Supplementary Information

A Base-Catalyzed Approach for the anti-Markovnikov Hydration of Styrene Derivatives

Spencer P. Pajk†, Zisong Qi†, Stephen J. Sujansky and Jeffrey S. Bandar*

Department of Chemistry, Colorado State University

Fort Collins, Colorado 80523, United States

Email: jeff.bandar@colostate.edu

Table of Contents

I. General Information

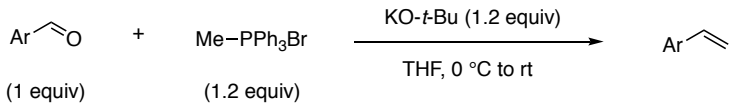
General Reagent Information: 1-*tert*-Butyl-4,4,4-tris(dimethylamino)-2,2-bis[tris(dimethylamino)-phosphoranylidenamino]-2λ^5,4λ^5-catenadi(phosphazene) (P_4-*t*-Bu, as a 0.8 M solution in hexanes) was purchased from Millipore Sigma (Product #79421) and stored in the freezer of a nitrogen-filled glovebox. Approximately 2 mL of the P_4-*t*-Bu solution was removed from the freezer on a weekly basis and stored at room temperature (rt) in the nitrogen-filled glovebox for routine use. Potassium *tert*-butoxide (KO-*t*-Bu) was purchased from Acros Organics (Product #27317) and stored in a nitrogen-filled glovebox. 1,4,7,10,13,16-Hexaoxacyclooctadecane (18-crown-6) was purchased from Chem-Impex (Catalog #03901) and stored in a nitrogen-filled glovebox. 1-Cyclopropylethanol was purchased from TCI (Catalog #C0984) and used as purchased. Borane tetrahydrofuran complex solution (catalog #176192), 9-borabicyclo[3.3.1]nonane solution (catalog #151076) and anhydrous 1,2-dimethoxyethane (catalog #259527) were purchased from Millipore Sigma and used as received. Tetrahydrofuran, dichloromethane, and toluene were deoxygenated and dried by passage over packed columns of neutral alumina and copper (II) oxide under positive pressure of nitrogen. All other solvents and reagents were purchased from Millipore Sigma, Combi-Blocks, TCI, Acros Organics, Matrix, or Alfa-Aesar and used as received unless otherwise noted. Flash Chromatography was performed on 40-63 μm silica gel (SiliaFlash® F60 from Silicycle).

General Analytical Information: All reported new compounds were characterized by ^{1}H, ^{13}C and ^{19}F NMR spectroscopy, FTIR spectroscopy and mass spectrometry. Melting point analysis was conducted if the compound was solid. ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were obtained on a Bruker Advanced NEO or Varian Inova 400 spectrometer. ^{1}H NMR data is reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, td = triplet of doublets, dq, doublet of quartets, m = multiplet), coupling constant (Hz), and integration.^{13}C NMR data is reported as follows: chemical shift (δ ppm), multiplicity (if applicable, q = quartet, d = doublet, dd = doublet of doublets). All ^{1}H NMR signals are reported as chemical shifts (δ ppm) relative to residual $CHCl_3$, at 7.26 ppm. All ^{13}C NMR signals are reported as chemical shifts (δ ppm) relative to $CDCl_3$ at 77.23 ppm. α,α,α-Trifluorotoluene (δ -62.61 ppm) internal standard was added to all ^{19}F NMR samples. High resolution mass spectra (HRMS) were recorded on an Agilent 6224 TOF LC-MS (ESI) provided by Colorado State University Central Instrumentation Facility. GC-MS data was recorded on an Agilent 7890B GC/5977A MSD system. Low resolution mass spectra (LRMS) were recorded on an Agilent 6130 Quadrupole LC-MS. Elemental analysis was performed by Atlantic Microlab, Inc., Norcross, GA. IR spectra were recorded using a Thermo Scientific Nicolet iS-50 FTIR Spectrometer and reported as frequency of absorption (cm^{-1}). Melting point analyses were conducted using a Mel-Temp capillary melting point apparatus. Thin-layer chromatography analysis was performed on silica gel 60Å F_{254} plates (250 μm, SiliaPlate from Silicycle, #TLG-R10014B-323) and interpreted using UV light (254 nm), I_2 or $KMnO_4$ stain.

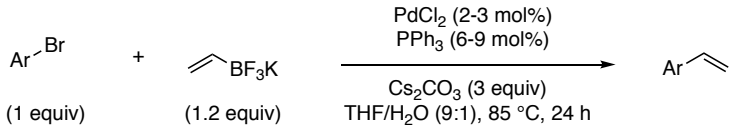
Note on nomenclature: The names provided for the structures below were obtained from ChemDraw Professional 16.0.

II. General Procedure for Preparation of Vinyl Arenes

Vinyl arene preparation: The majority of vinyl arenes were prepared according to known procedures and are known compounds: 2-chloro-3-vinylpyridine[1], 4-chloro-2-(trifluoromethyl)styrene[2], 3-chloro-2-vinylpyridine[3], 4-methyl-2-nitrostyrene[4], 3-nitrostyrene[5], 2,6-dichlorostyrene[6], 2-chloro-3-(trifluoromethyl)styrene[7], 4-vinylbenzophenone[8], 2-bromo-5-(trifluoromethyl)styrene[9], 1-bromo-2-vinylnaphthalene[10], 2-vinylquinoline[11], 3-bromo-4-vinylpyridine[12], and 2-bromo-6-vinylpyridine[13]. New vinyl arene substrates were prepared according to Methods A and B below and characterization is provided in Section VIII.



Method A: An oven-dried round bottom flask was charged with a magnetic stir bar and methyltriphenylphosphonium bromide (1.2 equiv). Anhydrous THF (20 mL per 1 g of aldehyde) was then added and the mixture was cooled to 0 °C in an ice bath with stirring. KO-*t*-Bu (1.2 equiv) was slowly added to the mixture resulting in a yellow-colored slurry. After the reaction mixture was stirred for 30 min at 0 °C, the aldehyde (1 equiv) was added dropwise into the mixture and the solution was then allowed to warm to rt for 4 h. At the completion of the reaction as indicated by TLC analysis, water (equal volume to THF used) was added to the reaction mixture and the resulting mixture was transferred to a separatory funnel. The mixture was extracted with EtOAc (3 x reaction volume), and the resulting organic solution was washed with brine (1 x reaction volume) and dried over Na_2SO_4. The solvent was removed *in vacuo* and the resulting residue was purified by silica gel chromatography using the given eluent conditions to provide the vinyl arene.



Method B: A flame-dried round bottom flask was charged with a magnetic stir bar, palladium(II) chloride (2-3 mol%), triphenylphosphine (6-9 mol%), aryl bromide (1 equiv), potassium vinyltrifluoroborate (1.2 equiv), and cesium carbonate (3 equiv) in a nitrogen-filled glovebox. The flask was removed from the glovebox, equipped with a reflux condenser with a rubber septum and evacuated and backfilled with nitrogen three times and left under positive pressure with a nitrogen balloon after the third cycle. A mixture of THF/H_2O (9/1) was then added via syringe. The reaction mixture was stirred for 24 h at 85 °C and then allowed to cool to rt. The reaction mixture was added to a separatory funnel, extracted with EtOAc (3 x reaction volume), and the organic solution was washed with brine (1 x reaction volume) and dried over anhydrous Na_2SO_4. After evaporation of the solvent *in vacuo*, the resulting residue was purified by silica gel chromatography using the given eluent conditions to provide the vinyl arene.

III. General Procedure for Screening of Alcohol

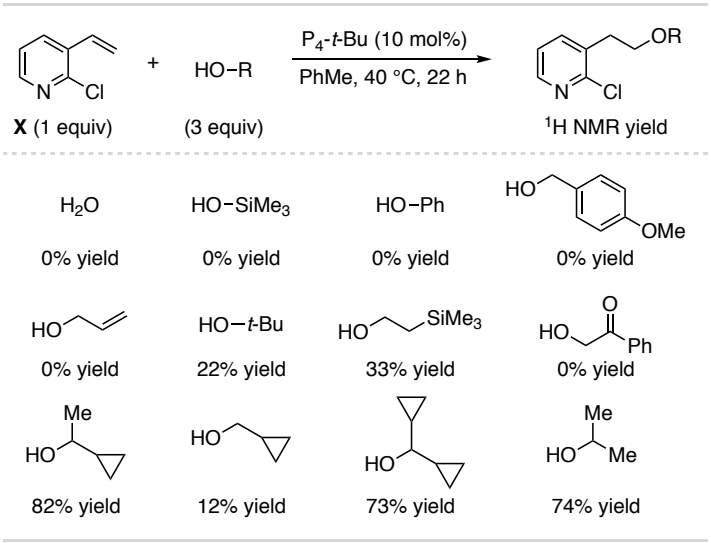
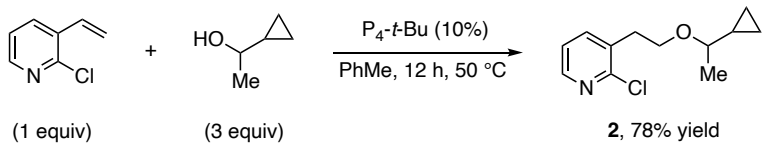


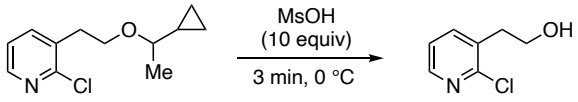
Table S1. Alcohol addition yields for various potential protected water equivalents.

General procedure for screening of alcohol: In a nitrogen-filled glovebox, 2-chloro-3-vinylpyridine (27.9 mg, 0.2 mmol, 1.0 equiv), alcohol (0.6 mmol, 3.0 equiv) and toluene (0.2 mL) were added to an oven-dried 1-dram reaction vial (Thermo Scientific B7990-2) containing a magnetic stir bar. A commercial 0.8 M solution of P_4-*t*-Bu in hexanes (25 µL, 0.02 mmol, 0.1 equiv) was then added to the reaction solution. The reaction vial was capped (Thermo Scientific C4015-1A with 10/50 septa), removed from the glovebox, and placed in a preheated aluminum reaction heating block (Chemglass CG-1991-04) with stirring at 40 °C for 22 h. The reaction mixture was then allowed to cool to rt before dibenzyl ether (9.5 µL, 0.05 mmol) was added and an aliquot (approximately 50 µL) of the reaction solution was directly transferred to an NMR tube with $CDCl_3$ (0.6 mL). The reaction conversion was determined by ^{1}H NMR spectroscopy by comparison of the product integration to the dibenzyl ether internal standard. The results are tabulated above in Table S1.



Independent preparation of ether 2: In a nitrogen filled glovebox, 2-chloro-3-vinylpyridine (139.6 mg, 1 mmol, 1 equiv), 1-cyclopropylethanol (293 µL, 3 mmol, 3 equiv), P_4-*t*-Bu (125 µL of a 0.8 M solution in hexanes, 0.1 mmol, 0.1 equiv) and PhMe (0.50 mL) were added to an oven-dried 2-dram reaction vial (Thermo Scientific B7999-3) with a magnetic stir bar. The vial was capped (Thermo Scientific B7995-15 with 10/90 septa), removed from the glovebox and placed in a preheated oil bath at 50 °C. The reaction mixture was stirred for 12 h. Direct subjection of the crude reaction material to silica gel flash chromatography (5% ethyl acetate/hexanes to 20% ethyl acetate/hexanes) yielded **2** as a colorless oil (176.1 mg, 0.78 mmol, 78% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 4.7 Hz, 1H), 7.63 (d, *J* = 7.5 Hz, 1H), 7.16 (dd, *J* = 7.5, 4.7 Hz, 1H),

3.86 – 3.76 (m, 1H), 3.71 – 3.61 (m, 1H), 2.97 (t, J = 6.6 Hz, 2H), 2.73 (p, J = 6.4 Hz, 1H), 1.17 (dd, J = 6.3, 1.2 Hz, 3H), 0.84 – 0.70 (m, 1H), 0.51 (m, 1H), 0.40 (m, 1H), 0.27 (m, 1H), 0.02 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.5, 147.6, 139.9, 133.9, 122.6, 80.3, 66.6, 34.1, 20.4, 16.6, 4.6, 1.1. **HRMS** (DART) $[M+H]^+$ calcd. for $[C_{12}H_{17}NOCl]^+$, 226.0993 found, 226.1017. **IR** (neat, cm^{-1}) 3078.2, 2970.4, 2859.8, 1562.7, 1407.7, 1102.3, 1078.7, 795.1, 747.8.

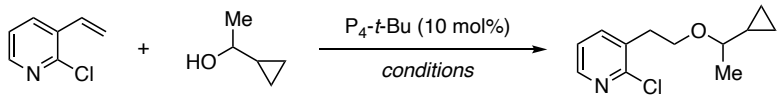


2 (1M in PhMe) **3**, 87% yield

Independent procedure for the deprotection of ether 2: To an oven-dried 2-dram vial (Thermo Scientific B7999-3) containing a magnetic stir bar was added 2-chloro-3-(2-(1-cyclopropylethoxy)ethyl)pyridine (**2**, 225.6 mg, 1 mmol, 1 equiv) and PhMe (1 mL). The vial was capped (Thermo Scientific B7995-15 with 10/90 septa), and the reaction solution was cooled to 0 °C in an ice bath and methanesulfonic acid (0.65 mL, 10 mmol, 10 equiv) was then added dropwise. The reaction mixture was stirred at 0 °C for 3 min. The biphasic mixture was then neutralized with saturated aqueous Na_2CO_3 (2 mL) and extracted with ethyl acetate (3 x 2 mL). The combined organic solution was washed with brine (5 mL), dried over Na_2SO_4, concentrated *in vacuo*, and purified via silica gel column chromatography (40% ethyl acetate/hexanes) to give 2-(2-chloropyridin-3-yl)ethan-1-ol (**3**, 138 mg, 0.87 mmol, 87% yield). See Section VIII for characterization data.

IV. Optimization and General Procedure for Hydration of Vinyl Arenes using P_4-*t*-Bu

Initial reaction condition optimization discussion: The initial conditions for P_4-*t*-Bu-catalyzed hydration and water surrogate screening were chosen based on our previous work in which PhMe was observed to provide the highest equilibrium ether yield.[14,15] Consistent with our prior work, Table S2 below shows the addition of 1-cyclopropylethanol (**4**) to be most favored in PhMe at 2 M concentration of the alkene. The "**General procedure for screening of alcohol**" from Section III above was followed to prepare Table S2. Other solvents are also effective but do not provide as high of equilibrium yields. Thus, PhMe was used in the General Procedure for the superbase conditions and for the comparison of **4** to other potential water surrogates shown in Table S1.



1 (1 equiv) **4** (3 equiv) **2**, ^{1}H NMR addition yield

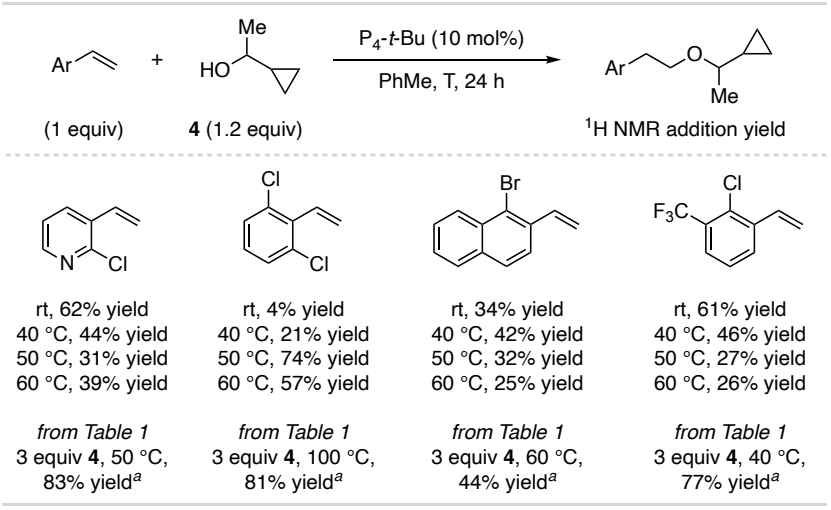
Solvent	Concentration of 1	Temperature (°C)	^{1}H NMR yield (%)
PhMe	1 M	50	39
PhMe	2 M	50	71
PhMe	2 M	rt	25
PhMe	2 M	40	82

PhMe	2 M	60	62
PhMe	2 M	70	38
DME	2 M	50	55
Dioxane	2 M	50	49
THF	2 M	50	49
DMSO	2 M	50	33
n-Bu_2O	2 M	50	59
DMF	2 M	50	35
MeCN	2 M	50	44

Table S2: Initial conditions examined for P_4-*t*-Bu-catalyzed addition of **4** to **1**.

Alcohol stoichiometry discussion: Excess alcohol (3 equiv of **4**) is typically used to provide high equilibrium addition yields. We have previously shown superbase-catalyzed alcohol addition to aryl alkenes can be efficient using 1.2 equiv of alcohol at lower reaction temperatures.[15] For this method using alcohol **4**, we typically obtained higher ether yields using 3 equiv of **4** at higher reaction temperatures. This is demonstrated in Table S3 with representative examples. However, this information does indicate that synthetically useful yields can be obtained using near stoichiometric amounts of **4** and styrene substrate.

Alcohol stoichiometry variation general procedure: In a nitrogen-filled glovebox, vinyl arene (0.1 mmol, 1.0 equiv), 1-cyclopropylethanol (11.7 µL, 0.12 mmol, 1.2 equiv) and PhMe (0.05 mL) were added to an oven-dried 1-dram reaction vial (Thermo Scientific B7990-2). A commercial 0.8 M solution of P_4-*t*-Bu in hexanes (12.5 µL, 0.01 mmol, 0.1 equiv) was then added to the reaction solution. The reaction vial was capped (Thermo Scientific C4015-1A with 10/50 septa), removed from the glovebox, and placed into a preheated aluminum reaction heating block (Chemglass CG-1991-04) and stirred for 24 h. The reaction solution was then allowed to cool to rt before dibenzyl ether (19.0 µL, 0.1 mmol, 1.0 equiv) was added and an aliquot (approximately 50 µL) of the reaction solution was directly transferred to an NMR tube with $CDCl_3$ (0.6 mL). The reaction yield was determined by ^{1}H NMR spectroscopy by comparison of the product integration to the dibenzyl ether internal standard. The results are tabulated in Table S3 below.

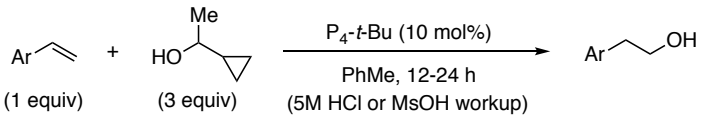


rt, 62% yield 40 °C, 44% yield 50 °C, 31% yield 60 °C, 39% yield	rt, 4% yield 40 °C, 21% yield 50 °C, 74% yield 60 °C, 57% yield	rt, 34% yield 40 °C, 42% yield 50 °C, 32% yield 60 °C, 25% yield	rt, 61% yield 40 °C, 46% yield 50 °C, 27% yield 60 °C, 26% yield
from Table 1 3 equiv **4**, 50 °C, 83% yield[a]	*from Table 1* 3 equiv **4**, 100 °C, 81% yield[a]	*from Table 1* 3 equiv **4**, 60 °C, 44% yield[a]	*from Table 1* 3 equiv **4**, 40 °C, 77% yield[a]

Table S3: Yield comparison using 1.2 equiv of **4** at various temperatures to using 3 equiv of **4** at the optimized temperature in Table 1. [a] yield of isolated alcohol product from Table 1.

Description of condition optimization on small scale for each styrene: We found that for each substrate examined, the optimal alcohol addition yield was temperature and concentration dependent as the reaction is under equilibrium control. Thus, for each substrate, we first obtained ^{1}H NMR yields of the reaction at a variety of temperatures (5 to 10 °C intervals) at 1 M in toluene. The reaction was then run at the highest yielding temperature at concentrations of 0.5 M and 2 M. Once optimal conditions were determined, the reaction was repeated on a 1.0 mmol scale and an isolated yield was obtained.

General procedure for condition optimization on small scale: In a nitrogen-filled glovebox, vinyl arene (0.15 mmol, 1.0 equiv), 1-cyclopropylethanol (44 μL, 0.45 mmol, 3.0 equiv) and toluene (0.15 mL) were added to an oven-dried 1-dram reaction vial (Thermo Scientific B7990-2) containing a magnetic stir bar. A commercial 0.8 M solution of P_4-*t*-Bu in hexanes (18.8 μL, 0.015 mmol, 0.1 equiv) was then added to the reaction solution. The reaction vial was capped (Thermo Scientific C4015-1A with 10/50 septa), removed from the glovebox, and placed in a preheated aluminum reaction heating block (Chemglass CG-1991-04) for 12 h. The reaction mixture was allowed to cool to rt before dibenzyl ether (14.3 μL, 0.075 mmol, 0.5 equiv) was added and an aliquot (approximately 50 μL) of the reaction solution was directly transferred to an NMR tube with $CDCl_3$ (0.6 mL). The alcohol addition yield was determined by ^{1}H NMR spectroscopy by comparison of the addition product integration to the dibenzyl ether internal standard.

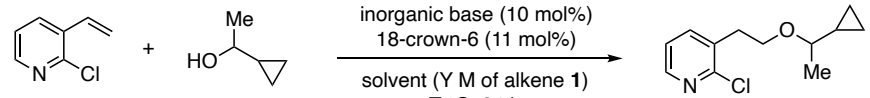


General procedure C for isolated hydration yields: In a nitrogen-filled glovebox, vinyl arene (1.0 mmol, 1.0 equiv), 1-cyclopropylethanol (293 μL, 3.0 mmol, 3.0 equiv) and toluene (amount indicated for each substrate) were added to a flame-dried 25 mL round bottom flask containing a magnetic stir bar. A commercial 0.8 M solution of P_4-*t*-Bu in hexanes (125 μL, 0.1 mmol, 0.1 equiv) was then added to the reaction solution. The reaction flask was sealed with a rubber septum, removed from the glovebox, and placed in an oil bath preheated to the indicated temperature. After 12-24 h (time indicated for each substrate), the flask was removed from the oil bath and inserted into a 0 °C ice bath. Methanesulfonic acid (667 μL, 10.3 mmol, 10.3 equiv) was then added dropwise and the resulting solution was stirred for the indicated time. For certain heterocyclic substrates, 5M aqueous HCl (4.0 mL, 20 mmol, 20 equiv) was used in place of methanesulfonic acid, with stirring at rt for 1 h. For both deprotection methods, the biphasic mixture was then neutralized with saturated aqueous Na_2CO_3 (amount equal to the total reaction volume) and extracted with ethyl acetate (3 x reaction volume). The combined organic layer was washed with brine (1 x reaction volume), concentrated *in vacuo* and the product was purified *via* silica gel column chromatography using the given eluent conditions.

V. Optimization and General Procedure for Inorganic Base-Catalyzed Hydration of Vinyl Arenes

Inorganic base discussion: In our prior work, we investigated many inorganic bases, additives and solvents for the catalytic addition of *n*-butanol to 4-(trifluoromethyl)styrene as a model reaction.[14,15] This led to the discovery of KO-*t*-Bu with 18-crown-6 additive as an effective inorganic base system for styrene hydroetherification in 1,2-dimethoxyethane (DME), with lower yields obtained in nonpolar aromatic solvents. Shown below in Table S4, we examined similar inorganic catalyst mixtures in a variety of solvents and conditions for the addition of 1-cyclopropylethanol (**4**) to 2-chloro-3-vinylpyridine (**1**). Moderate addition yields (50-60%) were obtained in a variety of solvents, although none outperformed the previously optimized conditions or the superbase conditions. In general, the trends in Table S4 are consistent with our prior studies, and more information regarding inorganic bases, additives, solvents and concentration effects can be found in our prior reports.[14,15] Therefore, KO-*t*-Bu with 18-crown-6 in DME was used as the standard inorganic catalyst system, with additional temperature optimization conducted for each substrate.

General procedure for optimization: In a nitrogen filled glovebox, inorganic base (0.1 equiv, 0.01 mmol), 18-crown-6 (2.9 mg, 0.011 mmol, 0.11 equiv), solvent (amount indicated as molarity of alkene in solvent), 1-cyclopropylethanol (0.3 to 0.5 mmol, 3.0 to 5.0 equiv) and 2-chloro-3-vinylpyridine (14.0 mg, 0.1 mmol, 1.0 equiv) were added to an oven-dried 1-dram reaction vial (Thermo Scientific B7990-2) containing a magnetic stir bar. The reaction vial was capped (Thermo Scientific C4015-1A with 10/50 septa) and placed in a preheated aluminum reaction heating block (Chemglass CG-1991-04) and stirred for 24 h. The reaction solution was allowed to cool to rt before dibenzyl ether (19.0 μL, 0.1 mmol, 1.0 equiv) was added and an aliquot (approximately 50 μL) of the reaction solution was directly transferred to an NMR tube with $CDCl_3$ (0.6 mL). The alcohol addition yield was determined by ^1H NMR spectroscopy by comparison of the product integration to the dibenzyl ether internal standard. The results are tabulated in Table S4 below.



1 (1 equiv) **4** (3 equiv) **2**, ^1H NMR yield

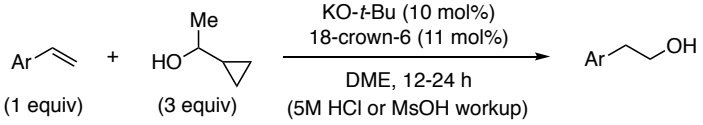
Entry	Base	Solvent (Y M)	Temp (°C)	4 (X equiv)	Yield %
1	KO-*t*-Bu	DME (2 M)	50 °C	3	60
2	KO-*t*-Bu, no 18-crown-6	DME (2 M)	50 °C	3	0
3	KOH	DME (2 M)	50 °C	3	51
4	$CsOH•H_2O$	DME (2 M)	50 °C	3	47
5	CsF+LiO-*t*-Bu	DME (2 M)	50 °C	3	54
6	KH	DME (2 M)	50 °C	3	0
7	KO-*t*-Bu	MeCN (2 M)	50 °C	3	56
8	KO-*t*-Bu	PhCN (2 M)	50 °C	3	59
9	KO-*t*-Bu	THF (2 M)	50 °C	3	53
10	KO-*t*-Bu	PhMe (2 M)	50 °C	3	54

11	KO-*t*-Bu	DME (0.5 M)	50 °C	3	44
12	KO-*t*-Bu	DME (1 M)	50 °C	3	19
13	KO-*t*-Bu	DME (1.5 M)	50 °C	3	56
14	KO-*t*-Bu	DME (2 M)	50 °C	4	62
15	KO-*t*-Bu	DME (2 M)	50 °C	5	67
16	KO-*t*-Bu	DME (2 M)	40 °C	3	56
17	KO-*t*-Bu	DME (2 M)	40 °C	4	63
18	KO-*t*-Bu	DME (2 M)	40 °C	5	70

Table S4. Condition and solvent effects for inorganic base-catalyzed addition of 1-cyclopropylethanol (**4**) to 2-chloro-3-vinylpyridine (**1**).

General procedure for inorganic condition optimization on small scale for each styrene: We found that for each substrate examined, the optimal addition yield was obtained at a specific temperature since the reaction is under equilibrium control. Thus, for each substrate, we first obtained ^{1}H NMR yields of the reaction at a variety of temperatures (5 °C intervals) at 2M concentration in 1,2-dimethoxyethane (DME). Once an optimal temperature was determined, the reaction was repeated on a 1.0 mmol scale and an isolated yield was obtained.

In the open air, KO-*t*-Bu (2.2 mg, 0.02 mmol, 0.1 equiv), 18-crown-6 (5.8 mg, 0.022 mmol, 0.11 equiv), 1,2-dimethoxyethane (0.1 mL), 1-cyclopropylethanol (58.7 µL ,0.6 mmol, 3.0 equiv) and vinyl arene (0.2 mmol, 1.0 equiv) were added to an oven-dried 1-dram reaction vial (Thermo Scientific B7990-2) containing a magnetic stir bar. The reaction vial was capped (Thermo Scientific C4015-1A with 10/50 septa) and placed in a preheated aluminum reaction heating block (Chemglass CG-1991-04) for 16 h. The reaction solution was allowed to cool to rt before dibenzyl ether (9.5 µL, 0.05 mmol, 0.25 equiv) was added and an aliquot (approximately 50 µL) of the reaction solution was directly transferred to an NMR tube with $CDCl_3$ (0.6 mL). The alcohol addition yield was determined by ^{1}H NMR spectroscopy by comparison of the product integration to the dibenzyl ether internal standard.



General procedure D for isolated yields: In the open air, KO-*t*-Bu (11.2 mg, 0.10 mmol, 0.1 equiv), 18-crown-6 (29.1 mg, 0.11 mmol, 0.11 equiv), 1,2-dimethoxyethane (0.5 mL), 1-cyclopropylethanol (293 µL, 3.0 mmol, 3.0 equiv) and vinyl arene (1.0 mmol, 1.0 equiv) were added in successive order to a flame-dried 25 mL round bottom flask containing a magnetic stir bar. The flask was capped with a rubber septum, a nitrogen-filled balloon was inserted and the flask was placed in a preheated oil bath at the indicated temperature with stirring. After the indicated time, the flask was removed from the oil bath and inserted into a 0 °C ice bath. To the reaction solution was then added methanesulfonic acid (667 µL, 10.3 mmol, 10.3 equiv) dropwise and the resulting mixture was stirred for the indicated time. For certain heterocyclic substrates, 5M aqueous HCl (4.0 mL, 20 mmol, 20 equiv) was used in place of methanesulfonic acid, with stirring at rt for 1 h. For both deprotection methods, the biphasic mixture was then neutralized with saturated aqueous sodium carbonate (amount equal to the total reaction volume) and extracted with

ethyl acetate (3 x reaction volume). The combined organic layer was washed with brine (1 x reaction volume), concentrated *in vacuo* and the product was purified *via* silica gel column chromatography using the given eluent conditions.

VI. Alcohol Addition Yield Comparisons Using Inorganic Base and Superbase Conditions

Purpose and discussion: Base-catalyzed addition yields of 1-cyclopropylethanol to vinyl arenes were compared using the organic superbase P_4-*t*-Bu and the inorganic base conditions KO-*t*-Bu with 18-crown-6. The reaction temperatures are not always the same between the superbase and inorganic conditions; semi-optimized temperatures were obtained from small scale optimizations described in the general procedures above (generally, optimal temperatures for the two conditions were within 10 °C of each other). These comparisons are summarized in Table S5 and show that P_4-*t*-Bu is a more general catalyst, typically giving higher addition yields, although the inorganic system also provides synthetically useful yields for many substrates. This information is provided to help users select proper bases for their intended applications or substrate of interest.

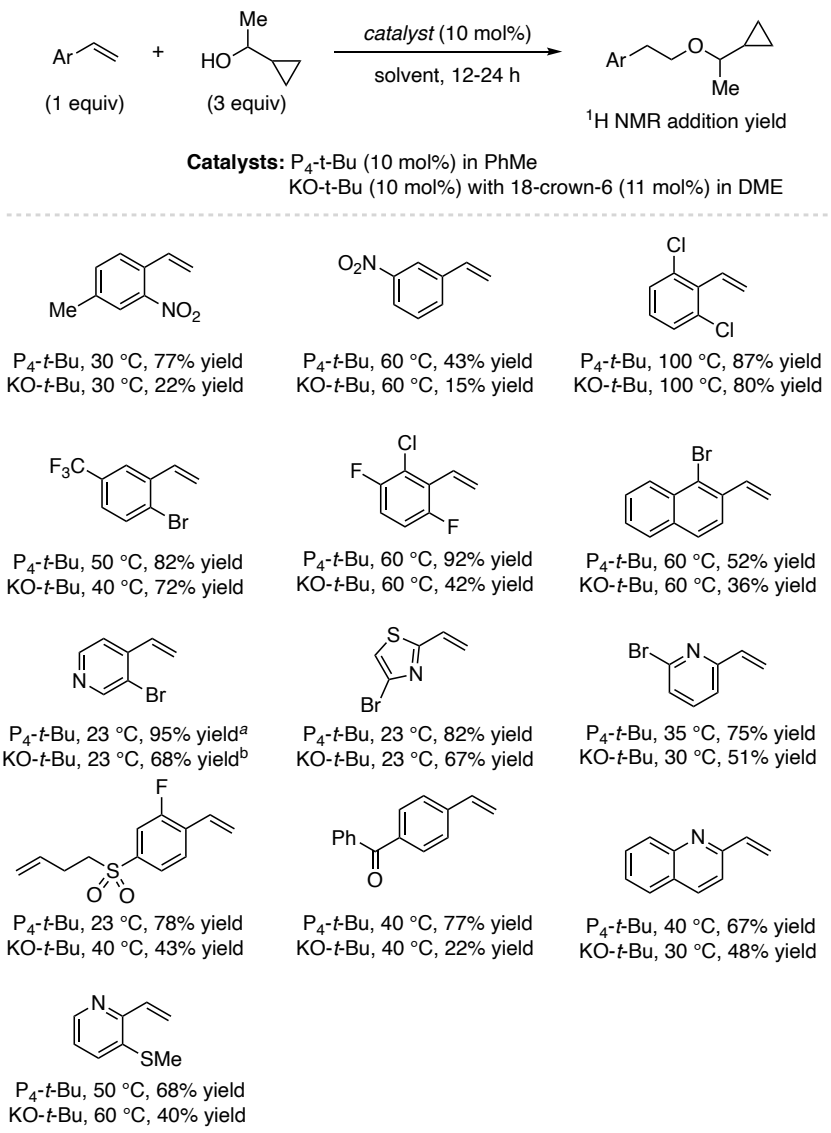


Table S5. Comparison of ^{1}H NMR alcohol addition yields using superbase and inorganic base conditions. [a] 6 h reaction time; [b] 10 min reaction time; mass balance decreased significantly over longer times.

