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Employing Arylacetylene as a Diene Precursor and Dienophile: Synthesis of Quinoline via the Povarov Reaction

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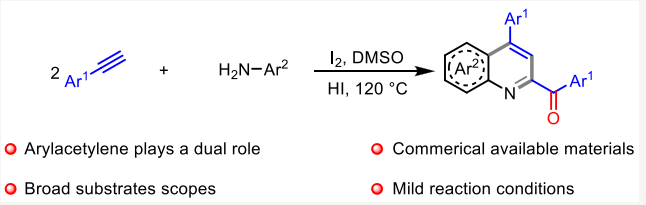
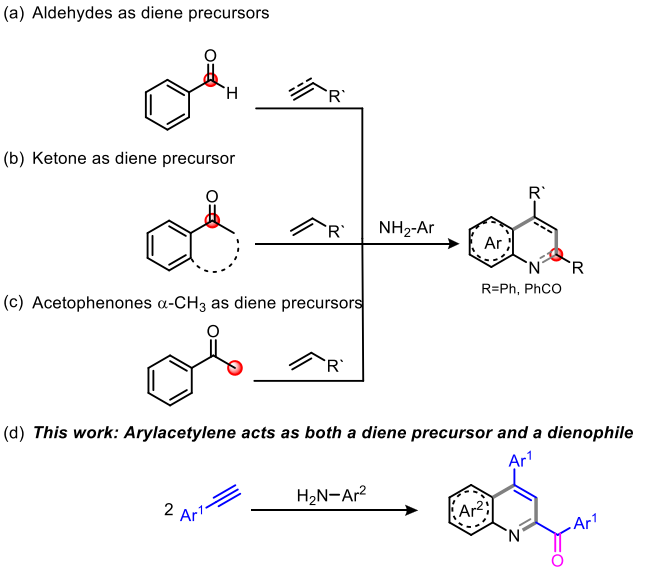
ABSTRACT: A novel I_2-mediated Povarov reaction of arylacetylenes and anilines for the synthesis of 2,4-substituted quinolines has been developed, in which arylacetylene first acts as both a diene precursor and dienophile. This work further develops the Povarov reaction to expand the types of diene precursors. Preliminary mechanistic studies indicate that the I_2/DMSO system realized the oxidative carbonylation of C(sp)−H of arylacetylene and then undergoes a [4 + 2] cycloaddition reaction.



Quinoline and their derivatives are important scaffolds widely found in natural products and pharmaceutical molecules.[1] In recent decades, numerous classic name reactions have been developed for the synthesis of quinoline, such as the Skraup quinoline synthesis[2] and the Friedländer quinoline synthesis.[3] Among them, the Povarov reaction, a formal [4 + 2] cycloaddition reaction of 2-azadienes with dienophiles, is a highly efficient strategy that has recently been widely used in quinoline synthesis.[4] Aromatic imines, used as the dienes, are key reaction intermediates in the Povarov reaction, and their generation has received considerable research attention accordingly.[5] However, strategies mainly focused on aldehydes as their precursors[6] (Scheme 1a). Only one study has reported using a ketone carbonyl as the aromatic imine precursor in the Povarov reaction[7] (Scheme 1b). In 2014, our group has developed methyl ketones as aromatic imines precursors to construct 2,4-substituted quinoline,[8] via the oxidation of methyl ketone C(sp^3)−H bonds (Scheme 1c). However, as aromatic imine precursors remain limited to carbonyl compounds, the development of new precursors has become a valuable research area. Arylacetylene is usually used as a dienophile in the Povarov reaction,[5e,6b,f,9] but to the best of our knowledge, there have been no reports employing arylacetylene as the diene precursor. Recently, we fortunately found that quinoline can be synthesized in the I_2/DMSO system from simple and easily available starting materials arylacetylene and aniline, showing that arylacetylene can first play a dual role simultaneously and more importantly, providing a completely new method for quinoline synthesis via the Povarov reaction (Scheme 1d).

Based on the above experimental findings and our group's continued interest in the synthesis of nitrogen heterocycles,[10] we first optimized conditions for the reaction between phenylacetylene (**1a**) and *p*-toluidine (**2a**) (Table 1). Initially, it was found that the reaction led to the desired 2,4-substituded quinoline in 28% yield with 0.5 equiv of iodine in DMSO when

Scheme 1. Transformation of Arylacetylenes to Quinoline by Povarov Reaction



$Cu(OTf)_2$ was added (entry 1). Considering the equivalents of iodine has influence on the reaction yield, we next optimized the iodine equivalent, and 1.0 equiv was chosen as the best condition (entries 2−4). Next, we screened the different temperatures, and 120 °C gave the best result (entries 5−9).

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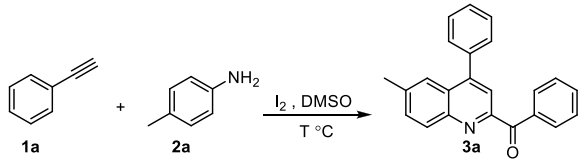
Table 1. Optimization of the Reaction Conditions[a]



Entry	I_2 (equiv)	Acid	Temp (°C)	Yield[b] (%)
1	0.5	$Cu(OTf)_2$	110	28
2	1.0	$Cu(OTf)_2$	110	32
3	1.6	$Cu(OTf)_2$	110	30
4	2.0	$Cu(OTf)_2$	110	25
5	1.0	$Cu(OTf)_2$	80	Trace
6	1.0	$Cu(OTf)_2$	100	30
7	1.0	$Cu(OTf)_2$	120	40
8	1.0	$Cu(OTf)_2$	130	38
9	1.0	$Cu(OTf)_2$	140	20
10[c]	1.0	$Cu(OTf)_2$	120	Trace
11[d]	1.0	$Cu(OTf)_2$	120	30
12[e]	1.0	$Cu(OTf)_2$	120	39
13	1.0	–	120	Trace
14	1.0	$Fe(OTf)_2$	120	30
15	1.0	$Fe(OTf)_3$	120	32
16	1.0	$FeCl_3$	120	30
17	1.0	HCl(36%)	120	20
18	1.0	HI(40%)	120	70
19	1.0	TfOH	120	40
20	1.0	TFA	120	45

