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Materials and Methods

Reactions were carried out under N_2 atmosphere unless otherwise noted. All air-sensitive compounds and reactions were performed under an inert atmosphere of nitrogen using standard Schlenk and glovebox techniques. All glassware was stored in an oven or flame-dried prior to use. Anhydrous solvents were obtained either by filtration through drying columns on an mBraun system (DCM, toluene), by distillation from CaH (MeCN, DMF) or Na/benzophenone (dioxane). Purified compounds were further dried under vacuum (0.01–0.2 Torr). Thin layer chromatography (TLC) was performed using EMD TLC plates pre-coated with 250 μm thickness silica gel 60 F_{254} plates and visualized by fluorescence quenching under UV light and $KMnO_4$ stain. Flash chromatography was performed using silica gel (230-400 mesh) purchased from Silicycle Inc. NMR spectra were recorded on either a Varian Unity/Inova 600 spectrometer operating at 600 MHz for ^1H acquisitions, a Varian Unity/Inova 500 spectrometer operating at 500 MHz and 125 MHz for ^1H and ^{13}C acquisitions, respectively, a Varian Mercury 400 spectrometer operating at 400 HMz, and 375 MHz for ^1H, and ^{19}F acquisitions, respectively, or Varian Mercury 300 spectrometer operating at 300 HMz, and 282 MHz for ^1H, and ^{19}F acquisitions, respectively. Chemical shifts for ^1H and ^{13}C acquisitions are reported in ppm with the solvent resonance as the internal standard (^1H: $CDCl_3$, δ 7.26; CD_3OD, δ 3.31; DMSO-*d6*, δ 2.50), (^{13}C: $CDCl_3$, δ 77.16; CD_3OD, δ 49.15). Chemical shifts for ^{19}F acquisitions are reported in ppm with $CFCl_3$ as the external standard (^{19}F: $CDCl_3$, δ 0). Data are reported as follows: s = singlet, br = broad, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constants in Hz; integration. All deuterated solvents were purchased from Cambridge Isotope Laboratories, dried over 4Å molecular sieves. High-resolution mass spectra were obtained using an Agilent ESI-TOF (6210) mass spectrometer or a Bruker q-TOF Maxis Impact mass spectrometer.

Experimental Data

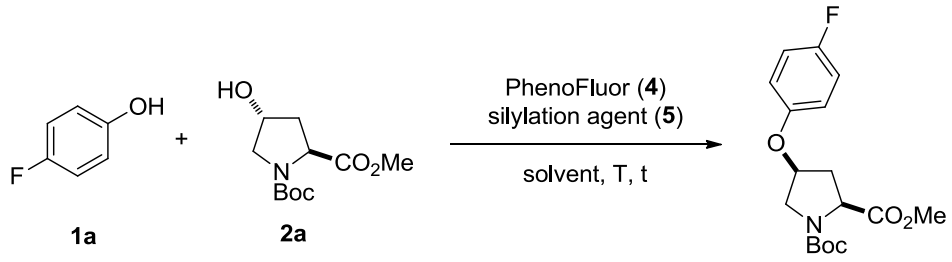
Experimental Procedures and Compound Characterization

General procedure for the cross coupling between alcohols and phenols with PhenoFluor

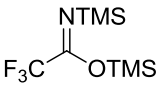
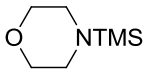
Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (128 mg, 0.300 mmol, 1.50 equiv), TMS-imidazole (85.0 mg, 88.9 μL, 0.606 mmol, 3.03 equiv.), and 1.5 mL of dioxane at 23 ℃. After 10 minutes, a phenol (0.300 mmol, 1.50 equiv.) in 1.0 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. An alcohol (0.200 mmol, 1.00 equiv.) in 1.5 mL dioxane was added and then the vial was sealed and heated at 80 ℃ for 24 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel.

Investigation of reaction conditions

Under N_2 atmosphere, to an oven-dried vial were added silylation reagent **5**, 4-fluorophenol (**1a**), and 1.5 mL of solvent at 23 ℃. After 5 minutes, PhenoFluor was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol **2a** in 1.5 mL solvent was added and then the vial was sealed and stirred at corresponding temperature for the time shown in the table below. Once cooled to 23 ℃, $PhCF_3$ was added as internal standard to determine the yield by ^{19}F NMR.

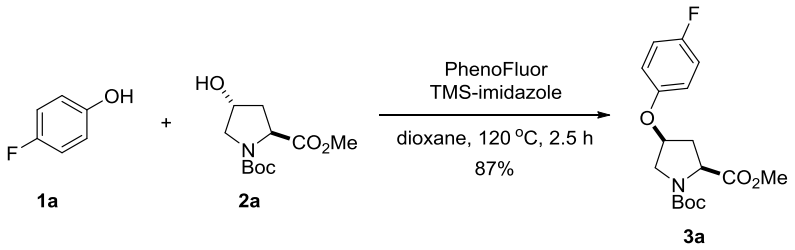


1a **2a** **3a**

entry	**4/5/1a/2a**	**5**	solvent	T (°C)	t (h)	**3a** (%)[a]
1	1/1/1/1		dioxane	120	2.5	<1
2	1/2/1/1	TMSOTf	dioxane	120	2.5	<1
3	1/1/1/1	$(TMS)_2NH$	dioxane	120	2.5	18
4	1/2/1/1		dioxane	120	2.5	47
5	1/2/1/1	$TMSNEt_2$	dioxane	120	2.5	50
6	1/2/1/1	TMS-imidazole	dioxane	120	2.5	60
7	1/2/1/1	TMS-imidazole	$PhCH_3$	120	2.5	60
8	1/2/1/1	TMS-imidazole	CH_2Cl_2	120	2.5	31
9	1/2/1/1	TMS-imidazole	CH_3CN	120	13	25
10	1/2/1/1	TMS-imidazole	DMF	120	13	28
11	2/4/1/2	TMS-imidazole	dioxane	120	2.5	97(87)[b]
12	2/4/1/2	TMS-imidazole	dioxane	60	23	97
13	2/4/1/2	TMS-imidazole	dioxane	rt	23	63
14	1.5/3/1.5/1	TMS-imidazole	dioxane	60	23	74(71)[b]

[a] Yield was determined by ^{19}F NMR with $PhCF_3$ (–62.6 ppm) as a internal standard. [b] Yield in the parentheses refers to the isolated yield.

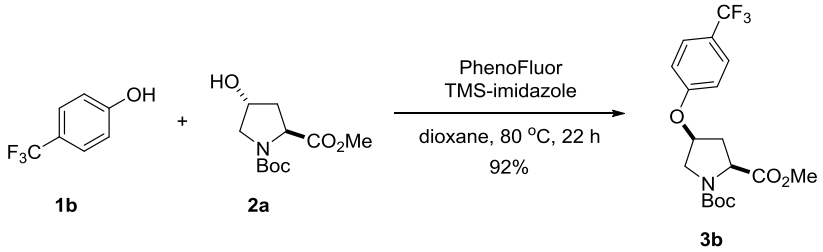
1-(*tert*-Butyl) 2-methyl (*2S,4S*)-4-(4-fluorophenoxy)pyrrolidine-1,2-dicarboxylate (3a)



Under N_2 atmosphere, to an oven-dried vial were added TMS-imidazole (170 mg, 178 μL, 1.21 mmol, 4.03 equiv.), 4-fluorophenol (**1a**) (33.6 mg, 0.300 mmol, 1.00 equiv.), and 3.0 mL of dioxane at 23 ℃. After 5 minutes, PhenoFluor (256 mg, 0.600 mmol, 2.00 equiv) was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol **2a** (147 mg, 0.599 mmol, 2.00 equiv.) in 2.0 mL dioxane was added and then the vial was sealed and heated at 120 ℃ for 2.5 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 4:1 (v/v), to afford 88.7 mg of the title compound as an off-white solid (87% yield).

R_f = 0.30 (hexane/EtOAc = 3/1 (v/v)). NMR Spectroscopy [mixture of 2 rotamers]: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ℃, δ): 7.00–6.92 (m, 4H, major+minor), 6.78–6.72 (m, 4H, major+minor), 4.80 (brs, 2H, major+minor), 4.54 (dd, *J* = 9.0, 2.5 Hz, 1H, minor), 4.42 (t, *J* = 5.8 Hz, 1H, major). 3.78–3.62 (m, 10 H, major+minor), 2.48–2.32 (m, 4H, major+minor), 1.47 (s, 9H, minor), 1.43 (s, 9H, major). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 172.6, 172.2, 157.8 (d, *J* = 239.4 Hz), 154.3, 153.9, 152.8 (d, *J* = 2.5 Hz), 117.0 (d, *J* = 8.3 Hz), 116.2 (d, *J* = 23.3 Hz), 80.5, 80.4, 76.4, 75.4, 57.9, 57.6, 52.4, 52.2, 52.0, 51.6, 36.4, 35.4, 28.5, 28.4. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ℃, δ): −122.77 (minor), −122.80 (major). HRMS (ESI-TOF) (m/z) calcd for $C_{17}H_{22}FNNaO_5$ $[M+Na]^+$, 362.1374; found, 362.1376.

1-(*tert*-Butyl) 2-methyl (*2S,4S*)-4-(4-(trifluoromethyl)phenoxy)pyrrolidine-1,2-dicarboxylate (3b)

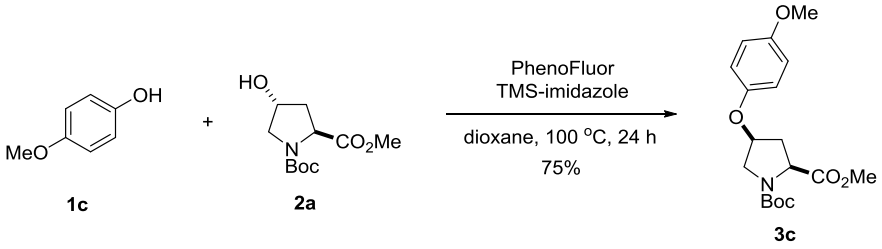


Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (256 mg, 0.600 mmol, 2.00 equiv), TMS-imidazole (170 mg, 178 μL, 1.21 mmol, 4.03 equiv.), and 1.0 mL of dioxane at 23 ℃. After 10 minutes, 4-(trifluoromethyl)phenol (**1b**) (49.0 mg, 0.302 mmol, 1.00 equiv.) in 0.75 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol **2a** (147 mg, 0.599

mmol, 2.00 equiv.) in 0.75 mL dioxane was added and then the vial was sealed and heated at 80 ℃ for 22 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 6:1 (v/v), to afford 108 mg of the title compound as a colorless oil (92% yield).

R_f = 0.25 (hexane/EtOAc = 4/1 (v/v)). NMR Spectroscopy [mixture of 2 rotamers]: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ℃, δ): 7.53 (t, *J* = 7.3 Hz, 4H, major+minor), 6.88–6.83 (m, 4H, major+ minor), 4.98–4.91 (2H, major+minor), 4.56 (dd, *J* = 8.1, 3.4 Hz, 1H, minor), 4.44 (dd, *J* = 8.7, 2.9 Hz, 1H, major), 3.84–3.64 (m, 10H, major+minor), 2.56–2.44 (m, 4H, major+minor), 1.48 (s, 9H, minor), 1.43 (s, 9H, major).^{13}C NMR (125 MHz, $CDCl_3$, 23 ℃, δ): 172.4, 171.9, 159.1, 154.1, 153.7, 127.1 (q, *J* = 4.1 Hz), 124.3 (q, *J* = 271.1 Hz), 123.7 (q, *J* = 32.4 Hz), 80.5, 80.4, 75.8, 74.7, 57.8, 57.4, 52.3, 52.1, 51.9, 51.5, 36.3, 35.4, 28.4, 28.3. ^{19}F NMR (471 MHz, $CDCl_3$, 23 ℃, δ): –61.68 (minor), –61.70 (major). HRMS (ESI-TOF) (m/z) calcd for $C_{18}H_{22}F_3NNaO_5$ $[M+Na]^+$, 412.1342; found, 412.1347.

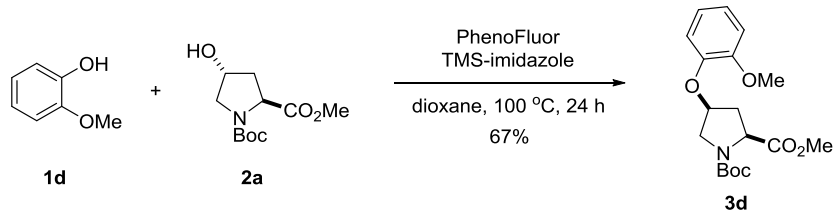
1-*tert*-Butyl 2-methyl (*2S,4S*)-4-(4-methoxyphenoxy)pyrrolidine-1,2-dicarboxylate (3c)



Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (128 mg, 0.300 mmol, 1.50 equiv), TMS-imidazole (85.0 mg, 88.9 μL, 0.606 mmol, 3.03 equiv.), and 1.5 mL of dioxane at 23 ℃. After 10 minutes, 4-methoxyphenol (**1c**) (37.2 mg, 0.300 mmol, 1.50 equiv.) in 1.0 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol **2a** (49.0 mg, 0.200 mmol, 1.00 equiv.) in 1.5 mL dioxane was added and then the vial was sealed and heated at 100 ℃ for 24 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 4:1 (v/v), to afford 53.0 mg of the title compound as a colorless oil (75% yield).

R_f = 0.28 (hexane/EtOAc = 3/1 (v/v)). NMR Spectroscopy [mixture of 2 rotamers]: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ℃, δ): 6.83–6.76 (m, 4H, major+minor), 6.75–6.70 (m, 4H), 4.82–4.75 (m, 2H, major+minor), 4.51 (dd, *J* = 9.1, 2.4 Hz, 1H, minor), 4.39 (t, *J* = 5.9 Hz, 1H, major), 3.78–3.61 (m, 16H, major+minor), 2.46–2.30 (m, 4H), 1.46 (s, 9H, minor), 1.42 (s, 9H, major).^{13}C NMR (125 MHz, $CDCl_3$, 23 ℃, δ): 172.6, 172.2, 154.4, 154.2, 153.8, 150.6, 117.0, 114.8, 80.2, 80.1, 76.3, 75.3, 57.9, 57.5, 55.7, 52.2, 52.1, 51.9, 51.5, 36.3, 35.4, 28.4, 28.3. HRMS (ESI-TOF) (m/z) calcd for $C_{18}H_{25}NNaO_6$ $[M+Na]^+$, 374.1574; found, 374.1580.

