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Regioselective Synthesis of 3-Bromoquinoline Derivatives and Diastereoselective Synthesis of Tetrahydroquinolines via Acid-Promoted Rearrangement of Arylmethyl Azides

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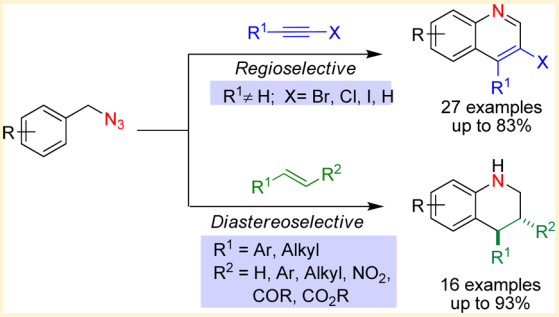
Supporting Information

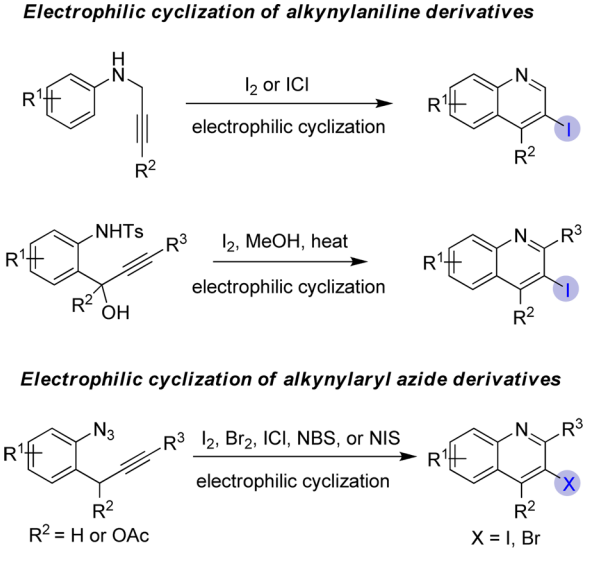
ABSTRACT: Regioselective synthesis of 3-bromoquinoline derivatives was achieved via a formal [4 + 2]-cycloaddition between *N*-arylimininium ion, generated from arylmethyl azides, and 1-bromoalkynes. This method could also be applied to other quinoline derivatives using appropriate alkynes. Moreover, the current strategy could be utilized for the diastereoselective synthesis of tetrahydroquinoline derivatives employing alkenyl substrates in good to excellent yields.



INTRODUCTION

Quinoline derivatives are one of the most prevalent core structures in bioactive compounds, both in natural products and synthetic compounds.[1] Nowadays, the investigation of biological activity of novel quinoline derivatives has continued to be of interest to many pharmaceutical companies. A number of quinoline derivatives have been clinically used as antifungal,[2] antibacterial,[3] antiprotozoal,[4] antimalarial,[5] as well as anticancer drugs.[6] A variety of synthetic methods have been reported for the preparation of quinoline derivatives.[7] Among these synthetic methods, aniline and *ortho*-functionalized aniline derivatives are well-established precursors which could react with several substrates to provide libraries of quinoline analogues. However, the structurally diverse quinoline compounds have been obtained by different synthetic approaches. There are limitations for each strategy, such as lengthy synthetic steps, difficulty in preparing starting materials and high reaction temperatures. Therefore, the development of a new synthetic method to enable the synthesis of diverse quinoline frameworks is still a challenging task. This included the development of a new synthetic method for preparing halogen-containing quinolines because the halogen atom could enhance the biological activity in many cases[8] and could also be used for further functionalization in preparing other complex molecules.[9] Several methods for the synthesis of haloquinoline have been revealed, including the direct halogenation which always suffers from poor regioselectivity and over halogenation,[10] but only few methods for the regioselective synthesis of 3-haloquinolines are known. A dependable method for preparing such quinoline system relies on the electrophilic cyclization of alkynylaniline[11] and alkynylaryl azide[12] derivatives (Scheme 1). However, the former methodology is well suited for the preparation of 3-iodoquinolines using electrophilic ICl and I_2, while electrophilic cyclization using molecular Br_2

Scheme 1. Previous Reported Methods



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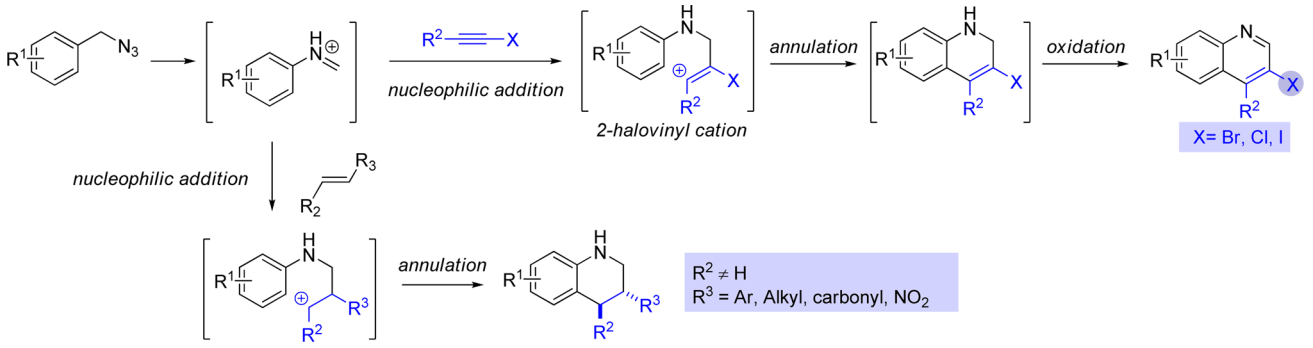
Scheme 2. Our Proposed Synthetic Methodology



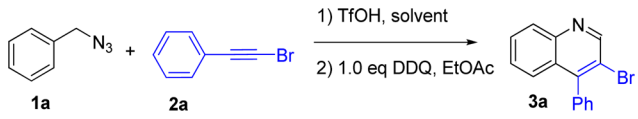
provided a complex mixture or low yields of the 3-bromoquinoline products.[11]

Recently, we presented the utility of benzylic azides in generating *N*-aryliminium ion[13] *in situ* under acidic conditions at ambient temperature. This iminium ion could be trapped by a variety of nucleophiles intermolecularly to furnish *N*-arylmethylarene, polycyclic alkaloid[14] and 2,4-unsubstitued quinoline compounds,[15] as well as intramolecularly to form phenanthridine compounds.[16] We found the reaction proceeded through a formal [4 + 2] cycloaddition by a stepwise process as demonstrated in our previous work. For example in the regioselective synthesis of quinoline-3-carboxylates, when ethyl-3-ethoxyacrylate was used as the nucleophile to trap with *N*-aryliminium ion intermediates, the reaction generated the oxocarbenium ion intermediate before further cyclization intramolecularly to give the products.[15] Therefore, we envision that haloacetylenes could serve as another class of two-atom component in a formal [4 + 2] cycloaddition with *N*-aryliminium ion intermediate to produce stable 2-halovinyl cation intermediates which would lead to the regioselective annulation to provide 3-haloquinoline as the final products. Moreover, we also aim to expand the scope of our methodology for the incorporation of other functional groups at 3-position such as a carbonyl moiety, an aryl and an alkyl group. Moreover, we have also applied our methodology for a diastereoselective synthesis of tetrahydroquinoline derivatives[17] as shown in Scheme 2.

RESULTS AND DISCUSSION

We initially investigated the synthesis of 3-bromoquinoline using benzyl azide (**1a**)[15] and bromophenyl acetylene (**2a**)[18] as the screening substrates. TfOH was employed to promote the rearrangement of benzyl azide in the first step, followed by the reaction with bromophenylacetylene to afford dihydroquinoline crude product which was then subjected to a well-established oxidizing conditions using 1.0 equiv of DDQ in EtOAc, in the second step. Several conditions have been investigated including equivalents of starting materials, TfOH, solvents, temperature and time as shown in Table 1. Using 1.0 equiv of **1a** and 1.2 equiv of **2a** could provide the desired product with excellent regioselectivity as anticipated in 58% yield, while the higher yield (68%) was obtained when 2.0 equiv of compound **2a** was employed (entry 2). Switching the numbers of equivalent between compounds **1a** and **2a** dramatically decreased the yield of the desired product (24%, entry 3). The effect of solvent was also investigated (entries 4−5) and DCE was found to be the most effective solvent. We next tried to perform the reaction at 0 °C for 1 h before allowing to stir at

Table 1. Optimization Conditions for the Synthesis of 3-Bromoquinoline Compound



entry	**1a** (equiv)	**2a** (equiv)	solvent	temp. (°C)	time (h)	yield (%)[a]
1	1.0	1.2	DCM	rt	18	58
2	1.0	2.0	DCM	rt	18	68
3	2.0	1.0	DCM	rt	18	24
4	1.0	2.0	DCE	rt	18	72
5	1.0	2.0	Toluene	rt	18	49
6[b]	1.0	2.0	DCE	0	18	69
7	1.0	2.0	DCE	rt	5	63
8	1.0	2.0	DCE, one pot	rt	18	63

[a]Isolated yield. [b]The reaction was carried out at 0 °C for 1 h before allowing to warm to room temperature for overnight.

room temperature for overnight. Unfortunately, the reaction gave a lower yield of the desired product (entry 6). Reducing the reaction time, the yield of the quinoline product could not be improved (entry 7). Moreover, we attempted the reaction in one-pot fashion by adding DDQ after the reaction was stirred for overnight. Unfortunately, we were unsuccessful in improving the yield of the corresponding product. On the basis of our results, we therefore adopted 1.0 equiv of arylmethyl azide, 2.0 equiv of haloacetylene and 1.2 equiv of TfOH in DCE in the first step and 1.0 equiv of DDQ in EtOAc in the second step as our optimal combination to further study the scope of the reaction.

