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A Microwave-Assisted Domino Benzannulation Reaction towards Functionalized Naphthalenes, Quinolines, and Isoquinolines

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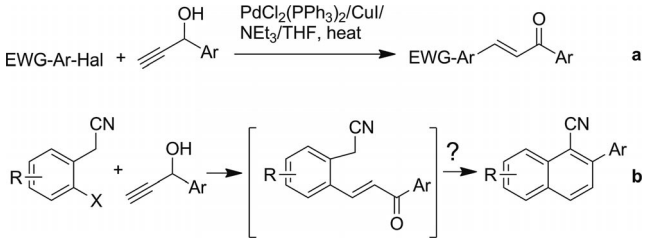
Keywords: Synthetic methods / Domino reactions / Cross-coupling / Isomerization / Nitrogen heterocycles

An efficient palladium/copper-catalyzed domino reaction was developed to yield functionalized naphthalenes, quinolines, and isoquinolines. The reactions of various substituted 1-phenylprop-2-yn-1-ols containing electron-donating (EDG) and electron-withdrawing (EWG) groups and 1-heteroarylprop-2-yn-1-ols worked well with this procedure. Both electron-rich and -deficient aryl halides were satisfactory substrates for this reaction. This domino benzannulation process involves a Sonogashira cross-coupling reaction, followed by isomerization to a chalcone, and finally an intramolecular condensation reaction.

Introduction

Naphthalenes, quinolines, and isoquinolines are important scaffolds, which are widely used in biological and medicinal chemistry[1] as well as synthetic chemistry.[2] Substituted naphthalene and its aza analogues are attractive as NK1 receptor antagonists,[3] antibacterial agents,[4] 17β-HSD1/2 inhibitors,[5] antitumor agents,[6] antimalarials,[7] antitumor antibiotics,[8] Rho-kinase inhibitors,[9] and as agrochemicals. Furthermore, they are interesting synthetic blocks in organic reactions. Because of their prevalence in active compounds, a number of synthetic methods have been developed to construct these structural units.[1d,10] Among these methods, transition-metal-catalyzed cross-coupling reactions have been the most powerful tools, using the readily available naphthalene, quinoline, and isoquinoline building blocks.[11] However, the development of new synthetic strategies, which are effective and versatile, remains an ever-present challenge.

To the best of our knowledge, the benzannulation reaction applied to the syntheses of aryl-substituted naphthalenes and quinolines has not been adequately explored.[12] In 2000, Müller et al. reported on a coupling–isomerization reaction (CIR) between electron-deficient aryl halides and arylpropargyl alcohols to furnish 1,3-diarylpropenones (see Scheme 1, reaction **a**).[13] This route proceeded through a Sonogashira coupling reaction followed by a base-catalyzed isomerization from the propargyl alcohol to the enone.



Scheme 1. (a) Coupling–isomerization reaction (CIR) between aryl halides and arylpropargyl alcohols. (b) This work.

Subsequently, a series of pharmaceutically relevant heterocycles, such as pyrazolines,[13] pyrimidines,[14] 1,5-benzoheteroazepines,[15] pyrroles,[16] pyridines,[17] tetrahydroquinolines,[17] annelated 2-aminopyridines,[18] and 2-arylquinolines,[7a] have been synthesized by using this palladium/copper-catalyzed domino cross-coupling–isomerization sequence. We predicted that *o*-halo-substituted phenylacetonitriles would react with arylpropargyl alcohols followed by a condensation reaction to furnish substituted naphthalenes through a one-pot cascade reaction sequence (see Scheme 1, reaction **b**). Therefore, we set out to develop a new and straightforward domino reaction with 2-(2-iodophenyl)-acetonitrile and 1-phenylprop-2-yn-1-ol as the starting materials to prepare the naphthalenes in a one-pot synthesis.

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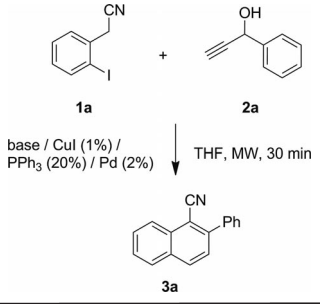
Results and Discussion

In 2006, Müller reported on a microwave-accelerated coupling–isomerization reaction (MACIR) to yield enones rapidly.[18] We conducted the reaction in a similar manner to Müller's approach.

As anticipated, this protocol yielded the desired compound 2-phenyl-1-naphthonitrile in 84% yield by using $Pd(PPh_3)_2Cl_2$ as a catalyst (see Table 1, Entry 1). Other Pd catalysts were less effective (see Table 1, Entries 2, 3, 4, and 5), resulting in lower yields. In addition, the yield decreased greatly by reducing the amount of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) to 1 equiv. (see Table 1, Entry 6). Increasing the amount of DBU to 3 equiv. also lowered the yield to 70% (see Table 1, Entry 7). When the reaction was conducted at 120 and 80 °C, similar results were obtained (see Table 1, Entries 9 and 10). Among the screened bases, 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (MTBD) was as effective as DBU (see Table 1, Entry 12). However, no product was obtained using Et_3N or the inorganic base K_2CO_3 (see Table 1, Entries 13 and 14). DBU was eventually selected as the base for our approach, as it is easily available and much cheaper than MTBD. Different solvents were further screened, and toluene afforded better results than dioxane and CH_3CN. When the reaction was con-

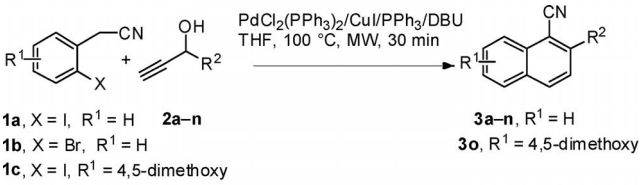
Table 1. Optimization of reaction conditions.[a]



