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Iron-Catalyzed Cyclization of Nitrones with Geminal-Substituted Vinyl Acetates: A Direct [4 + 2] Assembly Strategy Leading to 2,4-Disubstituted Quinolines

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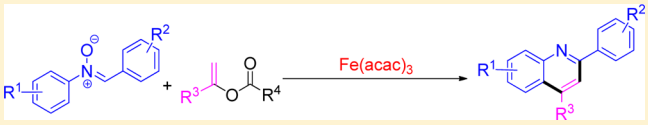
Supporting Information

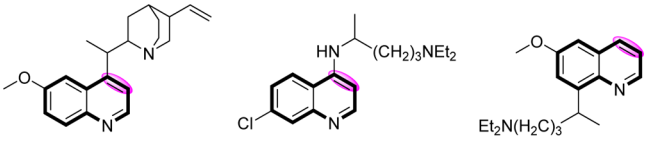
ABSTRACT: An iron-catalyzed intermolecular [4 + 2] cyclization of arylnitrones with geminal-substituted vinyl acetates was developed for the synthesis of 2,4-disubstituted quinolines in moderate to good yields with good functional group compatibilities. Preliminary mechanistic studies suggest a plausible iron-catalyzed C−H activation process under external-oxidant-free conditions.



INTRODUCTION

Quinoline derivatives exhibit pharmacologically privileged and synthetically important effects in medicinal chemistry, especially for the treatment of malaria (Scheme 1).[1] However, most natural quinolines metabolize too fast in human bodies, which restricts their clinical applications. Quinoline analogues, especially 2-substituted quinolines, have better pharmacological activities due to their higher inoxidizability.[2] Thus, it is meaningful to design or reform special structures of quinoline derivatives to obtain new, effective, and safe medicines. While there are numerous methods for the preparation of quinolines such as the classical Skraup quinoline synthesis, Niementowski quinoline synthesis, and other methods starting with anilines or substituted anilines,[3] these reactions suffer from a variety of disadvantages, viz.: (1) external oxidants for the aromatization, (2) harsh reaction conditions, and (3) noble and/or toxic metal catalysts or other additives.[4] Recently, versatile methods for rapid access to 2,3-disubstituted quinolines and quinoline-4-carboxylic acid derivatives starting from arylimines were reported,[5] in which palladium and indium catalysts were indispensable. In addition, production of extra wastes did not conform to the principles of green synthetic chemistry. Hence, development of a mild, efficient, and ecologically benign procedure to access such frameworks is highly desirable for organic chemists.

Scheme 1. Medicinal Quinoline Derivatives



Due to the nature of their easy preparation and fascinating polar nature of the N−O bond, nitrones are rising to the spotlight in heterocyclic chemistry for developing transition-metal-catalyzed C−H bond functionalization reactions.[6a] Scientists obtained a variety of useful structures such as indoles and O-containing heterocycles through cascade reactions of nitrones with alkynes.[6] Unfortunately, palladium, rhodium, cobalt, and other transition metals, which are expensive and/or toxic, always had to be used to activate the C−H bond of nitrones.[7] Iron with multiple valence states or its complexes is an ideal, cheap, and harmless catalyst for C−H activation in the literature.[8] Meanwhile, considering the emergence of geminal-substituted vinyl acetates as convenient acetylene equivalents,[9] and the special oxidizing N−O bond in nitrones which could serve as intramolecular oxidant,[7c] we envisioned an iron-catalyzed quinoline synthesis could be possible using nitrones and vinyl acetates. Herein, we present a new method for the preparation of 2,4-disubstituted quinolines from nitrones and IPA (isopropenyl acetate) derivatives catalyzed by iron, where no external oxidant was involved because of the inherent N−O bond.

RESULTS AND DISCUSSION

First, the reaction of nitrone **1a** (0.1 mmol) and IPA **2a** (4.0 equiv), in the presence of $FeCl_2$ (10 mol %), $AgSbF_6$ (20 mol %), and in MeOH (2 mL), under air at 100 °C for 10 h was examined. To our surprise, the desired product **3aa** was detected in trace yield (Table 1, entry 1). Delightedly, replacing $FeCl_2$ with $Fe(NO_3)_3$ obtained **3aa** in 20% yield (Table 1, entry 2). Other iron(III) salts, such as $FeBr_3$ and $FeCl_3$, provided moderately improved yields (Table 1, entries 3 and 4). Gratifyingly, the yield of **3aa** was increased to 78% in the presence of $Fe(acac)_3$ (Table 1, entry 5). Furthermore, simple solvent screening revealed dichloromethane (DCM) to be most effective for this reaction (Table 1, entries 6−9). Trace of **3aa**

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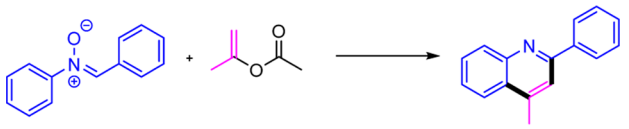
Table 1. Screening the Reaction Conditions[a,b]



