# Aromatic Ketone-Catalyzed Photochemical Synthesis of Imidazo-isoquinolinone Derivatives

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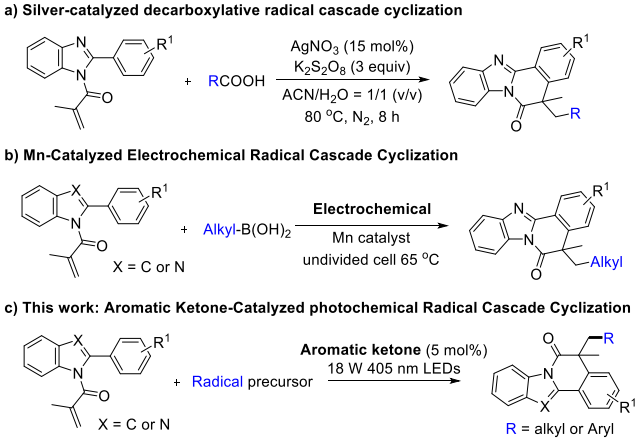
**ABSTRACT**: We have developed an efficient photocatalytic decarboxylative radical addition/cyclization strategy to synthesize imidazo-isoquinolinone derivatives using inexpensive aromatic ketone photocatalysts. This method not only tolerates a wide range of functional groups but also works well for both alkyl and aryl radicals.


## ■ INTRODUCTION

Imidazo- isoquinolinone derivatives possess unique properties that have been used in biological,[1-3] material science, and synthetic applications.[4] Consequently, many efficient synthetic methods have been developed.[3,5-11] For example, Song and co-workers proposed an elegant protocol via rhodium(III)-catalyzed [4+2] annulation of 2-arylimidazoles and α-diazoketoesters.[3] Yu's group[5] reported a silver-catalyzed decarboxylative radical cascade cyclization at 80 °C using 2-arylbenzoimidazoles and carboxylic acids in one-pot (Scheme 1a). Lei's group reported an Mn-catalyzed electrochemical radical cascade cyclization of activated olefins using arylbenzoimidazoles and alkyl boronic acid (Scheme 1b).[6] However, these methods still have some drawbacks, such as expensive metal catalysts or excess amounts of oxidants.

Radical generation from redox-active radical precursors is an attractive and straightforward method.[12,13] Redox-active radical precursors such as N-hydroxyphthalimide esters and N-halo-succinimide (NXS), can readily accept an electron from reductive species to generate a radical.[14-16] The visible-light-induced[17-19] radical generation has been utilized as a mild and yet versatile tool to access radicals from redox-active radical precursors.[20-24] Among commonly used photocatalysts, aromatic ketones are inexpensive and usually stable towards photo-degradation and are also well-studied examples of photoactive compounds.[25-33] Generally, due to the relatively high triplet energy and long triplet lifetime, the aromatic ketone is an efficient energy transfer sensitizer.[28,34-36] The excited aromatic ketone is capable of reacting with various organic molecules.[25,27,31,37-39] For example, an excited aromatic ketone may react with various hydrogen donors.[40,41] Herein, we report a simple and efficient aromatic ketone-catalyzed photochemical radical cascade cyclization to synthesize imidazo- isoquinolinone derivatives using N-hydroxyphthalimide esters and phenyl diazonium salts as radical precursors and dimethylacetamide (DMAc) as solvent (Scheme 1c).

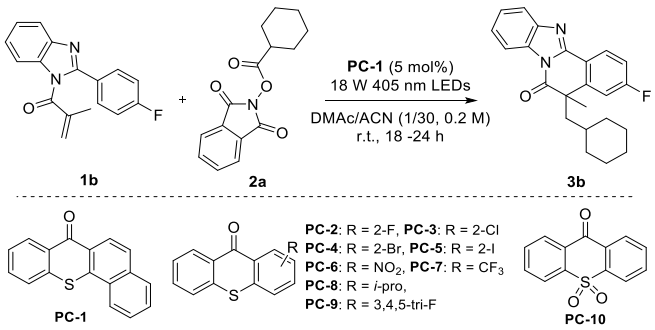



**Scheme 1 Literature Background.**

## ■ RESULTS AND DISCUSSION

We selected the reaction of N-methacryloyl-2-phenylbenzoimidazole (**1b**) with N-hydroxyphthalimide ester (**2a**) as our model system (Table 1). The desired product **3b** was obtained in 64% isolated yield using ketone **PC-1** as the photocatalyst (Table 1, entry 1). As the photocatalyst was changed from **PC-1** to **PC 2-10**, the yield of **3b** decreased (40% to 57%) (Table 1, entry 2). Commonly used transitional metal or dye photocatalysts showed lower efficiency (Table 1, entry 3). Solvents such as dimethylacetamide and acetonitrile were less effective (Table 1, entries 4 and 5). To our delight, decreasing the dimethylacetamide percentage improved the reaction outcome (Table 1, entry 6). A comparable yield was obtained using the light of 425 nm wavelength; the chemical yield decreased under a longer wavelength source (450 nm) (Table 1, entry 8). The photocatalyst is essential for the reaction, and lower loading reduced the chemical yield (Table 1, entry 9). Only a slight drop of yield was observed in the presence of air (Table 1, entry 10). As expected, no reaction occurred in the absence of light (Table 1, entry 11), and the intermittent illumination experiment re-confirmed that light was essential (see Table S4 in SI).

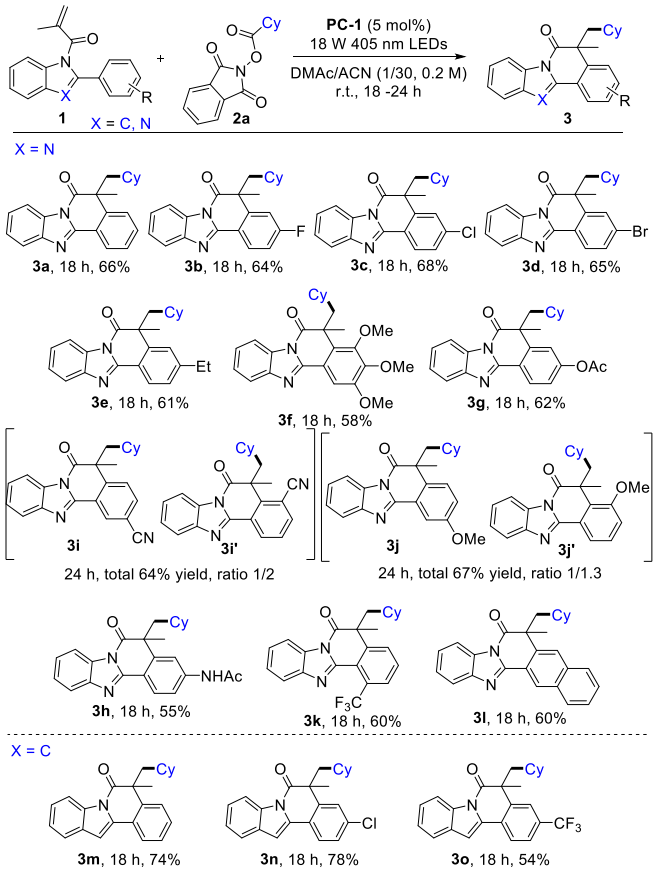
**Table 1. Optimization of reaction conditions.**[a]




| Entry | Variation(s) from standard conditions | Yields[b] |
|---|---|---|
| 1 | none | 69%(64%[c]) |
| 2 | **PC 2-10** as photocatalysts | 40-57%[d] |
| 3 | Ir, Ru complex or dye photocatalyst | 0-48% |
| 4 | DMAc (0.2 M) | 59% |
| 5 | ACN (0.2 M) | trace |
| 6 | DMAc/ACN (1/50, v/v, 0.2 M) | 68% |
| 7 | DMAc/ACN (1/30, v/v, 0.4 M) | 0[e] |
| 8 | 450, 425 or 365 nm 18 W LEDs | <10%, 67%, 64% |
| 9 | 0%, 1 mol%, 2.5 mol% photocatalyst | 0%, 30%, 67% |
| 10 | Under air | 67% |
| 11 | Dark | 0% |

[a] Standard conditions: **1b** (0.1 mmol), **2a** (1.05 equiv), **PC-1** (5 mol%), DMAc/ACN (1/30, v/v, 0.2 M), 405 nm 18W LEDs, rt, $N_2$, 18 h. [b]The yield was determined by GCMS using 9H-fluorene as the internal standard. [c] Isolated yield. [d] Solvent is DMAc. [e] Substrate is insoluble.

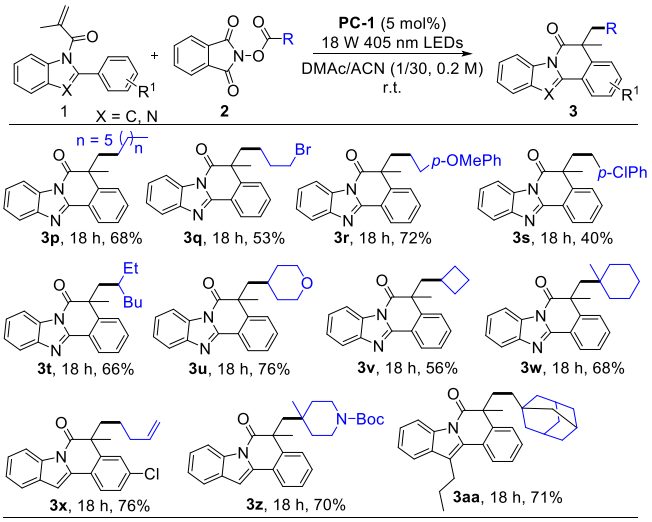
**Table 2. Substrate scopes of N-methacryloyl benzoimidazole or indole.**




Conditions: **1** (0.2 mmol), **2a** (1.05 equiv), **PC-1** (5 mol%), DMAc/ACN (1/30, v/v, 0.2 M), 405 nm 18W LEDs, rt, $N_2$, 18-24 h.