General procedure for P$_4$-*t*-Bu as catalyst: In a nitrogen-filled glovebox, vinyl arene (0.2 mmol, 1.0 equiv), 1-cyclopropylethanol (58.7 µL, 0.6 mmol, 3.0 equiv) and PhMe (0.2 mL) were added to an oven-dried 1-dram reaction vial (Thermo Scientific B7990-2). A commercial 0.8 M solution of P$_4$-*t*-Bu in hexanes (25 µL, 0.02 mmol, 0.1 equiv) was then added to the reaction solution. The reaction vial was capped (Thermo Scientific C4015-1A with 10/50 septa), removed from the glovebox, and placed into a preheated aluminum reaction heating block (Chemglass CG-1991-04) and stirred for 12-24 h (time as indicated in product characterization section for products from Table 1 and Scheme 2). The reaction solution was then allowed to cool to rt before dibenzyl ether (9.5 µL, 0.05 mmol, 0.25 equiv) was added and an aliquot (approximately 50 µL) of the reaction solution was directly transferred to an NMR tube with $CDCl_3$ (0.6 mL). The reaction yield was

determined by ^{1}H NMR spectroscopy by comparison of the product integration to the dibenzyl ether internal standard.

General procedure for KO-*t*-Bu/18-crown-6 as catalyst: On the bench top, KO-*t*-Bu (0.02 mmol, 0.1 equiv), 18-crown-6 (0.022 mmol, 0.11 equiv), 1,2-dimethoxyethane (0.2 mL), 1-cyclopropylethanol (58.7 μL, 0.6 mmol, 3.0 equiv) and vinyl arene (0.2 mmol, 1.0 equiv) were added to an oven-dried 1-dram reaction vial (Thermo Scientific B7990-2). The reaction vial was capped (Thermo Scientific C4015-1A with 10/50 septa), and placed in a preheated aluminum reaction heating block (Chemglass CG-1991-04) and stirred for 12-24 h (time as indicated in product characterization section for products from Table 1 and Scheme 2). The reaction solution was allowed to cool to rt before dibenzyl ether (9.5 μL, 0.05 mmol, 0.25 equiv) was added and an aliquot (approximately 50 μL) of the reaction solution was directly transferred to an NMR tube with $CDCl_3$ (0.6 mL). The reaction yield was determined by ^{1}H NMR spectroscopy by comparison of the product integration to the dibenzyl ether internal standard. **Note:** The general procedure used for inorganic conditions does not require the use of a strict inert atmosphere and thus these reactions were setup open to air. As a control, three substrates from Table S5 (4-methyl-2-nitrostyrene, 1-bromo-2-vinylnaphthalene and 2,6-dichlorostyrene; 4-(trifluoromethyl)styrene was also tested) were repeated using the general procedure above under a nitrogen atmosphere. These reactions led to near identical yields (± 2-3%) to those provided in Table S5.

VII. Discussion of Styrene Scope Limitations

Discussion: The base-catalyzed reversible addition of alcohols to styrenes provides the highest equilibrium yields for electron-deficient and heteroaryl derivatives.[14,15] To clarify the limitations of this protocol, Table S6 shows examples of mildly activated, unactivated and 1,1-disubstituted aryl-substituted alkenes varying the stoichiometry of alkene and 1-cyclopropylethanol.

Procedure: In a nitrogen-filled glovebox, the alkene (0.1 mmol, 1.0 equiv or 0.5 mmol, 5.0 equiv), 1-cyclopropylethanol (29.3 μL, 0.3 mmol, 3.0 equiv; 48.9 μL, 0.5 mmol, 5.0 equiv; 9.8 μL, 0.1 mmol, 1.0 equiv; 11.7 μL, 0.12 mmol, 1.2 equiv) and PhMe (0.05 mL) were added to an oven-dried 1-dram reaction vial (Thermo Scientific B7990-2). A commercial 0.8 M solution of P_4-*t*-Bu in hexanes (12.5 μL, 0.01 mmol, 0.1 equiv) was then added to the reaction solution. The reaction vial was capped (Thermo Scientific C4015-1A with 10/50 septa), removed from the glovebox, and placed into a preheated aluminum reaction heating block (Chemglass CG-1991-04) and stirred for 24 h. The reaction solution was then allowed to cool to rt before dibenzyl ether (19.0 μL, 0.1 mmol, 1.0 equiv) was added and an aliquot (approximately 50 μL) of the reaction solution was directly transferred to an NMR tube with $CDCl_3$ (0.6 mL). The reaction yield was determined by ^{1}H NMR spectroscopy by comparison of the product integration to the dibenzyl ether internal standard.

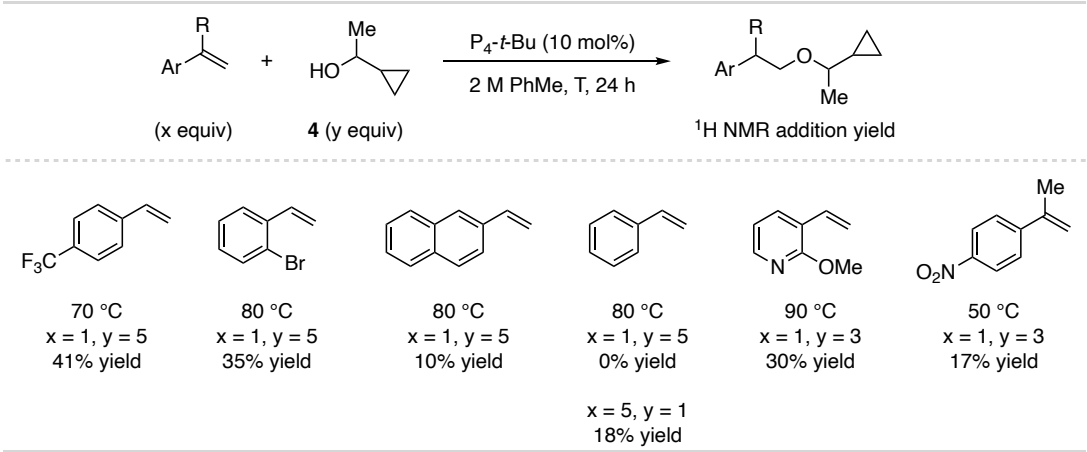
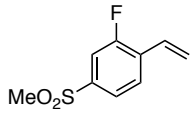


Table S6: Aryl alkene scope limitations, including electron-neutral to electron-rich aryl alkenes, and 1,1-disubstituted variants that provide low equilibrium ether yields.

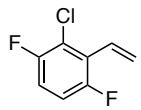
VIII. Synthesis and Characterization Data for Vinyl Arenes

2-Fluoro-4-(methylsulfonyl)styrene



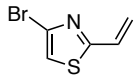
General Procedure B was followed with triphenylphosphine (94 mg, 0.36 mmol, 0.06 equiv), palladium(II) chloride (21 mg, 0.1 mmol, 0.02 equiv), cesium carbonate (5.87 g, 18 mmol, 3 equiv), potassium vinyltrifluoroborate, and 1-bromo-2-fluoro-4-(methylsulfonyl)benzene (1.52 g, 6.0 mmol, 1.0 equiv). Flash column chromatography (10% ethyl acetate/hexanes) yielded the title product as a yellow liquid (865 mg, 4.32 mmol, 72% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 – 7.55 (m, 3H), 6.90 (dd, *J* = 17.7, 11.3 Hz, 1H), 5.99 (dd, *J* = 17.7, 0.7 Hz, 1H), 5.59 (dd, *J* = 11.3, 0.8 Hz, 1H), 3.06 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.6 (d, J = 255.5 Hz), 140.7 (d, *J* = 6.9 Hz), 130.9 (d, *J* = 12.2 Hz), 128.2 (d, *J* = 3.8 Hz), 128.1 (d, *J* = 3.7 Hz), 123.1 (d, *J* = 3.8 Hz), 120.6 (d, *J* = 4.8 Hz), 115.3 (d, *J* = 25.7 Hz), 44.6. **^{19}F NMR** (376 MHz, CDCl3) δ -114.42. **HRMS** (DART) $[M+NH_4]^+$ calcd. for $[C_9H_{13}FNO_2S]^+$ 218.0646, found 218.0655. **IR** (neat, cm^{-1}) 3076.8, 3015.3, 2925.7, 1629.0, 1483.5, 1403.5, 1403.5, 1295.2, 1226.1, 1141.0, 991.3, 760.9, 529.4.

2-Chloro-3,6-difluorostyrene



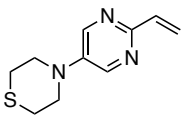
General Procedure A was followed with methyltriphenylphosphonium bromide (4.30 g, 12 mmol, 1.2 equiv), KO-*t*-Bu (1.35 g, 12 mmol, 1.2 equiv), and 2-chloro-3,6-difluorobenzaldehyde (1.76 g, 10 mmol, 1.0 equiv). Flash column chromatography with hexanes yielded the title product as a colorless liquid (1.20 g, 6.87 mmol, 69% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.06 – 6.90 (m, 2H), 6.79 (dd, *J* = 18.0, 12.0 Hz, 1H), 6.02 (dt, *J* = 18.0, 1.4 Hz, 1H), 5.71 (dt, *J* = 11.9, 1.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.1 (dd, *J* = 249.1, 1.9 Hz), 155.0 (dd, *J* = 244.5, 2.8 Hz), 127.1 (dd, *J* = 2.9, 1.5 Hz), 125.8 (d, *J* = 16.2 Hz), 123.5 (d, *J* = 11.8 Hz), 121.4 (dd, *J* = 19.4, 6.4 Hz), 115.0 (dd, *J* = 8.9, 2.3 Hz), 114.7 (dd, *J* = 8.9, 4.2 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.45 (d, *J* = 15.2 Hz), -118.02 (d, *J* = 15.2 Hz). **LRMS** $[M+H]^+$ calcd. for $[C_8H_6ClF_2]^+$ 175.0, found 175.0. **IR** (neat, cm^{-1}) 3100.3, 1851.7, 1473.0, 1383.6, 1231.9, 966.3, 933.6, 861.3, 808.1.

4-Bromo-2-vinylthiazole

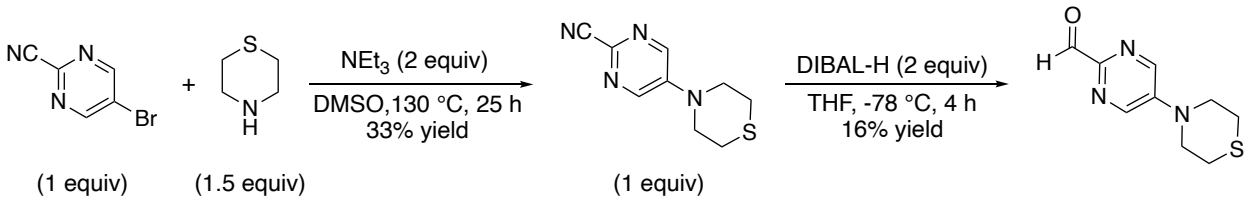


A slightly modified variant of General Procedure A was followed for this substrate. An oven-dried round bottom flask was charged with a magnetic stir bar and methyltriphenylphosphonium bromide (3.29 g, 9.6 mmol, 1.2 equiv), capped with a rubber septum, evacuated and backfilled with nitrogen three times and left under positive pressure with a nitrogen filled balloon. Anhydrous THF (30 mL) was added and the mixture was cooled to 0 °C in an ice bath with stirring. *n*-Butyllithium (5.50 mL of 1.6M solution in hexanes, 8.8 mmol, 1.1 equiv) was added dropwise with a nitrogen flushed syringe. Procedure A was then followed with 4-bromothiazole-2-carbaldehyde (1.54 g, 8.0 mmol, 1.0 equiv). Flash column chromatography (5% ethyl acetate/hexanes) yielded the title product as a yellow liquid (624 mg, 3.28 mmol, 41% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.13 (s, 1H), 6.86 (dd, *J* = 17.5, 10.9 Hz, 1H), 6.08 (d, *J* = 17.5 Hz, 1H), 5.58 (d, *J* = 10.9 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.9, 129.8, 125.9, 121.1, 116.4. **HRMS** (DART) $[M+H]^+$ calcd. for $[C_5H_5BrNS]^+$ 189.9321, found 189.9330. **IR** (neat, cm^{-1}) 3120.2, 1621.6, 1468.6, 1278.4, 1224.8, 1081.2, 974.5, 886.4, 832.3, 698.1.

4-(2-Vinylpyrimidin-5-yl)thiomorpholine



General Procedure A was followed with methyltriphenylphosphonium bromide (428.7 mg, 1.2 mmol, 1.2 equiv), KO-*t*-Bu (134.7mg, 1.2 mmol, 1.2 equiv), 5-thiomorpholinopyrimidine-2-carbaldehyde (209 mg, 1.0 mmol, 1.0 equiv, synthesis described below). Flash column chromatography (40% ethyl acetate/hexanes) yielded the title product as a clear liquid (100 mg, 0.48 mmol, 48% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 (s, 2H), 6.81 (dd, *J* = 17.4, 10.7 Hz, 1H), 6.39 (dd, *J* = 17.4, 1.7 Hz, 1H), 5.56 (dd, *J* = 10.7, 1.7 Hz, 1H), 3.76 – 3.47 (m, 4H), 2.88 – 2.35 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 144.9, 144.6, 142.3, 135.8, 120.8, 50.7, 26.4. **HRMS** (DART) $[M+H]^+$ calcd. for $[C_{10}H_{14}N_3S]^+$ 208.0903, found 208.0904. **IR** (neat, cm^{-1}) 2953.9, 2913.7, 1653.1, 1538.7, 1455.4, 1402.4, 1301.7, 1224.7, 1199.3, 997.0, 924.3, 817.2.

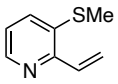


5-Thiomorpholinopyrimidine-2-carbaldehyde preparation: 5-bromopyrimidine-2-carbonitrile (4.60 g, 25 mmol, 1 equiv) was added to an oven-dried 100 mL round bottom flask containing a magnetic stirbar. The flask was sealed with a rubber septum and evacuated and backfilled with nitrogen three times and left under a positive pressure of nitrogen. DMSO (25 mL) was added *via* a nitrogen flushed syringe. Thiomorpholine (3.77 mL, 37.5 mmol, 1.5 equiv) and triethylamine (6.79 mL, 50 mmol, 2 equiv) were then added *via* nitrogen flushed syringes. The reaction flask was placed in a preheated oil bath at 130 °C and stirred for 25 h. The reaction mixture was cooled to room temperature and water (25 mL) was added. The resulting mixture was added to a separatory funnel, extracted with EtOAc (3 x reaction volume), and the organic solution was washed with brine (50 mL) and dried over Na_2SO_4. After evaporation of the solvent *in vacuo*, the resulting residue was purified by silica gel chromatography (10% ethyl acetate/1%

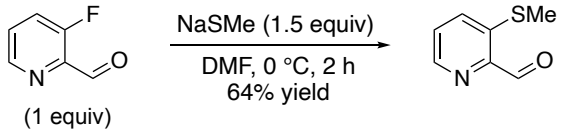
triethylamine/hexanes to 40% ethyl acetate/1% triethylamine/hexanes) to yield 5-thiomorpholinopyrimidine-2-carbonitrile as a brownish orange solid (1.695 g, 8.2 mmol, 33% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.29 (s, 2H), 3.86 – 3.79 (m, 4H), 2.78 – 2.71 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.7, 142.4, 133.0, 116.7, 49.2, 26.0.

5-Thiomorpholinopyrimidine-2-carbonitrile (1.25 g, 6.10 mmol, 1 equiv) was added to an oven-dried 100 mL round bottom flask containing a magnetic stirbar. The flask was sealed with a rubber septum and evacuated and backfilled with nitrogen three times and left under a positive pressure of nitrogen. THF (25 mL) was added *via* a nitrogen flushed syringe and the solution was cooled to -78 °C. DIBAL-H (1M solution in hexane, 12.2 mL, 12.2 mmol, 2 equiv) was added dropwise *via* a nitrogen flushed syringe. The reaction solution was allowed to warm to room temperature and stirred for 4 h. HCl (1 M aqueous solution, 15 mL) was added dropwise open to ambient air. A saturated solution of Rochelle's salt (50 mL) was added and stirred for 12 h. The solution was then filtered over a bed of celite. The resulting solution was added to a separatory funnel, extracted with EtOAc (3 x 75 mL), and the organic solution was washed with brine (1 x 100 mL) and dried over Na_2SO_4. After evaporation of the solvent *in vacuo*, the resulting residue was purified by silica gel chromatography (20% ethyl acetate/1% triethylamine/hexanes to 75% ethyl acetate/1% triethylamine/hexanes) to yield 5-thiomorpholinopyrimidine-2-carbaldehyde as a yellow solid (218.6 mg, 1.0 mmol, 16% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.94 (s, 1H), 8.43 (s, 2H), 3.94 – 3.79 (m, 4H), 2.84 – 2.68 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.0, 150.5, 143.5, 142.1, 49.4, 26.1.

3-(methylthio)-2-vinylpyridine

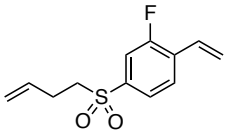


A slightly modified variant of General Procedure A was followed for this substrate. An oven-dried round bottom flask was charged with a magnetic stir bar and methyltriphenylphosphonium bromide (6.157 g, 17.24 mmol, 1.5 equiv), capped with a rubber septum, evacuated and backfilled with nitrogen three times and left under positive pressure with a nitrogen filled balloon. Anhydrous THF (72 mL) was then added, and the mixture was cooled to 0 °C in an ice bath with stirring. *n*-Butyllithium (10.77 mL of 1.6M solution in hexanes, 17.24 mmol, 1.5 equiv) was added dropwise with a nitrogen flushed syringe. Procedure A was then followed with 3-(methylthio)picolinaldehyde (1.76 g, 11.49 mmol, 1.0 equiv, synthesis described below). Flash column chromatography (5% ethyl acetate/hexanes to 15% ethyl acetate/hexanes) yielded the title product as a brown oil (128.4 mg, 0.8 mmol, 7% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.28 (d, J = 4.6 Hz, 1H), 7.40 (d, J = 8.0 Hz, 1H), 7.20 (dd, J = 16.9 Hz, 10.7 Hz, 1H), 7.10 (dd, J = 8.0, 4.6 Hz, 1H), 6.36 (dd, J = 10.8, 1.3 Hz 1H), 5.51 (dd, J = 10.8, 1.3 Hz, 1H), 2.41 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.0, 146.1, 134.7, 133.4, 132.8, 122.9, 120.2, 16.1. **HRMS** (DART) $[M+H]^+$ calcd. for $[C_8H_{10}NS]^+$, 152.0528 found, 152.0539. **IR** (neat, cm^{-1}) 3035.4, 2920.2, 1550.9, 1547.6, 1440.2, 1421.6, 1384.0, 1139.1, 1053.0, 982.2, 931.6, 785.1.

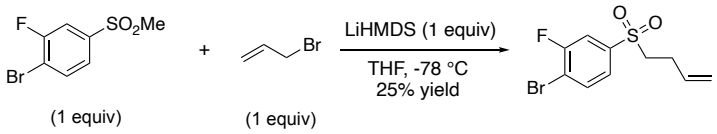


3-(methylthio)picolinaldehyde preparation: 3-Fluoropicolinaldehyde (2.5 g, 20.0 mmol, 1.0 equiv) was added to an oven-dried 250 mL round bottom flask with magnetic stir bar. DMF (100 mL) was added, and the solution was cooled to 0 °C with stirring. Sodium thiomethoxide (2.1 g, 30 mmol, 1.5 equiv) was slowly added. The reaction solution was stirred at 0 °C for 2 h. A saturated solution of ammonium chloride (50 mL) was then added. The resulting solution was transferred to a separatory funnel, extracted with EtOAc (3 x 50 mL), and the organic solution was washed with brine (1 x 100 mL) and dried over Na_2SO_4. After evaporation of the solvent *in vacuo*, the resulting residue was purified by silica gel chromatography (10% ethyl acetate/hexanes to 20% ethyl acetate/hexanes) to yield 3-(methylthio)picolinaldehyde as a brown oil (1.76 g, 12.5 mmol, 64% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.15 (s, 1H), 8.51 (dd, *J* = 4.5, 1.4 Hz, 1H), 7.67 (d, *J* = 8.3 Hz, 1H), 7.43 (dd, *J* = 8.3, 4.5 Hz, 1H), 2.45 (s, 3H).

4-(But-3-en-1-ylsulfonyl)-2-fluoro-1-vinylbenzene



General Procedure B was followed with triphenylphosphine (50.5 mg, 0.19 mmol, 0.09 equiv), palladium(II) chloride (11.4 mg, 0.06 mmol, 0.03 equiv), cesium carbonate (2.09 g, 6.42 mmol, 3.0 equiv), potassium vinyltrifluoroborate (344.0 mg, 2.57 mmol, 1.2 equiv), and 1-bromo-4-(but-3-en-1-ylsulfonyl)-2-fluorobenzene (626.0 mg, 2.14 mmol, 1.0 equiv, synthesis described below). Flash column chromatography (10% ethyl acetate/hexanes) yielded the title product as a light-yellow oil (340 mg, 1.41 mmol, 66% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 – 7.62 (m, 2H), 7.60 (dd, *J* = 9.7, 1.6 Hz, 1H), 6.90 (dd, *J* = 17.7, 11.2 Hz, 1H), 5.99 (dd, *J* = 17.7, 0.7 Hz, 1H), 5.79 – 5.66 (m, 1H), 5.59 (dd, *J* = 11.2, 0.7 Hz, 1H), 5.08 (dq, *J* = 8.2, 1.4 Hz, 1H), 5.05 (t, *J* = 1.5 Hz, 1H), 3.26 – 3.00 (m, 2H), 2.56 – 2.39 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.9 (d, *J* = 255.4 Hz), 139.3 (d, *J* = 6.8 Hz), 133.7, 131.2 (d, *J* = 12.4 Hz), 128.3 (d, *J* = 3.7 Hz), 128.2 (d, *J* = 3.8 Hz), 124.1 (d, *J* = 3.8 Hz), 120.7 (d, *J* = 4.8 Hz), 117.6, 116.2 (d, *J* = 25.4 Hz), 55.6, 27.1. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -114.52. **HRMS** (DART) $[M+H]^+$ calcd. for $[C_{12}H_{14}FO_2S]^+$ 241.0693, found 241.0680. **IR** (neat, cm^{-1}) 3081.4, 2983.1, 2922.9, 1642.4, 1629.7, 1567.0, 1486.8, 1407.1, 1310.2, 1270.7, 1226.9, 1183.7, 1141.7, 1114.9, 1072.9, 991.0, 920.7, 784.1.

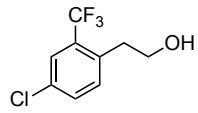


1-Bromo-4-(but-3-en-1-ylsulfonyl)-2-fluorobenzene preparation: 1-Bromo-2-fluoro-4-(methylsulfonyl)benzene (2.53 g, 10 mmol, 1 equiv) was added to an oven-dried 100 mL round bottom flask containing a magnetic stirbar. The flask was sealed with a rubber septum and evacuated and backfilled with nitrogen three times and left under a positive pressure of nitrogen. THF (40 mL) was added *via* a nitrogen flushed syringe. The reaction mixture was cooled to -78 °C. LiHMDS (0.9 – 1.1 M solution in hexane, 10 mL, 10 mmol, 1 equiv) was added dropwise *via* a nitrogen flushed syringe and the reaction mixture was stirred at -78 °C for 30 min. 3-Bromoprop-1-ene (0.87 mL, 10 mmol, 1 equiv) was then added dropwise *via* a nitrogen flushed syringe. The reaction mixture was stirred for 15 min at -78 °C, then allowed to warm to room temperature and stirred for 40 min. The reaction mixture was quenched with saturated NH_4Cl solution (1 x 50 mL). The resulting mixture was transferred to a separatory funnel, extracted with EtOAc (3 x 50 mL), and the organic solution was washed with brine (1 x 100 mL) and dried over Na_2SO_4. After

evaporation of the solvent *in vacuo*, the resulting residue was purified by silica gel chromatography (5% ethyl acetate/hexanes to 15% ethyl acetate/hexanes) to yield the title compound as a brown oil (0.724 g, 2.5 mmol, 25% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (m, 1H), 7.66 (d, *J* = 7.4, Hz, 1H), 7.59 (d, *J* = 8.3, Hz, 1H), 5.78 - 5.65 (m, 1H), 5.14 – 5.03 (m, 2H), 3.22 – 3.13 (m, 2H), 2.52 – 2.42 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.3 (d, J = 253.9 Hz), 140.3 (d, J = 5.5 Hz), 135.1, 133.5, 125.0 (d, J = 4.2 Hz), 117.8, 116.6 (d, J = 25 Hz), 116.5 (d, J = 21.0 Hz), 55.6, 27.0.

IX. Synthesis and Characterization Data for Hydration Products

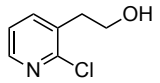
2-(4-Chloro-2-(trifluoromethyl)phenyl)ethan-1-ol (5)



General Procedure C was followed using 4-chloro-2-(trifluoromethyl)styrene (207 mg, 1.0 mmol, 1.0 equiv), 1-cyclopropylethanol (293 µL, 3.0 mmol, 3.0 equiv), P_4-*t*-Bu (0.8M, 125 µL, 0.1 mmol, 0.1 equiv) and toluene (667 µL) as the solvent at 40 °C for 12 h. Methanesulfonic acid (667 µL, 10.3 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (20% ethyl acetate/hexanes) yielded the title product as a yellow oil (135 mg, 0.60 mmol, 60% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 2.3 Hz, 1H), 7.44 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.35 (d, *J* = 8.3 Hz, 1H), 3.85 (q, *J* = 6.4 Hz, 2H), 3.02 (t, *J* = 6.7 Hz, 2H), 1.44 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 135.9 (q, *J* = 1.3 Hz), 133.5, 132.7, 131.9, 130.6 (q, *J* = 30.5 Hz), 126.6 (q, *J* = 5.9 Hz), 123.9 (q, *J* = 274.2 Hz), 63.1, 35.5 (q, *J* = 2.0 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -65.45. **LRMS** $[M+H]^+$ calcd. for $[C_9H_9ClF_3O]^+$ 225.0, found 225.0. **IR** (neat, cm^{-1}) 3322.2, 2917.2, 2848.9, 1486.6, 1410.4, 1304.8, 1118.9, 1054.1, 828.3, 697.9, 535.0.

For this substrate, General Procedure D was also followed using 4-chloro-2-(trifluoromethyl)styrene (207 mg, 1.0 mmol, 1.0 equiv), 1-cyclopropylethanol (293 µL, 3.0 mmol, 3.0 equiv), KO-*t*-Bu (11.2 mg, 0.1 equiv), 18-crown-6 (29.1 mg, 0.11 equiv) and 1,2-dimethoxyethane (0.5 mL) as the solvent at 60 °C for 24 h. Methanesulfonic acid (667 µL, 10.3 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (20% ethyl acetate/hexanes) yielded the title product as a yellow oil (110 mg, 0.49 mmol, 49% yield).

2-(2-Chloropyridin-3-yl)ethan-1-ol (3)

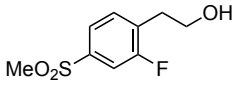


General Procedure C was followed using 2-chloro-3-vinylpyridine (139 mg, 1.0 mmol, 1.0 equiv), 1-cyclopropylethanol (293 µL, 3.0 mmol, 3.0 equiv), P_4-*t*-Bu (0.8M, 125 µL, 0.1 mmol, 0.1 equiv) and toluene (500 µL) as the solvent at 50 °C for 12 h. Methanesulfonic acid (667 µL, 10.3 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (40% ethyl acetate/hexanes) yielded the title product as a colorless oil (160 mg, 0.83 mmol, 83% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.25 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.62 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.17 (dd, *J* = 7.5, 4.8 Hz, 1H), 3.92 (t, *J* = 6.5 Hz, 2H), 2.98 (t, *J* = 6.5 Hz, 2H), 1.65 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.5, 147.7, 140.2, 133.4, 122.7, 61.1, 36.5. **HRMS** (DART) $[M+H]^+$ calcd. for $[C_7H_9ClNO]^+$ 158.0367, found 158.0370. **IR** (neat, cm^{-1}) 3330.9, 2935.8, 2877.6, 1564.6, 1407.3, 1078.3, 1047.7, 795.7, 746.5, 680.3.

For this substrate, General Procedure D was also followed using 2-chloro-3-vinylpyridine (139 mg, 1.0 mmol, 1.0 equiv), 1-cyclopropylethanol (484 µL, 5.0 mmol, 5.0 equiv), KO-*t*-Bu (11.2 mg, 0.1 equiv), 18-crown-6 (29.1 mg, 0.11 equiv) and 1,2-dimethoxyethane (0.5 mL) as the solvent

at 40 °C for 24 h. Methanesulfonic acid (667 µL, 10.3 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (40% ethyl acetate/hexanes) yielded the title product as a colorless oil (96 mg, 0.61 mmol, 61% yield).

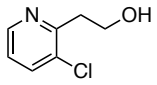
2-(2-Fluoro-4-(methylsulfonyl)phenyl)ethan-1-ol (6)



General Procedure C was followed using 2-fluoro-4-(methylsulfonyl)-1-vinylbenzene (200 mg, 1.0 mmol, 1.0 equiv), 1-cyclopropylethanol (488 µL, 5.0 mmol, 5.0 equiv), P_4-*t*-Bu (0.8M, 125 µL, 0.1 mmol, 0.1 equiv) and toluene (500 µL) as the solvent at rt for 12 h. Methanesulfonic acid (667 µL, 10.3 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (70% ethyl acetate/hexanes) yielded the title product as a white solid (139 mg, 0.64 mmol, 64% yield). **Melting point**: 72-73 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 (dd, *J* = 8.0, 1.9 Hz, 1H), 7.62 (dd, *J* = 8.9, 1.9 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 1H), 3.91 (q, *J* = 6.1 Hz, 2H), 3.05 (s, 3H), 2.99 (td, *J* = 6.4, 1.3 Hz, 2H), 1.60 (t, *J* = 5.5 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.1 (d, *J* = 251.3 Hz), 140.4 (d, *J* = 6.6 Hz), 133.0 (d, *J* = 16.0 Hz), 132.8 (d, *J* = 5.0 Hz), 123.2 (d, *J* = 3.9 Hz), 114.8 (d, *J* = 26.0 Hz), 61.8, 44.6, 32.6 (d, *J* = 1.6 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -113.98. **HRMS** (DART) $[M+NH_4]^+$ calcd. for $[C_9H_{15}FNO_3S]^+$ 236.0751, found 236.0752. **IR** (neat, cm^{-1}) 3520.6, 3381.7, 3012.7, 2930.0, 1406.7, 1299.6, 1229.3, 1139.2, 1054.7, 969.8, 764.1, 607.7.

For this substrate, General Procedure D was also followed using 2-fluoro-4-(methylsulfonyl)-1-vinylbenzene (200 mg, 1.0 mmol, 1.0 equiv), 1-cyclopropylethanol (488 µL, 5.0 mmol, 5.0 equiv), KO-*t*-Bu (11.2 mg, 0.10 mmol, 0.1 equiv), 18-crown-6 (29.1 mg, 0.11 mmol, 0.11 equiv) and 1,2-dimethoxyethane (0.5 mL) as the solvent at rt for 24 h. Methanesulfonic acid (667 µL, 10.3 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (70% ethyl acetate/hexanes) yielded the title product as a white solid (133 mg, 0.61 mmol, 61% yield).

