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Synthesis of 8-heteroaryl nitroxoline analogues via one-pot sequential Pd-catalyzed coupling reactions†

Helena Brodnik, Franc Požgan and Bogdan Štefane*

A series of 8-heteroaryl substituted quinolines were prepared, either by direct C–H arylation of five-membered heteroarenes, or Pd-catalyzed coupling of organoboron reagents with bromoquinolines. The use of (benzo)thiophenyl or (benzo)furanyl boron coupling partners allowed further C–H functionalization on the five-membered heteroaryl ring with aryl bromides in one flask to access a variety of polyconjugated molecular architectures. The developed methodology represents a simple approach towards 8-arylated analogues of the biologically interesting nitroxoline core.

Introduction

8-Arylquinoline is one of the pharmaceutically important scaffolds present in many molecules which have shown a variety of biological activity,¹ and has also been designed as a key structural element in materials science.² Recently, we have described the synthesis of new potential cathepsin B inhibitors based on 1,3,5-triazin-2(1*H*)-one³ and nitroxoline (8-hydroxy-5-nitroquinoline)⁴ scaffolds. To further explore the structure-activity relationship an efficient synthetic approach to obtain a variety of 8-(hetero)arylquinoline derivatives was required. Therefore, we focused on metal-catalyzed arylations, which have found a wide application in the synthesis of bi(hetero)-aryl systems. Indeed, the quinoline moiety has often been derivatized *via* Pd,⁵ Ni,⁶ Rh,⁷ Cu,⁸ and Ag-catalysed⁹ reactions producing mostly 2- and 4-arylated products. More recently, two methods for catalytic arylation of quinolines at the 8-position have been described,^{10,11} of which direct functionalization with a Rh(NHC)-based catalyst¹¹ appeared as the most attractive. In the course of development of cross-coupling synthetic methodologies some individual examples of quinoline arylation at the 8-position have also appeared in the literature. For example, the Suzuki reaction of 5-bromoindanone and (quinoline-8-yl)boronic acid gave the corresponding cross-coupling product in good yield.¹² Quinoline-8-yl triflate was used as a coupling partner in the decarboxylative arylation with potassium arylcarboxylates¹³ and arylation with potassium (hetero)aryltrifluoroborates¹⁴ catalyzed by Pd catalysts, while

5-methoxy-8-chloroquinoline coupled with phenylboronic acid in the presence of Ni(C) catalyst under relatively harsh reaction conditions.¹⁵ An example of Negishi cross-coupling of 8-chloroquinoline catalysed by a Ni(n)/diethyl phosphite system¹⁶ and regioselective functionalization of a quinoline moiety *via* magnesiation¹⁷ was described by Knochel and co-workers. Macdonald *et al.* described an elegant synthetic approach to phosphodiesterase type 4 photoaffinity probe by applying a cross-coupling step between 8-bromo-6-quinolinic acid and 3-aminobenzeneboronic acid.¹⁸

Results and discussion

From the retrosynthetic point of view, 8-heteroarylquinoline derivatives could simply be prepared by metal-catalyzed heteroarylation *via* C–H activation of furans, thiophenes, pyrroles, oxazoles, thiazoles, and their benzo derivatives with 8-haloquinolines. In most cases, intramolecular arylations or intermolecular C5-arylations of C2-substituted five membered heterocycles have been extensively studied.¹⁹ However, the direct arylation of some fundamental heterocycles, such as furan, thiophene, and pyrrole to prepare their 2-arylated derivatives was found to be problematic.²⁰ Guerchais, Doucet, and co-workers documented palladium-catalyzed direct heteroarylation of 8-bromoquinoline in moderate to good yields.²¹ Being aware of their successful examples we set out our synthetic approach towards 8-heteroarylquinoline derivatives *via* direct Pd-catalysed arylation of furan, thiophene, 1-methyl-1*H*-pyrrole, and their benzo derivatives. The starting material, 8-bromo-5-nitroquinoline (2), was prepared from commercially available 8-bromoquinoline (1). The most appropriate nitration reagent for 8-bromoquinoline was found to be an excess of

Faculty of Chemistry and Chemical Technology, University of Ljubljana, Večna pot 113, SI-1000 Ljubljana, Slovenia. E-mail: bogdan.stefane@fkkt.uni-lj.si

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KNO_3 in concentrated sulphuric acid, wherein the reaction time played a crucial role in obtaining a good yield (86%) of the product 2.

Having the starting materials in hand, we initiated the coupling chemistry with the model reaction of 8-bromoquinoline (1) with furan. After thorough screening of different catalytic systems and reaction conditions²² we found $\text{Pd}(\text{OAc})_2$ (5 mol%) in combination with SPhos (10 mol%) and K_3PO_4 as the base in NMP at 150 °C as optimal reaction conditions. When 5 equivalents of furan were used, we achieved a complete conversion of 8-bromoquinoline yielding 4a (Table 1) together with a significant amount of side product 5a (ratio 4a:5a = 1:2.4) produced by dimerization of 8-bromoquinoline. However, we were able to reduce the dimerization process of 8-bromoquinoline under the given reaction conditions only by applying a large excess of furan. When furan was used as a co-solvent (NMP-furan in a ratio of 1:1 (v/v)), the complete conversion of 8-bromoquinoline was achieved in 24 h at 150 °C and the ratio of products 4a:5a (10:1) changed in favour of the desired product 4a. Under the optimized reaction conditions both bromoquinolines 1 and 2 can be successfully coupled with furan, thiophene, and 1-methyl-1*H*-pyrrole only if they are used in a large excess (Table 1). On the other hand, the method, using a large excess of heteroarene, was found to be impractical for benzo[b]furan (3e) and benzo[b]thiophene (3f); for this reason only 5 equivalents of 3e and 3f were used. Even though, arylation of benzo[b]furan with 8-bromoquinino-

line (1) progressed up to 73% conversion in 24 h, it was accompanied by the pronounced dimerization of 8-bromoquinoline. Consequently, we were able to isolate only 8% of the pure product 4e. Slightly better but still unsatisfactory results were obtained with benzo[b]thiophene (Table 1, entry 6). It should be mentioned that the optimized reaction conditions failed for the coupling of 8-bromo-5-nitroquinoline (2) either with benzo[b]furan or benzo[b]thiophene resulting in a rather complex reaction mixture. For comparison, we also found that 8-bromoquinoline is much less reactive than the 2- or 3-bromo analogues, since they can be successfully coupled with furan at lower temperature (130 °C) using $\text{Pd}(\text{OAc})_2$ (1 mol%) and PPh_3 as a ligand.

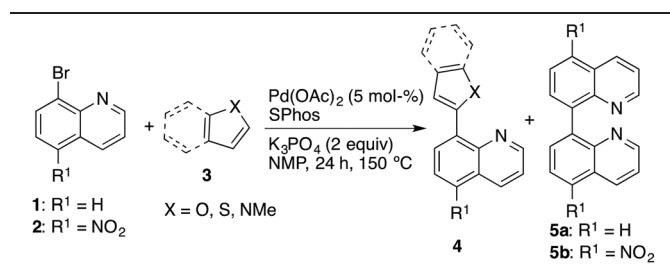
Since we found some limitations in the direct arylation approach with unsubstituted five-membered heteroarenes and being aware that it would be difficult to access targeted C3-quinolinyl heteroarenes we turned to the coupling chemistry with the model reaction of 8-bromoquinoline (1) with (furan-3-yl)-boronic acid testing different catalytic systems and reaction conditions.²² The reaction was found to be rather sluggish at temperatures below 80 °C in toluene in the presence of $\text{Pd}(\text{PPh}_3)_4$ or $\text{Pd}(\text{OAc})_2$ complexes. Thus, a set of different Pd-catalysts, most of which were generated *in situ* from a Pd-source and triphenylphosphine ligand, were tested in several solvents at 100 °C. Most of the commonly used Pd-precatalysts more or less successfully coupled 8-bromoquinoline with (furan-3-yl)-boronic acid. However, the catalyst system $\text{Pd}(\text{OAc})_2/\text{PPh}_3$, K_2CO_3 in the mixture of 1,4-dioxane/water 4:1 (v/v) was chosen to be the most practical. Moreover, the addition of water to the reaction mixture could also contribute to sufficiently solubilize the base.

In continuation, the scope of Suzuki–Miyaura cross-coupling of bromoquinolines 1 and 2 with different heteroarylboronic acids 6 was investigated by applying optimized reaction conditions. The reactions with both substrates 1 and 2 were complete in 3–24 h providing the corresponding 8-heteroarylquinoline coupling products 4 in good yields (Table 2). Since microwave (MW) conditions have been shown to be beneficial in some examples of Suzuki–Miyaura reactions,²³ we ran selected reactions under microwave irradiation at 100 °C in a 1,4-dioxane/water (4:1) solvent system for 3 h. However, our results show that there is no beneficial effect of using MW conditions, and in some cases even lower yields of the isolated products 4 were obtained (Table 2, yields in brackets).

Suzuki–Miyaura cross-coupling of 8-bromoquinolines 1 and 2 with heteroarylboronic acids 6a–g allowed the introduction of a variety of pyrrolyl, furanyl, thiophenyl, and their benzo analogues at the 8-position of the quinoline nucleus in good to excellent yields. In the case of using *N*-Boc-pyrrole-2-boronic acid (Table 2, entries 4 and 11) as the coupling partner the Boc group was removed in the course of the reaction, as also noticed by other researchers.²⁴

When 1 was coupled with (thiophene-3-yl)boronic acid (6c) in the presence of $\text{Pd}(\text{OAc})_2$ and PPh_3 at temperatures higher than 100 °C, beside 4l we also isolated a minor quantity (2%) of the side product 4l', 8,8'-(thiophene-2,3-diyl)diquinoline,

Table 1 Synthesis of the 8-heteroarylquinolines via Pd-catalyzed direct arylation



Entry	R^1	Heteroarene 3	Conversion % (4:5) ^c	4; (yield) ^d
1	H	Furan (3a)	100 (10:1) ^a	4a (48)
2	H	Thiophene (3b)	100 (10:1) ^a	4b (59)
3	H	2-Methylthiophene (3c)	100 (6:1) ^a	4c (39)
4	H	1-Methyl-1 <i>H</i> -pyrrole (3d)	100 (10:1) ^a	4d (61)
5	H	Benzo[b]furan (3e)	73 (1:2.7) ^b	4e (8)
6	H	Benzo[b]thiophene (3f)	100 (2:1) ^b	4f (28)
7	NO_2	Furan (3a)	100 ^a	4g (44)
8	NO_2	Thiophene (3b)	100 ^a	4h (53)
9	NO_2	2-Methylthiophene (3c)	100 (5:1) ^a	4i (35)
10	NO_2	1-Methyl-1 <i>H</i> -pyrrole (3d)	100	4j (57)

Conditions: ^a $\text{Pd}(\text{OAc})_2$ (5 mol%), SPhos (10 mol%), K_3PO_4 (1.0 mmol), 8-bromoquinoline 1 or 2 (0.5 mmol), heteroarene (1.0 mL), NMP (1.0 mL). ^b Heteroarene (2.5 mmol). ^c Ratio determined by ¹H NMR of the crude reaction mixture. ^d Isolated yields are given.

