Chapter 3
Base-Mediated Hydroamination of Terminal Alkynes
3.1 INTRODUCTION

Design of an effective and efficient catalytic carbon-to-heteroatom (C-X) bond formation reaction constitutes an active area of research that has a wide range of potential applications in both fine and industrial chemical syntheses. These products can not only be used in a number of synthetically useful transformations but also can be simply reduced to stable molecules. Many natural products and substituted nitrogen containing heterocycles can be successfully synthesized by inter- or intramolecular hydroamination of alkynes.

Hydroamination of alkynes have been involved successfully in the total synthesis of natural products like (+)-pseudodistomin D, (+)-preussin II, (+)-(S)-laudanosine III, and (–)-(S)-xylopinine VI (Figure 3.1).

![Figure 3.1. Natural products synthesized by the hydroamination of alkynes](image)

It can also be combined in a tandem process with several other reactions like Cope rearrangement, hydroarylation, hydrosilylation and with diverse addition reactions. Inter- or intramolecular hydroamination of alkynes was also found to be successful for the synthesis of substituted indoles and pyrroles (Scheme 3.1).
3.2 REVIEW OF LITERATURE

Since the pioneering studies of Stork, enamines have remained among the most widely used nucleophiles for the construction of C–C bonds under mild reaction conditions.\(^7\)

**Scheme 3.2.**

The profound impact of enamine chemistry on organic synthesis is well manifested by its widespread utility in a variety of reactions. To the best of our knowledge, hydroamination of alkynes is the most simplest and efficient process for the synthesis of enamines and imines.\(^9\)

Very first report on the addition of amines and terminal alkynes was given in 1977 by Riess et al.\(^10\) The addition of secondary amines XVII to electro-deficient perfluoroalkylethylenes XVI was successfully done in the presence of various solvents like ether, dioxane, CHCl\(_3\), CCl\(_3\) or CF\(_2\)ClCCl\(_2\), to obtain a series of selectively the E-isomer of perfluoroalkylamines XVIII (Scheme 3.3).

**Scheme 3.3.**

Later, many groups have reported metal-catalyzed addition of ammonia, primary amines or secondary amines onto alkynes.\(^9,11\) These reported methods were
either multistep or utilize harsh reaction conditions. Some procedures provided mixture of hydroaminated products or were accompanied by side reactions.

In 1992, Bergman and co-workers investigated the possibility of carrying out hydroamination catalyzed by zirconocene bisamides, \( \text{Cp}_2\text{Zr(NHR)} \) to form azametallacyclobutenes.\(^{12}\) During this course of time various catalytic or non-catalytic methods have been reported for the hydroamination of terminal alkynes using primary and secondary amines.

An intense literature study suggested that there were very few reports available on the addition of heterocyclic amines onto terminal alkynes. A notable work was reported by Knochel in 1999 for the addition of amines and alcohols to phenylacetylene using CsOH.H\(_2\)O in NMP (Scheme 3.4).\(^{13}\)

\[
\text{Scheme 3.4:}
\]

Recently, Liu and co-worker reported the Au(I)-catalyzed tandem hydroamination of terminal alkynes to synthesize the highly selective tertiary amines (Scheme 3.5).\(^{14}\) They discussed a diversity-oriented, and highly diastereoselective synthesis of tertiary amines XXVII with a broad substrate scope, thus rendering the method a valuable complementary approach to the conventional synthesis of amines.

\[
\text{Scheme 3.5:}
\]

Thus, the direct addition of amine N–H bonds to unsaturated substrates provides a simple, efficient, and atom-economic route to the synthetically useful
ketimines and enamines. It is also superior to the other available methods such as imination of ketones\textsuperscript{15} or the aminomercuration/demercuration of alkynes.\textsuperscript{16}

\(N\)-(1-Alkenyl)azoles or \(N\)-vinylimidazoles are important compounds in organic synthesis, and can be found in numerous biologically active molecules.\textsuperscript{17} However, there are many methods to prepare these compounds, most of these suffer from either harsh reaction conditions or lack of stereocontrol of the double-bond geometry.\textsuperscript{18} Hence, the addition of \(N\)-heterocycles onto terminal alkynes to yield vinyl-enamines still was an important area for researchers to work and explore.

An alternate and straightforward method for the synthesis of vinyl-enamines was recently reported by allowing vinylation of \(N\)-nucleophiles with various substituted (\(E\))-vinyl bromides under palladium-free and ligand-free conditions up to 95\% yield (Scheme 3.6).\textsuperscript{19}

**Scheme 3.6.**

3.3 **OBJECTIVE AND STRATEGY**

Due to the difficulties associated with hydroamination reactions and with very few reports on the addition of heterocyclic amines onto terminal alkynes to yield vinyl-enamines, we investigated the possibility of carrying out the stereo- and regioselective addition of these substrates. Encouraged by the successful results obtained in the hydroamination of internal alkynes with KOH; in this chapter we further extended the scope of this base for the regio- and stereoselective synthesis of stilbene type styryl indoles, pyrrole and imidazoles (Scheme 3.7).\textsuperscript{20}

**Scheme 3.7.** Synthesis of Styryl Indoles, pyrroles and imidazoles by the addition of \(N\)-heterocycles on terminal alkynes
3.4 RESULTS AND DISCUSSION

3.4.1 Hydroamination of Terminal Alkynes

3.4.1.1 Establishment of reaction conditions

In order to obtain the optimized reaction condition, we started our investigation using previous results used for the addition of heterocyclic amines onto internal alkynes. In the presence of 2.0 equiv of KOH, reaction of indole 1a and 1-ethynyl-4-methylbenzene 2a afforded a mixture of (Z)-1-(4-methylstyryl)-1H-indole 3a and (E)-1-(4-methylstyryl)-1H-indole 4a isomers in 85% yield and 50:50 stereoselectivity (Table 1, entry 1).

Table 3.1. Optimization of the Reaction Conditions.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>$T \degree C$</th>
<th>Stereoisomeric Ratio ($4a$:3a)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>KOH</td>
<td>DMSO</td>
<td>24</td>
<td>120</td>
<td>50:50</td>
<td>85</td>
</tr>
<tr>
<td>2</td>
<td>Cs$_2$CO$_3$</td>
<td>DMSO</td>
<td>24</td>
<td>120</td>
<td>0:100</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>KOtBu</td>
<td>DMSO</td>
<td>24</td>
<td>120</td>
<td>90:10</td>
<td>77</td>
</tr>
<tr>
<td>4</td>
<td>KOH</td>
<td>DMSO</td>
<td>24</td>
<td>30</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>KOH</td>
<td>DMSO</td>
<td>12</td>
<td>80</td>
<td>20:80</td>
<td>60</td>
</tr>
<tr>
<td>6</td>
<td>KOH</td>
<td>DMSO</td>
<td>0.5</td>
<td>120</td>
<td>0:100</td>
<td>90</td>
</tr>
<tr>
<td>7</td>
<td>KOH</td>
<td>DMSO</td>
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<td>89</td>
</tr>
<tr>
<td>8</td>
<td>KOH</td>
<td>DMSO</td>
<td><strong>0.5</strong></td>
<td><strong>120</strong></td>
<td><strong>2:98</strong></td>
<td><strong>92$^d$</strong></td>
</tr>
<tr>
<td>9</td>
<td>KOH</td>
<td>DMF</td>
<td>0.5</td>
<td>120</td>
<td>30:70</td>
<td>75$^d$</td>
</tr>
<tr>
<td>10</td>
<td>KOH</td>
<td>Toluene</td>
<td>0.5</td>
<td>120</td>
<td>40:60</td>
<td>10$^d$</td>
</tr>
<tr>
<td>11</td>
<td>KOH</td>
<td>DMA</td>
<td>0.5</td>
<td>120</td>
<td>30:70</td>
<td>54$^d$</td>
</tr>
<tr>
<td>12</td>
<td>KOH</td>
<td>NMP</td>
<td>0.5</td>
<td>120</td>
<td>10:90</td>
<td>85$^d$</td>
</tr>
</tbody>
</table>

