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Silver-Mediated Synthesis of Substituted Benzofuran- and Indole-Pyrroles via Sequential Reaction of *ortho*-Alkynylaromatics with Methylene Isocyanides

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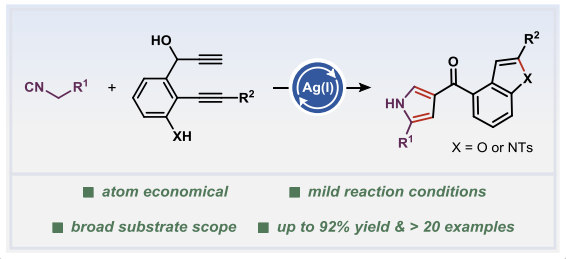


ABSTRACT: A silver-mediated reaction between 2-ethynyl-3-(1-hydroxyprop-2-yn-1-yl)phenols or 2-ethynyl-3-(1-hydroxyprop-2-yn-1-yl)anilines and methylene isocyanides has been developed. A sequential 5-*endo-dig* cyclization and [3+2] cycloaddition process is proposed. This synthetic strategy is atom- and step-efficient and applicable to a broad scope of substrates, allowing the synthesis of valuable substituted benzofuran- and indole-pyrroles in moderate to high yields.

KEYWORDS: alkynes; benzofurans; isocyanides; pyrroles; silver

INTRODUCTION

Isocyanides and alkynes are two classes of commercially available and extraordinarily versatile building blocks, widely applied in organic synthesis.[1,2] Although the reports describing the reactions between methylene isocyanates and alkynes are considerably rare, there have been noteworthy developments in the past years.[3] Likhar and coworkers described the synthesis of 2,4-disubstituted pyrroles via a Cu-catalyzed cycloaddition between isocyanides and terminal alkynes.[4] In contrast to Likhar's work, the Bi and Lei groups realized that the cycloaddition reaction of isocyanides with unactivated terminal alkynes in the presence of a silver catalyst afforded 2,3-disubstituted pyrroles (Figure 1a).[5] Following these reports, Bi and coworkers reported a conceptually distinct C–C coupling/oxygen transposition of terminal propargylic alcohols with isocyanides to give a variety of synthetically valuable 2,3-alleneamides (Figure 1b).[6a] Herein, we disclose our continued efforts to further expand the synthetic utility of these reactions to the synthesis of functionalized benzofuran- and indole-pyrroles (Figure 1c).[6b] Gratifyingly, a new silver-mediated sequential reaction of 2-ethynyl-3-(1-hydroxyprop-2-yn-1-yl)aromatics with activated methylene isocyanides was realized, providing a modular approach to benzofuran- and indole-pyrroles with broad substrate scope and in good to high yields. A reaction pathway including 5-*endo-dig* cyclization and regioselective [3+2] cycloaddition is proposed.

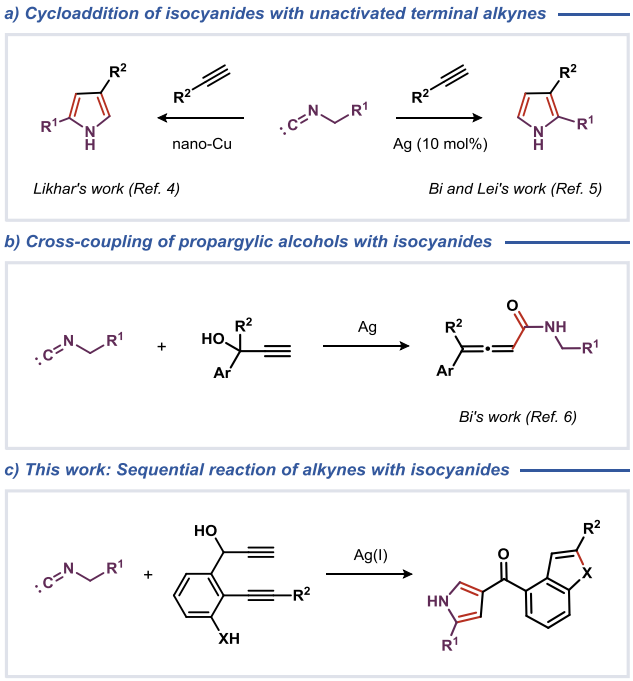


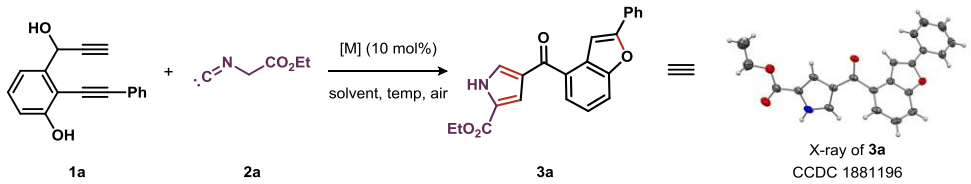
Figure 1. Metal-catalyzed reactions for synthesis of pyrroles.

RESULTS AND DISCUSSION

At the beginning, we concentrated on optimization of the reaction conditions with 3-(1-hydroxyprop-2-yn-1-yl)-2-(phenylethynyl)phenol (**1a**) and ethyl isocyanoacetate (**2a**) as the model substrates (Table 1). A range of silver catalysts, including AgOAc, AgF and $AgNO_2$, and other metal catalysts, such as CuI and $Pd(OAc)_2$, were initially screened in 1,4-dioxane at 80 °C (Table 1, entries 1–8). We found that Ag_2O displayed the best reactivity, affording product **3a** in 73% yield (Table 1, entry 6), while other metal catalysts were found to be less efficient. Next, the solvent effect was evaluated and proved that the use of *N*,*N*-dimethyl formamide (DMF) greatly increased the yield of **3a** to 91% (Table 1, entry 11). In contrast, aprotic and polar solvents, such as DCE and CH_3CN, had a negative effect, and delivered **3a** in 68% and 59% yields, respectively (Table 1, entries 9 and 10). Furthermore, the use of the protic solvent EtOH only resulted in formation of trace amounts of **3a**. A decrease in the reaction temperature from 80 °C to 40 °C or 25 °C, reduced the yield of the desired product (Table 1, entries 13 and 14). Gratifyingly, the reaction without addition of a silver catalyst

failed to produce the product (Table 1, entry 15). The conditions highlighted in Table 1 were therefore selected as optimal. The structure of product **3a** was further established by X-ray crystallography (CCDC 1881196, see Table 1).

Table 1. Optimization of the Reaction Conditions[a]



1a 2a 3a

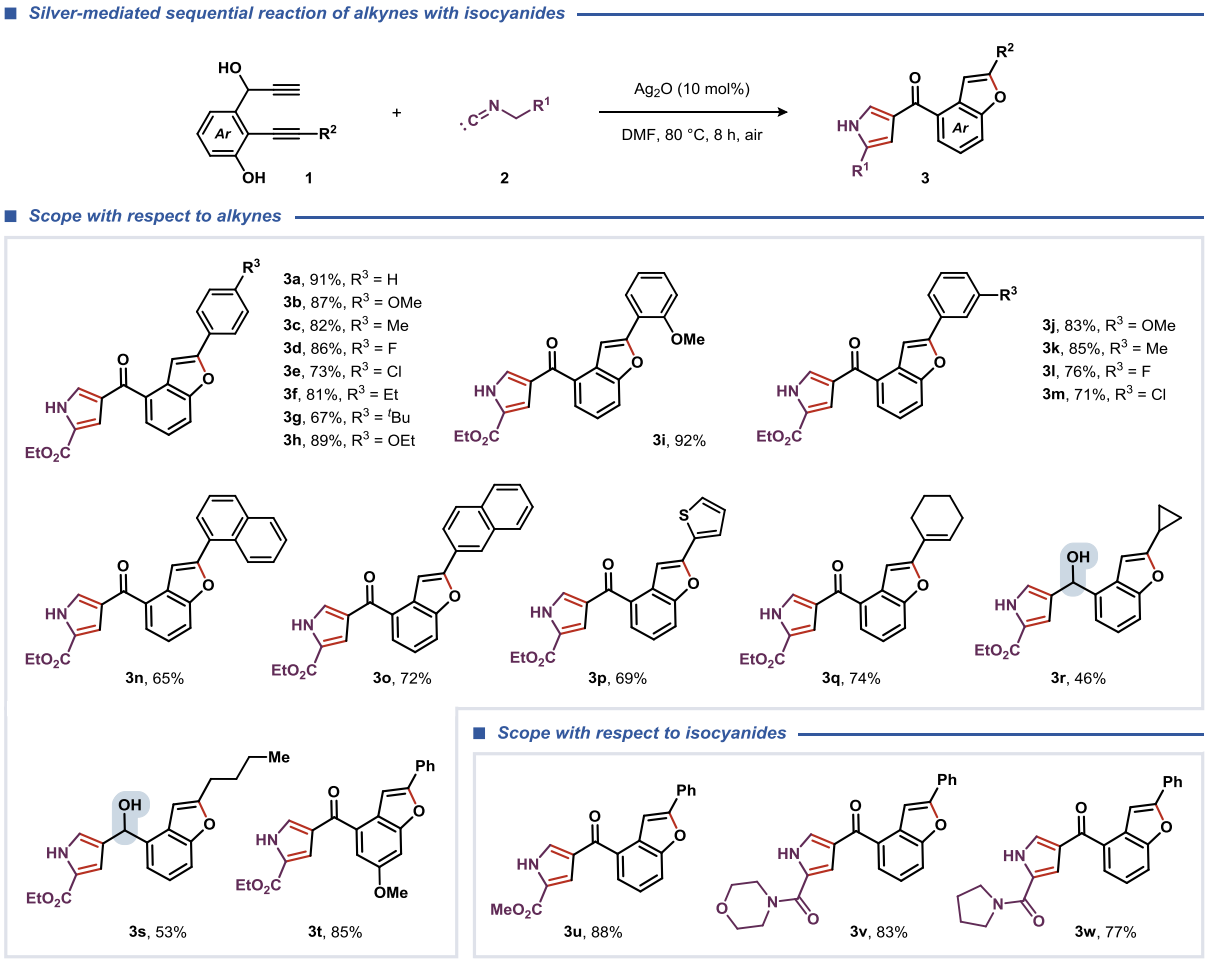
Entry	[M]	Solvent	Temp (°C)	Yield (%)[b]
1	AgOAc	1,4-dioxane	80	47
2	AgF	1,4-dioxane	80	46
3	$AgNO_2$	1,4-dioxane	80	38
4	Ag_2CO_3	1,4-dioxane	80	51
5	$AgBF_4$	1,4-dioxane	80	0
6	Ag_2O	1,4-dioxane	80	73
7	$Pd(OAc)_2$	1,4-dioxane	80	31[c]
8	CuI	1,4-dioxane	80	27[c]
9	Ag_2O	DCE	80	68
10	Ag_2O	CH_3CN	80	59
11	Ag_2O	DMF	80	91
12	Ag_2O	EtOH	80	trace
13	Ag_2O	DMF	40	62
14	Ag_2O	DMF	25	34
15	--	DMF	80	0

