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Metal-Free Synthesis 6-Benzylphenanthridines via Radical Addition/Cyclization of 2-Isocyanobiphenyls

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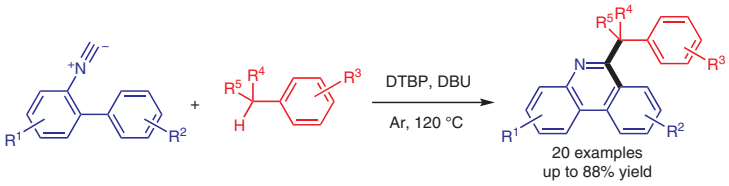

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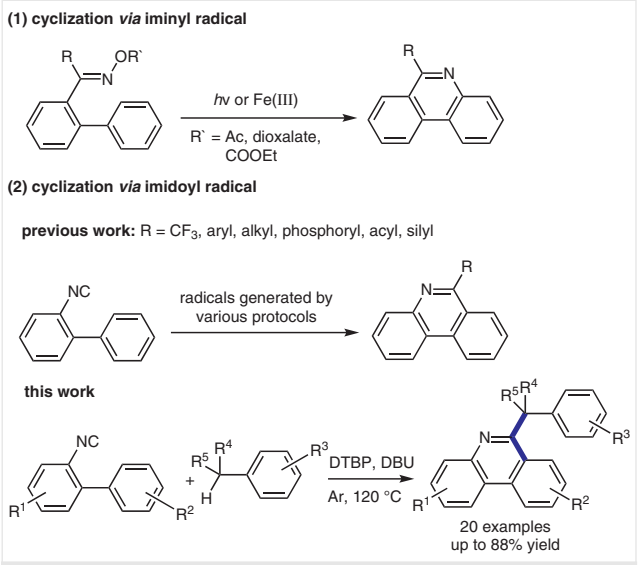
Abstract A simple and practical approach has been established for the synthesis of 6-benzylphenanthridines from benzylic hydrocarbons and 2-isocyanobiphenyls via C(sp^3)–H/C(sp^2)–H bond functionalization under metal-free condition. The reaction exhibits good functional group tolerance and delivers the target products in moderate to excellent yields. The preliminary mechanistic investigation revealed that a radical intermediate might be involved in this reaction.

Key words phenanthridine, metal-free, radical, isocyanobiphenyl, toluene

The cross-dehydrogenative coupling (CDC) reaction via C–H bond functionalization has become an increasingly powerful method for the construction of C–C bonds because of its step-economy and its effectiveness.[1] But direct functionalization of the C(sp^3)–H bond remains challenging because of its high bond-dissociation energy.[2] In the past decade, some progress has been made in C(sp^3)–C bond forming reactions through the functionalization of various C(sp^3)–H bonds,[3] while natural abundant hydrocarbon feedstocks were considered as an ideal source of C(sp^3)–H bonds.[4] Recently, the C(sp^3)–H bond functionalization of toluene has been extensively studied,[5] in which transition metals were usually used as catalysts.[5a–d,f–h] Compared to transition-metal-catalyzed functionalization of the C(sp^3)–H bond of toluene, metal-free activation[5i–l] of this inert bond to synthesize some biologically active compounds is still underdeveloped.[6]

Phenanthridine represents an essential moiety, widely found in many natural products, which exhibits antileukemic, antibacterial, anticancer activities.[7] Besides, phenanthridine derivatives also find applications in optoelectronic materials and DNA fluorescent dyes.[8] Thus, many efforts have been devoted to exploring synthetic methods to phenanthridines. Traditional synthetic methods, like the Pictet–Hubert reaction, usually require harsh conditions, while some new methods involving radical intermediates have been developed recently. One way is to generate iminyl radicals from oxime esters under photochemical or iron-catalyzed conditions, which then cyclize to afford phenanthridines (Scheme 1).[9] Another strategy is to cyclize through an imidoyl radical.[10] In 2012, Chatani, Tobisu, and co-workers envisioned that a radical from boronic acid could add to 2-isocyanobiphenyls to give an imidoyl radical, followed by cyclization to produce phenanthridines.[11] Later, it was found that 2-isocyanobiphenyls could also undergo similar reactions with other kinds of radicals to obtain various substituted phenanthridines, such as trifluoromethyl,[12]



Scheme 1 Synthesis of phenanthridines via a radical mechanism

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aryl,[13] phosphoryl,[14] alkyl,[15] acyl,[7e,16] and silyl[17] phenanthridines (Scheme 1). Inspired and encouraged by this excellent work and aiming to manufacture phenanthridines under greener reaction conditions, herein, we report a tandem addition and cyclization reaction of benzylic hydrocarbons with 2-isocyanobiphenyls to synthesis 6-benzylphenanthridines under metal-free conditions.

