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Rh(III)-Catalyzed Traceless Coupling of Quinoline *N*-Oxides with Internal Diarylalkynes

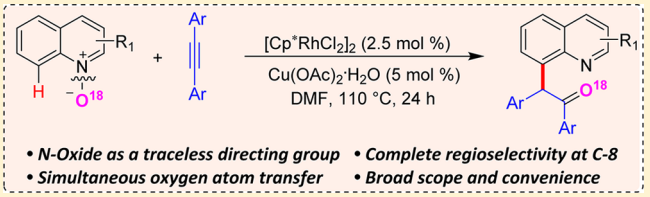
Upendra Sharma,[†,‡,§] Yoonsu Park,[‡,†] and Sukbok Chang*[,†,‡]

[†]Center for Catalytic Hydrocarbon Functionalizations, Institute for Basic Science (IBS), Daejeon 307-701, Korea

[‡]Department of Chemistry, Korea Advanced Institute of Science and Technology (KAIST), Daejeon 307-701, Korea

Supporting Information

ABSTRACT: Quinoline *N*-oxides were found to undergo Cp*Rh(III)-catalyzed coupling with internal diarylalkynes to provide 8-functionalized quinolines through a cascade process that involves remote C−H bond activation, alkyne insertion, and intramolecular oxygen atom transfer. In this reaction, the *N*-oxide plays a dual role, acting as a traceless directing group as well as a source of oxygen atom, as confirmed by an ^{18}O-labeling experiment.

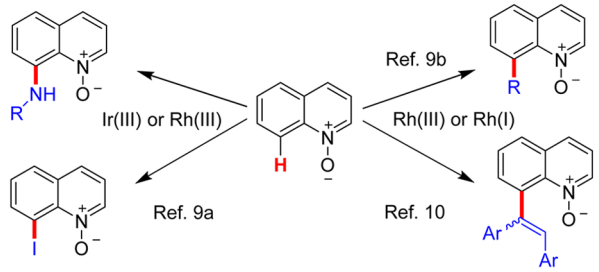


Substituted quinolines are among the most versatile structural motifs encountered in natural product,[1] medicinal,[2] and materials chemistry.[3] In this regard, the development of efficient methods for their synthesis[4] or functionalization at various positions is of high importance.[5] Indeed, while site-selective direct activation of C−H bonds of quinolines has been actively investigated, most of the previous studies demonstrated the catalytic transformation of quinolines at the C2 position.[6] In contrast, the direct activation of the C8−H bond has been much less explored, despite of high synthetic utility of C8-functionalized quinolone products. The first example of a direct catalytic C8 functionalization of unmodified quinolines was revealed by us in Rh(NHC)-mediated arylation.[7a] Sawamura also reported an elegant Ir(I)-catalyzed direct C8 borylation reaction of quinolines.[7b]

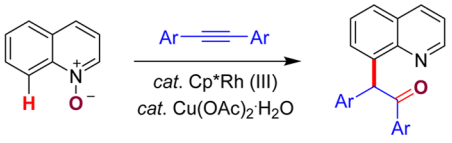
On the other hand, an alternative approach for the functionalization of quinolines at the C8 position has been investigated by employing their *N*-oxides as a directing group (Scheme 1a).[8] Recently, we applied this concept to C8 amination, iodination, alkylation, and alkynylation using Ir(III) or Rh(III) catalytic systems.[9a,b] At the same time, Shibata and Matsuo[10] also nicely utilized this concept for C8 olefination of quinoline *N*-oxides using a Rh(I) catalyst system. In this approach of using quinoline *N*-oxides, while complete C8 regioselectivity is secured in the C−H bond activation, an additional step of *N*-deoxygenation is required after the desired C−H functionalization to release the functionalized quinoline compounds, which are of high utility in medicinal and synthetic chemistry. Since *N*-oxide is known as an *oxidizing* directing group in C−H activation procedures,[11] we envisioned the development of a tandem process involving the desired C−H activation at the C8 position followed by a subsequent intramolecular oxygen atom transfer. By realizing this cascade process, we anticipated using the *N*-oxide as a *traceless* directing group giving rise to additionally oxygen-functionalized products at the end. Herein we disclose a Rh(III)-catalyzed

Scheme 1. C8 Functionalization of Quinoline *N*-Oxides

a) Previous Works: N-Oxide-Directed C-8 Functionalization



b) ***This Study: Traceless N-Oxide Directing Group*** *(see also Ref 12 of Li)*



C8 functionalization of quinoline *N*-oxides where the *N*-oxide acts as a directing group in the C−H bond activation as well as the source of an oxygen atom in the subsequent intramolecular rearrangement. It should be noted that during the preparation of this article, the Li group reported the same transformation using a similar catalytic system.[12]

We commenced our study by examining a reaction of quinoline *N*-oxide (**1a**) with diphenylacetylene (**2a**) under various catalytic conditions (Table 1). To our delight, the alkyne was incorporated at the C8 position of quinoline *N*-oxide with concomitant oxygen atom transfer, giving rise to 1,2-diphenyl-2-(quinolin-8-yl)-ethanone (**3a**), albeit in moderate yield, when $[Cp^*RhCl_2]_2$

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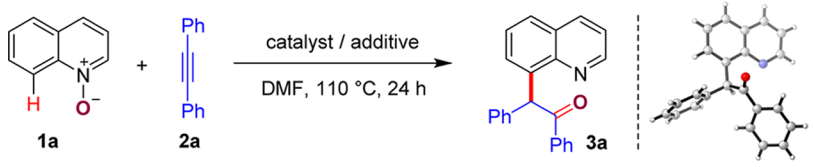
Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst (mol %)	additive (mol %)	yield (%)[b,c]
1	$[Cp^*RhCl_2]_2$ (5)	$Cu(OAc)_2{\cdot}H_2O$ (100)	41
2	–	$Cu(OAc)_2{\cdot}H_2O$ (100)	N.R.
3	$[Cp^*RhCl_2]_2$ (5)	–	N.R.
4	$[Cp^*RhCl_2]_2$ (5)	$Cu(OAc)_2{\cdot}H_2O$ (50)	51
5	$[Cp^*RhCl_2]_2$ (5)	$Cu(OAc)_2{\cdot}H_2O$ (10)	70
6	**$[Cp^*RhCl_2]_2$ (2.5)**	**$Cu(OAc)_2{\cdot}H_2O$ (5)**	**91 (89)**
7	$[Cp^*RhCl_2]_2$ (5)	$AgNTf_2$ (10)	17
8	$[Cp^*RhCl_2]_2$ (5)	$Cu(OAc)_2{\cdot}H_2O$ (10)	17[d]
9	$[Cp^*RhCl_2]_2$ (2.5)	$Cu(OAc)_2{\cdot}H_2O$ (5)	87 (85)[e]
10	$[Cp^*IrCl_2]_2$ (2.5)	$Cu(OAc)_2{\cdot}H_2O$ (5)	N.R.
11	$[Ru(p\text{-cymene})Cl_2]_2$ (2.5)	$Cu(OAc)_2{\cdot}H_2O$ (5)	N.R.

[a]Reaction conditions: **1a** (0.125 mmol), **2** (0.10 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol %), and $Cu(OAc)_2{\cdot}H_2O$ (5 mol %) in DMF (0.5 mL) at 110 °C for 24 h under an Ar atmosphere. [b]Crude yields were determined by ^1H NMR spectroscopy (internal standard: 1,1,2,2-tetrachloroethane). [c]Isolated yields are shown in parentheses. [d]Under an O_2 atmosphere (1 atm). [e]At 100 °C.

(5 mol %) was used in the presence of 1.0 equiv of $Cu(OAc)_2$ in DMF at 110 °C (Table 1, entry 1). The structure of the isolated product **3a** was unambiguously characterized by spectroscopic analysis and single-crystal X-ray diffraction. Control experiments showed that **3a** was not formed in the absence of either the rhodium catalyst or the copper additive (entries 2 and 3). Interestingly, the product yield increased when the the amount of the copper salt was reduced (entries 4 and 5). After extensive screening of the reaction parameters (see the Supporting Information for details), the highest reaction efficiency was obtained in a reaction using 2.5 mol % $[Cp^*RhCl_2]_2$ and 5 mol % $Cu(OAc)_2{\cdot}H_2O$ in DMF at 110 °C when the alkyne was employed as the limiting reagent (entry 6). Although an additional study is required, we presently assume that the copper additive converts the $[Cp^*RhCl_2]_2$ precursor to its acetate derivative in situ, which catalyzes the desired reaction more efficiently. The use of $AgNTf_2$ as the additive instead of the copper salt or reaction under an O_2 atmosphere resulted in decreased product yields (entries 7 and 8), and the reaction efficiency was slightly decreased at lower temperature (entry 9). The present reaction did not occur when other catalytic systems were applied, such as iridium or ruthenium catalysts (entries 10 and 11).