1a 2a 3aa

entry	catalysts	additive	solvent	yield[c] (%)
1	$FeCl_2$	$AgSbF_6$	MeOH	<5
2	$Fe(NO_3)_3$	$AgSbF_6$	MeOH	20
3	$FeBr_3$	$AgSbF_6$	MeOH	43
4	$FeCl_3$	$AgSbF_6$	MeOH	24
5	$Fe(acac)_3$	$AgSbF_6$	MeOH	78
6	$Fe(acac)_3$	$AgSbF_6$	EtOH	55
7	$Fe(acac)_3$	$AgSbF_6$	Acetone	81
8	$Fe(acac)_3$	$AgSbF_6$	Benzene	77
9	$Fe(acac)_3$	$AgSbF_6$	DCM	83, 79[d], 77[e]
10	$Fe(acac)_3$	AgCl	DCM	trace
11	$Fe(acac)_3$	Ag_2CO_3	DCM	trace
12	$Fe(acac)_3$	$NaSbF_6$	DCM	70
13	**$Fe(acac)_3$**	**$NaSbF_6$**[f]	**DCM**	**80**, 81[g], 75[h]
14	$Fe(acac)_3$	$NaSbF_6$[f]	DCM	37,[i] 61[j]

[a]Unless otherwise noted, the reaction was carried out on **1a** (0.1 mmol), **2a** (4.0 equiv), catalyst (10 mol %), and additive (20 mol %) in solvent (2.0 mL) at 100 °C for 10 h under air atmosphere in a sealed tube. [b]Detailed information please see Table S1, in Supporting Information. [c]Isolated yield. [d]At 90 °C. [e]At 120 °C. [f]$NaSbF_6$ (0.5 equiv). [g]Under N_2 atmophere. [h]Under O_2 atmophere. [i]Mole ratio, **1a**:**2a** = 1:1. [j]Mole ratio, **1a**:**2a** = 1:2.

was detected in the presence of other silver salts (Table 1, entries 10 and 11). Surprisingly, 70% yield of **3aa** was obtained when $NaSbF_6$ was used as the additive (Table 1, entry 12). Based on this result, 80% yield of **3aa** was obtained in the presence of 0.5 equiv of $NaSbF_6$ (Table 1, entry 13). Further screening of the parameters, such as reaction atmosphere and mole ratios between nitrones and IPA (Table 1, entries 13 and 14), established the optimized condition as follows: nitrone **1a** (0.1 mmol) and IPA **2a** (4.0 equiv) in the presence of $Fe(acac)_3$ (10 mol %) and $NaSbF_6$ (0.5 equiv), in DCM (2 mL) under air at 100 °C for 10 h.

With the optimal conditions in hand, we next investigated the substrate scope of arylnitrones (Table 2). Arylnitrones could be easily prepared from arylaldehyde and arylhydroxylamine easily according to the literature.[10] This reaction displayed excellent functional group tolerance. Both electron-donating and -withdrawing groups, such as 4-methyl (**1b**, **1o**), 4-methoxyl (**1i**), 4-methylthio (**1j**), 4-halogens (**1d-f**, **1l-m**), 4-trifluoromethyl (**1g**), and 4-cyano (**1h**), at the phenylimino moieties are compatible with this reaction, providing the corresponding quinoline products in moderate to good yields. The *meta*-substituted R^2 group also worked efficiently, affording **3ca** in 75% yield. Similar efficiencies were also observed, when R^1 groups were located at the *meta*- or *para*-positions with **3la**, **3ma**, **3na**, **3oa**, and **3pa** obtained in 78%−83% yields. In addition, nitrone containing the 2-naphthyl group also worked well in this reaction (**3ka**) with 89% yield. However, 1-naphthyl nitrone (**1k′**) failed to provide any products. Furthermore, other heterocyclic nitrones were also not compatible with this reaction (Figure S1, **1u**, **1v**, **1w**), most likely due to the strong metal−heteroatom coordination interactions, which were known to interfere with Fe-catalyzed *ortho*-C_{Ar}−H activations.[11] In addition, *ortho*-substitutions of either phenyl ring (Figure S1, **1q**, **1r**, **1s**, **1t**) only provided trace products, indicating this reaction is sensitive to steric hindrance. Lastly, all attempts to access 2-alkylquinolines failed (Figure S1, **1x**, **1y**, **1z**, **1a′**).

