Copper-Catalyzed Activation of α-Amino Peroxy and Hydroxy intermediates to Iminium ion Precursor: An Easy Access to C4-Substituted-3,4-dihydroquinazolines via Oxidative Cross Coupling Strategy

4.1 Introduction

C4-substituted 3,4-dihydroquinazolines are well-known alkaloids isolated from natural sources\(^1\) and showed different types of biological activities such as Trypanothione reductase (TryR) inhibitor,\(^2\) T-type calcium channel blocking agents\(^3\) and especially as anti-cancer agents.\(^4\) Number of methods have appeared in the literature to access this alkaloid involving multi-step schemes, special reaction conditions and usage of expensive, harmful and unstable intermediates such as carbodiimide, isocyanate, azide and isocyanide derivatives. Thus, these methods heavily impede their substrate scope and biological application.\(^5\)-\(^10\) Hence, the discovery of novel and most direct approach for synthesis of these compounds from simple starting material is highly welcome.

In recent years construction of carbon-carbon (C-C) and carbon-hetero atom (C-X) bonds through cross dehydrogenative coupling (CDC) or oxidative cross coupling (OCC) strategies via functionalization of C-H bonds are recognized as an elegant and more powerful approach in modern synthetic organic chemistry.\(^11\) Since these methods avoids pre-functionalised precursors and offer shorter routes for the synthesis of complex organic molecules making them more eco-friendly and atom-economical. In general, these reactions are accomplished by using transition metal catalysts with different oxidants such as organic peroxides, \(\text{H}_2\text{O}_2\), molecular oxygen (\(\text{O}_2\)) and so on. Among them functionalization of \(sp^3\)C-H bond adjacent to nitrogen atom (via reactive iminium ion intermediate) by CDC approach have been studied extensively over the last few years.\(^12\)-\(^28\)
4.2 State of the art:

Over the decade, the majority of reported CDC methods are devoted to synthesis of N-protected-C1-substituted tetrahydroisoquinoline (THIQ) derivatives via transition metal catalyzed oxidative cross coupling between N-protected- tetrahydroisoquinoline (THIQ) with variety of pro-nucleophiles.

Murahashi and co-workers synthesized N-protected-tetrahydroisoquinoline (THIQ) derivatives through ruthenium-catalyzed oxidative cross coupling of N-methoxycarbonyl THIQ with t-butyl hydroperoxide followed by treatment with different pro-nucleophiles in the presence of titanium tetrachloride (Scheme 1).\(^{(12)}\)

\[
\text{Scheme 1}
\]

Li and co-workers synthesized C1-substituted THIQ derivatives through cross dehydrogenative coupling reaction of THIQ with different pro-nucleophiles such as nitroalkanes, active methylene compounds, terminal alkynes, indoles, phenyl boronic acids using copper salts as catalyst and \(t\)-butylhydroperoxide (TBHP) as an external oxidant (Scheme 2).\(^{(13)}\)

\[
\text{Scheme 2}
\]
Klussmann and co-workers have elegantly described the copper-catalyzed aerobic oxidative cross dehydrogenative coupling of THIQ with different pro-nucleophiles to afford C-1 substituted THIQ derivatives under mild reaction conditions (Scheme 3).\(^{14}\)

![Scheme 3]

**Scheme 3**

Shu *et al.* developed an oxidant free CDC reaction for the synthesis of THIQ derivatives using platinum as a catalyst and nitroalkanes, dialkyl malonate, malononitrile and non-activated ketones are active participants in this coupling reaction (Scheme 4).\(^{15}\)

![Scheme 4]

**Scheme 4**

Zhu and co-workers have developed a highly efficient homogeneous gold-catalyzed oxidative C-C coupling method for THIQ with nitroalkanes and different unmodified ketones by using air as the sole oxidant under mild reaction conditions (Scheme 5).\(^{16}\)
Shirakawa et al. have demonstrated the iron catalyzed oxidative coupling of THIQ with various nucleophiles to give aminomethylarenes, α-aminonitroalkanes, and 2-(aminomethyl)-1,3-dicarbonyl compounds using stoichiometric amount of ditertiarybutyl peroxide (t-BuOOt-Bu) as an external oxidant (Scheme 6).\(^\text{(17)}\)

\[
\text{Scheme 6}
\]

Murahashi and co-workers have demonstrated the ruthenium-catalyzed oxidative cyanation of tertiary amines with molecular oxygen/hydrogen peroxide in the presence of sodium cyanide in acetic acid/hydrocyanic acid to provide the α-aminonitriles (Scheme 7).\(^\text{(18)}\)

\[
\text{Scheme 7}
\]

\[\text{R}^1 = \text{Methyl or Ethyl} \]
\[\text{R}^2 = \text{Me, OMe, Br} \]
Li and co-workers have developed the effective catalytic method to form propargylamine by using copper bromide as a catalyst and TBHP as an oxidant via α-amino-C-H bond functionalization of N,N-dimethylanilines with alkynes (Scheme 8). (13c)

\[
\begin{align*}
\text{N} & \quad \text{CuBr (5 mol\%)} \\
\text{R} & \quad \text{TBHP (1.0-1.2 equiv)} \\
100^\circ\text{C}, 3\text{h} & \\
\text{R} &= \text{Aryl and alkyl} \\
\end{align*}
\]

**Scheme 8**

Zhang and co-workers have demonstrated an efficient copper-catalyzed direct cross-coupling of N-heterocyclic sp\(^2\) C-H bonds with sp\(^3\) C-H bonds of anilines employing environmentally benign O\(_2\) or air as an oxidant under very mild reaction conditions (Scheme 9). (19)

\[
\begin{align*}
\text{N} & \quad \text{CuBr (5 mol\%)} \\
\text{air or O}_2 & \quad \text{50\,°C, 12\,h, CH}_3\text{CN} \\
\end{align*}
\]

**Scheme 9**

Fu and co-workers have developed a novel copper-catalyzed amidation of unactivated sp\(^3\) C-H bonds adjacent to a nitrogen atom in N-alkyltertiary amines by using simple catalytic system (CuBr/TBHP) under mild reaction conditions (Scheme 10). (20)

\[
\begin{align*}
\text{N} & \quad \text{CuBr (5 mol\%)} \\
\text{TBHP (2 equiv)} & \quad 80\,°\text{C, 6\,h} \\
\end{align*}
\]

**Scheme 10**
In 2006, Doyle and co-workers reported an oxidative Mannich reaction for the synthesis of valuable α-aminoalkyl butenolides from N-alkyl amines using dirhodium caprolactum complex \((\text{Rh}_2(\text{cap})_4)\) as a catalyst and TBHP as an oxidant\(^{(21a)}\) and very recently they have described the detailed mechanistic investigation of this transformation (Scheme 11).\(^{(21b)}\)

![Scheme 11](image)

Shirakawa et al. have reported the iron-catalyzed oxidative coupling of alkylamides with arenes to give α-arylalkylamides through a tandem reaction consisting of oxidation of alkylamides and the Friedel-Crafts alkylation with the resulting oxidized alkylamides using di-tertiarybutyl-peroxide (DTBP) as an oxidant (Scheme 12).\(^{(22)}\)

![Scheme 12](image)

Chen and co-workers have reported the iron-catalyzed direct C–N bond formation between azoles and amides is described. The oxidative coupling reactions of sp3 C–H bonds adjacent to a nitrogen atom in amides and sulfonamides with the N–H bond in azoles proceeded smoothly in the presence of FeCl\(_2\) and DTBP (Scheme 13).\(^{(23)}\)
Mao et al. have described a direct and regioselective amination reaction based on an efficient and inexpensive Fe(II) complex catalyst with TBHP as a benign oxidant. This reaction also offers a facile method for the construction of C–N bonds (Scheme 14).\(^{(24)}\)

**Scheme 14**

Xie et al. have demonstrated the copper-catalyzed oxidative cross coupling between amino acid derivatives and ketones through C-H bond functionalization of adjacent to nitrogen atom to afford \(\alpha\)-alkylaminoacid derivatives (Scheme 15).\(^{(25)}\)

**Scheme 15**

Wang and co-workers have developed an oxidative and enantioselective cross-coupling reaction of \(\text{N}\)-substituted glycine esters with \(\alpha\)-substituted \(\beta\)-ketoesters for the synthesis of various \(\alpha\) -alkyl \(\alpha\) -amino acids using chiral copper (II) complex as a catalyst and DDQ as an oxidant (Scheme 16).\(^{(26)}\)
Scheme 16

Zhang et al. have demonstrated a new approach to functionalize α-amino acid derivatives, which allows the efficient installation of a malonate or a phenylethynyl group at adjacent to nitrogen atom in amino acid derivatives using copper catalyst (Scheme 17). (27)

Scheme 17

Despite tremendous progress made on cross dehydrogenative coupling or oxidative cross coupling reaction at α-C-H bond adjacent to nitrogen atom of amines, majority of the reported methods are limited to N-protected tetrahydroisoquinoline (THIQ), N,N-dialkyl aniline, N-alkyl tertiary amine, amide and amino acid derivatives. Therefore, development of CDC reactions for
the synthesis of biologically important nitrogen based heterocycles through these direct routes are highly desirable. With these objectives in mind, recently our group have successfully demonstrated the transtion-metal free CDC reaction between THIQ and nitroalkanes in presence of KI and TBHP as an oxidant under mild conditions (Chapter 3). This CDC methodology was further explored for the first time towards the synthesis of biologically important 3,4-dihydroquinazoline derivatives from simple aldehydes and 1,3 diamine derivatives using nitroalkanes and dialkylmalonates as a pro-nucleophiles (Scheme 18).

**Scheme 18**

However, this method was unsuccessful with other pro-nucleophiles such as alkynes, indoles, ketones and so on. Therefore, we planned to use transition metal catalysts, where they can play dual role as a catalyst as well as an activator of pro-nucleophiles through dative or covalent bond interaction.
4.3 Present work:

In this chapter, we have described a simple and straightforward approach to access C4-substituted-3,4-dihydroquinazolines have achieved, where copper catalysed activation of α-amino peroxide and hydroxide intermediates to iminium ion precursors has been realized as an important step. Reactions of these intermediates with alkynes, indoles, pyrrole and silylenol ether afforded the structurally diverse C4-substituted-3,4-dihydroquinazoline derivatives in good yields (Scheme 19).