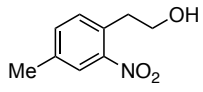
2-(3-Chloropyridin-2-yl)ethan-1-ol (7)



General Procedure C was followed using 3-chloro-2-vinylpyridine (140 mg, 1.0 mmol, 1.0 equiv), 1-cyclopropylethanol (293 µL, 3.0 mmol, 3.0 equiv), P_4-*t*-Bu (0.8M, 125 µL, 0.1 mmol, 0.1 equiv) and toluene (667 µL) as the solvent at 40 °C for 12 h. Methanesulfonic acid (533 µL, 8.2 mmol, 8.2 equiv) was used in the deprotection step and flash column chromatography (40% ethyl acetate/hexanes) yielded the title product as a colorless oil (102 mg, 0.65 mmol, 65% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.39 (dd, *J* = 4.7, 1.5 Hz, 1H), 7.66 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.13 (dd, *J* = 8.1, 4.7 Hz, 1H), 4.13 – 3.92 (m, 3H), 3.13 (t, *J* = 5.2 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.0, 146.8, 137.2, 131.7, 122.7, 60.6, 36.1. **HRMS** (DART) $[M+H]^+$ calcd. for $[C_7H_9ClNO]^+$ 158.0367, found 158.0370. **IR** (neat, cm^{-1}) 3326.4, 3059.5, 2933.5, 2877.0, 1575.9, 1426.3, 1045.2, 794.4.

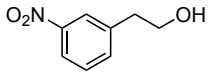
For this substrate, General Procedure D was also followed using 3-chloro-2-vinylpyridine (140 mg, 1.0 mmol, 1.0 equiv), 1-cyclopropylethanol (293 µL, 3.0 mmol, 3.0 equiv), KO-*t*-Bu (11.2 mg, 0.10 mmol, 0.1 equiv), 18-crown-6 (29.1 mg, 0.11 mmol, 0.11 equiv) and 1,2-dimethoxyethane (0.5 mL) as the solvent at 40 °C for 20 h. Methanesulfonic acid (667µL, 10.3 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (40% ethyl acetate/hexanes) yielded the title product as a colorless oil (80 mg, 0.51 mmol, 51% yield).

2-(4-Methyl-2-nitrophenyl)ethan-1-ol (8)



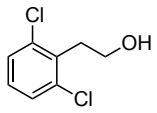
General Procedure C was followed using 4-methyl-2-nitrostyrene (163 mg, 1.0 mmol, 1.0 equiv), 1-cyclopropylethanol (293 µL, 3.0 mmol, 3.0 equiv), P_4-*t*-Bu (0.8M, 125 µL, 0.1 mmol, 0.1 equiv) and toluene (1.0 mL) as the solvent at 30 °C for 12 h. Methanesulfonic acid (667 µL, 10.3 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (25% to 40% ethyl acetate/hexanes) yielded the title product as an amorphous brown solid (115 mg, 0.64 mmol, 64% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.31 (d, *J* = 7.9 Hz, 1H), 7.27 – 7.19 (m, 1H), 3.87 (t, *J* = 6.4 Hz, 2H), 3.07 (t, *J* = 6.4 Hz, 2H), 2.36 (s, 3H), 1.73 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.8, 138.2, 134.0, 132.8, 130.8, 125.3, 63.0, 36.0, 20.9. **LRMS** $[M+H]^+$ calcd. for $[C_9H_{12}NO_3]^+$ 182.1, found 182.1. **IR** (neat, cm^{-1}) 3226.5, 2923.7, 2879.9, 1523.6, 1345.7, 1046.9, 831.9, 678.6.

2-(3-Nitrophenyl)ethan-1-ol (9)



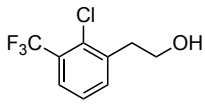
General Procedure C was followed using 3-nitrostyrene (149 mg, 1.0 mmol, 1.0 equiv), 1-cyclopropylethanol (293 µL, 3.0 mmol, 3.0 equiv), P_4-*t*-Bu (0.8M, 125 µL, 0.1 mmol, 0.1 equiv) and toluene (1.0 mL) as the solvent at 60 °C for 12 h. Methanesulfonic acid (667 µL, 10.3 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (25% ethyl acetate/hexanes) yielded the title product as an orange solid (81.0 mg, 0.48 mmol, 48% yield). **Melting point**: 47-48 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 – 8.05 (m, 2H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 3.93 (q, *J* = 6.0 Hz, 2H), 2.98 (t, *J* = 6.4 Hz, 2H), 1.58 (t, *J* = 5.0 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.6, 141.1, 135.6, 129.5, 124.0, 121.8, 63.1, 38.8. **HRMS** (DART) $[M+NH_4]^+$ calcd. for $[C_8H_{13}N_2O_3]^+$ 185.0921, found 185.0924. **IR** (neat, cm^{-1}) 3307.0, 3090.0, 2931.7, 2870.9, 1522.5, 1342.4, 1083.9, 1056.2, 883.1, 735.4. The characterization data is consistent with reported literature values.[16]

2-(2,6-Dichlorophenyl)ethan-1-ol (10)



General Procedure C was followed using 2,6-dichlorostyrene (173 mg, 1.0 mmol, 1.0 equiv),1-cyclopropylethanol (293 µL, 3.0 mmol, 3.0 equiv), P_4-*t*-Bu (0.8M, 125 µL, 0.1 mmol, 0.1 equiv) and toluene (1.0 mL) as the solvent at 100 °C for 12 h. Methanesulfonic acid (667 µL, 10.3 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (40% dichloromethane/hexanes to 20% ethyl acetate/hexanes) yielded the title product as a white solid (154 mg, 0.81 mmol, 81% yield). **Melting point**: 69-70 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.0 Hz, 2H), 7.10 (t, *J* = 8.0 Hz, 1H), 3.88 (q, *J* = 6.8 Hz, 2H), 3.27 (t, *J* = 7.2 Hz, 2H), 1.45 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 136.1, 134.5, 128.5, 128.4, 61.2, 34.8. The characterization data is consistent with reported literature values.[17]

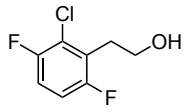
2-(2-Chloro-3-(trifluoromethyl)phenyl)ethan-1-ol (11)



General Procedure C was followed using 2-chloro-3-(trifluoromethyl)styrene (207 mg, 1.0 mmol, 1.0 equiv), 1-cyclopropylethanol (293 µL, 3.0 mmol, 3.0 equiv), P_4-*t*-Bu (0.8M, 125 µL, 0.1 mmol, 0.1 equiv) and toluene (1.0 mL) as the solvent at 40 °C for 12 h. Methanesulfonic acid (667 µL, 10.3 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (20% ethyl acetate/hexanes) yielded the title product as colorless liquid (173 mg, 0.77 mmol, 77% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.50 (d, *J* = 7.8 Hz, 1H), 7.32 (td, *J* =

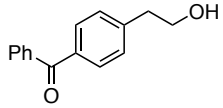
7.8, 0.9 Hz, 1H), 3.93 (t, J = 6.6 Hz, 2H), 3.11 (t, J = 6.6 Hz, 2H), 1.44 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.0, 134.9, 132.3, 129.3 (q, J = 30.7 Hz), 126.6, 126.3 (q, J = 5.5 Hz), 123.2 (q, J = 273.2 Hz), 61.8, 37.1. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.89. **LRMS** $[M+H]^+$ calcd. for $[C_9H_9ClF_3O]^+$ 225.0, found 225.0. **IR** (neat, cm^{-1}) 3326.1, 2939.6, 2885.0, 1586.2, 1434.1, 1314.7, 1129.1, 1045.7, 797.8, 732.7, 699.0.

2-(2-Chloro-3,6-difluorophenyl)ethan-1-ol (12)



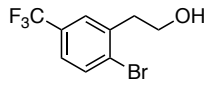
General Procedure C was followed using 2-chloro-3,6-difluorostyrene (175 mg, 1.0 mmol, 1.0 equiv),1-cyclopropylethanol (293 µL, 3.0 mmol, 3.0 equiv), P_4-*t*-Bu (0.8M, 125 µL, 0.1 mmol, 0.1 equiv) and toluene (1.0 mL) as the solvent at 65 °C for 12 h. Methanesulfonic acid (667 µL, 10.3 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (75% dichloromethane/hexanes) yielded the title product as a colorless oil (160 mg, 0.83 mmol, 83% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.09 – 6.81 (m, 2H), 3.85 (t, J = 6.9 Hz, 2H), 3.09 (td, J = 6.9, 2.3 Hz, 2H), 1.80 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.5 (dd, J = 258.2, 2.5 Hz), 155.1 (dd, J = 258.8, 2.5 Hz),126.4 (d, J = 20.7 Hz), 122.5 (dd, J = 19.2, 6.7 Hz), 114.8 (dd, J = 23.9, 9.5 Hz), 114.3 (dd, J = 25.7, 7.8 Hz), 61.3, 30.3 (t, J = 1.6 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -118.04 (d, J = 16.0 Hz), -118.71 (d, J = 16.0 Hz). **EA** Calc for $C_8H_7ClF_2O$: C, 49.89; H, 3.66; Found: C, 50.00; H, 3.62. **IR** (neat, cm^{-1}) 3319.5, 2944.4, 2885.6, 1472.7, 1231.0, 1039.5, 866.0, 808.2, 746.5, 726.5.

(4-(2-Hydroxyethyl)phenyl)(phenyl)methanone (13)



General Procedure C was followed using phenyl(4-vinylphenyl)methanone (208.3 mg, 1.0 mmol, 1.0 equiv), 1-cyclopropylethanol (488 µL, 5.0 mmol, 5.0 equiv), P_4-*t*-Bu (0.8M, 125 µL, 0.1 mmol, 0.1 equiv) and toluene (500 µL) as the solvent at 40 °C for 24 h. Methanesulfonic acid (667 µL, 10.3 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (10% ethyl acetate/hexanes) yielded the title product as a light yellow oil (110 mg, 0.49 mmol, 49% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (td, J = 8.1, 1.4 Hz, 4H), 7.59 (t, J = 7.1 Hz, 1H), 7.48 (m, 2H), 7.35 (d, J = 7.9 Hz, 2H), 3.93 (td, J = 6.5, 1.6 Hz, 2H), 2.96 (t, J = 6.5 Hz, 2H), 1.74 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.7, 144.0, 137.9, 136.1, 132.5, 130.7, 130.2, 129.2, 128.5, 63.5, 39.4. **HRMS** (DART) $[M+H]^+$ calcd. for $[C_{15}H_{15}O_2]^+$ 227.1067, found 227.1066. **IR** (neat, cm^{-1}) 3397.3, 3057.8, 2935.3, 2873.6, 1651.9, 1604.8, 1446.2, 1412.3, 1316.0, 1276.7, 1174.9, 1043.6, 938.0, 923.2, 698.8.

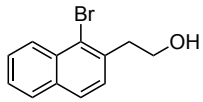
2-(2-Bromo-5-(trifluoromethyl)phenyl)ethan-1-ol (14)



General Procedure C was followed using 2-bromo-5-(trifluoromethyl)styrene (251 mg, 1.0 mmol, 1.0 equiv), 1-cyclopropylethanol (293 µL, 3.0 mmol, 3.0 equiv), P_4-*t*-Bu (0.8M, 125 µL, 0.1 mmol, 0.1 equiv) and toluene (667 µL) as the solvent at 50 °C for 12 h. Methanesulfonic acid (667 µL, 10.3 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (70% dichloromethane/hexanes) yielded the title product as a yellow oil (122 mg, 0.75 mmol, 75% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 (dd, J = 8.3, 0.9 Hz, 1H), 7.54 (d, J = 2.2 Hz, 1H), 7.33 (dd, J = 8.3, 2.2 Hz, 1H), 3.91 (td, J = 6.6, 5.6 Hz, 2H), 3.07 (t, J = 6.6 Hz, 2H), 1.43 (t, J = 5.6 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.3, 133.6, 130.1 (q, J = 33.0 Hz), 128.7, 128.1 (q, J = 3.6 Hz), 125.0 (q, J = 3.7 Hz), 124.0 (q, J = 272.2 Hz), 61.8, 39.4. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.69. **LRMS** $[M+H]^+$ calcd. for

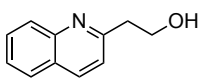
$[C_9H_9BrF_3O]^+$ 269.0, found 269.1. **IR** (neat, cm^{-1}) 3319.2, 2937.6, 2883.8, 1604.5, 1322.5, 1165.4, 1120.8, 1080.8, 1036.0, 823.2, 725.2.

2-(1-Bromonaphthalen-2-yl)ethan-1-ol (15)



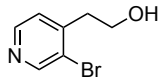
General Procedure C was followed using 1-bromo-2-vinylnaphthalene (206 mg, 0.88 mmol, 1.0 equiv), 1-cyclopropylethanol (258 µL, 2.64 mmol, 3.0 equiv), P_4-*t*-Bu (0.8M, 111 µL, 0.09 mmol, 0.1 equiv) and toluene (880 µL) as the solvent at 60 °C for 12 h. Methanesulfonic acid (587 µL, 9.1 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (20% to 40% ethyl acetate/hexanes) yielded the title product as a white solid (97 mg, 0.39 mmol, 44% yield). **Melting point**: 68-70 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.5 Hz, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.77 (d, *J* = 8.3 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.50 (m, 1H), 7.40 (d, *J* = 8.3 Hz, 1H), 3.99 (q, *J* = 6.5 Hz, 2H), 3.29 (t, *J* = 6.7 Hz, 2H), 1.42 (t, *J* = 5.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 136.3, 133.6, 132.8, 128.8, 128.2, 127.8, 127.6, 127.5, 126.3, 124.5, 62.5, 40.7. **HRMS** (DART) $[M+NH_4]^+$ calcd. for $[C_{12}H_{15}BrNO]^+$ 268.0332, found 268.0330. **IR** (neat, cm^{-1}) 3230.2, 2958.9, 2925.6, 2875.4, 1556.7, 1500.4, 1444.9, 1371.0, 1332.5, 1253.0, 1046.1, 970.7, 811.7, 749.4, 736.5.

2-(Quinolin-2-yl)ethan-1-ol (16)



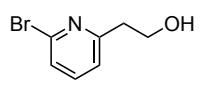
General Procedure C was followed using 2-vinylquinoline (155 mg, 1.0 mmol, 1.0 equiv), 1-cyclopropylethanol (293 µL, 3.0 mmol, 3.0 equiv), P_4-*t*-Bu (0.8M, 125 µL, 0.1 mmol, 0.1 equiv) and toluene (1 mL) as the solvent at 40 °C for 12 h. Aqueous 5M HCl (4.0 mL, 20 mmol, 20 equiv) was used in the deprotection step and flash column chromatography (100% ethyl acetate) yielded the title product as a white solid (108 mg, 0.62 mmol, 62% yield). **Melting point**: 101-102 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.4 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.67 (ddd, *J* = 8.4, 6.8, 1.5 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 1H), 7.25 (d, *J* = 8.2 Hz, 1H), 4.79 (s, 1H), 4.13 (t, *J* = 5.4 Hz, 2H), 3.18 (t, *J* = 5.4 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.6, 147.5, 136.7, 129.8, 128.9, 127.7, 127.0, 126.2, 122.0, 61.6, 39.5. **HRMS** (DART) $[M+H]^+$ calcd. for $[C_{11}H_{12}NO]^+$ 174.0913, found 174.0931. **IR** (neat, cm^{-1}) 3126.7, 2953.8, 2923.6, 2840.7, 1600.7, 1505.1, 1430.5, 1334.5, 1244.7, 1052.0, 818.2, 764.4.

2-(3-Bromopyridin-4-yl)ethan-1-ol (17)



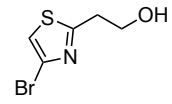
General Procedure C was followed using 3-bromo-4-vinylpyridine (184 mg, 1.0 mmol, 1.0 equiv), 1-cyclopropylethanol (259 µL, 3.0 mmol, 3.0 equiv), P_4-*t*-Bu (0.8M, 125 µL, 0.1 mmol, 0.1 equiv) and toluene (500 µL) as the solvent at rt for 1 h. Aqueous 5M HCl (4.0 mL, 20 mmol, 20 equiv) was used in the deprotection step and flash column chromatography (80% ethyl acetate/hexanes) yielded the title product as a white solid (152 mg, 0.75 mmol, 75% yield). **Melting point**: 48-49 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.35 (d, *J* = 4.9 Hz, 1H), 7.23 (d, *J* = 4.9 Hz, 1H), 3.92 (t, *J* = 6.4 Hz, 2H), 2.99 (t, *J* = 6.4 Hz, 2H), 2.49 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.9, 148.0, 147.7, 126.3, 123.5, 60.9, 38.7. **HRMS** (DART) $[M+H]^+$ calcd. for $[C_7H_9BrNO]^+$ 201.9862, found 201.9863. **IR** (neat, cm^{-1}) 3216.9, 3019.4, 2955.7, 2934.5, 2871.2, 1587.7, 1400.2, 1365.2, 1306.4, 1055.9, 1038.5, 694.3, 609.9.

2-(6-Bromopyridin-2-yl)ethan-1-ol (18)



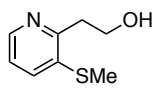
General Procedure C was followed using 2-bromo-6-vinylpyridine (184 mg, 1.0 mmol, 1.0 equiv), 1-cyclopropylethanol (293 µL, 3.0 mmol, 3.0 equiv), P_4-*t*-Bu (0.8M, 125 µL, 0.1 mmol, 0.1 equiv) and toluene (667 µL) as the solvent at 35 °C for 12 h. Aqueous 5M HCl (4.0 mL, 20 mmol, 20 equiv) was used in the deprotection step and flash column chromatography (50% ethyl acetate/hexanes) yielded the title product as a yellow oil (122 mg, 0.60 mmol, 60% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (t, J = 7.7 Hz, 1H), 7.33 (d, J = 7.9 Hz, 1H), 7.12 (d, J = 7.5 Hz, 1H), 3.99-4.00 (m, 2H), 2.97-3.00 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.8, 141.5, 139.0, 126.0, 122.6, 61.6, 39.6. **HRMS** (DART) $[M+H]^+$ calcd. for $[C_7H_9BrNO]^+$ 201.9862, found 201.9866. **IR** (neat, cm^{-1}) 3313.2, 2930.8, 2875.8, 1582.5, 1552.2, 1436.5, 1403.7, 1122.0, 1044.4, 781.9, 678.8.

2-(4-Bromothiazol-2-yl)ethan-1-ol (19)



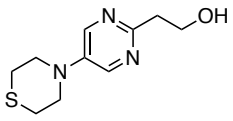
General Procedure C was followed using 4-bromo-2-vinylthiazole (190 mg, 1.0 mmol, 1.0 equiv), 1-cyclopropylethanol (391 µL, 4.0 mmol, 4.0 equiv), P_4-*t*-Bu (0.8M, 63 µL, 0.05 mmol, 0.05 equiv) and toluene (500 µL) as the solvent at rt for 12 h. Methanesulfonic acid (667 µL, 10.3 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (40% ethyl acetate/hexanes) yielded the title product as a yellow oil (153 mg, 0.74 mmol, 74% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.12 (s, 1H), 4.02 (t, J = 5.7 Hz, 2H), 3.22 (t, J = 5.7 Hz, 2H), 2.68 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.8, 124.4, 116.6, 61.2, 36.3. **HRMS** (DART) $[M+H]^+$ calcd. for $[C_5H_7BrNOS]^+$ 207.9426, found 207.9435. **IR** (neat, cm^{-1}) 3331.2, 3120.3, 2923.0, 2878.3, 1478.7, 1255.4, 1133.1, 1083.7, 1048.6, 830.9, 729.4.

2-(3-(Methylthio)pyridin-2-yl)ethan-1-ol (23)



General Procedure C was followed using 3-(methylthio)-2-vinylpyridine (75.6 mg, 0.5 mmol, 1.0 equiv), 1-cyclopropylethanol (145 µL, 1.5 mmol, 3.0 equiv), P_4-*t*-Bu (0.8M, 62.5 µL, 0.05 mmol, 0.1 equiv) and toluene (250 µL) as the solvent at 50 °C for 24 h. Methanesulfonic acid (332 µL, 5.15 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (5% methanol/dichloromethane) yielded the title product as a white solid (53.0 mg, 0.31 mmol, 63% yield). **Melting point**: 58-59 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.26 (dd, J = 4.9, 1.5 Hz, 1H), 7.47 (dd, J = 8.0, 1.5 Hz, 1H), 7.20 – 7.12 (m, 1H), 4.38 (s, 1H), 4.08 (t, J= 5.4 Hz, 2H), 3.02 (t, J = 5.4 Hz, 2H), 2.45 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.6, 144.1, 134.9, 132.6, 122.1, 60.7, 35.8, 15.2. **HRMS** (DART) $[M+H]^+$ calcd. for $[C_8H_{12}NOS]^+$ 170.0634, found 170.0653. **IR** (neat, cm^{-1}) 3243.7, 3053.0, 2959.1, 2920.1, 2867.3, 1568.5, 1442.5, 1416.0, 1370.0, 1048.2, 1015.6, 783.0, 756.3, 693.3, 671.4.

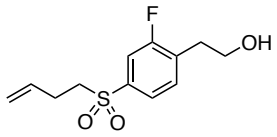
2-(5-Thiomorpholinopyrimidin-2-yl)ethan-1-ol (24)



General Procedure C was followed using 4-(2-vinylpyrimidin-5-yl)thiomorpholine (41.4 mg, 0.2 mmol, 1.0 equiv), 1-cyclopropylethanol (58 µL, 0.6 mmol, 3.0 equiv), P_4-*t*-Bu (0.8M, 25 µL, 0.02 mmol, 0.1 equiv) and toluene (100 µL) as the solvent at 50 °C for 24 h. Methanesulfonic acid (130 µL, 2.06 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (1% to 5% methanol/dichloromethane) yielded the title product as a light yellow oil (18.0 mg, 0.080 mmol, 40% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.30 (s, 2H), 4.04 (m, 2H), 3.63 – 3.55 (m, 4H), 3.15 (t, J = 5.5 Hz, 2H), 2.83 – 2.70 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.8,

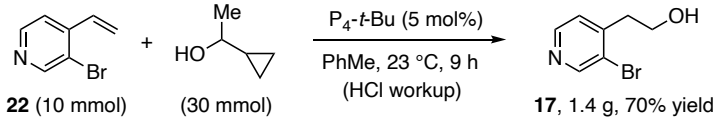
144.9, 142.7, 61.0, 50.9, 39.3, 26.5. **HRMS** (DART) $[M+H]^+$ calcd. for $[C_{10}H_{16}N_3OS]^+$ 226.1009, found 226.1022. **IR** (neat, cm^{-1}) 3337.7, 2920.8, 1683.8, 1458.0, 1031.8, 981.6, 954.1, 667.9.

2-(4-(But-3-en-1-ylsulfonyl)-2-fluorophenyl)ethan-1-ol (25)

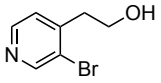


General Procedure C was followed using 4-(but-3-en-1-ylsulfonyl)-2-fluoro-1-vinylbenzene (96.1 mg, 0.4 mmol, 1.0 equiv), 1-cyclopropylethanol (194 µL, 2.0 mmol, 5.0 equiv), P_4-*t*-Bu (0.8M, 50 µL, 0.04 mmol, 0.1 equiv) and toluene (200 µL) as the solvent at rt for 24 h. Methanesulfonic acid (267 µL, 4.12 mmol, 10.3 equiv) was used in the deprotection step and flash column chromatography (50% ethyl acetate/hexanes) yielded the title product as a colorless oil (74 mg, 0.286 mmol, 72% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (dt, *J* = 7.9, 2.1 Hz, 1H), 7.59 (dt, *J* = 8.9, 2.1 Hz, 1H), 7.50 (t, *J* = 7.4 Hz, 1H), 5.80 – 5.65 (m, 1H), 5.11 – 5.05 (m, 1H), 5.05 (m, 1H), 3.93 (td, *J* = 6.4, 2.4 Hz, 2H), 3.21 – 3.10 (m, 2H), 3.00 (tt, *J* = 6.4, 1.6 Hz, 2H), 2.56 – 2.42 (m, 2H), 1.52 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.1 (d, *J* = 251.3 Hz), 139.1 (d, *J* = 6.6 Hz), 133.7, 133.0 (d, *J* = 16.1 Hz), 132.7 (d, *J* = 4.9 Hz), 124.0 (d, *J* = 3.8 Hz), 117.5, 115.6 (d, *J* = 25.7 Hz), 61.9, 55.5, 32.6 (d, *J* = 1.6 Hz), 27.0. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -114.06. **LRMS** $[M+H]^+$ calcd. for $[C_{12}H_{16}FO_3S]^+$ 259.1, found 259.1. **IR** (neat, cm^{-1}) 3503.5, 3072.8, 2931.1, 1642.6, 1576.8, 1489.1, 1407.1, 1304.0, 1271.3, 1227.7, 1136.7, 1117.4, 1071.4, 1046.2, 912.0, 784.9.

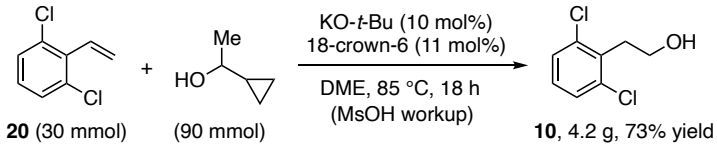
X. Large-scale anti-Markovnikov Hydration Reactions



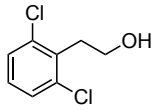
2-(3-Bromopyridin-4-yl)ethan-1-ol (17)



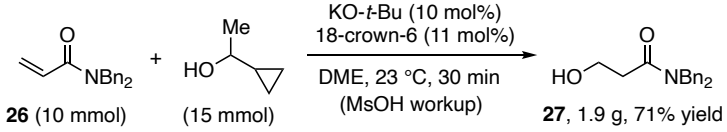
General Procedure C was followed using an oven-dried 100 mL round bottom flask and 3-bromo-4-vinylpyridine (**22**, 1.84 g, 10.0 mmol, 1.0 equiv), 1-cyclopropylethanol (2.9 mL, 30.0 mmol, 3.0 equiv), P_4-*t*-Bu (0.8M, 625 µL, 0.5 mmol, 0.05 equiv) and toluene (10 mL) as the solvent at rt for 9 h. The reaction solution was then cooled to 0 °C in an ice bath and aqueous 4M HCl (40.0 mL, 160 mmol, 16 equiv) was added dropwise with vigorous stirring. The biphasic mixture was allowed to warm to rt and stirred for 1 h before being quenched with saturated aqueous Na_2CO_3 (100 mL), extracted with ethyl acetate (3 x 100 mL), washed with brine (200 mL), and concentrated *in vacuo*. Purification of the resulting residue via flash column chromatography (80% ethyl acetate/hexanes) yielded the title product as a white solid (1.42 g, 7.03 mmol, 70% yield).



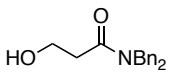
2-(2,6-Dichlorophenyl)ethan-1-ol (10)



General Procedure D was followed using an oven-dried 100 mL round bottom flask and 2,6-dichlorostyrene (5.20 g, 30 mmol, 1.0 equiv), 1-cyclopropylethanol (8.7 mL, 90 mmol, 3.0 equiv), KO-*t*-Bu (337 mg, 3 mmol, 0.1 equiv), 18-crown-6 (872 mg, 3.3 mmol, 0.11 equiv) and 1,2-dimethoxyethane (15 mL) as the solvent at 85 °C. After 18 h, the reaction flask was inserted into a 0 °C ice bath and methanesulfonic acid (20 mL, 10.3 equiv) was added dropwise with vigorous stirring. After 30 min, the reaction mixture was quenched with saturated aqueous Na_2CO_3 (50 mL), extracted with ethyl acetate (3 x 50 mL), washed with brine (150 mL), and concentrated *in vacuo*. Purification of the resulting residue via flash column chromatography (20% ethyl acetate/hexanes) yielded the title product as a white solid (4.20 g, 22.0 mmol, 73% yield).

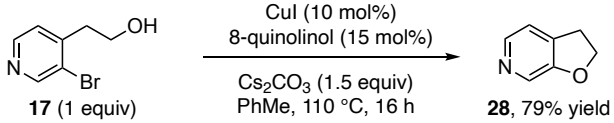


***N,N*-dibenzyl-3-hydroxypropanamide (27)**

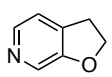


General Procedure D was followed using an oven-dried 50 mL round bottom flask and *N,N*-dibenzylacrylamide[18] (2.51 g, 10 mmol, 1.0 equiv), 1-cyclopropylethanol (1.29 g, 15 mmol, 1.5 equiv), KO-*t*-Bu (112 mg, 1.0 mmol, 0.1 equiv), 18-crown-6 (291 mg, 1.1 mmol, 0.11 equiv) and 1,2-dimethoxyethane (5 mL) as the solvent at rt. After 30 min, the reaction flask was inserted into a 0 °C ice bath and methanesulfonic acid (6.7 mL, 103 mmol, 10.3 equiv) was added dropwise with vigorous stirring. After 30 min, the reaction mixture was quenched with saturated aqueous Na_2CO_3 (50 mL), extracted with ethyl acetate (3 x 50 mL), washed with brine (150 mL), and concentrated *in vacuo*. Purification of the resulting residue via flash column chromatography (1 to 5% methanol/dichloromethane) yielded the title product as a viscous oil (1.92 g, 7.13 mmol, 71% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 – 7.34 (m, 2H), 7.34 – 7.27 (m, 4H), 7.25 – 7.19 (m, 2H), 7.17 – 7.12 (m, 2H), 4.63 (s, 2H), 4.45 (s, 2H), 3.92 (t, *J* = 5.3 Hz, 2H), 2.77 (s, 1H), 2.66 (t, *J* = 5.3 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.6, 137.1, 136.1, 129.3, 128.9, 128.5, 128.0, 127.8, 126.6, 59.0, 50.1, 48.4, 35.2. **LRMS** $[M+H]^+$ calcd. for $[C_{17}H_{20}NO_2]^+$ 270.2, found 270.2**. IR** (neat, cm^{-1}) 3415.2, 3061.7, 3028.9, 2924.3, 1623.8, 1494.8, 1471.1, 1450.4, 1420.7, 1359.5, 1206.2, 1044.6, 1028.4, 955.9, 731.8, 696.5.

