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Copper-Catalyzed Modular Amino Oxygenation of Alkenes: Access to Diverse 1,2-Amino Oxygen-Containing Skeletons

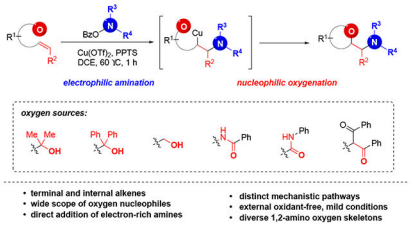
Brett N. Hemric, **Andy W. Chen**, **Qiu Wang***

Department of Chemistry, Duke University, Durham, North Carolina, United States

Abstract

Copper-catalyzed alkene amino oxygenation reactions using *O*-acylhydroxylamines have been achieved for a rapid and modular access to diverse 1,2-amino oxygen-containing molecules. This transformation is applicable to the use of alcohols, carbonyls, oximes and thio-carboxylic acids as nucleophiles on both terminal and internal alkenes. Mild reaction conditions tolerate a wide range of functional groups, including ether, ester, amide, carbamate, and halide. The reaction protocol allows for starting with free amines as the precursor of *O*-benzoylhydroxylamines to eliminate their isolation and purification, contributing to broader synthetic utilities. Mechanistic investigations reveal the amino oxygenation reactions may involve distinct pathways, depending on different oxygen nucleophiles.

Graphical Abstract



INTRODUCTION

1,2-Amino oxygen-containing skeletons are important and prevalent in pharmaceuticals, agrochemicals, and natural products.[1] Alkene amino oxygenation reactions, allowing for installation of an amino precursor and an oxygen group onto readily available alkenes, represents a direct, powerful transformation to construct these valued molecules.[2] Following the ground-breaking Sharpless aminohydroxylation reaction,[3] various methods have been developed for less toxic reagents, broader substrate scope, and higher levels of regioselectivity.[4] A particularly attractive approach is alkene amino oxygenation using an electrophilic amino source, which directs complementary chemo- and regio-selectivity and

*Corresponding Author: qiu.wang@duke.edu.

Supporting Information.

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eliminates the need of external oxidants in comparison to the methods involving nucleophilic amino precursors. Elegant examples have been reported to explore electrophilic amination-initiated alkene functionalization for direct addition of a sulfonamide,[5] azide,[6] *N*-carbamate,[7] and *N*-benzene sulfonimide[8] groups (Scheme 1). Yet less common is the installation of an electron-rich amino group directly in the alkene difunctionalization.[9–10]

In our own efforts in developing copper-catalyzed alkene amino difunctionalization methods, we recently reported an amino lactonization reaction that is enabled by a new alkene activation pathway involving *O*-benzoylhydroxylamine-mediated amination.[11] Such an alkene activation presents great potential as a powerful amination strategy in an analogous manner to electrophilic halogen and chalcogen reagents.[12] Herein, we report that this copper-catalyzed electrophilic alkene amination pathway enables the nucleophilic incorporation of different oxygen sources, such as alcohols, amides, oximes, and even thiocarboxylic acids for the synthesis of diverse amino-containing skeletons (Scheme 1). The reactions proceed within 2 h in a facile and regioselective manner on a broad variety of substrates with a good compatibility with functional groups. A great variety of skeletons obtained from this method represents an unprecedented class of 1,2 amino oxygen-containing compounds and a valuable addition to expand the chemical space. Furthermore, mechanistic investigations elucidate two distinct pathways that may be involved in the amino oxygenation reactions, depending on the nature of the oxygen nucleophile.

RESULTS AND DISCUSSION

Our studies began with the amino etherification reaction using the tertiary alcohol **1a** and 4-benzoyloxymorpholine **2a** as model substrates (Table 1). Under previously established amino lactonization conditions (entry 1),[11a] desired product **3a** was obtained in 36% yield. Among various additives examined (entries 2–8), pyridinium *p*-toluenesulfonate (PPTS) was found to be most effective, increasing the formation of **3a** to 66% yield (entry 8). Increasing the catalyst loading to 20 mol% ameliorates the reaction while reducing the loading to 5 mol % had no effect (entries 9–10). Finally, decreasing the reaction temperature to 60 °C gave comparable efficiency to the reaction at 80 °C, although further decreasing the temperature to 40 °C led to poorer efficacy (entries 11–12). Based on the results of reaction optimization studies,[13] we chose conditions in entry 11 as the standard conditions and confirmed the formation of **3a** in 76% isolation yield on a 0.4 mmol scale.

We next examined the scope of this amino etherification transformation under standard conditions (Table 2). Besides model substrate **1a**, tertiary alcohol **1b** gave trityl-substituted ether **3b** in 48% yield, which likely suffers from the increased steric strain. Secondary alcohols formed corresponding ether products **3c** and **3d** in comparable yields, showing no steric influence in this case. Analogous primary alcohol **1e** also formed **3e** in 38% yield. In addition to five-membered products, a six-membered ether **3f** was formed in 47% yield. Both electronic-rich and deficient substituents on the aromatic backbone were well tolerated, such as ether (**3g**), amide (**3h**), and halide (**3i**). Unsaturated alcohols bearing aliphatic backbones were effective in this transformation, regardless of substitution on the backbone (**3j–l**). Substitutions on the alkene were also examined. 1,1-Disubstituted alkenes were effective, ranging from unsaturated tertiary alcohols (**3m**, **3o**) to primary alcohols (**3n**, **3p–**

r). 1,2-Disubstituted internal alkenes were also tolerated (**3s–u**). The formation of **3s** from *E* and *Z* isomers in a mixture of two diastereomers also suggests common intermediates generated from both precursors. Even structurally complex, bridged cyclic ether **3u** was successfully formed, albeit in lower yield. The scope of amines was also examined using representative *O*-benzoylhydroxylamines. Six-membered amines bearing different functional groups were well tolerated (**3ab–ac**). Acyclic amines were readily installed, such as diethylamine (**3ad**), *N*-methylbenzyl amine (**3ae**) and *N*-methylphenethyl amine (**3af**). The inferior outcome of **3ae** suggests the presence of a reactive alpha-hydrogen may promote unwanted oxidation pathways, decreasing the efficiency. Additionally, highly sterically hindered amine precursors (i.e., dicyclohexylamine **3ag**) were not tolerated in this reaction.

The generality of this copper-catalyzed amino oxygenation reaction was examined on a more extensive range of potential oxygen sources (Table 3). We hypothesized that secondary amides would be potentially compatible oxygen nucleophiles, by a cyclization and deprotonation sequence. Benzamide-bearing terminal alkene **4a** and internal alkene **4b** both afforded desired 1,3-oxazine products **5a** and **5b** in 52% and 60% yields. The reaction with amide **4c** gave iminolactone **5c** in 35% yield, resulting from nucleophilic oxygen cyclization rather than nitrogen trapping.[14] Unsaturated 1,3-diones **4d–e** were examined in this reaction as potential oxygen nucleophile via the enol form, with **5d** formed in 31% yield. Oxime **4f** afforded desired dihydroisoxazole product **5f** under slightly modified conditions, with same efficacy on both 0.4 mmol and 2-mmol scales. Hydroxamic acids[4h] (**4g–h**) were ineffective in this reaction. Excitingly, unsaturated thioic acid **4i** was applicable for a copper-catalyzed aminothioation reaction, readily affording thiolactone **4i**, though in low yield. With such an extensive range of oxygen sources, this copper-catalyzed amino functionalization method provides rapid access to a great variety of 1,2 amino oxygen containing products that represents an unprecedented class of skeletons for an entirely new area of chemical space.

Mechanistically, this alkene amino etherification reaction was presumed to undergo a similar pathway to the previous amino lactonization reaction: electrophilic initiation by copper-catalyzed amination followed by nucleophilic trapping by the oxygen source. This hypothesis was probed and confirmed by the observations in mechanistic studies (Scheme 2). In the reaction of α-methyl substituted alkene **1v**, desired product **3v** formed in only 30% yield, along with an allylic amine **6** obtained in 16% yield (Scheme 2A). Two possible pathways may be involved in the formation of allylic amine **6**: (1) upon the electrophilic amination to the alkene, the resulting copper intermediate might undergo β-hydride elimination; alternatively (2) direct functionalization of C–H bond, without the involvement of the alkene. To elucidate the reaction pathways, α-CD_3 substituted alkene ***D*$_3$-1v** was subjected to the same conditions, providing amino oxygenation product ***D*$_2$-3v** in 43% yield along with the formation of allylic amine ***D*$_2$-6** in 15% yield. The lack of H-incorporation in any deuterium positions suggested the formation of ***D*$_2$-6** resulted from the elimination, rather than direct allylic C–H amination. To further elucidate the reaction pathways for different oxygen nucleophiles, we performed radical trapping experiments with 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) as a radical scavenger in the reaction of alcohol **1a**, amide **4a**, 1,3-dione **4d** and oxime **4f** (Scheme 4B). The reaction of **1a** in the presence of TEMPO generated TEMPO trapped product **7** in 33% yield while ether product **8** was not

observed. The reactions of amide **4a** and dione **4d** resulted in analogous TEMPO trapping products **9** and **11.** These result coincided with our earlier results[11a] (Scheme 2A), indicating that the amino etherification reaction was initiated by electrophilic amination of *O*-benzoylhydroxylamines followed by oxygen trapping as a secondary step.[15] However, the reaction of oxime **4f** in the presence of TEMPO did not provide expected TEMPO-trapping product **13**, but resulted in *exo*-cyclization product **14** with TEMPO trapping at the different vinyl position. This result implies that the oxime substrate class does not participate in the amination-initiation as the other classes of oxygen nucleophile, rather by an oxime radical cyclization followed by the amination trapping of *O*-benzoylhydroxylamines.[16] The TEMPO trapping was also attempted with thioic acid **4i**, yet with no TEMPO incorporated product observed. Another observation during our studies was that the geometric purity of the recovered internal alkenes was appreciably lower than the starting alkene (Scheme 2C). To further investigate this intriguing occurrence, we subjected 99% geometrically pure *E* and Z stilbenes to the reaction condition, as they had been shown to be poor substrates for the intermolecular amino oxygenation in the previous studies.[11b] The recovered stilbenes showed only 83% *E* and 84% Z, respectively. To exclude the possibility if the copper catalyst and/or heat was responsible for the observed isomerization, the control experiment in the absence of *O*-benzoylhydroxylamine **2a** was performed. In this case, quantitative recovery of each alkene was observed with over 99% retention, indicating the possibility that the amine addition to the alkene is reversible.

Based on these experimental results, the reaction mechanism is proposed in Scheme 3. Upon the reaction of Cu(I) salt (**I**) with *O*-benzoylhydroxylamine **2**, a highly reactive amino-Cu(III) complex would be formed, existing as either Cu(III) amino species or Cu(II) amino radical species (**II**). The addition of such reactive intermediates to the alkene (**1** or **4**) would produce Cu(III) intermediate (**III**), which eventually lead to the amino oxygenated product (**3** or **5**). Meanwhile, Cu-complex (**III**) may undergo β-hydride elimination to form allylic amine **6** as observed in Scheme 2A. Alternatively, this highly reactive Cu(III) intermediate could undergo homolytic cleavage to generate a radical (**IV**) that may be trapped by TEMPO, as evidenced in the formation of **7**, **9**, and **11** (Scheme 2B). The benefits of PPTS in this reaction possibly results from its role of assisting the release of copper catalyst from its coordination with the 1,2-amino oxygenated product, diminishing the unproductive pathways. It is important to note that the reaction pathways involving *O*-benzoylhydroxylamines can be distinctly different, depending on the choice of nucleophiles. For example, the reactions of unsaturated oximes do not involve the amination initiation as the other classes of oxygen nucleophile (Scheme 2B). In the copper-catalyzed analogous diamination reactions we reported previously,[16b] *O*-benzoylhydroxylamines also participate in the trapping step rather than in the initiation step.

We briefly demonstrated the unique advantages of the experimental protocol of this copper-catalyzed amino oxygenation reaction to highlight its practical use (Scheme 4). For example, starting with morpholine, treatment with BPO oxidation[17] followed by standard aminoetherification conditions successfully formed **3a** in 56% yield. Such adaptability that can eliminate the isolation step of *O*-benzoylhydroxylamines is particularly attractive. In another instance, the crude reaction mixture of **5a**, obtained from the amino oxygenation

reaction of benzamide **4a**, was readily converted into the free aniline either bearing benzoyl-protected alcohol (**15**) or free alcohol (**16**) by either acid-promoted or KOH-mediated hydrolysis, respectively.

CONCLUSION

In summary, we have developed a modular copper-catalyzed amino oxygenation of alkenes using *O*-benzoylhydroxylamines and a variety of oxygen nucleophiles, including alcohols, amides, and enols. Mechanistic investigations explicitly support reaction initiation by an electrophilic amination step from the *O*-benzoylhydroxylamine. Such distinct reaction pathways offer a new platform for alkene amino functionalization that directly installs electron-rich amine groups that were difficult in previous methods. The reaction also features mild conditions and good compatibility with broad substrate and functional groups. The diverse skeletons generated through this transformation are expected to greatly expand the chemical space and diversity of 1,2-amino oxy containing molecules that are highly valued and demanded, especially in organic synthesis and drug discovery.

EXPERIMENTAL SECTION

General Experimental Information.

Unless otherwise noted, reactions were performed without exclusion of air or moisture. All commercially available reagents and solvents were used as received unless otherwise stated. Analytical thin-layer chromatography (TLC) was performed using aluminum plates pre-coated with 0.25 mm of 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). TLC plates were visualized by exposure to ultraviolet light and/or exposure to $KMnO_4$ or vanillin stain. Organic solutions were concentrated *in vacuo* using a rotary evaporator. Column chromatography was performed with silica gel (60 Å, standard grade). Nuclear magnetic resonance spectra were recorded at ambient temperature (unless otherwise stated) on 400 MHz or 500 MHz spectrometers. All values for proton chemical shifts are reported in parts per million (ppm, δ) and are referenced to the residual protium in $CDCl_3$ (δ 7.26). All values for carbon chemical shifts are reported in parts per million (ppm, δ) and are referenced to the carbon resonances in $CDCl_3$ (δ 77.0). NMR data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, m = multiplet, br = broad), coupling constant (Hz), and integration. Infrared spectroscopic data was obtained on a Thermo Nicolet 380 or 6700 FTIR and is reported in wavenumbers (cm^{-1}). Most high-resolution mass spectra were obtained through the Duke University Mass Spectrometry Facility using a liquid chromatography-electrospray ionization mass spectrometer with TOF analysis. For some of these LCHRMS samples, LiBr was spiked in as a cationizing agent to stabilize the parent mass. Other high-resolution mass spectra were obtained through the Stapleton lab at Duke University using gas chromatography Thermo Q Exactive Hybrid Quadrupole-Orbitrap.

Amino Oxygenation Standard Conditions:

To a 4-mL vial with Teflon-coated micro stir bar was added alkene (0.4 mmol, 1.0 equiv), *O*-acylhydroxylamine (0.8 mmol, 2.0 equiv), copper(II) trifluoromethanesulfonate (28.8 mg,

0.08 mmol, 0.2 equiv), and pyridinium *p*-toluenesulfonate (100.6 mg, 0.4 mmol, 1.0 equiv), followed by addition of anhydrous 1,2-dichloroethane (2.0 mL). The resulting solution was stirred at 60 °C until the consumption of *O*-benzoylhydroxylamine (monitored by TLC using vanillin staining). The reaction mixture was filtered through a plug of activated, neutral (Brockman grade I, 58-60Å) Al_2O_3 and concentrated by rotary evaporation. The resulting crude mixture was subjected to flash column chromatography to provide amino oxygenation product.

4-((3,3-Dimethyl-1,3-dihydroisobenzofuran-1-yl)methyl)morpholine (3a).— Synthesized using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as a colorless oil (74.8 mg, 76%). $\mathbf{R_f}$ = 0.28 (5% MeOH– CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.30–7.20 (m, 3H), 7.09 (dd, *J* = 5.8, 1.7 Hz, 1H), 5.32 (dd, *J* = 7.5, 4.1 Hz, 1H), 3.75 (t, *J* = 4.6 Hz, 4H), 2.73–2.61 (m, 2H), 2.70 (dd, *J* = 13.0, 4.1 Hz, 1H), 2.61 (dd, *J* = 13.0, 7.5 Hz, 1H), 2.58–2.50 (m, 2H), 1.52 (s, 3H), 1.44 (s, 3H); **^{13}C {^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 147.2, 140.1, 127.7, 127.1, 121.6, 120.4, 85.3, 79.2, 66.8, 66.0, 54.4, 30.1, 29.0; **FTIR** (thin film): cm^{-1} 2966, 2806, 1454, 1116, 1034, 1009, 864, 760; **HRLCMS-ESI** (m/z) Calcd for ($C_{15}H_{22}NO_2$) ($[M+H]^+$): 248.1645; found: 248.1649.

4-((3,3-Diphenyl-1,3-dihydroisobenzofuran-1-yl)methyl)morpholine (3b).— Synthesized using standard conditions. Isolated by flash column chromatography (100% hexanes to 30% EtOAc–hexanes) as a white solid (71.0 mg, 48%). $\mathbf{R_f}$ = 0.29 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.35–7.17 (m, 14H), 5.39 (dd, *J* = 7.1, 4.3 Hz, 1H), 3.77–3.65 (m, 4H), 2.84 (dd, *J* = 13.2, 4.3 Hz, 1H), 2.73 (dd, *J* = 13.2, 7.1 Hz, 1H), 2.78–2.67 (m, 2H), 2.57–2.47 (m, 2H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 145.6, 144.6, 144.3, 141.3, 127.9, 127.8, 127.7, 127.6, 127.4, 127.2, 123.8, 121.6, 92.5, 80.1, 77.0, 67.0, 64.3, 54.3; **FTIR** (thin film): cm^{-1} 2853, 2810, 1446, 1117, 1009, 756, 699; **HRLCMS-ESI** (m/z) Calcd for ($C_{25}H_{26}NO_2$) ($[M+H]^+$): 372.1958; found: 372.1961.

4-((3-Methyl-1,3-dihydroisobenzofuran-1-yl)methyl)morpholine (3c).— Synthesized using standard conditions. Two diastereomers of **3c** were observed in the crude mixture in a ratio of 1.1:1 by ^{1}H NMR. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as a colorless oil (51.1 mg, 55%, as a mixture of two diastereomers in a ratio of 1.5:1 by ^{1}H NMR). $\mathbf{R_f}$ = 0.34 (5% MeOH– CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz, mixture of diastereomers): δ 7.33–7.19 (m, 3H [maj], 3H [min]), 7.18–7.10 (m, 1H [maj], 1H [min]), 5.49 (m, 1H [maj]), 5.34–5.21 (m, 1H [maj], 2H [min]), 3.76 (t, *J* = 4.7 Hz, 4H [maj], 4H [min]), 2.79 (dd, *J* = 13.1, 3.5 Hz), 2.74–2.52 (m, 5H [maj], 6H [min]), 1.51 (d, *J* = 6.3 Hz. 3H), 1.46 (d, *J* = 6.3 Hz, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 143.8, 143.6, 140.8, 140.4, 127.7, 127.7, 127.2, 121.4, 121.4, 120.8, 120.8, 80.5, 80.0, 79.3, 79.1, 66.8, 65.7, 64.7, 54.4, 54.2, 22.6, 22.1; **FTIR** (thin film): cm^{-1} 2964, 2852, 1453, 1116, 1069, 1035, 1009, 864, 748; **HRLCMS-ESI** (m/z) Calcd for ($C_{14}H_{20}NO_2$) ($[M+H]^+$): 234.1489; found: 234.1493.

4-((3-Phenyl-1,3-dihydroisobenzofuran-1-yl)methyl)morpholine (3d).— Synthesized using standard conditions. Two diastereomers of **3d** were observed in the crude mixture in a ratio of 1.1:1 by ^{1}H NMR. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as an off-white oil (76.3 mg, 66%, as a mixture of two diastereomers in a ratio of 1.4:1 by ^{1}H NMR). $\mathbf{R_f}$ = 0.30 (5% MeOH– CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz, mixture of diastereomers): δ 7.40–7.20 (m, 16H), 7.05 (d, *J* = 7.4 Hz, 1H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.25 (d, *J* = 2.7 Hz, 1H), 6.12 (d, *J* = 2.2 Hz, 1H), 5.68 (td, *J* = 5.8, 2.7 Hz, 1H), 5.48 (m, 1H), 3.78 (t, *J* = 4.7 Hz, 8H), 2.97 (dd, *J* = 13.2, 3.7 Hz, 1H), 2.82 (dd, *J* = 13.2, 7.5 Hz, 1H), 2.76 (d, *J* = 5.8 Hz, 2H), 2.86–2.68 (m, 4H), 2.67–2.56 (m, 4H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 142.6, 142.3, 142.2, 141.9, 128.4, 128.4, 128.0, 127.9, 127.6, 127.2, 126.8, 122.2, 121.5, 121.3, 85.6, 85.4, 81.6, 81.4, 66.9, 65.1, 64.7, 54.4, 52.2; **FTIR** (thin film): cm^{-1} 2852, 1454, 1115, 1035, 1009, 865, 750, 698; **HRLCMS-ESI** (m/z) Calcd for ($C_{19}H_{21}NO_2$) ($[M+H]^+$): 296.1645; found: 296.1649.

4-((1,3-Dihydroisobenzofuran-1-yl)methyl)morpholine (3e).—Synthesized using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as a clear, colorless oil (33.3 mg, 38%). $\mathbf{R_f}$ = 0.23 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.31–7.19 (m, 4H), 5.42–5.37 (m, 1H), 5.16 (dd, *J* = 12.3, 2.6 Hz, 1H), 5.06 (dd, *J* = 12.3, 1.0 Hz, 1H), 3.77 (t, *J* = 4.7 Hz, 4H), 2.71 (dd, *J* = 13.1, 3.7 Hz, 1H), 2.74–2.53 (m, 5H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 140.5, 139.4, 127.7, 127.2, 121.4, 120.9, 81.3, 72.7, 66.9, 64.5, 54.2; **FTIR** (thin film): cm^{-1} 2852, 1454, 1116, 1040, 1009, 865, 750; **HRLCMS-ESI** (m/z) Calcd for ($C_{13}H_{18}NO_2$) ($[M+H]^+$): 220.1332; found: 220.1335.

4-((1,1-Dimethylisochroman-3-yl)methyl)morpholine (3f).—Synthesized using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as a colorless oil (48.7 mg, 47%). $\mathbf{R_f}$ = 0.16 (5% MeOH– CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.21–7.04 (m, 4H), 4.13–4.02 (m, 1H), 3.74 (t, *J* = 4.7 Hz, 4H), 2.78–2.60 (m, 5H), 2.58–2.48 (m, 3H), 1.53 (s, 3H), 1.53 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 142.7, 132.7, 128.7, 126.0, 125.8, 125.0, 75.3, 66.8, 66.6, 63.7, 54.2, 33.8, 31.4, 28.5; **FTIR** (thin film): cm^{-1} 2931, 2853, 1448, 1270, 1117, 868, 759; **HRLCMS-ESI** (m/z) Calcd for ($C_{16}H_{24}NO_2$) ($[M+H]^+$): 262.1802; found: 262.1804.

4-((5-Methoxy-3,3-dimethyl-1,3-dihydroisobenzofuran-1-yl)methyl)morpholine (3g).—Synthesized using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as a white solid (99.9 mg, 90%). $\mathbf{R_f}$ = 0.27 (5% MeOH– CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.11 (d, *J* = 8.3 Hz, 1H), 6.77 (dd, *J* = 8.3, 2.3 Hz, 1H), 6.60 (d, *J* = 2.3 Hz, 1H), 5.26 (dd, *J* = 7.4, 4.0 Hz, 1H), 3.78 (s, 3H), 3.73 (t, *J* = 4.7 Hz, 4H), 2.69–2.61 (m, 2H), 2.65 (dd, *J* = 13.0, 4.0 Hz, 1H), 2.56 (dd, *J* = 13.0, 7.4 Hz, 1H), 2.55–2.49 (m, 2H), 1.50 (s, 3H), 1.42 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 159.8, 148.9, 132.1, 122.3, 113.0, 105.8, 85.0, 78.9, 66.8, 66.1, 55.3, 54.4, 29.9, 28.8; **FTIR** (thin film):

cm^{-1} 2965, 2853, 1613, 1496, 1454, 1290, 1228, 1115, 1033, 1008, 867; **HRLCMS-ESI** (m/z) Calcd for ($C_{16}H_{24}NO_3$) ($[M+H]^+$): 278.1751; found: 278.1755.

***N*-(3,3-Dimethyl-1-(morpholinomethyl)-1,3-dihydroisobenzofuran-5-yl)-*N*-methylbenzamide (3h).—**Synthesized using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc-hexanes with 5% NEt_3) as a tan solid (116.2 mg, 76%). $\mathbf{R_f}$ = 0.19 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.24–7.15 (m, 3H), 7.15–7.07 (m, 3H), 6.99 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.56 (s, 1H), 5.19 (dd, *J* = 7.1, 4.4 Hz, 1H), 3.70 (t, *J* = 4.7 Hz, 4H), 2.60 (dd, *J* = 13.0, 4.4 Hz, 1H), 2.53 (dd, *J* = 13.0, 7.1 Hz, 1H), 2.64–2.44 (m, 4H), 1.29 (s, 3H), 1.18 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 170.6, 148.3, 144.5, 138.2, 135.8, 129.3, 128.3, 127.6, 125.2, 122.2, 119.6, 84.8, 78.8, 66.8, 65.5, 54.3, 38.1, 29.6, 28.6; **FTIR** (thin film): cm^{-1} 2967, 2856, 1646, 1493, 1362, 1116, 1034, 1011, 796, 720, 701; **HRLCMS-ESI** (m/z) Calcd for ($C_{23}H_{29}N_2O_3$) ($[M+H]^+$): 381.2173; found: 381.2176.

