



Intramolecular Palladium-Catalyzed Aryl Amination and Aryl Amidation

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Abstract: Upon treatment with a palladium catalyst and a suitable base, aromatic halides undergo intramolecular substitution to form five, six, and seven-membered rings. In a similar fashion aryl halides with pendant amides or sulfonamides are cyclized to form five and six-membered rings. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

Nitrogen heterocycles are one of the most important classes of pharmacologically active compounds. A variety of methods are available for their synthesis via intramolecular aryl carbon-nitrogen bond formation.¹⁻⁷ However, most require the use of activated substrates or harsh reaction conditions. We felt that a technique which involved the transition metal catalyzed displacement of a suitable leaving group would be particularly useful, since many transition metal coupling reactions occur under mild conditions and are highly tolerant of a wide variety of functional groups.⁸

A transformation of this type which utilized a stoichiometric quantity of Pd(PPh₃)₄ was reported by Boger and coworkers several years ago in the total synthesis of lavendamycin methyl ester.¹ Migita previously reported a palladium-catalyzed arylamination using (N,N-diethylamino)tributyltin to form N,N-diethyl aniline derivatives.^{9a} We have generalized this methodology by employing a transamination process to allow for a more general transformation.^{9b} Further development led to a main group-free aryl amination protocol.^{9c} We now report a study of the intramolecular palladium-catalyzed amination reaction, and, as well, the cyclization of amides and sulfonamides. This methodology allows for easy access to a wide variety of nitrogen heterocycles.

RESULTS AND DISCUSSION

Aminostannane cyclizations. Modification of our aminostannane/aryl halide coupling protocol^{9b} to form heterocycles by cyclization proved to be an effective route to nitrogen heterocycles. The amino arylbromides were stannylated *in situ* by stirring with (N,N-diethylamino)tributyltin at room temperature under vacuum. The resulting stannylamines were treated with a catalytic amount of PdCl₂(o-tolyl₃P)₂ in toluene at 100 °C to effect cyclization (eq a). This method allows for the formation of five, six, and seven membered rings in moderate to good yields (Table 1).

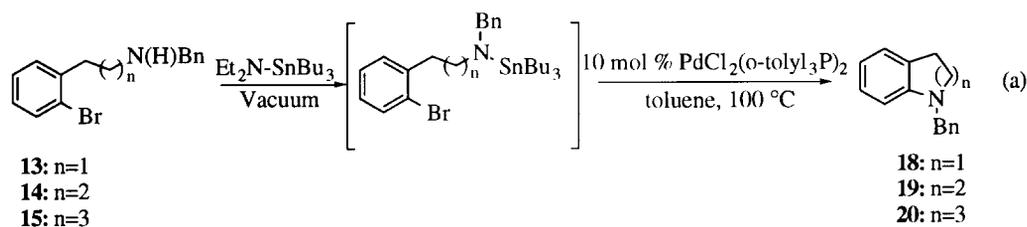


Table 1. Palladium-catalyzed Cyclization of Aminostannanes

Entry	X	n	Reaction Time	Isolated Yield
1	Br	1	14 h	87 %
2	Br	2	20 h	72 %
3	Br	3	24 h	61 %

A variety of catalysts were successfully employed (Table 2), including Pd(PPh₃)₄, which is not effective in the intermolecular reactions. A variety of reaction conditions were examined and we found that in general, chelating phosphines gave lower yields and larger amounts of dehalogenated starting material as side products, and lower reaction temperatures resulted in incomplete conversion. The aminostannane process has the significant drawback of requiring stoichiometric amounts of tributyltin reagents, and efforts to use aminoboranes eventually led to the discovery of main group-free conditions for the reaction.^{9c,10}

Table 2. Ligand Effects in the Palladium-Catalyzed Cyclization of **13** to **18** Using an Aminostannane Protocol

Catalyst	mol %	T (°C)	t (h)	%conversion (by GC)	yield % (isolated)
PdCl ₂ [(<i>o</i> -tolyl) ₃ P] ₂	10	100	20	100	82
Pd(PPh ₃) ₄	10	100	≤12	100	94
"	2	100	20	93	79
"	10	80	36	100	75
Pd(dba) ₂ /2(<i>o</i> -tolyl) ₃ P	10	40	14	100	60
"	10	rt.	12	53	41
Pd(OAc) ₂ /2(<i>o</i> -tolyl) ₃ P	10	100	40	74	40
PdCl ₂ (PPh ₃) ₂	10	100	44	100	69
PdCl ₂ (Ph ₂ P[CH ₂] ₂ PPh ₂)	10	100	26	80	65
PdCl ₂ (Ph ₂ P[CH ₂] ₃ PPh ₂)	10	100	70	100	66
PdCl ₂ (Ph ₂ P[CH ₂] ₄ PPh ₂)	10	100	40	75	60
PdCl ₂ (DPPF)	10	100	70	100	57
Pd ₂ (dba) ₃ •CHCl ₃ /2(2-furyl) ₃ P	10	80	65	86	67

Main group-free cyclizations. Treatment of amino arylhalides with a palladium catalyst and a base in toluene at 100 °C promoted the cyclization in the absence of a main group reagent (eq b, Table 3). Interestingly, the intramolecular amination proceeds in good yields when potassium carbonate is used as a base (entries 1-3). The effectiveness of K₂CO₃ contrasts with the intermolecular reaction which requires the use of a stronger base to achieve complete conversion and acceptable yields. A variety of other bases (Na₂CO₃, NaOAc, KOAc, Li₂CO₃, Ag₂CO₃, CaCO₃, and DBU) are less effective. Little difference was seen when DMF was used as the solvent. Formation of six and seven-membered rings required longer reaction times than were necessary for the formation of five-membered rings.

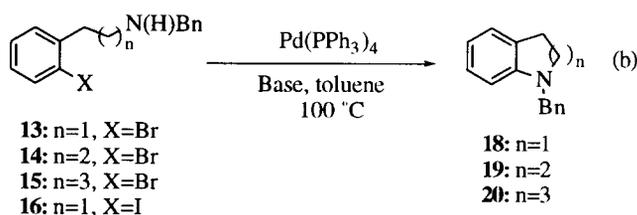
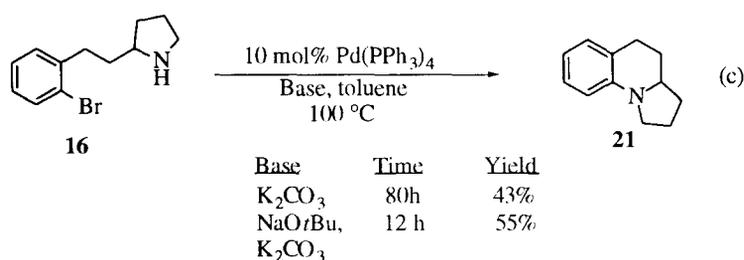


Table 3. Main Group Free Cyclizations

Entry	X	n	Base	Catalyst	mol %	Temp	Time	Isolated Yield
1	Br	1	K ₂ CO ₃	Pd(PPh ₃) ₄	10	100 °C	40 h	70%
2	Br	2	K ₂ CO ₃	Pd(PPh ₃) ₄	10	100 °C	68 h	67%
3	Br	3	K ₂ CO ₃	Pd(PPh ₃) ₄	10	100 °C	115 h	62%
4	Br	1	NaOtBu/K ₂ CO ₃	Pd(PPh ₃) ₄	1	100 °C	2.5 h	92%
5	Br	2	NaOtBu/K ₂ CO ₃	Pd(PPh ₃) ₄	1	100 °C	6 h	87%
6	Br	3	NaOtBu/K ₂ CO ₃	Pd(PPh ₃) ₄	1	100 °C	6 h	89%
7	Br	1	NaOtBu/K ₂ CO ₃	Pd/C + PPh ₃	5	100 °C	136 h	77%
8	I	1	NaOtBu/K ₂ CO ₃	Pd(PPh ₃) ₄	1	100 °C	0.5 h	93%
9	I	1	NaOtBu/K ₂ CO ₃	Pd(PPh ₃) ₄	1	65 °C	2 h	96%
10	I	1	XS Et ₃ N	Pd(PPh ₃) ₄	5	r.t.	40 h	83%
11	I	1	Et ₃ N (solvent)	Pd(PPh ₃) ₄	5	r.t.	15 h	87%

The rate and yield of the cyclization reaction were improved by using both NaOtBu and K₂CO₃ simultaneously instead of one single base. Although the use of K₂CO₃ was not found to be essential in the transformations, cleaner reactions were generally observed when it was employed. At 100 °C most reactions proceeded quickly (0.5-6 h) and in excellent yields. However, the cyclization of **16** to **21** under these conditions was very slow and afforded the desired product in moderate yield (eq c).

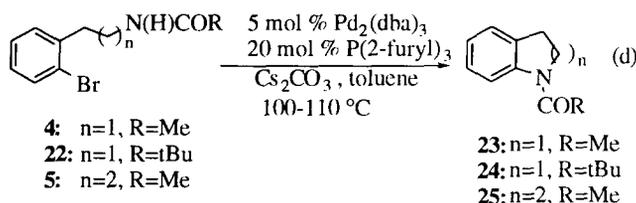


Good yields were generally also obtained when the reaction was carried out at 65 °C, although reaction rates tended to slow greatly as the reaction approached completion. Additionally, the use of Pd(PPh₃)₄ in the intramolecular reaction was superior to procedures employing catalysts with P(*o*-tolyl)₃ as the phosphine; this is in stark contrast to the results which we observed in our studies of the intermolecular reaction. We also determined that Pd/C with added triphenylphosphine was also a suitable catalyst system (entry 7), albeit slow.¹¹

In contrast to the intermolecular process, aryl iodides¹² proved to be superior substrates (entries 8 and 9). In fact, the cyclization of iodide **17** was accomplished at room temperature when triethylamine was used as the base or solvent (entries 10, 11).

