Chapter 4

Applications of Ionic Liquids as Catalyst
Application of ionic liquids as catalysts has enabled the researchers to explore not only the physical but also the chemical interactions of either their bulky cations or anions with the reactants under study. Following the literature on ionic liquids as catalysts (Section 1.8.2), attempts were made towards the development of a metal containing allyl functionalized morpholinium based ionic liquid for the purpose of catalyzing two well-known organic transformations - Biginelli reaction and Knoevenagel condensation. It has been proposed that when the allyl functionalized morpholinium based ionic liquid ‘[amm]Br’ is taken together with the metal salt Pd(OCOCH\(_3\))\(_2\), it is the complex ‘[amm]_2[PdBr_2(OCOCH_3)_2]’ (Figure 4.1), produced in the reaction mixture that is the actual catalytic species that participates in the reaction.

![Figure 4.1: Catalytic complex [amm]_2[PdBr_2(OCOCH_3)_2]](image)

### 4.1 INTRODUCTION

#### 4.1.1 Morpholinium ionic liquids – Ionic liquids based on morpholinium cation.

N-alkyl-N-methyl-morpholinium salts are increasingly under attention because of their moderate or low toxicity (EC\(_{50}\) between 0.15 mM and 14.13 mM), short synthesis time, simple purification steps, good product reproducibility and economical synthetic pathways.\(^1\)\(^2\) As reported by Lee et al.,\(^2\) in comparison to salts of imidazole and pyrrolidine, the ones based on morpholinium ions require cheap morpholinium cation sources as compared to organic cations such as 1-vinyl-2-pyrrolidinone, 1-methylpyrrolidine and 1-methyl imidazole. These thermally and electrochemically stable ILs have been expected to be potential candidates as electrolytes in batteries and other electronic devices.\(^3\)\(^4\) They have
also been used in the size controlled synthesis of crystalline palladium nanoparticles using [bmmor]BF₄ (N-butyl-N-methyl-morpholinium tetrafluoroborate) as a stabilizer.⁵

Morpholinium based ionic liquids are increasingly being used in the field of catalysis leading towards the development of new catalysts. Ionic liquid [morH]HSO₄ (morpholinium bisulfate) was found to be an effective catalyst for the condensation reaction of indoles with carbonyl compound to yield bis(indolyl)methanes at room temperature.⁶ The methodology has several merits such as mild reaction condition, inexpensive catalyst, stability at room temperature and it was also found that this catalyst could also be recovered quantitatively and reused without much loss of catalytic activity.

List et al. have reported a highly efficient method for the aldol condensation of acetone with aromatic aldehydes, using morpholinium trifluoroacetate as the catalyst.⁷ The easily availability of the catalyst together with high selectivity and functional group tolerance makes this a valuable procedure.

4.1.2 N-allyl-functionalised ionic liquids

Functionalised ionic liquids exhibit a range of physical and chemical properties that are well suited to specific applications (Catalytic applications: Section 1.8.2.2). As an example, ILs bearing the O,O-diphenylphosphonyl functionality have been evaluated as mechanical lubricants⁸ and ILs with fluorous chains can act as surfactants.⁹ Applications also include the use of acid-functionalised ionic liquids in the acetalisation of aldehydes ¹⁰,¹¹ and urea- and thiourea functionalized ILs in the extraction of metal ions from aqueous solutions.¹²,¹³ Thiol-functionalized ILs have been shown to stabilize gold and platinum nanoparticles.¹⁴,¹⁵ Similarly, nitrile-functionalised ILs can stabilize palladium nanoparticles, which also exhibit catalytic activity in many C-C coupling reactions.¹⁶,¹⁷

Amongst the allyl-functionalised ILs, N-allyl-imidazolium salts have been reported as early as 1971.¹⁸ At the time of discovery, the liquid nature of these compounds and hygroscopicity was not appreciated. However, the low melting temperature and the deliquescent nature has been attributed to high flexibility of the allyl group and intra-hydrogen bonding between H-atoms of the imidazole ring and the counter anion.

As yet, no extensive study on catalytic properties of ILs bearing alkene functionality has been reported, although it has been shown that 1-allyl-3-methylimidazolium chloride can
be used as a solvent for cellulose acetylation. Ohno et al have synthesized a series of
allyl-imidazolium halides and investigated their conductivities, viscosities and thermal
properties, indicating that the introduction of an allyl group onto the N-position of the
imidazole ring can effectively suppress their crystallization.

These alkene functionalized ILs have also been considered as useful synthons for the
synthesis of many other low melting molten salts or functionalized ILs. Addition
reactions to side chains of these allyl functionalized compounds can represent an
important synthetic route to a wide range of novel and potential ILs. Besides this
allyl-functionalized imidazole and pyrroline based ionic liquids, have also been
used as electrolytes for capacitors and dry sensitized solar cells respectively.

4.1.3 Metal containing ionic liquids and their applications

Ionic liquids and ionic liquid crystals (ILCs) of imidazolium salts composed of
various transition and main group metals have been reviewed extensively by Vasam et
al. ILCs are liquid crystalline, ionic compounds with melting point less than 100°C.
The presence of metal ions provides numerous additional properties such as color,
geometry and magnetism, which are distinguishable compared to simple ILCs. Metal-containing ILCs are also potentially very useful as an ordered media/potential
solvents, catalysts, catalyst precursors and reagents for organic transformations
and provide eco-friendly protocols. They have also been found to play key roles in
material science. Many of these IL systems are air and moisture stable and are
considered as alternatives for air and moisture sensitive chloroaluminate-based ILs.

Based on their melting point this study has been divided into three classes:

A Metal containing ionic liquids, ILs

B Metal containing ionic liquid crystals, ILCs

C IL supported metal catalysts – IL tagged to the ligand of a metal complex

(Section 1.8.2.3)

In this study only A and B have been considered

A Metal containing ionic liquids, ILs: The prolific works of Seddon, Welton,
DuPont and their coworkers from the period of 1990’s gave a special significance to
the ILs and their derivatives composed of transition-metals and main group metals.
Synthesis of two isomorphous imidazolium salts [(emim)]₂MCl₄, where M=Co or Ni (Figure 4.2 (a-b)) with melting point 90°C–100°C, were prepared directly by mixing the corresponding metal chloride with [emim]Cl under dry nitrogen atmosphere. Crystal structure studies of these ILs revealed that extended hydrogen bonding networks could be present between the MCl₄²⁻ and the ring hydrogens.