With the optimized conditions in hand, we successfully reacted a wide range of *N*-heteroaromatic oxides with diphenylacetylene to afford functionalized *N*-heteroaryl products (Scheme 2). The reaction was shown to be compatible with several substituents that are frequently employed in synthetic chemistry. In addition, the position of substituent(s) in the *N*-heteroaromatic oxide did not affect the reaction efficiency. For instance, quinoline *N*-oxides substituted with a methyl group at C2, C3, C4, and/or C6 underwent the desired reaction in high yields with excellent regioselectivity (**3b**–**f**). However, a reaction of 7-methylquinoline *N*-oxide was rather sluggish and give a moderate product yield (**3g**), presumably for steric reasons.

6-Methoxyquinoline *N*-oxide reacted smoothly under the optimal conditions to afford **3h** in good yield. Halide-substituted quinoline *N*-oxides were employed to examine the functional group tolerance of the present reaction conditions. Pleasingly, the reactions of substrates bearing a fluoro, chloro, bromo, or iodo group were smooth, leading to the corresponding halide-bearing products in moderate to good yields (**3i**–**m**). The solid-state structures of products **3m** and **3l** were obtained by X-ray diffraction analysis (see the Supporting Information). The functional group tolerance of the current conditions was also demonstrated in a reaction of a quinoline *N*-oxide substituted with a free hydroxyl group (**3n**). A range of carbonyl and carboxyl groups were observed to be compatible with the reaction conditions, including acetal, aldehyde, ketone, ester, and carbamate (**3o**–**s**). The present catalytic procedure is also applicable to the reaction of polyaromatic *N*-oxides such as anthracene (**3u**), phenanthridine (**3v**), and benzo[*f*]quinoline (**3w**).

Next, the scope of the alkyne coupling partner was examined (Scheme 3). While a wide range of symmetrical diarylacetylenes could readily be reacted with quinoline *N*-oxide **1a**, electron-withdrawing substituents afforded higher product yields (**5a**–**h**) compared with diphenylalkynes bearing electron-donating groups. Again, sensitive functional groups such as halides or carbonyls were completely compatible with the present reaction conditions. Not only diphenylacetylenes with *para* disubstitution but also a substrate disubstituted at the *meta* positions also underwent the desired reaction, albeit in moderate yield (**5i**).[13] In addition, reactions of **1a** with unsymmetrically substituted diarylacetylenes yielded mixtures of regioisomeric products in almost equal amounts. For instance, the reaction of 4-*tert*-butylphenyl-4′-methoxyphenylacetylene with **1a** afforded two isomers in similar yields (**5jA** and **5jB**). Reactions of diarylacetylenes substituted on only one aryl group were smooth but led to a similar ratio of two isomeric products (**5kA**/**B**–**5nA**/**B**). The solid-state structure of product **5kB** was obtained by X-ray diffraction analysis (see the Supporting Information). Interestingly, the coupling of a diyne reactant proceeded in moderate yields (**5nA**/**B**). On the other hand, monosubstituted aryl- or aliphatic alkynes did not react with quinoline *N*-oxides under the present conditions. It is interesting to compare our reaction procedure with that of Li[12] in that the

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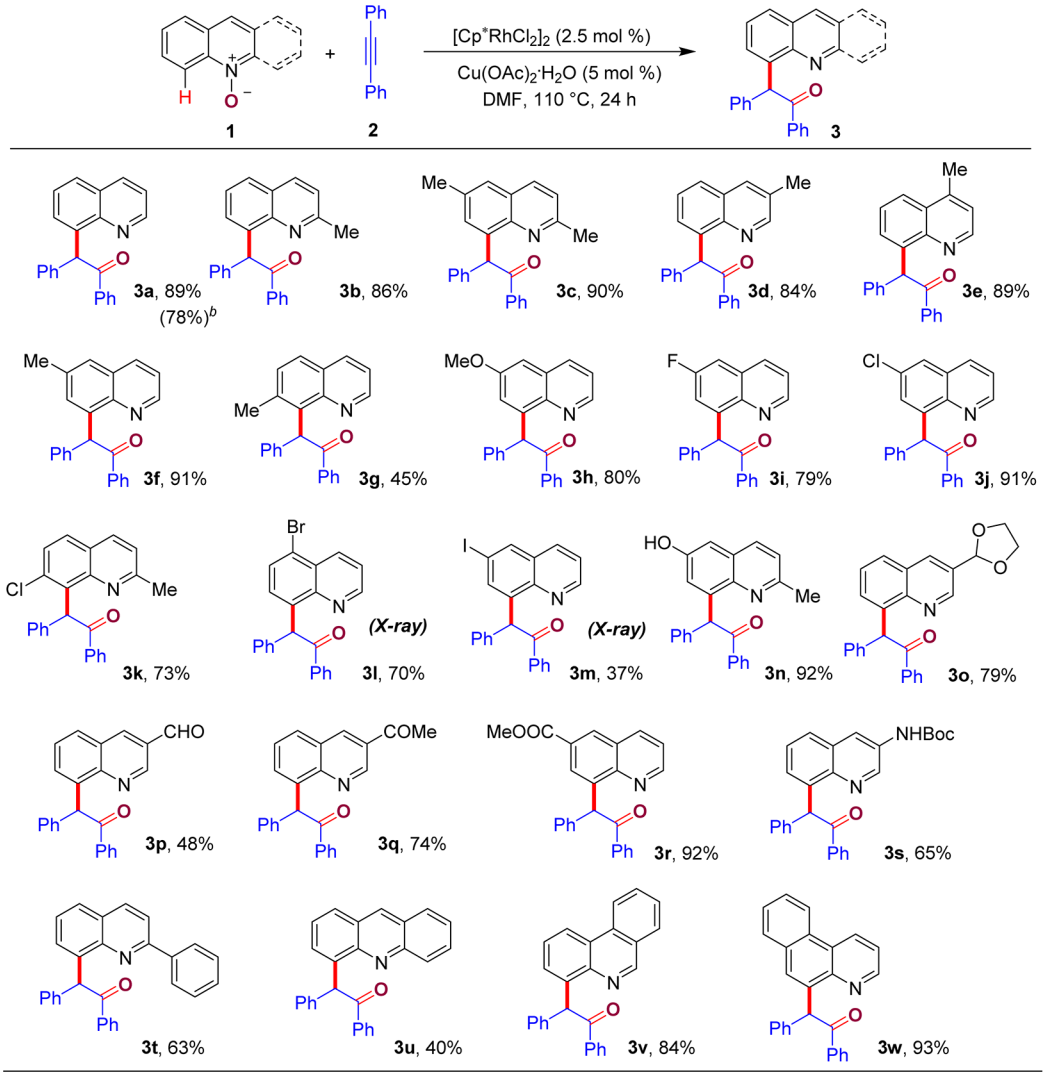
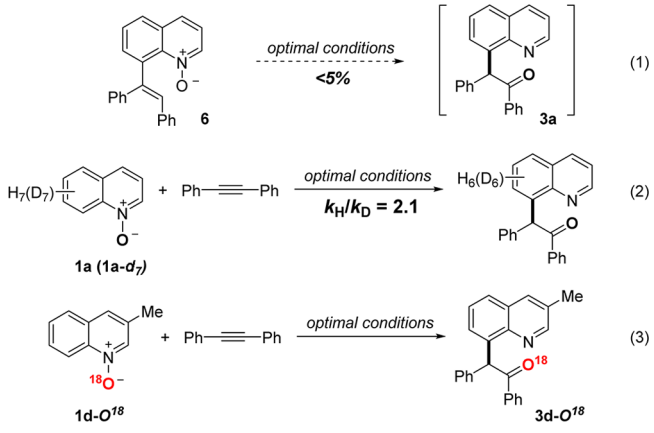
Scheme 2. Scope of *N*-Heteroaromatic *N*-Oxides[a]



[a]Reaction conditions: **1** (0.25 mmol), **2** (0.2 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol %), and $Cu(OAc)_2{\cdot}H_2O$ (5 mol %) in DMF (0.5 mL) at 110 °C for 24 h under an Ar atmosphere. [b]Reaction conditions: **1** (6.0 mmol), **2** (5.0 mmol), $[Cp^*RhCl_2]_2$ (5.0 mol %), and $Cu(OAc)_2{\cdot}H_2O$ (10 mol %) in DMF (12.5 mL) at 110 °C for 36 h under an Ar atmosphere.

present method employs only a copper additive (5 mol %) while acetic acid (2 equiv) and $Zn(OTf)_2$ (20 mol %) were added in addition to $AgSbF_6$ (20 mol %) in Li's procedure. In addition, more examples of functional group tolerance are presented in our study.