$^a$ Reactions were carried out using 1a (2.0 equiv), 2a (1.0 mmol) and base (2.5 equiv) in solvent (2.0 mL). $^b$ Stereoisomeric ratio. $^c$ Total yield of two isomers. $^d$ Base (0.20 equiv) was taken.
The effective addition of heterocyclic amines followed the anti-markovnikovs rule. When different bases were tested in this reaction, KOH proved to be the most effective (Table 1, entries 2 and 3). The stereoselectivity of product was found to be dependent on the nature of base, reaction time and temperature. Cs$_2$CO$_3$ afforded only Z-isomer (3a) in 80 % yield (entry 2), however KOrBu provided the E-isomer 4a as a major product (entry 3). Decrease in the reaction temperature showed that no addition product was formed at 30 °C and reaction initiated at 80 °C (entries 4 and 5). Monitoring the reaction at 120 °C suggested that the hydroaminated product 3a was formed within 30 min in 90 % yield (entry 6) and further increase in time led to the conversion of kinetically stable Z- isomer into thermodynamically stable E- isomer (entry 7).

In contrast to internal alkynes, terminal alkynes afforded 3a with catalytic amount of KOH (20 mol %) in good yield (entry 8). With this result in hand, finally the effect of various solvents was checked for the selective formation of 3a. It was interesting to see that high boiling solvents like DMF, toluene, DMA provided the mixture of E/Z isomers in low yields in comparison to DMSO (entries 9–11). Another high boiling and polar solvent N-methylpyrrolidone, NMP, provided the Z- isomer 3a in 90:10 stereoisomeric ratio and 85% yield (entry 12).

3.4.1.2 Characterization of compounds 3a and 4a

Compound 3a was prepared by the addition of 0.2 mmol of KOH in the solution of indole 1a and 4-ethynyltoluene 2a in DMSO. The reaction mixture was heated at 120 °C for 20-25 minutes. The structure of compound 3a was established on the basis of its spectral data analysis. Its high resolution mass spectrum showed [M]$^+$ peak at m/z 233.1205, which confirmed its molecular formula to be C$_{17}$H$_{15}$N. In the $^1$H NMR spectrum (CDCl$_3$, 300 MHz), the characteristic peaks of methyl group attached to C4
appeared at $\delta$ 2.30 as singlet for 3 protons. The styryl protons at C1 appeared at $\delta$ 6.89 and C2 came at 6.26 ppm as doublets and coupling constant, $J_{H-H} = 9.3$ Hz falling in the range of $cis$-coupled protons. This suggested that isomer 3a was with $Z$-configuration (Table 3.2). Similarly, in its $^{13}$C NMR spectrum obtained in CDCl$_3$ at 75 MHz, the characteristic peak of methyl carbon attached with C4" appeared at $\delta$ 21.3 and styryl carbons C1 at $\delta$ 128.5 and C2 at $\delta$ 110.1 ppm (Figure 3.3). The peaks of all other protons and carbons of the molecule were present in $^1$H and $^{13}$C NMR spectra of the molecule.

The structure of compound 4a was established in the same way, on the basis of its spectral data analysis, as done for 3a. The major difference in the two isomers was made with the help of $^1$H NMR spectrum. The styryl protons at C1 appeared at $\delta$ 6.89 and C2 came at 6.26 ppm as doublets and coupling constant, $J_{H-H} = 14.5$ Hz falling in the range of $trans$-coupled protons. This suggested that isomer 4a was of $E$-configuration (Figure 3.4). Rest peaks of all other protons and carbons of the molecule were present in $^1$H and $^{13}$C NMR spectra of the molecule.

Table 3.2. Spectral Comparison of regioisomers 3a and 4a

<table>
<thead>
<tr>
<th>Entry</th>
<th>3a</th>
<th>4a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Structure</td>
<td>![Structure of 3a]</td>
<td>![Structure of 4a]</td>
</tr>
<tr>
<td>2. Molecular formula</td>
<td>$C_{17}H_{15}N$</td>
<td>$C_{17}H_{15}N$</td>
</tr>
<tr>
<td>3. No. of H in $^1$H NMR</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>4. Coupling constant of styryl protons</td>
<td>9.3 Hz (Z-isomer)</td>
<td>14.4 Hz (E-isomer)</td>
</tr>
<tr>
<td>5. No. of C in $^{13}$C NMR</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>6. No. of quaternary C</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>
Figure 3.2: $^1$H NMR of (Z)-1-(4-methylstyryl)-1H-indole (3a)
Figure 3.3: $^{13}$C NMR of (Z)-1-(4-methylstyryl)-1H-indole (3a)
Figure 3.4: $^1$H NMR of (E)-1-(4-methylstyryl)-1H-indole (4a)
Figure 3.5: $^{13}$C NMR of (E)-1-(4-methylstyryl)-1H-indole (4a)
3.4.1.3 Scope of the reaction

Under the optimized reaction condition i.e. 20 mol % of KOH in DMSO at 120 °C (Table 3.1, entry 8), the scope and limitations of this process were examined by the addition of various N-heterocycles 1a–m onto terminal alkynes 2a–n (Table 3.3).

During the course of reaction, it was noticed that the nature of the heteroarenes and the substituents attached to the aryl group of triple bond were responsible for the success of the process. As seen from Table 3.3, the reaction tolerates a wide range of substituents (comprising electron-donating and electron-withdrawing groups) both in the N-heterocycle and acetylene, thus demonstrating a general character of the synthesis. In the case of indole 1a and electron rich alkynes 2a and 2b, the desired addition products 3a and 3b were obtained in 90 and 70% yields respectively (Table 3.3, entries 1 and 2). Heterocyclic amines with an electron-donating group such as 3-methylindole 1b, 2-methylindole 1c and 5-methoxyindole 1d afforded the addition products with Z-stereoselectivity in good yields in comparison to 1a (entries 3–13).