![Figure 4.2: (emim)]₂MCl₄ (a) M= Co, (b) M= Ni](image)

Amongst the palladium containing ILs, DuPont’s group has reported the synthesis and catalytic action of [(bmim)]₂PdCl₄ (Figure 4.3) in the hydrodimerization of 1,3-butadiene in [bmim]BF₄ medium. IR spectral data and crystal structure of this metal containing IL also showed the presence of strong hydrogen bonding between the chloride and imidazolium hydrogens. It has been found that during the catalytic process, the compound [(bmim)]₂PdCl₄ in [bmim]BF₄ underwent dealkylation and produced the catalyst precursor trans-[PdCl₂(mim)]₂ (Figure 4.4).

![Figure 4.3: [bmim]₂PdCl₄](image)

![Figure 4.4: trans-[PdCl₂(mim)]₂](image)
Later, Seddon’s group also used the [bmim]₂PdCl₄ (Figure 4.3) as a catalyst for Heck reaction conducted in a three-phase [bmim]PF₆/hexane/water system. In this case generation of metal-NHC (NHC= N-heterocyclic carbenes) in the catalytic cycle was anticipated. Soon, Ortwerth et al. characterized the structure of another palladium based IL, [emim]₂PdCl₄, which was prepared by the reaction of Pd(acac)₂ with an acidic [emim]Cl– AlCl₃ system.

Shreev and co-workers on the other hand, focused the formation of ionic liquid-coordinated compound (Figure 4.5 (b)) with the dissolution of PdCl₂ in an ionic liquid of mono-quaternary bis-2,2-bimidazole (Figure 4.5 (a)) for a Pd(II) catalyzed Heck reaction. This IL-coordinated Pd(II) complex (Figure 4.5 (b)) performed well for at least 10 times without significant loss in its activity.

Dyson and co-workers also prepared an ionic liquid-coordinated Pd(II) complex [Pd(N≡CC₃mim)₂-Cl₂]BF₄, Figure 4.6, (N≡CC₃mim = 1-butylnitrile-2,3-dimethylimidazolium) by using a nitrile functionalized ionic liquid. This complex (Figure 4.6) was employed as a solvent and recyclable catalyst during the hydrogenation of 1,3-cyclohexadiene.
B Metal containing ionic liquid crystals

The pioneering work has been done by Bruce’s and Seddon’s groups, who reported the synthesis of liquid crystalline \([C_n\text{-mim}]_2MCl_4\), where \(M=\text{Co, Ni or Pd}\) (Figure 4.7 (a-c)) and \(C_n = \text{alkyl chain of } C_nH_{2n+1}, n = 12–18\).\(^{36,37}\) The thermal stability of these compounds was found to be directly proportional to with the length of the alkyl chain attached to the imidazolium cation. The crystal and liquid polymorphism for compounds of \([C_n\text{-mim}]_2\text{PdCl}_4\) (Figure 4.7 (c)) was also investigated by these groups and was also found to be a function of alkyl chain length \((n = 12, 14, 16, 18)\).\(^{25}\) While the compounds of \(n = 10\) and \(12\) were found non mesogenic, the compounds with \(n=14, 16, 18\) showed liquid crystalline behavior. The melting point values for these compounds were higher than the counter parts with inorganic anions like Cl\(^-\), BF\(_4^-\) and PF\(_6^-\), but comparable with \([\text{CoCl}_4]^2-\) or \([\text{NiCl}_4]^2-\). Moreover, it was suggested that the use of these ordered liquid-crystal as a solvent could certainly influence the selectivity in catalytic reactions.

Metal containing ILCs composed of \(N,N^\prime\)-dialkylimidazolium salts of \(\text{Pd(II)}\) and \(\text{Cu(II)}\) i.e. \([((C_n)\text{-im})_2MCl_4]\), (Figure 4.8 (a,b)) where \(n = 8, 10, 12, 14, 16, 18\) for \(M = \text{Pd(II)}\) (Figure 4.8 (a)) and \(n = 10, 12, 14, 16, 18\) for \(M = \text{Cu(II)}\) (Figure 4.8 (b)) were prepared and structurally characterized by Lin’s group.\(^{27}\) The crystal structures of \([((C_{12})\text{-im})_2\text{PdCl}_4 \] and \([((C_{12})\text{-im})_2\text{CuCl}_4 \]. H\(_2\)O were found to be the first example of metal containing ILCs based on \([(C_n)\text{-im}] \) salts.
In this study, a palladium dicarbene complex \( \text{trans-}[(\text{C}_n\text{Y})_2\text{PdCl}_2] \) (Figure 4.9 (a)) and carbene-imidazole complex \( \text{trans-}[(\text{C}_n\text{Y})(\text{C}_n\text{im})\text{PdCl}_2] \) (Figure 4.9 (b)) were identified as the thermal decomposition products of Pd-IL complex Figure 4.8 (a).

**Figure 4.9:** (a) \( \text{trans-}[(\text{C}_n\text{Y})_2\text{PdCl}_2] \) (b) \( \text{trans-}[(\text{C}_n\text{Y})(\text{C}_n\text{im})\text{PdCl}_2]; \) (n=16) 27

### 4.1.4 Metal containing allyl-functionalised ionic liquids

Dyson *et al.* have described the synthesis and characterization of metal containing allyl functionalized imidazolium ionic liquid; \([\text{amim}]\text{PdBr}_2\text{Cl}_2\) (amim = 1-allyl-3-methyl-imidazolium) (Figure 4.10 (a)). The complex \([\text{amim}]\text{PdBr}_2\text{Cl}_2\) underwent de-alkylation in presence of AIBN and afforded the complex shown in (Figure 4.10 (b)). These researchers also discussed some nascent reactions that they could undergo, indicating that these compounds could be a source to a variety of other functionalized ionic liquids. 21

**Figure 4.10:** (a) Synthesis of metal containing allyl functionalized imidazolium ionic liquid; \([\text{amim}]\text{PdBr}_2\text{Cl}_2 \) (amim = 1-allyl-3-methyl-imidazolium) (b) polymerization of \([\text{amim}]\text{PdBr}_2\text{Cl}_2\) in presence of AIBN 21
4.1.5 Work Objective

Convinced by the easy synthetic procedure for morpholine based ionic liquids and catalytic applications of metal containing ionic liquids, an allyl-functionalized morpholine based ionic liquid, [amm]Br (N-allyl-N-methylmorpholinium bromide) has been treated with a metal salt (palladium acetate) so as to afford ‘[amm]Br-Pd(OCOCH$_3$)$_2$’ system. UV-spectrophotometric studies indicated the formation of metal containing ionic liquid complex ‘[amm]$_2$PdBr$_2$(OCOCH$_3$)$_2$’ (Figure 4.1). Catalytic performance of this ionic liquid-metal salt system: ‘[amm]Br-Pd(OCOCH$_3$)$_2$’ has been investigated through series of Biginelli condensation and Knoevenagel condensation in Sections 4A and Section 4B respectively.

