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NH_4I-mediated sp^3 C-H cross-dehydrogenative coupling of benzylamines with 2-methylquinoline for the synthesis of *E*-2-styrylquinolines

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Xue Li[1], Bin Huang[1], JiangWei Wang[2], YuanYuan Zhang[1] and WeiBo Liao[1]

Abstract

Without any metal catalyst, a simple and efficient method for the synthesis of *E*-2-styrylquinolines through sp^3 C-H cross-dehydrogenative coupling of benzylamines with 2-methylquinolines mediated by NH_4I under air is successfully developed. The oxidative olefination proceeded through deamination and sp^3 C–H bond activation. A plausible mechanism is proposed for the construction of *E*-2-styrylquinolines.

Keywords

2-methylquinolines, benzylamines, *E*-2-styrylquinolines, NH_4I, sp^3 C-H cross-dehydrogenative coupling

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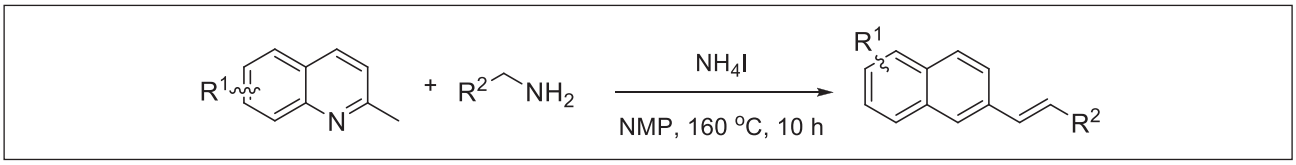
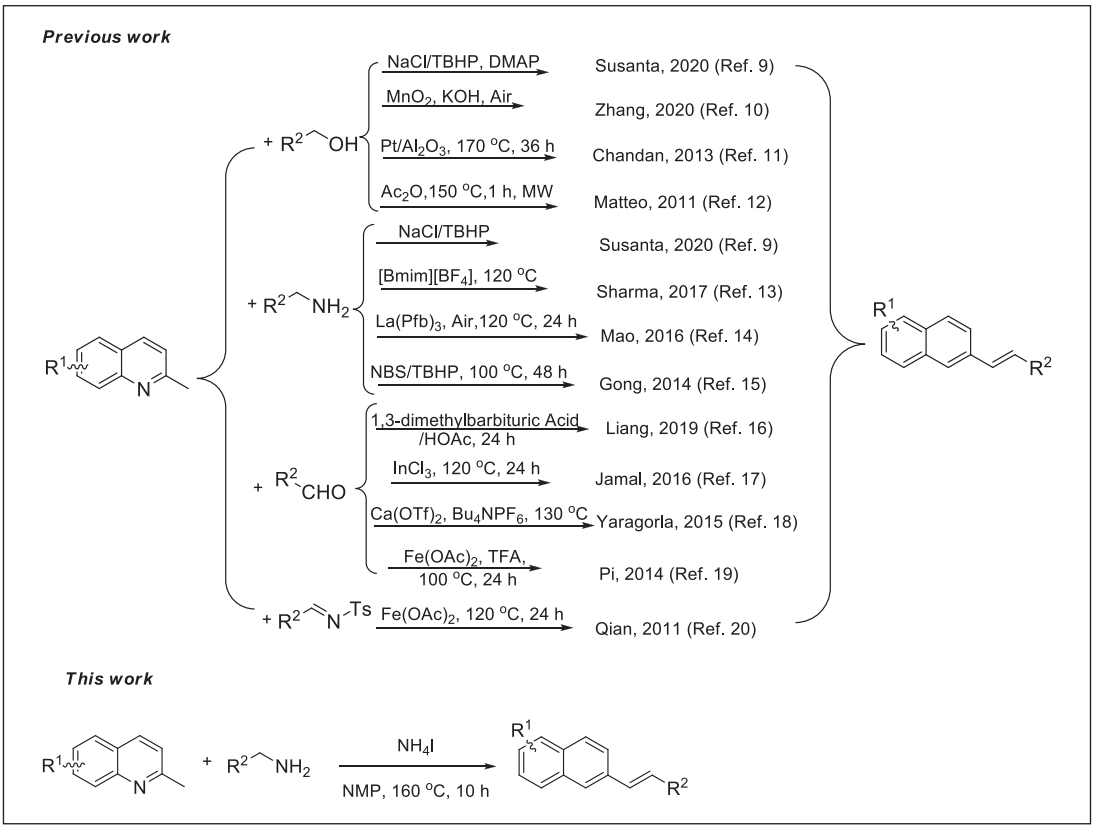


Introduction

On account of their unique structures and reactivities, quinoline and its derivatives are widely utilized to prepare various biologically important compounds.[1,2] Among quinoline derivatives, *E*-2-styrylquinolines are typical bioactive compounds acting as potent HIV-1 integrase inhibitors,[3–5] leukotriene receptor antagonists,[6,7] and antiallergic drugs.[8] The wide applications of *E*-2-styrylquinolines have attracted considerable attention in synthetic chemistry. In the past 10 years, widely used methods for the synthesis of *E*-2-styrylquinolines have mainly involved the reactions of 2-methylquinolines with benzyl alcohols,[9–12] benzyl amines,[9,13–15] aldehydes,[16–19] and *N*-benzylidene-4-methylbenzenesulfonamides[20] (Scheme 1). In 2011, Qian et al.[20] disclosed that $Fe(OAc)_2$ promoted the reactions of 2-methylquinolines and *N*-benzylidene-4-methylbenzenesulfonamides by removing a molecule of *p*-toluenesulfonamide to give *E*-2-styrylquinolines. In 2019, Liang et al.[16] reported that various 2-alkenylquinolines could be produced from 2-methylquinolines and aldehydes under the synergistic organocatalysis of 1,3-dimethylbarbituric acid/HOAc for 24 h. In 2020, Susanta et al.[9] reported that *E*-2-styrylquinolines could be prepared from 2-methylquinolines by reactions with primary alcohols or primary amines using the NaCl/TBHP oxidative system. In the same year, Zhang et al.[10] showed that reactions of 2-methylquinolines and primary alcohols catalyzed by MnO_2 in the presence of KOH eliminated molecule of H_2O and were transformed into *E*-2-styrylquinolines. Nevertheless, these methods suffer from environmental and economic concerns as they