Next, we surveyed the geminal-substituted vinyl acetate scope of this iron-catalyzed annulation (Table 3). Notably, when R^3 adopted aryl groups, these vinyl acetates could afford the corresponding quinolines (**3ac**−**3af**) in good yields of 75% to 83%. In the absence of the aryl group, however, **3ab** only gave 57% yield. This reactivity difference can be explained probably by the stability of the carbocation generated in intermediate D in our proposed mechanism.[12] Furthermore, 2-thiophenyl-substituted vinyl acetate **2g** was also a difficult partner for this reaction (Figure S2), probably due to the metal coordination−chelation interaction as discussed above. The reaction can be further diversified when methyl methacrylate and ^{t}butyl acrylate were used to replace vinyl acetate, affording the desired products **3aa** and **3ab** in 51% and 75% yield, respectively (Figure 1). According to our originally envisaged mechanism, we can roughly explain the reason that the R^3 group is hydrogen and the secondary carbocation is less stable in the solution (the intermediate **D** in the proposed mechanism).[12]

Preliminary mechanistic studies were conducted to get some insights into this transformation (Scheme 2). With the help of a Lewis acid, the attack of nitrone by vinyl acetate followed by an intramolecular addition may be involved. However, replacing $Fe(acac)_3$ with other strong Lewis acids, such as $Cu(OTf)_2$, $CeCl_3$, $BF_3{\cdot}OEt_2$, or Brønsted acid HOTf shut down the reaction. The absence of the desired product and possible byproduct (eq 1) indicated that this reaction was unlikely to follow a Lewis acid catalyzed pathway. Another mechanism starting with a [3 + 2] cycloaddition, followed by an iron-catalyzed ring-opening reaction, where Fe(III) acted as a Lewis acid was also reasonable. However, the potential [3 + 2] cyclization intermediate was also not detected (eq 2). Generally speaking, this transformation may not match the characteristics of a Lewis acid-catalyzed reaction.[13] Although at the current stage none of them can be thoroughly ruled out, an iron-catalyzed C−H activation pathway was favored.

Iron(III)-catalyzed C−H activation has been widely developed in the past decades.[8,14] In light of foregoing experiments and the literature, a plausible mechanism was proposed as shown in Scheme 3. Cleavage of the C−H bond by iron(III) at the *ortho*-position of the phenyl ring via N-oxide serving as a directing group generates intermediate **A**. IPA insertion to **A** followed by β-O elimination affords intermediate **C**. The iminium species **C1** can be delocalized to generate a carbocation **C2**. Imine addition or intramolecular olefin addition into the carbocation followed by E1 elimination provides the key intermediate **D**. Subsequent β-H elimination generates the quinoline N-oxide **E**, which might briefly show up in the system but was undetectable. Internal oxidation cleaves the N−O bond to produce the desired quinoline product and regenerates the iron(III) catalyst, thereby closing the catalytic cycle. Acetic acid and water were the only byproducts.

CONCLUSIONS

In conclusion, we have developed an iron-catalyzed annulation of nitrones with geminal-substituted vinyl acetates for the synthesis of 2,4-disubstituted quinolines. This transformation features: (1) iron-catalyzed C−H activation process based on preliminary mechanistic investigations; (2) mild conditions with inexpensive transition metal and internal oxidant; (3)

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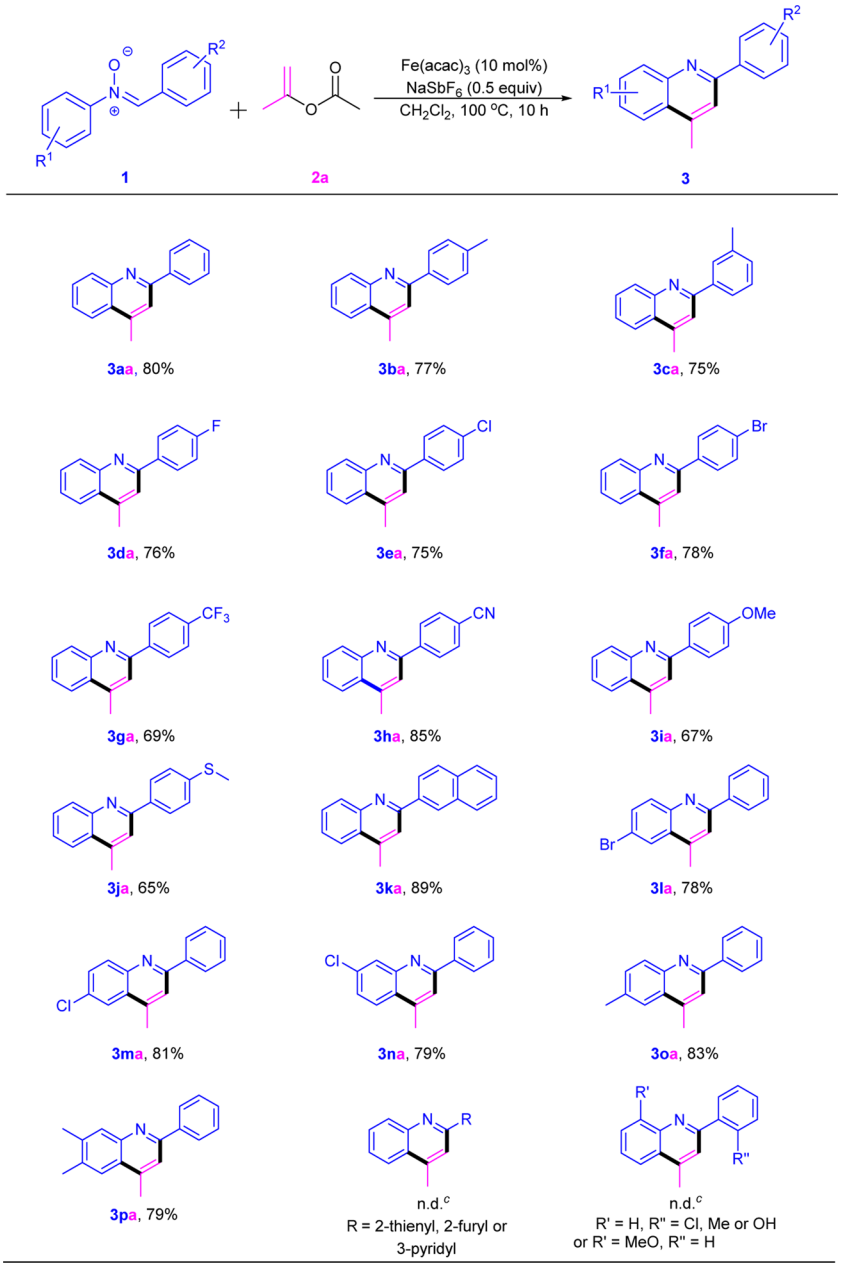
Table 2. Substrate Scope of Arylnitrones[a,b]



