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Synthesis of Functionalized Indolines and Dihydrobenzofurans by Iron and Copper Catalyzed Aryl C−N and C−O Bond Formation

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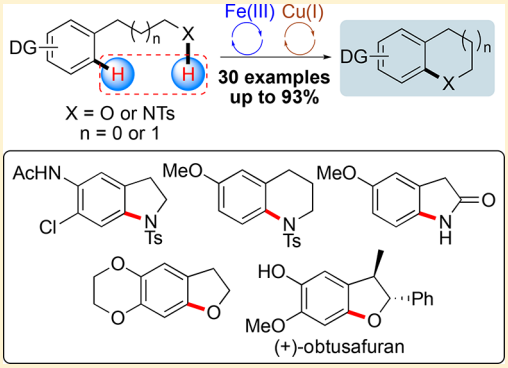
Supporting Information

ABSTRACT: A simple and effective one-pot, two-step intramolecular aryl C−N and C−O bond forming process for the preparation of a wide range of benzo-fused heterocyclic scaffolds using iron and copper catalysis is described. Activated aryl rings were subjected to a highly regioselective, iron(III) triflimide-catalyzed iodination, followed by a copper(I)-catalyzed intramolecular *N*- or *O*-arylation step leading to indolines, dihydrobenzofurans, and six-membered analogues. The general applicability and functional group tolerance of this method were exemplified by the total synthesis of the neolignan natural product, (+)-obtusafuran. DFT calculations using Fukui functions were also performed, providing a molecular orbital rationale for the highly regioselective arene iodination process.



INTRODUCTION

Indoline and dihydrobenzofuran scaffolds are privileged structures, represented in a wide range of natural products and pharmaceutically important agents.[1] For this reason, considerable efforts have focused on the discovery of efficient methods for the preparation of these heterocycles.[2] A commonly used approach for the synthesis of indolines and dihydrobenzofurans is the Buchwald−Hartwig or Ullmann-type C−N and C−O bond forming process of prefunctionalized, halogenated phenylethylamines and phenylethylalcohols (Figure 1a).[3−6] As well as five-membered rings, this strategy is highly effective for the preparation of six-membered benzo-fused heterocyclic systems and has been used for the preparation of a wide range of natural products such as (+)-isatisine A,[4g] corsifuran A,[5b] and a number of quinoline-containing alkaloids.[3b]

An alternative approach for preparing these ring systems has been developed more recently involving transition-metal-catalyzed aryl C−H activation and intramolecular cross-coupling with N−H or O−H bonds.[7,8] Pioneering work by the Yu group showed that triflimide-protected 2-phenylethylamines and Pd(II)/Cu(I) catalysis could be used for the one-pot preparation of indolines via a tandem C−H bond iodination−amination sequence.[8a] The palladium-catalyzed intramolecular aryl C(sp^2)−H amination process was improved using *N*-chelating groups and oxidizing agents such as hypervalent iodonium salts.[8−10] Among the range of *N*-protected amides used to direct the palladium-catalyzed functionalization of aryl C−H bonds, the Zhao group demonstrated the highly effective use of a *N*,*O*-bidentate oxalyl amide (Figure 1b).[8g]

Although this strategy has also been used to prepare dihydrobenzofurans from phenylethylalcohols, the oxidizing conditions can be problematic for substrates bearing primary and secondary alcohols.[11] More recently, Zakarian and co-workers reported a mechanistically distinct approach for the preparation of dihydrobenzofurans (Figure 1c).[12] A one-pot intramolecular aryl C−O bond forming process was achieved by formation of nonsymmetrical diaryliodonium salts by oxidation of electron-rich 2-phenylethylalcohols, followed by a copper-catalyzed C−O bond forming process. A key feature of this method was the room temperature conditions for copper-catalyzed cyclization.

While these methods provide an attractive entry to these ring systems, many of the approaches have been specifically developed for either C−N or C−O bond formation or for the preparation of a particular ring size. We were interested in developing a new approach for intramolecular C−N or C−O bond formation that would avoid a prefunctionalization step, precious transition metals, strong oxidizing conditions and could be used for the general preparation of both five- and six-membered heterocyclic systems. Herein, we describe a one-pot intramolecular C−N and C−O bond forming process that utilizes a highly regioselective iron-catalyzed iodination for initial arene activation, followed by a copper-catalyzed C−N and C−O cyclization (Figure 1d). As well as providing an electronic rationale for the high regioselectivity of the iron-catalyzed halogenation reaction, we show the general application of this process for the preparation of a wide range of ring systems and as the key step for the total synthesis of the natural product, (+)-obtusafuran.

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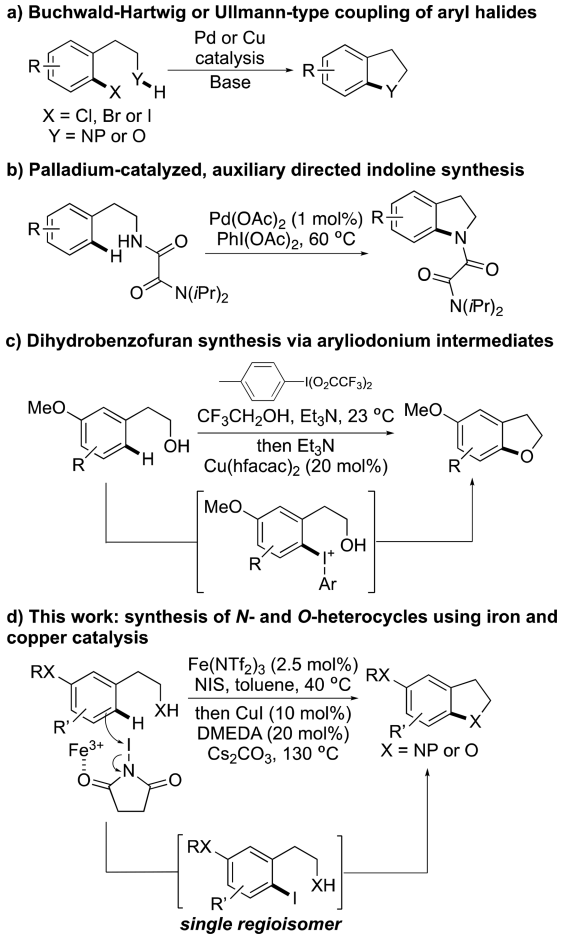


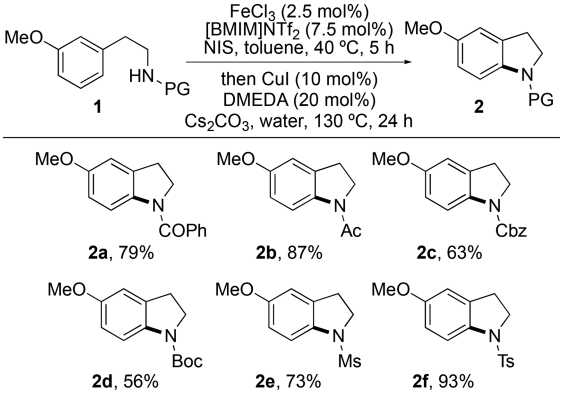
Figure 1. Synthesis of indolines and dihydrobenzofuran scaffolds.

RESULTS AND DISCUSSION

Previously, we have shown that the combination of iron(III) chloride and the inexpensive ionic liquid [BMIM]NTf_2 results in the formation of iron triflimide, which can be used as a super Lewis acid catalyst[13] to activate *N*-halosuccinimides for the fast and efficient regioselective halogenation of aromatic compounds.[14] In this current study, this transformation was investigated for the regioselective iodination of a new class of substrate, *N*-protected 2-phenylethylamines (Scheme 1). The initial aim was to evaluate the 3-methoxy substituent as a directing group for selective *para*-iodination and assess if the resulting activated aryl intermediate could undergo a copper-(I)-catalyzed *N*-arylation reaction for the one-pot synthesis of indolines. Using standard conditions for halogenation with iron(III) chloride (2.5 mol %) and [BMIM]NTf_2 (7.5 mol %), the iodination of *N*-benzoyl protected **1a** by *N*-iodosuccinimide (NIS) was complete in 5 h at 40 °C.[14a,15] Analysis of the crude reaction mixture by ^{1}H NMR spectroscopy showed the formation of the *para*-iodinated regioisomer as the sole product. The aryl ring of **1a** can undergo iodination with NIS, without the iron(III) triflimide catalyst; however, under the same conditions, full conversion was only achieved after 22 h giving a 10:1 mixture of *para*- and *ortho*-regioisomers. The regioselective iron(III) triflimide catalyzed activation of **1a** was then performed in combination with a Cu(I)-catalyzed *N*-arylation for the one-pot synthesis of indoline **2a**. Using copper iodide (10 mol %) and DMEDA (20 mol %) during the C−N bond forming step gave *N*-benzoyl-protected indoline **2a** in 79% overall yield. It should be noted that when the synthesis of **2a** was done by performing each step separately, the overall yield (59%) was significantly lower than that for the one-pot process. With the success of the one-pot synthesis of **2a**, a range of *N*-protecting groups were explored to evaluate the most suitable nucleophile for the Cu(I)-catalyzed *N*-arylation. While *N*-Cbz and *N*-Boc carbamate protected indolines **2c** and **2d** were prepared in good yields, the most efficient one-pot processes involved *N*-acetamide or *N*-sulfonamide protected compounds. In particular, one-pot activation and cyclization of *N*-tosyl phenylethylamine **1f** gave indoline **2f** in 93% yield.

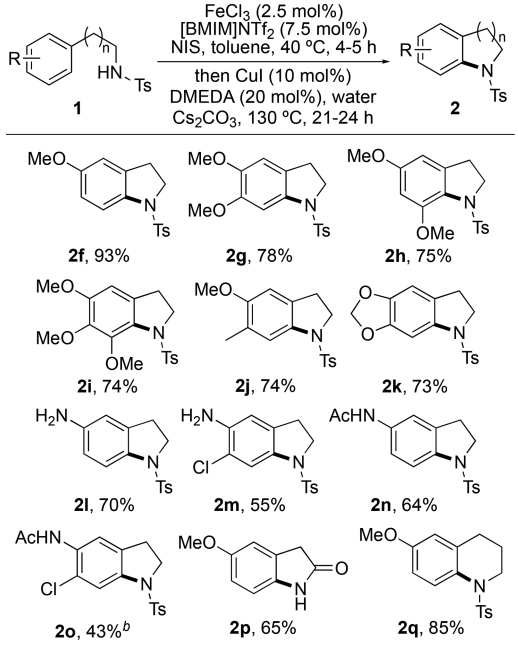
Having identified optimized conditions and the most efficient *N*-nucleophile, the scope of the one-pot activation and cyclization process was explored for the preparation of indolines (Scheme 2). Using a range of *N*-tosyl ethylamine

Scheme 1. One-Pot Activation and Cyclization of *N*-Protected 3-Methoxyphenylethylamines 1[a]



[a]Isolated yields are shown.

Scheme 2. One-Pot Activation and Cyclization for the Synthesis of *N*-Heterocycles[a]



[a]Isolated yields are shown. [b]The one-pot process was performed via the bromide intermediate using NBS for the activation step.

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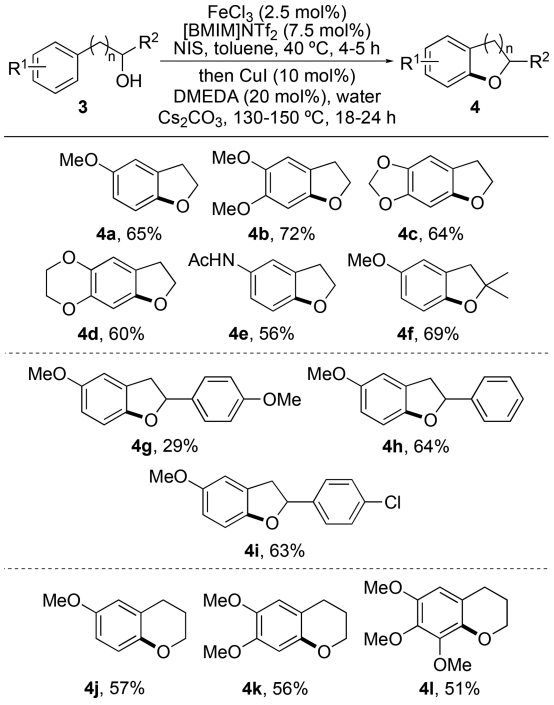
substituted anisoles, anilines, and acetanilides gave the corresponding indolines **2f**–**2o** as single regioisomers, in 43–93% yields.[16] As expected, substrates with multiple activating groups were converted to the indolines in shorter overall reaction times. Interestingly, phenylethylamine **1o** containing *N*-acetyl and chlorine substituents failed to undergo the iron(III)-catalyzed iodination even at 70 °C. Instead, activation was achieved by bromination using *N*-bromosuccinimide (NBS) at 40 °C. Completion of the one-pot process gave indoline **2o** in 43% yield. Access to other benzannulated heterocycles was also achieved using the one-pot process. Iron(III)-catalyzed iodination and copper(I)-catalyzed cyclization of 3-methoxyphenylacetamide (**1p**) gave 2-oxindole **2p** in 65% yield, while an *N*-tosyl propylamine substituted anisole led to the corresponding tetrahydroquinoline **2q** in 85% yield.[17]

The use of palladium-catalyzed C–H activation in the presence of phenyliodonium diacetate, followed by C–O cyclization for the synthesis of dihydrobenzofurans, can be done using tertiary[11a] or secondary benzylic alcohol nucleophiles.[11b] However, the general use of substrates bearing primary or secondary hydroxy groups for this process are problematic due to competitive oxidation.[12] Mild oxidative conditions such as those reported by the Zakarian group are required for general access to dihydrobenzofurans (Figure 1c).[12] Following the successful application of the one-pot iron(III)-catalyzed activation and copper(I)-catalyzed cyclization for the synthesis of *N*-heterocycles, we were interested to discover whether the mild oxidative conditions for this two-step process could also be applied for the preparation of dihydrobenzofurans. The transformation was initially attempted using 3-methoxyphenylethan-2′-ol (**3a**) for the synthesis of 2,3-dihydro-5-methoxybenzofuran (**4a**) (Scheme 3). While the standard iodination conditions could be used, a slightly higher temperature (150 °C) was required for complete conversion to the cyclized dihydrobenzofuran. This gave **4a** in 65% yield. The scope of this process was then explored using a range of substrates with various aryl activating groups and primary, secondary, or tertiary alcohol nucleophiles (**3a**–**3i**). In general, the one-pot processes were performed under the standard conditions developed for the *N*-heterocycles, giving the corresponding dihydrobenzofurans as single regioisomers in 56–72% yields. It should be noted that while other one-pot methods have had problems with overoxidation and the generation of benzofuran byproducts, especially with electron-rich substrates,[11b] analogous dihydrobenzofurans produced in this study (e.g., **4b**–**4d**) were formed cleanly as single products. The only limitation was found during the synthesis of natural product corsifuran A (**4g**).[18] Substrate **3g**, which contains two activated aryl rings, gave a mixture of products during the iodination step, resulting in the isolation of corsifuran A (**4g**) in only 29% yield.[19] However, using secondary benzylic alcohols with less electron-rich aryl rings (e.g., **3h** and **3i**) allowed selective iodination of the 3-methoxyphenyl moiety resulting in the synthesis of dihydrobenzofurans **4h** and **4i** in 64% and 63% yields, respectively. This approach was also effective for the one-pot synthesis of dihydrobenzopyrans. Application of (3-methoxyphenyl)-propan-3′-ol (**3j**) to the one-pot iron(III)-catalyzed activation and copper(I)-catalyzed cyclization gave dihydrobenzopyran **4j** as the sole product in 57% yield. Similar results were also obtained for dihydrobenzopyrans **4k** and **4l**.

To further explore the functional group tolerance of the one-pot process and illustrate its application for natural product synthesis, the method was investigated as a key step for the total synthesis of (+)-obtusafuran (**10**). The neolignan (+)-obtusafuran was first isolated from the heartwood of *Dalbergia retusa*[20] and more recently from several other *Dalbergia* species.[21−23] As well as possessing antiplasmodial activity,[21] (+)-obtusafuran has been shown to have anticarcinogenic activity as a potent inducer of the carcinogen-detoxifying enzyme, quinone reductase.[24] Racemic obtusafuran has been prepared by a thermal rearrangement of the neoflavanoid, obtusaquinol,[25] while the only asymmetric synthesis of (+)-obtusafuran was reported by Chen and Weisel, who used an enantioselective hydrogenation to produce a chiral alcohol that was then subjected to an S_NAr reaction to form the furan ring.[26] Our strategy involved the synthesis of α-methyl phenyl ketone **7** (Scheme 4) and the application of this to a Merck-type enantioselective hydrogenation involving a base-mediated dynamic kinetic resolution process.[27,28] The resulting secondary benzylic alcohol **8** would then be used in the one-pot iron(III)-catalyzed iodination and copper(I)-catalyzed cyclization to complete the synthesis of the dihydrobenzofuran skeleton. Initially, Weinreb amide **6** was prepared in two steps from phenylacetic acid **5**, by coupling with *N*,*O*-dimethylhydroxylamine using EDCI and HOBt, followed by TBDMS protection of the phenol under standard conditions. Reaction of **6** with phenylmagnesium bromide and then α-alkylation with LiHMDS and methyl iodide gave key intermediate **7** in good overall yield. This was then subjected to the Merck enantioselective hydrogenation using the commercially available Noyori-type chiral catalyst, $RuCl_2$[(*S*)-DM-Segphos][(*S*)-DAIPEN].[27−29] On screening various conditions and catalyst loadings, the best results were achieved by hydrogenation at 10 bar of pressure, using 2 mol % of the Ru(II)-catalyst. This gave secondary alcohol **8** as a single

Scheme 3. One-Pot Activation and Cyclization for the Synthesis of *O*-Heterocycles[a]



[a]Isolated yields are shown.