The large difference in pKa between the NH proton (~38)¹³ and the conjugate acid of K₂CO₃ (10.33)¹³ or NaOtBu (~17)¹³ suggests that deprotonation of the nitrogen occurs after coordination to the metal, and the large difference in reaction rates observed for bases of different strengths is consistent with this notion. We note that coordination chemistry involving the oxidative addition complexes of aryl iodides and aryl bromides is substantially different in intermolecular cases, however in intramolecular cases no differences were detectable.¹⁴

Amide Cyclizations. Slight modifications of our aminohalide cyclization protocol allowed for the cyclization of halo acetamides (eq d). Optimal results were obtained when Pd₂(dba)₃ / 2 (2-furyl)₃P was used as the catalyst, and Cs₂CO₃ was employed as the base. Other palladium catalysts (Pd(PPh₃)₄, Pd₂(dba)₃ / 2 P(o-tolyl)₃, Pd₂(dba)₃ / 2PPh₃) either required longer reaction times or gave lower yields. No cyclization products were formed when Ph₃As or (C₆F₅)₃P were used as ligands. Other alkali metal carbonates required slightly longer reaction times and/or gave lower yields. Protocols which used NaOtBu, Na₂CO₃, NaOAc, or KOAc as bases were also unsuccessful.



The reaction gave much better results in the formation of the N-acyl indolines than in the formation of six and seven membered ring heterocycles. The six membered ring could be formed, although yields were low. Attempts to form seven-membered rings resulted in dehalogenation of the starting material, and no desired products were detected by GC/MS. Pivaloyl amides were also effectively cyclized in good yields (Table 4). The amide cyclizations were, in general, much slower than the corresponding aminohalide cyclizations and required high catalyst loading to proceed to completion. Attempts to expand this protocol to intermolecular cases have been unsuccessful.^{15,16}

Table 4. Palladium-Catalyzed Cyclizations of Amides

entry	n	R	Temp	Time	Isolated Yield
1	1	Me	100 °C	8 h	99%
2	1	<i>t</i> -Bu	100 °C	23 h	87%
3	2	Me	110 °C	21h	44%

Benzamides of type **10** were also cyclized effectively using Pd₂(dba)₃/2 P(o-tolyl)₃ and K₂CO₃ (eq e). Use of Cs₂CO₃ as a base gave inferior results. These cyclizations were considerably slower than for the

cyclizations shown in (d), and the reaction was most effective in the formation of six-membered rings (Table 5).

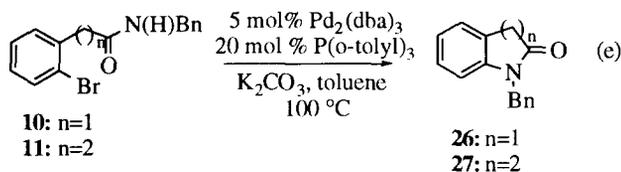


Table 5. Pd Catalyzed Cyclization of Benzamides

Entry	n	Catalyst	Temp.	Time	Yield
1	1	Pd ₂ (dba) ₃ 2 o-tolyl ₃ P	100 °C	42h	59%
2	2	Pd ₂ (dba) ₃ 2 o-tolyl ₃ P	100 °C	91h	82%
3	3	Pd ₂ (dba) ₃ 2 2-furyl ₃ P	110 °C	25h	~5%

Attempted cyclization to form a seven membered ring failed when P(o-tolyl)₃ was used as the ligand. Use of P(2-furyl)₃ as a ligand under conditions of high concentration and at elevated temperatures proceeded with complete consumption of starting material. However, the major product of the reaction was dehalogenated starting material, and only ~5% of the desired product could be isolated.

Sulfonamide Cyclizations. Conditions similar to those used to cyclize amides allowed for the cyclization of sulfonamides in good yields (eq f). These cyclizations were much faster and required lower catalyst loading than those for corresponding amides. We attribute this to the enhanced acidity of the sulfonamide N-H proton.¹⁷

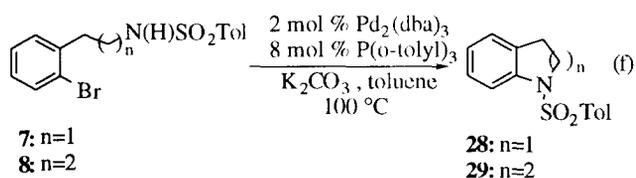


Table 6. Pd Catalyzed Cyclization of Sulfonamides

Entry	n	Time	Yield
1	1	5h	88%
2	2	14h	87%

Five and six membered rings were formed in high yields using 2 mol % Pd₂(dba)₃/2 P(*o*-tolyl)₃ and K₂CO₃ (Table 6). Again, attempts to form seven-membered rings were unsuccessful, and the reaction time was shortest for the formation of the five-membered ring. As was observed with amides, intermolecular coupling of sulfonamides with aryl halides was unsuccessful. The fact that sulfonamides and amides give satisfactory results for the formation of five and six membered rings, but the process fails for larger rings and in intermolecular cases suggests that nitrogen coordination of the sulfonamide or amide to the metal may be less facile than amine coordination. The nitrogen in amides and sulfonamides is considerably less basic than the amine nitrogen,^{17,18} and known complexes of the type MCl₂L₂ (where M = Pt or Pd, and L = DMF, NMA or DMA) have been shown to be O-bonded.¹⁹

CONCLUSION

In conclusion, we have demonstrated the cyclization of aryl bromoamines, bromoamides, and bromosulfonamides in good yields. This methodology should allow for easy access to a wide variety of substituted nitrogen heterocycles.

EXPERIMENTAL SECTION

General. All reactions were carried out under an argon atmosphere in oven dried glassware. Nuclear magnetic resonance (NMR) spectra were recorded on a Varian XL-300 or Unity-300 FT spectrometer. Infrared (IR) spectra were recorded on a Perkin Elmer Series 1600 FT spectrometer. Gas chromatographic analyses were performed on a Hewlett Packard model 5890 GC with a 3392 integrator and FID detector using a 25 mm capillary column with crosslinked SE-30 as a stationary phase. Mass spectra (GC/MS) were recorded on a Hewlett Packard model 5971 mass selective detector connected to a Hewlett Packard model 5890 GC. Elemental analyses were performed by E&R Microanalytical Laboratory Inc., Corona N.Y. Toluene, THF, and ether were continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen or argon. Dichloromethane was dried by continuous reflux and distillation from CaH₂ under nitrogen. Triethylamine was purchased from Fischer and distilled from CaH₂ before use. Tosyl chloride, thionyl chloride, anhydrous benzylamine, and tri(2-furyl) phosphine were obtained from Aldrich Chemical Co. and used without further purification. Sodium *t*-butoxide was purchased from Aldrich Chemical Co. and stored under nitrogen in a vacuum atmospheres glove box. Tetrakis (triphenylphosphine) palladium was prepared according to literature procedures.⁴⁷ Acetyl Chloride was purchased from Mallinckrodt Chemical Co. and used as received. Anhydrous potassium carbonate was purchased from Mallinckrodt Chemical Co. and was finely ground with a mortar and pestle before use. Cesium carbonate, Tris(dibenzylideneacetone)dipalladium (0) and tri-*o*-tolyl phosphine were purchased from Strem Chemical Co. and were used as received. All other reagents were purchased from commercial sources and used without further purification. Cyclization substrates were prepared according to literature procedures, or using standard synthetic methods. Preparative flash chromatography was performed on ICN Biomedicals Silitech 32-63d silica gel. Yields refer to isolated yields (average of two runs) of compounds estimated to be ≥95% pure as determined by ¹H NMR, and either capillary GC or combustion analysis.

General procedure for cyclization of amino arylbromides using NaOtBu as base. To a suspension of sodium *tert*-butoxide (1.60 mmol), potassium carbonate (1.60 mmol), and tetrakis(triphenylphosphine)palladium(0) in toluene (5 mL) was added the substrate (1.0 mmol). The mixture was then heated to 100°C with stirring until the starting material had been completely consumed as judged by GC analysis. The mixture was cooled to r.t. and, water and ether (5 mL each) were added. The layers were separated and the aqueous layer was extracted with ether (2 X 5 mL). The combined organic layers were dried over anhydrous MgSO₄, filtered, and concentrated *in vacuo*. When 5 or 10 mol % palladium catalyst was used, the following workup procedure was employed to remove the phosphine. The reaction mixture was cooled to room temperature, and water and ether (5 mL each) were added. The aqueous layer was extracted with ether (2 X 5 mL), and the combined organic layers were then stirred with 30% hydrogen peroxide (5 mL) for 10 to 20 minutes to oxidize the phosphine. The layers were separated and the organic layer was washed with water (10 mL). The combined aqueous layers were extracted with ether (2 X 20 mL). The combined ether layers were then washed with saturated ferrous sulfate (10 mL) and water (10 mL). The combined aqueous layers were extracted with ether (2 X 20 mL). The combined ether layers were then washed with brine, dried (MgSO₄), and concentrated *in vacuo*. The crude material was purified further by flash chromatography on silica gel, followed by kugelrohr distillation.

1-Benzylindoline (18).²⁰ The general procedure gave 192 mg (92%) of a colorless oil. ¹H NMR (CDCl₃, 300 MHz,) δ 7.38-7.03 (m, 5H), 6.77 (dd, 2H, *J* = 7.4 Hz, 7.2 Hz,), 6.62 (d, 2H, *J* = 7.5 Hz), 4.25 (s, 2H), 3.31 (t, 2H, *J* = 8.3 Hz), 2.96 (t, 2H, *J* = 8.2 Hz); ¹³C NMR (CDCl₃, 300 MHz,) δ 152.5, 138.4, 129.9, 128.4, 127.8, 127.2, 127.0, 124.4, 117.6, 106.9, 53.6, 53.5, 28.5; IR (neat, cm⁻¹) 3025, 2820, 1606, 1488, 743; GC/MS (*m/z*) 209, 132, 118, 117, 91, 77.