[a]Unless otherwise noted, the reaction was carried out on **1** (0.1 mmol), **2a** (4.0 equiv), $Fe(acac)_3$ (10 mol %), and $NaSbF_6$ (0.5 equiv) in DCM (2.0 mL) at 100 °C for 10 h under air atmosphere in a sealed tube. [b]Isolated yield. [c]For detailed information please see Figure S1, in Supporting Information.

diverse substrates and good functional group tolerance; (4) dual functionality of N-oxide as both a directing group and an oxidant; and (5) green chemistry with water and acetic acid as byproducts.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all chemicals were purchased from commercial suppliers and used without further purification. ^1H NMR and ^{13}C NMR spectra were recorded at ambient temperature on a 300 or 400 MHz NMR spectrometer (75 MHz for ^{13}C, 100 MHz for ^{13}C). NMR experiments are reported in δ units, parts per million (ppm), and were referenced to $CDCl_3$ (7.26 or 77.0 ppm) as the internal standard. The coupling constants J are given in Hz. Column chromatography was performed using silica gel 60 (300−400 mesh). Melting points were taken on an electrothermal melting point apparatus and without correction. IR spectra were recorded on an FT-IR spectrometer using KBr discs. HRMS spectra were recorded using a spectrometer with a TOF mass analyzer with an ESI ion source.

General Procedure for Preparation of Quinolones. Under air atmosphere, a sealed tube was charged with diarylnitrones (0.1 mmol), ferric acetylacetonate (3.5 mg, 10 mol %), geminal-substituted vinyl acetates (4.0 mmol), $NaSbF_6$ (12.9 mg, 50 mol %), and DCM (2.0 mL). The reaction mixture was stirred at 100 °C for 10 h in an oil bath. After the completion of the reaction, 2 mL of saturated sodium hydroxide solution and 3 × 2 mL of EtOAc were added. The combined organic phase was concentrated in vacuum, and the residue was purified by flash column chromatography on silica gel with petroleum ether-ethyl acetate as the eluent to give the desired product.

General Procedure for the Arylnitrones.[10a] Nitroarene (1.0 equiv), aldehyde (1.1 equiv), and NH_4Cl (1.2 equiv) were dissolved in

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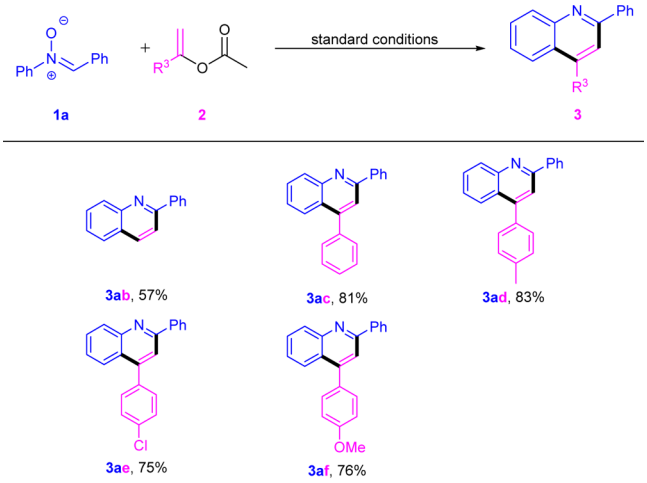
Table 3. Substrate Scope of Vinyl Acetates[a,b]



[a]Unless otherwise noted, the reaction was carried out on **1a** (0.1 mmol), **2** (4.0 equiv), $Fe(acac)_3$ (10 mol %), and $NaSbF_6$ (0.5 equiv) in DCM (2.0 mL) at 100 °C for 10 h under air atmosphere in a sealed tube. [b]Isolated yield.

a 1:1 mixture of EtOH and water (2 mL/mmol of starting material) and cooled to 0 °C (ice bath). Then zinc powder (2.0 equiv) was added to the resulting mixture, and the reaction was allowed to warm to room temperature and stirred for 16 h. The reaction mixture was filtered and washed with CH_2Cl_2. The filtrate was extracted with CH_2Cl_2 (4 × 50 mL), and the combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to give crude nitrones. Pure nitrones were obtained by recrystallization from ethyl acetate.

