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J. Org. Chem., **Just Accepted Manuscript** • Publication Date (Web): 22 Jan 2015

Just Accepted

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Palladium-Catalyzed Intramolecular C(sp^2)-H Imidoylation for the Synthesis of Six-Membered *N*-Heterocycles

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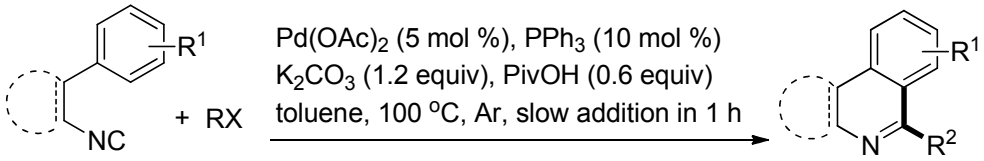


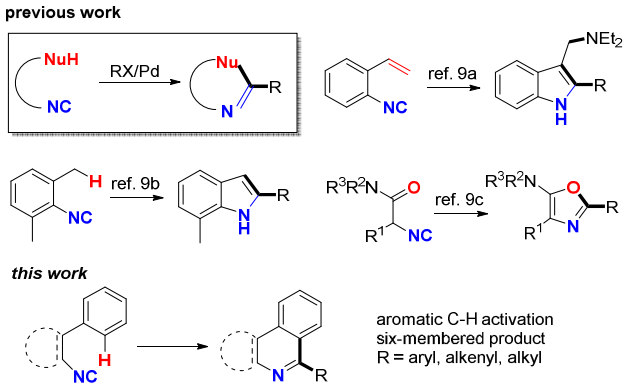
ABSTRACT: A new strategy for the construction of phenanthridine and isoquinoline scaffolds, starting from arenes containing a pending isocyanide moiety under palladium catalysis, has been developed. This process involves sequential intermolecular isocyanide insertion to an aryl palladium(II) intermediate and intramolecular aromatic C-H activation as key steps. Alkyl palladium(II) intermediate lacking β-hydrogen is also applicable to this reaction, generating unique bisheterocyclic scaffolds with three C-C bonds being formed consecutively.

INTRODUCTION

The versatility of isocyanide in generating molecular complexity has been adequately demonstrated in Ugi and related multicomponent reactions (MCRs) since 1960's. [1] In the past decade, another important and unique reactivity of isocyanide has been increasingly recognized, that is palladium-catalyzed imidoylation process.[2] Similar to carbon monoxide (CO) as its isoelectronic equivalent, isocyanide can undergo migratory insertion to a Pd(II) intermediate, followed by substitution with various nucleophiles and reductive elimination to generate amidines,[3a] amides,[3b,4] ketimines,[5] imidates, or thiomidates[6] accordingly. This palladium-catalyzed imidoylation reaction is particularly powerful in construction of het-

erocyclic skeletons through non-functionalized or functionalized isocyanide strategies. In non-functionalized isocyanide approach, only the terminal carbon of isocyanide is consisted in the constructed heterocyclic ring by reacting isocyanide with molecules either bearing two nucleophiles[7] or containing a nucleophile and a precursor of Pd(II) intermediate ready for isocyanide insertion.[8] In functionalized isocyanide strategy, however, the isocyanide substrate not only participates in migratory insertion, but also provides inbuilt functional groups which can react with the imidoyl palladium intermediate further (Scheme 1).[9] As a result, the isocyanide nitrogen is included in the cyclized product as a ring member. Therefore, this strategy for heterocycle synthesis takes full advantage of RNC in having a diversifiable R group over CO. For instance, in 2002, Takahashi reported a three-component coupling reaction of aryl iodides, *o*-alkenylphenyl isocyanides and secondary amines (Scheme 1).[9a] In this reaction, the imidoyl palladium intermediate was trapped by the *ortho* styrenic moiety followed by nucleophilic substitution and reductive elimination to build indole scaffold. Ten years later, Takemoto reported a Pd-catalyzed cascade process consisting of isocyanide insertion and benzylic C(sp^3)-H activation, leading to indole derivatives as well (Scheme 1).[9b] Very recently, we used α-isocyanoacetamides as a novel class of functionalized isocyanide for the synthesis of C2 diversified oxazoles[9c] as well as 2,2'-bisoxazoles.[9d] Herein, we would like to report a sequential process using arene-containing isocyanides as substrates to construct six-membered N-heterocycles including phenanthridines[10] and isoquinolines via intramolecular aromatic C-H activation as a key step (Scheme 1).

Scheme 1. Functionalized Isocyanide in Palladium-Catalyzed Imidoylative Cyclization



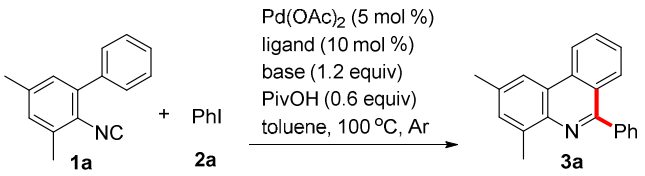
2-Isocyano-1,1'-biphenyls were originally selected as idea substrates in testing the hypothesis. In recent years, reactions using 2-isocyano-1,1'-biphenyls as radical acceptors to form multi-substituted phenanthridines have been frequently reported. Some carbon centered radicals including aryl,[11] CF_3,[12] alkyl,[13] acyl,[14] and alkoxycarbonyl[15] radicals as well as heteroatom-centered ones[16] were applied to react with 2-isocyano-1,1'-biphenyls, forming various imidoyl radical intermediates for the following intramolecular homolytic aromatic substitution (HAS) process.[17] In these radical based reactions, however, no examples of corresponding alkenylation or alkynylation were realized. Given the fruitfulness of Pd chemistry, we

anticipated that an alternative palladium-catalyzed imidoylation process would provide a new approach to multi-substituted six-membered N-heterocycles by using arene-containing isocyanides as a new class of functionalized isocyanides.

RESULTS AND DISCUSSION

Our initial effort was focused on using 2-isocyano-5-methyl-1,1'-biphenyl as a model substrate in a reaction with iodobenzene under palladium catalysis. Unfortunately, unstable products derived from consecutive isocyanide insertion were obtained. This unwanted side reaction was probably due to the unfavorable reaction distance between the phenyl ring and the Pd catalyst after isocyanide insertion. To circumvent multi isocyanide insertion, an additional substituent at the C3 position of the 2-isocyano-1,1'-biphenyl substrate was introduced to force the Pd center in a position closer to the pending phenyl ring. Indeed, when 2-isocyano-3,5-dimethyl-1,1'-biphenyl **1a** (0.2 mmol scale) was chosen in a reaction with iodobenzene **2a** in the presence of $Pd(OAc)_2$ (5 mol %), Ad_2PnBu (10 mol %), and 1.2 equivalents of Cs_2CO_3 in toluene at 100 °C, 2,4-dimethyl-6-phenylphenanthridine **3a** was formed in 20% yield (entry 1, Table 1). When Cs_2CO_3 was replaced by CsOPiv, the reaction was improved significantly to give **3a** in 78% yield (entry 2). It was found that the influence of phosphine ligand on the reaction efficiency was minimal (entries 3-6). Since CsOPiv was highly hygroscopic, in-situ formation of CsOPiv by mixing Cs_2CO_3 and PivOH was preferred, which indeed gave a slightly improved result (entry 7).[18] K_2CO_3 was proved the base of choice among the bases screened (entries 8-10). The reaction proceeded equally well in 0.5 mmol scale in the same amount of solvent (1.5 mL), and the product **3a** was isolated in 90% yield (entry 11). It is notable that in all of these cases, slow addition of a solution of **1a** in toluene via a syringe pump to a pre-stirred reaction mixture is applied to achieve maximum and reproducible result (see experimental section for details).