[1]Drug Research Center, Traditional Chinese Medicine Institute of Jiangxi, Nanchang, P.R. China
[2]Jiangxi Provincial Hospital of Traditional Chinese medicine, Nanchang, P.R. China

Corresponding author:
Xue Li, Drug Research Center, Traditional Chinese Medicine Institute of Jiangxi, Nanchang 330046, P.R. China.
Email: m18702635626@163.com



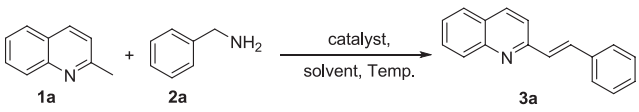
Scheme 1. Methods for the preparation of *E*-2-styrylquinolines.

utilize strong oxidants and transition-metal catalysts, which impede the applicability of these methods. To avoid these drawbacks, we successfully developed a method that involves deamination and sp^3 C-H cross-dehydrogenative coupling of 2-methylquinolines and benzylamines to give various *E*-2-styrylquinolines mediated by NH_4I in moderate to good yields (30%–93%) with NMP (*N*-methyl-2-pyrrolidone) as the solvent, without any other metal catalyst at 160 °C for 10 h (Scheme 1).

Results and discussion

The 2-Methylquinoline (**1a**) and benzylamine (**2a**) were selected as model substrates to optimize the reaction conditions for the synthesis of *E*-2-styrylquinoline (**3a**). The effects of different catalysts, solvents, and temperatures were investigated. The results are summarized in Table 1. First, different additives such as NBS (*N*-bromosuccinimide), NIS (*N*-iodosuccinimide), TBAI (tetra-*n*-butylammonium iodide), NH_4I, and KI were investigated and NH_4I was found to be the best, affording a 52% yield of **3a** (Table 1, entries 1–5). No product was formed in the absence of a catalyst, even on increasing the reaction temperature to 160 °C (Table 1, entry 6). Next, the solvent was optimized and NMP was found to be the best (Table 1, entries 4 and 7–9). With NMP as the solvent, the reaction temperature and time were further optimized. When the temperature was increased from 120–160 °C, the yield of **3a** increased from 52% to 85% (Table 1, entries 4, 10, and 11), which indicated that the reaction proceeded best at 160 °C. To further improve the yield of **3a**, increased reaction times of up to 24 h at 160 °C were tested; however, the yield was not

Table 1. Optimization of the reaction conditions for the synthesis of **3a**.[a]

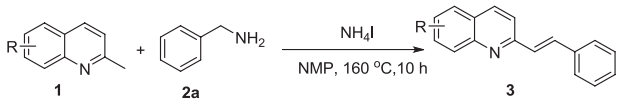


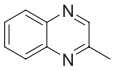
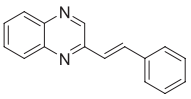
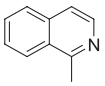
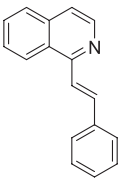
1a **2a** **3a**

Entry	Additive	Solvent	Temp (°C)	Yield of **3a** (%)[b]
1	NBS	NMP	120	Trace
2	NIS	NMP	120	Trace
3	TBAI	NMP	120	10
4	NH_4I	NMP	120	52
5	KI	NMP	120	Trace
6	None	NMP	160	0
7	NH_4I	CH_3CN	80	Trace
8	NH_4I	Toluene	110	Trace
9	NH_4I	DMSO	160	Trace
10	NH_4I	NMP	140	64
11	NH_4I	NMP	160	85
12[c]	NH_4I	NMP	160	85
13[d]	NH_4I	NMP	160	86
14[e]	NH_4I	NMP	160	85
15[f]	NH_4I	NMP	160	18
16[g]	NH_4I	NMP	160	86

NBS: *N*-bromosuccinimide; NIS: *N*-iodosuccinimide; TBAI: tetra-*n*-butylammonium iodide; DMSO: dimethyl sulfoxide.
[a]Reaction conditions: **1a** (1.0 mmol), **2a** (3.0 mmol), catalyst (1.2 equiv), solvent (4 mL), in air, 10 h.
[b]Isolated yield.
[c]Reaction time: 14 h.
[d]Reaction time: 18 h.
[e]Reaction time: 24 h.
[f]Under N_2.
[g]Under O_2.

Table 2. Substrate scope of various quinolines having sp^3 carbons in the oxidative cross-dehydrogenative coupling reaction.[a]



Entry	R	Product[b]	Yield (%)[c]
1	(**1a**) H	**3a**	85
2	(**1b**) 3-CH_3	**3b**	73
3	(**1c**) 3-Br	**3c**	80
4	(**1d**) 4-CH_3	**3d**	61
5	(**1e**) 4-Cl	**3e**	68
6	(**1f**) 6-CH_3	**3f**	82
7	(**1g**) 6-Cl	**3g**	93
8	(**1h**) 6-Br	**3h**	89
9	(**1i**) 7-CH_3	**3i**	83
10	(**1j**) 7-Cl	**3j**	90
11	(**1k**) 7-Br	**3k**	87
12	(**1l**) 8-CH_3	**3l**	54
13	(**1m**) 8-Cl	**3m**	59
14	(**1n**) 	**3n** 	60
15	(**1o**) 	**3o** 	51

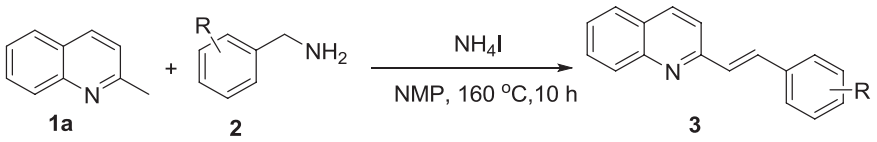
[a]Reaction condition: **1** (1.0 mmol), **2a** (3.0 mmol), NH_4I (1.2 equiv), NMP (4 mL), air, 160 °C, 10 h.
[b]Structures were confirmed by ^1H and ^{13}C nuclear magnetic resonance (NMR) spectroscopy.
[c]Isolated yield based on **1**.