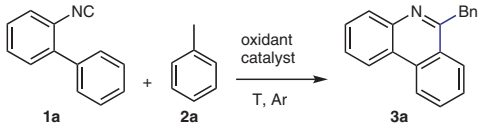
Initially, 2-isocyanobiphenyl (**1a**) and toluene (**2a**) were chosen as the model substrates to investigate the reaction conditions; the results are summarized in Table 1. To our delight, the desired product was obtained in 35% yield under argon at 120 °C after 24 h (entry 1). Firstly, a series of oxidants were examined, such as di-*tert*-butyl peroxide (DTBP), *tert*-butyl hydroperoxide (TBHP), *tert*-butyl peroxybenzoate (TBPB), dicumyl peroxide (DCP), and cumene hydroperoxide (CHP) (entry 1–5). It showed that compound **3aa** was obtained with a better yield when using DTBP (entry 5). Next, transitional metals, like copper, iron, or iridium, were used in the reaction; they can promote the formation of the *tert*-butoxide radical or facilitate transformation to the final product. However, all of them failed to give better results (entry 6–12), as did the use of tetrabutylammonium iodide (TBAI) as the catalyst (entry 13).

Investigating different bases as the catalyst showed the ideal base to be DBU (entry 14–17). The reaction temperature and the amounts of DTBP and DBU required were also screened (entry 18–23). Finally, DTBP (2 equiv) and DBU (0.5 equiv) at 120 °C were found to be optimal to give compound **3aa** in 65% yield (entry 17).

With the optimal conditions in hand, the substrate scope of 2-isocyanobiphenyls **1** and benzylic hydrocarbons **2** was investigated. As shown in Scheme 2, this reaction was successfully amenable to a range of 2-isocyanobiphenyl compounds with electron-withdrawing or electron-donating groups, generating the corresponding phenanthridines **3a–g** in moderate to good yields. To our surprise, the reaction of 2-isocyano-2′-methylbiphenyl, with a methyl located in the *ortho*-position of the phenyl ring, with toluene smoothly gave 6-benzyl-10-methylphenanthridine (**3h**) in 68% yield. The dimethyl-substituted substrate, 2-isocyano-3′,5′-dimethylbiphenyl, successfully underwent the reaction to afford the desired product **3i** in 79% yield. Furthermore, substituents on the isocyano-substituted phenyl ring of the biphenyl did not interfere with the reaction efficiency and gave products **3j–l** in 63–73% yields.

This reaction was further expended to a series of toluene substrates (Scheme 2). We were pleased to find that *m*-xylene, mesitylene, and 4-halotoluenes all performed well under the standard conditions and generated the corresponding products **4a–e** in satisfactory yields, but a lower yield of product **4f** was achieved using 4-methoxytoluene. Unfortunately, electron-deficient substrates, 4-nitrotoluene, and ethyl 2-phenylacetate, both failed to produce the desired products **4g**,**h**. Finally, ethylbenzene and cumene afforded the target compounds **4i** and **4j** in 78% and 57% yield, respectively.

Table 1 Optimization of Typical Reaction Conditions[a]