![Scheme 19](image)

4.4 Result and Discussion

4.4.1 One-pot synthesis of C4-alkynyl-3,4-dihydroquinazolines

We investigated the reaction to synthesize C4-alkynylated-3,4-dihydroquinazoline derivatives in one pot two step process using simple starting material 1,3-diamine (1a), benzaldehyde (2a) and phenylacetylene (5a) via CDC reaction using copper(I) bromide (CuBr) as a catalyst and 70 wt% tert-butyl hydroperoxide in water (TBHP) as an oxidant (Scheme 20, path a). To our delight, the desired product was obtained in 26% isolated yield along with unidentified by-products and which was further confirmed by $^1$H NMR, $^{13}$C NMR, IR and HRMS analysis (Figure 4a-4d). We investigated the reaction under various conditions, but the undesirable side reactions impaired the yield of the required product.
On the basis of the mechanistic understanding of our group\(^{28}\) and Klussmann group\(^{14b,30}\) we envisioned that catalytic amount of Lewis\(^{14b}\) or Bronsted acids\(^{30}\) could generate iminium ion species from the α-amino peroxy and hydroxy intermediates and which can be further trapped with different pro-nucleophiles. So, we attempted the reaction where the formation of α-amino peroxyether (4a) and hydroxy intermediate (7a) was achieved using the KI/TBHP catalytic system\(^{28}\) which was subsequently treated with phenylacetylene in presence of copper(I) bromide (CuBr) as a catalyst. Interestingly, the isolated yield of the desired product 6a was increased to 73\% (Scheme 20, path b).

**Scheme 20:** Synthesis of 4-(phenylethynyl)-2,3-diphenyl-3,4-dihydroquinazoline through oxidative cross coupling reaction.

Further optimizations were carried out by varying the copper salts, solvents, catalyst loading and reaction temperature and the results are shown in Table 1. Among the copper salts tested, CuBr and CuCl showed same catalytic activity (Table 1, entries 3 and 8) and CuCl was chosen as catalyst of choice for further studies. Control experiment shows that copper catalyst is crucial for the product formation and also plays the dual role in activating the alkyne as well as
Table 1: Optimization of reaction condition for synthesis of 3,4-dihydroquinazoline derivatives through α-amino peroxide and hydroxide intermediate. (a)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Copper salt (mol %)</th>
<th>5a (Equivalent)</th>
<th>Condition</th>
<th>Time (hour)</th>
<th>6a (%)</th>
<th>7a (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CuBr (20)</td>
<td>2</td>
<td>80°C</td>
<td>6</td>
<td>44</td>
<td>30</td>
</tr>
<tr>
<td>2</td>
<td>CuBr (20)</td>
<td>2.5</td>
<td>DME, 100°C</td>
<td>6</td>
<td>75</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>CuBr (10)</td>
<td>2</td>
<td>DME, 100°C</td>
<td>6</td>
<td>73</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>CuBr (5)</td>
<td>2</td>
<td>DME, 100°C</td>
<td>6</td>
<td>25</td>
<td>45</td>
</tr>
<tr>
<td>5</td>
<td>CuBr (10)</td>
<td>2</td>
<td>1,4-DIOXANE, 100°C</td>
<td>6</td>
<td>67</td>
<td>&lt;5</td>
</tr>
<tr>
<td>6</td>
<td>CuBr (10)</td>
<td>2</td>
<td>THF, 100°C</td>
<td>6</td>
<td>52</td>
<td>10</td>
</tr>
<tr>
<td>7</td>
<td>—</td>
<td>2</td>
<td>DME, 100°C</td>
<td>6</td>
<td>—</td>
<td>80</td>
</tr>
<tr>
<td>8</td>
<td>CuCl (10)</td>
<td>2</td>
<td>DME, 100°C</td>
<td>6</td>
<td>73</td>
<td>—</td>
</tr>
<tr>
<td>9</td>
<td>Cu(OAc) (10)</td>
<td>2</td>
<td>DME, 100°C</td>
<td>6</td>
<td>47</td>
<td>25</td>
</tr>
<tr>
<td>10</td>
<td>CuCl₂·5H₂O (10)</td>
<td>2</td>
<td>DME, 100°C</td>
<td>6</td>
<td>65</td>
<td>&lt;5</td>
</tr>
<tr>
<td>11</td>
<td>CuSO₄·5H₂O (10)</td>
<td>2</td>
<td>DME, 100°C,</td>
<td>6</td>
<td>10</td>
<td>55</td>
</tr>
</tbody>
</table>

(a) Reaction condition: (i) 1,3-diamine 1a (0.5 mmol), benzaldehyde 2a (0.5 mmol), EtOH (1.5 mL), r.t., 3 h. (ii) KI (0.1 mmol), 70 wt% TBHP in H₂O (4 equiv.), r.t., overnight. (iii) Copper salt (5-20 mol%), phenylacetylene 5a (1-1.25 mmol). (b) Isolated yield of the products after SiO₂ column chromatography.
Table 2: Synthesis of C4-alkynyl-3,4-dihydroquinazoline derivatives through oxidative cross coupling reaction.\(^{(a)}\)

\[ \begin{array}{c}
\text{1} \quad \text{2} \quad \text{1, EtOH, r.t., 3 h.} \\
\quad \text{II. 20 mol% KI TBHP (4 equiv.) r.t., over night.}
\end{array} \]

\[ \begin{array}{c}
\text{4a} \quad \text{II. 10 mol% CuCl DME, 100 °C, 6 h.} \\
\quad \text{6}
\end{array} \]

(a) Reaction conditions: (i) 1,3-diamine 1 (0.5 mmol), aldehyde 2 (0.5 mmol), EtOH (1.5 mL), rt, 3 h. (ii) KI (0.1 mmol), 70 wt% TBHP in H\(_2\)O (4 equiv.), r.t., overnight. (iii) CuCl (10 mol%), alkynes 5 (1 mmol), dimethoxy ethane (2 mL), 100 °C, 6 h. (b) Numbers in parentheses are isolated yield of the products after SiO\(_2\) column chromatography.
the intermediates 4a and 7a (Table 1, entry 7). It was found that 10 mol% of CuCl, in presence of 2 equivalent of phenylacetylene with 2 mL of DME at 100 °C was the best condition for the conversion of 4a and 7a to 6a (Table 1, entry 8).

Under the optimized reaction conditions, we synthesized structurally diverse C4-alkynyl-3,4-dihydroquinazolines and the results are summarized in Table 2. Although the yields are moderate to good for all the products (Table 2, 6a-6l), no definite pattern was observed by substitutional variations at 2-,3- and 4- positions of dihydroquinazolines with aldehydes, amines and alkynes respectively. Further the structure of 6a has been confirmed by single crystal X-ray analysis (Figure 1, 6a).

Figure 1: ORTEP drawing of compound 6a (CCDC 943358). Displacement ellipsoids are drawn at the 30% probability level and H atoms are represented by circles of arbitrary radii. The compound is crystallized in monoclinic space group P2₁ with two molecules in the asymmetric unit.
Table 3: Synthesis of C4-indolyl-3,4-dihydroquinazoline derivatives through oxidative cross coupling reaction.\(^{(a)}\)

\[
\begin{aligned}
&\text{1} & \begin{array}{c}
\text{H} \\
\text{NH}_2
\end{array} & \begin{array}{c}
\text{H} \\
\text{R}^1
\end{array} & \text{O} & \begin{array}{c}
\text{H} \\
\text{R}^2
\end{array} \\
\text{2}
\end{aligned}
\]

\[
\text{1} \rightarrow \text{2} \begin{array}{c}
\text{H} \\
\text{NH}_2
\end{array} \quad \text{i. EtOH, r.t., 3 h.} \quad \text{ii. 20 mol\% KI} \quad \text{TBHP (4 equiv.)} \quad \text{r.t., overnight.} \quad \text{iii.} \quad \text{10 mol\% CuCl} \quad \text{CH}_3\text{CN}, 100^\circ\text{C}, 6 \text{ h.}
\]

(a) Reaction conditions: (i) 1,3-diamine \( \text{1} \) (0.5 mmol), aldehyde \( \text{2} \) (0.5 mmol), EtOH (1.5 mL), r.t., 3 h. (ii) KI (0.1 mmol), 70 wt\% TBHP in H\(_2\)O (4 equiv.), r.t., overnight. (iii) CuCl (10 mol\%), indoles \( \text{8} \) (0.75 mmol), CH\(_3\)CN (2 mL), 80 \(^\circ\)C, 6 h. (b) Numbers in parentheses are isolated yield of the products after SiO\(_2\) column chromatography
4.4.2 One-pot synthesis of C4-indolyl and pyrrolyl-3,4-dihydroquinazolines

After the success in synthesis of 4-(alkynyl)-2,3-substituted-3,4-dihydroquinazolines (6), we next focused our attention in applying this method with other pro-nucleophile in place of alkynes. As indole\(^{31}\) and pyrrole\(^{32}\) rings are commonly observed structural units in several natural and pharmaceutically important products, we looked at these pro-nucleophiles for the next set of experiments under the similar reaction conditions.

![Figure 2: ORTEP drawing of compound 9f (CCDC 943359). Displacement ellipsoids are drawn at the 30% probability level and H atoms are represented by circles of arbitrary radii. The compound is crystallized in orthorhombic space group Pca2\(_1\) with one 9f molecule and two chloroform solvents in the asymmetric unit.](image)

The intermediates 4 and 7 were treated with various indoles to provide the corresponding C4-(indolyl)-3,4-dihydroquinazoline derivatives and the results are summarized in table 3 and the compounds were analysed by \(^1\)H NMR, \(^{13}\)C NMR, IR and HRMS (Figure 5a-5d). As reported earlier\(^{13c}\), the reaction selectively occurred at C3 position of indoles and which was confirmed
by single crystal X-ray analysis (Figure 2, 9f). The substitutional effects of indoles, amines and aldehydes on dihydroquinazoline chromophore were investigated and the results are shown in Table 3. Reactions of benzaldehydes with various substituents such as alkyl, alkoxy or fluoro groups with various C-5/C-7 substituted indoles afforded the desired products in good isolated yields (Table 3, 9a-9f). Also, C-5 halo-substituted indoles reacted with aromatic aldehydes smoothly to afford the corresponding product under this condition (Table 3, 9g-9i). When p-nitro-benzaldehyde and furan-2-carboxaldehyde were used as an aldehyde variant, the corresponding products were obtained in lower yields (Table 3, 9j and 9k). In case of N-methylindole, the desired product was obtained in a low yield (Table 3, 9l). Furthermore, we applied this method for the synthesis of C4-pyrrolyl-3,4-dihydroquinazoline derivatives and the desired products were obtained in good isolated yields (Scheme 21, 11a-b) and the compounds were analysed by ¹H NMR, ¹³C NMR, IR and HRMS (Figure 6a-6d).\(^{(14b)}\)

\[
\begin{align*}
\text{Scheme 21:} \quad &\text{Synthesis of C4-pyrrolyl-3,4-dihydroquinazoline derivatives through oxidative cross coupling reaction.} \\
&
\end{align*}
\]

We further tested the role of metal catalyst with indoles also. The blank experiment with intermediates 4a and 7a with indole in absence of copper catalyst shows the formation of oxidized product 2,3-diphenylquinazolinone, but not the desired product 9a, which clearly confirms that the copper catalyst is essential for the product formation.
4.4.3 One-pot synthesis of C4-alkyl-3,4-dihydroquinazolines

After successful in synthesis of C4-indolyl-3,4-dihydroquinazoline derivatives, we continued our investigation on the use of methyl ketones and acetophenone as a pro-nucleophile under the similar reaction conditions. However, the reaction did not proceeded even in the presence of additives *i.e* acetic acid, and L-proline.