With the optimal conditions in hand, we then applied these optimal conditions to a variety of arylmethyl azide substrates to verify the generality of the method (Table 2). The reactions proceeded readily when electronically neutral substrates, benzyl azide (**1a**) and *o*-tolylmethyl azide (**1b**), were employed to give the desired quinolines in 72% and 61% yields, respectively. 4-*tert*-Butylbenzyl azide (**1c**) could also provide the quinoline product **3c** in moderate yield (57%, entry 3). In the case of 2-naphthylmethyl azide (**1d**), the desired quinoline product was obtained in low yield (16%, entry 4), presumably because the steric hindrance of the 2-naphthyl iminium ion affected the annulation step thus providing a complex mixture instead. Arylmethyl azide with mildly electron-withdrawing group, *p*-phenyl substituent (**1e**) furnished the corresponding 3-bromoquinoline in good yield (75%, entry 5). Moreover, the effects of halogen-substituent of arylmethyl azides were explored (entries 6−14). The reaction of *o*-chloro- and *p*-

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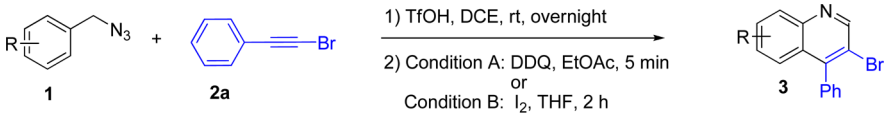
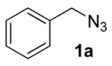
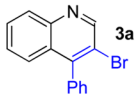
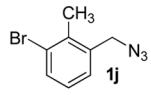
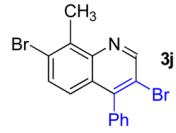
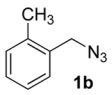
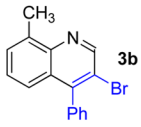
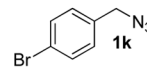
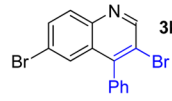
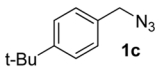
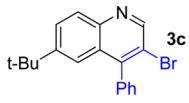
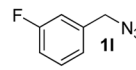
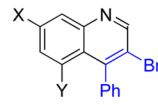
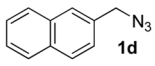
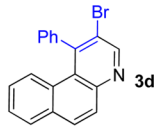
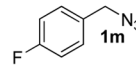
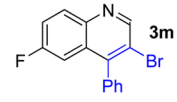
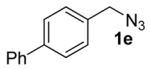
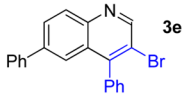
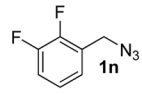
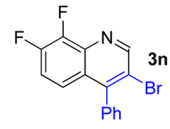
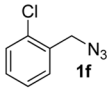
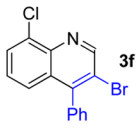
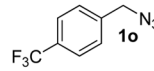
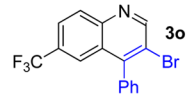
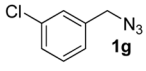
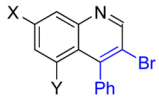
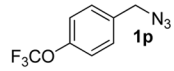
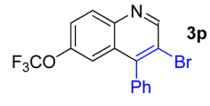
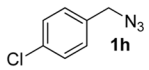
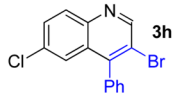
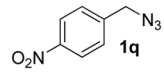
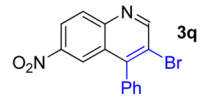
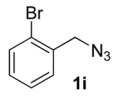
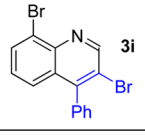
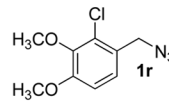
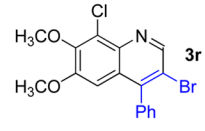
Table 2. Scope of Arylmethyl Azide Substrates



Entry	Substrate	Product	Yield (%)[a,b]	Entry	Substrate	Product	Yield (%)[a,b]
1	 1a	 3a	72	10	 1j	 3j	66
2	 1b	 3b	61	11	 1k	 3k	80
3	 1c	 3c	57 69[c]	12	 1l	 3l-1, X = F, Y= H: 13 3l-2, X = H, Y= F: 25	
4	 1d	 3d	16	13	 1m	 3m	61 76[c]
5	 1e	 3e	75 83[c]	14	 1n	 3n	36
6	 1f	 3f	65	15	 1o	 3o	40
7	 1g	 3g-1, X = Cl, Y= H: 13 3g-2, X = H, Y= Cl: 31		16	 1p	 3p	48
8	 1h	 3h	62	17	 1q	 3q	21 40[c]
9	 1i	 3i	74	18	 1r	 3r	- 26

[a]Isolated yield. [b]Condition A. [c]Condition B.

chlorophenylmethyl azides (entries 6 and 8) also proceeded well under these conditions and furnished the desired products in good yields (65% and 62%, respectively), whereas *m*-chlorophenylmethyl azide (entry 7) afforded the separable regioisomeric products (**3g-1** and **3g-2**) in lower combined yields (44%). These were presumably due to the inductive effect of the chlorine atom which decreased the nucleophilicity of the carbon atoms toward the cyclization. Surprisingly, compound **3g-2**, obtained via the cyclization at slightly more steric position, was obtained in higher yield than compound **3g-1**. The higher yields of the corresponding quinolines were obtained when various bromoarylmethyl azides (entries 9−11) were employed in this transformation. In addition, *m*-fluorophenylmethyl azide (**1l**) could provide the desired products **3l-1** and **3l-2** in 38% combined yields. Comparing to entry 7, the higher inductive effect of the fluorine atom could decrease the nucleophilicity of the aromatic nucleophile more than the chlorine atom, providing the quinoline products in lower yields (entry 12). *p*-Fluorophenylmethyl azide (**1m**) was capable of converting to the corresponding 3-bromoquinoline

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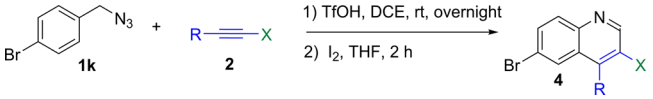
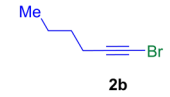
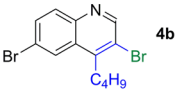
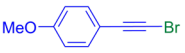
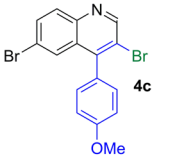
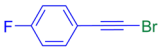
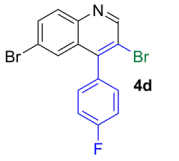
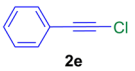
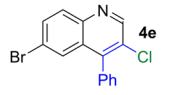
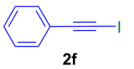
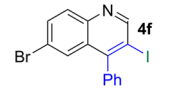
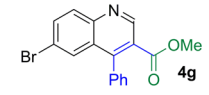
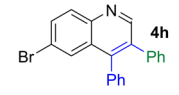
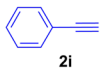
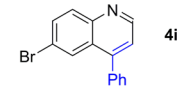
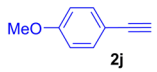
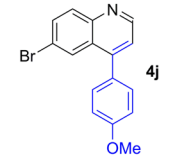
product in good yield (entry 13). However, the product yields dramatically dropped when increasing the electron-withdrawing effect of substituents on the arylmethyl azide substrates such as 2,3-difluoro, *p*-trifluoromethyl, *p*-trifluoromethoxy and *p*-nitro groups (entries 14−17). The unsuccessful results might possibly be caused by the difficulty of the electron-deficient aniline species to cyclize onto the vinyl carbocation intermediate, thus affording low yields of the quinoline products. In these cases, we observed the corresponding aniline derivatives as the results of hydrolysis of the iminium ions as well as complex mixtures of other unidentifiable products. In addition, the reaction of arylmethyl azide bearing electron-donating group 2-chloro-3,4-dimethoxybenzyl azide (**1r**) was also unsuccessful, leading to a complex mixture and no desired product was observed. Presumably, the arylmethyl azide substrates containing electron-donating groups, especially the methoxy group, provided the corresponding dihydroquinoline which may have undergone decomposition under the DDQ oxidation conditions. To avoid this decomposition, I_2-promoted oxidation[16] (condition B) was applied instead which could provide the desired product **3r** in 26% yield. These latter oxidation conditions could be applied to several prior cases (entries 3, 5, 13 and 17) to afford products in higher yields than DDQ oxidation while longer reaction time was needed.