General Procedure for the 1-Phenylvinyl Acetate.[15] To a mixture of acetophenone (4.85 mL, 5 g, 42.5 mmol) and 2-propenyl acetate (23.13 mL, 0.213 mol, 5.0 equiv) was added *p*-toluenesulfonic acid (0.75 g, 3.925 mmol, 0.09 equiv). The resulting mixture was refluxed for 20 h in a 100 mL flask equipped with a condenser and a drying tube. The solvent was then cooled to room temperature, and the solvent was evaporated in vacuo. Ether was added (100 mL), and the resulting solvent was washed with water (3 × 50 mL) and dried over $MgSO_4$. The solvent was evaporated in vacuo to give a dark orange/red oily residue. This residue was purified by column chromatography on silica gel to yield yellow oil. Sometimes a further distillation to remove remaining acetophenone is necessary.

*4-Methyl-2-phenylquinoline (**3aa**).*[13b] Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) give **3aa** (17.5 mg, 80% yield) as a yellow solid: mp 62–63 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.20–8.15 (m, 3H), 8.00 (d, J = 8.2 Hz, 1H), 7.71–7.74 (m, 2H), 7.45–7.51 (m, 4H), 2.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.0, 148.1, 144.8, 139.8, 130.2, 129.3, 129.1, 128.7, 127.5, 127.2, 126.0, 123.6, 119.7, 19.0; MS: (EI) 219 (M^+).

*4-Methyl-2-(p-tolyl)quinoline (**3ba**).*[13b] Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives the product **3ba** (18.0 mg, 77% yield) as a yellow solid: mp 76–78 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.18–8.15 (m, 1H), 8.07–8.04 (m, 2H), 8.01–7.98 (m, 1H), 7.74–7.68 (m, 2H), 7.56–7.51 (m, 1H), 7.34–7.31 (m, 2H), 2.76 (d, J = 0.9 Hz, 3H), 2.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 157.0, 148.0, 144.7, 139.2, 136.9, 130.1 129.5, 129.3, 127.4, 127.2, 125.8 123.6, 119.6, 21.3, 19.0; MS (EI): 233 (M^+).

*4-Methyl-2-(m-tolyl)quinoline (**3ca**).*[13b] Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3ca** (17.4 mg, 75% yield) as a yellowish solid: mp 77–78 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.17–8.14 (m, 1H), 7.99 (t, J = 4.0 Hz, 2H), 7.88 (d, J = 7.7 Hz, 1H), 7.71–7.66 (m, 2H), 7.54–7.49 (m, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.23 (s, 1H), 2.74 (d, J = 0.9 Hz, 3H), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 157.3, 148.0, 144.7, 139.7, 138.4, 130.2, 130.0, 129.3, 128.6, 128.2, 127.2, 126.0, 124.6, 123.6, 119.9, 21.6, 19.0; MS (EI): 233 (M^+).

*2-(4-Fluorophenyl)-4-methylquinoline (**3da**).*[13b] Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3da** (18.0 mg, 76% yield) as a yellowish oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.17–8.13 (m, 3H), 8.00 (d, J = 8.3 Hz, 1H), 7.74–7.67 (m, 2H), 7.57–7.53 (m, 1H), 7.20 (t, J = 8.7 Hz, 2H), 2.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 164.9, 162.5, 155.9, 148.0, 145.0, 135.9 (d, J_{C-F} = 4.0 Hz), 130.2, 129.3 (d, J_{C-F} = 16.0 Hz), 127.1, 126.1, 123.6, 119.4, 115.7 (d, J_{C-F} = 22.0 Hz), 19.0; MS (EI): 237 (M^+).

*2-(4-Chlorophenyl)-4-methylquinoline (**3ea**).*[13b] Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3ea** (18.5 mg, 75% yield) as a yellowish solid: mp 74–75 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.17–8.10 (m, 3H), 8.00 (d, J = 8.3 Hz, 1H), 7.75–7.68 (m, 2H), 7.58–7.48 (m, 3H), 2.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 155.7, 145.0, 138.2, 135.4, 130.3, 129.5, 129.3, 128.9, 128.76, 127.3, 126.2, 123.6, 119.3, 19.0; MS (EI): 253 (M^+).

*2-(4-Bromophenyl)-4-methylquinoline (**3fa**).*[13b] Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3fa** (23.2 mg, 78% yield) as a yellowish solid: mp 68–69 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.17–8.10 (m, 3H), 8.00 (d, J = 8.2 Hz, 1H), 7.74–7.68 (m, 2H), 7.55–7.48 (m, 3H), 2.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 155.7, 148.1, 145.0, 138.2, 135.2, 135.4, 130.2, 129.5, 128.9, 128.8, 127.3, 126.2, 123.6, 119.3,19.0; MS (EI): 297 (M^+).