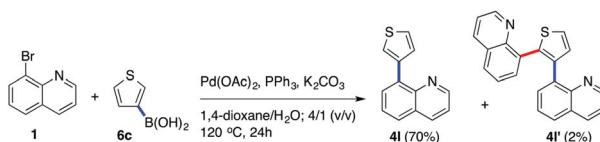


Table 2 Suzuki–Miyaura cross-coupling of **1** and **2** with heteroarylboronic acids **6**

	1: R¹ = H	Pd(OAc)₂, PPh₃, K₂CO₃, 1,4-dioxane/H₂O; 4/1 (v/v), 100 °C, 24 h	4
	2: R¹ = NO₂		
Entry	R ¹	Boronic acid 6	4; yield^a (MW-yield), %
1	H		4c; 70 (42)
2	H		4k; 85 (63)
3	H		4l; 70 (63)
4	H		4m; 57 (20)^b
5	H		4d; 96
6	H		4e; 97 (33)
7	H		4f; 92 (29)
8	NO ₂		4i; 74 (31)
9	NO ₂		4n; 85 (45)
10	NO ₂		4o; 90 (65)
11	NO ₂		4p; 62^b
12	NO ₂		4j; 99
13	NO ₂		4q; 79 (30)
14	NO ₂		4r; 69 (32)

^a Isolated yields are reported. ^b The Boc group was removed during the reaction.

arising from the arylation of the thiophene ring of the already formed Suzuki coupling product **4l** with 8-bromoquinoline (Scheme 1).

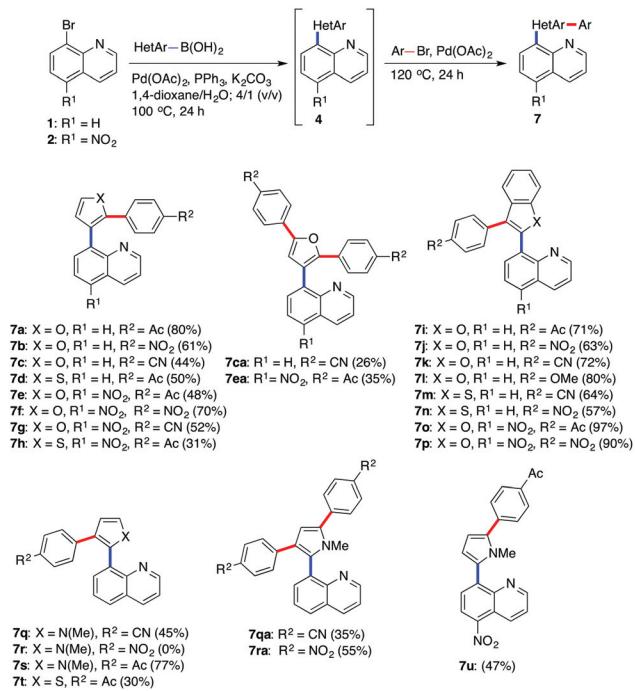


Scheme 1 Coupling reaction between **1** and **6c** at elevated temperature.

This result suggested that a one-pot Suzuki–Miyaura coupling reaction followed by C–H arylation of an already installed heteroarene moiety could be feasible. The development of multistep synthetic sequences in a single flask, such as tandem, cascade, or sequential reactions is highly desirable in the chemistry community. There are a number of advantages of such processes, such as reduction of cost, time, and waste. Additionally, such a methodology enables the production of large molecular diversity and the introduction of a wide degree of complexity in a single transformation.²⁵ There are several examples where the Suzuki–Miyaura coupling reaction was combined in a one-pot procedure, for example with C–H cross-coupling reaction,²⁶ Heck coupling,²⁷ isoxazole fragmentation,²⁸ Michael addition,²⁹ aza-Michael reaction,³⁰ and condensation reaction.³¹

Investigation towards one-pot sequential procedure was initiated with the Suzuki–Miyaura cross-coupling between 8-bromoquinoline (**1**) and (furan-3-yl)boronic acid (**6b**) employing the catalyst Pd(OAc)₂–PPh₃, and a 1,4-dioxane/H₂O solvent system. The subsequent C–H arylation was then carried out by simply adding 4-bromoacetophenone after the completion of the Suzuki coupling. In order to obtain high conversions, additional 5 mol% of the catalyst (Pd(OAc)₂) without the additional loading of the ligand (PPh₃) was required. The resulting reaction mixture was further stirred for 24 h while raising the temperature to 120 °C. Pleasingly, the expected arylated product **7a** was obtained in a high 80% isolated yield (Scheme 2). A 1,4-dioxane–H₂O, 4/1 (v/v) solvent system was found to be superior among the tested solvents (toluene, 1,4-dioxane, NMP, 2-propanol, and water). Even though 2-propano³² showed promising results in the Suzuki–Miyaura cross-coupling reaction, the subsequent C–H activation step was almost completely inhibited in this solvent. The Suzuki–Miyaura cross-coupling products of **1** and **2** with commercially available heteroarylboronic acids **6b**, **6c**, **6e**, **6f**, and **6g** allowed efficient subsequent C–H arylation of (benzo)furan, (benzo)thiophene, and pyrrole ring using different arylbromides as electrophiles, mostly affording monoarylated final products **7** (Scheme 2).

Detailed structural analysis of the monoarylated products **7a–h** using X-ray analysis and 2D NMR techniques confirmed the formation of C2 arylated products that is in consistency with the literature data published to a large extent by Doucet and co-workers on C3 substituted furans,³³ pyrroles,³⁴ and thiophenes.³⁵ The C–H arylation of 8-(thiophene-2-yl)- and 8-(*N*-methylpyrrol-2-yl)quinolines **4b** and **4d** (Scheme 2, products



Scheme 2 One-pot synthesis of quinoline derivatives 7 by sequential Suzuki–Miyaura cross-coupling/C–H arylation reaction.

7q–t) predominantly occurred at the C3 position rather than at C5. In case of arylation of nitro analogue 4j with 4-bromoacetophenone the C5 site selectivity was prevalent (Scheme 2, example 7u). To clarify the synthesis of 7t, the Suzuki–Miyaura reaction between 8-bromoquinoline (1) and potassium thiophene-2-yl trifluoroborate was achieved in 1,4-dioxane at 80 °C in the presence of a catalyst, which was synthesized from 2-aminobiphenyl, Pd(OAc)₂ and SPhos (catalyst A).³² However, our results indicate that the catalyst A is not successful in performing the C–H arylation synthetic step, consequently, the arylation step was then performed with loading of Pd(OAc)₂ (5 mol%), PPh₃ (10 mol%), and K₂CO₃ and heating the reaction mixture at 120 °C for 24 h. The final product 7t was isolated in a modest 30% yield.

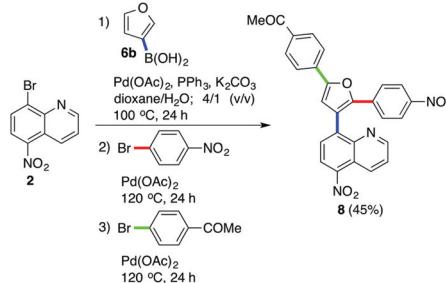
According to the ¹H NMR spectrum of the crude reaction mixtures only traces of diarylated products were detected. However, in four particular cases we were able to isolate the diarylated products 7ea, 7ea, 7qa and 7ra in pure form (Scheme 2). To minimize the formation of the diarylated products 0.80 equivalents of the aryl bromides were used in the arylation step assuming the complete conversion of the Suzuki–Miyaura cross-coupling reaction.

According to the results of regioselectivity in the above-mentioned examples one could suggest the directing influence of the quinoline nitrogen in C–H activations,³⁶ which is rather small due to a six-membered palladacyclic transition state and can be, in particular examples (Scheme 2, examples of mono-arylated product 7u and diarylated products 7ea and 7ea), overwritten by the greater reactivity of the C-5 position. Additionally,

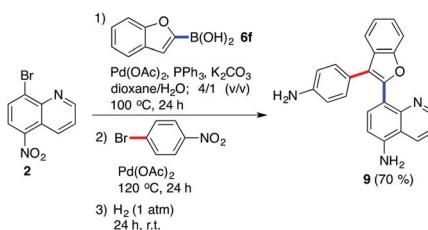
we speculate that the nitro group in the case of the C-5 arylated product 7u may also have influence on the reactivity of the C-5 position, since in the analogue product 7s (lacking nitro functionality) C-3 arylation occurred. The examination of the set of aryl bromides as the coupling partners revealed that the aryl halides bearing an electron-accepting group reacted relatively well with the 8-heteroarylquinoline derivatives under the given reaction conditions. 4-Bromoanisole, bearing an electron-donating group, was found to be less reactive. However, by simply elevating the reaction temperature from 120 °C to 150 °C we were able to isolate the desired product 7l in an 80% yield (Scheme 2).

Furthermore, we were able to accomplish a three-step one-pot transformation, which included the Suzuki–Miyaura cross-coupling reaction of 2 and 6b followed by two C–H arylations of the furan-3-yl moiety of the formed intermediate 4n using two different aryl bromides. The corresponding product 8 was isolated in a reasonable 45% yield (Scheme 3).

Finally, we examined the possibility of combining the Suzuki–Miyaura cross-coupling reaction, direct C–H arylation reaction, and hydrogenation reaction in a one-pot synthetic procedure. The Suzuki–Miyaura cross-coupling reaction of 8-bromo-5-nitroquinoline (2) and benzo[b]furan-2-yl boronic acid (6f) delivered product 4q which was arylated with 4-bromonitrobenzene and the crude reaction mixture was then exposed to the atmosphere (1 atm) of hydrogen at room temperature for 24 h. The final product 9 (Scheme 4) was isolated in good (70%) overall yield.



Scheme 3 One-pot synthesis of polyarylated furan.



Scheme 4 One-pot Suzuki–Miyaura cross-coupling/arylation/hydrogenation reaction sequence.



Conclusions

In summary, an original two-step single-flask palladium-catalyzed Suzuki–Miyaura cross-coupling/direct C–H arylation sequence was developed starting from readily available 8-bromo- and 8-bromo-5-nitroquinoline. The method enables a straightforward derivatization of primarily formed heteroaryl Suzuki–Miyaura cross-coupling products with aryl bromides as proelectrophiles. In addition, we have demonstrated that our single-flask multicoupling approach successfully allowed the preparation of a 2,5-non-symmetrically diarylated furanyl quinoline product **8** by implementing two consecutive arylation steps. This sequential synthetic approach supplies a variety of hetero(aryl) functionalized quinolines being potential inhibitors of the cathepsin family of enzymes. Furthermore, the photophysical and electrochemical properties of some synthesized products are under investigation.

Experimental

General information

Unless specified, commercial-grade reagents were used without further purification. Reactions were monitored by analytical thin-layer chromatography (TLC) or reverse-phase HPLC. Visualization of the developed TLC chromatogram was performed by UV absorbance or aqueous potassium permanganate. Flash chromatography was performed on 230–400-mesh silica gel with the indicated solvent system. Yields refer to chromatographically and spectroscopically (^1H and ^{13}C NMR) homogeneous materials. Melting points are uncorrected. Infra-red spectra were recorded on a FT-IR spectrometer and are reported in reciprocal centimeters (cm^{-1}). Routine nuclear magnetic resonance spectra were recorded either on a Bruker Avance DPX 300 or Avance III 500 MHz spectrometer. Chemical shifts for ^1H NMR spectra are recorded in parts per million (ppm) from tetramethylsilane as an internal standard. Data are reported as follows: chemical shift, multiplicity, (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, sext = sextet, sept = septet, m = multiplet, and br = broad), number of equivalent nuclei (by integration), coupling constants (J) quoted in Hertz to the nearest 0.25 Hz. Chemical shifts for the ^{13}C NMR spectra are recorded in parts per million from tetramethylsilane using the central peak of the solvent resonance as an internal standard. All spectra were obtained with complete proton decoupling. High-resolution mass spectra were recorded on an Agilent 6224 Accurate Mass TOF LC/MS instrument by electrospray ionization operating at a resolution of 15 000 full widths at half height.

