C(sp^3)H/N(sp^2) cross-coupling reaction for the synthesis of tertiary arylamines via fluxional SOX·Pd(II) catalysis

Supporting Information

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1. General Information

All commercially obtained reagents were used as received unless otherwise noted. $Pd(OAc)_2$ (Strem, 99+% (99.95+%-Pd)) was stored in a glove box and weighed out in the air at room temperature prior to use. (±)-MeO-SOX (MaSOX) was synthesized according to the reported literature procedure.[1] Toluene was used as received (Fisher Chemical), and dioxane was purified prior to use by passage through a bed of activated alumina (Al_2O_3) (Glass Contour, Laguna Beach, California). All $C(sp^3)H/N(sp^2)$ cross-coupling reactions were set up and run under ambient air with no precautions taken to exclude moisture. Slow addition protocols were performed using a New Era Pump Systems NE-300 syringe pump. Thin-layer chromatography (TLC) was conducted with Merck silica gel (SiO_2) 60 F254 precoated plates (0.25 mm) and visualized with UV, potassium permanganate, ninhydrin, cerium ammonium molybdate, and iodine stains. Flash column chromatography was performed using ZEOprep 60 ECO 43–60 micron silica gel (American International Chemical, Inc.) or Brockmann Grade I, activated, basic aluminum oxide, 58 Å, 60 mesh, 205 m^3/g S.A. (Thermofisher Scientific). Brockmann Grade I alumina was converted to Brockmann Grade III basic alumina via the addition of 0.056 mL H_2O/1 mL Al_2O_3. Solvent "NH_4OH-MeOH" noted in the text for purifications indicates a 10% v/v solution of 28–30% aqueous ammonium hydroxide ($NH_4OH_{(aq)}$) in methanol (MeOH), which was prepared and used directly. For example, 5 mL of 28–30% $NH_4OH_{(aq)}$ and 45 mL of MeOH made 50 mL NH_4OH-MeOH solution. Solvent "AcOH-EtOAc" noted in the text for purifications indicates a 5% v/v solution of glacial acetic acid (AcOH) in ethyl acetate (EtOAc), which was prepared and used directly. For example, 5 mL of AcOH and 95 mL of EtOAc made 100 mL AcOH-EtOAc solution. For flash column chromatography purifications using triethylamine deactivated silica, a silica slurry was made with a solution of 2% triethylamine in dichloromethane (DCM) (v/v). The slurry was added to the column, packed, and at least 2 column volumes of the starting eluent was passed through the column. The crude material was then introduced and purified, using the corresponding solvent(s) noted. Abbreviations in the text are as follows: dichloromethane (DCM), 1,2-dichloroethane (1,2-DCE), dimethylformamide (DMF), dimethyl sulfoxide (DMSO), dimethyl sulfide (DMS), tetrahydrofuran (THF), methyl *tert*-butyl ether (MTBE), isopropanol (IPA), acetonitrile (MeCN), diisopropyl azodicarboxylate (DIAD), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC·HCl), pyridinium chlorochromate (PCC), (diacetoxyiodo)benzene (PIDA), 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), azobisisobutyronitrile (AIBN), 1,1,1-tris(acetyloxy)-1,1-dihydro-1,2-benziodoxol-3-(1*H*)-one (DMP), tetrabutylammonium fluoride (TBAF), hydroxybenzotriazole (HOBt), sodium bis(trimethylsilyl)amide (NaHMDS), *N*,*N'*-dimethylpropyleneurea (DMPU), triethylamine (TEA), *N*,*N*-diisopropylethylamine (DIPEA), 4-dimethylaminopyridine (DMAP), trifluoroacetic acid (TFA), (±)-MeO-SOX (MaSOX), dibutyl phosphate (dbp), dibenzyl phosphate (dBnp), 2,5-dimethylbenzoquinone (2,5-DMBQ), 2,5-dimethylhydroquinone (2,5-DMHQ), toluenesulfonyl (Ts), cyclohexyl (Cy), phenyl (Ph), 1,4-di-tert-butylbenzene (DTTB), recovered starting material (RSM).

^1H NMR spectra were recorded on a Varian Unity Inova 400 (400 MHz), Varian Unity 500 (500 MHz), Varian Unity 500NB (500 MHz), Varian VXR 500 (500 MHz), HD-500 Bruker Avance III (500 MHz), or a NEO 600 Bruker (600 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ = 7.26 ppm, $(CD_3)_2SO$ = 2.5 ppm). All spectra are baseline corrected using Whittaker Smoother prior to analysis. Data reported as: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sext = sextet, hept = heptet, o = octet, dp = doublet of pentets, pt = pentet of triplets, m = multiplet, dm = doublet of multiplets, br = broad, app = apparent; coupling constant(s) in Hz; integration. ^{19}F NMR spectra were recorded on a HD-500 Bruker Avance III (500 MHz), a Varian Unity Inova 400 (400 MHz), or a Varian Unity 500 (500 MHz) spectrometer and are reported in ppm using C_6F_6 as an external standard ($CDCl_3$). Crude yields and recovered staring material (RSM) of the

amination reactions were analyzed using ^{1}H NMR (d1 = 10 seconds, nt = 16 scans) with benzotrifluoride or nitrobenzene as an internal standard. In compounds containing a mixture of rotamers, the wording "and" is used to differentiate the minor and major rotamers in the ^{1}H NMR and ^{13}C NMR writeup. In compounds containing a mixture of diastereomers, the minor diastereomer is noted in parentheses. Optical rotations were measured with a sodium lamp using a 1 mL cell with a 50 mm path length on a Jasco P-1020 polarimeter and are reported as follows: $[\alpha]_{\lambda}T^{o}C$ (*c* = g/100 mL solvent). High-resolution mass spectra were obtained at the University of Illinois Mass Spectrometry Laboratory. Electrospray ionization (ESI) spectra were performed on a Waters Q-Tof Ultima spectrometer, and electron ionization (EI) and field desorption (FD) spectra were performed on a Micromass 70-VSE spectrometer. Automated medium-pressure liquid chromatography (MPLC) was performed using a Teledyne ISCO CombiFlash Nextgen 300+ system. High-performance liquid chromatography (HPLC) analysis was performed on an Agilent 1100 Series or an Agilent 1260 Infinity II instrument. Gas chromatography (GC) analysis was performed on an Agilent 6890N Series instrument equipped with a J&W Cyclosil-B column (length = 30 m, thickness = 0.25 μm, diameter = 0.250 mm) with hydrogen as the carrier gas.

2. Reaction Development

2.1 Reaction development and optimization.

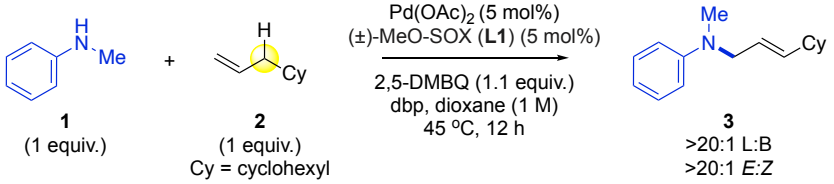
General procedure: To a ½ dram vial equipped with a stir bar was added $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.05 equiv.), MaSOX (5.2 mg, 0.015 mmol, 0.05 equiv.), 2,5-dimethylbenzoquinone (45 mg, 0.33 mmol, 1.1 equiv.), and *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.). A fresh solution of dibutyl phosphate in dioxane was added (0.3 mL, 1.0 M), followed by allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.). The vial was capped, sealed with Teflon tape and parafilm, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 12 h, with no precautions to exclude air and moisture. The vial was cooled to room temperature, diluted with $CDCl_3$, and benzotrifluoride (43.8 mg, 0.3 mmol, 1.0 equiv.) was added as an internal standard. The crude mixture was analyzed using ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) to determine the recovered olefin starting material. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes eluent) afforded the allylic arylamine product as a clear oil. Isolated yields are the average of two or three experiments.

In situ *N*-methyl phenylamine·BF_3 or *N*-methyl phenylamine·HBF_4 procedure: To a flame-dried 1 dram vial equipped with a stir bar was added *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and DCM (0.6 mL, 0.5 M). The vial was cooled to 0 °C and $BF_3{\cdot}OEt_2$ (41 μL, 0.33 mmol, 1.1 equiv.) or $HBF_4{\cdot}OEt_2$ (41 μL, 0.3 mmol, 1.0 equiv.) was added dropwise. The reaction was stirred at 0 °C for 15 minutes and then at room temperature for 1 h. The crude mixture was concentrated under reduced pressure and subsequently placed under vacuum for 8 hours to afford *N*-methyl phenylamine·BF_3 or *N*-methyl phenylamine·HBF_4, which was used directly without further purification. To the same vial was added $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.05 equiv.), MaSOX (5.2 mg, 0.015 mmol, 0.05 equiv.), and 2,5-dimethylbenzoquinone (45 mg, 0.33 mmol, 1.1 equiv.). A fresh solution of dibutyl phosphate in dioxane was added (0.3 mL, 1.0 M), followed by allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.). The vial was capped, sealed with Teflon tape and parafilm, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 12 h, with no precautions to exclude air and moisture. The vial was cooled to room temperature, diluted with $CDCl_3$, and benzotrifluoride (43.8 mg, 0.3 mmol, 1.0 equiv.) was added as an internal standard. The crude mixture was analyzed using ^{1}H NMR to determine the recovered olefin starting material (nt = 16 scans, d1 = 10 seconds). The material was

then diluted with 25 mL of EtOAc and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude material was diluted with $CDCl_3$, benzotrifluoride (43.8 mg, 0.3 mmol, 1.0 equiv.) was added as an internal standard, and the material was analyzed again using ^1H NMR (nt = 16 scans, d1 = 10 seconds) to determine the amination crude yield. Yields are the average of two experiments.

Table S1. Extended reaction development of the C(sp^3)H/N(sp^2) cross-coupling.

extended reaction development



1 (1 equiv.) + **2** (1 equiv.) Cy = cyclohexyl → **3** >20:1 L:B >20:1 *E*:*Z*

entry	*amine* ***1***	*palladium(II)*	*% dbp*	*% yield (% olefin RSM)*[a]
1	**1** · BF_3[b]	**cat-1**	25%	<5% (22%)[c]
2	**1** · HBF_4[b]	**cat-1**	5%	<5% (11%)[c]
3	**1**	**cat-1**	25%	64% (4%)
4	**1**	**cat-1**	10%	85% (0%)
5	**1**	**cat-1**	5%	90% (2%)
6[d]	**1**	**cat-1**	5%	90% (2%)
7[e]	**1**	**cat-1**	5%	89% (1%)
8[f]	**1**	**cat-1**	5%	91% (1%)
9[g]	**1**	**cat-1**	5%	90% (2%)
10	**1**	**cat-1**	—	35% (60%)
11[h]	**1**	**cat-1**	—	50% (46%)
12	**1**	**cat-1**	5% TFA	85% (6%)
13	**1**	**cat-1**	5% dBnp	89% (3%)
14	**1**	**4**	5%	<5% (83%)[c]
15	**1**	$Pd(OAc)_2$	5%	<5% (84%)[c]
16[h]	**1**	$Pd(OAc)_2$	5%	<5% (70%)[c]
17	**1**	$Pd(OAc)_2$	10%	<5% (72%)[c]
18	**1**	**4** · **L1**	5%	89% (2%)
19	**1**	2.5% **cat-1**	5%	62% (32%)
20	*slow add.*	2.5% **cat-1**	5%	84% (16%)

[a]Olefin recovered starting material (RSM) was determined by crude ^1H NMR analysis using benzotrifluoride as an internal standard. [b]The amine was complexed in situ without purification. [c]Yield was determined by crude ^1H NMR analysis using benzotrifluoride as an internal standard. [d]toluene as a solvent. [e]1,2-dichloroethane as a solvent. [f]methyl *tert*-butyl ether as a solvent. [g]chloroform as a solvent. [h]24 h.

Entry 1: The *N*-methyl phenylamine·BF_3 in situ procedure was followed using a 0.25 M of dibutyl phosphate in dioxane (0.3 mL, 0.075 mmol, 0.25 equiv.) as the solvent. Run 1: 4% yield (23% olefin RSM); Run 2: 4% yield (20% olefin RSM). **Average: 4% ± 0.02% yield (22% ± 2.4% olefin RSM).**

Entry 2: The *N*-methyl phenylamine·HBF_4 in situ procedure was followed using 0.05 M of dibutyl phosphate in dioxane (0.3 mL, 0.015 mmol, 0.05 equiv.) as the solvent. Run 1: 1% yield (11% olefin RSM); Run 2: 1% yield (12% olefin RSM). **Average: 1% ± 0.2% yield (11% ± 0.9% olefin RSM).**

Entry 3: The general procedure was followed using 0.25 M of dibutyl phosphate in dioxane (0.3 mL, 0.075 mmol, 0.25 equiv.) as the solvent. Run 1: 43.5 mg, 63% yield (4% olefin RSM); Run 2: 44.6 mg, 65% yield (3% olefin RSM). **Average: 64% ± 1.4% yield (4% ± 0.6% olefin RSM).**

Entry 4: The general procedure was followed using 0.1 M of dibutyl phosphate in dioxane (0.3 mL, 0.03 mmol, 0.1 equiv.) as the solvent. Run 1: 58.6 mg, 86% yield (0% olefin RSM); Run 2: 58.4 mg, 84% yield (0% olefin RSM). **Average: 85% ± 1.6% yield (0% olefin RSM).**

Entry 5: The general procedure was followed using 0.05 M of dibutyl phosphate in dioxane (0.3 mL, 0.015 mmol, 0.05 equiv.) as the solvent. Run 1: 62.3 mg, 92% yield (2% olefin RSM); Run 2: 62.4 mg, 91% yield (2% olefin RSM); Run 3: 61.4 mg, 88% yield (3% olefin RSM). **Average: 90% ± 1.7% yield (2% ± 0.3% olefin RSM).**

Entry 6: The general procedure was followed using 0.05 M of dibutyl phosphate in toluene (0.3 mL, 0.015 mmol, 0.05 equiv.) as the solvent. Run 1: 62.3 mg, 91% yield (2% olefin RSM); Run 2: 61.4 mg, 90% yield (2% olefin RSM). **Average: 90% ± 0.6% yield (2% ± 0.02% olefin RSM).**

Entry 7: The general procedure was followed using 0.05 M of dibutyl phosphate in 1,2-DCE (0.3 mL, 0.015 mmol, 0.05 equiv.) as the solvent. Run 1: 60.7 mg, 88% yield (1% olefin RSM); Run 2: 62.1 mg, 90% yield (0% olefin RSM). **Average: 89% ± 1.1% yield (1% ± 0.9% olefin RSM).**

Entry 8: The general procedure was followed using 0.05 M of dibutyl phosphate in MTBE (0.3 mL, 0.015 mmol, 0.05 equiv.) as the solvent. Run 1: 61.9 mg, 90% yield (1% olefin RSM); Run 2: 63.2 mg, 92% yield (1% olefin RSM). **Average: 91% ± 1.9% yield (1% ± 0.03% olefin RSM).**

Entry 9: The general procedure was followed using 0.05 M of dibutyl phosphate in chloroform (0.3 mL, 0.015 mmol, 0.05 equiv.) as the solvent. Run 1: 60.4 mg, 88% yield (3% olefin RSM); Run 2: 52.8 mg, 91% yield (0% olefin RSM). **Average: 90% ± 1.5% yield (2% ± 1.5% olefin RSM).**

Entry 10: The general procedure was followed using dioxane as the solvent. Run 1: 25.9 mg, 38% yield (60% olefin RSM); Run 2: 22.4 mg, 33% yield (61% olefin RSM). **Average: 35% ± 3.7% yield (60% ± 0.7% olefin RSM).**

Entry 11: The general procedure was followed using dioxane as the solvent and stirred for 24 hours. Run 1: 33.2 mg, 48% yield (49% olefin RSM); Run 2: 35.0 mg, 51% yield (43% olefin RSM). **Average: 50% ± 1.8% yield (46% ± 4.4% olefin RSM).**

Entry 12: The general procedure was followed using 0.05 M of trifluoroacetic acid in dioxane (0.3 mL, 0.015 mmol, 0.05 equiv.) as the solvent. Run 1: 57.9 mg, 84% yield (8% olefin RSM); Run 2: 58.6 mg, 86% yield (5% olefin RSM). **Average: 85% ± 1.1% yield (6% ± 1.9% olefin RSM).**

Entry 13: The general procedure was followed using dibenzyl phosphate (4.2 mg, 0.015 mmol, 0.05 equiv.) and dioxane (0.3 mL, 1.0 M) as the solvent. Run 1: 60.3 mg, 90% yield (4% olefin RSM); Run 2: 59.1 mg, 87% yield (3% olefin RSM). **Average: 89% ± 2.1% yield (3% ± 0.4% olefin RSM).**

Entry 14: To a ½ dram vial equipped with a stir bar was added $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.05 equiv.), a fresh solution of 0.05 M dibutyl phosphate in dioxane (0.3 mL, 0.015 mmol, 0.05 equiv.) as the solvent, and *N*-methyl phenylamine (3.2 mg, 0.03 mmol, 0.1 equiv.). The vial was capped, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 1 h. The vial was cooled to room temperature and 2,5-dimethylbenzoquinone (45 mg, 0.33 mmol, 1.1 equiv.), *N*-methyl phenylamine (28.9 mg, 0.27 mmol, 0.9 equiv.), and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were subsequently added. The vial was capped, sealed with Teflon tape and parafilm, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 12 h, with no precautions to exclude air and moisture. The crude mixture was analyzed using ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) with benzotrifluoride (43.8 mg, 0.3 mmol, 1.0 equiv.) added as an internal standard to determine the recovered olefin starting material as well as the cross-coupled product crude yields. A doublet at 2.26 ppm and a singlet at 2.09 ppm was observed, indicative of Wacker olefin oxidation side reactivity[2] (see spectra). Run 1: 3% yield (83% olefin RSM, 11% Wacker oxidation); Run 2: 2% yield (83% olefin RSM, 10% Wacker oxidation). **Average: 2% ± 0.1% yield (83% ± 0.4% olefin RSM, 10% ± 0.4% Wacker oxidation).**

Entry 15: The general procedure in the absence of MaSOX was followed using 0.05 M of dibutyl phosphate in dioxane (0.3 mL, 0.015 mmol, 0.05 equiv.) as the solvent. The crude mixture was analyzed using ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) to determine the recovered olefin starting material, the cross-coupled product, and Wacker oxidation byproduct crude yields. Run 1: 2% yield (84% olefin RSM, 8% Wacker oxidation); Run 2: 2% yield (84% olefin RSM, 10% Wacker oxidation). **Average: 2% ± 0.02% yield (84% ± 0.1% olefin RSM, 9% ± 0.8% Wacker oxidation).**

Entry 16: The general procedure in the absence of MaSOX was followed using 0.05 M of dibutyl phosphate in dioxane (0.3 mL, 0.015 mmol, 0.05 equiv.) as the solvent and stirred for 24 hours. The crude mixture was analyzed using ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) to determine the recovered olefin starting material, the cross-coupled product, and Wacker oxidation byproduct crude yields. Run 1: 3% yield (70% olefin RSM, 17% Wacker oxidation); Run 2: 6% yield (70% olefin RSM, 19% Wacker oxidation). **Average: 4% ± 1.9% yield (70% ± 0.4% olefin RSM, 18% ± 1.5% Wacker oxidation).**

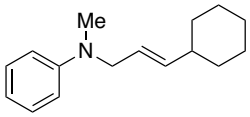
Entry 17: The general procedure in the absence of MaSOX was followed using 0.1 M of dibutyl phosphate in dioxane (0.3 mL, 0.03 mmol, 0.1 equiv.) as the solvent. The crude mixture was analyzed using ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) to determine the recovered olefin starting material, the cross-coupled product, and Wacker oxidation byproduct crude yields. Run

1: 3% yield (72% olefin RSM, 16% Wacker oxidation); Run 2: 3% yield (71% olefin RSM, 16% Wacker oxidation). **Average: 3% ± 0.1% yield (72% ± 0.7% olefin RSM, 16% ± 0.2% Wacker oxidation).**

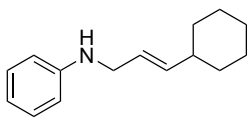
Entry 18: To a ½ dram vial equipped with a stir bar was added $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.05 equiv.), a fresh solution of 0.05 M dibutyl phosphate in dioxane (0.3 mL, 0.015 mmol, 0.05 equiv.) as the solvent, and *N*-methyl phenylamine (3.2 mg, 0.03 mmol, 0.1 equiv.). The vial was capped, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 1 h. The vial was cooled to room temperature and MaSOX (5.2 mg, 0.015 mmol, 0.05 equiv.), 2,5-dimethylbenzoquinone (45 mg, 0.33 mmol, 1.1 equiv.), *N*-methyl phenylamine (28.9 mg, 0.27 mmol, 0.9 equiv.), and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were subsequently added. The vial was capped, sealed with Teflon tape and parafilm, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 12 h, with no precautions to exclude air and moisture. The remainder of the general procedure was followed. Run 1: 61.1 mg, 89% yield (3% olefin RSM); Run 2: 61.6 mg, 89% yield (2% olefin RSM). **Average: 89% ± 0.6% yield (2% ± 0.9% olefin RSM).**

Entry 19: The general procedure was followed using $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 0.025 equiv.), MaSOX (3.4 mg, 0.01 mmol, 0.025 equiv.), 2,5-dimethylbenzoquinone (60 mg, 0.44 mmol, 1.1 equiv.), *N*-methyl phenylamine (42.9 mg, 0.4 mmol, 1.0 equiv.), a 0.05 M solution of dibutyl phosphate in dioxane (0.4 mL, 0.02 mmol, 0.05 equiv.) as the solvent, and allylcyclohexane (50 mg, 0.4 mmol, 1.0 equiv.). Run 1: 58.0 mg, 63% yield (28% olefin RSM); Run 2: 54.4 mg, 60% yield (35% olefin RSM). **Average: 62% ± 2.6% yield (32% ± 5.5% olefin RSM).**

Entry 20: To a 1 dram vial equipped with a stir bar was added $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 0.025 equiv.), MaSOX (3.4 mg, 0.01 mmol, 0.025 equiv.), and 2,5-dimethylbenzoquinone (60 mg, 0.44 mmol, 1.1 equiv.). A 0.05 M solution of dibutyl phosphate in dioxane as the solvent was added (0.4 mL, 0.02 mmol, 0.05 equiv.) followed by allylcyclohexane (50 mg, 0.4 mmol, 1.0 equiv.). The vial was sealed with Teflon tape and parafilm, and placed in a pre-heated 45 °C oil bath. A 1 mL syringe charged with 0.4 mL of a 1.0 M solution of *N*-methyl phenylamine in dioxane (0.4 mmol, 1.0 equiv.) was prepared and fitted with a 22Gx3 needle. The amine solution was then added at a rate of 0.04 mL/hour via syringe pump and stirred at 45 °C for 12 h total. The remainder of the general procedure was followed. Run 1: 76.4 mg, 84% yield (17% olefin RSM); Run 2: 76 mg, 85% yield (15% olefin RSM). **Average: 84% ± 0.1% yield (16% ± 2.2% olefin RSM).**



(*E*)-*N*-(3-cyclohexylallyl)-*N*-methylaniline (3): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (app t, *J* = 8.0 Hz, 2H), 6.87 (app d, *J* = 8.2 Hz, 2H), 6.82 (t, *J* = 7.3 Hz, 1H), 5.68 (dd, *J* = 15.5, 6.6 Hz, 1H), 5.53 (dt, *J* = 15.5, 5.7 Hz, 1H), 3.97 (d, *J* = 5.7 Hz, 2H), 3.01 (s, 3H), 2.15 – 2.01 (m, 1H), 1.87 – 1.79 (m, 4H), 1.79 – 1.73 (m, 1H), 1.42 – 1.32 (m, 2H), 1.28 (tt, *J* = 12.4, 2.9 Hz, 1H), 1.23 – 1.13 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.88, 139.20, 129.18, 122.65, 116.39, 112.81, 54.92, 40.54, 37.71, 33.10, 26.31, 26.16. HRMS (ESI) m/z calc'd for $C_{16}H_{23}N_2O_2$ $[M+H]^+$: 275.1760; found 275.1757.



(*E*)-*N*-(3-cyclohexylallyl)aniline: *Procedure A: 0 mol% dbp additive gives no allylic amine product.* The general procedure was followed using phenylamine (27.9 mg, 0.3 mmol, 1.0 equiv.) and dioxane as the solvent. The crude mixture was analyzed using ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) to

determine the recovered olefin starting material as well as the cross-coupled product crude yields. Run 1: 0% yield (97% olefin RSM); Run 2: 0% yield (93% olefin RSM). **Average: 0% yield (95% ± 2.4% olefin RSM).**

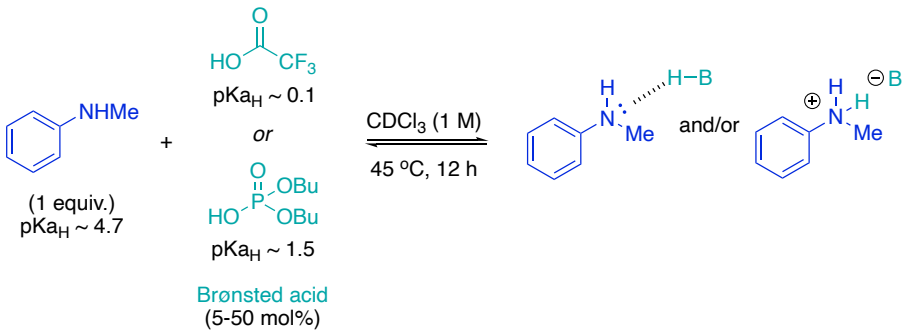
Procedure B: 25 mol% dbp additive gives trace allylic amine product and reduced mass balance. The general procedure was followed using phenylamine (27.9 mg, 0.3 mmol, 1.0 equiv.) and 0.25 M of dibutyl phosphate in dioxane (0.3 mL, 0.075 mmol, 0.25 equiv.) as the solvent. The crude mixture was analyzed using ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) to determine the recovered olefin starting material as well as the cross-coupled product crude yields. Run 1: 1% yield (62% olefin RSM); Run 2: 1% yield (59% olefin RSM) **Average: 1% ± 0.03% yield (60% ± 2.3% olefin RSM).**

Procedure C: 5 mol% dbp additive gives trace allylic amine product. The general procedure was followed using phenylamine (27.9 mg, 0.3 mmol, 1.0 equiv.) and 0.05 M of dibutyl phosphate in dioxane (0.3 mL, 0.015 mmol, 0.05 equiv.) as the solvent. The crude mixture was analyzed using ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) to determine the recovered olefin starting material as well as the cross-coupled product crude yields. Run 1: 4% yield (92% olefin RSM); Run 2: 6% yield (84% olefin RSM) **Average: 5% ± 1.4% yield (88% ± 6.4% olefin RSM).**

Procedure D: Increasing the catalyst loading to 10 mol% gave a small increase in yield and lower mass balance. The general procedure was followed using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), phenylamine (27.9 mg, 0.3 mmol, 1.0 equiv.), and 0.05 M of dibutyl phosphate in dioxane (0.3 mL, 0.015 mmol, 0.05 equiv.) as the solvent. The crude mixture was analyzed using ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) to determine the recovered olefin starting material as well as the cross-coupled product crude yields. Run 1: 7% yield (79% olefin RSM); Run 2: 6% yield (77% olefin RSM) **Average: 7% ± 0.6% yield (78% ± 1.5% olefin RSM).**

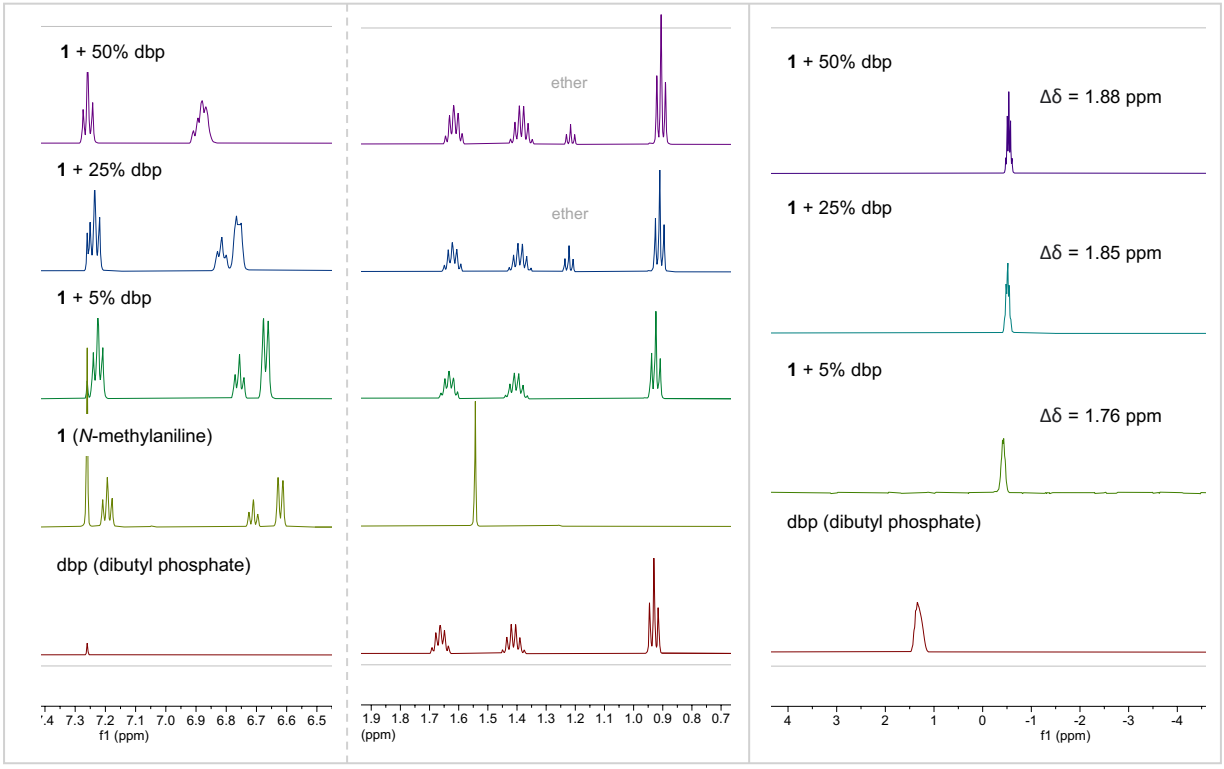
Procedure E: The slow addition protocol increased the total reactivity but afforded a mixture of mono- and di-allylated products. To a 1 dram vial equipped with a stir bar was added $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.05 equiv.), MaSOX (5.2 mg, 0.015 mmol, 0.025 equiv.), and 2,5-dimethylbenzoquinone (45 mg, 0.33 mmol, 1.1 equiv.). A 0.05 M solution of dibutyl phosphate in dioxane as the solvent was added (0.3 mL, 0.015 mmol, 0.05 equiv.) followed by allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.). The vial was sealed with Teflon tape and parafilm, and placed in a pre-heated 45 °C oil bath. A 1 mL syringe charged with 0.3 mL of a 1.0 M solution of phenylamine in dioxane (0.3 mmol, 1.0 equiv.) was prepared and fitted with a 22Gx3 needle. The amine solution was then added at a rate of 0.03 mL/hour via syringe pump and stirred at 45 °C for 12 h total. Purification via flash column chromatography (Brockmann Grade 3 basic alumina, Hexanes (200 mL) → 1% EtOAc/Hexanes (200 mL) → 2% EtOAc/Hexanes (200 mL) eluent) afforded the monoallylated 2° arylamine product as a red oil and the diallylated 3° arylamine product as a clear oil. Run 1: 7.1 mg, 11% yield (3.1 mg, 3% diallylation, 79% olefin RSM); Run 2: 6.9 mg, 11% yield (3.2 mg, 3% diallylation, 77% olefin RSM) **Average: 11% ± 0.4% yield (3% ± 0.4% yield diallylation, 75% ± 0.1% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (app t, *J* = 7.6 Hz, 2H), 6.73 (app t, *J* = 7.3 Hz, 1H), 6.65 (d, *J* = 8.0 Hz, 2H), 5.68 (dd, *J* = 15.4, 6.7 Hz, 1H), 5.56 (dt, *J* = 15.4, 5.9 Hz, 1H), 3.72 (d, *J* = 5.9 Hz, 2H), 2.03 – 1.93 (m, 1H), 1.88 – 1.69 (m, 4H), 1.71 – 1.63 (m, 1H), 1.36 – 1.23 (m, 2H), 1.19 (tt, *J* = 12.6, 3.0 Hz, 1H), 1.15 – 1.03 (m, 2H).The spectra are in accordance with those reported in the literature.[3]

2.2. Spectroscopic evaluation of *N*-methyl phenylamine with Brønsted acid additives.



To a ½ dram vial equipped with a stir bar was added *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and $CDCl_3$ (0.3 mL, 1.0 M), followed by addition of Brønsted acid additive dibutyl phosphate (dbp) or trifluoracetic acid (TFA). The vial was capped, sealed with Teflon tape and parafilm, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 12 h, with no precautions to exclude air and moisture. The vial was cooled to room temperature, half of the material was transferred to an NMR tube, and then diluted with an additional 0.5 mL of $CDCl_3$. The crude mixture was analyzed using ^{1}H NMR and ^{31}P NMR or ^{19}F NMR to determine the influence of the respective Brønsted acid additive on *N*-methyl phenylamine. pKa$_H$ values were retrieved from CAS SciFinder database.

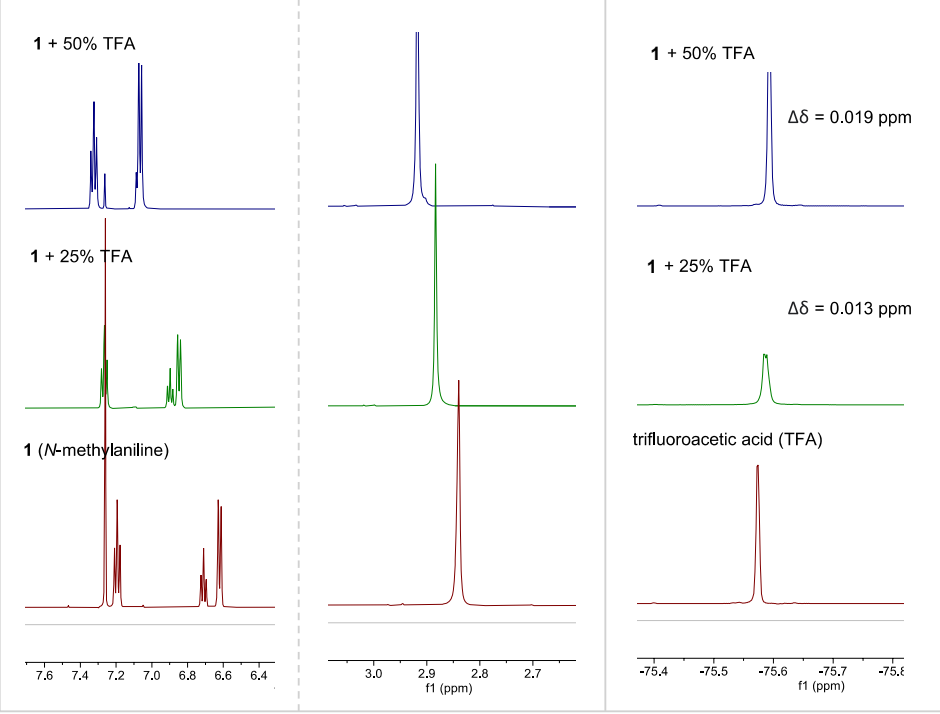
Figure S1. Spectroscopic analysis of *N*-methyl phenylamine **1** and dbp via ^{1}H NMR (left) and ^{31}P NMR (right) experiments.



Conclusion: ^{1}H NMR at various amounts of dbp demonstrated a downfield shift of the aromatic and methyl resonances of *N*-methyl phenylamine as well as an upfield shift of the alkyl resonances of dibutyl phosphate, with higher dbp concentrations resulting in greater Δδ (^{1}H) shifts. ^{31}P NMR analysis demonstrated an upfield shift relative to authentic dbp. Higher concentrations of dbp with *N*-methyl phenylamine resulted in larger Δδ (^{31}P) values. Due to the moderate pKa_H differences between dbp (~ 1.5) and *N*-methyl phenylamine (~ 4.7), this data is suggestive of a transient dbp/*N*-methyl phenylamine protonation and/or a hydrogen-bond-donor/hydrogen-bond-acceptor interaction.

An increase in catalytic reactivity at lower amounts of dbp (5 mol%) indicates that high dbp loadings may shift the equilibrium to higher concentrations of protonated and/or hydrogen-bonded arylamine, which may interfere with the ability for the free amine nucleophile to undergo functionalization to form the allylic tertiary amine product. NMR analysis at 5 mol% dbp resulted in a smaller Δδ (^{31}P) value of 1.76 ppm (versus 1.85 ppm and 1.88 ppm with 25% and 50% dbp, respectively) as well as a smaller Δδ (^{1}H) shifts, supporting a diminishment of this interaction.

Figure S2. Spectroscopic analysis of *N*-methyl phenylamine **1** and TFA via ^{1}H NMR (left) and ^{13}F NMR (right) experiments.



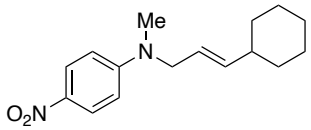
Conclusion: Exchange of dbp with TFA, a well-established strong hydrogen-bond-donor and weak hydrogen-bond-acceptor, afforded analogous results in which downfield shift of the aromatic and methyl resonances of *N*-methyl phenylamine were observed via ^{1}H NMR analysis and upfield shifts were observed via ^{19}F NMR analysis. Higher concentrations of TFA resulted in greater Δδ (^{1}H) and Δδ (^{19}F) values. This data supports that Brønsted acid additives (e.g. dbp, TFA) may afford a moderate protonation/hydrogen-bond-donor interaction with secondary arylamines.

3. Nucleophile, Electrophile, and Complex Examples Scope

3.1. General C(sp^3)H/N(sp^2) cross-coupling procedure: The following procedure was used with no precautions to exclude air and moisture. To a ½ dram vial equipped with a stir bar was added $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.05 equiv.), MaSOX (5.2 mg, 0.015 mmol, 0.05 equiv.), 2,5-dimethylbenzoquinone (45 mg, 0.33 mmol, 1.1 equiv.), and amine nucleophile (0.3 mmol, 1.0 equiv.). A fresh solution of dibutyl phosphate in solvent was added (0.3 mL, 1.0 M), followed by olefin electrophile (0.3 mmol, 1.0 equiv.). The vial was sealed with Teflon tape and parafilm, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 3–72 h. The vial was cooled to room temperature, diluted with $CDCl_3$, and benzotrifluoride (43.8 mg, 0.3 mmol, 1.0 equiv.) was added as an internal standard. The crude mixture was analyzed using quantitative ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) to determine the recovered olefin starting material. Unless otherwise noted, the crude reaction was then concentrated under reduced pressure and immediately subjected to flash column chromatography to afford the allylic arylamine product. Isolated yields are the average of two or three experiments.

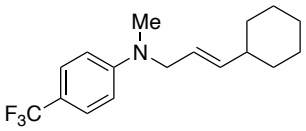
3.2. Slow addition C(sp^3)H/N(sp^2) cross-coupling procedure: The following procedure was used with no precautions to exclude air and moisture. To a 1 dram vial equipped with a stir bar was added $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.05 equiv.), MaSOX (5.2 mg, 0.015 mmol, 0.05 equiv.) and 2,5-dimethylbenzoquinone (45 mg, 0.33 mmol, 1.1 equiv.). A fresh solution of dibutyl phosphate in solvent was added (0.3 mL, 1.0 M), followed by olefin electrophile (0.3 mmol, 1.0 equiv.). The vial was sealed with Teflon tape and parafilm, and placed in a pre-heated 45 °C oil bath. A 1 mL syringe charged with 0.3 mL of a 1.0 M solution of amine nucleophile in dioxane (0.3 mmol, 1.0 equiv.) was prepared and fitted with a 22Gx3 needle. The amine solution was then added into the stirring reaction mixture via syringe pump and stirred at 45 °C for 4–24 h. The vial was cooled to room temperature, diluted with $CDCl_3$, and benzotrifluoride (43.8 mg, 0.3 mmol, 1.0 equiv.) was added as an internal standard. The crude mixture was analyzed using quantitative ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) to determine the recovered olefin starting material. Unless otherwise noted, the crude reaction was then concentrated under reduced pressure and immediately subjected to flash column chromatography to afford the allylic arylamine product. Isolated yields are the average of two or three experiments.

3.3. Synthesis and characterization of the nucleophile scope products.

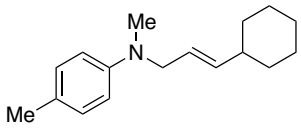


(*E*)-*N*-(3-cyclohexylallyl)-*N*-methyl-4-nitroaniline (5): *N*-methyl-4-nitroaniline (45.6 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (200 mL) → 3% EtOAc/Hexanes (200 mL) → 6% EtOAc/Hexanes (200 mL) eluent) afforded the product with 2,5-DMBQ. The material was then diluted with 25 mL of EtOAc and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a yellow solid. Run 1: 66.8 mg, 81% yield (13% olefin RSM); Run 2: 68.1 mg, 83% yield (14% olefin RSM); Run 3: 68.2 mg, 82% yield (12% olefin RSM). **Average: 82% ± 0.8% yield (14% ± 0.9% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (app d, *J* = 9.4 Hz, 2H), 6.61 (app d, *J* = 9.4 Hz, 2H), 5.53 (ddt, *J* = 15.5, 6.6, 1.6 Hz, 1H), 5.35 (dtd, *J* = 15.5,

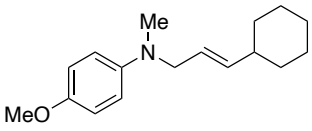
5.4, 1.1 Hz, 1H), 3.97 (app d, *J* = 5.4 Hz, 2H), 3.05 (s, 3H), 2.01 – 1.91 (m, 1H), 1.75 – 1.66 (m, 4H), 1.66 – 1.60 (m, 1H), 1.30 – 1.19 (m, 2H), 1.14 (tt, *J* = 12.4, 3.2 Hz, 1H), 1.09 – 0.99 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.84, 140.10, 136.98, 126.29, 120.43, 110.56, 54.51, 40.47, 38.24, 32.93, 26.20, 26.05. HRMS (ESI) m/z calc'd for $C_{16}H_{23}N_2O_2$ $[M+H]^+$: 275.1760; found 275.1757.



(*E*)-*N*-(3-cyclohexylallyl)-*N*-methyl-4-(trifluoromethyl)aniline (6): *N*-methyl-4-(trifluoromethyl)aniline (52.5 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes eluent) afforded the product as a clear oil. Run 1: 82.6 mg, 93% yield (0% olefin RSM); Run 2: 83.7 mg, 95% yield (0% olefin RSM); Run 3: 82.8 mg, 93% yield (0% olefin RSM). **Average: 93% ± 1.2% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.6 Hz, 2H), 6.71 (d, *J* = 8.6 Hz, 2H), 5.56 (dd, *J* = 15.5, 6.5 Hz, 1H), 5.38 (dt, *J* = 15.5, 5.5 Hz, 1H), 3.91 (d, *J* = 5.5 Hz, 2H), 2.96 (s, 3H), 2.02 – 1.91 (m, 1H), 1.77 – 1.67 (m, 4H), 1.68 – 1.61 (m, 1H), 1.27 (qt, *J* = 12.8, 3.5 Hz, 2H), 1.16 (tt, *J* = 12.4, 2.8 Hz, 1H), 1.13 – 1.01 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.68, 139.51, 126.46 (q, *J* = 3.7 Hz), 125.36 (q, *J* = 270.0 Hz), 121.52, 117.41 (q, *J* = 32.6 Hz), 111.38, 54.39, 40.51, 37.79, 33.04, 26.28, 26.13. ^{19}F NMR (471 MHz, $CDCl_3$) δ -60.66. HRMS (ESI) m/z calc'd for $C_{17}H_{23}NF_3$ $[M+H]^+$: 298.1783; found 298.1779.



(*E*)-*N*-(3-cyclohexylallyl)-*N*,4-dimethylaniline (7): *N*,4-dimethylaniline (36.4 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (300 mL) → 3% EtOAc/Hexanes (300 mL) eluent) afforded the product as a yellow oil. Run 1: 59.4 mg, 82% yield (13% olefin RSM); Run 2: 58.8 mg, 81% yield (13% olefin RSM); Run 3: 59.8 mg, 83% yield (11% olefin RSM). **Average: 82% ± 0.9% yield (13% ± 1.2% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05 (app d, *J* = 8.5 Hz, 2H), 6.69 (app d, *J* = 8.5 Hz, 2H), 5.57 (ddt, *J* = 15.5, 6.6, 1.4 Hz, 1H), 5.42 (dtd, *J* = 15.5, 5.7, 1.2 Hz, 1H), 3.81 (d, *J* = 5.7 Hz, 2H), 2.86 (s, 3H), 2.27 (s, 3H), 2.01 – 1.90 (m, 1H), 1.76 – 1.68 (m, 4H), 1.68 – 1.61 (m, 1H), 1.32 – 1.21 (m, 2H), 1.16 (tt, *J* = 12.3, 3.0 Hz, 1H), 1.12 – 1.02 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.98, 139.26, 129.67, 125.79, 122.88, 113.36, 55.39, 40.56, 37.94, 33.12, 26.32, 26.16, 20.38. HRMS (ESI) m/z calc'd for $C_{17}H_{26}N$ $[M+H]^+$: 244.2065; found 244.2065.

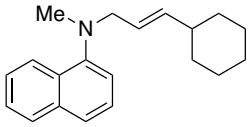


(*E*)-*N*-(3-cyclohexylallyl)-4-methoxy-*N*-methylaniline (8): <u>*Procedure A*</u>*:* 4-methoxy-*N*-methylaniline (41.2 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), 2,5-DMBQ (36.8 mg, 0.27 mmol, 0.9 equiv.), and 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 24 h. *Note: 1.1 equiv. and 0.9 equiv. of 2,5-DMBQ afforded comparable product yields and 0.9 equiv. was used for ease of purification purposes.* Purification via flash column chromatography (100 mL SiO_2 deactivated with 2% triethylamine, Hexanes (200 mL) → 1% Acetone/Hexanes (400 mL) → 2% Acetone/Hexanes (400 mL) → 5% Acetone/Hexanes (100 mL) eluent) afforded the product as a purple-tinted oil. Run 1: 65.5 mg, 84% yield (6% olefin RSM); Run 2: 64.1 mg, 83% yield (8% olefin RSM); Run 3: 63.8 mg, 83% yield (7%

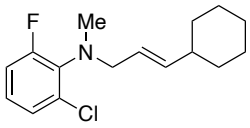
olefin RSM). **Average: 83% ± 1.1% yield (7% ± 1.3% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.74 (app d, *J* = 9.0 Hz, 2H), 6.66 (app d, *J* = 9.0 Hz, 2H), 5.47 (dd, *J* = 15.5, 6.6 Hz, 1H), 5.32 (app dt, *J* = 15.5, 6.0 Hz, 1H), 3.71 – 3.64 (m, 5H), 2.72 (s, 3H), 1.91 – 1.81 (m, 1H), 1.66 – 1.58 (m, 4H), 1.58 – 1.51 (m, 1H), 1.22 – 1.11 (m, 2H), 1.07 (tt, *J* = 12.3, 2.8 Hz, 1H), 1.03 – 0.92 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.88, 144.95, 139.52, 123.03, 115.26, 114.72, 56.34, 55.87, 40.56, 38.50, 33.10, 26.30, 26.14. HRMS (ESI) m/z calc'd for $C_{17}H_{26}NO$ $[M+H]^+$: 260.2014; found 260.2017.

Procedure B: Decreased catalyst loadings and time gave diminished yields. 4-methoxy-*N*-methylaniline (41.2 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (100 mL SiO_2 deactivated with 2% triethylamine, Hexanes (200 mL) → 1% Acetone/Hexanes (400 mL) → 2% Acetone/Hexanes (400 mL) → 5% Acetone/Hexanes (100 mL) eluent) afforded the product with 2,5-DMBQ. The material was then diluted with EtOAc (25 mL) and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a purple-tinted oil. Run 1: 32.2 mg, 41% yield (50% olefin RSM); Run 2: 32.7 mg, 42% yield (51% olefin RSM). **Average: 42% ± 0.7% yield (50% ± 0.7% olefin RSM).**

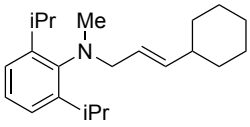
Procedure C: Alternatively, 4-methoxy-*N*-methylaniline (41.2 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the slow addition procedure, in which 0.3 mL of a 1.0 M solution of 4-methoxy-*N*-methylaniline was added at a rate of 0.015 mL/hour to the reaction mixture containing 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.), and stirred for 24 h. Procedure B's purification conditions were used to afford the product as a purple-tinted oil. Run 1: 56 mg, 73% yield (24% olefin RSM); Run 2: 58.6 mg, 76% yield (22% olefin RSM). **Average: 75% ± 2.1% yield (23% ± 2.0% olefin RSM).**



(*E*)-*N*-(3-cyclohexylallyl)-*N*-methylnaphthalen-1-amine (9): *N*-methylnaphthalen-1-amine (47.2 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (300 mL) → 3% EtOAc/Hexanes (200 mL) eluent) afforded the product as a clear oil. Run 1: 73.5 mg, 88% yield (7% olefin RSM); Run 2: 72.5 mg, 87% yield (9% olefin RSM); Run 3: 73.6 mg, 88% yield (7% olefin RSM). **Average: 88% ± 0.8% yield (8% ± 1.2% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (app d, *J* = 7.6 Hz, 1H), 7.84 (app d, *J* = 7.3 Hz, 1H), 7.54 (d, *J* = 8.1 Hz, 1H), 7.52 – 7.45 (m, 2H), 7.41 (app td, *J* = 7.8, 1.8 Hz, 1H), 7.09 (app d, *J* = 7.5 Hz, 1H), 5.69 (app dd, *J* = 15.6, 6.3 Hz, 1H), 5.62 (app dt, *J* = 15.6, 5.8 Hz, 1H), 3.65 (d, *J* = 5.8 Hz, 2H), 2.85 and 2.86 (two s, 3H), 2.10 – 1.99 (m, 1H), 1.84 – 1.73 (m, 4H), 1.73 – 1.65 (m, 1H), 1.38 – 1.27 (m, 2H), 1.22 (app t, *J* = 12.5 Hz, 1H), 1.18 – 1.09 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.39, 140.12, 134.95, 129.28, 128.43, 125.77, 125.20, 124.22, 124.17, 122.88, 115.20, 60.27, 40.79, 40.68, 33.17, 26.35, 26.18. *^{1}H-^{13}C HSQC analysis indicates that the carbon resonance at 125.77 ppm accounts for two nondegenerate carbons on the naphthalene ring (see spectra).* HRMS (ESI) m/z calc'd for $C_{20}H_{26}N$ $[M+H]^+$: 280.2065; found 280.2064.



(*E*)-2-chloro-*N*-(3-cyclohexylallyl)-6-fluoro-*N*-methylaniline (10): 2-chloro-6-fluoro-*N*-methylaniline (47.9 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.15 M solution of dibutyl phosphate in dioxane (0.15 equiv.) as a solvent, and stirred for 48 h. Purification via flash column chromatography (50 mL SiO_2 deactivated with 2% triethylamine, Hexanes eluent) afforded the product as a clear oil. Run 1: 61.2 mg, 72% yield (14% olefin RSM); Run 2: 63.0 mg, 74% yield (16% olefin RSM); Run 3: 59.1 mg, 70% yield (19% olefin RSM). **Average: 72% ± 2.1% yield (16% ± 2.4% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (app dt, *J* = 7.9, 1.5 Hz, 1H), 6.99 – 6.89 (m, 2H), 5.53 (dd, *J* = 15.5, 6.5 Hz, 1H), 5.44 (app dt, *J* = 15.5, 6.4, Hz, 1H), 3.59 (d, *J* = 6.4 Hz, 2H), 2.81 (d, *J* = 2.5 Hz, 3H), 1.98 – 1.86 (m, 1H), 1.74 – 1.56 (m, 5H), 1.29 – 1.18 (m, 2H), 1.13 (tt, *J* = 12.4, 3.0 Hz, 1H), 1.06 – 0.94 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.55 (d, *J* = 250.3 Hz), 140.29, 137.29 (d, *J* = 13.3 Hz), 134.30 (d, *J* = 6.7 Hz), 125.68 (d, *J* = 2.9 Hz), 125.14 (d, *J* = 9.5 Hz), 124.15, 115.18 (d, *J* = 21.6 Hz), 58.00 (d, *J* = 3.7 Hz), 40.49, 40.39 (d, *J* = 4.8 Hz), 33.01, 26.31, 26.10. ^{19}F NMR (471 MHz, $CDCl_3$) δ (-117.27) – (-117.39) (m). HRMS (ESI) m/z calc'd for $C_{16}H_{22}NFCl$ $[M+H]^+$: 282.1425; found 282.1424.



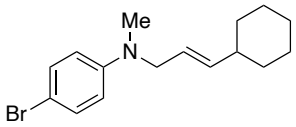
(*E*)-*N*-(3-cyclohexylallyl)-2,6-diisopropyl-*N*-methylaniline (11): <u>*Procedure A*</u>*:* 2,6-diisopropyl-*N*-methylaniline (57.4 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.15 M solution of dibutyl phosphate in dioxane (0.15 equiv.) as a solvent, and stirred for 48 h. Purification via flash column chromatography (10 mL Brockmann Grade 3 basic alumina, Hexanes (150 mL) eluent) followed by a second flash column chromatography (100 mL SiO_2, Hexanes (300 mL) → 1% EtOAc/Hexanes (400 mL) → 2% EtOAc/Hexanes (400 mL) eluent) afforded the product as a clear oil. Run 1: 61.3 mg, 66% yield (14% olefin RSM); Run 2: 57.0 mg, 61% yield (13% olefin RSM); Run 3: 57.6 mg, 61% yield (17% olefin RSM). **Average: 63% ± 2.7% yield (15% ± 2.4% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (app t, *J* = 7.6 Hz, 1H), 7.10 (app d, *J* = 7.6 Hz, 2H), 5.57 (dd, *J* = 15.4, 6.5 Hz, 1H), 5.49 (dt, *J* = 15.4, 6.2 Hz, 1H), 3.58 (d, *J* = 6.2 Hz, 2H), 3.42 (hept, *J* = 6.9 Hz, 2H), 2.76 (s, 3H), 2.05 – 1.95 (m, 1H), 1.80 – 1.71 (m, 4H), 1.71 – 1.63 (m, 1H), 1.36 – 1.26 (m, 2H), 1.24 (d, *J* = 4.4 Hz, 6H) and 1.22 (d, *J* = 4.4 Hz, 6H), 1.21 – 1.16 (m, 1H), 1.16 – 1.06 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.22, 147.61, 138.69, 126.24, 126.10, 123.98, 59.36, 40.86, 40.66, 33.28, 28.23, 26.37, 26.21, 24.55. HRMS (ESI) m/z calc'd for $C_{22}H_{36}N$ $[M+H]^+$: 314.2848; found 314.2852.

<u>*Procedure B*</u>*: Using 5 mol% dbp instead of 15 mol% dbp afforded diminished yields.* 2,6-diisopropyl-*N*-methylaniline (57.4 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 48 h. Purification using the conditions above afforded the product as a clear oil. 42.8 mg, 46% yield (27% olefin RSM).

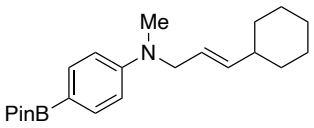
<u>*Procedure C*</u>*: Under the standard conditions (5 mol% catalyst, 5 mol% dbp, 12 hours), diminished yields were observed.* 2,6-diisopropyl-*N*-methylaniline (38.3 mg, 0.2 mmol, 1.0 equiv.) and allylcyclohexane (24.8 mg, 0.2 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 0.05 equiv.), MaSOX (3.4 mg, 0.01 mmol, 0.05 equiv.), 2,5-DMBQ (30 mg, 0.22 mmol, 1.1 equiv.), and 0.2 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. The crude mixture was analyzed using quantitative ^{1}H NMR (nt = 16 scans, d1

= 10 seconds) with benzotrifluoride as an internal standard to determine the product and recovered olefin starting material yields: 22% yield (70% olefin RSM).

Procedure D: The slow addition procedure did not improve reactivity under the standard conditions, suggestive that palladium-amine binding is not a major challenge, but rather, the steric-encumbrance of the nucleophile: 2,6-diisopropyl-*N*-methylaniline (57.4 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the slow addition procedure, in which 0.3 mL of a 1.0 M solution of 2,6-diisopropyl-*N*-methylaniline was added at a rate of 0.03 mL/hour to the reaction mixture containing 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.), and stirred for 12 h. The crude mixture was analyzed using quantitative ^{1}H NMR (nt = 8 scans, d1 = 10 seconds) with benzotrifluoride as an internal standard to determine the approximate product and recovered olefin starting material yields: 13% yield (83% olefin RSM).

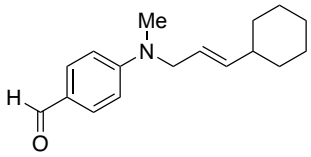


(*E*)-4-bromo-*N*-(3-cyclohexylallyl)-*N*-methylaniline (12): 4-bromo-*N*-methylaniline (55.8 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (50 mL SiO_2 deactivated with 2% triethylamine, Hexanes (200 mL) → 2% EtOAc/Hexanes (200 mL) → 4% EtOAc/Hexanes (200 mL) → 6% EtOAc/Hexanes (200 mL) → 8% EtOAc/Hexanes (100 mL) → 10% EtOAc/Hexanes (100 mL) eluent) afforded the product as a yellow oil, as well as the recovered 4-bromo-*N*-methylaniline. Due to a grease impurity in the recovered amine starting material, benzotrifluoride (14.6 mg, 0.1 mmol) was added and quantitative ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) analysis was used to determine the recovery yield. Run 1: 76.6 mg, 83% yield (10% olefin RSM, 4% amine RSM); Run 2: 75.9 mg, 82% yield (10% olefin RSM, 4% amine RSM). Run 3: 77.4 mg, 85% yield (11% olefin RSM, 12% amine RSM). **Average: 83% ± 1.1% yield (10% ± 0.5% olefin RSM, 7% ± 4.4% amine RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (app d, *J* = 9.1 Hz, 2H), 6.59 (app d, *J* = 9.0 Hz, 2H), 5.54 (dd, *J* = 15.5, 6.6 Hz, 1H), 5.36 (dtd, *J* = 15.5, 5.6, 0.8 Hz, 1H), 3.82 (d, *J* = 5.6 Hz, 2H), 2.87 (s, 3H), 2.01 – 1.89 (m, 1H), 1.77 – 1.67 (m, 4H), 1.67 – 1.60 (m, 1H), 1.26 (qt, *J* = 13.0, 3.6 Hz, 2H), 1.16 (tt, *J* = 12.3, 3.1 Hz, 1H), 1.12 – 1.00 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.72, 139.43, 131.77, 121.96, 114.30, 108.17, 54.84, 40.50, 37.90, 33.06, 26.28, 26.12. HRMS (ESI) m/z calc'd for $C_{16}H_{23}NBr$ $[M+H]^+$: 308.1012; found 308.1014.

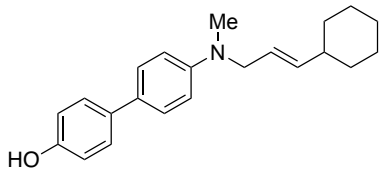


(*E*)-*N*-(3-cyclohexylallyl)-*N*-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (13): *N*-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (69.9 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (50 mL SiO_2, 2% EtOAc/Hexanes eluent) afforded the product alongside a mixture of the product with 2,5-DMBQ. The mixed fractions were purified via a second flash column chromatography (50 mL SiO_2, 2% EtOAc/Hexanes eluent). The combined pure fractions afforded the product as a light purple tinted solid. Run 1: 85.3 mg, 80% yield (2% olefin RSM); Run 2: 86.3 mg, 81% yield (1% olefin RSM); Run 3: 87.3 mg, 82% yield (0% olefin RSM). **Average: 81% ± 0.9% yield (1% ± 0.9% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (app d, *J* = 8.8 Hz, 2H), 6.68 (app d, *J* = 8.8 Hz, 2H), 5.53 (dd, *J* = 15.6, 6.6 Hz, 1H), 5.37 (dt, *J* = 15.6, 5.4 Hz, 1H), 3.88 (d, *J* = 5.4 Hz, 2H), 2.92 (s, 3H), 2.02 – 1.84 (m, 1H), 1.73 – 1.65 (m, 4H), 1.65 – 1.56 (m, 1H), 1.32 (s, 12H), 1.26 – 1.19 (m, 2H), 1.14 (tt, *J* = 12.3, 3.1 Hz, 1H), 1.09 – 0.99 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.88, 139.20, 136.30, 122.12, 111.45, 83.25,

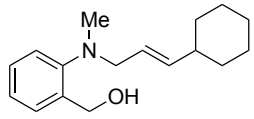
54.31, 40.52, 37.59, 33.07, 26.30, 26.14, 24.98. *Note: The carbon bound to boron was not observed due to quadrupole broadening from B^{11} nucleus. This is consistent to what is reported in the literature.* ^{11}B NMR (161 MHz, $CDCl_3$) δ 30.50. HRMS (ESI) m/z calc'd for $C_{22}H_{35}NO_2Br$ $[M+H]^+$: 356.2761; found 356.2770.



(*E*)-4-((3-cyclohexylallyl)(methyl)amino)benzaldehyde (14): 4-(methylamino)benzaldehyde (40.5 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (50 mL SiO_2, 5% Et_2O/Hexanes (600 mL) → 10% Et_2O/Hexanes (200 mL) → 15% Et_2O/Hexanes (200 mL) → 20% Et_2O/Hexanes (200 mL) eluent) afforded the product as a yellow oil. Run 1: 73.4 mg, 95% yield (0% olefin RSM); Run 2: 73.4 mg, 96% yield (0% olefin RSM); Run 3: 71.4 mg, 92% yield (0% olefin RSM). **Average: 95% ± 1.9% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.73 (s, 1H), 7.71 (d, *J* = 8.6 Hz, 2H), 6.70 (d, *J* = 8.6 Hz, 2H), 5.54 (dd, *J* = 15.6, 6.5 Hz, 1H), 5.36 (dt, *J* = 15.6, 5.4 Hz, 1H), 3.95 (d, *J* = 5.4 Hz, 2H), 3.02 (s, 3H), 2.01 – 1.87 (m, 1H), 1.75 – 1.66 (m, 4H), 1.66 – 1.59 (m, 1H), 1.29 – 1.19 (m, 2H), 1.14 (tt, *J* = 12.6, 3.1 Hz, 1H), 1.09 – 0.99 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 190.32, 153.89, 139.76, 132.13, 125.26, 120.91, 111.28, 54.29, 40.44, 37.93, 32.94, 26.20, 26.05. HRMS (ESI) m/z calc'd for $C_{17}H_{24}NO$ $[M+H]^+$: 258.1858; found 258.1858.

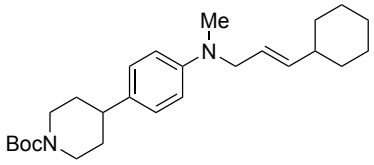


(*E*)-4'-((3-cyclohexylallyl)(methyl)amino)-[1,1'-biphenyl]-4-ol (15): 4'-(methylamino)-[1,1'-biphenyl]-4-ol (59.8 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Upon crude ^{1}H NMR analysis, a doublet at 2.22 ppm and a singlet at 2.04 ppm was observed, indicative of Wacker olefin oxidation side reactivity (see spectra). Wacker olefin oxidation yields were determined alongside the olefin RSM by quantitative crude ^{1}H NMR analysis. Purification via flash column chromatography (50 mL SiO_2, Hexanes (100 mL) → 5% EtOAc/Hexanes (400 mL) → 10% EtOAc/Hexanes (400 mL) → 15% EtOAc/Hexanes (200 mL) eluent) afforded the product as a light yellow solid. Run 1: 71.9 mg, 75% yield (10% olefin RSM, 12% Wacker oxidation); Run 2: 69.7 mg, 73% yield (5% olefin RSM, 11% Wacker oxidation); Run 3: 68.4 mg, 71% yield (3% olefin RSM, 9% Wacker oxidation). **Average: 73% ± 2.0% yield (6% ± 3.6% olefin RSM, 11% ± 1.2% Wacker oxidation).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.38 (m, 4H), 6.86 (app d, *J* = 8.6 Hz, 2H), 6.78 (app d, *J* = 8.8 Hz, 2H), 5.58 (app dd, *J* = 15.4, 6.6 Hz, 1H), 5.42 (dtd, *J* = 15.5, 5.7, 1.0 Hz, 1H), 4.61 (br s, 1H), 3.88 (d, *J* = 5.7 Hz, 2H), 2.92 (s, 3H), 2.03 – 1.87 (m, 1H), 1.75 – 1.66 (m, 4H), 1.66 – 1.59 (m, 1H), 1.32 – 1.19 (m, 2H), 1.15 (tt, *J* = 12.4, 2.9 Hz, 1H), 1.11 – 1.00 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.15, 148.87, 139.35, 134.42, 128.84, 127.61, 127.43, 122.53, 115.64, 113.05, 54.95, 40.56, 37.84, 33.11, 26.31, 26.16. HRMS (ESI) m/z calc'd for $C_{22}H_{28}NO$ $[M+H]^+$: 322.2171; found 322.2166. *The allylic carbon resonance at 54.95 ppm is indicative of an alpha-amino carbon. This data supports this method to chemoselectively functionalize at the amine in the presence of an unprotected phenol.*

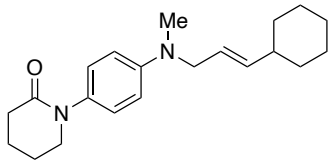


(*E*)-(2-((3-cyclohexylallyl)(methyl)amino)phenyl)methanol (16): (2-(methylamino)phenyl)methanol (41.2 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution

of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (50 mL SiO_2, Hexanes (200 mL) → 3% EtOAc/Hexanes (200 mL) → 6% EtOAc/Hexanes (200 mL) → 9% EtOAc/Hexanes (200 mL) → 12% EtOAc/Hexanes (200 mL) → 15% EtOAc/Hexanes (100 mL) eluent) afforded the product as a yellow oil. Run 1: 63.8 mg, 82% yield (14% olefin RSM); Run 2: 64.6 mg, 83% yield (17% olefin RSM); Run 3: 63.2 mg, 82% yield (15% olefin RSM). **Average: 83% ± 0.8% yield (15% ± 1.7% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (app t, *J* = 7.4 Hz, 1H), 7.18 (app d, *J* = 7.9 Hz, 1H), 7.15 (app dd, *J* = 7.6, 1.2 Hz, 1H), 7.08 (td, *J* = 7.4, 0.9 Hz, 1H), 5.68 (br s, 1H), 5.57 (dd, *J* = 15.4, 6.7 Hz, 1H), 5.43 (dtd, *J* = 15.4, 6.7, 0.9 Hz, 1H), 4.81 (s, 2H), 3.45 (d, *J* = 6.7 Hz, 2H), 2.65 (s, 3H), 2.01 – 1.90 (m, 1H), 1.76 – 1.59 (m, 5H), 1.25 (qt, *J* = 13.0, 3.4 Hz, 2H), 1.15 (tt, *J* = 12.3, 3.1 Hz, 1H), 1.11 – 1.00 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.49, 141.50, 135.97, 128.48, 128.10, 124.72, 123.21, 121.73, 65.22, 59.65, 41.25, 40.59, 32.98, 26.26, 26.07. HRMS (ESI) m/z calc'd for $C_{17}H_{26}NO$ $[M+H]^+$: 260.2014; found 260.2008. *^{1}H-^{13}C HSQC analysis denotes the allylic carbon resonance to be at 59.65 ppm, which is indicative of an alpha-amino carbon. Comparison of the starting amino alcohol and product ^{13}C NMR spectra show for the alpha-hydroxyl ^{13}C peak (65.01 ppm) to minimally shift. This data supports this method to chemoselectively functionalize at the amine in the presence of an unprotected benzylic alcohol (see spectra).*

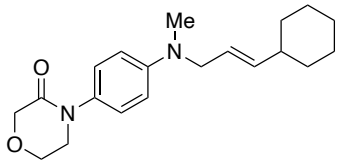


***tert*-butyl (*E*)-4-(4-((3-cyclohexylallyl)(methyl)amino)phenyl)piperidine-1-carboxylate (17):** *tert*-butyl 4-(4-(methylamino)phenyl)piperidine-1-carboxylate (87.1 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (100 mL) → 3% EtOAc/Hexanes (300 mL) → 6% EtOAc/Hexanes (300 mL) eluent) afforded the product with 2,5-DMBQ. The material was then diluted with EtOAc (25 mL) and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a beige solid. Run 1: 113.2 mg, 92% yield (6% olefin RSM); Run 2: 114.7 mg, 93% yield (6% olefin RSM); Run 3: 114.4 mg, 93% yield (6% olefin RSM). **Average: 93% ± 1.0% yield (6% ± 0.2% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.06 (app d, *J* = 8.5 Hz, 2H), 6.70 (app d, *J* = 8.5 Hz, 2H), 5.57 (dd, *J* = 15.5, 6.6 Hz, 1H), 5.41 (app dt, *J* = 15.5, 5.8 Hz, 1H), 4.23 (app br s, 2H), 3.82 (d, *J* = 5.6 Hz, 2H), 2.86 (s, 3H), 2.84 – 2.72 (m, 2H), 2.55 (tt, *J* = 12.1, 3.4 Hz, 1H), 2.00 – 1.90 (m, 1H), 1.80 (app d, *J* = 12.9 Hz, 2H), 1.75 – 1.67 (m, 4H), 1.67 – 1.53 (m, 3H), 1.493 and 1.491 (two s, 9H), 1.30 – 1.20 (m, 2H), 1.16 (tt, *J* = 12.4, 2.7 Hz, 1H), 1.12 – 1.01 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.00, 148.47, 139.15, 133.68, 127.37, 122.82, 112.92, 79.36, 55.07, 44.52, 41.72, 40.50, 37.73, 33.55, 33.06, 28.60, 26.26, 26.11. *^{1}H-^{13}C HSQC analysis confirms the weak carbon resonance at 44.52 ppm to correlate to 4 proton peaks on the piperidine ring (see spectra).* HRMS (ESI) m/z calc'd for $C_{26}H_{41}N_2O_2$ $[M+H]^+$: 413.3168; found 413.3160.

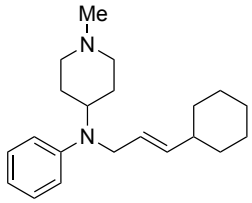


(*E*)-1-(4-((3-cyclohexylallyl)(methyl)amino)phenyl)piperidin-2-one (18): 1-(4-(methylamino)phenyl)piperidin-2-one (61.3 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, 5% EtOAc/Hexanes (200 mL) → 10% EtOAc/Hexanes (200 mL) → 15% EtOAc/Hexanes → 20% EtOAc/Hexanes (200 mL) → 25% EtOAc/Hexanes

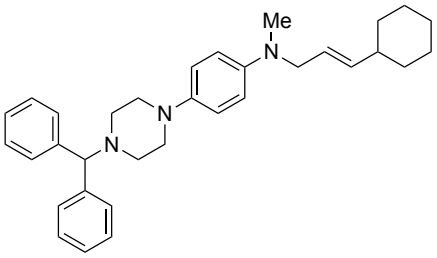
(200 mL) → 30% EtOAc/Hexanes (200 mL) → 35% EtOAc/Hexanes (200 mL) → 40% EtOAc/Hexanes (200 mL) eluent) followed by a second flash column chromatography (50 mL SiO_2, 50% EtOAc/Hexanes (600 mL) → 100% EtOAc (400 mL) eluent) afforded the product as a white solid. Run 1: 86.9 mg, 90% yield (3% olefin RSM); Run 2: 88.5 mg, 91% yield (3% olefin RSM); Run 3: 86.6 mg, 89% yield (2% olefin RSM). **Average: 90% ± 1.0% yield (3% ± 0.3% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05 (app d, *J* = 8.9 Hz, 2H), 6.70 (app d, *J* = 8.9 Hz, 2H), 5.55 (app dd, *J* = 15.5, 6.6 Hz, 1H), 5.39 (dtd, *J* = 15.5, 5.7, 0.9 Hz, 1H), 3.82 (d, *J* = 5.7 Hz, 2H), 3.60 – 3.54 (m, 2H), 2.87 (s, 3H), 2.57 – 2.48 (m, 2H), 1.98 – 1.92 (m, 1H), 1.93 – 1.87 (m, 4H), 1.73 – 1.66 (m, 4H), 1.66 – 1.59 (m, 1H), 1.30 – 1.19 (m, 2H), 1.15 (tt, *J* = 12.4, 3.1 Hz, 1H), 1.10 – 1.00 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.21, 148.53, 139.13, 132.36, 126.93, 122.50, 112.96, 54.92, 52.20, 40.44, 37.78, 33.01, 32.95, 26.23, 26.08, 23.74, 21.65. HRMS (ESI) m/z calc'd for $C_{21}H_{31}N_2O$ $[M+H]^+$: 327.2436; found 327.2434.



