Functionalized Benzofurans via Microwave-Promoted Tandem Claisen-Rearrangement/5-*endo*-dig Cyclization

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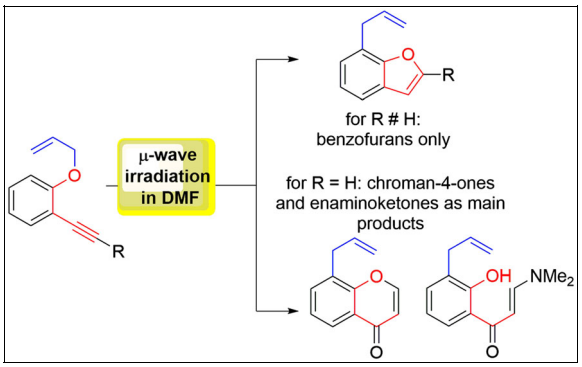

Ortho-allyloxy alkinyl benzenes undergo, upon microwave irradiation in dimethylformamide, a tandem sequence of Claisen-rearrangement and 5-*endo*-dig cyclization to furnish 7-allyl-substituted benzofurans. With terminal alkynes, chroman-4-ones and enaminoketones become the main products. A mechanistic proposal for this observation relies on a reaction of the starting material with the solvent dimethylformamide under the microwave conditions.

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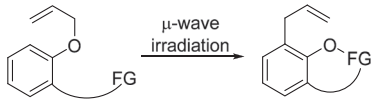
INTRODUCTION

Over the past few years, we investigated the development and application of microwave-promoted tandem sequences [1–3] for the synthesis of benzoannellated oxacycles with an aliphatic substituent at the benzo ring, starting from easily accessible acyclic precursors (Scheme 1). In general, these transformations start from allyl-protected *ortho*-substituted phenols (e.g., salicylic aldehyde derivatives) with a substituent containing a reactive, normally electrophilic, functional group FG. For the synthesis of the precursors, the allyl ether plays the role of a protecting group to mask the nucleophilic reactivity of the phenol. Instead of a traceless deprotection, the allyl ether is used to install an allyl side chain at the benzo ring, which can be further elaborated in various ways as required for the target structures to be addressed.

Along these lines, straightforward syntheses of pyranocoumarins [4], prenylcoumarins [5–7], furanocoumarins [8], chroman-4-ones [9], and chromene-4-ones [10,11] were developed and implemented in the total synthesis of several natural products. In the above-mentioned examples, the cyclization step proceeds through a nucleophilic acyl substitution (for the synthesis of coumarins) or through an addition across an electronically biased C─C-multiple bond (for the synthesis of chroman-4-ones and chromene-4-ones). In the present work, we aimed at an extension of the microwave-promoted Claisen-rearrangement/cyclization sequence to systems without an explicitly electrophilic functional group FG. This is, for example, the case with C─C-triple bonds directly attached to the *ortho*-position of the masked phenol. Upon Claisen rearrangement, the liberated *O*-nucleophile would undergo a 5-*endo*-dig cyclization to benzofurans. The development of methods for the synthesis of benzofurans has attracted continuous interest for many decades. Some of the most recent contributions include routes that involve the construction of the benzene ring as a key step, either by benzannulation to a preformed furan [12] or by a dehydration/oxidative dehydrogenation sequence of an in situ formed tetrahydrobenzofuran [13]. Many syntheses of benzofurans use 5-*endo*-dig cyclizations of *ortho*-alkinylphenols [14]. Traditionally, these reactions are mediated by bases such as Cs_2CO_3 in polar, aprotic solvents at elevated temperatures [15,16], but only for very few examples microwave irradiation was used to accelerate the reaction [17,18]. In recent years, metal catalysis has been intensively investigated for this intramolecular heteroannulation, including, inter alia, rhodium [19], palladium [20], and indium catalysts [21]. Transition metal catalysis offers the opportunity to combine the heteroannulation with additional steps to tandem sequences, which ultimately results in the formation of 2,3-disubstituted benzofurans. Examples for

Scheme 1. Generalized tandem Claisen-rearrangement/cyclization sequence.



such tandem sequences are a Rh-catalyzed cyclization of alkinylphenols in the presence of electron deficient alkenes [22] or cyclizations of alkinylphenol allyl ethers, which proceed through a metal catalyzed deallylation and intramolecular transfer of the allyl substituent to the 3-position of the benzofuran [23–26]. Allyl ethers of alkinyl phenols are also the envisaged starting materials for the tandem sequence investigated in this study, but in contrast to the transition metal catalyzed reactions mentioned earlier, the microwave-promoted Claisen-rearrangement/5-*endo*-dig cyclization will result in the formation of 7-allylbenzofurans, that is, the allyl substituent is installed at the benzo ring, rather than the furan part of the heterocycle [27]. We are aware of only one example from the patent literature for such a tandem Claisen-rearrangement/5-*endo*-dig cyclization, which describes a total synthesis of the natural product moracin S (Fig. 1) [28]. The authors used conventional heating in water for 9 h in a closed reaction vessel to promote the reaction, resulting in a yield of 31% of a 7-prenylated benzofuran. During preparation of this manuscript, Mino and coworkers published a closely related two-step approach to 7-allylbenzofurans from *ortho*-allyloxyalkinyl benzenes that uses a Lewis acid-mediated Claisen rearrangement, followed by a TBAF-catalyzed 5-*endo*-dig cyclization. Both steps can be conducted in one pot, but in this case, overstoichiometric amounts of TBAF are required to promote the cyclization [29].

The interest in the development of novel synthetic methods for functionalized benzofurans and 2,3-dihydrobenzofurans is stimulated by their ubiquitous occurrence in natural products [30] and drugs [31]. Examples for bioactive naturally occurring benzofurans are the moracins, which show antifungal and antibacterial activity [32]. 7-Aminomethyl-substituted benzofurans, such as the example shown in Figure 1 together with moracins S and L, were identified as kinase inhibitors and potent cytotoxic agents in a high throughput screening [33].

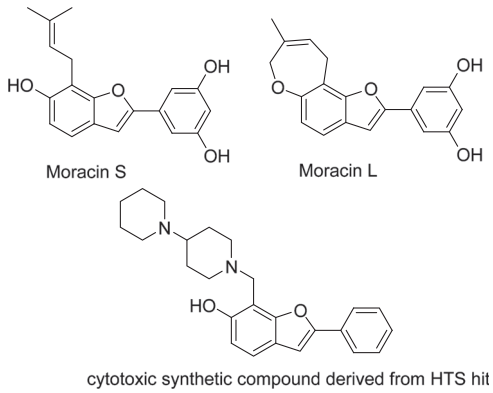


Figure 1. Natural and nonnatural bioactive C3-unsubstituted benzofurans.

RESULTS AND DISCUSSION

We started the investigation into the microwave-promoted tandem sequence with precursor **4a** [24,26], which was synthesized from 2-allyloxybenzaldehyde (**1a**) [10] in two steps via carbonyl alkynylation using the Bestmann–Ohira reagent **2** [34], followed by Sonogashira coupling of **3a** [35] with iodobenzene. For the latter step, the copper-free reaction conditions published by Liang et al. were used [36] (Scheme 2).

All microwave irradiation experiments were conducted at 250°C, because we [9] and others [7] have previously shown that the Claisen rearrangement remains incomplete at lower temperatures. In a first experiment (Table 1, entry 1), we tested toluene as a solvent. After 1 h, the starting material was completely consumed, but we could only isolate the product of the Claisen rearrangement **6a** and not the expected benzofuran **7a**. We reasoned that replacing toluene by the polar aprotic solvent dimethylformamide (DMF) should enhance the nucleophilicity of the phenol and thereby facilitate the ring closure. Benzofuran **5a** was indeed the sole product when the reaction was run in DMF. It could be isolated in a yield of 92% (Table 1, entry 2). Addition of K_2CO_3 under these conditions did not improve the yield further (Table 1, entry 3).

