization reactions (**Scheme 1.19**). The catalytic activity was affected by the steric and electronic environment of the Schiff base. High activity with excellent stability of the catalyst was due to combination of Schiff base ligands with a strong Lewis basic *N*-heterocyclic carbene ligand.[109]



Scheme 1.19 Schiff base ruthenium complexes for RCM and ROM reations

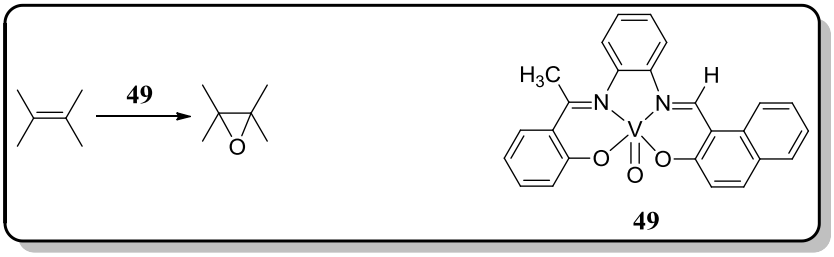
Schiff base metal complexes are very useful and efficient catalysts for the preparation of epoxides from alkenes. The manganese (III) Schiff base metal complex (**48**) was used as a catalyst for the asymmetric epoxidation of conjugated alkenes on addition of bulky Lewis acids (LA) such as zinc tetraphenylporphyrin (ZnTPP). The complexes showed increased turnover numbers in the catalytic asymmetric epoxidation of conjugated olefins (**Scheme 1.20**).[110]



Scheme 1.20 Manganese (III) Schiff base metal complex catalyzed epoxidation reaction

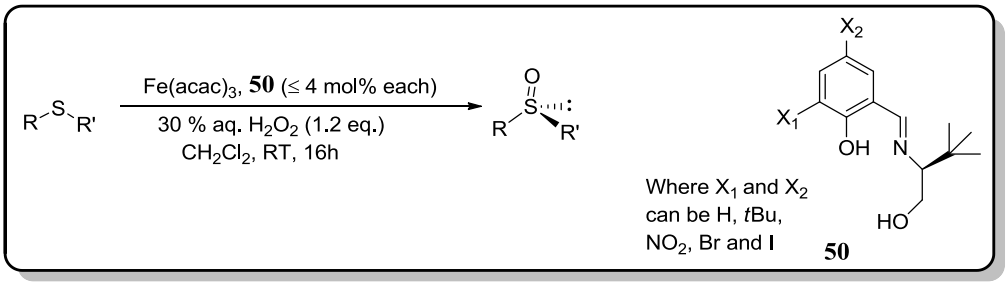
An oxidovanadium complex (IV) of asymmetrical tetradentate N_2O_2 Schiff base derived from 2-hydroxyacetophenon, 2-hydroxynaphthaldehyde and 1,2 phenylenediimine (**49**) was synthesized (**Scheme 1.21**). The complex showed good catalytic activity in epoxidation of

cyclooctene, cyclohexene, styrene, norbornene, 1-octene and indene using *tert*-butyl hydroperoxide as oxygen source.[111]



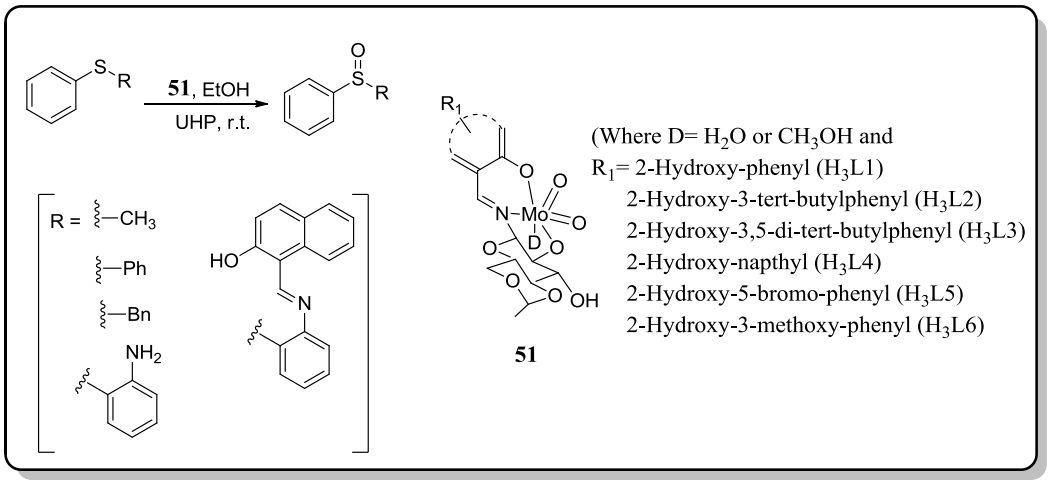
Scheme 1.21 Oxidovanadium (IV) tetradentate Schiff base complex for epoxidation reaction

Chiral sulfoxides are achieved using an iron catalyst formed *in situ* from [Fe(acac)$_3$] and a Schiff base (**50**) obtained from aminoalcohol and salicylaldehyde derivatives (**Scheme 1.22**).[112]



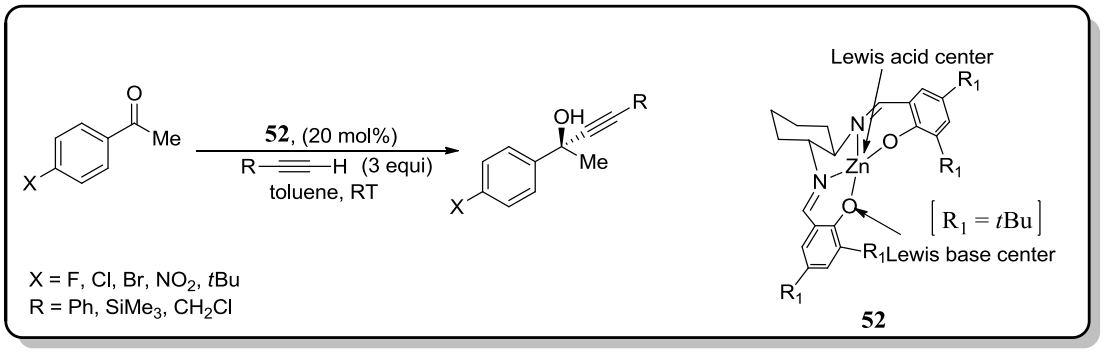
Scheme 1.22 Schiff base iron catalyst for the formation of chiral sulfoxides

Huang group prepared an artificial metalloenzyme based cobalt (II) Schiff base complex with bovine serum albumin. The catalytic activity of the artificial metalloenzyme was determined for enantioselective sulfoxidation of a variety of sulfides with H_2O_2.[113] A series of Mo(VI) complexes (**51**) based on 4,6-*O*-ethylidene-*β*-D-glucopyranosylamine derived ligands was synthesized. The complexes were used as efficient catalysts for the selective oxidation of organic sulfides to corresponding sulfoxides and all complexes showed competent recycling without much loss of catalytic activity for the reaction (**Scheme 1.23**).[114]



Scheme 1.23 *cis*-dioxo molybdenum (VI) complexes for the oxidation of sulfides.

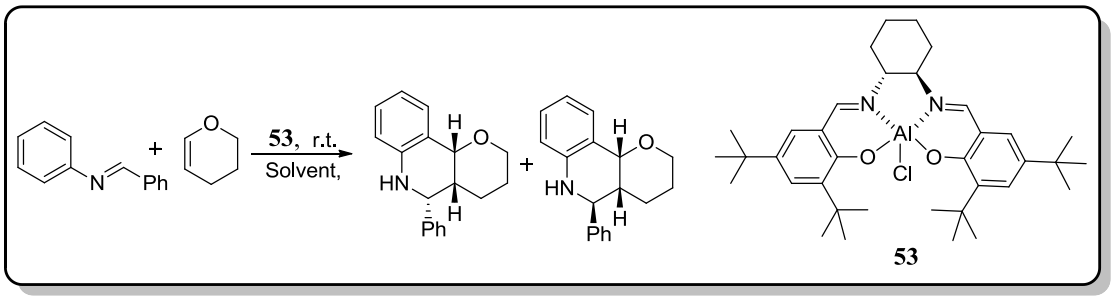
Schiff base complexes showed considerable applications in the reduction of ketones to alcohols. Cozzi group synthesized a series Zn(II) salen complexes (**52**) and used them for the enantioselective alkynylation of ketones. The protocol explained the general catalytic enantioselective addition of terminal alkynes to ketones (**Scheme 1.24**).[115]



Scheme 1.24 Zn(II) salen complexes for the enantioselective alkynylation of ketones

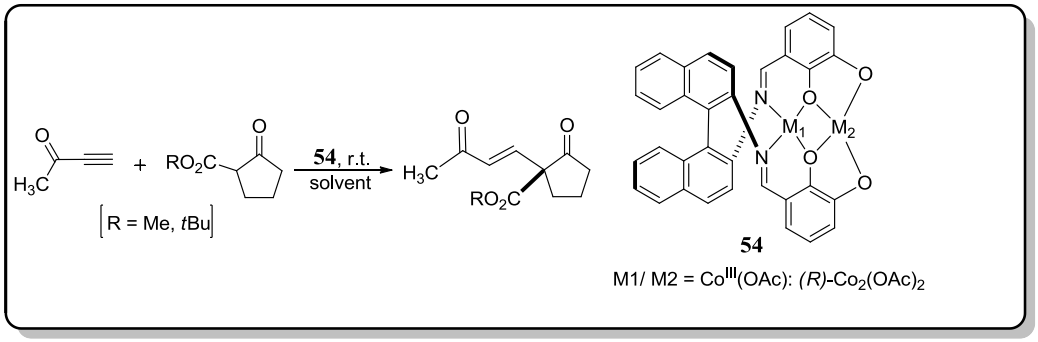
Himeda and co-workers reported the synthesis of a rhodium complex [Cp*Rh(bpy)Cl]Cl and used it as a catalyst in the transfer hydrogenation of a wide variety of ketones under mild reaction conditions.[116]

The target-oriented synthesis of pyranoquinolines was achieved by inverse electron demand (IED) Diels–Alder reaction using chiral Schiff base aluminium complex (**53**). The effect of solvent, substituents and molecular sieves were investigated to synthesize pyarnoquinoline as highly pure diastereomer (**Scheme 1.25**).[117]



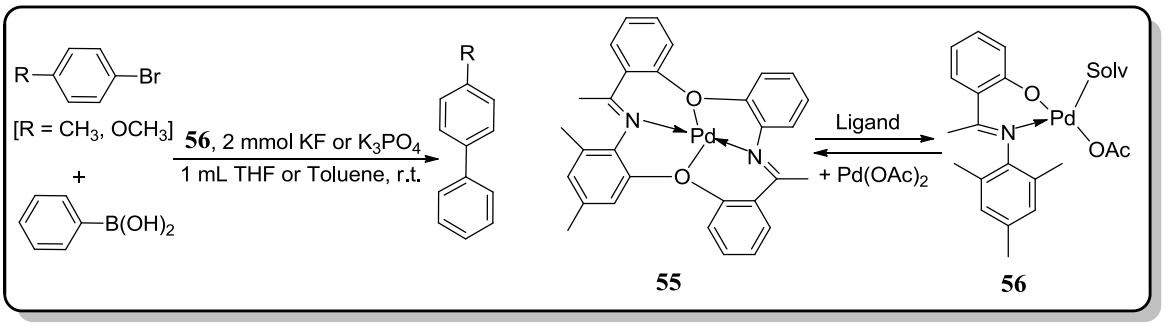
Scheme 1.25 Diels-Alder reaction catalyzed by salen-Al complex

A stable homodinuclear Schiff base cobalt complex (**54**) that expanded the scope of bimetallic cooperative Schiff base catalysis was used for the 1,4-addition of *β*-keto esters to alkynones and a nitroalkene (**Scheme 1.26**). High yields with high enantioselectivities were achieved at room temperature under highly concentrated conditions without air or moisture sensitivity.[118]



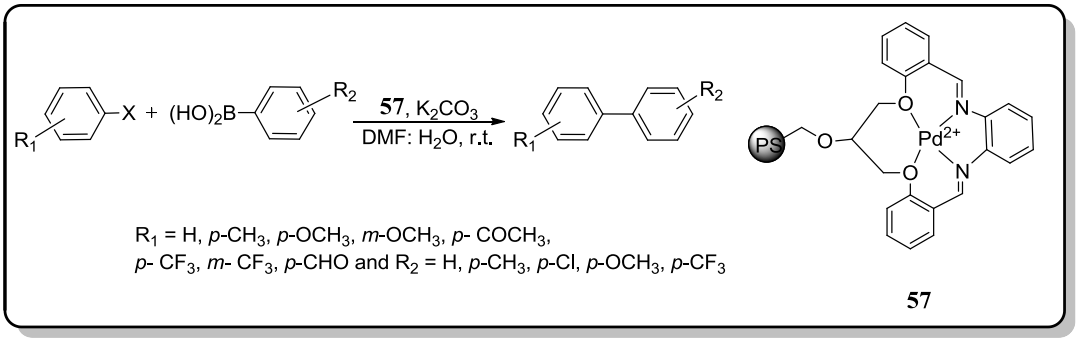
Scheme 1.26 Schiff base catalysts for the 1,4-addition of *β*-keto esters to alkynones

The coupling reactions are able to produce important class of organic compounds which have a great influence in pharmaceutical materials. Schiff base metal complexes form pronounced catalytic systems for the cross coupling reactions. *N,O*-bidentate ligand, 2-[1-(2,4,6-trimethyl-phenylimino)-ethyl]-phenol was used to synthesize a deprotonated 5,5′-chelated palladium acetate complex (**55**). The prepared complex was used as a catalyst for Suzuki cross-coupling reaction of substituted aryl bromides and boronic acids. The deprotonated palladium acetate complex (**56**), [5′Pd(II)(OAc)(solv)], was suggested as a precursor for the catalytically active species (**Scheme 1.27**).[119]



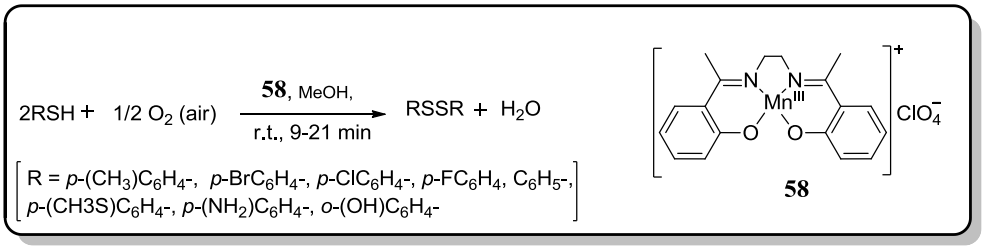
Scheme 1.27 Schiff base catalyst for Suzuki cross-coupling reaction

Cai group prepared a polymer-supported macrocyclic Schiff base palladium complex (**57**) and used it as a catalyst for the Suzuki cross-coupling reaction under ambient conditions. The catalyst showed excellent catalytic activity and stability and could be easily recovered by simple filtration and reused several times without much loss in catalytic activity (**Scheme 1.28**).[120]



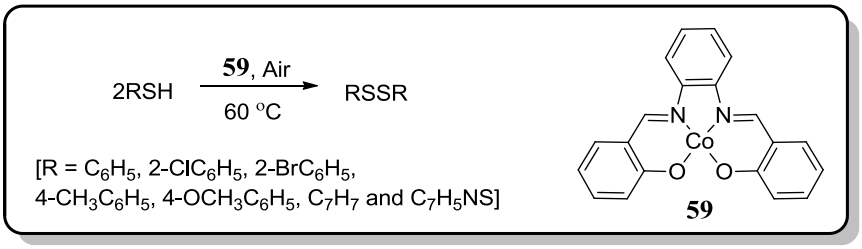
Scheme 1.28 PS-macrocyclic Schiff base palladium catalyst for Suzuki reaction

Disulfides play an important role in biological processes. Schiff-base metal complexes are known to act as efficient catalysts in the synthesis of disulfides. Golchoubian *et al.* prepared Schiff base manganese(III) complex (**58**) and used it as a catalyst in the oxidative coupling of aromatic thiols (**Scheme 1.29**). The disulfides were formed under aerated and mild conditions.[121]



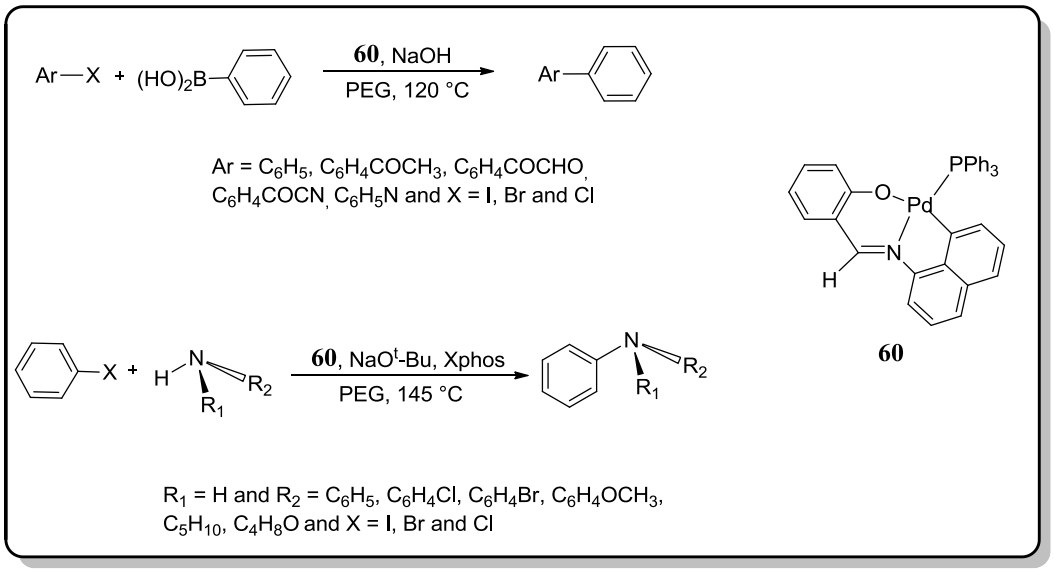
Scheme 1.29 Manganese(III) Schiff-base catalyst for the oxidative coupling of thiols

Tan and co-workers synthesized a cobalt salophen complex (**59**) and used it as a catalyst for the aerobic oxidation of thiols (**Scheme 1.30**). The catalytic oxidation system was found highly selective and very effective in the conversion of disulfides from thiols using air as oxidant.[122]



Scheme 1.30 Cobalt salophen complex for the synthesis of symmetrical disulfides.

Bhattacharya group prepared cyclopalladate [Pd(L)(PPh_3)] type of complexes (**60**) by the reaction of *N*-(naphthyl)-4-R-salicylaldimines, 2-hydroxy-*N*-(naphthyl)-naphthaldimine and $Na_2[PdCl_4]$. All the complexes (**Scheme 1.31**) were found to be suitable catalyst precursors for Suzuki-type C–C and Buchwald-type C–N bond coupling reactions.[123]



Scheme 1.31 Phosphene based palladium complex for the coupling reactions

1.7 Biological activities of Schiff base metal complexes

Schiff base metal complexes are well known for their wide spectrum of antimicrobial[124, 125] and DNA cleaving activities.[126-129] A variety of Schiff base metal complexes have been designed as DNA biosensors[130, 131] and have been successfully employed in DNA detection. Schiff base metal complexes of zinc (II) which strongly bind and cleave DNA, exhibit anticancer activities and control apoptosis.[132, 133]

A series of copper(II) complexes Schiff base derived from S-methyldithiocarbazate and S-benzyldithiocarbazate with methyl levulinate, levulinic acid and 4-carboxybenzaldehyde (**61**) were synthesized. The ligands and their respective copper (II) complexes showed moderate antibacterial activity against both Gram-positive and Gram-negative bacteria (**Figure 1.10**). The most biologically active two ligands were conjugated with various vector moieties *viz*. polyarginines, oligoethylene glycol and an efflux pump blocker, phenylalanine-arginine-*β*-naphthylamide. Conjugation of cell-penetrating peptides (CPPs) to dithiocarbazate compounds greatly enhanced the therapeutic potential.[127] Kandaswamy *et al*. prepared symmetrical oxyimine-based macrocyclic dinuclear zinc(II) complexes (**62**) and evaluated their DNA binding, DNA hydrolysis and the cytotoxic properties (**Figure 1.10**). Considerable changes in DNA binding mode and hydrolysis rate were observed by introducing and extending the aromatic moiety in the macrocyclic ring of the complex.[133] ONO tridentate Schiff base ligand was used to synthesize a series of Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) metal complexes (**63**). The synthesized complexes were screened for their antibacterial and antifungal activities (**Figure 1.10**). Complexes of Mn(II), Cu(II) and Zn(II) were tested for anticancer activity on human breast cancer cell line, MCF-7.[134]

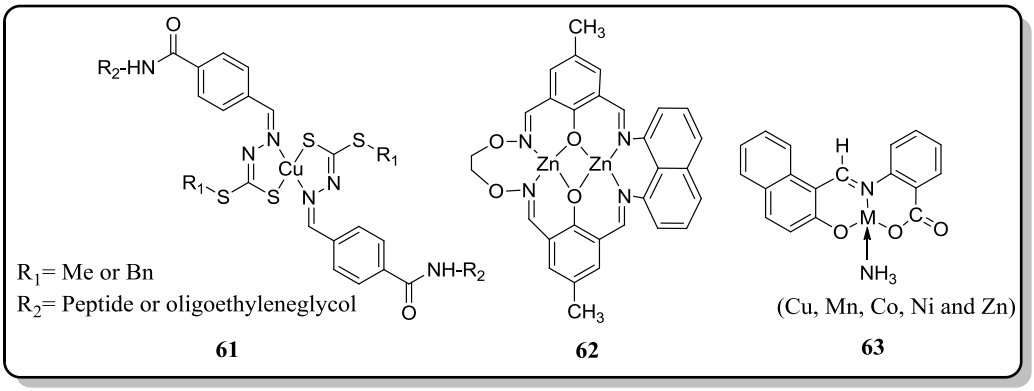


Figure 1.10 Biologically active Schiff base metal complexes

Cu(II) and Co(II) complexes of Schiff base ligands derived from the condensation of 1, 4-phenylenediamine with 5,7-dihydroxy-6-formyl-2-methylbenzopyran-4-one or 6-formyl-7-hydroxy-5-methoxy-2-methylbenzopyran-4-one showed antibacterial and antifungal activities.[135] Ni(II) complexes of amino acid reduced Schiff base ligands showed moderate anticancer activities against human hepatic (HepG2), human cervical cancer (HeLa) and human prostate (PC3) cell lines.[136] Copper (II) thiosemicarbazone complexes (**64-67**) showed good antiproliferative activity against breast adenocarcinoma MCF7, ovarian carcinoma (A2780 and A2780) and noncancerous human embryonic kidney cells (HEK293)

(**Figure 1.11**). The activity of complex can be attributed to the ability to induce ROS accumulation in cells followed by promotion of nrf_2-mediated antioxidant defense.[137]

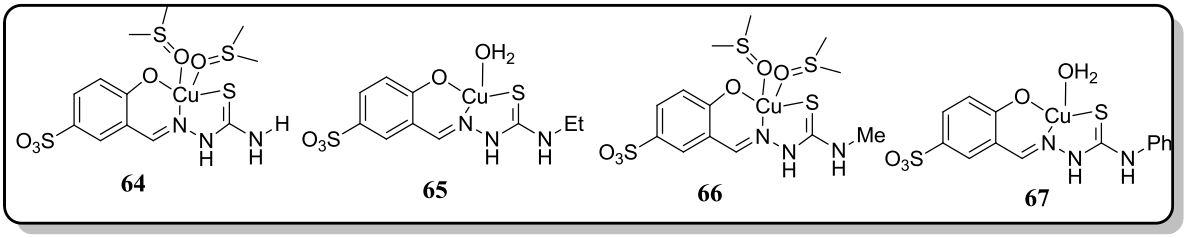


Figure 1.11 Biologically active thiosemicarbazone copper (II) complexes

Cytotoxicity tests using MTT assay with HeLa cells were performed using Ni(II), Cu(II) and Zn(II) complexes of biopolymeric Schiff bases of salicylaldehydes and chitosan.[138] Rahman and group synthesized a tetradentate ONNO Schiff base ligand and its Mn(II), Fe(II), Co(II) and Cd(II) complexes (**68**, **69**). The Schiff base ligand and complexes were examined for antimicrobial activity (**Figure 1.12**). Antimicrobial activities of both ligand and its metal complexes were tested against Gram positive and Gram negative bacteria. All the prepared compounds showed good results of inhibition against the selected pathogenic microorganisms. The acquired data revealed that the tested complexes displayed higher anticancer activity than their simple Schiff base ligands and were comparatively effective as anticancer agents. The binding ability of the complexes for DNA exhibited good results in binding *via* intercalation mode.[139] Manganese(II), cobalt(II), nickel(II), copper(II) and zinc(II) complexes of hexadentate N_2O_4 donor ligand, glyoxal bis(N-nitroso phenylglycine) were prepared and their antimicrobial activity were studied against *E.coli, B. cirroflagellosus, A. niger and C. albicans*. Among the all complexes, copper (II) complex (**70**) showed highest potential against all the microorganisms tested (**Figure 1.12**).[140]

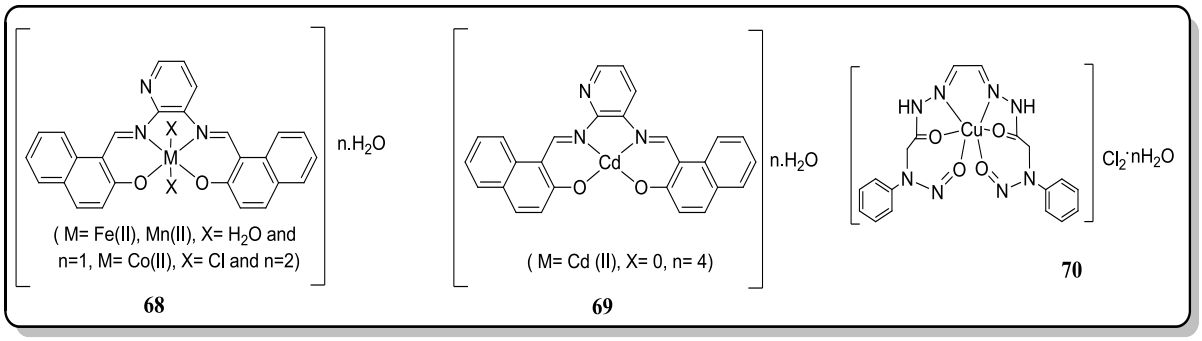


Figure 1.12 HNDAP Schiff base complexes as biologically active agent

Yazdi and co-workers reported a water-soluble sulfonato-substituted Schiff base ligand and its copper(II), zinc(II), and nickel(II) complexes. The compounds were investigated for cytotoxicity against the human chronic myeloid leukemia K562 cells by the MTT assay method. The strongest cytotoxicity was found for the copper complex. The copper compound further caused a visible decrease in viability of the K562 cells.[141] Sharaby *et al.* described biological activity of some selected metal complexes of sulfonamide Schiff base ligand and some mixed ligand complexes with glycine as a secondary ligand. The synthesized Schiff base, its metal (Cu^{II}, Zn^{II}, Cd^{II}, Fe^{III} and Fe^{II}) and mixed ligand complexes were screened for their antibacterial, antifungal and anticancer activity. The activity data showed that the metal complexes and mixed ligand complexes exhibited promising microbial and anticancer activities than their parent Schiff base ligand, the data also displayed that the mixed ligand complexes were found more effective than the metal complexes.[142]

1.8 Photophysical properties of Schiff base metal complexes

The luminescent properties of Schiff base metal complexes are studied due to their wide applications in light emitting diodes (OLEDs),[143-148] liquid crystal[149], laser technology[150] and biology. A variety of Schiff base Zn(II) complexes have shown their effects as powerful tools for the preparation of electroluminescent materials **71-75** (**Figure 1.13**). Xu *et al.* reported the synthesis of phenyl benzoimidazole ligand based zinc (II) complexes (**71**) and subsequently studied the blue-emitting properties of Zn(II) complexes.[151] Son and group reported a series of light-emitting Zn complexes (**72**) in which the emission could be expediently tuned from blue to green by changing different substituents at 4^{th} position of the oxazolylphenolate ligand.[152] Li group developed the effects of the carbazole functional moiety on the emission and electrical properties of the zinc(II) complexes (**73**).[153] A series of ionic zinc–salicylideneimine compounds were synthesized (**74**) by J. Y. Wu. These compounds showed intense fluorescence properties in both solid and solution phases.[154] Roh *et al.* explored several green-emitting Zn(II) complexes (**75**) with benzothiazole and its derivatives to yield white-light emission.[155]

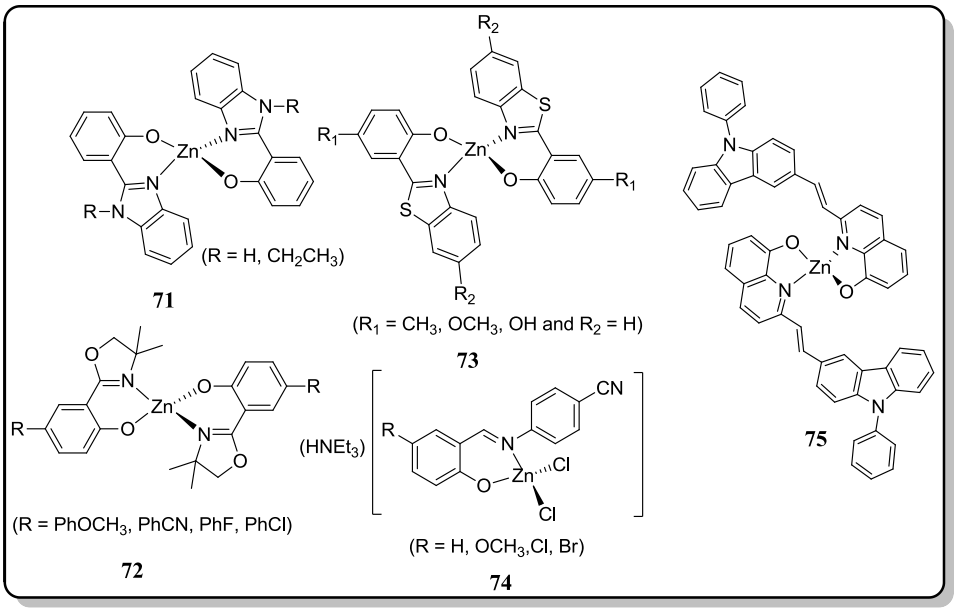


Figure 1.13 Schiff base zinc(II) complexes as luminescent materials

An imine conjugate Schiff base ligand was prepared and evaluated for its sensing properties. The ligand detected Zn^{2+} selectively among a wide range of metal ions. The sensing behavior of the ligand was recognized by UV-vis, fluorescence and ^1H NMR titration techniques. The single crystal X-ray studies revealed the formation of a binuclear complex (**76**) (**Figure 1.14**).[156] Che group reported a series of highly luminescent Pt(II) complexes (**77**) of bidentate Schiff base ligands. Due to the rigidity of the ligands, the synthesized complexes showed high thermal stability (**Figure 1.14**).[143]

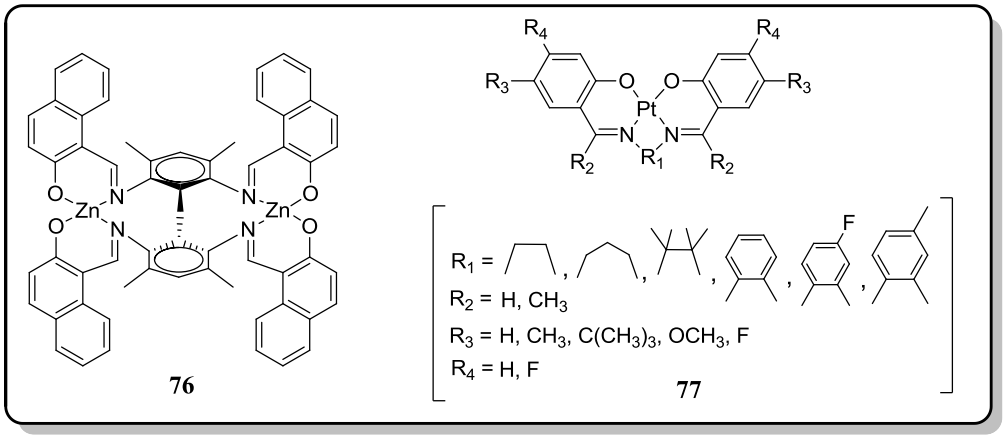


Figure 1.14 Luminescent Schiff base zinc(II) and Pt(II) complexes

Binuclear Zn(II) complexes of *N*, *N*-diethylamine were synthesized and were found to be highly selective and sensitive fluorescent chemosensors for picric acid.[157] Su *et al.* synthesized a novel class of zinc(II) Schiff base complexes and investigated their

photophysical and electrochemical properties in details. The complexes showed aggregation-induced emission enhancement (AIEE). The study presented a zinc(II) Schiff base system specifically showing the effect of substitution on the aggregation-induced emission enhancement activity.[158]

A series of diaminomaleonitrile (DAMN) and DAMN based asymmetric Schiff bases ligands and their Zn(II), Cd(II), Co(II), Ni(II), and Cu(II) metal complexes were synthesized and explored their photophysical applications.[153] Xiang and group prepared a series of colorful salen-type Schiff bases from a variety of organic groups. The occurrence of electron-accepting/donating substituents, donor-acceptor systems, and/or π-extended systems indicated not only full absorption and emission spectra in the visible region of light but also high fluorescence quantum yields up to 0.83 in solution. The experimental results and density functional theory (DFT) calculations proved that the energy gaps of these salen ligands could be well altered. Adding Cu^{2+} and Co^{2+} to the ligand (**78**) solution led to a drastic color change from pink into brownish red and purple, respectively, which was useful not only for the ratiometric detection but also for rapid visual sensing even with the naked eye. The properties of the *cis* and *trans* isomer of the ligand were examined and coordination chemistry of the salen ligands was similar to other well-known tetradentate porphyrin ligands (**Figure 1.15**).[159]

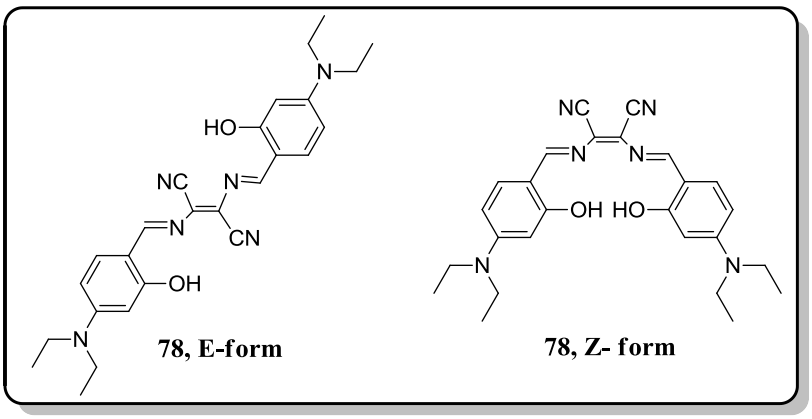


Figure 1.15 Fluorescent *cis* and *trans* forms of salen-type Schiff bases

A collection of Cu(II), Fe(III), Mn(III), Pt(II) and Zn(II) complexes of a symmetric porphyrin Schiff base ligand (**79**) were prepared (**Figure 1.16**). The photo physical properties of the ligand and its metal complexes were investigated. The compounds exhibited very interesting pholuminescence properties.[160]

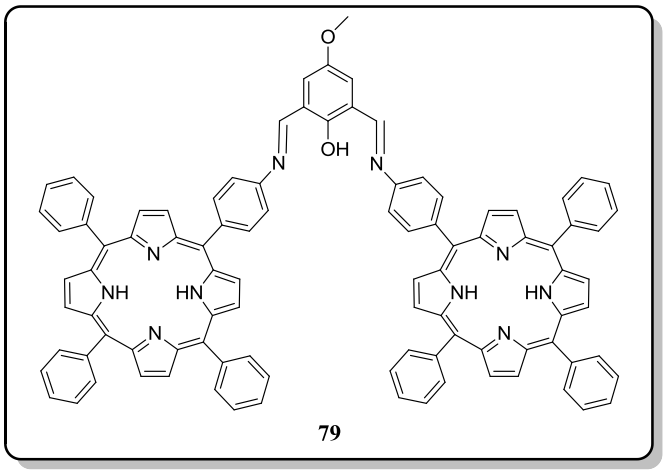


Figure 1.16 Luminescent symmetric porphyrin Schiff base ligands

Fu and group reported platinum and ruthenium metal based Schiff base complexes. The synthesized complexes were found highly luminescent and were used as photosensitizers for visible-light compelled hydrogen production reactions.[161] A series of mononuclear or binuclear *trans* zinc(II)/mercury(II) complexes of polydentate Schiff base ligands were synthesized. The properties of the synthesized complexes were fully characterized by UV-visible and fluorescence spectra in both solid and solution states at room temperature. The luminescence color of the complexes could be tuned from blue to green to red.[162] A series of zinc (II) complexes of different conjugated Schiff base systems were synthesized by Fan group and these complexes were investigated for their photophysical properties. The complexes showed high luminescence both in solid and solution states.[163] Das and co-workers prepared a series of complexes of Zn^{II}, Cd^{II} and Hg^{II} with the formula $[Zn_2(L)(SCN)_3]$, $[Cd_{2.5}(L)(SCN)_3(AcO)]_n$ and $[Hg_2(L)(SCN)_3]_n$ with a Schiff base ligand, 4-*tert*-butyl-2,6-bis-[(2-pyridin-2-yl-ethylimino)-methyl]-phenol (**80**). The synthesized complexes were found highly fluorescent in nature (**Figure 1.17**).[164] A tripodal Schiff base derived from tris(2-aminoethyl)amine and 2-hydroxynaphthalene-1-carboxaldehyde (**81**) acted as a chemosensor for metallic species. The fluorogenic response of the ligand towards Zn^{2+}, Cd^{2+}, Fe^{3+} and Fe^{2+} was estimated and the addition of metallic cations induced a remarkable colorimetric response (**Figure 1.17**).[165]

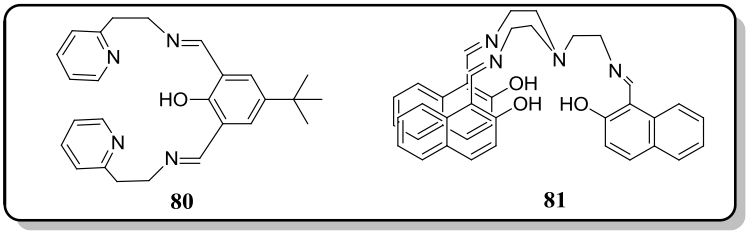


Figure 1.17 Luminescent Schiff base ligands

1.9 Conclusions

Recent developments show an improved interest in the chemistry of ionic liquid-tagged Schiff base metal complexes. This might be due to their utility in various fields such as medicinal chemistry, material science, organometallics and particularly in catalysis. This chapter summarizes an assorted report for the synthesis and applications of ionic liquid-tagged metal complexes. Since ionic liquid-tagged Schiff base metal complexes are found to have applications in diverse disciplines, the synthesis of novel Schiff base complexes, anchored with ionic liquids is open for further exploration.

1.10 References

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Chapter 2

Experimental and Theoretical Methods and Characterization Techniques

SECTION 2A

Materials and Methods

A variety of chemicals, instruments and characterization techniques have been used during the progression of this research work. The various techniques employed for the characterization of synthesized ligands and complexes comprises Fourier transform infrared (FTIR) spectroscopy, UV-visible spectroscopy, NMR spectroscopy, Mass spectrometry, EPR spectroscopy, Cyclic voltammogram and powdered XRD. Thermal analysis and photophysical properties of the ligands and complexes were also studied. This chapter presents the information regarding various instruments, basic principles of various techniques, chemicals and software used.

2A.1 Chemicals used

Allyl bromide, aniline, *p*-anisidine, benzaldehyde, benzyl acrylate, benzyl bromide, benzyl chloride, *p*-bromoaniline, 4-bromoanisole, *p*-bromobenzaldehyde, bromobenzene, 5-bromoindole, 1,3-dibromopropane, 4-bromostyrene, 4-bromothiophenol, 4-tertiary butylphenyl acetylene, *p*-chloroaniline, *p*-chlorobenzaldehyde, chlorobenzene, 4-chlorothiophenol, 4-chlorostyrene, copper acetatepentahydrate, DABCO, Et_3N, 2-ethynyl pyridine, 4-ethyl phenyl acetylene, 2-ethynyl-1,2,3-trimethylbenzene, *p*-fluoroaniline, 4-fluorophenyl acetylene, 1-heptyne, 2,4-dihydroxybenzaldehyde, indole, iodobenzene, 4-iodotoluene, 1-iodo-4-nitrobenzene, 1-iodonaphthalene, 2-iodotoluene, 2-iodoaniline, 4-iodoanisole, 2-iodothiophene, 2-iodo-1,3,5-trimethyl benzene, isopropyl amine, *p*-methoxybenzaldehyde, 4-methoxyphenyl acetylene, (3,4,5-trimethoxyphenyl)boronic acid, methyl acrylate, 1-methylimidazole, methyl iodide, 4-methyl styrene, 4-methylthiophenol, 2-naphthalenethiol, 1-naphthylamine, *p*-nitrobenzaldehyde, 1-octyne, palladium acetate, phenacyl bromide, phenyl acetylene, phenyl boronic acid, 5-phenyl-1-pentyne, piperidine, potassium carbonate, pyrrolidine, sodium azide, sodium bicarbonate, sodium carbonate, sodium hydroxide, styrene, thiophene-2-carbaldehyde, thiophenol, *p*-tolyl acetylene and zinc acetate tetrahydrate were purchased from chemicals companies *viz.* Sigma Aldrich, Alfa Aesar, SD fine, SRL, Spectrochem etc. The solvents acetone, acetonitrile, benzene, chloroform, DMF, DMSO, ethanol, ether, ethyl acetate, hexane, methanol and THF were acquired from Merck, India limited and were distilled and dried before use.

2A.2 Characterization and analysis techniques

The instrumental methods which were used for the detailed analysis and characterization of ionic liquid-tagged ligands and their metal complexes are summarized beneath.

2A.2.1 Infrared (IR) spectroscopy

The infrared spectroscopy is the study of the interaction of matter with light radiation when waves travel through the medium. The waves interact with the polarity of the chemical bonds of the molecules and are electromagnetic in nature. This spectroscopy deals with the analysis of infrared light interacting with a molecule, which can be examined in three means by measuring absorption, emission and reflection.[1] The main use of this technique is in organic and inorganic chemistry and is used to determine functional groups in the molecules.[2] According to the selection rule of IR spectroscopy, an electric dipole moment change must be accompanied with the 'IR active' vibrational mode. The basics of vibrational spectroscopy is governed by two laws, they are Hooke's law and Frank condon principle. Hooke's law states that, for two body harmonic oscillator the frequency of vibration is

$$\overline{\nu} = \frac{1}{2\pi c}\sqrt{\frac{K}{\mu}}$$

Where, c = speed of light, K = force constant, (5 x 10^5 dynes/cm) and μ = reduced mass ($m_1.m_2/m_1+m_2$). Hooke's law can be used to calculate the fundamental vibrations for diatomic molecules in infrared spectroscopy. According to Franck Condon Principle, in a vibrating molecule, the probability of finding of given atom at a certain point is inversely proportional to its velocity.[3] In this thesis work, infrared spectra (4000-450 cm^{-1}) of ionic liquid-tagged Schiff base ligands and their metal complexes were recorded with KBr pallets on ABB Bomen MB 3000 FTIR spectrometer (**Figure 2A.1**).

Figure 2A.1 Photograph of the (FT-IR) spectrometer (ABB Bomen MB 3000)

2A.2.2 UV-visible spectroscopy

Electron spectroscopy is an analytical technique which is used to study the electronic structure and its dynamics in atoms and molecules. Electronic spectroscopy deals with the interactions of ultraviolet and visible radiations of electromagnetic spectrum with the matter by promotion of the electrons from their ground state to a high energy excited state. The wavelength range of ultra violet-visible spectroscopy is in between 190-750 nm.[4] UV-Vis spectroscopy can be used to define the concentration of organic compound having high degree of conjugation dissolved in suitable solvent.[5] The solvent polarity and pH can affect the absorption spectrum of an organic compound. The absorption of light in this spectroscopy can be explained according to Lambert-Beer's Law, which states that the absorbance (*A*) of an absorbing species in a solution is directly proportional to the concentration (*c)* of the species and its molar extinction coefficient (ε) at the certain measuring wavelength λ and is given by the equation –

$$A = \log(I_0/I) = \varepsilon.c.l$$

where, I_0 and I are the intensities of the incident and transmitted light, respectively, and l is the path length for the light beam passing through the sample.[6] Many organic compounds as well as metal complexes can be characterized by the electronic spectroscopy.[7, 8]

In present work, UV-visible spectra were recorded both in solution and solid states and the comparative studies of the ionic liquid-tagged ligands and complexes were accomplished. The studies were performed using the Shimadzu Spectrophotometer with model UV-2450 and JASCO with model V-650 (**Figure 2A.2**).

Figure 2A.2 Photograph of the UV. spectrometers, Shimadzu model UV-2450 and JASCO with model V-650

2A.2.3 Nuclear magnetic resonance (NMR) spectroscopy

Nuclear magnetic resonance spectroscopy is a research technique that adventures the magnetic properties of certain atomic nuclei. The spectroscopy determines the physical and chemical properties of atoms or the molecules in which they are confined. It relies on the phenomenon of nuclear magnetic resonance and can provide detailed information about the structure and chemical environment of molecules. The intramolecular magnetic field which is present around an atom in a molecule changes the resonance frequency and thus gives access to details of the electronic structure of a molecule and its individual functional group.[9] NMR technique is applicable to any kind of sample that contains nuclei possessing spin e.g. ^{1}H or ^{13}C, placed in a magnetic field and absorbs electromagnetic radiation at a frequency characteristic of the isotope.[10] In the present thesis the ^{1}HNMR and ^{13}C NMR spectra of the ionic liquid-tagged ligands and their metal complexes were measured on a 400 MHz NMR spectrometer (Bruker AVANCE III) and Bruker Heaven 11400 (400 MHz) and Varian (500 MHz), using $CDCl_3$ and DMSO-d_6 as solvents (**Figure 2A.3**).

Figure 2A.3 Photograph of 400 MHz NMR spectrometer (Bruker AVANCE III).

2A.2.4 Mass spectrometry

Mass Spectrometry is a technique which causes the formation of the gaseous ions with or without their fragmentation. The gas phase ions are then characterized by their mass to charge ratios (*m/z*) and their relative abundances. If the amount of energy supplied to a molecule is greater than the ionization energy, a molecular ion known as the parent ion, is formed. Mass spectrometry is used in many different fields and is applied to pure samples as well as complex mixtures. Mass spectrometers are used to measure the difference in mass-to-charge ratio (m/z) of ionized atoms or molecules to separate them. Therefore, mass spectroscopy permits the quantitation of atoms or molecules and provides structural information by the identification of distinctive fragmentation patterns. The operations performed by the mass spectrometer are; to create gas-phase ions, to separate the ions in space or time based on their mass-to-charge ratio and also to measure the quantity of ions of each mass-to-charge ratio.[11-14] In the present thesis the mass spectra of the ionic liquid-tagged ligands and their metal complexes were recorded on AB SCIEX TOF/TOF 5800 spectrometer and 6545Q-TOF LC/MS, Model-G6545A (**Figure 2A.4**).

Figure 2A.4 Photograph of mass spectrometer (6545Q-TOF LC/MS, G6545A)

2A.2.5 Powder X-ray diffraction (PXRD)

Powder diffraction is a scientific technique which uses X-rays, neutron or electron on powder or micro crystalline samples for the structural interpretation of the material.[15] Powder diffractometer is the instrument which is used to perform such powder measurements. X-ray powder diffraction is one of the most potential characterization tools and a nondestructive technique for characterizing both organic and inorganic crystalline materials in molecular as well as crystalline form. The cathode ray tubes acts as the source of the X-ray, and before directed towards the sample, these rays are filtered to produce monochromatic radiation, collimated to concentrate.[16] The interaction between the material and the incident X-rays produces constructive conclusions about crystal structure if they satisfy Bragg's equation.[17, 18]

Bragg's equation is $2d \sin\theta = n\lambda$

Where ***n*** is a positive integer, **λ** is the wavelength of a beam of X-rays incident on a crystal with lattice planes separated by distance *d*, and θ is the angle of incident rays. In present work the powder X-ray diffraction (XRD) data of ionic liquid-tagged ligands and their metal complexes with CuK_α radiation (λ = 1.542 Å), were obtained on a Rigaku Miniflex II diffractometer and the

diffraction patterns were recorded over a range of 2θ angles from 10 to 50° with the scanning rate of 2°/min (**Figure 2A.5**).

Figure 2A.5 Photograph of powder X-ray diffractometer (RIGAKU MiniFlex II).

2A.2.6 Electron spin resonance (ESR) spectroscopy

Electron spin spectroscopy also known as electron paramagnetic resonance (EPR) or electron magnetic resonance (EMR), measures the transition frequency between different spin states of an electron. The energy difference between the electron states $m_s = -1/2$ and $m_s = 1/2$ in a reasonably strong magnetic field of 1 Tesla is $\Delta E = 1.86 \times 10^{-23} J$ corresponding to a frequency of 28 GHz in ESR. The excitation frequencies in electron spin resonance spectra depend on the total magnetic moment. The energy levels of a bound, unpaired electron are therefore different from that of a free electron mainly due to the electron orbital angular momentum. The corresponding *g*-factors then differ from that of the free electron ($g_e = 2.0023$) and can be stated as a function of the orbital angular momentum L and the total angular momentum *J*:

$$g = 1 + \frac{S(S+1) - L(L+1) + J(J+1)}{2J(J+1)}$$

ESR also observes the coupling of electron to nuclear spins, which is called as the 'hyperfine coupling' and carries information about the native environment of the electronic spin probe.[19-

[22]In the present work the ESR spectra of ionic liquid-tagged copper (II) complex was acquired on ESR spectrometer JEOL, Japan (JES-FA200 ESR Spectrometer with X and Q band)

Figure 2A.6 Photograph of ESR spectrometer JEOL, Japan (JES-FA200).

2A.2.7 Fluorescence spectroscopy

In a fluorescence spectrometry both an excitation spectrum and/or an emission spectrum can be measured. The concentration of the analyte is directly proportional to the intensity of the emission. When the external energy supply is by means of the absorption, the light emitted is called photoluminescence and this progression takes place in any fluorimetric analysis. In fluorescence spectroscopy the fluorophores play the central role and the assorted interactions of these fluorophores with light are investigated in fluorescence spectroscopy. The fluorophore is an element that causes a molecule to absorb energy of a specific wavelength and then re-remit energy at a different but equally specific wavelength.[23-26] In this thesis the Steady-state fluorescence measurements were executed on Horiba Jobin Yvon Fluoromax-4 scanning spectrofluorimeter (**Figure 2A.7**).

Figure 2A.7 Photograph of spectrofluorimeter (Horiba Jobin Yvon Fluoromax-4)

The quartz cuvettes of 1 cm path length, excitation and emission slit widths of 3 nm were used for the spectral measurements. Fluorescence quantum yields of the ionic liquid-tagged zinc(II) complex were estimated at room temperature for a variety of solvents by a relative method employing quinine sulfate (φ = 0.55 in 0.1 N H_2SO_4), as the secondary standard using the following equation:

$$\frac{\Phi_S}{\Phi_R} = \frac{I_S}{I_R} \times \frac{(OD)_R}{(OD)_S} \times \frac{\eta_S^2}{\eta_R^2}$$

Where *I* is the area under the curve, Φ is the fluorescence quantum yield, $\eta$is the refractive index of the medium, OD denotes absorbance at the wavelength of exciting light and the subscripts S and R stand for the parameters of studied sample and reference, respectively.

2A.2.8 Time resolved spectroscopy

Time resolved time-resolved spectroscopy is used to study the dynamic processes in materials or chemical compounds with the help of spectroscopic techniques. Most often these processes are studied after the illumination of a material occurs, but in principle, the technique can be pragmatic to any process that leads to a change in material properties. It is possible to study the processes that occurs on time scales as short as 10^{-16} seconds with the help of lasers.[27-30] In the present thesis the excited singlet state lifetimes were measured from intensity decays using a

Horiba Jobin Yvon Fluorocube-01-NL picosecond time-correlated single-photon counting (TCSPC) experimental setup (**Figure 2A.8**).

Figure 2A.8 Photograph of Horiba Jobin Yvon Fluorocube-01-NL (TCSPC)

A picosecond diode laser of 400 nm (Nano LED 400L, IBH, UK) was used as an excitation light source. A TBX photon detection module (TBX-07C) was used for the detection of fluorescence signals at magic angle (54.7°) polarization. The decays were analyzed using IBH DAS-6 decay analysis software. The fineness of the fits was judged by the χ^2criterion. Average fluorescence lifetime for the multi exponential decay curve was obtained from the decay time constants $(\tau)$and pre-exponential factors (α) using the following equation:

$$\langle \tau_f \rangle = \frac{\sum_i \alpha_i \tau_i^2}{\sum_i \alpha_i \tau_i}$$

Where α_i is the pre-exponential factor corresponding to the i^{th} decay time constant τ_i.

2A.2.9 Cyclic voltammetry

Cyclic voltammetry (CV) is an electrochemical technique that measures the current which develops in an electrochemical cell. In potentiometry, the electrochemical potential of one electrode (the reference electrode) is generally fixed, so the measured cell potential can be inferred in terms of an equilibrium half-cell reaction which involves an analyte species in contact

with the other electrode (the working electrode). Contrasting to a linear sweep, when the set potential is reached in a CV experiment, the working electrode's potential is ramped to the initial potential to return in the opposite direction. The cycles of ramps in potential can be repeated as many times as required. The current at the working electrode is plotted versus the applied voltage to give the cyclic voltammogram. Cyclic voltammetry is generally used to study the electrochemical properties of an analyte in solution. In the current work the cyclic voltammogram of an ionic liquid-tagged copper complex was recorded on the linear-sweep voltammogram of Ag_2S/Ag-1 and Ag_2S/Ag-2 and was obtained in the potential range of 01.8V to -1.5V vs. Ag/AgCl with a scan rate of 20 mV/S (**Figure 2A.9**).[31-34]

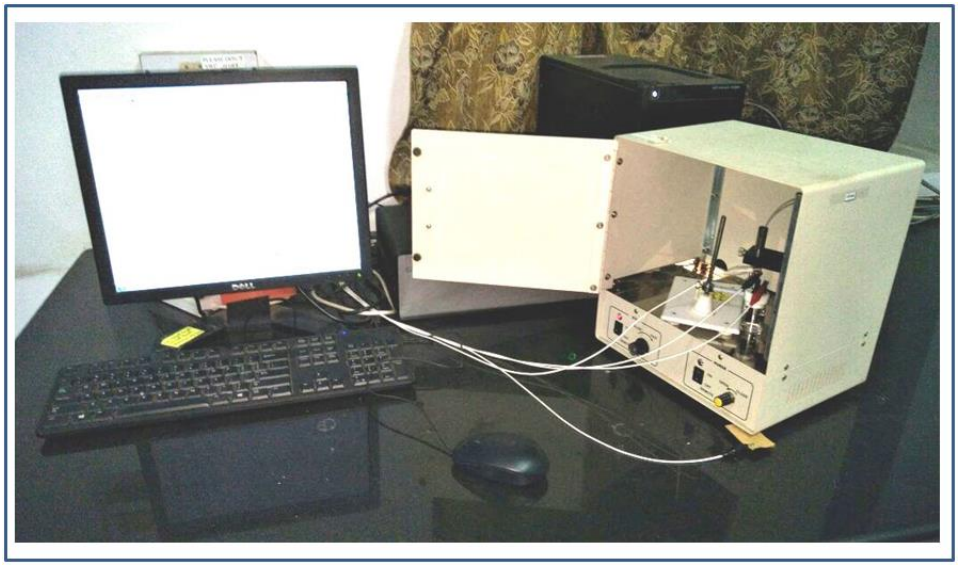

Figure 2A.9 Photograph of linear-sweep cyclic voltammogram

2A.2.10 Differential scanning calorimetry (DSC)

Differential scanning calorimetry (DSC) is a technique for measuring the energy which is required to establish a nearly zero temperature variation between a substance and an inert reference. This is a thermo analytical technique in which the change in the amount of heat necessary to increase the temperature of a sample and reference is measured as a function of temperature. Both the sample and reference are kept at nearly the same temperature throughout the experiment. DSC permits the measurements of the transition such as the glass transition, melting, and crystallization. Additionally, the chemical reaction such as thermal

curing, specific heat capacity, and purity analysis are also measurable with this technique.[35, 36]In the current thesis work the DSC of ionic liquid-tagged ligands and their metal complexes was recorded on Perkin Elmer DSC 4000 at a heating rate of 10 °C min^{-1} using nitrogen as the carrier gas in the range 30 °C to 400 °C (**Figure 2A.10**).

Figure 2A.10 Photograph of Perkin DSC (model DSC-4000)

2A.2.11 Thermo gravimetric analysis (TGA)

Thermogravimetric analysis (TGA) is the method of thermal analysis in which the changes in physical and chemical properties of materials are measured as a function of increasing temperature or time. The TGA instrument comprises of a sample pan in which a known amount of a starting material between 2 and 50 mg should be placed and it should cover bottom of the pan called initial weight. TGA helps to measure a variety of processes such as melting, crystallization or glass transition, absorption, desorption, sublimation, reduction, vaporization, oxidation and decomposition.[37, 38] The TGA instrument which was used to record the data of ionic liquid-tagged ligands and metal complexes, in the present thesis is Perkin Elmer Thermo Gravimetric Analyzer of model TGA – 4000 (**Figure 2A.11**).

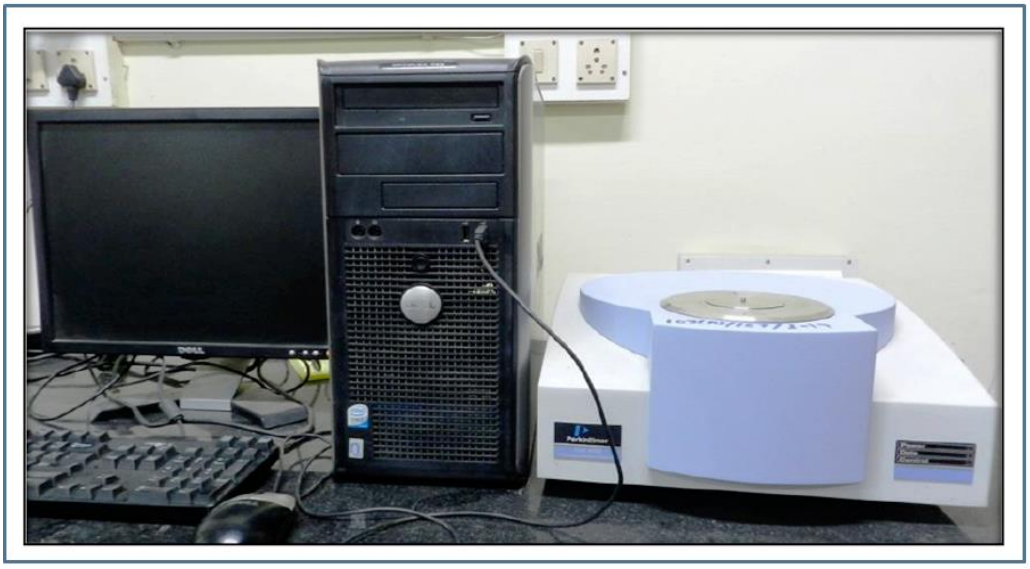

Figure 2A.11 Photograph of Perkin Thermo Gravimetric Analyzer of model TGA-4000

2A.3 Software used

The spectral data were plotted using Origin pro 8.0, while chemical structures were drawn using ChemBioDraw Ultra 12.0 and the NMR data were integrated using MestReNova.

2A.4 References

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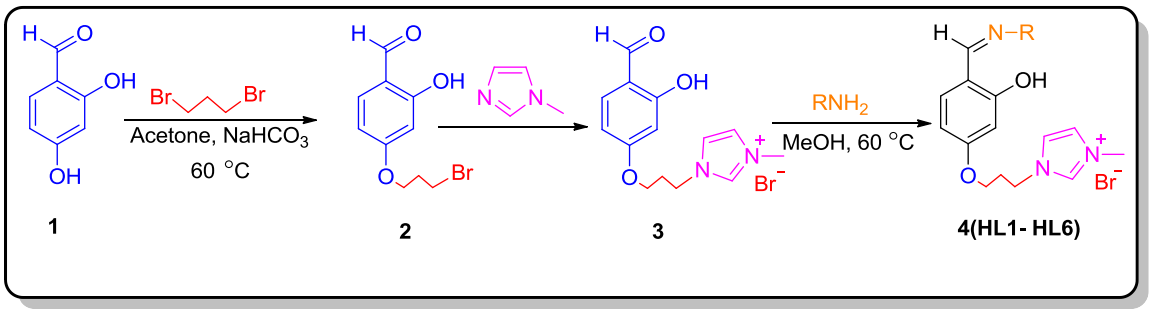
SECTION 2B

Synthesis and Characterization of Ionic liquid-tagged Schiff Base Ligands

2B.1 Synthesis and Characterization of Ionic Liquid-tagged Schiff Bases

2B.1.1 Results and discussion

In most functionalized ionic liquids, quaternization of ring nitrogen by alkyl halide to produce 3-alkylimidazolium salt is done after attaching the functional group to imidazole at the N-1 position. These reactions are generally performed in a narrow region of temperature and solvent parameters due to competing side reaction of the alkylating reagent with the incorporated functional group. We have designed a novel approach for the synthesis of functionalized ionic liquids where this alkylation of functional group can be avoided (**Scheme 2B.1**).