8-Bromo-5-nitroquinoline (2). 8-Bromoquinoline (**1**) (2.3 g, 11.2 mmol) was slowly added to a mixture of H_2SO_4 (7 mL, 98%) and KNO_3 (4.5 g, 44.6 mmol) at 0 °C. The reaction mixture was allowed to warm to room temperature at which it was stirred for 2 h. The mixture was basified with a saturated solution of Na_2CO_3 to pH = 9 and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over

anhydrous Na_2SO_4 , filtered and evaporated under reduced pressure to obtain 2.42 g (86%) of pure product **2**.

Light yellow solid; R_f (light petroleum/EtOAc = 5/3) 0.48. FT-IR (ATR, neat): 3087, 1594, 1511, 1487, 1393, 1323, 1286, 921, 841, 806, 776 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.17 (dd, J = 4.0, 1.5 Hz, 1H), 9.07 (dd, J = 9.0, 1.5 Hz, 1H), 8.26 (d, J = 8.5 Hz, 1H), 8.20 (d, J = 8.5 Hz, 1H), 7.74 (dd, J = 9.0, 4.5 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 152.2, 145.0, 144.9, 133.3, 132.6, 131.4, 124.7, 122.1. HRMS (ESI $^-$): m/z calcd for $\text{C}_9\text{H}_6\text{BrN}_2\text{O}_2$ ($\text{M} + \text{H}$) $^+$: 252.9607; found: 252.9609. Elemental analysis calcd for $\text{C}_9\text{H}_5\text{BrN}_2\text{O}_2$: C, 42.72; H, 1.99; N, 11.07; found: C, 42.76; H, 1.83; N, 10.90.

General procedure for the synthesis of 8-heteroarylquinolines via Pd-catalyzed direct arylation (4a–j)

The corresponding quinoline (**1**, **2**) (0.50 mmol), $\text{Pd}(\text{OAc})_2$ (5.6 mg, 0.025 mmol), SPhos (20.5 mg, 0.050 mmol) and K_3PO_4 (212 mg, 1.00 mmol) were dissolved in NMP. In the case of direct arylation of furan (**3a**), thiophene (**3b**), 2-methylthiophene (**3c**) and 1-methyl-1*H*-pyrrole (**3d**) the latter were added as a co-solvent (1 mL and 1 mL of NMP). In the case of direct arylation of benzo[b]furan (**3e**) and benzo[b]thiophene (**3f**) 5 equiv. (2.50 mmol) and 2 mL of NMP were added. The reaction mixture was stirred in a sealed glass tube at 150 °C for 24 h under an inert atmosphere. The mixture was allowed to cool to r.t. to which water was added (3 mL) and the product was extracted into dichloromethane (2 × 3 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent was evaporated under reduced pressure. The crude product was purified by radial chromatography to yield pure product **4**.

8-(Furan-2-yl)quinoline (4a). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 20/1). Colorless oil (47 mg, 48%); R_f (light petroleum/EtOAc = 10/1) 0.51. FT-IR (ATR, neat): 3060, 1582, 1501, 1015, 818, 790, 736 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.00 (dd, J = 4.0, 2.0 Hz, 1H), 8.24 (dd, J = 7.5, 1.5 Hz, 1H), 8.16 (dd, J = 8.5, 2.0 Hz, 1H), 7.81 (d, J = 3.5 Hz, 1H), 7.71 (dd, J = 8.0, 1.5 Hz, 1H), 7.60–7.75 (m, 2H), 7.43 (dd, J = 8.0, 4.0 Hz, 1H), 6.61 (dd, J = 3.5, 2.0 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 151.3, 149.9, 144.3, 141.9, 136.4, 128.9, 128.6, 127.0, 126.4, 126.0, 121.0, 113.0, 112.1. HRMS (ESI $^+$): m/z calcd for $\text{C}_{13}\text{H}_{10}\text{NO}$ ($\text{M} + \text{H}$) $^+$: 196.0757; found: 196.0756.

8-(Thiophen-2-yl)quinoline (4b). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 50/1). Light yellow oil (62 mg, 59%); R_f (light petroleum/EtOAc = 10/1) 0.44. FT-IR (ATR, neat): 3065, 1494, 1311, 937, 820, 787, 694 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.01 (dd, J = 4.0, 2.0 Hz, 1H), 8.16 (dd, J = 8.0, 2.0 Hz, 1H), 8.06 (dd, J = 7.5, 1.5 Hz, 1H), 7.79 (dd, J = 3.5, 1.0 Hz, 1H), 7.73 (dd, J = 8.0, 1.5 Hz, 1H), 7.55 (dd, J = 8.0, 7.5 Hz, 1H), 7.48 (dd, J = 5.0, 1.0 Hz, 1H), 7.43 (dd, J = 8.0, 4.0 Hz, 1H), 7.17 (dd, J = 5.0, 3.5 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 149.5, 144.6, 139.7, 136.3, 133.0, 128.7, 128.0, 127.9, 127.1, 126.7, 126.6, 126.4, 121.2. HRMS (ESI $^+$): m/z calcd for $\text{C}_{13}\text{H}_{10}\text{NS}$ ($\text{M} + \text{H}$) $^+$: 212.0528; found: 212.0528.



8-(5-Methylthiophen-2-yl)quinoline (4c). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 20/1). Light green oil (44 mg, 39%); R_f (light petroleum/EtOAc = 10/1) 0.49. FT-IR (ATR, neat): 2914, 1496, 1474, 1046, 827, 794, 753, 650 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.00 (dd, J = 4.0, 2.0 Hz, 1H), 8.15 (dd, J = 8.5, 2.0 Hz, 1H), 8.01 (dd, J = 7.5, 1.5 Hz, 1H), 7.70 (dd, J = 8.0, 1.5 Hz, 1H), 7.57 (d, J = 3.5 Hz, 1H), 7.55–7.52 (m, 1H), 7.42 (dd, J = 8.0, 4.0, 1H), 6.82 (dd, J = 3.5, 1.0 Hz, 1H), 2.57 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 149.3, 144.6, 142.6, 137.3, 136.3, 133.4, 128.7, 127.4, 126.7, 126.6, 126.4, 124.9, 121.1, 15.3. HRMS (ESI $^+$): m/z calcd for $\text{C}_{14}\text{H}_{12}\text{NS}$ ($\text{M} + \text{H}$) $^+$: 226.0685; found: 226.0684.

8-(1-Methyl-1*H*-pyrrol-2-yl)quinoline (4d). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 50/1). Colorless oil (63 mg, 61%); R_f (light petroleum/EtOAc = 5/3) 0.46. FT-IR (ATR, neat): 3046, 2940, 1498, 1314, 958, 831, 706 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 8.95 (dd, J = 4.0, 2.0 Hz, 1H), 8.18 (dd, J = 8.0, 2.0 Hz, 1H), 7.83 (dd, J = 8.0, 1.5 Hz, 1H), 7.73 (dd, J = 7.0, 1.5 Hz, 1H), 7.58–7.55 (m, 1H), 7.39 (dd, J = 8.0, 4.0 Hz, 1H), 6.84–6.83 (m, 1H), 6.32–6.29 (m, 2H), 3.47 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 150.4, 147.0, 136.1, 133.0, 132.2, 131.9, 128.5, 127.9, 126.1, 123.2, 120.9, 110.0, 107.7, 35.3. HRMS (ESI $^+$): m/z calcd for $\text{C}_{14}\text{H}_{13}\text{N}_2$ ($\text{M} + \text{H}$) $^+$: 209.1073; found: 209.1074.

8-(Benzofuran-2-yl)quinoline (4e). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 20/1). Yellow solid (9 mg, 8%); mp = 102–104 $^{\circ}\text{C}$; R_f (light petroleum/EtOAc = 3/1) 0.46. FT-IR (ATR, neat): 3030, 1499, 1450, 1259, 1109, 821, 792, 741 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.07 (dd, J = 4.1, 1.8 Hz, 1H), 8.50 (dd, J = 7.4, 1.4 Hz, 1H), 8.30 (d, J = 0.9 Hz, 1H), 8.22 (dd, J = 8.2, 1.8 Hz, 1H), 7.81 (dd, J = 8.1, 1.4 Hz, 1H), 7.70–7.64 (m, 2H), 7.57 (dd, J = 8.2, 0.9 Hz, 1H), 7.49 (dd, J = 8.2, 4.1 Hz, 1H), 7.34–7.30 (m, 1H), 7.27–7.24 (m, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 154.2, 153.0, 150.1, 144.9, 136.5, 129.9, 128.6, 128.4, 128.2, 127.4, 126.3, 124.5, 122.7, 121.6, 121.2, 110.9, 109.6. HRMS (ESI $^+$): m/z calcd for $\text{C}_{17}\text{H}_{12}\text{NO}$ ($\text{M} + \text{H}$) $^+$: 246.0913; found: 246.0914. Elemental analysis calcd for $\text{C}_{17}\text{H}_{11}\text{NO}$: C, 83.25; H, 4.52; N, 5.71; found: C, 82.79; H, 4.33; N, 5.62.

8-(Benzothiophen-2-yl)quinoline (4f). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 20/1). Yellow solid (37 mg, 28%); mp = 79–80 $^{\circ}\text{C}$; R_f (light petroleum/EtOAc = 3/1) 0.41. FT-IR (ATR, neat): 3049, 1508, 1379, 1306, 932, 822, 740 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.07 (dd, J = 4.2, 1.8 Hz, 1H), 8.21 (dd, J = 8.2, 1.9 Hz, 1H), 8.17 (dd, J = 7.3, 1.4 Hz, 1H), 8.10 (s, 1H), 7.90–7.85 (m, 2H), 7.82 (dd, J = 8.1, 1.4 Hz, 1H), 7.62–7.59 (m, 1H), 7.48 (dd, J = 8.2, 4.1 Hz, 1H), 7.38–7.31 (m, 2H). ^{13}C NMR (125 MHz, CDCl_3): δ 149.7, 145.1, 141.6, 140.4, 139.7, 136.5, 133.0, 129.2, 128.8, 128.1, 126.4, 124.2, 124.1, 123.9, 123.7, 121.9, 121.4. HRMS (ESI $^+$): m/z calcd for $\text{C}_{17}\text{H}_{12}\text{NS}$ ($\text{M} + \text{H}$) $^+$: 262.0685; found: 262.0683. Elemental analysis calcd for $\text{C}_{17}\text{H}_{11}\text{NS}$: C, 78.13; H, 4.28; N, 5.36; found: C, 77.64; H, 3.87; N, 5.21.

8-(Furan-2-yl)-5-nitroquinoline (4g). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 20/1). Yellow solid (53 mg, 44%); mp = 153–156 $^{\circ}\text{C}$; R_f (light petroleum/

EtOAc = 10/1) 0.47. FT-IR (ATR, neat): 3117, 2920, 1499, 1322, 1183, 1025, 948, 811, 787, 738 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.11 (dd, J = 9.0, 2.0 Hz, 1H), 9.07 (dd, J = 4.0, 2.0 Hz, 1H), 8.43 (d, J = 8.5 Hz, 1H), 8.28 (d, J = 8.5 Hz, 1H), 8.08 (d, J = 3.5 Hz, 1H), 7.67–7.65 (m, 2H), 6.66 (dd, J = 3.5, 2.0 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 150.5, 149.9, 143.9, 143.5, 143.1, 134.0, 132.3, 125.1, 123.7, 123.2, 121.8, 117.4, 113.0. HRMS (ESI $^+$): m/z calcd for $\text{C}_{13}\text{H}_9\text{N}_2\text{O}_3$ ($\text{M} + \text{H}$) $^+$: 241.0608; found: 241.0608.

