Imidazo[1,2-*a*]pyridine (IP) has been recognized as premium aza-heterocyclic system. In its functionalized forms it exhibits numerous biological applications, and found its presence in several commercialized drugs. Thus, functionalizing imidazo[1,2-*a*]pyridine under environmentally benign reaction conditions is in high demand. Development of methodologies for the formation of nascent chemical bonds under metal-catalyzed or metal-free conditions have become the foremost task of synthetic organic chemists in recent years. In particular, development of new methodologies by overcoming the demand of pre-activated starting materials have proved to be effective and advantageous protocols towards the construction of plethora of pharmaceutical leads and natural products. The ongoing periodical documentation of on imidazo[1,2-*a*]pyridines allude our interest towards developing novel metal-catalyzed and metal-free strategies for functionalizing imidazo-heterocycles.

Coequally, the upsurge concern for minimizing the waste and providing an environmental being reaction process, has endorsed the exploration of different imidazolium-supported reagents for the liquid-phase synthesis of small aromatics and heteroaromatics. Such strategies have offered unique advantages in organic synthesis by retaining the supremacy of product purification along with the solubility benefits of the reagents. In this regard, we have developed a novel imidazolium–supported benzotriazole reagent and exemplified its applicability in selective organic transformations. The present work was successfully executed in due diligence of sustainable chemistry, and the thesis has been divided into six chapters (Figure 6.1.1).

Figure 6.1.1: A diagram describing the systematic division of the thesis

The present thesis entitled **"C-H Functionalization of Imidazo-Heterocycles and Exploration of Imidazolium-Supported Benzotriazole Reagent for Selective Organic Transformations"** deals with the functionalization of imidazo[1,2-*a*]pyridine (IP) scaffold *via* conventional heterocyclization, metal-catalyzed C-H activation and metal-free oxidative coupling reactions. In addition the thesis systematically documents the synthesis and exploration of novel

imidazoliumsupported
benzotriazole reagent as carboxylic acid activator. A chapter wise summary is presented below:

6.2 Specific conclusions

In chapter 1, of the thesis, we have described the importance and chemical reactivity of
imidazo[1,2-*a*]pyridine skeleton as an introductory chapter to provide a background on
imidazo[1,2-*a*]pyridine based works conducted by synthetic chemists in the past (Figure 6.2.1).

Figure 6.2.1: A graphical representation on the functionalization of imidazo[1,2-*a*]pyridines

Chapter 2: Microwave-Assisted Expedite Synthesis of Imidazo[1,2-*a*]pyridyl Quinoxalin-2(1*H*)-ones

Inspired from the valuable medicinal importance of different imidazo[1,2-*a*]pyridyl-heterocyclic
conjugates, and the profound biological profile of quinoxalines derivatives. **In this chapter** we
have described a microwave-assisted strategy for the synthesis of imidazo[1,2-*a*]pyridyl
appended quinoxalin-2(1*H*)-ones. The desired product were synthesized by reacting prior
synthesized imidazo[1,2-*a*]pyridine-3-glyoxalates and *ortho*-phenylene diamine using
montmorillonite K-10 under solvent-free condition or $Yb(OTf)_3$ in THF. This Hinsberg
heterocyclization reaction showcased good compatibility with a wide variety of substituted
imidazo[1,2-*a*]pyridines resulting in the formation of described products in 20-82% yields under
environmentally being reaction conditions (Scheme 6.2.1).

Scheme 6.2.1: Montmorillonite K-10 or $Yb(OTf)_3$-catalyzed synthesis of imidazo[1,2-*a*]pyridyl
quinoxalinones

The synthesized imidazo[1,2-*a*]pyridine-3-glyoxalates and imidazo[1,2-*a*]pyridyl appended
quinoxalin-2(1*H*)-ones were well characterized by ^{1}H NMR, ^{13}C NMR and mass-spectrometry
analysis

The third chapter of the thesis describes a significant exploration of transition metal-catalyzed
strategies towards the direct synthesis of functionalized imidazo-heterocycles. The chapter is
divided into two parts:

Chapter 3A: Copper-Catalyzed Direct Dicarbonylation of Imidazo-

Heterocycles *via* C-H
Bond Activation

Chapter 3A, of the thesis is focused on the development of an oxidative coupling strategy for the formation of C-3 dicarbonylated imidazo-heterocycles using aryl actaldehydes under Cucatalyzed conditions without the prior activation of Csp^2-H bond of imidazo-heterocycles in the presence of aerial oxygen. This methodology is proposed to proceed by means of cleavage of sp^2-H and sp^3-H bonds between imidazo-heterocycles and aryl acetaldehyde, whereby oxidative cross-dehydrogenative coupling and oxidation of α-methylene of aryl acetaldehydes proceeds in a cumulative manner (Scheme 6.2.2). The versatility of the reaction was generalized with differently substituted electron-rich and electron-deficient imidazo[1,2-*a*]pyridines and aryl acetaldehydes. A detailed mechanistic pathway was proposed by performing a set of control experiments and mass-spectrometry study of the reaction mixture. The mechanism was believed to proceed *via* single electron transfer process (SET) with eventual introduction of oxygen atom from atmospheric air. The synthesized C-3 dicarbonylated imidazo[1,2-*a*]pyridines completely characterized by ^{1}H NMR, ^{13}C NMR and mass spectrometry analysis.

Scheme 6.2.2: Cu-catalyzed aerobic C-3 dicarbonylation of imidazo[1,2-*a*]pyridines

Chapter 3B: Ruthenium(II)-Catalyzed Regioselective *o*-Amidation of 2-Arylimidazo-
Heterocycles *via* C-H Bond Activation

In Chapter 3B, we have described a regioselective Ru(II)-catalyzed strategy for *ortho*-amidation of 2-arylimidazo[1,2-*a*]pyridines with aryl isocyanates *via* Csp^2-H bond activation. An array of *ortho*-amidated 2-arylimidazo[1,2-*a*]pyridines with different functionalities on aryl and pyridyl rings were synthesized in good-to-excellent yields (Scheme 6.2.3). The developed protocol was also applicable to the selective *ortho*-amidation of other 2-arylimidazo-heterocycles such as 2-phenylimidazo[2,1-*b*]thiazole, 2-phenylbenzo[*d*]imidazo[2,1-*b*]thiazole, and 2-phenyl imidazo[1,2-*a*]pyrimidine. Delightfully, the methodology was scalable at gram scale without any

noticeable declination in the yield. This is the first method for the coupling of aryl isocyanates
with the imidazo[1,2-*a*]pyridine system *via* a pentacyclometalated intermediate. Contentedly, the
mechanistic pathway of the reaction was advocated by several control experiments and by ESIMS
study of the reaction mixture. The cationic pentacyclometalated intermediate complex was
synthesized, and utilized for the catalytic and stoichiometric transformation of targeted product,
justifying the formation of described complex in the catalytic cycle. All of the synthesized *ortho*amidated
2-arylimidazo[1,2-*a*]pyridines were detailed characterized by detailed spectroscopic analysis. In addition, the X-ray crystal structure of one of the synthesized derivative provides a
transparent spectroscopic support.

Scheme 6.2.3: Ru(II)-catalyzed *ortho*-amidation of 2-arylimidazo[1,2-*a*]pyridines

The fourth chapter of the thesis describes the significant exploration of metal-free strategies
towards the homocoupling of imidazo-heterocycles. This chapter is also divided into two parts:

Chapter 4A: Transition Metal-Free Homocoupling of Imidazo-Heterocycles *via* Csp^2–Csp^2 Bond Formation

In chapter 4A, we have described a iodobenzene diacetate (PIDA)-mediated synthesis of 3,3′-biimidazo[1,2-*a*]pyridines by the oxidative homocoupling of 2-arylimidazo[1,2-*a*]pyridines
under ambient condition (Scheme 6.2.4a). A series of homocoupled 2,2′-diaryl-3,3′-biimidazo[1,2-*a*]pyridines were synthesized from wide range of electronically rich imidazo[1,2-
a]pyridyl substrates in moderate-to-good yields. This hypervalent iodine(III) mediated crossdehydrogenative
protocol was also applicable towards the homocoupling of other imidazoheterocycles,
such as imidazo[2,1-*b*]thiazoles and benzo[*d*]imidazo[2,1-*b*]thiazoles.

