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Synthesis of indoles, benzofurans, and related heterocycles *via* an acetylene-activated S_NAr/intramolecular cyclization cascade sequence in water or DMSO†

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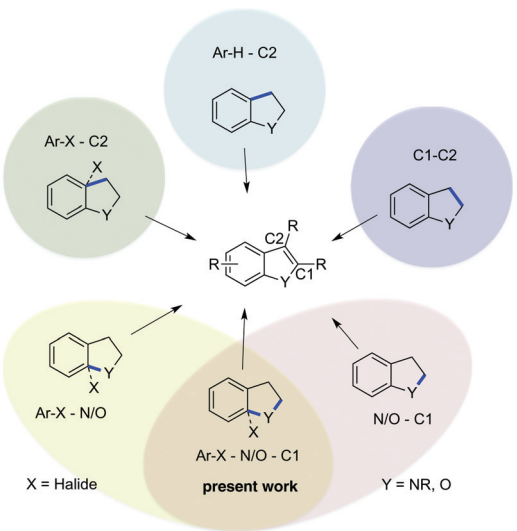
The synthesis of 2-substituted indoles and benzofurans was achieved by nucleophilic aromatic substitution, followed by subsequent 5-endo-dig cyclization between the nucleophile and an *ortho* acetylene. The acetylene serves the dual role of the electron withdrawing group to activate the substrate for S_NAr, and the C1–C2 carbon scaffold for the newly formed 5-membered heteroaromatic ring. This method allows for the bond forming sequence of Ar–X–N/O–C1 to proceed in a single synthetic step, furnishing indoles and benzofurans in moderate to high yields. Since the method is not transition metal mediated, brominated and chlorinated substrates are tolerated, and benzofuran formation can be conducted using water or water–DMSO mixtures as solvent.

Introduction

Indoles, benzofurans, and similar motifs are pervasive throughout nature,[1] and represent common building blocks for the synthesis of pharmaceuticals[2] or otherwise biologically relevant targets. The ubiquity of this type of scaffold and utility of products derived therefrom for transistors,[3] light emitting diodes,[4] photovoltaics,[5] biosensors[6] and other functional organic molecules[7] continues to drive the pursuit of new synthetic methodologies, which have been extensively reviewed for both indole[8] and benzofuran[9] moieties.

Considering routes to indoles that begin with an intact benzene ring, the formation of new bonds can occur between C1–C2,[10] Ar–H–C2,[11] Ar–X–C2,[12] Ar–H–N,[13] Ar–X–N,[14] or N–C1[15,16] (Scheme 1). Similarly, the formation of new bonds within a benzofuran motif can occur between C1–C2,[17] Ar–H–C2,[18] Ar–X–C2,[19] Ar–H–O,[20] Ar–X–O[21] or O–C1.[16,22] The present work describes a procedure for the generation of indoles and benzofurans in which the Ar–F–N/O–C1 bonds are formed in a single synthetic step, achieved through the coupling of various *N*- and *O*-nucleophiles with 2-fluoro-arylacetylenes. This bond formation sequence is less common, but not without precedent. Indeed, indoles can be formed from 2-halo-arylacetylenes and the desired *N*-coupling partner through Pd,[23] Cu,[24] or Ni[25] mediated processes. Similarly, benzofurans can be produced by Pd[26] or Cu[27] catalyzed hydroxylation of aryl halides, followed by subsequent intramolecular cyclization with an *ortho* acetylene. Even the analogous *S*-(benzothiophene),[28] and *P*-(benzophosphole)[29] heterocycles have been synthesized by similar routes. However, the reliance on transition metal mediated processes precludes the use of aryl fluorides as the reactive halogen species. The present work instead utilizes alkyne-activated S_NAr for the



Scheme 1 Strategies for the synthesis of indoles and benzofurans.

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Ar–X–N/O bond formation, allowing the use of aryl fluorides. Selectivity of *N*- and *O*-nucleophiles in an S_NAr context for fluorine over alternative halogens also means that our method is able to furnish Cl- and Br-substituted indoles and benzofurans, which are difficult to access using metal-mediated Ar–X–N/O–C1 bond forming schemes. Since S_NAr reactivity benefits from significant polar interactions to stabilize the transition state, water can be used as a sustainable reaction solvent,[30] or as a co-solvent along with DMSO, for the synthesis of benzofurans by this method.

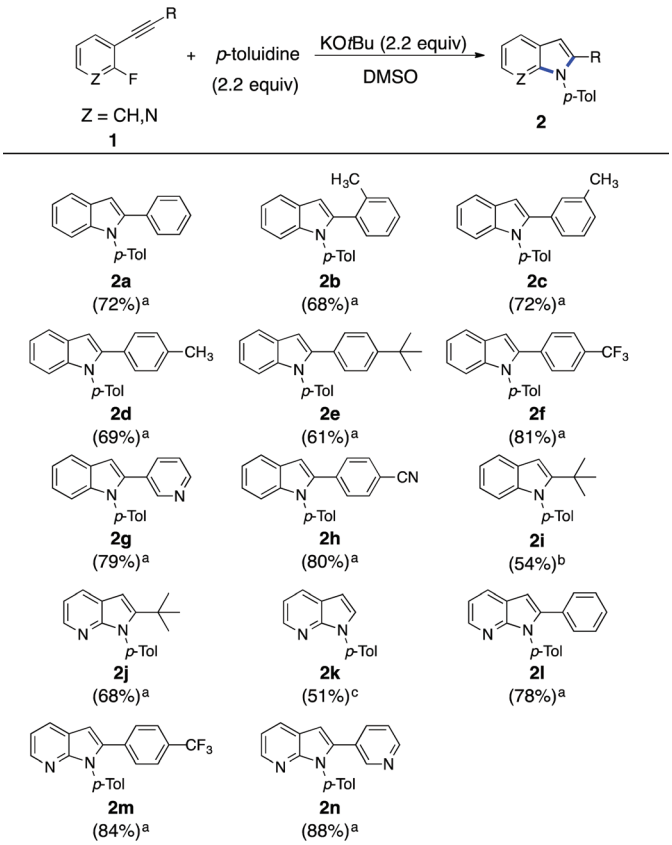
The use of alkynes as the sole electron-withdrawing group to promote S_NAr reactions has been only sparingly covered in the literature.[31] We recently probed the topic in detail,[32] determining reaction rates for the substitution of 4-fluorophenylacetylenes with *p*-cresol, as well as examining other *N*- and *O*-nucleophiles. We found that 2-fluoroarylacetylenes, when reacted with *p*-toluidine would, after the initial substitution, further cyclize to form the corresponding 2-substituted indole. Aside from examples in our initial report, analogous sequences have been limited to aromatics with multiple-alkynes for the synthesis of benzotrifurans and benzotripyrrols,[33] or the use of highly reactive selenium[34,35] or sulfur[34,36] nucleophiles. In the present work, we further develop the scope of our method for 2-substituted indole formation examining *p*-toluidine and acetamide nucleophiles with various electrophiles. Additionally, we expand the substitution/cyclization[37] cascade reactivity to hydroxide, which provides the corresponding benzofurans.

Results and discussion

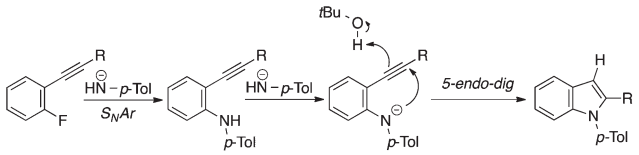
In order to probe the functional group tolerance of the electrophile and to determine the effects of these groups on S_NAr/cyclization, the study compared yields for various 2-fluoro-arylacetylenes **1** in the reaction with *p*-toluidine under KO*t*Bu conditions (Table 1) a mechanism for which is included in Scheme 2. As expected, the addition of a pyridine nitrogen *ortho* to the substituting fluorine further activated the substrates for S_NAr (**1j–n**), increasing the reaction yields relative to the benzene analogues. The nature of R pendant to the acetylene also significantly influenced reaction yields, generally following the trend for: aryl with EWG (**1f–h**, **1m–n**) > aryl (**1a**, **1l**) > aryl with EDG (**1b–e**) > *t*-butyl (**1i–j**) > H (**1k**). *t*-Butyl acetylene electrophile **1i** required prolonged reaction times and increased temperatures, although such reduced reactivity could be mitigated by use of the pyridine analogue **1j**. Benzene electrophiles substituted with terminal acetylenes proved problematic due to competing alkyne addition side reactions. Selectivity for the desired S_NAr pathway could be restored by use of the pyridine analogue **1k** at longer reaction time and lower temperature, although product yields remained modest.

The trends for electrophile reactivity observed with *p*-toluidine also held true for hydroxide and acetamide. Of the three nucleophiles, hydroxide reacted with the highest yield. The superior nucleophilicity of hydroxide was also evident through the formation of significant amounts of the corresponding benzofuran products in reactions with *N*-nucleophiles that were not rigorously dried prior to use. In a competition experiment reacting equimolar amounts of hydroxide and *p*-tolylamide with electrophile **1a**, hydroxide reacted overwhelmingly to form the corresponding benzofuran product in a 95 : 5 ratio over the indole. Acetamide proved an effective nucleophile as well as ammonia surrogate, by directly providing the corresponding *N*-H indole *via in situ* acetate cleavage, obviating the need for an anhydrous ammonia source to produce this product outcome.

Table 1 Reaction of *p*-toluidine with various 2-fluoro-arylacetylene electrophiles[a]

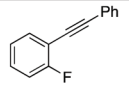
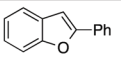
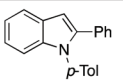
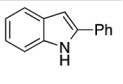
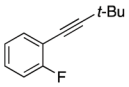
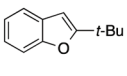
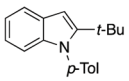
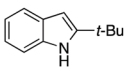
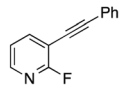
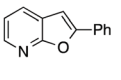
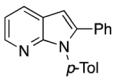
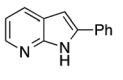
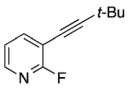
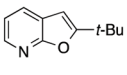
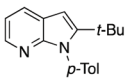
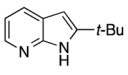
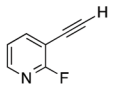
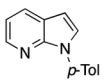


[a] Conditions: 100 °C, 18 h. [b] Conditions: 150 °C, 72 h. [c] Conditions: 80 °C, 48 h. **1a**: Z = CH, R = Ph, **1b**: Z = CH, R = *o*-Tol, **1c**: Z = CH, R = *m*-Tol, **1d**: Z = CH, R = *p*-Tol, **1e**: Z = CH, R = 4-*t*Bu-Ph, **1f**: Z = CH, R = 4-CF_3-Ph, **1g**: Z = CH, R = 3-Py, **1h**: Z = CH, R = 4-CN-Ph, **1i**: Z = CH, R = *t*Bu, **1j**: Z = N, R = *t*Bu, **1k**: Z = N, R = H, **1l**: Z = N, R = Ph, **1m**: Z = N, R = 4-CF_3-Ph, **1n**: Z = N, R = 3-Py.