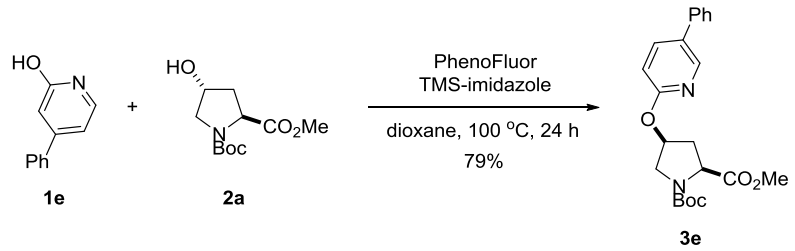
1-*tert*-Butyl 2-methyl (*2S,4S*)-4-(2-methoxyphenoxy)pyrrolidine-1,2-dicarboxylate (3d)



Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (128 mg, 0.300 mmol, 1.50 equiv), TMS-imidazole (85.0 mg, 88.9 μL, 0.606 mmol, 3.03 equiv.), and 1.5 mL of dioxane at 23 ℃. After 10 minutes, 2-methoxyphenol (**1d**) (37.2 mg, 0.300 mmol, 1.50 equiv.) in 1.0 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol **2a** (49.0 mg, 0.200 mmol, 1.00 equiv.) in 1.5 mL dioxane was added and then the vial was sealed and heated at 100 ℃ for 24 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 4:1 (v/v), to afford 47.0 mg of the title compound as a yellow solid (67% yield).

R_f = 0.25 (hexane/EtOAc = 3/1 (v/v)). NMR Spectroscopy [mixture of 2 rotamers]: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ℃, δ): 7.01–6.94 (m, 2H, major+minor), 6.91–6.85 (m, 4H, major+minor), 6.85–6.80 (m, 2H, major+minor), 4.98–4.84 (m, 2H, major+minor), 4.52 (dd, *J* = 9.0, 2.7 Hz, 1H, minor), 4.40 (dd, *J* = 7.8, 4.6 Hz, 1H, major). 3.81 (s, 3H, minor), 3.80 (s, 3H, major), 3.75 (s, 3H, major), 3.74 (s, 3H, minor), 3.88–3.68 (m, 4H, major+minor), 2.52–2.35 (m, 4H, major+minor), 1.47 (s, 9H, minor), 1.43 (s, 9H, major).^{13}C NMR (125 MHz, $CDCl_3$, 23 ℃, δ): 172.6, 172.2, 154.3, 153.8, 150.7, 150.7, 146.01, 146.0, 122.8, 122.8, 120.9, 120.8, 117.6, 117.5, 112.5, 80.1, 80.0, 76.9, 75.9, 57.9, 57.5, 55.8, 52.2, 52.04, 51.8, 51.3, 36.5, 35.6, 28.4, 28.3. HRMS (ESI-TOF) (m/z) calcd for $C_{18}H_{25}NNaO_6$ $[M+Na]^+$, 374.1574; found, 374.1584.

(*2S,4S*)-1-*tert*-Butyl 2-methyl 4-((5-phenylpyridin-2-yl)oxy)pyrrolidine-1,2-dicarboxylate (3e)

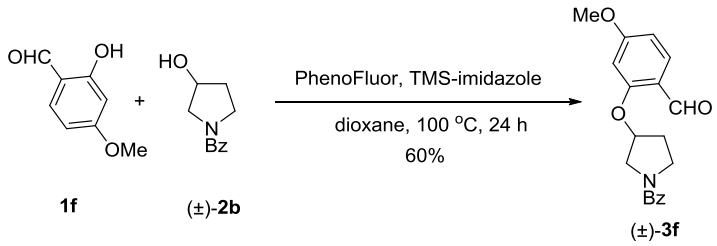


Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (256 mg, 0.600 mmol, 2.00 equiv), TMS-imidazole (170 mg, 178 μL, 1.21 mmol, 4.03 equiv.), and 1.0 mL of dioxane at 23 ℃. After 10 minutes, 4-phenylpyridin-2-ol (**1e**) (95% purity, 34.0 mg, 0.300 mmol, 1.00 equiv.) in 0.75 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol **2a** (147 mg, 0.599 mmol, 2.00 equiv.) in 1.0 mL dioxane was added and then the vial was sealed and heated at 100 ℃ for 24 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The

residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 2:1 (v/v), to afford 94.5 mg of the title compound as a colorless oil (79% yield).

R_f = 0.5 (hexane/EtOAc = 3/2 (v/v)). NMR Spectroscopy [mixture of 2 rotamers]: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.16–8.12 (m, 2H, major+minor), 7.56 (d, *J* = 8.0 Hz, 4H, major+minor), 7.46–7.37 (m, 6H, major+minor).7.08 (t, *J* = 5.0 Hz, 2H, major+minor), 6.83 (d, *J* = 10.2 Hz, 2H, major+minor), 5.58 (m, 1H, minor), 5.55 (m, 1H, major), 4.54 (dd, *J* = 9.3, 2.3 Hz, 1H, minor), 4.42 (dd, *J* = 9.3, 2.2 Hz, 1H, major), 3.91–3.81 (m, 2H, major+minor), 3.75–3.63 (m, 8H, major+minor), 2.63–2.55 (m, 1H, major), 2.55–2.47 (m, 1H, minor), 2.45 (s, 1H, major), 2.44 (s, 1H, minor), 1.47 (s, 9H, minor), 1.43 (s, 9H, major).^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 172.9, 172.5, 163.2, 163.2, 154.3, 153.8, 151.5, 147.1, 138.1, 138.0, 129.1, 129.0, 126.9, 115.8, 109.1, 109.0, 80.1, 80.0, 73.7, 72.7, 58.0, 57.6, 52.5, 52.2, 52.0, 51.9, 36.5, 35.7, 28.4, 28.3. HRMS (ESI-TOF) (m/z) calcd for $C_{22}H_{27}N_2O_5$ $[M+Na]^+$, 399.1914; found, 399.1930.

(±)-2-((1-Benzoylpyrrolidin-3-yl)oxy)-5-methoxybenzaldehyde ((±)-3f)

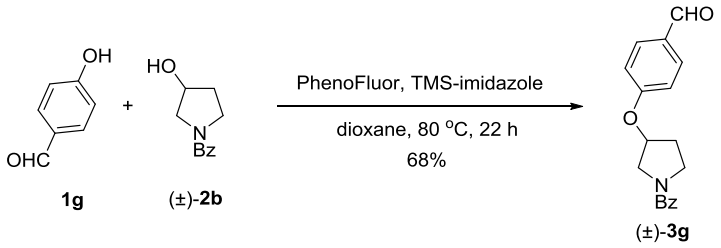


1f (±)-**2b** (±)-**3f**

Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (128 mg, 0.300 mmol, 1.50 equiv), TMS-imidazole (85.0 mg, 88.9 μL, 0.606 mmol, 3.03 equiv.), and 1.5 mL of dioxane at 23 ℃. After 10 minutes, 2-hydroxy-4-methoxybenzaldehyde (**1f**) (45.6 mg, 0.300 mmol, 1.50 equiv.) in 0.50 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol (±)-**2b** (38.0 mg, 0.199 mmol, 1.00 equiv.) in 1.0 mL dioxane was added and then the vial was sealed and heated at 100 ℃ for 24 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with EtOAc/hexane 2:1 (v/v), to afford 39.0 mg of the title compound as a light yellow solid (60% yield).

R_f = 0.20 (EtOAc/hexane = 2/1 (v/v)). NMR Spectroscopy [mixture of 2 rotamers]: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 10.30 (s, 1H, major), 10.21 (s, 1H, minor), 7.84 (d, *J* = 8.7 Hz, 1H, major), 7.81 (d, *J* = 8.8 Hz, 1H, minor), 7.53 (dd, *J* = 7.4 Hz, 2H, major), 7.51–7.47 (d, *J* = 6.5 Hz,, 2H, minor), 7.45–7.35 (m, 6H, major+minor), 6.58 (d, *J* = 8.7 Hz, 1H, major), 6.55 (d, *J* = 9.1 Hz, 1H, minor), 6.42 (s, 1H, major), 6.31 (s, 1H, minor), 5.09 (t, *J* = 4.2 Hz, 1H, major), 4.99–4.91(m, 1H, minor), 4.13–3.46 (m, 14H), 2.44–2.23 (m, 2H, major), 2.22–2.12 (m, 2H, minor). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 187.9, 187.8, 170.2, 170.1, 166.1, 165.9, 161.0, 160.9, 136.5, 136.3, 131.1, 131.1, 130.4, 130.3, 128.6, 128.5, 127.3, 127.2, 119.8, 106.5, 106.2, 100.1, 100.0, 77.2, 75.9, 55.8, 54.6, 51.8, 47.6, 44.3, 32.4, 30.2. HRMS (ESI-TOF) (m/z) calcd for $C_{19}H_{20}NO_4$ $[M+H]^+$, 326.1387; found, 326.1297.

(±)-4-((1-Benzoylpyrrolidin-3-yl)oxy)benzaldehyde ((±)-3g)

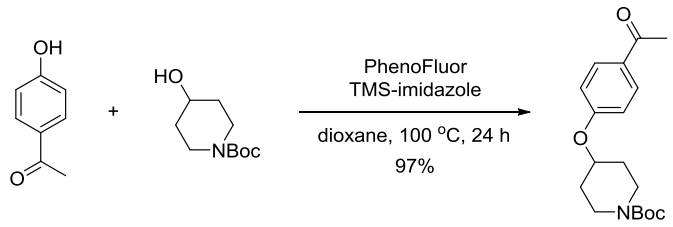


1g (±)-2b (±)-3g

Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (128 mg, 0.300 mmol, 1.50 equiv), TMS-imidazole (85.0 mg, 88.9 μL, 0.606 mmol, 3.03 equiv.), and 1.5 mL of dioxane at 23 ℃. After 10 minutes, 4-hydroxybenzaldehyde (**1g**) (36.6 mg, 0.300 mmol, 1.50 equiv.) in 0.50 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol (±)-**2b** (38.0 mg, 0.199 mmol, 1.00 equiv.) in 1.0 mL dioxane was added and then the vial was sealed and heated at 80 ℃ for 22 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with EtOAc/hexane 2:1 (v/v), to afford 40.0 mg of the title compound as a light yellow solid (68% yield).

R_f = 0.3 (EtOAc/hexane = 2/1 (v/v)). NMR Spectroscopy [mixture of 2 rotamers]: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 9.90 (s, 1H, major), 9.87 (s, 1H, minor), 7.85 (d, *J* = 8.1 Hz, 2H, major), 7.81 (d, *J* = 8.2 Hz, 2H, minor), 7.56 (d, *J* = 6.7 Hz, 2H, major), 7.50 (d, *J* = 7.1 Hz, 2H, minor), 7.45–7.36 (m, 6H, major+minor), 7.01 (d, *J* = 8.3 Hz, 2H, major), 6.93 (d, *J* = 8.3 Hz, 2H, minor), 5.10 (s, 1H, major), 4.99 (s, 1H, minor), 4.23–3.52 (m, 8H, major+minor), 2.36–2.22 (m, 2H, major), 2.22–2.10 (m, 2H, minor).^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 190.9, 190.8, 170.3, 170.0, 162.2, 162.0, 136.6, 136.5, 132.2, 130.5, 130.4, 130.3, 128.6, 128.5, 127.4, 127.3, 115.7, 115.6, 76.7, 75.6, 54.7, 52.1, 47.5, 44.4, 32.3, 30.2. HRMS (ESI-TOF) (m/z) calcd for $C_{18}H_{18}NO_3$ $[M+H]^+$, 296.1281; found, 296.1293.

***tert*-Butyl 4-(4-acetylphenoxy)piperidine-1-carboxylate (3h)**



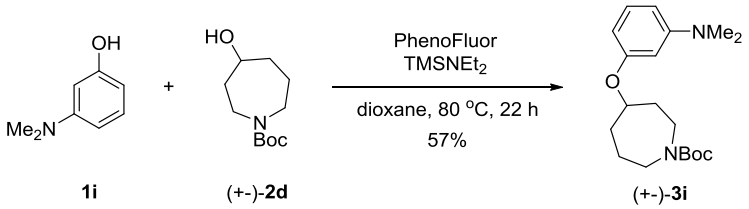
1h 2c 3h

Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (256 mg, 0.600 mmol, 3.00 equiv), TMS-imidazole (170 mg, 178 μL, 1.21 mmol, 6.05 equiv.), and 1.0 mL of dioxane at 23 ℃. After 10 minutes, 1-(4-hydroxyphenyl)ethan-1-one (**1h**) (27.2 mg, 0.200 mmol, 1.00 equiv.) in 1.0 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol **2c** (120.8 mg, 0.600 mmol, 3.00 equiv.) in 0.50 mL dioxane was added and then the vial was sealed and

heated at 100 ℃ for 24 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 4:1 (v/v), to afford 61.3 mg of the title compound as a white solid (97% yield).

R_f = 0.30 (hexane/EtOAc = 4/1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ℃, δ): 7.90 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 4.70–4.44 (m, 1H), 3.79–3.56 (m, 2H), 3.50–3.23 (m, 2H), 2.52 (s, 3H), 1.96-1.88 (m, 2H), 1.83–1.69 (m, 2H), 1.45 (s, 9H).^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 196.7, 161.2, 154.8, 130.7, 130.4, 115.2, 79.7, 72.2, 40.5, 30.3, 28.4, 26.3. HRMS (ESI-TOF) (m/z) calcd for $C_{18}H_{25}NNaO_4$ $[M+Na]^+$, 342.1676; found, 342.1683.

(±)-*tert*-Butyl 4-(3-(dimethylamino)phenoxy)azepane-1-carboxylate ((±)-3i)

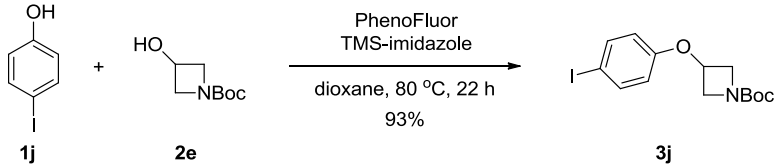


1i (+-)-**2d** (+-)-**3i**

Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (256 mg, 0.600 mmol, 1.50 equiv), $TMSNEt_2$ (175 mg, 227 μL, 1.21 mmol, 3.00 equiv.), and 1.0 mL of dioxane at 23 ℃. After 10 minutes, 3-(dimethylamino)phenol (**1i**) (82.3 mg, 0.600 mmol, 1.50 equiv.) in 0.75 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol (±)-**2d** (86.1 mg, 0.400 mmol, 1.00 equiv.) in 0.75 mL dioxane was added and then the vial was sealed and heated at 80 ℃ for 22 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 8:1 (v/v), to afford 76.0 mg of the title compound as a colorless oil (57% yield).