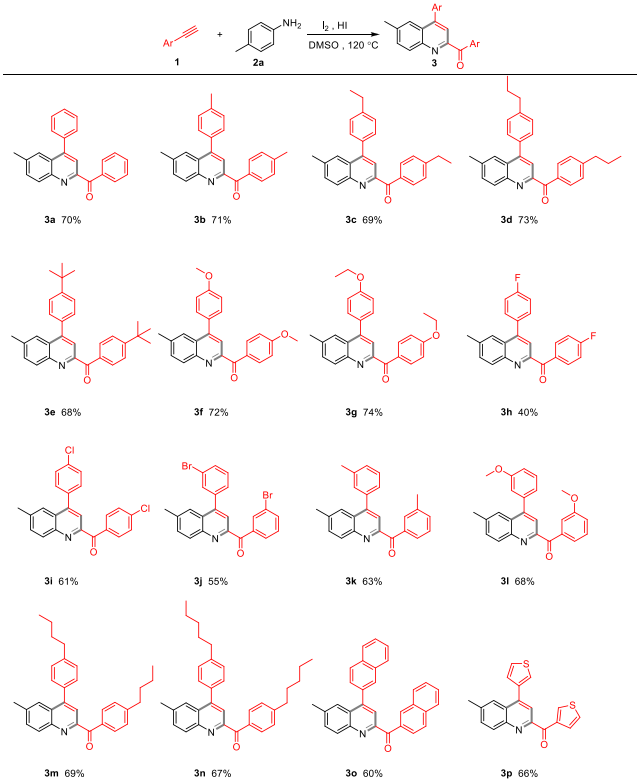
[a]Reaction conditions: **1a** (1.5 mmol), **2a** (0.5 mmol), I_2, acid (2.0 equiv), indicated temperature, DMSO 4 mL, 6 h, unless otherwise noted. [b]Products were obtained in isolated yields. [c]**1a** (0.5 mmol). [d]**1a** (1 mmol). [e]**1a** (2 mmol).

To further improve the reaction yield, we optimized the equivalent ratio of phenylacetylene to aniline, and 3:1 was the best ratio (entries 10−12). In addition, we also tried not to add any acid additives in the reaction, but the yield was trace (entry 13). Finally, various acid additives were further screened, including $Fe(OTf)_2$, $Fe(OTf)_3$, $FeCl_3$, HCl, HI, TfOH, and TFA (entries 14−20). To our delight, adding HI to the reaction afforded **3a** in a greatly improved yield of 70%.

With optimized conditions in hand, we next tested the effect of different phenylacetylene substituents on this transformation (Scheme 2). Phenylacetylene bearing electron-donating groups (−Me, −Et, −*n*-Pr, −*t*-Bu, −OMe, −OEt) at the *para*-position give the corresponding product in satisfactory yields (**3b**−**3g**, 68%−74%). Various halogen substituents, in either the *para*- or *meta*-position, were also compatible with the reaction (**3h**−**3j**, 40%−61%). The yields of products substituted by methyl and methoxy groups at the *meta*-position can also reach 63% and 68% (**3k**−**3l**) respectively. Long-chain substituents and large hindered substituents, such as naphthalene, afforded the desired compounds in moderate to good yields under the optimal conditions (**3m**−**3o**, 60%−69%). Fortunately, a heterocyclic thiophene-substituted alkyne was also compatible with this reaction, giving product **3p** in 66% yield. Finally, we tried to use alkyl alkynes in the reaction; unfortunately, alkyl alkynes were not compatible with the reaction under the optimal conditions.

To further examine the reaction scopes, a brief screening of other commercially available substituted aryl amines was conducted (Scheme 3). Both electron-donating groups (−Et, −*i*-Pr, −*t*-Bu, $-OCH_3$, and $-SCH_3$) and an electron-withdrawing group (−Ph) were compatible with the reaction, giving the product **4a**−**4f** in good yields (51%−72%). Furthermore, amines with a halogenated aromatic ring (−F, −Cl, −Br, $-OCF_3$) were readily transformed into halogenated products **4g**−**4j** in 50%−63% yields. A polysubstituted aromatic amine substrate also afforded corresponding polysubstituted quinoline product **4k** in 31% yield. Fortunately, large sterically hindered group naphthylamine was well tolerated in the reaction (**4l**, 40%). Finally, the reactions of *p*-OCH_3-amine with *p*-Et-arylacetylene and *p*-Et-amine with *m*-OCH_3-arylacetylene were conducted, giving the corresponding target compounds **4m** and **4n** in 68% and 67% yields, respectively.

Scheme 2. Substrate Scope for the Synthesis of 3[a,b]



[a]Reaction conditions: **1** (3 mmol), **2a** (1 mmol), I_2 (2 mmol), and HI (40% in water, 4 mmol) heated in 4 mL of DMSO. [b]Products were obtained in isolated yields.

To further understand the reaction mechanism of this novel process, a series of control experiments were conducted (Scheme 4). First, phenylacetylene reacted with iodine and DMSO at 120 °C when HI was added, giving phenylglyoxal in 43% yield (Scheme 4a). Next, under the standard conditions, we reacted *α*-iodophenone **1ab** as a substrate with *p*-toluidine **2a** and phenylacetylene **1a** giving the corresponding product **3a** in 72% yield (Scheme 4b). Furthermore, 2-hydroxyacetophenone (**1ac**) was reacted with **2a** and **1a** under the optimal conditions, affording **3a** in 74% yield (Scheme 4c). **3a** was also obtained in 73% yield when the hydrated species **1ad** was treated with *p*-toluidine (**2a**) and phenylacetylene (**1a**) under the optimal conditions (Scheme 4d). These results show that *α*-iodophenone, 2-hydroxyacetophenone, and phenylglyoxal were pivotal intermediates in this transformation. Finally, under the optimal conditions preprepared *C*-acylimine