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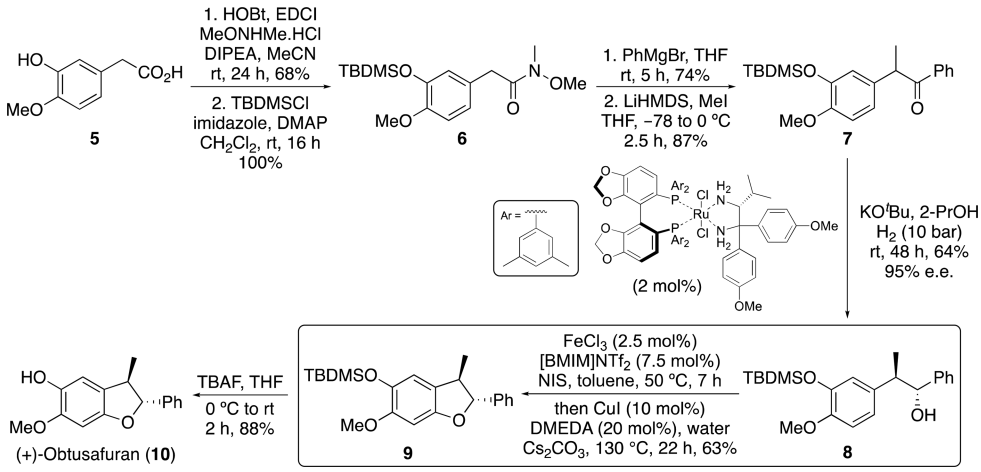
Scheme 4. Total Synthesis of (+)-Obtusafuran (10)[a]

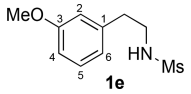


[a]Isolated yields are shown.

diastereomer, in 95% enantiomeric excess and 64% yield.[30] Our one-pot process was then investigated for the final key step. Activation of the aryl ring using the iron(III)-catalyzed iodination required a slightly higher temperature (50 °C) and longer reaction time (7 h) than the more simple substrates. Following this step, the standard conditions of the copper(I)-catalyzed cyclization were then used to complete the one-pot process, which gave dihydrobenzofuran **9** in 63% yield. Despite using a substrate with a highly activated aryl ring and a secondary alcohol, no byproducts from overiodination or oxidation were observed at either stage of the one-pot process. Finally, TBAF mediated removal of the silyl protecting group completed the eight-step synthesis of (+)-obtusafuran (**10**) in 16% overall yield. The spectroscopic data and optical rotation of **10** were entirely consistent with literature data.[20b,26]

Iron(III)-catalyzed activation of the *N*-protected 2-phenylethylamines and phenylethan-2′-ols gave the *para*-iodinated isomers as the sole product. As no reaction was observed at the other activated positions, including the most sterically accessible *ortho*-position, DFT calculations were used to explore electronic reasons for this reactivity.[31] The reactivities of different sites toward electrophilic or nucleophilic attack may be assessed using a computed descriptor such as partial (atomic) charge. In this study, the Hirshfeld partitioning scheme was used.[32] The Hirshfeld charges calculated for the (unsubstituted) aromatic carbons of *N*-mesyl protected 2-phenylethylamine **1e** single out C-5 as the least preferred site for electrophilic attack, but cannot distinguish which of C-2, C-4, or C-6 would be the most preferred site (Table 1, entry 1). A more refined and powerful reactivity descriptor is provided by the Fukui functions.[33,34] The electrophilic Fukui function $f^-(\boldsymbol{r})$ has more positive values at points in space where it is energetically favorable to remove electrons (see Supporting Information for background and derivations); that is, $f^-(\boldsymbol{r})$ identifies sites favored for electrophilic attack. If the reactivity is entirely controlled by the frontier orbitals, $f^-(\boldsymbol{r})$ is well approximated by the density of the HOMO. From Figure 2, it is evident that the most positive region of $f^-(\boldsymbol{r})$, and hence the most favorable site for electrophilic attack of **1e**, is located around C-6. More specifically, the p_z atomic orbital on C-6 makes the largest contribution to the HOMO. By contracting the continuous Fukui functions to distinct sites (e.g., atoms), "condensed" Fukui reactivity indices are obtained; a large

Table 1. Reactivity Descriptors Computed for the Aromatic Carbons of Methoxyphenylethylamine 1e[a]



1e

entry	reactivity descriptors[b]	C-2	C-4	C-5	C-6
1	q_H/e	−0.065	−0.071	−0.042	−0.065
2	$f^-(q_H)$	0.082	0.078	0.065	0.140
3	f^-(HOMO)	12	10	8	22
4	$\Delta f(q_H)$	0.045	0.019	0.068	−0.088
5	Δf(HOMO)	7	4	12	−15

[a]M06-2X/def2-TZVP/PCM(toluene). [b]q_H is the Hirshfeld charge (in units of the elementary charge, e). $f^-(q_H)$ and $\Delta f(q_H)$ are the condensed electrophilic Fukui function and the condensed "dual descriptor", respectively, calculated from Hirshfeld charges. f^-(HOMO) and Δf(HOMO) are the same descriptors but calculated from Hirshfeld-atomic contributions to the HOMO (expressed in %).

(positive) electrophilicity index f^- indicates a favored site for electrophilic attack. Using frontier-orbital terminology, f^- for a particular atom can be identified with the contribution of that atom to the HOMO. f^- values for the aromatic carbons in **1e** are presented in Table 1 (entries 2 and 3). The quantitative reactivity analysis using atomic Fukui indices thus clearly identifies C-6 as the most preferred site for electrophilic attack in this case, in agreement with experiment. C-2 and C-4 have significantly diminished, nearly equal reactivity; C-5 is predicted to be least reactive. Further analysis can be performed using a "dual descriptor" Δf, which combines the separate electrophilic and nucleophilic Fukui functions into one descriptor.[35] More positive values of Δf indicate sites for nucleophilic attack; more negative values indicate sites for electrophilic attack. As can be seen from Table 1 (entries 4 and 5), the analysis based on Δf values fully confirms the regioselectivity observed for activation of the substrates in this study.

CONCLUSIONS

In summary, a one-pot, two-step method involving iron(III)-catalyzed aryl ring activation and copper(I)-catalyzed C−N or C−O bond forming cyclization has been developed for the general synthesis of valuable *N*- and *O*-heterocyclic scaffolds.

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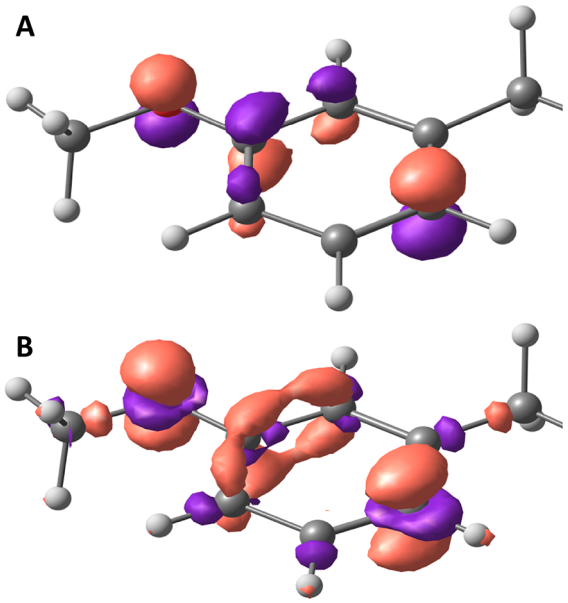

Figure 2. Isosurface plots of (A) the HOMO and (B) the electrophilic Fukui function $f^{-}(r)$ for **1e**. The aminoalkyl part is omitted, as its contribution to either function is negligible. Positive values are colored in orange, and negative values, in purple. Isosurface values: 0.006 au for $f^{-}(r)$, 0.1 au for the HOMO.

Following DFT calculations, which showed the molecular orbital basis for the highly regioselective halogenation step, the novel, one-pot method was applied to the efficient synthesis of indolines and dihydrobenzofurans, as well as six-membered analogues. This one-pot approach does not require prefunctionalization of the substrate as with the traditional Buchwald–Hartwig and Ullmann-type intramolecular couplings, and unlike the established palladium-catalyzed dehydrogenative processes, this method has no issues with overiodination or oxidation and could be applied to substrates with highly activated aryl ring systems and with primary and secondary alcohols. This was exemplified by the use of this one-pot process as the key step for the total synthesis of the neolignan natural product, (+)-obtusafuran. We expect this simple and effective approach to find utilization in the preparation of other heterocyclic scaffolds and for application in the synthesis of natural products and medicinal chemistry targets. Investigation of further applications of the one-pot process is currently underway.

EXPERIMENTAL SECTION

All reagents and starting materials were obtained from commercial sources and used as received unless otherwise stated. Dry solvents were purified using a solvent purification system. Brine refers to a saturated solution of sodium chloride. All reactions were performed in oven-dried glassware under an atmosphere of argon unless otherwise stated. Flash column chromatography was carried out using silica gel (40–63 μm) and neutral aluminum oxide (50–200 μm). Aluminum-backed plates precoated with silica gel 60 (UV_{254}) were used for thin layer chromatography and were visualized under ultraviolet light and by staining with $KMnO_4$ or ninhydrin. ^{1}H NMR spectra were recorded on an NMR spectrometer at 400 or 500 MHz, and data are reported as follows: chemical shift in ppm relative to tetramethylsilane or the solvent as the internal standard ($CDCl_3$, δ 7.26 ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or overlap of nonequivalent resonances, integration). ^{13}C{^{1}H} NMR spectra were recorded on an NMR spectrometer at 101 or 126 MHz, and data are reported as follows: chemical shift in ppm relative to tetramethylsilane or the solvent as an internal standard ($CDCl_3$, δ 77.0 ppm), multiplicity with respect to hydrogen (deduced from DEPT experiments, C, CH, CH_2 or CH_3). IR spectra were recorded on an FTIR spectrometer; wavenumbers are indicated in cm^{-1}. Mass spectra were recorded using electron impact or electrospray techniques. HRMS spectra were recorded using a dual-focusing magnetic analyzer mass spectrometer. Melting points are uncorrected. Optical rotations were determined as solutions irradiating with the sodium D line (λ = 589 nm) using a polarimeter. $[\alpha]_D$ values are given in units 10^{-1} deg cm^2 g^{-1}. Chiral HPLC methods were calibrated with the corresponding racemic mixtures.

3-Methoxy-1-[(*E*)-2′-nitrovinyl]benzene.[36] To a solution of *m*-anisaldehyde (0.890 mL, 7.30 mmol) in toluene (30 mL) were added nitromethane (2.00 mL, 37.0 mmol) and ammonium acetate (0.560 g, 7.30 mmol). The resulting solution was heated under reflux for 18 h. The reaction mixture was washed with water (2 × 30 mL), followed by brine (2 × 30 mL). Purification by flash column chromatography (dichloromethane) gave 3-methoxy-1-[(*E*)-2′-nitrovinyl]benzene (1.21 g, 97%) as a yellow solid. Mp 91–92 °C (lit.[36] 89–91 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85 (s, 3H), 7.02–7.08 (m, 2H), 7.14 (d, J = 7.6 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 7.57 (d, J = 13.6 Hz, 1H), 7.97 (d, J = 13.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 55.4 (CH_3), 114.0 (CH), 118.0 (CH), 121.7 (CH), 130.4 (CH), 131.4 (C), 137.4 (CH), 139.0 (CH), 160.2 (C); MS (EI) m/z 179 (M^+, 100), 136 (82), 135 (72), 84 (86), 77 (50).

3,4-Dimethoxy-1-[(*E*)-2′-nitrovinyl]benzene.[37] 3,4-Dimethoxy-1-[(*E*)-2′-nitrovinyl]benzene was synthesized as described for 3-methoxy-1-[(*E*)-2′-nitrovinyl]benzene using 3,4-dimethoxybenzaldehyde (1.00 g, 6.00 mmol). Purification by flash column chromatography (dichloromethane) gave 3,4-dimethoxy-1-[(*E*)-2′-nitrovinyl]benzene (1.04 g, 83%) as a yellow solid. Mp 134–136 °C (lit.[37] 135–137 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.93 (s, 3H), 3.95 (s, 3H), 6.91 (d, J = 8.3 Hz, 1H), 7.01 (d, J = 1.7 Hz, 1H), 7.18 (dd, J = 8.3, 1.7 Hz, 1H), 7.53 (d, J = 13.6 Hz, 1H), 7.96 (d, J = 13.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 56.0 (CH_3), 56.1 (CH_3), 110.3 (CH), 111.4 (CH), 122.8 (C), 124.6 (CH), 135.2 (CH), 139.3 (CH), 149.6 (C), 152.9 (C); MS (ESI) m/z 232 (M + Na^+, 100).

3,5-Dimethoxy-1-[(*E*)-2′-nitrovinyl]benzene.[38] 3,5-Dimethoxy-1-[(*E*)-2′-nitrovinyl]benzene was synthesized as described for 3-methoxy-1-[(*E*)-2′-nitrovinyl]benzene using 3,5-dimethoxybenzaldehyde (0.350 g, 2.10 mmol). The residue was recrystallized from diethyl ether which gave 3,5-dimethoxy-1-[(*E*)-2′-nitrovinyl]-benzene (0.357 g, 81%) as a yellow solid. Mp 81–83 °C (lit.[38] 78 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83 (s, 6H), 6.59 (t, J = 2.2 Hz, 1H), 6.66 (d, J = 2.2 Hz, 2H), 7.54 (d, J = 13.6 Hz, 1H), 7.92 (d, J = 13.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 55.5 (CH_3), 55.6 (CH_3), 102.8 (CH), 104.2 (CH), 107.0 (CH), 107.6 (CH), 133.4 (CH), 139.2 (C), 160.7 (C), 161.3 (C); MS (EI) m/z 209 (M^+, 100), 189 (48), 165 (90), 135 (34), 84 (98).

1-[(*E*)-2′-Nitrovinyl]-3,4,5-trimethoxybenzene.[37] 1-[(*E*)-2′-Nitrovinyl]-3,4,5-trimethoxybenzene was synthesized as described for 3-methoxy-1-[(*E*)-2′-nitrovinyl]benzene using 3,4,5-trimethoxybenzaldehyde (1.00 g, 6.00 mmol). The residue was recrystallized from hexane, which gave 1-[(*E*)-2′-nitrovinyl]-3,4,5-trimethoxybenzene (1.14 g, 94%) as a yellow solid. Mp 119–121 °C (lit.[37] 122–124 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.91 (s, 6H), 3.92 (s, 3H), 6.76 (s, 2H), 7.52 (d, J = 13.6 Hz, 1H), 7.94 (d, J = 13.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 56.3 (2 × CH_3), 61.1 (CH_3), 106.5 (2 × CH), 125.3 (C), 136.4 (CH), 139.3 (CH), 141.8 (C), 153.7 (2 × C); MS (ESI) m/z 262 (M + Na^+, 100).

3-Methoxy-4-methylbenzaldehyde.[39] To a stirred solution of lithium aluminum hydride (0.425 g, 11.1 mmol) in dry tetrahydrofuran (20 mL) was added a solution of methyl 3-methoxy-4-methylbenzoate (1.00 g, 5.55 mmol) in dry tetrahydrofuran (10 mL) dropwise at 0 °C. The resulting suspension was warmed to room temperature and stirred for 4 h after which, the solution was cooled to 0 °C and diluted with tetrahydrofuran (20 mL). Water (0.5 mL) was added slowly followed by 15% aqueous sodium hydroxide solution (0.5 mL) and water (1.5 mL). The resulting solution was warmed to room temperature, and magnesium sulfate (0.50 g) was

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added and stirred for 0.5 h. The suspension was filtered, and the filtrate was concentrated *in vacuo* to give 3-methoxy-4-methylbenzyl alcohol (0.767 g, 91%) as a colorless oil which was used without further purification. To a stirred solution of 3-methoxy-4-methylbenzyl alcohol (0.737 g, 4.85 mmol) in chloroform (25 mL) was added manganese dioxide (4.22 g, 48.5 mmol). The resulting suspension was stirred at room temperature for 18 h. The crude reaction mixture was filtered through Celite and concentrated *in vacuo* to give 3-methoxy-4-methylbenzaldehyde (0.621 g, 75%) as a white solid. Mp 34−36 °C (lit.[39] 39−40 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.29 (s, 3H), 3.90 (s, 3H), 7.29 (d, J = 7.5 Hz, 1H), 7.34 (d, J = 1.4 Hz, 1H), 7.36 (dd, J = 7.5, 1.4 Hz, 1H), 9.93 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.9 (CH_3), 55.5 (CH_3), 107.9 (CH), 124.5 (CH), 130.9 (C), 134.9 (CH), 135.9 (C), 158.3 (C), 192.0 (CH); MS (EI) m/z 150 (M^+, 100), 121 (19), 91 (28), 84 (21).

3-Methoxy-4-methyl-1-[(*E*)-2′-nitrovinyl]benzene. 3-Methoxy-4-methyl-1-[(*E*)-2′-nitrovinyl]benzene was synthesized as described for 3-methoxy-1-[(*E*)-2′-nitrovinyl]benzene using 3-methoxy-4-methylbenzaldehyde (0.624 g, 4.16 mmol). The residue was recrystallized from hexane which gave 3-methoxy-4-methyl-1-[(*E*)-2′-nitrovinyl]benzene (0.585 g, 73%) as a yellow solid. Mp 142−143 °C; IR (neat) 3119, 2945, 1629, 1602, 1573, 1494, 1414, 1343, 1328, 1248, 1159, 1035, 976, 814 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.26 (s, 3H), 3.87 (s, 3H), 6.92 (s, 1H), 7.06 (d, J = 7.6 Hz, 1H), 7.19 (d, J = 7.6 Hz, 1H), 7.57 (d, J = 13.6 Hz, 1H), 7.97 (d, J = 13.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.6 (CH_3), 55.4 (CH_3), 109.3 (CH), 122.2 (CH), 128.8 (C), 131.4 (CH), 132.4 (C), 136.3 (CH), 139.6 (CH), 158.3 (C); MS (ESI) m/z 216 (M + Na^+, 100); HRMS (ESI) calcd for $C_{10}H_{11}NNaO_3$ (M + Na^+) 216.0631, found 216.0626.

3,4-Methylenedioxy-1-[(*E*)-2′-nitrovinyl]benzene.[40] 3,4-Methylenedioxy-1-[(*E*)-2′-nitrovinyl]benzene was synthesized as described for 3-methoxy-1-[(*E*)-2′-nitrovinyl]benzene using piperonal (1.00 g, 6.00 mmol). The residue was recrystallized from hexane which gave 3,4-methylenedioxy-1-[(*E*)-2′-nitrovinyl]benzene (1.03 g, 80%) as a yellow solid. Mp 142−143 °C (lit.[40] 148 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.06 (s, 2H), 6.87 (d, J = 8.0 Hz, 1H), 7.00 (d, J = 1.8 Hz, 1H), 7.08 (dd, J = 8.0, 1.8 Hz, 1H), 7.47 (d, J = 13.6 Hz, 1H), 7.92 (d, J = 13.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 102.1 (CH_2), 107.0 (CH), 109.1 (CH), 124.2 (CH), 126.6 (CH), 135.5 (C), 139.1 (CH), 148.8 (C), 151.4 (C); MS (EI) m/z 193 (M^+, 100), 146 (98), 89 (65), 84 (51), 63 (44).

3-Nitro-1-[(*E*)-2′-nitrovinyl]benzene.[41] 3-Nitro-1-[(*E*)-2′-nitrovinyl]benzene was synthesized as described for 3-methoxy-1-[(*E*)-2′-nitrovinyl]benzene using 3-nitrobenzaldehyde (1.00 g, 6.00 mmol). Purification by flash column chromatography (petroleum ether/ethyl acetate, 9:1) gave 3-nitro-1-[(*E*)-2′-nitrovinyl]benzene (0.420 g, 31%) as a yellow solid. Mp 119−121 °C (lit.[41] 125−126 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 13.7 Hz, 1H), 7.69 (t, J = 8.0 Hz, 1H), 7.88 (dt, J = 8.0, 1.6 Hz, 1H), 8.05 (d, J = 13.7 Hz, 1H), 8.35 (dt, J = 8.0, 1.6 Hz, 1H), 8.43 (t, J = 1.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 123.5 (CH), 126.2 (CH), 130.6 (CH), 131.9 (C), 134.4 (CH), 136.2 (CH), 139.3 (CH), 148.9 (C); MS (EI) m/z 194 (M^+, 100), 147 (48), 118 (38), 102 (100), 84 (82), 76 (36).

4-Chloro-3-nitro-1-[(*E*)-2′-nitrovinyl]benzene. 4-Chloro-3-nitro-1-[(*E*)-2′-nitrovinyl]benzene was synthesized as described for 3-methoxy-1-[(*E*)-2′-nitrovinyl]benzene using 4-chloro-3-nitrobenzaldehyde (1.00 g, 6.00 mmol). Purification by flash column chromatography (petroleum ether/ethyl acetate, 7:3) gave 4-chloro-3-nitro-1-[(*E*)-2′-nitrovinyl]benzene (0.620 g, 26%) as a yellow solid. Mp 142−143 °C; IR (neat) 3109, 2945, 2361, 1605, 1540, 1342, 1049, 833 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 13.7 Hz, 1H), 7.66−7.72 (m, 2H), 7.96 (d, J = 13.7 Hz, 1H), 8.06 (d, J = 1.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 125.6 (CH), 130.1 (C), 130.4 (C), 132.6 (CH), 133.2 (CH), 133.8 (C), 135.1 (CH), 139.4 (CH); MS (EI) m/z 228 (M^+, 40), 181 (100), 152 (38), 136 (95), 115 (38), 101 (48), 89 (41), 75 (54); HRMS (EI) calcd for $C_8H_5{}^{35}ClN_2O_4$ (M^+) 227.9938, found 227.9929.

1′-(3-Methoxyphenyl)ethyl-2′-amine.[42] To a suspension of sodium borohydride (0.180 g, 4.80 mmol) in dry tetrahydrofuran (10 mL) was added boron trifluoride diethyl etherate (0.750 mL, 6.00 mmol) dropwise at 0 °C, and the contents were stirred at room temperature for 0.25 h. A solution of 3-methoxy-1-[(*E*)-2′-nitrovinyl]-benzene in tetrahydrofuran (3.0 mL) was added dropwise into the reaction mixture which was then heated under reflux for 6.5 h. After cooling to room temperature, the reaction was quenched by the slow addition of ice water (12 mL). The reaction mixture was acidified with 1 M aqueous hydrochloric acid (12 mL) and heated to 85 °C for 2 h. The reaction mixture was cooled to room temperature and washed with dichloromethane (2 × 10 mL), then 1 M aqueous sodium hydroxide was added until basic (ca. pH 12). The aqueous layer was extracted with dichloromethane (3 × 20 mL), dried ($MgSO_4$), and concentrated *in vacuo* to give 1′-(3-methoxyphenyl)-ethyl-2′-amine (0.140 g, 92%) as a yellow oil which was used without further purification. Spectroscopic data were consistent with the literature.[42] ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.99 (br s, 2H), 2.72 (t, J = 6.8 Hz, 2H), 2.96 (t, J = 6.8 Hz, 2H), 3.78 (s, 3H), 6.73−6.80 (m, 3H), 7.21 (t, J = 7.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 39.0 (CH_2), 43.0 (CH_2), 55.2 (CH_3), 111.6 (CH), 114.6 (CH), 121.2 (CH), 129.5 (CH), 140.9 (C), 159.8 (C); MS (ESI) m/z 152 (M + H^+, 100).