XI. Intramolecular C–O Coupling Reactions for Dihydrobenzofuran Synthesis

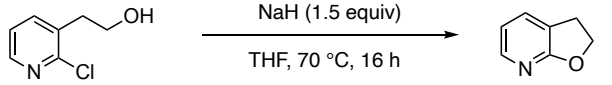


2,3-Dihydrofuro[2,3-*c*]pyridine (28)



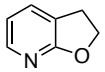
In a nitrogen-filled glovebox, to an oven-dried 2-dram reaction vial (Thermo Scientific B7999-3) containing a magnetic stir bar was added copper(I) iodide (7.6 mg, 0.04 mmol, 0.1 equiv), 8-quinolinol (8.7 mg, 0.06 mmol, 0.15 equiv), cesium carbonate (195.5 mg, 0.6 mmol, 1.5 equiv), PhMe (0.4 mL), and 2-(3-bromopyridin-4-yl)ethan-1-ol (80.8

mg, 0.4 mmol, 1.0 equiv) in successive order. The reaction vial was capped (Thermo Scientific B7995-15 with 10/90 septa), removed from the glovebox, and inserted into a preheated silicon oil bath at 110 °C. After stirring for 16 h, the reaction mixture was cooled to rt, water was added (3 mL), and the mixture was extracted with Et_2O (3 x 3 mL). The combined organic layer was washed with brine (10 mL) and concentrated *in vacuo*. Purification of the resulting residue *via* flash column chromatography (33% diethyl ether/hexanes) yielded the desired product as colorless oil (38.0 mg, 0.314 mmol, 79% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 8.12 (d, J = 4.7 Hz, 1H), 7.15 (dd, J = 4.7, 1.0 Hz, 1H), 4.58 (t, J = 8.8 Hz, 2H), 3.22 (td, J = 8.8, 1.1 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.5, 142.2, 136.3, 131.8, 120.3, 71.2, 29.6. The spectroscopic data is consistent with literature data.[19]

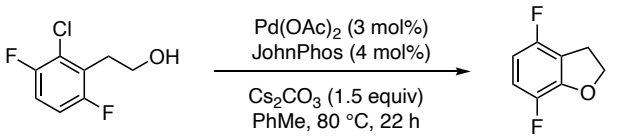


3 (1 equiv) **29**, 88% yield

2,3-Dihydrofuro[2,3-*b*]pyridine (29)

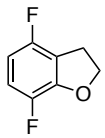


In a nitrogen-filled glovebox, to an oven-dried 2-dram vial (Thermo Scientific B7999-3) containing a magnetic stir bar was added 2-(2-chloropyridin-3-yl)ethan-1-ol (47.3 mg, 0.3 mmol, 1.0 equiv) and THF (0.6 mL). NaH (60% dispersion in mineral oil, 18 mg, 0.45 mmol, 1.5 equiv) was then added slowly to the mixture at rt in the glovebox. The reaction vial was capped (Thermo Scientific B7995-15 with 10/90 septa), removed from the glovebox, and inserted into a preheated silicon oil bath at 70 °C. After stirring for 16 h, the reaction mixture was cooled to rt and quenched with water (2 mL), extracted with Et_2O (3 x 3 mL), washed with brine (10 mL), and concentrated *in vacuo*. Purification of the resulting residue *via* flash column chromatography with (75% diethyl ether/hexanes) yielded the desired product as colorless oil (32.0 mg, 0.264 mmol, 88% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95 (m, 1H), 7.44 (dq, J = 7.2, 1.4 Hz, 1H), 6.74 (dd, J = 7.1, 5.2 Hz, 1H), 4.58 (t, J = 8.7 Hz, 2H), 3.22 (tt, J = 8.6, 1.2 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.8, 146.7, 133.7, 119.7, 116.6, 69.0, 28.2. The spectroscopic data is consistent with literature data.[20]



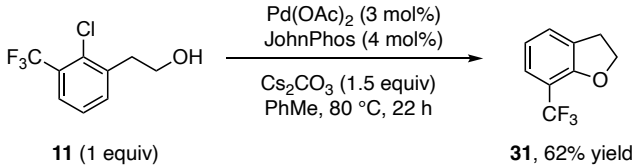
12 (1 equiv) **30**, 71% yield

4,7-Difluoro-2,3-dihydrobenzofuran (30)

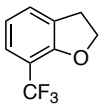


In a nitrogen-filled glovebox, to an oven-dried 2-dram vial (Thermo Scientific B7999-3) containing a magnetic stir bar was added palladium(II) acetate (2.0 mg, 0.009 mmol, 0.03 equiv), (2-biphenyl)di-*tert*-butylphosphine (JohnPhos, 3.6 mg, 0.012 mmol, 0.04 equiv), cesium carbonate (147 mg, 0.45 mmol, 1.5 equiv), PhMe (0.3 mL), and 2-(2-chloro-3,6-difluorophenyl)ethan-1-ol (57.8 mg, 0.3 mmol, 1.0 equiv) in successive order. The reaction vial was capped (Thermo Scientific B7995-15 with 10/90 septa), removed from the glovebox, and inserted into a preheated silicon oil bath at 80 °C. After stirring for 22 h, the reaction mixture was cooled to rt and quenched with water (2 mL), extracted with Et_2O (3 x 3 mL), washed with brine (10 mL), and concentrated *in vacuo*. Purification of the resulting residue *via* flash

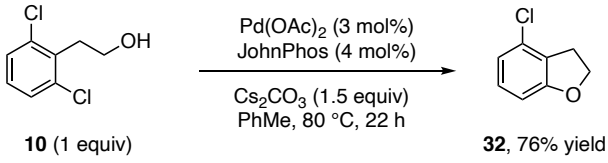
column chromatography (100% hexanes) yielded the desired product as colorless oil (33.0 mg, 0.211 mmol, 71% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.89 – 6.81, (m, 1H), 6.47 (ddd, *J* = 9.1, 7.8, 3.0 Hz, 1H), 4.72 (t, *J* = 8.7 Hz, 2H), 3.29 (tt, *J* = 8.7, 1.0 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.3 (dd, *J* = 242.7, 2.2 Hz), 148.4 (dd, *J* = 12.4, 8.7 Hz), 144.3 (dd, *J* = 240.4, 3.2 Hz), 116.6 (dd, *J* = 23.8, 3.0 Hz), 116.3 (dd, *J* = 19.7, 9.0 Hz), 107.4 (dd, *J* = 23.5, 6.1 Hz), 73.5, 27.6 (m). **^{19}F NMR** (377 MHz, $CDCl_3$) δ -122.43 (d, *J* = 20.5 Hz), -144.44 (d, *J* = 19.7 Hz). **IR** (neat, cm^{-1}) 2923.4, 2852.4, 1640.8, 1499.0, 1458.9, 1234.3, 1198.6, 1041.4, 994.0, 792.8. **GCMS** $[M]^+$ calc for $[C_8H_6F_2O]^+$ 156.0, found 156.



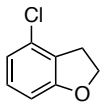
7-(Trifluoromethyl)-2,3-dihydrobenzofuran (31)



In a nitrogen-filled glovebox, to an oven-dried 2-dram vial (Thermo Scientific B7999-3) containing a magnetic stir bar was added palladium(II) acetate (2.0 mg, 0.009 mmol, 0.03 equiv), (2-biphenyl)di-*tert*-butylphosphine (JohnPhos, 3.6 mg, 0.012 mmol, 0.04 equiv), cesium carbonate (147 mg, 0.45 mmol, 1.5 equiv), PhMe (0.3 mL), and 2-(2-chloro-3-(trifluoromethyl)phenyl)ethan-1-ol (67.4 mg, 0.3 mmol, 1.0 equiv) in successive order. The reaction vial was capped (Thermo Scientific B7995-15 with 10/90 septa), removed from the glovebox, and inserted into a preheated silicon oil bath at 80 °C. After stirring for 22 h, the reaction mixture was cooled to rt and quenched with water (2 mL), extracted with Et_2O (3 x 3 mL), washed with brine (10 mL), and concentrated *in vacuo*. Purification of the resulting residue *via* flash column chromatography (100% hexanes) yielded the desired product as colorless oil (35.0 mg, 0.186 mmol, 62% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 (m, 2H), 6.96 – 6.82 (m, 1H), 4.71 (t, *J* = 8.8 Hz, 2H), 3.25 (t, *J* = 8.8 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.6 (q, *J* = 2.0 Hz), 129.4, 128.6, 125.0 (q, *J* = 4.5 Hz), 123.8 (q, *J* = 271.5 Hz), 120.3, 112.9, 72.6, 29.4. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -61.83. **IR** (neat, cm^{-1}) 2923.4, 2849.9, 1621.3, 1606.0, 1482.5, 1460.8, 1444.1, 1345.7, 1315.2, 1221.9, 1124.3, 1058.6, 986.7, 780.8. **LRMS** $[M-H]^-$ calc for $[C_9H_6F_3O]^-$ 187.0, found 187.1.



4-Chloro-2,3-dihydrobenzofuran (32)



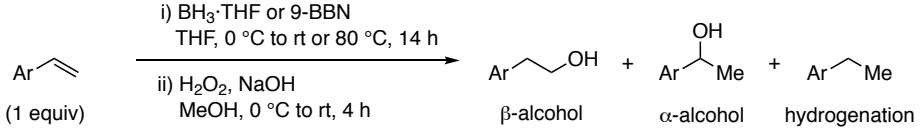
In a nitrogen-filled glovebox, to an oven-dried 2-dram vial (Thermo Scientific B7999-3) containing a magnetic stir bar was added palladium(II) acetate (3.4 mg, 0.015 mmol, 0.03 equiv), (2-biphenyl)di-*tert*-butylphosphine (JohnPhos, 6.0 mg, 0.02 mmol, 0.04 equiv), cesium carbonate (244 mg, 0.75 mmol, 1.5 equiv), PhMe (0.5 mL), and 2-(2,6-dichlorophenyl)ethan-1-ol (95.5 mg, 0.5 mmol, 1.0 equiv) in successive order. The reaction vial was capped (Thermo Scientific B7995-15 with 10/90 septa), removed from the glovebox, and inserted into a preheated silicon oil bath at 80 °C. After stirring for 22 h, the reaction mixture was

cooled to rt and quenched with water (2 mL), extracted with Et_2O (3 x 3 mL), washed with brine (10 mL), and concentrated *in vacuo*. Purification of the resulting residue *via* flash column chromatography (100% hexanes) yielded the desired product as colorless oil (59.0 mg, 0.382 mmol, 76% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.04 (tt, J = 8.0, 0.8 Hz, 1H), 6.83 (dd, J = 8.0, 0.8 Hz, 1H), 6.67 (dd, J = 8.0, 0.8 Hz, 1H), 4.61 (t, J = 8.8 Hz, 2H), 3.25 (t, J = 8.8 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.2, 130.9, 129.4, 126.2, 120.7, 107.9, 71.3, 29.6. **IR** (neat, cm^{-1}) 2972.8, 2898.0, 1606.5, 1588.2, 1478.2, 1467.4, 1450.8, 1437.1, 1236.9, 1156.1, 1139.8, 981.3, 944.6, 905.4, 761.2. **GCMS** $[M]^+$ calc for $[C_8H_7ClO]^+$ 154.0, found 154.

XII. Hydroboration/Oxidation Comparison of Vinyl Arene Substrates

Discussion. The purpose of these experiments was to compare a base-catalyzed styrene hydration approach to traditional hydroboration/oxidation protocols. Two common boranes (BH_3·THF and 9-BBN) were first employed for three control styrene substrates. Thus, styrene, 4-fluorostyrene and 4-*tert*-butylstyrene underwent high yielding hydroboration/oxidation using the general procedure described below. Next, several vinyl arenes from Table 2 were examined using the same general procedure and the results are provided in Table S7. The general experimental procedure is provided below with an example spectrum to illustrate how ^{1}H NMR yields were used to determine product distribution.

General procedure. Vinyl arene (0.2 mmol, 1.0 equiv) was added to an oven-dried 2-dram reaction vial (Thermo Scientific B7999-3) with a magnetic stir bar. The vial was capped (Thermo Scientific B7995-15 with 10/90 septa) and evacuated and filled with nitrogen three times. Anhydrous THF (0.4 mL) was added and the reaction solution was cooled to 0 °C using an ice bath. Borane solution, BH_3·THF (1.0 M solution in THF, 0.4 mL, 2.0 equiv) or 9-BBN (0.5 M solution in THF, 0.8 mL, 2.0 equiv) was then added dropwise. The reaction mixture was allowed to warm to rt or 80 °C and stirred for 14 h. After cooling the reaction mixture to 0 °C in an ice bath, MeOH (0.4 mL), aqueous NaOH (2 M, 0.95 mL, 9.5 equiv), and 30% H_2O_2 (0.14 mL, 6.0 equiv) were added successively to the reaction mixture. The reaction mixture was stirred for 4 h at rt and then dibenzyl ether (19.0 µL, 0.1 mmol, 0.5 equiv) was added as an internal standard. The reaction mixture was extracted with EtOAc (3 x 3 mL) and the organic layer was concentrated *in vacuo*. $CDCl_3$ (approximately 0.6 mL) was added to the concentrate, homogenized and transferred to an NMR tube. The product yield and distribution were determined by ^{1}H NMR spectroscopy by comparison of the product integration to the dibenzyl ether internal standard. The results are summarized in Table S7 below.



	BH_3·THF		**9-BBN**	
	0 °C to rt	0 °C to 80 °C	0 °C to rt	0 °C to 80 °C
vinyl arene	^{1}H NMR yield (%)		^{1}H NMR yield (%)	
styrene	85	75	100	100
4-fluorostyrene	71	63	77	77

4-*tert*-butylstyrene	79	83	96	97
2,6-dichlorostyrene (**20**)	15 (β), 34 (α)	-	15 (β)	63 (β), 11 (α)
4-methyl-2-nitrostyrene (**21**)	39	28	15	18
3-bromo-4-vinylpyridine (**22**)	no alcohol, hydrogenation	-	no alcohol, hydrogenation	-

Table S7. Comparison of multiple hydroboration/oxidation methods for the formal anti-Markovnikov hydration of various vinyl arenes (β = *liner alcohol,* α = *branch alcohol*).

Example NMR spectra interpretation for hydroboration/oxidation of 4-methyl-2-nitrostyrene (21). Provided below is an example ^{1}H NMR spectrum of the crude reaction mixture for the hydroboration/oxidation of 4-methyl-2-nitrostyrene (**21**) using BH_3·THF (0 °C to rt). Integration of dibenzyl ether chemical shifts compared to alcohol methylene chemical shifts were used to determine ^{1}H NMR yields. Yields for other reaction conditions and styrenes were determined analogously.

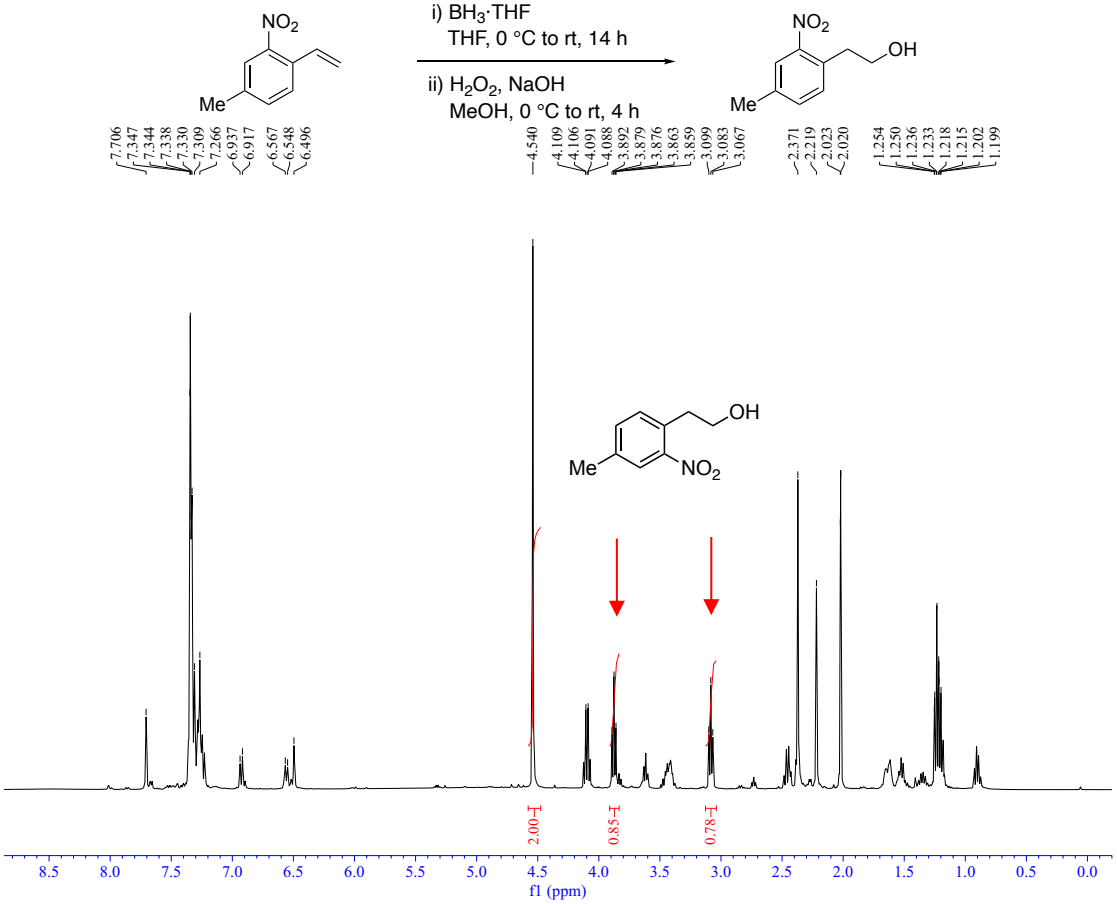
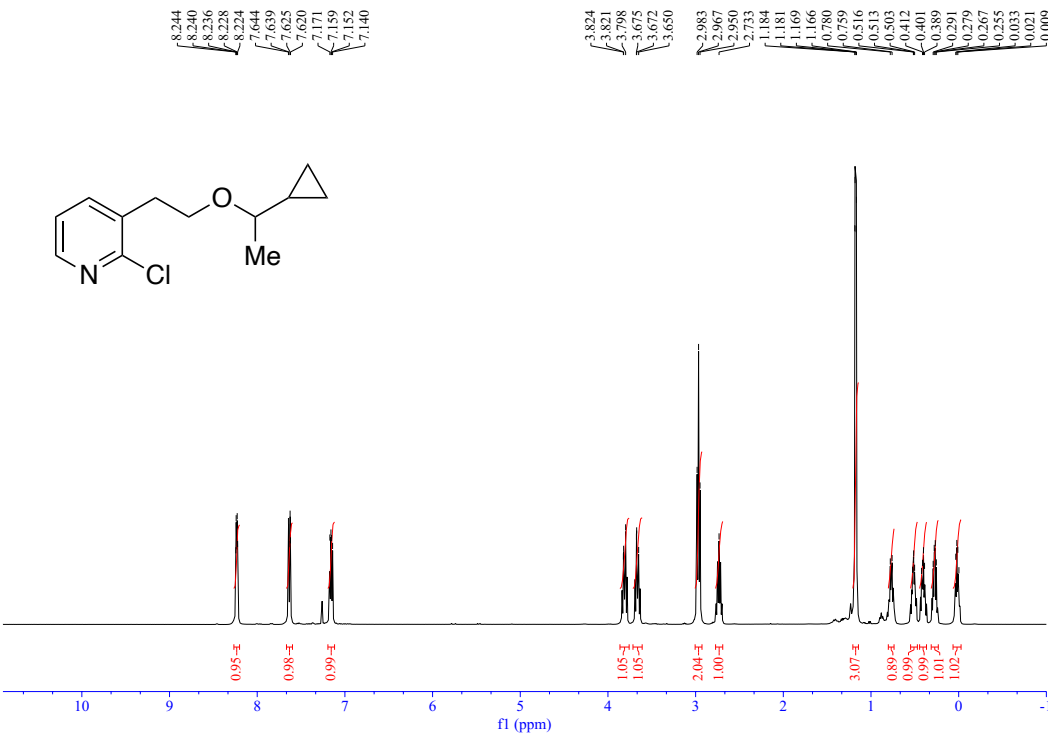


Figure S1. Example NMR spectrum for the hydroboration/oxidation of 4-methyl 2-nitrostyrene. A 39% yield is indicated by the integration of the product triplet at 3.08 ppm.

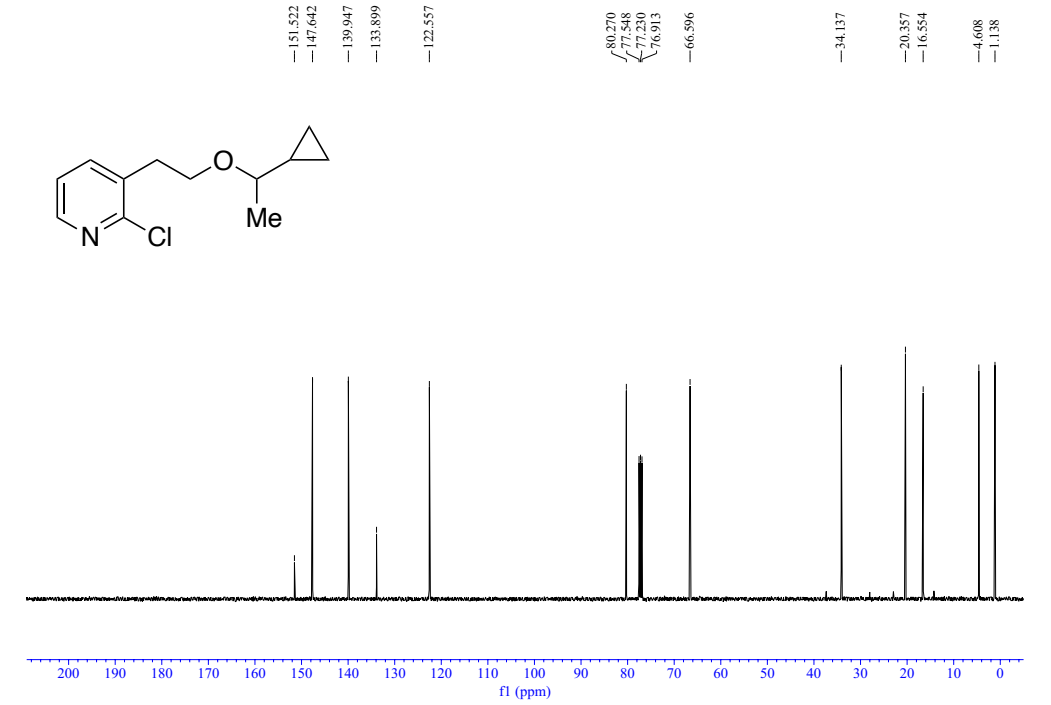
XIII. References

[1] K. Lafaye, L. Nicolas, A. Guérinot, S. Reymond, J. Cossy. *Org. Lett*. **2014**, *16*, 4972 – 4975.
[2] E. T. McBee, R. A. Sanford, *J. Am. Chem. Soc*. **1950**, *72*, 4053 – 4055.
[3] A. A. Friedman, J. Panteleev, J. Tsoung, V. Huynh, M. Lautens. *Angew. Chem. Int. Ed*. **2013**, *52*, 9755 – 9758.
[4] L. Yang, L. Shi, Q. Xing, K.-W. Huang, C. Xia, F. Li. *ACS Catal*. **2018**, *8*, 10340 – 10348.
[5] H. Lebel, M. Davi, S. Díez-González, S. P. Nolan. *J. Org. Chem*. **2007**, *72*, 144 – 149.
[6] C. R. Smith, T. V. RajanBabu. *Tetrahedron* **2010**, *66*, 1102 – 1110.
[7] T. R. Puleo, A. J. Strong, J. S. Bandar. *J. Am. Chem. Soc*. **2019**, *141*, 1467 – 1472.
[8] C.-T. Yang, J. Han, J. Liu, Y. Li, F. Zhang, H.-Z. Yu, S. Hu, X. Wang. *Chem. Eur. J*. **2018**, *24*, 10324 – 10328.
[9] R. Van Hoveln, B. M. Hudson, H. B. Wedler, D. M. Bates, G. Le Gros, D. J. Tantillo, J. M. Schomaker. *J. Am. Chem. Soc*. **2015**, *137*, 5346 – 5354.
[10] Y. Yang, S. L. Buchwald. *Angew. Chem. Int. Ed*. **2014**, *53*, 8677 – 8681.
[11] M. A. Fakhfakh, X. Franck, A. Fournet, R. Hocquemiller, B. Figadère. *Tetrahedron Lett*. **2001**, *42*, 3847 – 3850.
[12] S. He, P. Li, X. Dai, H. Liu, Z. Lai, D. Xiao, C. C. McComas, C. Du, Y. Liu, J. Yin, Q. Dang, N. Zorn, X. Peng, R. P. Nargund, A. Palani. *Tetrahedron Lett*. **2017**, *58,* 1373 – 1375.
[13] M. Zhang, J. Xie, C. Zhu. *Nat Commun* **2018**, *9*, 3517.
[14] C. Luo, J. S. Bandar, *J. Am. Chem. Soc*. **2018**, *140*, 3547 – 3550.
[15] C. Luo, J. V. Alegra-Requena, S. J. Sujansky, S. P. Pajk, L. C. Gallegos, R. S. Paton, J. S. Bandar, *J. Am. Chem. Soc*. **2022**, *144*, 9586 – 9596.
[16] B. P. Fors, S. L. Buchwald. *J. Am. Chem. Soc*. **2009**, *131*, 12898 – 12899.
[17] B. Plouvier, G. N. Beatch, G. L. Jung, A. Zolotoy, T. Sheng, L. Clohs, T. D. Barrett, D. Fedida, W. Q. Wang, J. J. Zhu, Y. Liu, S. Abraham, L. Lynn, Y. Dong, R. A. Wall, M. J. A. Walker. *J. Med. Chem*. **2007**, *50*, 2818 – 2841.
[18] A. S. Norgren, S. Zhang, P. I. Arvidsson. *Org. Lett.* **2006**, *8*, 4533 – 4536.
[19] D. A. De Bie, A. Ostrowicz, G. Geurtsen, H. C. van der Plas. *Tetrahedron*, **1988**, 44, 2977 – 2983
[20] A. E. Frissen, A. T. M. Marcelis, H. C. van der Plas. *Tetrahedron Lett*. **1987**, *28*, 1589 – 1592.

XIV. Copies of NMR Spectra

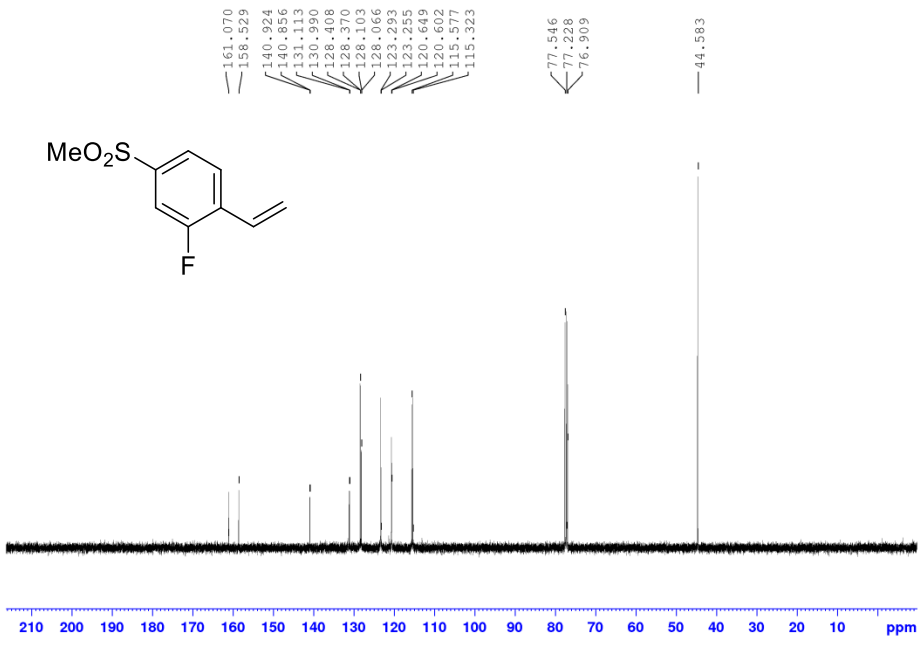


^{1}H NMR spectrum of **2** (400 MHz, $CDCl_3$)

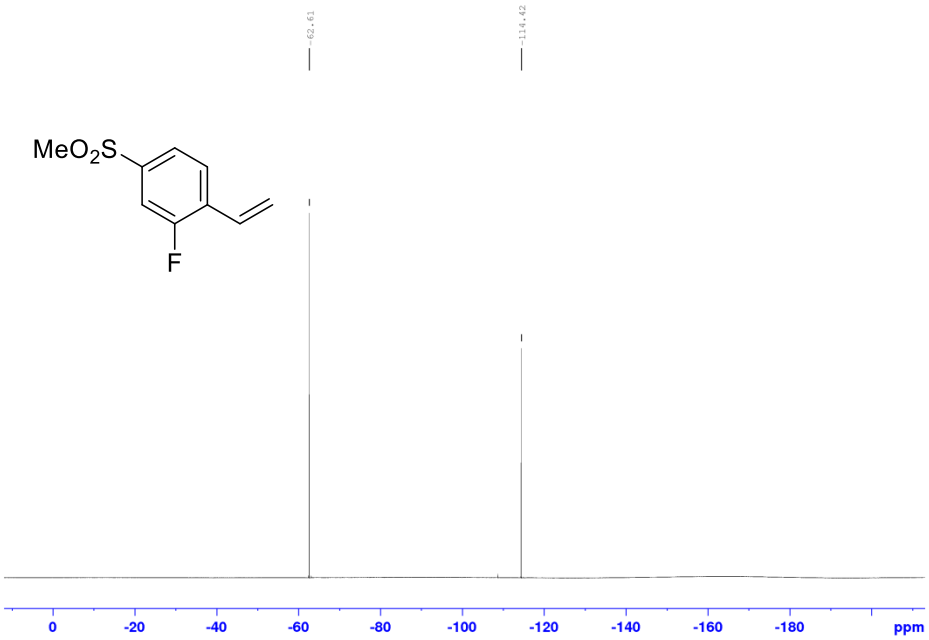


^{13}C NMR spectrum of **2** (101 MHz, $CDCl_3$)

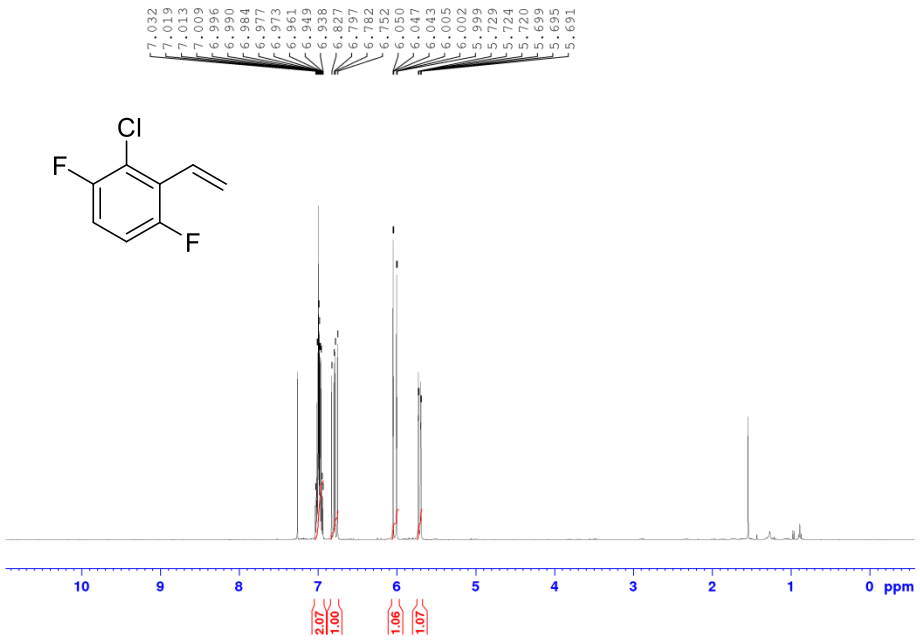
^{1}H NMR spectrum of 2-fluoro-4-(methylsulfonyl)styrene (400 MHz, $CDCl_3$)



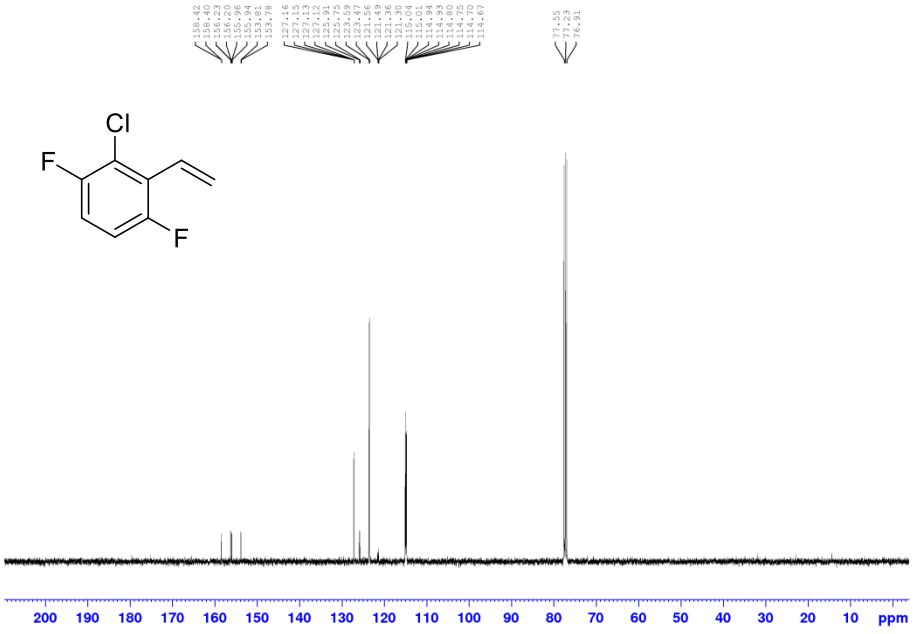
^{13}C NMR spectrum of 2-fluoro-4-(methylsulfonyl)styrene (101 MHz, $CDCl_3$)



^{19}F NMR spectrum of 2-fluoro-4-(methylsulfonyl)styrene (377 MHz, $CDCl_3$, $PhCF_3$ internal standard set at -62.61 ppm)

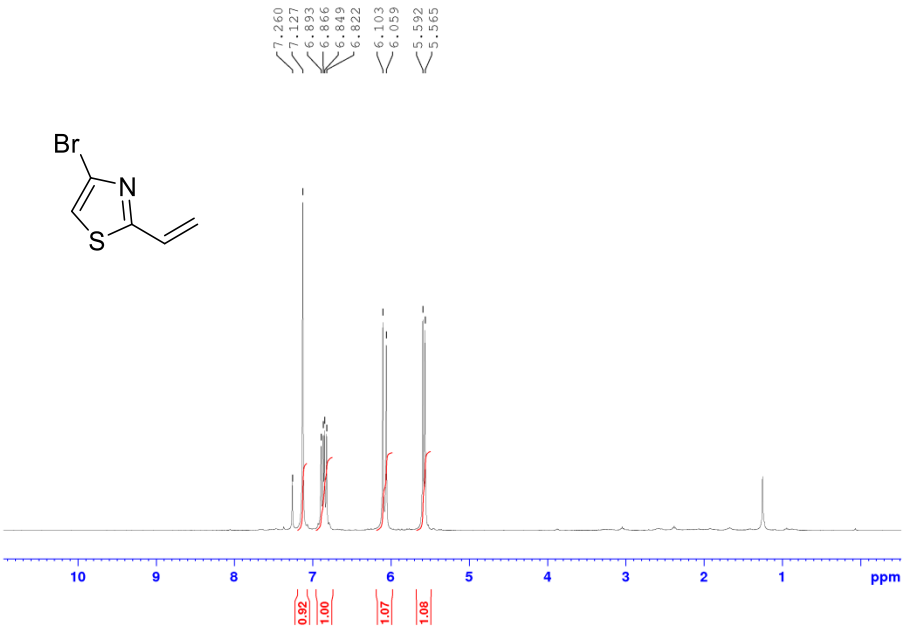


^{1}H NMR spectrum of 2-chloro-3,6-difluorostyrene (400 MHz, $CDCl_3$)