Diverse alkynyl nucleophiles were next examined (Table 3) to probe the scope of the methodology in the preparation of various quinoline analogues. In these experiments, we selected *p*-bromobenzyl azide (**1k**) as the substrate for this purpose and used iodine oxidation to avoid the decomposition of some electron-rich intermediates. Various substituted bromoacetylene compounds were applied under these conditions (entries 1−3). 1-Bromo-1-hexyne (**2b**) provided the desired product in low yield (19%, entry 1). The higher yields were obtained when the substituent groups of bromoacetylenes could better stabilize the carbocation intermediates as demonstrated in entry 10 of Table 1 and entries 2 and 3 of Table 3. Bromoethynylanisole (**2c**) could give the more stable vinyl cation intermediate than bromoethynyl-4-fluoro-benzene (**2d**), thus providing the corresponding product in higher yields. Moreover, this method could be applied to synthesize 3-chloro- and 3-iodoquinolines by using chloro-[18] and iodophenylacetylene[19] as nucleophiles (entries 5−6), providing 3-chloroquinoline **4e** and 3-iodoquinoline **4f** in 55% and 46% yields, respectively. These results illustrated that the bulkiness of iodine atom may affect lower yield of the quinoline product. Besides the halophenylacetylenes, this method was also compatible with methyl-3-phenylpropiolate (**2g**) for preparing quinoline-3-carboxylate in good yield (entry 7). Diphenylacethylene was then applied to these conditions to give the desired quinoline in 42% yied. This method could also be used to conveniently prepare quinolines in moderate yields starting from arylmethyl azide and terminal alkynes such as phenylacetylene (**2i**, entry 8) and 4-ethynylanisole (**2j**, entry 9). Surprisingly, the electron rich alkyne **2j** provided the desired product in lower yield, presumably because it could not tolerate well under the reaction conditions, leading to the decomposition of the starting material. An additional advantage of using this method for the synthesis of quinolines is the obliteration of the use of toxic metal catalyst, thus providing metal-free final products.[11b]

Having established the strategy for the synthesis of quinoline compounds using arylmethyl azide and alkyne precursors, we continued to further expand the scope of this method for

Table 3. Scope of Alkyne Substrates



Entry	Substrate	Product	Yield (%)[a]
1			19
2			76
3			54
4			55
5			46
6			60
7			42
8			65
9			56

[a]Isolated yields.

preparing tetrahydroquinoline scaffolds. The synthesis also involved with nucleophilic addition to the iminium ion intermediates with alkenyl nucleophiles. We found the reaction required less amounts of the alkenes (1.2 equiv) in the reaction due to their higher stability than the alkynes under the reaction conditions. Moreover we also discovered that DCM could be used as the optimal solvent for this process. Initially, chalcone derivatives were first employed to evaluate the ability of our method (entries 1−5, Table 4). When the chalcone derivatives

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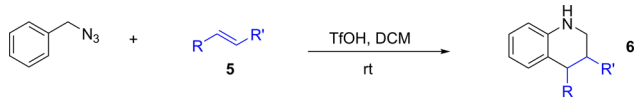
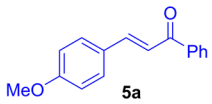
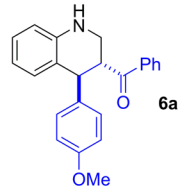
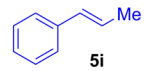
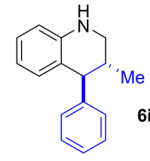
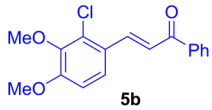
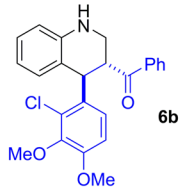
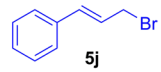
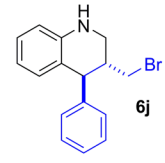
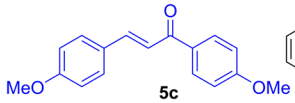
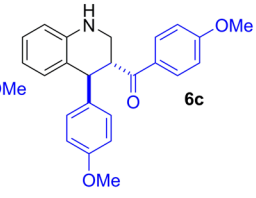
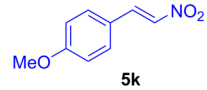
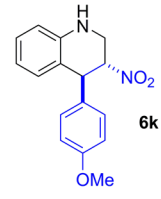
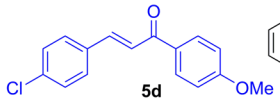
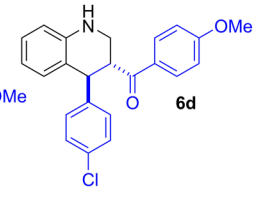
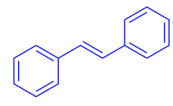
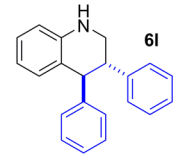
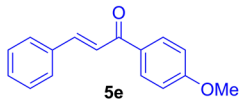
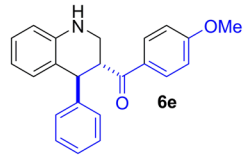
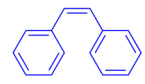
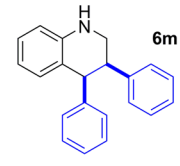
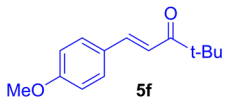
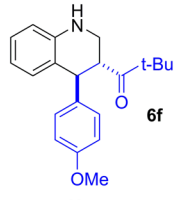
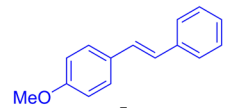
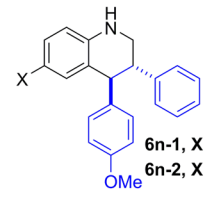
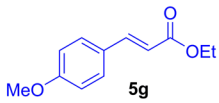
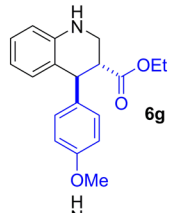
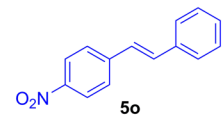
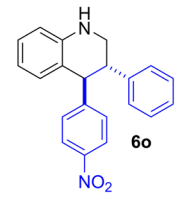
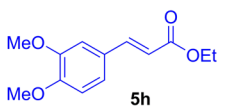
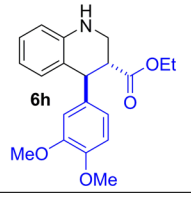
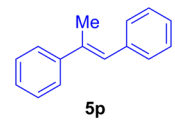
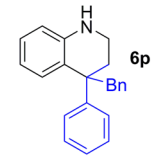
Table 4. Scope of Alkene Substrates



Entry	Substrate	Product	Yield (%)[a]	Entry	Substrate	Product	Yield (%)[a]
1	 **5a**	 **6a**	68	9	 **5i**	 **6i**	70
2	 **5b**	 **6b**	70	10	 **5j**	 **6j**	77
3	 **5c**	 **6c**	75	11	 **5k**	 **6k**	77
4	 **5d**	 **6d**	24	12	 **5l**	 **6l**	71
5	 **5e**	 **6e**	0	13	 **5m**	 **6m** (28%) + **6l** (28%)	
6	 **5f**	 **6f**	72	14	 **5n**	 **6n-1, X = H:** 93 **6n-2, X = Br:** 84[b]	
7	 **5g**	 **6g**	81	15	 **5o**	 **6o**	0
8	 **5h**	 **6h**	82	16	 **5p**	 **6p**	55

[a]Isolated yields. [b]Azide **2j** was employed.

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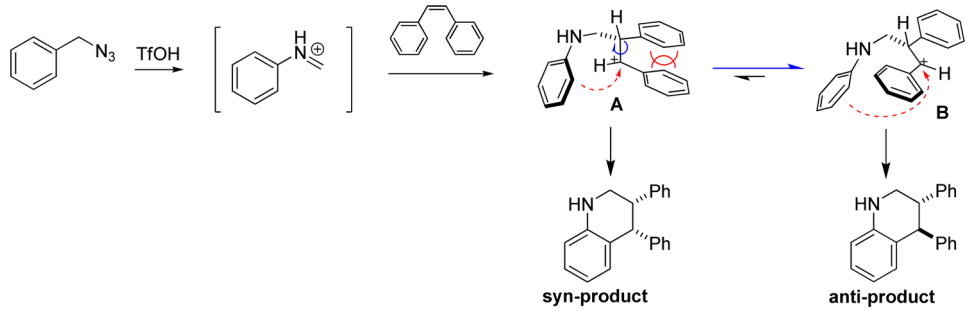
Scheme 3. Proposed Mechanism



containing electron donating groups on aromatic ring (**5a**–**5c**) were employed as the nucleophiles, all of tetrahydroquinoline products were obtained as single antidiastereomers in good yields (entries 1–3). Interestingly, chloro-substituted chalcone **5d** could provide tetrahydroquinoline **6d** in 24% yield, while chalcone **5e** failed to give the desired product **6e**, and starting material **5e** was recovered. These results indicated that chlorine atom could increase the nucleophilicity of the α,β-unsaturated ketone to facilitate the nucleophilic addition to the iminium ion intermediate. Moreover, both α,β-unsaturated ketone and ester were also applicable under these conditions to furnish the corresponding products in good yields (entries 6–8). Next, a series of styrene derivatives (entries 9–11) was also investigated using these conditions. The reaction of trans-methylstyrene **5i** provided the desired product **6i** in good yield with excellent regio- and diastereoselectivity. It is important to note that cinnamyl bromide **5j** could also tolerate under the employed conditions and offered tetrahydroquinoline **6j** in high yield as a single regioisomeric product. In addition, nitrostyrene **5k** was found to perform well under the reaction conditions, giving the corresponding product **6k** in good yield. In all alkenes, only anti-isomeric products were obtained. To further understand the stereochemical outcome including the reaction mechanism, both *trans*- and *cis*-stilbenes (**5l** and **5m**) were employed in this study. The reaction of *trans*-stilbene gave tetrahydroquinoline product **6l** as a single antidiastereomer in good yield, whereas *cis*-stilbene provided both *syn*- and *anti*-tetrahydroquinoline products (**6m** and **6l**, respectively) in 1:1 ratio in moderate combined yield (entries 12–13). These results indicated that the reaction mechanism involved with the formation of the benzylic carbocation intermediate. Therefore, the stability of carbocation intermediate played an important role in the stereochemical outcome of the desired product. In case of *trans*-stilbene (**5l**), the transient carbocation intermediate already attained the more stable conformation B which readily cyclized to give only the *anti*-isomeric product. However, in *cis*-stilbene (**5m**), the less stable conformer of carbocation intermediate (conformer A), initially formed and underwent the cyclization directly to form the syn-isomeric product, or underwent a bond rotation to give the more stable conformation of the carbocation intermediate (conformer B) which led to the anti-product as shown in Scheme 3.