5-Nitro-8-(thiophen-2-yl)quinoline (4h). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 25/1). Yellow solid (68 mg, 53%); mp = 144–147 $^{\circ}\text{C}$; R_f (light petroleum/EtOAc = 10/1) 0.35. FT-IR (ATR, neat): 3088, 1558, 1498, 1418, 1397, 1327, 1305, 902, 851, 812 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.15 (dd, J = 9.0, 1.5 Hz, 1H), 9.11 (dd, J = 4.0, 1.5 Hz, 1H), 8.44 (d, J = 8.5 Hz, 1H), 8.17, (d, J = 8.5 Hz, 1H), 7.94 (d, J = 4.0 Hz, 1H), 7.69 (dd, J = 9.0, 4.0 Hz, 1H), 7.65 (d, J = 5.0, 1H), 7.22 (d, J = 5.0, 4.0 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 149.9, 143.8, 143.1, 139.9, 137.8, 132.4, 131.9, 128.9, 126.9, 125.1, 124.8, 123.9, 122.0. HRMS (ESI $^+$): m/z calcd for $\text{C}_{13}\text{H}_8\text{N}_2\text{O}_2\text{S}$ ($\text{M} + \text{H}$) $^+$: 257.0385; found: 257.0387.

8-(5-Methylthiophen-2-yl)-5-nitroquinoline (4i). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 20/1). Yellow solid (47 mg, 35%); mp = 162–164 $^{\circ}\text{C}$; R_f (light petroleum/EtOAc = 3/1) 0.46. FT-IR (ATR, neat): 2916, 1497, 1469, 1442, 1393, 1356, 844, 803, 783 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.15 (dd, J = 8.9, 1.7 Hz, 1H), 9.08 (dd, J = 4.1, 1.7 Hz, 1H), 8.42 (d, J = 8.4 Hz, 1H), 8.09 (d, J = 8.4 Hz, 1H), 7.75 (d, J = 3.8, 1H), 7.67 (dd, J = 8.9, 4.1 Hz, 1H), 6.88 (d, J = 3.8 Hz, 1H), 2.60 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 149.6, 147.2, 143.6, 142.4, 140.2, 135.3, 132.4, 129.2, 125.4, 125.3, 123.9, 123.8, 122.1, 15.4. HRMS (ESI $^+$): m/z calcd for $\text{C}_{14}\text{H}_{11}\text{N}_2\text{O}_2\text{S}$ ($\text{M} + \text{H}$) $^+$: 271.0536; found: 271.0536. Elemental analysis calcd for $\text{C}_{14}\text{H}_{10}\text{N}_2\text{O}_2\text{S}$: C, 62.21; H, 3.73; N, 10.36; found: C, 62.15; H, 3.87; N, 10.37.

8-(1-Methyl-1*H*-pyrrol-2-yl)-5-nitroquinoline (4j). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 10/1). Orange solid (72 mg, 57%); mp = 119–120 $^{\circ}\text{C}$; R_f (light petroleum/EtOAc = 5/3) 0.51. FT-IR (ATR, neat): 3119, 1509, 1497, 1328, 1311, 846, 814, 793, 735 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.08–9.05 (m, 2H), 8.40 (d, J = 8.0 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.64 (dd, J = 9.0, 4.0 Hz, 1H), 6.91–6.90 (m, 1H), 6.44 (dd, J = 3.5, 2.0 Hz, 1H), 6.34–6.33 (m, 1H), 3.52 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 151.1, 146.3, 144.3, 140.0, 132.0, 130.8, 129.2, 125.2, 124.4, 123.6, 121.7, 112.4, 108.5, 35.8. HRMS (ESI $^+$): m/z calcd for $\text{C}_{14}\text{H}_{12}\text{N}_3\text{O}_2$ ($\text{M} + \text{H}$) $^+$: 254.0924; found: 254.0925. Elemental analysis calcd for $\text{C}_{14}\text{H}_{11}\text{N}_3\text{O}_2$: C, 66.40; H, 4.38; N, 16.59; found: C, 66.17; H, 4.11; N, 16.37.

General procedure for Suzuki–Miyaura coupling (4k–r). The corresponding quinoline (1, 2) (0.25 mmol), boronic acid (6a–g) (0.375 mmol), $\text{Pd}(\text{OAc})_2$ (2.8 mg, 0.0125 mmol), PPh_3 (6.6 mg, 0.025 mmol) and K_2CO_3 (69 mg, 0.5 mmol) were dissolved in a mixture of 1,4-dioxane (0.8 mL) and water (0.2 mL). The reaction mixture was stirred in a sealed glass tube at 100 $^{\circ}\text{C}$ for 24 h under an inert atmosphere. The mixture was



allowed to cool to r.t. to which water was added (3 mL) and the product was extracted into dichloromethane (2×3 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent was evaporated under reduced pressure. The crude product was purified by radial chromatography to yield pure product **4**.

8-(Furan-3-yl)quinoline (4k). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 50/1). Colourless oil (42 mg, 85%); R_f (light petroleum/EtOAc = 5/3) 0.44. FT-IR (ATR, neat): 3045, 1511, 1497, 1158, 1028, 871, 794, 756, 645 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 8.98 (dd, J = 4.1, 1.8 Hz, 1H), 8.56 (s, 1H), 8.18 (dd, J = 8.3, 1.8 Hz, 1H), 7.87 (dd, J = 7.2, 1.4 Hz, 1H), 7.73 (dd, J = 8.2, 1.4 Hz, 1H) 7.57–7.54 (m, 2H), 7.43 (dd, J = 8.2, 4.1 Hz, 1H), 7.00 (d, J = 1.9 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 149.7, 145.7, 143.1, 142.3, 136.4, 131.5, 128.8, 127.8, 126.8, 126.4, 122.8, 121.1, 110.6. HRMS (ESI $^+$): m/z calcd for $\text{C}_{13}\text{H}_{10}\text{NO}$ ($\text{M} + \text{H}$) $^+$: 196.0757; found: 196.0757.

8-(Thiophen-3-yl)quinoline (4l). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 20/1). Yellow oil (37 mg, 70%); R_f (light petroleum/EtOAc = 5/3) 0.48. FT-IR (ATR, neat): 3034, 1607, 1529, 1133, 866, 830, 793, 754 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 8.97 (dd, J = 4.1, 1.8 Hz, 1H), 8.16 (dd, J = 8.2, 1.8 Hz, 1H), 7.89 (dd, J = 3.0, 1.3 Hz, 1H), 7.85 (dd, J = 7.2, 1.5 Hz, 1H), 7.75 (dd, J = 8.1, 1.4 Hz, 1H), 7.66 (dd, J = 5.0, 1.4 Hz, 1H), 7.56–7.53 (m, 1H), 7.42 (dd, J = 5.0, 3.0 Hz, 1H), 7.39 (dd, J = 8.2, 4.1 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 150.0, 145.8, 139.5, 136.3, 135.1, 129.7, 129.4, 128.8, 127.3, 126.3, 124.7, 124.5, 121.0. HRMS (ESI $^+$): m/z calcd for $\text{C}_{13}\text{H}_{10}\text{NS}$ ($\text{M} + \text{H}$) $^+$: 212.0528; found: 212.0530. Elemental analysis calcd for $\text{C}_{13}\text{H}_9\text{NS}$: C, 73.90; H, 4.29; N, 6.63; found: C, 73.75; H, 4.16; N, 6.57.

8-(1H-Pyrrol-2-yl)quinoline (4m). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 20/1). Yellow solid (28 mg, 57%); mp = 86–90 $^{\circ}\text{C}$; R_f (light petroleum/EtOAc = 10/1) 0.46. FT-IR (ATR, neat): 3305, 1775, 1498, 1312, 1111, 1081, 802, 721 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 12.62 (s, 1H), 8.90 (dd, J = 4.2, 1.9 Hz, 1H), 8.18–8.11 (m, 2H), 7.61–7.58 (m, 1H), 7.55–7.50 (m, 1H), 7.41 (dd, J = 8.3, 4.2 Hz, 1H), 7.03–7.01 (m, 1H), 6.91–6.89 (m, 1H), 6.35–6.32 (m, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 148.5, 144.6, 137.1, 131.6, 129.1, 129.0, 126.8, 125.0, 124.9, 120.8, 119.1, 108.9, 107.0. HRMS (ESI $^+$): m/z calcd for $\text{C}_{13}\text{H}_{11}\text{N}_2$ ($\text{M} + \text{H}$) $^+$: 195.0917; found: 195.0916.

8-(Furan-3-yl)-5-nitroquinoline (4n). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 20/1). Yellow solid (51 mg, 85%); mp = 117–119 $^{\circ}\text{C}$; R_f (light petroleum/EtOAc = 3/1) 0.49. FT-IR (ATR, neat): 3121, 1510, 1500, 1315, 1158, 1143, 868, 808 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.09 (dd, J = 8.9, 1.7 Hz, 1H), 9.07–9.05 (m, 1H), 8.74 (s, 1H), 8.39 (d, J = 8.2 Hz, 1H), 7.90 (d, J = 8.2, 1H), 7.66 (dd, J = 8.9, 4.1 Hz, 1H), 7.59–7.58 (m, 1H), 7.01–7.00 (m, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 150.4, 145.5, 145.1, 143.4, 142.9, 138.9, 132.3, 125.2, 124.9, 123.7, 121.8 (2C), 110.2. HRMS (ESI $^+$): m/z calcd for $\text{C}_{13}\text{H}_9\text{N}_2\text{O}_3$ ($\text{M} + \text{H}$) $^+$: 241.0608; found: 241.0611. Elemental analysis calcd for $\text{C}_{13}\text{H}_8\text{N}_2\text{O}_3$: C, 65.00; H, 3.36; N, 11.66; found: C, 64.67; H, 3.50; N, 12.04.

5-Nitro-8-(thiophen-3-yl)quinoline (4o). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 20/1). Yellow solid (58 mg, 90%); mp = 143–145 $^{\circ}\text{C}$; R_f (light petroleum/EtOAc = 3/1) 0.44. FT-IR (ATR, neat): 3089, 1492, 1326, 1291, 1208, 1140, 851, 793, 774 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.11–9.07 (m, 2H), 8.40 (d, J = 8.2 Hz, 1H), 8.06 (dd, J = 3.0, 1.3 Hz, 1H), 7.93 (d, J = 8.2 Hz, 1H), 7.68–7.63 (m, 2H), 7.49–7.46 (m, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 150.9, 145.5, 144.1, 142.0, 138.0, 132.1, 129.6, 127.4, 127.2, 125.2, 124.6, 123.6, 121.9. HRMS (ESI $^+$): m/z calcd for $\text{C}_{13}\text{H}_9\text{N}_2\text{O}_2\text{S}$ ($\text{M} + \text{H}$) $^+$: 257.0379; found: 257.0376. Elemental analysis calcd for $\text{C}_{13}\text{H}_8\text{N}_2\text{O}_2\text{S}$: C, 60.93; H, 3.15; N, 10.93; found: C, 60.66; H, 2.94; N, 10.84.