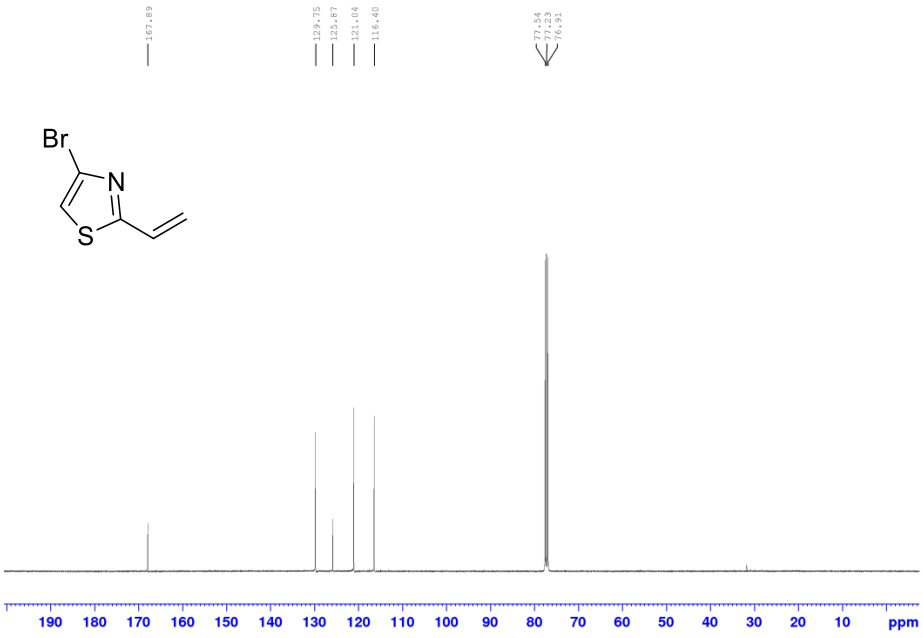


^{13}C NMR spectrum of 2-chloro-3,6-difluorostyrene (101 MHz, $CDCl_3$)

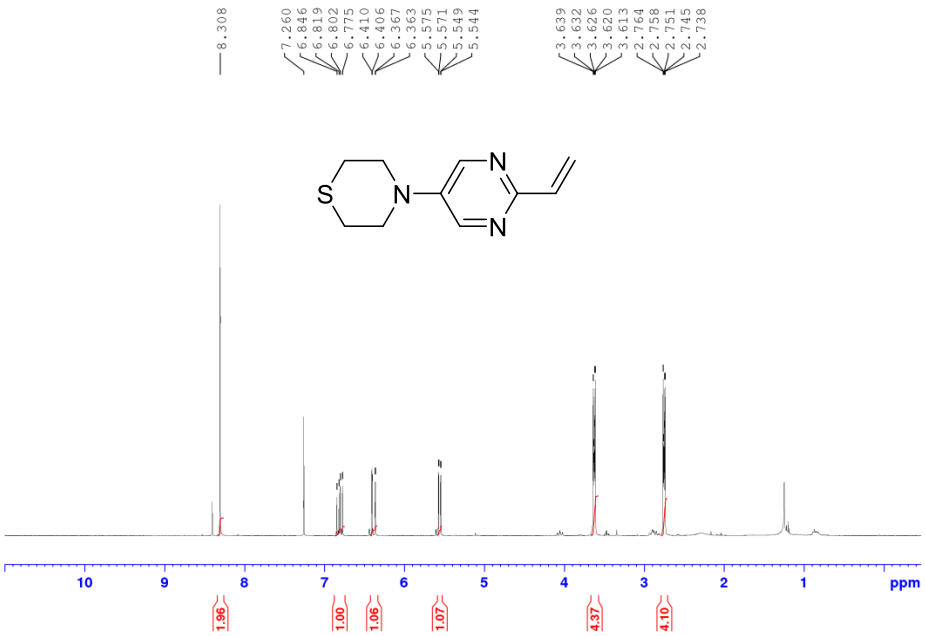
^{19}F NMR spectrum of 2-chloro-3,6-difluorostyrene (377 MHz, $CDCl_3$, $PhCF_3$ internal standard set at -62.61 ppm)



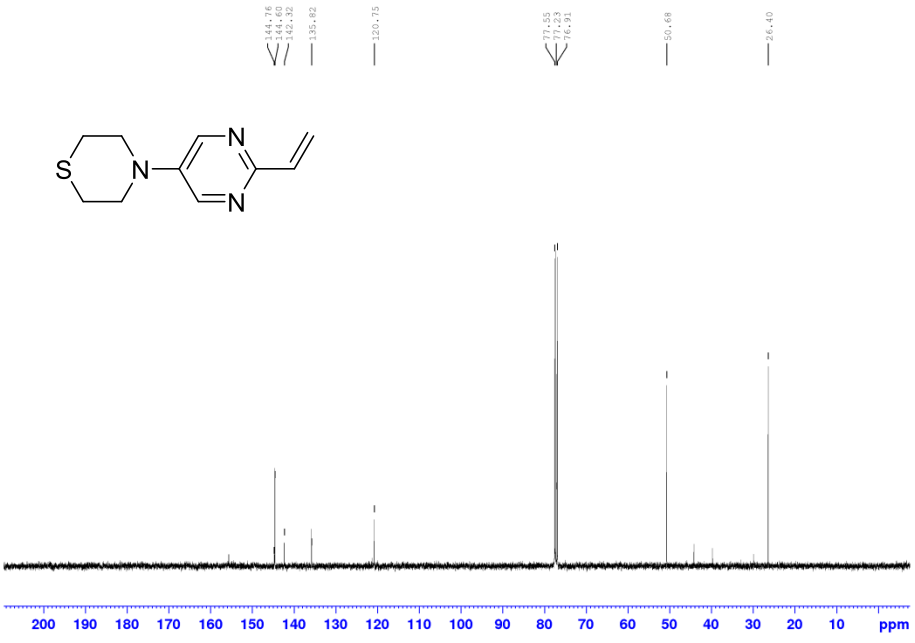
^{1}H NMR spectrum of 4-bromo-2-vinylthiazole (400 MHz, $CDCl_3$)



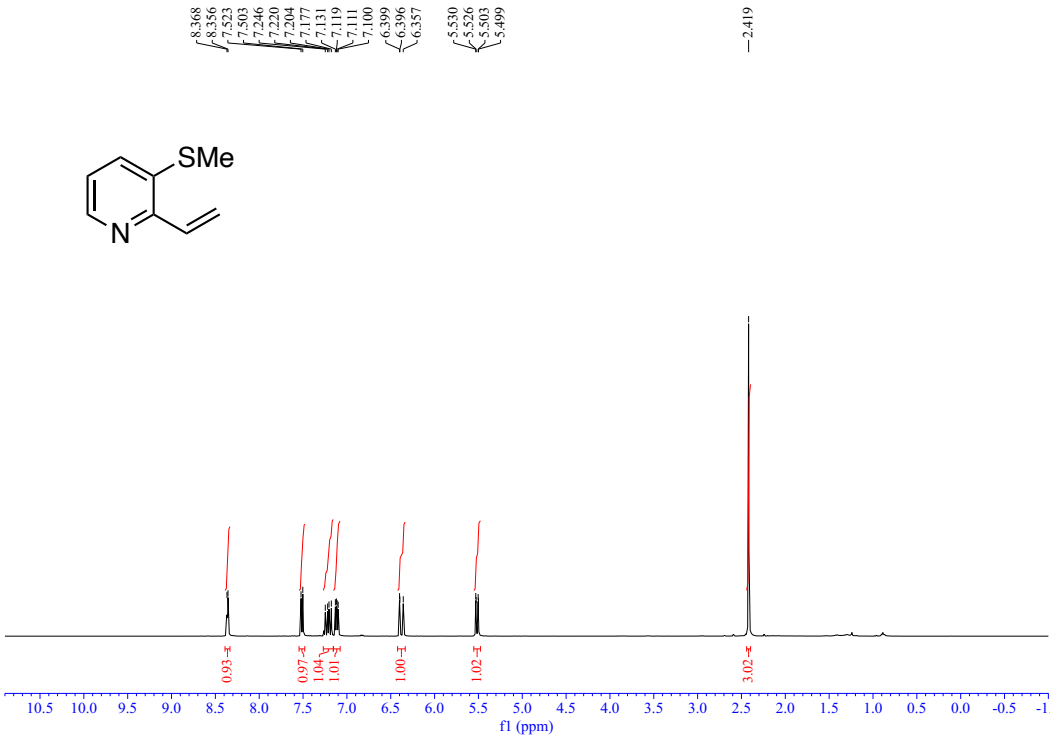
^{13}C NMR spectrum of 4-bromo-2-vinylthiazole (101 MHz, $CDCl_3$)



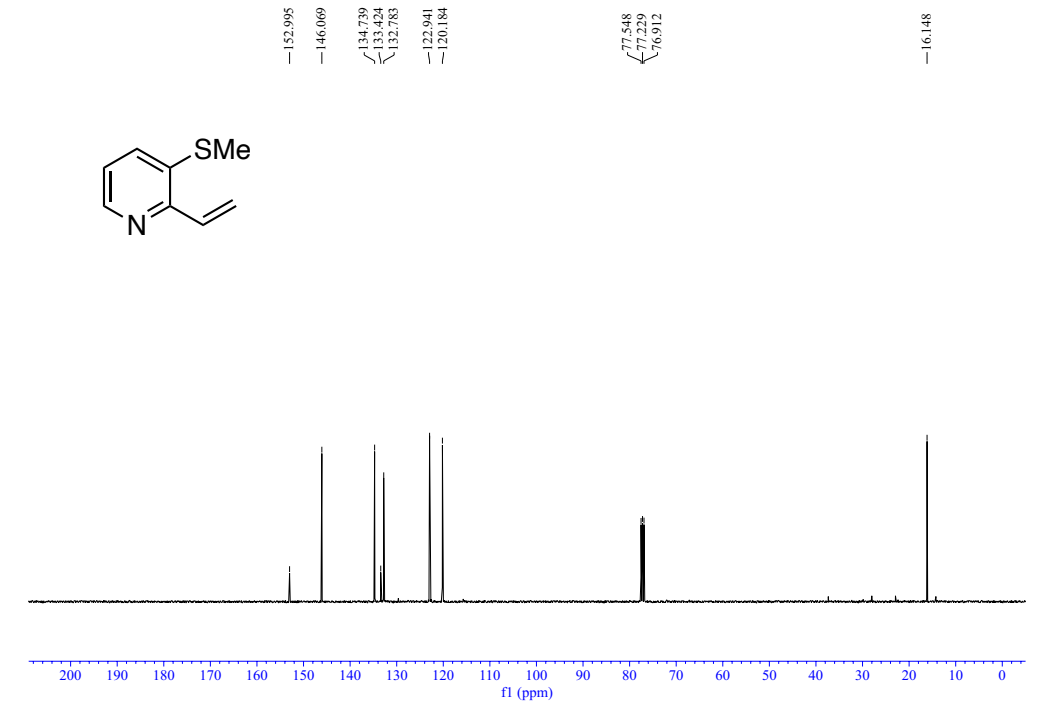
^{1}H NMR spectrum of 4-(2-vinylpyrimidin-5-yl)thiomorpholine (400 MHz, $CDCl_3$)



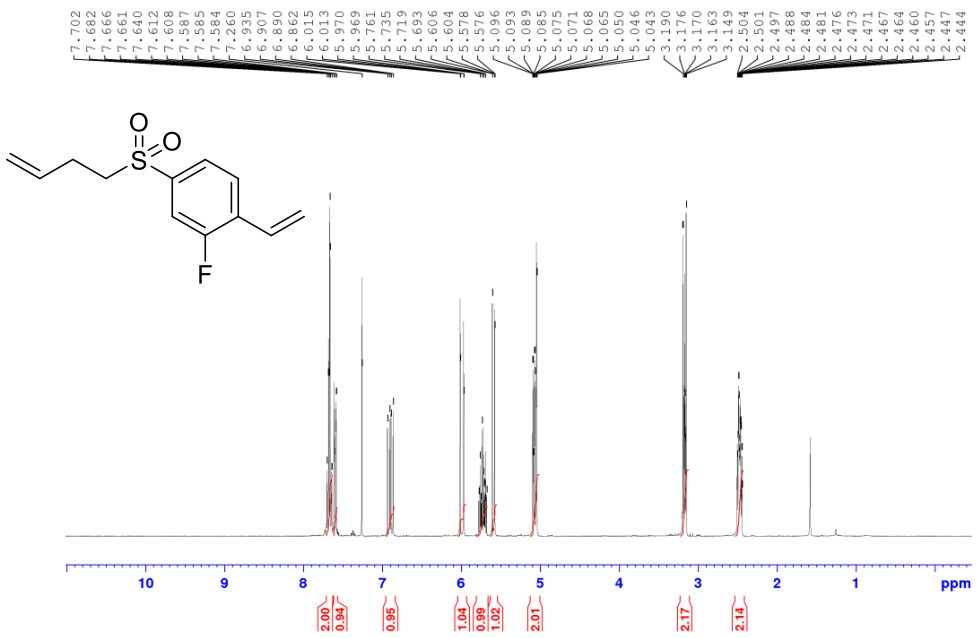
^{13}C NMR spectrum of 4-(2-vinylpyrimidin-5-yl)thiomorpholine (101 MHz, $CDCl_3$)



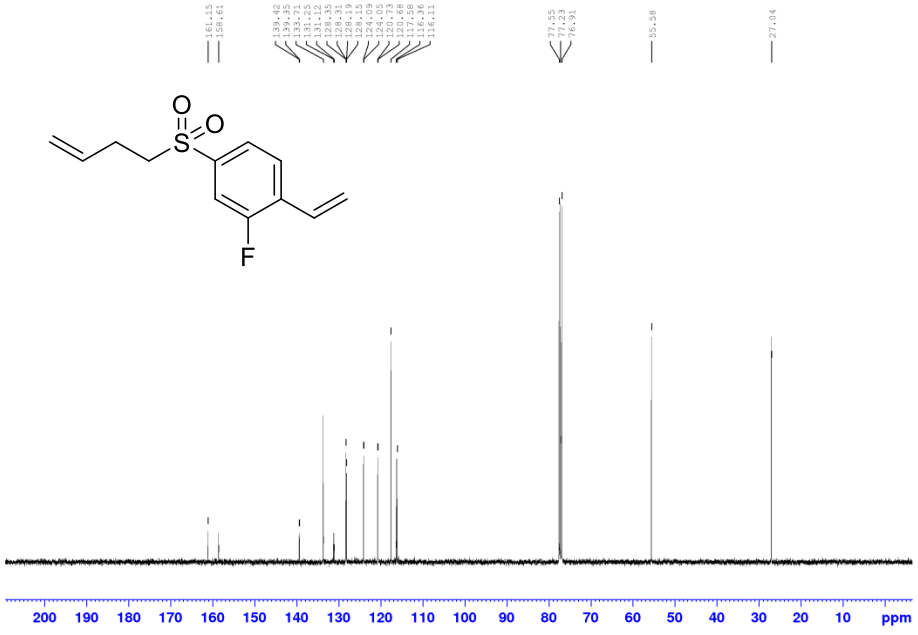
^{1}H NMR spectrum of 3-(methylthio)-2-vinylpyridine (400 MHz, $CDCl_3$)



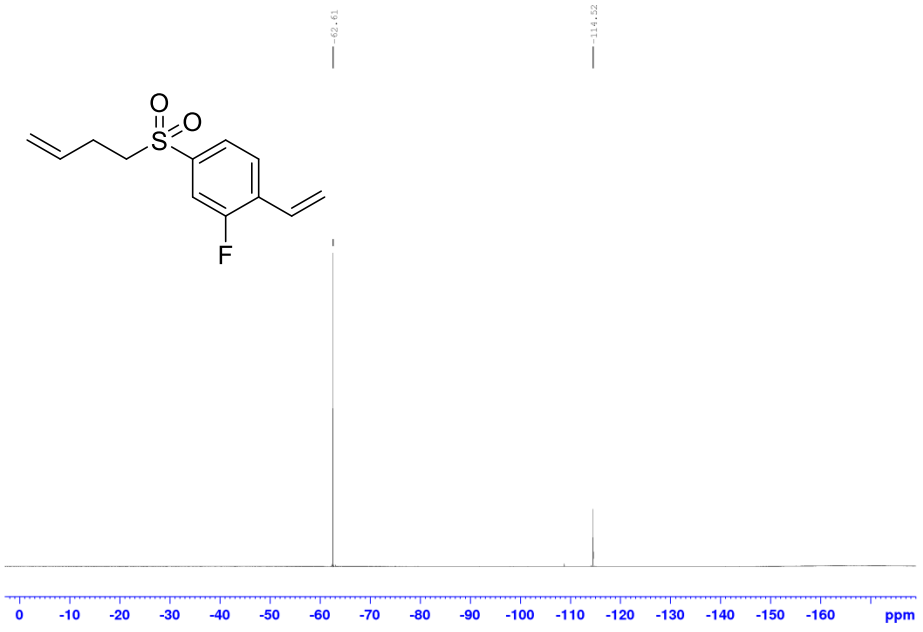
^{13}C NMR spectrum of 3-(methylthio)-2-vinylpyridine (101 MHz, $CDCl_3$)



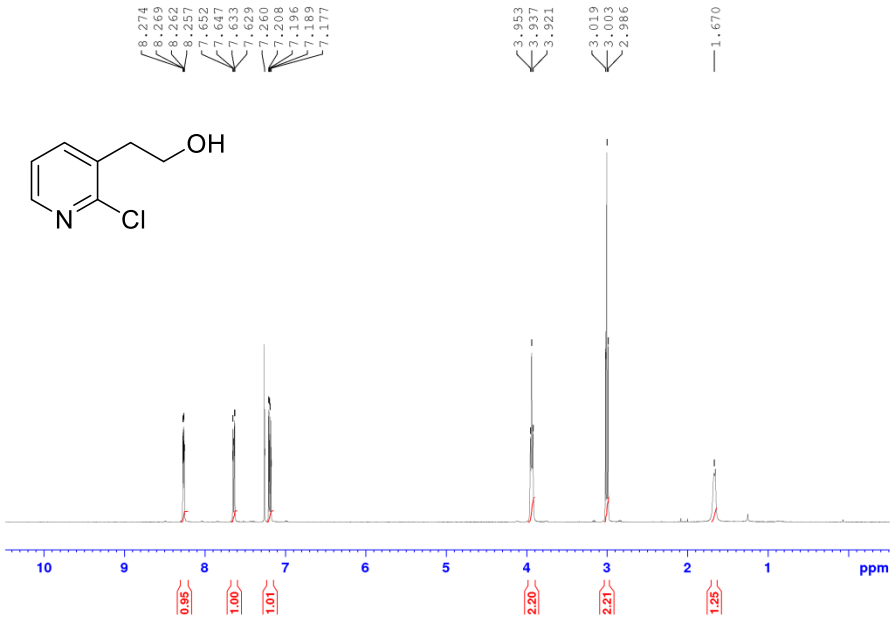
^{1}H NMR spectrum of 4-(but-3-en-1-ylsulfonyl)-2-fluoro-1-vinylbenzene (400 MHz, $CDCl_3$)



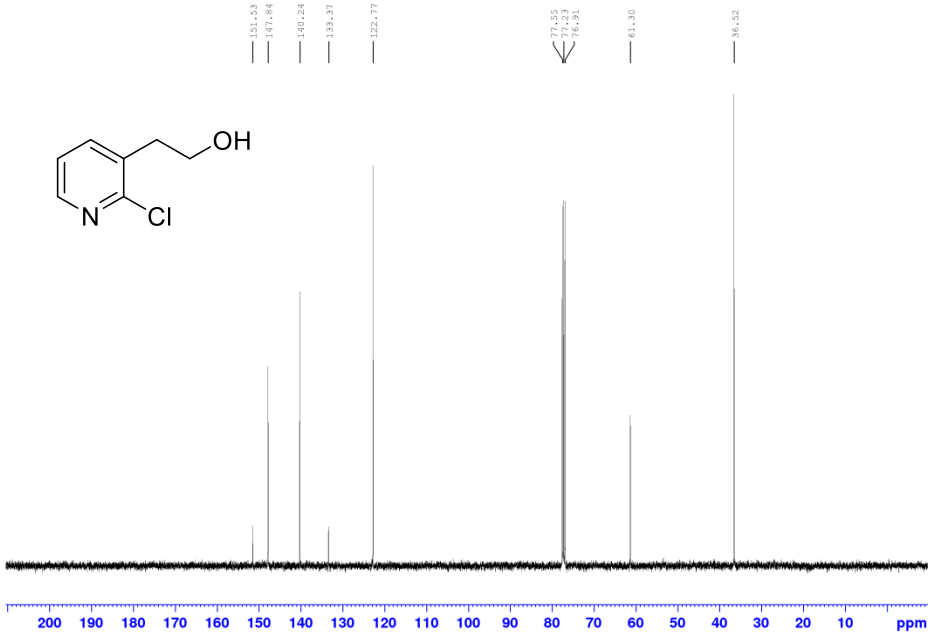
^{13}C NMR spectrum of 4-(but-3-en-1-ylsulfonyl)-2-fluoro-1-vinylbenzene (101 MHz, $CDCl_3$)



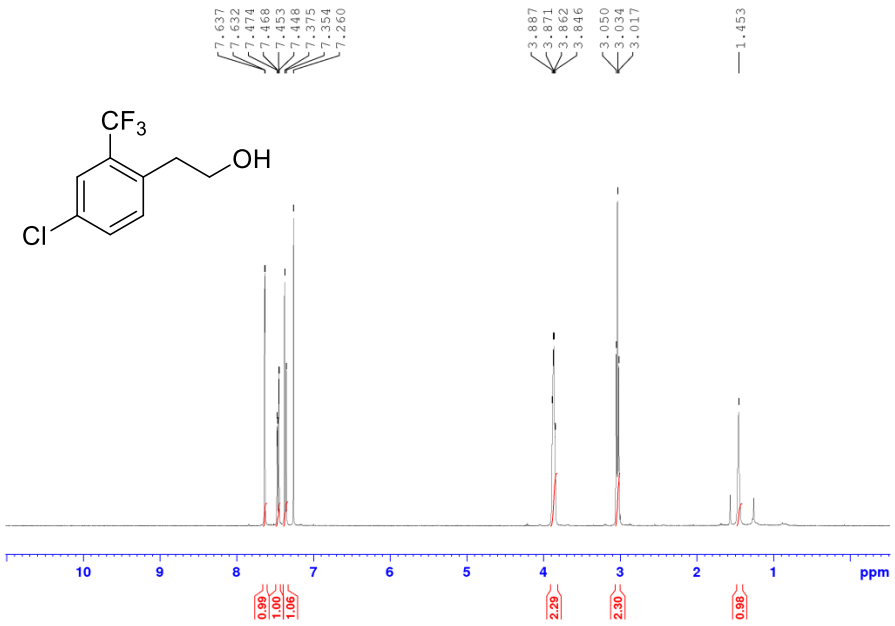
^{19}F NMR spectrum of 4-(but-3-en-1-ylsulfonyl)-2-fluoro-1-vinylbenzene (377 MHz, $CDCl_3$, $PhCF_3$ internal standard set at -62.61 ppm)



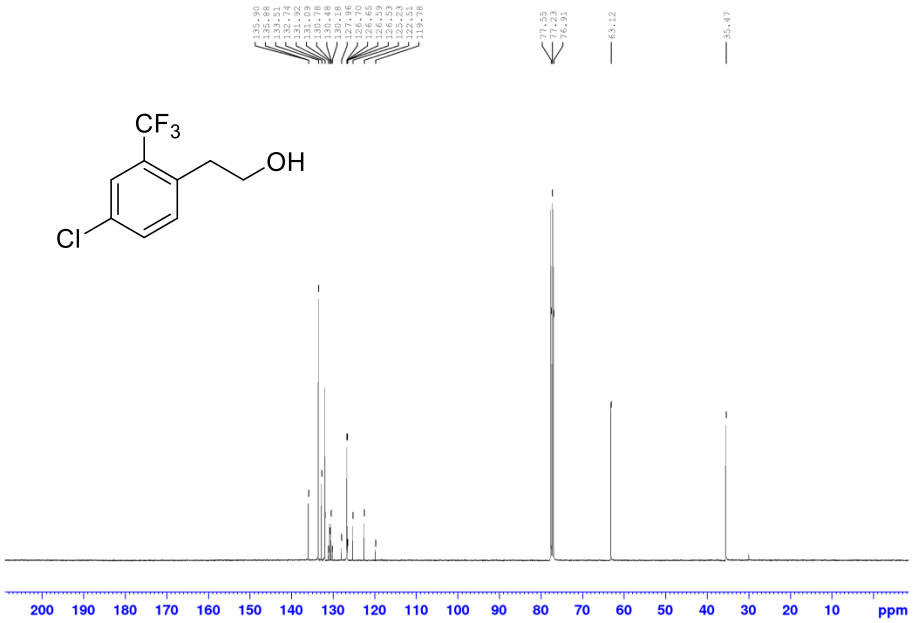
^{1}H NMR spectrum of **3** (400 MHz, $CDCl_3$)



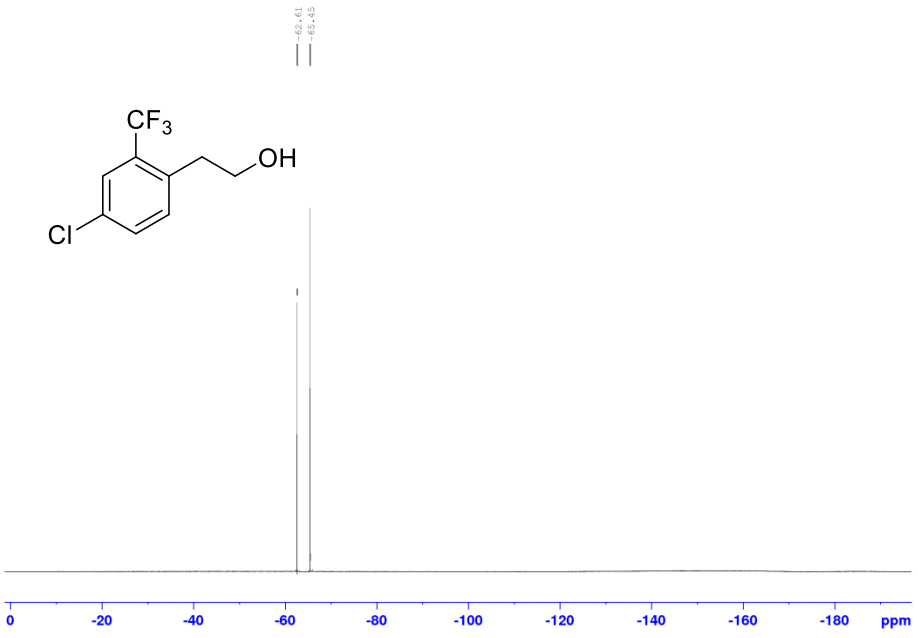
^{13}C NMR spectrum of **3** (101 MHz, $CDCl_3$)



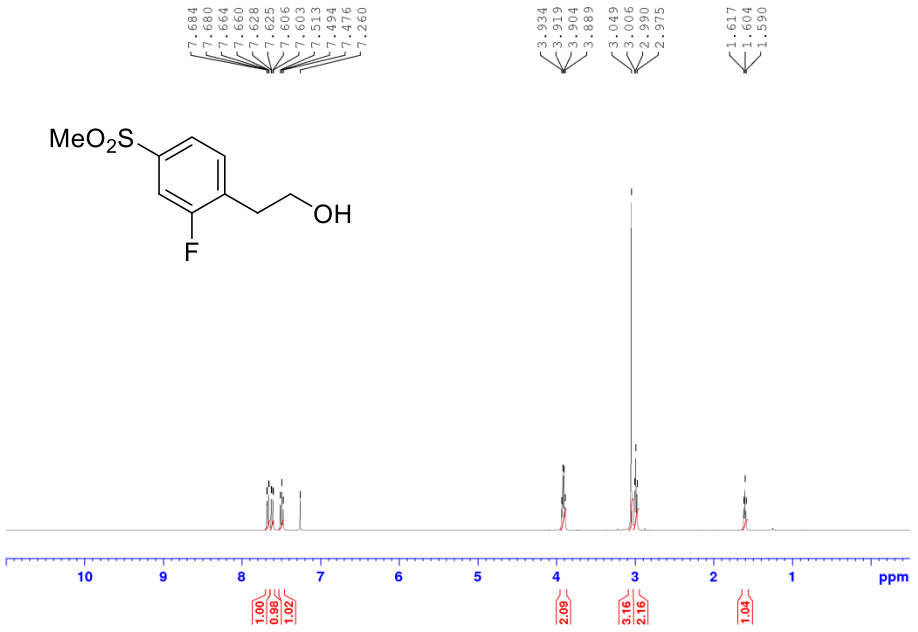
^{1}H NMR spectrum of **5** (400 MHz, $CDCl_3$)



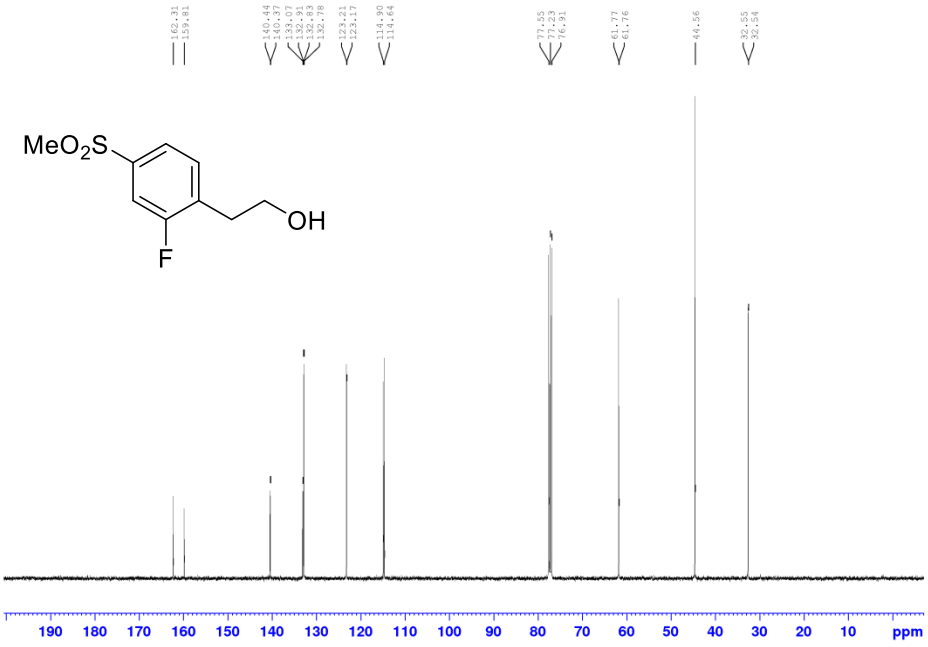
^{13}C NMR spectrum of **5** (101 MHz, $CDCl_3$)



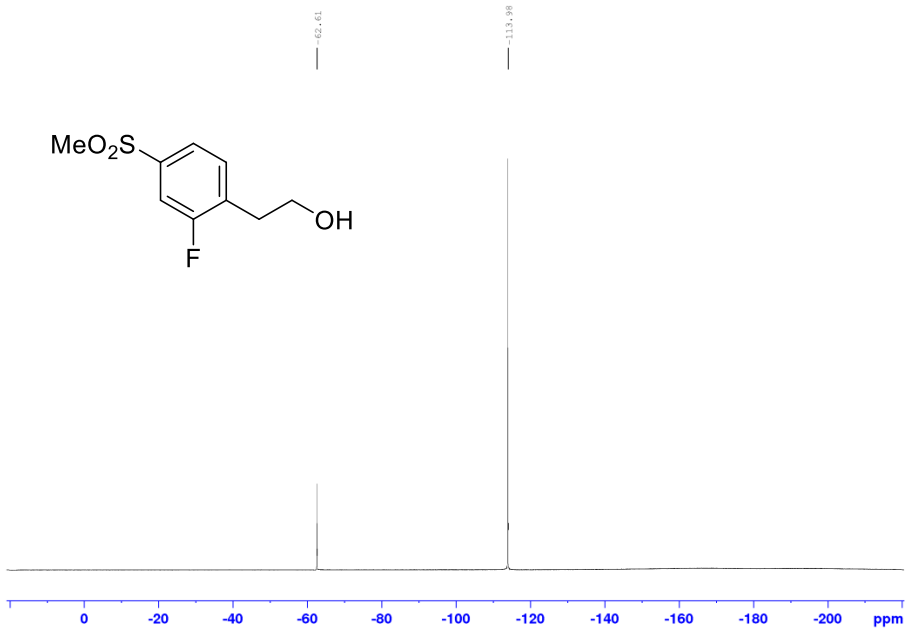
^{19}F NMR spectrum of **5** (377 MHz, $CDCl_3$, $PhCF_3$ internal standard set at -62.61 ppm)