***N*-[(3-Methoxyphenyl)ethyl]benzamide (1a).**[43] 1′-(3-Methoxyphenyl)ethyl-2′-amine (0.050 g, 0.33 mmol) was dissolved in dry dichloromethane (5 mL), and triethylamine (0.070 mL, 0.50 mmol) was added. The reaction mixture was cooled to 0 °C, and benzoyl chloride (0.039 mL, 0.33 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 0.5 h, warmed to room temperature, and stirred for 20 h. The reaction mixture was diluted with dichloromethane (10 mL), washed with 1 M aqueous hydrochloric acid (10 mL) and then brine (10 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/ethyl acetate, 7:3) gave *N*-[(3-methoxyphenyl)ethyl]benzamide (**1a**) (0.077 g, 91% yield) as a white solid. Mp 64−66 °C (lit.[43] 67 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.91 (t, J = 6.9 Hz, 2H), 3.71 (q, J = 6.9 Hz, 2H), 3.78 (s, 3H), 6.24 (br s, 1H), 6.76−6.84 (m, 3H), 7.20−7.26 (m, 1H), 7.36−7.42 (m, 2H), 7.44−7.50 (m, 1H), 7.67−7.72 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 35.8 (CH_2), 41.1 (CH_2), 55.2 (CH_3), 112.1 (CH), 114.4 (CH), 121.1 (CH), 126.8 (2 × CH), 128.6 (2 × CH), 129.7 (CH), 131.4 (CH), 134.7 (C), 140.5 (C), 159.9 (C), 167.5 (C); MS (EI) m/z 255 (M^+, 25), 134 (100), 105 (62), 77 (25).

***N*-[(3-Methoxyphenyl)ethyl]acetamide (1b).**[44] 1′-(3-Methoxyphenyl)ethyl-2′-amine (0.050 g, 0.33 mmol) was dissolved in dry dichloromethane (10 mL), and acetic anhydride (0.038 mL, 0.40 mmol) was added while stirring. The reaction mixture was stirred at room temperature for 20 h. The reaction mixture was diluted with dichloromethane (15 mL), washed with 1 M aqueous sodium carbonate (15 mL) and then brine (15 mL), dried ($MgSO_4$), and concentrated *in vacuo* to give *N*-[(3-methoxyphenyl)ethyl]acetamide (**1b**) (0.060 g, 94%) as a yellow oil which was used without further purification. Spectroscopic data were consistent with the literature.[44] ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.94 (s, 3H), 2.79 (t, J = 6.8 Hz, 2H), 3.51 (q, J = 6.8 Hz, 2H), 3.80 (s, 3H), 5.44 (br s, 1H), 6.72−6.82 (m, 3H), 7.23 (t, J = 7.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 23.4 (CH_3), 35.7 (CH_2), 40.5 (CH_2), 50.2 (CH_3), 111.9 (CH), 114.5 (CH), 121.1 (CH), 129.7 (CH), 140.5 (C), 159.9 (C), 170.0 (C); MS (ESI) m/z 216 (M + Na^+, 100).

Benzyl *N*-[(3-Methoxyphenyl)ethyl]carbamate (1c).[45] 1′-(3-Methoxyphenyl)ethyl-2′-amine (0.100 g, 0.660 mmol) was dissolved in dry dichloromethane (10 mL), and triethylamine (0.142 mL, 1.00 mmol) was added while stirring. The reaction mixture was cooled to 0 °C, and benzyl chloroformate (0.114 mL, 0.800 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 0.5 h, warmed to room temperature, and stirred for 5 h. The reaction mixture was diluted with dichloromethane (15 mL), washed with 1 M aqueous hydrochloric acid (15 mL) and then brine (15 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/ethyl acetate, 4:1) gave benzyl *N*-[(3-methoxyphenyl)ethyl]carbamate (**1c**) (0.134 g, 72%) as a colorless oil. Spectroscopic data were consistent with the literature.[45] ^{1}H NMR

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(400 MHz, $CDCl_3$) δ 2.79 (t, J = 6.6 Hz, 2H), 3.45 (q, J = 6.6 Hz, 2H), 3.78 (s, 3H), 4.76 (br s, 1H), 5.09 (s, 2H), 6.69−6.81 (m, 3H), 7.21 (t, J = 7.9 Hz, 1H), 7.28−7.38 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 36.1 (CH_2), 42.1 (CH_2), 55.2 (CH_3), 66.7 (CH_2), 111.9 (CH), 114.5 (CH), 121.1 (CH), 128.1 (2 × CH), 128.5 (2 × CH), 128.6 (CH), 129.6 (CH), 136.6 (C), 140.3 (C), 156.3 (C), 159.8 (C); MS (ESI) m/z 308 (M + Na^+, 100).

***tert*-Butyl-*N*-[(3-methoxyphenyl)ethyl]carbamate (1d).**[46] 1′-(3-Methoxyphenyl)ethyl-2′-amine (0.200 g, 1.32 mmol) was dissolved in dry dichloromethane (10 mL), and triethylamine (0.370 mL, 2.64 mmol) was added with stirring. Di-*tert*-butyl dicarbonate (0.870 g, 3.97 mmol) was added, and the resulting solution was stirred at room temperature for 16 h. The reaction mixture was concentrated *in vacuo*, and the residue was purified by column chromatography (petroleum ether/ethyl acetate, 4:1) to give *tert*-butyl-*N*-[(3-methoxyphenyl)ethyl]carbamate (**1d**) (0.253 g, 76%) as a yellow oil. Spectroscopic data were consistent with the literature.[46] ^{1}H NMR (400 MHz, $CHCl_3$) δ 1.44 (s, 9H), 2.77 (t, J = 6.9 Hz, 2H), 3.38 (q, J = 6.9 Hz, 2H), 3.80 (s, 3H), 4.55 (br s, 1H), 6.72−6.89 (m, 3H), 7.22 (t, J = 7.9 Hz, 1H); ^{13}C NMR (101 MHz, $CHCl_3$) δ 28.4 (3 × CH_3), 36.3 (CH_2), 41.7 (CH_2), 55.2 (CH_3), 79.2 (C), 111.8 (CH), 114.5 (CH), 121.1 (CH), 129.6 (CH), 140.6 (C), 155.9 (C), 159.8 (C); MS (EI) m/z 251 (M^+, 12), 195 (32), 134 (100), 121 (48), 91 (24).

***N*-[(3-Methoxyphenyl)ethyl]methanesulfonamide (1e).** 1′-(3-Methoxyphenyl)ethyl-2′-amine (0.198 g, 1.32 mmol) was dissolved in dry dichloromethane (10 mL), and triethylamine (0.370 mL, 2.64 mmol) was added with stirring. The reaction mixture was cooled to 0 °C, and methanesulfonyl chloride (0.120 mL, 1.59 mmol) was added. The reaction mixture was stirred at 0 °C for 0.5 h, warmed to room temperature, and stirred for 4 h. The reaction mixture was diluted with dichloromethane (15 mL), washed with 1 M aqueous hydrochloric acid (15 mL), and brine (15 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/ethyl acetate, 1:1) gave *N*-[(3-methoxyphenyl)ethyl]methanesulfonamide (**1e**) (0.184 g, 60%) as a yellow oil. IR (neat) 3287, 2936, 1586, 1489, 1312, 1258, 1146, 783 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.83−2.88 (m, 5H), 3.41 (q, J = 6.4 Hz, 2H), 3.81 (s, 3H), 4.24 (br s, 1H), 6.74−6.82 (m, 3H), 7.25 (t, J = 7.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 36.5 (CH_2), 40.4 (CH_3), 44.3 (CH_2), 55.2 (CH_3), 112.2 (CH), 114.7 (CH), 121.1 (CH), 129.9 (CH), 139.3 (C), 160.0 (C); MS (EI) m/z 229 (M^+, 35), 134 (100), 122 (76), 108 (62), 91 (25); HRMS (EI) calcd for $C_{10}H_{15}NO_3S$ (M^+) 229.0773, found 229.0780.

***N*-[(3-Methoxyphenyl)ethyl]-4′′-methylbenzenesulfonamide (1f).**[47] 1′-(3-Methoxyphenyl)ethyl-2′-amine (0.200 g, 1.32 mmol) was dissolved in dry dichloromethane (10 mL) and triethylamine (0.280 mL, 1.98 mmol) was added with stirring. The reaction mixture was cooled to 0 °C and *p*-toluenesulfonyl chloride (0.302 g, 1.58 mmol) was added. The reaction mixture was stirred at 0 °C for 0.5 h, warmed to room temperature and stirred for 6 h. The reaction mixture was diluted with dichloromethane (15 mL), washed with 1 M aqueous hydrochloric acid (15 mL), brine (15 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/ethyl acetate, 4:1) gave *N*-[(1-methoxyphenyl)ethyl]-4′′-methylbenzenesulfonamide (**1f**) (0.327 g, 81%) as a yellow oil. Spectroscopic data were consistent with the literature.[47] ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.45 (s, 3H), 2.75 (t, J = 6.9 Hz, 2H), 3.23 (q, J = 6.9 Hz, 2H), 3.79 (s, 3H), 4.54 (br s, 1H), 6.63 (br s, 1H), 6.69 (br d, J = 7.9 Hz, 1H), 6.78 (dd, J = 7.9, 2.5 Hz, 1H), 7.20 (t, J = 7.9 Hz, 1H), 7.31 (d, J = 8.2 Hz, 2H), 7.71 (d, J = 8.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.5 (CH_3), 35.8 (CH_2), 44.1 (CH_2), 55.1 (CH_3), 112.1 (CH), 114.4 (CH), 121.0 (CH), 127.1 (2 × CH), 129.7 (2 × CH), 129.8 (CH), 136.9 (C), 139.2 (C), 143.4 (C), 159.9 (C); MS (ESI) m/z 328 (M + Na^+, 100).

***N*-[(3,4-Dimethoxyphenyl)ethyl]-4′′-methylbenzenesulfonamide (1g).**[48] To a suspension of sodium borohydride (0.817 g, 21.6 mmol) in dry tetrahydrofuran (50 mL) was added boron trifluoride diethyl etherate (3.37 mL, 27.3 mmol) dropwise at 0 °C, and the mixture was stirred at room temperature for 0.25 h. A solution of 3,4-dimethoxy-1-[(*E*)-2′-nitrovinyl]benzene (0.950 g, 4.55 mmol) in tetrahydrofuran (15 mL) was added dropwise into the reaction mixture which was then heated under reflux for 6.5 h. After cooling to room temperature, the reaction was quenched by the slow addition of ice water (30 mL). The reaction mixture was acidified with 1 M aqueous hydrochloric acid (30 mL) and heated to 85 °C for 2 h. The reaction mixture was cooled to room temperature and washed with dichloromethane (2 × 40 mL), and then 1 M aqueous sodium hydroxide was added until basic (ca. pH 12). The aqueous layer was extracted with dichloromethane (3 × 40 mL), dried ($MgSO_4$), and concentrated *in vacuo* to give 1′-(3,4-dimethoxyphenyl)ethyl-2′-amine (0.582 g, 71%) as a yellow oil which was used without further purification. 1′-(3,4-Dimethoxyphenyl)ethyl-2′-amine (0.509 g, 2.81 mmol) was dissolved in dry dichloromethane (20 mL), and triethylamine (0.588 mL, 4.22 mmol) was added while stirring. The reaction mixture was cooled to 0 °C, and *p*-toluenesulfonyl chloride (0.643 g, 3.37 mmol) was added. The reaction mixture was stirred at 0 °C for 0.5 h, warmed to room temperature, and stirred for 6 h. The reaction mixture was diluted with dichloromethane (30 mL), washed with 1 M aqueous hydrochloric acid (30 mL) and brine (30 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/ethyl acetate, 7:3) gave *N*-[(3,4-dimethoxyphenyl)ethyl]-4′′-methylbenzenesulfonamide (**1g**) (0.716 g, 76%) as a yellow oil. Spectroscopic data were consistent with the literature.[48] ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 2.71 (t, J = 6.8 Hz, 2H), 3.19 (q, J = 6.8 Hz, 2H), 3.81 (s, 3H), 3.86 (s, 3H), 4.31 (t, J = 6.8 Hz, 1H), 6.55 (d, J = 2.0 Hz, 1H), 6.62 (dd, J = 8.1, 2.0 Hz, 1H), 6.76 (d, J = 8.1 Hz, 1H), 7.28 (d, J = 8.2 Hz, 2H), 7.67 (d, J = 8.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.5 (CH_3), 35.3 (CH_2), 44.3 (CH_2), 55.8 (CH_3), 56.0 (CH_3), 111.5 (CH), 111.8 (CH), 120.8 (CH), 127.1 (2 × CH), 129.7 (2 × CH), 130.1 (C), 136.9 (C), 143.4 (C), 148.0 (C), 149.2 (C); MS (EI) m/z 335 (M^+, 60), 184 (17), 164 (38), 151 (100), 107 (17), 91 (48).

***N*-[(3,5-Dimethoxyphenyl)ethyl]-4′′-methylbenzenesulfonamide (1h).**[49] *N*-[(3,5-Dimethoxyphenyl)ethyl]-4′′-methylbenzenesulfonamide (**1h**) was synthesized as described for *N*-[(3,4-dimethoxyphenyl)ethyl]-4′′-methylbenzenesulfonamide (**1g**) using 3,5-dimethoxy-1-[(*E*)-2′-nitrovinyl]benzene. Reduction of 3,5-dimethoxy-1-[(*E*)-2′-nitrovinyl]benzene (0.330 g, 1.58 mmol) using sodium borohydride (0.285 g, 7.51 mmol) and boron trifluoride diethyl etherate (1.17 mL, 9.48 mmol) gave 1′-(3,5-dimethoxyphenyl)ethyl-2′-amine (0.165 g, 58%) which was used without further purification. The *N*-protection step was carried out at room temperature for 18 h. Purification by flash column chromatography (petroleum ether/ethyl acetate, 4:1) gave *N*-[(3,5-dimethoxyphenyl)-ethyl]-4′′-methylbenzenesulfonamide (**1h**) (0.150 g, 50%) as a colorless oil. Spectroscopic data were consistent with the literature.[49] ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 2.69 (t, J = 6.9 Hz, 2H), 3.19 (q, J = 6.9 Hz, 2H), 3.74 (s, 6H), 4.48 (t, J = 6.9 Hz, 1H), 6.21 (d, J = 2.2 Hz, 2H), 6.31 (t, J = 2.2 Hz, 1H), 7.27 (d, J = 8.2 Hz, 2H), 7.68 (d, J = 8.2 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 21.5 (CH_3), 36.0 (CH_2), 44.0 (CH_2), 55.3 (2 × CH_3), 98.7 (CH), 106.7 (2 × CH), 127.1 (2 × CH), 129.7 (2 × CH), 136.9 (C), 140.0 (C), 143.4 (C), 161.1 (2 × C); MS (ESI) m/z 358 (M + Na^+, 100).

4′′-Methyl-*N*-[(3,4,5-trimethoxyphenyl)ethyl]benzenesulfonamide (1i).[50] 4′′-Methyl-*N*-[(3,4,5-trimethoxyphenyl)ethyl]-benzenesulfonamide (**1i**) was synthesized as described for *N*-[(3,4-dimethoxyphenyl)ethyl]-4′′-methylbenzenesulfonamide (**1g**) using 1-[(*E*)-2′-nitrovinyl]-3,4,5-trimethoxybenzene. Reduction of 1-[(*E*)-2′-nitrovinyl]-3,4,5-trimethoxybenzene (1.09 g, 4.56 mmol) using sodium borohydride (0.821 g, 21.7 mmol) and boron trifluoride diethyl etherate (3.90 mL, 27.4 mmol) gave 1′-(3,4,5-trimethoxyphenyl)ethyl-2′-amine (0.748 g, 78%) which was used without further purification. The *N*-protection step was carried out at room temperature for 6 h. Purification by flash column chromatography (petroleum ether/ethyl acetate, 3:2) gave 4′′-methyl-*N*-[(3,4,5-trimethoxyphenyl)ethyl]benzenesulfonamide (**1i**) (0.903 g, 71%) as a yellow oil. Spectroscopic data were consistent with the literature.[50] ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 2.71 (t, J = 6.8 Hz, 2H), 3.21 (q, J = 6.8 Hz, 2H), 3.80 (s, 6H), 3.81 (s, 3H), 4.48 (t, J = 6.8

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Hz, 1H), 6.28 (s, 2H), 7.28 (d, J = 8.3 Hz, 2H), 7.69 (d, J = 8.3 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.5 (CH_3), 36.1 (CH_2), 44.2 (CH_2), 56.1 (2 × CH_3), 60.8 (CH_3), 105.7 (2 × CH), 127.1 (2 × CH), 129.7 (2 × CH), 133.3 (C), 136.9 (C), 137.0 (C), 143.5 (C), 153.4 (2 × C); MS (ESI) m/z 388 (M + Na^+, 100).

***N*-[(3-Methoxy-4-methylphenyl)ethyl]-4′′-methylbenzenesulfonamide (1j).** *N*-[(3-Methoxy-4-methylphenyl)ethyl]-4′′-methylbenzenesulfonamide (**1j**) was synthesized as described for *N*-[(3,4-dimethoxyphenyl)ethyl]-4′′-methylbenzenesulfonamide (**1g**) using 3-methoxy-4-methyl-1-[(*E*)-2′-nitrovinyl]benzene. Reduction of 3-methoxy-4-methyl-1-[(*E*)-2′-nitrovinyl]benzene (0.585 g, 3.03 mmol) using sodium borohydride (0.757 g, 20.5 mmol) and boron trifluoride diethyl etherate (3.42 mL, 26.5 mmol) gave 1′-(3-methoxy-4-methylphenyl)ethyl-2′-amine (0.356 g, 71%) which was used without further purification. The *N*-protection step was carried out at room temperature for 24 h. Purification by flash column chromatography (petroleum ether/ethyl acetate, 4:1) gave *N*-[(3-methoxy-4-methylphenyl)ethyl]-4′′-methylbenzenesulfonamide (**1j**) (0.278 g, 45%) as a yellow oil. IR (neat) 3264, 2924, 1586, 1512, 1464, 1414, 1323, 1256, 1155, 1094, 814 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.17 (s, 3H), 2.42 (s, 3H), 2.72 (t, J = 6.8 Hz, 2H), 3.20 (q, J = 6.8 Hz, 2H), 3.76 (s, 3H), 4.34 (t, J = 6.8 Hz, 1H), 6.51 (d, J = 1.4 Hz, 1H), 6.51 (dd, J = 7.5, 1.4 Hz, 1H), 7.01 (d, J = 7.5 Hz, 1H), 7.27 (d, J = 8.2 Hz, 2H), 7.67 (d, J = 8.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 15.8 (CH_3), 21.5 (CH_3), 35.7 (CH_2), 44.2 (CH_2), 55.2 (CH_3), 110.4 (CH), 120.4 (CH), 125.2 (C), 127.1 (2 × CH), 129.7 (2 × CH), 130.8 (CH), 136.3 (C), 137.0 (C), 143.4 (C), 158.0 (C); MS (ESI) m/z 342 (M + Na^+, 100); HRMS (ESI) calcd for $C_{17}H_{21}NNaO_3S$ (M + Na^+) 342.1134, found 342.1125.