When the scope of various alkynes was checked with 1b, it was found that electron donating groups affected the yield of the product formed (entries 3 and 4). Electron withdrawing substituents attached to the alkyne substrate 2e and 2f enhanced the rate of reaction and fastened the conversion of desired isomer to more stable E-isomer, thus lowering the yield of the desired Z-product (entries 5 and 6).

No reaction was observed with heterocycle 1b and aliphatic alkynes 2g and 2h (entries 7 and 8). Electron-rich heterocycle 1c afforded the desired product with 2a and 2i in low yields (entries 9 and 10). 1d provided the products 3i–k in good yields (entries 11–13). 5-bromoindole 1e afforded the hydroaminated product 3l in 68% yield (entry 14).
### Table 3.3. Hydroamination of terminal alkyne\(^a\)

![Chemical structure]

<table>
<thead>
<tr>
<th>entry</th>
<th>(N)-heterocycle 1</th>
<th>alkyne 2</th>
<th>product 3</th>
<th>yield (%)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>2a</td>
<td>3a</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>1a</td>
<td>2b</td>
<td>3b</td>
<td>70</td>
</tr>
<tr>
<td>3</td>
<td>1b</td>
<td>2c</td>
<td>3c</td>
<td>96</td>
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<td>4</td>
<td>1b</td>
<td>2d</td>
<td>3d</td>
<td>78</td>
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<td>5</td>
<td>1b</td>
<td>2e</td>
<td>3e</td>
<td>65</td>
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<tr>
<td>6</td>
<td>1b</td>
<td>2f</td>
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<td>68</td>
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<td>7</td>
<td>1b</td>
<td>2g</td>
<td>nr</td>
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<td>2h</td>
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</tr>
<tr>
<td>9</td>
<td>1c</td>
<td>2a</td>
<td>3g</td>
<td>80</td>
</tr>
<tr>
<td>entry</td>
<td>N-heterocycle 1</td>
<td>alkyne 2</td>
<td>product 3</td>
<td>yield (%)$^b$</td>
</tr>
<tr>
<td>-------</td>
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</tr>
<tr>
<td>10</td>
<td>1c</td>
<td>2i</td>
<td>3h</td>
<td>82</td>
</tr>
<tr>
<td>11</td>
<td>1d</td>
<td>2c</td>
<td>3i</td>
<td>94</td>
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<tr>
<td>12</td>
<td>1d</td>
<td>2b</td>
<td>3j</td>
<td>65</td>
</tr>
<tr>
<td>13</td>
<td>1d</td>
<td>2j</td>
<td>3k</td>
<td>96</td>
</tr>
<tr>
<td>14</td>
<td>1e</td>
<td>2c</td>
<td>3l</td>
<td>86</td>
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<tr>
<td>15</td>
<td>1f</td>
<td>2k</td>
<td>3m</td>
<td>85</td>
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<td>2l</td>
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<td>2c</td>
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<td>94</td>
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<tr>
<td>18</td>
<td>1h</td>
<td>2m</td>
<td>3p</td>
<td>99$^c$</td>
</tr>
</tbody>
</table>
Modification in the indole ring by substituting a phenyl ring made no appreciable change in the reactivity of these substrates with the corresponding terminal alkynes (entries 15–17). Pyrrole 1h being more nucleophilic afforded the hydroamminated product 3p in lesser reaction time in 99% yield (entry 18). It is interesting to note that electron-deficient imidazole 1i and 2-ethyl-4-methylimidazole 1j reacted well with terminal alkynes 2d, 2n and 2a to afford the hydroamminated products 3q–s in 72%, 86% and 89% yields respectively (entries 19–21). It was interesting to observe that heterocycles with electron withdrawing groups like -CHO and -COOH in the indole moiety i.e. 1H-indole-3-carbaldehyde 1k and 1H-indole-2-carboxylic acid 1l did not reacted under the given conditions with 2a (entries 22 and 23). A cyclic secondary amine, pyrrolidine 1m also did not show any reaction with 2a (entry 24).

\[
\begin{array}{cccc}
\text{entry} & N\text{-heterocycle 1} & \text{alkyne 2} & \text{product 3} & \text{yield (%)}^b \\
19 & 1i & 2d & 3q & 72^d \\
20 & 1i & 2n & 3r & 86 \\
21 & 1j & 2a & 3s & 89^d \\
22 & 1k & 2a & \text{nr} & - \\
23 & 1l & 2a & \text{nr} & - \\
24 & 1m & 2a & \text{nr} & - \\
\end{array}
\]

\(^a\) The reactions were performed using \(N\)-heterocycle 1 (2.0 equiv), 1.0 mmol of the alkyne 2 and 0.2 equiv of KOH in 1.5 mL of DMSO at \(120^\circ\text{C}\) for 0.5–1 h unless otherwise noted. \(^b\) Yield of isolated product. \(^c\) Time = 15 min. \(^d\) Time = 2 h.
3.4.2 Hydroamination of 1, 3- and 1, 4-diethynylbenzenes

About two centuries back, with the discovery of over a thousand naturally occurring acetylenes, it was noticed that diynes and triynes also make an important constituent of the structure or substructure in many plants (Figure 3.6).21

![Panaxytriol XXXI (characteristic polyacetylene components of Panax ginseng)](image)

![Dehydromatricaria ester XXXII](image)

Figure 3.6. Selected naturally occurring diynes

Thus, the possibility of the reaction of \(N\)-heterocycles with dialkynes was next investigated after obtaining successful hydroamination of terminal alkynes.

3.4.2.1 Establishment of reaction conditions

When \(1b\) was reacted with 1, 3-diethynylbenzene \(4a\) and 0.2 equiv KOH at 120 °C, a complex mixture of three isomers was obtained in 30 minutes (Table 3.4, entry 1). Reaction monitoring at continuous interval time showed that the addition of the amine to the alkyne occurred very fast leading to the conversion of kinetically stable Z-isomer to thermodynamically stable E-isomer followed by the attack on another alkynyl group present in the substrate. Decrease in reaction time and temperature did not showed any major change and provided the mixture of addition products \(5aa\) and \(6ab\) in 78 and 80% yield respectively (entries 2 and 3). Use of CsCO\(_3\) (0.2 equiv) yielded the mixture of two stereoisomers \(5aa\) and \(5ab\) by the addition of \(1a\) only at one position of the dialkyne (entry 4). Increase in temperature provided the product \(5ab\) in 68% yield (entry 5).
Table 3.4. Optimization of Reaction Conditions for the Hydroamination of Dialkynes

<table>
<thead>
<tr>
<th>entry</th>
<th>base</th>
<th>t/ °C</th>
<th>time/min</th>
<th>product</th>
<th>yield (%)</th>
</tr>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5aa</td>
<td>5ab</td>
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<tr>
<td>1</td>
<td>KOH</td>
<td>120</td>
<td>30</td>
<td>45</td>
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<td>2</td>
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</tr>
<tr>
<td>3</td>
<td>KOH</td>
<td>80</td>
<td>15</td>
<td>70</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>Cs₂CO₃</td>
<td>80</td>
<td>20</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>5</td>
<td>Cs₂CO₃</td>
<td>120</td>
<td>10</td>
<td>10</td>
<td>90</td>
</tr>
</tbody>
</table>

* The reactions were performed using N-heterocycle 1b (3.0 equiv), 1.0 mmol of the alkyne 4a and 0.2 equiv of base in 1.5 mL of DMSO. † Yield of mixture of isolated product.