improved (Table **1**, entries 11–14). The optimum reaction time was therefore about 10 h (Table **1**, entry 11). When the reaction was carried out under N_2, the yield of **3a** decreased dramatically (Table 1, entry 15), which indicated that the mixture required the presence of O_2 or air. Subsequently, the reaction was carried out under an O_2 atmosphere and the yield of target product **3a** was found to be almost equal to the yield in air (Table 1, entries 11 and 16). So the optimal reaction conditions were established as follows: using NH_4I as the additive, NMP as the solvent, 160 °C, 10 h.

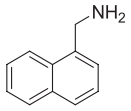
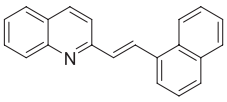
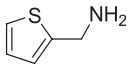
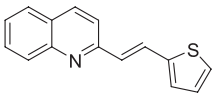
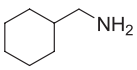
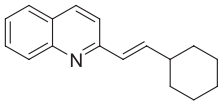
With optimized conditions in hand, we set out to explore the substrate scope of various quinolines having sp3 carbons for oxidative cross-dehydrogenative coupling reactions. The target products **3** were obtained in moderate to good yields ranging from 51% to 93% by reacting quinolines **1** with benzylamine (**2a**) in NMP under air at 160 °C for 10 h. The results are shown in Table 2. The nature of the substituents on substrates **1** affected the reaction yields to some degree. Both halogen-substituted and methyl-substituted 2-methylquinoline smoothly afforded the corresponding products in 54%–93% yields (Table 2, entries 2–12). Among them, when substituents were attached to C-3, C-4, C-6, C-7, or C-8, the yields of the halogen-substituted products were slightly higher than those of the methyl-substituted products. Notably, dimethyl-substituted quinolines only offered the products of olefination at the 2-methyl position, the methyls attached at other positions were unreactive (Table 2, entries 2, 4, 6, 9, and 12). Besides, 2-methylquinoxaline and 1-methylisoquinoline also exhibited excellent reactivity with benzylamine (**2a**) under the standard conditions and gave the olefination products **3n** in 60% and **3o** in 51% yields (Table 2, entries 14 and 15).

Subsequently, we set out to examine the substrate scope of various methanamines **2** in reactions with 2-methylquinoline (**1a**). The target products **3** were obtained in good yields ranging from 30% to 90% under the optimized conditions. The results are shown in Table 3. The nature of different R groups of benzylamines **2** affected the reaction yields slightly. Halogen-substituted benzylamines and methyl-substituted benzylamines reacted with **1a** to afford the corresponding olefination products in 72%–90% yields (Table 2, entries 1–8). It is worth noting that naphthalen-α-methanamine (**2i**) provided the desired product **3x** in excellent yield 88% (Table 2, entry 9). Besides, a heterocyclic methanamine such as 2-thiophene-methanamine (**2j**) and an aliphatic amine such as cyclohexyl methanamine (**2k**) also underwent deamination and were transformed effectively into the corresponding products **3y** and **3z** in yields of 73% and 30%, respectively (Table 2, entries 10 and 11). According to the ^1H nuclear magnetic resonance (NMR) spectra of olefination products **3** and earlier studies,[14–16] we were able to conform the (*E*)-configurations of the olefination products **3**.

Table 3. Substrate scope of various primary amines.[a]



1a 2 3

Entry	R	Product[b]	Yield (%)[c]
1	(**2a**) 2-CH_3	**3p**	89
2	(**2b**) 2-Cl	**3q**	72
3	(**2c**) 3-CH_3	**3r**	76
4	(**2d**) 3-F	**3s**	83
5	(**2e**) 3-Cl	**3t**	87
6	(**2f**) 4-CH_3	**3u**	90
7	(**2g**) 4-F	**3v**	86
8	(**2h**) 4-Cl	**3w**	80
9	(**2i**) 	**3x** 	88
10	(**2j**) 	**3y** 	73
11	(**2k**) 	**3z** 	30

[a]Reaction condition: **1a** (1.0 mmol), **2** (3.0 mmol), NH_4I (1.2 equiv), NMP (4 mL), air, 160 °C, 10 h.
[b]Structures were confirmed by ^1H and ^{13}C nuclear magnetic resonance (NMR) spectroscopy.
[c]Isolated yield based on **1a**.

To further explore the mechanism of oxidative olefination for the construction of *E*-2-styrylquinolines, several control experiments were carried out. First, when adding the radical scavenger TEMPO (1.0 equiv) to the standard reaction, **3a** could be afforded in 84% yield (Scheme 2(a)), which suggested that the reaction may not proceed through a radical intermediate. Second, when **2a** alone was subjected to the standard reaction conditions, 30% yield of phenylmethanimine, 10% yield of *N*-benzylbenzamide, and a trace amount of benzaldehyde were observed (Scheme 2(b)). Finally, when **1a** reacted with phenylmethanimine under the standard conditions, an 86% yield of **3a** was obtained (Scheme 2(c)), suggesting that phenylmethanimine might be an intermediate in this reaction.

Based on these observations and related references,[13,15] a plausible mechanism is proposed in Scheme 3. Initially, NH_4I is oxidized to a highly active "I^+" species in air. Second, the benzylamine is transformed into a phenylmethanimine by elimination under the influence of "I^+." Finally, phenylmethanimine is attacked by the 2-methylquinoline and is transformed into the corresponding olefination product *via* elimination of a molecule of NH_3.