5-Nitro-8-(1H-pyrrol-2-yl)quinoline (4p). Radial chromatography on silica gel (eluting with petroleum ether/dichloromethane; 2/1). Orange solid (37 mg, 62%); mp = 147–148 $^{\circ}\text{C}$; R_f (light petroleum/EtOAc = 3/1) 0.48. FT-IR (ATR, neat): 3307, 1562, 1494, 1311, 1044, 857, 743 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 12.68 (s, 1H), 9.25 (dd, J = 9.0, 1.5 Hz, 1H), 8.99 (dd, J = 4.0, 1.5 Hz, 1H), 8.42 (d, J = 8.5 Hz, 1H), 8.08 (d, J = 8.5 Hz, 1H), 7.66 (dd, J = 9.0, 4.0 Hz, 1H), 7.14–7.13 (m, 1H), 7.09–7.07 (m, 1H), 6.41–6.39 (m, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 149.1, 143.7, 140.9, 135.8, 133.2, 130.1, 126.1, 123.6, 122.9, 122.3, 122.2, 111.8, 110.4. HRMS (ESI $^+$): m/z calcd for $\text{C}_{13}\text{H}_{10}\text{N}_3\text{O}_2$ ($\text{M} + \text{H}$) $^+$: 240.0768; found: 240.0766. Elemental analysis calcd for $\text{C}_{13}\text{H}_9\text{N}_3\text{O}_2$: C, 65.27; H, 3.79; N, 17.56; found: C, 65.11; H, 3.69; N, 17.13.

8-(Benzofuran-2-yl)-5-nitroquinoline (4q). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 20/1). Yellow solid (57 mg, 79%); mp = 183–185 $^{\circ}\text{C}$; R_f (light petroleum/EtOAc = 3/1) 0.49. FT-IR (ATR, neat): 2919, 1562, 1499, 1449, 1312, 834, 812, 740 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.15–9.14 (m, 1H), 9.12–9.10 (m, 1H), 8.55–8.53 (m, 2H), 8.47–8.45 (m, 1H), 7.74–7.70 (m, 2H), 7.59–7.58 (m, 1H), 7.41–7.38 (m, 1H), 7.31–7.28 (m, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 154.7, 151.1, 150.7, 144.4, 144.1, 134.6, 132.4, 129.5, 126.0, 124.8 (2C), 123.8, 123.2, 122.3, 121.7, 113.6, 111.2. HRMS (ESI $^+$): m/z calcd for $\text{C}_{17}\text{H}_{11}\text{N}_2\text{O}_3$ ($\text{M} + \text{H}$) $^+$: 291.0764; found: 291.0766.

8-(Benz[b]thiophen-2-yl)-5-nitroquinoline (4r). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 20/1). Yellow solid (53 mg, 69%); mp = 149–152 $^{\circ}\text{C}$; R_f (light petroleum/EtOAc = 5/3) 0.49. FT-IR (ATR, neat): 3051, 1509, 1492, 1329, 1303, 815, 791, 739 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.17–9.14 (m, 2H), 8.46 (d, J = 8.5 Hz, 1H), 8.28 (d, J = 8.5 Hz, 1H), 8.24 (s, 1H), 7.93–7.90 (m, 2H), 7.73 (dd, J = 9.0, 4.0 Hz, 1H), 7.41–7.39 (m, 2H). ^{13}C NMR (125 MHz, CDCl_3): δ 150.1, 144.4, 143.8, 143.0, 139.8, 138.9, 138.3, 132.3, 126.2, 126.1, 125.4, 124.6, 124.5, 124.3, 124.0, 122.0, 121.9. HRMS (ESI $^+$): m/z calcd for $\text{C}_{17}\text{H}_{11}\text{N}_2\text{O}_2\text{S}$ ($\text{M} + \text{H}$) $^+$: 307.0536; found: 307.0538.

Procedure for Suzuki–Miyaura coupling with potassium thiophene-2-trifluoroborate

Quinoline **1** (0.50 mmol), potassium thiophene-2-trifluoroborate (1.50 mmol) and the Pd catalyst **A** (36 mg, 0.05 mmol)

were dissolved in 1,4-dioxane. The reaction mixture was stirred in a sealed glass tube at 80 °C for 48 h under an inert atmosphere. The mixture was allowed to cool to r.t. to which water was added (5 mL) and the product was further extracted into dichloromethane (2 × 5 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the solvent was evaporated under reduced pressure. The crude product was purified by radial chromatography to yield pure product **4b**.

General procedure for one-pot sequential Suzuki–Miyaura coupling and direct C–H functionalization

The corresponding quinoline (1, 2) (0.50 mmol), boronic acid 6 (0.75 mmol), $\text{Pd}(\text{OAc})_2$ (5.6 mg, 0.025 mmol), PPh_3 (13.1 mg, 0.05 mmol) and K_2CO_3 (207 mg, 1.5 mmol) were dissolved in a mixture of 1,4-dioxane (1.6 mL) and water (0.4 mL). The reaction mixture was stirred in a sealed glass tube at 100 °C for 24 h under an inert atmosphere. After allowing the mixture to cool to r.t. the glass tube was opened to which the aryl bromide (0.40 mmol) and $\text{Pd}(\text{OAc})_2$ (5.6 mg, 0.025 mmol) were added. The reaction mixture was again sealed and further stirred at 120 °C for 24 h under an inert atmosphere. The mixture was allowed to cool to r.t. to which water was added (5 mL) and the product was further extracted with dichloromethane (2 × 5 mL). The combined organic layers were dried (Na_2SO_4), filtered and the solvent was evaporated under reduced pressure. The crude product was purified by radial chromatography to yield pure product 7.

8,8'-(Thiophene-2,3-diyl)diquinoline (4l'). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 5/1). Yellow solid (3 mg, 2%); mp = 242–247 °C; R_f (light petroleum/EtOAc = 1/1) 0.48. FT-IR (ATR, neat): 3048, 1572, 1492, 905, 900, 825, 785, 750, 729, 667 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 8.90 (dd, J = 4.2, 1.8 Hz, 1H), 8.85 (dd, J = 4.2, 1.8 Hz, 1H), 8.13–8.09 (m, 2H), 7.65–7.60 (m, 3H), 7.47 (d, J = 5.2 Hz, 1H), 7.41 (dd, J = 7.2, 1.4 Hz, 1H), 7.38–7.33 (m, 3H), 7.21–7.18 (m, 2H). ^{13}C NMR (125 MHz, CDCl_3): δ 149.9, 149.8, 146.8, 146.6, 138.3, 136.9, 136.4, 136.0 (2C), 133.8, 132.3, 131.5, 131.2, 128.5, 128.4, 127.5, 127.0, 126.0, 125.9, 125.3, 120.9, 120.8. HRMS (ESI $^+$): m/z calcd for $\text{C}_{22}\text{H}_{15}\text{N}_2\text{S}$ (M + H) $^+$: 339.0950; found: 339.0951.

1-[4-[3-(Quinolin-8-yl)furan-2-yl]phenyl]ethan-1-one (7a). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 10/1). Yellow solid (100 mg, 80%); mp = 180–185 °C; R_f (light petroleum/EtOAc = 5/3) 0.48. FT-IR (ATR, neat): 2923, 1671, 1602, 1357, 1261, 831, 795, 730 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 8.91 (dd, J = 4.0, 2.0 Hz, 1H), 8.24 (dd, J = 8.5, 2.0 Hz, 1H), 7.89 (dd, J = 8.0, 1.5 Hz, 1H), 7.75–7.74 (AA'BB', J = 8.5 Hz, 2H), 7.71 (dd, J = 7.0, 1.5 Hz, 1H), 7.67 (d, J = 2.0 Hz, 1H), 7.57–7.54 (m, 1H), 7.46–7.43 (m, 3H), 6.76 (d, J = 1.7 Hz, 1H), 2.52 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 197.5, 150.5, 148.5, 146.5, 142.2, 136.4, 135.6, 135.1, 133.3, 131.1, 128.9, 128.3, 128.2, 126.4, 125.3, 122.2, 121.4, 116.4, 26.5. HRMS (ESI $^+$): m/z calcd for $\text{C}_{21}\text{H}_{16}\text{NO}_2$ (M + H) $^+$: 314.1176; found: 314.1171.

8-[2-(4-Nitrophenyl)furan-3-yl]quinoline (7b). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc;

10/1). Yellow solid (77 mg, 61%); mp = 217–220 °C; R_f (light petroleum/EtOAc = 5/3) 0.31. FT-IR (ATR, neat): 3124, 1771, 1753, 1240, 1056, 831, 693 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 8.88 (dd, J = 4.0, 2.0 Hz, 1H), 8.26 (dd, J = 8.5, 2.0 Hz, 1H), 8.01–7.99 (AA'BB', J = 9.0 Hz, 2H), 7.92 (dd, J = 8.0, 1.5 Hz, 1H), 7.73 (dd, J = 7.0, 1.5 Hz, 1H), 7.70 (d, J = 2.0 Hz, 1H), 7.61–7.58 (m, 1H), 7.50–7.44 (m, 3H), 6.77 (d, J = 2.0 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 150.7, 147.4, 146.3, 146.0, 143.0, 137.2, 136.5, 132.9, 131.0, 128.9, 128.6, 126.4, 125.6 (2C), 123.7, 123.6 (2C), 121.5, 116.7. HRMS (ESI $^+$): m/z calcd for $\text{C}_{19}\text{H}_{13}\text{N}_2\text{O}_3$ (M + H) $^+$: 317.0921; found: 317.0920.

4-[3-(Quinolin-8-yl)furan-2-yl]benzonitrile (7c). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 10/1). Orange solid (52 mg, 44%); mp = 106–110 °C; R_f (light petroleum/EtOAc = 5/3) 0.40. FT-IR (ATR, neat): 3108, 2219, 1605, 1499, 1063, 828, 797, 753 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 8.89 (dd, J = 4.0, 2.0 Hz, 1H), 8.24 (dd, J = 8.5, 2.0 Hz, 1H), 7.90 (dd, J = 8.0, 1.5 Hz, 1H), 7.71 (dd, J = 7.0, 1.5 Hz, 1H), 7.67 (d, J = 2.0 Hz, 1H), 7.59–7.56 (m, 1H), 7.46–7.40 (m, 5H), 6.75 (d, J = 2.0 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 150.6, 147.6, 146.3, 142.6, 136.4, 135.4, 133.0, 132.0 (2C), 131.0, 128.9, 128.5, 126.4, 125.6 (2C), 122.9, 121.5, 119.0, 116.5, 109.8. HRMS (ESI $^+$): m/z calcd for $\text{C}_{20}\text{H}_{13}\text{N}_2\text{O}$ (M + H) $^+$: 297.1022; found: 297.1022.

1-[4-[3-(Quinolin-8-yl)thiophen-2-yl]phenyl]ethan-1-one (7d). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 10/1). Yellow solid (66 mg, 50%); mp = 207–210 °C; R_f (light petroleum/EtOAc = 5/3) 0.38. FT-IR (ATR, neat): 3043, 1675, 1599, 1357, 1265, 828, 794, 723 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 8.90 (dd, J = 4.0, 2.0 Hz, 1H), 8.20 (dd, J = 8.5, 2.0 Hz, 1H), 7.81 (dd, J = 8.0, 2.0 Hz, 1H), 7.71–7.70 (AA'BB', J = 8.5 Hz, 2H), 7.49–7.48 (m, 1H), 7.46–7.40 (m, 3H), 7.35 (d, J = 5.0 Hz, 1H), 7.28–7.26 (m, 2H), 2.51 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 197.6, 150.4, 146.7, 139.6, 139.1, 137.1, 136.2, 135.6, 135.2, 132.7, 131.7, 130.9, 128.8 (2C), 128.3 (2C), 127.8, 126.2, 124.6, 121.2, 26.5. HRMS (ESI $^+$): m/z calcd for $\text{C}_{21}\text{H}_{16}\text{NOS}$ (M + H) $^+$: 330.0947; found: 330.0945.