4-((6-Chloro-3,3-dimethyl-1,3-dihydroisobenzofuran-1-yl)methyl)morpholine (3i).—Synthesized using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as a tan oil (78.1 mg, 69%). $\mathbf{R_f}$ = 0.33 (5% MeOH– CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.24–7.19 (m, 2H), 6.99 (d, *J* = 8.1 Hz, 1H), 5.25 (t, *J* = 5.8 Hz, 1H), 3.73 (t, *J* = 4.5 Hz, 1H), 2.69–2.57 (m, 4H), 2.56–2.48 (m, 2H), 1.49 (s, 3H), 1.41 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 145.8, 142.3, 132.9, 127.9, 122.0, 121.6, 85.1, 78.6, 66.8, 65.4, 54.4, 29.9, 28.8; **FTIR** (thin film): cm^{-1} 2967, 2854, 1455, 1280, 1116, 1035, 1009, 865, 820; **HRLCMS-ESI** (m/z) Calcd for ($C_{15}H_{21}ClNO_2$) ($[M+H]^+$): 282.1255; found: 282.1261.

4-((4,4-Diphenyltetrahydrofuran-2-yl)methyl)morpholine (3j).—Synthesized using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as an off-white solid (60.2 mg, 47%). $\mathbf{R_f}$ = 0.26 (5% MeOH– CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.37–7.15 (m, 10H), 4.64 (d, *J* = 8.8 Hz, 1H), 4.30–4.22 (m, 1H), 4.14 (d, *J* = 8.8 Hz, 1H), 3.72 (t, *J* = 4.8 Hz, 4H), 2.64–2.48 (m, 6H), 2.44 (dd, *J* = 13.0, 3.3 Hz, 1H), 2.35 (dd, *J* = 12.2, 9.7 Hz, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 146.0, 145.6, 128.4, 128.3, 127.1, 127.0, 126.4, 126.2, 76.9, 75.9, 66.8, 63.9, 55.4, 54.2, 43.4; **FTIR** (thin film): cm^{-1} 2854, 2808, 1494, 1447, 1116, 1067, 1014, 866, 700; **HRLCMS-ESI** (m/z) Calcd for ($C_{21}H_{26}NO_2$) ($[M+H]^+$): 324.1958; found: 324.1960.

4-((4,4-Dimethyltetrahydrofuran-2-yl)methyl)morpholine (3k).—Synthesized using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as a colorless oil (25.3 mg, 32%). $\mathbf{R_f}$ = 0.17 (5% MeOH– CH_2Cl_2); **^{1}H NMR** ($CDC1_3$, 400 MHz): δ 4.25–4.18 (m, 1H), 3.72 (dd, *J* = 5.3, 4.2 Hz, 4H), 3.51 (d, *J* = 8.2 Hz, 1H), 3.44 (d, *J* = 8.2 Hz, 1H), 2.57–2.46 (m, 5H), 2.38 (dd, *J* = 13.0, 3.1 Hz, 1H), 1.76 (dd, *J* = 12.2, 6.7 Hz, 1H), 1.34 (dd, *J* = 12.2, 9.1 Hz, 1H), 1.07 (s, 6H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ

80.2, 76.5, 66.8, 64.1, 54.2, 45.6, 39.1, 26.6, 26.4; **FTIR** (thin film): cm^{-1} 2955, 2853, 1454, 1293, 1118, 1064, 1010, 866; **HRLCMS-ESI** (m/z) Calcd for ($C_{11}H_{22}NO_2$) ($[M+H]^+$): 200.1645; found: 200.1646.

4-((Tetrahydrofuran-2-yl)methyl)morpholine (3l).—Synthesized using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as a colorless oil (16.3 mg, 24%). $\mathbf{R_f}$ = 0.05 (5% MeOH– CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 4.02 (tdd, *J* = 8.0, 6.7, 3.5 Hz, 1H), 3.87 (dt, *J* = 8.4, 6.8 Hz, 1H), 3.77–3.68 (m, 1H), 3.72 (t, *J* = 4.7 Hz, 4H), 2.55–2.49 (m, 4H), 2.47 (dd, *J* = 13.0, 8.0 Hz, 1H), 2.40 (dd, *J* = 13.0, 3.5 Hz, 1H), 1.97 (dddd, *J* = 11.8, 8.0, 6.8, 5.0 Hz, 1H), 1.90–1.78 (m, 2H), 1.48 (ddt, *J* = 11.8, 8.7, 8.0 Hz, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 76.3, 68.1, 66.8, 63.7, 54.2, 30.3, 25.3; **FTIR** (thin film): cm^{-1} 2955, 2855, 1454, 1118, 1068, 866; **HRLCMS-ESI** (m/z) Calcd for ($C_9H_{18}NO_2$) ($[M+H]^+$): 172.1332; found: 172.1335.

4-((3,3-Dimethyl-1-phenyl-1,3-dihydroisobenzofuran-1-yl)methyl)morpholine (3m).—Synthesized using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as a tan oil (67.4 mg, 52%). $\mathbf{R_f}$ = 0.10 (25% EtOAc–Hex); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.67–7.60 (m, 2H), 7.51–7.48 (m, 1H), 7.34–7.27 (m, 4H), 7.21 (tt, *J* = 7.3, 1.3 Hz, 1H), 7.13–7.08 (m, 1H), 3.55 (ddd, *J* = 10.9, 6.0, 3.3 Hz, 2H), 3.50 (ddd, *J* = 10.9, 6.0, 3.3 Hz, 2H), 2.98 (d, *J* = 14.0 Hz, 1H), 2.90 (d, *J* = 14.0, 1H), 2.49 (ddd, *J* = 11.3, 6.0, 3.3 Hz, 2H), 2.42 (ddd, *J* = 11.3, 6.0, 3.3 Hz, 2H), 1.66 (s, 3H), 1.43 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 147.3, 145.3, 142.3, 127.8, 127.1, 126.7, 125.7, 122.8, 120.6, 89.8, 85.2, 69.2, 67.1, 55.3, 30.0, 30.0; **FTIR** (thin film): cm^{-1} 2967, 1749, 1452, 1116, 1011, 970, 862, 758; **HRLCMS-ESI** (m/z) Calcd for ($C_{21}H_{26}NO_2$) ($[M+H]^+$): 324.1958; found: 324.1959.

4-((1-Phenyl-1,3-dihydroisobenzofuran-1-yl)methyl)morpholine (3n).—Synthesized using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as an orange oil (52.5 mg, 44%). $\mathbf{R_f}$ = 0.41 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.63–7.58 (m, 2H), 7.47–7.42 (m, 1H), 7.39–7.22 (m, 6H), 5.27 (d, *J* = 12.0 Hz, 1H), 5.19 (d, *J* = 12.0 Hz, 1H), 3.61–3.47 (m, 4H), 3.11 (d, *J* = 13.9 Hz, 1H), 3.03 (d, *J* = 13.9 Hz, 1H), 2.52 (ddd, *J* = 11.3, 5.7, 3.5 Hz, 2H), 2.41 (ddd, *J* = 11.3, 5.7, 3.5 Hz, 2H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 143.8, 143.5, 139.5, 128.0, 127.5, 127.0, 127.0, 125.5, 122.4, 120.9, 91.3, 72.0, 67.5, 67.2, 55.0; **FTIR** (thin film): cm^{-1} 2849, 2802, 1452, 1315, 1145, 1115, 1025, 864, 751, 726, 698; **HRLCMS-ESI** (m/z) Calcd for ($C_{19}H_{22}NO_2$) ($[M+H]^+$): 296.1645; found: 296.1647.

4-((2,5,5-Triphenyltetrahydrofuran-2-yl)methyl)morpholine (3o).—Synthesized using standard conditions. Isolated by flash column chromatography (100% hexanes to 30% EtOAc–hexanes) as an off-white oil (41.8 mg, 26%). $\mathbf{R_f}$ = 0.29 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.63–7.57 (m, 2H), 7.47–7.39 (m, 4H), 7.35–7.16 (m, 8H), 7.15–7.09 (m, 1H), 3.48 (t, *J* = 4.6 Hz, 4H), 2.86–2.79 (m, 1H), 2.76 (d, *J* = 13.8 Hz, 1H),

2.61 (d, *J* = 13.8 Hz, 1H), 2.55–2.40 (m, 3H), 2.38–2.21 (m, 4H); **$^{13}C\{^{1}H\}$ NMR** ($CDCl_3$, 125 MHz): δ 147.9, 147.4, 146.0, 127.9, 127.8, 127.4, 126.4, 126.3, 126.2, 125.8, 89.1, 89.0, 68.9, 67.1, 55.0, 37.2, 35.8; **FTIR** (thin film): cm^{-1} 2853, 2805, 1491, 1447, 1117, 749, 700; **HRLCMS-ESI** (m/z) Calcd for ($C_{27}H_{30}NO_2$) ($[M+H]^+$): 400.2271; found: 400.2274.

4-((2,4,4-Triphenyltetrahydrofuran-2-yl)methyl)morpholine (3p).—Synthesized using standard conditions. Isolated by flash column chromatography (100% hexanes to 40% EtOAc–hexanes) as an off-white solid (67.4 mg, 42%). $\mathbf{R_f}$ = 0.42 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.60–7.16 (m, 15H), 4.91 (d, *J* = 9.1 Hz, 1H), 4.41 (d, *J* = 9.1 Hz, 1H), 3.70–3.55 (m, 4H), 3.37 (d, *J* = 12.6 Hz, 1H), 3.26 (d, *J* = 12.6 Hz, 1H), 2.63 (d, *J* = 13.9 Hz, 1H), 2.55 (d, *J* = 13.9 Hz, 1H), 2.49–2.36 (m, 4H); **$^{13}C\{^{1}H\}$ NMR** ($CDCl_3$, 125 MHz): δ 146.9, 146.4, 145.7, 128.3, 128.0, 127.7, 127.2, 127.2, 126.3, 126.1, 125.9, 125.4, 88.1, 76.0, 68.5, 67.1, 56.4, 55.2, 49.2; **FTIR** (thin film): cm^{-1} 2851, 2803, 1493, 1446, 1116, 1059, 866, 757, 698; **HRLCMS-ESI** (m/z) Calcd for ($C_{27}H_{30}NO_2$) ($[M+H]^+$): 400.2271; found: 400.2276.

4-((4,4-Dimethyl-2-phenyltetrahydrofuran-2-yl)methyl)morpholine (3q).—Synthesized using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as a tan oil (68.8 mg, 62%). $\mathbf{R_f}$ = 0.31 (5% MeOH– CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.39–7.35 (m, 2H), 7.32–7.26 (m, 2H), 7.19 (tt, *J* = 7.2, 1.4 Hz, 1H), 3.64 (d, *J* = 8.0 Hz, 1H), 3.59 (ddd, *J* = 5.7, 3.6, 2.2 Hz, 4H), 3.51 (d, *J* = 8.0 Hz, 1H), 2.58–2.45 (m, 2H), 2.56 (d, *J* = 13.9 Hz, 1H), 2.48 (d, *J* = 13.9 Hz, 1H), 2.42 (ddd, *J* = 11.4, 5.7, 3.6 Hz), 2.27 (d, *J* = 12.3 Hz, 1H), 2.05 (d, *J* = 12.3, Hz, 1H), 1.16 (s, 3H),0.86 (s, 3H); **$^{13}C\{^{1}H\}$ NMR** ($CDCl_3$, 125 MHz): δ 146.8, 127.6, 126.1, 125.3, 88.4, 79.6, 68.9, 67.2, 55.2, 50.3, 40.0, 27.3, 26.9; **FTIR** (thin film): cm^{-1} 2955, 2850, 1447, 1317, 1117, 1059, 868, 703; **HRLCMS-ESI** (m/z) Calcd for ($C_{17}H_{26}NO_2$) ($[M+H]^+$): 276.1958; found: 276.1964.

4-((2-Phenyltetrahydrofuran-2-yl)methyl)morpholine (3r).—Synthesized using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as a tan solid (31.0 mg, 31%). $\mathbf{R_f}$ = 0.27 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.38 (d, *J* = 7.1 Hz, 2H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.21 (t, *J* = 6.9 Hz, 1H), 3.95 (q, *J* = 7.4 H, 1H), 3.86 (td, *J* = 7.9, 5.6 Hz, 1H), 3.65–3.56 (m, 4H), 2.66 (d, *J* = 13.8 Hz, 1H), 2.60–2.48 (m, 3H), 2.45–2.29 (m, 3H), 2.10 (ddd, *J* = 12.2, 7.7, 4.7 Hz, 1H), 2.01–1.90 (m, 1H), 1.82–1.70 (m, 1H); **$^{13}C\{^{1}H\}$ NMR** ($CDCl_3$, 125 MHz): δ 146.2, 127.8, 126.4, 125.5, 87.6, 67.8, 67.2, 55.2, 35.8, 25.7; **FTIR** (thin film): cm^{-1} 2955, 2851, 1452, 1118, 1060, 868, 703; **HRLCMS-ESI** (m/z) Calcd for ($C_{15}H_{22}NO_2$) ($[M+H]^+$): 248.1645; found: 248.1647.

4-((3,3-Dimethyl-1,3-dihydroisobenzofuran-1-yl)(phenyl)methyl)morpholine (3s).—From (*E*): Synthesized using standard conditions. Two diastereomers of **3s** were observed in the crude mixture in a ratio of 1.6:1 by GCMS. Isolated by flash column chromatography (100% hexanes to 40% EtOAc–hexanes) as a white solid (46.7 mg, 36%, as

a mixture of two diastereomers in a ratio of 1.6:1 by GCMS). From (*Z*): Synthesized using standard condition A. Two diastereomers of **3s** were observed in the crude mixture in a ratio of 1.3:1 by GCMS. Isolated by flash column chromatography (100% hexanes to 20% EtOAc–hexanes) as a white solid (37.9 mg, 29%, as a mixture of two diastereomers in a ratio of 1.3:1 by GCMS). $\mathbf{R_f}$ = 0.30 (5% MeOH– CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz, mixture of diastereomers): δ 7.43 (d, *J* = 7.5 Hz, 1H), 7.28–7.05 (m, 14H), 7.01–6.90 (m, 3H), 5.78 (d [broad], *J* = 5.6 Hz, 2H), 3.83–3.72, (m, 8H), 3.62 (d, *J* = 5.8 Hz, 1H), 3.59 (d, *J* = 5.0 Hz, 1H), 2.78–2.55 (m, 4H), 1.38 (s, 3H), 1.37 (s, 3H), 1.19 (s, 3H), 0.92 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 147.9, 147.3, 139.6, 138.2, 137.9, 136.2, 130.3, 130.2, 127.7, 127.6, 127.4, 127.2, 127.0, 126.8, 126.6, 123.4, 122.5, 120.3, 120.2, 85.4, 85.1, 81.5, 79.1, 74.9, 67.1, 52.8, 51.6, 29.7, 29.3, 28.7; **FTIR** (thin film): cm^{-1} 2965, 2851, 1451, 1360, 1116, 1013, 758, 703; **HRLCMS-ESI** (m/z) Calcd for ($C_{21}H_{26}NO_2$) ([M+H]$^+$): 324.1958; found: 324.1961.

4-(1-(3,3-Dimethyl-1,3-dihydroisobenzofuran-1-yl)ethyl)morpholine (3t).— Synthesized using standard conditions. Two diastereomers of **3t** were observed in the crude mixture in a ratio of 4:1 by ^{1}H NMR. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as a tan oil (73.1 mg, 70%, as a mixture of two diastereomers in a ratio of 5.4:1 by ^{1}H NMR). **Major diastereomer.** Isolated as a clear oil. $\mathbf{R_f}$ = 0.17 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.32–7.25 (m, 3H), 7.13–7.08 (m, 1H), 5.35 (d, *J* = 4.0 Hz, 1H), 3.80 (t, *J* = 4.6 Hz, 4H), 2.87–2.77 (m, 3H), 2.64 (dt, *J* = 11.6, 4.6 Hz, 2H), 1.54 (s, 3H), 1.45 (s, 3H), 0.94 (d, *J* = 6.7 Hz, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 147.2, 140.5, 127.5, 127.1, 121.8, 120.3, 85.0, 82.2, 67.3, 64.3, 50.0, 29.3, 28.9, 8.4; **FTIR** (thin film): cm^{-1} 2966, 2850, 1453, 1360, 1152, 1115, 1027, 992, 968, 854, 758; **HRLCMS-ESI** (m/z) Calcd for ($C_{16}H_{24}NO_2$) ([M+H]$^+$): 262.1802; found: 262.1800. **Minor diastereomer.** Isolated as a clear oil. $\mathbf{R_f}$ = 0.15 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.45 (d, *J* = 7.4 Hz, 1H), 7.32–7.22 (m, 2H), 7.10 (d, *J* = 6.9 Hz, 1H), 5.38 (d, *J* = 4.0 Hz, 1H), 3.74 (t, *J* = 4.6 Hz, 4H), 2.80 (qd, *J* = 6.7, 4.0 HZ, 1H), 2.75–2.66 (m, 4H), 1.59 (s, 3H), 1.45 (s, 3H), 0.96 (d, *J* = 6.7); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 148.1, 138.9, 127.5, 126.8, 122.9, 120.3, 84.6, 81.7, 67.5, 62.6, 51.5, 29.2, 28.8, 12.0; **FTIR** (thin film): cm^{-1} 2967, 2851, 2807, 1452, 1359, 1265, 1153, 1118, 1028, 970, 860, 761; **HRLCMS-ESI** (m/z) Calcd for ($C_{16}H_{24}NO_2$) ([M+H]$^+$): 262.1802; found: 262.1801.

4-(3,3,4-Trimethyl-2-oxabicyclo[2.2.1]heptan-6-yl)morpholine (3u).—Synthesized using standard conditions. Two diastereomers of **3u** were observed in the crude mixture in a ratio of 7:1 by both ^{1}H NMR and GCMS. The major isomer was isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as a white solid (15.8 mg, 18%). $\mathbf{R_f}$ = 0.13 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 4.19 (t, *J* = 2.3 Hz, 1H), 3.77–3.65 (m, 4H), 2.54–2.34 (m, 4H), 2.31–2.25 (m, 1H), 1.97 (ddd, *J* = 10.1, 3.7, 2.6 Hz, 1H), 1.71 (dt, *J* = 12.7, 3.5 Hz, 1H), 1.39 (dd, *J* = 12.7, 10.1 Hz, 1H), 1.34 (s, 3H), 1.27–1.23 (m, 1H), 1.09 (s, 3H), 1.04 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 82.1, 81.0, 76.0, 69.7, 69.0, 67.0, 60.4, 52.6, 51.6, 49.7, 48.1, 42.0, 39.8, 36.5, 31.5, 27.3, 26.6, 22.6, 21.6, 16.3, 14.1;

FTIR (thin film): cm^{-1} 2966, 2853, 2803, 1450, 1276, 1260, 1178, 1118; **HRLCMS-ESI** (m/z) Calcd for ($C_{13}H_{24}NO_2$) ($[M+H]^+$): 226.1802; found: 226.1805.

***Tert*-butyl 4-((3,3-dimethyl-1,3-dihydroisobenzofuran-1-yl)methyl)piperazine-1-carboxylate (3ab).—**Synthesized using standard conditions. Isolated by flash column chromatography (100% hexanes to 30% EtOAc–hexanes) as a colorless oil (87.6 mg, 63%). $\mathbf{R_f}$ = 0.23 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.30–7.19 (m, 3H), 7.09 (dd, *J* = 6.2, 1.8 Hz, 1H), 5.33 (dd, *J* = 7.5, 3.9 Hz, 1H), 3.48 (t, *J* = 4.6 Hz, 4H), 2.73 (dd, *J* = 13.1, 3.9 Hz, 1H), 2.67–2.58 (m, 3H), 2.56–2.44 (m, 2H), 1.53 (s, 3H), 1.45 (s, 9H), 1.45 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz, 60 °C): δ 154.8, 147.5, 140.3, 127.8, 127.2, 121.6, 120.5, 85.3, 79.7, 79.4, 65.5, 53.9, 43.7, 30.1, 29.0, 28.4; **FTIR** (thin film): cm^{-1} 2971, 2926, 2810, 1692, 1455, 1420, 1364, 1242, 1169, 1123, 1004, 760; **HRLCMS-ESI** (m/z) Calcd for ($C_{20}H_{31}N_2O_3$) ($[M+H]^+$): 347.2329; found: 347.2332.

Ethyl 1-((3,3-dimethyl-1,3-dihydroisobenzofuran-1-yl)methyl)piperidine-4-carboxylate (3ac).—Synthesized using standard conditions. Isolated by flash column chromatography (100% hexanes to 30% EtOAc–hexanes) as an orange oil (89.1 mg, 70%). $\mathbf{R_f}$ = 0.12 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.30–7.22 (m, 3H), 7.12–7.08 (m, 1H), 5.32 (dd, *J* = 7.1, 4.5 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.19–3.11 (m, 1H), 3.00–2.91 (m, 1H), 2.71 (dd, *J* = 13.1, 4.5 Hz, 1H), 2.62 (dd, *J* = 13.1, 7.1 Hz, 1H), 2.35–2.10 (m, 3H), 1.97–1.77 (m, 4H), 1.54 (s, 3H), 1.46 (s, 3H), 1.26 (t, *J* = 7.1 H, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 175.1, 147.2, 140.4, 127.6, 127.1, 121.7, 120.3, 85.2, 79.3, 65.7, 60.1, 54.0, 53.4, 41.0, 30.1, 29.0, 28.2, 28.1, 14.1; **FTIR** (thin film): cm^{-1} 2969, 1728, 1450, 1285, 1258, 1182, 1028, 760; **HRLCMS-ESI** (m/z) Calcd for ($C_{19}H_{28}NO_3$) ($[M+H]^+$): 318.2064; found: 318.2068.

***N*-((3,3-Dimethyl-1,3-dihydroisobenzofuran-1-yl)methyl)-N-ethylethanamine (3ad).—**Synthesized using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as a yellow oil (52.0 mg, 56%). $\mathbf{R_f}$ = 0.09 (10% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.30–7.22 (m, 3H), 7.13–7.08 (m, 1H), 5.27 (dd, *J* = 6.7, 5.3 Hz, 1H), 2.75 (d, *J* = 5.3 Hz, 1H), 2.74 (d, *J* = 6.7 Hz, 1H), 2.70 (q, *J* = 7.2 Hz, 2H), 2.69 (q, *J* = 7.2 Hz, 2H), 1.55 (s, 3H), 1.46 (s, 3H), 1.07 (t, *J* = 7.2 Hz, 6H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 147.4, 140.7, 127.5, 127.0, 121.8, 120.4, 85.0, 79.7, 60.2, 47.6, 30.1, 29.1, 11.6; **FTIR** (thin film): cm^{-1} 2968, 2805, 1455, 1376, 1359, 1154, 1029, 759; **HRLCMS-ESI** (m/z) Calcd for ($C_{15}H_{24}NO$) ($[M+H]^+$): 234.1852; found: 234.1854.

***N*-Benzyl-1-(3,3-dimethyl-1,3-dihydroisobenzofuran-1-yl)-*N*-methylmethanamine (3ae).—**Synthesized using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as a yellow oil (41.8 mg, 37%). $\mathbf{R_f}$ = 0.10 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.40–7.22 (m, 8H), 7.12 (dd, *J* = 6.3, 1.8 Hz, 1H), 5.41–5.36 (m, 1H), 3.70 (s, 2H), 2.74 (d, *J* = 5.2 Hz, 1H), 2.74 (d, *J* = 6.9 Hz, 1H), 2.43 (s, 3H), 1.53 (s, 3H), 1.49 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 147.3, 140.5, 138.8, 129.1, 128.1, 127.6, 127.1, 126.8, 121.7, 120.4, 85.2, 79.4, 63.8, 62.9,

43.0, 30.0, 29.1; **FTIR**(thin film): cm^{-1} 2969, 2790, 1454, 1360, 1154, 1024, 759, 737, 698; **HRLCMS-ESI** (m/z) Calcd for ($C_{19}H_{24}NO$) ($[M+H]^+$): 282.1852; found: 282.1855.

***N*-((3,3-Dimethyl-1,3-dihydroisobenzofuran-1-yl)methyl)-*N*-methyl-2-phenylethan-1-amine (3af).—**Synthesized using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) as an orange oil (84.9 mg, 72%). $\mathbf{R_f}$ = 0.20 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.34–7.12 (m, 9H), 5.35 (t, *J* = 6.0 Hz, 1H), 2.92–2.76 (m, 6H), 2.53 (s, 3H), E60 (s, 3H), 1.51 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 147.3, 140.5, 140.4, 128.6, 128.2, 127.6, 127.1, 125.8, 121.6, 120.4, 85.1, 79.2, 64.2, 60.2, 42.9, 33.4, 30.0, 29.0; **FTIR** (thin film): cm^{-1} 2969, 2793, 1453, 1359, 1028, 745, 698; **HRLCMS-ESI** (m/z) Calcd for ($C_{20}H_{26}NO$) ($[M+H]^+$): 296.2009; found: 296.2013.

4-(Morpholinomethyl)-2-phenyl-4*H*-benzo[*d*][1,3]oxazine (5a).—Synthesized using standard conditions. Isolated by flash column chromatography (100% Hexanes to 40% EtOAc–hexanes) as an off-white solid (64.0 mg, 52%). $\mathbf{R_f}$ = 0.35 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.20–8.14 (m, 2H), 7.53–7.42 (m, 3H), 7.35–7.28 (m, 2H), 7.18 (ddd, *J* = 7.5, 2.9 Hz, 1H), 7.07 (d, *J* = 7.5 Hz, 1H), 5.56 (dd, *J* = 7.9, 4.3 Hz, 1H), 3.71 (t, *J* = 4.6 Hz, 4H), 2.91 (dd, *J* = 13.8, 7.9 Hz, 1H), 2.65 (dd, *J* = 13.8, 4.3 Hz, 1H), 2.56 (t, *J* = 4.6 Hz, 4H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 156.6, 139.3, 132.7, 131.4, 129.0, 128.2, 128.0, 126.3, 124.9, 124.6, 124.4, 74.3, 67.1, 63.5, 54.1; **FTIR** (thin film): cm^{-1} 2956, 2852, 2809, 1623, 1598, 1573, 1483, 1450, 1261, 1116, 1081, 1070, 764, 694; **HRLCMS-ESI** (m/z) Calcd for ($C_{19}H_{21}N_2O_2$) ($[M+H]^+$): 309.1598; found: 309.1603.