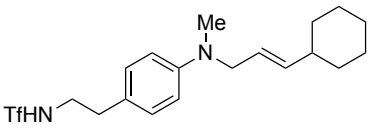
(*E*)-4-(4-((3-cyclohexylallyl)(methyl)amino)phenyl)morpholin-3-one (19): 4-(4-(methylamino)phenyl)morpholin-3-one (61.9 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (100 mL SiO_2, DCM (200 mL) → 0.5% NH_4OH-MeOH/DCM (200 mL) → 1% NH_4OH-MeOH/DCM (200 mL) → 1.5% NH_4OH-MeOH/DCM (200 mL) → 2% NH_4OH-MeOH/DCM (200 mL) → 2.5% NH_4OH-MeOH/DCM (200 mL) eluent) afforded the product with 2,5-DMHQ. The material was then diluted with EtOAc (25 mL) and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a light-yellow solid. Run 1: 90.7 mg, 92% yield (1% olefin RSM); Run 2: 94.2 mg, 97% yield (1% olefin RSM); Run 3: 91.1 mg, 93% yield (4% olefin RSM). **Average: 94% ± 2.3% yield (2% ± 1.4% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (app d, *J* = 8.9 Hz, 2H), 6.71 (app d, *J* = 8.9 Hz, 2H), 5.56 (dd, *J* = 15.5, 6.5 Hz, 1H), 5.38 (dt, *J* = 15.5, 5.6 Hz, 1H), 4.31 (s, 2H), 3.99 (app t, *J* = 5.0 Hz, 2H), 3.84 (d, *J* = 5.6 Hz, 2H), 3.69 (app t, *J* = 5.0 Hz, 2H), 2.89 (s, 3H), 1.99 – 1.89 (m, 1H), 1.73 – 1.66 (m, 4H), 1.66 – 1.60 (m, 1H), 1.30 – 1.19 (m, 2H), 1.15 (tt, *J* = 12.5, 3.0 Hz, 1H), 1.10 – 1.00 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.90, 148.78, 139.21, 130.07, 126.46, 122.23, 112.85, 68.68, 64.31, 54.80, 50.27, 40.43, 37.80, 32.99, 26.22, 26.07. HRMS (ESI) m/z calc'd for $C_{20}H_{29}N_2O_2$ $[M+H]^+$: 329.2229; found 329.2227.



Basic aliphatic amines are generally not compatible functionality under SOX·Pd(OAc)$_2$ catalysis. **(*E*)-*N*-(3-cyclohexylallyl)-1-methyl-*N*-phenylpiperidin-4-amine:** 1-methyl-*N*-phenylpiperidin-4-amine (38.1 mg, 0.2 mmol, 1.0 equiv.) and allylcyclohexane (24.8 mg, 0.2 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (4.5 mg, 0.02 mmol, 0.1 equiv.), MaSOX (6.8 mg, 0.02 mmol, 0.1 equiv.), 2,5-DMBQ (30 mg, 0.22 mmol, 1.1 equiv.) and 0.2 mL of a 0.05 M solution of di(2-ethylhexyl)phosphoric acid in dioxane (0.05 equiv.) as a solvent, and stirred for 24 h. The crude mixture was analyzed via ^{1}H NMR with benzotrifluoride as an internal standard to determine the approximate yield and recovered olefin starting material: 0% yield (83% olefin RSM).

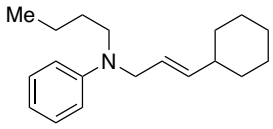


(*E*)-4-(4-benzhydrylpiperazin-1-yl)-*N*-(3-cyclohexylallyl)-*N*-methylaniline (20): 4-(4-benzhydrylpiperazin-1-yl)-*N*-methylaniline (107.3 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), 2,5-DMBQ (36.8 mg, 0.27 mmol, 0.9 equiv.) and 0.3 mL of a 0.1 M solution of dibutyl phosphate in dioxane (0.1 equiv.) as a solvent, and stirred for 24 h. *Note: 1.1 equiv. and 0.9 equiv. of 2,5-DMBQ afforded comparable product yields and 0.9 equiv. was used for ease of purification purposes.* Purification via flash column chromatography (50 mL SiO_2 deactivated with 2% triethylamine, Hexanes (200 mL) → 2% Acetone/Hexanes (200 mL) → 4% Acetone/Hexanes (200 mL) → 6% Acetone/Hexanes (200 mL) eluent) followed by a second flash column chromatography (same conditions) afforded the product as a beige-white solid. Run 1: 104.1 mg, 72% yield (9% olefin RSM); Run 2: 106.2 mg, 74% yield (11% olefin RSM); Run 3: 105.5 mg, 73% yield (11% olefin RSM). **Average: 73% ± 0.8% yield (10% ± 1.4% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.6 Hz, 4H), 7.20 (t, *J* = 7.5 Hz, 4H), 7.10 (t, *J* = 7.4 Hz, 2H), 6.78 (app d, *J* = 8.7 Hz, 2H), 6.65 (app d, *J* = 8.7 Hz, 2H), 5.47 (dd, *J* = 15.5, 6.6 Hz, 1H), 5.32 (dt, *J* = 15.5, 6.0 Hz, 1H), 4.19 (s, 1H), 3.67 (d, *J* = 5.9 Hz, 2H), 2.99 (app t, *J* = 4.5 Hz, 4H), 2.72 (s, 3H), 2.48 (app t, *J* = 4.5 Hz, 4H), 1.90 – 1.80 (m, 1H), 1.66 – 1.57 (m, 4H), 1.57 – 1.50 (m, 1H), 1.21 – 1.11 (m, 2H), 1.06 (tt, *J* = 12.5, 3.0 Hz, 1H), 1.02 – 0.92 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.76, 143.25, 142.93, 139.40, 128.64, 128.09, 127.07, 123.17, 118.24, 114.78, 76.43, 56.02, 52.30, 51.08, 40.56, 38.24, 33.11, 26.31, 26.15. HRMS (ESI) m/z calc'd for $C_{33}H_{42}N_3$ $[M+H]^+$: 480.3379; found 480.3367.

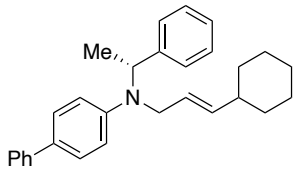


(*E*)-*N*-(4-((3-cyclohexylallyl)(methyl)amino)phenethyl)-1,1,1-trifluoromethanesulfonamide (22): *Procedure A:* 1,1,1-trifluoro-*N*-(4-(methylamino)phenethyl)methanesulfonamide (84.7 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (50 mL SiO_2 deactivated with 2% triethylamine, Hexanes (200 mL) → 3% Acetone/Hexanes (300 mL) → 6% Acetone/Hexanes (300 mL) → 9% Acetone/Hexanes (300 mL) eluent) afforded the product with a triethylamine impurity. The material was then diluted with EtOAc (25 mL) and washed with water (20 mL). The organic and aqueous layers were separated, and the aqueous layer was extracted with EtOAc (3 x 20 mL). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a purple-tinted oil. Run 1: 102.4 mg, 84% yield (5% olefin RSM); Run 2: 104.1 mg, 86% yield (5% olefin RSM); Run 3: 102.7 mg, 85% yield (5% olefin RSM). **Average: 85% ± 0.9% yield (5% ± 0.2% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (app d, *J* = 8.6 Hz, 2H), 6.70 (app d, *J* = 8.6 Hz, 2H), 5.56 (app dd, *J* = 15.5, 6.6 Hz, 1H), 5.39 (dtd, *J* = 15.5, 5.7, 1.1 Hz, 1H), 4.94 (br s, 1H), 3.84 (d, *J* = 5.7 Hz, 2H), 3.49 (t, *J* = 6.7 Hz, 2H), 2.88 (s, 3H), 2.79 (t, *J* = 6.7 Hz, 2H), 2.00 – 1.90 (m, 1H), 1.74 – 1.67 (m, 4H), 1.67 – 1.60 (m, 1H), 1.31 – 1.20 (m, 2H), 1.15 (tt, *J* = 12.3, 3.1 Hz, 1H), 1.11 – 1.01 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.07, 139.43, 129.58, 123.68, 123.62, 120.86 (q, *J* = 321.9 Hz), 113.28, 54.90, 45.79, 40.53, 37.82, 35.49, 33.09, 26.29, 26.14. ^{19}F NMR (471 MHz, $CDCl_3$) δ -77.30. *Minimal shift of the ^{19}F NMR resonance of the product (-77.30 ppm) from the starting amine 1,1,1-trifluoro-N-(4-(methylamino)phenethyl)methanesulfonamide (-77.31 ppm) supports this method's chemoselective functionalization of the N-methyl arylamine in the presence of an N-triflylamine.* HRMS (ESI) m/z calc'd for $C_{19}H_{28}N_2O_2SF_3$ $[M+H]^+$: 405.1824; found 405.1822.

Procedure B: Running the reaction in the absence of dibutyl phosphate required extended reaction times and higher catalyst loadings to promote catalysis. Diminished yields of the arylamine functionalized product and unidentifiable byproducts were observed (see spectra). 1,1,1-trifluoro-*N*-(4-(methylamino)phenethyl)methanesulfonamide (56.5 mg, 0.2 mmol, 1.0 equiv.) and allylcyclohexane (24.8 mg, 0.2 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (4.5 mg, 0.02 mmol, 0.1 equiv.), MaSOX (6.4 mg, 0.02 mmol, 0.1 equiv.), 2,5-DMBQ (30 mg, 0.22 mmol, 1.1 equiv.), and 0.2 mL of toluene as a solvent, and stirred for 72 h. Purification using the conditions above afforded the product as a purple-tinted oil. 35.5 mg, 44% yield (40% olefin RSM).

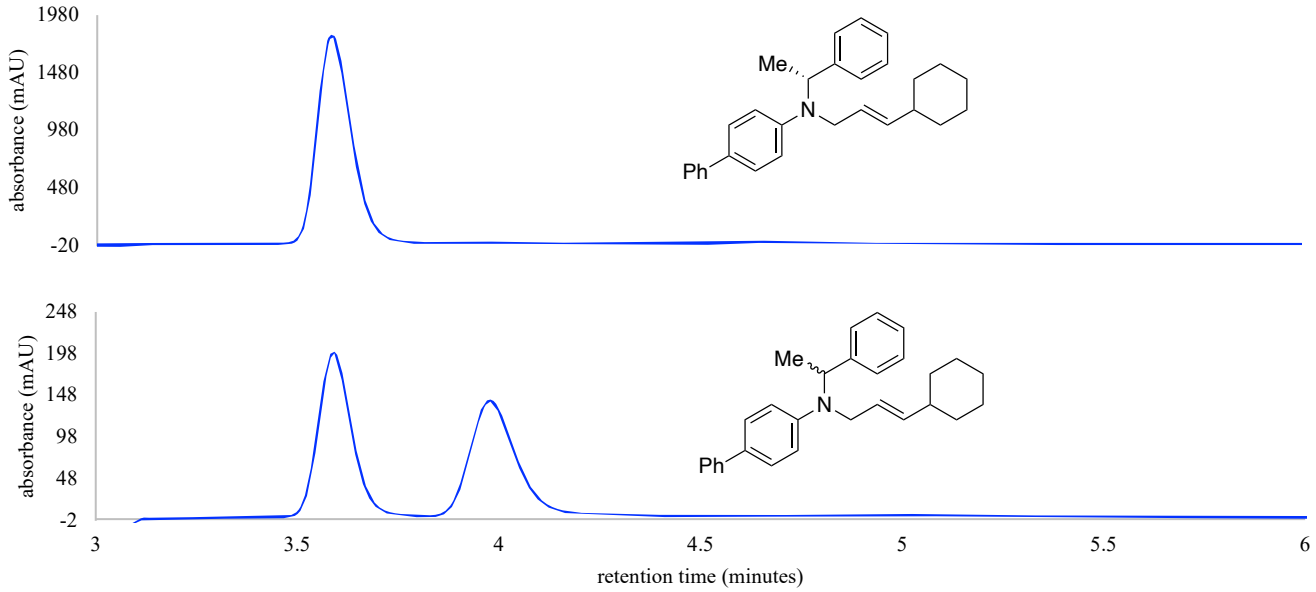


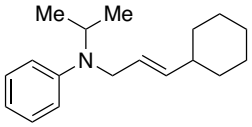
(*E*)-*N*-butyl-*N*-(3-cyclohexylallyl)aniline (23): *N*-butylaniline (44.8 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 24 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (300 mL) eluent) afforded the product as a clear oil. Run 1: 73.2 mg, 91% yield (7% olefin RSM); Run 2: 75.0 mg, 93% yield (6% olefin RSM); Run 3: 75.6 mg, 94% yield (4% olefin RSM). **Average: 93% ± 1.4% yield (6% ± 1.3% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (app t, *J* = 7.7 Hz, 2H), 6.68 (app d, *J* = 8.4 Hz, 2H), 6.64 (app t, *J* = 7.3 Hz, 1H), 5.54 (app dd, *J* = 15.5, 6.5 Hz, 1H), 5.40 (app dtt, *J* = 15.5, 5.5, 1.1 Hz, 1H), 3.84 (d, *J* = 5.4 Hz, 2H), 3.26 (app t, *J* = 7.7 Hz, 2H), 2.00 – 1.91 (m, 1H), 1.74 – 1.67 (m, 4H), 1.66 – 1.61 (m, 1H), 1.60 – 1.53 (m, 2H), 1.35 (sext, *J* = 7.5 Hz, 2H), 1.30 – 1.20 (m, 2H), 1.15 (tt, *J* = 12.3, 2.9 Hz, 1H), 1.10 – 1.00 (m, 2H), 0.95 (app td, *J* = 7.3, 1.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.77, 138.67, 129.20, 123.29, 115.57, 112.21, 52.80, 50.24, 40.54, 33.07, 29.55, 26.33, 26.17, 20.52, 14.18. HRMS (ESI) m/z calc'd for $C_{19}H_{30}N$ $[M+H]^+$: 272.2378; found 272.2378.



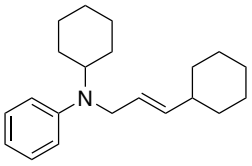
(*R*,*E*)-*N*-(3-cyclohexylallyl)-*N*-(1-phenylethyl)-[1,1'-biphenyl]-4-amine (24): (*R*)-*N*-(1-phenylethyl)-[1,1'-biphenyl]-4-amine (82 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.1 M solution of dibutyl phosphate in dioxane (0.1 equiv.) as a solvent, and stirred for 24 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (300 mL) → 2% Et_2O/Hexanes (200 mL) → 4% EtOAc/Hexanes (100 mL) eluent) afforded the product as a clear oil. Run 1: 63.7 mg, 54% yield, 98% e.e. (32% olefin RSM); Run 2: 64.5 mg, 55% yield, 98% e.e. (31% olefin RSM); Run 3: 66.1 mg, 56% yield, 98% e.e. (28% olefin RSM). **Average: 55% ± 0.8% yield, 98% e.e. (30% ± 1.9% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (app d, *J* = 7.9 Hz, 2H), 7.45 (app d, *J* = 8.8 Hz, 2H), 7.38 (app t, *J* = 7.7 Hz, 2H), 7.35 – 7.30 (m, 4H), 7.26 – 7.21 (m, 2H), 6.86 (app d, *J* = 8.8 Hz, 2H), 5.51 (dd, *J* = 15.6, 6.7 Hz, 1H), 5.37 (app dt, *J* = 15.6, 5.1 Hz, 1H), 5.16 (q, *J* = 7.0 Hz, 1H), 3.83 (d, *J* = 5.1 Hz, 2H), 1.97 – 1.86 (m, 1H), 1.73 – 1.63 (m, 5H), 1.62 (d, *J* = 7.0 Hz, 3H), 1.28 – 1.18 (m, 2H), 1.14 (tt, *J* = 12.4, 3.0 Hz, 1H), 1.07 – 0.97 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.65, 143.05, 141.34, 138.37, 129.15, 128.74, 128.57, 127.70, 127.15, 126.96, 126.35, 126.02, 124.90, 113.73, 56.54, 48.70, 40.58, 33.01, 32.97, 26.32, 26.13, 18.30. *^{1}H-^{13}C HSQC analysis indicates that the carbon resonances at 33.01 and 32.97 ppm account for two carbons on the cyclohexane ring; while it's anticipated for them to be degenerate, the carbon peaks are splitting, likely in result to the diastereotopic nature of the carbons on the cyclohexyl ring (see spectra).* HRMS (ESI) m/z calc'd for $C_{29}H_{34}N$ $[M+H]^+$: 396.2691; found 396.2698. % e.e. was determined

by HPLC analysis using a Chiralcel OD-H column (2% IPA/Hexanes eluent; 1.5 mL/min flow rate). $[\alpha]^{24}_{D}$ = +175.95° (*c* = 0.95, $CHCl_3$).



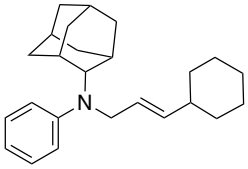


(*E*)-*N*-(3-cyclohexylallyl)-*N*-isopropylaniline (25): *N*-isopropylaniline (40.6 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.1 M solution of dibutyl phosphate in dioxane (0.1 equiv.) as a solvent, and stirred for 24 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes eluent) afforded the product as a clear oil. Run 1: 65.5 mg, 86% yield (9% olefin RSM); Run 2: 65.9 mg, 86% yield (9% olefin RSM); Run 3: 64.8 mg, 84% yield (8% olefin RSM). **Average: 85% ± 0.9% yield (9% ± 0.5% olefin RSM).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (app t, *J* = 7.9 Hz, 2H), 6.75 (d, *J* = 8.2 Hz, 2H), 6.65 (t, *J* = 7.2 Hz, 1H), 5.57 (app dd, *J* = 15.6, 6.6 Hz, 1H), 5.41 (dtd, *J* = 15.5, 4.8, 0.8 Hz, 1H), 4.10 (hept, *J* = 6.6 Hz, 1H), 3.75 (d, *J* = 4.8 Hz, 2H), 2.02 – 1.88 (m, 1H), 1.77 – 1.65 (m, 4H), 1.65 – 1.57 (m, 1H), 1.31 – 1.20 (m, 2H), 1.18 (d, *J* = 6.6 Hz, 6H), 1.18 – 1.11 (m, 1H), 1.10 – 0.99 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.34, 137.61, 129.13, 125.76, 115.89, 113.01, 47.99, 46.42, 40.54, 33.04, 26.35, 26.17, 20.12. HRMS (ESI) m/z calc'd for $C_{18}H_{28}N$ $[M+H]^+$: 258.2222; found 258.2229.

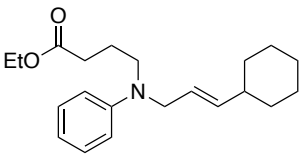


(*E*)-*N*-cyclohexyl-*N*-(3-cyclohexylallyl)aniline (26): *N*-cyclohexylaniline (52.6 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.1 M solution of dibutyl phosphate in dioxane (0.1 equiv.) as a solvent, and stirred for 48 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes eluent) afforded the product as a yellow-tinted solid. Run 1: 74.0 mg, 83% yield (4% olefin RSM); Run 2: 72.3 mg, 82% yield (3% olefin RSM); Run 3: 73.0 mg, 82% yield (4% olefin RSM). **Average: 82% ± 0.8% yield (4% ± 0.6% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (app dd, *J* = 8.6, 7.2 Hz, 2H), 6.75 (app d, *J* = 8.6 Hz, 2H), 6.66 (tt, *J* = 7.2, 1.0 Hz, 1H), 5.58 (ddt, *J* = 15.6, 6.6, 1.6 Hz, 1H), 5.41 (dtd, *J* = 15.6, 4.9, 1.2 Hz, 1H), 3.81 (app d, *J* = 4.9 Hz, 2H), 3.61 (tt, *J* = 11.2, 3.3 Hz, 1H),

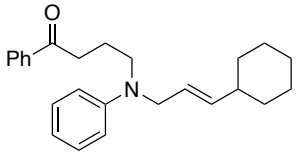
2.00 – 1.91 (m, 1H), 1.91 – 1.81 (m, 4H), 1.75 – 1.68 (m, 5H), 1.68 – 1.62 (m, 1H), 1.46 – 1.32 (m, 4H), 1.32 – 1.21 (m, 2H), 1.17 (tt, *J* = 12.4, 3.0 Hz, 2H), 1.12 – 1.02 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.25, 137.55, 129.13, 125.87, 115.74, 112.77, 57.11, 47.35, 40.52, 33.04, 30.73, 26.40, 26.35, 26.17, 26.14. HRMS (ESI) m/z calc'd for $C_{21}H_{32}N$ $[M+H]^+$: 298.2535; found 298.2532.



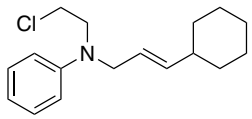
(*E*)-*N*-(3-cyclohexylallyl)-*N*-phenyladamantan-2-amine (27): *N*-phenyladamantan-2-amine (68.2 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.15 M solution of dibutyl phosphate in dioxane (0.15 equiv.) as a solvent, and stirred for 48 h. Purification via flash column chromatography (50 mL SiO_2 deactivated with 2% triethylamine, Hexanes (200 mL) → 1% Et_2O/Hexanes (200 mL) → 2% Et_2O/Hexanes (200 mL) eluent) afforded the product as a white solid. Run 1: 47.7 mg, 45% yield (36% olefin RSM); Run 2: 41.5 mg, 40% yield (40% olefin RSM); Run 3: 45.4 mg, 43% yield (41% olefin RSM). **Average: 43% ± 2.9% yield (39% ± 2.6% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (app t, *J* = 7.9 Hz, 2H), 6.97 (d, *J* = 7.8 Hz, 2H), 6.88 (t, *J* = 7.3 Hz, 1H), 5.28 (dt, *J* = 15.6, 6.1 Hz, 1H), 5.21 (dd, *J* = 15.6, 6.5 Hz, 1H), 3.58 (d, *J* = 6.1 Hz, 2H), 3.28 (br s, 1H), 2.04 (d, *J* = 12.2 Hz, 2H), 1.96 (br s, 2H), 1.82 – 1.69 (m, 5H), 1.68 – 1.55 (m, 6H), 1.55 – 1.48 (m, 3H), 1.30 (d, *J* = 12.1 Hz, 2H), 1.18 – 1.09 (m, 2H), 1.05 (tt, *J* = 12.4, 3.1 Hz, 1H), 0.89 (qd, *J* = 12.2, 2.8 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.96, 139.24, 128.42, 125.21, 123.11, 122.16, 60.56, 54.35, 40.69, 37.97, 37.33, 33.16, 31.50, 29.52, 27.62, 27.61, 26.32, 26.10. HRMS (ESI) m/z calc'd for $C_{25}H_{36}N$ $[M+H]^+$: 350.2848; found 350.2848.



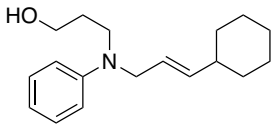
ethyl (*E*)-4-((3-cyclohexylallyl)(phenyl)amino)butanoate (28): ethyl 4-(phenylamino)butanoate (62.2 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (200 mL) → 2% EtOAc/Hexanes (200 mL) eluent) afforded the product with 2,5-DMBQ. The material was then diluted with EtOAc (25 mL) and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a clear-beige oil. Run 1: 83.1 mg, 85% yield (15% olefin RSM); Run 2: 83.1 mg, 84% yield (11% olefin RSM); Run 3: 84.3 mg, 86% yield (10% olefin RSM). **Average: 85% ± 1.1% yield (12% ± 2.3% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (app t, *J* = 7.9 Hz, 2H), 6.73 (d, *J* = 8.2 Hz, 2H), 6.67 (t, *J* = 7.3 Hz, 1H), 5.55 (dd, *J* = 15.5, 6.6 Hz, 1H), 5.41 (dtd, *J* = 15.5, 5.5, 0.8 Hz, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 3.86 (d, *J* = 5.5 Hz, 2H), 3.33 (app t, *J* = 7.5 Hz, 2H), 2.36 (t, *J* = 7.2 Hz, 2H), 2.00 – 1.89 (m, 3H), 1.75 – 1.67 (m, 4H), 1.67 – 1.61 (m, 1H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.31 – 1.20 (m, 2H), 1.16 (tt, *J* = 12.4, 2.8 Hz, 1H), 1.12 – 1.01 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.42, 148.55, 138.93, 129.24, 122.98, 116.01, 112.37, 60.50, 52.82, 49.60, 40.50, 33.02, 31.81, 26.28, 26.13, 22.73, 14.36. HRMS (ESI) m/z calc'd for $C_{21}H_{32}NO_2$ $[M+H]^+$: 330.2433; found 330.2434.



(*E*)-4-((3-cyclohexylallyl)(phenyl)amino)-1-phenylbutan-1-one (29): 1-phenyl-4-(phenylamino)butan-1-one (71.8 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 24 h. Purification via flash column chromatography (50 mL silica deactivated with 2% triethylamine, Hexanes (200 mL) → 3% Et_2O/Hexanes (200 mL) → 6% Et_2O/Hexanes (200 mL) → 9% Et_2O/Hexanes (200 mL) → 12% Et_2O/Hexanes (200 mL) eluent) afforded the product with 2,5-DMBQ. The material was then diluted with EtOAc (25 mL) and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a maroon-tinted oil. Run 1: 89.8 mg, 84% yield (12% olefin RSM); Run 2: 90.7 mg, 84% yield (11% olefin RSM); Run 3: 86.3 mg, 80% yield (11% olefin RSM). **Average: 82% ± 2.4% yield (11% ± 0.8% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (app d, *J* = 7.9 Hz, 2H), 7.57 (app t, *J* = 7.4 Hz, 1H), 7.46 (app t, *J* = 7.7 Hz, 2H), 7.20 (app t, *J* = 7.8 Hz, 2H), 6.74 (d, *J* = 8.3 Hz, 2H), 6.67 (t, *J* = 7.2 Hz, 1H), 5.55 (dd, *J* = 15.6, 6.5 Hz, 1H), 5.41 (dt, *J* = 15.6, 5.5 Hz, 1H), 3.87 (d, *J* = 5.5 Hz, 2H), 3.38 (app t, *J* = 7.4 Hz, 2H), 3.03 (t, *J* = 6.9 Hz, 2H), 2.05 (p, *J* = 7.2 Hz, 2H), 2.00 – 1.85 (m, 1H), 1.73 – 1.65 (m, 4H), 1.65 – 1.60 (m, 1H), 1.29 – 1.18 (m, 2H), 1.14 (tt, *J* = 12.5, 3.0 Hz, 1H), 1.09 – 0.98 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.88, 148.70, 138.97, 137.06, 133.14, 129.27, 128.72, 128.14, 123.05, 116.06, 112.57, 52.98, 49.71, 40.49, 35.88, 33.02, 26.29, 26.14, 21.96. HRMS (ESI) m/z calc'd for $C_{25}H_{32}NO$ $[M+H]^+$: 362.2484; found 362.2480.

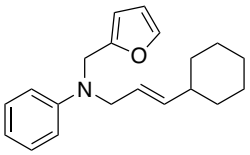


(*E*)-*N*-(2-chloroethyl)-*N*-(3-cyclohexylallyl)aniline (30): *N*-(2-chloroethyl)aniline (46.7 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 24 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (300 mL) eluent) afforded the product as a clear oil. Run 1: 69.0 mg, 83% yield (13% olefin RSM); Run 2: 69.9 mg, 84% yield (15% olefin RSM); Run 3: 88 mg, 88% yield (5% olefin RSM). **Average 85% ± 2.6% yield (11% ± 5.1% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (app t, *J* = 8.0 Hz, 2H), 6.75 – 6.68 (m, 3H), 5.57 (app dd, *J* = 15.6, 6.5 Hz, 1H), 5.41 (dtd, *J* = 15.6, 5.5, 1.0 Hz, 1H), 3.90 (d, *J* = 5.5 Hz, 2H), 3.67 – 3.57 (m, 4H), 2.05 – 1.89 (m, 1H), 1.76 – 1.66 (m, 4H), 1.66 – 1.60 (m, 1H), 1.32 – 1.20 (m, 2H), 1.15 (tt, *J* = 12.5, 3.1 Hz, 1H), 1.11 – 0.97 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.72, 139.55, 129.50, 122.67, 116.92, 112.28, 53.12, 52.32, 40.54, 40.48, 33.00, 26.28, 26.13. HRMS (ESI) m/z calc'd for $C_{17}H_{25}NCl$ $[M+H]^+$: 278.1676; found 278.1668.

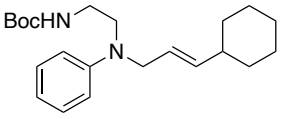


(*E*)-3-((3-cyclohexylallyl)(phenyl)amino)propan-1-ol (31): 3-(phenylamino)propan-1-ol (45.4 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (200 mL) → 2% EtOAc/Hexanes (200 mL) eluent) afforded the product with 2,5-DMBQ. The material was then diluted with EtOAc (25 mL) and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a clear-beige oil. Run 1: 75.0 mg, 92% yield (5% olefin RSM); Run 2: 71.4 mg, 87% yield (5% olefin RSM); Run 3: 71.4 mg, 87% yield (3% olefin RSM).

Average: 89% ± 2.9% yield (4% ± 1.5% olefin RSM). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (app t, *J* = 7.3 Hz, 2H), 6.77 (app d, *J* = 8.1 Hz, 2H), 6.70 (app t, *J* = 7.2 Hz, 1H), 5.57 (app dd, *J* = 15.5, 6.6 Hz, 1H), 5.43 (app dtt, *J* = 15.5, 5.6, 1.3 Hz, 1H), 3.86 (d, *J* = 5.5 Hz, 2H), 3.73 (t, *J* = 6.0 Hz, 2H), 3.42 (t, *J* = 7.0 Hz, 2H), 2.01 – 1.91 (m, 1H), 1.85 (p, *J* = 6.4 Hz, 2H), 1.80 (br s, 1H), 1.75 – 1.67 (m, 4H), 1.67 – 1.61 (m, 1H), 1.31 – 1.20 (m, 2H), 1.16 (app t, *J* = 12.4 Hz, 1H), 1.12 – 1.01 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.81, 139.17, 129.25, 122.99, 116.55, 113.22, 61.18, 53.38, 47.52, 40.52, 33.03, 30.21, 26.27, 26.13. *^{1}H-^{13}C HSQC analysis denotes the allylic carbon resonance to be at 53.38 ppm, which is indicative of an alpha-amino carbon. Comparison of the starting amino alcohol and product ^{13}C NMR spectra show for the alpha-hydroxyl ^{13}C peak (61.18 ppm) to minimally shift. This data supports this method to chemoselectively functionalize at the amine in the presence of an unprotected alcohol (see spectra).* HRMS (ESI) m/z calc'd for $C_{18}H_{28}NO$ $[M+H]^+$: 274.2171; found 274.2173.



(*E*)-*N*-(3-cyclohexylallyl)-*N*-(furan-2-ylmethyl)aniline (32): *N*-(furan-2-ylmethyl)aniline (52.0 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (300 mL) → 3% EtOAc/Hexanes (100 mL) eluent) afforded the product as a clear oil. Run 1: 76.7 mg, 88% yield (5% olefin RSM); Run 2: 78.9 mg, 90% yield (5% olefin RSM); Run 3: 78.6 mg, 89% yield (6% olefin RSM). **Average: 89% ± 1.4% yield (6% ± 0.2% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.34 (m, 1H), 7.22 (app t, *J* = 7.9 Hz, 2H), 6.83 (app d, *J* = 8.1 Hz, 2H), 6.72 (app t, *J* = 7.3 Hz, 1H), 6.34 – 6.28 (m, 1H), 6.16 (app d, *J* = 3.2 Hz, 1H), 5.59 (dd, *J* = 15.5, 6.5 Hz, 1H), 5.44 (app dt, *J* = 15.5, 5.5 Hz, 1H), 4.44 (s, 2H), 3.92 (d, *J* = 5.5 Hz, 2H), 2.03 – 1.91 (m, 1H), 1.76 – 1.68 (m, 4H), 1.68 – 1.61 (m, 1H), 1.33 – 1.22 (m, 2H), 1.17 (tt, *J* = 12.4, 2.9 Hz, 1H), 1.13 – 1.02 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.88, 148.93, 141.83, 139.40, 129.17, 122.57, 116.87, 113.08, 110.31, 107.24, 52.51, 47.09, 40.53, 33.05, 26.31, 26.15. HRMS (ESI) m/z calc'd for $C_{20}H_{26}NO$ $[M+H]^+$: 296.2014; found 296.2016.

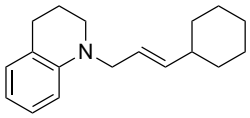


***tert*-butyl (*E*)-(2-((3-cyclohexylallyl)(phenyl)amino)ethyl)carbamate (33):** <u>*Procedure A*</u>*: tert*-butyl (2-(phenylamino)ethyl)carbamate (70.9 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (200 mL) → 3% EtOAc/Hexanes (400 mL) → 6% EtOAc/Hexanes (400 mL) → 9% EtOAc/Hexanes (100 mL) eluent) afforded the product with 2,5-DMBQ. The material was then diluted with EtOAc (25 mL) and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a maroon oil. Run 1: 104.9 mg, 98% yield (0% olefin RSM); Run 2: 105.1 mg, 98% yield (0% olefin RSM); Run 3: 102.7 mg, 96% yield (0% olefin RSM). **Average: 97% ± 1.2% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (app t, *J* = 7.8 Hz, 2H), 6.75 (d, *J* = 8.2 Hz, 2H), 6.69 (t, *J* = 7.3 Hz, 1H), 5.56 (dd, *J* = 15.5, 6.5 Hz, 1H), 5.41 (dt, *J* = 15.5, 5.4 Hz, 1H), 4.75 and 4.52 (two br s, 1H), 3.87 (d, *J* = 5.4 Hz, 2H), 3.48 – 3.37 (m, 2H), 3.36 – 3.21 (m, 2H), 2.00 – 1.91 (m, 1H), 1.75 – 1.67 (m, 4H), 1.67 – 1.60 (m, 1H), 1.46 (br s, 9H), 1.30 – 1.20 (m, 2H), 1.15 (tt, *J* = 12.6, 3.0 Hz, 1H), 1.11 – 1.01 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.12, 148.66, 139.27, 129.32,

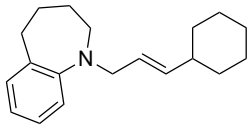
122.74, 116.54, 112.60, 79.38, 53.13, 50.10, 40.51, 38.56, 33.00, 28.54, 26.26, 26.12. HRMS (ESI) m/z calc'd for $C_{22}H_{35}N_2O_2$ $[M+H]^+$: 359.2699; found 359.2699.

Procedure B: Decreased catalyst loadings under the general procedure gave no reactivity. *tert*-butyl (2-(phenylamino)ethyl)carbamate (47.3 mg, 0.2 mmol, 1.0 equiv.) and allylcyclohexane (24.8 mg, 0.2 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 0.05 equiv.), MaSOX (3.4 mg, 0.01 mmol, 0.05 equiv.), 2,5-DMBQ (30 mg, 0.22 mmol, 1.1 equiv.), and 0.2 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Analysis by quantitative crude ^{1}H NMR with benzotrifluoride (nt = 16 scans, d1 = 10 seconds) as an internal standard determined the amount of product and remaining olefin starting material. Run 1: 0% yield (94% olefin RSM); Run 2: 0% yield (97% olefin RSM). **Average: 0% yield (95% ± 2.3% olefin RSM).**

Procedure C: Alternatively, *tert*-butyl (2-(phenylamino)ethyl)carbamate (70.9 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the slow addition procedure, in which 0.3 mL of a 1.0 M solution of *tert*-butyl (2-(phenylamino)ethyl)carbamate was added at a rate of 0.015 mL/hour to the reaction mixture containing 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.), and stirred for 24 h. Procedure A's purification conditions were used to afford the product as a maroon oil. Run 1: 96.5 mg, 90% yield (10% olefin RSM); Run 2: 103.1 mg, 95% yield (4% olefin RSM). **Average: 93% ± 3.6% yield (7% ± 4.2% olefin RSM).**

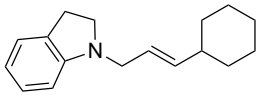


(*E*)-1-(3-cyclohexylallyl)-1,2,3,4-tetrahydroquinoline (34): 1,2,3,4-tetrahydroquinoline (39.9 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes eluent) afforded the product as a clear oil. Run 1: 67.9 mg, 90% yield (6% olefin RSM); Run 2: 69.3 mg, 91% yield (7% olefin RSM); Run 3: 66.3 mg, 87% yield (7% olefin RSM). **Average: 89% ± 2.3 yield (7% ± 0.9% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 (app t, *J* = 7.9 Hz, 1H), 6.95 (d, *J* = 7.2 Hz, 1H), 6.62 (d, *J* = 8.2 Hz, 1H), 6.57 (app t, *J* = 7.3 Hz, 1H), 5.58 (dd, *J* = 15.5, 6.6 Hz, 1H), 5.43 (dtd, *J* = 15.5, 5.6, 0.8 Hz, 1H), 3.82 (d, *J* = 5.6 Hz, 2H), 3.24 (app t, *J* = 5.6 Hz, 2H), 2.76 (app t, *J* = 6.3 Hz, 2H), 2.02 – 1.91 (m, 3H), 1.76 – 1.68 (m, 4H), 1.68 – 1.61 (m, 1H), 1.32 – 1.21 (m, 2H), 1.17 (tt, *J* = 12.4, 2.9 Hz, 1H), 1.13 – 1.02 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.68, 138.93, 129.07, 127.09, 122.62, 122.40, 115.65, 111.24, 53.43, 48.82, 40.55, 33.13, 28.30, 26.32, 26.17, 22.46. HRMS (ESI) m/z calc'd for $C_{18}H_{26}N$ $[M+H]^+$: 256.2065; found 256.2064.



(*E*)-1-(3-cyclohexylallyl)-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepine (35): 2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepine (44.2 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes eluent) afforded the product as a clear oil. Run 1: 68.8 mg, 85% yield (15% olefin RSM); Run 2: 70.7 mg, 87% yield (12% olefin RSM); Run 3: 69.5 mg, 86% yield (10% olefin RSM). **Average: 86% ± 1.1% yield (12% ± 2.5% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 – 7.08 (m, 2H), 6.92 (d, *J* = 7.8 Hz, 1H), 6.85 (app t, *J* = 7.3 Hz, 1H), 5.64 (dd, *J* = 15.5, 6.6 Hz, 1H), 5.51 (dt, *J* = 15.5, 6.0 Hz, 1H), 3.70 (d, *J* = 6.0 Hz, 2H), 2.95 – 2.87 (m, 2H), 2.84 – 2.77 (m, 2H), 2.06 – 1.96 (m, 1H), 1.81 – 1.58 (m, 9H), 1.37 – 1.24 (m, 2H), 1.20 (tt, *J* = 12.3, 3.0 Hz, 1H), 1.12 (qd, *J* = 12.9, 3.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.98, 139.51, 135.91, 130.11, 126.62, 125.60, 120.81, 117.65, 56.60,

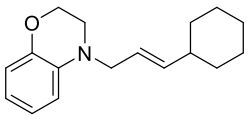
52.60, 40.64, 35.34, 33.20, 30.46, 26.35, 26.18, 26.00. HRMS (ESI) m/z calc'd for $C_{19}H_{28}N$ $[M+H]^+$: 270.2222; found 270.2226.



(*E*)-1-(3-cyclohexylallyl)indoline (36): *Procedure A:* indoline (35.8 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 24 h. Purification via flash column chromatography (50 mL SiO_2 deactivated with 2% triethylamine, Hexanes (300 mL) → 1% Et_2O/Hexanes (300 mL) → 2% Et_2O/Hexanes (300 mL) eluent) afforded the product as a beige solid. Run 1: 30.4 mg, 42% yield (29% olefin RSM); Run 2: 30.1 mg, 42% yield (32% olefin RSM); Run 3: 29.9 mg, 42% yield (30% olefin RSM). **Average: 42% ± 0.3 yield (30% ± 1.8% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 – 7.02 (m, 2H), 6.65 (t, *J* = 7.3 Hz, 1H), 6.52 (d, *J* = 7.8 Hz, 1H), 5.65 (dd, *J* = 15.4, 6.7 Hz, 1H), 5.48 (dtd, *J* = 15.4, 6.3, 1.0 Hz, 1H), 3.65 (d, *J* = 6.3 Hz, 2H), 3.30 (t, *J* = 8.3 Hz, 2H), 2.94 (t, *J* = 8.3 Hz, 2H), 2.05 – 1.92 (m, 1H), 1.78 – 1.68 (m, 4H), 1.68 – 1.60 (m, 1H), 1.33 – 1.21 (m, 2H), 1.17 (tt, *J* = 12.4, 3.0 Hz, 1H), 1.13 – 1.04 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.47, 140.21, 130.54, 127.33, 124.51, 122.96, 117.66, 107.59, 53.12, 51.68, 40.65, 33.10, 28.62, 26.31, 26.16. HRMS (ESI) m/z calc'd for $C_{17}H_{24}N$ $[M+H]^+$: 242.1909; found 242.1906. *Note: 1H-indole was collected as a mixture with the starting indoline amine and 2,5-DMBQ upon purification, and ^{1}H NMR is in accordance with literature values (see spectra).*[4] *Due to overlapping peaks in the crude ^{1}H NMR analysis and the volatility of 1H-indole upon isolation, a yield could not be reported. Observation of 1H-indole is indicative of indoline-palladium coordination followed by β-hydride elimination and sequential isomerization, with a driving force to form the fully aromatized indole amine. Lower allylic amination reactivity with indoline can be attributed to the amine's higher basicity, and thereby stronger affinity to electrophilic metals relative to other secondary arylamines.*[5]

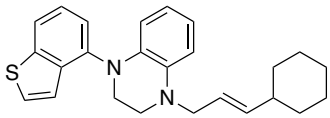
Procedure B: Decreased catalyst loadings gave diminished yields and poor mass balance. Indoline (35.8 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 48 h. The crude mixture was analyzed using quantitative ^{1}H NMR (nt = 8 scans, d1 = 10 seconds) with benzotrifluoride as an internal standard to determine the approximate yield and recovered olefin starting material: 15% yield (42% olefin RSM).

Procedure C: Alternatively, indoline (35.8 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the slow addition procedure, in which 0.3 mL of a 1.0 M solution of indoline was added at a rate of 0.03 mL/hour to the reaction mixture containing 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.), and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (300 mL) → 3% EtOAc/Hexanes (200 mL) eluent) afforded the product as a beige solid. Run 1: 47.6 mg, 66% yield (31% olefin RSM); Run 2: 49.6 mg, 69% yield (29% olefin RSM). **Average: 67% ± 2.0% yield (30% ± 1.7% olefin RSM).**

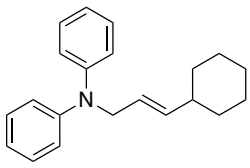


(*E*)-4-(3-cyclohexylallyl)-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazine (37): 3,4-dihydro-2*H*-benzo[*b*][1,4]oxazine (40.6 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (50 mL Brockmann Grade 3 basic alumina, Hexanes (400 mL) → 200 mL 1% EtOAc/Hexanes eluent) afforded the product as a rose colored oil. Run 1: 70.8 mg, 92% yield (0% olefin RSM); Run 2: 69.7 mg, 90% yield (0% olefin RSM); Run 3: 70.3 mg, 91%

yield (0% olefin RSM). **Average: 91% ± 0.8% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.83 (app td, *J* = 7.8, 1.6 Hz, 1H), 6.79 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.74 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.63 (app td, *J* = 7.6, 1.6 Hz, 1H), 5.63 (app dd, *J* = 15.7, 6.6 Hz, 1H), 5.44 (dtd, *J* = 15.4, 6.1, 1.2 Hz, 1H), 4.26 (app t, *J* = 4.3 Hz, 2H), 3.81 (d, *J* = 6.0 Hz, 2H), 3.28 (app t, *J* = 4.4 Hz, 2H), 2.03 – 1.91 (m, 1H), 1.78 – 1.67 (m, 4H), 1.70 – 1.62 (m, 1H), 1.33 – 1.21 (m, 2H), 1.17 (tt, *J* = 12.5, 3.0 Hz, 1H), 1.14 – 1.02 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.32, 140.30, 135.53, 121.87, 121.55, 117.70, 116.34, 112.96, 64.77, 53.18, 46.39, 40.60, 33.06, 26.26, 26.11. HRMS (ESI) m/z calc'd for $C_{17}H_{24}NO$ $[M+H]^+$: 258.1858; found 258.1858.



(*E*)-1-(benzo[*b*]thiophen-4-yl)-4-(3-cyclohexylallyl)-1,2,3,4-tetrahydroquinoxaline (38): 1-(benzo[*b*]thiophen-4-yl)-1,2,3,4-tetrahydroquinoxaline (79.9 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (100 mL SiO_2, 5% Et_2O/Hexanes eluent) afforded the product as a yellow oil. Run 1: 103.6 mg, 89% yield (4% olefin RSM); Run 2: 102.7 mg, 88% yield (4% olefin RSM); Run 3: 103.7 mg, 89% yield (3% olefin RSM). **Average: 89% ± 0.6% yield (4% ± 0.6% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.0 Hz, 1H), 7.38 – 7.33 (m, 2H), 7.25 (d, *J* = 4.8 Hz, 1H), 7.16 (d, *J* = 7.6 Hz, 1H), 6.79 – 6.70 (m, 2H), 6.45 (t, *J* = 7.3 Hz, 1H), 6.32 (d, *J* = 7.9 Hz, 1H), 5.67 (dd, *J* = 15.5, 6.5 Hz, 1H), 5.53 (app dt, *J* = 15.5, 5.8 Hz, 1H), 3.91 (d, *J* = 5.8 Hz, 2H), 3.79 (app t, *J* = 4.5 Hz, 2H), 3.44 (app t, *J* = 4.6 Hz, 2H), 2.07 – 1.95 (m, 1H), 1.80 – 1.70 (m, 4H), 1.70 – 1.62 (m, 1H), 1.35 – 1.23 (m, 2H), 1.19 (app t, *J* = 12.5 Hz, 1H), 1.15 – 1.05 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.46, 141.37, 139.87, 136.72, 136.15, 134.11, 125.79, 125.49, 122.72, 122.23, 120.66, 119.95, 119.16, 117.32, 116.03, 112.25, 53.70, 49.14, 47.20, 40.61, 33.13, 26.31, 26.16. HRMS (EI) m/z calc'd for $C_{25}H_{28}N_2S$ $[M]^+$: 388.1973; found 388.1976.

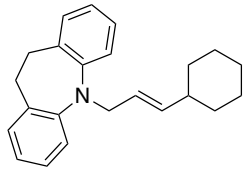


(*E*)-*N*-(3-cyclohexylallyl)-*N*-phenylaniline (39): <u>*Procedure A*</u>*:* diphenylamine (50.8 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.15 M solution of dibutyl phosphate in toluene (0.15 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (300 mL) eluent) afforded the product as a clear oil. Run 1: 54.3 mg, 62% yield (26% olefin RSM); Run 2: 51.0 mg 58% yield (27% olefin RSM); Run 3: 50.0 mg, 68% yield (32% olefin RSM). **Average 59% ± 2.3% yield (29% ± 3.1% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (app t, *J* = 7.5 Hz, 4H), 7.02 (d, *J* = 7.8 Hz, 4H), 6.94 (t, *J* = 7.3 Hz, 2H), 5.59 (dd, *J* = 15.6, 6.4 Hz, 1H), 5.51 (dt, *J* = 15.6, 5.2 Hz, 1H), 4.29 (d, *J* = 5.2 Hz, 2H), 2.03 – 1.85 (m, 1H), 1.79 – 1.58 (m, 5H), 1.33 – 1.19 (m, 2H), 1.14 (t, *J* = 12.3 Hz, 1H), 1.08 – 0.97 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.14, 139.20, 129.24, 123.07, 121.21, 121.06, 54.46, 40.51, 32.95, 26.30, 26.10. HRMS (ESI) m/z calc'd for $C_{21}H_{26}N$ $[M+H]^+$: 292.2065; found 292.2061.

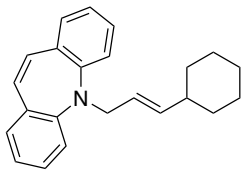
<u>*Procedure B*</u>*: Decreased amounts of dbp afforded diminished yields.* Diphenylamine (50.8 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in toluene (0.05 equiv.) as a solvent, and stirred for 12 h. The crude mixture was analyzed using ^{1}H NMR with benzotrifluoride as an internal standard to determine the approximate yield and recovered olefin starting material: 43% yield (46% olefin RSM).

<u>*Procedure C*</u>*: Increasing the reaction time afforded increased yields.* Diphenylamine (50.8 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.15 M

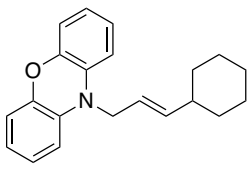
solution of dibutyl phosphate in toluene (0.15 equiv.) as a solvent, and stirred for 24 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (300 mL) eluent) afforded the product as a clear oil. Run 1: 67.2 mg, 77% yield (11% olefin RSM); Run 2: 64.6 mg, 74% yield (18% olefin RSM); Run 3: 67.9 mg, 78% yield (11% olefin RSM). **Average 76% ± 2.2% yield (13% ± 4.4% olefin RSM).**



(*E*)-5-(3-cyclohexylallyl)-10,11-dihydro-5*H*-dibenzo[*b*,*f*]azepine (40): 10,11-dihydro-5*H*-dibenzo[*b*,*f*]azepine (58.6 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.5 M solution of dibutyl phosphate in toluene (0.5 equiv.) as a solvent, and stirred for 48 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (300 mL) eluent) afforded the product as a clear oil. Run 1: 57.6 mg, 61% yield (17% olefin RSM); Run 2: 53.4 mg, 56% yield (21% olefin RSM); Run 3: 53.3 mg, 56% yield (23% olefin RSM). **Average: 58% ± 2.7% yield (20% ± 2.7% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 – 7.08 (m, 4H), 7.06 (app d, *J* = 8.1 Hz, 2H), 6.91 (tt, *J* = 7.3, 1.5 Hz, 2H), 5.59 (app dd, *J* = 15.6, 7.0 Hz, 1H), 5.34 (app dt, *J* = 15.6, 6.0 Hz, 1H), 4.35 (d, *J* = 6.0 Hz, 2H), 3.18 (app d, *J* = 1.5 Hz, 4H), 1.93 – 1.82 (m, 1H), 1.70 – 1.54 (m, 5H), 1.26 – 1.08 (m, 3H), 1.04 – 0.94 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.22, 139.85, 134.19, 129.68, 126.20, 124.57, 122.23, 120.83, 54.04, 40.57, 32.90, 32.67, 26.25, 25.99. HRMS (ESI) m/z calc'd for $C_{23}H_{28}N$ $[M+H]^+$: 318.2222; found 318.2216.

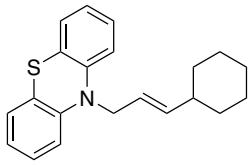


(*E*)-5-(3-cyclohexylallyl)-5*H*-dibenzo[*b*,*f*]azepine (41): 5*H*-dibenzo[*b*,*f*]azepine (57.9 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in toluene (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (300 mL) eluent) afforded the product as a bright yellow oil. Run 1: 78.9 mg, 84% yield (14% olefin RSM); Run 2: 82.4 mg, 87% yield (10% olefin RSM); Run 3: 79.0 mg, 84% yield (11% olefin RSM). **Average: 85% ± 2.0% yield (12% ± 2.1% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (td, *J* = 7.7, 1.7 Hz, 2H), 7.04 (dd, *J* = 7.5, 1.4 Hz, 2H), 6.96 (app t, *J* = 8.1 Hz, 4H), 6.74 (s, 2H), 5.63 (app dd, *J* = 15.6, 6.9 Hz, 1H), 5.31 (dtd, *J* = 15.6, 5.9, 1.0 Hz, 1H), 4.31 (d, *J* = 5.9 Hz, 2H), 1.90 – 1.80 (m, 1H), 1.67 – 1.51 (m, 5H), 1.23 – 1.14 (m, 2H), 1.13 (dt, *J* = 11.6, 2.9 Hz, 1H), 1.01 – 0.92 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.93, 140.40, 133.86, 132.31, 129.11, 128.60, 124.09, 123.25, 121.00, 53.17, 40.51, 32.82, 26.24, 25.96. HRMS (ESI) m/z calc'd for $C_{23}H_{26}N$ $[M+H]^+$: 316.2065; found 316.2063.

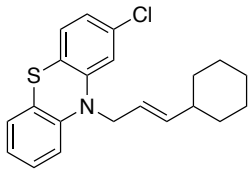


(*E*)-10-(3-cyclohexylallyl)-10*H*-phenoxazine (42): 10*H*-phenoxazine (54.9 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in toluene (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (300 mL) eluent) afforded the product as a beige oil. Run 1: 76.1 mg, 83% yield (1% olefin RSM); Run 2: 76.6 mg, 84% yield (2% olefin RSM); Run 3: 77.1 mg, 84% yield (3% olefin RSM). **Average 84% ± 0.7% yield (2% ± 0.9% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.88 – 6.70 (m, 2H), 6.68 – 6.62 (m, 4H), 6.47 (d, *J* = 8.0 Hz, 2H), 5.66 (ddt, *J* = 15.7, 6.6, 1.7 Hz, 1H), 5.40 (dtd, *J* = 15.7, 4.5, 1.3 Hz, 1H), 4.12 – 4.08 (m, 2H), 2.03 – 1.92 (m, 1H), 1.78 – 1.66 (m, 4H), 1.66 – 1.60 (m, 1H), 1.30 – 1.19 (m, 2H), 1.14 (tt, *J* = 12.6, 3.0 Hz, 1H), 1.10 – 1.00 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.44,

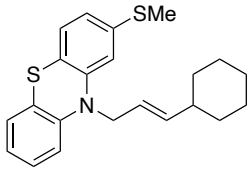
139.43, 134.09, 123.72, 120.93, 120.01, 115.24, 112.26, 47.32, 40.48, 32.91, 26.28, 26.11. HRMS (ESI) m/z calc'd for $C_{21}H_{23}NO$ $[M+H]^+$: 305.1780; found 305.1777.



(*E*)-10-(3-cyclohexylallyl)-10*H*-phenothiazine (43): 10*H*-phenothiazine (59.8 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of 0.05 M solution of dibutyl phosphate in 1,2-dichloroethane (0.05 equiv.) as a solvent, and stirred for 48 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (300 mL) eluent) afforded the product as a yellow oil. Run 1: 81.0 mg, 84% yield (16% olefin RSM); Run 2: 76.5 mg, 80% yield (9% olefin RSM); Run 3: 77.4 mg, 80% yield (11% olefin RSM). **Average 81% ± 2.5% yield (12% ± 3.8% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 – 6.98 (m, 4H), 6.91 – 6.83 (m, 4H), 5.64 (ddt, *J* = 15.8, 6.6, 1.7 Hz, 1H), 5.53 (dtd, *J* = 15.8, 4.3, 1.0 Hz, 1H), 4.42 (d, *J* = 4.3 Hz, 2H), 2.05 – 1.96 (m, 1H), 1.76 – 1.67 (m, 4H), 1.66 – 1.60 (m, 1H), 1.31 – 1.20 (m, 2H), 1.15 (tt, *J* = 12.3, 3.0 Hz, 1H), 1.11 – 1.02 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.72, 139.64, 127.10, 126.75, 123.01, 122.24, 122.01, 115.46, 50.81, 40.52, 32.73, 26.14, 25.94. HRMS (EI) m/z calc'd for $C_{21}H_{23}NS$ $[M]^+$: 321.1551; found 321.1540.

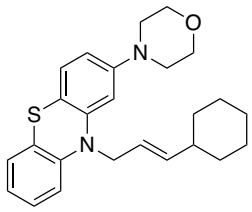


(*E*)-2-chloro-10-(3-cyclohexylallyl)-10*H*-phenothiazine (44): 2-chloro-10*H*-phenothiazine (70.1 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of 0.05 M solution of dibutyl phosphate in 1,2-dichloroethane (0.05 equiv.) as a solvent, and stirred for 48 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (300 mL) eluent) afforded the product as a clear oil. Run 1: 81.3 mg, 76% yield (12% olefin RSM); Run 2: 80.1 mg, 75% yield (13% olefin RSM); Run 3: 77.7 mg, 73% yield (9% olefin RSM). **Average: 75% ± 1.8% yield (11% ± 2.0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (app td, *J* = 7.8, 1.6 Hz, 1H), 7.05 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.94 (d, *J* = 7.9 Hz, 1H), 6.88 (td, *J* = 7.5, 1.0 Hz, 1H), 6.87 – 6.82 (m, 3H), 5.63 (ddt, *J* = 15.8, 6.9, 1.7 Hz, 1H), 5.50 (dtd, *J* = 15.8, 4.4, 1.0 Hz, 1H), 4.39 (d, *J* = 4.4 Hz, 2H), 2.10 – 1.93 (m, 1H), 1.80 – 1.68 (m, 4H), 1.67 – 1.61 (m, 1H), 1.35 – 1.21 (m, 2H), 1.17 (tt, *J* = 12.3, 3.1 Hz, 1H), 1.13 – 1.03 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.91, 144.24, 140.38, 133.10, 127.45, 127.29, 126.94, 122.85, 122.84, 122.09, 121.62, 121.39, 115.99, 115.76, 51.07, 40.68, 32.81, 26.23, 26.02. HRMS (EI) m/z calc'd for $C_{21}H_{22}NSCl$ $[M]^+$: 355.1161; found 355.1165.

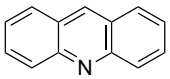


(*E*)-10-(3-cyclohexylallyl)-2-(methylthio)-10*H*-phenothiazine (45): 2-(methylthio)-10*H*-phenothiazine (73.6 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.15 M solution of dibutyl phosphate in 1,2-dichloroethane (0.15 equiv.) as a solvent, and stirred for 48 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, 3% Et_2O/Hexanes (300 mL) → 5% Et_2O/Hexanes (100 mL) eluent) afforded the product as a yellow oil. Run 1: 61.6 mg, 55% yield (21% olefin RSM); Run 2: 59.2 mg, 54% yield (13% olefin RSM); Run 3: 56.9 mg, 52% yield (16% olefin RSM). **Average 54% ± 2.1% yield (16% ± 3.9% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 – 7.03 (m, 2H), 6.95 (d, *J* = 7.9 Hz, 1H), 6.89 – 6.84 (m, 2H), 6.80 (app d, *J* = 1.7 Hz, 1H), 6.77 (app dd, *J* = 8.0, 1.8 Hz, 1H), 5.64 (ddt, *J* = 15.9, 6.7, 1.7 Hz, 1H), 5.53 (app dt, *J* = 15.9, 4.3 Hz, 1H), 4.42 (d, *J* = 4.3 Hz, 2H), 2.43 (s, 3H), 2.06 – 1.96 (m, 1H), 1.77 – 1.67 (m, 4H), 1.68 – 1.59 (m, 1H), 1.31 – 1.20 (m, 2H), 1.16 (tt, *J* = 12.5, 3.0 Hz, 1H), 1.12 – 1.03 (m, 2H). ^{13}C

NMR (126 MHz, $CDCl_3$) δ 145.18, 144.59, 139.94, 137.39, 127.25, 126.89, 126.86, 123.13, 122.50, 122.06, 120.68, 120.01, 115.64, 114.43, 51.04, 40.72, 32.91, 26.22, 26.05, 16.44. HRMS (EI) m/z calc'd for $C_{22}H_{25}NS_2$ $[M]^+$: 367.1428; found 367.1415.

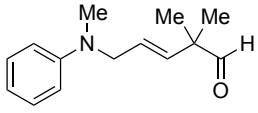


(*E*)-4-(10-(3-cyclohexylallyl)-10*H*-phenothiazin-2-yl)morpholine (46): 4-(10*H*-phenothiazin-2-yl)morpholine (85.3 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.1 M solution of dibutyl phosphate in toluene (0.1 equiv.) as a solvent, and stirred for 48 h. Purification via flash column chromatography (50 mL SiO_2 deactivated with 2% triethylamine, Hexanes (200 mL) → 2% EtOAc/Hexanes (200 mL) → 4% EtOAc/Hexanes (200 mL) → 6% EtOAc/Hexanes (200 mL) → 8% EtOAc/Hexanes (200 mL) → 10% EtOAc/Hexanes (200 mL) → 12% EtOAc/Hexanes (200 mL) eluent) afforded the product as a beige solid. Run 1: 94.2 mg, 77% yield (0% olefin RSM); Run 2: 96.5 mg, 79% yield (0% olefin RSM); Run 3: 90.1 mg, 74% yield (0% olefin RSM). **Average: 77% ± 2.7% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 – 7.02 (m, 2H), 6.93 (d, *J* = 8.4 Hz, 1H), 6.88 – 6.81 (m, 2H), 6.52 (s, 1H), 6.45 (d, *J* = 8.4 Hz, 1H), 5.66 (dd, *J* = 15.9, 6.9 Hz, 1H), 5.57 (dt, *J* = 15.9, 4.2 Hz, 1H), 4.43 (d, *J* = 4.2 Hz, 2H), 3.84 (app t, *J* = 4.8 Hz, 4H), 3.07 (app t, *J* = 4.8 Hz, 4H), 2.07 – 1.96 (m, 1H), 1.72 – 1.66 (m, 4H), 1.66 – 1.60 (m, 1H), 1.31 – 1.20 (m, 2H), 1.14 (tt, *J* = 12.3, 3.0 Hz, 1H), 1.11 – 1.01 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.29, 145.82, 144.85, 139.61, 127.07, 127.03, 126.83, 123.72, 122.83, 122.28, 115.48, 113.40, 109.96, 104.51, 66.95, 51.18, 49.77, 40.78, 33.02, 26.18, 26.02. HRMS (ESI) m/z calc'd for $C_{25}H_{31}N_2OS$ $[M+H]^+$: 407.2157; found 407.2154.

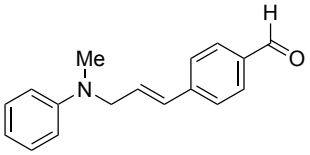


9,10-dihydroacridine did not undergo C(sp^3)H/N(sp^2) cross-coupling and underwent aromatization to afford acridine. 9,10-dihydroacridine (54.4 mg, 0.3 mmol, 1.0 equiv.) and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in toluene (0.05 equiv.) as a solvent, and stirred for 12 h. The crude mixture was analyzed using ^{1}H NMR benzotrifluoride as an internal standard to determine am approximate yield of the recovered olefin starting material and acridine product (see spectra): 87% yield (91% olefin RSM).

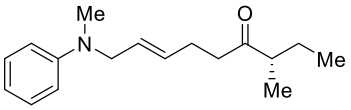
3.4. Synthesis and characterization of the electrophile scope products.



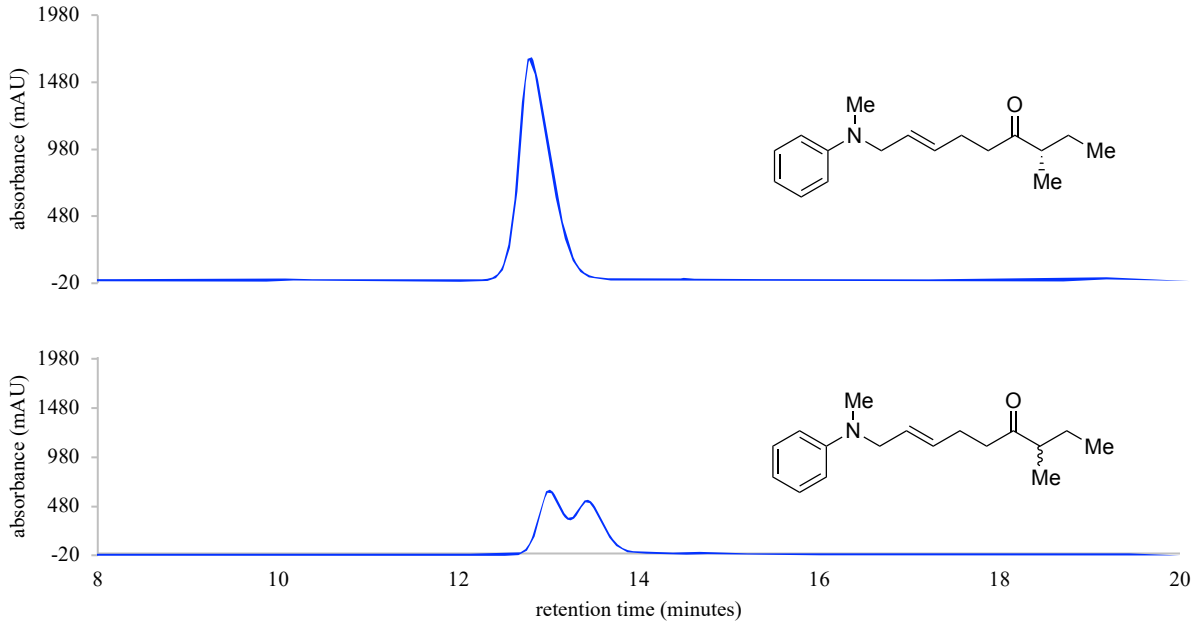
(*E*)-2,2-dimethyl-5-(methyl(phenyl)amino)pent-3-enal (47): *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and 2,2-dimethylpent-4-enal (33.7 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 24 h. Purification via flash column chromatography (40 mL SiO_2, 2% Acetone/Hexanes (400 mL) eluent) afforded the product as a pale amber oil. Run 1: 46.0 mg, 71% yield (5% olefin RSM); Run 2: 48.7 mg, 75% yield (5% olefin RSM); Run 3: 46.4 mg, 71% yield (6% olefin RSM). **Average: 72% ± 1.8% yield (5% ± 0.5% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.36 (s, 1H), 7.23 (t, *J* = 8.1 Hz, 2H), 6.75 – 6.69 (m, 3H), 5.63 – 5.53 (m, 2H), 3.93 (d, *J* = 3.3 Hz, 2H), 2.90 (s, 2H), 1.17 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.62, 149.57, 133.63, 129.30, 127.41, 116.82, 112.75, 54.93, 48.63, 37.95, 21.66. HRMS (ESI) m/z calc'd for $C_{14}H_{20}NO$ $[M+H]^+$: 218.1545; found 218.1554.

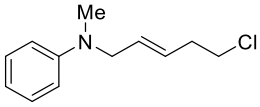


(*E*)-4-(3-(methyl(phenyl)amino)prop-1-en-1-yl)benzaldehyde (48): *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and 4-allylbenzaldehyde (43.9 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 3 h. Purification via flash column chromatography (50 mL SiO_2, 2% EtOAc/Hexanes (200 mL) → 3.5% EtOAc/Hexanes (200 mL) → 5% EtOAc/Hexanes (200 mL) eluent) afforded the product as a yellow oil. Run 1: 68.6 mg, 90% yield (0% olefin RSM); Run 2: 70.9 mg, 94% yield (0% olefin RSM); Run 3: 67.9 mg, 90% yield (0% olefin RSM). **Average: 92% ± 1.7% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.81 (d, *J* = 8.3 Hz, 2H), 7.49 (d, *J* = 8.1 Hz, 2H), 7.27 (app t, *J* = 7.2 Hz, 2H), 6.79 (d, *J* = 7.8 Hz, 1H), 6.75 (app t, *J* = 7.3 Hz, 1H), 6.58 (d, *J* = 15.9 Hz, 1H), 6.44 (dt, *J* = 15.9, 5.2 Hz, 1H), 4.13 (dd, *J* = 5.2, 1.7 Hz, 2H), 3.01 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.80, 149.44, 143.06, 135.38, 130.23, 130.12, 130.09, 129.37, 126.92, 116.93, 112.65, 55.00, 38.35. HRMS (ESI) m/z calc'd for $C_{17}H_{18}NO$ $[M+H]^+$: 252.1388; found 252.1390.

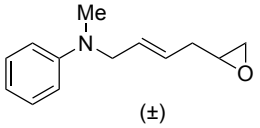


(+)-(*S*,*E*)-3-methyl-9-(methyl(phenyl)amino)non-7-en-4-one (49): *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and (*S*)-3-methylnon-8-en-4-one (46.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. The crude was then concentrated under reduced pressure, dissolved in EtOAc (25 mL), and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (40 mL SiO_2 deactivated with 2% triethylamine, Hexanes (200 mL) → 1% EtOAc/Hexanes (200 mL) → 2% EtOAc/Hexanes (200 mL) eluent) afforded the product as a beige oil. Run 1: 60.0 mg, 76% yield, 99% e.e. (6% olefin RSM); Run 2: 58.5 mg, 75% yield, 99% e.e. (14% olefin RSM); Run 3: 59.3 mg, 76% yield, 99% e.e. (12% olefin RSM). **Average: 76% ± 0.8% yield, 99% e.e. (11% ± 3.4% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (t, *J* = 7.7 Hz, 2H), 6.74 – 6.65 (m, 3H), 5.58 (dt, *J* = 15.4, 6.6 Hz, 1H), 5.49 (dt, *J* = 15.4, 5.4 Hz, 1H), 3.84 (d, *J* = 5.4 Hz, 2H), 2.89 (s, 3H), 2.49 (td, *J* = 7.2, 3.8 Hz, 2H), 2.41 (sext, *J* = 6.9 Hz, 1H), 2.29 (q, *J* = 6.9 Hz, 2H), 1.65 (app hept, *J* = 7.3 Hz, 1H), 1.36 (app hept, *J* = 7.3 Hz, 1H), 1.04 (d, *J* = 6.9 Hz, 3H), 0.85 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 214.08, 149.67, 131.27, 129.23, 126.26, 116.47, 112.67, 54.57, 48.05, 40.76, 37.94, 26.42, 26.03, 15.96, 11.84. HRMS (ESI) m/z calc'd for $C_{17}H_{26}NO$: $[M+H]^+$: 260.2014; found: 260.2016. % e.e. was determined by HPLC analysis using a Chiralcel OJ-H column (2% IPA/Hexanes eluent; 0.8 mL/min flow rate). $[\alpha]^{23}_D$ = +14.43 (*c* = 1.05, $CHCl_3$).





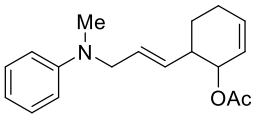
(*E*)-N-(5-chloropent-2-en-1-yl)-*N*-methylaniline (50): *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and 5-chloropent-1-ene (31.4 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.1 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (50 mL Brockmann Grade 3 basic alumina, Hexanes eluent) afforded the product as a colorless oil. Run 1: 43.4 mg, 69% yield (21% olefin RSM); Run 2: 46.6 mg, 74% yield (20% olefin RSM); Run 3: 45.9 mg, 73% yield (15% olefin RSM). **Average: 72% ± 2.2% yield (19% ± 2.6% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.20 (m, 2H), 6.82 – 6.64 (m, 3H), 5.66 – 5.56 (m, 2H), 3.89 (d, *J* = 2.7 Hz, 2H), 3.52 (t, *J* = 6.9 Hz, 2H), 2.92 (s, 3H), 2.50 (app tdt, *J* = 6.9, 4.5, 1.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.64, 129.27, 128.94, 128.16, 116.64, 112.75, 54.55, 44.21, 37.99, 35.56. HRMS (ESI) m/z calc'd for $C_{12}H_{17}NCl$ $[M+H]^+$: 210.1050; found 210.1046.



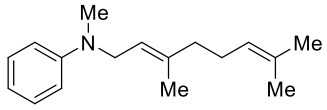
(±)

(±)-(*E*)-*N*-methyl-*N*-(4-(oxiran-2-yl)but-2-en-1-yl)aniline (51): *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and 2-(but-3-en-1-yl)oxirane (29.4 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (200 mL) → 1% EtOAc/Hexanes (200 mL) → 2% EtOAc/Hexanes (300 mL) eluent) afforded the product with a quinone impurity. The material was then concentrated under reduced pressure, dissolved in EtOAc (25 mL), and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a clear oil. Run 1: 43.4 mg, 71% yield (12% olefin RSM); Run 2: 45.7 mg, 75% yield (10% olefin RSM); Run 3: 46.3 mg, 76% yield (12% olefin RSM). **Average: 75% ± 2.2% yield (11% ± 0.9 olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.22 (m, 2H), 6.84 – 6.68 (m, 3H), 5.71 – 5.54 (m, 2H), 3.94 – 3.90 (m, 2H), 3.02 – 2.96 (m, 1H), 2.95 (s, 3H), 2.76 (dd, *J* = 5.0, 3.9 Hz, 1H), 2.50 (dd, *J* = 5.0, 2.7 Hz, 1H), 2.39 – 2.29 (m, 2H). ^{13}C NMR (126 MHz,

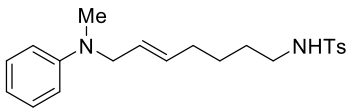
$CDCl_3$) δ 149.51, 129.16, 128.66, 126.60, 116.48, 112.59, 54.50, 51.43, 46.55, 46.53, 37.92, 35.04. HRMS (ESI) m/z calc'd for $C_{13}H_{18}NO$ $[M+H]^+$: 204.1388; found 204.1398.