[a] Reaction conditions: **1a** (0.3 mmol), **2a** (0.45 mmol), catalyst (0.03 mmol), solvent (2.0 mL), 80 °C under air, 8.0 h. [b] Isolated yields. [c] ^1H NMR yields using CH_2Br_2 as internal standard.

Guided by the preliminary findings, the scope of the transformation was explored (Scheme 1). An assortment of substituted 2-ethynyl-3-(1-hydroxyprop-2-yn-1-yl)phenols **1** reacted under the optimized reaction conditions with ethyl isocyanoacetate (**2a**) to furnish the corresponding products. The reaction was compatible with a variety of aryl motifs substituted at the *para*-, *meta*- and *ortho*-positions, furnishing benzofuran-pyrrole products **3b–3m** in moderate to good yields.

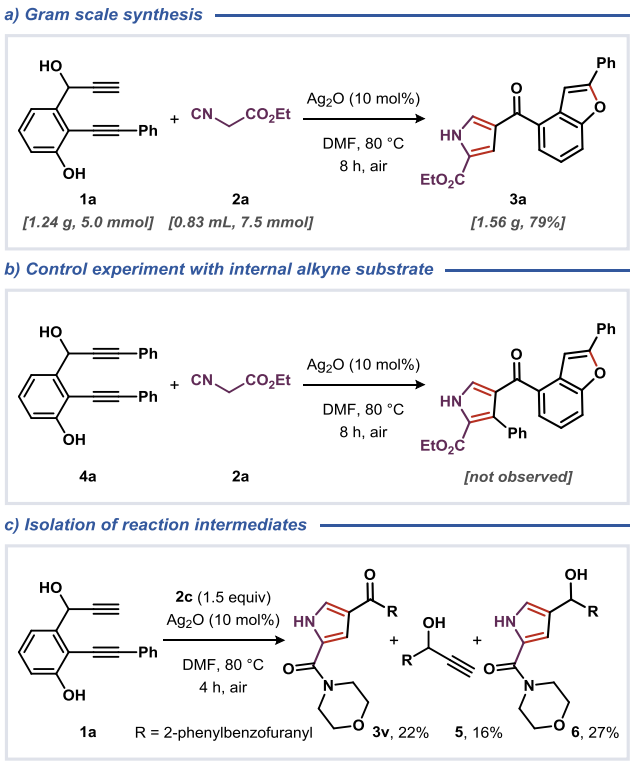
Importantly, a variety of synthetically valuable functional groups, including fluoride and chloride were well tolerated in the reaction to deliver the functionalized products in synthetically useful yields. The tolerance of these functional groups offers an opportunity for further elaboration of chemical space. Similarly, propargylic derivatives bearing aromatic substituents, including fused aryl and heteroaryl groups, underwent smooth reaction with **2a** to deliver the products **3n**–**3p** in 65–72% yields. Gratifyingly, the alkenyl substituent 1-cyclohexenyl was tolerated, producing **3q** in 74% yield. Furthermore, under the same conditions the cyclopropyl and *n*-butyl-derivatized substrates **1r** and **1s** generated products **3r** and **3s** in acceptable yields. According to NMR analysis and high resolution mass spectra, **3r** and **3s** are not oxidized product, which is presumably due to the delocalization of the electron density onto the aryl rings and is of great help to put forward a mechanism.[7] Attempts at obtaining the corresponding ketone products by prolonging the reaction time were unsuccessful. Additionally, the methoxy substituted substrate **1t** afforded the target product **3t** in decent yield. Finally, the scope with respect to isocyanides was investigated under the optimized conditions. A range of activated methylene isocyanides including methyl isocyanoacetate and isocyanoacetamide derivatives reacted with **1a**, delivering the expected products **3u**–**3w** in good yields.

Scheme 1. Substrate Scope



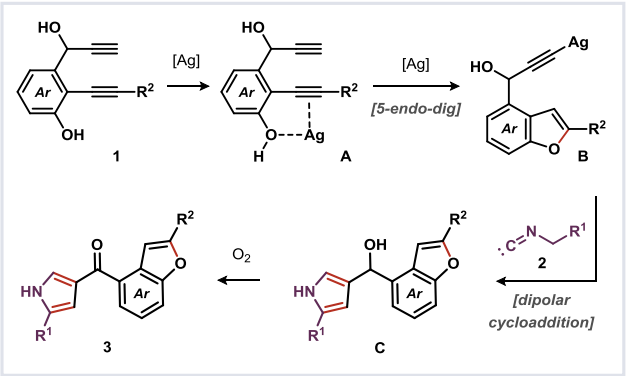
Encouraged by these findings, the applicability of the present transformation was evaluated by carrying out the reaction of 3-(1-hydroxyprop-2-yn-1-yl)-2-(phenylethynyl)phenol **1a** and ethyl isocyanoacetate **2a** on gram scale. The corresponding product **3a** was obtained with a slightly decreased yield of 79% (Scheme 2a). Unfortunately, subjecting the internal alkyne substrate **4a** and **2a** to the standard conditions resulted in no product (Scheme 2b). This implies that the formation of the corresponding silver acetylide is essential.[5,8] Furthermore, when terminating the reaction mixture of **1a** and **2c** after half of the standard reaction time, intermediates **5** and **6** were obtained in reasonable yields (Scheme 2c). Adducts **5** and **6** could be easily converted to the corresponding product **3a** in high yields, stressing the involvement of **5** and **6** as key intermediates in the developed transformation.

Scheme 2. Gram-Scale Synthesis and Mechanistic Studies



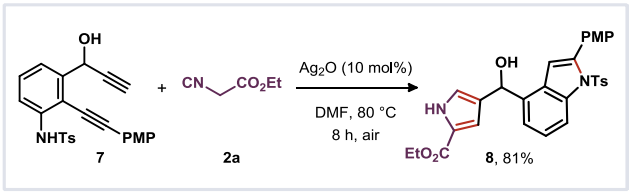
Based on related precedents[9,10] including previous reports on silver-catalyzed reactions of isocyanides with terminal alkynes and propargylic alcohols, a plausible reaction mechanism for the formation of benzofuran-pyrrole **3** was proposed (Scheme 3). Owing to the chelating effect of the hydroxyl and alkynyl units, silver complex **A** is initially formed. A subsequent 5-*endo-dig* cyclization of complex **A** generates benzofuran **B**.[11] Next, the terminal alkyne in **B** undergoes a [3+2] cycloaddition of the alkynyl unit with the isocyanide, thus affording intermediate **C**. Finally, oxidation of the alcohol moiety to the corresponding carbonyl group gives the final product **3**.

Scheme 3. Proposed Reaction Mechanism



Lastly, to expand the application of this transform, substrate **7** was synthesized from 2-bromo-3-nitro-benzaldehyde (for synthetic details, see the Supporting Information). As shown in Scheme 4, under the same reaction conditions, indole-pyrrole **8** could be generated in high yield. The product **8** is not further oxidized, which is presumably due to the electron-rich indole ring that increases the electron density around the hydroxy group and makes it less prone to undergo oxidation. These observations strongly support that formation of **8** occurs through a similar pathway as that of benzofuran-based derivatives **3**.