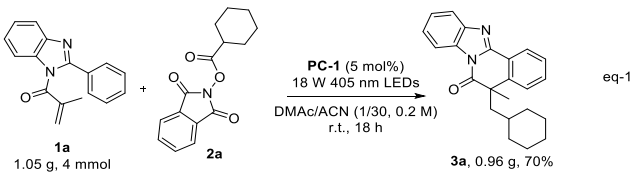
With the optimized conditions in hand, the scope of the reaction was evaluated (Table 2). Firstly, we investigated the scope of N-methacryloyl-2-phenylbenzoimidazole **1** using **2a** as the radical precursor. A wide range of functional groups such as halogens (**3b-d**), alkyl (**3e**), ether (**3f**, **3j**, and **3j'**), ester (**3g**), amide (**3h**), cyano (**3i** and **3i'**) trifluoromethyl (**3k**) and naphthyl (**3l**) were well tolerated. N-methacryloyl-2-phenylbenzoimidazole **1** equipped with an *ortho*- or *para*-substituted group on the 2-phenyl moiety selectively constructed the single regioisomer. Naphthyl-derived **3l** could also be accessed regio-selectively in 60% yield. However, substrates with a *meta*-substituted group usually gave a mixture of regio-isomers (Table 2, **3i-3j'**). The N-methacryloyl-2-phenylindole derivatives were also suitable substrates (Table 2, **3m-o**).

**Table 3. Substrate scopes of N-hydroxyphthalimide esters.**




Conditions: **1** (0.2 mmol), **2** (1.05 equiv), **PC-1** (5 mol%), DMAc/ACN (1/30, v/v, 0.2 M), 405 nm 18W LEDs, rt, $N_2$, 18 h.

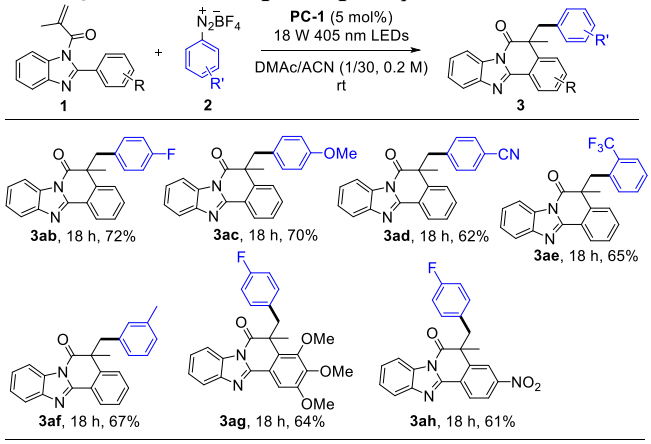
We then proceeded to study the scope of N-hydroxyphthalimide esters (NHPI) (Table 3). A wide range of NHPI derived from aliphatic carboxylic acids were suitable substrates, and both primary, secondary, and tertiary radicals could be generated. Diverse functional groups such as alkyl (**3p**, **3t**, and **3aa**), bromide (**3q**), ether (**3r** and **3u**), alkenes (**3x**), and N-Boc (**3z**) were compatible with the reaction conditions, and moderate to good yields were obtained. A slightly lower yield was observed for benzyl NHPI ester (40%, **3s**). The chemical yields were lower for NHPI esters containing 4-membered rings (**3v**). The scale-up reaction on a 1 gram scale gave a 70% yield (eq 1).




We investigated the functionalization of 2-arylbenzoimidazoles using aryldiazonium salts as radical precursors (Table 4). To our satisfaction, various substituted aryldiazonium salts, including an electron-withdrawing or an electron-donating group such as *p*-fluoro (**3ab**), *p*-methoxyl (**3ac**), *p*-cyano (**3ad**), *ortho*-trifluoromethyl (**3ae**), *meta*-methyl (**3af**) on the benzene ring afforded the desired product in yields ranging from 62% to 72%. It should

be noted that the electronic and steric effects played a minor role here; good yields of products were obtained regardless.

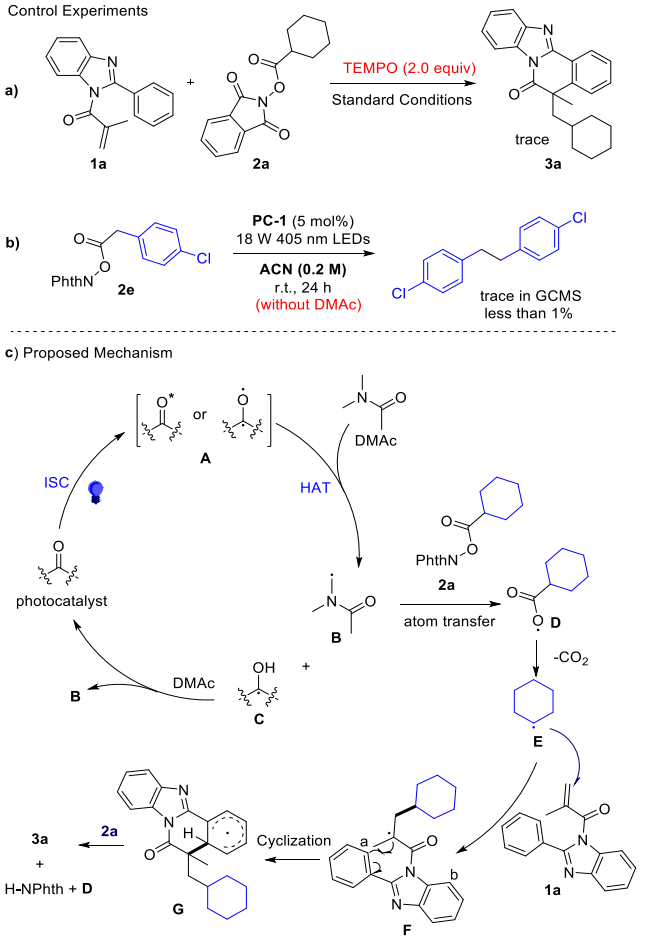
**Table 4. Substrate scopes of phenyl diazonium salts.**




Conditions: **1** (0.2 mmol), **2** (1.05 equiv), **PC-1** (5 mol%), DMAc/ACN (1/30, v/v, 0.2 M), 405 nm 18W LEDs, rt, $N_2$, 18 h.

To gain insights into the reaction mechanism, we conducted several control experiments (Scheme 2). No desired products were obtained in the presence of a radical scavenger (TEMPO), which provides support for a possible free radical mechanism (Scheme 2a). Although the N-hydroxyphthalimide esters[14,42-45] and phenyl diazonium salts[46] have been proven as efficient radical precursors under photoirradiation, **2e** was nearly inert in the absence of dimethylacetamide (Scheme 2b). This result suggested that dimethylacetamide played an essential role in this transformation.

Our proposed mechanism is presented in Scheme 2c. First, the aromatic ketone photocatalysts were irradiated by light to generate the excited state (ketone*, **A**). **A** might react with DMAc to generate DMAc radical **B** and radical **C** via a hydrogen atom transfer process. **B** might react with **2a** to generate radical **D**, which was further converted to the radical **E** by releasing one molecule of $CO_2$. Alkyl radical **E** underwent a radical addition to **1a** at the terminal olefin to generate the radical intermediate **F**, followed by an intramolecular radical cyclization to give the radical intermediate **G**. Eventually **G** was oxidized by **2a** to give the final product **3a**. At the same time, H-NPhth and radical **D** were also generated. It should be noted that the cyclization of the radical intermediate **F** selectively occurred at position 'a' rather than position 'b', which may result from the fact that the six-membered product from the 6-endo-trig cyclization is more energetically favorable, both kinetically and thermodynamically.[5]




**Scheme 2. Mechanistic Studies.**

## ■ CONCLUSIONS

In summary, we have developed a photochemical protocol to synthesize imidazo-isoquinolinone derivatives in moderate to good yields. Our protocol is based on readily available building blocks, 2-arylbenzoimidazoles, and N-hydroxyphthalimide esters or phenyl diazonium salts, using stable and inexpensive keone photocatalysts. This method has advantages of broad reactant scope, mild reaction conditions, and easy workup. Further application of this strategy is currently ongoing in our laboratory.

## ■ EXPERIMENTAL SECTION

**General Methods.** All reactions were carried out under an ambient atmosphere without protection. Commercial reagents and solvents were obtained from commercial providers and used without further purification. The products were purified using a commercial flash chromatography system or a regular glass column. TLC was developed on silica gel 60 F254 glass plates.

