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Copper-Catalyzed Activation of α-Amino Peroxy and Hydroxy Intermediates to Iminium Ion Precursor: An Access to C4-Substituted 3,4-Dihydroquinazolines via Oxidative Cross Coupling Strategy

R. Arun Kumar,[†] G. Saidulu,[†] Balasubramanian Sridhar,[‡] Shiuh Tzung Liu,*[,§] and K. Rajender Reddy*[,†]

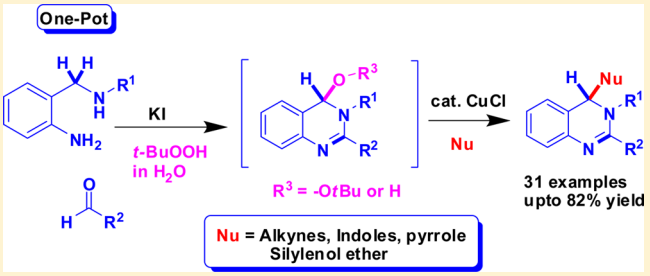
[†]Inorganic and Physical Chemistry Division, CSIR−Indian Institute of Chemical Technology, Tarnaka, Hyderabad 500 607, India

[‡]X-ray Crystallography Division, CSIR−Indian Institute of Chemical Technology, Tarnaka, Hyderabad 500 607, India

[§]Department of Chemistry, National Taiwan University, Taipei 106,Taiwan

Supporting Information

ABSTRACT: A simple and straightforward approach to access C4-substituted-3,4-dihydroquinazolines has been achieved, where copper-catalyzed 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.



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 anticancer agents.[4] Several multistep approaches are known for the synthesis of 3,4-dihydroquinazoline derivatives using highly expensive and unstable reagents such as carbodiimide, isocyanate, azide, and isocyanite derivatives.[5] The limitations of these methods for synthesizing such important alkaloids heavily impede their biological studies. Because of the broad applications of these compounds, new protocols incorporating an efficient and straightforward synthetic procedure to access these scaffolds are highly welcome.

In recent years construction of carbon−carbon (C−C) and carbon−heteroatom (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.[6] Since these methods avoid prefunctionalized precursors and offer shorter routes for the synthesis of complex organic molecules, making them more eco-friendly and atom-economical. Generally, these reactions are accomplished by using transition metal catalysts with different oxidants such as organic peroxides, H_2O_2, molecular oxygen (O_2) and so on.[6] Among them, functionalization of sp^3 C−H bond adjacent to nitrogen atom (via reactive iminium ion intermediate) by CDC approach has been studied extensively over the past few years.[6−13]

Despite tremendous progress made on oxidative α-C−H bond functionalization of amines, a majority of the reported methods are limited to N-protected tetrahydroisoquinoline (THIQ),[7−9] *N*,*N*-dialkyl aniline,[10] *N*-alkyl tertiary amine,[10−12] and amide[13] 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 we have demonstrated the transition-metal-free one-pot synthesis of C4-alkylated 3,4-dihydroquinazoline derivatives via α-C−H bond functionalization of amines using relatively acidic pronucleophile, i.e., nitroalkanes and dialkylmalonates by CDC approach.[8e] On the other hand, this method was unsuccessful with other pronucleophiles 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 pronucleophiles through dative or covalent bond interaction.[7f,m,10b,f]

RESULT AND DISCUSSION

One-Pot Synthesis of C4-Alkynyl-3,4-dihydroquinazolines. In continuation of our previous work,[8e] we started our investigation 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 1, path a). To our delight, the desired product was obtained in 26% isolated yield along with unidentified byproducts. We investigated the reaction under various conditions, but the

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Scheme 1. Synthesis of 4-(Phenylethynyl)-2,3-diphenyl-3,4-dihydroquinazoline through Oxidative Cross Coupling Reaction

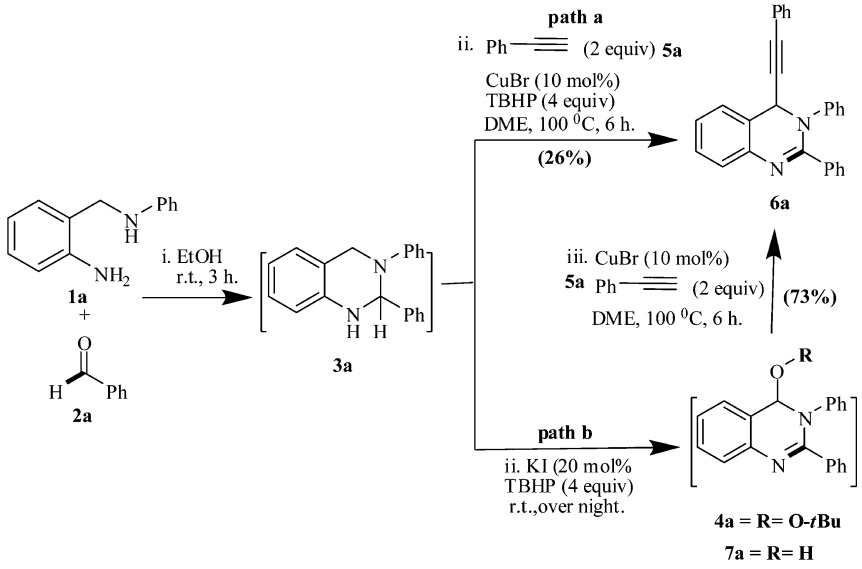
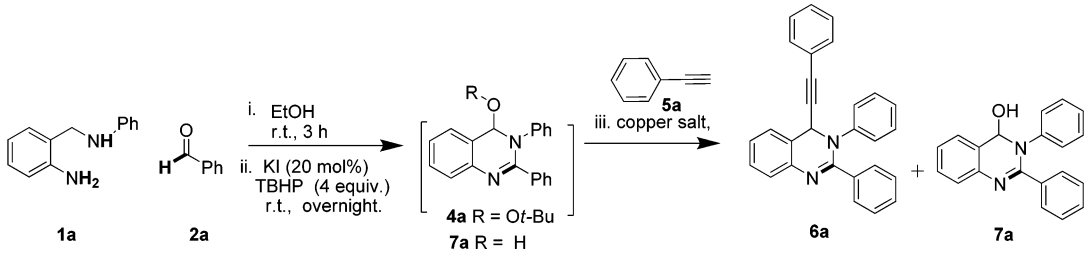


Table 1. Optimization of Reaction Condition for Synthesis of 3,4-Dihydroquinazoline Derivatives Through α-Amino Peroxide and Hydroxide Intermediate[a]



					yield[b]	
entry	copper salt (mol %)	**5a** (equiv)	condition	time (h)	**6a** (%)	**7a** (%)
1	CuBr (20)	2	80 °C	6	44	30
2	CuBr (20)	2.5	DME, 100 °C	6	75	–
3	CuBr (10)	2	DME, 100 °C	6	73	–
4	CuBr (5)	2	DME, 100 °C	6	25	45
5	CuBr (10)	2	1,4-dioxane, 100 °C	6	67	<5
6	CuBr (10)	2	THF, 100 °C	6	52	10
7	–	2	DME, 100 °C	6	–	80
8	**CuCl (10)**	**2**	**DME, 100 °C**	**6**	**73**	–
9	Cu(OAc) (10)	2	DME, 100 °C	6	47	25
10	$CuCl_2·5H_2O$ (10)	2	DME, 100 °C	6	65	<5
11	$CuSO_4·5H_2O$ (10)	2	DME, 100 °C	6	10	55

[a]Reaction condition: (i) 1,3-diamine **1a** (0.5 mmol), benzaldehyde **2a** (0.5 mmol), EtOH (1.5 mL), rt, 3 h. (ii) KI (0.1 mmol), 70 wt % TBHP in H_2O (4 equiv), rt, overnight. (iii.) Copper salt (5−20 mol %), phenylacetylene **5a** (1−1.25 mmol). [b]Isolated yield of the products after SiO_2 column chromatography.

undesirable side reactions impaired the yield of the required product.

