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Sequential catalytic process: synthesis of quinoline derivatives by $AuCl_3$/CuBr-catalyzed three-component reaction of aldehydes, amines, and alkynes

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Dedicated to Professor Hiroshi Suginome on the occasion of his 77th birthday

Abstract

A sequential catalytic process has been developed based on gold-catalyzed nucleophilic addition of terminal alkynes to imines, and gold-catalyzed intramolecular reaction of aromatic ring to alkynes. This one-pot reaction of aldehydes, amines, and alkynes gives quinoline derivatives in good yields.
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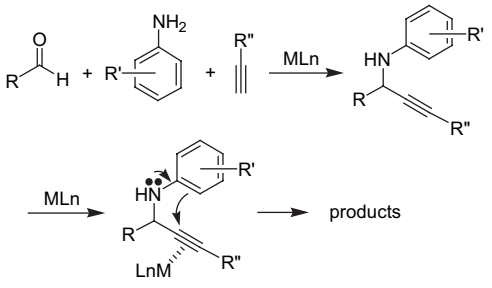
Keywords: Catalysis; Gold; Quinoline; Propargyl amine; Alkyne; Nucleophilic addition

1. Introduction

Gold has attracted more and more attentions in chemistry.[1] Generally, Au^I and Au^{III} act as soft Lewis acids, and they preferentially coordinate with soft Lewis bases, such as alkynes and allenes. The activated alkynes or allenes become susceptible to be attacked by various nucleophiles, such as alcohols/water,[2] nitrogen,[3] carbon nucleophiles,[4] carboxylic acids,[5] ketones,[6] and thiols.[7] Among the carbon nucleophiles, aromatic rings have unique properties and have received attentions recently.[8] For example, Nevado and Echavarren have recently demonstrated Au^I-catalyzed intramolecular hydroarylation of alkyne by electron rich aromatic moiety.[8c]

On the other hand, it has been reported that transition metal complexes, such as silver,[9] ruthenium,[10] and copper,[11] can catalyze the addition of terminal alkynes to imines to afford propargyl amine derivatives. A recent interesting development in this field has been reported by Wei and Li, who have demonstrated a highly efficient three-component coupling reaction of aldehydes, alkynes, and amines via C–H activation catalyzed by gold in water. The reaction affords propargyl amines in high yields.[12] On the other hand, the use of single catalytic system to mediate two or more transformations in a single synthetic operation has recently emerged as a new research area.[13] This strategy is efficient to build complex structures from simple starting materials in an environmentally compatible fashion. Inspired by these developments, we have conceived that it might be possible to combine the Au-catalyzed addition of terminal



Scheme 1. A sequential catalytic process.

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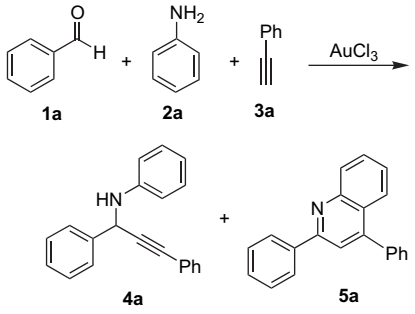
alkynes to imines and the Au-catalyzed reaction of alkynes in a one-pot sequential catalytic process (Scheme 1). Herein, we report a novel method to synthesize quinoline derivatives by the $AuCl_3$/CuBr-catalyzed three-component reaction of aldehydes, amines, and alkynes.

2. Results and discussions

On the outset of this investigation, we have examined the three-component reaction of benzaldehyde, aniline, and phenylacetylene with $AuCl_3$ as a catalyst (Scheme 2). The reaction afforded two products. One was the addition product **4a**, which was formed by nucleophilic addition of the terminal alkyne to the imine that was generated in situ. The other product was a quinoline derivative **5a**. The formation of **5a** suggested the further transformation of the addition product **4a** by Au catalysis under this reaction condition was indeed possible. This result prompted us to examine the Au-catalyzed reaction of propargyl amine **4a** in detail.

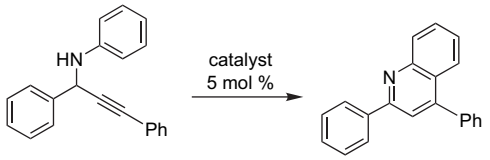


Scheme 2. $AuCl_3$-catalyzed three-component reaction of aldehydes **1a**, amine **2a**, and terminal alkyne **3a**.

AuCl and $AuCl_3$ were examined as catalysts for the reaction of propargyl amine **4a** under various conditions (Table 1). Both catalysts worked well to give **5a** in good yields. Reaction with $AuCl_3$ as catalyst gave better results. Addition of AgOTf did not improve the yield. Microwave or higher reaction temperature could significantly shorten the reaction time, but the yields were not improved (entries 1–5). $PtCl_2$ was also examined as a catalyst, but it gave **5a** in low yield (entry 9). The optimized reaction condition was to use $AuCl_3$ in MeOH at room temperature (entry 6). Under this condition the reaction gave the quinoline product **5a** in good yield, although the reaction took a long time (4 days). It was worthwhile to note that protonic acids failed to catalyze the reaction (entries 10–14).[14] Finally, control experiment indicated that no reaction occurred in the absence of a catalyst.