Conclusion

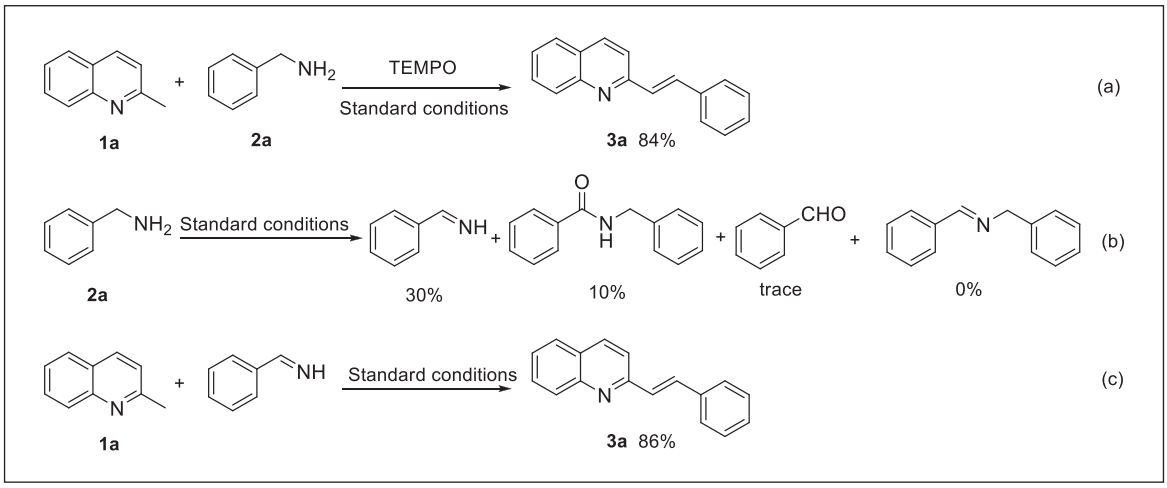
In summary, we have developed an efficient approach for the synthesis of a variety of *E*-2-styrylquinolines through sp^3 C-H cross-dehydrogenative coupling of benzylamines with 2-methylquinolines promoted by NH_4I under air without any metal catalyst. The approach provides relatively mild reaction conditions, moderate to good yields, and encompasses a broad substrate scope. A plausible mechanism has been proposed for the oxidative olefination through deamination.

Experimental

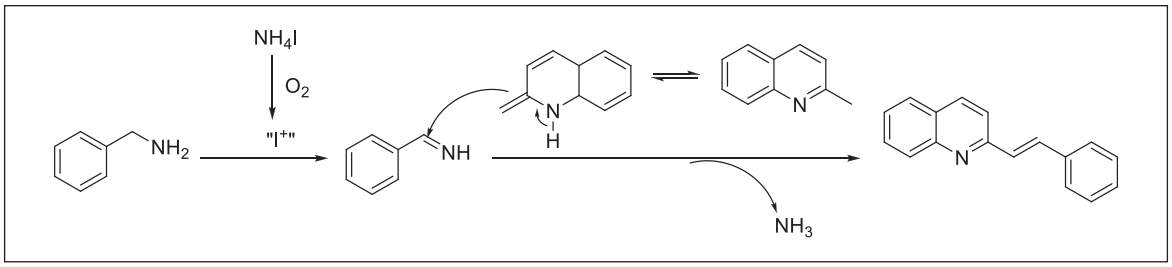
Infrared spectra were determined on a Nicolet Avatar-370 spectrometer in KBr (ν in cm^{-1}). Melting points were measured on a Büchi B-540 capillary melting point apparatus and are uncorrected. Mass spectra (ESI-MS) were recorded on a Thermo Finnigan LCQ-Advantage spectrometer. High-resolution mass spectra (ESI-HRMS) were obtained using an Agilent 6210 TOF instrument. ^1H NMR and ^{13}C NMR spectra were recorded on a Varian Mercury Plus-400 spectrometer (400 and 100 MHz), δ in parts per million, *J* in Hertz, using TMS as the internal standard. Signal multiplicities are assigned as singlet (s), doublet (d), multiplet (m). All analytical reagents were commercially available and were used directly without further purification.

*Synthesis of E-2-styrylquinolines (**3a** selected as an example); general procedure*

A mixture of 2-methylquinoline (**1a**) (0.14 g, 1 mmol), benzylamine (0.32 g, 3.0 mmol), and NH_4I (0.17 g, 1.2 mmol) in NMP (4 mL) was stirred at 160 °C for 10 h until the total



Scheme 2. Control experiments.



Scheme 3. A plausible mechanism.

consumption of **1a**. After cooling, the reaction mixture was washed with brine (20 mL) and extracted with CH_2Cl_2 (2 × 20 mL). The combined organic extract was dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography (petroleum ether/EtOAc = 6:1) to afford the target product **3a** (pale yellow solid, 85%, 0.20 g).

2-[(1E)-2-phenylethenyl]quinoline (**3a**). Pale yellow solid; 85%, 0.20 g; m.p. 91–92 °C (Lit.[21] 91–93 °C).[21] 1H NMR (400 MHz, $CDCl_3$): δ = 8.14–8.06 (m, 2H), 7.76 (d, *J* = 8.2 Hz, 1H), 7.74–7.64 (m, 5H), 7.55–7.46 (m, 1H), 7.43–7.38 (m, 3H), 7.34–7.30 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.4, 148.2, 136.6, 136.3, 134.5, 129.7, 129.3, 129.0, 128.9, 128.6, 127.6, 127.5, 127.2, 126.3, 118.9. MS (ESI): m/z (%) = 232.1 ($[M]^+$, 100). HRMS (ESI): m/z $[M]^+$ calcd for $C_{17}H_{14}N$: 232.1126, found: 232.1133.