Table 4: Synthesis of C4-alkyl-3,4-dihydroquinazoline derivatives *via* oxidative cross coupling reaction. (a)

(a) Reaction conditions: (i) 1,3-diamine 1 (0.5 mmol), aldehyde 2 (0.5 mmol), EtOH (1.5 mL), r.t., 3 h. (ii) KI (0.1 mmol), 70 wt% TBHP in H₂O (4 equiv.), r.t., overnight. (iii) CuCl (10 mol %), silylenol ether 12 (1.25 mmol), dimethoxy ethane (3 mL), 100 °C, 6 h. (b) Numbers in parentheses are isolated yields of the products after SiO₂ column chromatography.
While, we performed the reaction under the standard condition with silylenolethers i.e. trimethyl(1-phenylvinyl)oxy)silane (12), the desired coupling product was obtained in good isolated yields and the compounds were analysed by $^1$H NMR, $^{13}$C NMR, IR and HRMS (Figure 7a-7d).

The generality and scope of the substrates were investigated further and the results are summarized in Table 4. The electronic effect on aromatic aldehydes does not affect the yields of coupling products significantly and the desired products were obtained in good isolated yields (Table 4, 13a-13e) and structure of compound 13a has been confirmed by single crystal X-ray analysis (Figure 3, 13a).

**Figure 3:** ORTEP drawing of compound 13a (CCDC 943360). Displacement ellipsoids are drawn at the 30% probability level and H atoms are represented by circles of arbitrary radii. The compound is crystallized in triclinic space group P$ar{1}$ with two molecules in the asymmetric unit.

### 4.4.4 Mechanistic considerations

Based on our$^{(28)}$ and Klussmann group$^{(14b)}$ experimental results, we would like to propose the plausible mechanism for formation of C4-phenylacetylnyl-3,4-dihydroquinazoline derivatives as shown in scheme 22. The cyclic condensation product (3a) is oxidized by the KI/TBHP
system predominantly to yield 4-\textit{t}-butylperoxy-2,3-diphenylquinazoline (4a) and 2,3-diphenyl-3,4-dihydroquinazolin-4-ol (7a) through ionic catalytic cycle.\(^{(28)}\)

In the next step, the peroxy (4a) and hydroxyl (7a) intermediates are converted into iminium ions (\textbf{In 1} and \textbf{In 2}) \textit{via} a reversible heterolytic cleavage catalysed by Lewis acid (CuCl).\(^{(14b)}\) Subsequently, the iminium ion is trapped by phenylacetylene through the reactive copper phenylacetylide \textbf{In 3} to afford the final product 6a.\(^{(14,13c)}\) In a similar manner, indoles (8), pyrrole (10) and silylenol ethers (12) can react with 4a or 7a in the presence of copper catalyst to afford the corresponding coupling products 9, 11 and 13 respectively. Most of the prepared dihydroquinazolins are capable of stereoisomers, particularly at C-4 position. However, absence of any chiral directing agents results only in 1:1 mixture of diastereomeric products.

\textbf{Scheme 22.} Plausible mechanism for the formation of C4-phenylacetylenyl-3,4 dihydroquinazoline.

\textbf{4.5 Conclusions}

In summary, we have demonstrated one-pot synthesis of C4-alkynyl, C4-indolyl, C4-pyrrolyl and C4-alkyl 3,4-dihydroquinazoline derivatives through oxidative cross coupling strategy using simple starting materials (1,3-diamines and aldehydes) and catalysts (KI and
CuCl) under mild reaction conditions. Copper catalyst has been realised as an activator of α-amino peroxide and hydroxide intermediates to iminium ion. The structure of compounds 6a, 9f, and 13a are also been confirmed by single crystal X-ray analysis (Figure 1-3).

4.6. Experimental Section

We have not experienced any problem in working or handling with the peroxide compounds described in this work. However, precaution should be taken when working with peroxide compounds.

General Information

All the other chemicals and solvents were obtained from commercial sources, and purified by using standard methods. Silica gel (100–200 mesh) was used for column chromatography and thin-layer chromatography was performed on pre-coated silica gel 60-F254 plates and visualized by UV-light and developed by iodine. The IR values are reported in reciprocal centimeters (cm⁻¹). All ¹H and ¹³C {¹H} NMR spectra were recorded on a 300, 400, and 500 MHz spectrometer. Chemical shifts (δ) are reported in ppm, using TMS (δ =0) as an internal standard in CDCl₃. The peak patterns are indicated as follows: bs, broad singlet; s, singlet; d, doublet; t, triplet; dd, doublet of doublet; sep, septet; m, multiplet. The coupling constants (J), are reported in Hertz (Hz). Mass spectral data was compiled using MS (ESI), HRMS mass spectrometers and the orbitrap mass analyser was used for the HRMS measurement.

X-ray data for compounds 6a, 9f and 13a were collected at room temperature using a Bruker Smart Apex CCD diffractometer with graphite monochromated MoKα radiation (λ=0.71073 Å) with ω-scan method. Preliminary lattice parameters and orientation matrices were obtained from four sets of frames. Unit cell dimensions were determined from 5779 reflections for 6a, 5829 reflections for 9f and 6098 for 13a.
Integration and scaling of intensity data were accomplished using SAINT program.\(^{(34)}\) The structures were solved by Direct Methods using SHELXS97\(^{(34)}\) and refinement was carried out by full-matrix least-squares technique using SHELXL97.\(^{(34)}\) Anisotropic displacement parameters were included for all non-hydrogen atoms. The hydrogen atom attached to nitrogen atom of 9f was located in a difference density map and refined isotropically. All other H atoms were located in a difference density map but were positioned geometrically and included as riding atoms, with C-H = 0.93-0.98 Å and U_{iso}(H) = 1.2U_{eq}(c). The absolute configuration of the procured material was known in advance and was confirmed by unambiguous refinement of the absolute structure parameter\(^{(35)}\) for 9f. In the absence of significant anomalous scattering efforts, Friedel pairs were merged for 6a.

**General procedure for preparation of N-(2-aminobenzyl)aniline:**\(^{(28,36)}\)

A solution of 1.86 g (20 mmol) of aniline and 3.02 g (20 mmol) 2-nitrobenzaldehyde in 38 mL of benzene was refluxed for 5 hours to remove water with Dean Stark apparatus. Then the reaction mixture was concentrated by rotary evaporation and the residue was dissolved in 57 mL of ethanol. The solution was treated with 0.5 g of NaBH\(_4\) in small portion and the mixture was stirred at room temperature for overnight. The mixture was concentrated; the residue was extracted with water and CHCl\(_3\). The resulting extract was washed with brine and dried over Na\(_2\)SO\(_4\). The residue in 40 mL ethanol was catalytically hydrogenated with 0.057 g of PtO\(_2\) and after the completion of reaction; the catalyst was removed by filtration. The filtrate was evaporated under reduced pressure to give pale brown solid in quantitative yield. The product was purified by column chromatography using hexane/ethyl acetate mixture as eluent. Other N-(2-aminobenzyl) substituted anilines were prepared by the same method.
General procedure for one-pot synthesis of 4-(alkynyl)-2,3-Substituted-3,4-dihydroquinazolines

To a solution of N-(2-aminobenzyl) substituted anilines (1,3-diamine) (0.5 mmol) in 1.5 mL of ethanol, aldehyde (0.5 mmol) was added and stirred at room temperature for 3 hours. To the same solution, KI (16 mg, 0.1 mmol) and 0.25 mL of 70 wt% TBHP in H₂O (4 equivalent) was added drop wise for 5 minutes and stirred at room temperature for overnight. The solvent (EtOH) was removed completely under reduced pressure. Alkynes (1 mmol, 2 equiv.) and CuCl (5 mg, 0.05 mmol) were added in the resulted residue and diluted with 2 mL of dimethoxyethane (DME). The mixture was stirred magnetically at 100 °C for 6 hours. The progress of the reaction was monitored by TLC. After cooling to RT, the catalysts were removed by filtration through silica gel bed using ethyl acetate. The filtrate was concentrated under reduced pressure to afford crude product. The crude product was purified by column chromatography using petroleum ether/ethyl acetate mixture as an eluent and which was analyzed by ¹H NMR, ¹³C NMR, IR, ESI-MS and ESI-HRMS (Figure 4a-4d).

General procedure for one-pot synthesis of 4-(indolyl)-2,3-Substituted-3,4-dihydroquinazolines

To a solution of N-(2-aminobenzyl) substituted anilines (1,3-diamine) (0.5 mmol) in 1.5 mL of ethanol, aldehyde (0.5 mmol) was added and stirred at room temperature for 3 hours. To the same solution, KI (16 mg, 0.1 mmol) and 0.25 mL of 70 wt% TBHP in H₂O (4 equivalent) was added drop wise for 5 minutes and stirred at room temperature for overnight. The solvent (EtOH) was removed completely under reduced pressure. Indoles (0.75 mmol, 1.5 equiv.) and CuCl (5 mg, 0.05 mmol) were added in the resulted residue and diluted with 2 mL of acetonitrile (CH₃CN). The mixture was stirred magnetically at 80 °C for 6 hours. The progress of the
reaction was monitored by TLC. After cooling to RT, the catalysts were removed by filtration through silica gel bed using ethyl acetate. The filtrate was concentrated under reduced pressure to afford crude product. The crude product was purified by column chromatography using petroleum ether/ethyl acetate mixture as an eluent and which was analyzed by $^1$H NMR, $^{13}$C NMR, IR, ESI-MS and ESI-HRMS (Figure 5a-5d).

**General procedure for one-pot synthesis of 4-(pyrrolyl)-2,3-Substituted-3,4-dihydroquinazolines**

To a solution of $N$-(2-aminobenzyl) substituted anilines (1,3-diamine) (0.5 mmol) in 1.5 mL of ethanol, aldehyde (0.5 mmol) was added and stirred at room temperature for 3 hours. To the same solution, KI (16 mg, 0.1 mmol) and 0.25 mL of 70 wt% TBHP in H$_2$O (4 equivalent) was added drop wise for 5 minutes and stirred at room temperature for overnight. The solvent (EtOH) was removed completely under reduced pressure. Pyrrole (2 mmol, 4 equiv.) and CuCl (5mg, 0.05 mmol) were added in the resulted residue and diluted with 2 mL of acetonitrile (CH$_3$CN). The mixture was stirred magnetically at 80 °C for 6 hours. The progress of the reaction was monitored by TLC. After cooling to RT, the catalysts were removed by filtration through silica gel bed using ethyl acetate. The filtrate was concentrated under reduced pressure to afford crude product. The crude product was purified by column chromatography using petroleum ether/ethyl acetate mixture as an eluent and which was analyzed by $^1$H NMR, $^{13}$C NMR, IR, ESI-MS and ESI-HRMS(Figure 6a-6d).

