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Iodine mediated *in situ* generation of R-Se–I: application towards the construction of pyrano[4,3-*b*]quinoline heterocycles and fluorescence properties†

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In this paper, we report the iodine mediated *in situ* generation of R-Se–I and further its application towards the construction of pyrano[4,3-*b*]quinolin-1-one derivatives. The structural elaboration of 1-chloro-8-methyl-3-phenylbenzo[*b*][1,6]naphthyridine **6** was successfully achieved by Sonogashira, Suzuki coupling and dehalogenation reactions. Finally, the synthesized compounds **4a**, **5a**, **5b**, **6**, and **7a–7c** were studied for photophysical properties including UV-absorption, fluorescence, and quantum yield studies. The synthesized pyranoquinoline derivatives showed λ_{max}, F_{max} and Φ_f values in the range of 391–447 nm, 436–486 nm and 0.004–0.301, respectively in chloroform solvent.

Introduction

In modern organic synthesis, functionalized heterocyclic building blocks are of great importance because of their wide application in pharmaceutical and industrial applications.[1] Nitrogen-containing heterocycles are gaining more importance due to their interesting numerous applications in synthetic chemistry,[2] and natural products and because of their potent biological activities.[3] Among various N-heterocycles, pyranoquinoline derivatives have gained significant importance in natural products that are present in many alkaloids[4] such as flindersine, oricine, geibalasine and verprisine[5] and they exhibit a variety of biological activities such as anti-inflammatory,[6] antibacterial,[7] and anti-allergic activities.[8] Pyranoquinoline is also known for pharmacological activities such as anti-coagulant,[9] coronary constricting[10] and cancer cell growth inhibitory activity.[11] They are often used as synthetic precursors for the preparation of other natural products such as dimeric quinoline alkaloids and other polycyclic heterocycles.[12] Recently, Larock *et al.* have reported a two step synthesis of pyrano[4,3-*b*]quinolinones from the corresponding alkynylesters followed by intramolecular cyclization.[13] As per a literature survey, the generation of Ar–Se–X and its application is highly important, and the syntheses of pyranoquinolines and pyranoquinolinones are multistep and suffer from poor availability of starting materials.[14] In addition, there are a large number of methodologies in the literature for the synthesis of chalcogen-containing quinolines, including selenium derivatives.[15] Besides the pharmacological properties, the presence of selenium-containing quinolines in a potentially bioactive molecule can dramatically increase the biological activity of the substrate.[16] In our ongoing projects, we have successfully synthesized thieno[2,3-*b*]quinoline and selenopheno[2,3-*b*]quinoline,[17] thieno[2,3-*c*]acridine and furo[2,3-*c*]acridine,[18] 2-imino-1,3-thiaselenolanes,[19] and selenium-containing bicyclic β-lactams.[20a] The main feature of the current strategy includes the use of both iodine and diorganyl diselenide reagents in the cyclization reaction for their ability to transform acyclic substrates into different heterocycles and incorporate new functionality into the final product, thus making more useful heterocycles that are suitable for further transformations.[20b] Herein, we have successfully attempted the synthesis of 4-(arylselanyl)-3-aryl-1*H*-pyrano[4,3-*b*]quinolin-1-one derivatives from alkynylesters. Furthermore, we carried out photophysical studies including UV-absorption spectroscopy, fluorescence, and quantum yield studies.

Results and discussion

Our investigations began with the starting material 6-methyl-2-(phenylethynyl)quinoline-3-carbaldehyde[21] **2a** prepared from the corresponding 6-methyl-2-chloroquinoline-3-carbaldehyde[22] **1a** and phenyl acetylene under Sonogashira coupling reaction conditions. Furthermore, 2-phenylalkynylquinoline-3-carboxylate **3a** was obtained selectively in excellent yields without affecting the triple bond[13] by using I_2 and K_2CO_3 in methanol at room temperature (Scheme 1).

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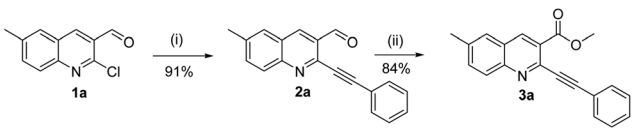
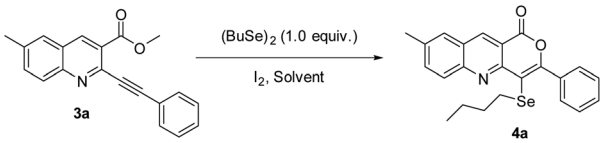


Scheme 1 Synthesis of methyl 6-methyl-2-(phenylethynyl)quinoline-3-carboxylate **3a**. Reaction conditions: (i) 2-Chloro-6-methylquinoline-3-carbaldehyde **1a** (2.43 mmol), $Pd(PPh_3)_2Cl_2$ (5 mol%), Et_3N (7.29 mmol), phenyl acetylene (3.65 mmol), CuI (5 mol%), THF (10 mL), rt, 15 h; (ii) I_2 (1.47 mmol), K_2CO_3 (2.21 mmol), methanol (5 mL), rt, 1 h.

We first examined the seleno-cyclization reaction of **3a** (0.05 g, 1.0 equiv.) with I_2 (0.126 g, 1.0 equiv.) and dibutyl diselenide (0.045 g, 1.0 equiv.) in CH_2Cl_2 (5 mL) under a nitrogen atmosphere, the cyclized product **4a** was obtained in 16% yield (Table 1, entry 1). Furthermore we increased the equivalents of iodine (1.5 and 3.0 equiv.); interestingly the yield was increased up to 66% (Table 1, entries 2–5). On the other hand, a higher loading of I_2 (4.0 equiv.) led to a slightly lower yield (Table 1, entries 4–6). Then, we carried out the reactions under reflux conditions. The experimental conditions described in Table 1 (entries 9–11) showed that the reaction proceeds under reflux conditions with the highest yields (83–89%). The chloroform solvent used for the reaction was found to be less effective (Table 1, entries 13 and 14). Also, the reaction did not proceed in acetonitrile solvent (Table 1, entry 15). The reaction temperature and iodine equivalents were found to have dramatic effects on the present intramolecular cyclization, and a higher yield of products was obtained when the reaction was performed under reflux conditions. Also, the reaction was carried out using $(Me\text{-}S)_2$ and $(Ph\text{-}S)_2$ but the reaction does not proceed for dialkyl disulfide as well as for diaryl disulfide.

Table 1 Optimization of reaction conditions on 4-(butylselanyl)-8-methyl-3-phenyl-1*H*-pyrano[4,3-*b*]quinolin-1-one **4a**



Entry	Solvent	I_2 (equiv.)	Temp. (°C)	Yield[a] **4a** (%)
1	CH_2Cl_2	1.0	rt	16
2	CH_2Cl_2	1.5	rt	20
3	CH_2Cl_2	2.0	rt	61
4	CH_2Cl_2	2.5	rt	64
5	CH_2Cl_2	3.0	rt	66
6	CH_2Cl_2	4.0	rt	59
7	CH_2Cl_2	3.0	rt	42[b]
8	CH_2Cl_2	1.5	Reflux	47[c]
9	CH_2Cl_2	2.5	Reflux	85[c]
10	CH_2Cl_2	3.0	Reflux	89[c]
11	CH_2Cl_2	3.5	Reflux	83[c]
12	$CHCl_3$	3.0	rt	22
13	$CHCl_3$	3.0	rt	14[b]
14	$CHCl_3$	3.0	Reflux	51[c]
15	CH_3CN	3.0	Reflux	NR[c]

[a] Reactions were performed under nitrogen, for 1 h. [b] Open flask, room temperature. [c] Reflux conditions. NR: no reaction.

Table 2 Substrate scopes of 4-(arylselanyl)-3-aryl-1*H*-pyrano[4,3-*b*]quinolin-1-one **4a–4t**