3-Methyl-2-[(1E)-2-phenylethenyl]quinoline (**3b**). Pale yellow solid; 73%, 0.18 g; m.p. 98–100 °C (Lit.21 98–100 °C).[21] 1H NMR (400 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 8.4 Hz, 1H), 8.02 (d, *J* = 15.6 Hz, 1H), 7.88 (s, 1H), 7.72–7.63 (m, 4H), 7.51 (d, *J* = 15.6 Hz, 1H), 7.47–7.39 (m, 3H), 7.35–7.32 (m, 1H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.9, 146.9, 137.1, 136.2, 135.6, 129.4, 129.1, 128.7, 128.6, 128.5, 127.8, 127.5, 126.7, 125.8, 124.3, 19.6. MS (ESI): m/z (%) = 246.1 ($[M]^+$, 100). HRMS (ESI): m/z $[M]^+$ calcd for $C_{18}H_{16}N$: 246.1283, found: 246.1290.

3-Bromo-2-[(1E)-2-phenylethenyl]quinoline (**3c**). Pale yellow solid; 80%, 0.25 g; m.p. 103–105 °C (Lit.21 103–105 °C).[21] 1H NMR (400 MHz, $CDCl_3$): δ = 8.37 (s, 1H), 8.08–8.03 (m, 2H), 7.80 (d, *J* = 15.6 Hz, 1H), 7.73–7.67 (m, 4H), 7.50 (t, *J* = 7.3 Hz, 1H), 7.45–7.40 (m, 2H), 7.37–7.32 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.9, 147.0, 139.1, 136.9, 136.6, 130.1, 129.2, 128.9, 128.6, 128.4, 127.7, 126.8, 126.5, 124.8, 118.3. MS (ESI): m/z (%) = 310.0 ($[M]^+$, 51), 312.0($[M]^+$, 49). HRMS (ESI): m/z $[M]^+$ calcd for $C_{17}H_{13}{}^{79}BrN$: 310.0231, found: 310.0239; $C_{17}H_{13}{}^{81}BrN$: 312.0211, found: 312.0218.

4-Methyl-2-[(1E)-2-phenylethenyl]quinoline[15] (**3d**). Pale yellow solid; 61%, 0.15 g; m.p. 122–124 °C (Lit.[15] 122–123 °C). 1H NMR (400 MHz, $CDCl_3$): δ = 8.04 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.56–7.47 (m, 4H), 7.37–7.32 (m, 2H), 7.28–7.24 (m, 3H), 7.22–7.17 (m, 1H), 2.61(s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.0, 148.2, 144.3, 136.8, 134.2, 129.8, 129.5, 129.2, 128.8, 128.5, 127.5, 127.3, 125.9, 123.7, 119.8, 19.2. MS (ESI): m/z (%) = 246.1 ($[M]^+$, 100). HRMS (ESI): m/z $[M]^+$ calcd for $C_{18}H_{16}N$: 246.1283, found: 246.1291.

4-Chloro-2-[(1E)-2-phenylethenyl]quinoline (**3e**). Pale yellow solid; 68%, 0.18 g; m.p. 109–111 °C (Lit.[21] 110–111 °C).[21] 1H NMR (400 MHz, $CDCl_3$): δ = 8.19–8.16 (m, 1H), 8.09 (d, *J* = 8.4 Hz, 1H), 7.77–7.72 (m, 2H), 7.69–7.63 (m, 3H), 7.60–7.56 (m, 1H), 7.43–7.37 (m, 2H), 7.36–7.31 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.1, 149.2, 142.7, 136.2, 135.3, 130.5, 129.5, 128.9, 128.7, 127.9, 127.3,

127.0, 125.3, 124.0, 119.0. MS (ESI): m/z (%) = 266.1 ($[M]^+$, 75), 268.1 ($[M]^+$, 25). HRMS (ESI): m/z $[M]^+$ calcd for $C_{17}H_{13}{}^{35}ClN$: 266.0736, found: 266.0743; $C_{17}H_{13}{}^{37}ClN$: 268.0707, found: 268.0716.

6-Methyl-2-[(1E)-2-phenylethenyl]quinoline (**3f**). Pale yellow solid; 82%, 0.20 g; m.p. 141–143 °C (Lit.[21] 142–144°C).[21] 1H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.4 Hz, 1H), 7.97 (d, *J* = 8.8 Hz, 1H), 7.67–7.62 (m, 4H), 7.55–7.53 (m, 2H), 7.43–7.38 (m, 3H), 7.34–7.31 (m, 1H), 2.49 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.3, 146.2, 136.9, 136.2, 135.7, 133.9, 132.0, 129.2, 128.8, 128.6, 128.5, 127.3, 127.2, 126.4, 118.9, 21.7. MS (ESI): m/z (%) = 246.1 ($[M]^+$, 100). HRMS (ESI): m/z $[M]^+$ calcd for $C_{18}H_{16}N$: 246.1283, found: 246.1290.

6-Chloro-2-[(1E)-2-phenylethenyl]quinoline (**3g**). White solid; 93%, 0.25 g; m.p. 147–149 °C (Lit.[21] 148–149°C).[21] 1H NMR (400 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 8.8 Hz, 1H), 8.03 (d, *J* = 9.0 Hz, 1H), 7.80–7.78 (m, 1H), 7.72–7.61 (m, 5H), 7.43–7.31 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.4, 146.3, 136.6, 135.5, 134.8, 131.7, 130.7, 130.5, 128.9, 128.6, 128.5, 127.8, 127.3, 126.2, 120.0. MS (ESI): m/z (%) = 266.1 ($[M]^+$, 75), 268.1 ($[M]^+$, 25). HRMS (ESI): m/z $[M]^+$ calcd for $C_{17}H_{13}{}^{35}ClN$: 266.0736, found: 266.0744; $C_{17}H_{13}{}^{37}ClN$: 268.0707, found: 268.0715.

6-Bromo-2-[(1E)-2-phenylethenyl]quinoline (**3h**). Pale yellow solid; 89%, 0.28 g; m.p. 164–166 °C (Lit.[21] 164–166°C).[21] 1H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.6 Hz, 1H), 8.05–7.98 (m, 2H), 7.71–7.68 (m, 1H), 7.69–7.61 (m, 4H),7.42–7.31 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.6, 147.0, 136.6, 135.5, 135.0, 133.0, 130.8, 129.5, 128.9, 128.8, 128.5, 128.4, 127.3, 120.5, 119.5. MS (ESI): m/z (%) = 310.0 ($[M]^+$, 51), 312.0 ($[M]^+$, 49). HRMS (ESI): m/z $[M]^+$ calcd for $C_{17}H_{13}{}^{79}BrN$: 310.0231, found: 310.0238; $C_{17}H_{13}{}^{81}BrN$: 312.0211, found: 312.0219.