*4-Methyl-2-(4-(trifluoromethyl)phenyl)quinoline (**3ga**).*[16] Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3ga** (19.8 mg, 69% yield) as a yellow solid: mp 117–118 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.27 (d, J = 10.7 Hz, 2H), 8.20–8.17 (m, 1H), 8.04–8.01 (m, 1H), 7.79–7.62 (m, 4H), 7.62–7.56 (m, 1H), 2.79 (d, J = 1.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 155.4, 148.0, 145.4, 137.1, 131.7 (d, J_{C-F} = 52.5 Hz), 129.7, 127.8, 127.5, 126.6, 125.7 (t, J_{C-F} = 4.1 Hz), 125.6, 123.7, 120.0, 19.1; MS (EI): 287 (M^+).

*4-(4-Methylquinolin-2-yl)benzonitrile (**3ha**).* Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3ha** (20.7 mg, 85% yield) as a yellowish solid: mp 146–147 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.30–8.27 (m, 2H), 8.17 (d, J = 8.5 Hz, 1H), 8.05–8.02 (m, 1H), 7.82–7.73 (m, 4H), 7.63–7.57 (m, 1H), 2.80 (d, J = 0.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 155.0, 144.4, 139.1, 127.6, 133.5, 129.5, 127.9, 127.6, 127.3, 126.8, 125.1, 121.2, 119.8, 21.4, 19.4; MS (EI): 244 (M+); HRMS (ESI) m/z calcd for $C_{17}H_{13}N_2$ $(M + H)^+$ 245.1073, found 245.1076; IR (KBr) ν 3030, 2921, 2850, 1636, 1465, 1384.

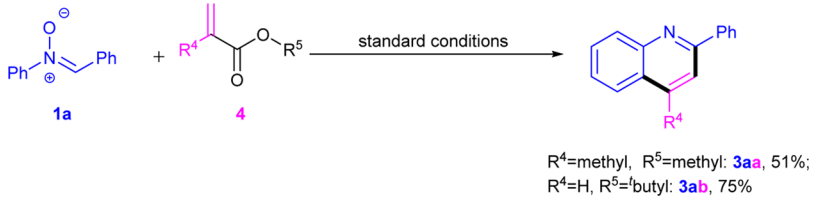


Figure 1. Substrate scope of acrylates in isolated yield. Unless otherwise noted, the reaction was carried out on **1a** (0.1 mmol), **4** (4.0 equiv), $Fe(acac)_3$ (10 mol %), and $NaSbF_6$ (0.5 equiv) in DCM (2.0 mL) at 100 °C for 10 h under air atmosphere in a sealed tube.

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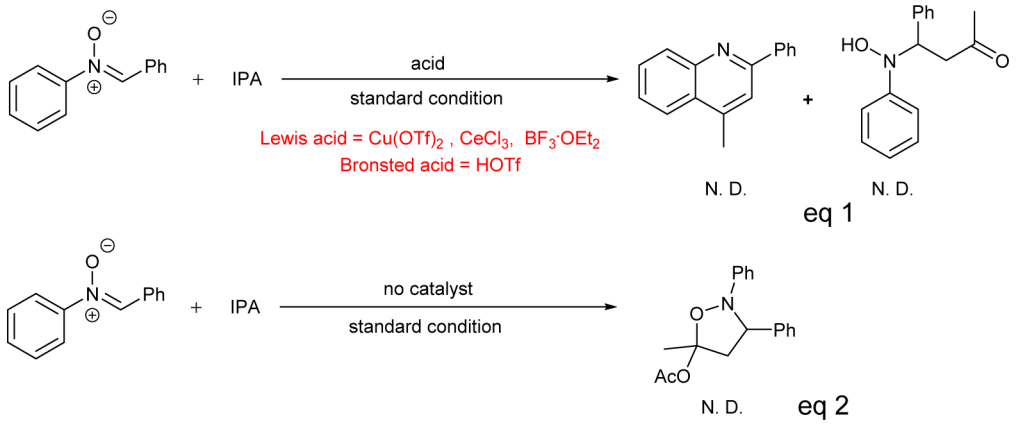
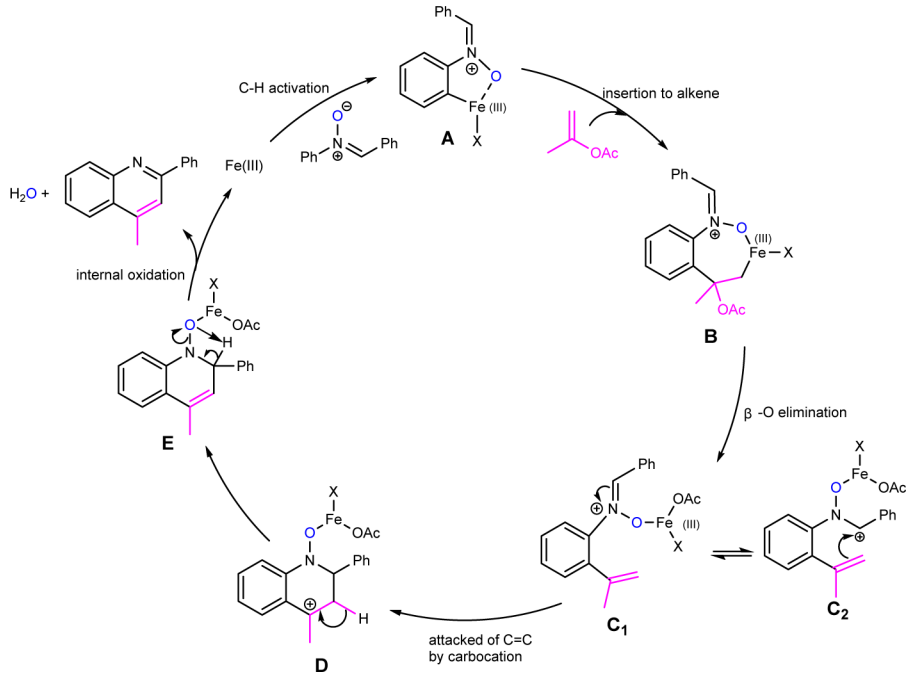
Scheme 2. Preliminary Mechanistic Studies