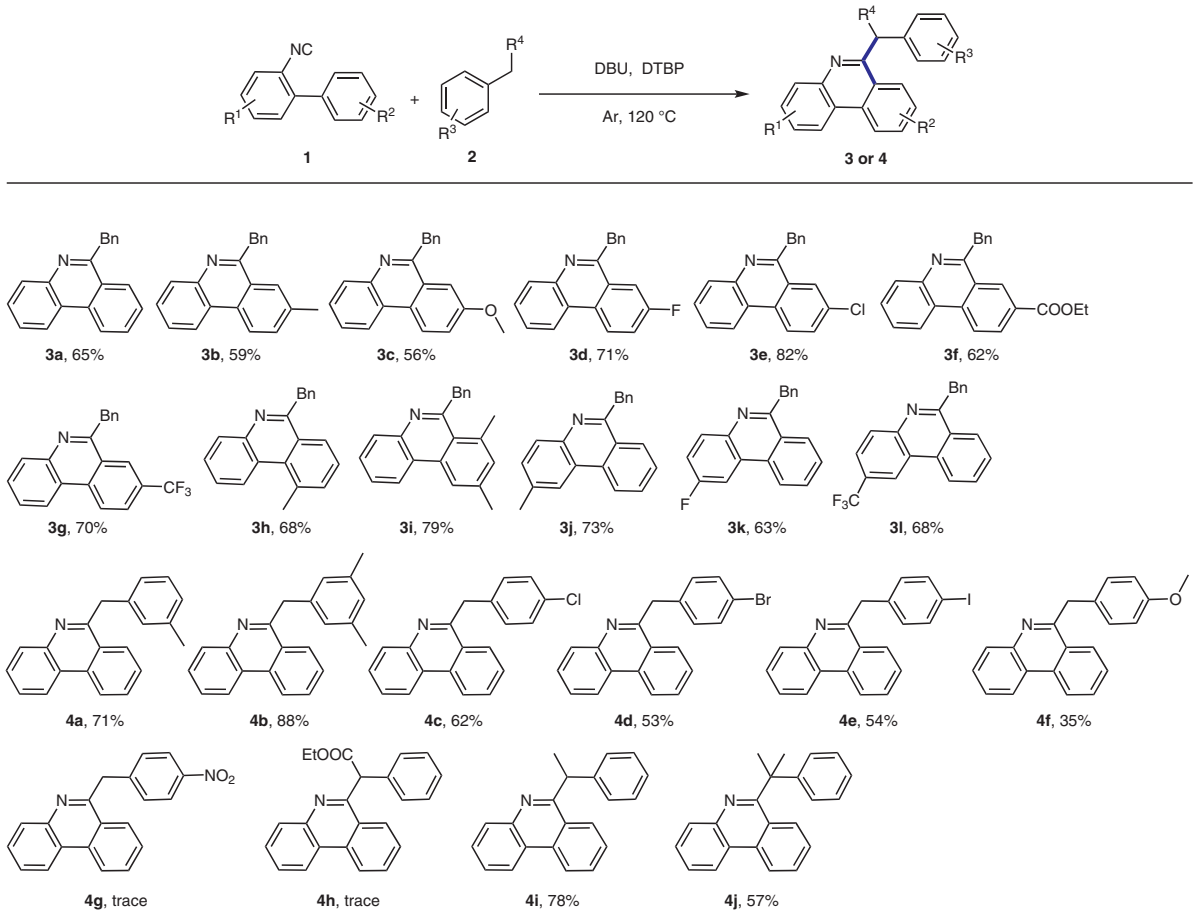


1a 2a 3a

Entry	Oxidant (equiv)	Catalyst (mol%)	Temp (°C)	Yield (%)[b]
1	TBHP (2.0)	–	120	35
2	TBPB (2.0)	–	120	20
3	DCP (2.0)	–	120	6
4	CHP (2.0)	–	120	6
5	DTBP (2.0)	–	120	42
6	DTBP (2.0)	CuO (5)	120	40
7	DTBP (2.0)	CuCl (5)	120	30
8	DTBP (2.0)	Cu_2O (5)	120	31
9	DTBP (2.0)	$Cu(OAc)_2$ (5)	120	0
10	DTBP (2.0)	$FeCl_3$ (5)	120	37
11	DTBP (2.0)	$Fe(Cp)_2$ (5)	120	37
12	DTBP (2.0)	$IrCl_3$ (5)	120	42
13	DTBP (2.0)	TBAI (5)	120	30
14	DTBP (2.0)	Cs_2CO_3 (50)	120	42
15	DTBP (2.0)	K_2CO_3 (50)	120	40
16	DTBP (2.0)	Et_3N (50)	120	53
17	DTBP (2.0)	DBU (50)	120	65
18	DTBP (2.0)	DBU (50)	110	23
19	DTBP (2.0)	DBU (50)	130	45
20	DTBP (1.0)	DBU (50)	120	55
21	DTBP (3.0)	DBU (50)	120	46
22	DTBP (2.0)	DBU (30)	120	59
23	DTBP (2.0)	DBU (10)	120	52
24	DTBP (2.0)	DBU (80)	120	63

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (2.0 mL), oxidant (0.4 mmol), Ar atmosphere, 24 h.
[b] Isolated yield.

To gain an insight into this transformation, we conducted some experiments to study the mechanism. Some control experiments were carried out (Scheme 3). Under the standard conditions but in the presence of a radical scavenger, 2,2,6,6-tetramethylpiperidin-1-yloxy (TEMPO), the reaction was completely inhibited [Scheme 3, (1)]. This result indicates that the reaction might proceed via a radical pathway. Then, kinetic isotope effect (KIE) experiments were conducted to gain insight into the transformation [Scheme 3, (2–4)]. KIE values, (k_H/k_D = 1.3 and 1.1, respectively), were obtained for both intramolecular and intermolecular com-



Scheme 2 Radical addition/cyclization of benzylic hydrocarbons with 2-isocyanobiphenyls. *Reagents and conditions*: **1** (0.25 mmol), DTBP (0.5 mmol), DBU (0.125 mmol), benzylic hydrocarbon **2** (2.0 mL), 120 °C, under Ar. Isolated yields are reported.