**General procedure for one-pot synthesis of 4-(alkyl)-2,3-Substituted-3,4-dihydroquinazolines**

To a solution of $N$-(2-aminobenzyl) substituted anilines (1,3-diamine) (0.5 mmol) in 1.5 mL of ethanol, aldehyde (0.5 mmol) was added and stirred at room temperature for 3 hours. To
the same solution, KI (16 mg, 0.1 mmol) and 0.25 mL of 70 wt% TBHP in H₂O (4 equivalent) was added drop wise for 5 minutes and stirred at room temperature for overnight. The solvent (EtOH) was removed completely under reduced pressure and the resulted residue was diluted with 3 mL dimethoxyethane (DME), which was stirred magnetically at 100 °C for 1 hours. The reaction mixture was cooled RT and Trimethyl(1-phenylvinylxilo)silane (1 mmol, 2 equiv.) and CuCl (5mg, 0.05 mmol) were added in the solution. The mixture was stirred magnetically at 100 °C for 5 hours. The progress of the reaction was monitored by TLC. After cooling to RT, the catalysts were removed by filtration through silica gel bed using ethyl acetate. The filtrate was concentrated under reduced pressure to afford crude product. The crude product was purified by column chromatography using petroleum ether/ethyl acetate mixture as an eluent and which was analyzed by ¹H NMR, ¹³C NMR, IR, ESI-MS and ESI-HRMS (Figure 7a-7d).

**Spectroscopic data of products**

![2,3-diphenyl-4-(phenylethynyl)-3,4-dihydroquinazoline](image)

**2,3-diphenyl-4-(phenylethynyl)-3,4-dihydroquinazoline:**(Table 2, 6a)

Yellow solid. (Hexane/Ethyl acetate = 4:1, Rf = 0.5). Isolated yield = 73%. IR ν max cm⁻¹: 3121, 3061, 3024, 2920, 1684, 1658, 1586, 1547, 1489, 1376, 1277, 1249, 1174, 1138, 1028, 967, 758, 694. ¹H NMR (CDCl₃, 500 MHz, ppm): δ 7.61 (d, J = 6.0Hz, 2H), 7.50 (d, J = 8.0 Hz, 1H), 7.40-7.36 (m, 3H), 7.29-7.17 (m, 12H), 7.03-7.01 (m, 1H), 5.9 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 154.1, 144.6, 141.4, 136.2, 131.7, 129.6, 129.5, 128.5, 128.8, 128.6, 128.4, 128.1, 128.0, 125.9, 125.0, 124.9, 124.4, 123.5, 122.3, 87.3, 86.3, 53.0. MS (ESI): m/z (amu) = 385 (M+H)⁺. (ESI-HRMS): calculated for C₂₈H₂₁N₂(M+H)⁺: 385.16993 amu, found: 385.16925 amu.
3-phenyl-2-p-tolyl-4-(p-tolylethynyl)-3,4-dihydroquinazoline:(Table 2, 6b)

Sticky Yellow solid. (Hexane/Ethyl acetate = 4:1, Rf = 0.5). Isolated yield = 70%. IR $v_{\text{max}}$ cm$^{-1}$:
3032, 2925, 2857, 1685, 1656, 1546, 1508, 1486, 1455, 1377, 1315, 1278, 1249, 1138, 1027, 819, 758. $^1$H NMR (CDCl$_3$, 300 MHz, ppm): $\delta$ 7.52-7.45 (m, 3H), 7.38-7.33 (m, 1H), 7.28-7.25 (m, 2H), 7.19-7.14 (m, 6H), 7.07-6.99 (m, 5H), 5.86 (s, 1H), 2.31 (s, 3H), 2.28 (s, 3H).

$^{13}$C NMR (CDCl$_3$, 75 MHz, ppm): $\delta$ 154.2, 144.9, 141.5, 139.6, 138.5, 133.3, 131.6, 129.6, 128.8, 128.7, 128.6, 125.6, 125.0, 124.7, 124.2, 123.7, 123.5, 119.3, 86.7, 86.3, 53.1, 21.3, 21.3. MS (ESI): m/z (amu) = 413 (M+H)$^+$. (ESI-HRMS): calculated for C$_{30}$H$_{25}$N$_2$ (M+H)$^+$: 413.20123 amu, found: 413.19992 amu.

3-phenyl-2-m-tolyl-4-(m-tolylethynyl)-3,4-dihydroquinazoline:(Table 2, 6c)

Sticky yellow solid. (Hexane/Ethyl acetate = 4:1, Rf = 0.5). Isolated yield = 73%. IR $v_{\text{max}}$ cm$^{-1}$:
3033, 2947, 2838, 1685, 1587, 1548, 1485, 1374, 1316, 1279, 1251, 1028, 780, 758. $^1$H NMR (CDCl$_3$, 300 MHz, ppm): $\delta$ 7.55 (s, 1H), 7.50-7.48 (d, $J = 8.30$, 1H), 7.39-7.26 (m, 3H), 7.21-7.15 (m, 8H), 7.12-7.07 (m, 3H), 7.04-6.99 (m, 1H), 5.87 (s, 1H), 2.29 (s, 3H), 2.27 (s, 3H). $^{13}$C NMR (CDCl$_3$, 75 MHz, ppm): $\delta$ 154.3, 144.7, 141.4, 137.8, 137.7, 136.0, 132.3, 130.3, 130.2,
129.3, 128.8, 128.6, 128.0, 127.7, 126.8, 125.8, 125.0, 124.8, 124.3, 123.5, 123.4, 122.1, 87.0, 86.4, 53.0, 21.2, 21.0. MS (ESI): m/z (amu) = 413 (M+H)^+. (ESI-HRMS): calculated for C_{30}H_{25}N_2(M+H)^+: 413.20123 amu, found: 413.20020 amu.

4-((4-methoxyphenyl)ethynyl)-2,3-diphenyl-3,4-dihydroquinazoline: (Table 2, 6d)

Yellow solid. (Hexane/Ethyl acetate = 4:1, Rf = 0.5). Isolated yield = 56%. IR ν \text{max} \text{ cm}^{-1}: 3061, 3033, 2952, 2837, 1685, 1604, 1547, 1490, 1375, 1280, 1248, 1173, 1137, 1030, 832, 765, 696.  

^1H NMR (CDCl\textsubscript{3}, 300 MHz, ppm): δ 7.61 (dd, J = 8.30 Hz, 1.51 Hz, 2H), 7.49 (d, J = 7.5 Hz, 1H), 7.40-7.28 (m, 4H), 7.24-7.16 (m, 8H), 7.04-6.98 (m, 1H), 6.78 (d, J = 9.0 Hz, 2H), 5.87 (s, 1H), 3.78 (s, 3H). ^13C NMR (CDCl\textsubscript{3}, 75 MHz, ppm): δ 159.7, 154.2, 144.7, 141.4, 136.3, 134.8, 133.3, 129.7, 129.6, 129.3, 129.0, 128.8, 128.7, 128.1, 128.0, 127.3, 127.2, 127.0, 125.9, 125.1, 124.9, 124.4, 123.8, 123.5, 114.4, 113.8, 86.3, 86.1, 55.3, 53.1. MS (ESI): m/z (amu) = 415 (M+H)^+. (ESI-HRMS): calculated for C_{29}H_{23}ON_2 (M+H)^+: 415.18049 amu, found: 415.17936 amu.
2,3-bis(4-methoxyphenyl)-4-((4-methoxyphenyl)ethynyl)-3,4-dihydroquinazoline: (Table 2, 6e)

Yellow solid. (Hexane/Ethyl acetate = 1:1, Rf = 0.5). Isolated yield = 69%. IR ν\textsubscript{max} cm\textsuperscript{-1}: 3001, 2958, 2932, 2837, 1684, 1606, 1541, 1508, 1465, 1292, 1247, 1172, 1030, 832, 770. \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 300 MHz, ppm): δ 7.54 (d, J = 8.6 Hz, 2H), 7.46 (d, J = 7.9 Hz, 1H), 7.37-7.25 (m, 3H), 7.16 (d, J = 3.9 Hz, 2H), 7.11 (d, J = 8.8 Hz, 2H), 6.86-6.70 (m, 6H), 5.79 (s, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 3.73 (s, 3H). \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 75 MHz, ppm): δ 160.5, 159.5, 156.5, 154.1, 141.5, 138.3, 134.5, 133.2, 131.3, 130.7, 129.9, 128.7, 128.4, 127.5, 127.1, 126.8, 125.4, 125.2, 125.0, 124.4, 123.4, 114.5, 114.2, 113.9, 113.7, 86.4, 85.9, 55.3, 55.2, 55.1, 53.6. MS (ESI): m/z (amu) = 475 (M+H)\textsuperscript{+}. (ESI-HRMS): calculated for C\textsubscript{31}H\textsubscript{27}O\textsubscript{3}N\textsubscript{2} (M+H)\textsuperscript{+}: 475.20162 amu, found: 475.20004 amu.

4-((4-fluorophenyl)ethynyl)-2-(4-methoxyphenyl)-3-phenyl-3,4-dihydroquinazoline: (Table 2, 6f)

Yellow solid. (Hexane/Ethyl acetate = 4:1, Rf = 0.4). Isolated yield = 52%. IR ν\textsubscript{max} cm\textsuperscript{-1}: 3007, 2932, 2839, 1664, 1603, 1544, 1507, 1375, 1309, 1251, 1030, 837, 758. \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 300
MHz, ppm): \(\delta 7.57 \text{ (d, } J = 8.3 \text{ Hz, } 2\text{H}), 7.47 \text{ (d, } J = 8.3 \text{ Hz, } 1\text{H}), 7.39-7.32 \text{ (m, } 3\text{H}), 7.22-7.13 \text{ (m, } 6\text{H}), 7.05-6.92 \text{ (m, } 3\text{H}), 6.96 \text{ (d, } J = 9 \text{ Hz, } 2\text{H}), 5.85 \text{ (s, } 1\text{H}), 3.76 \text{ (s, } 3\text{H}). \)

\(^{13}\)C NMR (CDCl\(_3\), 75 MHz, ppm): \(\delta 164.2, 160.8, 160.7, 153.9, 144.8, 141.4, 133.7, 133.6, 131.3, 128.9, 128.9, 128.7, 128.1, 125.6, 124.9, 124.5, 124.3, 124.2, 123.4, 120.1, 115.5, 115.3, 113.8, 113.4, 87.0, 85.0, 55.3, 55.1, 53.1. MS (ESI): \(m/z\) (amu) = 433 (M+H\(^+\)). (ESI-HRMS): calculated for C\(_{29}\)H\(_{22}\)FN\(_2\)O (M+H\(^+\)) : 433.17107 amu, found : 433.17053 amu.

