Chapter 1

A General Introduction
1.1 INTRODUCTION

Heterocyclic chemistry is one of the most valuable sources of novel compounds with diverse biological activity, mainly, because of the unique ability of the compounds to mimic the structure of peptides and to bind reversibly to proteins.\(^1\) The interface between chemistry and biology where substantially new scientific insights, discoveries and applications are taking place, has been bridged by many small heterocyclic compounds. To medicinal chemists, the true utility of heterocyclic structures is the ability to synthesize one library based on one core scaffold and to screen it against a variety of different receptors, yielding several active compounds. They also serve as important intermediates in organic synthesis, play an important role in biochemical processes because the side groups of the most typical and essential constituents of living cells DNA and RNA, are based on aromatic heterocycles.\(^2\) Almost unlimited combinations of fused heterocyclic structures can be designed, resulting in novel polycyclic frameworks with the most diverse physical, chemical, and biological properties. The fusion of several rings leads to geometrically well-defined rigid polycyclic structures and, thus, holds the promise of a high functional specialization resulting from the ability to orient substituents in three dimensional spaces.

Heterocyclic compounds are worth attention for above mentioned reasons; therefore, organic chemists have been making extensive efforts to produce these heterocyclic compounds by developing new and efficient synthetic transformations. Among a variety of new synthetic transformations, transition metal-catalyzed reactions are some of the most attractive methodologies for synthesizing heterocyclic compounds, since transition metal-catalyzed reactions can directly construct complicated molecules from readily accessible starting materials under mild conditions. The catalytic construction of heterocyclic skeletons is classified into two major processes (Scheme 1).\(^3\)

- C-C bond formation from the corresponding acyclic precursors and
- C-X bond formation from the corresponding acyclic precursors (X = heteroatom).

**Scheme 1. Two General Methods for the Synthesis of Heterocycle**

\[ \text{C-C bond formation} \quad \text{C-X bond formation} \]
The syntheses of heterocycles cover a large number of synthetic protocols, however, we tried to summarized some of them in Scheme 2.\textsuperscript{3} One of the common method for the synthesis of heterocycles is cycloaddition as shown in Scheme 2A. Formation of heterocycles may have another route, where activated carbon may attack to the carbon of a leaving group resulting in the formation of C-C bond or activated carbon may attack to allylic position of leaving group to form C-C bond (Scheme 2B). Alternatively, a heteroatom X may attack instead of C to form C-X bond (Scheme 2C). Furthermore, ring closing reactions of terminal or internal alkenes/alkynes may lead to the formation of heterocycles (Scheme 2D).

**Scheme 2.** Starting Substrates along with Reaction Patterns for the Synthesis of Heterocycles

Cyclization reaction of alkenes/alkynes may lead to the formation of heterocyclic compound using transition metal as catalyst. Lewis-acid catalyst such as I\textsubscript{2}, ICl etc may also be used for synthesis of heterocycles. Since a transition metal-
catalyzed reaction can directly construct complicated molecules, therefore, they have been employed in almost every type of organic synthesis to afford diverse arrays of heterocycles (Scheme 3).

**Scheme 3. Cyclization Reaction of Alkenes/Alkynes using Transition Metal/Lewis acid as Catalyst**

![Cyclization Reaction Scheme](image)

**1.2 REVIEW OF LITERATURE**

Particularly, transition metal-catalyzed cyclizations have shown inherently undeniable benefits, such as good chemo- or regioselectivity, mild conditions, as well as high economical and ecological merits. They can directly construct complex molecules from readily accessible starting materials under mild conditions. In the past few years, the area of π-acid catalysis has emerged as a powerful technique in synthetic organic chemistry. A survey of the literature revealed a plethora of reports involving π-acid-catalyzed reactions.\(^4\) Metals such as Pd, Pt, Cu, Au, Ag, Ni, Ru, Rh, Ir etc are the most widely used as π-acid catalysts for the activation of C-C multiple bonds.\(^5\) Similarly, Lewis-acids such as I\(_2\), ICl, Br\(_2\), NIS, NBS and NCS are also alkynophilic in nature and are extensively used for synthesis of heterocycles.\(^6\)

Among various π-substrates used, alkynes have been widely employed for synthesis of polyfused heteroaromatic compounds. Wide range of reactions are reported
using alkyne derivatives as a substrate. The alkynes have activated triple bond which plays important role in the electrophilic cyclization, annulation methodology etc. It is well-precedented that the transition metal or Lewis acid-catalyzed cyclization of alkynes possessing a nucleophile in their proximity is an important process in organic synthesis, which can construct various heterocycles in an efficient and atom-economic way.\(^7\)