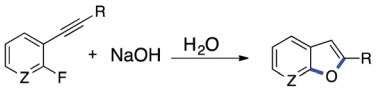
Scheme 2 Proposed S_NAr/intramolecular cyclization cascade mechanism.

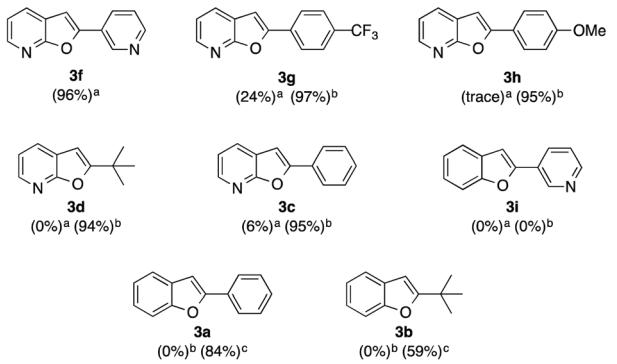
Table 2 Reaction of hydroxide, *p*-toluidine and acetamide with various 2-fluoro-arylacetylene electrophiles

Electrophile	NaOH[a]	*p*-toluidine[b]	Acetamide[c]
 **1a**	 **3a** (92%)[d]	 **2a** (72%)[d]	 **4a** (68%)[d]
 **1i**	 **3b** (89%)[e]	 **2i** (54%)[e]	 **4b** (51%)[e]
 **1l**	 **3c** (93%)[d]	 **2l** (78%)[d]	 **4c** (69%)[d]
 **1d**	 **3d** (90%)[d]	 **2j** (68%)[d]	 **4d** (67%)[d]
 **1k**	 **3e** (61%)[f]	 **2k** (51%)[f]	 **4e** (52%)[f]

[a] 1.2 equiv. NaOH. [b] 2.2 equiv. *p*-toluidine, 2.2 equiv. KO*t*Bu. [c] 2.2 equiv. acetamide, 2.2 equiv. KO*t*Bu. [d] Conditions: 100 °C, 18 h. [e] Conditions: 150 °C, 72 h. [f] Conditions: 80 °C, 48 h.

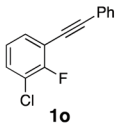
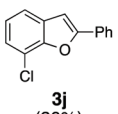
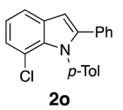
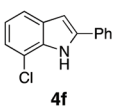
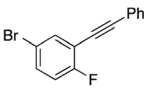
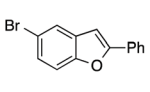
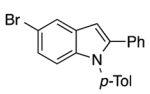
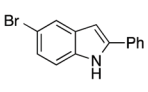
Table 3 Reaction of hydroxide with 2-fluoro-phenylacetylene electrophiles under aqueous conditions





[a] Reaction conditions: 0.5 mmol electrophile, 3 equiv. NaOH, H_2O (1 mL), 100 °C, 18 h, sealed tube. [b] Reaction conditions: 0.5 mmol electrophile, 3 equiv. NaOH, H_2O (1 mL), 125 °C, 48 h, sealed tube. [c] Reaction conditions: 0.5 mmol electrophile, 3 equiv. NaOH, H_2O–DMSO 1 : 1 v/v (1 mL), 155 °C, 48 h, sealed tube.

Table 4 Reaction of hydroxide, *p*-toluidine and acetamide with various brominated and chlorinated 2-fluoro-phenylacetylene electrophiles[a]

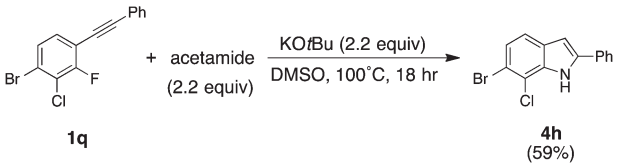
Electrophile	NaOH[b]	*p*-toluidine[c]	Acetamide[d]
 **1o**	 **3j** (80%)	 **2o** (73%)	 **4f** (67%)
 **1p**	 **3k** (82%)	 **2p** (76%)	 **4g** (62%)

[a] Conditions: 100 °C, 18 h. [b] 1.2 equiv. NaOH. [c] 2.2 equiv. *p*-toluidine, 2.2 equiv. KO*t*Bu. [d] 2.2 equiv. acetamide, 2.2 equiv. KO*t*Bu.

The excellent reactivity of hydroxide as a nucleophile for this transformation (Table 2) prompted us to investigate aqueous conditions for the synthesis of benzofurans (Table 3). Water could successfully be used as the exclusive reaction solvent for the more reactive S_NAr electrophiles possessing a pyridine nitrogen *ortho* to the substituting fluorine (**3c–d** and **3f–h**). For less electrophilic substrates, DMSO–water mixtures were required for efficient reactivity (**3a** and **3b**).

Given the enhanced reactivity of fluorine in S_NAr reactions, our substitution/cyclization method leaves additional halogens intact (Table 4), providing a handle for further functionalization of the indole and benzofuran products. Such halogenated heterocycles are not readily accessible by metal-mediated hydroxylation[26,27] or amination.[23–25] The S_NAr-cyclization sequence was even found to tolerate the presence of multiple halogens on one substrate (Scheme 3); the reaction between bromo- and chloro-substituted electrophile **1q** and acetamide provided indole **4h** in a 59% yield.

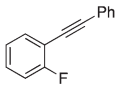
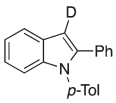
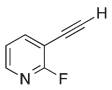
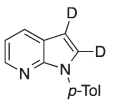
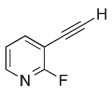
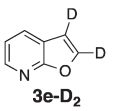
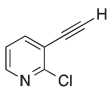
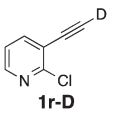
For the generation of both benzofurans and indoles, deuteration at C2 was observed when DMSO-D_6 was used as the reaction solvent (Table 5), indicating transient deprotonation of the DMSO under both hydroxide (entry 3) and *t*-butoxide conditions (entries 1 and 2). Additionally, deuteration at C1



1q **4h** (59%)

Scheme 3 Indolization of a multiply-halogenated electrophile.

Table 5 Deuteration experiments in DMSO-D_6

Entry	Electrophile	Nucleophile	Product[d]
1[a]	 **1a**	*p*-Toluidine	 **2a-D**
2[b]	 **1k**	*p*-Toluidine	 **2k-D_2**
3[c]	 **1k**	NaOH	 **3e-D_2**
4[d]	 **1r**	NaOH	 **1r-D**

[a] Reaction conditions: 0.5 mmol electrophile, 2.2 equiv. *p*-toluidine, 2.2 equiv. KO*t*Bu, DMSO-D_6 1 mL, 100 °C, 18 h. [b] 0.5 mmol electrophile, 2.2 equiv. *p*-toluidine, 2.2 equiv. KO*t*Bu, DMSO-D_6 1 mL, 80 °C, 72 h. [c] 0.5 mmol electrophile, 1.2 equiv. NaOH, DMSO-D_6 1 mL, 80 °C, 72 h. [d] Percent deuteration at each position determined by ^{1}H NMR spectroscopy to be greater than 95%.

was observed with the terminal acetylene electrophile in DMSO-D_6 (entries 2 and 3), most likely as a result of H/D exchange prior to cyclization. To test this assumption we reacted **1r** (entry 4), a substrate less active than the fluoro analogue **1k** toward S_NAr reaction, but which should possess similar terminal alkyne acidity. The substrate was found to undergo deuteration at the terminal alkyne position, but did not proceed with the rest of the regular S_NAr/cyclization sequence.

Conclusions

The S_NAr/intramolecular cyclization cascade sequence presented herein allows for the formation of Ar–X–N/O–C1 bonds in a single synthetic step between 2-fluoro-arylacetylenes and various *N*- or *O*-nucleophiles for the generation of the corresponding indoles, **1e** benzofurans or related heterocycles. This type of bond forming sequence is rare for such heterocycles, and our S_NAr-based approach allows the formation of brominated and chlorinated products, as well as reactivity in aqueous systems.

Materials and methods

Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were collected on a Varian 500 MHz NMR spectrometer. HRMS data were obtained from an Agilent Technologies 6230 TOF LC/MS with an Ion Sense DART 100 ionization interface. All IR spectra were recorded on a Perkin Elmer FT-IR Spectrum One instrument.

General procedure for 2-halo-arylacetylenes synthesis

In a sealed tube were added $PdCl_2(PPh_3)_2$ (0.13 mmol) and CuI (0.25 mmol). The mixture was purged with Argon for 5 minutes, and then degassed 2-fluoro-1-iodoarene (8.75 mmol), degassed terminal alkyne (9.50 mmol), and triethylamine (12 mL) were added in that order. The mixture was stirred at room temperature for 18 hours and then diluted with CH_2Cl_2 and aqueous NH_4Cl. The layers were separated and the aqueous phase extracted with CH_2Cl_2 (3 × 80 mL). The combined organic layers were washed with H_2O (80 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude product purified by silica gel flash column chromatography.

1-(*o*-Fluorophenyl)-2-(*o*-tolyl)ethyne (1b). Column chromatography eluent: hexanes. Colorless oil (85%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58–7.53 (td, J = 7.8 Hz, 1.9 Hz, 1H), 7.52–7.48 (d, J = 7.9 Hz, 2H), 7.36–7.30 (m, 1H), 7.21–7.19 (d, J = 7.8 Hz, 2H), 7.17–7.11 (q, 7.8 Hz, 2H), 2.41 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$): δ: 163.6, 161.6, 138.8, 131.6, 129.7, 129.6, 129.1, 123.9 (d, J = 3.8 Hz), 119.8, 115.6, 115.4, 94.6 (d, J = 3.3 Hz), 82.0, 21.5. TLC: R_f = 0.5 (hexanes). IR (ATR): 3031 (m), 2920 (m), 2216 (m), 1931 (m), 1800 (w), 1700 (m), 1600 (w), 1569 (m), 1486 (s), 1319 (w), 1271 (m), 1265 (s), 1221 (s). HRMS (DART): calculated for $[C_{15}H_{11}FH]^+$ 211.0918, measured 211.0921.