1-[4-[3-(5-Nitroquinolin-8-yl)furan-2-yl]phenyl]ethan-1-one (7e). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 10/1). Yellow solid (69 mg, 48%); mp = 218–220 °C; R_f (light petroleum/EtOAc = 5/3) 0.39. FT-IR (ATR, neat): 3137, 1673, 1601, 1515, 1500, 1335, 1250, 812 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.10 (dd, J = 8.9, 1.7 Hz, 1H), 8.99 (dd, J = 4.1, 1.7 Hz, 1H), 8.35 (d, J = 8.0 Hz, 1H), 7.81–7.78 (m, 3H), 7.70 (d, J = 1.8, 1H), 7.86 (dd, J = 8.9, 4.1 Hz, 1H), 7.43–7.42 (m, 2H), 6.79 (d, J = 1.8 Hz, 1H), 2.54 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 197.3, 151.3, 149.5, 146.2, 145.0, 142.6, 141.0, 135.7, 134.8, 132.2, 129.2, 128.5 (2C), 125.9 (2C), 124.3, 124.1, 121.9, 120.7, 116.0, 26.5. HRMS (ESI $^+$): m/z calcd for $\text{C}_{21}\text{H}_{15}\text{N}_2\text{O}_4$ (M + H) $^+$: 359.1026; found: 359.1023. Elemental analysis calcd for $\text{C}_{21}\text{H}_{14}\text{N}_2\text{O}_4$: C, 70.39; H, 3.94; N, 7.82; found: C, 70.40; H, 3.70; N, 7.52.

5-Nitro-8-[2-(4-nitrophenyl)furan-3-yl]quinoline (7f). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 10/1). Yellow solid (101 mg, 70%); mp = 254–256 °C; R_f (light petroleum/EtOAc = 5/3) 0.51. FT-IR (ATR, neat): 3091,



1595, 1500, 1324, 1103, 1072, 851, 795, 705 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.10 (dd, J = 8.9, 1.7 Hz, 1H), 8.96 (dd, J = 4.1, 1.7 Hz, 1H), 8.39 (d, J = 8.0 Hz, 1H), 8.06–8.04 (m, 2H), 7.82 (d, J = 8.0 Hz, 1H), 7.74 (d, J = 1.9 Hz, 1H), 7.69 (dd, J = 8.9, 4.1 Hz, 1H), 7.48–7.46 (m, 2H), 6.79 (d, J = 1.9 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 151.5, 148.3, 146.5, 146.0, 145.3, 143.3, 140.4, 136.6, 132.3, 129.1, 126.1 (2C), 124.3, 124.2, 123.9 (2C), 122.0, 121.9, 116.3. HRMS (ESI $^+$): m/z calcd for $\text{C}_{19}\text{H}_{12}\text{N}_3\text{O}_5$ ($\text{M} + \text{H}$) $^+$: 362.0771; found: 362.0770.

4-[3-(5-Nitroquinolin-8-yl)furan-2-yl]benzonitrile (7g). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 10/1). Yellow solid (71 mg, 52%); mp = 157–161 $^\circ\text{C}$; R_f (light petroleum/EtOAc = 5/3) 0.46. FT-IR (ATR, neat): 3084, 2221, 1604, 1504, 1328, 1068, 896, 840, 786, 728 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.09 (dd, J = 8.9, 1.6 Hz, 1H), 8.96 (dd, J = 4.2, 1.6 Hz, 1H), 8.38 (d, J = 8.0 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.71 (d, J = 1.7 Hz, 1H), 7.69 (dd, J = 8.9, 4.2 Hz, 1H), 7.48–7.46 (m, 2H), 7.42–7.40 (m, 2H), 6.78 (d, J = 1.7 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 151.4, 148.5, 146.0, 145.2, 143.0, 140.5, 134.7, 132.2, 132.1 (2C), 129.0, 126.0 (2C), 124.3, 124.2, 121.9, 121.3, 118.7, 116.2, 110.7. HRMS (ESI $^+$): m/z calcd for $\text{C}_{20}\text{H}_{12}\text{N}_3\text{O}_3$ ($\text{M} + \text{H}$) $^+$: 342.0873; found: 342.0870.

1-[4-[3-(5-Nitroquinolin-8-yl)thiophen-2-yl]phenyl]ethan-1-one (7h). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 10/1). Orange solid (46 mg, 31%); mp = 205–209 $^\circ\text{C}$; R_f (light petroleum/EtOAc = 5/3) 0.42. FT-IR (ATR, neat): 3100, 1675, 1597, 1513, 1333, 1263, 864, 797, 736, 725 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.06 (dd, J = 9.0, 2.0 Hz, 1H), 8.98 (dd, J = 4.0, 2.0 Hz, 1H), 8.24 (d, J = 8.0 Hz, 1H), 7.76–7.74 (AA'BB', J = 8.5 Hz, 2H), 7.64 (dd, J = 9.0, 4.0 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.52 (d, J = 5.0 Hz, 1H), 7.34 (d, J = 5.0 Hz, 1H), 7.26–7.24 (AA'BB', J = 8.5 Hz, 2H), 2.53 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 197.2, 151.2, 146.3, 144.7, 143.0, 140.8, 138.8, 135.7, 135.3, 132.3, 132.1, 129.8, 129.0 (2C), 128.6 (2C), 125.1, 124.2, 123.9, 121.8, 26.5. HRMS (ESI $^+$): m/z calcd for $\text{C}_{21}\text{H}_{15}\text{N}_2\text{O}_3\text{S}$ ($\text{M} + \text{H}$) $^+$: 375.0798; found: 375.0789.

4,4'-[3-(Quinolin-8-yl)furan-2,5-diyl]dibenzonitrile (7ca). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 5/1). Orange solid (41 mg, 26%); mp > 250 $^\circ\text{C}$; R_f (light petroleum/EtOAc = 1/1) 0.68. FT-IR (ATR, neat): 3117, 2221, 1599, 1497, 938, 827, 790, 758 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 8.90 (dd, J = 4.0, 2.0 Hz, 1H), 8.28 (dd, J = 8.5, 2.0 Hz, 1H), 7.95 (dd, J = 8.0, 1.5 Hz, 1H), 7.89–7.87 (AA'BB', J = 8.5 Hz, 2H), 7.75 (dd, J = 7.0, 1.5 Hz, 1H), 7.73–7.71 (AA'BB', J = 8.5 Hz, 2H), 7.63–7.60 (m, 1H), 7.52–7.45 (m, 5H), 7.17 (s, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 151.5, 150.8, 148.6, 146.2, 136.6, 134.6, 134.1, 132.7 (2C), 132.2, 132.1 (2C), 131.0, 129.0, 128.9, 126.5, 125.8 (2C), 125.4, 124.3 (2C), 121.7, 118.9, 118.8, 114.9, 110.9, 110.5. HRMS (ESI $^+$): m/z calcd for $\text{C}_{27}\text{H}_{16}\text{N}_3\text{O}$ ($\text{M} + \text{H}$) $^+$: 398.1288; found: 398.1282.

1,1'-(3-(5-Nitroquinolin-8-yl)furan-2,5-diyl)bis(4,1-phenylene)bis(ethan-1-one) (7ea). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 5/1). Yellow solid (67 mg, 35%); mp = 220–224 $^\circ\text{C}$; R_f (light petroleum/EtOAc = 5/3) 0.27. FT-IR (ATR, neat): 3131, 1669, 1598, 1505, 1328, 1261, 1181,

838, 787 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.12 (dd, J = 8.9, 1.7 Hz, 1H), 9.01 (dd, J = 4.1, 1.7 Hz, 1H), 8.39 (d, J = 8.0 Hz, 1H), 8.06–8.04 (m, 2H), 7.91–7.89 (m, 2H), 7.86 (d, J = 8.0, 1H), 7.84–7.82 (m, 2H), 7.71 (dd, J = 8.9, 4.1 Hz, 1H), 7.52–7.50 (m, 2H), 7.19 (s, 1H), 2.65 (s, 3H), 2.56 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 197.3, 197.2, 152.5, 151.5, 149.9, 146.1, 145.3, 140.4, 136.1, 136.0, 134.3, 134.0, 132.3, 129.2, 129.0 (2C), 128.6 (2C), 125.9 (2C), 124.3, 124.2, 124.0 (2C), 123.0, 121.9, 113.6, 26.6, 26.5. HRMS (ESI $^+$): m/z calcd for $\text{C}_{29}\text{H}_{21}\text{N}_2\text{O}_5$ ($\text{M} + \text{H}$) $^+$: 477.1445; found: 477.1443. Elemental analysis calcd for $\text{C}_{29}\text{H}_{20}\text{N}_2\text{O}_5$: C, 73.10; H, 4.23; N, 5.88; found: C, 73.18; H, 3.89; N, 5.59.

1-[4-[2-(Quinolin-8-yl)benzofuran-3-yl]phenyl]ethan-1-one (7i). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 10/1). Light yellow solid (103 mg, 71%); mp = 153–155 $^\circ\text{C}$; R_f (light petroleum/EtOAc = 5/3) 0.63. FT-IR (ATR, neat): 2917, 1678, 1604, 1266, 1182, 957, 831, 795, 750, 727 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 8.79 (dd, J = 4.0, 2.0 Hz, 1H), 8.20 (dd, J = 8.5, 2.0 Hz, 1H), 7.92 (dd, J = 8.0, 1.5 Hz, 1H), 7.84–7.77 (m, 4H), 7.64 (d, J = 8.0 Hz, 1H), 7.57–7.54 (m, 1H), 7.46–7.44 (AA'BB', J = 8.5 Hz, 2H), 7.41–7.38 (m, 2H), 7.35–7.32 (m, 1H), 2.56 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 197.7, 155.1, 151.4, 150.8, 146.5, 138.6, 136.2, 135.3, 132.5, 129.9, 129.0 (2C), 128.6, 128.5 (2C), 128.3, 127.4, 126.1, 124.8, 123.2, 121.5, 120.0, 119.5, 111.7, 26.5. HRMS (ESI $^+$): m/z calcd for $\text{C}_{25}\text{H}_{18}\text{NO}_2$ ($\text{M} + \text{H}$) $^+$: 364.1332; found: 364.1328. Elemental analysis calcd for $\text{C}_{25}\text{H}_{17}\text{NO}_2$: C, 82.63; H, 4.72; N, 3.85; found: C, 82.42; H, 4.51; N, 3.76.

8-[3-(4-Nitrophenyl)benzofuran-2-yl]quinoline (7j). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 20/1). Yellow solid (92 mg, 63%); mp = 71–76 $^\circ\text{C}$; R_f (light petroleum/EtOAc = 5/3) 0.60. FT-IR (ATR, neat): 3065, 1596, 1510, 1341, 1104, 851, 792, 746 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 8.71 (dd, J = 4.0, 2.0 Hz, 1H), 8.21 (dd, J = 8.5, 2.0 Hz, 1H), 8.10–8.08 (AA'BB', J = 9.0 Hz, 2H), 7.96 (dd, J = 8.0, 1.5 Hz, 1H), 7.89 (dd, J = 7.0, 1.5 Hz, 1H), 7.76 (d, J = 7.5 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.62–7.59 (m, 1H), 7.51–7.49 (AA'BB', J = 9.0 Hz, 2H), 7.44–7.35 (m, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 155.1, 151.7, 150.7, 146.3, 146.0, 140.9, 136.3, 132.3, 130.2, 129.4, 129.3 (2C), 128.7, 128.0, 126.2, 125.1, 123.7 (2C), 123.4, 121.7, 119.7, 118.7, 111.8. HRMS (ESI $^+$): m/z calcd for $\text{C}_{23}\text{H}_{15}\text{N}_2\text{O}_3$ ($\text{M} + \text{H}$) $^+$: 367.1077; found: 367.1073.