To shed light on the mechanistic understanding of the reaction, a brief series of preliminary experiments were carried out. When compound **6**, which could be formed by the insertion of diphenylacetylene into an initially generated rhodacycle of quinoline *N*-oxide, was prepared separately and subjected to the reaction conditions, significant conversion did not occur (eq 1), which implies that the reaction may not involve such a discrete insertion intermediate. Parallel competition reactions between **1a** and its deuterated analogue **1a-*d*$_7$** were performed and revealed a notable kinetic isotope effect (k_H/k_D = 2.1; eq 2), suggesting that the C−H bond cleavage would be rate-limiting in the overall process.[14] When a quinoline *N*-oxide labeled with ^{18}O (**1d-*O*^{18}**) was allowed to react with diphenylacetylene, the corresponding product (**3d-*O*^{18}**) was obtained with full incorporation of the ^{18}O atom in the ketone moiety in



the product (eq 3). This result clearly shows that the *N*-oxide of the substrate not only directs the remote C−H activation but also delivers an oxygen atom. Further detailed studies will be required to fully understand the exact pathway of this reaction, in particular in respect to the oxygen transfer process.

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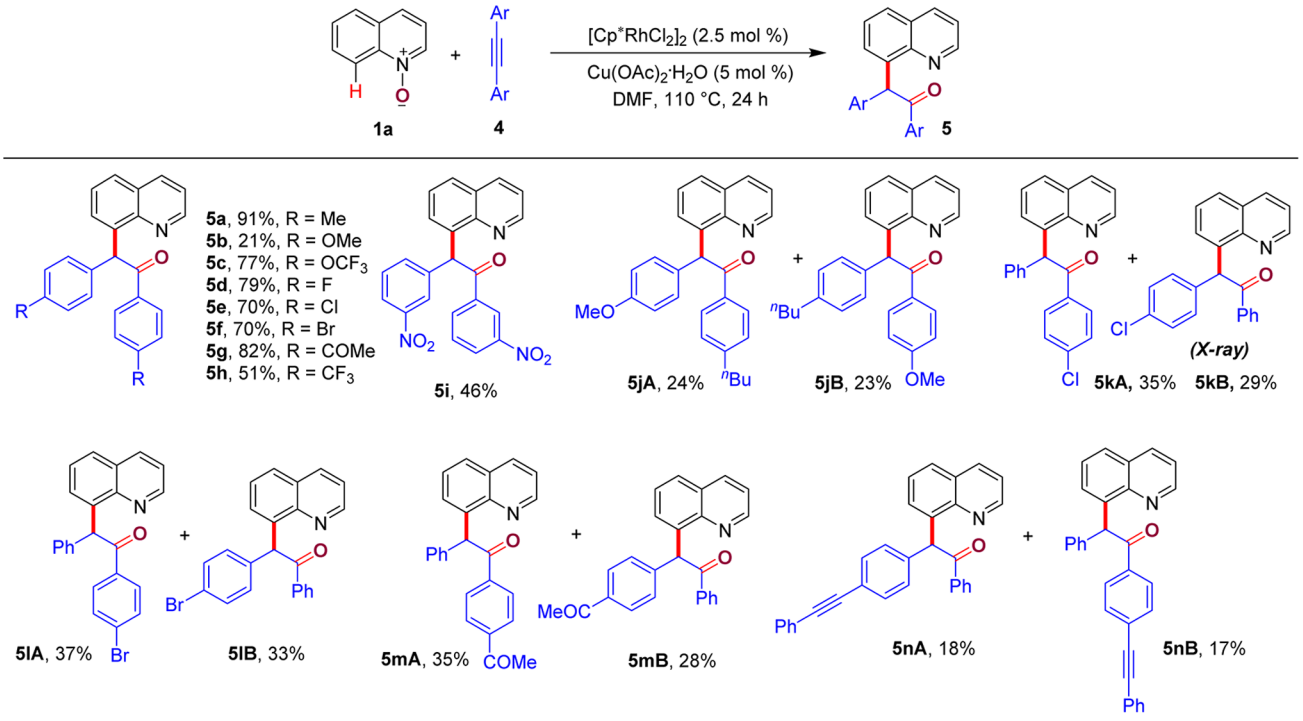
Scheme 3. Scope of Alkynes[a]



[a]Reaction conditions: **1** (0.25 mmol), **4** (0.2 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol %), and $Cu(OAc)_2·H_2O$ (5 mol %) in DMF (0.5 mL) at 110 °C for 24 h under an Ar atmosphere.

In conclusion, we have developed the Rh(III)-catalyzed direct C8 functionalization of quinoline *N*-oxides by reaction with internal diarylalkynes to deliver 2-(quinolin-8-yl)-1,2-diaryl-ethanone products. In this reaction, the *N*-oxide plays a dual role, acting as a traceless directing group as well as a source of oxygen atom, as confirmed by an ^{18}O-labeling experiment. This reaction proceeds with complete regioselectivity at the C8 position of the quinoline with good tolerance of various functional groups.

EXPERIMENTAL SECTION

General Methods. Unless otherwise stated, all reactions were carried out under an argon atmosphere in a glovebox. Qualitative analyses of reaction mixtures were performed by thin-layer chromatography. All isolated compounds were characterized by ^1H and ^{13}C NMR spectroscopy and high-resolution mass spectrometry (HRMS). Compounds were also characterized using gas chromatography−mass spectrometry (GC−MS) whenever required. ^1H NMR chemical shifts are reported in units of parts per million and were measured relative to the signals for residual chloroform (7.26 ppm) in the deuterated solvent or 0.0 ppm for tetramethylsilane. $^{13}C\{^1H\}$ NMR chemical shifts are reported in parts per million relative to deuterochloroform (77.0 ppm), unless otherwise stated, and all were obtained with ^1H decoupling. All coupling constant (J) values are reported in hertz. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of doublets of doublets (ddd), doublet of triplets (dt), triplet (t), triplet of doublets (td), quartet (q), and multiplet (m). HRMS spectra were obtained using the EI method (analyzer type: magnetic sector−electric sector, MS/MS) or the ESI method (analyzer type: quadrupole-TOF, MS/MS). Infrared spectra were collected with an FT-IR spectrometer using an ATR module.

Preparation of Substrates. Quinoline *N*-oxides **1**,[9] diarylalkynes **2**,[15] and (*E*)-8-(1,2-diphenylvinyl)quinoline *N*-oxide (**6**)[10] were prepared according to the previously reported procedures.

General Procedure for the Rhodium-Catalyzed Coupling of Quinoline *N*-Oxides with Alkynes To Give 2-(Quinolin-8-yl)-1,2-diarylethanones. To an oven-dried screw-capped vial (1 mL) charged with a Spinvane triangular-shaped Teflon stirbar were added $[Cp^*RhCl_2]_2$ (3.1 mg, 2.5 mol %), $Cu(OAc)_2·H_2O$ (2.0 mg, 5 mol %), quinoline *N*-oxide **1** (0.25 mmol), and alkyne **2** (0.20 mmol) under an argon atmosphere in a glovebox. Subsequently, solvent (0.5 mL) was added using a laboratory syringe. The reaction mixture was put in a preheated oil bath at 110 °C for 24 h with vigorous stirring. After cooling to room temperature, the reaction mixture was filtered through Celite and washed with EtOAc. The organic layer was further washed with water (3 mL × 5) to remove traces of DMF and copper salt and dried over sodium sulfate. Finally, the solvent was removed under reduced pressure. The residue was purified by flash chromatography using petroleum ether/ethyl acetate as the eluent.

*1,2-Diphenyl-2-(quinolin-8-yl)ethanone (Scheme 2, **3a**).*[12] White solid (57.5 mg, 89%); mp 131−132 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.87 (dd, J = 4.2, 1.8 Hz, 1H), 8.19−8.18 (m, 2H), 8.13 (dd, J = 8.3, 1.8 Hz, 1H), 7.73 (dd, J = 7.9, 1.8 Hz, 1H), 7.51−7.36 (m, 11H), 7.33−7.30 (m, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 199.1, 149.5, 145.7, 139.0, 138.3, 137.4, 136.3, 132.5, 129.9, 129.0, 128.8, 128.5, 128.4, 127.2, 127.1, 126.3, 121.2, 53.8; HRMS (EI) m/z calcd for $C_{23}H_{17}NO$ $[M]^+$ 323.1310, found 323.1307.

*2-(2-Methylquinolin-8-yl)-1,2-diphenylethanone (Scheme 2, **3b**).*[12] Greenish crystalline solid (58.0 mg, 86%); mp 161−162 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.18−8.17 (m, 2H), 8.00 (d, J = 8.3 Hz, 1H), 7.67 (dd, J = 8.1, 1.4 Hz, 1H), 7.50 (tt, J = 8.0, 1.4 Hz, 3H), 7.43−7.29 (m, 9H), 7.24 (d, J = 8.4 Hz, 1H), 2.53 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 199.6, 158.0, 145.1, 139.0, 138.0, 137.9, 136.2, 132.3, 130.1, 129.4, 128.9, 128.8, 128.3, 127.1, 126.6, 126.4, 125.3, 121.9, 54.2, 25.1; HRMS (EI) m/z calcd for $C_{24}H_{19}NO$ $[M]^+$ 337.1467, found 337.1469.