On the basis of the mechanistic understanding of our group[8e] and Klussmann group,[7o,8f] we envisioned that catalytic amount of Lewis[7o] or Bronsted acids[8f] could generate iminium ion species from the α-amino peroxy and hydroxy intermediates and can be further trapped with different pronucleophiles. 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,[8e] 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 1, path b). 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 the intermediates **4a** and **7a** (Table 1, entry 7). It was found that 10 mol % of CuCl, in presence of 2 equiv of phenylacetylene with 2 mL of DME at

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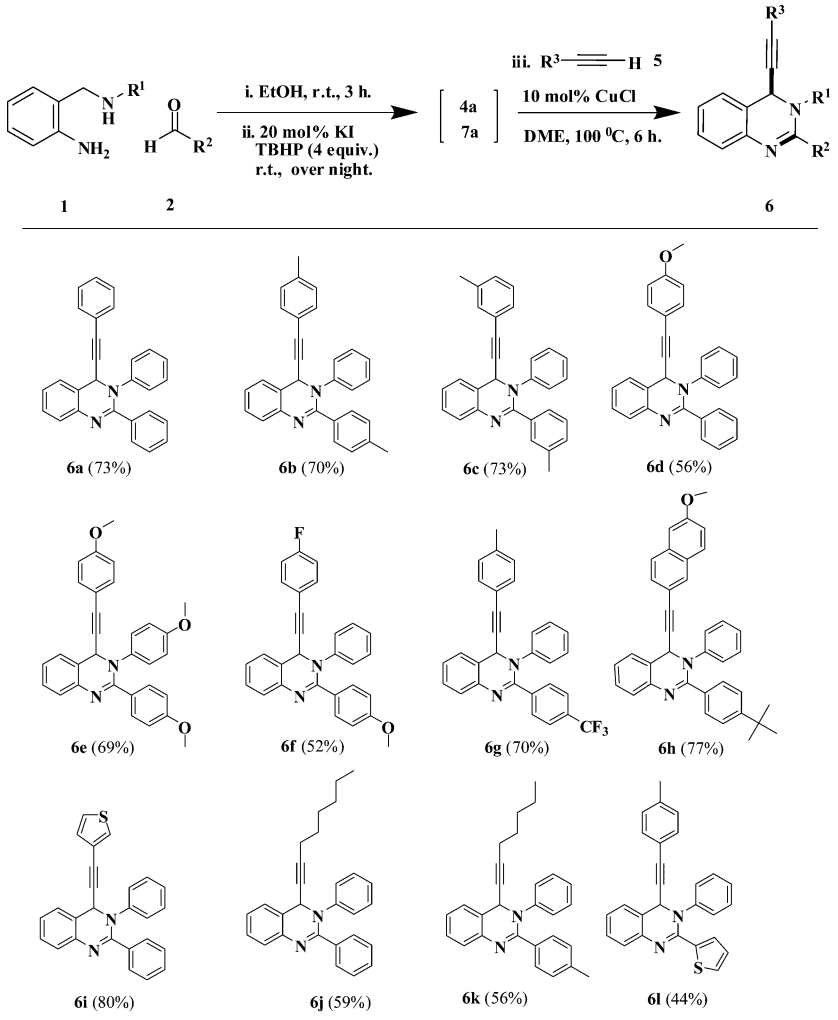
Table 2. Synthesis of C4-Alkynyl-3,4-dihydroquinazoline Derivatives through Oxidative Cross Coupling Reaction[a,b]



[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_2O (4 equiv), rt, 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.

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**).

One-Pot Synthesis of C4-Indolyl and Pyrrolyl-3,4-dihydroquinazolines. After the success in synthesizing of 4-(alkynyl)-2,3-substituted-3,4-dihydroquinazolines (**6**), we next focused our attention in applying this method with other pronucleophile in place of alkynes. As indole[14] and pyrrole[15] rings are commonly observed structural units in several natural and pharmaceutically important products, we looked at these pronucleophiles for the next set of experiments under the similar reaction conditions.

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. As reported earlier,[7b] the reaction selectively occurred at C3 position of indoles and 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*-nitrobenzaldehyde 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 2, **11a**,**b**).[7o] 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

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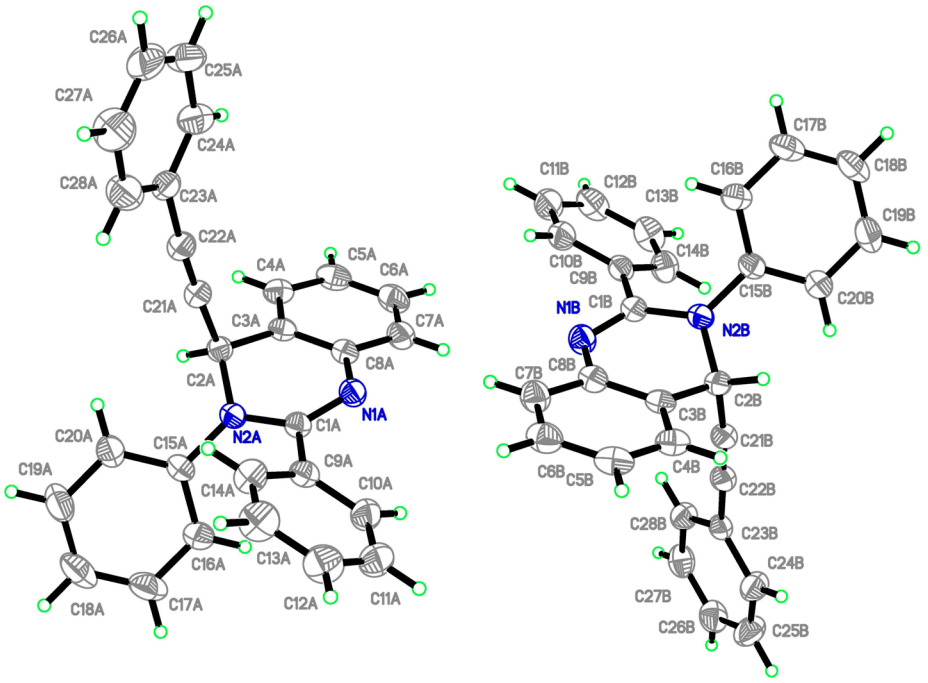

Figure 1. ORTEP drawing of compound **6a** (CCDC 943358). Displacement ellipsoids are drawn at the 30% probability level, and H atoms are represented by circles of arbitrary radii. The compound is crystallized in monoclinic space group $P2_1$ with two molecules in the asymmetric unit.

formation of oxidized product 2,3-diphenylquinazolinone (see Supporting Information) but not the desired product **9a**, which clearly confirms that the copper metal is essential for the product formation.

One-Pot Synthesis of C4-Alkyl-3,4-dihydroquinazolines. After successful synthesis of C4-indolyl-3,4-dihydroquinazoline derivatives, we continued our investigation on the use of methyl ketones and acetophenone as a pronucleophile under the similar reaction conditions. However, the reaction did not proceeded even in the presence of additives, i.e., acetic acid[7d] and L-proline.[7e] While we performed the reaction under the standard condition with silylenolethers, i.e., trimethyl(1-phenylvinyloxy)silane (**12**), the desired coupling product was obtained in good isolated yield. The ^{1}H NMR spectrum of blank experiment is very complex and does not provide any clue for the product formation (see Supporting Information). 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, 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**).

Mechanistic Considerations. On the basis of our[8e] and Klussmann group[7o] experimental results, we would like to propose the plausible mechanism for formation of C4-phenylacetynyl-3,4-dihydroquinazoline derivatives as shown in Scheme 3. The cyclic condensation product (**3a**) is oxidized by the KI/TBHP system predominantly to yield 4-*t*-butylperoxy-2,3-diphenylquinazoline (**4a**) and 2,3-diphenyl-3,4-dihydroquinazolin-4-ol (**7a**) through ionic catalytic cycle.[8e]

In the next step, the peroxy (**4a**) and hydroxyl (**7a**) intermediates are converted into iminium ions (**In 1** and **In 2**) via a reversible heterolytic cleavage catalyzed by Lewis acid (CuCl).[7o] Subsequently, the iminium ion is trapped by phenylacetylene through the reactive copper phenylacetylide **In 3** to afford the final product **6a**.[7n,o,10b] 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 dihydroquinazolines 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.