In addition, the nucleophilic addition of unsymmetrical stilbene **5n** to the iminium ion intermediate generated from azide **1a** was also examined (entry 14) and was found to afford the desired quinoline **6n-1** as a single regioisomeric product. To determine the regioselectivity of the product, stilbene **5n** was reacted with *N*-aryliminium ion generated from azide **1j**, resulting in quinoline **6n-2** as a single regioisomeric product, which was subjected to an NOE difference experiment to confirm the regiochemical outcome. In using stilbene **5o**, containing the electron-deficient nitro group, the reaction failed to give the corresponding product with nearly 60% of compound **5o** recovered. Trisubstituted stilbene **5p** was subjected to the usual conditions to evaluate the steric effect of the stilbene substrate. The results showed that stilbene **5p** underwent the isomerization of the double bond before trapping with the iminium ion to provide the corresponding product in moderate yield.

CONCLUSIONS

In conclusion, we have successfully developed the regioselective synthesis of 3-haloquinoline compounds via a formal [4 + 2] cycloaddition of *N*-aryliminium ions, generated *in situ* from the benzylic azide rearrangement, and haloacetylene analogues. Besides 3-bromo-, 3-chloro-, and 3-iodoquinolines, this method could be used for the construction of 3-alkyl-, 3-aryl-, 3-carbonyl as well as 3-unsubstituted quinoline compounds starting from appropriate nucleophilic alkyne derivatives. Moreover, our method could be used to prepare tetrahydroquinolines with high regio- and diastereoselectivity using nucleophilic alkenes. The method is highlighted from the readily available starting materials and tolerance of a variety of substituents under reaction conditions. Moreover, the corresponding quinoline products could be obtained under metal-free conditions, constituting a green chemistry approach for the synthesis of quinoline derivatives in modest to high yields.

EXPERIMENTAL SECTION

General Procedure. The commercial grade chemicals were used without further purification, unless otherwise specified. All solvents used were purified by the solvent purification system. The oven-dried glassware (110 °C at least for 2 h) was used for all reactions. Crude reaction mixtures were concentrated under reduced pressure by removing organic solvent with the rotary evaporator. Column chromatography was performed using silica gel 60 (particle size 0.06–0.2 mm; 70–230 mesh ASTM). Analytical thin layer chromatography (TLC) was performed with silica gel 60 F_{254} aluminum sheets. The nuclear magnetic resonance (NMR) spectra were recorded in deuterochloroform ($CDCl_3$) with 300 and 600 MHz spectrometers. Chemical shifts for ^{1}H NMR and ^{13}C NMR spectra were reported in part per million (ppm, δ), relative to tetramethylsilane (TMS) as the internal reference. Coupling constants (J) were reported in hertz (Hz). Infrared spectra were measured using FT-IR spectrometer and were reported in cm^{-1}. High resolution mass spectra (HRMS) were obtained using time-of-flight (TOF).

General Procedure for the Synthesis of Quinolines (3a–3r, 4b–4j). The arylmethyl azides (1.0 equiv) were placed in a round bottle flask and added with dry dichloroethane (DCE, 0.14 mmol/mL) under argon. TfOH (1.0 equiv) was subsequently added into a solution and the mixture was stirred for 5 min at room temperature before haloacetylenes (2.0 equiv) were added. The reaction was stirred

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for overnight and was then quenched with saturated sodium bicarbonate ($NaHCO_3$). The reaction mixture was extracted with EtOAc, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. For oxidation, the crude products were oxidized by either one of the following methods.

Method A: The crude product was dissolved in EtOAc (0.08 mmol/mL) and added with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (2.5 equiv). The reaction mixture was stirred for 5 min and concentrated to give a crude product which was purified by silica gel column chromatography using hexane to 4:1 hexane/EtOAc.

Method B: The crude product was dissolved in THF (0.08 mmol/mL) and added with I_2 (2.5 equiv) The reaction mixture was stirred at room temperature for 2 h and quenched with saturated $Na_2S_2O_3$. The mixture was extracted with EtOAc, dried over Na_2SO_4, concentrated and purified with silica gel column chromatography using hexane to 4:1 hexane/EtOAc to give the desired product.

*3-Bromo-4-phenylquinoline (**3a**).* Yield 84.3 mg (72%, yellow solid); mp 99−101 °C. IR (neat): ν_{max} 1569, 1489, 1102, 763, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.13 (d, 1H, J = 8.4 Hz), 7.71 (t, 1H, J = 7.2 Hz), 7.53−7.42 (m, 5H), 7.33−7.26 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.0, 147.6, 146.8, 136.7, 129.6, 129.4, 129.3, 128.8, 128.6, 128.5, 127.5, 126.3, 118.4; HRMS (ESI-TOF) calcd for $C_{15}H_{11}BrN$ (Br-79) (M + H^+) 284.0069, found 284.0063.

*3-Bromo-8-methyl-4-phenylquinoline (**3b**).* Yield 72.7 mg (61%, yellow solid); mp 72−74 °C. IR (neat): ν_{max} 3058, 2921, 2339, 1483, 1142, 761, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.07 (s, 1H), 7.58−7.51 (m, 4H), 7.34−7.29 (m, 4H), 2.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.6, 147.6, 145.9, 137.4, 137.2, 129.6, 129.3, 128.9, 128.4, 127.2, 124.4, 118.5, 18.2; HRMS (ESI-TOF) calcd for $C_{16}H_{13}BrN$ (Br-79) (M + H^+) 298.0226, found 298.0228.

*3-Bromo-6-(tert-butyl)-4-phenylquinoline (**3c**).* Condition A: Yield 102.2 mg (57%). Condition B: Yield 154.6 mg (69%, yellow solid); mp 101−102 °C. IR (neat): ν_{max} 3058, 2963, 2319, 1493, 1109, 701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.07 (d, 1H, J = 9 Hz), 7.81 (dd, 1H, J = 8.7, 2.1 Hz), 7.59−7.49 (m, 3H), 7.41 (d, 1H, J = 2.1 Hz), 7.33 (dd, 2H, J = 7.8, 1.5 Hz), 1.26 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.2, 150.5, 147.5, 145.3, 136.8, 129.3, 129.0, 128.6, 128.44, 128.35, 121.2, 118.4, 35.0, 31.0; HRMS (ESI-TOF) calcd for $C_{19}H_{19}BrN$ (Br-79) (M + H^+) 340.0695, found 340.0683.

*2-Bromo-1-phenylbenzo[f]quinoline (**3d**).* Yield 25.4 mg (16%, yellow solid); mp 176−178 °C. IR (neat): ν_{max} 3046, 2370, 1953, 1484, 1440, 1122, 834, 754 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.00 (app s, 2H), 7.87 (dd, 1H, J = 8.1, 1.2 Hz), 7.62−7.57 (m, 3H), 7.50−7.45 (m, 1H), 7.40 (d, 1H, J = 8.7 Hz), 7.33−7.26 (m, 2H), 7.14 (ddd, 1H, J = 8.4, 6.9, 1.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.8, 148.3, 147.4, 141.3, 133.3, 131.9, 129.6, 129.5, 128.8, 128.6, 128.6, 128.3, 128.1, 127.1, 126.1, 125.8, 121.7; HRMS (ESI-TOF) calcd for $C_{19}H_{13}BrN$ (Br-79) (M + H^+) 334.0226, found 334.0223.

*3-Bromo-4,6-diphenylquinoline (**3e**).* Condition A: Yield 138.9 mg (75%). Condition B: Yield 159.7 mg (83%, yellow solid); mp 145−146 °C. IR (neat): ν_{max} 3357, 2922, 1954, 1485, 1104, 761, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.22 (d, 1H, J = 9 Hz), 7.98 (dd, 1H, J = 9, 3 Hz), 7.66 (s, 1H), 7.61−7.51 (m, 5H), 7.45−7.33 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.7, 147.9, 146.1, 140.4, 140.1, 136.6, 129.9, 129.3, 129.0, 128.9, 128.7, 128.6, 127.9, 127.4, 124.0, 118.9; HRMS (ESI-TOF) calcd for $C_{21}H_{15}BrN$ (Br-79) (M + H^+) 360.0382, found 360.0386.