Scheme 4. Formation of Indole-Pyrrole



CONCLUSIONS

In summary, we have developed a silver-mediated sequential cyclization reaction of isocyanides with 2-ethynyl-3-(1-hydroxyprop-2-yn-1-yl)phenols or 2-ethynyl-3-(1-hydroxyprop-2-yn-1-yl)anilines, affording benzofuran- and indole-pyrroles in good to high yields. A mechanistic pathway for the formation of these versatile products was proposed. Considering the relevance of benzofuran-pyrroles as potentially useful building blocks, this practical methodology will certainly

find promising synthetic applications in the future.

EXPERIMENTAL SECTION

General Information. All reagents were purchased from commercial sources (Adamas, Aladdin, etc) and used without further treatment, unless otherwise indicated. The products were purified by column chromatography over silica gel. ^{1}H NMR and ^{13}C NMR spectra were recorded at 25 °C on a Varian 400 MHz and 100 MHz, respectively, and TMS was used as internal standard. High resolution mass spectra (HRMS) were recorded on Bruck MicroTof using ESI-TOF method.

General Procedure for the Synthesis of 1 (Using 1a as an Example). Triethylamine (0.5 mL, 3.5 mmol) and DMAP (0.012 g, 0.1 mmol) were added to a well-stirred solution of 2-bromo-3-hydroxybenzaldehyde (0.35 g, 1.7 mmol) in CH_2Cl_2 (10 mL) under N_2. The reaction mixture was cooled to 0 °C, and Ac_2O (0.35 mL, 3.6 mmol) was added drop-wise at the same temperature, followed by stirring for 1 h at room temperature. The reaction mixture was then poured into an aqueous saturated solution of $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate 7:1) afforded 2-bromo-3-formylphenyl acetate in 95% yield as a yellow solid.

To a mixture of 2-bromo-3-formylphenyl acetate (0.39 g, 1.64 mmol), CuI (0.019 g, 0.1 mmol) and $Pd(PPh_3)_2Cl_2$ (0.07 g, 0.1 mmol) in triethylamine (10.0 mL) stirred at 50 °C was added ethynylbenzene (219 µL, 2.0 mmol) under N_2, until 2-bromo-3-formylphenyl acetate was consumed as indicated by TLC (about 10 h). The resulting mixture was concentrated and the residue was taken up in CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate 10:1) afforded

3-formyl-2-(phenylethynyl)phenyl acetate in 89% yield as a white solid.[12a]

A mixture of 3-formyl-2-(phenylethynyl)phenyl acetate (0.40 g, 1.5 mmol) and K_2CO_3 (0.42 g, 3.0 mmol) in MeOH (6.0 mL) was stirred at room temperature for 0.5 h. The reaction mixture was then neutralized with 1 N HCl and the resulting solution was concentrated to remove MeOH. The residue was partitioned with EtOAc and water, and the organic layer was washed with brine, dried over $MgSO_4$, and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate 4:1) afforded 3-hydroxy-2-(phenylethynyl)benzaldehyde in 80% yield as a white solid.[12b]

A solution of 3-hydroxy-2-(phenylethynyl)benzaldehyde (0.222 g, 1.0 mmol) in distilled THF (2 mL) was treated at 0 °C with ethynylmagnesium bromide (3 mL, 1.5 mmol). The resulting mixture was stirred at 0 °C for 1 h and for 4 h at room temperature. After treatment with a saturated aqueous solution of NH_4Cl and extractions with Et_2O, the combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate 3:1) afforded **1a** in 94% yield as a yellow solid.[12c]

*3-(1-Hydroxyprop-2-yn-1-yl)-2-(phenylethynyl)phenol (**1a**).* Yield 94% (233 mg). Pale yellow solid; m.p. 86–87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58–7.56 (m, 2H), 7.41–7.39 (m, 3H), 7.32–7.27 (m, 2H), 6.99 (dd, *J* = 7.6 Hz, 1.6 Hz, 1H), 5.96 (s, 1H), 5.83 (s, 1H), 2.67 (d, *J* = 2.4 Hz, 1H), 2.59 (s, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 156.9, 142.1, 131.6 (2C), 130.4, 129.2, 128.6 (2C), 121.9, 118.5, 114.9, 108.0, 101.8, 82.8, 80.3, 74.7, 63.2; HRMS (ESI-TOF) m/z calculated for $C_{17}H_{13}O_2$ $[M+H]^+$: 249.0910, found: 249.0917.

*3-(1-Hydroxyprop-2-yn-1-yl)-2-((4-methoxyphenyl)ethynyl)phenol (**1b**).* Yield 92% (256 mg). Pale

yellow solid; m.p. 88–89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51–7.47 (m, 2H), 7.30–7.25 (m, 2H), 6.98–6.96 (m, 1H), 6.92–6.88 (m, 2H), 6.00 (s, 1H), 5.81 (dd, *J* = 6.0 Hz, 2.0 Hz, 1H), 3.84 (s, 3H), 2.72 (d, *J* = 6.0 Hz, 1H), 2.66 (d, *J* = 2.0 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.3, 156.7, 141.9, 133.1 (2C), 130.0, 118.5, 114.8, 114.2 (2C), 113.9, 108.3, 101.9, 82.8, 79.0, 74.6, 63.1, 55.4; HRMS (ESI-TOF) m/z calculated for $C_{18}H_{15}O_3$ $[M+H]^+$: 279.1016, found: 279.1021.

*3-(1-Hydroxyprop-2-yn-1-yl)-2-(p-tolylethynyl)phenol (**1c**).* Yield 87% (228 mg). Pale yellow solid; m.p. 86–87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.0 Hz, 2H), 7.29–7.25 (m, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.98 (dd, *J* = 7.2 Hz, 2.4 Hz, 1H), 5.98 (s, 1H), 5.82 (dd, *J* = 6.0 Hz, 2.0 Hz, 1H), 2.66–2.65 (m, 2H), 2.39 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 156.7, 142.0, 139.5, 131.4 (2C), 130.1, 129.3 (2C), 118.8, 118.5, 114.8, 108.2, 102.1, 82.8, 79.6, 74.6, 63.1, 21.5; HRMS (ESI-TOF) m/z calculated for $C_{18}H_{15}O_2$ $[M+H]^+$: 263.1067, found: 263.1069.

*2-((4-Fluorophenyl)ethynyl)-3-(1-hydroxyprop-2-yn-1-yl)phenol (**1d**).* Yield 81% (215 mg). Pale yellow solid; m.p. 92–93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54–7.50 (m, 2H), 7.28–7.25 (m, 2H), 7.06–7.02 (m, 2H), 6.93 (dd, *J* = 6.4 Hz, 2.8 Hz, 1H), 6.41 (s, 1H), 5.80 (d, *J* = 2.0 Hz, 1H), 3.34 (s, 1H), 2.64 (d, *J* = 2.0 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.8 (d, *J* = 250 Hz), 156.9, 142.4, 133.5 (d, *J* = 8.4 Hz, 2C), 130.2, 118.3, 118.2 (d, *J* = 3.6 Hz), 115.8 (d, *J* = 22 Hz, 2C), 114.9, 108.0, 100.1, 82.9, 80.5, 74.4, 62.8; HRMS (ESI-TOF) m/z calculated for $C_{17}H_{12}FO_2$ $[M+H]^+$: 267.0816, found: 267.0811.

*2-((4-Chlorophenyl)ethynyl)-3-(1-hydroxyprop-2-yn-1-yl)phenol (**1e**).* Yield 79% (222 mg). Pale yellow solid; m.p. 137–138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 7.6 Hz, 2H), 7.44–7.27 (m, 4H), 6.98 (dd, *J* = 7.6 Hz, 1.6 Hz, 1H), 5.89 (s, 1H), 5.80 (s, 1H), 2.67 (d, *J* = 2.4 Hz, 1H), 2.51 (s, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.0, 142.3, 135.5, 132.9 (2C), 130.7, 129.1 (2C), 120.5, 118.7, 115.1, 107.8, 100.7, 82.8, 81.4, 74.9, 63.2; HRMS (ESI-TOF) m/z calculated for $C_{17}H_{12}ClO_2$ $[M+H]^+$: 283.0520, found:

283.0526.

*2-((4-Ethylphenyl)ethynyl)-3-(1-hydroxyprop-2-yn-1-yl)phenol (**1f**).* Yield 73% (201 mg). Pale yellow solid; m.p. 88–89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89–7.84 (m, 2H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.48 (d, *J* = 7.2 Hz, 1H), 7.38–7.30 (m, 3H), 5.98 (s, 1H), 5.82 (dd, *J* = 6.0 Hz, 2.0 Hz, 1H), 2.82–2.71 (m, 3H), 2.39 (d, *J* = 6.0 Hz, 1H), 1.33 (t, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 156.6, 155.2, 145.3, 132.0, 128.4 (2C), 127.7, 127.4, 125.2 (2C), 123.9, 120.7, 111.7, 99.5, 83.0, 75.1, 63.5, 28.8, 15.5; HRMS (ESI-TOF) m/z calculated for $C_{19}H_{17}O_2$ $[M+H]^+$: 277.1223, found: 277.1221.