Subsequently, a series of propargyl amines **4b–o** were prepared according to the method developed by Li and co-workers, who used a combination of $RuCl_3$ and CuBr as catalyst.[10] These propargyl amines were subjected to the optimized reaction conditions with $AuCl_3$ catalyst in MeOH. As shown in Table 2, for most substrates the reaction provided good yields of quinoline derivatives, although in general the reaction required a long time. It was noted that the substituents R^1 did not significantly affect the reaction. Substrates bearing functional groups such as allyloxy and bromide (Table 2, entries 3, 4, 7, 8, and 10) were tolerated. This made possible the further derivatization of the quinoline products. However, R^2 and R^3 were found to

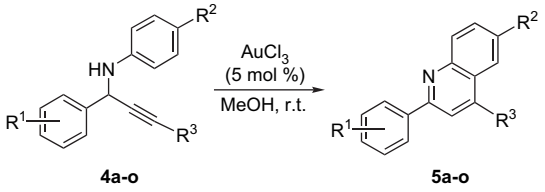
Table 1
Optimization of reaction conditions for acid-catalyzed of **4a**



Entry	Catalyst	Solvent	Temperature (°C)	Time	Yield[a] (%)
1	$AuCl_3$+3AgOTf	DCE	80	24 h	38
2	$AuCl_3$+3AgOTf	$PhCH_3$	110	14 h	66
3	AuCl+AgOTf	$PhCH_3$	110	12 h	48
4	$AuCl_3$+3AgOTf	MeOH	120[b]	10 min	71
5	$AuCl_3$+3AgOTf	MeOH	25	4 days	71
6	$AuCl_3$	MeOH	25	4 days	85
7	AuCl	MeOH	15	8 days	83
8	$AuCl_3$	MeOH	120[b]	15 min	68
9	$PtCl_2$	$PhCH_3$	110	27 h	44
10	TfOH	$PhCH_3$	25	2 days	—[c]
11	TfOH	$PhCH_3$	80	8 h	—[d]
12	TsOH	$PhCH_3$	25	8 days	—[c]
13	HCl	MeOH	25	8 days	—[c]
14	CuBr	MeOH	25	10 days	—[c]
15	No catalyst	MeOH	25	10 days	—[c]

[a] Yields after column chromatographic purification with silica gel.
[b] Reaction was carried out under microwave irradiation.
[c] Compound **5a** was not detected and **4a** was recovered.
[d] A complex mixture was obtained.

Table 2
$AuCl_3$-catalyzed propargyl amines **4a–o**



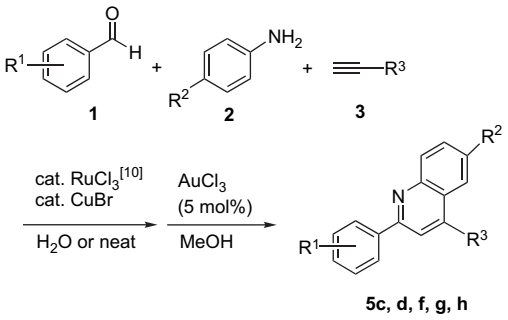
Entry	Substrate (**4a–o**)	Product (**5a–o**)	Time (days)	Yield[a] (%)
1	**4a**, R^1=R^2=H; R^3=Ph	**5a**	4	85
2	**4b**, R^1=H; R^2=CH_3; R^3=Ph	**5b**	2	79
3	**4c**, R^1=2-allyloxy; R^2=H; R^3=Ph	**5c**	3	86
4	**4d**, R^1=2-allyloxy; R^2=CH_3; R^3=Ph	**5d**	3	86
5	**4e**, R^1=2-Me; R^2=H; R^3=Ph	**5e**	4	72
6	**4f**, R^1=2-Me; R^2=CH_3; R^3=Ph	**5f**	1.5	65
7	**4g**, R^1=3-Br; R^2=H; R^3=Ph	**5g**	5	87
8	**4h**, R^1=3-Br; R^2=CH_3; R^3=Ph	**5h**	1.5	86
9	**4i**, R^1=3-OMe; R^2=H; R^3=Ph	**5i**	4	85
10	**4j**, R^1=4-Br; R^2=H; R^3=Ph	**5j**	2.5	74
11	**4k**, R^1=4-Cl, R^2=H; R^3=Ph	**5k**	2.5	83
12	**4l**, R^1=4-Ph; R^2=H; R^3=Ph	**5l**	4	72
13	**4m**, R^1=H; R^2=H; R^3=1-naphthyl	**5m**	4	74
14	**4n**, R^1=H; R^2=4-BrC_6H_4; R^3=H	**5n**	2	0
15	**4o**, R^1=H; R^2=H; R^3=CH_2CH_2OTHP	**5o**	3	0

[a] Yields after column chromatographic purification with silica gel.

markedly affect the reaction. R^3 could be phenyl or naphthyl. When R^2 was an aryl group bearing an electron-withdrawing group, such as 4-bromophenyl, the reaction didn't proceed even in refluxing MeOH (entry 14). When R^3 was an alkyl group, no desired product was obtained (entry 15).