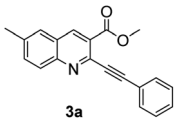
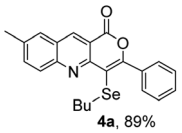
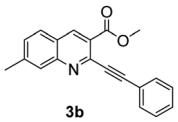
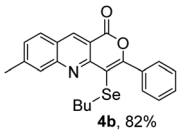
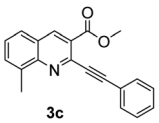
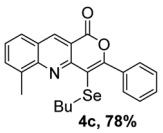
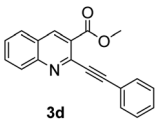
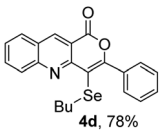
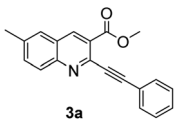
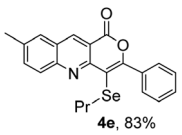
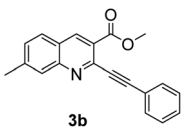
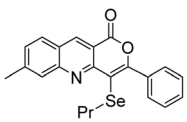
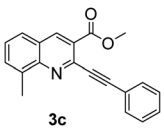
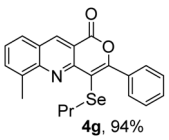
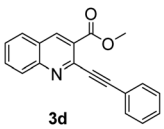
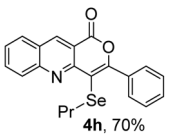
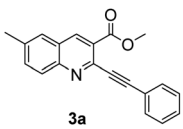
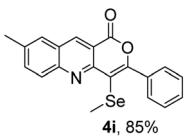
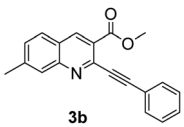
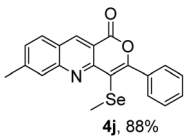
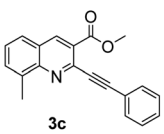
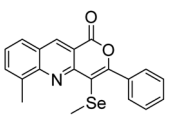
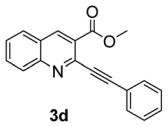
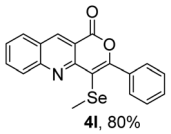
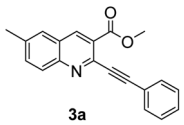
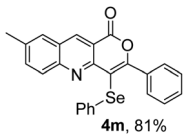
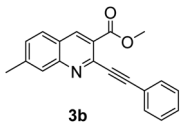
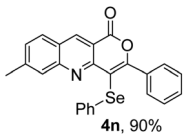
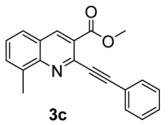
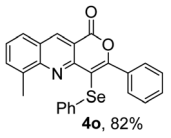
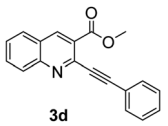
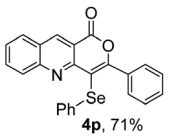
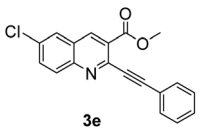
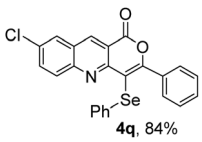
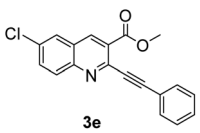
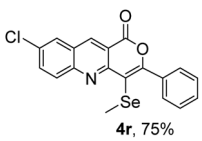
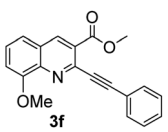
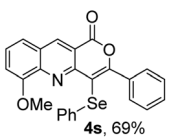
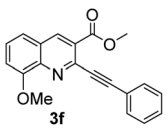
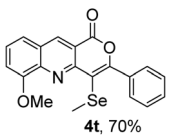
Entry	Alkynl ester (**3**)	Diorganyl diselenides	Product (**4**) % yield[a]
1	 **3a**	$(BuSe)_2$	 **4a**, 89%
2	 **3b**	$(BuSe)_2$	 **4b**, 82%
3	 **3c**	$(BuSe)_2$	 **4c, 78%**
4	 **3d**	$(BuSe)_2$	 **4d**, 78%
5	 **3a**	$(PrSe)_2$	 **4e**, 83%
6	 **3b**	$(PrSe)_2$	 **4f**, 89%
7	 **3c**	$(PrSe)_2$	 **4g**, 94%
8	 **3d**	$(PrSe)_2$	 **4h**, 70%
9	 **3a**	$(MeSe)_2$	 **4i**, 85%
10	 **3b**	$(MeSe)_2$	 **4j**, 88%
11	 **3c**	$(MeSe)_2$	 **4k**, 82%

Table 2 *(Contd.)*

Entry	Alkynl ester (**3**)	Diorganyl diselenides	Product (**4**) % yield[a]
12	 **3d**	$(MeSe)_2$	 **4l**, 80%
13	 **3a**	$(PhSe)_2$	 **4m**, 81%
14	 **3b**	$(PhSe)_2$	 **4n**, 90%
15	 **3c**	$(PhSe)_2$	 **4o**, 82%
16	 **3d**	$(PhSe)_2$	 **4p**, 71%
17	 **3e**	$(PhSe)_2$	 **4q**, 84%
18	 **3e**	$(MeSe)_2$	 **4r**, 75%
19	 **3f**	$(PhSe)_2$	 **4s**, 69%
20	 **3f**	$(MeSe)_2$	 **4t**, 70%

[a] Reactions were performed by using 0.15 mmol of **3**, I_2 (3.0 equiv.) and diorganyl diselenides (1.0 equiv.) in CH_2Cl_2 under reflux conditions for 1 h.

With the optimal reaction conditions in hand (Table 1, entry 10) we have successfully synthesized pyrano[4,3-*b*]quinolin-1-one derivatives **4a–4t** (Table 2). The alkyl substitution at the quinoline part well tolerated the effect of different diorganyl diselenides and iodine under the reflux reaction conditions. Our results showed that the cyclized products, 4-(alkylselanyl)-3-phenyl-1*H*-pyrano[4,3-*b*]quinolin-1-one derivatives **4a–4t** were obtained in excellent yields 70–94% (Table 2). The structures of all the synthesized compounds **3a–3f**, **4a–4t** were characterized by IR, HRMS, ^{1}H- and ^{13}C-NMR spectral analysis.

The plausible mechanism for the formation of pyrano[4,3-*b*]quinoline **4** is shown in Fig. 1.[23] First, the reaction of molecular iodine (I_2) and $(R\text{-}Se)_2$ was carried out, which resulted in the *in situ* generation of R-Se–I **I**. Furthermore, compound **3** reacts with R-Se–I **I** to generate a seleniranium ion **II**. Subsequently, the nucleophilic attack of the ester functional group takes place on the seleniranium ion which resulted in the intermediate **III**. Finally the intermediate **III** results in the target compound **4** by the elimination of Me–I. A control experiment was carried out to support the proposed reaction mechanism; for that purpose we carried out the reaction of **3a** (0.02 g, 1 equiv.), diphenyl diselenide (0.02 g, 1 equiv.) and iodine (0.05 g, 3.0 equiv.) in deuterated solvent $CDCl_3$ (1.5 mL) and we have investigated the formation of the R-Se–I intermediate, and also the formation of the by-product Me–I by NMR. For the by-product Me–I, the NMR spectra clearly showed the proton peak at 2.167 ppm and carbon peak at −23.149 ppm.

Next, the synthesized 4-(butylselanyl)-8-methyl-3-phenyl-1*H*-pyrano[4,3-*b*]quinolin-1-one **4a** was functionalized, providing chemical evidence of the cyclized product **4a**. The reaction of **4a** with an excess of 28% NH_4OH in DMF at 80 °C afforded compound **5a** and **5b** (Scheme 2)[24] which were characterized as 8-methyl-3-phenylbenzo[*b*][1,6]naphthyridin-1(2*H*)-one (**5a**) and 4-(butylselanyl)-8-methyl-3-phenylbenzo[*b*][1,6]naphthyridin-1(2*H*)-one (**5b**) from their spectral and analytical data. Furthermore, the compound **5a** was transformed into 1-chloro-8-methyl-3-phenylbenzo[*b*][1,6]naphthyridine **6** on reaction with $POCl_3$ under reflux conditions.[24] In addition, the presence of chlorine in the 8-methyl-3-phenylbenzo[*b*][1,6]naphthyridine product **6** is an interesting feature of the cycliza-

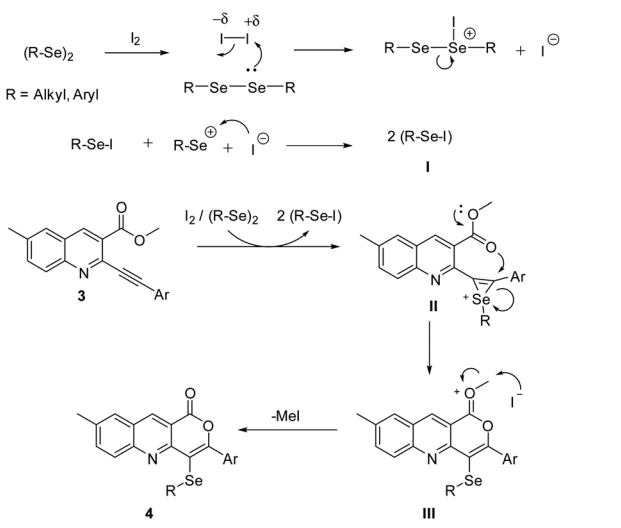
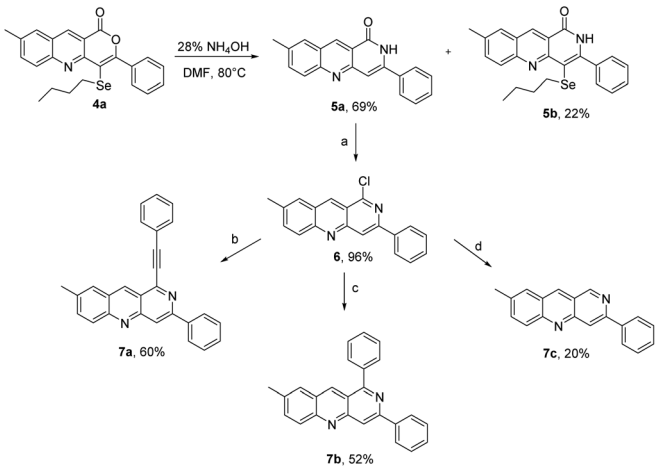


Fig. 1 Plausible mechanism.