3.4.2.2 Scope of the reaction

Therefore, under the optimized reaction conditions (Table 3.4, entry 5), selective hydroamination of dialkynes 4a and 4b was performed (Table 3.5). 4a provided the 1,3-bis((Z)-2-(1H-indol-1-yl)vinyl)benzene 6bc with 1a in 42% yield (entry 2). 1,4-diethynylbenzene 6b yielded the mixture of E:Z isomers with 1a and 1l in 64 and 57% yield respectively (entries 3 and 4). Pyrrole 1e provided the Z-isomer in 54% yield along with a complex mixture of other isomers (entry 5).
Table 3.5. Hydroamination of dialkynes<sup>a</sup>

<table>
<thead>
<tr>
<th>entry</th>
<th>N-Heterocycle 1</th>
<th>alkyne 4</th>
<th>product 5</th>
<th>yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1b</td>
<td>4a</td>
<td>5ab</td>
<td>68</td>
</tr>
<tr>
<td>2</td>
<td>1a</td>
<td>4a</td>
<td>6bc</td>
<td>42</td>
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<td>3</td>
<td>1b</td>
<td>4b</td>
<td>5bb</td>
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<tr>
<td>4</td>
<td>1a</td>
<td>4b</td>
<td>5cb</td>
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</tr>
<tr>
<td>5</td>
<td>1h</td>
<td>4b</td>
<td>5db</td>
<td>54</td>
</tr>
</tbody>
</table>

<sup>a</sup> The reactions were performed using N-heterocycle 1 (2.0 equiv), 1.0 mmol of the alkyne 4 and 0.2 equiv of Cs<sub>2</sub>CO<sub>3</sub> in 1.5 mL of DMSO at 120 °C for 10 min. <sup>b</sup> Yield of isolated product.

3.4.2.3 Characterization of compounds 5ab and 6bc

Compound 5ab was prepared by the addition of 0.2 mmol of Cs<sub>2</sub>CO<sub>3</sub> in the solution of 3-methylindole 1b and 1,3-diyneylbenzene 6a in DMSO. The reaction
mixture was heated at 120 °C for 10–15 min. The obtained product 5ab was confirmed to be formed on the basis of its spectral data analysis. The high resolution mass spectrum showed [M]+ peak at m/z 257.1201, which confirmed its molecular formula to be C_{19}H_{15}N. In the 'H NMR spectrum of 5ab done in CDCl₃ at 400 MHz, the presence of a peak at δ 3.03 ppm as singlet showed that there is one free alkynyl proton present in the molecule at C2″ (Figure 3.5). The appearance of the styryl protons attached with the C1’ and C2’ at δ 7.24 and 6.94 ppm respectively as doublets and coupling constant, 9.3 Hz falling in the range of cis-coupled protons suggested the formation of Z-isomer by the attack of N-heterocycle only at one of the two alkynyl positions. Further, the presence of characteristic peak of methyl carbon attached with C3 of indole ring at 9.6 ppm and quarternary alkynyl carbons C1‴ and C2‴ at δ 77.3 and 83.3 ppm in the 13C NMR spectrum done in CDCl₃ and 75 MHz confirms the formation of 5ab as the major product (Figure 3.6). The peaks of all other protons and carbons of the molecule were present in 'H and 13C NMR spectra of the molecule.

The structure of compound 6bc was established in the same way, on the basis of its spectral data analysis, as done for 5ab. The major difference in the two isomers was made with the help of 'H NMR spectrum (Figure 3.7). In 6bc, the styryl protons at C2′ and C1′ appeared at δ 6.96 and 6.20 ppm respectively as doublets and with coupling constant, J = 9.5 Hz falling in the range of cis-coupled protons. This suggested that isomer 6bc was of Z-configuration (Figure 3.8). The absence of the alkynyl proton in the 'H spectrum and quarternary alkynyl carbons in the 13C NMR spectra of the molecule 6bc suggested that the attack of nucleophile took place at both terminals of the alkyne substrate yielding the bis-vinylenamine. Spectral comparison of these two products 5ab and 6bc has been showed in Table 3.6.
### Table 3.6. Spectral Comparison of 5ab and 6bc

<table>
<thead>
<tr>
<th>Entry</th>
<th>5ab</th>
<th>6bc</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Molecular formula</td>
<td>C_{19}H_{13}N</td>
<td>C_{26}H_{26}N_{2}</td>
</tr>
<tr>
<td>3. HRMS data</td>
<td>257.1201</td>
<td>360.1625</td>
</tr>
<tr>
<td>4. No. of H in ¹H NMR</td>
<td>15</td>
<td>20 (10 x 2)</td>
</tr>
<tr>
<td>5. Coupling constant of styryl protons</td>
<td>9.5 Hz (Z-isomer)</td>
<td>9.3 Hz (Z-isomer)</td>
</tr>
<tr>
<td>6. No. of C in ¹³C NMR</td>
<td>19</td>
<td>14</td>
</tr>
<tr>
<td>7. No. of alkynyl carbons in ¹³C NMR</td>
<td>Yes (δ 83.3, 77.3 ppm)</td>
<td>No</td>
</tr>
<tr>
<td>8. Presence of acetylenic proton</td>
<td>Yes (at δ 3.03)</td>
<td>No</td>
</tr>
</tbody>
</table>
Figure 3.5: $^1$H NMR of (Z)-1-(3-ethynylstyryl)-3-methyl-1H-indole (5ab)
Figure 3.6: $^{13}$C NMR of (Z)-1-(3-ethynylstyryl)-3-methyl-1H-indole (5ab)
Figure 3.7: $^1$H NMR of 1,3-bis((Z)-2-(1H-indol-1-yl)vinyl)benzene (6bc)
Figure 3.8: $^{13}$C NMR of 1,3-bis((Z)-2-($1H$-indol-1-yl)vinyl)benzene (6bc)
3.5 PROBABLE MECHANISM

Our successful results in the hydroamination of N-heterocycles onto terminal alkynes led other researchers to show their interest on further extension of this work. Recently, Dvorko et al. have reported the synthesis of nitrogen stilbene analogs by utilizing a similar methodology i.e. KOH and DMSO for the hydroamination of arylacetylenes with pyrroles. They elaborated this work using a variety of pyrrole substrates and provided the experimental results for our observations. They showed that E/Z- isomer ratio of the adducts found to be controlled by the reaction conditions. The adducts initially formed as the Z-isomers (kinetic control, according to the classic trans-nucleophilic addition rule). Then, the Z- isomers undergo Z/E- isomerization until reaching the equilibrium state, i.e., the reaction stereochemistry is thermodynamically controlled which was explained by NMR monitoring of the addition of pyrrole 1h to phenylacetylene 2c in a solution of KOH/DMSO-d6 at 90 °C (Scheme 3.7).