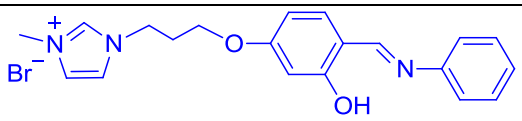
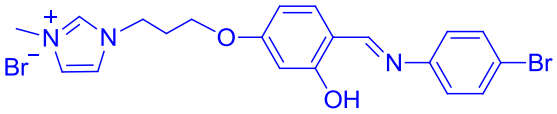
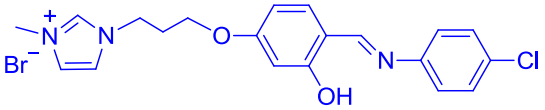
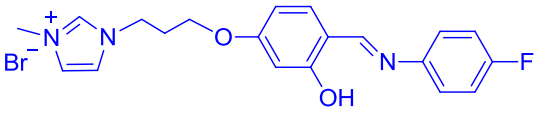
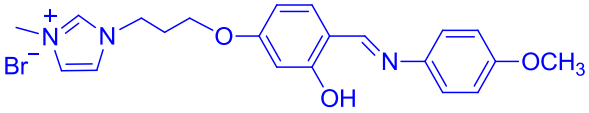
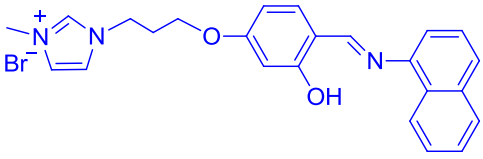


Scheme 2B.1 Synthesis of ionic liquid-tagged Schiff bases

The first step of the synthetic route involved the synthesis of 4-(3-bromopropoxy)-2-hydroxybenzaldehyde **2** by selective *O*-alkylation of 2,4-dihydroxybenzaldehyde **1**. The reaction gives a mixture of 4-(3-bromopropoxy)-2-hydroxybenzaldehyde **2** and 4,4′-(propane-1,3-diylbis(oxy))-bis(2-hydroxybenzaldehyde). Formation of dimeric 4,4′-(propane-1,3-diylbis(oxy))-bis(2-hydroxybenzaldehyde) was minimized by dilution method. Usage of mild reaction conditions and presence of hydrogen bonding resulted in *O*-alkylation selectively at the para-positon. The ^{1}H NMR spectrum of the compound showed singlet at δ11.02 for OH, singlet at δ 10.02 for aldehydic proton, triplet at δ 3.66 for CH_2Br, triplet at δ 4.10 for OCH_2, multiple at δ 2.28 for CH_2 along with aromatic protons at δ 6.49-7.64. The ESI-MS spectrum of **2** a peak at *m/z* 259.0 and 261.1 for $[M]^+$ and $[M + 2]^+$ ions, respectively. In the IR spectra a peak at 1624 cm^{-1} was observed for aldehydic C=O stretching and a sharper peak at 3080 cm^{-1} for OH stretching. There was no significant shift in the C=O stretching frequency that also indicates that intramolecular hydrogen bonding of ortho-hydroxy group with carbonyl group is not disturbed

and alkylation has occurred selectively at the para hydroxy group. In addition to this sharper peak at 3080 cm^{-1} for OH stretching also indicates alkylation at para-hydroxy group. In the subsequent step, 1-methylimidazole was reacted with **2** to form ionic liquid tagged aldehyde **3**. The ESI-MS spectrum of **3** displayed a peak at *m/z* 261.2 for $[M + H–Br]^+$ ion. The ^1H NMR spectrum showed an additional peak at δ 3.86 ppm for N-CH_3 and three new peaks at δ 9.25, 7.84 and 7.74 ppm for imidazolium ring protons in addition to other protons. In the third step, **3** was reacted with different aromatic amines to yield ionic liquid tagged Schiff base **4**. The yields of **4** were moderate and the nature of various substituents on the aromatic amines had no obvious effect on the yields. The details of yield and structure for different ionic liquid tagged Schiff bases are given in **Table 2B.1**.

Table 2B.1 Synthesis of ionic liquid-tagged Schiff bases **HL1-HL6**

S. No.	R	Structure of 4	Label	Yield[a] (%)
1.	C_6H_5		**HL1**	68
2.	4-BrC_6H_5		**HL2**	60
3.	4-ClC_6H_5		**HL3**	59
4.	4-FC_6H_5		**HL4**	64
5.	4-$OCH_3C_6H_5$		**HL5**	68
6.	$C_{10}H_7$		**HL6**	50

[a]Isolated yield.

Compound **HL1** exhibited absorption bands at 1620 cm^{-1} (C=N str.), 3100 cm^{-1} (H–C(=N) str.) and 3415 cm^{-1}(OH str.) in the IR spectrum. The ESI-MS spectrum (**Figure A01, Appendix-A**)

of **HL1** showed a peak at (*m/z*): 336.3 $[M - Br]^+$. In ^1H NMR azomethine proton appeared at δ 8.79 and hydroxyl proton at δ 13.77 along with other protons of the molecule. A peak appeared at δ 163.6 for azomethine carbon along with other carbons of the molecule in ^{13}CNMR spectra. The representative ^1H and ^{13}CNMR of **HL1** is shown in **Figure 2.12**. These spectral data are consistent with the structure of **HL1**.

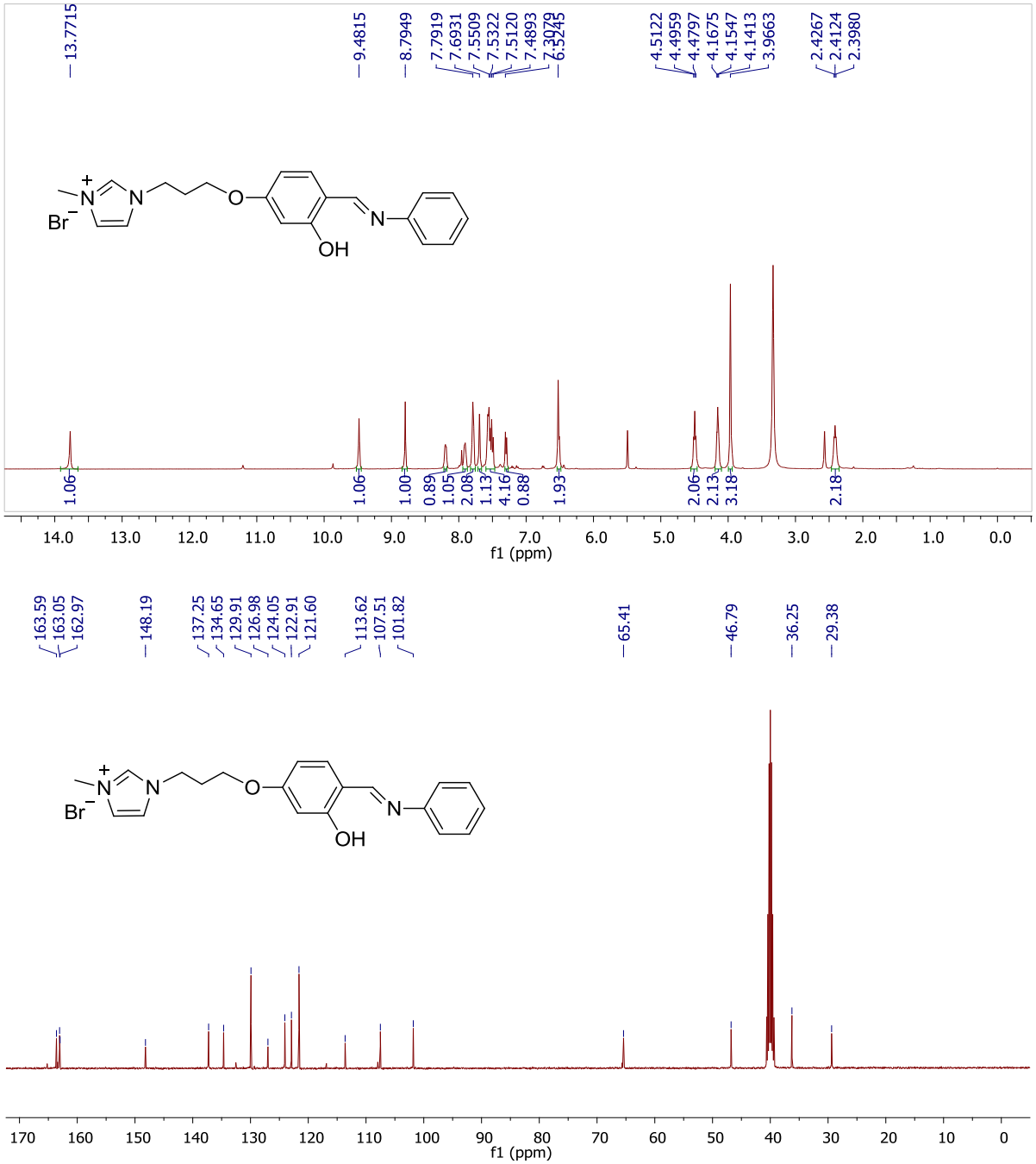


Figure 2B.1 ^1H and ^{13}C NMR spectra of **HL1** in deuterated DMSO

Similarly, spectroscopic data for all other compounds have been found to be consistent with their structure.

2B.2 Experimental Section

2B.2.1 General

All the solvents and reagents were purchased from Sigma-Aldrich, India and Spectrochem Pvt. Ltd., India and were used without further purification. Melting points were determined in open capillary tubes on a MPA120-Automated Melting Point apparatus and are uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Heaven 11400 (400 MHz) and Varian (500 MHz) spectrometers using $CDCl_3$ and DMSO-d_6 as solvents and the chemical shifts were expressed in ppm.

2B.2.2 Synthesis of ionic liquid tagged aldehyde (3)

In the first step, reaction of 1,3-dibromopropane (8.0 mmol), 2,4-dihydroxybenzaldehyde (6.0 mmol) and sodium bicarbonate (6.0 mmol) in acetone (50 mL) at 60 °C for 60 hours gave mixture of 4-(3-bromopropoxy)-2-hydroxybenzaldehyde **2** and 4,4′-(propane-1,3-diylbis(oxy))bis(2-hydroxybenzaldehyde). Column chromatography over silica gel gave pure **2** in 65% yield. Reaction of 1- methylimidazole (3.5 mmol) with **2** (3.5 mol) at 80 °C for 48 hours gave a viscous liquid which was washed with diethyl ether-ethyl acetate mixture to give ionic liquid tagged aldehyde **3** in almost quantitative yield.

2B.2.3 General procedure for synthesis of ionic liquid supported Schiff bases (4)

A mixture containing ionic liquid-tagged aldehyde (3.0 mmol) and amine (4.0 mmol) in ethanol was refluxed for 4 hours. On completion of the reaction, ethanol (30 mL) was added to the reaction mixture; the solid product formed was filtered off and washed with cold ethanol. The crude product was purified by recrystallization from ethanol/ethyl acetate (3: 1 *v/v*). All the compounds were characterized by IR, ESI-MS and ^{1}H NMR and ^{13}CNMR spectroscopic data (**Figure A02-A06, Appendix-A**).

2B.3 Physical and spectral data for HL1-HL6

HL1: Yield 849 mg (68%); mp 81- 83 °C; IR (cm^{-1})1620, 3416; ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.77 (s, 1H), 9.48 (s,1H), 8.79 (s, 1H), 8.20 (t, *J* = 1.8, 1H), 7.90 (t, *J* = 1.8 Hz, 1H),7.79–7.78 (m, 1H), 7.69 (s, 1H), 7.57–7.48 (m, 3H), 7.29 (d, *J* = 7.2 Hz, 1H), 6.58–6.47 (m, 2H), 4.50 (t, *J* = 6.5 Hz, 2H), 4.15 (t, *J* = 5.1 Hz, 2H), 3.97 (s, 3H), 2.50–2.31 (m, 2H); ^{13}CNMR (126 MHz, DMSO-d_6) δ 163.6, 162.9, 148.2, 148.7, 137.3, 134.7, 129.9, 129.3, 126.9, 124.0, 122.9, 121.6, 116.4,114.6, 113.6, 107.5, 101.8, 65.4, 46.8, 36.2, 31.2, 29.4; ESI-MS (*m/z*): 336.3 $[M - Br]^+$.

HL2: Yield 891 mg (60%); mp 180-184 °C; IR (cm^{-1}) 1612, 3425; ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.42 (s, 1H), 9.35 (s, 1H), 8.77 (s, 1H), 7.80 (t, *J* = 1.8 Hz, 1H), 7.70 (t, *J* = 1.7 Hz,1H), 7.55 (td, *J* = 8.7, 2.04 Hz, 2H), 7.46 (d, *J* = 8.5 Hz, 1H),7.27 (td, *J* = 8.7, 2.04 Hz, 2H), 6.49–6.45 (m, 2H), 4.45 (t, *J* = 6.9 Hz, 2H), 4.12 (t, *J* = 5.8 Hz, 2H), 3.93 (s, 3H), 2.40–2.34 (m, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.7, 163.4, 163.1, 147.7, 137.2, 134.7, 132.7, 124.1, 123.8, 122.9, 119.4,113.6, 107.7, 101.8, 65.4, 46.8, 36.2, 31.2, 29.3; ESI-MS (*m/z*): 414.1 $[M - Br]^+$, 416.1 $[M + 2 - Br]^+$.

HL3: Yield 797 mg (59%); mp 150-155 °C; IR (cm^{-1}) 1612, 3325; ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.45 (s, 1H), 9.33 (s,1H), 8.74 (s, 1H), 7.77 (t, *J* = 1.8 Hz, 1H), 7.67 (t, *J* = 1.7 Hz,1H), 7.44 (d, *J* =8.2 2H), 7.41 (td, *J* = 8.8, 2.08 Hz, 2H), 7.31 (td, *J* = 8.8, 2.16 Hz, 2H), 6.50–6.42 (m, 2H), 4.44 (t,*J* = 6.9 Hz, 1H), 4.12 (t, *J* = 5.8 Hz, 1H), 3.93 (s, 3H), 2.40–2.34 (m, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.6, 163.3,163.1, 147.3, 137.3, 134.7, 131.1, 129.8, 128.9, 124.1, 123.5, 122.9, 115.9, 113.6, 107.6, 101.8, 65.4, 46.8, 36.2, 29.4; ESI-MS (*m/z*): 370.1 $[M - Br]^+$, 372.1 $[M + 2 - Br]^+$, 373.1 $[M + 3 - Br]^+$.

HL4: Yield 833 mg (64%); mp 148-152 °C; IR (cm^{-1}) 1609, 3378; ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.52 (s, 1H), 9.36 (s, 1H), 8.74 (s, 1H), 7.80 (t, *J* = 1.8 Hz, 1H), 7.70 (t, *J* = 1.8 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.37–7.34 (m, 2H),7.18–7.14 (m, 2H), 6.53–6.28 (m, 2H), 4.45 (t, *J* = 6.8 Hz, 2H), 4.12 (t, *J* = 5.8 Hz, 2H), 3.93 (s, 3H), 2.40–2.34 (m, 2H);^{13}C NMR (126 MHz, DMSO-d_6) δ 163.2, 163.1, 162.9, 162.1,160.2, 144.8, 137.3, 134.6, 124.0, 123.5, 123.4, 122.9, 116.7,116.5, 113.6, 107.5, 101.8, 65.4, 46.8, 36.2, 29.4; ESI-MS (*m/z*): 354.17 $[M - Br]^+$.

HL5: Yield 910 mg (68%); mp 140-145 °C; IR (cm^{-1}) 1614, 3406; ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.85 (s, 1H), 9.38 (s,1H), 8.70 (s, 1H), 7.78 (t, *J* =1.8, 1H), 7.68 (t, *J* = 1.7, 1H), 7.40(d, *J* = 8.3, 1H) 7.30 (td, *J* = 8.9, 2.16 Hz, 2H), 6.95 (td, *J* = 8.9,2.16 Hz, 2H), 6.45–6.43 (m, 2H), 4.47

(t, *J* = 6.9 Hz, 2H), 4.11 (t, *J* = 5.8 Hz, 2H), 3.94 (s, 3H), 3.82 (s, 3H), 2.40-2.34 (m, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.3, 162.5, 161.0,158.6, 141.0, 137.3, 134.3, 124.0, 122.9, 122.8, 115.9, 115.1,114.9, 113.7, 107.3, 101.8, 65.3, 55.8, 55.7, 46.8, 36.2, 29.4; ESI-MS (*m/z*): 366.2 $[M - Br]^+$.

HL6: Yield 699 mg (50%); viscous liquid; IR (cm^{-1}) 1613, 3389; ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.70 (s, 1H), 9.43 (s,1H), 8.73 (s, 1H), 7.79 (t, *J*= 1.9 Hz, 1H), 7.69 (t, *J* = 1.9 Hz, 1H), 7.74 (d, *J* = 1H) 7.44–7.40 (m, 3H), 7.31–7.24 (m, 3H), 6.65–6.58 (m, 1H), 6.48–6.40 (m, 2H), 4.47 (t, *J* = 6.9 Hz, 2H), 4.12 (t, *J* = 5.8 Hz, 2H), 3.95 (s, 3H), 2.42–2.35 (m, 2H);^{13}C NMR (126 MHz, DMSO-d_6) δ 163.9, 163.4, 163.1, 145.7,137.3, 134.7, 134.1, 128.5, 128.2, 127.0, 126.8, 124.1, 122.9, 122.8, 114.8, 114.1, 107.7, 101.9, 65.5, 46.8, 36.3, 29.4; ESI-MS (*m/z*): 386.2 $[M - Br]^+$.

2B.4 Conclusion

In conclusion, a new approach for the synthesis of imidazolium ionic liquid-tagged Schiff bases was developed. Synthesis of ionic liquid tagged Schiff bases was achieved in three steps from 2, 4-dihydroxybenzaldehyde by selective alkylation with 1, 3-dibromopropane, followed by reaction with 1-methylimidazole and Schiff base formation with aromatic amines.

Chapter 3

Synthesis, Characterization and Catalytic Applications of Ionic Liquid-tagged Schiff Base Complexes of Pd, Cu and Zn

SECTION 3A

Synthesis, Characterization and Catalytic Applications of Ionic Liquid-tagged Schiff Base Palladium Complex

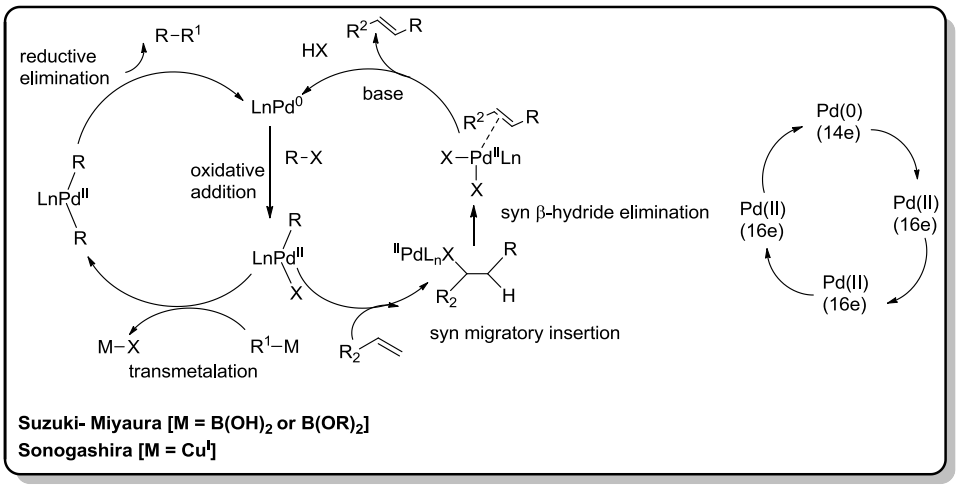
3A.1 Introduction

The cross-coupling reactions have noteworthy contribution in organic synthesis to build C-C bonds.[1-6] Heck reaction is a selective method for the formation of new C-C bonds in a single operational step and is a palladium-catalyzed coupling of alkenyl or aryl (sp^2) halides with alkenes to yield products resulting from the substitution of a hydrogen atom in the alkene coupling partner.[7-12] The first examples of the Heck reaction were independently reported by Mizoroki[13] and later improved protocol by Heck.[14] This reaction is a significantly robust and efficient method for the preparation of various substituted olefins, dienes, and precursors of conjugated polymers with the generation of tertiary and quaternary stereocenters and intramolecular ring formation.[15-17] The catalytic mechanism of the Heck reaction involves a series of transformations around the palladium catalyst. The palladium(0) compound is required in this cycle and is generally prepared *in situ* from a palladium(II) precursor.[18, 19] The first step of the reaction is an oxidative addition in which palladium inserts itself in the aryl to halide bond. The second step of the mechanism involves a π-complex formation of palladium via *syn* addition insertion of the alkene in the palladium-carbon bond. Then the β-hydride elimination takes place and a new palladium-alkene π-complex forms. This complex is destroyed and the palladium(0) compound is regenerated by reductive elimination of the palladium(II) species by the base in the final step (**Scheme 3A.1**).[20, 21]

The Suzuki reaction is another useful palladium-catalyzed carbon–carbon bond-forming reaction which involves palladium-mediated coupling of organic electrophiles with organoboron compounds in the presence of a base. The first example of this protocol was reported by the Suzuki group.[22, 23] This reaction is an important method for the synthesizing conjugated dienes and higher polyene systems with high stereoisomeric purity and biaryls. Besides this, remarkable progress has been reported for the Suzuki coupling reactions of unactivated alkyl halides, that enables the $C(sp^2)$-$C(sp^3)$ and even $C(sp^3)$-$C(sp^3)$ bond forming processes.[24, 25] The broad functional group tolerance and the substrate scope of the reaction towards sterically hindered substrates, inert aryl and vinyl chlorides, sulfonate derivatives, nucleophiles such as thermally unstable polyfluorophenyl and 2-heteroaryl boron reagents can be attained easily.[26-31] The mechanism of the palladium catalyzed Suzuki reaction involves oxidative addition of palladium to the halide to form the organopalladium species. In the next step the organopalladium complex

breaks and the transmetalation takes place and the boron-ate complex (produced by reaction of the boronic acid with base) is formed. The reductive elimination then takes place and completes the catalytic process (**Scheme 3A.1**).[21, 32]

Sonogashira reaction is an important cross-coupling reaction and an efficient method for the synthesis of arylated internal alkyne compounds. The original Sonogashira reaction demonstrated that the reaction could be accelerated by the addition of a co-catalytic CuI salt to the reaction mixture.[33, 34] This reaction is utilized for the synthesis of pharmaceuticals, agrochemicals and fine chemicals.[35, 36] A typical Sonogashira reaction is executed in organic solvents under inert conditions using palladium catalyst, a co-catalyst, and a stoichiometric amount of base.[37] Use of copper (I) iodide as a co-catalyst, enhances the reaction rate, but makes it necessary to avoid oxygen. In oxygen environment, Glaser-type[38] oxidative homocoupling of alkyne occurs that reduces the alkyne availability and makes the product separation tedious. To evade this limitaion copper free Sonogashira protocol i.e. the original Cassar–Heck version of this reaction has been rediscovered in past few years.[39] In the catalytic cycle of the Sonogashira reaction, an inactive Pd(II) catalyst is activated by reduction to a Pd(0) compound. The active palladium catalyst reacts with the aryl or vinyl halide in an oxidative addition to produce a Pd(II). In the transmetallation step, this intermediate reacts with the copper acetylide and forms a complex with copper halide. In the final step reductive elimination takes place to produce the alkyne, with regeneration of the palladium catalyst (**Scheme 3A.1**).[8, 21]



Scheme 3A.1 General catalytic cycle for the Pd-catalyzed reactions

An intriguing aspect of these cross coupling reactions is the broad synthetic applications that has played pivotal task in the synthesis of fine chemicals and advanced functional materials.[40] Palladium-catalyzed C-C coupling reactions without using any ligands have been reported, but the major drawbacks associated with them is the use of toxic solvents, requirement of high temperature and long reaction time.[41] Many catalytic systems have been developed using different palladium catalysts together with phosphane and phosphorous ligands. However, these ligands are toxic, expensive, sensitive to air oxidation and unstable at high temperatures. Homogeneous Pd-catalysts have been extensively employed because of high catalytic activity and selectivity.[42-44] These homogeneous catalyst systems have a drawback of the separation and recycling of the catalysts, additionally they induce contamination of the ligand residue in the products. Therefore there has always been demanding upsurge to develop robust, efficient and cost effective catalyst that can circumvent the limitations posed by the existing catalysts.[45, 46] Moreover, environmental concerns and economic considerations also make it essential to develop catalytic systems that can be recovered and recycled, especially when noxious transition metals are involved.[47, 48]

A plethora of palladium-based catalytic systems have been developed with the aim of obtaining increased activity and selectivity. NHC ligands in general have an excellent air and moisture stability and have been employed for homogeneous transition metal catalysis. The difficulty of separation of the homogenous catalyst from the reaction product can be easily achieved by using polymer-supported and insoluble transition-metal complexes. Advantages of both homogeneous and heterogeneous catalysts for the C-C coupling reactions were achieved using polymer-supported NHC-Pd catalysts by immobilization of the homogeneous complexes on Wang resin, Merrifield resin and polystyrene.[49-51]

Lee and co-workers developed a poly(1-methylimidazoliummethyl styrene)-surface grafted-poly(styrene) resin as a polymer supported NHC precursor (**1**) which readily formed a stable complex with palladium. The synthesized polymer-supported NHC-Pd complex (**2**) (**Figure 3A.1**) was used as a recyclable catalyst for the Suzuki cross-coupling reaction.[51]

Adsorbed ionic liquids or covalently linked ionic liquids to several supports have the properties of true ionic liquids, behaving as bulk ionic liquids and the advantages of a solid support. Imidazolium-based networks have been used as catalyst for the Heck reaction. Palladium (10 wt%) on a highly cross-linked imidazolium-based material (**3**) was used as catalyst for the Heck

and Suzuki reaction. The Heck reaction was catalyzed by both leached and supported Pd species while the Suzuki reaction took place with the leached Pd species and the reaction was quenched when a large amount of support is added.[52]

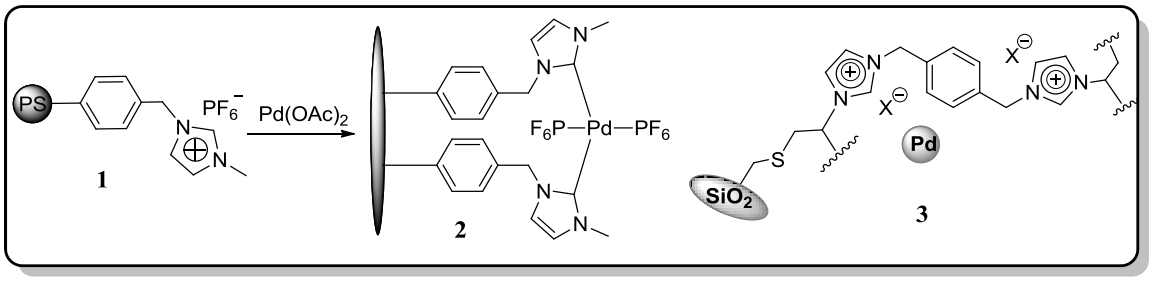


Figure 3A.1 2, 2′ -Biimidazolium-based palladium complex and imidazolium salts immobilized palladium species

A catalytic system (**4**) based on the concept of simultaneous covalent anchoring of a N-heterocyclic carbene palladium/ionic liquid matrix on the silica surface (**Figure 3A.2**). TEM coupled with EDX analysis of the catalyst indicated the formation of Pd nanoparticles within the immobilized IL layer. The catalyst was thermally stable and could be recovered and reused for four reaction cycles with high turnover number of 36, 600 for the Heck reaction.[53] Wei *et al.* synthesized an efficient and reusable catalyst with PdEDTA immobilized in an ionic liquid brush (**5**) for Suzuki reaction in water under aerobic conditions (**Figure 3A.2**). The catalyst was used effectively with no apparent loss of catalyst efficiency until the 10th cycle.[54]

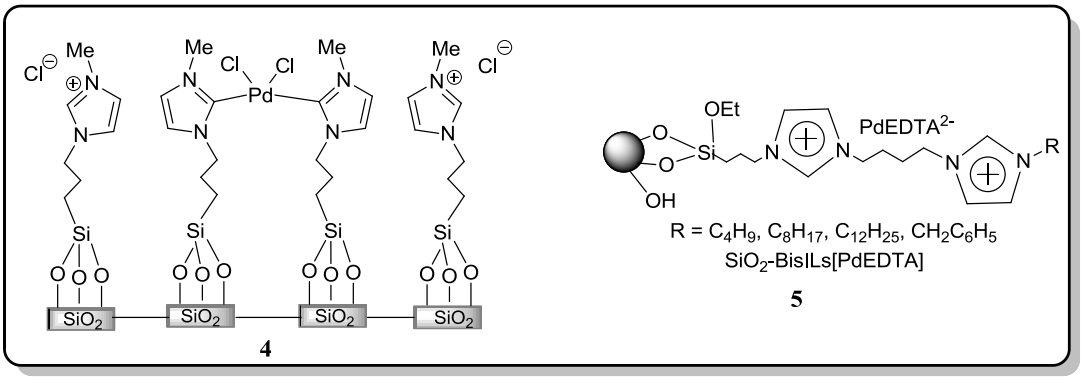


Figure 3A.2 Silica enchored and polymer-supported N-heterocyclic carbene- Pd complexes

Nanosized palladium particles suspended in organic solvents or aqueous solutions have good catalytic efficiency due to increased surface area and rotational degrees of freedom.[55]

Imidazolium salt based ILs are excellent stabilizing agents for monodispersed metal nanoparticles (NPs), preventing them from agglomeration to form bulk metal. An alternative to the traditional palladium on carbon (Pd/C) precatalyst system (**6**) was developed by protecting palladium nanoparticles (Pd NPs) with an imidazolium-based ionic polymer (IP) in a functionalized ionic liquid (**Figure 3A.3**). The precatalyst was used for the Heck and Suzuki coupling reactions under solvent-free conditions. The high stability of catalyst was apparent by the fact that it could be stored without undergoing degradation for at least two years.[56] Palladium-supported periodic mesoporous organosilica based on alkylimidazolium ionic liquid (Pd@PMO-IL) (**7**) was prepared in which the imidazoilium ionic liquid was uniformly distributed in the silica mesoporous framework (**Figure 3A.3**). PMO-IL nanostructure acted as a nanoscaffold to recapture the Pd nanoparticles into the mesochannels thus preventing agglomeration of Pd and was used as a recyclable catalyst for the Suzuki–Miyaura coupling reaction of various types of iodo-, bromo-, and even deactivated aryl chlorides in water.[57]

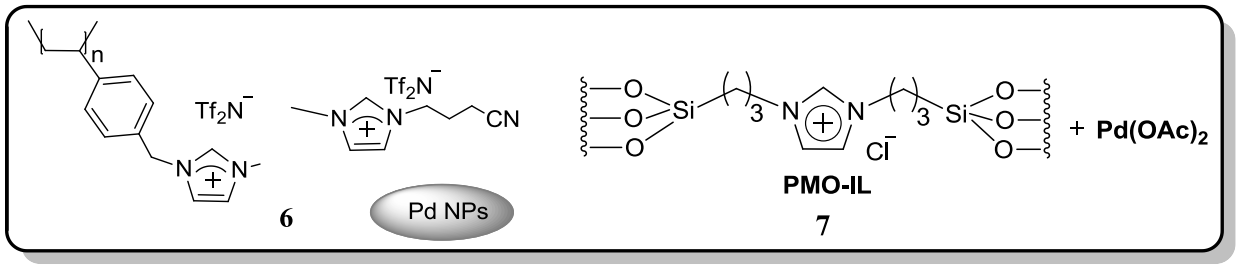


Figure 3A.3 Polymer-supported, pyrazolyl-functionalized *N*-heterocyclic carbine Pd complexes and Pd NPs stabilized by an ionic polymer

Support structure and functional groups grafted on the support plays a significant role in preventing the aggregation of palladium nanoparticles. The mesoporous materials due to their high surface area and regularly arranged pore structure are good supports for immobilizing palladium catalysts. An *N*-heterocyclic carbene palladium complex and ionic liquid were grafted on the mesoporous cage-like material SBA-16 (**8**) and used as highly recyclable heterogeneous catalyst for the Heck and Suzuki reactions (**Figure 3A.4**). Complete conversion of the unactivated bromobenzene was observed at a low catalyst loading of 0.01 mol%. Better recyclability than that of the catalyst prepared from amorphous silica was due to isolated nanocages of SBA-16 that prevented aggregation and agglomeration of Pd particles formed

during the catalytic reaction.[58] Bhaumik group used ortho-metalated palladium(II) complex (**9**) anchored in a ordered mesoporous silica matrix for the Suzuki reaction (**Figure 3A.4**).[59]

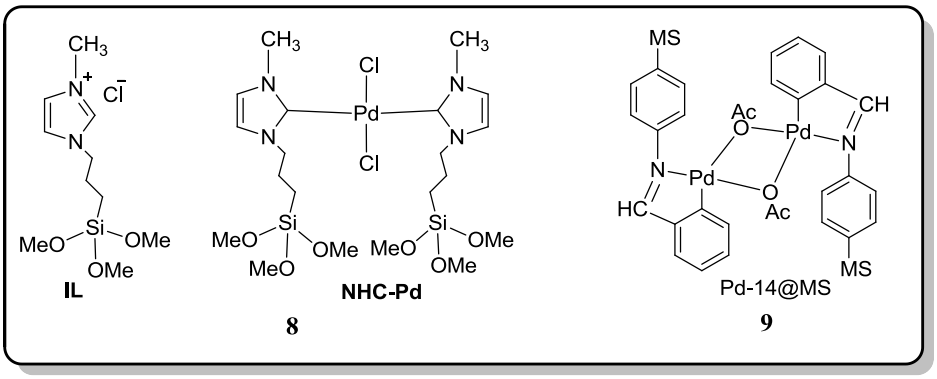


Figure 3A.4 NHC palladium complex, Palladium-supported (Pd@PMO-IL) and 2D-hexagonal mesoporous organosilica anchored Pd(II) complex

A palladium catalyst comprising of nanostructured silica bearing trialkyl-(4-pyridyl)-ammonium binding sites (**10**) was synthesized and used as a heterogeneous catalyst for the Sonogashira reaction (**Figure 3A.5**). The catalyst showed enhanced catalytic activity with low Pd leaching due to non-covalent anchoring and coulombic interactions between pyridine binding site and the immobilized Pd species.[60] Movassagh group synthesized an air, moisture stable and recyclable palladium(II) Schiff base complex (**11**) which was anchored to multi-walled carbon nanotubes (Pd-Schiff base@MWCNTs) (**Figure 3A.5**) and used it as a catalyst for the Suzuki-Miyaura reaction.[61]

Magnetic nanoparticles (MNPs) have been used as support for the immobilization of homogeneous catalysts. These supported catalysts on MNP show high catalytic activity, possess high thermal and mechanical Stability and can be reused by using an external magnet. A Pd-isatin Schiff base complex (**12**) immobilized on γ-Fe_2O_3 (Pd-isatin Schiff base-γ-Fe_2O_3) was synthesized (**Figure 3A.5**) and used as a magnetically reusable Pd catalyst for the Heck cross-coupling reaction.[62]

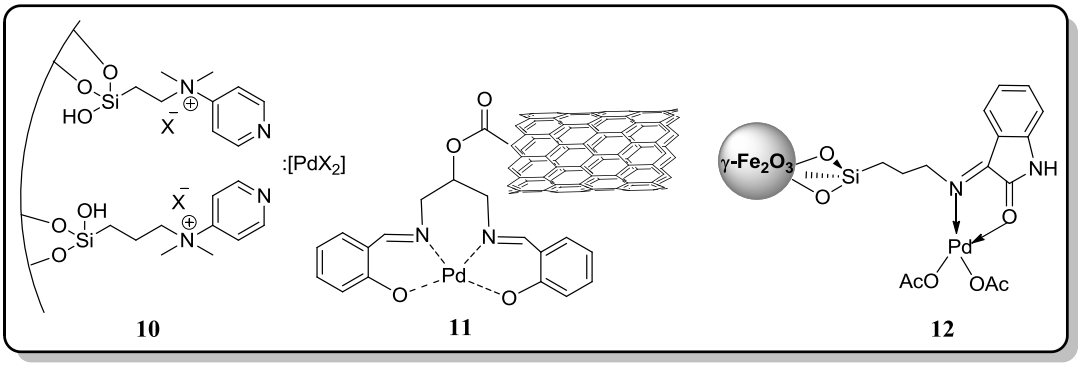


Figure 3A.5 Silica functionalized palladium with pyridine sites, Palladium-supported on WCNTs and Pd-isatin Schiff base complex

Phan *et al.* synthesized a superparamagnetic nanoparticles based palladium complex (**13**) and used as a catalyst for the Sonogashira reaction (**Figure 3A.6**).[63] Chitosan is an inexpensive, biodegradable polysaccharide and has been employed as stable support for Pd-catalyzed cross-coupling reactions. Movassagh *et al.* synthesized a magnetic porous chitosan-thienyl imine palladium(II) complex, MPCS-TI/Pd (**14**). The synthesized complex was found to be highly active heterogeneous catalyst (**Figure 3A.6**) for the Heck reaction in aqueous media. The catalyst was easily reused for seven cycles and could be easily separated by an external magnet.[64] Zwitterionic palladium complexes of ligands with different pendent alkyl chain length were applied as metal precursors to generate Pd NPs (**15**). These nanoparticles worked efficiently as catalyst for the Heck reaction (**Figure 3A.6**).[65]

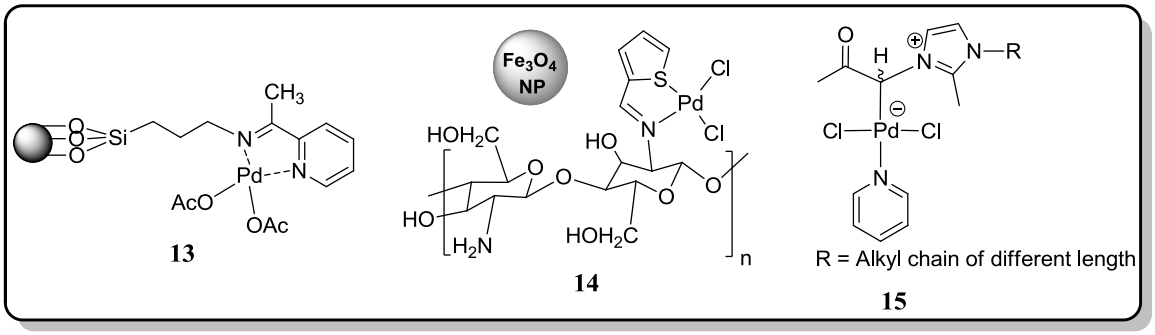


Figure 3A.6 Superparamagnetic nanoparticles-supported palladium catalyst, chitosan-thienyl imine palladium(II) complex and zwitterionic palladium complexes

Poly (ethylene glycol) (PEG) is an environmental friendly reaction medium for organic synthesis and catalytic process. Various PEG supported ligands and catalysts have been synthesized. The PEG based functionalized ionic liquids display special chemical and physical properties and are extensively used as solvents and (or) catalyst for the Heck and Suzuki reaction.[66, 67] Luo group prepared a catalytic system (**16**) based on 8-hydroxyquinoline functionalized poly (ethylene glycol) bridged dicationic ionic liquid ([HQ-PEG_{1000}-DIL][BF_4]) and $Pd(OAc)_2$ (**Figure 3A.7**). The prepared system was used as a catalyst for Pd-catalyzed Heck reaction under solvent-free conditions.[68]

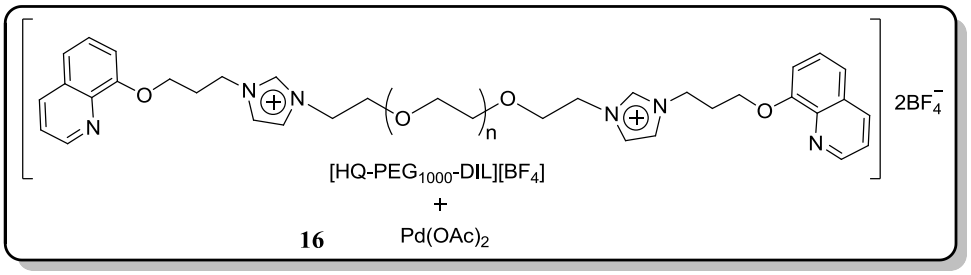


Figure 3A.7 [HQ-PEG_{1000}-DIL][BF_4] and $Pd(OAc)_2$ system

Shreeve group synthesized a monoquaternary room temperature ionic liquid 1, 3, 1′-tributyl-2, 2′-biimidazolium hexafluorophosphate (**17**) and used it as a ligand and solvent for palladium-catalyzed Suzuki cross coupling reactions (**Figure 3A.8**). The catalyst could be recycled at least 14 times without a significant decrease in catalytic performance. Due to the coordination ability, the monoquaternary ionic liquid the palladium leaching was not observed in the recycling experiments.[69] As pyrazolyl ring is weakly coordinating to metal centers, the pyrazolyl-functionalized NHCs transition metal complexes readily facilitate oxidative additions in the catalytic cycle of C-C coupling reaction. A hemilabile pyrazolyl-functionalized *N*-heterocyclic carbene complex of palladium(II) (**18**) was used as a recyclable catalyst for the Heck and Suzuki cross-coupling reactions in ionic liquids (**Figure 3A.8**).[70] Piperidine-appended dimethyl-imidazolium-NTf_2 ionic liquid (**19**) was used both as solvent and base (**Figure 3A.8**) for the Sonogashira cross-coupling reaction with $PdCl_2(PPh_3)_2$. The protocol was extended to synthesize SF_5-substituted diaryls, aryl-alkyl-acetylenes and homocoupled products of terminal acetylenes.[71]

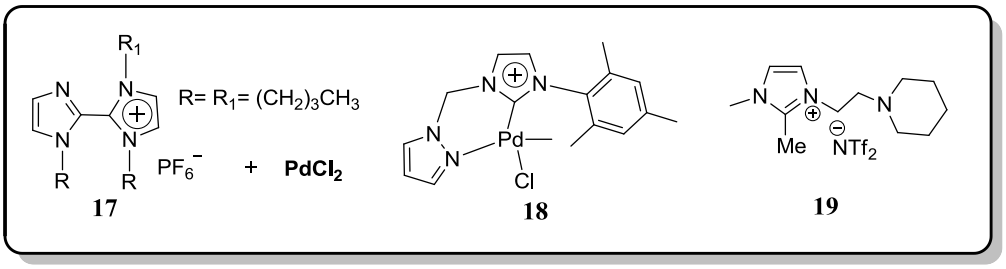


Figure 3A.8 1,3,1′-Tributyl-2, 2′-biimidazolium, pyrazolyl-functionalized NHC palladium(II) complexes and piperidine-appended dimethyl-imidazolium-NTf_2 ionic liquid

$Pd(OAc)_2$/(2-mesitylindenyl)dicyclohexylphosphine/$Me(octyl)_3N^+Cl^-/K_3PO_4 \cdot 3H_2O$ catalytic system (**20**) worked efficiently with ultra-low loading and high turnover number for the Suzuki–Miyaura cross-coupling reactions of a variety of aryl and heteroaryl chlorides (**Figure 3A.9**).[72] Separation of catalyst by filtration or extraction can be readily achieved by binding the active metal complexes to insoluble or water-soluble carriers. A precatalyst system (**21**) for the Heck and Suzuki cross-coupling reactions was developed by the reaction of $Pd(OAc)_2$ with an acetate anion bearing an imidazolium cation as its charge tag (**Figure 3A.9**). The *in situ* formation of a bidentate imidazolic carbene-carboxylate ligand upon proton abstraction from a charged-tagged Pd complex after base addition gave better catalytic performance of the catalyst as compared to $Pd(OAc)_2$.[73] A carbapalladacycle catalyst (**22**) with enhanced ionophilicity was synthesized by anchoring it to a catalytically inert ammonium tag. The ammonium tag improved the solubility in ionic liquid media, reduced the palladium leaching and facilated the heterogenisation of **22** in the layers of montmorillonite clay resulting in the formation of another organic-inorganic hybrid catalyst (**Figure 3A.9**). Both the catalyst were used for the Sonogashira cross coupling reaction.[74]

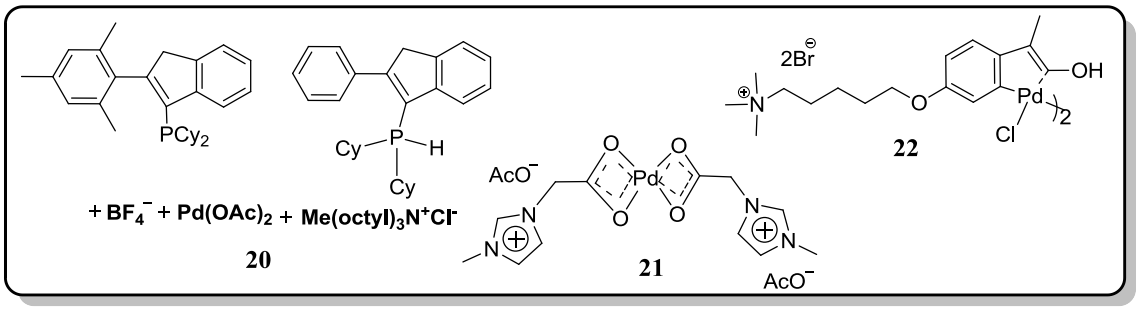


Figure 3A.9 Palladium-supported (Pd@PMO-IL), charge-tagged palladium complex and a carbapalladacycle catalyst

The Pd(0) complexes of phase-tagged phosphines 1-($CH_2NEt_3^+$), 4-($CH_2P(1\text{-}Ad)_2$)C_6H_4.Br^- and 1-(CH_2-PPh_3^+), 4-($CH_2PH^+(1\text{-}Ad)_2$)C_6H_4.$2Br^-$ (**23-25**) were used as catalyst for the Sonogashira coupling reaction (**Figure 3A.10**).[75]

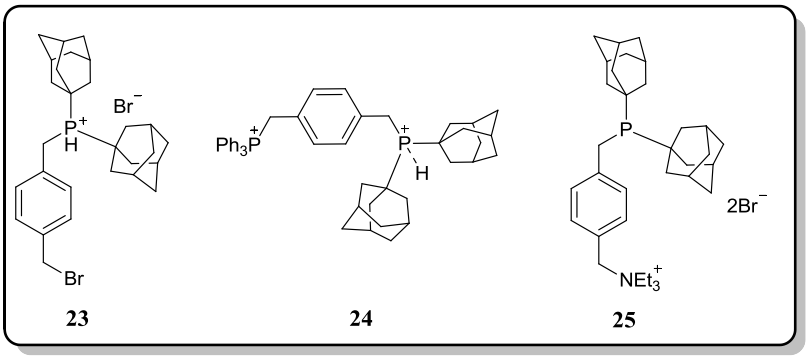


Figure 3A.10 Catalysts with cationic phase tags and piperidine-appended dimethyl-imidazolium-NTf_2 ionic liquid.

The Schiff base metal complexes of palladium metal also showed improved catalytic activity with good efficiency in the Heck, Suzuki and Sonogashira cross coupling reactions.[76-80] Hu and co-workers synthesized a water-soluble palladium-salen catalyst (**26**) modified by pyridinium salt and used it as a catalyst for the Heck reaction (**Figure 3A.11**). 0.5 mol% of the catalyst could achieve 98.3% conversion with 99% selectivity. The catalytic activity of catalyst modified by pyridinium salt was higher than that of unmodified one. The catalyst could be easily separated from reaction system by water wash and recycled for six runs without significant loss of catalytic activity and selectivity.[81] The effect of pendent alkyl chain lengths on Heck and Sonogashira coupling was studied using air and moisture insensitive palladium complexes (**27**) of Se, N, O type Schiff base ligands. The length of pendent alkyl chain of ligand do not affect the Sonogasira reaction, while the Heck reaction showed change in catalytic efficiency. This change was due to the effect of length on the nature and dispersion of nano-phases containing Pd involved in catalysis. (**Figure 3A.11**).[82] Schiff base palladium complex (**28**) immobilized on magnetic polymer microspheres (**Figure 3A.11**) was used as a recyclable catalyst for the Suzuki reaction.[83]

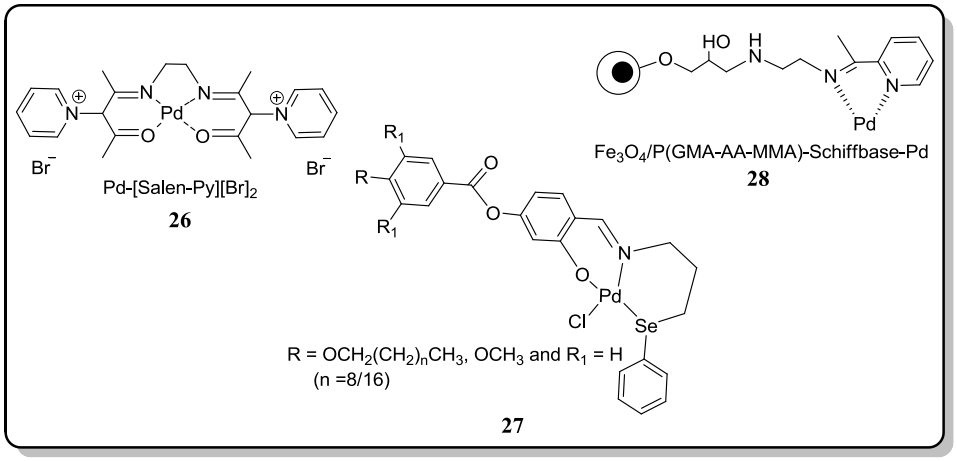


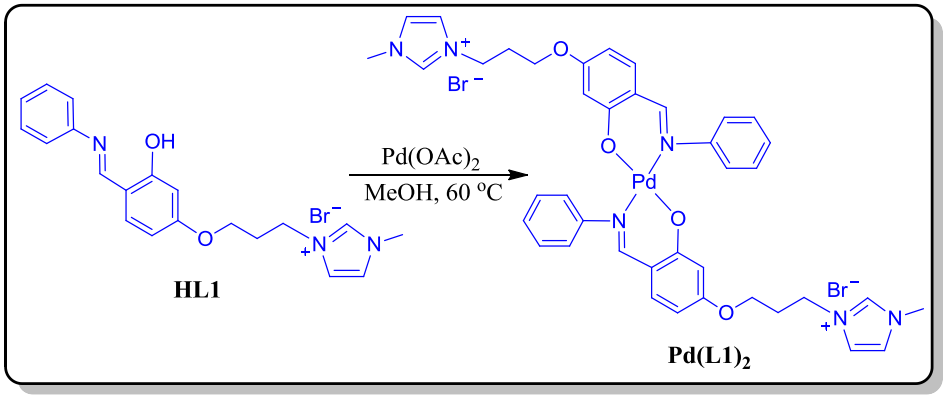
Figure 3A.11 Pyridinium salt modified palladium-salen catalyst, selenated palladium(II) complexes and microspheres supported Schiff base palladium complex

This chapter deals with the synthesis, characterization and catalytic application of novel imidazolium ionic liquid-tagged Schiff base complex of palladium. The synthesized complex was screened for its catalytic applications in the Heck, Suzuki and Sonogashira cross coupling reaction in aqueous medium. Our catalytic system was found highly efficient for all Heck, Suzuki and Sonogashira reactions without the aid of phase transfer catalyst or organic solvents.

3A.2 Results and discussion

3A.2.1 Synthesis of $(Pd(L1)_2$

The required amount of (672 mg, 2.0 mmol) of **HL1** (synthetic procedure is described in Chapter 2B), was stirred with ethanol (20 mL) in a 25 mL round bottom flask for 15 min. To the resulting solution, palladium acetate (224 mg, 1.0 mmol) was added and refluxed for 4 hours till the product precipitated completely. After cooling, the product was separated by filtration and recrystallized from the mixture of petroleum ether (2 mL) and methanol (15 mL), **Scheme 3A.2**.



Scheme 3A.2 Synthesis of ionic liquid-tagged palladium complex **Pd(L1)$_2$**

3A.2.2 Characterization of Pd(L1)$_2$

The compound was isolated as an orange colored solid. The complex obtained was aerially stable and soluble in water, ethanol, methanol, ACN, DMF and DMSO. A variety of analytical techniques were used for the structure elucidation of **HL1** and **Pd(L1)$_2$**. In the FTIR spectrum of **Pd(L1)$_2$**, the azomethine peak shifted towards lower frequency than the corresponding value of 1620 cm^{-1} in **HL1** and appeared at 1596 cm^{-1} and the band in the region of 3400 cm^{-1} (OH stretch) for **HL1** disappeared in **Pd(L1)$_2$**, indicated the coordination of metal ion through nitrogen of the C=N group and oxygen of OH group.[84, 85] An absorption band at 1288 cm^{-1} owing to ν(C–O) peak was also observed in the spectrum of **HL1** and after complexation with the palladium metal this peak shifted towards higher frequency value of 1303 cm^{-1} (**Figure 3A.12**).[86]

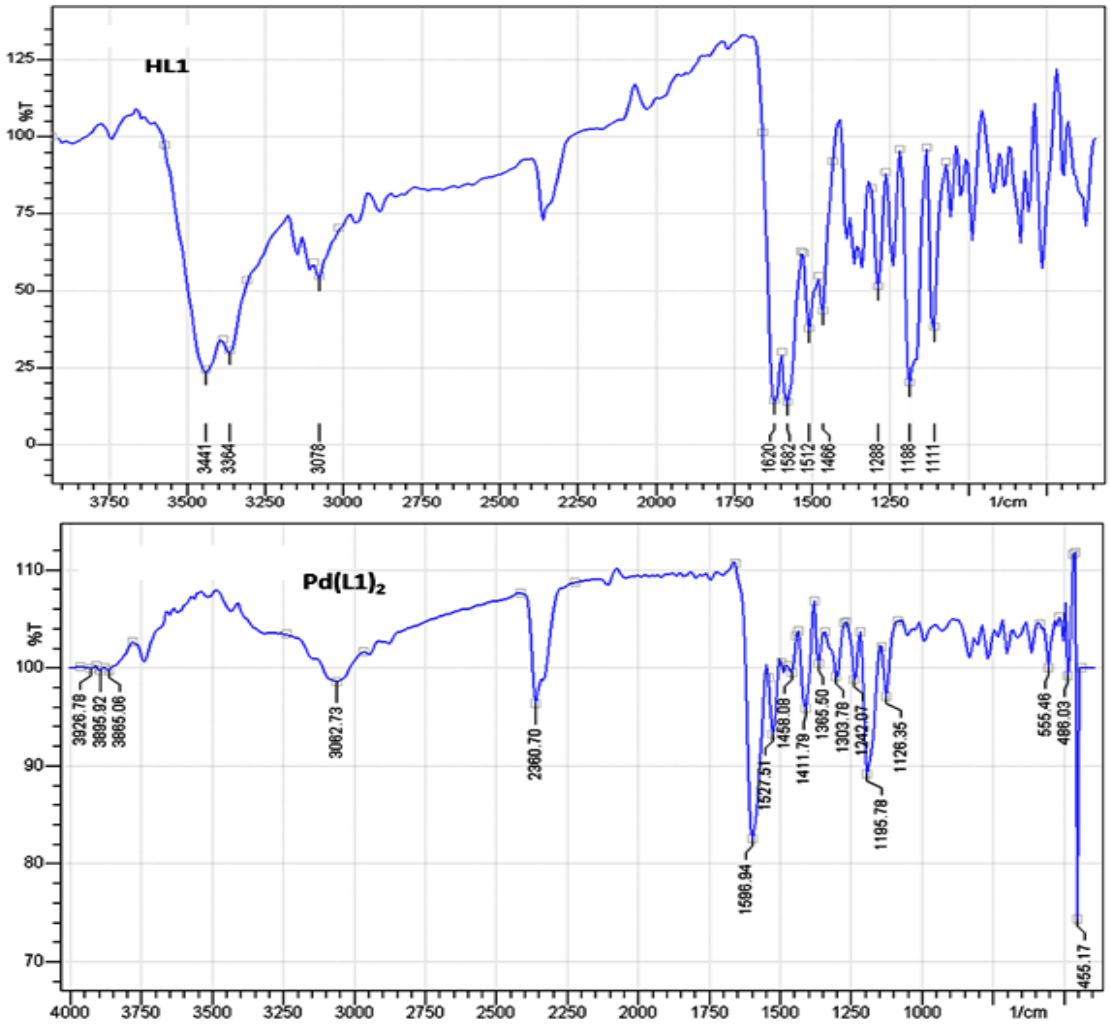


Figure 3A.12 FT-IR spectra of **HL1** and **Pd(L1)$_2$**

The solution state electronic spectra of **HL1** and the complex **Pd(L1)$_2$** were recorded in distilled DMSO. The free ligand **HL1** exhibited two absorption bands at 280 nm and 321 nm, which can be attributed to π-π* and n–π* transitions of the ligand. Shift of these bands towards shorter wavelengths (264 and 304 nm respectively) and the appearance of a new band at 395 nm in absorption spectrum of **Pd(L1)$_2$** suggested complexation of **HL1** with palladium. In the solid state electronic spectra also, blue shift was observed after complexation (**Figure 3A.13**).

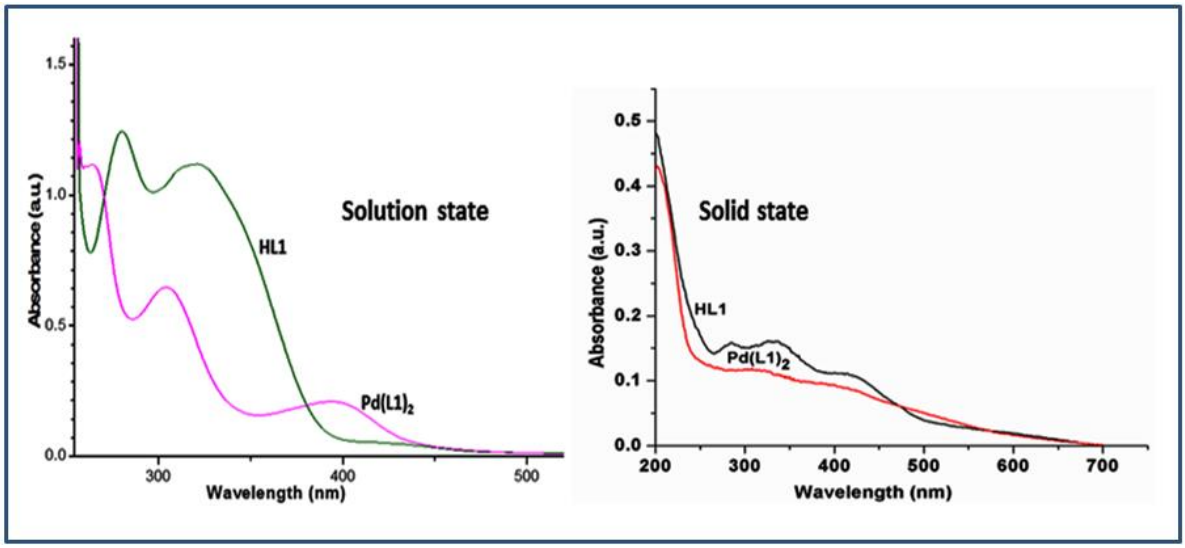


Figure 3A.13 UV-visible spectra of **HL1** and **Pd(L1)$_2$**

The ^{1}H NMR spectrum of **HL1** showed resonance signals at δ 8.79 and 13.77 ppm assigned to azomethine and hydroxyl protons respectively along with other protons. In the spectrum of complex **Pd(L1)$_2$** the azomethine peak shifted up field at δ 7.93 and the hydroxyl proton peak was absent, indicating the complexation of palladium metal ion with the nitrogen of azomethine group and oxygen of hydroxyl group (**Figure 3A.14**). The ^{13}C NMR of **HL1** contained a characteristic peak of azomethine carbon at δ 163.6 and after getting coordinated with palladium metal this peak shifted downfield at δ 166.1, showing the complexation of palladium ion with the ligand. The other peaks in ^{13}C NMR were also consistent with the structure of **HL1** and **Pd(L1)$_2$** (**Figure 3A.15**).