1-(*o*-Fluorophenyl)-2-(*m*-tolyl)ethyne (1c). Column chromatography eluent: hexanes. Yellow oil (88%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61–56 (td, J = 6.8 Hz, 1.9 Hz, 1H), 7.48–7.43 (d, J = 10.3 Hz, 2H), 7.38–7.29 (m, 2H), 7.25–7.21 (d, J = 7.8 Hz, 1H), 7.20–7.13 (q, J = 7.3 Hz, 2H), 7.42 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 163.7, 161.7, 138.1, 133.5 (d, J = 1.3 Hz), 132.3, 129.9 (d, J = 7.6 Hz), 129.6, 128.6 (d, J = 65.5 Hz), 124.0 (d, J = 3.8 Hz), 122.8, 115.6 (d, J = 21.4 Hz), 112.1 (d, J = 16.4 Hz), 94.8 (d, J = 2.5 Hz), 82.3, 21.2. TLC: R_f = 0.5 (hexanes). IR (ATR): 3038 (s), 2921 (s), 2212 (m), 1946 (w), 1793 (w), 1698 (w), 1598 (s), 1572 (s), 1495 (s), 1481 (s), 1380 (w), 1318 (w), 1264 (m), 1226 (s), 1205 (m), 1167 (w), 1155 (w), 1131 (w), 1098 (s), 1030 (m). HRMS (DART): calculated for $[C_{15}H_{11}FH]^+$ 211.0918, measured 211.0896.

1-(*o*-Fluorophenyl)-2-(*p*-tolyl)ethyne (1d). Column chromatography eluent: hexanes. White solid (90%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67–7.59 (m, 3H), 7.41–7.36 (m, 1H),

7.29–7.25 (d, J = 8 Hz, 2H), 7.24–7.18 (m, 2H), 2.46 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ: 163.6, 161.8, 138.8, 133.4 (d, J = 1.5 Hz), 131.6, 129.7 (d, J = 8.2 Hz), 129.1, 123.9 (d, J = 4.0 Hz), 119.8, 115.5 (d, J = 21.0 Hz), 112.1 (d, J = 15.6), 94.6 (d, J = 3.5 Hz), 21.5. TLC: R_f = 0.5 (hexanes). IR (ATR): 3027 (m), 2919 (m), 2219 (m), 1915 (m), 1805 (w), 1699 (m), 1662 (w), 1602 (w), 1566 (m), 1556 (m), 1542 (w), 1535 (w), 1509 (s), 1488 (s), 1444 (s), 1318 (w), 1276 (m), 1263 (s), 1219 (s), 1180 (m), 1139 (w), 1096 (m), 966 (w), 942 (m). HRMS (DART): calculated for $[C_{15}H_{11}FH]^+$ 211.0918, measured 211.0918.

2-(*o*-Fluorophenyl)-1-[*p*-(*tert*-butyl)phenyl]ethyne (1e). Column chromatography eluent: hexanes. White solid (87%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55–7.49 (m, 3H), 7.42–7.37 (d, J = 8.5 Hz, 2H), 7.34–7.28 (m, 1H), 7.16–7.08 (m, 2H), 1.35 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 163.5, 161.6, 151.9, 133.4, 131.4, 129.7 (d, J = 7.9 Hz), 125.4, 123.9 (d, J = 3.8 Hz), 120.0, 115.5 (d, J = 21.4 Hz), 112.2 (d, J = 15.8 Hz), 94.6 (d, J = 3.4 Hz), 34.8, 31.2. TLC: R_f = 0.5 (hexanes). IR (ATR): 2964 (s), 2860 (m), 2221 (w), 1918 (w), 1844 (w), 1733 (w), 1716 (w), 1698 (m), 1674 (w), 1616 (w), 1555 (m), 1567 (m), 1519 (m), 1502 (m), 1485 (s), 1450 (s), 1405 (w), 1362 (m), 1263 (s), 1213 (s), 1144 (w), 1094 (s), 1015 (m). HRMS (DART): calculated for $[C_{18}H_{17}FH]^+$ 253.1387, measured 253.1417.

2-(*o*-Fluorophenyl)-1-[*p*-(trifluoromethyl)phenyl]ethyne (1f). Column chromatography eluent: hexanes. White solid (80%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69–7.66 (d, J = 8.5 Hz, 2H), 7.64–7.61 (d, J = 8.5 Hz), 7.57–7.53 (td, J = 7.4 Hz, 1.8 Hz, 1H), 7.40–7.34 (m, 1H), 7.19–7.11 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ: 163.7, 161.7, 133.5 (d, J = 0.9 Hz), 131.9, 130.6 (d, J = 7.9 Hz), 126.7, 125.3 (q, J = 3.8 Hz), 124.9, 124.1 (d, J = 3.8 Hz), 115.6 (d, J = 20.5 Hz), 111.2 (d, J = 15.8 Hz), 92.8 (d, J = 3.2 Hz), 85.0. TLC: R_f = 0.5 (hexanes). IR (ATR): 3060 (w), 2928 (w), 2225 (m), 1927 (w), 1806 (w), 1698 (w), 1675 (w), 1615 (m), 1604 (s), 1555 (m), 1542 (m), 1521 (w), 1489 (s), 1449 (s), 1405 (m), 1324 (s), 1265 (s), 1223 (s), 1156 (s), 1104 (s). HRMS (DART): calculated for $[C_{15}H_8F_4H]^+$ 265.0635, measured 265.0661.

2-(*o*-Fluorophenyl)-1-(2-pyridyl)ethyne (1g). Column chromatography eluent: hexanes to CH_2Cl_2, step gradient. Brown oil (78%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.82 (s, 1H), 8.60 (s, 1H), 7.84–7.80 (d, J = 7.5 Hz, 1H), 7.54–7.50 (td, J = 7.5 Hz, 1.7 Hz, 1H), 7.36–7.26 (m, 2H), 7.16–7.08 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 163.6, 161.6, 152.2, 149.7, 138.5, 133.4, 130.6 (d, J = 7.6 Hz), 124.1 (d, J = 3.8 Hz), 123.2, 115.6 (d, J = 21.4 Hz), 111.2 (d, J = 16.4 Hz), 90.2 (d, J = 2.9 Hz), 86.0. TLC: R_f = 0.4 (CH_2Cl_2). IR (ATR): 3421 (w), 3033 (m), 2226 (w), 1917 (w), 1844 (w), 1795 (w), 1733 (w), 1716 (w), 1698 (w), 1662 (w), 1612 (w), 1572 (m), 1561 (s), 1542 (w), 1524 (w), 1492 (s), 1473 (m), 1452 (m), 1406 (s), 1329 (w), 1264 (s), 1221 (s), 1187 (m), 1159 (w), 1145 (w), 1120 (w), 1098 (s), 1022 (s), 943 (w). HRMS (DART): calculated for $[C_{13}H_8FNH]^+$ 198.0714, measured 198.0697.

2-(*o*-Fluorophenyl)-1-(4-cyanophenyl)ethyne (1h). Column chromatography eluent: hexanes to EtOAc–hexanes, 1/9, step gradient. White solid (15%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66–7.61 (m, 4H), 7.55–7.51 (td, J = 7.5 Hz, 1.7 Hz, 1H), 7.41–7.35 (m, 1H), 7.19–7.11 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 163.7, 161.7, 133.5, 132.1 (d, J = 12.6 Hz), 130.9 (d, J = 7.6 Hz), 127.8, 124.1 (d, J = 15.0 Hz), 118.4, 115.7 (d, J = 85.0 Hz), 111.8, 111.0 (d, J = 17.6), 92.5 (d, J = 3.4), 87.0. TLC: R_f = 0.5 (EtOAc–hexanes, 1/9). IR (ATR): 3030 (w), 2924 (m), 2880 (w), 2221 (s), 1931 (m), 1796 (w), 1716 (w), 1698 (w), 1676 (w), 1600 (s), 1574 (m), 1555 (m), 1542 (w), 1535 (w), 1504 (s), 1485 (s), 1442 (m), 1409 (m), 1320 (w), 1263 9s), 1216 (s), 1179 (m), 1155 (w), 1136 (w), 1108 (w), 1096 (s), 1029 (m), 1017 (m). HRMS (DART): calculated for $[C_{15}H_8FNH]^+$ 222.0714, measured 222.0695.

2-Fluoro-3-(*tert*-butylethynyl)pyridine (1j). Column chromatography eluent: hexanes to EtOAc–hexanes, 1/9, step gradient. Brown oil (66%). ^{1}H NMR (500 MHz, $CDCl_3$): δ: 8.10–8.07 (ddd, J = 4.9 Hz, 2.0 Hz, 1.0 Hz, 1H), 7.79–7.74 (dd, J = 7.5 Hz, 2.0 Hz, 1H), 7.13–7.09 (dd, J = 5.0 Hz, 1.8 Hz, 1H), 1.34 (s, 9H).^{13}C NMR (126 MHz, $CDCl_3$): δ: 163.7, 161.8, 145.7 (d, J = 14.5 Hz), 143.3 (d, J = 2.9 Hz), 120.8 (d, J = 4.5 Hz), 105.7 (d, J = 1.9 Hz), 71.0 (d, J = 4.6 Hz), 30.7, 28.2. TLC: R_f = 0.6 (EtOAc–hexanes, 1/9). IR (ATR): 3056 (m), 2223 (m), 1955 (w), 1884 (w), 1748 (w), 1716 (w), 1698 (w), 1674 (w), 1593 (m), 1562 (m), 1491 (s), 1430 (s), 1391 (w), 1316 (w), 1291 (w), 1278 (w), 1252 (s), 1212 (m), 1178 (w), 1151 (m), 1069 (m), 1027 (m). HRMS (DART): calculated for $[C_{11}H_{12}FNH]^+$ 178.1027, measured 178.1025.

3-Ethynyl-2-fluoropyridine (1k). See ESI† for full synthesis details. TMS-acetylene coupled through general procedure described above, then cleaved with TBAF to afford terminal alkyne **1k**. Column chromatography eluent: CH_2Cl_2 to MeOH–CH_2Cl_2, 1/19. Yellow solid (81%).^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22–8.17 (m, 1H), 7.92–7.87 (m, 1H), 7.20–7.16 (m, 1H), 3.38 (s, 1H).^{13}C NMR (126 MHz, $CDCl_3$): δ 164.2, 162.2, 147.3 (d, J = 14.5 Hz), 144.2 (d, J = 2.5 Hz), 120.1 (d, J = 3.8 Hz), 106.3 (d, J = 31.5 Hz), 84.1 (d, J = 2.0 Hz). TLC: R_f = 0.8 (MeOH–CH_2Cl_2, 1/19). IR (ATR): 3243 (s), 3096 (m), 3054 (m), 2926 (m), 2172 (w), 2109 (s), 1971 (m), 1938 (m), 1906 (m), 1765 (m), 1599 (s), 1566 (s), 1552 (m), 1443 (s), 1421 (s), 1325 (m), 1291 (s), 1252 (s), 1172 (s), 1107 (s). HRMS (DART): calculated for $[C_7H_4FNH]^+$ 122.0401, measured 122.0408.