(*E*)-6-(3-(methyl(phenyl)amino)prop-1-en-1-yl)cyclohex-2-en-1-yl acetate (52): *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and (±)-6-allylcyclohex-2-en-1-yl acetate (54.1 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (50 mL SiO_2, 5% EtOAc/Hexanes eluent) afforded the product as a clear oil. Run 1: 70.2 mg, 82% yield (0% olefin SM); Run 2: 68.5 mg, 80% yield (0% olefin RSM); Run 3: 70.3 mg, 82% yield (0% olefin RSM). **Average: 81% ± 0.9% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (app t, *J* = 7.8 Hz, 2H), 6.84 – 6.61 (m, 3H), 5.96 (app dt, *J* = 10.0, 3.5 Hz, 0.61H), 5.89 – 5.84 (m, 0.38H), 5.81 – 5.74 (m, 0.62H), 5.64 (app dd, *J* = 15.5, 7.2 Hz, 0.61H), 5.61 – 5.49 (m, 1.72H), 5.24 (t, *J* = 4.1 Hz, 0.60H), 5.22 – 5.18 (m, 0.38H), 3.98 – 3.79 (m, 2H), 2.90 (s, 1.74H), 2.89 (s, 1.12H), 2.54 – 2.45 (m, 0.61H), 2.42 – 2.32 (m, 0.39H), 2.23 – 2.13 (m, 0.67H), 2.12 – 2.00 (m, 1.48H), 1.99 (s, 1.10H), 1.94 (s, 1.81H), 1.87 – 1.76 (m, 0.41H), 1.76 – 1.65 (m, 1.23H), 1.65 – 1.49 (m, 0.42H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (170.87), 170.72, 149.62, (133.52), 132.78, 132.52, (131.30), 129.19, (126.62), 126.42, (126.09), 125.04, (116.56), 116.49, (112.76), 112.65, (72.61), 69.25, 54.67, (42.01), 40.34, 37.84, (37.83), (26.58), 24.66, (24.11), 23.68, (21.31), 21.18. HRMS (ESI) m/z calc'd for $C_{18}H_{24}NO_2$ $[M+H]^+$: 286.1807; found 286.1813. *Note: The major and minor diastereomers in the ^{13}C spectrum were assigned by ^{1}H-^{13}C HSQC analysis and the minor diastereomer was weighted to 0.38H and the major diastereomer was weighted to 0.62H.*

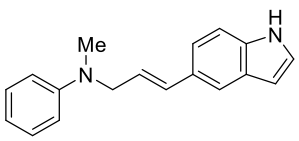


(*E*)-*N*-(3,7-dimethylocta-2,6-dien-1-yl)-*N*-methylaniline (53): *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and 3,7-dimethylocta-1,6-diene (41.5 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 48 h. Purification via flash column chromatography (60 mL Brockmann Grade 3 basic alumina, Hexanes eluent) afforded the product as a clear oil. Run 1: 52.3 mg, 72% yield (25% olefin RSM); Run 2: 51.8 mg, 71% yield (24% olefin RSM); Run 3: 51.9 mg, 71% yield (27% olefin RSM). **Average: 71% ± 0.5% yield (25% ± 1.2% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (app t, *J* = 8.2 Hz, 2H), 6.75 (d, *J* = 8.2 Hz, 2H), 6.71 (t, *J* = 7.2 Hz, 1H), 5.22 (app t, *J* = 6.4 Hz, 1H), 5.16 (app t, *J* = 6.0 Hz, 0.12H), 5.07 (app t, *J* = 6.9 Hz, 0.86H), 3.91 (d, *J* = 6.3 Hz, 2H), 2.89 (s, 3H), 2.18 – 2.06 (m, 2H), 2.06 – 2.01 (m, 2H), 1.71 (br s, 3H), 1.67 (s, 3H), 1.65, (s, 0.35H), 1.59 (s, 2.71H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.04, (149.93), (138.38), 138.18, (132.14), 131.69, (129.23), 129.21, 124.16, (124.07), (121.88), 121.08, 116.56, (116.52), 113.14, (113.06), 50.64, (50.37), 39.74, (38.04), 38.00, (32.31), 26.58, (25.91), 25.84, (23.42), 17.83, 16.38. HRMS (ESI) m/z calc'd for $C_{17}H_{26}N$ $[M+H]^+$: 244.2065 found 244.2061. *Note: The product is formed as an 8:1 mixture of E/Z isomers, quantified by ^{13}C qNMR analysis. The isomers were identified by comparison to an authentic E-isomer prepared by an allylic substitution[6] and an authentic mixture of E/Z isomers prepared by reductive amination.[7] The major isomer (E) was confirmed by ^{1}H-^{1}H 1D-NOESY analysis (see spectra).*

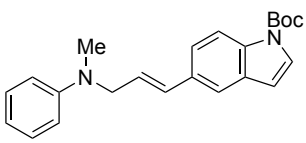


(*E*)-4-methyl-*N*-(7-(methyl(phenyl)amino)hept-5-en-1-yl)benzenesulfonamide (54): *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and *N*-(hept-6-en-1-yl)-4-

methylbenzenesulfonamide (80.2 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (50 mL SiO_2, 20% EtOAc/Hexanes eluent) afforded the product with a hydroquinone impurity. The material was then concentrated under reduced pressure, dissolved in EtOAc (25 mL), and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a pale oil. Run 1: 100.6 mg, 90% yield (7% olefin RSM); Run 2: 95.4 mg, 85% yield (5% olefin RSM); Run 3: 98.9 mg, 88% yield (7% olefin RSM). **Average: 88% ± 2.1% yield (6% ± 0.9% olefin RSM).** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 (app d, *J* = 8.3 Hz, 2H), 7.30 (app d, *J* = 8.0 Hz, 2H), 7.22 (app t, *J* = 8.0 Hz, 2H), 6.73 – 6.66 (m, 3H), 5.49 (dt, *J* = 15.4, 6.6 Hz, 1H), 5.40 (dt, *J* = 15.4, 5.5 Hz, 1H), 4.49 (t, *J* = 6.2 Hz, 1H), 3.83 (t, *J* = 5.5 Hz, 2H), 2.89 (q, *J* = 6.6 Hz, 2H), 2.88 (s, 3H), 2.42 (s, 3H), 1.96 (q, *J* = 6.8 Hz, 2H), 1.41 (app p, *J* = 7.7 Hz, 2H), 1.32 (app p, *J* = 7.6 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.64, 143.46, 137.04, 132.10, 129.80, 129.19, 127.21, 125.94, 116.44, 112.76, 54.56, 43.12, 37.96, 31.65, 28.99, 26.15, 21.64. HRMS (ESI) m/z calc'd for $C_{21}H_{29}N_2O_2S$ $[M+H]^+$: 373.1950; found 373.1953.



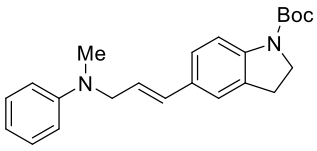
(*E*)-*N*-(3-(1*H*-indol-5-yl)allyl)-*N*-methylaniline (55): *N*-methyl phenylamine (42.9 mg, 0.4 mmol, 1.0 equiv.) and 5-allyl-1*H*-indole (62.9 mg, 0.4 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 0.025 equiv.), MaSOX (3.4 mg, 0.01 mmol, 0.025 equiv.), 2,5-DMBQ (60 mg, 0.44 mmol, 1.1 equiv.), and 0.4 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. The crude was then concentrated under reduced pressure, dissolved in EtOAc (25 mL), and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (60 mL SiO_2, 10% EtOAc/Hexanes eluent) afforded the product as a tan oil. Run 1: 109.8 mg, 98% yield (0% olefin RSM); Run 2: 101.8 mg, 97% yield (0% olefin RSM); Run 3: 100.7 mg, 96% yield (0% olefin RSM). **Average: 97% ± 0.8% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (br s, 1H), 7.60 (s, 1H), 7.32 – 7.29 (m, 2H), 7.26 (app t, *J* = 7.3 Hz, 2H), 6.82 (d, *J* = 8.1 Hz, 2H), 6.73 (t, *J* = 7.3 Hz, 1H), 6.64 (d, *J* = 15.9 Hz, 1H), 6.51 (app t, *J* = 2.7 Hz, 1H), 6.20 (dt, *J* = 15.9, 5.8 Hz, 1H), 4.10 (d, *J* = 5.8 Hz, 2H), 2.99 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.88, 135.53, 132.68, 129.30, 129.24, 128.24, 124.76, 122.86, 120.65, 119.23, 116.57, 112.85, 111.21, 103.06, 55.22, 38.03. HRMS (ESI) m/z calc'd for $C_{11}H_{10}N$ $[M+H]^+$: 156.0813; found 156.0815.



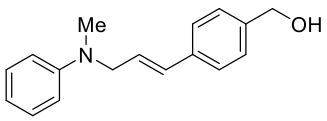
***tert*-butyl (*E*)-5-(3-(methyl(phenyl)amino)prop-1-en-1-yl)-1*H*-indole-1-carboxylate (56):** *N*-methyl phenylamine (42.9 mg, 0.4 mmol, 1.0 equiv.) and *tert*-butyl 5-allyl-1*H*-indole-1-carboxylate (102.9 mg, 0.4 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 0.025 equiv.), MaSOX (3.4 mg, 0.01 mmol, 0.025 equiv.), 2,5-DMBQ (60 mg, 0.44 mmol, 1.1 equiv.), and 0.4 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. The crude was then concentrated under reduced pressure, dissolved in EtOAc (25 mL), and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (60 mL Brockmann Grade 3 basic alumina, Hexanes (200 mL)

→ 1% EtOAc/Hexanes (200 mL) → 2% EtOAc/Hexanes (200 mL) → 3% EtOAc/Hexanes (400 mL) eluent) afforded the product as a beige solid. Run 1: 143.5 mg, 99% yield (0% olefin RSM); Run 2: 140.7 mg, 97% yield (0% olefin RSM); Run 3: 142.7 mg, 98% yield (0% olefin RSM). **Average: 98% ± 0.8% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (br d, *J* = 8.5 Hz, 1H), 7.56 (d, *J* = 3.7 Hz, 1H), 7.51 (d, *J* = 1.7 Hz, 1H), 7.35 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.29 – 7.22 (m, 2H), 6.81 (app d, *J* = 8.3 Hz, 1H), 6.73 (app t, *J* = 7.6 Hz, 1H), 6.61 (app d, *J* = 16.0 Hz, 1H), 6.52 (d, *J* = 3.7 Hz, 1H), 6.25 (dt, *J* = 16.0, 5.6 Hz, 1H), 4.10 (dd, *J* = 5.6, 1.7 Hz, 2H), 3.00 (s, 3H), 1.67 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.77, 134.76, 131.85, 131.78, 130.99, 129.32, 126.50, 124.52, 122.81, 118.98, 116.65, 115.25, 112.79, 107.49, 83.85, 55.12, 38.13, 28.34. HRMS (ESI) m/z calc'd for $C_{23}H_{27}N_2O_2$ $[M+H]^+$: 363.2073 found 363.2048.

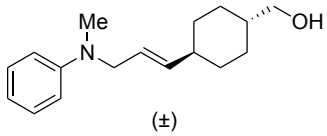
This reaction was successfully scaled up to yield over 1 gram of cross-coupled product. N-methyl phenylamine (375 mg, 3.5 mmol, 1.0 equiv.) and *tert*-butyl 5-allyl-1*H*-indole-1-carboxylate (900.7 mg, 3.5 mmol, 1.0 equiv.) were reacted according to the general procedure in a round-bottom flask equipped with a stir bar using $Pd(OAc)_2$ (19.6 mg, 0.088 mmol, 0.025 equiv.), MaSOX (30 mg, 0.088 mmol, 0.025 equiv.), 2,5-DMBQ (524 mg, 3.85 mmol, 1.1 equiv.), and 3.5 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. The crude was then concentrated under reduced pressure, dissolved in EtOAc (50 mL), and washed with NaOH (30 mL, 1 M), $NaHSO_3$ (30 mL, sat.), NaOH (30 mL, 1 M), $NaHSO_3$ (30 mL, sat.), NaOH (30 mL, 1 M), $NaHSO_3$ (30 mL, sat.), NaOH (30 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (250 mL Brockmann Grade 3 basic alumina, Hexanes (400 mL) → 1% EtOAc/Hexanes (400 mL) → 2% EtOAc/Hexanes (400 mL) → 3% EtOAc/Hexanes (600 mL) eluent) afforded the product as a beige solid. Run 1: 1.17 g, 92% yield (0% olefin RSM); Run 2: 1.14 g, 90% yield (0% olefin RSM). **Average: 91% ± 1.0% yield (0% olefin RSM).**



***tert*-butyl (*E*)-5-(3-(methyl(phenyl)amino)prop-1-en-1-yl)indoline-1-carboxylate (57):** *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and *tert*-butyl 5-allylindoline-1-carboxylate (77.8 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 3 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (200 mL) → 1% EtOAc/Hexanes (800 mL) → 2% EtOAc/Hexanes (400 mL) eluent) afforded the product with a 2,5-DMBQ impurity. The mixture was then dissolved in EtOAc (25 mL) and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a light orange oil. Run 1: 106.1 mg, 97% yield (0% olefin RSM); Run 2: 103.9 mg, 95% yield (0% olefin RSM); Run 3: 105.0 mg, 96% yield (0% olefin RSM). **Average: 96% ± 0.8% yield (0% olefin RSM).** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.77 and 7.39 (two br s, 1H), 7.25 (app t, *J* = 7.1 Hz, 2H), 7.18 (s, 1H), 7.14 (d, *J* = 8.4 Hz, 1H), 6.80 (d, *J* = 8.1 Hz, 2H), 6.73 (t, *J* = 7.1 Hz, 1H), 6.46 (d, *J* = 15.9 Hz, 1H), 6.13 (dt, *J* = 15.9, 5.7 Hz, 2H), 4.07 (d, *J* = 5.6 Hz, 2H), 3.97 (br s, 2H), 3.05 (t, *J* = 8.7 Hz, 2H), 2.98 (s, 3H), 1.57 (br s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 152.58, 149.69, 142.54 and 141.58, 132.34, 131.30, 131.23, 129.28, 126.27, 123.58, 122.32, 116.60, 114.59, 112.74, 80.58, 55.03, 47.87, 38.07, 28.58, 27.36. HRMS (ESI) m/z calc'd for $C_{23}H_{27}N_2O_2$ $[M+H]^+$: 363.2073; found 363.2068. *Note: Boc-induced rotamers gave similar resonance splitting patterns in the ^{1}H and ^{13}C spectra of the starting allyl indoline olefin. ^{1}H-^{13}C HSQC analysis confirmed the identity of the product (see spectra).*

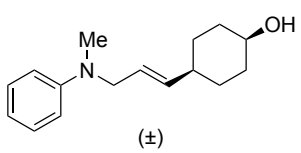


(*E*)-(4-(3-(methyl(phenyl)amino)prop-1-en-1-yl)phenyl)methanol (58): *N*-methyl phenylamine (42.9 mg, 0.4 mmol, 1.0 equiv.) and (4-allylphenyl)methanol (59.3 mg, 0.4 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 0.025 equiv.), MaSOX (3.4 mg, 0.01 mmol, 0.025 equiv.), 2,5-DMBQ (60 mg, 0.44 mmol, 1.1 equiv.), and 0.4 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. The crude mixture was then concentrated under reduced pressure, dissolved in EtOAc (25 mL), and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (50 mL SiO_2, 20% EtOAc/Hexanes (500 mL) eluent) afforded the product as a yellow solid. Run 1: 85.1 mg, 84% yield (0% olefin RSM); Run 2: 86.1 mg, 85% yield (0% olefin RSM); Run 3: 90.2 mg, 89% yield (0% olefin RSM). **Average: 86% ± 2.2% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.3 Hz, 2H), 7.28 – 7.23 (m, 2H), 6.79 (d, *J* = 7.8 Hz, 1H), 6.73 (t, *J* = 7.3 Hz, 1H), 6.52 (dt, *J* = 15.9, 1.7 Hz, 1H), 6.26 (dt, *J* = 15.9, 5.5 Hz, 1H), 4.66 (s, 2H), 4.09 (dd, *J* = 5.5, 1.7 Hz, 2H), 2.99 (s, 3H), 1.67 (br s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.68, 140.15, 136.52, 130.97, 129.33, 127.36, 126.64, 126.02, 116.74, 112.76, 65.25, 55.03, 38.17. HRMS (EI) m/z calc'd for $C_{17}H_{19}NO$ $[M]^+$: 253.14667; found 253.14653.



(±)

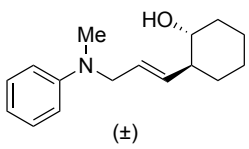
(±)-*trans*-4-((*E*)-3-(methyl(phenyl)amino)prop-1-en-1-yl)cyclohexyl)methanol (59): *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and (±)-*trans*-(4-allylcyclohexyl)methanol (46.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (50 mL SiO_2, 20% EtOAc/Hexanes eluent) afforded the product with a 2,5-DMBQ impurity. The mixture was then dissolved in EtOAc (25 mL) and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a tan oil. Run 1: 73.9 mg, 95% yield (0% olefin SM); Run 2: 73.0 mg, 94% yield (0% olefin RSM); Run 3: 74.2 mg, 95% yield (0% olefin RSM). **Average: 95% ± 0.5% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (app t, *J* = 7.4 Hz, 2H), 6.75 (app d, *J* = 8.1 Hz, 2H), 6.71 (app td, *J* = 7.2, 1.2 Hz, 1H), 5.57 (dd, *J* = 15.5, 6.6 Hz, 1H), 5.44 (dt, *J* = 15.5, 5.6 Hz, 1H), 3.86 (d, *J* = 5.7 Hz, 2H), 3.45 (d, *J* = 6.4 Hz, 2H), 2.90 (s, 1H), 1.97 – 1.88 (m, 1H), 1.80 (app t, *J* = 11.1 Hz, 4H), 1.59 – 1.36 (m, 2H), 1.11 (app qd, *J* = 13.2, 3.7 Hz, 2H), 0.98 (app qd, *J* = 13.1, 3.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.81, 138.63, 129.16, 122.96, 116.42, 112.79, 68.71, 54.85, 40.69, 40.18, 37.74, 32.35, 29.20. HRMS (ESI) m/z calc'd for $C_{17}H_{26}NO$ $[M+H]^+$: 260.2014; found 260.2011.



(±)

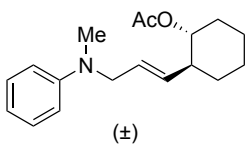
(±)-*cis*-4-((*E*)-3-(methyl(phenyl)amino)prop-1-en-1-yl)cyclohexan-1-ol (60): *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and 4-allylcyclohexan-1-ol (42.1 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. The crude was then concentrated under reduced pressure, dissolved in EtOAc (25 mL), and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column

chromatography (40 mL SiO_2, 20% EtOAc/Hexanes eluent) afforded the product as a yellow oil. Run 1: 61.1 mg, 83% yield (0% olefin RSM); Run 2: 59.6 mg, 81% yield (0% olefin RSM); Run 3: 64.0 mg, 87% yield (0% olefin RSM). **Average: 84% ± 2.5% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (t, *J* = 7.9 Hz, 2H), 6.74 (d, *J* = 8.2 Hz, 2H), 6.69 (t, *J* = 7.3 Hz, 1H), 5.60 (dd, *J* = 15.5, 6.4 Hz, 1H), 5.45 (dt, *J* = 15.5, 5.6 Hz, 1H), 3.97 – 3.90 (m, 1H), 3.86 (d, *J* = 5.6 Hz, 2H), 2.89 (s, 3H), 2.10 – 2.02 (m, 1H), 1.73 – 1.64 (m, 2H), 1.62 – 1.46 (m, 6H), 1.27 – 1.20 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.83, 137.80, 129.21, 123.62, 116.47, 112.84, 67.04, 54.90, 38.73, 37.82, 32.17, 27.09. HRMS (ESI) m/z calc'd for $C_{16}H_{24}NO$ $[M+H]^+$: 246.1858; found 246.1857.



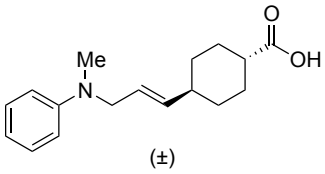
(±)-*trans*-2-((*E*)-3-(methyl(phenyl)amino)prop-1-en-1-yl)cyclohexan-1-ol (61): <u>*Procedure A*</u>*: N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and 2-allylcyclohexan-1-ol (42.1 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. The crude was then concentrated under reduced pressure, dissolved in EtOAc (25 mL), and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (40 mL SiO_2, 10% EtOAc/Hexanes (200 mL) → 15% EtOAc/Hexanes (200 mL) → 20% EtOAc/Hexanes (300 mL) eluent) afforded the product as a red oil. Run 1: 29.4 mg, 40% yield (9% olefin RSM); Run 2: 30.2 mg, 41% yield (9% olefin RSM); Run 3: 28.7 mg, 39% yield (10% olefin RSM). **Average: 40% ± 0.8% yield (9% ± 0.5% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.18 (m, 2H), 6.89 – 6.58 (m, 3H), 5.60 (dt, *J* = 15.5, 5.5 Hz, 1H), 5.45 (dd, *J* = 15.5, 8.6 Hz, 1H), 3.95 (dd, *J* = 16.4, 5.6 Hz, 1H), 3.88 (dd, *J* = 16.4, 5.6 Hz, 1H), 3.18 (td, *J* = 10.0, 4.2 Hz, 1H), 2.93 (s, 3H), 2.04 – 1.97 (m, 1H), 1.93 – 1.83 (m, 1H), 1.81 – 1.61 (m, 4H), 1.34 – 1.10 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.47, 134.90, 129.23, 127.64, 116.75, 112.95, 73.16, 54.74, 49.99, 38.15, 33.89, 31.51, 25.27, 24.89. HRMS (ESI) m/z calc'd for $C_{16}H_{24}NO$ $[M+H]^+$: 246.1858; found 246.1864.

<u>*Procedure B*</u>*: Running this reaction in the absence of N-methyl phenylamine showed significant olefin decomposition.* 2-allylcyclohexan-1-ol (42.1 mg, 0.3 mmol, 1.0 equiv.) was reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. The crude mixture was analyzed using quantitative ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) with benzotrifluoride as an internal standard to determine the recovered olefin starting material. Run 1: 52% olefin RSM; Run 2: 47% olefin RSM. **Average**: **49% ± 2.0% olefin RSM.** *These results suggest that the proximal Lewis-basic hydroxyl group may be engaging with the palladium-metal, leading to undesired reactivity and/or decomposition pathways.*



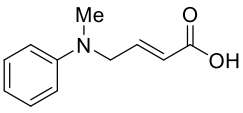
(±)-*trans*-2-((*E*)-3-(methyl phenyl)amino)prop-1-en-1-yl)cyclohexyl acetate (62): *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and 2-allylcyclohexyl acetate (54.7 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. The crude was then concentrated under reduced pressure, dissolved in EtOAc (25 mL), and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (40 mL SiO_2, 5% EtOAc/Hexanes eluent) afforded the product as a clear oil. Run 1: 76.7 mg, 89% yield (0% olefin RSM);

Run 2: 74.1 mg, 86% yield (0% olefin RSM); Run 3: 72.4 mg, 84% yield (0% olefin RSM). **Average: 86% ± 2.1% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (app dt, *J* = 7.3, 6.6 Hz, 2H), 6.73 – 6.65 (m, 3H), 5.50 (dt, *J* = 15.4, 5.1 Hz, 1H), 5.44 (dd, *J* = 15.4, 7.3 Hz, 1H), 4.57 (td, *J* = 10.2, 4.3 Hz, 1H), 3.87 (dd, *J* = 16.0, 4.7 Hz, 1H), 3.80 (dd, *J* = 16.2, 5.5 Hz, 1H), 2.87 (s, 3H), 2.14 – 2.04 (m, 1H), 1.97 – 1.92 (m, 1H), 1.91 (s, 3H), 1.80 – 1.71 (m, 2H), 1.70 – 1.63 (m, 1H), 1.39 – 1.11 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.69, 149.66, 134.51, 129.23, 126.28, 116.50, 112.70, 75.63, 54.64, 46.40, 37.80, 31.75, 31.72, 25.00, 24.63, 21.36. HRMS (ESI) m/z calc'd for $C_{18}H_{26}NO_2$ $[M+H]^+$: 288.1964; found 288.1975.

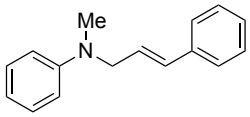


(±)

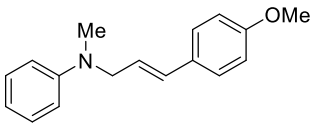
(±)-*trans*-4-((*E*)-3-(methyl(phenyl)amino)prop-1-en-1-yl)cyclohexane-1-carboxylic acid (63): *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and (±)-*trans*-4-allylcyclohexane-1-carboxylic acid (50.5 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.2 M solution of dibutyl phosphate in dioxane (0.2 equiv.) as a solvent, and stirred for 24 h. Purification via flash column chromatography (60 mL SiO_2, Hexanes (200 mL) → 5% Acetone/Hexanes (200 mL) → 10% Acetone/Hexanes (200 mL) → 20% Acetone/Hexanes (200 mL) → 30% Acetone/Hexanes (250 mL) eluent) afforded the product as a white solid. Run 1: 50.8 mg, 62% yield (6% olefin SM); Run 2: 48.4 mg, 59% yield (6% olefin RSM); Run 3: 50.9 mg, 62% yield (4% olefin RSM). **Average: 61% ± 1.2% yield (5% ± 0.9% olefin RSM).** ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.90 (s, 1H), 7.22 (t, *J* = 7.7 Hz, 2H), 6.73 (d, *J* = 8.2 Hz, 2H), 6.70 (t, *J* = 7.3 Hz, 1H), 5.53 (dd, *J* = 15.6, 6.8 Hz, 1H), 5.43 (dt, *J* = 15.6, 5.6 Hz, 1H), 3.85 (d, *J* = 5.5 Hz, 2H), 2.88 (s, 3H), 2.24 (tt, *J* = 12.2, 3.6 Hz, 1H), 2.05 – 2.00 (m, 2H), 1.99 – 1.91 (m, 1H), 1.84 – 1.79 (m, 2H), 1.45 (qd, *J* = 13.1, 3.5 Hz, 2H), 1.10 (qd, *J* = 13.1, 3.5 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.87, 149.76, 137.85, 129.21, 123.49, 116.54, 112.83, 54.84, 42.75, 39.73, 37.84, 31.90, 28.55. HRMS (ESI) m/z calc'd for $C_{17}H_{24}NO_2$ $[M+H]^+$: 274.1807; found 274.1812. *Note: Fully homogenizing the carboxylic acid starting material into the reaction mixture using the solvent solution was important in obtaining consistent results.*



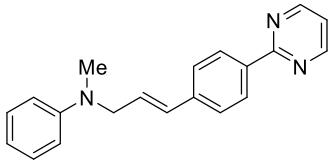
(*E*)-4-(methyl(phenyl)amino)but-2-enoic acid (64): *N*-methyl phenylamine (64.3 mg, 0.6 mmol, 1.0 equiv.) and but-3-enoic acid (51.6 mg, 0.6 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.025 equiv.), MaSOX (5.3 mg, 0.015 mmol, 0.025 equiv.), 2,5-DMBQ (90 mg, 0.66 mmol, 1.1 equiv.), and 0.6 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 4 h. Purification via flash column chromatography (25 mL SiO_2, 10% Acetone/Hexanes (100 mL) → 15% Acetone/Hexanes (100 mL) → 20% Acetone/Hexanes (300 mL) eluent) afforded the product with a hydroquinone impurity. The mixture was dissolved in EtOAc (30 mL) and extracted with 1.5 M aqueous K_2CO_3 (3 x 25 mL). The combined aqueous layers were acidified with 1 M HCl (60 mL) until it reached a pH ~ 5 and then extracted with DCM (3 x 50 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the pure product as a beige solid. Run 1: 95.9 mg, 84% yield (0% olefin RSM); Run 2: 98.7 mg, 86 % yield (0% olefin RSM); Run 3: 96.4 mg, 84 % yield (0% olefin RSM). **Average: 85% ± 0.9% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (app t, *J* = 7.9 Hz, 2H), 7.08 (dt, *J* = 15.7, 4.4 Hz, 1H), 6.75 (t, *J* = 7.3 Hz, 1H), 6.68 (d, *J* = 8.2 Hz, 2H), 5.94 (dt, *J* = 15.6, 2.0 Hz, 1H), 4.10 (dd, *J* = 4.4, 2.0 Hz, 2H), 2.98 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.37, 148.91, 147.60, 129.41, 121.31, 117.29, 112.48, 54.09, 38.61. HRMS (ESI) m/z calc'd for $C_{11}H_{14}NO_2$ $[M+H]^+$: 192.1025; found 192.1026.



***N*-cinnamyl-*N*-methylaniline (65):** *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and allylbenzene (35.5 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 3 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes eluent) afforded the product as a clear oil. Run 1: 66.3 mg, 99% yield (0% olefin RSM); Run 2: 65.0 mg, 97% yield (0% olefin RSM); Run 3: 64.3 mg, 96% yield (0% olefin RSM). **Average: 97% ± 1.2% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (app dt, *J* = 8.1, 1.8 Hz, 2H), 7.31 (td, *J* = 7.7, 1.9 Hz, 2H), 7.28 – 7.20 (m, 2H), 6.82 – 6.78 (m, 2H)), 6.74 (tdt, *J* = 7.4, 2.4, 1.1 Hz, 1H), 6.54 (dq, *J* = 15.9, 1.8 Hz, 1H), 6.26 (dtd, *J* = 15.9, 5.5, 1.8 Hz, 1H), 4.10 (dt, *J* = 5.5, 1.7 Hz, 2H), 2.99 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.71, 137.04, 131.39, 129.32, 128.67, 127.54, 126.45, 125.89, 116.72, 112.76, 55.04, 38.15. HRMS (ESI) m/z calc'd for $C_{16}H_{18}N$ $[M+H]^+$: 224.1439; found 224.1429.

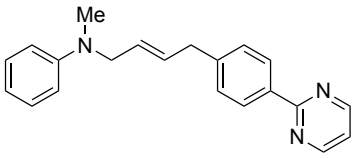


(*E*)-*N*-(3-(4-methoxyphenyl)allyl)-*N*-methylaniline (66): *N*-methyl phenylamine (42.9 mg, 0.4 mmol, 1.0 equiv.) and 1-allyl-4-methoxybenzene (59.3 mg, 0.4 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 0.025 equiv.), MaSOX (3.4 mg, 0.01 mmol, 0.025 equiv.), 2,5-DMBQ (60 mg, 0.44 mmol, 1.1 equiv.), and 0.4 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (100 mL) → 1% EtOAc/Hexanes (400 mL) eluent) afforded the product with a quinone impurity. The material was then concentrated under reduced pressure, dissolved in EtOAc (25 mL), and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a tan oil. Run 1: 91.1 mg, 90% yield (0% olefin RSM); Run 2: 91.3 mg, 90% yield (0% olefin RSM); Run 3: 89.1 mg, 88% yield (0% olefin RSM). **Average: 89% ± 0.9% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (app d, *J* = 8.7 Hz, 2H), 7.27 – 7.23 (m, 2H), 6.84 (app d, *J* = 8.8 Hz, 2H), 6.80 (app d, *J* = 7.8 Hz, 2H), 6.73 (tt, *J* = 7.3, 1.1 Hz, 2H), 6.47 (app d, *J* = 15.8, 1H), 6.11 (dt, *J* = 15.8, 5.5 Hz, 1H), 4.07 (dd, *J* = 5.6, 1.7 Hz, 2H), 3.80 (s, 3H), 2.98 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.21, 149.76, 130.86, 129.86, 129.30, 127.59, 123.58, 116.63, 114.08, 112.77, 55.43, 55.07, 38.08. HRMS (ESI) m/z calc'd for $C_{17}H_{20}NO$ $[M+H]^+$: 254.1545; found 254.1538.

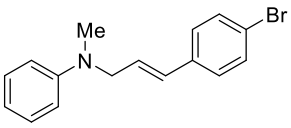


(*E*)-*N*-methyl-N-(3-(4-(pyrimidin-2-yl)phenyl)allyl)aniline (67): *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and 2-(4-allylphenyl)pyrimidine (58.9 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 3 h. Purification via flash column chromatography (50 mL SiO_2, 15% EtOAc/Hexanes eluent) afforded the product with a hydroxyquinone impurity. The material was dissolved in EtOAc (25 mL) and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a white solid. Run 1: 76.0 mg, 84% yield (5% olefin RSM); Run 2: 78.0 mg, 86% yield (11% olefin RSM); Run 3: 75.1 mg, 82% yield (13% olefin RSM). **Average: 84% ± 1.2% yield (10% ± 3.4% olefin RSM).** ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.79 (d, *J* = 4.8 Hz, 2H), 8.38 (app d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.32 – 7.21 (m, 2H), 7.17 (t, *J* = 4.8 Hz, 1H), 6.80 (app d, *J* = 7.8 Hz, 2H), 6.73 (app t, *J* = 7.2 Hz, 1H), 6.58 (app d, *J* = 15.9 Hz, 1H), 6.37 (dt, *J* = 15.9, 5.4 Hz, 1H), 4.12 (dd, *J* = 5.4, 1.7 Hz, 2H), 3.01

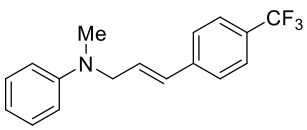
(s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.59, 157.36, 149.63, 139.43, 136.65, 130.86, 129.37, 128.50, 127.46, 126.72, 119.08, 116.76, 112.70, 55.07, 38.26. HRMS (ESI) m/z calc'd for $C_{20}H_{20}N_3$ $[M+H]^+$: 302.1657; found 302.1651.



The unactivated one-carbon homologue of this pyrimidine electrophile afforded diminished reactivity. **(*E*)-*N*-methyl-*N*-(4-(4-(pyrimidin-2-yl)phenyl)but-2-en-1-yl)aniline:** *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and 2-(4-(but-3-en-1-yl)phenyl)pyrimidine (63.1 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 24 h. Purification via flash column chromatography (50 mL SiO_2, 15% EtOAc/Hexanes eluent) afforded the product with a hydroxyquinone impurity. The material was dissolved in EtOAc (25 mL) and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a beige solid. 28.4 mg, 30% yield (50% olefin RSM). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.79 (d, J = 4.8 Hz, 2H), 8.35 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.2 Hz, 2H), 7.25 – 7.21 (m, 2H), 7.17 (t, J = 4.8 Hz, 1H), 5.78 (dt, J = 15.3, 6.8 Hz, 1H), 5.60 (dt, J = 15.3, 5.5 Hz, 1H), 3.92 (d, J = 5.4 Hz, 2H), 3.44 (d, J = 6.8 Hz, 2H), 2.92 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.88, 157.35, 149.68, 143.54, 135.67, 130.96, 129.26, 128.96, 128.40, 127.49, 119.02, 116.60, 112.81, 54.61, 38.71, 38.05. HRMS (ESI) m/z calc'd for $C_{21}H_{22}N_3$ $[M+H]^+$: 316.1814; found 316.1817.



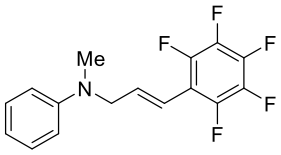
(*E*)-*N*-(3-(4-bromophenyl)allyl)-*N*-methylaniline (68): *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and 1-allyl-4-bromobenzene (59.1 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 48 h. Purification via flash column chromatography (60 mL Brockmann Grade 3 basic alumina, Hexanes eluent) afforded the product as a tan solid. Run 1: 80.6 mg, 89% yield (0% olefin RSM); Run 2: 81.0 mg, 89% yield (0% olefin RSM); Run 3: 83.7 mg, 92% yield (0% olefin RSM). **Average: 90% ± 1.4% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (app d, J = 8.5 Hz, 2H), 7.30 – 7.25 (m, 2H), 7.23 (app d, J = 8.4 Hz, 2H), 6.80 (app d, J = 7.9 Hz, 2H), 6.76 (t, J = 7.3 Hz, 1H), 6.47 (dt, J = 15.9, 1.8 Hz, 1H), 6.26 (dt, J = 15.9, 5.3 Hz, 1H), 4.09 (dd, J = 5.3, 1.7 Hz, 2H), 3.00 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.56, 135.95, 131.72, 130.09, 129.34, 127.98, 126.81, 121.22, 116.80, 112.68, 54.94, 38.22. HRMS (EI) m/z calc'd for $C_{16}H_{15}BrN$ $[M-H]^+$: 300.0388; found 300.0376.



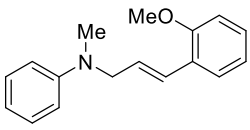
(*E*)-*N*-methyl-*N*-(3-(4-(trifluoromethyl)phenyl)allyl)aniline (69): <u>*Procedure A*</u>: *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and 1-allyl-4-(trifluoromethyl)benzene (55.9 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 3 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes eluent) afforded the product as a tan solid. Run 1: 85.6 mg, 98% yield (0% olefin RSM); Run 2: 82.2 mg, 94% yield (0% olefin RSM); Run 3: 81.4 mg, 93% yield (0% olefin RSM). **Average: 95% ± 2.2% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, J = 8.1 Hz, 2H), 7.44 (d, J = 8.1 Hz, 2H), 7.29 – 7.23 (m, 2H), 6.84 – 6.77 (m, 2H), 6.75 (td, J = 7.3, 1.3 Hz, 1H), 6.55 (dt, J = 15.9, 1.6 Hz, 1H), 6.36 (dt, J = 15.9, 5.2 Hz, 1H), 4.12 (d, J = 5.1 Hz, 2H),

3.00 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.41, 140.38, 129.79, 129.26, 129.22 (q, J = 32.5 Hz), 128.76, 126.48, 125.50 (q, J = 3.8 Hz), 124.67 (q, J = 272.1Hz), 116.80, 112.57, 54.84, 38.20. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.57. HRMS (ESI) m/z calc'd for $C_{17}H_{17}NF_3$ $[M+H]^+$: 292.1313; found 292.1315.

Procedure B: Alternatively, *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and 1-allyl-4-(trifluoromethyl)benzene (55.9 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the slow addition procedure, in which 0.3 mL of a 1.0 M solution of *N*-methyl phenylamine was added at a rate of 0.1 mL/hour to the reaction mixture containing 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) and stirred for 4 hours. Procedure A's purification conditions were used to afford the product as a tan solid. Run 1: 83.0 mg, 95% yield (0% olefin RSM); Run 2: 81.3 mg, 93% yield (0% olefin RSM); Run 3: 83.9 mg, 96% yield (0% olefin RSM). **Average: 95% ± 1.2% yield (0% olefin RSM).**

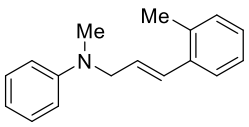


(*E*)-*N*-methyl-*N*-(3-(perfluorophenyl)allyl)aniline (70): *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and 1-allyl-2,3,4,5,6-pentafluorobenzene (62.4 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes eluent) afforded the product as a tan oil. Run 1: 91.3 mg, 97% yield (0% olefin RSM); Run 2: 92.8 mg, 99% yield (0% olefin RSM); Run 3: 91.4 mg, 97% yield (0% olefin RSM). **Average: 98% ± 0.9% yield (0% olefin RSM).** The spectra are in accordance with those reported in the literature.[8] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.22 (m, 2H), 6.80 – 6.72 (m, 3H), 6.59 (app dtd, J = 16.4, 5.0, 1.8 Hz, 1H), 6.44 (dq, J = 16.4, 1.8 Hz, 1H), 4.13 (d, J = 4.9 Hz, 2H), 3.03-2.99 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.41, 144.74 (dm, J = 249.9 Hz), 139.95 (dm, J = 254.3 Hz), 137.39 (dm, J = 246.0 Hz), 135.94 (td, J = 7.4, 2.5 Hz), 129.37, 117.16, 115.19, 112.75, 111.97 (td, J = 14.1, 4.2 Hz), 55.73, 38.35. ^{19}F NMR (471 MHz, $CDCl_3$) δ -142.96 (dd, J = 21.8, 7.9 Hz), -156.68 (t, J = 20.8 Hz), -163.03 (app td, J = 21.4, 8.0 Hz). HRMS (ESI) m/z calc'd for $C_{16}H_{13}NF_5$ $[M+H]^+$: 314.0968; found 314.0974.



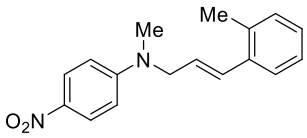
(*E*)-*N*-(3-(2-methoxyphenyl)allyl)-*N*-methylaniline (71): *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and 1-allyl-2-methoxybenzene (44.5 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 4 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (100 mL) → 1% EtOAc/Hexanes (200 mL) → 2% EtOAc/Hexanes (300 mL) eluent) afforded the product with a quinone impurity. The material was then concentrated under reduced pressure, dissolved in EtOAc (25 mL), and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a tan oil. Run 1: 66.2 mg, 87% yield (0% olefin RSM); Run 2: 67.1 mg, 88% yield (0% olefin RSM); Run 3: 66.3 mg, 87% yield (0% olefin RSM). **Average: 87% ± 0.5% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (app d, J = 7.7 Hz, 1H), 7.25 (app t, J = 8.0 Hz, 2H), 7.21 (app t, J = 7.8 Hz, 1H), 6.90 (t, J = 7.3 Hz, 1H), 6.91 – 6.84 (m, 2H), 6.81 (d, J = 8.2 Hz, 2H), 6.72 (t, J = 7.2 Hz, 1H), 6.27 (dt, J = 16.0, 5.8 Hz, 1H), 4.10 (d, J = 6.0 Hz, 2H), 3.84 (s, 3H), 2.98 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.67, 149.87, 129.28, 128.58, 127.00, 126.57, 126.07, 120.76, 116.64, 112.91, 111.03, 55.61, 55.49, 38.01. HRMS (ESI) m/z calc'd for $C_{17}H_{20}NO$ $[M+H]^+$: 254.1545; found 254.1541. *Note:*

The ^{13}C resonance at 126.57 ppm accounts for both a vinylic and aryl (C–H) carbon, confirmed via ^{1}H-^{13}C HSQC analysis (see spectra).

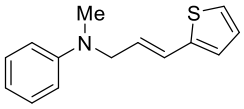


(*E*)-*N*-methyl-*N*-(3-(*o*-tolyl)allyl)aniline (72): <u>*Procedure A*</u>: *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and 1-allyl-2-methylbenzene (39.4 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the slow addition procedure, in which 0.3 mL of a 1.0 M solution of *N*-methyl phenylamine was added at a rate of 0.03 mL/hour to the reaction mixture containing 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.), and stirred for 12 hours. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes eluent) afforded the product as a clear oil. Run 1: 62.3 mg, 89% yield (0% olefin RSM); Run 2: 65.2 mg, 92% yield (0% olefin RSM); Run 3: 62.6 mg, 88% yield (0% olefin RSM). **Average: 90% ± 1.7% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 – 7.38 (m, 1H), 7.25 – 7.21 (m, 2H), 7.17 – 7.09 (m, 3H), 6.81 (d, *J* = 9.0 Hz, 1H), 6.75 – 6.69 (m, 2H), 6.10 (dt, *J* = 15.7, 5.5 Hz, 1H), 4.11 (app d, *J* = 5.5 Hz, 1H), 3.00 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.59, 136.17, 135.24, 130.22, 129.47, 129.16, 127.33, 126.97, 126.06, 125.72, 116.63, 112.77, 55.12, 38.03, 19.80. HRMS (ESI) m/z calc'd for $C_{17}H_{18}N$ $[M+H]^+$: 236.1439; found 236.1430.

<u>*Procedure B:*</u> *The standard conditions using higher catalyst loadings and longer reaction times gave diminished yields.* *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and 1-allyl-2-methylbenzene (39.4 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 24 h. Analysis by crude ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) using benzotrifluoride as an internal standard was used to determine the amount of product and remaining olefin starting material. Run 1: 8% yield (80% olefin RSM); Run 2: 5% yield (82% olefin RSM). **Average: 7% ± 1.5% yield (81% ± 1.0% olefin RSM).**

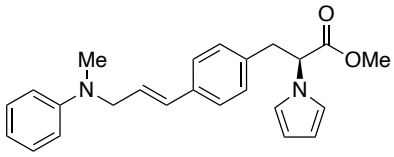


(*E*)-*N*-methyl-4-nitro-*N*-(3-(*o*-tolyl)allyl)aniline (73): *N*-methyl-4-nitroaniline (45.6 mg, 0.3 mmol, 1.0 equiv.) and 1-allyl-2-methylbenzene (39.4 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.), and stirred for 24 hours. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, 2% EtOAc/Hexanes eluent) afforded the product with a quinone impurity. The material was then dissolved in EtOAc (25 mL) and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a crystalline yellow solid. Run 1: 78.8 mg, 93% yield (0% olefin RSM); Run 2: 77.1 mg, 91% yield (0% olefin RSM); Run 3: 77.8 mg, 92% yield (0% olefin RSM). **Average: 92% ± 0.8% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.06 (app d, *J* = 8.4 Hz, 2H), 7.76 – 7.34 (m, 1H), 7.13 (app d, *J* = 1.9 Hz, 3H), 6.86 (app d, *J* = 8.1 Hz, 2H), 6.71 (d, *J* = 15.9, 1H), 6.13 (dt, *J* = 15.9, 5.5 Hz, 1H), 4.30 (d, *J* = 5.5 Hz, 2H), 3.15 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 153.74, 135.77, 135.28, 134.81, 130.18, 129.07, 127.47, 126.10, 125.83, 125.38, 125.14, 111.05, 53.73, 38.28, 19.27. HRMS (ESI) m/z calc'd for $C_{17}H_{19}N_2O_2$ $[M+H]^+$: 283.1447; found 283.1442.

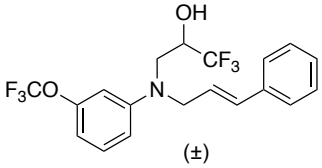


(*E*)-*N*-methyl-*N*-(3-(thiophen-2-yl)allyl)aniline (74): *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.) and 2-allylthiophene (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 24 h. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes eluent) afforded the product as an amber oil. Run 1: 61.8 mg, 90% yield (0% olefin RSM); Run 2: 61.3 mg, 89% yield (0% olefin RSM); Run 3: 63.2 mg, 92% yield (0% olefin RSM). **Average: 90% ± 1.3% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (app t, *J* =7.9 Hz, 2H), 7.13 (d, *J* = 5.1 Hz, 1H), 6.94 (app t, *J* = 44 Hz, 1H), 6.91 (app d, *J* = 3.5 Hz, 1H), 6.78 (app d, *J* = 7.6 Hz, 2H), 6.73 (t, *J* = 7.3 Hz, 1H), 6.64 (d, *J* = 15.7 Hz, 1H), 6.09 (dt, *J* = 15.7, 5.3 Hz, 1H), 4.05 (dd, *J* = 5.4, 1.7 Hz, 2H), 2.98 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.61, 142.25, 129.34, 127.44, 125.70, 125.46, 124.39, 124.09, 116.74, 112.65, 54.76, 38.19. HRMS (ESI) m/z calc'd for $C_{14}H_{15}NS$ $[M+H]^+$: 230.1003; found 230.0998.

3.5. Synthesis and characterization of the complex example products.

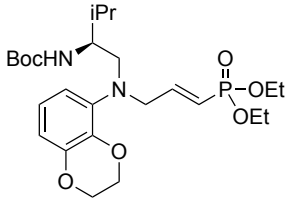


(-)-methyl (*S*,*E*)-3-(4-(3-(methyl(phenyl)amino)prop-1-en-1-yl)phenyl)-2-(1*H*-pyrrol-1-yl)propanoate (75): *N*-methyl phenylamine (42.9 mg, 0.4 mmol, 1.0 equiv.) and methyl (*S*)-3-(4-allylphenyl)-2-(1*H*-pyrrol-1-yl)propanoate (107.7 mg, 0.4 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 0.025 equiv.), MaSOX (3.4 mg, 0.01 mmol, 0.025 equiv.), 2,5-DMBQ (60 mg, 0.44 mmol, 1.1 equiv.), and 0.4 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (50 mL SiO_2, 10% EtOAc/Hexanes eluent) afforded the product with a quinone impurity. The material was then dissolved in EtOAc (25 mL) and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a pale oil that solidified at 0 °C to a white solid. Run 1: 142.3 mg, 95% yield (0% olefin RSM); Run 2: 138.2 mg, 92% yield (0% olefin RSM); Run 3: 137.8 mg, 92% yield (0% olefin RSM). **Average: 93% ± 0.9% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 2H), 7.26 – 7.24 (m, 2H), 6.98 (d, *J* = 8.3 Hz, 2H), 6.81 (d, *J* = 8.3 Hz, 2H), 6.78 – 6.75 (m, 1H), 6.75 – 6.73 (m, 2H), 6.49 (d, *J* = 15.9 Hz, 1H), 6.23 (dt, *J* = 15.9, 5.5 Hz, 1H), 6.20 – 6.15 (m, 2H), 4.76 (app ddd, *J* = 8.9, 6.4, 1.3 Hz, 1H), 4.09 (d, *J*= 5.5 Hz, 2H), 3.73 (s, 3H), 3.42 (dd, *J* = 13.9, 6.4 Hz, 1H), 3.27 (dd, *J* = 13.9, 8.9 Hz, 1H), 3.00 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.63, 149.59, 135.79, 135.57, 130.83, 129.28, 129.12, 126.58, 125.77, 120.18, 116.67, 112.66, 108.83, 63.57, 54.92, 52.66, 39.27, 38.13. HRMS (ESI) m/z calc'd for $C_{24}H_{27}N_2O_2$ $[M+H]^+$: 375.2073; found 375.2058. $[\alpha]^{22}_D$ = -73.58° (c = 0.585, $CHCl_3$).



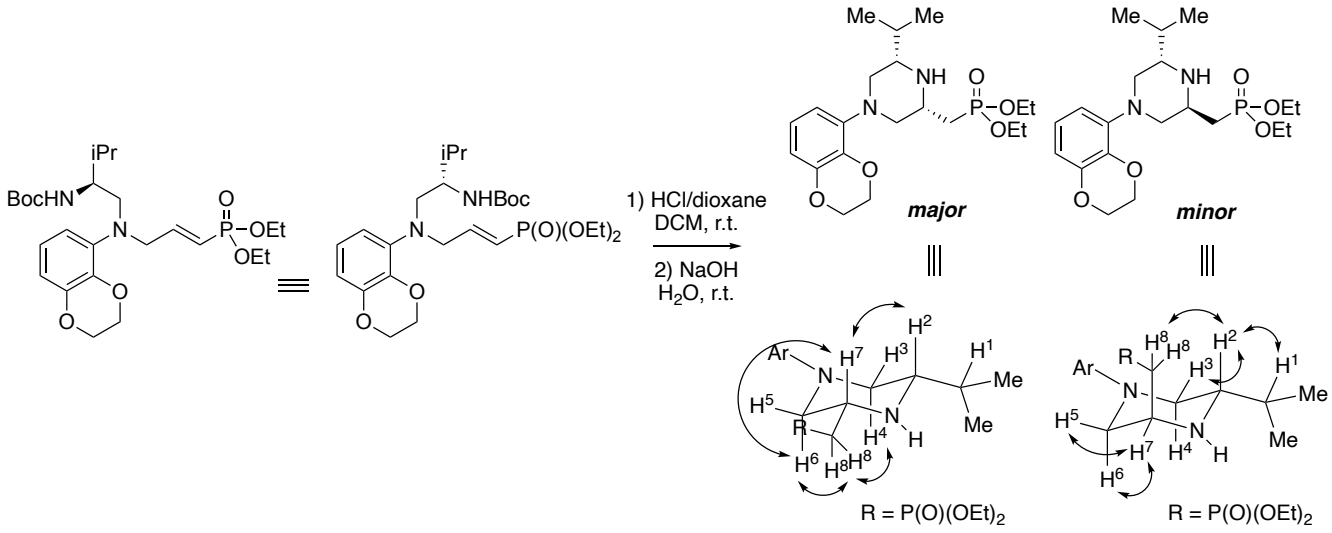
(±)-3-(cinnamyl(3-(trifluoromethoxy)phenyl)amino)-1,1,1-trifluoropropan-2-ol (76): 1,1,1-trifluoro-3-((3-(trifluoromethoxy)phenyl)amino)propan-2-ol (115.7 mg, 0.4 mmol, 1.0 equiv.) and allylbenzene (47.3 mg, 0.4 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 0.025 equiv.), MaSOX (3.4 mg, 0.01 mmol, 0.025 equiv.), 2,5-DMBQ (60 mg, 0.44 mmol, 1.1 equiv.), and 0.4 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. The crude mixture was diluted with EtOAc (10 mL) and washed with $NaHCO_3$

(10 mL, 1 M), $NaHSO_3$ (10 mL, sat.), $NaHCO_3$ (10 mL, 1 M), $NaHSO_3$ (10 mL, sat.), $NaHCO_3$ (10 mL, 1 M), $NaHSO_3$ (10 mL, sat.), $NaHCO_3$ (10 mL, 1 M) – 7 washes in total. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification via flash chromatography (40 mL SiO_2, 1% MeOH / 3% EtOAc / 96% Hexanes (500 mL) eluent) afforded the product as a yellow solid. Run 1: 155.8 mg, 96% yield (0% olefin RSM); Run 2: 154.8 mg, 94% yield (0% olefin RSM); Run 3: 150.3 mg, 93% yield (0% olefin RSM). **Average: 95% ± 1.4% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (app d, *J* = 7.8 Hz, 2H), 7.31 (app t, *J* = 7.5 Hz, 2H), 7.26 – 7.21 (m, 2H), 6.72 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.65 – 6.62 (m, 2H), 6.52 (app d, *J* = 16.0 Hz, 1H), 6.21 (dt, *J* = 16.0, 5.4 Hz, 1H), 4.36 – 4.27 (m, 1H), 4.22 (ddd, *J* = 17.3, 5.5, 1.4 Hz, 1H), 4.17 (ddd, *J* = 17.4, 5.5, 1.4 Hz, 1H), 3.79 (dd, *J* = 15.5 Hz, 1H), 3.57 (dd, *J* = 15.4, 9.0 Hz, 1H), 2.53 – 2.43 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.77 (d, *J* = 1.9 Hz), 149.41, 136.48, 132.60, 130.58, 128.77, 127.98, 126.54, 124.58 (q, *J* = 283.6 Hz), 124.19, 120.65 (q, *J* = 257.5 Hz), 111.15, 109.67, 105.75, 68.95 (q, *J* = 29.9 Hz), 54.09, 50.85 (q, *J* = 2.3 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ -57.44, -78.62 (d, *J* = 6.8 Hz). HRMS (ESI) m/z calc'd for $C_{19}H_{18}NO_2F_6$ $[M+H]^+$: 406.1242; found 406.1242. *The allylic carbon resonance at 54.09 ppm is indicative of an alpha-amino carbon. Comparison of the starting amino alcohol and product ^{13}C NMR spectra show for the alpha-hydroxyl ^{13}C peak (68.95 ppm) to minimally shift. This data supports this method to chemoselectively functionalize at the amine in the presence of an unprotected alcohol (see spectra).*



(-)-*tert*-butyl (*S*,*E*)-(1-((3-(diethoxyphosphoryl)allyl)(2,3-dihydrobenzo[*b*][1,4]dioxin-5-yl)amino)-3-methylbutan-2-yl)carbamate (77): *tert*-butyl (*S*)-(1-((2,3-dihydrobenzo[*b*][1,4]dioxin-5-yl)amino)-3-methylbutan-2-yl)carbamate (67.3 mg, 0.2 mmol, 1.0 equiv.) and diethyl allylphosphonate (35.6 mg, 0.2 mmol, 1.0 equiv.) were reacted according to the slow addition procedure using $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 0.05 equiv.), MaSOX (3.4 mg, 0.01 mmol, 0.05 equiv.), and 2,5-DMBQ (30 mg, 0.22 mmol, 1.1 equiv.), in which 0.2 mL of a 1.0 M solution of (*S*)-(1-((2,3-dihydrobenzo[*b*][1,4]dioxin-5-yl)amino)-3-methylbutan-2-yl)carbamate was added at a rate of 0.02 mL/hour to the reaction mixture containing 0.2 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.), and stirred at room temperature for 12 h. The crude material was diluted with EtOAc (25 mL) and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. Purification via flash column chromatography (50 mL SiO_2 deactivated with 2% triethylamine, 10% Acetone/Hexanes (200 mL) → 15% Acetone/Hexanes (200 mL) → 20% Acetone/Hexanes (200 mL) → 25% Acetone/Hexanes (200 mL) → 30% Acetone/Hexanes (200 mL) → 35% Acetone/Hexanes (200 mL) → 40% Acetone/Hexanes (200 mL) eluent) followed by a second flash column chromatography (100 mL SiO_2, EtOAc (200 mL) → 1% MeOH/EtOAc (200 mL) → 2% MeOH/EtOAc (200 mL) → 3% MeOH/EtOAc (200 mL) eluent) afforded the product as a beige oil. Run 1: 80.4 mg, 78% yield (10% olefin RSM); Run 2: 78.5 mg, 77% yield (12% olefin RSM); Run 3: 80.7 mg, 79% yield (12% olefin RSM). **Average: 78% ± 1.0% yield (11% ± 1.3% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.76 – 6.63 (m, 2H), 6.54 – 6.48 (m, 2H), 5.79 (dd, *J* = 20.2, 17.5 Hz, 1H), 4.79 (br d, *J* = 7.2 Hz, 1H), 4.30 – 4.26 (m, 2H), 4.26 – 4.19 (m, 2H), 4.02 – 3.90 (m, 4H), 3.91 – 3.86 (m, 2H), 3.63 (br s, 1H), 3.16 – 3.00 (m, 2H), 1.93 – 1.69 (m, 1H), 1.40 (s, 9H), 1.24 (app q, *J* = 7.8 Hz, 6H), 0.86 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.25, 150.25 (d, *J* = 5.0 Hz), 144.45, 139.53, 137.35, 120.63, 118.75 (d, *J* = 186.2 Hz), 114.36, 111.99, 78.85, 64.21, 64.17, 61.72 (d, *J* = 5.2 Hz), 54.18, 54.16 (d, *J* = 22.6 Hz), 53.34, 30.30, 28.52, 19.01, 17.58, 16.44 (d, *J* = 2.8 Hz), 16.38 (d, *J* = 2.8 Hz). *Note: the methyl protons of the isopropyl functionality are diastereotopic, with two protons (0.86 and 0.82 ppm) and two carbon (19.01 and 17.58 ppm) resonances observed; the methyl*

protons of the diethyl phosphate functionality are diastereotopic, with two carbon (16.44 and 16.38 ppm) resonances observed. HRMS (ESI) m/z calc'd for $C_{25}H_{42}N_2O_7P$ $[M+H]^+$: 513.2730; found 513.2739. $[\alpha]^{24}_D$ = -66.45° (c = 0.89, $CHCl_3$).

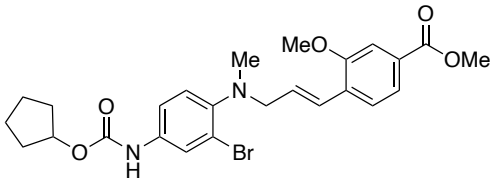


diethyl (((2*S*,6*S*)-4-(2,3-dihydrobenzo[*b*][1,4]dioxin-5-yl)-6-isopropylpiperazin-2-yl)methyl)phosphonate and **diethyl (((2*R*,6*S*)-4-(2,3-dihydrobenzo[*b*][1,4]dioxin-5-yl)-6-isopropylpiperazin-2-yl)methyl)phosphonate (78):** A 4.0 M solution of HCl in dioxane (0.31 mL, 1.25 mmol, 8.0 equiv.) was added dropwise to a solution of *tert*-butyl (*S*,*E*)-(1-((3-(diethoxyphosphoryl)allyl)(2,3-dihydrobenzo[*b*][1,4]dioxin-5-yl)amino)-3-methylbutan-2-yl)carbamate (80.4 mg, 0.16 mmol, 1.0 equiv.) in DCM (0.2 mL, 1.0 M), and the reaction was stirred at room temperature for 17 hours. The reaction mixture was then concentrated under reduce pressure and azeotroped with pentane (x 3) to afford the crude Boc-deprotected amine hydrochloride as an off-white solid. The material was then diluted with H_2O (0.2 mL, 1.0 M) and subsequently, a 1.0 M solution of NaOH (0.17 mL, 0.17 mmol, 1.1 equiv.) was added dropwise, and the reaction was stirred at room temperature for 24 hours. The mixture was diluted with DCM (5 mL) and water (5 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (100 mL SiO_2, 3% MeOH/EtOAc (200 mL) → 6% MeOH/EtOAc (200 mL) → 9% MeOH/EtOAc (200 mL) → 12% MeOH/EtOAc (200 mL) → 15% MeOH/EtOAc (200 mL) → 18% MeOH/EtOAc (200 mL) → 20% MeOH/EtOAc (200 mL) eluent) partially separated the diastereomers. Pure fractions of the major and minor diastereomers were separately collected for spectroscopic characterization, and all fractions were then combined to afford the product as a beige-tinted oil (59.8 mg, 0.14 mmol, 92% yield, d.r. = 4:1 *cis*:*trans*). *Note: the diastereomeric ratio was determined by ^{13}C qNMR analysis (see combined spectra).* HRMS (ESI) m/z calc'd for $C_{20}H_{34}N_2O_5P$ $[M+H]^+$: 413.2205; found 413.2207.

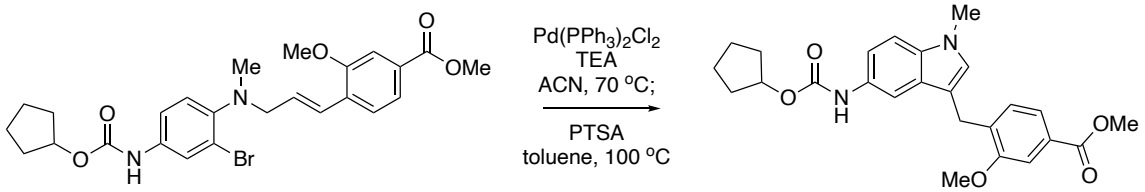
Characterization of major diastereomer: ^1H NMR (500 MHz, $CDCl_3$) δ 6.76 (t, *J* = 8.2 Hz, 1H), 6.58 (d, *J* = 8.2 Hz, 1H), 6.53 (d, *J* = 8.0 Hz, 1H), 4.35 – 4.29 (m, 2H), 4.27 – 4.21 (m, 2H), 4.18 – 4.07 (m, 4H), 3.44 (d, *J* = 11.0 Hz, 1H), 3.41 – 3.32 (m, 2H), 2.70 (app t, *J* = 8.4 Hz, 1H), 2.70 (br s, 1H), 2.35 (app t, *J* = 10.2 Hz, 2H), 2.01 – 1.79 (m, 2H), 1.68 – 1.55 (m, 1H), 1.33 (td, *J* = 7.1, 2.3 Hz, 6H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.25, 141.80, 136.60, 120.78, 112.11, 111.17, 64.45, 64.11, 61.98 (d, *J* = 6.5 Hz), 61.85 (d, *J* = 6.2 Hz), 61.30, 57.64 (d, *J* = 21.1 Hz), 54.43, 50.64, 31.33, 30.56 (d, *J* = 146.3 Hz), 19.36, 19.21, 16.65 (d, *J* = 3.4 Hz), 16.61 (d, *J* = 3.4 Hz). *Notes: the methyl protons of*

the isopropyl functionality are diastereotopic, with two proton (1.00 and 0.95 ppm) and two carbon (19.36 and 19.21 ppm) resonances observed. The methyl and methylene protons of the diethyl phosphate functionality are diastereotopic, with two carbon resonances (16.65 and 16.61 ppm; 61.98 and 61.85 ppm) observed each. The structure was assigned with the help of ^{1}H-^{1}H COSY and ^{1}H-^{1}H 2D NOESY analysis (see spectra).

Characterization of minor diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.76 (t, *J* = 8.1 Hz, 1H), 6.59 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.50 (dd, *J* = 8.0, 1.2 Hz, 1H), 4.31 – 4.26 (m, 2H), 4.26 – 4.22 (m, 2H), 4.18 – 4.09 (m, 4H), 3.68 – 3.57 (m, 1H), 3.15 (app t, *J* = 9.9 Hz, 2H), 2.98 (d, *J* = 11.1 Hz, 1H), 2.92 – 2.84 (m, 1H), 2.83 – 2.76 (m, 1H), 2.56 (app q, *J* = 14.2 Hz, 1H), 2.03 (ddd, *J* = 18.6, 15.7, 3.2 Hz, 1H), 2.03 (br s, 1H), 1.98 – 1.87 (m, 1H), 1.33 (t, *J* = 7.0 Hz, 6H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.24, 141.91, 136.61, 120.86, 112.11, 111.22, 64.26, 64.18, 61.99 (app t, *J* = 6.7 Hz), 56.56, 56.29 (d, *J* = 20.0 Hz), 53.48, 47.59, 29.56, 28.49, 19.66, 19.11, 16.63 (app t, *J* = 6.1 Hz). *Notes: the methyl protons of the isopropyl functionality are diastereotopic, with two proton (1.02 and 0.97 ppm) and two carbon (19.66 and 19.11 ppm) resonances observed. The methyl and methylene protons of the diethyl phosphate functionality are also diastereotopic, however, the carbon resonances are overlapping (two app t, 61.99 and 16.63 ppm). Note: the structure was assigned with the help of ^{1}H-^{1}H COSY and ^{1}H-^{1}H 2D NOESY analysis (see spectra).*

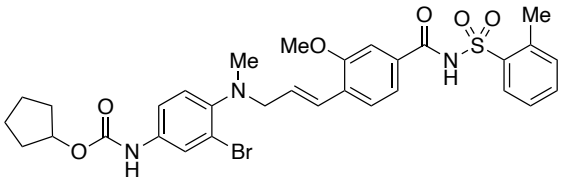


methyl (*E*)-4-(3-((2-bromo-4-(((cyclopentyloxy)carbonyl)amino)phenyl)(methyl)amino)prop-1-en-1-yl)-3-methoxybenzoate (81): cyclopentyl (3-bromo-4-(methylamino)phenyl)carbamate (94.0 mg, 0.3 mmol, 1.0 equiv.) and methyl 4-allyl-3-methoxybenzoate (61.9 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. The crude material was diluted with EtOAc (25 mL) and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. Purification via flash column chromatography (100 mL SiO_2 deactivated with 2% triethylamine, 20% Et_2O/Hexanes (400 mL) → 25% Et_2O/Hexanes (400 mL) → 30% Et_2O/Hexanes (200 mL) → 40% Et_2O/Hexanes (200 mL) → 50% Et_2O/Hexanes (200 mL) → 60% Et_2O/Hexanes (200 mL) eluent) afforded the product as a yellow solid. Run 1: 127.2 mg, 82% yield (0% olefin RSM); Run 2: 126.0 mg, 82% yield (0% olefin RSM); Run 3: 132.7 mg, 86% yield (0% olefin RSM). **Average: 83% ± 2.5% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (br s, 1H), 7.59 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.52 (d, *J* = 1.6 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.31 – 7.26 (m, 1H), 7.04 (d, *J* = 8.7 Hz, 1H), 6.91 (d, *J* = 16.2 Hz, 1H), 6.56 (s, 1H), 6.42 (dt, *J* = 16.1, 6.5 Hz, 1H), 5.22 – 5.15 (m, 1H), 3.91 (s, 3H), 3.89 (s, 3H), 3.74 (d, *J* = 6.5 Hz, 2H), 2.74 (s, 3H), 1.95 – 1.81 (m, 2H), 1.80 – 1.68 (m, 4H), 1.65 – 1.55 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.07, 156.39, 153.56, 146.59, 134.31, 130.80, 130.13, 129.94, 126.78, 126.61, 124.16, 122.17, 122.03, 120.29, 118.48, 111.77, 78.37, 59.62, 55.79, 52.26, 40.77, 32.87, 23.76. HRMS (ESI) m/z calc'd for $C_{25}H_{30}N_2O_5Br$ $[M+H]^+$: 517.1338; found 517.1344.



methyl 4-((5-(((cyclopentyloxy)carbonyl)amino)-1-methyl-1*H*-indol-3-yl)methyl)-3-methoxybenzoate (82): To an oven-dried ½ dram vial fitted with a Teflon cap and stir bar was added bis(triphenylphosphine)palladium chloride (3.5 mg, 0.005 mmol, 0.10 equiv.) in the glovebox followed by quick addition of methyl (*E*)-4-(3-((2-bromo-4-(((cyclopentyloxy)carbonyl)amino)phenyl)(methyl)amino)prop-1-en-1-yl)-3-methoxybenzoate (25.9 mg, 0.05 mmol, 1.0 equiv.). The vial was placed under vacuum for 10 minutes and then introduced to an atmosphere of N_2. MeCN (0.5 mL, 0.1 M), pre-sparged with argon, was added followed the addition of freshly distilled Et_3N (35 µL, 0.25 mmol, 5.0 equiv.). The reaction was quickly replaced with a new Teflon cap under an atmosphere of argon. The reaction vial was sealed with Teflon tape and parafilm and placed into an oil bath such that the solvent line and oil line were level, leaving the empty headspace exposed above the oil. The reaction was stirred at 70 °C for 48 hours under an atmosphere of argon. The reaction was cooled to room temperature, diluted with EtOAc, filtered through a Celite plug – rinsing with EtOAc – and concentrated under reduced pressure. To the round-bottom flask equipped with a stir bar containing the crude product was added toluene (1 mL) and *p*-toluenesulfonic acid monohydrate (8.6 mg, 0.05 mmol, 1.0 equiv.). The reaction was stirred at 100 °C for 1 hour. The reaction was then cooled to room temperature, diluted with EtOAc, quenched with aqueous 1 M $NaHCO_3$, and then carefully extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification via flash chromatography (100 mL SiO_2, 20% EtOAc/Hexanes (600 mL) eluent) afforded the product as a yellow solid. Run 1: 14.9 mg, 68% yield. Run 2: 15.6 mg, 71% yield. **Average 70% ± 1.4% yield.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 – 7.48 (m, 3H), 7.22 – 7.16 (m, 2H), 7.13 (d, *J* = 7.8 Hz, 1H), 6.75 (s, 1H), 6.49 (br s, 1H), 5.24 – 5.16 (m, 1H), 4.07 (s, 2H), 3.93 (s, 3H), 3.89 (s, 3H), 3.70 (s, 3H), 1.94 – 1.83 (m, 2H), 1.82 – 1.67 (m, 4H), 1.66 – 1.56 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.37, 157.22, 154.25, 135.59, 134.37, 130.14, 129.74, 129.13, 128.34, 128.18, 122.14, 115.22, 112.58, 110.94, 109.82, 109.49, 77.79, 55.71, 52.18, 32.95, 32.88, 25.36, 23.81. HRMS (ESI) m/z calc'd for $C_{25}H_{29}N_2O_5$ $[M+H]^+$: 437.2068; found 437.2076.