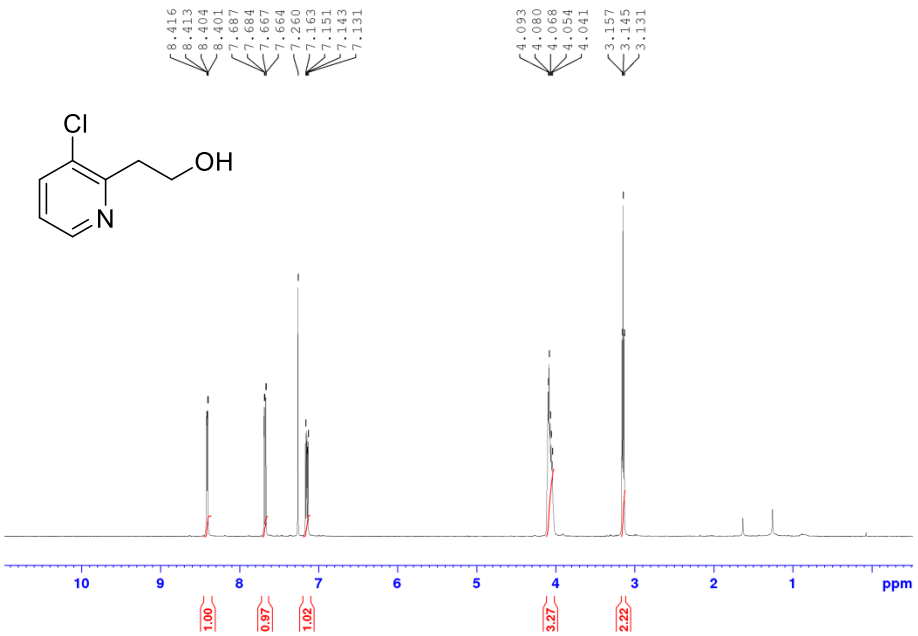
^{1}H NMR spectrum of **6** (400 MHz, $CDCl_3$)



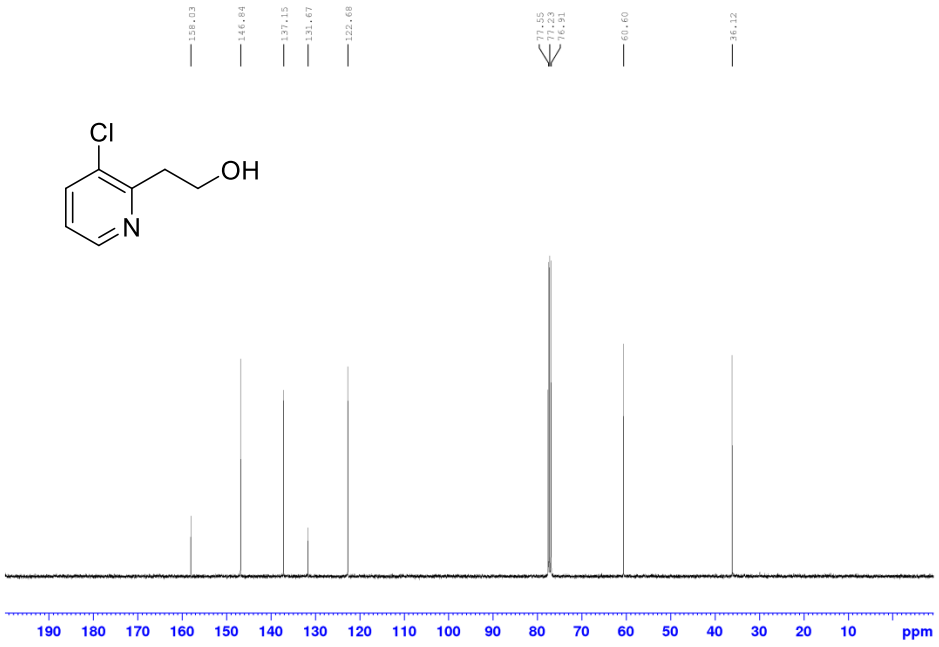
^{13}C NMR spectrum of **6** (101 MHz, $CDCl_3$)



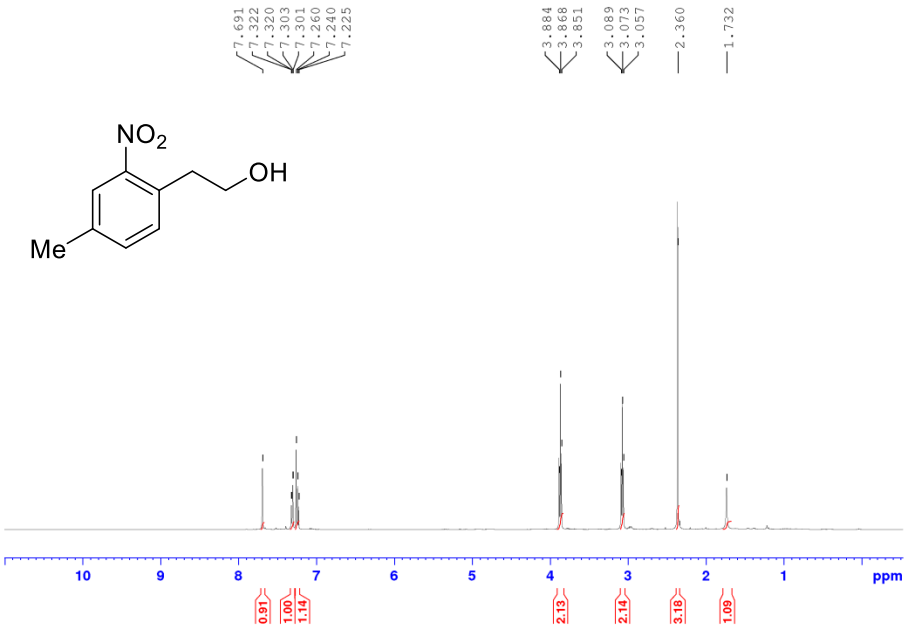
^{19}F NMR spectrum of **6** (377 MHz, $CDCl_3$, $PhCF_3$ internal standard set at -62.61 ppm)



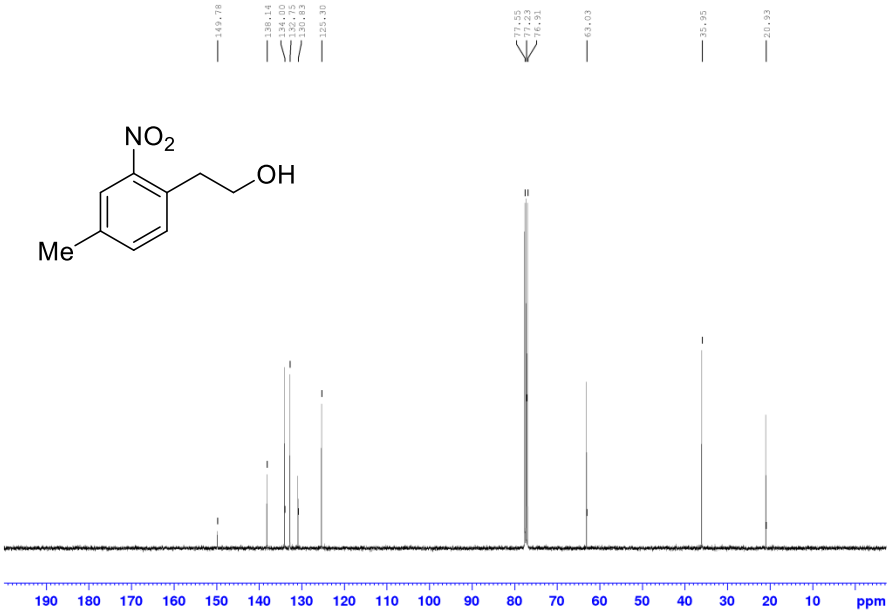
^{1}H NMR spectrum of **7** (400 MHz, $CDCl_3$)



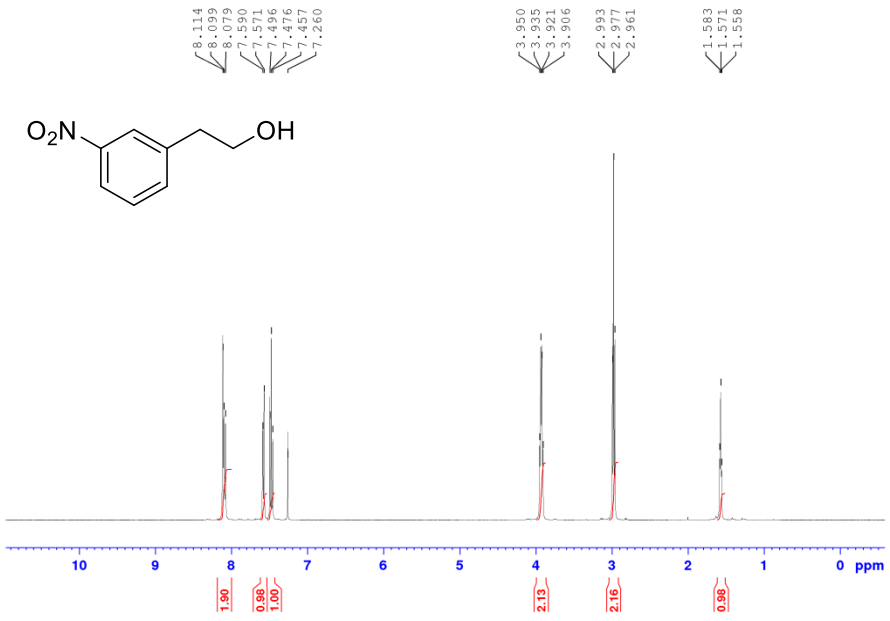
^{13}C NMR spectrum of **7** (101 MHz, $CDCl_3$)



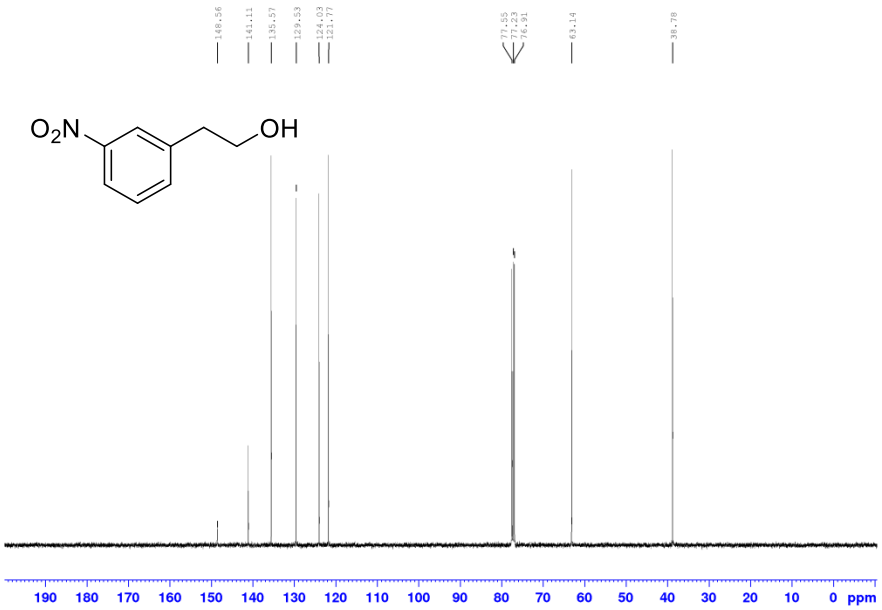
^{1}H NMR spectrum of **8** (400 MHz, $CDCl_3$)



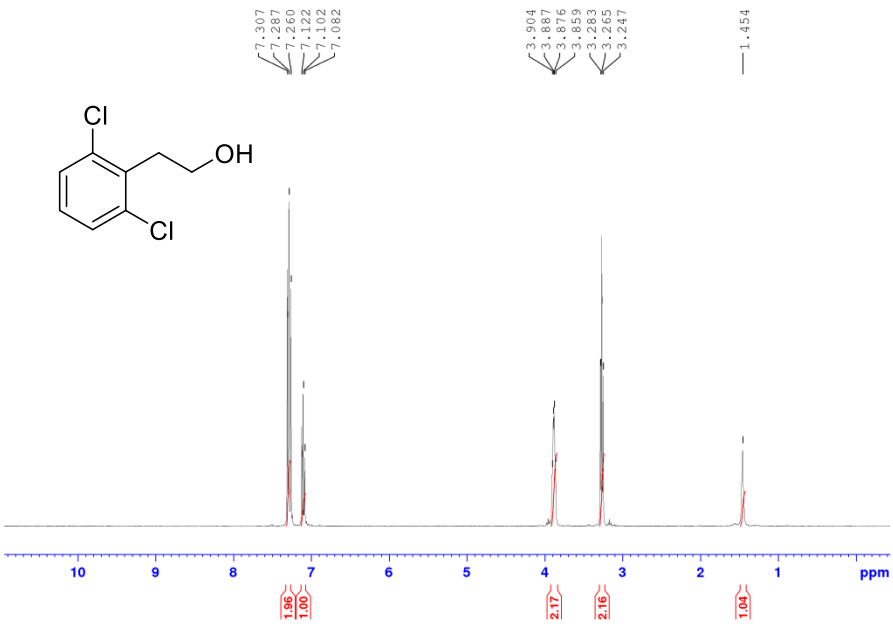
^{13}C NMR spectrum of **8** (101 MHz, $CDCl_3$)



^{1}H NMR spectrum of **9** (400 MHz, $CDCl_3$)

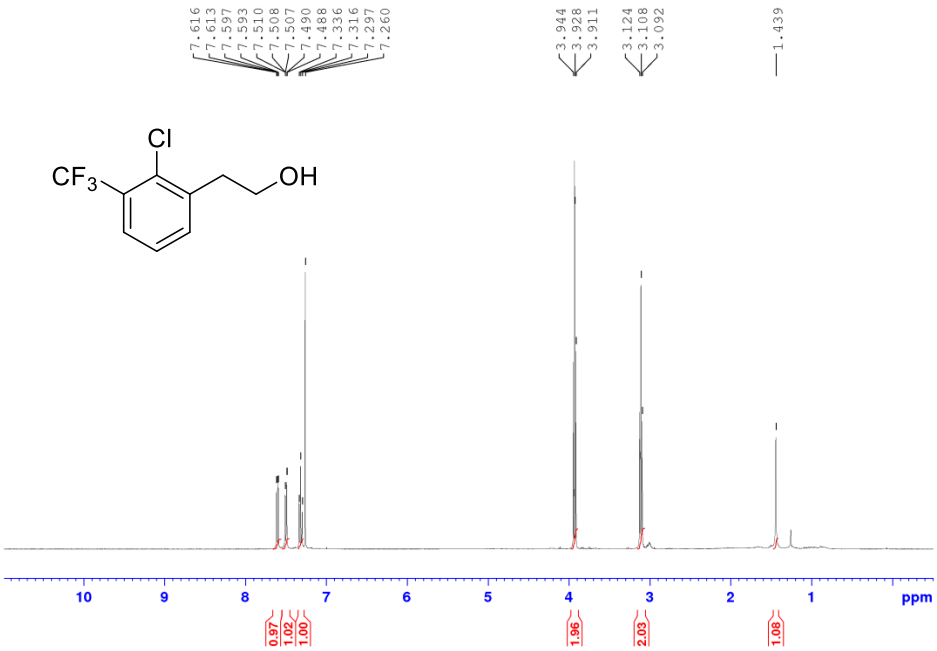


^{13}C NMR spectrum of **9** (101 MHz, $CDCl_3$)

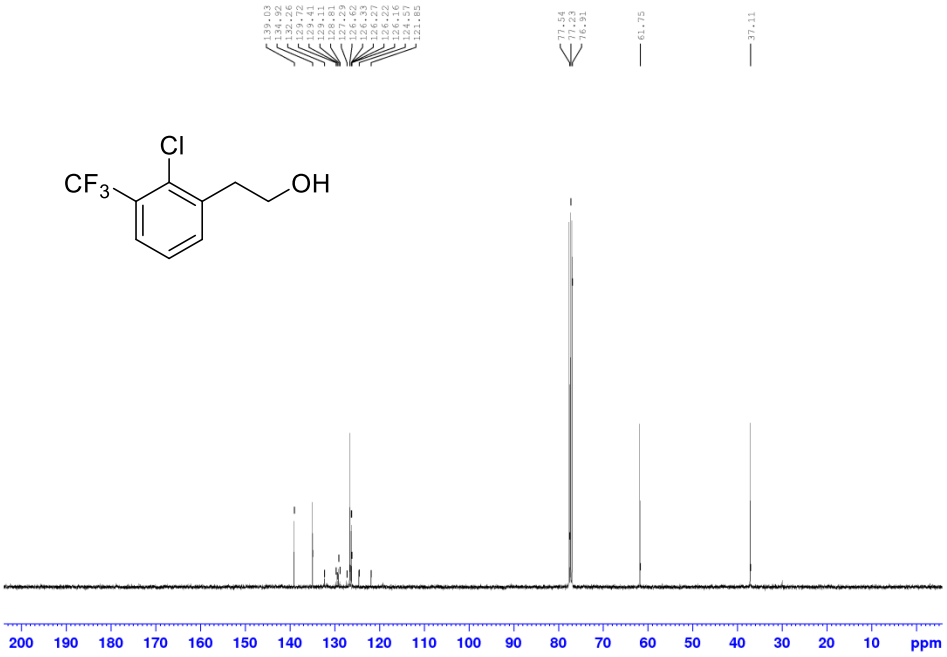


^{1}H NMR spectrum of **10** (400 MHz, $CDCl_3$)

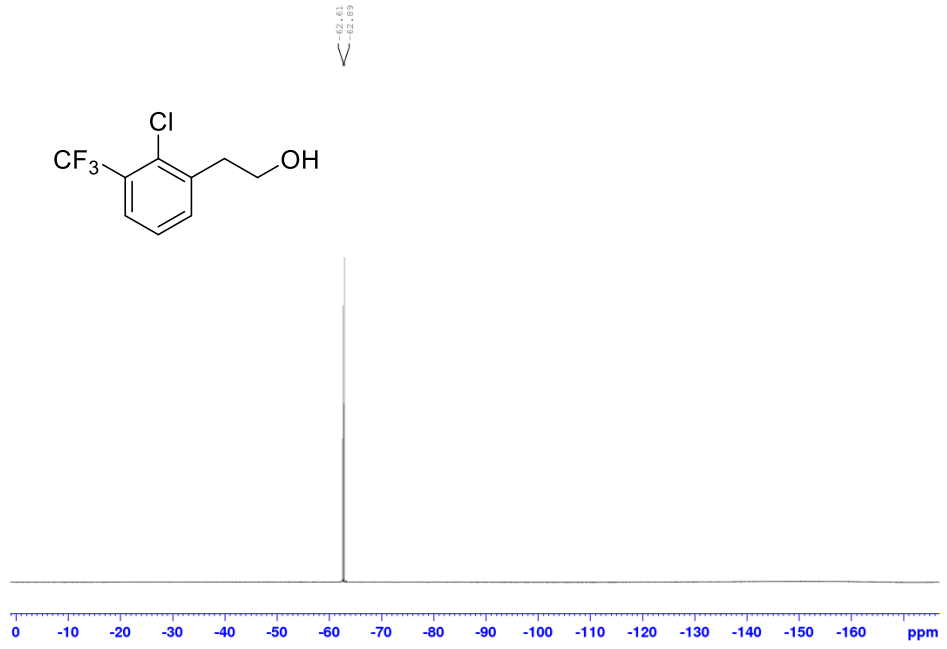
^{13}C NMR spectrum of **10** (101 MHz, $CDCl_3$)



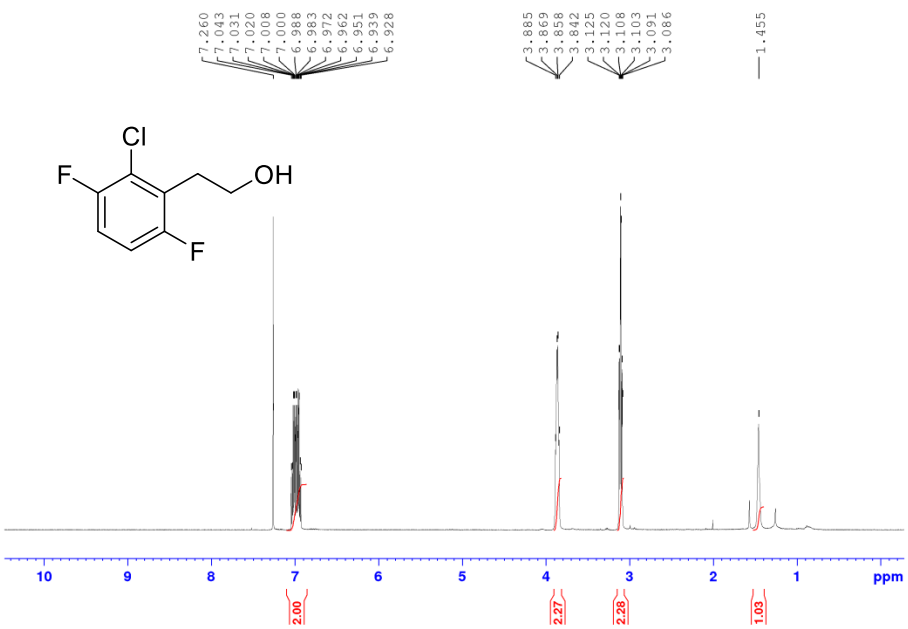
^{1}H NMR spectrum of **11** (400 MHz, $CDCl_3$)



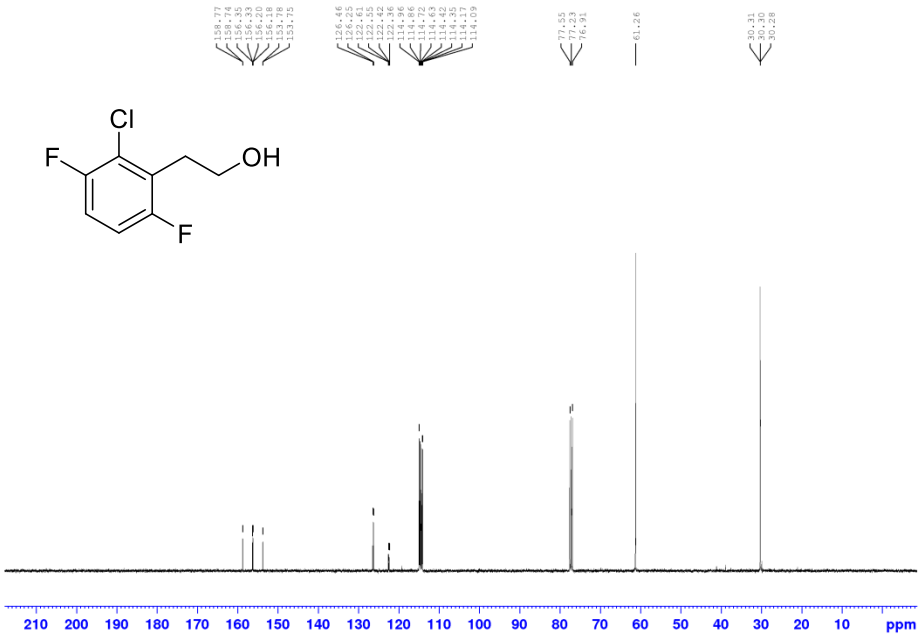
^{13}C NMR spectrum of **11** (101 MHz, $CDCl_3$)



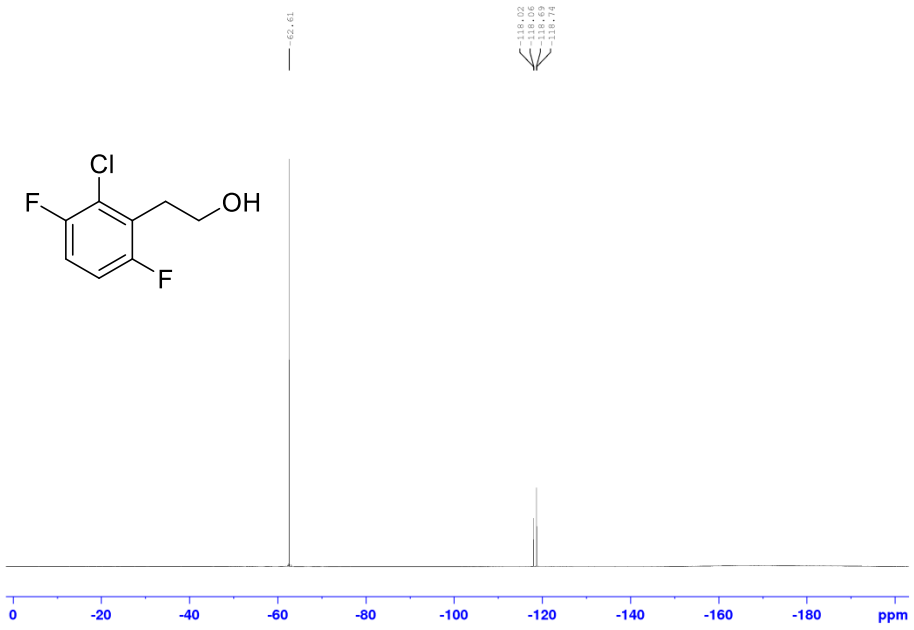
^{19}F NMR spectrum of **11** (377 MHz, $CDCl_3$, $PhCF_3$ internal standard set at -62.61 ppm)



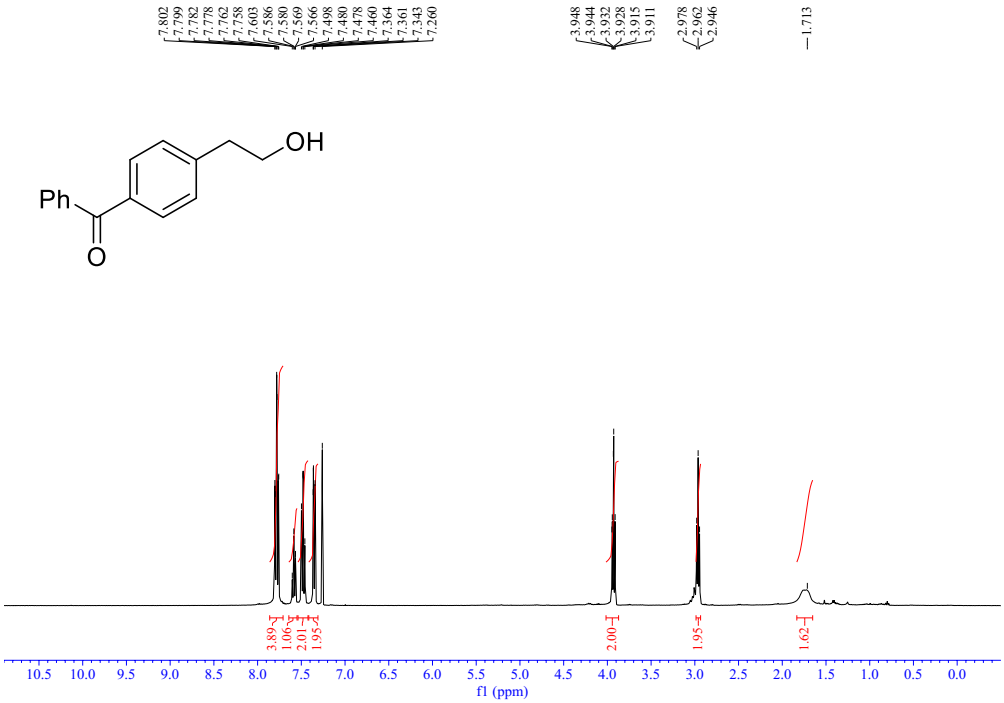
^{1}H NMR spectrum of **12** (400 MHz, $CDCl_3$)



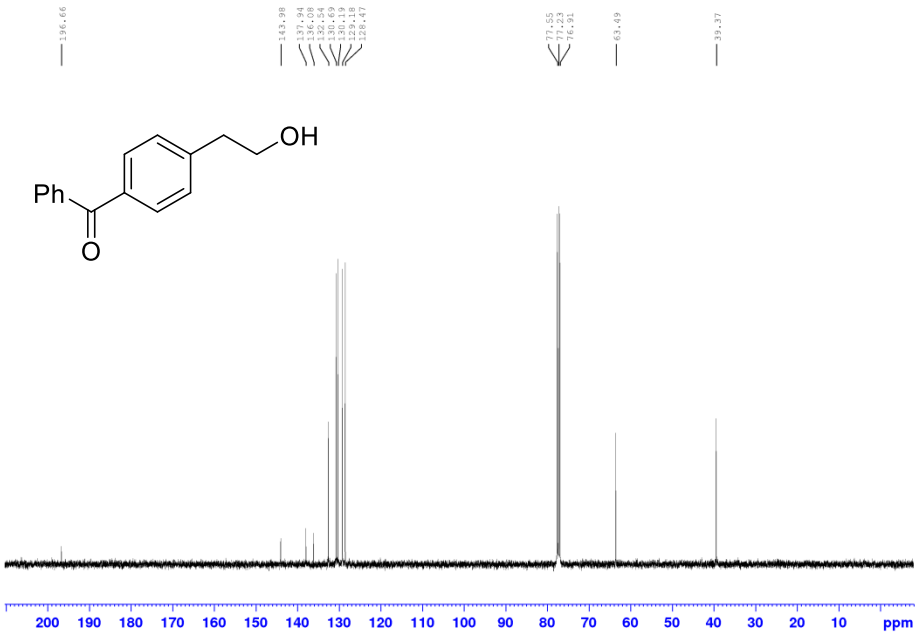
^{13}C NMR spectrum of **12** (101 MHz, $CDCl_3$)



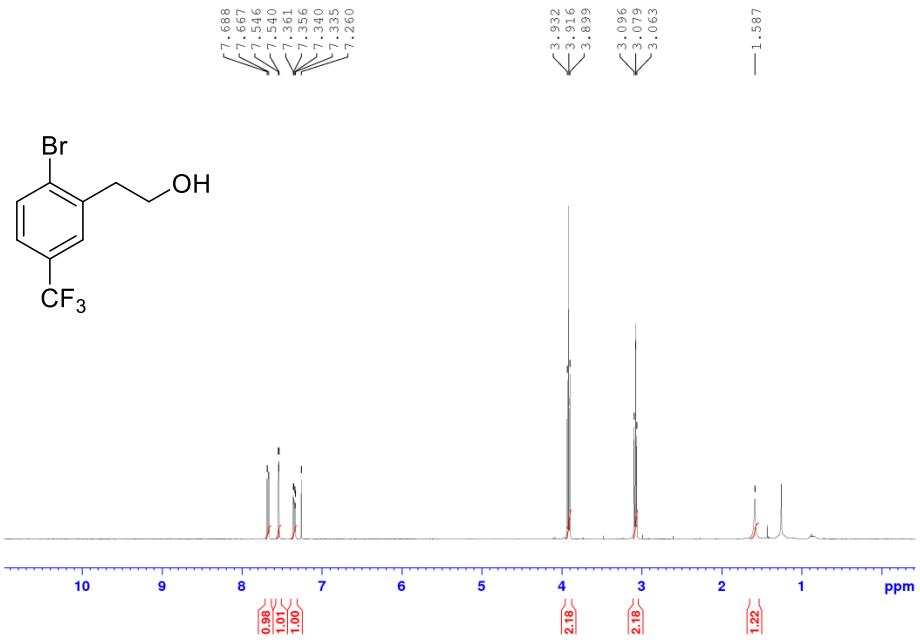
^{19}F NMR spectrum of **12** (377 MHz, $CDCl_3$, $PhCF_3$ internal standard set at -62.61 ppm)



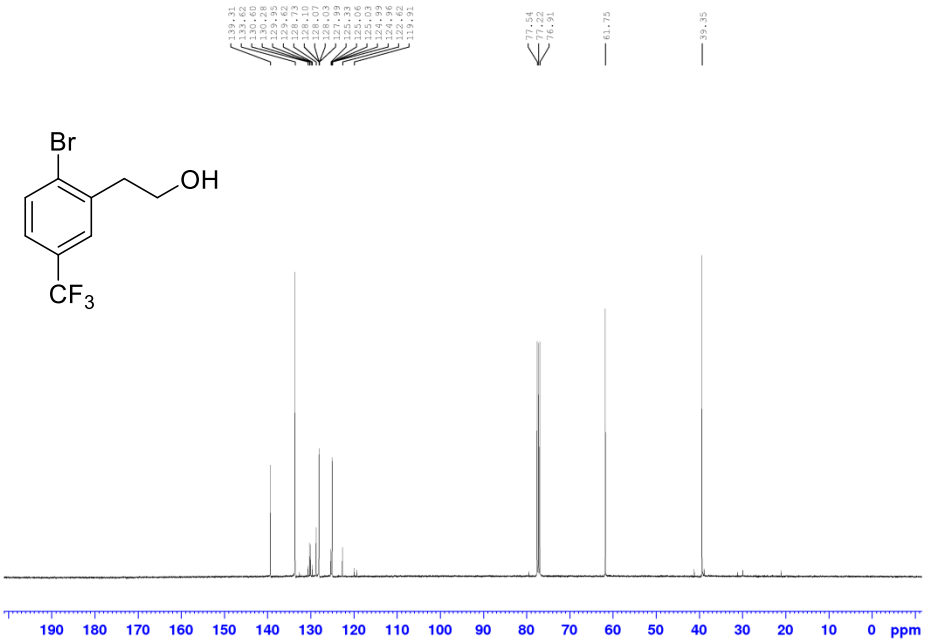
^{1}H NMR spectrum of **13** (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of **13** (101 MHz, $CDCl_3$)