2-Fluoro-3-(phenylethynyl)pyridine (1l). Column chromatography eluent: hexanes to EtOAc–hexanes, 1/9, step gradient. Brown solid (81%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10–8.07 (dt, J = 5 Hz, 0.9 Hz, 1H), 7.84–7.79 (m, 1H), 7.53–7.48 (m, 2H), 7.33–7.28 (m, 3H), 7.11–7.07 (m, 1H).^{13}C NMR (126 MHz, $CDCl_3$): δ 163.4, 161.5, 146.5 (d, J = 13.8 Hz), 143.3 (d, J = 2.5 Hz), 131.7, 129.1, 128.5, 122.1, 121.1 (d, J = 4.3 Hz), 107.4 (d, J = 31.5 Hz), 96.0 (d, J = 1.9 Hz), 81.0 (d, J = 5.3 Hz). TLC: R_f = 0.4 (EtOAc–hexanes, 1/9). IR (ATR): 3057 (m), 2223 (m), 1955 (w), 1884 (w), 1748 (w), 1716 (w), 1698 (w), 1674 (w), 1593 (s), 1562 (s), 1491 (s), 1430 (s), 1391 (s), 1291 (w), 1278 (w), 1252 (s), 1212 (s), 1178 (w), 1151 (m), 1097 (s), 1069 (w), 1027 (m). HRMS (DART): calculated for $[C_{13}H_8FNH]^+$ 198.0714, measured 198.0714.

2-Fluoro-3-((4-(trifluoromethyl)phenyl)ethynyl)pyridine (1m). Column chromatography eluent: hexanes to EtOAc–hexanes, 1/9, step gradient. White solid (74%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22–8.19 (dq, J = 5.0 Hz, 1.0 Hz, 1H), 7.96–7.91 (m, 1H), 7.69–7.60 (m, 4H), 7.24–7.20 (m, 1H).^{13}C NMR (126 MHz,

$CDCl_3$): δ 163.6, 161.7, 147.2 (d, J = 13.9 Hz), 143.5 (d, J = 2.4 Hz), 132.0, 130.7 (q, J = 32.8 Hz), 126.0 (d, J = 1.4 Hz), 125.4 (q, J = 3.8 Hz), 121.1 (d, J = 4.4 Hz), 106.9 (d, J = 31.5), 94.3, 83.1 (d, J = 5.3 Hz). TLC: R_f = 0.5 (EtOAc–hexanes, 1/9). IR (ATR): 3050 (w), 2890 (w), 1931 (w), 1748 (w), 1699 (w), 1675 (w), 1614 (w), 1595 (m), 1562 (m), 1524 (w), 1501 (w), 1456 (m), 1437 (s), 1403 (w), 1321 (s), 1255 (m), 1216 (w), 1184 (w), 1162 (s), 1125 (m), 1063 (s), 1013 (s). HRMS (DART): calculated for $[C_{14}H_7FNH]^+$ 266.0587, measured 266.0597.

2-Fluoro-3-(2-pyridylethynyl)pyridine (1n). Column chromatography eluent: CH_2Cl_2 → MeOH–CH_2Cl_2, 1/19, step gradient. Yellow solid (72%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.73–8.69 (d, J = 1.5 Hz, 1H), 8.53–8.50 (dd, J = 5.0 Hz, 1.5 Hz, 1H), 8.15–8.10 (dq, J = 5.0 Hz, 0.9 Hz, 1H), 7.89–7.84 (m, 1H), 7.78–7.75 (dt, J = 8.0 Hz, 2.0 Hz, 1H), 7.26–7.22 (ddd, J = 8.0 Hz, 5.0 Hz, 0.8 Hz, 1H), 7.17–7.13 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 163.4, 161.6, 152.3, 149.3, 147.2 (d, J = 14.5 Hz), 143.4 (d, J = 2.4 Hz), 138.6, 123.1, 121.1 (d, J = 2.5 Hz), 119.4, 92.4 (d, J = 1.9 Hz), 84.1 (d, J = 12.6 Hz). TLC: R_f = 0.2 (CH_2Cl_2). IR (ATR): 3084 (w), 3028 (w), 2228 (w), 1907 (w), 1748 (w), 1716 (w), 1699 (w), 1675 (w), 1602 (m), 1563 (s), 1542 (m) 1501 (w), 1477 (s), 1433 (s), 1409 (m), 1318 (m), 1297 (w), 1250 (s), 1216 (m), 1188 (m), 1160 (w), 1118 (m), 1096 (s), 1033 (w), 1023 (m). HRMS (DART): calculated for $[C_{12}H_7FN_2H]^+$ 199.0666, measured 199.0664.

1-Chloro-2-fluoro-3-(phenylethynyl)benzene (1o). Column chromatography eluent: hexanes. Yellow solid (85%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65–7.60 (m, 2H), 7.49–7.36 (m, 5H), 7.11–7.07 (td, J = 8.0 Hz, 1.3 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 159.3, 157.2, 131.8, 131.7, 130.6, 129.0, 128.5, 124.4 (d, J = 5.0 Hz), 122.6, 113.7 (d, J = 15.1), 95.7 (d, J = 3.8 Hz), 81.8. TLC: R_f = 0.7 (hexanes). IR (ATR): 3054 (m), 2197 (w), 1946 (w), 1869 (w), 1797 (w), 1747 (w), 1716 (w), 1698 (w), 1676 (w), 1603 (m), 1571 (m), 1556 (w), 1542 (w), 1524 (w), 1492 (s), 1464 (m), 1448 (s), 1314 (w), 1272 (w), 1239 (s), 1179 (w), 1156 (m), 1136 (m), 1061 (w), 1071 (m), 1027 (m). HRMS (DART): calculated for $[C_{14}H_8ClFH]^+$ 231.0371, measured 231.0377.

4-Bromo-1-fluoro-2-(phenylethynyl)benzene (1p). Column chromatography eluent: hexanes. Yellow oil (83%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71–7.68 (dd, J = 6.5 Hz, 2.5 Hz, 1H), 7.65–7.60 (m, 2H), 7.46–7.38 (m, 4H), 7.04–6.99 (t, J = 9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 162.8, 160.8, 135.8, 132.8 (d, J = 7.6 Hz), 131.9, 129.0, 128.5, 122.5, 117.2 (d, J = 22.7 Hz), 116. 3(d, J = 3.8 Hz), 114.1 (d, J = 16.4 Hz), 95.6 (d, J = 3.3 Hz), 81.4. TLC: R_f = 0.7 (hexanes). IR (ATR): 3061 (m), 2222 (m), 1947 (w), 1877 (w), 1748 (w), 1716 (w), 1697 (w), 1675 (w), 1605 (w), 1572 (w), 1555 (w), 1541 (w), 1495 (s), 1479 (s), 1442 (m), 1392 (s), 1276 (w), 1255 (s), 1222 (s), 1178 (w), 1158 (w), 1144 (w), 1107 (s), 1069 (s), 1025 (m). HRMS (DART): calculated for $[C_{14}H_8BrFH]^+$ 274.9866, measured 274.9852.

1-Bromo-2-chloro-3-fluoro-4-(phenylethynyl)benzene (1q). Column chromatography eluent: hexanes. Off-white solid (73%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62–7.56 (m, 2H), 7.44–7.22 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 159.7, 157.7, 132.5, 131.8, 131.3 (d, J = 1.6 Hz), 129.2 (d, J = 16.4 Hz), 128.5 (d, J = 1.5 Hz), 123.8, 122.3, 121.8, 112.6 (d, J = 16.8), 95.6 (d, J = 3.8), 81.4 (d, J = 63 Hz). TLC: R_f = 0.7 (hexanes). IR (ATR): 3053 (m), 2538 (w), 2206 (m), 1951 (w), 1885 (w), 1795 (w), 1748 (w), 1716 (w), 1700 (w), 1670 (w), 1587 (m), 1571 (w), 1542 (w), 1525 (w), 1489 (s), 1458 (s), 1441 (m), 1411 (s), 1318 (w), 1260 (w), 1222 (m), 1182 (m), 1142 (w), 1157 (w), 1127 (w), 1069 (w), 1025 (w). HRMS (DART): calculated for $[C_{14}H_7BrClFH]^+$ 308.9476, measured 308.9473.

2-Chloro-3-ethynylpyridine (1r). See ESI† for full synthesis details. Cleaved from commercially available 2-chloro-3-trimethylsilanylethynyl-pyridine with TBAF. Column chromatography eluent: hexanes to EtOAc–hexanes, 3/7, step gradient. White solid (97%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.33–8.29 (m, 1H), 7.81–7.77 (m, 1H), 7.20–7.16 (m, 1H) 3.48 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 152.5, 148.8, 142.1, 121.8, 119.4, 85.0, 78.2. TLC: R_f = 0.4 (EtOAc–hexanes, 1/9). IR (ATR): 3212 (s), 2106 (m), 1962 (w) 1926 (w), 1839 (w), 1748 (w), 1716 (w), 1698 (w), 1675 (w), 1646 (w), 1578 (m), 1556 (s), 1535 (m), 1501 (w), 1473 (w), 1440 (m), 1389 (s), 1275 (m), 1262 (m), 1125 (s), 1092 (w), 1077 (s), 1070 (s). HRMS (DART): calculated for $[C_7H_4ClNH]^+$ 138.0105, measured 138.0107.

2-Fluoro-3-((4-methoxyphenyl)ethynyl)pyridine (1s). Column chromatography eluent: hexanes–CH_2Cl_2 1 : 1 to CH_2Cl_2, step gradient. Yellow solid (97%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10–8.07 (dq, J = 5 Hz, 1H), 7.85–7.80 (ddd, J = 9.3 Hz, 7.5 Hz, 2 Hz, 1H), 7.47–7.43 (m, 2H), 7.14–7.10 (ddd, J = 7.5 Hz, 5 Hz, 2 Hz, 1H), 6.86–6.82 (m, 2H), 3.77 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 163.4, 161.4, 160.2, 146.2–146.0 (d, J = 13.9 Hz) 143.1–143.0 (d, J = 2.5 Hz), 133.3, 121.1–121.0 (d, J = 4.4 Hz), 114.1, 108.0–107.3 (d, J = 125 Hz), 96.2 (d, J = 1.9 Hz), 79.8 (d, J = 5.0 Hz), 55.2. TLC: R_f = 0.5 (CH_2Cl_2). IR (ATR): 3056 (w), 3006 (w), 2962 (m), 2936 (m), 2838 (m), 2539 (m), 2221 (s), 2192 (m), 2015 (w), 1889 (w), 1607 (s), 1596 (s), 1561 (s), 1508 (s), 1456 (s), 1431 (s), 1319 (s), 1288 (s), 1247 (s), 1212 (s), 1174 (s), 1146 (s), 1107 (s), 1096 (s), 1027 (s). HRMS (DART): calculated for $[C_{14}H_{10}FNOH]^+$ 228.0819, measured 228.0820.