4′′-Methyl-*N*-[(3,4-methylenedioxyphenyl)ethyl]benzenesulfonamide (1k).[51] 4′′-Methyl-*N*-[(3,4-methylenedioxyphenyl)-ethyl]benzenesulfonamide (**1k**) was synthesized as described for *N*-[(3,4-dimethoxyphenyl)ethyl]-4′′-methylbenzenesulfonamide (**1g**) using 3,4-methylenedioxy-1-[(*E*)-2′-nitrovinyl]benzene. Reduction of 3,4-methylenedioxy-1-[(*E*)-2′-nitrovinyl]benzene (1.03 g, 5.32 mmol) using sodium borohydride (0.957 g, 25.3 mmol) and boron trifluoride diethyl etherate (3.90 mL, 31.9 mmol) gave 1′-(3,4-methylenedioxyphenyl)ethyl-2′-amine (0.587 g, 66%) which was used without further purification. The *N*-protection step was carried out at room temperature for 6 h. Purification by flash column chromatography (petroleum ether/ethyl acetate, 4:1) gave 4′′-methyl-*N*-[(3,4-methylenedioxyphenyl)ethyl]benzenesulfonamide (**1k**) (0.679 g, 76%) as a white solid. Mp 86−88 °C (lit.[51] 89−90 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 2.67 (t, J = 6.8 Hz, 2H), 3.16 (q, J = 6.8 Hz, 2H), 4.34 (br s, 1H), 5.92 (s, 2H), 6.49−6.54 (m, 2H), 6.70 (dd, J = 7.1, 1.3 Hz, 1H), 7.29 (d, J = 8.4 Hz, 2H), 7.69 (d, J = 8.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.5 (CH_3), 35.5 (CH_2), 44.3 (CH_2), 101.0 (CH_2), 108.5 (CH), 109.0 (CH), 121.8 (CH), 127.1 (2 × CH), 129.7 (2 × CH), 131.3 (C), 137.0 (C), 143.5 (C), 146.5 (C), 147.9 (C); MS (ESI) m/z 342 (M + Na^+, 100).

4′′-Methyl-*N*-[(3-nitrophenyl)ethyl]benzenesulfonamide. 4′′-Methyl-*N*-[(3-nitrophenyl)ethyl]benzenesulfonamide was synthesized as described for *N*-[(3,4-dimethoxyphenyl)ethyl]-4′′-methylbenzenesulfonamide (**1g**) using 3-nitro-1-[(*E*)-2′-nitrovinyl]benzene. Reduction of 3-nitro-1-[(*E*)-2′-nitrovinyl]benzene (0.281 g, 1.45 mmol) using sodium borohydride (0.363 g, 9.78 mmol) and boron trifluoride diethyl etherate (1.59 mL, 12.3 mmol) gave 1′-(3-nitrophenyl)ethyl-2′-amine (0.186 g, 77%) which was used without further purification. The *N*-protection step was carried out at room temperature for 6 h. Purification by flash column chromatography (petroleum ether/ethyl acetate, 1:1) gave 4′′-methyl-*N*-[(3-nitrophenyl)ethyl]benzenesulfonamide (0.142 g, 82%) as a yellow oil. IR (neat) 3285, 1597, 1526, 1348, 1325, 1155, 1094, 814 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 2.88 (t, J = 7.0 Hz, 2H), 3.25 (q, J = 7.0 Hz, 2H), 5.03 (br s, 1H), 7.27 (d, J = 7.9 Hz, 2H), 7.42 (t, J = 7.8 Hz, 1H), 7.47 (dt, J = 7.8, 1.5 Hz, 1H), 7.68 (d, J = 7.9 Hz, 2H), 7.90 (t, J = 1.5 Hz, 1H), 8.03 (dt, J = 7.8, 1.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.5 (CH_3), 35.5 (CH_2), 43.8 (CH_2), 121.8 (CH), 123.6 (CH), 127.0 (2 × CH), 129.5 (CH), 129.8 (2 × CH), 135.2 (CH), 136.7 (C), 140.0 (C), 143.7 (C), 148.3 (C); MS (ESI) m/z 343 (M + Na^+, 100); HRMS (ESI) calcd for $C_{15}H_{16}N_2NaO_4S$ (M + Na^+) 343.0723, found 343.0712.

***N*-[(4-Chloro-3-nitrophenyl)ethyl]-4′′-methylbenzenesulfonamide.** *N*-[(4-Chloro-3-nitrophenyl)ethyl]-4′′-methylbenzenesulfonamide was synthesized as described for *N*-[(3,4-dimethoxyphenyl)ethyl]-4′′-methylbenzenesulfonamide (**1g**) using 4-chloro-3-nitro-1-[(*E*)-2′-nitrovinyl]benzene. Reduction of 4-chloro-3-nitro-1-[(*E*)-2′-nitrovinyl]benzene (0.255 g, 1.12 mmol) using sodium borohydride (0.280 g, 7.55 mmol) and boron trifluoride diethyl etherate (1.23 mL, 9.52 mmol) gave 1′-(4-chloro-3-nitrophenyl)ethyl-2′-amine (0.174 g, 78%) which was used without further purification. The *N*-protection step was carried out at room temperature for 6 h. Purification by flash column chromatography (petroleum ether/ethyl acetate, 7:3) gave *N*-[(4-chloro-3-nitrophenyl)ethyl]-4′′-methylbenzenesulfonamide (0.238 g, 79%) as a yellow solid. Mp 84−86 °C; IR (neat) 3271, 2922, 2361, 1532, 1327, 1157, 1088, 810 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 2.82 (t, J = 6.8 Hz, 2H), 3.22 (q, J = 6.8 Hz, 2H), 5.13 (t, J = 6.8 Hz, 1H), 7.24−7.30 (m, 3H, 6-H), 7.38 (d, J = 8.2 Hz, 1H), 7.55 (d, J = 2.0 Hz, 1H), 7.65 (d, J = 8.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.6 (CH_3), 34.9 (CH_2), 43.6 (CH_2), 125.2 (C), 125.8 (CH), 127.0 (2 × CH), 129.8 (2 × CH), 131.9 (CH), 133.8 (CH), 136.5 (C), 138.6 (C), 143.9 (C), 147.7 (C); MS (ESI) m/z 377 (M + Na^+, 100); HRMS (ESI) calcd for $C_{15}H_{15}{}^{35}ClN_2NaO_4S$ (M + Na^+) 377.0333, found 377.0326.

***N*-[(3-Aminophenyl)ethyl]-4′′-methylbenzenesulfonamide (1l).** To a stirred solution of 4′′-methyl-*N*-[(3-nitrophenyl)ethyl]-benzenesulfonamide (0.142 g, 0.40 mmol) in ethanol (20 mL) was added tin(II) dichloride dihydrate (0.758 g, 3.36 mmol), and the resulting solution was heated under reflux for 18 h. After cooling to room temperature, the reaction mixture was diluted with saturated aqueous sodium hydrogen carbonate solution (20 mL) and extracted with dichloromethane (4 × 50 mL). The combined extracts were washed with brine (2 × 200 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/ethyl acetate, 1:1) gave *N*-[(3-aminophenyl)ethyl]-4′′-methylbenzenesulfonamide (**1l**) (0.102 g, 79%) as a white solid. Mp 80−82 °C; IR (neat) 3268, 2922, 1601, 1495, 1460, 1319, 1153, 1093, 814 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 2.66 (t, J = 6.8 Hz, 2H), 3.17 (q, J = 6.8 Hz, 2H), 3.62 (br s, 2H), 4.38 (br s, 1H), 6.39 (t, J = 1.7 Hz, 1H), 6.42−6.48 (m, 1H), 6.53 (dd, J = 7.6, 1.7 Hz, 1H), 7.04 (t, J = 7.6 Hz, 1H), 7.29 (d, J = 7.9 Hz, 2H), 7.69 (d, J = 7.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.5 (CH_3), 35.7 (CH_2), 44.1 (CH_2), 113.6 (CH), 115.3 (CH), 118.8 (CH), 127.1 (2 × CH), 129.7 (2 × CH), 129.8 (CH), 137.0 (C), 138.8 (C), 143.4 (C), 146.8 (C); MS (ESI) m/z 313 (M + Na^+, 100); HRMS (ESI) calcd for $C_{15}H_{18}N_2NaO_2S$ (M + Na^+) 313.0981, found 313.0984.

***N*-[(3-Amino-4-chlorophenyl)ethyl]-4′′-methylbenzenesulfonamide (1m).** *N*-[(3-Amino-4-chlorophenyl)ethyl]-4′′-methylbenzenesulfonamide (**1m**) was synthesized as described for *N*-[(3-aminophenyl)ethyl]-4′′-methylbenzenesulfonamide (**1l**) using 4′′-methyl-*N*-[(3-nitro-4-chlorophenyl)ethyl]benzenesulfonamide (0.278 g, 0.790 mmol). Purification by flash column chromatography (petroleum ether/ethyl acetate, 7:3) gave *N*-[(3-amino-4-chlorophenyl)ethyl]-4′′-methylbenzenesulfonamide (**1m**) (0.226 g, 89%) as a colorless oil. IR (neat) 3372, 3279, 2924, 2361, 1620, 1497, 1435, 1319, 1156, 1088, 810 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 2.62 (t, J = 6.8 Hz, 2H), 3.13 (q, J = 6.8 Hz, 2H), 4.00 (br s, 2H), 4.88 (t, J = 6.8 Hz, 1H), 6.36 (dd, J = 8.1, 2.0 Hz, 1H), 6.49 (d, J = 2.0 Hz, 1H), 7.06 (d, J = 8.1 Hz, 1H), 7.26 (d, J = 8.3 Hz, 2H), 7.67 (d, J = 8.3 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.6 (CH_3), 35.3 (CH_2), 44.0 (CH_2), 116.1 (CH), 117.7 (C), 119.2 (CH), 127.1 (2 × CH), 129.6 (CH), 129.7 (2 × CH), 136.8 (C), 137.5 (C), 143.0 (C), 143.5 (C); MS (ESI) m/z 347 (M + Na^+, 100); HRMS (ESI) calcd for $C_{15}H_{17}{}^{35}ClN_2NaO_2S$ (M + Na^+) 347.0591, found 347.0582.

***N*-[(3-Acetamidophenyl)ethyl]-4′′-methylbenzenesulfonamide (1n).** Acetic anhydride (0.110 mL, 1.17 mmol) was added to a stirred solution of *N*-[(3-aminophenyl)ethyl]-4′′-methylbenzenesulfonamide (**1l**) (0.225 g, 0.780 mmol) in dry dichloro-

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methane (10 mL) and stirred at room temperature for 16 h. The reaction mixture was washed with saturated sodium carbonate (15 mL) and brine (15 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/ethyl acetate, 3:7) gave *N*-[(3-acetamidophenyl)-ethyl]-4′′-methylbenzenesulfonamide (**1n**) (0.245 g, 95%) as a colorless oil. IR (neat) 3282, 2921, 1669, 1613, 1595, 1549, 1489, 1440, 1319, 1153, 1094, 814 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.14 (s, 3H), 2.42 (s, 3H), 2.72 (t, J = 6.8 Hz, 2H), 3.18 (q, J = 6.8 Hz, 2H), 4.69 (t, J = 6.8 Hz, 1H), 6.81 (d, J = 7.5 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 7.25−7.30 (m, 3H), 7.39 (d, J = 7.5 Hz, 1H), 7.46 (br s, 1H), 7.69 (d, J = 7.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.5 (CH_3), 24.6 (CH_3), 35.8 (CH_2), 44.1 (CH_2), 118.3 (CH), 120.2 (CH), 124.5 (CH), 127.1 (2 × CH), 129.3 (CH), 129.8 (2 × CH), 136.8 (C), 138.3 (C), 138.8 (C), 143.5 (C), 168.6 (C); MS (ESI) m/z 355 ($M + Na^+$, 100); HRMS (ESI) calcd for $C_{17}H_{20}N_2NaO_3S$ ($M + Na^+$) 355.1087, found 355.1080.

N-[(3-Acetamido-4-chlorophenyl)ethyl]-4′′-methylbenzenesulfonamide (1o). *N*-[(3-Acetamido-4-chlorophenyl)-ethyl]-4′′-methylbenzenesulfonamide (**1o**) was synthesized as described for *N*-[(3-acetamidophenyl)ethyl]-4′′-methylbenzenesulfonamide (**1n**) using *N*-[(3-amino-4-chlorophenyl)ethyl]-4′′-methylbenzenesulfonamide (**1m**) (0.109 g, 0.340 mmol). Purification by flash column chromatography (petroleum ether/ethyl acetate, 1:1) gave *N*-[(3-acetamido-4-chlorophenyl)ethyl]-4′′-methylbenzenesulfonamide (**1o**) (0.121 g, 99%) as a colorless oil. IR (neat) 3279, 2932, 2361, 1674, 1582, 1528, 1427, 1319, 1157, 1096 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.22 (s, 3H), 2.42 (s, 3H), 2.72 (t, J = 6.9 Hz, 2H), 3.19 (q, J = 6.9 Hz, 2H), 4.73 (t, J = 6.9 Hz, 1H), 6.78 (dd, J = 8.2, 1.7 Hz, 1H), 7.23 (d, J = 8.2 Hz, 1H), 7.27 (d, J = 8.2 Hz, 2H), 7.59 (br s, 1H), 7.69 (d, J = 8.2 Hz, 2H), 8.11 (br s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.5 (CH_3), 24.9 (CH_3), 35.6 (CH_2), 44.0 (CH_2), 121.0 (C), 121.8 (CH), 125.1 (CH), 127.1 (2 × CH), 129.0 (CH), 129.7 (2 × CH), 134.6 (C), 136.9 (C), 137.9 (C), 143.4 (C), 168.4 (C); MS (ESI) m/z 389 ($M + Na^+$, 100); HRMS (ESI) calcd for $C_{17}H_{19}{}^{35}ClN_2NaO_3S$ ($M + Na^+$) 389.0697, found 389.0685.

3-Methoxyphenylacetamide (1p).[52] To a stirred solution of 3-methoxyphenylacetic acid (0.500 g, 3.00 mmol) in dry dichloromethane (15 mL) was added thionyl chloride (2.63 mL, 63.0 mmol) at 0 °C. The reaction mixture was heated under reflux for 2.5 h after which the solvent was removed *in vacuo*. The residue was dissolved in tetrahydrofuran (20 mL), and 25% aqueous ammonium hydroxide (4 mL) was added slowly at 0 °C. The reaction mixture was then stirred at room temperature for 16 h. The mixture was concentrated *in vacuo*, and water (15 mL) was added. The solution was heated for 0.5 h. The suspension was cooled to 0 °C, and the resulting white powder was collected by vacuum filtration and washed with ice−water to give 3-methoxyphenylacetamide (**1p**) (0.209 g, 42%) as a white solid. Mp 139−141 °C (lit.[52] 137−139 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 3.56 (s, 2H), 3.81 (s, 3H), 5.41 (br s, 1H), 5.52 (br s, 1H), 6.80−6.88 (m, 3H), 7.28 (t, J = 7.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 43.4 (CH_2), 55.2 (CH_3), 113.0 (CH), 115.0 (CH), 121.6 (CH), 130.1 (CH), 136.3 (C), 160.1 (C), 173.2 (C); MS (ESI) m/z 186 ($M + Na^+$, 100).

1′-(3-Methoxyphenyl)acrylonitrile.[53] To a solution of *m*-anisaldehyde (1.79 mL, 14.7 mmol) in dry dichloromethane (25 mL) was added cyanomethylene triphenylphosphorane (4.88 g, 16.2 mmol), and the resulting mixture was stirred at room temperature for 16 h. After this time, the reaction mixture was concentrated *in vacuo* and the residue was purified by flash column chromatography (petroleum ether/ethyl acetate, 9:1) to give 1′-(3-methoxyphenyl)-acrylonitrile (3:1 ratio of *E* to *Z* isomers) (1.81 g, 79%) as a colorless oil. Spectroscopic data are reported for the major *E* isomer. Spectroscopic data were consistent with the literature.[53] ^1H NMR (400 MHz, $CDCl_3$) δ 3.84 (s, 3H), 5.87 (t, J = 16.6 Hz, 1H), 6.93−7.05 (m, 3H), 7.30−7.43 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 55.4 (CH_3), 96.7 (CH), 112.5 (CH), 116.9 (CH), 117.1 (C), 120.0 (CH), 130.2 (CH), 134.8 (C), 150.5 (CH), 160.0 (C); MS (EI) m/z 159 (M^+, 100), 116 (20), 89 (20).

N-[(1-Methoxyphenyl)propyl]-4′′-methylbenzenesulfonamide (1q).[54] To a solution of 1′-(3-methoxyphenyl)-acrylonitrile (1.00 mL, 6.29 mmol) in ethanol (25 mL) were added 37% aqueous hydrochloric acid (3 mL) and 10% palladium on charcoal (0.073 g). The reaction mixture was hydrogenated at 2.5 bar for 72 h. The reaction mixture was filtered through Celite and concentrated *in vacuo*. The crude hydrochloride salt was dissolved in dichloromethane (25 mL), and triethylamine (0.700 mL, 5.00 mmol) was added. *p*-Toluenesulfonyl chloride (0.572 g, 3.00 mmol) was added at 0 °C, and the resulting solution was stirred at room temperature for 16 h. The reaction mixture was diluted with dichloromethane (20 mL) and washed with 1 M aqueous hydrochloric acid (30 mL) and brine (30 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/ethyl acetate, 7:3) gave *N*-[(1-methoxyphenyl)-propyl]-4′′-methylbenzenesulfonamide (**1q**) (0.499 g, 63%) as a colorless oil. Spectroscopic data were consistent with the literature.[54] ^1H NMR (400 MHz, $CDCl_3$) δ 1.70−1.80 (m, 2H), 2.40 (s, 3H), 2.56 (t, J = 7.7 Hz, 2H), 2.94 (q, J = 6.7 Hz, 2H), 3.75 (s, 3H), 5.04 (t, J = 6.7 Hz, 1H), 6.62−6.68 (m, 2H), 6.70 (ddd, J = 8.0, 2.5, 0.8 Hz, 1H), 7.14 (t, J = 8.0 Hz, 1H), 7.28 (d, J = 8.3 Hz, 2H), 7.74 (d, J = 8.3 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.5 (CH_3), 31.0 (CH_2), 32.8 (CH_2), 42.6 (CH_2), 55.2 (CH_3), 111.5 (CH), 114.1 (CH), 120.8 (CH), 127.1 (2 × CH), 129.4 (CH), 129.8 (2 × CH), 137.0 (C), 142.7 (C), 143.4 (C), 159.7 (C); MS (ESI) m/z 342 ($M + Na^+$, 100).

1-Benzoyl-5-methoxyindoline (2a). Iron(III) chloride (0.50 mg, 3.0 μmol) was dissolved in 1-butyl-3-methylimidazolium bis(trifluoromethanesulfonyl)imide (3.0 μL, 10 μmol) and stirred for 0.5 h at room temperature and then added to a solution of *N*-iodosuccinimide (0.031 g, 0.14 mmol) in toluene (1.0 mL). *N*-[(3-Methoxyphenyl)ethyl]benzamide (**1a**) (0.035 g, 0.14 mmol) was then added, and the mixture was stirred at 40 °C for 5 h. Upon completion of the iodination step, the reaction mixture was cooled to room temperature and copper(I) iodide (3.0 mg, 14 μmol), cesium carbonate (0.088 g, 0.27 mmol), *N*,*N*′-dimethylethylenediamine (3.0 μL, 28 μmol), and water (0.5 mL) were added. The reaction mixture was degassed under argon for 0.1 h and then heated to 130 °C for 24 h. The reaction mixture was then cooled to room temperature, diluted with ethyl acetate (10 mL), and washed with a 1 M aqueous sodium thiosulfate solution (10 mL). The aqueous layer was extracted with ethyl acetate (3 × 10 mL), and the combined organic layers were washed with brine (10 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/ethyl acetate, 4:1) gave 1-benzoyl-5-methoxyindoline (**2a**) (0.027 g, 79%) as a brown solid. Mp 102−104 °C; IR (neat) 2922, 1624, 1595, 1487, 1400, 1294, 1140, 1026, 833 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, 100 °C) δ 3.08 (t, J = 8.2 Hz, 2H), 3.76 (s, 3H), 4.00 (t, J = 8.2 Hz, 2H), 6.71 (dd, J = 8.7, 2.4 Hz, 1H), 6.88 (d, J = 2.4 Hz, 1H), 7.46−7.62 (m, 6H); ^{13}C NMR (126 MHz, DMSO-d_6, 100 °C) δ 28.4 (CH_2), 50.8 (CH_2), 56.1 (CH_3), 111.6 (CH), 112.6 (CH), 117.4 (CH), 127.3 (2 × CH), 128.8 (2 × CH) 130.2 (CH), 134.7 (C), 137.0 (C), 137.9 (C), 156.8 (C), 167.9 (C); MS (EI) m/z 253 (M^+, 43), 148 (12), 105 (100), 77 (29); HRMS (EI) calcd for $C_{16}H_{15}NO_2$ (M^+) 253.1103, found 253.1114.