Scheme 2 Functionalization of **4a**, **5a** and **6**. Reaction conditions: (a) $POCl_3$, 80 °C, (b) phenyl acetylene, $Pd(PPh_3)_2Cl_2$, Et_3N, THF, room temperature. (c) Phenylboronic acid, $Pd(OAc)_2$, Cs_2CO_3, DMF, 110 °C. (d) Methylacrylate, PPh_3, $Pd(OAc)_2$, K_2CO_3, DMF, 110 °C.

tion which allowed further structural elaboration, most notably by the Sonogashira coupling, Suzuki coupling and dehalogenation reactions to afford the corresponding diversified pyrano[4,3-*b*]quinoline moieties **7a–7c**. (Scheme 2).[25]

The UV-Vis absorption spectra of **4a**, **5a–5b**, **6**, **7a–7c** in chloroform are shown in Fig. 2. In the pyranoquinoline derivatives **4a** and **5b** bearing the R-Se group, the absorption maximum (λ_{max}) and molar extinction coefficient (ε) values were found to be (**4a:** λ_{max} = 391 nm, ε = 4, 960) and (**5b:** λ_{max} = 405 nm, ε = 4, 861) (Fig. 2), while the compounds **5a**, **6** and **7a–7c** show the absorption maximum (λ_{max}) and molar extinction coefficient (ε) values (**5a:** λ_{max} = 399 nm, ε = 7, 279; **6:** λ_{max} = 425 nm, ε = 5, 220; **7a:** λ_{max} = 447 nm, ε = 5, 524; **7b:** λ_{max} = 434 nm, ε = 4, 051; **7c:** λ_{max} = 425 nm, ε = 2, 305). The fluorescence spectra of **4a**, **5a–5b**, **6** and **7a–7c** in chloroform are shown in Fig. 3.

The fluorescence maximum (F_{max}) and Stokes shift values were in the range of 436 to 486 nm and 2 to 146 nm, respectively. The fluorescence quantum yield (Φ_f) values were relatively low (Φ_f: 0.004–0.301) probably because of the heavy atom effect.[26] The effect of the heavy atom (R-Se) reflects on the fluorescence,[27] and compounds **4a** and **5b** bearing a heavy atom do not show fluorescence; on the other hand compounds **5a**, **6**, **7a–7c** showed higher fluorescence (Fig. 3). Furthermore, the fluorescence quantum yield (Φ_f) value for **5a**, **6**, **7a–7c** was found to be (Φ_f = 0.025–0.301) which was higher than the fluorescence quantum yield (Φ_f) values of **4a** (Φ_f = 0.004) and **5b** (Φ_f = 0.008) probably due to the absence of the heavy atom (R-Se) group in **5a**.

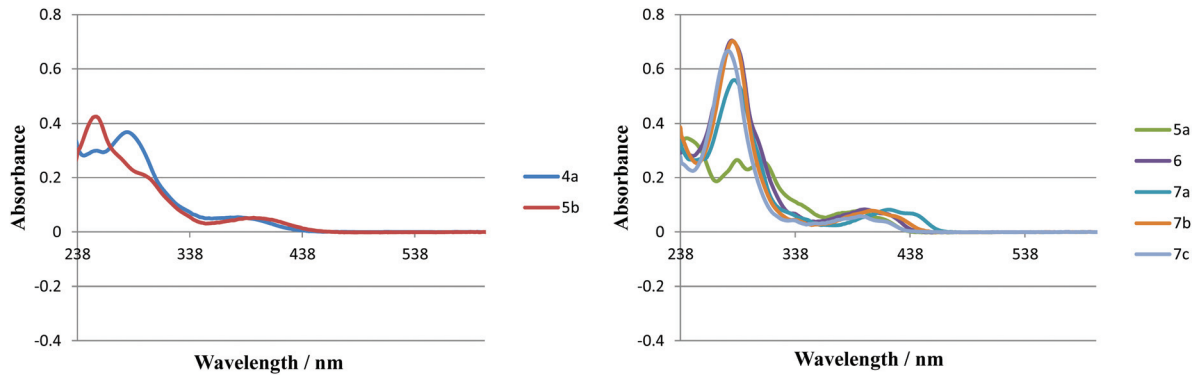


Fig. 2 UV-Vis absorption spectra in chloroform of compounds **4a**, **5a–5b**, **6** and **7a–7c**.

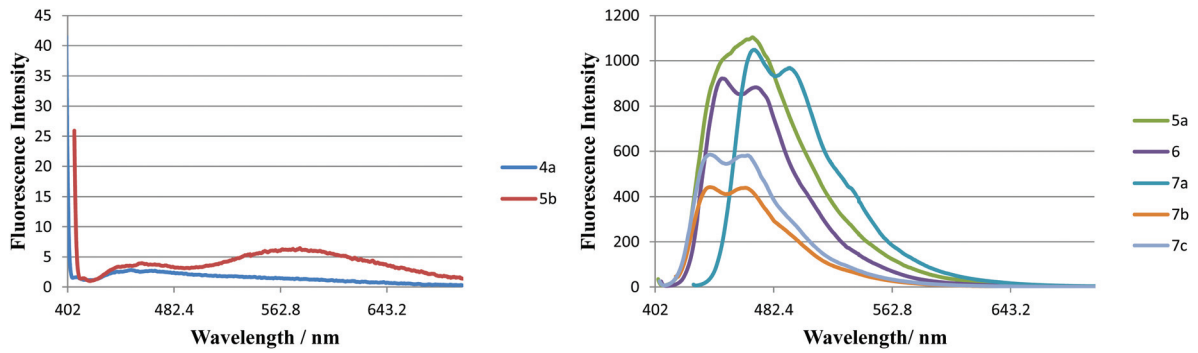


Fig. 3 Normalized fluorescence spectra in chloroform of compounds **4a**, **5a–5b**, **6** and **7a–7c**.

Conclusions

We have developed a synthetic route for the preparation of pyrano[4,3-*b*]quinolin-1-one derivatives **4** *via* the intramolecular cyclization of alkynylesters promoted by diorganyl diselenide. Next, the structural elaboration of pyrano[4,3-*b*]quinolin-1-one **4** was done by Sonogashira coupling, Suzuki coupling and dehalogenation reactions. Finally, the synthesized compounds were studied for photophysical properties including UV-absorption spectroscopy, fluorescence, and quantum yield studies. The synthesized pyranoquinoline derivatives showed λ_{max}, F_{max} and Φ_f values in the range from 391–447 nm, 436–486 nm and 0.004–0.301, respectively in chloroform solvent. The structures of the products were confirmed by IR, NMR, and HRMS as well as fluorescence properties. Further expansion of current strategies and evaluation of biological activity are in progress.

Experimental: general

All solvents and reagents were purchased from the suppliers and used without further purification. IR spectra were recorded on a JASCO FT/IR-460 Plus spectrophotometer. Reactions were monitored by thin-layer chromatography (TLC) carried on silica plates using UV-light or Iodine chamber for visualization.

Column chromatography was performed on silica gel (60–120 mesh) using *n*-hexane and ethyl acetate as eluents. Evaporation and condensation were carried out *in vacuo*. NMR spectra were recorded with JEOL JNM-ECS 400 spectrometers with tetramethylsilane as an internal standard. Chemical shifts δ and coupling constants J are given in ppm (parts per million) and Hz (hertz), respectively. The following abbreviations were used as follows: s: singlet, d: doublet, t: triplet, m: multiplet. Additionally unknown compounds are characterized by HRMS analysis. All known compound data are consistent with the given literature reports. Melting points were measured by using a Yanaco micromelting point apparatus.

Diselenide preparation

Preparation of 1,2-dibutyldiselenide. Selenium (200 mg, 2.53 mmol) was added to a stirred solution of sodium borohydride (191 mg, 5.07 mmol) in ethanol (20 mL) at 0 °C. Stirring was continued for 30 min, at this temperature. Additionally, selenium (200 mg, 2.53 mmol) was added to the reaction mixture and stirred for 30 min at 0 °C. Finally, iodobutane (1.01 mL, 8.87 mmol) was added over a period of 5 min. After stirring for an hour at room temperature, the reaction mixture was extracted with *n*-hexane and washed with water, dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified over silica gel column chromatography (SiO_2: *n*-hexane/toluene = 20/1) to afford dibutyl diselenide as an orange coloured liquid.

Yield: 72%; orange coloured liquid; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.92 (t, J = 7.6 Hz, 4H), 1.68–1.75 (m, 4H), 1.42 (q, J = 7.5 Hz, 4H), 0.93 (t, J = 7.3 Hz, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 33.2, 30.0, 22.7, 13.7; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 307.8.

Preparation of 1,2-dipropyldiselenide. Yield: 68%; orange coloured liquid; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.86–2.94 (m, 4H), 1.72–1.81 (m, 4H), 1.00 (t, J = 7.3 Hz, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 32.4, 24.3, 14.2; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 303.4.