To explore the scope of the tandem sequence, three other diarylacetylenes **4b–d** were synthesized from

Scheme 2. Synthesis of precursor **4a**.

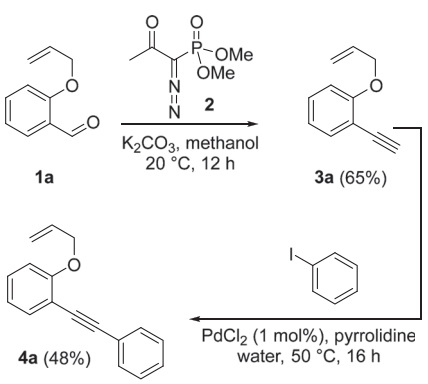
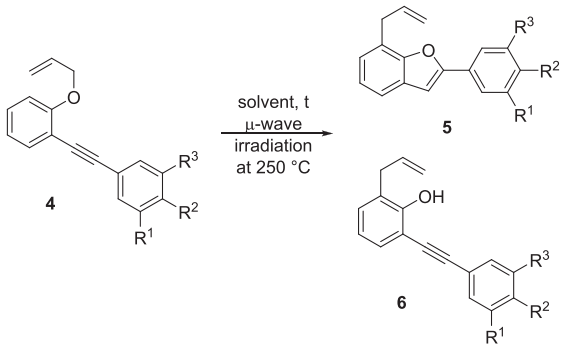


Table 1

Synthesis of 7-allyl-2-arylbenzofurans.



Entry	4	R^1	R^2	R^3	Solvent	t (min)	Product (yield, %)
1	**4a**	H	H	H	Toluene	60	**6a** (45)
2	**4a**	H	H	H	DMF	15	**5a** (92)
3[a]	**4a**	H	H	H	DMF	15	**5a** (90)
4	**4b**	H	OMe	H	DMF	15	**5b** (n. d.)[b]
5	**4b**	H	OMe	H	DMF	30	**5b** (67)
6	**4c**	OMe	H	OMe	DMF	15	**5c** (n. d.)[b]
7	**4c**	OMe	H	OMe	DMF	30	**5c** (63)
8	**4d**	OMe	OMe	OMe	DMF	15	**5d** (n. d.)[b]
9	**4d**	OMe	OMe	OMe	DMF	30	**5d** (54)

DMF, dimethylformamide.
[a]K_2CO_3 (4 equiv.) used as an additive.
[b]Not determined, incomplete conversion (thin-layer chromatography).

commercially available benzaldehydes **7** in three steps (Table 2) and irradiated at 250°C in DMF in a microwave reactor. In all cases, unreacted starting material was detected by thin-layer chromatography (TLC) after 15 min (Table 1, entries 4, 6, and 8), but the conversion was quantitative after 30 min and the expected benzofurans **5b–d** were isolated in yields between 54% and 67% (Table 1, entries 5, 7, and 9).

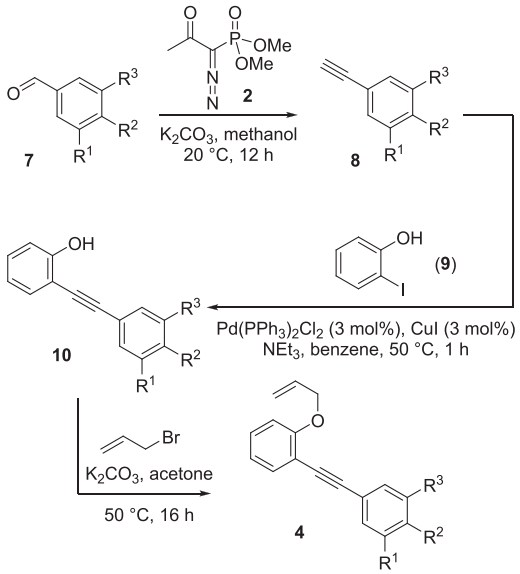
The optimized conditions for the tandem Claisen-rearrangement/5-*endo*-dig cyclization sequence could also be successfully applied to an acetylene substituted with an electron-withdrawing group. The required precursor, propiolate **4e**, was synthesized from acetylene **3a** by lithiation and electrophilic trapping with methyl chloroformiate [37]. Microwave irradiation at 250°C in DMF furnished 7-allyl-2-methoxycarbonylbenzofuran (**5e**) in 54% yield (Scheme 3).

We concluded our investigation into this microwave-promoted tandem sequence with five monosubstituted acetylenes **3a–e**. Compound **3a** is an intermediate en route to the test substrate **4a** and its synthesis from aldehyde **1a** via carbonyl alkynylation with the Bestmann–Ohira reagent is shown in Scheme 2. The other four arylacetylenes **3b–e** were synthesized analogously from the known *ortho*-allyloxybenzaldehydes **1b–e** (Table 3).

In a first experiment, **3a** was subjected to microwave irradiation in DMF for 15 min (Table 4, entry 1). Surprisingly, neither the expected 7-allylbenzofuran (**12a**) nor the Claisen rearrangement product **11a** were detected, although the starting material was fully consumed as indicated by TLC. Instead, the enaminoketone **13a** and 7-allylchromene-4-one (**14a**) were isolated in more than 60% combined yield. The enaminoketone **13a** must result from a reaction between the starting material **3a** and the solvent DMF, and **14a** is apparently formed from **13a** via an intramolecular conjugate addition followed by elimination of dimethylamine [40]. In toluene as a solvent (Table 4, entry 2), the reaction stops at the stage of the Claisen rearrangement as previously observed for the diarylacetylene **4a**, and the phenol **11a** was isolated in moderate yield. The assumption that the chromene-4-one **14a** results from **13a** is supported by the observation that its yield increases at longer reaction times at the expense of the intermediary product **13a** (Table 4, entry 3). From the four other monosubstituted acetylenes tested in this study, only **3b** and **3d**, both with an electron-donating substituent in *para*-position to the allyloxy group, reacted to benzofurans (Table 4, entries 4 and 6). While 7-allyl-5-methoxybenzofuran (**12b**) was isolated in a fair yield of 47%, along with equal amounts of the enaminoketone **13b** and its secondary product **14b**, the MOM-protected

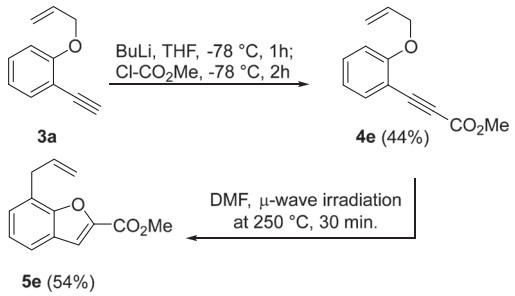
Table 2

Synthesis of precursors **4b–d**.



Entry	7	R^1	R^2	R^3	8 (yield, %)	10 (yield, %)	4 (yield, %)
1	**7b**	H	OMe	H	**8b** (53)	**10b** (96)	**4b** (65)
2	**7c**	OMe	H	OMe	**8c** (57)	**10c** (81)	**4c** (78)
3	**7d**	OMe	OMe	OMe	**8d** (58)	**10d** (93)	**4d** (62)

Scheme 3. Tandem Claisen-rearrangement/cyclization sequence of propiolate **4e**.

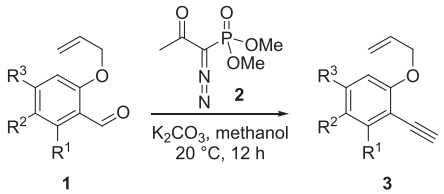


derivative **12d** was obtained only in a poor yield of 18%. We could not observe any products resulting from a reaction with DMF in this case. Without an electron-donating substituent in *para*-position to the allyloxy group (Table 4, entries 5 and 7), we observed either decomposition of the starting material (in the case of **3c**) or the formation of a 5:1 mixture of enaminoketone **13e** and chromene-4-one **14e** (in the case of **3e**). These observations suggest that an electron-donating group *para* to the allyloxy substituent increases the nucleophilicity of the phenol intermediate **11** and accelerates the 5-*endo*-dig cyclization over the reaction with the solvent DMF.