Table 1. Optimization of the Reaction Conditions[a]



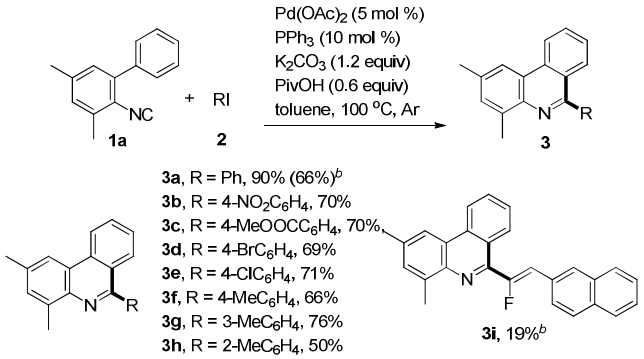
entry	base	ligand	additive	yield[b]
1	Cs_2CO_3	Ad_2PnBu		20%
2	CsOPiv	Ad_2PnBu		78%

3	CsOPiv	Cy_3P		78%
4	CsOPiv	dppe		76%
5	CsOPiv	PPh_3		77%
6	CsOPiv	BINAP		78%
7	Cs_2CO_3	PPh_3	PivOH	84%
8	CsF	PPh_3	PivOH	80%
9	K_2CO_3	PPh_3	PivOH	88%
10	Na_2CO_3	PPh_3	PivOH	trace
11[c]	K_2CO_3	PPh_3	PivOH	90%

[a]Reaction conditions: **1a** (0.2 mmol, 1.0 equiv, in 1 mL of toluene), **2a** (0.3 mmol, 1.5 equiv), $Pd(OAc)_2$ (5 mol %), ligand (10 mol %), base (1.2 equiv), additive (0.6 equiv), toluene (0.5 mL), 100 °C, Ar, syringe pump addition within 1 h. [b] Isolated yield of **3a**. [c] **1a** (0.5 mmol), in the same amount of solvent (0.5 + 1 mL).

With the optimal conditions in hand, we first investigated the scope of halides in this Pd-catalyzed imidoylative cyclization reaction with **1a** (Scheme 2). Aryliodides bearing a variety of functional groups including electron-withdrawing NO_2, methoxycarbonyl, Br, and Cl as well as electron-donating methyl at the *para* position gave the corresponding products **3b**-**3f** in yields ranging from 66 to 71%. 3-Methylphenyl iodide reacted smoothly with **1a** to give **3g** in 76% yield, while a methyl group located at the *ortho* position of phenyl iodide affected the product formation significantly (**3h**, 50%). Phenylbromide could also be used in this reaction, furnishing the same product **3a** in 66% yield. Besides, alkenylated phenanthridine derivative **3i** was also accessible by employing the corresponding vinyl bromide[19] as a substrate, albeit in only 19% yield. Unfortunately, a reaction between **1a** and bromoethynylbenzene under otherwise identical conditions couldn't yield the desired product.

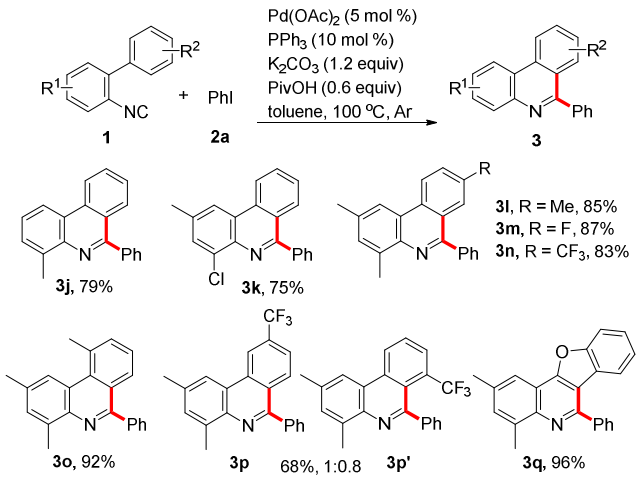
Scheme 2. Scope of Halides[a]



[a]Reaction conditions: **1a** (0.5 mmol, 1.0 equiv, in 1 mL of toluene), **2** (0.75 mmol, 1.5 equiv), $Pd(OAc)_2$ (5 mol %), PPh_3 (10 mol %), PivOH (0.6 equiv), K_2CO_3 (1.2 equiv), toluene (0.5 mL), 100 °C, Ar, syringe pump addition within 1 h. Isolated yields of **3** were reported. [b]Corresponding bromide was used.

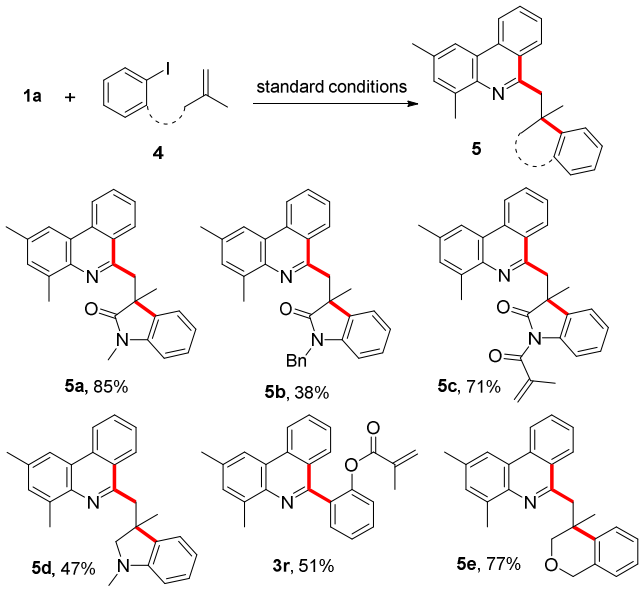
Then the reaction was investigated using various substituted 2-isocyano biphenyls (Scheme 3). Changing the substituent on the 2-position from methyl to chloride also gave the desired product **3k** in 75% yield. The reaction was not sensitive to the electronic nature of substituents on the non-isocyano bearing aromatic ring, delivering F, CF_3, and Me substituted 6-phenyl phenanthridines **3l-3m** in good yields. 2-Isocyano-3,5,2'-trimethyl-1,1'-biphenyl furnished **3o** in a surprisingly high yield (92%). Unfortunately, poor regio-selectivity was obtained for *meta* CF_3 substituted 2-isocyano biphenyl (**3p** and **3p'**). C-H bond in a heteroaromatic ring could also be activated by the imidoyl palladium(II) intermediate, giving benzofuro[3,2-c]quinolone derivative **3q** in an excellent 96% yield.

Scheme 3. Scope of 2-Isocyano Biphenyls[a]



[a]Reaction conditions: **1** (0.5 mmol, 1.0 equiv, in 1 mL of toluene), **2a** (0.75 mmol, 1.5 equiv), $Pd(OAc)_2$ (5 mol %), PPh_3 (10 mol %), PivOH (0.6 equiv), K_2CO_3 (1.2 equiv), toluene (0.5 mL), 100 °C, Ar, syringe pump addition within 1 h. Isolated yields of **3** were reported.

Scheme 4. Cascade Imidoylative Cyclization[a]

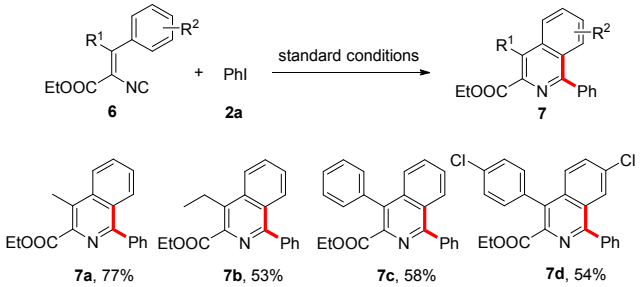


[a]Standard conditions, isolated yields of **5** and **3r**.