*3-Bromo-8-chloro-4-phenylquinoline (**3f**).* Yield 85.6 mg (65%, yellow solid); mp 140−146 °C. IR (neat): ν_{max} 3061, 3023, 1682, 1478, 1116, 757 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.17 (s, 1H), 7.84 (dd, 1H, J = 6.9, 1.5 Hz), 7.57−7.55 (m, 3H), 7.45−7.26 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.4, 148.1, 143.1, 136.3, 133.7, 130.1, 129.6, 129.1, 128.8, 128.6, 127.3, 125.5, 119.6; HRMS (ESI-TOF) calcd for $C_{15}H_{10}BrClN$ (Br-79) (Cl-35) (M + H^+) 317.9680, found 317.9686.

*3-Bromo-7-chloro-4-phenylquinoline (**3g-1**).* Yield 33.2 mg (13%, white solid); mp 80−81 °C. IR (neat): ν_{max} 1598, 1478, 1070, 888 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 9.06 (s, 1H), 8.14 (d, 1H, J = 1.2 Hz), 7.58−7.53 (m, 3H), 7.44 (d, 1H, J = 9.0 Hz), 7.40 (dd, 1H, J = 8.4, 1.8 Hz), 7.31−7.30 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.0, 147.9, 147.2, 136.3, 135.6, 129.2, 128.9, 128.7, 128.6, 28.5, 127.7, 127.3, 118.7; HRMS (ESI-TOF) calcd for $C_{15}H_{10}BrClN$ (Br-79) (Cl-35) (M + H^+) 317.9680, found 317.9672.

*3-Bromo-5-chloro-4-phenylquinoline (**3g-2**).* Yield 79.9 mg (31%, yellow solid); mp 78−79 °C. IR (neat): ν_{max} 1601, 1480, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.06 (s, 1H), 8.10 (dd, 1H, J = 7.8, 1.8 Hz), 7.63−7.54 (m, 2H), 7.48−7.45 (m, 3H), 7.24−7.21 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.2, 148.5, 146.7, 139.5, 130.8, 130.5, 129.9, 129.1, 129.0, 128.3, 128.0, 125.9, 122.3; HRMS (ESI-TOF) calcd for $C_{15}H_{10}BrClN$ (Br-79) (Cl-35) (M + H^+) 317.9680, found 317.9677.

*3-Bromo-6-chloro-4-phenylquinoline (**3h**).* Yield 135.8 mg (62%, yellow solid); mp 156−157 °C. IR (neat): ν_{max} 3048, 2319, 1603, 1483, 1105, 826, 704 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.06 (d, 1H, J = 9 Hz), 7.66−7.56 (m, 4H), 7.45 (s, 1H), 7.31−7.26 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.2, 146.9, 145.3, 136.0, 133.6, 131.2, 130.4, 129.5, 129.2, 129.0, 128.8, 125.1, 119.6; HRMS (ESI-TOF) calcd for $C_{15}H_{10}BrClN$ (Br-79) (Cl-35) (M + H^+) 317.9680, found 317.9678.

*3,8-Dibromo-4-phenylquinoline (**3i**).* Yield 67.5 mg (74%, yellow solid); mp 122−123 °C. IR (neat): ν_{max} 2922, 2852, 1475, 1113, 982, 755, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.16 (s, 1H), 8.05 (dd, 1H, J = 7.5, 1.2 Hz), 7.60−7.45 (m, 5H), 7.32−7.26 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.7, 148.1, 144.0, 136.4, 133.2, 130.1, 129.2, 128.8, 128.6, 127.8, 126.3, 124.9, 119.7; HRMS (ESI-TOF) calcd for $C_{15}H_{10}Br_2N$ (Br-79) (M + H^+) 361.9175, found 361.9181.

*3,7-Dibromo-8-methyl-4-phenylquinoline (**3j**).* Yield 116.8 mg (66%, yellow solid); mp 113−114 °C. IR (neat): ν_{max} 2922, 1268, 1126, 901, 762, 706 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.04 (s, 1H), 7.57−7.51 (m, 4H), 7.30−7.25 (m, 2H), 7.18 (d, 1H, J = 9.0 Hz), 2.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.4, 147.7, 146.2, 137.3, 136.6, 131.5, 129.2, 128.7, 128.5, 127.8, 125.9, 124.8, 118.7, 17.8; HRMS (ESI-TOF) calcd for $C_{16}H_{12}Br_2N$ (Br-79) (M + H^+) 375.9331, found 375.9318.

*3,6-Dibromo-4-phenylquinoline (**3k**).* Yield 102.0 mg (80%, yellow solid); mp 160−161 °C. IR (neat): ν_{max} 3049, 2324, 1599, 1480, 1103, 824, 704 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.05 (s, 1H), 7.99 (d, 1H, J = 8.7 Hz), 7.78 (dd, 1H, J = 9, 2.1 Hz), 7.63−7.52 (m, 4H), 7.34−7.26 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.4, 146.8, 145.5, 136.0, 133.0, 131.3, 130.0, 129.2, 129.0, 128.8, 128.3, 121.9, 119.6; HRMS (ESI-TOF) calcd for $C_{15}H_{10}Br_2N$ (Br-79) (M + H^+) 361.9175, found 361.9180.

*3-Bromo-7-fluoro-4-phenylquinoline (**3l-1**).* Yield 33.2 mg (13%, yellow solid); mp 100−101 °C. IR (neat): ν_{max} 1621, 1485, 1191, 761 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.05 (s, 1H), 7.76 (dd, 1H, J = 9.7, 2.5 Hz), 7.60−7.48 (m, 4H), 7.35−7.29 (m, 2H), 7.27−7.20 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.9 (d, J_{CF} = 250 Hz), 153.1, 147.88 (d, J_{CF} = 12 Hz), 147.87, 136.5, 129.2, 128.8, 128.7 (d, J_{CF} = 9 Hz), 128.6, 125.94 (d, J_{CF} = 3 Hz), 125.87, 117.9 (d, J_{CF} = 25 Hz), 113.2 (d, J_{CF} = 20 Hz); HRMS (ESI-TOF) calcd for $C_{15}H_{10}BrFN$ (Br-79) (M + H^+) 301.9975, found 301.9975.

*3-Bromo-5-fluoro-4-phenylquinoline (**3l-2**).* Yield 62.8 mg (25%, yellow solid); mp 75−76 °C. IR (neat): ν_{max} 1623, 1567, 1460, 756 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.00 (d, 1H, J = 8.4 Hz), 7.68 (ddd, 1H, J = 8.0, 8.0, 5.4 Hz), 7.54−7.51 (m, 3H), 7.31−7.26 (m, 2H), 7.16 (ddd, 1H, J = 11.9, 7.8, 1.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.5 (d, J_{CF} = 258 Hz), 152.7 (d, J_{CF} = 1 Hz), 148.2, 144.6 (d, J_{CF} = 5 Hz), 139.2 (d, J_{CF} = 3 Hz), 129.3 (d, J_{CF} = 9 Hz), 128.1, 128.0, 127.9 (d, J_{CF} = 3 Hz), 126.0 (d, J_{CF} = 4 Hz), 120.7, 119.1 (d, J_{CF} = 9 Hz), 112.8 (d, J_{CF} = 22 Hz); HRMS (ESI-TOF) calcd for $C_{15}H_{10}BrFN$ (Br-79) (M + H^+) 301.9975, found 301.9981.

*3-Bromo-6-fluoro-4-phenylquinoline (**3m**).* Condition A: Yield 182.8 mg (61%). Condition B: Yield 154.9 mg (76%, yellow solid); mp 65−66 °C. IR (neat): ν_{max} 3058, 1622, 1490, 1192, 831, 736, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.01 (s, 1H), 8.16−8.11 (m, 1H), 7.59−7.53 (m, 3H), 7.51−7.44 (m, 1H), 7.32−7.30 (m, 2H), 7.10 (dd, 1H, J = 9.9, 2.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0 (d, J_{CF} = 248 Hz), 151.1 (d, J_{CF} = 3 Hz), 147.3 (d, J_{CF} = 5 Hz), 143.8,

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136.2, 132.0 (d, J_{CF} = 9 Hz), 129.7 (d, J_{CF} = 10 Hz), 129.1, 128.9, 128.7, 119.7 (d, J_{CF} = 26 Hz), 119.4, 109.8 (d, J_{CF} = 24 Hz); HRMS (ESI-TOF) calcd for $C_{15}H_{10}BrFN$ (Br-79) (M + H^+) 301.9975, found 301.9983.

*3-Bromo-7,8-difluoro-4-phenylquinoline (**3n**).* Yield 78.0 mg (36%, white solid); mp 142−143 °C. IR (neat): ν_{max} 2927, 1634, 1475, 1386, 1288, 822 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.10 (s, 1H), 7.59−7.55 (m, 3H), 7.37−7.24 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.2, 149.2 (dd, J_{CF} = 250, 11 Hz), 147.8 (t, J_{CF} = 8 Hz), 144.7 (dd, J_{CF} = 256, 12 Hz), 138.3 (dd, J_{CF} = 9, 4 Hz), 135.9, 129.1, 129.0, 128.7, 126.5, 122.2 (dd, J_{CF} = 8, 6 Hz), 119.0 (d, J_{CF} = 3 Hz), 118.2 (d, J_{CF} = 21 Hz); HRMS calcd for $C_{15}H_9BrF_2N$ (Br-79) (M + H^+) 319.9881, found 319.9872.