R_f =0.3 (hexane /EtOAc = 8/1 (v/v)). NMR Spectroscopy [mixture of rotamers]: ^{1}H NMR (300 MHz, $CDCl_3$, 23 ºC, δ): 7.14 (t, *J* = 8.1 Hz, 2H, major+minor), 6.38 (d, *J* = 8.5 Hz, 2H, major+minor), 6.30 (s, 2H, major+minor), 6.29 (d, *J* = 7.4 Hz, 2H, major+minor), 4.48–4.37 (m, 2H, major+minor), 3.68–3.20 (m, 8H, major+minor), 2.93 (s, 12H, major+minor), 2.15–1.83 (m, 10H, major+minor), 1.73–1.59 (m, 2H, major+minor), 1.47 (s, 18H, major+minor).^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 158.5, 155.6, 129.8, 106.2, 103.6, 101.6, 79.3, 75.6, 75.4, 46.6, 45.9, 41.9, 41.5, 40.8, 34.3, 34.0, 32.0, 31.4, 28.5, 22.8, 22.3. HRMS (ESI-TOF) (m/z) calcd for $C_{19}H_{31}N_2O_3$ $[M+H]^+$, 335.2329; found, 335.2343.

***tert*-Butyl 3-(4-iodophenoxy)azetidine-1-carboxylate (3j)**

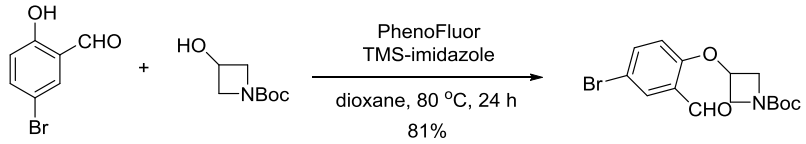


1j **2e** **3j**

Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (256 mg, 0.600 mmol, 1.50 equiv), TMS-imidazole (170 mg, 178 μL, 1.21 mmol, 3.00 equiv.), and 1.0 mL of dioxane at 23 ℃. After 10 minutes, 4-iodophenol (**1j**) (132 mg, 0.600 mmol, 1.50 equiv.) in 0.75 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol **2e** (70.0 mg, 0.404 mmol, 1.00 equiv.) in 0.75 mL dioxane was added and then the vial was sealed and heated at 80 ℃ for 22 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 20:1 (v/v), to afford 138.8 mg of the title compound as a off-white solid (93% yield).

R_f = 0.2 (hexane/EtOAc = 10/1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ℃, δ): 7.57 (d, *J* = 8.8 Hz, 2H), 6.52 (d, *J* = 8.7 Hz, 2H), 4.86–4.80 (m, 1H), 4.31–4.26 (m, 2H), 3.99 (dd, *J* = 9.8, 4.0 Hz, 2H), 1.45 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ℃, δ): 156.4, 156.1, 138.5, 116.9, 83.8, 79.9, 65.8, 56.3, 28.4. HRMS (ESI-TOF) (m/z) calcd for $C_{14}H_{18}INNaO_3$ $[M+Na]^+$, 398.0224; found, 398.0224.

tert-Butyl 3-(4-bromo-2-formylphenoxy)azetidine-1-carboxylate (3k)

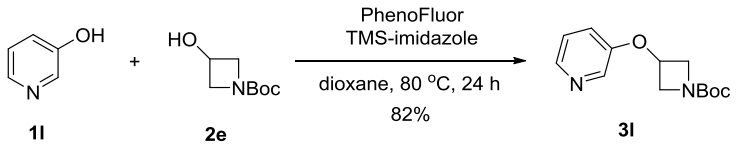


1k **2e** **3k**

Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (191 mg, 0.449 mmol, 1.50 equiv), TMS-imidazole (127 mg, 133 μL, 0.905 mmol, 3.00 equiv.), and 1.0 mL of dioxane at 23 ℃. After 10 minutes, 5-bromo-2-hydroxybenzaldehyde (**1o**) (90.0 mg, 0.450 mmol, 1.50 equiv.) in 0.75 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol **2e** (52.0 mg, 0.301 mmol, 1.00 equiv.) in 0.75 mL dioxane was added and then the vial was sealed and heated at 80 ℃ for 24 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 4:1 (v/v), to afford 86.2 mg of the title compound as a yellow solid (81% yield).

R_f = 0.23 (hexane /EtOAc = 4/1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ℃, δ): 10.41 (s, 1H), 7.94 (d, *J* = 2.4 Hz, 1H), 7.59 (dd, *J* = 9.8, 2.4 Hz, 1H), 6.51 (d, *J* = 8.8 Hz, 1H), 4.98–4.93 (m, 1H), 4.34 (ddd, *J* = 9.8, 6.1, 1.0 Hz, 2H), 4.05 (ddd, *J* = 10.3, 4.5, 1.0 Hz, 2H), 1.46 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ℃, δ): 187.7, 157.6, 155.9, 138.3, 131.6, 126.3, 114.6, 114.2, 80.2, 66.7, 56.1, 28.3. HRMS (ESI-TOF) (m/z) calcd for $C_{15}H_{18}BrNNaO_4$ $[M+Na]^+$, 378.0311; found, 378.0306.

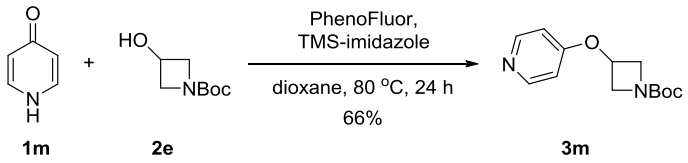
***tert*-Butyl 3-(pyridin-3-yloxy)azetidine-1-carboxylate (3l)**



Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (256 mg, 0.600 mmol, 1.50 equiv), TMS-imidazole (170 mg, 178 μL, 1.21 mmol, 3.00 equiv.), and 1.0 mL of dioxane at 23 ℃. After 10 minutes, pyridin-3-ol (**1l**) (57.5 mg, 0.605 mmol, 1.50 equiv.) in 0.6 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol **2e** (70.0 mg, 0.404 mmol, 1.00 equiv.) in 0.9 mL dioxane was added and then the vial was sealed and heated at 80 ℃ for 24 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 1:1 (v/v), to afford 82.0 mg of the title compound as a brown solid (82% yield).

R_f = 0.50 (hexane/EtOAc = 2/3 (v/v)). NMR Spectroscopy : ^{1}H NMR (500 MHz, $CDCl_3$, 23 ℃, δ): 8.20 (s, 1H), 8.11 (s, 1H), 7.20–7.15 (m, 1H), 6.99 (d, *J* = 8.3 Hz, 1H), 4.89–4.84 (m, 1H), 4.29–4.23 (m, 2H), 3.98–3.93 (m, 2H), 1.39 (s, 9H).^{13}C NMR (125 MHz, $CDCl_3$, 23 ℃, δ): 156.0, 152.8, 142.9, 137.5, 124.0, 121.5, 79.9, 66.1, 56.2, 28.3. HRMS (ESI-TOF) (m/z) calcd for $C_{13}H_{19}N_2O_3$ $[M+H]^+$, 251.1390; found, 251.1399.

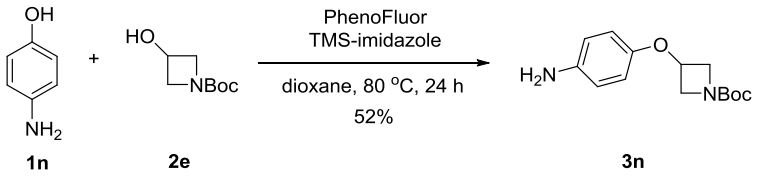
***tert*-Butyl 3-(pyridin-4-yloxy)azetidine-1-carboxylate (3m)**



Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (256 mg, 0.600 mmol, 1.50 equiv), TMS-imidazole (170 mg, 178 μL, 1.21 mmol, 3.00 equiv.), and 1.0 mL of dioxane at 23 ℃. After 10 minutes, pyridin-4(1H)-one (**1m**) (57.5 mg, 0.605 mmol, 1.50 equiv.) in 0.6 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol **2e** (70.0 mg, 0.404 mmol, 1.00 equiv.) in 0.9 mL dioxane was added and then the vial was sealed and heated at 80 ℃ for 24 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 2:3 (v/v), to afford 66.3 mg of the title compound as a yellow solid (66% yield).

R_f = 0.2 (hexane /EtOAc = 1/2 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ℃, δ): 8.43 (d, *J* = 6.3 Hz, 2H), 6.64 (d, *J* = 6.4 Hz, 2H), 4.94–4.88 (m, 1H), 4.31 (dd, *J* = 9.8, 6.4 Hz, 2H), 4.00 (dd, *J* = 10.0, 4.0 Hz, 2H), 1.43 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ℃, δ): 162.6, 155.9, 151.4, 110.3, 80.1, 65.8, 56.2, 28.3. HRMS (ESI-TOF) (m/z) calcd for $C_{13}H_{19}N_2O_3$ $[M+H]^+$, 251.1390; found, 251.1395.

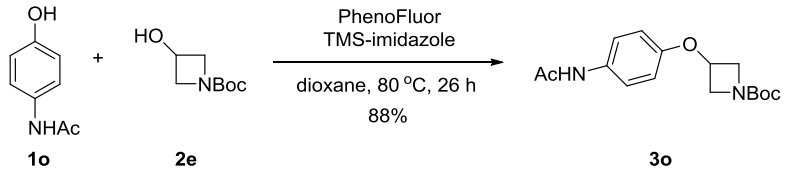
***tert*-Butyl 3-(4-aminophenoxy)azetidine-1-carboxylate (3n)**



Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (256 mg, 0.600 mmol, 1.50 equiv), TMS-imidazole (170 mg, 178 μL, 1.21 mmol, 3.00 equiv.), and 1.0 mL of dioxane at 23 ℃. After 10 minutes, 4-aminophenol (**1n**) (65.4 mg, 0.600 mmol, 1.50 equiv.) in 0.75 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol **2e** (70.0 mg, 0.404 mmol, 1.00 equiv.) in 0.75 mL dioxane was added and then the vial was sealed and heated at 80 ℃ for 24 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 3:2 (v/v), to afford 55.0 mg of the title compound as a yellow solid (52% yield).

R_f = 0.5 (hexane/EtOAc = 1/1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 6.64–6.55 (m, 4H), 4.79–4.74 (m, 1H), 4.23 (dd, *J* = 9.6, 6.5 Hz, 2H), 3.96 (dd, *J* = 9.7, 4.6 Hz, 2H), 3.47 (brs, 2H), 1.44 (s, 9H).^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 156.2, 149.6, 140.8, 116.4, 115.7, 79.7, 66.1, 26.5, 28.4. HRMS (ESI-TOF) (m/z) calcd for $C_{14}H_{20}N_2NaO_3$ $[M+Na]^+$, 287.1366 ; found, 287.1368.

***tert*-Butyl 3-(4-acetamidophenoxy)azetidine-1-carboxylate (3o)**

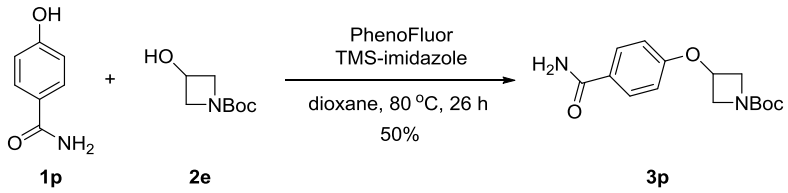


Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (192 mg, 0.450 mmol, 1.50 equiv), TMS-imidazole (127 mg, 133 μL, 0.905 mmol, 3.00 equiv.), and 1.0 mL of dioxane at 23 ℃. After 10 minutes, N-(4-hydroxyphenyl)acetamide (**1o**) (68.0 mg, 0.450 mmol, 1.50 equiv.) in 0.75 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol **2e** (52.0 mg, 0.301 mmol, 1.00 equiv.) in 0.75 mL dioxane was added and then the vial was sealed and heated at 80 ℃ for 26 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 1:2 (v/v), to afford 80.6 mg of the title compound as a white solid (88% yield).

R_f = 0.23 (hexane /EtOAc = 1/2 (v/v)). NMR Spectroscopy: ^{1}H NMR (600 MHz, CD_3OD, 23 ℃, δ) 7.44 (d, *J* = 9.0 Hz, 2H), 6.76 (d, *J* = 9.0 Hz, 2H), 4.98–4.91 (m, 1H), 4.31 (brs, 2H), 3.88 (brs, 2H), 2.09 (s, 3H), 1.45 (s, 9H). ^{13}C NMR (125 MHz, CD_3OD, 23 ºC, δ): 171.6, 158.2, 154.8, 133.9, 123.3, 116.0, 81.5, 67.3, 57.2, 28.8, 23.7. HRMS (ESI-TOF) (m/z) calcd for $C_{16}H_{22}N_2NaO_4$

$[M+Na]^+$, 329.1472; found, 329.1478.

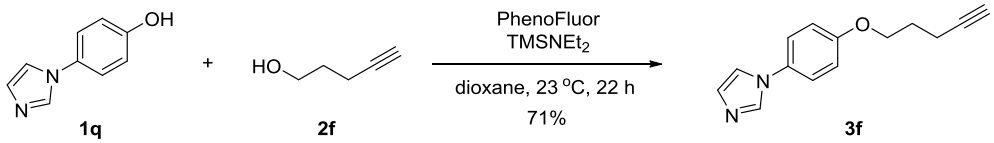
***tert*-Butyl 3-(4-carbamoylphenoxy)azetidine-1-carboxylate (3p)**



Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (192 mg, 0.450 mmol, 1.5 equiv), TMS-imidazole (127 mg, 133 μL, 0.905 mmol, 3.00 equiv.), and 1.00 mL of dioxane at 23 ℃. After 10 minutes, 4-hydroxybenzamide (**1p**) (62.0 mg, 0.452 mmol, 1.50 equiv.) in 0.75 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol **2e** (52.0 mg, 0.301 mmol, 1.00 equiv.) in 0.75 mL dioxane was added and then the vial was sealed and heated at 80 ℃ for 26 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 1:2~0/1 (v/v), to afford 42.8 mg of the title compound as a white solid (50% yield).

R_f = 0.23 (EtOAc). NMR Spectroscopy: ^{1}H NMR (600 MHz, CD_3OD, 23 ℃, δ): 7.85 (d, J = 8.3 Hz, 2H), 6.88 (d, J = 8.3 Hz, 2H), 5.04 (brs, 1H), 4.99 (brs, 2H), 4.36 (brs, 2H), 3.92 (brs, 2H), 1.43 (s, 9H). ^{13}C NMR (125 MHz, CD_3OD, 23 ºC, δ): 171.8, 161.0, 158.0, 130.9, 128.0, 115.5, 81.4, 67.3, 28.6. HRMS (ESI-TOF) (m/z) calcd for $C_{15}H_{20}N_2NaO_4$ $[M+Na]^+$, 315.1315; found, 315.1314.