Enaminoketones are valuable intermediates for the synthesis of heterocycles [41]. Precedence for their preparation from DMF and alkynes is scarce, and we are aware of only two examples remotely resembling the transformation observed by us. One example is the Rh-catalyzed reaction of DMF, sulfonylazides, and terminal alkynes to α-amino enaminoketones [42,43]. In another synthesis, *ortho*-hydroxy acetophenones undergo an acid catalyzed, microwave-promoted condensation with the dimethylacetal of DMF to furnish enaminoketones as intermediates, which then undergo a cyclization to chromene-4-ones [40]. A tentative mechanism to explain the formation of enaminoketones **13** and their secondary products **14** from alkynes **3** and DMF is outlined in Scheme 4. We assume that the reaction with DMF occurs after the Claisen rearrangement and that a hydrogen bond between the phenol and the oxygen of DMF increases the nucleophilicity at the terminal sp-carbon through an *ortho*-quinonemethide structure. Nucleophilic attack at the DMF carbon yields intermediate **A**, from which aromaticity is restored via intramolecular nucleophilic migration of the DMF-oxygen to the inner carbon of the former C—C-triple bond.

Table 3

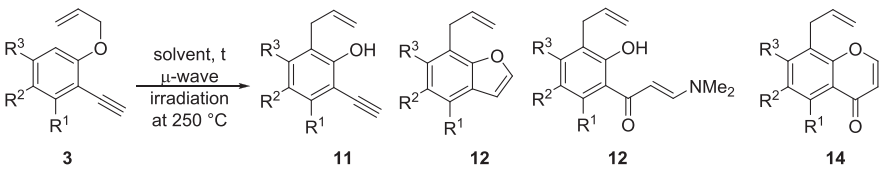
Synthesis of (*o*-allyloxyaryl)acetylenes **3b–d**.



Entry	**1**[Ref.]	R^1	R^2	R^3	**3** (yield, %)
1	**1b** [38]	H	OMe	H	**3b** (39)
2	**1c** [5]	OMe	H	OMe	**3c** (16)
3	**1d** [6]	H	OMe	OMOM	**3d** (35)
4	**1e** [39]	H	H	OMe	**3e** (39)

Table 4

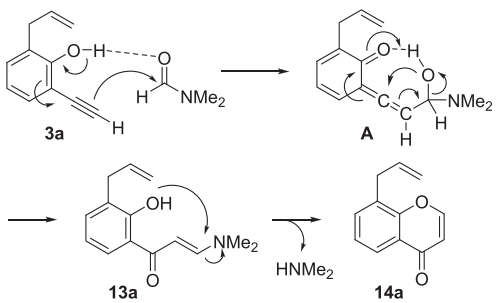
Microwave irradiation of (*o*-allyloxyaryl)acetylenes **3**.



Entry	**3**	R^1	R^2	R^3	Solvent	t (min)	**11** (yield, %)	**12** (yield, %	**13** (yield, %	**14** (yield, %
1	**3a**	H	H	H	DMF	15	**11a** (--)[a]	**12a** (--)[a]	**13a** (23)	**14a** (40)
2	**3a**	H	H	H	Toluene	60	**11a** (41)[a]	**12a** (--)[a]	**13a** (--)[a]	**14a** (--)[a]
3	**3a**	H	H	H	DMF	30	**11a** (--)[a]	**12a** (--)[a]	**13a** (13)	**14a** (49)
4	**3b**	H	OMe	H	DMF	30	**11b** (--)[a]	**12b** (47)	**13b** (15)	**14b** (16)
5	**3c**	OMe	H	OMe	DMF	30	--[b]	--[b]	--[b]	--[b]
6	**3d**	H	OMe	OMOM	DMF	30	**11d** (--)[a]	**12d** (18)	**13d** (--)[a]	**14d** (--)[a]
7	**3e**	H	H	OMe	DMF	30	**11e** (--)[a]	**12e** (--)[a]	**13e** (52)	**14e** (10)

DMF, dimethylformamide.
--, Not detected.
[a]Not detected
[b]Complex mixture of products formed

Scheme 4. Tentative mechanism for the formation of products **13a** and **14a**.



CONCLUSIONS

In summary, we have devised a route to 7-allyl-substituted benzofurans via a microwave-promoted tandem Claisen-rearrangement/5-*endo*-dig cyclization sequence of *ortho*-allyloxy alkinyl arenes. For monosubstituted alkynes, an unexpected and to the best of our knowledge unprecedented reaction with the solvent DMF was observed, which leads to enaminoketones and in a subsequent step to chromene-4-ones.

EXPERIMENTAL SECTION

General methods. All experiments were conducted in dry reaction vessels under an atmosphere of dry nitrogen. Solvents were purified by standard procedures. ^{1}H NMR spectra were obtained at 300 or 600 MHz in $CDCl_3$ with $CHCl_3$ (δ = 7.26 ppm) as an internal standard. Coupling

constants are given in Hz. ^{13}C NMR spectra were recorded at 75 or 150 MHz in $CDCl_3$ with $CDCl_3$ (δ = 77.1 ppm) as an internal standard. Whenever the solubility or stability of the sample or signal separation was insufficient in $CDCl_3$, it was replaced by acetone-d_6 (acetone-d_5 as internal standard for ^1H NMR spectroscopy, δ = 2.05 ppm, CD_3COCD_3 as internal standard for ^{13}C NMR spectroscopy, δ = 29.8 ppm). IR spectra were recorded as ATR-FTIR spectra. Wavenumbers (ν) are given in cm^{-1}. The peak intensities are defined as strong (s), medium (m), or weak (w). Low-resolution and high-resolution mass spectra were obtained by EI-TOF or ESI-TOF. Microwave reactions were carried out in Anton-Paar-monowave 300 or 400 reactors (monowave, maximum power 850 W, temperature control by IR-sensor, 20-mL vial volume).

General procedure for the synthesis of arylacetylenes 3 and **8**. To a solution of the appropriate benzaldehydes **1** or **7** (1.00 mmol) in methanol (10 mL) was added K_2CO_3 (276 mg, 2.00 mmol). Dimethyl (1-diazo-2-oxopropyl) phosphonate (**2**, 307 mg, 1.60 mmol) was added and the solution was stirred at ambient temperature until the starting material was fully consumed (TLC). All volatiles were evaporated and the residue partitioned between brine (10 mL) and ethyl acetate (30 mL). The organic layer was separated and the aqueous layer extracted with ethyl acetate (twice, 30 mL each). The combined organic extracts were dried with $MgSO_4$, filtered, and evaporated. The residue was purified by column chromatography, using hexanes/MTBE mixtures of increasing polarity as eluent.

1-(Allyloxy)-2-ethynylbenzene (3a) *[44].* Following the general procedure, **1a** (162 mg, 1.00 mmol) was converted to **3a** (103 mg, 0.65 mmol, 65%): yellowish oil; ^1H NMR (300 MHz, $CDCl_3$) δ 7.49 (dm, J = 7.6 Hz, 1H), 7.35–7.27 (m, 1H), 6.94 (dm, J = 7.5 Hz, 1H), 6.92–6.87 (m, 1H), 6.09 (ddt, J = 17.3, 10.5, 5.0 Hz, 1H), 5.50 (dq, J = 17.3, 1.7 Hz, 1H), 5.32 (dq, J = 10.5, 1.7 Hz, 1H), 4.66 (dt, J = 5.0, 1.7 Hz, 2H), 3.32 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8, 134.3, 133.0, 130.2, 120.7, 117.7, 112.5, 111.9, 81.3, 80.2, 69.4; IR (ATR) ν 3283 (m), 2868 (w), 2106 (w), 1595 (m), 1575 (m), 1487 (s), 1444 (s), 1287 (m), 1249 (s), 1229 (s); HRMS: no $[M^+]$ signal observed with different ionization methods.