1-Acetyl-5-methoxyindoline (2b).[55] 1-Acetyl-5-methoxyindoline (**2b**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using *N*-[(3-methoxyphenyl)ethyl]acetamide (**1b**) (0.049 g, 0.25 mmol). Purification by flash column chromatography (petroleum ether/ethyl acetate, 1:1) gave 1-acetyl-5-methoxyindoline (**2b**) (0.042 g, 87%) as a colorless oil. Spectroscopic data were consistent with the literature.[55] NMR spectra showed a 5:1 mixture of rotamers. Only signals for the major rotamer are recorded. ^1H NMR (400 MHz, $CDCl_3$) δ 2.20 (s, 3H), 3.17 (t, J = 8.4 Hz, 2H), 3.78 (s, 3H), 4.04 (t, J = 8.4 Hz, 2H), 6.68−6.76 (m, 2H), 8.12 (d, J = 8.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 24.0 (CH_3), 28.2 (CH_2), 48.9 (CH_2), 55.6 (CH_3), 110.9 (CH), 111.9 (CH), 117.5 (CH), 132.7 (C), 136.7 (C), 156.2 (C), 167.9 (C); MS (EI) m/z 191 (M^+, 80), 149 (60), 134 (100).

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1-(Benzyloxycarbonyl)-5-methoxyindoline (2c). 1-(Benzyloxycarbonyl)-5-methoxyindoline (**2c**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using benzyl *N*-[(3-methoxyphenyl)ethyl]carbamate (**1c**) (0.048 g, 0.17 mmol). Purification by flash column chromatography (petroleum ether/ethyl acetate, 9:1) gave 1-(benzyloxycarbonyl)-5-methoxyindoline (**2c**) (0.030 g, 63%) as a colorless oil. IR (neat) 2953, 1701, 1493, 1406, 1325, 1263, 1132, 1024, 756 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, 100 °C) δ 3.09 (t, J = 8.6 Hz, 2H), 3.74 (s, 3H), 4.01 (t, J = 8.6 Hz, 2H), 5.25 (s, 2H), 6.72 (dd, J = 8.7, 2.6 Hz, 1H), 6.84 (d, J = 2.6 Hz, 1H), 7.31−7.45 (m, 5H), 7.56 (d, J = 8.7 Hz, 1H); ^{13}C NMR (126 MHz, DMSO-d_6, 100 °C) δ 27.7 (CH_2), 48.0 (CH_2), 56.2 (CH_3), 66.8 (CH_2), 112.0 (CH), 112.9 (CH), 115.2 (CH), 128.1 (2 × CH), 128.3 (CH), 128.8 (2 × CH), 133.4 (C), 136.3 (C), 137.3 (C), 152.9 (C), 156.2 (C); MS (ESI) m/z 306 ($M + Na^+$, 100); HRMS (ESI) calcd for $C_{17}H_{17}NNaO_3$ ($M + Na^+$) 306.1101, found 306.1095.

1-(*tert*-Butoxycarbonyl)-5-methoxyindoline (2d).[56] 1-(*tert*-Butoxycarbonyl)-5-methoxyindoline (**2d**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using *tert*-butyl-*N*-[(3-methoxyphenyl)ethyl]carbamate (**1d**) (0.063 g, 0.25 mmol). Purification by flash column chromatography (petroleum ether/diethyl ether, 9:1) gave 1-(*tert*-butoxycarbonyl)-5-methoxyindoline (**2d**) (0.035 g, 56%) as a white solid. Mp 84−86 °C (lit.[56] Mp 87−88 °C); ^1H NMR (500 MHz, DMSO-d_6, 100 °C) δ 1.53 (s, 9H), 3.04 (t, J = 8.6 Hz, 2H), 3.73 (s, 3H), 3.91 (t, J = 8.6 Hz, 2H), 6.71 (dd, J = 8.7, 2.5 Hz, 1H), 6.81 (d, J = 2.5 Hz, 1H), 7.50 (d, J = 8.7 Hz, 1H); ^{13}C NMR (126 MHz, DMSO-d_6, 100 °C) δ 27.5 (CH_2), 28.7 (3 × CH_3), 48.1 (CH_2), 56.2 (CH_3), 80.4 (C), 111.9 (CH), 112.8 (CH), 115.1 (CH), 133.3 (C), 136.6 (C), 152.3 (C), 155.8 (C); MS (EI) m/z 249 (M^+, 15), 193 (100), 149 (28), 134 (62), 84 (30).

1-(Methanesulfonyl)-5-methoxyindoline (2e). 1-(Methanesulfonyl)-5-methoxyindoline (**2e**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using *N*-[(3-methoxyphenyl)-ethyl]methanesulfonamide (**1e**) (0.057 g, 0.25 mmol). Purification by flash column chromatography (petroleum ether/ethyl acetate, 1:1) gave 1-(methanesulfonyl)-5-methoxyindoline (**2e**) (0.041 g, 73%) as a colorless oil. IR (neat) 2932, 1489, 1343, 1157, 1030, 818 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.81 (s, 3H), 3.12 (t, J = 8.5 Hz, 2H), 3.78 (s, 3H), 3.97 (t, J = 8.5 Hz, 2H), 6.72 (dd, J = 8.8, 2.5 Hz, 1H), 6.79 (d, J = 2.5 Hz, 1H), 7.32 (d, J = 8.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 28.4 (CH_2), 33.9 (CH_3), 50.7 (CH_2), 55.7 (CH_3), 111.6 (CH), 112.8 (CH), 115.1 (CH), 133.1 (C), 135.4 (C), 156.8 (C); MS (EI) m/z 227 (M^+, 45), 148 (100%), 133 (69), 117 (38), 77 (33); HRMS (EI) calcd for $C_{10}H_{13}NO_3S$ (M^+) 227.0616, found 227.0617.

5-Methoxy-1-(4′-methylbenzenesulfonyl)indoline (2f). 5-Methoxy-1-(4′-methylbenzenesulfonyl)indoline (**2f**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using *N*-[(3-methoxyphenyl)ethyl]-4′′-methylbenzenesulfonamide (**1f**) (0.077 g, 0.25 mmol). Purification by flash column chromatography (petroleum ether/ethyl acetate, 4:1) gave 5-methoxy-1-(4′-methylbenzenesulfonyl)indoline (**2f**) (0.070 g, 93%) as a yellow oil. IR (neat) 2943, 1597, 1485, 1350, 1163, 1032, 814 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 3H), 2.77 (t, J = 8.2 Hz, 2H), 3.77 (s, 3H), 3.92 (t, J = 8.2 Hz, 2H), 6.64 (d, J = 2.5 Hz, 1H), 6.75 (dd, J = 8.8, 2.5 Hz, 1H), 7.22 (d, J = 8.2 Hz, 2H), 7.58 (d, J = 8.8 Hz, 1H), 7.63 (d, J = 8.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.5 (CH_3), 28.3 (CH_2), 50.4 (CH_2), 55.6 (CH_3), 111.0 (CH), 112.6 (CH), 116.7 (CH), 127.4 (2 × CH), 129.6 (2 × CH), 133.9 (C), 134.0 (C), 135.5 (C), 143.9 (C), 156.9 (C); MS (ESI) m/z 326 ($M + Na^+$, 100); HRMS (ESI) calcd for $C_{16}H_{17}NNaO_3S$ ($M + Na^+$) 326.0821, found 326.0810.

5,6-Dimethoxy-1-(4′-methylbenzenesulfonyl)indoline (2g). 5,6-Dimethoxy-1-(4′-methylbenzenesulfonyl)indoline (**2g**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using *N*-[(3,4-dimethoxyphenyl)ethyl]-4′′-methylbenzenesulfonamide (**1g**) (0.084 g, 0.25 mmol). The *N*-arylation step was carried out at 130 °C for 21 h. Purification by flash column chromatography (petroleum ether/ethyl acetate, 4:1) gave 5,6-dimethoxy-1-(4′-methylbenzenesulfonyl)indoline (**2g**) (0.065 g, 78%) as a white solid. Mp 116−118 °C; IR (neat) 2955, 1597, 1505, 1456, 1348, 1211, 1159, 1089, 814 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 2.70 (t, J = 8.2 Hz, 2H), 3.80 (s, 3H), 3.90 (t, J = 8.2 Hz, 2H), 3.94 (s, 3H), 6.60 (s, 1H), 7.20 (d, J = 8.7 Hz, 2H), 7.32 (s, 1H), 7.59 (d, J = 8.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.5 (CH_3), 28.1 (CH_2), 50.7 (CH_2), 56.3 (CH_3), 56.3 (CH_3), 101.2 (CH), 108.2 (CH), 123.6 (C), 127.4 (2 × CH), 129.6 (2 × CH), 133.9 (C), 135.4 (C), 143.9 (C), 146.4 (C), 148.7 (C); MS (ESI) m/z 356 ($M + Na^+$, 100); HRMS (ESI) calcd for $C_{17}H_{19}NNaO_4S$ ($M + Na^+$) 356.0927, found 356.0918.

5,7-Dimethoxy-1-(4′-methylbenzenesulfonyl)indoline (2h). 5,7-Dimethoxy-1-(4′-methylbenzenesulfonyl)indoline (**2h**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using *N*-[(3,5-dimethoxyphenyl)ethyl]-4′′-methylbenzenesulfonamide (**1h**) (0.082 g, 0.25 mmol). The iodination step was carried out at 40 °C for 4 h, and the *N*-arylation step, at 130 °C for 21 h. Purification by flash column chromatography (dichloromethane/diethyl ether, 19:1) gave 5,7-dimethoxy-1-(4′-methylbenzenesulfonyl)indoline (**2h**) (0.061 g, 75%) as a colorless oil; IR (neat) 2361, 1558, 1350, 1165, 813 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.32 (t, J = 7.4 Hz, 2H), 2.40 (s, 3H), 3.77 (s, 3H), 3.85 (s, 3H), 4.02 (t, J = 7.4 Hz, 2H), 6.25 (d, J = 2.2 Hz, 1H), 6.38 (d, J = 2.2 Hz, 1H), 7.19 (d, J = 8.6 Hz, 2H), 7.54 (d, J = 8.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.6 (CH_3), 29.9 (CH_2), 53.1 (CH_2), 55.6 (CH_3), 56.2 (CH_3), 99.1 (CH), 101.7 (CH), 124.5 (C), 127.7 (2 × CH), 129.3 (2 × CH), 135.6 (C), 139.6 (C), 143.6 (C), 152.9 (C), 152.6 (C); MS (ESI) m/z 356 ($M + Na^+$, 100); HRMS (ESI) calcd for $C_{17}H_{19}NNaO_4S$ ($M + Na^+$) 356.0927, found 356.0917.

1-(4′-Methylbenzenesulfonyl)-5,6,7-trimethoxyindoline (2i). 1-(4′-Methylbenzenesulfonyl)-5,6,7-trimethoxyindoline (**2i**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using 4′-methyl-*N*-[(3,4,5-trimethoxyphenyl)ethyl]benzenesulfonamide (**1i**) (0.092 g, 0.25 mmol). The iodination step was carried out at 40 °C for 4 h, and the *N*-arylation step, at 130 °C for 22 h. Purification by flash column chromatography (petroleum ether/ethyl acetate, 7:3) gave 1-(4′-methylbenzenesulfonyl)-5,6,7-trimethoxyindoline (**2i**) (0.068 g, 74%) as a white solid. Mp 126−128 °C; IR (neat) 2940, 1597, 1470, 1418, 1350, 1236, 1163, 1125, 1067, 816 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.30 (t, J = 7.6 Hz, 2H), 2.40 (s, 3H), 3.80 (s, 3H), 3.87 (s, 3H), 4.00 (s, 3H), 4.02 (t, J = 7.6 Hz, 2H), 6.38 (s, 1H), 7.18 (d, J = 8.3 Hz, 2H), 7.53 (d, J = 8.3 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.6 (CH_3), 29.6 (CH_2), 53.1 (CH_2), 56.3 (CH_3), 60.3 (CH_3), 61.2 (CH_3), 102.9 (CH), 127.6 (C), 127.7 (2 × CH), 129.3 (2 × CH), 132.5 (C), 135.5 (C), 141.5 (C), 143.7 (C), 146.9 (C), 152.4 (C); MS (ESI) m/z 386 ($M + Na^+$, 100); HRMS (ESI) calcd for $C_{18}H_{21}NNaO_5S$ ($M + Na^+$) 386.1033, found 386.1022.

5-Methoxy-6-methyl-1-(4′-methylbenzenesulfonyl)indoline (2j). 5-Methoxy-6-methyl-1-(4′-methylbenzenesulfonyl)indoline (**2j**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using *N*-[(3-methoxy-4-methylphenyl)ethyl]-4′′-methylbenzenesulfonamide (**1j**) (0.058 g, 0.18 mmol). Purification by flash column chromatography (hexane/ethyl acetate, 7:3) gave 5-methoxy-6-methyl-1-(4′-methylbenzenesulfonyl)indoline (**2j**) (0.042 g, 74%) as a colorless oil; IR (neat) 2947, 1597, 1497, 1350, 1157, 1088, 1026, 810 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.23 (s, 3H), 2.36 (s, 3H), 2.71 (t, J = 8.2 Hz, 2H), 3.75 (s, 3H), 3.88 (t, J = 8.2 Hz, 2H), 6.55 (s, 1H), 7.19 (d, J = 8.1 Hz, 2H), 7.46 (s, 1H), 7.59 (d, J = 8.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.7 (CH_3), 21.5 (CH_3), 28.3 (CH_2), 50.4 (CH_2), 55.6 (CH_3), 107.0 (CH), 118.3 (CH), 126.0 (C), 127.4 (2 × CH), 129.6 (2 × CH), 130.6 (C), 134.0 (C), 134.8 (C), 143.8 (C), 155.0 (C); MS (ESI) m/z 340 ($M + Na^+$, 100); HRMS (ESI) calcd for $C_{17}H_{19}NNaO_3S$ ($M + Na^+$) 340.0978, found 340.0970.

1-(4′-Methylbenzenesulfonyl)-(5,6-methylenedioxy)-indoline (2k). 5,6-Methylenedioxy-1-(4′-methylbenzenesulfonyl)-indoline (**2k**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using 4′′-methyl-*N*-[(3,4-methylenedioxyphenyl)ethyl]benzenesulfonamide (**1k**) (0.078 g, 0.25 mmol). The iodination step was carried out at 40 °C for 4 h, and the *N*-arylation step, at 130 °C for 21 h. Purification by flash column chromatography

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(petroleum ether/ethyl acetate, 9:1) gave 1-(4′-methylbenzenesulfonyl)-(5,6-methylenedioxy)indoline (**2k**) (0.056 g, 73%) as a white solid. Mp 139−141 °C; IR (neat) 2955, 1597, 1476, 1454, 1352, 1306, 1163, 1038, 937 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 2.66 (t, J = 8.2 Hz, 2H), 3.90 (t, J = 8.2 Hz, 2H), 5.94 (s, 2H), 6.51 (s, 1H), 7.22 (d, J = 8.3 Hz, 2H), 7.24 (s, 1H), 7.62 (d, J = 8.3 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.5 (CH_3), 28.0 (CH_2), 50.9 (CH_2), 99.0 (CH), 101.4 (CH_2), 105.2 (CH), 124.7 (C), 127.4 (2 × CH), 129.6 (2 × CH), 134.0 (C), 136.0 (C), 144.0 (C), 144.6 (C), 147.2 (C); MS (ESI) m/z 340 (M + Na^+, 100); HRMS (ESI) calcd for $C_{16}H_{15}NNaO_4S$ (M + Na^+) 340.0614, found 340.0603.

5-Amino-1-(4′-methylbenzenesulfonyl)indoline (2l). 5-Amino-1-(4′-methylbenzenesulfonyl)indoline (**2l**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using *N*-[(3-aminophenyl)ethyl]-4′′-methylbenzenesulfonamide (**1l**) (0.080 g, 0.28 mmol). The iodination step was carried out at 40 °C for 4 h, and the *N*-arylation step, at 130 °C for 21 h. Purification by flash column chromatography (hexane/ethyl acetate, 1:1) gave 5-amino-1-(4′-methylbenzenesulfonyl)indoline (**2l**) (0.055 g, 70%) as a colorless oil. IR (neat) 3475, 3365, 1624, 1597, 1488, 1343, 1161, 1091, 814 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 3H), 2.64 (t, J = 8.2 Hz, 2H), 3.53 (br s, 2H), 3.86 (t, J = 8.2 Hz, 2H), 6.41 (d, J = 2.3 Hz, 1H), 6.53 (dd, J = 8.5, 2.3 Hz, 1H), 7.19 (d, J = 8.1 Hz, 2H), 7.45 (d, J = 8.5 Hz, 1H), 7.58 (d, J = 8.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.5 (CH_3), 28.3 (CH_2), 50.3 (CH_2), 111.9 (CH), 114.3 (CH), 117.3 (CH), 127.4 (2 × CH), 129.5 (2 × CH), 133.9 (C), 134.0 (2 × C), 143.4 (C), 143.7 (C); MS (ESI) m/z 311 (M + Na^+, 100); HRMS (ESI) calcd for $C_{15}H_{16}N_2NaO_2S$ (M + Na^+) 311.0825, found 311.0826.

5-Amino-6-chloro-1-(4′-methylbenzenesulfonyl)indoline (2m). 5-Amino-6-chloro-1-(4′-methylbenzenesulfonyl)indoline (**2m**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using *N*-[(3-amino-4-chlorophenyl)ethyl]-4′′-methylbenzenesulfonamide (**1m**) (0.059 g, 0.18 mmol). The iodination step was carried out at 40 °C for 4 h. Purification by flash column chromatography (hexane/ethyl acetate, 1:1) gave 5-amino-6-chloro-1-(4′-methylbenzenesulfonyl)indoline (**2m**) (0.032 g, 55%) as a colorless oil. IR (neat) 3472, 3372, 2924, 2361, 1620, 1597, 1481, 1342, 1159, 1088, 810 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 2.66 (t, J = 8.2 Hz, 2H), 3.71−3.96 (m, 4H), 6.49 (s, 1H), 7.22 (d, J = 8.2 Hz, 2H), 7.58 (s, 1H), 7.61 (d, J = 8.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.5 (CH_3), 28.0 (CH_2), 50.3 (CH_2), 112.1 (CH), 117.0 (CH), 118.1 (C), 127.4 (2 × CH), 129.7 (2 × CH), 132.4 (C), 133.7 (C), 134.2 (C), 139.7 (C), 144.0 (C); MS (ESI) m/z 345 (M + Na^+, 100); HRMS (ESI) calcd for $C_{15}H_{15}{}^{35}ClN_2NaO_2S$ (M + Na^+) 345.0435, found 345.0422.

5-Acetamido-1-(4′-methylbenzenesulfonyl)indoline (2n). 5-Acetamido-1-(4′-methylbenzenesulfonyl)indoline (**2n**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using *N*-[(3-acetamidophenyl)ethyl]-4′′-methylbenzenesulfonamide (**1n**) (0.148 g, 0.45 mmol). The iodination step was carried out at 40 °C for 4 h, and the *N*-arylation step, at 130 °C for 21 h. Purification by flash column chromatography (hexane/ethyl acetate, 7:3) gave 5-acetamido-1-(4′-methylbenzenesulfonyl)indoline (**2n**) (0.094 g, 64%) as a white solid. Mp 168−170 °C; IR (neat) 3320, 2924, 1675, 1546, 1487, 1351, 1163, 1091, 815 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.13 (s, 3H), 2.37 (s, 3H), 2.83 (t, J = 8.1 Hz, 2H), 3.89 (t, J = 8.1 Hz, 2H), 7.05 (dd, J = 8.3, 1.6 Hz, 1H), 7.21 (d, J = 7.7 Hz, 2H), 7.24 (br s, 1H), 7.49 (br s, 1H), 7.54 (d, J = 8.3 Hz, 1H), 7.62 (d, J = 7.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.5 (CH_3), 24.4 (CH_3), 28.1 (CH_2), 50.2 (CH_2), 115.4 (CH), 117.6 (CH), 119.3 (CH), 127.3 (2 × CH), 129.7 (2 × CH), 133.0 (C), 133.7 (C), 134.2 (C), 138.4 (C), 144.2 (C), 168.3 (C); MS (ESI) m/z 353 (M + Na^+, 100); HRMS (ESI) calcd for $C_{17}H_{18}N_2NaO_3S$ (M + Na^+) 353.0930, found 353.0925.