Entry	Pd catalyst	Base [equiv.]	Solvent	Temp. [°C]	% Yield[b]
1	$Pd(PPh_3)_2Cl_2$	DBU (2)	THF	100	84
2	$Pd(dppf)Cl_2$	DBU (2)	THF	100	66
3	$Pd_2(dba)_3$	DBU (2)	THF	100	67
4	$Pd(CH_3CN)_2Cl_2$	DBU (2)	THF	100	69
5	$Pd(PPh_3)_4$	DBU (2)	THF	100	69
6	$Pd(PPh_3)_2Cl_2$	DBU (1)	THF	100	36
7	$Pd(PPh_3)_2Cl_2$	DBU (3)	THF	100	70
8[c]	$Pd(PPh_3)_2Cl_2$	DBU (2)	THF	100	52
9	$Pd(PPh_3)_2Cl_2$	DBU (2)	THF	120	68
10	$Pd(PPh_3)_2Cl_2$	DBU (2)	THF	80	71
11	$Pd(PPh_3)_2Cl_2$	DBN (2)	THF	100	60
12	$Pd(PPh_3)_2Cl_2$	MTBD (2)	THF	100	85
13	$Pd(PPh_3)_2Cl_2$	Et_3N (2)	THF	100	0
14	$Pd(PPh_3)_2Cl_2$	K_2CO_3 (2)	THF	100	0
15	$Pd(PPh_3)_2Cl_2$	DBU (2)	toluene	100	83
16	$Pd(PPh_3)_2Cl_2$	DBU (2)	dioxane	100	78
17	$Pd(PPh_3)_2Cl_2$	DBU (2)	CH_3CN	100	76
18[d]	$Pd(PPh_3)_2Cl_2$	DBU (2)	THF	100	75

[a] Reagent and conditions: **1a** (122 mg, 0.5 mmol), **2a** (66 mg, 0.5 mmol), solvent (3 mL), MW (microwave), 30 min. [b] Isolated yield. [c] No PPh_3 was added to reaction mixture. [d] The reaction was heated in an oil bath for 3 h.

Table 2. Domino reaction of 2-(2-halophenyl)acetonitrile with substituted 1-arylprop-2-yn-1-ols.[a]



1a, X = I, R^1 = H **2a–n**
1b, X = Br, R^1 = H
1c, X = I, R^1 = 4,5-dimethoxy

3a–n, R^1 = H
3o, R^1 = 4,5-dimethoxy

Entry	1	2	Product	Yield[b] (%)
1	**1a**	**2a**	**3a**	84
2[c]	**1a**	**2b**	**3b**	68
3	**1a**	**2c**	**3c**	88
4[c]	**1a**	**2d**	**3d**	76
5[c]	**1a**	**2e**	**3e**	77
6	**1a**	**2f**	**3f**	83
7[c]	**1a**	**2g**	**3g**	70
8	**1a**	**2h**	**3h**	73
9	**1a**	**2i**	**3i**	55
10	**1a**	**2j**	**3j**	56
11	**1a**	**2k**	**3k**	67
12	**1a**	**2l**	**3l**	67
13	**1a**	**2m**	**3m**	94
14	**1a**	**2n**	**3n**	90
15	**1c**	**2c**	**3o**	46
16	**1b**	**2a**	**3a**	72

[a] Reagents and conditions: **1a** (122 mg, 0.5 mmol), **2a**–**2n** (0.5 mmol), $Pd(PPh_3)_2Cl_2$ (7 mg, 0.01 mmol), CuI (1 mg, 0.005 mmol), PPh_3 (26 mg, 0.1 mmol), solvent (3 mL), MW, 30 min. [b] Isolated yield. [c] Reaction time was 3 h.

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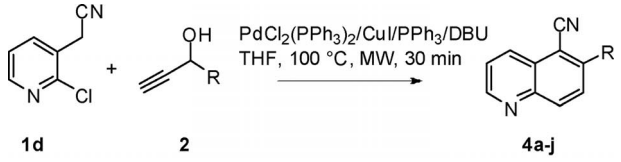
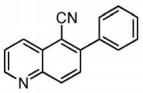
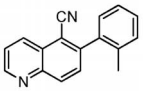
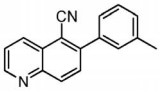
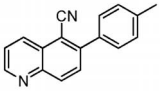
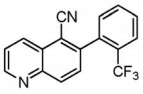
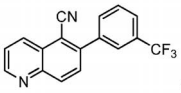
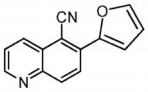
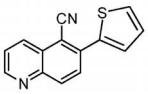
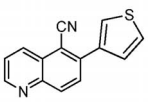
ducted under conventional heating in THF (tetrahydrofuran) for 3 h, **3a** was obtained in 75% yield (see Table 1, Entry 18).

Using the optimized reaction conditions [2 mol-% equiv. $Pd(PPh_3)_2Cl_2$, 1 mol-% equiv. CuI, 20 mol-% equiv. PPh_3, THF, 100 °C], we next explored the scope and generality of this palladium/copper-catalyzed domino cross-coupling isomerization–condensation reaction.

As shown in Table 2, various 1-arylprop-2-yn-1-ols were tested in this method. The electronic nature of the propargyl alcohols plays an important role in this transformation. When propargyl alcohols were substituted by aryl groups with electron-donating groups in the *meta* position, very good yields were obtained (see Table 2, Entries 3 and 6). However, propargyl alcohols substituted by aryl groups with electron-donating groups in the *ortho* and *para* positions needed prolonged reaction times to achieve good yields. This is presumably because the electron-donating groups did not favor the isomerization step in this domino reaction sequence. Electron-withdrawing group substitutents (such as CF_3) at the *meta* and *para* positions of the aryl group gave moderate yields (see Table 2, Entries 9 and 10), whereas substitution at *ortho* position afforded a good yield (see Table 2, Entry 8). With the 1-heteroarylprop-2-yn-1-ols, excellent yields were obtained using 1-(thiophen-3-yl)prop-2-yn-1-ol and 1-(pyridin-3-yl)prop-2-yn-1-ol (see Table 2, Entries 13 and 14). However, only moderate yields of the products were obtained with 1-(furan-2-yl)prop-2-yn-1-ol and 1-(thiophen-2-yl)prop-2-yn-1-ol (see Table 2, Entries 11 and 12). Subsequently, the reaction was performed under the standard conditions using the less active 2-(2-bromophenyl)acetonitrile with 1-phenylprop-2-yn-1-ol, resulting in 72% yield of the product (see Table 2, Entry 16), which was a lower yield than that of the same reaction with 2-(2-iodophenyl)acetonitrile. Furthermore, under these reaction conditions, the electron-rich 2-(2-iodo-4,5-dimethoxyphenyl)acetonitrile also gave an acceptable yield (see Table 2, Entry 15). Using this CIR procedure, the reactions went smoothly with the electron-deficient 2-(2-chloropyridin-3-yl)acetonitrile and various 1-arylprop-2-yn-1-ols as shown in Table 3. Both electron-rich and -deficient aryl alcohols exhibited similar reaction activity as those shown in Table 2.