1-(Allyloxy)-2-ethynyl-4-methoxybenzene (3b) *[45].* Following the general procedure, **1b** (192 mg, 1.00 mmol) was converted to **3b** (73 mg, 0.39 mmol, 39%): yellowish oil; ^1H NMR (300 MHz, $CDCl_3$) δ 7.00 (dd, J = 2.7, 0.6 Hz, 1H), 6.85 (dd, J = 9.0, 2.7 Hz, 1H), 6.80 (dd, J = 9.0, 0.6 Hz, 1H), 6.05 (ddt, J = 17.3, 10.3, 5.1 Hz, 1H), 5.44 (dq, J = 17.3, 1.7 Hz, 1H), 5.27 (dq, J = 10.3, 1.7 Hz, 1H), 4.58 (dt, J = 5.1 1.6 Hz, 2H), 3.75 (s, 3H), 3.29 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 153.5, 133.4, 118.7, 117.6, 116.3, 114.5, 112.8, 81.3, 80.1, 70.5, 55.9; IR (ATR) ν 3284 (m), 2938 (w), 2106 (w), 1579 (w), 1494 (s), 1463 (w), 1463 (m), 1277 (m), 1219 (s), 1159 (m); HRMS (ESI) calcd for $C_{12}H_{13}O_2$ $[M + H]^+$ 189.0916, found 189.0927.

1-(Allyloxy)-2-ethynyl-3,5-dimethoxybenzene (3c) *.* Following the general procedure, **1c** (222 mg, 1.00 mmol) was converted to **3c** (35 mg, 0.16 mmol, 16%): yellowish oil; ^1H NMR (300 MHz, $CDCl_3$) δ 6.05 (s, 1H), 6.05 (s, 1H), 6.02 (ddt, J = 17.3, 10.5, 5.0 Hz, 1H), 5.43 (dq, J = 17.3, 1.7 Hz, 1H), 5.25 (dq, J = 10.6, 1.7 Hz, 1H), 4.57 (dt, J = 5.0, 1.7 Hz, 2H), 3.83 (s, 3H), 3.76 (s, 3H), 3.29 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.0, 162.1, 161.7, 132.9, 117.5, 93.8, 92.0, 90.7, 83.9, 76.5, 69.5, 56.0, 55.4; IR (ATR) ν 3274 (m), 2940 (w), 2101 (m), 1601 (s), 1575 (s), 1456 (m), 1418 (m), 1337 (w), 1225 (m); HRMS (ESI) calcd for $C_{13}H_{15}O_3$ $[M + H]^+$ 219.1021, found 219.1000.

1-(Allyloxy)-2-ethynyl-4-methoxy-5-(methoxymethoxy) benzene (3d) *.* Following the general procedure, **1d** (252 mg, 1.00 mmol) was converted to **3d** (87 mg, 0.35 mmol, 35%): yellowish oil; ^1H NMR (300 MHz, $CDCl_3$) δ 6.91 (s, 1H), 6.76 (s, 1H), 5.99 (ddt, J = 17.2, 10.4, 5.2 Hz, 1H), 5.39 (dm, J = 17.2 Hz, 1H), 5.22 (dm, J = 10.4 Hz, 1H), 5.16 (s, 2H), 4.53 (dm, J = 5.2 Hz, 2H), 3.77 (s, 3H), 3.45 (s, 3H), 3.21 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.8, 148.1, 143.7, 133.2, 117.6, 116.8, 104.8, 103.5, 95.5, 80.3, 80.1, 70.4, 56.4, 56.2; IR (ATR) ν 3260 (s), 2937 (w), 2105 (w), 1604 (w), 1504 (s), 1463 (m), 1417 (m), 1390 (m), 1268 (s), 1212 (s); HRMS (ESI) calcd for $C_{14}H_{16}O_4$ $[M + H]^+$ 249.1127, found 249.1120.

2-(Allyloxy)-1-ethynyl-4-methoxybenzene (3e) *[45].* Following the general procedure, **1e** (192 mg, 1.00 mmol) was converted to **3e** (73 mg, 0.39 mmol, 39%): yellowish oil; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38 (dm, J = 7.8 Hz, 1H), 6.47–6.41 (2H), 6.05 (ddt, J = 17.3, 10.6, 5.0 Hz, 1H), 5.47 (dq, J = 17.3, 1.7 Hz, 1H), 5.29 (dq, J = 10.6, 1.7 Hz, 1H), 4.61 (dt, J = 5.0 Hz, 2H), 3.79 (s, 3H), 3.21 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.4, 161.0, 135.0, 132.9, 117.7, 105.4, 104.5, 100.1, 80.3, 79.9, 69.5, 55.5; IR (ATR) ν 3281 (m), 2937 (w), 2103 (w), 1604 (s), 1571 (m), 1500 (s), 1462 (m), 1443 (m), 1420 (m), 1301 (s); HRMS (ESI) calcd for $C_{12}H_{13}O_2$ $[M + H]^+$ 189.0916, found 189.0929.

1-Ethynyl-4-methoxybenzene (8b) *[46].* Following the general procedure, **7b** (136 mg, 1.00 mmol) was converted to **8b** (70 mg, 0.53 mmol, 53%): yellowish oil; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44 (d, J = 8.9 Hz, 2H), 6.85 (d, J = 8.9 Hz, 1H), 3.80 (s, 3H), 3.01 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1, 133.7, 114.3, 114.1, 83.8, 75.9, 55.4; IR (ATR) ν 3286 (m), 2838 (w), 2106 (w), 1605 (s), 1571 (w), 1505 (s), 1464 (m), 1441 (m),

1289 (s), 1245 (s); HRMS (EI) calcd for C_9H_8O [M^+] 132.0575, found 132.0573.

1-Ethynyl-3,5-dimethoxybenzene (8c) *[46].* Following the general procedure, **7c** (166 mg, 1.00 mmol) was converted to **8c** (92 mg, 0.57 mmol, 57%): yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.65 (d, *J* = 2.3 Hz, 2H), 6.47 (t, *J* = 2.3 Hz, 1H), 3.78 (s, 6H), 3.04 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.7, 123.5, 110.1, 102.4, 83.8, 76.8, 55.5; IR (ATR) *v* 3286 (m), 2838 (w), 2117 (w), 1587 (s), 1453 (m), 1419 (s), 1344 (m), 1321 (m), 1295 (m), 1204 (s), 1153(s); HRMS (EI) calcd for $C_{10}H_{10}O_2$ [M^+] 162.0681, found 162.0678.

5-Ethynyl-1,2,3-trimethoxybenzene (8d) *[47].* Following the general procedure, **7d** (196 mg, 1.00 mmol) was converted to **8d** (111 mg, 0.58 mmol, 58%): yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.72 (s, 2H), 3.84 (s, 3H), 3.85 (s, 6H), 3.02 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.2, 139.5, 117.2, 109.6, 83.8, 76.3, 61.1, 56.3; IR (ATR) *v* 3282 (m), 2939 (w), 2104 (w), 1575 (s), 1501 (s), 1449 (m), 1409 (s), 1331 (s), 1233 (s), 1183 (m), 1122(s); HRMS (EI) calcd for $C_{11}H_{12}O_3$ [M^+] 192.0786, found 192.0787.

1-(Allyloxy)-2-(phenylethynyl)benzene (4a) *[26].* Alkyne **3a** (158 mg, 1.00 mmol), iodobenzene (204 mg, 1.00 mmol), and pyrrolidine (410 μL, 5.00 mmol) were suspended in water (5 mL). $PdCl_2$ (2 mg, 1 mol%) was added and the mixture was heated to 50°C for 16 h and then cooled to ambient temperature and diluted with ethyl acetate (30 mL). The mixture was washed with brine, the organic layer was separated, dried with $MgSO_4$, filtered, and evaporated. The residue was purified by column chromatography on silica using hexanes/MTBE mixtures of increasing polarity as eluent to furnish **4a** (112 mg, 0.48 mmol, 48%): colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59–7.54 (2H), 7.52 (dm, *J* = 7.6 Hz, 1H), 7.38–7.28 (m, 4H), 6.96 (tm, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 8.3 Hz, 1H), 6.12 (ddt, *J* = 17.2, 10.6, 4.8 Hz, 1H), 5.56 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.32 (dq, *J* = 10.6, 1.6 Hz, 1H), 4.66 (dt, *J* = 4.8, 1.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 133.6, 133.4, 131.8, 129.7, 128.9, 128.4, 128.2, 124.1, 121.1, 117.2, 113.3, 93.8, 86.1, 69.8; IR (ATR) *v* 3061 (w), 2918 (w), 1592 (w), 1572 (w), 1496 (m), 1482 (m), 1443 (m), 1276 (m), 1239 (m), 1225 (m); HRMS (EI) calcd for $C_{17}H_{14}O$ [M^+] 234.1045, found 234.1048.