*2-(2,6-Dimethylquinolin-8-yl)-1,2-diphenylethanone (Scheme 2, **3c**).*[12] Colorless gummy solid (63.2 mg, 90%); ^1H NMR (600 MHz, $CDCl_3$) δ 8.18−8.16 (m, 2H), 7.91 (d, J = 8.3 Hz, 1H), 7.49 (tt, J = 7.1, 1.4 Hz, 3H), 7.43−7.39 (m, 5H), 7.33−7.29 (m, 2H), 7.20 (d, J = 8.3 Hz, 1H), 7.14 (d, J = 1.9 Hz, 1H), 2.52 (s, 3H), 2.41 (d, J = 1.0 Hz, 3H);

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$^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 199.7, 157.0, 143.7, 138.5, 138.0, 135.5, 135.0, 132.3, 131.5, 130.0, 128.9, 128.7, 128.3, 127.1, 126.5, 125.6, 121.9, 54.0, 25.0, 21.7; HRMS (EI) m/z calcd for $C_{25}H_{21}NO$ $[M]^+$ 351.1623, found 351.1624.

*2-(3-Methylquinolin-8-yl)-1,2-diphenylethanone (Scheme 2, **3d**).*[12] Yellow solid (56.7 mg, 84%); mp 110−111 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.71 (d, J = 2.2 Hz, 1H), 8.15−8.13 (m, 2H), 7.89 (dd, J = 2.3, 1.2 Hz, 1H), 7.65 (dd, J = 8.1, 1.4 Hz, 1H), 7.49−7.26 (m, 11H), 2.49 (d, J = 1.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 199.2, 151.5, 144.1, 138.7, 138.3, 137.5, 134.9, 132.5, 130.5, 129.9, 129.0, 128.8, 128.7, 128.4, 128.2, 127.1, 126.5, 126.3, 53.9, 18.6; HRMS (EI) m/z calcd for $C_{24}H_{19}NO$ $[M]^+$ 337.1467, found 337.1463.

*2-(4-Methylquinolin-8-yl)-1,2-diphenylethanone (Scheme 2, **3e**).*[12] Light-yellow solid (60.1 mg, 89%); mp 143−144 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.70 (d, J = 4.3 Hz, 1H), 8.14 (dt, J = 7.1, 1.4 Hz, 2H), 7.91 (dd, J = 8.3, 1.4 Hz, 1H), 7.49−7.45 (m, 5H), 7.41−7.35 (m, 5H), 7.30−7.27 (m, 1H), 7.21−7.20 (m, 1H), 2.68 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 199.2, 149.2, 145.5, 144.4, 139.5, 138.4, 137.5, 132.5, 129.9, 129.5, 129.0, 128.8, 128.4, 128.4, 127.1, 125.9, 123.1, 122.0, 54.2, 18.9; HRMS (ESI) m/z calcd for $C_{24}H_{20}NO$ $[M + H]^+$ 338.1545, found 338.1537.

*2-(6-Methylquinolin-8-yl)-1,2-diphenylethanone (Scheme 2, **3f**).*[12] White solid (61.4 mg, 91%); mp 130−131 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.79 (dd, J = 4.3, 1.8 Hz, 1H), 8.13 (dt, J = 7.3, 1.4 Hz, 2H), 8.04 (dd, J = 8.4, 1.8 Hz, 1H), 7.49−7.44 (m, 5H), 7.40−7.33 (m, 5H), 7.30−7.26 (m, 2H), 2.44 (d, J = 1.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 199.2, 148.7, 138.3, 137.4, 136.1, 135.5, 132.6, 132.0, 129.8, 129.0, 128.7, 128.5, 128.4, 127.1, 126.0, 121.2, 53.6, 21.8; HRMS (EI) m/z calcd for $C_{24}H_{19}NO$ $[M]^+$ 337.1467, found 337.1463.

*2-(7-Methylquinolin-8-yl)-1,2-diphenylethanone (Scheme 2, **3g**).* White solid (30.4 mg, 45%); mp 156−157 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.82 (dd, J = 4.3, 1.8 Hz, 1H), 8.04 (dd, J = 8.2, 1.8 Hz, 1H), 7.81 (dt, J = 7.5, 1.3 Hz, 2H), 7.65 (d, J = 8.3 Hz, 1H), 7.38−7.36 (m, 1H), 7.29−7.14 (m, 10H), 6.92 (s, 1H), 2.50 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 199.1, 149.3, 145.9, 138.7, 138.5, 138.3, 136.2, 135.9, 131.6, 130.7, 129.8, 128.1, 128.0, 127.9, 127.0, 126.9, 126.5, 120.4, 54.4, 21.9; IR (diamond) 1685, 1597, 1494, 1446, 1265, 1208, 1003, 825, 730, 693 cm^{-1}; HRMS (EI) m/z calcd for $C_{24}H_{19}NO$ $[M]^+$ 337.1467, found 337.1466.

*2-(6-Methoxyquinolin-8-yl)-1,2-diphenylethanone (Scheme 2, **3h**).*[12] White solid (56.5 mg, 80%); mp 131−132 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.68 (t, J = 3.0 Hz, 1H), 8.13−8.12 (m, 2H), 8.03 (d, J = 8.2 Hz, 1H), 7.50−7.44 (m, 3H), 7.41−7.26 (m, 7H), 7.06 (s, 1H), 6.97 (d, J = 2.8 Hz, 1H), 3.85 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 198.7, 157.3, 147.0, 142.1, 140.9, 137.7, 137.4, 134.8, 132.5, 129.8, 129.5, 129.0, 128.8, 128.4, 127.2, 123.1, 121.5, 104.1, 55.3, 53.9; HRMS (EI) m/z calcd for $C_{24}H_{19}NO_2$ $[M]^+$ 353.1416, found 353.1415.

*2-(6-Fluoroquinolin-8-yl)-1,2-diphenylethanone (Scheme 2, **3i**).*[12] White solid (53.9 mg, 79%); mp 107−108 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.78 (dd, J = 4.2, 1.7 Hz, 1H), 8.16−8.14 (m, 2H), 8.07 (dd, J = 8.3, 1.7 Hz, 1H), 7.52−7.31 (m, 11H), 7.18 (dd, J = 9.6, 2.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 198.4, 160.2 (d, J = 246.7 Hz), 148.6 (d, J = 2.7 Hz), 143.0, 142.6 (d, J = 8.7 Hz), 137.3 (d, J = 23.4 Hz), 135.7 (d, J = 5.6 Hz), 132.7, 129.8, 129.1, 129.1 (d, J = 9.0 Hz), 129.0, 129.0, 128.5, 127.5, 121.9, 120.7 (d, J = 27.2 Hz), 109.7 (d, J = 21.4 Hz), 54.0; HRMS (EI) m/z calcd for $C_{23}H_{16}FNO$ $[M]^+$ 341.1216, found 341.1215.

*2-(6-Chloroquinolin-8-yl)-1,2-diphenylethanone (Scheme 2, **3j**).*[12] White solid (65.1 mg, 91%); mp 145−146 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.80 (dd, J = 4.3, 1.7 Hz, 1H), 8.15−8.13 (m, 2H), 8.03 (dd, J = 8.3, 1.7 Hz, 1H), 7.71 (d, J = 2.3 Hz, 1H), 7.50−7.30 (m, 11H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 198.4, 149.6, 144.2, 141.4, 137.3, 137.2, 135.4, 132.7, 132.3, 130.9, 129.8, 129.1, 129.0, 128.9, 128.5, 127.5, 125.6, 122.0, 53.8; HRMS (EI) m/z calcd for $C_{23}H_{16}ClNO$ $[M]^+$ 357.0920, found 357.0920.

*2-(7-Chloro-2-methylquinolin-8-yl)-1,2-diphenylethanone (Scheme 2, **3k**).* White solid (54.3 mg, 73%); mp 184−185 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 7.84 (d, J = 8.4 Hz, 1H), 7.77−7.75 (m, 2H), 7.5−7.43 (m, 4H), 7.31−7.22 (m, 4H), 7.18−7.12 (m, 3H), 6.49 (s, 1H), 2.65 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 197.5, 159.0, 145.4, 138.8, 138.1, 136.6, 135.9, 134.9, 131.3, 130.4, 128.1, 127.8, 127.7, 127.6, 127.5, 126.9, 125.3, 122.0, 55.9, 24.5; IR (diamond) 1693, 1593, 1493, 1205, 1129, 831, 752, 693, 562 cm^{-1}; HRMS (EI) m/z calcd for $C_{24}H_{18}ClNO$ $[M]^+$ 371.1077, found 371.1075.

*2-(5-Bromoquinolin-8-yl)-1,2-diphenylethanone (Scheme 2, **3l**).* White crystalline solid (56.3 mg, 70%); mp 177−178 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.84 (dd, J = 4.2, 1.6 Hz, 1H), 8.53 (dd, J = 8.5, 1.6 Hz, 1H), 8.10 (dd, J = 8.1, 1.4 Hz, 2H), 7.73 (d, J = 7.8 Hz, 1H), 7.51−7.48 (m, 2H), 7.42−7.34 (m, 7H), 7.31−7.28 (m, 1H), 7.21 (d, J = 7.9 Hz, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 198.7, 150.0, 146.4, 136.7, 132.7, 130.3, 123.0, 129.8, 129.0, 128.5, 127.6, 127.3, 122.2, 121.0, 53.9; IR (diamond) 2922, 2853, 1677, 1486, 1447, 1211, 826, 734, 626, 531 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{16}BrNO$ $[M]^+$ 401.0415, found 401.0411.