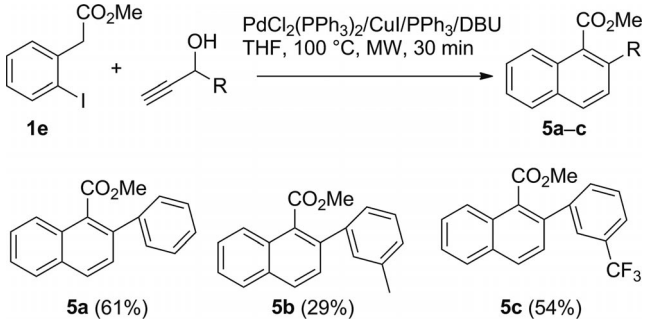
Table 3. Reaction of 2-(2-chloropyridin-3-yl)acetonitrile and substituted 1-arylprop-2-yn-1-ols.[a]



Entry	2	Product	Yield[b] (%)
1	**2a**	 **4a**	66
2[c]	**2b**	 **4b**	68
3	**2c**	 **4c**	84
4[c]	**2d**	 **4d**	73
5	**2h**	 **4e**	60
6	**2i**	 **4f**	69
7	**2k**	 **4g**	89
8	**2l**	 **4h**	76
9	**2m**	 **4i**	73

[a] Reagents and conditions: **1d** (76 mg, 0.5 mmol), **2** (0.5 mmol), $Pd(PPh_3)_2Cl_2$ (7 mg, 0.01 mmol), CuI (1 mg, 0.005 mmol), PPh_3 (26 mg, 0.1 mmol), solvent (3 mL), MW, 30 min. [b] Isolated yield. [c] Reaction time was 3 h.

Additionally, methyl 2-(2-iodophenyl)acetate (**1e**) was further explored using this method (see Scheme 2). With the exception of **5c**, this protocol resulted in a decreased yield of the products compared to that of **1a**. This could be explained by the fact that the electron-withdrawing ability of the ester group is weaker than that of nitrile group, which would make the condensation step slower and, therefore, result in lower yields.



Scheme 2. Reaction of methyl 2-(2-iodophenyl)acetate with substituted 1-arylprop-2-yn-1-ols.

Furthermore, the electron-deficient heteroaryl halides **1f** and **1g** were tested under this protocol (Scheme 3). 6-Phenylisoquinoline (**5d**) and 7-phenylquinoline (**5e**) were ob-

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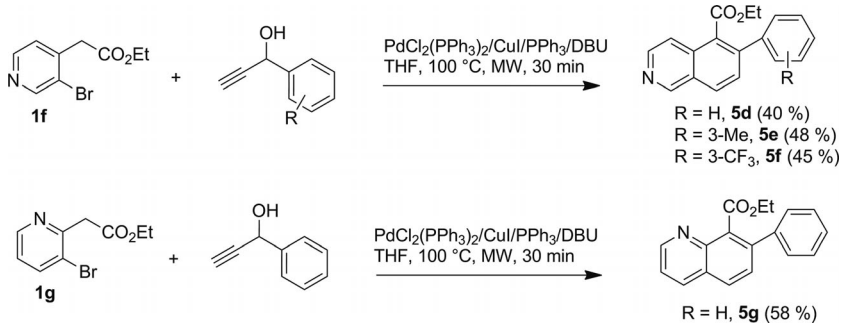

Scheme 3. Reaction of electron-deficient heteroaryl halides with substituted 1-phenylprop-2-yn-1-ol.

tained with acceptable yields. These results suggest that this useful methodology could easily be used to achieve structural diversity.

Conclusions

By using a facile one-pot procedure under mild conditions, we have developed a versatile palladium/copper-catalyzed domino cross-coupling–isomerization–condensation sequence to access functionalized naphthalenes, quinolones, and isoquinolines. The reaction went smoothly with both electron-rich and -deficient aryl halides. This protocol has a broad group tolerance with propargyl alcohols. Further studies directed at taking advantage of this methodology with other heterocyclic syntheses are currently under progress.

Experimental Section

General Information: All of the reagents, with the exception of **1a**, were commercially available products that were used without further purification. Analytical thin-layer chromatography was performed using HSGF 254 (0.15–0.2 mm thickness, Yantai Huiyou Company, China). Column chromatography was carried out on silica gel (200–300 mesh). ^{1}H and ^{13}C NMR spectroscopic data were recorded with Varian Mercury-400 and Varian Mercury-500 spectrometers. Tetramethylsilane was used as an internal standard. The chemical shifts were reported in parts per million (ppm, δ). Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), mutiplet (m), and broad (br.). Low and high resolution mass spectra were recorded with a Finnigan/MAT-95 spectrometer. Melting points were measured with a Büchi 510 melting point apparatus. The microwave reaction was performed with a CEM microwave reactor.

Ethyl 2-(3-Bromopyridin-4-yl)acetate (1f) and Ethyl 2-(3-Bromopyridin-2-yl)acetate (1g): Compound **1f** and **1g** were prepared according to the procedure described in ref.[19]

General Procedure for the Synthesis of Substituted Naphthalenes, Quinolines, and Isoquinolines: To the mixture of aryl halides (0.5 mmol), arylpropargyl alcohols (0.5 mmol), $Pd(PPh_3)_2Cl_2$ (7 mg, 0.01 mmol), CuI (1 mg, 0.005 mmol), and PPh_3 (26 mg, 0.1 mmol) in anhydrous THF (3 mL) was added DBU (0.15 mL) under nitrogen. Then, the reaction was performed in a microwave reactor at 100 °C. When the reaction was complete, the solvent was removed in vacuo, and the crude product was eluted on silica gel with petroleum ether/ethyl acetate to give the corresponding products.

2-Phenyl-1-naphthonitrile (3a): Light yellow powder; m.p. 120–121 °C; ref.[20] m.p. 119 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.36 (d, J = 8.0 Hz, 1 H), 8.11 (d, J = 8.5 Hz, 1 H), 7.95 (d, J = 8.1 Hz, 1 H), 7.74 (td, J = 8.4, 1.3 Hz, 1 H), 7.70–7.60 (m, 4 H), 7.57–7.49 (m, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 145.89, 138.64, 133.12, 132.95 (CH), 131.81, 129.21 (CH), 128.96 (CH), 128.90 (CH), 128.79 (CH), 128.46 (CH), 127.38 (CH), 127.18 (CH), 125.68 (CH), 117.56, 108.08 ppm.