General procedure for *N*-tolyl indole synthesis

In a reaction flask under Ar, 2-halo-arylacetylene (0.5 mmol), *p*-toluidine (1.1 mmol), and DMSO (1.0 mL) were added. The reaction was started with the addition of KO*t*Bu (1.1 mmol). The reaction was stirred on an aluminum heating block at 100 °C for 18 h. The reaction was quenched by dilution with CH_2Cl_2 and addition of NH_4Cl. The layers were separated and the aqueous phase extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with H_2O (80 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude product purified by silica gel flash column chromatography.

2-(*o*-Tolyl)-1-(*p*-tolyl)-1*H*-indole (2b). Column chromatography eluent: hexanes to CH_2Cl_2, step gradient. Colorless oil (83%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74–7.69 (m, 1H), 7.40–7.36 (m, 1H), 7.28–7.23 (m, 1H), 7.23–7.18 (m, 3H), 7.16–7.11 (m, 4H), 7.09–7.06 (m, 2H), 6.65 (s, 1H), 2.35 (s, 3H), 2.13 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 140.2, 137.7, 137.6, 136.4, 135.5, 132.7, 131.5, 129.9, 129.5, 128.2, 128.1, 127.1, 125.2, 121.9, 120.4, 120.4, 110.6, 104.0, 21.1, 20.4. TLC: R_f = 0.5

(CH_2Cl_2). IR (ATR): 3015 (s), 2221 (m), 2066 (w), 1634 (s), 1512 (s), 1488 (s), 1453 (s), 1262 (m), 1220 (m), 1097 (m), 1030 (w). HRMS (DART): calculated for $[C_{22}H_{19}NH]^+$ 298.1590, measured 298.1581.

2-(*m*-Tolyl)-1-(*p*-tolyl)-1*H*-indole (2c). Column chromatography eluent: hexanes to CH_2Cl_2, step gradient. White solid (72%). ^{1}H NMR (500 MHz, $CDCl_3$): δ: 7.78–7.74 (m, 1H), 7.37–7.34 (m, 1H), 7.30–7.16 (m, 8H), 7.13–7.07 (m, 2H), 6.87 (d, J = 0.8 Hz), 2.47 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 141.0, 139.2, 137.8, 137.0, 136.0, 132.6, 129.9, 129.7, 128.3, 128.1, 128.0, 127.9, 126.1, 122.2, 120.6, 120.5, 110.7, 103.4, 21.5, 21.2. TLC: R_f = 0.5 (CH_2Cl_2). IR (ATR): 3031 (m), 2920 (m), 2862 (w), 1880 (w), 1606 (s), 1510 (s), 1483 (w), 1452 (s), 1376 (m), 1352 (m), 1316 (m), 1274 (w), 1261 (w), 1211 (m), 1173 (w), 1147 (w), 1108 (w), 1095 (w), 1078 (w), 1039 (w), 1014 (w). HRMS (DART): calculated for $[C_{22}H_{19}NH]^+$ 298.1590, measured 298.1598.

1,2-di-*p*-Tolyl-1*H*-indole (2d). Column chromatography eluent: hexanes to CH_2Cl_2–hexanes, 4/6, step gradient. White solid (69%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74–7.70 (m, 1H), 7.33–7.29 (m, 1H), 7.28–7.17 (m, 8H), 7.12–7.09 (d, J = 8 Hz, 2H) 6.81 (d, J = 0.6 Hz, 1H), 2.45 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 140.9, 139.1, 137.1, 137.0, 136.0, 129.9, 129.8, 128.9, 128.8, 128.3, 127.9, 122.0, 120.5, 120.4, 110.7, 103.0, 21.2, 21.2. TLC: R_f = 0.2 (hexanes). IR (ATR): 3029 (m), 2960 (m), 1844 (w), 1749 (w), 1716 (w), 1699 (w), 1674 (w), 1606 (w), 1555 (w), 1542 (m), 1513 (s), 1500 (m), 1455 (s), 1412 (w), 1380 (m), 1357 (m), 1320 (w), 1307 (m), 1255 (w), 1187 (w), 1174 (w), 1147 (w), 1113 (w), 1021 (w). HRMS (DART): calculated for $[C_{22}H_{19}NH]^+$ 298.1590, measured 298.1573.

2-(4-(*tert*-Butyl)phenyl)-1-(*p*-tolyl)-1*H*-indole (2e). Column chromatography eluent: hexanes to CH_2Cl_2–hexanes, 1/1, step gradient. White solid (67%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73–7.68 (m, 1H), 7.32–7.23 (m, 7H), 7.21–7.16 (m, 4H), 6.81 (d, J = 0.8 Hz, 1H), 2.45 (s, 3H), 1.33 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 150.2, 140.8, 139.2, 137.0, 136.1, 129.9, 129.6, 128.4, 128.3, 127.9.2, 125.0, 122.0, 120.5, 120.3, 110.7, 103.0, 34.5, 31.3, 21.2. TLC: R_f = 0.2 (hexanes). IR (ATR): 3031 (w), 2960 (m), 2864 (w), 1844 (w), 1734 (w), 1716 (w), 1699 (w), 1675 (w), 1606 (w), 1564 (w), 1555 (w), 1541 (w), 1535 (w), 1513 (s), 1503 (m), 1473 (w), 1409 (w), 1378 (m), 1360 (w), 1347 (m), 1321 (m), 1259 (m), 1200 (m), 1175 (w), 1113 (m), 1017 (m). HRMS (DART): calculated for $[C_{25}H_{25}NH]^+$ 340.2060, measured 340.2037.

1-(*p*-Tolyl)-2-(4-(trifluoromethyl)phenyl)-1*H*-indole (2f). Column chromatography eluent: hexanes to CH_2Cl_2–hexanes 1/1, step gradient. White solid (81%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72–7.49 (m, 1H), 7.53–7.38 (d, J = 8.5 Hz, 2H), 7.30–7.17 (m, 7H), 7.16–7.12 (dt, J = 8.5 Hz, 2 Hz, 2H). 6.88 (d, J = 0.7 Hz), 2.45 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 139.5, 139.0, 137.5, 136.1, 135.5, 130.2, 128.8, 128.0, 127.7, 125.1 (q, J = 3.8 Hz), 123.1, 122.9, 120.8 (d, J = 12.6 Hz), 110.8, 104.7, 29.7, 21.1. TLC: R_f = 0.3 (hexanes). IR (ATR): 3034 (m), 2920 (m), 1617 (s), 1514 (s), 1474 (w), 1453 (s), 1412 (m), 1379 (m), 1320 (s), 1257 (w), 1212 (m), 1165 (s), 1123 (s), 1109 (s), 1079 (s), 1063 (s), 1016 (s). HRMS (DART): calculated for $[C_{22}H_{16}F_3NH]^+$ 352.1313, measured 352.1317.

2-(Pyridin-3-yl)-1-(*p*-tolyl)-1*H*-indole (2g). Column chromatography eluent: hexanes to CH_2Cl_2, step gradient. Brown solid (79%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.65–8.62 (m, 1H), 8.48–8.44 (m, 1H), 7.72–7.68 (m, 1H), 5.54–5.50 (m, 1H), 7.27–7.11 (m, 8H), 6.87 (s, 1H), 2.42 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 149.5, 148.1, 139.7, 137.6, 137.2, 135.6, 135.5, 130.0, 128.9, 128.2, 122.7, 120.8, 120.7, 110.7, 104.4, 20.9. TLC: R_f = 0.6 (CH_2Cl_2). IR (ATR): 3029 (m), 2920 (m), 1920 (w), 1771 (w), 1697 (w), 1661 (w), 1607 (m), 1571 (m), 1555 (w), 1541 (w), 1535 (w), 1510 (s), 1448 (s), 1421 (m), 1376 (m), 1364 (m), 1350 (m), 1324 (m), 1310 (m), 1254 (m), 1208 (m), 1173 (m), 1143 (w), 1127 (w), 1108 (w), 1104 (m), 1038 (w), 1024 (m), 1016 (m). HRMS (DART): calculated for $[C_{20}H_{16}N_2H]^+$ 285.1386, measured 285.1362.

4-(1-(*p*-Tolyl)-1*H*-indol-2-yl)benzonitrile (2h). Column chromatography eluent: CH_2Cl_2 to MeOH–CH_2Cl_2, 1/39, step gradient. Off-white solid (80%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72–7.68 (m, 3H), 7.38–7.34 (dt, J = 8.8 Hz, 2 Hz, 2H), 7.30–7.28 (m, 1H), 7.25–7.22 (m, 2H), 7.22–7.17 (m, 2H), 7.15–7.12 (m, 2H), 6.89 (d, J = 0.8 Hz), 2.42 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 168.9, 139.5, 137.4, 136.3, 135.6, 131.6, 130.1, 128.7, 128.0, 127.7, 127.7, 122.9, 120.8, 120.7, 110.8, 104.5, 21.2. TLC: R_f = 0.1 (CH_2Cl_2), 0.4 (MeOH–CH_2Cl_2, 1/39). IR (ATR): 3480 (m), 3365 (w), 3149 (s), 2922 (w), 1905 (w), 1793 (w), 1680 (s), 1663 (s), 1605 (s), 1563 (m), 1541 (w), 1535 (w), 1472 (w), 1453 (m), 1411 (w), 1380 (s), 1352 (m), 1321 (m), 1282 (m), 1259 (m), 1210 (m), 1139 (m), 1106 (m), 1017 (m). HRMS (DART): calculated for $[C_{22}H_{16}N_2H]^+$ 309.1386, measured 309.1380.