3-phenyl-4-(p-tolylethynyl)-2-(4-(trifluoromethyl)phenyl)-3,4- dihydroquinazoline:

(Table 2, 6g)

Sticky Yellow solid. (Hexane/Ethyl acetate = 4:1, Rf = 0.6). Isolated yield = 70%. IR \(v_{\text{max}}\) cm\(^{-1}\): 3121, 3032, 2927, 2854, 1685, 1550, 1509, 1491, 1378, 1322, 1280, 1249, 1166, 1128, 1066, 1019, 846, 816, 754. \(^1\)H NMR (CDCl\(_3\), 300 MHz, ppm): \(\delta 7.75 \text{ (d, } J = 8.12 \text{ Hz, } 2\text{H}), 7.51-7.47 \text{ (m, } 3\text{H}), 7.41-7.36 \text{ (m, } 1\text{H}), 7.28-7.13 \text{ (m, } 8\text{H}), 7.08-7.03 \text{ (m, } 3\text{H}), 5.89 \text{ (s, } 1\text{H}), 2.31 \text{ (s, } 3\text{H}). \)

\(^{13}\)C NMR (CDCl\(_3\), 75 MHz, ppm): \(\delta 152.5, 144.1, 141.0, 139.8, 138.8, 131.6, 129.8, 128.9, 126.4, 125.1, 125.0, 124.9, 124.8, 123.5, 123.4, 119.0, 86.7, 86.4, 53.0, 21.3. MS (ESI): \(m/z\) (amu) = 467 (M+H\(^+\)). (ESI-HRMS): calculated for C\(_{30}\)H\(_{22}\)N\(_2\)F\(_3\) (M+H\(^+\)) : 467.17296 amu, found : 467.17059 amu.
2-(4-tert-butylphenyl)-4-((6-methoxynaphthalen-2-yl)ethynyl)-3-phenyl-3,4-
dihydroquinazoline: (Table 2, 6h)

Pale yellow solid. (Hexane/Ethyl acetate = 4:1, Rf = 0.6). Isolated yield = 77%. IR $\nu_{\text{max}}$ cm$^{-1}$: 3063, 2961, 2932, 2866, 1685, 1627, 1601, 1543, 1484, 1376, 1315, 1271, 1246, 1198, 1030, 844, 758, 697. $^1$H NMR (CDCl$_3$, 300 MHz, ppm): $\delta$ 7.83 (s, 1H), 7.64-7.55 (m, 4H), 7.49 (d, $J$ = 7.93 Hz, 1H), 7.40-7.34 (m, 2H), 7.27-7.24 (m, 3H), 7.21-7.20 (m, 5H), 7.13-7.00 (m, 3H), 5.92 (s, 1H), 3.90 (s, 3H), 1.24 (s, 9H). $^{13}$C NMR (CDCl$_3$, 75 MHz, ppm): $\delta$ 158.3, 154.0, 152.8, 145.0, 141.7, 134.1, 133.4, 131.6, 129.3, 129.2, 129.0, 128.8, 128.6, 128.2, 126.6, 125.7, 125.0, 124.9, 124.2, 123.7, 123.4, 119.3, 117.3, 87.1, 86.7, 55.2, 53.2, 34.6, 31.1. MS (ESI): m/z (amu) = 521 (M+H)$^+$. (ESI-HRMS): calculated for C$_{37}$H$_{33}$ON$_2$ (M+H)$^+$: 521.25874 amu, found : 521.25781 amu.

2,3-diphenyl-4-(thiophen-3-ylethynyl)-3,4-dihydroquinazoline: (Table 2, 6i)

Brown solid. (Hexane/Ethyl acetate = 4:1, Rf = 0.4). Isolated yield = 80%. IR $\nu_{\text{max}}$ cm$^{-1}$: 3117, 3035, 2931, 1681, 1657, 1586, 1546, 1489, 1454, 1376, 1315, 1277, 1249, 1138, 1023, 764, 696. $^1$H NMR (CDCl$_3$, 300 MHz, ppm): $\delta$ 7.63-7.59 (m, 2H), 7.49 (d, $J$ = 8.32 Hz, 1H), 7.41-
7.34 (m, 2H), 7.28-7.13 (m, 10H), 7.08-6.99 (m, 2H), 5.87 (s, 1H). $^{13}$C NMR (CDCl$_3$, 75 MHz, ppm): $\delta$ 154.1, 144.7, 141.4, 136.2, 129.9, 129.6, 129.5, 129.3, 128.9, 128.7, 128.0, 125.9, 125.2, 125.0, 124.9, 124.4, 123.5, 121.4, 87.0, 81.4, 53.1. MS (ESI): m/z (amu) = 391 (M+H)$^+$. (ESI-HRMS): calculated for C$_{26}$H$_{19}$N$_2$S (M+H)$^+$ = 391.12635 amu, found: 391.12570.

4-(oct-1-ynyl)-2,3-diphenyl-3,4-dihydroquinazoline:(Table 2, 6j)

Yellow sticky solid. (Hexane/Ethyl acetate = 4:1, Rf = 0.6). Isolated yield = 59%. IR $\nu_{max}$ cm$^{-1}$: 3064, 3037, 2954, 2929, 2857, 1721, 1689, 1586, 1560, 1490, 1376, 1316, 1276, 1250, 1124, 1028, 763, 696. $^1$H NMR (CDCl$_3$, 300 MHz, ppm): $\delta$ 7.59-7.56 (m, 2H), 7.45 (d, $J$ = 6.98 Hz, 1H), 7.36-7.31 (m, 1H), 7.27-7.09 (m, 9H), 7.01-6.96 (m, 1H), 5.63 (t, $J$ = 2 Hz, 1H), 2.20-2.15 (m, 2H), 1.50-1.41 (m, 2H), 1.38-1.18 (m, 6H), 0.83 (t, $J$ = 6.7 Hz, 3H). $^{13}$C NMR (CDCl$_3$, 75 MHz, ppm): $\delta$ 154.1, 144.6, 141.1, 136.1, 134.6, 129.6, 129.4, 129.2, 129.0, 128.5, 127.9, 127.2, 127.1, 125.7, 124.8, 124.6, 124.2, 123.3, 87.3, 78.7, 52.5, 34.3, 31.4, 31.1, 28.3, 24.8, 22.4, 18.7, 13.9, 0.9. MS (ESI): m/z (amu) = 393 (M+H)$^+$. (ESI-HRMS): calculated for C$_{28}$H$_{29}$N$_2$(M+H)$^+$ = 393.23253 amu: found: 393.23187 amu.
4-(hept-1-ynyl)-3-phenyl-2-p-tolyl-3,4-dihydroquinazoline: (Table 2, 6k)

Yellow sticky solid. (Hexane/Ethyl acetate = 4:1, Rf = 0.6). Isolated yield = 56%. IR $\nu_{\text{max}}$ cm$^{-1}$: 3064, 2929, 2857, 1688, 1547, 1489, 1455, 1378, 1316, 1277, 1249, 1143, 1123, 1027, 763, 696. $^1$H NMR (CDCl$_3$, 300 MHz, ppm): $\delta$ 7.48-7.43 (m, 3H), 7.35-7.30 (m, 1H), 7.18-7.09 (m, 6H), 7.04-6.96 (m, 3H), 5.61 (t, $J$ = 2 Hz, 1H), 2.28 (s, 3H), 2.19-2.24 (m, 2H), 1.50-1.41 (m, 2H), 1.35-1.21 (m, 4H), 0.84 (t, $J$ = 6.9 Hz, 3H). $^{13}$C NMR (CDCl$_3$, 75 MHz, ppm): $\delta$ 144.9, 141.3, 139.5, 134.6, 133.3, 129.6, 128.6, 128.5, 125.5, 124.7, 124.6, 124.4, 124.0, 123.3, 87.2, 78.7, 56.6, 30.8, 28.1, 22.0, 21.3, 18.7, 13.8, 0.9. MS (ESI): m/z (amu) = 393 (M+H)$^+$. (ESI-HRMS): calculated for C$_{28}$H$_{29}$N$_2$(M+H)$^+$ = 393.23253 amu: found : 393.23175 amu.

3-phenyl-2-(thiophen-2-yl)-4-(p-tolylethynyl)-3,4-dihydroquinazoline (Table 2, 6l)

Brown sticky solid. (Hexane/Ethyl acetate = 4:1, Rf = 0.4). Isolated yield = 44%. IR $\nu_{\text{max}}$ cm$^{-1}$: 3061, 3040, 1688, 1604, 1546, 1511, 1493, 14 3040, 1688, 1604, 1546, 1511, 1493, 1479, 1426, 1377, 1278, 1253, 1129, 1109, 817, 758, 703. $^1$H NMR (CDCl$_3$, 500 MHz, ppm): $\delta$ 7.43 (d, $J$ = 7.78 Hz, 1H), 7.38-7.25 (m, 8H), 7.18-7.31 (m, 3H), 7.05 (d, $J$ = 7.93 Hz, 2H), 6.89 (d, $J$ = 3.05 Hz, 1H), 6.83-6.81 (m, 1H), 5.80 (s, 1H), 2.30 (s, 3H). $^{13}$C NMR (CDCl$_3$, 75 MHz, ppm): $\delta$
148.5, 144.8, 141.4, 139.8, 138.5, 131.6, 128.8, 128.0, 125.7, 125.2, 124.9, 124.7, 124.3, 123.6, 119.2, 86.7, 86.3, 53.4, 23.3, 128.8, 128.8, 127.0, 125.7, 125.2, 124.9, 124.7, 124.3, 123.6, 119.2, 86.7, 86.3, 53.4, 23.3. MS (ESI): m/z (amu) = 405 (M+H)+. (ESI-HRMS): calculated for C\textsubscript{27}H\textsubscript{21}N\textsubscript{2}S (M+H)+ = 405.14200: found : 405.14189 amu.

4-(1H-indol-3-yl)-2,3-diphenyl-3,4-dihydroquinazoline: (Table 3, 9a)

Yellow solid. (Hexane/Ethyl acetate = 1:1, Rf = 0.5). Isolated yield = 82%. IR \nu max cm\textsuperscript{-1}: 3059, 3035, 2923, 2855, 1685, 1655, 1545, 1487, 1454, 1394, 1361, 1283, 1244, 1109, 1025, 763, 744. 1H NMR (CDCl\textsubscript{3}, 300 MHz, ppm): \delta 8.34 (bs, 1H), 7.89 (d, \textit{J} = 7.1 Hz, 1H), 7.59 (d, \textit{J} = 6.6 Hz, 2H), 7.47 (d, \textit{J} = 7.9 Hz, 1H), 7.35 (d, \textit{J} = 7.36 Hz, 1H), 7.28-7.05 (m, 10H), 6.98-6.95 (m, 3H) 6.23 (s, 1H). 13C NMR (CDCl\textsubscript{3}+DMSO-D\textsubscript{6}, 75 MHz, ppm): \delta 153.1, 144.2, 139.4, 135.2, 134.9, 127.8, 127.0, 126.4, 126.0, 125.5, 124.0, 123.7, 122.8, 122.6, 120.6, 119.9, 117.7, 117.5, 110.3, 57.37. MS (ESI): m/z (amu) = 400 (M+H)+. (ESI-HRMS): calculated for C\textsubscript{28}H\textsubscript{22}N\textsubscript{3}(M+H)+ = 400.18082 amu: found : 400.17987 amu.