*2-(6-Iodoquinolin-8-yl)-1,2-diphenylethanone (Scheme 2, **3m**).* White crystalline solid (33.2 mg, 37%); mp 149−150 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.80 (dd, J = 4.2, 1.7 Hz, 1H), 8.12−8.09 (m, 3H), 7.99 (dd, J = 8.3, 1.7 Hz, 1H), 7.56 (d, J = 1.9 Hz, 1H), 7.51−7.47 (m, 1H), 7.43−7.34 (m, 8H), 7.31−7.28 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 198.5, 149.9, 144.9, 141.2, 138.4, 137.3, 137.2, 135.9, 135.0, 132.7, 129.9, 129.8, 129.1, 129.0, 128.5, 127.5, 121.8, 92.3, 53.6; IR (diamond) 2922, 2853, 1679, 1580, 1445, 1242, 1211, 875, 779, 757, 696, 682, 569 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{16}INNaO$ $[M + Na]^+$ 472.0174, found 472.0178.

*2-(6-Hydroxy-2-methylquinolin-8-yl)-1,2-diphenylethanone (Scheme 2, **3n**).* White solid (65.0 mg, 92%); mp 187−188 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.17 (dd, J = 8.2, 1.5 Hz, 2H), 7.59 (d, J = 8.4 Hz, 1H), 7.52−7.49 (m, 1H), 7.46−7.41 (m, 4H), 7.35 (t, J = 7.7 Hz, 2H), 7.30−7.26 (m, 1H), 7.21 (s, 1H), 7.10 (d, J = 8.4 Hz, 1H), 6.81 (d, J = 2.6 Hz, 1H), 6.60 (d, J = 2.7 Hz, 1H), 6.00 (d, J = 5.0 Hz, 1H), 2.43 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 200.6, 155.1, 152.9, 140.9, 140.5, 137.8, 137.1, 134.8, 132.6, 130.0, 129.0, 129.0, 128.3, 127.3, 127.3, 122.0, 122.0, 108.0, 54.4, 24.7; IR (diamond) 3375, 1665, 1618, 1598, 1385, 1211, 854, 719, 689, 577 cm^{-1}; HRMS (EI) m/z calcd for $C_{24}H_{19}NO_2$ $[M]^+$ 353.1416, found 353.1412.

*2-[3-(1,3-Dioxolan-2-yl)quinolin-8-yl]-1,2-diphenylethanone (Scheme 2, **3o**).* Light-yellow solid (62.5 mg, 79%); mp 109−110 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.97 (d, J = 2.2 Hz, 1H), 8.23 (d, J = 2.1 Hz, 1H), 8.14−8.12 (m, 2H), 7.76 (dd, J = 8.0, 1.5 Hz, 1H), 7.50−7.27 (m, 11H), 6.03 (s, 1H), 4.17−4.03 (m, 4H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 199.0, 148.3, 146.0, 139.0, 138.2, 137.4, 134.2, 132.6, 131.0, 130.2, 129.9, 129.0, 128.8, 128.4, 127.6, 127.4, 127.2, 126.7, 102.3, 65.5, 65.5, 53.9; IR (diamond) 2884, 1677, 1492, 1211, 1072, 982, 763, 731, 572 cm^{-1}; HRMS (EI) m/z calcd for $C_{26}H_{21}NO_3$ $[M]^+$ 395.1521, found 395.1523.

*8-(2-Oxo-1,2-diphenylethyl)quinoline-3-carbaldehyde (Scheme 2, **3p**).* Light-yellow solid (33.7 mg, 48%); mp 182−183 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 10.20 (s, 1H), 9.25 (d, J = 2.1 Hz, 1H), 8.58 (d, J = 2.1 Hz, 1H), 8.11 (dd, J = 8.2, 1.4 Hz, 2H), 7.86 (dd, J = 8.0, 1.6 Hz, 1H), 7.55−7.35 (m, 10H), 7.30−7.28 (m, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 198.7, 190.7, 148.3, 148.1, 140.1, 139.8, 137.6, 137.2, 133.0, 132.7, 129.8, 129.0, 128.9, 128.6, 128.5, 128.5, 127.6, 127.4, 127.1, 54.0; IR (diamond) 1698, 1676, 1596, 1492, 1212, 761, 733, 696, 571 cm^{-1}; HRMS (EI) m/z calcd for $C_{24}H_{17}NO_2$ $[M]^+$ 351.1259, found 351.1260.

*2-(3-Acetylquinolin-8-yl)-1,2-diphenylethanone (Scheme 2, **3q**).* Light-yellow solid (54.1 mg, 74%); mp 198−199 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 9.34 (d, J = 2.2 Hz, 1H), 8.69 (d, J = 2.2 Hz, 1H), 8.13−8.12 (m, 2H), 7.84 (dd, J = 8.0, 1.5 Hz, 1H), 7.54−7.37 (m, 10H), 7.31−7.29 (m, 1H), 2.71 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 198.8, 196.7, 148.3, 147.3, 139.5, 137.7, 137.5, 132.7, 132.2, 129.8, 129.3, 129.0, 129.0, 128.5, 128.5, 127.4, 127.3, 126.9, 54.0, 26.8; IR (diamond) 1681, 1596, 1269, 1214, 767, 694, 615, 567 cm^{-1}; HRMS (EI) m/z calcd for $C_{25}H_{19}NO_2$ $[M]^+$ 365.1416, found 365.1414.

*Methyl 8-(2-Oxo-1,2-diphenylethyl)quinoline-6-carboxylate (Scheme 2, **3r**).* Light-yellow solid (70.2 mg, 92%); mp 98−99 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.92 (dd, J = 4.4, 1.8 Hz, 1H), 8.51

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(d, J = 1.8 Hz, 1H), 8.23 (dd, J = 8.2, 1.5 Hz, 1H), 8.14−8.12 (m, 2H), 8.01 (d, J = 1.8 Hz, 1H), 7.50−7.37 (m, 9H), 7.31−7.29 (m, 1H), 3.91 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 198.6, 166.5, 151.5, 147.5, 139.7, 137.7, 137.6, 137.2, 132.7, 130.3, 129.8, 129.2, 129.0, 128.5, 127.9, 127.5, 127.4, 121.9, 53.9, 52.3; IR (diamond) 1711, 1679, 1437, 1220, 1186, 784, 733, 577 cm^{-1}; HRMS (EI) m/z calcd for $C_{25}H_{19}NO_3$ $[M]^+$ 381.1365, found 381.1364.

tert-Butyl 8-(2-Oxo-1,2-diphenylethyl)quinolin-3-ylcarbamate (Scheme 2, ***3s****).* Light-yellow solid (57.0 mg, 65%); mp 193−194 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.49 (d, J = 2.5 Hz, 1H), 8.17 (s, 1H), 8.09 (dd, J = 8.2, 1.4 Hz, 2H), 7.58 (dd, J = 8.2, 1.3 Hz, 1H), 7.48−7.43 (m, 3H), 7.35 (q, J = 8.2 Hz, 5H), 7.28−7.24 (m, 2H), 7.18 (d, J = 7.1 Hz, 1H), 6.95 (s, 1H), 1.52 (s, 9H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 199.5, 152.7, 142.6, 141.9, 138.6, 137.9, 137.4, 132.5, 132.2, 129.9, 128.9, 128.8, 128.4, 128.0, 127.2, 126.8, 126.7, 121.8, 81.0, 54.2, 28.3; IR (diamond) 3324, 1723, 1673, 1485, 1243, 1157, 1064, 756, 734 cm^{-1}; HRMS (EI) m/z calcd for $C_{28}H_{26}N_2O_3$ $[M]^+$ 438.1943, found 438.1941.

1,2-Diphenyl-2-(2-phenylquinolin-8-yl)ethanone (Scheme 2, ***3t****).* Light-brown solid (50.3 mg, 63%); mp 144−145 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.20 (d, J = 8.2 Hz, 3H), 7.89 (d, J = 8.5 Hz, 1H), 7.83−7.81 (m, 2H), 7.73 (dd, J = 8.0, 1.4 Hz, 1H), 7.58−7.52 (m, 3H), 7.43 (dt, J = 14.9, 7.4 Hz, 6H), 7.35−7.21 (m, 5H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 198.9, 155.8, 145.4, 139.9, 139.2, 137.6, 137.4, 137.1, 132.6, 130.1, 130.0, 129.1, 129.1, 129.0, 128.6, 128.5, 127.3, 127.2, 126.7, 126.0, 118.5, 54.5; IR (diamond) 1683, 1596, 1487, 1445, 1323, 1205, 831, 764, 686, 630 cm^{-1}; HRMS (EI) m/z calcd for $C_{29}H_{21}NO$ $[M]^+$ 399.1623, found 399.1621.