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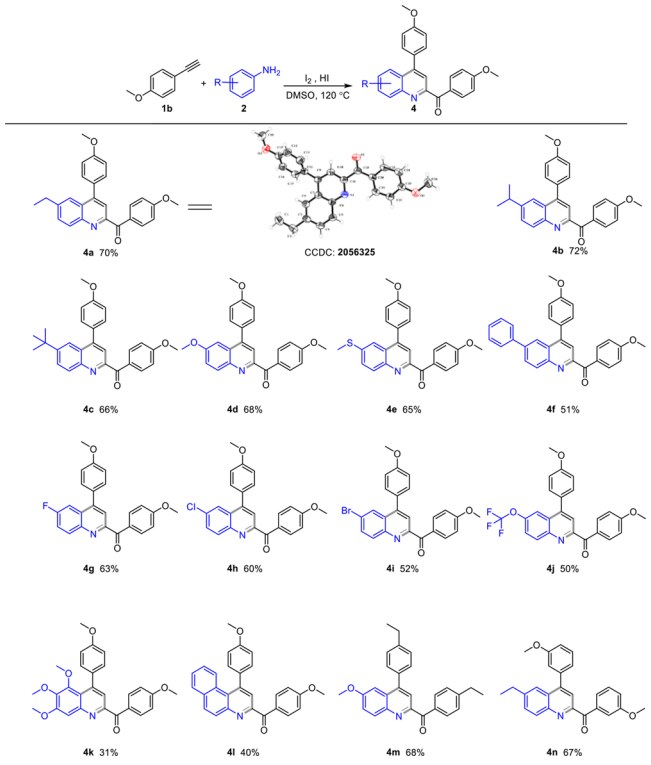
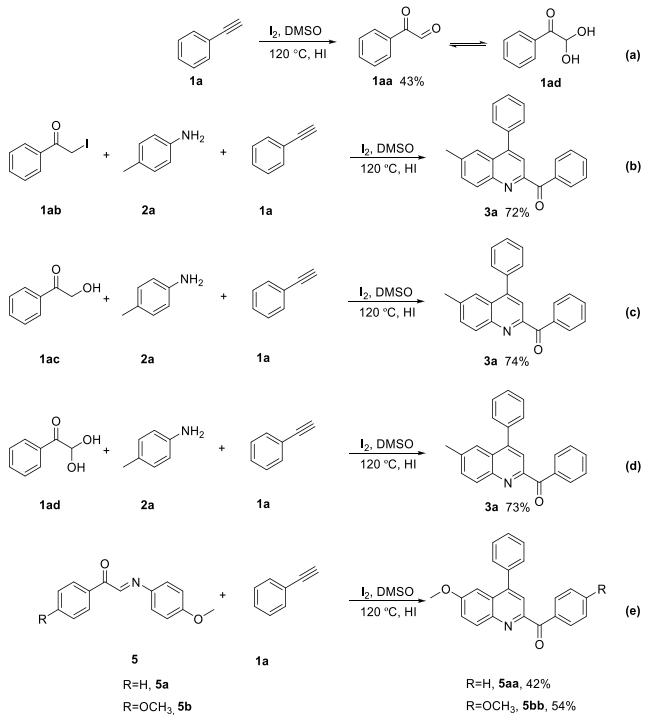
Scheme 3. Substrate Scope for the Synthesis of 4[a,b]



[a]Reaction conditions: **1a** (3 mmol), **2** (1 mmol), I_2 (2 mmol), and HI (40% in water, 4 mmol) heated in 4 mL of DMSO. [b]Products were obtained in isolated yields.

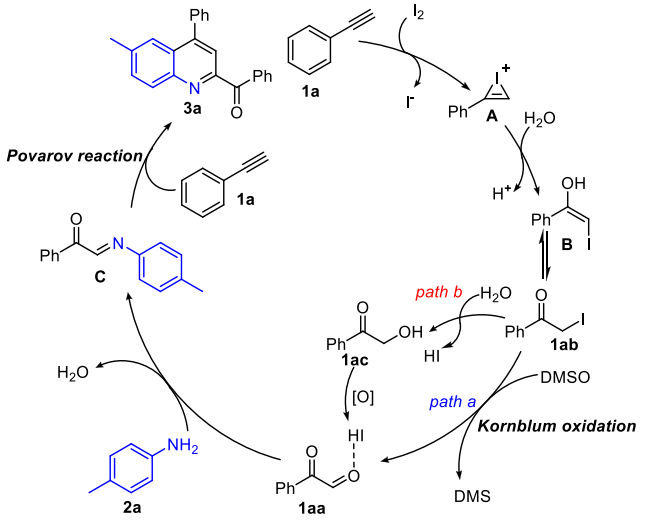
Scheme 4. Control Experiments



substrates **5** were reacted with **1a**; when R = H, the yield of **5aa** was 42%, and when R = OCH_3, asymmetric product **5bb** can be obtained in 54% yield (Scheme 4e), which showed that *C*-acylimine was a key intermediate in this reaction. Furthermore, the ^{18}O-labling experiment indicated that the source of carbonyl oxygen was mainly from H_2O (see the Supporting Information for details).

From the above control experiments and previous studies, the possible mechanism[10d,11] for the present reaction was proposed (Scheme 5). First, iodine activates phenylacetylene

Scheme 5. Proposed Mechanism



1a to afford iodonium cation **A** with release of I^-.[10d] Species **A** is then attacked by H_2O to give enol intermediate **B**. The enol intermediate **B** is then isomerized to α-iodophenone **1ab**. The conversion of **1ab** into **1aa** has two paths. In path a, **1ab** is converted to **1aa** by Kornblum oxidation, while, in path b, **1ab** reacts with H_2O to generate 2-hydroxyacetophenone **1ac**, which is then oxidized to **1aa**. Next, **1aa** is attacked by *p*-toluidine (**2a**) to afford *C*-acylimine **C**, which then reacts with another molecule of phenylacetylene (**1a**) via the Povarov reaction to obtain final product **3a**.

CONCLUSION

In conclusion, we have developed a novel method to generate quinolines using the Povarov reaction, in which arylacetylene first acts as both a diene precursor and dienophile. The C(sp)−H of arylacetylene is oxidized to an aldehyde by the I_2/DMSO system and then generates diene *C*-acylimine by reacting with aniline in situ. This development of the Povarov reaction greatly broadens the types of diene precursors applicable and expands the substrate scopes beyond carbonyl compounds. Further research of the new kind of diene precursor in the Povarov reaction to construct more nitrogen-containing heterocycles is underway in our laboratory.

EXPERIMENTAL SECTION

General Methods. All other substrates and reagents were commercially available and used without further purification. All new compounds were fully characterized. TLC analysis was performed using precoated glass plates. Column chromatography was performed using silica gel (200−300 mesh). ^1H, ^{13}C, and ^{19}F spectra were recorded in $CDCl_3$ on 400 MHz NMR spectrometers, and chemical shifts of ^1H NMR are reported in ppm, relative to the internal standard of tetramethylsilane (TMS, δ = 0.00 ppm). Chemical shifts of $^{13}C\{^1H\}$ NMR were reported in ppm with the solvent as the internal standard ($CDCl_3$, δ = 77.0 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d =

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doublet, t = triplet, m = multiplet), coupling constants (Hz), and integration. $^{13}C\{^1H\}$ spectra were recorded in $CDCl_3$ on 100 MHz NMR spectrometers, and resonances (δ) are given in ppm. ^{19}F spectra were recorded in $CDCl_3$ on 376 MHz NMR spectrometers, and resonances (δ) are given in ppm. HRMS data were obtained on a Bruker 7-T FT-ICR MS equipped with an electrospray source. The X-ray crystal-structure determinations of **4a** were obtained on a Bruker SMART APEX CCD system. Melting points were determined using an XT-4 apparatus and not corrected.