1-(4-(Pent-4-yn-1-yloxy)phenyl)-1H-imidazole (3q)

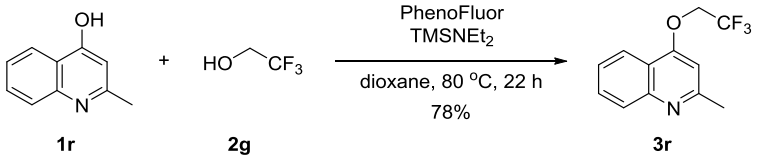


Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (341 mg, 0.800 mmol, 2.00 equiv), $TMSNEt_2$ (233 mg, 303 μL, 1.60 mmol, 4.00 equiv.), and 1.5 mL of dioxane at 23 ℃. After 10 minutes, 4-(1H-imidazol-1-yl)phenol (**1q**) (64 mg, 0.400 mmol, 1.00 equiv.) in 1.0 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol **2f** (67.3 mg, 74 μL, 0.800 mmol, 2.00 equiv.) was added and then the vial was sealed and the mixture was stirred at 23 ℃ for 22 h. The reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with EtOAc, to afford 64.0 mg of the title compound as a white solid (71% yield).

R_f = 0.25 (EtOAc). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.76 (s, 1H), 7.29 (d, J = 8.9 Hz, 2H), 7.19 (d, J = 8.9 Hz, 2H), 6.99 (d, J = 8.9 Hz, 2H), 4.11 (t, J = 6.1 Hz, 2H), 2.43 (td, J = 6.9, 2.6 Hz, 2H), 2.03 (p, J = 6.5 Hz, 2H), 1.98 (t, J = 2.6 Hz, 1H). ^{13}C NMR (125

MHz, $CDCl_3$, 23 ºC, δ): 158.4, 136.0, 130.9, 130.3, 123.4, 118.9, 115.6, 83.4, 69.12, 66.7, 28.2, 15.3. HRMS (ESI-TOF) (m/z) calcd for $C_{14}H_{15}N_2O$ $[M+H]^+$, 227.1179; found, 227.1188.

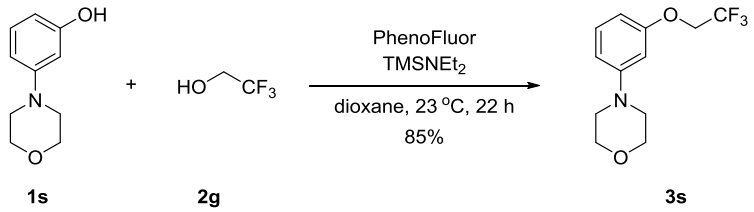
2-Methyl-4-(2,2,2-trifluoroethoxy)quinoline (3r)



Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (341 mg, 0.800 mmol, 2.00 equiv), $TMSNEt_2$ (233 mg, 303 μL, 1.60 mmol, 4.00 equiv.), and 1.0 mL of dioxane at 23 ℃. After 10 minutes, 2-methylquinolin-4-ol (**1r**) (64.0 mg, 0.402 mmol, 1.00 equiv.) in 1.0 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. 2,2,2-Trifluoroethanol (**2g**) (80.6 mg, 58 μL, 0.806 mmol, 2.00 equiv.) was added and then the vial was sealed and heated at 80 ℃ for 22 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 2:1 (v/v), to afford 75.2 mg of the title compound as a white solid (78% yield).

R_f = 0.40 (hexane/EtOAc = 2/1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ℃, δ): 8.12 (d, *J* = 8.3 Hz, 1H), 7.95 (d, *J* = 8.3 Hz, 1H), 7.67 (d, *J* = 7.9 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 6.51 (s, 1H), 4.49 (q, 7.8 Hz, 2H), 2.67 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 159.8, 148.9, 130.3, 128.2, 125.4, 123.0 (q, *J* = 278.3 Hz), 121.9, 121.4, 119.2, 101.1, 65.3 (q, *J* = 36.9 Hz), 25.8. ^{19}F NMR (282 MHz, $CDCl_3$, 23 ºC, δ): −73.6 (t, *J* =7.9 Hz). HRMS (ESI-TOF) (m/z) calcd for $C_{12}H_{11}F_3NO$ $[M+H]^+$, 242.0787; found, 242.0798.

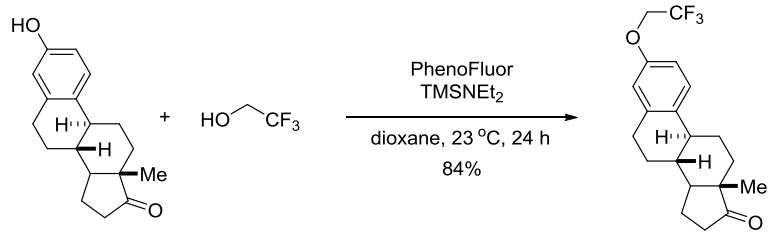
4-(3-(2,2,2-Trifluoroethoxy)phenyl)morpholine (3s)



Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (341 mg, 0.800 mmol, 2.00 equiv), $TMSNEt_2$ (233 mg, 303 μL, 1.60 mmol, 4.00 equiv.), and 1.0 mL of dioxane at 23 ℃. After 10 minutes, 3-morpholinophenol (**1s**) (71.7 mg, 0.400 mmol, 1.00 equiv.) in 1.0 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. 2,2,2-Trifluoroethanol (**2g**) (80.6 mg, 58 μL, 0.806 mmol, 2.00 equiv.) was added and then the vial was sealed and the mixture was stirred at 23 ℃ for 22 h. The reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 10:1 (v/v), to afford 88.6 mg of the title compound as a colorless oil (85% yield).

R_f = 0.20 (hexane/EtOAc = 10/1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ℃, δ): 7.21 (t, *J* = 8.2 Hz, 1H), 6.61 (dd, *J* = 8.3, 2.3 Hz, 1H), 6.51 (t, *J* = 2.4 Hz, 1H), 6.42 (dd, *J* = 8.1, 2.4 Hz, 1H), 4.34 (q, *J* = 8.2 Hz, 2H), 3.91–3.82 (m, 4H), 3.21–3.12 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 158.6, 153.0, 130.2, 123.5 (q, *J* = 277.8 Hz), 110.1, 105.1, 103.4, 66.9, 66.0 (q, *J* = 35.5 Hz), 49.2. ^{19}F NMR (282 MHz, $CDCl_3$, 23 ºC, δ): −74.0 (t, *J* = 8.2 Hz). HRMS (ESI-TOF) (m/z) calcd for $C_{12}H_{15}F_3NO_2$ $[M+H]^+$, 262.1049; found, 262.1060.

(8*R*,9*S*,13*S*)-13-Methyl-3-(2,2,2-trifluoroethoxy)-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (3t)

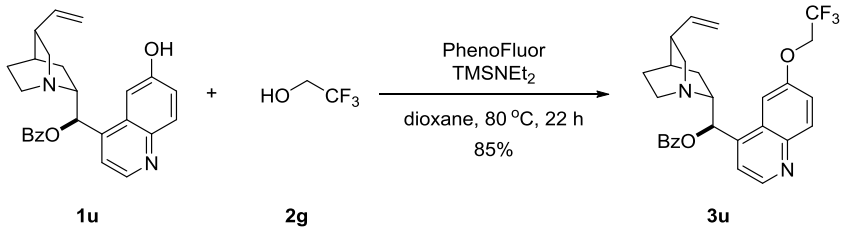


1t **2g** **3t**

Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (341 mg, 0.800 mmol, 2.00 equiv), $TMSNEt_2$ (233 mg, 303 μL, 1.60 mmol, 4.00 equiv.), and 1.0 mL of dioxane at 23 ℃. After 10 minutes, estrone (**1t**) (108 mg, 0.400 mmol, 1.00 equiv.) in 1.0 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. 2,2,2-Trifluoroethanol (**2g**) (80.6 mg, 58 μL, 0.806 mmol, 2.00 equiv.) was added and then the vial was sealed and the mixture was stirred at 23 ℃ for 24 h. The reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 8:1 (v/v), to afford 117.5 mg of the title compound as a white solid (78% yield).

R_f = 0.30 (hexane/EtOAc = 8/1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ℃, δ): 7.23 (dd, *J* = 8.6, 1.1 Hz, 1H), 6.78–6.72 (m, 1H), 6.69 (d, *J* = 2.7 Hz, 1H), 4.32 (q, *J* = 8.2 Hz, 2H), 2.99–2.86 (m, 2H), 2.51 (dd, *J* = 18.9, 8.8Hz, 1H), 2.45–2.39 (m, 1H), 2.26 (td, *J* = 10.5, 3.8 Hz, 1H), 2.15 (dt, *J* = 18.8, 8.9 Hz, 1H), 2.10–1.99 (m, 2H), 2.00–1.92 (m, 1H), 1.70–1.30 (m, 6H), 0.92 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 220.8, 155.5, 138.2, 134.0, 126.6, 123.4 (q, *J* = 278.1 Hz), 115.1, 112.4, 65.9 (q, *J* = 35.4 Hz), 50.4, 48.0, 44.0, 38.2, 35.9, 31.6, 29.6, 26.4, 25.9, 21.6, 13.8. ^{19}F NMR (282 MHz, $CDCl_3$, 23 ºC, δ): −74.0 (t, *J* = 8.2 Hz). HRMS (ESI-TOF) (m/z) calcd for $C_{20}H_{24}F_3O_2$ $[M+H]^+$, 353.1723; found, 353.1737.

(*R*)-(6-(2,2,2-Trifluoroethoxy)quinolin-4-yl)((1*R*,2*R*,4*R*,5*S*)-5-vinylquinuclidin-2-yl)methyl benzoate (3u)

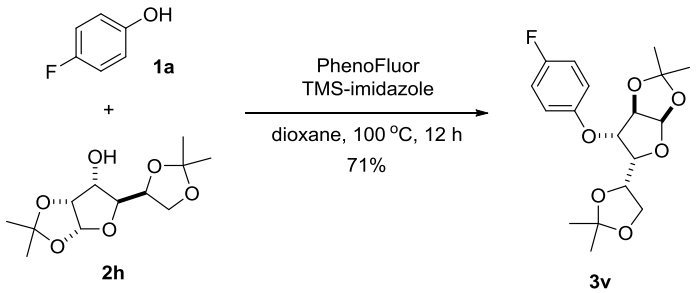


1u **2g** **3u**

Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (256 mg, 0.600 mmol, 2.00 equiv), $TMSNEt_2$ (175 mg, 224 μL, 1.20 mmol, 4.00 equiv.), and 1.0 mL of dioxane at 23 ℃. After 10 minutes, (*R*)-(6-hydroxyquinolin-4-yl)((1*R*,2*R*,4*R*,5*S*)-5-vinylquinuclidin-2-yl)methyl benzoate (**1u**) (124.2 mg, 0.301 mmol, 1.00 equiv.) in 1.0 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. 2,2,2-Trifluoroethanol (**2g**) (60.1 mg, 44 μL, 0.601 mmol, 2.00 equiv.) was added and then the vial was sealed and heated at 80 ℃ for 22 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc/Et_3N 100:150/1 (v/v/v), to afford 125.5 mg of the title compound as a yellow oil (85% yield).

R_f = 0.20 (hexane/EtOAc/Et_3N = 100/150/1 (v/v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.77 (d, *J* = 4.4 Hz, 1H), 8.11–8.05 (m, 3H), 7.69 (brs, 1H), 7.61 (t, *J* = 7.3 Hz, 1H), 7.51–7.43 (m, 4H), 6.84 (brs, 1H), 5.88–5.78 (m, 1H), 5.04 (d, *J* = 9.2 Hz, 1H), 5.02 (s, 1H), 4.74–4.51 (m, 2H), 3.47 (q, *J* = 7.9 Hz, 1H), 3.25 (s, 1H), 3.14 (t, *J* = 11.4 Hz, 1H), 2.72 (s, 2H), 2.37 (s, 1H), 2.00–1.90 (m, 2H), 1.82 (brs, 2H), 1.64 (brs, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 165.6, 155.7, 148.4, 145.3, 144.2, 141.6, 133.6, 132.5, 129.7, 129.6, 128.7, 126.6, 123.3 (q, *J* = 277.8 Hz), 121.6, 118.9, 114.7, 103.4, 77.3, 74.2, 66.0 (q, *J* = 36.4 Hz), 59.4, 56.6, 42.5, 39.6, 27.8, 27.6, 24.1. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –73.6 (t, *J* = 8.0 Hz). HRMS (ESI-TOF) (m/z) calcd for $C_{28}H_{28}F_3N_2O_3$ $[M+H]^+$, 497.2047; found, 497.2066.

(3a*R*,5*R*,6*S*,6a*R*)-5-((*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-6-(4-fluorophenoxy)-2,2 dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole (3v)



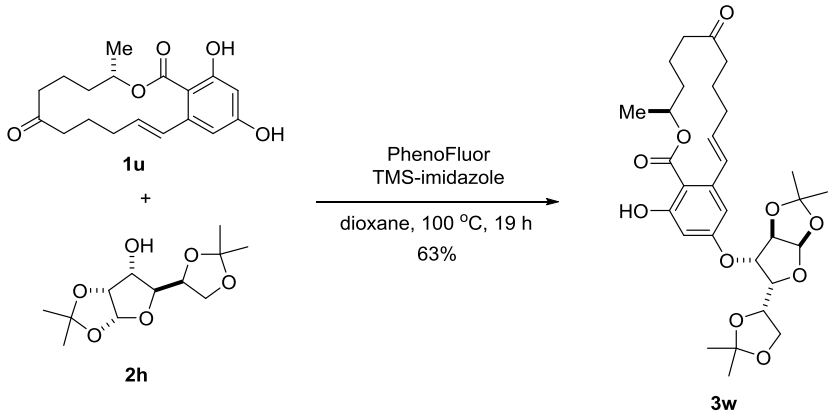
2h **3v**

Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (128 mg, 0.300 mmol, 1.50

equiv), TMS-imidazole (85 mg, 88.9 μL, 0.605 mmol, 3.00 equiv.), and 1.5 mL of dioxane at 23 ℃. After 10 minutes, 4-fluorophenol (**1a**) (33.6 mg, 0.300 mmol, 1.50 equiv.) and 1.0 mL dioxane were added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol **2h** (52.1 mg, 0.200 mmol, 1.00 equiv.) in 1.5 mL dioxane was added and then the vial was sealed and heated at 100 ℃ for 12 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 25:1 (v/v), to afford 50.5 mg of the title compound as a white solid (71% yield).

R_f = 0.30 (hexane/EtOAc = 8/1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ℃, δ): 7.04–6.97 (m, 2H), 6.9 –6.90 (m, 2H), 6.00–5.88 (m, 1H), 4.65 (d, *J* = 3.0 Hz, 1H), 4.58 (d, *J* = 3.8 Hz, 1H), 4.45 (dd, *J* = 13.4, 5.8 Hz, 1H), 4.30 (dd, *J* = 7.7, 3.1 Hz, 1H), 4.18–4.07 (m, 2H), 1.54 (s, 3H), 1.44 (s, 3H), 1.33 (s, 3H), 1.31 (s, 3H).^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 157.8 (d, *J* = 239.8 Hz), 153.1 (d, *J* = 2.5 Hz), 116.8 (d, *J* = 8.2 Hz), 116.1 (d, *J* = 23.3 Hz), 112.1, 109.2, 105.2, 82.1, 80.7, 80.5, 72.2, 67.1, 26.9, 26.7, 26.2, 25.3. ^{19}F NMR (282 MHz, $CDCl_3$, 23 ºC, δ): –122.45. HRMS (ESI-TOF) (m/z) calcd for $C_{18}H_{24}FO_6$ $[M+H]^+$, 355.1551; found, 355.1562.