2-(*o*-Tolyl)-1-naphthonitrile (3b): Light yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.33 (d, J = 8.3 Hz, 1 H), 8.10 (d, J = 8.4 Hz, 1 H), 7.98 (d, J = 8.2 Hz, 1 H), 7.75 (td, J = 8.1, 1.0 Hz, 1 H), 7.66 (td, J = 8.1, 1.0 Hz, 1 H), 7.47 (d, J = 8.4 Hz, 1 H), 7.41–7.30 (m, 4 H), 2.24 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 146.46, 138.52, 135.77, 132.72, 132.51 (CH), 131.82, 130.53 (CH), 129.56 (CH), 128.90 (CH), 128.53 (CH), 127.53 (CH), 127.39 (CH), 125.96 (CH), 125.50 (CH), 116.96, 109.75, 20.02 (CH_3) ppm. MS (EI): m/z (%) = 243 (65) $[M]^+$, 242 (100). HRMS (EI): calcd. for $C_{18}H_{13}N$ 243.1048; found 243.1048.

2-(*m*-Tolyl)-1-naphthonitrile (3c): White powder; m.p. 89–90 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.36 (d, J = 8.4 Hz, 1 H), 8.10 (d, J = 8.6 Hz, 1 H), 7.95 (d, J = 8.1 Hz, 1 H), 7.73 (td, J = 8.3, 1.2 Hz, 1 H), 7.66–7.59 (m, 2 H), 7.52–7.47 (m, 2 H), 7.43 (t, J = 8.0 Hz, 1 H), 7.31 (d, J = 8.0 Hz 1 H), 2.47 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 146.07, 138.62, 138.48, 133.12, 132.85 (CH), 131.78, 129.86 (CH), 129.65 (CH), 128.91 (CH), 128.68 (CH), 128.45 (CH), 127.30 (CH), 127.22 (CH), 126.32 (CH), 125.66 (CH), 117.58, 108.02, 21.52 (CH_3) ppm. MS (EI): m/z (%) = 243 (65) $[M]^+$, 242 (100). HRMS (EI): calcd. for $C_{18}H_{13}N$ 243.1048; found 243.1056.

2-(*p*-Tolyl)-1-naphthonitrile (3d): White crystalline solid; m.p. 151–152 °C; ref.[21] m.p. 147–150 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.34 (d, J = 8.5 Hz, 1 H), 8.08 (d, J = 8.6 Hz, 1 H), 7.93 (d, J = 8.2 Hz, 1 H), 7.72 (t, J = 7.6 Hz, 1 H), 7.63–7.57 (m, 4 H), 7.35 (d, J = 7.9 Hz, 2 H), 2.45 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 145.95, 138.96, 135.75, 133.16, 132.88 (CH), 131.71, 129.52 (2 CH), 129.09 (2 CH), 128.88 (CH), 128.44 (CH), 127.24 (CH), 127.20 (CH), 125.62 (CH), 117.74, 107.86, 21.34 (CH_3) ppm.

2-(2-Methoxyphenyl)-1-naphthonitrile (3e): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33 (dd, J = 8.1, 1.0 Hz, 1 H), 8.08 (d, J = 8.5 Hz, 1 H), 7.94 (d, J = 8.2 Hz, 1 H), 7.71 (td, J = 7.6, 1.3 Hz, 1 H), 7.62 (td, J = 7.5, 1.2 Hz, 1 H), 7.57 (d, J = 8.5 Hz, 1 H), 7.46 (ddd, J = 9.2, 7.8, 1.6 Hz, 1 H), 7.39 (dd, J = 7.5, 1.5 Hz, 1 H), 7.11–7.06 (m, 2 H), 3.85 (s, 3 H) ppm. ^{13}C NMR (125 MHz,

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$CDCl_3$): δ = 156.58, 143.14, 132.83, 132.21 (CH), 131.84, 131.20 (CH), 130.51 (CH), 128.58 (CH), 128.40 (CH), 128.19 (CH), 127.66, 127.20 (CH), 125.55 (CH), 120.84 (CH), 117.39, 111.42 (CH), 110.07, 55.54 (CH_3) ppm. MS (EI): *m*/*z* (%) = 259 (100) $[M]^+$. HRMS (EI): calcd. for $C_{18}H_{13}NO$ 259.0997; found 259.0990.

2-(3-Methoxyphenyl)-1-naphthonitrile (3f): White powder; m.p. 99–100 °C; ref.[22] m.p. 97–98 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.36 (d, *J* = 8.4 Hz, 1 H), 8.10 (d, *J* = 8.6 Hz, 1 H), 7.95 (d, *J* = 8.1 Hz, 1 H), 7.73 (dd, *J* = 11.2, 4.1 Hz, 1 H), 7.63 (t, *J* = 7.9 Hz, 2 H), 7.45 (t, *J* = 7.9 Hz, 1 H), 7.27–7.20 (m, 2 H), 7.03 (dd, *J* = 8.3, 2.5 Hz, 1 H), 3.90 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.71, 145.72, 139.94, 133.09, 132.92, 131.87, 129.86, 128.97, 128.46, 127.40, 127.10, 125.69, 121.61, 117.49, 114.72, 114.66, 108.10, 55.45 ppm. MS (EI): *m*/*z* (%) = 259 (100) $[M]^+$.

2-(4-Methoxyphenyl)-1-naphthonitrile (3g): White powder; m.p. 134–135 °C; ref.[21] m.p. 133.5–136.5 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.34 (d, *J* = 8.4 Hz, 1 H), 8.07 (d, *J* = 8.6 Hz, 1 H), 7.93 (d, *J* = 8.3 Hz, 1 H), 7.71 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1 H), 7.66–7.57 (m, 4 H), 7.07 (dt, *J* = 8.9, 2.1 Hz, 2 H), 3.90 (d, *J* = 4.2 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.24, 145.61, 133.22, 132.87 (CH), 131.58, 130.94, 130.52 (2 C, CH), 128.88 (CH), 128.42 (CH), 127.18 (CH), 127.14 (CH), 125.57 (CH), 117.87, 114.28 (2 C, CH), 107.55, 55.41 (CH_3) ppm. MS (EI): *m*/*z* (%) = 259 (100) $[M]^+$.