General procedure for the synthesis of diarylacetylenes 10. The corresponding alkyne **8** (1.00 mmol), 2-iodophenol (219 mg, 1.00 mmol), and NEt_3 (277 μL, 2.00 mmol) were dissolved in dry and degassed benzene (5 mL). CuI (6 mg, 3 mol %) and Pd $(PPh_3)_2Cl_2$ (21 mg, 3 mol %) were added and the mixture was heated to 50°C for 1 h. After cooling to ambient temperature, the mixture was diluted with ethyl acetate (30 mL) and washed with brine (10 mL). The organic layer was separated, dried with $MgSO_4$, filtered, and evaporated. The residue was purified by column chromatography on silica, using hexanes/MTBE mixtures of increasing polarity as eluent.

2-((4-Methoxyphenyl)ethynyl)phenol (10b) *[16,48].* Following the general procedure, **8b** (132 mg, 1.00 mmol) was converted to **10b** (215 mg, 0.96 mmol, 96%): yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (dm, J = 8.9 Hz, 2H), 7.44 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.29 (ddd, *J* = 8.2, 7.5, 1.7 Hz, 1H), 7.01 (dd, *J* = 8.2, 1.0 Hz, 1H), 6.96–6.93 (m, 1H), 6.92 (dm, *J* = 8.9 Hz, 2H), 5.90 (s, 1H), 3.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1, 156.5, 133.3, 131.6, 130.3, 120.5, 114.7, 114.5, 114.3, 110.0, 96.6, 81.8, 55.5; IR (ATR) *v* 3504 (br), 2934 (w), 2836 (w), 2206 (w), 1602 (m), 1505 (s), 1483 (m), 1452 (m), 1287 (m), 1245 (s), 1174 (s); HRMS (EI) calcd for $C_{15}H_{12}O_2$ [M^+] 224.0832, found 224.0842.

2-((3,5-Dimethoxyphenyl)ethynyl)phenol (10c) *[48].* Following the general procedure, **8c** (162 mg, 1.00 mmol) was converted to **10c** (206 mg, 0.81 mmol, 81%): yellowish oil; ^{1}H NMR (300 MHz, acetone-d_6) δ 8.51 (s, 1H), 7.42 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.25 (ddd, *J* = 8.6, 7.3, 1.7 Hz, 1H), 6.95 (dd, *J* = 8.5, 1.0 Hz, 1H), 6.88 (ddd, *J* = 7.5, 7.5, 1.2 Hz, 1H), 6.71 (d, *J* = 2.3 Hz, 2H), 6.51 (t, *J* = 2.3 Hz, 1H), 3.81 (s, 6H); ^{13}C NMR (75 MHz, acetone-d_6) δ 161.8, 158.9, 133.7, 131.0, 125.8, 120.6, 116.5, 111.1, 110.0, 102.2, 94.5, 85.8, 55.8; IR (ATR) n 3436 (br), 2937 (w), 2838 (w), 2206 (w), 1585 (s), 1488 (m), 1451 (m), 1418 (m), 1356 (m), 1203 (s), 1150 (s); HRMS (EI) calcd for $C_{16}H_{14}O_3$ [M^+] 254.0943, found 254.0950.

2-((3,4,5-Dimethoxyphenyl)ethynyl)phenol (10d) *[48].* Following the general procedure, **8d** (192 mg, 1.00 mmol) was converted to **10d** (264 mg, 0.93 mmol, 93%): yellowish oil; ^{1}H NMR (300 MHz, acetone-d_6) δ 8.41 (s, 1H), 7.41 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.24 (ddd, *J* = 8.3, 7.4, 1.7 Hz, 1H), 6.95 (dd, *J* = 8.3, 1.0 Hz, 1H), 6.88 (ddd, *J* = 7.5, 7.5, 1.2 Hz, 1H), 6.85 (s, 2H), 3.85 (s, 6H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, acetone-d_6) δ 158.8, 154.3, 140.2, 133.6, 130.9, 120.6, 119.3, 116.5, 111.3, 109.9, 94.8, 85.0, 60.7, 56.6; IR (ATR) *v* 3407 (br), 2938 (w), 2837 (w), 1574 (s), 1504 (m), 1448 (m), 1409 (m), 1356 (m), 1233 (s), 1122 (s); HRMS (EI) calcd for $C_{17}H_{16}O_4$ [M^+] 284.1043, found 284.1053.

General procedure for the synthesis of allyl ethers 4b–d. To a solution of the corresponding phenol **10** (1.00 mmol) in acetone (5 mL) were added allyl bromide (128 μL, 1.50 mmol) and K_2CO_3 (280 mg, 2.00 mmol). The mixture was heated to 50°C for 16 h and then cooled to ambient temperature and partitioned between brine (20 mL) and ethyl acetate (30 mL). The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (twice, 30 mL each). The combined organic

extracts were dried with $MgSO_4$, filtered, and evaporated. The residue was purified by column chromatography on silica, using hexanes/MTBE mixtures of increasing polarity as eluent.

1-(Allyloxy)-2-((4-methoxyphenyl)ethynyl)benzene (4b). Following the general procedure, **10b** (224 mg, 1.00 mmol) was converted to **4b** (172 mg, 0.65 mmol, 65%): yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52–7.47 (m, 3H), 7.26 (ddd, *J* = 8.7, 7.6, 1.8 Hz, 1H), 6.95 (dd, *J* = 7.5, 0.9 Hz, 1H), 6.92–6.86 (3H), 6.11 (ddt, *J* = 17.2, 10.5, 4.8 Hz, 1H), 5.55 (dm, *J* = 17.2 Hz, 1H), 5.31 (dm, *J* = 10.5 Hz, 1H), 4.65 (dt, *J* = 4.8, 1.7 Hz, 2H), 3.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7, 159.1, 133.4, 133.3, 133.2, 129.4, 120.9, 117.2, 116.0, 114.1, 113.7, 112.8, 93.7, 84.6, 69.5, 55.4; IR (ATR) *ν* 2933 (w), 2836 (w), 2214 (w), 1605 (m), 1571 (w), 1509 (s), 1443 (m), 1285 (s), 1243 (s), 1173 (m), 1104 (m); HRMS (EI) calcd for $C_{18}H_{16}O_2$ [M^+] 264.1150, found 264.1144.

1-((2-Allyloxy)phenyl)ethynyl)-3,5-dimethoxybenzene (4c). Following the general procedure, **10c** (254 mg, 1.00 mmol) was converted to **4c** (229 mg, 0.78 mmol, 78%): yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.28 (ddd, *J* = 8.4, 7.6, 1.7 Hz, 1H), 6.95 (td, *J* = 7.5, 1.0 Hz, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 6.72 (d, *J* = 2.3 Hz, 2H), 6.46 (t, *J* = 2.3 Hz, 1H), 6.11 (ddt, *J* = 17.2, 10.6, 4.8 Hz, 1H), 5.56 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.31 (dq, *J* = 10.6, 1.7 Hz, 1H), 4.65 (dt, *J* = 4.8, 1.7 Hz, 2H), 3.81 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.7, 159.3, 133.6, 133.2, 129.8, 125.1, 120.9, 117.2, 113.2, 112.7, 109.5, 101.8, 93.7, 85.6, 69.4, 55.5; IR (ATR) *ν* 2936 (w), 2838 (w), 2214 (w), 1585 (s), 1493 (m), 1447 (m), 1419 (m), 1357 (m), 1259 (m), 1203 (s), 1152 (s); HRMS (EI) calcd for $C_{19}H_{18}O_3$ [M^+] 294.1256, found 294.1249.