1-Benzyl-1,2,3,4-tetrahydroquinoline (19).²⁰ The general procedure gave 194 mg (87%) of a colorless oil. ¹H NMR (CDCl₃, 300 MHz) δ 7.34-7.21 (m, 5H), 6.99-6.94 (m, 2H), 6.59-6.48 (m, 2H), 4.48 (s, 2H), 3.62 (dd, 2H, *J* = 5.9, 5.3 Hz,), 2.82 (t, 2H, *J* = 6.4 Hz), 2.05-1.97 (m, 2H); ¹³C NMR (CDCl₃, 300 MHz) δ 145.5, 138.8, 128.9, 128.5, 127.1, 126.7, 126.5, 122.1, 115.8, 110.9, 55.1, 49.8, 28.1, 22.3; IR (neat, cm⁻¹) 2925, 2842, 1602, 1506, 1451, 1345, 743; GC/MS (*m/z*) 223, 146, 132, 117, 91, 77.

1-Benzyl-2,3,4,5-tetrahydro-1H-1-benzazepin (20).²¹ The general procedure gave 211 mg (89%) of a colorless oil. ¹H NMR (CDCl₃, 300 MHz) δ 7.45-6.88 (m, 9H), 4.32 (s, 2H), 2.88 (br, 4H), 1.60 (br, 4H); ¹³C NMR (CDCl₃, 300 MHz) δ 152.6, 139.8, 136.1, 129.9, 128.3, 128.2, 126.9, 126.6, 121.2, 117.5, 58.4, 53.3, 35.0, 30.0, 25.8; IR (neat, cm⁻¹) 3025, 2925, 2840, 1596, 1495, 1450, 1140, 940, 750; GC/MS (*m/z*) 237, 160, 146, 130, 118, 91, 77.

Benzo[e]indolizidine (21).^{22,23} The general procedure gave 96 mg (55%) of a colorless oil. ¹H NMR (CDCl₃, 300 MHz) δ 7.06 (dd, 1H, *J* = 7.9, 7.8 Hz), 6.98 (d, 1H, *J* = 7.3, Hz), 6.54 (t, 1H, *J* = 7.3 Hz), 6.39 (d, 1H, *J* = 8.3 Hz), 3.46-3.16 (m, 3H), 2.91-2.70 (m, 2H), 2.17-1.86 (m, 4H), 1.53-1.35 (m, 2H); ¹³C NMR (CDCl₃, 300 MHz) δ 144.7, 128.3, 127.1, 121.1, 114.6, 109.8, 57.9, 46.8, 33.1, 28.1, 27.3, 23.9; IR (neat, cm⁻¹) 2933, 2839, 1604, 1502, 1459, 1357, 1323, 740; GC/MS (*m/z*) 173, 172, 145, 144, 130, 117, 77.

General procedure for cyclization of amino arylbromides using K_2CO_3 as the base. To a suspension of finely ground potassium carbonate (2.0 mmol), and tetrakis(triphenylphosphine)palladium(0) (0.1 mmol) in toluene (2 mL) was added the bromoamine (1.0 mmol) and the reaction mixture was heated to 100 °C with stirring until the starting material had been completely consumed as judged by GC analysis. The mixture was then cooled to r.t., and water and ether (5 mL each) were added. The aqueous layer was extracted with ether (2 X 5 mL) and the combined organic layers were then stirred with 30% hydrogen peroxide (5 mL) for 10 to 20 minutes to oxidize the triphenylphosphine. The layers were separated and the organic layer was washed with water (10 mL). The combined aqueous layers were extracted with ether (2 X 20 mL). The combined ether layers were then washed with saturated ferrous sulfate (10 mL) and then water (10 mL). The combined aqueous layers were extracted with ether (2 X 20 mL). The combined ether layers were then washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated. The crude product was purified further by flash chromatography on silica gel, followed by kugelrohr distillation.

General procedure for cyclizations using aminostannanes. The amino arylhalide (1.0 mmol) and (N,N-diethylamino)tributyltin (1.0 mmol) were mixed together and stirred under vacuum (0.01 mm Hg) for one hour. Toluene (2 mL) and $PdCl_2(o\text{-tolyl}_3P)_2$ (0.1 mmol) were added and the reaction mixture was heated to 100 °C with stirring until the starting material had been consumed as judged by GC analysis. The reaction mixture was cooled to room temperature and water and ether (5 mL each) were added. The layers were separated and the aqueous layer was extracted with ether (2 X 5 mL). The combined organic fractions were then stirred with 30% hydrogen peroxide (5 mL) for 10 to 20 minutes to oxidize the triphenylphosphine. The layers were separated and the organic layer was washed with water (10 mL). The combined aqueous layers were extracted with ether (2 X 20 mL). The combined ether layers were then washed with saturated ferrous sulfate (10 mL) and then water (10 mL). The combined aqueous layers were extracted with ether (2 X 20 mL). The combined ether layers were then washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated. The crude product was purified further by flash chromatography on silica gel followed by kugelrohr distillation.

General procedure for the synthesis of amino arylbromides. To a solution of the appropriate mesylate or iodide²⁴ (7.17 mmol), in THF (7 mL), was added potassium carbonate (35.8 mmol), followed by benzylamine (35.8 mmol). The reaction mixture was heated to reflux until all starting material had been consumed as judged by GC analysis. The mixture was cooled to room temperature, water (30 mL) was added, and the layers were separated. The aqueous layer was extracted with ether (2 x 20 mL) and the combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated. The crude product was purified further by flash chromatography on silica gel.

N-benzyl-*o*-bromophenethylamine (13).²⁵ The general procedure afforded 1.58 g (76%) of a pale yellow oil. 1H NMR ($CDCl_3$, 300 MHz) δ 7.51 (d, 1H, $J = 7.4$ Hz), 7.31-7.20 (m, 7H), 7.08-7.03 (m, 1H), 3.82 (s, 2H), 2.98-2.88 (m, 4H), 1.61 (br, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 140.2, 139.3, 132.8, 130.6, 128.3, 128.0, 127.8, 127.3, 126.8, 124.6, 53.7, 48.9, 36.6; IR (neat, cm^{-1}) 3026, 2923, 2821, 1472, 1451, 1113, 1026, 744, 687; GC/MS (m/z) 290, 288, 210, 171, 169, 120, 91.

N-Benzyl-3-(*o*-bromophenyl)propylamine (14).²⁵ The general procedure (on a 3.45 mmol scale) afforded 936 mg (89%) of a colorless oil. ¹H NMR (CDCl₃, 300 MHz) δ 7.54 (d, 1H, *J* = 8.2 Hz), 7.37-7.20 (m, 7H), 7.05-7.01 (m, 1H), 3.79 (s, 2H), 2.77 (dd, 2H, *J* = 7.2 Hz, 6.6 Hz,), 2.68 (dd, 2H, *J* = 7.0 Hz, 6.4 Hz), 1.72-1.59 (m, 2H), 1.22 (br, 1H); ¹³C NMR (CDCl₃, 300 MHz) δ 141.2, 140.3, 132.4, 130.0, 128.1, 127.8, 127.2, 127.1, 126.6, 124.2, 53.7, 48.5, 33.6, 29.9; IR (neat, cm⁻¹) 3061, 3026, 2930, 2860, 2815, 1494, 1470, 1453, 1439, 1121, 1022, 749, 698, 658; GC/MS (*m/z*) 304, 302, 224, 171, 169, 120, 91.

N-Benzyl-4-(*o*-bromophenyl)butylamine (15). The general procedure (on a 5 mmol scale) gave 1.45 g (85%) of a colorless oil. ¹H NMR (CDCl₃, 300 MHz) δ 7.55 (d, 1H, *J* = 7.9 Hz), 7.37-7.21 (m, 7H), 7.07-7.03 (m, 1H), 3.82 (s, 2H), 2.83 (dd, 2H, *J* = 7.8 Hz, 7.7 Hz), 2.73 (t, 2H, *J* = 7.0 Hz), 1.92-1.84 (m, 4H), 1.28 (br, 1H); ¹³C NMR (CDCl₃, 300 MHz) δ 141.3, 140.2, 132.4, 129.9, 128.0, 127.7, 127.1, 127.0, 126.4, 124.1, 53.7, 48.8, 35.6, 29.4, 27.3; IR (neat, cm⁻¹) 3061, 3026, 2930, 2858, 2813, 1494, 1470, 1454, 1439, 1119, 1022, 749, 698, 658; GC/MS (*m/z*) 319, 317, 238, 171, 169, 120, 91; HRMS calcd for C₁₇H₂₀BrN: 317.077911, found 317.07806.

2-(*o*-bromophenyl)-1-(2-pyrrolidine)ethane (16). To a solution of 2-(*o*-bromophenethyl)-1-pyrroline (**43**) (5 g, 19.8 mmol) in methanol (20 mL) was slowly added solid sodium borohydride (749 mg, 19.8 mmol). The solution was stirred at r.t. until all starting material had been consumed (2 h) as judged by GC, and TLC. Water (150 mL) and dichloromethane (75 mL) were added and stirring was continued for 0.5 h. The layers were separated and the aqueous layer was extracted with dichloromethane (3 X 100 mL). The combined organic layers were dried (MgSO₄), filtered, and concentrated. The crude product was purified further by flash chromatography on silica gel using 3% triethylamine in dichloromethane to afford 3.98 g (79%) of a colorless oil. ¹H NMR (CDCl₃, 300 MHz) δ 7.52 (d, 1H, *J* = 7.8 Hz), 7.27-7.18 (m, 2H), 7.07-7.01 (m, 1H), 3.07-2.97 (m, 2H), 2.89-2.72 (m, 3H), 1.98-1.88 (m, 1H), 1.81-1.68 (m, 4H), 1.57 (br, 1H), 1.38-1.26 (m, 1H); ¹³C NMR (CDCl₃, 300 MHz) δ 140.7, 131.8, 129.3, 126.5, 126.5, 123.5, 57.8, 45.8, 35.8, 33.2, 31.0, 24.6; IR (neat, cm⁻¹) 2955, 2865, 1566, 1471, 1403, 1361, 1023, 750, 658; GC/MS (*m/z*) 254, 252, 174, 70; HRMS calcd for C₁₂H₁₆BrN: 252.038786, found 252.03856.