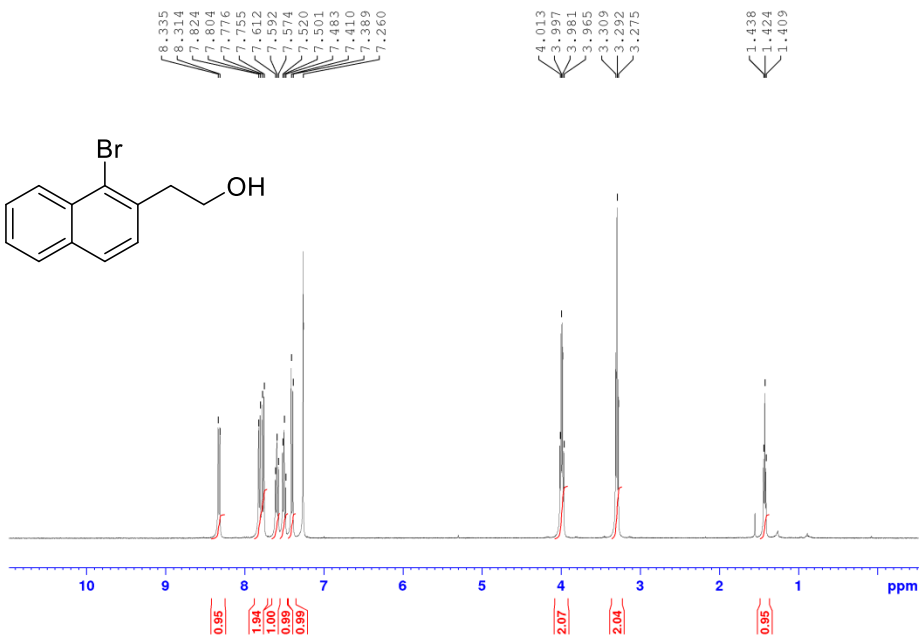


^{1}H NMR spectrum of **14** (400 MHz, $CDCl_3$)

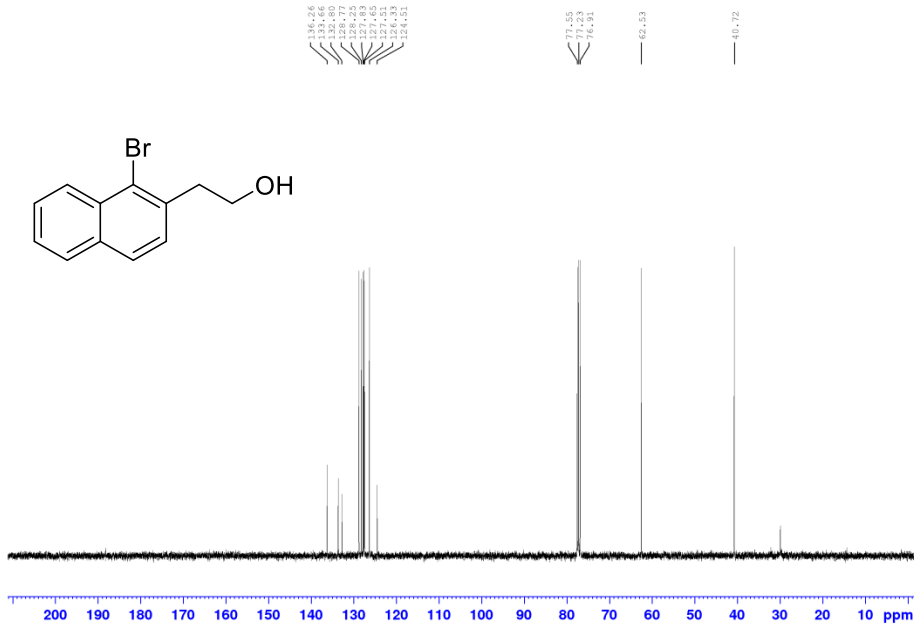


^{13}C NMR spectrum of **14** (101 MHz, $CDCl_3$)

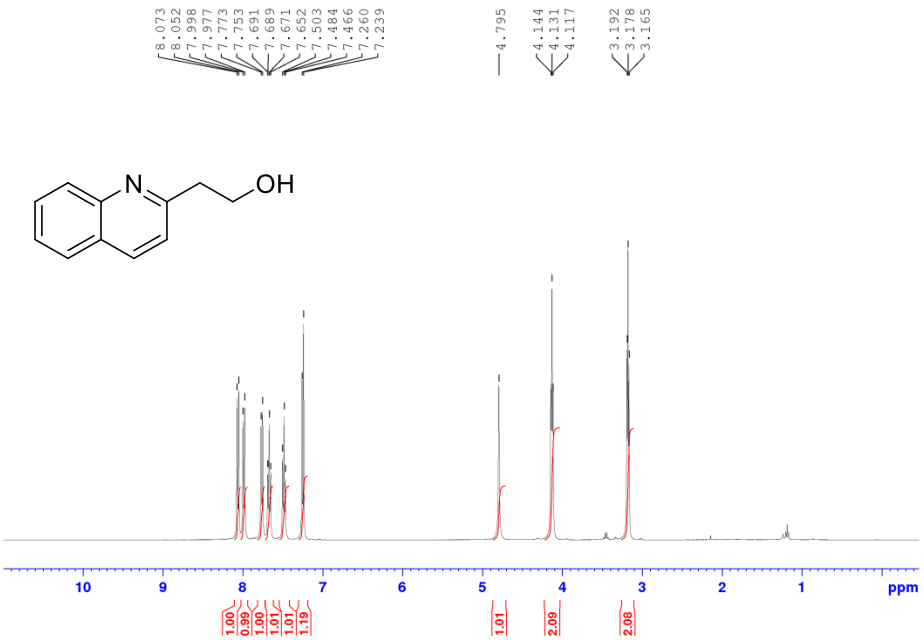
^{19}F NMR spectrum of **14** (377 MHz, $CDCl_3$, $PhCF_3$ internal standard set at -62.61 ppm)



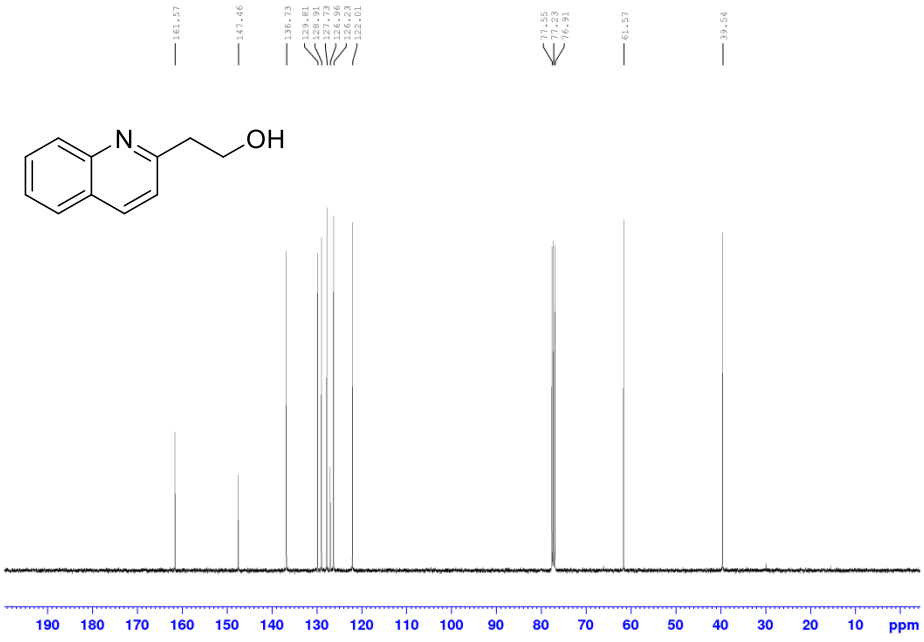
^{1}H NMR spectrum of **15** (400 MHz, $CDCl_3$)



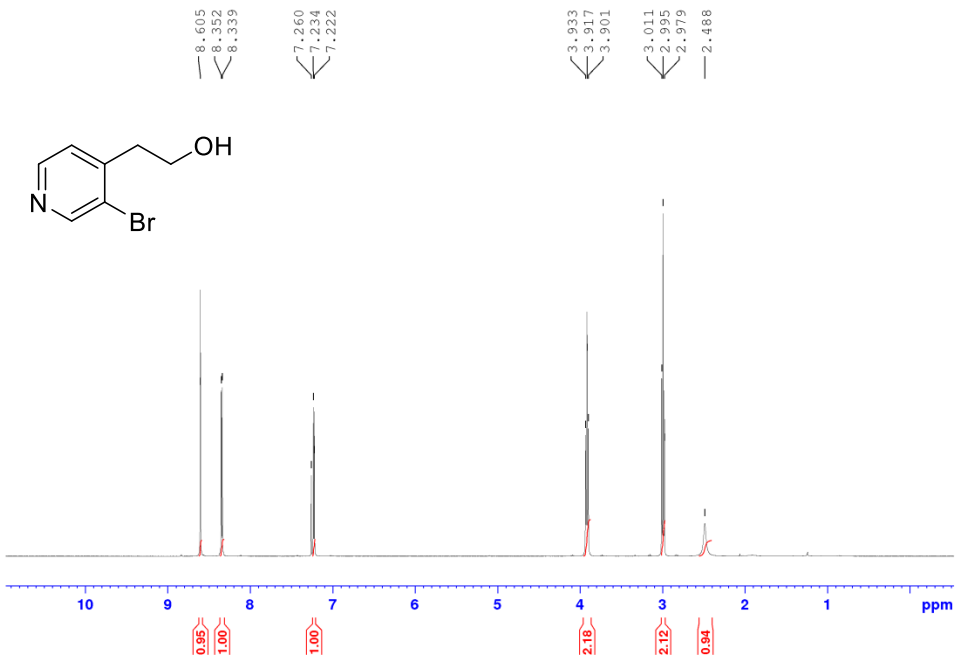
^{13}C NMR spectrum of **15** (101 MHz, $CDCl_3$)



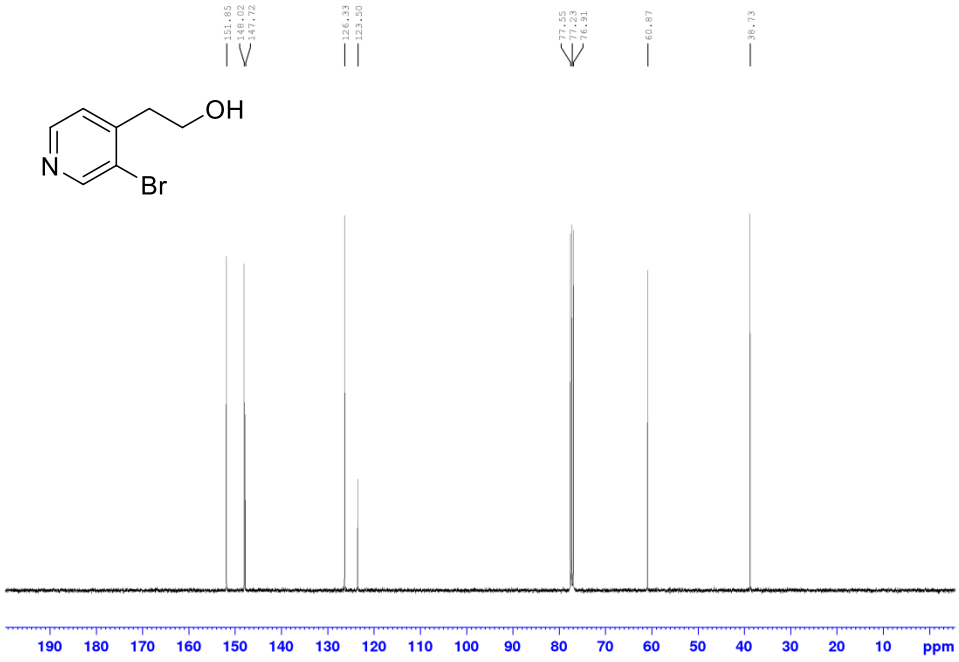
^{1}H NMR spectrum of **16** (400 MHz, $CDCl_3$)



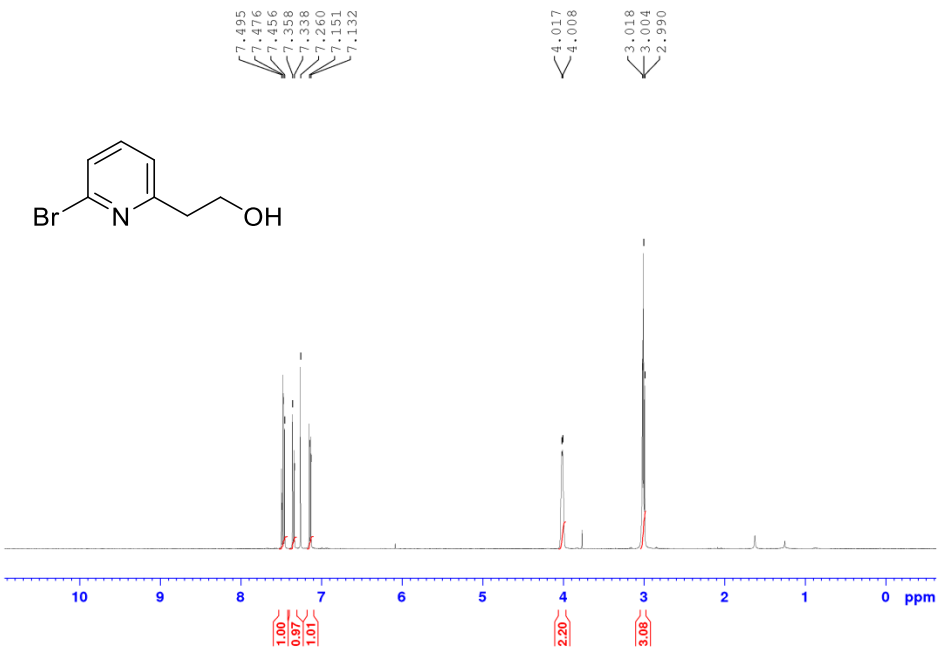
^{13}C NMR spectrum of **16** (101 MHz, $CDCl_3$)



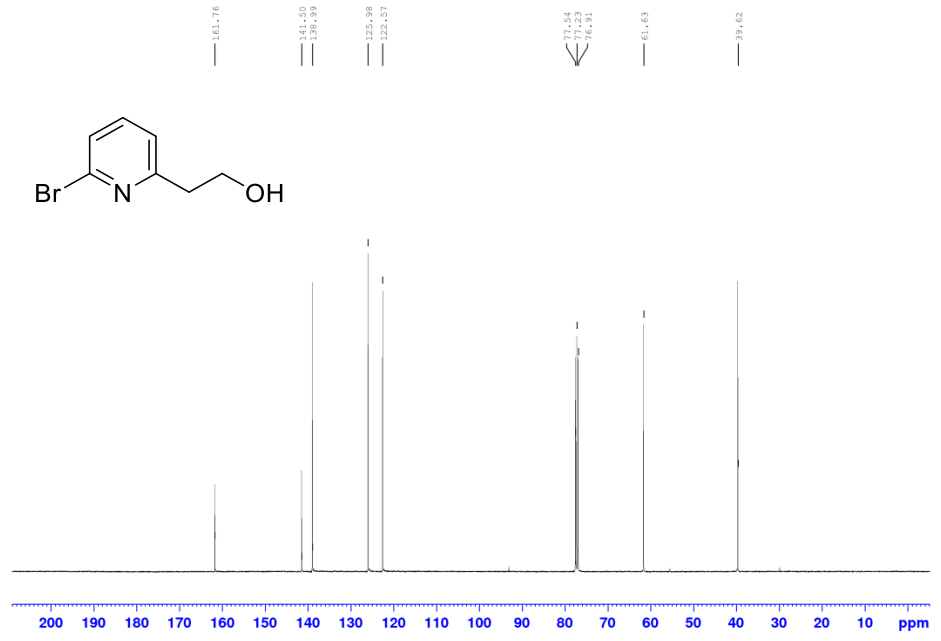
^{1}H NMR spectrum of **17** (400 MHz, $CDCl_3$)



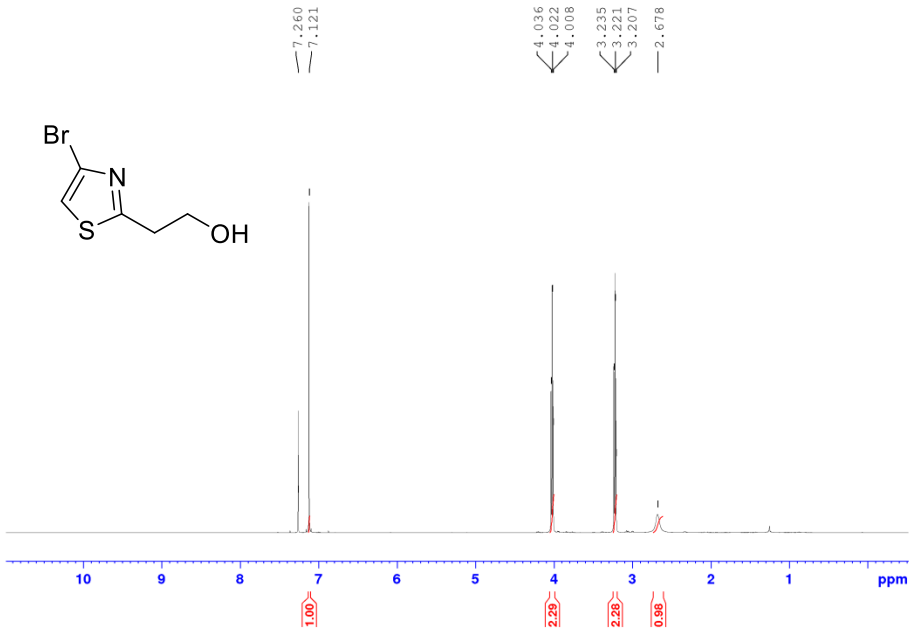
^{13}C NMR spectrum of **17** (101 MHz, $CDCl_3$)



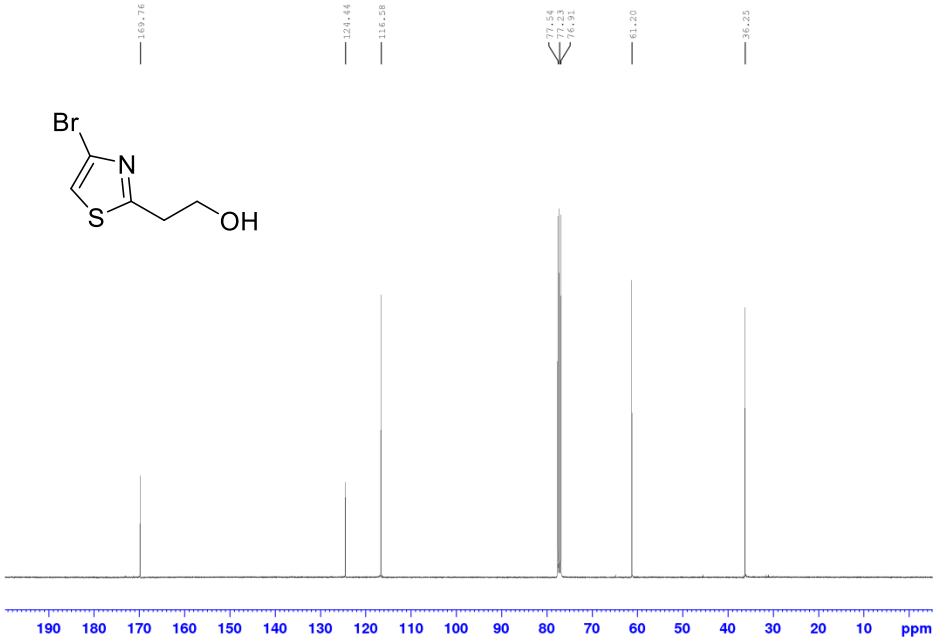
^{1}H NMR spectrum of **18** (400 MHz, $CDCl_3$)



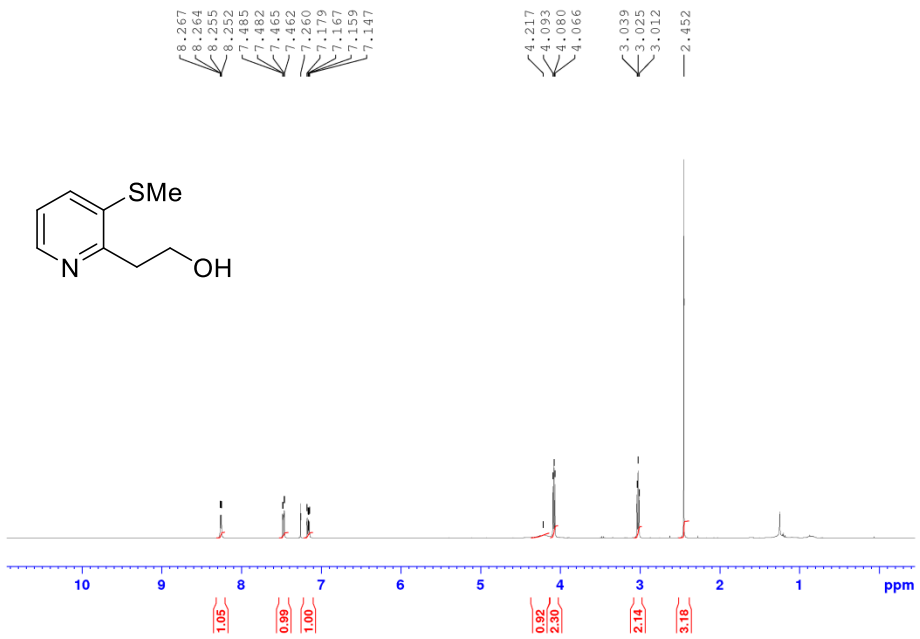
^{13}C NMR spectrum of **18** (101 MHz, $CDCl_3$)



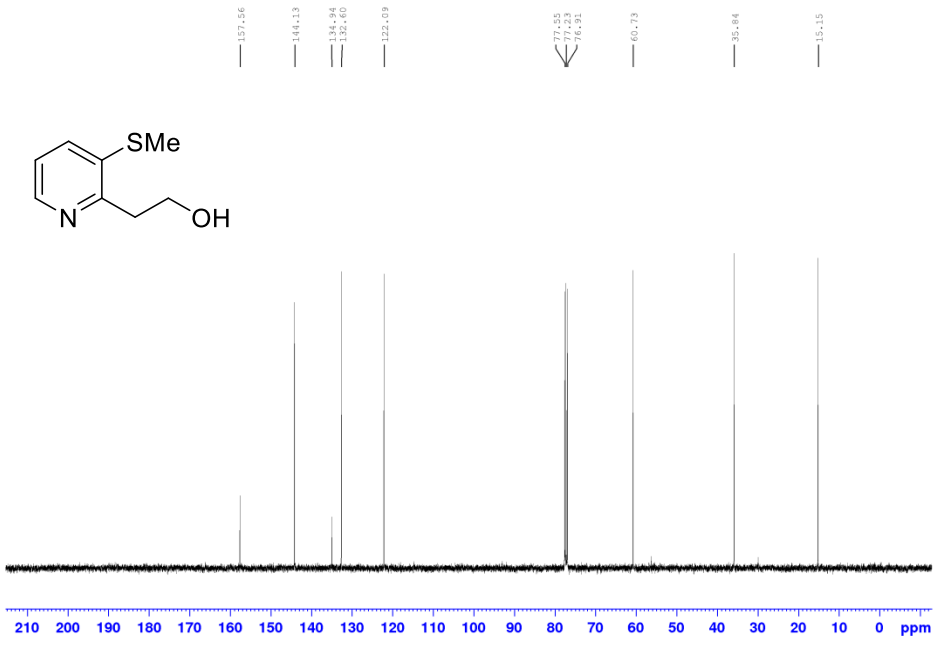
^{1}H NMR spectrum of **19** (400 MHz, $CDCl_3$)



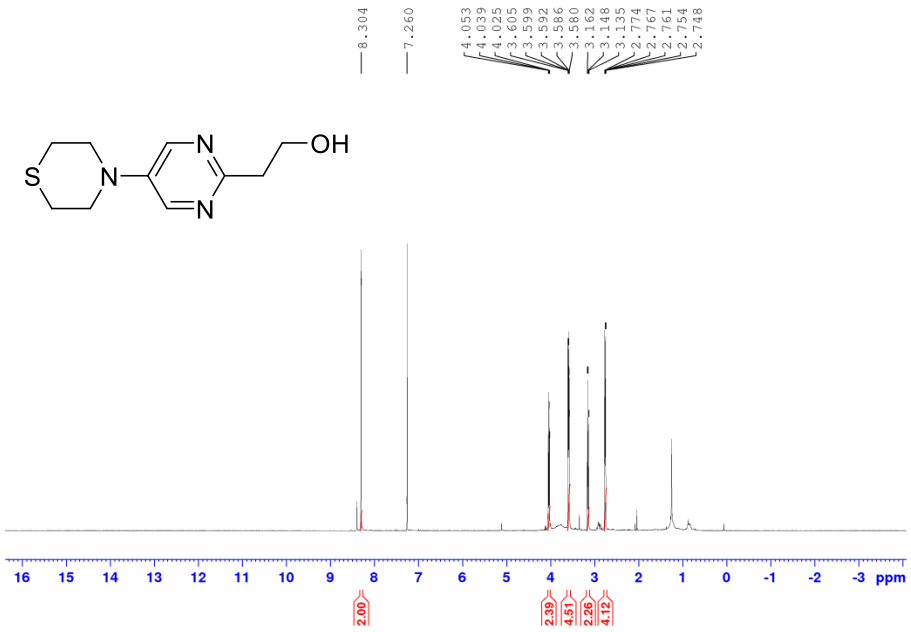
^{13}C NMR spectrum of **19** (101 MHz, $CDCl_3$)



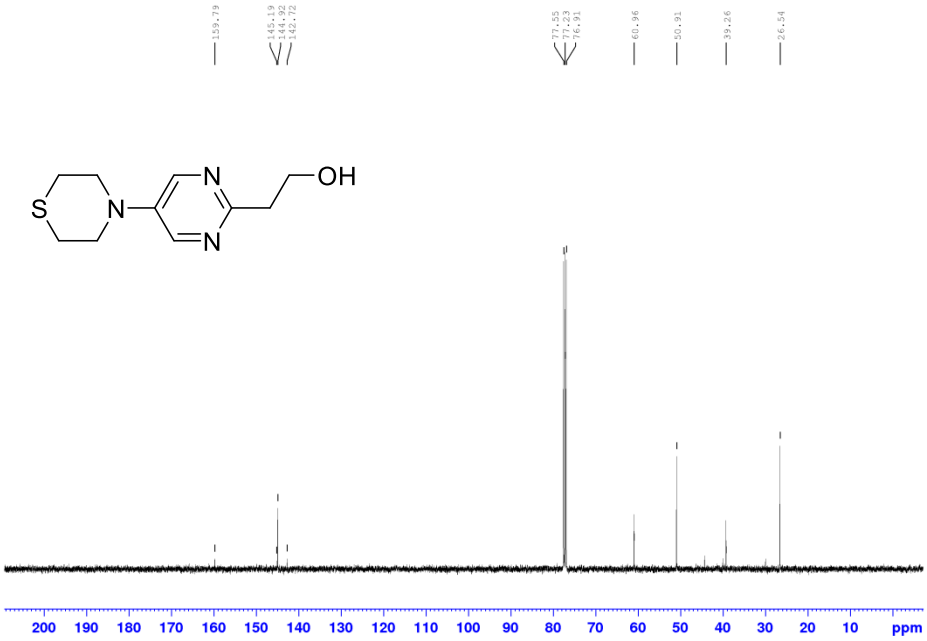
^{1}H NMR spectrum of **23** (400 MHz, $CDCl_3$)



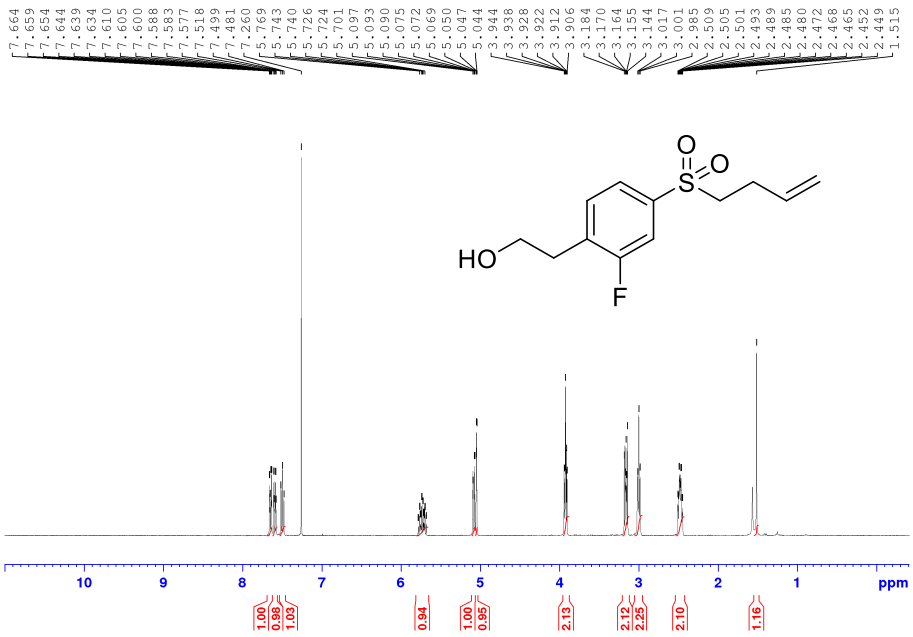
^{13}C NMR spectrum of **23** (101 MHz, $CDCl_3$)



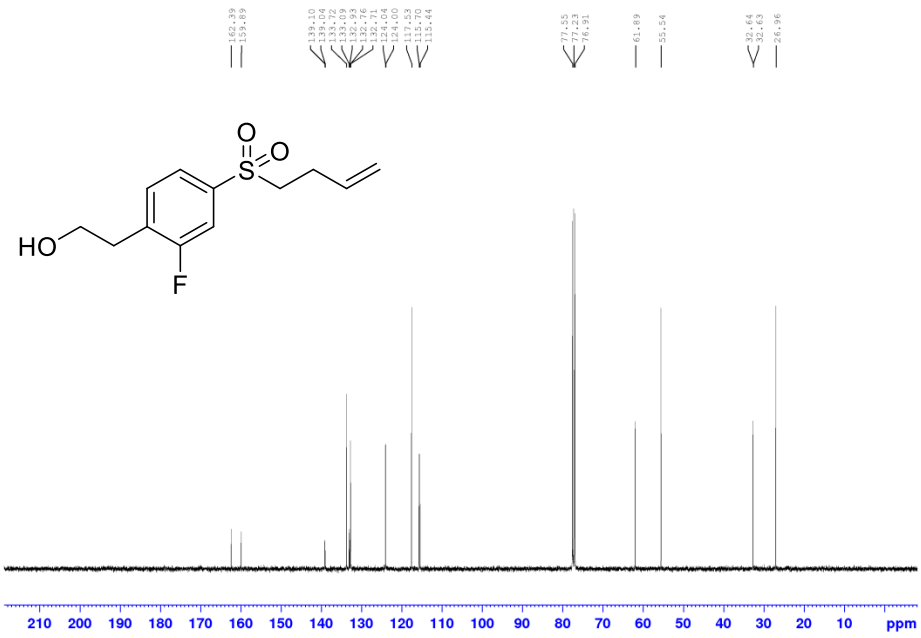
^{1}H NMR spectrum of **24** (400 MHz, $CDCl_3$)