2-(*tert*-Butyl)-1-(*p*-tolyl)-1*H*-pyrrolo[2,3-*b*]pyridine (2j). Column chromatography eluent: hexanes to CH_2Cl_2, step gradient. Brown solid (68%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22–8.19 (dd, J = 4.7 Hz, 1.5 Hz, 1H), 7.86–7.83 (dd, J = 7.8 Hz, 1.5 Hz, 1H), 7.34–7.31 (d, J = 2 Hz, 2H), 7.29–7.25 (m, 2H), 7.04–7.00 (dd, J = 8 Hz, 4.5 Hz, 1H), 6.41 (s, 1H), 2.46 (s, 3H), 1.29 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 151.6, 151.2, 142.8, 138.7, 136.2, 130.5, 129.7, 127.3, 119.5, 116.0, 96.9, 33.5, 30.7, 21.4. TLC: R_f = 0.6 (CH_2Cl_2), 0.7 (MeOH–CH_2Cl_2, 1/19), 0.2 (CH_2Cl_2–hexanes, 1/1). IR (ATR): 3041 (m), 2958 (s), 2924 (s), 2869 (s), 1593 (m), 1574 (m), 1525 (s), 1515 (s), 1470 (m), 14 010 (s), 1393 (m), 1361 (s), 1311 (s), 1285 (s), 1246 (s), 1216 (m), 1199 (m), 1132 (w), 1107 (m), 1041 (w), 1023 (w). HRMS (DART): calculated for $[C_{18}H_{20}N_2H]^+$ 265.1705, measured 265.1703.

1-(*p*-Tolyl)-1*H*-pyrrolo[2,3-*b*]pyridine (2k). Column chromatography eluent: hexanes to CH_2Cl_2–hexanes 1/1, step gradient. Brown solid (51%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39–8.36 (d, J = 4.5 Hz, 1H), 7.99–7.96 (d, J = 9 Hz), 7.64–7.61 (d, J = 8 Hz, 2H), 7.51–7.48 (d, J = 3.5 Hz, 1H), 7.35–7.32 (d, J = 8.5 Hz, 2H), 7.15–7.11 (ddd, J = 8.0 Hz, 4.5 Hz, 0.7 Hz, 1H), 6.63–6.61 (dd, 3.8 Hz, 0.7 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 143.5, 136.2, 135.9, 129.9, 128.0, 124.0, 116.5, 108.2, 107.7, 101.2, 21.0. TLC: R_f = 0.8 (CH_2Cl_2), 0.4 (CH_2Cl_2–hexanes, 1/1). IR (ATR): 2923 (s), 1594 (s), 1530 (s),

1476 (m), 1424 (s), 1359 (m), 1323 (s), 1269 (m), 1235 (m), 1210 (w), 1147 (w), 1110 (m), 1039 (w). HRMS (DART): calculated for $[C_{14}H_{12}N_2H]^+$ 209.1079, measured 209.1083.

2-Phenyl-1-(*p*-tolyl)-1*H*-pyrrolo[2,3-*b*]pyridine (2l). Column chromatography eluent: hexanes to CH_2Cl_2, step gradient. Yellow solid (78%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.36–8.33 (dd, J = 4.5 Hz, 1.6 Hz, 1H), 7.99–7.96 (dd, J = 8.0 Hz, 1.7 Hz, 1H), 7.35–7.27 (m, 5H), 7.26–7.21 (m, 4H), 7.15–7.12 (dd, 8.0 Hz, 4.8 Hz, 1H), 6.74 (s, 1H), 2.40 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 150.0, 143.7, 141.1, 137.1, 134.3, 132.2, 129.7, 128.8, 128.3, 128.2, 128.1, 127.7, 120.8, 116.9, 101.1, 21.2. TLC: R_f = 0.7 (CH_2Cl_2), 0.4 (EtOAc–hexanes, 1/9). IR (ATR): 3058 (w), 3034 (w), 2917 (w), 1920 (w), 1884 (w), 1845 (w), 1734 (w), 1699 (w), 1675 (w), 1604 (w), 1589 (m), 1567 (m), 1541 (m), 1512 (s), 1489 (w), 1473 (m), 1447 (w), 1417 (s), 1371 (s), 1315 (m), 1297 (m), 1277 (m), 1241 (m), 1211 (w), 1195 (w), 1183 (m), 1108 (m), 1073 (w), 1028 (m). HRMS (DART): calculated for $[C_{20}H_{16}N_2H]^+$ 285.1386, measured 285.1396.

1-(*p*-Tolyl)-2-(4-(trifluoromethyl)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine (2m). Column chromatography eluent: hexanes to EtOAc–hexanes, 1/9, step gradient. Brown solid (84%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39–8.36 (dd, J = 4.6 Hz, 1.6 Hz, 1H), 8.02–7.98 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.56–7.53 (d, J = 8.0 Hz, 2H), 7.45–7.41 (d, J = 8.0 Hz, 2H), 7.28–7.25 (d, J = 8.0 Hz, 2H), 7.23–7.19 (dt, J = 9.0 Hz, 2.2 Hz, 2H), 7.18–7.14 (dd, J = 7.5 Hz, 4.8 Hz, 1H), 6.81 (s, 1H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 150.3, 144.3, 139.3, 137.7, 135.7, 134.0, 130.0, 129.6, 129.4, 128.9, 128.8, 128.1, 125.2 (q, J = 3.8 Hz), 120.6, 117.2, 102.4, 21.2. TLC: R_f = 0.8 (CH_2Cl_2), 0.4 (EtOAc–hexanes, 1/9). IR (ATR): 3006 (w), 2990 (w), 1844 (w), 1738 (w), 1716 (w), 1699 (w), 1674 (w), 1617 (w), 1555 (w), 1542 (w), 1513 (w), 1501 (w), 1473 (w), 1456 (w), 1403 (w), 1325 (s), 1275 (s), 1260 (s), 1160 (s), 1122 (s), 1109 (s), 1084 (m), 1063 (m), 1018 (m). HRMS (DART): calculated for $[C_{21}H_{15}F_3NH]^+$ 353.1260, measured 353.1239.

2-(Pyridin-3-yl)-1-(*p*-tolyl)-1*H*-pyrrolo[2,3-*b*]pyridine (2n). Column chromatography eluent: CH_2Cl_2 to MeOH–CH_2Cl_2, 1/9, step gradient. Brown solid (88%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.66 (s, 1H), 8.51 (s, 1H), 8.37–8.35 (dd, J = 4.5 Hz, 1.5 Hz, 1H), 8.01–7.98 (dd, J = 8.0 Hz, 1.5 Hz, 1H), 7.53–7.49 (dt, J = 8.0 Hz, 2.0 Hz, 1H), 7.26–7.23 (d, J = 8.0 Hz, 2.0 Hz, 1H), 7.26–7.23 (d, J = 8.0 Hz, 2H), 7.22–7.17 (m, 3H), 7.17–7.14 (dd, J = 7.8 Hz, 4.5 Hz, 1H), 6.8 (s, 1H), 2.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 150.2, 149.5, 148.7, 144.3, 137.8, 137.4, 135.8, 133.8, 130.0, 128.7, 128.1, 123.0, 120.5, 117.2, 109.8, 101.9, 21.2. TLC: R_f = 0.1 (CH_2Cl_2), 0.2 (MeOH–CH_2Cl_2, 1/19). IR (ATR): 3037 (m), 2923 (m), 2855 (m), 1897 (w), 1693 (m), 1592 (m), 1567 (m), 1512 (s), 1462 (m), 1430 (s), 1403 (s), 1371 (m), 1316 (s), 1294 (s), 1247 (m), 1211 (w), 1178 (m), 1110 (m), 1023 (m). HRMS (DART): calculated for $[C_{19}H_{15}N_3H]^+$ 286.1344, measured 286.1344.

7-Chloro-2-phenyl-1-(*p*-tolyl)-1*H*-indole (2o). Column chromatography eluent: hexanes to CH_2Cl_2–hexanes, 1/4, step gradient. White solid (73%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65–7.62 (dd, J = 7.8 Hz, 1.1 Hz, 1H), 7.32–7.25 (m, 5H), 7.25–7.21 (dt, J = 8.5 Hz, 2.0 Hz, 2H), 7.21–7.19 (dd, J = 7.7 Hz, 1.1 Hz, 1H), 7.18–7.15 (m, 2H), 7.14–7.10 (t, J = 7.8 Hz, 1H), 6.8 (s, 1H), 2.43 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 143.3, 138.1, 136.2, 134.0, 132.4, 130.9, 130.3, 129.5, 128.7, 128.0, 127.6, 124.0, 120.8, 119.3, 117.4, 103.5, 21.3. TLC: R_f = 0.6 (hexanes). IR (ATR): 3064 (w), 3038 (w), 2924 (m), 2853 (w), 1897 (w), 1785 (w), 1609 (m), 1581 (m), 1513 (w), 1491 (m), 1470 (s), 1456 (m), 1443 (m), 1422 (s), 1377 (w), 1351 (w), 1322 (w), 1289 (s), 1272 (w), 1256 (w), 1236 (m), 1206 (w), 1192 (m), 1169 (m), 1143 (s), 1107 (w), 1097 (w), 1071 (w), 1050 (w), 1038 (m), 1020 (s). HRMS (DART): calculated for $[C_{21}H_{16}ClNH]^+$ 318.1044, measured 318.1045.

5-Bromo-2-phenyl-1-(*p*-tolyl)-1*H*-indole (2p). Column chromatography eluent: hexanes to CH_2Cl_2–hexanes, 1/4, step gradient. White solid (76%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83–7.81 (d, J = 1.8 Hz, 1H), 7.31–7.22 (m, 8H), 7.16–7.11 (m, 3H), 6.74 (d, J = 0.6 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 141.9, 137.5, 135.4, 132.1, 130.0, 129.8, 128.9, 128.2, 127.7, 127.6, 124.9, 122.8, 113.6, 112.2, 102.6, 21.2. TLC: R_f = 0.4 (hexanes). IR (ATR): 3033 (m), 2923 (s), 2855 (m), 1902 (w), 1602 (m), 1514 (s), 1486 (m), 1456 (s), 1441 (s), 1378 (s), 1324 (m), 1302 (w), 1285 (w), 1255 (w), 1204 (m), 1170 (m), 1109 (w), 1077 (w), 1052 (m), 1029 (m). HRMS (DART): calculated for $[C_{21}H_{16}BrNH]^+$ 362.0539, measured 362.0538.

General procedure for benzofuran synthesis

In a reaction flask 2-halo-arylacetylene (0.5 mmol), and DMSO (1.0 mL) were added. The reaction was started with the addition of NaOH (0.6 mmol). The reaction was stirred on an aluminum heating block at 100 °C for 18 h. The reaction was quenched by dilution with CH_2Cl_2 and addition of NH_4Cl. The layers were separated and the aqueous phase extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with H_2O (80 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude product purified by silica gel flash column chromatography.