4-(1H-indol-3-yl)-3-phenyl-2-p-tolyl-3,4-dihydroquinazoline: (Table 3, 9b)

Yellow solid. (Hexane/Ethyl acetate = 1:1, Rf = 0.6). Isolated yield = 73%. IR \nu max cm\textsuperscript{-1}: 3062, 2926, 2857, 1652, 1543, 1510, 1487, 1454, 1394, 1361, 1245, 1111, 1019, 743. 1H NMR (CDCl\textsubscript{3}, 300 MHz, ppm): \delta 8.41 (bs, 1H), 7.88 (d, \textit{J} = 9.0 Hz, 1H), 7.51-7.46 (m, 3H), 7.35(d, \textit{J} = 8.3 Hz, 1H), 7.25-6.97 (m, 12H), 6.22 (s, 1H), 2.24 (s, 3H). 13C NMR (CDCl\textsubscript{3}, 75 MHz, ppm):
δ 155.7, 145.6, 140.1, 136.3, 132.6, 129.6, 128.9, 128.7, 128.0, 127.1, 125.7, 125.3, 124.7, 124.5, 124.4, 124.0, 122.3, 122.0, 119.9, 199.2, 118.7, 111.80, 58.99, 21.35. MS (ESI): m/z (amu) = 414 (M+H)+. (ESI-HRMS): calculated for C29H24N3(M+H)+ = 414.19647 amu: found : 414.19568 amu.

2-(4-isopropylphenyl)-4-(7-methyl-1H-indol-3-yl)-3-phenyl-3,4-dihydroquinazoline:(Table 3, 9c)

Brown solid. (Hexane/Ethyl acetate = 3:2, Rf = 0.6). Isolated yield = 68%. IR ν max cm⁻¹: 2961, 2928, 2872, 1639, 1612, 1540, 1489, 1455, 1387, 1358, 1316, 1247, 1114, 759. ¹H NMR (CDCl₃, 300 MHz, ppm): δ 8.12 (bs, 1H), 7.76 (d, J = 7.7 Hz, 1H), 7.52 (d, J = 7.7 Hz, 2H), 7.45 (d, J = 7.3 Hz, 1H), 7.23-7.20 (m, 2H), 7.14-6.94 (m, 10H), 6.21 (s, 1H), 2.81 (sep, J = 6.9 Hz, 1H), 1.15 (dd, J = 6.9 Hz, 6H). ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 155.4, 150.6, 145.8, 140.5, 135.8, 133.4, 129.7, 128.5, 127.8, 127.2, 126.1, 125.1, 124.4, 124.2, 124.0, 122.6, 122.01, 120.8, 120.2, 120.1, 116.5, 58.8, 33.8, 23.6, 23.6, 16.6. MS (ESI): m/z (amu) = 456 (M+H)+. (ESI-HRMS): calculated for C₃₂H₃₀N₃(M+H)+ = 456.24342 amu: found : 456.24121 amu.
2,3-bis(4-methoxyphenyl)-4-(7-methyl-1H-indol-3-yl)-3,4-dihydroquinazoline: (Table 3, 9d)

Brown solid. (Hexane/Ethyl acetate = 3:1, Rf = 0.5). Isolated yield = 61%. IR $\nu_{\text{max}}$ cm$^{-1}$: 2930, 2838, 1606, 1582, 1540, 1507, 1481, 1393, 1354, 1299, 1246, 1175, 1031, 835, 767. $^1$H NMR (CDCl$_3$, 300 MHz, ppm): $\delta$ 8.38 (bs, 1H), 7.69 (d, $J = 8.3$ Hz, 1H), 7.51-7.45 (m, 3H) 7.21-7.00 (m, 5H), 6.90 (d, $J = 9.0$ Hz, 2H), 6.75-6.68 (m, 2H), 6.59 (d, $J = 9.0$ Hz, 2H) , 6.11 (s, 1H), 3.72 (s, 3H), 3.68 (s, 3H), 2.46 (s, 3H). $^{13}$C NMR (CDCl$_3$, 75 MHz, ppm): $\delta$ 160.6, 156.8, 155.7, 139.6, 138.8, 135.8, 131.3, 127.8, 127.5, 126.3, 125.4, 125.2, 124.0, 123.5, 122.5, 122.1, 121.0, 120.1, 120.0, 116.3, 113.8, 113.4, 59.3, 55.2, 55.1. MS (ESI): m/z (amu)= 474 (M+H)$^+$. (ESI-HRMS): calculated for C$_{31}$H$_{28}$O$_2$N$_3$(M+H)$^+$ = 474.21760 amu: found : 474.21646 amu.

3-(2-(4-fluorophenyl)-3-phenyl-3,4-dihydroquinazolin-4-yl)-1H-indole-5-carbonitrile:

(Table 3, 9e)

Yellow solid. (Hexane/Ethyl acetate = 3:2, Rf = 0.4). Isolated yield = 65%. IR $\nu_{\text{max}}$ cm$^{-1}$: 2928, 2852, 2221, 1603, 1545, 1509, 1484, 1356, 1228, 1155, 843, 809, 697. $^1$H NMR (DMSO-D6 + CDCl$_3$, 300 MHz, ppm): $\delta$ 10.67 (bs, 1H), 7.66 (s, 1H), 7.15-7.11 (m, 2H), 7.03-6.78 (m, 5H), 6.66-6.42 (m, 9H), 5.77 (s, 1H). $^{13}$C NMR (DMSO-D6+CDCl$_3$, 75 MHz, ppm): $\delta$ 161.8, 159.5, 151.4, 143.4, 138.8, 136.4, 130.6, 129.6, 126.9, 125.9, 124.7, 123.7, 122.9, 122.9, 122.9, 122.7, 122.4,
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122.2, 122.1, 118.7, 118.1, 113.2, 113.0, 111.3, 99.6, 55.8. MS (ESI): m/z (amu) = 443 (M+H)+
calculated for C_{29}H_{20}N_{4}F (M+H)^{+} = 443.16665: found amu: 443.16478 amu.

4-(5-nitro-1H-indol-3-yl)-2,3-diphenyl-3,4-dihydroquinazoline: (Table 3, 9f)

Yellow solid. (Hexane/Ethyl acetate = 3:2, Rf = 0.4). Isolated yield = 63%. IR ν_{max} cm^{-1}: 3064,
3033, 2922, 2857, 1622, 1585, 1541, 1483, 1395, 1334, 1245, 765, 698. ^1^H NMR (CDCl₃, 300
MHz, ppm): δ 10.13 (bs, 1H), 8.83 (d, J = 2.2 Hz, 1H), 8.06 (dd, J = 10.57, 2.2 Hz, 1H), 7.58 (d,
J = 6.7 Hz, 2H), 7.48 (d, J = 7.5 Hz, 1H) 7.33-7.28 (m, 2H), 7.21-6.92 (m, 10H), 6.24 (s, 1H).
^13^C NMR (CDCl₃ + DMSO-D₆, 75 MHz, ppm): δ 152.9, 143.7, 139.5, 139.4, 138.2, 134.5, 127.8,
127.7, 127.1, 126.3, 124.8, 124.3, 124.0, 123.9, 122.9, 122.8, 122.6, 122.0, 119.7, 115.2, 114.8,
110.5, 56.4. MS (ESI): m/z (amu) = 445 (M+H)^+. (ESI-HRMS): calculated for
C_{28}H_{21}O_{2}N_{4}(M+H)^{+} = 445.16590 amu: found : 445.16434 amu.

4-(5-fluoro-1H-indol-3-yl)-3-phenyl-2-(4-(trifluoromethyl)phenyl)-3,4-dihydroquinazoline:

(Table 3, 9g)

Yellow solid. (Hexane/Ethyl acetate = 3:2, Rf = 0.4). Isolated yield = 56%. IR ν_{max} cm^{-1}: 3047,
2924, 1584, 1544, 1485, 1456, 1409, 1323, 1168, 1128, 1110, 1066, 1017, 937, 848, 794, 762,
698, 605. ^1^H NMR (CDCl₃, 300 MHz, ppm): δ 8.46 (bs, 1H), 7.69 (d, J = 8.3 Hz, 2H), 7.51-7.43
(m, 4H), 7.32-7.23 (m, 2H), 7.14-7.09 (m, 5H), 7.05-6.94 (m, 4H), 6.16 (s, 1H). $^{13}$C NMR (CDCl$_3$, 75 MHz, ppm): $\delta$ 159.7, 156.6, 153.9, 145.0, 140.5, 139.8, 132.8, 129.7, 129.0, 128.9, 128.2, 126.6, 126.4, 125.4, 125.2, 125.2, 124.7, 124.5, 123.9, 119.6, 112.4, 112.3, 111.0, 110.7, 104.0, 103.7, 58.5. MS (ESI): m/z (amu) = 486 (M+H)$^+$. (ESI-HRMS): calculated for C$_{29}$H$_{20}$N$_3$F$_4$(M+H)$^+$ amu = 486.15879: found : 486.15758 amu.

![Chemical structure](image)

4-(5-chloro-1H-indol-3-yl)-3-phenyl-2-m-tolyl-3,4-dihydroquinazoline: (Table 3, 9h) Yellow solid. (Hexane/Ethyl acetate = 3:2, Rf = 0.5). Isolated yield = 52%. IR $\nu$ max cm$^{-1}$: 3065, 3029, 2923, 2897, 1586, 1542, 1484, 1454, 1389, 1346, 1371, 1285, 1250, 1112, 1047, 907, 731. $^1$H NMR (CDCl$_3$, 300 MHz, ppm): $\delta$ 8.72 (bs, 1H), 7.83 (s, 1H), 7.55-7.43 (m, 2H), 7.25-6.86 (m, 13H), 6.15 (s, 1H), 2.23 (s, 3H). $^{13}$C NMR (CDCl$_3$, 75 MHz, ppm): $\delta$ 155.7, 145.1, 140.0, 137.9, 135.3, 134.5, 130.7, 130.2, 128.7, 128.1, 127.8, 126.6, 125.8, 125.5, 125.3, 125.1, 124.9, 124.4, 124.0, 123.7, 122.3, 118.6, 117.9, 112.7, 58.5, 21.2. MS (ESI): m/z amu = 448 (M+H)$^+$. (ESI-HRMS): calculated for C$_{29}$H$_{23}$N$_3$Cl(M+H)$^+$ = 448.15750 amu: found : 448.15579 amu.
4-(5-bromo-1H-indol-3-yl)-2-(4-tert-butylphenyl)-3-phenyl-3,4-dihydroquinazoline: (Table 3, 9i)

Brown solid. (Hexane/Ethyl acetate = 3:2, Rf = 0.4). Isolated yield = 67%. IR ν max cm⁻¹: 2960, 2927, 2864, 1585, 1567, 1539, 1482, 1456, 1392, 1311, 1282, 1250, 1114, 885, 842, 793, 760, 697. ¹H NMR (CDCl₃, 300 MHz, ppm): δ 8.85 (bs, 1H), 8.00 (d, J = 1.5 Hz, 1H), 7.53-7.46 (m, 5H), 7.29-6.94 (m, 12H), 6.14 (s, 1H), 1.21 (s, 9H). ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 155.4, 153.3, 145.2, 143.1, 134.8, 132.3, 129.3, 128.7, 128.0, 126.9, 126.0, 125.7, 125.1, 125.0, 124.9, 124.7, 124.1, 123.9, 123.7, 120.8, 118.1, 113.2, 113.0, 58.5, 31.0. MS (ESI): m/z amu = 534 (M+H)⁺. (ESI-HRMS): calculated for C₃₂H₂₉N₃Br (M+H)⁺ = 534.15394 amu: found : 534.15237 amu.