In the preparation of propargyl amines **4a–o**, we have followed Li's approach, which is a $RuCl_3$/CuBr-catalyzed three-component reaction of aldehyde, amine, and alkyne.[10] We have found that it is not necessary to purify the propargyl amine products for the subsequent $AuCl_3$-catalyzed reaction. The $AuCl_3$-catalyzed reaction can be successfully carried out by simple extraction or filtration of the reaction mixture, followed by addition of $AuCl_3$ and MeOH. As shown by the data collected in Table 3, the quinoline products could be isolated in good to excellent yields in this way.

Table 3
Sequential catalytic process with two catalytic system



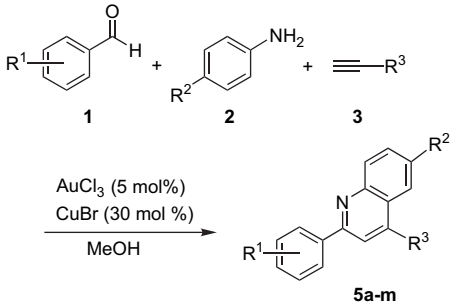
5c, d, f, g, h

Entry	R^1, R^2, R^3	Product	Time[a] (days)	Yield[b] (%)
3	R^1=2-allyloxy; R^2=H; R^3=Ph	**5c**	7.5	76
4	R^1=2-allyloxy; R^2=CH_3; R^3=Ph	**5d**	5.5	94
6	R^1=2-Me; R^2=CH_3; R^3=Ph	**5f**	6.5	55
7	R^1=3-Br; R^2=H; R^3=Ph	**5g**	2.5	65
8	R^1=3-Br; R^2=CH_3; R^3=Ph	**5h**	2.5	80

[a] The total reaction time for two steps.
[b] Yields after column chromatographic purification with silica gel.

Since Li and co-workers have previously reported the gold-catalyzed three-component reaction of aldehydes, alkynes, and amines to provide propargyl amines,[12] we further conceived that a sequential $AuCl_3$-catalyzed reaction of aldehydes, alkynes, and amines to generate quinoline derivatives might be possible. As shown by the results in Scheme 2, the initial experiment suggested that quinoline derivative was formed by the $AuCl_3$-catalyzed three-component reaction, but the reaction proceeded very slowly. Inspired by Li's catalytic system with $RuCl_3$/CuBr in the preparation of propargyl amine, we introduced CuBr as co-catalyst in the $AuCl_3$-catalyzed three-component reaction. It was then found that the yield of the reaction could be improved by adding 30 mol % CuBr, although the reaction time remained essentially the same. As shown in Table 4, a series of quinoline derivates were obtained in moderate to good yields in this three-component reaction catalyzed by $AuCl_3$/CuBr. We suggest that the role of CuBr is to activate the imine intermediate, which is attacked by gold alkynilide.

Table 4
Sequential catalytic process with $AuCl_3$/CuBr

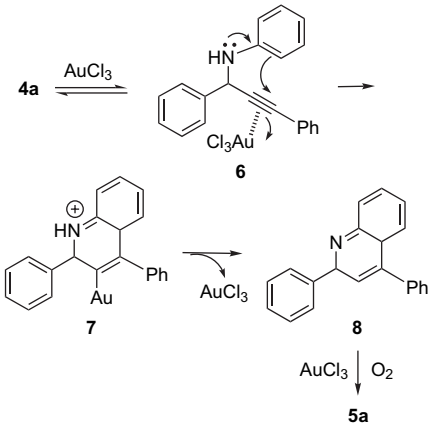


5a-m

Entry	R^1, R^2, R^3	Product	Time (days)	Yield[a] (%)
1	R^1=R^2=H; R^3=Ph	**5a**	12	55
2	R^1=H; R^2=CH_3; R^3=Ph	**5b**	7	67
3	R^1=2-allyloxy; R^2=H; R^3=Ph	**5c**	8	62
4	R^1=2-allyloxy; R^2=CH_3; R^3=Ph	**5d**	7	73
5	R^1=2-Me; R^2=H; R^3=Ph	**5e**	4	64
6	R^1=2-Me; R^2=CH_3; R^3=Ph	**5f**	4	77
7	R^1=3-Br; R^2=H; R^3=Ph	**5g**	5	65
8	R^1=3-Br; R^2=CH_3; R^3=Ph	**5h**	7	87
9	R^1=3-OMe; R^2=H; R^3=Ph	**5i**	7	52
10	R^1=4-Br; R^2=H; R^3=Ph	**5j**	7	84
11	R^1=4-Cl, R^2=H; R^3=Ph	**5k**	7	86
12	R^1=4-Ph; R^2=H; R^3=Ph	**5l**	7	48
13	R^1=H; R^2=H; R^3=1-naphthyl	**5m**	6	69

[a] Yields after column chromatographic purification with silica gel.

A mechanism for the formation of the quinoline derivatives is proposed in Scheme 3. The triple bond of **4a** could be activated by $AuCl_3$ to promote an intramolecular nucleophilic attack by the *N*-substituted phenyl ring attached to the nitrogen. The dihydroquinoline intermediate **8** could be further oxidized by air O_2 to afford quinoline product **5a**.