4.2 SYNTHESIS OF CATALYTIC SYSTEM: [amm]Br-Pd(OCOCH$_3$)$_2$

The catalytic system: [amm]Br-Pd(OCOCH$_3$)$_2$ was synthesized from [amm]Br and Pd(OCOCH$_3$)$_2$ (Scheme 4.1, Figure 4.11). The precursor, allyl functionalized ionic liquid: N-methyl-N-(prop-2-enyl) morpholinium bromide or N-allyl-N-methyl morpholinium bromide, [amm]Br was synthesized from N-methyl morpholine as per simple and efficient method proposed by Feng et al.$^{38}$ [amm]Br was then characterized by $^1$H and $^{13}$C NMR studies. This was found to be a stable hydrophilic ionic liquid. In the next step an equimolar mixture of [amm]Br was reacted with palladium acetate in a suitable solvent. To a solution of [amm]Br (1mole) in ethanol (5.0ml) palladium acetate (1mole) was added. The mixture that turned dark red (Figure 4.12), was stirred for not more than 36 hours and the catalytic complex was isolated by evaporation of the solvent under reduced pressure.
Evidence for the complexation between the hydrophilic ionic liquid [amm]Br and the metal salt palladium acetate was laid forward by UV-Visible spectrophotometry studies. A solution of palladium acetate absorbed at 400 nm of UV-Visible spectrum. When palladium acetate was stirred with hydrophilic allyl-functionalized morpholinium ionic liquid; [amm]Br (N-allyl-N-methylmorpholinium bromide), its absorbance shifted to a lower wavelength with a decrease in intensity. This implies a
hypsochromic shift and was indicative of a complex formation (Figure 4.13). Wavelength shift from 399nm in palladium acetate to 327nm in the complex obtained could be attributed to the formation of complex \([\text{amm}]_2\text{[PdBr}_2(\text{OCOCH}_3)_2]\).

Figure 4.13: UV-Vis absorbance spectrum of (b) catalytic system \([\text{amm}]\text{Br-}
\text{Pd(OCOCH}_3)_2\); w.r.t (a) palladium acetate

4.4 CONCLUSION

Morpholinium based ionic liquid require easy synthetic steps compared to those containing an imidazole nucleus. Allyl-functionalized morpholinium based ionic liquid could be easily synthesized with less moisture sensitivity compared to imidazolium based ionic liquid such as \([\text{bmim}]\text{BF}_4\). Complexation of the hydrophilic ionic liquid \([\text{amm}]\text{Br}\) with a metal salt further reduced its moisture sensitivity and increased the stability. The metal salt-ionic liquid conjugate system \(([\text{amm}]\text{Br-}
\text{Pd(OCOCH}_3)_2\), as prepared by the method, was further employed for the synthesis of Biginelli derivatives and Knoevenagel adducts.
SECTION 4A

Application of Novel hydrophilic ionic liquid-metal salt system; ‘[amm]Br- Pd(OCOCH$_3$)$_2$’ towards catalytic synthesis of series of Biginelli derivatives under solventless conditions.

A novel hydrophilic palladium containing morpholine based ionic liquid (derived from N-allyl-N-methylmorpholinium bromide with an easy synthetic procedure) has been used to catalyze the synthesis of wide series of Biginelli derivatives (Scheme 4A.1); 3,4-dihydropyrimidin-2(1H)-ones or -thiones and 3,4,5,6,7,8-hexahydroquinazolin-2(1H)-ones or thiones in a one pot three component reaction. Urea/thiourea, an aromatic aldehyde and a β-ketoester/enolisable ketone (substituted acetophenone/cyclohexanone) couple in the presence of [amm]Br- Pd(OCOCH$_3$)$_2$ system at room temperature under solventless conditions to afford the heterocyclic derivatives in good yields.

![Scheme 4A.1: Synthesis of 3,4-dihydropyrimidin-2(1H)-ones or -thiones and 3,4,5,6,7,8-hexahydroquinazolin-2(1H)-ones or thiones using [amm]Br-Pd(OCOCH$_3$)$_2$]
4A.1 INTRODUCTION

4A.1.1 ‘3,4-dihydropyrimidin-2-ones’ and conventional methods of synthesis

In 1893 Italian chemist Pietro Biginelli (at University of Florence) reported this reaction for the first time which is taken as the birth of this reaction. It is popularly named after him i.e. Biginelli Reaction. Classically, the reaction was reported as acid-catalyzed condensation of ethyl acetoacetate, benzaldehyde and urea in ethanol which upon refluxing followed by cooling gives a solid crystalline product 3,4-dihydropyrimidin-2(1H)-one. Thus this was apparently a three component reaction (Scheme 4A.2) and the acid used was hydrochloric acid.39

\[
\begin{align*}
\text{Scheme 4A.2: Conventional acid catalyzed Biginelli reaction}^{39}
\end{align*}
\]

The scope of this reaction was gradually extended by the variation of all the three building blocks, allowing access to a large number of multifunctionalized dihydropyrimidines (DHPMs) of medicinal use.40-48 Dihydropyrimidines show a diverse range of biological activities. They are known to possess activities such as antibacterial and antiviral (nitractin), antitumor, analgesic and anti-inflammatory,49 antiplatelet aggregation and antihypertensive activity. Thus, development of methodologies for efficient lead structure identification and for pharmacophore variation of dihydropyrimidine motif has always attracted the attention of pharmaceutical industry.50,51

Catalysts employed till date can be broadly categorized into five variants-Bronsted acids, Lewis acids, ionic liquids, biocatalysts and organocatalysts. In addition, few rate enhancement processes have also been adopted like sonication, microwave irradiation and certain other miscellaneous processes.
The reaction conditions traditionally employed involve strong Bronsted and Lewis acids, such as LiClO₄, LaCl₃·7H₂O, InCl₃, Bi(OTf)₃, BiCl₃, Mn(OAc)₃, Cu(OTf)₂, FeCl₃·6H₂O, ZrCl₄ or SnCl₂·2H₂O. Among the Si-MCM-41 or montomorillonite K-10 clay supported ZnCl₂, AlCl₃, GaCl₃, InCl₃ and FeCl₃ catalysts, FeCl₃/Si-MCM-41 has shown best results for microwave assisted synthesis of dihydropyrimidinones. Formic acid has been used under solventless conditions for microwave irradiated synthesis of these compounds while Cu(OTf)₂ has also been used at 100°C in the presence of ethanol. There have also been previous reports on the use of solid-phase protocols which allow higher degree of throughput and automation. An earlier method to synthesize dihydropyrimidinones in ionic liquid, as reported by Sain et al., involved heating and this was the possible reason why the catalyst could not be recycled. Additionally, the yields obtained with some of the aldehydes were low. Similarly, Azhar et al. have synthesized dihydropyrimidinones using Cu(BF₄)₂·xH₂O as a catalyst, but as in the previous case, the catalyst had recyclability issues.