*2-((4-(Tert-butyl)phenyl)ethynyl)-3-(1-hydroxyprop-2-yn-1-yl)phenol (**1g**).* Yield 59% (179 mg). Pale yellow solid; m.p. 76–77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.54 (m, 2H), 7.48–7.45 (m, 2H), 7.36–7.32 (m, 2H), 7.03 (dd, *J* = 6.4 Hz, 2.8 Hz, 1H), 6.10 (s, 1H), 5.88 (s, 1H), 2.84 (s, 1H), 2.39 (d, *J* = 2.0 Hz, 1H), 1.39 (s, 9H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 156.9, 152.7, 142.1, 131.4 (2C), 130.2, 125.7 (2C), 118.7, 118.5, 114.9, 108.3, 102.1, 82.9, 79.7, 74.7, 63.2, 35.0, 31.2 (3C); HRMS (ESI-TOF) m/z calculated for $C_{21}H_{21}O_2$ $[M+H]^+$: 305.1542, found: 305.1557.

*2-((4-Ethoxyphenyl)ethynyl)-3-(1-hydroxyprop-2-yn-1-yl)phenol (**1h**).* Yield 80% (233 mg). Pale yellow solid; m.p. 94–96 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.51 (m, 2H), 7.35–7.30 (m, 2H), 7.02 (dd, *J* = 7.6 Hz, 2.4 Hz, 1H), 6.97–6.92 (m, 2H), 6.06 (s, 1H), 5.87 (s, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 2.75 (s, 1H), 2.71 (d, *J* = 2.0 Hz, 1H), 1.47 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.8, 156.8, 142.0, 133.2 (2C), 130.1, 118.5, 114.8, 114.7 (2C), 113.7, 108.5, 102.1, 82.9, 78.9, 74.7, 63.7, 63.2, 14.8; HRMS (ESI-TOF) m/z calculated for $C_{19}H_{17}O_3$ $[M+H]^+$: 293.1178, found: 293.1179.

*3-(1-Hydroxyprop-2-yn-1-yl)-2-((2-methoxyphenyl)ethynyl)phenol (**1i**).* Yield 73% (202 mg). Pale yellow solid; m.p. 68–69 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 7.6 Hz, 1.6 Hz, 1H), 7.45–7.35 (m, 1H), 7.37–7.28 (m, 2H), 7.08–6.98 (m, 3H), 6.83 (m, 1H), 5.86 (m, 1H), 4.03 (s, 3H), 3.31 (d, *J* = 8.0 Hz,

1H), 2.72 (d, *J* = 2.4 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 159.7, 157.5, 141.4, 131.5, 130.5, 130.2, 120.9, 118.5, 114.9, 111.4, 110.4, 108.4, 98.7, 86.4, 82.7, 74.8, 63.5, 55.9; HRMS (ESI-TOF) m/z calculated for $C_{18}H_{15}O_3$ $[M+H]^+$: 279.1021, found: 279.1032.

*3-(1-Hydroxyprop-2-yn-1-yl)-2-((3-methoxyphenyl)ethynyl)phenol (**1j**).* Yield 84% (234 mg). Pale yellow solid; m.p. 81–82 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.30 (m, 3H), 7.24–7.20 (m, 1H), 7.15–7.12 (m, 1H), 7.07–6.99 (m, 2H), 6.01 (s, 1H), 5.87 (dd, *J* = 6.4 Hz, 2.4 Hz, 1H), 3.89 (s, 3H), 2.72 (d, *J* = 2.4 Hz, 1H), 2.63 (d, *J* = 6.0 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 159.5, 156.9, 142.2, 130.5, 129.7, 124.2, 122.9, 118.6, 116.5, 115.8, 115.0, 108.0, 101.8, 82.8, 80.1, 74.7, 63.2, 55.4; HRMS (ESI-TOF) m/z calculated for $C_{18}H_{15}O_3$ $[M+H]^+$: 279.1021, found: 279.1036.

*3-(1-Hydroxyprop-2-yn-1-yl)-2-(m-tolylethynyl)phenol (**1k**).* Yield 85% (223 mg). Pale yellow solid; m.p. 86–87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.34 (m, 2H), 7.33–7.26 (m, 3H), 7.19 (d, *J* = 7.6 Hz, 1H), 6.97 (dd, *J* = 6.8 Hz, 2.4 Hz, 1H), 5.99 (s, 1H), 5.82 (s, 1H), 2.68–2.66 (m, 2H), 2.34 (s, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 156.9, 142.2, 138.5, 132.2, 130.4, 130.2, 128.6, 128.5, 121.8, 118.6, 115.0, 108.2, 102.2, 82.9, 80.0, 74.8, 63.3, 21.3; HRMS (ESI-TOF) m/z calculated for $C_{18}H_{15}O_2$ $[M+H]^+$: 263.1067, found: 263.1072.

*2-((3-Fluorophenyl)ethynyl)-3-(1-hydroxyprop-2-yn-1-yl)phenol (**1l**).* Yield 77% (204 mg). Pale yellow solid; m.p. 112–113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.39 (m, 2H), 7.38–7.34 (m, 3H), 7.19–7.13 (m, 1H), 7.03 (dd, *J* = 7.6 Hz, 1.6 Hz, 1H), 6.00 (s, 1H), 5.85 (s, 1H), 2.72 (d, *J* = 2.4 Hz, 1H), 2.67 (s, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 163.6 (d, *J* = 246 Hz), 157.0, 142.3, 130.8, 130.3 (d, *J* = 8.7 Hz), 127.5 (d, *J* = 3.1 Hz), 123.8 (d, *J* = 9.4 Hz), 118.6, 118.4 (d, *J* = 23 Hz), 116.6 (d, *J* = 21 Hz), 115.1, 107.6, 100.3 (d, *J* = 3.5 Hz), 82.7, 81.4, 74.8, 63.1; HRMS (ESI-TOF) m/z calculated for $C_{17}H_{12}FO_2$ $[M+H]^+$: 267.0816, found: 267.0820.

*2-((3-Chlorophenyl)ethynyl)-3-(1-hydroxyprop-2-yn-1-yl)phenol (**1m**).* Yield 76% (215 mg). Pale yellow solid; m.p. 134–135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71–7.25 (m, 6H), 7.04 (d, *J* = 8.0 Hz, 1H), 5.93 (s, 1H), 5.85 (s, 1H), 2.73 (d, *J* = 2.4 Hz, 1H), 2.55 (s, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 157.1, 142.4, 134.6, 131.5, 130.9, 129.8, 129.5, 123.9, 118.7, 115.2, 107.7, 100.3, 100.1, 82.8, 81.6, 74.9, 63.2; HRMS (ESI-TOF) m/z calculated for $C_{17}H_{12}ClO_2$ $[M+H]^+$: 283.0520, found: 283.0527.

*3-(1-Hydroxyprop-2-yn-1-yl)-2-(naphthalen-1-ylethynyl)phenol (**1n**).* Yield 62% (185 mg). Pale yellow solid; m.p. 143–144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.4 Hz, 1H), 7.95–7.87 (m, 2H), 7.80 (dd, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.67–7.46 (m, 3H), 7.37–7.32 (m, 2H), 7.07–7.01 (m, 1H), 6.07 (s, 1H), 5.93 (dd, *J* = 6.0 Hz, 2.4 Hz, 1H), 2.70 (d, *J* = 2.0 Hz, 1H), 2.58 (d, *J* = 2.0 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 157.0, 142.1, 133.2, 133.0, 131.0, 130.5, 129.9, 128.5, 127.4, 126.8, 125.9, 125.3, 119.6, 118.6, 115.1, 108.3, 100.1, 84.9, 82.9, 74.9, 63.3; HRMS (ESI-TOF) m/z calculated for $C_{21}H_{15}O_2$ $[M+H]^+$: 299.1067, found: 299.1083.

*3-(1-Hydroxyprop-2-yn-1-yl)-2-(naphthalen-2-ylethynyl)phenol (**1o**).* Yield 73% (217 mg). Pale yellow solid; m.p. 130–131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.87–7.79 (m, 3H), 7.61–7.48 (m, 3H), 7.35–7.27 (m, 2H), 7.05–6.96 (m, 1H), 6.03 (s, 1H), 5.87 (dd, *J* = 6.0 Hz, 2.0 Hz, 1H), 2.68 (d, *J* = 2.4 Hz, 1H), 2.65 (d, *J* = 6.0 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 157.0, 142.2, 133.2, 132.9, 131.8, 130.5, 128.4, 127.95, 127.94, 127.9, 127.3, 126.9, 119.2, 118.6, 115.0, 108.1, 102.3, 82.9, 80.7, 74.8, 63.3; HRMS (ESI-TOF) m/z calculated for $C_{21}H_{15}O_2$ $[M+H]^+$: 299.1067, found: 299.1073.