Consequently, during the last few years an explosive increase of interest in electrophilic heteroatom cyclization has taken place. Thus, they have become an extremely active and original field of heterocycle synthesis. This methodology takes advantages, in most cases, of the presence of a residual halogen atom which is suitable to suffer further transformations. Electrophilic cyclizations may be defined as those processes that involve addition of the electrophilic source to C(sp) or C(sp\(^2\)) bonds of alkenes, alkynes, allenes, conjugated dienes, and other carbon-carbon multiple bonds. These heterocycle rings can be formed through \textit{endo} or \textit{exo} cyclization modes, depending on the chain length, the substitution pattern on the chain, and the electrophile employed. Larock and co-workers have reported synthesis of polycyclic aromatic iodides. The reaction of 2-(arylethynyl)biphenyls 1 bearing either electron-donating or electron-withdrawing groups with ICl at -78 °C affords substituted polycyclic aromatic iodides 2 in good to excellent yields (Scheme 4).\(^8\)

**Scheme 4.** Synthesis of Polycyclic Aromatic Iodides via Electrophilic Iodo-cyclization (Larock approach)

Further, Larock and Waldo have shown that functionally substituted 2-alkyn-1-one \(o\)-methyl oximes 3 can be cyclized under mild reaction conditions in the presence of ICl to give the corresponding 4-iodoisoxazoles 4 in moderate to excellent yields (Scheme 5).\(^9\)
Scheme 5. Synthesis of Substituted Isoxazoles by Electrophilic Cyclization (Larock approach)

\[
\begin{align*}
\text{R1} & = \text{H, Me, Ar, } n-C_{6}H_{13}, \text{t-Bu, etc} \\
\text{R2} & = \text{Me, Ar, t-Bu, etc} \\
N^\text{OMe} \quad \text{ICI (1.2 equiv)} \quad 0.5-1 \text{ h, r.t.} \quad \text{CH}_2\text{Cl}_2 \quad N^\text{OMe} \\
\end{align*}
\]

Further, to solve the mystery of functional group effect, Larock and co-workers have studied relative reactivity of various functional groups toward alkyne electrophilic cyclization reactions. They prepared diarylalkynes 5 by consecutive Sonogashira reactions of appropriately substituted aryl halides and competitive cyclizations have been performed using I₂, ICl, NBS and PhSeCl as electrophiles. They found that the nucleophilicity of the competing functional groups, polarization of the triple bond, and the cationic nature of the intermediate are the most important factors in determining the outcome of these reactions (Scheme 6).¹⁰

Scheme 6. Competition Studies in Alkyne Electrophilic Cyclization Reactions (Larock approach)

Further, extending this methodology in iterative fashion, Larock and Mehta have shown straightforward strategy for the synthesis of polyheterocyclic compounds 10, which involved iterative cycles of palladium-catalyzed Sonogashira coupling, followed by iodocyclization using I₂ or ICl. They have synthesized a variety of heterocyclic units including benzofurans, benzothiophenes, indoles, and isocoumarins, under mild reaction conditions (Scheme 7).¹¹

Scheme 7. Iodine/Palladium Approaches to the Synthesis of Polyheterocyclic Compounds (Larock approach)
Use of palladium-catalyzed methodology for library approaches in the synthesis of small-molecule and numerous natural products along with biologically active molecules is well-established. Palladium complexes exist in three oxidation states Pd(0), Pd(II) and Pd(IV). The facile interconversion between these oxidation states is responsible for the broad utility of palladium in organic chemistry. Hegedus and co-workers have reported the preparation of indoles using intramolecular Heck cyclization by carrying out the reaction of 2-iodoanilines 11 with catalytic Pd(OAc)$_2$, Et$_3$N, and MeCN at 110 °C which afforded substituted indoles 12 in good yields (Scheme 8).\textsuperscript{12}

**Scheme 8.** Palladium-Catalyzed Synthesis of Indoles (**Hegedus approach**)

![Scheme 8](image)

Harned and Tello-Aburto achieved the synthesis of heterocyclic compound 14 via palladium-catalyzed regioselective cyclizations of alkyne-tethered cyclohexadienones 13. They proposed that cyclization involved an initial Pd-mediated acetoxylation of the alkyne, followed by migratory insertion and protonolysis of the resulting palladium enolate (Scheme 9).\textsuperscript{13}