4-(1-Morpholinoethyl)-2-phenyl-4H-benzo[d][1,3]oxazine (5b).—Synthesized using standard conditions. Two diastereomers of **5b** were observed in the crude mixture in a ratio of 3.3:1 by ^{1}H NMR. Isolated by flash column chromatography (100% Hexanes to 25% EtOAc–hexanes) to yield **5b** (77.7 mg, 60%). **Major diastereomer.** Isolated as a clear oil (60.6 mg, 47%). $\mathbf{R_f}$ = 0.27 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.17–8.10 (m, 2H), 7.54–7.40 (m, 3H), 7.33–7.24 (m, 2H), 7.18 (td, *J* = 7.1, 1.8 Hz, 1H), 7.04 (d, *J* = 7.4 Hz, 1H), 5.61 (d, *J* = 4.0 Hz, 1H), 3.75–3.63 (m, 4H), 2.92 (qd, *J* = 6.8, 4.0 Hz, 1H), 2.71 (ddd, *J* = 11.2 5.8, 3.3 Hz, 2H), 2.62 (ddd, *J* = 11.2, 5.8, 3.3 Hz, 2H), 1.11 (d, *J* = 6.8 Hz, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 156.6, 139.1, 132.4, 131.2, 128.6, 128.2, 127.6, 126.0, 125.0, 124.8, 123.9, 77.7, 67.2, 66.0, 50.0, 8.7; **FTIR** (thin film): cm^{-1} 2958, 2853, 1625, 1598, 1573, 1484, 1449, 1263, 1116, 1068, 1026, 762, 694; **HRLCMS-ESI** (m/z) Calcd for ($C_{20}H_{23}N_2O_2$) ($[M+H]^+$): 323.1754; found: 323.1762. **Minor diastereomer.** Isolated as a white solid (17.1 mg, 13%). $\mathbf{R_f}$ = 0.47 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.30–8.23 (m, 2H), 7.54–7.42 (m, 3H), 7.36–7.29 (m, 2H), 7.17 (td, *J* = 7.0, 2.2 Hz, 1H), 7.07 (d, *J* = 7.8 Hz, 1H), 5.29 (d, *J* = 7.7 Hz, 1H), 3.68 (t, *J* = 4.4 Hz, 4H), 3.00–2.90 (m, 1H), 2.69 (dt, *J* = 11.2, 4.4 Hz, 2H), 2.43 (dt, *J* = 11.2, 4.4 Hz, 2H), 0.97 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 157.2, 139.8, 132.7, 131.4, 128.8, 128.4, 128.1, 125.8, 125.6, 124.7, 124.4, 67.4, 61.9, 49.4, 9.3; **FTIR** (thin film): cm^{-1} 2953, 2853, 1620, 1596, 1572, 1481, 1449, 1242, 1117, 1069, 1027, 765, 694; **HRLCMS-ESI** (m/z) Calcd for ($C_{20}H_{23}N_2O_2$) ($[M+H]^+$): 323.1754; found: 323.1762.

(*Z*)-3-(Morpholinomethyl)-*N*-phenylisobenzofuran-1(3*H*)-imine (5c).—Synthesized using standard conditions. Isolated by flash column chromatography (5% EtOAc–hexanes to 50% EtOAc–hexanes) as a yellow oil (43.2 mg, 35%). $\mathbf{R_f}$ = 0.30 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.96 (d, *J* = 7.4 Hz, 1H), 7.59–7.46 (m, 3H), 7.37–7.27 (m, 4H), 7.10 (tt, *J* = 7.1, 1.6 Hz, 1H), 5.63 (dd, *J* = 6.8, 4.8 Hz, 1H), 3.70 (dt, *J* = 5.9, 3.6 Hz, 4H), 2.86 (dd, *J* = 13.6, 4.8 Hz, 1H), 2.74 (dd, *J* = 13.6, 6.8 Hz, 1H), 2.68 (ddd, *J* = 11.6, 5.8, 3.6 Hz, 2H), 2.51 (ddd, *J* = 11.6, 5.8, 3.6 Hz, 2H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 158.2, 146.5, 145.3, 131.8, 130.9, 129.0, 128.5, 123.9, 123.9, 123.3, 121.8, 82.5, 67.0, 62.8, 54.2; **FTIR** (thin film): cm^{-1} 2852, 2811, 1681, 1593, 1488, 1294, 1199, 1116, 1070, 1009, 866, 753, 695; **HRLCMS-ESI** (m/z) Calcd for ($C_{19}H_{21}N_2O_2$) ($[M+H]^+$): 309.1598; found: 309.1602.

(5-Methyl-5-(morpholinomethyl)-2-phenyl-4,5-dihydrofuran-3-yl) (phenyl)methanone (5e).—Synthesized using standard conditions. Isolated by flash column chromatography (100% hexanes to 30% EtOAc–hexanes) as a clear oil (44.6 mg, 31%). $\mathbf{R_f}$ = 0.30 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.42 (d, *J* = 7.8 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 1H), 7.17–7.12 (m, 3H), 7.09–7.00 (m, 4H), 3.71 (t, *J* = 4.6 Hz, 4H), 3.35 (d, *J* = 14.8 Hz, 1H), 2.96 (d, *J* = 14.8 Hz, 1H), 2.70–2.62 (m, 4H), 2.59 (ddd, *J* = 11.6, 4.6 Hz, 2H), 1.55 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 193.7, 164.7, 139.2, 130.9, 130.4, 129.8, 129.1, 128.8, 127.5, 112.0, 88.8, 67.1, 66.2, 55.1, 42.6, 24.8; **FTIR** (thin film): cm^{-1} 2925, 2852, 1611, 1592, 1573, 1491, 1446, 1367, 1272, 1249, 1117, 1069, 893, 865, 695; **HRLCMS-ESI** (m/z) Calcd for ($C_{23}H_{26}NO_3$) ($[M+H]^+$): 364.1907; found: 364.1912.

4-((3-Phenyl-4,5-dihydroisoxazol-5-yl)methyl)morpholine (5f).—Synthesized using standard conditions with the following modification: with copper(II) acetate instead of copper(II) trifluoromethanesulfonate and 1,2-dimethoxyethane instead of 1,2-dichloroethane. Isolated by flash column chromatography (100% hexanes to 70% EtOAc–hexanes) as a clear oil (49.1 mg, 50%).$\mathbf{R_f}$ = 0.23 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.68–7.64 (m, 2H), 7.41–7.37 (m, 3H), 4.90 (dddd, *J* = 10.5, 8.1, 6.5, 5.0 Hz, 1H), 3.69 (t, *J* = 4.7 Hz, 4H), 3.39 (dd, *J* = 16.6, 10.5 Hz, 1H), 3.18 (dd, *J* = 16.6, 8.1 Hz, 1H), 2.67 (dd, *J* = 13.2, 6.5 Hz, 1H), 2.62–2.49 (m, 4H), 2.57 (dd, *J* = 13.2, 5.0 Hz, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 156.4, 129.9, 129.5, 128.6, 126.5, 79.3, 66.8, 62.1, 54.1, 38.7; **FTIR** (thin film): cm^{-1} 2853, 1676, 1447, 1356, 1114, 1010, 905, 865, 760, 692; **HRLCMS-ESI** (m/z) Calcd for ($C_{14}H_{19}N_2O_2$) ($[M+H]^+$): 247.1441; found: 247.1443.

3-Methyl-3-(morpholinomethyl)benzo[*c*]thiophen-1(3H)-one (5i).—Synthesized using standard conditions. Isolated by flash column chromatography (100% hexanes to 30% EtOAc–hexanes) as a yellow oil (16.7 mg, 16%). $\mathbf{R_f}$ = 0.57 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.76 (d, *J* = 7.4 Hz, 1H), 7.59 (td, *J* = 7.4, 1.4 Hz, 1H), 7.55 (d, *J* = 7.4 Hz, 1H), 7.44 (td, *J* = 7.4, 1.4 Hz, 1H), 3.61 (ddd, *J* = 11.4, 6.1, 3.2 Hz, 2H), 3.56 (ddd, *J* = 11.4, 6.1, 3.2 Hz, 2H), 2.88 (d, *J* = 14.1 Hz, 1H), 2.77 (d, *J* = 14.1 Hz, 1H), 2.55 (ddd, *J* = 11.4, 6.1, 3.2 Hz, 2H), 2.48 (ddd, *J* = 11.4, 6.1, 3.2 Hz, 2H), 1.85 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 196.6, 154.0, 136.1, 133.0, 128.3, 123.6, 123.5, 68.9, 67.2, 62.1, 55.4,

25.8; **FTIR** (thin film): cm^{-1} 2958, 2849, 2806, 1682, 1455, 1116, 1010, 909, 863, 774; **HRLCMS-ESI** (m/z) Calcd for ($C_{14}H_{18}NO_2S$) ($[M+H]^+$): 264.1053; found: 264.1057.

4-((1,3,3-Trimethyl-1,3-dihydroisobenzofuran-1-yl)methyl)morpholine (3v).— Run using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3), followed by flash column chromatography (100% hexanes to 50% EtOAc–hexanes). Isolated as a white solid (30.9 mg, 30%). $\mathbf{R_f}$ = 0.32 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.44–7.36 (m, 2H), 7.26–7.21 (m, 2H), 3.78 (td, *J* = 5.8, 3.3 Hz, 4H), 2.81–2.74 (m, 2H), 2.72 (d, *J* = 13.8 Hz, 1H), 2.66 (d, *J* = 13.8 Hz, 1H), 2.63–2.55 (m, 2H), 1.68 (s, 3H), 1.66 (s, 3H), 1.64 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 146.8, 144.1, 127.6, 127.2, 121.3, 120.6, 87.1, 84.6, 68.9, 67.1, 55.4, 31.1, 30.3, 26.9; **FTIR** (thin film): cm^{-1} 2967, 2852, 1454, 1363, 1117, 1078, 978, 866, 756; **HRLCMS-ESI** (m/z) Calcd for ($C_{16}H_{24}NO_2$) ($[M+H]^+$): 262.1802; found: 262.1805.

2-(2-(3-Morpholinoprop-1-en-2-yl)phenyl)propan-2-ol (6).—Run using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3), followed by flash column chromatography (100% hexanes to 50% EtOAc–hexanes). Isolated as a clear, colorless oil (16.8 mg, 16%). $\mathbf{R_f}$ = 0.15 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.34 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.24 (td, *J* = 7.4, 1.5 Hz), 7.17 (td, *J* = 7.4, 1.5 Hz, 1H), 7.00 (dd, *J* = 7.4, 1.5 Hz, 1H), 5.30–5.28 (m, 1H), 5.05 (d, *J* = 1.9 Hz, 1H), 3.68 (t, *J* = 4.7 Hz, 4H), 3.22 (s, 2H), 2.59 (s, 1H), 2.56–2.47 (m, 4H), 1.60 (s, 6H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 148.7, 147.0, 139.2, 131.5, 127.0, 126.4, 126.1, 116.2, 73.2, 66.7, 66.0, 54.0, 33.2; **FTIR** (thin film): cm^{-1} 3443 (br), 2965, 2807, 1686, 1454, 1116, 1010, 865, 759; **HRLCMS-ESI** (m/z) Calcd for ($C_{16}H_{24}NO_2$) ($[M+H]^+$): 262.1802; found: 262.1803.

4-((3,3-Dimethyl-1-(methyl-*d*$_3$)-1,3-dihydroisobenzofuran-1-yl)methyl)morpholine (*D*$_3$-3v).—Synthesized using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3), followed by flash column chromatography (100% hexanes to 50% EtOAc–hexanes) as a yellow solid (46.0 mg, 43%). $\mathbf{R_f}$ = 0.32 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.44–7.36 (m, 2H), 7.27–7.21 (m, 2H), 3.78 (td, *J* = 5.8, 3.2 Hz, 4H), 2.81– 2.74 (m, 2H), 2.71 (d, *J* = 13.8 Hz, 1H), 2.66 (d, *J* = 13.8 Hz, 1H), 2.63–2.55 (m, 2H), 1.68 (s, 3H), 1.64 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 146.8, 144.2, 127.6, 127.2, 121.3, 120.6, 87.0, 84.6, 68.9, 67.2, 55.5, 31.1, 30.4, 26.1 (multiplet); **FTIR** (thin film): cm^{-1} 2966, 2852, 2804, 1453, 1117, 1073, 1036, 997, 971, 867, 759; **HRLCMS-ESI** (m/z) Calcd for ($C_{16}H_{21}D_3NO_2$) ($[M+H]^+$): 265.1989; found: 265.1991.

2-(2-(3-Morpholinoprop-1-en-2-yl-1,1-*d*$_2$)phenyl)propan-2-ol (*D*$_2$-6).—Synthesized using standard conditions. Isolated by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3), followed by flash column chromatography (100% hexanes to 50% EtOAc–hexanes)

as a colorless oil (16.1 mg, 15%). $\mathbf{R_f}$ = 0.23 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.34 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.24 (td, *J* = 7.5, 1.5 Hz, 1H), 7.17 (td, *J* = 7.5, 1.5 Hz, 1H), 7.00 (dd, *J* = 7.5, 1.5 Hz, 1H), 3.68 (t, *J* = 4.6 Hz, 4H), 3.22 (s, 2H), 2.57–2.46 (m, 4H), 1.72 (s, 1H), 1.60 (s, 6H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 148.5, 147.0, 139.2, 131.6, 127.1, 126.5, 126.1, 73.2, 66.7, 66.0, 54.0, 33.2 (note that the carbon peak for CD_2 could not be found); **FTIR** (thin film): cm^{-1} 3340 (broad), 2970, 1467, 1379, 1305, 1160, 1128, 950, 816; **HRLCMS-ESI** (m/z) Calcd for ($C_{16}H_{22}D_2NO_2$) ($[M+H]^+$): 264.1927; found: 264.1928.

2-(2-(2-Morpholino-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)ethyl)phenyl)propan-2-ol (7).—Synthesized using standard conditions with addition of TEMPO (1.0 equiv). Isolated by flash column chromatography (100% hexanes to 70% EtOAc–hexanes) as a colorless oil (53.2 mg, 33%). $\mathbf{R_f}$ = 0.29 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.54 (d, *J* = 7.5 Hz, 1H), 7.32–7.22 (m, 2H), 7.15 (t, *J* = 7.5 Hz, 1H), 6.83 (s, 1H), 5.99 (dd, *J* = 9.9, 5.1 Hz, 1H), 3.54–3.41 (m, 4H), 3.16 (dd, *J* = 13.2, 5.1 Hz, 1H), 2.52 (dd, *J* = 13.2, 9.9 Hz, 1H), 2.58–2.39 (m, 2H), 2.12–1.98 (m, 2H), 1.66 (s, 6H), 1.53–1.41 (m, 4H), 1.37 (s, 3H), 1.34–1.26 (m, 2H), 1.16 (s, 3H), 0.99 (s, 3H), 0.44 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 146.5, 142.0, 129.6, 126.8, 126.8, 125.1, 79.7, 72.4, 66.6, 64.6, 60.6, 59.1, 54.6, 40.6, 40.4, 33.8, 33.5, 33.4, 32.9, 20.4, 20.2, 17.0; **FTIR** (thin film): cm^{-1} 2970, 2929, 1456, 1360, 1116, 1004, 957, 867, 756; **HRLCMS-ESI** (m/z) Calcd for ($C_{24}H_{41}N_2O_3$) ($[M+H]^+$): 405.3112; found: 405.3115.

***N*-(2-(2-Morpholino-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)ethyl)phenyl)benzamide (9).—**Synthesized by standard conditions with addition of TEMPO (1.0 equiv). Isolated by flash column chromatography (100% hexanes to 50% EtOAc–hexanes) as a white solid (55.9 mg, 30%). $\mathbf{R_f}$ = 0.27 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 10.0 (s, 1H), 8.11 (d, *J* = 7.6 Hz, 1H), 7.98 (d, *J* = 7.3 Hz, 2H), 7.54 (t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.3 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.29–7.24 (m, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 5.00 (dd, *J* = 8.0, 5.3 Hz, 1H), 3.46 (t, *J* = 4.5 Hz, 1H), 3.12 (dd, *J* = 13.2, 5.3 Hz, 1H), 2.77 (13.2, 8.0 Hz, 1H), 2.44 (dt, *J* = 11.3, 4.5 Hz, 2H), 2.30 (dt, *J* = 11.3, 4.5 Hz, 2H), 1.54–1.26 (m, 6H), 1.31 (s, 3H), 1.21 (s, 3H), 0.96 (s, 3H), 0.62 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 165.6, 136.5, 135.4, 133.4, 131.6, 128.5, 128.3, 128.0, 127.3, 124.4, 123.4, 66.8, 62.7, 60.7, 59.9, 54.7, 40.5, 40.4, 33.8, 33.4, 20.7, 20.5, 17.0; **FTIR** (thin film): cm^{-1} 2931, 2851, 1674, 1588, 1520, 1450, 1303, 1117, 911, 754, 705; **HRLCMS-ESI** (m/z) Calcd for ($C_{28}H_{40}N_3O_3$) ($[M+H]^+$): 466.3064; found: 466.3070.

2-(2-Methyl-3-morpholino-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propyl)-1,3-diphenylpropane-1,3-dione (11).—Synthesized by standard conditions with addition of TEMPO (1.0 equiv). Isolated by flash column chromatography (100% hexanes to 75% EtOAc–hexanes) as a colorless oil (33.1 mg, 16%). $\mathbf{R_f}$ = 0.40 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.06 (d, *J* = 7.6 Hz, 4H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.40 (t, *J* = 7.6 Hz, 4H), 5.58 (dd, *J* = 5.9, 4.2 Hz, 1H), 3.39 (t, *J* = 4.7 Hz, 4H), 2.85 (dd, *J* = 14.5, 5.9 Hz, 1H), 2.77 (dd, *J* = 14.5, 4.2 Hz, 1H), 2.63 (d, *J* = 13.7 Hz, 1H), 2.53 (d, *J* = 13.7 Hz, 1H), 2.45–2.37 (m, 4H), 1.47–1.40 (m, 4H), 1.31 (s, 3H), 1.29–1.23 (m, 2H), 1.12 (s, 3H), 1.10 (s, 3H), 1.06 (s, 3H), 1.02 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 196.3, 195.9,

136.5, 136.1, 133.1, 133.1, 129.3, 129.2, 128.5, 82.0, 67.1, 66.7, 59.6, 59.4, 56.8, 55.1, 41.0, 38.8, 34.7, 34.6, 24.8, 21.1, 16.9; **FTIR** (thin film): cm^{-1} 2970, 2932, 1699, 1663, 1597, 1579, 1448, 1375, 1269, 1218, 1118, 1016, 920, 756, 692; **HRLCMS-ESI** (m/z) Calcd for ($C_{32}H_{44}N_2O_4$) ($[M+H]^+$): 521.3374; found: 521.3381.

3-Phenyl-5-(((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)-4,5-dihydroisoxazole (14).—Synthesized by standard condition with the following modification: with copper(II) acetate instead of copper(II) trifluoromethanesulfonate, 1,2-dimethoxyethane instead of 1,2-dichloroethane, and with addition of TEMPO (1.0 equiv). Isolated by flash column chromatography (100% hexanes to 70% EtOAc–hexanes) as a white solid (38.2 mg, 60%). $\mathbf{R_f}$ 0.56 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.73–7.65 (m, 2H), 7.44–7.36 (m, 3H), 4.87 (ddt, *J* = 10.9, 7.5, 4.7 Hz, 1H), 4.04–3.93 (m, 2H), 3.38 (dd, *J* = 16.4, 10.9 Hz, 1H), 3.25 (dd, *J* = 16.4, 7.5 Hz, 1H), 1.49–1.27 (m, 6H), 1.19 (s, 6H), 1.07 (s, 6H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 156.0, 129.8, 129.6, 128.6, 126.5, 79.1, 77.5, 60.0, 39.5, 37.0, 33.0, 32.9, 20.0, 16.9; **FTIR** (thin film): cm^{-1} 2971, 2929, 2869, 1469, 1447, 1374, 1357, 1262, 1246, 1132, 1060, 966, 912, 759, 692; **HRLCMS-ESI** (m/z) Calcd for ($C_{19}H_{29}N_2O_2$) ($[M+H]^+$): 317.2224; found: 317.2226.

Sequential Amino Oxidation/Amino Oxygenation Reaction.

To the solution of benzoyl peroxide (242.2 mg, 1 mmol, 2.5 equiv) and Na_2HPO_4 (212.9 mg, 3.75 equiv) in DMF (2.0 mL), was added morpholine (114 μL, 3.25 equiv). The reaction was stirred at room temperature for 1 h, until the consumption of BPO (monitored by TLC). The solution was concentrated *in vacuo* using a PhMe azeotrope. The crude was filtered through a short pad of silica, and washed with EtOAc to remove insoluble components. The filtrate was concentrated *in vacuo*. To the resulting crude residue, was added 1,2-dichloroethane (2.0 mL), followed by 2-(2-vinylphenyl)propan-2-ol **1a** (64.9 mg, 0.4 mmol, 1.0 equiv), $Cu(OTf)_2$ (28.9 mg, 0.2 equiv), and PPTS (100.5 mg, 1.0 equiv). The resulting solution was stirred at 60 °C for 1 h, until the consumption of **2a** (monitored by TLC). The resulting solution was filtered through activated, neutral (Brockman Grade I, 58–60Å mesh powder) Al_2O_3 and concentrated *in vacuo*. Purification by flash column chromatography (addition of 0.2 mL TFA to crude reaction mixture, 50% EtOAc–hexanes, then 50% EtOAc–hexanes with 5% NEt_3) afforded the product (**3a**) as a clear oil (55.8 mg, 0.23 mmol, 56%).

1-(2-Aminophenyl)-2-morpholinoethyl benzoate (15).—In a 1-Dram vial, was added *N*-(2-vinylphenyl)benzamide **4a** (44.7 mg, 0.2 mmol, 1.0 equiv), 4-benzoyloxymorpholine **2a** (82.9 mg, 2.0 equiv), copper (II) trifluoromethanesulfonate (14.4 mg, 0.2 equiv), pyridine *p*-toluenesulfonate (50.3 mg, 1.0 equiv), and 1,2-dichloroethane (1.0 mL). The vial was capped and charged with Teflon-coated stir bar. The reaction was stirred at 60 °C, until the consumption of **2a** (monitoring by TLC). The resulting solution was filtered through activated, neutral (Brockman Grade I, 58–60Å mesh powder) Al_2O_3 and concentrated *in vacuo* to yield the crude product. To the crude product in a 2-Dram vial, was added MeOH (2.7 mL) and concentrated aqueous HCl (1.3 mL). The resulting solution was stirred at room temperature for 13 h and then was concentrated *in vacuo*. Purification by flash column chromatography (100% hexanes with 2% NEt_3 to 100% EtOAc) afforded the pure aniline (**15**) as a clear oil (31.5 mg, 48%). $\mathbf{R_f}$ = 0.29 (5% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400

MHz): δ 8.07 (d, *J* = 7.8 Hz, 2H), 7.57 (t, *J* = 7.8 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.32 (d, *J* = 7.5 Hz, 1H), 7.11 (t, *J* = 7.5 HZ, 1H), 6.78 (t, *J* = 7.5 Hz, 1H), 6.70 (d, *J* = 7.5 Hz, 1H), 6.28 (dd, *J* = 7.3, 5.1 HZ, 1H), 4.33 (br, 2H), 3.65 (t, *J* = 4.5 Hz, 4H), 3.14 (dd, *J* = 13.4, 7.3 Hz, 1H), 2.83 (dd, *J* = 13.4, 5.1 Hz, 1H), 2.65–2.55 (m, 4H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 166.0, 144.7, 133.0, 130.2, 129.6, 129.0, 128.4, 127.2, 124.2, 118.6, 116.8, 70.5, 67.0, 62.6, 54.0; **FTIR** (thin film): cm^{-1} 3351 (broad), 2853, 2812, 1716, 1497, 1452, 1269, 1114, 1070, 1026, 1009, 869, 753, 711; **HRLCMS-ESI** (m/z) Calcd for ($C_{19}H_{23}N_2O_3$) ([M +H]$^+$): 327.1703; found: 327.1711.

1-(2-Aminophenyl)-2-morpholinoethan-1-ol (16).—To a 1-Dram vial, was added *N*-(2-vinylphenyl)benzamide **4a** (44.7 mg, 0.2 mmol, 1.0 equiv), 4-benzoyloxymorpholine **2a** (82.9 mg, 2.0 equiv), copper (II) trifluoromethanesulfonate (14.4 mg, 0.2 equiv), pyridine *p*-toluenesulfonate (50.3 mg, 1.0 equiv), and 1,2-dichloroethane (1.0 mL). The vial was capped and charged with Teflon-coated stir bar. The reaction was stirred at 60 °C, until the consumption of **2a** (monitored by TLC). The resulting solution was filtered through activated, neutral (Brockman Grade I, 58–60Å mesh powder) Al_2O_3 and concentrated *in vacuo*. To the crude residue in a 2-Dram vial was added a solution of 6 M KOH (4 mL, 3:1 EtOH:H_2O, sonication required for solubility). The resulting solution was stirred at 75 °C for 13 h. The reaction was then quenched with a saturated aqueous solution of NH_4Cl (5 mL) and acidified with 2 M HCl (15 mL). The aqueous layer was washed with EtOAc (10 mL x 3). The aqueous layer was then basified with a saturated aqueous solution of $NaHCO_3$ to pH 9.5 and extracted with EtOAc (10 mL x 3). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*, affording the pure aniline (**16**) as a white solid (18.0 mg, 40%). $\mathbf{R_f}$ = 0.08 (20% MeOH–CH_2Cl_2); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.08 (t, *J* = 7.5 Hz, 1H), 7.01 (d, *J* = 7.5 Hz, 1H), 6.70 (t, *J* = 7.5 Hz, 1H), 6.64 (d, *J* = 7.5 Hz, 1H), 4.77 (dd, *J* = 11.0, 3.4 Hz, 1H), 4.22 (br, 3H), 3.85–3.69 (m, 4H), 2.96 (dd, *J* = 12.5, 11.0 Hz, 1H), 2.81–2.70 (m, 2H), 2.55–2.45 (m, 2H), 2.48 (dd, *J* = 12.5, 3.4 Hz, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 145.8, 128.6, 127.9, 124.0, 118.0, 116.7, 69.3, 67.0, 62.0, 53.3; **FTIR** (thin film): cm^{-1} 3425 (broad), 3352 (broad), 2855, 2816, 1616, 1496, 1456, 1297, 1114, 1068, 1005, 868, 752; **HRLCMS-ESI** (m/z) Calcd for ($C_{12}H_{19}N_2O_2$) ([M+H]$^+$): 223.1441; found: 223.1443.