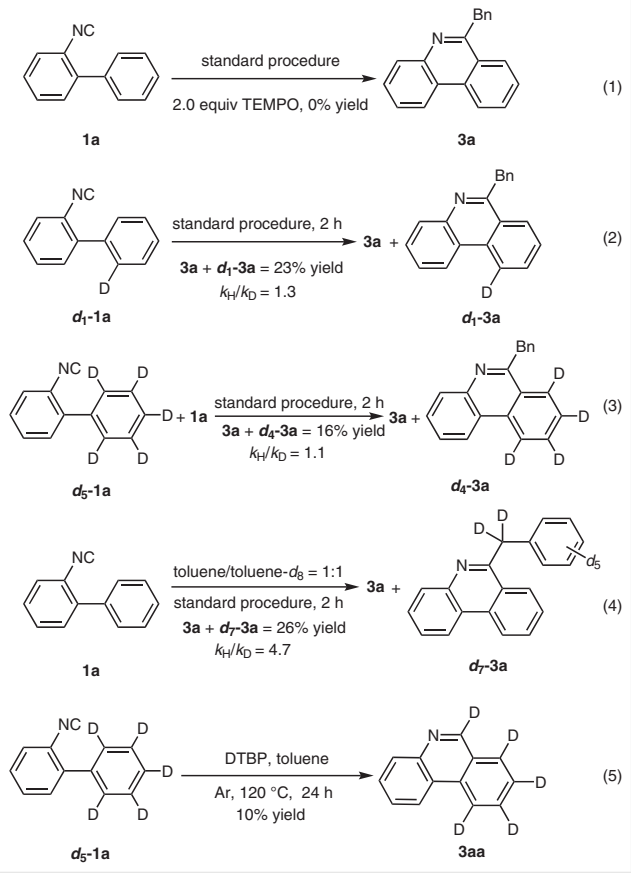
peting experiments, which suggested the cleavage of phenyl C(sp^2)–H is not the rate-determining step. At the same time, when a competing experiment between toluene and toluene-d_8 was carried out, a high KIE value (k_H/k_D = 4.7) was observed, which implied that the cleavage of the benzyl C(sp^3)–H bond may be the rate-determining step. It was also found that the C6–H of compound **3aa** originates from the phenyl ring of compound **1a** [Scheme 3, (5)].

A plausible mechanism is proposed for this reaction based on our results and previous mechanistic studies (Scheme 4). Initially, thermal homolytic cleavage of DTBP generates the *tert*-butoxy radical, and it abstracts a hydrogen atom from toluene and forms a benzyl radical. The benzyl radical then adds to isocyanobiphenyl to give an imidoyl radical **5** which next cyclizes to form the cyclohexadienyl radical **6**. Subsequently, in the absent of DBU, oxidation of **6** produces the final product **3a**. But in the presence of DBU, deprotonation of **6** gives radical anion **7** which is then oxidized to deliver the final product **3a** along with a *tert*-butoxy anion.

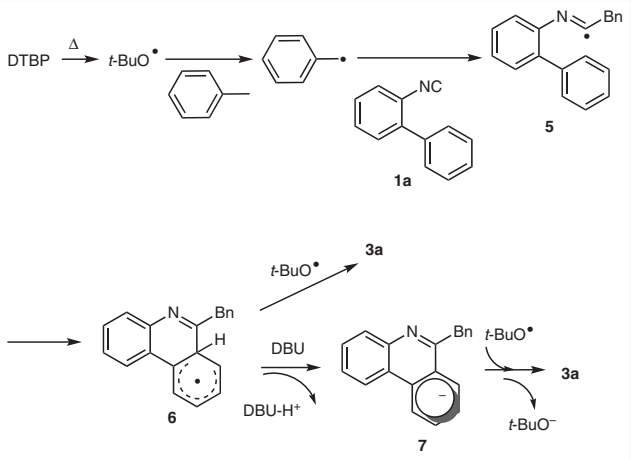
In summary, we have developed a practical and green approach for the synthesis of 6-benzylphenanthridines from 2-isocyanobiphenyls and benzylic hydrocarbons. This method is achieved under metal-free condition with good functional group tolerance and can be employed in the preparation of biologically interesting phenanthridines in moderate to excellent yields.

CAUTION! Reactions and work-up involving peroxy compounds should be conducted behind a safety shield.

Unless otherwise noted, the commercial chemicals were used without further purification. TLC was performed using silica gel 60 F254 and visualized using UV light. Column chromatography was performed with silica gel (mesh 300–400). ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker ARX400. ^{1}H NMR spectra were recorded in $CDCl_3$ and referenced to residual $CHCl_3$ at δ = 7.26. ^{13}C NMR spectra were referenced to the central peak of $CDCl_3$ at δ = 77.0.



Scheme 3 Preliminary mechanism investigation



Scheme 4 Proposed mechanism

6-Benzylphenanthridines 3a–l, 4a–j; General Procedure

To a Schlenk tube were added 2-isocyanobiphenyl **1** (0.25 mmol), DBU (0.125 mmol), DTBP (0.5 mmol), and toluene **2** (2 mL). The mixture was stirred at 120 °C for 24 h. After completion of the reaction, the mixture was evaporated under reduced pressure, and the residue was poured into water and extracted with EtOAc. The combined organic extracts were dried (Na_2SO_4) and filtered, and then the solvent was removed by rotary evaporation. The obtained crude product was purified by column chromatography (silica gel, PE/EtOAc 5:1) to give the product.

6-Benzylphenanthridine (3a)

Yellow solid; yield: 43.7 mg (65%); mp 116–117 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.60 (d, *J* = 8.3 Hz, 1 H), 8.54 (d, *J* = 7.5 Hz, 1 H), 8.19 (t, *J* = 7.0 Hz, 2 H), 7.79–7.69 (m, 2 H), 7.68–7.60 (m, 1 H), 7.60–7.52 (m, 1 H), 7.31 (d, *J* = 7.5 Hz, 2 H), 7.23 (dd, *J* = 8.9, 6.1 Hz, 2 H), 7.15 (t, *J* = 7.3 Hz, 1 H), 4.75 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.4, 144.0, 139.4, 133.5, 130.6, 130.1, 128.9, 128.8, 128.7, 127.5, 127.3, 126.9, 126.5, 125.6, 124.2, 122.6, 122.2, 43.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{15}NNa$: 292.1102; found: 292.1098.