*3-(1-Hydroxyprop-2-yn-1-yl)-2-(thiophen-2-ylethynyl)phenol (**1p**).* Yield 69% (176 mg). Pale yellow solid; m.p. 134–135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.40 (m, 2H), 7.39–7.30 (m, 2H), 7.11 (dd, *J* = 5.2 Hz, 3.6 Hz, 1H), 7.02 (dd, *J* = 7.6 Hz, 2.0 Hz, 1H), 6.12 (s, 1H), 5.85 (s, 1H), 2.73 (s, 1H), 2.71 (d, *J* = 2.0 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 157.0, 142.3, 132.9, 130.7, 128.6, 127.4, 121.8, 118.6,

115.1, 107.9, 94.6, 84.1, 82.8, 74.7, 63.1; HRMS (ESI-TOF) m/z calculated for $C_{15}H_{11}O_2S$ $[M+H]^+$: 255.0474, found: 255.0476.

*2-(Cyclohex-1-en-1-ylethynyl)-3-(1-hydroxyprop-2-yn-1-yl)phenol (**1q**).* Yield 53% (134 mg). m.p. 89–90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.18 (m, 2H), 6.92 (dd, *J* = 6.8 Hz, 2.4 Hz, 1H), 6.32–6.26 (m, 1H), 5.92 (s, 1H), 5.71 (dd, *J* = 5.6 Hz, 2.0 Hz, 1H), 2.75 (d, *J* = 6.0 Hz, 1H), 2.63 (d, *J* = 2.4 Hz, 1H), 2.29–2.12 (m, 4H), 1.75–1.57 (m, 4H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 156.5, 141.7, 136.9, 129.7, 119.9, 118.4, 114.6, 108.5, 103.9, 82.8, 77.5, 74.5, 63.1, 29.0, 25.7, 22.1, 21.2; HRMS (ESI-TOF) m/z calculated for $C_{17}H_{17}O_2$ $[M+H]^+$: 253.1223, found: 253.1233.

*2-(Cyclopropylethynyl)-3-(1-hydroxyprop-2-yn-1-yl)phenol (**1r**).* Yield 59% (125 mg). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.33 (m, 2H), 7.21–7.15 (m, 1H), 6.65 (s, 1H), 5.68 (dd, *J* = 5.6 Hz, 2.0 Hz, 1H), 2.69 (d, *J* = 3.0 Hz, 1H), 2.23 (t, *J* = 5.6 Hz, 1H), 2.11–2.01 (m, 1H), 1.05–0.95 (m, 4H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 161.1, 154.7, 131.1, 127.1, 122.9, 120.4, 111.2, 99.1, 83.1, 74.9, 63.5, 9.4, 7.5 (2C); HRMS (ESI-TOF) m/z calculated for $C_{14}H_{13}O_2$ $[M+H]^+$: 213.0910, found: 213.0922.

*2-(Hex-1-yn-1-yl)-3-(1-hydroxyprop-2-yn-1-yl)phenol (**1s**).* Yield 63% (143 mg). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.34 (m, 2H), 7.23–7.17 (m, 1H), 6.66 (d, *J* = 1.2 Hz, 1H), 5.69 (dd, *J* = 5.2 Hz, 2.40 Hz, 1H), 2.83–2.75 (m, 2H), 2.69 (d, *J* = 2.4 Hz, 1H), 2.33 (d, *J* = 6.0 Hz, 1H), 1.80–1.68 (m, 2H), 1.49–1.37 (m, 2H), 0.94 (t, *J* = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.3, 155.1, 131.4, 127.0, 123.0, 120.3, 111.3, 100.6, 83.1, 74.9, 63.4, 29.8, 28.2, 22.4, 13.9; HRMS (ESI-TOF) m/z calculated for $C_{15}H_{17}O_2$ $[M+H]^+$: 229.1223, found: 229.1227.

*3-(1-Hydroxyprop-2-yn-1-yl)-5-methoxy-2-(phenylethynyl)phenol (**1t**).* Yield 86% (239 mg). Pale yellow solid; m.p. 139–140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.2 Hz, 2H), 7.47–7.28 (m, 5H), 6.73 (d, *J* = 8.4 Hz, 1H), 5.69 (dd, *J* = 5.6 Hz, 2.0 Hz, 1H), 4.03 (s, 3H), 2.71 (d, J = 2.0 Hz, 1H), 2.43–2.31

(m, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 156.4, 145.7, 144.3, 130.1, 128.9, 128.8, 128.7 (2C), 125.2 (2C), 124.6, 121.9, 106.1, 100.6, 83.2, 74.9, 63.2, 56.2; HRMS (ESI-TOF) m/z calculated for $C_{18}H_{15}O_3$ $[M+H]^+$: 279.1016, found: 279.1020.

General Procedure for the Synthesis of 7. A mixture of 2-bromo-3-nitrobenzaldehyde (1.0 g, 4.3 mmol) and sodium borohydride (1.6 g, 4.3 mmol) in MeOH (8.0 mL) was stirred at room temperature until 2-bromo-3-nitrobenzaldehyde was consumed as indicated by TLC (about 4 h). The resulting mixture was concentrated and the residue was taken up in CH_2Cl_2. The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure to give (2-bromo-3-nitrophenyl)methanol in 98% yield as a white solid, which was used directly in the next step without additional purification.

A reaction flask was charged with the (2-bromo-3-nitrophenyl)methanol (0.9 g, 4.0 mmol), $FeCl_3$ (16.2 mg, 0.1 mmol), activated carbon (2.0 g) and ethanol (20.0 mL). The mixture was heated to 80 °C, followed by drop-wise addition of hydrazine hydrate (2.0 mL, 80%) under N_2. The heating was continued until (2-bromo-3-nitrophenyl)methanol was consumed as indicated by TLC (about 2 h). The insoluble matter was removed by filtration while hot, and the filtrate was collected. The filtrate was concentrated under reduced pressure and the residue was taken up in CH_2Cl_2. The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure to give (3-amino-2-bromophenyl)methanol in 92% yield as a white solid, which was used directly in the next step without additional purification.

A mixture of (3-amino-2-bromophenyl)methanol (0.6 g, 3.0 mmol), *p*-toluenesulfonyl chloride (0.6 g, 3.2 mmol) and pyridine (325 µL, 4.0 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature until (3-amino-2-bromophenyl)methanol was consumed as indicated by TLC (about 4 h). The resulting

mixture was concentrated and the residue was taken up in CH_2Cl_2. The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure to give *N*-(2-bromo-3-(hydroxymethyl)phenyl)-4-methylbenzenesulfonamide in 98% yield as a white solid, which was used directly in the next step without additional purification.

A mixture of *N*-(2-bromo-3-(hydroxymethyl)phenyl)-4-methylbenzenesulfonamide (0.7 g, 2.0 mmol) and pyridinium chlorochromate (0.86 g, 4.0 mmol) in MeOH (10 mL) was stirred at room temperature, until the *N*-(2-bromo-3-(hydroxymethyl)phenyl)-4-methylbenzenesulfonamide was consumed as indicated by TLC (about 2 h). The resulting mixture was concentrated and the residue was taken up in CH_2Cl_2. The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure to give *N*-(2-bromo-3-formylphenyl)-4-methylbenzenesulfonamide in 87% yield as a pale yellow solid, which was used directly in the next step without additional purification.

A mixture of *N*-(2-bromo-3-formylphenyl)-4-methylbenzenesulfonamide (0.53 g, 1.5 mmol), CuI (0.019 g, 0.1 mmol) and $Pd(PPh_3)_2Cl_2$ (0.07 g, 0.1 mmol) in triethylamine (10.0 mL) was stirred at 50 °C, followed by addition of 1-ethynyl-4-methoxybenzene (233 µL, 1.8 mmol) under N_2. The heating was continued until *N*-(2-bromo-3-formylphenyl)-4-methylbenzenesulfonamide was consumed as indicated by TLC (about 10 h). The resulting mixture was concentrated and the residue was taken up in CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate 8:1) afforded *N*-(3-formyl-2-((4-methoxyphenyl)ethynyl)phenyl)-4-methylbenzenesulfonamide in 87% yield as a pale yellow solid.

A solution of *N*-(3-formyl-2-((4-methoxyphenyl)ethynyl)phenyl)-4-methylbenzenesulfonamide (0.4

g, 1 mmol) in distilled THF (2 mL) was treated at 0 °C with ethynylmagnesium bromide (3 mL, 1.5 mmol). The resulting mixture was stirred at 0 °C for 1 h and for 4 h at room temperature. After treatment with a saturated aqueous solution of NH_4Cl and extractions with Et_2O, the combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate 4:1) afforded **7** in 92% yield as a yellow solid.