Photocatalyzed experiments were performed under visible light irradiation by a blue LED at 20-30 °C. An EvoluChem™ 8-position PhotoRedOx Box manufactured by HepatoChem Inc was used in this system. One 18 W blue LEDs were equipped in this photoreactor. The blue LED's energy peak wavelength was 405 nm, peak width at half-height was about 23 nm, and irradiance between Vis band (380-780) was 338.206 W/m². The reaction vessel was a borosilicate glass test tube, and no filters were applied. The

distance from the light source to the irradiation vessel was approximately 5-10 cm. The wavelength of LEDs was showed in SI. $^1$H NMR (399 MHz or 500MHz), $^{13}$C{1H} NMR (100 MHz) and $^{19}$F NMR (376 MHz) spectra were recorded on a Bruker NMR apparatus. The chemical shifts are reported in δ (ppm) values ($^1$H and $^{13}$C{1H} NMR relative to $CHCl_3$, δ 7.26 ppm for $^1$H NMR and δ 77.0 ppm for $^{13}$C{1H} NMR). Or alternatively, $^1$H NMR chemical shifts were referenced to tetramethylsilane signal (0 ppm). Multiplicities are recorded by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), m (multiplet) and br (broad). Coupling constants (*J*), are reported in Hertz (Hz). GC analyses were performed using a Shimadzu GC-2010 ultra gas chromatography–mass spectrometry instrument equipped with a Shimadzu AOC-20s autosampler. High-resolution mass spectra (HRMS) were analyzed by MSF Staff on the high-resolution GC-EI-QTOF or ESI/APCI Orbitrap. N-methacryloyl-2-phenylbenzoimidazole **1a – 1l** and **1q** were prepared according to Lei's method[6] (**1a-1e, 1j** were known compounds[6,47,48]). N-methacryloyl-2-phenylindole **1m – 1p** were prepared according to Kim's method (**1m** was known compounds).[49-51] N-hydroxyphthalimide esters **2a – 2l** were all known compounds and prepared according to Baran's method[14,41,42,52-56]. The aryl diazonium tetrafluoroborates **2m – 2q** were all known compounds and prepared according to our previous work.[57-59]

**General Procedure for Photochemical Synthesis of Phenanthridine.** The specified N-methacryloyl-2-phenylbenzoimidazole and N-methacryloyl-2-phenylindole (0.2 mmol), N-hydroxyphthalimide esters and aryl diazonium tetrafluoroborates (1.05 equiv), 7H-benzo[c]thioxanthen-7-one (**PC-1**, 5 mol%), and 1 mL DMAc / ACN (1/30, 0.2 M) were capped inside a reactor. Then the mixture was agitated under blue LED irradiation (405 nm, 18 W) at room temperature for 18 to 24 hours. The progress of the reaction was monitored by GC-MS or/and TLC. After the completion of the reaction, the solvent was removed, and the residue was purified by flash silica chromatography using hexanes and ethyl acetate as the eluent (typically, ethyl acetate/*n*-hexanes = 2/98).

2-Methyl-1-(2-(3,4,5-trimethoxyphenyl)-1H-benzo[d]imidazol-1-yl)prop-2-en-1-one (**1f**): Purified by flash silica chromatography (ethyl acetate/n-hexanes = 5/95), colorless oil, 40% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 7.79 (dd, *J* = 6.5, 2.6 Hz, 1H), 7.67 (dd, *J* = 6.6, 2.6 Hz, 1H), 7.38 – 7.28 (m, 2H), 6.80 (s, 2H), 5.57 (q, *J* = 1.5 Hz, 1H), 5.27 (d, *J* = 1.1 Hz, 1H), 3.86 (d, *J* = 1.5 Hz, 9H), 1.97 (s, 3H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 170.3, 153.4, 153.2, 142.5, 139.9, 139.6, 134.5, 128.4, 126.7, 124.6, 124.3, 119.9, 112.4, 106.0, 60.8, 56.2, 18.0. HRMS (APCI): m/z calculated for $C_{20}H_{21}N_2O_4$ $[M+H]^+$, 353.1496; found, 353.1500.

4-(1-Methacryloyl-1H-benzo[d]imidazol-2-yl)phenyl acetate (**1g**): Purified by flash silica chromatography (ethyl acetate/n-hexanes = 5/95), white solid, 48% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 7.85 – 7.79 (m, 1H), 7.73 – 7.67 (m, 1H), 7.65 – 7.59 (m, 2H), 7.41 – 7.32 (m, 2H), 7.24 – 7.18 (m, 2H), 5.62 (d, *J* = 1.5 Hz, 1H), 5.38 – 5.35 (m, 1H), 2.30 (s, 3H), 2.01 (s, 3H). $^{13}$C{$^1$H } NMR (100 MHz, Chloroform-*d*): δ 170.1, 168.7, 152.6, 151.9, 142.7, 140.2, 134.6, 129.9, 128.9, 128.8, 124.7, 124.4, 121.9, 120.1, 112.7, 21.1, 18.0. HRMS (APCI): m/z calculated for $C_{19}H_{17}N_2O_3$ $[M+H]^+$, 321.1234; found, 321.1238.

N-(4-(1-methacryloyl-1H-benzo[d]imidazol-2-yl)phenyl)acetamide (**1h**): Purified by flash silica chromatography (ethyl acetate/n-hexanes = 5/95), white solid, 45% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.06 (s, 1H), 7.81 (dd, *J* = 6.4, 2.7 Hz, 1H), 7.70 (dd, *J* = 6.5, 2.7 Hz, 1H), 7.63 (d, *J* = 8.5 Hz, 2H), 7.53 (d, *J* = 8.6 Hz, 2H), 7.41 – 7.32 (m, 2H), 5.65 – 5.60 (m, 1H), 5.38 (s, 1H), 2.16 (s, 3H), 2.01 (s, 3H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 170.2, 168.7, 153.1, 142.5, 140.2, 140.0, 134.6, 129.6, 129.0, 126.4, 124.7, 124.5, 119.8, 119.4, 112.7, 24.6, 18.1. HRMS (APCI): m/z calculated for $C_{19}H_{18}N_3O_2$ $[M+H]^+$, 320.1394; found, 320.1397.

3-(1-Methacryloyl-1H-benzo[d]imidazol-2-yl)benzonitrile (**1i**): Purified by flash silica chromatography (ethyl acetate/n-hexanes = 5/95), white solid, 41% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 7.95 (s, 1H), 7.88 – 7.81 (m, 2H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.69 (dd, *J* = 6.2, 3.1 Hz, 1H), 7.59 (t, *J* = 7.8 Hz, 1H), 7.44 – 7.36 (m, 2H), 5.79 (s, 1H), 5.57 (s, 1H), 2.09 (s, 3H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 169.5, 151.2, 142.6, 140.2, 134.6, 133.2, 132.8, 132.6, 132.2, 129.5, 125.4, 124.8, 120.5, 117.8, 113.2, 113.0, 18.1. HRMS (APCI): m/z calculated for $C_{18}H_{14}N_3O$ $[M+H]^+$, 288.1131; found, 288.1135.

2-Methyl-1-(2-(2-(trifluoromethyl)phenyl)-1H-benzo[d]imidazol-1-yl)prop-2-en-1-one (**1k**): Purified by flash silica chromatography (ethyl acetate/n-hexanes = 5/95), colorless oil, 46% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 7.85 (dt, *J* = 7.1, 3.0 Hz, 1H), 7.81 – 7.76 (m, 1H), 7.72 (dt, *J* = 6.8, 4.0 Hz, 1H), 7.66 – 7.57 (m, 2H), 7.54 – 7.49 (m, 1H), 7.43 – 7.34 (m, 2H), 5.69 (d, *J* = 1.5 Hz, 1H), 5.61 (s, 1H), 1.96 (s, 3H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 168.8, 150.3, 142.7, 139.4, 133.4, 131.9, 131.4, 130.3, 129.9, 128.9 (q, *J* = 31.2 Hz), 127.6, 126.6 (q, *J* = 4.9 Hz), 125.0, 124.9, 123.6 (d, *J* = 273.8 Hz), 120.6, 113.6, 18.1. $^{19}$F NMR (376 MHz, Chloroform-*d*): δ -58.7 (s, 3F). HRMS (APCI): m/z calculated for $C_{18}H_{14}F_3N_2O$ $[M+H]^+$, 331.1053; found, 331.1056.

2-Methyl-1-(2-(naphthalen-2-yl)-1H-benzo[d]imidazol-1-yl)prop-2-en-1-one (**1l**): Purified by flash silica chromatography (ethyl acetate/n-hexanes = 5/95), white solid, 44% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.13 (s, 1H), 7.95 – 7.83 (m, 4H), 7.79 (dd, *J* = 6.6, 2.6 Hz, 1H), 7.71 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.59 – 7.49 (m, 2H), 7.45 – 7.35 (m, 2H), 5.47 (s, 1H), 5.34 (s, 1H), 1.97 (s, 3H). $^{13}$C{$^1$H} NMR (100 MHz, cdcl$_3$) δ 170.4, 153.6, 142.9, 140.4, 134.8, 133.8, 132.9, 129.0, 128.8, 128.7, 128.5, 128.5, 127.9, 127.4, 127.0, 125.6, 124.8, 124.6, 120.2, 112.9, 77.1, 18.1. HRMS (APCI): m/z calculated for $C_{21}H_{17}N_2O$ $[M+H]^+$, 313.1335; found, 313.1339.

1-(2-(4-Chlorophenyl)-1H-indol-1-yl)-2-methylprop-2-en-1-one (**1n**): Purified by flash silica chromatography (ethyl acetate/n-hexanes = 5/95), white solid, 48% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 7.9 (d, *J* = 8.2 Hz, 1H), 7.6 (d, *J* = 7.1 Hz, 1H), 7.4 – 7.3 (m, 2H), 7.3 – 7.2 (m, 4H), 6.7 (s, 1H), 5.4 (d, *J* = 1.4 Hz, 1H), 5.2 (s, 1H), 1.9 (s, 3H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 171.0, 141.2, 139.5, 137.9, 133.7, 132.6, 129.0, 128.8, 126.6, 124.5, 123.2, 120.7, 113.8, 109.1, 18.3. HRMS (APCI): m/z calculated for $C_{18}H_{15}NOCl$ $[M+H]^+$, 296.0837; found, 296.0840.