5-((2-Allyloxy)phenyl)ethynyl)-1,2,3-trimethoxybenzene (4d). Following the general procedure, **10d** (284 mg, 1.00 mmol) was converted to **4d** (201 mg, 0.62 mmol, 62%): yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.27 (ddd, *J* = 8.4, 7.5, 1.7 Hz, 1H), 6.95 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1H), 6.90 (d, *J* = 8.4 Hz, 1H), 6.79 (s, 2H), 6.11 (ddt, *J* = 17.2, 10.6, 4.8 Hz, 1H), 5.56 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.30 (dq, *J* = 10.6, 1.7 Hz, 1H), 4.65 (dt, *J* = 4.8, 1.7 Hz, 2H), 3.87 (s, 6H), 3.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 153.2, 133.4, 133.3, 129.7, 120.9, 118.8, 118.3, 117.1, 113.2, 112.7, 109.0, 93.7, 85.0, 69.4, 61.1, 56.3; IR (ATR) *ν* 2938 (w), 2841 (w), 2252 (w), 1573 (s), 1504 (s), 1446 (m), 1409 (m), 1355 (m), 1261 (m), 1233 (s), 1126 (s); HRMS (EI) calcd for $C_{20}H_{20}O_4$ [M^+] 324.1356, found 324.1351.

Methyl-3-(2-allyloxy)phenyl)propiolate (4e) [37]. A solution of **3a** (158 mg, 1.00 mmol) was cooled to −78°C. Butyllithium (2.5 M sol. in hexane, 0.60 mL, 1.50 mmol) was added and the mixture was stirred at −78°C for 2 h. The reaction was quenched by addition of an aqueous saturated solution of NH_4Cl (5 mL) and then warmed to ambient temperature. Ethyl acetate (30 mL) was added, the organic layer was separated, and the aqueous layer was extracted with ethyl acetate (twice, 30 mL each). The combined organic extracts were dried with $MgSO_4$, filtered, and evaporated. The crude product was purified by column chromatography on silica, using hexanes/MTBE mixtures of increasing polarity as eluent, to furnish **4e** (95 mg, 0.44 mmol, 44%): yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.36 (ddd, *J* = 8.5, 7.5, 1.7 Hz, 1H), 6.92 (ddd, *J* = 7.5, 7.5, 0.9 Hz, 1H), 6.88 (d, *J* = 8.5 Hz, 1H), 6.04 (ddt, *J* = 17.3, 10.6, 4.8 Hz, 1H), 5.49 (dq, *J* = 17.3, 1.6 Hz, 1H), 5.30 (dq, *J* = 10.6, 1.6 Hz, 1H), 4.62 (dt, *J* = 4.8, 1.6 Hz, 2H), 3.82 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.8, 154.7, 134.9, 132.6, 132.3, 120.8, 117.6, 112.5, 109.4, 84.5, 83.7, 69.3, 52.7; IR (ATR) *ν* 2953 (m), 2219 (s), 1704 (s), 1595 (m), 1574 (m), 1489 (s), 1446 (s), 1279 (s), 1162 (s); HRMS (ESI) calcd for $C_{13}H_{12}O_3Na$ [M + Na]$^+$ 239.0684, found 239.0679.

General procedure for microwave-promoted reactions of alkynes 4. The appropriate precursor **4** (1.00 mmol) was dissolved in toluene (7 mL) or DMF (7 mL) (Tables 1 and 4 or Scheme 2) in a vessel suited for microwave irradiation. The vessel was sealed, placed in a dedicated microwave reactor, and heated at 250°C for the time period indicated in the respective tables and schemes. After cooling to ambient temperature, the solvent was evaporated and the residue purified by column chromatography on silica with hexanes/MTBE mixtures as eluent.

2-Allyl-6-(phenylethynyl)phenol (6a). Table 1, entry 1 (solvent toluene; reaction time 60 min): following the general procedure, **4a** (234 mg, 1.00 mmol) was converted to **6a** (105 mg, 0.45 mmol, 45%): yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58–7.52 (2H), 7.41–7.36 (3H), 7.33 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.16 (dm, *J* = 7.6 Hz, 1H), 6.88 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.04 (ddt, *J* = 17.3, 11.0, 6.6 Hz, 1H), 5.96 (s, 1H), 5.12 (dm, *J* = 17.3 Hz, 1H), 5.11 (dm, *J* = 11.0 Hz, 1H), 3.46 (dm, *J* = 6.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.7, 136.5, 131.8, 131.2, 129.9, 128.9, 128.7, 126.3, 122.8, 120.4, 115.9, 109.7, 96.4, 83.7, 34.4; IR (ATR) *ν* 3508 (m), 3059 (w), 2918 (w), 1638 (w), 1585 (w), 1491 (m), 1451 (s), 1334 (m), 1229 (s), 1069 (m); HRMS (EI) calcd for $C_{17}H_{14}O$ [M^+] 234.1045, found 234.1040.

7-Allyl-2-phenylbenzofuran (5a). Table 1, entry 2 (solvent DMF; reaction time 15 min): following the general procedure, **4a** (234 mg, 1.00 mmol) was converted to **5a** (215 mg, 0.92 mmol, 92%): yellowish oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92–7.88 (m, 2H), 7.49–7.46 (3H), 7.38 (tt, *J* = 7.4, 1.3 Hz, 1H), 7.21 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.14 (dm, *J* = 7.3 Hz, 1H), 7.04 (s,

1H), 6.17 (ddt, J = 16.8, 10.0, 6.8 Hz, 1H), 5.26 (dm, J = 17.0 Hz, 1H), 5.17 (dm, J = 10.0 Hz, 1H), 3.78 (d, J = 6.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.7, 153.4, 136.1, 130.7, 129.1, 128.9, 128.6, 125.0, 124.4, 123.8, 123.3, 119.1, 116.3, 101.7, 34.2; IR (ATR) ν 3061 (w), 1638 (w), 1638 (w), 1608 (w), 1565 (w), 1480 (m), 1424 (m), 1289 (m), 1203 (s), 1172 (m); HRMS (EI) calcd for $C_{17}H_{14}O$ [M^+] 234.1045, found 234.1053.

7-Allyl-2-(4-methoxyphenyl)benzofuran (5b). Table 1, entry 5 (solvent DMF; reaction time 30 min): following the general procedure, **4b** (264 mg, 1.00 mmol) was converted to **5b** (177 mg, 0.67 mmol, 67%): yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (dm, J = 8.9 Hz, 2H), 7.43 (dd, J = 7.6, 1.1 Hz, 1H), 7.17 (dd, J = 7.5, 7.5 Hz, 1H), 7.09 (dm, J = 7.5 Hz, 1H), 6.99 (d, J = 8.9 Hz, 2H), 6.89 (s, 1H), 6.16 (ddt, J = 16.8, 10.0, 6.7 Hz, 1H), 5.24 (dm, J = 17.0 Hz, 1H), 5.15 (dm, J = 10.0 Hz, 1H), 3.87 (s, 3H), 3.76 (dm, J = 6.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1, 155.9, 153.3, 136.2, 129.4, 126.5, 123.9, 123.7, 123.6, 123.2, 118.8, 116.2, 114.4, 100.1, 55.5, 34.2; IR (ATR) ν 2933 (w), 2836 (w), 1614 (m), 1506 (s), 1482 (w), 1454 (w), 1429 (w), 1249 (s), 1173 (m); HRMS (ESI) calcd for $C_{18}H_{17}O_2$ [M + H]$^+$ 265.1229, found 265.1245.