N-benzyl-*o*-Iodophenethylamine (17). The general procedure gave 653 mg (65%) of a colorless oil. ¹H NMR (CDCl₃, 300 MHz) δ 7.72 (d, 1H, *J* = 7.8 Hz), 7.24-7.12 (m, 7H), 6.83-6.77 (m, 1H), 3.76 (s, 2H), 2.89-2.77 (m, 4H), 1.85 (br, 1H); ¹³C NMR (CDCl₃, 300 MHz) δ 142.3, 140.0, 139.2, 129.4, 128.0, 127.9, 127.7, 127.6, 126.5, 100.6, 53.4, 48.8, 40.9; IR (neat, cm⁻¹) 3059, 3025, 2925, 2818, 1494, 1464, 1454, 1435, 1117, 1028, 1010, 749, 698, 647; GC/MS (*m/z*) 338, 217, 120, 91; HRMS calcd for C₁₅H₁₆IN: 337.032752, found 337.03254.

General procedure for cyclization of acetamides. A Schlenk tube was charged with the acetamide (1 mmol), Cesium carbonate (2 mmol), tris(dibenzylideneacetone)dipalladium(0) (0.05 mmol, 10 mol% Pd), and tri-(2-furyl) phosphine (0.2 mmol). The flask was purged with argon for 1 min, then toluene (2 mL) was added and the reaction mixture was heated to 100-110 °C with stirring until the starting material had been completely consumed as judged by GC analysis. The solution was then allowed to cool to room temperature,

taken up in ether (15 mL), filtered, and concentrated. The crude product was then purified further by flash chromatography on silica gel.

N-acetyllindoline (23).^{26-28,48} The general procedure gave 157 mg (98%) of a colorless solid; mp=108-111 °C (lit=104-105 °C). The NMR spectra showed a mixture of rotamers ¹H NMR (CDCl₃, 300 MHz) δ 2.22 (s, 3H), 2.44 (s, 3H), 3.0 (t, 2H, *J*= 8.1 Hz), 3.19 (t, 2H, *J*= 8.4 Hz), 4.04 (t, 2H, *J*= 8.5 Hz), 4.13 (t, 2H, *J*= 8.3 Hz), 7.01 (t, 1H, *J*= 7.4 Hz), 7.16-7.22 (m, 2H), 8.21 (d, 1H, *J*= 7.7 Hz); ¹³C NMR (CDCl₃, 300 MHz) δ 24.0, 27.7, 48.5, 116.6, 123.3, 124.3, 127.2, 131.0, 142.7, 168.5; IR (KBr, cm⁻¹) 1649, 1598, 1483, 1464, 1408, 1344, 1323, 1264, 769. Anal Calcd for C₁₀H₁₁NO: C, 74.51; H, 6.88. Found: C, 74.77; H, 7.06.

N-acetyl-1,2,3,4-tetrahydroquinoline (25).²⁹ The general procedure gave 75 mg (43%) of a pale yellow oil. ¹H NMR (CDCl₃, 300 MHz) δ 1.96 (p, 2H, *J*= 6.3 Hz), 2.23 (s, 3H), 2.72 (t, 2H, *J*= 6.6 Hz), 3.79 (t, 2H, *J*= 6.3 Hz), 7.13-7.20 (m, 4H); ¹³C NMR (CDCl₃, 300 MHz) δ 170.0, 128.4, 126.0, 125.1, 124.5, 26.8, 24.0, 23.1; IR (neat, cm⁻¹) 3064, 2947, 1652, 1494, 1260, 732, 617. Anal Calcd for C₁₁H₁₃NO: C, 75.4; H, 7.48. Found C, 75.24; H, 7.66.

N-pivaloyllindoline (24). The general procedure afforded 176 mg (87%) of a white solid; mp = 66-67 °C. ¹H NMR (CDCl₃, 300 MHz) δ 8.24 (d, 1H, *J* = 8.4 Hz), 7.22-7.16 (m, 2H), 7.01 (t, 1H, *J* = 7.4 Hz), 4.13 (t, 2H, *J* = 8.3 Hz), 4.04 (t, 2H, *J* = 8.5 Hz), 3.19 (t, 2H, *J* = 8.4 Hz), 3.0 (t, 2H, *J* = 8.1 Hz), 2.44 (s, 3H), 2.22 (s, 3H); ¹³C NMR (CDCl₃, 300 MHz) δ 176.2, 144.5, 130.6, 127.0, 124.0, 123.3, 118.0, 49.2, 39.9, 29.0, 27.4; IR (KBr, cm⁻¹) 2969, 2929, 1642, 1599, 1476, 1401, 1371, 1360, 1165, 768. Anal. Calcd for C₁₃H₁₇NO: C, 76.81; H, 8.43. Found: C, 76.81; H, 8.36.

General procedure for the preparation of acetamides. To a solution of amine (4.0 mmol) and triethylamine (4.4 mmol) in dichloromethane (4 mL) at 0° C was slowly added acetyl chloride (4.4 mmol); a white precipitate formed. The reaction mixture was stirred at 0° C for 15 min, then warmed to ambient temperature and stirred for 2 h. The mixture was then diluted with ether (10 mL) and washed with brine (5 mL). The organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated. The crude product was then purified further by flash chromatography on silica gel.

N-acetyl-2-*o*-bromophenethylamine (4). To a solution of 2-*o*-bromophenethylamine (8.0 g, 40 mmol) in ether (100 mL) was slowly added triethylamine (8.09 g, 40.0 mmol), and acetyl chloride (6.28 g, 80 mmol); a white precipitate formed. The reaction mixture was stirred at ambient temperature for 14 h, then poured into 6 N NaOH (120 mL). The aqueous layer was extracted with ether (2 x 170 mL). The combined organic layers were washed with brine (170 mL), then dried over anhydrous magnesium sulfate. The solvent was removed *in vacuo* and recrystallization of the crude product from ether/pentane gave 6.77 g (70%) of an opaque solid; mp=74-75 °C. ¹H NMR (CDCl₃, 300 MHz) δ 1.96 (s, 3H), 2.97 (t, 2H, *J*= 7.2 Hz), 3.53 (q, 2H, *J*= 6.7 Hz), 5.60 (br, 1H), 7.10-7.13 (m, 1H), 7.22-7.27 (m, 2H), 7.55 (d, 1H, *J*= 8.0 Hz); ¹³C NMR (CDCl₃, 300 MHz) δ 22.7, 35.4, 39.0, 124.2, 127.2, 127.8, 130.4, 132.5, 138.1, 170.2; IR (KBr, cm⁻¹) 3444, 3250, 3070, 1646, 1558, 1541, 1437, 757. Anal Calcd for C₁₀H₁₂NOBr: C, 49.61; H, 4.99. Found: C, 49.59; H, 4.83.

N-acetyl-3-(*o*-bromophenyl)propylamine (5). The general procedure (on a 5 mmol scale) gave 0.625 g (49%) of a colorless oil. $^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ 1.84 (p, 2H, $J = 7.8$ Hz), 1.97 (s, 3H), 2.77 (t, 2H, $J = 7.5$ Hz), 3.31 (q, 2H, $J = 6.6$ Hz), 5.55 (br, 1H), 7.03-7.54 (m, 4H); $^{13}\text{C NMR}$ (CDCl_3 , 300 MHz) δ 23.1, 29.4, 33.3, 38.9, 124.1, 127.4, 127.6, 130.2, 132.6, 140.5, 170.2; IR (neat, cm^{-1}) 3284, 3083, 2933, 1654, 1560, 1471, 1438, 1368, 1021, 749. Anal Calcd for $\text{C}_{11}\text{H}_{14}\text{NOBr}$: C, 51.58; H, 5.51. Found: C, 51.38; H, 5.31.

N-acetyl-4-(*o*-bromophenyl)butylamine (6). The general procedure gave 0.875 g (81%) of a colorless oil. $^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ 1.53-1.70 (m, 4H), 1.97 (s, 3H), 2.75 (t, 2H, $J = 7.5$ Hz), 3.29 (q, 2H, $J = 6.3$ Hz), 5.47 (br, 1H), 7.02-7.53 (m, 4H); $^{13}\text{C NMR}$ (CDCl_3 , 300 MHz) δ 23.0, 27.0, 28.9, 25.5, 39.1, 124.1, 127.2, 127.4, 130.1, 132.5, 141.1, 170.1; IR (neat, cm^{-1}) 3283, 3083, 2933, 2861, 1647, 1558, 1471, 1438, 1368, 1292, 1022, 750. Anal Calcd for $\text{C}_{12}\text{H}_{16}\text{NOBr}$: C, 53.35; H, 5.97. Found: C, 53.23; H, 6.15.

N-pivaloyl-2-*o*-bromophenethylamine (22). To a solution of 2-*o*-bromophenethylamine (4.00 g, 20.0 mmol) in ether (80 mL) was added triethylamine (4.05 g, 40.0 mmol) followed by slow dropwise addition of pivaloyl chloride (4.82 g, 40.0 mmol); a white precipitate formed. The reaction was stirred for 2 h, then poured into 6 N sodium hydroxide (100 mL). The layers were separated and the aqueous layer was extracted with ether (2 X 65 mL). The combined organic layers were washed with brine (50 mL), dried (MgSO_4), filtered, and concentrated. The crude product was recrystallized from ether/hexane to afford 5.35 g (94%) of a white solid; mp = 95-96 °C. $^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ 7.56 (d, 1H, $J = 7.0$ Hz), 7.28-7.20 (m, 2H), 7.13-7.09 (m, 1H), 5.68 (s, 1H), 3.53 (q, 2H, $J = 6.5$ Hz), 2.99 (t, 2H, $J = 6.8$ Hz), 1.15 (s, 3H); $^{13}\text{C NMR}$ (CDCl_3 , 300 MHz) δ 178.4, 138.4, 132.8, 131.0, 128.2, 127.4, 124.4, 38.1, 38.5, 35.5, 27.5; IR (KBr, cm^{-1}) 3322, 2967, 1626 1538, 1471, 1366, 1216, 1017, 755, 662. Anal. Calcd for $\text{C}_{13}\text{H}_{18}\text{BrNO}$: C, 54.94; H, 6.38. Found: C, 55.04; H, 6.38.