(*S*,*E*)-14-(((3a*S*,4*S*,5*R*,6a*S*)-5-((*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-4-yl)oxy)-16-hydroxy-3-methyl-3,4,5,6,9,10-hexahydro-1*H*-benzo[*c*][1]oxacyclotetradecine-1,7(8*H*)-dione (3w)

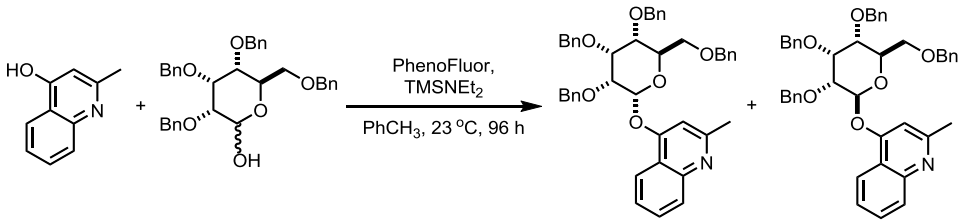


Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (85.2 mg, 0.200 mmol, 2.00 equiv), TMS-imidazole (56.6 mg, 59.2 μL, 0.403 mmol, 4.03 equiv.), and 0.9 mL of dioxane at 23 ℃. After 10 minutes, Zearalenone (**1u**) (31.8 mg, 0.100 mmol, 1.00 equiv.) in 0.6 mL dioxane was added, and the mixture was stirred at 23 ℃ for 10 min. Alcohol **2h** (52.0 mg, 0.201 mmol, 2.01 equiv.) was added and then the vial was sealed and heated at 100 ℃ for 19 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 5:1 (v/v), to afford 35.3 mg of the title compound as a off-white solid (63% yield).

R_f = 0.25 (hexane/EtOAc = 5/1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ℃, δ): 12.06 (s, 1H), 7.00 (d, *J* = 15.8 Hz, 1H), 6.51 (s, 2H), 5.94 (d, *J* = 3.9 Hz, 1H), 5.71 (ddd, *J* =

14.7, 10.7 Hz, 4.3 Hz, 1H), 5.04-4.97 (m, 1H), 4.74 (d, *J* = 3.1 Hz, 1H), 4.56 (d, *J* = 3.5 Hz, 1H), 4.43–4.37 (m, 1H), 4.31–4.28 (m 1H), 4.15–4.06 (m, 2H), 2.86–2.77 (m, 1H), 2.63–2.56 (m, 1H), 2.40–2.32 (m, 1H), 2.56–2.09 (m, 4H), 1.81–1.58 (m, 5H), 1.54 s, 3H), 1.42 (s, 3H), 1.38 (d, *J* = 6.3 Hz, 3H), 1.31 (s, 3H), 1.30 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 210.9, 171.3, 165.5, 161.3, 143.6, 132.9, 132.8, 112.3, 109.3, 109.1, 105.2, 104.4, 101.4, 82.2, 80.3, 79.8, 73.6, 72.1, 67.1, 42.9, 36.6, 34.7, 31.0, 26.9, 26.7, 26.2, 25.3, 22.2, 20.9, 20.8. HRMS (ESI-TOF) (m/z) calcd for $C_{30}H_{40}NaO_{10}$ $[M+Na]^+$, 583.2514; found, 583.2500.

Phenyl 2,3,4,6-Tera-O-4-(2)-methylquinolinyl-α-D-galactose (3x)

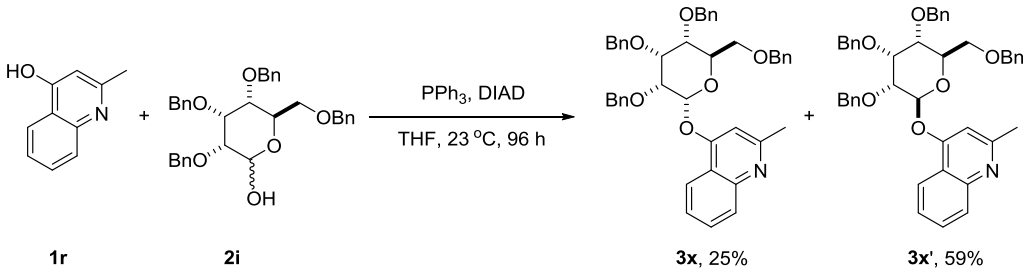


1r **2i** **3x**, 50% **3x'**, 0.4%

Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (128 mg, 0.300 mmol, 1.50 equiv.), $TMSNEt_2$ (87.5 mg, 112 μL, 0.60 mmol, 1.50 equiv.), and 1.0 mL of $PhCH_3$ at 23 ℃. After 10 minutes, 2-methylquinolin-4-ol (**1r**) (48.0 mg, 0.301 mmol, 1.50 equiv.) in 1.0 mL $PhCH_3$ were added, and the mixture was stirred at 23 ℃. After 30 min, 2,3,4,6-tetra-O-benzyl-D-galactose (**2i**) (108 mg, 0.199 mmol, 1.00 equiv.) was added and then the vial was sealed. After being stirred at 23 ℃ for 96 h, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 2:1 (v/v), to afford 68.0 mg of α-anomer **3x** as a colorless oil (50% yield) and 0.5 mg of β-anomer **3x'** as white solid (0.4%). β-anomer **3x'**was obtained as the major isomer via Mitsunobu reaction and characterized (see next page).

R_f = 0.20 (hexane/EtOAc = 2/1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ℃, δ): 8.21 (d, *J* = 8.3 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.72 (t, *J* = 7.7 Hz, 1H), 7.54–7.41 (m, 5H), 7.41–7.26 (m, 11H), 7.24–7.17 (m, 5H), 6.87 (s, 1H), 5.73 (anomeric H, d, *J* = 3.3 Hz, 1H), 5.13–4.98 (m, 2H), 4.96–4.88 (m, 2H), 4.75–4.65 (m, 2H), 4.47–4.27 (m, 4H), 4.12 (s, 1H), 4.07 (t, *J* = 6.5 Hz, 1H), 3.68–3.59 (m, 1H), 3.56 (dt, *J* = 12.3, 6.1 Hz, 1H), 2.65 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 160.2, 159.7, 148.9, 138.5, 138.4, 137.7, 129.8, 128.5, 128.4, 128.3, 128.3, 128.2, 128.1, 127.8, 127.7, 127.7, 127.6, 125.0, 121.9, 120.0, 104.5, 96.4 (anomeric carbon), 78.4, 76.4, 75.0, 74.7, 73.5, 73.4, 73.2, 70.9, 68.6, 25.8. HRMS (ESI-TOF) (m/z) calcd for $C_{44}H_{44}NO_6$ $[M+H]^+$, 682.3163; found, 682.3184.

Phenyl 2,3,4,6-Tera-O-4-(2)-methylquinolinyl-β-D-galactose (3x') prepared by Mitsunobu reaction



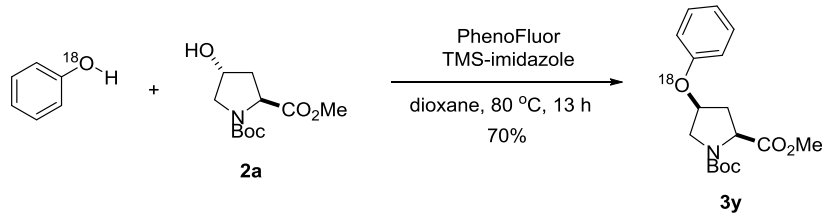
1r **2i** **3x**, 25% **3x'**, 59%

Under N_2 atmosphere, to an oven-dried vial were added 2-methylquinolin-4-ol (**1r**) (57.0 mg, 0.358 mmol, 1.20 equiv.), 2,3,4,6-tetra-O-benzyl-D-galactose (**2i**) (162 mg, 0.300 mmol, 1.00 equiv.), PPh_3 (94.5 mg, 0.360 mmol, 1.20 equiv.) and 2.0 mL of THF at 23 ℃. After 10 minutes, diisopropyl azodicarboxylate (DIAD, 72.9 mg, 71 μL, 0.361 mmol, 1.20 equiv.) was added slowly in 2 minutes. After being stirred at 23 ℃ for 24 h, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 2:1~1:1 (v/v), to afford 52.0 mg of α-anomer **3x** as a colorless oil (25% yield), and 122.0 mg of β-anomer **3x'** as a white solid (59% yield). The ratio of α-anomer/β-anomer was determined to be 30/70.

Characterization of β-anomer **3x'**: R_f = 0.10 (hexane/EtOAc = 2/1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.14 (d, *J* = 8.3 Hz, 1H), 7.95 (d, *J* = 8.5 Hz, 1H), 7.66 (t, *J* = 7.7 Hz, 1H), 7.48–7.18 (m, 21H), 6.83 (s, 1H), 5.27 (anomeric H, d, *J* = 7.6 Hz, 1H), 5.03 (d, *J* = 7.4 Hz, 1H), 5.01 (d, *J* = 8.3 Hz, 1H), 4.93 (d, *J* = 10.6 Hz, 1H), 4.83–4.77 (m, 2H), 4.68 (d, *J* = 11.6 Hz, 1H), 4.47 (d, *J* = 11.6 Hz, 1H), 4.41 (d, *J* = 11.6 Hz, 1H), 4.36–4.28 (m, 1H), 4.00 (d, *J* = 2.6 Hz, 1H), 3.81 (t, *J* = 6.3 Hz, 1H), 3.75–3.65 (m, 2H), 3.62–3.57 (m, 1H), 2.59 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 160.2, 159.9, 149.2 138.4, 138.3, 138.1, 137.9, 129.9, 128.6, 128.6, 128.5, 128.5, 128.5, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 125.2, 121.9, 119.8, 104.1, 100.7 (anomeric carbon), 82.3, 79.0, 75.9, 74.8, 74.6, 73.9, 73.4, 73.3, 69.2, 26.0. HRMS (ESI-TOF) (m/z) calcd for $C_{44}H_{44}NO_6$ $[M+H]^+$, 682.3163; found, 682.3182.

Incorporation of ^{18}O from phenol to ether

1-*tert*-Butyl 2-methyl (*2S,4S*)-4-(phenoxy)pyrrolidine-1,2-dicarboxylate (3y)



2a **3y**

Under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (128 mg, 0.300 mmol, 1.50

equiv), TMS-imidazole (85.0 mg, 88.9 μL, 0.606 mmol, 3.03 equiv.), and 1.0 mL of dioxane at 23 ℃. After 10 minutes, $Ph^{18}OH$ (68.5% purity in ^{18}O; 29.0 mg, 0.304 mmol, 1.52 equiv.) in 1.0 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h. Alcohol **2a** (49.0 mg, 0.200 mmol, 1.00 equiv.) in 1.0 mL dioxane was added and then the vial was sealed and heated at 80 ℃ for 13 h. Once cooled to 23 ℃, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 8:1 (v/v), to afford 44.5 mg of the title compound as a colorless oil (70% yield).

R_f = 0.25 (hexane/EtOAc = 5/1 (v/v)). $[\alpha]_D^{23}$ = –32.2 ^{o} (*c* = 1.0, $CHCl_3$). NMR Spectroscopy [mixture of 2 rotamers]: ^{1}H NMR (500 MHz, DMSO-*d6*, 23 ℃, δ): 7.32–7.25 (m, 4H, major+minor), 6.99–6.90 (m, 2H, major+minor), 6.88–6.78 (m, 4H, major+minor), 5.09–4.97 (m, 2H, major+ minor), 4.40 (dd, *J* = 8.3, 4.4 Hz, 1H, minor), 4.36 (dd, *J* = 9.4, 2.0 Hz, 1H, major), 3.75–3.65 (m, 2H, major+minor), 3.64 (s, 3H, major), 3.61 (s, 3H, minor), 3.46–3.36 (m, 2H, major+minor), 2.60–2.51 (m, 2H, major+minor), 2.20 (s, 1H, major), 2.17 (s, 1H, minor), 1.40 (s, 9H, minor), 1.34 (s, 9H,major). The above data is consistent with the reported data.[4]

VT NMR analysis of **3y** at 99 ℃ in DMSO-*d6* reflects an e.r. ≥ 97 : 3.

HRMS analysis shows a 67.7% incorporation of ^{18}O in the product, with the $Ph^{18}OH$ (68.5% purity of ^{18}O) as the starting material, indicating that the oxygen in the ether bond is predominantly from phenol. For the mass spectra of ^{18}O incorporation determination, see SI-$Ph^{18}OH$ and SI-^{18}O-3y.