ILs are considered as the green solvent of the present century which obey the twelve principles of the green chemistry and are used extensively as catalysts or solvent or both in the organic synthesis. In this decade, the use of ILs in Biginelli reaction have attracted much attention either to enhance rate of reaction or to make a synthetic protocol greener. In the synthesis of DHPMs a variety of ILs viz. task-specific, polymer-supported, chiral ionic liquid have been used. Few amongst these are: [bmim]FeCl₄, [Hmim]HSO₄, [C₄mim]HSO₄, [bmim]BF₄, immobilized Cu(acac)₂, [bmim]Sac, [bmim]PF₆, [bmim]BF₄, [bmim]Cl×2AlCl₃, n-butyl-pyridinium tetrafluoroborate, tri-(2-hydroxyethyl) ammonium acetate, etc. It is worthwhile to note that all the ionic liquids used have been based upon the imidazolium nuclei.  

4A.1.2 Work objective

An ionic liquid-metal salt system-'[amm]Br-Pd(OCOCH₃)₂' expected to form a metal containing ionic liquid complex-'[amm]₂PdBr₂(OCOCH₃)₂' (Figure 4.1) was used as a catalyst for the synthesis of a series of biologically active heterocyclic compounds.
‘3,4-dihydropyrimidin-2-ones’ and ‘3,4,5,6,7,8-hexahydroquinazolin-2(1H)-ones’ at room temperature under atmospheric pressure. The advantage of using this system for Biginelli reaction over other ILs was the ease in the synthetic procedure for morpholine based molten salts over imidazole based or pyridine based molten salts. Metal salt- ionic liquid system could be easily recycled for further turns without significant loss in its activity. It was envisaged that the use of a metal containing olefin functionalized ionic liquid complex for catalytic purposes could open new avenues for research in the field of ionic liquid catalysis. The purpose of choosing a palladium salt over other metal salts can be attributed to the high catalytic efficiency and low melting temperature of its complexes over certain other commonly used metal salt complexes.

4A.2 GENERAL PROCEDURE FOR [amm]Br-Pd(OCOCH$_3$)$_2$ CATALYZED SYNTHESIS OF BIGINELLI DERIVATIVES UNDER SOLVENTLESS CONDITIONS.

In a mixture containing active methylene compound/ketonic compound (2mmole) (as per Scheme 4A.4, Scheme 4A.5 and Scheme 4A.6), aromatic aldehyde (2mmole), urea or thiourea (3mmole), 10-15 mole% of liquid ‘palladium acetate-ionic liquid’ complex system (synthesized as per procedure given in Section 4.2) was added and was allowed to stir at room temperature till the reaction reached completion (as indicated by TLC). 5 ml of cold water was added to the reaction mixture and stirred. The solid material obtained was filtered and the washings were retained. The product was further washed with cold water and recrystallized from ethyl acetate/n-hexane or ethanol to afford the pure product. The aqueous washings were evaporated in vacuum to afford the liquid catalytic system which could be recycled at least five turns with no loss in its activity.
4A.3 RESULTS AND DISCUSSION

The study was started by reacting 2mmole of benzaldehyde with 2mmole of ethylacetoacetate and 3mmole of urea at room temperature in the presence of a catalytic amount of ionic liquid, [amm]Br (N-allyl-N-methylmorpholinium bromide) (Scheme 4A.3). Even in presence of this allyl functionalized morpholinium ionic liquid, TLC indicated the product formation but the yield of the product was rather low. Upon complexation of [amm]Br with other metal salts, the complexes were formed, but were not stable in air and moisture. However, with palladium acetate a red colored complex was formed (Figure 4.11 and Figure 4.12) that was not only stable in air and moisture but gave a high percentage yield. Thereby, upon functionalization of the ionic liquid with a transition metal salt its catalytic efficiency increased many folds.

Based on these preliminary investigations, three series of compounds were formed by varying the active methylene compound/ketonic compound in the conventional Biginelli reaction. The first series involved urea/thiourea, aromatic aldehyde and an active methylene compound (ethylacetoacetate) (Scheme 4A.4, Table 4A.1). In this 3,4-dihydropyrimidin-2(1H)-ones were formed as the product with ethoxycarbonyl substituent at 5th position of the parent nucleus. The mechanism is presumed to involve the condensation of the aldehyde with the urea molecule followed by the nucleophilic addition of the 1,3-dicarbonyl compound (ethylacetoacetate). As shown in Figure 4A.1, the mechanistic steps could be facilitated by the catalytic complex ‘[amm]2PdBr2(OCOCH3)2’ formed by the complexation reaction between [amm]Br and Pd(OCOCH3)2, thereby increasing the rate of the reaction.

![Scheme 4A.3: Synthesis of 5-ethoxycarbonyl-4-phenyl-6-methyl-3,4-dihydropyrimidin-2(1H)-one](image)

*Reaction condition: 1mmole of benzaldehyde, 1mmole of ethylacetoacetate and 2mmole of urea reacted at room temperature in the presence of a catalytic amount of ionic liquid [amm]Br*
The second series involved urea, aromatic aldehyde and acetophenone derivatives (Scheme 4A.5, Table 4A.2) yielding 3,4-dihydropyrimidin-2(1H)-ones (phenyl substituent at the 5th position) as products and third involved the use of cyclohexanone as the ketonic compound so as to afford 3,4,5,6,7,8-hexahydroquinazolin-2(1H)-ones (Scheme 4A.6, Table 4A.3).

Synthesis of 3,4-dihydropyrimidin-2(1H)-ones (Scheme 4A.4) with ethoxycarbonyl substituent at 5th position of the pyrimidine-one nucleus was a bit faster as compared to the synthesis of 3,4-dihydropyrimidin-2(1H)-ones with phenyl derivative at 5th position (Scheme 4A.5). This could be attributed to the greater nucleophilicity of the carbanion formed in case of ethylacetocetate as compared to that of the carbanion formed from the acetophenone derivatives.
Scheme 4A.4: Synthesis of 5-ethoxycarbonyl-3,4-dihydropyrimidin-2(1H)-ones

*Reaction condition:* Condensation of 2mmole of aromatic aldehyde, 2mmole of ethylacetoacetate and 3mmole of urea/thiourea in presence of 10 mole% of catalytic system [amm]Br- Pd(OCOCH₃)₂ at room temperature.

Scheme 4A.5: Synthesis of 5-phenyl substituted-3,4-dihydropyrimidin-2(1H)-ones

*Reaction condition:* Condensation of 2mmole of aromatic aldehyde, 2mmole of acetophenone derivative and 3mmole of urea/thiourea in presence of 15 mole% of catalytic system [amm]Br-Pd(OCOCH₃)₂ at room temperature.