**Scheme 9.** Palladium-Catalyzed Reactions of Cyclohexadienones (**Harned approach**)

![Scheme 9](image)

Recently, Liang and co-workers demonstrated a palladium-catalyzed tandem cyclization/C–H functionalization using two alkynes to construct a series of polycyclic functionalized indoles. They used a range of internal alkynes 15 bearing synthetically useful functional groups and successfully synthesized polycyclic compounds 16 (Scheme 10).\textsuperscript{14}
Scheme 10. Pd(II)-Catalyzed Synthesis of Functionalized Indoles via Tandem Cyclization (Liang approach)

Coming to the coinage metals, Ag, Au and Cu are extensively used for the synthesis of heterocycles. The applications of silver salts in organic synthesis are indeed mostly driven by its Lewis acidity. The d^{10} electronic configuration favoured interactions of Ag salt with unsaturated systems having low-lying empty orbitals, especially alkynes, and to a lesser extent allenes and alkenes. This alkynophilicity is probably reinforced by f orbitals and relativistic effects. Porco and Su reported an elegant synthesis of pyrroloisoquinolines 18 using AgOTf as catalyst through cascade cyclization/[3+2] dipolar cycloaddition of alkynyl N-benzylidene glycinates 17 in toluene (Scheme 11).^{15}

Scheme 11. Synthesis of Pyrroloisoquinolines through Cascade Cyclization/ [3+2] Dipolar Cycloaddition (Porco approach)

Further, Peng and co-workers have shown a facile synthesis of halo-substituted benzo[a]fluorenols 20 via silver tetrafluoroborate catalyzed electrophilic cascade cyclization under mild conditions at 10 °C in CH_2Cl_2. The reaction proceeded with good chemical selectivity (Scheme 12).^{16}

Scheme 12. Synthesis of Halo-substituted Benzo[a]fluorenols (Peng approach)
Recently, Patil and co-workers have reported the synthesis of fused isoquinolines 23 using \(\sigma\)-alkynylbenzaldehyde 21 and aromatic amines having tethered nucleophiles 22 using AuCl as a catalyst in dichloroethane (Scheme 13).\(^{17}\)

**Scheme 13.** Synthesis of Fused Isoquinolines via Tandem Nucleophilic Addition and Cyclization (Patil approach)

![Scheme 13](image)

Balamurugan and Gudla have shown an intramolecular cyclization of arylmethyl ketone 24 tethered with arylalkyne results in 1-arylnaphthalene 25 lignan scaffold under gold catalysis. Using this method, it has been shown that 1-arylnaphthalenes fused with furan, pyran and cyclopentane could be made in good yields (Scheme 14).\(^{18}\)

**Scheme 14.** Synthesis of Arylnaphthalene by Gold-Catalyzed Intramolecular Sequential Electrophilic Addition and Benzannulation (Balamurugan approach)

![Scheme 14](image)

Ohno and co-workers have reported the synthesis of 3-(aminomethyl) isoquinoline-fused polycyclic compounds 29. The reaction began with a Mannich-type reaction of 2-ethynylbenzaldehyde 26 with paraformaldehyde 27 and a secondary amine 28, followed by treatment with a diamine component which gave tricyclic isoquinolines through cascade cyclization and oxidation reaction (Scheme 15).\(^{19}\)

**Scheme 15.** Synthesis of 3-(aminomethyl)isoquinoline-fused Polycyclic Compounds (Ohno approach)

![Scheme 15](image)
Zora and Kivrak have shown that when α,β-alkynic hydrazones 32, prepared readily from hydrazines 31 and propargyl aldehydes and ketones 30, is treated with copper(I) iodide in the presence of triethylamine in refluxing acetonitrile, underwent electrophilic cyclization to afford pyrazole 33 derivatives in good to excellent yields (Scheme 16).20

Scheme 16. Synthesis of Pyrazoles via CuI-Mediated Electrophilic Cyclizations (Zora approach)

Chatani and co-workers have shown Rh-catalyzed reaction of alkynes 35 with 2-bromophenylboronic acids 34 involved carbonylative cyclization to give indenones 36. They have shown that regioselectivity was dependent on both the electronic and the steric nature of the substituents on the alkynes. Presence of a bulky group and an electron-withdrawing group favoured the α-position of indenones. In the case of silyl- or ester-substituted alkynes, the regioselectivity was extremely high. The selectivity increased in the order SiMe3 > COOME . aryl . alkyl (Scheme 17).21