2-[2-(Trifluoromethyl)phenyl]-1-naphthonitrile (3h): White powder; m.p. 97–99 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.30 (d, *J* = 8.4 Hz, 1 H), 8.08 (d, *J* = 8.5 Hz, 1 H), 7.98 (d, *J* = 8.2 Hz, 1 H), 7.85 (d, *J* = 8.2 Hz, 1 H), 7.75 (td, *J* = 7.8, 1.2 Hz, 1 H), 7.70–7.76 (m, 2 H), 7.61 (t, *J* = 7.7 Hz, 1 H), 7.49 (d, *J* = 8.5 Hz, 1 H), 7.44 (d, *J* = 7.5 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.71, 139.82, 137.44, 132.28, 132.15, 131.94 (CH), 131.78 (CH), 131.59 (CH), 129.90, 129.09 (CH), 129.06 (CH), 128.68, 128.57 (CH), 127.78 (CH), 127.13 (CH), 126.46 (q, *J* = 3.8 Hz, CH-C-CF_3), 125.58 (CH), 123.78 (d, *J* = 274.5 Hz, CF_3), 122.69, 116.42, 110.24 ppm. MS (EI): *m*/*z* (%) = 297 (100) $[M]^+$. HRMS (EI): calcd. for $C_{18}H_{11}F_3N$ 297.0765; found 297.0773.

2-[3-(Trifluoromethyl)phenyl]-1-naphthonitrile (3i): Light yellow powder; m.p. 92–94 °C; ref.[22] m.p. 94–95 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.36 (dd, *J* = 8.4, 0.8 Hz, 1 H), 8.15 (d, *J* = 8.5 Hz, 1 H), 7.97 (d, *J* = 8.2 Hz, 1 H), 7.92–7.86 (m, 2 H), 7.79–7.74 (m, 2 H), 7.70–7.64 (m, 2 H), 7.60 (d, *J* = 8.5 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.13, 139.38, 133.31 (CH), 133.00, 132.59 (CH), 132.09, 131.44, 131.18, 129.35 (CH), 129.28 (CH), 128.54 (CH), 127.84 (CH), 126.72 (CH), 126.03 (q, *J* = 3.7 Hz, CH), 125.74 (CH), 125.63 (q, *J* = 3.7 Hz, CH), 123.92 (d, *J* = 273.0 Hz, CF_3) 117.10, 108.52 ppm. MS (EI): *m*/*z* (%) = 297 (100) $[M]^+$.

2-[4-(Trifluoromethyl)phenyl]-1-naphthonitrile (3j): White crystalline solid; m.p. 100–101 °C; ref.[22] m.p. 91–93 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.37 (d, *J* = 8.4 Hz, 1 H), 8.16 (d, *J* = 8.5 Hz, 1 H), 7.98 (d, *J* = 8.1 Hz, 1 H), 7.83–7.78 (m, 4 H), 7.77 (t, *J* = 7.5 Hz, 1 H), 7.68 (t, *J* = 7.5 Hz, 1 H), 7.60 (d, *J* = 8.5 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 145.57, 143.54, 134.68 (CH), 134.38, 133.52, 132.32 (d, *J* = 33 Hz, C-C-F_3), 131.02 (2 CH), 130.69 (CH), 129.93 (CH), 129.26 (CH), 128.06 (CH), 127.23–127.01 (m, 3 CH), 125.40 (d, *J* = 271 Hz, CF_3), 118.52, 109.86 ppm. MS (EI): *m*/*z* (%) = 297 (100) $[M]^+$.

2-(Furan-2-yl)-1-naphthonitrile (3k): Light brown powder; m.p. 154–155 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.29 (dd, *J* = 8.3, 3.5 Hz, 1 H), 8.05–7.95 (m, 2 H), 7.86 (dd, *J* = 8.0, 3.3 Hz, 1 H), 7.68 (ddd, *J* = 8.5, 5.4, 2.3 Hz, 1 H), 7.63 (d, *J* = 1.6 Hz, 1 H), 7.56 (ddd, *J* = 8.9, 7.1, 2.2 Hz, 1 H), 7.52–7.46 (m, 1 H), 6.62 (dd, *J* = 3.5, 1.8 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.24, 143.82 (CH), 133.31, 133.21, 133.05 (CH), 131.60, 129.02 (CH), 128.42 (CH), 127.27 (CH), 125.51 (CH), 122.95 (CH), 117.86, 112.59 (CH), 111.82 (CH), 102.97 ppm. MS (EI): *m*/*z* (%) = 219 (100) $[M]^+$. HRMS (EI): calcd. for $C_{15}H_9NO$ 219.0684; found 219.0684.

2-(Thiophen-2-yl)-1-naphthonitrile (3l): White powder; m.p. 87–88 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.33 (d, *J* = 8.4 Hz, 1 H), 8.04 (d, *J* = 8.5 Hz, 1 H), 7.90 (dd, *J* = 8.1, 0.5 Hz, 1 H), 7.82 (dd, *J* = 4.6, 1.2 Hz, 1 H), 7.74–7.69 (m, 2 H), 7.60 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1 H), 7.52 (dd, *J* = 4.6, 1.2 Hz, 1 H), 7.22 (q, *J* = 4.7 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.06, 137.81, 133.38, 133.12 (CH), 131.77, 129.18 (CH), 128.51 (CH), 128.45 (CH), 128.39 (CH), 128.11 (CH), 127.45 (CH), 126.78 (CH), 125.72 (CH), 117.80, 106.37 ppm. MS (EI): *m*/*z* (%) = 235 (100) $[M]^+$. HRMS (EI): calcd. for $C_{15}H_9NS$ 235.0456; found 235.0451.

2-(Thiophen-3-yl)-1-naphthonitrile (3m): White powder; m.p. 97–98 °C. ^1H NMR (400 MHz, $[D_6]$DMSO): δ = 8.31 (d, *J* = 8.6 Hz, 1 H), 8.16 (d, *J* = 8.4 Hz, 1 H), 8.11 (d, *J* = 8.5 Hz, 2 H), 7.84–7.76 (m, 3 H), 7.69 (t, *J* = 7.3 Hz, 1 H), 7.63 (dd, *J* = 5.0, 0.9 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $[D_6]$DMSO): δ = 140.14, 138.91, 134.04 (CH), 132.81, 131.85, 130.00 (CH), 129.32 (CH), 128.50 (CH), 128.00 (CH), 127.89 (CH), 127.44 (CH), 127.05 (CH), 125.01 (CH), 117.98, 106.08 ppm. MS (EI): *m*/*z* (%) = 235 (100) $[M]^+$. HRMS (EI): calcd. for $C_{15}H_9NS$ 235.0456; found 235.0454.