*N-(3-(1-hydroxyprop-2-yn-1-yl)-2-((4-methoxyphenyl)ethynyl)phenyl)-4-methylbenzenesulfonamide (**7**).* Yield 73% (314 mg). Pale yellow solid; m.p. 78–79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.4 Hz, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.43–7.39 (m, 2H), 7.35–7.31 (m, 1H), 7.27–7.25 (m, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.95–6.93 (m, 2H), 6.77 (d, *J* = 0.4 Hz, 1H), 5.66 (s, 1H), 3.87 (s, 3H), 2.64–2.63(m, 1H), 2.43–2.33 (m, 1H), 2.27 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.0, 144.6, 142.1, 138.4, 134.7, 131.8 (2C), 131.1, 129.3 (2C), 128.4, 126.8 (2C), 124.5, 124.4, 122.0, 116.9, 112.9 (2C), 110.9, 82.8, 75.2, 62.9, 55.3, 21.5; HRMS (ESI-TOF) m/z calculated for $C_{25}H_{22}NO_4S$ $[M+H]^+$: 432.1264, found: 432.1271.

General Procedure for the Synthesis of 3 and 8 (**Using 3a as an Example**)**.** To a 25 mL Schlenk tube equipped with a stirring bar was added ethyl 2-isocyanoacetate (50 µL, 0.45 mmol), 1-(2-(phenylethynyl)phenyl)prop-2-yn-1-ol (131 mg, 0.3 mmol), DMF (2.0 mL) and Ag_2O (11 mg, 0.05 mmol). The mixture was stirred at 80 °C for about 8 h under air. The resulting mixture was concentrated and the residue was taken up in CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate 3:1) afforded **3a.**

*Ethyl 4-(2-phenylbenzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3a**).* Yield 91% (98 mg). Pale

yellow solid; m.p. 166–167 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 7.91–7.89 (m, 2H), 7.72–7.69 (m, 2H), 7.59–7.58 (m, 1H), 7.51 (d, *J* = 0.8 Hz, 1H), 7.48–7.44 (m, 2H), 7.42–7.41 (m, 1H), 7.40–7.33 (m, 2H), 4.37 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 189.7, 161.0, 157.7, 155.4, 131.3, 130.0, 129.2, 129.0, 128.8 (2C), 128.0, 126.6, 125.2 (2C), 125.0, 124.2, 123.3, 116.4, 114.6, 101.9, 61.0, 14.4; HRMS (ESI-TOF) m/z calculated for $C_{22}H_{18}NO_4$ $[M+H]^+$: 360.1230, found: 360.1233.

*Ethyl 4-(2-(4-methoxyphenyl)benzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3b**).* Yield 87% (101 mg). Pale yellow solid; m.p. 224–226 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (s, 1H), 7.83 (d, *J* = 8.8 Hz, 2H), 7.68 (t, *J* = 8.0 Hz, 2H), 7.59–7.57 (m, 1H), 7.42 (s, 1H), 7.38 (s, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 6.98 (d, *J* = 8.8 Hz, 2H), 4.36 (d, *J* = 7.2 Hz, 2H), 3.86 (s, 3H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 189.9, 161.0, 160.3, 157.9, 155.2, 130.9, 129.5, 128.1, 126.7 (2C), 126.6, 124.9, 124.1, 122.8, 122.7, 116.4, 114.4, 114.3 (2C), 100.3, 61.0, 55.4, 14.3; HRMS (ESI-TOF) m/z calculated for $C_{23}H_{20}NO_5$ $[M+H]^+$: 390.1336, found: 390.1349.

*Ethyl 4-(2-(p-tolyl)benzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3c**).* Yield 82% (92 mg). Pale yellow solid; m.p. 171–172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (s, 1H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.70–7.67 (m, 2H), 7.59–7.57 (m, 1H), 7.45 (d, *J* = 0.4 Hz, 1H), 7.42–7.41 (m, 1H), 7.35–7.31 (m, 1H), 7.28 (s, 1H), 7.26 (s, 1H), 4.37 (q, *J* = 6.8 Hz, 2H), 2.40 (s, 3H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 189.8, 161.0, 158.0, 155.3, 139.2, 131.1, 129.5 (2C), 129.3, 128.0, 127.3, 126.6, 125.2 (2C), 124.9, 124.1, 123.0, 116.4, 114.5, 101.2, 61.0, 21.4, 14.4; HRMS (ESI-TOF) m/z calculated for $C_{23}H_{20}NO_4$ $[M+H]^+$: 374.1387, found: 374.1401.

*Ethyl 4-(2-(4-fluorophenyl)benzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3d**).* Yield 86% (97 mg). Yellow solid; m.p. 161–162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (s, 1H), 7.90–7.85 (m, 2H), 7.70

(t, *J* = 8.0 Hz, 2H), 7.60–7.58 (m, 1H), 7.46 (s, 1H), 7.42–7.41 (m, 1H), 7.35 (t, *J* = 8.0 Hz, 1H), 7.18–7.12 (m, 2H), 4.37 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 189.7, 163.1 (d, *J* = 248 Hz), 161.0, 156.8, 155.3, 131.3, 129.2, 128.0, 127.1 (d, *J* = 8.2 Hz, 2C), 126.5, 126.3 (d, *J* = 3.3 Hz), 125.1, 124.2, 123.3, 116.4, 116.0 (d, *J* = 20 Hz, 2C), 114.6, 101.6, 61.0, 14.4; HRMS (ESI-TOF) m/z calculated for $C_{22}H_{17}FNO_4$ $[M+H]^+$: 378.1136, found: 378.1147.

*Ethyl 4-(2-(4-chlorophenyl)benzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3e**).* Yield 73% (86 mg). Pale yellow solid; m.p. 183–184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 7.84–7.81 (m, 2H), 7.70 (t, *J* = 8.0 Hz, 2H), 7.59–7.58 (m, 1H), 7.51 (d, *J* = 1.2 Hz, 1H), 7.45–7.40 (m, 3H), 7.39–7.33 (m, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 189.6, 160.9, 156.6, 155.4, 134.9, 131.4, 129.1 (2C), 129.0, 128.5, 127.9, 126.5, 126.4 (2C), 125.1, 124.2, 123.6, 116.4, 114.6, 102.4, 61.0, 14.4; HRMS (ESI-TOF) m/z calculated for $C_{22}H_{17}ClNO_4$ $[M+H]^+$: 394.0841, found: 394.0852.

*Ethyl 4-(2-(4-ethylphenyl)benzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3f**).* Yield 81% (94 mg). Pale yellow solid; m.p. 176–177 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 7.83–7.80 (m, 2H), 7.70–7.67 (m, 2H), 7.59–7.57 (m, 1H), 7.46 (d, *J* = 0.8 Hz, 1H), 7.42–7.41 (m, 1H), 7.35–7.28 (m, 3H), 4.37 (q, *J* = 7.2 Hz, 2H), 2.70 (q, *J* = 8.0 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H), 1.27 (t, *J* = 7.6 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 189.8, 161.0, 158.1, 155.3, 145.5, 131.1, 129.4, 128.4 (2C), 128.0, 127.5, 126.6, 125.3 (2C), 124.9, 124.2, 123.0, 116.4, 114.5, 101.2, 61.0, 28.8, 15.4, 14.4; HRMS (ESI-TOF) m/z calculated for $C_{24}H_{22}NO_4$ $[M+H]^+$: 388.1543, found: 388.1547.

*Ethyl 4-(2-(4-(tert-butyl)phenyl)benzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3g**).* Yield 67% (83 mg). Pale yellow solid; m.p. 185–187 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (s, 1H), 7.85–7.82 (m, 2H), 7.71–7.68 (m, 2H), 7.59–7.58 (m, 1H), 7.50–7.47 (m, 3H), 7.42–7.41 (m, 1H), 7.35–7.31 (m, 1H),

4.37 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H), 1.36 (s, 9H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 189.8, 161.0, 158.0, 155.3, 152.3, 131.1, 129.4, 128.1, 127.2, 126.6, 125.8 (2C), 125.0 (2C), 124.9, 124.2, 123.0, 116.4, 114.5, 101.3, 61.0, 34.8, 31.2 (3C), 14.3; HRMS (ESI-TOF) m/z calculated for $C_{26}H_{26}NO_4$ $[M+H]^+$: 416.1856, found: 416.1850.

*Ethyl 4-(2-(4-ethoxyphenyl)benzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3h**).* Yield 89% (107 mg). Yellow solid; m.p. 176–178 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (s, 1H), 7.84–7.80 (m, 2H), 7.68 (t, *J* = 8.0 Hz, 2H), 7.59–7.57 (m, 1H), 7.42–7.41 (m, 1H), 7.37 (d, *J* = 0.8 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 7.00–6.95 (m, 2H), 4.37 (q, *J* = 7.2 Hz, 2H), 4.10 (q, *J* = 7.2 Hz, 2H), 1.45 (t, *J* = 7.2 Hz, 3H), 1.38 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 189.8, 160.9, 159.8, 158.0, 155.2, 130.9, 129.6, 127.9, 126.8 (2C), 126.6, 124.9, 124.1, 122.7, 122.6, 116.4, 114.8 (2C), 114.4, 100.3, 63.6, 61.0, 14.8, 14.4; HRMS (ESI-TOF) m/z calculated for $C_{24}H_{22}NO_5$ $[M+H]^+$: 404.1492, found: 404.1501.