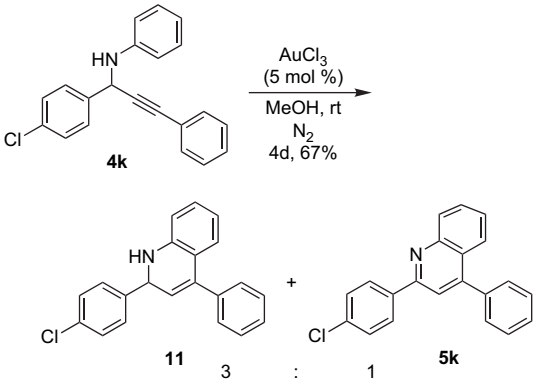


Scheme 3. Mechanistic proposal.

Although it is known that dihydroquinoline can be easily oxidized,[15] we wondered if $AuCl_3$ had effect on the oxidation. Thus, 1,2-dihydroquinoline **9** was prepared through the reduction of quinoline with $LiAlH_4$.[16] Stirring 1,2-dihydroquinoline **9** with 5 mol % $AuCl_3$ in MeOH afforded quinoline **10** in 90% yield within 1 h (Scheme 4), while in the absence of $AuCl_3$ the oxidation proceeded very slowly.

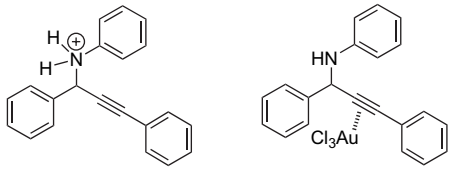
Scheme 4. Oxidation of 1,2-dihydroquinoline.

The $AuCl_3$-catalyzed reaction of **4k** was further carried out under the condition in which oxygen was strictly excluded. As expected, dihydroquinoline **11** was observed in the crude ^1H NMR. Due to its rapid oxidation in the workup, a mixture of dihydroquinoline **11** and quinoline derivative **5k** was isolated in 67% yield with 3:1 ratio (Scheme 5). It was noted that **11** was completely converted to **5k** when keeping in $CDCl_3$ for 2 days.



Scheme 5. $AuCl_3$-catalyzed reaction of **4k** under N_2 atmosphere.

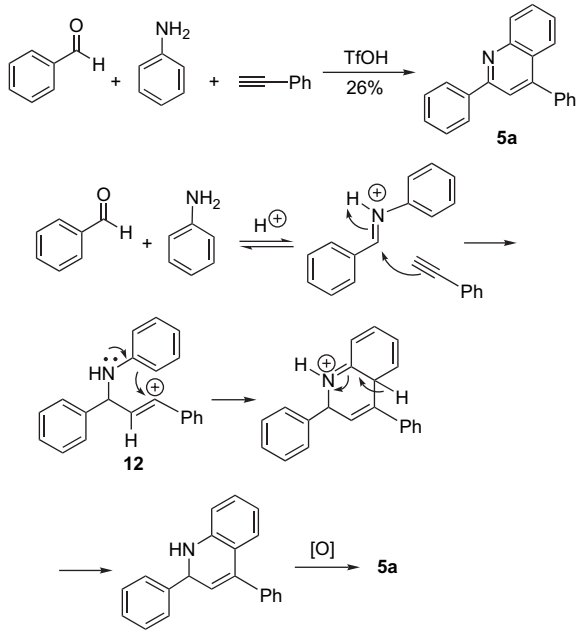
To optimize the acid-catalyzed reaction of **4a**, several protic acids, such as TsOH, TfOH, and HCl, were tested but did not catalyze the reaction (Table 1, entries 10–13). This could be rationalized by the fact that proton as hard acid preferentially interacts with amino nitrogen, while Au^I or Au^{III} as soft Lewis acid favorably coordinates with triple bond.



Interestingly, TfOH-catalyzed three-component reaction gave **5a** in 26% isolated yield (Scheme 6). This result could be rationalized as follows. In TfOH-catalyzed three-component reaction, the formation of **5a** might not be through **4a**, rather it formed through a vinylic cation intermediate.[17]

3. Conclusion

In conclusion, we have developed a simple and effective catalytic method to form quinoline derivatives by using a $AuCl_3$-catalyzed reaction of propargyl amines, or by a $AuCl_3$/CuBr-catalyzed three-component reaction of aldehydes, amines, and alkynes. These processes can provide a diverse range of quinoline derivatives in moderate to good yields from simple starting materials.



Scheme 6. TfOH-catalyzed three-component reaction.

4. Experimental section

4.1. General information

For chromatography, 200–300 mesh silica gel (Qingdao, China) was employed. ^1H and ^{13}C NMR spectra were recorded at 200 and 50 MHz with a Varian Mercury 200 spectrometer, or 300 and 75 MHz with a Varian Mercury 300 spectrometer. Chemical shifts are reported in parts per million using tetramethylsilane (TMS) as internal standard. Mass spectra were obtained on a VG ZAB-HS mass spectrometer. The Au catalysts, $RuCl_3$ hydrate and CuBr are commercially available and are used without further purification.