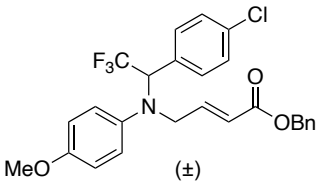
Additional Heck cyclization reaction conditions in the presence of unprotected arylamines can be found in the following literature references.[9]



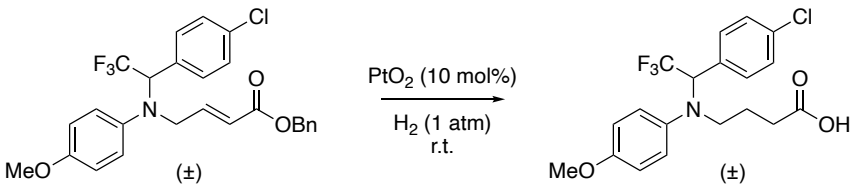
cyclopentyl (*E*)-(3-bromo-4-((3-(2-methoxy-4-((*o*-tolylsulfonyl)carbamoyl)phenyl)allyl)(methyl)amino)phenyl)carbamate (83): cyclopentyl (3-bromo-4-(methylamino)phenyl)carba-mate (62.6 mg, 0.2 mmol, 1.0 equiv.) and 4-allyl-3-methoxy-N-(o-tolylsulfonyl)benzamide (69.1 mg, 0.2 mmol, 1.0 equiv.) were reacted according to the slow addition procedure using $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 0.05 equiv.), MaSOX (3.4 mg, 0.01 mmol, 0.05 equiv.), and 2,5-DMBQ (30 mg, 0.22 mmol, 1.1 equiv.), in which 0.2 mL of a 1.0 M solution of cyclopentyl (3-bromo-4-(methylamino)phenyl)carbamate was added at a rate of 0.01 mL/hour to the reaction mixture containing 0.2 mL of 0.1 M solution of dibutyl phosphate in dioxane (0.10 equiv.), and stirred for 24 h. The vial was cooled to room temperature, diluted with CD_3OD, and nitrobenzene (24.6 mg, 0.2 mmol, 1.0 equiv.) was added as an internal standard. The crude mixture was analyzed using quantitative ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) in CD_3OD to determine the recovered olefin starting

material. Purification via MPLC (dry load; 40 g RediSepGold HP column, 25% → 60% Acetone/Hexanes eluent over 14 minutes then 60% Acetone/Hexanes → 100% Acetone over 1 minute then 100% Acetone over 3 minutes; 60 mL/min flow rate) followed by a second flash column chromatography (50 mL SiO_2, 5% AcOH-EtOAc/toluene (200 mL) → 10% AcOH-EtOAc/toluene (200 mL) → 15% AcOH-EtOAc/toluene (200 mL) → 20% AcOH-EtOAc/toluene (200 mL) eluent) afforded the product as a yellow solid. Run 1: 83.3 mg, 63% yield (19% olefin RSM); Run 2: 76.4 mg, 58% yield (14% olefin RSM); Run 3: 76.7 mg, 58% yield (14% olefin RSM). **Average: 60% ± 3.0% yield (16% ± 2.8% olefin RSM).** ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.65 (br s, 1H), 9.57 (br s, 1H), 8.04 (d, J = 7.9 Hz, 1H), 7.77 (br s, 1H), 7.60 – 7.53 (m, 2H), 7.51 (d, J = 1.1 Hz, 1H), 7.47 (dd, J = 8.2, 1.1 Hz, 1H), 7.44 (t, J = 7.7 Hz, 1H), 7.40 – 7.33 (m, 2H), 7.15 (d, J = 8.8 Hz, 1H), 6.82 (d, J = 16.0 Hz, 1H), 6.43 (dt, J = 16.0, 6.4 Hz, 1H), 5.11 – 5.02 (m, 1H), 3.85 (s, 3H), 3.68 (d, J = 6.4 Hz, 2H), 2.63 (s, 3H), 2.61 (s, 3H), 1.90 – 1.78 (m, 2H), 1.72 – 1.61 (m, 4H), 1.61 – 1.52 (m, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.91, 155.80, 153.29, 145.02, 138.07, 136.85, 135.73, 133.31, 132.29, 131.53, 130.41, 130.18, 129.69, 126.36, 126.15, 125.72, 122.58, 122.51, 120.94, 119.39, 118.01, 110.96, 76.88, 58.53, 55.77, 40.78, 32.30, 23.26, 19.65. HRMS (ESI) m/z calc'd for $C_{31}H_{35}N_3O_6SBr$ $[M+H]^+$: 656.1430; found 656.1424.

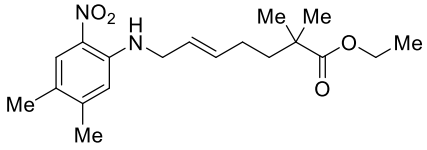
Note: SEM-protection of the sulfonyl benzamide olefin fragment afforded productive catalysis in an estimated 60% yield via crude ^{1}H NMR analysis with 2-nitrobenzene as an internal standard (see spectra). This supports our hypothesis that the more basic aniline nucleophile is deprotonating the acidic N—H sulfonyl benzamide functionality to access an anionic intermediate that is likely deactivating the catalyst.



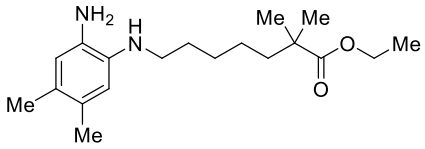
(±)-benzyl (*E*)-4-((1-(4-chlorophenyl)-2,2,2-trifluoroethyl)(4-methoxyphenyl)amino)but-2-enoate (85): *N*-(1-(4-chlorophenyl)-2,2,2-trifluoroethyl)-4-methoxyaniline (126.3 mg, 0.4 mmol, 1.0 equiv.) and benzyl but-3-enoate (70.5 mg, 0.4 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 0.025 equiv.), MaSOX (3.4 mg, 0.01 mmol, 0.025 equiv.), 2,5-DMBQ (60 mg, 0.44 mmol, 1.1 equiv.), and 0.4 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred at room temperature for 24 h. Purification via flash column chromatography (100 mL SiO_2 deactivated with 2% triethylamine, Hexanes (200 mL) → 1% Acetone/Hexanes (300 mL) → 2% Acetone/Hexanes (300 mL) → 3% Acetone/Hexanes (300 mL) → 4% Acetone/Hexanes (300 mL) → 5% Acetone/Hexanes (300 mL) → 6% Acetone/Hexanes (300 mL) eluent) afforded the product as an orange oil. Run 1: 156.9 mg, 80% yield (7% olefin RSM); Run 2: 155.4 mg, 80% yield (10% olefin RSM); Run 3: 155.5 mg, 81% yield (12% olefin RSM). **Average: 81% ± 0.6% yield (9% ± 2.5% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 7H), 7.28 – 7.24 (m, 2H), 6.86 (app d, J = 9.1 Hz, 2H), 6.83 (app d, J = 9.1 Hz, 2H), 6.78 (dt, J = 15.8, 4.6 Hz, 1H), 5.87 (app d, J = 15.8 Hz, 1H), 5.20 (q, J = 8.2 Hz, 1H), 5.10 (s, 2H), 3.86 (app dd, J = 18.4, 4.0 Hz, 1H), 3.76 (s, 3H), 3.71 (app dd, J = 18.2, 4.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.00, 154.61, 145.49, 141.65, 135.99, 134.88, 131.22, 129.74, 129.17, 128.67, 128.39, 128.36, 125.9 (q, J = 286.3 Hz) 122.47, 119.75, 114.83, 66.89 (q, J = 28.9 Hz), 66.37, 55.65, 48.20. ^{19}F NMR (471 MHz, $CDCl_3$) δ -68.02 (d, J = 8.1 Hz). HRMS (ESI) m/z calc'd for $C_{26}H_{24}NO_3ClF_3$ $[M+H]^+$: 490.1397; found 490.1397. *Note: increased temperatures afforded diminished yields and poor mass balance with formation of acetate and 2,5-DMBQ functionalized byproducts observed.*



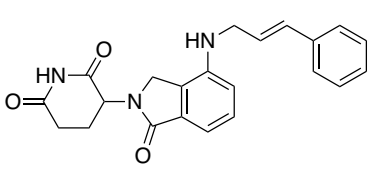
(±)-4-((1-(4-chlorophenyl)-2,2,2-trifluoroethyl)(4-methoxyphenyl)amino)butanoic acid (86): To a ½ dram vial equipped with a stir bar was added PtO_2 (3.2 mg, 0.014 mmol, 0.1 equiv.) and MeOH (0.2 mL), which was sparged with H_2 for 5 min. In a separate vial, a solution of benzyl (*E*)-4-((1-(4-chlorophenyl)-2,2,2-trifluoroethyl)(4-methoxyphenyl)amino)but-2-enoate (69.5 mg, 0.14 mmol, 1.0 equiv.) in a mixture of MeOH (0.7 mL) and EtOAc (0.2 mL) was sparged with H_2 for 5 minutes and subsequently added dropwise to the reaction mixture. The reaction was stirred at room temperature under H_2 (1 atm) for 20 hours. The crude mixture was filtered over celite – rinsing with MeOH and EtOAc – and then concentrated under reduced pressure. Purification via flash column chromatography (100 mL SiO_2, 5% Acetone/Hexanes (200 mL) → 10% Acetone/Hexanes (200 mL) → 15% Acetone/Hexanes (200 mL) → 20% Acetone/Hexanes (200 mL) → 25% Acetone/Hexanes (200 mL) → 30% Acetone/Hexanes (200 mL) eluent) afforded the product as a light-yellow oil (47.7 mg, 0.12 mmol, 84% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (app d, *J* = 8.6 Hz, 2H), 7.24 (app d, *J* = 8.4 Hz, 2H), 6.98 (app d, *J* = 9.1 Hz, 2H), 6.87 (app d, *J* = 9.1 Hz, 2H), 4.96 (q, *J* = 8.5 Hz, 1H), 3.82 (s, 3H), 3.17 – 3.03 (m, 1H), 3.03 – 2.89 (m, 1H), 2.38 – 2.24 (m, 2H), 1.78 – 1.58 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 179.53 – 179.22 (m), 155.30, 141.55, 134.60, 131.41, 130.03, 128.94, 126.57 (q, *J* = 285.6 Hz), 122.54, 114.72, 69.00 (q, *J* = 28.6 Hz), 55.64, 46.08, 30.80, 22.15. ^{19}F NMR (471 MHz, $CDCl_3$) δ -67.95 (d, *J* = 8.6 Hz). HRMS (ESI) m/z calc'd for $C_{19}H_{20}NO_3ClF_3$ $[M+H]^+$: 402.1084; found 402.1084. *Note: Pd/C as the catalyst led to significant amounts of the free N—H amine, likely proceeding via a tandem palladium(0)-mediated deallylation, decarboxylation mechanism.*[10]



ethyl (*E*)-7-((4,5-dimethyl-2-nitrophenyl)amino)-2,2-dimethylhept-5-enoate (87): 4,5-dimethyl-2-nitroaniline (49.9 mg, 0.3 mmol, 1.0 equiv.) and ethyl 2,2-dimethylhept-6-enoate (55.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.1 M solution of dibutyl phosphate in dioxane (0.10 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (50 mL SiO_2, 10% EtOAc/Hexanes eluent) afforded the product as a bright red oil. Run 1: 91.4 mg, 87% yield (0% olefin RSM); Run 2: 92.0 mg, 88% yield (0% olefin RSM); Run 3: 91.9 mg, 88% yield (0% olefin RSM). **Average: 88% ± 0.5% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (br t, J = 5.6 Hz, 1H), 7.92 (s, 1H), 6.60 (s, 1H), 5.70 (app dt, J = 15.4, 6.6 Hz, 1H), 5.56 (app dt, J = 15.4, 5.6 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.87 (app t, J = 5.6, 1.4 Hz, 2H), 2.25 (s, 3H), 2.17 (s, 3H), 2.05 – 1.94 (m, 2H), 1.68 – 1.53 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H), 1.17 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.82, 147.30, 144.09, 133.65, 129.99, 126.55, 125.31, 124.61, 114.53, 60.44, 44.94, 42.11, 40.10, 28.05, 25.26, 20.87, 18.70, 14.38. HRMS (ESI) m/z calc'd for $C_{19}H_{29}N_2O_4$ $[M+H]^+$: 349.2127; found 349.2129. *Note: the mono-allylation product was the only product observed.*

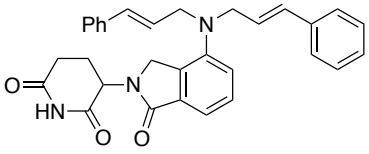


ethyl 7-((2-amino-4,5-dimethylphenyl)amino)-2,2-dimethylheptanoate: ethyl (*E*)-7-((4,5-dimethyl-2-nitrophenyl)amino)-2,2-dimethylhept-5-enoate (104.4 mg, 0.3 mmol, 1.0 equiv.) and EtOAc (3 mL, 0.1 M) were added to a flame-dried round-bottom flask equipped with a stir bar under an atmosphere of N_2. PtO_2 (13.6 mg, 0.06 mmol, 0.2 equiv.) was added and the mixture was sparged with H_2 for 30 minutes. Afterwards, the reaction was stirred at room temperature under H_2 (1 atm) overnight. The crude mixture was filtered over celite – rinsing with MeOH – and concentrated under reduced pressure, and then filtered a second time over a small plug of SiO_2 – rinsing with DCM – and concentrated under reduced pressure to afford ethyl 7-((2-amino-4,5-dimethylphenyl)amino)-2,2-dimethylheptanoate as a pale golden oil (91.5 mg, 0.29 mmol, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.52 (s, 1H), 6.45 (s, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.17 (br s, 3H), 3.06 (t, *J* = 7.1 Hz, 2H), 2.18 (s, 3H), 2.13 (s, 3H), 1.65 (p, *J* = 7.2 Hz, 2H), 1.56 – 1.50 (m, 2H), 1.41 (p, *J* = 7.2 Hz, 2H), 1.32 – 1.22 (m, 5H), 1.17 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.18, 136.07, 131.98, 128.20, 126.03, 118.53, 114.01, 60.33, 44.70, 42.26, 40.79, 29.81, 27.88, 25.30, 24.94, 19.43, 18.92, 14.40. HRMS (ESI) m/z calc'd for $C_{19}H_{33}N_2O_2$ $[M+H]^+$: 321.2542; found 321.2539. *Note: Pd/C conditions gave incomplete reduction of the olefin and no reduction of the nitro group. Although $Pd(OH)_2$ was competent to furnish both reductions, an impurity was introduced, which was not observed when using PtO_2. This diamine product was found to rapidly decompose (even when stored under argon and at low temperatures) and should be prepared as needed.*



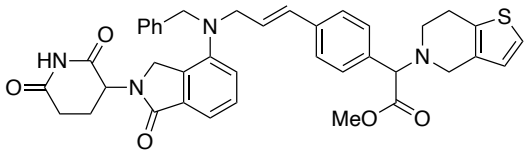
(±)

(±)-3-(4-(cinnamylamino)-1-oxoisoindolin-2-yl)piperidine-2,6-dione (89): 3-(4-amino-1-oxoisoindolin-2-yl)piperidine-2,6-dione (51.9 mg, 0.2 mmol, 1.0 equiv.) and allylbenzene (23.6 mg, 0.2 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (4.5 mg, 0.02 mmol, 0.1 equiv.), MaSOX (6.8 mg, 0.02 mmol, 0.1 equiv.), 2,5-DMBQ (30 mg, 0.22 mmol, 1.1 equiv.), and 0.2 mL of a 0.05 M solution of dibutyl phosphate in 1,2-DCE (0.05 equiv.) as a solvent, and stirred for 72 h. The crude mixture was analyzed in CD_3CN to determine the recovered olefin starting material. Purification via MPLC (dry load; 12 g RediSepGold HP column, 1% → 5% MeOH/DCM eluent over 40 column volumes; 30 mL/min flow rate) afforded the product as a yellow solid. *Note: the product is not greatly soluble in organic solvents and therefore MPLC purification provided the best consistency in both separation and yield.* Run 1: 61.6 mg, 83% yield (0% olefin RSM); Run 2: 58.8 mg, 78% yield (0% olefin RSM); Run 3: 60.4 mg, 81% yield (0% olefin RSM). **Average: 81% ± 2.3% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.01 (s, 1H), 7.41 (app d, *J* = 7.7 Hz, 2H), 7.35 – 7.26 (m, 3H), 7.22 (app t, *J* = 7.3 Hz, 1H), 6.95 (d, *J* = 7.4 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 6.62 (d, *J* = 16.0 Hz, 1H), 6.37 (dt, *J* = 16.0, 5.5 Hz, 1H), 6.01 (t, *J* = 5.7 Hz, 1H), 5.12 (dd, *J* = 13.3, 5.1 Hz, 1H), 4.29 (d, *J* = 17.2 Hz, 1H), 4.18 (d, *J* = 17.2 Hz, 1H), 3.98 (app t, *J* = 5.3 Hz, 2H), 2.93 (ddd, *J* = 17.3, 13.5, 5.4 Hz, 1H), 2.62 (app d, *J* = 17.1 Hz, 1H), 2.33 (qd, *J* = 13.3, 4.5 Hz, 1H), 2.04 (dtd, *J* = 12.7, 5.3, 2.3 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 172.92, 171.26, 168.83, 143.49, 136.64, 132.08, 130.22, 129.17, 128.60, 127.59, 127.36, 126.70, 126.13, 112.30, 110.30, 51.52, 45.75, 44.65, 31.25, 22.82. HRMS (ESI) m/z calc'd for $C_{22}H_{22}N_3O_3$ $[M+H]^+$: 376.1661; found 376.1656.

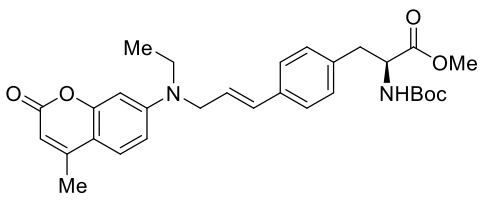


(±)

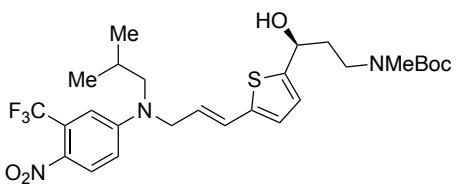
(±)-3-(4-(cinnamylamino)-1-oxoisoindolin-2-yl)piperidine-2,6-dione (89b): the diallylated product was isolated (~10% yield) with an unknown impurity, and characterization was determined by ^{1}H NMR and HRMS analysis. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.98 (s, 1H), 7.41 (app d, J = 7.6 Hz, 4H), 7.37 (d, J = 7.9 Hz, 1H), 7.30 (app t, J = 7.7 Hz, 4H), 7.24 – 7.16 (m, 4H), 6.60 (d, J = 15.9 Hz, 2H), 6.34 (dt, J = 16.0, 5.9 Hz, 2H), 5.10 (dd, J = 13.3, 5.1 Hz, 1H), 4.58 (d, J = 17.0 Hz, 1H), 4.47 (d, J = 17.0 Hz, 1H), 4.07 (d, J = 5.9 Hz, 4H), 2.91 (ddd, J = 17.3, 13.7, 5.4 Hz, 1H), 2.65 – 2.55 (m, 1H), 2.49 – 2.44 (m, 1H), 2.04 – 1.96 (m, 1H). HRMS (ESI) m/z calc'd for $C_{31}H_{30}N_3O_3$ $[M+H]^+$: 492.2287; found 492.2288.



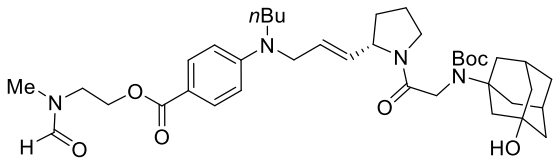
methyl (*E*)-2-(4-(3-(benzyl(2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-4-yl)amino)prop-1-en-1-yl)phenyl)-2-(6,7-dihydrothieno[3,2-*c*]pyridin-5(4*H*)-yl)acetate (90): 3-(4-(benzylamino)-1-oxoisoindolin-2-yl)piperidine-2,6-dione (69.8 mg, 0.2 mmol, 1.0 equiv.) and methyl 2-(4-allylphenyl)-2-(6,7-dihydrothieno[3,2-*c*]pyridin-5(4*H*)-yl)acetate (65.5 mg, 0.2 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (4.5 mg, 0.02 mmol, 0.1 equiv.), MaSOX (6.8 mg, 0.02 mmol, 0.1 equiv.), 2,5-DMBQ (30 mg, 0.22 mmol, 1.1 equiv.), and 0.2 mL of a 0.1 M solution of dibutyl phosphate in dioxane (0.10 equiv.) as a solvent, and stirred for 72 h. The reaction was filtered over a frit, rinsing with EtOAc, and concentrated under reduced pressure. The crude material was then diluted with $CDCl_3$ and benzotrifluoride (43.8 mg, 0.3 mmol, 1.0 equiv.) was added as an internal standard for crude ^{1}H NMR analysis. Upon crude ^{1}H NMR analysis, a doublet at 6.8 ppm (1H), a doublet of triplets at 6.31 ppm (1H), and a singlet at 2.1 ppm (3H) was observed, indicative of acetate functionalization of the olefin as a byproduct. Purification via flash column chromatography (100 mL SiO_2, 50% EtOAc/Hexanes (500 mL) → DCM (300 mL) → 4% MeOH/DCM (100 mL) eluent) afforded the product with the starting amine. A second flash column chromatography (100 mL SiO_2, 4% isopropanol/DCM eluent) afforded the product alongside a mixture of the product with the starting amine, and the mixed fractions were resubjected to flash column chromatography (100 mL SiO_2, 4% isopropanol/DCM eluent). The combined pure fractions afforded the product as an orange-tinted solid. Run 1: 92.4 mg, 68% yield (0% olefin RSM, 13% acetate functionalized byproduct); Run 2: 87.2 mg, 65% yield (0% olefin RSM, 11% acetate functionalized byproduct); Run 3: 83.4 mg, 63% yield (0% olefin RSM, 13% acetate functionalized byproduct). **Average: 65% ± 2.9% yield (0% olefin RSM, 12% ± 1.5% acetate functionalized byproduct).** ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.98 (s, 1H), 7.41 (d, J = 8.3 Hz, 2H), 7.36 (d, J = 8.2 Hz, 2H), 7.35 – 7.28 (m, 5H), 7.25 (d, J = 5.1 Hz, 1H), 7.24 – 7.19 (m, 2H), 7.13 (d, J = 8.1 Hz, 1H), 6.75 (d, J = 5.1 Hz, 1H), 6.55 (d, J = 15.9 Hz, 1H), 6.36 (dt, J = 15.9, 6.0 Hz, 1H), 5.10 (dd, J = 13.3, 5.1 Hz, 1H), 4.57 (d, J = 17.0 Hz, 1H), 4.49 (s, 2H), 4.46 (d, J = 17.0 Hz, 1H), 4.38 (s, 1H), 4.03 (d, J = 6.0 Hz, 2H), 3.63 (s, 3H), 3.54 – 3.44 (m, 2H), 2.91 (ddd, J = 17.2, 13.7, 5.3 Hz, 1H), 2.79 – 2.66 (m, 4H), 2.60 (app d, J = 16.9 Hz, 1H), 2.46 (qd, J = 13.2, 4.5 Hz, 1H), 2.04 – 1.95 (m, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 172.90, 171.45, 171.04, 168.15, 145.66, 138.47, 136.55, 135.30, 133.55, 133.34, 132.67, 131.55, 131.33, 128.91, 128.80, 128.40, 127.52, 126.96, 126.88, 126.48, 125.48, 123.10, 120.94, 114.73, 71.27, 54.45, 53.70, 51.82, 51.59, 50.03, 47.63, 47.51, 31.19, 25.03, 22.37. HRMS (ESI) m/z calc'd for $C_{39}H_{39}N_4O_5S$ $[M+H]^+$: 675.2641; found 675.2650.



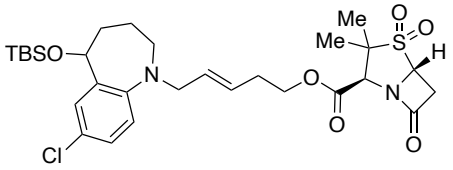
(+)-methyl (*S*,*E*)-2-((*tert*-butoxycarbonyl)amino)-3-(4-(3-(ethyl(4-methyl-2-oxo-2*H*-chromen-7-yl)amino)prop-1-en-1-yl)phenyl)propanoate (91): 7-(ethylamino)-4-methyl-2*H*-chromen-2-one (81.3 mg, 0.4 mmol, 1.0 equiv.) and methyl (*S*)-3-(4-allylphenyl)-2-((*tert*-butoxycarbonyl)amino)propanoate (127.8 mg, 0.4 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 0.025 equiv.), MaSOX (3.4 mg, 0.01 mmol, 0.025 equiv.), 2,5-DMBQ (60 mg, 0.44 mmol, 1.1 equiv.), and 0.4 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (60 mL SiO_2 deactivated with 1% triethylamine, Hexanes (200 mL) → 5% EtOAc/Hexanes (200 mL) → 20% EtOAc/Hexanes (250 mL) → 40% EtOAc/Hexanes (500 mL) eluent) afforded the product as a beige solid. Run 1: 195.8 mg, 94% yield (0% olefin RSM); Run 2: 193.7 mg, 93% yield (0% olefin RSM); Run 3: 197.8 mg, 95% yield (0% olefin RSM). **Average: 94% ± 0.8% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.50 (d, J = 9.0 Hz, 1H), 7.32 (d, J = 7.8 Hz, 2H), 7.27 (app d, J = 8.1 Hz, 1H), 7.16 (d, J = 7.8 Hz, 2H), 6.75 (app d, J = 9.0 Hz, 1H), 6.58 (app d, J = 2.4 Hz, 1H), 6.49 (d, J = 16.0 Hz, 1H), 6.28 (dt, J = 16.0, 5.3 Hz, 1H), 5.94 (s, 1H), 4.17 (d, J = 5.4 Hz, 2H), 4.16 – 4.10 (m, 1H), 3.60 (s, 3H), 3.50 (q, J = 7.0 Hz, 2H), 2.95 (dd, J = 13.8, 5.2 Hz, 1H), 2.81 (dd, J = 13.8, 10.0 Hz, 1H), 2.32 (s, 3H), 1.30 and 1.24 (two s, 9H), 1.24 (s, 2H), 1.16 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 172.54, 160.72, 155.43, 155.37, 153.52, 150.82, 136.91, 134.70, 130.49, 129.34, 126.14, 126.10, 124.99, 108.99, 108.64, 107.92, 97.28, 78.28, 55.15, 51.78, 51.50, 44.58, 36.12, 28.10, 17.94, 12.17. HRMS (ESI) m/z calc'd for $C_{30}H_{37}N_2O_6$ $[M+H]^+$: 521.2652; found 521.2645. $[\alpha]^{23}_D$ = +41.03° (c = 0.78, $CHCl_3$).



(+)-*tert*-butyl (*S*,*E*)-(3-hydroxy-3-(5-(3-(isobutyl(4-nitro-3-(trifluoromethyl)phenyl) amino)prop-1-en-1-yl)thiophen-2-yl)propyl)(methyl)carbamate (92): *N*-isobutyl-4-nitro-3-(trifluoromethyl)aniline (78.7 mg, 0.3 mmol, 1.0 equiv.) and *tert*-butyl (*S*)-(3-(5-allylthiophen-2-yl)-3-hydroxypropyl)(methyl)carbamate (93.4 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.1 equiv.), MaSOX (10.3 mg, 0.03 mmol, 0.1 equiv.), and 0.3 mL of a 0.1 M solution of dibutyl phosphate in dioxane (0.10 equiv.) as a solvent, and stirred for 48 h. The solvent was removed under reduced pressure, the crude residue was dissolved in EtOAc (25 mL), and washed with NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M), $NaHSO_3$ (5 mL, sat.), NaOH (5 mL, 1 M) – 7 washes in total. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (100 mL SiO_2, 5% Acetone/Benzene eluent) afforded the product as a yellow solid. Run 1: 120.2 mg, 70% yield (0% olefin RSM); Run 2: 124.1 mg, 72% yield (0% olefin RSM); Run 3: 126.8 mg, 74% yield (0% olefin RSM). **Average: 72% ± 1.6% yield (0% olefin RSM).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, J = 9.4 Hz, 1H), 7.00 (d, J = 2.8 Hz, 1H), 6.82 – 6.72 (m, 3H), 6.49 (d, J = 15.9 Hz, 1H), 5.88 (dt, J = 15.8, 5.1 Hz, 1H), 4.88 – 4.65 (m, 2H), 4.17 (d, J = 5.0 Hz, 2H), 3.95 – 3.78 (m, 1H), 3.28 (d, J = 7.4 Hz, 2H), 3.12 – 2.95 (m, 1H), 2.85 (s, 3H), 2.19 – 2.04 (m, 1H), 2.06 – 1.99 (m, 1H), 1.91 – 1.77 (m, 1H), 1.45 (s, 9H), 0.99 (d, J = 6.7 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.40, 151.81, 147.96, 139.76, 135.56, 129.07, 126.63 (q, J = 33.4 Hz), 126.06, 126.03, 123.30, 122.55 (q, J = 271.3 Hz), 121.46, 112.87, 110.36 (q, J = 6.6 Hz), 80.44, 66.55, 58.95, 53.45, 44.95, 36.85, 34.52, 28.48, 27.46, 20.42. ^{19}F NMR (471 MHz, $CDCl_3$) δ -60.08. HRMS (ESI) m/z calc'd for $C_{27}H_{36}N_3O_5NaSF_3$ $[M+Na]^+$: 594.2225; found 594.2220. $[\alpha]^{23}_D$ = +9.9° (c = 1.055, $CHCl_3$).



(-)-2-(*N*-methylformamido)ethyl 4-(((*E*)-3-((*S*)-1-(*N*-(*tert*-butoxycarbonyl)-*N*-((1*r*,3*R*,5*R*,7*S*)-3-hydroxyadamantan-1-yl)glycyl)pyrrolidin-2-yl)allyl)(butyl)amino)benzoate (93): 2-(*N*-methylformamido)ethyl 4-(butylamino)benzoate (83.5 mg, 0.3 mmol, 1.0 equiv.) and *tert*-butyl (2-((*S*)-2-allylpyrrolidin-1-yl)-2-oxoethyl)((1*r*,3*R*,5*R*,7*S*)-3-hydroxyadamantan-1-yl)carbamate (125.6 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 24 h. Purification via flash column chromatography (100 mL SiO_2, 40% Acetone/Hexanes (300 mL) → 50% Acetone/Hexanes (500 mL) → 60% Acetone/Hexanes (500 mL) → 80% Acetone/Hexanes (500 mL) eluent) afforded the product as an off-white crystalline solid. Run 1: 149.7 mg, 72% yield (12% olefin RSM); Run 2: 146.3 mg, 70% yield (18% olefin RSM); Run 3: 146mg, 70% yield (16% olefin RSM). **Average: 71% ± 0.9% yield (15% ± 2.5% olefin RSM).** ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.03 (app d, J = 7.1 Hz, 1H), 7.79 – 7.64 (m, 2H), 6.96 – 6.55 (m, 2H), 5.60 (dd, J = 15.6, 5.9 Hz, 0.66H), 5.55 – 5.46 (m, 1H), 5.40 (dt, J = 15.6, 5.3 Hz, 0.35H), 4.50 – 4.39 (m, 2H), 4.35 – 4.22 (m, 2H), 4.13 – 3.86 (m, 3H), 3.78 – 3.65 (m, 0.6H), 3.68 – 3.53 (m, 2H), 3.42 – 3.27 (m, 4.5H), 2.98 (s, 1H), 2.80 (s, 2H), 2.24 – 2.04 (m, 2H), 2.04 – 1.81 (m, 6H), 1.81 – 1.59 (m, 4H), 1.57 – 1.43 (m, 6H), 1.41 – 1.18 (m, 13H), 0.90 (t, J = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6, 70 °C) δ 168.12, 165.16, 162.39, 154.01, 151.38, 132.40, 130.58, 130.54, 125.30, 115.18, 110.55, 110.51, 78.14, 67.54, 60.43, 60.36, 57.96, 56.95, 50.92, 49.55, 47.77, 47.49, 45.66, 43.88, 42.50, 38.65, 34.60, 34.19, 30.31, 28.98, 28.74, 27.78, 19.25, 13.31. *Note: The ^{13}C spectrum was acquired at 70 °C to coalesce rotamers for characterization.* HRMS (ESI) m/z calc'd for $C_{39}H_{59}N_4O_7$ $[M+H]^+$: 695.4384; found 695.4395. $[\alpha]^{21}_D$ = -20.78° (c = 0.995, $CHCl_3$).



(*E*)-5-(5-((*tert*-butyldimethylsilyl)oxy)-7-chloro-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-1-yl)pent-3-en-1-yl (2*S*,5*R*)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4,4-dioxide (94): 5-((*tert*-butyldimethylsilyl)oxy)-7-chloro-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepine (93.6 mg, 0.3 mmol, 1.0 equiv.) and pent-4-en-1-yl (2*S*,5*R*)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4,4-dioxide (90.4 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the general procedure using 0.3 mL of a 0.1 M solution of dibutyl phosphate in dioxane (0.10 equiv.) as a solvent, and stirred for 12 h. Purification via flash column chromatography (150 mL SiO_2, 20% Acetone/Hexanes eluent) afforded the product alongside a mixture of the product with the starting olefin, and the mixed fractions were resubjected to flash column chromatography (150 mL SiO_2, 20% Acetone/Hexanes eluent). The combined pure fractions afforded the product as a beige solid. *Note: TLC analysis was best visualized using Cerium Ammonium Molybdate stain.* Run 1: 127.6 mg, 70% yield (19% olefin RSM); Run 2: 135.3 mg, 74% yield (18% olefin RSM); Run 3: 131.3 mg, 74% yield (13% olefin RSM). **Average: 72% ± 2.4% yield (16% ± 3.3% olefin RSM).** The reaction was characterized as a mixture of diastereomers and the diastereomeric ratio was determined by ^{1}H NMR (1:1 d.r.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, J = 2.0 Hz, 1H), 7.08 (dd, J = 8.5, 2.5 Hz, 1H), 6.76 (d, J = 8.5 Hz, 1H), 5.67 – 5.52 (m, 2H), 4.94 – 4.87 (m, 1H), 4.63 – 4.57 (m, 1H), 4.36 (s, 1H), 4.29 – 4.18 (m, 2H), 3.79 (app dt, J = 14.2, 3.4 Hz, 1H), 3.57 (dd, J = 14.2, 4.8 Hz, 1H), 3.48 (dd, J = 16.2, 4.2 Hz, 1H), 3.43 (dd, J = 16.1, 1.5 Hz, 1H), 3.15 – 3.07 (m, 1H), 2.55 – 2.39 (m, 2H), 2.02 – 1.92 (m, 1H), 1.74 – 1.64 (m, 1H), 1.59 and 1.59 (two s, 3H), 1.56 – 1.45 (m, 2H), 1.40 and 1.40 (two s, 3H), 0.94 (s, 9H), 0.08 (s, 3H), 0.04 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.83, 167.03, 146.70, (146.67), 140.27, (140.25), 131.58, (131.52), 127.37, (127.32), 126.90, (126.89), 126.64, 125.70, 118.95, 71.15, 65.73, 63.36, 62.73, 61.22, 55.98, (55.94), 52.49, (52.46), 38.45, 35.03,

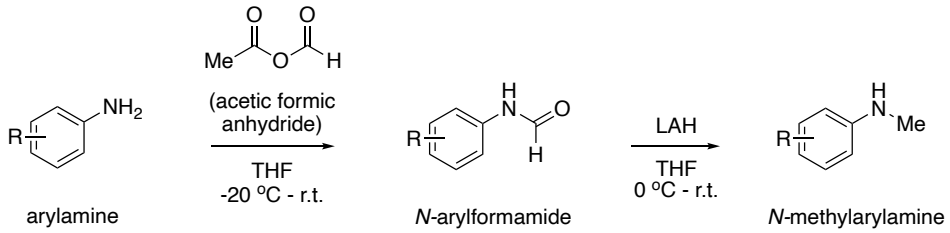
(35.00), 31.74, 26.03, 25.98, (25.95), 20.44, 18.64, 18.43, -4.67, -4.75. HRMS (ESI) m/z calc'd for $C_{29}H_{44}N_2O_6SiSCl$ $[M+H]^+$: 611.2378; found 611.2374.

The free benzylic alcohol afforded diminished reactivity. 7-chloro-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-5-ol (39.5 mg, 0.2 mmol, 1.0 equiv.) and pent-4-en-1-yl (2*S*,5*R*)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4,4-dioxide (60.3 mg, 0.2 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (4.5 mg, 0.02 mmol, 0.1 equiv.), MaSOX (6.8 mg, 0.02 mmol, 0.1 equiv.), 2,5-DMBQ (30 mg, 0.22 mmol, 1.1 equiv.), and 0.2 mL of a 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv.) as a solvent, and stirred for 24 h. The crude mixture was analyzed via ^1H NMR (nt = 16 scans, d1 = 10 seconds) with benzotrifluoride as an internal standard to determine the yield and recovered olefin starting material: 34% yield (53% olefin RSM).

4. Synthesis and Characterization of Starting Materials

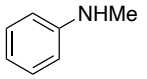
4.1. Synthesis and characterization of nucleophile starting materials.

_N_-methylation Procedure A:[11]

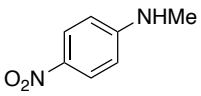


<u>*Part 1*</u>*:* To a round-bottom flask equipped with a stir bar and a reflux condenser was added acetic anhydride (2.6 equiv.). The flask was cooled to 0 °C and formic acid (88%, 3.2 equiv.) was added dropwise. The reaction was stirred at 60 °C for 2 h to provide acetic formic anhydride. The mixture was then diluted with THF (5.0 M) and cooled to -20 °C, in which a solution of the arylamine (1.0 equiv.) in THF (2.5 M) was added dropwise. The reaction was allowed to stir at -20 °C to room temperature, monitoring via TLC. Following full consumption of the arylamine, the reaction was diluted with DCM and quenched with water. The material was transferred to a separatory funnel and the organic layer was then washed with saturated $NaHCO_3$ (3 x), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The *N*-arylformamide was carried to the next step without further purification.

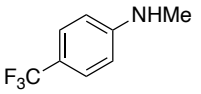
<u>*Part 2*</u>*:* To a flame-dried flask equipped with a stir bar was added lithium aluminum hydride (1.2 equiv.) and THF (0.25 M). The flask was cooled to 0 °C and a solution of *N*-arylformamide (1.0 equiv.) in THF (1.5 M) was added dropwise. The reaction was allowed to stir at 0 °C to room temperature, monitoring via TLC. Upon full consumption of the *N*-arylformamide, the reaction was cooled to 0 °C and quenched dropwise with EtOAc followed by a small amount of water. The mixture was filtered over celite, rinsing with EtOAc, and concentrated under reduced pressure. Purification via flash column chromatography afforded the *N*-methyl arylamine derivative.



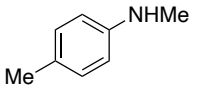
***N*-methyl phenylamine** was purchased from Sigma-Aldrich and purified via distillation to afford the amine as a yellow-tinted oil.



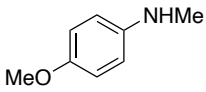
***N*-methyl-4-nitroaniline** was purchased from Oakwood Chemicals and used without further purification.



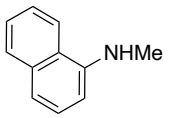
***N*-methyl-4-(trifluoromethyl)aniline** was prepared from 4-(trifluoromethyl)aniline (1.0 g, 6 mmol, 1.0 equiv.) following *N*-methylation procedure A. Purification via flash column chromatography (SiO_2, 5% → 10% EtOAc/Hexanes eluent) afforded the product as a clear oil (0.6 g, 3.4 mmol, 57% yield over 2 steps). Spectral data were in accordance with literature values.[12] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.3 Hz, 1H), 6.60 (d, *J* = 8.3 Hz, 1H), 4.04 (s, 0H), 2.87 (s, 1H).



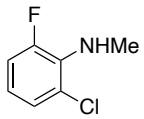
***N*,4-dimethylaniline** was purchased from Sigma-Aldrich and purified via distillation to afford the amine as a yellow-tinted oil.



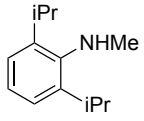
4-methoxy-*N*-methylaniline was purchased from Ambeed and purified via flash column chromatography (SiO_2, 10% EtOAc/Hexanes eluent) to afford the amine as a light-yellow solid. *The material should be stored under argon and kept in the freezer to maintain its purity.*



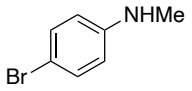
***N*-methylnaphthalen-1-amine** was synthesized following a modified literature procedure.[13] To a flame-dried round-bottom flask equipped with a stir bar and a reflux condenser was added naphthalen-1-amine (0.72 g, 5 mmol, 1.0 equiv.), trimethylamine borane (0.36 g, 5 mmol, 1.0 equiv.), sodium hydride (90%; 0.33 g, 12.5 mmol, 2.5 equiv.), and DMF (60 mL, 0.08 M). The reaction was stirred at 80 °C for 19 h. The reaction was then cooled to 0 °C, quenched with saturated NH_4Cl (30 mL), and diluted with EtOAc (20 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with saturated $NaHCO_3$ (30 mL), water (3 x 30 mL), and 50:50 brine:water (30 mL). The organic layer was then dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (SiO_2, 5% EtOAc/Hexanes eluent) afforded the product as a deep-red oil (0.52 g, 3.3 mmol, 66% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (app t, *J* = 8.2 Hz, 2H), 7.45 (app pt, *J* = 7.1, 1.7 Hz, 2H), 7.39 (app td, *J* = 7.9, 2.6 Hz, 1H), 7.28 – 7.24 (m, 1H), 6.62 (app d, *J* = 7.6 Hz, 1H), 4.44 (br s, 1H), 3.03 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.66, 134.35, 128.80, 126.81, 125.84, 124.82, 123.57, 119.91, 117.43, 103.90, 31.17. HRMS (ESI) m/z calc'd for $C_{11}H_{12}N$ $[M+H]^+$: 158.0970; found 158.0968.



2-chloro-6-fluoro-*N*-methylaniline was prepared from 2-chloro-6-fluoroaniline (0.87 g, 6 mmol, 1.0 equiv.) following *N*-methylation procedure A. Purification via flash column chromatography (SiO_2, 2% → 4% → 6% EtOAc/Hexanes eluent) afforded the product as a clear oil (0.49 g, 3.0 mmol, 51% yield over 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05 (app dt, *J* = 8.1, 1.3 Hz, 1H), 6.91 (ddd, *J* = 12.6, 8.3, 1.4 Hz, 1H), 6.63 (td, *J* = 8.2, 5.2 Hz, 1H), 3.97 (br s, 1H), 3.07 (d, *J* = 4.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.08 (d, *J* = 243.0 Hz), 135.24 (d, *J* = 11.7 Hz), 124.97 (d, *J* = 3.1 Hz), 122.43 (d, *J* = 6.5 Hz), 118.15 (d, *J* = 8.6 Hz), 115.45 (d, *J* = 20.8 Hz), 33.94 (d, *J* = 9.2 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ -127.28 (app dp, *J* = 12.6, 4.4 Hz). HRMS (ESI) m/z calc'd for C_7H_8NFCl $[M+H]^+$: 160.0329; found 160.0326.

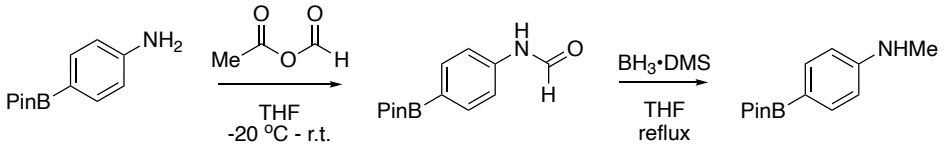


2,6-diisopropyl-*N*-methylaniline was prepared from 2,6-diisopropylaniline (1.2 g, 7 mmol, 1.0 equiv.) following *N*-methylation procedure A. Purification via flash column chromatography (SiO_2, DCM eluent) afforded the product as a clear oil (0.63 g, 3.3 mmol, 82% yield over 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 – 7.09 (m, 2H), 7.06 (app dd, *J* = 8.7, 6.3 Hz, 1H), 3.28 (hept, *J* = 6.9 Hz, 2H), 3.00 (br s, 1H), 2.75 (s, 3H), 1.26 (d, *J* = 6.9 Hz, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.93, 142.33, 123.82, 123.74, 38.66, 27.83, 24.38. HRMS (ESI) m/z calc'd for $C_{13}H_{22}N$ $[M+H]^+$: 192.1752; found 192.1758.



4-bromo-*N*-methylaniline was purchased from AA Blocks and used without further purification.

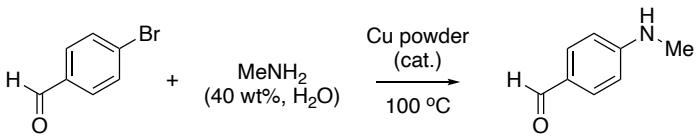
Synthesis of *N*-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline:



N-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)formamide was prepared from 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (1.8 g, 8 mmol, 1.0 equiv.) following Part 1, *N*-methylation procedure A.

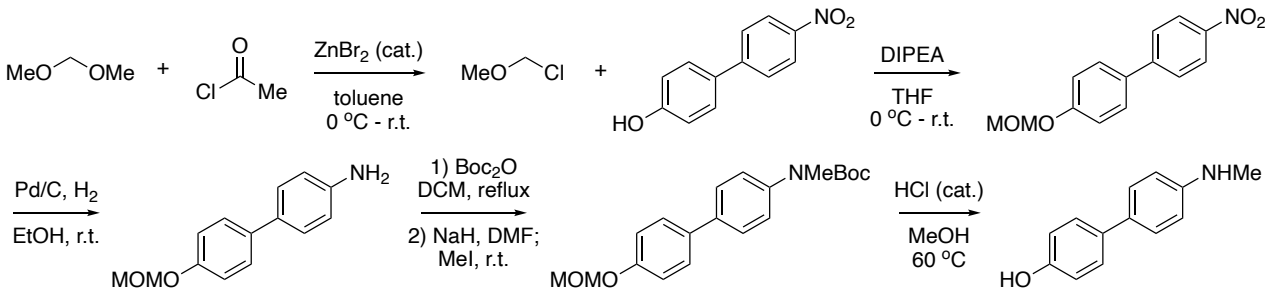
N-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline. To an oven-dried round-bottom flask equipped with a stir bar and reflux condenser was added *N*-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)formamide (8 mmol, 1.0 equiv.) and THF (10 mL, 0.8 M). The reaction flask was cooled to 0 °C and a 2.0 M solution of BH_3·DMS in THF (8 mL, 16 mmol, 2.0 equiv.) was added dropwise. Then the reaction was stirred at reflux for 16 hours. The reaction mixture was cooled to 0 °C, quenched by dropwise addition of MeOH (10 mL), and stirred for 1 hour. The reaction mixture was then concentrated under reduced pressure, azeotroping with pentane. Purification via flash chromatography (100 mL SiO_2, 10% EtOAc/Hexanes eluent) afforded the product as a white solid (0.83 g, 3.6 mmol, 45% yield over 2 steps). Spectral data were in accordance with literature values.[14] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.4 Hz, 2H), 6.58 (d, *J* = 8.4 Hz, 2H), 3.92 (br s, 1H), 2.85 (s, 3H), 1.32 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.92, 136.45, 111.57, 83.31, 30.42, 24.98. *Note: the carbon bound to boron was not observed in the ^{13}C NMR spectrum due to quadrupole broadening from B^{11} nucleus. This is consistent to what is reported in the literature.* ^{11}B NMR (161 MHz, $CDCl_3$) δ 30.84.

Synthesis of 4-(methylamino)benzaldehyde:



4-(methylamino)benzaldehyde was prepared according to the literature procedure, and spectral data were in accordance with literature values.[15]1H NMR (500 MHz, $CDCl_3$) δ 9.73 (s, 1H), 7.70 (d, J = 8.6 Hz, 2H), 6.61 (d, J = 8.4 Hz, 2H), 4.44 (br s, 1H), 2.92 (d, J = 4.5 Hz, 3H).

Synthesis of 4'-(methylamino)-[1,1'-biphenyl]-4-ol:



chloro(methoxy)methane was prepared according to a modified literature procedure.[16] To a flame-dried round-bottom flask equipped with a stir bar and an addition funnel was added dimethoxymethane (1.3 mL, 15 mmol, 1.0 equiv.), toluene (4 mL, 3.7 M), and zinc bromide (34 mg, 0.15 mmol, 0.01 equiv.). The solution was cooled to 0 °C, acetyl chloride (1.1 mL, 15 mmol, 1.0 equiv.) was added dropwise via the addition funnel over 5 minutes, and the reaction was stirred at 0 °C to room temperature for 2 h. The clear solution of chloro(methoxy)methane was used directly in the next step without manipulation. *Note: chloro(methoxy)methane is a very hazardous chemical and should be handled with extreme care.*

4-(methoxymethoxy)-4'-nitro-1,1'-biphenyl. Subsequently, a solution of 4'-nitro-[1,1'-biphenyl]-4-ol (1.3 g, 6 mmol, 0.4 equiv.) in THF (6 mL) was added in one portion to the reaction flask via the addition funnel. The addition funnel was then charged with DIPEA (2.6 mL, 15 mmol, 1.0 equiv.), which was added dropwise to the reaction mixture at 0 °C. The reaction was stirred at 0 °C to room temperature overnight. The solution was then cooled to 0 °C, diluted with EtOAc (10 mL), quenched with saturated NH_4Cl (10 mL), and let stir for 1 h. The aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (30 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (SiO_2, 5% → 10% → 15% → 20% → 25% EtOAc/Hexanes eluent) afforded the product as a light yellow solid (1.3 g, 4.8 mmol, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (app d, J = 8.9 Hz, 2H), 7.70 (app d, J = 8.9 Hz, 2H), 7.58 (app d, J = 8.8 Hz, 2H), 7.16 (app d, J = 8.8 Hz, 2H), 5.24 (s, 2H), 3.51 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.18, 147.29, 146.82, 132.41, 128.73, 127.37, 124.30, 116.96, 94.47, 56.30. HRMS (ESI) m/z calc'd for $C_{14}H_{14}NO_4$ $[M+H]^+$: 260.0923; found 260.0913.

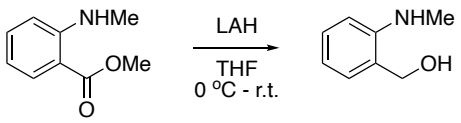
4'-(methoxymethoxy)-[1,1'-biphenyl]-4-amine. To a round-bottom flask equipped with a stir bar was added 4-(methoxymethoxy)-4'-nitro-1,1'-biphenyl (1.2 g, 4.6 mmol, 1.0 equiv.), 5 wt. % Pd/C (0.49 g, 0.23 mmol, 0.05 equiv.), EtOH (31 mL, 0.15 M), and the solution was sparged with argon for 5 minutes. Subsequently, the reaction was slowly introduced to an atmosphere of H_2 and sparged with H_2 for 5 minutes. The reaction was stirred at room temperature under H_2 (1 atm) for 22 h. The crude mixture was filtered over celite – rinsing with MeOH and EtOAc – and then concentrated under reduced pressure to afford 4'-(methoxymethoxy)-[1,1'-biphenyl]-4-amine as an off-white solid (1.01 g, 4.4 mmol, 95% yield). The material was carried forward without further purification.

tert-butyl (4'-(methoxymethoxy)-[1,1'-biphenyl]-4-yl)carbamate. To a flame-dried round-bottom flask equipped with a stir bar and a reflux condenser was added 4'-(methoxymethoxy)-[1,1'-biphenyl]-4-amine (1.0 g, 4.4 mmol, 1.0 equiv.), di-*tert*-butyl decarbonate (1.04 g, 4.8 mmol, 1.1 equiv.), and DCM (2.2 mL, 2.0 M). The reaction was heated to reflux and stirred for 21 h. The reaction was cooled to room temperature, diluted with DCM (5 mL) and quenched with water (5 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 5 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the product as a pink-white solid (1.4 g, 4.4 mmol, >99% yield). The crude was carried forward without further purification.

tert-butyl (4'-(methoxymethoxy)-[1,1'-biphenyl]-4-yl)(methyl)carbamate. To a solution of *tert*-butyl (4'-(methoxymethoxy)-[1,1'-biphenyl]-4-yl)carbamate (1.3 g, 3.9 mmol, 1.0 equiv.) in DMF (13 mL, 0.3 M) was added sodium hydride (60% dispersion in mineral oil; 0.3 g, 7.9 mmol, 2.0 equiv.) in one portion. The mixture was stirred at room temperature for 30 minutes and then methyl iodide (0.37 mL, 5.9 mmol, 1.5 equiv.) was added dropwise. The reaction stirred at room temperature for 6 h. The reaction was quenched with saturated $NaHCO_3$ (10 mL) at 0 °C and then diluted with water (5 mL) and EtOAc (20 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with water (3 x 40 mL), 50:50 water:brine (50 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude orange solid was carried forward without further purification.

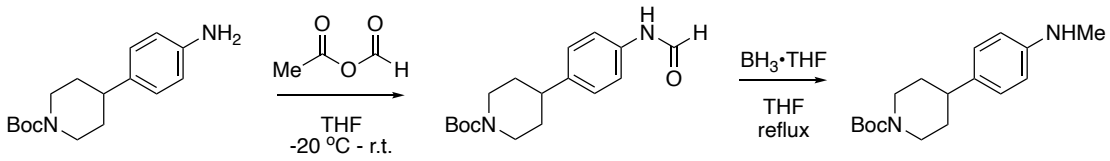
4'-(methylamino)-[1,1'-biphenyl]-4-ol. To a round-bottom flask equipped with a stir bar and reflux condenser was added *tert*-butyl (4'-(methoxymethoxy)-[1,1'-biphenyl]-4-yl)(methyl)carbamate (0.8 g, 2.3 mmol, 1.0 equiv.), MeOH (23 mL, 0.1 M), and HCl (37 wt. % in H_2O, 0.2 mL), and stirred at 60 °C for 36 h. The reaction was cooled to 0 °C, diluted with EtOAc (20 mL), and quenched slowly with saturated $NaHCO_3$ (10 mL) until the aqueous layer maintained a neutral pH. The aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (100 mL SiO_2, 10% EtOAc/Hexanes (500 mL) → 15% EtOAc/Hexanes (500 mL) → 20% EtOAc/Hexanes (500 mL) → 30% EtOAc/Hexanes (500 mL) eluent) followed by recrystallization in a mixture of Hexanes and EtOAc afforded the product as a light-yellow solid (0.3 g, 1.5 mmol, 63% yield over two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (app d, J = 8.6 Hz, 2H), 7.39 (app d, J = 8.6 Hz, 2H), 6.86 (app d, J = 8.6 Hz, 2H), 6.67 (app d, J = 8.6 Hz, 2H), 4.63 (br s, 1H), 3.75 (br s, 1H), 2.88 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.25, 148.47, 134.47, 130.08, 127.68, 127.65, 115.65, 112.86, 30.99. HRMS (ESI) m/z calc'd for $C_{13}H_{14}NO$ $[M+H]^+$: 200.1075; found 200.1075.

Synthesis of (2-(methylamino)phenyl)methanol:



(2-(methylamino)phenyl)methanol was synthesized following a modified literature procedure.[17] To a flame-dried round-bottom flask equipped with a stir bar was added lithium aluminum hydride (0.28 g, 7.5 mmol, 1.5 equiv.) and THF (12.5 mL, 0.6 M). The flask was cooled to 0 °C, a solution of methyl 2-(methylamino)benzoate (0.82 g, 5 mmol, 1.0 equiv.) in THF (3.5 mL, 1.6 M) was added dropwise, and the reaction was stirred 0 °C to room temperature overnight. The mixture was then cooled to 0 °C, quenched dropwise with EtOAc (2 mL) followed by a water (0.5 mL), filtered over celite – rinsing with EtOAc – and then concentrated under reduced pressure. Purification via flash column chromatography (100 mL SiO_2 deactivated with 2% triethylamine, 5% → 10% → 15% → 20% Acetone/Hexanes eluent) afforded (2-(methylamino)phenyl)methanol as a light yellow, sticky solid (0.53 g, 3.9 mmol, 77% yield). Spectral data were in accordance with literature values. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (app td, J = 7.6, 1.6 Hz, 1H), 7.06 (app dd, J = 7.5, 1.6 Hz, 1H), 6.71 – 6.65 (m, 2H), 4.65 (s, 2H), 2.88 (s, 3H).

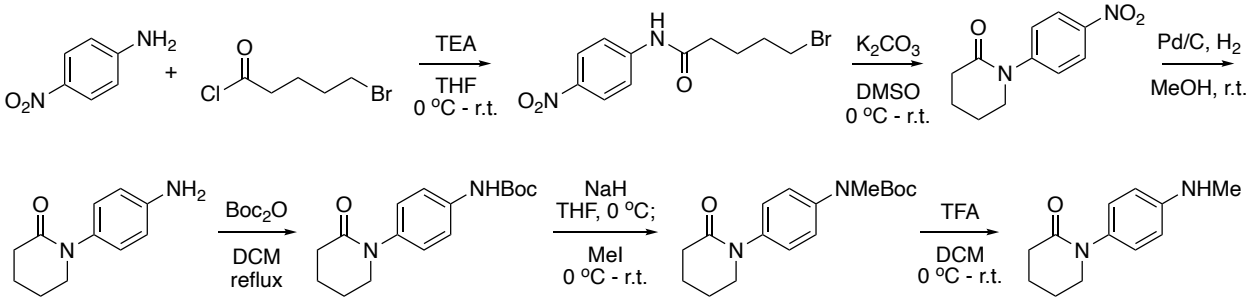
Synthesis of *tert*-butyl 4-(4-(methylamino)phenyl)piperidine-1-carboxylate:



tert-butyl 4-(4-formamidophenyl)piperidine-1-carboxylate was prepared from *tert*-butyl 4-(4-aminophenyl)piperidine-1-carboxylate (0.83 g, 3.0 mmol, 1.0 equiv.) following Part 1, *N*-methylation procedure A.

tert-butyl 4-(4-(methylamino)phenyl)piperidine-1-carboxylate. To a flame-dried flask equipped with a stir bar and a reflux condenser was added crude *tert*-butyl 4-(4-formamidophenyl)piperidine-1-carboxylate (3 mmol, 1.0 equiv.) and THF (0.5 M, 6 mL). The flask was cooled to 0 °C and a 1.0 M solution of BH_3·THF (6 mL, 6 mmol, 2.0 equiv.) was added dropwise. The reaction was subsequently heated to reflux and stirred overnight. Following consumption of the *N*-arylformamide, the reaction was cooled to 0 °C, quenched dropwise with MeOH (10 mL), and stirred for 30 min. The mixture was then concentrated under reduced pressure and azeotroped with DCM (3 x 15 mL). Purification via flash column chromatography (100 mL SiO_2, 15% → 20% EtOAc/Hexanes eluent) followed by recrystallization in a mixture of DCM and hexanes afforded *tert*-butyl 4-(4-(methylamino)phenyl)piperidine-1-carboxylate as a white solid (0.65 g, 2.3 mmol, 75% yield over 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (d, *J* = 8.5 Hz, 2H), 6.58 (d, *J* = 8.5 Hz, 2H), 4.21 (app br s, 2H), 3.62 (s, 1H), 2.82 (s, 3H), 2.82 – 2.71 (m, 2H), 2.53 (tt, *J* = 12.2, 3.5 Hz, 1H), 1.78 (app d, *J* = 13.0 Hz, 2H), 1.65 – 1.52 (m, 2H), 1.48 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.06, 147.97, 134.84, 127.59, 112.67, 79.46, 44.68, 41.92, 33.63, 31.07, 28.65. *^{1}H-^{13}C HSQC analysis confirms the weak carbon resonance at 44.68 ppm to correlate to 4 proton peaks from the piperidine ring (see spectra).* HRMS (ESI) m/z calc'd for $C_{17}H_{27}N_2O_2$ $[M+H]^+$: 291.2073; found 291.2058.

Synthesis of 1-(4-(methylamino)phenyl)piperidin-2-one:



5-bromo-N-(4-nitrophenyl)pentanamide. To a flame-dried round-bottom flask equipped with a stir bar was added 4-nitroaniline (1.8 g, 13.1 mmol, 1.0 equiv.), THF (1.0 M, 13 mL), and triethylamine (3.7 mL, 26.2 mmol, 2.0 equiv.). The reaction flask was cooled to 0 °C and 5-bromopentanoyl chloride[18] (3.9 g, 19.6 mmol, 1.5 equiv.) was added dropwise, and then stirred 0 °C to room temperature for 5.5 h. The reaction was added to a flask with ice-cold water (0 °C) and allowed to stir for 30 minutes, in which an orange solid precipitated. The solid was filtered (rinsing with cold water followed by pentane) and dried to afford 5-bromo-*N*-(4-nitrophenyl)pentanamide as a beige-orange solid, which was carried forward without further purification.

1-(4-nitrophenyl)piperidin-2-one. A solution of 5-bromo-*N*-(4-nitrophenyl)pentanamide (13.1 mmol, 1.0 equiv.), K_2CO_3 (2.0 g, 14.4 mmol, 1.1 equiv.), and DMSO (19 mL, 0.7 M) was heated to reflux and stirred for 6 hours. The reaction was then cooled to room temperature, diluted with EtOAc (20 mL), and quenched with water (20 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine (30 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (300 mL SiO_2 deactivated with 2% triethylamine, 10% Acetone/Hexanes (500 mL) → 15% Acetone/Hexanes (500 mL) → 20% Acetone/Hexanes (500 mL) → 25% Acetone/Hexanes (500 mL) → 30% Acetone/Hexanes (500 mL) → 35% Acetone/Hexanes (500 mL) eluent) afforded 1-(4-nitrophenyl)piperidin-2-one as a yellow solid (2.5 g, 11.3 mmol, 86% yield over 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (app d, J = 9.1 Hz, 2H), 7.49 (app d, J = 9.1 Hz, 2H), 3.73 (t, J = 5.8 Hz, 2H), 2.61 (t, J = 6.6 Hz, 2H), 2.05 – 1.93 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.38, 149.06, 145.35, 125.99, 124.49, 51.04, 33.26, 23.56, 21.40. HRMS (ESI) m/z calc'd for $C_{11}H_{13}N_2O_3$ $[M+H]^+$: 221.0926; found 221.0928.

1-(4-aminophenyl)piperidin-2-one. To a round-bottom flask equipped with a stir bar was added 1-(4-nitrophenyl)piperidin-2-one (1.2 g, 5.5 mmol, 1.0 equiv.) and MeOH (18 mL, 0.3 M). The solution was sparged with argon for 5 minutes and subsequently, 5 wt. % Pd/C (0.59 g, 0.28 mmol, 0.05 equiv.) was added. The reaction was slowly introduced to an atmosphere of H_2 and sparged with H_2 for 5 minutes. Afterwards, the reaction was stirred at room temperature under H_2 (1 atm) overnight. The crude mixture was filtered over celite – rinsing with MeOH – and then concentrated under reduced pressure to afford 1-(4-aminophenyl)piperidin-2-one as a white solid (0.96 g, 5.05 mmol, 92% yield). The material was carried forward without further purification.

tert-butyl (4-(2-oxopiperidin-1-yl)phenyl)carbamate. To a flame-dried round-bottom flask equipped with a stir bar and a reflux condenser was added 1-(4-aminophenyl)piperidin-2-one (0.38 g, 2 mmol, 1.0 equiv.), di-*tert*-butyl dicarbonate (0.48 g, 2.2 mmol, 1.1 equiv.), and DCM (1 mL, 2.0 M). The reaction was heated to reflux and stirred for 18 hours. The reaction was cooled to room temperature, diluted with DCM (5 mL) and quenched with water (5 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 5 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting solid was recrystallized in a mixture of DCM and hexanes to afford the product as a white solid (0.46 g, 1.6 mmol, 79% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (app d, J = 8.7 Hz, 2H), 7.16 (app d, J = 8.7 Hz, 2H), 6.51 (br s, 1H), 3.64 – 3.56 (m, 2H), 2.60 – 2.50 (m, 2H), 1.98 – 1.87 (m, 4H), 1.51 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.24, 152.85, 138.48, 136.99, 126.97, 119.39, 80.77, 51.96, 33.01, 28.47, 23.72, 21.64. HRMS (ESI) m/z calc'd for $C_{16}H_{23}N_2O_3$ $[M+H]^+$: 291.1709; found 291.1702.

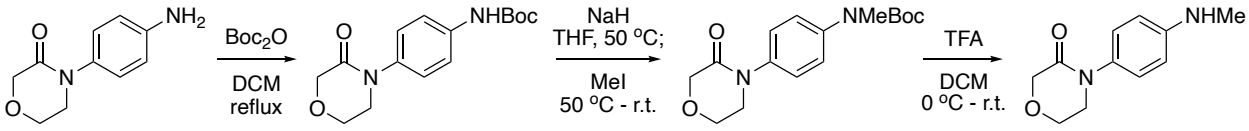
tert-butyl methyl(4-(2-oxopiperidin-1-yl)phenyl)carbamate. To a flame-dried round-bottom flask equipped with a stir bar was added *tert*-butyl (4-(2-oxopiperidin-1-yl)phenyl)carbamate (0.65 g, 2.2 mmol, 1.0 equiv.) and THF (28 mL, 0.08 M). The solution was cooled to 0 °C, sodium hydride (60% dispersion in mineral oil; 0.18 g, 4.5 mmol, 2.0 equiv.) was added in one portion, and the reaction was stirred at 0 °C for 60 minutes. Subsequently, methyl iodide (0.21 mL, 3.36 mmol, 1.5 equiv.) was added and the reaction was stirred at 0 °C to room temperature for 22 hours. Following consumption of the starting amine, the mixture was cooled to 0 °C and quenched with saturated $NaHCO_3$ (15 mL). The mixture was then diluted with EtOAc (15 mL), the aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude solid was carried forward without further purification.

1-(4-(methylamino)phenyl)piperidin-2-one. Trifluoroacetic acid (1.9 mL, 24.6 mmol, 11 equiv.) was added dropwise to a solution of *tert*-butyl methyl(4-(2-oxopiperidin-1-yl)phenyl)carbamate (2.2 mmol, 1.0 equiv.) in DCM (16 mL, 0.14 M) at 0

°C. The reaction was stirred at 0 °C to room temperature for 6 hours. 1 M NaOH was then slowly added to the mixture stirring at 0 °C until the aqueous layer maintained a neutral pH. The aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (100 mL SiO_2, 2% MeOH/DCM eluent) followed by recrystallization in a mixture of DCM and hexanes afforded 1-(4-(methylamino)phenyl)piperidin-2-one as a white solid (0.4 g, 1.9 mmol, 87% yield over 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 (app d, J = 8.8 Hz, 2H), 6.60 (app d, J = 8.8 Hz, 2H), 3.75 (br s, 1H), 3.62 – 3.54 (m, 2H), 2.83 (s, 3H), 2.59 – 2.48 (m, 2H), 1.98 – 1.84 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.30, 148.23, 133.42, 127.32, 112.92, 52.32, 33.02, 30.99, 23.82, 21.74. HRMS (ESI) m/z calc'd for $C_{12}H_{17}N_2O_2$ $[M+H]^+$: 205.1341; found 205.1340.

Note: the coupling of 4-bromo-N-methylaniline with piperidin-2-one using Ullmann cross-coupling conditions afforded inconsistent yields. We found this alternative route to be a more robust and consistent synthesis.

Synthesis of 4-(4-(methylamino)phenyl)morpholin-3-one:



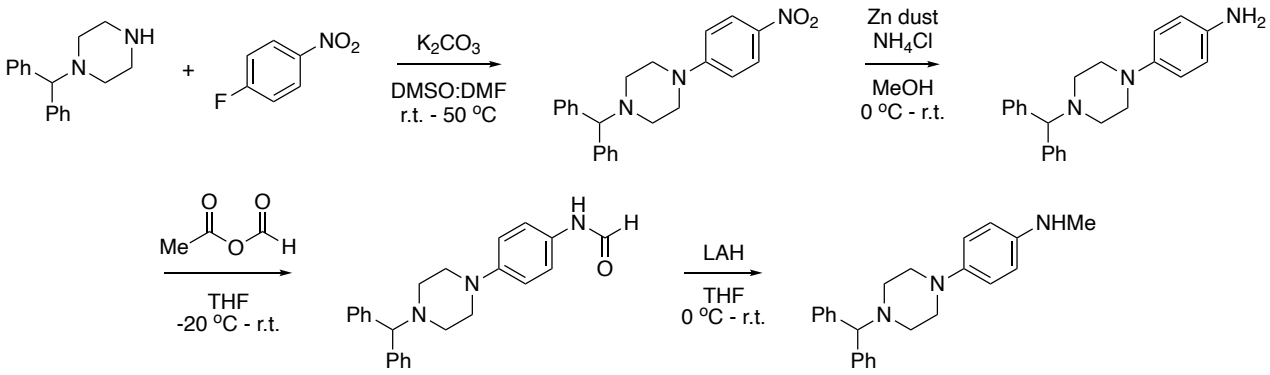
tert-butyl (4-(3-oxomorpholino)phenyl)carbamate. To a flame-dried round-bottom flask equipped with a stir bar and a reflux condenser was added 4-(4-aminophenyl)morpholin-3-one (2.3 g, 12 mmol, 1.0 equiv.), di-*tert*-butyl dicarbonate (2.9 g, 13.2 mmol, 1.1 equiv.), and DCM (6 mL, 2.0 M). The reaction was heated to reflux and stirred for 16 hours. The reaction was cooled to 0 °C, diluted with EtOH (15 mL), and stirred for 30 minutes, in which a white precipitate formed. The resulting solid was filtered, washing with EtOH, to afford the product as a white solid (3.4 g, 11.6 mmol, 97% yield), which was carried to the next step without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (app d, J = 8.8 Hz, 2H), 7.24 (app d, J = 8.8 Hz, 2H), 6.51 (br s, 1H), 4.33 (s, 2H), 4.02 (app t, J = 5.1 Hz, 2H), 3.72 (app t, J = 5.1 Hz, 2H), 1.52 (s, 9H).

tert-butyl methyl(4-(3-oxomorpholino)phenyl)carbamate. To a flame-dried round-bottom flask equipped with a stir bar was added *tert*-butyl (4-(3-oxomorpholino)phenyl)carbamate (3.2 g, 11 mmol, 1.0 equiv.) and THF (138 mL, 0.08 M). The solution was cooled to 0 °C, sodium hydride (60% dispersion in mineral oil; 0.9 g, 22 mmol, 2.0 equiv.) was added in one portion, and the reaction was then stirred at 50 °C for 2 hours. Subsequently, methyl iodide (1.0 mL, 16.5 mmol, 1.5 equiv.) was added and the reaction was stirred at 50 °C for 22 hours. Following consumption of the starting amine by crude ^{1}H NMR analysis, the mixture was cooled to 0 °C and quenched with saturated $NaHCO_3$ (50 mL). The mixture was then diluted with EtOAc (50 mL), the aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 40 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (500 mL SiO_2, 0% → 1% → 2% → 3% MeOH/DCM eluent) afforded the product as an orange-beige solid (1.9 g, 6.3 mmol, 57% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (app s, 4H), 4.34 (s, 2H), 4.03 (app t, J = 5.0 Hz, 2H), 3.74 (app t, J = 5.1 Hz, 2H), 3.26 (s, 3H), 1.47 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.85, 154.77, 142.62, 138.30, 126.25, 125.70, 80.77, 68.73, 64.29, 49.83, 37.34, 28.49.

4-(4-(methylamino)phenyl)morpholin-3-one. Trifluoroacetic acid (0.84 mL, 11 mmol, 11.0 equiv.) was added dropwise to a solution of *tert*-butyl methyl(4-(3-oxomorpholino)phenyl)carbamate (0.31 g, 1 mmol, 1.0 equiv.) in DCM (7 mL, 0.14 M) at 0 °C. The reaction was stirred at 0 °C to room temperature, monitoring via TLC. The mixture was then cooled to 0 °C and

quenched with saturated $NaHCO_3$ until the aqueous layer maintained a neutral pH. The aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (SiO_2, 0% → 1% → 2% → 3% MeOH/DCM eluent) followed by recrystallization in a mixture of DCM and hexanes afforded 4-(4-(methylamino)phenyl)morpholin-3-one as a gray-white solid (0.16 g, 0.77 mmol, 77% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (app d, *J* = 8.8 Hz, 2H), 6.62 (app d, *J* = 8.8 Hz, 2H), 4.32 (s, 2H), 4.00 (app t, *J* = 5.1 Hz, 2H), 3.80 (br s, 1H), 3.69 (app t, *J* = 5.1 Hz, 2H), 2.84 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.03, 148.60, 131.15, 126.88, 112.87, 68.77, 64.39, 50.42, 30.91. HRMS (ESI) m/z calc'd for $C_{11}H_{15}N_2O_2$ $[M+H]^+$: 207.1134; found 207.1134.