2-Phenylbenzofuran (3a). Column chromatography eluent: hexanes. White solid (92%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94–7.91 (m, 2H), 7.65–7.62 (ddd, J = 7.7 Hz, 1.4 Hz, 0.7 Hz, 1H), 7.60–7.57 (dq, J = 8.0 Hz, 0.8 Hz, 1H), 7.52–7.47 (m, 2H), 7.43–7.38 (tt, J = 7.4 Hz, 1.3 Hz, 1H), 7.37–7.32 (m, 1H), 7.31–7.27 (m, 1H), 7.07–7.06 (d, J = 1.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 155.9, 154.9, 130.5, 129.2, 128.8, 128.6, 124.9, 124.3, 123.0, 120.9, 111.2, 101.2. TLC: R_f = 0.5 (hexanes). IR (ATR): 3034 (m), 1896 (w), 1673 (w), 1604 (w), 1587 (w), 1561 (m), 1490 (m), 1470 (m), 1455 (s), 1440 (s), 1350 (w), 1333 (w), 1321 (w), 1304 (w), 1295 (w), 1272 (w), 1257 (m), 1207 (m), 1168 (m), 1105 (m), 1073 (m), 1038 (m), 1019 (m). HRMS (DART): calculated for $[C_{14}H_{10}OH]^+$ 195.0804, measured 195.0776.

2-(*tert*-Butyl)benzofuran (3b). Column chromatography eluent: hexanes. White solid (89%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51–7.48 (m, 1H), 7.45–7.42 (m, 1H), 7.24–7.16 (m, 2H), 6.37–6.36 (d, J = 0.9 Hz, 1H), 1.39 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 167.4, 154.6, 128.9, 123.0, 122.2, 120.3, 110.8, 98.9, 33.0, 28.9. TLC: R_f = 0.7 (hexanes). IR (ATR): 2924 (s), 2854 (m), 1844 (w), 1734 (m), 1716 (m), 1699 (s), 1674 (m),

1647 (w), 1555 (m), 1523 (s), 1498 (m), 1456 (m), 1260 (m). HRMS (DART): calculated for $[C_{12}H_{14}OH]^+$ 175.1117, measured 175.1115.

2-Phenylfuro[2,3-*b*]pyridine (3c). Column chromatography eluent: hexanes to CH_2Cl_2, step gradient. Brown solid (93%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.33–8.30 (dd, J = 5 Hz, 1.3 Hz, 1H), 7.95–7.91 (m, 3H), 7.51–7.46 (m, 2H), 7.43–7.39 (tt, J = 7.5 Hz, 1.3 Hz, 1H), 7.26–7.22 (dd, J = 8.0 Hz, 4.9 Hz, 1H), 7.03 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 161.9, 155.7, 143.9, 129.7, 129.5, 129.3, 128.9, 128.5, 125.2, 119.5, 100.0. TLC: R_f = 0.6 (CH_2Cl_2). IR (ATR): 3056 (w), 2974 (m), 2927 (w), 1952 (w), 1888 (w), 1734 (w), 1688 (m), 1657 (m), 1596 (m), 1585 (m), 1562 (m), 1542 (w), 1535 (w), 1491 (m), 1471 (w), 1446 (m), 1431 (m), 1416 (w), 1401 (s), 1363 (m), 1334 (m), 1305 (w), 1297 (m), 1277 (w), 1243 (s), 1170 (s), 1112 (m), 1071 (w), 1037 (w), 1045 (w), 1020 (s), 1000 (w). HRMS (DART): calculated for $[C_{13}H_9NOH]^+$ 196.0757, measured 196.0732.

2-(*tert*-Butyl)furo[2,3-*b*]pyridine (3d). Column chromatography eluent: hexanes to CH_2Cl_2–hexanes, 1/1, step gradient. Brown oil (90%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.26–8.20 (d, J = 4.0 Hz, 1H), 7.82–7.79 (dd, J = 7.5 Hz, 1.7 Hz, 1H), 7.18–7.15 (dd, J = 7.5 Hz, 5.0 Hz, 1H), 6.37 (s, 1H), 1.41 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 167.3, 161.8, 142.7, 128.9, 121.1, 118.9, 98.1, 33.1, 28.6. TLC: R_f = 0.7 (CH_2Cl_2), 0.3 (CH_2Cl_2–hexanes, 1/1). IR (ATR): 2926 (s), 1580 (s), 1460 (m), 1403 (s), 1364 (m), 1341 (m), 1286 (s), 1252 (s), 1224 (m), 1203 (s), 1166 (m), 1115 (m), 1086 (s). HRMS (DART): calculated for $[C_{11}H_{13}NOH]^+$ 176.1075, measured 176.1075.

Furo[2,3-*b*]pyridine (3e). Column chromatography eluent: hexanes to CH_2Cl_2, step gradient. Yellow solid (61%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.37–8.34 (dd, J = 5.0 Hz, 2.0 Hz, 1H), 7.98–7.95 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.74–7.72 (d, J = 2.5 Hz, 1H), 7.27–7.23 (dd, J = 8.0 Hz, 4.5 Hz, 1H), 6.81–6.79 (d, J = 2.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 162.0, 144.7, 144.2, 130.1, 119.2, 106.0, 103.8. TLC: R_f = 0.6 (CH_2Cl_2). IR (ATR): 2923 (s), 2880 (m), 1288 (s), 1135 (s). HRMS (DART): calculated for $[C_{11}H_{13}NOH]^+$ 176.1070, measured 176.1070.

7-Chloro-2-phenylbenzofuran (3j). Column chromatography eluent: hexanes. Yellow solid (80%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94–7.90 (m, 2H), 7.50–7.46 (m, 3H), 7.43–7.38 (tt, J = 7.5 Hz, 2 Hz, 1H), 7.32–7.29 (dd, J = 7.8 Hz, 0.9 Hz, 1H), 7.20–7.15 (t, J = 7.8 Hz, 1H), 7.04 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 156.8, 150.6, 130.8, 129.8, 129.0, 128.8, 125.1, 124.4, 123.8, 119.4, 116.6, 101.7. TLC: R_f = 0.5 (hexanes). IR (ATR): 3063 (w), 1609 (m), 1580 (m), 1491 (m), 1470 (s), 1447 (w), 1422 (s), 1351 (w), 1322 (w), 1288 (s), 1236 (s), 1192 (m), 1170 (s), 1143 (s), 1097 (w), 1071 (w), 1050 (w), 1038 (m), 1020 (s). HRMS (DART): calculated for $[C_{14}H_9ClOH]^+$ 229.0420, measured 229.0428.

5-Bromo-2-phenylbenzofuran (3k). Column chromatography eluent: hexanes. Yellow solid (82%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89–7.85 (m, 2H), 7.73–7.71 (m, 2H), 7.51–7.46 (m, 2H), 7.45–7.37 (m, 3H), 6.96 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 157.2, 153.6, 131.2, 129.9, 129.0, 128.8, 127.1, 125.1, 123.5, 112.6, 100.7. TLC: R_f = 0.3 (hexanes). IR (ATR): 3091 (w), 3060 (w), 3030 (w), 2926 (w), 2601 (w), 2545 (w), 2237 (w), 2079 (w), 1959 (w), 1889 (w), 1871 (w), 1831 (w), 1740 (w), 1684 (w), 1604 (m), 1577 (s), 1490 (m), 1449 (s), 1437 (s), 1428 (s), 1326 9m), 1275 (m), 1260 (s), 1206 (m), 1156 (m), 1116 (m), 1072 (m), 1050 (s), 1037 (s), 1020 (m), 1001 (w). HRMS (DART): calculated for $[C_{14}H_9BrOH]^+$ 272.9910, measured 272.9921.

General procedure for aqueous benzofuran synthesis

In a reaction flask 2-halo-arylacetylene (0.5 mmol), and H_2O (1 mL) were added. The reaction was started with the addition of NaOH (1.5 mmol). The reaction was stirred on an aluminum heating block at 125 °C for 48 h. The reaction was quenched by dilution with ethyl acetate and addition of NH_4Cl. The layers were separated and the aqueous phase extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with H_2O (80 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude product purified by silica gel flash column chromatography.

2-(4-(Trifluoromethyl)phenyl)furo[2,3-*b*]pyridine (3g). Column chromatography eluent: hexanes–CH_2Cl_2, 1 : 1 to CH_2Cl_2. Yellow oil (97%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.37–8.35 (dd, J = 5 Hz, 1.5 Hz, 1H), 8.04–8.01 (d, J = 8.5 Hz, 2H), 7.98–7.95 (m, 1H), 7.76–7.72 (d, J = 8.5 Hz, 2H), 7.29–7.25 (m, 1H), 7.14 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 162,0, 153.9, 144.7, 130.1, 126.0–125.8 (q, J = 3.8 Hz), 125.3, 121.1, 119.8, 102.0, 29.7. TLC: R_f = 0.6 (CH_2Cl_2). IR (ATR): 2924 (m), 2852 (m), 1930 (w), 1732 (m), 1615 (m), 1596 (s), 1562 (s), 1511 (w), 1456 (m), 1438 (s), 1415 (w), 1403 (m), 1324 (s), 1295 (s), 1255 (s), 1216 (s), 1186 (m), 1162 (s), 1128 (m), 1120 (s), 1067 (s), 1031 (w), 1014 (s). HRMS (DART): calculated for $[C_{14}H_8F_3NOH]^+$ 264.0631, measured 264.0631.

2-(4-Methoxyphenyl)furo[2,3-*b*]pyridine (3h). Column chromatography eluent: CH_2Cl_2. Yellow oil (95%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.28–8.25 (dd, J = 4.8 Hz, 1.5 Hz, 1H), 7.89–7.84 (m, 3H), 7.3–7.19 (dd, J = 7 Hz, 5 Hz, 1H), 7.02–6.99 (m, 2H), 6.88 (s, 1H), 3.88 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 160.5, 155.8, 143.2, 141.2, 129.0, 126.7, 121.2, 119.4, 110.0, 98.3, 55.4. TLC: R_f = 0.3 (CH_2Cl_2). IR (ATR): 2920 (s), 2855 (s), 1735 (s), 1615 (s), 1598 (s), 1507 (s), 1256 (s), 1037 (s). HRMS (DART): calculated for $[C_{14}H_{11}NO_2H]^+$ 226.0863, measured 226.0864.

General procedure for N–H indole synthesis

In a reaction flask under Ar 2-halo-arylacetylene (0.5 mmol), acetamide (1.1 mmol), and DMSO (1.0 mL) were added. The reaction was started with the addition of KO*t*Bu (1.1 mmol). The reaction was stirred on an aluminum heating block at 100 °C for 18 h. The reaction was quenched by dilution with CH_2Cl_2 and addition of NH_4Cl. The layers were separated and the aqueous phase extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with H_2O (80 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude product purified by silica gel flash column chromatography.