Scheme 3. Proposed Mechanism



*2-(4-Methoxyphenyl)-4-methylquinoline (**3ia**).*[13b] Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3ia** (16.7 mg, 67% yield) as a yellowish solid: 110−112 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.15−8.10 (m, 3H), 8.00−7.96 (m, 1H), 7.68 (s, 1H), 7.54−7.44 (m, 2 H), 7.07−7.02 (m, 2H), 3.89 (s, 3H), 2.75 (d, J = 0.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 160.7, 156.6, 148.1, 144.6, 130.0, 129.3, 129.2, 128.8, 127.7, 125.7, 123.6, 119.3, 114.1, 55.4, 19.0; MS (EI): 249 (M^+).

*4-Methyl-2-(4-(methylthio)phenyl)quinoline (**3ja**).* Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3ja** (17.2 mg, 65% yield) as a yellowish solid: 135−136 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.19−8.11 (m, 3H), 8.01 (d, J = 8.3 Hz, 1H), 7.75−7.71 (m, 2H), 7.58−7.54 (m, 1H), 7.41 (d, J = 8.4 Hz, 2H), 2.79 (s, 3H), 2.57 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.3, 148.1, 144.8, 140.2, 136.4, 130.1, 129.4, 127.8, 126.4, 125.9, 123.6, 119.3, 112.8, 19.0, 15.5; MS (EI): 265 (M^+); HRMS (ESI) m/z calcd for $C_{17}H_{16}NS$ $(M + H)^+$ 266.0998, found 266.1002; IR (KBr) ν 3030, 2920, 2850, 1634, 1595, 1494, 1385.

*4-Methyl-2,2′-binaphthalene (**3ka**).*[13b] Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3ka** (23.9 mg, 89% yield) as a yellowish solid: mp 96−97 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.35 (d, J = 8.4 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H), 8.05 (d, J = 8.3 Hz, 1H), 7.98−7.95 (m, 2H), 7.81−7.76 (m, 2H), 7.64−7.50 (m, 5H), 2.73 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.8, 147.6, 144.2, 138.5, 133.7, 131.0, 129.9, 129.2, 128.7, 128.1, 127.4, 126.8, 126.3, 126.0, 125.7, 125.5, 125.1, 123.6, 126.4, 18.5; MS (EI): 269 (M^+).

*6-Bromo-4-methyl-2-phenylquinoline (**3la**).*[13b] Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3la** (23.2 mg, 78% yield) as yellowish solid: 77−79 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.15−8.12 (m, 3H), 8.02 (d, J = 8.9 Hz, 1H), 7.79−7.72 (m, 2H), 7.53−7.47 (m, 3H), 2.72 (d, J = 1.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 157.4, 146.7, 144.0, 139.3, 132.7, 131.9, 129.5, 128.8, 127.5, 126.1, 120.4, 120.0, 19.0; MS (EI): 297 (M^+).

*6-Chloro-4-methyl-2-phenylquinoline (**3ma**).*[13b] Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3ma** (20.4 mg, 81% yield) as a yellowish solid: mp 78−79 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.15−8.09 (m, 3H), 7.96 (d, J = 2.2 Hz, 1H), 7.73 (s, 1H), 7.66−7.63 (m, 1H), 7.55−7.46 (m, 3H), 2.73 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 157.3, 146.5, 144.0, 139.3, 131.8, 130.2, 129.4, 129.0, 128.8, 127.4, 122.8, 120.4, 113.9, 19.0; MS (EI): 253 (M^+).

*7-Chloro-4-methyl-2-phenylquinoline (**3na**).*[13b] Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3na** (20.1 mg, 79% yield) as a yellowish solid: mp 81−83 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.17−8.12 (m, 3H), 7.90 (m, 1H), 7.69

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(d, J = 1.1 Hz, 1H), 7.56−7.34 (m, 4H), 2.73 (d, J = 1.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.0, 144.9, 139.2, 135.1, 129.5, 129.0, 128.8, 128.7, 127.5, 127.4, 126.8, 125.0, 119.9, 19.0; MS (EI): 253 (M^+).