Synthesis of 4-(4-benzhydrylpiperazin-1-yl)-*N*-methylaniline:



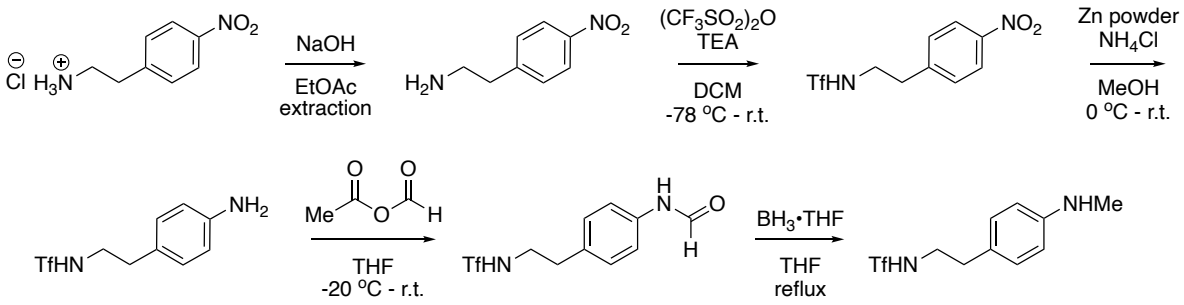
1-benzhydryl-4-(4-nitrophenyl)piperazine. To a suspension of 1-benzhydrylpiperazine (2.1 g, 8.5 mmol, 1.0 equiv.) and K_2CO_3 (1.2 g, 8.5 mmol, 1.0 equiv.) in 1:1 DMF/DMSO (12 mL each, 0.35 M) was added 1-fluoro-4-nitrobenzene (1.2 g, 8.5 mmol, 1.0 equiv.) dropwise. The reaction was stirred at room temperature for 17 h and then at 40 °C, monitoring by TLC. Following full consumption of the starting materials, the mixture was cooled to room temperature and diluted with EtOAc (20 mL) and water (15 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with water (3 x 30 mL) and 50:50 brine:water (30 mL). The organic layer was then dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting solid was recrystallized in EtOH to afford the product as a bright yellow solid (2.0 g, 5.4 mmol, 65% yield). Spectral data were in accordance with literature values.[19] ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (app d, *J* = 9.4 Hz, 2H), 7.45 (app d, *J* = 7.6 Hz, 4H), 7.30 (app t, *J* = 7.6 Hz, 4H), 7.21 (tt, *J* = 7.4, 1.3 Hz, 2H), 6.78 (app d, *J* = 9.4 Hz, 2H), 4.27 (s, 1H), 3.41 (app t, *J* = 5.1 Hz, 4H), 2.55 (app t, *J* = 5.2 Hz, 4H).

4-(4-benzhydrylpiperazin-1-yl)aniline. To suspension of 1-benzhydryl-4-(4-nitrophenyl)piperazine (1.9 g, 5.1 mmol, 1.0 equiv.) in MeOH (67 mL, 0.076 M) was added saturated NH_4Cl (aq.) (14 mL, 0.38 M). The solution was cooled to 0 °C, zinc power (3.3 g, 50.9 mmol, 10.0 equiv.) was added in one portion, and the reaction was stirred at 0 °C to room temperature for 20 h. The mixture was then filtered over a bed of celite, rinsing with MeOH. The mother liquor was concentrated under reduced pressure and subsequently transferred to a separatory funnel with EtOAc (20 mL) and H_2O (20 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with saturated $NaHCO_3$ (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (100 mL SiO_2, 0% → 1% → 2% → 4% MeOH/DCM eluent) followed by a second flash column

chromatography (50 mL SiO_2, 10% → 15% → 20% Acetone/Hexanes eluent) afforded 4-(4-benzhydrylpiperazin-1-yl)aniline as a beige solid (1.3 g, 3.9 mmol, 76% yield). Spectral data were in accordance with literature values.[19] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (app d, J = 7.4 Hz, 4H), 7.28 (app t, J = 7.7 Hz, 4H), 7.19 (app t, J = 7.4 Hz, 2H), 6.79 (app d, J = 8.8 Hz, 2H), 6.64 (app d, J = 8.8 Hz, 2H), 4.27 (s, 1H), 3.40 (br s, 2H), 3.06 (app t, J = 4.9 Hz, 4H), 2.55 (app t, J = 4.9 Hz, 4H).

4-(4-benzhydrylpiperazin-1-yl)-N-methylaniline was prepared from 4-(4-benzhydrylpiperazin-1-yl)aniline (1.2 g, 3.5 mmol, 1.0 equiv.) following *N*-methylation procedure A. Purification via flash column chromatography (150 mL SiO_2 deactivated with 2% triethylamine, 20% Acetone/Hexanes (500 mL) → 25% Acetone/Hexanes (1000 mL) eluent) afforded 4-(4-benzhydrylpiperazin-1-yl)-*N*-methylaniline as an beige-white solid (0.67 g, 1.9 mmol, 54% yield over 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (app d, *J* = 7.7 Hz, 4H), 7.28 (app t, *J* = 7.7 Hz, 4H), 7.18 (app t, *J* = 7.4 Hz, 2H), 6.85 (app d, *J* = 8.8 Hz, 2H), 6.59 (app d, *J* = 8.8 Hz, 2H), 4.27 (s, 1H), 3.44 (br s, 1H), 3.06 (app t, *J* = 4.8 Hz, 4H), 2.80 (s, 3H), 2.56 (app t, *J* = 4.8 Hz, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.85, 143.84, 142.93, 128.65, 128.10, 127.09, 76.44, 67.25, 52.30, 51.34, 31.58. HRMS (EI) m/z calc'd for $C_{24}H_{27}N_3$ $[M]^+$: 357.2205; found 357.2214.

Synthesis of 1,1,1-trifluoro-*N*-(4-(methylamino)phenethyl)methanesulfonamide (21):



2-(4-nitrophenyl)ethan-1-amine. To a separatory funnel was added 2-(4-nitrophenyl)ethan-1-amine hydrochloride (1.0 g, 5 mmol, 1.0 equiv.), EtOAc (25 mL) and a solution of 5 M NaOH (25 mL). The contents were mixed, the aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (4 x 25 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford 2-(4-nitrophenyl)ethan-1-amine, which was carried forward without further purification. *Note: the free amine is not greatly soluble in organic solvents following concentration.*

1,1,1-trifluoro-N-(4-nitrophenethyl)methanesulfonamide. To a flame-dried round-bottom flask equipped with a stir bar was added 2-(4-nitrophenyl)ethan-1-amine (5 mmol, 1.0 equiv.), DCM (17 mL, 0.3 M), and triethylamine (0.73 mL, 5.3 mmol, 1.05 equiv.). The reaction flask was cooled to -78 °C and trifluoromethanesulfonic anhydride (0.84 mL, 5 mmol, 1.0 equiv.) was added dropwise over 15 minutes. The reaction was allowed to stir at -78 °C to room temperature for 15 h. The reaction was then quenched with water (10 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (500 mL SiO_2, 5% → 15% Acetone/Hexanes eluent) afforded 1,1,1-trifluoro-*N*-(4-nitrophenethyl)methanesulfonamide as a light-orange solid (1.3 g, 4.4 mmol, 89% yield over 2 steps). *Note: performing the N-Tf protection from the amine hydrochloride salt instead of the free amine afforded significant di-Tf protection.* ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (app d, *J* = 8.7 Hz, 2H), 7.39 (app d, *J* = 8.7 Hz, 2H), 4.82 (br s, 1H), 3.62 (t, *J* = 6.9 Hz,

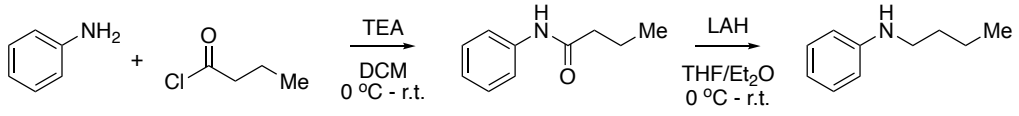
2H), 3.05 (t, J = 6.9 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.32, 144.55, 129.97, 124.30, 119.67 (q, J = 320.9 Hz), 45.00, 36.83. ^{19}F NMR (471 MHz, $CDCl_3$) δ -77.25. HRMS (ESI-TOF ES-) m/z calc'd for $C_9H_8N_2O_4SF_3$ $[M-H]^-$: 297.0157; found 297.0164.

N-(4-aminophenethyl)-1,1,1-trifluoromethanesulfonamide. To suspension of 1,1,1-trifluoro-*N*-(4-nitrophenethyl)methanesulfonamide (2.2 g, 7.2 mmol, 1.0 equiv.) in MeOH (95 mL, 0.076 M) was added saturated NH_4Cl (aq.) (19 mL, 0.38 M). The solution was cooled to 0 ºC, zinc power (4.7 g, 72.3 mmol, 10 equiv.) was added in one portion, and the reaction was stirred at 0 ºC to room temperature for 18 h. The mixture was then filtered over celite, rinsing with MeOH. The mother liquor was concentrated under reduced pressure and subsequently transferred to a separatory funnel with EtOAc (20 mL) and H_2O (20 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with saturated $NaHCO_3$ (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford *N*-(4-aminophenethyl)-1,1,1-trifluoromethanesulfonamide as a beige solid (1.9 g, 7.1 mmol, 98% yield), which was used without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.91 (app d, J = 8.3 Hz, 2H), 6.59 (app d, J = 8.3 Hz, 2H), 4.74 (br s, 1H), 3.57 (br s, 2H), 3.42 (t, J = 6.7 Hz, 2H), 2.71 (t, J = 6.7 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.61, 129.82, 126.39, 119.77 (q, J = 321.2 Hz), 115.83, 45.75, 35.72. ^{19}F NMR (471 MHz, $CDCl_3$) δ -77.32.

N-(4-(2-((trifluoromethyl)sulfonamido)ethyl)phenyl)formamide was prepared from *N*-(4-aminophenethyl)-1,1,1-trifluoromethanesulfonamide (1.8 g, 6.7 mmol, 1.0 equiv.) following Part 1, *N*-methylation procedure A.

1,1,1-trifluoro-N-(4-(methylamino)phenethyl)methanesulfonamide. To a flame-dried flask equipped with a stir bar and a reflux condenser was added crude *N*-(4-(2-((trifluoromethyl)sulfonamido)ethyl)phenyl)formamide (6.7 mmol, 1.0 equiv.) and THF (13.5 mL, 0.5 M). The flask was cooled to 0 ºC and a 1.0 M solution of BH_3·THF (13.4 mL, 13.4 mmol, 2.0 equiv.) was added dropwise. The reaction was subsequently heated to reflux and stirred overnight. Following consumption of the *N*-arylformamide, the reaction was cooled to 0 ºC, quenched dropwise with MeOH (10 mL), and stirred for 30 min. The mixture was then concentrated under reduced pressure and azeotroped with DCM (x 3). Purification via flash column chromatography (300 mL SiO_2, 5% → 25% Acetone/Hexanes eluent) afforded 1,1,1-trifluoro-*N*-(4-(methylamino)phenethyl)methanesulfonamide as a beige-tinted solid (1.0 g, 3.6 mmol, 54% yield over 3 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.01 (app d, J = 8.4 Hz, 2H), 6.59 (app d, J = 8.5 Hz, 2H), 4.70 (br s, 1H), 3.74 (br s, 1H), 3.50 (t, J = 6.6 Hz, 2H), 2.83 (s, 3H), 2.81 (t, J = 6.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.67, 129.74, 124.83, 119.78 (q, J = 321.6 Hz), 113.11, 45.81, 35.65, 30.93. ^{19}F NMR (471 MHz, $CDCl_3$) δ -77.31. HRMS (ESI) m/z calc'd for $C_{10}H_{14}N_2O_2F_3S$ $[M+H]^+$: 283.0728; found 283.0703.

Synthesis of *N*-butylaniline:



N-phenylbutyramide. Butyryl chloride (1.0 mL, 10 mmol, 1.0 equiv.) was added dropwise to a solution of aniline (0.91 mL, 10 mmol, 1.0 equiv.) and triethylamine (1.7 mL, 12.5 mmol, 1.25 equiv.) in DCM (25 mL, 0.4 M) cooled to 0 ºC. The reaction was stirred 0 ºC to room temperature and following full consumption of aniline, the solution was quenched with water

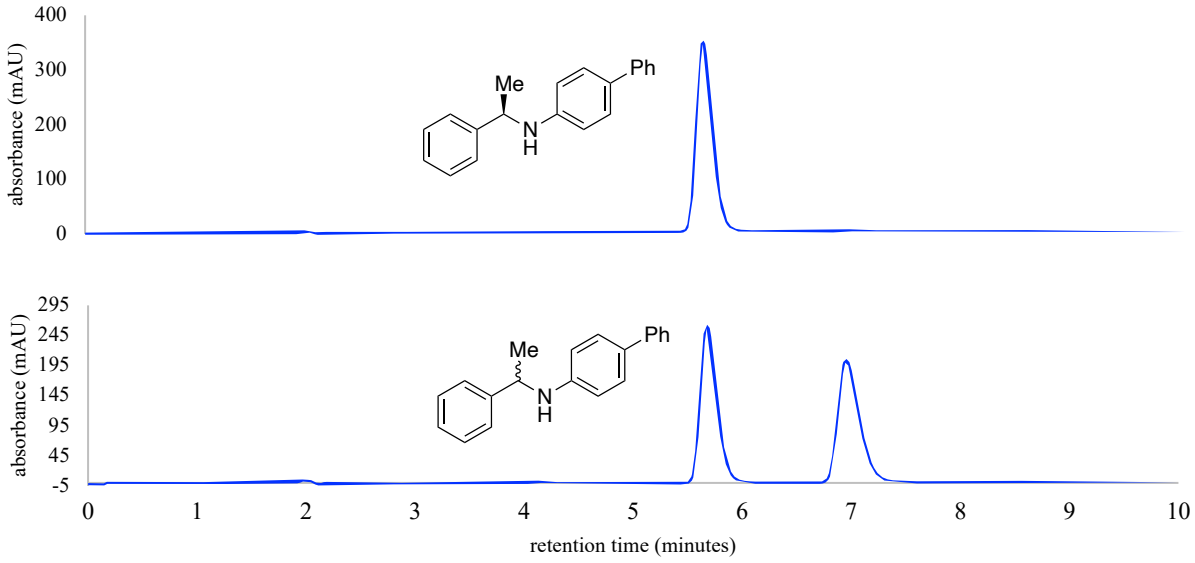
(15 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford *N*-phenylbutyramide as a white solid (1.6 g, 9.9 mmol, 99% yield), which was carried forward without further purification.

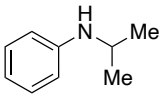
N-butylaniline. To a flame-dried flask equipped with a stir bar was added lithium aluminum hydride (0.88 g, 23.2 mmol, 2.9 equiv.) and Et_2O (24 mL, 1.0 M) The flask was cooled to 0 °C and a solution of *N*-phenylbutyramide (1.3 g, 8 mmol, 1.0 equiv.) in THF (9 mL, 0.9 M) was added dropwise. The reaction was allowed to stir at 0 °C to room temperature and upon full consumption of the amide, the reaction was cooled to 0 °C and quenched dropwise with water (0.88 mL), 15% NaOH (0.88 mL), and then water (2.6 mL). The mixture was diluted with Et_2O (20 mL), $MgSO_4$ was added, and the mixture was stirred for 30 min. The slurry was subsequently filtered over celite, rinsing with Et_2O, and solvent was concentrated under reduced pressure. Purification via flash column chromatography (SiO_2, 0% → 1% → 2% → 3% → 4% → 5% EtOAc/Hexanes eluent) afforded the product as a yellow-tinted oil (1.18 g, 7.9 mmol, 99% yield). The product was then distilled to ensure high purity. Spectral data were in accordance with literature values.[20] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (t, *J* = 7.8 Hz, 2H), 6.69 (t, *J* = 7.3 Hz, 1H), 6.61 (d, *J* = 7.9 Hz, 2H), 3.59 (br s, 1H), 3.11 (t, *J* = 7.1 Hz, 2H), 1.61 (p, *J* = 7.4 Hz, 2H), 1.44 (sext, *J* = 7.5 Hz, 2H), 0.96 (t, *J* = 7.4 Hz, 3H).

Synthesis of (*R*)-*N*-(1-phenylethyl)-[1,1'-biphenyl]-4-amine:

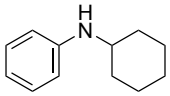
(R)-N-(1-phenylethyl)-[1,1'-biphenyl]-4-amine was prepared according to the literature procedure.[21] To a flame-dried sealed tube equipped with a stir bar was added $Pd(OAc)_2$ (56.1 mg, 0.25 mmol, 0.05 equiv.), 1,1'Bis(diphenylphosphino)ferrocene (DPPF) (0.55 g, 1 mmol, 0.2 equiv.), and NaO*t*Bu (0.6 g, 6.25 mmol, 1.3 equiv.) from the glovebox, followed by 4-bromo-1,1'-biphenyl (1.2 g, 5 mmol, 1.0 equiv.). The flask was capped with a septum, placed under vacuum, and purged with argon (x 3). (*R*)-1-phenylethan-1-amine (0.76 g, 6.25 mmol, 1.25 equiv.) and THF (5 mL, 1.0 M), both separately pre-sparged with argon for 15 minutes, were subsequently added to the reaction flask under positive argon pressure. The flask was quickly sealed and stirred overnight at 100 °C behind a blast shield. The reaction mixture was then cooled to room temperature, diluted with Et_2O, and filtered over celite, rinsing with Et_2O. The filtrate was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (SiO_2, 2% Et_2O/Hexanes eluent) afforded the product as an off-white solid (0.7 g, 2.4 mmol, 48% yield, 99% e.e.). Spectral data were in accordance with literature values. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (app d, *J* = 7.7 Hz, 1H), 7.40 (app d, *J* = 7.8 Hz, 1H), 7.38 – 7.31 (m, 3H), 7.26 – 7.21 (m, 1H), 6.59 (app d, *J* = 8.6 Hz, 1H), 4.54 (q, *J* = 6.7 Hz, 1H), 4.13 (br s, 1H), 1.55 (d, *J* = 6.7 Hz, 2H). % e.e. was determined by HPLC analysis using a Chiralcel OD-H column (10% IPA/Hexanes eluent; 1.5 mL/min flow rate). $[\alpha]^{23}_D$ = +57.23° (*c* = 0.95, $CHCl_3$).

N-(1-phenylethyl)-[1,1'-biphenyl]-4-amine. The racemic analogue was prepared using 1-phenylethan-1-amine (0.3 g, 2.5 mmol, 1.25 equiv.) and 4-bromo-1,1'-biphenyl (0.47 g, 2 mmol, 1.0 equiv.) following the same protocol. Purification via flash column chromatography (SiO_2, 2% Et_2O/Hexanes eluent) afforded the product as an off-white solid (0.32 g, 1.4 mmol, 59% yield).



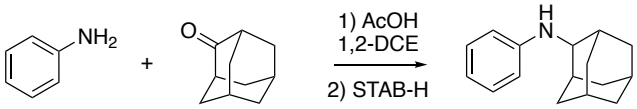


***N*-isopropylaniline** was purchased from AA Blocks and used without further purification.



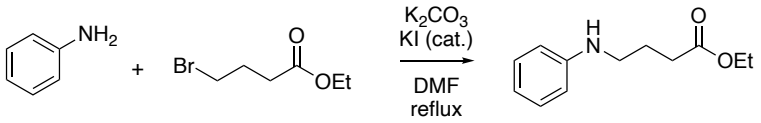
***N*-cyclohexylaniline** was purchased from Ambeed and used without further purification.

Synthesis of *N*-phenyladamantan-2-amine:



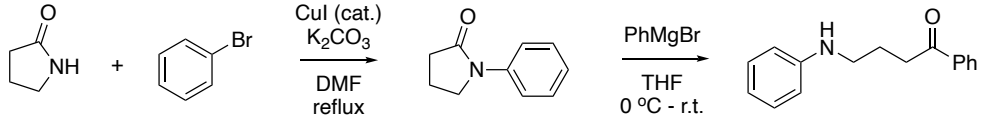
AcOH (5 mL, 1.0 M) was added dropwise to a solution of aniline (0.46 g, 5.0 mmol 1.0 equiv.) and 2-adamantanone (1.1 g, 7.5 mmol, 1.5 equiv.) in 1,2-dichloroethane (10 mL, 0.5 M), and the mixture stirred at room temperature for 1 hour. Subsequently, sodium triacetoxyborohydride (1.6 g, 7.5 mmol, 1.5 equiv.) was added portion-wise, and the reaction stirred at room temperature for 2 hours. Following consumption of the aniline starting amine, the mixture was diluted with water (15 mL) and DCM (10 mL), and NaOH pellets were slowly introduced until the aqueous layer maintained a basic pH. The aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (SiO_2, 0% → 2% → 4% → 6% → 8% → 20% Et_2O/Hexanes eluent) afforded *N*-phenyladamantan-2-amine as a white solid (1.1 g, 4.9 mmol, 98% yield). Spectral data were in accordance with literature values.[22] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (app t, J = 7.7 Hz, 2H), 6.65 (t, J = 7.3 Hz, 1H), 6.60 (app d, J = 8.1 Hz, 2H), 3.97 (br s, 1H), 3.55 (br s, 1H), 2.03 (br s, 2H), 1.96 – 1.88 (m, 5H), 1.87 – 1.81 (m, 3H), 1.76 (br s, 2H), 1.61 (d, J = 12.8 Hz, 2H). HRMS (ESI) m/z calc'd for $C_{16}H_{22}N$ $[M+H]^+$: 228.1752; found 228.1754.

Synthesis of ethyl 4-(phenylamino)butanoate:



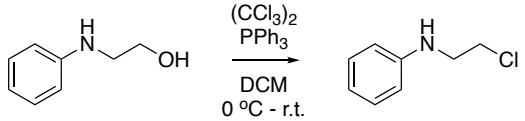
To a flame-dried round-bottom flask equipped with a stir bar and a reflux condenser was added K_2CO_3 (1.5 g, 11 mmol, 2.2 equiv.), potassium iodide (0.17 g, 1.0 mmol, 0.2 equiv.), aniline (0.5 mL, 5 mmol, 1.0 equiv.), and DMF (5 mL, 1.0 M). Ethyl 4-bromobutanoate (0.7 mL, 5 mmol, 1.0 equiv.) was added dropwise and the reaction was stirred at 60 °C for 18 h. The mixture was then cooled to room temperature, diluted with Et_2O (10 mL), and quenched with water (10 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic layers were washed with water (3 x 30 mL), 50:50 brine:water (30 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (SiO_2, 5% → 10% → 15% → 20% → 25% Et_2O/Hexanes eluent) afforded the product as a white solid (0.5 g, 2.4 mmol, 48% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (app t, J = 7.9 Hz, 2H), 6.69 (app t, J = 7.3 Hz, 1H), 6.60 (app d, J = 8.0 Hz, 2H), 4.14 (q, J = 7.2 Hz, 2H), 3.71 (br s, 1H), 3.18 (t, J = 6.9 Hz, 2H), 2.43 (t, J = 7.2 Hz, 2H), 1.95 (p, J = 7.1 Hz, 2H), 1.26 (t, J = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.59, 148.29, 129.41, 117.46, 112.84, 60.64, 43.43, 32.10, 24.83, 14.37. HRMS (ESI) m/z calc'd for $C_{12}H_{18}NO_2$ $[M+H]^+$: 208.1338; found 208.1334.

Synthesis of 1-phenyl-4-(phenylamino)butan-1-one:

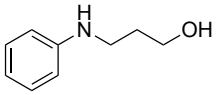


1-phenyl-4-(phenylamino)butan-1-one was prepared according to the literature procedure.[23] To a flame-dried round-bottom flask equipped with a stir bar and reflux condenser was added 1-phenylpyrrolidin-2-one[24] (0.8 g, 5.0 mmol, 1.0 equiv.) and THF (5 mL, 1.0 M). The solution was cooled to 0 °C, a freshly prepared solution of phenylmagnesium bromide (2.5 M in THF, 5.9 mmol, 1.1 equiv.) was added dropwise, and the reaction was stirred at 0 °C to room temperature for 5 h. The solution was then cooled to 0 °C, quenched with saturated NH_4Cl (10 mL), and diluted with EtOAc (20 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (250 mL SiO_2, 5% → 20% Et_2O/Hexanes eluent) afforded 1-phenyl-4-(phenylamino)butan-1-one as an off-white solid (0.71 g, 3.0 mmol, 60% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (app d, J = 8.0 Hz, 2H), 7.56 (app t, J = 7.4 Hz, 1H), 7.46 (app t, J = 7.7 Hz, 2H), 7.17 (app t, J = 7.9 Hz, 2H), 6.69 (t, J = 7.3 Hz, 1H), 6.62 (d, J = 7.9 Hz, 2H), 3.74 (br s, 1H), 3.24 (t, J = 6.8 Hz, 2H), 3.12 (t, J = 7.0 Hz, 2H), 2.09 (p, J = 7.0 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.98, 148.40, 137.02, 133.25, 129.41, 128.76, 128.17, 117.46, 112.88, 43.62, 36.22, 23.98. HRMS (ESI) m/z calc'd for $C_{16}H_{18}NO$ $[M+H]^+$: 240.1388; found 240.1390. *Note: 1-phenyl-4-(phenylamino)butan-1-one should be stored under argon in the fridge to maintain high purity and should be used within a week to afford reproducibility in the allylic amination.*

Synthesis of *N*-(2-chloroethyl)aniline:

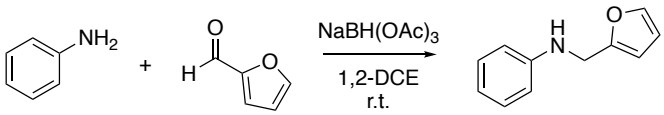


N-(2-chloroethyl)aniline was prepared according to a modified literature procedure.[25] To an oven-dried round-bottom flask equipped with a stir bar was added 2-(phenylamino)-ethan-1-ol (0.6 mL, 5.0 mmol, 1.0 equiv.) and DCM (10 mL, 0.5 M). The solution was cooled to 0 °C and hexachloroethane (1.3 g, 5.5 mmol, 1.1 equiv.) was added, followed by portion-wise addition of triphenylphosphine (1.4 g, 5.5 mmol, 1.1 equiv.). The reaction mixture was stirred at 0 °C to room temperature overnight, in which a white precipitate formed. The crude material was diluted with water (10 mL) and washed with 1 M $NaHCO_3$ (15 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 7 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (50 mL SiO_2, Hexanes (200 mL) → 5% EtOAc/Hexanes (300 mL) eluent) afforded *N*-(2-chloroethyl)aniline as a yellow oil (0.42 g, 2.68 mmol, 54% yield). Spectral data were in accordance with literature values.[26] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (app t, *J* = 7.8 Hz, 2H), 6.77 (app t, *J* = 7.4 Hz, 1H), 6.66 (app d, *J* = 8.2 Hz, 2H), 4.12 (br s, 1H), 3.70 (t, *J* = 6.0 Hz, 2H), 3.49 (t, *J* = 6.0 Hz, 2H).



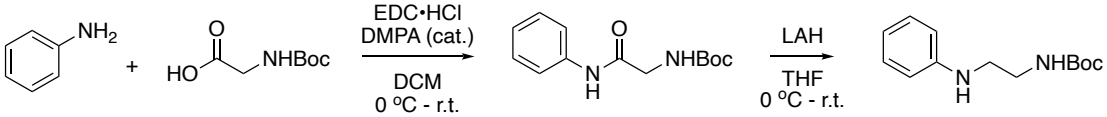
3-(phenylamino)propan-1-ol was purchased from A2B Chem and used without further purification.

Synthesis of *N*-(furan-2-ylmethyl)aniline:



N-(furan-2-ylmethyl)aniline was prepared according to the literature procedure, and spectral data were in accordance with literature values.[27] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.36 (m, 1H), 7.20 (app t, *J* = 8.0 Hz, 2H), 6.75 (app t, *J* = 7.4 Hz, 1H), 6.69 (app d, *J* = 8.0 Hz, 2H), 6.33 (dd, *J* = 3.0, 1.8 Hz, 1H), 6.25 (app d, *J* = 3.0 Hz, 1H), 4.33 (s, 2H), 4.02 (br s, 1H).

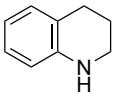
Synthesis of *tert*-butyl (2-(phenylamino)ethyl)carbamate:



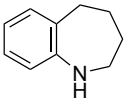
tert-butyl (2-oxo-2-(phenylamino)ethyl)carbamate. To a flame-dried round-bottom flask equipped with a stir bar was added (*tert*-butoxycarbonyl)glycine (1.1 g, 6.4 mmol, 1.06 equiv.), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (1.5 g, 7.2 mmol, 1.2 equiv.), 4-dimethylaminopyridine (0.07 g, 0.6 mmol, 0.1 equiv.), and DCM (12 mL, 0.5 M) at 0 °C, and the mixture was stirred for 15 minutes. Subsequently, aniline (0.56 g, 6 mmol, 1.0 equiv.) was added dropwise

and the reaction was stirred at 0 ºC to room temperature overnight. Following consumption of aniline, the mixture was concentrated under reduced pressure and transferred to a separatory funnel with EtOAc (20 mL) and water (20 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with 1 M HCl (2 x 20 mL), $NaHCO_3$ (2 x 20 mL), and brine, and then dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting white solid was triturated with Et_2O and carried forward without further purification (1.3 g, 5.4 mmol, 90% yield).

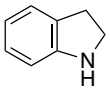
tert-butyl (2-(phenylamino)ethyl)carbamate. To a flame-dried round-bottom flask equipped with a stir bar was added lithium aluminum hydride (0.15 g, 4 mmol, 2.0 equiv.) and THF (5 mL, 0.4 M). The flask was cooled to 0 ºC, a solution of *tert*-butyl (2-oxo-2-(phenylamino)ethyl)carbamate (0.5 g, 2 mmol, 1.0 equiv.) in THF (4 mL, 0.4 M) was added dropwise, and the reaction was stirred at 0 ºC to room temperature overnight. The mixture was then cooled to 0 ºC, quenched dropwise with EtOAc (2 mL) followed by a water (0.5 mL), stirred for 30 minutes, and then filtered over celite, rinsing with EtOAc. Purification via flash column chromatography (100 mL SiO_2, 0% → 4% → 8% → 12% → 16% → 20% EtOAc/Hexanes eluent) afforded *tert*-butyl (2-(phenylamino)ethyl)carbamate as an off-white solid (0.3 g, 1.3 mmol, 65% yield). Spectral data were in accordance with literature values.[28] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (app t, J = 8.0 Hz, 2H), 6.74 (app t, J = 7.3 Hz, 1H), 6.64 (app d, J = 7.9 Hz, 2H), 4.81 and 4.51 (two br s, 1H) 3.99 (br s, 1H), 3.45 – 3.35 (m, 2H), 3.29 (t, J = 5.8 Hz, 2H), 1.48 (s, 9H).



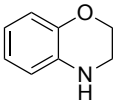
1,2,3,4-tetrahydroquinoline was purchased from a Sigma-Aldrich and purified via distillation to afford the amine as a yellow-tinted oil.



2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepine was purchased from Ambeed and used without further purification.

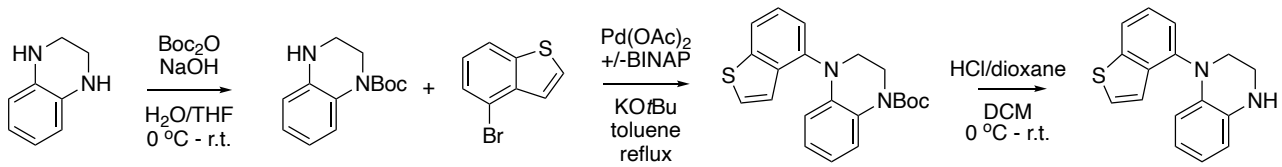


indoline was purchased from Acros Organics and purified via short-path vacuum distillation to afford the amine as a clear oil.



3,4-dihydro-2*H*-benzo[*b*][1,4]oxazine was purchased from Oakwood Chemicals and used without further purification.

Synthesis of 1-(benzo[*b*]thiophen-4-yl)-1,2,3,4-tetrahydroquinoxaline:

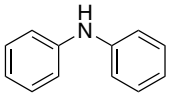


tert-butyl 3,4-dihydroquinoxaline-1(2H)-carboxylate. NaOH (0.32 g, 8 mmol, 2.0 equiv.) was added to a solution of 1,2,3,4-tetrahydroquinoxaline (0.54 g, 4 mmol, 1.0 equiv.) in THF (8 mL, 0.5 M) and H_2O (2 mL, 2.0 M), and stirred for 10 minutes. The solution was subsequently cooled to 0 ºC, di-*tert*-butyl dicarbonate (0.83 g, 3.8 mmol, 0.95 equiv.) was added

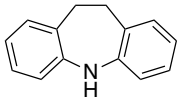
portion-wise, and the reaction was stirred at 0 °C to room temperature. Following consumption of the starting amine, the mixture was diluted with water (5 mL) and DCM (10 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (SiO_2, 5% → 10% → 15% → 20% → 25% → 30% EtOAc/Hexanes eluent) afforded the product as a gray-tinted solid (0.8 g, 3.2 mmol, 85% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 – 7.42 (m, 1H), 6.89 (t, *J* = 7.6 Hz, 1H), 6.65 (t, *J* = 7.7 Hz, 1H), 6.56 (d, *J* = 8.0 Hz, 1H), 3.95 (br s, 1H), 3.76 (app t, *J* = 5.0 Hz, 2H), 3.41 (app t, *J* = 5.0 Hz, 2H), 1.52 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.45, 136.88, 124.88, 124.79, 124.75, 116.82, 114.66, 81.06, 42.22, 41.60, 28.53. HRMS (EI) m/z calc'd for $C_{13}H_{18}N_2O_2$ $[M]^+$: 234.13683; found 234.13592.

tert-butyl 4-(benzo[b]thiophen-4-yl)-3,4-dihydroquinoxaline-1(2H)-carboxylate. To a flame-dried round-bottom flask equipped with a stir bar and a reflux condenser was added $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 0.05 equiv.), (±)-BINAP (34.3 mg, 0.055 equiv., 0.055 mmol), and potassium *tert*-butoxide (157 mg, 1.4 mmol, 1.4 equiv.) from the glovebox, followed by *tert*-butyl 3,4-dihydroquinoxaline-1(2*H*)-carboxylate (0.28 g, 1.2 mmol, 1.2 equiv.) and 4-bromobenzo[*b*]thiophene (0.21 g, 1 mmol, 1.0 equiv.). The flask was placed under vacuum and purged with argon (x 3). Toluene (1.7 mL, 0.6 M), pre-sparged with argon for 15 minutes, was added to the reaction flask, and the reaction was stirred at 100 °C for 36 hours. The crude mixture was cooled to room temperature and filtered over celite, rinsing with EtOAc, and then concentrated under reduced pressure. Purification via flash column chromatography (SiO_2, 5% → 10% EtOAc/Hexanes eluent) afforded the product as a light-yellow solid (0.26 g, 0.7 mmol, 71% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.1 Hz, 1H), 7.65 – 7.57 (m, 1H), 7.42 – 7.37 (m, 2H), 7.26 (d, *J* = 7.5 Hz, 1H), 7.15 (d, *J* = 5.5 Hz, 1H), 6.76 (ddd, *J* = 7.3, 6.8, 1.6 Hz, 1H), 6.71 (app td, *J* = 7.6, 1.5 Hz, 1H), 6.31 (dd, *J* = 8.1, 1.5 Hz, 1H), 3.99 (app t, *J* = 5.0 Hz, 2H), 3.75 (app t, *J* = 5.1 Hz, 2H), 1.57 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.44, 141.88, 141.75, 137.82, 137.68, 126.76, 125.65, 125.53, 124.64, 124.52, 122.93, 121.93, 120.84, 117.46, 115.09, 81.31, 51.04, 42.30, 28.58. HRMS (ESI) m/z calc'd for $C_{21}H_{22}N_2O_2NaS$ $[M+Na]^+$: 389.1300; found 389.1295.

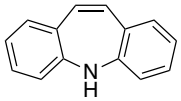
1-(benzo[b]thiophen-4-yl)-1,2,3,4-tetrahydroquinoxaline. A 4.0 M solution of HCl in dioxane (0.5 mL, 2 mmol, 4.0 equiv.) was added dropwise to a solution of *tert*-butyl 4-(benzo[*b*]thiophen-4-yl)-3,4-dihydroquinoxaline-1(2*H*)-carboxylate (183 mg, 0.5 mmol, 1.0 equiv.) in DCM (0.5 mL, 1.0 M), and the reaction was stirred at room temperature for 5 hours. The reaction was then diluted with DCM (2 mL) and quenched dropwise with 1 M NaOH until the aqueous layer maintained a neutral pH. The aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (100 mL SiO_2 deactivated with 2% triethylamine, 2% → 4% → 6% → 8% → 10% → 12% → 14% → 16% → 20% Acetone/Hexanes eluent) followed by azeotroping with pentane afforded the product as a yellow solid (0.11 g, 0.4 mmol, 83% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.1 Hz, 1H), 7.39 – 7.33 (m, 2H), 7.28 (d, *J* = 5.6 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 6.66 (app td, *J* = 7.6, 1.3 Hz, 1H), 6.62 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.48 (ddd, *J* = 7.3, 7.1, 1.7 Hz, 1H), 6.33 (dd, *J* = 8.1, 1.2 Hz, 1H), 3.89 (br s, 1H), 3.80 (app t, *J* = 4.6 Hz, 2H), 3.56 (app t, *J* = 4.7 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.30, 141.43, 136.82, 134.55, 133.64, 125.91, 125.49, 122.63, 120.92, 119.75, 119.32, 118.59, 116.37, 114.84, 49.70, 41.46. HRMS (ESI) m/z calc'd for $C_{16}H_{15}N_2S$ $[M+H]^+$: 267.0956; found 267.0950.



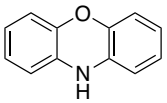
diphenylamine was purchased from Sigma-Alrich and used without further purification.



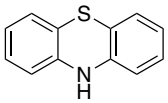
10,11-dihydro-5*H*-dibenzo[*b*,*f*]azepine was purchased from TCI America and used without further purification.



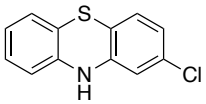
5*H*-dibenzo[*b*,*f*]azepine was purchased from Enamine and used without further purification.



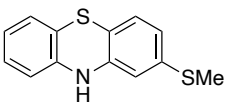
10*H*-phenoxazine was purchased from Ambeed and used without further purification. *Note: when the amine was purchased from Ambeed, the C(sp^3)H/N(sp^2) cross-coupling afforded consistent reactivity. Other vendors gave variable yields.*



10*H*-phenothiazine was purchased from Sigma-Aldrich and used without further purification.

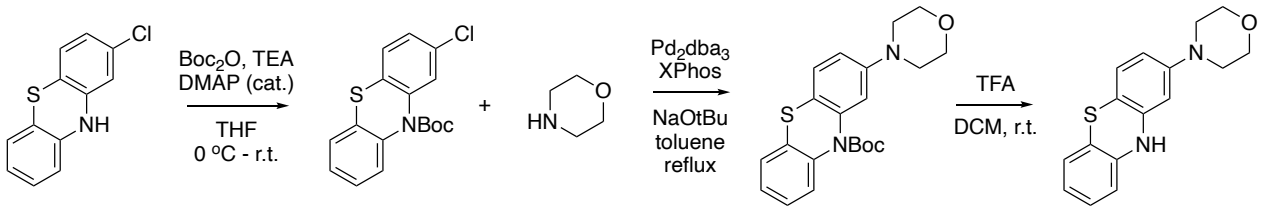


2-chloro-10*H*-phenothiazine was purchased from Oakwood Chemicals and used without further purification.



2-(methylthio)-10*H*-phenothiazine was purchased from Oakwood Chemicals and used without further purification.

Synthesis of 4-(10*H*-phenothiazin-2-yl)morpholine:



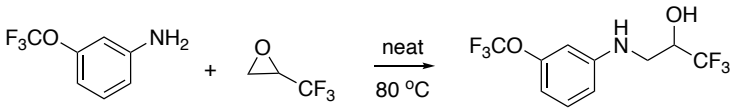
tert-butyl 2-chloro-10H-phenothiazine-10-carboxylate. To an oven-dried round-bottom flask equipped with a stir bar was added 2-chloro-10*H*-phenothiazine (0.23 g, 1 mmol, 1.0 equiv.), THF (5 mL, 0.2 M), and triethylamine (0.82 mL, 4 mmol, 4.0 equiv.). The reaction was cooled to 0 °C and a solution of Boc_2O (0.44 g, 2 mmol, 2.0 equiv.) and DMAP (1.2 mg, 0.01 mmol, 0.01 equiv.) in THF (2 mL, 0.5 M) was added dropwise. The reaction was stirred at 0 °C to room temperature overnight. The reaction was then quenched at 0 °C with water (10 mL). The aqueous layer was extracted with DCM (3 x 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting solid was recrystallized in EtOH to afford a light-purple solid (0.31 g, 0.93 mmol, 93% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 2.1 Hz, 1H), 7.50 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.33 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.28 (td, *J* = 7.5, 1.5 Hz, 1H), 7.25 (d, *J*

= 8.4 Hz, 1H), 7.17 (td, *J* = 7.6, 1.2 Hz, 1H), 7.14 (dd, *J* = 8.4, 2.2 Hz, 1H), 1.50 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.17, 139.86, 138.37, 132.42, 131.76, 130.80, 128.12, 127.61, 127.54, 127.33, 126.92, 126.43, 126.35, 82.73, 28.26.

tert-butyl 2-morpholino-10H-phenothiazine-10-carboxylate. To an oven-dried three-neck round-bottom flask equipped with a stir bar fitted with a reflux condenser was added Pd_2dba_3 (42.6 mg, 0.05 mmol, 0.05 equiv.), XPhos (44.3 mg, 0.09 mmol, 0.1 equiv.), and NaO*t*Bu (0.18 g, 1.9 mmol, 2.0 equiv.) from the glovebox, followed by the addition of 2-chloro-10*H*-phenothiazine (0.3 g, 0.93 mmol, 1.0 equiv.). The reaction flask was placed under vacuum for 5 minutes and was then purged with an argon balloon and an outlet needle for 15 minutes. In a separate flask, toluene (4.7 mL, 0.2 M) and morpholine (0.16 g, 1.86 mmol, 2.0 equiv.) were sparged with argon for 30 minutes and were then added via syringe to the reaction flask. The reaction was stirred at reflux for 18 hours. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. Purification via flash column chromatography (SiO_2, 10% → 15% → 20% → 25% EtOAc/Hexanes eluent) afforded the product as a beige solid (0.29 g, 0.7 mmol, 75% yield). Spectral data were in accordance with literature values.[29] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (app d, *J* = 8.0 Hz, 1H), 7.33 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.24 (app t, *J* = 7.5 Hz, 1H), 7.21 (d, *J* = 8.7 Hz, 1H), 7.16 – 7.10 (m, 2H), 6.75 (dd, *J* = 8.6, 2.6 Hz, 1H), 3.86 (app t, *J* = 4.8 Hz, 4H), 3.14 (app t, *J* = 4.8 Hz, 4H), 1.49 (s, 9H).

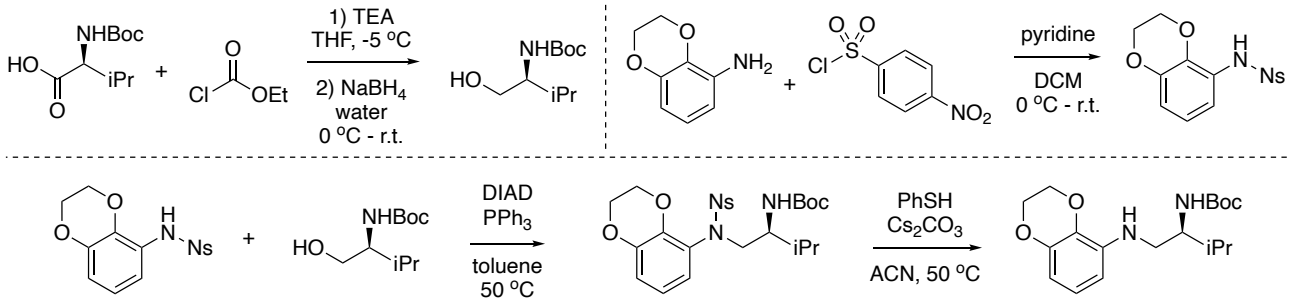
4-(10H-phenothiazin-2-yl)morpholine. To an oven-dried round-bottom flask equipped with a stir bar was added *tert*-butyl 2-morpholino-10*H*-phenothiazine-10-carboxylate (0.29 g, 0.7 mmol, 1.0 equiv.) and DCM (7 mL, 0.1 M). The reaction flask was cooled to 0 ºC and trifluoroacetic acid (1.4 mL, 18.8 mmol, 27 equiv.) was added dropwise. The reaction was taken out of the ice bath and stirred at room temperature for 24 hours. The reaction was then neutralized with careful addition of 1 M NaOH. The aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Recrystallization in a mixture of DCM and hexanes afforded the product as a white solid (127 mg, 0.45 mmol, 65 % yield). Spectral data were in accordance with literature values.[29] ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 8.47 (s, 1H), 6.97 (t, *J* = 7.8 Hz, 1H), 6.90 (d, *J* = 7.6 Hz, 1H), 6.78 – 6.70 (m, 2H), 6.67 (d, *J* = 7.9 Hz, 1H), 6.41 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.30 (d, *J* = 2.3 Hz, 1H), 3.71 (app t, *J* = 4.8 Hz, 4H), 3.00 (app t, *J* = 4.8 Hz, 4H).

Synthesis of 1,1,1-trifluoro-3-((3-(trifluoromethoxy)phenyl)amino)propan-2-ol:



1,1,1-trifluoro-3-((3-(trifluoromethoxy)phenyl)amino)propan-2-ol was prepared according to a modified procedure.[30] 3-(trifluoromethoxy)aniline (1.34 mL, 10 mmol, 2.5 equiv.) and 2-(trifluoromethyl)oxirane (0.38 mL, 4 mmol, 1.0 equiv.) were added to a sealed tube and heated at 80° C for 24 hours behind a blast shield. The product was purified via Kugelrohr distillation of the starting aniline to afford the product as a light tan solid (977 mg, 3.4 mmol, 85% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (t, *J* = 8.2 Hz, 1H), 6.64 (app d, *J* = 8.1, 1H), 6.59 (dd, *J* = 8.2, 2.0 Hz, 1H), 6.50 (app br s, 1H), 4.26 – 4.17 (m, 1H), 4.13 (br s, 1H), 3.58 (dd, *J* = 14.0, 3.6 Hz, 1H), 3.36 (dd, *J* = 14.0, 8.1 Hz, 1H), 2.54 (br s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.66 (q, *J* = 1.6 Hz), 148.66, 130.65, 124.57 (q, *J* = 282.2 Hz), 120.62 (q, *J* = 257.2 Hz), 111.85, 110.82, 106.04, 68.73 (q, *J* = 30.7 Hz), 43.47 (q, *J* = 2.2 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ -57.51, -78.42 (d, *J* = 6.9 Hz). HRMS (ESI) m/z calc'd for $C_{10}H_{10}NO_2F_6$ $[M+H]^+$: 290.0616; found 290.0616.

Synthesis of *tert*-butyl (*S*)-(1-((2,3-dihydrobenzo[*b*][1,4]dioxin-5-yl)amino)-3-methylbutan-2-yl)carbamate:



tert-butyl (S)-(1-hydroxy-3-methylbutan-2-yl)carbamate was prepared according to the literature.[31] To a flame-dried round-bottom flask equipped with a stir bar was added (*tert*-butoxycarbonyl)-*L*-valine (2.2 g, 10 mmol, 1.0 equiv.) and THF (13 mL, 0.8 M), followed by triethylamine (1.7 mL, 12 mmol, 1.2 equiv.). The solution was cooled to -5 °C, ethyl chloroformate (0.95 mL, 10 mmol, 1.0 equiv.) was added dropwise, and the reaction was stirred for 1 hour at -5 °C in which a white precipitate crashed out. The white solid was filtered and rinsed with THF. The filtrate was subsequently added dropwise to a solution of $NaBH_4$ (1 g, 25 mmol, 2. equiv.) in water (13 mL, 0.8 M) at 0 °C, and the reaction stirred at 0 °C to room temperature overnight. The solution was then diluted with DCM and water, the aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (SiO_2, 15% → 20% → 25% → 35% → 45% → 50% EtOAc/Hexanes eluent) afford the product as a clear oil (1.7 g, 8.4 mmol, 84% yield over 2 steps). Spectral data were in accordance with literature values.[31] $[\alpha]^{24}_D$ = -25.47° (*c* = 0.97, $CHCl_3$).

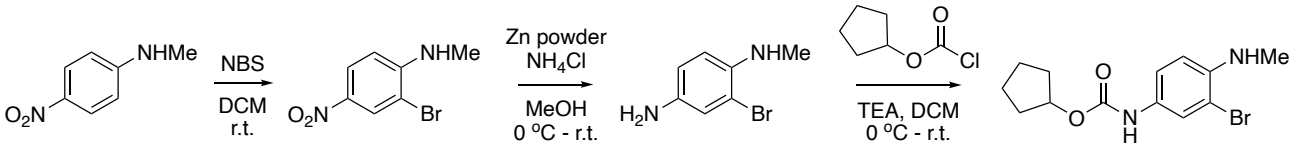
N-(2,3-dihydrobenzo[b][1,4]dioxin-5-yl)-4-nitrobenzenesulfonamide. A solution of 4-nitrobenzenesulfonyl chloride (0.66 g, 3 mmol, 1.0 equiv.) in DCM (55 mL, 0.06 M) was added dropwise to a solution of 2,3-dihydrobenzo[*b*][1,4]dioxin-5-amine (0.5 g, 3.3 mmol, 1.1 equiv.), DMAP (37 mg, 0.3 mmol, 0.1 equiv.), and pyridine (0.27 mL, 3.3 mmol, 1.1 equiv.) in DCM at 0 °C. The reaction was stirred at 0 °C to room temperature, monitoring by TLC. Following reaction completion, the crude was washed with 1 M HCl (3 x 50 mL) and then brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting solid was washed with EtOH and subsequently recrystallized in DCM to afford the product as a beige solid (0.7 g, 2.1 mmol, 70% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (app d, *J* = 8.9 Hz, 2H), 7.88 (app d, *J* = 8.9 Hz, 2H), 7.05 (dd, *J* = 8.1, 1.3 Hz, 1H), 6.78 (br s, 1H), 6.74 (t, *J* = 8.2 Hz, 1H), 6.60 (dd, *J* = 8.3, 1.4 Hz, 1H), 4.05 – 4.01 (m, 2H), 4.00 – 3.96 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.35, 144.97, 143.77, 134.76, 128.76, 124.77, 124.13, 121.41, 114.87, 114.48, 64.71, 64.08. HRMS (ESI) m/z calc'd for $C_{14}H_{13}N_2O_6S$ $[M+H]^+$: 337.0494; found 337.0492.

tert-butyl (S)-(1-((N-(2,3-dihydrobenzo[b][1,4]dioxin-5-yl)-4-nitrophenyl)sulfonamido)-3-methylbutan-2-yl)carbamate. To a flame-dried round-bottom flask equipped with a stir bar and a reflux condenser was added *N*-(2,3-dihydrobenzo[b][1,4]dioxin-5-yl)-4-nitrobenzenesulfonamide (0.75 g, 2.2 mmol, 1.0 equiv.), *tert*-butyl (*S*)-(1-hydroxy-3-methylbutan-2-yl)carbamate (0.91 g, 4.4 mmol, 2.0 equiv.), triphenylphosphine (1.2 g, 4.4 mmol, 2.0 equiv.), and toluene (22 mL, 0.1 M), and then dropwise addition of DIAD (0.88 mL, 4.4 mmol, 2.0 equiv.). The reaction was stirred at 50 °C for 3 hours, monitoring by TLC. *Note: careful monitoring of the reaction is recommended to prevent undesired byproduct formation.* The reaction mixture was then cooled to room temperature and concentrated under reduced pressure. The crude material was purified via flash column chromatography (SiO_2, 5% → 10% → 15% → 20% → 25% → 30% EtOAc/Hexanes eluent) followed

by a second flash column chromatography (SiO_2, 0% → 2% → 4% → 6% → 8% EtOAc/DCM eluent). The purified material was azeotroped with pentane (x 3) to afford the product as a light yellow solid (1.1 g, 2.1 mmol, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (app d, *J* = 8.8 Hz, 2H), 7.84 (app d, *J* = 8.8 Hz, 2H), 7.02 – 6.75 (m, 3H), 4.66 (br s, 1H), 4.10 – 3.94 (m, 2H), 3.95 – 3.27 (m, 5H), 1.81 (app br s, 1H), 1.44 and 1.38 (two s, 9H), 0.94 – 0.80 (m, 6H).

tert-butyl (S)-(1-((2,3-dihydrobenzo[b][1,4]dioxin-5-yl)amino)-3-methylbutan-2-yl)carbamate. To a flask equipped with a stir bar and a reflux condenser was added *tert*-butyl (*S*)-(1-((*N*-(2,3-dihydrobenzo[*b*][1,4]dioxin-5-yl)-4-nitrophenyl)sulfonamido)-3-methylbutan-2-yl)carbamate (1.0 g, 1.85 mmol, 1.0 equiv.), Cs_2CO_3 (1.2 g, 3.7 mmol, 2.0 equiv.), and MeCN (19 mL, 0.1 M), followed by dropwise addition of thiophenol (0.38 mL, 3.7 mmol, 1.0 equiv.). The reaction was stirred at 50 °C. Following consumption of the starting amine, the bright yellow crude mixture was filtered over celite, rinsing with EtOAc. The filtrate was concentrated under reduced pressure and subsequent purification via flash column chromatography (SiO_2, 15% Acetone/Hexanes eluent) afforded the product as a clear oil (0.59 g, 1.7 mmol, 94% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.71 (t, *J* = 8.2 Hz, 1H), 6.27 (d, *J* = 8.3 Hz, 1H), 6.22 (d, *J* = 7.9 Hz, 1H), 4.50 (br d, *J* = 9.0 Hz, 1H), 4.34 – 4.20 (m, 5H), 3.79 – 3.59 (m, 1H), 3.26 (dd, *J* = 12.4, 4.0 Hz, 1H), 3.11 – 2.94 (m, 1H), 1.95 – 1.78 (m, 1H), 1.45 (s, 9H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.46, 143.24, 138.70, 130.91, 121.21, 106.07, 103.04, 79.43, 64.48, 64.44, 55.49, 46.57, 30.44, 28.50, 19.66, 18.21. HRMS (ESI) m/z calc'd for $C_{18}H_{29}N_2O_4$ $[M+H]^+$: 337.2127; found 337.2135. *Note: the methyl protons of the isopropyl functionality are diastereotopic, with two proton (0.99 and 0.96 ppm) and two carbon (19.66 and 18.21 ppm) resonances observed.* $[\alpha]^{24}_D$ = -5.29° (*c* = 0.85, $CHCl_3$).

Synthesis of cyclopentyl (3-bromo-4-(methylamino)phenyl)carbamate (79):



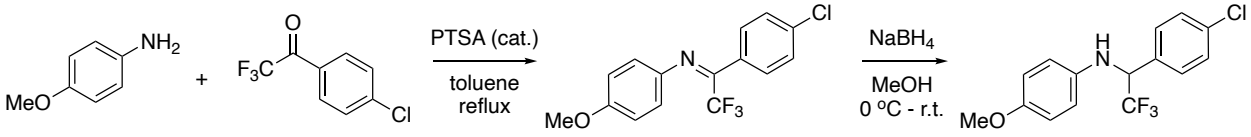
2-bromo-N-methyl-4-nitroaniline. To an oven-dried round-bottom flask equipped with a stir bar was added *N*-methyl-4-nitroaniline (1.8 g, 12 mmol, 1.0 equiv.), *N*-bromo-succinimide (2.1 g, 12 mmol, 1.0 equiv.), and DCM (48 mL, 0.25 M). The reaction was stirred for 3 hours at room temperature. The reaction was then cooled to 0 °C and quenched with saturated $Na_2S_2O_3$ (20 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 15 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification via a silica plug (20 mL SiO_2, EtOAc eluent) afforded the product as a neon yellow solid (2.77 g, 11.5 mmol, 96% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (d, *J* = 2.4 Hz, 1H), 8.14 (dd, *J* = 9.1, 2.4 Hz, 1H), 6.58 (d, *J* = 9.1 Hz, 1H), 5.17 (br s, 1H), 3.02 (d, *J* = 4.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.77, 137.83, 128.80, 125.60, 108.46, 107.76, 30.58. HRMS (ESI) m/z calc'd for $C_7H_8N_2O_2Br$ $[M+H]^+$: 230.9769; found 230.9767.

2-bromo-N^1-methylbenzene-1,4-diamine. To an oven-dried round-bottom flask equipped with a stir bar was added 2-bromo-*N*-methyl-4-nitroaniline (2.77 g, 11.5 mmol, 1.0 equiv.) and MeOH (60 mL, 0.2 M). The solution was cooled to 0 °C, saturated NH_4Cl (30 mL, 0.4 M) and zinc powder (5.9 g, 60 mmol, 5.2 equiv.) were added, and the reaction was stirred at 0 °C to room temperature for 16 hours. The reaction mixture was diluted with EtOAc (50 mL) and filtered over celite to remove the zinc powder to afford a light purple solution. The solution was transferred to a separatory funnel and the organic layer was

washed with water (2 x 20 mL), brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude was purified via flash column chromatography (80 mL SiO_2, 20% → 50% EtOAc/Hexanes eluent) to give the product as a dark red-brown oil (2.0 g, 10.1 mmol, 87% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 (d, J = 2.5 Hz, 1H), 6.64 (dd, J = 8.5, 2.5 Hz, 1H), 6.52 (d, J = 8.5 Hz, 1H), 3.46 (br s, 3H), 2.84 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.60, 137.97, 120.15, 116.34, 112.26, 110.60, 31.55. HRMS (EI) m/z calc'd for $C_7H_9N_2Br$ $[M]^+$: 199.9949; found 199.9943.

cyclopentyl (3-bromo-4-(methylamino)phenyl)carbamate. To an oven-dried round-bottom flask equipped with a stir bar was added 2-bromo-4-amino-*N*-methylaniline (2.0 g, 10.1 mmol, 1.0 equiv.) and DCM (40 mL, 0.25 M). The reaction flask was cooled to 0 °C and stirred for 10 minutes and subsequently, cyclopentyl carbonochloridate (1.5 g, 10.1 mmol, 1.0 equiv.) was added dropwise. The dark-red solution was stirred at 0 °C to room temperature for 24 hours. The reaction mixture was then brought to a neutral pH upon addition of 1 M HCl. The aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 15 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (100 mL SiO_2, 5% EtOAc/Hexanes (400 mL) → 10% EtOAc/Hexanes (300 mL) → 15% EtOAc/Hexanes (300 mL) eluent) afforded cyclopentyl (3-bromo-4-(methylamino)phenyl)carbamate as a tan-brown solid (2.1 g, 6.4 mmol, 64% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (app br s, 1H), 7.18 – 7.12 (br m, 1H), 6.56 (d, J = 8.7 Hz, 1H), 6.28 (app br s, 1H), 5.23 – 5.12 (m, 1H), 4.18 (br s, 1H), 2.87 (d, J = 4.8 Hz, 3H), 1.93 – 1.82 (m, 2H), 1.82 – 1.67 (m, 4H), 1.66 – 1.58 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.05, 142.60, 128.43, 124.10, 120.33, 110.63, 109.26, 77.84, 32.77, 30.88, 23.68. HRMS (ESI) m/z calc'd for $C_{13}H_{18}N_2O_2Br$ $[M+H]^+$: 313.0552; found 313.0549.

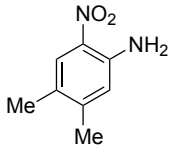
Synthesis of *N*-(1-(4-chlorophenyl)-2,2,2-trifluoroethyl)-4-methoxyaniline:



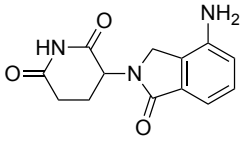
(Z)-1-(4-chlorophenyl)-2,2,2-trifluoro-N-(4-methoxyphenyl)ethan-1-imine was prepared according to the literature procedure,[32] and was carried forward without purification.

N-(1-(4-chlorophenyl)-2,2,2-trifluoroethyl)-4-methoxyaniline. To a flame-dried round-bottom flask equipped with a stir bar was added crude (*Z*)-1-(4-chlorophenyl)-2,2,2-trifluoro-*N*-(4-methoxyphenyl)ethan-1-imine (5 mmol, 1.0 equiv.) and MeOH (13 mL, 0.4 M). The mixture was cooled to 0 °C, $NaBH_4$ (0.38 g, 10 mmol, 2.0 equiv.) was added in one portion, and the reaction was stirred at 0 °C to room temperature for 12 hours. The reaction mixture was then cooled to 0 °C and quenched with 1 M HCl (10 mL). The mixture was diluted with EtOAc (20 mL) and 1 M NaOH was slowly added until the aqueous layer maintained a neutral pH. The aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (SiO_2, 5% → 10% EtOAc/Hexanes eluent) afforded *N*-(1-(4-chlorophenyl)-2,2,2-trifluoroethyl)-4-methoxyaniline as a yellow oil (1.48 g, 4.7 mmol, 94% yield over 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 – 7.34 (m, 4H), 6.74 (app d, J = 8.9 Hz, 2H), 6.57 (app d, J = 8.9 Hz, 2H), 4.79 (app p, J = 7.2 Hz, 1H), 4.05 (br d, J = 6.9 Hz, 1H), 3.72 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.60, 139.18, 135.23, 132.89, 129.48, 129.28, 124.97 (q, J = 281.8

Hz), 115.90, 115.01, 61.29 (q, J = 29.7 Hz), 55.78. ^{19}F NMR (471 MHz, $CDCl_3$) δ -74.07 (d, J = 7.4 Hz). HRMS (ESI) m/z calc'd for $C_{15}H_{14}NOF_3Cl$ $[M+H]^+$: 316.0716; found 316.0714.

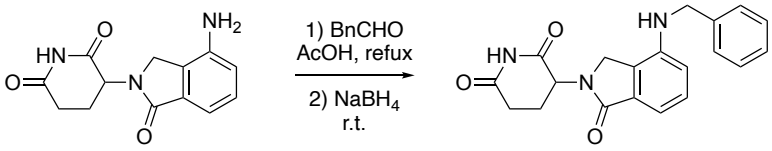


4-methyl-6-nitrobenzene-1,3-diamine was purchased from Sigma-Aldrich and used without additional purification.



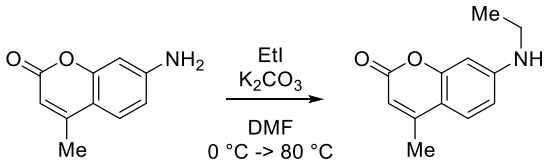
3-(4-amino-1-oxoisoindolin-2-yl)piperidine-2,6-dione was purchased from Ambeed and used without further purification.

Synthesis of 3-(4-(benzylamino)-1-oxoisoindolin-2-yl)piperidine-2,6-dione:



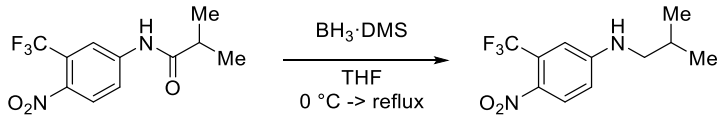
3-(4-(benzylamino)-1-oxoisoindolin-2-yl)piperidine-2,6-dione was synthesized following a modified literature procedure.[33] 3-(4-amino-1-oxoisoindolin-2-yl)piperidine-2,6-dione (1.3 g, 5 mmol, 1.0 equiv.), acetic acid (50 mL, 0.1 M), and benzaldehyde (0.51 mL, 5 mmol, 1.0 equiv.) were added to a flame-dried round-bottom flask equipped with a stir bar and a reflux condenser, and stirred at reflux for 2 hours. Subsequently, the mixture was cooled to room temperature and $NaBH_4$ (0.2 g, 5.5 mmol, 1.1 equiv.) was added in one portion. The reduction was allowed to stir at room temperature overnight in which a beige solid crashed out. The suspension was filtered and rinsed with acetic acid followed by cold ethyl acetate and then hexanes to afford 3-(4-(benzylamino)-1-oxoisoindolin-2-yl)piperidine-2,6-dione as an off-white solid (1.05 g, 3 mmol, 60% yield). Spectral data were in accordance with literature values.[33] ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.01 (s, 1H), 7.38 (d, J = 7.6 Hz, 2H), 7.32 (t, J = 7.6 Hz, 2H), 7.26 – 7.16 (m, 2H), 6.92 (d, J = 7.4 Hz, 1H), 6.64 (d, J = 8.0 Hz, 1H), 6.37 (t, J = 5.9 Hz, 1H), 5.12 (dd, J = 13.3, 5.1 Hz, 1H), 4.39 (d, J = 5.9 Hz, 2H), 4.31 (d, J = 17.2 Hz, 1H), 4.20 (d, J = 17.2 Hz, 1H), 2.93 (ddd, J = 17.4, 13.7, 5.3 Hz, 1H), 2.62 (app d, J = 17.1 Hz, 1H), 2.32 (qd, J = 13.3, 4.5 Hz, 1H), 2.11 – 1.99 (m, 1H).

Synthesis of 7-(ethylamino)-4-methyl-2*H*-chromen-2-one:



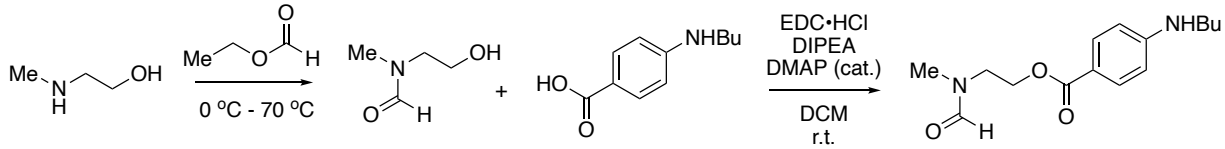
7-(ethylamino)-4-methyl-2H-chromen-2-one was prepared according to the literature procedure, and the spectral data were in accordance with literature values.[34] ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.43 (d, J = 8.7 Hz, 1H), 6.61 (t, J = 5.2 Hz, 1H), 6.59 (dd, J = 8.8, 2.3 Hz, 1H), 6.37 (d, J = 2.3 Hz, 1H), 5.90 (q, J = 1.2 Hz, 1H), 3.11 (qd, J = 7.2, 5.2 Hz, 2H), 2.30 (d, J = 1.1 Hz, 3H), 1.17 (t, J = 7.2 Hz, 3H).

Synthesis of *N*-isobutyl-4-nitro-3-(trifluoromethyl)aniline:



To a flame-dried flask equipped with a stir bar and a reflux condenser was added *N*-(4-nitro-3-(trifluoromethyl)phenyl)isobutyramide (2.76 g, 10 mmol, 1.0 equiv.) and THF (0.3 M, 34 mL). The flask was cooled to 0 ºC and a 2.0 M solution of BH_3·DMS (10 mL, 20 mmol, 2.0 equiv.) was added dropwise. The reaction was subsequently heated to reflux and stirred overnight. Following consumption of the *N*-arylbutyramide, the reaction was cooled to 0 ºC, quenched dropwise with MeOH (10 mL), and stirred for 30 minutes. The mixture was then concentrated under reduced pressure and azeotroped with pentane (3 x). Purification via flash column chromatography (100 mL SiO_2, 10% Acetone/Hexanes eluent) afforded the product as a bright yellow solid (2.37 g, 9.0 mmol, 90% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 9.1 Hz, 1H), 6.88 (d, *J* = 2.7 Hz, 1H), 6.64 (dd, *J* = 9.1, 2.7 Hz, 1H), 4.66 (br s, 1H), 3.05 (dd, *J* = 6.7, 5.7 Hz, 2H), 1.93 (h, *J* = 6.7 Hz, 1H), 1.02 (d, *J* = 6.7 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.02, 136.34, 129.24, 126.72 (q, *J* = 33.0 Hz), 122.29 (q, *J* = 273.2 Hz), 112.36, 111.14 (q, *J* = 6.2 Hz), 51.07, 28.03, 20.28. ^{19}F NMR (471 MHz, $CDCl_3$) δ -60.21. HRMS (ESI) m/z calc'd for $C_{11}H_{14}N_2O_2F_3$ $[M+H]^+$: 263.1007; found 263.1008.

Synthesis of 2-(*N*-methylformamido)ethyl 4-(butylamino)benzoate:

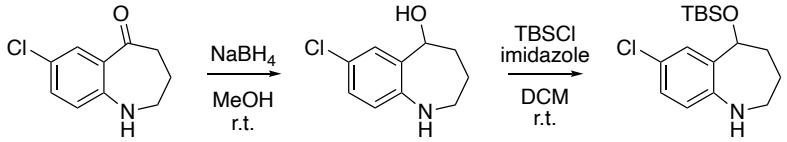


N-(2-hydroxyethyl)-N-methylformamide. To a flame-dried round-bottom flask equipped with a stir bar and a reflux condenser was added 2-(methylamino)ethan-1-ol (1.6 mL, 20 mmol, 1.0 equiv.) and ethyl formate (2.4 mL, 30 mmol, 1.5 equiv.) at 0 °C. The mixture was then heated at reflux for 24 h. The crude material was directly purified via flash column chromatography (100 mL SiO_2, 10% MeOH/DCM eluent) and azeotroped with pentane at low temperatures to afford *N*-(2-hydroxyethyl)-*N*-methylformamide as a colorless oil (1.99 g, 19.3 mmol, 96% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (s, 0.44H), 8.03 (s, 0.55H), 3.79 (t, *J* = 5.3 Hz, 0.89H), 3.73 (t, *J* = 5.1 Hz, 1.08H), 3.50 (t, *J* = 5.3 Hz, 0.9H), 3.36 (d, *J* = 5.1 Hz, 1.1H), 3.03 (s, 1.37H), 2.89 (s, 1.67H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.06, (163.67), 60.68 (59.07), 52.18, (47.96), 36.04, (30.02). HRMS (ESI) m/z calc'd for $C_4H_{10}NO_2$ $[M+H]^+$: 104.0712; found 104.0712. *Note: Rotamers induced by the N-formyl group account for a doubling of the resonances in both the ^{1}H and ^{13}C NMR spectra.*

2-(N-methylformamido)ethyl 4-(butylamino)benzoate. To a flame-dried round-bottom flask fitted with a stir bar was added 4-(butylamino)benzoic acid (870 mg, 4.5 mmol, 1.0 equiv.), anhydrous DCM (5 mL, 1.0 M), EDC·HCl (1.3 g, 6.8 mmol, 1.5 equiv.), DMAP (55 mg, 0.45 mmol, 0.1 equiv.), and DIPEA (2.8 mL, 15.8 mmol, 3.5 equiv.). The mixture was stirred at room temperature for 15 minutes, then *N*-(2-hydroxyethyl)-*N*-methylformamide (700 mg, 6.8 mmol 1.5 equiv.) was added as a solution in DCM (1 mL). The reaction was stirred at room temperature for 48 h, tracking by TLC. Upon consumption of the

carboxylic acid, the mixture was diluted with DCM (20 mL), transferred to a separatory funnel, and subsequently washed with 1 M HCl (3 x 10 mL), 2 M NaOH (3 x 10 mL), brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (100 mL SiO_2, 20% EtOAc/Hexanes (500 mL) → 40% EtOAc/Hexanes (500 mL) → 80% EtOAc/Hexanes (500 mL) eluent) afforded the product as a white crystalline solid (808 mg, 2.9 mmol, 65% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (s, 0.61H), 8.08 (s, 0.39H), 7.83 (app d, *J* = 8.7 Hz, 0.76H), 7.80 (app d, *J* = 8.7 Hz, 1.25H), 6.57 – 6.45 (m, 2H), 4.41 (t, *J* = 5.4 Hz, 0.78H), 4.37 (t, *J* = 5.2 Hz, 1.23H), 4.16 (br s, 1H), 3.71 (t, *J* = 5.4 Hz, 0.79H), 3.58 (t, *J* = 5.2 Hz, 1.24H), 3.16 (t, *J* = 7.1 Hz, 2H), 3.05 (s, 1.17H), 2.96 (s, 1.83H), 1.61 (p, *J* = 7.3 Hz, 2H), 1.43 (sext, *J* = 7.4 Hz, 2H), 0.96 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.66, (166.48), 163.13, (162.98), 152.63, (152.48), 131.82, 117.54, (117.06), 111.52, (111.48), 61.56, (60.64), 48.86, (43.67), 43.16, (43.14), 35.74, (30.12), 31.50, (31.48), 20.33, 13.97. HRMS (ESI) m/z calc'd for $C_{15}H_{22}N_2O_3Na$ $[M+Na]^+$: 301.1528; found 301.1528. *Note: Rotamers are apparent in both the ^{1}H and ^{13}C spectra as a result of the N-formyl group. The pairing of carbon resonances was validated by ^{1}H-^{13}C-HSQC analysis (see spectra).*

Synthesis of 5-((*tert*-butyldimethylsilyl)oxy)-7-chloro-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepine:

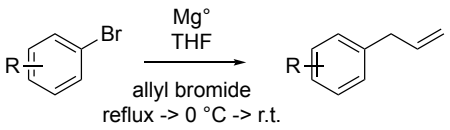


7-chloro-2,3,4,5-tetrahydro-1H-benzo[b]azepin-5-ol. $NaBH_4$ (0.15 g, 4 mmol, 2.0 equiv.) was added portion-wise to a solution of 7-chloro-1,2,3,4-tetrahydro-5*H*-benzo[*b*]azepin-5-one (0.39 g, 2 mmol, 1.0 equiv.) in MeOH (20 mL, 0.1 M), and the reaction was stirred at room temperature for 1 hour. The mixture was then cooled to 0 °C and quenched with dropwise addition of saturated NH_4Cl (15 mL) and diluted with DCM (15 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (SiO_2, 15% Acetone/Hexanes eluent) afforded the product as a white solid (0.39 g, 1.9 mmol, 98% yield). Spectral data were in accordance with literature values.[35]

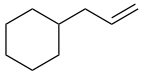
5-((tert-butyldimethylsilyl)oxy)-7-chloro-2,3,4,5-tetrahydro-1H-benzo[b]azepine. tert-Butyldimethylsilyl chloride (0.43 g, 2.9 mmol, 1.5 equiv.) was added in one portion to a solution of 7-chloro-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-5-ol (0.38 g, 1.9 mmol, 1.0 equiv.) and imidazole (0.26 g, 3.8 mmol, 2.0 equiv.) in DCM (4 mL, 0.5 M), and the reaction was stirred at room temperature for 6 hours. Following consumption of the starting amine, the reaction was then diluted with DCM (15 mL) and water (10 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (SiO_2, 0% → 20% Acetone/Hexanes eluent) afforded the product as a white solid (0.57 g, 1.8 mmol, 96% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 2.5 Hz, 1H), 7.00 (dd, *J* = 8.2, 2.5 Hz, 1H), 6.64 (d, *J* = 8.2 Hz, 1H), 4.69 (app d, *J* = 10.3 Hz, 1H), 3.68 (br s, 1H), 3.26 (dt, *J* = 12.7, 3.9 Hz, 1H), 2.72 – 2.60 (m, 1H), 2.03 – 1.96 (m, 1H), 1.87 – 1.77 (m, 2H), 1.64 – 1.55 (m, 1H), 0.95 (s, 9H), 0.09 (s, 3H), 0.06 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.91, 138.39, 126.76, 126.70, 126.36, 120.90, 72.76, 48.02, 36.50, 27.98, 26.05, 18.48, -4.77. HRMS (ESI) m/z calc'd for $C_{16}H_{27}NOSiCl$ $[M+H]^+$: 312.1550; found 312.1560.