*Ethyl 4-(2-(2-methoxyphenyl)benzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3i**).* Yield 92% (107 mg). Pale yellow solid; m.p. 195–197 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.49 (s, 1H), 8.08 (dd, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.75 (d, *J* = 0.8 Hz, 1H), 7.70–7.67 (m, 2H), 7.59–7.58 (m, 1H), 7.43–7.42 (m, 1H), 7.38–7.32 (m, 2H), 7.11–7.07 (m, 1H), 7.02 (d, *J* = 8.4 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 3.98 (s, 3H), 1.38 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 190.0, 161.0, 157.0, 154.5, 154.2, 131.5, 129.9, 129.8, 128.0, 127.4, 126.9, 124.7, 124.2, 123.2, 120.8, 119.1, 116.5, 114.3, 111.2, 106.7, 61.1, 55.6, 14.5; HRMS (ESI-TOF) m/z calculated for $C_{23}H_{20}NO_5$ $[M+H]^+$: 390.1336, found: 390.1338.

*Ethyl 4-(2-(3-methoxyphenyl)benzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3j**).* Yield 83% (97 mg). Pale yellow solid; m.p. 159–160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1H), 7.72–7.69 (m, 2H), 7.59–7.58 (m, 1H), 7.52–7.49 (m, 2H), 7.44–7.41 (m, 2H), 7.39–7.34 (m, 2H), 6.95–6.92 (m, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 3.89 (s, 3H), 1.38 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 189.7, 160.9,

159.9, 157.6, 155.3, 131.3 (2C), 129.9, 129.1, 128.0, 126.5, 125.0, 124.2, 123.4, 117.8, 116.4, 115.2, 114.6, 110.1, 102.2, 61.0, 55.4, 14.4; HRMS (ESI-TOF) m/z calculated for $C_{23}H_{20}NO_5$ $[M+H]^+$: 390.1336, found: 390.1342.

*Ethyl 4-(2-(m-tolyl)benzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3k**).* Yield 85% (95 mg). Pale yellow solid; m.p. 177–178 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.54 (s, 1H), 7.74–7.69 (m, 4H), 7.59–7.58 (m, 1H), 7.49 (d, *J* = 0.8 Hz, 1H), 7.42–7.41 (m, 1H), 7.35 (t, *J* = 8.8 Hz, 2H), 7.20 (d, *J* = 7.6 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 2.43 (s, 3H), 1.39 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 189.7, 160.9, 157.9, 155.4, 138.5, 131.2, 129.9, 129.8, 129.2, 128.8, 127.9, 126.6, 125.8, 124.9, 124.2, 123.2, 122.4, 116.4, 114.6, 101.8, 61.0, 21.5, 14.4; HRMS (ESI-TOF) m/z calculated for $C_{23}H_{20}NO_4$ $[M+H]^+$: 374.1387, found: 374.1397.

*Ethyl 4-(2-(3-fluorophenyl)benzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3l**).* Yield 76% (86 mg). Pale yellow solid; m.p. 198–199°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1H), 7.73–7.66 (m, 3H), 7.61–7.58 (m, 2H), 7.54 (d, *J* = 1.2 Hz, 1H), 7.44–7.36 (m, 3H), 7.09–7.04 (m, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 189.6, 163.1 (d, *J* = 244 Hz), 161.0, 156.3 (d, *J* = 3.1 Hz), 155.4, 132.1 (d, *J* = 8.4 Hz), 131.5, 130.4 (d, *J* = 8.3 Hz), 128.9, 128.1, 126.4, 125.1, 124.2, 123.8, 120.9 (d, *J* = 2.9 Hz), 116.4, 115.8 (d, *J* = 21.3 Hz), 114.7, 112.1 (d, *J* = 23.5 Hz), 103.0, 61.0, 14.4; HRMS (ESI-TOF) m/z calculated for $C_{22}H_{17}FNO_4$ $[M+H]^+$: 378.1136, found: 378.1144.

*Ethyl 4-(2-(3-chlorophenyl)benzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3m**).* Yield 71% (84 mg). Pale yellow solid; m.p. 209–211 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (s, 1H), 7.90 (t, *J* = 1.6 Hz, 1H), 7.78–7.75 (m, 1H), 7.73–7.70 (m, 2H), 7.59–7.58 (m, 1H), 7.54 (d, *J* = 0.8 Hz, 1H), 7.42–7.33 (m, 4H), 4.37 (q, *J* = 7.2 Hz, 2H), 1.39 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 189.6, 160.9, 156.1, 155.4, 134.9, 131.7, 131.5, 130.1, 128.9, 128.8, 127.9, 126.5, 125.2, 125.1, 124.3, 123.8, 123.3,

116.3, 114.7, 103.0, 61.0, 14.4; HRMS (ESI-TOF) m/z calculated for $C_{22}H_{17}ClNO_4$ $[M+H]^+$: 394.0841, found: 394.0857.

*Ethyl 4-(2-(naphthalen-1-yl)benzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3n**).* Yield 65% (80 mg). Pale yellow solid; m.p. 211–213 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 8.52–8.49 (m, 1H), 7.95–7.91 (m, 3H), 7.80–7.75 (m, 2H), 7.62–7.54 (m, 5H), 7.45–7.40 (m, 2H), 4.37 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 189.8, 160.9, 157.4, 155.4, 133.9, 131.5, 130.5, 129.9, 128.9, 128.6, 128.0, 127.7, 127.5, 127.1, 126.6, 126.2, 125.4, 125.2, 124.9, 124.2, 123.4, 116.4, 114.7, 106.4, 61.0, 14.4; HRMS (ESI-TOF) m/z calculated for $C_{26}H_{20}NO_4$ $[M+H]^+$: 410.1387, found: 410.1388.

*Ethyl 4-(2-(naphthalen-2-yl)benzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3o**).* Yield 72% (88 mg). Pale yellow solid; m.p. 203–204 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 8.41 (s, 1H), 7.96–7.83 (m, 4H), 7.75–7.71 (m, 2H), 7.63 (d, *J* = 0.8 Hz, 1H), 7.61–7.60 (m, 1H), 7.55–7.48 (m, 2H), 7.44–7.43 (m, 1H), 7.37 (t, *J* = 8.0 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 189.7, 161.0, 157.8, 155.5, 133.5, 133.3, 131.3, 129.3, 128.6, 128.5, 128.0, 127.8, 127.3, 126.7 (2C), 126.6, 125.0, 124.4, 124.2, 123.4, 122.9, 116.4, 114.6, 102.6, 61.0, 14.4; HRMS (ESI-TOF) m/z calculated for $C_{26}H_{20}NO_4$ $[M+H]^+$: 410.1387, found: 410.1393.

*Ethyl 4-(2-(thiophen-2-yl)benzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3p**).* Yield 69% (76 mg). Pale yellow solid; m.p. 225–227 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.51 (s, 1H), 7.72–7.66 (m, 2H), 7.59–7.58 (m, 1H), 7.55–7.54 (m, 1H), 7.41–7.33 (m, 4H), 7.14–7.11 (m, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 1.39 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 189.6, 160.8, 155.1, 153.2, 132.8, 131.1, 129.2, 128.0, 127.8, 126.6, 126.5, 125.4, 125.1, 124.2, 123.3, 116.3, 114.5, 101.7, 61.0, 14.4; HRMS (ESI-TOF) m/z calculated for $C_{20}H_{16}NO_4S$ $[M+H]^+$: 366.0795, found: 366.0788.

*Ethyl 4-(2-(cyclohex-1-en-1-yl)benzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3q**).* Yield 80% (87 mg). Pale yellow solid; m.p. 146–147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (s, 1H), 7.65–7.63 (m, 1H), 7.60–7.57 (m, 1H), 7.56–7.55 (m, 1H), 7.40–7.39 (m, 1H), 7.29 (t, *J* = 8.0 Hz, 1H), 6.97 (s, 1H), 6.69–6.66 (m, 1H), 4.36 (q, *J* = 7.2 Hz, 2H), 2.41–2.38 (m, 2H), 2.30–2.26 (m, 2H), 1.78–1.77 (m, 2H), 1.70–1.66 (m, 2H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 189.9, 160.9, 159.3, 155.0, 130.9, 129.2, 127.9, 127.4, 127.2, 126.6, 124.5, 124.1, 122.8, 116.4, 114.1, 100.7, 61.0, 25.5, 24.8, 22.3, 22.0, 14.4; HRMS (ESI-TOF) m/z calculated for $C_{22}H_{22}NO_4$ $[M+H]^+$: 364.1543, found: 364.1553.

*Ethyl 4-((2-cyclopropylbenzofuran-4-yl)(hydroxy)methyl)-1H-pyrrole-2-carboxylate (**3r**).* Yield 46% (45 mg). Pale yellow solid; m.p. 78–79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (s, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.22–7.13 (m, 2H), 6.73 (t, *J* = 6.8 Hz, 1H), 6.47 (s, 1H), 6.39 (d, *J* = 4.4 Hz, 1H), 5.88 (t, *J* = 2.4 Hz, 1H), 4.59 (s, 1H), 4.36 (q, *J* = 7.2 Hz, 2H), 2.04–1.95 (m, 1H), 1.38 (t, *J* = 7.2 Hz, 3H) 0.96–0.93 (m, 4H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.4, 160.0, 154.4, 135.6, 134.7, 127.2, 122.6, 121.6, 120.1, 118.6, 111.1, 109.7, 99.9, 68.5, 60.8, 14.4, 9.3, 7.2 (2C); HRMS (ESI-TOF) m/z calculated for $C_{19}H_{20}NO_4$ $[M+H]^+$: 326.1387, found: 326.1389.