Synthesis of *O*-Benzoylhydroxylamines 2.

***O*-Benzoylhydroxylamines (2a-2e)** were synthesized as previously reported. [11a, 17]

***O*-Benzoyl-*N*-methyl-*N*-phenethylhydroxylamine (2f).—**To a solution of Na_2HPO_4 (2.13 g, 1.5 equiv) and benzoyl peroxide (2.42 g, 10 mmol, 1.0 equiv) in DMF (26 mL) was added *N*-methyl-2-phenylethan-1-amine (1.9 mL, 1.3 equiv). The reaction was stirred at room temperature for 1.5 h, and was then quenched with DI H_2O (15 mL) followed by addition of EtOAc (40 mL). The organic layer was washed with a saturated aqueous solution of $NaHCO_3$ (20 mL x 3). The combined aqueous layers were extracted with EtOAc (25 mL x 3). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc–hexanes to 20% EtOAc–hexanes) afforded *O*-benzoyl-*N*-methyl-*N*-phenethylhydroxylamine (**2f**) as a clear oil (2.24 g, 8.8 mmol, 88%). $\mathbf{R_f}$ = 0.55 (25% EtOAc–hexanes).**^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.99

(dd, *J* = 8.2, 1.3 Hz, 2H), 7.56 (tt, *J* = 7.4, 1.2 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.29–7.14 (m, 5H), 3.23 (t, *J* = 7.7 Hz, 2H), 2.97–2.92 (m, 2H), 2.92 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 165.1, 139.1, 133.0, 129.3, 129.1, 128.6, 128.4, 128.3, 126.1, 62.5, 47.0, 33.7; **FTIR** (thin film): cm^{-1} 3027, 2846, 1735, 1451, 1247, 1175, 1080, 1057, 1024, 699; **HRLCMS-ESI** (m/z) Calcd for ($C_{16}H_{18}NO_2$) ($[M+H]^+$): 256.1332; found: 256.1337.

***O*-Benzoyl-*N*,*N*-dicyclohexylhydroxylamine (2g).—**To a solution of Na_2HPO_4 (4.26 g, 30 mmol, 1.5 equiv) and benzoyl peroxide (4.84 g, 20 mmol, 1.0 equiv) in DMF (52 mL), was added dicyclohexylamine (5.2 mL, 26 mmol, 1.3 equiv). The solution was stirred at room temperature for 3 h followed by addition of dicyclochexylamine (4.8 mL, 24 mmol, 1.2 equiv). The reaction was stirred at room temperature for another 21 h, and was then quenched with DI H_2O (28 mL) followed by addition of EtOAc (80 mL). The organic layer was washed with a saturated aqueous solution of $NaHCO_3$ (40 mL x 3). The combined aqueous layers were extracted with EtOAc (40 mL x 3). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc–hexanes) afforded *O*-benzoyl-*N,N*-dicyclohexylhydroxylamine (**2g**) as a white solid (3.45 g, 11.4, mmol, 57%). $\mathbf{R_f}$ = 0.47 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.07–8.02 (m, 2H), 7.57 (tt, *J* = 7.5, 1.4 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 2H), 3.09 (tt, *J* = 10.8, 3.5 Hz, 2H), 1.95–1.86 (m, 4H), 1.85–1.75 (m, 4H), 1.67–1.58 (m, 2H), 1.43–1.18 (m, 8H), 1.14 (tt, *J* = 12.4, 3.1 Hz, 2H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz, 60 °C): δ 132.7, 129.6, 129.5, 128.3, 60.9, 29.1, 26.0, 25.3; **FTIR** (thin film): cm^{-1} 2930, 2853, 1744, 1449, 1251, 1237, 1176, 1080, 1059, 1024, 707; **HRLCMS-ESI** (m/z) Calcd for ($C_{19}H_{28}NO_2$) ($[M+H]^+$): 302.2115; found: 302.2120.

Preparation of Unsaturated Alcohol Substrates

2-(2-Vinylphenyl)propan-2-ol (1a).—To a solution of 2-vinylbenzoic acid (**1a-i**)[11a] (6.67 g, 45.0 mmol, 1.0 equiv) and K_2CO_3 (9.33 g, 1.5 equiv) in DMF (90 mL), was added MeI (5.6 mL, 2.0 equiv). The solution was stirred at room temperature for 16.5 h and was then quenched with addition of DI H_2O (100 mL) followed by EtOAc (100 mL). The organic layer was washed with a saturated aqueous solution of $NaHCO_3$ (40 mL x 2). The combined aqueous layers were extracted with EtOAc (50 mL x 3). The combined organic layers were washed with brine (75 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc–hexanes) afforded methyl 2-vinylbenzoate **1a-ii** as a colorless oil (7.03 g, 43.4 mmol, 96%). $\mathbf{R_f}$= 0.85 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.88 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.59 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.51–7.42 (m,2H), 7.32 (td, *J* = 7.7, 1.4 Hz, 1H), 5.65 (dd, *J* = 17.5, 1.4 Hz, 1H), 5.36 (dd, *J* = 10.9, 1.4 Hz, 1H), 3.90 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 167.8, 139.5, 135.8, 132.1, 130.3, 128.5, 127.4, 127.2, 116.4, 52.1; **FTIR** (thin film): cm^{-1} 2951, 1720, 1483, 1433, 1297, 1255, 1132, 1078, 917, 770, 716; **HRLCMS-ESI** (m/z) Calcd for ($C_{10}H_{11}O_2$) ($[M+H]^+$): 163.0754; found: 163.0750.

To an air-free solution of methyl 2-vinylbenzoate (**1a-ii**) (6.48 g, 40.0 mmol, 1.0 equiv) in Et_2O (160 mL) at 0 °C under N_2, was added MeMgBr (3 M in Et_2O, 40.0 mL, 3.0 equiv). The solution was allowed to stir at 0 °C for 30 min, at room temperature for 16 h and was then quenched with slow addition of a saturated aqueous solution of NH_4Cl (30 mL) and DI

H_2O (20 mL). The solution was acidified with HCl (2 M, 50 mL). The aqueous layer was extracted with Et_2O (50 mL x 3). The combined organic layers were washed with brine (70 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (1% EtOAc–hexanes to 14% EtOAc–hexanes) afforded 2-(2-vinylphenyl)propan-2-ol (**1a**) as a semisolid (6.13 g, 37.8 mmol, 94%). $\mathbf{R_f}$ = 0.68 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.64 (dd, *J* = 17.4, 10.9 Hz, 1H), 7.50–7.43 (m, 2H), 7.27–7.23 (m, 2H), 5.52 (dd, *J* = 17.4, 1.7 Hz, 1H), 5.27 (dd, *J* = 10.9, 1.7 Hz, 1H), 1.83 (s, 1H), 1.67 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 144.7, 138.1, 137.2, 128.5, 127.4, 127.3, 124.9, 115.2, 73.6, 31.3; **FTIR** (thin film): cm^{-1} 3356 (broad), 2974, 1478, 1365, 1164, 1142, 942, 912, 758; **HRGCMS-ESI** (m/z) Calcd for ($C_{11}H_{14}O$) ($[M]^+$): 162.1039; found: 162.1039.

Diphenyl(2-vinylphenyl)methanol (1b).—To an air-free solution of methyl 2-vinylbenzoate (**1a-ii**) (486.6 mg, 3.0 mmol, 1.0 equiv) in THF (12 mL) at 0 °C under N_2, was added dropwise PhMgBr (3 M in Et_2O, 3.0 mL, 3.0 equiv) over 10 min. The reaction solution was stirred at reflux for 14 h and was then cooled to room temperature. The reaction was quenched with slow addition of DI H_2O (3 mL), followed by a saturated aqueous solution of NH_4Cl (5 mL). The solution was acidified with HCl (2 M, 5 mL) and THF was removed *in vacuo* (~90%). The aqueous layer was extracted with Et_2O (10 mL x 3). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc–hexanes to 20% EtOAc–hexanes) afforded diphenyl(2-vinylphenyl)methanol (**1b**) as a yellow oil (378.2 mg, 1.4 mmol, 44%). $\mathbf{R_f}$ 0.54 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.51 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.39–7.25 (m, 11H), 7.12 (td, *J* = 7.7, 1.5 Hz, 1H), 6.81 (dd, *J* = 17.3, 10.9 Hz, 1H), 6.69 (dd, *J* = 7.9, 1.3 Hz, 1H), 5.54, (dd, *J* = 17.3, 1.6 Hz, 1H), 5.13 (dd, *J* = 10.9, 1.6 Hz, 1H), 3.39 (s, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 146.5, 143.9, 137.7, 137.1, 129.3, 128.3, 127.9, 127.8, 127.7, 127.1, 126.8, 116.2, 82.7; **FTIR** (thin film): cm^{-1} 3553 (broad), 3058, 1490, 1473, 1445, 1326, 1158, 1001, 907, 749, 732, 698, 636; **HRLCMS-ESI** (m/z) Calcd for ($C_{21}H_{18}OLi$) ($[M+^7Li]^+$): 293.1513; found: 293.1512.

1-(2-Vinylphenyl)ethan-1-ol (1c).—A solution of 2-bromobenzaldehyde (2.32 g, 12.0 mmol, 1.0 equiv) and tetrakis (triphenylphosphine)palladium (138.7 mg, 0.01 equiv) in DME (96 mL) was stirred at room temperature for 20 min. Then, K_2CO_3 (1.66 g, 1.0 equiv), potassium trifluorovinylborate (2.41 g, 1.5 equiv), and DI H_2O (29 mL) were added. The reaction was refluxed for 16 h, and was then cooled to room temperature. DME was removed *in vacuo* (~90%). The reaction was quenched with a saturated aqueous solution of NH_4Cl (60 mL). The aqueous layer was extracted with Et_2O (50 mL x 3). The combined organic layers were washed with brine (50 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc–hexanes) afforded olefin 2-vinylbenzaldehyde **1c-i** as a colorless oil (1.21 g, 9.2 mmol, 76%). $\mathbf{R_f}$ = 0.51 (5% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 10.30 (s, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.62–7.48 (m, 3H), 7.47–7.39 (m, 1H), 5.71 (dd, *J* = 17.4, 1.3 Hz, 1H), 5.52 (dd, *J* = 11.0, 1.3 Hz, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 192.3, 140.4, 133.7, 133.2, 132.7, 131.1, 127.8, 127.3, 119.3; **FTIR** (thin film): cm^{-1} 2851, 2736, 1689, 1596, 1565, 1479, 1296, 1205,

1186, 987, 922, 861, 830, 771, 741; **HRLCMS-ESI** (m/z) Calcd for (C_9H_9O) ($[M+H]^+$): 133.0648; found: 133.0646.

To an air-free solution of 2-vinylbenzaldehyde **1c-i** (396.5 mg, 3.0 mmol, 1.0 equiv) in Et_2O (12 mL) at 0 °C under N_2, was added dropwise MeMgBr (3 M in Et_2O, 2.0 mL, 2.0 equiv) over 10 min. The reaction solution was stirred at room temperature for 16 h, and was then quenched with slow addition of with DI H_2O (3 mL), followed by a saturated aqueous solution of NH_4Cl (3 mL). The solution was acidified with HCl (2 M, 5 mL). The aqueous layer was extracted with Et_2O (10 mL x 3). The combined organic layers were washed with brine (25 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc–hexanes to 20% EtOAc–hexanes) afforded 1-(2-vinylphenyl)ethan-1-ol (**1c**) as a colorless oil (338.4 mg, 2.3 mmol, 76%). $\mathbf{R_f}$ = 0.24 (10% EtOAc–hexanes).**^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.54 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.46 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.32 (td, *J* = 7.5, 1.6 Hz, 1H), 7.29–7.23 (m, 1H), 7.06 (dd, *J* = 17.3, 11.0 Hz, 1H), 5.63 (dd, *J* = 17.3, 1.5 Hz, 1H), 5.34 (dd, *J* = 11.0, 1.5 Hz, 1H), 5.23 (qd, *J* = 6.5, 3.3 Hz, 1H), 1.78 (d, *J* = 3.3 Hz, 1H), 1.49 (d, *J* = 6.5 Hz, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 142.7, 135.3, 134.0, 128.1, 127.4, 126.1, 124.7, 116.5, 66.8, 24.2; **FTIR** (thin film): cm^{-1} 3340 (broad), 2973, 1481, 1450, 1413, 1369, 1118, 1072, 1005, 913, 774, 757; **HRLCMS-ESI** (m/z) Calcd for ($C_{10}H_{12}OLi$) ($[M+^7Li]^+$): 155.1043; found: 155.1041.

Phenyl(2-vinylphenyl)methanol (1d).—To an air-free solution of 2-vinylbenzaldehyde (**1c-i**) (337.0 mg, 2.55 mmol, 1.0 equiv) in Et_2O (10.2 mL) at 0 °C under N_2, was added dropwise PhMgBr (3 M in Et_2O, 1.7 mL, 2.0 equiv) over 10 min. The reaction solution was stirred at room temperature for 13 h, and was then quenched with slow addition of DI H_2O (2 mL), followed by a saturated aqueous solution of NH_4Cl (5 mL). The solution was acidified with HCl (2 M, 5 mL). The aqueous layer was extracted with Et_2O (10 mL x 3). The combined organic layers were washed with brine (25 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc–hexanes to 20% EtOAc–hexanes) afforded phenyl(2-vinylphenyl)methanol (**1d**) as a colorless oil (499.2 mg, 2.4 mmol, 93%). $\mathbf{R_f}$ = 0.33 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.52–7.44 (m, 2H), 7.38–7.23 (m, 7H), 7.01 (dd, *J* = 17.3, 10.9 Hz, 1H), 6.13 (d, *J* = 4.0 Hz, 1H), 5.61 (dd, *J* = 17.3, 1.4 Hz, 1H), 5.28 (dd, *J* = 10.9, 1.4 Hz, 1H), 2.18 (d, *J* = 4.0 Hz, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 142.9, 140.3, 136.2, 134.2, 128.4, 127.9, 127.8, 127.4, 126.8, 126.3, 116.6, 72.9; **FTIR** (thin film): cm^{-1} 3340 (broad), 3062, 3028, 1494, 1480, 1450, 1177, 1015, 916, 760, 730, 699; **HRLCMS-ESI** (m/z) Calcd for ($C_{15}H_{14}OLi$) ($[M+^7Li]^+$): 217.1199; found: 217.1199.

(2-(1-Phenylvinyl)phenyl)methanol (1e).—To an air-free solution of methyl 2-vinylbenzoate (**1a-ii**) (1.62 g, 10.0 mmol, 1.0 equiv) in PhMe (10.0 mL) at −50 °C under N_2, was added dropwise DIBAL (1 M in Hexanes, 22.0 mL, 2.2 equiv) over 20 min. The solution was stirred at −50 °C for 2.5 h and was then warmed to 0 °C followed by the addition of Et_2O (20 mL). The reaction was quenched with slow addition of DI H_2O (0.9 mL), an aqueous solution of NaOH (15%, 0.9 mL), and DI H_2O (2.2 mL) in sequence. The mixture was warmed to room temperature and stirred for 15 min. $MgSO_4$ was added. The mixture was stirred for another 15 min, and was then filtered through a silica pale with

EtOAc (250 mL). The filtrate was concentrated *in vacuo*. Purification by flash column chromatography (20% EtOAc-hexanes) afforded (2-(1-phenylvinyl)phenyl)methanol (**1e**) as a colorless oil (1.31 g, 9.7 mmol, 97%). $\mathbf{R_f}$ = 0.49 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.54 (dd, *J* = 7.3, 2.0 Hz, 1H), 7.37 (dd, *J* = 6.9, 2.0 Hz, 1H), 7.34–7.27 (m, 2H), 7.06 (dd, *J* = 17.4, 11.0 Hz, 1H), 5.71 (dd, *J* = 17.4, 1.3 Hz, 1H), 5.37 (dd, *J* = 11.0, 1.3 Hz, 1H), 4.76 (d, *J* = 5.8 Hz, 2H), 1.62 (t, *J* = 5.8 Hz, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 137.5, 136.5, 133.7, 128.2, 128.1, 127.8, 125.9, 116.4, 63.2; **FTIR** (thin film): cm^{-1} 3311, 2885, 1483, 1452, 1414, 1184, 1003, 914, 772, 762, 731; **HRGCMS-ESI** (m/z) Calcd for ($C_9H_{10}O$) ($[M]^+$): 134.0726; found: 134.0726.

2-(2-Allylphenyl)propan-2-ol (1f).—To an air-free solution of methyl 2-iodobenzoate (0.88 mL, 6.0 mmol, 1.0 equiv) in THF (12 mL) at −40 °C under N_2, was added LiCl·*i*-PrMgCl (1.3 M in THF, 7.0 mL, 1.5 equiv). The mixture was stirred at −40 °C for 1 h, and was then added a freshly prepared solution of CuCN (537.4 mg, 6.0 mmol) and LiCl (509.0 mg, 12.0 mmol) in THF (12 mL), followed by dropwise addition of allyl bromide (1.6 mL, 3.0 equiv) over 30 min at −40 °C. The mixture was warmed to room temperature and stirred for another 2.5 h. The mixture was then filtered through a pale of silica with EtOAc. The solution was washed with a saturated aqueous solution of NH_4Cl (50 mL x 2). The aqueous layers were extracted with EtOAc (30 mL). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo*, yielding 1.05 g of the crude olefin which was used without further purification. To solution of the crude olefin (969.2 mg, 5.5 mmol, 1.0 equiv) in Et_2O (22 mL) under N_2, was added dropwise MeMgBr (3 M in Et_2O, 5.5 mL, 3.0 equiv) over 5 min. The solution was stirred at room temperature overnight, and was then quenched with slow addition of a saturated aqueous solution of NH_4Cl (25 mL) and DI H_2O (10 mL). The solution was acidified with HCl (2 M, 10 mL). The aqueous layer was extracted with Et_2O (20 mL x 3). The combined organic layers were washed with brine (50 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (100% Hexanes to 20% EtOAc–hexanes) afforded 2-(2-allylphenyl)propan-2-ol (**1f**) as a colorless oil (710.6 mg, 4.0 mmol, 72% over two steps). $\mathbf{R_f}$ = 0.83 (25% EtOAc–hexanes).**^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.41 (d, *J* = 7.5 Hz, 1H), 7.24–7.15 (m, 3H), 6.06 (ddt, *J* = 17.0, 10.2, 6.1 Hz, 1H), 5.06 (dq, *J* = 10.2, 1.7 Hz, 1H), 4.98 (dq, *J* = 17.0, 1.7 Hz, 1H), 3.81 (dt, *J* = 6.1, 1.7 Hz, 1H), 1.87 (s, 1H), 1.66 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 145.6, 139.5, 137.8, 132.3, 127.1, 125.9, 125.5, 115.3, 73.8, 38.3, 31.7; **FTIR** (thin film): cm^{-1} 3356 (broad), 2975, 1636, 1486, 1442, 1365, 1243, 1162, 995, 944, 910, 760; **HRLCMS-ESI** (m/z) Calcd for ($C_{12}H_{14}$) ($[M–H_2O]^+$): 158.10900; found: 158.10894.

2-(5-Methoxy-2-vinylphenyl)propan-2-ol (1g).—A solution of methyl 5-methoxy-2-bromobenzoate (1.72 g, 7 mmol, 1.0 equiv) and tetrakis (triphenylphosphine)palladium (80.9 mg, 0.01 equiv) in DME (35 mL) was stirred at room temperature for 20 min. Then K_2CO_3 (967.5 mg, 1.0 equiv), potassium trifluorovinylborate (1.41 g, 1.5 equiv), and DI H_2O (7 mL) were added. The reaction was refluxed for 17 h, then cooled to room temperature, and quenched with a saturated aqueous solution of NH_4Cl (30 mL). The aqueous layer was extracted with Et_2O (25 mL x 3). The combined organic layers were washed with brine (50 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (5% EtOAc–hexanes to 10% EtOAc–hexanes) afforded

methyl 5-methoxy-2-vinylbenzoate (**1g-i**) as a colorless oil (710.9 mg, 3.7 mmol, 53%). $\mathbf{R_f}$ = 0.55 (5% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.52 (d, *J* = 8.7 Hz, 1H), 7.42 – 7.33 (m, 2H), 7.03 (dd, *J* = 8.7, 2.8 Hz, 1H), 5.56 (dd, *J* = 17.5, 1.4 Hz, 1H), 5.26 (dd, *J* = 10.9, 1.4 Hz, 1H), 3.90 (s, 3H), 3.84 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 167.6, 158.7, 135.1, 132.1, 129.5, 128.3, 118.6, 114.7, 114.4, 55.4, 52.1; **FTIR** (thin film): cm^{-1} 2950, 1718, 1604, 1493, 1434, 1288, 1253, 1218, 1070, 1046, 1024, 828, 792; **HRLCMS-ESI** (m/z) Calcd for ($C_{11}H_{13}O_3$) ($[M+H]^+$): 193.0859; found: 193.0858.

To an air-free solution of the above methyl 5-methoxy-2-vinylbenzoate (**1g-i**) (480.5 mg, 2.5 mmol, 1.0 equiv) in Et_2O (10 mL) at 0 °C under N_2, was added slowly MeMgBr (3 M in Et_2O, 2.5 mL, 3.0 equiv) over 10 min. The reaction solution was stirred at room temperature for 15 h and was then quenched with slow addition of DI H_2O (3 mL), followed by a saturated aqueous solution of NH_4Cl (4 mL). The solution was acidified with HCl (2 M, 4 mL). The aqueous layer was extracted with Et_2O (15 mL x 3). The combined organic layers were dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc–hexanes to 25% EtOAc–hexanes) afforded 2-(5-methoxy-2-vinylphenyl)propan-2-ol (**1g**) as a colorless oil (387.1 mg, 2.0 mmol, 81%). $\mathbf{R_f}$ = 0.45 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.51 (dd, *J* = 17.3, 10.9 Hz, 1H), 7.43 (d, *J* = 8.5 Hz, 1H), 7.04 (d, *J* = 2.7 HZ, 1H), 6.78 (dd, *J* = 8.5, 2.7 Hz, 1H), 5.43 (dd, *J* = 17.3, 1.7 Hz, 1H), 5.18 (dd, *J* = 10.9, 1.7 Hz, 1H), 3.82 (s, 3H), 1.84 (s, 1H), 1.65 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 158.9, 146.4, 137.4, 129.6, 129.6, 113.6, 111.7, 111.5, 73.4, 55.2, 31.1; **FTIR** (thin film): cm^{-1} 3416 (broad), 2974, 2937, 1605, 1567, 1483, 1292, 1246, 1217, 1048, 906, 827; **HRLCMS-ESI** (m/z) Calcd for ($C_{12}H_{16}O_2Li$) ($[M+^7Li]^+$): 199.1305; found: 199.1306.

***N*-(3-(2-hydroxypropan-2-yl)-4-vinylphenyl)-*N*-methylbenzamide (1h).—**To a solution of 5-amino-2-bromobenzoic acid (4.32 g, 20.0 mmol, 1.0 equiv) in MeOH (40 mL) at 0 °C, was added dropwise $SOCl_2$ (2.2 mL, 1.5 equiv) over 10 min. The solution was stirred at room temperature for 1.5 h, refluxed for 3 h, and stirred at room temperature for 13 h. The reaction was quenched with DI H_2O (50 mL). MeOH was removed *in vacuo* (~90%). To the resulting residue, was added a saturated aqueous solution of $NaHCO_3$ (60 mL) and brine (50 mL). The aqueous layers were extracted with EtOAc (40 mL x 6). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (1% MeOH–CH_2Cl_2 to 5% MeOH–CH_2Cl_2) afforded methyl 5-amino-2-bromobenzoate (**1h-i**) as an orange oil (4.38 g, 19.0 mmol, 95%). $\mathbf{R_f}$ 0.73 (5% MeOH–CH_2Cl_2). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.38 (d, *J* = 8.6 Hz, 1H), 7.10 (d, *J* = 2.9 Hz, 1H), 6.64 (dd, *J* = 8.6, 2.9 Hz , 1H), 3.90 (s, 3H), 3.77 (br, 2H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 166.7, 145.6, 134.6, 132.2, 119.1, 117.2, 108.6, 52.2; **FTIR** (thin film): cm^{-1} 3468 (broad), 3377 (broad), 2950, 1722, 1626, 1597, 1476, 1439, 1324, 1239, 1111, 1026, 822, 777; **HRLCMS-ESI** (m/z) Calcd for ($C_8H_9BrNO_2$) ($[M+H]^+$): 229.9811; found: 229.9810.

To a solution of methyl 5-amino-2-bromobenzoate (**1h-i**) (2.30 g, 10.0 mmol, 1.0 equiv) and triethylamine (1.7 mL, 1.2 equiv) in CH_2Cl_2 (75 mL) at 0 °C, was added BzCl (1.4 mL, 1.2 equiv) dropwise over 10 min. The reaction was stirred at room temperature for 18 h. The

organic layer was washed with HCl (2 M, 50 mL x 2), a saturated aqueous solution of $NaHCO_3$ (50 mL x 2), dried over Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc–hexanes to 25% EtOAc–hexanes) afforded methyl 5-benzamido-2-bromobenzoate (**1h-ii**) as a highly viscous oil (3.04 g, 9.1 mmol, 91%). $\mathbf{R_f}$ = 0.38 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.06 (d, *J* = 2.7 Hz, 1H), 8.01 (br, 1H), 7.88–7.84 (m, 2H), 7.76 (dd, *J* = 8.7, 2.7 Hz, 1H), 7.63 (d, *J* = 8.7 Hz, 1H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 2H), 3.92 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 166.1, 165.8, 137.3, 134.9, 134.2, 132.3, 132.2, 128.8, 127.0, 124.2, 122.7, 116.1, 52.6; **FTIR** (thin film): cm^{-1} 3313 (broad), 2951, 1733, 1655, 1581, 1530, 1474, 1395, 1308, 1255, 1222, 1109, 1027, 707; **HRLCMS-ESI** (m/z) Calcd for ($C_{15}H_{13}BrNO_3$) ($[M+H]^+$): 334.0073; found: 334.0067.