4-[2-(Quinolin-8-yl)benzofuran-3-yl]benzonitrile (7k). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 10/1). Yellow solid (100 mg, 72%); mp = 89–93 $^\circ\text{C}$; R_f (light petroleum/EtOAc = 5/3) 0.58. FT-IR (ATR, neat): 3047, 2224, 1607, 1494, 1451, 960, 829, 793, 745, 727 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 8.72 (dd, J = 4.0, 2.0 Hz, 1H), 8.20 (dd, J = 8.5, 2.0 Hz, 1H), 7.94 (dd, J = 8.0, 1.5 Hz, 1H), 7.87 (dd, J = 7.0, 1.5 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.65 (d, J = 8.0, 1H), 7.61–7.58 (m, 1H), 7.52–7.50 (AA'BB', J = 8.5 Hz, 2H), 7.45–7.43 (AA'BB', J = 8.5 Hz, 2H), 7.42–7.39 (m, 2H), 7.36–7.33 (m, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 155.1, 151.4, 150.6, 146.0, 138.8, 136.2, 132.3, 132.1 (2C), 130.0, 129.5, 129.4 (2C), 128.7, 128.0, 126.1, 125.0, 123.3, 121.6, 119.7, 119.0, 118.9, 111.8, 110.0.



HRMS (ESI⁺): *m/z* calcd for C₂₄H₁₅N₂O (M + H)⁺: 347.1179; found: 347.1174.

8-[3-(4-Methoxyphenyl)benzofuran-2-yl]quinoline (7l). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 10/1). Yellow solid (112 mg, 80%); mp = 51–57 °C; *R*_f (light petroleum/EtOAc = 5/1) 0.54. FT-IR (ATR, neat): 2834, 1512, 1450, 1286, 1244, 1171, 1017, 828, 792, 744 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.88 (dd, *J* = 4.0, 2.0 Hz, 1H), 8.18 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.87 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.76–7.75 (m, 2H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.52–7.49 (m, 1H), 7.40 (dd, *J* = 8.5, 4.0 Hz, 1H), 7.37–7.34 (m, 1H), 7.31–7.28 (m, 3H), 6.80–6.79 (AA'BB', *J* = 8.5 Hz, 2H), 3.76 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 158.4, 155.0, 150.8, 150.2, 146.9, 136.1, 132.7, 130.4, 130.2 (2C), 129.4, 129.0, 128.6, 126.0, 125.3, 124.4, 122.7, 121.4, 120.2, 119.8, 113.9 (2C), 111.6, 55.1. HRMS (ESI⁺): *m/z* calcd for C₂₄H₁₈NO₂ (M + H)⁺: 352.1332; found: 352.1329.

4-[2-(Quinolin-8-yl)benzo[b]thiophen-3-yl]benzonitrile (7m). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 10/1). Yellow solid (93 mg, 64%); mp = 181–184 °C; *R*_f (light petroleum/EtOAc = 5/3) 0.58. FT-IR (ATR, neat): 3055, 2227, 1603, 1488, 1362, 969, 823, 788, 738 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.86 (dd, *J* = 4.0, 2.0 Hz, 1H), 8.17 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.93–7.92 (m, 1H), 7.82 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.70–7.68 (m, 1H), 7.57 (dd, *J* = 7.0, 1.5 Hz, 1H), 7.49–7.48 (AA'BB', *J* = 8.5 Hz, 2H), 7.46–7.43 (m, 1H), 7.41–7.38 (m, 5H). ¹³C NMR (125 MHz, CDCl₃): δ 150.4, 146.5, 141.0, 140.6, 138.8, 138.6, 136.2, 133.9, 132.9, 132.8, 131.9, 130.7, 129.0, 128.5, 125.9, 124.8, 124.6, 122.6, 122.3, 121.4, 118.9, 110.4. HRMS (ESI⁺): *m/z* calcd for C₂₄H₁₅N₂S (M + H)⁺: 363.0950; found: 363.0949.

8-[3-(4-Nitrophenyl)benzo[b]thiophen-2-yl]quinoline (7n). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 10/1). Yellow solid (87 mg, 57%); mp = 153–156 °C; *R*_f (light petroleum/EtOAc = 5/3) 0.63. FT-IR (ATR, neat): 2916, 1594, 1511, 1342, 1307, 1101, 824, 788, 735 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.86 (dd, *J* = 4.0, 2.0 Hz, 1H), 8.18 (dd, *J* = 8.5, 2.0 Hz, 1H), 8.07–8.05 (AA'BB', *J* = 9.0 Hz, 2H), 7.95–7.93 (m, 1H), 7.84 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.72–7.70 (m, 1H), 7.60 (dd, *J* = 7.0, 1.5 Hz, 1H), 7.47–7.44 (m, 3H), 7.43–7.39 (m, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 150.5, 146.5, 143.1, 140.6, 139.0, 138.8, 136.3, 133.6, 132.9, 132.7, 130.8 (3C), 129.1, 128.5, 126.0, 124.9, 124.7, 123.5 (2C), 122.6, 122.3, 121.5. HRMS (ESI⁺): *m/z* calcd for C₂₃H₁₅N₂O₂S (M + H)⁺: 383.0849; found: 383.0851.

1-[4-[2-(5-Nitroquinolin-8-yl)benzofuran-3-yl]phenyl]ethan-1-one (7o). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 10/1). Yellow solid (158 mg, 97%); mp = 148–152 °C; *R*_f (light petroleum/EtOAc = 5/3) 0.63. FT-IR (ATR, neat): 1676, 1605, 1531, 1515, 1329, 1265, 953, 828, 737 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.99 (dd, *J* = 9.0, 2.0 Hz, 1H), 8.72 (dd, *J* = 4.0, 2.0 Hz, 1H), 8.37 (d, *J* = 8.0 Hz, 1H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.87–7.85 (AA'BB', *J* = 8.5 Hz, 2H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.57 (dd, *J* = 9.0, 4.0 Hz, 1H), 7.46–7.35 (m, 4H), 2.57 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 197.5, 155.3, 151.1, 148.6, 145.8, 145.6, 138.2, 136.6,

135.6, 131.9, 130.0, 129.0 (2C), 128.6 (2C), 128.2, 125.8, 124.1, 124.0, 123.6, 121.9, 121.6, 120.4, 111.8, 26.6. HRMS (ESI⁺): *m/z* calcd for C₂₅H₁₇N₂O₄ (M + H)⁺: 409.1183; found: 409.1186. Elemental analysis calcd for C₂₅H₁₆N₂O₄: C, 73.52; H, 3.95; N, 6.86; found: C, 73.22; H, 3.68; N, 6.46.

5-Nitro-8-[3-(4-nitrophenyl)benzofuran-2-yl]quinoline (7p). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 10/1). Yellow solid (148 mg, 90%); mp = 189–194 °C; *R*_f (light petroleum/EtOAc = 7/1) 0.44. FT-IR (ATR, neat): 3080, 1597, 1508, 1492, 1340, 854, 746, 703 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 9.00 (dd, *J* = 9.0, 2.0 Hz, 1H), 8.64 (dd, *J* = 4.0, 1.5 Hz, 1H), 8.42 (d, *J* = 8.0 Hz, 1H), 8.13 (AA'BB', *J* = 9.0 Hz, 2H), 8.10 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.57 (dd, *J* = 9.0, 4.0 Hz, 1H), 7.49–7.45 (m, 3H), 7.38 (m, 1H). ¹³C NMR (125 MHz, CDCl₃): δ 155.2, 151.0, 148.9, 146.6, 145.9, 145.2, 140.6, 136.1, 132.0, 129.9, 129.5 (2C), 128.0, 126.0, 124.2, 124.0, 123.8 (3C), 121.6, 121.0, 120.1, 111.9. HRMS (ESI⁺): *m/z* calcd for C₂₃H₁₄N₃O₅ (M + H)⁺: 409.1183; found: 409.1186.

4-[1-Methyl-5-(quinolin-8-yl)-1H-pyrrol-3-yl]benzonitrile (7q). Radial chromatography on silica gel (eluting with petroleum ether/diethyl ether; 2/1). White solid (56 mg, 45%); mp = 136–141 °C; *R*_f (light petroleum/EtOAc = 5/3) 0.63. FT-IR (ATR, neat): 2918, 2212, 1601, 1345, 1178, 930, 844, 829, 797, 714 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.96 (dd, *J* = 4.0, 2.0 Hz, 1H), 8.26 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.93 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.56–7.51 (m, 2H), 7.46 (dd, *J* = 8.5, 4.0 Hz, 1H), 7.30–7.28 (AA'BB', *J* = 8.5 Hz, 2H), 7.09–7.08 (AA'BB', *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 3.0 Hz, 1H), 6.55 (d, *J* = 3 Hz, 1H), 3.35 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 151.0, 147.6, 141.8, 136.4, 133.4, 131.8 (2C), 131.7, 129.8, 129.1, 128.7, 127.3 (2C), 126.4, 123.1, 122.2, 121.4, 119.6, 107.7, 107.4, 35.0. HRMS (ESI⁺): *m/z* calcd for C₂₁H₁₆N₃ (M + H)⁺: 310.1339; found: 310.1337.

1-[4-[1-Methyl-2-(quinolin-8-yl)-1H-pyrrol-3-yl]phenyl]ethan-1-one (7s). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 10/1). Yellow solid (100 mg, 77%); mp = 75–78 °C; *R*_f (light petroleum/EtOAc = 5/3) 0.46. FT-IR (ATR, neat): 2923, 1670, 1597, 1354, 1265, 1223, 1182, 832, 796, 726 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.98 (dd, *J* = 4.0, 2.0 Hz, 1H), 8.26 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.91 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.65–7.63 (AA'BB', *J* = 8.5 Hz, 2H), 7.56 (dd, *J* = 7.0, 1.5 Hz, 1H), 7.53–7.50 (m, 1H), 7.46 (dd, *J* = 8.5, 4.0 Hz, 1H), 7.11–7.09 (AA'BB', *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 3.0 Hz, 1H), 3.37 (s, 3H), 2.47 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 197.7, 151.0, 147.8, 142.1, 136.4, 133.5, 133.4, 132.1, 129.6, 128.9, 128.7, 128.3 (2C), 126.9 (2C), 126.5, 122.9, 122.8, 121.4, 107.8, 35.0, 26.4. HRMS (ESI⁺): *m/z* calcd for C₂₂H₁₉N₂O (M + H)⁺: 327.1492; found: 327.1488.

1-[4-[2-(Quinolin-8-yl)thiophen-3-yl]phenyl]ethan-1-one (7t). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 10/1). Yellow solid (39 mg, 30%); mp = 122–123 °C; *R*_f (light petroleum/EtOAc = 5/1) 0.49. FT-IR (ATR, neat): 2918, 2850, 1671, 1594, 1493, 1358, 1264, 1109, 955, 829, 759 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 9.07 (dd, *J* = 4.0, 2.0 Hz, 1H), 8.22 (dd, *J* = 8.0, 2.0 Hz, 1H), 8.14 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.01–7.99 (AA'BB', *J* = 8.5 Hz, 2H), 7.83–7.78 (m, 4H),

7.662–7.59 (m, 1H), 7.52–7.48 (m, 2H), 2.64 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 197.4, 149.5, 145.0, 144.5, 140.9, 139.3, 136.5, 135.5, 132.6, 129.1 (2C), 128.8, 127.6 (2C), 127.5, 126.5, 125.4 (2C), 124.3, 121.4, 26.6. HRMS (ESI $^+$): m/z calcd for $\text{C}_{21}\text{H}_{16}\text{NOS}$ ($\text{M} + \text{H}$) $^+$: 330.0947; found: 330.0944.