*3-Bromo-4-phenyl-6-(trifluoromethyl)quinolone (**3o**).* Yield 108.5 mg (40%, white solid); mp 107−108 °C. IR (neat): ν_{max} 1308, 1126, 1065, 835 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.16 (s, 1H), 8.25 (d, 1H, J = 8.7 Hz), 7.89 (dd, 1H, J = 9.0, 2.1 Hz), 7.80 (d, 1H, J = 0.6 Hz), 7.61−7.57 (m, 3H), 7.34−7.31 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.1, 148.6, 147.8, 135.7, 130.9, 129.4 (q, J_{CF} = 33 Hz), 129.22, 129.18, 128.9, 128.0, 125.2 (q, J_{CF} = 3 Hz), 124.2 (q, J_{CF} = 4 Hz), 123.7 (q, J_{CF} = 271 Hz), 119.9; HRMS (ESI-TOF) calcd for $C_{16}H_{10}BrF_3N$ (Br-79) (M + H^+) 351.9943, found 351.9944.

*3-Bromo-4-phenyl-6-(trifluoromethoxy)quinolone (**3p**).* Yield 97.0 mg (48%, yellow solid); mp 168−169 °C. IR (neat): ν_{max} 2927, 1490, 1249, 1216, 1165, 1098, 833, 759, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.07 (s, 1H), 8.17 (d, 1H, J = 9.3 Hz), 7.60−7.56 (m, 4H), 7.33−7.31 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.5, 147.7 (q, J_{CF} = 1.8 Hz), 147.5, 145.1, 135.9, 131.9, 129.2, 129.1, 129.0, 128.8, 123.3, 120.4 (q, J_{CF} = 257 Hz), 119.7, 116.8; HRMS (ESI-TOF) calcd for $C_{16}H_{10}BrF_3NO$ (Br-79) (M + H^+) 367.9892, found 367.9895.

*3-Bromo-6-nitro-4-phenylquinoline (**3q**).* Condition A: Yield 32.7 mg (21%). Condition B: Yield 80.0 mg (40%, yellow solid); mp 159−160 °C. IR (neat): ν_{max} 3357, 2922, 2853, 1529, 1347, 744 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.21 (s, 1H), 8.49−8.44 (m, 2H), 8.27 (d, 1H, J = 9.0 Hz), 7.64−7.60 (m, 3H), 7.36−7.33 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.4, 149.5, 148.8, 146.2, 135.1, 131.6, 129.5, 129.1, 129.0, 127.9, 123.1, 122.9, 120.6; HRMS (ESI-TOF) calcd for $C_{15}H_{10}BrN_2O_2$ (Br-79) (M + H^+) 328.9920, found 328.9898.

*3-Bromo-8-chloro-6,7-dimethoxy-4-phenylquinoline (**3r**).* Yield 75.9 mg (36%, yellow solid); mp 163−164 °C. IR (neat): ν_{max} 3352, 2920, 2334, 1481, 1042, 707 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.01 (s, 1H), 7.60−7.50 (m, 3H), 7.32−7.27 (m, 2H), 6.68 (s, 1H), 4.00 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.4, 150.1, 149.0, 146.4, 140.0, 136.7, 129.0, 128.8, 128.7, 126.8, 126.2, 118.9, 103.4, 60.9, 55.8; HRMS (ESI-TOF) calcd for $C_{17}H_{14}BrClNO_2$ (Br-79) (Cl-35) (M + H^+) 377.9891, found 377.9884.

*3,6-Dibromo-4-butylquinoline (**4b**).* Yield 35.1 mg (19%, dark brown liquid); IR (neat): ν_{max} 2957, 2927, 2859, 1726, 1487, 1073, 827 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.15 (d, 1H, J = 2.1 Hz), 7.94 (d, 1H, J = 9.0 Hz), 7.77 (dd, 1H, J = 8.7, 2.1 Hz), 3.17 (t, 2H, J = 8.0 Hz), 1.70−1.51 (m, 4H), 1.02 (t, 3H, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.5, 146.5, 145.6, 132.6, 132.0, 129.5, 126.2, 121.7, 120.5, 31.6, 31.2, 23.0, 13.8; HRMS (ESI-TOF) calcd for $C_{13}H_{14}Br_2N$ (Br-79) (M + H^+) 341.9488, found 341.9504.

*3,6-Dibromo-4-(4-methoxyphenyl)quinoline (**4c**).* Yield 156.1 mg (76%, yellow solid); mp 113−114 °C. IR (neat): ν_{max} 1610, 1513, 1481, 1248 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.02 (s, 1H), 7.97 (d, 1H, J = 9.0 Hz), 7.76 (dd, 1H, J = 8.7, 2.1 Hz), 7.69 (d, 1H, J = 2.1 Hz), 7.26−7.22 (m, 2H), 7.11−7.07 (m, 2H), 3.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.9, 152.4, 146.6, 145.5, 132.9, 131.3, 130.6, 130.2, 128.5, 128.1, 121.8, 120.0, 114.2, 55.3; HRMS (ESI-TOF) calcd for $C_{16}H_{12}Br_2NO$ (Br-79) (M + H^+) 391.9280, found 391.9292.

*3,6-Dibromo-4-(4-fluorophenyl)quinoline (**4d**).* Yield 116.6 mg (54%, yellow solid); mp 178−179 °C. IR (neat): ν_{max} 3073, 1603, 1508, 1481, 1222, 840, 826 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.00 (d, 1H, J = 9.0 Hz), 7.79 (dd, 1H, J = 9.0, 2.1 Hz), 7.61 (d, 1H, J = 2.4 Hz), 7.33−7.25 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.9 (d, J_{CF} = 248 Hz), 152.3, 145.7, 145.4, 133.0, 131.8 (d, J_{CF} = 4 Hz), 131.4, 131.1(d, J_{CF} = 8 Hz), 129.8, 128.0, 122.0, 119.7, 116.0 (d, J_{CF} = 22 Hz); HRMS (ESI-TOF) calcd for $C_{15}H_9Br_2FN$ (Br-79) (M + H^+) 379.9080, found 379.9097.

*6-Bromo-3-chloro-4-phenylquinoline (**4e**).* Yield 107.9 mg (55%, yellow solid); mp 106−107 °C. IR (neat): ν_{max} 3058, 2929, 1726, 1482, 1112, 828, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.00 (d, 1H, J = 9.0 Hz), 7.77 (dd, 1H, J = 8.7, 2.1 Hz), 7.65 (d, 1H, J = 2.1 Hz), 7.60−7.54 (m, 3H), 7.35−7.32 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.4, 145.2, 144.3, 134.0, 132.8, 131.3, 129.4, 129.0, 128.8, 128.3, 128.1, 121.9; HRMS (ESI-TOF) calcd for $C_{15}H_{10}BrClN$ (Br-79) (Cl-35) (M + H)$^+$ 317.9680, found 317.9681.

*6-Bromo-3-iodo-4-phenylquinoline (**4f**).* Yield 100.0 mg (46%, yellow solid); mp 183−184 °C. IR (neat): ν_{max} 2923, 1732, 1481, 1068, 966, 703 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.25 (s, 1H), 7.99 (d, 1H, J = 9.0 Hz), 7.79 (dd, 1H, J = 9.0, 2.4 Hz), 7.62−7.56 (m, 4H), 7.28−7.25 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.0, 151.4, 145.7, 139.6, 133.2, 131.2, 129.8, 129.0, 128.9, 128.8, 128.7, 121.6, 97.5; HRMS (ESI-TOF) calcd for $C_{15}H_{10}BrIN$ (M + H) $^+$ (Br-79) 409.9036, found 409.9049.

*Methyl 6-Bromo-4-phenylquinoline-3-carboxylate (**4g**).* Yield 118.1 mg (60%, yellow solid); mp 170−172 °C. IR (neat): ν_{max} 3750, 3057, 1729, 1220, 1125, 759 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.32 (s, 1H), 8.05 (d, 1H, J = 9.0 Hz), 7.85 (dd, 1H, J = 9.0, 2.1 Hz), 7.73 (d, 1H, J = 2.1 Hz), 7.54−7.52 (m, 3H), 7.30−7.26 (m, 2H), 3.68 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.45, 150.2, 149.1, 147.8, 135.5, 134.5, 131.3, 129.5, 128.7, 128.6, 128.5, 128.3, 123.7, 121.7, 52.3; HRMS (ESI-TOF) calcd for $C_{17}H_{13}BrNO_2$ (M + H) $^+$ (Br-79) 342.0124, found 342.0128.

*6-Bromo-3,4-diphenylquinoline (**4h**).* Yield 100.9 mg (42%, yellow solid); mp 220−221 °C. IR (neat): ν_{max} 3058, 2370, 1893, 1481, 1063, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.05 (d, 1H, J = 8.4 Hz), 7.80 (d, 2H, J = 15.3 Hz), 7.36−7.16 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.2, 146.1, 144.6, 137.6, 135.5, 133.9, 132.6, 131.3, 130.4, 130.0, 128.6, 128.5, 128.4, 128.1, 128.0, 127.3, 121.1; HRMS (ESI-TOF) calcd for $C_{21}H_{15}BrN$ (M + H^+) (Br-79) 360.0382, found 360.0392.