Scheme 3.7. NMR monitoring of the addition of pyrrole 1h to phenylacetylene 2c by Dvorko et al.

3.6 CONCLUSION

In summary, we have described a versatile and efficient regio- and stereoselective synthetic method to produce a broad range of functionalized Z- vinylenamines in good
to excellent yields. This methodology utilizes a simple and economical bases KOH and CsCO$_3$ for the addition of $N$-heterocycles not only onto terminal alkynes but also for 1,3- and 1,4- dialkynes.

This work also provides a study of effect of using different bases, temperatures and time on the stereoselectivity of products which has not been done till yet. The developed chemistry provides an efficient and green protocol for the selective synthesis of enamines without making use of expensive catalysts and ligands. Based upon this, we believe that the current strategy can be very helpful to develop new synthetic methods to variety of fused heterocycles of pharmaceutical interest.

3.7 EXPERIMENTAL SECTION

3.7.1 General procedure for the preparation of Z-styryl enamines

In an oven dried pressure tube, to a solution of $N$-heterocycle (2.0 equiv) in DMSO and finely crushed KOH (0.2 equiv), alkyne (1.0 mmol) was added. The resulting reaction mixture was heated at 120 °C. Progress of the reaction was monitored by TLC and after the completion of reaction; reaction mixture was brought to room temperature. The reaction mixture was extracted with ethylacetate (5 mL X 3), and evaporated under reduced pressure. The crude reaction mixture was purified using silica gel column chromatography.

3.7.2 Analytical data

(Z)-1-styryl-1H-indole (3a): The product was obtained as a yellow oil. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.61 (d, $J = 6.9$ Hz, 1H), 7.36 (d, $J = 8.4$ Hz, 1H), 7.23 (td, $J =1.2$, 6.9 Hz, 1H), 7.16 (td, $J = 1.2$, 6.6 Hz, 1H), 7.08–7.01 (m, 5H), 6.89 (d, $J = 9.3$ Hz, 1H), 6.49 (d, $J = 3.0$ Hz, 1H), 6.26 (d, $J = 9.3$ Hz, 1H), 2.30 (s, 3H); $^{13}$C NMR (CDCl$_3$, 75 MHz): $\delta$ 137.4, 135.9, 131.9, 129.1, 128.6, 128.5, 127.2, 122.6, 122.3, 120.8, 120.6, 120.0, 110.1, 103.7, 21.3. HRMS (ESI): [M]$^+$ Calcd for [C$_{17}$H$_{13}$N]: 233.1204, found : 233.1209.
(Z)-4-(2-(1H-indol-1-yl)vinyl)-N,N-dimethylaniline (3b): The product was obtained as a brown solid, mp: 130–132 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.62 (dd, $J = 3.0$ Hz, 1H), 7.36 (d, $J = 8.1$ Hz, 1H), 7.23–7.11 (m, 3H), 7.00 (dd, $J = 1.5$, 7.9 Hz, 2H), 6.73 (d, $J = 9.0$ Hz, 1H), 6.55–6.52 (m, 3H), 6.24 (d, $J = 9.0$ Hz, 1H), 2.90 (s, 6H); $^{13}$C NMR (CDCl$_3$, 75 MHz): $\delta$ 149.8, 135.9, 129.9, 128.5, 127.5, 120.2, 122.5, 122.4, 122.2, 120.8, 120.3, 111.9, 110.4, 103.3, 40.3. HRMS (ESI): [M]$^+$ Calcd for [C$_{18}$H$_{18}$N$_2$]: 262.1470, found: 262.1472.

(Z)-3-methyl-1-styryl-1H-indole (3c): The product was obtained as a yellow solid, mp: 126–128 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$: 7.54 (d, $J = 7.5$ Hz, 1H), 7.32 (d, $J = 8.1$ Hz, 1H), 7.28–7.14 (m, 6H), 7.16 (d, $J = 6.9$ Hz, 1H), 6.91 (d, $J = 9.3$ Hz, 1H), 6.82 (s, 1H), 6.16 (d, $J = 9.3$ Hz, 1H), 2.23 (s, 3H); $^{13}$C NMR (CDCl$_3$, 75 MHz): $\delta$ 136.3, 135.4, 129.1, 128.8, 128.4, 127.3, 124.4, 123.3, 122.5, 120.2, 118.9, 117.6, 113.4, 110.0, 9.7. HRMS (ESI): [M]$^+$ Calcd for [C$_{17}$H$_{15}$N]: 233.1204, found: 233.1204.

(Z)-1-(4-(tert-butyl)styryl)-3-methyl-1H-indole (3d): The product was obtained as orange crystals, mp: 110–115 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$: 7.56 (d, $J = 7.3$ Hz, 1H), 7.32 (d, $J = 8.0$ Hz, 1H), 7.28–7.24 (m, 2H), 7.22 (dd, $J = 1.4$ Hz, 1H), 7.19–7.15 (m, 3H), 6.88 (d, $J = 1.7$ Hz, 1H), 6.86 (d, $J = 8.8$ Hz, 1H), 6.15 (d, $J = 9.5$ Hz, 1H), 2.25 (s, 3H), 1.30 (s, 9H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 149.7, 135.9, 133.5, 129.6, 129.3, 125.9, 125.7, 125.2, 122.9, 122.7, 121.1, 120.3, 119.2, 114.6, 112.3, 109.4, 34.5, 31.3, 9.7. HRMS (ESI): [M]$^+$ Calcd for [C$_{21}$H$_{23}$N]: 289.1830, found: 289.1831.

(Z)-3-methyl-1-(4-nitrostyryl)-1H-indole (3e): The product was obtained as yellow needles, mp: 142–145 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.95 (dt, $J = 2.2$, 9.5 Hz, 1H), 7.62–7.56 (m, 2H), 7.19–7.14 (m, 2H), 7.12–7.07 (m, 1H), 7.04–6.97 (m, 1H), 6.91–6.86 (m, 2H), 6.73 (t, $J = 8.8$ Hz, 1H), 6.43 (s, 1H), 2.34 (s, 3H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 145.5, 141.6, 136.2, 134.4, 130.9, 130.2, 127.9, 123.7, 121.3, 119.4, 119.3, 116.4, 115.6, 111.7.
111.6, 108.2, 9.8. HRMS (ESI): [M]$^+$ Calcd for [C$_{17}$H$_{14}$N$_2$O$_2$] : 278.1055, found : 278.1051.