Qualitative Compound Report

Data File	PHENOPOS1-141014-07710.d	**Sample Name**	phenopos
Sample Type	Unknown	**Position**	P1-A07
Instrument Name	Instrument 1	**User Name**	Sunia Trauger
Acq Method	OA_FIA_POS.M	**Acquired Time**	10/14/2014 1:39:51 PM
IRM Calibration Status	Success	**DA Method**	protein2.m
Comment	Easy-Access Method: 'OA FIA POS FORMULA'|C6H6O		

Sample Group		**Info.**	
MFC0	C6H6O	**MFC1**	
MFC2		**MFC3**	
Report Destination	F=D:\MassHunter\Data\SAT\Data\141014-133709		

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)	MFG Formula	DB Formula
Cpd 2: C6 H6 [18O]	0.23	96.0465	4539	C6 H6 [18O]	96.0461	4.56	C6 H6 [18O]	C6 H6 [18O]
Cpd 1: C6 H6 O	0.23	94.0418	2252	C6 H6 O	94.0419	-0.29	C6 H6 O	C6 H6 O

Compound Label	*m/z*	RT	Algorithm	Mass
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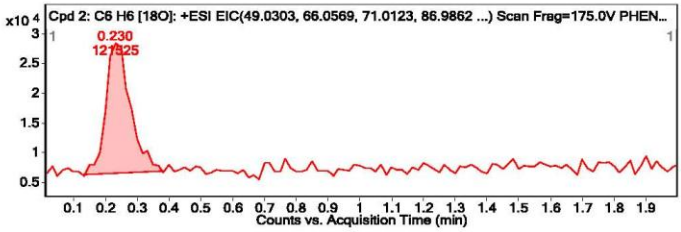
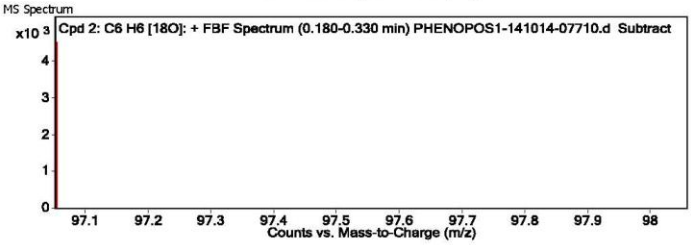
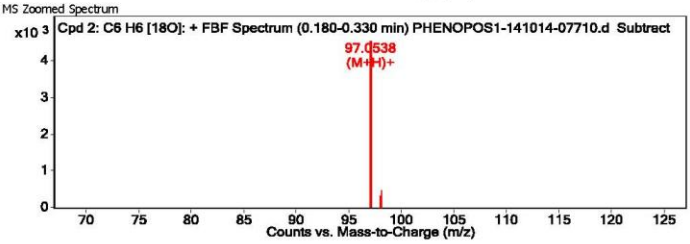


MS Spectrum



MS Zoomed Spectrum

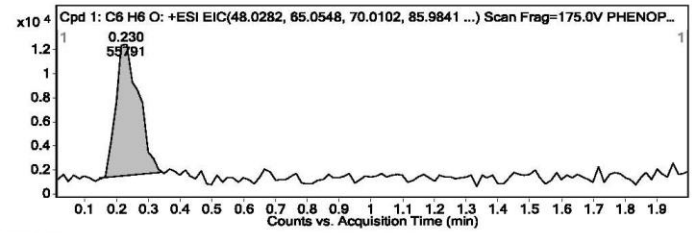


Qualitative Compound Report

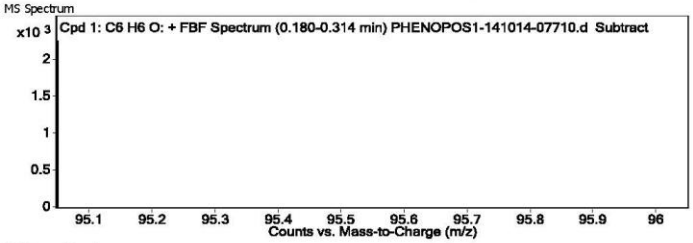
MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
97.0538	1	4539.22	C6H6[18O]	(M+H)+
98.0574	1	488.86	C6H6[18O]	(M+H)+

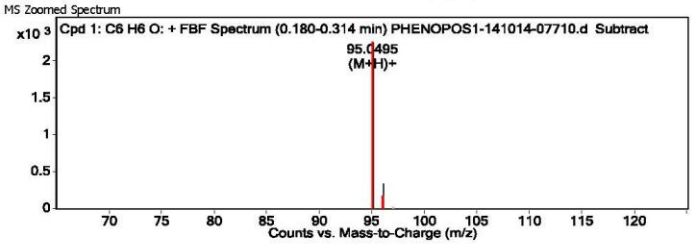
Compound Label	m/z	RT	Algorithm	Mass
Cpd 1: C6 H6 O	95.0495	0.23	Find By Formula	94.0418



MS Spectrum



MS Zoomed Spectrum



MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
95.0495	1	2251.58	C6H6O	(M+H)+
96.05	1	350.21	C6H6O	(M+H)+

--- End Of Report ---

SI-Ph^{18}OH

Qualitative Compound Report

Data File	XS_01205A1-141014-07715.d	Sample Name	XS_01205a
Sample Type	Unknown	Position	P1-B03
Instrument Name	Instrument 1	User Name	Sunia Trauger
Acq Method	OA_FIA_POS.M	Acquired Time	10/14/2014 4:26:53 PM
IRM Calibration Status	Success	DA Method	protein2.m
Comment	Easy-Access Method: 'OA FIA POS FORMULA'|C17H23NO5, C17H23NO4[18O]		

Sample Group		Info.	
MFC0	C17H23NO5	MFC1	C17H23NO4[18O]
MFC2		MFC3	
Report Destination	F=D:\MassHunter\Data\SAT\Data\141014-162417		

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)	MFG Formula	DB Formula
Cpd 2: C17 H23 N O4 [18O]	0.245	323.1628	88234	C17 H23 N O4 [18O]	323.1619	2.79	C17 H23 N O4 [18O]	C17 H23 N O4 [18O]
Cpd 1: C17 H23 N O5	0.245	321.1581	591128	C17 H23 N O5	321.1576	1.61	C17 H23 N O5	C17 H23 N O5

Compound Label	m/z	RT	Algorithm	Mass
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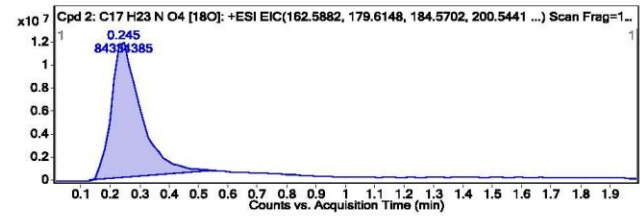
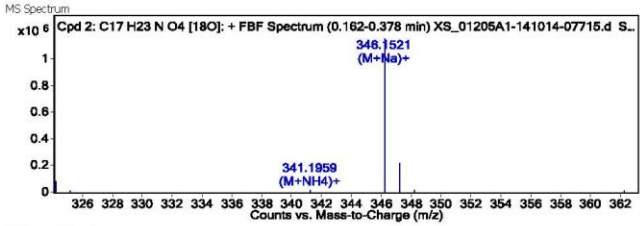
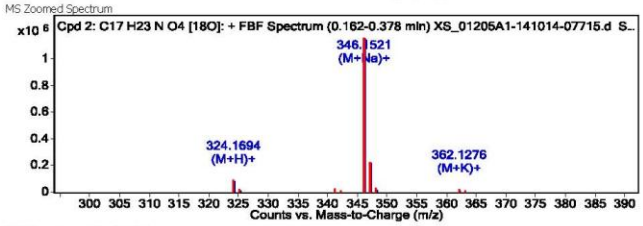


MS Spectrum



MS Zoomed Spectrum



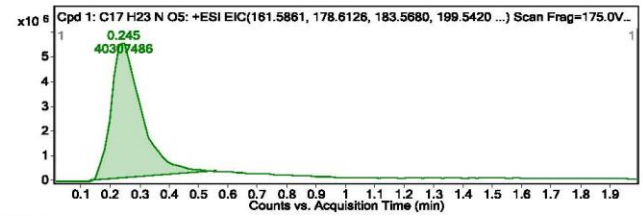
MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
324.1694	1	88234.43	C17H23NO4[18O]	(M+H)+
325.1727	1	16972.19	C17H23NO4[18O]	(M+H)+
341.1959	1	22418.55	C17H23NO4[18O]	(M+NH4)+

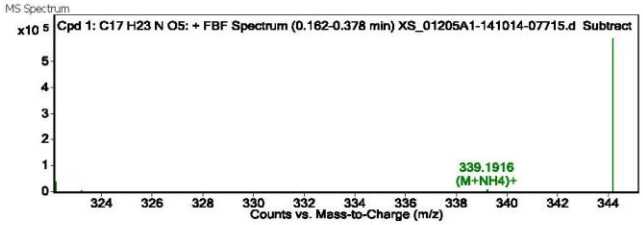
Qualitative Compound Report

342.1926	1	6686.67	C17H23NO4[18O]	(M+NH4)+
346.1521	1	1154158.38	C17H23NO4[18O]	(M+Na)+
347.155	1	223356.27	C17H23NO4[18O]	(M+Na)+
348.1576	1	25899.46	C17H23NO4[18O]	(M+Na)+
349.1646	1	3035.42	C17H23NO4[18O]	(M+Na)+
362.1276	1	20054.89	C17H23NO4[18O]	(M+K)+
363.1332	1	4466.87	C17H23NO4[18O]	(M+K)+

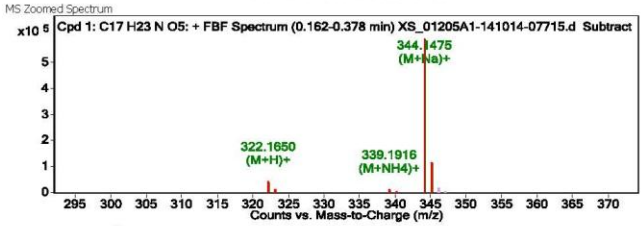
Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C17 H23 N O5	344.1475	0.245	Find By Formula	321.1581



MS Spectrum



MS Zoomed Spectrum



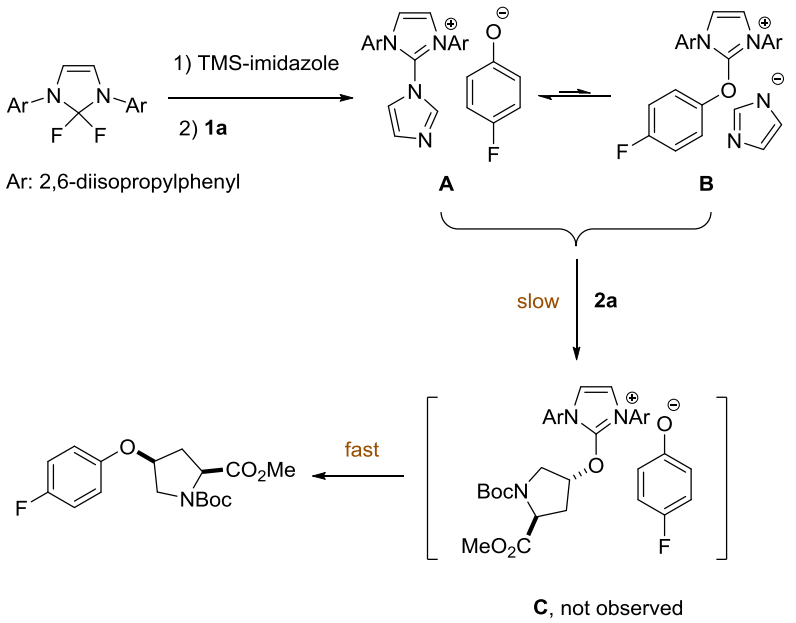
MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
322.165	1	42761.55	C17H23NO5	(M+H)+
323.1679	1	9477.4	C17H23NO5	(M+H)+
339.1916	1	11314.91	C17H23NO5	(M+NH4)+
340.1968	1	3201.07	C17H23NO5	(M+NH4)+
344.1475	1	591127.75	C17H23NO5	(M+Na)+
345.1503	1	116692.28	C17H23NO5	(M+Na)+

--- End Of Report ---

SI-^{18}O-3y

Tracking the reaction of 1a and 2a with ^{19}F NMR and HRMS (ESI-TOF)



Reaction 1: under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (42.7 mg, 0.100 mmol, 1.00 equiv), TMS-imidazole (28.2 mg, 29.7 μL, 0.201 mmol, 1.01 equiv.), and 1.0 mL of dioxane at 23 ℃. After 10 minutes, 4-fluorophenol (**1a**) (11.2 mg, 0.100 mmol, 1.00 equiv.) in 0.5 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h, after which $PhCF_3$ (20 μL, 0.162 mmol) was added as the internal standard for ^{19}F NMR analysis (see **Figure S1**). ^{19}F NMR shows that a yield of 97% was found for 4-fluorophenolate at −132.4 ppm. HRMS (ESI-TOF) shows a major signal at 455.3191, which is in consistent with the calculated MS for the cation of ion pair A ($C_{30}H_{39}N_4$; 455.3169). Although ion pair B was not observed in ^{19}F NMR, a very small peak at 499.3124 was observed via HRMS (ESI-TOF), which is consistent with the calculated MS for the cation of ion pair B ($C_{33}H_{40}FN_2O^+$; 499.3119). For the mass spectra, see SI-reaction 1.

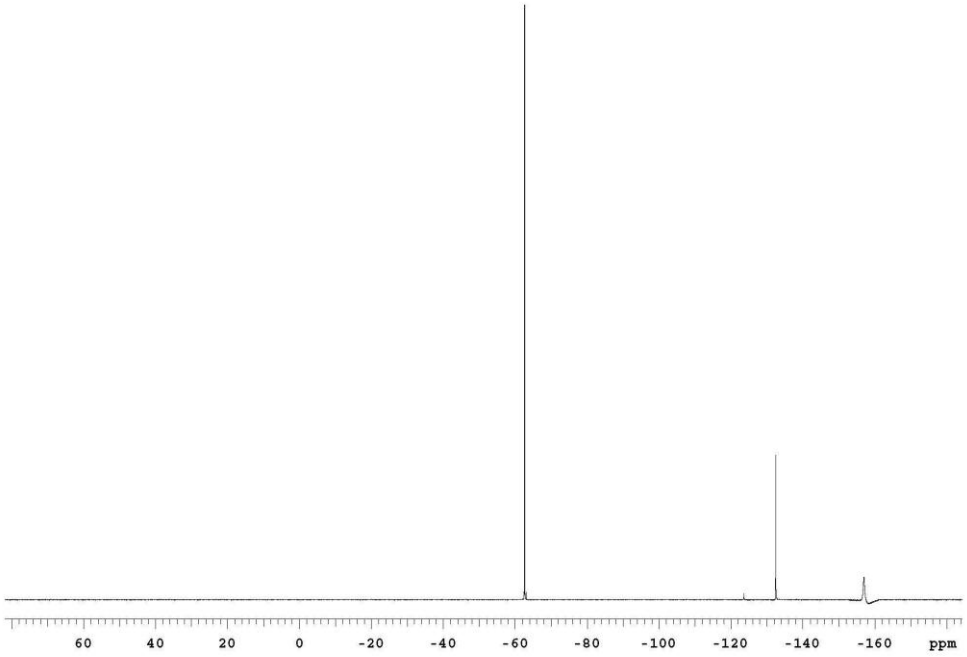


Figure S1 ^{19}F NMR of reaction 1

Reaction 2: under N_2 atmosphere, to an oven-dried vial were added PhenoFluor (42.7 mg, 0.100 mmol, 1.00 equiv), TMS-imidazole (28.2 mg, 29.7 μL, 0.201 mmol, 2.01 equiv.), and 1.0 mL of dioxane at 23 ℃. After 10 minutes, 4-fluorophenol (**1a**) (11.2 mg, 0.100 mmol, 1.00 equiv.) in 0.5 mL dioxane was added, and the mixture was stirred at 23 ℃ for 0.5 h, after which 1-(tert-butyl) 2-methyl (2*S*,4*R*)-4-hydroxypyrrolidine-1,2-dicarboxylate **2a** (24.5 mg, 0.100 mmol, 1.00 equiv.) in 1.0 mL of dioxane were added. The mixture was then heated at 60 ℃. After 3 h, $PhCF_3$ (10 μL, 0.081 mmol) was added as the internal standard for ^{19}F NMR analysis (see **Figure S2**). ^{19}F NMR showed a yield of 48% for ether **3a**, and a yield of 52% for 4-fluorophenolate. The cations of A and B can still be observed via HRMS (ESI-TOF), and A is the major intermediate. The anticipated ion pair C was not observed. For the mass spectra, see SI-reaction 2.