2-Methyl-1-(2-(4-(trifluoromethyl)phenyl)-1H-indol-1-yl)prop-2-en-1-one (**10**): Purified by flash silica chromatography (ethyl acetate/n-hexanes = 5/95), colorless oil, 52% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 7.94 (d, *J* = 8.2 Hz, 1H), 7.64 (t, *J* = 6.8 Hz, 3H), 7.45 (d, *J* = 8.2 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 1H), 7.29 (t, *J* = 7.4 Hz, 1H), 6.79 (s, 1H), 5.49 (s, 1H), 5.33 (s, 1H), 1.96 (s, 3H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 170.8, 141.3, 139.2, 138.1, 137.6, 129.7 (q, *J* = 32.6 Hz), 128.8, 127.9, 126.8, 125.6(q, *J* = 3.5 Hz), 123.3, 121.0, 113.9, 110.1, 18.3. $^{19}$F NMR (376 MHz, Chloroform-*d*): δ -62.24 (s, 3F). HRMS (APCI): m/z calculated for $C_{19}H_{15}NOF_3$ [M+H]$^+$, 330.1100; found, 330.1103.

2-Methyl-1-(2-phenyl-3-propyl-1H-indol-1-yl)prop-2-en-1-one (**1p**): Purified by flash silica chromatography (ethyl acetate/n-hexanes = 5/95), colorless oil, 60% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.12 (d, *J* = 7.9 Hz, 1H), 7.68 (d, *J* = 7.4 Hz, 1H), 7.48 – 7.41 (m, 2H), 7.41 – 7.34 (m, 3H), 7.34 – 7.29 (m, 2H), 5.32 (s, 1H), 5.20 (s, 1H), 2.79 – 2.72 (m, 2H), 1.85 (s, 3H), 1.75 (h, *J* = 7.4 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 171.1, 141.2, 136.9, 135.8, 133.8, 129.6, 129.5, 128.3, 127.4, 124.7, 124.3, 122.7, 120.6, 119.2, 114.1, 26.2, 23.5, 18.2, 14.2. HRMS (APCI): m/z calculated for $C_{21}H_{22}NO$ [M+H]$^+$, 304.1696; found, 304.1699.

2-Methyl-1-(2-(4-nitrophenyl)-1H-benzo[d]imidazol-1-yl)prop-2-en-1-one (**1q**): Purified by flash silica chromatography (ethyl acetate/n-hexanes = 5/95), pale yellow solid, 50% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.32 (d, *J* = 8.7 Hz, 2H), 7.91 – 7.85 (m, 1H), 7.82 (d, *J* = 8.7 Hz, 2H), 7.73 – 7.67 (m, 1H), 7.46 – 7.38 (m, 2H), 5.78 (d, *J* = 1.5 Hz, 1H), 5.56 (s, 1H), 2.09 (s, 3H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 169.5, 151.2, 148.4, 142.7, 140.3, 137.2, 134.7, 129.7, 129.7, 125.6, 124.9, 123.9, 120.7, 113.0, 18.1. HRMS (APCI): m/z calculated for $C_{17}H_{14}N_3O_3$ [M+H]$^+$, 308.1030; found, 308.1033.

5-(Cyclohexylmethyl)-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one[6] (**3a**): Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 2/98), white solid, 66% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.49 (d, *J* = 7.8 Hz, 1H), 8.42 – 8.34 (m, 1H), 7.85 – 7.79 (m, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.50 – 7.35 (m, 4H), 2.47 (dd, *J* = 14.1, 7.9 Hz, 1H), 2.04 (dd, *J* = 14.2, 4.2 Hz, 1H), 1.65 (s, 3H), 1.46 – 1.32 (m, 3H), 1.28 – 1.18 (m, 2H), 1.03 – 0.74 (m, 6H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 173.4, 149.8, 144.0, 141.8, 131.5, 131.4, 127.5, 126.5, 125.9, 125.7, 125.4, 122.5, 119.7, 115.7, 48.7, 48.2, 34.8, 34.2, 32.8, 31.7, 25.9, 25.8.

5-(Cyclohexylmethyl)-3-fluoro-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (**3b**): Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 2/98), white solid, 64% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.49 (dd, J = 8.7, 5.8 Hz, 1H), 8.36 (dd, J = 6.5, 2.4 Hz, 1H), 7.81 (dd, J = 6.4, 2.2 Hz, 1H), 7.48 – 7.38 (m, 2H), 7.23 – 7.11 (m, 2H), 2.49 (dd, J = 14.3, 8.0 Hz, 1H), 1.98 (dd, J = 14.3, 5.0 Hz, 1H), 1.65 (s, 3H), 1.52 – 1.35 (m, 3H), 1.48 – 1.19 (m, 2H), 1.06 – 0.75 (m, 6H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 172.8, 164.9 (d, *J* = 252.6 Hz), 149.0, 144.7 (d, *J* = 7.9 Hz), 144.0, 131.3, 128.5 (d, *J* = 9.2 Hz), 125.9, 125.5, 119.6, 119.1, 115.6 (d, *J* = 19.4 Hz), 113.4 (d, *J* = 22.9 Hz), 48.8, 48.5, 34.9, 34.2, 32.9, 31.7, 25.9, 25.8. $^{19}$F NMR (376 MHz, Chloroform-*d*): δ -106.66 – -106.72 (m, 1F). HRMS (ESI): m/z calculated for $C_{23}H_{24}FN_2O$ [M+H]$^+$, 363.1867; found, 363.1868.

3-Chloro-5-(cyclohexylmethyl)-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one[6] (**3c**): Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 2/98), white solid, 68% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.41 (d, *J* = 8.2 Hz, 1H), 8.36 – 8.34 (m, 1H), 7.81 – 7.79 (m, 1H), 7.45 – 7.49 (m, 4H), 2.47 (dd, *J* = 14.3, 8.0 Hz, 1H), 1.99 (dd, *J* = 14S.2, 5.0 Hz, 1H), 1.65 (s, 3H), 1.46 – 1.39 (m, 3H), 1.26 – 1.25 (m, 1H), 1.16 (br, 1H), 1.00 – 0.75 (m, 6H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 172.6, 148.8, 143.9, 143.5, 137.7, 131.3, 128.1, 127.3, 126.6, 125.9, 125.8, 125.6, 121.2, 119.7, 115.7, 48.7, 48.3, 34.8, 34.1, 32.8, 31.5, 25.8, 25.8.

3-Bromo-5-(cyclohexylmethyl)-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (**3d**): Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 2/98), white solid, 65% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.37 – 8.34 (m, 2H), 7.83 – 7.81 (m, 1H), 7.63 – 7.60 (m, 2H), 7.47 – 7.41 (m, 2H), 2.47 (dd, *J* = 14.3, 7.9 Hz, 1H), 2.00 (dd, *J* = 14.3, 5.1 Hz, 1H), 1.66 (s, 3H), 1.49 – 1.39 (m, 3H), 1.29 – 1.17 (m, 2H), 1.01 – 0.76 (m, 6H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 172.6, 148.9, 144.0, 143.7, 131.4, 131.1, 129.7, 127.4, 126.2, 126.0, 125.7, 121.6, 119.8, 115.8, 48.8, 48.3, 34.9, 34.2, 32.9, 31.5, 25.9, 25.8. HRMS (ESI): m/z calculated for $C_{23}H_{24}BrN_2O$[M+H]$^+$, 423.1067; found, 423.1066.

5-(Cyclohexylmethyl)-3-ethyl-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (**3e**): Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 2/98), white solid, 61% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.39 (d, *J* = 8.2 Hz, 1H), 8.38 – 8.36 (m, 1H), 7.82 – 7.80 (m, 1H), 7.41 (qd, *J* = 7.3, 1.3 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.26 (s, 1H), 2.76 (q, *J* = 7.6 Hz, 2H), 2.45 (dd, *J* = 14.2, 7.7 Hz, 1H), 2.04 (dd, *J* = 14.2, 5.1 Hz, 1H), 1.66 (s, 3H), 1.47 – 1.35 (m, 3H), 1.29 (t, *J* = 7.6 Hz, 3H), 1.27 – 1.17 (m, 2H), 1.03 – 0.73 (m, 6H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 173.6, 150.0, 148.3, 144.1, 141.9, 131.4, 127.4, 125.9, 125.8, 125.7, 125.2, 120.1, 119.5, 115.7, 48.8, 48.3, 34.9, 34.2, 33.0, 31.6, 29.2, 25.9, 25.9, 25.8, 15.3. HRMS (ESI): m/z calculated for $C_{25}H_{29}N_2O$ [M+H]$^+$, 373.2274; found, 373.2275.

5-(Cyclohexylmethyl)-2,3,4-trimethoxy-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (**3f**): Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 5/95), white solid, 58% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.38 – 8.35 (m, 1H), 7.81 (s, 1H), 7.80 – 7.78 (m, 1H), 7.41 (q, *J* = 7.4 Hz, 2H), 4.02 (d, *J* = 4.5 Hz, 6H), 3.91 (s, 3H), 2.57 (dd, *J* = 13.9, 4.3 Hz, 1H), 2.32 (dd, *J* = 13.9, 8.0 Hz, 1H), 1.73 (s, 3H), 1.51 – 1.28 (m, 4H), 1.10 – 1.07 (m, 1H), 0.95 – 0.69 (m, 6H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 174.7, 153.4, 152.4, 149.9, 145.3, 144.1, 131.5, 127.1, 125.7, 125.2, 119.3, 118.3, 115.8, 103.5, 60.7, 60.6, 56.2, 48.4, 46.4, 35.6, 33.9, 32.7, 28.2, 26.0, 26.0, 25.9. HRMS (ESI): m/z calculated for $C_{26}H_{31}N_2O_4$[M+H]$^+$, 435.2278; found, 435.2280.