It was anticipated that alkyl Pd(II)-intermediate lacking β-hydrogen was also applicable to this reaction to generate alkyl substituted phenanthridine derivatives. Therefore, a cascade process involving oxidative addition of Pd(0) to aryl iodides **4** linking a 2-propene moiety and alkene insertion, followed by imidoylative cyclization, was investigated (Scheme 4). Indeed, a range of unique bisheterocyclic scaffolds with a methylene tether were obtained in moderate to good yields (**5a-5d**). When 2-iodophenyl methacrylate was used, the desired intramolecular alkene insertion to aryl Pd(II) intermediate did not take place, furnishing aryl substituted phenanthridine **3r** in 51% yield. Satisfyingly, when the terminal alkene was one more carbon away from the aryl ring in a benzyl ether substrate, the cascade reaction occurred again (**5e**, 77%). It was notable that three C-C bonds were formed consecutively in this one-pot reaction, enabling to install indolinone, indoline, or isochromane to phenanthridine with high step and bond-forming efficiency.

To extend this Pd-catalyzed functionalized isocyanide strategy to other six-membered heterocycle synthesis, vinyl isocyanides **6** were used as substrates under the same reaction conditions (Scheme 5).[20] Ethyl 4-methyl(ethyl)-1-phenylisoquinoline-3-carboxylates **7a-b** were prepared smoothly starting from the corresponding vinyl isocyanides. 1,4-Diaryl isoquinolines **7c-d** were also accessible by employing this method in acceptable yields.

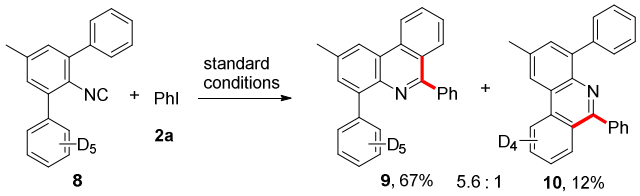
Scheme 5. Synthesis of Isoquinolines[a]



[a]Standard conditions, isolated yields of **7**.

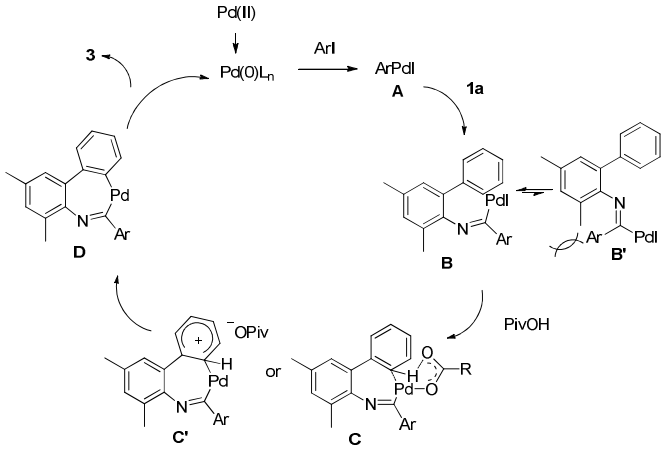
To gain insight into the reaction mechanism, intramolecular kinetic isotope effect was investigated using 2,6-diphenyl aryl isocyanide **8** with one of the phenyl rings fully deuterium labeled. The ratio of **9** to **10**, determined by ^{1}H NMR, was about 5.6:1, which indicated that C-H cleavage might be a rate-limiting step.

Scheme 6. Mechanistic study



A plausible mechanism of this imidoylative cyclization process was depicted in Scheme 6.[5] Initial oxidative addition of aryl halide to Pd(0) affords aryl Pd(II) intermediate **A**. Then, coordination and migratory insertion of the isocyano moiety to intermediate **A** generates imidoyl palladium species **B** and **B'**. The steric hindrance of the *ortho* methyl group helps the presence of conformer **B** in the equilibrium. Next, activation of the C(sp^2)-H bond aided by the coordinated pivalate through a concerted metalation deprotonation (CMD) intermediate **C** gives palladacycle **D**.[21] Finally, reductive elimination delivers the cyclized phenanthridine product **3** and regenerates Pd(0) for the next catalytic cycle. However, an electrophilic aromatic substitution process involving intermediate **C'** cannot be excluded.

Scheme 7. Possible mechanism



CONCLUSION

In summary, we have demonstrated the feasibility of functionalized isocyanide strategy in palladium-catalyzed imidoylation in heterocycle synthesis. In this imidoylative cyclization process, 2-isocyano-1,1'-biphenyls as well as *Z*-2-isocyanostyrenes react smoothly with arylhalides to generate aryl substituted six-membered phenanthridines and isoquinolines, respectively. Aryliodides bearing *ortho* alkenes by a variety of N or O linkage are also applied in this reaction. Therefore, a process including alkene insertion, migratory insertion of isocyanide, and intramolecular C(sp^2)-H activation takes place sequentially, allowing to install other heterocycles to phenanthridine by a methylene tether. Three C-C bonds are formed consecutively, representing high bond-forming efficiency of the reaction. Mechanistic study suggests that C(sp^2)-H activation is likely a rate-determining step.

EXPERIMENTAL SECTION

General Information. Reactions were monitored using thin-layer chromatography (TLC) on commercial silica gel plates (GF254). Solvents for flash column chromatography (FC), crystallization and extractions have been distilled once. Visualization of the developed plates was performed under UV light (254 nm). Flash column chromatography was performed on silica gel (200-300 mesh). ^{1}H and ^{13}C NMR spectra were recorded on a 400 or 500 MHz spectrometer. Chemical shifts (δ) were reported in ppm referenced to an internal tetramethylsilane standard for ^{1}H NMR. Chemical shifts of ^{13}C NMR are reported relative to $CDCl_3$ (δ 77.0). Coupling constants, *J*, were reported in Hertz unit (Hz). High resolution mass spectra (HRMS) were obtained on an ESI-LC-MS/MS spectrometer.

General Procedure A: An oven-dried 25 mL Schlenk tube was charged with $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), PPh_3 (0.05 mmol, 13.1 mg), K_2CO_3 (0.6 mmol, 84 mg), PivOH (0.3 mmol, 31 mg), and the tube was refilled with Ar for 3 times. Then a solution of aryl(vinyl) halide **2** (0.75 mmol) in 0.5 mL of toluene was added. After the mixture was stirred at 100 °C for 0.5 h, 2-isocyano-1,1'-biphenyl **1** (0.5 mmol) was dissolved in 1.0 mL of toluene and the solution was added via a syringe pump within 1 h. The crude reaction mixture was extracted with ethyl acetate (20 mL × 3) and washed with brine (20 mL). The organic phase was concentrated in vacuum and the product **3** was purified by flash chromatography using ethyl acetate and petroleum ether (1:100) as an eluent.

General Procedure B: An oven-dried 25 mL Schlenk tube was charged with $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), PPh_3 (0.05 mmol, 13.1 mg), K_2CO_3 (0.6 mmol, 84 mg), PivOH (0.3 mmol, 31 mg), and the tube was refilled with Ar for 3 times. Then, 0.5 mL of toluene was added, and the mixture was stirred at 100 °C for 0.5 h. To this mixture, a solution of aryliodide **4** containing an ortho pending alkene moiety (0.75 mmol) in 0.5 mL of toluene was added. Besides, a solution of 2-isocyano-3,5-dimethyl-1,1'-biphenyl (**1a**, 0.5 mmol, 103.6 mg) in 0.5 mL of toluene was introduced via a syringe pump within 1 h. The crude reaction mixture was extracted with ethyl acetate (20 mL × 3) and washed with brine (20 mL). The organic phase was concentrated in vacuum and the product **5** was purified by flash chromatography using ethyl acetate and petroleum ether (1:50) as an eluent.