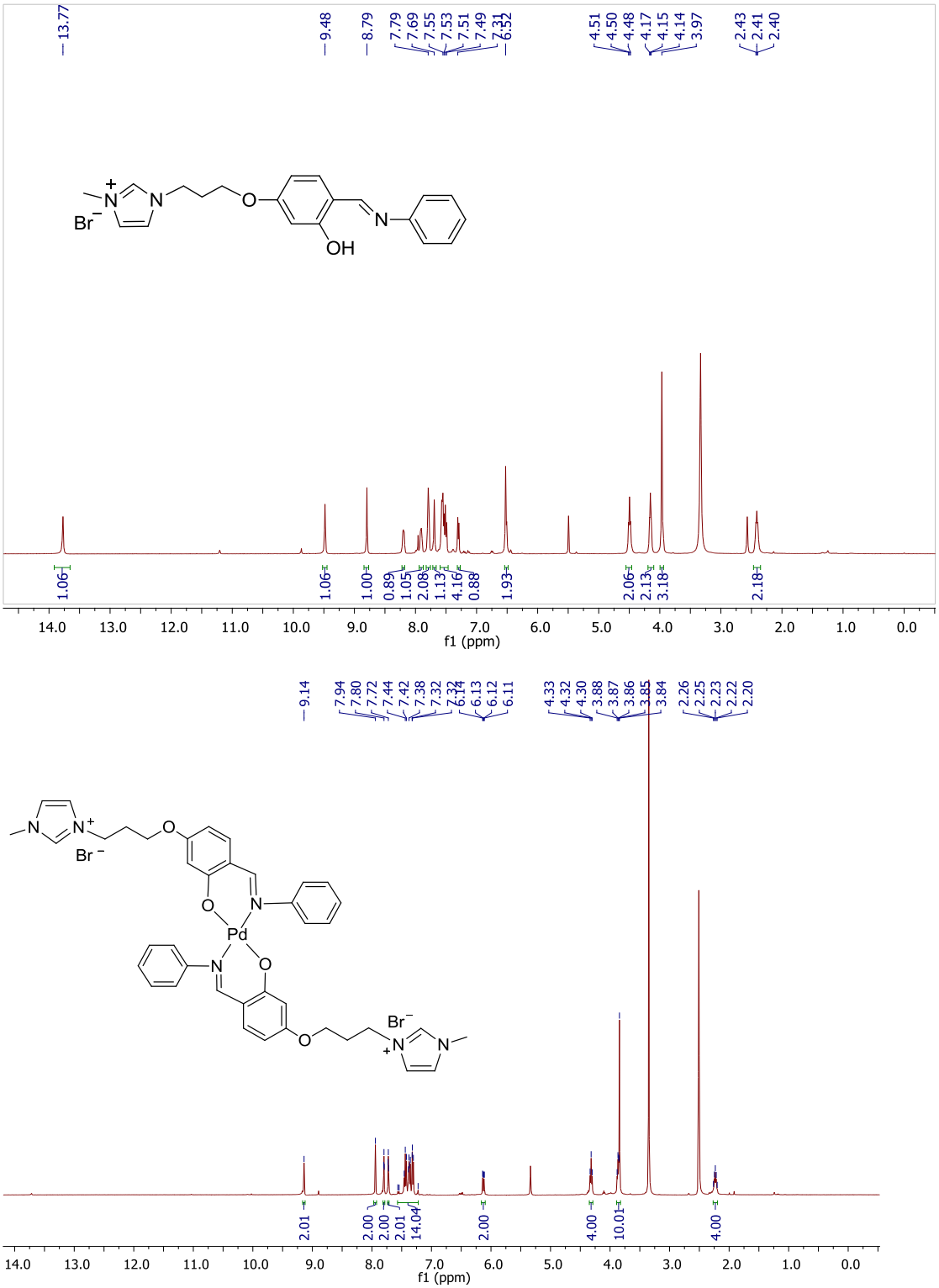


Figure 3A.14 ^{1}H NMR spectra of **HL1** and **Pd(L1)$_2$** in deuterated DMSO

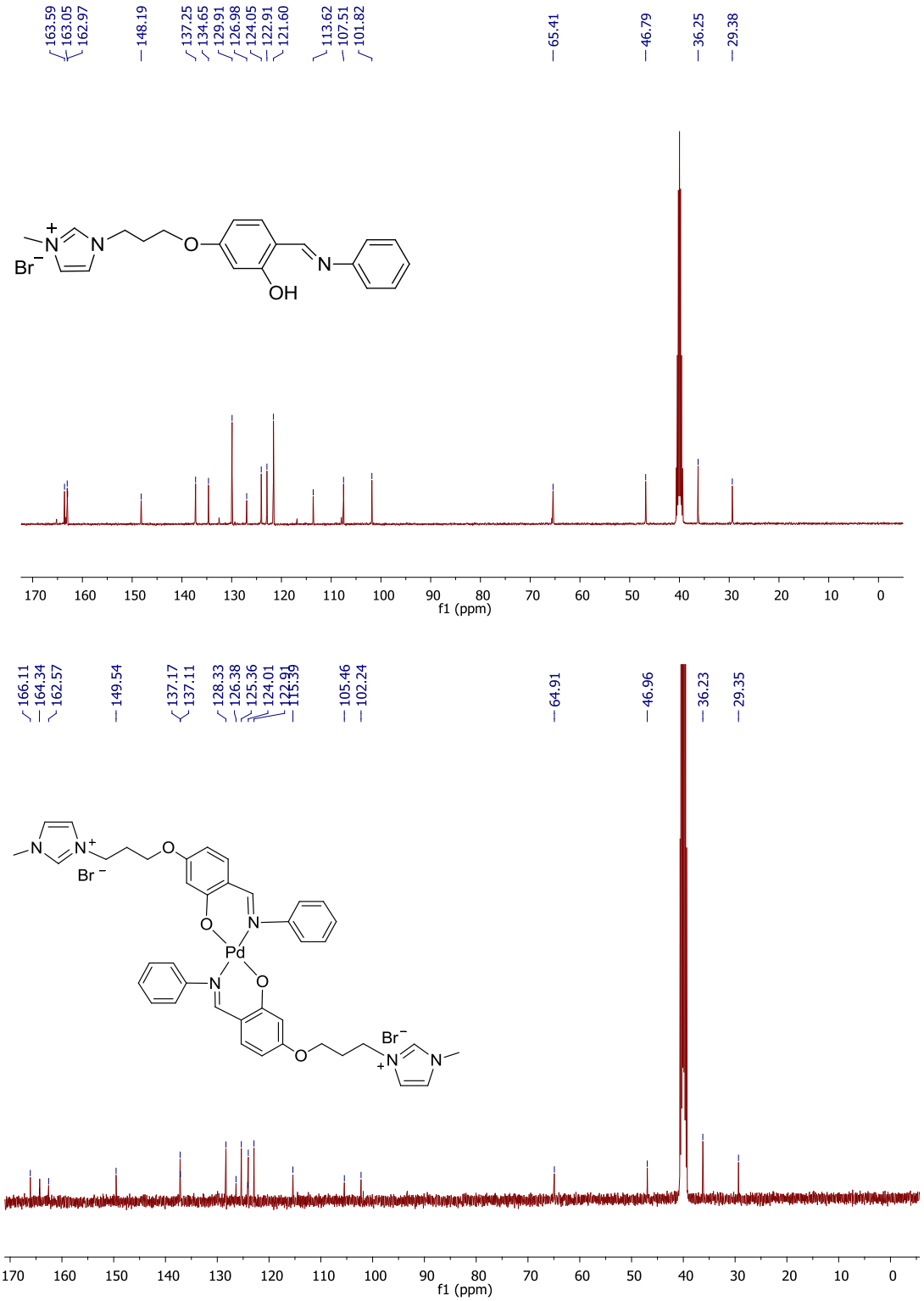


Figure 3A.15 ^{13}C NMR spectra of **HL1** and **Pd(L1)$_2$** in deuterated DMSO

The MALDI mass spectrum of the complex **Pd(L1)$_2$** showed a peak at *m/z* 777.32, that corresponds to the $[M+H-2Br]^+$ ion (**Figure A07, Appendix-A**). The powder XRD pattern of **HL1** showed sharp peaks revealing its crystalline nature. On complexation with the metal the peak intensities in XRD diminished, with line broadening indicating change in the nature from crystalline to amorphous state (**Figure 3A.16**).[87] The powder XRD of **Pd(L1)$_2$** was also recorded after heating it at 200 °C for 4 hours and it was found that there was no significant change, indicating the high thermal stability of **Pd(L1)$_2$** .

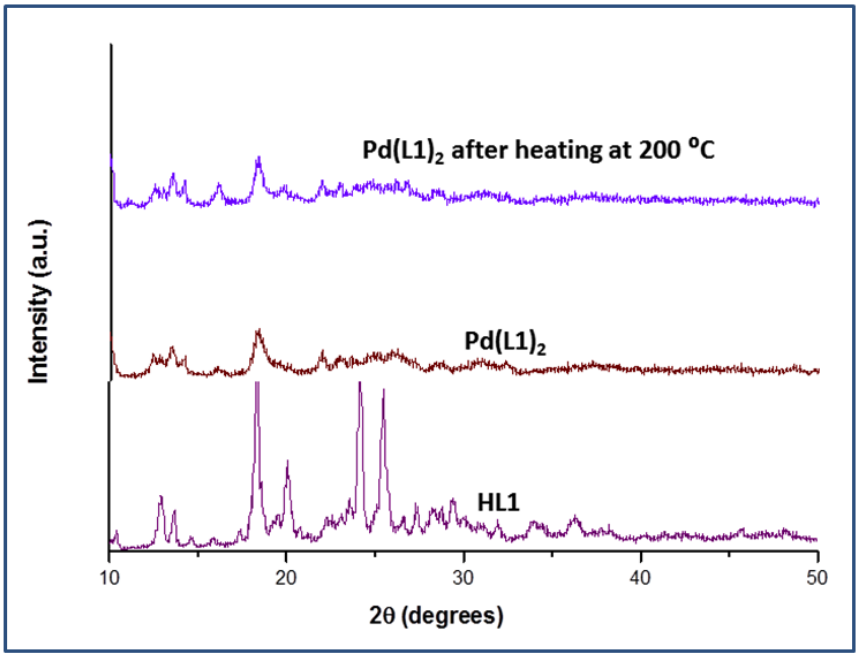


Figure 3A.16 Powdered XRD spectra of **HL1** and **Pd(L1)$_2$**

In the DSC thermogram of **HL1** an endothermic peak, corresponding to its melting point was observed at 81 ^oC. One more peak in a broad range at 130-200 ^oC indicated the glass transition temperature of **HL1**.[88, 89] After complexation the stability of compound enhanced as there was not any significant peak up to the range of 200 ^oC and after this temperature, there was a gradual and continuous decomposition of **Pd(L1)$_2$** indicating its higher thermal stability than **HL1** (**Figure 3A.17**).

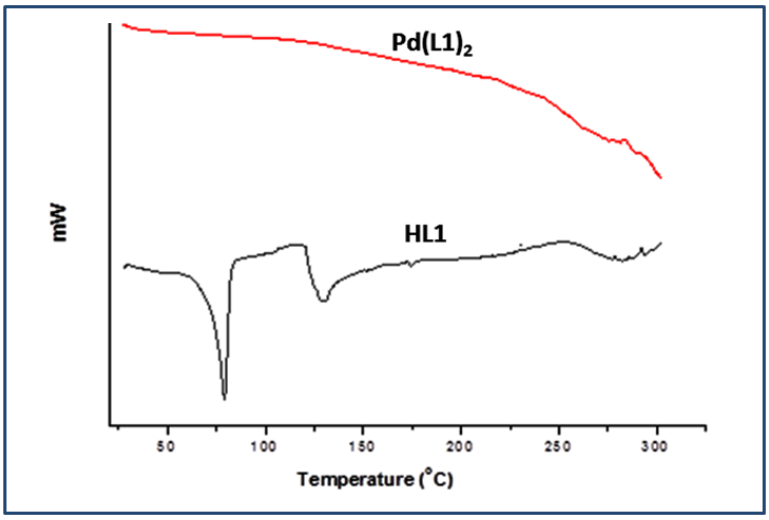


Figure 3A.17 DSC thermogram of **HL1** and **Pd(L1)$_2$**

The synthesized ligand (**HL1**) and complex (**Pd(L1)$_2$**) were further screened for their fluorescence studies and both **HL1** and **Pd(L1)$_2$** showed steady state fluorescence (**Figure A08, Appendix-A**). The time correlated single photon counting (*TCSPC*) lifetime of **HL1** and **Pd(L1)$_2$** were measured (in a nanosecond time scale) and the fluorescence decays of both ligand and complex were obtained at an excitation of 300 nm (λ_{ex} 300 nm) and emission of 400 nm (λ_{em} 400 nm). In case of **HL1**, fluorescence decays were properly fitted to a monoexponential and the life time for excited state was observed at 3.96 nano seconds. After complexation with palladium metal, the fluorescence decays were only properly fitted to a biexponential decay law because two life times were observed and the average life time 11.47 nano seconds, this noticeably indicated increased excitation state stability and enhanced fluorescence of **Pd(L1)$_2$** (**Figure 3A.18**).

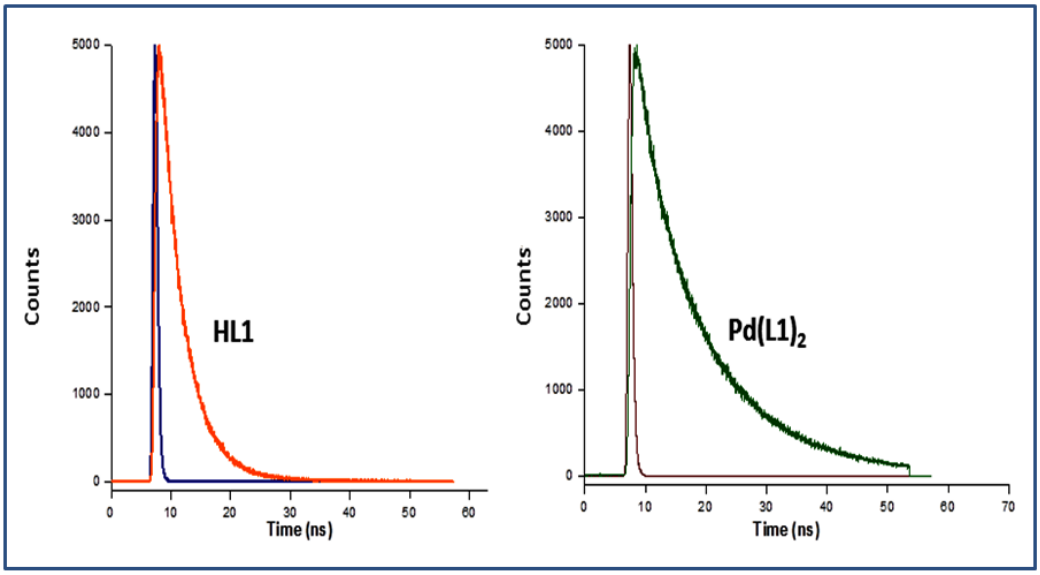


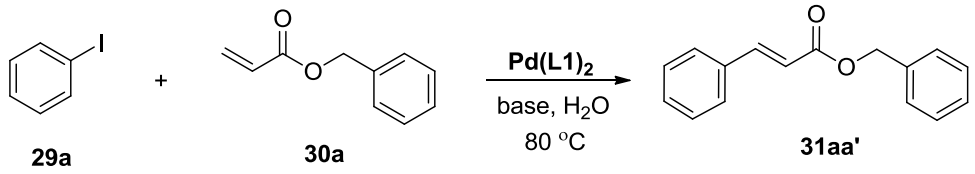
Figure 3A.18 Time-resolved fluorescence decay of **HL1** and **Pd(L1)$_2$** in DMSO recorded after 300 nm excitation. The emission wavelength settled was 400 nm.

3A.2.3 Catalytic activity of Pd(L1)$_2$

3A.2.3.1 Catalytic activity of Pd(L1)$_2$ for the Heck reaction

The synthesized complex **Pd(L1)$_2$** was explored as a catalyst for carbon-carbon bond forming Heck reaction in aqueous medium. Initially the reaction conditions for the Heck reaction were optimized by performing the model reaction between iodobenzene (**29a**) and benzyl acrylate (**30a**). The results from different reaction conditions are summarized in Table 3A.1. It was found that reaction at 80 °C with 1 mol % of **Pd(L1)$_2$** in the presence of K_2CO_3 gave benzyl cinnamate (**31aa′**) in 96% yield (Table 3A.1, entry 6). The use of organic base such as triethylamine resulted in poor yield of **31aa′** and this may be attributed to the poor solubility of triethylamine in aqueous medium.

Table 3A.1 Optimization of the reaction conditions for the Heck reaction catalyzed by **Pd(L1)$_2$**.[a]



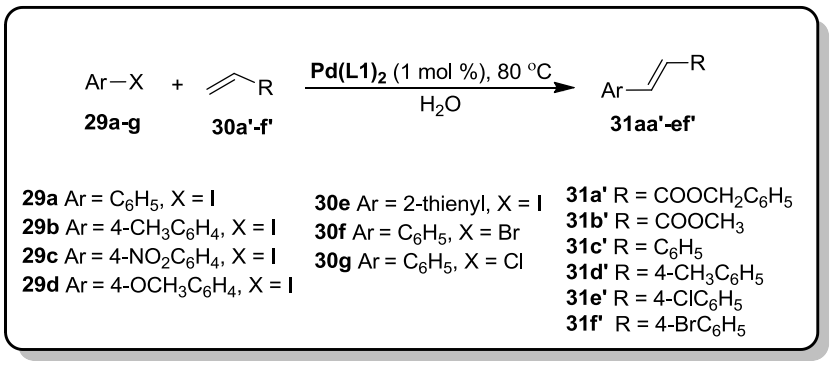
29a **30a** **31aa'**

Entry	**Pd(L1)$_2$** (mol %)	Base	Yield[b] (%)
1.	1.0	Et_3N	26
2.	1.0	NaOH	74
3.	1.0	$NaHCO_3$	84
4.	1.0	Cs_2CO_3	88
5.	3.0	K_2CO_3	98
6.	**1.0**	**K_2CO_3**	**96**
7.	0.2	K_2CO_3	88
8.	0.1	K_2CO_3	87
9.	0.01	K_2CO_3	86

[a]Reaction conditions: Iodobenzene (1 mmol), benzyl acrylate (2 mmol), **Pd(L1)$_2$** (x mol %), base (2 mmol), water (2 mL). [b]Isolated yield.

With the optimized reaction conditions in hand, the scope of the Heck reaction was investigated by employing substituted aryl halides **29a-g** to react with substituted olefins **30a′-f′** (Scheme 3A.3). Aryl iodide with electron donating methyl and methoxy group and electron withdrawing nitro group both reacted well under these conditions to give the desired coupled products in excellent yields (Table 3A.2, entries 11−16). Similarly different substituted alkenes also reacted smoothly to afford corresponding coupled products in excellent yields. It is worth mentioning that electron withdrawing groups on both substrates resulted in better yields as compared to substrates bearing electron donating groups. The more demanding substrates *viz.* aryl bromides and aryl chlorides were also allowed to react with styrene and benzyl acrylate under these conditions (Table 3A.2, entries 2, 3 and 6, 7). To our delight, hetroaryl iodides such as 2-iodothiophene (**29e**) also underwent the Heck coupling with **30a′** to give the corresponding coupled product **31ea′** in 82% yield (Table 3A.2, entry 17). The catalyst was found to be very effective for various substrates including heteroaromatic halides to give the coupled product in

good to excellent yield (76−98%) in short reaction time. The identity of the products was confirmed by melting points and ^{1}H and ^{13}C NMR data and they were found to be consistent with the reported values.



Scheme 3A.3 Heck reaction catalyzed by **Pd(L1)$_2$** in aqueous medium

3A.2.3.2 Reusability of Pd(L1)$_2$ for Heck reaction

The reusability of **Pd(L1)$_2$** was evaluated for the model Heck reaction. As shown in **Figure 3A.20**, the catalyst could be effectively used for up to six cycles without much loss in catalytic activity. Leaching of the catalyst during extraction may be one of the factors responsible for the gradual decrease in the yield of the product during recycling.

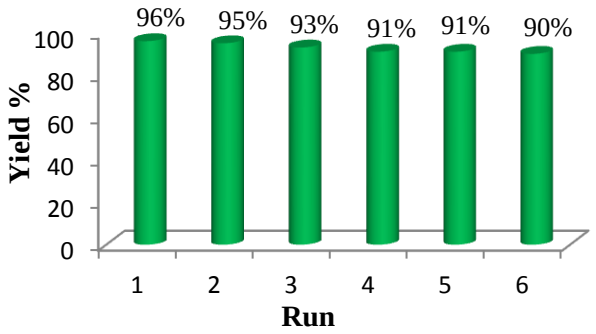


Figure 3A.20 Reusability of **Pd(L1)$_2$** for Heck reaction

Table 3A.2 Heck reaction between aryl halides and alkenes catalyzed by **Pd(L1)$_2$** in water[a]

S. No.	X	Ar	R	Product	Time (h)	Yield[b] (%)
1.	I	C_6H_5	$COOCH_2C_6H_5$	**31aa′**	4.0	96
2.	Br	C_6H_5	$COOCH_2C_6H_5$	**31aa′**	5.5	86
3.	Cl	C_6H_5	$COOCH_2C_6H_5$	**31aa′**	6.0	82
4.	I	C_6H_5	$COOCH_3$	**31ab′**	3.5	96
5.	I	C_6H_5	C_6H_5	**31ac′**	5.5	80
6.	Br	C_6H_5	C_6H_5	**31ac′**	6.0	79
7.	Cl	C_6H_5	C_6H_5	**31ac′**	6.5	76
8.	I	C_6H_5	4-$CH_3C_6H_5$	**31ad′**	4.5	82
9.	I	C_6H_5	4-ClC_6H_5	**31ae′**	4.5	81
10.	I	C_6H_5	4-BrC_6H_5	**31af′**	4.5	83
11.	I	4-$CH_3C_6H_4$	$COOCH_2C_6H_5$	**31ba′**	4.5	80
12.	I	4-$NO_2C_6H_4$	$COOCH_2C_6H_5$	**31ca′**	4.0	98
13.	I	4-$NO_2C_6H_4$	C_6H_5	**31cc′**	4.5	88
14.	I	4-$NO_2C_6H_4$	4-$CH_3C_6H_5$	**31cd′**	5.0	81
15.	I	4-$NO_2C_6H_4$	4-ClC_6H_5	**31ce′**	5.0	78
16.	I	4-$OCH_3C_6H_4$	$COOCH_2C_6H_5$	**31da′**	5.0	86
17.	I	2-C_4H_3S	$COOCH_2C_6H_5$	**31ea′**	6.0	82

[a]Reaction conditions: Arylhalide (1.0 mmol) alkene (2.0 mmol), **Pd(L1)$_2$** (1 mol %), K_2CO_3 (2 mmol), water (2 mL). [b]Isolated yield.

The representative ^{1}H and ^{13}C NMR of **31aa'** is shown in **Figure 3A.19**.

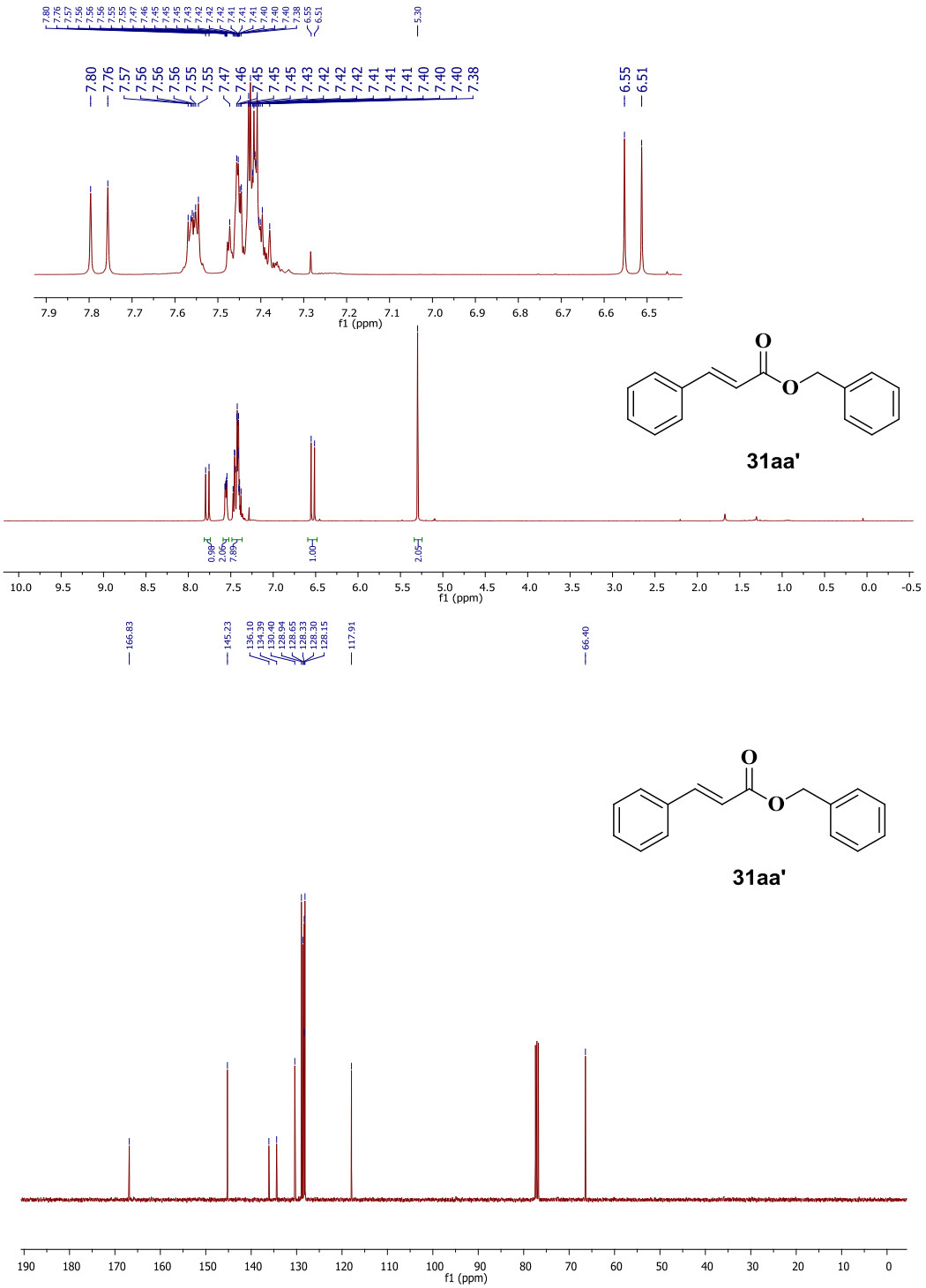
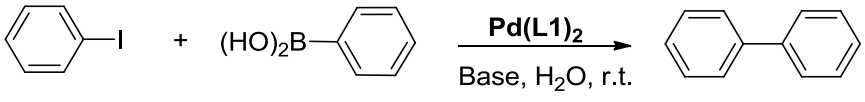


Figure 3A.19 ^{1}H and ^{13}C NMR spectra (in $CDCl_3$) of (E)-Benzyl cinnamate (**31aa'**)

3A.2.3.3 Catalytic activity of $Pd(L1)_2$ for the Suzuki reaction

Encouraged with the excellent results for the Heck reaction using **$Pd(L1)_2$** as catalyst in aqueous medium, we set out to optimize the reaction condition for Suzuki reaction in aqueous medium. As the Suzuki reaction is largely affected by the amount of catalyst and type of the base used, we optimized the reaction conditions taking reaction of iodobenzene (**29a**) and phenylboronic acid (**32a′**) to give biphenyl (**33aa′**) as model reaction. The results from various experiments are summarized in Table 3A.3. It was found that 0.1 mol % of **$Pd(L1)_2$** in presence of K_2CO_3 as base was most suitable condition for an efficient conversion at room temperature with excellent yield of **33aa′** (Table 3A.3, entry 5). The yield of **33aa′** was not much affected by increasing the concentration of catalyst up to 3 mol % (Table 3A.3, entries 5-9).

Table 3A.3 Optimization of the reaction conditions for the Suzuki reaction catalyzed by **$Pd(L1)_2$**.[a]

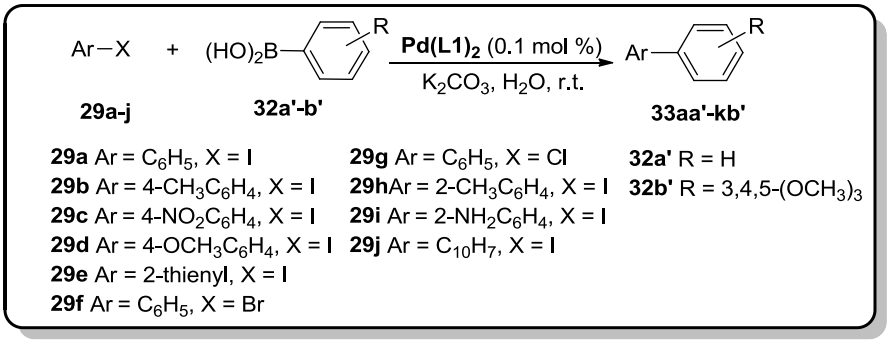


29a **32a′** **33aa′**

Entry	**$Pd(L1)_2$** (mol %)	Base	Yield[b] (%)
1.	0.1	Et_3N	69
2.	0.1	NaOH	68
3.	0.1	$NaHCO_3$	71
4.	0.1	Cs_2CO_3	76
5.	**0.1**	**K_2CO_3**	**80**
6.	0.5	K_2CO_3	80
7.	1	K_2CO_3	81
8.	3	K_2CO_3	82
9.	0.01	K_2CO_3	80

[a]Reaction conditions: Iodobenzene (1.0 mmol), phenylboronic acid (1.2 mmol), **$Pd(L1)_2$** (x mol %), base (2.0 mmol), deionized water (2 mL). [b]Isolated yield.

The scope of Suzuki reaction catalyzed by **Pd(L1)$_2$** in aqueous medium was investigated by employing various aryl halides and arylboronic acids (Scheme 3A.4). The results are summarized in Table 3A.4. The reaction of substituted iodobenzenes (**29a-e**, **29h-j**) with arylboronic acids gave corresponding coupled products in excellent yields (80-87%). The reaction of bromobenzene (**29f**) and chlorobenzene (**29g**) with arylboronic acids also afforded good yields of the coupled products (71–76%) (Table 3A.4, entries 2–3, 5–6, 11 and 13−14). However, the time required for completion of reaction for bromobenzene (**29f**) and chlorobenzene (**29g**) was more than that for iodobenzene (**29a**). The method is equally applicable for both electron-withdrawing and electron-donating group substituted aryl iodides. For example 4-nitro-, 4-methyl, 4-methoxy and 2-aminoiodobenzenes were smoothly converted to the corresponding coupled products in high yields. The identity of the products was confirmed by melting points and ^{1}H and ^{13}C NMR data and they were found to be consistent with the reported values.



Scheme 3A.4 Suzuki reaction catalyzed by **Pd(L1)$_2$** in aqueous medium

Table 3A.4 Suzuki reaction between aryl halides (**29**) and arylboronic acids (**32**) catalyzed by **Pd(L1)$_2$** in water.[a]

S. No.	X	Ar	R	Product	Time (min.)	Yield[b] (%)
1.	I	C_6H_5	H	**33aa′**	30	80
2.	Br	C_6H_5	H	**33aa′**	50	76
3.	Cl	C_6H_5	H	**33aa′**	55	71
4.	I	C_6H_5	3,4,5-$(OCH_3)_3$	**33ab′**	50	79
5.	Br	C_6H_5	3,4,5-$(OCH_3)_3$	**33ab′**	55	73
6.	Cl	C_6H_5	3,4,5-$(OCH_3)_3$	**33ab′**	55	70
7.	I	4-$CH_3C_6H_4$	H	**33ba′**	30	75
8.	I	4-$NO_2C_6H_4$	H	**33ca′**	40	89
9.	I	2-$CH_3C_6H_4$	H	**33ha′**	50	65
10.	I	4-$OCH_3C_6H_4$	H	**33da′**	35	89
11.	Br	4-$OCH_3C_6H_4$	H	**33da′**	55	74
12.	I	2-$NH_2C_6H_4$	H	**33ia′**	60	70
13.	Br	$C_{10}H_7$	H	**33ja′**	40	76
14.	Cl	$C_{10}H_7$	H	**33ja′**	45	74
15.	I	2-C_4H_3S	H	**33ea′**	30	82

[a]Reaction conditions: Arylhalide (1.0 mmol), arylboronic acid (1.2 mmol), **Pd(L1)$_2$** (0.1 mol %), K_2CO_3 (2.0 mmol), water (2 mL). [b]Isolated yield

The representative ^{1}H and ^{13}C NMR of **33aa'** is shown in **Figure 3A.21**.

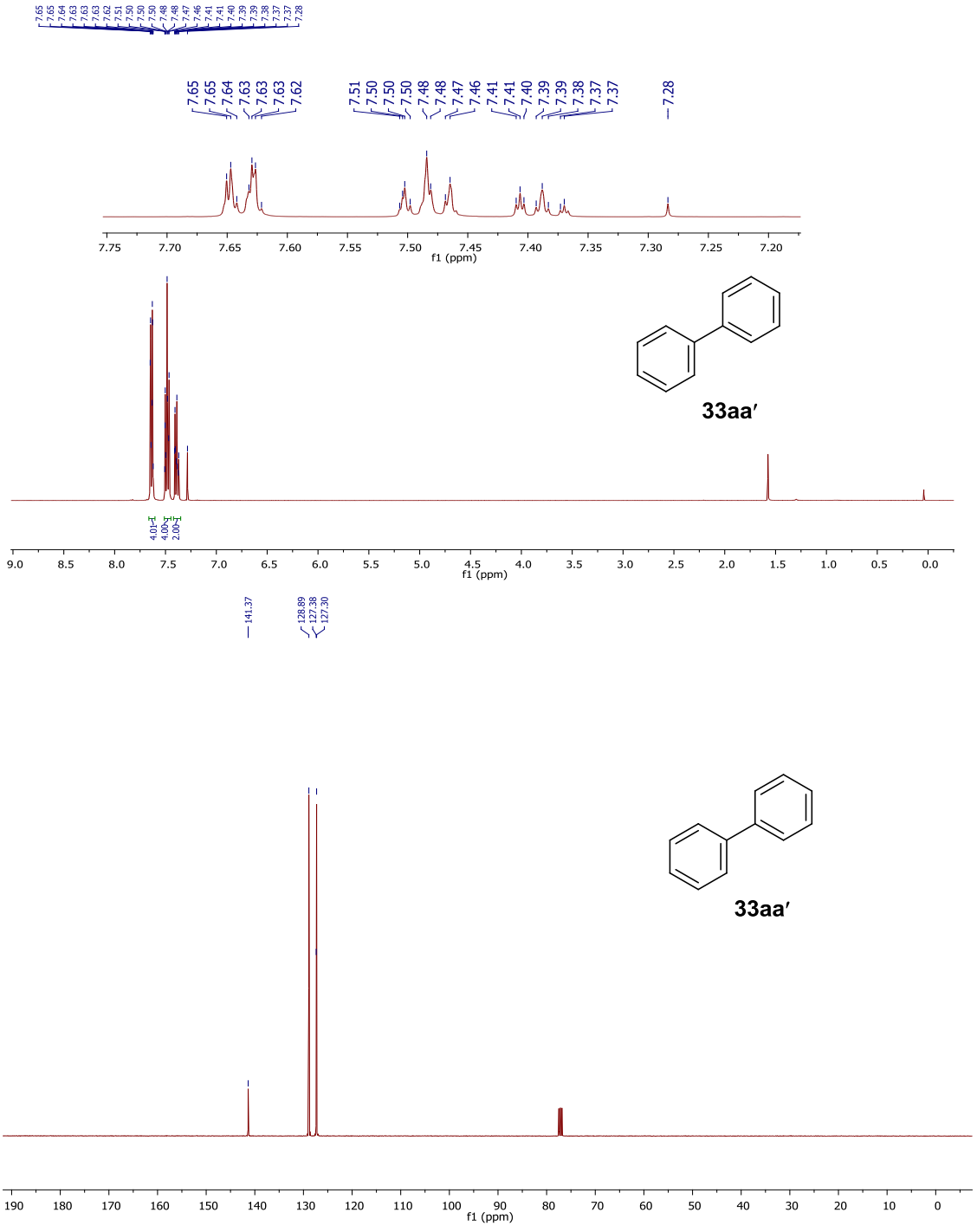


Figure 3A.21 ^{1}H and ^{13}C NMR spectra (in deuterated $CDCl_3$) of 1,1'-Biphenyl (**33aa'**)

3A.2.3.4 Reusability of $Pd(L1)_2$ for Suzuki reaction

The reusability of **$Pd(L1)_2$** was evaluated for the model Suzuki reaction. As shown in **Figure 3A.22**, the catalyst could be efficiently used for up to six cycles without much loss in catalytic activity. The discharge of the catalyst through extraction may be one of the factors responsible for the gradual decrease in the yield of the product during recycling.

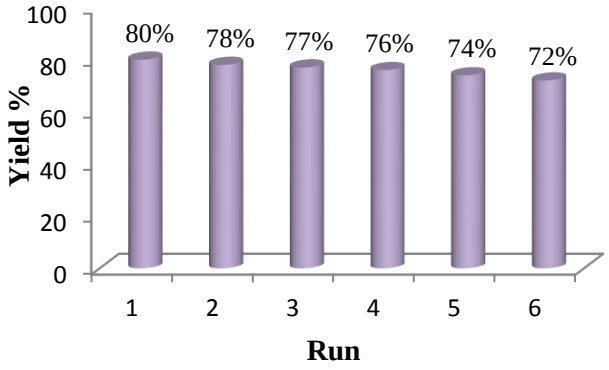
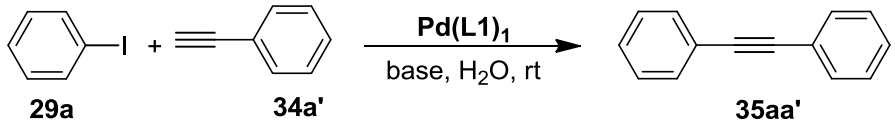


Figure 3A.22 Reusability of **$Pd(L1)_2$** for Suzuki reaction

3A.2.3.5 Catalytic activity of $Pd(L1)_2$ for Sonogashira reaction

The **$Pd(L1)_2$** further screened as a catalyst for the Sonogashira cross coupling reaction. The reaction was performed without adding copper as an additive. The preliminary optimization of the reaction conditions were performed on the reaction of iodobenzene (**29a**) with phenyl acetylene (**34a′**) in presence of different bases (Table 3A.5).

Table 3A.5 Optimization of the reaction conditions for the Sonogashira reaction catalyzed by **$Pd(L1)_2$.** [a]

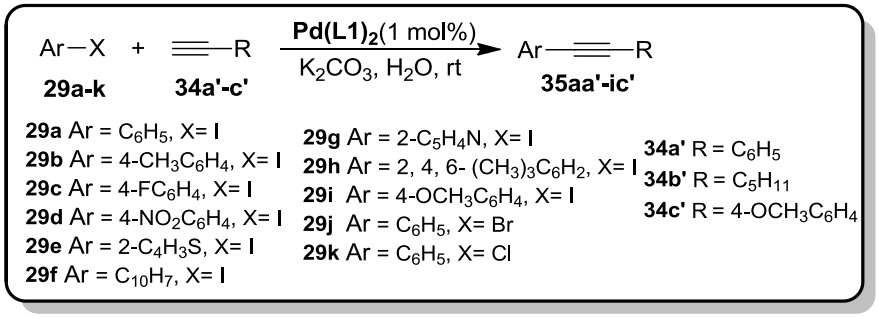


Entry	Base	**$Pd(L1)_2$** (mol%)	Time (h)	Yield[b] (%)
1	Piperidine	1.0	3	65

2	Pyrrolidine	1.0	3	68
3	Isopropyl amine	1.0	3	68
4	DABCO	1.0	3	65
5	Et_3N	1.0	4.5	30
6	NaOH	1.0	2.5	65
7	Cs_2CO_3	1.0	2	77
8	Na_2CO_3	1.0	2.5	60
9	**K_2CO_3**	**1.0**	**2**	**79**
10	K_2CO_3	0.2	2	77
11	K_2CO_3	0.1	2	75
12	K_2CO_3	0.01	2	73

[a]Reaction conditions: Iodobenzene (2.5 mmol), Phenyl acetylene (3 mmol), base (5 mmol), 2 (x mol %), water (10 mL), 2-4.5 h, rt. [b]Isolated yield.

After optimizing the reaction conditions, a collection of terminal acetylenes (**34**) were coupled with different aryl halides (**29**) (Scheme 3A.5), and moderate to good yields were obtained (Table 3A.6).



Scheme 3A.5 Sonogashira reaction catalyzed by **$Pd(L1)_2$** in aqueous medium

Table 3A.6 Copper-free Sonogashira reaction of terminal alkynes with aryl halides catalyzed by **$Pd(L1)_2$**.[a]

Entry	X	Ar	R	Product	Time (h)	Yield[b] (%)
1.	I	C_6H_5	C_6H_5	**35aa′**	2	78

2.	Br	C_6H_5	C_6H_5	**35aa′**	2	70
3.	Cl	C_6H_5	C_6H_5	**35aa′**	4	65
4.	I	4-$CH_3C_6H_4$	C_6H_5	**35ba′**	3	75
5.	I	4-FC_6H_4	C_6H_5	**35ca′**	2	75
6.	Br	4-FC_6H_4	C_6H_5	**35ca′**	2.5	65
7.	I	4-$NO_2C_6H_4$	C_6H_5	**35da′**	2	75
8.	Br	4-$NO_2C_6H_4$	C_6H_5	**35da′**	4	65
9.	I	2-C_4H_3S	C_6H_5	**35ea′**	3	75
10.	I	$C_{10}H_7$	C_6H_5	**35fa′**	3	75
11.	I	2-C_5H_4N	C_6H_5	**35ga′**	3	75
12.	I	2, 4, 6- $(CH_3)_3C_6H_2$	C_6H_5	**35ha′**	4	60
13.	I	C_6H_5	C_5H_{11}	**35ab′**	4	55
14.	I	4-$OCH_3C_6H_4$	4-$OCH_3C_6H_4$	**35ic′**	3	75

[a] Reaction conditions: aryl halide (2.5 mmol), terminal alkyne (3 mmol), **Pd(L1)$_2$** (1 mol %) K_2CO_3 (5 mmol), water (25 ml). [b]Isolated yield

It is noteworthy that moderately reactive aryl bromide also showed good reactivity (Table 3A.6, entry 2), while the reaction with aryl chloride was less effective (Table 3A.6, entry 3). Good product yields were obtained for the coupling reaction of aryl halides with both electron donating (Table 3A.6, entries 4 and 14) and electron withdrawing (Table 3A.6, entry 5-8) groups. The hetero aromatic halides also gave products in good yields (Table 3A.6, entry 9, 11). The product yield with aliphatic acetylenes was moderate (Table 3A.6, entry 13). The identity of the products was confirmed by melting points and ^{1}H and ^{13}C NMR data and they were found to be consistent with the reported values.

The representative ^{1}H and ^{13}C NMR of **33aa'** is shown in **Figure 3A.23**.

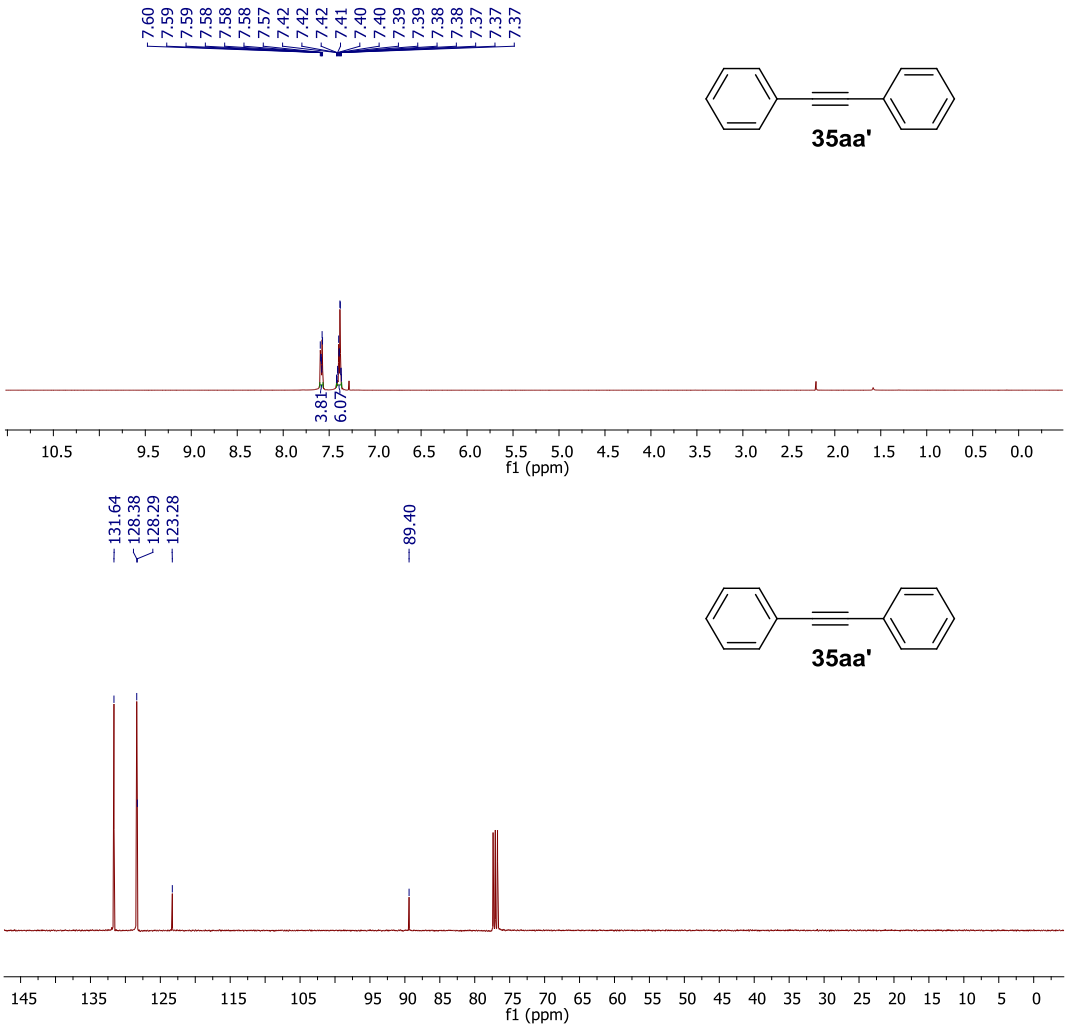


Figure 3A.23 ^{1}H and ^{13}C NMR spectra (in $CDCl_3$) of 1, 2-Diphenylethyne (**35aa'**)

3A.2.3.6 Reusability of Pd(L1)$_2$ for the Sonogashira reaction

The reusability of **Pd(L1)$_2$** was evaluated for the model Sonogashira reaction. The catalyst could effectively be used up to six cycles without much loss in the catalytic activity (**Figure 3A.24**). Leaching of the catalyst during extraction might be responsible for the gradual decrease in the yield of the product during recycling.

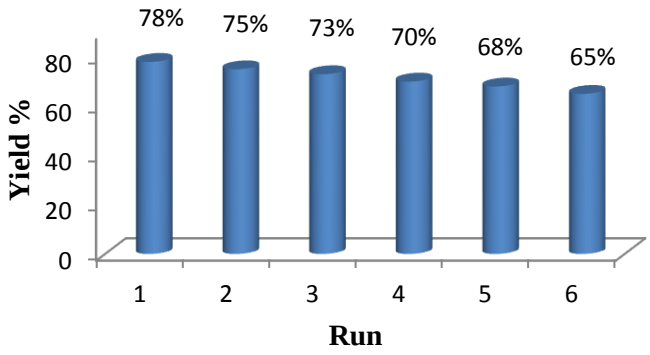


Figure 3A.24 Reusability of **Pd(L1)$_2$** for the Sonogashira reaction

3A.3 Experimental section

3A.3.1 Synthesis (Pd(L1)$_2$)

Ionic liquid-tagged Schiff base **HL1** (672 mg, 2.0 mmol) was stirred with ethanol (20 mL) in a 25 mL round bottom flask for 15 min. To the resulting solution, palladium acetate (224 mg, 1.0 mmol) was added and refluxed for 4 hrs till the product precipitated completely. After cooling, the product **Pd(L1)$_2$** was separated by filtration and recrystallized from mixture of petroleum ether (2 mL) and methanol (15 mL).

3A.3.2 General procedure for the Heck reaction in water

A 50 mL round bottom flask containing a mixture of aryl halide (1.0 mmol), alkene (2.0 mmol), K_2CO_3 (2.0 mmol) and **Pd(L1)$_2$** (1.0 mol %) in water (2 mL) was heated to a temperature of 80 °C in an oil bath. The advancement of the reaction was monitored with TLC at regular time intervals. After completion of the reaction, the reaction mixtures was added to water (20 mL) and extracted with ethyl acetate (3 × 10 mL). The organic layer was dried with anhydrous Na_2SO_4, and concentrated to give crude product which was purified by column chromatography over silica gel (mesh 60−120) using *n*-hexane and ethyl acetate as an eluent. The products were analyzed by ^{1}H and ^{13}C NMR spectroscopy.

3A.3.3 General procedure for the Suzuki reaction in water

To a 50 mL round bottom flask were added aryl halide (1.0 mmol), arylboronic acid (1.2 mmol), **Pd(L1)$_2$** (0.1 mol %), K_2CO_3 (2.0 mmol) and water (2 mL) under continuous stirring at room temperature (25 °C). Progress of the reaction was monitored by means of TLC at regular intervals of 5 minutes. After completion of the reaction, the reaction mixture was diluted with water (20 mL) and extracted with mixture of hexane and ethyl acetate (1: 1 *v/v*, 3 × 10 mL). Diethyl ether was used for extraction in case of **33ha′**, **33ia′** and **33ja′**. The organic layer was dried with anhydrous Na_2SO4, and then the solvent was evaporated under reduced pressure. The resulting residue was purified by column chromatography over silica gel (mesh 60−120) using *n*-hexane/ethyl acetate as an eluent to give the desired product. The products were analyzed by ^{1}H and ^{13}C NMR spectroscopy.

3A.3.4 General procedure for the Sonogashira reaction in water

Under an aerial atmosphere, a 25 mL round bottom flask was charged with aryl halide (2.45 mmol, 500 mg.), acetylene (2.94 mmol, 500 mg), potassium carbonate (4.90 mmol, 677 mg) and catalyst **Pd(L1)$_2$** (0.02 mmol, 27.2 mg.) in water (10 mL). The resulting mixture was kept on continuous stirring at room temperature for 2 hours. The progress of the reaction was continuously monitored by TLC. On completion of the reaction, the product was extracted in ethyl acetate and after evaporation the residue was purified by column chromatography over silica gel (mesh 100−200) using *n*-hexane/ethyl acetate as an eluent to get the desired product. The products were analyzed by ^{1}H and ^{13}C NMR spectroscopy.

3A.3.5 Reusability and recovery of the catalyst

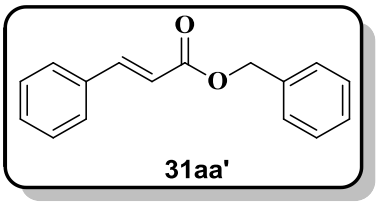
After the completion of the first run of the reactions the product was directly extracted in organic layer and catalyst remained in the water layer was reused for the next cycle of the reaction, following same procedure as mentioned above for Heck, Suzuki and Sonogashira reactions.

3A.3.6 Spectroscopic data of Pd(L1)$_2$

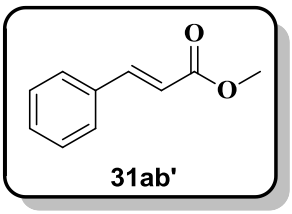
The compound was isolated as orange apparent solid in 91% yield with melting point of 209-211 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.14 (s, 2H), 7.94 (s, 2H), 7.80 (t, J = 1.8, 2H), 7.72 (t, J =

1.8 Hz, 2H), 7.56–7.22 (m, 14H), 6.12 (dd, *J* = 8.8, 2.3 Hz, 2H), 4.32 (t, *J* = 6.9 Hz, 4H), 3.88 – 3.84 (m, 10H), 2.26–2.20 (m, 4H). ^{13}C NMR (75 MHz, DMSO) δ 166.1, 164.3, 162.5, 149.5, 137.2, 137.1, 128.3, 126.4, 125.4, 124.0, 122.9, 115.4, 105.5, 102.2, 64.9, 46.9, 36.2, 29.3.

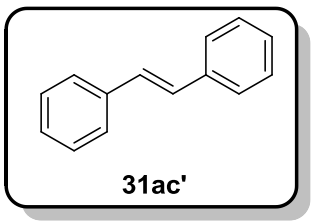
3A.3.7 ^{1}H and ^{13}C NMR analysis of the Heck coupling products



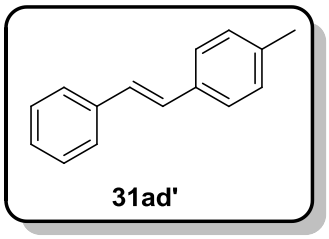
(*E*)-Benzyl cinnamate (31aa′): Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 16.0 Hz, 1H), 7.59 – 7.53 (m, 2H), 7.49 – 7.33 (m, 8H), 6.53 (d, *J* = 16.0 Hz, 1H), 5.30 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 145.2, 136.10, 134.4, 130.4, 128.9, 128.6, 128.3, 128.3, 128.1, 117.9, 66.4.



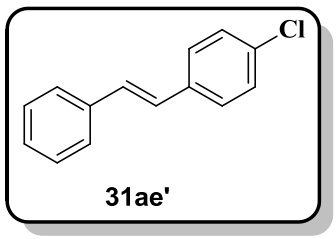
(*E*)-Methyl cinnamate (31ab′): Colorless liquid;[90] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 16.0 Hz, 1H), 7.59 – 7.52 (m, 2H), 7.45 – 7.37 (m, 3H), 6.47 (d, *J* = 16.0 Hz, 1H), 3.83 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 144.9, 134.4, 130.3, 128.9, 128.1, 117.8, 51.7.



(*E*)-1,2-Diphenylethene (31ac′): Colorless solid; mp 122 – 123 °C (Lit. mp 120 – 122 °C);[91] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 8.2, 1.2 Hz, 4H), 7.39 – 7.34 (m, 4H), 7.28 – 7.23 (m, 2H), 7.11 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.4, 128.7, 128.7, 127.7, 126.5.

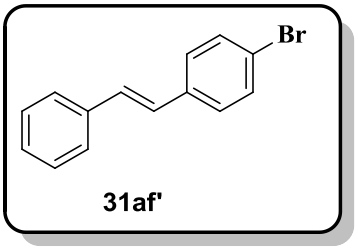


(*E*)-1-Methyl-4-styrylbenzene (31ad′): Colorless solid, mp 114 – 116 °C (Lit. mp 119 − 122 °C);[90] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.54 (m, 2H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.44 – 7.38 (m, 2H), 7.34 – 7.28 (m, 1H), 7.23 (d, *J* = 7.9 Hz, 2H), 7.14 (d, *J* = 2.6 Hz, 2H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6, 134.6, 129.5, 128.7, 128.7, 127.7, 127.5, 126.5, 126.5, 21.3.

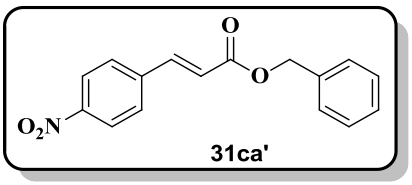


(*E*)-1-Chloro-4-styrylbenzene (31ae′): Colorless solid, mp 128 – 129 °C (Lit. mp 126 − 128 °C);[92] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 8.2, 1.1 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 2H), 7.39 – 7.29 (m, 4H) 7.26 (d, *J* = 4.5 Hz, 1H), 7.07 (d, *J* = 2.8 Hz, 2H). ^{13}C NMR (100

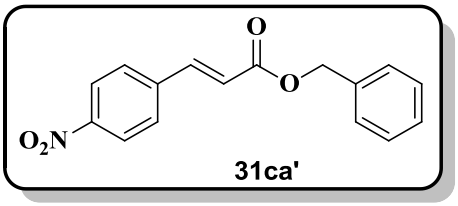
MHz, $CDCl_3$) δ 137.0, 135.9, 133.2, 129.3, 128.9, 128.8, 127.9, 127.8, 127.4, 126.6.



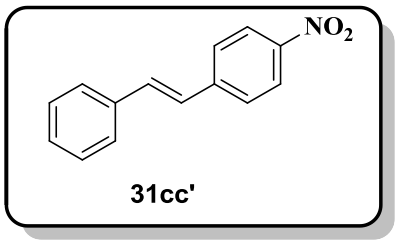
(*E*)-1-Bromo-4-styrylbenzene (31af′): Colorless solid, mp 136 – 138 °C (Lit. mp 136.5 − 139);[92] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.48 (m, 4H), 7.43 – 7.36 (m, 4H), 7.31 (dt, *J* = 4.1, 1.7 Hz, 1H), 7.13 (d, *J* = 16.3 Hz, 1H), 7.06 (d, *J* = 16.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.9, 136.3, 131.8, 129.4, 128.7, 128.0, 127.9, 127.3, 126.6, 121.3.



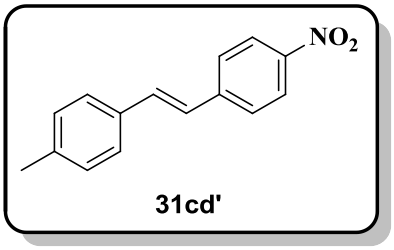
(*E*)-Benzyl 3-(4-methylphenyl)acrylate (31ba′): Yellow crystalline solid, mp 87 – 88 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 16.0 Hz, 1H), 7.46 – 7.35 (m, 7H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.47 (d, *J* = 16.0 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 145.2, 140.8, 136.2, 131.7, 129.6, 128.6, 128.3, 128.2, 128.1, 116.8, 66.3, 21.5.



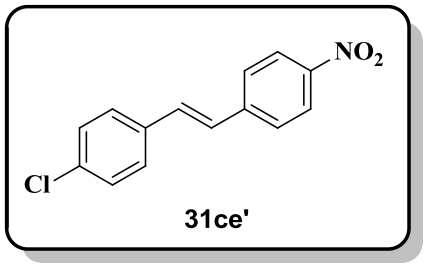
(*E*)-Benzyl 3-(4-nitrophenyl)acrylate (31ca′): Pale yellow solid, mp 110 – 112 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.6 Hz, 2H), 7.77 (d, *J* = 16.0 Hz, 1H), 7.69 (d, *J* = 8.6 Hz, 2H), 7.49 – 7.27 (m, 5H), 6.63 (d, *J* = 16.0 Hz, 1H), 5.30 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 148.5, 142.2, 140.5, 135.6, 128.7, 128.5, 128.4, 124.4, 124.2, 122.2, 66.9.



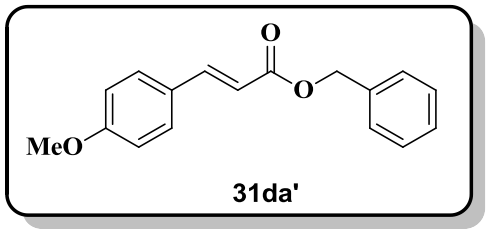
1-(4-Nitrostyryl)benzene (31cc′): Yellow solid, mp 151 – 152 °C (Lit. mp 155 °C); [91] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.6 Hz, 2H), 7.64 (d, *J* = 8.5 Hz, 2H), 7.58 (d, *J* = 7.5 Hz, 2H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.37 (t, *J* = 7.2 Hz, 1H), 7.32 – 7.24 (m, 1H), 7.16 (d, *J* = 16.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.8, 143.9, 136.2, 133.3, 128.9, 128.9, 127.0, 126.9, 126.3, 124.2.



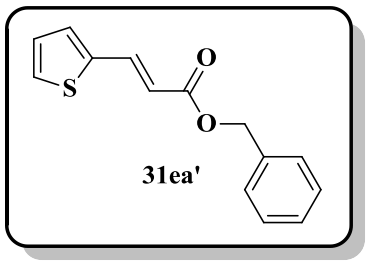
1-(4-Nitrostyryl)-4-methylbenzene (31cd′): Yellow solid, mp 144 – 146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.5 Hz, 2H), 7.63 (d, *J* = 8.5 Hz, 2H), 7.48 (d, *J* = 7.6 Hz, 2H), 7.29 – 7.23 (m, 3H), 7.12 (d, *J* = 16.3 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.6, 144.1, 139.0, 133.4, 133.3, 129.6, 127.0, 126.7, 125.3, 124.1, 21.4.



1-(4-Nitrostyryl)-4-chlorobenzene (31ce′): Yellow solid, mp 187 – 188 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.6 Hz, 2H), 7.65 (d, *J* = 8.6 Hz, 2H), 7.50 (d, *J* = 8.3 Hz, 2H), 7.39 (d, *J* = 8.3 Hz, 2H), 7.30 – 7.21 (m, 1H), 7.14 (d, *J* = 16.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.9, 143.5, 134.7, 134.6, 131.9, 129.1, 128.2, 126.9, 126.9, 124.2.

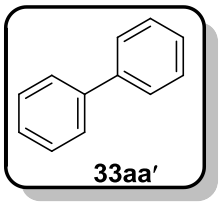


(*E*)-Benzyl 3-(4-methoxyphenyl)acrylate (31da′): Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 16.0 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.47 – 7.36 (m, 5H), 6.93 (d, *J* = 8.8 Hz, 2H), 6.40 (d, *J* = 16.0 Hz, 1H), 5.28 (s, 2H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 161.4, 144.9, 136.2, 129.8, 128.6, 128.3, 128.2, 127.1, 115.3, 114.3, 66.2, 55.4.

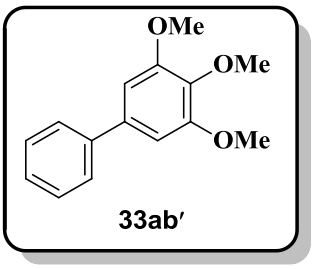


(*E*)-Benzyl 3-(thiophen-2-yl)acrylate (31ea'): Yellow solid, mp 46 − 47 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 15.7 Hz, 1H), 7.47 – 7.35 (m, 6H), 7.30 – 7.24 (m, 1H), 7.08 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.32 (d, *J* = 15.7 Hz, 1H), 5.27 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 139.5, 137.6, 136.1, 131.1, 128.6, 128.6, 128.3, 128.3, 128.1, 116.6, 66.4.

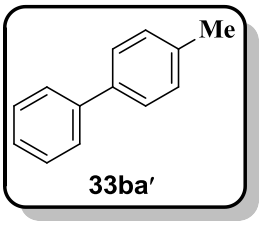
3A.3.8 ^{1}H and ^{13}C NMR analysis of the Suzuki coupling products



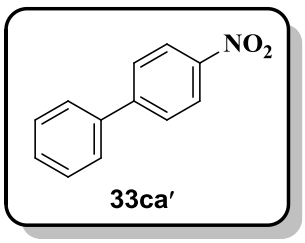
1,1'-Biphenyl (33aa′): Colorless solid; mp 68 – 70 °C (Lit. mp 71 – 72 °C);[4] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.61 (m, 2H), 7.52 – 7.45 (m, 2H), 7.41 – 7.36 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.4, 128.9, 127.4, 127.3.



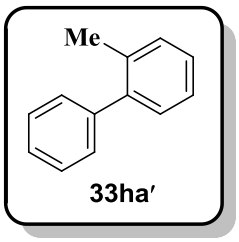
3,4,5-Trimethoxy-1,1'-biphenyl (33ab′): Colorless solid, mp 141 – 141.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.56 (m, 2H), 7.50 – 7.43 (m, 2H), 7.41 – 7.34 (m, 1H), 6.81 (s, 2H), 3.95 (s, 6H), 3.92 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 141.4, 137.6, 137.3, 128.8, 127.3, 127.1, 104.5, 61.0, 56.2.



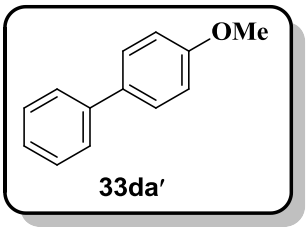
4-Methyl-1,1'-biphenyl (33ba′): Colorless solid, mp 49–50 °C (Lit. mp 49 − 51 °C);[91] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.60 (m, 2H), 7.57 – 7.52 (m, 2H), 7.50 – 7.44 (m, 2H), 7.40 – 7.34 (m, 1H), 7.29 (d, *J* = 7.3 Hz, 2H), 2.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.2, 138.4, 137.1, 129.5, 128.8, 128.8, 127.1, 127.0, 21.2.



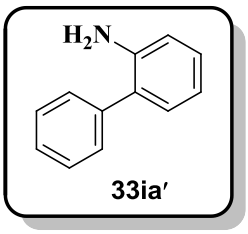
4-Nitro-1,1'-biphenyl (33ca′): Pale yellow coloured solid, mp 113–114 °C (Lit. mp 113 − 115);[91] ^{1}H NMR (400 MHz, $CDCl_3$) δ ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (dt, *J* = 8.8, 2.4 Hz, 2H), 7.77 (dt, *J* = 8.8, 2.4 Hz, 2H), 7.66 – 7.63 (m, 2H), 7.55 – 7.45 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.7, 147.1, 138.8, 129.2, 128.9, 127.8, 127.4, 124.1.