General procedure for the synthesis of 6-methyl-2-(phenylethynyl)quinoline-3-carbaldehyde 2a–2f

To a solution of 2-chloro-6-methylquinoline-3-carbaldehyde[22] **1a** (500 mg, 2.43 mmol, 1.0 equiv.) in dry THF (10 mL) was added $Pd(PPh_3)_2Cl_2$ (85.33 mg, 5 mol%), triethylamine (738.13 mg, 7.29 mmol, 3.0 equiv.), phenyl acetylene (372.50 mg, 3.65 mmol, 1.5 equiv.), and copper(I) iodide (23.15 mg, 5 mol%) under nitrogen. The mixture was stirred at room temperature for 15 h.[21] After completion of the reaction, the solvent was evaporated under reduced pressure. The residue was extracted with ethyl acetate and the organic phase was washed successively with water and brine. The organic layer was dried over Na_2SO_4. The resulting crude product was purified by column chromatography using *n*-hexane : ethyl acetate (92 : 8) as the eluent to afford **2a**, yellow solid. Yield: 91%; melting point: 136–138 °C; IR (neat): 2361, 2016, 1965, 1700, 1572, 1191, 1099, 946, 830, 803, 769, 582, 564, 528 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.75 (s, 1H), 8.59 (s, 1H), 8.02 (d, J = 9.2 Hz, 1H), 7.64–7.68 (m, 4H), 7.40 (dd, J = 6.9, 4.6 Hz, 3H), 2.53 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 190.7, 148.7, 142.9, 138.5, 136.2, 135.4, 132.3, 129.8, 128.9, 128.8, 128.6, 128.3, 126.4, 121.5, 95.1, 85.8, 21.7; HRMS (ESI): $CDCl_3$ m/z = 272.1075 calcd. For $C_{19}H_{14}NO$, found 272.1050 $[M + H]^+$.

7-Methyl-2-(phenylethynyl)quinoline-3-carbaldehyde (2b). Yield: 85%; melting point: 196–198 °C; IR (neat): 2986, 2409, 2212, 1689, 1579, 1546, 1487, 1440, 1379, 1145, 1092, 1066, 918, 880, 706, 685, 674, 523 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.71 (s, 1H), 8.60 (s, 1H), 7.88 (s, 1H), 7.77 (d, J = 8.2 Hz, 1H), 7.67–7.69 (m, 2H), 7.41 (dd, J = 7.3, 4.6 Hz, 4H), 2.55 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 190.7, 150.3, 144.2, 143.9, 136.6, 132.3, 130.6, 129.8, 129.3, 128.6, 128.3, 124.5, 121.5, 95.2, 85.8, 22.4; HRMS (ESI): m/z = 272.1075 calcd. For $C_{19}H_{14}NO$, found 272.1046 $[M + H]^+$.

8-Methyl-2-(phenylethynyl)quinoline-3-carbaldehyde (2c). Yield: 81%; melting point: 150–152 °C; IR (neat): 2211, 1781, 1691, 1583, 1564, 1492, 1482, 1441, 1409, 1387, 1369, 1169, 1119, 1073, 1042, 945, 912, 883, 844, 776, 757, 693, 536, 472 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.80 (s, 1H), 8.68 (s, 1H), 7.78 (d, J = 8.2 Hz, 1H), 7.69–7.71 (m, 3H), 7.51 (d, J = 6.9 Hz, 1H), 7.43 (dd, J = 4.4, 3.0 Hz, 3H), 2.86 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 191.3, 149.4, 142.8, 137.7, 137.3, 133.1, 132.4, 129.8, 128.7, 128.1, 127.7, 126.6, 121.7, 94.9, 86.2, 18.2; HRMS (ESI): m/z = 272.1075 calcd. For $C_{19}H_{14}NO$, found 272.1062 $[M + H]^+$.

2-(Phenylethynyl)quinoline-3-carbaldehyde (2d). Yield: 89%; melting point: 111–113 °C; IR (neat): 2209, 1774, 1692, 1612, 1580, 1556, 1493, 1444, 1372, 1166, 1146, 1087, 879, 783, 686, 522, 486, 475 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.80 (s, 1H),

8.74 (s, 1H), 8.17 (d, J = 7.8 Hz, 1H), 7.97 (s, 1H), 7.85–7.89 (m, 1H), 7.70–7.72 (m, 2H), 7.64 (d, J = 6.9 Hz, 1H), 7.42–7.45 (m, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 190.8, 150.2, 144.0, 137.2, 133.1, 132.4, 130.0, 129.8, 129.4, 128.9, 128.7, 128.3, 126.5, 121.4, 95.7, 85.6; HRMS (ESI): m/z = 258.0919 calcd. For $C_{18}H_{12}NO$, found 258.0891 $[M + H]^+$.

6-Chloro-2-(phenylethynyl)quinoline-3-carbaldehyde (2e). Yield: 78%; melting point: 134–136 °C; IR (neat): 3046, 2207, 1690, 1575, 1474, 1364, 1168, 1074, 944, 937, 829, 750, 688, 570, 524 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.79 (s, 1H), 8.65 (s, 1H), 8.11 (d, J = 9.2 Hz, 1H), 7.94 (d, J = 2.3 Hz, 1H), 7.78–7.80 (m, 1H), 7.70 (dd, J = 6.0, 1.8 Hz, 2H), 7.42–7.46 (m, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 190.5, 148.6, 144.1, 136.5, 134.2, 134.0, 132.4, 130.9, 130.1, 129.4, 128.7, 128.1, 127.1, 121.2, 96.2, 85.4; HRMS (ESI): m/z = 292.0529 calcd. For $C_{18}H_{12}NO$, found 292.0518 $[M + H]^+$.

8-Methoxy-2-(phenylethynyl)quinoline-3-carbaldehyde (2f). Yield: 83%; melting point: 142–144 °C; IR (neat): 3010, 2205, 1689, 1583, 1459, 1373, 1270, 1126, 1073, 939, 765, 751, 717, 686, 524 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.83 (s, 1H), 8.71 (s, 1H), 7.69 (dd, J = 7.6, 2.1 Hz, 2H), 7.54–7.59 (m, 2H), 7.41–7.43 (m, 3H), 7.20–7.22 (m, 1H), 4.13 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 191.1, 155.0, 142.8, 142.1, 136.9, 132.4, 129.8, 129.3, 128.6, 127.6, 121.7, 121.2, 110.9, 95.6, 86.1, 56.4; HRMS (ESI): m/z = 288.1025 calcd. For $C_{18}H_{12}NO$, found 288.1006 $[M + H]^+$.

General procedure for the synthesis of methyl 6-methyl-2-(phenylethynyl)quinoline-3-carboxylate 3a–3f

To a solution of 6-methyl-2-(phenylethynyl)quinoline-3-carbaldehyde[21] **2a** (200 mg, 0.737 mmol, 1.0 equiv.) in methanol (5 mL) was added I_2 (374 mg, 1.47 mmol, 2.0 equiv.) and K_2CO_3 (306 mg, 2.21 mmol, 3.0 equiv.). The resulting reaction mixture was stirred at room temperature until the total disappearance of the starting material monitored by TLC. After completion, the reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$ and water. The resulting reaction mixture was extracted using ethyl acetate. The organic layer was dried over Na_2SO_4. The resulting product was purified by column chromatography using *n*-hexane : ethyl acetate (80 : 20) as the eluent to afford **3a**, yellow solid. Yield: 84%; melting point: 91–93 °C; IR (neat): 2216, 1726, 1582, 1559, 1486, 1440, 1266, 1194, 1174, 1134, 1065, 912, 827, 777, 765, 685, 563, 527 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.03 (d, J = 8.7 Hz, 1H), 7.72 (s, 2H), 7.60–7.63 (m, 2H), 7.38 (t, J = 3.2 Hz, 3H), 4.02 (s, 3H), 2.53 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.8, 147.7, 140.7, 139.1, 138.3, 134.7, 132.4, 129.3, 128.8, 128.5, 127.4, 125.9, 125.5, 122.6, 93.1, 88.7, 52.7, 21.7; HRMS (ESI): m/z = 302.1181 calcd. For $C_{20}H_{16}NO_2$, found 302.1162 $[M + H]^+$.

Methyl 7-methyl-2-(phenylethynyl)quinoline-3-carboxylate (3b). Yield: 86%; melting point: 97–99 °C; IR (neat): 2215, 1726, 1620, 1596, 1545, 1495, 1436, 1421, 1276, 1261, 1230, 1193, 1065, 931, 812, 792, 752, 686, 530, 470 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 7.93 (s, 1H), 7.72–7.78 (m, 3H), 7.38–7.44 (m, 4H), 4.03 (s, 3H), 2.58 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.8, 149.4, 143.3, 141.7, 139.6, 132.5, 130.4, 129.3, 128.5, 128.3, 128.2, 124.8, 124.0, 122.6, 93.3, 88.7, 52.6, 22.3; HRMS (ESI): m/z = 302.1181 calcd. For $C_{20}H_{16}NO_2$, found 302.1163 $[M + H]^+$.

Methyl 8-methyl-2-(phenylethynyl)quinoline-3-carboxylate (3c). Yield: 83%; melting point: 67–69 °C; IR (neat): 2216, 1727, 1711, 1612, 1587, 1565, 1491, 1439, 1404, 1261, 1240, 1198, 1154, 1092, 1035, 789, 753, 688, 667, 514 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.65 (s, 1H), 7.71 (q, J = 3.2 Hz, 2H), 7.60 (dd, J = 17.6, 7.6 Hz, 2H), 7.36–7.41 (m, 4H), 3.99 (s, 3H), 2.81 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.9, 148.2, 140.4, 139.9, 137.4, 132.4, 132.3, 129.3, 128.5, 127.8, 126.5, 125.8, 125.3, 122.8, 92.8, 89.3, 52.6, 18.1; HRMS (ESI): m/z = 302.1181 calcd. For $C_{20}H_{16}NO_2$, found 302.1159 $[M + H]^+$.