Scheme 17. Rh(I)-Catalyzed Carbonylative Cyclization Reactions Leading to Indenones (Chatani approach)

Cheng and co-workers have developed a rhodium-catalyzed chelation-assisted C-H activation of α,β-unsaturated ketoxime 37. The reaction of ketoxime with alkynes 38 afforded substituted pyridine 39 derivatives in good to excellent yields (Scheme 18).22
Scheme 18. Rhodium-Catalyzed One-Pot Synthesis of Substituted Pyridine Derivatives (Cheng approach)

\[ \text{R}^2 \text{N}=\text{OH} + \text{R}^4 \equiv \text{R}^4 \xrightarrow{\text{Rhl(Ph$_3$)}(3.0 \text{ mol \%)}} \text{toluene, 130 °C} \rightarrow \text{R}^2 \text{N}=\text{R}^4 \]

Similar to rhodium, ruthenium was also used for the synthesis of heterocyclic compounds comprising of alkyne as one of the substrate. Ackermann and Lygin have reported the ruthenium catalyzed oxidative annulation of alkynes 41 by aniline derivatives 40. They have shown that catalysis was accomplished with a cationic ruthenium(II) complex in water as a sustainable solvent, thereby setting the stage for an expedient synthesis of bioactive indoles with ample scope (Scheme 19).23

Scheme 19. Cationic Ruthenium(II) Catalyzed Synthesis of Indole in Water (Ackermann approach)

Further, Ackermann and co-workers have achieved ruthenium catalysed oxidative annihilations of alkynes by acrylamides, which allowed the preparation of 2-pyridones 45 using various electron-rich and electron-deficient acrylamides 43 as well as (di)aryl- and (di)alkyl-substituted alkynes 44 (Scheme 20).24

Scheme 20. Ruthenium-Catalyzed Oxidative Synthesis of 2-Pyridones (Ackermann approach)

Odom and co-workers have shown that a titanium-catalyzed three-component coupling reaction can be used to generate tautomers of N-aryl-1,3-diimines 49. They
treated N-aryl-1,3-diimines with acetic acid leading to cyclization forming quinoline 50 derivatives via one-pot procedure (Scheme 21).\textsuperscript{25}

**Scheme 21.** Titanium-Catalyzed Direct Access to Substituted Quinolines (Odom approach)

Lei and co-workers have developed a strategy towards the cyclic addition of 2,2'-dihydroxybiphenyl 51 to terminal alkynes 52 using Lewis acid TiCl\(_4\) as catalyst. They synthesized dibenzo[\(d,f\)][1,3]-dioxepines derivatives 53 in good yields with excellent regio-selectivity (Scheme 22).\textsuperscript{26}

**Scheme 22.** Synthesis of Dibenzo[\(d,f\)][1,3]-dioxepines Catalyzed by Lewis Acid TiCl\(_4\) (Lei approach)

Gandon and co-workers have synthesized 1,2-dibromobenzene derivative 55 by the cyclization of a triyne 54. For this purpose they have synthesized air stable cobalt complex, which led to the cyclised product in good yield (Scheme 23).\textsuperscript{27}

**Scheme 23.** Cobalt-Catalyzed Synthesis of 1,2-Dibromobenzene derivative (Gandon approach)
Echavarren and co-workers have shown Pt(II)-catalyzed synthesis of fused dipyrane derivatives 57 starting from 1,6-enynes substrate 56. The reaction was proposed to go via Pt(II)-catalyzed nucleophilic additions to 1,6-enynes, and cyclopropyl metal carbene formed in the 6-endo-dig cyclization was evolved from seven-membered ring intermediates (Scheme 24). 28

**Scheme 24.** Platinum(II)-Catalyzed Cyclization of 1,6-enynes (Echavarren approach)

1.3 BALDWIN’S RULE

The key bond-forming step which transforms an acyclic precursor into the desired cyclic structure in a regio- and stereocontrolled manner remains critical to the construction of complex molecules. These heterocycle rings can be formed through endo or exo cyclization modes, depending on the chain length, the substitution pattern on the chain, and the electrophile employed (Figure 1). 29