4-(5-methoxy-1H-indol-3-yl)-2-(4-nitrophenyl)-3-phenyl-3,4-dihydroquinazoline:(Table 3, 9j)

Yellow solid. (Hexane/Ethyl acetate = 3:2, Rf = 0.4). Isolated yield = 26%. IR ν max cm⁻¹: 2928, 2855, 1584, 1546, 1520, 1485, 1456, 1345, 1283, 1214, 1173, 1108, 1055, 1029, 856, 760. ¹H NMR (CDCl₃, 300 MHz, ppm): δ 8.22 (bs, 1H), 8.02 (d, J = 8.3 Hz, 2H), 7.72 (d, J = 8.3 Hz, 2H), 7.45 (d, J = 7.5 Hz, 1H), 7.31-7.23 (m, 2H), 7.15-6.86 (m, 9H), 6.19 (s, 1H), 3.73 (s, 3H).
$^{13}$C NMR (CDCl$_3$, 75 MHz, ppm): δ 154.5, 153.1, 147.9, 145.0, 140.5, 131.5, 130.2, 129., 128.1, 126.5, 126.3, 125.7, 125.5, 125.0, 124.8, 123.2, 122.5, 120.2, 112.7, 112.3, 100.9, 59.12, 55.7. MS (ESI): m/z (amu) = 475 (M+H$^+\)). (ESI-HRMS): calculated for C$_{29}$H$_{23}$O$_3$N$_4$(M+H)$^+$ = 475.17647 amu: found : 475.17453 amu.

2-(furan-2-yl)-4-(1H-indol-3-yl)-3-phenyl-3,4-dihydroquinazoline: (Table 3, 9k)

Brown solid. (Hexane/Ethyl acetate = 1:1, Rf = 0.5). Isolated yield = 34%. IR $\nu_{\text{max}}$ cm$^{-1}$: 3060, 2927, 2858, 1584, 1536, 1481, 1454, 1397, 1286, 1249, 1111, 1012, 911, 824, 744, 696. $^1$H NMR (DMSO-d6 + CDCl$_3$, 300 MHz, ppm): δ 10.57 (bs, 1H), 7.75-7.63 (m, 2H), 7.75-7.63 (m, 2H), 7.40-7.37 (m, 3H), 7.20-7.03 (m, 10H), 6.35-6.34 (m, 2H), 6.15 (s, 1H). $^{13}$C NMR (DMSO-D6, 75 MHz, ppm): δ 148.9, 145.3, 144.5, 140.6, 136.7, 128.8, 127.7, 127.0, 125.9, 125.3, 124.7, 124.1, 123.9, 123.1, 124.4, 121.3, 117.8, 114.3, 111.7, 58.3. MS (ESI): m/z (amu) = 390 (M+H$^+\)). (ESI-HRMS): calculated for C$_{26}$H$_{20}$O$_3$N$_3$(M+H)$^+$ = 390.16009 amu: found : 390.15999 amu.

4-(1-methyl-1H-indol-3-yl)-2,3-diphenyl-3,4-dihydroquinazoline: (Table 3, 9l)

Yellow solid. (Hexane/Ethyl acetate = 1:1, Rf = 0.5). Isolated yield = 34%. IR $\nu_{\text{max}}$ cm$^{-1}$: 3056, 2928, 1586, 1541, 1481, 1477, 1373, 1329, 1281, 1247, 765, 743, 698. $^1$H NMR (CDCl$_3$, 500 MHz, ppm): δ 7.87 (d, $J = 7.9$Hz, 1H), 7.61-7.60 (m, 2H), 7.46 (d, $J = 7.7$ Hz, 1H), 7.31-7.17 (m,
2,3-diphenyl-4-(1H-pyrrol-2-yl)-3,4-dihydroquinazoline: (Scheme 9, 11a)

Brown color solid. (Hexane/Ethyl acetate = 3:2, Rf = 0.5). Isolated yield = 66%. IR $v_{\text{max}}$ cm$^{-1}$: 3060, 2929, 2853, 1585, 1540, 1490, 1381, 1283, 1247, 1128, 1028, 763, 720, 697. $^1$H NMR (CDCl$_3$, 300 MHz, ppm): $\delta$ 8.45 (bs, 1H), 7.57-7.48 (m, 3H), 7.35-7.30 (m, 1H), 7.23-6.98 (m, 10H), 6.64-6.61 (m, 1H), 6.42-6.37 (m, 1H), 6.16-6.14 (m, 1H), 5.96 (s, 1H). $^{13}$C NMR (CDCl$_3$, 75 MHz, ppm): $\delta$ 155.5, 145.5, 140.9, 135.8, 133.7, 129.8, 129.6, 128.9, 128.4, 128.0, 126.0, 125.6, 125.4, 124.5, 124.2, 119.2, 107.9, 105.3, 59.3. MS (ESI): m/z (amu) = 350 (M+H)$^+$. (ESI-HRMS): calculated for C$_{24}$H$_{20}$N$_3$ (M+H)$^+ = 350.16517$ amu; found : 350.16510 amu.

3-phenyl-4-(1H-pyrrol-2-yl)-2-p-tolyl-3,4-dihydroquinazoline:(Scheme 9, 11b)

Brown color solid. (Hexane/Ethyl acetate = 3:2, Rf = 0.5). Isolated yield = 61%. IR $v_{\text{max}}$ cm$^{-1}$: 3060, 3038, 2920, 1583, 1537, 1510, 1482, 1453, 1381, 1320, 1282, 1248, 1180, 1115, 1093,
1030, 827, 759, 723, 696. $^1$H NMR (CDCl$_3$, 300 MHz, ppm): $\delta$ 8.41 (bs, 1H), 7.49-7.44 (m, 3H), 7.32 (t, $J = 6.6$ Hz, 1H), 7.17-6.99 (m, 9H), 6.63-6.59 (m, 1H), 6.40-6.35 (m, 1H), 6.16-6.13 (m, 1H), 5.94 (s, 1H), 2.26 (s, 3H). $^{13}$C NMR (CDCl$_3$, 75 MHz, ppm): 155.5, 145.7, 141.0, 140.1, 133.7, 132.8, 129.6, 128.8, 128.6, 128.4, 125.8, 125.5, 124.5, 124.4, 124.1, 119.1, 107.9, 105.2, 59.3, 21.3. MS (ESI): m/z (amu) = 364 (M+H)$^+$. (ESI-HRMS): calculated for C$_{25}$H$_{22}$N$_3$ (M+H)$^+ =$364.18082 amu; found : 364.18034 amu.

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\text{2-(2,3-diphenyl-3,4-dihydroquinazolin-4-yl)-1-phenylethanone: (Table 4, 13a)}
\]

Pale Yellow solid. (Hexane/Ethyl acetate = 4:1, Rf = 0.5). Isolated yield = 66%. IR $\nu$ max cm$^{-1}$: 3059, 2928, 2865, 1681, 1596, 1583, 1541, 1492, 1476, 1447, 1274, 1247, 1032, 768, 757, 691, 600, 558. $^1$H NMR (CDCl$_3$, 300 MHz, ppm): $\delta$ 7.88-7.85 (m, 2H), 7.65-7.62 (m, 2H), 7.53-7.48 (m, 2H), 7.38-7.28 (m, 4H), 7.23-7.11 (m, 6H), 7.02-6.93 (m, 3H), 5.69 (t, $J = 6.7$ Hz 1H), 3.58 (dd, $J = 16, 6.7$ Hz, 1H), 3.40 (dd, $J = 16, 6.9$ Hz, 1H). $^{13}$C NMR (CDCl$_3$, 125 MHz, ppm): $\delta$ 198.0, 154.9, 145.0, 141.8, 136.9, 135.7, 133.4, 130.0, 129.6, 128.8, 128.5, 128.3, 128.1, 126.8, 125.9, 125.2, 124.5, 124.0, 123.3, 58.6, 43.6. MS (ESI): m/z (amu) = 403 (M+H)$^+$. (ESI-HRMS): calculated for C$_{28}$H$_{23}$ON$_2$ (M+H)$^+ =$403.18049 amu; found : 403.18027 amu.
1-phenyl-2-(3-phenyl-2-p-tolyl-3,4-dihydroquinazolin-4-yl)ethanone: (Table 4, 13b)

Pale Yellow solid. (Hexane/Ethyl acetate = 4:1, Rf = 0.5). Isolated yield = 65%. IR $v_{\text{max}}$ cm$^{-1}$:

3059, 2918, 1596, 1581, 1540, 1493, 1477, 1448, 1374, 1274, 1247, 1179, 1053, 1000, 821, 771, 692, 598. $^1$H NMR (CDCl$_3$, 300 MHz, ppm): $\delta$ 7.87-7.84 (m, 2H), 7.54-7.47 (m, 4H), 7.38-7.27 (m, 3H), 7.15-7.07 (m, 4H), 7.02-6.93 (m, 5H), 5.68 (t, $J = 6.7$ Hz 1H), 3.57 (dd, $J = 16.6$, 6.7 Hz, 1H), 3.36 (dd, $J = 16.6$, 6.9 Hz, 1H), 2.27 (s, 1H). $^{13}$C NMR (CDCl$_3$, 75 MHz, ppm): $\delta$ 198.0, 154.9, 145.3, 141.9, 140.2, 136.9, 133.3, 132.9, 129.6, 128.8, 128.7, 128.5, 128.3, 128.2, 126.9, 125.7, 125.1, 124.4, 123.8, 123.3, 58.6, 43.6, 21.3. MS (ESI): m/z (amu) = 417 (M+H)$^+$. (ESI-HRMS): calculated for C$_{29}$H$_{25}$ON$_2$ (M+H)$^+ =$ 417.1961 amu: found : 417.1950 amu.