Methyl 2-(phenylethynyl)quinoline-3-carboxylate (3d). Yield: 92%; melting point: 97–99 °C; IR (neat): 2217, 1728, 1615, 1595, 1584, 1489, 1434, 1414, 1227, 1201, 1127, 1063, 1026, 954, 945, 795, 755, 687, 525, 469 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.17 (d, J = 8.7 Hz, 1H), 7.89 (d, J = 7.8 Hz, 1H), 7.83 (dd, J = 8.7, 6.9 Hz, 1H), 7.73 (q, J = 3.2 Hz, 2H), 7.62 (d, J = 8.2 Hz, 1H), 7.39–7.41 (m, 3H), 4.05 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.7, 149.1, 141.7, 139.9, 132.5, 132.3, 129.4, 129.3, 128.6, 128.5, 128.0, 125.9, 125.6, 122.5, 93.5, 88.6, 52.7; HRMS (ESI): m/z = 288.1025 calcd. For $C_{19}H_{14}NO_2$, found 288.0996 $[M + H]^+$.

Methyl 6-chloro-2-(phenylethynyl)quinoline-3-carboxylate (3e). Yield: 83%; melting point: 151–153 °C; IR (neat): 3067, 2209, 1707, 1579, 1489, 1437, 1248, 1234, 1064, 833, 752, 688, 655, 528, 513 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.10 (d, J = 9.2 Hz, 1H), 7.87 (d, J = 2.3 Hz, 1H), 7.70–7.77 (m, 3H), 7.40 (q, J = 2.3 Hz, 3H), 4.05 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.4, 147.5, 141.9, 138.8, 133.9, 133.2, 132.5, 130.8, 129.6, 128.6, 127.1, 126.5, 126.5, 122.3, 94.2, 88.2, 52.9; HRMS (ESI): m/z = 322.0635 calcd. For $C_{19}H_{14}NO_2$, found 322.0611 $[M + H]^+$.

Methyl 8-methoxy-2-(phenylethynyl)quinoline-3-carboxylate (3f). Yield: 97%; yellow liquid; IR (neat): 2952, 2218, 1735, 1614, 1560, 1492, 1463, 1274, 1186, 1157, 1058, 985, 792, 749, 728, 665, 527 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.74 (s, 1H), 7.71 (q, J = 3.2 Hz, 2H), 7.50 (t, J = 8.0 Hz, 1H), 7.43 (d, J = 7.3 Hz, 1H), 7.38 (t, J = 3.2 Hz, 3H), 7.13 (d, J = 7.8 Hz, 1H), 4.09 (s, 3H), 4.03 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.8, 154.8, 141.0, 140.5, 139.6, 132.4, 129.2, 128.4, 128.4, 127.0, 126.2, 122.7, 120.1, 110.1, 93.5, 89.0, 56.3, 52.7; HRMS (ESI): m/z = 318.1130 calcd. For $C_{19}H_{14}NO_2$, found 318.1102 $[M + H]^+$.

General procedure for the synthesis of 4-(butylselanyl)-8-methyl-3-phenyl-1*H*-pyrano[4,3-*b*]quinolin-1-one 4a–4t

To a solution of I_2 (126 mg, 0.497 mmol, 3.0 equiv.), dibutyl diselenide (45 mg, 0.166 mmol, 1.0 equiv.) in CH_2Cl_2 (5 mL) were added, and the resulting mixture was stirred for 20 min. After this time period, methyl 6-methyl-2-(phenylethynyl)quinoline-3-carboxylate[14] **3a** (50 mg, 0.166 mmol, 1.0 equiv.) was added at the same temperature. The reaction was monitored by TLC, and after completion, the reaction mixture was

quenched with saturated aqueous $Na_2S_2O_3$ and water. The resulting solution was extracted using dichloromethane. The organic layer was dried over Na_2SO_4. The crude product was purified by column chromatography using *n*-hexane : ethyl acetate (82 : 18) as the eluent to afford **4a**, yellow solid. Yield: 89%; melting point: 109–111 °C; IR (neat): 2944, 1737, 1608, 1594, 1485, 1456, 1445, 1200, 1187, 1070, 1045, 932, 826, 749, 608, 621, 647, 480 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1H), 8.18 (d, J = 8.7 Hz, 1H), 7.74–7.78 (m, 4H), 7.49 (t, J = 3.4 Hz, 3H), 2.96 (t, J = 7.3 Hz, 2H), 2.60 (s, 3H), 1.52 (t, J = 7.6 Hz, 2H), 1.25 (q, J = 7.5 Hz, 2H), 0.78 (t, J = 7.3 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.3, 158.6, 151.7, 150.4, 139.8, 137.8, 136.0, 134.2, 130.2, 130.1, 129.6, 127.9, 127.8, 127.0, 115.4, 107.9, 31.9, 28.5, 22.8, 21.8, 13.6; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 198.13; HRMS (ESI): m/z = 424.0816 calcd. For $C_{23}H_{22}NO_2Se$, found 424.0817 $[M + H]^+$.

4-(Butylselanyl)-7-methyl-3-phenyl-1*H* pyrano[4,3-*b*]quinolin-1-one (4b). Yield: 82%; melting point: 146–148 °C; IR (neat): 2950, 1723, 1613, 1598, 1499, 1444, 1425, 1377, 1215, 1172, 1145, 1066, 1049, 1038, 953, 809, 797, 695, 632, 479 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.13 (s, 1H), 8.07 (s, 1H), 7.91 (d, J = 8.2 Hz, 1H), 7.76–7.78 (m, 2H), 7.49 (t, J = 3.2 Hz, 4H), 2.96 (t, J = 7.3 Hz, 2H), 2.63 (s, 3H), 1.53 (q, J = 7.3 Hz, 2H), 1.26 (t, J = 7.3 Hz, 2H), 0.78 (t, J = 7.3 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.3, 158.9, 152.5, 151.9, 144.6, 140.3, 134.2, 130.2, 130.1, 130.0, 128.9, 128.8, 127.9, 125.1, 114.7, 107.9, 32.0, 28.5, 22.8, 22.4, 13.6; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 198.59; HRMS (ESI): m/z = 424.0816 calcd. For $C_{23}H_{22}NO_2Se$, found 424.0824 $[M + H]^+$.

4-(Butylselanyl)-6-methyl-3-phenyl-1*H*-pyrano[4,3-*b*]quinolin-1-one (4c). Yield: 78%; melting point: 92–94 °C; IR (neat): 2923, 1743, 1594, 1567, 1459, 1370, 1229, 1170, 1066, 1027, 784, 692, 648, 619, 530 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 7.85 (d, J = 8.2 Hz, 1H), 7.77 (q, J = 3.2 Hz, 3H), 7.49–7.54 (m, 4H), 3.05 (t, J = 7.6 Hz, 2H), 2.92 (s, 3H), 1.51 (t, J = 7.6 Hz, 2H), 1.24 (q, J = 7.5 Hz, 2H), 0.78 (t, J = 7.3 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.3, 158.9, 151.2, 150.7, 140.9, 138.0, 134.3, 133.3, 130.2, 130.1, 127.9, 127.4, 127.2, 127.0, 115.1, 108.2, 32.0, 27.9, 22.9, 18.2, 13.6; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 204.0; HRMS (ESI): m/z = 446.0635 calcd. For $C_{23}H_{21}NO_2NaSe$, found 446.0621 $[M + Na]^+$.

4-(Butylselanyl)-3-phenyl-1*H*-pyrano[4,3-*b*]quinolin-1-one (4d). Yield: 78%; melting point: 114–116 °C; IR (neat): 2951, 1738, 1615, 1595, 1558, 1425, 1412, 1213, 1178, 1146, 1071, 1043, 970, 797, 754, 700, 626, 478 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.20 (s, 1H), 8.28 (d, J = 8.7 Hz, 1H), 8.03 (d, J = 7.8 Hz, 1H), 7.90–7.94 (m, 1H), 7.78 (dt, J = 5.3, 2.1 Hz, 2H), 7.65 (t, J = 7.6 Hz, 1H), 7.48–7.51 (m, 3H), 2.97 (t, J = 7.6 Hz, 2H), 1.54 (q, J = 7.3 Hz, 2H), 1.23–1.30 (m, 2H), 0.79 (d, J = 7.3 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.1, 159.0, 152.5, 151.6, 140.8, 134.2, 133.4, 130.3, 130.1, 129.9, 129.3, 127.9, 127.5, 126.9, 115.5, 107.8, 31.9, 28.5, 22.8, 13.6; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 199.21; HRMS (ESI): m/z = 410.0659 calcd. For $C_{22}H_{20}NO_2Se$, found 410.0658 $[M + H]^+$.