General Procedure C: An oven-dried 25 mL Schlenk tube was charged with $Pd(OAc)_2$ (0.01 mmol, 2.3 mg), PPh_3 (0.02 mmol, 5.3 mg), K_2CO_3 (0.24 mmol, 33 mg), PivOH (0.12 mmol, 12 mg), and the tube was refilled with Ar for 3 times. Then a solution of PhI (**2a**, 0.3 mmol, 61.8 mg) in 0.5 mL of toluene was added. The mixture was stirred at 100 °C for 0.5 h, followed by adding a solution of vinyl isocyanide **6** (0.2 mmol) in 1.0 mL of toluene via a syringe pump within 1 h. The reaction mixture was extracted with ethyl acetate (20 mL × 3) and washed with brine (20 mL). The organic phase was concentrated in vacuum and the product **7** was purified by flash chromatography using ethyl acetate and petroleum ether (1:100) as an eluent.

2,4-dimethyl-6-phenylphenanthridine (3a)[22]

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (104 mg, 0.5 mmol, 1.0 equiv) and iodobenzene (153 mg, 0.75 mmol, 1.5 equiv) according to the general procedure A. Isolated as a white solid (128 mg, 0.45 mmol), yield: 90%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (d, *J* = 8.4 Hz, 1H), 8.25 (s, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.82-7.78 (m, 3H), 7.60-7.49 (m, 4H), 7.45 (s, 1H), 2.85 (s, 3H), 2.60 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.3, 140.9, 137.8, 136.1, 133.6, 131.2, 130.2, 129.8, 128.5, 128.4, 128.1, 126.6, 124.8, 123.3, 122.4, 119.3, 21.9, 18.2; FTIR: ν_{max}/cm^{-1} 3047, 2910, 1566, 1517, 1442, 1360, 1319, 955, 850, 778, 761, 700, 672, 582; HRMS (ESI-TOF): calcd for $C_{21}H_{17}N$ ($M+H^+$) 284.1434; found: 284.1436; mp: 123-125 °C.

2,4-dimethyl-6-(4-nitrophenyl)phenanthridine (3b)

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (104 mg, 0.5 mmol, 1.0 equiv) and 1-iodo-4-nitrobenzene (187 mg, 0.75 mmol, 1.5 equiv) according to the general procedure A. Isolated as a pale yellow solid (111 mg, 0.35 mmol), yield: 70%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.72 (d, *J* = 8.4 Hz, 1H), 8.42 (d, *J* = 8.4 Hz, 2H), 8.27 (s, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.99 (d, *J* = 8.8 Hz, 2H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.49 (s, 1H), 2.83 (s, 3H), 2.62 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.7, 147.9, 146.7, 140.8, 138.1, 137.1, 133.6, 131.6, 131.1, 130.3, 127.5, 127.1, 124.2, 123.5, 123.5, 122.8, 119.4, 22.0, 18.1; FTIR: ν_{max}/cm^{-1} 3069, 2919, 1597, 1517, 1348, 1319, 852, 773, 694, 584; HRMS (ESI-TOF): calcd for $C_{21}H_{16}N_2O_2$ ($M+H^+$) 329.1285; found:329.1285; mp: 213-215 °C.

methyl 4-(2,4-dimethylphenanthridin-6-yl)benzoate (3c)

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (104 mg, 0.5 mmol, 1.0 equiv) and methyl 4-iodobenzoate (196 mg, 0.75 mmol, 1.5 equiv) according to the general procedure A. Isolated as a white solid (120 mg, 0.35 mmol), yield: 70%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (d, *J* = 8.0 Hz, 1H), 8.24 (s, 1H), 8.22 (d, *J* = 8.4 Hz, 2H), 8.08 (d, *J* = 8.4 Hz, 1H), 8.88 (d, *J* = 8.0 Hz, 2H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.46 (s, 1H), 3.98 (s, 3H), 2.83 (s, 3H), 2.60 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.0, 157.1, 144.8, 140.9, 138.0, 136.6, 133.6, 131.4, 130.3, 130.1, 130.0, 129.5, 128.0, 126.8, 124.5, 123.4, 122.6, 119.3, 52.2, 22.0, 18.2; FTIR: ν_{max}/cm^{-1} 3070, 2919, 1724, 1609, 1434, 1321, 1288, 1103, 777, 704; HRMS (ESI-TOF): calcd for $C_{23}H_{19}NO_2$ ($M+H^+$) 342.1489; found: 342.1489; mp: 191-193 °C.

6-(4-bromophenyl)-2,4-dimethylphenanthridine (3d)

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (104 mg, 0.5 mmol, 1.0 equiv) and 1-bromo-4-iodobenzene (212 mg, 0.75 mmol, 1.5 equiv) according to the general procedure A. Isolated as a white solid (126 mg, 0.35 mmol), yield: 69%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.69 (d, *J* = 8.0 Hz, 1H), 8.25 (s, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.84-7.80 (m, 1H), 7.69 (m, 4H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.46 (s, 1H), 2.83 (s, 3H), 2.60 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.0, 140.9, 139.3, 137.8, 136.4, 133.6, 131.8, 131.4, 130.0, 128.1, 126.8, 124.5, 123.3, 122.9, 122.6, 119.3, 22.0, 18.2; FTIR: ν_{max}/cm^{-1} 3070, 2920, 1485, 1370, 1361, 1317, 1912, 841, 831, 794, 767, 583; HRMS (ESI-TOF): calcd for $C_{21}H_{16}BrN$ ($M+H^+$) 362.0539; found: 362.0539; mp: 176-178 °C.

6-(4-chlorophenyl)-2,4-dimethylphenanthridine (3e)

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (104 mg, 0.5 mmol, 1.0 equiv) and 1-chloro-4-iodobenzene (178 mg, 0.75 mmol, 1.5 equiv) according to the general procedure A. Isolated as a white solid (120 mg, 0.36 mmol), yield: 71%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.67 (d, *J* = 8.4 Hz, 1H), 8.24 (s, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.80 (t, *J* = 7.6 Hz, 1H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.45 (s, 1H), 2.83 (s, 3H), 2.59 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.0, 140.8, 138.8, 137.8, 136.4, 134.6, 133.6, 131.5, 131.3, 130.0, 128.4, 128.1, 126.8, 124.6, 123.3, 122.6, 119.3, 22.0, 18.2;

FTIR: ν_{max}/cm^{-1} 3072, 2919, 1488, 1362, 1318, 1090, 834, 795, 763; HRMS (ESI-TOF): calcd for $C_{21}H_{16}ClN$ ($M+H^+$) 318.1044; found: 318.1046; mp: 187-189 °C.

2,4-dimethyl-6-(p-tolyl)phenanthridine (3f)

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (104 mg, 0.5 mmol, 1.0 equiv) and 1-iodo-4-methylbenzene (164 mg, 0.75 mmol, 1.5 equiv) according to the general procedure A. Isolated as a white solid (99 mg, 0.33 mmol), yield: 66%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.66 (d, *J* = 8.4 Hz, 1H), 8.23 (s, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 7.78 (t, *J* = 6.8 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.43 (s, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 2.84 (s, 3H), 2.59 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.3, 141.0, 138.3, 137.8, 137.6, 136.0, 133.6, 131.2, 130.2, 130.1, 129.9, 129.8, 128.9, 128.6, 128.2, 126.5, 124.9, 123.2, 122.4, 119.3, 22.0, 21.4, 18.3; FTIR: ν_{max}/cm^{-1} 3069, 2914, 1449, 1361, 1318, 1181, 845, 797, 769, 582; HRMS (ESI-TOF): calcd for $C_{22}H_{19}N$ ($M+H^+$) 298.1590; found: 298.1593; mp: 139-141 °C.