5-Acetamido-6-chloro-1-(4′-methylbenzenesulfonyl)-indoline (2o). 5-Acetamido-6-chloro-1-(4′-methylbenzenesulfonyl)-indoline (**2o**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using *N*-[(3-acetamido-4-chlorophenyl)ethyl]-4′′-methylbenzenesulfonamide (**1o**) (0.042 g, 0.11 mmol). The bromination step was carried out at 40 °C for 4 h, and the *N*-arylation step, at 130 °C for 21 h. Purification by flash column chromatography (hexane/ethyl acetate, 2:3) gave 5-acetamido-6-chloro-1-(4′-methylbenzenesulfonyl)indoline (**2o**) (0.017 g, 43%) as a white solid. Mp 138−140 °C; IR (neat) 3350, 2925, 1653, 1356, 1162 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.21 (s, 3H), 2.39 (s, 3H), 2.85 (t, J = 8.4 Hz, 2H), 3.90 (t, J = 8.4 Hz, 2H), 7.25 (d, J = 8.5 Hz, 2H), 7.49 (s, 1H), 7.65 (d, J = 8.5 Hz, 2H), 7.68 (s, 1H), 8.05 (br s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.5 (CH_3), 24.7 (CH_3), 27.9 (CH_2), 50.3 (CH_2), 115.4 (CH), 118.4 (CH), 121.9 (C), 127.3 (2 × CH), 129.8 (2 × CH), 130.5 (C), 131.6 (C), 133.6 (C), 138.6 (C), 144.4 (C), 168.2 (C); MS (ESI) m/z 387 (M + Na^+, 100); HRMS (ESI) calcd for $C_{17}H_{17}{}^{35}ClN_2NaO_3S$ (M + Na^+) 387.0541, found 387.0527.

5-Methoxyindolin-2-one (2p).[57] 5-Methoxyindolin-2-one (**2p**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using 3-methoxyphenylacetamide (**1p**) (0.042 g, 0.25 mmol). The *N*-arylation step was carried out at 130 °C for 21 h. Purification by flash column chromatography (hexane/ethyl acetate, 1:1) gave 5-methoxyindolin-2-one (**2p**) (0.027 g, 65%) as a white solid. Mp 128−130 °C (lit.[57] 132−134 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 3.53 (s, 2H), 3.78 (s, 3H), 6.75 (dd, J = 8.5, 2.4 Hz, 1H), 6.79 (d, J = 8.5 Hz, 1H), 6.85 (br s, 1H), 8.53 (br s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 36.7 (CH_2), 55.8 (CH_3), 110.0 (CH), 111.8 (CH), 112.5 (CH), 126.7 (C), 135.9 (C), 155.7 (C), 177.5 (C); MS (ESI) m/z 186 (M + Na^+, 100).

6-Methoxy-1-(4′-methylbenzenesulfonyl)-1,2,3,4-tetrahydroquinoline (2q). 6-Methoxy-1-(4′-methylbenzenesulfonyl)-2,3,4-tetrahydroquinoline (**2q**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using *N*-[(1-methoxyphenyl)-propyl]-4′′-methylbenzenesulfonamide (**1q**) (0.083 g, 0.50 mmol). Purification by flash column chromatography (hexane/ethyl acetate, 4:1) gave 6-methoxy-1-(4′-methylbenzenesulfonyl)-1,2,3,4-tetrahydroquinoline (**2q**) (0.071 g, 85%) as a colorless oil. IR (neat) 2943 (CH), 1609, 1597 (C═C), 1493, 1339, 1162, 1090, 812 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.51−1.59 (m, 2H), 2.33 (t, J = 6.8 Hz, 2H), 2.38 (s, 3H), 3.73−3.77 (m, 2H), 3.78 (s, 3H), 6.52 (d, J = 2.8 Hz, 1H), 6.75 (dd, J = 9.0, 2.8 Hz, 1H), 7.18 (d, J = 8.3 Hz, 2H), 7.42 (d, J = 8.3 Hz, 2H), 7.70 (d, J = 9.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.3 (CH_2), 21.5 (CH_3), 26.6 (CH_2), 46.4 (CH_2), 55.4 (CH_3), 112.1 (CH), 113.7 (CH), 127.0 (CH), 127.2 (2 × CH), 129.5 (2 × CH), 129.9 (C), 132.7 (C), 136.7 (C), 143.4 (C), 157.0 (C); MS (ESI) m/z 340 (M + Na^+, 100); HRMS (ESI) calcd for $C_{17}H_{19}NNaO_3S$ (M + Na^+) 340.0978, found 340.0965.

(3,4-Methylenedioxy)phenethan-2′-ol (3c).[58] To a stirred suspension of lithium aluminum hydride (0.211 g, 5.55 mmol) in dry tetrahydrofuran (15 mL) was added 3,4-(methylenedioxy)phenylacetic acid (0.500 g, 2.78 mmol) in tetrahydrofuran (5 mL) dropwise under a constant stream of argon at 0 °C. The suspension was stirred at room temperature for 5 h, cooled to 0 °C, and quenched with water (0.20 mL). To this solution was added 15% aqueous sodium hydroxide (0.20 mL), followed by water (0.60 mL). Magnesium sulfate was added, and the suspension was stirred for 0.5 h, filtered, and then concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/ethyl acetate, 1:1) gave (3,4-methylenedioxy)phenethan-2′-ol (**3c**) (0.308 g, 67%) as a colorless oil. Spectroscopic data were consistent with the literature.[58] ^1H NMR (400 MHz, $CDCl_3$) δ 1.50 (br s, 1H), 2.78 (t, J = 6.6 Hz, 2H), 3.79 (br s, 2H), 5.93 (s, 2H), 6.67 (dd, J = 7.9, 1.6 Hz, 1H), 6.72 (d, J = 1.6 Hz, 1H), 6.75 (d, J = 7.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 38.9 (CH_2), 63.7 (CH_2), 100.9 (CH_2), 108.3 (CH), 109.3 (CH), 121.9 (CH), 132.2 (C), 146.2 (C), 147.8 (C); MS (EI) m/z 166 (M^+, 30), 135 (100).

1′-(Dihydro-3,4-benzodioxinyl)ethan-2′-ol (3d).[59] 1′-(Dihydro-3,4-benzodioxinyl)ethan-2′-ol (**3d**) was synthesized as described for (3,4-methylenedioxy)phenethan-2′-ol (**3c**) using 1,4-benzodioxane-6-acetic acid (0.469 g, 2.51 mmol). Purification by flash column chromatography (petroleum ether/ethyl acetate, 1:1) gave 1′-(dihydro-3,4-benzodioxinyl)ethan-2′-ol (**3d**) (0.425 g, 94%) as a

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colorless oil. Spectroscopic data were consistent with the literature.[59] ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.78 (br s, 1H), 2.74 (t, J = 6.5 Hz, 2H), 3.78 (br s, 2H), 4.22 (s, 4H), 6.68 (dd, J = 8.2, 2.0 Hz, 1H), 6.73 (d, J = 2.0 Hz, 1H), 6.79 (d, J = 8.2 Hz, 1H); δ_C (101 MHz, $CDCl_3$) δ 38.4 (CH_2), 63.6 (CH_2), 64.3 (CH_2), 64.4 (CH_2), 117.3 (CH), 117.6 (CH), 121.9 (CH), 131.7 (C), 142.1 (C), 143.4 (C); MS (ESI) m/z 203 (M + Na^+, 100).

1′-(3-Aminophenyl)ethan-2′-ol.[60] To a stirred solution of 1′-(3-nitrophenyl)ethan-2′-ol (0.350 g, 2.09 mmol) in ethanol (25 mL) was added tin(II) dichloride dihydrate (2.40 g, 10.5 mmol), and the resulting solution was heated under reflux for 18 h. After cooling to room temperature, the reaction mixture was diluted with saturated aqueous sodium hydrogen carbonate solution (20 mL) and extracted with dichloromethane (5 × 50 mL). The combined extracts were washed with brine (2 × 200 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/ethyl acetate, 3:7) gave 1′-(3-aminophenyl)ethan-2′-ol (0.090 g, 32%) as a colorless oil. Spectroscopic data were consistent with the literature.[60] ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.54 (br s, 1H), 2.78 (t, J = 6.5 Hz, 2H), 3.64 (br s, 2H), 3.83 (t, J = 6.5 Hz, 2H), 6.54−6.58 (m, 2H), 6.60−6.65 (m, 1H), 7.07−7.13 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 39.2 (CH_2), 63.6 (CH_2), 113.3 (CH), 115.7 (CH), 119.2 (CH), 129.6 (CH), 139.7 (C), 146.6 (C); MS (EI) m/z 137 (M^+, 70), 106 (100), 84 (38), 78 (37), 63 (42).

1′-(3-Acetamidophenyl)ethan-2′-ol (3e). Acetic anhydride (0.085 mL, 0.900 mmol) was added to a stirred solution of 1′-(3-aminophenyl)ethan-2′-ol (0.082 g, 0.600 mmol) in dichloromethane (10 mL) and stirred for 24 h at room temperature. The reaction mixture was washed with aqueous saturated sodium carbonate (15 mL) and brine (15 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. Recrystallization from diethyl ether gave 1′-(3-acetamido)phenylethan-2′-ol (**3e**) (0.042 g, 42%) as a white solid. Mp 102−104 °C; IR (neat) 3294, 2924, 1667, 1612, 1551, 1489, 1435, 1319, 1041, 787 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.67 (br s, 1H), 2.16 (s, 3H), 2.84 (t, J = 6.6 Hz, 2H), 3.85 (t, J = 6.6 Hz, 2H), 6.95−7.00 (m, 1H), 7.23−7.45 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 24.6 (CH_3), 39.1 (CH_2), 63.5 (CH_2), 118.1 (CH), 120.5 (CH), 125.0 (CH), 129.2 (CH), 138.1 (C), 139.6 (C), 168.4 (C); MS (ESI) m/z 202 (M + Na^+, 100); HRMS (ESI) calcd for $C_{10}H_{13}NNaO_2$ (M + Na^+) 202.0838, found 202.0838.

Methyl (3-Methoxyphenyl)acetate.[61] To a stirred solution of 3-methoxyphenylacetic acid (2.00 g, 12.0 mmol) in methanol (20 mL) were added a few drops of concentrated sulfuric acid. The resulting mixture was heated under reflux for 16 h. The methanol was removed *in vacuo*, and the residue was diluted with dichloromethane (50 mL). The solution was washed with water (4 × 50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated to give methyl (3-methoxyphenyl)acetate (2.12 g, 99%) as a colorless oil. Spectroscopic data were consistent with the literature.[61] ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.59 (s, 2H), 3.67 (s, 3H), 3.78 (s, 3H), 6.76−6.88 (m, 3H), 7.21 (t, J = 7.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 41.2 (CH_2), 52.0 (CH_3), 55.2 (CH_3), 112.6 (CH), 114.9 (CH), 121.6 (CH), 129.6 (CH), 135.4 (C), 159.8 (C), 171.9 (C); MS (ESI) m/z 203 (M + Na^+, 100).

2′,2′-Dimethyl-1′-(3-methoxyphenyl)ethan-2′-ol (3f). Methylmagnesium bromide (3.0 M in diethyl ether, 2.20 mL, 6.50 mmol) was added dropwise to a 0 °C solution of methyl (3-methoxyphenyl)acetate (0.390 g, 2.17 mmol) in dry tetrahydrofuran (20 mL). The yellow solution was warmed to room temperature and stirred for 5 h. The reaction mixture was quenched with saturated aqueous ammonium chloride (30 mL) and diluted with diethyl ether (30 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 30 mL). The combined ethereal extracts were washed with brine (30 mL), dried ($MgSO_4$), and concentrated. Purification by flash column chromatography (petroleum ether/ethyl acetate, 4:1) gave 2′,2′-dimethyl-1′-(3-methoxyphenyl)ethan-2′-ol (**3f**) (0.301 g, 77%) as a colorless oil. IR (neat) 3426, 2969, 1601, 1489, 1261, 1153, 1047 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23 (s, 6H), 2.74 (s, 2H), 3.79 (s, 3H), 6.75−6.81 (m, 3H), 7.21 (t, J = 7.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 29.2 (2 × CH_3), 49.8 (CH_2), 55.2 (CH_3), 70.7 (C), 111.8 (CH), 116.3 (CH), 122.9 (CH), 129.2 (CH), 139.4 (C), 159.5 (C); MS (ESI) m/z 203 (M + Na^+, 100); HRMS (ESI) calcd for $C_{11}H_{16}NaO_2$ (M + Na^+) 203.1043, found 203.1044.

***N*-Methoxy-1′-(3-methoxyphenyl)-*N*-methylacetamide.**[62] To a solution of 3-methoxyphenylacetic acid (1.50 g, 9.03 mmol) in dichloromethane (50 mL) were added 1-ethyl-3-(3-(dimethylamino)-propyl)carbodiimide hydrochloride (1.70 g, 9.03 mmol), 1-hydroxybenzotriazole hydrate (1.35 g, 9.94 mmol), *N*,*O*-dimethylhydroxylamine hydrochloride (0.88 g, 9.03 mmol) and *N*,*N*-diisopropylethylamine (6.3 mL, 36.1 mmol). The mixture was stirred at room temperature for 24 h. Water (30 mL) and sodium hydrogen carbonate (30 mL) were added, and the mixture extracted with dichloromethane (4 × 100 mL). The combined extracts were washed with brine (2 × 200 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/ethyl acetate, 1:1) gave *N*-methoxy-1′-(3-methoxyphenyl)-*N*-methylacetamide (1.40 g, 74%) as a yellow oil. Spectroscopic data were consistent with the literature.[62] ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.19 (s, 3H), 3.60 (s, 3H), 3.74 (s, 2H), 3.79 (s, 3H), 6.79 (dd, J = 8.0, 2.6 Hz, 1H), 6.83−6.92 (m, 2H), 7.23 (t, J = 8.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 32.2 (CH_3), 39.4 (CH_2), 55.2 (CH_3), 61.3 (CH_3), 112.4 (CH), 114.8 (CH), 121.7 (CH), 129.4 (CH), 136.4 (C), 159.7 (C), 172.3 (C); MS (ESI) m/z 232 (M + Na^+, 100).

1′-(3-Methoxyphenyl)-2′-(4′′-methoxyphenyl)ethan-2′-one.[5b] An oven-dried three-neck flask was flushed with argon and charged with magnesium turnings (0.070 g, 2.3 mmol), a crystal of iodine, and dry tetrahydrofuran (12 mL). 4-Bromoanisole (0.29 mL, 2.3 mmol) was added, and the solution was heated under reflux for 1 h. This solution was then transferred via cannula to a solution of *N*-methoxy-1′-(3-methoxyphenyl)-*N*-methylacetamide (0.40 g, 1.9 mmol) in dry tetrahydrofuran (15 mL). The resulting suspension was stirred at room temperature for 16 h. The reaction mixture was quenched with saturated ammonium chloride solution (30 mL) and extracted with ethyl acetate (2 × 30 mL). The combined organic layers were washed with brine (30 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/ethyl acetate, 4:1) gave 1′-(3-methoxyphenyl)-2′-(4′′-methoxyphenyl)ethan-2-one (0.19 g, 45%) as a colorless oil. Spectroscopic data were consistent with the literature.[5b] ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 (s, 3H), 3.85 (s, 3H), 4.19 (s, 2H), 6.78 (dd, J = 8.0, 2.4 Hz, 1H), 6.80−6.83 (m, 1H), 6.85−6.88 (m, 1H), 6.91 (d, J = 9.0 Hz, 2H), 7.22 (t, J = 8.0 Hz, 1H), 7.99 (d, J = 9.0 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 45.4 (CH_2), 55.2 (CH_3), 55.5 (CH_3), 112.3 (CH), 113.8 (2 × CH), 115.0 (CH), 121.8 (CH), 129.6 (CH), 131.0 (2 × CH), 136.5 (2 × C), 159.8 (C), 163.5 (C), 196.1 (C); MS (ESI) m/z 279 (M + Na^+, 100).

1′-(3-Methoxyphenyl)-2′-phenylethan-2′-one.[63] An oven-dried three-neck flask was flushed with argon and charged with *N*-methoxy-1′-(3-methoxyphenyl)-*N*-methylacetamide (0.349 g, 1.67 mmol) in dry tetrahydrofuran (15 mL). Phenylmagnesium bromide (1.84 mL, 1.84 mmol; 1.0 M in tetrahydrofuran) was added dropwise at 0 °C, and the solution was warmed to room temperature and stirred for 2.5 h. The reaction mixture was quenched with saturated aqueous ammonium chloride solution (15 mL) and extracted with diethyl ether (4 × 30 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/ethyl acetate, 19:1) gave 1′-(3-methoxyphenyl)-2′-phenylethan-2′-one (0.210 g, 56%) as a colorless oil. Spectroscopic data were consistent with the literature.[63] ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (s, 3H), 4.25 (s, 2H), 6.78−6.83 (m, 2H), 6.86 (br d, J = 7.6 Hz, 1H), 7.24 (t, J = 7.6 Hz, 1H), 7.45 (t, J = 7.8 Hz, 2H), 7.55 (t, J = 7.8 Hz, 1H), 8.01 (d, J = 7.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 45.6 (CH_2), 55.2 (CH_3), 112.4 (CH), 115.1 (CH), 121.8 (CH), 128.6 (4 × CH), 129.7 (CH), 133.2 (CH), 136.0 (C), 136.6 (C), 159.8 (C), 197.5 (C); MS (ESI) m/z 249 (M + Na^+, 100).

2′-(4′′-Chlorophenyl)-1′-(3-methoxyphenyl)ethan-2′-one. The reaction was carried out as described for 1′-(3-methoxyphenyl)-2′-phenylethan-2′-one using *N*-methoxy-1′-(3-methoxyphenyl)-*N*-methylacetamide (0.387 g, 1.85 mmol). This gave 2′-(4′′-

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chlorophenyl)-1′-(3-methoxyphenyl)ethan-2′-one (0.339 g, 70%) as a colorless oil. IR (neat) 2940, 2361, 1682, 1589, 1489, 1265, 1157, 1088, 1049, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.78 (s, 3H), 4.22 (s, 2H), 6.78−6.85 (m, 3H), 7.24 (t, J = 7.6 Hz, 1H), 7.42 (d, J = 8.6 Hz, 2H), 7.94 (d, J = 8.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 45.6 (CH_2), 55.2 (CH_3), 112.5 (CH), 115.1 (CH), 121.7 (CH), 129.0 (2 × CH), 129.8 (CH), 130.1 (2 × CH), 134.8 (C), 135.6 (C), 139.6 (C), 159.9 (C), 196.3 (C); MS (ESI) m/z 283 (M + Na^+, 100); HRMS (ESI) calcd for $C_{15}H_{13}{}^{35}ClNaO_2$ (M + Na^+) 283.0496, found 283.0500.