Scheme 4A.6: Synthesis of 3,4,5,6,7,8-hexahydroquinazolin-2(1H)-ones

*Reaction condition:* Condensation of 2mmole of aromatic aldehyde, 2mmole of cyclohexanone and 3mmole of urea/thiourea in presence of 12 mole% of catalytic system [amm]Br-Pd(OCOCH₃)₂ at room temperature.
4A.3.1 Catalyst concentration

Concentration of catalyst required for conversion of 1mmole of benzaldehyde, 1mmole ethylacetoacetate and 1.5mmole of urea to 5-ethoxycarbonyl-4-phenyl-6-methyl-3,4-dihydropyrimidin-2(1H)-one was 10mole% (Table 4A.1, Entry 4A.2.1). However, for converting 1mmole of benzaldehyde, 1mmole of acetophenone and 1.5mmole of urea to the corresponding product 4-phenyl-3,4-dihydropyrimidin-2(1H)-one a little higher concentration of the catalyst was needed i.e. 15mole% (Table 4A.2, Entry 4A.2.1). This could be attributed to reduced acidic character of the methyl proton in acetophenone as compared to that in the active methylene group in ethylacetoacetate. Synthesis of 3,4,5,6,7,8-hexahydroquinazolin-2(1H)-ones required 12 mole% of the catalyst (Table 4A.3, Entry 4A.3.1).

Table 4A.1: [amm]Br-Pd(OCOCH₃)₂ catalyzed synthesis of ethoxy carbonyl substituted 3,4-dihydropyrimidin-2(1H)-ones

<table>
<thead>
<tr>
<th>S. No.</th>
<th>X</th>
<th>R</th>
<th>Product</th>
<th>Yield (%)</th>
<th>Time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4A.1</td>
<td>O</td>
<td>H</td>
<td><img src="image1.png" alt="Product 1" /></td>
<td>98</td>
<td>12</td>
</tr>
<tr>
<td>4A.2</td>
<td>O</td>
<td>4-Cl-</td>
<td><img src="image2.png" alt="Product 2" /></td>
<td>95</td>
<td>14</td>
</tr>
<tr>
<td>4A.3</td>
<td>O</td>
<td>4-(OCH₃)-</td>
<td><img src="image3.png" alt="Product 3" /></td>
<td>98</td>
<td>12</td>
</tr>
<tr>
<td>4A.4</td>
<td>O</td>
<td>4-(NO₂)-</td>
<td><img src="image4.png" alt="Product 4" /></td>
<td>92</td>
<td>15</td>
</tr>
<tr>
<td>S. No.</td>
<td>X</td>
<td>R</td>
<td>Product&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Yield (%)</td>
<td>Time (min)</td>
</tr>
<tr>
<td>-------</td>
<td>---</td>
<td>--------------------</td>
<td>-----------------------------------</td>
<td>-----------</td>
<td>------------</td>
</tr>
<tr>
<td>4A.5</td>
<td>O</td>
<td>2-(OCH&lt;sub&gt;3&lt;/sub&gt;)&lt;br&gt;4(OCH&lt;sub&gt;3&lt;/sub&gt;)</td>
<td><img src="image1.png" alt="Image" /></td>
<td>96</td>
<td>18</td>
</tr>
<tr>
<td>4A.6</td>
<td>O</td>
<td>3-(OCH&lt;sub&gt;3&lt;/sub&gt;)&lt;br&gt;4(OH)</td>
<td><img src="image2.png" alt="Image" /></td>
<td>90</td>
<td>20</td>
</tr>
<tr>
<td>4A.7</td>
<td>O</td>
<td>4-(CH&lt;sub&gt;3&lt;/sub&gt;)</td>
<td><img src="image3.png" alt="Image" /></td>
<td>84</td>
<td>15</td>
</tr>
<tr>
<td>4A.8</td>
<td>O</td>
<td>4-(OH)</td>
<td><img src="image4.png" alt="Image" /></td>
<td>88</td>
<td>20</td>
</tr>
<tr>
<td>4A.9</td>
<td>S</td>
<td>H</td>
<td><img src="image5.png" alt="Image" /></td>
<td>87</td>
<td>10</td>
</tr>
<tr>
<td>4A.10</td>
<td>S</td>
<td>4-(OCH&lt;sub&gt;3&lt;/sub&gt;)</td>
<td><img src="image6.png" alt="Image" /></td>
<td>90</td>
<td>12</td>
</tr>
<tr>
<td>4A.11</td>
<td>S</td>
<td>4-Cl-</td>
<td><img src="image7.png" alt="Image" /></td>
<td>84</td>
<td>15</td>
</tr>
</tbody>
</table>

<sup>a</sup>Reaction condition: Condensation of 2mmole of aromatic aldehyde, 2mmole of ethylacetoacetate and 3mmole of urea/thiourea in presence of 10 mole% of catalytic system [amm]Br-Pd(OCOCH<sub>3</sub>)<sub>2</sub> at room temperature. <sup>b</sup>Isolated pure crystallized product, characterization using <sup>1</sup>H-NMR, <sup>13</sup>C-NMR and mass spectrum studies.
Table 4A.2: [amm]Br-Pd(OCOCH$_3$)$_2$ catalyzed synthesis of phenyl substituted 3,4-dihydropyrimidin-2(1H)-ones$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>R</th>
<th>R'$</th>
<th>Product$^b$</th>
<th>Yield (%)</th>
<th>Time(min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4A.2.1.</td>
<td>O</td>
<td>H</td>
<td>H</td>
<td></td>
<td>86</td>
<td>10</td>
</tr>
<tr>
<td>4A.2.2.</td>
<td>O</td>
<td>4-Cl</td>
<td>H</td>
<td></td>
<td>90</td>
<td>12</td>
</tr>
<tr>
<td>4A.2.3.</td>
<td>O</td>
<td>4-(OCH$_3$)</td>
<td>H</td>
<td></td>
<td>97</td>
<td>10</td>
</tr>
<tr>
<td>4A.2.4.</td>
<td>O</td>
<td>4-(NO$_2$)</td>
<td>H</td>
<td></td>
<td>87</td>
<td>14</td>
</tr>
<tr>
<td>4A.2.5.</td>
<td>O</td>
<td>2-(OCH$_3$)-4(OCH$_3$)</td>
<td>H</td>
<td></td>
<td>98</td>
<td>15</td>
</tr>
<tr>
<td>4A.2.6.</td>
<td>O</td>
<td>3-(OCH$_3$)-4(OH)</td>
<td>H</td>
<td></td>
<td>96</td>
<td>08</td>
</tr>
<tr>
<td>Entry</td>
<td>X</td>
<td>R</td>
<td>R’</td>
<td>Product</td>
<td>Yield (%)</td>
<td>Time(min)</td>
</tr>
<tr>
<td>-------</td>
<td>----</td>
<td>-------------</td>
<td>----</td>
<td>---------</td>
<td>-----------</td>
<td>-----------</td>
</tr>
<tr>
<td>4A.2.7.</td>
<td>O</td>
<td>4-(CH₃)-</td>
<td>H</td>
<td><img src="image1" alt="Product" /></td>
<td>90</td>
<td>14</td>
</tr>
<tr>
<td>4A.2.8.</td>
<td>O</td>
<td>4-(OH)-</td>
<td>H</td>
<td><img src="image2" alt="Product" /></td>
<td>95</td>
<td>12</td>
</tr>
<tr>
<td>4A.2.9.</td>
<td>S</td>
<td>H</td>
<td>H</td>
<td><img src="image3" alt="Product" /></td>
<td>98</td>
<td>14</td>
</tr>
<tr>
<td>4A.2.10.</td>
<td>S</td>
<td>4-(OCH₃)</td>
<td>H</td>
<td><img src="image4" alt="Product" /></td>
<td>94</td>
<td>10</td>
</tr>
<tr>
<td>4A.2.11.</td>
<td>S</td>
<td>4-Cl</td>
<td>H</td>
<td><img src="image5" alt="Product" /></td>
<td>86</td>
<td>15</td>
</tr>
<tr>
<td>4A.2.12</td>
<td>O</td>
<td>H</td>
<td>4-OCH₃</td>
<td><img src="image6" alt="Product" /></td>
<td>92</td>
<td>18</td>
</tr>
<tr>
<td>4A.2.13</td>
<td>O</td>
<td>4-OCH₃</td>
<td>4-OCH₃</td>
<td><img src="image7" alt="Product" /></td>
<td>94</td>
<td>18</td>
</tr>
</tbody>
</table>