■ CONCLUSIONS

In summary, we have demonstrated one-pot synthesis of C4-alkylnyl, 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 realized as an activator of α-amino peroxide and hydroxide intermediates to iminium ion. The structures of compounds **6a**, **9f**, and **13a** have also been confirmed by single crystal X-ray analysis (Figures 1−3). Further research on the detailed mechanistic explanations as well as application of this methodology to synthesize biologically important molecules having 3,4-dihydroquinazoline as a core structure are currently ongoing in our laboratory.

■ EXPERIMENTAL SECTION

Caution! *Mixing neat peroxides directly with metal and metal salts is highly dangerous.* 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 precoated silica gel 60-F_{254} plates, visualized by UV light, and developed by iodine. The IR values are reported in reciprocal centimeters (cm^{-1}). All ^{1}H and $^{13}C\{^1H\}$ NMR spectras were recorded

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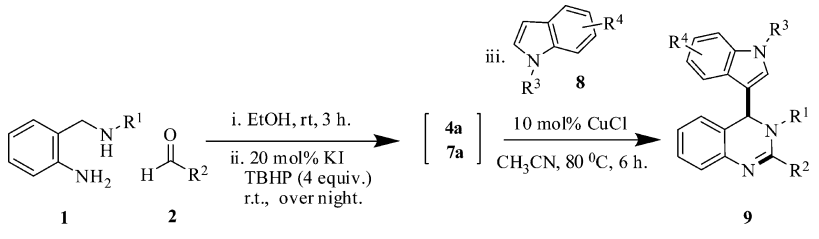
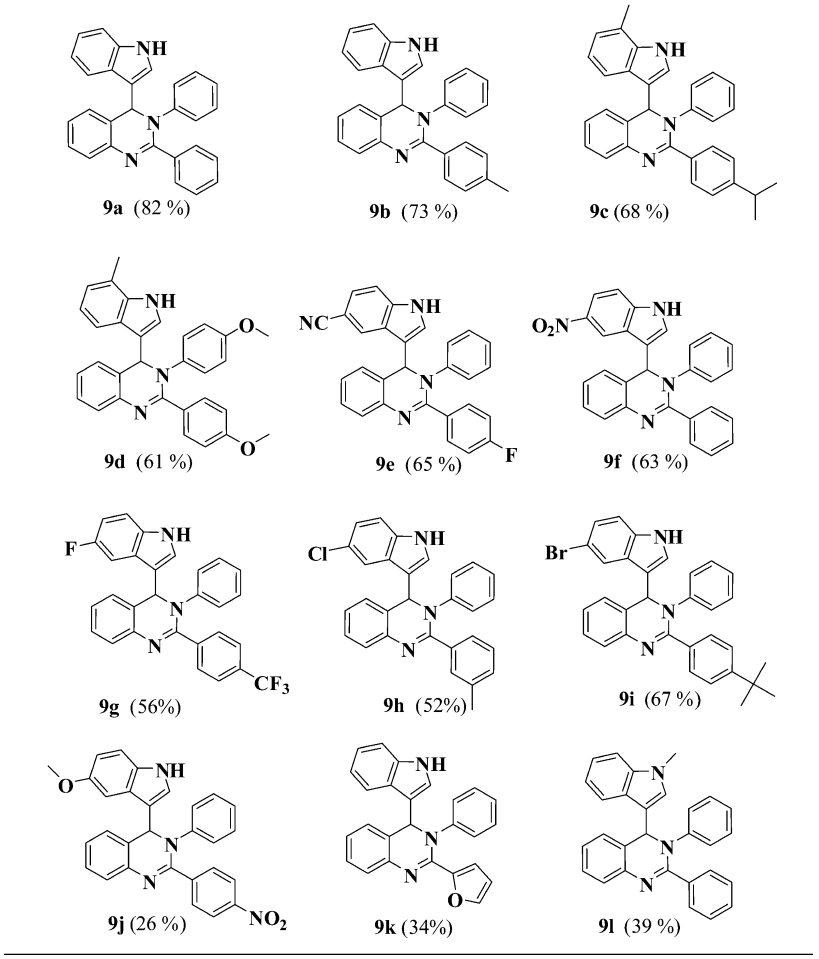
Table 3. Synthesis of C4-Indolyl-3,4-dihydroquinazoline Derivatives through Oxidative Cross Coupling Reaction[a,b]





[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_2O (4 equiv), rt, overnight. (iii) CuCl (10 mol %), indoles **8** (0.75 mmol), CH_3CN (2 mL), 80 °C, 6 h. [b]Numbers in parentheses are isolated yield of the products after SiO_2 column chromatography.

on a 300, 400, and 500 MHz spectrometer. Chemical shifts (δ) are reported in ppm, using TMS ($\delta = 0$) as an internal standard in $CDCl_3$. 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) and HRMS mass spectrometers, and the Orbitrap mass analyzer was used for the HRMS measurement.

General Procedure for Preparation of *N*-(2-Aminobenzyl)-aniline.[8e,16] A solution of 1.86 g (20 mmol) of aniline and 3.02 g (20 mmol) 2-nitrobenzaldyhyde in 38 mL of benzene was refluxed for 5 h 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 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_2SO_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 h. To the same solution, KI (16 mg, 0.1 mmol) and 0.25 mL of 70 wt % TBHP in H_2O (4 equiv) was added dropwise for 5 min and stirred at room temperature 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 h. The progress of the reaction was monitored by TLC. After cooling to RT, the catalysts

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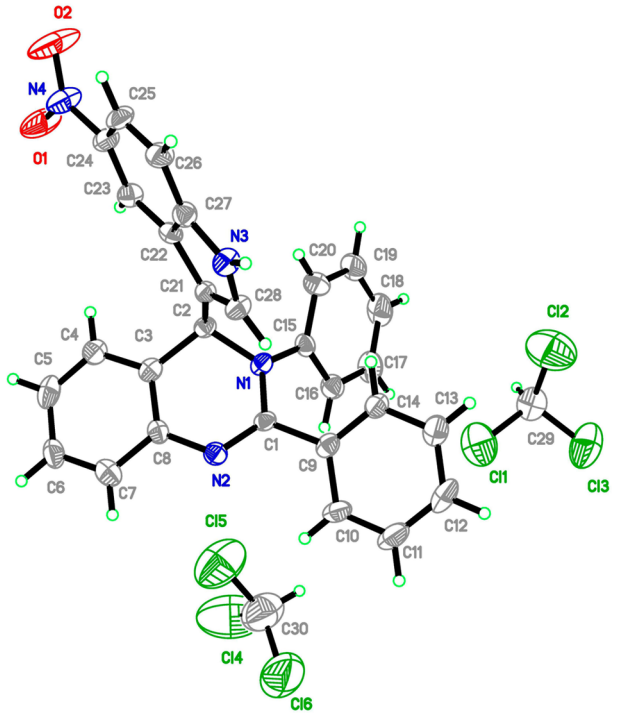


Figure 2. ORTEP drawing of compound **9f** (CCDC 943359). Displacement ellipsoids are drawn at the 30% probability level, and H atoms are represented by circles of arbitrary radii. The compound is crystallized in orthorhombic space group $Pca2_1$ with one **9f** molecule and two chloroform solvents in the asymmetric unit.

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 was analyzed by ^{1}H NMR, ^{13}C NMR, IR, ESI-MS, and ESI-HRMS.