2-(Pyridin-3-yl)-1-naphthonitrile (3n): White powder; m.p. 157–158 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.90 (s, 1 H), 8.75 (s, 1 H), 8.35 (dd, *J* = 8.4, 0.8 Hz, 1 H), 8.16 (d, *J* = 8.5 Hz, 1 H), 8.06 (dt, *J* = 8.1, 1.6 Hz, 1 H), 7.98 (d, *J* = 8.2 Hz, 1 H), 7.76 (ddd, *J* = 8.2, 7.0, 1.3 Hz, 1 H), 7.67 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1 H), 7.60 (d, *J* = 8.5 Hz, 1 H), 7.49 (dd, *J* = 7.7, 4.9 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 149.93 (CH), 149.67 (CH), 142.10, 136.50 (CH), 134.60, 133.41 (CH), 133.05, 132.13, 129.31 (CH), 128.56 (CH), 127.89 (CH), 126.61 (CH), 125.68 (CH), 123.53 (CH), 117.07, 108.73 ppm. MS (EI): *m*/*z* (%) = 230 (100) $[M]^+$. HRMS (EI): calcd. for $C_{16}H_{10}N_2$ 230.0844; found 230.0850.

6,7-Dimethoxy-2-(*m*-tolyl)-1-naphthonitrile (3o): White powder; m.p. 218–220 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 8.3 Hz, 1 H), 7.57 (s, 1 H), 7.47–7.38 (m, 4 H), 7.29–7.26 (m, 1 H), 7.18 (s, 1 H), 4.09 (s, 3 H), 4.04 (s, 3 H), 2.46 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 151.88, 150.31, 143.92, 138.91, 138.29, 130.96 (CH), 129.76 (CH), 129.65, 129.26 (CH), 128.51 (CH), 127.66, 126.18 (CH), 125.36 (CH), 118.06, 106.55 (CH), 106.20, 104.17 (CH), 56.21 (CH_3), 56.03 (CH_3), 21.47 (CH_3) ppm. MS (EI): *m*/*z* (%) = 303 (100) $[M]^+$. HRMS (EI): calcd. for $C_{20}H_7N_2O_2$ 303.1259; found 303.1259.

6-Phenylquinoline-5-carbonitrile (4a): White powder; m.p. 140–142 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.04 (dd, *J* = 4.2, 1.6 Hz, 1 H), 8.65 (ddd, *J* = 8.5, 1.6, 0.9 Hz, 1 H), 8.37 (dd, *J* = 8.8, 0.8 Hz, 1 H), 7.86 (d, *J* = 8.8 Hz, 1 H), 7.71–7.67 (m, 2 H), 7.65 (dd, *J* = 8.5, 4.2 Hz, 1 H), 7.58–7.50 (m, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 151.64 (CH), 146.62, 146.39, 137.84, 134.68 (CH), 133.84 (CH), 130.90 (CH), 129.31 (CH), 129.15 (2 CH), 128.96 (2 CH), 128.66, 123.53 (CH), 116.55, 108.08 ppm. MS (EI): *m*/*z* (%) = 230 (100) $[M]^+$. HRMS (EI): calcd. for $C_{16}H_{10}N_2$ 230.0844; found 230.0842.

6-(*o*-Tolyl)quinoline-5-carbonitrile (4b): White powder; m.p. 134–135 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.06 (dd, *J* = 4.2, 1.6 Hz, 1 H), 8.61 (d, *J* = 8.5 Hz, 1 H), 8.36 (d, *J* = 8.7 Hz, 1 H), 7.71 (d, *J* = 8.7 Hz, 1 H), 7.65 (dd, *J* = 8.5, 4.2 Hz, 1 H), 7.43–7.30 (m, 4 H), 2.23 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 151.65

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(CH), 146.98, 146.52, 137.66, 135.61, 134.15 (CH), 133.60 (CH), 131.23 (CH), 130.61 (CH), 129.44 (CH), 129.16 (CH), 128.19, 126.03 (CH), 123.42 (CH), 115.90, 109.77, 19.97 (CH_3) ppm. MS (EI): *m*/*z* (%) = 244 (100) $[M]^+$. HRMS (EI): calcd. for $C_{17}H_{12}N_2$ 244.1000; found 244.0998.

6-(*m*-Tolyl)quinoline-5-carbonitrile (4c): Yellowish powder; m.p. 118–119 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.03 (dd, *J* = 4.2, 1.6 Hz, 1 H), 8.64 (ddd, *J* = 8.5, 1.6, 0.9 Hz, 1 H), 8.35 (dd, *J* = 8.8, 0.8 Hz, 1 H), 7.85 (d, *J* = 8.8 Hz, 1 H), 7.64 (dd, *J* = 8.5, 4.2 Hz, 1 H), 7.51–7.42 (m, 3 H), 7.32 (d, *J* = 7.6 Hz, 1 H), 2.47 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 151.57 (CH), 146.61, 146.57, 138.71, 137.82, 134.60 (CH), 133.80 (CH), 130.94 (CH), 130.05 (CH), 129.80 (CH), 128.85 (CH), 128.65, 126.27 (CH), 123.49 (CH), 116.58, 108.00, 21.52 (CH_3) ppm. MS (EI): *m*/*z* (%) = 244 (100) $[M]^+$. HRMS (EI): calcd. for $C_{17}H_{12}N_2$ 244.1000; found 244.0998.

6-(*p*-Tolyl)quinoline-5-carbonitrile (4d): White powder; m.p. 129–130 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.02 (dd, *J* = 4.2, 1.6 Hz, 1 H), 8.63 (ddd, *J* = 8.5, 1.6, 0.9 Hz, 1 H), 8.35 (dd, *J* = 8.8, 0.7 Hz, 1 H), 7.85 (d, *J* = 8.8 Hz, 1 H), 7.63 (dd, *J* = 8.5, 4.2 Hz, 1 H), 7.61–7.57 (m, 2 H), 7.36 (d, *J* = 7.8 Hz, 2 H), 2.45 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 151.41 (CH), 146.47, 146.37, 139.40, 134.87, 134.54 (CH), 133.70 (CH), 130.85 (CH), 129.62 (CH), 128.97 (CH), 128.62, 123.40 (CH), 116.67, 107.71, 21.30 (CH_3) ppm. HRMS (EI): calcd. for $C_{17}H_{12}N_2$ 244.1000; found 244.0995.