5-(Cyclohexylmethyl)-5-methyl-6-oxo-5,6-dihydrobenzo[4,5]imidazo[2,1-a]isoquinolin-3-yl acetate (**3g**): Prepared

by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 5/95), white solid, 62% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.55 (d, *J* = 8.5 Hz, 1H), 8.43 – 8.41 (m, 1H), 7.88 – 7.86 (m, 1H), 7.51 – 7.45 (m, 2H), 7.30 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.26 (s, 1H), 2.52 (dd, *J* = 14.3, 7.9 Hz, 1H), 2.40 (s, 3H), 2.04 (dd, *J* = 14.2, 5.0 Hz, 1H), 1.71 (s, 3H), 1.56 – 1.40 (m, 3H), 1.37 – 1.21 (m, 2H), 1.12 – 0.81 (m, 6H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 173.0, 168.7, 153.3, 149.1, 144.0, 143.5, 131.3, 127.4, 125.8, 125.5, 121.3, 120.2, 119.7, 115.7, 48.9, 48.4, 34.8, 34.1, 32.9, 31.5, 25.9, 25.8, 21.2. HRMS (ESI): m/z calculated for $C_{25}H_{27}N_2O_3[M+H]^+$, 403.2016; found, 403.2016.

N-(5-(cyclohexylmethyl)-5-methyl-6-oxo-5,6-dihydrobenzo[4,5]imidazo[2,1-a]isoquinolin-3-yl)acetamide **(3h):** Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 5/95), white solid, 55% yield. $^1$H NMR (399 MHz, DMSO-$d_6$): δ 10.30 (s, 1H), 8.28 (d, *J* = 8.6 Hz, 1H), 8.23 (d, *J* = 6.8 Hz, 1H), 7.86 (s, 1H), 7.76 (t, *J* = 7.4 Hz, 2H), 7.41 (q, *J* = 7.3 Hz, 2H), 2.31 (dd, *J* = 14.1, 7.9 Hz, 1H), 2.11 (s, 3H), 2.00 (d, *J* = 4.7 Hz, 1H), 1.59 (s, 3H), 1.46 – 1.18 (m, 4H), 1.08 (s, 1H), 1.00 – 0.66 (m, 6H). $^{13}$C{$^1$H} NMR (100 MHz, DMSO-$d_6$): δ 173.1, 169.0, 149.4, 143.8, 142.6, 142.6, 130.9, 126.3, 125.7, 125.0, 119.3, 118.4, 116.7, 116.3, 115.1, 48.5, 47.9, 34.4, 33.7, 32.4, 31.0, 25.4, 25.3, 24.2. HRMS (ESI): m/z calculated for $C_{25}H_{28}N_3O_2[M+H]^+$, 402.2176; found, 402.2177.

5-(Cyclohexylmethyl)-5-methyl-6-oxo-5,6-dihydrobenzo[4,5]imidazo[2,1-a]isoquinoline-2-carbonitrile **(3i)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 2/98), white solid, **3i**/**3i'** is 1/2, total 64% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.79 (d, *J* = 1.6 Hz, 1H), 8.40 – 8.33 (m, 1H), 7.87 – 7.75 (m, 2H), 7.59 (d, *J* = 8.3 Hz, 1H), 7.52 – 7.43 (m, 2H), 2.53 (dd, *J* = 14.4, 8.0 Hz, 1H), 2.05 (dd, *J* = 14.3, 4.9 Hz, 1H), 1.68 (s, 3H), 1.53 – 1.35 (m, 3H), 1.25 – 1.13 (m, 2H), 1.02 – 0.73 (m, 6H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 172.0, 147.4, 146.2, 143.8, 133.8, 131.3, 129.9, 127.7, 126.3, 126.2, 124.0, 120.2, 117.6, 115.8, 112.1, 48.7, 48.5, 34.9, 34.2, 32.8, 31.4, 25.8, 25.7. HRMS (ESI): m/z calculated for $C_{24}H_{24}N_3O[M+H]^+$, 370.1914; found, 370.1915.

5-(cyclohexylmethyl)-5-methyl-6-oxo-5,6-dihydrobenzo[4,5]imidazo[2,1-a]isoquinoline-4-carbonitrile **(3i')**: $^1$H NMR (500 MHz, Chloroform-*d*): δ 8.82 (d, *J* = 8.0 Hz, 1H), 8.42 – 8.36 (m, 1H), 7.93 (d, *J* = 7.6 Hz, 1H), 7.87 – 7.82 (m, 1H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.51 – 7.47 (m, 2H), 2.96 (dd, *J* = 14.9, 4.1 Hz, 1H), 2.56 (dd, *J* = 15.0, 7.9 Hz, 1H), 1.94 (s, 3H), 1.51 – 1.33 (m, 5H), 0.98 – 0.80 (m, 6H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 172.2, 147.8, 143.9, 138.4, 130.7, 128.1, 126.3, 126.3, 124.7, 120.1, 118.5, 116.0, 111.5, 49.2, 46.0, 35.4, 33.7, 32.7, 29.7, 29.0, 25.8, 25.8. HRMS (ESI): m/z calculated for $C_{24}H_{24}N_3O[M+H]^+$, 370.1914; found, 370.1915.

5-(Cyclohexylmethyl)-2-methoxy-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one[6] **(3j)**: $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.38 (dd, *J* = 6.3, 2.7 Hz, 1H), 7.93 (d, *J* = 2.7 Hz, 1H), 7.85 – 7.82 (m, 1H), 7.74 – 7.40 (m, 2H), 7.34 (d, *J* = 8.8 Hz, 1H), 7.14 (dd, *J* = 8.8, 2.7 Hz, 1H), 3.97 (s, 3H), 2.44 (dd, *J* = 14.2, 8.0 Hz, 1H), 2.01 (dd, *J* = 14.1, 4.9 Hz, 1H), 1.63 (s, 3H), 1.53 – 1.35 (m, 3H), 1.31 – 1.12 (m, 2H), 1.04 – 0.71 (m, 6H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 173.8, 158.7, 149.9, 143.9, 134.2, 131.5, 127.9, 125.8, 125.5, 123.5, 120.4, 119.6, 115.8, 107.7, 55.7, 48.8, 47.9, 34.9, 34.2, 32.9, 31.8, 26.0, 25.9.

5-(Cyclohexylmethyl)-4-methoxy-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one[6] **(3j')**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 5/95), white solid, **3j**/**3j'** is 1/1.3, 67% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.40 – 8.38 (m, 1H), 8.19 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.83 – 7.81 (m, 1H), 7.49 – 7.39 (m, 3H), 7.08 (d, *J* = 8.2 Hz, 1H), 3.93 (s, 3H), 2.74 (dd, *J* = 13.9, 4.1 Hz, 1H), 2.33 (dd, *J* = 13.9, 7.6 Hz, 1H), 1.75 (s, 3H), 1.48 – 1.24 (m, 4H), 1.11 (d, *J* = 7.1 Hz, 1H), 0.97 – 0.70 (m, 6H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 174.6, 157.6, 150.0, 144.2, 131.4, 129.2, 128.8, 125.8, 125.3, 124.1, 119.6, 118.7, 115.9, 114.1, 55.4, 48.7, 45.5, 35.6, 34.0, 32.9, 27.2, 26.0, 25.8.

5-(Cyclohexylmethyl)-5-methyl-1-(trifluoromethyl)benzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one **(3k)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 2/98), white solid, 60% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.44 – 8.37 (m, 1H), 8.00 – 7.87 (m, 2H), 7.72 (d, *J* = 7.9 Hz, 1H), 7.64 (t, *J* = 7.9 Hz, 1H), 7.48 (dt, *J* = 5.7, 4.0 Hz, 2H), 2.52 (dd, *J* = 14.4, 8.0 Hz, 1H), 2.05 (dd, *J* = 14.3, 4.8 Hz, 1H), 1.68 (s, 3H), 1.52 – 1.36 (m, 3H), 1.30 – 1.14 (m, 2H), 1.02 – 0.73 (m, 6H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 172.3, 145.6, 144.5, 143.9, 130.8, 130.6, 130.2, 128.2 (q, *J* = 32.8 Hz), 127.2 (q, *J* = 7.1 Hz), 126.4, 125.9, 123.6 (d, *J* = 273.4 Hz), 121.5, 120.8, 115.7, 48.9, 48.4, 34.8, 34.2, 32.8, 31.7, 25.9, 25.8. $^{19}$F NMR (376 MHz, Chloroform-*d*): δ -59.3. HRMS (ESI): m/z calculated for $C_{24}H_{24}F_3N_2O$ $[M+H]^+$, 413.1835; found, 413.1836.