Scheme 6.2.4: PIDA/PhI-mediated/catalyzed synthesis of 2,2′-diaryl-3,3′-biimidazo[1,2-
a]pyridines

The reaction mechanism was believed to proceed with the reversal of the polarity at the C-3
position of imidazo[1,2-*a*]pyridine in the presence of stoichiometric amount of

iodobenzene
diacetate, followed by $SN_{2'}$ nucleophilic substitution with another molecule of imidazo[1,2-*a*]pyridine. All of the synthesized homocoupled biimidazo-heterocycles were detailed characterized by spectroscopic analysis including ^{1}H NMR, ^{13}C NMR and mass spectrometry. In addition, the X-ray crystal structure of one of the synthesized compound provides a clear evidence for the formation of described products. In addition, an organocatalytic approach for the desired transformation employing catalytic amount of iodobenzene with *m*-CPBA/AcOH was also executed (Scheme 6.2.4b).

Chapter 4B: Transition Metal-Free Homocoupling of Imidazo-Heterocycles Linked *via* Sulfur Bridges

In chapter 4B` we have explored the utility of molecular iodine for the oxidative direct homocoupling of imidazo-heterocycles using Na_2S as a sulfur source for predominant synthesis of bis(imidazo[1,2-*a*]pyridin-3-yl)sulfanes and bis(imidazo[1,2-*a*]pyridin-3-yl)disulfanes. The methodology was efficiently controlled under variable solvent conditions in straightforward manner. These direct oxidative strategies for the synthesis of bis-sulfanes and bis-disulfanes were well exemplified with a broad range of substituted 2-arylimidazo[1,2-*a*]pyridines (Scheme 6.2.5). The detailed mechanistic pathway for the synthesis of bis-sulfanes and bis-disulfanes is been properly advocated through a series of control experiments and ESI-MS studies.

Intriguingly, 2-arylimidazo[2,1-*b*]thiazole were also explored towards the formation of bissulfanes and bis-disulfanes in fairly good yields. All of the synthesized bis(imidazo[1,2-*a*]pyridin-3-yl)sulfanes and bis(imidazo[1,2-*a*]pyridin-3-yl)disulfanes were well characterized by ^{1}H NMR, ^{13}C NMR and mass spectrometry analysis. The structures of both sulfur bridge homocoupled products were unambiguously confirmed by X-ray crystallographic studies.

Scheme 6.2.5: I_2-mediated synthesis of bis(imidazo[1,2-*a*]pyridin-3-yl)sulfanes and bis(imidazo[1,2-*a*]pyridin-3-yl)disulfanes

Chapter 5: Exploration of Imidazolium-Supported Benzotriazole Reagent for Selective

Organic Transformations

In Chapter 5, we have presented a brief background of different imidazolium-supported reagents, and their application in various organic transformations. Later on, the chapter deals with a detailed synthetic protocol for the synthesis of imidazolium-supported benzotriazole reagent (Im-BtH) as a novel synthetic auxiliary. Thereafter, eight different *N*-acylated imidazolium-supported benzotriazole reagents (Im-BtCOR) were prepared and exemplified as greener carboxyl group activating reagents for the synthesis of library of amides, esters and thioesters in aqueous medium under microwave irradiation (Scheme 6.2.6). Gratifyingly, Im-BtH was efficiently used in one-pot fashion for the synthesis of an amide in comparable yield as a representative example. The application of imidazolium-supported *N*-acetyl benzotriazole (Im-$BtCOCH_3$) leads to synthesis of Paracetamol on the gram scale under green conditions in 93% yield. The reagent was successfully reused five times without any noticeable loss in activity

Scheme 6.2.6: Synthesis of amides, esters and thioesters, using novel imidazolium-supported benzotriazole reagent.

6.3 Future Scope

The current thesis reflects the development of new methodology for the synthesis of biologically active compounds under metal-catalyzed and metal-free conditions. Although the thesis mainly focused on the exploration of chemistry on imidazo[1,2-*a*]pyridine scaffold, yet there exist enormous scope for developing different imidazo[1,2-*a*]pyridyl fused heterocyclic frameworks.

In addition, introducing other nascent functionalities, at the expense of chelation-assistance of nitrogen of IP is an area left to explore for further the tandem cyclization reactions under appropriate reaction conditions. In concordance with the literatures precedence, we can expect to perceive good bioactivity of all functionalized imidazo-heterocycles.

On the other hand the broad range applications of benzotriazole chemistry, further provides a strong need for the exploration of imidazolium-supported benzotriazole reagent (ImBtH) to

achieve various organic molecules in constantly greener approaches.