8-Methyl-3-phenyl-4-(propylselanyl)-1*H*-pyrano[4,3-*b*]quinolin-1-one (4e). Yield: 83%; melting point: 143–145 °C; IR (neat): 2966, 1732, 1610, 1595, 1556, 1484, 1443, 1343, 1202, 1188, 1067, 1048, 1028, 953, 937, 828, 750, 703, 697, 620, 649 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 1H), 8.18 (d, J = 8.7 Hz, 1H), 7.74–7.78 (m, 4H), 7.49 (q, J = 3.4 Hz, 3H), 2.93 (t, J = 7.3 Hz, 2H), 2.59 (s, 3H), 1.56 (q, J = 7.3 Hz, 2H), 0.83 (t, J = 7.3 Hz, 3H; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.3, 158.7, 151.7, 150.4, 139.9, 137.8, 136.0, 134.2, 130.2, 130.1, 129.6, 127.9, 127.8, 127.0, 115.4, 107.8, 30.9, 23.3, 21.8, 14.4; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 195.4; HRMS (ESI): m/z = 410.0659 calcd. For $C_{22}H_{20}NO_2Se$, found 410.0668 $[M + H]^+$.

7-Methyl-3-phenyl-4-(propylselanyl)-1*H*-pyrano[4,3-*b*]quinolin-1-one (4f). Yield: 89%; melting point: 163–165 °C; IR (neat): 2964, 1726, 1612, 1593, 1497, 1441, 1372, 1212, 1167, 1066, 1044, 1028, 934, 810, 795, 763, 699, 631, 475 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.13 (s, 1H), 8.07 (s, 1H), 7.92 (d, J = 8.7 Hz, 1H), 7.76–7.78 (m, 2H), 7.47–7.49 (m, 4H), 2.94 (t, J = 7.3 Hz, 2H), 2.63 (s, 3H), 1.56 (q, J = 7.3 Hz, 2H), 0.83 (t, J = 7.1 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.3, 159.0, 152.5, 151.9, 145.0, 140.3, 134.2, 130.2, 130.1, 130.0, 129.0, 129.0, 128.0, 125.1, 114.7, 107.8, 31.0, 23.3, 22.4, 14.4; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 195.67; HRMS (ESI): m/z = 410.0659 calcd. For $C_{22}H_{20}NO_2Se$, found 410.0658 $[M + H]^+$.

6-Methyl-3-phenyl-4-(propylselanyl)-1*H*-pyrano[4,3-*b*]quinolin-1-one (4g). Yield: 94%; melting point: 127–129 °C; IR (neat): 2962, 1725, 1595, 1566, 1488, 1443, 1421, 1371, 1179, 1092, 1076, 1064, 787, 771, 764, 689, 624, 649, 611, 599 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.13 (s, 1H), 7.85 (d, J = 7.8 Hz, 1H), 7.75–7.78 (m, 3H), 7.48–7.54 (m, 4H), 3.03 (t, J = 7.3 Hz, 2H), 2.92 (s, 3H), 1.55 (q, J = 7.5 Hz, 2H), 0.84 (d, J = 7.3 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.3, 159.0, 151.1, 151.0, 141.0, 138.0, 134.2, 133.3, 130.2, 130.1, 128.0, 127.4, 127.2, 127.0, 115.1, 108.1, 30.2, 23.3, 18.2, 14.4; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 200.75; HRMS (ESI): m/z = 432.0479 calcd. For $C_{22}H_{19}NO_2NaSe$, found 432.0460 $[M + Na]^+$.

3-Phenyl-4-(propylselanyl)-1*H*-pyrano[4,3-*b*]quinolin-1-one (4h). Yield: 70%; melting point: 146–148 °C; IR (neat): 2963, 1738, 1614, 1591, 1559, 1441, 1377, 1243, 1210, 1175, 1066, 1041, 953, 798, 773, 759, 697, 625, 478 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.21 (s, 1H), 8.29 (d, J = 8.7 Hz, 1H), 8.04 (d, J = 8.2 Hz, 1H), 7.92 (t, J = 7.6 Hz, 1H), 7.77 (q, J = 3.2 Hz, 2H), 7.65 (t, J = 7.6 Hz, 1H), 7.49 (t, J = 3.4 Hz, 3H), 2.94 (t, J = 7.3 Hz, 2H), 1.56 (q, J = 7.3 Hz, 2H), 0.84 (t, J = 7.3 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.1, 159.1, 152.5, 151.6, 140.8, 134.1, 133.4, 130.3, 130.1, 129.9, 129.3, 127.9, 127.6, 126.9, 115.5, 107.7, 30.9, 23.3, 14.4; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 196.13; HRMS (ESI): m/z = 396.0503 calcd. For $C_{21}H_{18}NO_2Se$, found 396.0507 $[M + H]^+$.

8-Methyl-4-(methylselanyl)-3-phenyl-1*H*-Pyrano[4,3-*b*]quinolin-1-one (4i). Yield: 85%; melting point: 163–165 °C; IR (neat): 2930, 1737, 1626, 1161, 1486, 1442, 1373, 1345, 1203, 1188, 1024, 946, 904, 832, 755, 701, 693, 622, 479 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.18 (d, J = 8.7 Hz, 1H), 7.76–7.80 (m, 4H), 7.50 (t, J = 3.2 Hz, 3H), 2.59 (s, 3H), 2.29 (d, J = 6.4 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.2, 157.8, 151.5, 150.3, 139.9, 137.8, 136.0, 134.0, 130.4, 130.0, 129.5, 128.0, 127.8, 127.0, 115.5, 108.8, 21.8, 9.7; ^{77}Se-NMR (75 MHz,

$CDCl_3$) δ 124.39; HRMS (ESI): m/z = 382.0346 calcd. For $C_{20}H_{16}NO_2Se$, found 382.0342 $[M + H]^+$.

7-Methyl-4-(methylselanyl)-3-phenyl-1*H*-pyrano[4,3-*b*]quinolin-1-one (4j). Yield: 88%; melting point: 154–156 °C; IR (neat): 2995, 1665, 1623, 1595, 1570, 1499, 1380, 1218, 1170, 1066, 1049, 1025, 882, 811, 795, 702, 631, 471 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.08 (s, 1H), 7.91 (d, J = 8.2 Hz, 1H), 7.78–7.81 (m, 2H), 7.50 (t, J = 3.2 Hz, 4H), 2.63 (s, 3H), 2.29 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.2, 158.2, 152.3, 151.8, 144.7, 140.3, 134.1, 130.4, 130.0, 128.9, 128.8, 128.0, 125.1, 114.7, 108.8, 22.4, 9.7; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 124.70; HRMS (ESI): m/z = 382.0346 calcd. For $C_{20}H_{16}NO_2Se$, found 382.0348 $[M + H]^+$.

6-Methyl-4-(methylselanyl)-3-phenyl-1*H*-pyrano[4,3-*b*]quinolin-1-one (4k). Yield: 82%; melting point: 147–149 °C; IR (neat): 2929, 1733, 1595, 1569, 1487, 1442, 1373, 1229, 1172, 1090, 1066, 1026, 903, 785, 759, 699, 695, 621 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.13 (s, 1H), 7.85 (d, J = 8.2 Hz, 1H), 7.75–7.81 (m, 3H), 7.49–7.54 (m, 4H), 2.93 (s, 3H), 2.34 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.2, 158.0, 151.0, 150.6, 140.8, 137.9, 134.1, 133.4, 130.4, 130.0, 128.0, 127.4, 127.2, 126.9, 115.1, 109.2, 18.1, 9.2; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 129.01; HRMS (ESI): m/z = 404.0166 calcd. For $C_{20}H_{15}NO_2NaSe$, found 404.0151 $[M + Na]^+$.

4-(Methylselanyl)-3-phenyl-1*H*-pyrano[4,3-*b*]quinolin-1-one (4l). Yield: 80%; melting point: 155–157 °C; IR (neat): 3046, 1730, 1609, 1590, 1574, 1442, 1336, 1212, 1175, 1028, 916, 796, 756, 699, 691, 627, 471 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.18 (s, 1H), 8.28 (d, J = 9.2 Hz, 1H), 8.02 (d, J = 8.2 Hz, 1H), 7.90–7.94 (m, 1H), 7.79–7.81 (m, 2H), 7.64 (t, J = 7.6 Hz, 1H), 7.50 (t, J = 3.2 Hz, 3H), 2.29 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.0, 158.3, 152.3, 151.6, 140.8, 134.0, 133.5, 130.5, 130.0, 130.0, 129.3, 128.1, 127.6, 126.9, 115.5, 108.7, 9.7; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 125.77; HRMS (ESI): m/z = 368.0190 calcd. For $C_{19}H_{14}NO_2Se$, found 368.0183 $[M + H]^+$.