4,4'-[1-Methyl-5-(quinolin-8-yl)-1H-pyrrole-2,4-diyl]dibenzonitrile (7qa). Radial chromatography on silica gel (eluting with petroleum ether/diethyl ether; 1/1). Light yellow solid (57 mg, 35%); mp = 147–151 °C; R_f (light petroleum/EtOAc = 1/1) 0.44. FT-IR (ATR, neat): 2921, 2224, 1602, 1491, 1171, 913, 836, 791, 729 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.01 (dd, J = 4.0, 2.0 Hz, 1H), 8.30 (dd, J = 8.5, 2.0 Hz, 1H), 7.97 (dd, J = 8.0, 2.0 Hz, 1H), 7.75–7.73 (AA'BB', J = 8.5 Hz, 2H), 7.69–7.67 (AA'BB', J = 8.5 Hz, 2H), 7.61–7.54 (m, 2H), 7.51 (dd, J = 8.5, 4.0 Hz, 1H), 7.34–7.33 (AA'BB', J = 8.5 Hz, 2H), 7.13–7.12 (AA'BB', J = 8.5 Hz, 2H), 6.74 (s, 1H), 3.37 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 151.2, 147.4, 141.0, 137.4, 136.6, 134.1, 133.6, 133.3, 132.3 (2C), 131.9 (2C), 131.3, 129.5, 128.8, 128.7 (2C), 127.5 (2C), 126.6, 122.9, 121.7, 119.4, 118.9, 110.2, 110.1, 108.2, 33.8. HRMS (ESI $^+$): m/z calcd for $\text{C}_{28}\text{H}_{19}\text{N}_4$ ($\text{M} + \text{H}$) $^+$: 411.1604; found: 411.1597.

8-[1-Methyl-3,5-bis(4-nitrophenyl)-1H-pyrrol-2-yl]quinoline (7ra). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 3/1). Orange solid (99 mg, 55%); mp = 123–127 °C; R_f (light petroleum/EtOAc = 1/1) 0.43. FT-IR (ATR, neat): 2925, 1589, 1505, 1330, 1105, 852, 725 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.02 (dd, J = 4.0, 2.0 Hz, 1H), 8.33–8.31 (m, 3H), 8.00 (dd, J = 8.0, 2.0 Hz, 1H), 7.94–7.92 (AA'BB', J = 9.0 Hz, 2H), 7.75–7.73 (AA'BB', J = 9.0 Hz, 2H), 7.62 (dd, J = 7.0, 1.5 Hz, 1H), 7.59–7.56 (m, 1H), 7.53 (dd, J = 8.0, 4.0 Hz, 1H), 7.18–7.17 (AA'BB', J = 9.0 Hz, 2H), 6.84 (s, 1H), 3.41 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 151.3, 147.3, 146.3, 145.1, 143.1, 139.2, 136.7, 134.3, 134.0, 133.6, 131.1, 129.7, 128.9, 128.6 (2C), 127.4 (2C), 126.6, 124.0 (2C), 123.6 (2C), 122.7, 121.8, 110.9, 34.0. HRMS (ESI $^+$): m/z calcd for $\text{C}_{26}\text{H}_{19}\text{N}_4\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 451.1401; found: 451.1394.

1-[4-[1-Methyl-5-(5-nitroquinolin-8-yl)-1H-pyrrol-2-yl]phenyl]ethan-1-one (7u). Radial chromatography on silica gel (eluting with petroleum ether/EtOAc; 5/1). Orange solid (68 mg, 47%); mp = 191–195 °C; R_f (light petroleum/EtOAc = 2/1) 0.35. FT-IR (ATR, neat): 2921, 1673, 1599, 1318, 1268, 789, 754, 732 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.13–9.10 (m, 2H), 8.45 (d, J = 8.0 Hz, 1H), 8.05–8.04 (AA'BB', J = 8.5 Hz, 2H), 7.87 (d, J = 8.0 Hz, 1H), 7.70–7.66 (m, 3H), 6.60 (d, J = 4 Hz, 1H), 6.57 (d, J = 4 Hz, 1H), 3.51 (s, 3H), 2.65 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 197.6, 151.3, 146.2, 144.5, 139.5, 137.7, 137.2, 135.3, 134.4, 132.2, 129.4, 128.6 (2C), 128.5 (2C), 124.5, 123.8, 121.9, 113.1, 110.8, 35.1, 26.6. HRMS (ESI $^+$): m/z calcd for $\text{C}_{22}\text{H}_{18}\text{N}_3\text{O}_3$ ($\text{M} + \text{H}$) $^+$: 372.1343; found: 372.1341.

Procedure for the three-step one-pot transformation (Suzuki-Miyaura coupling followed by C–H functionalization and hydrogenation)

8-Bromo-5-nitroquinoline (2) (127 mg, 0.50 mmol), (furan-3-yl)boronic acid (6b) (84 mg, 0.75 mmol), Pd(OAc)₂ (5.6 mg, 0.025 mmol), PPh₃ (13.1 mg, 0.05 mmol) and K₂CO₃ (207 mg, 1.5 mmol) were dissolved in a mixture of 1,4-dioxane (1.6 mL) and water (0.4 mL). The reaction mixture was stirred in a sealed glass tube at 100 °C for 24 h under an inert atmosphere. After allowing the mixture to cool to r.t. the glass tube was opened to which 1-bromo-4-nitrobenzene (81 mg, 0.40 mmol) and Pd(OAc)₂ (5.6 mg, 0.025 mmol) were added. The reaction mixture was again sealed and further stirred at 120 °C for 24 h under an inert atmosphere. The mixture was allowed to cool to r.t. to which a flow of H₂ (1 atm) was passed. The reaction mixture was further stirred at r.t. for 24 h. After the reaction was complete, water was added (5 mL) and the product was further extracted with dichloromethane (2 × 5 mL). The combined organic layers were dried (Na₂SO₄), filtered and the solvent was evaporated under reduced pressure. The crude product was purified by radial chromatography to yield pure product 9.

8-[3-(4-Aminophenyl)benzofuran-2-yl]quinolin-5-amine (9). Radial chromatography on silica gel (eluting with petroleum

and water (0.4 mL). The reaction mixture was stirred in a sealed glass tube at 100 °C for 24 h under an inert atmosphere. After allowing the mixture to cool to r.t. the glass tube was opened to which 1-bromo-4-nitrobenzene (81 mg, 0.40 mmol) and Pd(OAc)₂ (5.6 mg, 0.025 mmol) were added. The reaction mixture was again sealed and further stirred at 120 °C for 24 h under an inert atmosphere. The mixture was allowed to cool to r.t. to which water was added (5 mL) and the product was further extracted with dichloromethane (2 × 5 mL). The combined organic layers were dried (Na₂SO₄) and filtered, and the solvent was evaporated under reduced pressure. The crude product was purified by radial chromatography to yield pure product 8.

1-[4-[5-(4-Nitrophenyl)-3-(5-nitroquinolin-8-yl)furan-2-yl]phenyl]ethan-1-one (8). Radial chromatography on silica gel (eluting with petroleum ether/dichloromethane; 1/1). Orange solid (87 mg, 45%); mp > 250 °C; R_f (light petroleum/EtOAc = 1/1) 0.68. FT-IR (ATR, neat): 2852, 1671, 1596, 1509, 1501, 1329, 1262, 1229, 850, 815, 704 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 9.12 (dd, J = 9.0, 1.5 Hz, 1H), 8.98 (dd, J = 4.0, 1.5 Hz, 1H), 8.43 (d, J = 8.0 Hz, 1H), 8.10–8.05 (m, 4H), 7.92–7.88 (m, 3H), 7.72 (dd, J = 7.0, 4.0 Hz, 1H), 7.56–7.54 (AA'BB', J = 9.0 Hz, 2H), 7.18 (s, 1H), 2.66 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 197.2, 153.3, 151.6, 148.6, 146.6, 146.0, 145.6, 139.9, 136.4, 136.1, 133.7, 132.4, 129.1 (3C), 126.1 (2C), 124.4 (2C), 124.3, 124.2 (2C), 124.0 (2C), 121.9, 113.7, 26.6. HRMS (ESI $^+$): m/z calcd for $\text{C}_{27}\text{H}_{18}\text{N}_3\text{O}_6$ ($\text{M} + \text{H}$) $^+$: 480.1190; found: 480.1187.

Procedure for the three-step one-pot transformation (Suzuki-Miyaura coupling followed by C–H functionalization and hydrogenation)

8-Bromo-5-nitroquinoline (2) (127 mg, 0.50 mmol), benzo[b]furan-2-ylboronic acid (6f) (121 mg, 0.75 mmol), Pd(OAc)₂ (5.6 mg, 0.025 mmol), PPh₃ (13.1 mg, 0.05 mmol) and K₂CO₃ (207 mg, 1.5 mmol) were dissolved in a mixture of 1,4-dioxane (1.6 mL) and water (0.4 mL). The reaction mixture was stirred in a sealed glass tube at 100 °C for 24 h under an inert atmosphere. After allowing the mixture to cool to r.t. the glass tube was opened to which 1-bromo-4-nitrobenzene (81 mg, 0.40 mmol) and Pd(OAc)₂ (5.6 mg, 0.025 mmol) were added. The reaction mixture was again sealed and further stirred at 120 °C for 24 h under an inert atmosphere. The mixture was allowed to cool to r.t. to which a flow of H₂ (1 atm) was passed. The reaction mixture was further stirred at r.t. for 24 h. After the reaction was complete, water was added (5 mL) and the product was further extracted with dichloromethane (2 × 5 mL). The combined organic layers were dried (Na₂SO₄), filtered and the solvent was evaporated under reduced pressure. The crude product was purified by radial chromatography to yield pure product 9.

ether/EtOAc; 1/1). Orange solid (98 mg, 70%); mp = 202–204 °C; R_f (dichloromethane/methanol = 10/1) 0.38. FT-IR (ATR, neat): 3369, 3340, 1585, 1448, 1361, 1273, 1173, 1024, 823, 745 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 8.88 (dd, J = 4.0, 1.5 Hz, 1H), 8.15 (dd, J = 8.5, 1.5 Hz, 1H), 7.72 (d, J = 7.7 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.52 (d, J = 7.8 Hz, 1H), 7.34 (dd, J = 8.5, 4.0 Hz, 1H), 7.31–7.28 (m, 1H), 7.27–7.24 (m, 1H), 7.19–7.17 (AA'BB', J = 8.5 Hz, 2H), 6.72 (d, J = 8.0 Hz, 1H), 6.58–6.57 (AA'BB', J = 8.5 Hz, 2H), 4.35 (s, 2H), 3.61 (s, 2H). ^{13}C NMR (125 MHz, CDCl_3): δ 154.8, 151.0, 150.6, 147.8, 144.9, 143.6, 133.7, 130.0 (2C), 129.4, 129.2, 123.8, 123.5, 122.4, 120.7, 120.1, 119.7, 119.0, 118.4, 115.1 (2C), 111.4, 109.3. HRMS (ESI $^+$): m/z calcd for $\text{C}_{23}\text{H}_{17}\text{N}_3\text{O}$ ($\text{M} + \text{H}$) $^+$: 352.1444; found: 352.1443.

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Notes and references

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