2-(Acridin-4-yl)-1,2-diphenylethanone (Scheme 2, ***3u****).* Yellow solid (29.9 mg, 40%); mp 149−150 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.23−8.21 (m, 2H), 7.97−7.95 (m, 1H), 7.90−7.88 (m, 1H), 7.85−7.83 (m, 1H), 7.64 (ddd, J = 8.5, 6.6, 1.4 Hz, 1H), 7.55−7.52 (m, 3H), 7.48−7.38 (m, 7H), 7.34−7.30 (m, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 199.5, 148.1, 146.6, 139.9, 138.1, 137.5, 135.9, 132.4, 130.1, 130.1, 129.8, 129.6, 128.9, 128.8, 128.4, 127.9, 127.3, 127.2, 126.6, 126.6, 125.6, 125.4, 54.7; IR (diamond) 1671, 1446, 1204, 985, 756, 738, 693, 561 cm^{-1}; HRMS (EI) m/z calcd for $C_{27}H_{19}NO$ $[M]^+$ 373.1467, found 373.1463.

2-(Phenanthridin-4-yl)-1,2-diphenylethanone (Scheme 2, ***3v****).* White crystalline solid (62.7 mg, 84%); mp 166−167 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 9.22 (s, 1H), 8.58 (d, J = 8.3 Hz, 1H), 8.49 (d, J = 8.2 Hz, 1H), 8.18−8.17 (m, 2H), 7.98 (d, J = 7.9 Hz, 1H), 7.81 (m, 1H), 7.66 (t, J = 7.5 Hz, 1H), 7.61−7.57 (m, 2H), 7.53−7.37 (m, 8H), 7.29 (t, J = 7.5 Hz, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 199.3, 152.5, 141.7, 139.6, 138.5, 137.5, 132.7, 132.5, 130.9, 129.9, 129.2, 129.0, 128.8, 128.6, 128.4, 127.4, 127.1, 126.7, 126.3, 124.2, 122.1, 121.4, 54.4; IR (diamond) 1679, 1587, 1445, 1237, 1212, 1009, 749, 703, 658 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{19}NNaO$ $[M + Na]^+$ 396.1364, found 396.1365.

2-(Benzo[f]quinolin-5-yl)-1,2-diphenylethanone (Scheme 2, ***3w****).* White solid (69.5 mg, 93%); mp 145−146 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.92 (dd, J = 8.4, 1.6 Hz, 1H), 8.85 (dd, J = 4.3, 1.6 Hz, 1H), 8.55 (d, J = 8.1 Hz, 1H), 8.19−8.18 (m, 2H), 7.79 (dd, J = 7.9, 1.4 Hz, 1H), 7.64−7.48 (m, 7H), 7.43−7.40 (m, 5H), 7.35−7.32 (m, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 199.1, 148.7, 146.0, 137.8, 137.6, 132.5, 131.4, 131.1, 130.9, 130.1, 129.3, 129.0, 128.9, 128.9, 128.5, 127.3, 127.3, 126.9, 125.6, 122.3, 121.4, 54.5; IR (diamond) 1680, 1449, 1378, 1235, 1205, 750, 688, 586 cm^{-1}; HRMS (EI) m/z calcd for $C_{27}H_{19}NO$ $[M]^+$ 373.1467, found 373.1468.

2-(Quinolin-8-yl)-1,2-di-p-tolylethanone (Scheme 3, ***5a****).*[12] Light-yellow resin (64.0 mg, 91%); ^1H NMR (600 MHz, $CDCl_3$) δ 8.85 (dd, J = 4.2, 1.8 Hz, 1H), 8.12−8.06 (m, 3H), 7.71 (dd, J = 7.5, 2.0 Hz, 1H), 7.47−7.43 (m, 3H), 7.37−7.35 (m, 3H), 7.19 (t, J = 7.6 Hz, 4H), 2.35 (d, J = 8.8 Hz, 6H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 198.8, 149.5, 145.9, 143.2, 139.3, 136.6, 136.2, 135.4, 134.9, 129.8, 129.7, 129.5, 129.1, 128.4, 127.0, 126.3, 121.1, 53.3, 21.6, 21.1; HRMS (EI) m/z calcd for $C_{25}H_{21}NO$ $[M]^+$ 351.1623, found 351.1620.

1,2-Bis(4-methoxyphenyl)-2-(quinolin-8-yl)ethanone (Scheme 3, ***5b****).*[12] Light-yellow resin (16.1 mg, 21%); ^1H NMR (600 MHz, $CDCl_3$) δ 8.84 (dd, J = 4.2, 1.8 Hz, 1H), 8.12−8.09 (m, 3H), 7.70 (dd, J = 7.8, 1.8 Hz, 1H), 7.46−7.42 (m, 2H), 7.38−7.34 (m, 4H), 6.89−6.84 (m, 4H), 3.80 (s, 3H), 3.77 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 197.8, 163.0, 158.6, 149.5, 145.8, 139.4, 136.2, 131.2, 130.8, 130.7, 130.3, 129.7, 128.4, 126.9, 126.3, 121.1, 114.2, 113.6, 55.3, 55.2, 52.5; HRMS (EI) m/z calcd for $C_{25}H_{21}NO_3$ $[M]^+$ 383.1521, found 383.1520.

2-(Quinolin-8-yl)-1,2-bis(4-(trifluoromethoxy)phenyl)ethanone (Scheme 3, ***5c****).* White solid (75.7 mg, 77%); mp 116−117 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.88 (dd, J = 4.2, 1.8 Hz, 1H), 8.17−8.14 (m, 3H), 7.76 (dd, J = 8.1, 1.5 Hz, 1H), 7.49−7.41 (m, 6H), 7.22−7.19 (m, 4H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 197.3, 152.4, 149.8, 148.4, 145.4, 137.9, 136.6, 136.4, 135.3, 131.1, 131.1, 130.9, 129.4, 128.6, 127.6, 126.3, 121.4, 121.0, 120.5 (q, J = 256.5 Hz), 120.3 (q, J = 256.5 Hz), 120.2, 52.8; IR (diamond) 1674, 1602, 1508, 1305, 1242, 1203, 1157, 1077, 997, 815, 538 cm^{-1}; HRMS (EI) m/z calcd for $C_{25}H_{15}F_6NO_3$ $[M]^+$ 491.0956, found 491.0957.

1,2-Bis(4-fluorophenyl)-2-(quinolin-8-yl)ethanone (Scheme 3, ***5d****).* Light-yellow crystalline solid (56.8 mg, 79%); mp 138−139 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.86 (dd, J = 4.2, 1.8 Hz, 1H), 8.15−8.12 (m, 3H), 7.74 (dd, J = 8.2, 1.4 Hz, 1H), 7.46 (t, J = 7.7 Hz, 1H), 7.42−7.38, 5H), 7.04 (td, J = 8.7, 2.6 Hz, 4H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 197.5, 165.4 (d, J = 253.5 Hz), 162.0 (d, J = 246.0 Hz), 149.7, 145.5, 138.5, 136.3, 133.8 (d, J = 3.0 Hz), 133.5 (d, J = 3.0 Hz), 131.5 (d, J = 9.0 Hz), 131.3 (d, J = 7.5 Hz), 129.5, 128.4, 127.4, 126.3, 121.3, 115.7 (d, J = 10.5 Hz), 115.6 (d, J = 12.0 Hz), 52.8; IR (diamond) 1676, 1593, 1505, 1211, 1152, 997, 811, 760, 757, 596 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{15}F_2NNaO$ $[M + Na]^+$ 382.1019, found 382.0997.

1,2-Bis(4-chlorophenyl)-2-(quinolin-8-yl)ethanone (Scheme 3, ***5e****).*[12] Light-yellow crystalline solid (54.9 mg, 70%); mp 137−138 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.84 (dd, J = 4.2, 1.7 Hz, 1H), 8.14 (dd, J = 8.2, 1.7 Hz, 1H), 8.03−8.01 (m, 2H), 7.74 (dd, J = 8.2, 1.4 Hz, 1H), 7.46 (t, J = 7.7 Hz, 1H), 7.41−7.31 (m, 9H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 197.6, 149.7, 145.5, 139.1, 138.1, 136.5, 136.3, 135.4, 133.2, 131.1, 130.3, 129.5, 128.9, 128.8, 128.5, 127.5, 126.3, 121.4, 53.0; HRMS (ESI) m/z calcd for $C_{23}H_{15}Cl_2NNaO$ $[M + Na]^+$ 414.0428, found 414.0412.