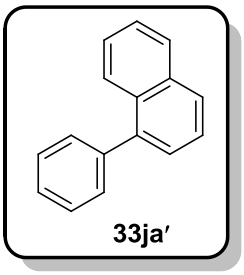
2-Methyl-1,1'-biphenyl (33ha′): Colorless liquid;[5] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.63 (m, 1H), 7.54 – 7.44 (m, 3H), 7.44 – 7.40 (m, 1H), 7.40 – 7.36 (m, 1H), 7.35 – 7.28 (m, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.98, 135.39, 130.35, 129.84, 129.24, 128.80, 128.11, 127.29, 127.22, 126.81, 125.81, 20.52.



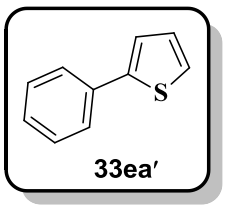
4-Methoxy-1,1'-biphenyl (33da′): Colorless solid, mp 87 – 90 °C (Lit. mp 88 − 92 °C);[91] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.52 (m, 4H), 7.47 – 7.42 (m, 2H), 7.37 – 7.30 (m, 1H), 7.01 (dt, *J* = 8.8, 2.4 Hz, 2H), 3.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 140.9, 133.8, 128.8, 128.2, 126.8, 126.7, 114.2, 55.4.



2-Amino-1,1'-biphenyl (33ia′): Colorless solid, mp 47–50 °C (Lit. mp 50 – 53 °C);[54] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.45 (m, 4H), 7.44 – 7.35 (m, 1H), 7.26 – 7.15 (m, 2H), 6.88 (dt, *J* = 7.5, 3.8 Hz, 1H), 6.84 – 6.79 (m, 1H), 3.77 (br s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.5, 139.6, 130.5, 129.1, 128.9, 128.5, 127.7, 127.2, 118.7, 115.6.

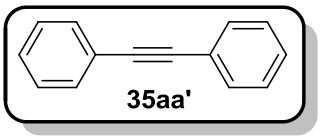


4-Naphthyl-1,1'-biphenyl (33ja′): Colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17–8.04 (m, 3H), 7.73 – 7.59 (m, 9H). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.8 Hz, 1H), 8.09 (d, *J* = 8.8 Hz, 1H), 8.04 (d, *J* = 8.2 Hz, 1H), 7.72 – 7.65 (m, 5H), 7.66 – 7.58 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.0, 140.5, 134.0, 131.9, 130.3, 129.0, 128.5, 128.4, 127.9, 127.4, 127.2, 126.2, 125.9, 125.6.

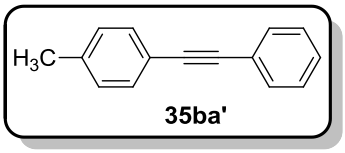


2-phenylthiophene (33ea′): Low melting colorless solid (Lit. mp 34 – 36 °C);[93] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.65 (m, 2H), 7.47 – 7.40 (m, 2H), 7.37 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.36 – 7.31 (m, 2H), 7.13 (dd, *J* = 5.1, 3.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.5, 134.5, 128.9, 128.1, 127.5, 126.0, 124.9, 123.1.

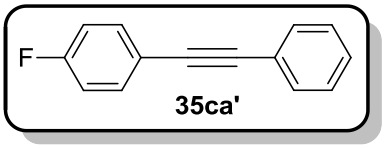
3A.3.9 ^{1}H and ^{13}C NMR analysis of the Sonogashira coupling products



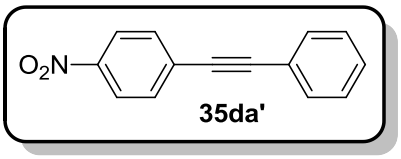
1, 2-Diphenylethyne (35aa'): White solid; mp 61 – 62 °C (Lit. mp 60 – 61 °C);[35] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.56 (m, 4H), 7.42 – 7.37 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.6, 128.3, 128.2, 123.2, 89.4.



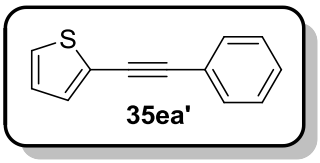
1-Methyl-4-(phenylethynyl) benzene (35ba'): White solid; mp 62 – 65 °C (Lit. mp 66 – 68 °C);[94] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.54 (m, 2H), 7.48 – 7.45 (m, 2H), 7.40 – 7.33 (m, 3H), 7.20 – 7.18 (d, *J* = 7.6 Hz, 2H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.4, 131.6, 131.5, 129.1, 128.4, 128.1, 123.5, 120.2, 89.6, 88.7, 21.6.



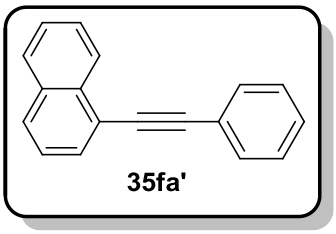
1-Fluoro-4-(phenylethynyl) benzene (35ca'): White solid; mp 109 – 111 °C (Lit. mp 109 – 110 °C);[95] ^{1}H NMR (400 MHz, $CDCl_3$) δ7.57 – 7.56 (m, 2H), 7.55 – 7.52 (m, 2H), 7.42 – 7.33 (m, 3H), 7.11 – 7.04 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.7, 161.2, 134.5 (d, *J* = 8.5 Hz), 133.5 (d, *J* = 8.3 Hz), 131.6, 128.4 (d, *J* = 3.8 Hz), 123.1, 116.0, 115.8 (d, *J* = 5.0 Hz), 115.5, 89.0, 88.3.



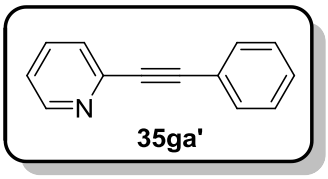
1-Nitro-4-(phenylethynyl) benzene (35da'): Yellow solid; mp 118 – 120 °C (Lit. mp 120 – 121 °C);[96] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.9 Hz, 2H), 7.69 (d, *J* = 9.0 Hz, 2H), 7.59 – 7.57 (m, 2H), 7.44 – 7.40 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.9, 132.2, 131.8, 130.2, 129.3, 128.5, 123.6, 122.1, 94.7, 87.5.



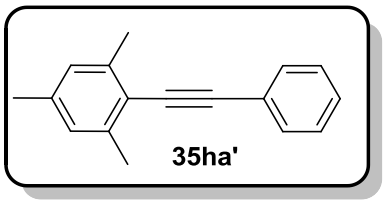
2-(Phenylethynyl) thiophene (35ea'): Colorless oil;[95] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.55 (m, 2H), 7.42 – 7.38 (m, 3H), 7.34 – 7.32 (m, 2H), 7.07 – 7.05 (dd, *J* = 5.1, 3.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.5, 131.9, 131.4, 129.2, 128.6, 128.3, 127.2, 122.9, 93.0, 82.6.



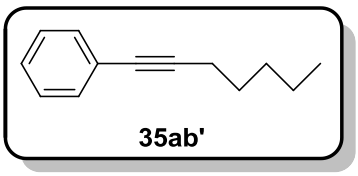
1-(Phenylethynyl) naphthalene (35fa'): Colorless oil;[97] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 8.3 Hz, 1H), 7.98 – 7.87 (m, 3H), 7.78 (dd *J* = 3.9, 2.1 Hz, 2H), 7.74 – 7.69 (m, 1H), 7.66 – 7.61 (m, 1H), 7.57 – 7.43 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.4, 133.3, 131.8, 130.5, 128.9, 128.6, 128.5, 128.4, 126.9, 126.6, 126.3, 125.4, 123.5, 121.0, 94.5, 87.7.



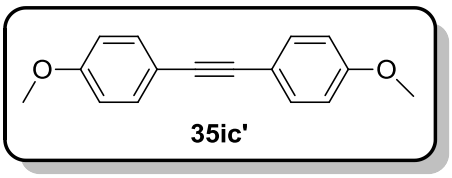
2-(Phenylethynyl) pyridine (35ga'): Yellow green oil;[95] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, *J* = 4.8 Hz, 1H), 7.63 (d, *J* = 6.8 Hz, 1H), 7.61 – 7.56 (m, 2H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.33 (dd, J = 4.1, 1.6 Hz, 3H), 7.21 – 7.16 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.0, 143.4, 136.1, 132.0, 129.0, 128.4, 127.1, 122.7, 122.2, 89.2, 88.6.



1-(2-mesitylethynyl) benzene (35ha'): Colorless liquid (very low melting white solid); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (m, 2H), 7.41 (m, 3H), 6.97 (m, 2H), 2.57 (s, 6H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.1, 137.8, 131.4, 128.4, 127.9, 127.6, 124.1, 120.0, 97.1, 87.4, 21.4, 21.0.



Hept-1-ynylbenzene (35ab'): Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.40 (m, 2H), 7.35 – 7.27 (m, 3H), 2.44 (t, *J* = 7.1 Hz, 2H), 1.70 – 1.60 (m, 2H), 1.52 – 1.43 (m, 2H), 1.38 (m, *J* = 10.3, 7.4, 4.9 Hz, 2H), 0.96 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (10 MHz, $CDCl_3$) δ 131.5, 128.1, 127.4, 124.1, 90.4, 80.5, 31.1, 28.5, 22.2, 19.4, 14.0.

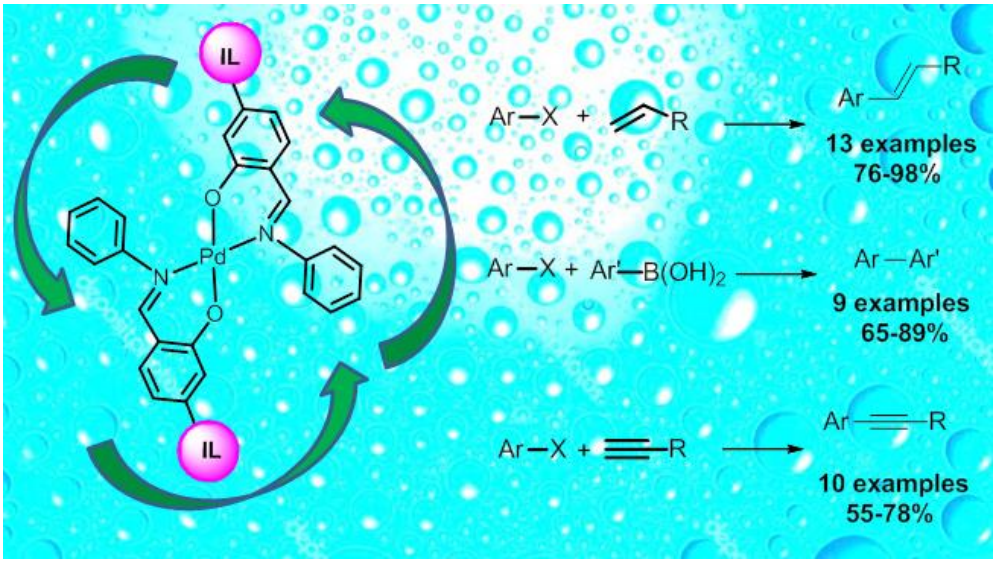


1, 2-bis(4-methoxyphenyl) ethyne (35ic'): Crystalline white solid; mp 49-50 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.56 (m, 4H), 6.73 – 6.69 (m, 4H), 3.80 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 138.1, 116.3, 82.7, 55.3.

3A.4 Conclusion

In summary, we have synthesized and systematically characterized a novel imidazolium ionic liquid-tagged palladium Schiff base complex and explored its catalytic activity for the Heck, Suzuki and Sonogashira reactions in aqueous medium. The complex showed high activity with excellent yields for these reactions. The catalyst is moisture insensitive; highly stable under thermal and aerobic conditions. The reaction condition for the palladium catalyzed coupling reactions are simple and are effective for more challenging substrates such as chlorides. Use of

aqueous medium, and recycling of the catalyst are the advantages that make this method economic and environmental friendly.



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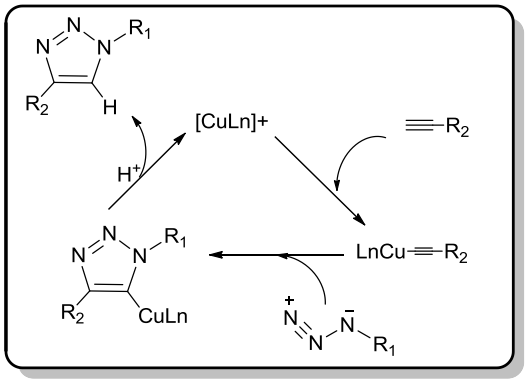
SECTION 3B

Synthesis, Characterization and Catalytic Applications of Ionic Liquid-tagged Schiff Base Copper Complex

3B.1 Introduction

Click chemistry has emerged as a fast and efficient approach for the synthesis of novel compounds with desired functional groups.[1, 2] 1,2,3-Triazoles have attracted much attention in recent years because of their wide applications in organic synthesis and biology.[3-6] Several synthetic methods for the preparation of 1,2,3-triazole derivatives have been developed, among them 1,3-dipolar cycloaddition between an alkyne and an azide is the traditional and broadly used method.[7-9] These 1, 3-dipolar cycloaddition reactions are widely used for preparing five-membered heterocyclic rings, such as the 1,4-disubstituted-1,2,3-triazoles because of their wide substrate scope, 100% atom economy, exclusive regioselectivity, and mild reaction conditions. Furthermore the 1,4-disubstituted-1,2,3-triazoles have tremendous applications in various research fields, including synthetic organic chemistry,[10, 11] biological science,[12, 13] medicinal chemistry[14, 15] and material chemistry.[16, 17] The reaction has gained significant attention in the recent years because Meldal[18] and Sharpless[19] initiated the use of Cu(I) catalysts under composed conditions that selectively formed 1,4-disubstituted 1,2,3- triazoles in high yields.

The mechanism of the reaction involves three steps. In the first step, the copper(I) ion is inserted into the terminal alkyne and forms the copper(I) acetylide. The copper(I) acetylide then reacts with the organic azide and after subsequent rearrangement the final product forms (**Scheme 3B.1**). Due to the presence of copper the reaction is regiospecific and only the 1,4-disubstituted 1,2,3-triazole forms.[19]



Scheme 3B.1 Mechanism of 1,3-dipolar cycloaddition reaction

A number of procedures have been developed including the use of Cu(I) salts directly, Cu(I) complexes, Cu(II) salts, Cu(II) salts/reductants and copper containing nanoparticles.[20-24] These

procedures are competent methods for the synthesis of 1,4-disubstituted 1,2,3-triazoles but have certain limitations *viz.* use of costly catalyst, reductants and organic solvents. Recent progress has been made to circumvent these limitations and few modified methods have emerged as alternatives. A stable Cu(I) complex $Cu(PPh_3)NO_3$,[25] PTA-iminophosphorane based Cu(I) complex[26] and $Cu(OAc)_2$/MCM-41 catalyst[27] were reported for the synthesis of 1,4-disubstituted 1,2,3-triazoles. The activity of the nanoparticle-supported catalysts could be dramatically increased because the size of the supported material affects the catalysis. Functionalized nanoparticles are efficient heterogeneous catalyst supports with high-surface-area.[28, 29] A magnetically recoverable nano ferrite-glutathione-copper (nano-FGT-Cu) catalyst (**1**, **Figure 3B.1**)[30] and copper nanoparticles in Guar-gum (**2**, **Figure 3B.1**)[31] were synthesized and used as the effective catalytic systems for the synthesis of 1,4-disubstituted 1,2,3-triazoles.

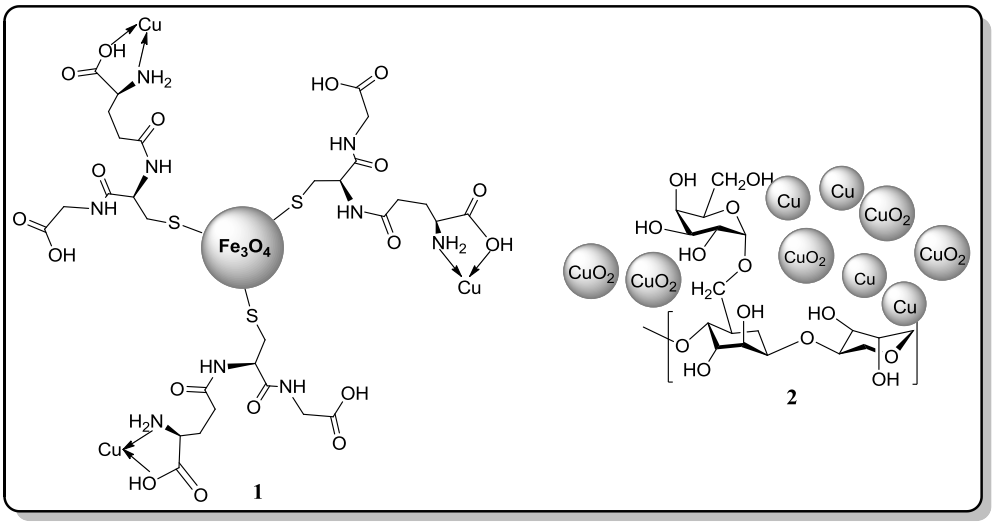


Figure 3B.1 Copper catalysts in nano-FGT and Guar-gum

In past few years, ionic liquids have been widely used as soluble support in the field of click chemistry. The catalytic systems anchored on ionic liquids can be recycled and separated with ease while retaining their original reactivity. Another advantage of ILs supported synthesis is use of spectroscopic analysis during the synthetic process which is not possible with the solid supported synthesis. The copper catalyzed one-pot synthesis of 1,4-disubsituted-1,2,3-triazoles in ionic liquids or with ionic tags have emerged as an efficient tool in the field of click chemistry. A varied number of catalytic systems such as cross-linked polymeric ionic liquid-supported copper

(Cu-CPSIL), imidazolium enclosed Merrifield resin-supported copper (Cu-PSIL), and silica dispersed CuO (CuO/SiO_2),[32] copper nanoparticles in ionic liquids[33] were used as highly effective catalytic systems. The ligated ionic copper(I) complex (**3**, **Figure 3B.2**),[34] $[Cu(Im^{12})_2]CuCl_2$ complex in $[bmim]BF_4$,[35] an octahedral copper(II) coordinated ionic liquid, $Cu[(OHCH_2CH_2)_2NH]_6[CF_3SO_3]$,[36] heterogeneous copper catalyst in poly(1-vinyl imidazole co-ionic liquid) as a solid support,[37] immobilized Cu(I) ionic liquid system,[38] heterogeneous catalyst CuI@SBA-15/PrEn/$ImPF_6$ in mesoporous silica SBA-15 skeleton with supported ethylenediamine/CuI complex.[39] (**4**, **Figure 3B.2**), copper(II) complexes of 1,2-*bis*(4-pyridylthio)ethane immobilized on polystyrene (**5**, **Figure 3B.2**) and silica (**6**, **Figure 3B.2**) nanoparticles were employed for the synthesis of 1,4-disubsituted-1,2,3-triazoles.[40, 41]

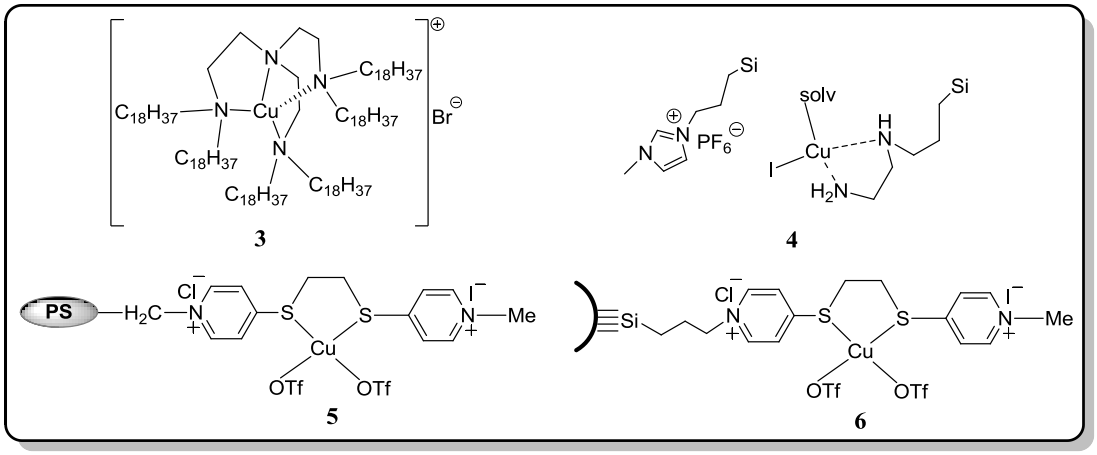


Figure 3B.2 A variety of Cu(I) and Cu(II) complexes with ionic liquids

The Schiff base copper complexes work as efficient and robust catalytic systems for the regioselective synthesis of 1,4-disubstituted-1,2,3 triazoles.[42-45] Functionalized chitosan based biopolymer-supported catalyst[46] (**7**, **Figure 3B.3**), microporous SNW-polymer based Cu(I) catalyst[47] (**8**, **Figure 3B.3**), The PMMA-supported catalyst with an unsymmetrical ferrocenyl moiety[48] (**9**, **Figure 3B.3**), 1-((4-bromophenylimino)methyl)naphthalen-2-ol and 2-(2-hydroxyphenyl)-2-oxazoline based tetra-coordinated copper (II) complexes[49] (**10** and **11, Figure 3B.3**) were used for the synthesis of 1,4-disubstituted-1,2,3 triazoles.

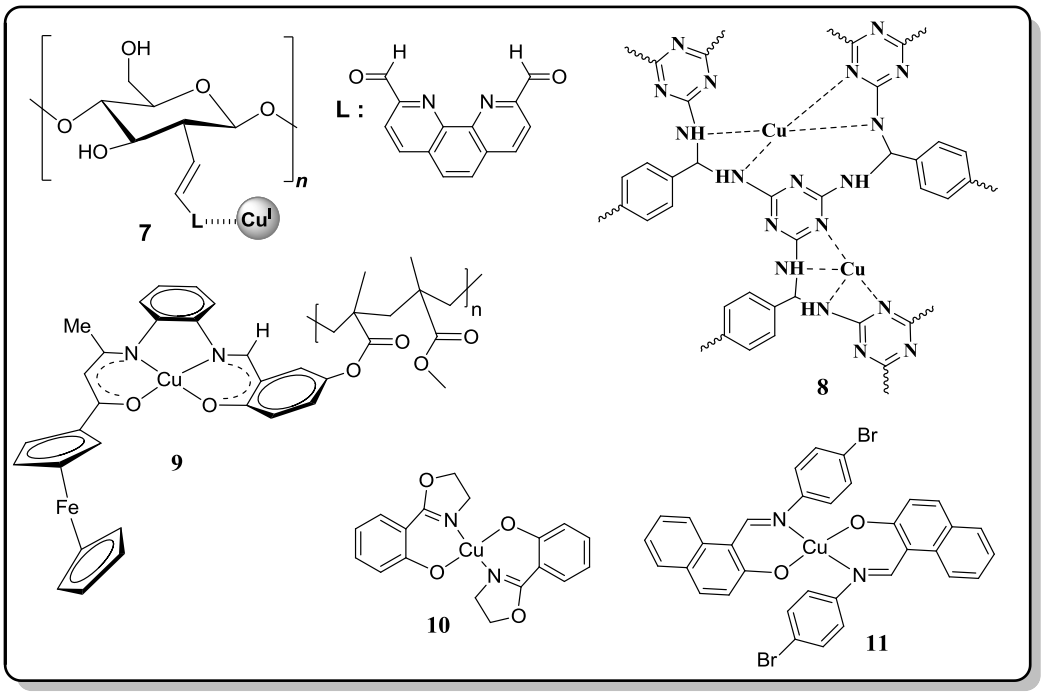
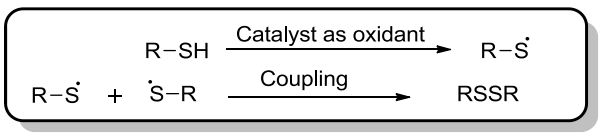


Figure 3B.3 Schiff-base copper(II) complexes

The disulfide bond formation is an important transformation in many biological processes, since it is responsible for the creation of the secondary and tertiary structures in proteins and helps in the stabilization of peptides in proteins. The diaryl disulfide derivatives have often been employed as significant intermediates in the synthesis of bio-active molecules owing to the reversibility of S–S bond formation, which permits them to participate in different addition and exchange reactions.[50-52] The most commonly employed procedure for the synthesis of diaryl disulfides includes the oxidation of the corresponding thiols with diverse array of metal-containing oxidants in presence of a base.[53-56] Although the mechanism of the reaction is not entirely clear, but is considered to involve the coupling reaction of sulfur radicals. The sulfur radicals are formed from thiolate anions by one-electron oxidation process with the metal complex or salt (**Scheme 3B.2**).[55, 57]



Scheme 3B.2 Mechanism of disulfide formation from thiols

Reagents mostly used in the preparation of disulfides includes permanganates,[58, 59] ferric chlorides,[60] sodium perborate,[61] copper salt,[62] rhenium-sulfoxide complex,[63] chromate and dichromate compounds,[54, 64] etc. The limitations associated with these reagents are the toxicity, high price of some of them and also the over-oxidation of the disulfide to thiosulfinates and derivatives. A variety of improved procedures have been employed *viz.* Chauhan *et al*. synthesized cobalt(II) phthalocyanine [CoPc] and cobalt(II) tetranitrophthalocyanine [CoTNPc] complexes (**12**, **13**) and used them as catalysts in the oxidation of thiols to disulfides with molecular oxygen. The complexes were used in dissolved form with ionic liquid [bmim][BF_4] at room temperature (**Figure 3B.4**). The catalysts were found highly efficient and delivered excellent yields of the products. The catalyst could effectively be recycled up to 5-6 recycling experiments without much loss in the catalytic activity. Catalyst **13** showed better catalytic activity and offered higher yields than that of **12**.[53]

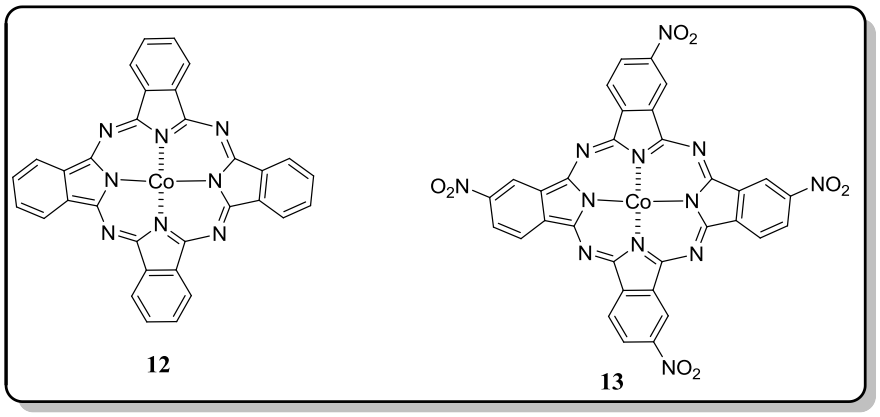


Figure 3B.4 Phthalocyanine based cobalt(II) complexes

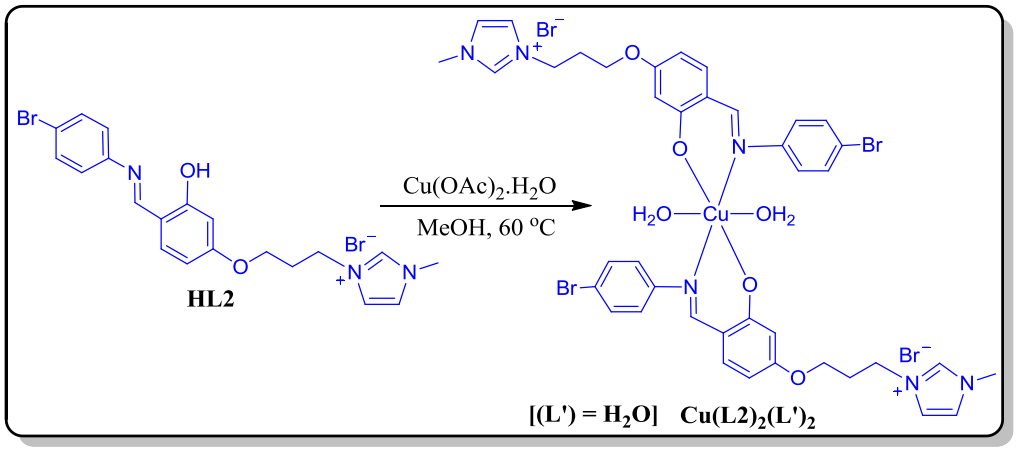
Garcia *et al*. developed an efficient method to synthesize alkyl, aryl and heteroaryl symmetrical disulfides from the corresponding thiols. The reactions were enhanced by ultrasounds, heated at 80 °C with Et_3N in DMF under atmospheric oxygen. Aromatic groups bearing electron donating and electron withdrawing groups, heteroaromatic, and alkyl thiols all were found effectively active and good to excellent yields of the products were achieved.[65]

3B.2 Results and discussion

3B.2.1 Synthesis of $[Cu(L2)_2(L')_2]$

The synthetic procedure of **HL2** is described in chapter 3. **HL2** (500 mg, 2.0 mmol) was stirred with ethanol (20mL) in a 25 mL round bottom flask for 15 minutes. The resulting solution was

treated with copper acetate monohydrate (120 mg, 1.0 mmol) and refluxed for 4 hours till the product precipitated completely. After cooling, the product was separated by simple filtration and recrystallized from the mixture of petroleum ether (2 mL) and methanol (15 mL), **Scheme 3B.3.**



Scheme 3B.3 Synthesis of ionic liquid-tagged copper complex **[Cu(L2)$_2$(L′)$_2$]**

3B.2.2 Characterization of [Cu(L2)$_2$(L′)$_2$]

The compound was isolated as brown colored solid. The complex obtained was aerially stable and soluble in water, ethanol, methanol, ACN, DMF and DMSO. The comparative structural analysis of **HL2** and **[Cu(L2)$_2$(L′)$_2$]** was done using various spectroscopic techniques. The FT-IR spectrum of **HL2** exhibited a peak at 1630 cm^{-1}, attributed to azomethine (ν(C=N)) group, whereas in **[Cu(L2)$_2$(L′)$_2$]** this peak shifted to 1593 cm^{-1}. The shifting of the azomethine peak to lower frequency confirms the complexation and indicated that the azomethine nitrogen is involved in the coordination with copper metal ion.[85] A broad band at 3423 cm^{-1} due to ν(OH) stretching was observed in the spectrum of **HL2** and this band was absent in [**Cu(L2)$_2$(L′)$_2$**], suggesting the involvement of hydroxyl (-OH) group of **HL2** in the coordination to metal ion through deprotonation.[86] The appearance of a peak at 3456 cm^{-1} in the spectrum of [**Cu(L2)$_2$(L′)$_2$**] indicated the presence of water molecules bound to copper metal in the complex. One more band, belonged to ν(C–O) peak at 1161 cm^{-1} appeared in the spectrum of **HL2** and after complexation with the copper metal this peak shifted towards higher frequency[87] and appeared at 1185 cm^{-1} (**Figure 3B.5**).

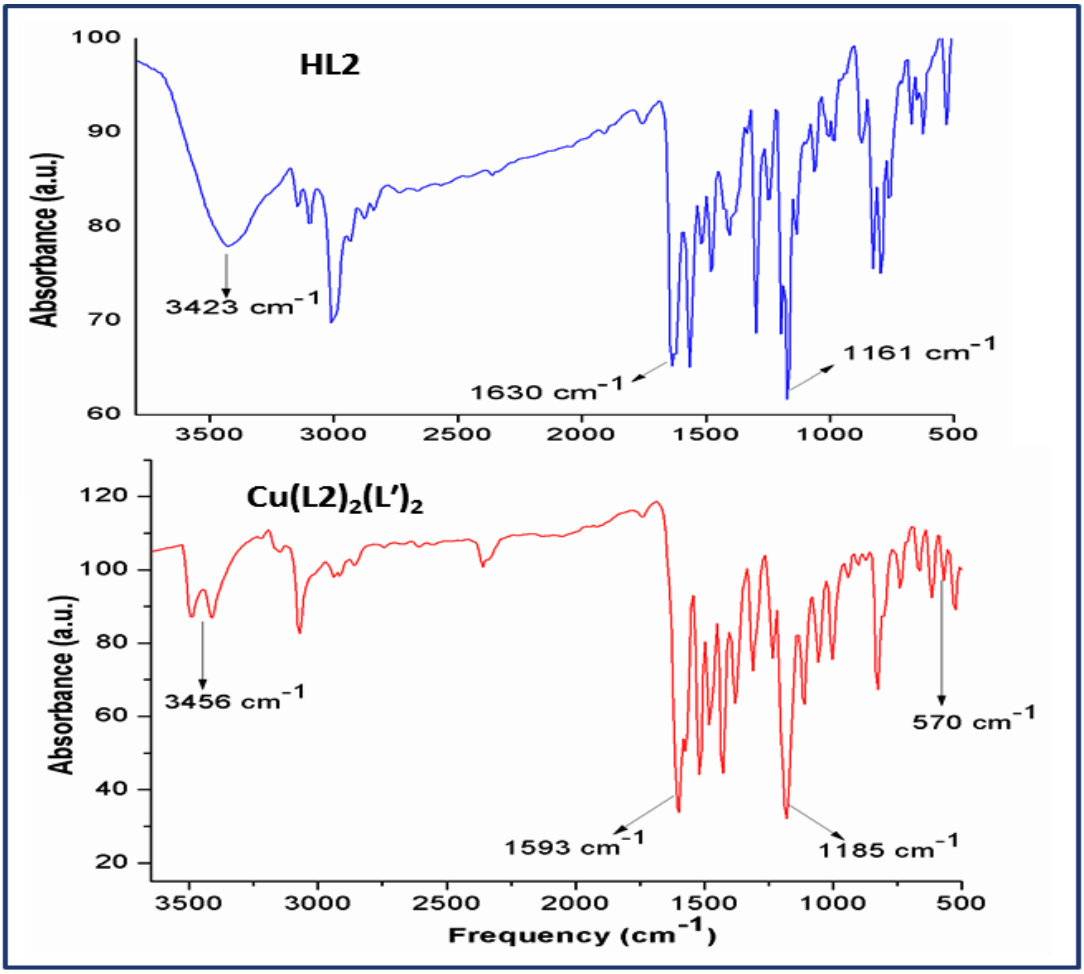


Figure 3B.5 FT-IR spectra of **HL2** and **[Cu(L2)$_2$(L′)$_2$]**

The solution state electronic spectra of **HL2** and the complex **[Cu(L2)$_2$(L′)$_2$]** were recorded in distilled DMSO. The free ligand **HL2** exhibited two absorption bands at 288 nm and 344 nm, which can be attributed to π-π* and n–π* transitions of the ligand. Shift of these bands towards longer wavelengths (297 and 352 nm respectively) suggested the complexation of **HL2** with copper metal. Also, in the solid state electronic spectra, red shift was observed after complexation. In the spectrum of **[Cu(L2)$_2$(L′)$_2$]** a broad low-intensity band was observed in a range of 660-820 nm which could be attributed to the *d-d* transitions ($^2E_g \rightarrow {}^2T_{2g}$) of the copper(II) ion and was the indicative of distorted octahedral geometry of the complex[88-91] (**Figure 3B.6**).

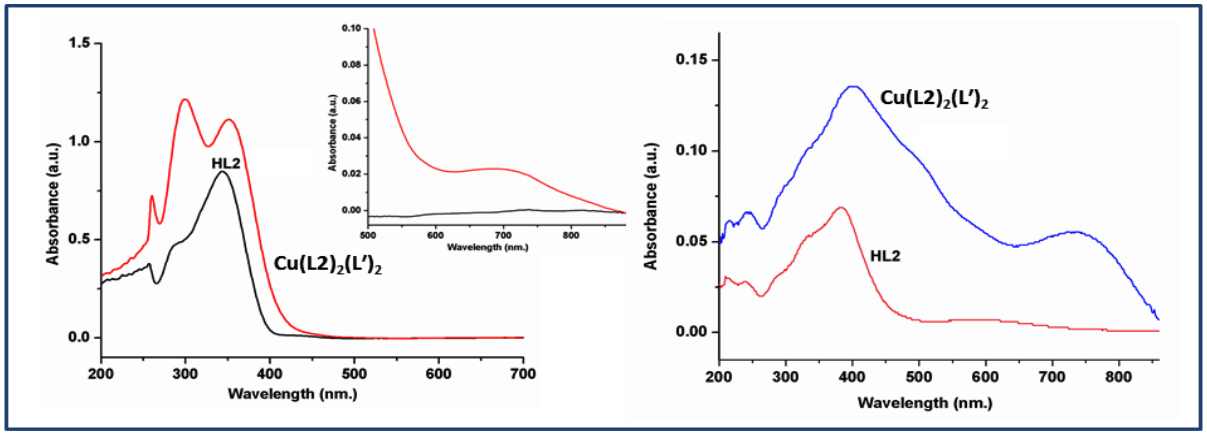


Figure 3B.6 U.V. spectra of **HL2** and **[Cu(L2)$_2$(L′)$_2$]**

In the powder XRD pattern of **HL2**, the appearance of sharp peaks indicated its crystalline nature. On complexation with the metal, the intensity of the peaks in the XRD patterns of **HL2** lessened and line broadening was observed, showing a change in nature from crystalline to amorphous.[92] The occurrence of some new peaks in the spectrum of **[Cu(L2)$_2$(L′)$_2$]**, displayed the presence of copper metal ion in the complex[93] (**Figure 3B.7**).

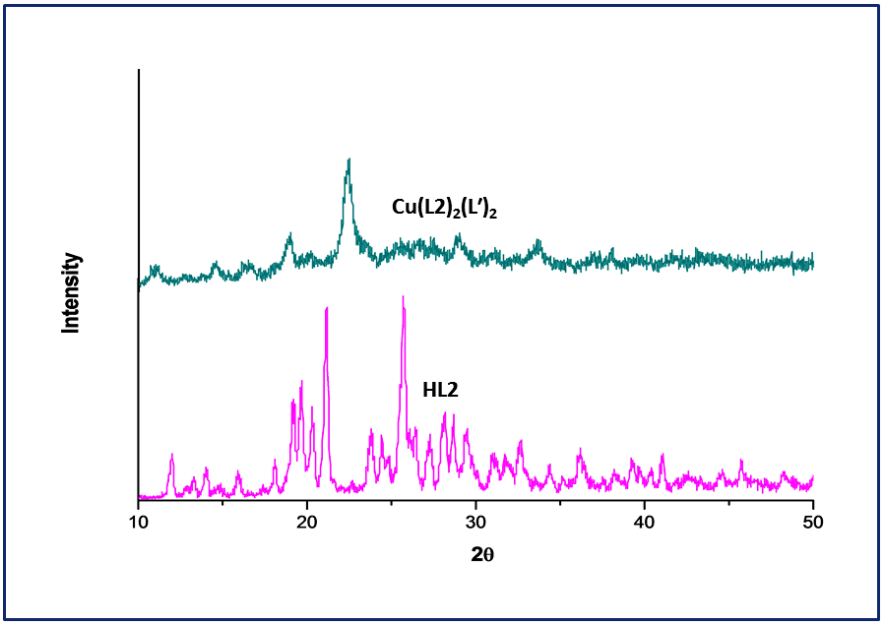


Figure 3B.7 Powdered XRD spectra of **HL2** and **[Cu(L2)$_2$(L′)$_2$]**

The thermal stabilities of **HL2** and **[Cu(L2)$_2$(L′)$_2$]** were determined by DSC and thermo gravimetric analysis (TGA) under nitrogen atmosphere. In the DSC scan of **HL2**, a sharp

endothermic peak corresponding to the melting point was observed at 200 °C. In case of **[Cu(L2)$_2$(L′)$_2$]**, an endothermic peak in the range of 96-110 °C indicated the removal of water molecules from the complex. The peak at 200 °C showed the elimination of organic part (ligand molecules) from the complex. The TGA of **HL2** did not show any specific loss in weight up to 250 °C, signifying its good thermal stability and in the TGA thermogram of **[Cu(L2)$_2$(L′)$_2$]** a weight loss near 100 °C, indicated the breakdown of water molecules from the complex and after this temperature no specific peak was observed till 250 °C, showing the thermal stability of the complex (**Figure 3B.8**).

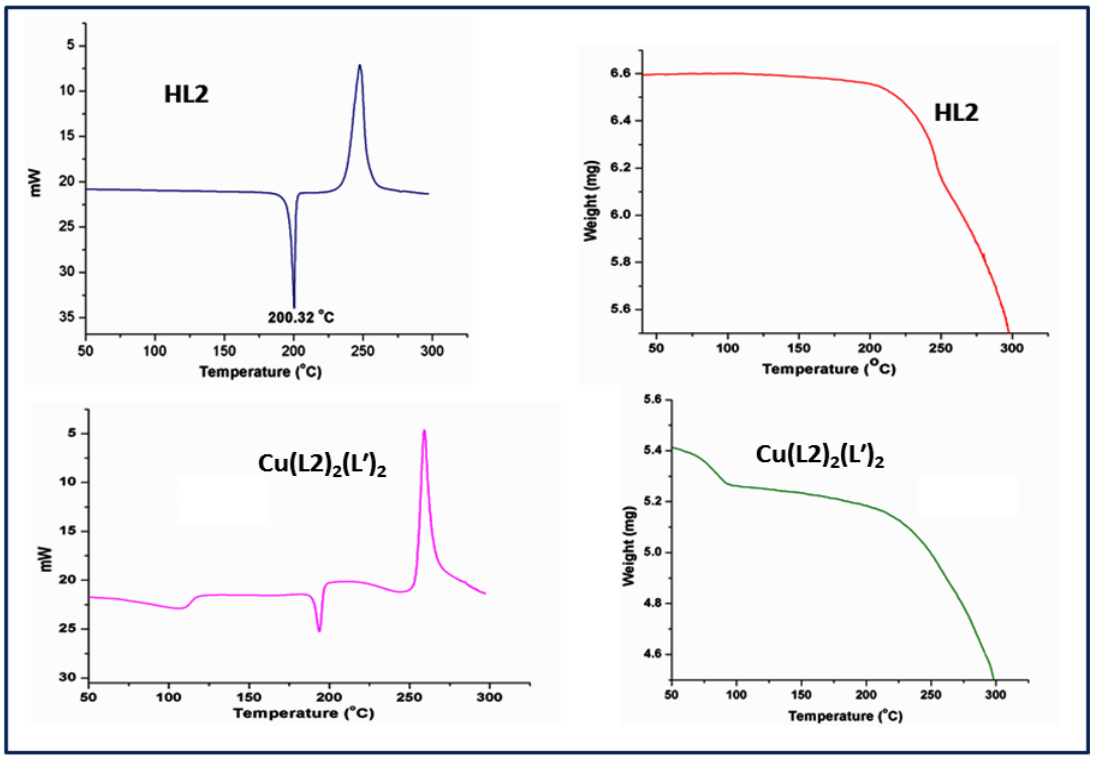


Figure 3B.8 DSC and TGA thermograms of **HL2** and **[Cu(L2)$_2$(L′)$_2$]**

In the HRMS spectrum (**Figure 3B.9**) of the complex a peak at *m/z* 925.2632 was observed and matched with the exact mass of **[Cu(L2)$_2$(L′)$_2$]** and it belongs to $[M - 2Br]^+$ ion. The $[M + 2H - 2Br]^+$ peak was also observed at *m/z* 927.26. The two other peaks at *m/z* 929.26 and 931.22 were also present in the spectrum and indicated the presence of two bromine atoms in the complex. These peaks were present in the 1:2:1 intensity ratio and resemble the $[M + 2 + 2H - 2Br]^+$ and the $[M + 4+ 2H - 2Br]^+$ ions, respectively.

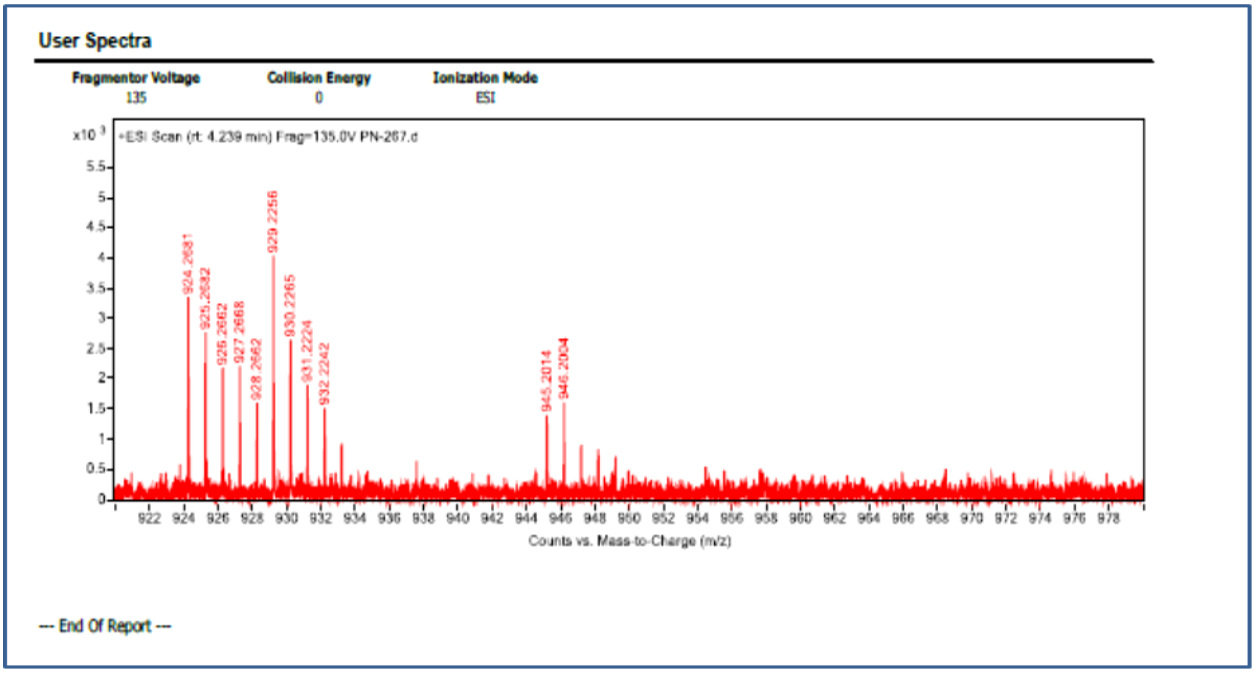


Figure 3B.9 The HRMS- mass spectrum of **$[Cu(L2)_2(L')_2]$**

In the ESI-MS, mass spectrum (**Figure 3B.10**), the peak present at *m/z* 924.16 matched with the exact mass of **$[Cu(L2)_2(L')_2]$** and it belongs to $[M - H - 2Br]^+$ ion.

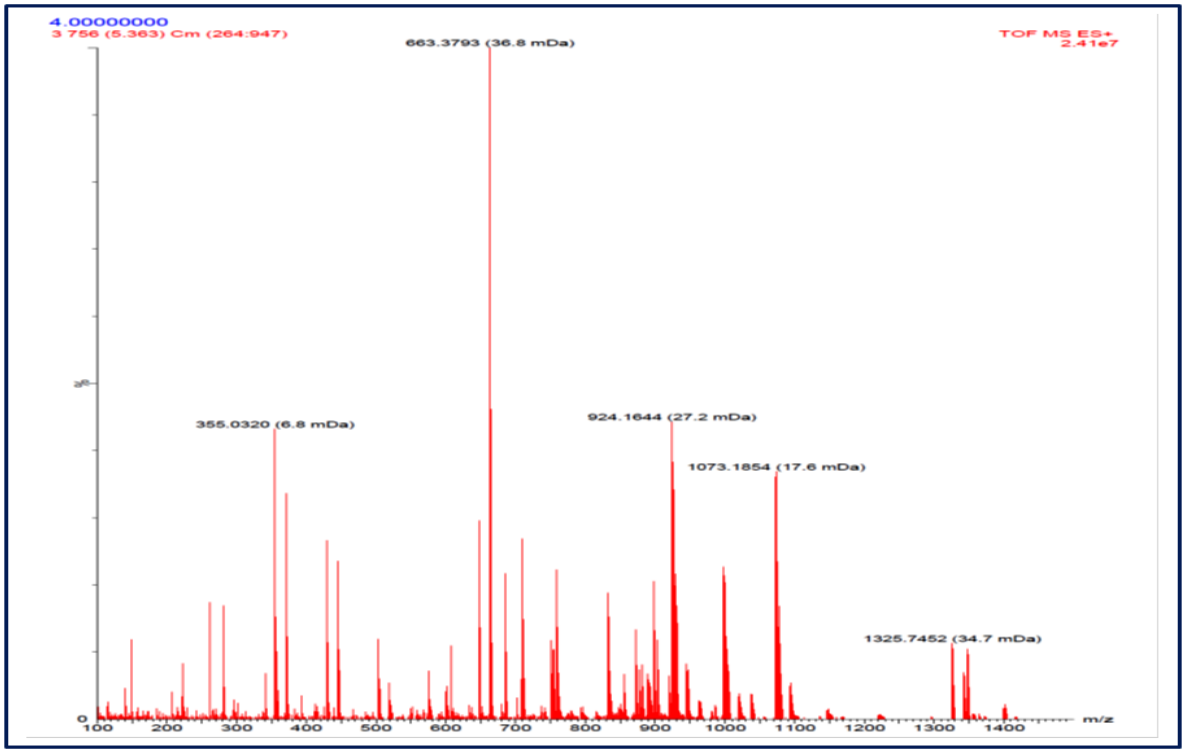


Figure 3B.10 The ESI mass spectrum of **$[Cu(L2)_2(L')_2]$**

EPR of **[Cu(L2)$_2$(L′)$_2$** was recorded in powder form both at liquid nitrogen temperature and at room temperature (**Figure 3B.11)**. In both the states the complex showed four resolved peaks with low field region and the g-parallel ($g_{\|}$) and g-perpendicular ($g_{\perp}$) values were calculated for both the conditions and summarized below.

Liquid nitrogen temperature		**Room temperature**	
$g_{\|}$	$g_{\perp}$	$g_{\|}$	$g_{\perp}$
2.235	2.046	2.172	2.047

On the basis of above mentioned *g* values it can be accredited that the complex bearing the axial co-ordination with the predominant $d_{x^2-y^2}$ ground state. The EPR analysis of the complex also revealed the presence of copper as Cu(II) and the distorted octahedral geometry around the metal centre.

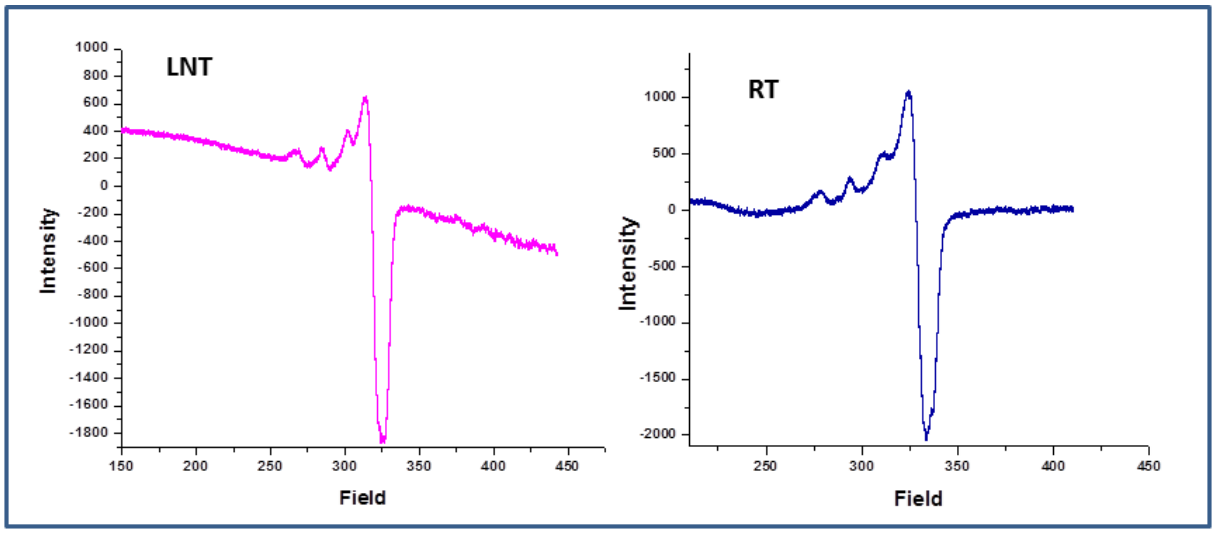


Figure 3B.11 The EPR (X-band) spectra of **[Cu(L2)$_2$(L′)$_2$]**

The cyclic voltamogram of **[Cu(L2)$_2$(L′)$_2$]** (1μM) in acetonitrile (2.2 to -1.3 V potential range), was recorded at room temperature (**Figure 3B.12**), showed a quasi-reversible peak for the redox couple copper(II)→copper(I) at cathodic potential; **Epc** = -0.65 and the cathodic current peak was observed at **Ipa** = -1.88. The two anodic potential peaks at **Epa=0.77, 1.01** with their

corresponding anodic potentials Ipc = **2.03**, **2.61** may be attributed to the oxidation processes of the oganic part of the complex.

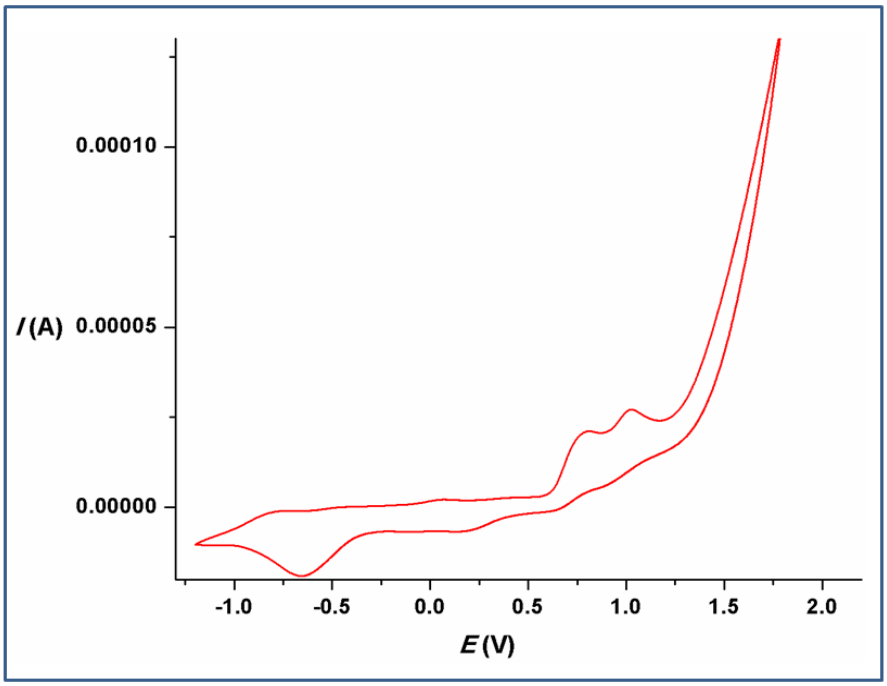


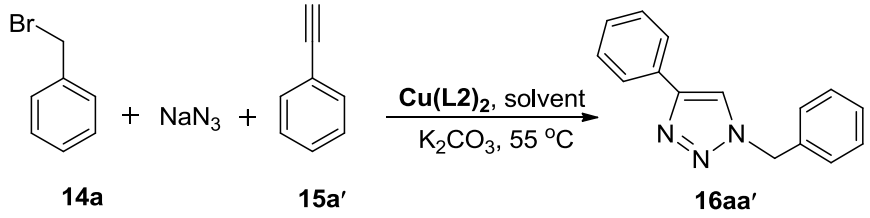
Figure 3B.12 The cyclic voltammogram of **$[Cu(L2)_2(L')_2]$**

3B.2.3 Catalytic activity of $[Cu(L2)_2(L')_2]$

3B.2.3.1 Catalytic activity of $[Cu(L2)_2(L')_2]$ in the synthesis of 1,4- disubstituted 1,2,3- triazoles

The complex **$[Cu(L2)_2(L')_2]$** was used as a catalyst in Huisgen 1,3-dipolar cycloaddition reactions to synthesize 1,4-disubstituted 1,2,3-triazoles in water. The reaction conditions were optimized for the 1,3-dipolar cycloaddition reaction of benzyl bromide, sodium azide and phenylacetylene using different solvents and varied amount of catalyst (Table 3B.1).

Table 3B.1 Optimization of the reaction conditions for the synthesis of 1,4-disubstituted 1,2,3-triazoles catalyzed by **$[Cu(L2)_2(L')_2]$**.[a]



14a 15a′ 16aa′

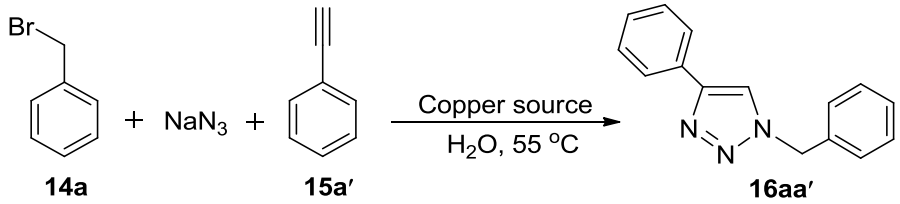
Entry	Solvent	$[Cu(L2)_2(L')_2]$ mol%	Time (h)	Yield[b] (%)
1 .	Ethanol	3	3	85
2.	Water	5	3	95
3.	Water	3	2.5	95
4.	**Water**	**0.5**	**2.5**	**95**
5.	THF	5	5	65
6.	THF	3	3	60
7.	DMSO	3	3	75
8.	ACN	3	3	80
9.	Dioxane	3	3	70
10.	Toluene	3	6	Trace

[a]Reaction conditions: benzyl bromide (1mmol), phenyl acetylene (1mmol), sodium azide (2 mmol), potassium carbonate (2 mmol) and **$[Cu(L2)_2(L')_2]$** (x mol %), solvent (2 mL).

[b]Isolated yield

Further the reaction was also carried out by taking different amounts of copper sources and among them the synthesized complex **$[Cu(L2)_2(L')_2]$** was found the best copper source for the reaction, the results are mentioned in table 3B.2.

Table 3B.2 Optimization of the reaction conditions for the synthesis of 1,4-disubstituted 1,2,3-triazoles catalyzed by **[Cu(L2)$_2$(L′)$_2$]**.[a]

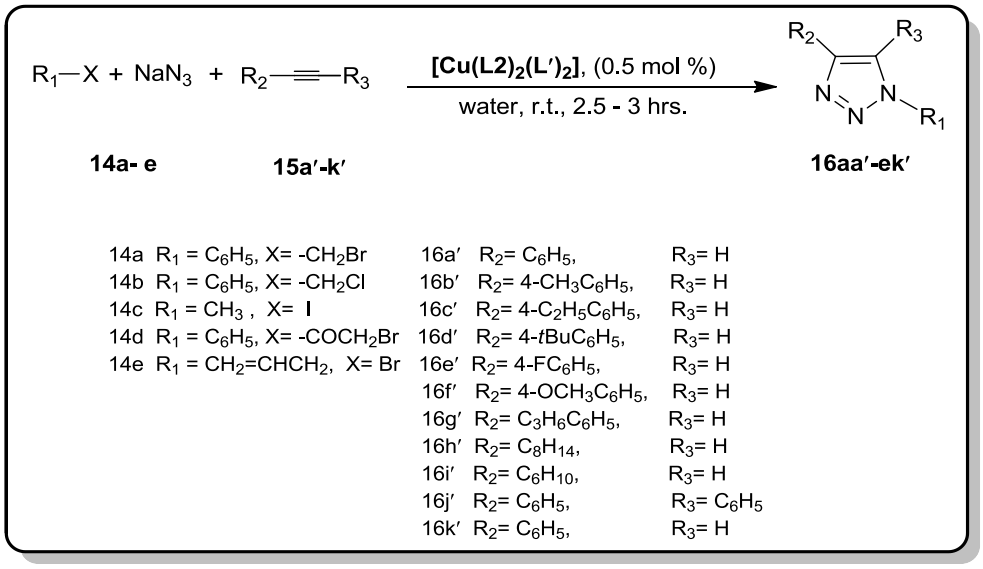


Entry	Copper source	Mol %	Time (h)	Runs	Yield[b] (%)
1	$Cu(OAc)_2.5H_2O$	5	10	0	50%
2	CuI	5	7	2	80%
3	CuBr	5	15	1	70%
4	$CuSO_4.5H_2O$	10	6	1	80%
5.	$CuCl_2$	10	6	1	60%
6.	**[Cu(L2)$_2$(L′)$_2$]**	0.5	3	10	95%

[a]Reaction conditions: benzyl bromide (1mmol), phenyl acetylene (1 mmol), sodium azide (2 mmol), potassium carbonate (2 mmol) and Cu-source (x mol %), water (2 mL). [b]Isolated yield.

Benzyl bromide, phenyl acetylene, sodium azide and potassium carbonate with [**Cu(L2)$_2$(L′)$_2$**] were treated to react and the reaction started quickly (checked by TLC) even after 10 minutes. After 2 hours the reaction could be monitored visually as the product separataed clearly from the aqueous reaction medium (free floated product, Figure 3B.13) and provided quantitative yield of the desired product. Subsequently, we decided to use 0.5 mol% of the catalyst for additional studies. After establishment of the optimized reaction conditions the scope of the catalyst was extended for the cycloaddition reaction of aromatic/aliphatic halides **14a-g**, sodium azide and aromatic/aliphatic acetylenes, **15a′-f′** (**Scheme 3B.4**).

Figure 3B.13



Scheme 3B.4 Multi component cycloaddition reactions between organic halides, sodium azide and alkynes catalyzed by **$[Cu(L2)_2(L')_2]$** in water

A variety of acetylenes were treated with benzyl bromide using ionic liquid-supported copper catalyst in water under ambient conditions and good to excellent yields were achieved. The acetylenes with both electron donating and withdrawing groups provided good yields (Table 3B.3, entries 1–7). Even the aliphatic and internal alkynes were also found highly efficient towards the cycloaddition reaction (Table 3B.3, entries 8, 9 and 10). Less active benzyl chloride also gave good yields of the products. (Table 3B.3, entries 12–14). In case of phenacyl bromide, allyl bromide and methyl iodide good to admirable yields were attained (Table 3B.3, entries 15–23).