General Procedures for the Synthesis of Products 3 (3a as an Example). A mixture of phenylacetylene **1a** (3.0 mmol, 3 equiv), **2a** (1.0 mmol, 1 equiv) and hydriodic acid (40% in water, 4.0 mmol, 4 equiv), and iodine (2.0 mmol, 2 equiv) in DMSO (4 mL) was stirred at 120 °C in the metal heating block, until almost complete conversion of the substrates by TLC analysis. The mixture was then quenched with saturation $Na_2S_2O_3$ solution (50 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 40:1) to afford the product **3a**.

Analytical Data for Products 3a–4n. *(6-Methyl-4-phenylquinolin-2-yl)(phenyl)methanone (**3a**).* Yield 70%; 226.5 mg; yellow solid; column chromatography, silica gel (PE/EA, 40:1); mp 139–141 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.27–8.25 (m, 2H), 8.16 (d, J = 8.4 Hz, 1H), 8.02 (s, 1H), 7.75 (s, 1H), 7.64–7.61 (m, 2H), 7.56–7.50 (m, 7H), 2.51 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 193.9, 153.3, 148.8, 145.9, 138.8, 137.8, 136.3, 132.9, 132.2, 131.4, 130.6, 129.5, 128.6, 128.5, 128.1, 127.4, 124.5, 121.1, 22.0. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{23}H_{18}NO^+$, 324.1383; found, 324.1388.

*(6-Methyl-4-(p-tolyl)quinolin-2-yl)(p-tolyl)methanone (**3b**).* Yield 71%; 249.5 mg; yellow solid; column chromatography, silica gel (PE/EA, 40:1); mp 137–139 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.17–8.15 (m, 3H), 7.97 (s, 1H), 7.78 (s, 1H), 7.62–7.60 (m, 1H), 7.46 (d, J = 8.0 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 2.51 (s, 3H), 2.48 (s, 3H), 2.46 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 193.7, 153.7, 148.9, 145.8, 143.9, 138.6, 138.5, 134.9, 133.7, 132.1, 131.6, 130.5, 129.5, 129.3, 128.9, 127.5, 124.6, 121.1, 22.0, 21.8, 21.3. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{25}H_{22}NO^+$, 352.1696; found, 352.1705.

*(4-Ethylphenyl)(4-(4-ethylphenyl)-6-methylquinolin-2-yl)methanone (**3c**).* Yield 69%; 261.9 mg; white solid; column chromatography, silica gel (PE/EA, 40:1); mp 105–107 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.20–8.15 (m, 3H), 7.98 (s, 1H), 7.79 (s, 1H), 7.61 (d, J = 8.8 Hz, 1H), 7.49 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 2.78 (q, J = 7.6 Hz, 2H), 2.75 (q, J = 7.6 Hz, 2H), 2.51 (s, 3H), 1.34 (t, J = 7.6 Hz, 3H), 1.29 (t, J = 7.6 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 193.7, 153.7, 150.0, 148.9, 145.9, 144.7, 138.5, 135.2, 133.9, 132.1, 131.7, 130.5, 129.5, 128.1, 127.7, 127.5, 124.6, 121.1, 29.1, 28.7, 22.0, 15.4, 15.2. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{27}H_{26}NO^+$, 380.2009; found, 380.2014.

*(6-Methyl-4-(4-propylphenyl)quinolin-2-yl)(4-propylphenyl)methanone (**3d**).* Yield 73%; 297.5 mg; yellow solid; column chromatography, silica gel (PE/EA, 40:1); mp 92–94 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.20–8.15 (m, 3H), 7.98 (s, 1H), 7.80 (s, 1H), 7.60 (d, J = 8.8 Hz, 1H), 7.47 (d, J = 8.0 Hz, 2H), 7.37–7.31 (m, 4H), 2.73–2.66 (m, 4H), 2.51 (s, 3H), 1.77–1.67 (m, 4H), 1.03 (t, J = 7.2 Hz, 3H), 0.98 (t, J = 7.6 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 193.6, 153.7, 148.9, 148.5, 145.8, 143.2, 138.5, 135.2, 133.9, 132.1, 131.6, 130.5, 129.4, 128.7, 128.3, 127.5, 124.6, 121.1, 38.2, 37.8, 24.5, 24.2, 22.0, 13.9, 13.8. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{29}H_{30}NO^+$, 408.2322; found, 408.2335.

*(4-(tert-Butyl)phenyl)(4-(4-(tert-butyl)phenyl)-6-methylquinolin-2-yl)methanone (**3e**).* Yield 68%; 296.2 mg; column chromatography, silica gel (PE/EA, 40:1); yellow solid; mp 153–155 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.22–8.16 (m, 3H), 7.99 (s, 1H), 7.83 (s, 1H), 7.63–7.50 (m, 7H), 2.53 (s, 3H), 1.43 (s, 9H), 1.38 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 193.6, 156.7, 153.7, 151.6, 148.8, 145.9, 138.5, 134.9, 133.6, 132.1, 131.5, 130.6, 129.3, 127.5, 125.6, 125.2, 124.7, 121.2, 35.1, 34.8, 31.4, 31.1, 22.0. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{31}H_{34}NO^+$, 436.2635; found, 436.2650.

*(4-Methoxyphenyl)(4-(4-methoxyphenyl)-6-methylquinolin-2-yl)methanone (**3f**).* Yield 72%; 276.1 mg; yellow solid; column chromatography, silica gel (PE/EA, 15:1); mp 177–179 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 8.8 Hz, 2H), 8.14 (d, J = 8.4 Hz, 1H), 7.95 (s, 1H), 7.79 (s, 1H), 7.59 (d, J = 8.4 Hz, 1H), 7.50 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.4 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 3.89 (s, 3H), 3.88 (s, 3H), 2.50 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 192.4, 163.6, 159.8, 154.0, 148.4, 145.8, 138.3, 133.8, 132.0, 130.8, 130.4, 130.1, 129.0, 127.4, 124.5, 121.0, 114.0, 113.4, 55.4, 55.3, 21.9. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{25}H_{22}NO_3^+$, 384.1594; found, 384.1593.

*(4-Ethoxyphenyl)(4-(4-ethoxyphenyl)-6-methylquinolin-2-yl)methanone (**3g**).* Yield 74%; 304.5 mg; yellow solid; column chromatography, silica gel (PE/EA, 15:1); mp 170–172 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 8.4 Hz, 2H), 8.15 (d, J = 8.4 Hz, 1H), 7.94 (s, 1H), 7.79 (s, 1H), 7.59 (d, J = 8.4 Hz, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.06 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 8.4 Hz, 2H), 4.14 (d, J = 6.8 Hz, 2H), 4.11 (d, J = 6.8 Hz, 2H), 2.50 (s, 3H), 1.48 (t, J = 4.8 Hz, 3H), 1.45 (t, J = 4.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 192.4, 163.0, 159.3, 154.1, 148.5, 145.8, 138.3, 133.9, 132.0, 130.8, 130.4, 130.0, 128.9, 127.4, 124.6, 121.0, 114.6, 113.9, 63.7, 63.5, 22.0, 14.8, 14.7. HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{27}H_{25}NO_3Na^+$, 434.1727; found, 434.1734.