6-Benzyl-8-methylphenanthridine (3b)

White solid; yield: 41.7 mg (59%); mp 103–104 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.50 (dd, *J* = 7.8, 4.5 Hz, 2 H), 8.17 (d, *J* = 8.1 Hz, 1 H), 7.97 (s, 1 H), 7.70 (dd, *J* = 11.1, 4.1 Hz, 1 H), 7.65–7.56 (m, 2 H), 7.32 (d, *J* = 7.5 Hz, 2 H), 7.24 (dd, *J* = 8.4, 6.6 Hz, 2 H), 7.16 (t, *J* = 7.3 Hz, 1 H), 4.73 (s, 2 H), 2.49 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.9, 143.5, 139.3, 137.3, 132.2, 131.3, 129.9, 128.7, 128.6, 128.3, 126.7, 126.6, 126.4, 125.7, 124.2, 122.5, 121.9, 43.0, 22.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{17}NNa$: 306.1259; found: 306.1254.

6-Benzyl-8-methoxyphenanthridine (3c)

Yellow solid; yield: 41.9 mg (56%); mp 98–101 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.51 (d, *J* = 9.1 Hz, 1 H), 8.49–8.44 (m, 1 H), 8.19 (dd, *J* = 8.1, 1.0 Hz, 1 H), 7.72–7.68 (m, 1 H), 7.65–7.61 (m, 1 H), 7.50 (d, *J* = 2.6 Hz, 1 H), 7.39 (dd, *J* = 9.0, 2.6 Hz, 1 H), 7.34 (d, *J* = 7.4 Hz, 2 H), 7.26 (dd, *J* = 8.4, 6.5 Hz, 2 H), 7.18 (t, *J* = 7.3 Hz, 1 H), 4.73 (s, 2 H), 3.82 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.4, 158.6, 143.0, 139.3, 129.9, 128.7, 128.7, 127.8, 127.7, 126.8, 126.7, 126.5, 124.2, 124.2, 121.6, 121.0, 107.5, 55.5, 43.7.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{17}NNaO$: 322.1208; found: 322.1202.

6-Benzyl-8-fluorophenanthridine (3d)

Yellow solid; yield: 50.9 mg (71%); mp 127–128 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.62 (dd, *J* = 9.1, 5.4 Hz, 1 H), 8.50 (d, *J* = 8.2 Hz, 1 H), 8.22 (dd, *J* = 8.2, 1.0 Hz, 1 H), 7.82 (dd, *J* = 9.8, 2.6 Hz, 1 H), 7.79–7.73 (m, 1 H), 7.70–7.66 (m, 1 H), 7.56–7.51 (m, 1 H), 7.34 (d, *J* = 7.2 Hz, 2 H), 7.28 (dd, *J* = 8.3, 6.6 Hz, 2 H), 7.20 (t, *J* = 7.2 Hz, 1 H), 4.72 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.4 (d, *J* = 247 Hz), 159.4, 143.5, 138.7, 130.2, 130.1 (d, *J* = 2 Hz), 128.8, 128.7, 128.6, 127.2, 126.8 (d, *J* = 8 Hz), 126.7, 125.1 (d, *J* = 8 Hz), 123.6, 121.9, 119.7 (d, *J* = 23 Hz), 111.7 (d, *J* = 21 Hz), 43.2.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{14}FNNa$: 310.1008; found: 310.1005.

6-Benzyl-8-chlorophenanthridine (3e)

White solid; yield: 62.1 mg (82%); mp 113–114 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.51 (d, *J* = 8.9 Hz, 1 H), 8.47 (d, *J* = 8.2 Hz, 1 H), 8.21 (dd, *J* = 8.2, 0.8 Hz, 1 H), 8.17 (d, *J* = 2.1 Hz, 1 H), 7.79–7.73 (m, 1 H), 7.70 (dd, *J* = 8.8, 2.1 Hz, 1 H), 7.68–7.63 (m, 1 H), 7.34 (d, *J* = 7.4 Hz, 2 H), 7.28 (dd, *J* = 10.1, 4.8 Hz, 2 H), 7.20 (t, *J* = 7.2 Hz, 1 H), 4.71 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.1, 143.8, 138.7, 133.3, 131.8, 131.0, 130.1, 129.1, 128.8, 128.7, 127.2, 126.7, 126.4, 126.3, 124.3, 123.4, 121.9, 43.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{14}ClNNa$: 326.0712; found: 326.0705.