Table 3B.3 Synthesis of 1, 4-Disubstituted-1,2,3-Triazoles catalyzed by **$[Cu(L2)_2(L')_2]$** in water under aerobic conditions[a]

Entry	R_1	X	R_2	R_3	Product	Time (hrs.)	Yield[b] (%)
1.	C_6H_5	-CH_2Br	C_6H_5	H	**16aa'**	2.5	95
2.	C_6H_5	-CH_2Br	4-$CH_3C_6H_5$	H	**16ab'**	2.5	90
3.	C_6H_5	-CH_2Br	4-$C_2H_5C_6H_5$	H	**16ac'**	2.5	90

4.	C_6H_5	-CH_2Br	4-*t*BuC_6H_5	H	**16ad'**	2.5	85
5.	C_6H_5	-CH_2Br	4-FC_6H_5	H	**16ae'**	2.5	95
6.	C_6H_5	-CH_2Br	4-O$CH_3C_6H_5$	H	**16af'**	2.5	90
7.	C_6H_5	-CH_2Br	$C_3H_6C_6H_5$	H	**16hg'**	2.5	90
8.	C_6H_5	-CH_2Br	C_8H_{14}	H	**16ah'**	3	80
9.	C_6H_5	-CH_2Br	C_6H_{10}	H	**16ai'**	3	80
10.	C_6H_5	-CH_2Br	C_6H_5	C_6H_5	**16aj'**	6.5	75
11.	C_6H_5	*p*-NO_2-CH_2Br	C_6H_5	H	**16ak'**	2.5	90
12.	C_6H_5	-CH_2Cl	C_6H_5	H	**16ba'**	2.5	88
13.	C_6H_5	-CH_2Cl	4-FC_6H_5	H	**16be'**	2.5	78
14.	C_6H_5	-CH_2Cl	4-O$CH_3C_6H_5$	H	**16bf'**	2.5	76
15.	CH_3	I	C_6H_5	H	**16ca'**	3	90
16.	CH_3	I	4-FC_6H_5	H	**16ce'**	3	90
17.	CH_3	I	4-O$CH_3C_6H_5$	H	**16cf'**	3	90
18.	C_6H_5	-$COCH_2$Br	C_6H_5	H	**16da'**	2.5	85[c]
19.	C_6H_5	-$COCH_2$Br	4-FC_6H_5	H	**16de'**	2.5	90[c]
20.	C_6H_5	-$COCH_2$Br	4-O$CH_3C_6H_5$	H	**16df'**	2.5	85[c]
21.	CH_2=CH-CH_2	Br	C_6H_5	H	**16ea'**	3	90
22.	CH_2=CH-CH_2	Br	4-FC_6H_5	H	**16ee'**	3	90
23.	CH_2=CH-CH_2	Br	4-O$CH_3C_6H_5$	H	**16ef'**	3	90

[a]Reaction conditions: Aromatic/aliphatic halides (1 mmol), acetylenes (1mmol), sodium azide (2 mmol), potassium carbonate (2 mmol) and **[Cu(L2)$_2$(L′)$_2$]** (0.5 mol %), water (2 mL). [b]Isolated yield by simple washing, [c]Isolated yield by column chromatography.

3B.2.3.2 Reusability of $[Cu(L2)_2(L')_2]$ for the synthesis of 1,4-disubstituted 1,2,3-triazoles

The reusability of **$[Cu(L2)_2(L')_2]$** was evaluated for the synthesis of 1,4-disubstituted 1,2,3-triazoles in water, as shown in **Figure 3B.14**, the catalyst could be effectively used for up to ten cycles. Leaching of the catalyst during extraction may be one of the factors responsible for the gradual decrease in the yield of the product during recycling.

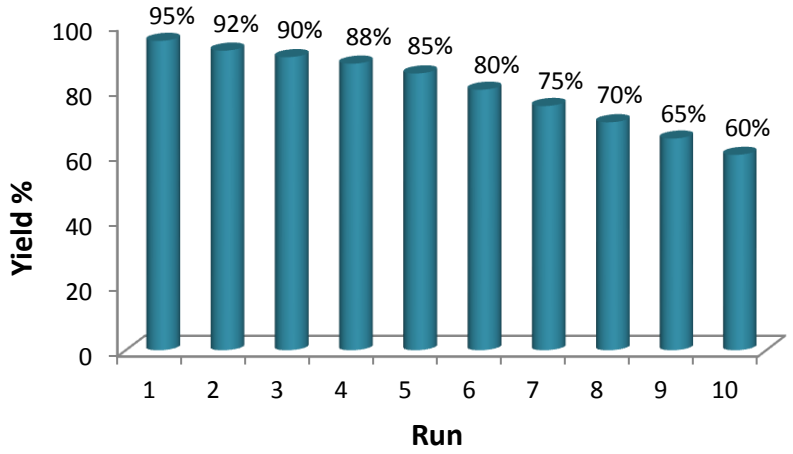


Figure 3B.14 Reusability of **$[Cu(L2)_2(L')_2]$** for the synthesis of 1,4-disubstituted-1,2,3-triazoles

The representative ^{1}H and ^{13}C NMR of **16aa'** is shown in **Figure 3B.15**.

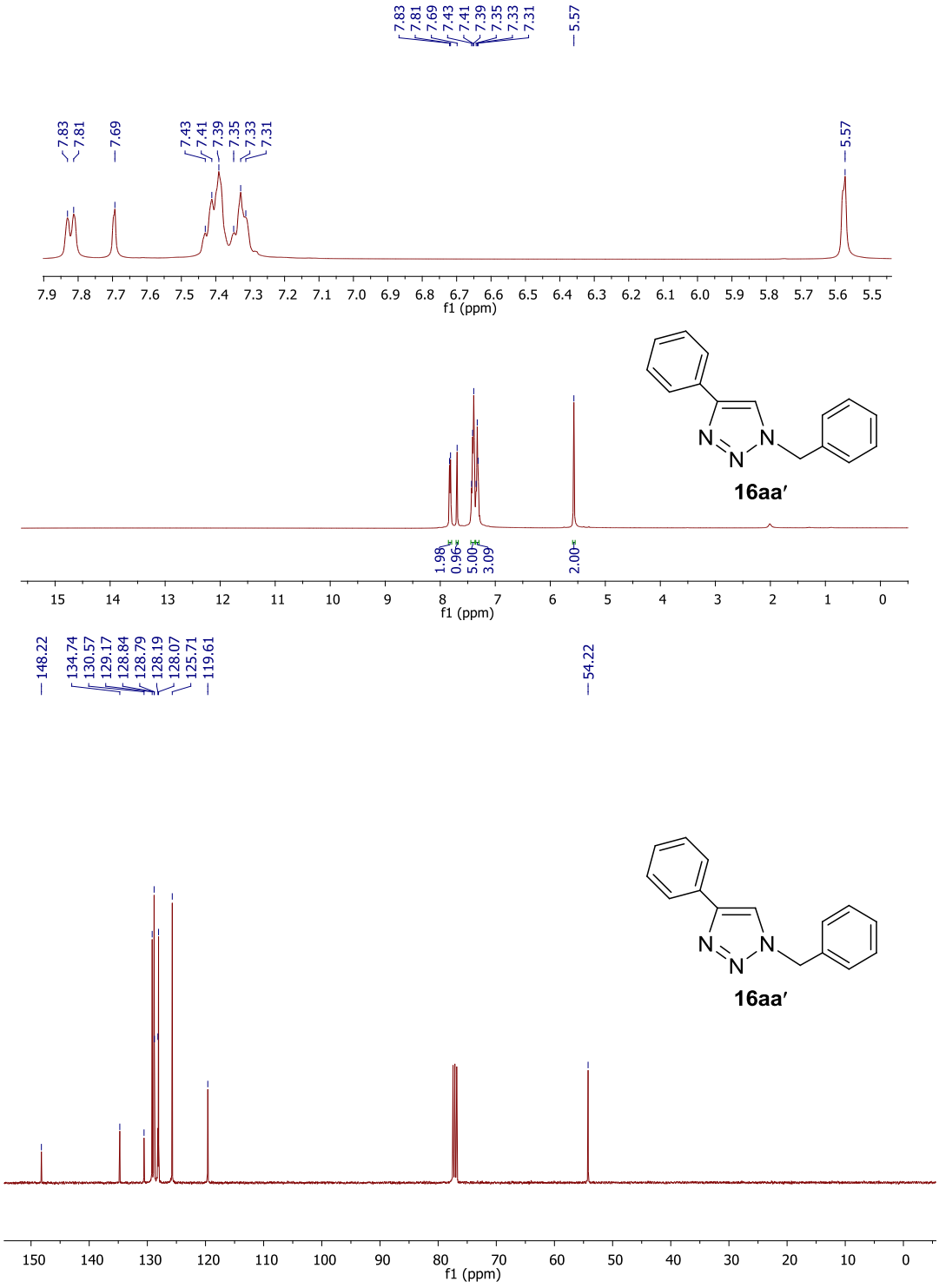
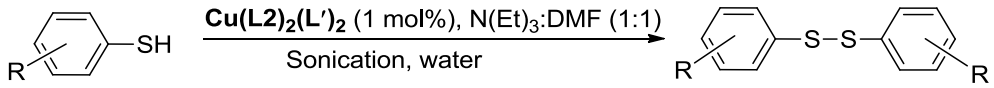


Figure 3B.15 ^{1}H and ^{13}C NMR spectra (in deuterated $CDCl_3$) of 1-benzyl-phenyl-1*H*-1,2,3-triazole (**16aa'**)

3B.2.3.3 Catalytic activity of [Cu(L2)$_2$(L′)$_2$] for the synthesis of aryl disulfides from thiols

The prepared catalyst was also used as a catalyst for the synthesis of diaryl disulfides from thiols. The reaction conditions were optimized using thiophenol (3.5 mmol), triethyl amine (1.2 mmol) and DMF + water (1:1) as solvent under sonication process. The effect of substituents on thiols was also determined and the results are summarized in table 3B.4.

Table 3B.4 Synthesis of diaryl sulfides catalyzed by **[Cu(L2)$_2$(L′)$_2$]** under aerobic conditions.[a]



17 **18 (a-f)**

Entry	R	Time (min.)	18	Yield[b] (%)
1.	H	40	18a	96
2.	*p*-Cl	45	18b	95
3.	*p*-Br	35	18c	95
4.	*p*-CH_3	35	18d	98
5.	*o*-NH_2	40	18e	96
6.	C_4H_7	45	18f	90

[a]Reaction conditions: Thiols (3.5 mmol), triethylamine (1.2 mmol), **[Cu(L2)$_2$(L′)$_2$]** (1 mol %), water and DMF (1:1). [b]Isolated yield

The representative ^{1}H and ^{13}C NMR of **18a** is shown in **Figure 3B.16**.

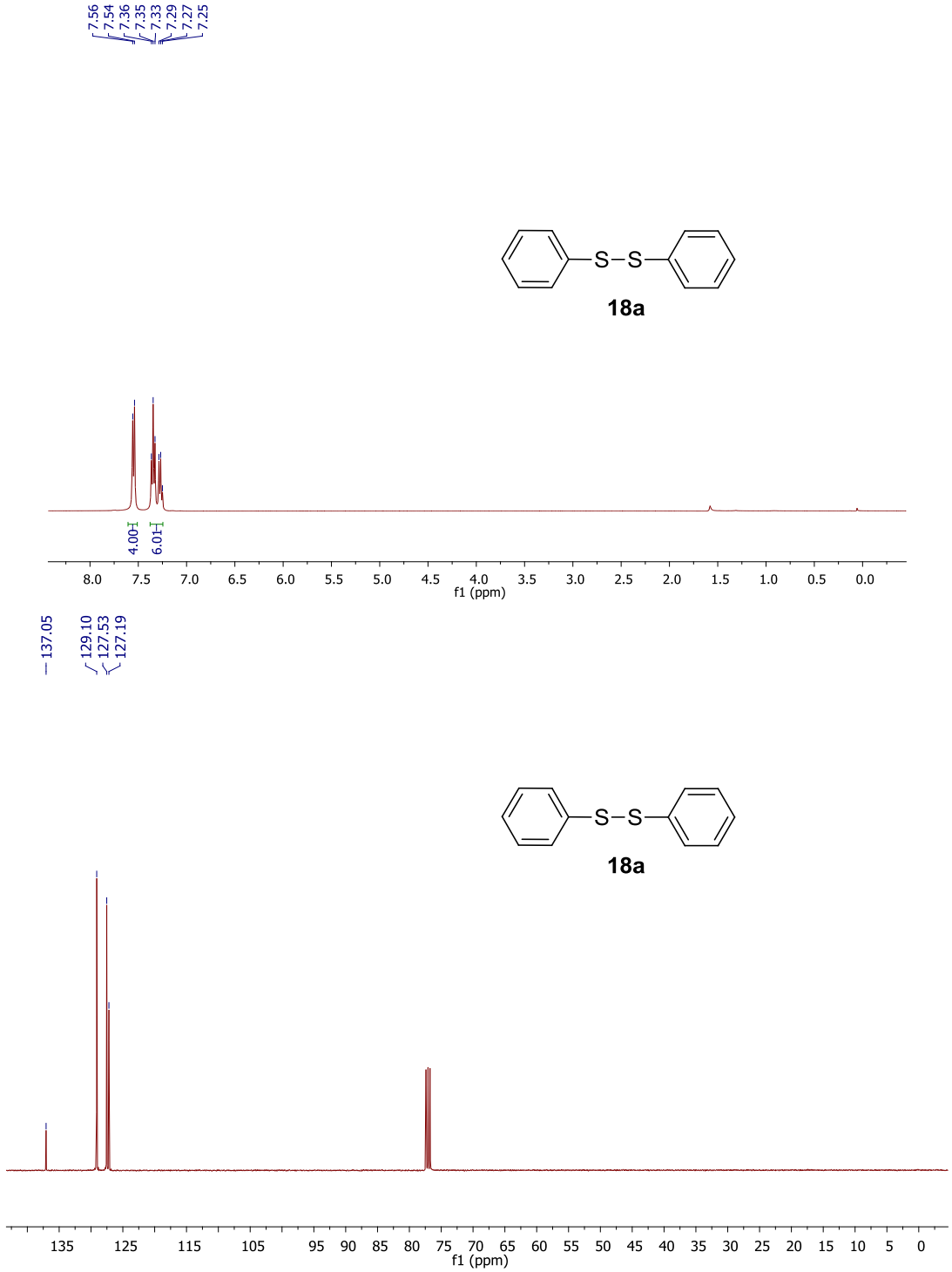


Figure 3B.16 ^{1}H and ^{13}C NMR spectra (in deuterated $CDCl_3$) of 1, 2-diphenyldisulfide **(18a)**

3B.3 Experimental section

3B.3.1 Synthesis of $[Cu(L2)_2(L')_2]$

The ligand **HL2** (500 mg, 2.0 mmol) was stirred with methanol in a 25 mL round bottom flask for 20 minutes, copper acetate monohydrate (199 mg, 1.0 mmol) was added to the resultant solution, and the mixture was refluxed for 4 h until the product precipitated completely. After cooling for 20 minutes the product **$[Cu(L2)_2(L')_2]$** was separated by simple filtration and recrystallized from a mixture of petroleum ether (5 mL) and methanol (20 mL).

3B.3.2 General procedure for the synthesis of 16aa' catalyzed by $[Cu(L2)_2(L')_2]$ in water

1 mmol of benzyl bromide, 1.0 mmol of alkyne, 2 mmol of potassium carbonate, 2 mmol of sodium azide and 0.5 mol% of the ionic liquid-tagged copper catalyst, **$[Cu(L2)_2(L')_2]$** were placed in a 25 ml round bottom flask. To this 10 mL of distilled water and a stirring bead were added. The reaction flask was kept on a magnetic stirrer and the reaction mixture was stirred for 2.5–3h at 55 °C. After the completion of the reaction, the product was separated using ethyl acetate extraction in almost all cases. All the products, except phenacyl bromide were purified by simple washing with hexane. These compounds were purified by column chromatography over silica gel (mesh 100−200) using *n*-hexane/ethyl acetate as an eluent. All the synthesized products with were the isolated products were analyzed by ^{1}H and ^{13}C NMR spectroscopy. The NMR spectra for some of the products are given in (**Appendix-A, Figure A09-A14**)**.** The recovered catalyst was dried and reused at least for ten times without losing its catalytic activity.

3B.3.3 Reusability and recovery of the catalyst

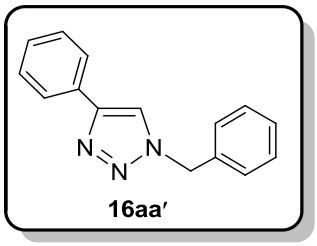
We optimized the reprocess of the reaction by taking benzyl bromide (1 mmol), phenyl acetylene (1 mmol), sodium azide (2 mmol), potassium carbonate (2 mmol) and **$[Cu(L2)_2(L')_2]$** (0.5 mol%) as catalyst. After the completion of the reaction we isolated the free floating product with ethyl acetate. In the remaining reaction mass (the water layer) when no starting material was left, since it was checked by TLC, the same amount of all starting materials viz. phenyl acetylene, benzyl bromide and sodium azide were added and TLC was checked after 2 hours and it was found that the reaction arose properly. Similar conditions were applied for the next cycle.

3B.3.4 General procedure for the synthesis of 18a catalyzed by $[Cu(L2)_2(L')_2]$

Thiophenol (3.5 mmol), 1.2 mmol of triethylamine and 1 mol% of **$[Cu(L2)_2(L')_2]$** were placed in a 25 ml round bottom flask. To this 10 mL of distilled water and DMF (1:1) were added. The reaction flask was kept on a sonicator, initially for 10 minutes and the progress of the reaction was checked by TLC. After 10 minutes the reaction mixture was further kept on sonication to complete the reaction at room temperature. After the completion of the reaction, the product was purified by column chromatography over silica gel (mesh 100−200) using *n*-hexane/ethyl acetate as an eluent. The synthesized products were analyzed by NMR spectra.

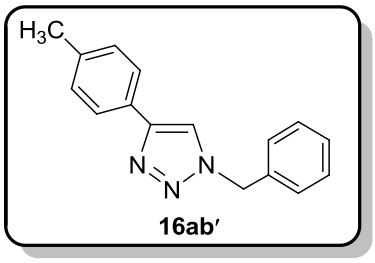
3B.3.5 Spectroscopic data of the synthesized 1,4-disubstituted 1,2,3-triazoles and disulfides

1-benzyl-phenyl-1*H*-1,2,3-triazole (16aa')



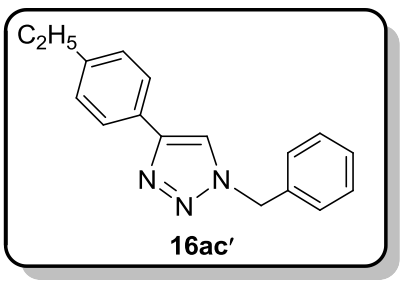
Yield 98%; white crystalline solid; mp 124 –126 ^{0}C (Lit. mp 126 – 128 °C);[94] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, *J* = 7.2 Hz, 2H), 7.69 (s, 1H), 7.46 – 7.37 (m, 5H), 7.33 (t, *J* = 7.1 Hz, 3H), 5.57 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 148.2, 134.7, 130.6, 129.2, 128.8, 128.7, 128.2, 128.0 125.7, 119.6, 54.2.

1-benzyl-4-*p*-tolyl-phenyl-1*H*-1,2,3-triazole (16ab')



Yield 96%; white crystalline solid; mp 152 –154 ^{0}C (Lit. mp 151 – 153 °C);[95] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 8.1 Hz, 2H), 7.65 (s, 1H), 7.43 – 7.30 (m, 5H), 7.23 (d, *J* = 7.9 Hz, 2H), 5.57 (s, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 138.0, 134.8, 129.5, 129.1, 128.7, 128.1, 127.7, 125.6, 119.2, 54.2, 21.2.

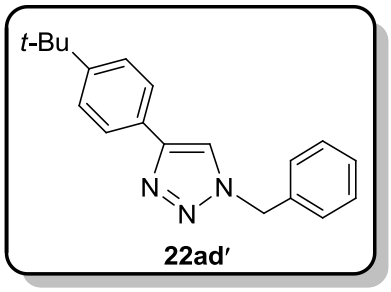
1-benzyl-4-(4-ethylphenyl)-1*H*-1,2,3-triazole (16ac')



Yield 96%; white crystalline solid; mp 143–145 ^{0}C (Lit. mp 147 – 148 °C);[96] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.65 (s, 1H), 7.40 (t, *J* = 6.6 Hz, 3H), 7.32 (dd, *J* = 7.4, 1.9 Hz, 2H), 7.26 (d, *J* = 8.2 Hz, 2H), 5.59 (s, 2H), 2.68 (q,

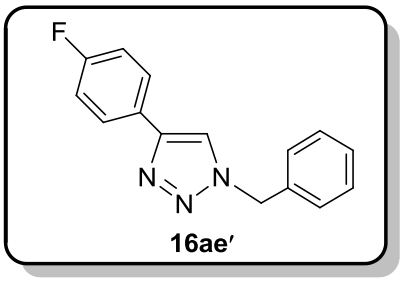
J = 7.6 Hz, 2H), 1.26 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.3, 144.4, 134.8, 129.2, 128.8, 128.3, 128.0, 127.9, 125.7, 119.2, 54.2, 28.8, 15.5.

1-benzyl-4-(4-tert-butylphenyl)-1*H*-1,2,3-triazole (16ad')



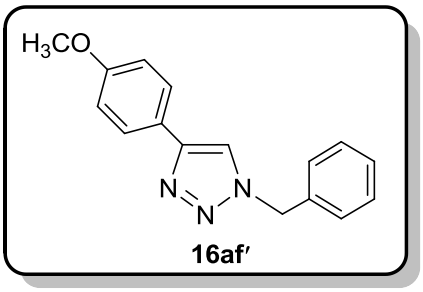
Yield 96%; white crystalline solid; mp 105–109 ^{0}C (Lit. mp 112 – 113 °C);[96] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.4 Hz, 2H), 7.68 (s, 1H), 7.42 (dd, *J* = 23.8, 7.7 Hz, 5H), 7.34 – 7.29 (m, 2H), 5.57 (s, 2H), 1.36 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 151.3, 148.2, 134.9, 129.1, 128.7, 128.0, 127.8, 125.8, 125.5, 119.4, 54.2, 34.7, 31.3.

1-benzyl-4-(4-flourophenyl)-1*H*-1,2,3-triazole (16ae')



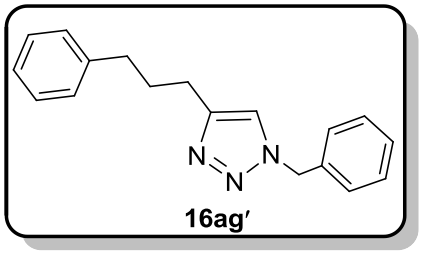
Yield 90%; white solid; mp 109–115 ^{0}C (Lit. mp 113 – 115 °C);[25] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 8.2, 5.4 Hz, 2H), 7.68 (s, 1H), 7.36 (dt, *J* = 7.5, 5.9 Hz, 5H), 7.10 (t, *J* = 8.5 Hz, 2H), 5.58 (s, 2H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 161.4, 134.6, 129.2, 128.8, 128.1, 127.5, 127.4, 126.8, 119.5, 115.9, 115.7, 54.

1-benzyl-4-(4-methoxyphenyl)-1H-1,2,3-triazole (16af'):



Yield 90%; white solid; mp 111–115 ^{0}C (Lit. mp 116–118 °C) ;[94] ^{1}H NMR (400 MHz, DMSO-d_6): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.72 (d, *J* = 8.7 Hz, 2H), 7.37 – 7.25 (m, 5H), 6.95 (d, *J* = 8.8 Hz, 2H), 5.57 (s, 2H), 3.72 (s, 3H). ^{13}C NMR (100 MHz, DMSO- d_6) δ 160.0, 147.4, 136.9, 129.6, 128.9, 128.7, 127.3, 124.1, 121.4, 115.2, 55.9, 53.8.

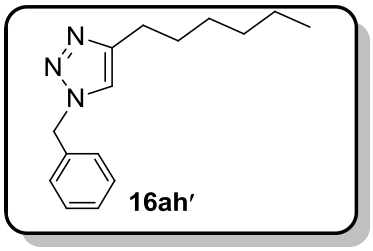
1-benzyl-4-(3-phenylpropyl)-1*H*-1,2,3-triazole (16ag')



Yield 90%; white solid; mp 62–63 ^{0}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.35 (m, 3H), 7.29 (d, *J* = 14.8 Hz, 4H), 7.23

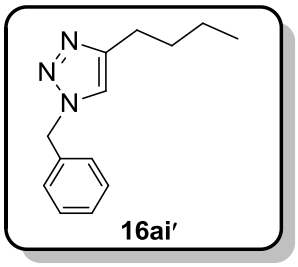
– 7.16 (m, 4H), 5.51 (s, 2H), 2.80 – 2.72 (m, 2H), 2.69 (t, *J* = 7.7 Hz, 2H), 2.06 – 1.95 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.5, 141.9, 135.0, 129.1, 128.8, 128.0, 125.9, 120.7, 54.0, 35.4, 31.1, 25.3.

1-benzyl-4-hexyl-1*H*-1,2,3-triazole (16ah')



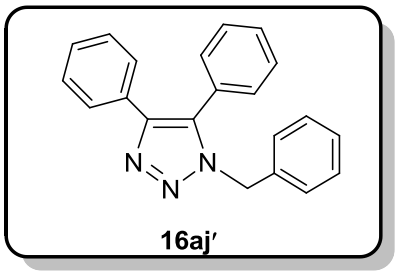
Yield 90%; white solid; mp 44–46 ^{0}C (Lit. mp 47–48 °C)[97]; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.41–7.25 (m, 6H), 5.5 (s, 2H), 2.69 (t, *J* = 7.9 Hz, 2H), 1.67–1.64 (m, 2H), 1.36–1.29 (m, 6H), 0.87 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.0, 135.0, 129.0, 128.6, 128.0, 120.6, 54.1, 31.5, 29.3, 28.9, 25.7, 22.6, 14.1.

1-benzyl-4-butyl-1*H*-1,2,3-triazole (16ai')



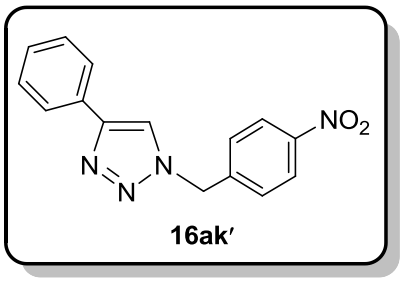
Yield 90%; white solid; mp 44–46 ^{0}C (Lit. mp 47–48 °C);[25] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 22.7, 6.2 Hz, 1H), 7.26 (d, *J* = 7.7 Hz, 1H), 7.20 (s, 1H), 5.50 (s, 1H), 2.74 – 2.63 (m, 1H), 1.63 (dt, *J* = 15.4, 7.5 Hz, 1H), 1.44 – 1.30 (m, 1H), 0.92 (t, *J* = 7.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.9, 135.0, 129.0, 128.6, 127.9, 120.5, 53.9, 31.5, 25.4, 22.3, 13.8.

1-benzyl-4,5-diphenyl-1*H*-1,2,3-triazole (16aj')



Yield 90%; white solid; mp 109–111 ^{0}C (Lit. mp 107–108 °C);[98] ^{1}H NMR (400 MHz, DMSO): δ 7.55 – 7.47 (m, 5H), 7.32 – 7.26 (m, 8H), 7.00 – 6.98 (m, 2H), 5.48 (s, 2H); ^{13}C NMR (100 MHz, DMSO): δ 143.9, 136.1, 134.4, 131.3, 130.4, 130.3, 129.7, 129.1, 129.0, 128.3, 128.2, 127.7, 127.6, 126.7, 51.7.

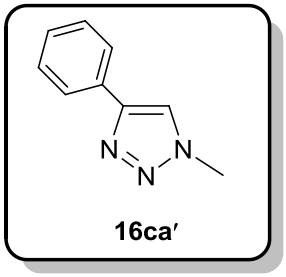
1-(4-nitrobenzyl)-4-phenyl-1*H*-1,2,3-triazole (16ak')



Yield 85%; white solid; mp 157–159 ^{0}C (Lit. mp 156–157 °C);[99] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.6 Hz, 2H), 7.84 – 7.79 (m, 3H), 7.40 (ddd, *J* = 30.0, 11.7, 5.4 Hz, 5H),

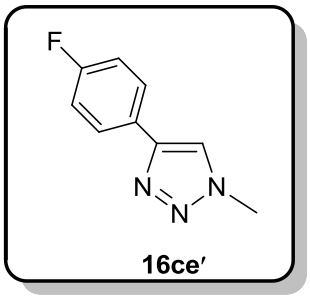
5.71 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.6, 148.0, 141.8, 130.1, 128.9, 128.6, 128.5, 125.7, 124.3, 119.8, 53.2.

1-methyl-4-phenyl)-1*H*-1,2,3-triazole (16ca')



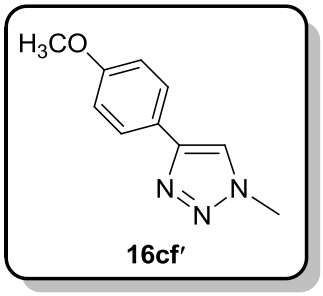
Yield 90%; white solid; mp 116–121 ^{0}C (Lit. mp 122 °C);[100] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.1 Hz, 2H), 7.76 (s, 1H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.35 (t, *J* = 6.8 Hz, 1H), 4.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 130.6, 128.8, 128.2, 125.7, 120.6, 36.8.

4-(4-fluorophenyl)-1-methyl-*H*-1,2,3-triazole (16ce')



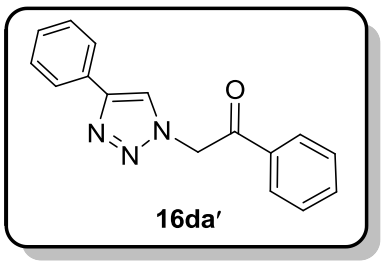
Yield 90%; white solid; mp 136–138 ^{0}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.79 (m, 2H), 7.73 (s, 1H), 7.16 – 7.11 (m, 2H), 4.17 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 161.4, 147.2, 127.4 (d, *J* = 8.1 Hz), 126.8 (d, *J* = 3.3 Hz), 120.3, 115.9, 115.7, 36.8.

4-(4-methoxyphenyl)-1-methyl-*H*-1,2,3-triazole (16cf')



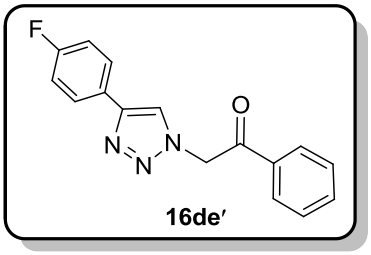
Yield 85%; white solid; 142–145 ^{0}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.71 (m, 2H), 7.65 (s, 1H), 6.98 – 6.90 (m, 2H), 4.09 (s, 3H), 3.83 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 147.8, 127.0, 123.3, 119.9, 114.2, 55.3, 36.7.

1-phenyl-2(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethanone (16da')



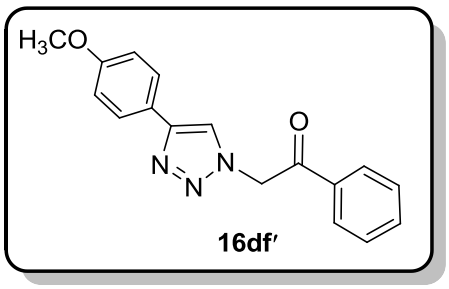
Yield 85%; white solid; mp 160–165 ^{0}C (Lit. mp 166–169 °C);[101] ^{1}H NMR (400 MHz, DMSO) δ 8.54 (s, 1H), 8.11 (d, *J* = 7.4 Hz, 2H), 7.89 (d, *J* = 7.3 Hz, 2H), 7.76 (t, *J* = 7.4 Hz, 1H), 7.64 (t, *J* = 7.7 Hz, 2H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 1H), 6.28 (s, 2H). ^{13}C NMR (100 MHz, DMSO) δ 192.7, 146.8, 134.8, 134.6, 131.2, 129.5, 128.7, 128.3, 125.6, 123.5, 56.5.

2-(4-(4-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)-1-phenylethanone (16de')



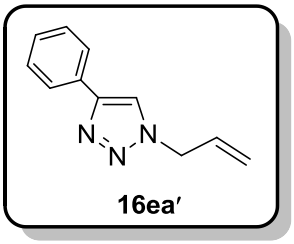
Yield 90%; white solid; mp 176–182 ^{0}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.10 (d, *J* = 7.4 Hz, 2H), 7.92 (dd, *J* = 8.6, 5.6 Hz, 2H), 7.75 (t, *J* = 7.4 Hz, 1H), 7.63 (t, *J* = 7.7 Hz, 2H), 7.31 (t, *J* = 8.9 Hz, 2H), 6.27 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.62 – 197.42 (m), 150.7, 139.5 (d, *J* = 2.6 Hz), 139.3, 134.2, 133.5, 132.73 – 132.20 (m), 128.20 (d, *J* = 7.6 Hz), 121.2, 121.0.

2-(4-(4-methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)-1-phenylethanone (16df')



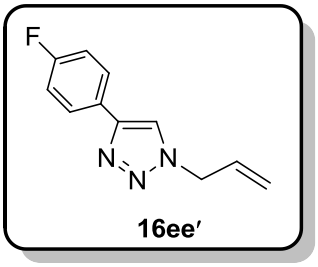
Yield 85%; white solid; mp 108–111 ^{0}C (Lit. mp 106–109 °C);[102] ^{1}H NMR (400 MHz, DMSO) δ 8.45 (s, 1H), 8.13 (d, *J* = 7.9 Hz, 2H), 7.83 (s, 2H), 7.66 (t, *J* = 7.6 Hz, 3H), 7.07 (d, *J* = 8.5 Hz, 2H), 6.27 (s, 2H), 3.83 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 192.7, 159.5, 146.7, 134.7, 134.6, 129.5, 128.7, 126.9, 123.8, 122.6, 114.8, 56.4, 55.6.

1-allyl-4-phenyl-1*H*-1,2,3-triazole (16ea')



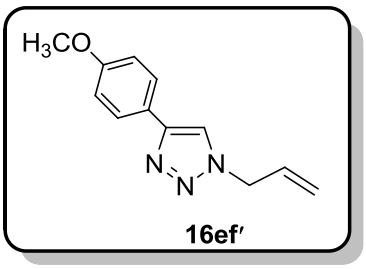
Yield 90%; white solid; mp 58–61 ^{0}C (Lit. mp 57–58 °C);[103] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 5.2, 3.2 Hz, 2H), 7.78 (s, 1H), 7.43 (dd, *J* = 10.3, 4.7 Hz, 2H), 7.37 – 7.30 (m, 1H), 6.06 (ddt, *J* = 16.4, 10.2, 6.1 Hz, 1H), 5.42 – 5.28 (m, 2H), 5.01 (dt, *J* = 6.1, 1.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.0, 131.3, 130.6, 128.8, 128.2, 125.7, 120.2, 119.5, 52.8.

1-allyl-4-(4-fluorophenyl)-1*H*-1,2,3-triazole (16ee')



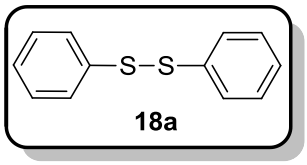
Yield 90%; white solid; mp 64–68 ^{0}C; ^{1}H NMR (400 MHz, DMSO) δ 8.56 (s, 1H), 7.95 – 7.87 (m, 2H), 7.29 (t, *J* = 8.9 Hz, 2H), 6.19 – 6.00 (m, 1H), 5.28 (ddd, *J* = 18.4, 13.7, 1.2 Hz, 2H), 5.07 (d, J = 5.9 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 161.4, 147.5, 131.3, 127.5 (d, *J* = 8.1 Hz), 126.8 (d, *J* = 3.2 Hz), 120.3, 119.2, 115.9, 115.7, 52.8.

1-allyl-4-(4-methoxyphenyl)-1*H*-1,2,3-triazole (16ef')



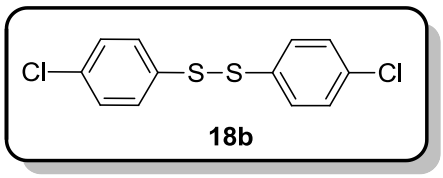
Yield 90%; white solid; mp 90–92 ^{0}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.74 (m, 2H), 7.69 (s, 1H), 6.98 – 6.94 (m, 2H), 6.05 (ddt, *J* = 16.4, 10.2, 6.1 Hz, 1H), 5.34 (ddd, *J* = 6.3, 3.8, 1.2 Hz, 2H), 5.00 (dt, *J* = 6.1, 1.4 Hz, 2H), 3.84 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 147.9, 131.4, 127.0, 123.3, 120.1, 118.7, 114.2, 55.3, 52.7.

1, 2-diphenyldisulfide (18a)



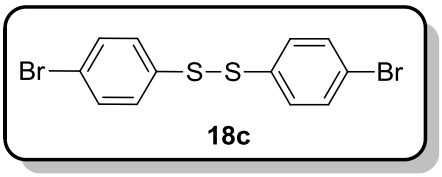
Yield 96%; white solid; mp 59–60 ^{0}C (Lit. mp 59–60 °C);[53] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.4 Hz, 4H), 7.31 (dt, *J* = 30.9, 7.3 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.1, 129.1, 127.5, 127.2.

1, 2-bis(4-chlorophenyl)disulfane (18b)



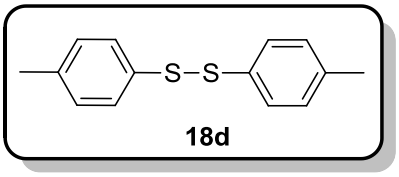
Yield 98%; white solid; mp 55–58 ^{0}C (Lit. mp 56–57 °C);[104] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.36 (m, 4H), 7.33 – 7.27 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.1, 133.6, 129.3 (d, *J* = 1.0 Hz).

1, 2-bis(4-bromophenyl)disulfane (18c)



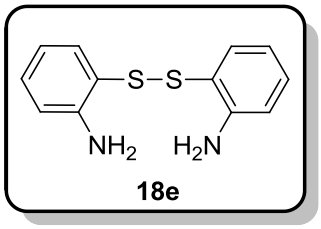
Yield 95%; white solid; mp 93–95 ^{0}C (Lit. mp 95–96 °C);[104] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.36 (m, 4H), 7.33 – 7.27 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.1, 134.6, 130.32 (d, *J* = 1.0 Hz).

1, 2-di-*p*-tolyldisulfane (18d)



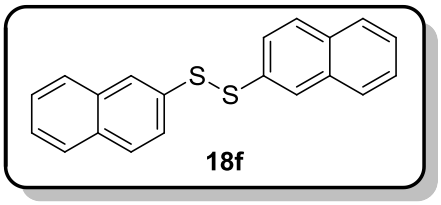
Yield 98%; white solid; mp 46–49 ^{0}C (Lit. mp 47– 49 °C);[65] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.2 Hz, 4H), 7.25 (d, *J* = 8.0 Hz, 4H), 2.47 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.4, 133.8, 129.7, 21.0

2,2-bissulfanediyldianiline (18e)



Yield 95%; white solid; mp 92–94 ^{0}C (Lit. mp 95–96 °C);[65] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (ddt, *J* = 7.4, 3.1, 1.6 Hz, 4H), 6.77 – 6.70 (m, 2H), 6.62 (td, *J* = 7.6, 1.3 Hz, 2H), 4.36 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.6, 136.8, 131.6, 118.7, 118.3, 115.3.

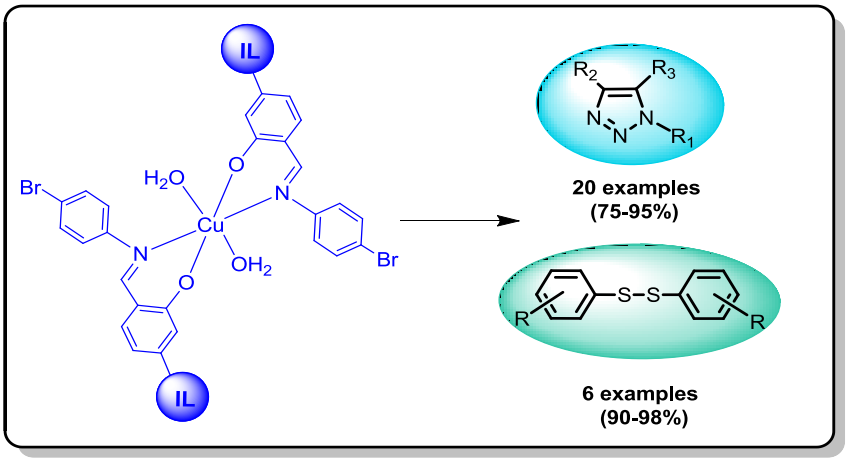
1,2-di(naphthalene-2-yl)disulfane (18f)



Yield 90%; white solid; mp 133–135 ^{0}C (Lit. mp 128–132 °C);[65] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 2H), 7.84 – 7.75 (m, 6H), 7.66 (dd, *J* = 8.7, 1.8 Hz, 2H), 7.52 – 7.45 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.3, 133.5, 132.5, 129.0, 127.8, 127.5, 126.8, 126.6, 126.3, 125.7.

3B.4 Conclusion

In conclusion, an imidazolium ionic liquid-tagged copper(II) complex was synthesized and methodically characterized. The complex was used as a catalyst in the synthesis of 1,4-disubstituted 1,2,3-triazoles in water. The complex was found highly efficient catalyst as excellent yields of the products were achieved and the complex was initiated also active towards the less active internal alkynes. The same complex showed good catalytic activity towards the synthesis of diaryl sulfides from thiols.



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SECTION 3C

Synthesis, Characterization and Catalytic Applications of Ionic Liquid-tagged Schiff Base Zinc Complex

3C.1 Introduction

Zinc metal ion forms complexes with Schiff base ligands having π-conjugated system in various coordination numbers and suitable geometries leading to alteration in properties.[1, 2] Schiff base zinc metal complexes are widely studied for their optical properties,[3, 4] and catalytic activities.[5, 6] The photoluminescence efficiency of a Schiff base luminescent ligand enhances on coordination with zinc and can be controlled by tuning the steric and/or electronic properties of the ligand. The photoluminescence behavior of dinuclear zinc(II) complexes of tetraiminodiphenol macrocycles (**1**) with the composition $[Zn_2L^1](ClO_4)_2$, $[Zn_2L^2(H_2O)_2](ClO_4)_2$, $[Zn_2L^2(\mu\text{-}O_2CR)](ClO_4)$ (R= CH_3, C_6H_5, *p*-$CH_3C_6H_4$, *p*-$OCH_3C_6H_4$, *p*-ClC_6H_4, *p*-$NO_2C_6H_4$), and $[Zn_2L_3(\mu\text{-}OAc)](ClO_4)$ were studied for photoluminescent properties (**Figure 3C.1**). Zinc-induced fluorescence enhancement of the macrocyclic ligand which could be considered as a photoinduced charge-transfer fluorophore was observed.[7] Qian group developed naked-eye and ratiometric fluorescent zinc sensor (**2)** of carboxamidoquinoline with an alkoxyethylamino chain as receptor (**Figure 3C.1**). It showed good water solubility and high selectivity for sensing and also signal the presence of Zn^{2+}. Increase in fluorescence quantum yield and a 75 nm red-shift of fluorescence emission upon binding Zn^{2+} in buffer aqueous solution was observed.[8] Majumder *et al*. synthesized dinuclear zinc(II) complexes of tetra imino diphenol macrocyclic ligand (**3**) having composition $[Zn_2L(H_2O)_2]\text{-}(ClO_4)_2\cdot 2CH_3CN$, $[Zn_2L(H_2O)_2](ClO_4)_2\cdot 2dmf$, $[Zn_2L(H_2O)_2](NO_3)_2\cdot 2dmf$, $[Zn_2LCl_2]$, $[Zn_2L(N_3)_2]$, $[Zn_2L(NCS)_2]$, $[Zn_2L(NCO)_2]$, $[Zn_2L\text{-}(NCSe)_2]_2\cdot dmf$ (**Figure 3C.1**). Relationship between radiative rate constant and quantum yield for the dizinc(II) complexes was established. The increase of the radiative rate constant from time resolved studies indicated enhancement of the ligand fluorescence by zinc(II).[9]

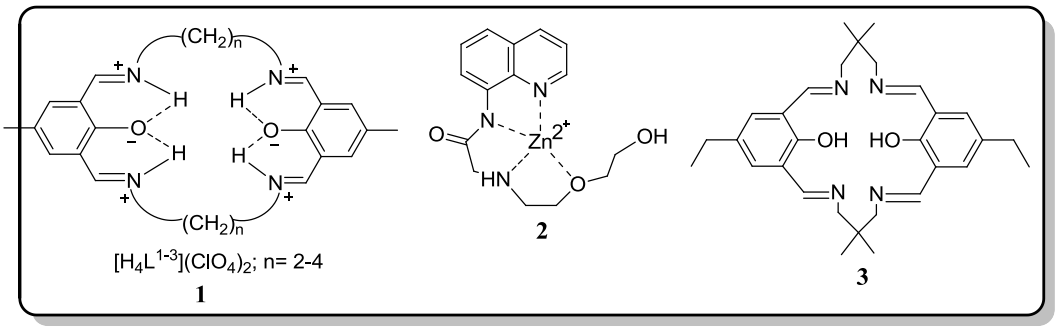


Figure 3C.1 Fluorescent tetraiminodiphenol macrocycles, ratiometric zinc sensor and tetra imino diphenol ligand

Yang group synthesized three paeonol Schiff base ligands and their Zn(II) complexes (**4**, **5** and **6**). All the synthesized complexes were found highly fluorescent in nature and they could emit bright fluorescence at room temperature in both solution (DMF) and solid state (**Figure 3C.2**).

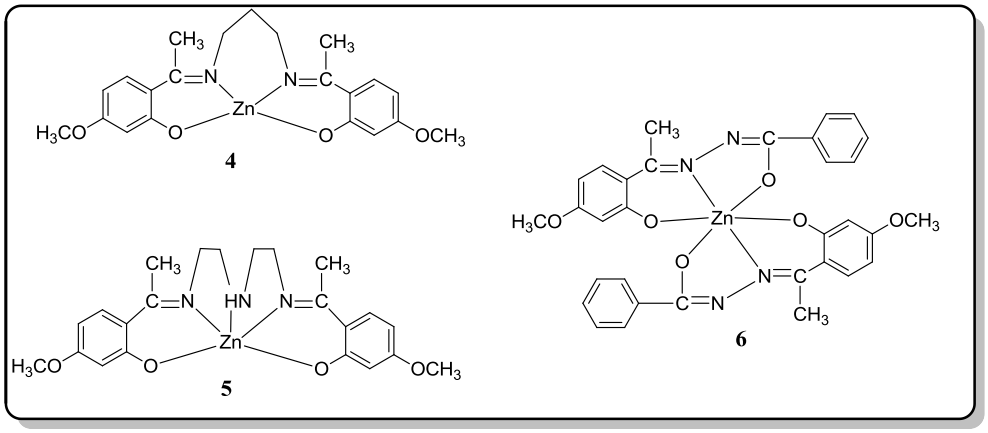
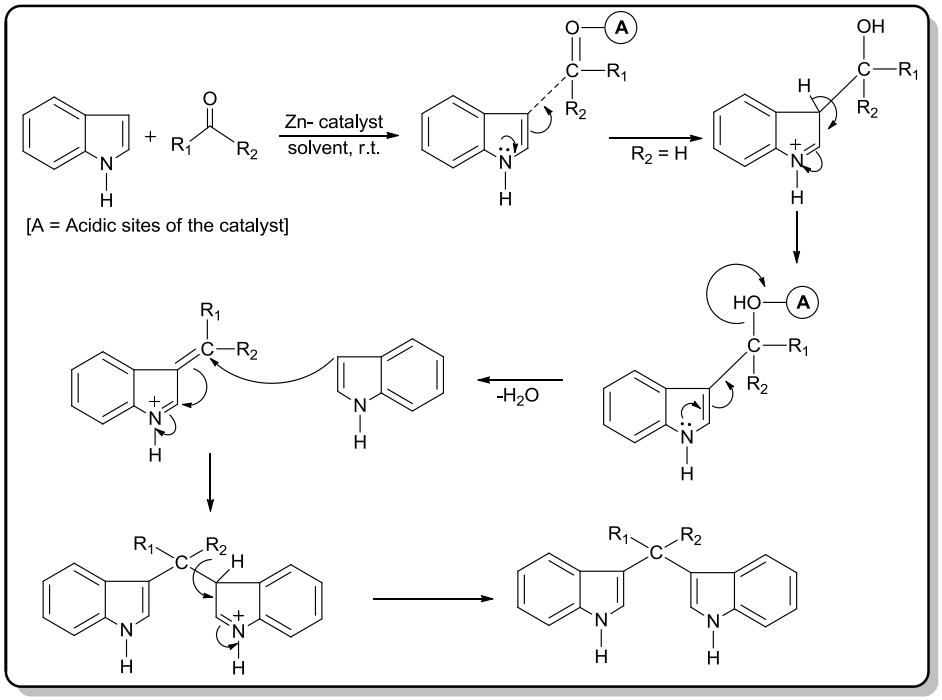


Figure 3C.2 Fluorescent Zn(II) complexes of paeonol Schiff base ligands

Indole fragments such as bis(indolyl)methanes (BIMs) are an important class of compounds, which have a wide range of biological and pharmaceutical applications.[10, 11] Condensation of indole derivatives with carbonyl compounds leads to the formation of bis(indolyl)methanes. The reaction involves the electrophilic substitution reaction of indole with aromatic aldehydes. The steps involves in the synthesis are depicted in **Scheme 3C.1**.[12]



Scheme 3C.1 Mechanism for the zinc catalyzed reaction of indole with aromatic aldehyde.

A variety of reports are accessible where a range of catalysts *viz.* $CuBr_2$, I_2, CAN, NBS, $InCl_3$, $In(OTf)_3$, tris(hydroxymethyl)methane ammonium hydrogensulphate and BF_3 are employed.[13-15] Few limitations are associated with these methodologies including, the use of volatile organic solvents, toxic reagents, tedious work-up, poor yields etc., therefore advanced and improved methods to synthesize (BIMs) in laboratories are being developed.[16] Silveira and co-workers developed an efficient and recyclable medium of glycerin and $CeCl_3.7H_2O$ and used it in the synthesis of bis(indolyl)methanes.[17] Mendes *et al*. developed an efficient and green procedure for the synthesis of bis(indolyl) methanes using ammonium niobium oxalate as the catalyst and water or glycerol as the solvent. Good to excellent yields of the products were obtained under conventional heating or under sonication, while taking water as solvent, the catalyst was easily reused.[18] Mulla group developed a simple and rapid protocol for an efficient synthesis of bis(indolyl) methane in excellent yields using ethyl ammonium nitrate as a reusable ionic liquid at room temperature.[19] In summary, an operationally simple and green method for the synthesis of a wide range of bis(1H-indol-3-yl)methanes, under mild conditions, with good yields, has been developed. This simple protocol has the advantages of environmental friendliness, higher yields, shorter reaction times and convenient operation, which only requires stirring the reaction mixture at ambient temperature, without the use of any additional energy source like heating or sonication. *Cis*-dioxido-molybdenum (VI) complexes (**7** and **8**) of hydrazine based Schiff base were used for their catalytic activity on the electrophilic reaction of indole with aldehydes to obtain bis(indolyl)methanes (**Figure 3C.3**).[20] Sah group used a *cis*-dioxomolybdenum (VI) complex (**9**) as an efficient catalyst in the selective synthesis of a series of bis(indolyl)methanes (BIMs) by the condensation of indoles with carbonyl compounds.[21] The adopted synthetic procedure was green in nature as the reaction was carried out under solvent free conditions (**Figure 3C.3**).

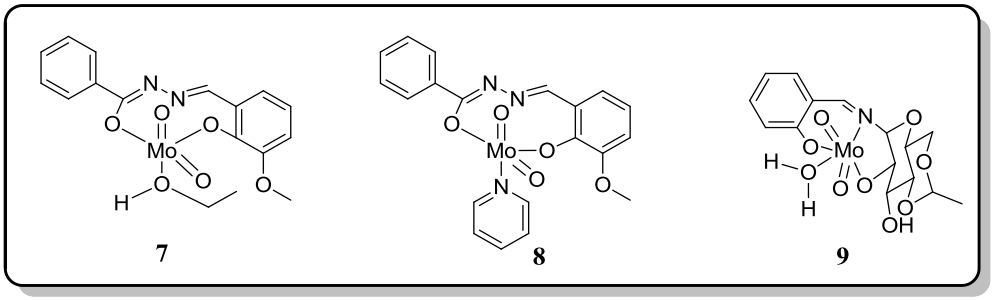


Figure 3C.3 *Cis*-dioxido-molybdenum (VI) complexes

A magnetic nanoparticles-supported Cu-isatin Schiff base complex (**10**) was synthesized and found to be efficient and recyclable catalyst in the synthesis of bis(indolyl)methanes in aqueous media. The catalyst was easily removed from the reaction mixture using an external magnet and reused eight times without any significant loss in activity (**Figure 3C.4**).[22] Yang *et al.* synthesized a series of 1,2,4-triazole based thiol Schiff bases and screened them as catalysts for the synthesis of bis(indolyl)methanes. The ligand (**11**, L_2) was found effective catalyst among the all with copper(II) salt.[23]

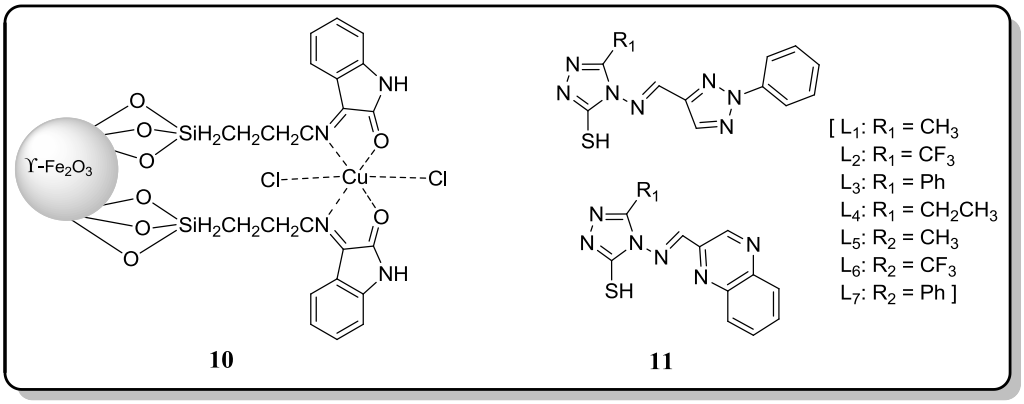


Figure 3C.4 Cu-isatin Schiff base complex and triazole-thiol based Schiff bases

The current chapter deals with the synthesis, characterization, photophysical properties, and catalytic activities of novel ionic liquid-supported Schiff base zinc(II) complex. The synthesized complex was found fluorescent in nature and was also explored for its catalytic activity. The complex showed good catalytic activity in the synthesis of bis(indolyl)methanes.

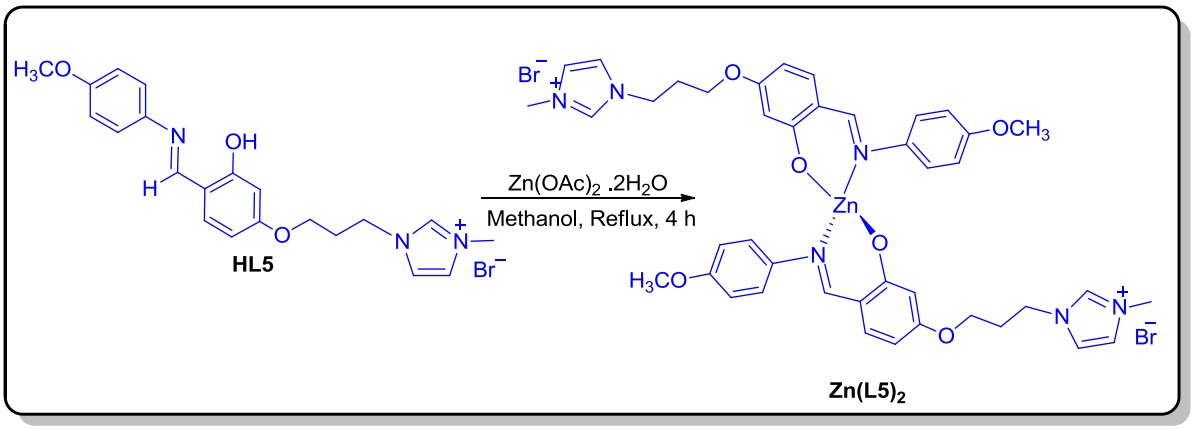
3C.2 Results and discussion

3C.2.1 Synthesis and characterization of $Zn(L5)_2$

3C.2.1.1 Synthesis of $Zn(L5)_2$

Ionic liquid-tagged Schiff base **HL5** was synthesized as described in chapter 2B**.** The ligand **HL5** (600 mg, 2.0 mmol) and zinc acetate dihydrate (148 mg, 1.0 mmol) were mixed and the mixture was refluxed for 4h. After cooling, the product was separated by filtration and

recrystallized from the mixture of petroleum ether (2 mL) and methanol (15 mL). **Zn(L5)$_2$** was separated as fine yellow colored powder, **Scheme 3C.2**.



Scheme 3C.2 Synthesis of **Zn(L5)$_2$**

3C.2.1.2 Characterization of Zn(L5)$_2$

The compound was isolated as yellow colored solid. The complex obtained was aerially stable and soluble in water, ethanol, methanol, ACN, DMF and DMSO. **HL5** and **Zn(L5)$_2$** both were studied comparatively through collection of structural investigations. The FT-IR spectrum of **HL5** contained a peak at 1620 cm^{-1}, attributed to azomethine (ν(C=N)) group, whereas in **Zn(L5)$_2$** this peak shifted to 1612 cm^{-1}. This shifting of the azomethine peak to lower frequency indicates that the azomethine nitrogen is involved in the coordination with zinc metal ion. In the spectrum of **HL5,** another absorption band was observed at 3418 cm^{-1} due to ν(OH) stretching. This band was absent in **Zn(L5)$_2$,** suggesting the involvement of -OH group of **HL5** in the coordination to metal ion through deprotonation.[24, 25] One more peak at 1165 cm^{-1} due to ν(C–O) stretch was observed in the spectrum of **HL5,** which on complexation with the zinc metal shifted towards higher frequency[26] value of 1180 cm^{-1} (**Figure 3C.5**).

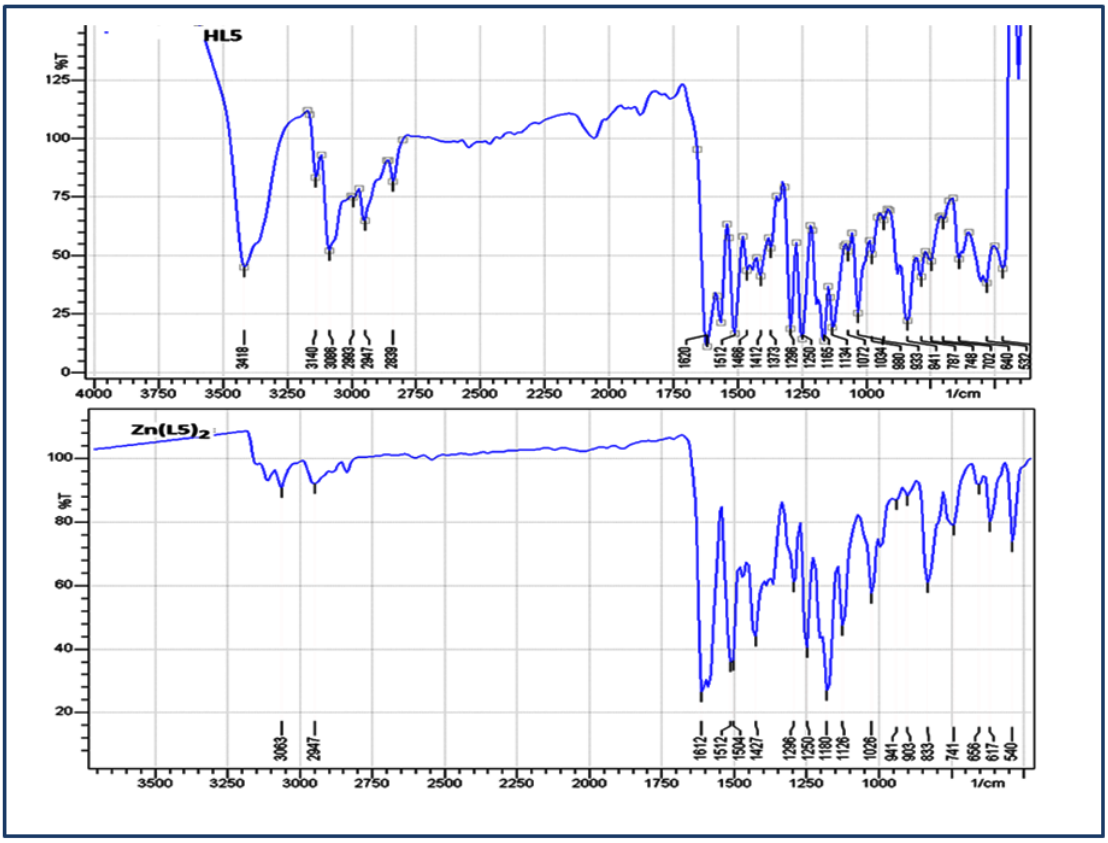


Figure 3C.5 FT-IR spectra of **HL5** and **$Zn(L5)_2$**

In the ^{1}H NMR spectrum of **HL5**, a signal representing the azomethine proton (CH=N) appeared at δ 8.87, and the hydroxyl proton resonated at δ 13.86. Signals corresponding to other protons were also revealing the structure of **HL5**. The azomethine proton signal of **$Zn(L5)_2$** appeared at δ 8.37 and there was no signal nearby δ 13-14. These spectral inferences indicated the complexation of **HL5** with zinc metal (**Figure 3C.6**). In ^{13}C NMR spectrum of **HL5** the azomethine carbon appeared at δ 163.30 and after complexation with zinc metal this value shifted at δ 172.67 in **$Zn(L5)_2$**. Other signals were also consistent with the structure (**Figure 3C.7**). The MALDI mass spectrum (**Figure A15, Appendix-A**) of **$Zn(L5)_2$** showed a peak at 793.35 corresponding to $[M + H- 2Br]^{+}$ ion. The presence of zinc ion was indicated in terms of M (793.35), M + 2 (795.34) and M + 4 (797.35) isotopic peaks and their intensities; also M + 1, M + 3 and M + 5 isotopic peak corresponding to the number of carbon atoms of the complex were evident shown by similar systems.[27, 28] The distorted tetrahedral geometry may be undergoing a transition five coordinated state during the catalytic cycle.