7-Allyl-2-(3,5-dimethoxyphenyl)benzofuran (5c). Table 1, entry 7 (solvent DMF; reaction time 30 min): following the general procedure, **4c** (294 mg, 1.00 mmol) was converted to **5c** (185 mg, 0.63 mmol, 63%): yellowish oil; ^{1}H NMR (300 MHz, acetone-d_6) δ 7.50 (dd, J = 7.4, 1.5 Hz, 1H), 7.31 (s, 1H), 7.20 (dd, J = 7.4, 7.4 Hz, 1H), 7.17–7.12 (m, 3H), 6.55 (t, J = 2.3 Hz, 1H), 6.15 (ddt, J = 16.8, 10.0, 6.7 Hz, 1H), 5.25 (dq, J = 17.0, 1.8 Hz, 1H), 5.12 (dm, J = 10.0 Hz, 1H), 3.89 (s, 6H), 3.75 (dm, J = 6.7 Hz, 2H); ^{13}C NMR (75 MHz, acetone-d_6) δ 162.3, 156.3, 154.1, 137.1, 133.1, 129.9, 125.4, 124.4, 124.2, 120.0, 116.5, 103.8, 103.2, 101.5, 55.8, 34.6; IR (ATR) n 2936 (w), 2836 (w), 1595 (s), 1571 (s), 1455 (m), 1420 (m), 1357 (w), 1203 (s), 1152 (s); HRMS (ESI) calcd for $C_{19}H_{19}O_3$ [M + H]$^+$ 295.1334, found 295.1315.

7-Allyl-2-(3,4,5-trimethoxyphenyl)benzofuran (5d). Table 1, entry 9 (solvent DMF; reaction time 30 min): following the general procedure, **4d** (324 mg, 1.00 mmol) was converted to **5d** (175 mg, 0.54 mmol, 54%): yellowish oil; ^{1}H NMR (300 MHz, acetone-d_6) δ 7.47 (dd, J = 7.5, 1.3 Hz, 1H), 7.26 (s, 2H), 7.25 (s, 1H), 7.18 (dd, J = 7.5, 7.5 Hz, 1H), 7.12 (dm, J = 7.5 Hz, 1H), 6.12 (ddt, J = 16.8, 10.0, 6.8 Hz, 1H), 5.25 (dq, J = 17.0, 1.9 Hz, 1H), 5.12 (dm, J = 10.0 Hz, 1H), 3.94 (s, 6H), 3.79 (s, 3H), 3.74 (dm, J = 6.8 Hz, 2H); ^{13}C NMR (75 MHz, acetone-d_6) δ 156.4, 154.8, 154.0, 140.1, 137.1, 130.2, 126.8, 125.1, 124.3, 124.1, 119.8, 116.5, 103.4, 102.3, 60.7, 56.6, 34.7; IR (ATR) ν 2936 (w), 2836 (w), 1589 (m), 1568 (m), 1501 (m), 1414 (m), 1337 (m), 1251 (m), 1123 (s); HRMS (ESI) calcd for $C_{20}H_{21}O_4$ [M + H]$^+$ 325.1440, found 325.1444.

Methyl-7-allylbenzofuran-2-carboxylate (5e). Scheme 2 (solvent DMF; reaction time 30 min): following the general procedure, **4e** (216 mg, 1.00 mmol) was converted to **5e** (117 mg, 0.54 mmol, 54%): yellowish oil; ^{1}H NMR (300 MHz, acetone-d_6) δ 7.64 (dd, J = 7.1, 2.0 Hz, 1H), 7.64 (s, 1H), 7.33 (dm, J = 7.6 Hz, 1H), 7.29 (dd, J = 7.5, 7.5 Hz, 1H), 6.10 (ddt, J = 17.0, 10.0, 6.6 Hz, 1H), 5.15 (dq, J = 17.0, 1.7 Hz, 1H), 5.10 (dq, J = 10.0, 1.7 Hz, 1H), 3.93 (s, 3H), 3.70 (dm, J = 6.6 Hz, 2H); ^{13}C NMR (75 MHz, acetone-d_6) δ 160.2, 155.1, 146.4, 136.5, 128.3, 127.8, 125.5, 125.0, 121.9, 116.8, 114.9, 52.5, 34.1; IR (ATR) ν 2952 (w), 1720 (s), 1639 (w), 1566 (m), 1435 (m), 1335 (w), 1293 (s), 1176 (s); HRMS (ESI) calcd for $C_{13}H_{13}O_3$ [M + H]$^+$ 217.0865, found 217.0879.

2-Allyl-6-ethynylphenol (11a). Table 4, entry 2 (solvent toluene; reaction time 60 min): following the general procedure, **3a** (158 mg, 1.00 mmol) was converted to **11a** (65 mg, 0.41 mmol, 41%): yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (dd, J = 7.7, 1.7 Hz, 1H), 7.15 (dm, J = 7.5 Hz, 1H), 6.83 (dd, J = 7.6, 7.6 Hz, 1H), 6.01 (ddt, J = 17.5, 9.6, 6.5 Hz, 1H), 5.90 (s, 1H), 5.14–5.05 (m, 2H), 3.46 (s, 1H), 3.42 (dm, J = 6.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.5, 136.4, 131.6, 130.2, 126.4, 120.3, 116.0, 108.4, 84.1, 79.0, 34.3; IR (ATR) ν 3507 (w), 3284 (w), 2919 (w), 1637 (m), 1451 (s), 1328 (m), 1245 (m), 1213 (m), 1071 (m), 994 (m); HRMS: no [M^+] signal observed with different ionization methods.

(E)-1-(3-allyl-2-hydroxyphenyl)-3-(dimethylamino)prop-2-ene-1-one (13a) *and* ***8-allyl-4H-chromene-4-one (14a).*** Table 4, entry 3 (solvent DMF; reaction time 30 min): following the general procedure, **3a** (158 mg, 1.00 mmol) was converted to **13a** (30 mg, 0.13 mmol, 13%) and **14a** (91 mg, 0.49 mmol, 49%). Analytical data for **13a**: yellowish oil; ^{1}H NMR (600 MHz, acetone-d_6) δ 14.81 (s, 1H), 7.89 (d, J = 12.0 Hz, 1H), 7.74 (dm, J = 8.0, 1.8 Hz, 1H), 7.22 (dm, J = 7.3 Hz, 1H), 6.74 (dd, J = 8.0, 7.5 Hz, 1H), 6.01 (ddt, J = 17.0, 10.0, 6.8 Hz, 1H), 5.98 (d, J = 12.1 Hz, 1H), 5.07 (dm, J = 17.1 Hz, 1H), 4.99 (dm, J = 10.0 Hz, 1H), 3.37 (d, J = 6.8 Hz, 2H), 3.27 (s, 3H), 3.04 (s, 3H); ^{13}C NMR (150 MHz, acetone-d_6) δ 192.1, 162.0, 156.0, 137.8, 134.3, 129.3, 127.4, 120.6, 118.1, 115.6, 90.3, 45.4, 37.6, 34.3; IR (ATR) ν 2912 (w), 2811 (w), 1624 (s), 1592 (m), 1541 (s), 1471 (s), 1419 (s), 1343 (s), 1274 (s); HRMS (ESI) calcd for $C_{14}H_{18}NO_2$ [M + H]$^+$ 232.1338, found 232.1345. Analytical data of **14a**: [10] yellowish oil; ^{1}H NMR (600 MHz, acetone-d_6) δ 8.19 (d, J = 6.0 Hz, 1H), 7.98 (dd, J = 7.9, 1.7 Hz, 1H), 7.62 (dm, J = 7.4 Hz, 1H), 7.40 (dd, J = 7.6, 7.6 Hz, 1H), 6.29 (d, J = 6.0 Hz, 1H), 6.06 (ddt, J = 17.1, 10.1, 6.6 Hz, 1H), 5.12 (dq,

J = 17.1, 1.8 Hz, 1H), 5.09 (dm, J = 10.1 Hz, 1H), 3.64 (d, J = 6.6 Hz, 2H); ^{13}C NMR (150 MHz, acetone-d_6) δ 177.3, 156.7, 155.3, 136.6, 134.8, 130.8, 125.9, 125.7, 124.3, 116.9, 113.2, 34.1; IR (ATR) v 3076 (w), 2913 (w), 1641 (s), 1597 (m), 1481 (m), 1437 (m), 1405 (m), 1346 (m), 1321 (m); HRMS (ESI) calcd for $C_{12}H_{11}O_2$ $[M + H]^+$ 187.0759, found 187.0757.