2,4-dimethyl-6-(m-tolyl)phenanthridine (3g)

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (104 mg, 0.5 mmol, 1.0 equiv) and 1-iodo-3-methylbenzene (163 mg, 0.75 mmol, 1.5 equiv) according to the general procedure A. Isolated as a pale yellow solid (113 mg, 0.38 mmol), yield: 76%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.66 (d, *J* = 8.4 Hz, 1H), 8.24 (s, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 7.79 (t, *J* = 7.6 Hz, 1H), 7.60-7.53 (m, 3H), 7.45-7.41 (m, 2H), 7.32 (d, *J* = 7.6 Hz, 1H), 2.84 (s, 3H), 2.59 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.5, 141.0, 140.4, 137.8, 137.7, 136.0, 133.5, 131.2, 130.8, 130.2, 129.8, 129.2, 128.6, 128.5, 128.4, 128.2, 128.0, 127.3, 126.6, 126.5, 124.9, 123.3, 122.4, 122.3, 119.3, 22.0, 21.6, 18.3; FTIR: ν_{max}/cm^{-1} 3075, 2911, 1570, 1357, 1318, 849, 792, 779, 766, 706; HRMS (ESI-TOF): calcd for $C_{22}H_{19}N$ ($M+H^+$) 298.1590; found: 298.1591; mp: 133-135 °C.

2,4-dimethyl-6-(o-tolyl)phenanthridine (3h)

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (104 mg, 0.5 mmol, 1.0 equiv) and 1-iodo-2-methylbenzene (163 mg, 0.75 mmol, 1.5 equiv) according to the general procedure A. Isolated as a pale yellow solid (75 mg, 0.25 mmol), yield: 50%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.67 (d, *J* = 8.0 Hz, 1H), 8.27 (s, 1H), 7.80-7.76 (m, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.53-7.49 (m, 1H), 7.45 (s, 1H), 7.42-7.32 (m, 4H), 2.81 (s, 3H), 2.60 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.0, 140.9, 139.8, 137.9, 136.8, 136.1, 133.1, 131.1, 130.4, 130.0, 129.9, 129.8, 128.4, 128.2, 126.7, 125.6, 125.5, 123.4, 122.3, 119.3, 21.9, 20.0, 18.4; FTIR: ν_{max}/cm^{-1} 3049, 2915, 1573, 1452, 1361, 1317, 854, 778, 760, 737, 726; HRMS (ESI-TOF): calcd for $C_{22}H_{19}N$ ($M+H^+$) 298.1590; found: 298.1592; mp: 145-147 °C.

(*Z*)-6-(1-fluoro-2-(naphthalen-2-yl)vinyl)-2,4-dimethylphenanthridine (3i)

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (104 mg, 0.5 mmol, 1.0 equiv) and (*E*)-2-(2-bromo-2-fluorovinyl)naphthalene (188 mg, 0.75 mmol, 1.5 equiv) according to the general procedure A. Isolated as an orange solid (35 mg, 0.10 mmol), yield: 19%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (d, *J* = 8.4 Hz, 1H), 8.60 (d, *J* = 9.2 Hz, 1H), 8.23 (d, *J* = 10.0 Hz, 1H), 7.98-7.95 (m, 1H), 7.91-7.83 (m, 4H), 7.73-7.69 (m, 1H), 7.53-7.48 (m, 3H), 7.01 (d, *J* = 38.4 Hz, 1H), 2.91 (s, 3H), 2.62 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.8 (d, *J* = 265.0 Hz, 1C), 149.3 (d, *J* = 30.6 Hz, 1C), 140.5, 138.0, 137.3, 133.6, 133.5, 132.8 (d, *J* = 1.6 Hz, 1C), 131.4, 131.1 (d, *J* = 3.6 Hz, 1C), 130.2, 129.0, 128.9, 128.3, 128.1, 127.6, 127.4, 127.2, 127.14, 127.07, 126.3, 126.2, 124.1, 123.9 (d, *J* = 3.6 Hz, 1C), 122.5, 119.4, 112.61, 112.56, 22.1, 18.2; FTIR: ν_{max}/cm^{-1} 3052, 2917, 1367,1313, 1165, 905, 817, 766, 748, 482; HRMS (ESI-TOF): calcd for $C_{27}H_{20}FN$ ($M+H^+$) 378.1653; found: 378.1654; mp:195-197 °C.

4-methyl-6-phenylphenanthridine (3j)[23]

Prepared from 2-isocyano-3-methyl-1,1'-biphenyl (97 mg, 0.5 mmol, 1.0 equiv) and iodobenzene (153 mg, 0.75 mmol, 1.5 equiv) according to the general procedure A. Isolated as a white solid (106 mg, 0.40 mmol), yield: 79%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (d, *J* = 8.4 Hz, 1H), 8.45 (d, *J* = 8.0 Hz, 1H), 8.17 (d, *J* = 8.4 Hz, 1H),7.82-7.79 (m, 3H), 7.61-7.49 (m, 6H), 2.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.2, 142.6, 140.3, 138.2, 133.9, 130.2, 130.1, 129.4, 128.6, 128.5, 128.4, 128.2, 126.8, 126.4, 124.7, 123.4, 122.5, 119.7, 18.4; FTIR: ν_{max}/cm^{-1} 3059, 2957, 1567, 1467, 1361, 750, 689, 668; HRMS (ESI-TOF): calcd for $C_{20}H_{15}N$ ($M+H^+$) 270.1277; found: 270.1278; mp:137-139 °C.

4-chloro-2-methyl-6-phenylphenanthridine (3k)

Prepared from 3-chloro-2-isocyano-5-methyl-1,1'-biphenyl (114 mg, 0.5 mmol, 1.0 equiv) and iodobenzene (153 mg, 0.75 mmol, 1.5 equiv) according to the general procedure A. Isolated as a white solid (113 mg, 0.38 mmol), yield: 75%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.65 (d, *J* = 8.0 Hz, 1H), 8.30 (s, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 7.86-7.81 (m, 3H), 7.70 (s, 1H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.58-7.50 (m, 3H), 2.61 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.5, 139.6, 138.4, 136.8, 134.2, 133.1, 130.7, 130.5, 130.3, 128.9, 128.8, 128.3, 127.5, 125.2, 125.1, 122.4, 120.5, 21.7; FTIR: ν_{max}/cm^{-1} 3048, 2914, 1360, 1317, 855, 829, 779, 762, 702,673; HRMS (ESI-TOF): calcd for $C_{20}H_{14}ClN$ ($M+H^+$) 304.0888; found: 304.0886; mp:189-191 °C.

2,4,8-trimethyl-6-phenylphenanthridine (3l)

Prepared from 2-isocyano-3,4',5-trimethyl-1,1'-biphenyl (111 mg, 0.5 mmol, 1.0 equiv) and iodobenzene (153 mg, 0.75 mmol, 1.5 equiv) according to the general procedure A. Isolated as a white solid (126 mg, 0.43 mmol), yield: 85%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54 (d, *J* = 8.0 Hz, 1H), 8.19 (s, 1H), 7.91 (s, 1H), 7.81-7.78 (m, 1H), 7.62-7.48 (m, 4H), 7.40 (s, 1H), 2.83 (s, 3H), 2.57 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.0, 140.7, 140.6, 137.8, 136.5, 136.0, 131.6, 131.5, 130.8, 130.2, 128.3, 128.2, 127.8, 125.0, 123.4, 122.4, 119.1, 22.0, 21.7, 18.3; FTIR: ν_{max}/cm^{-1} 3050, 2919, 2850, 1565, 1524, 1441, 1365, 1315, 818, 766, 700, 581; HRMS (ESI-TOF): calcd for $C_{22}H_{19}N$ ($M+H^+$) 298.1590; found: 298.1592; mp:147-149 °C.