(Z)-3-methyl-1-(4-(trifluoromethoxy)styryl)-1H-indole (3f): The product was obtained as yellow oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.54 (d, $J = 7.4$ Hz, 1H), 7.31–7.29 (m, 1H), 7.25–7.21 (m, 3H), 7.19–7.16 (m, 1H), 7.09 (d, $J = 8.1$ Hz, 2H), 6.94 (d, $J = 8.8$ Hz, 1H), 6.76 (d, $J = 1.1$ Hz, 1H), 6.12 (d, $J = 8.8$ Hz, 1H), 2.24 (s, 3H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 148.1, 136.2, 134.0, 130.0, 129.2, 126.5, 124.0, 123.9, 122.6, 120.7, 120.4, 119.0, 116.0, 113.9, 109.9, 9.6. HRMS (ESI): [M]$^+$ Calcd for [C$_{18}$H$_{14}$F$_3$NO] : 317.1027, found : 317.1025.

(Z)-2-methyl-1-(4-methylstyryl)-1H-indole (3g): The product was obtained as off–white crystals, mp: 120–125 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.54 (dd, $J = 1.5$ Hz, 1H), 7.13 (dd, $J = 1.5$ Hz, 1H), 7.08 (td, $J = 1.4$, 5.1 Hz, 2H), 6.94 (d, $J = 8.0$ Hz, 2H), 6.79 (d, $J = 8.8$ Hz, 2H), 6.68 (d, $J = 8.8$ Hz, 1H), 6.59 (d, $J = 8.8$ Hz, 1H), 6.36 (s, 1H), 2.24 (s, 3H), 2.22 (s, 3H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 138.0, 136.4, 135.8, 131.6, 129.3, 129.2, 128.7, 128.5, 121.8, 120.9, 120.0, 119.4, 110.5, 101.7, 21.2, 13.0. HRMS (ESI): [M]$^+$ Calcd for [C$_{18}$H$_{17}$N] : 247.1361, found : 247.1362.

(Z)-2-methyl-1-(4-phenoxystyryl)-1H-indole (3h): The product was obtained as yellow crystals, mp: 130–135 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.51 (dd, $J = 2.2$, 2.9 Hz, 1H), 7.29 (t, $J = 7.7$ Hz, 2H), 7.12–7.03 (m, 4H), 6.92 (dd, $J = 2.2$, 7.3 Hz, 2H), 6.83 (dt, $J = 2.6$, 8.8 Hz, 2H), 6.73 (dt, $J = 2.9$, 8.8 Hz, 2H), 6.68 (d, $J = 8.8$ Hz, 1H), 6.59 (d, $J = 8.8$ Hz, 1H), 6.35 (s, 1H), 2.25 (s, 3H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 157.1, 156.5, 136.2, 135.6, 130.1, 129.7, 129.4, 128.7, 128.5, 123.6, 121.7, 120.9, 120.1, 119.5, 119.3, 118.3, 110.6, 101.8, 13.0. HRMS (ESI): [M]$^+$ Calcd for [C$_{23}$H$_{19}$NO] : 325.1467, found : 325.1465.
(Z)-5-methoxy-1-styryl-1H-indole (3i): The product was obtained as a yellow solid, mp: 85–90 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.26–7.16 (m, 6H), 7.07 (d, \(J = 2.4\) Hz, 1H), 6.99 (d, \(J = 3.0\) Hz, 1H), 6.90 (d, \(J = 9.3\) Hz, 1H), 6.86 (d, \(J = 2.7\) Hz, 1H), 6.42 (d, \(J = 3.3\) Hz, 1H), 6.24 (d, \(J = 9.3\) Hz, 1H), 3.85 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz): \(\delta\) 154.9, 135.1, 131.0, 129.1, 128.7, 128.4, 127.7, 127.5, 123.44, 119.2, 112.3, 110.9, 103.7, 102.9, 55.9. HRMS (ESI): [M]+ Calcd for [C\(_{17}\)H\(_{15}\)NO]: 249.1154, found: 249.1154.

(Z)-4-(2-(5-methoxy-1H-indol-1-yl)vinyl)-N,N-dimethylaniline (3j): The product was obtained as a brown solid, mp 140–145 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.23 (d, \(J = 9.0\) Hz, 1H), 7.12–7.08 (m, 2H), 6.99 (d, \(J = 8.7\) Hz, 2H), 6.86 (dd, \(J = 2.4, 6.3\) Hz, 1H), 6.69 (d, \(J = 9.0\) Hz, 1H), 6.55–6.52 (m, 2H), 6.45 (d, \(J = 3.0\) Hz, 1H), 6.22 (d, \(J = 9.0\) Hz, 1H), 3.85 (s, 3H), 2.91 (s, 6H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz): \(\delta\) 154.6, 149.7, 131.0, 129.8, 128.9, 127.9, 122.5, 122.1, 120.3, 112.3, 112.1, 110.6, 102.9, 102.7, 55.8, 40.3. HRMS (ESI): [M]+ Calcd for [C\(_{19}\)H\(_{20}\)N\(_2\)O]: 292.1576, found: 292.1575.

(Z)-5-methoxy-1-(2-methylstyryl)-1H-indole (3k): The product was obtained as a white solid, mp 90–100 °C; \(^1\)HNMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.29 (d, \(J = 9.0\) Hz, 1H), 7.24–7.16 (m, 2H), 7.14–7.07 (m, 2H), 7.03 (d, \(J = 9.0\) Hz, 2H), 6.89 (dd, \(J = 2.4, 6.6\) Hz, 1H), 6.77 (d, \(J = 3.0\) Hz, 1H), 6.30 (s, 1H), 6.17 (d, \(J = 9.3\) Hz, 1H), 3.84 (s, 3H), 2.22 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 154.9, 136.4, 134.9, 131.1, 130.9, 128.9, 128.8, 127.5, 127.1, 125.9, 123.5, 114.7, 112.2, 110.4, 103.8, 102.9, 55.8, 19.9. HRMS (ESI): [M]+ Calcd for [C\(_{18}\)H\(_{17}\)NO]: 263.1310, found: 263.1314.

(Z)-5-bromo-1-styryl-1H-indole (3l): The product was obtained as white crystals, mp: 130–135 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.73 (d, \(J = 2.2\) Hz, 1H), 7.29 (dd, \(J = 1.4, 6.6\) Hz, 1H), 7.26–7.19 (m, 4H), 7.12 (dd, \(J = 2.2, 5.1\) Hz, 2H), 7.01 (d, \(J = 2.9\) Hz, 1H), 6.89 (d, \(J = 9.5\) Hz, 1H), 6.44 (d, \(J = 2.9\) Hz, 1H), 6.35 (d, \(J = 8.8\) Hz, 1H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 134.5, 134.4,
Chapter 3  Base catalyzed hydroamination of terminal alkynes

130.2, 128.6, 128.5, 128.3, 127.8, 125.2, 123.4, 122.9, 121.2, 113.9, 111.6, 103.4.