4.2. Synthesis and characterization of electrophile starting materials.

Aryl Allylation Procedure:[36]

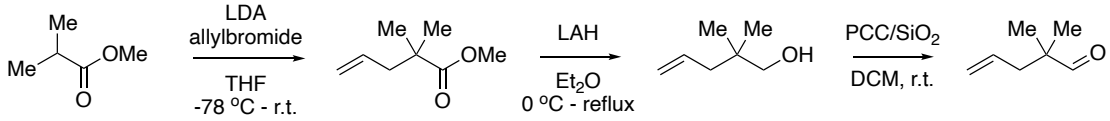


A round-bottom flask containing magnesium turnings (1.2 equiv.) and equipped with a stir bar and reflux condenser was flame-dried under vacuum then allowed to cool to room temperature. A single crystal of I_2 was added under an atmosphere of N_2, followed by anhydrous THF (2.0 M). A solution of arylbromide (1.0 equiv.) in anhydrous THF (2.0 M) was added portion-wise, allowing the Grignard reagent to initiate and reach a steady reflux. Upon consumption of the starting material (tracked by titration against I_2), the reaction was cooled to room temperature and the solids were allowed to settle. The Grignard was transferred dropwise by syringe to a flame-dried round-bottom flask equipped with a stir bar containing a solution of allyl bromide (3.0 equiv.) in anhydrous THF (0.25 M) at 0 °C. The reaction was warmed to room temperature over 4 hours and then diluted with Et_2O and quenched with water. The organic and aqueous layers were separated, and the aqueous phase was extracted with Et_2O (x 3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography afforded the allylbenzene derivative.



allylcyclohexane was purchased from TCI America and used without additional purification.

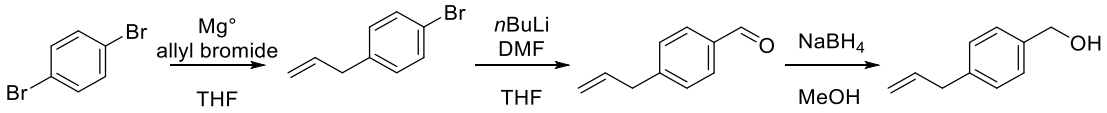
Synthesis of 2,2-dimethylpent-4-enal:



2,2-dimethylpent-4-en-1-ol was prepared according to the literature procedure and spectral data were in accordance with literature values.[37] ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.92 – 5.77 (m, 1H), 5.10 – 5.01 (m, 2H), 3.33 (d, J = 5.8 Hz, 2H), 2.02 (d, J = 7.5 Hz, 2H), 1.39 (t, J = 3.3 Hz, 1H), 0.89 (s, 6H).

2,2-dimethylpent-4-enal was prepared using a modified literature procedure.[38] To a flame dried round-bottom flask equipped with a stir bar was added pyridinium chlorochromate (1.9 g, 8.8 mmol, 2.0 equiv.) and silica gel (2.4 g, 1.5:1 w/w to PCC). The solid mixture was rapidly stirred under a N_2 atmosphere to disperse the reagent, and then anhydrous DCM (20 mL) was added to afford a heterogeneous suspension. 2,2-dimethylpent-4-en-1-ol (502 mg, 4.4 mmol, 1.0 equiv.) was added as a solution in DCM (5 mL) and vigorously stirred at room temperature overnight. The reaction mixture was then filtered over a plug of silica, eluting with DCM, and the filtrate was concentrated in vacuo at low temperatures to produce 2,2-dimethylpent-4-enal as a colorless oil (229 mg, 2 mmol, 56% yield). The spectral data were in accordance with literature values.[38] ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.48 (s, 1H), 5.71 (ddt, J = 16.8, 10.4, 7.4 Hz, 1H), 5.11 – 5.03 (m, 2H), 2.22 (dt, J = 7.5, 1.2 Hz, 2H), 1.06 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.10, 133.29, 118.63, 45.89, 41.60, 21.32. *Note: This olefin was found to decompose quickly, and its purity should be checked by ^{1}H NMR prior to use.*

Synthesis of 4-allylbenzaldehyde and (4-allylphenyl)methanol:

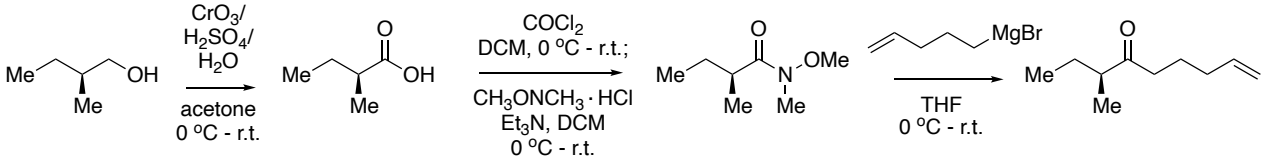


1-allyl-4-bromobenzene was prepared according to the aryl allylation procedure and 5.0 mmol of 1,4-dibromobenzene was used as the limiting reagent. Purification via flash column chromatography (300 mL SiO_2, Hexanes eluent) afforded the product as a clear oil (749 mg, 3.8 mmol, 76% yield). The spectral data were in accordance with literature values.[36] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (app d, *J* = 8.3 Hz, 2H), 7.07 (app d, *J* = 8.3 Hz, 2H), 5.93 (ddtd, *J* = 16.9, 10.3, 6.7, 1.0 Hz, 1H), 5.12 – 5.04 (m, 2H), 3.34 (d, *J* = 6.6 Hz, 2H).

4-allylbenzaldehyde. To a flame-dried round-bottom flask equipped with a stir bar was added 1-allyl-4-bromobenzene (1.1 g, 5.6 mmol, 1.0 equiv.) and anhydrous THF (4 mL, 1.3 M). The flask was cooled to -78 °C and *n*BuLi (4.1 mL, 6.2 mmol, 1.1 equiv., 1.5 M solution in hexanes) was added dropwise. The reaction was stirred for 30 minutes at -78 °C and subsequently, anhydrous DMF (0.5 mL, 6.2 mmol, 1.1 equiv.) was added dropwise. The reaction was allowed to warm to room temperature over 3 hours and then quenched with water. The layers were separated, and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (150 mL SiO_2, Hexanes (200 mL) → 1% EtOAc/Hexanes (200 mL) → 2% EtOAc/Hexanes (200 mL) → 5% EtOAc/Hexanes (400 mL) → 10% EtOAc/Hexanes (200 mL) eluent) afforded the product as a clear oil (601 mg, 4.1 mmol, 73% yield). The spectral data were in accordance with literature values.[39] ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.82 (app d, *J* = 8.1 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 5.96 (ddt, *J* = 16.8, 10.1, 6.7 Hz, 1H), 5.15 – 5.09 (m, 1H), 3.47 (d, *J* = 6.7 Hz, 2H).

(4-allylphenyl)methanol was prepared according to the literature procedure,[40] and the spectral data were in accordance with literature values.[41] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 7.9 Hz, 2H), 7.19 (d, *J* = 7.9 Hz, 2H), 5.96 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.13 – 5.04 (m, 2H), 4.67 (s, 2H), 3.39 (d, *J* = 6.7 Hz, 2H).

Synthesis of (*S*)-3-methylnon-8-en-4-one:



(S)-2-methylbutanoic acid. The Jones reagent was prepared by dissolving CrO_3 (3.3 g, 33 mmol, 1.65 equiv.) in H_2O (6 mL) in a round-bottom flask equipped with a stir bar followed by dropwise addition of concentrated H_2SO_4 (3.2 mL) at 0 °C. The reagent was stirred for 30 minutes, forming a deep red color, then transferred dropwise to a solution of (*S*)-2-methylbutan-1-ol (1.76 g, 20 mmol, 1.0 equiv.) in acetone (20 mL, 0.1 M) at 0 °C. The mixture was stirred for 2 hours, quenched by dropwise addition of isopropanol (4 mL), and then extracted with Et_2O (3 x 20 mL). The combined organic layers were washed with 1 M HCl (2 x 20 mL), brine (20 mL), dried over Na_2SO_4, filtered, and then concentrated under reduced pressure at low temperatures. Purification via flash column chromatography (100 mL SiO_2, Pentane (100 mL) → 10% Et_2O/Pentane (200 mL)

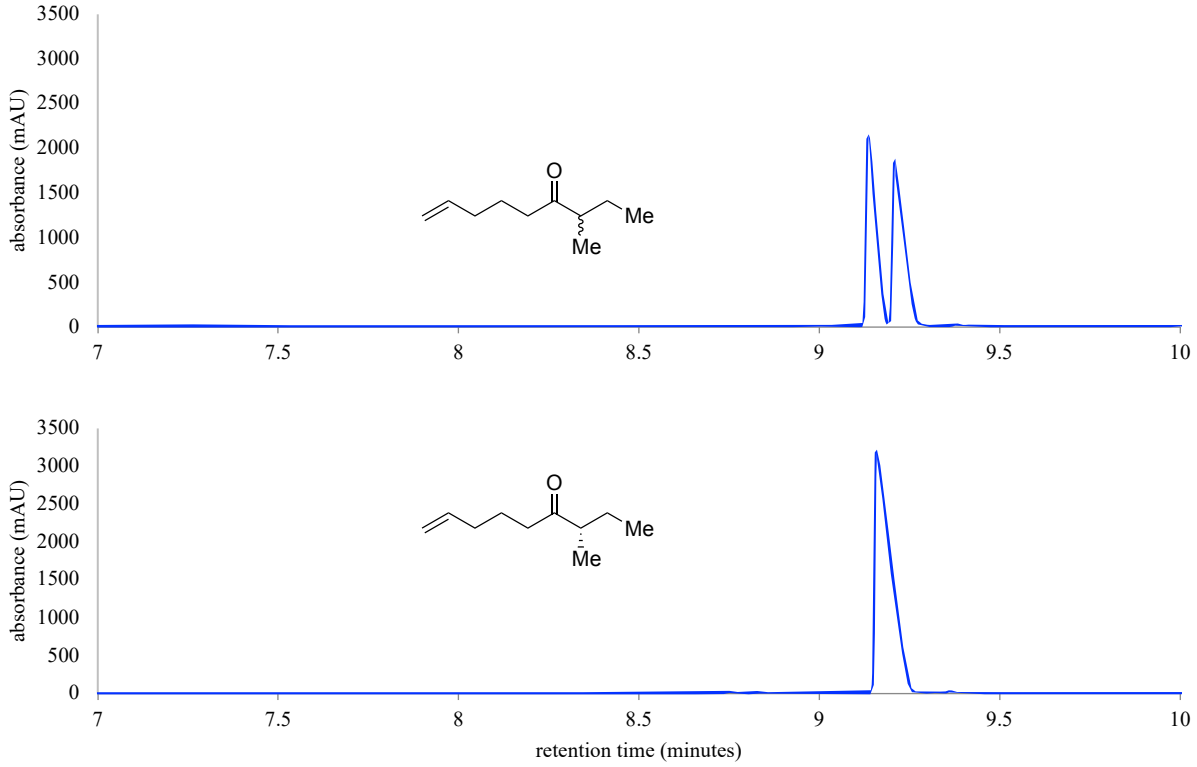
→ 20% Et_2O/Pentane (200 mL) → 40% Et_2O/Pentane (200 mL) → 60% Et_2O/Pentane (200 mL) eluent) afforded the product with some starting alcohol as an impurity. The mixture was then dissolved in Et_2O (50 mL) and made basic with 10% Na_2CO_3 (aq.) until the aqueous layer maintained a pH ~ 9. The layers were separated, and the organic layer was extracted with 10% Na_2CO_3 (3 x 30 mL). The combined aqueous portions were acidified with 1 M HCl to a pH ~ 3 and then extracted with Et_2O (4 x 40 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure at low temperature to afford the pure product as a colorless oil (1.74 g, 17 mmol, 85% yield). The spectral and optical data were in accordance with literature values.[42] ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.58 (br s, 1H), 2.41 (sext, *J* = 7.0 Hz, 1H), 1.71 (dp, *J* = 13.7, 7.3 Hz, 1H), 1.51 (dp, *J* = 13.9, 7.3 Hz, 1H), 1.18 (d, *J* = 7.0 Hz, 3H), 0.95 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.14, 40.96, 26.67, 16.51, 11.69. HRMS (ESI) m/z calc'd for $C_5H_9O_2$: $[M-H]^-$: 101.0603; found: 101.0604. $[\alpha]^{24}_D$ = +19.08° (*c* = 1.025, $CHCl_3$).

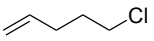
(S)-2-methylbutanoyl chloride. A flame-dried round-bottom flask equipped with a stir bar and charged with (*S*)-2-methylbutanoic acid (1.8 g, 17 mmol, 1.0 equiv.) and DCM (21 mL, 0.8 M) was cooled to 0 °C, in which oxalyl chloride (1.7 mL, 20 mmol, 1.2 equiv.) was added dropwise. The reaction was stirred at 0 ºC to room temperature for 4 hours. The reaction was then concentrated under reduced pressure, azeotroped with DCM (3 x), and the crude acyl chloride was carried forward without further purification.

(S)-N-methoxy-N,2-dimethylbutanamide. A round-bottom flask equipped with a stir bar and charged with *N*,*O*-dimethylhydroxylamine hydrochloride (2.0 g, 20 mol, 1.2 equiv.), DCM (21 mL, 0.8 M), and Et_3N (5.6 mL, 40 mmol, 2.4 equiv.) was cooled to 0 °C followed by dropwise addition of the crude (*S*)-2-methylbutanoyl chloride (17 mmol, 1.0 equiv.) in DCM (17 mL, 1 M). The reaction was stirred from 0 ºC to room temperature overnight. The reaction was then diluted with DCM (40 mL) and quenched with H_2O (20 mL). The layers were separated, and the organic layer was washed with 1 M HCl (20 mL), 5% aqueous $NaHCO_3$ (20 mL), and brine (20 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (100 mL SiO_2, 20% EtOAc/Hexanes eluent) afforded the product as a pale-yellow oil (1.4 g, 9.5 mmol, 56% yield over two steps). The spectral data were in accordance with literature values.[43] ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.68 (s, 3H), 3.19 (s, 3H), 2.79 (m, 1H), 1.69 (dp, *J* = 13.5, 7.4 Hz, 1H), 1.41 (dp, *J* = 13.5, 7.4 Hz, 1H), 1.10 (d, *J* = 6.8 Hz, 2H), 0.89 (t, *J* = 7.4 Hz, 3H). HRMS (ESI) m/z calc'd for $C_7H_{16}NO_2$: $[M+H]^+$: 146.1181; found: 146.1183. $[\alpha]^{22}_D$ = +30.29° (*c* = 1.035, $CHCl_3$).

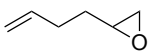
(S)-3-methylnon-8-en-4-one. To a flame-dried round-bottom flask equipped with a stir bar was added *(S)-N*-methoxy-*N*,2-dimethylbutanamide (1.3 g, 9 mmol, 1.0 equiv.) and THF (30 mL, 0.3 M) and cooled to 0 °C. Freshly prepared pent-4-en-1-ylmagnesium bromide (33 mL of a 0.55 M solution in THF, 18 mmol, 2.0 equiv.) was added dropwise, and the reaction was allowed to stir at 0 ºC to room temperature, monitoring the consumption of the starting material by TLC (ca. 5 hours). The reaction was diluted with Et_2O (20 mL), quenched with saturated aqueous NH_4Cl (20 mL). The layers were separated, and the organic phase was washed with H_2O (3 x 20 mL). The combined aqueous washes were then washed with Et_2O (2 x 40 mL). The organic phases were combined, dried over $MgSO_4$, filtered, and concentrated under reduced pressure at low temperatures. Purification via flash column chromatography (100 mL SiO_2, Pentane (500 mL) → 1% Et_2O/Pentane (200 mL) → 2% Et_2O/Pentane (200 mL) eluent) afforded the product as a clear oil (200 mg, 1.3 mmol, 65% yield, 99% ee). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.76 (ddt, *J* = 17.0, 10.4, 6.7 Hz, 1H), 5.03 – 4.93 (m, 2H), 2.50 – 2.36 (m, 3H), 2.05 (app q, *J* = 7.3 Hz, 2H), 1.73 – 1.62 (m, 3H), 1.37 (app hept, *J* = 7.3 Hz, 1H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.86 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 214.84, 138.27, 115.25, 48.06, 40.39, 33.30, 26.08, 22.79, 16.06, 11.85. HRMS (ESI) m/z calc'd for $C_{10}H_{19}O$: $[M+H]^+$: 155.1436; found: 155.1433. $[\alpha]^{20}_D$ = +24.66° (*c* = 1.035, $CHCl_3$). % e.e. was determined by GC analysis (Method: Isothermal:

50 °C, 3 min → Ramp: 17 °C/min to 90 °C → Isothermal: 90 °C, 1 min → Ramp: 17 °C/min to 200 °C → Isothermal: 200 °C, 4 min).



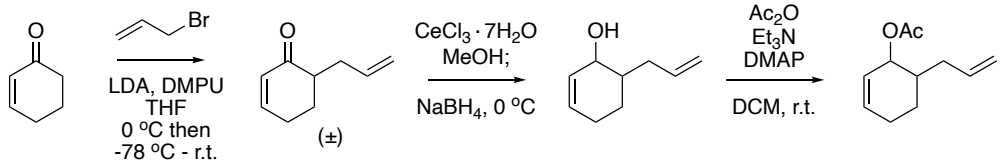


5-chloropent-1-en was purchased from Ambeed Chemical and used without additional purification.



2-(but-3-en-1-yl)oxirane was purchased from Oakwood Chemicals and used without additional purification.

Synthesis of 6-allylcyclohex-2-en-1-yl acetate:



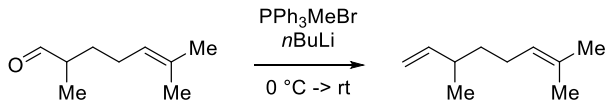
(±)-6-allylcyclohex-2-en-1-one was prepared according to a reported procedure and spectral data were in accordance with literature values.[44] ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 – 6.89 (m, 1H), 6.17 – 5.92 (m, 1H), 5.93 – 5.63 (m, 1H), 5.30 – 4.86 (m, 2H), 2.80 – 2.55 (m, 1H), 2.51 – 2.27 (m, 3H), 2.25 – 2.01 (m, 2H), 1.84 – 1.65 (m, 1H).

6-allylcyclohex-2-en-1-ol. A flame-dried round-bottom flask equipped with a stir bar was charged with (±)-6-allylcyclohex-2-en-1-one (871 mg, 6.4 mmol, 1.0 equiv.) and MeOH (13 mL, 0.5 M) was cooled to 0 °C. $CeCl_3 \cdot 7H_2O$ (2.87 g, 7.7 mmol, 1.2 equiv.) was added in one portion, and the mixture was stirred for 30 minutes at 0 °C. $NaBH_4$ (290 mg, 7.7 mmol, 1.2 equiv.) was then added and the reaction was stirred an additional 30 minutes. MeOH was removed via rotary evaporation, and the residue was dissolved in Et_2O (20 mL) and quenched with saturated aqueous NH_4Cl (10 mL). The layers were separated, and the aqueous phase was extracted with Et_2O (3 x 20 mL). The combined organic layers were washed with brine (20 mL),

dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (100 mL SiO_2, 25% Et_2O/Pentane eluent) afforded the product as a clear oil (726 mg, 5.2 mmol, 82% yield, 1.6:1 d.r.). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.92 – 5.82 (m, 2.19H), 5.81 – 5.76 (m, 0.38H), 5.65 (dq, *J* = 10.0, 2.3 Hz, 0.36H), 5.14 – 4.99 (m, 2H), 4.05 (t, *J* = 4.2 Hz, 0.59H), 4.03 – 3.87 (m, 0.36H), 2.50 – 2.34 (m, 0.36H), 2.28 (app p, *J* = 7.1 Hz, 0.64H), 2.18 – 1.93 (m, 3H), 1.79 (app dq, *J* = 13.0, 4.5 Hz, 0.39H), 1.68 – 1.50 (m, 2H), 1.48 – 1.23 (m, 2.61H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.55, 137.36, 131.71, 130.13, 129.85, 128.77, 116.47, 116.10, 71.31, 65.88, 41.91, 39.31, 37.33, 36.17, 25.84, 25.40, 24.66, 22.56. HRMS (EI) m/z/ calc'd for $C_9H_{13}O$ $[M-H]^-$: 137.09665; found: 137.09636. *Note*: *the diastereomeric ratio was determined by ^{1}H NMR, in which the minor diastereomer was weighted to an integration of 0.36H and the major diastereomer was weighted to an integration of 0.59H.*

6-allylcyclohex-2-en-1-yl acetate. A flame-dried round-bottom flask equipped with a stir bar was charged with (±)-6-allylcyclohex-2-en-1-ol (726 mg, 5.2 mmol, 1.0 equiv.), DCM (21 mL, 0.25 M), Et_3N (2.6 mL, 18.4 mmol, 3.5 equiv.), and DMAP (64 mg, 0.5 mmol, 0.1 equiv.). Acetic anhydride (1.24 mL, 13.1 mmol, 2.5 equiv.) was then added dropwise and the reaction was stirred at room temperature for 5 hours, tracking by TLC. Upon consumption of the starting alcohol, the reaction was quenched with H_2O (10 mL). The layers were separated, and the aqueous phase was extracted with DCM (3 x 15 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (50 mL SiO_2, 5% Et_2O/Pentane eluent) afforded the product as a clear oil (887 mg, 4.9 mmol, 93% yield, 1.8:1 d.r.). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.96 (ddd, *J* = 9.9, 4.8, 2.5 Hz, 0.63H), 5.88 (app dtd, *J* = 9.4, 3.6, 1.4 Hz, 0.36H), 5.85 – 5.73 (m, 1.62H), 5.59 (dq, *J* = 10.0, 2.4 Hz, 0.35H), 5.18 (t, *J* = 4.5 Hz, 0.63H), 5.12 – 5.07 (m, 0.36H), 5.06 – 4.98 (m, 2H), 2.34 – 2.12 (m, 1.71H), 2.06 (s, 1.05H), 2.05 (s, 1.98H), 2.05 – 1.90 (m, 2.25H), 1.91 – 1.70 (m, 1.37H), 1.67 – 1.58 (m, 0.74H), 1.57 – 1.47 (m, 0.73H), 1.46 – 1.36 (m, 0.40H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.13, (170.91), 136.75, (136.41), 133.23, (131.72), (125.95), 125.12, (116.58), 116.38, (73.01), 68.77, (37.92), 37.47, (36.42), 35.86, 25.46, (24.76), (23.99), 23.17, (21.50), 21.30. HRMS (EI) m/z calc'd for $C_{11}H_{16}O_2$ $[M]^+$: 180.11503; found: 180.11421. *Note*: *the diastereomeric ratio was determined by ^{1}H NMR, in which the minor diastereomer was weighted to an integration of 0.36H and the major diastereomer was weighted to an integration of 0.63H.*

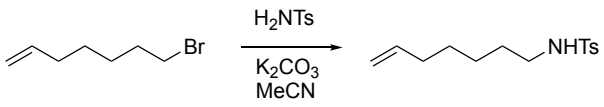
Synthesis of 3,7-dimethylocta-1,6-diene:



A flame-dried round-bottom flask equipped with a stir bar was charged with methyltriphenylphosphoniumbromide (5.4 g, 15.1 mmol, 1.5 equiv.) and THF (45 mL, 0.32 M) was cooled to 0 °C. *n*BuLi (10.1 mL, 14.8 mmol, 1.48 equiv., 1.6 M in hexanes) was added over 10 minutes, and the reaction was stirred at 0 °C for an additional 30 minutes. A solution of 2,6-dimethylhept-5-enal (1.6 mL, 10 mmol, 1.0 equiv.) in THF (20 mL, 0.5 M) was added dropwise, and the reaction was allowed to warm to room temperature overnight. The reaction was quenched with saturated aqueous NH_4Cl (30 mL), and the aqueous and organic layers were separated. The aqueous phase was extracted with Et_2O (3 x 40 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure at 0 °C, azeotroping with pentane. The material was purified via flash column chromatography (600 mL SiO_2, Pentane eluent) to afford 3,7-dimethylocta-1,6-diene as a clear,

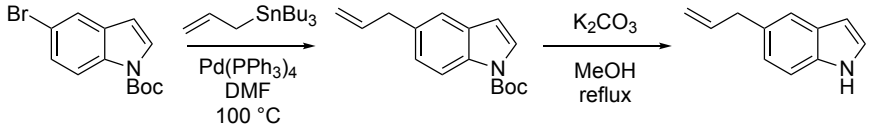
fragrant oil (980 mg, 7.1 mmol, 71% yield). The spectral data were in agreement with those reported in the literature.[45] ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.70 (ddd, *J* = 17.5, 10.3, 7.5 Hz, 1H), 5.10 (app tt, *J* = 7.1, 1.4 Hz, 1H), 4.95 (app dt, *J* = 17.2, 1.6 Hz, 1H), 4.95 – 4.88 (m, 1H), 2.12 (hept, *J* = 6.9 Hz, 1H), 2.04 – 1.89 (m, 2H), 1.68 (s, 3H), 1.60 (s, 3H), 1.43 – 1.20 (m, 2H), 0.99 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.92, 131.44, 124.81, 112.61, 37.51, 36.90, 25.89, 25.87, 20.30, 17.83.

Synthesis of *N*-(hept-6-en-1-yl)-4-methylbenzenesulfonamide:



N-(hept-6-en-1-yl)-4-methylbenzenesulfonamide was prepared according to the literature procedure, and the spectral data were in accordance with literature values.[46] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 5.74 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.06 – 4.84 (m, 2H), 4.32 (br m, 1H), 2.93 (q, *J* = 6.8 Hz, 2H), 2.43 (s, 3H), 1.99 (app q, *J* = 6.9 Hz, 2H), 1.46 (p, *J* = 7.2 Hz, 2H), 1.37 – 1.18 (m, 4H).

Synthesis of tert-butyl 5-allyl-1*H*-indole-1-carboxylate and 5-allyl-1*H*-indole:

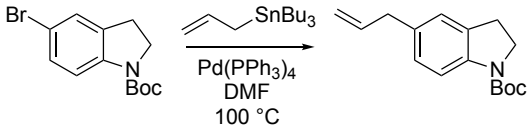


tert-butyl 5-allyl-1H-indole-1-carboxylate. To a flame-dried three-necked round-bottom flask equipped with a stir bar and a reflux condenser was added *tert*-butyl 5-bromo-1*H*-indole-1-carboxylate (1.48 g, 5 mmol, 1.0 equiv.), freshly distilled DMF (17 mL, 0.3 M), and allyltributylstannane (2 mL, 6 mmol, 1.2 equiv.) under an atmosphere of Argon. The solution was sparged with Argon for one hour, placed under an Argon atmosphere, then $Pd(PPh_3)_4$ (289 mg, 0.25 mmol, 0.05 equiv.) was quickly added to the flask. The reaction was then heated to 100 °C for 24 h. Upon completion, the flask was cooled to room temperature and diluted with EtOAc (40 mL). 1 M NaOH (20 mL) was added and the mixture was then stirred for 30 minutes. The aqueous and organic layers were separated, and the organic layer was washed with brine (5 x 40 mL), dried over Na_2SO_4, filtered, and then concentrated under reduced pressure. Purification via flash column chromatography (100 mL 10% w/w K_2CO_3/SiO_2, Hexanes (200 mL) → 2% EtOAc/Hexanes (300 mL) eluent) afforded *tert*-butyl 5-allyl-1*H*-indole-1-carboxylate as a clear, viscous oil (1.0 g, 4.1 mmol, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (br d, *J* = 8.5 Hz, 1H), 7.57 (d, *J* = 3.7 Hz, 1H), 7.37 (d, *J* = 1.6 Hz, 1H), 7.14 (dd, *J* = 8.5, 1.6 Hz, 1H), 6.02 (ddt, *J* = 16.8, 10.0, 6.6 Hz, 1H), 5.13 – 5.04 (m, 2H), 3.48 (dt, *J* = 6.7, 1.6 Hz, 2H), 1.67 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.95, 138.22, 134.50, 133.92, 131.00, 126.20, 125.24, 120.69, 115.59, 115.13, 107.27, 83.67, 40.26, 28.36. HRMS (ESI) m/z calc'd for $C_{16}H_{20}NO_2$ $[M+H]^+$: 258.1494; found 258.1486. *Note: the use of a 10% w/w K_2CO_3/SiO_2 stationary phase in the flash chromatography helped greatly in trapping the tin byproducts.*

5-allyl-1H-indole. To a flame-dried round-bottom flask equipped with a stir bar and a reflux condenser was added *tert*-butyl 5-allyl-1*H*-indole-1-carboxylate (678 mg, 2.6 mmol, 1.0 equiv.), freshly distilled MeOH (90 mL, 0.03 M), and finely

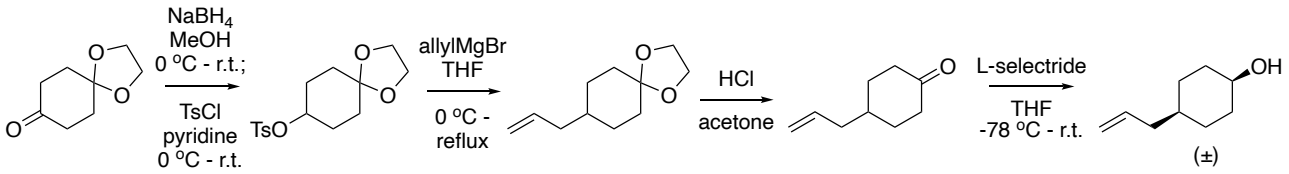
ground K_2CO_3 (546 mg, 4 mmol, 1.5 equiv.). The suspension was rapidly stirred at reflux for 48 hours, then cooled to room temperature, and the solvent was removed under reduced pressure. The residue was dissolved in DCM (30 mL) and washed with water (25 mL). The phases were separated, and the aqueous layer was extracted with DCM (3 x 20 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (100 mL SiO_2, 10% EtOAc/Hexanes eluent) afforded the product as a yellow oil (364 mg, 2.3 mmol, 89% yield). The spectral data were in agreement with those reported in the literature.[47] ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (br s, 1H), 7.46 (br s, 1H), 7.33 (d, *J* = 8.3 Hz, 1H), 7.19 (app t, *J* = 2.8 Hz, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.58 – 6.37 (m, 1H), 6.05 (app ddt, *J* = 16.8, 10.0, 6.7 Hz, 1H), 5.14 – 5.08 (m, 1H), 5.07 – 5.03 (m, 1H), 3.50 (d, *J* = 6.7 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.82, 134.64, 131.55, 128.29, 124.46, 123.27, 120.27, 115.14, 110.99, 102.52, 40.53.

Synthesis of tert-butyl 5-allylindoline-1-carboxylate:



tert-butyl 5-allylindoline-1-carboxylate. To a flame-dried three-necked round-bottom flask equipped with a stir bar and a reflux condenser was added *tert*-butyl 5-bromoindoline-1-carboxylate (2.0 g, 6.8 mmol, 1.0 equiv.), freshly distilled DMF (23 mL, 0.3 M), and allyltributylstannane (2.7 mL, 8.1 mmol, 1.2 equiv.) under an atmosphere of argon. The solution was sparged with argon for 1 hour, placed under an argon atmosphere, then $Pd(PPh_3)_4$ (393 mg, 0.34 mmol, 0.05 equiv.) was quickly added to the flask. The reaction was stirred at 100 °C for 24 h and upon completion, the flask was cooled to room temperature, diluted with EtOAc (40 mL), then 1 M NaOH (20 mL) was added and the mixture was stirred for 30 minutes. The aqueous and organic layers were separated and the organic layer was washed with brine (5 x 40 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (100 mL 10% K_2CO_3/SiO_2, Hexanes (500 mL) → 1% EtOAc/Hexanes (200 mL) → 2% EtOAc/Hexanes (200 mL) → 3% EtOAc/Hexanes (200 mL) eluent) followed by a second flash column chromatography (100 mL SiO_2, 3% EtOAc/Hexanes (250 mL) → 5% EtOAc/Hexanes (500 mL) eluent) afforded *tert*-butyl 5-allylindoline-1-carboxylate as a white solid (904 mg, 3.5 mmol, 52% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 and 7.37 (two br s, 1H), 6.98 (app s, 2H), 5.94 (ddt, *J* = 16.8, 10.1, 6.7 Hz, 1H), 5.11 – 4.99 (m, 2H), 3.96 (br s, 2H), 3.32 (d, *J* = 6.7 Hz, 2H), 3.06 (t, *J* = 8.7 Hz, 2H), 1.56 (br s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 152.72, 141.34 and 140.48, 138.03, 133.98, 132.18 and 131.26, 127.61, 125.24 and 124.94, 115.54, 114 .63, 81.41 and 80.34, 47.79, 39.81, 28.60, 27.53 and 27.10. HRMS (EI) m/z calc'd for $C_{16}H_{21}NO_2$ $[M]^+$: 259.1572; found 259.15647. *Note: The signals at 7.76 and 7.36 ppm in the ^{1}H NMR correspond to a single aryl-H; the doubling of resonances is due to the Boc-induced rotamers, which are also observed in the paired ^{13}C resonances at 141.34 and 140.48, 132.18 and 131.26, 125.24 and 124.94, 81.41 and 80.34, and 27.53 and 27.10 ppm, confirmed by ^{1}H-^{13}C HSQC analysis (see spectra).*

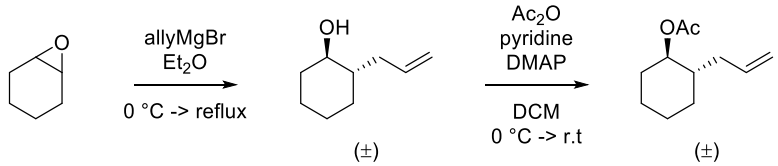
Synthesis of (±)-cis-4-allylcyclohexan-1-ol:



4-allylcyclohexan-1-one was prepared according to the literature procedure, and the spectral data were in accordance with literature values.[48] ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 (ddt, *J* = 16.4, 10.9, 7.2 Hz, 1H), 5.09 – 4.99 (m, 2H), 2.48 – 2.24 (m, 4H), 2.18 – 1.92 (m, 4H), 1.92 – 1.71 (m, 1H), 1.41 (qd, *J* = 12.0, 5.3 Hz, 2H).

(±)-cis-4-allylcyclohexan-1-ol. To a flame-dried round-bottom flask equipped with a stir bar was added 4-allylcyclohexan-1-one (308 mg, 2.2 mmol, 1.0 equiv.) and THF (9 mL, 0.25 M) under an atmosphere of argon and cooled to -78 °C. L-Selectride (4.6 mL, 4.5 mol, 2.0 equiv., 0.96 M in THF) was added dropwise and the reaction was allowed to slowly warm to room temperature overnight. The flask was cooled to 0 °C, vented, carefully quenched with aqueous 1 M HCl (5 mL), and the mixture was stirred for an additional 30 minutes. The aqueous and organic phases were separated, and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (250 mL SiO_2, Hexanes (200 mL) → 5% EtOAc/Hexanes (200 mL) → 10% EtOAc/Hexanes (200 mL) → 15% EtOAc/Hexanes (200 mL) → 20% EtOAc/Hexanes (400 mL) eluent) afforded the product as a clear oil and as a single diastereomer (204 mg, 1.46 mmol, 65% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.78 (ddt, *J* = 17.2, 10.2, 7.1 Hz, 1H), 5.03 – 4.94 (m, 2H), 3.96 (tt, *J* = 5.0, 3.0 Hz, 1H), 2.01 (app t, *J* = 6.5 Hz, 2H), 1.74 – 1.67 (m, 2H), 1.61 – 1.48 (m, 4H), 1.44 – 1.35 (m, 3H), 1.34 – 1.30 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.58, 115.66, 67.21, 40.68, 36.30, 32.36, 26.81. *Note: We found that the use of a sterically demanding reducing agent such as L-Selectride (versus $NaBH_4$)[48] afforded the cis-product as a single diastereomer. The proton alpha to the hydroxyl group has J values consistent with an equatorial configuration (5.0 and 3.0 Hz), whereas in an analogous compound trans-4-(tert-butyl)cyclohexan-1-ol, the proton alpha to the hydroxyl group displays comparatively larger J values of 10.9 and 4.4 Hz, which is consistent with an axial-axial interaction.*[49]

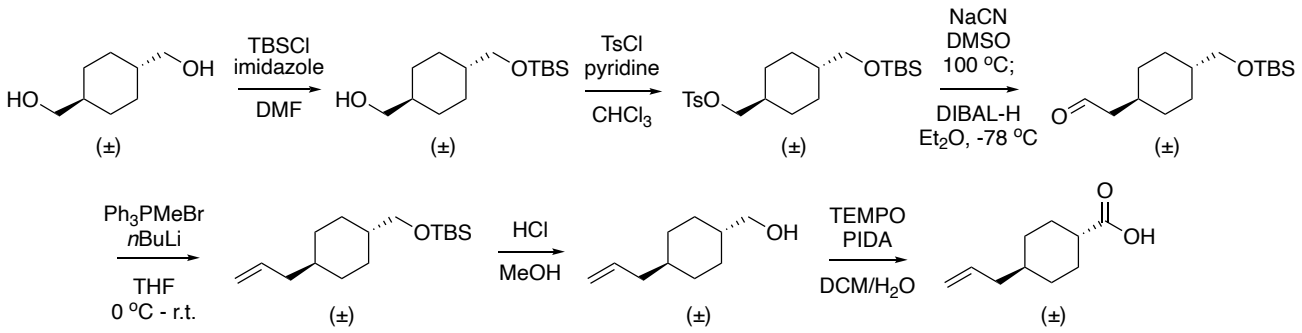
Synthesis of (±)-*trans*-2-allylcyclohexan-1-ol and (±)-*trans*-2-allylcyclohexyl acetate:



(±)-trans-2-allylcyclohexan-1-ol was prepared according to a literature procedure, and the spectral data were in accordance with literature values.[51] ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.86 (ddt, *J* = 17.2, 10.1, 7.2 Hz, 1H), 5.10 – 4.99 (m, 2H), 3.27 (td, *J* = 9.7, 4.5 Hz, 1H), 2.49 – 2.41 (m, 1H), 2.03 – 1.89 (m, 2H), 1.82 – 1.69 (m, 2H), 1.67 – 1.60 (m, 1H), 1.57 (s, 1H), 1.39 – 1.22 (m, 3H), 1.18 (tt, *J* = 12.6, 3.2 Hz, 1H), 0.95 (app qd, *J* = 12.8, 3.6 Hz, 1H).

(±)-trans-2-allylcyclohexyl acetate was prepared according to a literature procedure, and the spectral data were in accordance with literature values.[51] ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.74 (dddd, *J* = 15.7, 11.4, 7.9, 6.5 Hz, 1H), 5.02 – 4.93 (m, 2H), 4.50 (td, *J* = 10.1, 4.3 Hz, 1H), 3.95 (ddd, *J* = 10.9, 9.2, 4.4 Hz, 2.24 (m, 1H), 2.04 (s, 3H), 2.00 – 1.93 (m, 1H), 1.93 – 1.80 (m, 2H), 1.77 – 1.70 (m, 1H), 1.67 – 1.60 (m, 1H), 1.58 – 1.47 (m, 1H), 1.37 – 1.24 (m, 2H), 1.18 (qt, *J* = 12.4, 3.8 Hz, 1H), 1.01 (qd, *J* = 12.3, 3.7 Hz, 1H).

Synthesis of (±)-*trans*-4-allylcyclohexyl)methanol and (±)-*trans*-4-allylcyclohexane-1-carboxylic acid:



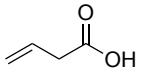
(±)-trans-2-(4-(((tert-butyldimethylsilyl)oxy)methyl)cyclohexyl)acetaldehyde was prepared according to the literature procedure, and the spectral data were in accordance with literature values.[50] ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.78 (s, 1H), 3.42 (d, *J* = 6.2 Hz, 2H), 2.56 – 2.07 (m, 2H), 1.96 – 1.68 (m, 5H), 1.49 – 1.34 (m, 1H), 1.24 – 0.95 (m, 4H), 0.91 (s, 9H), 0.06 (s, 6H).

(±)-trans-(4-allylcyclohexyl)methoxy)(tert-butyl)dimethylsilane. n-Butyllithium (3 mL, 4.1 mmol, 1.4 equiv., 1.36 M in hexanes) was added dropwise to a vigorously stirring suspension of methyltriphenylphosphonium bromide (1.6 g, 4.4 mmol, 1.5 equiv.) in THF (15 mL, 0.3 M) at 0°C, and the resulting yellow suspension was stirred for 1 hour. (±)-*trans*-2-(4-(((*tert*-butyldimethylsilyl)oxy)methyl)cyclohexyl)acetaldehyde (798 mg, 2.95 mmol, 1.0 equiv.) was slowly added as a solution in THF (2 mL, 1.6 M), and the reaction mixture was allowed warm up to room temperature overnight. The solvent was concentrated under reduced pressure and the crude mixture was then filtered over a pad of SiO_2, rinsing with Et_2O. The mother liquor was concentrated under reduced pressure to afford the product as a clear oil (418 mg, 1.6 mmol, 53% yield) and carried forward without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.79 (ddt, *J* = 17.3, 10.4, 7.1 Hz, 1H), 5.08 – 4.86 (m, 2H), 3.39 (d, *J* = 6.4 Hz, 2H), 1.95 (t, *J* = 6.9 Hz, 2H), 1.76 (d, *J* = 9.4 Hz, 4H), 1.46 – 1.34 (m, 1H), 1.33 – 1.18 (m, 1H), 0.98 – 0.82 (m, 13H), 0.03 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.85, 115.37, 69.00, 42.01, 40.70, 38.09, 32.61, 29.71, 26.14, 18.56, -5.17. HRMS (EI) m/z calc'd for $C_{16}H_{32}SiO$ $[M]^+$: 268.22225; found 268.22328.

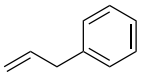
(±)-trans-(4-allylcyclohexyl)methanol. (±)-*trans*-(4-allylcyclohexyl)methoxy)(*tert*-butyl)dimethylsilane (655 mg, 2.5 mmol, 1.0 equiv.) was dissolved in MeOH (25 mL, 0.1 M) at room temperature, then a 3 M solution of HCl in MeOH (8 mL, 25 mmol, 10 equiv.) was added and the reaction was stirred for 30 minutes. The MeOH was concentrated under reduced pressure and the residue was dissolved in EtOAc (20 mL) and washed with saturated aqueous $NaHCO_3$ (10 mL). The aqueous and organic layers were separated and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (50 mL SiO_2, 10% EtOAc/Hexanes eluent) afforded the product as a clear oil (361.3 mg, 2.3 mmol, 94% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.79 (ddt, *J* = 17.2, 10.3, 7.2 Hz, 1H), 5.02 – 4.92 (m, 2H), 3.45 (d, *J* = 6.3 Hz, 2H), 1.96 (app t, *J* = 6.9 Hz,

2H), 1.79 (app d, J = 6.8 Hz, 4H), 1.52 – 1.38 (m, 1H), 1.37 – 1.21 (m, 2H), 0.98 – 0.89 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.68, 115.50, 68.89, 41.92, 40.68, 37.94, 32.46, 29.53. HRMS (EI) m/z calc'd for $C_{10}H_{18}O$ $[M]^+$: 154.13577; found 154.13626.

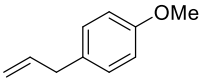
(±)-trans-4-allylcyclohexane-1-carboxylic acid. (±)-*trans*-(4-allylcyclohexyl)methanol (403 mg, 2.6 mmol, 1.0 equiv.) was dissolved in DCM (13 mL, 0.2 M) and H_2O (13 mL, 0.2 M), and TEMPO (123 mg, 0.78 mmol, 0.3 equiv.) and PIDA (2.5 g, 7.8 mmol, 3.0 equiv.) were added. The biphasic mixture was rapidly stirred for 5 hours, the reaction was quenched with $Na_2S_2O_3$ (1.5 g), and the mixture was stirred for an additional 30 minutes. The aqueous and organic layers were separated, and the aqueous phase was extracted with DCM (5 x 50 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and then passed through a plug of SiO_2, eluting with DCM (100 mL). The solution was concentrated to a volume of 20 mL and subsequently treated with 1 M NaOH until basic. The layers were separated and the aqueous phase was re-acidified with 1 M HCl until it reached a pH ~ 2, then extracted with DCM (3 x 40 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to afford the product as a clear, light yellow oil (425 mg, 2.5 mmol, 97% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.63 (br s, 1H), 5.77 (ddt, J = 16.1, 10.7, 7.1 Hz, 1H), 5.03 – 4.92 (m, 2H), 2.25 (tt, J = 12.2, 3.6 Hz, 1H), 2.09 – 1.98, 2H), 1.96 (t, J = 6.9 Hz, 2H), 1.87 – 1.79 (m, 2H), 1.42 (qd, J = 13.2, 3.5 Hz, 2H), 1.38 – 1.25 (m, 1H), 0.95 (qd, J = 13.2, 3.5 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.62, 137.20, 115.88, 43.27, 41.66, 36.96, 31.97, 28.87. HRMS (EI) m/z calc'd for $C_{10}H_{16}O_2$ $[M]^+$: 168.11503; found 168.11491.



but-3-enoic acid was purchased from a Sigma-Aldrich and used as received without additional purification.

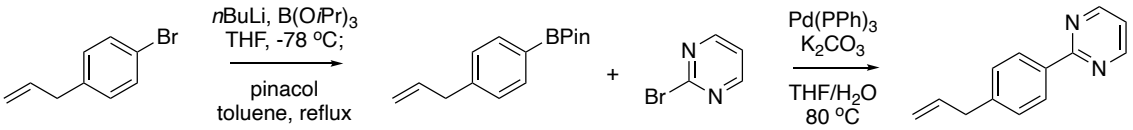


allylbenzene was purchased from Oakwood Chemicals and used as received without additional purification.



1-allyl-4-methoxybenzene was purchased from Sigma-Aldrich and used as received without additional purification.

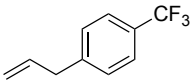
Synthesis of 2-(4-allylphenyl)pyrimidine:



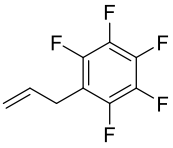
2-(4-allylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. To a flame-dried round-bottom flask equipped with a stir bar was added 1-allyl-4-bromobenzene (1.4 g, 7 mmol, 1.0 equiv.), THF (15 mL, 0.5 M), and triisopropylborate (1.8 mL, 8.4 mmol, 1.2 equiv.). The flask was cooled to -78 °C and *n*BuLi (6 mL, 8.4 mmol, 1.2 equiv., 1.36 M in Hexanes) was added dropwise. The reaction was stirred at -78 °C for 2 hours, then allowed to warm to room temperature overnight. The reaction was quenched with H_2O (20 mL), the layers were separated, and the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude material was carried forward without further purification. The crude borylation product was dissolved in benzene (15

mL, 0.5 M) in a round-bottom flask containing a stir bar and equipped with a Dean-Stark apparatus. Pinacol (1.0 g, 8.4 mmol, 1.2 equiv.) was added in one portion and the reaction was stirred at reflux for 24 h. The reaction was cooled to room temperature, H_2O (20 mL) and EtOAc (20 mL) were added, and the layers were separated. The aqueous phase was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. Purification via flash column chromatography (200 mL SiO_2, 5% EtOAc/20% Benzene/70% Hexanes eluent) afforded the product as a clear oil with a pinacol impurity that was carried forward (870 mg, 3.6 mmol, 51% yield over two steps). The spectral data were in accordance with literature values.[52] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.8 Hz, 2H), 7.20 (d, *J* = 7.8 Hz, 2H), 5.96 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.25 – 4.94 (m, 2H), 3.40 (d, *J* = 6.7 Hz, 2H), 1.34 (s, 12H).

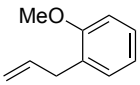
2-(4-allylphenyl)pyrimidine. To a flame-dried three-neck round-bottom flask containing a stir bar and fixed with a reflux condenser was added 2-(4-allylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.85 g, 3.5 mmol, 1.2 equiv.), 2-bromopyrimidine (463 mg, 3 mmol, 1.0 equiv.), anhydrous K_2CO_3 (830 mg, 6 mmol, 2.0 equiv.), THF (25 mL, 0.12 M), and H_2O (5 mL, 0.6 M). The mixture was degassed with N_2 for one hour and then placed under an atmosphere of N_2. $Pd(PPh_3)_4$ (175 mg, 0.15 mmol, 0.05 equiv.) was added and the reaction was stirred at 80 °C for 24 hours. The reaction was cooled to room temperature and quenched with saturated aqueous NH_4Cl (15 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (75 mL SiO_2, 5% EtOAc/Hexanes eluent) afforded the product as a clear oil (323 mg, 1.6 mmol, 51% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.79 (d, *J* = 4.8 Hz, 2H), 8.37 (app d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.3 Hz, 2H), 7.16 (t, *J* = 4.8 Hz, 1H), 6.01 (ddt, *J* = 16.8, 10.1, 6.7 Hz, 1H), 5.12 (app dq, *J* = 11.0, 1.7 Hz, 1H), 5.11 – 5.08 (m, 1H), 3.46 (d, *J* = 6.7 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.87, 157.34, 143.17, 137.11, 135.69, 129.05, 128.39, 119.01, 116.31, 40.22. HRMS (ESI) m/z calc'd for $C_{13}H_{13}N_2$ $[M+H]^+$: 197.1079; found 197.1080.



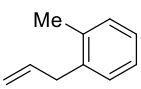
1-allyl-4-(trifluoromethyl)benzene was prepared according to the aryl allylation procedure and 10.0 mmol of 1-bromo-4-(trifluoromethyl)benzene was used as the limiting reagent Purification via flash column chromatography (250 mL SiO_2, Hexanes eluent) afforded the product as a clear oil (1.0 g, 5.4 mmol, 54% yield). The spectral data were in accordance with literature values.[53] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 5.96 (ddt, *J* = 16.8, 10.1, 6.7 Hz, 1H), 5.24 – 4.98 (m, 2H), 3.45 (d, *J* = 6.7 Hz, 2H).



1-allyl-2,3,4,5,6-pentafluorobenzene was purchased from Sigma-Aldrich and used without additional purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.87 (ddt, *J* = 16.6, 10.1, 6.2 Hz, 1H), 5.15 – 5.03 (m, 2H), 3.44 (app d, *J* = 6.3 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.04 (dm, *J* = 245.7 Hz), 140.10 (dm, *J* = 250.9 Hz), 137.45 (dm, *J* = 249.3 Hz), 133.01, 117.27, 113.11 (td, *J* = 18.4, 4.2 Hz), 26.45.



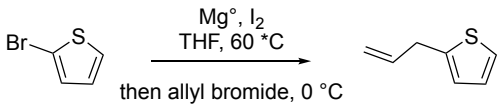
1-allyl-2-methoxybenzene was purchased from Sigma-Aldrich and used as received without additional purification.



1-allyl-2-methylbenzene was prepared according to the aryl allylation procedure and 10.0 mmol of 1-bromo-2-methylbenzene was used as the limiting reagent. Purification via flash column chromatography (150 mL SiO_2, Hexanes eluent) afforded the product as a clear oil (1.2 g, 9.2 mmol, 92% yield). The spectral data were in accordance with

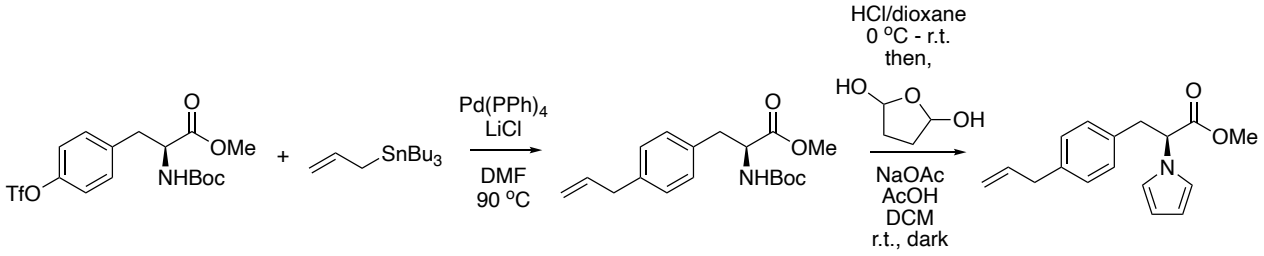
literature values.[54] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 – 7.11 (m, 4H), 6.02 – 5.91 (m, 1H), 5.07 (app dp, *J* = 10.1, 1.4 Hz, 1H), 5.01 (app. dp, *J* = 17.1, 1.7 Hz, 1H), 3.38 (d, *J* = 6.4 Hz, 2H), 2.30 (s, 3H).

Synthesis of 2-allylthiophene:



2-allylthiophene. To a flame-dried three-necked round-bottom flask equipped with a stir bar fitted with a reflux condenser was added magnesium turnings (729 mg, 30 mmol, 2 equiv.), THF (10 mL, 3 M), and a single crystal of I_2. A solution of 2-bromothiophene (1.5 mL, 15 mmol, 1.0 equiv.) in THF (5 mL, 3.0 M) was separately prepared and a small aliquot (100 μL) was added to initiate the Grignard. The remainder of the solution was added slowly, stirred at reflux for 2 hours, and then cooled to room temperature. To a cooled (0 ºC) solution of allylbromide (865 μL, 10 mmol, 1.0 equiv.) in THF (40 mL, 0.25 M) was added the prepared Grignard (8.8 mL, 10 mmol, 1.0 equiv., 1.14 M) via dropwise addition, and the reaction was allowed to slowly warm to room temperature over 6 hours. The reaction was quenched with saturated NH_4Cl (20 mL), and the organic and aqueous layers were separated. The aqueous layer was extracted with Et_2O (3 x 20 mL), and the combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure at 0 °C. Purification via flash column chromatography (SiO_2, Pentane eluent) afforded 2-allylthiophene as a clear oil (1.14 g, 9.2 mmol, 92% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 (dd, *J* = 5.2, 1.2 Hz, 1H), 6.95 (dd, *J* = 5.2, 3.3 Hz, 1H), 6.82 (dq, *J* = 3.3, 1.2 Hz, 1H), 6.01 (ddt, *J* = 16.7, 10.0, 6.7 Hz, 1H), 5.16 (dq, *J* = 16.7, 1.4 Hz, 2H), 5.11 (dq, *J* = 10.0, 1.4 Hz, 2H), 3.59 (app dq, *J* = 6.7, 1.4 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.92, 136.54, 126.89, 124.61, 123.63, 116.23, 34.20. HRMS (EI) m/z calc'd for C_7H_8S $[M]^+$: 124.03467 found 124.03439.

Synthesis of methyl (*S*)-3-(4-allylphenyl)-2-((*tert*-butoxycarbonyl)amino)propanoate and methyl (*S*)-3-(4-allylphenyl)-2-(1*H*-pyrrol-1-yl)propanoate:

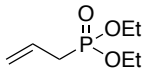


methyl (S)-3-(4-allylphenyl)-2-((tert-butoxycarbonyl)amino)propanoate was prepared according to the literature procedure using 5 mmol of methyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-3-(4-(((trifluoromethyl)sulfonyl)oxy)phenyl)propanoate as the limiting reagent, and the spectral data were in accordance with literature values (1.25 g, 3.9 mmol, 78% yield).[55] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (d, *J* = 7.8 Hz, 2H), 7.05 (d, *J* = 7.8 Hz, 2H), 5.95 (ddt, *J* = 16.9, 10.4, 6.7 Hz, 1H), 5.10 – 5.03 (m, 2H), 4.95 and 4.66 (d, *J* = 8.3 Hz and br s, 1H), 4.57 and 4.37 (q, *J* = 6.4 Hz and br s,1H), 3.71 (s, 3H), 3.36 (d, *J* = 6.8 Hz, 2H), 3.09 and 3.02 and 2.92 (dd, *J* = 13.9, 5.7 Hz and dd, *J* = 13.9, 6.2 Hz and br s, 2H), 1.42 (s, 9H). $[\alpha]^{22}_D$ = +7.48° (*c* = 1.065,

$CHCl_3$). *Note: The N-Boc induced rotamers account for additional ^1H NMR resonances at 4.66, 4.37, and 2.92 ppm that correspond to the N-H, methine, and methylene protons on the amino ester.*

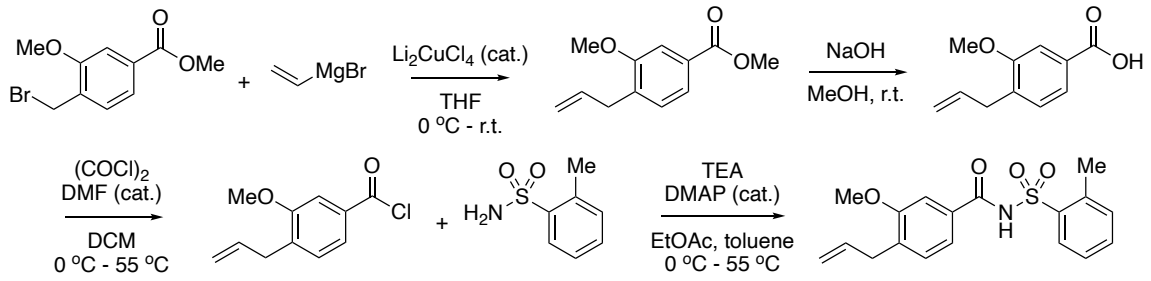
methyl (S)-3-(4-allylphenyl)-2-aminopropanoate. To a flame-dried round-bottom flask equipped with a stir bar was added methyl (*S*)-3-(4-allylphenyl)-2-((tert-butoxycarbonyl)amino)propanoate (913 mg, 2.86 mmol, 1.0 equiv.) and freshly distilled dioxane (3 mL, 1.0 M). The solution was cooled to 0 °C, a 4 M solution of HCl in dioxane (3.5 mL, 14.3 mmol, 5 equiv.) was added dropwise, and stirred 0 ºC to room temperature overnight. The solution was cooled back to 0 °C, quenched with H_2O (5 mL) and saturated aqueous K_2CO_3 (5 mL), and stirred for 15 minutes. The layers were separated and the aqueous phase was extracted with EtOAc (3 x 20 mL). The organic phases were combined, dried over Na_2SO_4, filtered, concentrated, passed through a plug of SiO_2 – eluting with EtOAc – and concentrated under reduced pressure to afford methyl (*S*)-3-(4-allylphenyl)-2-aminopropanoate as a clear oil which was carried forward without further purification.

methyl (S)-3-(4-allylphenyl)-2-(1H-pyrrol-1-yl)propanoate. To a round-bottom flask equipped with a stir bar and reflux condenser was added 2,5-dimethoxytetrahydrofuran (391 mL, 3.02 mmol, 1.02 equiv.) and H_2O (4 mL, 0.66 M). The solution was stirred and heated at reflux for 2 h, then cooled to room temperature. The condenser was exchanged with a rubber septa, the flask was wrapped in foil to exclude light, and then methyl (*S*)-3-(4-allylphenyl)-2-aminopropanoate (552 mg, 2.52 mmol, 1.0 equiv.), NaOAc (207 mg, 2.52 mmol, 1.0 equiv.), AcOH (144 µL, 2.52 mmol, 1.0 equiv.), and DCM (5 mL, 0.5 M) was added. The mixture was stirred in the dark at room temperature for 15 h, then basified with saturated aqueous Na_2CO_3 (10 mL). The layers were separated and the aqueous phase was extracted with DCM (3 x 15 mL). The organic phases were combined, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (100 mL SiO_2, 5% EtOAc/Hexanes eluent) afforded methyl (*S*)-3-(4-allylphenyl)-2-(1*H*-pyrrol-1-yl)propanoate as a clear oil (617 mg, 2.3 mmol, 80% yield over two steps). ^1H NMR (500 MHz, $CDCl_3$) δ 7.07 (d, *J* = 8.1 Hz, 2H), 6.95 (d, *J* = 8.1 Hz, 2H), 6.73 (app q, *J* = 2.1 Hz, 2H), 6.16 (app q, *J* = 2.1 Hz, 2H), 6.00 – 5.88 (m, 1H), 5.07 (app q, *J* = 1.4 Hz, 1H), 5.06 – 5.01 (m, 1H), 4.78 – 4.71 (m, 1H), 3.71 (s, 3H), 3.40 (dd, *J* = 13.9, 6.6 Hz, 1H), 3.35 (d, *J* = 6.6 Hz, 2H), 3.24 (dd, *J* = 13.9, 8.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.76, 138.92, 137.45, 134.15, 129.01, 128.91, 120.22, 115.96, 108.81, 63.74, 52.67, 39.92, 39.20. HRMS (ESI) m/z calc'd for $C_{17}H_{20}NO_2$ $[M+H]^+$: 270.1494; found 270.1494. $[\alpha]^{23}_D$ = -60.68° (*c* = 1.225, $CHCl_3$). *Note: this modification to the Claussen-Kass pyrrole synthesis[56] was optimal for the efficient formation of the heterocycle. Non-specific decomposition occurred when using other conditions that required elevated temperatures, unbuffered acids, and/or other activating agents (e.g. P_2O_5, $Sc(OTf)_3$).*



diethyl allylphosphonate was purchased from Ambeed and used without further purification.

Synthesis of methyl 4-allyl-3-methoxybenzoate (80a) and 4-allyl-3-methoxy-*N*-(*o*-tolylsulfonyl)benzamide (80b):



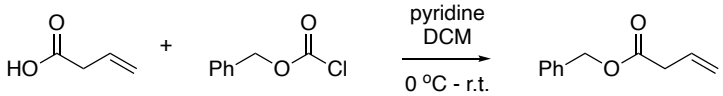
methyl 4-allyl-3-methoxybenzoate (80a). To an oven-dried round-bottom flask equipped with a stir bar was added methyl 4-(bromomethyl)-3-methoxybenzoate (4.9 g, 19 mmol, 1.0 equiv.), freshly distilled *N*-methyl-2-pyrrolidone (7.3 mL, 76 mmol, 4.0 equiv.), and THF (29 mL, 0.7 M). A 0.1 M solution of dilithium tetrachlorocuprate(II) in THF (5.7 mL, 0.57 mmol, 0.03 equiv.) was added, the reaction flask was cooled to 0 °C, and a 1.0 M solution of vinylmagnesium bromide in THF (26.6 mL, 26.6 mmol, 1.4 equiv.) was added dropwise. The reaction was allowed to warm to room temperature and stirred for 1.5 hours. The reaction was then cooled to 0 °C, quenched dropwise with 1 M HCl (13 mL), diluted with H_2O (5 mL), and then extracted with EtOAc (5 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (300 mL SiO_2, 5% → 8% EtOAc/Hexanes eluent) afforded the product as a clear oil (2.5 g, 11.4 mmol, 60% yield). *Note: dropwise addition of vinylmagnesium bromide was important to avoid clumping of solids.* ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.51 (app d, *J* = 1.1 Hz, 1H), 7.19 (d, *J* = 7.8 Hz, 1H), 5.97 (ddt, *J* = 15.7, 10.9, 6.6 Hz, 1H), 5.11 – 4.99 (m, 2H), 3.90 (s, 3H), 3.88 (s, 3H), 3.41 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.23, 157.21, 136.07, 134.34, 129.66, 129.41, 122.16, 116.16, 111.03, 55.64, 52.16, 34.40. HRMS (ESI) m/z calc'd for $C_{12}H_{15}O_3$ $[M+H]^+$: 207.1021; found 207.1020.

4-allyl-3-methoxybenzoic acid. 1 M NaOH (57.1 mL, 5.0 equiv.) was added to a solution of methyl 4-allyl-3-methoxybenzoate (2.5 g, 11.4 mmol, 1.0 equiv.) in MeOH (38 mL, 0.3 M), and the reaction was stirred for 2 hours at room temperature. The reaction was cooled to 0 °C, brought to a pH of 1 upon acidification with 1 M HCl, and then diluted with EtOAc (80 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 40 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give the product as a white solid (2.0 g, 10.4 mmol, 91% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.56 (br s, 1H), 7.69 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.57 (d, *J* = 1.6 Hz, 1H), 7.24 (d, *J* = 7.8 Hz, 1H), 5.98 (ddt, *J* = 16.6, 10.7, 6.6 Hz, 1H), 5.12 – 5.03 (m, 2H), 3.90 (s, 3H), 3.45 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.45, 157.34, 135.95, 135.51, 129.86, 128.41, 123.00, 116.38, 111.45, 55.72, 34.53. HRMS (ESI-TOF ES-) m/z calc'd for $C_{11}H_{11}O_3$ $[M-H]^-$: 191.0708; found 191.0707.

4-allyl-3-methoxybenzoyl chloride. To a round-bottom flask equipped with a stir bar and a reflux condenser was added 4-allyl-3-methoxybenzoic acid (2.0 g, 10.4 mmol, 1.0 equiv.) and DCM (21 mL, 0.5 M). The mixture was cooled to 0 °C and oxalyl chloride (1.3 mL, 15.6 mmol, 1.5 equiv.) was added, followed by dropwise addition of DMF (0.11 mL, 1 mmol, 0.1 equiv.). The reaction was warmed to 55 °C and stirred for 24 hours. The reaction was cooled to room temperature, diluted with water, and quenched with 5% $NaHCO_3$. The aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 60 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford the product as a dark oil, which was used in the next step without further purification.

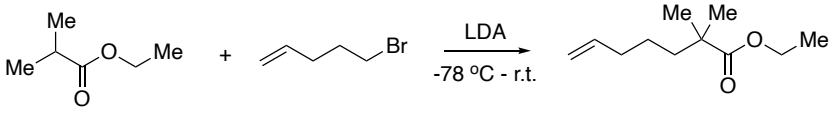
4-allyl-3-methoxy-N-(o-tolylsulfonyl)benzamide (80b). To an oven-dried round-bottom flask equipped with a stir bar was added *o*-toluenesulfonamide (2.0 g, 11.4 mmol, 1.1 equiv.), EtOAc (21 mL, 0.5 M), triethylamine (3.6 mL, 26 mmol, 2.5 equiv.), and 4-dimethylaminopyridine (63 mg, 0.52 mmol, 0.05 equiv.). The mixture was cooled to 0 °C and a solution of 4-allyl-3-methoxybenzoyl chloride (2.2 g, 10.4 mmol, 1.0 equiv.) in toluene (8 mL, 1.3 M) was added dropwise. The reaction was warmed to 55 °C and stirred for 24 hours. The reaction was then cooled to room temperature and quenched with 1 M HCl until the aqueous layer maintained a pH of 1. The aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification via flash chromatography (250 mL SiO_2, 10% EtOAc/DCM eluent) achieved the product as a light tan solid (2.2 g, 6.4 mmol, 62% yield over two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.61 – 9.27 (m, 1H), 8.28 (d, *J* = 8.1 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 1H), 7.37 – 7.30 (m, 3H), 7.19 (d, *J* = 8.1 Hz, 1H), 5.92 (ddt, *J* = 16.8, 10.1, 6.6 Hz, 1H), 5.09 – 5.00 (m, 2H), 3.79 (s, 3H), 3.38 (d, *J* = 6.6 Hz, 2H), 2.73 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.26, 157.81, 137.77, 136.70, 135.62, 135.49, 134.25, 132.65, 131.71, 130.14, 130.08, 126.65, 119.72, 116.56, 109.81, 55.75, 34.36, 20.60. HRMS (ESI) m/z calc'd for $C_{18}H_{19}NO_4S$ $[M+H]^+$: 346.1113; found 346.1113.

Synthesis of benzyl but-3-enoate:



Benzyl but-3-enoate was prepared according to the literature procedure,[57] and spectral data were in accordance with literature values. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.31 (m, 5H), 5.95 (ddt, *J* = 17.5, 9.8, 6.9 Hz, 1H), 5.20 – 5.15 (m, 2H), 5.14 (s, 2H), 3.15 (dt, *J* = 6.9, 1.4 Hz, 2H).

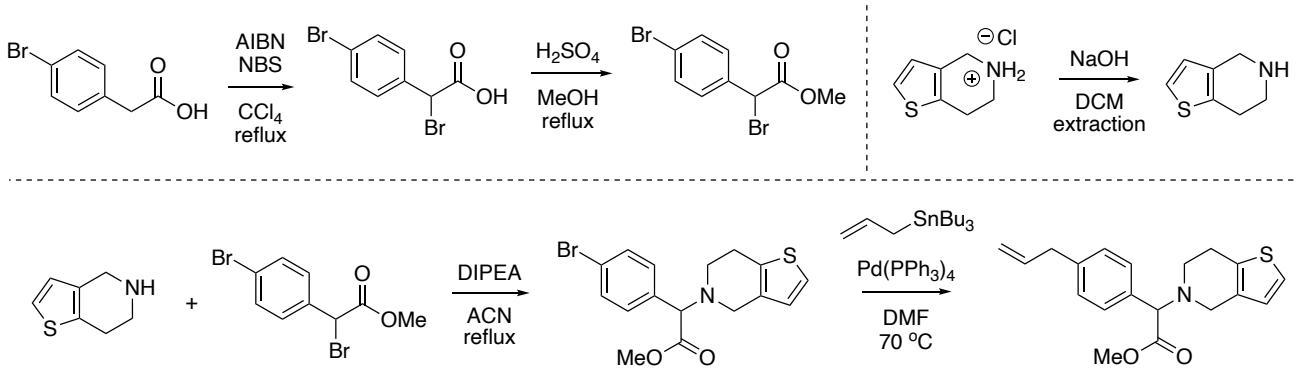
Synthesis of ethyl 2,2-dimethylhept-6-enoate:



ethyl 2,2-dimethylhept-6-enoate was synthesized following a modified literature procedure.[37] To a flame-dried round-bottom flask equipped with a stir bar was added freshly distilled diisopropylamine (1.6 mL, 12 mmol, 1.2 equiv.) and THF (40 mL, 0.25 M). The flask was cooled to -78 °C, *n*-Butyllithium (7.2 mL, 11 mmol, 1.1 equiv., 1.53 M solution in Hexanes) was added dropwise, and the reaction was stirred for 30 minutes. Ethyl *iso*butyrate (1.35 mL, 10 mmol, 1.0 equiv.) was then added dropwise, the reaction was stirred for 30 minutes, then 5-bromopentene (1.2 mL, 10 mmol, 1.0 equiv.) was added slowly, and the reaction was stirred from -78 °C to room temperature overnight. The reaction was then quenched at 0 °C with 1 M HCl (20 mL). The organic and aqueous layers were separated, the aqueous layer was extracted with Et_2O (3 x 20 mL), and the combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure at 0 °C. Purification via flash column chromatography (100 mL SiO_2, Pentane (250 mL) → 5% Et_2O/Pentane (250 mL) → 10% Et_2O/Pentane (250 mL) eluent) afforded ethyl 2,2-dimethylhept-6-enoate as a clear oil (1.6 g, 8.5 mmol, 85% yield). ^{1}H NMR

(500 MHz, $CDCl_3$) δ 5.78 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 4.99 (dq, *J* = 16.9, 1.7 Hz, 1H), 4.94 (app ddt, *J* = 10.2, 2.3, 1.3 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 2.02 (qt, *J* = 7.1, 1.5 Hz, 2H), 1.54 – 1.49 (m, 2H), 1.38 – 1.28 (m, 2H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.16 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.14, 138.78, 114.68, 60.33, 42.23, 40.31, 34.25, 25.29, 24.38, 14.39. HRMS (ESI) m/z calc'd for $C_{12}H_{21}O_2$ $[M+H]^+$: 185.1542; found: 185.1543.