Ethyl 6-Benzylphenanthridine-8-carboxylate (3f)

White solid; yield: 52.9 mg (62%); mp 149–150 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.00 (d, *J* = 1.5 Hz, 1 H), 8.63 (d, *J* = 8.6 Hz, 1 H), 8.55 (d, *J* = 8.3 Hz, 1 H), 8.36 (dd, *J* = 8.6, 1.7 Hz, 1 H), 8.21 (dd, *J* = 8.2, 0.9 Hz, 1 H), 7.83–7.76 (m, 1 H), 7.72–7.64 (m, 1 H), 7.40 (d, *J* = 7.3 Hz, 2 H), 7.26 (dd, *J* = 8.3, 6.7 Hz, 2 H), 7.17 (t, *J* = 7.3 Hz, 1 H), 4.79 (s, 2 H), 4.43 (q, *J* = 7.1 Hz, 2 H), 1.45 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.1, 160.9, 144.7, 139.0, 136.4, 130.2, 130.2, 129.9, 129.5, 129.1, 128.9, 128.8, 127.1, 126.6, 124.9, 123.4, 122.8, 122.7, 61.5, 43.2, 14.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{19}NNaO_2$: 364.1313; found: 364.1305.

6-Benzyl-8-(trifluoromethyl)phenanthridine (3g)

Yellow solid; yield: 59.0 mg (70%); mp 105–106 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.71 (d, *J* = 8.7 Hz, 1 H), 8.58–8.51 (m, 2 H), 8.24 (dd, *J* = 8.2, 0.9 Hz, 1 H), 7.96 (dd, *J* = 8.7, 1.5 Hz, 1 H), 7.82 (dd, *J* = 8.2, 1.2 Hz, 1 H), 7.76–7.65 (m, 1 H), 7.36 (d, *J* = 7.5 Hz, 2 H), 7.32–7.24 (m, 2 H), 7.20 (t, *J* = 7.3 Hz, 1 H), 4.78 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.2, 144.6, 138.6, 135.7, 130.3, 130.0, 129.3, 128.9, 128.7, 127.4, 126.8, 126.3 (q, *J* = 3.0 Hz), 124.8, 124.6 (q, *J* = 4.0 Hz), 124.1 (d, *J* = 271.0 Hz), 123.7, 123.1, 122.5, 43.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{14}F_3NNa$: 360.0976; found: 360.0968.

6-Benzyl-10-methylphenanthridine (3h)

Yellow oil; yield: 48.1 mg (68%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.82 (d, *J* = 8.4 Hz, 1 H), 8.28 (dd, *J* = 8.1, 1.1 Hz, 1 H), 8.15 (d, *J* = 8.0 Hz, 1 H), 7.80–7.73 (m, 1 H), 7.68–7.62 (m, 2 H), 7.53–7.44 (m, 1 H), 7.31 (d, *J* = 7.4 Hz, 2 H), 7.25 (dd, *J* = 10.5, 5.1 Hz, 2 H), 7.17 (t, *J* = 7.2 Hz, 1 H), 4.79 (s, 2 H), 3.12 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.6, 145.0, 139.5, 135.7, 134.7, 132.9, 130.3, 128.6, 128.6, 128.0, 127.0, 126.9, 126.7, 126.4, 126.0, 125.8, 125.5, 43.8, 27.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{17}NNa$: 306.1259; found: 306.1251.

6-Benzyl-7,9-dimethylphenanthridine (3i)

Yellow solid; yield: 58.7 mg (79%); mp 109–110 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.57 (d, *J* = 8.1 Hz, 1 H), 8.38 (s, 1 H), 8.12 (d, *J* = 8.1 Hz, 1 H), 7.72–7.68 (m, 1 H), 7.64–7.61 (m, 1 H), 7.26–7.19 (m, 3 H), 7.15 (t, *J* = 7.2 Hz, 1 H), 7.03 (d, *J* = 7.1 Hz, 2 H), 4.93 (s, 2 H), 2.80 (s, 3 H), 2.56 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3, 143.3, 140.2, 136.5, 135.3, 133.8, 129.5, 128.6, 128.6, 128.3, 126.6, 126.1, 124.6, 124.1, 122.4, 120.8, 46.8, 25.5, 21.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{19}NNa$: 320.1415; found: 320.1409.

6-Benzyl-2-methylphenanthridine (3j)

Yellow solid; yield: 51.6 mg (73%); mp 104–105 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.63 (d, *J* = 8.3 Hz, 1 H), 8.36 (s, 1 H), 8.20 (d, *J* = 8.3 Hz, 1 H), 8.11 (d, *J* = 8.3 Hz, 1 H), 7.78 (dd, *J* = 8.2, 7.1 Hz, 1 H), 7.58 (t, *J* = 8.2 Hz, 2 H), 7.33 (d, *J* = 7.6 Hz, 2 H), 7.30–7.22 (m, 2 H), 7.18 (t, *J* = 6.9 Hz, 1 H), 4.77 (s, 2 H), 2.65 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.1, 142.0, 139.3, 136.5, 133.1, 130.3, 130.1, 129.6, 128.5, 128.5, 127.1, 127.0, 126.2, 125.5, 123.8, 122.4, 121.6, 43.0, 21.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{17}NNa$: 306.1259; found: 306.1257.