7-(Cyclohexylmethyl)-7-methylbenzo[g]benzo[4,5]imidazo[2,1-a]isoquinolin-6(7H)-one **(3l)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 2/98), white solid, 60% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.65 (d, *J* = 8.6 Hz, 1H), 8.57 – 8.51 (m, 1H), 8.42 (dd, *J* = 6.7, 2.4 Hz, 1H), 7.96 (dd, *J* = 8.9, 6.8 Hz, 2H), 7.87 (dd, *J* = 6.7, 2.4 Hz, 1H), 7.63 – 7.57 (m, 2H), 7.51 – 7.43 (m, 2H), 2.90 (dd, *J* = 14.5, 4.5 Hz, 1H), 2.75 (dd, *J* = 14.6, 7.6 Hz, 1H), 2.05 (s, 3H), 1.31 (d, *J* = 11.5 Hz, 3H), 1.17 – 1.06 (m, 2H), 0.86 – 0.62 (m, 6H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 174.8, 150.3, 144.4, 138.0, 136.0, 131.3, 130.9, 130.2, 129.6, 127.0, 126.6, 126.0, 125.6, 122.5, 121.3, 119.7, 115.8, 50.5, 48.3, 35.4, 33.7, 32.8, 29.5, 25.8, 25.7, 25.7. HRMS (ESI): m/z calculated for $C_{27}H_{27}N_2O[M+H]^+$, 395.2118; found, 395.2118.

5-(Cyclohexylmethyl)-5-methylindolo[2,1-a]isoquinolin-6(5H)-one **(3m)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 2/98), white solid, 74% yield. $^1$H NMR (500 MHz, Chloroform-*d*): δ 8.63 (d, *J* = 8.1 Hz, 1H), 7.89 – 7.85 (m, 1H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.41 – 7.31 (m, 5H), 7.04 (s, 1H), 2.47 (dd, *J* = 14.1, 7.9 Hz, 1H), 1.99 (dd, *J* = 14.1, 5.0 Hz, 1H), 1.64 (s, 3H), 1.49 – 1.35 (m, 3H), 1.32 – 1.23 (m, 2H), 1.09 – 0.76 (m, 6H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 173.5, 138.6, 135.5, 135.3, 130.6, 128.6, 127.0, 126.8, 125.0, 124.4, 124.4, 123.7, 120.3, 116.8, 102.6, 49.0, 47.6, 34.9, 34.3, 32.8, 31.5, 26.0, 26.0, 25.9. HRMS (ESI): m/z calculated for $C_{24}H_{25}NONa[M+Na]^+$, 366.1828; found, 366.1827.

3-Chloro-5-(cyclohexylmethyl)-5-methylindolo[2,1-a]isoquinolin-6(5H)-one **(3n)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 2/98), white solid, 78% yield. $^1$H NMR (500 MHz, Chloroform-*d*): δ 8.60 (d, *J* = 8.1 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.63 – 7.59 (m, 1H), 7.42 – 7.30 (m, 4H), 7.01 (s, 1H), 2.46 (dd, *J* = 14.2, 7.9 Hz, 1H), 1.93 (dd, *J* = 14.3, 5.2 Hz, 1H), 1.63 (s, 3H), 1.52 – 1.39 (m, 3H), 1.32 – 1.21 (m, 2H), 1.09 – 0.93 (m, 3H), 0.83 (tt, *J* = 7.8, 2.5 Hz, 3H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 172.7, 140.4, 135.3, 134.5, 134.4, 130.4, 127.5, 126.8, 125.3, 125.1, 124.6, 123.0, 120.4, 116.8, 103.1, 49.0, 47.7, 34.8, 34.2, 32.8, 31.4, 26.0, 25.9. HRMS (APCI): m/z calculated for $C_{24}H_{25}ClNO$ $[M+H]^+$, 378.1619; found, 378.1625.

5-(Cyclohexylmethyl)-5-methyl-3-(trifluoromethyl)indolo[2,1-a]isoquinolin-6(5H)-one **(3o)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 2/98), white solid, 54% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.73 (d, *J* = 8.0 Hz, 1H), 8.08 (d, *J* = 8.1 Hz, 1H), 7.80 – 7.69 (m, 3H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.38 (s, 1H), 2.60 (dd, *J* = 14.3, 7.6 Hz, 1H), 2.09 (dd, *J* = 14.2, 5.1 Hz, 1H), 1.78 (s, 3H), 1.61 – 1.50 (m, 3H), 1.36 – 1.31 (m, 2H), 1.12 – 0.86 (m, 6H). $^{13}$C{1H} NMR (100 MHz, Chloroform-*d*): δ 172.6, 139.3, 135.5, 134.0, 130.3, 127.7, 125.9, 124.8, 124.2, 123.9, 120.8, 117.0, 104.7, 49.0, 47.9, 34.9, 34.2, 33.0, 31.2, 26.0, 25.9. $^{19}$F NMR (376 MHz, Chloroform-*d*): δ -62.8 (s, 3F). HRMS (APCI): m/z calculated for $C_{25}H_{25}F_3NO$ $[M+H]^+$, 412.1883; found, 412.1885.

5-Methyl-5-octylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one **(3p)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 2/98), colorless oil, 68% yield. $^1$H NMR (500 MHz, Chloroform-*d*): δ 8.48 (d, *J* = 7.5 Hz, 1H), 8.37 (dd, *J* = 6.5, 2.1 Hz, 1H), 7.82 (dd, *J* = 6.4, 2.0 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.49 – 7.41 (m, 4H), 2.39 (td, *J* = 12.8, 4.6 Hz, 1H), 1.97 (td, *J* = 12.9, 4.3 Hz, 1H), 1.72 (s, 3H), 1.22 – 1.02 (m, 10H), 0.96 – 0.88 (m, 1H), 0.84 – 0.76 (m, 4H). $^{13}$C{1H} NMR (100 MHz, Chloroform-*d*): δ 173.3, 149.9, 144.0, 141.9, 131.8, 131.3, 127.5, 126.0, 125.8, 125.4, 122.9, 119.7, 115.6, 49.4, 43.1, 31.6, 29.4, 29.0, 29.0, 28.8, 25.0, 22.5, 14.0. HRMS (ESI): m/z calculated for $C_{24}H_{29}N_2O$ $[M+H]^+$, 361.2274; found, 361.2276.

5-(4-Bromobutyl)-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one **(3q)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 2/98), white solid, 53% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.49 (d, *J* = 7.8 Hz, 1H), 8.36 (dd, *J* = 6.5, 2.6 Hz, 1H), 7.85 – 7.80 (m, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.52 – 7.40 (m, 4H), 3.19 (qd, *J* = 7.8, 2.7 Hz, 2H), 2.44 (td, *J* = 12.9, 4.9 Hz, 1H), 2.02 (td, *J* = 12.9, 4.9 Hz, 1H), 1.79 – 1.64 (m, 5H), 1.13 – 0.95 (m, 2H). $^{13}$C{1H} NMR (100 MHz, Chloroform-*d*): δ 173.1, 149.7, 144.0, 141.3, 131.9, 131.2, 127.8, 125.9, 125.6, 122.9, 119.8, 115.6, 49.3, 41.6, 32.5, 29.2, 23.8. HRMS (ESI): m/z calculated for $C_{20}H_{20}BrN_2O$ $[M+H]^+$, 383.0754; found, 383.0754.

5-(3-(4-Methoxyphenyl)propyl)-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one **(3r)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 2/98), white solid, 72% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.48 (d, *J* = 7.8 Hz, 1H), 8.38 (dd, *J* = 5.9, 2.6 Hz, 1H), 7.82 (dd, *J* = 5.9, 2.8 Hz, 1H), 7.57 – 7.34 (m, 5H), 6.88 (d, *J* = 8.5 Hz, 2H), 6.72 (d, *J* = 8.5 Hz, 2H), 3.73 (s, 3H), 2.51 – 2.33 (m, 3H), 2.00 (td, *J* = 13.0, 4.0 Hz, 1H), 1.70 (s, 3H), 1.34 – 1.25 (m, 1H), 1.16 – 1.07 (m, 1H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 173.2, 157.7, 149.8, 144.0, 141.6, 133.2, 131.8, 131.2, 129.0, 127.6, 126.0, 125.8, 125.5, 122.9, 119.7, 115.6, 113.6, 55.1, 49.3, 42.1, 34.5, 29.0, 26.7. HRMS (ESI): m/z calculated for $C_{26}H_{25}N_2O_2$ $[M+H]^+$, 397.1911; found, 397.1912.

5-(4-Chlorophenethyl)-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one **(3s)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 2/98), white solid, 40% yield. $^1$H NMR (500 MHz, Chloroform-*d*): δ 8.52 (d, *J* = 7.8 Hz, 1H), 8.28 (dd, *J* = 6.8, 1.9 Hz, 1H), 7.82 (dd, *J* = 6.4, 1.6 Hz, 1H), 7.62 (td, *J* = 7.6, 1.3 Hz, 1H), 7.52 (t, *J* = 8.3 Hz, 2H), 7.47 – 7.40 (m, 2H), 7.03 (d, *J* = 8.3 Hz, 2H), 6.83 (d, *J* = 8.3 Hz, 2H), 2.79 (dt, *J* = 13.2, 8.1 Hz, 1H), 2.28 (dt, *J* = 13.2, 8.1 Hz, 1H), 2.20 (t, *J* = 8.0 Hz, 2H), 1.74 (s, 3H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 172.8, 149.6, 144.0, 141.1, 138.5, 132.0, 131.9, 131.2, 129.5, 128.3, 127.9, 126.0, 125.9, 125.6, 123.2, 119.7, 115.6, 49.1, 44.0, 31.0, 29.5. HRMS (ESI): m/z calculated for $C_{24}H_{20}ClN_2O$ $[M+H]^+$, 387.1259; found, 387.1260.