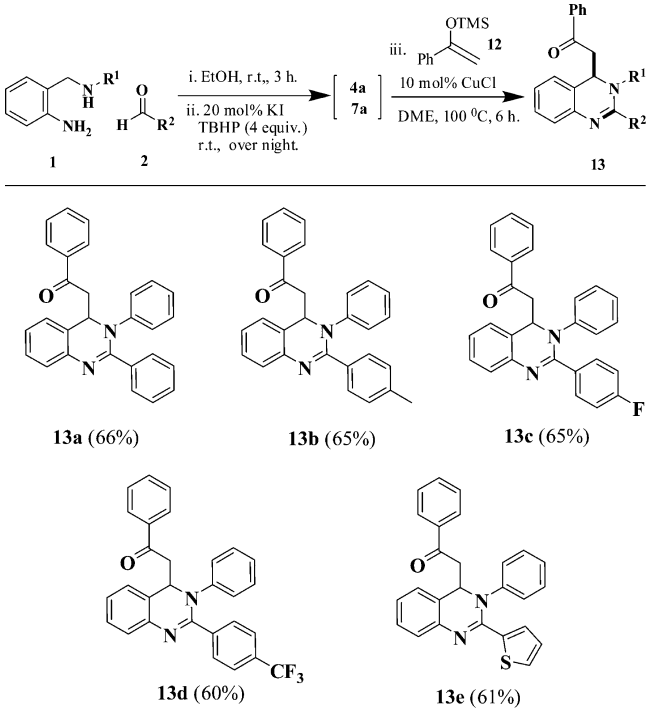
*2,3-Diphenyl-4-(phenylethynyl)-3,4-dihydroquinazoline (**6a**).* Yellow solid. mp 113−115 °C. Isolated yield 140 mg (73%) (hexane/ethyl acetate = 4:1, R_f = 0.5): IR ν_{max} cm^{-1} 3121, 3061, 3024, 2920, 1684, 1658, 1586, 1547, 1489, 1376, 1277, 1249, 1174, 1138, 1028, 967, 758, 694; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 7.61 (d, J = 6.0 Hz, 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); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) δ 154.1, 144.6, 141.4, 136.2, 131.7, 129.6, 129.5, 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 = 385 (M + H)$^+$; (ESI-HRMS) calculated for $C_{28}H_{21}N_2$ (M + H)$^+$ 385.16993, found 385.16925.

*3-Phenyl-2-p-tolyl-4-(p-tolylethynyl)-3,4-dihydroquinazoline (**6b**).* Yellow solid. mp 107−109 °C. Isolated yield 145 mg (70%) (hexane/ethyl acetate = 4:1, R_f = 0.5): IR ν_{max} cm^{-1} 3032, 2925, 2857, 1685, 1656, 1546, 1508, 1486, 1455, 1377, 1315, 1278, 1249, 1138, 1027, 819, 758; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 7.51−7.47 (m, 3H), 7.37−7.33 (m, 1H), 7.27−7.24 (m, 2H), 7.19−7.14 (m, 6H), 7.06−6.99 (m, 5H), 5.86 (s, 1H), 2.30 (s, 3H), 2.27 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) δ 154.2, 144.9, 141.5, 139.6, 138.5, 133.3, 131.6, 129.6, 128.8, 128.7, 128.64, 125.6, 125.0, 124.7, 124.2, 123.7, 123.5, 119.3, 86.7, 86.3, 53.1, 21.38, 21.32; MS (ESI) m/z = 413 (M + H)$^+$; (ESI-HRMS) calculated for $C_{30}H_{25}N_2$ (M + H)$^+$ 413.20123, found 413.19992.

*3-Phenyl-2-m-tolyl-4-(m-tolylethynyl)-3,4-dihydroquinazoline (**6c**).* Yellow semisolid. Isolated yield 150 mg (73%) (hexane/ethyl acetate = 4:1, R_f = 0.5): IR ν_{max} cm^{-1} 3033, 2947, 2838, 1685, 1587, 1548, 1485, 1374, 1316, 1279, 1251, 1028, 780, 758; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 7.56 (s, 1H), 7.49 (d, J = 7.9 Hz, 1H), 7.37 (m, 1H), 7.30−7.23 (m, 1H), 7.2−7.12 (m, 9H), 7.08−6.98 (m, 4H), 5.87 (s, 1H), 2.28 (s, 3H), 2.26 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) δ 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 = 413 (M + H)$^+$; (ESI-HRMS) calculated for $C_{30}H_{25}N_2$ (M + H)$^+$ 413.20123, found 413.20020.

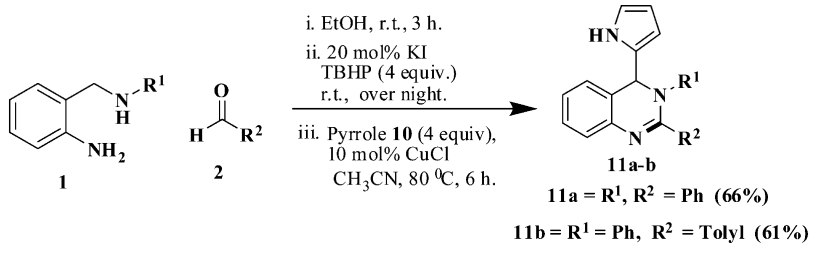
*4-((4-Methoxyphenyl)ethynyl)-2,3-diphenyl-3,4-dihydroquinazoline (**6d**).* Yellow solid. mp 77−79 °C. Isolated yield 115 mg (56%)

Table 4. Synthesis of C4-Alkyl-3,4-dihydroquinazoline Derivatives via Oxidative Cross Coupling Reaction[a,b]



[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_2O (4 equiv), rt, 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 SiO_2 column chromatography.

Scheme 2. Synthesis of C4-Pyrrolyl-3,4-dihydroquinazoline Derivatives through Oxidative Cross Coupling Reaction



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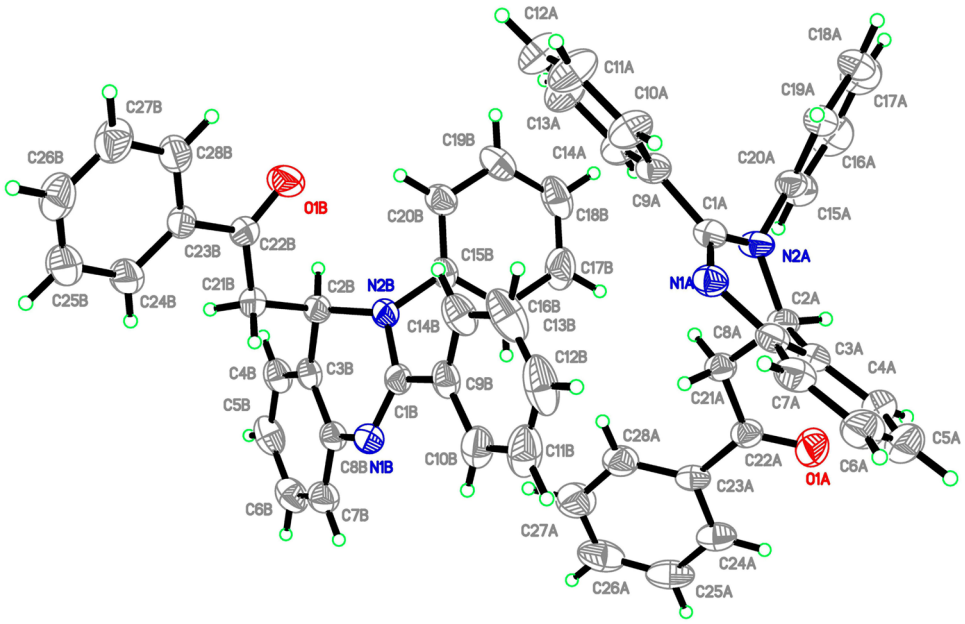
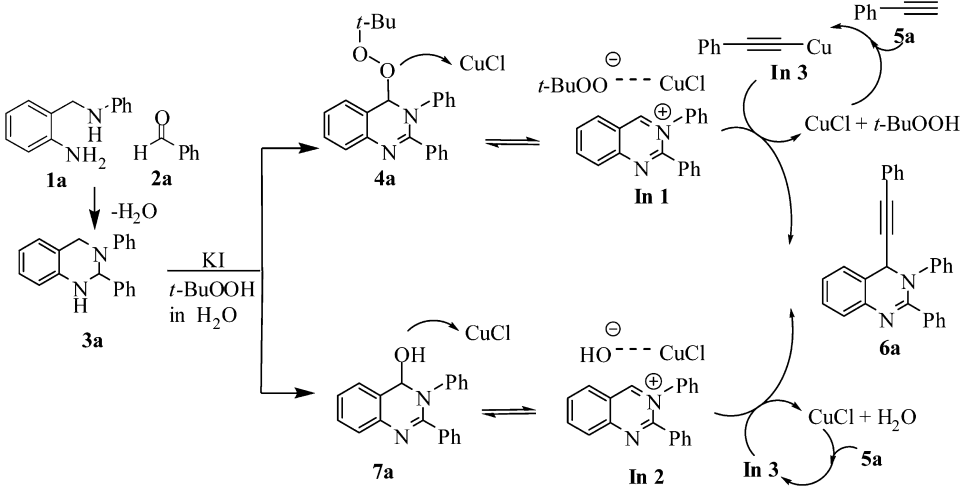