6-Benzyl-2-fluorophenanthridine (3k)

Yellow solid; yield: 45.2 mg (63%); mp 92–93 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.42 (d, *J* = 8.2 Hz, 1 H), 8.17 (t, *J* = 8.3 Hz, 2 H), 8.10 (d, *J* = 10.0 Hz, 1 H), 7.73 (t, *J* = 7.6 Hz, 1 H), 7.58 (t, *J* = 7.6 Hz, 1 H), 7.45 (dd, *J* = 11.9, 5.0 Hz, 1 H), 7.31 (d, *J* = 7.2 Hz, 2 H), 7.24 (t, *J* = 7.4 Hz, 2 H), 7.20–7.12 (m, 1 H), 4.72 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.3 (d, *J* = 245.0 Hz), 159.4 (d, *J* = 3.0 Hz), 140.7, 139.1, 132.8, 132.1 (d, *J* = 9.0 Hz), 130.5, 128.7, 128.7, 128.0, 127.2, 126.5, 125.5, 125.3 (d, *J* = 10.0 Hz), 122.7, 117.5 (d, *J* = 24.0 Hz), 107.0 (d, *J* = 23.0 Hz), 43.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{14}FNNa$: 310.1008; found: 310.1005.

6-Benzyl-2-(trifluoromethyl)phenanthridine (3l)

Yellow oil; yield: 72.3 mg (68%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.82 (s, 1 H), 8.62 (d, *J* = 8.3 Hz, 1 H), 8.27 (dd, *J* = 15.9, 8.4 Hz, 2 H), 7.94 (dd, *J* = 8.6, 1.7 Hz, 1 H), 7.88–7.78 (m, 1 H), 7.71–7.59 (m, 1 H), 7.33 (d, *J* = 7.5 Hz, 2 H), 7.27 (dd, *J* = 9.0, 6.0 Hz, 2 H), 7.19 (t, *J* = 7.2 Hz, 1 H), 4.78 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.7, 145.3, 138.8, 133.0, 131.1, 130.9, 128.8, 128.7, 128.4127.4, 126.7, 125.8, 124.8 (q, *J* = 3.0 Hz), 124.5 (d, *J* = 270.0 Hz), 124.2, 123.7, 122.6, 120.0 (q, *J* = 5.0 Hz), 43.2.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{14}F_3NNa$: 360.0976; found: 360.0970.

6-(3-Methylbenzyl)phenanthridine (4a)

Yellow oil; yield: 50.2 mg (71%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.61 (d, *J* = 8.3 Hz, 1 H), 8.56 (d, *J* = 7.8 Hz, 1 H), 8.23 (t, *J* = 8.1 Hz, 2 H), 7.78–7.73 (m, 2 H), 7.68–7.63 (m, 1 H), 7.62–7.54 (m, 1 H), 7.15 (d, *J* = 6.0 Hz, 3 H), 6.99 (d, *J* = 5.7 Hz, 1 H), 4.74 (s, 2 H), 2.27 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.4, 143.9, 139.2, 138.3, 133.4, 130.4, 130.0, 129.4, 128.7, 128.5, 127.4, 127.2, 126.7, 125.7, 125.6, 124.1, 122.5, 122.1, 43.2, 21.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{17}NNa$: 306.1259; found: 306.1258.

6-(3,5-Dimethylbenzyl)phenanthridine (4b)

Yellow oil; yield: 65.3 mg (88%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.62 (d, *J* = 8.3 Hz, 1 H), 8.56 (dd, *J* = 8.2, 1.1 Hz, 1 H), 8.24 (dd, *J* = 11.5, 4.3 Hz, 2 H), 7.79–7.74 (m, 2 H), 7.68–7.64 (m, 1 H), 7.61–7.57 (m, 1 H), 6.94 (s, 2 H), 6.81 (s, 1 H), 4.70 (s, 2 H), 2.23 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.5, 143.8, 139.1, 138.1, 133.4, 130.4, 130.0, 128.8, 128.2, 127.5, 127.3, 126.7, 126.5, 125.6, 124.1, 122.5, 122.1, 43.1, 21.4.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{19}NNa$: 320.1415; found: 320.1411.

6-(4-Chlorobenzyl)phenanthridine (4c)

White solid; yield: 47.0 mg (62%); mp 151–153 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.63 (d, *J* = 8.3 Hz, 1 H), 8.60–8.53 (m, 1 H), 8.20 (dd, *J* = 8.1, 1.0 Hz, 1 H), 8.13 (d, *J* = 8.3 Hz, 1 H), 7.81–7.73 (m, 2 H), 7.69–7.65 (m, 1 H), 7.61–7.57 (m, 1 H), 7.26–7.20 (m, 4 H), 4.72 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.7, 143.7, 137.7, 133.5, 132.3, 130.6, 130.0, 129.9, 128.9, 128.8, 127.5, 127.0, 126.9, 125.3, 124.1, 122.7, 122.1, 42.4.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{14}ClNNa$: 326.0712; found: 326.0705.