5-(2-Ethylhexyl)-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one **(3t)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/*n*-hexanes = 2/98), white solid, 66% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.47 (d, *J* = 7.4 Hz, 1H), 8.35 (d, *J* = 7.3 Hz, 1H), 7.81 (d, *J* = 7.4 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.47 – 7.36 (m, 4H), 2.37 (td, *J* = 14.1, 5.6 Hz, 1H), 1.98 (ddd, *J* = 13.3, 6.3, 2.3 Hz, 1H), 1.72 (d, *J* = 3.0 Hz, 3H), 1.02 – 0.67 (m, 11H), 0.58 – 0.51 (m, 4H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 173.4, 173.4, 149.8, 144.0, 141.8, 141.8, 131.4, 131.3, 127.5, 126.6, 126.5, 125.7, 125.7, 125.4, 122.9, 122.8, 119.6, 115.6, 48.6, 48.5, 47.2, 46.9, 35.9, 35.8, 33.0, 32.6, 29.6, 29.4, 28.1, 27.8, 26.4, 25.8, 22.6, 22.5, 13.8, 13.7, 10.3, 9.9. HRMS (ESI): m/z calculated for $C_{24}H_{29}N_2O[M+H]^+$, 361.2274; found, 361.2274.

5-Methyl-5-((tetrahydro-2H-pyran-4-yl)methyl)benzo[4, 5]imidazo[2,1-a]isoquinolin-6(5H)-one **(3u)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/n-hexanes = 2/98), white solid, 76% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.49 (d, *J* = 7.8 Hz, 1H), 8.40 – 8.34 (m, 1H), 7.82 (d, *J* = 7.0 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.53 – 7.38 (m, 4H), 3.65 (t, *J* = 11.9 Hz, 2H), 3.07 – 2.91 (m, 2H), 2.53 (dd, *J* = 14.3, 6.2 Hz, 1H), 2.09 (dd, *J* = 14.2, 4.2 Hz, 1H), 1.68 (s, 3H), 1.28 – 1.01 (m, 5H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 173.1, 149.6, 144.0, 141.5, 131.7, 131.3, 127.7, 126.4, 126.0, 125.9, 125.6, 122.5, 119.8, 115.7, 67.4, 67.4, 48.4, 48.1, 33.7, 32.8, 32.4, 31.6. HRMS (ESI): m/z calculated for $C_{22}H_{23}N_2O_2[M+H]^+$, 347.1754; found, 347.1755.

5-(Cyclobutylmethyl)-5-methylbenzo[4,5]imidazo[2,1-a] isoquinolin-6(5H)-one[6] **(3v)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/n-hexanes = 2/98), white solid, 56% yield. $^1$H NMR (399 MHz, Chloroform-*d*): δ 8.47 – 8.45 (m, 1H), 8.35 (dd, *J* = 6.4, 2.5 Hz, 1H), 7.81 (dd, *J* = 6.3, 1.9 Hz, 1H), 7.56 – 7.52 (m, 1H), 7.48 – 7.38 (m, 4H), 2.46 (dd, *J* = 13.5, 8.0 Hz, 1H), 2.07 (dd, *J* = 13.5, 6.4 Hz, 1H), 1.89 – 1.81 (m, 1H), 1.73 (s, 3H), 1.54 – 1.41 (m, 5H), 1.34 – 1.25 (m, 1H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 173.2, 149.9, 144.0, 141.8, 131.5, 131.3,

127.5, 126.4, 125.7, 125.7, 125.4, 122.8, 119.7, 115.6, 51.3, 48.5, 32.8, 28.8, 28.4, 27.8, 18.5.

5-Methyl-5-((1-methylcyclohexyl)methyl)benzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one **(3w)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/n-hexanes = 2/98), colorless oil, 68% yield. $^{1}$H NMR (399 MHz, Chloroform-*d*): δ 8.48 (d, *J* = 7.5 Hz, 1H), 8.41 – 8.35 (m, 1H), 7.86 – 7.79 (m, 1H), 7.54 – 7.39 (m, 5H), 2.59 (d, *J* = 14.5 Hz, 1H), 2.20 (d, *J* = 14.5 Hz, 1H), 1.70 (s, 3H), 1.32 – 0.97 (m, 8H), 0.83 – 0.75 (m, 2H), 0.39 (s, 3H). $^{13}$C{$^{1}$H} NMR (100 MHz, Chloroform-*d*): δ 173.5, 149.8, 144.1, 142.2, 131.4, 131.0, 127.5, 125.8, 125.7, 125.4, 122.2, 119.7, 115.8, 55.3, 47.3, 39.2, 39.1, 34.4, 33.2, 25.9, 23.9, 21.7, 21.6. HRMS (ESI): m/z calculated for $C_{24}H_{27}N_2O[M+H]^+$, 359.2118; found, 359.2120.

3-Chloro-5-methyl-5-(pent-4-en-1-yl)indolo[2,1-a]isoquinolin-6(5H)-one **(3x)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/n-hexanes = 2/98), colorless oil, 76% yield. $^{1}$H NMR (399 MHz, Chloroform-*d*): δ 8.59 (d, *J* = 8.1 Hz, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.42 – 7.28 (m, 4H), 7.00 (s, 1H), 5.66 – 5.54 (m, 1H), 4.90 (d, *J* = 5.0 Hz, 1H), 4.86 (s, 1H), 2.39 (td, *J* = 12.9, 4.6 Hz, 1H), 1.90 (ddt, *J* = 17.6, 12.9, 5.2 Hz, 3H), 1.69 (s, 3H), 1.14 – 0.91 (m, 2H). $^{13}$C{$^{1}$H} NMR (100 MHz, Chloroform-*d*): δ 172.4, 140.3, 137.8, 135.2, 134.6, 134.5, 130.5, 127.7, 126.3, 125.4, 125.0, 124.7, 123.5, 120.5, 116.7, 115.0, 103.2, 48.8, 42.5, 33.5, 28.6, 24.2. HRMS (APCI): m/z calculated for $C_{22}H_{21}ClNO$ $[M+H]^+$, 350.1306; found, 350.1309.

Tert-butyl 4-methyl-4-((5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)methyl)piperidine-1-carboxylate **(3z)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/n-hexanes = 5/95), white solid, 70% yield. $^{1}$H NMR (399 MHz, Chloroform-*d*): δ 8.60 (d, *J* = 7.9 Hz, 1H), 7.85 (dt, *J* = 5.2, 3.2 Hz, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.46 – 7.29 (m, 5H), 7.05 (s, 1H), 3.53 – 3.38 (m, 2H), 2.92 – 2.82 (m, 1H), 2.81 – 2.70 (m, 1H), 2.61 (d, *J* = 14.4 Hz, 1H), 2.11 (d, *J* = 14.4 Hz, 1H), 1.69 (s, 3H), 1.39 (s, 9H), 1.33 – 1.24 (m, 1H), 1.07 – 0.93 (m, 2H), 0.71 (d, *J* = 13.7 Hz, 1H), 0.47 (s, 3H). $^{13}$C{$^{1}$H} NMR (100 MHz, Chloroform-*d*): δ 173.3, 154.8, 138.4, 135.2, 130.6, 128.4, 127.6, 127.3, 125.2, 124.6, 123.9, 123.7, 120.4, 116.9, 103.0, 79.2, 54.7, 46.5, 38.1, 38.0, 33.0, 32.9, 28.4, 22.0. HRMS (APCI): m/z calculated for $C_{29}H_{35}N_2O_3$ $[M+H]^+$, 459.2642; found, 259.2642.

5-(2-(Adamantan-1-yl)ethyl)-5-methyl-12-propylindolo[2, 1-a]isoquinolin-6(5H)-one **(3aa)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/n-hexanes = 2/98), pale yellow oil, 71% yield. $^{1}$H NMR (399 MHz, Chloroform-*d*): δ 8.64 (d, *J* = 7.8 Hz, 1H), 7.96 (d, *J* = 7.2 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.43 – 7.33 (m, 5H), 3.10 (t, *J* = 7.3 Hz, 2H), 2.34 (td, *J* = 13.0, 4.5 Hz, 1H), 1.94 – 1.79 (m, 6H), 1.68 – 1.50 (m, 9H), 1.39 – 1.25 (m, 6H), 1.14 (t, *J* = 7.3 Hz, 3H), 0.78 (td, *J* = 13.1, 4.4 Hz, 1H), 0.63 (td, *J* = 13.1, 4.0 Hz, 1H). $^{13}$C{$^{1}$H} NMR (100 MHz, Chloroform-*d*): δ 173.2, 139.0, 134.2, 132.2, 129.5, 127.9, 126.9, 126.5, 126.4, 125.5, 124.6, 124.0, 119.2, 118.4, 116.8, 48.3, 42.0, 38.9, 37.1, 35.4, 31.9, 29.1, 28.6, 27.3, 22.3, 14.5. HRMS (ESI): m/z calculated for $C_{32}H_{37}NONa$ $[M+Na]^+$, 474.2767; found, 474.2766.