Figure 3. ORTEP drawing of compound **13a** (CCDC 943360). Displacement ellipsoids are drawn at the 30% probability level, and H atoms are represented by circles of arbitrary radii. The compound is crystallized in triclinic space group $P\bar{1}$ with two molecules in the asymmetric unit.

Scheme 3. Plausible Mechanism for the Formation of C4-Phenylacetylenyl-3,4-dihydroquinazoline



(hexane/ethyl acetate = 4:1, R_f = 0.5): IR ν_{max} cm^{-1}3061, 3033, 2952, 2837, 1685, 1604, 1547, 1490, 1375, 1280, 1248, 1173, 1137, 1030, 832, 765, 696; ^{1}H NMR ($CDCl_3$, 300 MHz, ppm) δ 7.61 (dd, J = 8.30, 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); ^{13}C NMR ($CDCl_3$, 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 = 415 (M + H)$^+$; (ESI-HRMS) calculated for $C_{29}H_{23}ON_2$ (M + H)$^+$ 415.18049, found 415.17936.

*2,3-Bis(4-methoxyphenyl)-4-((4-methoxyphenyl)ethynyl)-3,4-dihydroquinazoline (**6e**).* Yellow solid. mp 72−74 °C. Isolated yield 165 mg (69%) (hexane/ethyl acetate = 1:1, R_f = 0.5): IR ν_{max} cm^{-1} 3001, 2958, 2932, 2837, 1684, 1606, 1541, 1508, 1465, 1292, 1247, 1172, 1030, 832, 770; ^{1}H NMR ($CDCl_3$, 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); ^{13}C NMR ($CDCl_3$, 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 = 475 (M + H)$^+$; (ESI-HRMS) calculated for $C_{31}H_{27}O_3N_2$ (M + H)$^+$ 475.20162, found 475.20004.

*4-((4-Fluorophenyl)ethynyl)-2-(4-methoxyphenyl)-3-phenyl-3,4-dihydroquinazoline (**6f**).* Yellow solid. mp 108−110 °C. Isolated yield 115 mg (52%) (hexane/ethyl acetate = 4:1, R_f = 0.4): IR ν_{max} cm^{-1} 3007, 2932, 2839, 1664, 1603, 1544, 1507, 1375, 1309, 1251, 1030, 837, 758; ^{1}H NMR ($CDCl_3$, 300 MHz, ppm) δ 7.57 (d, J = 8.3 Hz, 2H), 7.47 (d, J = 8.3 Hz, 1H), 7.39−7.32 (m, 3H), 7.22−7.13 (m, 6H), 7.05−6.92 (m, 3H), 6.96 (d, J = 9 Hz, 2H), 5.85 (s, 1H), 3.76 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) δ 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 = 433 (M + H)$^+$; (ESI-HRMS) calculated for $C_{29}H_{22}FN_2O$ (M + H)$^+$ 433.17107, found 433.17053.

*3-Phenyl-4-(p-tolylethynyl)-2-(4-(trifluoromethyl)phenyl)-3,4-dihydroquinazoline (**6g**).* Yellow semisolid. mp 103−105 °C. Isolated yield 165 mg (70%) (hexane/ethyl acetate = 4:1, R_f = 0.6): IR ν_{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 ($CDCl_3$,

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500 MHz, ppm) δ 7.73 (d, J = 8.2 Hz, 2H), 7.51−7.47 (m, 3H), 7.42−7.37 (m, 1H), 7.27−7.19 (m, 6H), 7.15 (d, J = 7.6 Hz, 2H) 7.08−7.04 (m, 3H), 5.89 (s, 1H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) δ 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 = 467 (M + H)$^+$; (ESI-HRMS) calculated for $C_{30}H_{22}N_2F_3$ (M + H)$^+$ 467.17296, found 467.17059.

*2-(4-tert-Butylphenyl)-4-((6-methoxynaphthalen-2-yl)ethynyl)-3-phenyl-3,4- dihydroquinazoline (**6h**).* Yellow solid. mp 95−97 °C. Isolated yield 200 mg (77%) (hexane/ethyl acetate = 4:1, R_f = 0.6): IR ν_{max} cm^{-1} 3063, 2961, 2932, 2866, 1685, 1627, 1601, 1543, 1484, 1376, 1315, 1271, 1246, 1198, 1030, 844, 758, 697; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 7.83 (bs, 1H), 7.63−7.56 (m, 4H), 7.49 (d, J = 7.6 Hz, 1H), 7.39−7.37 (m, 2H), 7.26−7.21 (m, 8H), 7.12−7.03 (m, 3H), 5.92 (s, 1H), 3.90 (s, 3H), 1.24 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) δ 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 = 521 (M + H)$^+$; (ESI-HRMS) calculated for $C_{37}H_{33}ON_2$ (M + H)$^+$ 521.25874, found 521.25781.

*2,3-Diphenyl-4-(thiophen-3-ylethynyl)-3,4-dihydroquinazoline (**6i**).* Brown solid. mp 125−127 °C. Isolated yield 160 mg (80%) (hexane/ethyl acetate = 4:1, R_f = 0.4): IR ν_{max} cm^{-1} 3117, 3035, 2931, 1681, 1657, 1586, 1546, 1489, 1454, 1376, 1315, 1277, 1249, 1138, 1023, 764, 696; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 7.62−7.60 (m, 2H), 7.49 (d, J = 7.6 Hz, 1H), 7.40−7.35 (m, 2H), 7.27−7.14 (m, 10H), 7.06−7.0 (m, 2H), 5.87 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) δ 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 = 391 (M + H)$^+$; (ESI-HRMS) calculated for $C_{26}H_{19}N_2S$ (M + H)$^+$ = 391.12635 found 391.12570.

*4-(Oct-1-ynyl)-2,3-diphenyl-3,4-dihydroquinazoline (**6j**).* Yellow semisolid. Isolated yield 116 mg (59%) (hexane/ethyl acetate = 4:1, R_f = 0.6): IR ν_{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) δ 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) δ 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 = 393 (M + H)$^+$; (ESI-HRMS) calculated for $C_{28}H_{29}N_2$(M + H)$^+$ = 393.23253, found 393.23187.

*4-(Hept-1-ynyl)-3-phenyl-2-p-tolyl-3,4-dihydroquinazoline (**6k**).* Yellow semisolid. Isolated yield 110 mg (56%) (hexane/ethyl acetate = 4:1, R_f = 0.6): IR ν_{max} cm^{-1} 3064, 2929, 2857, 1688, 1586, 1547, 1489, 1455, 1378, 1316, 1277, 1249, 1143, 1123, 1027, 763, 696; ^{1}H NMR ($CDCl_3$, 300 MHz, ppm) δ 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) δ 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 =393 (M + H)$^+$; (ESI-HRMS) calculated for $C_{28}H_{29}N_2$(M + H)$^+$ = 393.23253, found 393.23175.