Cyclization of benzamides

N-benzyl-2-indolinone (26).³⁰⁻³² A Schlenk tube was charged with **10** (152 mg, 0.50 mmol), potassium carbonate (97 mg, 0.7 mmol), tris(dibenzylideneacetone)dipalladium(0) (9 mg, 0.01 mmol, 4% Pd), and tri-*o*-tolyl phosphine (12 mg, 0.04 mmol). The tube was purged with argon for 1 min, then toluene (4 mL) was added and the reaction mixture was heated to 100 °C with stirring. After 15 h GC analysis showed incomplete conversion. Tris(dibenzylideneacetone)dipalladium(0) (5 mg, 0.005 mmol, 2% Pd), and tri-*o*-tolyl phosphine (6 mg, 0.02 mmol) was added. The reaction mixture was heated for an additional 22 h, at which time GC analysis showed complete consumption of starting material. The reaction mixture was cooled to room temperature, taken up in ether (15 mL), filtered, and concentrated. The crude product was purified further by flash chromatography on silica gel using 8/1 hexane/ethyl acetate as the elutant to give 68 mg (61%) of a yellow oil. $^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ 3.60 (s, 2H), 4.90 (s, 2H), 6.71(d, 1H, $J = 7.8$ Hz), 6.96-7.31 (m, 8H); $^{13}\text{C NMR}$ (CDCl_3 , 300 MHz) δ 35.6, 43.6, 109.0, 122.2, 124.3, 124.4, 127.2, 127.5, 127.7, 128.6, 135.8, 144.2, 175.0; IR (neat, cm^{-1}) 1708, 1614, 1488, 1466, 1347, 1197, 1166, 750; GC/MS (m/z) 223, 132, 91. HRMS calcd for $\text{C}_{15}\text{H}_{14}\text{NO}$: 223.099714. Found: 223.09973.

N-benzyl-1,2,3,4-tetrahydroisoquinoline-2-one (27).³³ A Schlenk tube was charged with **11** (159 mg, 0.5 mmol), potassium carbonate (97 mg, 0.7 mmol), tris(dibenzylideneacetone)dipalladium(0) (18 mg, 0.02 mmol, 8 mol% Pd), and tri-*o*-tolyl phosphine (24 mg, 0.08 mmol). The tube was purged with argon for 1 min, then toluene (4 mL) was added and the mixture was heated to 100 °C with stirring. GC analysis after 68 h showed incomplete consumption of starting material. Tris(dibenzylideneacetone)dipalladium(0) (5 mg, 0.005 mmol, 2 mol% Pd), and tri-*o*-tolyl phosphine (6 mg, 0.02 mmol) was added and the mixture was heated for an additional 24 h, when GC analysis showed complete consumption of starting material. The reaction mixture was cooled to room temperature, taken up in ether (15 mL), filtered, and concentrated. The crude product was purified further by flash chromatography on silica gel using 5/1 hexane/ethyl acetate as the elutant to give 91 mg (76%) of a colorless oil which solidified upon standing to give a white solid; mp=49.8-51.2 °C. ¹H NMR (CDCl₃, 300 MHz) δ 2.77-3.01 (m, 4H), 5.18 (s, 2H), 6.86-7.31 (m, 9H); ¹³C NMR (CDCl₃, 300 MHz) δ 25.5, 31.8, 46.1, 115.5, 122.8, 126.3, 127.0, 127.4, 127.8, 128.7, 136.9, 139.8, 170.5; IR (KBr, cm⁻¹) 3087, 3060, 3026, 2961, 2943, 1674, 1599, 1588, 1496, 1469, 1454, 1427, 1381, 1191, 755, 728, 708. Anal Calcd for C₁₆H₁₅NO: C, 80.98; H, 6.37. Found: C, 80.88; H, 6.45.

N-Benzyl-2-*o*-bromophenylethylamide (10).³⁴ To a -15 °C solution of nitrosylhexafluorophosphate (2.10 g, 12.0 mmol) in nitromethane (20 mL) was slowly added *o*-bromophenylacetonitrile (2.94 g, 15.0 mmol), and benzylbromide (1.71 g, 10.0 mmol) in nitromethane (5 mL). The reaction mixture was stirred for 20 min at -15 °C, then water (25 mL) was added. The layers were separated and the aqueous layer was extracted with ether (2 x 50 mL). The combined organic layers were washed with saturated aqueous sodium bicarbonate (50 mL), water (50 mL), and brine (50 mL). The organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated. The product was purified further by flash chromatography on silica gel using 2/1 hexane/ethyl acetate as the elutant to give 1.67 g (75%) of a white solid; mp=132-134 °C. ¹H NMR (CDCl₃, 300 MHz) δ 3.78 (s, 2H), 4.45 (d, 2H, *J*= 5.7 Hz), 5.72 (br, 1H), 7.13-7.39 (m, 8H), 7.69 (d, 1H, *J*= 7.9 Hz); ¹³C NMR (CDCl₃, 300 MHz) δ 43.4, 43.7, 124.8, 127.2, 127.4, 127.8, 128.4, 129.0, 131.6, 132.9, 134.7, 138.0, 169.4; IR (KBr, cm⁻¹) 3273, 2359, 1643, 1541, 1455, 736, 694. Anal Calcd for C₁₅H₁₄NOBr: C, 59.23; H, 4.64. Found: C, 59.57; H, 4.55.

General procedure for preparation of N-benzyl amides. To solid carboxylic acid (5 mmol) in a round bottom flask was added thionyl chloride (4 mL). The solution was stirred at room temperature for 2.5 h. Excess thionyl chloride was removed *in vacuo* and dichloromethane (2.5 mL) was added. This solution was slowly added to a solution of benzylamine (12.5 mmol) in dichloromethane (2.5 mL) at 0 °C; a white solid precipitated. The reaction mixture was stirred at 0 °C for 15 min, then warmed to ambient temperature and stirred for 2 h. The reaction mixture was then diluted with ether (10 mL), washed with saturated aqueous sodium bicarbonate (5 mL), and washed with brine (5 mL). The organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated. The crude product was then purified further by flash chromatography on silica gel.

N-benzyl-3-(*o*-bromophenyl)propionylamide (11).^{25,45} The general procedure gave 1.271 g (80%) of a white solid; mp=90.4- 91.6 °C (lit=70-73 °C). ¹H NMR (CDCl₃, 300 MHz) δ 2.53 (t, 2H, *J*= 8.1 Hz), 3.12 (t, 2H, *J*= 7.2 Hz), 4.42 (d, 2H, *J*= 5.7 Hz), 5.66 (br, 1H), 7.05-7.53 (m, 9H); ¹³C NMR (CDCl₃, 300 MHz) δ

31.9, 36.1, 43.3, 124.1, 127.1, 127.39, 127.43, 127.8, 128.4, 130.5, 132.6, 139.9, 171.6; IR (KBr, cm^{-1}) 3296, 3030, 2940, 1641, 1542, 1469, 1553, 1024, 752, 697.

N-benzyl-4-(*o*-bromophenyl)butylamide (12). The general procedure (on a 6 mmol scale) gave 1.328 g (67%) of a white solid; mp=110.6-112.0 °C. ^1H NMR (CDCl_3 , 300 MHz) δ 2.00 (p, 2H, $J= 7.5$ Hz), 2.28 (t, 2H, $J= 7.5$ Hz), 2.80 (t, 2H, $J= 7.2$ Hz), 4.45 (d, 2H, $J= 5.4$ Hz), 5.70 (br, 1H), 7.02-7.53 (m, 9H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 25.7, 35.3, 35.8, 43.6, 124.4, 127.4, 127.5, 127.7, 127.8, 128.7, 130.4, 132.7, 138.3, 140.7, 172.3; IR (KBr, cm^{-1}) 3293, 3052, 2951, 1636, 1559, 1545, 1458, 745, 698. Anal Calcd for $\text{C}_{17}\text{H}_{18}\text{NOBr}$: C, 61.46; H, 5.46. Found: C, 61.66; H, 5.46.

General procedure for Pd-catalyzed cyclization of sulfonamides. A Schlenk tube was charged with the sulfonamide (0.5 mmol), potassium carbonate (0.7 mmol), tris(dibenzylideneacetone)dipalladium(0) (0.01 mmol, 4 mol% Pd), and tri-*o*-tolyl phosphine (0.04 mmol). The tube was purged with argon for 1 min, then toluene (4 mL) was added. The solution was heated to 100 °C with stirring until the starting material had been completely consumed as judged by TLC analysis. The solution was then cooled to room temperature, taken up in ether (15 mL), filtered, and concentrated. The crude product was then purified further by flash chromatography on silica gel.

N-(*p*-toluenesulfonyl)-indoline (28).³⁵ The general procedure gave 120 mg (88%) of a white solid; mp=101.5-102.3 °C. ^1H NMR (CDCl_3 , 300 MHz) δ 2.36 (s, 3H), 2.88 (t, 2H, $J= 8.1$ Hz), 3.91 (t, 2H, $J= 8.1$ Hz), 6.96-7.26 (m, 5H), 7.66 (t, 3H, $J= 8.4$ Hz); ^{13}C NMR (CDCl_3 , 300 MHz) δ 21.5, 27.8, 49.9, 114.9, 123.6, 125.0, 127.2, 127.6, 129.6, 131.7, 133.9, 141.9, 144.0; IR (KBr, cm^{-1}) 3029, 2874, 2853, 1597, 1480, 1460, 1348, 1307, 1239, 1168, 1104, 1090, 1044, 975, 754. Anal Calcd for $\text{C}_{15}\text{H}_{15}\text{NSO}_2$: C, 65.91; H, 5.53. Found: C, 65.99; H, 5.50.