6-[2-(Trifluoromethyl)phenyl]quinoline-5-carbonitrile (4e): Colorless crystalline solid; m.p. 135–136 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.09 (dd, *J* = 4.2, 1.6 Hz, 1 H), 8.60 (ddd, *J* = 8.5, 1.6, 0.9 Hz, 1 H), 8.36 (dd, *J* = 8.8, 0.8 Hz, 1 H), 7.87 (d, *J* = 7.6 Hz, 1 H), 7.75–7.62 (m, 4 H), 7.45 (d, *J* = 7.6 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 152.16 (CH), 146.84, 144.31, 136.65, 133.74 (CH), 131.92 (CH), 131.43 (CH), 130.83 (CH), 129.40 (CH), 128.82 (d, *J* = 30.2 Hz, C-CF_3), 127.85, 126.60 (q, *J* = 5.0 Hz, CH-C-CF_3), 123.71 (d, *J* = 274.7 Hz, CF_3) 123.70 (CH), 115.40, 110.45 ppm. MS (EI): *m*/*z* (%) = 298 (100) $[M]^+$. HRMS (EI): calcd. for $C_{17}H_9F_3N_2$ 298.0718; found 298.0721.

6-[3-(Trifluoromethyl)phenyl]quinoline-5-carbonitrile (4f): Light yellow solid; m.p. 118–120 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.08 (dd, *J* = 4.2, 1.6 Hz, 1 H), 8.65 (d, *J* = 8.4 Hz, 1 H), 8.42 (d, *J* = 8.8 Hz, 1 H), 7.93–7.89 (m, 2 H), 7.86 (d, *J* = 8.8 Hz, 1 H), 7.79 (d, *J* = 7.8 Hz, 1 H), 7.72–7.66 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 152.12 (CH), 146.82, 144.63, 138.60, 135.11 (CH), 133.88 (CH), 132.50 (CH), 131.51 (d, *J* = 32.7 Hz, C-CF_3), 130.45 (CH), 129.55 (CH), 128.60, 126.03 (m, 2 CH-C-CF_3), 123.82 (d, *J* = 273.4 Hz, CF_3), 123.81 (CH), 116.09, 108.62 ppm. MS (EI): *m*/*z* (%) = 298 (100) $[M]^+$. HRMS (EI): calcd. for $C_{17}H_9F_3N_2$ 298.0718; found 298.0716.

6-(Furan-2-yl)quinoline-5-carbonitrile (4g): Yellow solid; m.p. 159–160 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.95 (dd, *J* = 4.2, 1.5 Hz, 1 H), 8.57 (dd, *J* = 8.5, 0.7 Hz, 1 H), 8.28 (d, *J* = 9.1 Hz, 1 H), 8.20 (d, *J* = 9.1 Hz, 1 H), 7.65 (dd, *J* = 2.0, 0.8 Hz, 1 H), 7.58 (dd, *J* = 8.5, 4.2 Hz, 1 H), 7.50 (d, *J* = 3.6 Hz, 1 H), 6.63 (dd, *J* = 3.6, 1.8 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 151.33 (CH), 149.60, 146.45, 144.41 (CH), 134.82 (CH), 133.69, 133.55 (CH), 128.89, 126.67 (CH), 123.61 (CH), 116.86, 112.81 (CH), 112.58 (CH), 102.62 ppm. MS (EI): *m*/*z* (%) = 220 (100) $[M]^+$. HRMS (EI): calcd. for $C_{14}H_8N_2O$ 220.0637; found 220.0637.

6-(Thiophen-2-yl)quinoline-5-carbonitrile (4h): Yellow powder; m.p. 154–155 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.99 (dd, *J* = 4.2, 1.6 Hz, 1 H), 8.60 (ddd, *J* = 8.5, 1.5, 0.8 Hz, 1 H), 8.30 (d, *J* = 8.9 Hz, 1 H), 7.95 (d, *J* = 8.9 Hz, 1 H), 7.85 (dd, *J* = 3.7, 1.1 Hz, 1 H), 7.62 (dd, *J* = 8.5, 4.2 Hz, 1 H), 7.55 (dd, *J* = 5.1, 1.1 Hz, 1 H), 7.23 (dd, *J* = 5.1, 3.8 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 151.56 (CH), 146.56, 139.24, 138.32, 134.88 (CH), 133.77 (CH), 130.38 (CH), 129.01, 128.96 (CH), 128.81 (CH), 128.59 (CH), 123.71 (CH), 116.83, 106.02 ppm. MS (EI): *m*/*z* (%) = 236 (100) $[M]^+$. HRMS (EI): calcd. for $C_{14}H_8N_2S$ 236.0408; found 236.0409.

6-(Thiophen-3-yl)quinoline-5-carbonitrile (4i): Light yellow powder; m.p. 204–205 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.00 (dd, *J* = 4.2, 1.5 Hz, 1 H), 8.60 (d, *J* = 8.4 Hz, 1 H), 8.32 (d, *J* = 8.9 Hz, 1 H), 7.90 (d, *J* = 8.9 Hz, 1 H), 7.85 (dd, *J* = 2.9, 1.4 Hz, 1 H), 7.61 (dd, *J* = 8.5, 4.2 Hz, 1 H), 7.56 (dd, *J* = 5.0, 1.3 Hz, 1 H), 7.50 (dd, *J* = 5.0, 2.9 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 151.51 (CH), 146.56, 140.44, 138.19, 134.82 (CH), 133.73 (CH), 130.36 (CH), 128.83, 127.77 (CH), 126.95 (CH), 126.15 (CH), 123.56 (CH), 116.89, 106.86 ppm. MS (EI): *m*/*z* (%) = 236 (100) $[M]^+$. HRMS (EI): calcd. for $C_{14}H_8N_2S$ 236.0408; found 236.0399.

Methyl 2-Phenyl-1-naphthoate (5a): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00–7.95 (m, 2 H), 7.91 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.60–7.38 (m, 8 H), 3.71 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.09, 140.92, 138.08, 132.33, 130.00 (CH), 129.95, 128.53 (2 CH), 128.48 (2 CH), 128.17 (CH), 127.64 (CH), 127.51 (CH), 127.44 (CH), 126.38 (CH), 125.09 (CH), 52.23 (CH_3) ppm. MS (EI): *m*/*z* (%) = 262 (85) $[M]^+$, 231 (100). HRMS (EI): calcd. for $C_{18}H_{14}O_2$ 262.0994; found 236.0991.