4.2. General procedure for the preparation of propargyl amines *4a–m*[10]

A mixture of aldehyde (2 mmol) and aniline (2.4 mmol) was heated at 60 °C for about 2 h. Then $RuCl_3$ (3 mol %), CuBr (30 mol %), phenylacetylene (1.2 mmol), and water (2 mL) or solvent free were added into the mixture under N_2. The mixture was stirred at room temperature for 10 min and at 40 °C overnight. The reaction mixture was poured into water, and extracted with diethyl ether (or methylene chloride). The organic layer was washed with water and dried over anhydrous $MgSO_4$. The solvent was removed in vacuo. The product was isolated by column chromatography on silica gel eluting with EtOAc–hexane.

4.3. General procedure for the preparation of quinoline derivatives *5a–m* from propargyl amines

To a solution of propargyl amine (0.5 mmol) in anhydrous MeOH (5 mL) at room temperature under air was added $AuCl_3$ (5 mol %). After being stirred at room temperature

for enough time, the starting material disappeared as judged by TLC. The solvent was removed by evaporation under reduced pressure and the crude product was purified by chromatography to afford quinoline derivatives.

4.4. General procedure for the preparation of quinoline derivatives **5a–m** from three-component material

First, a mixture of aldehyde (1 mmol) and aniline (1.2 mmol) was heated at 60 °C for about 2 h. Then $AuCl_3$ (5 mol %), CuBr (30 mol %), phenylacetylene (1.2 mmol), and MeOH (1 mL) were added into the mixture under N_2. The mixture was stirred at room temperature for 10 min then at 40 °C overnight. Then the mixture was stirred at room temperature for enough time when TLC showed that the reaction had completed. The solvent was removed by evaporation under reduced pressure and the crude product was purified by chromatography to yield quinoline derivative.

4.4.1. N-{1-[2-(Allyloxy)phenyl]-3-phenylprop-2-ynyl}-benzenamine (**4c**)

IR (film): 691, 751, 1245, 1490, 1501, 1601; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.35 (s, 1H), 4.58–4.63 (m, 2H), 5.21–5.26 (m, 1H), 5.39–5.46 (m, 1H), 5.83 (s, 1H), 5.96–6.08 (m, 1H), 6.73–6.80 (m, 3H), 6.89 (d, J=7.5 Hz, 1H), 6.98 (dt, J=7.8, 1.2 Hz, 1H), 7.15–7.41 (m, 8H), 7.66 (dd, J=1.5, 7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 45.82, 68.87, 83.55, 89.02, 112.32, 114.17, 117.14, 118.30, 121.04, 123.01, 128.00, 128.08, 128.20, 128.41, 128.99, 129.14, 131.64, 131.94, 146.75, 155.60; EIMS (*m*/*z*, relative intensity): 339 (M^+, 11), 298 (8), 247 (100), 232 (6), 205 (17), 178 (17), 165 (5), 152 (9), 141(29), 115 (13), 103 (11); HRMS calcd for $C_{24}H_{21}ON$: 339.1623; found: 339.1620.

4.4.2. 2-[2-(Allyloxy)phenyl]-4-phenylquinoline (**5c**)

IR (film): 702, 754, 763, 1239, 1277, 1356, 1449, 1546, 1590; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.58 (dt, J=4.8, 1.8 Hz, 2H), 5.15–5.20 (m, 1H), 5.28–5.36 (m, 1H), 5.92–6.04 (m, 1H), 6.70–7.02 (m, 1H), 7.14 (dt, J=7.5, 0.9 Hz, 1H), 7.36–7.57 (m, 7H), 7.68–7.13 (m, 1H), 7.90–7.93 (m, 3H), 8.23–8.26 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 69.28, 112.97, 117.17, 121.56, 123.86, 125.53, 125.57, 126.17, 128.13, 128.43, 129.02, 129.59, 130.00, 130.06, 130.23, 131.53, 133.01, 138.50, 147.23, 148.79, 156.24, 156.58; EIMS (*m*/*z*, relative intensity): 337 (M^+, 49), 322 (18), 308 (32), 296 (27), 280 (100), 267 (18), 241 (5), 202 (9), 176 (7); HRMS calcd for $C_{24}H_{19}ON$: 337.1467; found: 337.1460.

4.4.3. N-{1-[2-(Allyloxy)phenyl]-3-phenylprop-2-ynyl}-4-methylbenzenamine (**4d**)

IR (film): 692, 754, 808, 1244, 1490, 1518, 3020, 3405; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.22 (s, 3H), 4.23 (s, 1H), 4.59–4.66 (m, 2H), 5.22–5.26 (m, 1H), 5.40–5.47 (m, 1H), 5.77 (s, 1H), 5.97–6.10 (m, 1H), 6.69–6.72 (m, 2H), 6.88–7.00 (m, 4H), 7.19–7.40 (m, 6H), 7.64 (dd, J=1.8, 7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.44, 46.24, 68.92, 83.54, 89.24, 112.32, 114.54, 117.19, 121.06, 123.11, 127.60, 127.99, 128.09, 128.39, 128.46, 129.10, 129.52, 131.67, 133.01, 144.49, 155.64; EIMS (*m*/*z*, relative intensity): 353 (M^+, 21), 312 (6), 247 (100), 232 (7), 205 (10), 178 (14), 141 (27), 115 (12); HRMS calcd for $C_{25}H_{23}ON$: 353.1780; found: 353.1772.