(Z)-1-(3,5-dimethoxystyryl)-5-phenyl-1H-indole (3m):
The product was obtained as brown crystals, mp: 90–95 °C;
^1H NMR (400 MHz, CDCl$_3$): δ 7.80 (s, 1H), 7.64 (dd, J = 1.5, 8.0 Hz, 2H), 7.51–7.40 (m, 4H), 7.32 (td, J = 1.5, 8.0 Hz, 1H), 7.12 (d, J = 3.6 Hz, 1H), 6.97 (d, J = 8.8 Hz, 1H), 6.55 (d, J = 8.8 Hz, 1H), 6.35 (s, 3H), 6.24 (d, J = 9.5 Hz, 1H), 3.63 (s, 6H); ^13C NMR (CDCl$_3$, 100 MHz): δ 160.6, 142.2, 136.6, 135.4, 134.2, 129.0, 128.7, 127.9, 127.3, 126.5, 123.5, 122.2, 119.6, 119.4, 110.4, 106.5, 104.3, 100.3, 55.2. HRMS (ESI): [M]^+ Calcd for [C$_{24}$H$_{21}$NO$_2$] : 355.1572, found : 355.1568.

(Z)-1-(2-(6-methoxyphenanthren-2-yl)vinyl)-5-phenyl-1H-indole (3n):
The product was obtained as light brown crystals, mp: 130–135 °C; ^1H NMR (400 MHz, CDCl$_3$): δ 7.83 (s, 1H), 7.68–7.61 (m, 5H), 7.56 (d, J = 8.8 Hz, 1H), 7.52–7.42 (m, 5H), 7.33 (d, J = 7.3 Hz, 1H), 7.20 (dd, J = 2.2, 7.3 Hz, 1H), 7.11–7.07 (m, 3H), 7.02 (d, J = 9.5 Hz, 1H), 6.53 (d, J = 2.9 Hz, 1H), 6.44 (d, J = 9.5 Hz, 1H), 3.91 (s, 3H); ^13C NMR (CDCl$_3$, 100 MHz): δ 157.9, 142.2, 135.4, 134.2, 133.9, 130.1, 129.5, 129.1, 128.7, 128.6, 127.9, 127.8, 127.3, 126.9, 126.8, 126.4, 122.9, 122.2, 120.1, 119.4, 119.1, 110.4, 105.7, 104.2, 55.3. HRMS (ESI): [M]^+ Calcd for [C$_{31}$H$_{23}$NO]: 425.1780, found : 425.1778.

(Z)-5-(4-methoxyphenyl)-1-styryl-1H-indole (3o):
The product was obtained as a yellow solid, mp: 100–105 °C;
^1H NMR (300 MHz, CDCl$_3$): δ 7.78 (s, 1H), 7.59–7.54 (m, 3H), 7.49–7.38 (m, 3H), 7.28–7.19 (m, 5H), 7.00 (m, 2H), 6.53 (d, J = 3.6 Hz, 1H), 6.30 (d, J = 9.0 Hz, 1H), 3.9 (s, 3H); ^13C NMR (CDCl$_3$, 75 MHz): δ 158.6, 135.1, 134.9, 133.9, 129.1, 128.7, 128.5, 128.3, 127.7, 127.6, 123.3, 122.0, 119.6, 118.9, 114.1, 110.3, 104.2, 55.4. HRMS (ESI): [M]^+ Calcd for [C$_{23}$H$_{19}$NO]: 325.1467, found : 325.1462.
**Chapter 3  Base catalyzed hydroamination of terminal alkynes**

**Z**-1-(3-methylstyryl)-1H-pyrrole (3p): The product was obtained as a yellow oil; $^1$H NMR (400 MHz, CDCl$_3$): δ 7.05 (dd, $J = 3.2$, 8.7 Hz, 2H), 6.78 (dd, $J = 3.2$, 8.7 Hz, 2H), 6.65–6.62 (m, 3H), 6.14 (t, $J = 1.8$ Hz, 2H), 6.05 (d, $J = 9.2$ Hz, 1H), 3.78 (s, 3H); $^{13}$C NMR (CDCl$_3$, 100 MHz): δ 159.0, 129.9, 127.2, 125.1, 120.7, 119.1, 113.7, 109.2, 55.2. HRMS (ESI): [M]$^+$ Calcd for [C$_{13}$H$_{13}$NO]: 199.0997, found: 199.0991.

**Z**-1-(4-(tert-butyl)styryl)-1H-imidazole (3q): The product was obtained as a colorless oil; $^1$H NMR (400 MHz, CDCl$_3$): δ 7.51 (s, 1H), 7.30 (d, $J = 8.0$ Hz, 2H), 7.08 (s, 1H), 7.01 (d, $J = 8.8$ Hz, 2H), 6.92 (s, 1H), 6.69 (d, $J = 9.5$ Hz, 1H), 6.35 (d, $J = 9.5$ Hz, 1H), 1.29 (s, 9H); $^{13}$C NMR (CDCl$_3$, 100 MHz): δ 151.7, 136.9, 130.4, 129.1, 128.3, 127.9, 125.8, 125.7, 124.3, 121.6, 118.6, 34.8, 31.2. HRMS (ESI): [M]$^+$ Calcd for [C$_{15}$H$_{18}$N$_2$]: 226.1470, found: 226.1469.

**Z**-1-(2-(thiophen-3-yl)vinyl)-1H-imidazole (3r): The product was obtained as a yellow solid, mp: 65–70 °C; $^1$H NMR (300 MHz, CDCl$_3$): δ: 7.51 (s, 1H), 7.25–7.20 (m, 1H), 7.10 (d, $J = 9.6$ Hz, 2H), 6.94 (d, $J = 1.2$ Hz, 1H), 6.62 (d, $J = 9.0$ Hz, 1H), 6.56 (dd, $J = 1.2$, 3.9 Hz, 1H), 6.44 (d, $J = 9.0$ Hz, 1H); $^{13}$C NMR (CDCl$_3$, 75 MHz): δ 136.9, 134.1, 129.7, 127.0, 126.2, 125.8, 121.3, 120.8, 118.7. HRMS (ESI): [M]$^+$ Calcd for [C$_9$H$_8$N$_2$S]: 176.0408, found: 176.0408.

**Z**-2-ethyl-4-methyl-1-(3-methylstyryl)-1H-imidazole (3s): The product was obtained as a brown oil; $^1$H NMR (300 MHz, CDCl$_3$): δ 6.92 (dt, $J = 1.8$, 4.8 Hz, 2H), 6.78 (dt, $J = 2.7$, 6.6 Hz, 2H), 6.48 (d, $J = 8.7$ Hz, 2H), 6.32 (d, $J = 9.0$ Hz, 1H), 3.78 (s, 3H), 2.58 (q, $J = 7.8$ Hz, 2H), 2.19 (s, 3H), 1.26 (t, $J = 3.0$ Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 160.5, 148.6, 136.9, 130.1, 126.6, 126.4, 120.6, 114.7, 114.1, 55.3, 20.6, 13.5, 12.3. HRMS (ESI): [M]$^+$ Calcd for [C$_{15}$H$_{18}$N$_2$]: 226.1470, found: 226.1470.
3.7.3. General procedure for the addition of N-heterocycles with dialkynes: To a solution of N-heterocycle (2.0 mmol) in DMSO and finely crushed Cs₂CO₃ (0.2 equiv), alkyne (1.0 mmol) was added. Resulting mixture was heated at 120 °C. Progress of the reaction was monitored by TLC. After the complete consumption of alkynes, reaction mixture was brought to room temperature. The reaction mixture was extracted with ethylacetate (5 mL X 3) and evaporated under reduced pressure.