*3-Phenyl-2-(thiophen-2-yl)-4-(p-tolylethynyl)-3,4-dihydroquinazoline (**6l**).* Brown semisolid. Isolated yield 90 mg (44%) (hexane/ethyl acetate = 4:1, R_f = 0.4): IR ν_{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) δ 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) δ 148.5, 144.8, 141.4, 139.8, 138.5, 131.6, 130.6, 128.85, 128.81, 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 = 405 (M + H)$^+$; (ESI-HRMS) calculated for $C_{27}H_{21}N_2S$ (M + H)$^+$ = 405.14200, found 405.14189.

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 h. To the same solution, KI (16 mg, 0.1 mmol) and 0.25 mL of 70 wt % TBHP in H_2O (4 equiv) were added dropwise for 5 min and stirred at room temperature 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 (CH_3CN). The mixture was stirred magnetically at 80 °C for 6 h. 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 was analyzed by ^{1}H NMR, ^{13}C NMR, IR, ESI-MS, and ESI-HRMS.

*4-(1H-Indol-3-yl)-2,3-diphenyl-3,4-dihydroquinazoline (**9a**).* Yellow solid. mp 123−125 °C. Isolated yield 165 mg (82%) (hexane/ethyl acetate = 1:1, R_f = 0.5): IR ν_{max} cm^{-1} 3059, 3035, 2923, 2855, 1685, 1655, 1545, 1487, 1454, 1394, 1361, 1283, 1244, 1109, 1025, 763, 744; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 8.53 (bs, 1H), 7.87 (d, J = 7.7 Hz, 1H), 7.58 (d, J = 7.3 Hz, 2H), 7.48 (d, J = 7.9 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.25−7.11 (m, 7H), 7.06 (t, J = 7.9 Hz, 3H), 6.97 (d, J = 7.3 Hz, 3H), 6.22 (s, 1H); ^{13}C NMR ($CDCl_3$+DMSO−D_6, 75 MHz, ppm) δ 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, 57.3; MS (ESI) m/z = 400 (M + H)$^+$; (ESI-HRMS) calculated for $C_{28}H_{22}N_3$(M + H)$^+$ = 400.18082, found 400.17987.

*4-(1H-Indol-3-yl)-3-phenyl-2-p-tolyl-3,4-dihydroquinazoline (**9b**).* Yellow solid. mp 126−128 °C. Isolated yield 150 mg (73%) (hexane/ethyl acetate = 1:1, R_f = 0.6): IR ν_{max} cm^{-1} 3062, 2926, 2857, 1652, 1543, 1510, 1487, 1454, 1394, 1361, 1245, 1111, 1019, 743; ^{1}H NMR ($CDCl_3$, 300 MHz, ppm) δ 8.50 (bs, 1H), 7.88 (d, J = 7.7 Hz, 1H), 7.49−7.47 (m, 3H), 7.34 (d, J = 7.7 Hz, 1H), 7.24−7.05 (m, 8H), 6.99−6.96 (m, 5H), 6.21(s, 1H), 2.23 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) δ 155.6, 145.5, 140.1, 136.2, 132.5, 129.5, 128.8, 128.5, 127.08, 127.0, 125.6, 125.2, 124.6, 124.4, 123.8, 122.2, 121.9, 119.8, 119.0, 118.6, 111.6, 58.8, 21.23; MS (ESI) m/z = 414 (M + H)$^+$; (ESI-HRMS) calculated for $C_{29}H_{24}N_3$ (M + H)$^+$ = 414.19647, found 414.19568.

*2-(4-Isopropylphenyl)-4-(7-methyl-1H-indol-3-yl)-3-phenyl-3,4-dihydroquinazoline (**9c**).* Brown solid. mp 111−113 °C. Isolated yield 155 mg (68%) (hexane/ethyl acetate = 3:2, R_f = 0.6): IR ν_{max} cm^{-1} 2961, 2928, 2872, 1639, 1612, 1540, 1489, 1455, 1387, 1358, 1316, 1247, 1114, 759; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 8.57 (bs, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.53−7.54 (m, 3H), 7.20 (t, J = 8.0 Hz, 1H), 7.13−6.96 (m, 12H), 6.20 (s, 1H), 2.79 (sep, J = 6.8 Hz, 1H), 2.45 (s, 3H), 1.14 (dd, J = 6.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 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, 125.5, 125.1, 124.4, 124.2, 124.0, 122.6, 122.0, 120.8, 120.2, 120.1, 116.5, 58.8, 33.8, 23.6, 23.6, 16.6; MS (ESI) m/z = 456 (M + H)$^+$; (ESI-HRMS) calculated for $C_{32}H_{30}N_3$ (M + H)$^+$ = 456.24342, found 456.24121.

*2,3-Bis(4-methoxyphenyl)-4-(7-methyl-1H-indol-3-yl)-3,4-dihydroquinazoline (**9d**).* Brown solid. mp 116−118 °C. Isolated yield 148 mg (61%) (hexane/ethyl acetate = 3:1, R_f = 0.5): IR ν_{max} cm^{-1} 2930, 2838, 1606, 1582, 1540, 1507, 1481, 1393, 1354, 1299, 1246, 1175, 1031, 835, 767; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 8.78 (bs, 1H), 7.68 (d, J = 7.9 Hz, 1H), 7.47−7.43 (m, 3H) 7.18 (t, J = 9.0 Hz, 1H), 7.09−7.05 (m, 3H), 6.99 (d, J = 6.2 Hz, 2H), 6.86 (d, J = 8.8 Hz, 2H), 6.63 (d, J = 8.2 Hz, 2H), 6.57 (d, J = 8.8 Hz, 2H) 6.08 (s, 1H), 3.667 (s, 3H), 3.662 (s, 3H), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) δ 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 = 474 (M + H)$^+$; (ESI-HRMS) calculated for $C_{31}H_{28}O_2N_3$ (M + H)$^+$ = 474.21760, found 474.21646.

*3-(2-(4-Fluorophenyl)-3-phenyl-3,4-dihydroquinazolin-4-yl)-1H-indole-5-carbonitrile (**9e**).* Yellow solid. mp 121−123 °C. Isolated yield 145 mg (65%) (hexane/ethyl acetate = 3:2, R_f = 0.4): IR ν_{max} cm^{-1} 2928, 2852, 2221, 1603, 1545, 1509, 1484, 1356, 1228, 1155,

843, 809, 697; ^{1}H NMR (DMSO-d_6, 300 MHz, ppm) δ 11.53 (bs, 1H), 8.16−8.03 (m, 2H), 7.58−6.89 (m, 15H), 6.38 (s, 1H); ^{13}C NMR (DMSO-d_6 + $CDCl_3$, 75 MHz, ppm) δ 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, 122.7, 122.4, 122.2, 122.1, 118.7, 118.1, 113.2, 113.0, 111.3, 99.6, 55.8; MS (ESI) m/z = 443 (M + H)$^+$ calculated for $C_{29}H_{20}N_4F$ (M + H)$^+$ = 443.16665, found 443.16478.

*4-(5-Nitro-1H-indol-3-yl)-2,3-diphenyl-3,4-dihydroquinazoline (**9f**).* Yellow solid. mp 243−245 °C. Isolated yield 140 mg (63%) (hexane/ethyl acetate = 3:2, R_f = 0.4): IR ν_{max} cm^{-1} 3064, 3033, 2922, 2857, 1622, 1585, 1541, 1483, 1395, 1334, 1245, 765, 698; ^{1}H NMR (DMSO-d_6, 500 MHz, ppm) 8.83 (d, J = 1.9 Hz, 1H), 7.99 (dd, J = 9.0, 2.1 Hz, 1H), 7.57−7.54 (m, 4H), 7.35−7.23 (m, 6H), 7.17−7.10 (m, 3H), 7.02−6.95 (m, 3H), 6.60 (s, 1H); ^{13}C NMR ($CDCl_3$ + DMSO−D_6, 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 = 445(M + H)$^+$; (ESI-HRMS) calculated for $C_{28}H_{21}O_2N_4$ (M + H)$^+$ = 445.16590, found 445.16434.