8-fluoro-2,4-dimethyl-6-phenylphenanthridine (3m)

Prepared from 4'-fluoro-2-isocyano-3,5-dimethyl-1,1'-biphenyl (113 mg, 0.5 mmol, 1.0 equiv) and iodobenzene (153 mg, 0.75 mmol, 1.5 equiv) according to the general procedure A. Isolated as a white solid (131 mg, 0.44 mmol), yield: 87%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.67-8.66 (m, 1H), 8.17 (s, 1H), 7.80-7.77 (m, 3H), 7.58-7.50 (m, 4H), 7.44 (s, 1H), 2.83 (s, 3H), 2.59 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.0 (d, *J* = 246.9 Hz, 1C), 157.4 (d, *J* = 4.1 Hz, 1C), 140.7, 139.9, 138.0, 136.6, 131.1, 130.2 (d, J = 1.8 Hz, 1C), 130.0, 128.6, 128.3, 126.0 (d, *J* = 7.9 Hz, 1C), 125.0 (d, *J* = 8.4 Hz, 1C), 122.9, 119.2, 119.03, 118.99, 112.8, 112.6, 22.0, 18.2; FTIR: ν_{max}/cm^{-1} 3057, 2917, 1524, 1372, 1315, 1196, 875, 824, 765, 693, 580; HRMS (ESI-TOF): calcd for $C_{21}H_{16}FN$ ($M+H^+$) 302.1340; found: 302.1343; mp:147-149 ^{o}C.

2,4-dimethyl-6-phenyl-8(trifluoromethyl)phenanthridine (3n)

Prepared from 2-isocyano-3,5-dimethyl-4'-(trifluoromethyl)-1,1'-biphenyl (138 mg, 0.5 mmol, 1.0 equiv) and iodobenzene (153 mg, 0.75 mmol, 1.5 equiv) according to the general procedure A. Isolated as a white solid (145 mg, 0.42 mmol), yield: 83%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.73 (d, *J* = 8.0 Hz, 1H), 8.45 (s, 1H), 8.20 (s, 1H), 7.97-7.94 (m, 1H), 7.80-7.78 (m, 2H), 7.60-7.52 (m, 3H), 7.49 (s, 1H), 2.83 (s, 3H), 2.58 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.0, 141.6, 139.5, 138.2, 136.9, 132.4, 130.2, 128.9, 128.5, 128.4 (q, *J* = 32.9 Hz, 1C), 125.9 (q, *J* = 4.1 Hz, 1C), 125.6 (q, *J* = 3.2 Hz, 1C), 124.1 (q, *J* = 273.5 Hz, 1C), 124.0, 123.5, 122.4, 119.5, 21.9, 18.2; FTIR: ν_{max}/cm^{-1} 3056, 2920, 1372, 1330, 1303, 1225, 1162, 1119, 828, 769; HRMS (ESI-TOF): calcd for $C_{22}H_{16}F_3N$ ($M+H^+$) 352.1308; found:352.1309; mp:142-144 ^{o}C.

2,4,10-trimethyl-6-phenylphenanthridine (3o)

Prepared from 2-isocyano-2',3,5-trimethyl-1,1'-biphenyl (111 mg, 0.5 mmol, 1.0 equiv) and iodobenzene (153 mg, 0.75 mmol, 1.5 equiv) according to the general procedure A. Isolated as a white solid (137 mg, 0.46 mmol), yield: 92%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.46 (s, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.76-7.74 (m, 2H), 7.63 (d, *J* = 4.0 Hz, 1H), 7.55-7.53 (m, 3H), 7.51-7.43 (m, 2H), 3.15 (s, 3H), 2.86 (s, 3H), 2.59 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.0, 141.9, 141.1, 137.7, 135.2, 134.8, 134.1, 133.2, 130.5, 130.2, 128.2, 128.1, 127.3, 126.5, 126.0, 124.7, 124.2, 27.1, 22.3, 18.9; FTIR: ν_{max}/cm^{-1} 3051, 2915, 1442, 1379, 1362, 1322, 845, 779, 766, 700; HRMS (ESI-TOF): calcd for $C_{22}H_{19}N$ ($M+H^+$) 298.1590; found: 298.1591; mp:161-163 ^{o}C.

2,4-dimethyl-6-phenyl-9(trifluoromethyl)phenanthridine (3p)

Prepared from 2-isocyano-3,5-dimethyl-3'-(trifluoromethyl)-1,1'-biphenyl (138mg, 0.5 mmol, 1.0 equiv) and iodobenzene (153 mg, 0.75 mmol, 1.5 equiv) according to the general procedure A. Isolated as a white solid (67 mg, 0.19 mmol), yield: 38%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.94 (s, 1H), 8.29 (d, *J* = 8.0 Hz, 1H), 8.25 (s, 1H), 7.80-7.76 (m, 3H), 7.59-7.54 (m, 3H), 7.51 (s, 1H), 2.85 (s, 3H), 2.63 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.6, 141.3, 139.8, 138.2, 137.1, 133.3, 132.1, 131.3 (q, *J* = 32.7 Hz, 1C), 130.1, 129.5, 128.8, 128.3, 126.1, 124.1 (q, *J* = 272.7 Hz, 1C), 122.8, 122.5 (q, *J* = 3.2 Hz, 1C), 120.0 (q, *J* = 4.0 Hz, 1C), 119.2,

21.9, 18.1; FTIR: ν_{max}/cm^{-1} 3063, 2920, 1349, 1316, 1161, 1152, 1119, 1072, 771, 703; HRMS (ESI-TOF): calcd for $C_{22}H_{16}F_3N$ ($M+H^+$) 352.1308; found: 352.1309; mp: 187-189 °C.

2,4-dimethyl-6-phenyl-7(trifluoromethyl)phenanthridine (3p')

Another isomer **3p'** was isolated as a white solid (57 mg, 0.15 mmol), yield: 30%. ^1H NMR (400 MHz, $CDCl_3$): δ 8.86 (d, *J* = 8.0 Hz, 1H), 8.17 (s, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.86 (t, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 4.0 Hz, 2H), 7.46-7.42 (m, 4H), 2.81 (s, 3H), 2.59 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.9, 143.6 (q, *J* = 1.8 Hz, 1C), 140.0, 137.5, 136.6, 135.5, 131.9, 129.3, 128.5, 128.4 (q, *J* = 31.5 Hz, 1C), 128.3, 127.6 (q, *J* = 6.2 Hz, 1C), 127.5, 126.2, 123.8 (q, *J* = 274.4 Hz, 1C), 121.7, 120.5, 119.0, 22.0, 17.7; FTIR: ν_{max}/cm^{-1} 3058, 2919, 1298, 1185, 1128, 1112, 1092, 822, 776, 700; HRMS (ESI-TOF): calcd for $C_{22}H_{16}F_3N$ ($M+H^+$) 352.1308; found: 352.1306; mp:199-201 °C.

2,4-dimethyl-6-phenyl-9H-cyclopenta[4,5]furo[3,2-*c*]quinolonep (3q)

Prepared from 2-(2-isocyano-3,5-dimethylphenyl)benzofuran (120mg, 0.5 mmol, 1.0 equiv) and iodobenzene (153 mg, 0.75 mmol, 1.5 equiv) according to the general procedure A. Isolated as a white solid (151 mg, 0.48 mmol), yield: 96%. ^1H NMR (400 MHz, $CDCl_3$): δ 8.04-8.01 (m, 3H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.62-7.54 (m, 3H), 7.46 (t, *J* = 8.0 Hz, 2H), 7.28-7.24 (m, 1H), 2.87 (s, 3H), 2.58 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.4, 156.0, 153.1, 144.7, 140.4, 137.6, 136.2, 132.1, 129.3, 129.1, 128.5, 126.7, 123.3, 123.2, 122.3, 117.4, 115.9, 114.1, 111.8, 21.8, 18.4; FTIR: ν_{max}/cm^{-1} 3050, 2916, 1589, 1489, 1446, 1355, 1319, 1185, 1120, 851, 775, 745, 694; HRMS (ESI-TOF): calcd for $C_{23}H_{17}NO$ ($M+H^+$) 324.1383; found: 324.1383; mp:185-187 °C.