To a suspension of potassium *tert*-butoxide (942.6 mg, 1.2 equiv) in THF (5 mL) was slowly added a solution of methyl 5-benzamido-2-bromobenzoate (**1h-ii**) (2.35 g, 7.0 mmol, 1.0 equiv) in THF (20 mL). To this solution was added MeI (0.65 mL, 1.5 equiv) slowly over 15 min. The resulting reaction solution was stirred for 19 h at room temperature and was then quenched with DI H_2O (15 mL). THF was removed *in vacuo* (~90%). To the resulting residue, was added a saturated aqueous solution of $NaHCO_3$ (15 mL). The aqueous layers were extracted with EtOAc (25 mL x 3). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc–hexanes to 50% EtOAc–hexanes) afforded methyl 2-bromo-5-(*N*-methylbenzamido) benzoate (**1h-iii**) as a highly viscous oil (1.14 g, 3.3 mmol, 47%). $\mathbf{R_f}$ = 0.26 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.58 (d, *J* = 2.7 Hz, 1H), 7.46 (d, *J* = 8.5 Hz, 1H), 7.33–7.27 (m, 3H), 7.25–7.20 (m, 2H), 6.92 (dd, *J* = 8.5, 2.7 Hz, 1H), 3.90 (s, 3H), 3.46 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 170.4, 165.5, 144.0, 135.0, 134.9, 132.6, 130.8, 130.0, 129.0, 128.5, 128.0, 119.0, 52.6, 38.2; **FTIR** (thin film): cm^{-1} 2951, 1732, 1645, 1472, 1435, 1350, 1314, 1281, 1243, 1107, 1015, 719, 697; **HRLCMS-ESI** (m/z) Calcd for ($C_{16}H_{15}BrNO_3$) ($[M+H]^+$): 348.0230; found: 348.0230.

A solution of 2-bromo-5-(*N*-methylbenzamido)benzoate (**1h-iii**) (1.04 g, 3.0 mmol, 1.0 equiv) and tetrakis (triphenylphosphine)palladium (277.0 mg, 0.08 equiv) in DME (15 mL) was stirred at room temperature for 20 min. Then K_2CO_3 (622.0 mg, 1.5 equiv), potassium trifluorovinylborate (643.0 mg, 1.6 equiv), and DI H_2O (4 mL) were added. The reaction was refluxed for 22 h, then cooled to room temperature, and quenched with a saturated aqueous solution of NH_4Cl (15 mL). The aqueous layer was extracted with Et_2O (20 mL x 3). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc–hexanes to 50% EtOAc–hexanes) afforded methyl 5-(*N*-methylbenzamido)-2-vinylbenzoate (**1h-iv**) as a viscous oil (707.4 mg, 2.4 mmol, 80%). $\mathbf{R_f}$ = 0.37 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.65 (d, *J* = 2.4 Hz, 1H), 7.42–7.24 (m, 5H), 7.22–7.17 (m, 2H), 7.06 (dd, *J* = 8.5, 2.4 Hz, 1H), 5.58 (dd, *J* = 17.4, 1.2 HZ, 1H), 5.34 (dd, *J* = 11.0 1.2 Hz, 1H), 3.87 (s, 3H), 3.50 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 170.5, 166.8, 143.9, 137.4, 135.4, 134.7, 130.5, 129.8, 129.2, 128.6, 127.9, 117.0, 52.2, 38.2; **FTIR** (thin film): cm^{-1} 2950, 1718, 1643, 1600, 1492, 1435, 1351, 1316, 1237, 1112, 1073, 1015, 920, 841, 791, 722, 699; **HRLCMS-ESI** (m/z) Calcd for ($C_{18}H_{18}NO_3$) ($[M+H]^+$): 296.1281; found: 296.1284.

To a solution of methyl 5-(*N*-methylbenzamido)-2-vinylbenzoate **1h-iv** (590.7 mg, 2.0 mmol, 1.0 equiv) in Et_2O (8 mL) and THF (3 mL, for solubility) at 0 °C under N_2, was added dropwise MeMgBr (3 M in Et_2O, 2.0 mL, 3.0 equiv) over 10 min. The reaction mixture was stirred at room temperature for 15 h and was then quenched with slow addition of DI H_2O (3 mL), followed by a saturated aqueous solution of NH_4Cl (5 mL). The solution was acidified with HCl (2 M, 5 mL). The aqueous layer was extracted with EtOAc (15 mL x 3). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc–hexanes to 50% EtOAc–hexanes) afforded *N*-(3-(2-hydroxypropan-2-yl)-4-vinylphenyl)-*N*-methylbenzamide (**1h**) as a viscous oil (248.2 mg, 0.84 mmol, 42%). $\mathbf{R_f}$ = 0.13 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.47 (dd, *J* = 17.4, 10.9 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 1H), 7.30–7.14 (m, 5H), 7.01 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.94–6.92 (m, 1H), 5.47 (dd, *J* = 17.4, 1.5 Hz, 1H), 5.24 (dd, *J* = 10.9, 1.5 Hz, 1H), 3.51 (s, 3H), 1.60 (s, 1H), 1.41 (s, 6H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 170.5, 145.7, 143.4, 136.9, 135.9, 134.8, 129.3, 128.8, 128.4, 127.6, 124.2, 124.1, 115.1, 72.8, 37.8, 30.8; **FTIR** (thin film): cm^{-1} 3406, 2973, 1627, 1598, 1486, 1360, 1306, 1112, 1018, 911, 753, 724, 697; **HRLCMS-ESI** (m/z) Calcd for ($C_{19}H_{22}NO_2$) ($[M+H]^+$): 296.1645; found: 296.1647.

2-(4-Chloro-2-vinylphenyl)propan-2-ol (1i).—To a solution of 2-bromo-4-chlorobenzoic acid (3.53 g, 15.0 mmol, 1.0 equiv) in methanol (45 mL), was added concentrated H_2SO_4 (1.7 mL, 2.0 equiv). The resulting solution was refluxed for 17 h, cooled to room temperature, and concentrated *in vacuo* to remove ~85% of the MeOH. The resulting residue was quenched with slow addition of a saturated aqueous solution of $NaHCO_3$ (50 mL). The resulting aqueous layer was extracted with EtOAc (35 mL x 3). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (20% EtOAc-hexanes) afforded methyl 2-bromo-4-chlorobenzoate (**1i-i**) as a clear oil (2.93 g, 11.7 mmol, 78%). $\mathbf{R_f}$ = 0.74 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.77 (d, *J* = 8.4 Hz, 1H), 7.69 (d, *J* = 2.0 Hz, 1H), 7.35 (dd, *J* = 8.4, 2.0 HZ, 1 H), 3.93 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 165.6, 138.2, 134.1, 132.3, 130.2, 127.5, 122.5, 52.6; **FTIR** (thin film): cm^{-1} 2951, 1736, 1582, 1433, 1371, 1287, 1245, 1121, 1102, 1039, 832, 768; **HRLCMS-ESI** (m/z) Calcd for ($C_8H_7BrClO_2$) ($[M+H]^+$): 248.9312; found: 248.9315.

A solution of methyl 2-bromo-4-chlorobenzoate (**1i-i**) (1.99 g, 8.0 mmol, 1.0 equiv) and tetrakis (triphenylphosphine)palladium (92.4 mg, 0.01 equiv) in DME (40 mL) was stirred at room temperature for 20 min. Then K_2CO_3 (1.11 g, 1.0 equiv), potassium trifluorovinylborate (1.61 g, 1.5 equiv), and DI H_2O (8 mL) were added. The reaction was refluxed for 23 h, cooled to room temperature, and then quenched with a saturated aqueous solution of NH_4Cl (30 mL). The aqueous layer was extracted with Et_2O (30 mL x 3). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (100% hexanes to 10% EtOAc–hexanes) afforded methyl 4-chloro-2-vinylbenzoate (**1i-ii**) as a colorless oil (656.0 mg, 3.3 mmol, 42%). $\mathbf{R_f}$ = 0.68 (5% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.84 (d, *J* = 8.4 Hz, 1H), 7.55 (d, *J* = 2.2 Hz, 1H), 7.44 (dd, *J* = 17.4, 11.0 Hz, 1H), 7.29 (dd, *J* = 8.4, 2.2 Hz, 1H), 5.66 (dd, *J* = 17.4, 1.2 Hz, 1H), 5.40 (dd, *J* = 11.0, 1.2 Hz, 1H), 3.90 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125

MHz): δ 166.8, 141.5, 138.4, 134.8, 31.9, 127.4, 127.2, 126.7, 117.6, 52.2; **FTIR** (thin film): cm^{-1} 2951, 1721, 1589, 1555, 1475, 1434, 1273, 1247, 1105, 1076, 866, 784; **HRLCMS-ESI** (m/z) Calcd for ($C_{10}H_{10}ClO_2$) ($[M+H]^+$): 197.0364; found: 197.0358.

To the solution of methyl 4-chloro-2-vinylbenzoate (**1i-ii**) (590.0 mg, 3.0 mmol, 1.0 equiv) in Et_2O (12 mL) at 0 °C under N_2, was added dropwise MeMgBr (3 M in Et_2O, 3.0 mL, 3.0 equiv) over 10 min. The reaction solution was stirred at room temperature for 12 h and was then quenched with slow addition of DI H_2O (3 mL), followed by a saturated aqueous solution of NH_4Cl (5 mL). The solution was acidified with HCl (2 M, 6 mL). The aqueous layer was extracted with Et_2O (10 mL x 3). The combined organic layers were washed with brine (25 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc–hexanes to 20% EtOAc–hexanes) afforded 2-(4-chloro-2-vinylphenyl)propan-2-ol (**1i**) as a colorless oil (551.1 mg, 2.8 mmol, 93%). $\mathbf{R_f}$ = 0.35 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.56 (dd, *J* = 17.3, 10.9 Hz, 1H), 7.44 (d, *J* = 2.4 Hz, 1H), 7.37 (d, *J* = 8.5 Hz, 1H), 7.19 (dd, *J* = 8.5, 2.4 Hz, 1H), 5.53 (dd, *J* = 17.3, 1.5 Hz, 1H), 5.31 (dd, *J* = 10.9, 1.5 Hz, 1H), 1.78 (s, 1H), 1.64 (s, 6H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 143.2, 139.0, 137.0, 133.0, 128.2, 127.1, 126.5, 116.3, 73.3, 31.3; **FTIR** (thin film): cm^{-1} 3380 (broad), 2976, 1556, 1475, 1365, 1116, 918, 877, 817; **HRGCMS-ESI** (m/z) Calcd for ($C_{11}H_{13}ClO$) ($[M]^+$): 196.0649; found: 196.0649.

2,2-Diphenylpent-4-en-1-ol (1j).—To a solution of diphenylacetic acid (14.9 g, 70.0 mmol, 1.0 equiv) in MeOH (210 mL), was added concentrated H_2SO_4 (7.8 mL, 2.0 equiv). The resulting solution was refluxed for 13.5 h, cooled to room temperature and concentrated *in vacuo* to remove ~75% of the MeOH. The resulting residue was quenched with slow addition of a saturated aqueous solution of $NaHCO_3$ (75 mL). The resulting aqueous layer was extracted with EtOAc (50 mL x 3). The combined organic layers were washed with brine (75 mL), dried with Na_2SO_4, and concentrated *in vacuo*, affording the crude ester which was used without further purification. To a solution of the resulting ester (1.25 g, 5.5 mmol, 1.0 equiv) in THF (6 mL) at −78 °C under N_2, was added slowly LDA (2 M in THF, 3.3 mL, 1.2 equiv) over 15 min. The resulting solution was stirred at −78 °C for 15 min and was added slowly allyl bromide (0.64 mL, 1.35 equiv) over 5 min. The resulting reaction was stirred at −78 °C for 15 min, and was then allowed to warm to room temperature overnight. The reaction was quenched with a saturated aqueous solution of NH_4Cl (10 mL). The aqueous layer was extracted with EtOAc (15 mL x 3). The combined organic layers were washed with brine (30 mL), dried with Na_2So_4, and concentrated *in vacuo*. Purification by flash column chromatography (100% Hexanes to 5% EtOAc–Hexanes) afforded methyl 2,2-diphenylpent-4-enoate (**1j-i**) as a colorless oil (1.39 g, 5.2 mmol, 93% over two steps), which matched previously reported spectra.[18] $\mathbf{R_f}$ = 0.81 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.36–7.22 (m, 10 H), 5.61 (ddt, *J* = 17.5, 9.8, 7.0 Hz, 1H), 4.99–4.90 (m, 2H), 3.71 (s, 3H), 3.18 (d, *J* = 7.0 Hz, 2H).

To the solution of ester **1j-i** (1.07 g, 4.0 mmol, 1.0 equiv) in PhMe (4 mL) at −50 °C under N_2, was added slowly DIBAL (1 M in PhMe, 8.8 mL, 2.2 equiv) over 10 min. The solution was stirred at −50 °C for 2 h, then warmed to 0 °C, and diluted with Et_2O (5 mL). The reaction was quenched with the addition of DIH_2O (0.4 mL), an aqueous solution of NaOH

(15%, 0.4 mL), and DI H_2O (0.9 mL) in sequence. The mixture was warmed to room temperature and stirred for 15 min. $MgSO_4$ was added. The mixture was stirred for another 15 min, and was then filtered through a silica pale with EtOAc. The filtrate was concentrated *in vacuo*. Purification by flash column chromatography (100% hexanes to 10% EtOAc–hexanes) afforded 2,2-diphenylpent-4-en-1-ol (**1j**) as a white solid (901.5 mg, 3.8 mmol, 95%), which matched previously reported spectra.[18] $\mathbf{R_f}$ = 0.67 (25% EtOAc–Hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.36–7.16 (m, 10H), 5.44 (ddt, *J* = 17.1, 10.2, 7.1 Hz, 1H), 5.10 (dd, *J* = 17.1, 2.0 Hz, 1H), 5.00 (dd, *J* = 10.2, 2.0 Hz, 1H), 4.16 (d, *J* = 4.2 Hz, 2H), 2.98 (d, *J* = 7.1 Hz, 2H), 1.16 (m, 1H).

2,2-Dimethylpent-4-en-1-ol (1k).—To a solution of LAH (250.5 mg, 2.2 equiv) in Et_2O (18 mL) at 0 °C under N_2, was added slowly the solution of 2,2-dimethylpent-4-enoic acid (412.1 μL, 2.0 mmol, 1.0 equiv) in Et_2O (3 mL) over 15 min. The reaction mixture was stirred at 0 °C for 1.5 h and was then diluted with Et_2O (12 mL). The reaction was quenched with the addition of DI H_2O (0.25 mL), an aqueous solution of NaOH (15%, 0.25 mL), and DI H_2O (0.75 mL) in sequence. The reaction mixture was warmed to room temperature and stirred for 15 min. $MgSO_4$ was added. The resulting mixture was stirred for another 15 min and was then filtered through a pale of silica with EtOAc. The filtrate was concentrated *in vacuo*. Purification by flash column chromatography (100% Hexanes to 20% EtOAc–hexanes) afforded the 2,2-dimethylpent-4-en-1-ol (**1k**) as a colorless oil (189.4 mg, 1.7 mmol, 55%), which matched previously reported spectra.[18] $\mathbf{R_f}$ = 0.62 (25% EtOAc–Hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 5.89–5.76 (m, 1H), 5.07–4.98 (m, 2H), 3.30 (s, 2H), 2.00 (d, *J* = 7.5 Hz, 2H), 1.83 (s, 1H), 0.86 (s, 6H). Note: this compound is surprisingly volatile, so be careful when removing solvent under reduced presssure.

2-(2-(1-Phenylvinyl)phenyl)propan-2-ol (1m).—To a solution of 2-(1-phenylvinyl)benzoic acid (**1m-i**)[11a] (1.68 g, 7.5 mmol, 1.0 equiv) and K_2CO_3 (1.55 g, 1.5 equiv) in DMF (15 mL), was added MeI (0.93 mL, 2.0 equiv). The solution was stirred at room temperature for 16 h. The reaction was quenched with DI H_2O (25 mL), followed by addition of EtOAc (20 mL). The organic layer was separated and washed with a saturated aqueous solution of $NaHCO_3$ (25 mL x 3). The combined aqueous layers were extracted with EtOAc (30 mL x 3). The combined organic layers were washed with brine (50 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc–hexanes) afforded methyl 2-(1-phenylvinyl)benzoate (**1m-ii**) as a colorless oil (1.67 g, 7.0 mmol, 93%), which matched previously reported spectra.[19] $\mathbf{R_f}$ = 0.60 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.82 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.53 (td, *J* = 7.7, 1.5 Hz, 1H), 7.45–7.37 (m, 2H), 7.31–7.21 (m, 5H), 5.68 (d, *J* = 1.1 Hz, 1H), 5.26 (d, *J* = 1.1 Hz, 1H), 3.50 (s, 3H).

To a solution of methyl 2-(1-phenylvinyl)benzoate (**1m-ii**) (1.19 g, 5.0 mmol, 1.0 equiv) in Et_2O (20 mL) at 0 °C under N_2, was added dropwise MeMgBr (3 M in Et_2O, 5.0 mL, 3.0 equiv) over 10 min. The reaction solution was stirred at room temperature for 16 h and was then quenched with slow addition of DI H_2O (5 mL), followed by a saturated aqueous solution of NH_4Cl (5 mL). The mixture was acidified with HCl (2 M, 10 mL). The aqueous layer was extracted with Et_2O (15 mL x 3). The combined organic layers were washed with

brine (25 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (100% hexanes to 20% EtOAc–hexanes) afforded 2-(2-(1-phenylvinyl)phenyl)propan-2-ol (**1m**) as a colorless oil (896.0 mg, 3.7 mmol, 75%). $\mathbf{R_f}$ = 0.37 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.51 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.34 (td, *J* = 7.6, 1.5 Hz, 1H), 7.31–7.23 (m,6H), 7.11 (dd, *J* = 7.6, 1.5 Hz, 1H), 5.87 (d, *J* = 1.3 Hz, 1H), 5.23 (d, *J* = 1.3 Hz, 1H), 2.25 (s, 1H), 1.49 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 151.4, 146.4, 140.8, 138.3, 132.4, 128.2, 127.7, 127.4, 126.5, 126.5, 126.4, 114.2, 74.2, 32.3; **FTIR** (thin film): cm^{-1} 3396 (broad), 2972, 1494, 1363, 1164, 950, 903, 783, 761, 711; **HRLCMS-ESI** (m/z) Calcd for ($C_{17}H_{18}OLi$) ($[M+^7Li]^+$): 245.1513; found: 245.1513.

(2-(1-Phenylvinyl)phenyl)methanol (1n).—To a solution of methyl 2-(1-phenylvinyl)benzoate (**1m-ii**) (197.8 mg, 0.83 mmol, 1.0 equiv) in PhMe (0.83 mL) at −50 °C under N_2, was added dropwise DIBAL (1 M in PhMe, 1.83 mL, 2.2 equiv) over 10 min. The solution was stirred at −50 °C for 2 h, then warmed to 0 °C, and diluted with Et_2O (3 mL). The reaction was quenched with the addition of DI H_2O (0.1 mL), an aqueous solution of NaOH (15%, 0.1 mL), and DI H_2O (0.2 mL) in sequence. The mixture was warmed to room temperature and stirred for 15 min. $MgSO_4$ was added. The resulting mixture was stirred for another 15 min and filtered through a silica pale with EtOAc (125 mL). The filtrate was concentrated *in vacuo*. Purification by flash column chromatography (20% EtOAc-hexanes) afforded (2-1-phenylvinyl)phenyl)methanol (**1n**) as a colorless oil (165.7 mg, 0.79 mmol, 95%). $\mathbf{R_f}$ = 0.58 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.50 (dd, *J* = 7.4, 1.0 Hz, 1H), 7.39 (td, *J* = 7.4, 1.6 Hz, 1H), 7.36–7.24 (m, 7H), 5.80 (d, *J* = 1.3 Hz, 1H), 5.26 (d, *J* = 1.3 Hz, 1H), 4.44 (d, *J* = 6.2 Hz, 1H), 1.40 (d, *J* = 6.2 Hz, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 148.3, 140.6, 140.4, 138.6, 130.2, 128.5, 128.0 127.5, 126.5, 115.6, 63.1; **FTIR** (thin film): cm^{-1} 3339, 3059, 3025, 1494, 1444, 1027, 906, 782, 769, 707; **HRLCMS-ESI** (m/z) Calcd for ($C_{15}H_{14}OLi$) ($[M+^7Li]^+$): 217.1199; found: 217.1201.

1,1,4-Triphenylpent-4-en-1-ol (1o).—To a solution of 4-phenylpent-4-enoic acid (**1o-i**)[11a] (2.12 g, 12.0 mmol, 1.0 equiv) and K_2CO_3 (2.49 g, 1.5 equiv) in DMF (24 mL) at room temperature, was added MeI (1.5 mL, 2.0 equiv). The solution was stirred at room temperature for 17 h, and was then quenched with DI H_2O (36 mL), followed by EtOAc (30 mL). The layers were separated and the organic layer was washed with a saturated aqueous solution of $NaHCO_3$ (25 mL x 3). The combined aqueous layers were extracted with EtOAc (40 mL x 3). The combined organic layers were washed with brine (50 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc–hexanes) afforded methyl 4-phenylpent-4-enoate (**1o-ii**) as a colorless oil (2.20 g, 11.5 mmol, 96%). $\mathbf{R_f}$ = 0.54 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.43–7.25 (m, 5H), 5.31 (s, 1H), 5.09 (d, *J* = 1.3 Hz, 1H), 3.66 (s, 3H), 2.88–2.82 (m, 2H),2.49 (t, *J* = 7.7 Hz, 2H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 173.4, 146.8, 140.4, 128.3, 127.5, 126.0, 112.7, 51.5, 33.0, 30.4; **FTIR** (thin film): cm^{-1} 2951, 1733, 1628, 1495, 1435, 1254, 1196, 1156, 898, 778, 702; **HRLCMS-ESI** (m/z) Calcd for ($C_{12}H_{15}O_2$) ($[M+H]^+$): 191.1068; found: 191.1066.

To a solution of methyl 4-phenylpent-4-enoate (**1o-ii**) (761.0 mg, 4.0mmol, 1.0 equiv) in THF (16mL) at 0 °C under N_2, was added dropwise PhMgBr (3 M in Et_2O, 4.0 mL, 3.0 equiv) over 10 min. The reaction solution was stirred at room temperature for 19 h and was then quenched with slow addition of DI H_2O (3 mL), followed by a saturated aqueous solution of NH_4Cl (5 mL). The solution was acidified with HCl (2 M, 5 mL). THF was removed *in vacuo* (~90%). The aqueous layer was extracted with Et_2O (15 mL x 3). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (5% EtOAc–hexanes to 10% EtOAc–hexanes) afforded 1,1,4-triphenylpent-4-en-1-o1 (**1o**) as a yellow oil (1.25 g, 4.0 mmol, 99%). $\mathbf{R_f}$ = 0.44 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.46–7.39 (m, 4H), 7.38–7.21 (m, 11H), 5.29 (d, *J* = 1.3 Hz, 1H), 5.08 (d, *J* = 1.3 Hz, 1H), 2.56–2.49 (m, 2H), 2.48–2.41 (m, 2H), 2.15 (s, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 148.4, 146.7, 140.7, 128.2, 128.1, 127.4, 126.8, 126.0, 126.0, 112.3, 78.2, 40.7, 29.7; **FTIR** (thin film): cm^{-1} 3558 (broad), 3468 (broad), 3056, 3024, 1493, 1446, 1057, 1026, 896, 775, 697; **HRLCMS-ESI** (m/z) Calcd for ($C_{23}H_{22}OLi$) ($[M+^7Li]^+$): 321.1826; found: 321.1826.

2,2-Diphenylpent-4-en-1-ol (1p).—2-Phenyl-3-bromopropene (**1p-i**) was synthesized as previously reported.[20] $\mathbf{R_f}$ = 0.66 (2% EtOAc–Hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.53–7.47 (m, 2H), 7.41–7.31 (m, 3H), 5.57 (s, 1H), 5.50 (s, 1H), 4.40 (s, 2H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 144.2, 137.5, 128.5, 128.2, 126.0, 117.2, 34.2; **FTIR** (thin film): cm^{-1} 3058, 1740, 1496, 1450, 1212, 910, 776, 716, 697, 549; **HRGCMS-ESI** (m/z) Calcd for (C_9H_9Br) ($[M]^+$): 195.9882; found: 195.9881.

To a solution of diphenylacetic acid (14.86 g, 70.0 mmol, 1.0 equiv) in MeOH (210 mL), was added H_2SO_4 (7.8 mL, 2.0 equiv). The resulting solution was refluxed for 13.5 h and cooled to room temperature. The mixture concentrated *in vacuo* to remove ~75% of the MeOH. The resulting residue was quenched with slow addition of a saturated aqueous solution of $NaHCO_3$ (75 mL). The aqueous layer was extracted with EtOAc (50 mL x 3). The combined organic layers were washed with brine (75 mL), dried with Na_2SO_4, and concentrated *in vacuo*, affording the crude ester which was used without further purification. To an air-free solution of this ester (1.25 g, 5.5 mmol, 1.0 equiv) in THF (6 mL) at −78 °C. was added slowly LDA (2 M in THF, 3.3 mL, 1.2 equiv) over 15 min. The resulting solution was stirred at −78 °C for 15 min, after which 2-phenyl-3-bromopropene (**1p-i**) (0.64 mL, 1.35 equiv) was added slowly over 5 min. The resulting reaction was stirred at −78 °C for 15 min and was then allowed to warm to room temperature overnight. The reaction was quenched with a saturated aqueous solution of NH_4Cl (10 mL). The aqueous layer was extracted with EtOAc (15 mL x 3). The combined organic layers were washed with brine (30 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (100% Hexanes to 5% EtOAc–Hexanes) afforded methyl 2,2-diphenylpent-4-enoate (**1p-ii**) as a colorless oil (1.69 g, 4.9 mmol, 88% over two steps). $\mathbf{R_f}$ = 0.81 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.36–7.14 (m, 15H), 5.11 (s, 1H), 4.67 (s, 1H), 3.66 (s, 2H), 3.36 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 173.7, 145.0, 143.1, 142.5, 129.0, 127.8, 127.6, 126.9, 126.8, 126.6, 118.3,, 60.1, 51.7, 43.6; **FTIR** (thin film): cm^{-1} 3056, 3026, 2948, 1733, 1495, 1446, 1202, 697; **HRLCMS-ESI** (m/z) Calcd for ($C_{24}H_{23}O_2$) ($[M+H]^+$): 343.1698; found: 343.1688.