Synthesis of methyl 2-(4-allylphenyl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetate:



2-bromo-2-(4-bromophenyl)acetic acid. To a flame-dried round-bottom flask equipped with a stir bar and a reflux condenser was added 2-(4-bromophenyl)acetic acid (2.2 g, 10 mmol, 1.0 equiv.) and freshly recrystallized *N*-bromosuccinimide (2.0 g, 11 mmol, 1.1 equiv.). The flask was placed under vacuum and purged with argon (x 3). A separate flask containing CCl_4 was degassed under argon for 40 minutes. CCl_4 (20 mL, 0.5 M) was then added to the mixture followed by quick addition of freshly recrystallized AIBN (82 mg, 0.5 mmol, 0.05 equiv.), and the reaction was stirred at reflux for 16 h. The reaction was then cooled to room temperature, diluted with Hexanes, and filtered over celite – rinsing with DCM. Purification via flash column chromatography (100 mL SiO_2, 0% → 1% → 3% → 5% → 7% MeOH/DCM eluent) afforded the product with the pyrrolidine-2,5-dione byproduct. The mixture was transferred to a separatory funnel with EtOAc (20 mL) and brought to a basic pH upon addition of 1 M NaOH. The aqueous layer was extracted with EtOAc (3 x 15 mL). The basic aqueous layer was subsequently brought to an acidic pH upon slow addition of 1 M HCl, and then extracted with EtOAc (3 x 20 mL). The combined second organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford 2-bromo-2-(4-bromophenyl)acetic acid as a white solid with 9% of the pyrrolidine-2,5-dione byproduct, which was carried forward to the next step. ^1H NMR (500 MHz, $CDCl_3$) δ 7.51 (app d, *J* = 8.6 Hz, 2H), 7.44 (app d, *J* = 8.6 Hz, 2H), 5.31 (s, 1H).

methyl 2-bromo-2-(4-bromophenyl)acetate. To a round-bottom flask equipped with a stir bar and reflux condenser was added 2-bromo-2-(4-bromophenyl)acetic acid (2.6 g, 8.9 mmol, 1.0 equiv.), MeOH (30 mL, 0.3 M), and H_2SO_4 (25 μL, 0.45 mmol, 0.05 equiv.), and stirred at reflux overnight. The reaction was cooled to 0 °C, diluted with EtOAc (20 mL), and quenched slowly with saturated $NaHCO_3$ until the aqueous layer maintained a neutral pH. The aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (150 mL SiO_2, 0% → 4% → 8% → 12% EtOAc/Hexanes eluent) afforded methyl 2-bromo-2-(4-bromophenyl)acetate as a light-yellow oil (2.0 g, 6.6 mmol, 66% yield over 2 steps). ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (app d, *J* = 8.5 Hz, 2H), 7.42 (app d, *J* = 8.6 Hz, 2H),

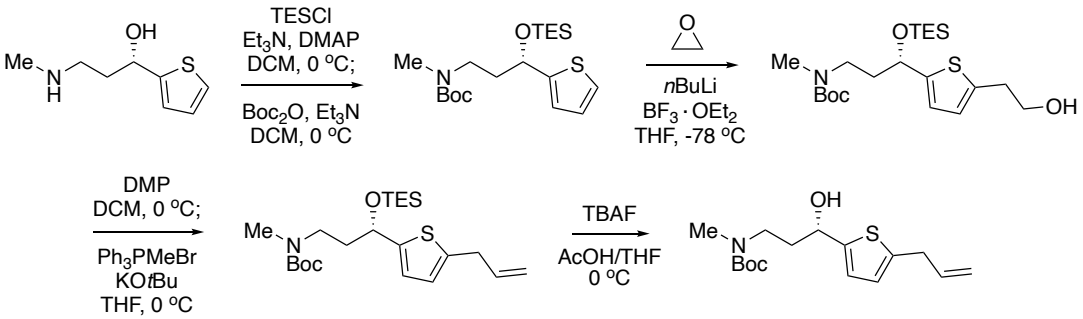
5.30 (s, 1H), 3.79 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.58, 134.89, 132.18, 130.46, 123.74, 53.65, 45.49. HRMS (EI) m/z calc'd for $C_9H_8O_2Br_2$ $[M]^+$: 305.88913; found 305.88909.

4,5,6,7-tetrahydrothieno[3,2-c]pyridine. To a separatory funnel was added 4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine hydrochloride (1.09 g, 6.2 mmol, 1.0 equiv.), DCM (25 mL), and a solution of 1 M NaOH (25 mL). The contents were mixed, the aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 25 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford 4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine, which was carried forward without further purification.

methyl 2-(4-bromophenyl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetate. To a solution of 4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine (6.2 mmol, 1.0 equiv.) and methyl 2-bromo-2-(4-bromophenyl)acetate (1.9 g, 6.2 mmol, 1.0 equiv.) in acetonitrile (21 mL, 0.3 M) was added *N,N*-diisopropylethylamine (0.8 g, 6.2 mmol, 1.0 equiv.). The reaction was stirred at reflux, monitoring by TLC. Following consumption of the starting materials, the mixture was cooled to room temperature, diluted with EtOAc (20 mL), and quenched with water (10 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (150 mL SiO_2, 5% → 10% → 15% EtOAc/Hexanes eluent) afforded methyl 2-(4-bromophenyl)-2-(6,7-dihydrothieno[3,2-*c*]pyridin-5(4*H*)-yl)acetate as a beige-tinted oil (2.1 g, 5.9 mmol, 94% yield over two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (app d, *J* = 8.5 Hz, 2H), 7.38 (app d, *J* = 8.4 Hz, 2H), 7.07 (d, *J* = 5.1 Hz, 1H), 6.66 (d, *J* = 5.1 Hz, 1H), 4.26 (s, 1H), 3.73 (s, 3H), 3.63 (d, *J* = 14.2 Hz, 1H), 3.58 (d, *J* = 14.2 Hz, 1H), 2.90 – 2.83 (m, 3H), 2.83 – 2.75 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.72, 135.28, 133.41, 133.20, 132.02, 130.55, 125.36, 123.02, 122.74, 72.34, 52.38, 51.05, 48.40, 25.39. HRMS (ESI) m/z calc'd for $C_{16}H_{17}NO_2SBr$ $[M+H]^+$: 366.0163; found 328.1059.

methyl 2-(4-allylphenyl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetate. To a flame-dried three-neck round-bottom flask equipped with a stir bar and a reflux condenser was added methyl 2-(4-bromophenyl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetate (0.55 g, 1.5 mmol, 1.0 equiv.). The flask was placed under vacuum and purged with argon (x 3). DMF (15 mL, 0.1 M), pre-sparged with argon for 15 minutes, was added to the reaction flask, and then $Pd(PPh_3)_4$ (173 mg, 0.15 mmol, 0.1 equiv.) and allyltributylstannane (0.6 mL, 1.8 mmol, 1.2 equiv.) were added sequentially. The reaction was stirred at 70 ºC for 13 h under an argon atmosphere. *Notes: (1) the starting aryl-bromide and product have a nearly identical Rf by TLC. To monitor the reaction, an aliquot was taken, passed through a silica plug rinsing with EtOAc, and concentrated under a stream of nitrogen. The crude mixture was evaluated by TLC in 10 mL of DCM with 2 drops of NH_4OH-MeOH; (2) lithium chloride, elevated temperatures, and prolonged reaction times afforded formation of the olefin-isomerized styrene isomer.* The reaction mixture was then cooled to room temperature and concentrated over a stream of nitrogen. Purification via flash column chromatography (50 mL SiO_2, 0% → 1% → 2% → 3% → 4% → 5% → 6% → 7% → 8% → 10% → 12% → 20% EtOAc/Hexanes eluent) followed by a second flash column chromatography (100 mL SiO_2, 0.5% NH_4OH/DCM eluent) afforded the product as a clear oil (0.41 g, 1.26 mmol, 82% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 6.98 (d, *J* = 5.1 Hz, 1H), 6.58 (d, *J* = 5.1 Hz, 1H), 5.90 (ddt, *J* = 16.9, 10.0, 6.8 Hz, 1H), 5.09 – 4.95 (m, 2H), 4.20 (s, 1H), 3.65 (s, 3H), 3.57 (d, *J* = 14.3 Hz, 1H), 3.52 (d, *J* = 14.3 Hz, 1H), 3.33 (d, *J* = 6.9 Hz, 2H), 2.87 – 2.75 (m, 3H), 2.74 – 2.63 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.31, 140.65, 137.22, 133.80, 133.49, 133.42, 129.02, 129.00, 125.43, 122.86, 116.24, 72.79, 52.24, 51.13, 48.43, 40.07, 25.41. HRMS (ESI) m/z calc'd for $C_{19}H_{22}NO_2S$ $[M+H]^+$: 328.1371; found 328.1371.

Synthesis of *tert*-butyl (*S*)-(3-(5-allylthiophen-2-yl)-3-hydroxypropyl)(methyl)carbamate:



(S)-N-methyl-3-(thiophen-2-yl)-3-((triethylsilyl)oxy)propan-1-amine. To a flame-dried round-bottom flask equipped with a stir bar was added (*S*)-3-(methylamino)-1-(thiophen-2-yl)propan-1-ol (856 mg, 5 mmol, 1.0 equiv.), DCM (20 mL, 0.25 M), Et_3N (1.7 mL, 12 mmol, 2.4 equiv.), and DMAP (61 mg, 0.5 mmol, 0.1 equiv.). The solution was cooled to 0 °C, triethylsilylchloride (1 mL, 6 mmol, 1.2 equiv.) was added dropwise, and the reaction was stirred at 0 °C for 30 minutes and then at room temperature for 1 hour, tracking conversion of the starting alcohol by TLC. Upon full conversion of the starting material, the reaction was diluted with DCM and quenched with water. The layers were separated, the aqueous phase was extracted with DCM (3 x 20 mL), and the combined organic phases were washed with brine (30 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude material was carried forward without further purification.

tert-butyl (S)-methyl(3-(thiophen-2-yl)-3-((triethylsilyl)oxy)propyl)carbamate. The crude silyl ether was dissolved in DCM (20 mL, 0.25 M) and Et_3N (1.4 mL, 10 mmol, 2.0 equiv.) was added. The mixture was cooled to 0 °C, di-*tert*-butyldicarbonate (2.2 g, 10 mmol, 2.0 equiv.) was added, and then stirred at 0 °C to room temperature overnight. The reaction was diluted with DCM and quenched with water. The layers were separated, the aqueous phase was extracted with DCM (3 x 20 mL), and the combined organic phases were washed with brine (30 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (150 mL SiO_2, 5% EtOAc/Hexanes eluent) afforded the product as a clear oil (1.84 g, 4.8 mmol, 96% yield over two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (d, *J* = 4.9 Hz, 1H), 6.93 – 6.88 (m, 2H), 4.96 (t, *J* = 6.1 Hz, 1H), 3.32 – 3.21 (m, 1.45H), 3.20 – 3.07 (m, 0.56H), 2.80 (s, 3H), 2.08 – 1.99 (m, 1H), 1.99 – 1.90 (m, 1H), 1.43 (s, 9H), 0.90 (t, *J* = 8.0 Hz, 9H), 0.55 (q, *J* = 8.0 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.80, 149.54 and 149.25, 126.34, 124.12, 123.18, 79.32, 69.12, 45.83, 39.08, 34.43, 28.55, 6.88, 4.87. $[\alpha]^{21}_D$ = -15.74° (*c* = 1.68, $CHCl_3$). HRMS (ESI) m/z calc'd for $C_{19}H_{35}NO_3NaSiS$ $[M+Na]^+$: 408.2005; found 408.2006. *Note: N-Boc rotamers account for broadened and separated signals in the ^{1}H NMR spectrum as well as for doubling of signals in the ^{13}C NMR spectrum.*

tert-butyl (S)-(3-(5-(2-hydroxyethyl)thiophen-2-yl)-3-((triethylsilyl)oxy)propyl)(methyl)carbamate. To a flame-dried round-bottom flask equipped with a stir bar was added *tert*-butyl *(S)*-methyl(3-(thiophen-2-yl)-3-((triethylsilyl)oxy)propyl)carbamate (1.84 g, 4.8 mmol, 1.0 equiv.) and THF (48 mL, 0.1 M). The solution was cooled to -78 °C and *n*BuLi (3.6 mL of a 1.58 M solution in hexanes, 5.7 mmol, 1.2 equiv.) was added dropwise, and the reaction was stirred at -78 °C for 30 minutes. Ethylene oxide (2.2 mL of a 2.5 M solution in THF, 5.7 mmol, 1.2 equiv.) was added dropwise and stirred for 10 minutes and subsequently, $BF_3{\cdot}OEt_2$ (710 µL, 5.7 mmol, 1.2 equiv.) was added dropwise. The reaction was held at -78 °C for 90 minutes, warmed to room temperature over 30 minutes, and then diluted with Et_2O and quenched with water. The layers were separated, the aqueous phase was extracted with Et_2O (3 x 40 mL), and the combined organic layers were washed with brine (40 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column

chromatography (100 mL SiO_2, 10% EtOAc/Hexanes (300 mL) → 20% EtOAc/Hexanes (500 mL) → 40% EtOAc/Hexanes (300 mL) eluent) afforded the product as a pink oil (1.37 g, 3.2 mmol, 66% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.73 (app br s, 1H), 6.67 (d, *J* = 3.4 Hz, 1H), 4.88 (t, *J* = 6.2 Hz, 1H), 3.83 (q, *J* = 6.2 Hz, 2H), 3.26 (br s, 1.46H, 3.16 (br s, 0.55H), 3.02 (t, *J* = 6.3 Hz, 2H), 2.80 (s, 3H), 2.07 – 1.98 (m, 1H), 1.96 – 1.88 (m, 1H), 1.68 (br s, 1H), 1.43 (s, 9H), 0.90 (t, *J* = 7.9 Hz, 9H), 0.55 (q, *J* = 7.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.85, 148.14 and 147.86, 139.73, 124.92, 123.29, 79.39, 69.25, 63.61, 45.88, 38.90, 34.50, 33.79, 28.60, 6.93, 4.91. $[\alpha]^{21}_D$ = -8.58° (*c* = 3.21, $CHCl_3$). HRMS (ESI) m/z calc'd for $C_{21}H_{39}NO_4NaSiS$ $[M+H]^+$: 452.2267; found 452.2267.

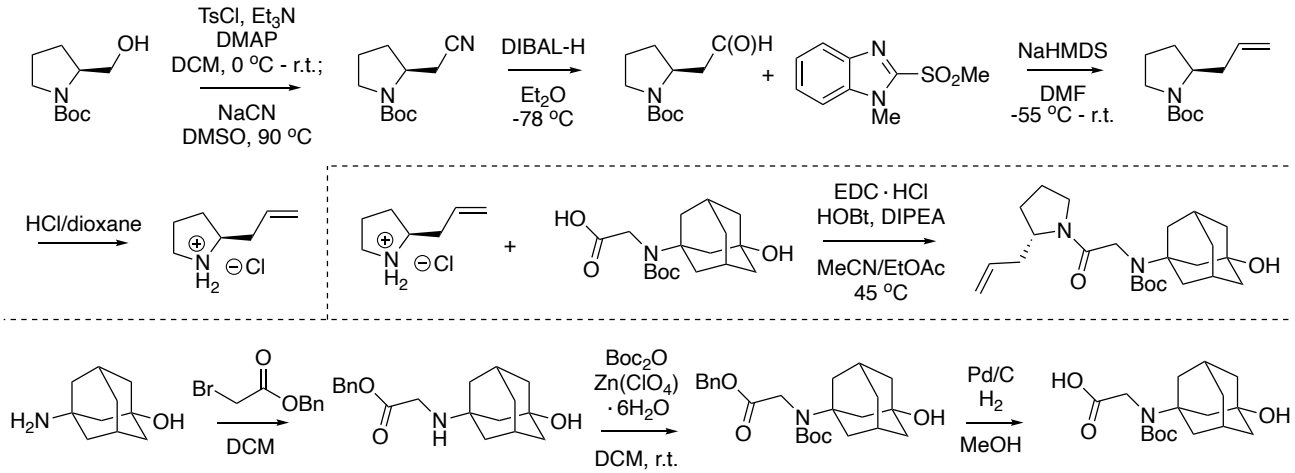
tert-butyl (S)-methyl(3-(5-(2-oxoethyl)thiophen-2-yl)-3-((triethylsilyl)oxy)propyl)carbamate. To a flame-dried round-bottom flask equipped with a stir bar was added *tert*-butyl (*S*)-(3-(5-(2-hydroxyethyl)thiophen-2-yl)-3-((triethylsilyl)oxy)propyl)(methyl)carbamate (1.37 g, 3.2 mmol, 1.0 equiv.) and DCM (13 mL, 0.25 M). The solution was cooled to 0 °C, Dess-Martin periodinane (1.62 g, 3.8 mmol, 1.2 equiv.) was added, and the reaction was stirred at 0 °C for 10 minutes and then at room temperature for 1 hour. Upon full conversion of the starting material by TLC, the reaction was filtered through a short plug of SiO_2, eluting with 20% EtOAc/Hexanes, and concentrated under reduced pressure. The material was dissolved in Et_2O (50 mL), washed with saturated $NaHCO_3$ (3 x 20 mL), brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude aldehyde (yellow oil) was carried forward without further purification.

tert-butyl (S)-(3-(5-allylthiophen-2-yl)-3-((triethylsilyl)oxy)propyl)(methyl)carbamate. To a flame-dried round-bottom flask equipped with a stir bar was added methyltriphenylphosphonium bromide (1.2 g, 3.4 mmol, 1.1 equiv.) and THF (32 mL, 0.1 M). The solution was cooled to 0 °C, KO*t*Bu (365 mg, 3.2 mmol, 1.0 equiv.) was added, and the bright yellow suspension was brought to room temperature and stirred for 30 minutes. The reaction was cooled back to 0 °C and the crude aldehyde in THF (10 mL) was added dropwise. The reaction was stirred at 0 ºC for 1 hour, tracking by TLC, and then quenched with water and diluted with EtOAc. The layers were separated, the aqueous phase was extracted with EtOAc (3 x 40 mL), and the combined organic layers were washed with brine (40 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (100 mL SiO_2, 5% EtOAc/Hexanes eluent) afforded the product as a clear oil (637 mg, 1.5 mmol, 44% yield over two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.70 (d, *J* = 3.5 Hz, 1H), 6.59 (d, *J* = 3.5 Hz, 1H), 5.96 (ddt, *J* = 16.6, 10.0, 6.6 Hz, 1H), 5.16 – 5.05 (m, 2H), 4.86 (t, *J* = 6.2 Hz, 1H), 3.51 (d, *J* = 6.8 Hz, 2H), 3.30 – 3.20 (m, 1.45H), 3.16 – 3.11 (m, 0.55H), 2.81 (s, 3H), 2.07 – 1.97 (m, 1H), 1.96 – 1.84 (m, 1H), 1.43 (s, 9H), 0.90 (t, *J* = 8.0 Hz, 9H), 0.55 (q, *J* = 8.0 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.82, 147.58 and 147.26, 141.75, 136.63, 123.80, 123.13, 116.19, 79.30, 69.24, 45.91, 38.93, 34.56, 34.44, 28.56, 6.91, 4.88. $[\alpha]^{21}_D$ = -15.92° (*c* = 2.075, $CHCl_3$). HRMS (ESI) m/z calc'd for $C_{22}H_{39}NO_3SSiNa$ $[M+Na]^+$: 448.2318; found 448.2321.

tert-butyl (S)-(3-(5-allylthiophen-2-yl)-3-hydroxypropyl)(methyl)carbamate. To a flame-dried round-bottom flask equipped with a stir bar was added *tert*-butyl (*S*)-(3-(5-allylthiophen-2-yl)-3-((triethylsilyl)oxy)propyl)(methyl)carbamate (766 mg, 1.8 mmol, 1.0 equiv.) and THF (7 mL, 0.5 M). The flask was cooled to 0 °C and glacial acetic acid (7 mL, 0.5 M) was added followed by a dropwise addition of TBAF (7 mL, 7.0 mmol, 3.9 equiv., 1.0 M solution in THF). The reaction was stirred at 0 °C for two hours, tracking by TLC, and then quenched by the careful addition of saturated aqueous $NaHCO_3$ (50 mL) and diluted with EtOAc (25 mL). The layers were separated, the aqueous layer was extracted with EtOAc (3 x 25 mL), and the combined organic layers were sequentially washed with 10% aqueous Na_2CO_3 (20 mL), water (20 mL), brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (75 mL SiO_2, 20% EtOAc/Hexanes eluent) afforded the product as a clear oil (482 mg, 1.54 mmol, 86% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.73 (d, *J* = 3.5 Hz, 1H), 6.59 (d, *J* = 3.5 Hz, 1H), 5.92 (ddt, *J* = 16.6, 10.0, 6.6 Hz, 1H), 5.10 (app d, *J* = 17.1 Hz, 1H), 5.04

(app d, J = 9.8 Hz, 1H), 4.88 – 4.54 (m, 1H), 3.79 – 3.64 (m, 0.69H), 3.47 (d, J = 6.7 Hz, 2H), 3.37 – 3.25 (m, 0.31H), 3.25 – 3.14 (m, 0.36H), 3.09 – 3.03 (m, 0.64H), 2.81 (s, 3H), 2.13 – 1.75 (m, 2H), 1.41 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.86 and 155.66, 146.29 and 142.04, 141.56, 136.39, 123.91 and 123.43, 122.85, 116.06, 79.97 and 79.66, 67.47 and 66.58, 45.77 and 45.00, 37.19 and 36.67, 34.35, 34.33, 28.31. HRMS (ESI) m/z calc'd for $C_{16}H_{25}NO_3SNa$ $[M+Na]^+$: 334.1453; found 334.1449.). $[\alpha]^{22}_D$ = -25.4° (c = 1.07, $CHCl_3$). *Note: the signals at 34.35 and 34.33 ppm in the ^{13}C spectrum account for the N-methyl and allylic carbons, verified by ^{1}H-^{13}C HSQC analysis (see spectra).*

Synthesis of *tert*-butyl (2-((*S*)-2-allylpyrrolidin-1-yl)-2-oxoethyl)((1*r*, 3*R*, 5*R*, 7*S*)-3-hydroxyadamantan-1-yl)carbamate:



tert-butyl (S)-2-((tosyloxy)methyl)pyrrolidine-1-carboxylate. A flame-dried round-bottom flask equipped with a stir bar was charged with *tert*-butyl (*S*)-2-(hydroxymethyl)pyrrolidine-1-carboxylate (6.0 g, 30 mmol, 1.0 equiv.) and DCM (40 mL, 0.75 M) followed by DMAP (733 mg, 6 mmol, 0.1 equiv.) and Et_3N (28.4 mL, 60 mmol, 2.0 equiv.) at 0 °C. A solution of TsCl (6.3 g, 33 mmol, 1.1 equiv.) in DCM (20 mL, 1.6 M) was added slowly and the reaction was stirred at room temperature for 4 hours. Upon consumption of the starting alcohol by TLC, the reaction was quenched with H_2O (20 mL). The layers were separated, and the aqueous phase was extracted with DCM (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude mixture was passed through a plug of SiO_2, eluting with DCM, and used without further purification.

tert-butyl (S)-2-(cyanomethyl)pyrrolidine-1-carboxylate. DMSO (100 mL, 0.3 M) was added to a round-bottom flask equipped with a stir bar and containing the crude tosylate followed by addition of NaCN (3.6 g, 90 mmol, 3.0 equiv.) in one portion. The flask was capped and sealed with Teflon tape, and vigorously stirred at 90 °C for 16 h. The reaction was cooled to room temperature and quenched with H_2O (50 mL) and diluted with EtOAc (100 mL). The layers were separated, and the aqueous phase was extracted with EtOAc (5 x 40 mL). The combined organic layers were washed with brine (3 x 25 mL), dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. Purification via flash column chromatography (150 mL SiO_2, 10% EtOAc/Hexanes (300 mL) → 20% EtOAc/Hexanes (500 mL) eluent) afforded the product as a clear oil (5.5 g, 26 mmol, 87% yield over two steps). The spectral data were in accordance with literature values.[58] ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.12 – 3.89 (m, 1H), 3.55 – 3.20 (m, 2H), 2.96 – 2.43 (m, 2H), 2.25 – 2.12 (m, 1H), 2.06 – 1.72 (m, 3H), 1.47 (s, 9H).

tert-butyl (S)-2-(2-oxoethyl)pyrrolidine-1-carboxylate. A flame-dried round-bottom flask equipped with a stir bar and charged with *tert*-butyl *(S)*-2-(cyanomethyl)pyrrolidine-1-carboxylate (2.5 g, 12.5 mmol, 1.0 equiv.) and Et_2O (40 mL, 0.3 M)

was cooled to -78 °C in which DIBAL-H (15 mL, 15.8 mmol, 1.2 equiv., 1 M solution in heptane) was added dropwise over 15 minutes. The reaction was stirred at -78 °C for 3 hours and upon consumption of the starting material, the reaction was quenched with MeOH (5 mL). The mixture was warmed up to room temperature, 1 M aqueous citric acid (30 mL) was added, and the solution was stirred until the layers were clearly defined (ca. 2 hours). The layers were separated, and the aqueous phase was extracted with Et_2O (5 x 30 mL). The combined organic layers were washed with brine (2 x 30 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure at low temperatures. Purification via flash column chromatography (100 mL SiO_2, 10% Et_2O/Hexanes (200 mL) → 20% Et_2O/Hexanes (200 mL) → 40% Et_2O/Hexanes (300 mL) eluent) afforded the product as a clear oil (1.8 g, 8.4 mmol, 67% yield). The spectral data were in accordance with literature values.[59] ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.77 (t, *J* = 2.2 Hz, 1H), 4.35 – 4.17 (m, 1H), 3.50 – 3.22 (m, 2H), 3.01 – 2.66 (m, 1H), 2.47 (dd, *J* = 16.3, 7.5 Hz, 1H), 2.23 – 2.07 (m, 1H), 1.84 (p, *J* = 7.5 Hz, 2H), 1.65 (br s, 1H), 1.45 (s, 9H).

tert-butyl (S)-2-allylpyrrolidine-1-carboxylate was synthesized using a modified literature procedure.[60] A flame-dried round-bottom flask equipped with a stir bar was charged with *tert*-butyl *(S)*-2-(2-oxoethyl)pyrrolidine-1-carboxylate (214 mg, 1.0 mmol, 1.0 equiv.), DMF (430 µL, 0.2 M), and freshly made and recrystallized 1-methyl-2-(methylsulfonyl)-1*H*-benzo[*d*]imidazole (210 mg, 1.0 mmol, 1.0 equiv.). The flask was cooled to -55 °C, NaHMDS (1.3 mL, 1.3 mmol, 1.3 equiv., 1 M solution in THF) was added over 5 minutes, the reaction was slowly warmed to room temperature over 2 hours, and then stirred at room temperature for an additional 2 hours. Upon consumption of the starting aldehyde via TLC analysis, the reaction was quenched with saturated aqueous NH_4Cl (5 mL) and diluted with Et_2O (5 mL). The layers were separated and the aqueous phase was extracted with Et_2O (5 x 5 mL). The combined organic layers were washed with water (3 x 5 mL), brine (3 x 5 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure at low temperatures. Purification via flash column chromatography (40 mL SiO_2, Hexanes (100 mL) → 5% Et_2O/Hexanes (200 mL) → 10% Et_2O/Hexanes (200 mL) → 20% Et_2O/Hexanes (200 mL) eluent) afforded the product as a clear oil (154 mg, 0.73 mmol, 73% yield). The optical and spectral data were in accordance with literature values.[61] ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.81 – 5.62 (m, 1H), 5.31 – 4.84 (m, 2H), 3.85 and 3.76 (two br s, 1H), 3.38 and 3.31 (two br s, 2H), 2.54 and 2.41 (two br s, 1H), 2.11 (dt, *J* = 13.6, 8.3 Hz, 1H), 1.94 – 1.75 (m, 3H), 1.74 – 1.67 (m, 1H), 1.46 (s, 9H). $[\alpha]^{23}_D$ = -52.9° (*c* = 1.03, $CHCl_3$).

(S)-2-allyl-pyrrolidine hydrochloride. A flame-dried round-bottom flask equipped with a stir bar was charged with *tert*-butyl *(S)*-2-allylpyrrolidine-1-carboxylate (636 mg, 3 mmol, 1.0 equiv.) and dioxane (7.5 mL, 0.36 M). A 4 M solution of HCl in dioxane (7.5 mL, 30 mmol, 10 equiv.) was added at room temperature and the reaction was stirred for 90 minutes. Upon full conversion of the starting material, the solvent was removed under reduced pressure, azeotroping with DCM (3 x 10 mL). Purification via flash column chromatography (50 mL SiO_2, 5% MeOH/DCM (100 mL) → 10% MeOH DCM (500 mL) eluent) afforded the product as an orange semi-solid (337 mg, 2.3 mmol, 76% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.82 (br s, 1H), 9.29 (br s, 1H), 5.75 (app ddt, *J* = 17.2, 10.2, 6.8 Hz, 1H), 5.21 (app d, *J* = 17.1 Hz, 1H), 5.12 (app d, *J* = 10.2 Hz, 1H), 3.56 (p, *J* = 7.8 Hz, 1H), 3.44 – 3.32 (m, 1H), 3.32 – 3.23 (m, 1H), 2.73 (app dt, *J* = 14.2, 6.8 Hz, 1H), 2.48 (app dt, *J* = 14.0, 7.4 Hz, 1H), 2.17 – 2.00 (m, 2H), 1.98 – 1.83 (m, 1H), 1.82 – 1.59 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 132.62, 119.25, 59.52, 44.75, 36.26, 29.91, 23.46. HRMS (ESI) m/z calc'd for $C_7H_{14}N$ $[M+H]^+$: 112.1126; found 112.1124.

benzyl ((1r,3s,5R,7S)-3-hydroxyadamantan-1-yl)glycinate. A flame-dried round-bottom flask equipped with a stir bar was charged with 1-amino-3-hydoxyadamantane (6.7 g, 40 mmol, 4.0 equiv.), DCM (80 mL, 0.125 M), and benzyl 2-bromoacetate (1.6 mL, 10 mmol, 1.0 equiv.), and stirred at room temperature overnight. Upon consumption of the starting bromide, the solids were filtered off, rinsing with DCM, and the filtrate was concentrated under reduced pressure. Purification via flash column chromatography (200 mL SiO_2, DCM (250 mL) → 2% MeOH/DCM (250 mL) → 4% MeOH/DCM (250 mL) → 6%

MeOH/DCM (250 mL) → 10% MeOH/DCM (250 mL) eluent) afforded the product as a viscous clear oil (3.1 g, 9.8 mmol, 98% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.31 (m, 5H), 5.16 (s, 2H), 3.47 (s, 2H), 2.33 – 2.21 (m, 2H), 1.69 – 1.59 (m, 5H), 1.56 (s, 2H), 1.53 – 1.51 (m, 4H), 1.51 – 1.47 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.15, 135.69, 128.75, 128.61, 128.56, 69.74, 66.87, 53.72, 50.16, 44.47, 43.40, 41.31, 35.20, 30.80. HRMS (ESI) m/z calc'd for $C_{19}H_{26}NO_3$ $[M+H]^+$: 316.1913; found 316.1915 *Note: the filtered solids may be dissolved in EtOAc and basified with aqueous 1 M NaOH, extracted with EtOAc, and repurified to recover the unreacted starting adamantane.*

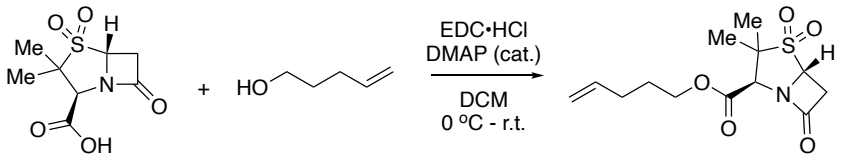
benzyl N-(tert-butoxycarbonyl)-N-((1r,3s,5R,7S)-3-hydroxyadamantan-1-yl)glycinate. A round-bottom flask equipped with a stir bar and charged with benzyl ((1*r*,3*s*,5*R*,7*S*)-3-hydroxyadamantan-1-yl)glycinate (1.9 g, 6.0 mmol, 1.0 equiv.), DCM (12 mL, 0.5 M), $Zn(ClO_4)_2 \cdot 6H_2O$ (225 mg, 0.6 mmol, 0.1 equiv.), and Boc_2O (1.97 g, 9.0 mmol, 1.5 equiv.) was stirred at room temperature for 72 hours. The solvent was removed under reduced pressure and then dissolved in H_2O (10 mL) and EtOAc (20 mL). The layers were separated, and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (100 mL SiO_2, Hexanes (200 mL) → 10% EtOAc/Hexanes (200 mL) → 20% EtOAc/Hexanes (200 mL) → 40% EtOAc/Hexanes (200 mL) eluent) afforded the product as a clear semi-solid (1.75 g, 4.2 mmol, 70% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 – 7.26 (m, 5H), 5.13 (s, 2H), 4.05 (br s, 2H), 2.29 – 2.17 (m, 2H), 2.09 – 1.93 (m, 6H), 1.82 (br s, 1H), 1.70 – 1.55 (m, 4H), 1.53 – 1.39 (m, 2H), 1.36 (br s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.31, (171.18), 154.60, 135.66, 128.59, 128.51, 128.40, 80.22, 69.73, 66.68, 59.08, 48.45, 45.92, 44.01, 39.27, 34.79, 31.07, 28.34. HRMS (ESI) m/z calc'd for $C_{24}H_{33}NO_5Na$ $[M+Na]^+$: 438.2256; found 438.2256. *Note: Conventional N-Boc conditions gave either low yields or competitive O-Boc reactivity. Lewis acidic metals[62] yielded better reactivity and high selectivity for N-Boc protection. The single resonance at 80 ppm (RC(O)O**C**$(CH_3)_3$) in the ^{13}C NMR spectrum confirms the incorporation of only one Boc-group, while the preserved resonance at 69.73 ppm (R_3**C**OH) and the shifting of the resonance at 44.47 ppm (R_3**C**NHR') from the starting secondary amine confirms the selectivity for N-Boc over O-Boc incorporation.*

N-(tert-butoxycarbonyl)-N-((1r,3s,5R,7S)-3-hydroxyadamantan-1-yl)glycine. To a flame-dried round-bottom flask equipped with a stir bar was added benzyl *N*-(*tert*-butoxycarbonyl)-*N-((1r,3s,5R,7S)*-3-hydroxyadamantan-1-yl)glycinate (1.75 g, 4.2 mmol, 1.0 equiv.), MeOH (100 mL, 0.025 M), and 5 wt. % Pd/C (100 mg, 0.05 mmol, 0.01 equiv.) under an atmosphere of N_2. The solution was then degassed with H_2 (1 atm) for 30 minutes, placed under an atmosphere of H_2, and then allowed to stir overnight. The reaction was placed back under an atmosphere of N_2, celite was added, the mixture was stirred for 30 minutes, and then filtered over a pad of celite, rinsing with MeOH (200 mL). The solvent was removed under reduced pressure to afford the product as a white crystalline solid. (1.3 g, 4.0 mmol, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.58 (br s, 2H), 4.02 (s, 2H), 2.23 (s, 2H), 2.14 – 1.88 (m, 6H), 1.73 – 1.60 (m, 4H), 1.57 – 1.48 (m, 2H), 1.43 (br s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.26, 155.49, 80.61, 70.15, 59.24, 48.25, 46.26, 43.86, 39.41, 34.89, 31.16, 28.56. HRMS (ESI) m/z calc'd for $C_{17}H_{27}NO_5Na$ $[M+Na]^+$: 348.1787; found 348.1782.

tert-butyl (2-((S)-2-allylpyrrolidin-1-yl)-2-oxoethyl)((1r,3R,5R,7S)-3-hydroxyadamantan-1-yl)carbamate. To a flame-dried round-bottom flask equipped with a stir bar and charged with *(S)*-2-allyl-pyrrolidine hydrochloride (337 mg, 2.3 mmol, 1.2 equiv.) and MeCN (5 mL, 0.4 M) was added DIPEA (400 µL, 2.3 mmol, 1.2 equiv.) and then stirred at room temperature for 20 minutes. Subsequently, *N*-(*tert*-butoxycarbonyl)-*N-((*1*r*,3*s*,5*R*,7*S*)-3*-hydroxyadamantan-1-yl)glycine (683 mg, 2.1 mmol, 1.0 equiv.), EDC·HCl (594 mg, 3.1 mmol, 1.5 equiv.), and HOBt (420 mg, 3.1 mmol, 1.5 equiv.) were added, an additional solution of DIPEA (700 µL, 4.0 mmol, 1.9 equiv.) in EtOAc (3 mL) was added, and the reaction was stirred at 45 °C for 24 hours. Upon consumption of the carboxylic acid starting material, the reaction was cooled to room temperature and

quenched with saturated aqueous NH_4Cl (10 mL) and diluted with EtOAc (20 mL). The layers were separated, the aqueous layer was extracted with EtOAc (5 x 20 mL), and the combined organic phases were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (100 mL SiO_2, 30% Acetone/Hexanes eluent) afforded the product as a white crystalline solid (752 mg, 1.8 mmol, 86% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80 – 5.67 (m, 1H), 5.30 – 4.76 (m, 2H), 4.19 – 4.11 (m, 1H), 4.05 – 3.94 (m, 1.7H), 3.93 – 3.83 (m, 0.29H), 3.57 – 3.50 (m, 0.25H), 3.48 – 3.38 (m, 1H), 3.38 – 3.31 (m, 0.75H), 2.77 – 2.54 (m, 0.76H), 2.37 – 2.27 (m, 0.24H), 2.24 (br s, 2H), 2.14 – 2.07 (m, 4H), 2.06 – 1.94 (m, 3H), 1.93 – 1.71 (m, 4H), 1.65 (app q, J = 12.2 Hz, 4H), 1.59 – 1.50 (m, 2H), 1.46 (br s, 1H), 1.43 (br s, 9H). ^{13}C NMR (126 MHz, DMSO-d_6, 60 °C) δ 167.71, 154.00, 135.12, 116.53, 78.10, 67.65, 58.03, 56.07, 47.84, 45.89, 45.17, 43.95, 38.63, 36.72, 34.66, 30.35, 27.83, 23.32. HRMS (ESI) m/z calc'd for $C_{24}H_{39}N_2O_4$ $[M+H]^+$: 419.2910; found 419.2918. $[\alpha]^{21}_D$ = -35.96° (c = 1.07, $CHCl_3$). *Note: The ^{13}C NMR spectrum was analyzed using variable temperature (60 °C) in DMSO to coalesce N-Boc and amide rotamers.*

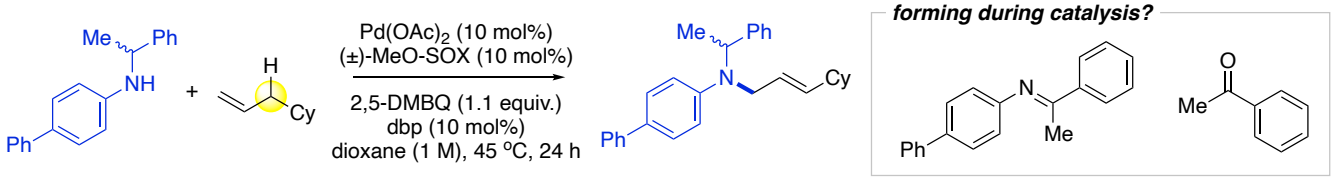
Synthesis of pent-4-en-1-yl (2*S*,5*R*)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4,4-dioxide:



To a flame-dried round-bottom flask equipped with a stir bar was added (2*S*,5*R*)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid 4,4-dioxide (1.6 g, 7 mmol, 1.0 equiv.), 4-dimethylaminopyridine (86 mg, 0.7 mmol, 0.1 equiv.), and DCM (18 mL, 0.4 M). The solution was cooled to 0 °C and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (1.4 g, 9.1 mmol, 1.3 equiv.) was added portion-wise, followed by dropwise addition of pent-4-en-1-ol (0.66 g, 7.7 mmol, 1.2 equiv.). The reaction was stirred at 0 °C to room temperature overnight. The crude mixture was diluted with water (10 mL), the aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification via flash column chromatography (300 mL SiO_2, 5% → 10% → 15% → 20% → 25% Acetone/Hexanes eluent) afforded the product as a yellow oil (1.6 g, 5.4 mmol, 78% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.79 (ddt, J = 16.9, 10.2, 6.6 Hz, 1H), 5.15 – 4.96 (m, 2H), 4.61 (dd, J = 4.2, 2.1 Hz, 1H), 4.38 (s, 1H), 4.22 (app td, J = 6.7, 1.6 Hz, 2H), 3.50 (dd, J = 16.2, 4.2 Hz, 1H), 3.44 (dd, J = 16.2, 2.2 Hz, 1H), 2.22 – 2.08 (m, 2H), 1.89 – 1.69 (m, 2H), 1.62 (s, 3H), 1.42 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.84, 167.11, 136.87, 116.07, 66.00, 63.41, 62.80, 61.24, 38.47, 30.05, 27.69, 20.51, 18.77. *Note: the methyl protons diastereotopic, with two proton (1.62 and 1.42 ppm) and two carbon (20.51 and 18.77 ppm) resonances observed.* HRMS (ESI) m/z calc'd for $C_{13}H_{20}NO_5S$ $[M+H]^+$: 302.1062; found 302.1060. $[\alpha]^{24}_D$ = +181.24° (c = 0.98, $CHCl_3$).

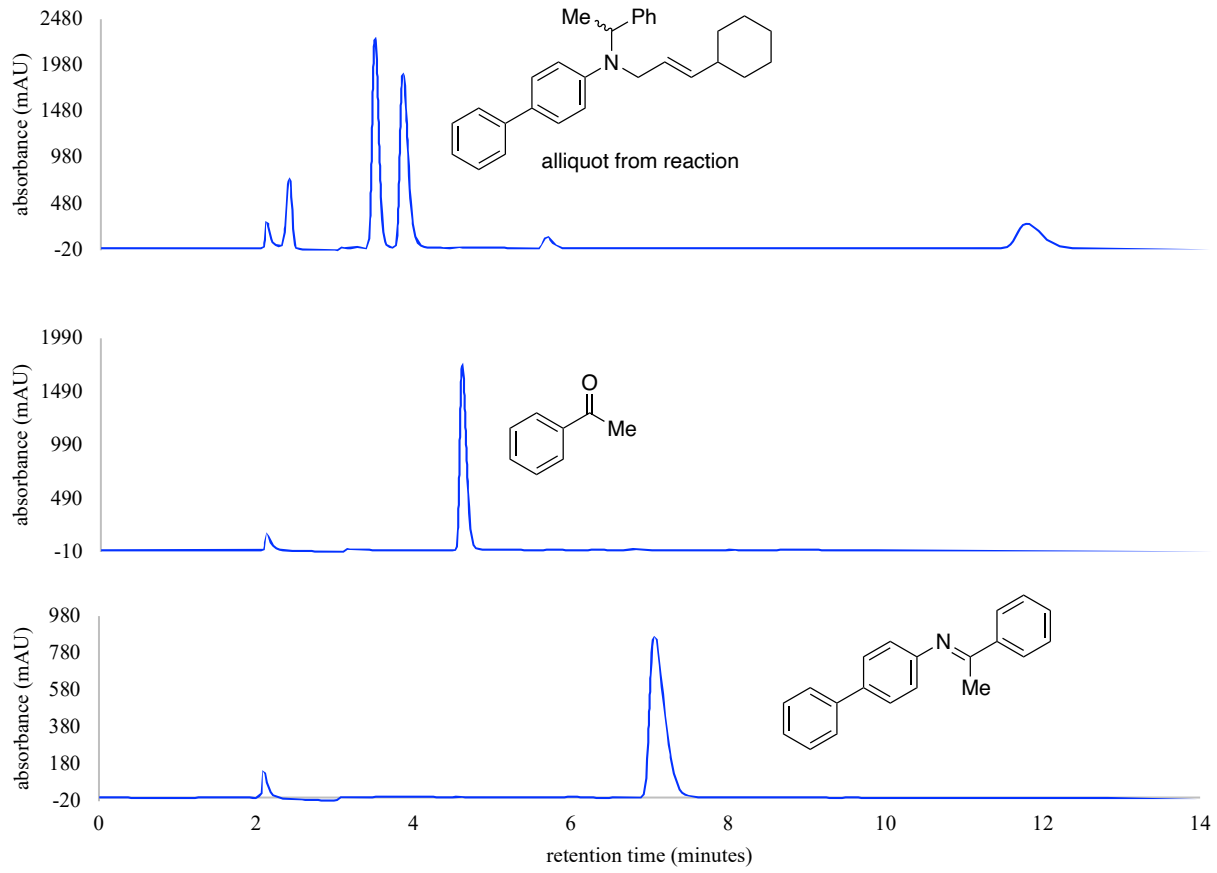
5. Mechanistic Investigations

5.1. Investigating palladium-amine β-hydride elimination side reactivity.



N-(1-phenylethyl)-[1,1'-biphenyl]-4-amine and allylcyclohexane were reacted according to the general procedure (reference substrate **24**) and at the end of the reaction, an aliquot was taken by dipping a pipette tip into the reaction vial. The aliquot was filtered through a pipette silica plug and rinsed with Et_2O. The crude material, acetophenone, and *N*-([1,1'-biphenyl]-4-yl)-1-phenylethan-1-imine were separately analyzed by HPLC using a Chiralcel OD-H column (2% IPA/Hexanes eluent, 1.5 mL/min flow rate).

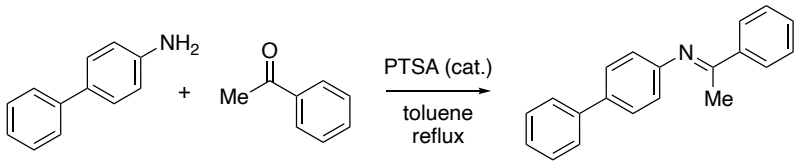
Figure S3. Stacked HPLC traces of the crude (*E*)-*N*-(3-cyclohexylallyl)-*N*-(1-phenylethyl)-[1,1'-biphenyl]-4-amine reaction, acetophenone, and *N*-([1,1'-biphenyl]-4-yl)-1-phenylethan-1-imine.



Conclusion: This study shows that no imine nor hydrolyzed imine side reactivity is observed under these C(sp^3)H/N(sp^2) cross-coupling conditions. These results suggest that this amination likely proceeds through an outer-sphere functionalization of the

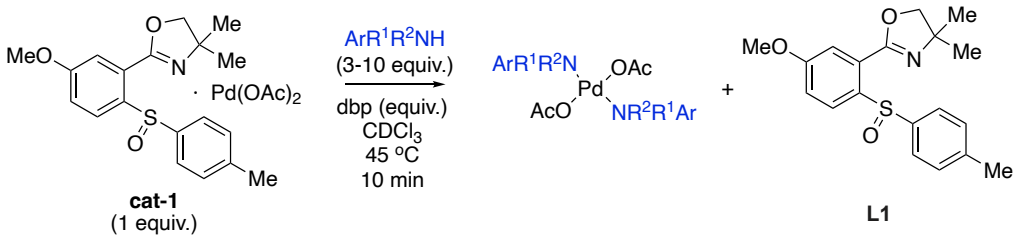
arylamine and/or with neutral arylamines, contrary to the mechanism observed in C(sp^2)—N cross couplings of aryl halides with amines that proceed via palladium-alkylamido intermediates.

Synthesis of *N*-([1,1'-biphenyl]-4-yl)-1-phenylethan-1-imine:



To a flame-dried round-bottom flask eqipped with a stir bar, Dean-Stark apparatus, and a reflux condenser was added [1,1'-biphenyl]-4-amine (0.4 g, 2.4 mmol, 1.2 equiv.), acetophenone (0.24 g, 2 mmol, 1.0 equiv.), toluene (5 mL, 0.4 M), and *p*-toluenesulfonic acid (19 mg, 0.1 mmol, 0.05 equiv.). The reaction was stirred at reflux for 48 h. The mixture was then cooled to room temperature and concentrated under reduced pressure. Purification via flash column chromatography (SiO_2, 0% → 2% → 3% → 4% → 5% EtOAc/Hexanes eluent) afforded a mixture of the product with acetophenone. The resulting solid was triturated with pentane to afford *N*-([1,1'-biphenyl]-4-yl)-1-phenylethan-1-imine as a bright-yellow solid (83.2 mg, 0.31 mmol, 15% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (app d, *J* = 7.0 Hz, 2H), 7.65 (app d, *J* = 7.7 Hz, 2H), 7.63 (app d, *J* = 8.3 Hz, 2H), 7.53 – 7.44 (m, 5H), 7.36 (app t, *J* = 7.4 Hz, 1H), 6.91 (app d, *J* = 8.0 Hz, 2H), 2.33 and 2.32 (two s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.81, 151.09, 141.07, 139.61, 136.30, 130.68, 128.89, 128.55, 127.80, 127.35, 127.01, 126.93, 120.04, 17.66. HRMS (ESI) m/z calc'd for $C_{20}H_{18}N$ $[M+H]^+$: 272.1439; found 272.1439.

5.2. Spectroscopic investigation of the MaSOX·Pd(OAc)$_2$ catalyst with amines.



Amine-palladium(II) binding procedure: To a ½ dram vial equipped with a stir bar was added Pd(OAc)$_2$ (3.4 mg, 0.015 mmol, 1.0 equiv.) and MaSOX (5.2 mg, 0.015 mmol, 1.0 equiv.). $CDCl_3$ (0.3 mL, 0.05 M) or a fresh solution of dibutyl phosphate in $CDCl_3$ was then added (0.3 mL, 0.05 M). The vial was sealed, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 1 h to precomplex the catalyst. *Note: 1 hour was found to be optimal for complexation and diminished stirring times led to variable results.* Subsequently, amine (10, 5, or 3 equiv.) was added, and the reaction was stirred for 10 min at 45 °C. 1,3,5-trimethoxybenzene (5 mg, 0.03 mmol, 2.0 equiv.) was then added as an internal standard followed by dilution with 0.4 mL of $CDCl_3$. The mixture was made homogenous and immediately transferred to an NMR tube for analysis. The amount of decomplexed MaSOX **L1** was determined by quantitative ^{1}H NMR using a Bruker 600 MHz spectrometer (nt = 32 scans, d1 = 21 seconds, aq = 4 seconds). **L1** and Pd(OAc)$_2$(amine)$_2$ as a mixture of diastereomers (e.g. complex **4**) were the major species observed spectroscopically. **L1** provided the most distinguishable peaks for analysis and the **L1** proton resonance at 8.21 ppm (1 proton) was integrated in reference to the internal standard proton resonance at 6.09 ppm (3 protons)

to determine yield of decomplexed **L1**. Yields are the average of two or three experiments. *Note: (1) 0.05 M of dibutyl phosphate in $CDCl_3$ (0.3 mL, 0.015 mmol, 1.0 equiv.) is representative of 5 mol% dbp under catalytic conditions and 0.25 M of dibutyl phosphate in $CDCl_3$ (0.3 mL, 0.375 mmol, 5.0 equiv.) is representative of 25 mol% dbp under catalytic conditions. (2) In experiments where 10 equivalents of amine afforded complete ligand decomplexation, the experiment was also assessed with 3 equivalents of amine which generally afforded more distinguishable trends.*

A control experiment was conducted following the amine-palladium(II) binding procedure with $CDCl_3$ as a solvent.

0 equiv. amine: Run 1: 7% yield **L1**; Run 2: 7% yield **L1**; Run 3: 5% yield **L1**. **Average: 6% ± 1.0% yield L1.**

1,1,1-trifluoro-*N*-phenethylmethanesulfonamide was used following the amine-palladium(II) binding procedure with $CDCl_3$ as a solvent.

10 equiv. amine: Run 1: 0% yield **L1**; Run 2: 0% yield **L1**. Run 3: 0% yield **L1**. **Average: 0% yield L1.**

Piperidine was used following the amine-palladium(II) binding procedure with $CDCl_3$ as a solvent.

10 equiv. amine: Run 1: 100% yield **L1**; Run 2: 101% yield **L1**. **Average: 100% ± 1.2% yield L1.**

5 equiv. amine: Run 1: 100% yield **L1**; Run 2: 99% yield **L1**. **Average: 100% ± 0.7% yield L1.**

3 equiv. amine: Run 1: 101% yield **L1**; Run 2: 100% yield **L1**. **Average: 101% ± 1.1% yield L1.**

Phenylamine was used following the amine-palladium(II) binding procedure with $CDCl_3$ as a solvent.

10 equiv. amine: Run 1: 100% yield **L1**; Run 2: 99% yield **L1**; Run 3: 100% yield **L1**. **Average: 100% ± 0.8% yield L1.**

5 equiv. amine: Run 1: 95% yield **L1**; Run 2: 93% yield **L1**; Run 3: 96% yield **L1**. **Average: 95% ± 1.6% yield L1.**

3 equiv. amine: Run 1: 93% yield **L1**; Run 2: 91% yield **L1**; Run 3: 91% yield **L1**. **Average: 92% ± 0.9% yield L1.**

***N*-methyl phenylamine** was used following the amine-palladium(II) binding procedure with $CDCl_3$ as a solvent.

10 equiv. amine: Run 1: 97% yield **L1**; Run 2: 96% yield **L1**; Run 3: 96% yield **L1**. **Average: 96% ± 0.9% yield L1.**

5 equiv. amine: Run 1: 93% yield **L1**; Run 2: 90% yield **L1**; Run 3: 92% yield **L1**. **Average: 92% ± 1.6% yield L1.**

3 equiv. amine: Run 1: 80% yield **L1**; Run 2: 84% yield **L1**; Run 3: 80% yield **L1**. **Average: 81% ± 2.6% yield L1.**

***N*-methyl phenylamine** was used following the amine-palladium(II) binding procedure with 0.05 M of dibutyl phosphate in $CDCl_3$ (0.3 mL, 0.015 mmol, 1.0 equiv.) as a solvent.

10 equiv. amine: Run 1: 93% yield **L1**; Run 2: 96% yield **L1**; Run 3: 93% yield **L1**. **Average: 94% ± 1.4% yield L1.**

***N*-methyl-4-nitroaniline** was used following the amine-palladium(II) binding procedure with $CDCl_3$ as a solvent.

10 equiv. amine: Run 1: 15% yield **L1**; Run 2: 13% yield **L1**; Run 3: 12% yield **L1**. **Average: 14% ± 1.4% yield L1.**

4-methoxy-*N*-methylaniline was used following the amine-palladium(II) binding procedure with $CDCl_3$ as a solvent.

10 equiv. amine: Run 1: 99% yield **L1**; Run 2: 100% yield **L1**; Run 3: 99% yield **L1**. **Average: 99% ± 0.2% yield L1.**

3 equiv. amine: Run 1: 96% yield **L1**; Run 2: 95% yield **L1**; Run 3: 97% yield **L1**. **Average: 96% ± 1.5% yield L1.**

***N*-butylaniline** was used following the amine-palladium(II) binding procedure with $CDCl_3$ as a solvent.

10 equiv. amine: Run 1: 92% yield **L1**; Run 2: 93% yield **L1**; Run 3: 96% yield **L1**. **Average: 93% ± 2% yield L1.**

Indoline was used following the amine-palladium(II) binding procedure with $CDCl_3$ as a solvent.

10 equiv. amine: Run 1: 96% yield **L1**; Run 2: 95% yield **L1**; Run 3: 93% yield **L1**. **Average: 95% ± 1.3% yield L1.**

3 equiv. amine: Run 1: 95% yield **L1**; Run 2: 97% yield **L1**; Run 3: 98% yield **L1**. **Average: 97% ± 1.5% yield L1.**

Diphenylamine was used following the amine-palladium(II) binding procedure with $CDCl_3$ as a solvent.

10 equiv. amine: Run 1: 8% yield **L1**; Run 2: 7% yield **L1**; Run 3: 8% yield **L1**. **Average: 8% ± 0.5% yield L1.**

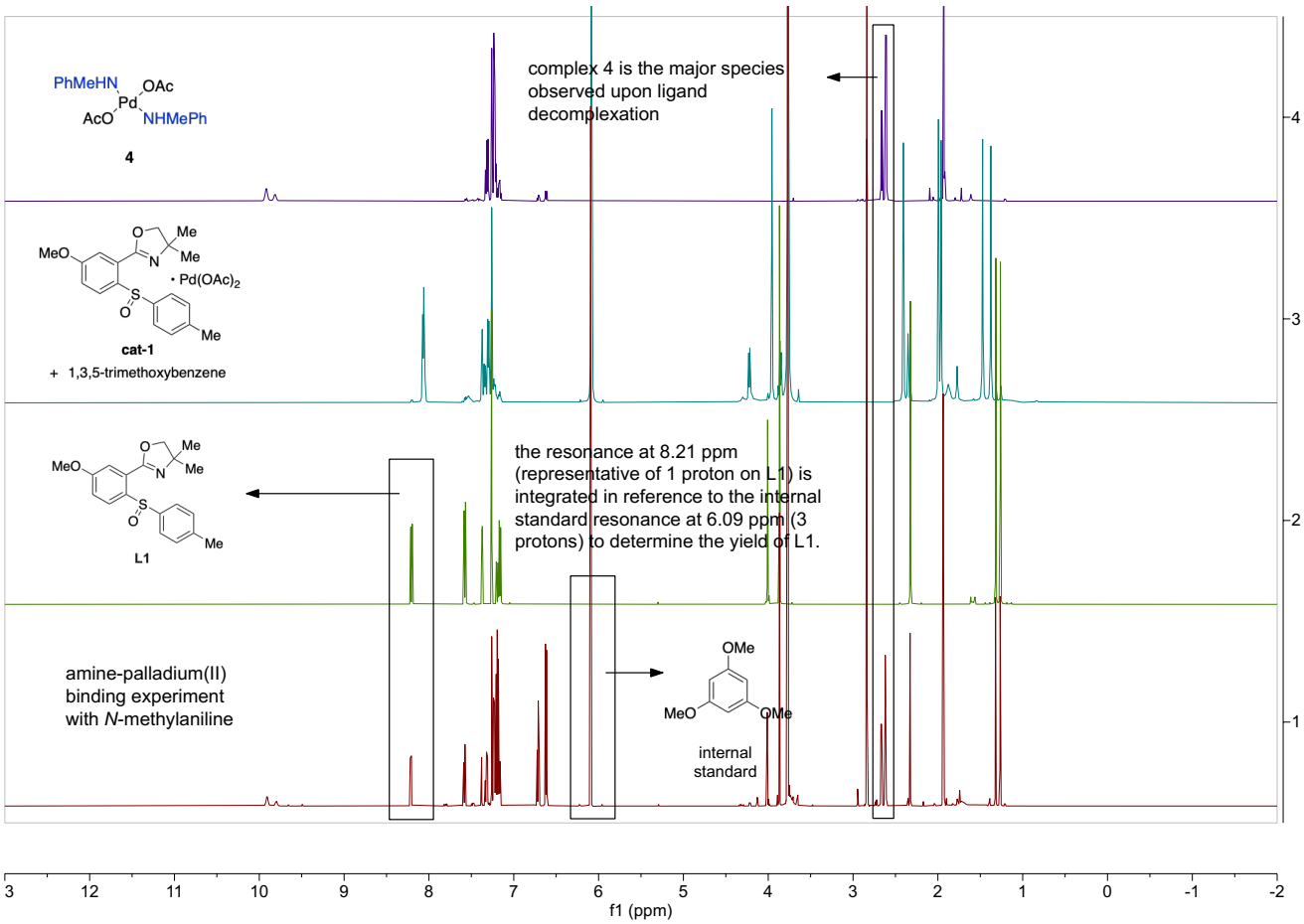
(*E*)-*N*-(3-cyclohexylallyl)-*N*-methylaniline was used following the amine-palladium(II) binding procedure with $CDCl_3$ as a solvent.

10 equiv. amine: Run 1: 19% yield **L1**; Run 2: 21% yield **L1**; Run 3: 23% yield **L1**. **Average: 21% ± 1.9% yield L1.**

(*E*)-1-(3-cyclohexylallyl)-4-phenylpiperidine was used following the amine-palladium(II) binding procedure with $CDCl_3$ as a solvent.

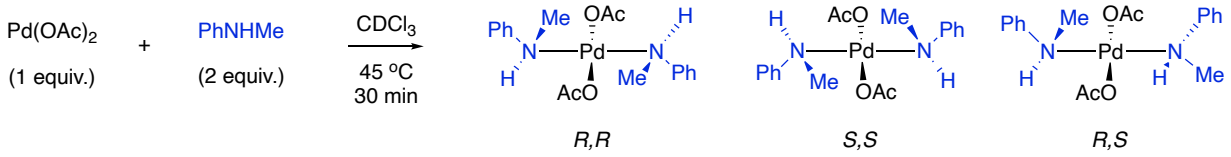
10 equiv. amine: Run 1: 58% yield **L1**; Run 2: 63% yield **L1**; Run 3: 63% yield **L1**. **Average: 61% ± 2.9% yield L1.**

Figure S4. Stacked spectra of the amine-palladium(II) binding experiment with *N*-methyl phenylamine, MaSOX **L1,** MaSOX·Pd(OAc)$_2$ **cat-1**, and complex **4**.



This shows a representative example of the amine-palladium(II) binding analysis with *N*-methyl phenylamine. The **L1** proton resonance at 8.21 ppm (1 proton) was integrated in reference to the internal standard proton resonance at 6.09 ppm (3 protons) to determine the yield of decomplexed **L1**. Authentic standard synthesis confirmed complex **4** as the major species observed upon ligand decomplexation.

In situ synthesis of Pd(OAc)$_2$(PhNHMe)$_2$:

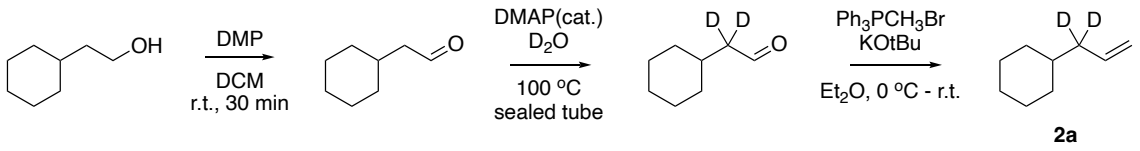


To a ½ dram vial equipped with a stir bar was added Pd(OAc)$_2$ (3.4 mg, 0.015 mmol, 1.0 equiv.), *N*-methyl phenylamine (3.2 mg, 0.03 mmol, 2.0 equiv.), and $CDCl_3$ (0.3 mL, 0.05 M), and the reaction was stirred for 30 min at 45 °C. The mixture was cooled to room temperature, diluted with 0.4 mL of $CDCl_3$, made homogenous by mixing, and transferred to an NMR tube for analysis. *Note: Amine ligands with three non-equivalent substituents affords a stereogenic nitrogen atom following coordination to a metal, resulting in a mixture of isomers (a pair of enantiomers and a meso isomer). This is in correspondence*

to the reported literature.[63] The reaction was characterized as a mixture of diastereomers and the diastereomeric ratio was determined by ^{1}H NMR (1:1.9 d.r.); the minor diastereomer is indicated in parentheses in the ^{13}C NMR characterization. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.97 – 9.87 (m, 1.23H), 9.86 – 9.77 (m, 0.73H), 7.35 – 7.29 (m, 2.69H), 7.25 – 7.16 (m, 7.42H), 2.66 (d, J = 5.6 Hz, 2.12H), 2.61 (d, J = 5.6 Hz, 3.94H), 1.93 (s, 3.77H), 1.92 (s, 2.14H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.09, (182.01), 147.01, (146.84), 129.43, (129.25), 125.42, (120.92), 120.69, (37.28), 36.68, 24.51, (24.39).

5.3. Kinetic isotope effect studies.

Synthesis of (allyl-1,1-*d*$_2$)cyclohexane (2a):



This sequence was synthesized following a modified literature procedure and spectral data were in accordance with the reported values.[64]

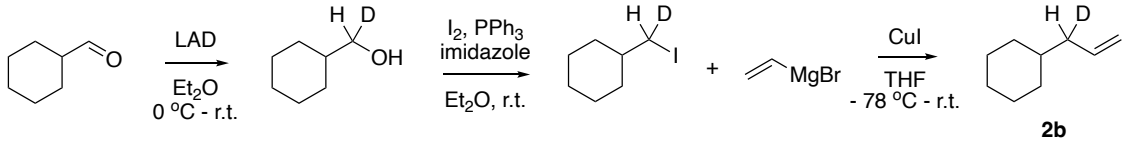
2-cyclohexylacetaldehyde. To a flame-dried round-bottom flask equipped with a stir bar was added Dess-Martin periodinane (7.6 g, 18 mmol, 1.2 equiv.) and DCM (43 mL, 0.35 M). The flask was cooled to 0 °C, 2-cyclohexylethan-1-ol (1.9 g, 15 mmol, 1.0 equiv.) was added dropwise, and the reaction was stirred at room temperature for 30 minutes. The reaction was then cooled to 0 °C, diluted with Et_2O (30 mL), and quenched with saturated $NaHCO_3$ (20 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with Et_2O (3 x 20 mL). The combined organic layers were washed with saturated $NaHCO_3$ (20 mL), water (20 mL), brine (20 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure at 0 °C. Purification via flash column chromatography (120 mL SiO_2, 5% Et_2O/Pentane eluent) afforded the product as a clear oil (1.4 g, 11.4 mmol, 76% yield). *Note: an impurity elutes right before the product and doesn't stain a bright yellow color in $KMnO_4$ stain.*

2-cyclohexylacetaldehyde-2,2-d$_2$. To a flame-dried sealed tube equipped with a stir bar was added 2-cyclohexylacetaldehyde (1.4 g, 11.4 mmol, 1.0 equiv.), D_2O (4.6 mL, 2.5 M), and DMAP (0.14 g, 1.1 mmol, 0.1 equiv.), and the reaction was stirred at 130 °C behind a blast shield for 2 hours. The reaction mixture was cooled to room temperature and then transferred to a separatory funnel with DCM (10 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with DCM (3 x 10 mL). The combined organic layers were washed with saturated 1 M HCl (2 x 20 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure at 0 °C, azeotroping with Pentane. The crude material was resubjected to the reaction two more times until 2-cyclohexylacetaldehyde-2,2-d_2 was achieved in >95% D incorporation via 1H NMR analysis (1.14 g, 8.9 mmol, 78% yield).

(allyl-1,1-d$_2$*)cyclohexane*. To a flame-dried round-bottom flask equipped with a stir bar was added Ph_3PMeBr (5.4 g, 15.2 mmol, 1.7 equiv.) and Et_2O (75 mL, 0.2 M), the mixture was cooled to 0 °C, and potassium *t*-butoxide (1.5 g, 13.4 mmol, 1.5 equiv.) was added portion-wise. The reaction was stirred at 0 °C for 30 minutes and subsequently, a solution of 2-cyclohexylacetaldehyde-2,2-d_2 (1.14 g, 8.9 mmol, 1.0 equiv.) in Et_2O (18 mL, 0.5 M) was added dropwise. The reaction was let stir at 0 °C to room temperature overnight. Following reaction completion, the mixture was cooled to 0 °C and quenched with dropwise addition of saturated NH_4Cl (30 mL). The aqueous and organic layers were separated, and the aqueous layer

was extracted with Et_2O (3 x 50 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure at 0 °C, azeotroping with Pentane. Purification via flash column chromatography (SiO_2, Pentane eluent) afforded the product as a clear oil (0.74 g, 5.9 mmol, 66% yield).

Synthesis of (allyl-1-*d*)cyclohexane (2b):



2b

This sequence was synthesized following a modified literature procedure and spectral data were in accordance with the reported values.[64]

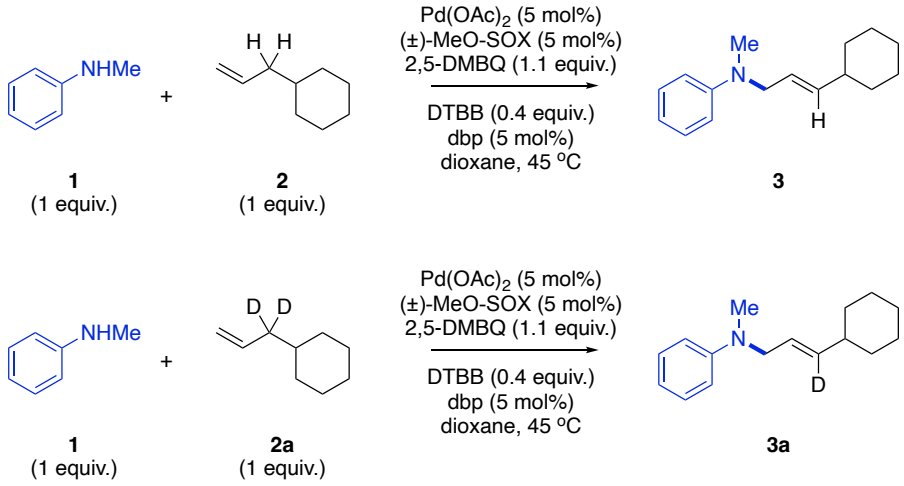
cyclohexylmethan-d-ol. To a flame-dried round-bottom flask equipped with a stir bar was added lithium aluminum deuteride (0.25 g, 6 mmol, 1.0 equiv.) from the glovebox followed by Et_2O (12 mL, 0.5 M). The mixture was cooled to 0 °C and a solution of cyclohexanecarbaldehyde (0.67 g, 6 mmol, 1.0 equiv.) in Et_2O (6 mL, 1.0 M) was added dropwise. The reaction was allowed to stir at 0 °C to room temperature, monitoring via TLC with Cerium Ammonium Molybdate stain. Following full consumption of the aldehyde, the reaction was cooled to 0 °C and quenched dropwise with water (0.25 mL), 15% NaOH (0.25 mL), and then water (0.75 mL). The mixture was diluted with Et_2O (20 mL), $MgSO_4$ was added, and the mixture was stirred for 30 min. The slurry was subsequently filtered over celite, rinsing with Et_2O, and the solvent was concentrated under reduced pressure. Purification via flash column chromatography (SiO_2, 0% → 2% → 4% → 6% → 8% → 10% → 15% Acetone/Hexanes eluent) afforded the product as clear oil (0.5 g, 4.4 mmol, 72% yield). *Note: upon purification, an impurity elutes at the tail-end with the product, which stains a vibrant yellow color with $KMnO_4$ stain (versus the product, which stains white). The impure fractions were collected separately and resubjected to the same column conditions.*

(iodomethyl-d)cyclohexane. To a flame-dried round-bottom flask equipped with a stir bar was added iodine (1.4 g, 5.6 mmol, 1.3 equiv.) and Et_2O (14 mL, 0.32 M), followed by imidazole (0.44 g, 6.5 mmol, 1.5 equiv.) and PPh_3 (1.4 g, 5.2 mmol, 1.2 equiv.). The flask was wrapped in aluminum foil to shield the reaction from the light and then a solution of cyclohexylmethan-*d*-ol (0.5 g, 4.3 mmol, 1.0 equiv.) in Et_2O (9 mL, 0.48 M) was added dropwise. The reaction was stirred at room temperature for 24 hours. *Note: principates clump at the bottom of the flask and to ensure the progression of the reaction, the solids were broken up with a spatula after ca. 14 hours.* The crude mixture was then filtered over celite, rinsing with Et_2O, and concentrated under reduced pressure at 0 °C. Purification via flash column chromatography (150 mL SiO_2, Pentane eluent) afforded the product as a clear oil (0.84 g, 3.8 mmol, 87% yield). *Note: the alkyl iodide is sensitive to light and will turn purple if not properly handled. Work should be completed in a dimly lit space, if possible.*

(allyl-1-d)cyclohexane. To a flame-dried round-bottom flask equipped with a stir bar was added copper iodide (1.1 g, 5.6 mmol, 1.5 equiv.) from the glovebox, followed by (iodomethyl-*d*)cyclohexane (0.83 g, 3.7 mmol, 1.0 equiv.) and THF (8 mL, 0.5 M). The flask was placed under an atmosphere of argon, cooled to -78 °C, and a 0.437 M solution of vinylmagnesium bromide in THF (11 mL, 4.8 mmol, 1.3 equiv.) was added dropwise. The reaction was stirred at -78 °C to 0 °C for 2 hours, and then at 0 °C to room temperature for another two hours. The mixture was then quenched by dropwise addition of saturated NH_4Cl (10 mL) at 0 °C and then diluted with H_2O (5 mL) and Pentane (20 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with Pentane (3 x 20 mL). The combined organic layers were washed with water, (30 mL), brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure at 0 °C. Purification via flash column

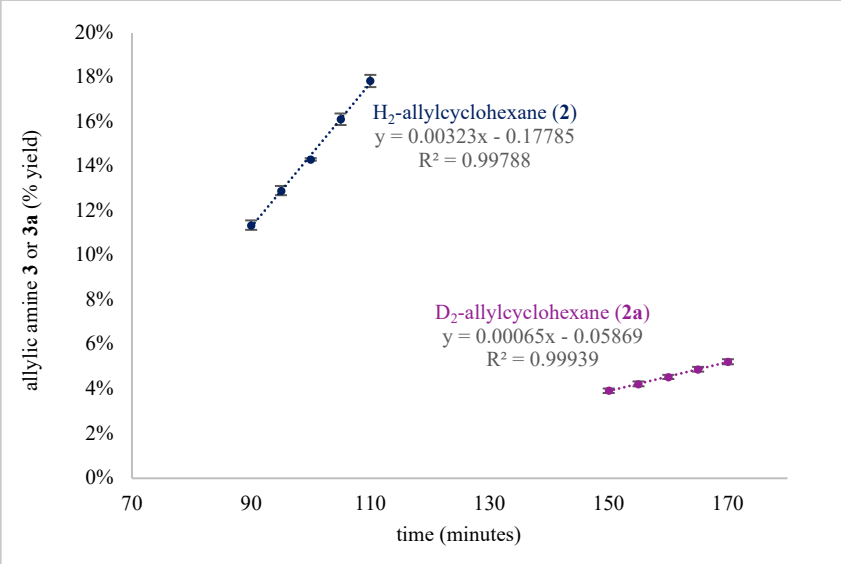
chromatography (300 mL SiO_2, Pentane eluent) afforded the product as a clear oil (0.15 g, 1.2 mmol, 32% yield). *Note: running the reaction under N_2 instead of argon lead to poorer yields. Upon purification, an impurity elutes out immediately after the product, which can be visualized by $KMnO_4$ stain upon careful inspection.*

Intermolecular kinetic isotope effect with dbp additive.