*4-(5-Fluoro-1H-indol-3-yl)-3-phenyl-2-(4-(trifluoromethyl)-phenyl)-3,4-dihydroquinazoline (**9g**).* Yellow solid. mp 105−107 °C. Isolated yield 135 mg (56%) (hexane/ethyl acetate = 3:2, R_f = 0.4): 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 ($CDCl_3$, 300 MHz, ppm) δ 8.41 (bs, 1H), 7.69 (d, J = 8.1 Hz, 2H), 7.53−7.33 (m, 4H), 7.33−7.24 (m, 3H), 7.14−6.09 (m, 9H), 6.16 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) δ 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, 58.7; MS (ESI) m/z = 486 (M + H)$^+$; (ESI-HRMS) calculated for $C_{29}H_{20}N_3F_4$ (M + H)$^+$ = 486.15879, found 486.15758.

*4-(5-Chloro-1H-indol-3-yl)-3-phenyl-2-m-tolyl-3,4-dihydroquinazoline (**9h**).* Yellow solid (hexane/ethyl acetate = 3:2, R_f = 0.5). Isolated yield 115 (52%): IR ν_{max} cm^{-1} 3065, 3029, 2923, 2897, 1586, 1542, 1484, 1454, 1389, 1346, 1371, 1285, 1250, 1112, 1047, 907, 731; ^{1}H NMR (DMSO-d_6, 300 MHz, ppm) δ 11.19 (bs, 1H), 8.19 (s, 1H), 7.78 (m, 1H), 7.50 (m, 1H), 7.37−6.93 (m, 14H), 6.34 (s, 1H), 2.23 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) δ 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 = 448 (M + H)$^+$; (ESI-HRMS) calculated for $C_{29}H_{23}N_3Cl$ (M + H)$^+$ = 448.15750, found 448.15579.

*4-(5-Bromo-1H-indol-3-yl)-2-(4-tert-butylphenyl)-3-phenyl-3,4-dihydroquinazoline (**9i**).* Brown solid. mp 114−116 °C. Isolated yield 180 mg (67%) (hexane/ethyl acetate = 3:2, R_f = 0.4): IR ν_{max} cm^{-1} 2960, 2927, 2864, 1585, 1567, 1539, 1482, 1456, 1392, 1311, 1282, 1250, 1114, 885, 842, 793, 760, 697; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 9.17 (bs, 1H), 7.98−7.95 (m, 1H), 7.51−7.48 (m, 3H), 7.26−7.23 (m, 2H), 7.18−7.09 (m, 7H), 7.01−6.98 (m, 2H), 6.95 (d, J = 7.6 Hz, 2H), 6.13 (s, 1H), 1.19 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) δ 155.4, 153.3, 145.3, 140.2, 134.8, 132.3, 129.3, 128.7, 128.0, 126.9, 126.0, 125.7, 125.1, 124.9, 124.8, 124.7, 124.2, 124.0, 123.7, 120.9, 118.2, 113.2, 113.1, 58.5, 34.6, 31.1, 31.0, 29.6; MS (ESI) m/z = 534 (M + H)$^+$; (ESI-HRMS) calculated for $C_{32}H_{29}N_3Br$ (M + H)$^+$ = 534.15394, found 534.15237.

*4-(5-Methoxy-1H-indol-3-yl)-2-(4-nitrophenyl)-3-phenyl-3,4-dihydroquinazoline (**9j**).* Yellow solid (hexane/ethyl acetate = 3:2, R_f = 0.4). Isolated yield 60 mg (26%): IR ν_{max} cm^{-1} 2928, 2855, 1584, 1546, 1520, 1485, 1456, 1345, 1283, 1214, 1173, 1108, 1055, 1029, 856, 760; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 8.26 (bs, 1H), 8.01 (d, J = 8.8 Hz, 2H), 7.71 (d, J = 8.8 Hz, 2H), 7.47 (d, J = 7.5 Hz, 1H), 7.30−7.23 (m, 4H), 7.14−7.08 (m, 4H), 7.02 (t, J = 7.3 Hz, 1H), 6.96 (m, 1H), 6.18 (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, 129.0, 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, 59.1, 55.7; MS (ESI) m/z = 475 (M + H)$^+$; (ESI-HRMS) calculated for $C_{29}H_{23}O_3N_4$ (M + H)$^+$ = 475.17647, found 475.17453.

*2-(Furan-2-yl)-4-(1H-indol-3-yl)-3-phenyl-3,4-dihydroquinazoline (**9k**).* Brown solid. mp 194−196 °C. Isolated yield 65 mg (34%) (hexane/ethyl acetate = 1:1, R_f = 0.5): IR ν_{max} cm^{-1} 3060, 2927, 2858, 1584, 1536, 1481, 1454, 1397, 1286, 1249, 1111, 1012, 911, 824, 744, 696; ^{1}H NMR (DMSO-d_6, 500 MHz, ppm) δ 11.04 (bs, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.61 (s, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.31 (d, J = 7.4 Hz, 1H), 7.26−7.21 (m, 5H), 7.11 (m, 3H), 7.01 (d, J = 7.6 Hz, 2H), 6.96 (t, J = 7.9 Hz, 1H), 6.60 (d, J = 3.3 Hz, 1H), 6.48−6.47 (m, 1H), 6.30 (s, 1H); ^{13}C NMR (DMSO-d_6, 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 = 390 (M + H)$^+$; (ESI-HRMS) calculated for $C_{26}H_{20}$ ON_3 (M + H)$^+$ = 390.16009, found 390.15999.

*4-(1-Methyl-1H-indol-3-yl)-2,3-diphenyl-3,4-dihydroquinazoline (**9l**).* Yellow solid. mp 107−109 °C. Isolated yield 80 mg (39%) (hexane/ethyl acetate = 1:1, R_f = 0.5): IR ν_{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, 8H), 7.12−7.06 (m, 5H), 7.01−6.95 (m, 3H), 6.22 (s, 1H), 3.67 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm) δ155.1, 145.8, 140.8, 136.9, 136.5, 129.6, 129.5, 128.5, 128.0, 127.8, 127.3, 126.6, 125.6, 125.1, 124.9, 124.7, 124.4, 121.8, 119.7, 119.0, 118.7, 109.5, 58.6, 32.8; MS (ESI) m/z = 414 (M + H)$^+$; (ESI-HRMS) calculated for $C_{29}H_{24}N_3$ (M + H)$^+$ = 414.19647, found 414.19604.

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 h. To the same solution, KI (16 mg, 0.1 mmol) and 0.25 mL of 70 wt % TBHP in H_2O (4 equiv) were added dropwise for 5 min and stirred at room temperature overnight. The solvent (EtOH) was removed completely under reduced pressure. Pyrrole (2 mmol, 4 equiv) and CuCl (5 mg, 0.05 mmol) were added in the resulted residue and diluted with 2 mL of acetonitrile (CH_3CN). The mixture was stirred magnetically at 80 °C for 6 h. 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 was analyzed by ^{1}H NMR, ^{13}C NMR, IR, ESI-MS, and ESI-HRMS.