7-Methyl-2-[(1E)-2-phenylethenyl]quinoline (**3i**). Pale yellow solid; 83%, 0.20 g; m.p. 106–108 °C (Lit.[21] 106–108 °C).[21] 1H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.6 Hz, 1H), 7.89–7.86 (m, 1H), 7.66–7.59 (m, 5H), 7.41–7.35 (m, 3H), 7.32–7.29 (m, 2H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.2, 148.6, 140.0, 136.2, 136.0, 134.1, 129.1, 128.8, 128.5, 128.4, 128.2, 127.3, 127.1, 125.5, 118.0, 21.9. MS (ESI): m/z (%) = 246.1 ($[M]^+$, 100). HRMS (ESI): m/z $[M]^+$ calcd for $C_{18}H_{16}N$: 246.1283, found: 246.1291.

7-Chloro-2-[(1E)-2-phenylethenyl]quinoline (**3j**). Pale yellow solid; 90%, 0.24 g; m.p. 118–120 °C (Lit.[21] 118–119°C).[21] 1H NMR (400 MHz, $CDCl_3$): δ = 7.98–7.97 (m, 2H), 7.82 (d, *J* = 8.2 Hz, 1H), 7.80–7.74 (m, 5H), 7.50–7.47 (m, 1H), 7.40–7.37 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.7, 148.5, 136.3, 136.0, 135.6, 135.0, 128.9, 128.7, 128.6, 128.4, 128.1, 127.4, 127.0, 125.6, 119.3. MS (ESI): m/z (%) = 266.1 ($[M]^+$, 75), 268.1 ($[M]^+$, 25). HRMS (ESI): m/z $[M]^+$ calcd for $C_{17}H_{13}{}^{35}ClN$: 266.0736, found: 266.0742; $C_{17}H_{13}{}^{37}ClN$: 268.0707, found: 268.0717.

7-Bromo-2-[(1E)-2-phenylethenyl]quinoline (**3k**). Pale yellow solid; 87%, 0.27 g; m.p. 127–129 °C (Lit.[14] 127–129°C).[14] 1H NMR (400 MHz, $CDCl_3$): δ = 8.22 (d, *J* = 1.6 Hz, 1H), 8.08 (d, *J* = 8.8 Hz, 1H), 7.79–7.74 (m, 5H), 7.65–7.62 (m, 1H), 7.41–7.32 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.8, 148.7, 136.4, 136.2, 135.2, 131.7, 129.6, 128.9, 128.8, 128.7, 128.4, 127.5, 125.8, 123.8, 119.6. MS (ESI): m/z (%) = 310.0 ($[M]^+$, 51), 312.0 ($[M]^+$, 49). HRMS (ESI): m/z $[M]^+$ calcd for $C_{17}H_{13}{}^{79}BrN$: 310.0231, found: 310.0238; $C_{17}H_{13}{}^{81}BrN$: 312.0211, found: 312.0219.

8-Methyl-2-[(1E)-2-phenylethenyl]quinoline (**3l**). Pale yellow solid; 54%, 0.13 g; m.p. 72–73 °C (Lit.[21] 72°C).[21] 1H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 8.6 Hz, 1H), 7.76 (d, *J* = 16.2 Hz, 1H), 7.68–7.62 (m, 4H), 7.56 (d, *J* = 6.7 Hz, 1H), 7.43–7.31 (m, 5H), 2.76 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.7, 147.2, 137.1, 136.7, 136.3, 133.7, 129.7, 129.4, 128.7, 128.4, 127.2, 127.1, 125.8, 125.3, 119.2, 18.4. MS (ESI): m/z (%) = 246.1 ($[M]^+$, 100). HRMS (ESI): m/z $[M]^+$ calcd for $C_{18}H_{16}N$: 246.1283, found: 246.1289.

8-Chloro-2-[(1E)-2-phenylethenyl]quinoline (**3m**). Pale yellow solid; 59%, 0.16 g; m.p. 88–90 °C (Lit.[16] 88–90 °C).[16] 1H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.3 Hz, 1H), 7.80–7.75 (m, 2H), 7.64–7.68 (m, 4H), 7.47–7.31 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.8, 144.3, 136.6, 136.4, 135.2, 133.1, 129.7, 128.8, 128.7, 128.4, 127.3, 127.1, 126.4, 125.8, 119.6. MS (ESI): m/z (%) = 266.1 ($[M]^+$, 75), 268.1 ($[M]^+$, 25). HRMS (ESI): m/z $[M]^+$ calcd for $C_{17}H_{13}{}^{35}ClN$: 266.0736, found: 266.0745; $C_{17}H_{13}{}^{37}ClN$: 268.0707, found: 268.0715.

2-[(1E)-2-phenylethenyl]quinoxaline (**3n**). Pale yellow solid; 60%, 0.14 g; m.p. 101–103 °C (Lit.[21] 101–103 °C).[21] 1H NMR (400 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.08 (d, *J* = 7.9 Hz, 2H), 7.88 (d, *J* = 16.3 Hz, 1H), 7.75–7.62 (m, 4H), 7.44–7.33 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.4, 144.7, 142.4, 141.6, 136.6, 135.9, 130.0, 129.4, 129.3, 129.2, 129.1, 128.9, 127.4, 125.1. MS (ESI): m/z (%) = 233.1 ($[M]^+$, 100). HRMS (ESI): m/z $[M]^+$ calcd for $C_{18}H_{16}N$: 233.1079, found: 233.1086.