*aReaction condition*: Condensation of 2mmole of aromatic aldehyde, 2mmole of acetophenone derivative and 3mmole of urea/thiourea in presence of 15 mole% of catalytic system [amm]Br-Pd(OCOCH₃)₂ at room temperature. *Isolated pure crystallized product, characterization using ¹H-NMR, ¹³C-NMR and mass spectrum studies*
Table 4A.3: [amm]Br-Pd(OCOCH$_3$)$_2$ catalyzed synthesis of 3,4,5,6,7,8-hexahydroquinazolin-2(1H)-ones$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>R</th>
<th>Product$^b$</th>
<th>Yield (%)</th>
<th>Time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4A.3.1</td>
<td>O</td>
<td>H</td>
<td><img src="image1.png" alt="Structure" /></td>
<td>95</td>
<td>10</td>
</tr>
<tr>
<td>4A.3.2</td>
<td>O</td>
<td>4-Cl</td>
<td><img src="image2.png" alt="Structure" /></td>
<td>88</td>
<td>15</td>
</tr>
<tr>
<td>4A.3.3</td>
<td>O</td>
<td>4-(OCH$_3$)</td>
<td><img src="image3.png" alt="Structure" /></td>
<td>98</td>
<td>08</td>
</tr>
<tr>
<td>4A.3.4</td>
<td>O</td>
<td>4-(NO$_2$)</td>
<td><img src="image4.png" alt="Structure" /></td>
<td>85</td>
<td>14</td>
</tr>
<tr>
<td>4A.3.5</td>
<td>O</td>
<td>2-(OCH$_3$)-4(OCH$_3$)</td>
<td><img src="image5.png" alt="Structure" /></td>
<td>95</td>
<td>09</td>
</tr>
<tr>
<td>4A.3.6</td>
<td>O</td>
<td>3-(OCH$_3$)-4-(OH)</td>
<td><img src="image6.png" alt="Structure" /></td>
<td>98</td>
<td>12</td>
</tr>
</tbody>
</table>
### Reaction condition:
Condensation of 2mmole of aromatic aldehyde, 2mmole of cyclohexanone and 3mmole of urea/thiourea in presence of 12 mole% of catalytic system [amm]Br-Pd(OCOCH₃)₂ at room temperature. Isolated pure crystallized product, characterization using ¹H-NMR, ¹³C-NMR and mass spectrum studies.

### 4A.3.2 Catalyst recyclability
The catalytic complex [amm]Br-Pd(OCOCH₃)₂ could be recycled by separating it from the aqueous residue of the reaction mixture by simply evaporating the solvent in vacuum. It could be re-used over five subsequent turns in each of the reaction schemes so as to yield 3,4-dihydropyrimidin-2(1H)-ones and 3,4,5,6,7,8-hexahydroquinazolin-2(1H)-ones in high yields. The data for recyclability of catalyst

<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>R</th>
<th>Product</th>
<th>Yield (%)</th>
<th>Time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4A.3.7</td>
<td>O</td>
<td>4-(CH₃)-</td>
<td><img src="image1.png" alt="Image" /></td>
<td>92</td>
<td>14</td>
</tr>
<tr>
<td>4A.3.8</td>
<td>O</td>
<td>4-(OH)-</td>
<td><img src="image2.png" alt="Image" /></td>
<td>95</td>
<td>12</td>
</tr>
<tr>
<td>4A.3.9</td>
<td>S</td>
<td>H</td>
<td><img src="image3.png" alt="Image" /></td>
<td>94</td>
<td>16</td>
</tr>
<tr>
<td>4A.3.10</td>
<td>S</td>
<td>4-(OCH₃)</td>
<td><img src="image4.png" alt="Image" /></td>
<td>97</td>
<td>12</td>
</tr>
<tr>
<td>4A.3.11</td>
<td>S</td>
<td>4-Cl</td>
<td><img src="image5.png" alt="Image" /></td>
<td>89</td>
<td>15</td>
</tr>
</tbody>
</table>
for the model reaction (1mmole of benzaldehyde, 1mmole of ethylacetoacetate and 1.5mmole urea reacted in presence of 10mole% [amm]Br-Pd(OCOCH$_3$)$_2$) has been plotted as a bar graph in Figure 4A.2. It was observed that with each subsequent cycle, the catalytic activity of palladium containing ionic liquid decreased negligibly (as observed by a decrease in the yields of the product).