5-(4-Fluorobenzyl)-5-methylbenzo[4,5]imidazo[2,1-a]iso - quinolin-6(5H)-one **(3ab):** Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/n-hexanes = 2/98), white solid, 72% yield. $^{1}$H NMR (399 MHz, Chloroform-*d*): δ 8.35 – 8.26 (m, 2H), 7.72 – 7.66 (m, 1H), 7.63 – 7.55 (m, 2H), 7.49 – 7.44 (m, 1H), 7.49 – 7.31 (m, 2H), 6.49 (d, *J* = 7.0 Hz, 4H), 3.53 (d, *J* = 13.2 Hz, 1H), 3.13 (d, *J* = 13.2 Hz, 1H), 1.91 (s, 3H). $^{13}$C{$^{1}$H} NMR (100 MHz, Chloroform-*d*): δ 172.4, 161.7 (d, *J* = 246.0 Hz), 149.3, 143.7, 140.4, 131.5, 130.9 (d, *J* = 8.8 Hz), 130.8, 130.5, 130.4, 127.9, 126.5, 125.7, 125.7, 125.4, 125.4, 123.5, 119.7, 115.3, 114.6 (d, *J* = 21.4 Hz)., 51.0, 49.7, 26.0. $^{19}$F NMR (376 MHz, Chloroform-*d*): δ -115.0 (q, *J* = 7.0 Hz, 1F). HRMS (ESI): m/z calculated for $C_{23}H_{18}N_2OF[M+H]^+$, 357.1398; found, 357.1399.

5-(4-Methoxybenzyl)-5-methylbenzo[4,5]imidazo[2,1-a] isoquinolin-6(5H)-one **(3ac)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/n-hexanes = 2/98), white solid, 70% yield. $^{1}$H NMR (500 MHz, Chloroform-*d*): δ 8.36 – 8.31 (m, 1H), 8.29 (d, *J* = 7.8 Hz, 1H), 7.72 – 7.67 (m, 1H), 7.58 (dt, *J* = 13.1, 7.1 Hz, 2H), 7.46 (t, *J* = 7.9 Hz, 1H), 7.39 (q, *J* = 5.3, 3.7 Hz, 2H), 6.45 (d, *J* = 8.6 Hz, 2H), 6.34 (d, *J* = 8.6 Hz, 2H), 3.52 (s, 3H), 3.50 (d, *J* = 13.3 Hz, 1H), 3.12 (d, *J* = 13.3 Hz, 1H), 1.90 (s, 3H). $^{13}$C{$^{1}$H} NMR (100 MHz, Chloroform-*d*): δ 172.7, 158.4, 149.5, 143.8, 140.8, 131.4, 131.0, 130.0, 127.7, 127.1, 126.6, 125.6, 125.3, 123.5, 119.6, 115.4, 113.2, 54.9, 51.2, 49.9, 25.9. HRMS (ESI): m/z calculated for $C_{24}H_{21}N_2O_2$ $[M+H]^+$, 369.1598; found, 369.1598.

4-((5-Methyl-6-oxo-5,6-dihydrobenzo[4,5]imidazo[2,1-a] isoquinolin-5-yl)methyl)benzonitrile **(3ad)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/n-hexanes = 2/98), white solid, 62% yield. $^{1}$H NMR (399 MHz, Chloroform-*d*): δ 8.34 – 8.27 (m, 2H), 7.73 – 7.69 (m, 1H), 7.66 – 7.59 (m, 2H), 7.49 (ddd, *J* = 8.3, 6.7, 1.8 Hz, 1H), 7.43 – 7.38 (m, 2H), 7.11 (d, *J* = 8.3 Hz, 2H), 6.66 (d, *J* = 8.3 Hz, 2H), 3.64 (d, *J* = 13.0 Hz, 1H), 3.23 (d, *J* = 13.0 Hz, 1H), 1.94 (s, 3H). $^{13}$C{$^{1}$H} NMR (100 MHz, Chloroform-*d*): δ 171.9, 149.0, 143.8, 140.7, 139.7, 131.7, 131.5, 130.8, 129.7, 128.2, 126.4, 126.0, 125.9, 125.7, 123.4, 119.9, 118.3, 115.3, 111.0, 50.8, 49.8, 26.8. HRMS (ESI): m/z calculated for $C_{24}H_{18}N_3O$ $[M+H]^+$, 364.1444; found, 364.1443.

5-Methyl-5-(2-(trifluoromethyl)benzyl)benzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one **(3ae)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/n-hexanes = 2/98), white solid, 65% yield. $^{1}$H NMR (399 MHz, Chloroform-*d*): δ 8.48 – 8.43 (m, 1H), 8.35 – 8.31 (m, 1H), 7.83 (dd, *J* = 6.6, 2.1 Hz, 1H), 7.53 – 7.38 (m, 6H), 7.12 (t, *J* = 7.6 Hz, 1H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.55 (d, *J* = 7.8 Hz, 1H), 4.06 (d, *J* = 16.4 Hz, 1H), 3.70 (d, *J* = 16.5 Hz, 1H), 1.85 (s, 3H). $^{19}$F NMR (376 MHz, Chloroform-*d*): δ -59.25 (s, 3F). $^{13}$C{$^{1}$H} NMR (100 MHz, Chloroform-*d*): δ 172.5, 149.5, 144.1, 140.8, 135.0, 132.0, 131.4, 129.2, 127.9, 126.5, 126.4, 126.3, 126.3, 126.2, 126.0, 125.9, 125.7, 125.6, 122.9, 119.8, 115.6, 49.3, 40.8, 30.8. HRMS (ESI): m/z calculated for $C_{24}H_{18}N_2O[M+H]^+$, 407.1366; found, 407.1367.

5-Methyl-5-(3-methylbenzyl)benzo[4,5]imidazo[2,1-a]iso quinolin-6(5H)-one **(3af)**: Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/n-hexanes = 2/98), white solid, 67% yield. $^{1}$H NMR (399 MHz, Chloroform-*d*): δ 8.34 (dd, *J* = 5.9, 3.3 Hz, 1H), 8.24 (d, *J* = 7.8 Hz, 1H), 7.68 (dd, *J* = 5.8, 3.2 Hz, 1H), 7.64 – 7.56 (m, 2H), 7.48 – 7.36 (m, 3H), 6.69 – 6.66 (m, 2H), 6.33 (s, 1H), 6.23 – 6.16 (m, 1H), 3.48 (d, *J* = 12.8 Hz, 1H), 3.08 (d, *J* = 12.9 Hz, 1H), 1.95 (s, 3H), 1.77 (s, 3H). $^{13}$C{$^{1}$H} NMR (100 MHz, Chloroform-*d*): δ 172.7, 149.5, 143.8, 140.6, 137.3, 134.7, 131.4,

131.0, 129.6, 127.7, 127.5, 126.4, 125.9, 125.6, 125.4, 125.3, 123.8, 119.6, 115.3, 51.5, 51.2, 25.1, 20.6. HRMS (ESI): m/z calculated for $C_{24}H_{21}N_2O[M+H]^+$, 353.1648; found, 353.1648.

5-(4-Fluorobenzyl)-2,3,4-trimethoxy-5-methylbenzo[4,5] imidazo[2,1-a]isoquinolin-6(5H)-one (**3ag**): Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/n-hexanes = 5/95), white solid, 64% yield. $^1$H NMR (500 MHz, Chloroform-d): δ 8.37 – 8.32 (m, 1H), 7.71 – 7.66 (m, 1H), 7.62 (s, 1H), 7.40 – 7.36 (m, 2H), 6.65 (dd, J = 8.6, 5.5 Hz, 2H), 6.51 (t, J = 8.7 Hz, 2H), 4.14 (s, 3H), 3.98 (s, 6H), 3.77 (d, J = 13.2 Hz, 1H), 3.49 (d, J = 13.2 Hz, 1H), 1.98 (s, 3H). $^{19}$F NMR (376 MHz, Chloroform-*d*): δ -116.0 – -116.1(m, 1F). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-*d*): δ 173.6, 161.5 (d, *J* = 245.3 Hz), 153.5, 152.2, 149.5, 145.5, 143.7, 132.5 (d, *J* = 2.6 Hz), 131.0, 130.2 (d, *J* = 7.8 Hz), 128.8, 128.4, 126.0, 125.8, 125.3, 119.3, 118.9, 115.5, 114.6 (d, *J* = 21.3 Hz), 103.4, 61.1, 60.7, 56.2, 51.2, 44.7, 25.7. HRMS (ESI): m/z calculated for $C_{26}H_{24}N_2O_4F$ $[M+H]^+$, 447.1715; found, 447.1713.

5-(4-Fluorobenzyl)-5-methyl-3-nitrobenzo[4,5]imidazo[2, 1-a]isoquinolin-6(5H)-one (**3ah**): Prepared by the general procedure, purified by flash silica chromatography (ethyl acetate/n-hexanes = 5/95), white solid, 61% yield. $^1$H NMR (500 MHz, DMSO-$d_6$): δ 8.66 (d, *J* = 1.9 Hz, 1H), 8.36 – 8.23 (m, 3H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 1H), 6.63 (t, *J* = 8.8 Hz, 2H), 6.53 (dd, *J* = 8.4, 5.7 Hz, 2H), 3.42 (s, 2H), 1.96 (s, 3H). $^{19}$F NMR (376 MHz, DMSO-$d_6$): δ -115.13 – -115.05 (m, 1F). $^{13}$C{$^1$H} NMR (100 MHz, DMSO-$d_6$) δ 171.5, 161.0 (d, *J* = 243.4 Hz), 149.3, 147.5, 143.3, 142.1, 131.2, 130.7 (d, *J* = 8.1 Hz), 130.6, 128.4, 126.4, 126.2, 126.1, 122.9, 122.7, 120.0, 115.0, 114.5 (d, *J* = 21.3 Hz), 51.2, 48.6, 39.7, 24.6. HRMS (ESI): m/z calculated for $C_{23}H_{17}N_3O_3F[M+H]^+$, 402.1248; found, 402.1247.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Optimization of the reaction conditions, copies of NMR spectra, the reaction setup.

## ■ AUTHOR INFORMATION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