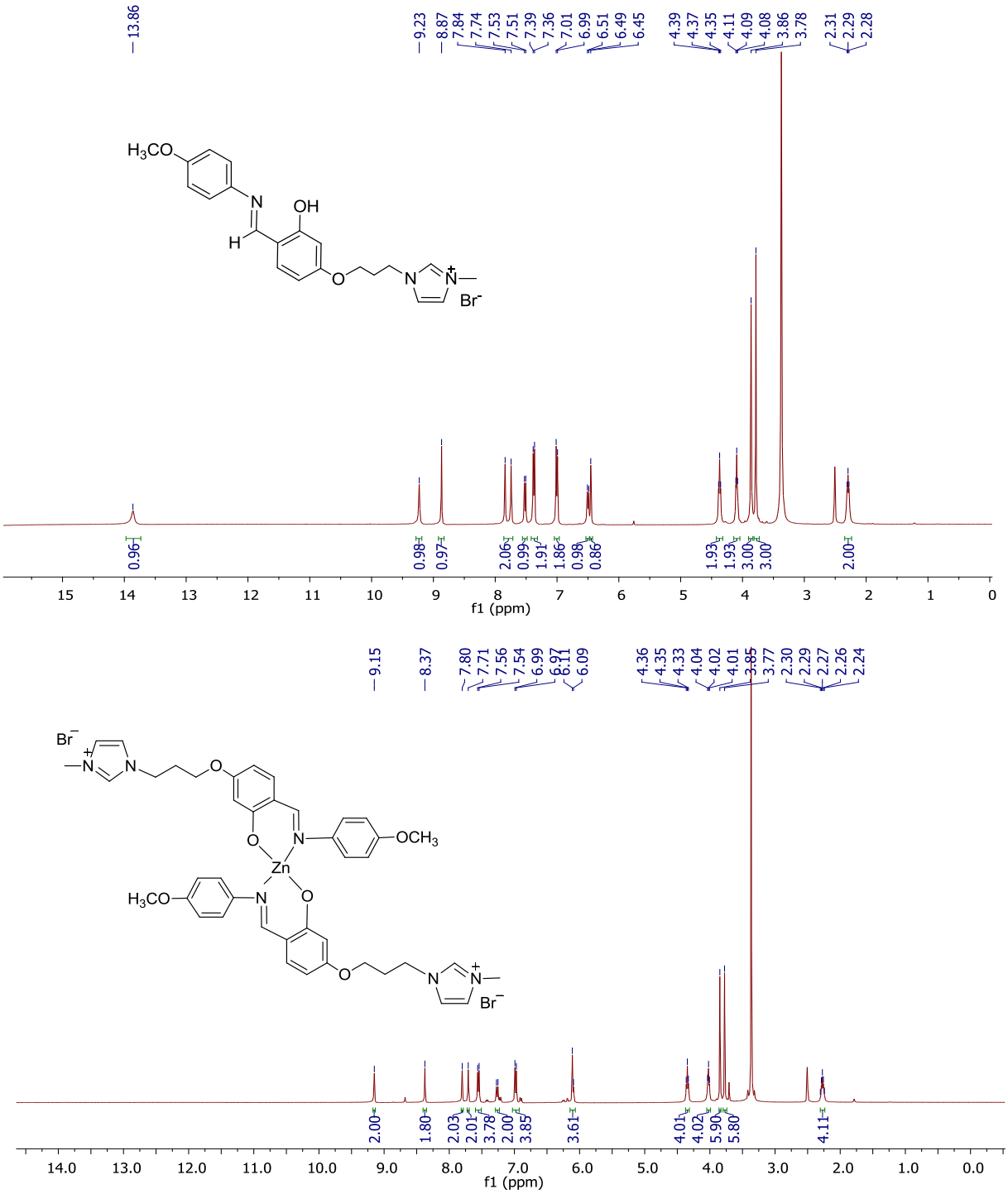


Figure 3C.6 ^{1}H NMR spectra of **HL5** and **Zn(L5)$_2$**

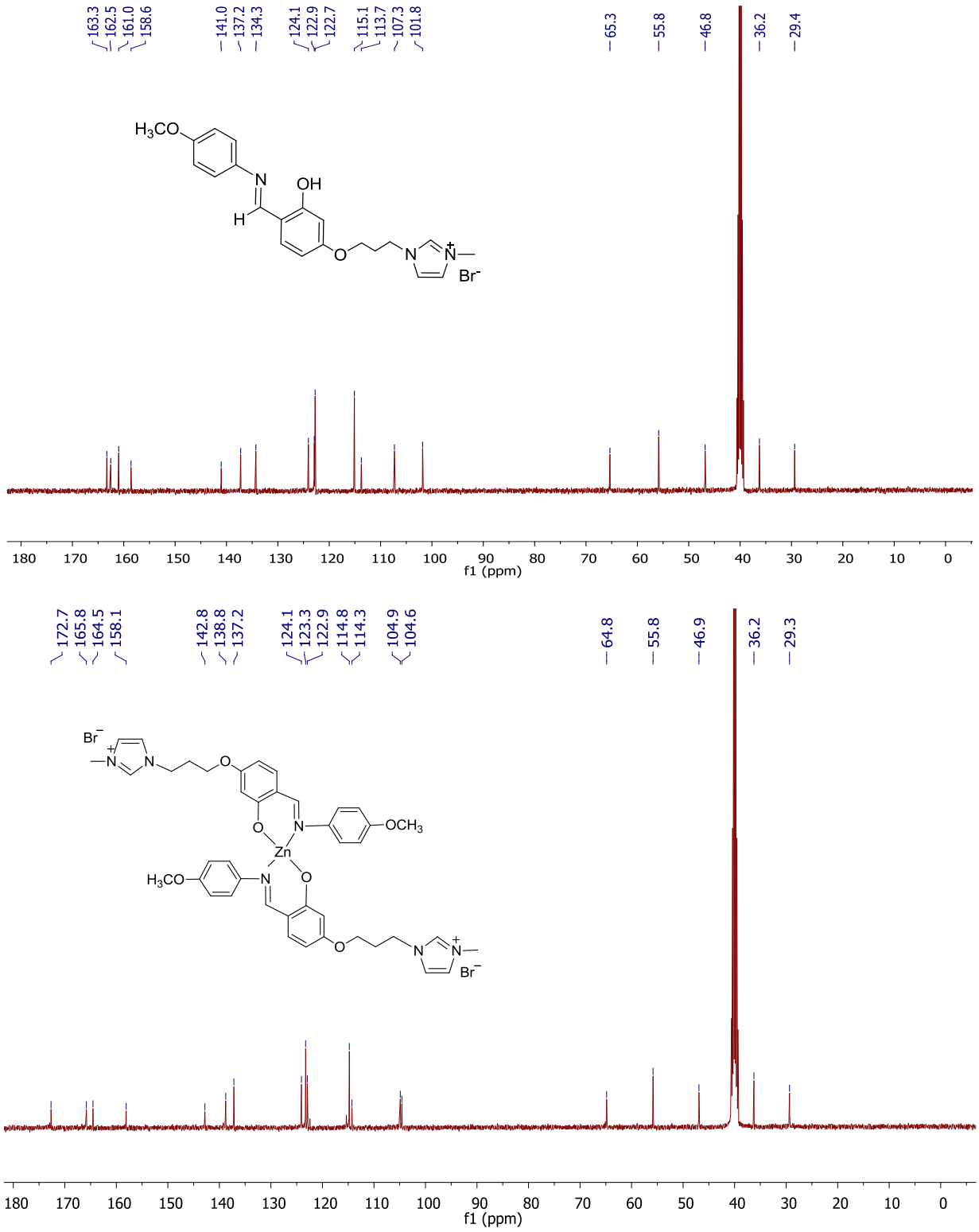


Figure 3C.7 ^{13}CNMR spectra of **HL5** and **Zn(L5)$_2$**

The powder XRD patterns indicated crystalline nature for both **HL5** and **Zn(L5)$_2$** however, the broad peaks indicated the major portion of the compound is amorphous in nature. In the XRD pattern of **Zn(L5)$_2$**, the appearance of new pattern indicated complex formation with the inclusion of zinc(II). No significant changes were observed in the powder XRD of 2 after heating at 200 °C for 2 h, showing its stabilityThe powder XRD patterns indicated crystalline nature for both **HL5** and **Zn(L5)$_2$**. In the XRD pattern of **Zn(L5)$_2$**, appearance of new peaks indicated presence of zinc(II). No significant changes were observed in the powder XRD of **Zn(L5)$_2$** after heating at 200 °C for 2 h, showing its high thermal stability (**Figure 3C.8**).

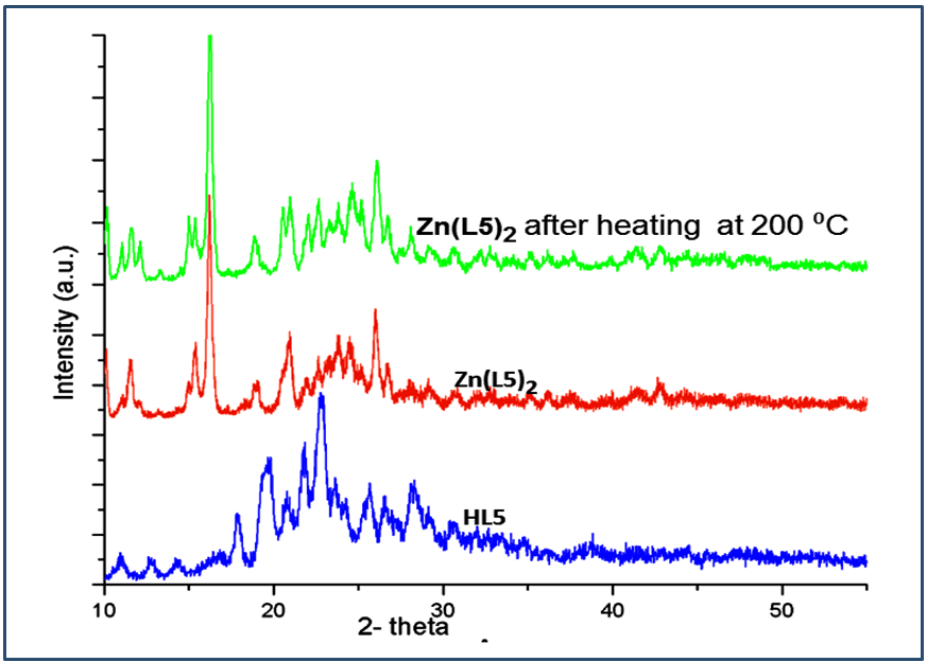


Figure 3C.8 Powder XRD pattern of **HL5** and **Zn(L5)$_2$**

The thermal stabilities of **HL5** and **Zn(L5)$_2$** were further determined by DSC and thermogravimetric analysis (TGA) under nitrogen atmosphere. In the DSC scan of **HL5**, a sharp endothermic peak corresponding to the melting point was observed at 151 °C. In case of **Zn(L5)$_2$**, the melting peak was observed at 322 °C suggesting good thermal stability in contrast to **HL5**. The TGA of **Zn(L5)$_2$**did not show any specific loss in weight up to 200 °C, indicating absence of both crystal and coordinated water molecules (**Figure 3C.9**).

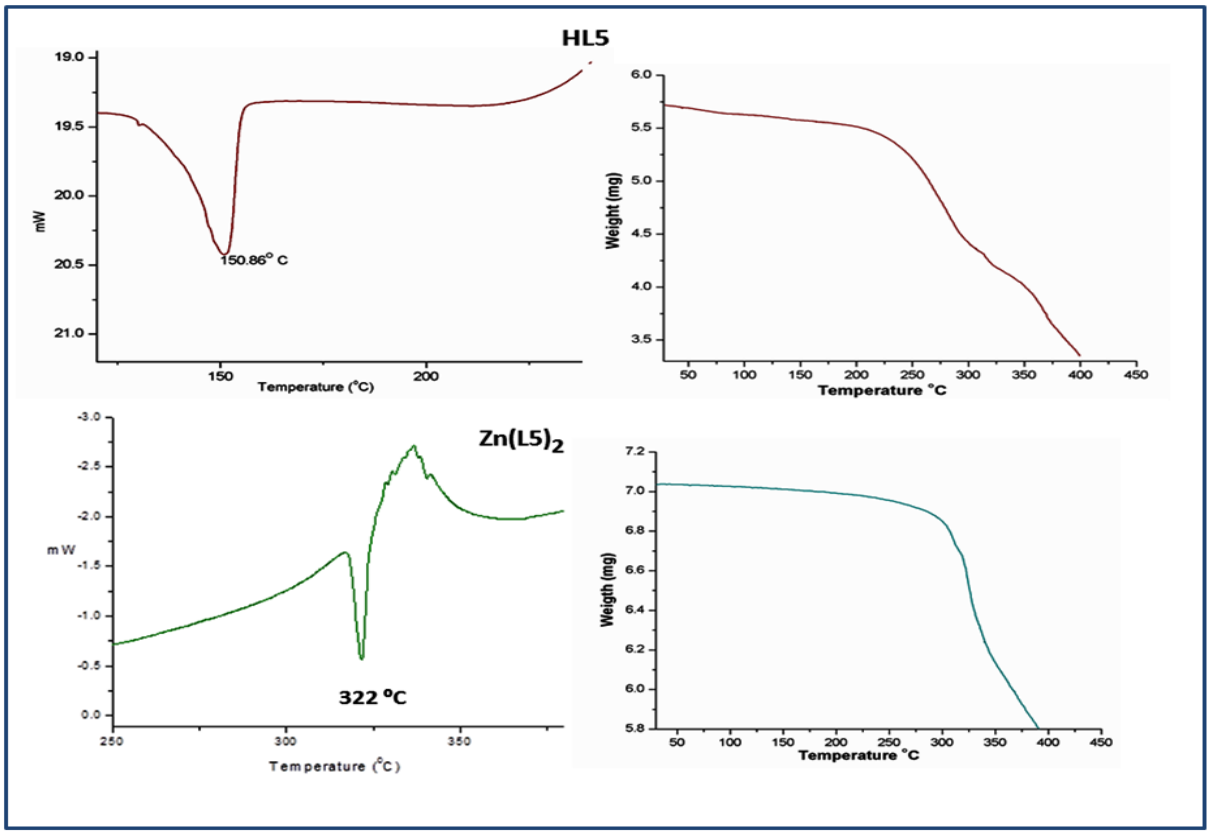


Figure 3C.9 DSC and TGA thermograms of **HL5** and **Zn(L5)$_2$**

3C.2.2 Photophysical properties of Zn(L5)$_2$

The photophysical properties of **HL5** and **Zn(L5)$_2$** were thoroughly studied by UV/vis, steady state and time resolved fluorescence spectroscopy. Both the ligand and complex were found fluorescent in nature (**Figure 3C.10**).

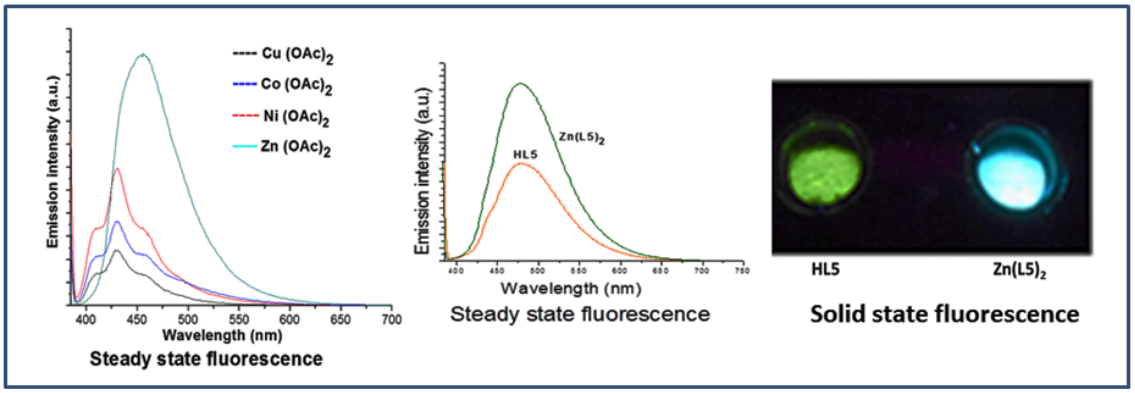


Figure 3C.10 Solution and solid state fluorescence spectra of **HL5** and **Zn(L5)$_2$**

The solution state electronic spectra of **HL5** in DMSO exhibited two absorption bands at 305 nm and 380 nm due to the π–π^* and n–π^* transitions respectively. In the solid state, these bands appeared at 335 nm and 426 nm. On complexation with zinc metal, hypsochromic shift was observed, resulting in appearance of bands at 275 nm and 343 nm in DMSO and at 318 nm and 403 nm in solid state (**Figure 3C.11**).

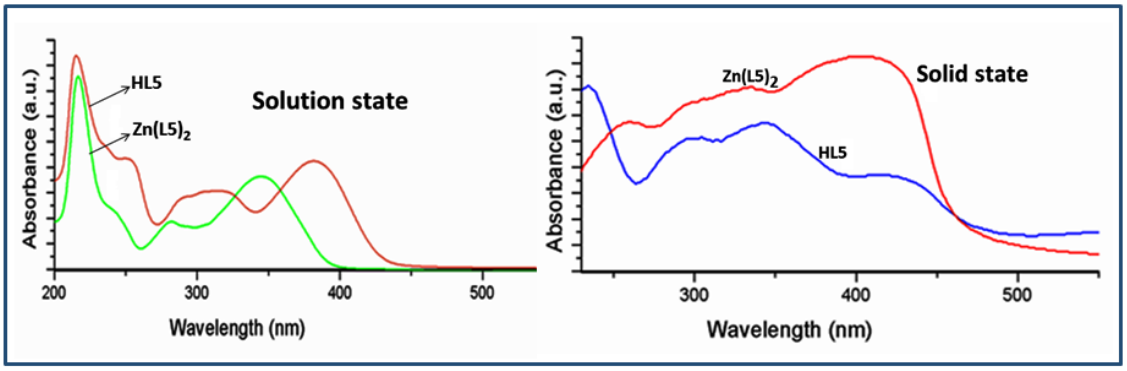


Figure 3C.11 U.V. spectra of **HL5** and **Zn(L5)$_2$**

The absorption and emission spectra (**Figure 3C.12**) of **Zn(L5)$_2$** were recorded in different solvents. The quantum yields at different excitations are summarized in table 3C.1.

Table 3C.1 Photophysical data of **Zn(L5)$_2$**[a]

S. No.	Solvent	$\lambda_{max, abs,}$ nm (ε, 1 x 10^{-5} M^{-1} cm^{-1})	λ_{ex}, nm	λ_{em}, nm	Quantum yield, Φ_{em} (solution, r.t.)[a]
1.	DMSO	348 (0.34), 284 (0.21)	280	425	0.05
			350	430	0.003
2.	Water	410 (0.10), 322 (0.11), 280 (0.17)	400	467	0.05
			325	368	0.008
			280	420	0.02
3.	Ethanol	343 (0.32), 280 (0.24)	350	344	0.006
4.	Acetonitrile	385 (0.33), 294(0.11)	350	446	0.06
			380	430	0.02

[a]Quantum yields were measured relative to quinine sulfate in 0.1 N H_2SO_4 (Φ_{em} = 0.55). All data were measured at 298K.

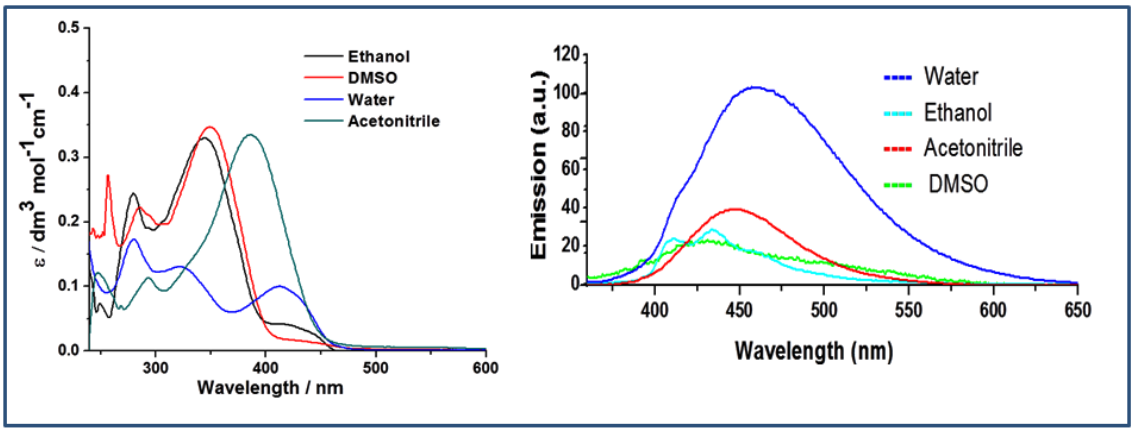


Figure 3C.12 Absorption and emission spectra of **$Zn(L5)_2$**

The life time was measured by time correlated single photon counting of **HL5** and **$Zn(L5)_2$**. The increase in life time from 0.3 nano seconds for **HL5** to 0.8 nano seconds for **$Zn(L5)_2$** (**Figure 3C.13**) indicated enhancement in conformational rigidity on complexation with Zn(II).

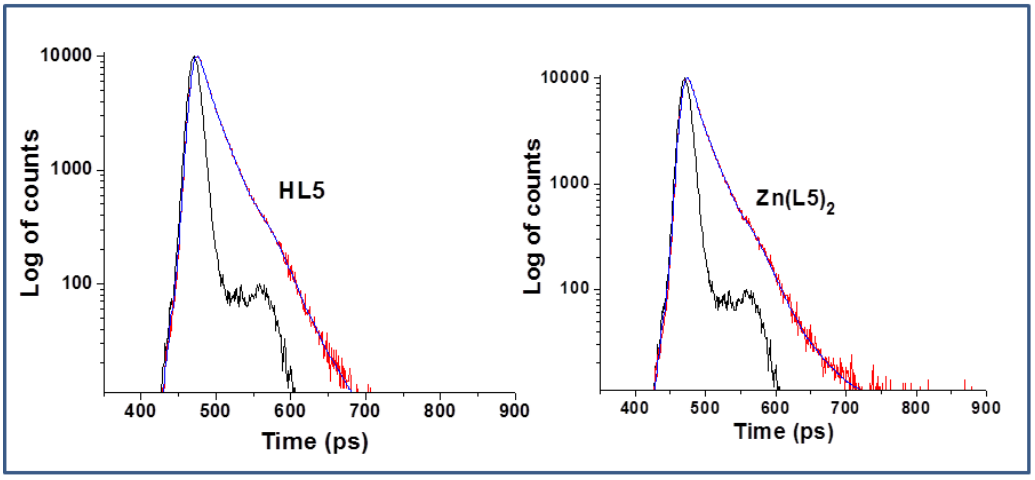
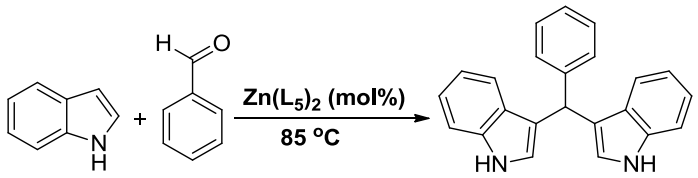


Figure 3C.13 Time-resolved fluorescence decay of **HL5** and **$Zn(L5)_2$**, fluorescence was monitored at 385 nm

3C.2.3 Catalytic application of $Zn(L5)_2$

$Zn(L5)_2$ was used as a catalyst for the synthesis of bis(indolyl)methanes using aromatic aldehydes and indole substrates. A varied mol% of **$Zn(L5)_2$** and variety of solvents were tested for the reaction. 3 mol% of **$Zn(L5)_2$** and water gave the best results (Table 3C.2, entry 4).

Table 3C.2 Optimization of reaction conditions for the synthesis of bis(indolyl)methanes catalyzed by **$Zn(L5)_2$**[a]



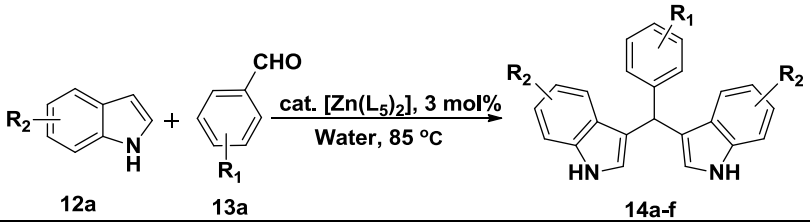
12a 13a 14a

Entry	Solvent	$Zn(L5)_2$(mol%)	Time (h)	Yield[b] (%)
1.	THF	3	6	80
2.	Water	5	6	80
3.	Ethanol	5	6	80
4.	**Water**	**3**	**6**	**80**
5.	DCM	3	7	65
6.	MeOH	3	6	75

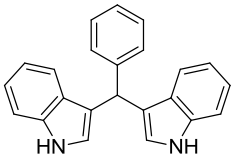
[a]Reaction conditions: indole (2.0 mmol), benzaldehyde (1.0 mmol), **$Zn(L5)_2$** (3 mol%) and water (5 mL). [b]Isolated yield

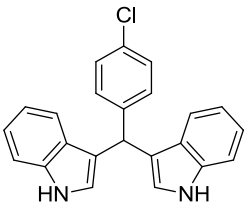
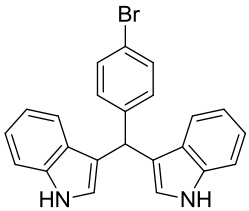
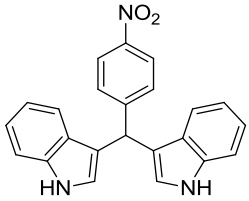
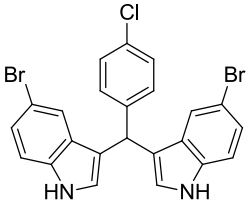
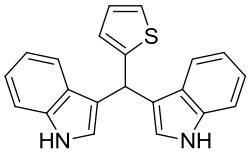
To expand the scope of the methodology, other kinds of indoles and aldehydes were tested for the same reaction and a variety of bis(indolyl)methanes were synthesized under the optimized condition (Table 3C.3).

Table **3C.3** Formation of bis(indolyl)methanes, catalyzed by **$Zn(L5)_2$**



12a 13a 14a-f

Entry	Product	14	Time/h	Yield (%)
1.		14a	6	90

2.		14b	6	95
3.		14c	6	90
4.		14d	7	75
5.		14e	7	80
6.		14f	8	85

[a]Reaction conditions: indole derivative (2.0 mmol), aromatic aldehyde (1.0 mmol), **Zn(L5)$_2$** (3 mol%) and water (5 mL). [b]Isolated yield

The representative ^{1}H and ^{13}C NMR of **14a** is shown in **Figure 3C.14**

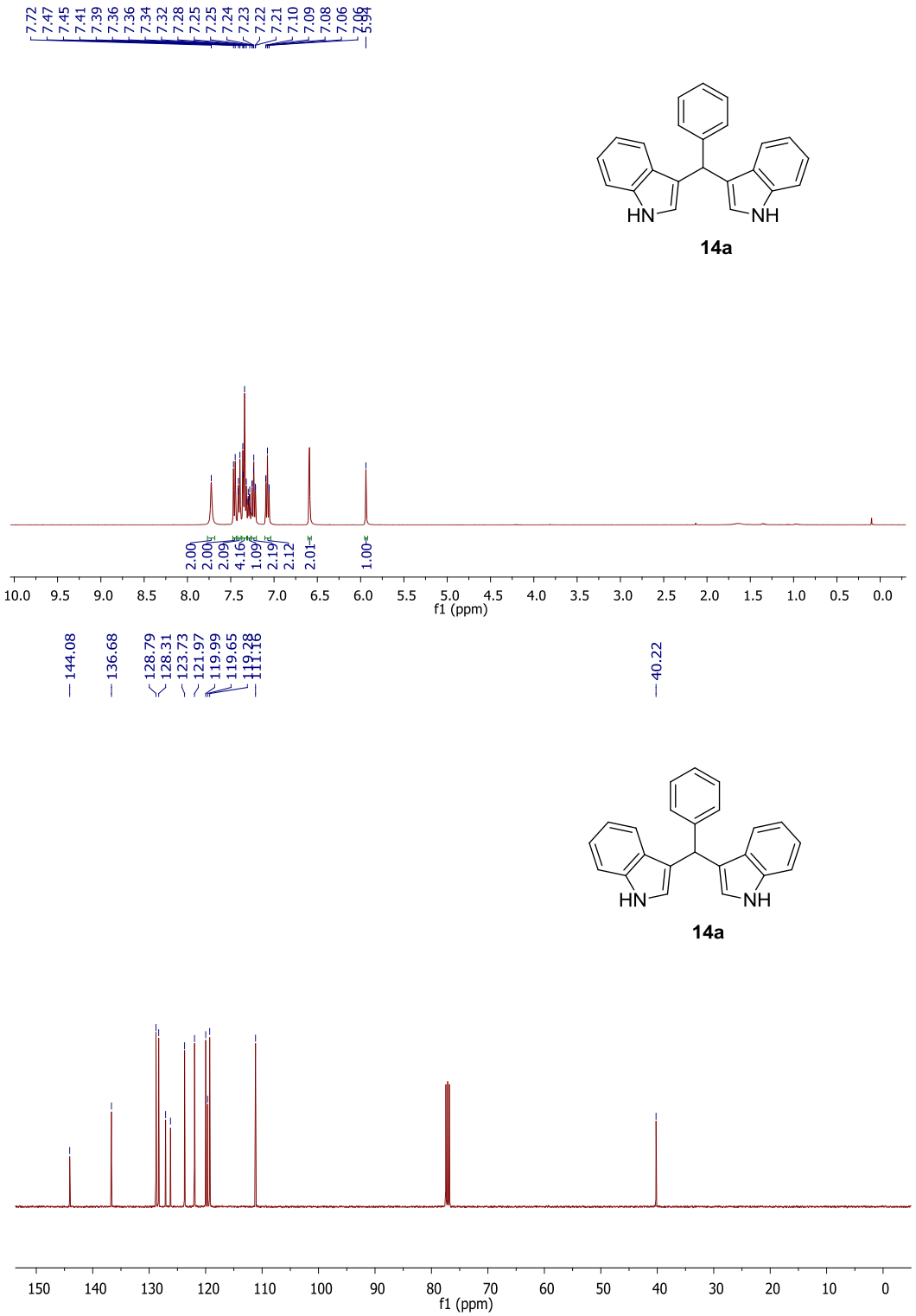


Figure 3C.14 ^{1}H and ^{13}C NMR spectra (in $CDCl_3$) of 3, 3′-(Phenylmethylene)bis(1*H*-indole) (**14a**)

3C.2.3.1 Recycling of $Zn(L5)_2$

The reusability of **$Zn(L5)_2$** was estimated for the synthesis of bis(indolyl)methanes. In **Figure 3C.15**, it is mentioned that the catalyst could be effectively used up to six repeated cycles without much loss in catalytic activity. The gradual decrease in the yield of the product during recycling may be due to the leaching of the catalyst during extraction.

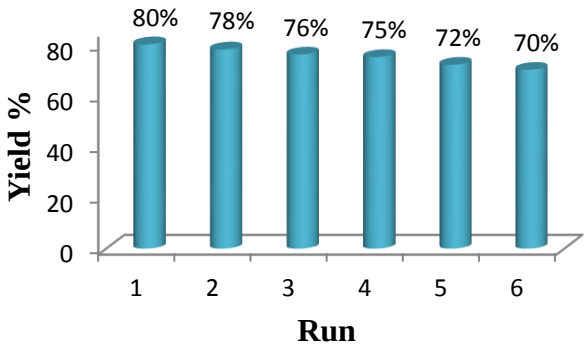


Figure 3C.15 Reusability of **$Zn(L5)_2$** for the synthesis of bis(indolyl)methanes

3C.3 Experimental section

3C.3.1 Synthesis of $Zn(L5)_2$

The ligand **HL5** (600 mg 2.0 mmol) was stirred with methanol in a 25 mL round bottom flask for 15 minutes, zinc acetate dihydrate (220 mg, 1.0 mmol) was added to the resultant solution, and the mixture was refluxed for 4 h until the product precipitated completely. After cooling for 20 minutes the product **2** was separated by simple filtration and recrystallized from a mixture of petroleum ether (5 mL) and methanol (20 mL).

3C.3.2 General procedure for the synthesis of bis(indolyl)methanes

A mixture of indole derivative (2.0 mmol), aromatic aldehyde (1.0 mmol) and **$Zn(L5)_2$** (3 mol%) as a catalyst in water (5 mL) were stirred at 85 °C temperature for 6-8 h. The progress of the reaction was continuously monitored by TLC. After completion of the reaction, the product was extracted in ethyl acetate and purified by column chromatography over silica gel (mesh 100−200) using *n*-hexane/ethyl acetate as an eluent. The isolated products were analyzed by ^{1}H and ^{13}C NMR spectroscopy.

3C.3.3 Reusability and recovery of the catalyst

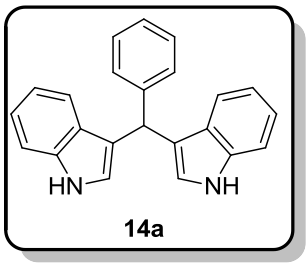
After the first run, when the reaction was completed, the product was directly extracted into the organic layer, and the catalyst which remained in the aqueous layer was reused for the next cycle of the reaction, following the same procedure for the synthesis of bis(indolyl)methanes.

3C.3.4 Spectroscopic data of $Zn(L5)_2$

Light yellow colored solid; Yield 90%; mp 315-325 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.15 (s, 2H), 8.37 (s, 2H), 7.80 (s, 2H), 7.71 (s, 2H), 7.55 (d, *J* = 8.7 Hz, 4H), 7.26 (d, *J* = 9.3 Hz, 2H), 6.98 (d, *J* = 8.7 Hz, 4H), 6.10 (d, *J* = 7.0 Hz, 4H), 4.35 (t, *J*= 6.7 Hz, 4H), 4.02 (t, *J* = 5.8 Hz, 4H), 3.85 (s, 6H), 3.77 (s, 6H), 2.32 – 2.22 (m, 4H).^{13}C NMR (101 MHz, DMSO-*d6*) δ 172.7, 165.8, 164.5, 158.1, 142.8, 138.8, 137.2, 124.1, 123.3, 122.9, 114.8, 114.3, 104.9, 104.6, 64.8, 55.8, 46.9, 36.2, 29.3.

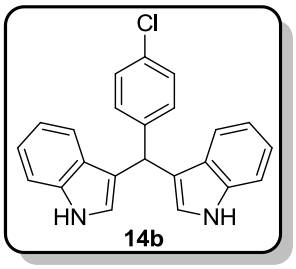
3C.3.4 Spectroscopic data of the synthesized bis(indolyl)methanes

3, 3′-(Phenylmethylene)bis(1*H*-indole), 14a: Yield (80%); pink solid; mp 146-148°C;[29] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (bs, 2H), 7.46 (d, *J* = 7.9 Hz, 2H), 7.42 – 7.39 (m, 2H), 7.36 –7.32 (m, 4H), 7.29 (dt, *J* = 8.4, 2.1 Hz, 1H), 7.25 – 7.21 (m, 2H), 7.10 – 7.06 (m, 2H), 6.59 (s, 2H), 5.94 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.1, 136.7, 128.8, 128.3, 127.1, 126.2, 123.7, 121.9, 119.9, 119.6, 119.3, 111.2, 40.2.

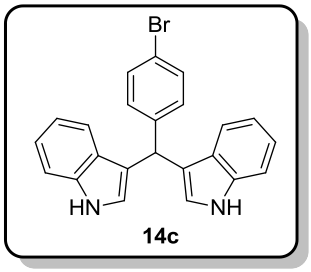


14a

3, 3′-((4-Chlorophenyl)methylene)bis(1*H*-indole), 14b: Yield (85%); pink solid; mp 80-82 °C;[29] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (bs, 2H), 7.39 (d, *J* = 8.2 Hz, 4H), 7.28 (q, *J* = 8.8 Hz, 4H), 7.21 (t, *J* = 7.7 Hz, 2H), 7.04 (t, *J* = 7.4 Hz, 2H), 6.66 (s, 2H), 5.89 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.5, 136.7, 131.7, 130.0, 128.3, 126.8, 123.6, 122.0, 119.8, 119.3, 119.1, 111.1, 39.6.

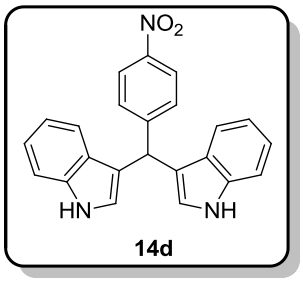


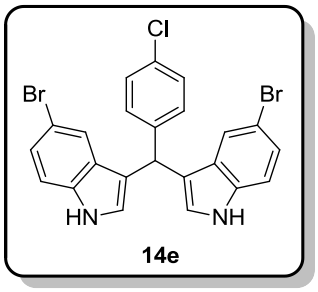
14b



3, 3′-((4-Bromophenyl)methylene)bis(1*H*-indole), 14c: Yield (80%); off white solid; mp 110-112 °C;[30] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (bs, 2H), 7.43 – 7.37 (m, 6H), 7.25– 7.20 (m, 4H), 7.05 (t, *J* = 7.5 Hz, 2H), 6.65 (s, 2H), 5.87 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.1, 136.7, 131.3, 130.5, 126.9, 123.6, 122.1, 119.9, 119.8, 119.4, 119.1, 111.1, 39.7.

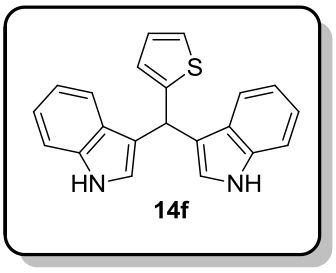
3, 3′-((4-Nitrophenyl)methylene)bis(1*H*-indole), 14d: Yield (65%); yellow solid; mp 125-127 °C;[31] ^{1}H NMR (400 MHz, DMSO- d_6) δ 10.96 (bs, 2H), 8.16 (d, *J* = 8.7 Hz, 2H), 7.62 (d, *J* = 8.7 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 7.9 Hz, 2H), 7.06 (t, *J* = 7.4 Hz, 2H), 6.91–6.87 (m, 4H), 6.04 (s, 1H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 153.6, 146.2, 137.0, 129.9, 126.8, 124.3, 123.9, 121.6, 119.4, 118.9, 117.1, 112.1, 39.8.





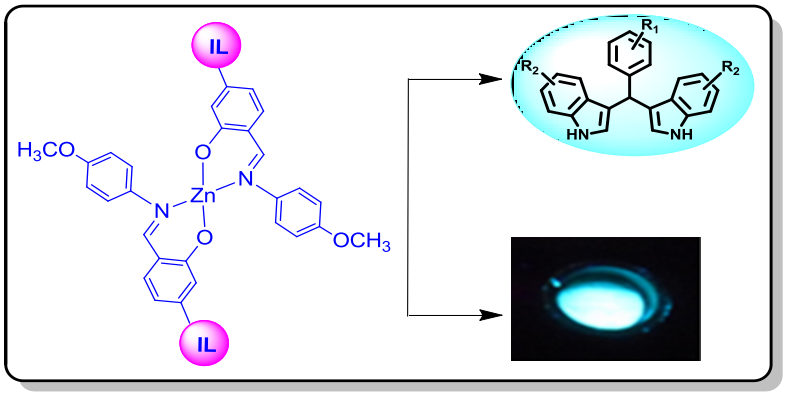
3, 3′-((4-Chlorophenyl)methylene)bis(5-bromo-1*H*-indole), 14e: Yield (82%); pink solid; mp 209-212 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (bs, 2H), 7.48 (s, 2H), 7.30 – 7.22 (m, 8H), 6.65 (s, 2H), 5.75 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.6, 135.3, 132.2, 129.9, 128.6, 128.5, 125.1, 124.8, 122.1, 118.5, 112.8, 112.7, 39.3.

3,3′-(Thiophen-2-ylmethylene)bis(1*H*-indole), 14f: Yield (75%); off white solid; mp 140-145 °C;[32] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (bs, 2H), 7.50 (d, *J* = 7.9 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.21 (dd, *J* = 14.2, 6.6 Hz, 3H), 7.07 (t, *J* = 7.4 Hz, 2H), 6.95 (dd, *J* = 7.8, 2.8 Hz, 2H), 6.84 (s, 2H), 6.19 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.6, 136.6, 126.7, 126.4, 125.1, 123.6, 123.2, 122.0, 119.8, 119.7, 119.4, 111.1, 35.4.



3C.4 Conclusion

In conclusion, a fluorescent imidazolium ionic liquid-tagged zinc(II) complex was synthesized and well characterized. The steady state fluorescence reflected enhancement in fluorescence, while increment in the excited singlet state lifetime indicating conformational rigidity of the complex. The complex showed good catalytic activity for the reaction of aromatic aldehydes and indoles to synthesize bis(indolyl)methanes in water.



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Chapter 4

Biological Activities of Ionic Liquid-tagged Schiff Base Ligands and Complexes

4.1 Introduction

Although at the beginning, applications of ILs were limited to chemical separations, catalysis and electrochemistry, but later the scope became much broader and covered the area of biological applications.[1] Imidazolium and pyridinium ionic liquids based architectures are found to have good antimicrobial activities.[2] Many ionic liquids displayed biocidal activity against Gram-positive, Gram-negative bacteria, fungi and algae.[3-5] *N*, *N*, *N*-trimethyl chitosan, *N*–*N*-propyl-*N*, *N*-dimethyl chitosan and *N*-furfuryl-*N*, *N*-dimethyl chitosan based quaternary ammonium salts (**1**) were prepared (**Figure 4.1**) and their antibacterial activities were explored against *Escherichia coli.* The antibacterial activities of quaternized chitosan against *E. coli* were stronger than that of chitosan and were affected by the molecular weight.[6] Selenium functionalized imidazolium based ionic liquids (**2**) were synthesized and evaluated for their antimicrobial activity (**Figure 4.1)**. Among the microbes tested, algae proved to be particularly susceptible towards the action of selenium ILs. The minimum inhibitory concentration (MIC) showed that the activity of the compounds was altered by structural modifications in the aryl group on selenium moiety as well as by the counter ion associated with the cationic part.[7]

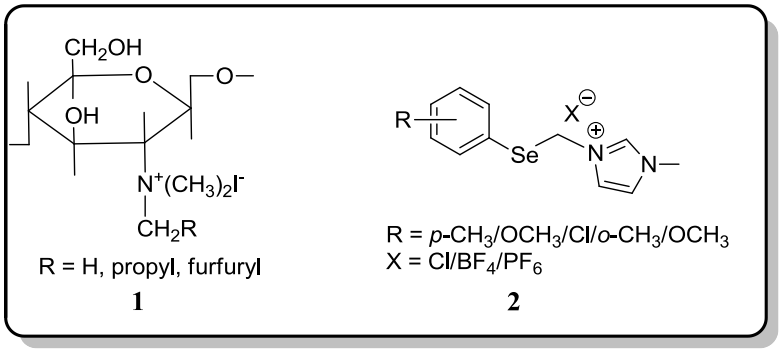


Figure 4.1 Quaternized *N*- alkyl chitosan and selenium based ionic liquids

1-alkylimidazolium and 1-alkoxymethylimidazolium ionic liquids with lactates (**3**, **4**) were synthesized and screened for their minimum inhibitory concentrations (MIC) and minimum biocidal concentrations (MBC) against rods, cocci and fungi (**Figure 4.2**). It was found that the anti-microbial activities of the protic ionic liquids were strongly related to the length of the substituent and also to the DL- or L-type anion.[8]

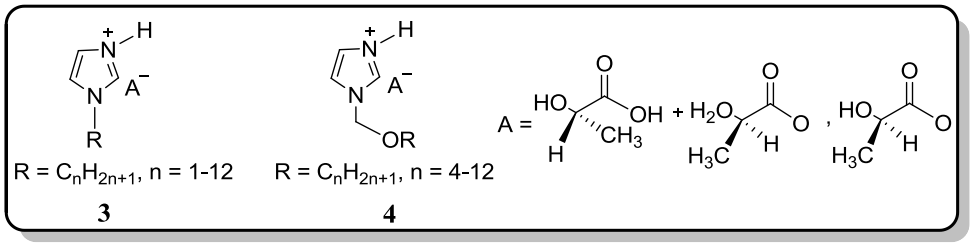


Figure 4.2 Lactate based protic ionic liquids

Antimicrobial studies of long-chain imidazolium and pyridinium based amphiphilic ionic liquids, 1-alkyl-3-methylimidazolium (**5**), 1-alkylpyridinium bromides (**6**), 3-methyl-1 alkyloxy carbonyl methyl imidazolium bromides (**7**), 1-alkyloxycarbonylmethylpyridinium bromides (**8**) and surface active amide functionalized ionic liquids (**9**, **10**) were investigated against Gram-negative and Gram-positive bacteria and fungi (**Figure 4.3**). The antimicrobial efficacy was dependent on the length of the alkyl chain. Compounds with short alkyl substituents were not active against bacteria and fungi whereas the ILs containing 10, 12 and 14 carbon atoms in their alkyl chain showed significant antimicrobial activity and the C_{14} homologous were the most active compounds.[9-11]

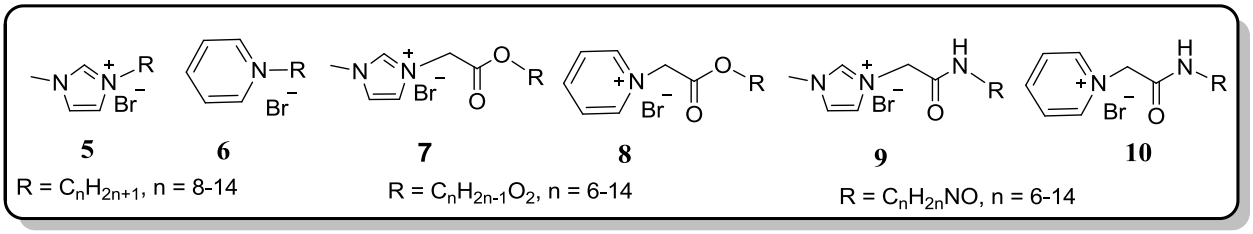


Figure 4.3 Imidazolium and pyridinium based functionalized ionic liquids

Hossain and co-workers synthesized 1-(2-hydroxylethyl)-3-alkylimidazolium chloride ionic liquids (**11**) and established their anti-microbial activities (**Figure 4.4**). The minimum inhibitory concentrations (MICs) and *EC*50 values for the present ILs were compared to a standard antibiotic, gentamicin. The *EC50* values were correlated to the chain length of alkyl substituents on the cation ring.[12] Elshaarawy *et al*. synthesized water-soluble methylimidazolium ionic liquids (**12**) bearing *N*,*N*′-bis (salicylidene)-*R*,*R*-1,2- diaminocyclohexane (saldach) scaffold with the chemical formula $H_2(R^1)_2$saldach(2-MeIm$^+X^-)_2$ (**Figure 4.4**). The synthesized compound established a noticeably enhanced biocidal effect towards methicillin resistant *Staphylococcus aureus* (MRSA) and multidrug-resistant *Escherichia coli* (MDREC).[13]

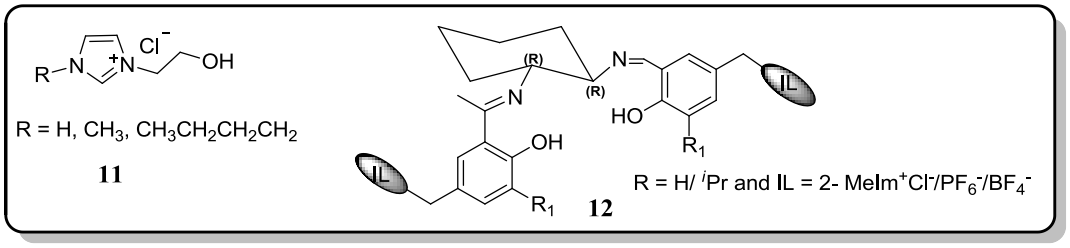


Figure 4.4 Imidazolium based ionic liquids and Ionic liquid-supported chiral saldach

Tawfik group synthesized gemini cationic surfactant-based ionic liquids (**13**) and screened their antimicrobial activity against Gram-negative and Gram-positive bacteria as well as fungi. The antimicrobial efficacy of the compounds was increased with the hydrophobicity and spacer length of the gemini ionic liquids (**Figure 4.5**).[14]

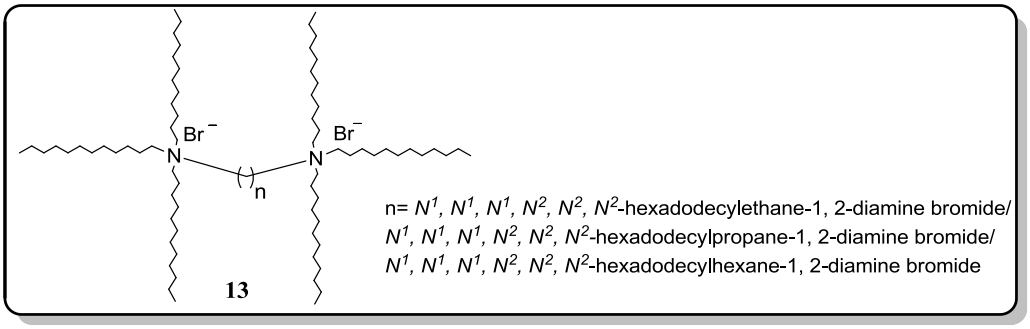


Figure 4.5 Gemini surfactant-based ionic liquids

Saraiva and co-workers studied the impact on efficacy of ionic liquids based on the association of choline with non-steroidal anti-inflammatory drugs, ketoprofen and naproxen forming IL-APIs (**14**, **15**). Enhanced drug bioavailability and thus efficacy of IL-APIs was due to interaction with biological membranes and improvement in the solubility. The IL-APIs exhibited promising properties regarding their incorporation in pharmaceutical formulations (**Figure 4.6**).[15]

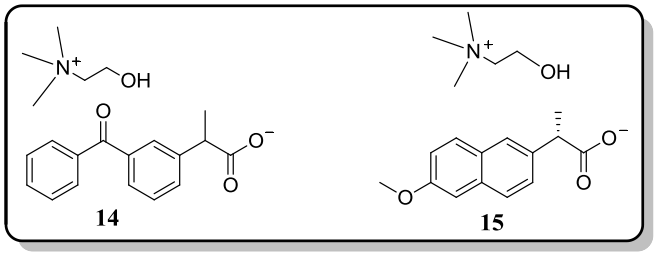


Figure 4.6 Choline based ionic liquids

Schiff bases constitute an important class of organic compounds because of their biological, analytical and pharmaceutical applications.[16-18] They possess excellent characteristics, structural similarities with natural biological substances. They are well known for broad spectrumbiological activities such as antiviral,[19, 20] anticancer,[21, 22] antifungal,[23, 24] antibacterial.[25, 26] The microbiocidal activities associated with them is due to the presence of the toxophoric C = N linkage in them.

A phenol based Schiff base polydentate ligand derived from 2,6-diformyl-4-methylphenol with *N*-aminopyrimidine (**16**) was prepared and evaluated for antimicrobial activity against four Gram-positive bacteria (*Staphylococcus aureus* ATCC 6538, *S.aureus* ATCC 25923, *Bacillus cereus* ATCC 7064 and *Micrococcus luteus* ATCC 9345), one Gram-negative bacterium (*Escherichia coli* ATCC 4230), and three yeast (*Candida albicans* ATCC 14053, *Candida krusei* ATCC 6258 and *Candida parapsilosis* ATCC 22019) strains. The ligand showed good biological activity against all tested bacteria and yeast strains (**Figure 4.7**).[27] A series of pyrazole based Schiff bases (**17**) were prepared and screened for their antibacterial (*Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Pseudomonas aeruginosa*) activity. The compounds exhibited significant biological activity against the tested microorganisms (**Figure 4.7**).[28] Kathiravan group synthesized a pyrene containing Schiff base (4-[(pyren-1-ylmethylene) amino] phenol) (**18**) and used it for antimicrobial and bioimaging studies. The compound showed excellent antimicrobial properties against Gram-positive (*Rhodococcus rhodochrous* and *Staphylococcus aureus*), Gram-negative (*Escherichia coli* and *Pseudomonas aeruginosa*) bacterial and fungal species (*Candida albicans*) (**Figure 4.7**).[29]

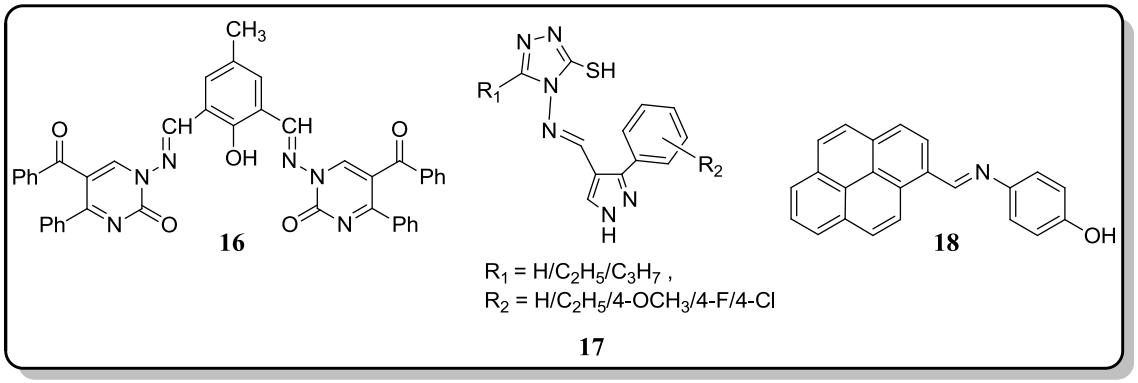


Figure 4.7 Phenol, pyrazole and pyrene based Schiff bases as antimicrobial agents

A series of Schiff bases from arylidene-2-(4-(4-methoxy/bromophenyl) thiazol-2-yl) hydrazines and 1-(4-(4-methoxy/bromophenyl) thiazol-2-yl)-2-cyclohexylidene/cyclopentylidene hydrazines was synthesized (**19**, **20** and **21**). The synthesized compounds were screened for their anti-bacterial and anti-fungal activities and were found to show moderate to good activities (**Figure 4.8**).[30]

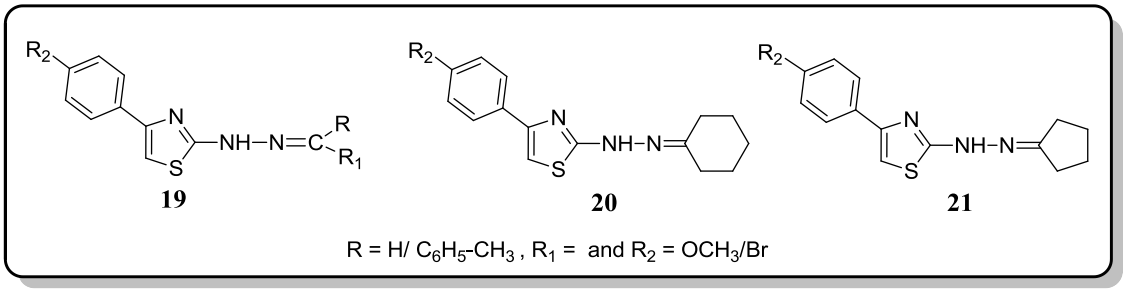


Figure 4.8 Thiazole based Schiff bases

The antimicrobial activity of the Schiff bases derived from chitosan and 3-(4-substituted-phenyl)-1-phenyl-1H-pyrazole-4-carbaldehyde (**22**) was explored against *Streptococcus pneumonia*, *Bacillis subtilis*, *Escherichia coli* and *Aspergillus fumigatus*, *Geotricum candidum* and *Syncephalastrum recemosum*. The antimicrobial activity of the Schiff bases was found to be stronger than that of chitosan and was dependent on the substituent group (**Figure 4.9**).[31] Salehi and co-workers prepared two Schiff bases derived from isophthalaldehyde (**23**) and screened them for *in vitro* antibacterial activities against four human pathogenic bacteria and their minimum inhibitory concentrations showed reasonable antibacterial activities (**Figure 4.9**).[32]

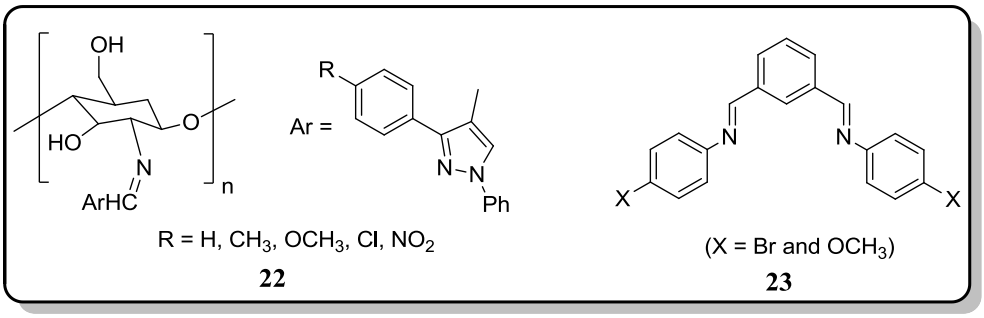


Figure 4.9 Chitosan and isophthalaldehyde derived Schiff bases

Schiff bases derived from benzaldehydes and 3, 3′-diaminodipropylamine (**24**) evaluated *in vitro* for their antimicrobial activity against a number of pathogenic Gram-positive and Gram-negative bacteria. The compounds showed bacteriostatic activities rather than bactericidal activities

(**Figure 4.10**).[33] Mohanan and co-workers prepared Schiff bases by the condensation of 2-aminophenol, 2-amino-4-nitrophenol, 2-amino-4-methylphenol, 2-amino benzimidazole with thiophene-2-carboxaldehyde and pyrrole-2-carboxaldehyde (**25**). The *in vitro* antibacterial activity of the synthesized compounds was tested against *Salmonella typhi*, *Bacillus coagulans*, *Bacillus pumills*, *Escherichia coli*, *Bacillus circulans*, *Pseudomonas*, *Clostridium* and *Klebsilla pneumonia* by disk diffusion method. All the prepared compounds were found to be effective antimicrobial agents (**Figure 4.10**).[34] Mohammadi group synthesized Schiff base ligands of macrocyclic bridged dianilines tetradentate with N_4 coordination sphere (**26**). All the Schiff bases were screened for their antibacterial activities and were found highly potent against two Gram-negative strains (*Escherichia coli* and *Pseudomonas aeruginosa*) and two Gram-positive (*Staphylococcus aureus* and *Staphylococcus epidermidis*) bacteria (**Figure 4.10**).[35]

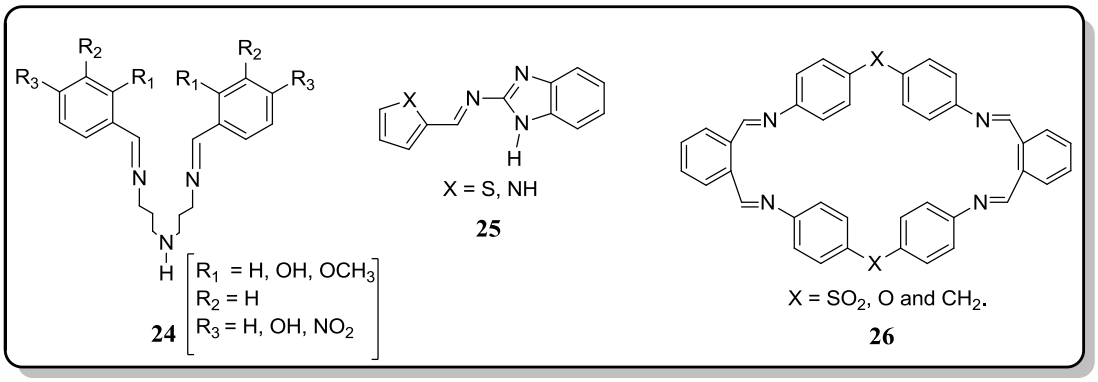


Figure 4.10 3, 3′-diaminodipropylamine and benzaldehyde derived, heterocyclic and macrocyclic Schiff bases

Schiff base copper complexes are well known for their extensive range of biological applications.[36-40] A number of copper complexes containing Schiff bases have been tested for their antimicrobial[41-45] and DNA cleaving activities.[46-50] Ferrocene-based amino acid reduced Schiff base ternary copper(II) complexes (**27**) of phenanthroline bases were synthesized (**Figure 4.11**) and tested towards their DNA cleaving ability. The complexes showed efficient DNA binding affinity and significant DNA cleavage activity in red light. Substantial role of the ferrocene moiety in enhancing the DNA photocleavage activity was also observed in comparison to the mononuclear copper(II) complex.[51] Reddy *et al.* synthesized two ternary copper(II) complexes (**28**, **29**) of Schiff base with neutral coligands 1, 10 phenathroline and 2, 2′ bipyridine (**Figure 4.11**). The absorption, fluorescence spectroscopy and viscosity measurements

confirmed an intercalative mode of interaction of both the complexes with calf thymus DNA (ct-DNA). Both the complexes cleaved DNA hydrolytically and the DNA binding and cleavage ability of phenanthroline system (**28**) was higher than the bipyridine system (**29**).[52]

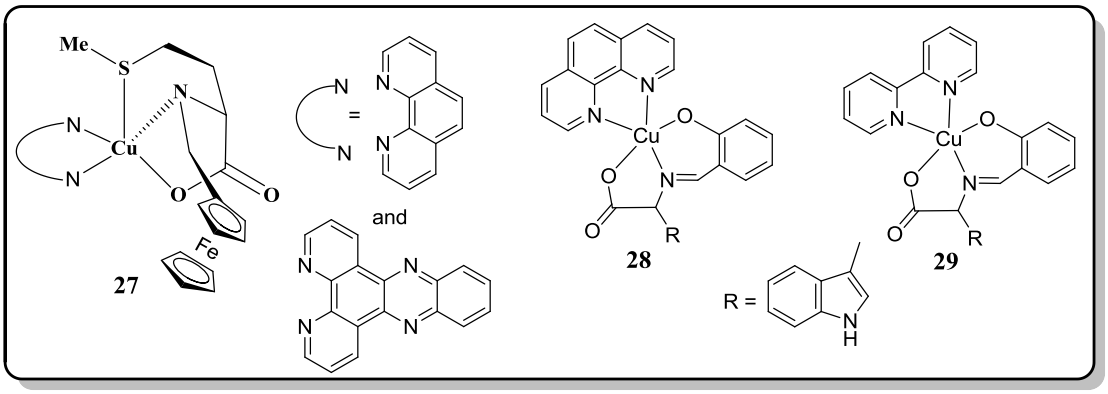


Figure 4.11 Ferrocene appended ternary amino acid and phen/bipy based Schiff base copper(II) complexes

Karipcin and co-workers prepared tetradentate diimine-dioxime ligand based mononuclear and heterodinuclear copper(II) complexes (**30**, **31**) and screened them towards their biological activities (**Figure 4.12**). The interaction of the complexes and DNA was investigated by agarose gel electrophoresis. It was observed that both the homo and heterodinuclear copper complexes could effectively cleave the supercoiled pBR322 DNA to nicked and linear forms.[53] A copper(II) complex of Schiff base, derived from salicylaldehyde and 1,10-phenanthroline (**32**) was synthesized and screened for its biological activities (**Figure 4.12**). It was observed that the complex could bind to ct-DNA through an intercalative mode and showed effective cleavage activity in the absence and presence of reducer. The intrinsic binding constant K_b of the complex (1.66×10^4 M^{-1}) was calculated by absorption spectra and the linear Stern-Volmer quenching constant K_{sq} (3.05) was obtained from florescence spectroscopy. Furthermore the cleaving reaction rate constant k_1 of the complex was also assimilated from agarose gel electrophoresis and was found to be 2.0×10^{-4} s^{-1}.[54]

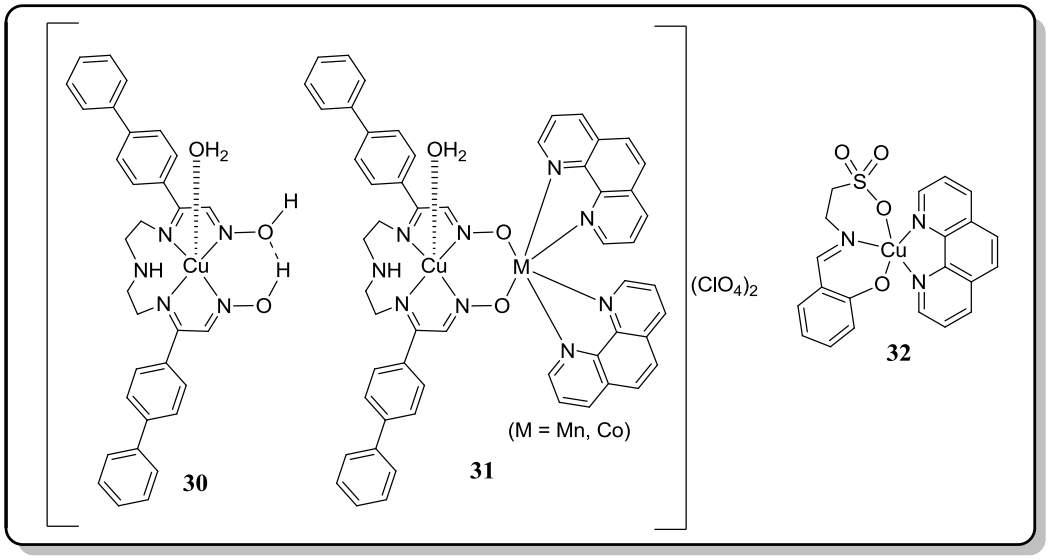


Figure 4.12 Diimine-dioxime ligand based mononuclear and heterodinuclear copper(II) complexes and 1,10-phenanthroline based copper(II) complex

Zinc is an important metal in the area of chemistry and biology, it constructs the active sites of many hydrolytic enzymes and acts as Lewis acid catalyst.[55, 56] It is the second most abundant trace element in bio-systems after iron and plays ubiquitous biological roles in living systems.[57] It helps in metabolism of RNA, DNA, signal transduction, regulating apoptosis and gene expression.[58, 59] Schiff base metal complexes are also known for their wide spectrum antimicrobial[60-62] and DNA cleaving activities.[63, 64] Various zinc(II) complexes have been screened for their biological applications.[65, 66] Hirota group studied DNA cleavage activities of *trans* and *cis* forms of azobenzene-linked photoactive dizinc complex (**33, 34**). The binding affinities of both the forms of the complex to DNA were due to the electrostatic interaction of positively charged complex with the negatively charged phosphate groups of DNA. However, the *cis* form showed more hydrolytic DNA cleavage activity as compared to the *trans* form (**Figure 4.13**).[67]

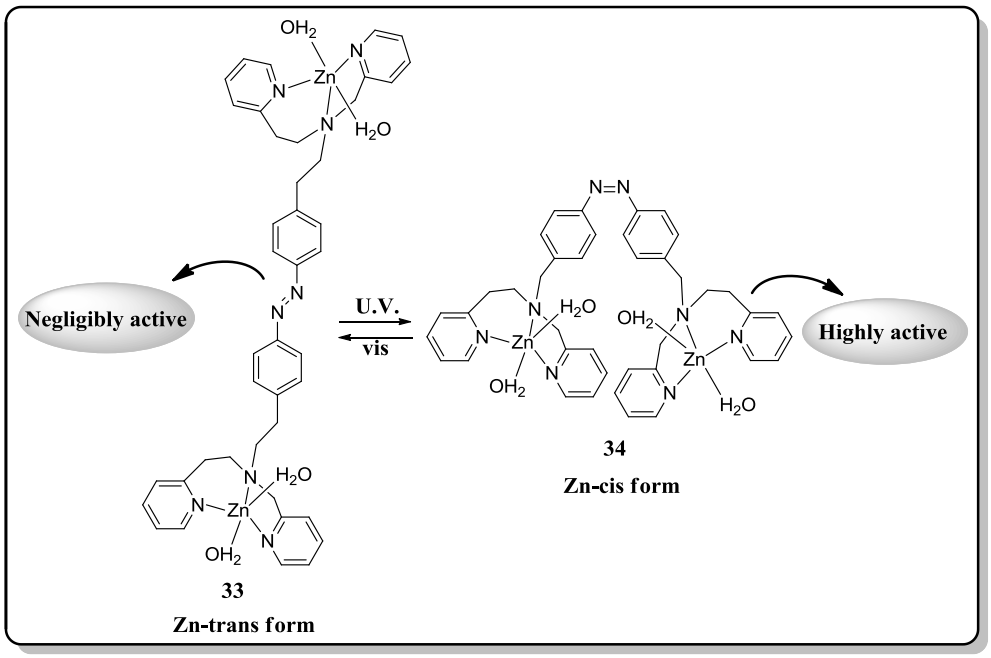


Figure 4.13 Hydrolytic DNA cleavage activity of azobenzene-linked dizinc complex

Antonella *et al*. reported substituent effect on DNA interaction of zinc-salophen complexes. Change in the electronic properties of the substituents at the 5,5′ positions, particularly the electron-withdrawing nitro substituents on the complexes (**35**) increased the electrophilic character of the metal center, leading to the strong interaction with plasmid DNA (**Figure 4.14**).[68] (E)-N-(pyridin-2-ylmethylene)arylamines were used as ligands to synthesize water soluble Zn(II) complexes **36**, **37** and **38** (**Figure 4.14**). The compounds exhibited *in vitro* tumour-inhibiting activities against the HeLa cell line. DNA binding of several transcription factors to its promoter sites, thus inhibiting gene transcription required for the biological activity of cells was interfered by the interaction of complexes with DNA.[69]

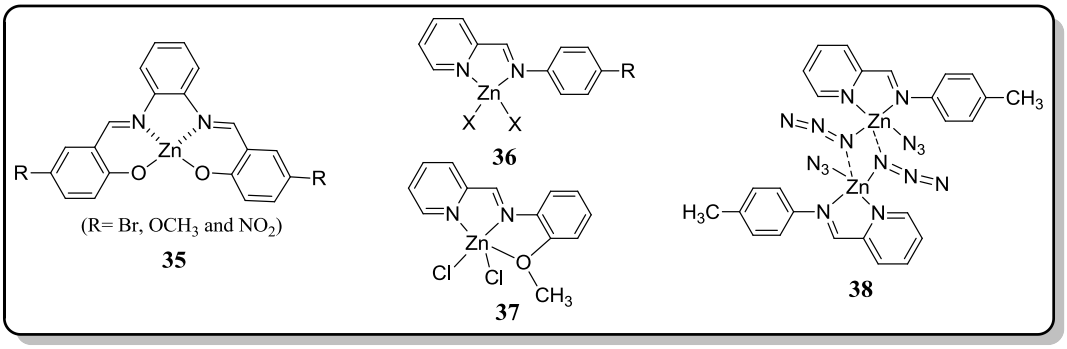


Figure 4.14 (E)-*N*-(pyridin-2-ylmethylene) arylamine based zinc(II) complexes

An acetato-bridged trinuclear Zn(II) complex was found to be efficient towards the cleavage of double stranded DNA. The complex also showed significant cytotoxicity against a human hepatocarcinoma cell line (HepG2).[70]

The present chapter deals with the biological applications of ionic liquid-supported Schiff base ligands and their copper and zinc complexes. The synthesized ligands were screened for their antimicrobial activities and were found active towards both the bacterial and fungal strains. The complexes were screened for its biological activity and it was observed that the complexes showed moderate to good antimicrobial activity with worthy DNA cleaving ability.