1′-(3-Methoxyphenyl)-2′-(4′′-methoxyphenyl)ethan-2′-ol (3g).[5b] To a stirred solution of 1′-(3-methoxyphenyl)-2′-(4′′-methoxyphenyl)ethan-2-one (0.530 g, 2.07 mmol) in methanol (15 mL) was added sodium borohydride (0.196 g, 5.17 mmol). The resulting suspension was stirred at room temperature for 4 h after which time the reaction was quenched with water (15 mL) and extracted with dichloromethane (3 × 30 mL). The combined organic layers were washed with water (2 × 60 mL) and brine (60 mL), dried ($MgSO_4$), and concentrated *in vacuo* to give 1′-(3-methoxyphenyl)-2′-(4′′-methoxyphenyl)ethan-2′-ol (**3g**) (0.508 g, 95%) as a colorless oil. Spectroscopic data were consistent with the literature.[5b] ^1H NMR (400 MHz, $CDCl_3$) δ 1.97 (br s, 1H), 2.94 (dd, J = 13.5, 8.0 Hz, 1H), 2.99 (dd, J = 13.5, 5.6 Hz, 1H), 3.76 (s, 3H), 3.80 (s, 3H), 4.84 (ddd, J = 8.0, 5.6, 2.7 Hz, 1H), 6.70−6.73 (m, 1H), 6.75−6.80 (m, 2H), 6.87 (d, J = 8.7 Hz, 2H), 7.21 (t, J = 7.9 Hz, 1H), 7.27 (d, J = 8.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 46.1 (CH_2), 55.2 (CH_3), 55.3 (CH_3), 74.9 (CH), 112.1 (CH), 113.8 (2 × CH), 115.1 (CH), 121.9 (CH), 127.2 (2 × CH), 129.5 (CH), 136.0 (C), 139.8 (C), 159.1 (C), 159.7 (C); MS (ESI) m/z 281 (M + Na^+, 100).

1′-(3-Methoxyphenyl)-2′-phenylethan-2′-ol (3h).[64] The reaction was carried out as described for 1′-(3-methoxyphenyl)-2′-(4′′-methoxyphenyl)ethan-2′-ol (**3g**) using 1′-(3-methoxyphenyl)-2′-phenylethan-2-one (0.188 g, 0.830 mmol), except that the reaction was stirred at room temperature for 1 h. This gave 1′-(3-methoxyphenyl)-2′-phenylethan-2′-ol (**3h**) (0.169 g, 89%) as a colorless oil. Spectroscopic data were consistent with the literature.[64] ^1H NMR (400 MHz, $CDCl_3$) δ 1.97 (d, J = 3.0 Hz, 1H), 2.96 (dd, J = 13.7, 8.4 Hz, 1H), 3.03 (dd, J = 13.7, 5.0 Hz, 1H), 3.77 (s, 3H), 4.89 (ddd, J = 8.4, 5.0, 3.0 Hz, 1H), 6.71−6.74 (m, 1H), 6.76−6.83 (m, 2H), 7.22 (t, J = 7.9 Hz, 1H), 7.26−7.40 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 46.2 (CH_2), 55.2 (CH_3), 75.2 (CH), 112.2 (CH), 115.1 (CH), 121.8 (CH), 125.9 (2 × CH), 127.6 (CH), 128.4 (2 × CH), 129.5 (CH), 139.6 (C), 143.8 (C), 159.7 (C); MS (ESI) m/z 251 (M + Na^+, 100).

2′-(4′′-Chlorophenyl)-1′-(3-methoxyphenyl)ethan-2′-ol (3i). The reaction was carried out as described for 1′-(3-methoxyphenyl)-2′-(4′′-methoxyphenyl)ethan-2′-ol (**3g**) using 2′-(4′′-chlorophenyl)-1′-(3-methoxyphenyl)ethan-2′-one (0.243 g, 0.930 mmol). This gave 2′-(4′′-chlorophenyl)-1′-(3-methoxyphenyl)ethan-2′-ol (**3i**) (0.210 g, 86%) as a colorless oil. IR (neat) 3402, 2940, 2361, 1597, 1489, 1258, 1157, 1088, 1049, 833, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.98 (d, J = 2.9 Hz, 1H), 2.91 (dd, J = 13.7, 8.5 Hz, 1H), 2.99 (dd, J = 13.7, 5.0 Hz, 1H), 3.78 (s, 3H), 4.88 (ddd, J = 8.5, 5.0, 2.9 Hz, 1H), 6.71 (t, J = 2.0 Hz, 1H), 6.74−6.82 (m, 2H), 7.22 (t, J = 8.0 Hz, 1H), 7.27 (d, J = 8.8 Hz, 2H), 7.32 (d, J = 8.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 46.2 (CH_2), 55.2 (CH_3), 74.5 (CH), 112.2 (CH), 115.1 (CH), 121.8 (CH), 127.3 (2 × CH), 128.5 (2 × CH), 129.6 (CH), 133.2 (C), 139.1 (C), 142.2 (C), 159.8 (C); MS (ESI) m/z 285 (M + Na^+, 100); HRMS (ESI) calcd for $C_{15}H_{15}{}^{35}ClNaO_2$ (M + Na^+) 285.0653, found 285.0646.

Ethyl (*E*)-1′-(3-Methoxyphenyl)acrylate.[65] A solution of lithium chloride (0.310 g, 7.30 mmol), triethyl phosphonoacetate (1.45 mL, 7.30 mmol), and 1,8-diazabicyclo[5,4,0]undec-7-ene (1.09 mL, 7.30 mmol) in dry acetonitrile (30 mL) was stirred for 0.5 h. *m*-Anisaldehyde (0.890 mL, 7.30 mmol) was added, and the solution was stirred at room temperature for 18 h. The reaction mixture was quenched with brine (30 mL) and concentrated, and the residue was extracted with diethyl ether (5 × 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. Purification by flash column chromatography (petroleum ether/ethyl acetate, 9:1) gave ethyl (*E*)-1′-(3′-methoxyphenyl)acrylate (1.36 g, 91%) as a colorless oil. Spectroscopic data were consistent with the literature.[65] ^1H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, J = 7.2 Hz, 3H), 3.82 (s, 3H), 4.26 (q, J = 7.2 Hz, 2H), 6.42 (d, J = 15.9 Hz, 1H), 6.91 (ddd, J = 8.1, 2.5, 0.8 Hz, 1H), 7.04 (t, J = 2.5 Hz, 1H), 7.10 (br d, J = 8.1 Hz, 1H), 7.29 (t, J = 8.1 Hz, 1H), 7.64 (d, J = 15.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 55.3 (CH_3), 60.5 (CH_2), 112.9 (CH), 116.1 (CH), 118.6 (CH), 120.7 (CH), 129.9 (CH), 135.8 (C), 144.5 (CH), 159.9 (C), 166.9 (C); MS (ESI) m/z 207 (M + H^+, 100).

Ethyl (*E*)-1′-(3,4,5-trimethoxyphenyl)acrylate.[66] The reaction was conducted as described for the synthesis of ethyl (*E*)-1′-(3′-methoxyphenyl)acrylate using trimethoxybenzaldehyde (1.00 g, 5.10 mmol). The resulting off-white solid was recrystallized from hot hexane which gave ethyl (*E*)-1′-(3,4,5-trimethoxyphenyl)acrylate (0.713 g, 53%) as a white solid. Mp 50−52 °C (lit.[66] 53−55 °C); ^1H NMR (500 MHz, $CDCl_3$) δ 1.34 (t, J = 7.2 Hz, 3H), 3.88 (s, 3H), 3.89 (s, 6H), 4.26 (q, J = 7.2 Hz, 2H), 6.35 (d, J = 15.9 Hz, 1H), 6.76 (s, 2H), 7.60 (d, J = 15.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.3 (CH_3), 56.1 (2 × CH_3), 60.5 (CH_2), 61.0 (CH_3), 105.2 (2 × CH), 117.5 (CH), 130.0 (C), 140.1 (C), 144.5 (CH), 153.4 (2 × C), 166.9 (C); MS (ESI) m/z 289 (M + H^+, 100).

1′-(3-Methoxyphenyl)propan-3′-ol (3j).[67] To a stirred suspension of lithium aluminum hydride (0.150 g, 3.94 mmol) in dry tetrahydrofuran (10 mL) was added ethyl (*E*)-1′-(3-methoxyphenyl)-acrylate (0.325 g, 1.58 mmol) in tetrahydrofuran (10 mL) dropwise under a constant stream of argon at 0 °C. The suspension was stirred at room temperature for 5 h, then cooled to 0 °C and quenched with a saturated aqueous solution of potassium sodium tartrate (20 mL), and stirred overnight. The suspension was extracted with diethyl ether (5 × 50 mL), and the combined organic extracts were dried ($MgSO_4$) and concentrated. Purification by flash column chromatography (petroleum ether/ethyl acetate, 7:3) gave 1′-(3-methoxyphenyl)-propan-3′-ol (**3j**) (0.179 g, 69%) as a colorless oil. Spectroscopic data were consistent with the literature.[67] ^1H NMR (400 MHz, $CDCl_3$) δ 1.85−1.94 (m, 2H), 2.69 (t, J = 7.9 Hz, 2H), 3.68 (t, J = 6.5 Hz, 2H), 3.80 (s, 3H), 6.72−6.77 (m, 2H), 6.78−6.82 (m, 1H), 7.21 (t, J = 7.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 32.1 (CH_2), 34.1 (CH_2), 55.1 (CH_3), 62.3 (CH_2), 111.1 (CH), 114.2 (CH), 120.8 (CH), 129.4 (CH), 143.5 (C), 159.7 (C); MS (ESI) m/z 189 (M + Na^+, 100).

1′-(3,4,5-Trimethoxyphenyl)propan-3′-ol (3l).[68] The reaction was conducted as described for the synthesis of 1′-(3-methoxyphenyl)propan-3′-ol (**3j**) using ethyl (*E*)-1′-(3,4,5-trimethoxyphenyl)acrylate (0.596 g, 2.24 mmol). The suspension was stirred at room temperature for 5 h, cooled to 0 °C, and quenched with water (0.25 mL). To this solution was added 15% aqueous sodium hydroxide (0.25 mL), followed by water (0.75 mL). Magnesium sulfate was added, and the suspension was stirred for 0.5 h, filtered, and concentrated *in vacuo*. Purification by flash column chromatography (ethyl acetate/petroleum ether, 3:2) gave 1′-(3,4,5-trimethoxyphenyl)propan-3′-ol (**3l**) (0.228 g, 45%) as a colorless oil. Spectroscopic data were consistent with the literature.[68] ^1H NMR (400 MHz, $CDCl_3$) δ 1.42 (br s, 1H), 1.85−1.95 (m, 2H), 2.63−2.69 (m, 2H), 3.68 (t, J = 6.5 Hz, 2H), 3.83 (s, 3H), 3.85 (s, 6H), 6.42 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 32.6 (CH_2), 34.3 (CH_2), 56.1 (2 × CH_3), 60.9 (CH_3), 62.3 (CH_2), 105.3 (2 × CH), 136.1 (C), 137.7 (C), 153.2 (2 × C); MS (ESI) m/z 249 (M + Na^+, 100).

2,3-Dihydro-5-methoxybenzofuran (4a).[12] 2,3-Dihydro-5-methoxybenzofuran (**4a**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using 3-methoxyphenylethan-2′-ol (**3a**) (0.071 mL, 0.50 mmol). The *O*-arylation step was carried out at 150 °C for 21 h. Purification by flash column chromatography (petroleum ether/ethyl acetate, 19:1) gave 2,3-dihydro-5-methoxybenzofuran (**4a**) (0.046 g, 65%) as a colorless oil. Spectroscopic data were consistent with the literature.[12] ^1H NMR (400 MHz, $CDCl_3$) δ 3.17 (t, J = 8.6 Hz, 2H), 3.75 (s, 3H), 4.53 (t, J = 8.6 Hz, 2H), 6.64 (dd, J = 8.6, 2.6 Hz, 1H), 6.68 (d, J = 8.6 Hz, 1H), 6.78 (d, J = 2.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 30.3 (CH_2), 56.1 (CH_3), 71.3 (CH_2), 109.1 (CH), 111.4 (CH), 112.8 (CH), 128.0 (C), 154.1 (C), 154.2 (C); MS (ESI) m/z 173 (M + Na^+, 100).

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2,3-Dihydro-5,6-dimethoxybenzofuran (4b). 2,3-Dihydro-5,6-dimethoxybenzofuran (**4b**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using 3,4-dimethoxyphenylethan-2′-ol (**3b**) (0.091 g, 0.50 mmol). Purification by flash column chromatography (petroleum ether/ethyl acetate, 9:1) gave 2,3-dihydro-5,6-dimethoxybenzofuran (**4b**) (0.065 g, 72%) as a white solid. Mp 58−60 °C; IR (neat) 2940, 1614, 1502, 1446, 1304, 1208, 1186, 1169, 1095, 1003, 828 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.15 (t, J = 8.7 Hz, 2H), 3.82 (s, 3H), 3.83 (s, 3H), 4.54 (t, J = 8.7 Hz, 2H), 6.45 (s, 1H), 6.78 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 30.0 (CH_2), 56.1 (CH_3), 57.0 (CH_3), 71.7 (CH_2), 94.9 (CH), 109.3 (CH), 116.6 (C), 143.2 (C), 149.2 (C), 154.3 (C); MS (ESI) m/z 203 (M + Na^+, 100); HRMS (ESI) calcd for $C_{10}H_{12}NaO_3$ (M + Na^+) 203.0679, found 203.0679.

2,3-Dihydro-5,6-methylenedioxybenzofuran (4c). 2,3-Dihydro-5,6-methylenedioxybenzofuran (**4c**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using (3,4-methylenedioxy)-phenethan-2′-ol (**3c**) (0.083 g, 0.50 mmol). Purification by flash column chromatography (petroleum ether/ethyl acetate, 9:1) gave 2,3-dihydro-5,6-methylenedioxybenzofuran (**4c**) (0.053 g, 64%) as a white solid. Mp 54−56 °C; IR (neat) 2893, 2361, 1620, 1474, 1296, 1142, 1034, 941 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.10 (t, J = 8.7 Hz, 2H), 4.54 (t, J = 8.7 Hz, 2H), 5.87 (s, 2H), 6.37 (s, 1H), 6.65 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 30.0 (CH_2), 72.0 (CH_2), 93.0 (CH), 101.1 (CH_2), 105.0 (CH), 117.7 (C), 141.4 (C), 147.1 (C), 154.6 (C); MS (EI) m/z 164 (M^+, 100), 133 (18), 84 (48), 78 (20); HRMS (EI) calcd for $C_9H_8O_3$ (M^+) 164.0473, found 164.0469.

2,3-Dihydro-5,6-ethylenedioxybenzofuran (4d). 2,3-Dihydro-5,6-ethylenedioxybenzofuran (**4d**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using 1′-(dihydro-3,4-benzodioxinyl)ethan-2′-ol (**3d**) (0.106 g, 0.590 mmol). The iodination step was carried out at 40 °C for 4 h. Purification by flash column chromatography (petroleum ether/ethyl acetate, 9:1) gave 2,3-dihydro-5,6-ethylenedioxybenzofuran (**4d**) (0.062 g, 60%) as a white solid. Mp 64−66 °C; IR (neat) 2992, 1607, 1486, 1327, 1185, 1060, 931 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.10 (t, J = 8.3 Hz, 2H), 4.15−4.23 (m, 4H), 4.50 (t, J = 8.3 Hz, 2H), 6.34 (s, 1H), 6.70 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 29.6 (CH_2), 64.1 (CH_2), 64.5 (CH_2), 71.6 (CH_2), 98.4 (CH), 113.2 (CH), 119.2 (C), 137.3 (C), 142.8 (C), 154.3 (C); MS (EI) m/z 178 (M^+, 100), 122 (92), 69 (25); HRMS (EI) calcd for $C_{10}H_{10}O_3$ (M^+) 178.0630, found 178.0625.

5-Acetamido-2,3-dihydrobenzofuran (4e).[69] 5-Acetamido-2,3-dihydrobenzofuran (**4e**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using 1′-(3-acetamidophenyl)ethan-2′-ol (**3e**) (0.027 g, 0.15 mmol). The iodination step was carried out at 40 °C for 4 h. Purification by flash column chromatography (petroleum ether/ethyl acetate, 1:1) gave 5-acetamido-2,3-dihydrobenzofuran (**4e**) (0.014 g, 56%) as a white solid. Mp 94−96 °C (lit.[69] 93−95 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 2.12 (s, 3H), 3.17 (t, J = 8.4 Hz, 2H), 4.54 (t, J = 8.4 Hz, 2H), 6.69 (d, J = 8.5 Hz, 1H), 7.00 (dd, J = 8.5, 2.2 Hz, 1H) 7.44−7.49 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 24.2 (CH_3), 29.9 (CH_2), 71.5 (CH_2), 109.0 (CH), 118.6 (CH), 120.7 (CH), 127.6 (C), 130.8 (C), 157.0 (C), 168.6 (C); MS (ESI) m/z 200 (M + Na^+, 100).

2,3-Dihydro-2,2-dimethyl-5-methoxybenzofuran (4f).[12] 2,3-Dihydro-2,2-dimethyl-5-methoxybenzofuran (**4f**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using 2′,2′-dimethyl-1′-(3-methoxyphenyl)ethan-2′-ol (**3f**) (0.120 g, 0.670 mmol). Purification by flash column chromatography (petroleum ether/diethyl ether, 19:1) gave 2,3-dihydro-2,2-dimethyl-5-methoxybenzofuran (**4f**) (0.082 g, 69%) as a colorless oil. Spectroscopic data were consistent with the literature.[12] ^1H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 6H), 2.98 (s, 2H), 3.74 (s, 3H), 6.60−6.67 (m, 2H), 6.71−6.75 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 28.1 (2 × CH_3), 43.3 (CH_2), 56.0 (CH_3), 86.5 (C), 109.3 (CH), 111.6 (CH), 112.8 (CH), 128.1 (C), 153.1 (C), 153.8 (C); MS (ESI) m/z 201 (M + Na^+, 100).

2,3-Dihydro-2-(4′-methoxyphenyl)-5-methoxybenzofuran (4g).[5b] 2,3-Dihydro-2-(4′-methoxyphenyl)-5-methoxybenzofuran (**4g**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using 1′-(3-methoxyphenyl)-2′-(4′′-methoxyphenyl)ethan-2′-ol (**3g**) (0.050 g, 0.19 mmol). The *O*-arylation step was carried out at 130 °C for 18 h. Purification by flash column chromatography (hexane/dichloromethane, 1:1) gave 2,3-dihydro-2-(4′-methoxyphenyl)-5-methoxybenzofuran (**4g**) (0.013 g, 29%) as a colorless oil. Spectroscopic data were consistent with the literature.[5b] ^1H NMR (400 MHz, $CDCl_3$) δ 3.19 (dd, J = 15.7, 8.3 Hz, 1H), 3.55 (dd, J = 15.7, 9.0 Hz, 1H), 3.77 (s, 3H), 3.81 (s, 3H), 5.68 (dd, J = 9.0, 8.3 Hz, 1H), 6.65−6.84 (m, 3H), 6.89 (d, J = 8.7 Hz, 2H), 7.33 (d, J = 8.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 38.7 (CH_2), 55.3 (CH_3), 56.1 (CH_3), 84.2 (CH), 109.2 (CH), 111.2 (CH), 113.0 (CH), 114.0 (2 × CH), 127.3 (2 × CH), 127.7 (C), 133.9 (C), 153.7 (C), 154.2 (C), 159.5 (C); MS (ESI) m/z 279 (M + Na^+, 100).

2,3-Dihydro-5-methoxy-2-phenylbenzofuran (4h).[12] 2,3-Dihydro-5-methoxy-2-phenylbenzofuran (**4h**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using 1′-(3-methoxyphenyl)-2′-phenylethan-2′-ol (**3h**) (0.084 g, 0.37 mmol). The iodination step was carried out at 40 °C for 4 h, and the *O*-arylation step, at 130 °C for 22 h. Purification by flash column chromatography (petroleum ether/ethyl acetate, 19:1) gave 2,3-dihydro-5-methoxy-2-phenylbenzofuran (**4h**) (0.053 g, 64%) as a colorless oil. Spectroscopic data were consistent with the literature.[12] ^1H NMR (400 MHz, $CDCl_3$) δ 3.18 (dd, J = 15.7, 8.2 Hz, 1H), 3.59 (dd, J = 15.7, 9.4 Hz, 1H), 3.76 (s, 3H), 5.72 (dd, J = 9.4, 8.2 Hz, 1H), 6.69 (dd, J = 8.7, 2.6 Hz, 1H), 6.74−6.80 (m, 2H), 7.26−7.43 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 38.9 (CH_2), 56.1 (CH_3), 84.3 (CH), 109.2 (CH), 111.2 (CH), 113.1 (CH), 125.8 (2 × CH), 127.5 (C), 128.0 (CH), 128.7 (2 × CH), 142.1 (C), 153.8 (C), 154.3 (C); MS (ESI) m/z 249 (M + Na^+, 100).