4.4.4. 2-[2-(Allyloxy)phenyl]-6-methyl-4-phenylquinoline (**5d**)

IR (film): 684, 701, 753, 827, 1274, 1423, 1491, 1547, 1587, 1600; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.46 (s, 3H), 4.56 (dd, J=1.5, 3.3 Hz, 2H), 5.15–5.34 (m, 2H), 5.91–6.02 (m, 1H), 6.99 (d, J=8.1 Hz, 1H), 7.13 (dt, J=0.6, 7.5 Hz, 1H), 7.34–7.55 (m, 7H), 7.67 (s, 1H), 7.86 (s, 1H), 7.91 (dd, J=1.5, 7.5 Hz, 1H), 8.14 (d, J=8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.67, 69.23, 112.93, 117.07, 121.50, 123.88, 124.25, 125.46, 128.00, 128.39, 129.53, 129.66, 130.06, 131.45, 132.99, 136.05, 138.67, 146.55, 147.27, 155.56, 156.17; EIMS (*m*/*z*, relative intensity): 351 (M^+, 66), 336 (24), 322 (35), 310 (44), 294 (73), 280 (55), 267 (13), 202 (6), 189 (8), 165 (4), 139 (4); HRMS calcd for $C_{25}H_{21}ON$: 351.1623; found: 351.1618.

4.4.5. N-[3-Phenyl-1-(o-tolyl)prop-2-ynyl]benzenamine (**4e**)

IR (film): 690, 723, 1501, 1601; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.45 (s, 3H), 4.01 (s, 1H), 5.56 (d, J=4.8 Hz, 1H), 6.73–6.80 (m, 3H), 7.18–7.77 (m, 10H), 7.78–7.80 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.95, 48.12, 84.73, 88.30, 113.75, 118.39, 122.83, 126.42, 127.17, 128.15, 128.18, 128.21, 129.18, 130.83, 131.71, 136.16, 137.42, 146.65; EIMS (*m*/*z*, relative intensity): 297 (M^+, 10), 205 (100), 190 (6), 127 (5); HRMS calcd for $C_{22}H_{19}N$: 297.1518; found: 297.1512.

4.4.6. 4-Phenyl-2-(o-tolyl)quinoline (**5e**)

IR (film): 701, 728, 766, 1355, 1406, 1444, 1489, 1574, 1547, 1590; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.45 (s, 3H), 7.27–7.30 (m, 3H), 7.45–7.54 (m, 8H), 7.68–7.74 (m, 1H), 7.93 (d, J=8.1 Hz, 1H), 8.21 (d, J=8.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.40, 122.53, 125.21, 125.58, 125.97, 126.39, 128.36, 128.47, 128.54, 129.41, 129.56, 129.72, 129.99, 130.85, 136.00, 138.11, 140.60, 148.38, 159.80; EIMS (*m*/*z*, relative intensity): 295 (M^+, 64), 294 (100), 218 (78), 133 (3); HRMS calcd for $C_{22}H_{17}N$: 295.1361; found: 295.1359.

4.4.7. 4-Methyl-N-[3-phenyl-1-(o-tolyl)prop-2-ynyl]benzenamine (**4f**)

IR (film): 691, 756, 807, 1489, 1518, 1616, 2919, 3020, 3406; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.31 (s, 3H), 2.51 (s, 3H), 3.94 (s, 1H), 5.59 (s, 1H), 6.73 (d, J=7.8 Hz, 2H), 7.08 (d, J=7.8 Hz, 2H), 7.25–7.48 (m, 8H), 7.83–7.86 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.93, 20.44, 48.33, 84.64, 88.50, 113.89, 122.87, 126.34, 127.13, 127.58, 128.07, 128.15, 129.66, 130.77, 131.70, 136.15, 137.55, 144.36; EIMS (*m*/*z*, relative intensity): 311 (M^+, 12), 205 (100), 190 (6), 178 (5), 127 (5), 107 (4); HRMS calcd for $C_{23}H_{21}N$: 311.1674; found: 311.1673.

4.4.8. 6-Methyl-4-phenyl-2-(o-tolyl)quinoline (**5f**)

IR (film): 701, 728, 756, 828, 1353, 1489, 1574, 1588, 2921, 3057; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.46 (s, 3H), 2.48 (s, 3H), 7.30–7.71 (m, 12H), 8.13 (d, J=8.4 Hz, 1H); ^{13}C NMR

(75 MHz, $CDCl_3$) δ 20.39, 21.79, 122.59, 124.30, 125.15, 125.93, 128.24, 128.35, 128.53, 129.53, 129.70, 130.80, 131.63, 135.99, 136.31, 138.34, 140.68, 146.96, 147.66, 158.85; EIMS (*m*/*z*, relative intensity): 309 (M^+, 72), 308 (100), 292 (6), 232 (76), 217 (9); HRMS calcd for $C_{23}H_{19}N$: 309.1518; found: 309.1529.