*4,6-Dimethyl-2-phenylquinoline (**3oa**).*[13b] Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3oa** (19.3 mg, 83% yield) as a yellow solid: mp 81−83 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.14−8.11 (m, 2H), 8.07 (d, J = 8.6 Hz, 1H), 7.72 (s, 1H), 7.62 (s, 1H), 7.57−7.43 (m, 4H), 2.72 (d, J = 0.8 Hz, 3H), 2.58 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 157.3, 148.0, 144.7, 138.4, 130.2, 130.0, 129.3, 128.6, 128.2, 126.0, 124.6, 123.6, 119.9, 21.6, 19.0; MS (EI): 233 (M^+).

*4,6,7-Trimethyl-2-phenylquinoline (**3pa**).* Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3pa** (19.5 mg, 79% yield) as yellowish solid: mp 85−87 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.14−8.11 (m, 2H), 8.07 (d, J = 8.6 Hz, 1H), 7.75 (s, 1H), 7.68 (s, 1H), 7.57−7.43 (m, 3H), 2.74 (d, J = 0.8 Hz, 3H), 2.58 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.2, 147.2, 143.8, 140.1, 139.4, 135.8, 129.6, 128.9, 128.7, 127.4, 125.7, 123.0, 119.1, 20.3, 19.0; MS (EI): 247 (M^+); HRMS (ESI) m/z calcd for $C_{18}H_{18}N$ $(M + H)^+$ 248.1434, found 248.1436; IR (KBr) ν 2922, 852, 1637, 1551, 1452.

*2-Phenylquinoline (**3ab**).*[13b] Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3ab** (15.3 mg, 75% yield) as a yellowish oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.25−8.14 (m, 4H), 7.89 (d, J = 8.6 Hz, 1H), 7.85−7.82 (m, 1H), 7.76−7.71 (m, 1H), 7.57−7.44 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 157.4, 148.3, 139.7, 136.8, 129.7, 129.6, 129.3, 128.8, 127.6, 127.4, 127.2, 126.3, 119.0; MS (EI): 205 (M^+).

*2,4-Diphenylquinoline (**3ac**).*[17] Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3ac** (22.7 mg, 81% yield) as a yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.28 (d, J = 8.4 Hz, 1H), 8.09−8.07 (m, 2H), 7.80−7.76 (m, 1H), 7.68 (s, 1H), 7.64−7.58 (m, 1H), 7.42−7.32 (m, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.8, 149.1, 148.8, 139.6, 138.3, 130.1, 129.5, 129.5, 129.3, 128.8, 128.5, 128.4, 127.5, 126.3, 125.7, 125.6, 119.3; MS (EI): 281 (M^+).

*2-Phenyl-4-(p-tolyl)quinoline (**3ad**).*[17] Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3ad** (24.5 mg, 83% yield) as a yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.13−8.04 (m, 3H), 7.79 (d, J = 8.4 Hz, 1H), 7.66 (s, 1H), 7.57 (t, J = 7.6 Hz, 1H), 7.40−7.28 (m, 6H), 7.20 (m, 2H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.8, 149.1, 148.7, 139.6, 138.2, 135.3, 130.0, 129.4, 129.2, 128.7, 127.5, 126.1, 125.8, 125.6, 119.2, 21.2; MS (EI): 295 (M^+).

*4-(4-Chlorophenyl)-2-phenylquinoline (**3ae**).*[17] Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3ae** (23.6 mg, 75% yield) as a yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.28−8.25 (m, 1H), 8.21−8.17 (m, 2H), 7.87−7.83 (m, 1H), 7.79−7.70 (m, 2H), 7.57−7.44 (m, 8H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.8, 148.7, 147.8, 193.4, 136.7, 134.6, 130.8, 130.2, 129.6, 129.4, 128.8, 128.7, 127.5, 126.5, 125.4, 125.2, 119.2; MS (EI): 315 (M^+).

*4-(4-Methoxyphenyl)-2-phenylquinoline (**3af**).*[17] Flash column chromatography on a silica gel (ethyl acetate:petroleum ether, 1:10) gives **3af** (23.7 mg, 76% yield) as a yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.16−8.13 (m, 1H), 8.09−8.05 (m, 2H), 7.85−7.81 (m, 1H), 7.67 (s, 1H), 7.63−7.57 (m, 1H), 7.43−7.31 (m, 6H), 6.97−6.92 (m, 2H), 3.76 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 159.8, 156.9, 148.8, 139.7, 130.8, 130.6, 130.1, 129.4, 129.3, 128.8, 127.5, 126.2, 125.9, 125.6, 119.3, 114.0, 55.4; MS (EI): 311 (M^+).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01910.

Experimental details on the reaction condition studied, along with copies of ^{1}H and ^{13}C NMR spectra of compounds **3aa**−**3pa** and **3ab**−**3af** (PDF)

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Notes

The authors declare no competing financial interest.

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