1-[(1E)-2-phenylethenyl]isoquinoline (**3o**). Pale yellow solid; 51%, 0.12 g; m.p. 97–99 °C (Lit.[21] 97–98 °C).[21] 1H NMR (400 MHz, $CDCl_3$): δ = 8.58 (d, *J* = 5.6 Hz, 1H), 8.36 (d, *J* = 8.5 Hz, 1H), 8.01 (d, *J* = 1.2 Hz, 2H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.72–7.66 (m, 3H), 7.65–7.62 (m, 1H), 7.57 (d, *J* = 5.5 Hz, 1H), 7.44–7.41 (m, 2H), 7.35–7.32 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.6, 142.7, 136.9, 136.7, 135.8, 129.9, 128.7, 128.6, 127.4, 127.3, 127.1, 126.7, 124.5, 122.8, 119.7. MS (ESI): m/z (%) = 232.1 ($[M]^+$, 100). HRMS (ESI): m/z $[M]^+$ calcd for $C_{17}H_{14}N$: 232.1126, found: 232.1134.

2-[(1E)-2-(2-Methyl)-phenylethenyl]quinoline (**3p**). Pale yellow solid; 89%, 0.22 g; m.p. 69–71 °C (Lit.[22] 69–71 °C).[21] 1H NMR (400 MHz, $CDCl_3$): δ = 8.30 (d, *J* = 8.4 Hz, 1H), 8.06–8.01 (m, 2H), 7.98–7.92 (m, 2H), 7.83–7.77 (m, 2H), 7.60–7.57 (m, 1H), 7.37 (d, *J* = 16.2 Hz, 1H), 7.27–7.21 (m, 3H), 2.48 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.4,

148.2, 136.9, 136.8, 135.2, 131.9, 131.0, 130.4, 130.3, 129.1, 129.0, 128.2, 127.6, 126.9, 126.7, 126.2, 120.5, 20.0. MS (ESI): m/z (%) = 246.1 ([M]$^+$, 100). HRMS (ESI): m/z [M]$^+$ calcd for $C_{18}H_{16}N$: 246.1283, found: 246.1291.

2-[(1E)-2-(2-Chloro)-phenylethenyl]quinoline (**3q**). Pale yellow solid; 72%, 0.19 g; m.p. 78–80 °C (Lit.22 78–80 °C).[21] 1H NMR (400 MHz, $CDCl_3$): δ = 8.35 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 16.2 Hz, 1H), 8.06–7.98 (m, 2H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.83–7.76 (m, 2H), 7.60–7.53 (m, 3H), 7.44–7.37 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.6, 148.2, 137.3, 134.2, 133.4, 132.0, 130.5, 130.4, 130.3, 129.4, 129.2, 128.3, 128.1, 127.8, 127.7, 126.9, 121.0. MS (ESI): m/z (%) = 266.1 ([M]$^+$, 75), 268.1 ([M]$^+$, 25). HRMS (ESI): m/z [M]$^+$ calcd for $C_{17}H_{13}{}^{35}ClN$: 266.0736, found: 266.0744; $C_{17}H_{13}{}^{37}ClN$: 268.0707, found: 268.0715.

2-[(1E)-2-(3-Methyl)-phenylethenyl]quinoline (**3r**). Pale yellow solid; 76%, 0.19 g; m.p. 68–69 °C (Lit.[22] 68–69 °C).[22] 1H NMR (400 MHz, $CDCl_3$): δ = 8.33 (d, *J* = 8.4 Hz, 1H), 8.10 (d, *J* = 16.2 Hz, 1H), 8.04–7.95 (m, 3H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.81–7.78 (m, 1H), 7.40–7.33 (m, 3H), 7.24–7.16 (m, 2H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.4, 148.2, 138.3, 136.9, 135.6, 132.1, 131.2, 130.5, 130.3, 129.2, 129.0, 128.3, 127.5, 126.7, 126.5, 126.2, 120.7, 21.1. MS (ESI): m/z (%) = 246.1 ([M]$^+$, 100). HRMS (ESI): m/z [M]$^+$ calcd for $C_{18}H_{16}N$: 246.1283, found: 246.1292.

2-[(1E)-2-(3-Fluoro)-phenylethenyl]quinoline (**3s**). Yellow solid; 83%, 0.21 g; m.p. 91–93 °C (Lit.[16] 91–93 °C).[16] 1H NMR (400 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 8.4 Hz, 1H), 8.07–48.0 (m, 1H), 7.72–7.67 (m, 2H), 7.58–7.53 (m, 2H), 7.52–7.46 (m, 1H), 7.41–317 (m, 4H), 7.01 (t, *J* = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.1 (d, *J* = 243 Hz), 155.2, 148.1, 138.8 (d, *J* = 8 Hz), 136.3, 132.9 (d, *J* = 3 Hz), 130.2, 130.0, 129.6, 129.1, 127.4, 127.3, 126.1, 123.1 (d, *J* = 3 Hz), 119.3, 115.2 (d, *J* = 21 Hz), 113.3 (d, *J* = 22 Hz). MS (ESI): m/z (%) = 250.1 ([M]$^+$, 100). HRMS (ESI): m/z [M]$^+$ calcd for $C_{17}H_{13}FN$: 250.1032, found: 250.1039.

2-[(1E)-2-(3-Chloro)-phenylethenyl]quinoline (**3t**). Yellow solid; 87%, 0.23 g; m.p. 90–92 °C (Lit.[21] 90–91 °C).[21] 1H NMR (400 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 8.5 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 7.79–37.7 (m, 2H), 7.64–7.61 (m, 3H), 7.53–7.49 (m, 2H), 7.38 (d, *J* = 16.2 Hz, 1H), 7.34–7.29 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.6, 148.2, 138.4, 136.5, 134.6, 132.8, 130.2, 130.1, 129.8, 129.3, 128.4, 127.5, 127.3, 127.0, 126.4, 125.4, 119.6. MS (ESI): m/z (%) = 266.1 ([M]$^+$, 75), 268.1 ([M]$^+$, 25). HRMS (ESI): m/z [M]$^+$ calcd for $C_{17}H_{13}{}^{35}ClN$: 266.0736, found: 266.0742; $C_{17}H_{13}{}^{37}ClN$: 268.0707, found: 268.0715.