*4.4.9. 2-(3-Bromophenyl)-4-phenylquinoline (**5g**)*

IR (film): 701, 773, 793, 878, 1073, 1545, 1588, 3062; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36 (t, J=7.8 Hz, 1H), 7.44–7.58 (m, 7H), 7.70–7.73 (s, 1H), 7.75 (s, 1H), 7.90 (dd, J=0.75, 8.11 Hz, 1H), 8.09 (dt, J=0.72, 7.8 Hz, 1H), 8.21–8.24 (m, 1H), 8.38 (t, J=1.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 118.95, 123.09, 125.63, 125.87, 126.01, 126.65, 128.48, 128.60, 129.49, 129.69, 130.11, 130.27, 130.56, 132.18, 138.11, 141.57, 148.67, 149.42, 155.06; EIMS (*m*/*z*, relative intensity): 360 [$(M+1)^+$, 100], 359 (M^+, 93), 278 (36), 252 (6), 176 (13), 151 (7), 139 (26); HRMS calcd for $C_{21}H_{14}N^{79}Br$: 359.0310; found: 359.0300.

*4.4.10. N-[1-(3-Bromophenyl)-3-phenylprop-2-ynyl]-4-methylbenzenamine (**4h**)*

IR (film): 690, 756, 788, 807, 1518, 1616, 3020; ^1H NMR (300 MHz, $CDCl_3$) δ 2.24 (s, 3H), 4.03 (d, J=6.4 Hz, 1H), 5.41 (d, J=6.4 Hz, 1H), 7.01 (dd, J=0.6, 8.4 Hz, 1H), 7.21–7.30 (m, 4H), 7.38–7.46 (m, 3H), 7.54–7.58 (m, 1H), 7.80 (t, J=1.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.44, 50.45, 85.40, 87.85, 114.30, 122.45, 122.74, 125.83, 128.11, 128.22, 129.68, 130.24, 130.28, 131.06, 131.73, 142.25, 143.88; EIMS (*m*/*z*, relative intensity): 375 (M^+, 16), 368 (3), 269 (100), 220 (22), 189 (38), 163 (3), 139 (2); HRMS calcd for $C_{22}H_{18}N^{79}Br$: 375.0623; found: 375.0621.

*4.4.11. 2-(3-Bromophenyl)-6-methyl-4-phenylquinoline (**5h**)*

IR (film): 700, 765, 790, 825, 1491, 1546, 1587, 1714, 3058; ^1H NMR (300 MHz, $CDCl_3$) δ 2.45 (s, 3H), 7.34 (t, J=7.8 Hz, 1H), 7.49–7.56 (m, 7H), 7.63 (s, 1H), 7.70 (s, 1H), 8.07 (d, J=8.4 Hz, 1H), 8.11 (d, J=8.4 Hz, 1H), 8.36 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.80, 118.98, 123.06, 124.35, 125.82, 125.88, 128.35, 128.57, 129.46, 129.83, 130.21, 130.44, 131.92, 131.97, 136.64, 138.34, 141.68, 147.26, 148.65, 154.15; EIMS (*m*/*z*, relative intensity): 373 (M^+, 100), 358 (38), 294 (23), 278 (16), 265 (2), 252 (2), 261 (10), 202 (5), 187 (3), 139 (24), 125 (6); HRMS calcd for $C_{22}H_{16}N^{79}Br$: 373.0466; found: 373.0467.

*4.4.12. N-[1-(3-Methoxyphenyl)-3-phenylprop-2-ynyl]benzenamine (**4i**)*

IR (film): 690, 754, 787, 871, 1046, 1154, 1255, 1433, 1489, 1501, 1600, 2924; ^1H NMR (300 MHz, $CDCl_3$) δ 3.80 (s, 3H), 4.14 (br, 1H), 5.46 (s, 1H), 6.75–7.42 (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 50.60, 55.24, 84.96, 88.34, 112.86, 113.53, 114.04, 118.56, 119.53, 122.71, 128.18, 128.27, 129.13, 129.77, 131.71, 141.29, 146.48, 159.90; EIMS (*m*/*z*, relative intensity): 313 (M^+, 9), 221 (100), 211 (45), 178 (14), 167 (6); HRMS calcd for $C_{22}H_{19}ON$: 313.1467; found: 313.1469.

*4.4.13. 2-(3-Methoxyphenyl)-4-phenylquinoline (**5i**)*

IR (film): 701, 770, 1044, 1209, 1357, 1431, 1489, 1547, 1589, 3060; ^1H NMR (300 MHz, $CDCl_3$) δ 3.91 (s, 3H), 7.00 (dd, J=2.4, 8.1 Hz, 1H), 7.38–7.84 (m, 7H), 7.68–7.74 (m, 3H), 7.80 (s, 1H), 7.89 (d, J=8.1 Hz, 1H), 8.24 (d, J=8.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.36, 112.63, 115.41, 119.37, 119.98, 125.58, 125.80, 126.31, 128.36, 128.54, 129.45, 129.52, 129.75, 130.10, 138.34, 141.09, 148.71, 149.07, 156.60, 160.10; EIMS (*m*/*z*, relative intensity): 311 (M^+, 75), 310 (100), 281 (35), 267 (7), 241 (3), 204 (9), 176 (3), 156 (7), 140 (6), 133 (8), 121 (5), 105 (2); HRMS calcd for $C_{22}H_{17}ON$: 311.1310; found: 311.1312.