3.7.4. Analytical data

**1-(3-ethynylstyryl)-3-methyl-1H-indole (5ab):** The product was obtained as a yellow oil; ^1^H NMR (400 MHz, CDCl₃): δ 7.54 (d, J = 8.0 Hz, 1H), 7.41 (s, 1H), 7.35–7.30 (m, 2H), 7.24 (t, J = 9.5 Hz, 1H), 7.19–7.16 (m, 3H), 6.94 (d, J = 9.5 Hz, 1H), 6.77 (s, 1H), 6.08 (d, J = 8.8 Hz, 1H), 3.03 (s, 1H), 2.23 (s, 3H); ^13^C NMR (CDCl₃, 100 Hz): δ 136.7, 135.7, 132.4, 130.9, 129.2, 128.9, 128.4, 124.1, 123.9, 122.6, 122.2, 120.4, 119.0, 115.7, 113.8, 109.9, 83.3, 77.3, 9.6. HRMS (ESI): [M]^+ Calcd for [C₁₉H₁₅N]: 257.1204, found: 257.1201.

**1,3-bis((Z)-2-(1H-indol-1-yl)vinyl)benzene (6bc):** The product was obtained as a yellow oil; ^1^H NMR (400 MHz, CDCl₃): δ 7.67 (d, J = 7.3 Hz, 2H), 7.39 (d, J = 8.1 Hz, 2H), 7.30 (td, J = 5.8, 1.5 Hz, 2H), 7.26–7.22 (m, 2H), 7.15–7.13 (m, 2H), 7.08–7.04 (m, 4H), 6.96 (d, J = 8.8 Hz, 2H), 6.50 (d, J = 2.9 Hz, 2H), 6.20 (d, J = 9.5 Hz, 2H); ^13^C NMR (CDCl₃, 100 MHz): δ 135.8, 135.2, 129.1, 128.5, 128.4, 127.6, 126.9, 123.6, 123.4, 120.5, 118.9, 110.1, 104.0. HRMS (ESI): [M]^+ Calcd for [C₂₆H₂₀N₂]: 360.1626, found: 360.1625.

**1-(4-ethynylstyryl)-3-methyl-1H-indole (5bb):** The product was obtained as a light yellow semi–solid; ^1^H NMR (400 MHz, CDCl₃): δ 7.60 [d, J = 14.6 Hz, 0.17H; (for minor)], 7.47 [d, J = 8.1 Hz, 1.0H; (for major)], 7.43–7.39 [m, 0.5H; (for minor)], 7.30 [d, J = 8.3 Hz, 2.4H; (2.0H for major
Chapter 3

Base catalyzed hydroamination of terminal alkynes

+ 0.4H for minor]), 7.24–7.22 [m, 1.2H; (1.0H for major + 0.4H for minor]), 7.19–7.17 [m, 3.5H; (3.0H for major + 0.5H for minor]), 6.86 [d, J = 8.8 Hz, 1.0H; (for major)], 6.72 [s, 1H; (for major)], 6.46 [d, J = 13.9 Hz, 0.22H; (for minor)], 6.04 [d, J = 8.8 Hz, 1.0H; (for major)], 3.04 [s, 0.17H; (17% for minor regioisomer)], 3.02 [s, 1.0H; (83% for major regioisomer)], 2.29 [s, 0.58H; (for major)], 2.17 [s, 3H; (for minor)]; 13C NMR (CDCl3, 100 MHz) : δ 135.9, 132.1, 128.6, 125.2, 124.1, 124.0, 122.6, 120.4, 119.0, 116.4, 113.9, 109.9, 83.6, 77.7, 9.6 (for major regioisomer); 136.2, 132.6, 129.2, 123.0, 120.8, 120.6, 119.4, 111.2, 109.4, 9.8 (for minor regioisomer). HRMS (ESI): [M]+ Calcd for [C19H15N] : 257.1204, found : 257.1202.

1-(4-ethynylstyryl)-1H-indole (5cb): The product was obtained as a brown oil; 1H NMR (400 MHz, CDCl3): δ 7.71 [d, J = 14.6 Hz, 0.5H; (for minor)], 7.61 [d, J = 8.1 Hz, 1.5H; (1.0H for major + 0.5H for minor)], 7.55 [d, J = 8.0 Hz, 0.5H; (for minor)], 7.52–7.48 [m, 1.5H; (1.0H for major + 0.5H for minor)], 7.40 [d, J = 8.1 Hz, 1H; (for major)], 7.37–7.35 [m, 3H; (2.0H for major + 1.0H for minor)], 7.31–7.30 [m, 0.6H; (for minor)], 7.22–7.21 [m, 1H; (for major)], 7.19–7.13 [m, 2H; (for major)], 7.00–6.98 [m, 2H; (for major)], 6.69–6.63 [m, 1H; (for minor)], 6.50 [d, J = 2.9 Hz, 1.0H; (for major)], 6.24 [d, J = 8.8 Hz, 1.0H; (for major)], 3.13 [s, 0.3H; (30% for minor regioisomer)], 3.09 [s, 1H; (70% for major regioisomer)]; 13C NMR (CDCl3, 100 MHz): δ 136.7, 135.7, 132.6, 129.2, 125.4, 124.4, 123.6, 122.9, 121.3, 121.2, 120.2, 112.9, 110.9, 109.6, 105.9, 83.7, 77.7 (for major regioisomer); 128.6, 123.9, 121.9, 120.7, 119.8, 110.9, 102.6 (for minor regioisomer). HRMS (ESI): [M+1]+ Calcd for [C19H15N] : 257.1204, found : 257.1202.

(Z)-1-(4-ethynylstyryl)-1H-pyrrole (5db): The product was obtained as a white needles, mp: 115–119 °C; 1H NMR (400 MHz, CDCl3): δ 7.32 (d, J = 8.1 Hz, 2H), 7.06 (d, J = 8.8 Hz, 2H), 6.67 (d, J = 9.5 Hz, 1H), 6.56 (t, J = 2.2 Hz, 2H), 6.08 (t, d, J = 2.2 Hz, 2H), 5.98 (d, J = 9.5 Hz, 1H), 3.02 (s, 1H); 13C NMR (CDCl3, 100 MHz) : δ 136.3, 132.5, 127.8, 125.5, 120.3, 119.1, 113.3, 110.8, 83.6, 77.7. HRMS (ESI): [M]+ Calcd for [C14H11N] : 193.0891, found : 193.0891.

NOTE: All the data mentioned here has been published in Org. Lett. 2011, 13, 1630 and J. Org. Chem. 2012, Manuscript jo-2012-00782n (Revisions submitted to Editorial Office). Therefore, selected spectras has been added in Appendix-II to avoid wastage of paper.
3.8 REFERENCES