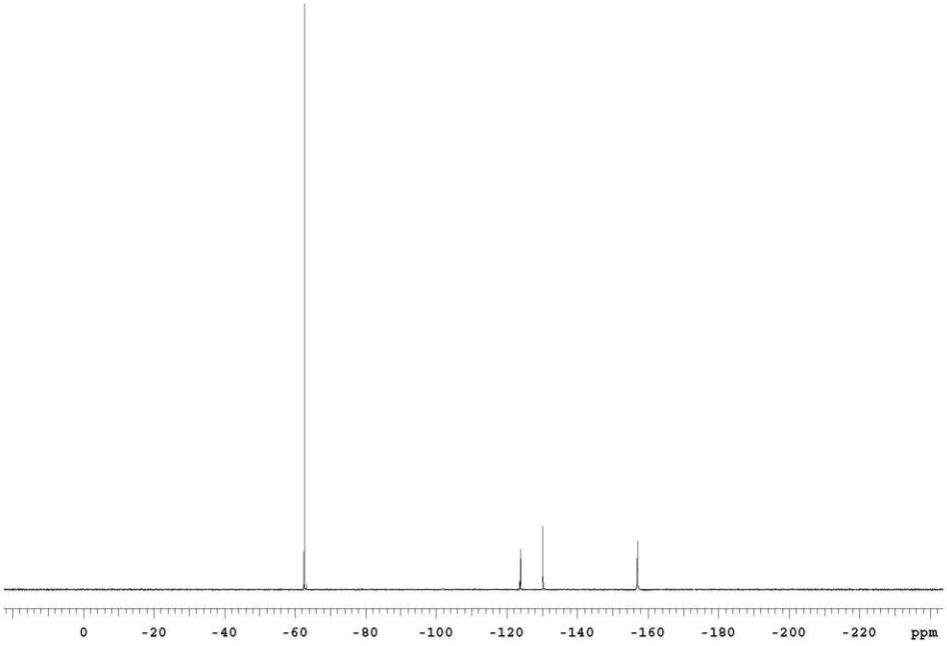
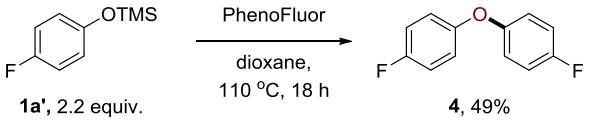


Figure S2 ^{19}F NMR of reaction 2

PhenoFluor mediated homo coupling of (4-fluorophenoxy)trimethylsilane (1a').



Under N_2 atmosphere, the mixture of PhenoFluor (427.0 mg, 1.00 mmol, 1.00 equiv), (4-fluorophenoxy)trimethylsilane (**1a'**, 405.4 mg, 2.20 mmol, 2.20 equiv.), and dioxane (6 mL) was heated at 110 ℃ for 18 h. The reaction was quenched with water (10 mL), and the mixture was extracted with Et_2O (20 mL × 3). The organic phase was dried with anhydrous $MgSO_4$. The solvent was removed under vacuo. The residue was purified by chromatography on silica gel, eluting with pentane, to afford 101 mg of the title compound as a colorless oil (49% yield).

Characterization of compound **4**: NMR Spectroscopy: ^{1}H NMR (400 MHz, $CDCl_3$, 23 ºC, δ): 7.06–6.99 (m, 4H), 6.97–6.92 (m, 4H). ^{13}C NMR (125 MHz, 23 ºC, δ) 158.86 (d, *J* = 241.7 Hz), 153.49 (d, *J* = 3.0 Hz), 120.05 (d, *J* = 8.4 Hz), 116.47 (d, *J* = 23.4 Hz). ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): −120.2. MS (EI) (m/z): 206 (M^+).

References

(1) Shriver, D. F.; Drezdon, M. A. Inert-Atmosphere Glove Boxes. The Manipulation of Air-Sensitive Compounds, 2nd ed.; John Wiley & Sons: New York, 1986; pp. 45–67.

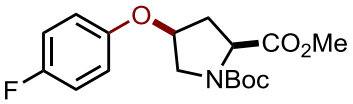
(2) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518–1520.

(3) Fulmer, G. R.; Miller, A. J. M.; Sherden, N. H.; Gottlieb, H. E.; Nudelman, A.; Stoltz, B. M.; Bercaw, J. E.; Goldberg, K. I. *Organometallics* **2010**, *29*, 2176-2179.

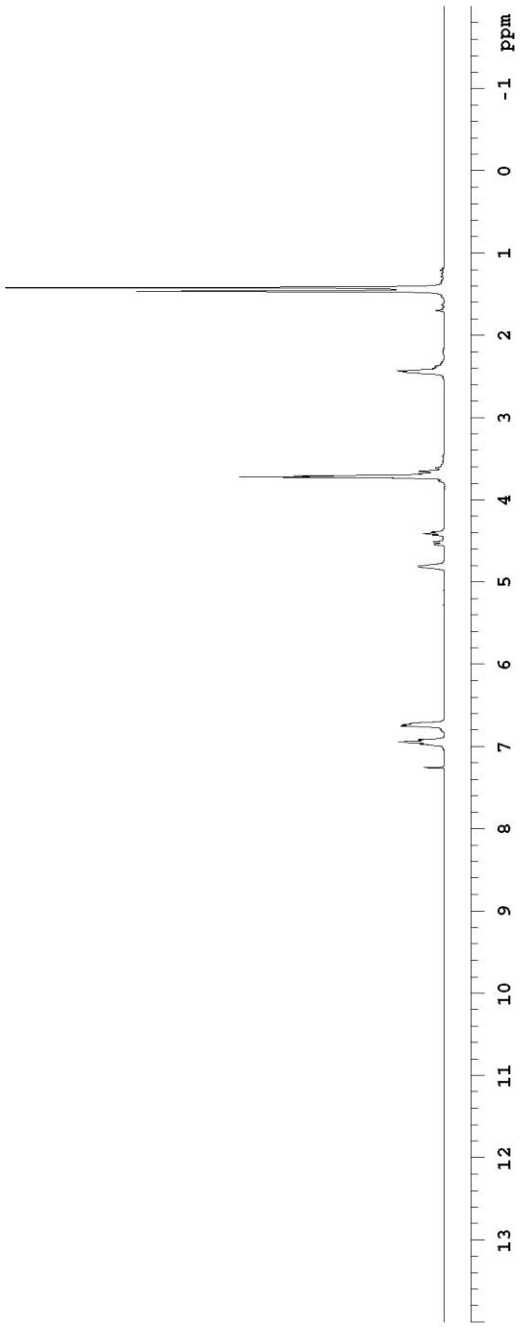
(4) Bellier, B.; McCort-Tranchepain, I.; Ducos, B.; Danascimento, S.; Meudal, H.; Noble, F.; Garbay, C.; Roques, B. P. *J. Med. Chem.* **1997**, *40*, 3947.

Spectroscopic Data

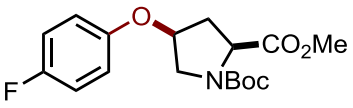
^{1}H NMR of **3a** ($CDCl_3$, 500 MHz, 23 ℃)



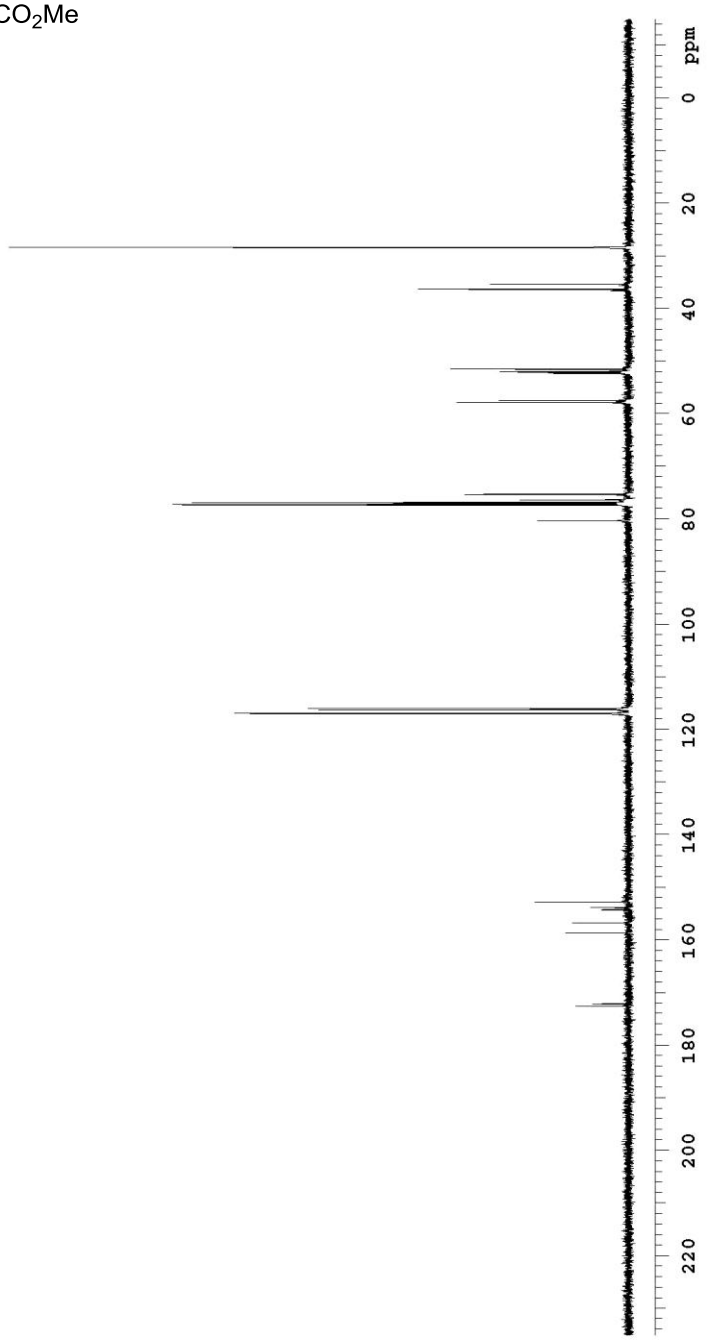
3a



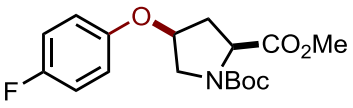
^{13}C NMR of **3a** ($CDCl_3$, 125 MHz, 23 ℃)



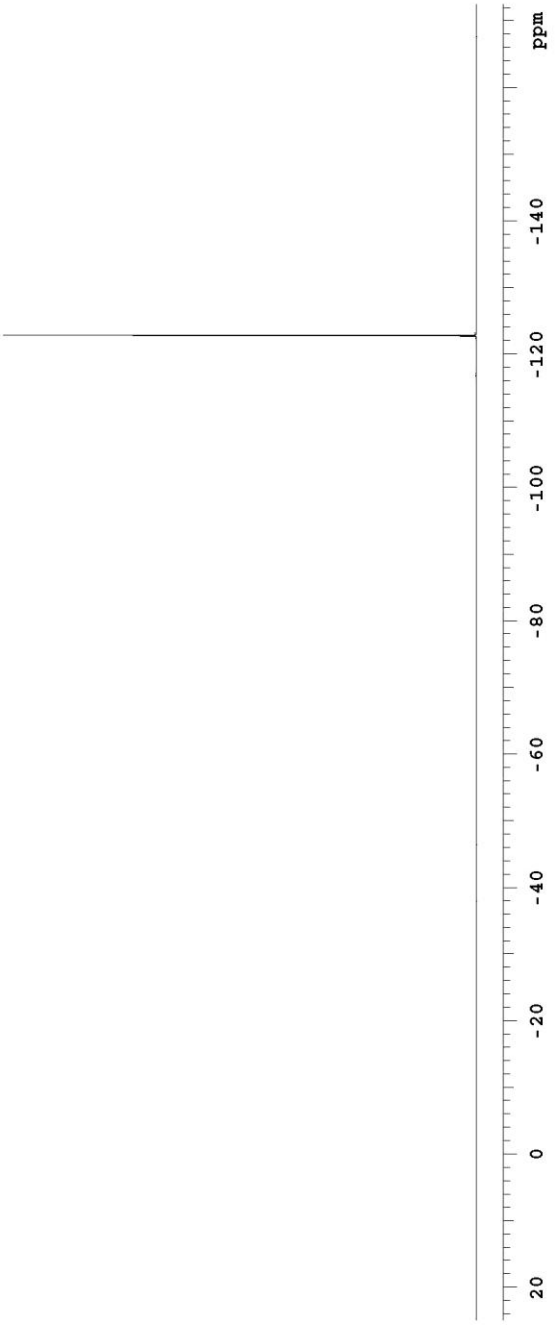
3a



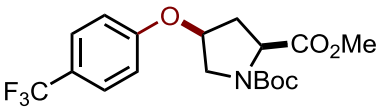
^{19}F NMR of **3a** ($CDCl_3$, 375 MHz, 23 ℃)



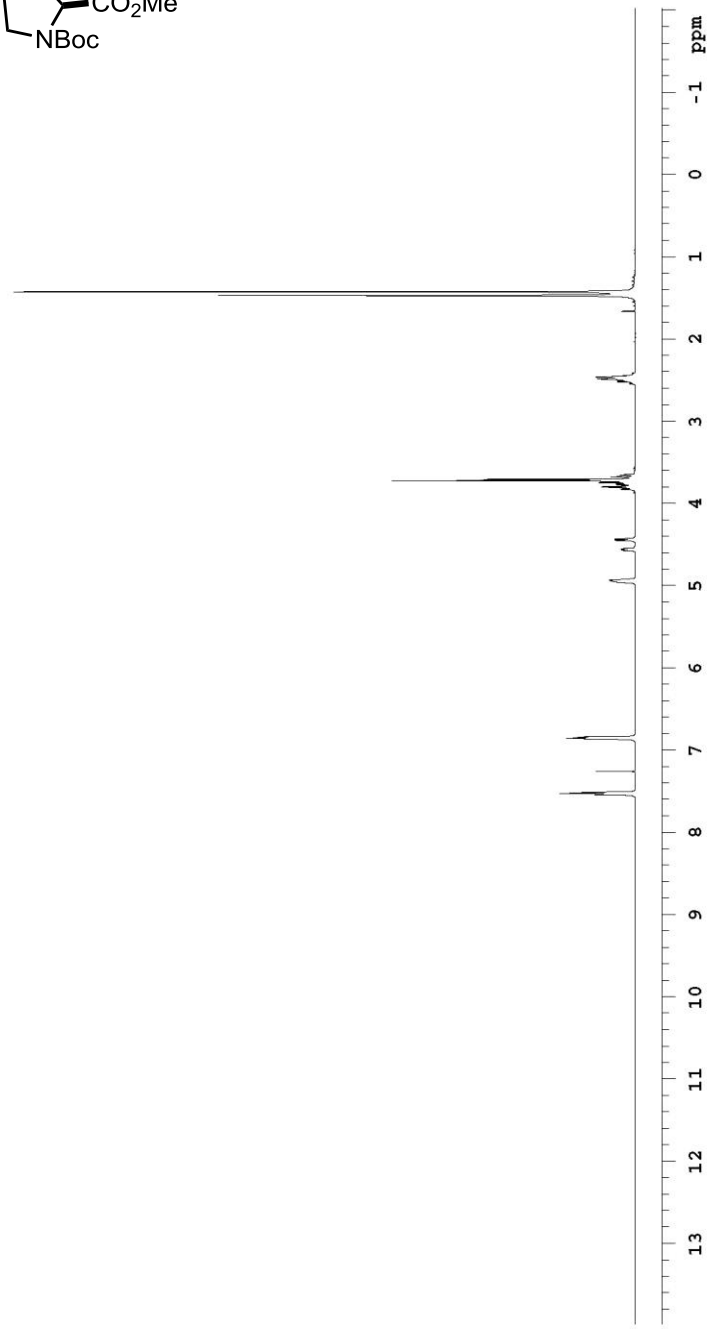
3a



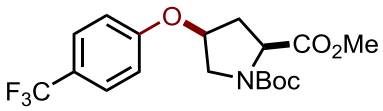
^{1}H NMR of **3b** ($CDCl_3$, 500 MHz, 23 ℃)