*(4-Fluorophenyl)(4-(4-fluorophenyl)-6-methylquinolin-2-yl)methanone (**3h**).* Yield 40%; 143.8 mg; white solid; column chromatography, silica gel (PE/EA, 40:1); mp 108–110 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.38–8.34 (m, 2H), 8.15 (d, J = 8.4 Hz, 1H), 8.01 (s, 1H), 7.70 (s, 1H), 7.65–7.62 (m, 1H), 7.55–7.51 (m, 2H), 7.28–7.17 (m, 4H), 2.52 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 192.0, 165.8 (d, J = 253.0 Hz, $^1J_{CF}$), 163.0 (d, J = 247.0 Hz, $^1J_{CF}$), 153.1, 147.9, 145.8, 139.2, 134.2 (d, J = 9.0 Hz, $^3J_{CF}$), 133.7 (d, J = 3.0 Hz, $^4J_{CF}$), 132.5 (d, J = 3.0 Hz, $^4J_{CF}$), 132.4, 131.2 (d, J = 8.0 Hz, $^3J_{CF}$), 130.6, 127.4, 124.3, 121.1, 115.8 (d, J = 22.0 Hz, $^2J_{CF}$), 115.2 (d, J = 21.0 Hz, $^2J_{CF}$), 22.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ −105.17, −112.88. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{23}H_{16}F_2NO^+$, 360.1194; found, 360.1203.

*(4-Chlorophenyl)(4-(4-chlorophenyl)-6-methylquinolin-2-yl)methanone (**3i**).* Yield 61%; 239.3 mg; white solid; column chromatography, silica gel (PE/EA, 40:1); mp 180–182 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 8.4 Hz, 2H), 8.14 (d, J = 8.4 Hz, 1H), 8.01 (s, 1H), 7.68 (s, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.55–7.48 (m, 6H), 2.52 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 192.3, 152.9, 147.6, 145.8, 139.5, 139.4, 136.2, 134.8, 134.6, 132.9, 132.4, 130.8, 130.7, 129.0, 128.4, 127.3, 124.2, 120.9, 22.1. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{23}H_{16}Cl_2NO^+$, 392.0603; found, 392.0618.

*(3-Bromophenyl)(4-(3-bromophenyl)-6-methylquinolin-2-yl)methanone (**3j**).* Yield 55%; 264.7 mg; yellow solid; column chromatography, silica gel (PE/EA, 40:1); mp 151–153 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 8.21 (d, J = 8.0 Hz, 1H), 8.16 (d, J = 8.4 Hz, 1H), 8.02 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.70–7.64 (m, 4H), 7.47–7.38 (m, 3H), 2.53 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 192.0, 152.5, 147.3, 145.8, 139.7, 139.6, 138.0, 135.7, 134.3, 132.6, 132.3, 131.7, 130.8, 130.2, 130.0, 129.6, 128.2, 127.3, 124.1, 122.8, 122.3, 120.9, 22.1. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{23}H_{16}Br_2NO^+$, 479.9593; found, 479.9603.

*(6-Methyl-4-(m-tolyl)quinolin-2-yl)(m-tolyl)methanone (**3k**).* Yield 63%; 221.4 mg; yellow solid; column chromatography, silica gel (PE/EA, 40:1); mp 99–101 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 8.4 Hz, 1H), 8.04 (s, 2H), 7.98 (s, 1H), 7.76 (s, 1H), 7.62–7.59 (m, 1H), 7.45–7.31 (m, 6H), 2.50 (s, 3H), 2.47 (s, 3H), 2.44 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 194.3, 153.5, 148.9, 145.9, 138.6, 138.4, 137.8, 136.3, 135.1, 133.7, 132.1, 131.6, 130.6, 130.1, 129.2, 128.8, 128.4, 127.9, 127.5, 126.6, 124.5, 121.0, 22.0, 21.5, 21.4. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{25}H_{22}NO^+$, 352.1696; found, 352.1706.

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*(3-Methoxyphenyl)(4-(3-methoxyphenyl)-6-methylquinolin-2-yl)methanone (**3l**).* Yield 68%; 260.7 mg; yellow solid; column chromatography, silica gel (PE/EA, 15:1); mp 127−129 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 8.4 Hz, 1H), 8.01 (s, 1H), 7.84 (d, J = 8.0 Hz, 2H), 7.77 (s, 1H), 7.62−7.59 (m, 1H), 7.48−7.39 (m, 2H), 7.18−7.04 (m, 4H), 3.87 (s, 3H), 3.87 (s, 3H), 2.50 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 193.6, 159.7, 159.3, 153.3, 148.6, 145.8, 139.1, 138.8, 137.4, 132.2, 130.6, 129.6, 129.0, 127.4, 124.5, 124.4, 121.9, 120.9, 119.7, 115.3, 115.1, 114.0, 55.40, 55.35, 22.0. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{25}H_{22}NO_3^+$, 384.1594; found, 384.1605.

*(4-Butylphenyl)(4-(4-butylphenyl)-6-methylquinolin-2-yl)methanone (**3m**).* Yield 69%; 300.6 mg; yellow solid; column chromatography, silica gel (PE/EA, 40:1); mp 88−90 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20−8.14 (m, 3H), 7.98 (s, 1H), 7.80 (s, 1H), 7.59 (d, J = 8.8 Hz, 1H), 7.47 (d, J = 8.0 Hz, 2H), 7.37−7.30 (m, 4H), 2.78−2.71 (m, 2H), 2.70−2.68 (m, 2H), 2.50 (s, 3H), 1.74−1.68 (m, 2H), 1.67−1.61(m, 2H), 1.46−1.43 (m, 2H), 1.40−1.36 (m, 2H), 0.99 (d, J = 7.2 Hz, 3H), 0.94 (d, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 193.6, 153.7, 148.8, 148.7, 145.9, 143.4, 138.4, 135.1, 133.8, 132.0, 131.6, 130.5, 129.4, 128.6, 128.2, 127.4, 124.6, 121.1, 35.8, 35.4, 33.5, 33.2, 22.4, 22.3, 22.0, 14.0, 13.9. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{31}H_{34}NO^+$, 436.2635; found, 436.2651.