6-(4-Bromobenzyl)phenanthridine (4d)

Yellow solid; yield: 46.0 mg (53%); mp 171–173 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.64 (d, *J* = 8.3 Hz, 1 H), 8.57 (d, *J* = 7.8 Hz, 1 H), 8.19 (d, *J* = 8.1 Hz, 1 H), 8.13 (d, *J* = 8.1 Hz, 1 H), 7.84–7.72 (m, 2 H), 7.71–7.64 (m, 1 H), 7.60 (t, *J* = 7.6 Hz, 1 H), 7.36 (d, *J* = 8.4 Hz, 2 H), 7.19 (d, *J* = 8.4 Hz, 2 H), 4.70 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.6, 143.7, 138.2, 133.5, 131.8, 130.7, 130.4, 130.0, 128.9, 127.6, 127.0, 126.9, 125.3, 124.1, 122.7, 122.1, 120.4, 42.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{14}BrNNa$: 370.0207; found: 370.0201.

6-(4-Iodobenzyl)phenanthridine (4e)

Yellow solid; yield: 53.3 mg (54%); mp 183–184 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.63 (d, *J* = 8.3 Hz, 1 H), 8.56 (d, *J* = 7.6 Hz, 1 H), 8.19 (dd, *J* = 8.1, 0.8 Hz, 1 H), 8.13 (d, *J* = 8.2 Hz, 1 H), 7.81–7.73 (m, 2 H), 7.69–7.64 (m, 1 H), 7.62–7.53 (m, 3 H), 7.07 (d, *J* = 8.3 Hz, 2 H), 4.69 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.6, 143.8, 138.9, 137.7, 133.4, 130.8, 130.6, 130.0, 128.9, 127.6, 127.0, 126.9, 125.3, 124.1, 122.7, 122.1, 91.8, 42.6.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{14}INNa$: 418.0069; found: 418.0065.

6-(4-Methoxybenzyl)phenanthridine (4f)

Yellow solid; yield: 26.1 mg (35%); mp 112–114 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.62 (d, *J* = 8.3 Hz, 1 H), 8.56 (d, *J* = 8.9 Hz, 1 H), 8.21 (d, *J* = 8.1 Hz, 2 H), 7.81–7.71 (m, 2 H), 7.69–7.62 (m, 1 H), 7.62–7.55 (m, 1 H), 7.28–7.20 (m, 2 H), 6.78 (t, *J* = 7.4 Hz, 2 H), 4.70 (s, 2 H), 3.73 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.5, 158.1, 143.6, 133.3, 131.2, 130.4, 129.7, 129.5, 128.7, 127.3, 127.1, 126.7, 125.3, 123.9, 122.4, 122.0, 114.0, 55.2, 42.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{17}NNaO$: 322.1208; found: 322.1200.

6-(1-Phenylethyl)phenanthridine (4i)

White solid; yield: 55.2 mg (78%); mp 94–96 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.63 (d, *J* = 8.3 Hz, 1 H), 8.57 (d, *J* = 8.1 Hz, 1 H), 8.30 (d, *J* = 8.1 Hz, 1 H), 8.25 (d, *J* = 8.3 Hz, 1 H), 7.82–7.71 (m, 2 H), 7.71–7.63 (m, 1 H), 7.61–7.53 (m, 1 H), 7.40 (d, *J* = 7.3 Hz, 2 H), 7.28 (t, *J* = 7.5 Hz, 2 H), 7.18 (t, *J* = 7.3 Hz, 1 H), 5.14 (q, *J* = 6.9 Hz, 1 H), 1.97 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.4, 145.9, 143.7, 133.2, 130.3, 129.9, 128.6, 128.5, 127.6, 127.1, 126.5, 126.4, 126.2, 125.2, 123.7, 122.4, 121.9, 44.1, 22.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{17}NNa$: 306.1259; found: 306.1252.

6-(2-Phenylpropan-2-yl)phenanthridine (4j)

White solid; yield: 42.3 mg (57%); mp 87–88 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.63 (d, *J* = 8.3 Hz, 1 H), 8.57 (d, *J* = 7.9 Hz, 1 H), 8.27 (d, *J* = 8.1 Hz, 1 H), 7.83–7.72 (m, 2 H), 7.70–7.64 (m, 2 H), 7.36–7.25 (m, 5 H), 7.23–7.19 (m, 1 H), 1.99 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.8, 150.5, 143.2, 134.1, 130.5, 129.3, 129.2, 128.7, 128.5, 126.8, 126.1, 125.9, 124.3, 124.0, 122.6, 121.8, 48.0, 31.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{19}NNa$: 320.1415; found: 320.1410.

[6,7,8,9,10-$^2H_5$]Phenanthridine (3aa)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.63–8.57 (m, 1 H), 8.21 (d, *J* = 8.2 Hz, 1 H), 7.79–7.74 (m, 1 H), 7.74–7.67 (m, 1 H).

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Supporting Information

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