N-(*p*-toluenesulfonyl)-1,2,3,4-tetrahydroquinoline (29).³⁶ The general procedure gave 121 mg (84%) of a white solid; mp=94.6- 95.4 °C (lit= 95-96 °C). ^1H NMR (CDCl_3 , 300 MHz) δ 1.63 (p, 2H, $J= 5.4$ Hz), 2.38 (s, 3H), 2.44 (t, 2H, $J= 6.9$ Hz), 3.80 (t, 2H, $J= 6.9$ Hz), 7.01-7.80 (m, 8H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 21.5, 21.7, 26.6, 46.5, 124.9, 126.5, 127.1, 129.0, 129.5, 130.6, 136.9, 137.8, 143.4; IR (KBr, cm^{-1}) 3057, 2950, 1598, 1488, 1453, 1356, 1340, 1309, 1163, 1092, 1071, 1019, 840, 762, 687, 579. Anal Calcd for $\text{C}_{16}\text{H}_{17}\text{NSO}_2$: C, 66.87; H, 5.96. Found: C, 66.87; H, 6.08.

General Procedure for the preparation of *p*-toluenesulfonamides. To a solution of the amine (5 mmol), and triethylamine (5.5 mmol) in dichloromethane (2.5 mL) at 0°C was slowly added a solution of *p*-toluenesulfonyl chloride (5.5 mmol) in dichloromethane (2.5 mL); a white precipitate formed. The reaction mixture was stirred at 0°C for 15 min, then warmed to ambient temperature and stirred for 2 h. The reaction mixture was then diluted with ether (10 mL), washed with aqueous saturated sodium bicarbonate (5 mL), and washed with brine (5 mL). The organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated. The crude product was then purified further by flash chromatography on silica gel.

N-(*p*-toluenesulfonyl)-*o*-bromophenylethylamine (7). The general procedure gave 1.21 g (68%) of a white solid; mp=71.2-72.0 °C. ¹H NMR (CDCl₃, 300 MHz) δ 2.42 (s, 3H), 2.92 (t, 2H, *J*= 6.9 Hz), 3.24 (q, 2H, *J*= 6.9 Hz), 4.06 (br, 1H), 7.08-7.30 (m, 5H), 7.50 (d, 1H, *J*= 8.1 Hz), 7.71 (d, 2H, *J*= 8.4 Hz); ¹³C NMR (CDCl₃, 300 MHz) δ 21.5, 36.3, 42.5, 124.4, 127.0, 127.6, 128.5, 129.7, 131.1, 132.9, 136.8, 137.1, 143.4; IR (KBr, cm⁻¹) 3249, 2946, 1599, 1567, 1469, 1437, 1323, 1163, 1092, 1068, 1021, 889, 813, 762, 748, 653. Anal Calcd for C₁₅H₁₆NSO₂Br: C, 50.86; H, 4.55. Found: C, 50.90; H, 4.64.

N-(*p*-toluenesulfonyl)-3-(*o*-bromophenyl)propylamine (8). The general procedure gave 1.187 g (65%) of a colorless oil which solidified upon the addition of hexane. The hexane was removed *in vacuo* to give a white solid; mp=58.2-59.3 °C. ¹H NMR (CDCl₃, 300 MHz) δ 1.78 (p, 2H, *J*= 7.5 Hz), 2.43 (s, 3H), 2.72 (t, 2H, *J*= 7.5 Hz), 3.00 (q, 2H, *J*= 6.6 Hz), 4.51 (br, 1H), 7.05-7.32 (m, 5H), 7.49 (d, 1H, *J*= 9.0 Hz), 7.74 (d, 2H, *J*= 8.4 Hz); ¹³C NMR (CDCl₃, 300 MHz) δ 21.4, 29.5, 32.9, 42.5, 124.2, 127.0, 127.4, 127.7, 129.6, 130.3, 132.7, 137.0, 140.2, 143.2; IR (KBr, cm⁻¹) 3283, 3063, 2929, 2867, 1598, 1495, 1471, 1439, 1325, 1159, 1094, 1020, 814, 752, 661. Anal Calcd for C₁₆H₁₈NSO₂Br: C, 52.18; H, 4.93. Found: C, 52.28; H, 4.95.

N-(*p*-toluenesulfonyl)-4-(*o*-bromophenyl)butylamine (9). To a suspension of sodium cyanide (1.11 g, 22.7 mmol) in THF (25 mL)/DMSO (36 mL) was added **40** in THF (11 mL). The reaction mixture was heated to 65 °C with stirring until all starting material had been consumed (6 h) as judged by TLC. The reaction mixture was cooled to room temperature, diluted with ether (75 mL), filtered, and concentrated. The crude product was purified further by flash chromatography on silica gel using 9/1 hexane/ethyl acetate as the elutant to afford 4-(*o*-bromophenyl)-butyronitrile (**49**) as a colorless oil (2.534 g, 62%). ¹H NMR (CDCl₃, 300 MHz) δ 2.01 (p, 2H, *J*= 6.3 Hz), 2.37 (t, 2H, *J*= 6.9 Hz), 2.91 (t, 2H, *J*= 7.5 Hz), 7.10-7.13 (m, 1H), 7.24-7.27 (m, 2H), 7.55 (d, 1H, *J*= 8.4 Hz); ¹³C NMR (CDCl₃, 300 MHz) δ 139.1, 133.0, 130.5, 128.2, 127.6, 124.2, 119.3, 34.7, 25.3, 16.5; IR (neat, cm⁻¹) 3056, 3011, 2935, 2246, 1471, 1456, 1440, 1019, 755.

A Schlenk flask was charged with solid aluminum chloride (1.51 g, 11.3 mmol) and cooled to 0 °C. Ether (25 mL) was added, followed by 1M Lithium Aluminum Hydride in ether (14.7 mL, 14.7 mmol). To this suspension was added **49** (2.53 g, 11.3 mmol) in ether (5 mL). The reaction mixture was warmed to ambient temperature with stirring for 11 h. The mixture was then cooled to 0 °C and slowly quenched with ice water. Sulfuric acid (2M, ~20 mL) was added until all solids dissolved. The layers were separated, and the aqueous layer was extracted with ether (40 mL). The aqueous layer was then brought to pH 11 with 1M NaOH, and extracted with ether (3 x 50 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated to afford 4-(*o*-bromophenyl)butylamine (**3**) as a colorless oil (1.93 g, 75%). ¹H NMR (CDCl₃, 300 MHz) δ 1.52 (br, 2H), 1.45-1.71 (m, 4H), 2.70-2.80 (m, 4H), 7.00-7.10 (m, 1H), 7.15-7.29 (m, 2H), 7.50-7.55 (m, 1H); ¹³C NMR (CDCl₃, 300 MHz) δ 141.5, 132.6, 130.1, 127.3, 127.2, 124.2, 41.6, 35.7, 32.8, 27.0; IR (neat, cm⁻¹) 3287, 3055, 3011, 2929, 1566, 1471, 1438, 1022, 749.

3 was tosylated using the general procedure (on a 3 mmol scale) to afford 1.026 g (90%) of a colorless oil which solidified upon the addition of hexane. The hexane was removed *in vacuo* to give N-(*p*-toluenesulfonyl)-4-(*o*-bromophenyl)butylamine as a white solid; mp=91.0-92.5 °C. ¹H NMR (CDCl₃, 300 MHz) δ 1.53-1.60 (m, 4H), 2.42 (s, 3H), 2.66 (t, 2H, *J*= 6.7 Hz), 2.99 (q, 2H, *J*= 6.7 Hz), 4.45 (br, 1H), 7.05-7.31 (m, 5H), 7.50 (d, 1H, *J*= 8.1 Hz), 7.74 (d, 2H, *J*= 8.3 Hz); ¹³C NMR (CDCl₃, 300 MHz) δ 21.4, 26.6, 29.0, 35.3, 42.9, 124.2, 127.0, 127.3, 127.5, 129.6, 130.2, 132.6, 136.8, 141.0, 143.2; IR (KBr, cm⁻¹) 3262,

3062, 2952, 1598, 1566, 1493, 1482, 1468, 1458, 1425, 1333, 1304, 1156, 1117, 1094, 1077, 1066, 1046, 1020, 810, 753. Anal Calcd for C₁₇H₂₀NSO₂Br: C, 53.41, H, 5.27. Found: C, 53.57; H, 5.27.

2-(*o*-bromophenethyl)-1-pyrroline (43). To a solution of diisopropylamine (4.00 g, 39.5 mmol) in THF (150 ml) at -20 °C was added 2.5 M *n*-butyllithium in hexanes (15.8 mL, 39.5 mmol) dropwise via syringe over a ten minute period. The resulting light yellow solution was stirred for thirty minutes and warmed to -10 °C. The solution was cooled to -78 °C and 2-methyl-1-pyrroline (**42**) (2.98 g, 35.9 mmol) was added dropwise via syringe over a ten minute period. The resulting yellow-orange solution was stirred for an additional thirty minutes at -78 °C. A solution of *o*-bromobenzyl bromide (8.97 g, 35.9 mmol) in THF (50 mL) was added dropwise via cannula over a ten minute period. The resulting bright yellow solution was slowly allowed to warm to room temperature and stirred for 14 h. The reaction mixture was poured into ether (250 mL), then washed with water (2 X 250 mL) and brine (250 mL). The organic layer was dried (MgSO₄), filtered and concentrated. The crude product was subjected to flash chromatography on silica gel using 2/1 hexane/ethyl acetate as the elutant to afford 3.37 g of a yellow oil. Kugelrohr distillation at 0.005 mm Hg and 90 °C afforded 6.25g (69%) of a colorless oil. ¹H NMR (CDCl₃, 300 MHz) δ 7.52 (d, 1H, *J* = 7.8 Hz), 7.27-7.19 (m, 2H), 7.08-7.03 (m, 1H), 3.87-3.80 (m, 2H), 3.08-3.02 (m, 2H), 2.66-2.61 (m, 2H), 2.52-2.46 (m, 2H), 1.93-1.82 (m, 2H); ¹³C NMR (CDCl₃, 300 MHz) δ 176.1, 140.1, 132.0, 129.6, 127.0, 126.8, 123.6, 60.2, 36.8, 33.0, 32.2, 21.9; IR (neat, cm⁻¹) 2958, 2864, 1644, 1566, 1471, 1440, 1315, 1303, 1044, 1022, 753, 656; GC/MS (*m/z*) 252, 251, 250, 172; HRMS calcd for C₁₂H₁₄BrN: 251.030961, found 251.03066.