*4.4.14. 2-(4-Bromophenyl)-4-phenylquinoline (**5j**)*

IR (film): 702, 772, 829, 1009, 1071, 1357, 1417, 1487, 1543, 1589; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44–7.76 (m, 10H), 7.89 (d, J=8.1 Hz, 1H), 8.07 (d, J=8.7 Hz, 2H), 8.21 (d, J=8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 118.80, 123.91, 125.65, 125.78, 126.53, 128.47, 128.60, 129.05, 129.49, 129.67, 130.04, 131.91, 138.17, 138.41, 148.71, 149.37, 155.49; EIMS (*m*/*z*, relative intensity): 361 (91), 359 (M^+, 100), 278 (27), 261 (23), 202 (14), 181 (5), 169 (37), 139 (20); HRMS calcd for $C_{21}H_{14}N^{79}Br$ 359.0310; found: 359.0302.

*4.4.15. 2-(4-Phenyphenyl)-4-phenylquinoline (**5l**)*

IR (film): 699, 721, 731, 769, 847, 1007, 1358, 1415, 1445, 1487, 1542, 1589; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.55 (m, 9H), 7.66–7.75 (m, 5H), 7.76–7.91 (m, 2H), 8.24–8.29 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 119.18, 125.62, 125.76, 126.30, 127.11, 127.50, 127.54, 127.93, 128.38, 128.57, 128.80, 129.53, 129.54, 130.09, 138.36, 138.45, 140.53, 142.02, 148.82, 149.11, 156.35; EIMS (*m*/*z*, relative intensity): 357 (M^+, 100), 280 (3), 202 (14), 178 (10), 170 (2); HRMS calcd for $C_{27}H_{19}N$: 357.1518; found: 357.1521.

*4.4.16. N-[3-(Naphthalen-1-yl)-1-phenylprop-2-ynyl]benzenamine (**4m**)*

IR (film): 696, 749, 774, 799, 1501, 1601, 3054, 3401; ^1H NMR (200 MHz, $CDCl_3$) δ 4.30 (br, 1H), 5.54 (s, 1H), 5.67–6.89 (m, 3H), 7.19–7.50 (m, 8H), 7.61–7.92 (m, 5H), 8.06–8.12 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 51.20, 83.40, 93.34, 114.66, 118.99, 120.42, 125.07, 126.18, 126.31, 126.75, 127.47, 128.16, 128.20, 128.76, 128.84, 129.22, 130.49, 133.10, 133.39, 139.56, 146.50; EIMS (*m*/*z*, relative intensity): 333 (M^+, 7), 241 (100), 149 (3), 77 (2); HRMS calcd for $C_{25}H_{19}N$: 333.1518; found: 333.1513.

*4.4.17. 4-(Naphthalen-1-yl)-2-phenylquinoline (**5m**)*

IR (film): 694, 731, 770, 804, 908, 1396, 1547, 1590, 3381; ^1H NMR (300 MHz, $CDCl_3$) δ 7.29–7.73 (m, 11H), 7.91–8.00 (m, 3H), 8.19–8.22 (m, 2H), 8.30 (d, J=8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 120.47, 125.27, 125.96, 126.12, 126.16, 126.34, 126.48, 127.00, 127.38, 127.62, 128.30, 128.76, 128.84, 129.43, 129.71, 129.87, 131.92, 133.47, 135.89, 139.36, 148.11, 148.35, 156.78; EIMS (*m*/*z*, relative intensity): 331 (M^+, 100), 252 (16), 226 (10), 164 (14); HRMS calcd for $C_{25}H_{17}N$: 331.1361; found: 331.1367.

*4.4.18. N-(1-Phenyl-5-(tetrahydro-2H-pyran-2-yloxy)-pent-2-ynyl)benzenamine (**4o**)*

IR (film): 697, 750, 1032, 1502, 1601, 2941; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.23–1.78 (m, 6H), 2.50 (dt, J=2.1, 7.2 Hz, 2H), 3.41–3.54 (m, 2H), 3.74–3.83 (m, 2H), 4.04 (s, 1H), 4.58 (dd, J=3, 6.6 Hz, 1H), 5.22 (s, 1H), 6.67 (m, 3H), 7.13–7.38 (m, 5H), 7.54–7.58 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.23, 20.28, 25.36, 30.45, 50.05, 61.96, 61.98, 65.60, 65.65, 80.21, 82.31, 98.58, 98.64, 113.82, 118.28, 127.15, 127.48, 127.83, 128.58, 128.73, 129.04, 140.13, 146.61; EIMS (*m/z*, relative intensity): 335 (M^+, 30), 263 (4), 250 (26), 232 (15), 219 (10), 206 (10), 187 (12), 171 (30), 141 (74); HRMS calcd for $C_{22}H_{25}O_2N$: 335.1885; found: 335.1881.

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