3-((2,4-dimethylphenanthridin-6-yl)methyl)-1,3-dimethylindolin-2-one (5a)

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (104 mg, 0.5 mmol, 1.0 equiv) and *N*-(2-iodophenyl)-*N*-methylmethacrylamide (227 mg, 0.75 mmol, 1.5 equiv) according to the general procedure B. Isolated as a yellow solid (162 mg, 0.43 mmol), yield: 85%. ^1H NMR (400 MHz, $CDCl_3$): δ 8.52 (d, J = 8.0 Hz, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 8.06 (s, 1H), 7.75-7.71 (m, 1H), 7.64-7.60 (m, 1H), 7.22 (s, 1H), 7.16-7.12 (m, 1H), 7.04-7.02 (m, 1H), 6.84-6.80 (m, 2H), 4.11 (d, *J* = 16.8 Hz, 1H), 4.04 (d, *J* = 16.8 Hz, 1H), 3.30 (s, 3H), 2.47 (s, 3H), 2.34 (s, 3H), 1.58 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 181.1, 154.0, 143.5, 140.3, 137.0, 135.4, 134.8, 132.5, 130.6, 129.7, 126.9, 126.7, 125.5, 125.2, 123.1, 122.5, 121.9, 121.8, 119.1, 107.9, 47.1, 40.8, 27.3, 26.4, 21.7, 18.2; FTIR: ν_{max}/cm^{-1} 3046, 2962, 1704, 1612, 1491, 1467, 1450, 1376, 1313, 791, 752; HRMS (ESI-TOF): calcd for $C_{26}H_{24}N_2O$ ($M+H^+$) 381.1961; found: 381.1963; mp:174-176 °C.

1-benzyl-3-((2,4-dimethylphenanthridin-6-yl)methyl)-3-methylindolin-2-one (5b)

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (104 mg, 0.5 mmol, 1.0 equiv) and *N*-benzyl-*N*-(2-iodophenyl)methacrylamide (283 mg, 0.75 mmol, 1.5 equiv) according to the general procedure B. Isolated as a yellow solid (87 mg, 0.19 mmol), yield: 38%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54 (d, *J* = 8.0 Hz, 1H), 8.32 (d, *J* = 8.0 Hz, 1H), 8.09 (s, 1H), 7.73 (t, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.23(s, 1H), 7.17-7.15 (m, 3H), 7.12-7.11 (m, 3H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.83 (t, *J* = 7.6 Hz, 1H), 6.67 (d, *J* = 7.6 Hz, 1H), 5.32 (d, *J* = 15.6 Hz, 1H), 4.66 (d, *J* = 15.6 Hz, 1H), 4.17 (d, *J* = 16.4 Hz, 1H), 4.02 (d, *J* = 16.4 Hz, 1H), 2.49 (s, 3H), 2.34 (s, 3H), 1.66 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 180.9, 154.1, 142.4, 140.3, 137.1, 136.4, 135.5, 134.7, 132.7, 130.7, 129.7, 128.6, 127.3, 127.1, 126.9, 126.8, 125.8, 125.3, 123.2, 122.4, 122.3, 121.9, 119.1, 108.9, 47.6, 43.6, 40.8, 27.2, 21.2, 18.2; FTIR: ν_{max}/cm^{-1} 3060, 2914, 1718, 1613, 1489, 1464, 1340, 1305, 1168, 790, 746; HRMS (ESI-TOF): calcd for $C_{32}H_{28}N_2O$ ($M+H^+$) 457.2274; found: 457.2278; mp:174-176 °C.

3-((2,4-dimethylphenanthridin-6-yl)methyl)-1-methacryloyl-3-methylindolin-2-one (5c)

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (104 mg, 0.5 mmol, 1.0 equiv) and *N*-(2-iodophenyl)-*N*-methacryloylmethacrylamide (266 mg, 0.75 mmol, 1.5 equiv) according to the general procedure B. Isolated as a white solid (154 mg, 0.36 mmol), yield: 71%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54 (d, *J* = 8.4 Hz, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 8.06 (s, 1H), 7.78-7.74 (m, 1H), 7.68-7.64 (m, 1H), 7.25-7.21 (m, 1H), 7.10-7.08 (m, 1H), 7.03-6.99 (m, 1H), 5.40 (s, 1H), 5.37 (s, 1H), 4.21 (d, *J* = 16.0 Hz, 1H), 4.13 (d, *J* = 16.0 Hz, 1H), 2.47 (s, 3H), 2.28 (s, 3H), 2.05 (s, 3H), 1.67 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 180.3, 171.2, 153.0, 141.7, 140.2, 139.7, 137.2, 135.7, 134.6, 132.6, 131.0, 129.9, 127.3, 126.9, 125.1, 125.0, 124.7, 123.2, 122.6, 121.1, 119.8, 119.1, 115.7, 47.0, 41.2, 28.3, 21.7, 18.9, 18.4; FTIR: ν_{max}/cm^{-1} 3075, 2965, 1766, 1681, 1480, 1451, 1352, 1311, 1259, 1150, 790, 751; HRMS (ESI-TOF): calcd for $C_{29}H_{26}N_2O_2$ ($M+H^+$) 435.2067; found: 435.2065; mp: 227-229 °C.

6-((1,3-dimethylindolin-3-yl)methyl)-2,4-dimethylphenanthridine (5d)

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (104 mg, 0.5 mmol, 1.0 equiv) and 2-iodo-*N*-methyl-*N*-(2-methylallyl)aniline (215 mg, 0.75 mmol, 1.5 equiv) according to the general procedure B. Isolated as a pale yellow oil (86 mg, 0.24 mmol), yield: 47%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (d, *J* = 8.4 Hz, 1H), 8.17 (s, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.70 (t, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.41 (s, 1H), 7.10 (t, *J* = 8.0 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.63 (t, *J* = 8.0 Hz, 1H), 6.51 (d, *J* = 8.0 Hz, 1H), 3.78-3.74 (m, 2H), 3.54 (d, *J* = 14.8 Hz, 1H), 4.22 (d, *J* = 8.8 Hz, 1H), 2.84 (s, 3H), 2.76 (s, 3H), 2.56 (s, 3H), 1.56 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.5, 152.2, 140.5, 138.9, 137.2, 135.5, 132.6, 130.9, 129.5, 127.7, 126.6, 126.3, 126.2, 123.1, 122.4, 122.3, 119.3, 117.6, 107.3, 68.2, 44.4, 43.2, 35.8, 24.6, 21.9, 18.6; FTIR: ν_{max}/cm^{-1} 3020, 2952, 2803, 1605, 1489, 1460, 1450, 1372, 1361, 1300, 849, 795, 777; HRMS (ESI-TOF): calcd for $C_{26}H_{26}N_2$ ($M+H^+$) 367.2169; found: 367.2169.