2-Phenyl-1*H*-indole (4a). Column chromatography eluent: hexanes to CH_2Cl_2–hexanes, 1/1, step gradient. Yellow solid (68%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.34 (s, 1H), 7.71–7.63 (m,

3H), 7.49–7.41 (m, 3H), 7.37–7.32 (tt, J = 7.5 Hz, 1.0 Hz, 1H), 7.24–7.19 (m, 1H), 7.16–7.12 (m, 1H), 6.86–6.85 (dd, J = 2.0 Hz, 1.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 137.9, 136.8, 132.4, 129.3, 129.0, 127.7, 125.1, 122.3, 120.7, 120.3, 101.8, 100.0. TLC: R_f = 0.9 (CH_2Cl_2), 0.5 (EtOAc–hexanes, 1/9). IR (ATR): 3445 (s), 3050 (m), 2924 (m), 2853 (m), 1891 (w), 1686 (m), 1616 (m), 1542 (w), 1481 (m), 1457 (s), 1447 (s), 1403 (m), 1352 (m), 1339 (w), 1299 (s), 1241 (w), 1189 (w), 1148 (w), 1114 (w), 1074 (w), 1050 (w), 1028 (w). HRMS (DART): calculated for $[C_{14}H_{11}NH]^+$ 194.0964, measured 194.0965.

2-(*tert*-Butyl)-1*H*-indole (4b). Column chromatography eluent: hexanes to CH_2Cl_2–hexanes, 1/1, step gradient. White solid (61%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95 (s, 1H), 7.57–7.54 (m, 1H), 7.35–7.32 (m, 1H), 7.16–7.12 (m, 1H), 7.11–7.06 (m, 1H), 6.29–6.27 (dd, J = 2.5 Hz, 1.0 Hz, 1H), 1.42 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 148.7, 135.7, 128.5, 121.1, 120.0, 119.6, 110.3, 97.0, 31.8, 30.3. TLC: R_f = 0.9 (CH_2Cl_2), 0.6 (EtOAc–hexanes, 1/9). IR (ATR): 3406 (s), 2957 (s), 2925 (s), 2863 (m), 1702 (w), 1612 (w), 1582 (w), 1542 (m), 1488 (w), 1458 (s), 1407 (s), 1394 (m), 1365 (s), 1348 (s), 1290 (s), 1246 (w), 1231 (w), 1202 (w), 1189 (w), 1148 (w), 1116 (w), 1012 (s). HRMS (DART): calculated for $[C_{12}H_{15}NH]^+$ 174.1277, measured 174.1277.

2-Phenyl-1*H*-pyrrolo[2,3-*b*]pyridine (4c). Column chromatography eluent: CH_2Cl_2 to MeOH–CH_2Cl_2, 1/39, step gradient. Pale yellow solid (69%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 12.55 (s, 1H), 8.34–8.31 (d, J = 4.0 Hz, 1H), 8.00–7.97 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.94–7.90 (m, 2H), 7.57–7.52 (m, 2H), 7.45–7.40 (tt, J = 7.5 Hz, 1.0 Hz, 1H), 7.15–7.10 (dd, J = 8.0 Hz, 4.5 Hz, 1H), 6.82 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 150.0, 142.0, 139.5, 132.4, 129.0, 128.7, 128.2, 125.9, 122.4, 116.1, 97.4. TLC: R_f = 0.8 (MeOH–CH_2Cl_2, 1/19), 0.4 (MeOH–CH_2Cl_2, 1/39). IR (ATR): 3160 (s), 3032 (s), 2972 (m), 2787 (m), 1904 (w), 1870 (w), 1833 (w), 1716 (w), 1698 (w), 1675 (w), 1588 (m), 1541 (m), 1486 (m), 1456 (m), 1431 (m), 1410 (m), 1363 (m), 1330 (m), 1280 (s), 1223 (w), 1195 (m), 1111 (m), 1074 (w), 1045 (w), 1029 (w). HRMS (DART): calculated for $[C_{13}H_{10}N_2H]^+$ 195.0917, measured 195.0895.

2-(*tert*-Butyl)-1*H*-pyrrolo[2,3-*b*]pyridine (4d). Column chromatography eluent: CH_2Cl_2 to MeOH–CH_2Cl_2, 2/23, step gradient. Yellow solid (67%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.76 (s, 1H), 8.28–8.26 (dd, J = 5.0 Hz, 1.5 Hz, 1H), 7.87–7.83 (ddd, J = 7.5 Hz, 1.5 Hz, 0.5 Hz, 1H), 7.07–7.03 (dd, J = 7.5 Hz, 5.0 Hz, 1H), 6.23–6.21 (d, J = 2.5 Hz, 1H), 1.48 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 150.2, 149.1, 141.4, 127.9, 127.7, 121.2, 94.7, 32.2, 30.1. TLC: R_f = 0.1 (MeOH–CH_2Cl_2, 1/19), 0.5 (MeOH–CH_2Cl_2, 2/23). IR (ATR): 3157 (m), 3088 (m), 2964 (s), 2869 (m), 1647 (m), 1605 (m), 1588 (s), 1540 (m), 1494 (w), 1417 (s), 1363 (s), 1326 (m), 1276 (s), 1226 (w), 1173 (s), 1109 (w), 1027 (w). HRMS (DART): calculated for $[C_{11}H_{14}N_2H]^+$ 175.1235, measured 175.1236.

1*H*-Pyrrolo[2,3-*b*]pyridine (4e). Column chromatography eluent: CH_2Cl_2 to MeOH–CH_2Cl_2, 2/23, step gradient. Yellow solid (52%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.49 (s, 1H), 8.36–8.30 (dd, J = 5.0 Hz, 1.3 Hz, 1H), 7.98–7.95 (dd, J = 8.0 Hz, 1.5 Hz, 1H), 7.36–7.33 (dd, J = 3.5 Hz, 1.5 Hz, 1H), 7.12–7.09 (dd, J = 8.0 Hz, 4.5 Hz, 1H), 6.54–6.52 (dd, J = 3.5 Hz, 1.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 148.5, 143.0, 129.0, 124.8, 120.1, 116.0, 101.0. TLC: R_f = 0.4 (MeOH–CH_2Cl_2, 2/23). IR (ATR): 3070 (m), 3061 (m), 2922 (s), 1584 (s), 1421 (s), 1279 (s). HRMS (DART): calculated for $[C_7H_6N_2H]^+$ 119.0609, measured 119.0614.

7-Chloro-2-phenyl-1*H*-indole (4f). Column chromatography eluent: hexanes to CH_2Cl_2–hexanes, 1/1, step gradient. Yellow solid (67%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.53 (s, 1H), 7.74–7.71 (m, 2H), 7.58–7.55 (dt, J = 8.0 Hz, 0.5 Hz, 1H), 7.52–7.47 (m, 2H), 7.41–7.37 (m, 1H), 7.24–7.21 (dd, J = 8.0 Hz, 1.0 Hz, 1H), 7.12–7.07 (t, J = 7.5 Hz, 1H), 6.89–6.88 (d, J = 2.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 138.7, 134.0, 131.8, 130.6, 129.1, 128.2, 125.3, 121.6, 121.0, 119.2, 116.3, 100.8. TLC: R_f = 0.1 (hexanes), 0.7 (CH_2Cl_2–hexanes, 1/1). IR (ATR): 3854 (w), 3748 (w), 3673 (w), 3650 (w), 3438 (s), 3067 (w), 3038 (w), 1957 (w), 1879 (w), 1834 (w), 1771 (w), 1685 (w), 1617 (w), 1602 (m), 1568 (m), 1542 (w), 1485 (s), 1451 (s), 1431 (s), 1391 (s), 1352 (s), 1324 (s), 1299 (s), 1244 (s), 1195 (s), 1163 (w), 1141 (m), 1097 (w), 1073 (w), 1050 (w), 1028 (w). HRMS (DART): calculated for $[C_{14}H_{10}ClNH]^+$ 228.0580, measured 228.0589.

5-Bromo-2-phenyl-1*H*-indole (4g). Column chromatography eluent: hexanes to CH_2Cl_2–hexanes, 1/1, step gradient. Yellow solid (62%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39 (s, 1H), 7.78–7.76 (q, J = 1.0 Hz), 7.69–7.65 (m, 2H), 7.50–7.45 (tt, J = 7.0 Hz, 2.0 Hz, 2H), 7.40–7.35 (tt, J = 7.0 Hz, 1.0 Hz, 1H), 7.30–7.28 (d, J = 1.0 Hz, 2H), 6.79–6.77 (d, J = 2.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 139.1, 135.4, 131.8, 131.0, 129.1, 128.2, 125.3, 125.1, 123.1, 113.4, 112.3, 99.5. TLC: R_f = 0.7 (CH_2Cl_2–hexanes, 1/1). IR (ATR): 3436 (s), 3082 (w), 3060 (w), 3037 (w), 2923 (w), 2853 (w), 1570 (w), 1488 (m), 1453 (s), 1393 (m), 1310 (m), 1282 (m), 1180 (w), 1128 (w), 1053 (m). HRMS (DART): calculated for $[C_{14}H_{10}BrNH]^+$ 272.0075, measured 272.0083.

6-Bromo-7-chloro-2-phenyl-1*H*-indole (4h). Column chromatography eluent: hexanes to CH_2Cl_2–hexanes, 1/1, step gradient. Yellow solid (59%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.51 (s, 1H), 7.71–7.67 (m, 2H), 7.51–7.46 (m, 2H), 7.42–7.37 (m, 2H), 7.36–7.33 (d, J = 8.5 Hz, 1H), 6.84–6.82 (d, J = 2.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 139.3, 134.9, 131.4, 129.3, 129.2, 128.4, 125.3, 125.0, 120.0, 116.6, 115.0, 100.9. TLC: R_f = 0.1 (hexanes), 0.7 (CH_2Cl_2–hexanes, 1/1). IR (ATR): 3426 (s), 3080 (m), 3057 (m), 3036 (m), 2924 (m), 2854 (m), 1939 (w), 1866 (w), 1735 (w), 1604 (m), 1567 (m), 1488 (s), 1473 (s), 1450 (s), 1432 (s), 1375 (s), 1338 (s), 1309 (m), 1296 (m), 1273 (w), 1227 (s), 1182 (w), 1153 (s), 1119 (w), 1097 (w), 1050 (w), 1029 (w), 1000 (w). HRMS (DART): calculated for $[C_{14}H_9BrClNH]^+$ 305.9685, measured 305.9697.

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