8-Methyl-3-phenyl-4-(phenylselanyl)-1*H*-pyrano[4,3-*b*]quinolin-1-one (4m). Yield: 81%; melting point: 137–139 °C; IR (neat): 3043, 1626, 1591, 1484, 1476, 1438, 1437, 1372, 1202, 1188, 1067, 1045, 935, 830, 738, 703, 692, 649, 621, 613, 478 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.06 (s, 1H), 8.03 (d, J = 8.7 Hz, 1H), 7.67–7.73 (m, 4H), 7.37–7.44 (m, 5H), 7.09 (t, J = 3.2 Hz, 3H), 2.55 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.1, 160.5, 151.1, 150.4, 139.8, 137.9, 136.0, 133.9, 132.1, 131.6, 130.4, 130.0, 129.6, 129.0, 128.0, 127.7, 127.1, 126.8, 115.4, 109.6, 21.7; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 312.05; HRMS (ESI): m/z = 444.0503 calcd. For $C_{25}H_{18}NO_2Se$, found 444.0499 $[M + H]^+$.

7-Methyl-3-phenyl-4-(phenylselanyl)-1*H*-pyrano[4,3-*b*]quinolin-1-one (4n). Yield: 90%; melting point: 149–151 °C; IR (neat): 3056, 1743, 1733, 1622, 1596, 1567, 1498, 1475, 1443, 1212, 1172, 1143, 1070, 1041, 1018, 794, 730, 691, 632, 589, 473 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.10 (s, 1H), 7.93 (s, 1H), 7.87 (d, J = 8.2 Hz, 1H), 7.72 (dd, J = 8.0, 1.6 Hz, 2H), 7.37–7.44 (m, 6H), 7.10 (t, J = 3.2 Hz, 3H), 2.57 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.1, 161.0, 151.9, 151.9, 144.7, 140.3, 134.0, 132.2, 131.4, 130.4, 130.1, 129.9, 129.0, 128.8, 127.9, 126.7, 125.2, 114.7, 109.5, 22.4; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 311.89; HRMS (ESI): m/z = 444.0503 calcd. For $C_{25}H_{18}NO_2Se$, found 444.0492 $[M + H]^+$.

6-Methyl-3-phenyl-4-(phenylselanyl)-1*H*-pyrano[4,3-*b*]quinolin-1-one (4o). Yield: 82%; melting point: 161–163 °C; IR (neat): 3051, 1743, 1593, 1574, 1488, 1477, 1444, 1248, 1171, 1084, 1072, 1021, 949, 784, 773, 731, 699, 687, 651, 620 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1H), 7.77–7.81 (m, 3H), 7.65 (d, J = 6.9 Hz, 1H), 7.47 (dd, J = 13.1, 5.7 Hz, 4H), 7.34 (dd, J = 7.3, 2.3 Hz, 2H), 7.08–7.11 (m, 3H), 2.55 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.1, 160.7, 150.6, 150.3, 140.7, 138.4, 133.9, 133.2, 132.5, 130.5, 130.4, 130.0, 128.9, 128.0, 127.4, 127.0, 126.4, 115.1, 109.6, 17.8; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 319.28; HRMS (ESI): m/z = 466.0322 calcd. For $C_{25}H_{17}NO_2NaSe$, found 466.0319 $[M + Na]^+$.

3-Phenyl-4-(phenylselanyl)-1*H*-pyrano[4,3-*b*]quinolin-1-one (4p). Yield: 71%; melting point: 169–171 °C; IR (neat): 3061, 1735, 1592, 1573, 1557, 1490, 1334, 1214, 1182, 1056, 1020, 952, 798, 759, 734, 688, 700, 628, 475 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.18 (s, 1H), 8.14 (d, J = 7.8 Hz, 1H), 7.99 (d, J = 8.2 Hz, 1H), 7.84–7.88 (m, 1H), 7.72–7.74 (m, 2H), 7.59–7.63 (m, 1H), 7.38–7.46 (m, 5H), 7.08–7.11 (m, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.0, 161.0, 151.8, 151.7, 140.8, 133.9, 133.4, 132.0, 131.6, 130.5, 130.0, 129.2, 129.0, 128.0, 127.6, 127.0, 126.9, 115.5, 109.6; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 312.97; HRMS (ESI): m/z = 430.0346 calcd. For $C_{24}H_{16}NO_2Se$, found 430.0356 $[M + H]^+$.

8-Chloro-3-phenyl-4-(phenylselanyl)-1*H*-pyrano[4,3-*b*]quinolin-1-one (4q). Yield: 84%; melting point: 157–159 °C; IR (neat): 3065, 1732, 1611, 1594, 1574, 1474, 1436, 1196, 1172, 1070, 1047, 833, 734, 690, 681, 635, 617, 486 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.05 (d, J = 9.2 Hz, 1H), 7.92 (d, J = 2.3 Hz, 1H), 7.71–7.77 (m, 3H), 7.37–7.48 (m, 5H), 7.10 (t, J = 3.2 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 161.6, 161.2, 152.1, 150.0, 139.7, 134.3, 133.7, 133.5, 131.9, 131.6, 131.4, 130.6, 129.9, 129.3, 129.0, 128.0, 127.8, 127.5, 127.4, 126.9, 116.2, 109.3; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 314.51; HRMS (ESI): m/z = 463.9957 calcd. For $C_{24}H_{16}NO_2Se$, found 463.9968 $[M + H]^+$.

8-Chloro-4-(methylselanyl)-3-phenyl-1*H*-pyrano[4,3-*b*]quinolin-1-one (4r). Yield: 75%; melting point: 184–186 °C; IR (neat): 2970, 1738, 1592, 1474, 1442, 1366, 1229, 1217, 1204, 1066, 840, 775, 696, 637, 527 cm^{-1}; ^{1}H-NMR (400 MHz, CDCl3) δ 9.10 (s, 1H), 8.23 (d, J = 9.2 Hz, 1H), 8.00 (d, J = 2.3 Hz, 1H), 7.78–7.86 (m, 3H), 7.50–7.52 (m, 3H), 2.28 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 161.6, 158.6, 152.5, 149.9, 139.8, 134.4, 133.8, 133.5, 131.4, 130.6, 130.0, 128.1, 127.6, 127.4, 116.2, 108.5, 9.7; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 127.01; HRMS (ESI): m/z = 401.9800 calcd. For $C_{24}H_{16}NO_2Se$, found 401.9780 $[M + H]^+$.

6-Methoxy-3-phenyl-4-(phenylselanyl)-1*H*-pyrano[4,3-*b*]quinolin-1-one (4s). Yield: 69%; melting point: 173–175 °C; IR (neat): 3051, 1742, 1594, 1572, 1557, 1464, 1267, 1161, 1113, 1070, 1035, 941, 782, 732, 694, 682, 652, 560 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.07 (s, 1H), 7.74 (dd, J = 7.3, 2.3 Hz, 2H), 7.56 (dd, J = 7.3, 2.3 Hz, 2H), 7.50–7.51 (m, 2H), 7.42–7.44 (m, 3H), 7.17 (t, J = 4.6 Hz, 1H), 7.06–7.09 (m, 3H), 4.07 (s, 3H);

^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.0, 160.0, 155.8, 150.7, 143.8, 140.4, 133.9, 133.5, 131.3, 130.4, 130.1, 128.7, 128.1, 127.9, 127.9, 127.3, 120.7, 115.8, 111.6, 110.8, 56.6; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 314.05; HRMS (ESI): m/z = 460.0452 calcd. For $C_{24}H_{16}NO_2Se$, found 460.0424 $[M + H]^+$.

6-Methoxy-4-(methylselanyl)-3-phenyl-1*H*-pyrano[4,3-*b*]quinolin-1-one (4t). Yield: 70%; melting point: 191–193 °C; IR (neat): 2332, 1731, 1595, 1490, 1464, 1263, 1224, 1166, 1114, 1064, 1042, 974, 783, 746, 709, 690, 563 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 7.80–7.82 (m, 2H), 7.55–7.58 (m, 2H), 7.50 (q, J = 2.1 Hz, 3H), 7.21 (dd, J = 7.1, 1.6 Hz, 1H), 4.12 (s, 3H), 2.35 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.1, 157.3, 155.7, 151.1, 143.7, 140.4, 133.9, 130.4, 130.0, 128.1, 128.0, 127.9, 120.7, 115.7, 111.2, 109.4, 56.5, 9.7; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 130.24; HRMS (ESI): m/z = 398.0295 calcd. For $C_{24}H_{16}NO_2Se$, found 398.0270 $[M + H]^+$.

General procedure for the synthesis of 8-methyl-3-phenylbenzo[*b*][1,6]naphthyridin-1(2*H*)-one (5a) and 4-(butylselanyl)-8-methyl-3-phenylbenzo[*b*][1,6]naphthyridin-1(2*H*)-one (5b)

To a solution of **4a** (1 mmol) in 5 mL DMF was added an excess of 28% NH_4OH and stirred at 80 °C. After completion of the reaction, monitored by TLC, the reaction mixture was poured into ice-cold water. The solid product was filtered and washed with water and dried over Na_2SO_4. The resulting product was purified by column chromatography using *n*-hexane : ethyl acetate (70 : 30) as the eluent to afford **5a** and **5b** as yellow solids.