*6-Bromo-4-phenylquinoline (**4i**).* Yield 88.8 mg (65%, brown solid); mp 76−77 °C. IR (neat): ν_{max} 3057, 1919, 1583, 1486, 1350, 845, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.93 (d, 1H, J = 4.5 Hz), 8.05 (d, 1H, J = 2.1 Hz), 8.03 (s, 1H), 7.78 (dd, 1H, J = 9.0, 2.1 Hz), 7.58−7.45 (m, 5H), 7.34 (d, 1H, J = 4.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.2, 147.7, 147.2, 137.2, 132.8, 131.6, 129.4, 128.8, 128.7, 127.94, 127.92, 122.0, 120.8; HRMS (ESI-TOF) calcd for $C_{15}H_{11}BrN$ (M + H) $^+$ (Br-79) 284.0069, found 284.0057.

*6-Bromo-4-(4-methoxyphenyl)quinoline (**4j**).* Yield 79.0 mg (56%, yellow solid); mp 110−113 °C. IR (neat): ν_{max} 2957, 1731, 1609, 1489, 1248, 830 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.90 (d, 1H, J = 4.5 Hz), 8.09 (d, 1H, J = 2.4 Hz), 8.02 (d, 1H, J = 9.0 Hz), 7.76 (dd, 1H, J = 9.0, 2.4 Hz), 7.43- 7.40 (m, 2H), 7.31 (d, 1H, J = 4.5 Hz), 7.08−7.05 (m, 2H), 3.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.0, 150.2, 147.3, 147.2, 132.6, 131.5, 130.6, 129.4, 128.1, 128.0, 121.9, 120.7, 114.2, 55.3; HRMS (ESI-TOF) calcd for $C_{16}H_{13}BrNO$ (M + H) $^+$ (Br-79) 314.0175, found 314.0180.

General Procedure for the Synthesis of Quinolines (6a−6d, 6f−6p). The arylmethyl azides (1.0 equiv) were placed in a round bottle flask and added with dry dichloroethane (DCM, 0.14 mmol/mL) under argon. TfOH (1.2 equiv) was subsequently added into a solution and the mixture was stirred for 5 min at room temperature before alkene substrates (1.2 equiv) were added. The reaction was stirred for overnight and was then quenched with saturated sodium bicarbonate ($NaHCO_3$). The reaction mixture was extracted with EtOAc, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude products were purified by silica gel column chromatography.

*(4-(4-Methoxyphenyl)-1,2,3,4-tetrahydroquinolin-3-yl)(phenyl)-methanone (**6a**).* Yield 113 mg (68%, light yellow solid); mp 157−158 °C; IR (neat): ν_{max} 3399, 3053, 2933, 2835, 1676, 1607, 1508, 1241, 1177, 1033, 829, 750, 701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.78−7.75 (m, 2H), 7.51−7.45 (m, 1H), 7.38−7.33 (m, 2H), 7.12−7.07 (m, 2H), 7.01 (td, 1H, J = 7.8, 0.9 Hz), 6.76−6.72 (m, 3H), 6.62−6.57 (m, 2H), 4.57 (d, 1H, J = 9.3 Hz), 4.08−4.00 (m, 2H),

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3.71(s, 3H), 3.48−3.40 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.2, 158.2, 144.0, 136.7, 136.6, 133.3, 130.4, 130.1, 128.5, 128.1, 127.0, 124.6, 117.9, 114.4, 113.8, 55.2, 48.8, 45.0, 44.3; HRMS (ESI-TOF) calcd for $C_{23}H_{22}NO_2$ $(M + H)^+$ 344.1645, found 344.1643.

(4-(2-Chloro-3,4-dimethoxyphenyl)-1,2,3,4-tetrahydroquinolin-3-yl)(phenyl)methanone ***(6b)***. Yield 140 mg (70%, yellow solid); mp 72−73 °C; IR (neat): ν_{max} 3397, 2939, 2830, 1681, 1487, 1271, 1039, 750 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (dd, 2H, J = 7.2, 1.2 Hz), 7.50−7.46 (m, 1H), 7.38−7.33 (m, 2H), 6.99 (td, 1H, J = 8.1, 0.9 Hz), 6.75−6.53 (m, 5H), 3.94 (d, 1H, J = 4.2 Hz), 4.14−3.98 (m, 1H), 3.80 (s, 3H), 3.77 (s, 3H), 3.48−3.37 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.6, 152.1, 143.9, 136.3, 132.8, 129.9, 128.4, 128.2, 128.1, 127.0, 126.2, 122.6, 118.0, 114.4, 110.3, 60.4, 55.9, 45.9, 42.7; HRMS (ESI-TOF) calcd for $C_{24}H_{22}ClNNaO_3$ $(M + Na)^+$ (Cl-35) 430.1180, found 430.1187.

(4-Methoxyphenyl)(4-(4-methoxyphenyl)-1,2,3,4-tetrahydroquinolin-3-yl)methanone ***(6c)***. Yield 129 mg (75%, light yellow solid), mp 139−140 °C; IR (neat): ν_{max} 3394, 2837, 1664, 1598, 1508, 1252, 1168, 1029, 828, 749 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80−7.75 (m, 2H), 7.12−7.07 (m, 2H), 7.03−6.98 (m, 1H), 6.85−6.80 (m, 2H), 6.76−6.70 (m, 3H), 6.61−6.56 (m, 2H), 4.55 (d, 1H, J = 9.3 Hz), 4.08−3.97 (m, 2H), 3.81 (s, 3H), 3.71 (s, 3H), 3.44 (d, 2H, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.5, 163.4, 158.1, 144.0, 136.2, 130.4, 130.3, 130.0, 129.6, 126.9, 124.8, 117.7, 114.3, 113.7, 113.6, 55.3, 55.0, 48.2, 45.1, 44.5; HRMS (ESI-TOF) calcd for $C_{24}H_{23}NNaO_3$ $(M + Na)^+$ 396.1570, found 396.1573.

(4-(4-Chlorophenyl)-1,2,3,4-tetrahydroquinolin-3-yl)(4-methoxyphenyl)methanone ***(6d)***. Yield 43 mg (24%, yellow oil); IR (neat): ν_{max} 3393, 2935, 2839, 1165, 1599, 1489, 1259, 1169, 750 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 7.79−7.75 (m, 2H), 7.18−7.10 (m, 5H), 7.04−6.99 (m, 1H), 6.86−6.81 (m, 2H), 6.66−6.56 (m, 3H), 4.60 (d, 1H, J = 9.6 Hz) 3.99 (d, 1H, J = 9.3, 4.2 Hz), 3.81 (s, 3H), 3.48−3.36 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.0, 163.6, 144.0, 142.8, 132.2, 130.5, 130.4, 130.3, 129.3, 128.5, 127.2, 124.0, 117.9, 114.5, 113.8, 55.4, 48.2, 45.2, 44.6; HRMS (ESI-TOF) calcd for $C_{23}H_{20}ClNNaO_2$ $(M + Na)^+$ (Cl-35) 400.1075, found 400.1076.

1-(4-(4-Methoxyphenyl)-1,2,3,4-tetrahydroquinolin-3-yl)-2,2-dimethylpropan-1-one ***(6f)***. Yield 108.3 mg (72%, yellow crystal): mp 124−126 °C; IR (neat): ν_{max} 3398, 1695, 1608, 1586, 1509, 1240. 1176 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.05−6.96 (m, 3H), 6.80−6.76 (m, 2H), 6.69−6.67 (m, 1H), 6.58−6.54 (m, 2H), 4.40 (d, 1H, J = 12.0 Hz), 3.77 (s, 3H), 3.54 (td, 1H, J = 21.0, 3.0 Hz), 3.35−3.19 (m, 2H), 0.80 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 216.0, 158.4, 143.9, 135.8, 130.5, 130.3, 126.9, 125.2, 117.7, 114.2, 113.7, 55.2, 48.9, 46.1, 45.8, 44.8, 25.4; HRMS (ESI-TOF) calcd for $C_{21}H_{25}NNaO_2$ $(M + Na)^+$ 346.1778, found 346.1775.

Ethyl 4-(4-Methoxyphenyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate ***(6g)***. Yield 119 mg (81%, yellow oil); IR (neat): ν_{max} 3404, 2980, 2836, 2308, 1727, 1608, 1509, 1247, 1176, 1034, 829, 749 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.07−7.05 (m, 2H), 6.99 (td, 1H, J = 7.2, 0.9 Hz), 6.83−6.80 (m, 2H), 6.70 (d, 1H, J = 7.5 Hz), 6.58−6.51 (m, 2H), 4.38 (d, 1H, J = 8.4 Hz), 4.01 (qd, 2H, J = 7.2, 1.2 Hz), 3.76 (s, 3H), 3.53−3.37 (m, 2H), 2.95 (td, 1H, J = 8.1, 3.6 Hz), 1.07 (t, 3H, J = 7.2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.1, 158.2, 143.8, 136.0, 130.1, 129.9, 127.1, 123.0, 117.4, 114.1, 113.6, 60.4, 55.1, 46.8, 44.8, 42.2, 13.9; HRMS (ESI-TOF) calcd for $C_{19}H_{21}NNaO_3$ $(M + Na)^+$ 334.1414, found 334.1414.