**Figure 1.** Exo/endo-Modes of Cyclization

A series of guidelines that describe the propensity of various systems to participate in ring-forming reactions was put forth by Baldwin in the 1970s. 30 This set of guidelines, which describe the relative ease of ring formation, has become known as Baldwin’s rules of ring closure and has been proved to be a useful tool in evaluating the feasibility of ring-forming reactions. Baldwin described his rules in terms of three features of the reaction:

- The ring size being formed (indicated through a numerical prefix).
- The hybridized state of the carbon atom undergoing the ring closing reaction ($sp =$ digonal, $sp^2 =$ trigonal, and $sp^3 =$ tetrahedral).
• The nature of the breaking bond (exo, the breaking bond is external to the newly formed ring, and endo, the breaking bond is within newly formed ring).

For example six-membered ring closing is shown in Figure 2

![Figure 2. Patterns of Ring Closure for 6-membered Ring](image)

The original “Baldwin rules” are reproduced in Table 1. All three factors involved in the classification (ring size, exo versus endo attack and hybridization at the site of attack) are critical in determining whether a particular cyclization mode is favourable.

**Table 1. Baldwin’s Rules for Ring Closure**

<table>
<thead>
<tr>
<th>Nucleophilic, Electrophilic, Radical</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>-tet (sp³)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>endo-</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>exo-</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>-trig (sp²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>endo-</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>exo-</td>
<td>✓</td>
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<tr>
<td>-dig (sp)</td>
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<td></td>
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<tr>
<td>endo-</td>
<td>✓</td>
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<tr>
<td>exo-</td>
<td>✓</td>
<td>✓</td>
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</tr>
</tbody>
</table>

**1.4 AIM AND OBJECTIVES OF THE PRESENT WORK**

Literature survey revealed that transition metal-catalyzed cyclization reactions have shown inherently undeniable benefits, such as good chemo- or regioselectivity, mild conditions, as well as high economical and ecological merits. They can directly construct complex molecules from readily accessible starting materials under mild conditions. Similarly, non metal Lewis-acids such as I₂, ICl, Br₂, NIS, NBS and NCS widely used media for the synthesis of heterocyclic compounds. In the past few years,
the area of \( \pi \)-acid catalysis has emerged as a powerful technique in synthetic organic chemistry. Thus, involving \( \pi \)-acid-catalyzed transition metal or other Lewis-acids which are alkynophilic in nature and can be used for synthesis of heterocycles.

Among various \( \pi \)-substrates used, alkynes have been widely employed for synthesis of polyfused heteroaromatic compounds. Wide range of reactions are reported using alkyne derivatives as a substrate. The alkynes have activated triple bond which plays important role in the electrophilic cyclization, annulation methodology etc.

In view of the above facts, we laid down the objectives to develop efficient synthetic route for the synthesis of fused tricyclic and tetracyclic pyrrolo[1,2-\( \alpha \)]quinolines and indolo[1,2-\( \alpha \)]quinolines using I\(_2\)/Pd-catalyzed protocol. We also conceived silver-catalyzed methodology for the synthesis of substituted acridinols, quinolinols and naphthalenols (Scheme 25).

**Scheme 25.**

\[
\begin{align*}
X &\quad \text{C} \quad n \\
\text{H} &\quad \text{R'} \\
\text{I} &\quad \text{Pd / Ag} \\
6\text{-endo-dig cyclization}
\end{align*}
\]

\( X = \text{hetero-atom} \)

Our main objectives of the work are:

1. Considering importance and various advantages of Iodine-mediated reactions, we wished to synthesize medicinally and materialistically important pyrrolo[1,2-\( \alpha \)]quinoline via electrophilic iodo-cyclization. This methodology takes advantages of the presence of a residual halogen atom which is suitable to suffer further transformations.

2. With our objective to develop parallel methodologies capable of furnishing regioisomeric heterocyclic compounds starting from similar substrates, governed by various catalytic protocols, palladium-catalyzed tandem (one-pot) synthesis of indolo[1,2-\( \alpha \)]quinoline and pyrrolo[1,2-\( \alpha \)]quinoline was envisioned.
3. With our ongoing efforts in the synthesis of heterocycles by the electrophilic cyclization of alkynes, we envisioned a straightforward approach for the synthesis of acridinol, quinolinol, naphthalenol and benzothiophenol via silver-catalyzed electrophilic cyclization.

1.5 DISSERTATION ORGANIZATION

This thesis work consists of four chapters including A General Introduction (Chapter 1).