8-Methyl-3-phenylbenzo[*b*][1,6]naphthyridin-1(2*H*)-one (5a). Yield: 69%; melting point: 235–237 °C; IR (neat): 3007, 2918, 1675, 1654, 1621, 1591, 1499, 1490, 1444, 1220, 934, 862, 823, 771, 752, 688, 556, 498 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.26 (s, 1H), 9.17 (s, 1H), 8.05 (d, J = 8.7 Hz, 1H), 7.76 (dd, J = 8.0, 1.6 Hz, 4H), 7.54–7.58 (m, 3H), 7.14 (s, 1H), 2.59 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 150.3, 142.6, 137.3, 136.6, 135.5, 134.1, 130.3, 129.6, 128.6, 127.9, 126.6, 126.1, 119.7, 106.1, 21.8; HRMS (ESI): m/z = 287.1184 calcd. For $C_{19}H_{15}N_2O$, found 287.1183 $[M + H]^+$.

4-(Butylselanyl)-8-methyl-3-phenylbenzo[*b*][1,6]naphthyridin-1(2*H*)-one (5b). Yield: 22%; melting point: 214–216 °C; IR (neat): 2918, 2867, 1655, 1588, 1569, 1484, 1465, 1440, 1372, 1326, 1293, 1188, 1125, 1029, 938, 823, 702, 633, 496, 480 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.31 (s, 1H), 9.15 (s, 1H), 8.19 (d, J = 9.2 Hz, 1H), 7.79 (s, 1H), 7.71 (dd, J = 8.7, 2.3 Hz, 1H), 7.54 (qd, J = 6.8, 3.1 Hz, 5H), 2.95 (t, J = 7.3 Hz, 2H), 2.60 (s, 3H), 1.45 (q, J = 7.5 Hz, 2H), 1.21–1.26 (m, 2H), 0.76 (t, J = 7.3 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 163.3, 152.3, 150.1, 146.4, 137.6, 136.9, 136.8, 135.1, 129.8, 129.5, 129.3, 128.4, 127.5, 126.4, 119.7, 106.7, 32.0, 28.4, 22.8, 21.8, 13.6; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 190.74; HRMS (ESI): m/z = 423.0976 calcd. For $C_{23}H_{23}N_2OSe$, found 423.0982 $[M + H]^+$.

General procedure for the synthesis of 1-chloro-8-methyl-3-phenylbenzo[*b*][1,6]naphthyridine (6)

To a solution of **5a** (1.0 mmol) was added $POCl_3$ (1.0 mmol mL^{-1}) and refluxed for 12 h. After completion of the reaction, monitored by TLC, the resulting reaction mixture was poured into ice-cold water. The solid product was filtered and washed with water. The resulting product was purified by column chromatography using *n*-hexane : ethyl acetate (70 : 30) as the eluent to afford **6** as an orange solid. Yield: 96%; melting point: 150–152 °C; IR (neat): 3023, 2916, 1921, 1624, 1603, 1553, 1507, 1447, 1395, 1287, 1280, 1136, 1027, 966, 822, 688, 665, 643, 469 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.28 (s, 1H), 8.17–8.19 (m, 2H), 8.08 (d, J = 9.2 Hz, 1H), 7.69–7.74 (m, 2H), 7.53 (d, J = 7.3 Hz, 2H), 7.45 (t, J = 7.1 Hz, 1H), 2.53 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 152.3, 152.2, 150.6, 137.4, 137.3, 136.5, 135.7, 129.7, 129.0, 128.4, 127.4, 127.1, 120.1, 116.1, 21.9; HRMS (ESI): m/z = 305.0846 calcd. For $C_{19}H_{14}N_2Cl$, found 305.0849 $[M + H]^+$.

General procedure for the synthesis of 8-methyl-3-phenyl-1(phenylethynyl)benzo[*b*][1,6]naphthyridine (7a)

To a solution of 1-chloro-8-methyl-3-phenylbenzo[*b*][1,6]naphthyridine **6** (0.062 mmol, 1.0 equiv.) in 10 mL THF was added phenyl acetylene (0.080 mmol, 1.5 equiv.), NEt_3 (3.0 equiv.), $PdCl_2(PPh_3)_2Cl_2$ (4.4 mg, 5 mol%) and copper(I) iodide (1.19 mg, 5 mol%). The resulting mixture was stirred under a nitrogen atmosphere at room temperature for 15 h. After completion of the reaction, the solvent was removed under reduced pressure, the residue was extracted with ethyl acetate and purified by silica gel column chromatography using *n*-hexane : ethyl acetate (70 : 30) as the eluent to afford **7a** as a yellow solid. Yield: 60%; melting point: 147–149 °C; IR (neat): 2918, 2850, 2206, 1633, 1595, 1553, 1504, 1492, 1467, 1415, 1344, 1174, 1136, 1026, 922, 866, 820, 752, 738, 685, 668, 658, 650, 549, 527 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.23 (s, 1H), 8.37 (d, J = 0.9 Hz, 1H), 8.25–8.27 (m, 2H), 8.11 (d, J = 8.7 Hz, 1H), 7.80–7.83 (m, 3H), 7.70–7.73 (m, 1H), 7.54 (t, J = 7.6 Hz, 2H), 7.47 (dd, J = 6.6, 2.5 Hz, 4H), 2.58 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 153.6, 151.1, 149.7, 146.4, 138.7, 136.8, 135.9, 135.6, 132.5, 129.8, 129.3, 129.0, 128.94, 128.7, 127.4, 122.3, 122.0, 117.1, 94.9, 86.7, 21.9; HRMS (ESI): m/z = 371.1548 calcd. For $C_{27}H_{19}N_2$, found 371.1532 $[M + H]^+$.

General procedure for the synthesis of 8-methyl-1,3-diphenylbenzo[*b*][1,6]naphthyridine (7b)

To a solution of 1-chloro-8-methyl-3-phenylbenzo[*b*][1,6]naphthyridine **6** (20 mg, 0.050 mmol, 1.0 equiv.) in 4 mL DMF was added phenylboronic acid (9.1 mg, 0.075 mmol, 1.3 equiv.), $Pd(OAc)_2$ (1.1 mg, 1 mol%), and Cs_2CO_3 (48.7 mg, 0.150 mmol, 3.0 equiv.). The resulting mixture was heated at 110 °C for 12 h. The solvent was removed under reduced pressure; the residue was extracted with ethyl acetate and brine. The crude was purified by silica gel chromatography using *n*-hexane : ethyl acetate (70 : 30) as the eluent to afford **7b** as a yellow solid. Yield: 52%; melting point: 212–214 °C; IR (neat): 3056, 1634, 1598, 1557, 1514, 1492, 1446, 1338, 1192, 1176, 1127, 1028, 925, 820, 792, 705, 693, 656 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.42 (d, J = 0.9 Hz, 1H), 8.32–8.34 (m, 2H), 8.13 (d, J = 9.6 Hz, 1H), 7.88 (dd, J = 8.0, 1.6 Hz, 2H), 7.70–7.72 (m, 2H), 7.60–7.64 (m, 3H), 7.53 (t, J = 7.6

Hz, 2H), 7.44 (t, J = 7.3 Hz, 1H), 2.55 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.6, 152.7, 151.0, 150.6, 139.2, 139.1, 136.5, 136.2, 135.7, 130.4, 129.3, 129.1, 128.9, 128.8, 128.7, 127.5, 127.4, 127.1, 119.9, 115.7, 21.8. HRMS (ESI): m/z = 347.1548 calcd. For $C_{19}H_{14}N_2Cl$, found 347.1535 $[M + H]^+$.

General procedure for the synthesis of 8-methyl-3-phenylbenzo[*b*][1,6]naphthyridine (7c)

To a solution of the corresponding 1-chloro-8-methyl-3-phenylbenzo[*b*][1,6]naphthyridine **6** in 4 mL DMF (20 mg, 0.037 mmol, 1.0 equiv.) was added methyl acrylate (6.5 mg, 0.074 mmol, 2.0 equiv.), $Pd(OAc)_2$ (0.4 mg, 0.5 mol%), PPh_3 (9.8 mg, 0.037 mmol, 1.0 equiv.) and K_2CO_3 (10.3 mg, 0.074 mmol, 2.0 equiv.). The resulting mixture was heated under a nitrogen atmosphere for 12 h.[24] The solvent was removed under reduced pressure, and the residue was extracted with ethyl acetate and purified by silica gel column chromatography using *n*-hexane : ethyl acetate (70 : 30) as the eluent to afford **7c**, yellow solid. Yield: 20%; melting point: 184–186 °C; IR (neat): 2919, 1720, 1634, 1611, 1573, 1557, 1446, 1435, 1399, 1258, 1127, 951, 924, 911, 886, 824, 752, 700, 655, 601, 561 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.56 (s, 1H), 8.82 (s, 1H), 8.42 (s, 1H), 8.23–8.25 (m, 2H), 8.14 (d, J = 9.2 Hz, 1H), 7.80 (s, 1H), 7.73 (dd, J = 8.7, 1.8 Hz, 1H), 7.56 (dd, J = 7.1, 1.6 Hz, 2H), 7.44–7.48 (m, 1H), 2.60 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 154.7, 153.5, 151.1, 150.0, 139.1, 136.5, 136.1, 135.7, 129.2, 129.1, 129.0, 127.3, 127.1, 121.4, 116.8, 21.9. HRMS (ESI): m/z = 217.1235 calcd. For $C_{19}H_{14}N_2Cl$, found 217.1223 $[M + H]^+$.

Conflicts of interest

There are no conflicts to declare.

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