*2,3-Diphenyl-4-(1H-pyrrol-2-yl)-3,4-dihydroquinazoline (**11a**).* Brown solid. mp 143−146 °C. Isolated yield 115 mg (66%) (hexane/ethyl acetate = 3:2, R_f = 0.5): IR ν_{max} cm^{-1} 3060, 2929, 2853, 1585, 1540, 1490, 1381, 1283, 1247, 1128, 1028, 763, 720, 697; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 8.55 (bs, 1H), 7.54 (d, J = 7.1 Hz, 2H), 7.47 (d, J = 7.7 Hz, 1H), 7.35−7.29 (m, 2H), 7.26−7.23 (m, 2H), 7.20−7.16 (m, 2H), 7.13 (t, J = 7.7 Hz, 3H), 7.08−7.05 (m, 3H) 7.00 (t, J = 7.1 Hz, 1H), 6.62 (s, 1H), 6.39 (s, 1H), 6.16−6.14 (m, 1H), 5.95 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) δ155.5, 145.5, 140.9, 135.8, 133.7, 129.8, 129.6, 128.9, 128.7, 128.4, 128.0, 126.0, 125.6, 125.4, 124.6, 124.5, 124.2, 119.2, 107.9, 105.3, 59.3; MS (ESI) m/z = 350 (M + H)$^+$; (ESI-HRMS) calculated for $C_{24}H_{20}N_3$ (M + H)$^+$ = 350.16517, found 350.16510.

*3-Phenyl-4-(1H-pyrrol-2-yl)-2-p-tolyl-3,4-dihydroquinazoline (**11b**).* Brown solid. mp 101−103 °C. Isolated yield 110 mg (61%) (hexane/ethyl acetate = 3:2, R_f = 0.5): IR ν_{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 ($CDCl_3$, 500 MHz, ppm) δ 8.42 (bs, 1H), 7.49−7.45 (m, 3H), 7.32 (t, J = 8.8 Hz, 1H), 7.11−7.13 (m, 3H), 7.02−7.00 (m, 3H), 6.61−6.60 (m, 1H), 6.39−6.37 (m, 1H), 6.15−6.13 (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 = 364 (M + H)$^+$; (ESI-HRMS) calculated for $C_{25}H_{22}N_3$ (M + H)$^+$ = 364.18082, found 364.18034.

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 h. To the same solution, KI (16 mg, 0.1 mmol) and 0.25 mL of 70 wt % TBHP in H_2O (4 equiv) were added dropwise for

5 min and stirred at room temperature overnight. The solvent (EtOH) was removed completely under reduced pressure, and the resulted residue was diluted with 3 mL of dimethoxyethane (DME), which was stirred magnetically at 100 °C for 1 h. The reaction mixture was cooled to rt, and trimethyl(1-phenylvinyloxy)silane (1.25 mmol, 2.5 equiv) and CuCl (5 mg, 0.05 mmol) were added in the solution. The mixture was stirred magnetically at 100 °C for 5 h. 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 was analyzed by ^{1}H NMR, ^{13}C NMR, IR, ESI-MS, and ESI-HRMS.

*2-(2,3-Diphenyl-3,4-dihydroquinazolin-4-yl)-1-phenylethanone (**13a**).* Yellow solid. mp 140−142 °C. Isolated yield 133 mg (66%) (hexane/ethyl acetate = 4:1, R_f = 0.5): IR ν_{max} cm^{-1} 3059, 2928, 2865, 1681, 1596, 1583, 1541, 1492, 1476, 1447, 1274, 1247, 1032, 768, 757, 691, 600, 558; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 7.86 (d, J = 7.4 Hz, 2H), 7.63 (d, J = 7.3 Hz, 2H), 7.49 (t, J = 7.4 Hz, 2H), 7.37−7.25 (m, 4H), 7.20 (t, J = 7.2 Hz, 2H), 7.13−7.09 (m, 4H), 7.01 (d, J = 7.7 Hz, 2H), 6.95 (t, J = 7.1 Hz, 1H), 5.69 (t, J = 6.7 Hz 1H), 3.58 (dd, J = 16.1, 6.5 Hz, 1H), 3.39 (dd, J = 16.6, 6.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm) δ 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 = 403 (M + H)$^+$; (ESI-HRMS) calculated for $C_{28}H_{23}ON_2$ (M + H)$^+$ = 403.18049, found 403.18027.

*1-Phenyl-2-(3-phenyl-2-p-tolyl-3,4-dihydroquinazolin-4-yl)-ethanone (**13b**).* Yellow solid. mp 90−92 °C. Isolated yield 135 mg (65%) (hexane/ethyl acetate = 4:1, R_f = 0.5): IR ν_{max} cm^{-1} 3059, 2918, 1681, 1596, 1581, 1540, 1493, 1477, 1448, 1374, 1274, 1247, 1179, 1053, 1000, 821, 771, 692, 598; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 7.87−7.85 (m, 2H), 7.54−7.48 (m, 4H), 7.37−7.29 (m, 3H), 7.14−7.08 (m, 4H), 7.02−6.94 (m, 5H), 5.67 (t, J = 6.8 Hz 1H), 3.57 (dd, J = 16.1, 6.7 Hz, 1H), 3.37 (dd, J = 16.3, 7.0 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) δ 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 = 417 (M + H)$^+$; (ESI-HRMS) calculated for $C_{29}H_{25}ON_2$ (M + H)$^+$ = 417.1961, found 417.1950.

*2-(2-(4-Fluorophenyl)-3-phenyl-3,4-dihydroquinazolin-4-yl)-1-phenylethanone (**13c**).* Yellow solid. mp 134−136 °C. Isolated yield 135 mg (65%) (hexane/ethyl acetate = 4:1, R_f = 0.5): IR ν_{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) δ 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 Hz, 1H), 3.32 (dd, J = 16.0, 6.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm) δ 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; MS (ESI) m/z = 421 (M + H)$^+$; (ESI-HRMS) calculated for $C_{28}H_{22}ON_2F$ (M + H)$^+$ = 421.17017, found 421.16934.

*1-Phenyl-2-(3-phenyl-2-(4-(trifluoromethyl)phenyl)-3,4-dihydroquinazolin-4-yl)ethanone (**13d**).* Yellow semisolid. Isolated yield 140 mg (60%) (hexane/ethyl acetate = 4:1, R_f = 0.6): IR ν_{max} cm^{-1} 3063, 2927, 1683, 1597, 1584, 1542, 1494, 1448, 1408, 1325, 1275, 1167, 1126, 1066, 1017, 852, 753, 691; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 7.86 (d, J = 8.3 Hz, 2H), 7.74 (d, J = 8.2 Hz, 2H), 7.53−7.50 (m, 2H), 7.44 (d, J = 8.2 Hz, 2H), 7.38−7.32 (m, 3H), 7.16−7.13 (m, 4H), 7.01−6.98 (m, 3H), 5.69 (t, J = 6.8 Hz, 1H), 3.57 (dd, J = 16.0, 7.0 Hz, 1H), 3.33 (dd, J = 16.1, 6.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) δ 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; MS (ESI) m/z = 471 (M + H)$^+$; (ESI-HRMS) calculated for $C_{29}H_{22}ON_2F_3$ (M + H)$^+$ = 471.16787, found 471.16542.

*1-Phenyl-2-(3-phenyl-2-(thiophen-2-yl)-3,4-dihydroquinazolin-4-yl)ethanone (**13e**).* Yellow solid. mp 145−146 °C. Isolated yield 125 mg (61%) (hexane/ethyl acetate = 4:1, R_f = 0.5): IR ν_{max} cm^{-1} 3059, 2956, 2926, 2854, 1683, 1596, 1545, 1515, 1491, 1475, 1425, 1273, 1053, 856, 756, 693; ^{1}H NMR ($CDCl_3$, 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); ^{13}C NMR ($CDCl_3$, 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 = 409 (M + H)$^+$; (ESI-HRMS) calculated for $C_{26}H_{21}ON_2S$ (M + H)$^+$ = 409.13691, found 409.13597.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H, ^{13}C NMR and HRMS spectra of all new compounds and detailed crystallographic data (CIF) of crystals **6a**, **9f**, and **13a**. This material is available free of charge via Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: stliu@ntu.edu.tw.

*E-mail: rajender@iict.res.in; rajenderkallu@yahoo.com.

Notes

The authors declare no competing financial interest.

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