*(6-Methyl-4-(4-pentylphenyl)quinolin-2-yl)(4-pentylphenyl)methanone (**3n**).* Yield 67%; 310.7 mg; yellow solid; column chromatography, silica gel (PE/EA, 40:1); mp 90−92 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20−8.14 (m, 3H), 7.98 (s, 1H), 7.80 (s, 1H), 7.60 (d, J = 8.4 Hz, 1H), 7.47 (d, J = 8.0 Hz, 2H), 7.37−7.31 (m, 4H), 2.73 (d, J = 9.6 Hz, 2H), 2.69 (d, J = 9.6 Hz, 2H), 2.51 (s, 3H), 1.74−1.70 (m, 2H), 1.69−1.65 (m, 2H), 1.40−1.38 (m, 4H), 1.37−1.33 (m, 4H), 0.94 (t, J = 6.0 Hz, 3H), 0.90 (t, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 193.7, 153.8, 148.81, 148.77, 145.9, 143.5, 138.5, 135.1, 133.8, 132.0, 131.6, 130.6, 129.5, 128.6, 128.2, 127.4, 124.6, 121.1, 36.1, 35.7, 31.6, 31.4, 31.1, 30.8, 22.6, 22.5, 22.0, 14.04, 13.99. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{33}H_{38}NO^+$, 464.2948; found, 464.2966.

*(6-Methyl-4-(naphthalen-2-yl)quinolin-2-yl)(naphthalen-2-yl)methanone (**3o**).* Yield 60%; 254.1 mg; white solid; column chromatography, silica gel (PE/EA, 40:1); mp 178−180 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (s, 1H), 8.32−8.29 (m, 1H), 8.21−8.16 (m, 2H), 8.05−8.01 (m, 2H), 7.98−7.89 (m, 5H), 7.80 (s, 1H), 7.69−7.67 (m, 1H), 7.64−7.51 (m, 5H), 2.49 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 193.8, 153.7, 148.8, 145.9, 138.9, 135.6, 135.3, 134.1, 133.6, 133.2, 133.0, 132.4, 132.3, 130.7, 129.9, 128.8, 128.5, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6, 127.3, 126.74, 126.68, 126.5, 124.6, 121.4, 22.0. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{31}H_{22}NO^+$, 424.1696; found, 424.1705.

*(6-Methyl-4-(thiophen-3-yl)quinolin-2-yl)(thiophen-3-yl)methanone (**3p**).* Yield 66%; 221.4 mg; yellow solid; column chromatography, silica gel (PE/EA, 40:1); mp 150−152 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (d, J = 1.6 Hz, 1H), 8.16−8.13 (m, 2H), 7.97 (d, J = 5.2 Hz, 1H), 7.88 (s, 1H), 7.61−7.56 (m, 2H), 7.52−7.50 (m, 1H), 7.37−7.33 (m, 2H), 2.52 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.8, 153.4, 146.0, 143.3, 139.8, 138.9, 138.3, 137.3, 132.1, 130.6, 129.5, 128.8, 127.5, 126.3, 125.2, 125.0, 124.4, 120.4, 22.0. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{19}H_{14}NOS_2^+$, 336.0511; found, 336.0522.

*(6-Ethyl-4-(4-methoxyphenyl)quinolin-2-yl)(4-methoxyphenyl)methanone (**4a**).* Yield 70%; 278.2 mg; yellow solid; column chromatography, silica gel (PE/EA, 15:1); mp 117−119 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 8.8 Hz, 2H), 8.18 (d, J = 8.4 Hz, 1H), 7.95 (s, 1H), 7.81 (s, 1H), 7.65−7.63 (m, 1H), 7.51 (d, J = 8.8 Hz, 2H), 7.08 (d, J = 8.8 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 3.90 (s, 3H), 3.89 (s, 3H), 2.83−2.77 (m, 2H), 1.30−1.26 (t, J = 7.6 Hz, 3H)). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.4, 163.6, 159.8, 154.0, 148.6, 146.0, 144.5, 133.8, 130.84, 130.77, 130.6, 130.1, 129.0, 127.4, 123.3, 121.0, 114.0, 113.4, 55.4, 55.3, 29.2, 15.4. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{26}H_{24}NO_3^+$, 398.1751; found, 398.1762.

*(6-Isopropyl-4-(4-methoxyphenyl)quinolin-2-yl)(4-methoxyphenyl)methanone (**4b**).* Yield 72%; 296.3 mg; yellow solid; column chromatography, silica gel (PE/EA, 15:1); mp 108−110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 8.4 Hz, 2H), 8.20 (d, J = 8.8 Hz, 1H), 7.96 (s, 1H), 7.85 (s, 1H), 7.70 (d, J = 8.8 Hz, 1H), 7.53 (d, J = 8.4 Hz, 2H), 7.09 (d, J = 8.4 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 3.91 (s, 3H), 3.89 (s, 3H), 3.08−3.05 (m, 1H), 1.30 (d, J = 6.8 Hz, 6H), 1.29 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.5, 163.6, 159.9, 154.1, 149.0, 148.7, 146.2, 133.8, 130.8, 130.7, 130.2, 129.3, 129.1, 127.4, 122.0, 121.0, 114.1, 113.4, 55.4, 55.3, 34.4, 23.8. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{27}H_{26}NO_3^+$, 412.1907; found, 412.1923.

*(6-(tert-Butyl)-4-(4-methoxyphenyl)quinolin-2-yl)(4-methoxyphenyl)methanone (**4c**).* Yield 66%; 280.8 mg; orange solid; column chromatography, silica gel (PE/EA, 15:1); mp 124−126 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 8.8 Hz, 2H), 8.20 (d, J = 8.8 Hz, 1H), 8.03 (s, 1H), 7.97 (s, 1H), 7.88 (d, J = 8.8 Hz, 1H), 7.54 (d, J = 8.4 Hz, 2H), 7.08 (d, J = 8.4 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 3.89 (s, 3H), 3.88 (s, 3H), 1.37 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.4, 163.5, 159.8, 154.2, 151.1, 148.9, 145.7, 133.8, 130.7, 130.2, 130.1, 129.0, 128.6, 126.9, 120.9, 120.6, 114.0, 113.4, 55.4, 55.2, 35.1, 31.0. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{28}H_{28}NO_3^+$, 426.2064; found, 426.2069.

*(6-Methoxy-4-(4-methoxyphenyl)quinolin-2-yl)(4-methoxyphenyl)methanone (**4d**).* Yield 68%; 271.6 mg; white solid; column chromatography, silica gel (PE/EA, 15:1); mp 142−144 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 8.8 Hz, 2H), 8.14 (d, J = 9.2 Hz, 1H), 7.97 (s, 1H), 7.51 (d, J = 8.4 Hz, 2H), 7.42−7.39 (m, 1H), 7.30 (d, J = 2.4 Hz, 1H), 7.07 (d, J = 8.4 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 3.89 (s, 3H), 3.88 (s, 3H), 3.82 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.2, 163.5, 159.8, 159.2, 152.5, 147.5, 143.2, 133.8, 132.3, 130.5, 130.2, 129.2, 128.7, 122.3, 121.4, 114.1, 113.3, 103.5, 55.5, 55.4, 55.3. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{25}H_{22}NO_4^+$, 400.1543; found, 400.1544.