2-(2-(4-fluorophenyl)-3-phenyl-3,4-dihydroquinazolin-4-yl)-1-phenylethanone: (Table 4, 13c)

Yellow solid. (Hexane/Ethyl acetate = 4:1, Rf = 0.5). Isolated yield = 65%. IR $v_{\text{max}}$ cm$^{-1}$:

3068, 2927, 2853, 1681, 1598, 1543, 1505, 1494, 1448, 1275, 1226, 1155, 1032, 846, 756, 692. $^1$H NMR (CDCl$_3$, 500 MHz, ppm): $\delta$ 7.88-7.86 (m, 2H), 7.63-7.60 (m, 2H), 7.53-7.48 (m, 2H), 7.38-7.30 (m, 3H), 7.15-7.12 (m, 4H), 7.00-6.98 (m, 3H), 6.89-6.86 (m, 2H), 5.66 (t, $J = 6.8$ Hz
1H), 3.59 (dd, \( J = 16.0, 7.6 \text{ Hz}, 1\text{H} \)), 3.32 (dd, \( J = 16.0, 6.7 \text{ Hz}, 1\text{H} \)). \(^{13}\text{C} \text{NMR} (\text{CDCl}_3, 125 \text{ MHz, ppm}): \delta 198.0, 164.7, 162.7, 154.0, 144.9, 141.6, 136.9, 133.5, 131.8, 131.7, 131.6, 128.9, 128.6, 128.4, 128.3, 126.8, 126.1, 125.2, 124.5, 124.2, 123.4, 115.3, 115.1, 58.9, 43.6. \text{MS (ESI): } m/z (\text{amu}) = 421 (\text{M+H})^+ . (\text{ESI-HRMS}): \text{calculated for } C_{28}H_{22}ON_2F (\text{M+H})^+ = 421.17017 \text{ amu}: \text{found : } 421.16934 \text{ amu.}

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\text{1-phenyl-2-(3-phenyl-2-(4-(trifluoromethyl)phenyl)-3,4-dihydroquinazolin-4-yl)ethanone:}
\]

(\text{Table 4, 13d})

Yellow sticky solid. (Hexane/Ethyl acetate = 4:1, Rf = 0.6). Isolated yield = 60%. IR \( \nu_{\text{max}} \text{ cm}^{-1} \): 3063, 2927, 1683, 1597, 1584, 1542, 1494, 1448, 1408, 1325, 1275, 1167, 1126, 1066, 1017, 852, 753, 691. \(^1\text{H} \text{NMR} (\text{CDCl}_3, 500 \text{ MHz, ppm}) : \delta 7.86 (\text{d, } J = 8.3 \text{ Hz}, 2\text{H}), 7.74 (\text{d, } J = 8.2 \text{ Hz}, 2\text{H}), 7.53-7.50 (\text{m, } 2\text{H}), 7.44 (\text{d, } J = 8.2 \text{ Hz}, 2\text{H}), 7.38-7.32 (\text{m, } 3\text{H}), 7.16-7.13 (\text{m, } 4\text{H}), 7.01-6.98 (\text{m, } 3\text{H}), 5.69 (\text{t, } J = 6.8 \text{ Hz, } 1\text{H}), 3.57 (\text{dd, } J = 16.0, 7.0 \text{ Hz, } 1\text{H}), 3.33 (\text{dd, } J = 16.1, 6.7 \text{ Hz, } 1\text{H}). \(^{13}\text{C} \text{NMR} (\text{CDCl}_3, 75 \text{ MHz, ppm}) : \delta 197.8, 153.4, 144.6, 141.4, 139.2, 136.8, 133.5, 129.8, 129.0, 128.6, 128.5, 128.2, 126.7, 126.6, 125.2, 125.0, 125.0, 124.7, 124.4, 123.3, 58.8, 43.7. \text{MS (ESI): } m/z (\text{amu}) = 471 (\text{M+H})^+ . (\text{ESI-HRMS}): \text{calculated for } C_{29}H_{22}ON_2F_3 (\text{M+H})^+ = 471.16787 \text{ amu}: \text{found : } 471.16542 \text{ amu.}
1-phenyl-2-(3-phenyl-2-(thiophen-2-yl)-3,4-dihydroquinazolin-4-yl)ethanone: (Table 4, 13e)

Yellow solid. (Hexane/Ethyl acetate = 4:1, Rf = 0.5). Isolated yield = 61%. IR ṽ max cm⁻¹: 3059, 2956, 2926, 2854, 1683, 1596, 1545, 1491, 1475, 1425, 1273, 1053, 856, 756, 693. ¹H NMR (CDCl₃, 300 MHz, ppm): δ 7.88-7.85 (m, 2H), 7.52-7.44 (m, 2H), 7.37-7.25 (m, 4H), 7.21-7.16 (m, 2H), 7.11-7.01 (m, 5H), 6.85-6.84 (m, 1H), 6.78-6.76 (m, 1H), 5.56 (t, J = 6.9 Hz, 1H), 3.61 (dd, J = 16.0, 6.9 Hz, 1H), 3.30 (dd, J = 16.1, 6.7 Hz, 1H). ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 198.0, 149.8, 145.4, 141.6, 140.2, 136.9, 134.7, 133.4, 130.6, 129.7, 129.0, 128.9, 128.5, 128.4, 128.3, 127.3, 126.7, 125.9, 125.2, 124.5, 124.4, 123.5, 59.1, 43.6. MS (ESI): m/z (amu) = 409 (M+H)⁺. (ESI-HRMS): calculated for C₂₆H₂₁ON₂S (M+H)⁺ = 409.13691 amu: found: 409.13597 amu.

4-(tert-butylperoxy)-2,3-diphenyl-3,4-dihydroquinazoline: (Scheme 8, 4a)

Pale yellow gummy solid, (Hexane/Ethyl acetate = 3:2 ;, Rf = 0.6). ¹H NMR (CDCl₃, 300 MHz, ppm): δ 7.71-7.68 (m, 2H), 7.54-7.41 (m, 3H), 7.31-7.21 (m, 7H), 7.17-7.12 (m, 1H), 7.02-6.98 (m, 1H), 6.26 (s, 1H), 1.19 (s, 9H). ¹³C NMR (75 MHz, CDCl₃, ppm): δ 153.8, 144.7, 136.2, 131.0, 129.9, 129.4, 128.8, 128.6, 127.9, 127.4, 125.4, 125.3, 125.0, 124.9, 122.2, 122.2, 120.3, 90.6, 80.5, 26.2.
2,3-diphenylquinazolin-4-ol: (Scheme 8, 7a)
White solid, (Hexane/Ethyl acetate = 1:1 : , Rf = 0.5). IR \( \nu \) max \( \text{cm}^{-1} \): 3061, 2930, 1588, 1547, 1487, 1405, 1250, 1029, 763. \( ^1H \) NMR (CDCl\(_3\), 300 MHz, ppm): \( \delta \) 7.29-6.95 (m, 14 H), 5.98 (s, 1H). \( ^{13}C \) NMR (75 MHz, CDCl\(_3\), ppm): \( \delta \) 144.9, 140.2, 134.1, 130.5, 129.3, 129.1, 128.5, 127.4, 126.0, 125.5, 125.1, 124.9, 124.2, 123.7.

X-ray Crystallography data of Compound:

Crystal data of compound 6a

Compound 6a was crystallized by slow evaporation method in methanol. \( \text{C}_{28}\text{H}_{20}\text{N}_{2} \), \( M = 384.46 \), colorless needle, 0.15 x 0.08 x 0.06 mm\(^3\), monoclinic, space group \( P2_1 \) (No. 4), \( a = 10.0155(9), b = 12.2702(11), c = 17.6705(15) \) \( \text{Å} \), \( \beta = 98.496(0)^\circ \), \( V = 2147.7(3) \text{Å}^3 \), \( Z = 4 \), \( D_c = 1.189 \text{g/cm}^3 \), \( F_{\text{000}} = 808 \), CCD Area Detector, MoK\( \alpha \) radiation, \( \lambda = 0.71073 \text{Å}, T = 294(2)\text{K}, 2\theta_{\text{max}} = 50.0^\circ \), 20815 reflections collected, 7546 unique (\( R_{\text{int}} = 0.0185 \)). Final \( GooF = 1.101, R1 = 0.0291, wR2 = 0.0752 \), \( R \) indices based on 7048 reflections with \( I>2\sigma(I) \) (refinement on \( F^2 \)), 541 parameters, 1 restraint, \( \mu = 0.070 \text{mm}^{-1} \). CCDC 943358 contains supplementary Crystallographic data for the structure. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk.

Crystal data of compound 9f

Compound 9f was crystallized by slow evaporation method in chloroform. \( \text{C}_{30}\text{H}_{22}\text{Cl}_{6}\text{N}_{4}\text{O}_{2} \), \( M = 683.22 \), colorless needle, 0.15 x 0.08 x 0.05 mm\(^3\), orthorhombic, space group \( Pca2_1 \) (No. 29), \( a = 11.7756(7), b = 14.3426(8), c = 18.5462(11) \) \( \text{Å} \), \( V = 3132.3(3) \text{Å}^3 \), \( Z = 4 \), \( D_c = 1.449 \text{ g/cm}^3 \), \( F_{\text{000}} = 1392 \), CCD Area Detector, MoK\( \alpha \) radiation, \( \lambda = 0.71073 \text{Å}, T = 294(2)\text{K}, 2\theta_{\text{max}} = 50.0^\circ \), 28563 reflections collected, 5504 unique (\( R_{\text{int}} = 0.0366 \)). Final \( GooF =
1.035, $RI = 0.0797$, $wR2 = 0.2195$, $R$ indices based on 4477 reflections with $I > 2\sigma(I)$ (refinement on $F^2$), 383 parameters, 1 restraint. $\mu = 0.584 \text{ mm}^{-1}$. Absolute structure parameter = 0.01(15). CCDC 943359 contains supplementary Crystallographic data for the structure.

**Crystal data of compound 13a**

Compound 13a was crystallized by slow evaporation method in chloroform. $C_{28}H_{22}N_2O$, $M = 402.48$, colorless plate, 0.15 x 0.14 x 0.06 mm$^3$, triclinic, space group $P-1$ (No. 2), $a = 9.7121(11)$, $b = 14.0265(15)$, $c = 18.387(2)$ Å, $\alpha = 102.350(2)$, $\beta = 105.074(2)$, $\gamma = 107.157(2)^\circ$, $V = 2193.4(4)$ Å$^3$, $Z = 4$, $D_c = 1.219$ g/cm$^3$, $F_{000} = 848$, CCD Area Detector, MoK$\alpha$ radiation, $\lambda = 0.71073$ Å, $T = 294(2)$K, $2\theta_{\text{max}} = 50.0^\circ$, 20856 reflections collected, 7709 unique ($R_{\text{int}} = 0.0247$). Final $GooF = 1.016$, $RI = 0.0432$, $wR2 = 0.1083$, $R$ indices based on 5288 reflections with $I > 2\sigma(I)$ (refinement on $F^2$), 559 parameters, 0 restraints, $\mu = 0.074 \text{ mm}^{-1}$. CCDC 943360 contains supplementary Crystallographic data for the structure. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk.

**References**


Chapter I


Figure 4a: $^1$H NMR of compound 6a.

Figure 4b: $^{13}$C NMR of compound 6a.
Figure 4c: IR spectrum of compound 6a.

Figure 4d: HRMS of compound 6a.
Figure 5a: $^1$H NMR of compound 9a.

Figure 5b: $^{13}$C NMR of compound 9a.
Figure 5c: IR spectrum of compound 9a.

Figure 5d: HRMS of compound 9a.
Figure 6a: $^1$H NMR of compound 11a.

Figure 6b: $^{13}$C NMR of compound 11a.
Figure 6c: IR spectrum of compound 11a.

Figure 6d: HRMS of compound 11a.
Figure 7a: $^1$H NMR of compound 13a.

Figure 7b: $^{13}$C NMR of compound 13a.
Figure 7c: IR Spectrum of compound 13a.

Figure 7d: HRMS of compound 13a.