7-Allyl-5-methoxybenzofuran (12b), (E)-1-(3-allyl-2-hydroxy-5-methoxyphenyl)-3-(dimethylamino)prop-2-ene-1-one (13b), and 8-allyl-6-methoxy-4H-chromene-4-one (14b). Table 4, entry 4 (solvent DMF; reaction time 30 min): following the general procedure, **3b** (188 mg, 1.00 mmol) was converted to **12b** (88 mg, 0.47 mmol, 47%), **13b** (39 mg, 0.15 mmol, 15%), and **14b** (35 mg, 0.16 mmol, 16%). Analytical data for **12b**: yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, J = 2.1 Hz, 1H), 6.93 (d, J = 2.5 Hz, 1H), 6.78–6.75 (m, 1H), 6.71 (d, J = 2.2 Hz, 1H), 6.08 (ddt, J = 17.1, 10.0, 6.6 Hz, 1H), 5.17 (dq, J = 17.1, 1.7 Hz, 1H), 5.12 (dm, J = 10.0 Hz, 1H), 3.84 (s, 3H), 3.65 (d, J = 6.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.3, 148.8, 145.5, 135.8, 127.8, 124.7, 116.5, 113.4, 107.0, 101.5, 56.0, 34.1; IR (ATR) v 2927 (m), 1606 (m), 1474 (s), 1426 (s), 1298 (w), 1196 (s), 1141 (s), 1034 (m); HRMS (EI) calcd for $C_{12}H_{12}O_2$ $[M^+]$ 188.0832, found 188.0836. Analytical data for **13b**: yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.75 (s, 1H), 7.86 (d, J = 12.1 Hz, 1H), 7.07 (d, J = 3.0 Hz, 1H), 6.89 (d, J = 3.0 Hz, 1H), 6.02 (ddt, J = 17.1, 10.1, 6.6 Hz, 1H), 5.71 (d, J = 12.1 Hz, 1H), 5.14–5.04 (m, 2H), 3.78 (s, 3H), 3.42 (d, J = 6.6 Hz, 2H), 3.16 (s, 3H), 2.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.5, 155.3, 154.9, 150.8, 136.6, 130.0, 121.2, 119.7, 116.0, 110.4, 90.3, 56.2, 45.5, 37.5, 33.9; IR (ATR) v 2910 (w), 1627 (s), 1539 (s), 1462 (m), 1362 (m), 1265 (s), 1194 (m), 1079 (s); HRMS (EI) calcd for $C_{15}H_{19}NO_3$ $[M^+]$ 261.1359, found 261.1360. Analytical data for **14b**: yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 5.9 Hz, 1H), 7.45 (d, J = 3.1 Hz, 1H), 7.13 (d, J = 3.1 Hz, 1H), 6.33 (d, J = 5.9 Hz, 1H), 5.98 (ddt, J = 17.1, 10.3, 6.6 Hz, 1H), 5.16–5.07 (m, 2H), 3.87 (s, 3H), 3.58 (d, J = 6.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.9, 156.8, 154.9, 149.8, 135.0, 131.6, 125.8, 124.1, 117.3, 112.2, 103.2, 56.0, 33.7; IR (ATR) v 3079 (w), 2935 (w), 1641 (s), 1607 (s), 1471 (s), 1430 (m), 1400 (m), 1327 (s), 1214 (m); HRMS (EI) calcd for $C_{13}H_{12}O_3$ $[M^+]$ 216.0781, found 216.0782.

7-Allyl-5-methoxy-6-(methoxymethoxy)benzofuran (12d). Table 4, entry 6 (solvent DMF; reaction time 30 min): following the general procedure, **3d** (248 mg, 1.00 mmol) was converted to **12d** (45 mg, 0.18 mmol, 18%): yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, J = 2.2 Hz, 1H), 6.96 (s, 1H), 6.67 (d, J = 2.1 Hz, 1H), 6.10 (ddt, J = 17.1, 10.0, 6.2 Hz, 1H), 5.11 (s, 2H), 5.09 (dq, J = 17.1, 1.6 Hz, 1H), 5.03 (dq, J = 10.1, 1.7 Hz, 1H), 3.87 (s, 3H), 3.74 (dt, J = 6.2, 1.6 Hz, 2H), 3.62 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.8, 148.6, 145.2, 142.3, 135.9, 122.6, 118.3, 115.6, 106.8, 101.1, 99.6, 57.7, 56.3, 29.1; IR (ATR) v 2924 (m), 1638 (w), 1602 (m), 1456 (m), 1429 (m), 1295 (m), 1208 (m), 1155 (m); HRMS (EI) calcd for $C_{14}H_{16}O_4$ $[M^+]$ 248.1043, found 248.1046.

(E)-1-(3-allyl)-2-hydroxy-4-methoxyphenyl)-3-(dimethylamino)prop-2-ene-1-one (13e) and 8-allyl-7-methoxy-4 H-chromene-4-one (14e). Table 4, entry 7 (solvent DMF; reaction time 30 min): following the general procedure, **3e** (188 mg, 1.00 mmol) was converted to **13e** (136 mg, 0.52 mmol, 52%) and **14e** (22 mg, 0.10 mmol, 10%). Analytical data for **13e**: yellowish oil; ^{1}H NMR (300 MHz, acetone-d_6) δ 14.93 (s, 1H), 7.83 (d, J = 12.1 Hz, 1H), 7.77 (d, J = 9.0 Hz, 1H), 6.48 (d, J = 9.0 Hz, 1H), 5.91 (ddt, J = 17.1, 10.0, 6.4 Hz, 1H), 5.88 (d, J = 12.1 Hz, 1H), 4.97 (dm, J = 17.1 Hz, 1H), 4.86 (dm, J = 10.0 Hz, 1H), 3.85 (s, 3H), 3.36 (d, J = 6.4, 1.6 Hz, 2H), 3.22 (s, 3H), 3.00 (s, 3H); ^{13}C NMR (75 MHz, acetone-d_6) δ 191.5, 163.4, 162.4, 155.2, 137.4, 128.9, 115.5, 115.2, 114.4, 101.9, 90.2, 56.0, 45.3, 37.5, 27.4; IR (ATR) v 2912 (w), 1613 (s), 1540 (s), 1485 (m), 1417 (m), 1348 (s), 1285 (m), 1244 (s); HRMS (EI) calcd for $C_{15}H_{19}NO_3$ $[M^+]$ 261.1359, found 261.1365. Analytical data for **14e**: yellowish oil; ^{1}H NMR (300 MHz, acetone-d_6) δ 8.10 (d, J = 6.0 Hz, 1H), 8.00 (d, J = 8.9 Hz, 1H), 7.20 (d, J = 8.9 Hz, 1H), 6.19 (d, J = 6.0 Hz, 1H), 5.94 (ddt, J = 17.1, 10.0, 6.4 Hz, 1H), 4.99 (dq, J = 17.1, 1.7 Hz, 1H), 4.94 (dq, J = 10.0, 1.7 Hz, 1H), 3.99 (s, 3H), 3.57 (dt, J = 6.2, 1.7 Hz, 2H); ^{13}C NMR (75 MHz, acetone-d_6) δ 177.0, 162.1, 156.6, 156.1, 136.2, 125.6, 119.8, 116.7, 115.5, 112.8, 110.1, 56.8, 27.6; IR (ATR) v 3077 (w), 2976 (w), 1636 (s), 1618 (s), 1592 (s), 1427 (m), 1405 (m), 1352 (m), 1267 (s); HRMS (EI) calcd for $C_{13}H_{12}O_3$ $[M^+]$ 216.0781, found 216.0783.

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