*Ethyl 4-((2-butylbenzofuran-4-yl)(hydroxy)methyl)-1H-pyrrole-2-carboxylate (**3s**).* Yield 53% (54 mg). Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.23–7.17 (m, 2H), 6.78 (d, *J* = 2.8 Hz, 1H), 6.50 (d, *J* = 0.8 Hz, 1H), 6.41 (d, *J* = 4.8 Hz, 1H), 5.91 (t, *J* = 2.8 Hz, 1H), 4.52 (s, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 2.74 (t, *J* = 8.0 Hz, 2H), 1.73–1.67 (m, 2H), 1.43–1.40 (m, 2H), 1.36 (t, *J* = 7.2 Hz, 3H), 0.94 (t, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.3, 159.3, 154.8, 134.9, 127.1, 122.9, 122.8, 121.5, 120.0, 118.7, 111.2, 109.8, 101.3, 68.6, 60.9, 29.7, 28.2, 22.3, 14.4, 13.8; HRMS (ESI-TOF) m/z calculated for $C_{20}H_{24}NO_4$ $[M+H]^+$: 342.1700, found: 342.1707.

*Ethyl 4-(6-methoxy-2-phenylbenzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3t**).* Yield 85% (99 mg). Pale yellow solid; m.p. 236–237 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.57 (s, 1H), 7.95–7.92 (m, 2H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.63 (s, 1H), 7.58–7.57 (m, 1H), 7.48–7.44 (m, 2H), 7.40–7.36 (m, 2H), 6.84 (d, *J* = 8.4 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 4.13 (s, 3H), 1.39 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 188.9, 160.9, 157.8, 148.3, 144.2, 131.3, 129.9, 129.0, 128.8 (2C), 127.7, 127.4, 126.8, 125.3 (2C), 124.2, 123.9, 116.4, 105.4, 102.7, 60.9, 56.3, 14.4; HRMS (ESI-TOF) m/z calculated for $C_{23}H_{20}NO_5$ $[M+H]^+$: 390.1336, found: 390.1340.

*Methyl 4-(2-phenylbenzofuran-4-carbonyl)-1H-pyrrole-2-carboxylate (**3u**).* Yield 88% (91 mg). Pale yellow solid; m.p. 172–173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (s, 1H), 7.91–7.89 (m, 2H), 7.70 (d, *J* = 7.6 Hz, 2H), 7.60–7.59 (m, 1H), 7.51 (s, 1H), 7.48–7.44 (m, 2H), 7.42–7.41 (m, 1H), 7.40–7.33 (m, 2H), 3.90 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 189.7, 161.3, 157.7, 155.4, 131.2, 130.0, 129.2, 129.0, 128.8 (2C), 128.1, 126.6, 125.2 (2C), 125.0, 123.8, 123.3, 116.6, 114.6, 101.9, 52.0; HRMS (ESI-TOF) m/z calculated for $C_{21}H_{16}NO_4$ $[M+H]^+$: 346.1074, found: 346.1077.

*(5-(Morpholine-4-carbonyl)-1H-pyrrol-3-yl)(2-phenylbenzofuran-4-yl)methanone (**3v**).* Yield 83% (100 mg). Pale yellow solid; m.p. 215–217 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.87 (s, 1H), 7.90–7.88 (m, 2H), 7.70–7.65 (m, 2H), 7.47–7.43 (m, 4H), 7.39–7.32 (m, 2H), 7.12–7.11 (m, 1H), 3.90 (s, 4H), 3.78–3.75 (m, 4H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 190.0, 161.5, 157.7, 155.5, 131.7, 130.1, 129.2, 129.1, 129.0 (2C), 127.8, 127.7, 126.0, 125.6, 125.3 (2C), 124.7, 123.4, 114.6, 113.4, 101.9 (2C), 66.8 (2C); HRMS (ESI-TOF) m/z calculated for $C_{24}H_{21}N_2O_4$ $[M+H]^+$: 401.1496, found: 401.1499.

*(4-(2-Phenylbenzofuran-4-carbonyl)-1H-pyrrol-2-yl)(pyrrolidin-1-yl)methanone (**3w**).* Yield 80% (92 mg). Pale yellow solid; m.p. 203–205 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.53 (s, 1H), 7.91–7.89 (m, 2H), 7.71–7.68 (m, 2H), 7.50–7.44 (m, 4H), 7.40–7.34 (m, 2H), 7.21–7.20 (m, 1H), 3.83 (t, *J* = 6.8 Hz, 2H),

3.70 (t, *J* = 6.8 Hz, 2H), 2.11–2.04 (m, 2H), 1.98–1.93 (m, 2H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 190.1, 159.7, 157.5, 155.4, 131.8, 130.0, 129.1, 129.0, 128.8 (2C), 127.4, 127.3, 126.4, 125.2 (2C), 124.6, 123.3, 114.4, 113.1, 101.9, 48.1, 47.3, 26.6, 23.9; HRMS (ESI-TOF) m/z calculated for $C_{24}H_{21}N_2O_3$ $[M+H]^+$: 385.1547, found: 385.1544.

*Ethyl 4-(hydroxy(2-(4-methoxyphenyl)-1-tosyl-1H-indol-4-yl)methyl)-1H-pyrrole-2-carboxylate (**8**).* Yield 81% (132 mg). Pale yellow solid; m.p. 214–215 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.27–8.22 (m, 1H), 7.43–7.41 (m, 2H), 7.33–7.32 (m, 2H), 7.28–7.27 (m, 1H), 7.25, (s, 1H), 7.03 (d, *J* = 0.8 Hz, 2H), 6.93–6.91 (m, 1H), 6.67 (t, *J* = 2.8 Hz, 1H), 6.62 (d, *J* = 0.8 Hz, 2H), 6.35 (d, *J* = 4.4 Hz, 1H), 5.57 (t, *J* = 2.4 Hz, 1H), 4.65, (s, 1H), 4.36–4.30 (m, 2H), 3.87 (s, 3H), 2.29 (s, 3H), 1.32 (t, *J* = 6.8 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 161.3, 159.9, 144.4, 141.6, 138.4, 135.7, 134.53, 134.50, 131.6 (2C), 129.1 (2C), 128.9, 126.8 (2C), 124.9, 124.5, 122.1, 121.4, 118.7, 115.9, 112.8 (2C), 112.3, 111.2, 68.1, 60.9, 55.3, 21.5, 14.4; HRMS (ESI-TOF) m/z calculated for $C_{30}H_{29}N_2O_6S$ $[M+H]^+$: 545.1741, found: 545.1753.

Characterization of Intermediates 5 and 6

*1-(2-Phenylbenzofuran-4-yl)prop-2-yn-1-ol (**5**).* Yield 16% (12 mg). Pale yellow solid; m.p. 48–49 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89–7.86 (m, 2H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.46–7.42 (m, 2H), 7.41–7.33 (m, 2H), 7.31–7.24 (m, 2H), 5.75 (dd, *J* = 6.0 Hz, 2.4 Hz, 1H), 2.71 (d, *J* = 2.4 Hz, 1H), 2.47 (d, *J* = 5.6 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 156.2, 155.2, 132.1, 130.2, 128.8 (2C), 128.7, 127.2, 125.0 (2C), 124.1, 120.7, 111.7, 100.1, 83.0, 75.1, 63.4; HRMS (ESI-TOF) m/z calculated for $C_{17}H_{13}O_2$ $[M+H]^+$: 249.0910, found: 249.0917.

*(5-(Hydroxy(morpholino)methyl)-1H-pyrrol-3-yl)(2-phenylbenzofuran-4-yl)methanone (**6**).* Yield 27% (33 mg). Pale yellow solid; m.p. 134–135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.56 (s, 1H), 7.84–7.81

(m, 2H), 7.49–7.41 (m, 3H), 7.36–7.27 (m, 3H), 7.06 (d, *J* = 0.8 Hz, 1H), 6.77–6.75 (m, 1H), 6.49–6.48 (m, 1H), 6.12 (d, *J* = 3.2 Hz, 1H), 3.79–3.77 (m, 4H), 3.69–3.66 (m, 4H), 2.50 (d, *J* = 3.6 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 161.5, 155.7, 155.2, 136.4, 130.2, 128.8 (2C), 128.6, 128.0, 126.9, 124.9 (2C), 124.6, 124.1, 120.2, 119.4, 110.8, 110.6, 100.4, 69.7 (2C), 66.7 (2C); HRMS (ESI-TOF) m/z calculated for $C_{24}H_{23}N_2O_4$ $[M+H]^+$: 403.1652, found: 403.1659.

ASSOCIATED CONTENT

Supporting Information

NMR spectra of compounds **1**, **3** and **5**–**8**, and X-ray crystallographic data for compound **3a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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