Methyl 2-(*m*-Tolyl)-1-naphthoate (5b): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97–7.93 (m, 2 H), 7.89 (dd, *J* = 8.4, 1.6 Hz, 1 H), 7.59–7.50 (m, 3 H), 7.35–7.26 (m, 3 H), 7.20 (d, *J* = 7.6 Hz, 1 H), 3.71 (s, 3 H), 2.42 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.16, 140.84, 138.17, 138.13, 132.29, 130.01, 129.93 (CH), 129.87, 129.25 (CH), 128.41 (CH), 128.36 (CH), 128.15 (CH), 127.49 (CH), 127.45 (CH), 126.30 (CH), 125.59 (CH), 125.08 (CH), 52.21 (CH_3), 21.52 (CH_3) ppm. MS (EI): *m*/*z* (%) = 276 (88) $[M]^+$, 245 (100). HRMS (EI): calcd. for $C_{19}H_{16}O_2$ 276.1150; found 276.1149.

Methyl 2-[3-(Trifluoromethyl)phenyl]-1-naphthoate (5c): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00–7.94 (m, 2 H), 7.91 (dd, *J* = 7.6, 1.6 Hz, 1 H), 7.75 (s, 1 H), 7.68–7.63 (m, 2 H), 7.61–7.54 (m, 3 H), 7.50 (d, *J* = 8.4 Hz, 1 H), 3.72 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.64, 141.66, 136.39, 132.58, 131.92 (CH), 131.04, 130.78, 130.33 (CH), 129.94, 128.97 (CH), 128.21 (CH), 127.77 (CH), 126.92 (CH), 126.80 (CH), 125.37 (q, *J* = 3.8 Hz, CH), 125.20 (CH), 124.39 (q, *J* = 3.8 Hz, CH), 122.98, 52.26 (CH_3) ppm. MS (EI): *m*/*z* (%) = 330 (90) $[M]^+$, 299 (100). HRMS (EI): calcd. for $C_{19}H_{13}F_3O_2$ 330.0868; found 330.0871.

Ethyl 6-Phenylisoquinoline-5-carboxylate (5d): Light yellow solid; m.p. 98–100 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.31 (s, 1 H), 8.62 (d, *J* = 6.0 Hz, 1 H), 8.10 (d, *J* = 8.4 Hz, 1 H), 7.85 (d, *J* = 6.0 Hz, 1 H), 7.66 (d, *J* = 8.4 Hz, 1 H), 7.47–7.42 (m, 5 H), 4.17 (q, *J* = 7.2 Hz, 2 H), 0.97 (t, *J* = 7.2 Hz, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.38, 152.82 (CH), 144.73 (CH), 143.03, 140.45, 133.16, 129.79 (CH), 129.22 (CH), 129.05, 128.72 (CH), 128.64 (CH), 128.34 (CH), 127.44, 117.98 (CH), 61.78 (CH_2), 13.82 (CH_3) ppm. MS (EI): *m*/*z* (%) = 277 (65) $[M]^+$, 232 (100). HRMS (EI): calcd. for $C_{18}H_{15}NO_2$ 277.1103; found 277.1111.

Ethyl 6-(*m*-Tolyl)isoquinoline-5-carboxylate (5e): Light yellow solid; m.p. 74–76 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.32 (s, 1 H), 8.63 (s, 1 H), 8.09 (d, *J* = 8.5 Hz, 1 H), 7.86 (d, *J* = 5.0 Hz, 1 H), 7.66 (d, *J* = 8.5 Hz, 1 H), 7.35 (t, *J* = 7.5 Hz, 1 H), 7.30–7.22 (m, 3 H), 4.20 (q, *J* = 7.1 Hz, 2 H), 2.42 (s, 3 H), 1.01 (t, *J* = 7.1 Hz, 3

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H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.09, 147.41 (CH), 139.28 (CH), 137.77, 134.98, 133.03, 127.78, 124.36 (CH), 123.97 (CH), 123.92 (CH), 123.70 (CH), 123.61, 123.28 (CH), 120.39 (CH), 112.65 (CH), 56.39 (CH_2), 16.27 (CH_3), 8.49 (CH_3) ppm. MS (EI): *m*/*z* (%) = 291 (65) $[M]^+$, 246 (100). HRMS (EI): calcd. for $C_{19}H_{17}NO_2$ 291.1259; found 291.1260.

Ethyl 6-[3-(Trifluoromethyl)phenyl]isoquinoline-5-carboxylate (5f): White solid; m.p. 114–116 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.38 (s, 1 H), 8.68 (d, *J* = 5.4 Hz, 1 H), 8.17 (d, *J* = 8.4 Hz, 1 H), 7.90 (d, *J* = 5.9 Hz, 1 H), 7.77 (s, 1 H), 7.73 (d, *J* = 7.7 Hz, 1 H), 7.70–7.65 (m, 2 H), 7.63 (t, *J* = 7.7 Hz, 1 H), 4.22 (q, *J* = 7.2 Hz, 2 H), 1.04 (t, *J* = 7.2 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.71, 152.72 (CH), 144.79 (CH), 141.20, 141.09, 132.98, 131.87 (CH), 130.01 (CH), 129.31, 129.11 (CH), 128.59 (CH), 127.50, 125.34 (q, *J* = 3.8 Hz, CH-C-CF_3), 124.92 (q, *J* = 3.8 Hz, CH-C-CF_3), 122.83, 117.90 (CH), 61.78 (CH_2), 13.60 (CH_3) ppm. MS (EI): *m*/*z* = 345 (60) $[M]^+$, 300 (100). HRMS (EI): calcd. for $C_{19}H_{14}F_3NO_2$ 345.0977; found 345.0975.

Ethyl 7-Phenylquinoline-8-carboxylate (5g): Light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.00 (dd, *J* = 4.2, 1.7 Hz, 1 H), 8.19 (dd, *J* = 8.3, 1.7 Hz, 1 H), 7.91 (d, *J* = 8.5 Hz, 1 H), 7.59 (d, *J* = 8.4 Hz, 1 H), 7.58–7.54 (m, 2 H), 7.48–7.40 (m, 4 H), 4.31 (q, *J* = 7.1 Hz, 2 H), 1.05 (t, *J* = 7.2 Hz, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.88, 151.39 (CH), 145.27, 140.33, 139.62, 135.72 (CH), 132.52, 128.85 (CH), 128.66 (CH), 128.38 (CH), 128.14 (CH), 127.92 (CH), 126.90, 121.48 (CH), 61.41 (CH_2), 13.78 (CH_3) ppm.

Supporting Information (see footnote on the first page of this article): Copies of the ^{1}H and ^{13}C NMR spectra for all new products.

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