*(4-Methoxyphenyl)(4-(4-methoxyphenyl)-6-(methylthio)quinolin-2-yl)methanone (**4e**).* Yield 65%; 270.1 mg; yellow solid; column chromatography, silica gel (PE/EA, 15:1); mp 133−135 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 8.8 Hz, 2H), 8.12 (d, J = 9.2 Hz, 1H), 7.97 (s, 1H), 7.75 (s, 1H), 7.64−7.61 (m, 1H), 7.51 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.4 Hz, 2H), 7.00 (d, J = 8.8 Hz, 2H), 3.90 (s, 3H), 3.89 (s, 3H), 2.49 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.2, 163.6, 159.9, 153.8, 147.6, 145.4, 139.8, 133.8, 130.8, 130.7, 129.8, 129.0, 128.8, 127.8, 121.6, 120.1, 114.1, 113.4, 55.4, 55.3, 15.3. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{25}H_{22}NO_3S^+$, 416.1315; found, 416.1330.

*(4-Methoxyphenyl)(4-(4-methoxyphenyl)-6-phenylquinolin-2-yl)methanone (**4f**).* Yield 51%; 227.2 mg; orange solid; column chromatography, silica gel (PE/EA, 15:1); mp 154−156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, J = 8.4 Hz, 3H), 8.23 (d, J = 1.2 Hz, 1H), 8.05−8.00 (m, 2H), 7.64 (d, J = 7.2 Hz, 2H), 7.55 (d, J = 8.4 Hz, 2H), 7.48−7.44 (m, 2H), 7.39 (d, J = 7.2 Hz, 1H), 7.09 (d, J = 8.4 Hz, 2H), 7.01 (d, J = 8.8 Hz, 2H), 3.90 (s, 3H), 3.86 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.3, 163.7, 160.0, 154.7, 149.4, 146.6, 140.8, 140.2, 133.9, 132.3, 131.2, 130.9, 129.9, 129.5, 128.9, 127.9, 127.6, 127.5, 123.5, 121.4, 114.2, 113.5, 55.5, 55.4. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{30}H_{24}NO_3^+$, 446.1751; found, 446.1769.

*(6-Ffluoro-4-(4-methoxyphenyl)quinolin-2-yl)(4-methoxyphenyl)methanone (**4g**).* Yield 63%; 244.1 mg; yellow solid; column chromatography, silica gel (PE/EA, 15:1); mp 178−180 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 8.8 Hz, 2H), 8.26−8.23 (m, 1H), 8.00 (s, 1H), 7.67−7.64 (m, 1H), 7.55−7.47 (m, 3H), 7.08 (d, J = 8.8 Hz, 2H), 7.00 (d, J = 8.8 Hz, 2H), 3.90 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.0, 163.7, 161.6 (d, J = 249.0 Hz, $^1J_{CF}$), 160.1, 154.3 (d, J = 2.0 Hz, $^4J_{CF}$), 148.8 (d, J = 6.0 Hz, $^4J_{CF}$), 144.3, 133.8, 133.3 (d, J = 9.0 Hz, $^3J_{CF}$), 130.6, 129.4, 128.8, 128.4 (d, J = 10.0 Hz, $^3J_{CF}$), 121.4, 120.0 (d, J = 26.0 Hz, $^2J_{CF}$), 114.3, 113.5, 109.3 (d, J = 23.0 Hz, $^2J_{CF}$), 55.44, 55.35. ^{19}F NMR (376 MHz, $CDCl_3$) δ −104.02. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{24}H_{19}FNO_3^+$, 388.1343; found, 388.1353.

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*(6-Chloro-4-(4-methoxyphenyl)quinolin-2-yl)(4-methoxyphenyl)methanone (**4h**).* Yield 60%; 242.3 mg; yellow soild; column chromatography, silica gel (PE/EA, 15:1); mp 167−169 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 8.8 Hz, 2H), 8.18 (d, J = 8.8 Hz, 1H), 8.02−7.99 (m, 2H), 7.72−7.69 (m, 1H), 7.49 (d, J = 8.4 Hz, 2H), 7.09 (d, J = 8.4 Hz, 2H), 7.00 (d, J = 8.8 Hz, 2H), 3.92 (s, 3H), 3.91 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.0, 163.8, 160.2, 155.1, 148.6, 145.7, 134.2, 133.9, 132.3, 130.8, 129.3, 128.8, 128.2, 124.7, 121.7, 114.3, 113.5, 55.5, 55.4. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{24}H_{19}ClNO_3^+$, 404.1048; found, 404.1047.

*(6-Bromo-4-(4-methoxyphenyl)quinolin-2-yl)(4-methoxyphenyl)methanone (**4i**).* Yield 52%; 233.1 mg; orange soild; column chromatography, silica gel (PE/EA, 15:1); mp 168−170 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 8.8 Hz, 2H), 8.18 (d, J = 1.6 Hz, 1H), 8.09 (d, J = 8.8 Hz, 1H), 7.98 (s, 1H), 7.83−7.80 (m, 1H), 7.47 (d, J = 8.4 Hz, 2H), 7.08 (d, J = 8.4 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 3.90 (s, 3H), 3.89 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 191.9, 163.7, 160.1, 155.1, 148.4, 145.8, 133.8, 133.2, 132.3, 130.7, 129.1, 128.7, 128.5, 127.9, 122.5, 121.6, 114.3, 113.5, 55.4, 55.3. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{24}H_{19}BrNO_3^+$, 448.0543; found, 448.0545.

*(4-Methoxyphenyl)(4-(4-methoxyphenyl)-6-(trifluoromethoxy)quinolin-2-yl)methanone (**4j**).* Yield 50%; 226.7 mg; yellow soild; column chromatography, silica gel (PE/EA, 15:1); mp 126−128 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32−8.28 (m, 3H), 8.03 (s, 1H), 7.88 (s, 1H), 7.65 (d, J = 8.8 Hz, 1H), 7.50 (d, J = 8.4 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 7.01 (d, J = 8.4 Hz, 2H), 3.92 (s, 3H), 3.91 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 191.9, 163.9, 160.3, 155.4, 149.4, 148.2, 145.5, 133.9, 133.0, 130.7, 129.1, 128.7, 127.9, 123.7, 121.7, 120.5 (q, J = 256.0 Hz, $^1J_{CF}$), 116.4, 114.4, 113.6, 55.5, 55.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ −57.66. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{25}H_{19}F_3NO_4^+$, 454.1261; found, 454.1270.