![Figure 4A.2: Recyclability of catalytic system [amm]Br-Pd(OCOCH$_3$)$_2$ for the formation of 3,4-dihydropyrimidin-2(1H)-ones$^a$](image)

$^a$Reaction conditions: 1mmole of benzaldehyde, 1mmole of ethylacetoacetate and 1.5mmole urea stirred in presence of 10mole% [amm]Br-Pd(OCOCH$_3$)$_2$

### 4A.4 CONCLUSION

A hydrophilic palladium containing ionic liquid has been developed, which is catalytically active towards the synthesis of three series of Biginelli derivatives that can serve as precursors to the synthesis of numerous pharmacologically active compounds. All the compounds isolated were in their crude form which could be recrystallized to give pure crystalline compounds with sharp and distinct melting points. The catalyst could not only be recovered but also re-used over a number of turns and this demonstrated the catalytic property of the complex. Due to the presence of the catalytic transition metal element palladium, the complex [amm]Br-Pd(OCOCH$_3$)$_2$ can be explored for other organic transformations as well.
SECTION 4B

Application of novel hydrophilic ionic liquid-metal salt system ‘[amm]Br-Pd(OCOCH$_3$)$_2$’ towards catalytic synthesis of Knoevenagel adducts under solventless conditions.

A useful reaction for the synthesis of substituted olefins has been carried out using a novel catalytic system ‘[amm]Br-Pd(OCOCH$_3$)$_2$’. The reaction commences under neutral conditions (without the addition of base) under solventless conditions. The metal salt- ionic liquid system catalyses the condensation between aromatic aldehydes and active methylene compounds (ethylenyanoacetate, malononitrile and malonic acid) efficiently giving excellent product yields. The catalytic metal containing ionic liquid complex system could be recycled and re-used up to five subsequent turns without the need for additional reagent.

EWG= CN, COOEt, COOH

Scheme 4B.1 Knoevenagel condensation catalyzed by [amm]Br-Pd(OCOCH$_3$)$_2$
Chapter 4

4B.1 INTRODUCTION

4B.1.1 Knoevenagel condensation and conventional methods of synthesis

The Knoevenagel condensation is a useful carbon-carbon bond formation reaction, possessing variety of applications in the synthesis of fine chemicals, hetero-Diels-Alder reactions and in the synthesis of carbocyclic as well as heterocyclic compounds. The reaction has been extensively utilized in the preparation of coumarin derivatives, cosmetics, perfumes and pharmaceutical chemicals. The conventional Knoevenagel condensation between a carbonyl compound and an active methylene compound has been carried out using bases such as ethylenediamine, piperidine or corresponding ammonium salts, amino acids, dimethylaminopyridine and potassium fluoride mixture. These electrophilic alkenes have also been synthesized under heterogeneous conditions using inorganic salts such as Al₂O₃, zeolite and calcite. Ionic liquids have also played a vital role as a reaction media for this condensation. However, some of these processes require harsh conditions and hence certain milder methods need to be developed for obtaining these condensation products under conditions which can be tolerated by sensitive functional groups (from both synthetic and environmental point of view). The synthetic challenge is thus, to carry out this reaction in a neutral medium thus avoiding the use of bases.

Room temperature ionic liquids (which have very low vapor pressure and are thermally stable) have been recognized as a possible environmentally benign alternative to volatile solvents in the chemical industry. Several classical organic processes have been successfully performed in ionic liquids (using them as solvents or catalysts). The application of task-specific ionic liquids with specific functional groups, which can be used as both as reagent and medium, but can also catalyze special reactions can further enhance the versatility of the ionic liquids.

Typically, ionic liquids cited in literature that have been employed for the Knoevenagel condensation, have an acidic counter anion such as nitrate in n-butylpyridinium nitrate and ethylammonium nitrate. Although a task specific ionic liquid [NH₃(CH₂CH₂OH)]CH₃COO with weak basic character has been used for condensation of aldehydes with certain active methylene compounds, but this...
ionic liquid also required acetic acid for its synthesis and in some cases the reaction required to be carried out at an elevated temperature. In another case, the common room temperature ionic liquid [bmim]PF₆ has been used, but required the presence of an additional catalyst sodium methoxide for the synthesis of 3-substituted coumarin derivatives via Knoevenagel condensation.

4B.1.2 Work Objective

In order to circumvent the problems encountered in all the methods which have been used till date for catalyzing the well-known Knoevenagel condensation, catalytically active, metal containing, hydrophilic and neutral ionic liquid-metal salt complex [amm]Br-Pd(OCOCH₃)₂ could be used as a major breakthrough. As already discussed before, the complex system was not only catalytically active but also stable over reaction completion and could be recycled over subsequent turns.

4B.2 TYPICAL PROCEDURE FOR THE SYNTHESIS OF KNOEVENAGEL ADDUCTS USING [amm]Br-Pd(OCOCH₃)₂ UNDER SOLVENTLESS CONDITIONS

To a mixture of aldehyde (5.0 mmol) and active methylene compound (6.0 mmol), 10mole% of metal salt- ionic liquid complex system (as prepared in Section 4.2) was added. The resulting reaction mixture was stirred at room temperature for a specified period (Table 4B.1). The progress of the reaction was monitored by thin layer chromatography (TLC). Upon complete conversion (as indicated by TLC) the reaction mixture was diluted by adding ethyl acetate (50 ml) and washed with water thrice followed by a brine wash. The organic layer was dried over anhydrous sodium sulphate (Na₂SO₄) followed by evaporation of the solvent using a rotary evaporator under reduced pressure so as to give the desired product, which after recrystallisation afforded the pure Knoevenagel products (Table 4B.1). The complete spectral analysis and compositional data revealed the formation of Knoevenagel products with excellent purity.
Subsequently, the first aqueous washing of the reaction mixture containing ethyl acetate was retained and this was evaporated under reduced pressure to retain the original catalytically active ionic liquid complex.

4B.3 RESULTS AND DISCUSSIONS

In order to investigate the versatility of the reaction, various aromatic aldehydes were reacted with active methylene compounds viz. malononitrile, malonic acid and ethylcyanoacetate (Scheme 4B.1). As expected, the yield of the products and the time required for condensing 5mmole of an aldehyde with 6 mmole of an active methylene compound was dependent upon the acidic character of the methylene protons in the active methylene compound (Table 4B.1). In general, substituent at the ortho-position of the aromatic aldehydes (Table 4B.1: Entries 4B.1.1, 4B.1.3 and 4B.1.5) seemed to decrease the rate of the reaction together with the overall yield and this may be because of steric constraints offered to the incoming nucleophile. Ketones showed no reactivity at all under similar conditions (Table 4B.1: Entry 4B.18).

4B.3.1 Catalyst concentration

Concentration of a catalyst is one of the major parameters in optimizing the yield of the product. It has been observed in this case that increase in the concentration of the catalyst beyond 10mole% did not affect the yield further. Hence, this was selected to be the optimum concentration (Figure 4B.1). This data has been plotted for the model reaction under study (Table 4B.1, Entry 4B.1).
4B.3.2 Catalyst recyclability

Applicability of hydrophilic ionic liquid-metal salt catalytic system [amm]Br-Pd(OCOCH$_3$)$_2$ as a recyclable catalyst was tested by carrying out repeated runs of the reaction (Table 4B.1, Entry 4B.1) using the same batch of the catalyst (Figure 4B.2). The data shows a gradual decrease in catalytic activity with increasing number of cycles. This may be because of possibility of wear and tear in case of ionic liquids (as compared to conventional catalysts) is low because of their distinct physiochemical properties.