To an air-free solution of **1p-ii** (1.37 g, 4.0 mmol, 1.0 equiv) in PhMe (4 mL) at −50 °C under N_2, was added slowly DIBAL (1 M in PhMe, 8.8 mL, 2.2 equiv) over 10 min. The reaction solution was stirred at −50 °C for 2 h, then warmed to 0 °C and diluted with Et_2O (5 mL). The reaction was quenched with addition of DI H_2O (0.4 mL), an aqueous solution of NaOH (15%, 0.4 mL), and DI H_2O (0.9 mL) in sequence. The mixture was warmed to room temperature and stirred for 15 min. $MgSO_4$ was added. The resulting mixture was stirred for another 15 min and filtered through a silica pale with EtOAc (150 mL). The filtrate was concentrated *in vacuo*. Purification by flash column chromatography (100% Hexanes to 10% EtOAc–hexanes) afforded 2,2-diphenylpent-4-en-1-ol (**1p**) as a colorless oil (1.01 g, 3.2 mmol, 80%). $\mathbf{R_f}$ = 0.67 (25% EtOAc–Hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.25–7.10 (m, 15H), 5.9 (s, 1H), 4.72 (s, 1H), 4.01 (d, *J* = 6.7 Hz, 2H), 3.47 (s, 2H), 1.2 (t, *J* = 6.7 Hz, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 145.6, 145.5, 142.9, 128.4, 127.9, 126.8, 126.4, 126.2, 118.4, 66.8, 52.6, 41.0; **FTIR** (thin film): cm^{-1} 3545 (broad), 3433 (broad), 3055, 3023, 1494, 1444, 905, 776, 757, 697; **HRLCMS-ESI** (m/z) Calcd for ($C_{23}H_{22}ONa$) ([M +Na]$^+$): 337.1563; found: 337.1556.

2,2-Dimethyl-4-phenylpent-4-en-1-ol (1q).—To an air-free solution of methyl isobutyrate (458.5 mg, 4.0 mmol, 1.0 equiv) in THF (12 mL) at −78 °C under N_2, was added slowly LDA (2 M in THF, 2.4 mL, 1.2 equiv) over 5 min. The resulting solution was stirred at −78 °C for 10 min and at 0 °C for 10 min. Then 2-phenyl-3-bromopropene (**1p-i**) (0.86 mL, 1.5 equiv) was added slowly over 3 min. The resulting reaction was stirred at 0 °C for 10 min and at room temperature for 30 min. The reaction was quenched with a saturated aqueous solution of NH_4Cl (20 mL). The aqueous layer was extracted with EtOAc (30 mL x 3). The combined organic layers were washed with brine (50 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (100% Hexanes to 5% EtOAc–Hexanes) afforded methyl 2,2-dimethyl-4-phenylpent-4-enoate (**1q-i**) as a colorless oil (719.4 mg, 3.3 mmol, 82%). $\mathbf{R_f}$ = 0.67 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.32–7.18 (m, 5H), 5.21 (d, *J* = 1.7 Hz, 1H), 5.03 (m, 1H), 3.27 (s, 2H), 2.77 (s, 2H), 1.11 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 177.5, 146.1, 142.1, 128.0, 127.2, 126.7, 117.0, 51.2, 46.0, 42.5, 25.5; **FTIR** (thin film): cm^{-1} 2972, 1731, 1199, 1137, 900, 779, 698; **HRLCMS-ESI** (m/z) Calcd for ($C_{14}H_{19}O_2$) ([M+H]$^+$): 219.1380; found: 219.1378.

To the solution of LAH (296.0 mg, 2.6 equiv) in Et_2O (18 mL) at 0 °C under N_2, was added slowly the solution of methyl 2,2-dimethyl-4-phenylpent-4-enoate (**1q-i**) (654.9 mg, 3.0 mmol, 1.0 equiv) in Et_2O (3 mL) over 4 min. The reaction solution was stirred at 0 °C for 15 min and then at room temperature for 2.5 h. The reaction was diluted with Et_2O (12 mL) and quenched at 0 °C with addition of DI H_2O (0.3 mL), an aqueous solution of NaOH (15%, 0.3 mL), and DI H_2O (0.9 mL) in sequence. The mixture was warmed to room temperature and stirred for 15 min. $MgSO_4$ was added. The resulting mixture was stirred for another 15 min and filtered through a silica pale with Et_2O. The filtrate was concentrated *in vacuo*. Purification by flash column chromatography (5% EtOAc–hexanes) afforded the alcohol (**1q**) as a white solid (514.0 mg, 2.7 mmol, 90%). $\mathbf{R_f}$ = 0.57 (25% EtOAc–Hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.42–7.22 (m, 5H), 5.26 (d, *J* = 1.8 Hz, 1H), 5.08 (d, *J* = 1.8 Hz, 1H), 3.17 (d, *J* = 6.1 Hz, 2H), 2.53 (s, 2H), 1.15 (t, *J* = 6.1 Hz, 1H), 0.79 (s, 3H);

$^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 146.9, 143.4, 128.3, 127.3, 126.4, 116.8, 71.2, 43.7, 36.5, 24.7; **FTIR** (thin film): cm^{-1} 3356 (broad), 2960, 1042, 897, 778, 703; **HRLCMS-ESI** (m/z) Calcd for ($C_{13}H_{19}O$) ($[M+H]^+$): 191.1430; found: 191.1432.

4-Phenylpent-4-en-1-ol (1r).—To an air-free solution of methyl 4-phenylpent-4-enoate (**1o-ii**) (570.7 mg, 3.0 mmol, 1.0 equiv) in PhMe (3 mL) at −50 °C under N_2, was added dropwise DIBAL (1 M in PhMe, 6.6 mL, 2.2 equiv) over 10 min. The reaction solution was stirred at −50 °C for 2 h and was then warmed to 0 °C and diluted with Et_2O (5 mL). The reaction was quenched with slow addition of DI H_2O (0.4 mL), an aqueous solution of NaOH (15%, 0.4 mL), and DI H_2O (0.9 mL) in sequence. The mixture was warmed to room temperature and stirred for 15 min. $MgSO_4$ was added. The resulting mixture was stirred for another 15 min and filtered through a silica pale with EtOAc (150 mL). The filtrate was concentrated *in vacuo*. Purification by flash column chromatography (20% EtOAc–hexanes to 25% EtOAc–hexanes) afforded 4-phenylpent-4-en-1-ol (**1r**) as a colorless oil (461.2 mg, 2.8 mmol, 95%). $\mathbf{R_f}$ = 0.39 (25% EtOAc–hexanes). **^1H NMR** ($CDCl_3$, 400 MHz): δ 7.42–7.37 (m, 2H), 7.34–7.22 (m, 3H), 5.28 (d, *J* = 1.4 Hz, 1H) 5.08 (q, *J* = 1.4 Hz, 1H),3.71–3.59 (m, 2H), 2.59 (td, *J* = 7.5, 1.0 Hz, 2H), 1.71 (tt, *J* = 7.5, 6.5 Hz, 2H), 1.31–1.21 (m, 1H); **$^{13}C\{^1H\}$ NMR** ($CDCl_3$, 125 MHz): δ 147.9, 140.9, 128.3, 127.4, 126.0, 112.5, 62.3, 31.5, 31.1; **FTIR** (thin film): cm^{-1} 3323 (broad), 2940, 1626, 1494, 1443, 1057, 896, 778, 703; **HRLCMS-ESI** (m/z) Calcd for ($C_{11}H_{15}O$) ($[M+H]^+$): 163.1117; found: 163.1116.

(*E*)-2-(2-styrylphenyl)propan-2-ol (*E*-1s).—To an air-free solution of methyl (*E*)-2-styrylbenzoate (***E*-1s-i**)[11a] (1.69 g, 7.0 mmol, 1.0 equiv) in Et_2O (28 mL) at 0 °C under N_2, was added dropwise MeMgBr (3 M in Et_2O, 7.0 mL, 3.0 equiv) over 10 min. The reaction solution was stirred at room temperature for 14 h and was then quenched with slow addition of DI H_2O (8 mL), followed by a saturated aqueous solution of NH_4Cl (10 mL). The solution was acidified with HCl (2 M, 10 mL). The aqueous layer was extracted with Et_2O (20 mL x 3). The combined organic layers were dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (5% EtOAc–hexanes to 20% EtOAc–hexanes) afforded (*E*)-2-(2-styrylphenyl)propan-2-ol (***E*-1s**) as a colorless oil (1.40 g, 5.9 mmol, 84%, with 464:1 *E*:*Z* by GCMS). $\mathbf{R_f}$ = 0.29 (10% EtOAc–hexanes). **^1H NMR** ($CDCl_3$, 400 MHz): δ 8.13 (d, *J* = 16.2 Hz, 1H), 7.61 (dd, *J* = 7.4, 1.8 Hz, 1H), 7.56–7.52 (m, 2H), 7.47 (dd, *J* = 7.4, 1.8 Hz, 1H), 7.37 (t, *J* = 7.4 HZ, 1H), 7.32–7.23 (m, 3H), 6.85 (d, *J* = 16.2 Hz, 1H), 1.83 (s, 1H), 1.71 (s, 6H); **$^{13}C\{^1H\}$ NMR** ($CDCl_3$, 125 MHz): δ 144.9, 137.8, 136.8, 129.8, 128.6, 128.3, 127.4, 127.3, 126.6, 125.2, 73.7, 31.5; **FTIR** (thin film): cm^{-1} 3370 (broad), 2974, 1598, 1493, 1446, 1364, 1162, 965, 756, 691; **HRLCMS-ESI** (m/z) Calcd for ($C_{17}H_{18}OLi$) ($[M+^7Li]^+$): 245.1513; found: 245.1512.

(*Z*)-2-(2-Styrylphenyl)propan-2-ol (*Z*-1s).—To an air-free solution of methyl (*Z*)-2-styrylbenzoate (***Z*-1s-ii**)[11a] (834.0 mg, 3.5 mmol, 1.0 equiv, 10:1 *Z*:*E* ratio) in Et_2O (14 mL) at 0 °C under N_2, was added slowly MeMgBr (3 M in Et_2O, 3.5 mL, 3.0 equiv). The reaction solution was stirred at 0 °C for 5 min, at room temperature for 18 h, and then quenched with slow addition of a saturated aqueous solution of NH_4Cl (10 mL) and DI H_2O (10 mL). The solution was acidified with HCl (2 M, 5 mL). The aqueous layer was extracted with EtOAc (30 mL x 3). The combined organic layers were washed with brine (50 mL), dried with

Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (100% Hexanes to 10% EtOAc–hexanes) afforded (*Z*)-2-(2-styrylphenyl)propan-2-ol (***Z*-1s**) as a colorless oil (795.8 mg, 4.0 mmol, 95%, with 12:1 *Z*:*E* ratio by GCMS). $\mathbf{R_f}$ = 0.62 (25% EtOAc–Hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.57 (d, *J* = 8.1 Hz, 1H), 7.32–7.03 (m, 9H), 6.59 (d, *J* = 12.2 Hz, 1H), 2.17 (s, 1H), 1.69 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 146.0, 136.5, 135.8, 131.9, 131.2, 129.5, 129.3, 128.0, 127.3, 127.2, 127.0, 125.3, 73.6, 30.7; **FTIR** (thin film): cm^{-1} 3356 (broad), 2973, 1598, 1494, 1445, 1363, 1163, 946, 784, 760, 698; **HRLCMS-ESI** (m/z) Calcd for ($C_{17}H_{18}ONa$) ($[M+Na]^+$): 261.1250; found: 261.1249.

(*E*)-2-(2-(Prop-1-en-1-yl)phenyl)propan-2-ol (*E*-1t).—To an air-free solution of methyl (*E*)-2-(prop-1-en-1-yl)benzoate (***E*-1t-i**)[11a] (352.4 mg, 2.0 mmol, 1.0 equiv) in Et_2O (8 mL) at 0 °C under N_2, was added dropwise MeMgBr (3 M in Et_2O, 2.0 mL, 3.0 equiv) over 10 min. The reaction solution was stirred at room temperature for 15 h and was then quenched with slow addition of DI H_2O (3 mL), followed by a saturated aqueous solution of NH_4Cl (3 mL). The solution was acidified with HCl (2 M, 6 mL). The aqueous layer was extracted with Et_2O (10 mL x 3). The combined organic layers were dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (5% EtOAc–hexanes to 20% EtOAc–hexanes) afforded (*E*)-2-(2-(prop-1-en-1-yl)phenyl)propan-2-ol (***E*-1t**) as a colorless oil (317.8 mg, 1.8 mmol, 90%). $\mathbf{R_f}$ = 0.32 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.45–7.36 (m, 1H), 7.26–7.17 (m, 3H), 5.96 (dq, *J* = 15.6, 6.6 Hz, 1H), 1.92 (s, 1H), 1.91 (dd, *J* = 6.6, 1.8 Hz, 1H), 1.66 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 144.2, 137.1, 131.8, 128.8, 127.2, 126.6, 124.8, 73.6, 31.2, 18.8; **FTIR** (thin film): cm^{-1} 3371 (broad), 2972, 1478, 1442, 1364, 1239, 1163, 1142, 1050, 966, 952, 862, 758, 741; **HRLCMS-ESI** (m/z) Calcd for ($C_{12}H_{15}$) ($[M+H-H_2O)^+$]: 159.1168; found: 159.1168.

2-(1-Methylcyclopent-3-en-1-yl)propan-2-ol (1u).—To a solution of 3-cyclopentenecarboxylic acid (1.0 mL, 10.0 mmol, 1.0 equiv) in MeOH (30 mL), was added H_2SO_4 (1.1 mL, 2.0 equiv). The resulting solution was stirred at room temperature for 16.5 h. The reaction was concentrated *in vacuo* to remove ~75% of the MeOH. The resulting residue was quenched with slow addition of a saturated aqueous solution of $NaHCO_3$ (10 mL). The aqueous layer was extracted with Et_2O (30 mL x 3). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo*, affording the crude ester (volatile) which was used without further purification. To a solution of this crude ester (504.6 mg, 4.0 mmol, 1.0 equiv) in THF (4 mL) at −78 °C, was added slowly LDA (2 M in THF, 2.4 mL, 1.2 equiv) over 15 min. The resulting solution was stirred at −78 °C for 15 min, after which MeI (348.6 μL, 1.4 equiv) was added slowly. The resulting reaction was stirred at −78 °C for 5 min, and was then allowed to warm to room temperature overnight. The reaction was quenched with a saturated aqueous solution of NH_4Cl (10 mL). The aqueous layer was extracted with Et_2O (20 mL x 3). The combined organic layers were washed with brine (50 mL), dried with Na_2SO_4, and concentrated *in vacuo*. The crude residue was flushed through a plug of silica, washing with hexanes, and concentrated *in vacuo*, affording a colorless oil that was used without further purification. To a solution of the crude olefin (308.4 mg, 2.2 mmol, 1.0 equiv) in Et_2O (9 mL) at 0 °C, was added slowly MeMgBr (3 M in Et_2O, 2.2 mL, 3.0 equiv). The reaction solution was stirred at 0 °C for 1 h, at room temperature for 20 h,

and quenched with slow addition of a saturated aqueous solution of NH_4Cl (10 mL) and DI H_2O (5 mL). The aqueous layer was extracted with Et_2O (20 mL x 3). The combined organic layers were washed with brine (50 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (5% EtOAc–Hexanes to 15% EtOAc–hexanes) afforded 2-(1-methylcyclopent-3-en-1-yl)propan-2-ol (**1u**) as a colorless oil (191.3 mg, 1.4 mmol, 17% over three steps). $\mathbf{R_f}$ = 0.67 (25% EtOAc–Hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 5.60 (s, 2H), 2.62 (d, *J* = 14.6 Hz, 1H), 1.91 (d, *J* = 14.6 Hz, 1H), 1.27 (s, 1H), 1.20 (s, 6H), 1.05 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 129.0, 74.5, 49.4, 42.1, 26.2, 25.2; **FTIR** (thin film): cm^{-1} 3420, 2974, 1372, 669; **HRGCMS-ESI** (m/z) Calcd for (C_9H_{14}) ($[M–H_2O]^+$): 122.1090; found: 122.1090.

Preparation of Other Unsaturated Oxygen Source Substrates

***N*-(2-Vinylphenyl)benzamide (4a).—**To a solution of 2-bromoaniline (3.44 g, 20.0 mmol, 1.0 equiv) in CH_2Cl_2 (50 mL), was added NEt_3 (3.6 mL, 1.3 equiv) and BzCl (2.6 mL, 1.1 equiv). The reaction solution was stirred at room temperature for 12 h and was then quenched with a saturated aqueous solution of NH_4Cl (20 mL). The organic layer was washed with HCl (2 M, 30 mL), a saturated aqueous solution of $NaHCO_3$ (30 mL), and brine (50 mL). The organic layer was dried with Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (20% EtOAc–hexanes to 30% EtOAc–hexanes) afforded *N*-(2-bromophenyl)benzamide (**4a-i**) as a fluffy, off-white solid (4.93 g, 17.9 mmol, 89%). $\mathbf{R_f}$ = 0.50 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.56 (dd, *J* = 8.3, 1.6 Hz, 1H), 8.51–8.44 (br, 1H), 7.98–7.91 (m, 2H), 7.62–7.49 (m, 4H), 7.38 (td, *J* = 7.8, 1.6 Hz, 1H), 7.02 (td, *J* = 7.8, 1.6 Hz, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 165.2, 135.7, 134.5, 132.2, 132.1, 128.9, 128.5, 127.0, 125.2, 121.7, 113.7; **FTIR** (thin film): cm^{-1} 3277 (broad), 3058, 1651, 1601, 1578, 1526, 1491, 1434, 1304, 1262, 1027, 749, 705, 690; **HRLCMS-ESI** (m/z) Calcd for ($C_{13}H_{11}BrNO$) ($[M+H]^+$): 276.0019; found: 276.0022.

A solution of *N*-(2-bromophenyl)benzamide (**4a-i**) (1.38 g, 5.0 mmol, 1.0 equiv) and tetrakis (triphenylphosphine)palladium (288.9 mg, 0.05 equiv) in DME (40 mL) was stirred at room temperature for 10 min. At this time, K_2CO_3 (1.04 g, 1.5 equiv), potassium trifluorovinylborate (2.41 g, 1.5 equiv), and DI H_2O (12 mL) were added. The reaction was refluxed for 15 h, then cooled to room temperature, and quenched with a saturated aqueous solution of NH_4Cl (30 mL). The aqueous layer was extracted with EtOAc (30 mL x 3). The combined organic layers were washed with brine (50 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (20% EtOAc–hexanes to 40% EtOAc–hexanes) afforded *N*-(2-vinylphenyl)benzamide (**4a**) as a chalky, off-white powder (1.01 g, 4.5 mmol, 90%). $\mathbf{R_f}$ = 0.16 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.03 (d, *J* = 8.0 Hz, 1H), 7.94–7.85 (m, 3H), 7.60–7.43 (m, 4H), 7.35 (td, *J* = 8.0, 1.4 Hz, 1H), 7.23–7.16 (m, 1H), 6.87 (dd, *J* = 17.5, 11.0 Hz, 1H), 5.72 (dd, *J* = 17.5, 1.3 Hz, 1H), 5.47 (dd, *J* = 11.0, 1.3 Hz, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 165.6, 134.7, 134.4, 132.3, 131.9, 130.6, 128.8, 128.5, 127.1, 125.4, 123.5, 118.4; **FTIR** (thin film): cm^{-1} 3239, 1647, 1600, 1579, 1521, 1480, 1305, 1270, 911, 767, 744, 713, 690; **HRLCMS-ESI** (m/z) Calcd for ($C_{15}H_{14}NO$) ($[M+H]^+$): 224.1070; found: 224.1073.

(*E*)-*N*-(2-(Prop-1-en-1-yl)phenyl)benzamide (4b).—A solution of *N*-(2-bromophenyl)benzamide (**4a-i**) (1.24 g, 4.5 mmol, 1.0 equiv) and tetrakis (triphenylphosphine)palladium (260.0 mg, 0.05 equiv) in DME (36 mL) was stirred at room temperature for 10 min. At this time, K_2CO_3 (0.93 g, 1.5 equiv), potassium *trans*-1-propenyltrifluoroborate (0.96 g, 1.4 equiv), and DI H_2O (11 mL) were added. The reaction was refluxed for 17 h, then cooled to room temperature, and quenched with a saturated aqueous solution of NH_4Cl (30 mL). The aqueous layer was extracted with EtOAc (30 mL x 3). The combined organic layers were washed with brine (50 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc–hexanes to 50% EtOAc–hexanes) afforded (*E*)-*N*-(2-(prop-1-en-1-yl)phenyl)benzamide (**4b**) as a chalky, off-white powder (0.87 g, 3.7 mmol, 82%). $\mathbf{R_f}$ = 0.28 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.090–801 (m, 1H), 7.92–7.83 (m, 3H), 7.58 (t, *J* = 7.0 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 2H), 7.38 (d, *J* = 7.6 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 6.51 (d, *J* = 15.5 Hz, 1H), 6.18 (dq, *J* = 15.5, 6.6 Hz, 1H), 1.96 (d, *J* = 6.6 Hz, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 165.5, 134.9, 134.1, 131.8, 130.8, 130.5, 128.8, 127.7, 127.2, 127.0, 125.8, 125.2, 123.1, 19.0; **FTIR** (thin film): cm^{-1} 3262, 1648, 1523, 1483, 1298, 748; **HRLCMS-ESI** (m/z) Calcd for ($C_{16}H_{16}NO$) ($[M+H]^+$): 238.1226; found: 238.1232.

***N*-Phenyl-2-vinylbenzamide (4c).—**To a solution of 2-vinylbenzoic acid (**1a-i**) (0.74 g, 5.0 mmol, 1.3 equiv) in CH_2Cl_2 (10 mL), was added $SOCl_2$ (0.73 mL, 2.0 equiv). The resulting solution was refluxed for 4 h, cooled to room temperature, and then concentrated *in vacuo*, yielding the crude acid chloride which was used in the next step without further purification. To a solution of this acid chloride and NEt_3 (1.4 mL, 2.0 equiv) in CH_2Cl_2 (10 mL), was added aniline (0.35 mL, 1.2 equiv). The reaction was stirred at room temperature for 18 h and was then quenched with DI H_2O (20 mL). The organic layer was washed with a saturated aqueous solution of $NaHCO_3$ (30 mL). The aqueous layer was extracted with CH_2Cl_2 (20 mL x 3). The combined organic layers were washed with brine and concentrated *in vacuo*. Purification by flash column chromatography (5% EtOAc–hexanes to 15% EtOAc–hexanes) afforded *N*-phenyl-2-vinylbenzamide (**4c**) as an off-white solid (0.70 g, 3.1 mmol, 63%). $\mathbf{R_f}$ = 0.58 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.65–7.56 (m, 4H), 7.51 (br, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.39–7.30 (m, 3H), 7.16 (t, *J* = 1.5 Hz, 1H), 7.10 (dd, *J* = 17.4, 10.9 Hz, 1H), 5.76 (d, *J* = 17.4 Hz, 1H), 5.39 (d, *J* = 10.9 Hz, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 167.5, 137.9, 135.7, 135.0, 134.1, 130.2, 127.5, 127.3, 126.1, 124.2, 119.8, 116.7; **FTIR** (thin film): cm^{-1} 3273 (broad), 3060, 1648, 1597, 1529, 1491, 1438, 1321, 1259, 914, 753, 691; **HRLCMS-ESI** (m/z) Calcd for ($C_{15}H_{14}NO$) ($[M+H]^+$): 224.1070; found: 224.1074.

2-Allyl-1,3-diphenylpropane-1,3-dione (4d).—To an air-free solution of acetophenone (3.5 mL, 30.0 mmol, 1.0 equiv) in THF (30 mL) at −78 °C under N_2, was added slowly LDA (2 M in THF, 18.0 mL, 1.2 equiv). The solution was stirred at −78 °C for 20 min, upon which BzCl (3.8 mL, 1.1 equiv) was added over 2 min. The resulting reaction solution was stirred at −78 °C for 5 min, at room temperature for 18 h, and then quenched with HCl (2 M, 15 mL). The reaction mixture was extracted with EtOAc (30 mL x 3). The combined organic layers were washed with brine (70 mL), dried with Na_2SO_4, and concentrated *in vacuo*.

Purification by flash column chromatography (5% EtOAc–hexanes) afforded 3-hydroxy-1,3-diphenylprop-2-en-1-one (**4d-i**) as an off-white/yellow solid (3.41 g, 15.2 mmol, 51%) in exclusively the enol isomer that matched previously reported spectra.[21] – = 0.57 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 16.88 (s, 1H), 8.03–7.98 (m, 4H), 7.59–7.54 (, 2H), 7.54–7.46 (m, 4H), 6.87 (s, 1H).