2-(2,4-dimethylphenanthridin-6-yl)phenyl methacrylate (3r)

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (104 mg, 0.5 mmol, 1.0 equiv) and 2-iodophenyl methacrylate (216 mg, 0.75 mmol, 1.5 equiv) according to the general procedure A. Isolated as a pale yellow oil (93 mg, 0.26 mmol), yield: 51%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.65 (d, *J* = 8.4 Hz, 1H), 8.25 (s, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.80-7.76 (m, 1H), 7.67-7.65 (m, 1H), 7.60-7.53 (m, 2H), 7.45-7.40 (m, 3H), 5.65 (s, 1H), 5.25 (s, 1H), 2.78 (s, 3H), 2.60 (s, 3H), 1.56 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.3, 155.1, 149.0, 140.9, 138.0, 136.4, 135.4, 133.0, 132.8, 131.7, 131.2, 130.0, 129.4, 128.3, 126.7, 126.6, 125.6, 125.3, 123.4, 123.1, 122.2, 119.3, 22.0, 18.2, 17.9; FTIR: ν_{max}/cm^{-1} 3068, 2923, 1737, 1447, 1363, 1319, 1294, 1196, 1130, 773, 758; HRMS (ESI-TOF): calcd for $C_{25}H_{21}NO_2$ ($M+H^+$) 368.1645; found: 368.1647.

2,4-dimethyl-6-((4-methylisochroman-4-yl)mthyl)phenanthridine (5e)

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (104 mg, 0.5 mmol, 1.0 equiv) and 1-iodo-2-(((2-methylallyl)oxy)methyl)benzene (216 mg, 0.75 mmol, 1.5 equiv) according to the general procedure B. Isolated as a pale yellow oil (141 mg, 0.39 mmol), yield: 77%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.60 (d, *J* = 8.4 Hz, 1H), 8.22 (s, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 7.73 (t, *J* = 8.0 Hz, 1H), 5.02 (t, *J* = 14.8 Hz, 1H), 4.92 (d, *J* = 14.8 Hz, 1H), 4.29 (d, *J* = 11.6 Hz, 1H), 3.84 (d, *J* = 14.0 Hz, 1H), 3.76 (d, *J* = 13.6 Hz, 1H), 3.64 (d, *J* = 11.2 Hz, 1H), 2.86 (s, 3H), 2.60 (s, 3H), 1.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.6, 142.2, 140.5, 137.3, 135.6, 133.7, 132.7, 130.9, 129.4, 126.5, 126.5, 126.5, 125.8, 124.0, 123.1, 122.3, 119.3, 74.3, 69.1, 44.0, 38.0, 23.5, 21.9, 18.4; FTIR: ν_{max}/cm^{-1} 3071, 2921, 1578, 1490, 1453, 1363, 1097, 773, 795, 745; HRMS (ESI-TOF): calcd for $C_{26}H_{25}NO$ ($M+H^+$) 368.2009; found: 368.2009.

ethyl 4-methyl-1-phenylisoquinoline-3-carboxylate (7a)[24]

Prepared from ethyl (*Z*)-2-isocyano-3-phenylbut-2-enoate (43 mg, 0.2 mmol, 1.0 equiv) and iodobenzene (61 mg, 0.3 mmol, 1.5 equiv) according to the general procedure C. Isolated as a pale yellow solid (45 mg, 0.16 mmol), yield: 77%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.80-7.76 (m, 1H), 7.71-7.68 (m, 2H), 7.61-7.57 (m, 1H), 7.54-7.46 (m, 3H), 4.50 (q, *J* = 8.0 Hz, 2H), 1.45 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.0, 158.7, 142.1, 139.1, 136.6, 130.3, 130.2, 128.6, 128.3, 128.2, 127.9, 126.9, 124.3, 61.6, 14.32, 14.27; FTIR: ν_{max}/cm^{-1} 3039, 2921, 1713, 1374, 1331, 1309, 1238, 1214, 1057, 772, 762, 704; HRMS (ESI-TOF): calcd for $C_{19}H_{17}NO_2$ ($M+H^+$) 292.1332; found: 292.1334; mp: 92-94 ^{o}C.

ethyl 4-ethyl-1-phenylisoquinoline-3-carboxylate (7b)

Prepared from ((*Z*)-1,1-diisocyanobut-1-en-2-yl)benzene (46 mg, 0.2 mmol, 1.0 equiv) and iodobenzene (61 mg, 0.3 mmol, 1.5 equiv) according to the general procedure C. Isolated as a pale yellow solid (33mg, 0.11 mmol), yield: 53%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (d, *J* = 8.8 Hz, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.79-7.75 (m, 1H), 7.70-7.68 (m, 2H), 7.57 (t, *J* = 8.0 Hz, 1H), 7.53-7.45 (m, 3H), 4.49 (q, *J* = 8.0 Hz, 2H), 3.27 (q, *J* = 8.0 Hz, 2H), 1.46-1.42(m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.9, 158.8, 141.9, 139.1, 135.7, 132.5, 130.3, 130.2, 128.6, 128.4, 128.3, 127.7, 127.3, 124.1, 61.6, 21.6, 15.4, 14.3; FTIR: ν_{max}/cm^{-1} 2966, 1716,

1445, 1372, 1309, 1286, 1256, 1208, 1160, 1071, 1052, 774, 705; HRMS (ESI-TOF): calcd for $C_{20}H_{19}NO_2$ ($M+H^+$) 306.1489; found: 306.1486; mp:91-93 °C.

ethyl 1,4-diphenylisoquinoline-3-carboxylate (7c)[25]

Prepared from (*Z*)-ethyl 2-isocyano-3,3-diphenylacrylate (55 mg, 0.2 mmol, 1.0 equiv) and iodobenzene (61 mg, 0.3 mmol, 1.5 equiv) according to the general procedure C. Isolated as a pale yellow solid (41 mg, 0.12 mmol), yield: 58%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, *J* = 8.0 Hz, 1H), 7.78-7.41 (m, 13H), 4.12 (q, *J* = 8.0 Hz, 2H), 0.98 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.5, 160.3, 142.3, 138.9, 136.4, 136.1, 131.9, 130.5, 130.2, 130.0, 128.8, 128.5, 128.3, 128.2, 128.1, 128.0, 127.7, 127.0, 126.5, 61.2, 13.7; FTIR: ν_{max}/cm^{-1} 3061, 2977, 1732, 1723, 1401, 1384, 1227, 1185, 1113, 782, 758, 700, 672; HRMS (ESI-TOF): calcd for $C_{24}H_{19}NO_2$ ($M+H^+$) 354.1489; found: 354.1487; mp:108-110 °C.

ethyl 7-chloro-4-(4-chlorophenyl)-1-phenylisoquinoline-3-carboxylate (7d)

Prepared from (*Z*)-4,4'-(2,2-diisocyanoethene-1,1-diyl)bis(chlorobenzene) (70 mg, 0.2 mmol, 1.0 equiv) and iodobenzene (61 mg, 0.3 mmol, 1.5 equiv) according to the general procedure C. Isolated as a pale yellow oil (46 mg, 0.11 mmol), yield: 54%. ^{1}H NMR (400 MHz, CDCl3): δ 8.15 (s, 1H), 7.75-7.73 (m, 2H), 7.63-7.49 (m, 7H), 7.36-7.32 (m, 2H), 4.16 (q, *J* = 8.0 Hz, 2H), 1.07 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (125 MHz, CDCl3): δ 166.9, 159.7, 142.4, 138.2, 134.7, 134.53, 134.46, 134.1, 131.6, 131.3, 130.6, 130.1, 129.2, 128.7, 128.6, 128.1, 127.7, 126.6, 61.5, 13.8; FTIR: νmax/cm^{-1} 3060, 2980, 1721, 1495, 1300, 1222, 1173, 1087, 841, 701, 533, 521; HRMS (ESI-TOF): calcd for C24H17Cl2NO2 ($M+H^+$) 422.0709; found: 422.0708.

ASSOCIATED CONTENT

Supporting Information

Proton and carbon NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

We are grateful to the National Science Foundation of China (21402203, 21472190) for financial support of this work.

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