CHAPTER 2

Iodine-Mediated Synthesis of 5-Iodopyrrolo[1,2-α]quinolines

The second chapter describes the synthesis of pyrrolo[1,2-α]quinolines by electrophilic cyclization of the alkynes using Lewis acidic I₂ in two steps in mild reaction condition (Scheme 26).

Scheme 26. Synthesis of Pyrrolo[1,2-α]quinolines

This chapter demonstrates the endo-cyclic ring closure of 1-(2-(subst-ethynyl)phenyl)-1H-pyrroles 60a–t mediated by Lewis acid, I₂ under mild conditions affording substituted 5-Iodo-pyrrolo[1,2-α]quinolines 61a–t in good to excellent yields. The reaction shows selective C–C bond formation on more electrophilic alkynyl carbon
resulting in the regioselective 6-endo-dig cyclized product. This method allows functional group variation on the quinoline nucleus which subsequently proves highly desirable for structural and biological activity assessments. Also iodine-catalysis system has undoubtedly extended the applications of electrophilic reactions and replaced the use of more expensive metal-catalysts. The chemistry outlined here is extremely versatile and accommodates various functional groups which makes it ideal for the generation of various functionally-substituted scaffolds. Furthermore, this cyclization method leads to the synthesis of halogen containing quinoline derivatives which thereafter has been elaborated using palladium and copper catalyzed coupling reactions, such as Suzuki-Miyaura, Heck, Alkyne-annulation and Ullmann coupling reactions.

CHAPTER 3
Palladium-Catalyzed Synthesis of Indolo[1,2-α]quinolines and Pyrrolo[1,2-α]quinolines

With our objective to develop parallel methodologies capable of furnishing regioisomeric heterocyclic compounds starting from similar substrates, governed by various catalytic protocols, and in keeping with well-established palladium-catalyzed methodologies used for library approaches in the synthesis of small-molecules and numerous natural products along with biologically active ingredient, in this chapter we have demonstrated one-pot alternative route for the synthesis of indolo[1,2-α]quinolines and pyrrolo[1,2-α]quinolines (Scheme 27).

**Scheme 27.** Synthesis of Indolo[1,2-α]quinolines and Pyrrolo[1,2-α]quinolines

![Scheme 27](image)

In chapter 3, an operationally simple tandem strategy for the regioselective synthesis of indolo[1,2-α]quinolines (64a–v) and pyrrolo[1,2-α]quinolines (65a–k) from 1-(2-bromophenyl)-1H-indole/pyrrole by the palladium-catalyzed sequential C-C bond formation is described. The developed new methodology combining sonogashira...
step with palladium catalyzed regioselective 6-endo-dig C–C bond formation in a tandem fashion, is advantageous, as it improved the efficiency, atom economy, and modularity of the synthesis. This synthetic methodology accommodates wide functional group variation on alkyne, which proves to be advantageous for structural and biological activity assessments. The formation of cyclized products was well established by $^1$H NMR, $^{13}$C NMR and HRMS datas.

**CHAPTER 4**

**Silver-Catalyzed Synthesis of Acridines, Quinolines and Naphthalenes**

This chapter describes the synthesis of AgOTf catalyzed synthesis of acridinols, quinolinols, naphthalenols, and dibenzothiophenol (Scheme 28).

**Scheme 28.** Synthesis of Acridinols, Quinolinols, Naphthalenols, and Dibenzothiophenol

In chapter 4, a facile, efficient and general synthetic method for a wide range of medicinally useful 2-carboxylate derivatives of acridinols (69a–k), quinolinols (69l–n), naphthalenols (69o–s), and dibenzothiophenol (69t) has been developed via silver-catalyzed intramolecular electrophilic cyclization of 3-(2-alkynyl)aryl-$\beta$-ketoesters (68a–t). The reaction shows selective C–C bond formation on more electrophilic alkynyl carbon resulting in the regioselective 6-endo-dig cyclized product, which was confirmed by charge density calculation and X-ray crystallographic studies. The deuterium labeling experiments were performed to ascertain the mechanism. The salient feature of our pathway demonstrated tolerance for various substrates like quinolinecarbaldehyde, nicotinaldehyde, benzaldehyde and benzothiophenecarbaldehyde, which afforded various 2-carboxylate derivatives of acridinol, quinolinol, naphthalenol and benzo thiophenol respectively under mild reaction condition in good yields.
1.6 REFERENCES


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