*(4-Methoxyphenyl)(5,6,7-trimethoxy-4-(4-methoxyphenyl)quinolin-2-yl)methanone (**4k**).* Yield 31%; 142.4 mg; orange soild; column chromatography, silica gel (PE/EA, 12:1); mp 140−142 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, J = 8.8 Hz, 2H), 7.70 (s, 1H), 7.45 (s, 1H), 7.37 (d, J = 8.8 Hz, 2H), 7.01−6.95 (m, 4H), 4.04 (s, 3H), 3.97 (s, 3H), 3.90 (s, 3H), 3.89 (s, 3H), 3.31 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.4, 163.6, 158.9, 155.8, 153.7, 148.6, 147.7, 145.7, 143.7, 133.7, 133.6, 129.8, 129.0, 121.9, 118.5, 113.5, 112.6, 106.0, 61.3, 60.9, 56.1, 55.5, 55.3. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{27}H_{26}NO_6^+$, 460.1755; found, 460.1749.

*(4-Methoxyphenyl)(1-(4-methoxyphenyl)benzo[f]quinolin-3-yl)methanone (**4l**).* Yield 40%; 167.8 mg; yellow solid; column chromatography, silica gel (PE/EA, 15:1); mp 197−199 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, J = 8.4 Hz, 2H), 8.10 (d, J = 9.2 Hz, 1H), 8.01 (d, J = 6.0 Hz, 2H), 7.90−7.87 (m, 2H), 7.55−7.22 (m, 1H), 7.39 (d, J = 8.4 Hz, 2H), 7.26−7.21 (m, 1H), 7.06−7.00 (m, 4H), 3.92 (s, 3H), 3.91 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.0, 163.7, 159.7, 153.4, 149.3, 148.4, 134.5, 133.9, 133.5, 131.8, 129.6, 129.5, 129.1, 128.9, 128.6, 128.5, 127.4, 125.7, 125.3, 124.5, 114.7, 113.5, 55.5, 55.4. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{28}H_{22}NO_3^+$, 420.1594; found, 420.1611.

*(4-Ethylphenyl)(4-(4-ethylphenyl)-6-methoxyquinolin-2-yl)methanone (**4m**).* Yield 68%; 268.9 mg; yellow solid; column chromatography, silica gel (PE/EA, 30:1); mp 144−146 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21−8.14 (m, 3H), 8.01 (s, 1H), 7.50 (d, J = 7.6 Hz, 2H), 7.43−7.32 (m, 6H), 3.82 (s, 3H), 2.79−2.71 (m, 4H), 1.33 (t, J = 7.6 Hz, 3H), 1.29 (t, J = 7.6 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 193.5, 159.3, 152.2, 149.8, 147.9, 144.7, 143.3, 135.3, 134.0, 132.4, 131.7, 129.3, 128.8, 128.2, 127.6, 122.3, 121.5, 103.6, 55.5, 29.0, 28.6, 15.4, 15.2. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{27}H_{26}NO_2^+$, 396.1958; found, 396.1969.

*(6-Ethyl-4-(3-methoxyphenyl)quinolin-2-yl)(3-methoxyphenyl)methanone (**4n**).* Yield 67%; 266.1 mg; yellow solid; column chromatography, silica gel (PE/EA, 15:1); mp 104−106 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 8.8 Hz, 1H), 8.01 (s, 1H), 7.84−7.80 (m, 3H), 7.68−7.66 (m, 1H), 7.49−7.40 (m, 2H), 7.20−7.14 (m, 2H), 7.10−7.05 (m, 2H), 3.89 (s, 3H), 3.89 (s, 3H), 2.84−2.78 (m, 2H), 1.31−1.27 (m, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 193.6, 159.7, 159.4, 153.3, 149.0, 145.9, 145.1, 139.1, 137.4, 131.2, 130.6, 129.7, 129.1, 127.4, 124.5, 123.4, 122.0, 121.0, 119.9, 115.2, 115.0, 114.2, 55.5, 55.4, 29.3, 15.5; HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{26}H_{24}NO_3^+$, 398.1751; found, 398.1762.

*(6-Methoxy-4-phenylquinolin-2-yl)(phenyl)methanone (**5aa**).* Yield 42%; 142.5 mg; white solid; column chromatography, silica gel (PE/EA, 20:1); mp 206−208 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 7.2 Hz, 2H), 8.13 (d, J = 9.2 Hz, 1H), 8.04 (s, 1H), 7.60−7.47 (m, 9H), 7.41−7.38 (m, 1H), 3.77 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 193.6, 159.4, 151.8, 147.8, 143.2, 137.9, 136.4, 132.7, 132.3, 131.3, 129.2, 128.6, 128.5, 127.9, 122.4, 121.4, 103.4, 55.4. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{23}H_{18}NO_2^+$, 340.1332; found, 340.1331.

*(6-Methoxy-4-phenylquinolin-2-yl)(4-methoxyphenyl)methanone (**5bb**).* Yield 54%; 199.3 mg; yellow solid; column chromatography, silica gel (PE/EA, 12:1); mp 165−167 °C. ^{1}H NMR (400 MHz, $CDCl_3$) 8.32 (d, J = 8.8 Hz, 2H), 8.15 (d, J = 8.8 Hz, 1H), 8.00 (s, 1H), 7.56−7.49 (m, 6H), 7.42 (d, J = 8.8 Hz, 1H), 6.99 (d, J = 8.4 Hz, 2H), 3.89 (s, 3H), 3.81 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.1, 163.5, 159.3, 152.5, 147.8, 143.2, 138.0, 133.8, 132.3, 129.3, 129.2, 128.7, 128.6, 128.5, 122.4, 121.5, 113.4, 103.5, 55.5, 55.4. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{24}H_{20}NO_3^+$, 370.1438; found, 370.1436.

*2-Oxo-2-phenylacetaldehyde (**1aa**).*[12] Yield 43%; 57.7 mg; white solid; column chromatography, silica gel (PE/EA, 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 7.6 Hz, 2H), 7.60−7.57 (t, J = 7.6 Hz, 1H), 7.50−7.43 (t, J = 7.6 Hz, 2H), 6.39 (d, J = 8.8 Hz, 1H), 5.13 (d, J = 9.6 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.7, 134.6, 132.1, 129.9, 128.7, 88.6.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00793.

Crystallographic data and copies of the ^{1}H and ^{13}C{^{1}H} NMR spectra (PDF)

Accession Codes

CCDC 2056325 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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