1,2-Bis(4-bromophenyl)-2-(quinolin-8-yl)ethanone (Scheme 3, ***5f****).*[12] Light-yellow solid (67.4 mg, 70%); mp 151−152 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.85 (dd, J = 4.2, 1.8 Hz, 1H), 8.16 (dd, J = 8.2, 1.8 Hz, 1H), 7.96−7.94 (m, 2H), 7.75 (dd, J = 8.1, 1.4 Hz, 1H), 7.53−7.51 (m, 2H), 7.49−7.46 (m, 3H), 7.42 (dd, J = 8.2, 4.2 Hz, 1H), 7.39−7.35 (m, 2H), 7.3−7.29 (m, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 197.7, 149.6, 145.3, 137.9, 137.0, 136.5, 135.8, 131.9, 131.8, 131.5, 130.5, 129.6, 128.5, 127.9, 127.5, 126.3, 121.4, 121.3, 53.0; HRMS (EI) m/z calcd for $C_{23}H_{15}Br_2NO$ $[M]^+$ 478.9520, found 478.9520.

1,2-Bis(4-acetylphenyl)-2-(quinolin-8-yl)ethanone (Scheme 3, ***5g****).* Light-yellow resin (66.8 mg, 82%); ^1H NMR (600 MHz, $CDCl_3$) δ 8.84 (dd, J = 4.3, 1.7 Hz, 1H), 8.16−8.14 (m, 3H), 7.93 (dd, J = 8.5, 2.2 Hz, 4H), 7.75 (dd, J = 8.1, 1.4 Hz, 1H), 7.53−7.52 (m, 2H), 7.48−7.44 (m, 2H), 7.41−7.40 (m, 1H), 7.37−7.36 (m, 1H), 2.57 (s, 1H), 2.56 (s, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 198.0, 197.6, 197.4, 149.7, 145.4, 143.3, 140.4, 139.9, 137.7, 136.4, 136.1, 130.1, 129.5, 129.0, 128.8, 128.5, 128.4, 127.7, 126.3, 121.5, 54.0, 26.8, 26.6; IR (diamond) 1670, 1603, 1496, 1357, 1261, 957, 818, 791, 728 cm^{-1}; HRMS (EI) m/z calcd for $C_{27}H_{21}NO_3$ $[M]^+$ 407.1521, found 407.1519.

2-(Quinolin-8-yl)-1,2-bis[4-(trifluoromethyl)phenyl]ethanone (Scheme 3, ***5h****).*[12] Light-yellow solid (46.9 mg, 51%); mp 167−168 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.87 (dd, J = 4.2, 1.7 Hz, 1H), 8.22−8.16 (m, 3H), 7.77 (dd, J = 8.2, 1.4 Hz, 1H), 7.65−7.61 (m, 4H), 7.57 (d, J = 8.2 Hz, 2H), 7.51 (s, 1H), 7.48 (t, J = 7.7 Hz, 1H), 7.43 (dd, J = 8.3, 4.2 Hz, 1H), 7.40 (dd, J = 7.3, 1.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 197.6, 149.8, 145.3, 141.7, 139.8, 137.5, 136.4, 134.1 (q, J = 31.5 Hz), 130.2, 129.7, 129.5, 129.4, 128.6, 127.8, 126.3, 125.7, 125.7, 125.6 (q, J = 271.5 Hz), 123.8 (q, J = 271.5 Hz), 121.5, 53.7; HRMS (ESI) m/z calcd for $C_{25}H_{16}F_6NO$ $[M + H]^+$ 460.1136, found 460.1138.

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*1,2-Bis(3-nitrophenyl)-2-(quinolin-8-yl)ethanone (Scheme 3, **5i**).* Light-yellow solid (38.0 mg, 46%); mp 189−190 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.99−8.96 (m, 2H), 8.36 (dt, J = 7.8, 1.3 Hz, 1H), 8.34 (t, J = 2.0 Hz, 1H), 8.30−8.31 (m, 1H), 8.18 (dd, J = 8.3, 1.7 Hz, 1H), 8.12−8.14 (m, 1H), 7.83−7.79 (m, 2H), 7.66 (s, 1H), 7.55−7.47 (m, 5H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 196.1, 150.3, 148.5, 148.4, 145.0, 139.8, 138.0, 136.6, 136.3, 135.9, 134.2, 129.8, 129.4, 129.2, 128.8, 128.4, 127.3, 126.4, 124.7, 123.9, 122.4, 121.9, 52.8; IR (diamond) 1686, 1530, 1349, 1217, 1088, 815, 705 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{15}N_3O_5$ [M]$^+$ 413.1012, found 413.1009.

*1-(4-Butylphenyl)-2-(4-methoxyphenyl)-2-(quinolin-8-yl)-ethanone (Scheme 3, **5jA**).* Light-yellow resin (19.7 mg, 24%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.85 (dd, J = 4.2, 1.8 Hz, 1H), 8.13 (dd, J = 8.3, 1.8 Hz, 1H), 8.05−8.03 (m, 2H), 7.71 (dd, J = 8.1, 1.5 Hz, 1H), 7.46 (t, J = 7.6 Hz, 1H), 7.42−7.41 (m, 1H), 7.39−7.35 (m, 4H), 7.20−7.18 (m, 2H), 6.91−6.89 (m, 2H), 3.78 (s, 3H), 2.63−2.60 (m, 2H), 1.61−1.56 (m, 2H), 1.37−1.31 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 198.9, 158.6, 149.5, 148.0, 145.8, 139.4, 136.1, 135.0, 130.8, 130.5, 129.7, 129.1, 128.5, 128.4, 126.9, 126.2, 121.1, 114.2, 55.2, 52.8, 35.6, 33.1, 22.3, 13.9; IR (diamond) 2928, 1679, 1605, 1509, 1464, 1245, 1176, 819, 790, 603, 534 cm^{-1}; HRMS (EI) m/z calcd for $C_{28}H_{27}NO_2$ [M]$^+$ 409.2042, found 409.2040.

*2-(4-Butylphenyl)-1-(4-methoxyphenyl)-2-(quinolin-8-yl)-ethanone (Scheme 3, **5jB**).* Light-yellow resin (18.8 mg, 23%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.86 (dd, J = 4.2, 1.8 Hz, 1H), 8.14−8.11 (m, 3H), 7.71 (dd, J = 6.7, 2.8 Hz, 1H), 7.47−7.43 (m, 3H), 7.37 (dd, J = 8.2, 4.2 Hz, 1H), 7.34 (d, J = 8.0 Hz, 2H), 7.16−7.15 (m, 2H), 6.89−6.85 (m, 2H), 3.81 (s, 3H), 2.60−2.57 (m, 2H), 1.61−1.56 (m, 2H), 1.38−1.32 (m, 2H), 0.92 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 197.7, 163.0, 149.5, 145.9, 141.5, 139.2, 136.2, 135.8, 131.3, 130.4, 129.8, 129.6, 128.7, 128.4, 126.9, 126.3, 121.0, 113.6, 55.3, 52.8, 35.3, 33.5, 22.4, 13.9; IR (diamond) 2927, 1673, 1597, 1574, 1503, 1310, 1252, 1216, 1105, 795, 600 cm^{-1}; HRMS (EI) m/z calcd for $C_{28}H_{27}NO_2$ [M]$^+$ 409.2042, found 409.2039.

*1-(4-Chlorophenyl)-2-phenyl-2-(quinolin-8-yl)ethanone (Scheme 3, **5kA**).* White solid (25.0 mg, 35%); mp 115−116 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.83 (dd, J = 4.2, 1.7 Hz, 1H), 8.15 (dd, J = 8.2, 1.8 Hz, 1H), 8.08−8.05 (m, 2H), 7.74−7.73 (m, 1H), 7.45−7.43 (m, 3H), 7.40−7.36 (m, 7H), 7.32−7.28 (m, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 197.9, 149.5, 145.7, 138.9, 138.8, 137.8, 136.2, 135.8, 130.7, 129.8, 129.8, 128.9, 128.7, 128.4, 127.3, 127.2, 126.3, 121.2, 53.9; IR (diamond) 1681, 1585, 1396, 1206, 1091, 993, 783 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{16}ClNO$ [M]$^+$ 357.0920, found 357.0922.

*2-(4-Chlorophenyl)-1-phenyl-2-(quinolin-8-yl)ethanone (Scheme 3, **5kB**).* White crystalline solid (20.8 mg, 29%); mp 156−157 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.87 (dd, J = 4.2, 1.8 Hz, 1H), 8.15 (dd, J = 8.2, 1.8 Hz, 1H), 8.09−8.07 (m, 2H), 7.74 (dd, J = 8.2, 1.5 Hz, 1H), 7.50−7.45 (m, 3H), 7.42−7.36 (m, 6H), 7.32−7.30 (m, 2H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 198.8, 149.7, 145.6, 138.3, 137.1, 136.9, 136.3, 133.0, 132.7, 131.1, 129.5, 128.9, 128.8, 128.5, 128.5, 127.3, 126.3, 121.3, 52.9; IR (diamond) 2922, 1675, 1491, 1087, 756, 716, 687, 602 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{16}ClNO$ [M]$^+$ 357.0920, found 357.0919.