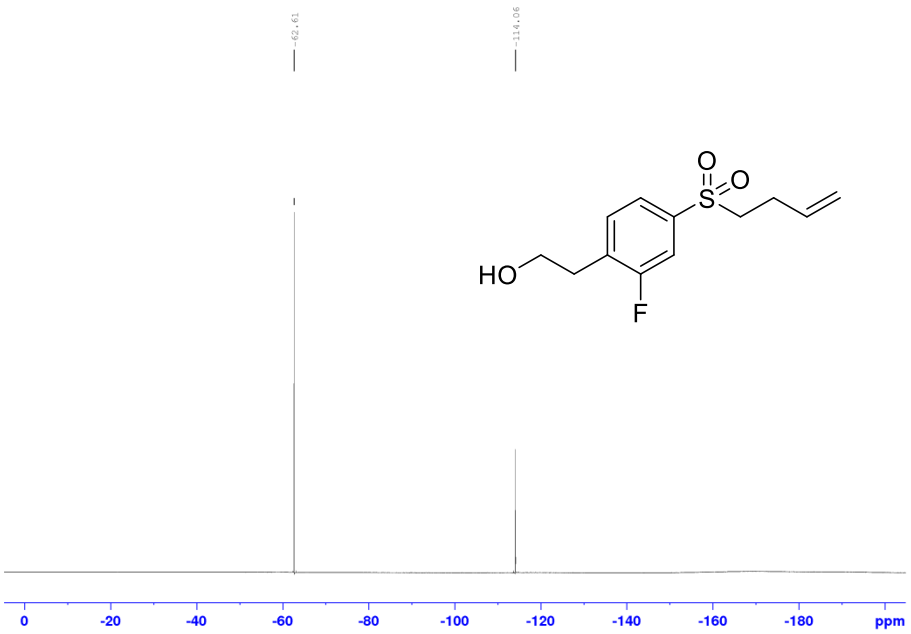
^{13}C NMR spectrum of **24** (101 MHz, $CDCl_3$)



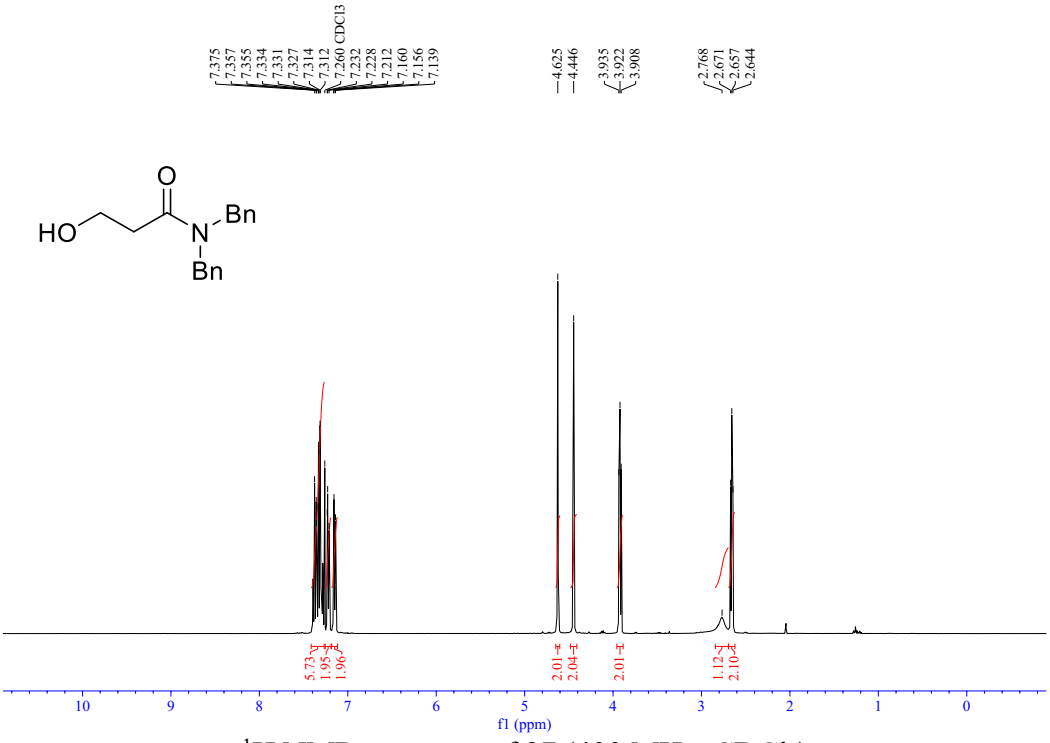
^{1}H NMR spectrum of **25** (400 MHz, $CDCl_3$)



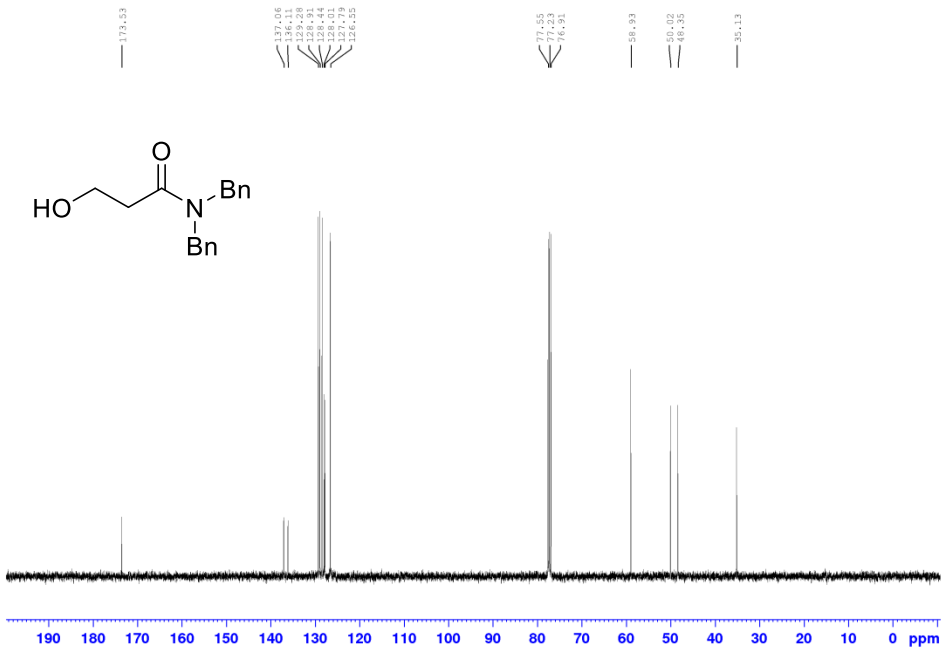
^{13}C NMR spectrum of **25** (101 MHz, $CDCl_3$)



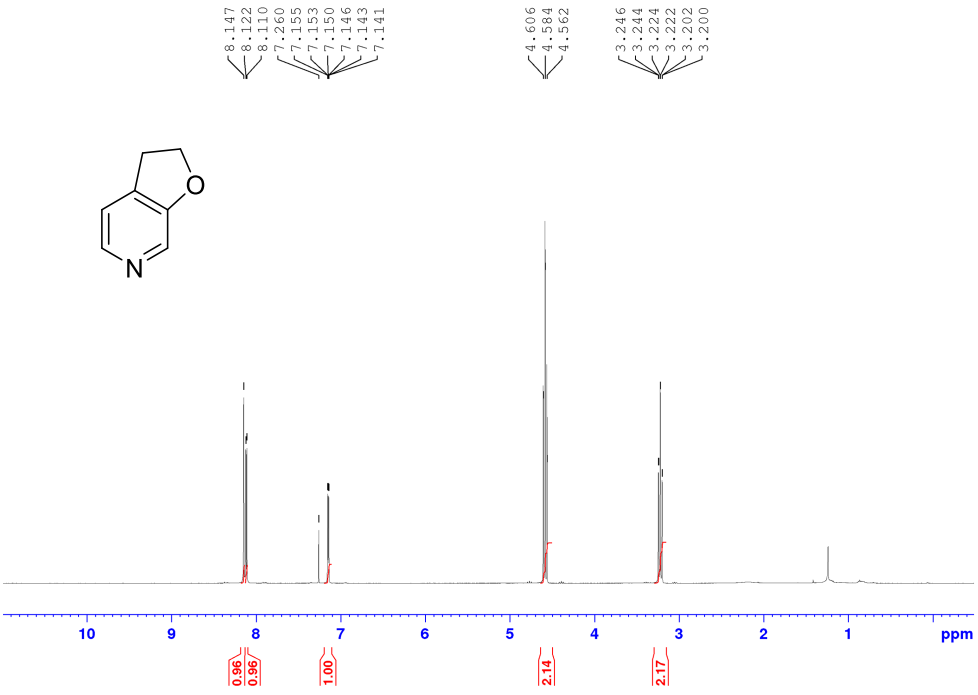
^{19}F NMR spectrum of **25** (377 MHz, $CDCl_3$, $PhCF_3$ internal standard set at -62.61 ppm)



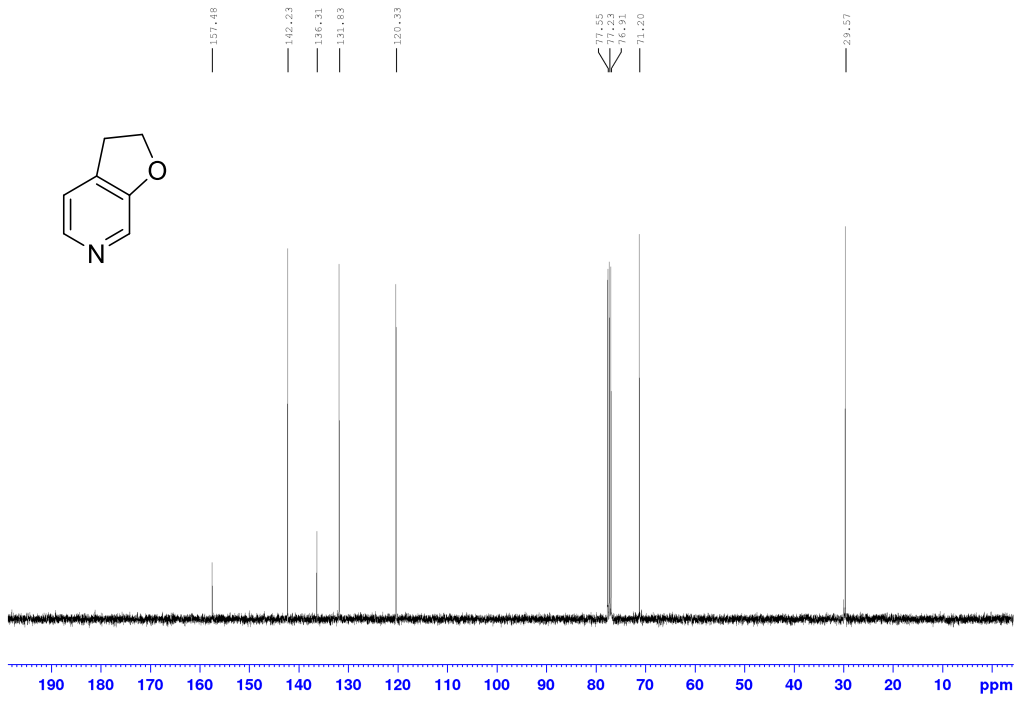
^{1}H NMR spectrum of **27** (400 MHz, $CDCl_3$)



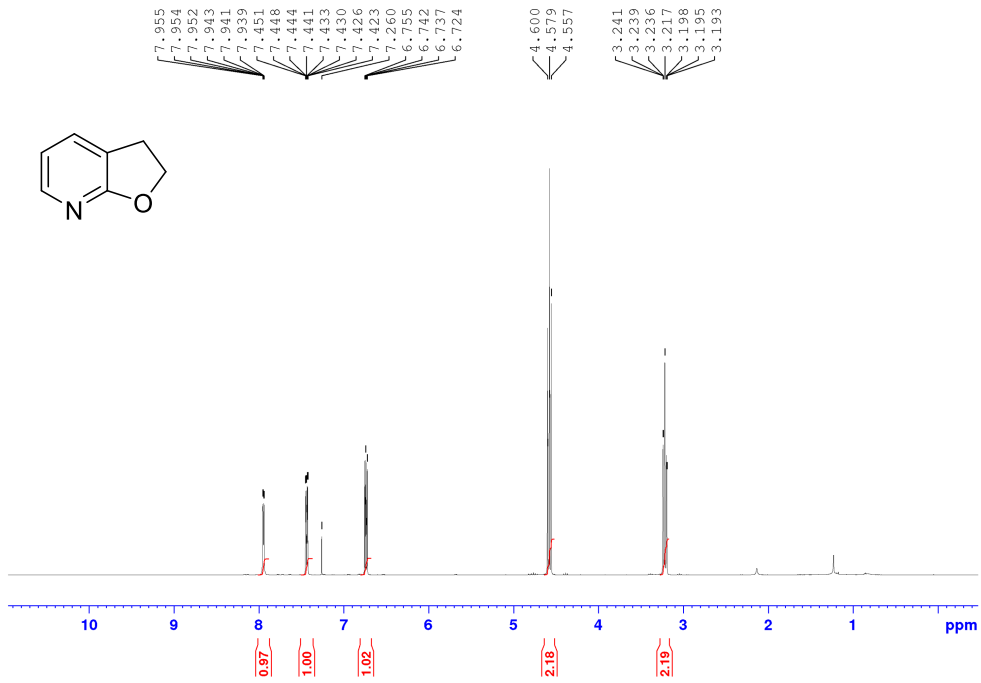
^{13}C NMR spectrum of **27** (101 MHz, $CDCl_3$)



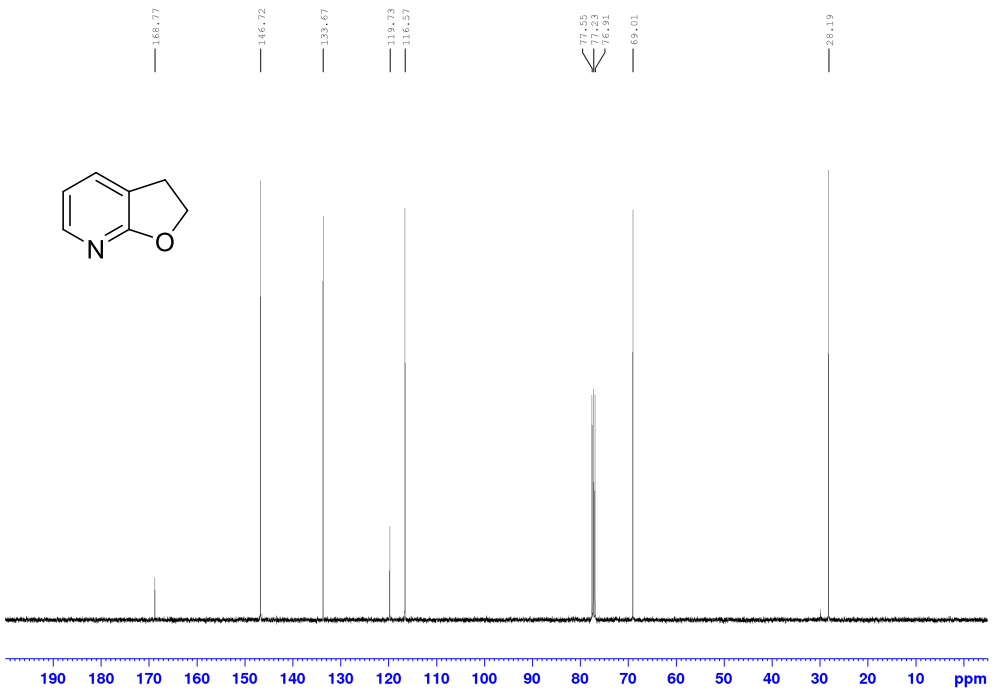
^{1}H NMR spectrum of **28** (400 MHz, $CDCl_3$)



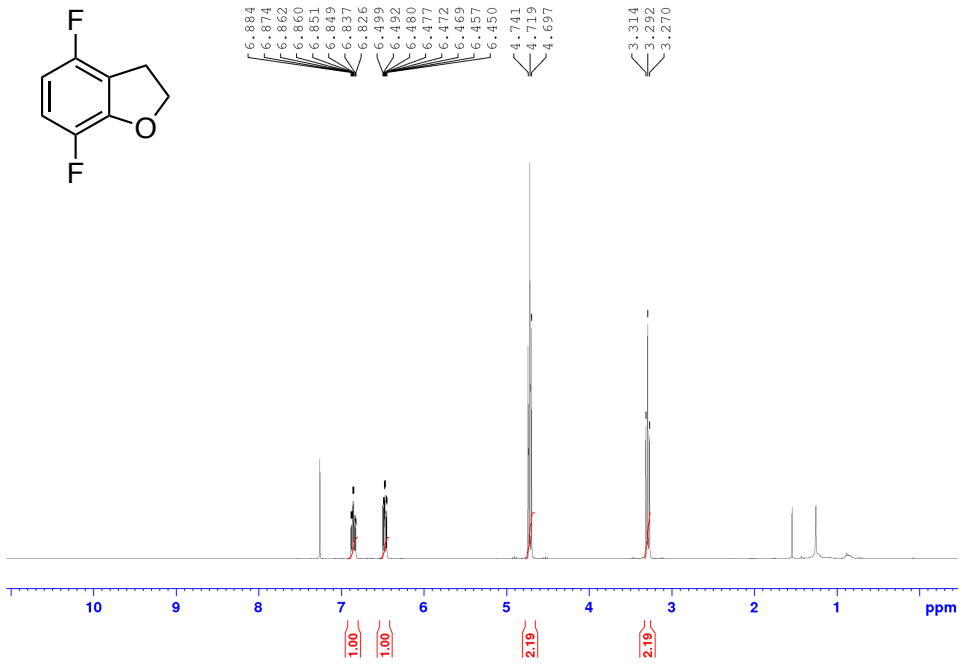
^{13}C NMR spectrum of **28** (101 MHz, $CDCl_3$)



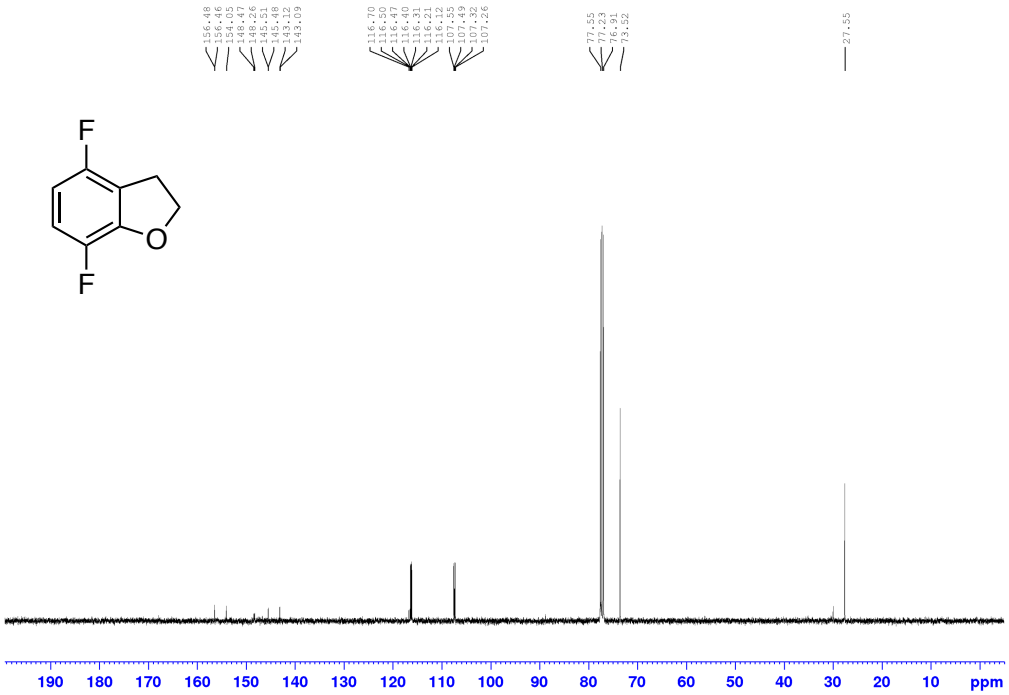
^{1}H NMR spectrum of **29** (400 MHz, $CDCl_3$)



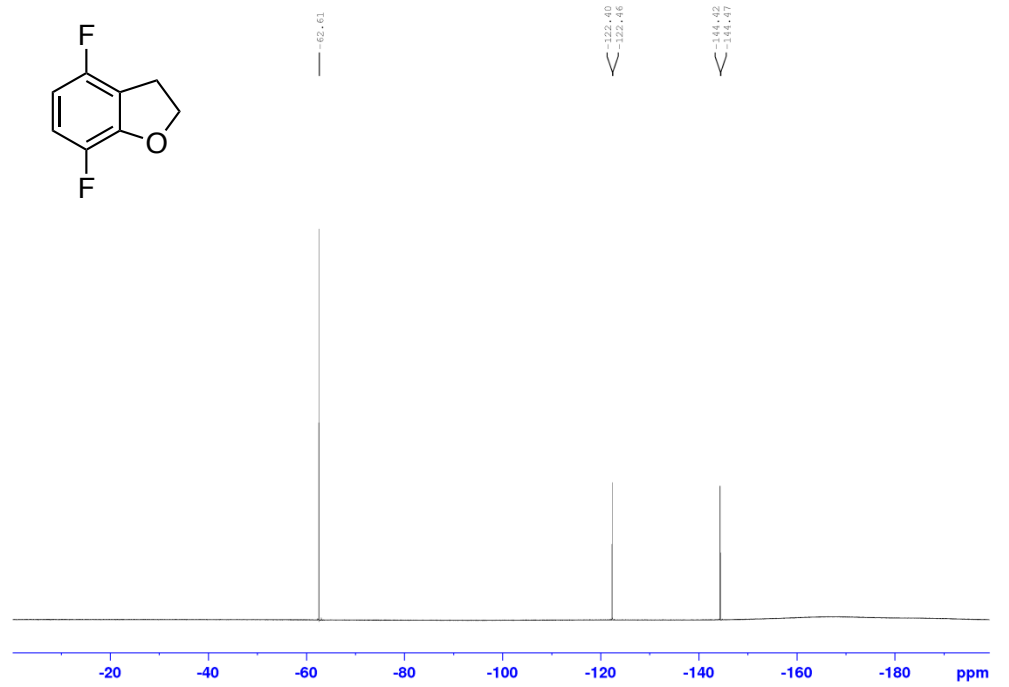
^{13}C NMR spectrum of **29** (101 MHz, $CDCl_3$)



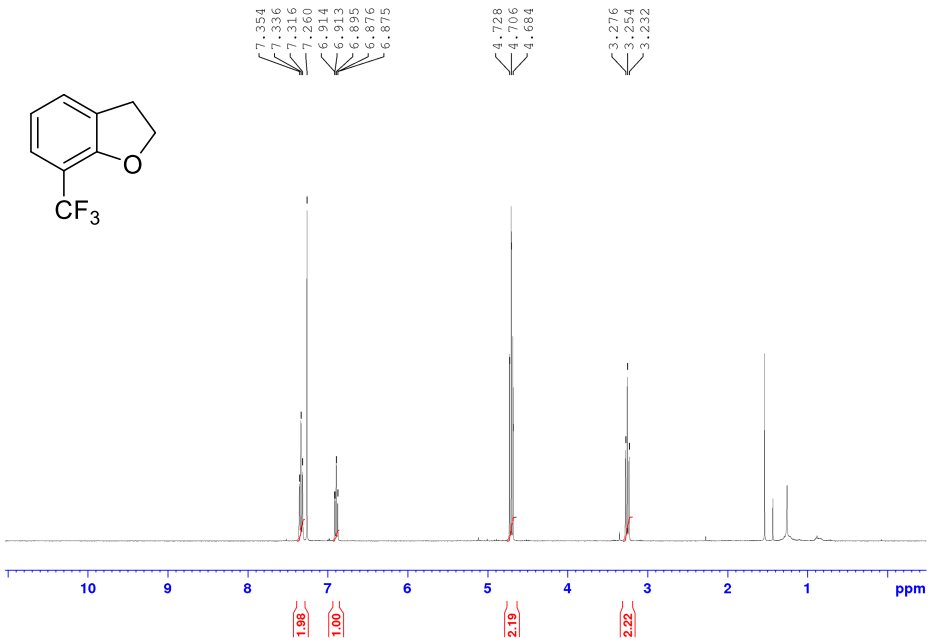
^{1}H NMR spectrum of **30** (400 MHz, $CDCl_3$)



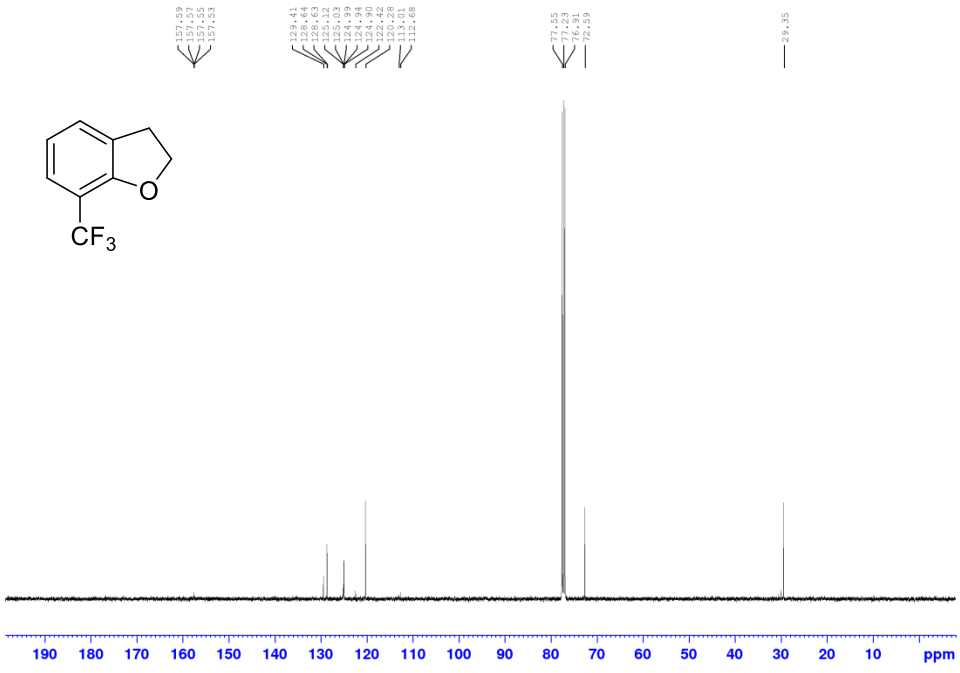
^{13}C NMR spectrum of **30** (101 MHz, $CDCl_3$)



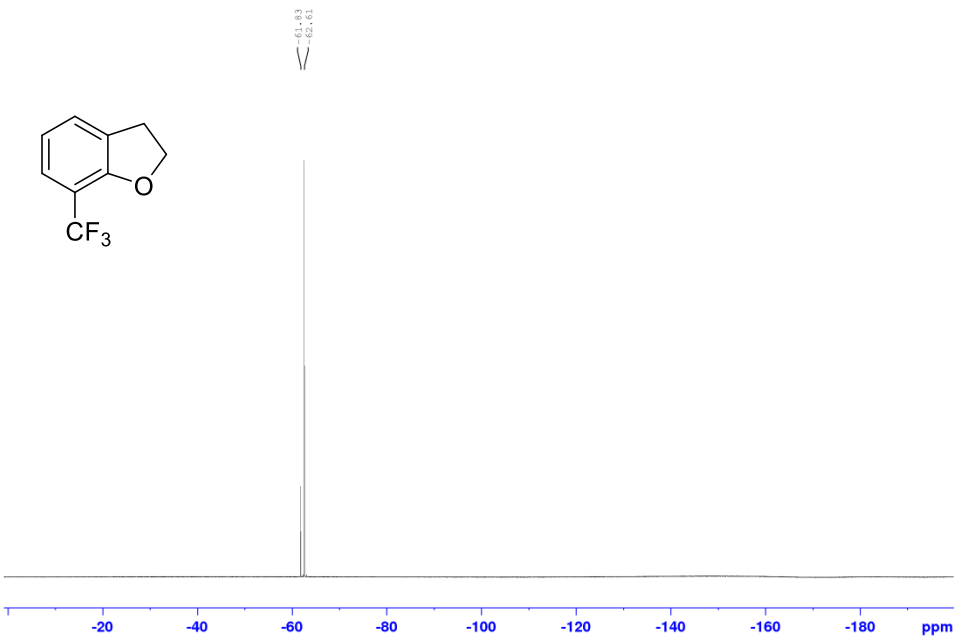
^{19}F NMR spectrum of **30** (377 MHz, $CDCl_3$, $PhCF_3$ internal standard set at -62.61 ppm)



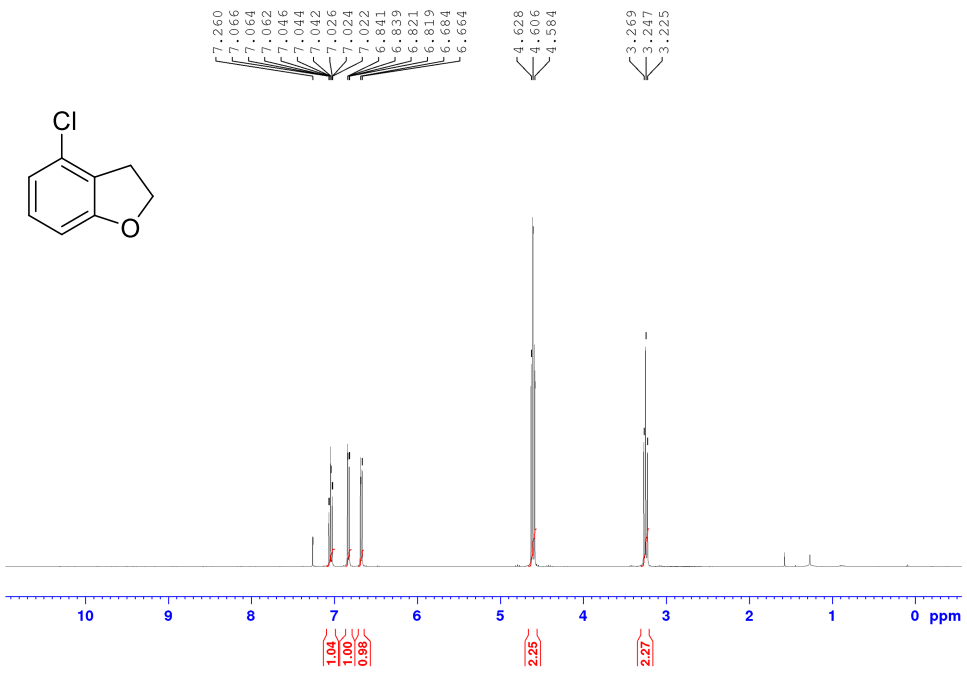
^{1}H NMR spectrum of **31** (400 MHz, $CDCl_3$)



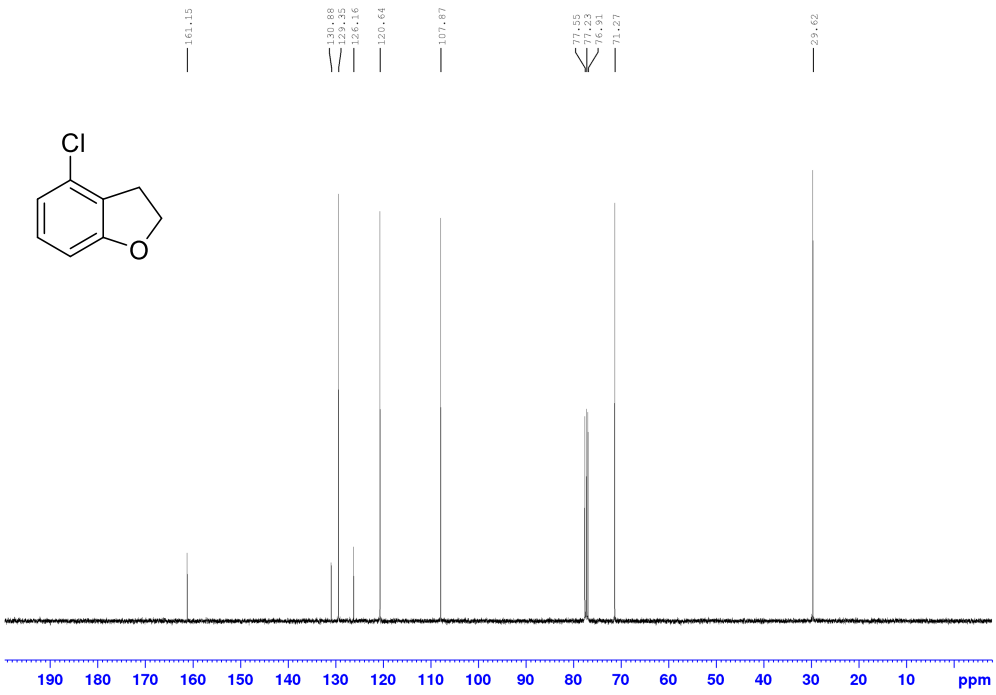
^{13}C NMR spectrum of **31** (101 MHz, $CDCl_3$)



^{19}F NMR spectrum of **31** (377 MHz, $CDCl_3$, $PhCF_3$ internal standard set at -62.61 ppm)



^{1}H NMR spectrum of **32** (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of **32** (101 MHz, $CDCl_3$)