General procedure for reduction of nitriles.³⁸ A Schlenk flask was charged with solid aluminum chloride (15.71 mmol) and cooled to 0 °C. Ether (35 mL) was added, followed by 1M Lithium Aluminum Hydride in ether (20.4 mmol). To this suspension was added the appropriate nitrile (15.71 mmol) in ether (8 mL). The reaction mixture was warmed to ambient temperature with stirring for 18 h. The mixture was then cooled to 0 °C and slowly quenched with ice water. Sulfuric acid (2M, ~20 mL) was added until all solids dissolved. The layers were separated, and the aqueous layer was extracted with ether (40 mL). The aqueous layer was then brought to pH 11 with 1M NaOH, and extracted with ether (3 x 50 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated. The crude product was purified by flash chromatography on silica gel.

2-*o*-bromophenethylamine (1).²⁵ The general procedure (77 mmol scale, chromatography step omitted) afforded a yellow oil. Distillation of the crude product at 71-74 °C and 0.01 mm Hg afforded 13.8 g (90%) of a colorless oil. ¹H NMR (CDCl₃, 300 MHz) δ 7.52 (d, 1H, *J* = 7.7 Hz), 7.23-7.20 (m, 2H), 7.09-7.03 (m, 1H), 2.99-2.85 (m, 4H), 1.21 (s, 2H); ¹³C NMR (CDCl₃, 300 MHz) δ 138.1, 131.7, 129.8, 126.7, 126.3, 123.5, 41.0, 39.3; IR (neat, cm⁻¹) 3362, 2933, 2869, 1560, 1473, 1438, 1328, 1023, 749, 657. Anal. Calcd for C₈H₁₀BrN: C, 48.03; H, 5.04. Found: C, 48.09; H, 5.26.

3-(*o*-bromophenyl)-propylamine (2).²⁵ The general procedure (on a 15.71 mmol scale) gave a colorless oil (2.827 g, 84%). ¹H NMR (CDCl₃, 300 MHz) δ 1.33 (br, 2H), 1.77 (p, 2H, *J* = 7.2Hz), 2.74-2.80 (m, 4H), 7.04-7.08 (m, 1H), 7.22-7.26 (m, 2H), 7.52 (d, 1H, *J* = 7.8 Hz); ¹³C NMR (CDCl₃, 300 MHz) δ 141.0, 132.8,

130.3, 127.5, 127.4, 124.4, 41.8, 34.0, 33.5; IR (neat, cm^{-1}) 3363, 3062, 2930, 2860, 1587, 1567, 1471, 1439, 1022, 750, 658.

***o*-bromocinnamionitrile (44).**^{37,39} A Schlenk flask was charged with 2-iodo-bromobenzene (2.7 mL, 21 mmol), acrylonitrile (2.0 mL, 30 mmol), sodium bicarbonate (4.2 g, 50 mmol), tetra-*n*-butyl ammonium chloride (5.6 g, 20 mmol), palladium acetate (90 mg, 0.4 mmol, 2 mol% Pd), and DMF (20 mL). The flask was purged with argon for 1 min, then heated to 40 °C with stirring. GC analysis after 24 h showed that there was incomplete conversion of starting material. Palladium acetate (23 mg, 0.1 mmol, 0.5 mol% Pd) was added and the reaction mixture was heated for an additional 24h, then cooled to room temperature. The mixture was diluted with ether (80 mL), filtered, and concentrated. The crude product was purified further by flash chromatography on silica gel using 9/1 hexane/ethyl acetate as the elutant to give a colorless oil which turned to a gummy solid upon standing (4.357 g, 99%, mixture of *E/Z* isomers). ¹H NMR (CDCl_3 , 300 MHz) δ 5.57 (s, 1H), 5.61 (s, 1H), 5.83 (s, 1H), 5.89 (s, 1H), 7.25-8.04 (m, 12H); ¹³C NMR (CDCl_3 , 300 MHz) δ 148.8, 147.7, 133.4, 133.3, 133.0, 132.0, 131.7, 129.1, 127.8, 127.7, 126.9, 124.6, 124.4, 117.5, 116.3, 98.9, 98.2; IR (neat, cm^{-1}) 3061, 2219, 1615, 1587, 1436, 1028, 752.

3-(*o*-bromophenyl)propionitrile (45).^{40,42} To a suspension of sodium borohydride (0.87 g, 23 mmol) in DME (20 mL) was added anhydrous methanol (0.93 mL, 23 mmol). After evolution of H₂ ceased, **44** (4.0 g, 19.2 mmol) in DME (20 mL) was added slowly. The mixture was heated to 70 °C with stirring until the starting material had been consumed (15h) as judged by GC analysis. The reaction mixture was cooled to room temperature and quenched with brine (15 mL). Water (10 mL) was added to dissolve all solids, and the mixture was acidified with 1M HCl to pH 3. The layers were separated and the aqueous layer was extracted with ether. The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated. The crude product was purified further by flash chromatography on silica gel using 12/1 hexane/ethyl acetate as the elutant to give a colorless oil (3.553 g, 88%). ¹H NMR (CDCl_3 , 300 MHz) δ 2.67 (t, 2H, *J* = 7.2 Hz), 3.07 (t, 2H, *J* = 7.2 Hz), 7.14-7.17 (m, 1H), 7.29-7.32 (m, 2H), 7.55 (d, 1H, *J* = 7.8 Hz); ¹³C NMR (CDCl_3 , 300 MHz) δ 137.1, 133.0, 130.7, 129.0, 127.9, 123.9, 118.8, 31.9, 17.4; IR (neat, cm^{-1}) 3059, 2938, 2247, 1471, 1440, 1423, 1027, 753.

4-(*o*-bromophenyl)-1-butene (54).⁴¹ To a solution of 2-bromobenzyl bromide (7.5 g, 30 mmol) in THF (35 mL) was slowly added 1 M allylmagnesium bromide in ether (159 mL, 159 mmol) using an ice bath to control exothermicity. The reaction mixture was then heated to reflux for 1.5 h with stirring. The mixture was then cooled to 0 °C and carefully quenched with 2M sulfuric acid (~ 20 mL). Water (~20 mL) was added to dissolve all solids, and the layers were separated. The aqueous layer was extracted with ether (3 x 40 mL), and the combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated to give a pale yellow oil (6.09 g, 96%). ¹H NMR showed that it contained slight impurities. The product was used without further purification. ¹H NMR (CDCl_3 , 300 MHz) δ 2.34-2.41 (m, 2H), 2.80-2.86 (m, 2H), 4.98-5.09 (m, 2H), 5.82-5.92 (m, 1H), 7.03-7.09 (m, 1H), 7.21-7.26 (m, 2H), 7.52 (d, 1H, *J* = 7.5 Hz); IR (neat, cm^{-1}) 3073, 2976, 2927, 2862, 1640, 1469, 1453, 1437, 1024, 913, 748, 657.

***o*-bromophenethanol (36).**^{43,44} To a solution of 0.5 M 9-BBN in THF (109 mL, 54.6 mmol) was added *o*-bromostyrene (10.0 g, 54.6 mmol) and THF (40 mL). The reaction was stirred at room temperature until the starting material had been completely consumed (18 h) as judged by GC analysis. 6 M sodium hydroxide (10 mL, 60.1 mmol) was added followed by careful addition of 30% hydrogen peroxide (17.1 mL, 175 mmol) to the reaction mixture while cooling with an ice bath. The reaction mixture was heated to 50 °C for one hour and then allowed to cool to room temperature. The solution was saturated with solid sodium carbonate, and the layers were separated. The organic layer was washed with saturated sodium sulfite, water, and saturated sodium chloride (150 mL each). The combined aqueous layers were extracted with ether (2 X 100 mL) and the combined organic layers were dried (MgSO₄), filtered, and concentrated. The crude product was subjected to flash chromatography on silica gel using 2/1 hexane/ethyl acetate as the elutant to afford 9.13 g (83%) of a colorless oil. ¹H NMR (CDCl₃, 300 MHz) δ 7.54 (d, 1H, *J* = 7.5 Hz), 7.28-7.21 (m, 7H), 7.11-7.05 (m, 1H), 3.87 (t, 2H, *J* = 6.7 Hz), 3.02 (t, 2H, *J* = 6.7 Hz), 1.42 (br, 1H); ¹³C NMR (CDCl₃, 300 MHz) δ 137.7, 132.6, 131.1, 127.9, 127.2, 124.5, 61.6, 39.1; IR (neat, cm⁻¹) 3332, 2927, 1567, 1471, 1440, 1040, 750, 659; GC/MS (*m/z*) 202, 200, 172, 171, 170, 169, 121, 91, 90, 89.