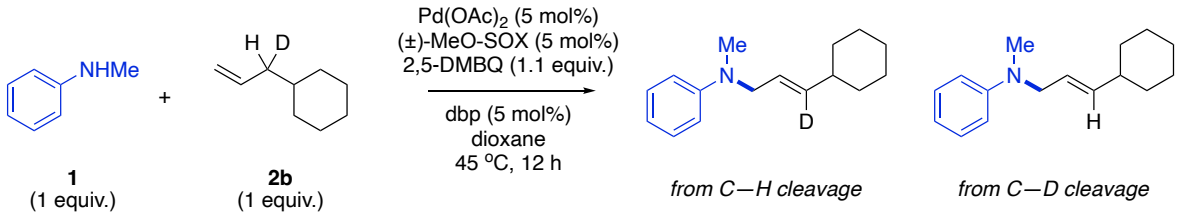
To a ½ dram vial equipped with a stir bar was added $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.05 equiv.), MaSOX (5.2 mg, 0.015 mmol, 0.05 equiv.), 2,5-dimethylbenzoquinone (45 mg, 0.33 mmol, 1.1 equiv.), 1,4-Di-tert-butylbenzene (22.8 mg, 0.12 mmol, 0.4 equiv.) as an internal standard, and *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.). A fresh 0.05 M solution of dibutyl phosphate in dioxane (0.05 equiv., 0.3 mL) and an additional 0.3 mL of dioxane was added (0.5 M total), and the vial was sealed with a Teflon cap. Allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) or (allyl-1,1-d_2)cyclohexane (37.9 mg, 0.3 mmol, 1.0 equiv.) was added via injection through the cap, and the vial was subsequently placed in a pre-heated 45 °C aluminum block. Aliquots (10 μL) were taken at the corresponding reactions times from the reaction vial and filtered through a silica plug with Et_2O for HPLC analysis (Agilent Poroshell 120 EC-C18, 90% ACN/water, 1.5 mL/min). The yield was determined by integration of the product peak (~7.5 min) relative to the internal standard peak (~6.2 min) and corrected by a standard curve. Yields are reported as the average of three runs with error bars denoting the standard deviation.

Figure S5: Initial rates with H_2-allylcyclohexane (**2**) and D_2-allylcyclohexane (**2a**) with dbp to determine the intermolecular KIE.



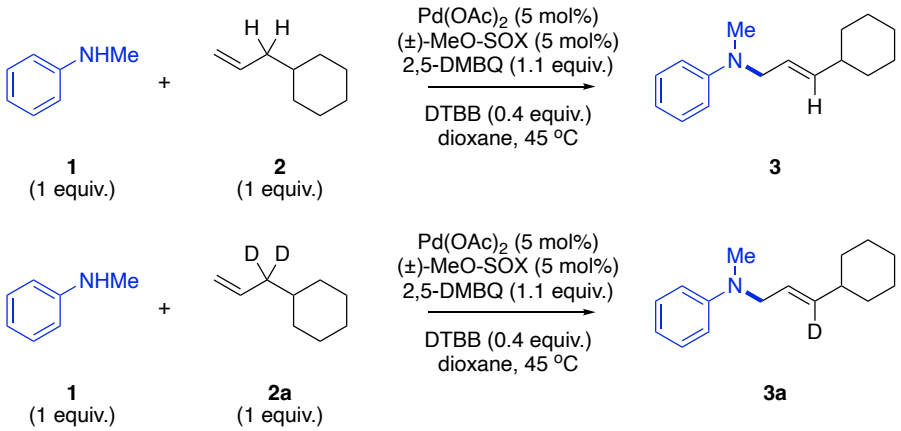
Intermolecular KIE = k_H/k_D = 0.00323/0.00065 = 4.95 ± 0.06

Intramolecular kinetic isotope effect with dbp additive.



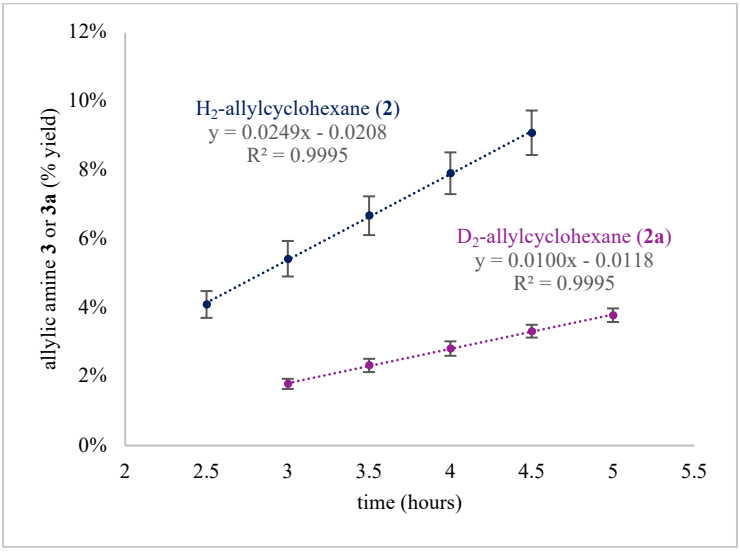
To a ½ dram vial equipped with a stir bar was added $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.05 equiv.), MaSOX (5.2 mg, 0.015 mmol, 0.05 equiv.), 2,5-dimethylbenzoquinone (45 mg, 0.33 mmol, 1.1 equiv.), and *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.). A fresh 0.05 M solution of dibutyl phosphate in dioxane was added (0.3 mL, 1.0 M), followed by (allyl-1-*d*)cyclohexane (37.6 mg, 0.3 mmol, 1.0 equiv.). The vial was sealed with Teflon tape and parafilm, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 12 h. The vial was cooled to room temperature, diluted with $CDCl_3$, and benzotrifluoride (43.8 mg, 0.3 mmol, 1.0 equiv.) was added as an internal standard. The crude mixture was analyzed using quantitative ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) for crude analysis. The crude reaction was then concentrated under reduced pressure and immediately subjected to flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (300 mL) → 3% EtOAc/Hexanes (100 mL) eluent) to afford the product as a clear oil. The ratio of products was determined by quantitative ^{1}H NMR analysis (nt = 16 scans, d1 = 10 seconds). Run 1: k_H/k_D = 5.06 (51.6 mg, 75% yield); Run 2: k_H/k_D = 5.03 (51.7 mg, 75% yield); Run 3: k_H/k_D = 5.07 (51.2 mg, 74% yield). **Average: k_H/k_D = 5.05 ± 0.02 (75% ± 0.4% yield).**

Intermolecular kinetic isotope effect without dbp additive.



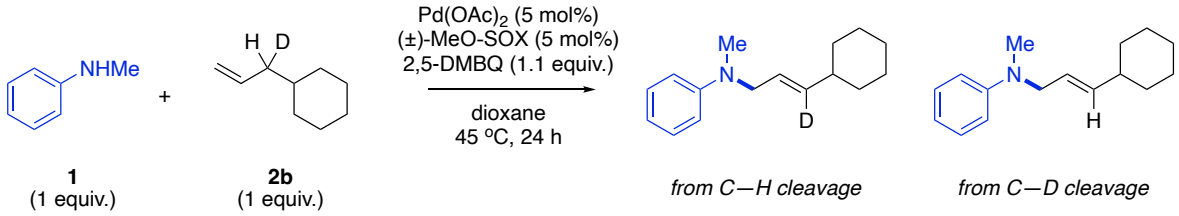
To a ½ dram vial equipped with a stir bar was added $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.05 equiv.), MaSOX (5.2 mg, 0.015 mmol, 0.05 equiv.), 2,5-dimethylbenzoquinone (45 mg, 0.33 mmol, 1.1 equiv.), 1,4-Di-tert-butylbenzene (22.8 mg, 0.12 mmol, 0.4 equiv.) as an internal standard, and *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.), followed by 0.6 mL of dioxane (0.5 M). The vial was sealed with a Teflon cap, allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) or (allyl-1,1-d_2)cyclohexane (37.9 mg, 0.3 mmol, 1.0 equiv.) was added via injection through the cap, and the vial was subsequently placed in a pre-heated 45 °C aluminum block. Aliquots (10 µL) were taken at the corresponding times from the reaction vial and filtered through a silica plug with diethyl ether for HPLC analysis (Agilent Poroshell 120 EC-C18, 90% ACN/water, 1.5 mL/min). The yield was determined by integration of the product peak (~7.5 min) relative to the internal standard peak (~6.2 min) and corrected by a standard curve. Yields are reported as the average of three runs with error bars denoting the standard deviation.

Figure S6: Initial rates with H_2-allylcyclohexane (**2**) and D_2-allylcyclohexane (**2a**) without dbp to determine the intermolecular KIE.



Intermolecular KIE = k_H/k_D = 0.0249/0.01 = 2.50 ± 0.08

Intramolecular kinetic isotope effect without dbp additive.

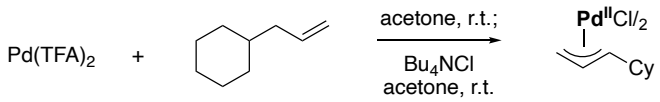


To a ½ dram vial equipped with a stir bar was added $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.05 equiv.), MaSOX (5.2 mg, 0.015 mmol, 0.05 equiv.), 2,5-dimethylbenzoquinone (45 mg, 0.33 mmol, 1.1 equiv.), *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.), dioxane (0.3 mL, 1.0 M), and (allyl-1-*d*)cyclohexane (37.6 mg, 0.3 mmol, 1.0 equiv.). The vial was sealed with Teflon tape and parafilm, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 24h. The vial was cooled to room temperature, diluted with $CDCl_3$, and benzotrifluoride (43.8 mg, 0.3 mmol, 1.0 equiv.) was added as an internal standard. The crude mixture was analyzed using quantitative ^1H NMR (nt = 16 scans, d1 = 10 seconds) for crude analysis. The crude reaction was then concentrated under reduced pressure and immediately subjected to flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (300 mL) → 3% EtOAc/Hexanes (100 mL) eluent) to afford the product as a clear oil. The ratio of products was determined by quantitative ^1H NMR analysis (nt = 16 scans, d1 = 10 seconds). Run 1: k_H/k_D = 4.35 (12.5 mg, 18% yield); Run 2: k_H/k_D = 4.33 (14 mg, 20% yield); Run 3: k_H/k_D = 4.48 (21.4 mg, 31% yield). **Average: k_H/k_D = 4.38 ± 0.08, (23% ± 6.9% yield).**

Conclusion: C—H cleavage is the rate determining step in this C(sp^3)H/N(sp^2) cross-coupling with the dbp additive.

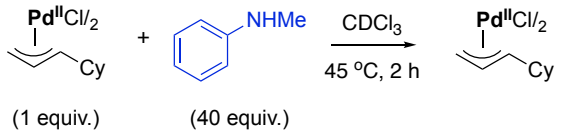
5.4. Stoichiometric π-allyl studies.

Synthesis of allylcyclohexane π-allyl-Pd(II) chloride dimer:

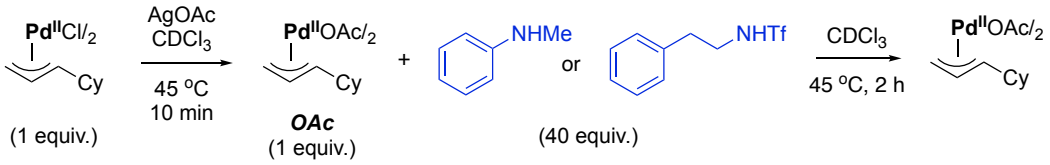


The π-allyl-Pd(II) chloride dimer was synthesized following a literature procedure and spectral data were in accordance with the reported values.[64] To a flame-dried round-bottom flask equipped with a stir bar was added $Pd(TFA)_2$ (0.67 g, 2 mmol, 1.0 equiv.) and Acetone (20 mL, 0.1 M), and stirred at room temperature for 10 minutes. Allylcyclohexane (0.31 mL, 2 mmol, 1.0 equiv.) was added dropwise, the reaction was stirred for 30 minutes, and then a solution of Bu_4NCl (0.61 g, 2.2 mmol, 1.1 equiv.) in Acetone (6 mL) was added dropwise and stirred for an additional 15 minutes. The crude mixture was filtered over a bed of celite (rinsing with Acetone), concentrated under reduced pressure, and then dry loaded onto celite. Purification via flash column chromatography (SiO_2, 5% → 10% → 15% → 25% → 50% EtOAc/Hexanes eluent) afforded the product as a bright yellow solid (0.3 g, 0.6 mmol, 56% yield).

Investigating functionalization of amines with palladium(II)-π-allyl complexes:

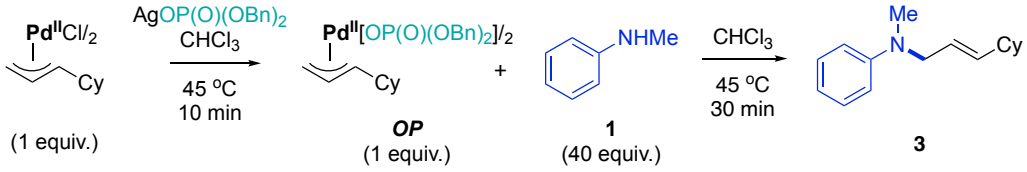


To a ½ dram vial equipped with a stir bar was added the π-allyl-Pd(II) chloride dimer (10.6 mg, 0.02 mmol, 1.0 equiv.), $CDCl_3$ (0.16 mL, 0.13 M), and *N*-methyl phenylamine (87 μL, 0.8 mmol, 40 equiv. (20 equiv. to palladium)). The vial was sealed, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 2 h. The mixture was cooled to room temperature, transferred to an NMR tube, and diluted with an additional 0.5 mL of $CDCl_3$. Crude ^{1}H NMR analysis afforded the recovered π-allyl-Pd(II) chloride dimer and no allylic amine functionalized product (see spectra).



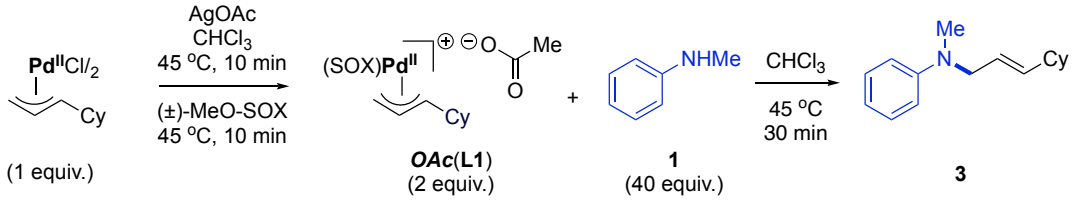
To a ½ dram vial equipped with a stir bar was added AgOAc (6.7 mg, 0.04 mmol, 2.0 equiv. (1.0 equiv. to palladium)) from the glovebox, the π-allyl-Pd(II) chloride dimer (10.6 mg, 0.02 mmol, 1.0 equiv.), and $CDCl_3$ (0.16 mL, 0.13 M). The vial was sealed, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 10 minutes. The mixture was cooled to room temperature and the π-allyl-Pd(II) acetate dimer ***OAc*** was filtered through a pipette with glass wool into a separate ½ dram vial equipped with a stir bar, rinsing with $CDCl_3$ (0.3 mL). *N*-methyl phenylamine (87 μL, 0.8 mmol, 40 equiv. (20 equiv. to palladium)) was added, the vial was sealed, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for an additional 2 h. The mixture was cooled to room temperature, transferred to an NMR tube, and diluted with an additional 0.3 mL of $CDCl_3$. Crude ^{1}H NMR analysis afforded the recovered π-allyl-Pd(II) acetate dimer and no allylic amine functionalized product (see spectra).

Alternatively, the procedure was followed using 1,1,1-trifluoro-*N*-phenethylmethanesulfonamide[65] (202.6 mg, 0.8 mmol, 40 equiv. (20 equiv. to palladium)) which afforded the recovered π-allyl-Pd(II) acetate dimer and no allylic amine functionalized product (see spectra).

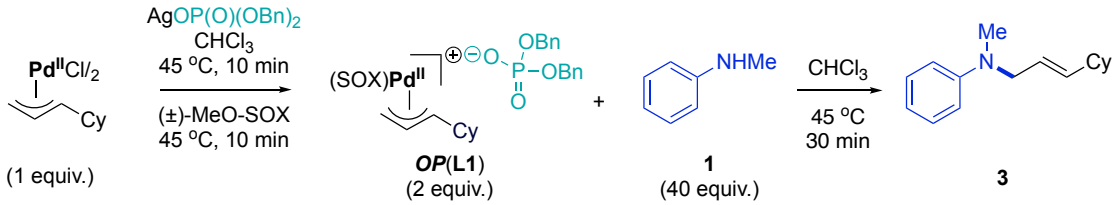


To a ½ dram vial equipped with a stir bar was added $AgOP(O)(OBn)_2$ (15.4 mg, 0.04 mmol, 2.0 equiv. (1.0 equiv. to palladium)) from the glovebox, the π-allyl-Pd(II) chloride dimer (10.6 mg, 0.02 mmol, 1.0 equiv.), and $CHCl_3$ (0.16 mL, 0.13 M). The vial was sealed, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 10 minutes. The mixture was cooled to room temperature and the π-allyl-Pd(II) phosphate dimer ***OP*** was filtered through a pipette with glass wool into a

separate ½ dram vial equipped with a stir bar, rinsing with $CHCl_3$ (0.5 mL). *N*-methyl phenylamine (87 μL, 0.8 mmol, 40 equiv. (20 equiv. to palladium)) was added, the vial was sealed, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 30 minutes. The mixture was immediately filtered through a silica plug and rinsed with EtOAc. The solution was concentrated under reduced pressure and then placed on high vacuum for 2 minutes. 1,3,5-trimethoxybenzene (6.7 mg, 0.04 mmol, 2.0 equiv.) was added as an internal standard followed by dilution with $CDCl_3$. The mixture was made homogenous, and half the material was transferred to an NMR tube for analysis. The amount of allylic amine product **3** was determined by quantitative ^{1}H NMR using a Bruker 600 MHz spectrometer (nt = 16 scans, d1 = 21 seconds, aq = 4 seconds). Run 1: 2% yield; Run 2: 2% yield; Run 3: 2% yield. **Average: 2% ± 0.3% yield.** *Note: prolonging the reaction to 2 hours afforded product **3** in preparative yield (84% yield).*



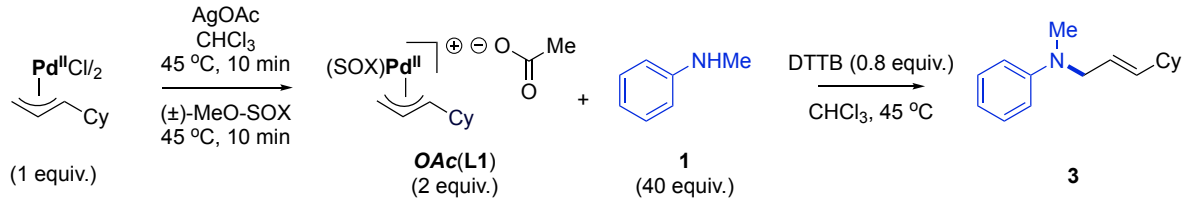
To a ½ dram vial equipped with a stir bar was added AgOAc (6.7 mg, 0.04 mmol, 2.0 equiv. (1.0 equiv. to palladium)) from the glovebox, the π-allyl-Pd(II) chloride dimer (10.6 mg, 0.02 mmol, 1.0 equiv.), and $CHCl_3$ (0.16 mL, 0.13 M). The vial was sealed, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 10 minutes. MaSOX (13.7 mg, 0.04 mmol, 2.0 equiv. (1.0 equiv. to palladium)) was subsequently added and the reaction was stirred at 45 °C for another 10 minutes, and then cooled to room temperature. Complex ***OAc*(L1)** was filtered through a pipette with glass wool into a separate ½ dram vial equipped with a stir bar, rinsing with $CHCl_3$ (0.5 mL). *N*-methyl phenylamine (87 μL, 0.8 mmol, 40 equiv. (20 equiv. to palladium)) was added, the vial was sealed, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 30 minutes. The mixture was immediately filtered through a silica plug and rinsed with EtOAc. The solution was concentrated under reduced pressure and then placed on high vacuum for 2 minutes. 1,3,5-trimethoxybenzene (6.7 mg, 0.04 mmol, 2.0 equiv.) was added as an internal standard followed by dilution with $CDCl_3$. The mixture was made homogenous, and half the material was transferred to an NMR tube for analysis. The amount of allylic amine product **3** was determined by quantitative ^{1}H NMR using a Bruker 600 MHz spectrometer (nt = 16 scans, d1 = 21 seconds, aq = 4 seconds). Run 1: 59% yield; Run 2: 62% yield; Run 3: 61% yield (isolated 5.7 mg, 62% yield). **Average: 61% ± 1.3% yield.**



To a ½ dram vial equipped with a stir bar was added $AgOP(O)(OBn)_2$ (15.4 mg, 0.04 mmol, 2.0 equiv. (1.0 equiv. to palladium)) from the glovebox, the π-allyl-Pd(II) chloride dimer (10.6 mg, 0.02 mmol, 1.0 equiv.), and $CHCl_3$ (0.16 mL, 0.13 M). The vial was sealed, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 10 minutes. MaSOX (13.7 mg, 0.04 mmol, 2.0 equiv. (1.0 equiv. to palladium)) was subsequently added and the reaction was stirred at 45 °C for another 10

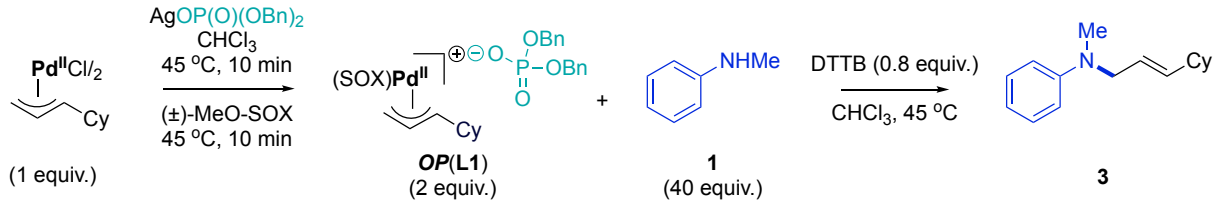
minutes, and then cooled to room temperature. Complex ***OP*(L1)** was filtered through a pipette with glass wool into a separate ½ dram vial equipped with a stir bar, rinsing with $CHCl_3$ (0.5 mL). *N*-methyl phenylamine (87 μL, 0.8 mmol, 40 equiv. (20 equiv. to palladium)) was added, the vial was sealed, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 30 minutes. The mixture was immediately filtered through a silica plug and rinsed with EtOAc. The solution was concentrated under reduced pressure and then placed on high vacuum for 2 minutes. 1,3,5-trimethoxybenzene (6.7 mg, 0.04 mmol, 2.0 equiv.) was added as an internal standard followed by dilution with $CDCl_3$. The mixture was made homogenous, and half the material was transferred to an NMR tube for analysis. The amount of allylic amine product **3** was determined by quantitative ^{1}H NMR using a Bruker 600 MHz spectrometer (nt = 16 scans, d1 = 21 seconds, aq = 4 seconds). Run 1: 88% yield; Run 2: 88% yield; Run 3: 85% yield. **Average: 87% ± 1.4% yield.**

Initial rates with complex *OAc*(L1) and *N*-methyl phenylamine [*N*-Ph, *OAc*(L1)].



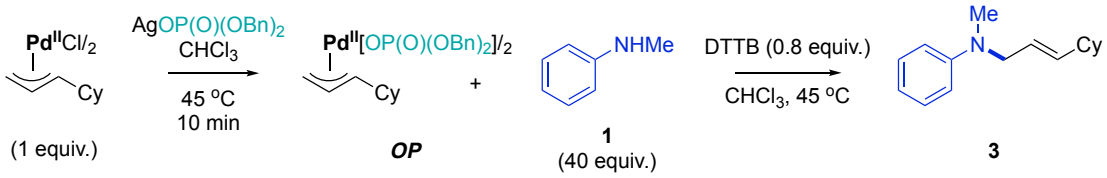
To a ½ dram vial equipped with a stir bar was added AgOAc (13.4 mg, 0.08 mmol, 2.0 equiv. (1.0 equiv. to palladium)) from the glovebox, the π-allyl-Pd(II) chloride dimer (21.2 mg, 0.04 mmol, 1.0 equiv.), and $CHCl_3$ (0.3 mL, 0.13 M). The vial was sealed, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 10 minutes. MaSOX (27.5 mg, 0.08 mmol, 2.0 equiv. (1.0 equiv. to palladium)) was subsequently added and the reaction was stirred at 45 °C for another 10 minutes, and then cooled to room temperature to afford complex ***OAc*(L1)**. To a 2 dram vial equipped with a stir bar was added 1,4-Di-tert-butylbenzene (6.1 mg, 0.032 mmol, 0.8 equiv.) as an internal standard. Complex ***OAc*(L1)** was filtered through a pipette with glass wool into the 2 dram vial, rinsing with $CHCl_3$ (5 mL, 0.008 M). The vial was sealed with a Teflon cap, *N*-methyl phenylamine (0.17 mL, 1.6 mmol, 40 equiv. (20 equiv. to palladium)) was added via injection through the cap, and the vial was immediately placed in a pre-heated 45 °C aluminum block. Aliquots (50 μL) were taken at the corresponding reaction times from the reaction vial and filtered through a silica plug with Et_2O for HPLC analysis (Agilent Poroshell 120 EC-C18, 90% ACN/water, 1.5 mL/min). The yield was determined by integration of the product peak (~7.5 min) relative to the internal standard peak (~6.2 min) and corrected by a standard curve. Yields are reported as the average of three runs with error bars denoting the standard deviation. $k_{initial}$ = 1.395 ± 0.031.

Initial rates with complex *OP*(L1) and *N*-methyl phenylamine [*N*-Ph, *OP*(L1)].



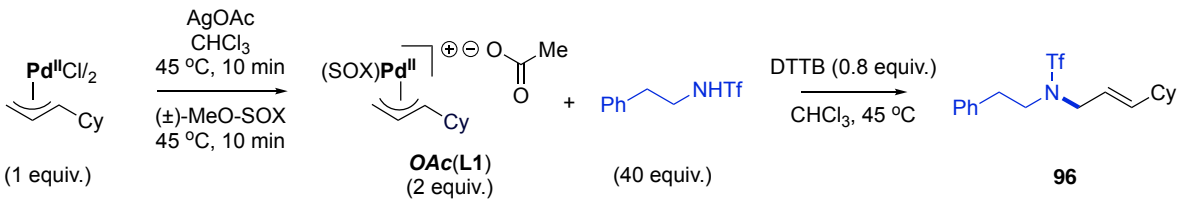
To a ½ dram vial equipped with a stir bar was added $AgOP(O)(OBn)_2$ (30.8 mg, 0.08 mmol, 2.0 equiv. (1.0 equiv. to palladium)) from the glovebox, the π-allyl-Pd(II) chloride dimer (21.2 mg, 0.04 mmol, 1.0 equiv.), and $CHCl_3$ (0.3 mL, 0.13 M). The vial was sealed, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 10 minutes. MaSOX (27.5 mg, 0.08 mmol, 2.0 equiv. (1.0 equiv. to palladium)) was subsequently added and the reaction was stirred at 45 °C for another 10 minutes, and then cooled to room temperature to afford complex ***OP*(L1)**. To a 2 dram vial equipped with a stir bar was added 1,4-Di-tert-butylbenzene (6.1 mg, 0.032 mmol, 0.8 equiv.) as an internal standard. Complex ***OP*(L1)** was filtered through a pipette with glass wool into the 2-dram vial, rinsing with $CHCl_3$ (5 mL, 0.008 M). The vial was sealed with a Teflon cap, *N*-methyl phenylamine (0.17 mL, 1.6 mmol, 40 equiv. (20 equiv. to palladium)) was added via injection through the cap, and the vial was immediately placed in a pre-heated 45 °C aluminum block. Aliquots (50 μL) were taken at the corresponding reactions times from the reaction vial and filtered through a silica plug with Et_2O for HPLC analysis (Agilent Poroshell 120 EC-C18, 90% ACN/water, 1.5 mL/min). The yield was determined by integration of the product peak (~7.5 min) relative to the internal standard peak (~6.2 min) and corrected by a standard curve. $k_{initial}$ = 9.269 ± 0.604.

Initial rates with the π-allyl-Pd(II) phosphate dimer *OP* and *N*-methyl phenylamine [*N*-Ph, *OP*].



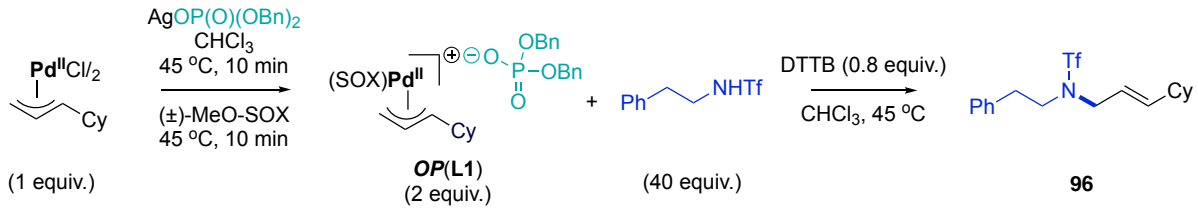
To a ½ dram vial equipped with a stir bar was added $AgOP(O)(OBn)_2$ (30.8 mg, 0.08 mmol, 2.0 equiv. (1.0 equiv. to palladium)) from the glovebox, the π-allyl-Pd(II) chloride dimer (21.2 mg, 0.04 mmol, 1.0 equiv.), and $CHCl_3$ (0.3 mL, 0.13 M). The vial was sealed, placed in a pre-heated 45 °C aluminum block, stirred at 45 °C for 10 minutes, and then cooled to room temperature to afford the palladium(II)-π-allyl phosphate dimer ***OP***. To a 2 dram vial equipped with a stir bar was added 1,4-Di-tert-butylbenzene (6.1 mg, 0.032 mmol, 0.8 equiv.) as an internal standard. The palladium(II)-π-allyl phosphate dimer was filtered through a pipette with glass wool into the 2 dram vial, rinsing with $CHCl_3$ (5 mL, 0.008 M). The vial was sealed with a Teflon cap, *N*-methyl phenylamine (0.17 mL, 1.6 mmol, 40 equiv. (20 equiv. to palladium)) was added via injection through the cap, and the vial was immediately placed in a pre-heated 45 °C aluminum block. Aliquots (50 μL) were taken at the corresponding reactions times from the reaction vial and filtered through a silica plug with Et_2O for HPLC analysis (Agilent Poroshell 120 EC-C18, 90% ACN/water, 1.5 mL/min). The yield was determined by integration of the product peak (~7.5 min) relative to the internal standard peak (~6.2 min) and corrected by a standard curve. $k_{initial}$ = 0.267 ± 0.004.

Initial rates with complex *OAc*(L1) and *N*-Tf phenethylamine [*N*-Tf, *OAc*(L1)].



To a ½ dram vial equipped with a stir bar was added AgOAc (13.4 mg, 0.08 mmol, 2.0 equiv. (1.0 equiv. to palladium)) from the glovebox, the π-allyl-Pd(II) chloride dimer (21.2 mg, 0.04 mmol, 1.0 equiv.), and $CHCl_3$ (0.3 mL, 0.13 M). The vial was sealed, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 10 minutes. MaSOX (27.5 mg, 0.08 mmol, 2.0 equiv. (1.0 equiv. to palladium)) was subsequently added and the reaction was stirred at 45 °C for another 10 minutes, and then cooled to room temperature to afford complex ***OAc*(L1)**. To a 2 dram vial equipped with a stir bar was added 1,4-Di-tert-butylbenzene (6.1 mg, 0.032 mmol, 0.8 equiv.) as an internal standard. Complex ***OAc*(L1)** was filtered through a pipette with glass wool into the 2 dram vial, rinsing with $CHCl_3$ (5 mL, 0.008 M). 1,1,1-trifluoro-*N*-phenethylmethanesulfonamide[65] (0.4 g, 1.6 mmol, 40 equiv. (20 equiv. to palladium)) was added, the vial was sealed with a Teflon cap, and the vial was immediately placed in a pre-heated 45 °C aluminum block. Aliquots (50 μL) were taken at the corresponding reactions times from the reaction vial and filtered through a silica plug with Et_2O for HPLC analysis (Agilent Poroshell 120 EC-C18, 85% ACN/water, 1.5 mL/min). The yield was determined by integration of the product peak (~8.6 min) relative to the internal standard peak (~7.1 min) and corrected by a standard curve. $k_{initial}$ = 3.430 ± 0.189.

Initial rates with complex *OP*(L1) and *N*-Tf phenethylamine [*N*-Tf, *OP*(L1)].



To a ½ dram vial equipped with a stir bar was added $AgOP(O)(OBn)_2$ (30.8 mg, 0.08 mmol, 2.0 equiv. (1.0 equiv. to palladium)) from the glovebox, the π-allyl-Pd(II) chloride dimer (21.2 mg, 0.04 mmol, 1.0 equiv.), and $CHCl_3$ (0.3 mL, 0.13 M). The vial was sealed, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 10 minutes. MaSOX (27.5 mg, 0.08 mmol, 2.0 equiv. (1.0 equiv. to palladium)) was subsequently added and the reaction was stirred at 45 °C for another 10 minutes, and then cooled to room temperature to afford complex ***OP*(L1)**. To a 2 dram vial equipped with a stir bar was added 1,4-Di-tert-butylbenzene (6.1 mg, 0.032 mmol, 0.8 equiv.) as an internal standard. Complex ***OP*(L1)** was filtered through a pipette with glass wool into the dram vial, rinsing with $CHCl_3$ (5 mL, 0.008 M). 1,1,1-trifluoro-*N*-phenethylmethanesulfonamide[65] (0.4 g, 1.6 mmol, 40 equiv. (20 equiv. to palladium)) was added, the vial was sealed with a Teflon cap, and the vial was immediately placed in a pre-heated 45 °C aluminum block. Aliquots (50 μL) were taken at the corresponding reactions times from the reaction vial and filtered through a silica plug with Et_2O for HPLC analysis (Agilent Poroshell 120 EC-C18, 85% ACN/water, 1.5 mL/min). The yield was determined by integration of the product peak (~8.6 min) relative to the internal standard peak (~7.1 min) and corrected by a standard curve. $k_{initial}$ = 0.549 ± 0.013.

Figure S7. Initial rates of the stoichiometric π-allyl-Pd(II) complexes ***OAc*(L1)** and ***OP*(L1)** with *N*-methyl phenylamine and *N*-Tf phenethylamine.

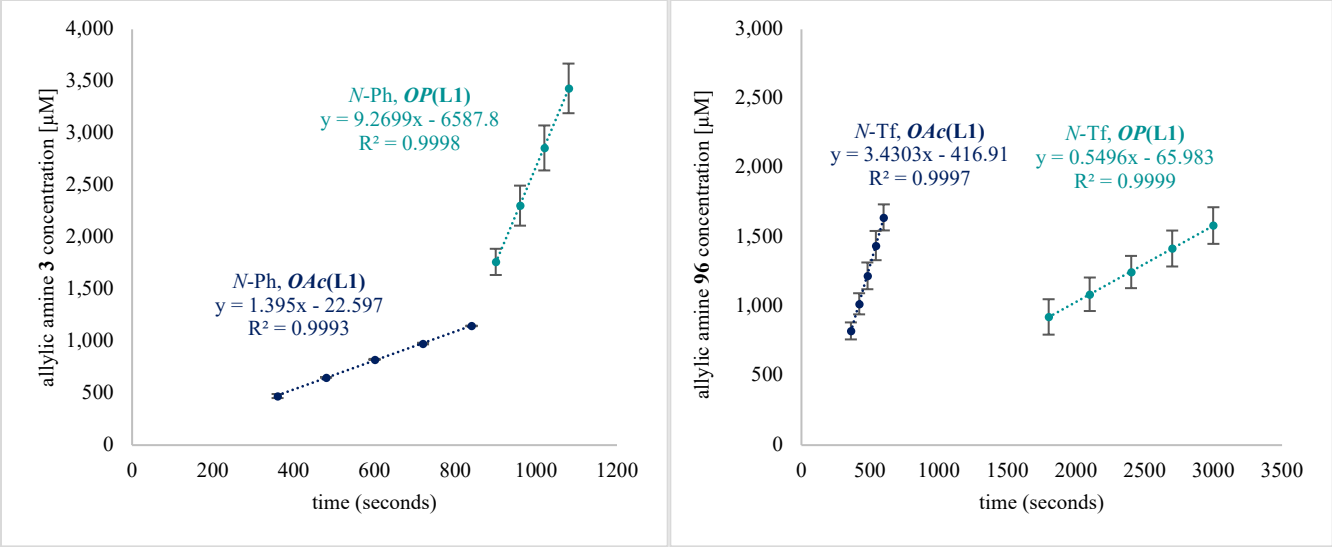


Figure S8. Initial rates of the stoichiometric π-allyl-Pd(II) complexes ***OP*** and ***OP*(L1)** with *N*-methyl phenylamine.

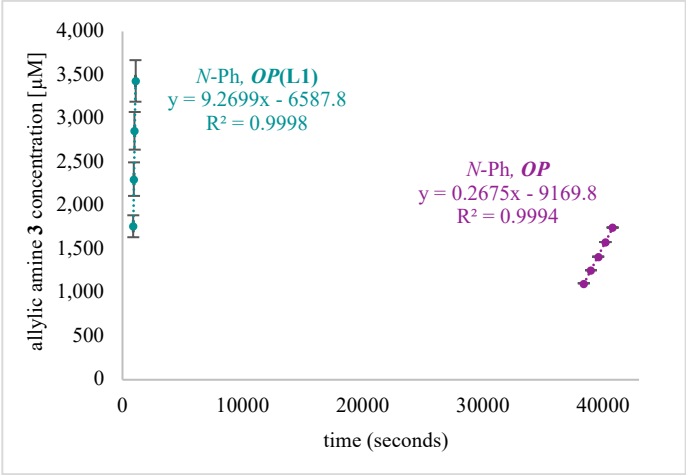


Figure S9. Reaction profiles of stoichiometric π-allyl-Pd(II) complexes ***OAc*(L1)** and ***OP*(L1)** with *N*-methyl phenylamine.

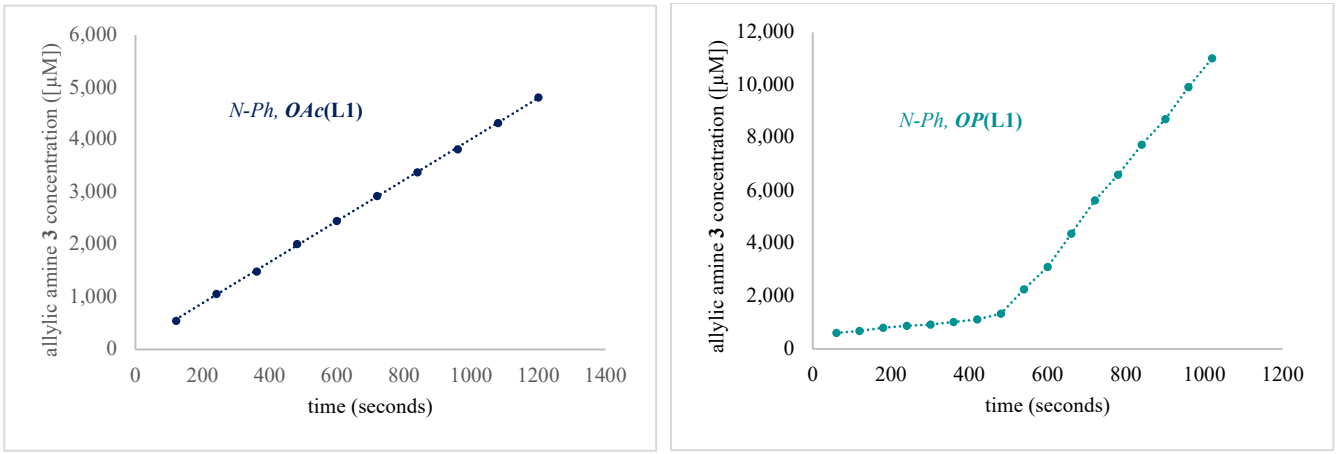


Figure S10. Reaction profiles of stoichiometric π-allyl-Pd(II) phosphate dimer ***OP*** with *N*-methyl phenylamine.

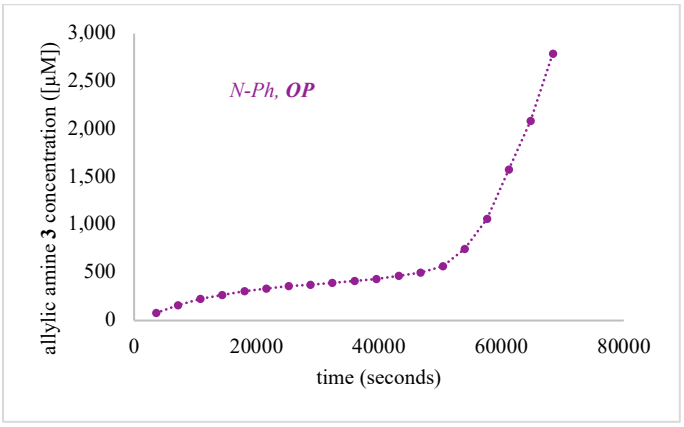
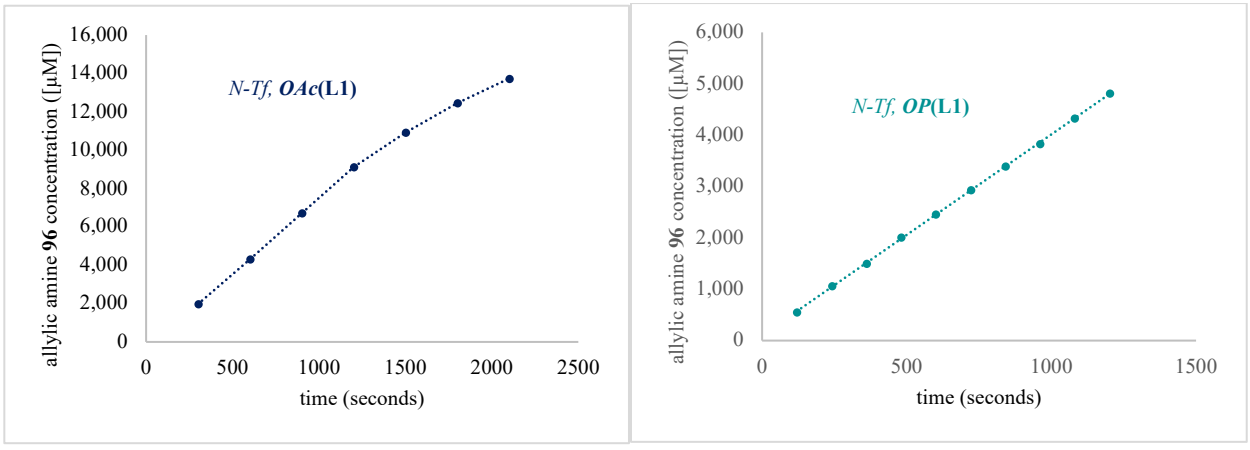
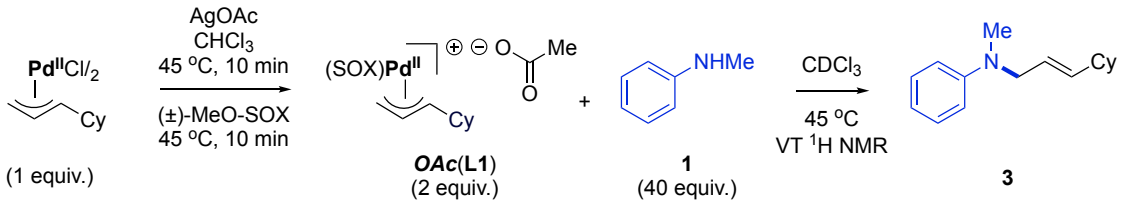


Figure S11. Reaction profiles of stoichiometric π-allyl-Pd(II) complexes ***OAc*(L1)** and ***OP*(L1)** with *N*-Tf phenethylamine.

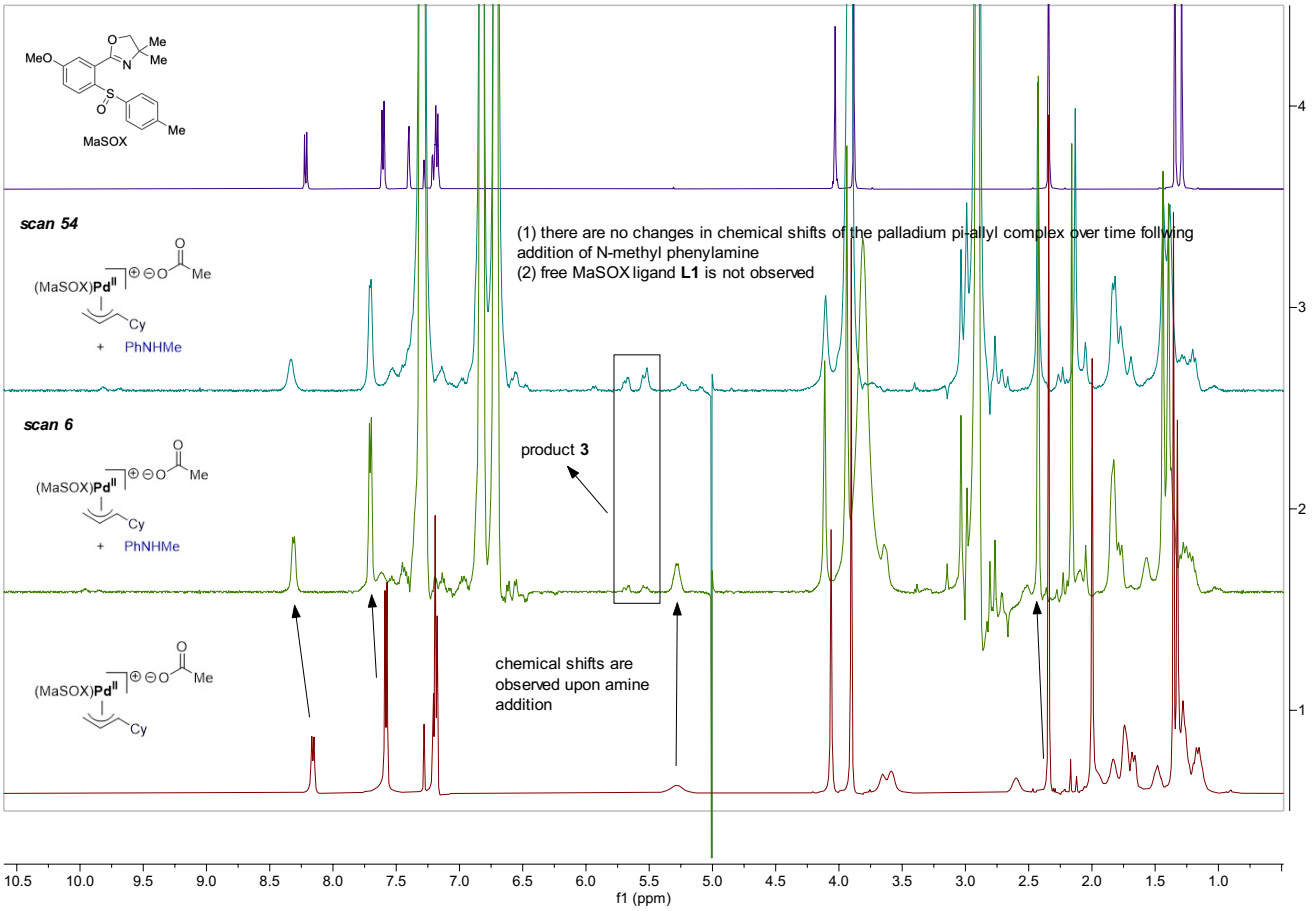


5.5. Spectroscopic investigation of complexes *OAc*(L1) and *OP*(L1) with *N*-methyl phenylamine.

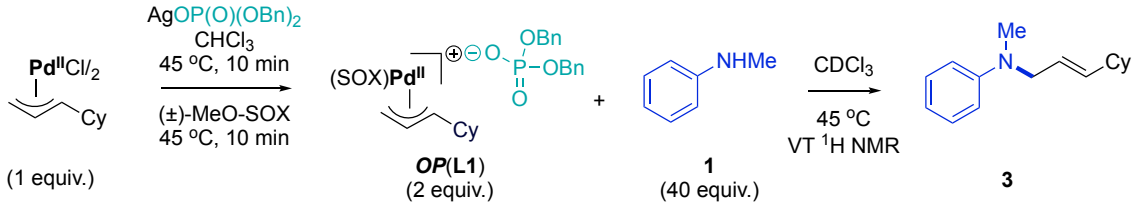


VT ^{1}H NMR procedure with complex *OAc*(L1): To a ½ dram vial equipped with a stir bar was added AgOAc (6.7 mg, 0.04 mmol, 2.0 equiv. (1.0 equiv. to palladium)) from the glovebox, the π-allyl-Pd(II) chloride dimer (10.6 mg, 0.02 mmol, 1.0 equiv.), and $CDCl_3$ (0.16 mL, 0.13 M). The vial was sealed, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 10 minutes. MaSOX (13.7 mg, 0.04 mmol, 2.0 equiv. (1.0 equiv. to palladium)) was subsequently added and the reaction was stirred at 45 °C for another 10 minutes, and then cooled to room temperature. Complex ***OAc*(L1)** was filtered through a pipette with glass wool into an NMR tube, rinsing with $CDCl_3$ (0.5 mL). ^{1}H NMR spectral data of complex ***OAc*(L1)** was acquired using a Varian VXR 500 MHz spectrometer at 45 °C (nt = 16 scans, d1 = 4 seconds, aq = 4 seconds). The NMR tube was allowed to cool to room temperature and then *N*-methyl phenylamine (87 μL, 0.8 mmol, 40 equiv. (20 equiv. to palladium)) was added. The tube was sealed, shaken, placed back into the spectrometer, and heated to 45 °C. ^{1}H NMR spectral data of the mixture was acquired every 2 scans over a series of scans at 45 °C.

Figure S12. Stacked spectra of the VT ^{1}H NMR ***OAc*(L1)/1** experiment (scans 6 and 54) with MaSOX **L1** and complex ***OAc*(L1)** at 45°C.



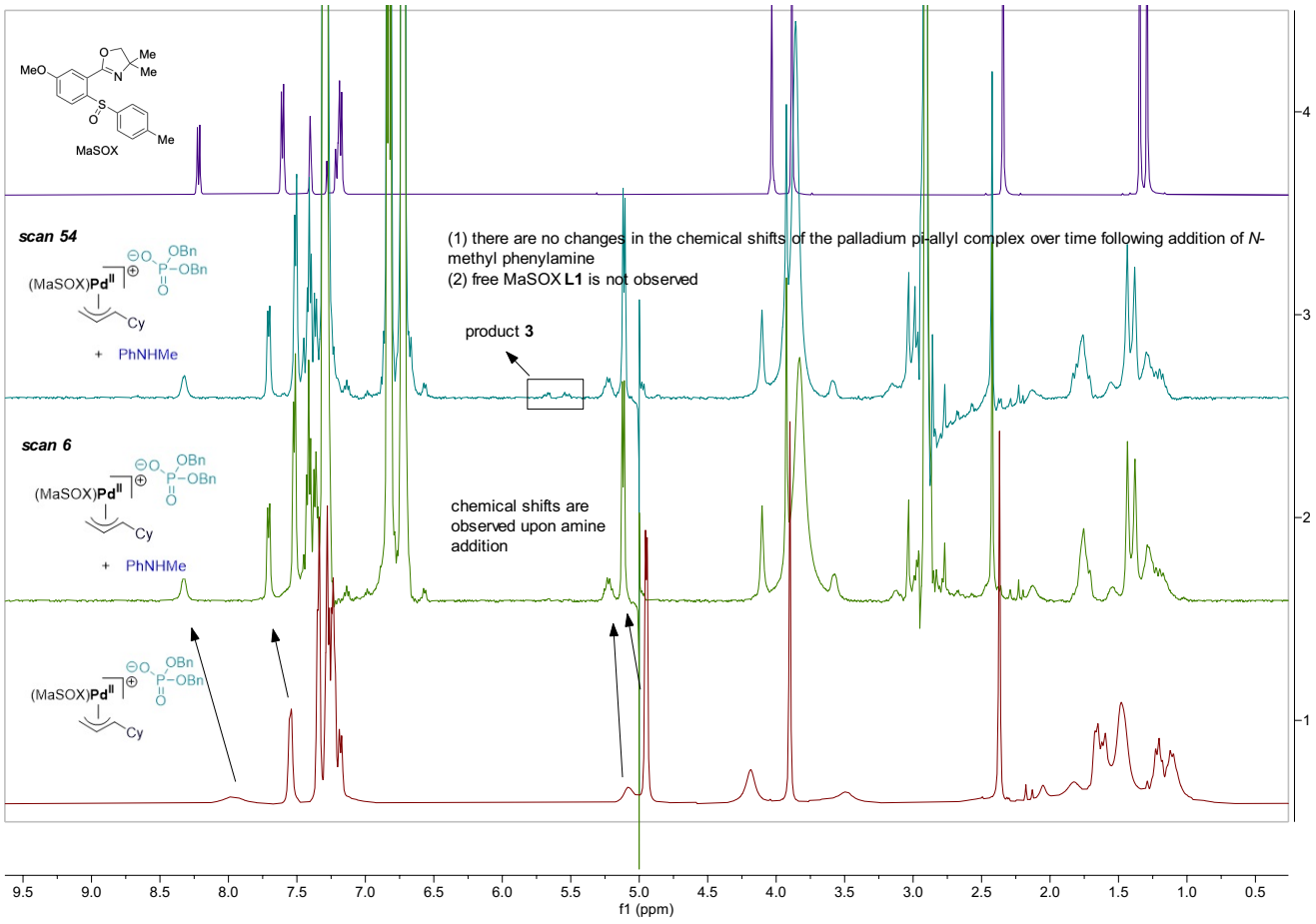
Conclusion: Addition of *N*-methyl phenylamine to complex ***OAc*(L1)** revealed downfield shifts and peak broadening of the ***OAc*(L1)** proton resonances. These shifts remain constant, and product **3** formation (5.38 and 5.53 ppm) is observed over the course of the experiment. This data suggests an altered binding of **L1** to the π-allyl-Pd(II) complex, however, no free **L1** was observed.



VT ^{1}H NMR procedure with complex *OP*(L1): To a ½ dram vial equipped with a stir bar was added AgOP(O)(OBn)$_2$ (15.4 mg, 0.04 mmol, 2.0 equiv. (1.0 equiv. to palladium)) from the glovebox, the π-allyl-Pd(II) chloride dimer (10.6 mg, 0.02 mmol, 1.0 equiv.), and $CDCl_3$ (0.16 mL, 0.13 M). The vial was sealed, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 10 minutes. MaSOX (13.7 mg, 0.04 mmol, 2.0 equiv. (1.0 equiv. to palladium)) was subsequently added and the reaction was stirred at 45 °C for another 10 minutes, and then cooled to room temperature. Complex ***OP*(L1)** was filtered through a pipette with glass wool into an NMR tube, rinsing with $CDCl_3$ (0.5 mL). ^{1}H NMR spectral data of complex ***OP*(L1)** was

acquired using a Varian Unity 500 MHz spectrometer at 45 °C (nt = 16 scans, d1 = 4 seconds, aq = 4 seconds). The NMR tube was allowed to cool to room temperature and then *N*-methyl phenylamine (87 μL, 0.8 mmol, 40 equiv. (20 equiv. to palladium)) was added. The tube was sealed, shaken, placed back into the spectrometer, and heated to 45 °C. ^{1}H NMR spectral data of the mixture was acquired every 2 scans over a series of scans at 45 °C.

Figure S13. Stacked spectra of the VT ^{1}H NMR ***OP*(L1)/1** experiment (scans 6 and 54) with MaSOX **L1** and complex ***OP*(L1)** at 45°C.

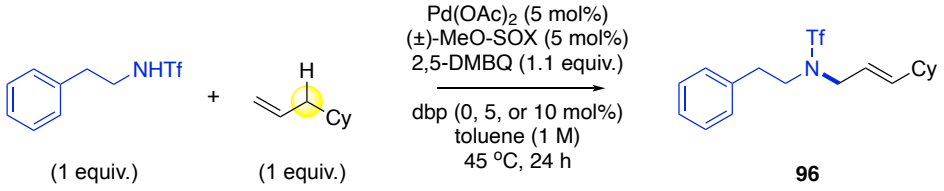


Conclusion: Analogous to the experiment with ***OAc*(L1)**, addition of *N*-methyl phenylamine to complex ***OP*(L1)** revealed downfield shifts and peak broadening of the ***OP*(L1)** proton resonances. These shifts remain constant, and product **3** formation (5.38 and 5.53 ppm) is observed over the course of the experiment. This data suggests an altered binding of **L1** to the π-allyl-Pd(II) complex, however, no free **L1** was observed.

*Note: An analogous experiment was performed using a total of 0.57 mL of $CDCl_3$ to offset the volume of N-methyl phenylamine **1** added. Chemical shifts were in agreement with the spectra shown above, ruling out concentration-dependent changes in chemical shifts of **OP(L1)**, **OP(L1) + 1**, and **L1**.*

5.6. Investigating the chemoselectivity between arylamines and *N*-Tf amines under MaSOX·Pd(OAc)$_2$ catalysis.

Influence of dbp additive on reactivity.

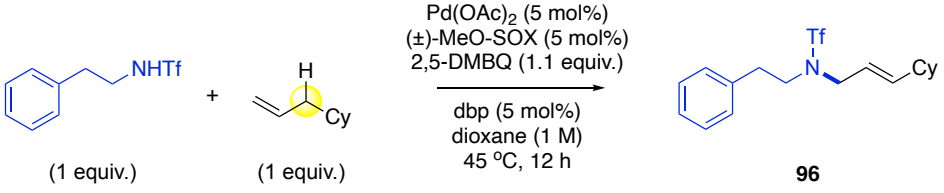


(1 equiv.) (1 equiv.) **96**

Procedure A: 0% dbp – the originally reported conditions from reference 64 – run for 24 hours instead of 72 hours. To a ½ dram vial equipped with a stir bar was added $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.05 equiv.), MaSOX (5.2 mg, 0.015 mmol, 0.05 equiv.), 2,5-dimethylbenzoquinone (45 mg, 0.33 mmol, 1.1 equiv.), and 1,1,1-trifluoro-*N*-phenethylmethanesulfonamide[65] (76 mg, 0.3 mmol, 1.0 equiv.). Toluene was added (0.3 mL, 1.0 M), followed by allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.). The vial was capped, sealed with Teflon tape and parafilm, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 24 h, with no precautions to exclude air and moisture. The vial was cooled to room temperature, diluted with $CDCl_3$, and benzotrifluoride (43.8 mg, 0.3 mmol, 1.0 equiv.) was added as an internal standard. The crude mixture was analyzed using ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) to determine the recovered olefin starting material. Purification via flash column chromatography (50 mL SiO_2, Hexanes (200 mL) → 5% DCM/Hexanes (200 mL) → 10% DCM/Hexanes (200 mL) → 15% DCM/hexanes (200 mL) → 20% DCM/Hexanes (100 mL) eluent) afforded the product as a clear oil. The spectral data were in accordance with literature values.[65] Run 1: 46.4 mg, 41% yield (40% olefin RSM); Run 2: 47.3 mg, 42% yield (42% olefin RSM). **Average: 42% ± 0.3% yield (41% ± 1.3% olefin RSM).**

Procedure B: 5 mol% dbp had a minimal impact on yields. 1,1,1-trifluoro-*N*-phenethylmethanesulfonamide (76 mg, 0.3 mmol, 1.0 equiv.). and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the above procedure using 0.3 mL of a 0.05 M solution of dibutyl phosphate in toluene (0.05 equiv.) as a solvent, and stirred for 24 h. The purification conditions above were used to afford the product as a clear oil. Run 1: 47 mg, 42% yield (52% olefin RSM); Run 2: 48.2 mg, 43% yield (51% olefin RSM). **Average: 42% ± 0.8% yield (52% ± 0.7% olefin RSM**).

Procedure C: 10 mol% dbp afforded diminished yields. 1,1,1-trifluoro-*N*-phenethylmethanesulfonamide (76 mg, 0.3 mmol, 1.0 equiv.). and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted according to the above procedure using 0.3 mL of a 0.1 M solution of dibutyl phosphate in toluene (0.1 equiv.) as a solvent, and stirred for 24 h. The purification conditions above were used to afford the product as a clear oil. Run 1: 10.7 mg, 10% yield (78% olefin RSM); Run 2: 12.9 mg, 11% yield (75% olefin RSM). **Average: 11% ± 1.4% yield (76% ± 2.6% olefin RSM**).

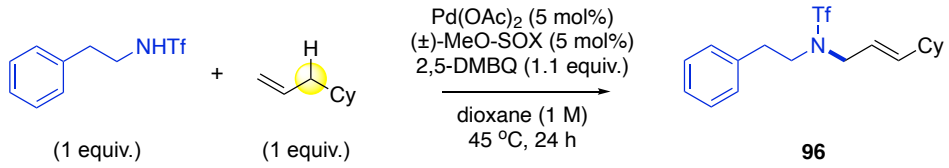


(1 equiv.) (1 equiv.) **96**

Using the general 2° arylamine conditions for an N-Tf nucleophile presents a direct reactivity comparison: 1,1,1-trifluoro-*N*-phenethylmethanesulfonamide (76 mg, 0.3 mmol, 1.0 equiv.). and allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.) were reacted

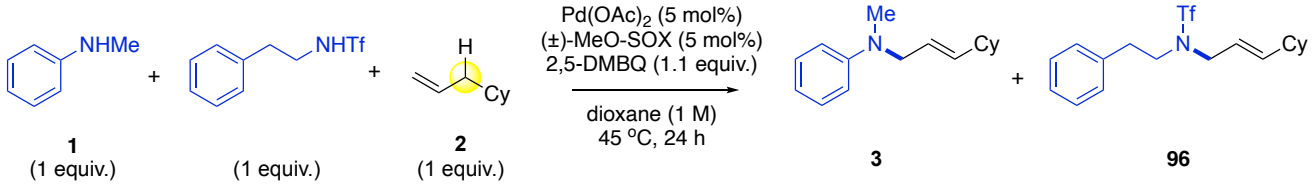
according to the general procedure using 0.3 mL of dioxane as a solvent, and stirred for 12 h. The crude mixture was analyzed using ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) with benzotrifluoride (43.8 mg, 0.3 mmol, 1.0 equiv.) added as an internal standard to determine the recovered olefin starting material. Purification via flash column chromatography (50 mL SiO_2, Hexanes (200 mL) → 5% DCM/Hexanes (200 mL) → 10% DCM/Hexanes (200 mL) → 15% DCM/hexanes (200 mL) → 20% DCM/Hexanes (100 mL) eluent) afforded the product as a clear oil. Run 1: 30.4 mg, 27% yield (63% olefin RSM); Run 2: 32.2 mg, 29% yield (54% olefin RSM). **Average: 28% ± 1.1% yield (59% ± 6.4% olefin RSM).** *Note: Using N-methyl phenylamine **1** as the nucleophile under these conditions affords 90% yield (2% olefin RSM) (Table **S1**, entry 5).*

Parallel reaction experiment (arylamine and *N*-Tf amine) without dbp additive.



To a ½ dram vial equipped with a stir bar was added $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.05 equiv.), MaSOX (5.2 mg, 0.015 mmol, 0.05 equiv.), 2,5-dimethylbenzoquinone (45 mg, 0.33 mmol, 1.1 equiv.), and 1,1,1-trifluoro-*N*-phenethylmethanesulfonamide[65] (76 mg, 0.3 mmol, 1.0 equiv.). Dioxane was added (0.3 mL, 1.0 M), followed by allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.). The vial was capped, sealed with Teflon tape and parafilm, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 24 h, with no precautions to exclude air and moisture. The vial was cooled to room temperature, diluted with $CDCl_3$, and benzotrifluoride (43.8 mg, 0.3 mmol, 1.0 equiv.) was added as an internal standard. The crude mixture was analyzed using ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) to determine the recovered olefin starting material. Purification via flash column chromatography (50 mL SiO_2, Hexanes (200 mL) → 5% DCM/Hexanes (200 mL) → 10% DCM/Hexanes (200 mL) → 15% DCM/hexanes (200 mL) → 20% DCM/Hexanes (100 mL) eluent) afforded the product as a clear oil. Run 1: 46.2 mg, 41% yield (58% olefin RSM); Run 2: 44.6 mg, 40% yield (57% olefin RSM). **Average: 40% ± 1.0% yield (58% ± 0.8% olefin RSM).** *Note: Using N-methyl phenylamine **1** as the nucleophile under these conditions affords 50% yield (46% olefin RSM) (Table **S1**, entry 11).*

Intermolecular competition experiment (arylamine versus *N*-Tf amine) without dbp additive.

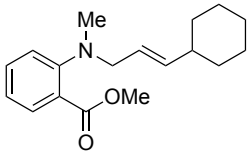


To a ½ dram vial equipped with a stir bar was added $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.05 equiv.), MaSOX (5.2 mg, 0.015 mmol, 0.05 equiv.), 2,5-dimethylbenzoquinone (45 mg, 0.33 mmol, 1.1 equiv.), 1,1,1-trifluoro-*N*-phenethylmethanesulfonamide[65] (76 mg, 0.3 mmol, 1.0 equiv.), and *N*-methyl phenylamine (32.1 mg, 0.3 mmol, 1.0 equiv.). Dioxane was added (0.3 mL, 1.0 M), followed by allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv.). The vial was capped, sealed with Teflon tape and parafilm, placed in a pre-heated 45 °C aluminum block, and stirred at 45 °C for 24 h, with no precautions to exclude air and moisture. The vial was cooled to room

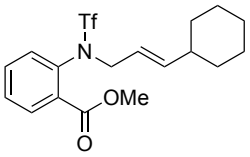
temperature, diluted with $CDCl_3$, and benzotrifluoride (43.8 mg, 0.3 mmol, 1.0 equiv.) was added as an internal standard. The crude mixture was analyzed using ^{1}H NMR (nt = 16 scans, d1 = 10 seconds) to determine the recovered olefin starting material. Purification via flash column chromatography (40 mL Brockmann Grade 3 basic alumina, Hexanes (200 mL) → 2% EtOAc/Hexanes (150 mL) eluent) afforded the arylamine functionalized product as a clear oil and the *N*-Tf functionalized product as an impure mixture. Benzotrifluoride (4.4 mg, 0.03 mmol, 0.1 equiv.) was added as an internal standard and the yield of the *N*-Tf functionalized product was determined using ^{1}H NMR (nt = 16 scans, d1 = 10 seconds). Run 1: 25.5 mg, 37% yield product **3** (44% olefin RSM, 3% *N*-Tf functionalized product); Run 2: 27.1 mg, 39% yield product **3** (41% olefin RSM, 3% *N*-Tf functionalized product). **Average: 38% ± 1.7% yield product 3 (42% ± 2.3% olefin RSM, 3% ± 0.2% *N*-Tf functionalized product).**

Conclusion: Arylamines have an inhibitory effect on the functionalization of less basic nucleophiles that were previously demonstrated under (SOX)·Pd(II) catalysis.

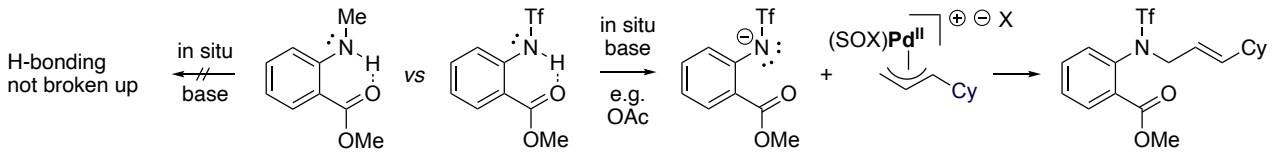
Reactivity differences of *N*-methyl versus *N*-Tf derived methyl anthranilate nucleophiles.



methyl (*E*)-2-((3-cyclohexylallyl)(methyl)amino)benzoate: methyl 2-(methylamino)benzoate (16.5 mg, 0.1 mmol, 1.0 equiv.) and allylcyclohexane (12.4 mg, 0.1 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 0.1 equiv.), MaSOX (3.4 mg, 0.01 mmol, 0.1 equiv.), 2,5-DMBQ (15 mg, 0.11 mmol, 1.1 equiv.), and 0.1 mL of a 0.15 M solution of dibutyl phosphate in dioxane (0.15 equiv.) as a solvent, and stirred for 24 h. The crude mixture was analyzed using ^{1}H NMR with benzotrifluoride as an internal standard to determine the approximate yield and recovered olefin starting material: 8% yield (66% olefin RSM).



methyl (*E*)-2-((*N*-(3-cyclohexylallyl)-1,1,1-trifluoromethyl)sulfonamido)benzoate: methyl 2-((trifluoromethyl)sulfonamido)benzoate (56.6 mg, 0.2 mmol, 1.0 equiv.) and allylcyclohexane (24.8 mg, 0.2 mmol, 1.0 equiv.) were reacted according to the general procedure using $Pd(OAc)_2$ (4.5 mg, 0.02 mmol, 0.1 equiv.), MaSOX (6.8 mg, 0.02 mmol, 0.1 equiv.), 2,5-DMBQ (30 mg, 0.22 mmol, 1.1 equiv.), and 0.2 mL of toluene as a solvent, and stirred for 48 h. The crude mixture was analyzed using ^{1}H NMR (nt = 10 scans, d1 = 10 seconds) with benzotrifluoride as an internal standard to determine the approximate yield and recovered olefin starting material: 88% yield (0% olefin RSM).



Conclusion: These results indicate a possible divergent mode of functionalization between the two classes of amine nucleophiles. *N*-Tf amines may be pronucleophiles that are deprotonated by the acetate counterion prior to functionalization. Arylamines may functionalize as the neutral amine and display higher reactivity with the less-basic phosphate counterion which accesses a more electrophilic π-allyl-(SOX)·Pd(II) intermediate.

6. References

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