4.2 Results and discussion

4.2.1 Antimicrobial activity of ligands HL1-HL6

Bactericidal assay of all the synthesized compounds (**HL1-HL6**) was performed against common food pathogenic bacteria to evaluate their usability as efficient alternative to well-established chemo therapeutic agents. The zone of inhibition and minimum inhibitory concentration (MIC) values were measured to determine the antibacterial efficiency of the tested compounds. Gram positive and Gram negative bacterial strains were selected on the basis of their clinical importance. The compounds (**HL1-HL6**) exhibited moderate to good antibacterial activity against both Gram positive bacteria (**Table 4.1, 4.2 and Figure 4.1**).

Table 4.1 Zone of inhibition and minimum inhibitory concentration (MIC) values of compounds against Gram positive bacteria

Compound	*B. cereus*		*S. aureus*		*P. putida*	
	Zone of inhibition (mm)	MIC (mg mL^{-1})	Zone of inhibition (mm)	MIC (mg mL^{-1})	Zone of inhibition (mm)	MIC (mg mL^{-1})
HL1	**11**	**128**	**13**	**64**	**13**	**64**
HL2	10	>128	11	128	11	128
HL3	10	128	11	128	10	>128
HL4	*	>128	*	>128	*	>128
HL5	10	>128	12	64	10	>128
HL6	11	>128	11	128	10	>128

*:No activity was observed.

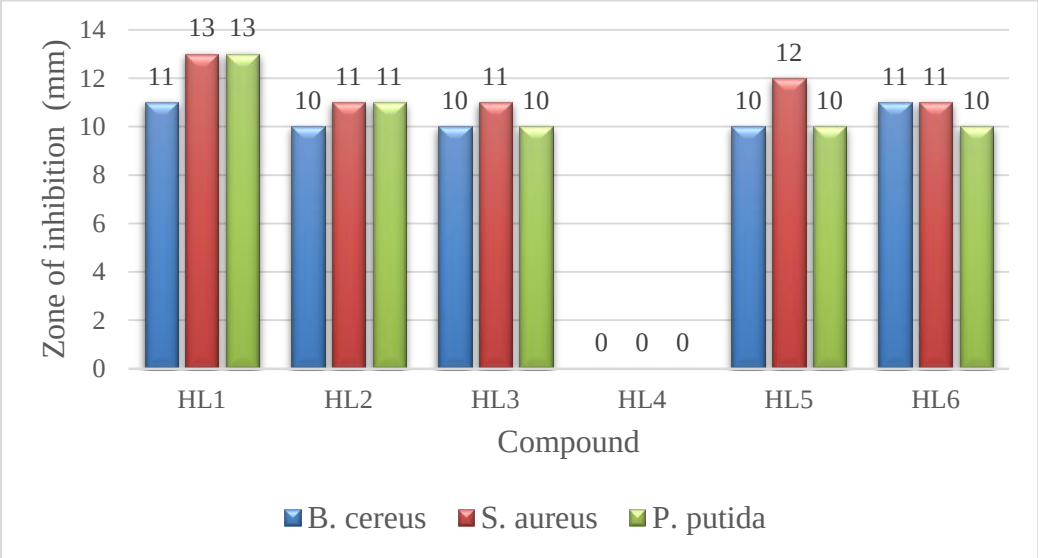


Figure 4.15 Zone of inhibitionvalues of compounds against Gram positive bacteria

Table 4.2 Zone of inhibition and minimum inhibitory concentration (MIC) values of compounds against Gram negative bacteria

Compound	*E. coli*		*K. pneumoniae*		*S. typhimurium*	
	Zone of inhibition (mm)	MIC (mg mL^{-1})	Zone of inhibition (mm)	MIC (mg mL^{-1})	Zone of inhibition (mm)	MIC (mg mL^{-1})
HL1	**11**	**128**	**12**	**64**	**11**	**64**
HL2	*	>128	*	>128	*	>128
HL3	*	>128	*	>128	*	>128
HL4	*	>128	*	>128	*	>128
HL5	*	>128	*	>128	*	>128
HL6	*	>128	*	>128	*	>128

*:No activity was observed.

This may be due to the interactions between peptidoglycan component of Gram positive cells and compounds which leads to disruption of cell wall resulting in cell death. Out of all the tested compounds, only **HL1**showed inhibition of both Gram positive and Gram negative bacteria, whereas **HL4** did not show any inhibition for both bacterial groups. Except **HL1**, all the compounds were found to be insensitive against the tested gram negative bacterial strains. All the synthesized compounds (**HL1-HL6**) were screened for *in vitro* antifungal activity. **Table 4.3**

shows zone of inhibition (**Figure 4.16**) and MIC values for the tested pathogenic fungal species. Similar to the antibacterial activity, compound **HL1** was found to exhibit broad spectrum antifungal activity against all the tested fungi.

Table 4.3 Zone of inhibition values of compounds against various tested fungi

Compound	*A. flavus*		*A. niger*		*F. oxysporum*		*C. acutatum*	
	Zone of inhibition (mm)	*MIC* (μg/mL)	*Zone of inhibition (mm)*	*MIC* (μg/mL)	*Zone of inhibition (mm)*	*MIC* (μg/mL)	*Zone of inhibition (mm)*	*MIC* (μg/mL)
HL1	15	64	16	64	15	64	15	64
HL2	14	128	13	128	13	>128	14	128
HL3	12	>128	16	64	15	64	14	128
HL4	13	128	13	>128	14	128	13	>128
HL5	13	>128	14	128	14	128	13	>128
HL6	14	128	18	32	14	128	15	64

The highest MIC value was observed with **HL6** followed by **HL1** and **HL3** against *A. niger* which was found to be the most sensitive fungal strain. Further studies are required to characterize the mode of action of these compounds against microbes.

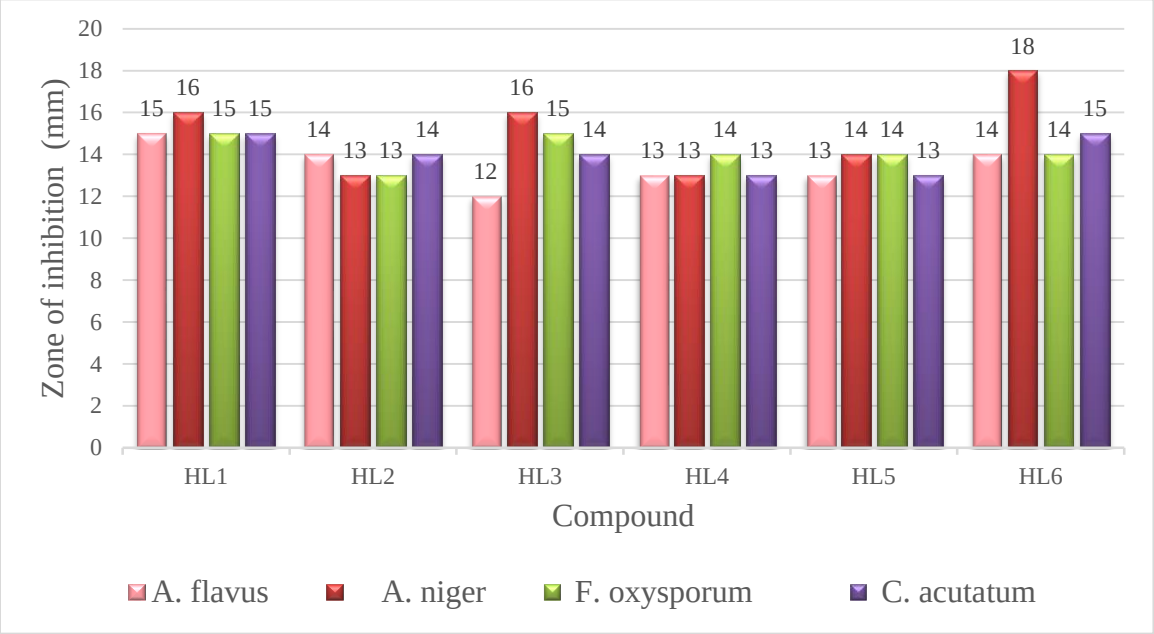


Figure 4.16 Zone of inhibition values of compounds against the tested fungi

4.2.2 Biological evaluation of $[Cu(L2)_2(L')_2]$

The zone of inhibition and minimum inhibitory concentration values were measured to evaluate the antibacterial and antifungal efficiency of **$[Cu(L2)_2(L')_2]$**. It exhibited moderate to good antibacterial (Table 4.4 and **Figure 4.17**) and antifungal activity (Table 4.5)

Table 4.4 Zone of inhibition and minimum inhibitory concentration (MIC) values of **$[Cu(L2)_2(L')_2]$** against bacteria.

Compound	**Bacteria**							
Code	*P. putida*		*Serratia marcescens*		*B. subtilis*		*S. aureus*	
	Zone of inhibition (mm)	*MIC* (μg/mL)	*Zone of inhibition (mm)*	*MIC* (μg/mL)	*Zone of inhibition (mm)*	*MIC* (μg/mL)	*Zone of inhibition (mm)*	*MIC* (μg/mL)
$[Cu(L2)_2(L')_2]$	17	6.25	19	3.125	18	12.5	18	6.25
Straptomycin	21	6.25	23	6.25	22	12.5	21	12.5

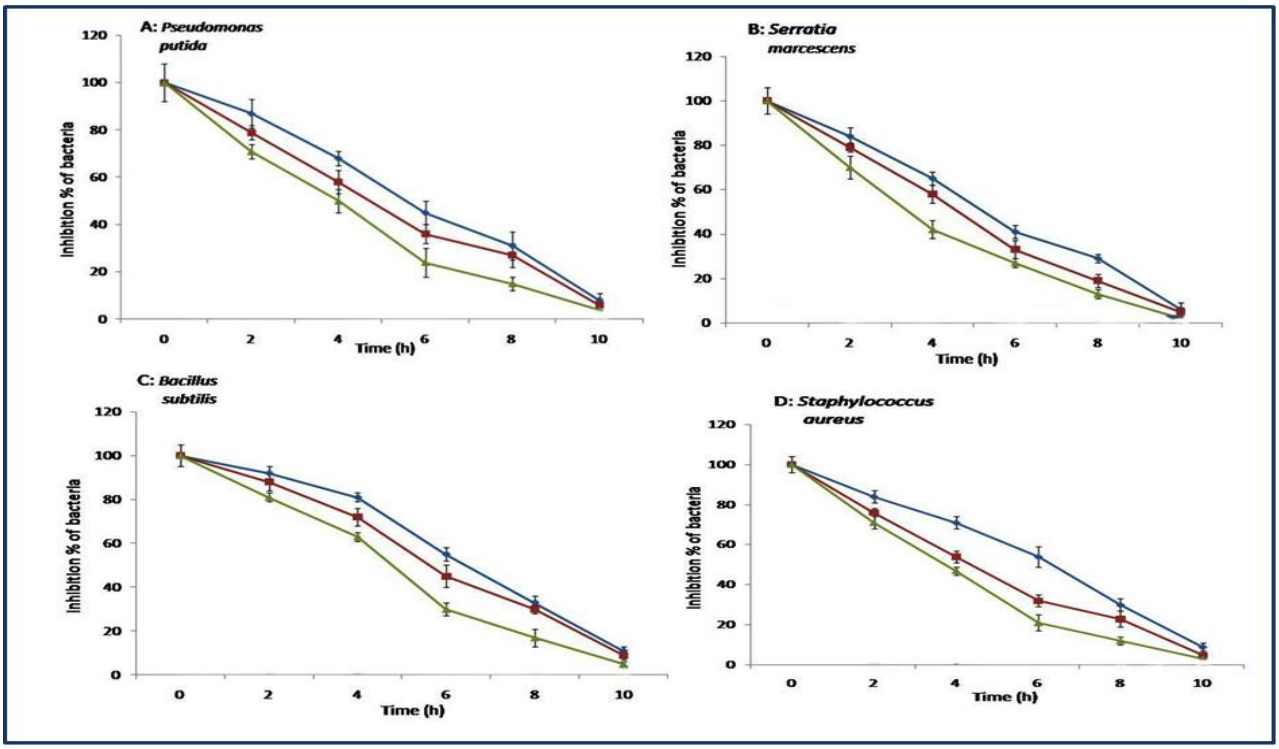


Figure 4.17 Zone of inhibition values of **$[Cu(L2)_2(L')_2]$** against bacteria

Table 4.5 Zone of inhibition and minimum inhibitory concentration (MIC) values of **$[Cu(L2)_2(L')_2]$** against fungi

Compound Code	**Fungi**							
	Candida albicans		*Aspergillus niger*		*Fusarium graminearum*		*Fusarium oxysporum*	
	Zone of inhibition (mm)	*MIC* (μg/mL)	*Zone of inhibition (mm)*	*MIC* (μg/mL)	*Zone of inhibition (mm)*	*MIC* (μg/mL)	*Zone of inhibition (mm)*	*MIC* (μg/mL)
$[Cu(L2)_2(L')_2]$	16	12.5	18	>12.5	18	6.25	17	6.25
Fluconazole	22	16	21	8	22	4	20	4

DNA cleavage activity of the compound was examined using pUC 19 plasmid as target. When circular plasmid DNA is run on gel electrophoresis, the fastest migration was observed for the supercoiled (form I). While after cleavage of one strand, the supercoil was relaxed to produce a slower moving nicked form (Form II). The DNA cleavage activity was monitored at variable temperature and solvents (**Figure 4.18**).

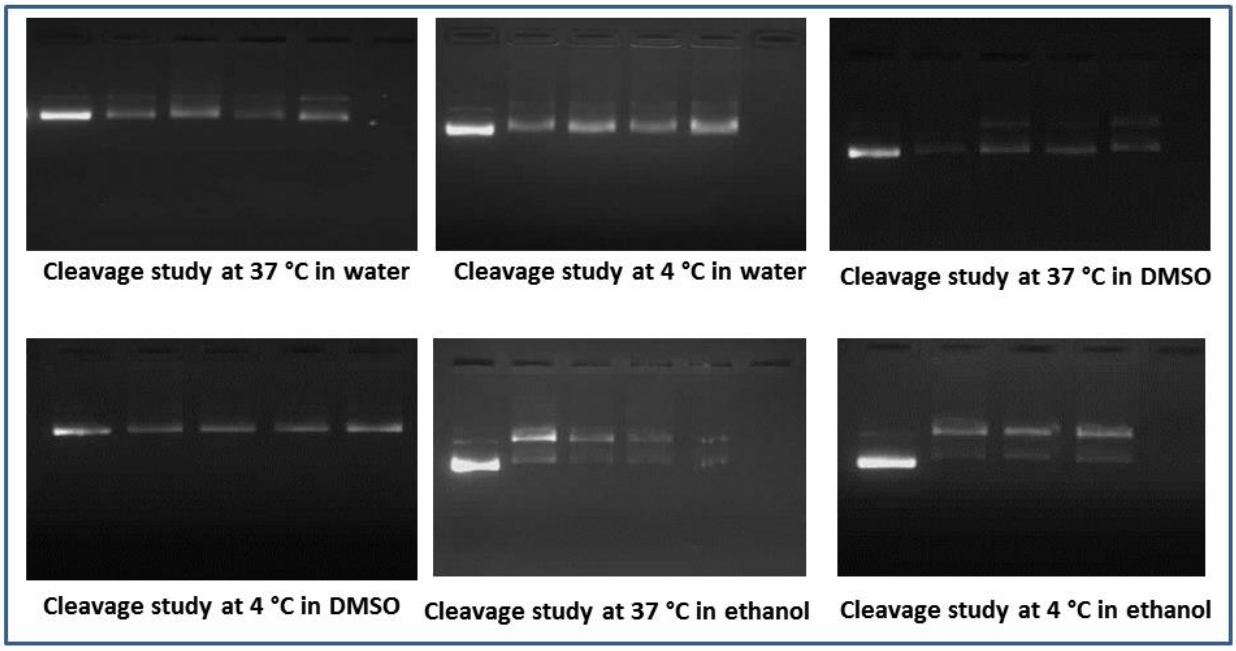


Figure 4.18 DNA cleavage activity of **$[Cu(L2)_2(L')_2]$** in variety of solvents at different temperatures

4.2.3 Biological evaluation of $Zn(L5)_2$

The zone of inhibition and minimum inhibitory concentration (MIC) values were measured to evaluate the antibacterial and antifungal efficiency of **$Zn(L5)_2$**. It exhibited moderate to good antibacterial activity against the tested bacterial strains and is comparable to standard drug. The maximum zone of inhibition was 18 mm in case of Gram +ve bacteria (MIC value of 12.5 μg/mL), whereas it was 19 mm against the tested Gram –ve bacterial strains (**Figure 4.19**) (MIC value in range of 12.5 to 6.25 μg/mL) (Table 4.6).

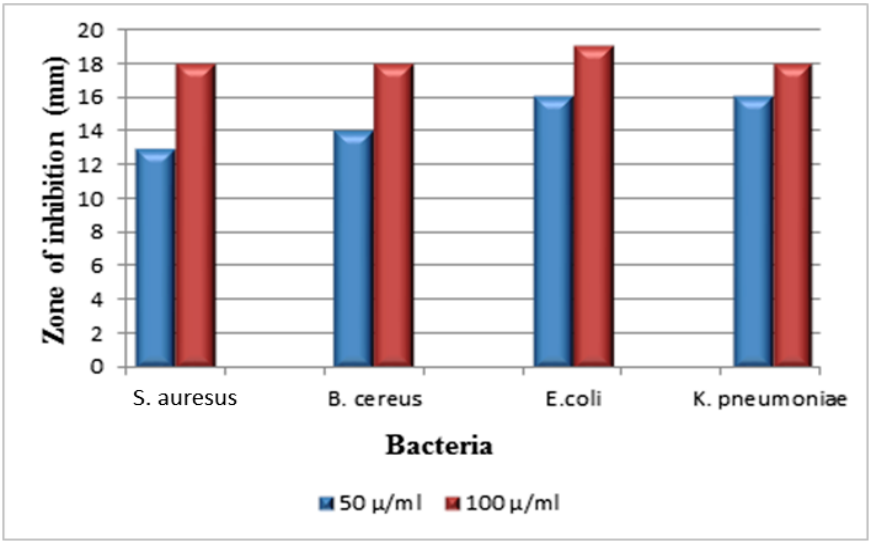


Figure 4.19 Zone of inhibition values of **$Zn(L5)_2$** against bacteria

Table 4.6 Zone of inhibition and minimum inhibitory concentration (MIC) values of **$Zn(L5)_2$** against bacteria

Compound	Gram +ve						Gram –ve					
	S. auresus			*B. cereus*			*E.coli*			*K. pneumoniae*		
	Zone of inhibition (mm)		*MIC* (μg/mL)	*Zone of inhibition (mm)*		*MIC* (μg/mL)	*Zone of inhibition (mm)*		*MIC* (μg/mL)	*Zone of inhibition (mm)*		*MIC* (μg/mL)
	50μg/Ml	100μg/mL		50μg/mL	100μg/mL		50μg/mL	100μg/mL		50μg/mL	100μg/mL	
$Zn(L5)_2$	13	18	>25	14	18	50	16	19	25	16	18	>25
Chloram-phenicol	28	33	12.5	29	35	12.5	27	31	>12.5	30	34	>6.25

Zn(L5)$_2$ was active in the range of 25-50 μg/mL to inhibit the mycelia growth of tested fungal strains (**Figure 4.20**), comparable to standard drug Amphotericin B (Table 4.7).

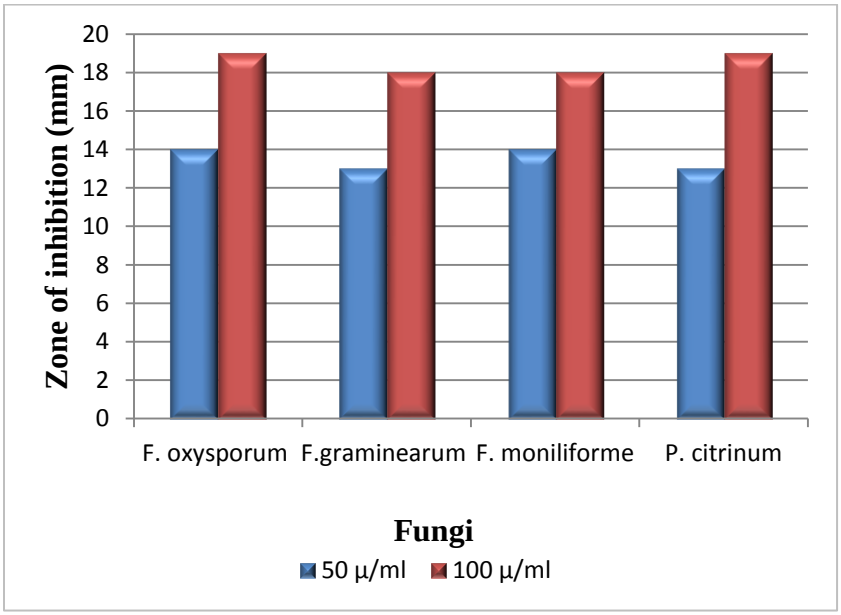


Figure 4.20 Zone of inhibition values of **Zn(L5)$_2$** against fungi

Table 4.7. Zone of inhibition and minimum inhibitory concentration (MIC) values of **Zn(L5)$_2$** against fungi

Compound	*F. oxysporum*			*F.graminearum*			*F. moniliforme*			*P. citrinum*		
	Zone of inhibition (mm)		*MIC* (μg/mL)	*Zone of inhibition (mm)*		*MIC* (μg/mL)	*Zone of inhibition (mm)*		*MIC* (μg/mL)	*Zone of inhibition (mm)*		*MIC* (μg/mL)
	50μg/mL	100μg/mL		50μg/mL	100μg/mL		50μg/mL	100μg/mL		50μg/mL	100μg/mL	
Zn(L5)$_2$	14	19	50	13	18	>25	14	18	50	13	19	25
Ampho-tericin B	25	28	25	24	27	25	25	30	>25	24	28	>12.5

Agarose gel electrophoresis was used to detect the molecular weight of DNA as well as to confirm the conformational changes upon cleavage. DNA cleavage activity of the **Zn(L5)$_2$** was examined using pUC19 plasmid as target. When circular plasmid DNA is run on gel electrophoresis, the fastest migration will be observed for the supercoiled (Form I). While after

cleavage of one strand, the supercoil will relax to produce a slower moving nicked form (Form II). It was observed that amount of cleaved DNA increases as the concentration of **$Zn(L5)_2$** increases from 10-40 μg (**Figure 4.21**).

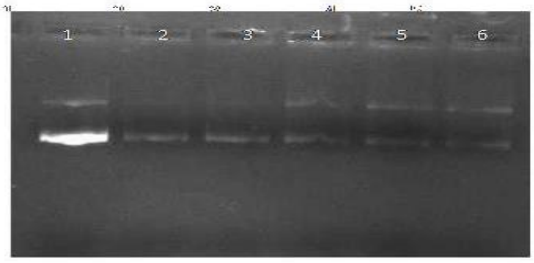


Figure 4.21 Concentration dependent DNA cleavage. Lane 1 control DNA, Lane 2, 3, 4, 5, 6 at concentration 10, 20, 30, 40, 50 μg respectively

Similarly time course of pUC19 DNA cleavage (**Figure 4.22**) reveals the more transformation from form (I) to form (II). However absence of linear form (III) of DNA agreed with the result observed by Mao *et al.*[71] using Zn^{2+} complexes.

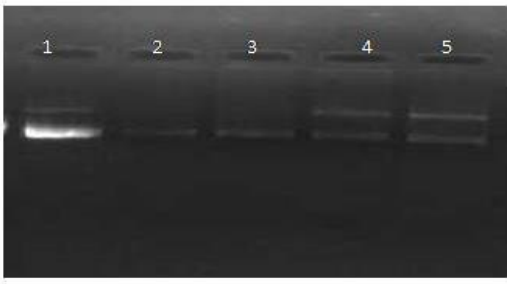


Figure 4.22 Time dependent DNA cleavage. Lane 1. Control DNA, Lane 2, 3, 4, 5 with the incubation time 1/2h, 1h, 1.5h, 2h respectively

4.3 Experimental section

4.3.1 *In vitro* antibacterial assay of ligands

Bactericidal assay of the synthesized compounds (**HL1-HL6**) was tested against common food pathogenic bacteria. The bacterial strains included Gram-positive *Bacillus cereus* (MTCC 430), *Staphylococcus aureus* (MTCC 96), *Pseudomonas putida* (MTCC 102) and Gram-negative

Escherichia coli (MTCC 1652), *Klebsiella pneumoniae* (MTCC 432) and *Salmonella typhimurium* (MTCC 98). All the cultures were purchased from Microbial Type Culture Collection (MTCC), IMTECH, India and revived as per suggested guidelines using standard microbiological methods. The cultures were maintained and sub-cultured on nutrient agar medium (HiMedia, India).

In vitro antibacterial activities were studied using the disc diffusion method[72] using semi-solid agar medium in Petri dishes at 128 μg mL^{-1} concentration for all the compounds with DMSO as a solvent. For this purpose, Mueller-Hilton (HiMedia, India) agar medium was prepared and sterilized by autoclaving at 121 °C at 15 psi for 15 min. Medium was poured into sterile Petri dishes (90 mm diameter) under aseptic conditions using laminar air flow chamber. After the solidification of medium, the suspension of the test organism (10^6 cfu mL^{-1}) was swabbed onto the individual agar media plates using a sterile glass spreader. A sterile disc (9 mm diameter) impregnated with compound was placed over media surface and the plates were incubated at 37 °C for 18-24 h under dark conditions. Negative controls (DMSO) were included to confirm that the solvent had no effect on the antibacterial activity. Positive controls (chloramphenicol, 0.03 mg mL^{-1}) were included to confirm the susceptibility of test organisms. Three replicates were maintained for each compound and their mean values were calculated.

4.3.2 *In vitro* antifungal assay of ligands

In vitro antifungal activity of the synthesized compounds was determined by standard agar well diffusion method[73] at 128 μg mL^{-1} concentration for all the compounds. Fungal strains used were *Aspergillus niger* (MTCC 282), *Aspergillus flavus* (MTCC 6674), *Fusarium oxysporum* (MTCC 6045), *Colletotrichum acutatum* (MTCC 2247) and were procured from MTCC, IMTECH, India. Autoclaved Potato Dextrose Agar (PDA) medium (Hi-media, India) was poured into sterile Petri dishes (90 mm diameter) under aseptic conditions in a laminar air flow chamber. Medium was allowed to solidify and then inoculated with 100 μl of 3 days old axenic fungal broth culture. After inoculation, wells of 9 mm diameter were prepared using sterile metallic borer. 100 μl of compound solution was poured in respective well and the plates were incubated at 28 °C for 4 days under dark conditions. DMSO and carbendazim (Methyl *1H*-benzimidazol-2-ylcarbamate, a standard broad spectrum antifungal antibiotic) were used as negative and positive

controls, respectively. Mean diameter of zone of inhibition was measured to determine the magnitude of antifungal activity. The experiment was performed in triplicates.

4.3.3 Biological assay of $[Cu(L2)_2(L')_2]$

Antibacterial activity

The synthesized complex was screened for antibacterial activity against the two gram (-) negative bacteria *Pseudomonas putida*, *Serratia marcescens* and two gram (+) positive bacteria *Bacillus subtilis*, *Staphylococcus aureus* following the standard protocol (NCCL 1993). Autoclaved nutrient-agar medium (Himedia, India) was poured into sterile glass petri-dishes (90 mm) under aseptic conditions using laminar air flow chamber. The tested pathogenic microorganisms were grown in nutrient-broth medium and suspension (100 μL) of each pathogenic microorganism (10^7 cfu mL^{-1}) was spread onto the individual media plates using a sterile glass spreader. After adsorption of bacterial suspension, well size of 6 mm diameter was made by the sterile metallic borer and the solution of working compound of different concentration (0, 3.125, 6.25, 12.5, 25, 50, 100 and 200 mg $mL^{-1)}$ was poured into the wells. The plates were incubated at 37 °C for 18-24 h under controlled condition of incubator (Labtech, India). The determination as to whether the organism is susceptible, intermediate or resistant was made by measuring the size of zone of inhibition in comparison with standard antibiotic. For the MIC assay, serial diluted samples of each compound (150 μL) were added in 96 well micro-trays. The same amount of test microorganism was added to obtain a final volume of 300 μL and incubated at 37 °C for 24 h. A control test with solvent DMSO at the same dilution was also used to ensure that the solvent had no effect on bacterial growth. DMSO was used as negative control. A broad spectrum antibiotic chloramphenicol effective against gram (+) and gram (-) bacterium was used as positive control. All assays were performed in duplicate sets.

Antifungal activity

The inhibition of fungal mycelium by the complex was performed against *Candida albicans*, *Aspergillus flavus*, *Fusarium graminearum* and *Fusarium oxysporum*. For the assay, each fungal strain was grown in freshly prepared sterile Potato dextrose broth (Himedia, India) medium at 28 °C for 5-6 days under dark conditions. Separate potato

dextrose agar (PDA) plate was made for each fungus and 100 μL of each fungal inoculum was uniformly spread. Following the adsorption of inoculums, well size of 6 mm diameter was prepared and compound solution was added in respective wells. For the MIC assay, glass tubes containing fungal inoculums were mixed with appropriate amount of compound to achieve the desired concentrations. The tubes were incubated at 28 °C for 5-6 days under dark conditions and carefully observed for the presence of turbidity. Fluconazole was used as positive control.

Cell viability assay

The effect of synthesized complex on bactericidal activity was evaluated by quantifying bacterial cell population after treating with different concentrations of complex. The concentration dependent curve was determined for compounds against log phase (1×10^7 cfu mL^{-1}) freshly grown cultures of tested bacterial strains. Bacterial culture was treated with compounds with 1x, 2x and 3x MIC for 2-10 h and the percentage in reduction of bacterial cell viability was measured by standard plate count assay. The number of cells in the control was assumed to be 100%. The decrease in cellular viability in treated samples was calculated with respect to the control. All treatments were performed in triplicate sets.

DNA cleavage assay

The DNA cleavage activity of the compound was studied by using 1% Agarose gel electrophoresis. Supercoiled plasmid pUC 19 DNA (2μL) was mixed with compound (100μmol) and the total volume was maintained up to 18μL with 50mM Tris buffer pH 7.4. The mixture was incubated at 4℃ and 37℃, different time intervals from 1-4 hrs using ethanol as a solvent. Before performing the gel electrophoresis the samples were mixed with loading buffer containing 25% bromophenol blue, 0.25% xylene cyanol and 30% glycerol. Each sample (5 μL) was loaded into 1 w/v % agarose gel for 40 min at 60 V in Tris-acetate-EDTA buffer (TAE) buffer. The gel was stained with ethidium bromide for 5 min after electrophoresis and them photographed under UV light in Gel doc system (Bio-rad)[71].

4.3.4 Biological activity of $Zn(L5)_2$

In vitro antibacterial assay of **$Zn(L5)_2$** was evaluated by agar-well diffusion method following the standard protocol.[74]The cultures of Gram positive bacteria *Staphylococcus aureus*, *Bacillus cereus* and Gram negative bacteria *Escherichia coli*, *Klebsiella pneumoniae* were freshly inoculated into sterile LB broth and suspension was adjusted to 1.5×10^8 CFU/mL. Autoclaved Muller–Hilton agar medium was poured into glass petri plates and swabbed with 100 μl inoculum of each organism. After the adsorption, well of 9 mm diameter was made by the sterile metallic borer. **$Zn(L5)_2$** was dissolved in DMSO and added to well at 50 and 100 μg/mL concentration using sterile pipettes. All the plates were incubated at 37 °C for 18-24 h. Antibacterial activity of **$Zn(L5)_2$** was evaluated by measuring the zone of inhibition with zone reader (Antibiotic zone scale). DMSO was used as a negative control to evaluate the solvent effect on the tested pathogens, whereas chloramphenicol (16 μg/mL) was used as a positive control. MIC values were evaluated at 6.25, 12.5, 25, 50, 100, and 200 μg/mL concentration using broth micro dilution method. A set of tubes containing Luria-Burtani broth medium with different concentrations of **$Zn(L5)_2$** were prepared. The tubes were inoculated with bacterial cultures 1.5×10^8 CFU/mL and incubated on a rotary shaker (180 rpm) at 37 °C for 18-24 h.

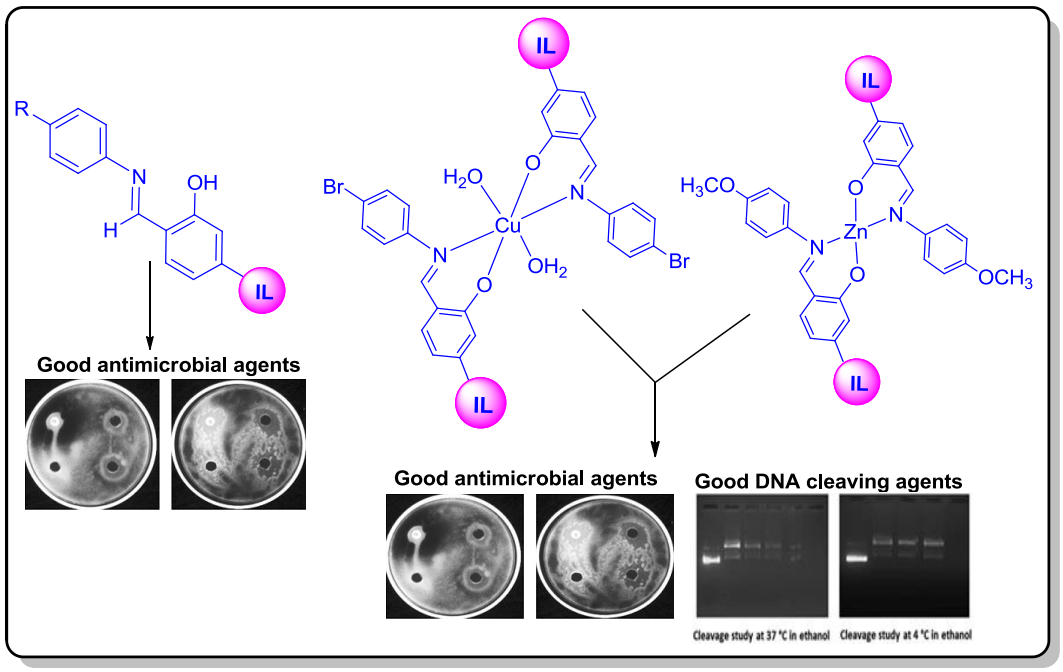
In vitro antifungal assay of **$Zn(L5)_2$** was determined by agar-well diffusion method against *Fusarium oxysporum, Fusarium graminearum, Fusarium moniliforme* and *Penicillium citrinum* at varying concentrations.[75] For the experimental work, potato dextrose agar was freshly prepared and autoclaved at 121 °C at 15 psi for 15 min. After cooling to room temperature, 100 μL of fungal inoculum was uniformly spread on the plate. Following the adsorption of inoculum, well of 9 mm diameter was prepared by the sterile metallic borer and the solution of **$Zn(L5)_2$** at 50 and 100 μg/mL concentration was added to the wells. Plates were incubated at 28 °C for 4 days under dark conditions. The experiments were performed in duplicates.

MIC assay of **$Zn(L5)_2$** was performed at 6.25, 12.5, 25, 50, 100, and 200 μg/mL concentrations. Tubes containing 10 mL of sterilized czapekdox broth medium was inoculated with 100 μl of freshly grown culture. Appropriate amount of **$Zn(L5)_2$**was added to achieve the desired concentrations. The tubes were incubated at 28 °C for 4 days under dark conditions and observed for the presence of visible turbidity. Broth without **$Zn(L5)_2$** was used as control.[71]

The DNA cleavage activity of **Zn(L5)$_2$** was studied using 1 % agarose gel electrophoresis. Supercoiled plasmid pUC19 DNA (2 μL) was mixed with varying concentrations of **Zn(L5)$_2$** (10 - 100 μM) and the total volume was maintained up to 18 μL with 50 *m*M Tris buffer (pH 7.4). The mixture was incubated at 37 °C. Similarly another set of mixture was incubated at different time intervals from 1-4 h using DMSO as a solvent. Before performing the gel electrophoresis, the samples were mixed with loading buffer containing 25% bromophenol blue, 0.25% xylene cyanol and 30% glycerol. Each sample (4 μL) was loaded into 1 *w*/*v* % agarose gel for 40 min at 60 V in Tris-acetate-EDTA buffer (TAE) buffer. The gel was stained with ethidium bromide for 5 min after electrophoresis and then photographed under UV light in Gel doc system (Bio-rad).[71]

4.4 Conclusion

In conclusion the present series of the ligands exhibited significant antimicrobial activity against both bacteria and fungi. The ionic liquid-tagged copper and zinc complexes showed good antimicrobial activity against both the bacterial and fungal strains. The DNA cleavage activity of the complexes was also deliberated and these were found highly efficient DNA cleaving agents. This analysis opens the avenue to utilize the compounds as broad spectrum chemotherapeutic agents. Further the scope of these studies can be extended to synthesize a library of ionic liquid tagged Schiff bases and metal complexes and to carry out their antimicrobial and DNA cleaving activities evaluation.



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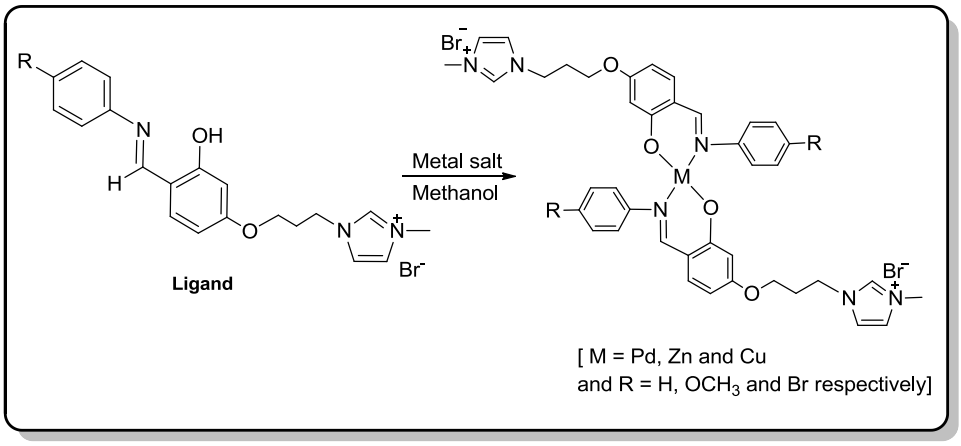
Chapter 5

Conclusion and Future Scope

5.1. Scope and Nature of present study

The promising diverse applications of ILs are due to their uncommon physical and chemical properties like high thermal stability, lack of inflammability, chemical stability, low volatility, and excellent solubility with many organic compounds. These properties of ionic liquids can be tailored by varying the combination of cations and anions. Due to high possibility for synthetic variations ILs are referred as designer fluids. Ionic liquids offer the advantage of both homogeneous and heterogeneous catalytic media. Transition metal complexes of Schiff bases are powerful catalysts for organic reactions, when Schiff base ligands are associated with the metal center, they can offer chemioselectivity, regioselectivity, or stereoselectivity under mild conditions. The current study combines all these aspects of ionic liquids, Schiff bases and transition metal complexes to explore the advanced applications of the resultant ionic liquid-tagged Schiff base metal complexes. In the present work we have synthesized six ionic liquid-tagged Schiff base ligands and some of their transition metal complexes (**Scheme 5.1 and 5.2**).



Scheme 5.1 Ionic liquid-tagged Schiff base ligands and their metal complexes

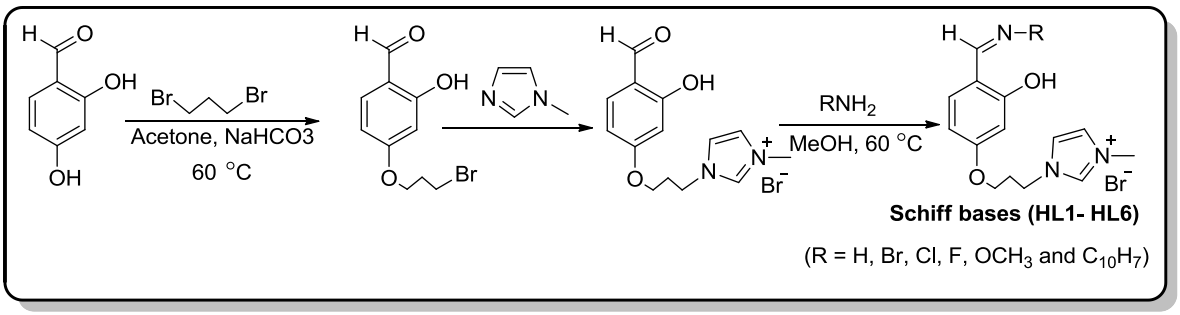
All the synthesized metal complexes are well characterized with the help of NMR, FT-IR, UV-visible spectroscopy, mass spectrometry and powder X-ray diffraction. The ligands and complexes are also analyzed by fluorescence spectroscopy, TCSPC, DSC and TGA. The thesis is divided into four chapters and the content description of these chapters is briefly discussed as follows:

Chapter 1

This chapter presents the general discussion about the ionic liquids and Schiff base metal complexes. The catalytic and biological based applications of these compounds have been explained thoroughly. Furthermore, the advantages of heterogeneous catalyst with ionic liquid-tag over the homogeneous counter parts are also discussed and literature surveys on the catalytic activity of these systems on the various organic transformations are presented. Beside this the reports based on biological and photophysical properties of these materials are also explained.

Chapter 2

This chapter deals with the materials, methodologies and characterization tools which are used for the synthesis and characterization of ionic liquid-tagged Schiff base ligands and some of their metal complexes. The concepts of characterization and analysis using NMR, Mass, FT-IR, EPR, UV-visible spectroscopy, cyclic voltammetry (C.V.) and powder X-ray diffraction, fluorescence spectroscopy, TCSPC, DSC and TGA is discussed. The second part of this chapter explains the synthesis, characterization and biological applications of novel ionic liquid-supported Schiff base ligands (Scheme 5.2). In most functionalized ionic liquids, quaternization of ring nitrogen by alkyl halide to produce 3-alkylimidazolium salt is done after attaching the functional group to imidazole at the *N*-1 position. These reactions are generally performed in a narrow region of temperature and solvent parameters due to competing side reaction of the alkylating reagent with the incorporated functional group. A novel approach has been designed for the synthesis of functionalized ionic liquids where this alkylation of functional group can be avoided. Using this strategy Schiff bases (**HL1-HL6**) were obtained in moderate yields and the nature of various substituents on the aromatic amines had no obvious effect on the yields.



Scheme 5.2 Synthesis of ionic liquid-tagged Schiff bases

Chapter 3

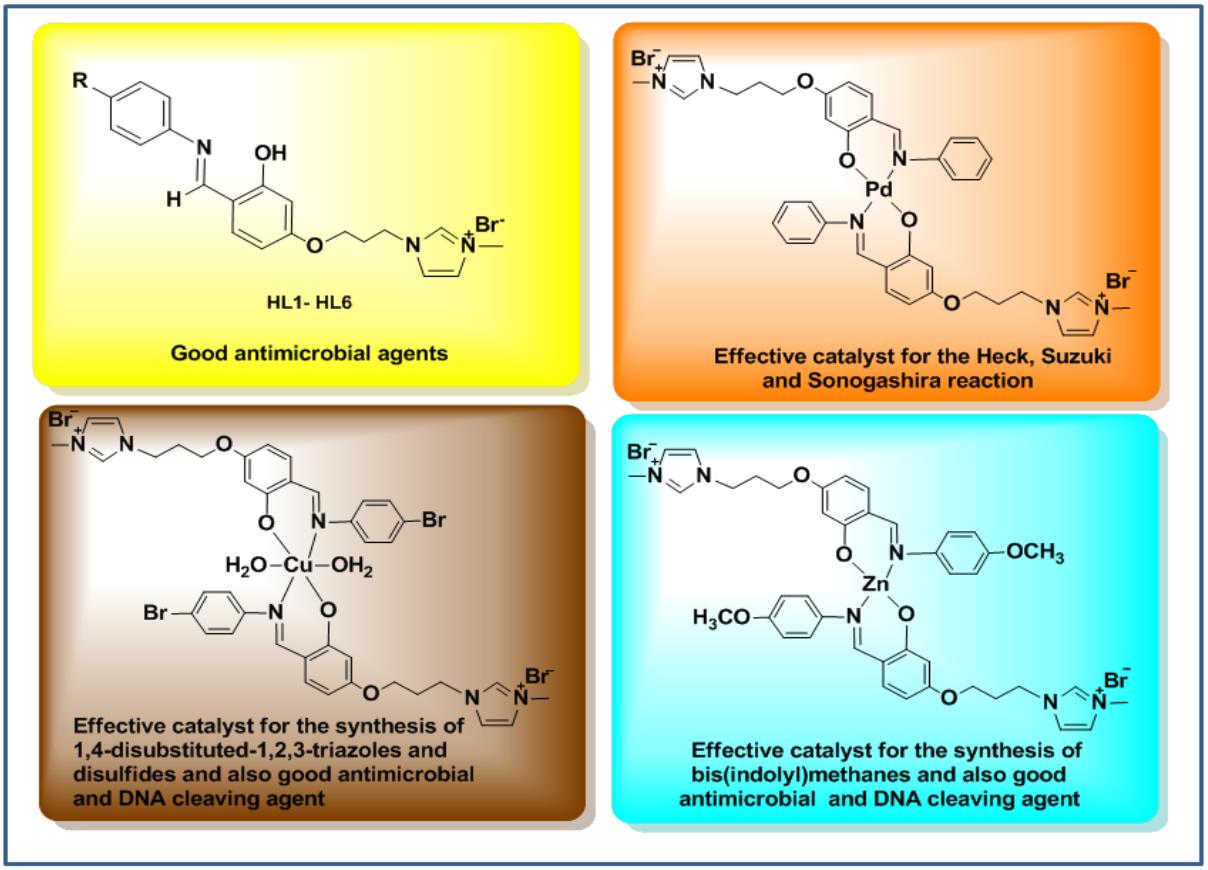
This chapter presents the synthesis, characterization and catalytic application of imidazolium ionic liquid-tagged Schiff base complex of palladium, copper and zinc. The ligands **HL1, HL2** and **HL5** were reacted with the respective metal salts (palladium acetate, copper acetate and zinc acetate) and the resultant complexes $\mathbf{Pd(L1)_2}$, $\mathbf{Cu(L2)_2(L')_2}$ and $\mathbf{Zn(L5)_2}$ were prepared. The synthesized complexes are moisture insensitive; highly stable under thermal and aerobic conditions. The palladium complex was screened for its catalytic applications in the Heck, Suzuki and Sonogashira cross coupling reaction in aqueous medium. The catalyst was found highly efficient for all the Heck, Suzuki and Sonogashira reactions without the aid of phase transfer catalyst or organic solvents in water. The reaction conditions for the palladium catalyzed coupling reactions are simple and are effective for more challenging substrates such as chlorides. Good to excellent yields, TONs and TOFs of the products were achieved and moreover the catalyst could be effectively recovered for many cycles without any significant loss in catalytic activity. The synthesized copper complex was screened for its catalytic applications in the synthesis of 1, 4- disubstituted 1,2,3-triazoles under aqueous conditions and in the formation of disulfide compounds from thiols under sonication. The catalyst was found highly efficient for both of the reactions. Good to excellent yields of the products were achieved and the catalyst was effectively recycled for up to 10 consecutive cycles in the synthesis of 1, 4- disubstituted 1,2,3-triazoles. The zinc complex was found to be a good catalyst for the reactions of aromatic aldehydes, and indole substrates in water to synthesize bis(indolyl)methanes.

Chapter 4

In this chapter the biological applications of the ionic liquid-tagged Schiff bases and their metal complexes were explained. The present series of the ligands exhibited significant antimicrobial activity against Gram +ve and Gram –ve bacteria and fungi. The ionic liquid-tagged copper and zinc complexes showed good antimicrobial activity against both the bacterial and fungal strains. The DNA cleavage activity of the complexes was also deliberated and these were found highly efficient DNA cleaving agents.

5.2. Overall Conclusion of Present Work

- Synthesis of ionic liquid-tagged Schiff base ligands and metal complexes (Pd, Zn and Cu) is achieved.
- Detailed characterization and analysis of the ligands and complexes have been carried out with the help of different characterization tools like NMR, Mass, IR, UV-Vis, fluorescence, EPR and time resolved spectroscopy, powder XRD, DSC, TGA and cyclic voltammetry.
- Ionic liquid-tagged Schiff base ligands have been synthesized and characterized. The synthesized ligands are found to be active antimicrobial agents towards selected bacterial and fungal strains.
- The catalytic activity of the synthesized ionic liquid-tagged palladium complex is explored towards the cross-coupling reactions and it has been observed that the complex showed excellent catalytic activity towards the Heck, Suzuki and Sonogashira reaction in aqueous medium. Good to admirable turn over numbers and turn over frequencies of the catalyst with excellent yields of the products are accomplished.
- The ionic liquid-tagged Schiff base copper complex has been synthesized and used as a catalyst for the synthesis of 1, 4- disubstituted 1,2,3-triazoles and disulfides under aqueous conditions. The complex is found highly efficient catalyst as good to excellent yields of the products are achieved. The complex has shown competent antimicrobial and DNA cleaving activity.
- An ionic liquid-tagged zinc complex is synthesized and its photo physical properties are investigated. The biological activities of the same complex have been investigated and the complex is found effective antimicrobial and DNA cleaving agent. The complex also acted as a good catalyst for the reactions of aromatic aldehydes, and indole substrates in water to synthesize bis(indolyl)methanes.



5.3. Future Scope

In the present thesis ionic liquid-tagged Schiff base ligands and their metal complexes have been synthesized and variety of applications has been studied. As per future scope is concerned, one can prepare a large number of parallel ionic liquid-tagged ligands following the established methodology. The synthesized ligands are expected to be important from chemical, biological, pharmaceutical and catalysis point of view. The same methodology for anti-bacterial and antifungal studies has been established and one can further look for their anti-inflammatory, analgesic, anti-diabetic and anti-cancerous properties. The synthesized metal complexes (Pd and Cu) with ionic liquid-tag can be used in a variety of other organic transformation such as Aldol reaction, Michael addition, Friedel craft reaction, Buchwald-Hartwig, Negishi and Hiyama coupling and many oxidation reactions. The synthesized zinc complex can be further used for photo physical applications. The antimicrobial and DNA cleaving activity of the synthesized complexes (Cu and Zn) can be further explored towards anti-inflammatory, anti- analgesic, anti-

diabetic and anti-cancerous properties. The same ligands can be complexed with other metals and metal complexes obtained can be explored for varied applications such as chemical, biological, pharmaceutical and catalysis.