3-(*o*-bromophenyl)-propanol (37).^{29,45} To anhydrous methanol (20 mL) was slowly added sodium borohydride (1.134 g, 30 mmol) with stirring. After H₂ evolution ceased, **48** (4.26g, 20 mmol) was added and the mixture was stirred at ambient temperature. TLC analysis of the reaction mixture after 14 h showed that little reaction had taken place. The solution was then heated to reflux until all starting material had been consumed (3.5 h) as judged by TLC analysis. The reaction mixture was cooled to room temperature, quenched slowly with water (15 mL), then acidified to pH 3 with 2M sulfuric acid (~20 mL). Ether was added (50 mL), and the layers were separated. The aqueous layer was extracted with ether (3 x 30 mL), and the combined organic layers were washed with brine (15 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated to give a pale yellow oil with solid impurities. The crude product was purified further by passing through a short column of silica gel using 3/1 hexane/ethyl acetate as the elutant. Removal of solvent gave 3.37 g (78%) of a colorless oil. ¹H NMR (CDCl₃, 300 MHz) δ 1.37 (br, 1H), 1.92 (p, 2H, *J* = 4.8 Hz), 2.84 (t, 2H, *J* = 7.8 Hz), 3.71 (t, 2H, *J* = 6.6 Hz), 7.05-7.09 (m, 1H), 7.23-7.26 (m, 2H), 7.53 (d, 1H, *J* = 8.1 Hz); IR (neat, cm⁻¹) 3344, 3064, 2937, 1471, 1438, 1057, 1020, 750, 658.

4-(*o*-bromophenyl)-butanol (38). To a solution of 0.5M 9-BBN in hexanes (88 mL, 44 mmol) was slowly added **54** (6.09 g, 28.9 mmol). The mixture was stirred at ambient temperature until the starting olefin had been consumed (17 h) as judged by TLC. NaOH (6M, 5 mL, 30 mmol) was added, followed by 10 mL of THF. 30% hydrogen peroxide (10.2 mL, 90 mmol) was slowly added and the mixture was heated to 50 °C for 1.5 h, then cooled to room temperature. The layers were separated, and the organic layer was washed with saturated aqueous sodium sulfite (20 mL), water (20 mL), and brine (20 mL). The aqueous extracts were combined, saturated with potassium carbonate, and extracted with ether (3 x 30 mL). The combined organic fractions were dried over anhydrous magnesium sulfate, filtered, and concentrated. The product was purified further by passing through a short column of silica gel using 2/1 hexane/ethyl acetate as the elutant to give a colorless oil (4.81 g, 73%). ¹H NMR (CDCl₃, 300 MHz) δ 7.50 (d, 1H, *J* = 8.0 Hz), 7.18-7.21 (m, 2H), 7.01-7.05 (m, 1H), 3.64 (t, 2H, *J* = 6.0 Hz), 2.74 (t, 2H, *J* = 7.3 Hz), 2.14 (br, 1H), 1.60-1.70 (m, 4H); ¹³C NMR (CDCl₃, 300 MHz) δ 141.5, 132.6, 130.2, 127.4, 127.3, 124.3, 62.4, 35.7, 32.2, 26.0; IR (neat, cm⁻¹) 3332,

3064, 2936, 2862, 1566, 1470, 1439, 1059, 1022, 750, 658; GC/MS (*m/z*) 230, 128, 184, 182, 171, 169, 149, 131, 91; HRMS calcd for C₁₀H₁₃BrO: 228.014976, found 228.01486.

4-(*o*-bromophenyl)-butyric acid (47).⁴⁶ To a solution of chromium trioxide (6.46 g, 64.6 mmol) in 1.5 M sulfuric acid (103 mL) at 0 °C was added **38** (3.76 g, 16.4 mmol) in acetone (200 mL) with stirring over 4 h. The reaction mixture was warmed to room temperature and stirred until all starting material had been consumed (1.5h) as judged by TLC analysis. The mixture was taken up in ether (200 mL), washed with brine (100 mL), and concentrated. The resulting oily solid was taken up in ether (100 mL) and extracted with 2M NaOH (3 x 50 mL). The aqueous layer was acidified to pH 3 with 2 M sulfuric acid and extracted with ether (3 x 75 mL). The ether extracts were combined, dried over anhydrous magnesium sulfate, filtered through a pad of florisil, and concentrated to give a white solid (2.62 g, 66%), mp=75.4-78.5 °C (lit=88-89 °C). ¹H NMR analysis showed slight impurities. The product was used without further purification. ¹H NMR (CDCl₃, 300 MHz) δ 1.98 (p, 2H, *J*= 7.5 Hz), 2.43 (t, 2H, *J*= 7.4 Hz), 2.80 (t, 2H, *J*= 7.5 Hz), 7.00-7.09 (m, 1H), 7.20-7.25 (m, 2H), 7.52 (d, 1H, *J*= 7.8 Hz); IR (neat, cm⁻¹) 3250-2500 (br), 1709, 1472, 1404, 1346, 1294, 1266, 1214, 1026, 902, 757.

3-(*o*-bromophenyl)-propanal (48).⁴⁵ A Schlenk flask was charged with 2-bromiodobenzene (3.85 mL, 30 mmol), allyl alcohol (3.06 mL, 45 mmol), sodium bicarbonate (6.3 g, 75 mmol), tetra-*n*-butyl ammonium chloride (8.34 g, 30 mmol), palladium acetate (135 mg, 0.6 mmol, 2 mol% Pd) and DMF (30 mL). The flask was purged with argon for 1 min, then heated to 40 °C with stirring until all starting material had been consumed (18.5h) as judged by GC analysis. The mixture was cooled to room temperature, taken up in ether (100 mL), filtered, and concentrated. The product was purified further by flash chromatography on silica gel using 5/1 hexane/ethyl acetate as the elutant to give a colorless oil (5.19 g, 81%). ¹H NMR analysis showed slight impurities. The product was used without further purification. ¹H NMR (CDCl₃, 300 MHz) δ 2.78-2.83 (m, 2H), 3.05-3.10 (m, 2H), 7.06-7.11 (m, 1H), 7.23-7.26 (m, 2H), 7.54 (d, 1H, *J*= 7.8 Hz), 9.84 (s, 1H); IR (neat, cm⁻¹) 3057, 3013, 2934, 2823, 2723, 1723, 1471, 1440, 1022, 751.

General procedure for mesylation of alcohols. To a solution of the appropriate alcohol (46.8 mmol) in pyridine (50 mL) at 0 °C was added via syringe methanesulfonyl chloride (65.5 mmol). The resulting solution was then placed in a refrigerator at 0 °C until all starting material had been consumed as judged by GC analysis. The reaction was poured into ice (100 g) and the organic layer was washed with saturated cupric sulfate (3 X 150 mL), water (1 X 150 mL), and saturated sodium chloride (1 X 150 mL). The organic layer was dried (MgSO₄), filtered, and concentrated. The crude product was purified further by flash chromatography on silica gel

***o*-Bromophenethylmethanesulfonate (39).** The general procedure (46.8 mmol scale) afforded 11.4 g (88%) of a colorless oil. ¹H NMR (CDCl₃, 300 MHz) δ 7.52 (d, 1H, *J*= 7.9 Hz), 7.25-7.22 (m, 7H), 7.13-7.08 (m, 1H), 4.40 (dd, 2H, *J*= 7.0 Hz, 6.7 Hz), 3.17 (dd, 2H, *J*= 7.1 Hz, 6.6 Hz), 2.84 (s, 3H); ¹³C NMR (CDCl₃, 300 MHz) δ 135.4, 132.8, 131.4, 128.7, 127.5, 124.2, 68.3, 37.0, 35.6; IR (neat, cm⁻¹) 3026, 2932, 1473, 1442, 1355, 1174, 1023, 958, 905, 804, 754; GC/MS (*m/z*) 280, 278, 184, 182, 171, 169, 103, 90, 89, 79, 77; HRMS calcd for C₉H₁₁BrO₃S: 277.961227, found 277.96136.

3-(*o*-bromophenyl)-propylmethanesulfonate (40). The general procedure (20 mmol scale, chromatography omitted) afforded 5.329 g (91%) of a pale yellow oil. ^1H NMR (CDCl_3 , 300 MHz) δ 7.52 (d, 1H, $J = 7.4$ Hz), 7.22-7.24 (m, 2H), 7.06-7.10 (m, 1H), 4.25 (t, 2H, $J = 6.2$ Hz), 3.00 (s, 3H), 2.86 (m, 2H), 2.05-2.13 (m, 2H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 139.3, 132.5, 130.2, 126.8, 127.3, 123.9, 68.9, 36.8, 31.6, 28.6; IR (neat, cm^{-1}) 3055, 3026, 2939, 1567, 1472, 1439, 1353, 1175, 1022, 1001, 974, 928, 838, 813, 754; GC/MS (m/z) 294, 292, 198, 196, 171, 169, 117; HRMS calcd for $\text{C}_{10}\text{H}_{13}\text{BrO}_3\text{S}$: 291.976877, found 291.97730.

4-(*o*-Bromophenyl)butylmethanesulfonate (41). The general procedure (5 mmol scale) afforded 1.45 g (91%) of a colorless oil. ^1H NMR (CDCl_3 , 300 MHz) δ 7.51 (d, 1H, $J = 8.1$ Hz), 7.24-7.17 (m, 2H), 7.07-7.02 (m, 1H), 4.24 (dd, 2H, $J = 6.4, 5.7$ Hz), 2.98 (s, 3H), 2.76 (dd, 2H, $J = 7.4$ Hz, 7.3 Hz), 1.84-1.70 (m, 4H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 140.6, 132.5, 130.1, 127.6, 127.3, 124.0, 69.7, 37.0, 35.1, 28.4, 25.5; IR (neat, cm^{-1}) 3055, 3026, 2940, 2865, 1566, 1471, 1440, 1356, 1174, 1070, 1037, 1021, 932, 754, 657; GC/MS (m/z) 308, 306, 227, 184, 182, 171, 169, 131; HRMS calcd for $\text{C}_{11}\text{H}_{15}\text{BrO}_3\text{S}$: 305.992527, found 305.99270.

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