*1-(4-Bromophenyl)-2-phenyl-2-(quinolin-8-yl)ethanone (Scheme 3, **5lA**).* White solid (29.8 mg, 37%); mp 72−73 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.82 (dd, J = 4.2, 1.8 Hz, 1H), 8.13 (dd, J = 8.2, 1.8 Hz, 1H), 7.99−7.97 (m, 2H), 7.72 (dd, J = 8.2, 1.4 Hz, 1H), 7.53−7.51 (m, 2H), 7.46−7.41 (m, 3H), 7.38−7.33 (m, 5H), 7.30−7.27 (m, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 198.1, 149.5, 145.7, 138.8, 137.7, 136.2, 136.2, 131.7, 130.5, 129.8, 129.8, 128.9, 128.4, 127.6, 127.3, 127.2, 126.2, 121.2, 53.9; IR (diamond) 2918, 1680, 1581, 1493, 1392, 1206, 1070, 992, 784, 700, 570 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{16}BrNO$ [M]$^+$ 401.0415, found 401.0416.

*2-(4-Bromophenyl)-1-phenyl-2-(quinolin-8-yl)ethanone (Scheme 3, **5lB**).* White crystalline solid (26.6 mg, 33%); mp 149−150 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.85 (dd, J = 4.2, 1.8 Hz, 1H), 8.14 (dd, J = 8.2, 1.7 Hz, 1H), 8.08−8.06 (m, 2H), 7.73 (dd, J = 8.1, 1.5 Hz, 1H), 7.49−7.43 (m, 5H), 7.41−7.36 (m, 4H), 7.32−7.29 (m, 2H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 198.7, 149.7, 145.6, 138.2, 137.5, 137.0, 136.3, 132.7, 131.7, 131.5, 129.5, 128.9, 128.5, 128.5, 127.3, 126.3, 121.3, 121.2, 52.9; IR (diamond) 2919, 1674, 1485, 1011, 895, 789, 773, 686, 667, 593 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{16}BrNO$ [M]$^+$ 401.0415, found 401.0411.

*1-(4-Acetylphenyl)-2-phenyl-2-(quinolin-8-yl)ethanone (Scheme 3, **5mA**).* Light-yellow resin (25.6 mg, 35%); ^{1}H NMR (600 MHz, $CDCl_3$) 8.80 (dd, J = 4.2, 1.7 Hz, 1H), 8.18−8.16 (m, 2H), 8.14−8.13 (m, 1H), 7.96−7.94 (m, 2H), 7.73 (dd, J = 8.2, 1.3 Hz, 1H), 7.46−7.42 (m, 3H), 7.39−7.35 (m, 3H), 7.32−7.29 (m, 3H), 2.58 (s, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 198.6, 197.5, 149.5, 145.6, 141.0, 139.6, 138.8, 137.4, 136.2, 129.9, 129.7, 129.0, 128.9, 128.4, 128.3, 127.4, 127.2, 126.2, 121.2, 54.5, 26.8; IR (diamond) 1670, 1596, 1493, 1259, 1210, 1075, 995, 787, 697, 589 cm^{-1}; HRMS (EI) m/z calcd for $C_{25}H_{19}NO_2$ [M]$^+$ 365.1416, found 365.1412.

*2-(4-Acetylphenyl)-1-phenyl-2-(quinolin-8-yl)ethanone (Scheme 3, **5mB**).* Light-yellow resin (20.5 mg, 28%); ^{1}H NMR (600 MHz, $CDCl_3$) 8.87 (dd, J = 4.2, 1.8 Hz, 1H), 8.14 (dd, J = 8.3, 1.8 Hz, 1H), 8.09−8.07 (m, 2H), 7.95−7.91 (m, 2H), 7.74 (dd, J = 7.9, 1.6 Hz, 1H), 7.57 (s, 1H), 7.53−7.51 (m, 2H), 7.49−7.36 (m, 6H), 2.56 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 198.5, 197.7, 149.8, 145.56, 144.1, 137.8, 137.0, 136.3, 135.9, 132.8, 130.0, 129.6, 128.9, 128.6, 128.5, 128.5, 127.5, 126.3, 121.3, 53.4, 26.5; IR (diamond) 1677, 1603, 1495, 1357, 1265, 819, 792 cm^{-1}; HRMS (EI) m/z calcd for $C_{25}H_{19}NO_2$ [M]$^+$ 365.1416, found 365.1414.

*1-Phenyl-2-[4-(phenylethynyl)phenyl]-2-(quinolin-8-yl)ethanone (Scheme 3, **5nA**).* Light-yellow solid (15.2 mg, 18%); mp 145−146 °C; ^{1}H NMR (600 MHz, $CDCl_3$) 8.86 (dd, J = 4.5, 1.7 Hz, 1H), 8.17 (d, J = 8.2 Hz, 1H), 8.11 (d, J = 8.1 Hz, 2H), 7.74 (d, J = 8.1 Hz, 1H), 7.54−7.50 (m, 4H), 7.49−7.40 (m, 5H), 7.38−7.34 (m, 5H), 7.29 (t, J = 7.4 Hz, 2H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 198.3, 149.4, 138.7, 138.0, 136.6, 131.7, 131.6, 130.0, 129.8, 128.9, 128.8, 128.6, 128.4, 128.4, 127.6, 127.2, 127.2, 126.4, 122.8, 121.2, 92.3, 88.8, 53.89; IR (diamond) 2923, 2853, 2210, 1680, 1594, 1492, 1211, 753, 685, 569 cm^{-1}; HRMS (EI) m/z calcd for $C_{31}H_{21}NO$ [M]$^+$ 423.1623, found 423.1625.

*2-Phenyl-1-[4-(phenylethynyl)phenyl]-2-(quinolin-8-yl)ethanone (Scheme 3, **5nB**).* Light-brown solid (14.4 mg, 17%); mp 193−194 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.87 (dd, J = 4.1, 1.8 Hz, 1H), 8.18−8.14 (m, 1H), 8.12 (dd, J = 8.1, 1.5 Hz, 2H), 7.75 (dd, J = 8.2, 1.4 Hz, 1H), 7.54−7.47 (m, 7H), 7.44−7.36 (m, 6H), 7.34−7.30 (m, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 198.8, 149.6, 145.7, 138.7, 138.8, 137.2, 136.5, 132.7, 131.9, 131.6, 129.8, 129.7, 128.9, 128.4, 128.4, 128.3, 128.2, 127.2, 126.3, 123.3, 122.1, 121.2, 89.6, 89.1, 53.6; IR (diamond) 2924, 1679, 1595, 1494, 1199, 1001, 814, 757, 689 cm^{-1}; HRMS (EI) m/z calcd for $C_{31}H_{21}NO$ [M]$^+$ 423.1623, found 423.1626.

Procedure for the Kinetic Isotope Effect Studies (eq 2). To a J. Young NMR tube were added quinoline *N*-oxide (**1a**) (18.1 mg, 0.125 mmol) or quinoline-*N*-oxide-d_7 (**1a-*d*$_7$**) (19.0 mg, 0.125 mmol), diphenylacetylene (**2a**) (17.8 mg, 0.10 mmol), $[Cp^*RhCl_2]_2$ (6.2 mg, 10 mol %), and $Cu(OAc)_2{\cdot}H_2O$ (4.0 mg, 20 mol %) in 1,1,2,2-tetrachloroethane (16.8 mg, 0.10 mmol, internal standard), and *N*,*N*-dimethylformamide-d_7 (0.5 mL) under an Ar atmosphere. The crude product yield was recorded using NMR spectroscopy relative to 1,1,2,2,-tetrachloroethane as an internal standard every 1 min for 6 h at 90 °C. The initial rate was measured by plotting points to give a KIE value of 2.08.

Preparation of ^{18}O-Labeled 3-Methylquinoline *N*-Oxide (eq 3, 1d-*O*^{18}).[16] A mixture of 3-methylquinoline (71.6 mg, 0.5 mmol) and $MeReO_3$ (1.24 mg, 1 mol %) in dichloromethane (2 mL) was treated with 1 mL of 2−3% aqueous $H_2{}^{18}O_2$ (0.5 mmol in $H_2{}^{18}O$) and stirred for 6 h at 25 °C. The reaction mixture was then treated with a catalytic amount of MnO_2 (1 mg) and stirred until oxygen evolution ceased (1 h). Following phase separation, the water layer was extracted with EtOAc (3 × 5 mL), and the combined organic layers were dried over Na_2SO_4 and filtered. The solvent was evaporated, and the residue was purified by flash chromatography using petroleum ether/ethyl acetate as the eluent to give ^{18}O-labeled 3-methylquinoline *N*-oxide in 15% yield (12 mg).

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■ ASSOCIATED CONTENT

Supporting Information

Optimization details; X-ray crystallographic data for **3a**, **3l**, **3m**, and **5kB**, including CIF files; KIE experiment; HRMS data for eq 3; and copies of ^{1}H and ^{13}C NMR spectra data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: sbchang@kaist.ac.kr.

Present Address

[§]U.S.: Natural Plant Products, CSIR-Institute of Himalayan Bioresource Technology, Kangra, Himachal Pradesh 176061, India.

Notes

The authors declare no competing financial interest.

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