Figure 4B.1: Catalyst concentration optimization for Knoevenagel condensation$^a$

$^a$Reaction conditions: 5mmole of benzaldehyde reacted with 6mmole of ethylcyanoacetate in presence of catalyst [amm]Br-Pd(OCOCH$_3$)$_2$

4B.3.2 Catalyst recyclability

Applicability of hydrophilic ionic liquid-metal salt catalytic system [amm]Br-Pd(OCOCH$_3$)$_2$ as a recyclable catalyst was tested by carrying out repeated runs of the reaction (Table 4B.1, Entry 4B.1) using the same batch of the catalyst (Figure 4B.2). The data shows a gradual decrease in catalytic activity with increasing number of cycles. This may be because of possibility of wear and tear in case of ionic liquids (as compared to conventional catalysts) is low because of their distinct physiochemical properties.

Figure 4B.2: Catalyst recyclability study for Knoevenagel condensation$^a$.

$^a$Reaction Condition: 5mmole of benzaldehyde reacted with 6mmole of ethylcyanoacetate in presence of 10mole% of catalyst [amm]Br-Pd(OCOCH$_3$)$_2$
<table>
<thead>
<tr>
<th>Entry</th>
<th>Aldehyde</th>
<th>Active methylene compound</th>
<th>Product</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4B.1.1</td>
<td>CHO</td>
<td><img src="image1" alt="Active methylene compound" /></td>
<td><img src="image2" alt="Product" /></td>
<td>0.30</td>
<td>98</td>
</tr>
<tr>
<td>4B.1.2</td>
<td>CHO</td>
<td><img src="image3" alt="Active methylene compound" /></td>
<td><img src="image4" alt="Product" /></td>
<td>0.58</td>
<td>97</td>
</tr>
<tr>
<td>4B.1.3</td>
<td>CHO</td>
<td><img src="image5" alt="Active methylene compound" /></td>
<td><img src="image6" alt="Product" /></td>
<td>0.33</td>
<td>98</td>
</tr>
<tr>
<td>4B.1.4</td>
<td>CHO</td>
<td><img src="image7" alt="Active methylene compound" /></td>
<td><img src="image8" alt="Product" /></td>
<td>0.50</td>
<td>92</td>
</tr>
<tr>
<td>4B.1.5</td>
<td>CHO</td>
<td><img src="image9" alt="Active methylene compound" /></td>
<td><img src="image10" alt="Product" /></td>
<td>0.75</td>
<td>95</td>
</tr>
<tr>
<td>4B.1.6</td>
<td>CHO</td>
<td><img src="image11" alt="Active methylene compound" /></td>
<td><img src="image12" alt="Product" /></td>
<td>0.25</td>
<td>97</td>
</tr>
<tr>
<td>4B.1.7</td>
<td>CHO</td>
<td><img src="image13" alt="Active methylene compound" /></td>
<td><img src="image14" alt="Product" /></td>
<td>1.00</td>
<td>81</td>
</tr>
<tr>
<td>4B.1.8</td>
<td>CHO</td>
<td><img src="image15" alt="Active methylene compound" /></td>
<td><img src="image16" alt="Product" /></td>
<td>1.16</td>
<td>92</td>
</tr>
<tr>
<td>4B.1.9</td>
<td>CHO</td>
<td><img src="image17" alt="Active methylene compound" /></td>
<td><img src="image18" alt="Product" /></td>
<td>1.41</td>
<td>97</td>
</tr>
<tr>
<td>4B.1.10</td>
<td>CHO</td>
<td><img src="image19" alt="Active methylene compound" /></td>
<td><img src="image20" alt="Product" /></td>
<td>0.83</td>
<td>94</td>
</tr>
<tr>
<td>4B.1.11</td>
<td>CHO</td>
<td><img src="image21" alt="Active methylene compound" /></td>
<td><img src="image22" alt="Product" /></td>
<td>0.41</td>
<td>85</td>
</tr>
<tr>
<td>Entry</td>
<td>Aldehyde</td>
<td>Active methylene compound</td>
<td>Product</td>
<td>Time (h)</td>
<td>Yield (%)</td>
</tr>
<tr>
<td>---------</td>
<td>-------------------</td>
<td>---------------------------</td>
<td>--------------------</td>
<td>----------</td>
<td>-----------</td>
</tr>
<tr>
<td>4B.1.12</td>
<td>HO—C—CHO</td>
<td>N=C—O</td>
<td>O</td>
<td>0.75</td>
<td>89</td>
</tr>
<tr>
<td>4B.1.13</td>
<td>NO₂—C—CHO</td>
<td>N=C—O</td>
<td>O</td>
<td>0.83</td>
<td>91</td>
</tr>
<tr>
<td>4B.1.14</td>
<td>C₂H₅—C—CHO</td>
<td>N=C—O</td>
<td>O</td>
<td>1.33</td>
<td>72</td>
</tr>
<tr>
<td>4B.1.15</td>
<td>H₂C₃—CHO —OCHO₃</td>
<td>N=C—O</td>
<td>O</td>
<td>1.25</td>
<td>80</td>
</tr>
<tr>
<td>4B.1.16</td>
<td>H₂C₃—CHO —HO—C—CHO</td>
<td>N=C—O</td>
<td>O</td>
<td>0.41</td>
<td>83</td>
</tr>
<tr>
<td>4B.1.17</td>
<td>CH₃—CHO</td>
<td>N=C—O</td>
<td>O</td>
<td>4.16</td>
<td>5</td>
</tr>
<tr>
<td>4B.1.18</td>
<td>CH₃CCH₃</td>
<td>N=C—O</td>
<td>O</td>
<td>12.0</td>
<td>-</td>
</tr>
</tbody>
</table>

*Reaction Condition:* 5mmole of carbonyl compound reacted with 6mmole of active methylene compound in presence of 10mole% of catalyst [amm]Br-Pd(OCOCH₃)₂

### 4B.4 CONCLUSION

Metal containing room temperature ionic liquid complex system- [amm]Br-Pd(OCOCH₃)₂ has been proved efficient for the well-known Knoevenagel reaction. The ionic liquid under study is neutral, leaving no toxic residues into the atmosphere and has an easy synthesis method and a work up procedure. Moreover, it does not even require the presence of an additional acidic or alkaline promoter to the reaction. The study opens avenues for exploring other such metal containing ionic liquids or complexes with enhanced and task specific catalytic activity.
REFERENCES