2-[(1E)-2-(4-Methyl)-phenylethenyl]quinoline (**3u**). Yellow solid; 90%, 0.22 g; m.p. 110–112 °C (Lit.[16] 110–112 °C).[16] 1H NMR (400 MHz, $CDCl_3$): δ = 8.08 (m, 2H), 7.77–7.66 (m, 4H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.46 (t, *J* = 7.4 Hz, 1H), 7.38 (d, *J* = 16.2 Hz, 1H), 7.22 (d, *J* = 7.9 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.3, 148.2, 138.6, 136.3, 134.5, 133.6, 129.6, 129.3, 129.0, 127.9, 127.5, 127.2, 127.1, 126.2, 119.1, 21.2. MS (ESI): m/z (%) = 246.1 ([M]$^+$, 100). HRMS (ESI): m/z [M]$^+$ calcd for $C_{18}H_{16}N$: 246.1283, found: 246.1292.

2-[(1E)-2-(4-Fluoro)-phenylethenyl]quinoline (**3v**). Yellow solid; 86%, 0.21 g; m.p. 120–122 °C (Lit.[16] 120–122 °C).[21] 1H NMR (400 MHz, $CDCl_3$): δ = 8.10–8.06 (m, 2H), 7.78 (d, *J* = 8.2 Hz, 1H), 7.74–637 (m, 5H), 7.56–7.49 (m, 1H), 7.32 (d, *J* = 16.2 Hz, 1H), 7.13–77.0 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.0 (d, *J* = 246 Hz), 155.9, 148.3, 136.3, 133.4, 132.8 (d, *J* = 3 Hz), 129.8, 129.2, 128.9, 128.6 (d, *J* = 3 Hz), 127.6, 127.3, 126.4, 119.6, 115.9 (d, *J* = 22 Hz). MS (ESI): m/z (%) = 250.1 ([M]$^+$, 100). HRMS (ESI): m/z [M]$^+$ calcd for $C_{17}H_{13}FN$: 250.1032, found: 250.1040.

2-[(1E)-2-(4-Chloro)-phenylethenyl]quinoline (**3w**). Yellow solid; 80%, 0.21 g; m.p. 141–143 °C (Lit.[16] 141–142 °C).[16] 1H NMR (400 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 8.4 Hz, 2H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.72–7.68 (m, 1H), 7.65–87.5 (m, 2H), 7.55–67.4 (m, 3H), 7.36–17.3 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.7, 148.3, 136.3, 135.1, 134.2, 132.8, 129.8, 129.5, 129.1, 128.9, 128.4, 127.5, 127.4, 126.2, 119.2. MS (ESI): m/z (%) = 266.1 ([M]$^+$, 75), 268.1 ([M]$^+$, 25). HRMS (ESI): m/z [M]$^+$ calcd for $C_{17}H_{13}{}^{35}ClN$: 266.0736, found: 266.0742; $C_{17}H_{13}{}^{37}ClN$: 268.0707, found: 268.0715.

2-[(1E)-2-(2-(Naphthalen-1-yl))vinyl]quinoline (**3x**). Yellow solid; 88%, 0.25 g; m.p. 104–106 °C (Lit.[22] 105–106 °C).[17] 1H NMR (400 MHz, $CDCl_3$): δ = 8.50 (d, *J* = 16.2 Hz, 1H), 8.32 (d, *J* = 8.4 Hz, 1H), 8.12 (d, *J* = 8.4 Hz, 2H), 7.86–7.71 (m, 6H), 7.56–7.45 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.2, 148.3, 136.2, 134.1, 133.7, 131.6, 131.5, 131.3, 129.6, 129.3, 128.8, 128.6, 127.5, 127.4, 126.3, 126.2, 125.8, 125.7, 124.1, 123.8, 119.5. MS (ESI): m/z (%) = 282.1 ([M]$^+$, 100). HRMS (ESI): m/z [M]$^+$ calcd for $C_{21}H_{16}N$: 282.1283, found: 282.1292.

2-[(1E)-2-(2-(Thiophen-2-yl))vinyl]quinoline (**3y**). Yellow solid; 73%, 0.17 g; m.p. 89–91 °C (Lit.[17] 89–91 °C).[17] 1H NMR (400 MHz, $CDCl_3$): δ = 8.07–8.00 (m, 2H), 7.84 (d, *J* = 16.2 Hz, 1H), 7.77–7.72 (m, 2H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.50–7.47 (m, 1H), 7.30–7.19 (m, 3H), 7.05–7.02 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.6, 155.5, 148.2, 142.1, 136.2, 129.8, 129.1, 128.2, 128.0, 127.7, 127.4, 127.2, 126.0, 125.9, 119.2. MS (ESI): m/z (%) = 238.1 ([M]$^+$, 100). HRMS (ESI): m/z [M]$^+$ calcd for $C_{15}H_{12}NS$: 238.0690, found: 238.0697.

2-[(1E)-2-(2-Cyclohexylvinyl)]quinoline (**3z**). Pale yellow oil; 30%, 0.07 g.[17] 1H NMR (400 MHz, $CDCl_3$): δ = 8.07–8.02 (m, 2H), 7.76–7.72 (m, 1H), 7.68–7.63 (m, 1H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.47–7.43 (m, 1H), 6.80–6.76 (m, 1H), 6.66 (d, *J* = 16.2 Hz, 1H), 2.30–2.15 (m, 1H), 1.77–1.64 (m, 4H), 1.33–1.19 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.6, 148.2, 143.5, 136.2, 129.4, 129.1, 128.5, 127.4, 127.2, 125.8, 118.6, 41.0, 32.3, 26.1, 26.0. MS (ESI): m/z (%) = 238.2 ([M]$^+$, 100). HRMS (ESI): m/z [M]$^+$ calcd for $C_{17}H_{20}N$: 238.1596, found: 238.1604.

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ORCID iD

Xue Li https://orcid.org/0000-0002-9499-2033

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