To a stirred solution of 3-hydroxy-1,3-diphenylprop-2-en-1-one (**4d-i**) (1.12 g, 5.0 mmol, 1.0 equiv) in DMF (10 mL) was added allyl bromide (0.48 mL, 1.1 equiv), then K_2CO_3 (1.04 g, 1.5 equiv). The resulting solution was heated at 60 °C for 6 h, then cooled to room temperature and quenched with H_2O (30 mL) and an aqueous solution of HCl (2M, 10 mL). The solution was extracted with EtOAc (20 mL x 3). The combined organic layers were washed with brine (40 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (100% hexanes to 5% EtOAc–hexanes) afforded 2-allyl-1,3-diphenylpropane-1,3-dione (**4d**) as a white solid (1.12 g, 4.2 mmol, 85%) that matched previously reported spectra.[22] $\mathbf{R_f}$ = 0.38 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.96 (d, *J* = 7.6 Hz, 4H), 7.57 (t, *J* = 7.6 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 4H), 5.88 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1H), 5.30 (t, *J* = 6.8 Hz, 1H), 5.10 (dt, *J* = 17.0, 1.3 Hz, 1H), 5.03 (d, *J* = 10.2 Hz, 1H), 2.88 (td, *J* = 6.8, 1.3 Hz, 2H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 195.4, 135.8, 134.9, 133.5, 128.8, 128.5, 117.1, 56.5, 33.5; **FTIR** (thin film): cm^{-1} 3064, 1693, 1669, 1595, 1580, 1447, 1327, 1267, 1237, 1198, 1180, 999, 920, 751, 688, 585; **HRLCMS-ESI** (m/z) Calcd for ($C_{18}H_{17}O_2$) ($[M+H]^+$): 265.1223; found: 265.1231.

2-(2-Methylallyl)-1,3-diphenylpropane-1,3-dione (4e).—To a solution of 3-hydroxy-1,3-diphenylprop-2-en-1-one (**4d-i**) (0.90 g, 4.0 mmol, 1.0 equiv) in DMF (8 mL), was added 3-bromo-2-methylpropene (0.44 mL, 1.1 equiv) and K_2CO_3 (0.83 g, 1.5 equiv). The resulting solution was heated at 60 °C for 6 h, then cooled to room temperature and quenched with DI H_2O (30 mL). The solution was extracted with EtOAc (20 mL x 3). The combined organic layers were washed with brine (50 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (5% EtOAc–hexanes) afforded 2-(2-methylallyl)-1,3-diphenylpropane-1,3-dione (**4e**) as a white solid (0.65 g, 2.3 mmol, 59%) that matched previously reported spectra.[22] $\mathbf{R_f}$ = 0.58 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.00–7.95 (m, 4H), 7.57 (tt, *J* = 7.4, 1.5 Hz, 2H), 7.48–7.43 (m, 4H), 5.43 (t, *J* = 6.6 Hz, 1H), 4.78 (s, 1H), 4.69 (s, 1H), 2.85 (d, *J* = 6.6 Hz, 2H), 1.78 (s, 3H).

(*E*)-1-phenylbut-3-en-1-one oxime (4f).—To an anhydrous solution of allyl bromide (3.46 mL, 40.0 mmol, 2.0 equiv) in THF (50 mL) at 0 °C, was added zinc dust (2.62 g, 40.0 mmol, 2.0 equiv). The mixture was stirred at 0 °C for 5 min and then was added benzaldehyde (2.03 mL, 20.0 mmol, 1.0 equiv). The reaction was stirred at 4 °C for 18 h and was then quenched with a saturated aqueous solution of NH_4Cl (30 mL). The solution was stirred at 0 °C for 30 min (a white precipitate formed). The mixture was warmed to room temperature, followed by addition of HCl (2 M, 15 mL). The aqueous layer was extracted with EtOAc (40 mL x 3). The combined organic layers were washed with brine (50 mL), dried (Na_2SO_4), and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc–hexanes to 15% EtOAc–hexanes) afforded 1-phenylbut-3-en-1-ol (**4f-i**) as a

clear oil (2.70, 18.2 mmol, 91%). $\mathbf{R_f}$ = 0.57 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.39–7.32 (m, 4H), 7.31–7.25 (m, 1H), 5.81 (ddt, *J* = 17.2, 10.0, 7.1 Hz, 1H), 5.20–5.12 (m, 2H), 4.74 (dd, *J* = 7.6, 5.3 Hz, 1H), 2.58–2.44 (m, 2H), 2.05 (s, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 143.8, 134.4, 128.3, 127.4, 125.7, 118.3, 73.2, 43.7; **FTIR** (thin film): cm^{-1} 3362 (broad), 3029, 2906, 1641, 1493, 1454, 1046, 988, 915, 757, 699; **HRLCMS-ESI** (m/z) Calcd for ($C_{10}H_{12}ONa$) ($[M+Na]^+$): 171.0780; found: 171.0781.

To an air-free suspension of pyridinium chlorochromate (4.74 g, 2.0 equiv) and Celite (4.74 g) in CH_2Cl_2 (67.5 mL) under N_2, was added slowly a solution of 1-phenylbut-3-en-1-ol (**4f-i**) (1.63 g, 11.0 mmol, 1.0 equiv) in CH_2Cl_2 (12.5 mL) over 6 min. The reaction was stirred at room temperature for 14 h and was then filtered through a pale of silica. The filtrate was concentrated *in vacuo*. Purification by flash column chromatography (100% hexanes to 10% EtOAc–hexanes) afforded 1-phenylbut-3-en-1-one (**4f-ii**) as a clear oil (1.04 g, 7.1 mmol, 65%). $\mathbf{R_f}$ = 0.50 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.97 (d, *J* = 8.2 Hz, 2H), 7.60–7.55 (m, 1H), 7.47 (t, *J* = 7.4 Hz, 2H), 6.09 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.27–5.18 (m, 2H), 3.77 (dd, *J* = 6.7, 1.2 Hz, 2H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 197.9, 136.4, 133.1, 131.0, 128.5, 128.2, 118.6, 43.3; **FTIR** (thin film): cm^{-1} 3080, 1681, 1597, 1580, 1448, 1332, 1208, 1003, 919, 753, 689; **HRLCMS-ESI** (m/z) Calcd for ($C_{10}H_{11}O$) ($[M+H]^+$): 147.0804; found: 147.0804.

To a slurry of $NH_2OH{\cdot}HCl$ (2.26 g, 5.0 equiv) in EtOH (20 mL), was added a solution of NaOAc (3.73 g, 7.0 equiv) in H_2O (20 mL). Upon the resulting solution becoming clear, a solution of 1-phenylbut-3-en-1-one (**4f-ii**) (0.95 g, 6.5 mmol, 1.0 equiv) in EtOH (20 mL) was added. The resulting reaction was stirred at room temperature for 15 h. EtOH was removed *in vacuo*. The aqueous layer was extracted with EtOAc (40 mL x 3). The combined organic layers were washed with brine (50 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (5% EtOAc–hexanes to 10% EtOAc–hexanes) afforded (*E*)-1-phenylbut-3-en-1-one oxime (**4f**) as a white solid (884.4 mg, 5.5 mmol, 84%). $\mathbf{R_f}$ = 0.26 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.83 (s, 1H), 7.68–7.61 (m, 2H), 7.43–7.35 (m, 3H), 5.95 (ddt, *J* = 17.1, 10.2, 6.3 Hz, 1H), 5.18 (d, *J* = 17.1 Hz, 1H), 5.12 (d, *J* = 10.2 Hz, 1H), 3.60 (d, *J* = 6.3 Hz, 2H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 156.7, 135.5, 132.0, 129.3, 128.5, 126.3, 117.1, 31.2; **FTIR** (thin film): cm^{-1} 3212 (broad), 3059, 2912, 1639, 1497, 1445, 1293, 1051, 943, 915, 758, 692; **HRLCMS-ESI** (m/z) Calcd for ($C_{10}H_{12}NO$) ($[M+H]^+$): 162.0913; found: 162.0918.

***N*-hydroxy-*N*-methyl-2-vinylbenzamide (4g).—**To a solution of 2-vinylbenzoic acid (**1a-i**) (0.74 g, 5.0 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) and DMF (15 drops), was added $SOCl_2$ (0.73 mL, 2.0 equiv). The resulting solution was refluxed for 2 h, cooled to room temperature and concentrated *in vacuo*, affording the crude acid chloride which was used in the next step without further purification. To a solution of $MeNHOH{\cdot}HCl$ (0.585 g, 1.4 equiv) and $NaHCO_3$ (1.01 g, 2.4 equiv) in THF (5 mL) and DI H_2O (1 mL), was added dropwise a solution of the crude acid chloride in THF (5 mL) over 10 min. The reaction was stirred at room temperature for 15 h and was then quenched with DI H_2O (8 mL). The aqueous layer was extracted with CH_2Cl_2 (20 mL x 3). The combined organic layers were washed with brine (25 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by

flash column chromatography (25% EtOAc-hexanes to 50% EtOAc-hexanes) afforded *N*-hydroxy-*N*-methyl-2-vinylbenzamide (**4g**) as a white solid (0.708 g, 4.0 mmol, 80%). $\mathbf{R_f}$ = 0.34 (50% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.73 (br, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.46–7.40 (m, 1H), 7.35–7.31 (m, 2H), 6.75 (dd, *J* = 17.5, 11.1 Hz, 1H), 5.78 (d, *J* = 17.5 Hz, 1H), 5.37 (d, *J* = 11.1 Hz, 1H), 3.18 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 165.3, 135.2, 133.0, 131.9, 130.1, 127.9, 127.2, 125.6, 117.2, 37.6; **FTIR** (thin film): cm^{-1} 3160 (broad), 2924, 1613, 1391, 768; **HRLCMS-ESI** (m/z) Calcd for ($C_{10}H_{12}NO_2$) ([M+H]$^+$): 178.0868; found: 178.0861.

***N*-hydroxy-*N*-phenyl-2-vinylbenzamide (4h).—**To a solution of 2-vinylbenzoic acid (**1a-i**) (0.77 g, 5.2 mmol, 1.3 equiv) in CH_2Cl_2 (10.4 mL) and DMF (15 drops), was added $SOCl_2$ (0.76 mL, 2.6 equiv). The resulting solution was refluxed for 2 h. The reaction was cooled to room temperature and concentrated *in vacuo*, yielding the crude acid chloride which was used in the next step without further purification. To a solution of PhNHOH (0.437 g, 4.0 mmol, 1.0 equiv) and $NaHCO_3$ (0.706 g, 2.1 equiv) in THF (3.5 mL) and DI H_2O (0.82 mL), was added dropwise a solution of the crude acid chloride in THF (6 mL) over 10 min. The resulting reaction mixture was stirred at room temperature for 15 h. The reaction was quenched with DI H_2O (8 mL). The aqueous layer was extracted with CH_2Cl_2 (20 mL x 3). The combined organic layers were washed a saturated aqueous solution of $NaHCO_3$ (30 mL x 3), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc-hexanes to 50% EtOAc-hexanes) afforded *N*-hydroxy-*N*-phenyl-2-vinylbenzamide (**4h**) as a gray solid (0.674 g, 2.8 mmol, 70%). $\mathbf{R_f}$ = 0.67 (50% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 9.26 (br, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.33 (td, *J* = 7.4, 2.2 Hz, 1H), 7.23–7.05 (m, 7H), 6.85 (dd, *J* = 17.4, 11.0 Hz, 1H), 5.68 (d, *J* = 17.4 Hz, 1H), 5.32 (d, *J* = 11.0 Hz, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 165.2, 138.6, 135.7, 133.3, 132.1, 130.0, 128.6, 128.0, 127.6, 127.4, 125.5, 125.0, 117.0; **FTIR** (thin film): cm^{-1} 3065, 2884 (broad), 1622, 1589, 1491, 1377, 919, 761, 692; **HRLCMS-ESI** (m/z) Calcd for ($C_{15}H_{14}NO_2$) ([M+H]$^+$): 240.1019; found: 240.1024.

***N*-hydroxy-*N*-methyl-2-(prop-1-en-2-yl)benzamide (4j).—**To a solution of 2-(prop-1-en-2-yl)benzoic acid (**4j-i**)[11a] (0.568 g, 3.5 mmol, 1.0 equiv) in CH_2Cl_2 (7 mL) and DMF (10 drops), was added thionyl chloride (0.51 mL, 2.0 equiv). The resulting solution was refluxed for 2 h. The reaction was cooled to room temperature and concentrated *in vacuo*, yielding the crude acid chloride which was used in the next step without further purification. To a solution of MeNHOH·HCl (0.409 g, 1.4 equiv) and $NaHCO_3$ (0.706 g, 2.4 equiv) in THF (3 mL) and DI H_2O (0.7 mL), was added dropwise a solution of the above crude acid chloride in THF (4 mL) over 5 min. The reaction was stirred at room temperature for 18 h and was then quenched with addition of a saturated aqueous solution of NH_4Cl (3 mL) and DI H_2O (5 mL). The aqueous layer was extracted with CH_2Cl_2 (20 mL x 3). The combined organic layers were washed with brine (25 mL), dried with Na_2SO_4, and concentrated *in vacuo* to afford the crude product. Purification by flash column chromatography (25% EtOAc-hexanes to 50% EtOAc-hexanes) afforded *N*-hydroxy-*N*-methyl-2-(prop-1-en-2-yl)benzamide (**4j**) as a white solid (0.483 g, 2.5 mmol, 72%). $\mathbf{R_f}$ = 0.42 (50% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.64 (br, 1H), 7.45–7.38 (m, 1H), 7.36–7.29 (m, 3H), 5.19 (s, 1H), 5.03 (s, 1H), 3.17 (s, 3H), 2.09 (s, 3H); **^{13}C{$_1$H} NMR** ($CDCl_3$, 125

MHz): δ 165.6, 143.3, 141.5, 131.2, 129.9, 128.1, 127.6, 127.3, 116.3, 37.3, 23.2; **FTIR** (thin film): cm^{-1} 3152 (broad), 2917, 1593, 1428, 1388, 1214, 1187, 909, 771; **HRLCMS-ESI** (m/z) Calcd for ($C_{11}H_{14}NO_2$) ($[M+H]^+$): 192.1019; found: 192.1025.

***N*-hydroxy-*N*,2,2-trimethylpent-4-enamide (4k).—**To a solution of 2,2-dimethyl-4-pentenoic acid (384.5 mg, 3.0 mmol, 1.0 equiv) in CH_2Cl_2 (7.5 mL) and DMF (5 drops) at 0 °C, was added oxalyl chloride (0.5 mL, 2.0 equiv) over 10 min. The solution was warmed to room temperature and stirred for 1.5 h. The solvents were then removed *in vacuo*, affording the crude acid chloride which was used in the next step without further purification. To a solution of MeNHOH·HCl (501.1 mg, 2.0 equiv) and $NaHCO_3$ (1.01 g, 4.0 equiv) in THF (3 mL) and H_2O (0.7 mL), was added slowly a solution of the crude acid chloride in THF (4 mL) over 10 min. The reaction was stirred at room temperature for 17 h. The reaction was quenched with a saturated aqueous solution of NH_4Cl (5 mL) and DI H_2O (5 mL). The aqueous layer was extracted with EtOAc (25 mL x 3). The combined organic layers were washed with brine (40 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification flash column chromatography (20% EtOAc–hexanes to 35% EtOAc–hexanes) afforded *N*-hydroxy-*N*,2,2-trimethylpent-4-enamide (**4k**) as a clear oil (308.7 mg, 2.0 mmol, 65%). $\mathbf{R_f}$ = 0.57 (50% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 5.73 (ddt, *J* = 17.8, 9.8, 7.3 Hz, 1H), 5.06 (d, *J* = 17.8 Hz, 1H), 5.05 (d, *J* = 9.8 Hz, 1H), 3.35 (s, 3H), 2.39 (d, *J* = 7.3 Hz, 2H), 1.25 (s, 6H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 176.4, 134.6, 117.5, 43.6, 42.2, 38.0, 25.1; **FTIR** (thin film): cm^{-1} 3176 (broad), 2927, 1590, 1475, 1385, 1210, 916; **HRLCMS-ESI** (m/z) Calcd for ($C_8H_{15}NO_2Na$) ($[M+H]^+$): 180.0995; found: 180.0998.

2-(Prop-1-en-2-yl)benzothioic *S*-acid (4i).—To a solution of 2-(prop-1-en-2-yl)benzoic acid (**4j-i**) (0.811 g, 5.0 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) and DMF (10 drops) at room temperature, was added thionyl chloride (0.73 mL, 10.0 mmol, 2.0 equiv). The resulting solution was refluxed for 2 h, cooled to room temperature, and concentrated *in vacuo*, yielding the crude acid chloride which was used in the next step without further purification. To a solution of thioacetamide (0.564 g, 1.5 equiv) in THF (12 mL), was added dropwise a solution of the crude acid chloride in THF (8 mL) over 10 min. The resulting reaction mixture was stirred at room temperature for 19 h, and quenched with the addition of the aqueous solution of NaOH (15%, 15 mL) and HCl (2 M, 25 mL) in sequence. The mixture was diluted with Et_2O (40 mL) and washed with an aqueous solution of NaOH (15%, 30 mL x 3). The organic layer was dried with Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (100% hexanes to 5% EtOAc-hexanes) afforded 2-(prop-1-en-2-yl)benzothioic *S*-acid (**4i**) as an off-white waxy solid (278.4 mg, 1.56 mmol, 31%). $\mathbf{R_f}$ = 0.20 (10% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.63 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.47 (td, *J* = 7.7, 1.4 Hz, 1H), 7.36–7.28 (m, 2H), 5.21–5.17 (m, 1H), 4.97 (s, 1H), 2.13 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 188.2, 144.1, 143.0, 137.2, 131.8, 129.0, 128.1, 127.1, 116.9, 24.0; **FTIR** (thin film): cm^{-1} 3082, 2970, 1739, 1685, 1187, 853, 768, 731, 643; **HRLCMS-ESI** (m/z) Calcd for ($C_{10}H_{11}OS$) ($[M+H]^+$): 179.0525; found: 179.0524.

Mechanism-Probing Substrates and Precursors

2-(2-(Prop-1-en-2-yl)phenyl)propan-2-ol (1v).—To an air-free solution of 2-(prop-1-en-2-yl)benzoic acid (*4j-i*) (1.95 g, 12.0 mmol, 1.0 equiv) and K_2CO_3 (2.49 g, 1.5 equiv) in DMF (24 mL) at room temperature under N_2, was added MeI (1.5 mL, 2.0 equiv). The solution was stirred at room temperature for 12 h. The reaction was quenched with DI H_2O (30 mL). The aqueous layer was extracted with EtOAc (50 mL x 4). The combined organic layers were washed with a saturated aqueous solution of $NaHCO_3$ (40 mL x 2) and brine (50 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (100% Hexanes to 10% EtOAc–hexanes) afforded methyl 2-(prop-1-en-2-yl)benzoate (**1v-i**) as a colorless oil (1.94 g, 11.1 mmol, 92%). $\mathbf{R_f}$ = 0.62 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.76 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.42 (td, *J* = 7.6, 1.5 HZ, 1H), 7.29 (td, *J* = 7.6, 1.4 Hz, 1H), 7.22 (dd, *J* = 7.6, 1.5 Hz, 1H), 5.09–5.07 (m, 1H), 4.82 (s, 1H), 3.83 (s, 3H), 2.06 (s, 3H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 168.4, 146.4, 145.1, 131.5, 129.7, 129.4, 129.2, 126.9, 113.7, 52.0, 24.1; **FTIR** (thin film): cm^{-1} 2950, 1728, 1446, 1432, 1289, 1252, 1124, 1075, 896, 769; **HRLCMS-ESI** (m/z) Calcd for ($C_{11}H_{13}O_2$) ($[M+H]^+$): 177.0910; found: 177.0910.

To an air-free solution of methyl 2-(prop-1-en-2-yl)benzoate (**1v-i**) (528.6 mg, 3.0 mmol, 1.0 equiv) in Et_2O (12 mL) at room temperature under N_2, was added MeMgBr (3 M in Et_2O, 3.0 mL, 3.0 equiv). The reaction was stirred at room temperature for 12 h and was then quenched with slow addition of a saturated aqueous solution of NH_4Cl (15 mL) and DI H_2O (10 mL). The solution was acidified with HCl (2 M, 10 mL). The aqueous layer was extracted with EtOAc (15 mL x 3). The combined organic layers were washed with brine (40 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (100% Hexanes to 20% EtOAc–hexanes) afforded 2-(2-(Prop-1-en-2-yl)phenyl)propan-2-ol (**1v**) as a white solid (387.0 mg, 2.2 mmol, 73%). $\mathbf{R_f}$ = 0.83 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.36 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.25–7.14 (m, 2H), 7.01 (dd, *J* = 7.4, 1.7 Hz, 1H), 5.23–5.20 (m, 1H), 4.91–4.89 (m, 1H), 3.0 (s, 1H), 2.19–2.17 (m, 3H), 1.62 (s, 6H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 150.5, 145.5, 140.9, 129.8, 126.8, 126.2, 126.1, 114.5, 32.8, 27.1; **FTIR** (thin film): cm^{-1} 3445 (broad), 3061, 2972, 1637, 1434, 1364, 1175, 955, 901, 759, 548; **HRGCMS-ESI** (m/z) Calcd for ($C_{12}H_{14}$) ($[M–H_2O]^+$): 158.1090; found: 158.1090.

2-(2-(Prop-1-en-2-yl-3,3,3-*d*$_3$)phenyl)propan-2-ol (*D*$_3$-1v).—To a two-neck reaction vessel charge with magnesium turnings (1.65 g, 1.7 equiv) and an I_2 spike, was added Et_2O (40 mL) followed by dropwise addition of iodomethane-d_3 (2.6 mL, 40.0 mmol, 1.0 equiv). The reaction was refluxed for 2 h, then cooled to room temperature and Schlenk filtered. In a separate air-free flask, a solution of 2-bromobenzaldehyde (2.1 mL, 18.0 mmol, 1.0 equiv) and Et_2O (54 mL) was stirred at 0 °C for 10 min and was then added slowly to the above methyl-d_3-magnesium bromide solution. The reaction mixture was allowed to stir at 0 °C for 15 min and then at room temperature for 12 h. The reaction was quenched with a saturated aqueous solution of NH_4Cl (20 mL) followed by DI H_2O (10 mL). The aqueous layer was extracted with Et_2O (30 mL x 2). The combined organic layers were dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (100% Hexanes to 10% EtOAc–hexanes) afforded 1-(2-bromophenyl)ethan-2,2,2-d_3-1-ol (**D$_3$-1v-i**) as a clear oil

(3.45 g, 16.9 mmol, 94%). $\mathbf{R_f}$ = 0.68 (25% EtOAc–Hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.59 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.51 (dd, *J* = 7.7, 1.2 Hz, 1H),7.35 (td, *J* = 7.7, 1.6 Hz, 1H), 7.13 (td, *J* = 7.7, 1.2 Hz, 1H), 5.23 (s, 1H), 1.99 (s, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 144.5, 132.3, 128.4, 127.6, 126.5, 121.4, 68.7, 22.6 (septet, $^1J_{D–C}$ = 19.1 Hz); **FTIR** (thin film): cm^{-1} 3329 (broad), 2228, 1568, 1467, 1439, 1123, 1039, 1018, 749; **HRLCMS-ESI** (m/z) Calcd for ($C_8H_6D_3BrOLi$) ($[M+^7Li]^+$): 210.0180; found: 210.0178.

To an air-free suspension of pyridinium chlorochromate (4.10 g, 2.0 equiv) and Celite (4.09 g) in CH_2Cl_2 (58.5 mL) under N_2, was added slowly an air-free solution of 1-(2-bromophenyl)ethan-2,2,2-*d*$_3$-1-ol (**D*$_3$*-1v-i**) (1.94 g, 9.5 mmol, 1.0, equiv) in CH_2Cl_2 (11.0 mL) over 15 min. The reaction was stirred at room temperature for 11 h and was then diluted with CH_2Cl_2 (30 mL). The reaction mixture was filtered through a pale of silica. The filtrate was concentrated *in vacuo*. Purification by flash column chromatography (3% EtOAc–hexanes to 6% EtOAc–hexanes) afforded 1-(2-bromophenyl)ethan-1-one-2,2,2-*d*$_3$ (***D*$_3$*-1v-ii**) as a colorless oil (1.80 g, 8.9 mmol, 94%). $\mathbf{R_f}$ = 0.79 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.61 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.46 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.37 (td, *J* = 7.6, 1.2 Hz, 1H), 7.29 (td, *J* = 7.6, 1.8 Hz, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 201.1, 141.1, 133.6, 131.6, 128.8, 127.3, 118.7, 29.4 (septet, $^1J_{D–C}$ = 19.7 Hz); **FTIR** (thin film): cm^{-1} 160, 1587, 1465, 1427, 1280, 1242, 1109, 1027, 980, 752, 726, 649, 567; **HRLCMS-ESI** (m/z) Calcd for ($C_8H_5D_3BrO$) ($[M+H]^+$): 201.9941; found: 201.9937.

To an air-free solution of methyltriphenylphosphonium bromide (982.4 mg, 1.1 equiv) in THF (12 mL) at 0 °C under N_2, was added slowly *n*-BuLi (2.5 M in hexanes, 1.0 mL, 2.5 mmol, 1.0 equiv). The reaction was stirred at 0 °C for 5 min and then at room temperature for 25 min. To the resulting ylide solution, was added slowly a solution of 1-(2-bromophenyl)ethan-1-one-2,2,2-*d*$_3$ (***D3*-1v-ii**) (606.2 mg, 1.2 equiv). The reaction was stirred at room temperature for 14.5 h and was then quenched with slow addition of D_2O (2 mL). After 10 min, a saturated aqueous solution of NH_4Cl (30 mL) was added. The aqueous layer was extracted with Et_2O (30 mL x 3). The combined organic layers were washed with brine (50 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (100% hexanes to 10% EtOAc–hexanes) afforded 1-bromo-2-(prop-1-en-2-yl-3,3,3-*d*$_3$)benzene (***D*$_3$*-1v-iii**) as a colorless oil (345.4 mg, 1.7 mmol, 69%). $\mathbf{R_f}$ = 0.89 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.55, (dd, *J* = 7.6, 1.3 Hz, 1H), 7.26 (td, *J* = 7.6, 1.3 Hz, 1H), 7.19 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.11 (td, *J* = 7.6, 1.8 Hz, 1H), 5.22 (d, *J* = 1.8 Hz, 1H), 4.94 (d, *J* = 1.8 Hz, 1H); **^{13}C{^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 145.5, 144.7, 132.6, 129.6, 128.2, 127.1, 121.5, 116.0, 22.6 (septet, $^1J_{D–C}$ = 19.4 Hz); **FTIR** (thin film): cm^{-1} 3081, 1634, 1589, 1561, 1469, 1433, 1304, 1116, 1039, 1023, 907, 868, 751, 729, 651, 550; **HRGCMS-ESI** (m/z) Calcd for ($C_9H_6D_3Br$) ($[M]^+$): 199.0070; found: 199.0070. [Note: it is vital to avoid any excess base, which will erode the *d*-labeling.]