2-(4′-Chlorophenyl)-2,3-dihydro-5-methoxybenzofuran (4i).[70] 2-(4′-Chlorophenyl)-2,3-dihydro-5-methoxybenzofuran (**4i**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using 2′-(4′′-chlorophenyl)-1′-(3-methoxyphenyl)ethan-2′-ol (**3i**) (0.154 g, 0.590 mmol). The iodination step was carried out at 40 °C for 4 h, and the *O*-arylation step, at 130 °C for 22 h. Purification by flash column chromatography (petroleum ether/ethyl acetate, 19:1) gave 2-(4′-chlorophenyl)-2,3-dihydro-5-methoxybenzofuran (**4i**) (0.096 g, 63%) as a white solid. Mp 58−60 °C (lit.[70] 60−61 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 3.13 (dd, J = 15.7, 8.0 Hz, 1H), 3.60 (dd, J = 15.7, 9.4 Hz, 1H), 3.76 (s, 3H), 5.70 (dd, J = 9.4, 8.0 Hz, 1H), 6.70 (dd, J = 8.7, 2.6 Hz, 1H), 6.74−6.80 (m, 2H), 7.33 (br s, 4H); δ_C (101 MHz, $CDCl_3$) δ 38.9 (CH_2), 56.0 (CH_3), 83.4 (CH), 109.3 (CH), 111.2 (CH), 113.1 (CH), 127.1 (2 × CH), 127.1 (C), 128.8 (2 × CH), 133.7 (C), 140.6 (C), 153.6 (C), 154.4 (C); MS (ESI) m/z 283 (M + Na^+, 100).

2,3-Dihydro-6-methoxy-1-benzopyran (4j).[12] 2,3-Dihydro-6-methoxybenzopyran (**4j**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using 1′-(3-methoxyphenyl)propan-3′-ol (**3j**) (0.083 g, 0.50 mmol). The *O*-arylation step was carried out at 150 °C for 24 h. Purification by flash column chromatography (hexane/dichloromethane, 1:1) gave 2,3-dihydro-6-methoxy-1-benzopyran (**4j**) (0.046 g, 57%) as a colorless oil. Spectroscopic data were consistent with the literature.[12] ^1H NMR (400 MHz, $CDCl_3$) δ 1.94−2.02 (m, 2H), 2.77 (t, J = 6.5 Hz, 2H), 3.74 (s, 3H), 4.13 (t, J = 5.2 Hz, 2H), 6.58 (d, J = 2.9 Hz, 1H), 6.66 (dd, J = 8.8, 2.9 Hz, 1H), 6.71 (d, J = 8.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 22.5 (CH_2), 25.2 (CH_2), 55.7 (CH_3), 66.3 (CH_2), 113.3 (CH), 114.4 (CH), 117.2 (CH), 122.7 (C), 149.0 (C), 153.2 (C); MS (EI) m/z 164 (M^+, 100), 149 (42), 136 (22), 108 (14), 84 (28), 77 (11).

2,3-Dihydro-6,7-dimethoxy-1-benzopyran (4k).[71] 2,3-Dihydro-6,7-dimethoxybenzopyran (**4k**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using 1′-(3,4-dimethoxyphenyl)-propan-3′-ol (**3k**) (0.049 g, 0.25 mmol). The *O*-arylation step was carried out at 150 °C for 24 h. Purification by flash column chromatography (hexane/ethyl acetate, 4:1) gave 2,3-dihydro-6,7-dimethoxy-1-benzopyran (**4k**) (0.027 g, 56%) as a colorless oil. Spectroscopic data were consistent with the literature.[71] ^1H NMR (500 MHz, $CDCl_3$) δ 1.95−2.02 (m, 2H), 2.70 (t, J = 6.6 Hz, 2H), 3.81 (s, 3H), 3.81 (s, 3H), 4.10−4.14 (m, 2H), 6.38 (s, 1H), 6.53 (s,

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1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 22.6 (CH_2), 24.3 (CH_2), 55.9 (CH_3), 56.5 (CH_3), 66.3 (CH_2), 100.9 (CH), 112.6 (C), 112.7 (CH), 143.0 (C), 148.3 (C), 148.7 (C); MS (EI) m/z 194 (M^+, 100), 179 (86), 149 (25), 123 (15), 57 (25).

2,3-Dihydro-6,7,8-trimethoxy-1-benzopyran (4l). 2,3-Dihydro-6,7-trimethoxy-1-benzopyran (**4l**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using 1′-(3,4,5-trimethoxyphenyl)propan-3′-ol (**3l**) (0.057 g, 0.25 mmol). The *O*-arylation step was carried out at 150 °C for 22 h. Purification by flash column chromatography (petroleum ether/ethyl acetate, 4:1) gave 2,3-dihydro-6,7,8-trimethoxy-1-benzopyran (**4l**) (0.029 g, 51%) as a colorless oil. IR (neat) 2932, 1489, 1462, 1420, 1277, 1219, 1126, 1099, 1072, 1011 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.95−2.03 (m, 2H), 2.73 (t, J = 6.5 Hz, 2H), 3.79 (s, 3H), 3.87 (s, 3H), 3.89 (s, 3H), 4.16−4.21 (m, 2H), 6.34 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 22.4 (CH_2), 24.8 (CH_2), 56.4 (CH_3), 61.1 (CH_3), 61.3 (CH_3), 66.4 (CH_2), 107.5 (CH), 117.1 (C), 141.4 (C), 142.3 (C), 142.6 (C), 146.6 (C); MS (ESI) m/z 247 (M + Na^+, 100); HRMS (ESI) calcd for $C_{12}H_{16}NaO_4$ (M + Na^+) 247.0941, found 247.0932.

1′-(3-Hydroxy-4-methoxyphenyl)-*N*-methoxy-*N*-methylacetamide. The reaction was carried out as described for *N*-methoxy-1′-(3-methoxyphenyl)-*N*-methylacetamide using 3-hydroxy-4-methoxyphenylacetic acid (**5**) (1.00 g, 5.49 mmol), except that the solvent used was acetonitrile (30 mL). Purification by flash column chromatography (petroleum ether/ethyl acetate, 3:7) gave 1′-(3-hydroxy-4-methoxyphenyl)-*N*-methoxy-*N*-methylacetamide (0.831 g, 68%) as a white solid. Mp 62−64 °C; IR (neat) 3323, 2939, 1642, 1590, 1511, 1440, 1271, 1131, 1006, 761 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.18 (s, 3H), 3.61 (s, 3H), 3.67 (s, 2H), 3.85 (s, 3H), 5.85 (s, 1H), 6.73−6.82 (m, 2H), 6.87 (d, J = 1.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 32.3 (CH_3), 38.7 (CH_2), 56.0 (CH_3), 61.3 (CH_3), 110.8 (CH and C), 115.7 (CH), 120.7 (CH), 128.1 (C), 145.6 (C), 172.7 (C); MS (ESI) m/z 248 (M + Na^+, 100); HRMS (ESI) calcd for $C_{11}H_{15}NNaO_4$ (M + Na^+) 248.0893, found 248.0889.

1′-(3-*tert*-Butyldimethylsilyloxy-4-methoxyphenyl)-*N*-methoxy-*N*-methylacetamide (6). To a solution of 1′-(3-hydroxy-4-methoxyphenyl)-*N*-methoxy-*N*-methylacetamide (1.23 g, 5.46 mmol) and imidazole (0.740 g, 10.9 mmol) in dry dichloromethane (40 mL) was added *tert*-butyldimethylsilyl chloride (0.99 g, 6.56 mmol) portionwise. 4-Dimethylaminopyridine (0.070 g, 0.55 mmol) was added, and the resulting suspension was stirred at room temperature for 16 h. The reaction was quenched with water (30 mL), and the mixture was extracted with dichloromethane (4 × 50 mL). The combined organic layers were washed with aqueous sodium hydrogen carbonate (100 mL) and brine (100 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/ethyl acetate, 4:1) gave 1′-(3-*tert*-butyldimethylsilyloxy-4-methoxyphenyl)-*N*-methoxy-*N*-methylacetamide (**6**) (1.87 g, 100%) as a colorless oil. IR (neat) 2932, 1663, 1512, 1271, 1136, 988, 839 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.15 (s, 6H), 0.99 (s, 9H), 3.18 (s, 3H), 3.58 (s, 3H), 3.65 (s, 2H), 3.78 (s, 3H), 6.78 (d, J = 8.2 Hz, 1H), 6.80 (d, J = 2.0 Hz, 1H), 6.83 (dd, J = 8.2, 2.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ − 4.6 (2 × CH_3), 18.4 (C), 25.8 (3 × CH_3), 32.8 (CH_3), 38.8 (CH_2), 55.6 (CH_3), 61.3 (CH_3), 112.2 (CH), 122.1 (CH), 122.3 (CH), 127.5 (C), 144.9 (C), 149.9 (C), 172.7 (C); MS (ESI) m/z 362 (M + Na^+, 100); HRMS (ESI) calcd for $C_{17}H_{29}NNaO_4Si$ (M + Na^+) 362.1758, found 362.1745.

1′-(3-*tert*-Butyldimethylsilyloxy-4-methoxyphenyl)-2′-phenylethan-2′-one. The reaction was carried out as described for 1′-(3-methoxyphenyl)-2′-phenylethan-2′-one using 1′-(3-*tert*-butyldimethylsilyloxy-4-methoxyphenyl)-*N*-methoxy-*N*-methylacetamide (**6**) (1.71 g, 5.03 mmol). Purification by flash column chromatography (petroleum ether/ethyl acetate, 4:1) gave 1′-(3-*tert*-butyldimethylsilyloxy-4-methoxyphenyl)-2′-phenylethan-2′-one (1.32 g, 74%) as a white solid. Mp 60−62 °C; IR (neat) 2930, 1680, 1510, 1271, 1136, 984, 839 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.12 (s, 6H), 0.97 (s, 9H), 3.77 (s, 3H), 4.16 (s, 2H), 6.76 (d, J = 1.4 Hz, 1H), 6.77−6.82 (m, 2H), 7.40−7.46 (m, 2H), 7.50−7.55 (m, 1H), 7.94−8.01 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ −4.6 (2 × CH_3), 18.4 (C), 25.7 (3 × CH_3), 45.0 (CH_2), 55.5 (CH_3), 112.4 (CH), 122.2 (CH), 122.5 (CH), 127.0 (C), 128.6 (2 × CH), 128.7 (2 × CH), 133.0 (CH), 136.7 (C), 145.1 (C), 149.9 (C), 197.9 (C); MS (ESI) m/z 379 (M + Na^+, 100); HRMS (ESI) calcd for $C_{21}H_{28}NaO_3Si$ (M + Na^+) 379.1700, found 379.1686.

1′-(3-*tert*-Butyldimethylsilyloxy-4-methoxyphenyl)-1′-methyl-2′-phenylethan-2′-one (7). An oven-dried three-neck flask was flushed with argon and charged with 1′-(3-*tert*-butyldimethylsilyloxy-4-methoxyphenyl)-2′-phenylethan-2′-one (1.32 g, 3.69 mmol) in dry tetrahydrofuran (30 mL). To this solution was added lithium bis(trimethylsilyl)amide (4.06 mL, 4.06 mmol, 1.0 M in tetrahydrofuran) dropwise at −78 °C. The reaction mixture was stirred at −78 °C for 0.5 h before methyl iodide (0.690 mL, 11.1 mmol) was added dropwise. The resulting solution was stirred for 1 h, at −78 °C, then slowly warmed to 0 °C, and stirred for a further 1 h. A saturated solution of ammonium chloride (30 mL) was added at 0 °C, and the solution was extracted with diethyl ether (3 × 50 mL). The combined ethereal extracts were washed with brine (100 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/ethyl acetate, 19:1) gave 1′-(3-*tert*-butyldimethylsilyloxy-4-methoxyphenyl)-1′-methyl-2′-phenylethan-2′-one (**7**) (1.19 g, 87%) as a colorless oil. IR (neat) 2930, 1684, 1506, 1275, 1138, 970, 837 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.09 (s, 6H), 0.96 (s, 9H), 1.48 (d, J = 6.8 Hz, 3H), 3.73 (s, 3H), 4.53 (q, J = 6.8 Hz, 1H), 6.74 (d, J = 8.5 Hz, 1H), 6.75 (d, J = 2.0 Hz, 1H), 6.79 (dd, J = 8.5, 2.0 Hz, 1H), 7.32−7.39 (m, 2H), 7.42−7.48 (m, 1H), 7.89−7.94 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ − 4.6 (2 × CH_3), 18.5 (C), 19.3 (CH_3), 25.7 (3 × CH_3), 47.3 (CH), 55.5 (CH_3), 112.6 (CH), 120.7 (CH), 120.8 (CH), 128.4 (2 × CH), 128.8 (2 × CH), 132.6 (CH), 134.1 (C), 136.6 (C), 145.3 (C), 149.9 (C), 200.4 (C); MS (ESI) m/z 393 (M + Na^+, 100); HRMS (ESI) calcd for $C_{22}H_{30}NaO_3Si$ (M + Na^+) 393.1856, found 393.1848.

(1′*R*,2′*R*)-1′-(3-*tert*-Butyldimethylsilyloxy-4-methoxyphenyl)-1′-methyl-2′-phenylethan-2′-ol (8). To an oven-dried conical flask was added potassium *tert*-butoxide (0.023 g, 0.16 mmol) and dichloro[(*S*)-(−)-5,5′-bis[di(3,5-xylyl)phosphino]-4,4′-bi-1,3-benzodioxole][(2S-(+)-1,1-bis(4-methoxyphenyl)-3-methyl-1,2-butanediamine]ruthenium(II) (0.025 g, 0.012 mmol). Distilled 2-propanol (1 mL) was added, and the resulting yellow solution was stirred at room temperature for 2 h under a constant stream of argon. 1′-(3-*tert*-Butyldimethylsilyloxy-4-methoxyphenyl)-1′-methyl-2′-phenylethan-2′-one (**7**) (0.270 g, 0.730 mmol) in 2-propanol (2 mL) was added to the conical flask containing the catalyst solution and hydrogenated at 10 bar for 48 h. The reaction mixture was treated with activated carbon and stirred for 1 h. The mixture was filtered through Celite and concentrated in vacuo. Purification by flash column chromatography (hexane/diethyl ether, 7:3) gave (1′*R*,2′*R*)-1′-(3-*tert*-butyldimethylsilyloxy-4-methoxyphenyl)-1′-methyl-2′-phenylethan-2′-ol (**8**) (0.192 g, 64%) as a colorless oil. IR (neat) 3454, 2929, 1508, 1275, 1139, 962, 836 cm^{-1}; $[\alpha]_D^{23}$ +34.4 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.15 (s, 6H), 1.00 (s, 9H), 1.03 (d, J = 7.2 Hz, 3H), 1.90 (d, J = 1.4 Hz, 1H), 2.89 (dq, J = 8.6, 7.2 Hz, 1H), 3.80 (s, 3H), 4.55 (dd, J = 8.6, 1.4 Hz, 1H), 6.73−6.77 (m, 1H), 6.80−6.84 (m, 2H), 7.24−7.36 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ −4.5 (2 × CH_3), 18.3 (CH_3), 18.5 (C), 25.8 (3 × CH_3), 47.5 (CH), 55.6 (CH_3), 79.7 (CH), 112.2 (CH), 120.6 (CH), 121.2 (CH), 127.0 (2 × CH), 127.7 (CH), 128.2 (2 × CH), 135.6 (C), 142.5 (C), 145.2 (C), 149.9 (C); MS (ESI) m/z 395 (M + Na^+, 100); HRMS (ESI) calcd for $C_{22}H_{32}NaO_3Si$ (M + Na^+) 395.2013, found 395.2023. Enantiomeric excess was determined by HPLC analysis, using a chiralcel AD-H column (hexane/*i*-propanol 98:2, flow rate 1.0 mL min^{-1}); t_{minor} = 10.65 min, t_{major} = 14.55 min, er = 2.5:97.5.

(2*R*,3*R*)-5-(*tert*-Butyldimethylsilyloxy)-2,3-dihydro-6-methoxy-3-methyl-2-phenylbenzofuran (9). (2*R*,3*R*)-5-(*tert*-Butyldimethylsilyloxy)-2,3-dihydro-6-methoxy-3-methyl-2-phenylbenzofuran (**9**) was synthesized as described for 1-benzoyl-5-methoxyindoline (**2a**) using (1′*R*,2′*R*)-1′-(3-*tert*-butyldimethylsilyloxy-4-methoxyphenyl)-1′-methyl-2′-phenylethan-2′-ol (**8**) (0.060 g, 0.16 mmol). The iodination step was carried out at 50 °C for 7 h. Purification by flash column chromatography (hexane/dichloromethane, 3:2) gave (2*R*,3*R*)-5-(*tert*-butyldimethylsilyloxy)-2,3-dihy-

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dro-6-methoxy-3-methyl-2-phenylbenzofuran (**9**) (0.038 g, 63%) as a colorless oil. IR (neat) 2929, 1493, 1449, 1215, 1188, 1169, 904, 837 cm^{-1}; $[\alpha]_D^{20}$ +23.0 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.14 (s, 3H), 0.14 (s, 3H), 1.00 (s, 9H), 1.37 (d, *J* = 6.7 Hz, 3H), 3.36 (dq, *J* = 8.9, 6.7 Hz, 1H), 3.77 (s, 3H), 5.11 (d, *J* = 8.9, 1H), 6.46 (s, 1H), 6.61 (s, 1H), 7.27−7.45 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ −4.7 (CH_3), −4.6 (CH_3), 18.4 (CH_3), 18.5 (C), 25.8 (3 × CH_3), 45.6 (CH), 55.7 (CH_3), 92.9 (CH), 95.0 (CH), 115.7 (CH), 122.4 (C), 126.1 (2 × CH), 128.1 (CH), 128.6 (2 × CH), 139.0 (C), 141.1 (C), 150.8 (C), 153.6 (C); MS (EI) *m*/*z* 370 (M^+. 61), 313 (47), 298 (100), 257 (33), 146 (32), 91 (37), 73 (40); HRMS (EI) calcd for $C_{22}H_{30}O_3Si$ (M^+) 370.1964, found 370.1955.

(2*R*,3*R*)-2,3-Dihydro-5-hydroxyl-6-methoxy-3-methyl-2-phenylbenzofuran (10), [(+)-Obtusafuran].[26] To a stirred solution of (2*R*,3*R*)-5-(*tert*-butyldimethylsilyloxy)-2,3-dihydro-6-methoxy-3-methyl-2-phenylbenzofuran (**9**) (0.038 g, 0.10 mmol) in dry tetrahydrofuran (10 mL) was added tetrabutylammonium fluoride solution (0.15 mL, 0.15 mmol; 1.0 M in tetrahydrofuran) at 0 °C. The resulting solution was stirred at room temperature for 2 h. The reaction mixture was diluted with diethyl ether (10 mL), washed with water (2 × 10 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by flash column chromatography (hexane/diethyl ether, 7:3) gave (2*R*,3*R*)-2,3-dihydro-5-hydroxyl-6-methoxy-3-methyl-2-phenylbenzofuran (**10**) (0.023 g, 88%) as a white solid. Mp 108−110 °C (lit.[26] 111−113 °C); $[\alpha]_D^{23}$ +48.2 (*c* 0.5, MeOH), lit.[26] $[\alpha]_D^{25}$ +50.0 (*c* 0.33, MeOH); ^1H NMR (400 MHz, $CDCl_3$) δ 1.37 (d, *J* = 6.9 Hz, 3H), 3.38 (dq, *J* = 8.6, 6.9 Hz, 1H), 3.87 (s, 3H), 5.11 (d, *J* = 8.6 Hz, 1H), 5.24 (s, 1H), 6.50 (s, 1H), 6.72 (s, 1H), 7.29−7.44 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 18.4 (CH_3), 45.7 (CH), 56.2 (CH_3), 92.8 (CH), 94.2 (CH), 109.5 (CH), 122.9 (C), 126.0 (2 × CH), 128.1 (CH), 128.6 (2 × CH), 139.9 (C), 141.0 (C), 146.2 (C), 152.4 (C); MS (EI) *m*/*z* 256 (M^+, 100), 239 (11), 165 (12), 91 (10).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.8b02888.

Computational reactivity analyses, synthetic routes to all one-pot substrates, HPLC traces for **8** and ^1H and ^{13}C NMR spectra for all compounds (PDF)

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Notes

The authors declare no competing financial interest.

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