Appendices

Appendix-A

Chapter 2 (section B)

Figure A01: ESI-MS spectrum of **HL1**

Figure A02: ^{1}H NMR and ^{13}CNMR spectra of **HL2**

Figure A03: ^{1}H NMR and ^{13}CNMR spectra of **HL3**

Figure A04: ^{1}H NMR and ^{13}CNMR spectra of **HL4**

Figure A05: ^{1}H NMR and ^{13}CNMR spectra of **HL5**

Figure A06: ^{1}H NMR and ^{13}CNMR spectra of **HL6**

Chapter 3 (section A)

Figure A07: MALDI-Mass spectrum of **Pd(L1)$_2$**

Chapter 3 (section B)

Figure A08: ^{1}H NMR and ^{13}CNMR spectra of **16ag'**

Figure A09: ^{1}H NMR and ^{13}CNMR spectra of **16ce'**

Figure A10: ^{1}H NMR and ^{13}CNMR spectra of **16cf'**

Figure A11: ^{1}H NMR and ^{13}CNMR spectra of **16de'**

Figure A12: ^{1}H NMR and ^{13}CNMR spectra of **16ee'**

Figure A13: ^{1}H NMR and ^{13}CNMR spectra of **16ef'**

Chapter 3 (section C)

Figure A14: MALDI-Mass spectrum of **Zn(L5)$_2$**

Figure A15: HRMS-Mass spectrum of **Zn(L5)$_2$**

Chapter 4

Figure A16: Antibacterial and antifungal activities of **Zn(L5)$_2$**

Chapter 2 (section B)

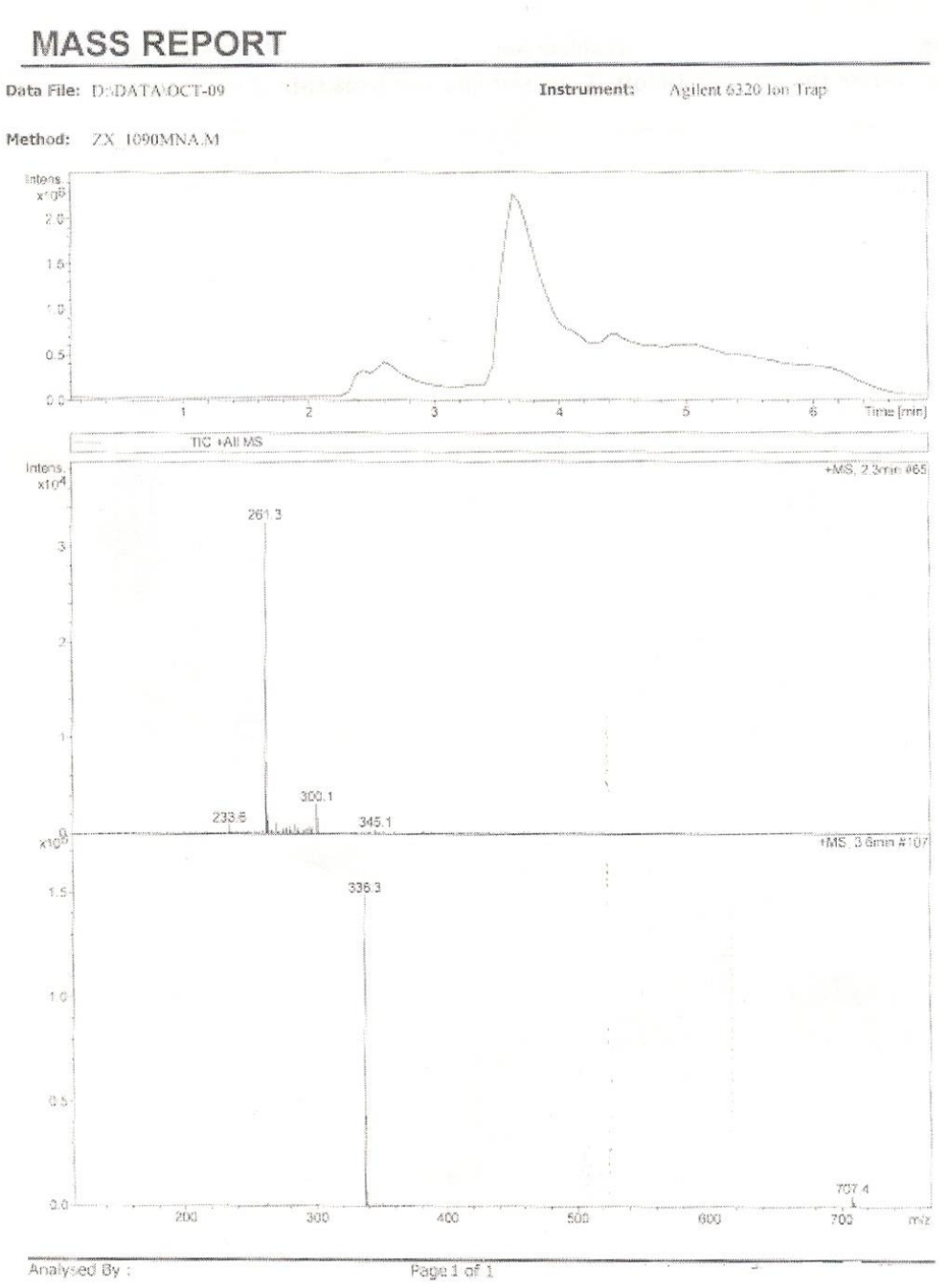


Figure A01: ESI-MS spectrum of **HL1**

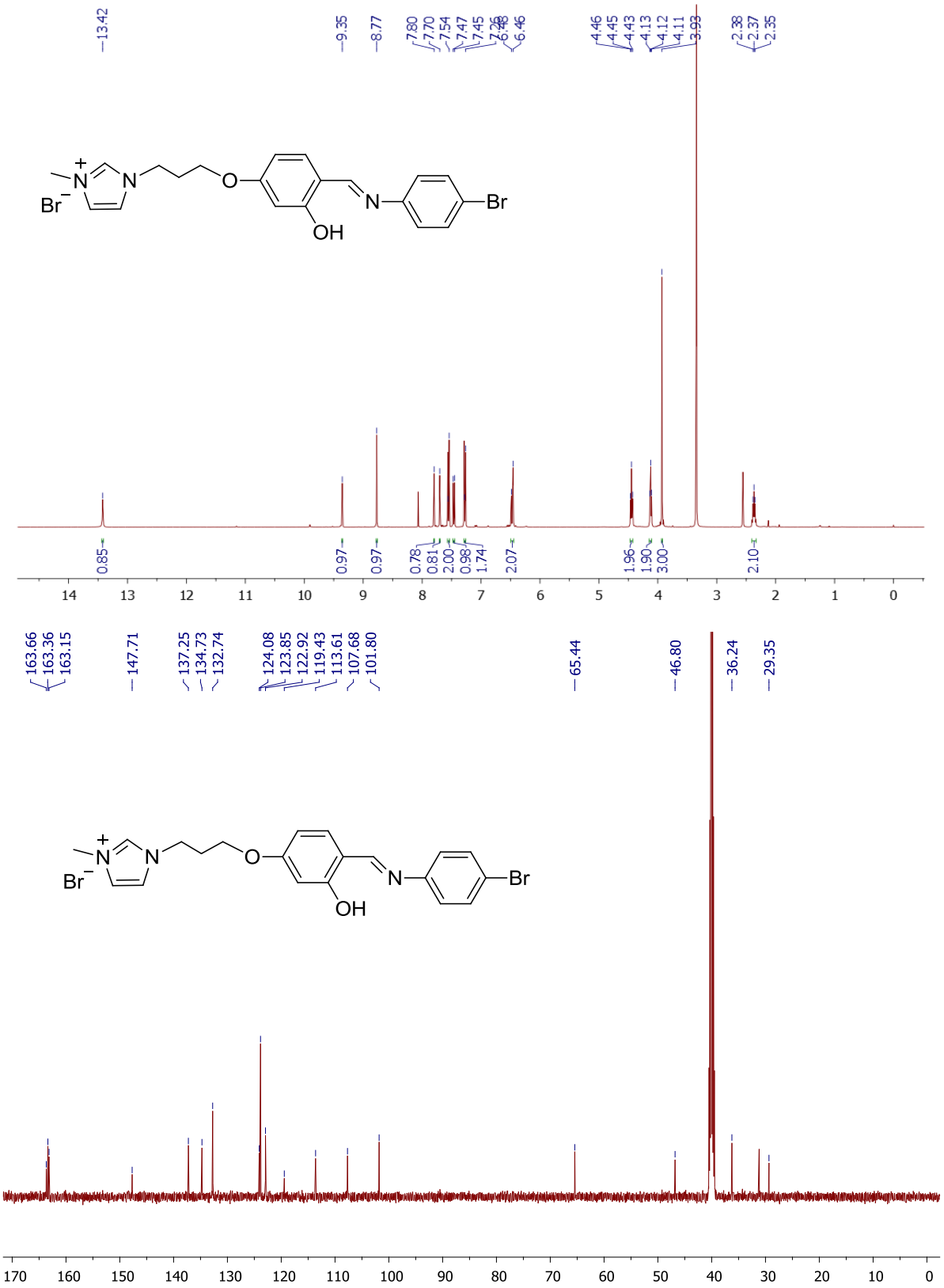


Figure A02: ^{1}H NMR and ^{13}CNMR spectra of **HL2**

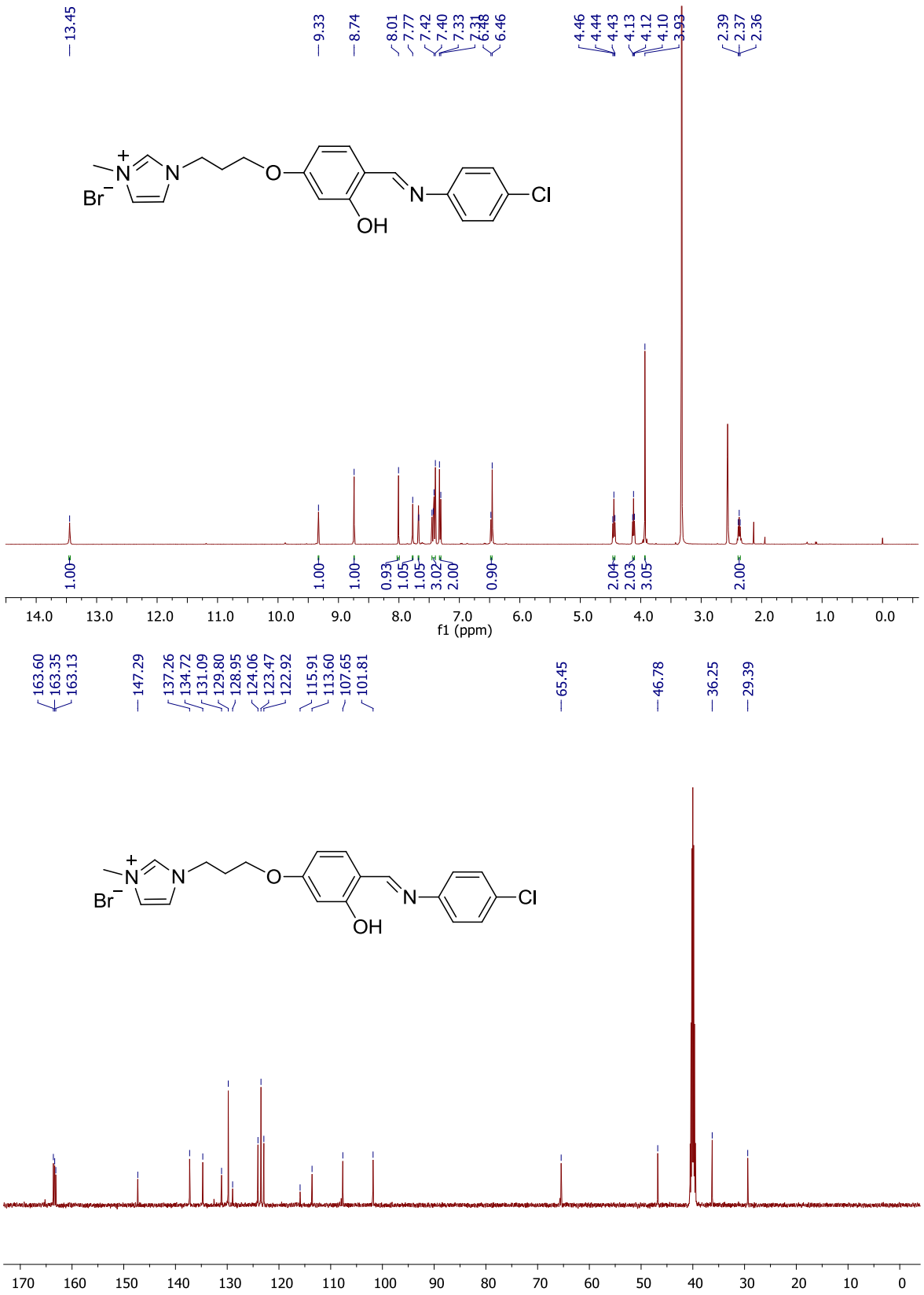


Figure A03: ^{1}H NMR and ^{13}CNMR spectra of **HL3**

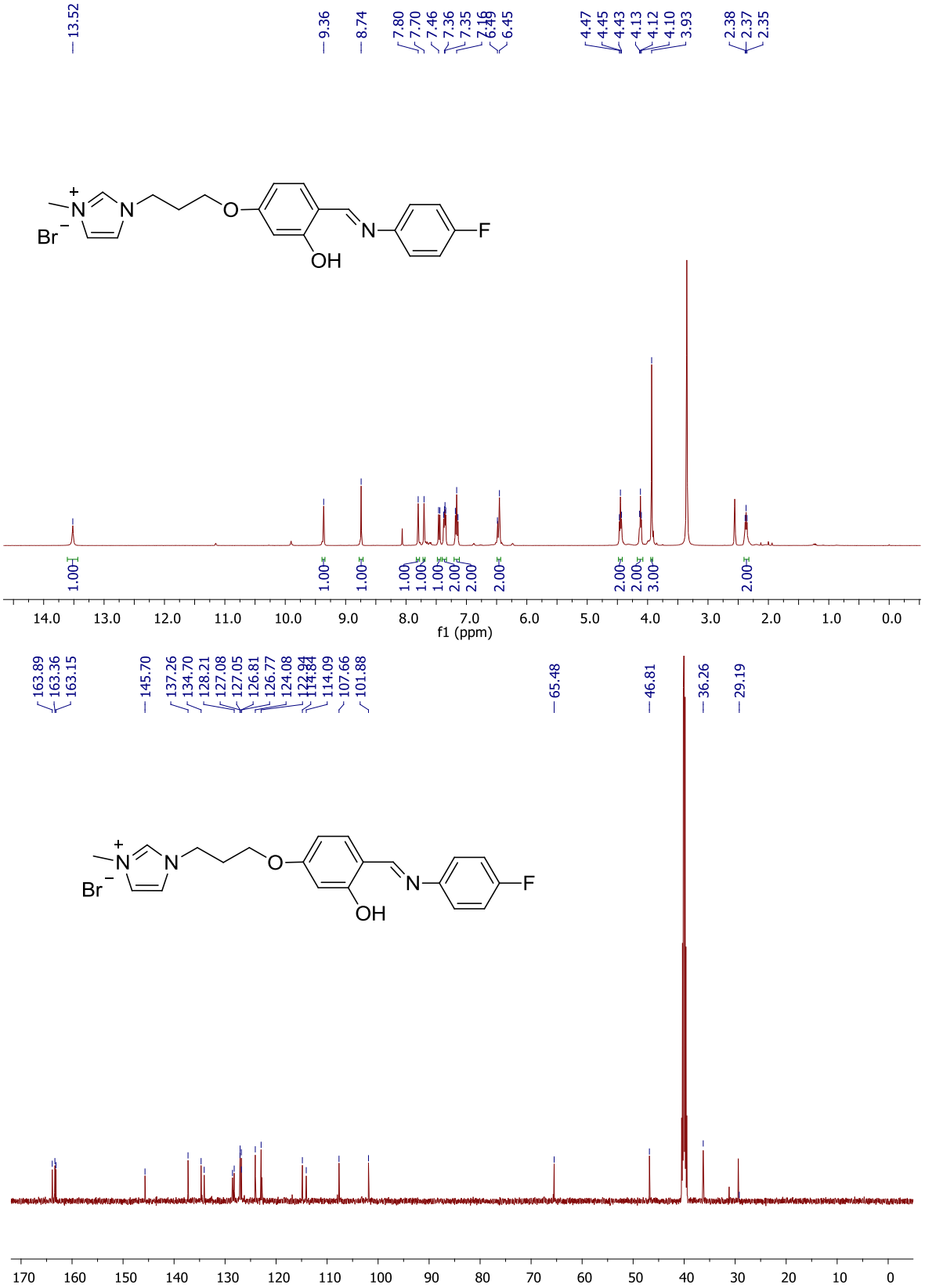


Figure A04: ^{1}H NMR and ^{13}CNMR spectra of **HL4**

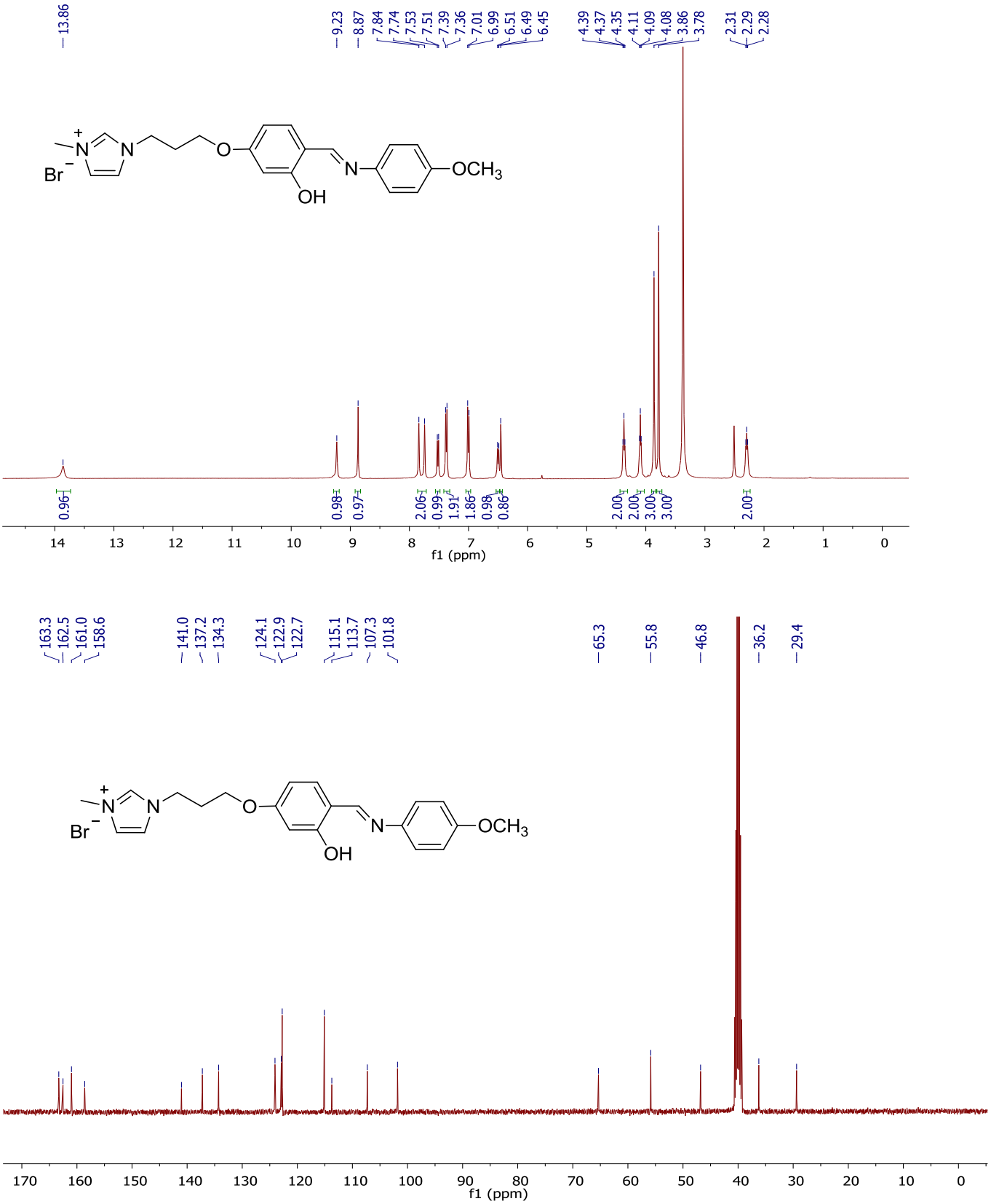


Figure A05: ^{1}H NMR and ^{13}CNMR spectra of **HL5**

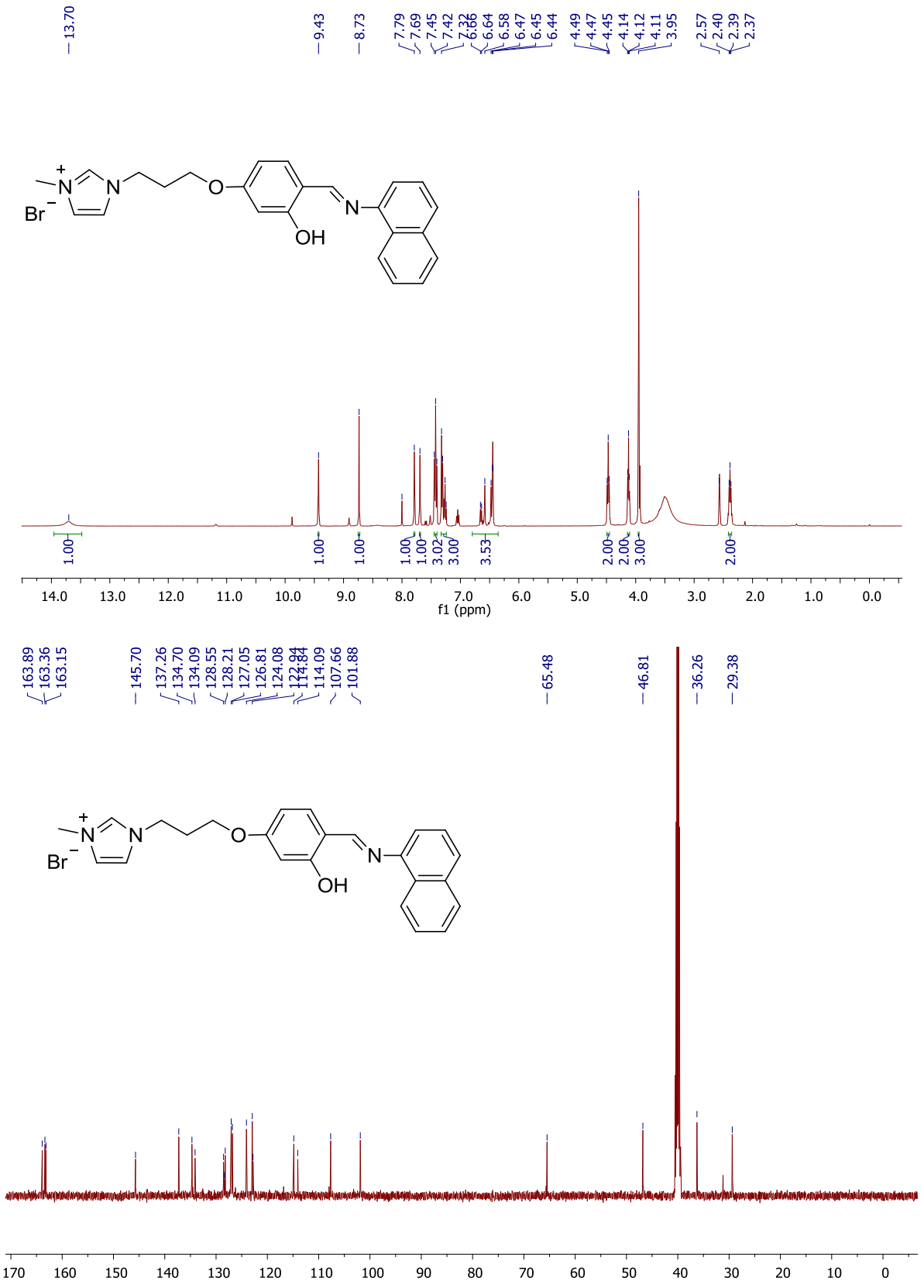


Figure A06: ^{1}H NMR and ^{13}CNMR spectra of **HL6**

Chapter 3 (section A)

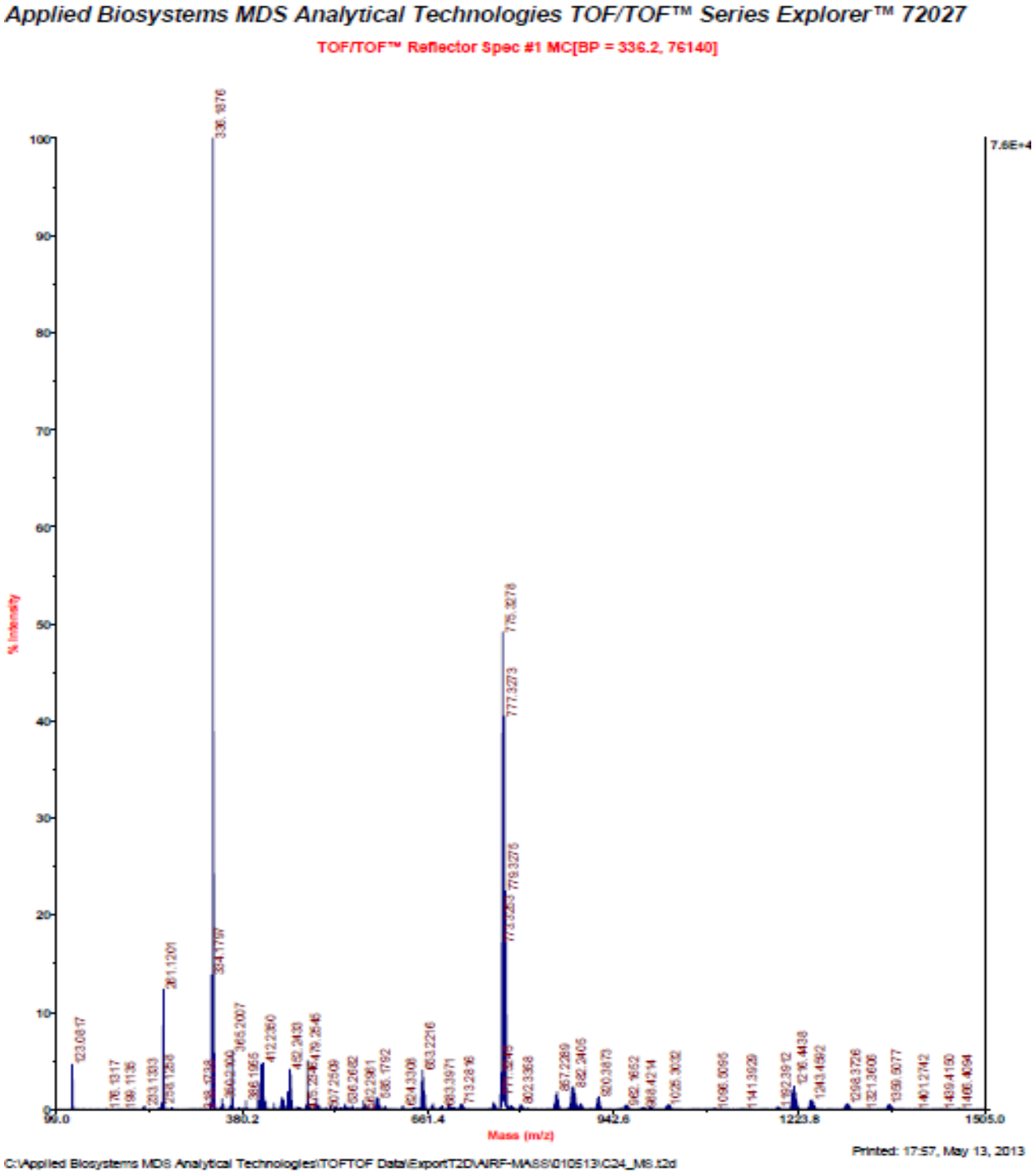


Figure A07: MALDI-Mass spectrum of **Pd(L1)$_2$**

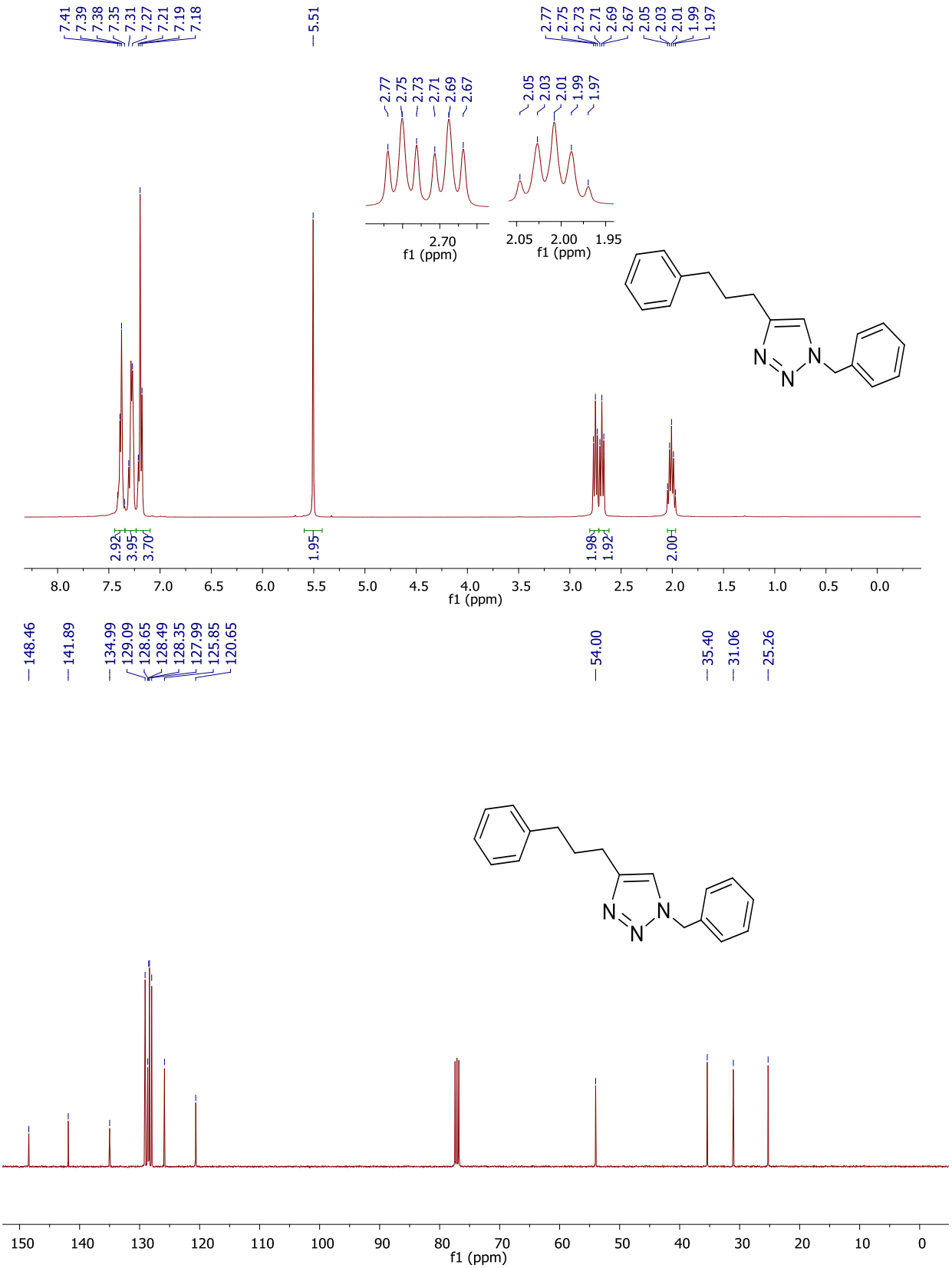


Figure A08: ^{1}H NMR and ^{13}CNMR spectra of **16ag'**

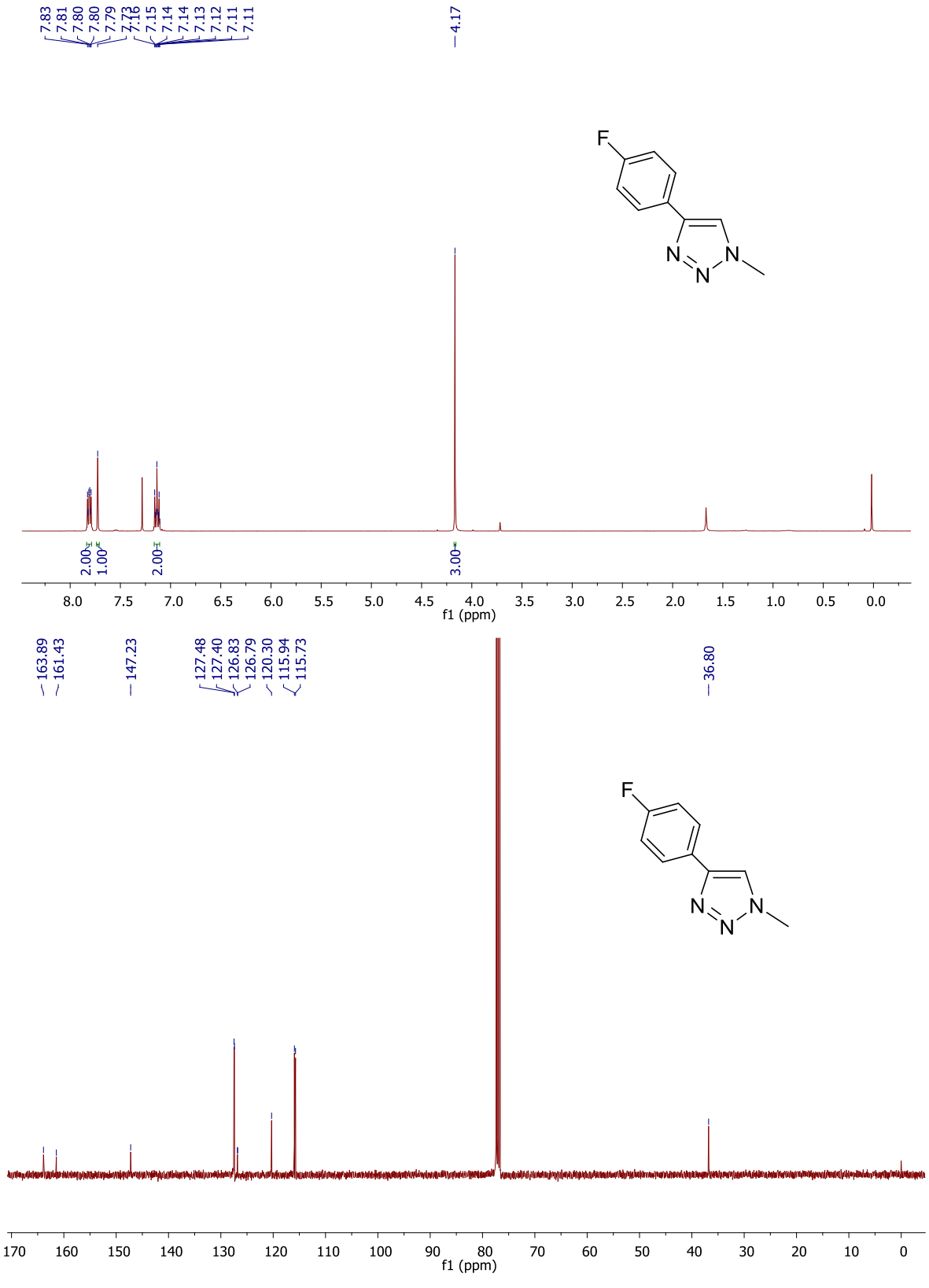


Figure A09: ^{1}H NMR and ^{13}CNMR spectra of **16ce'**

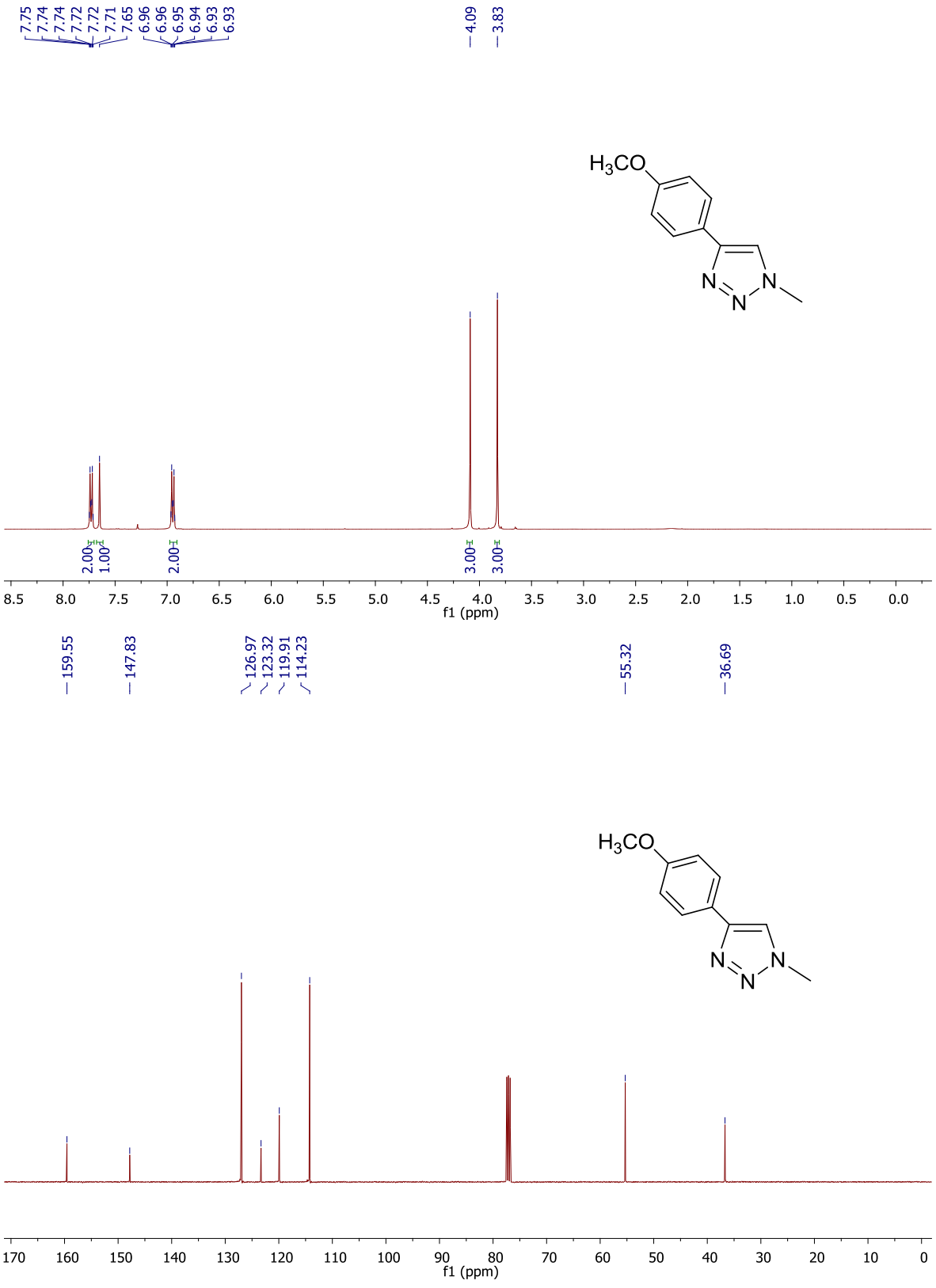


Figure A10: ^{1}H NMR and ^{13}CNMR spectra of **16cf'**

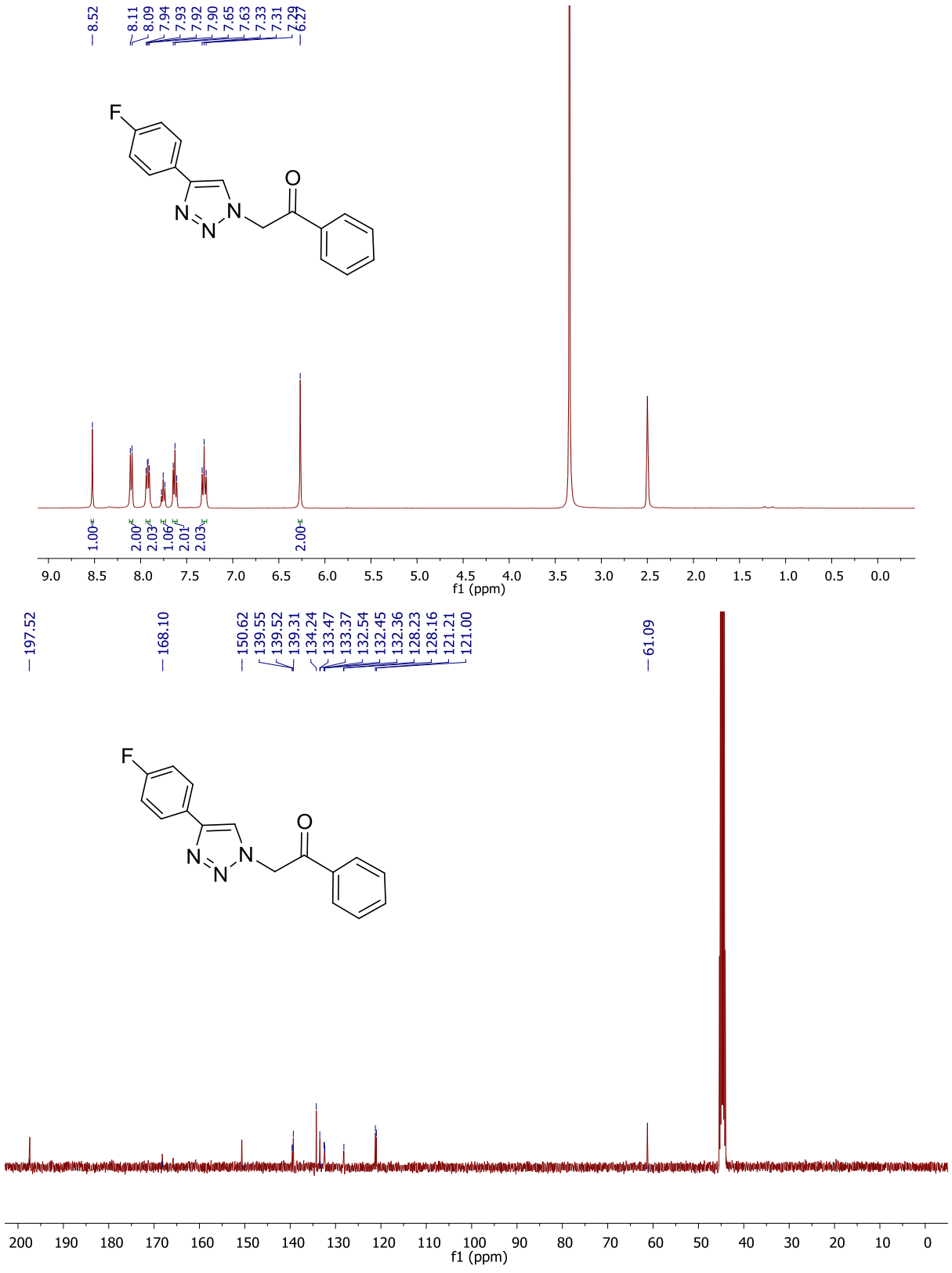


Figure A11: ^{1}H NMR and ^{13}CNMR spectra of **16de'**

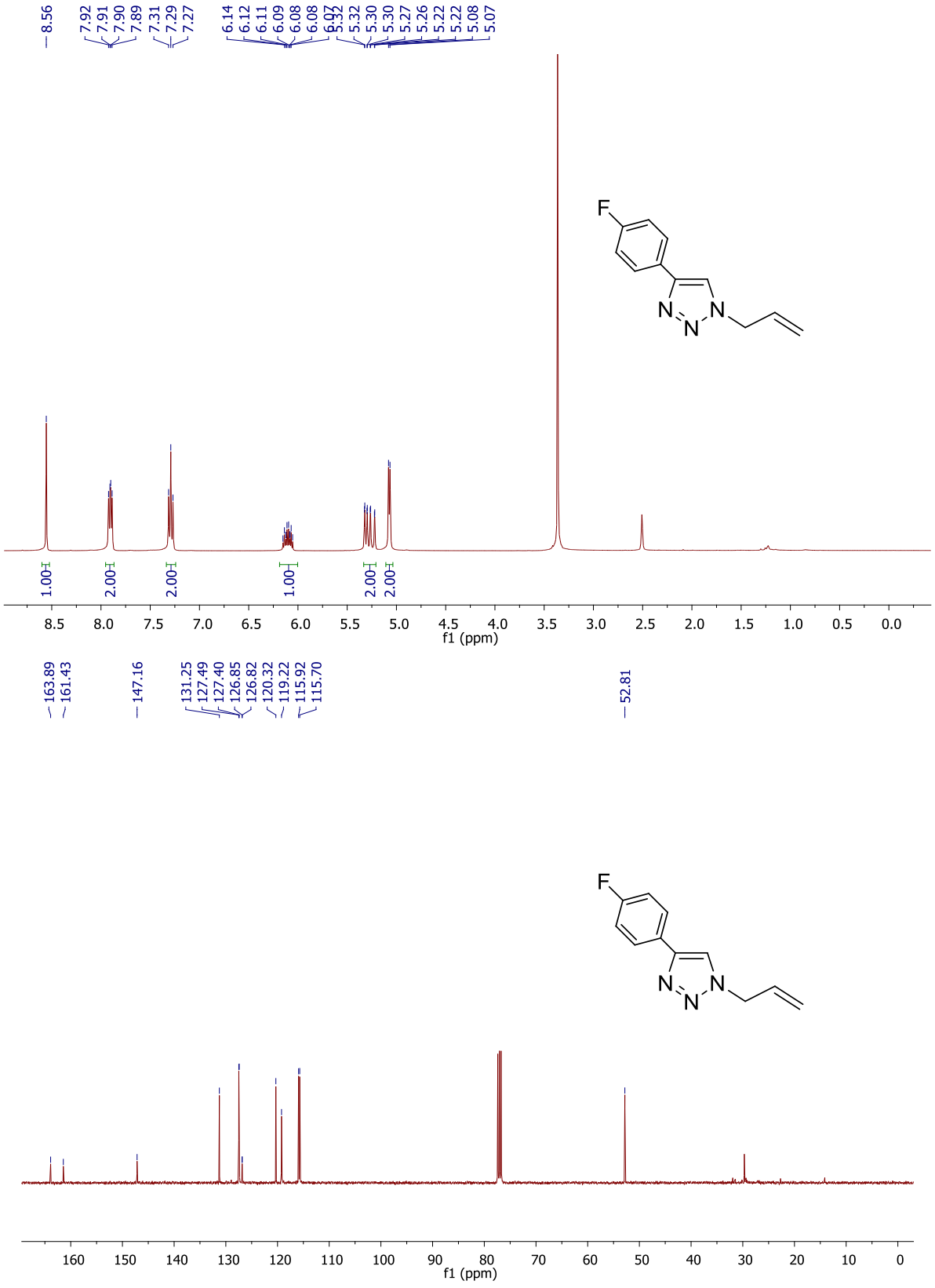


Figure A12: ^{1}H NMR and ^{13}CNMR spectra of **16ee'**

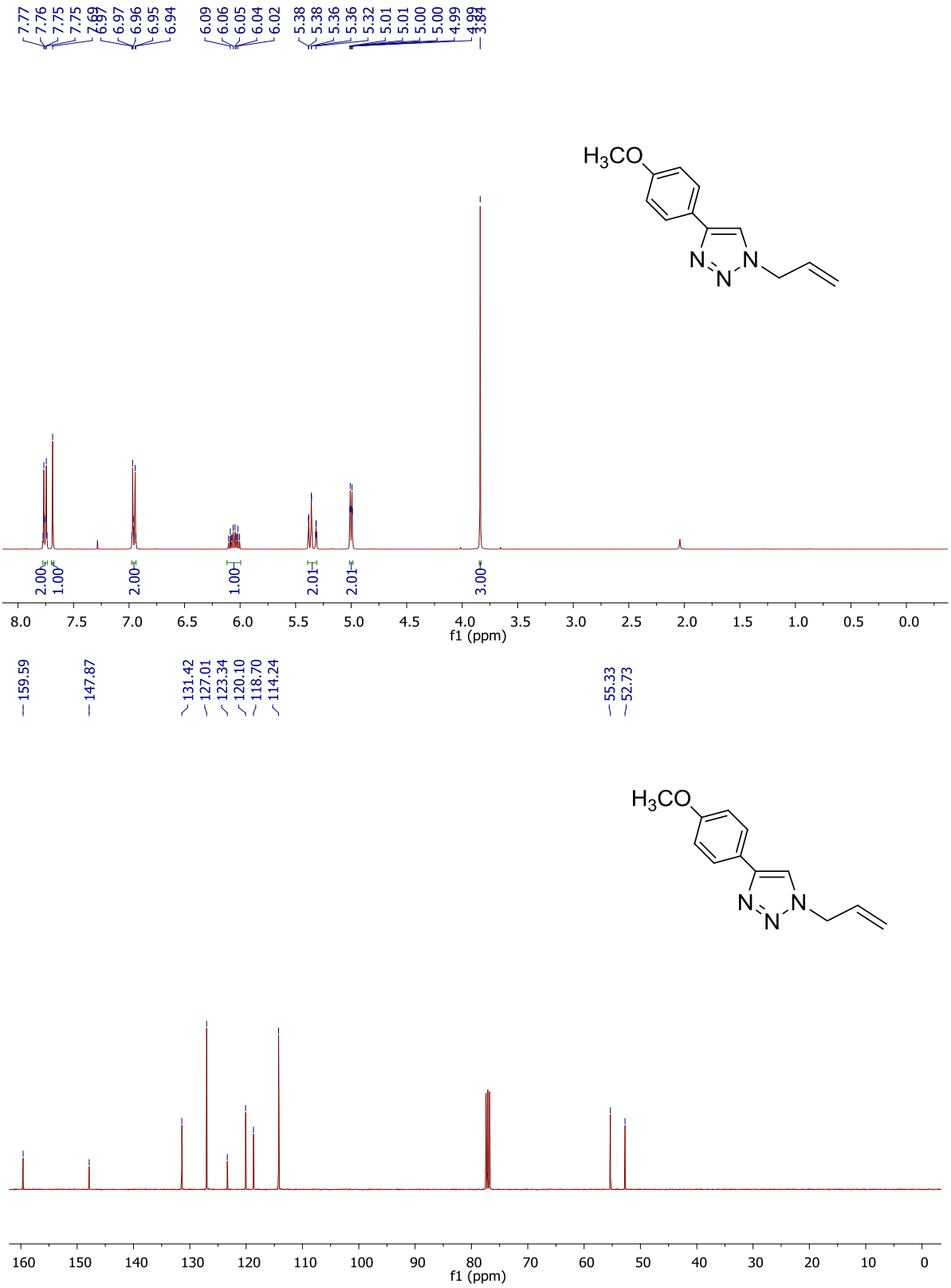


Figure A13: ^{1}H NMR and ^{13}CNMR spectra of **16ef'**

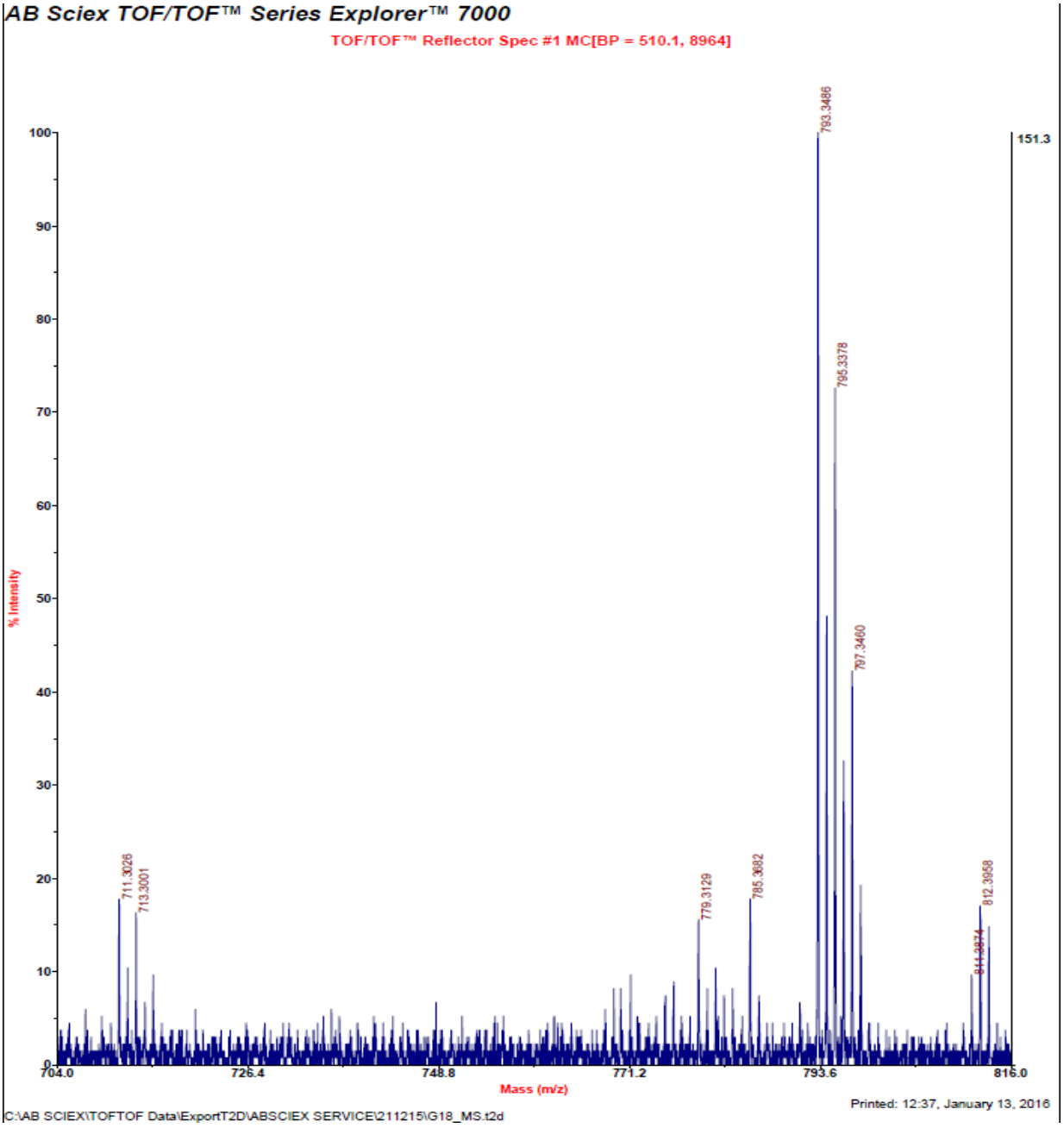


Figure A14: MALDI-Mass spectrum of **$Zn(L5)_2$**

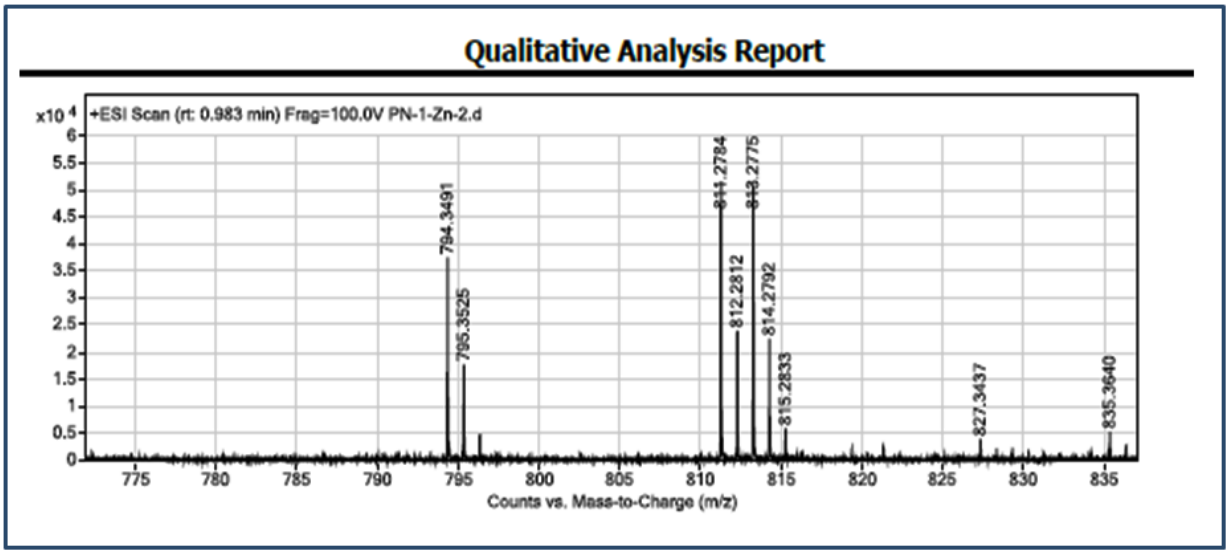


Figure A15: HRMS-Mass spectrum of **Zn(L5)$_2$**

Figure A16: Antibacterial and antifungal activities of **Zn(L5)$_2$**

Appendix-B

List of Publications *[B-1]*

1. Khungar, B.; Rao, M. S. Pericherla K. **Nehra, P**.; Jain, N. Panwar, J.; Kumar, A., "Synthesis, characterization and microbiocidal studies of novel ionic liquid-tagged Schiff bases" *C. R. Chimie*. **2012,** 15, 669–674.
2. **Nehra, P**.; Khungar, B.; Pericherla K.; Sivasubramanian, S. C.; Kumar, A., "Imidazolium ionic liquid-tagged palladium complex: an efficient catalyst for the Heck and Suzuki reactions in aqueous media" *Green chem.* **2014**, 16, 4266–4271.
3. **Nehra, P**.; Khungar, B.; Singh, R. P.; Sivasubramanian, S. C.; Jha P. N.; Saini V., Synthesis, characterization and applications of imidazolium ionic liquid-tagged zinc(II) Complex, *Inorg. Chim. Acta* **2018**, 478, 260-267.
4. **Nehra, P**.; Khungar, B.; Singh, R. P.; Sivasubramanian, S. C.; Jha P. N., An efficient, biologically active and recyclable ionic liquid-tagged copper(II) catalyst for azide–alkyne cycloaddition reactions (manuscript under prepration).
5. **Nehra, P**.; Khungar, B.; Sivasubramanian, S. C., Copper free Sonogashira coupling reaction with imidazolium ionic liquid-tagged palladium complex in water under aerobic conditions (manuscript under prepration).
6. **Nehra, P**.; Saini V.; Khungar, B.; Sivasubramanian, S. C., "An efficient and recyclable ionic liquid-tagged copper(II) catalyst for the oxidation of alcohols and thiols" (manuscript under prepration).

List of attended conferences *[B-2]*

1. **Nehra, P**.; Kumar, A. ; Khungar, B., "Synthesis, Characterization and Applications of Ionic liquid-Supported Schiff bases" at National Conference on Material Science Current Trends and Future Prospects, from 6th to 7th February-2012, organized by Lachoo Memorial college of science and Technology Jodhpur, India.
2. **Nehra, P**.; Khungar, B.; Pericherla K.; Sivasubramanian, S. C.; Kumar, A., "Copper Mediated Oxidation of Alcohols in Presence of Ionic Liquid-Supported Schiff bases" at National Symposium on Recent Trends in Chemical Science and Technology from 3rd to 4th March -2012, organized by the Department of Chemistry, IIT Patna, Patna.
3. **Nehra, P**.; Khungar, B.; Sivasubramanian, S. C.; Kumar, A., "Ionic liquid-supported metal complexes a green approach for catalysis" at National conference on Advances in Chemical Sciences organized by Maharshi Dayanand University Rohtak, Rohtak India from 1nd-2nd March, 2013.
4. **Nehra, P**.; Khungar, B.; Sivasubramanian, S. C., "Ionic Liquid-Supported Metal Complexes – an Environmentally Benign Catalytic Approach" at International Conference on Emerging Trends in Chemical Sciences organized by Central University of Gujarat Gandhinagar, India from 14th-15th March, 2013.
5. **Nehra, P**.; Khungar, B.; Pericherla K.; Sivasubramanian, S. C.; Kumar, A., "Ionic Liquid - Supported Palladium Complex: An Efficient and Recyclable Catalyst for the Suzuki Cross-Coupling Reaction in aqueous medium" 19th ISCB International Conference (ISCBC-2013) from 2nd-5th March, 2013 organized by the Department of Chemistry, Mohanlal Sukhadia University, Udaipur.
6. **Nehra, P**.; Khungar, B.; Pericherla K.; Sivasubramanian, S. C.; Kumar, A., "Synthesis, and Characterization of Ionic liquid-Supported Schiff base Ligands" at the conference in March-2013, organized by Department of Chemistry, BITS Pilani, Pilani Campus.
7. **Nehra, P**.; Khungar, B.; Saini, V.; Sivasubramanian, S. C., "Synthesis, Characterization and Catalytic Applications of Palladium Complex for C-C Coupling Reactions" at BITS Pilani, Pilani Campus, department of Physics, (23rd March, 2014)
8. **Nehra, P**.; Sivasubramanian, S. C.; Khungar, B., "Ionic Liquid-Tagged Copper Complex: An Eco-Friendly Catalyst for the Aerobic Oxidative Synthesis of 1, 4 disubstituted 1, 2, 3

Triazoles" (oral presentation) at National Conference on Nano and Functional Materials from 7th to 8th November-2014, organized by the Department of Chemistry BITS Pilani, Pilani Campus.

9. **Nehra, P**.; Khungar, B.; Pericherla K.; Sivasubramanian, S. C.; Kumar, R.; Kumar, A., "Ionic Liquid-Supported Palladium Complex: An Efficient and Recyclable Catalyst for Sonogashira Cross-Coupling Reaction" at 16th CRSI National Symposium in Chemistry from 7th to 9th February-2014, organized by the Department of Chemistry, IIT Bombay, Mumbai.
10. **Nehra, P**.; Singh, R. P.; Sivasubramanian, S. C.; Jha, P. N.; Khungar, B., "Synthesis, Characterization, Biological Activities and Photo physical Properties of an Ionic Liquid-Supported Schiff Base Zinc Complex" at national conference "FACSI-15", organized by Department of Chemistry, university of Rajasthan, Jaipur. (13-14th March).
11. **Nehra, P**.; Khungar, B.; Saini, V.; Sivasubramanian, S. C., "Ionic Liquid-Supported Schiff Base Copper Complex: An Efficient Catalyst for the Oxidation of Thiols to Disulfides" International conference on Organic Chemistry in Sustainable Development: Recent Advances and Future Challenge, from August 29th to 30th, 2016, organized by Department of Chemistry BITS-Pilani, Pilani Campus.
12. Attended Workshop on Analytical Instruments for Chemical & Environmental Engineers – WAICEE-2013 held in BITS Pilani.

BRIEF BIOGRAPHY OF THE CANDIDATE *[B-3]*

Ms. Pankaj Nehra completed her M.Sc. in Organic Chemistry from R. R. Morarka. Govt. PG college, Jhunjhunu in 2010. In 2011 she joined in BITS-Pilani, Pilani Campus, for her doctoral studies under the supervision of Prof. Bharti Khungar and co-supervision of Prof. S. C. Sivasubramanian. During her doctoral tenure, she received BITS Pilani institute fellowship (from 2011 to 2013) and UGC-Basic scientific research fellowship (from March-2013 to 2016). She has published three research articles in well renowned international journals and her three more publications are in pipeline. She has presented papers in national and international conferences/symposium.

BRIEF BIOGRAPHY OF THE SUPERVISOR *[B-4]*

Dr. Bharti Khungar is an Associate Professor at the Department of Chemistry, BITS Pilani, Pilani Campus. She carried out her doctoral research in Chemistry at University of Rajasthan, Jaipur under the Supervision of Prof. U. D. Tripaathi and Co-Supervision of Dr. A. K. Varshney and obtained the Ph.D. degree in 2002. After this, she worked as a Lecturer in the Department of Chemistry, Laxmi Devi Institute of Engineering and Technology, Alwar, Rajasthan till 2005. Before joining BITS, she worked at the post of Senior Lecturer at Banasthali University, Rajasthan for two years.

BRIEF BIOGRAPHY OF THE CO-SUPERVISOR *[B-5]*

Prof. S. C. Sivasubramanian is a Professor at the Department of Chemistry, BITS Pilani, Pilani Campus. He carried out his doctoral research at IIT Kanpur in Dec, 1989 under the Supervision of Prof. P. Raghunathan. He completed his M.Sc. from University of Hyderabad in 1982. While his post PhD experience he worked at Nuclear Engineering and Technology Dept. IIT Kanpur (6 months); Chemistry Dept. IIT Kanpur (7 months); IPCL Vadodara (4 months); BITS Pilani (25 years 11 months). His current designation, with start date is as Professor, Chemistry Dept., Pilani Campus BITS Pilani, 01 Feb 2005.