To an air-free solution of ***D*$_3$*-1v-iii** (280.1 mg, 1.4 mmol, 1.0 equiv) in THF (4.2 mL) at −78 °C under N_2, was added dropwise *n*-BuLi (2.5 M in hexanes, 0.53 mL, 1.0 equiv) over 5 min. The resulting yellow solution was stirred at −78 °C for 35 min, followed by slow addition of acetone (165 μL, 1.6 equiv). The resulting solution was stirred at −78 °C for 5 min and the yellow color became clear. The solution was then warmed to room temperature and quenched with a saturated aqueous solution of NH_4Cl (3 mL). The aqueous layer was

extracted with EtOAc (15 mL x 3). The combined organic layers were washed with brine (30 mL), dried with Na_2SO_4, and concentrated *in vacuo*. Purification by flash column chromatography (100% hexanes to 10% EtOAc–hexanes) afforded 2-(2-(prop-1-en-2-yl-3,3,3-d_3)phenyl)propan-2-ol (***D*~3~-1v**) as a white solid (135.7 mg, 0.76 mmol, 54%). $\mathbf{R_f}$ = 0.75 (25% EtOAc–hexanes). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.36 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.23 (td, *J* = 7.4, 1.5 Hz, 1H), 7.18 (td, *J* = 7.4, 1.3 Hz, 1H), 7.01 (dd, *J* = 7.4, 1.5 Hz, 1H), 5.21 (d, *J* = 2.2 Hz, 1H), 4.90 (d, *J* = 2.2 Hz, 1H), 3.01 (s, 1H), 1.62 (s, 3H); **^{13}{C^{1}H} NMR** ($CDCl_3$, 125 MHz): δ 150.4, 145.5, 140.9, 129.8, 126.8, 126.2, 126.1, 114.5, 74.5, 26.2 (septet, $^1J_{D–C}$ = 19.2 Hz); **FTIR** (thin film): cm^{-1} 3446 (broad), 2974, 1631, 1482, 1436, 1362, 1260, 1173, 1047, 954, 906, 858, 759, 543; **HRGCMS-ESI** (m/z) Calcd for ($C_{12}H_{13}D_3O$) ($[M]^+$): 179.1384; found: 179.1383. [Note: it is vital to avoid any excess base, which will erode the *d*-labeling.]

Supplementary Material

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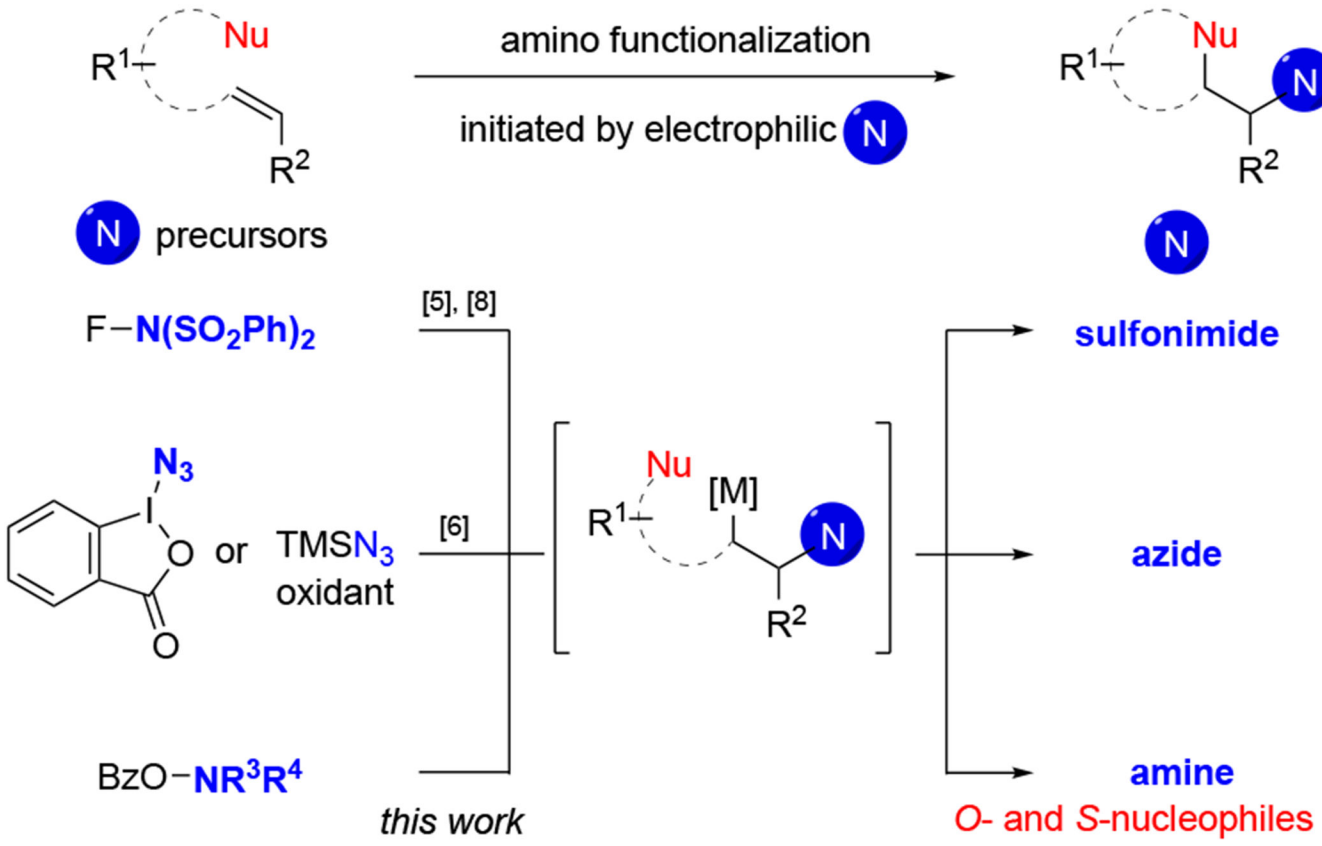
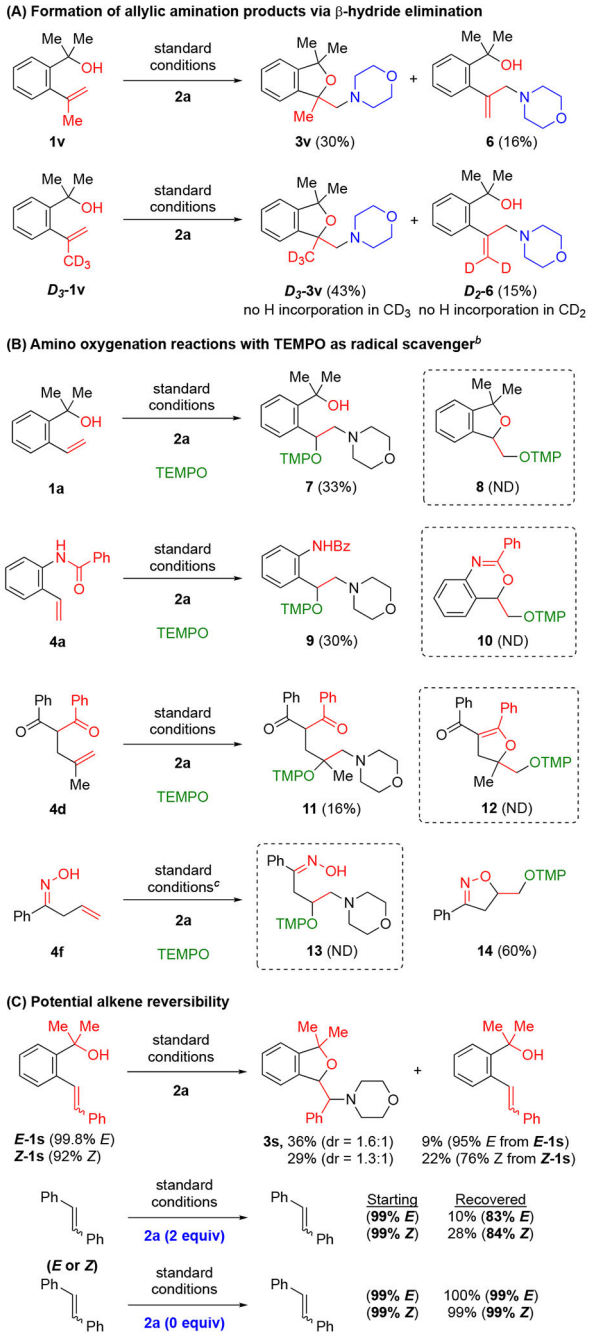


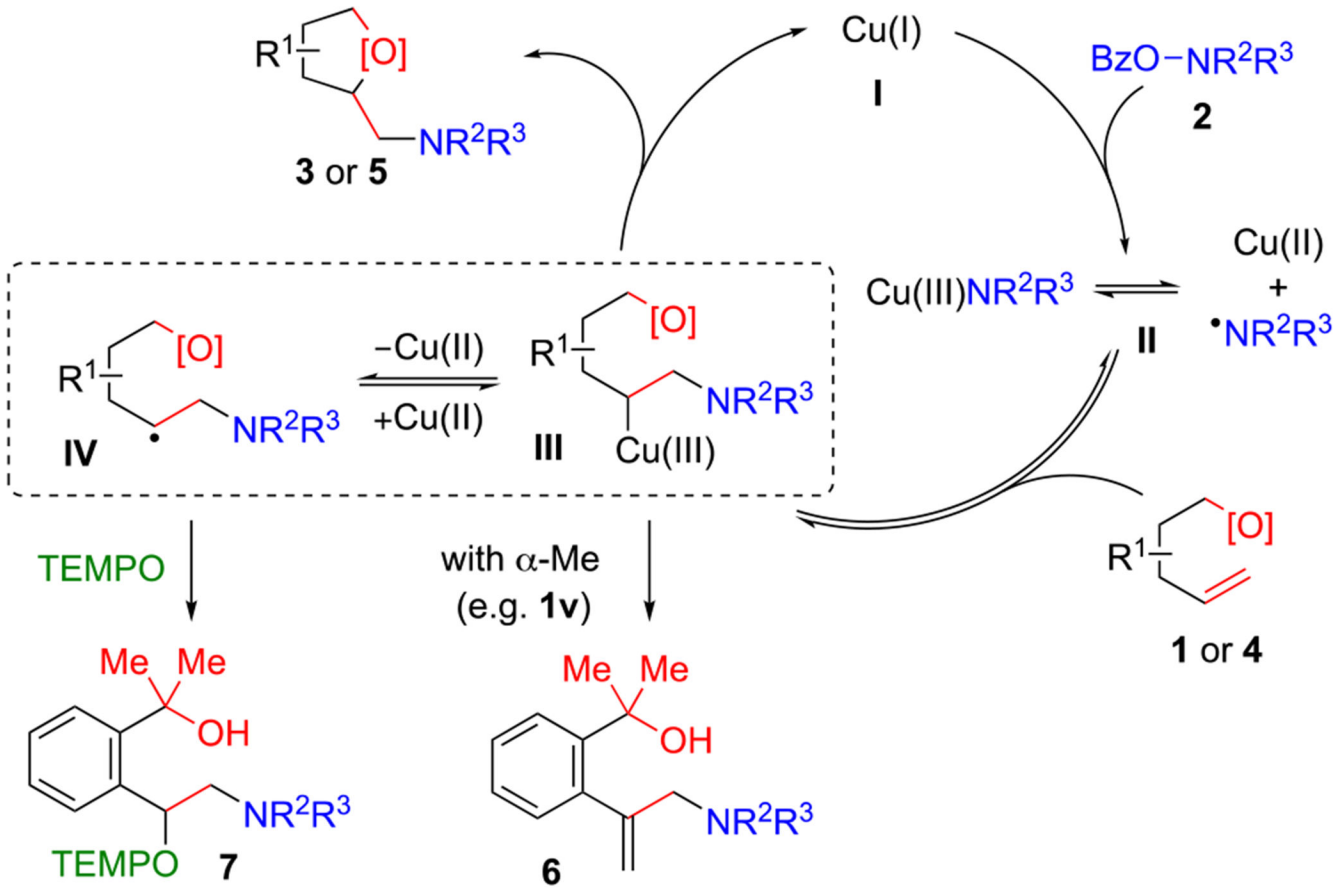
Scheme 1.

Alkene Amino Oxygenation Reactions Using Electrophilic Amino Addition to Alkenes

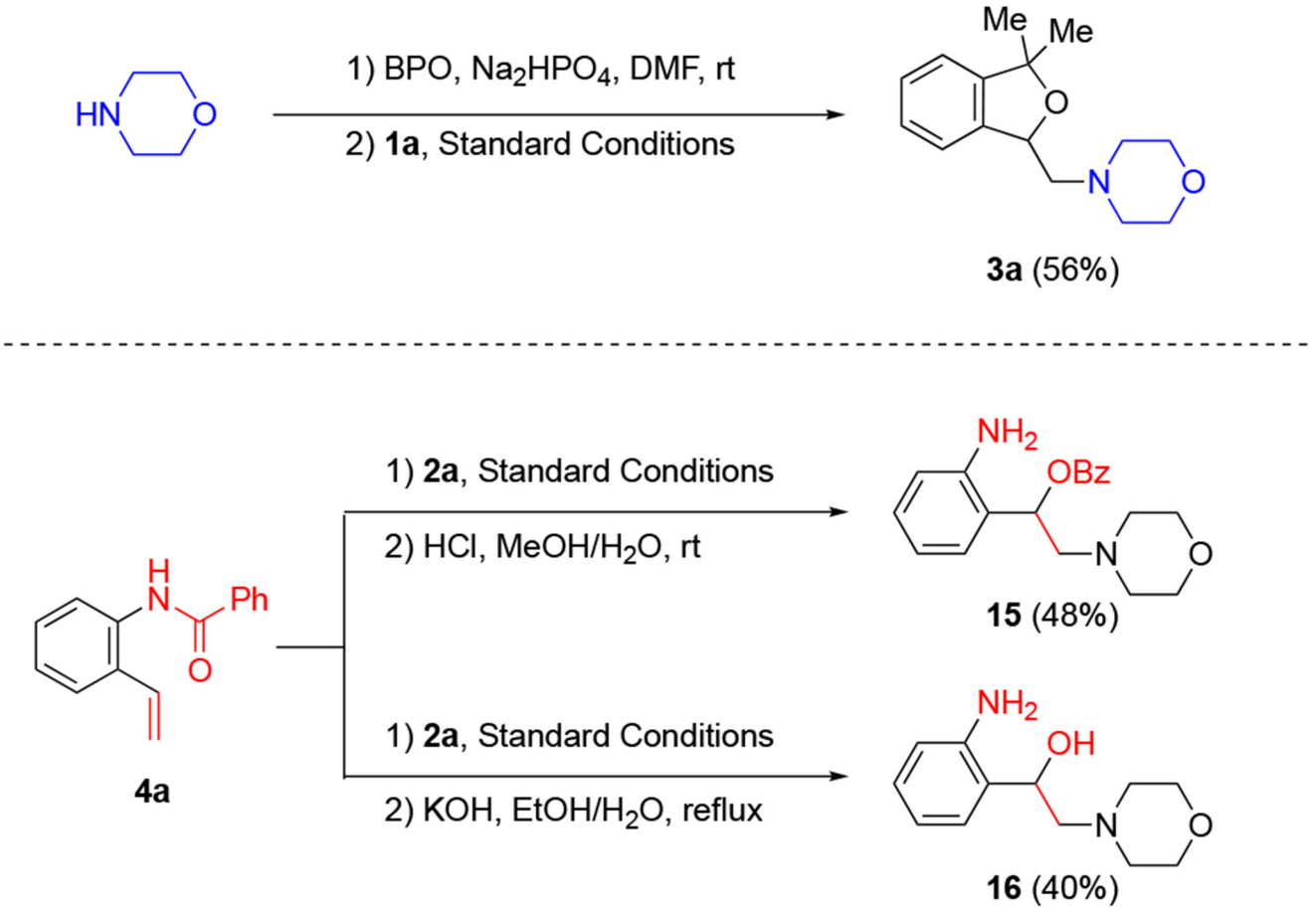


Scheme 2. Mechanistic Investigations[a]

[a]Isolation Yields. Standard Conditions: **1** or **4** (0.4 mmol, 1.0 equiv), **2a** (2.0 equiv), $Cu(OTf)_2$ (20 mol %), PPTS (1.0 equiv), DCE (1.0 mL), 60 °C. [b] Reactions in the presence of TEMPO (1.0 equiv). [c] Run without PPTS using $Cu(OAc)_2$ in 1,2-dimethoxyethane instead of $Cu(OTf)_2$ in DCE. ND = Not Detected. E/Z isomer ratios determined by GCMS.



Scheme 3.
Proposed Reaction Pathways

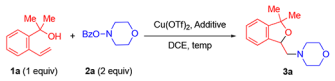


Scheme 4. Amino Oxygenation Reaction in Sequence[a]

[a]Isolation yields shown. Standard Conditions: **4a** (0.2 mmol, 1.0 equiv), **2a** (2.0 equiv), $Cu(OTf)_2$ (20 mol %), PPTS (1.0 equiv), DCE (1.0 mL), 60 °C.

Table 1.

Optimization of Copper-Catalyzed Amino Etherification of Unsaturated Alcohol 1a[a]



entry	$Cu(OTf)_2$(mol%)	additive	temp (°C)	3a (%)[b]
1	10	none	80	36
2	10	K_2CO_3	80	37
3	10	lutidine	80	35
4	10	DIPEA	80	trace
5	10	MsOH	80	trace
6	10	HCO_2H	80	43
7	10	NaH_2PO_4	80	38
8	10	PPTS	80	66
9	5	PPTS	80	66
10	20	PPTS	80	78
11	**20**	**PPTS**	**60**	**78 (76)[c]**
12	20	PPTS	40	68

[a]Conditions: **1a** (0.2 mmol, 1.0 equiv), **2a** (2.0 equiv), $Cu(OTf)_2$, additive (1.0 equiv), DCE (1.0 mL).

[b]Yields determined by ^1H NMR with CH_2Br_2 as an internal standard.

[c]Isolation yield in parentheses on 0.4 mmol scale. MsOH = Methanesulfonic acid. PPTS = pyridinium *p*-toluenesulfonate.

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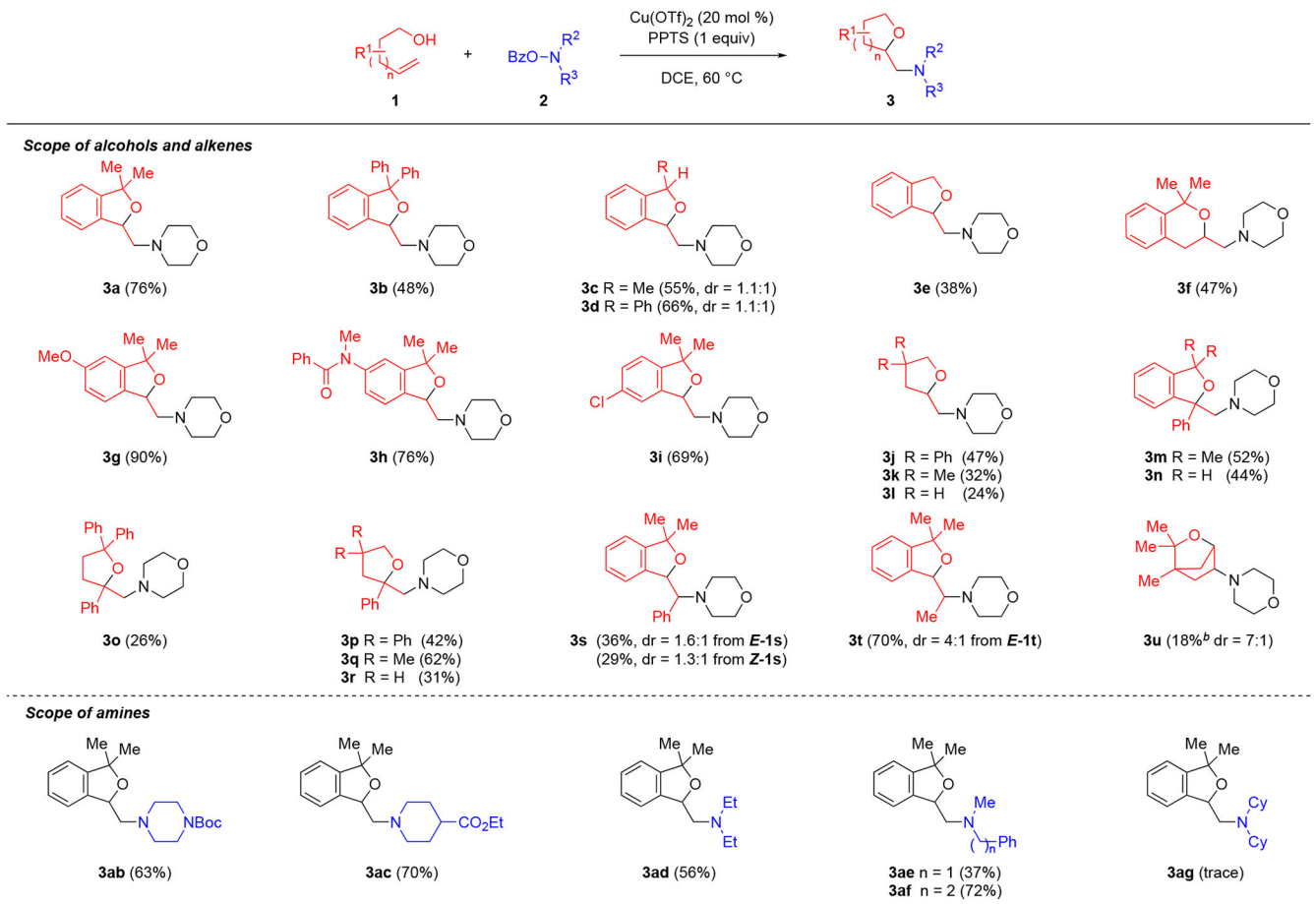
Table 2.

Scope of Copper-Catalyzed Amino Etherification of Alkenes[a]

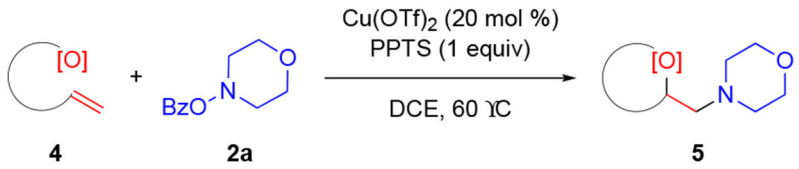


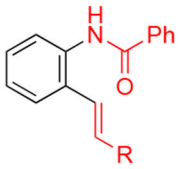
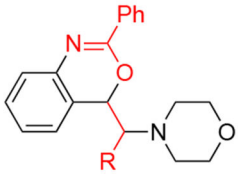
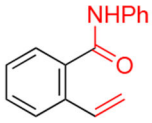
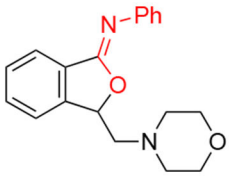
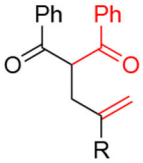
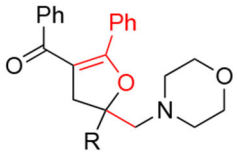
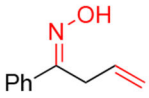
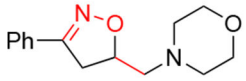
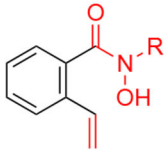
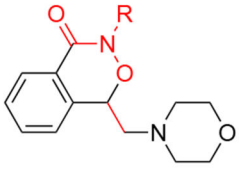
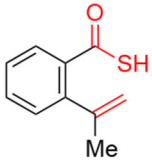
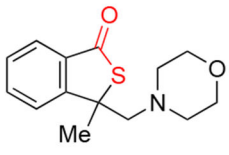
[a]Isolation yields shown. Reaction conditions: **1** (0.4 mmol, 1.0 equiv), **2a** (2.0 equiv), $Cu(OTf)_2$ (20 mol %), PPTS (1.0 equiv), DCE (1.0 mL), 60 °C.

[b]Yield of the major isomer. dr = diastereomeric ratio, determined by ^1H NMR and/or GCMS of the crude reaction mixture.

Table 3.

Amino Oxygenation and Thioation Reactions with More Extensive Variety of *O*- and *S*-Nucleophiles[a]



entry	alkene	product	yield
1	 **4a** R = H		**5a** 52%
2	**4b** R = Me		**5b** 60% (dr = 3:1)
3	 **4c**		**5c** 35%
4	 **4d** R = H		**5d** ND
5	**4e** R = Me		**5e** 31%
6	 **4f**		**5f**[b] 50% (0.4 mmol) 50% (2 mmol)
7	 **4g** R = Me		**5g** ND
8	**4h** R = Ph		**5h** ND
9	 **4i**		**5i** 16%

[a]Isolation yields shown. Reaction conditions: **4** (0.4 mmol, 1.0 equiv), **2a** (2.0 equiv), $Cu(OTf)_2$ (20 mol %), PPTS (1.0 equiv), DCE (1.0 mL), 60 °C.

[b]Run without PPTS using $Cu(OAc)_2$ in 1,2-dimethoxyethane instead of $Cu(OTf)_2$ in DCE. dr = diastereomeric ratio, determined by ^1H NMR and/or GCMS of the crude reaction mixture. ND = Not Detected.