Ethyl 4-(3,4-Dimethoxyphenyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate ***(6h)***. Yield 127.1 mg (82%, white solids): mp 125−127 °C; IR (neat): ν_{max} 3399, 1726, 1513, 1464, 1250, 1026 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.01 (td, 1H, J = 6.0, 0.9 Hz), 6.80−6.77 (m, 1H), 6.72−6.78 (m, 3H), 6.60−6.55 (m, 2H), 4.38 (d, 1H, J = 9.0 Hz), 4.10−3.98 (m, 3H), 3.86 (s, 3H), 3.81 (s, 3H), 3.56−3.41 (m, 2H), 2.99 (td, 1H, J = 9.0, 3.0 Hz), 1.09 (t, 3H, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.1, 148.8, 147.7, 143.8, 136.4, 130.2, 127.2, 122.9, 121.4, 117.5, 114.2, 111.9, 110.3, 60.5, 55.80, 55.76, 46.9, 45.3, 42.5, 14.0; HRMS (ESI-TOF) calcd for $C_{20}H_{24}NO_4$ $(M + H)^+$ 342.1700, found 342.1703.

3-Methyl-4-phenyl-1,2,3,4-tetrahydroquinoline ***(6i)***. Yield 98.6 mg (70%, white crystals): mp 84−85 °C; IR (neat): ν_{max} 3412, 1605, 1492,1452, 1317, 1266 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31−7.20 (m, 3H), 7.13−7.11 (m, 2H), 6.97 (td, 1H, J = 6.0, 3.0 Hz), 6.63−6.60 (m, 1H), 6.54−6.49 (m, 2H), 3.64 (d, 1H, J = 9.0 Hz), 3.28 (dd, 1H, J = 12.0, 6.0 Hz), 3.01 (dd, 1H, J = 12.0, 9.0 Hz), 2.19−2.09 (m, 1H), 0.92 (d, 3H, J = 6.0 Hz) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.7, 144.6, 130.7, 129.2, 128.2, 126.9, 126.2, 123.9, 117.1, 113.9, 51.2, 47.0, 34.9, 18.0; HRMS (ESI-TOF) calcd for $C_{16}H_{18}N$ $(M + H)^+$ 224.1434, found 224.1432.

3-(Bromomethyl)-4-phenyl-1,2,3,4-tetrahydroquinoline ***(6j)***. Yield 223.1 mg (77%, white crystals): mp 95−96 °C; IR (neat): ν_{max} 3414, 2919, 1605, 1492, 1316, 746, 700 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24−7.11 (m, 3H), 7.03 (dd, 2H, J = 8.4, 1.5 Hz), 6.94 (td, 1H, J = 7.8, 1.2 Hz), 6.66 (d, 1H, J = 7.2 Hz), 6.51 (t, 2H, J = 7.2 Hz), 3.99 (d, 1H, J = 6.0 Hz), 3.76 (br s, 1H), 3.37 (dd, 1H, J = 10.2, 5.1 Hz), 3.32−3.25 (m, 2H), 3.20 (dd, 1H, J = 11.7, 6.3 Hz), 2.32−2.22 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.2, 143.9, 131.2, 128.9, 128.5, 127.5, 126.5, 121.5, 117.8, 114.2, 46.9, 42.2, 42.1, 36.0; HRMS (ESI-TOF) calcd for $C_{16}H_{17}BrN$ (Br-79) $(M + H)^+$ 302.0539, found 302.0537.

4-(4-Methoxyphenyl)-3-nitro-1,2,3,4-tetrahydroquinoline ***(6k)***. Yield 117 mg (77%, yellow solid); mp 106−107 °C; IR (neat): ν_{max} 3412, 2837, 1607, 1544, 1509, 1248, 1030, 830, 750 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.10−7.06 (m, 3H), 6.88−6.80 (m, 3H), 6.70−6.60 (m, 2H), 4.86−4.79 (m, 2H), 4.00 (br s, 1H), 3.88−3.81 (m, 1H), 3.79 (s, 3H), 3.63 (dd, 1H, J = 12.0, 2.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 142.7, 133.4, 130.5, 129.9, 127.9, 120.3, 118.7, 114.7, 114.3, 85.3, 55.3, 45.8, 42.4; HRMS (ESI-TOF) calcd for $C_{16}H_{17}N_2O_3$ $(M + H)^+$ 285.1234, found 285.1231.

3,4-Diphenyl-1,2,3,4-tetrahydroquinoline ***(6l)***. Yield 101.6 mg (71%, reddish-orange solid): mp 98−99 °C; IR (neat): ν_{max} 3409, 1495, 1452 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21−7.07 (m, 6H), 7.05−6.97 (m, 5H), 6.69 (d, 1H, J = 6.0 Hz), 6.59−6.53 (m, 2H), 4.24 (d, 1H, J = 9.0 Hz), 3.47−3.38 (m, 2H), 3.23 (td, 1H, J = 9.0, 3.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.0, 144.7, 142.7, 130.7, 129.1, 128.2, 128.0, 127.7, 127.0, 126.4, 126.1, 124.7, 117.4, 114.2, 50.1, 47.4, 46.9; HRMS (ESI-TOF) calcd for $C_{21}H_{20}N$ $(M + H)^+$ 286.1590, found 286.1582.

3,4-Diphenyl-1,2,3,4-tetrahydroquinoline ***(6m)***. Yield 76.1 mg (28%, white solid): mp 155−156 °C; IR (neat): ν_{max} 3415, 2889, 1606, 1493, 669 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18−7.00 (m, 7H), 6.90 (d, 1H, J = 7.5 Hz), 6.72 (dd, 2H, J = 5.4, 1.8 Hz), 6.64−6.57 (m, 4H), 4.25 (d, 1H, J = 4.5 Hz), 3.85 (br s, 1H), 3.66 (dd, 1H, J = 11.7, 11.7 Hz), 3.50 (dt, 1H, J = 12.3, 3.6 Hz), 3.28 (dd, 1H, J = 11.1, 2.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.5, 142.1, 141.1, 130.5, 130.2, 128.0, 127.8, 127.5, 127.1, 126.4, 126.0, 123.7, 117.0, 113.9, 49.9, 42.9, 40.9; HRMS (ESI-TOF) calcd for $C_{21}H_{20}N$ $(M + H)^+$ 286.1590, found 286.1600.

4-(4-Methoxyphenyl)-3-phenyl-1,2,3,4-tetrahydroquinoline ***(6n-1)***. Yield 260.1 mg (93%, white solid); mp 106−107 °C; IR (neat): ν_{max} 3410, 2908, 1496, 1244, 1034, 699 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24−7.11 (m, 3H), 7.05−6.99 (m, 3H), 6.90 (d, 2H, J = 8.7 Hz), 6.70 (app d, 3H, J = 8.4 Hz), 6.60−6.54 (m, 2H), 4.19 (d, 1H, J = 9.0 Hz), 4.08 (br s, 1H), 3.72 (s, 3H), 3.52−3.40 (m, 2H), 3.24−3.16 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.9, 144.8, 142.9, 137.1, 130.7, 130.0, 128.3, 127.8, 127.1, 126.4, 125.1, 117.5, 114.3, 113.5, 55.1, 49.3, 47.5, 47.1; HRMS (ESI-TOF) calcd for $C_{22}H_{22}NO$ $(M + H)^+$ 316.1696, found 316.1698.

6-Bromo-4-(4-methoxyphenyl)-3-phenyl-1,2,3,4-tetrahydroquinoline ***(6n-2)***. Yield 223.0 mg (84%, white solid); mp 87−88 °C; IR (neat): ν_{max} 3414, 2952, 1493, 1247, 1033, 670 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23−7.14 (m, 3H), 7.09 (dd, 1H, J = 8.4, 2.1 Hz), 7.04−7.01 (m, 2H), 6.90−6.86 (m, 2H), 6.81 (dd, 1H, J = 2.1, 0.6 Hz), 6.74−6.70 (m, 2H), 6.46 (d, 1H, J = 8.4 Hz), 4.13 (d, 1H, J = 8.7 Hz), 4.12 (br s, 1H), 3.74 (s, 3H), 3.44−3.42 (m, 2H), 3.19−3.12 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.0, 143.7, 142.4, 136.3, 133.0, 129.91, 129.87, 128.3, 127.7, 126.9, 126.5, 115.7, 113.7, 108.9, 55.1, 49.0, 46.8, 46.6; HRMS (ESI-TOF) calcd for $C_{22}H_{21}BrNO$ (Br-79) $(M + H)^+$ 394.0801, found 394.0802.

4-Benzyl-4-phenyl-1,2,3,4-tetrahydroquinoline ***(6p)***. Yield 83.2 mg (55%, white solid): mp 121−122 °C; IR (neat): ν_{max} 1678, 1596, 1573, 1511, 1256, 1076 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ

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7.39 (dd, 1H, J = 9.0, 3.0 Hz), 7.26−7.03 (m, 9H), 6.93−6.90 (m, 2H), 6.77−6.71 (m, 1H), 6.48 (dd, 1H, J = 9.0, 3.0 Hz), 3.47 (d, 1H, J = 12.0 Hz), 3.42 (d, 1H, J = 12.0 Hz), 3.05−2.88 (m, 2H), 2.22 (dt, 1H, J = 12.0, 6.0 Hz), 2.13−2.03 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.3, 145.2, 138.2, 131.1, 129.4, 128.0, 127.9, 127.6, 127.4, 126.1, 125.8, 125.1, 116.3, 114.7, 47.5, 45.0, 38.2, 33.3; HRMS (ESI-TOF) calcd for $C_{22}H_{22}N$ $(M + H)^+$ 300.1747, found 300.1737.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra of all prepared products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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