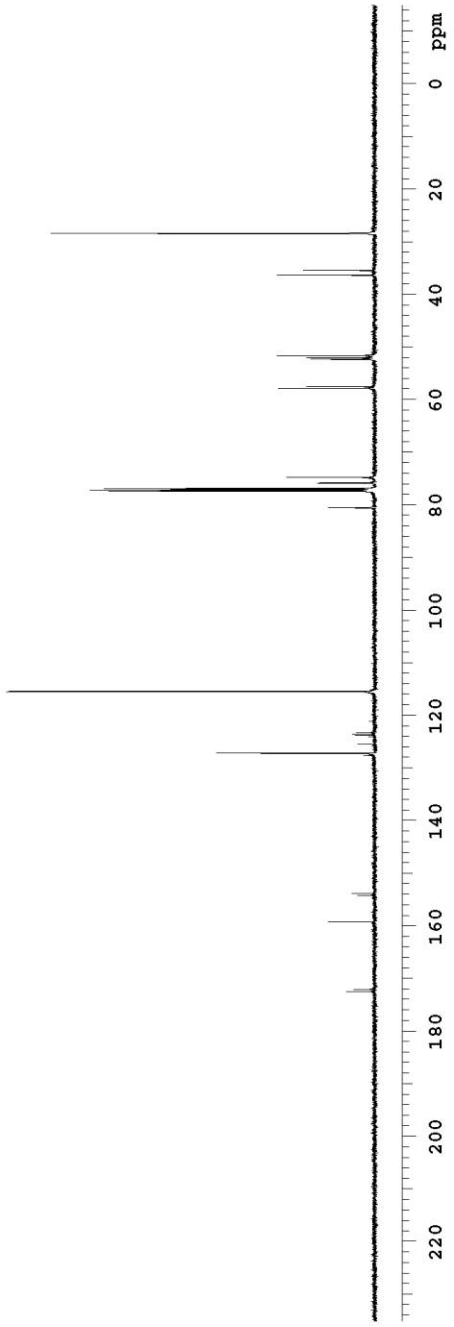
3b



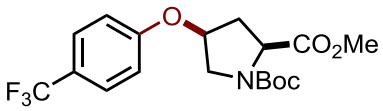
^{13}C NMR of **3b** ($CDCl_3$, 125 MHz, 23 ℃)



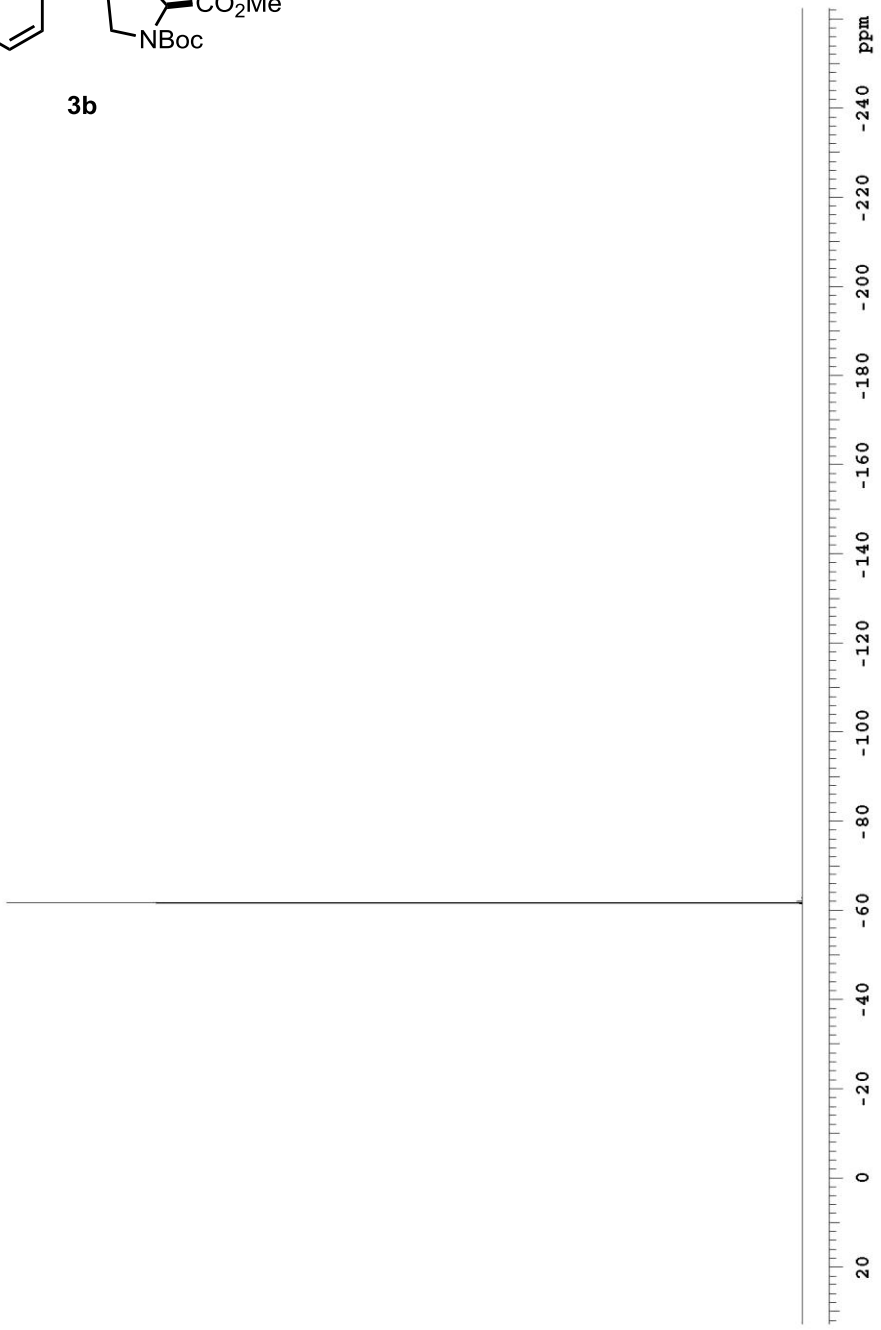
3b



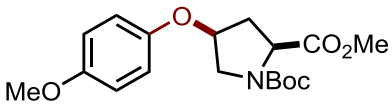
^{19}F NMR of **3b** ($CDCl_3$, 471 MHz, 23 °C)



3b



^{1}H NMR of **3c** ($CDCl_3$, 500 MHz, 23 ℃)



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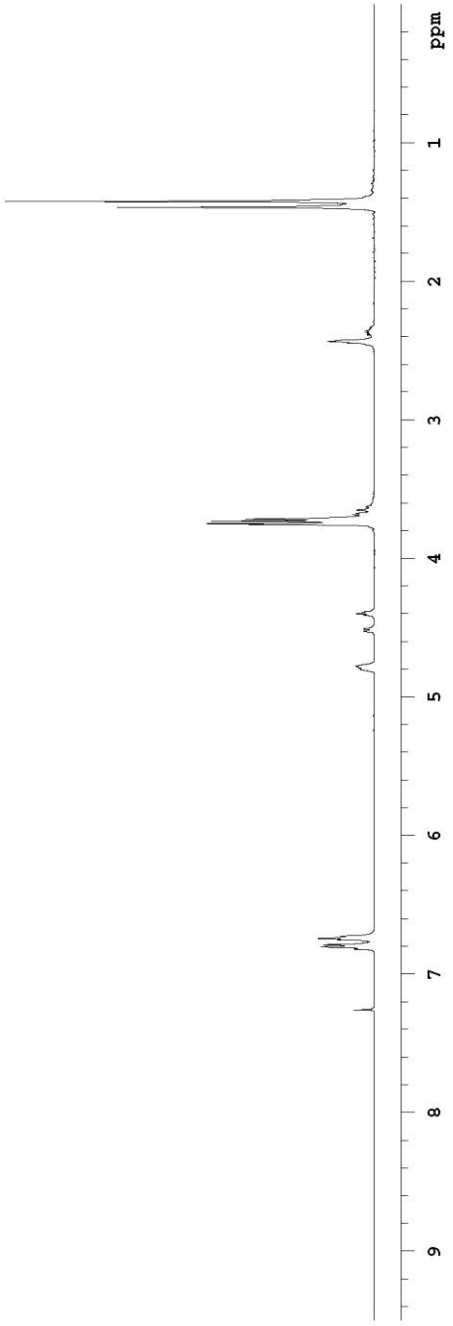
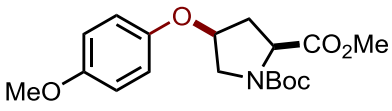
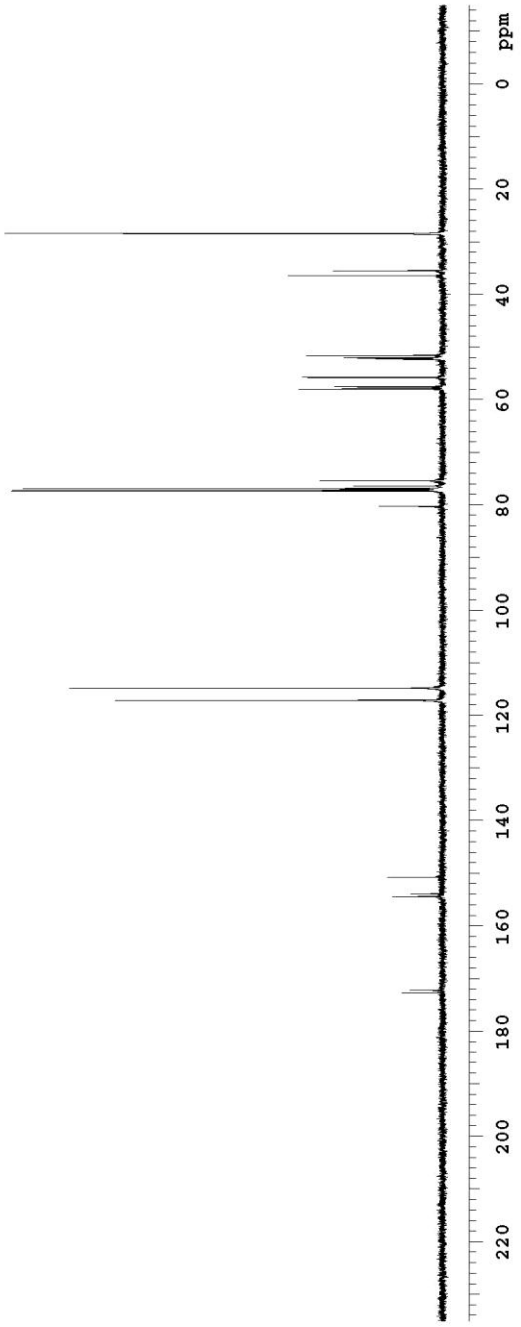


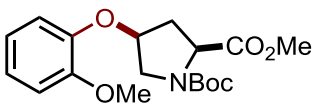
^{13}C NMR of **3c** ($CDCl_3$, 125 MHz, 23 ℃)



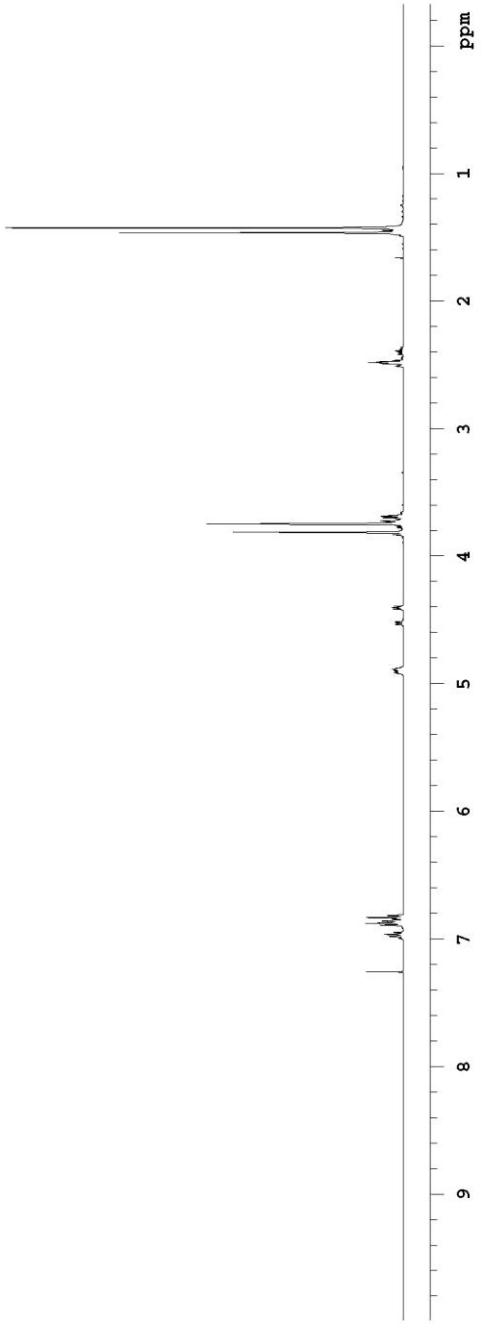
3c



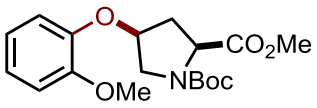
^{1}H NMR of **3d** ($CDCl_3$, 500 MHz, 23 ℃)



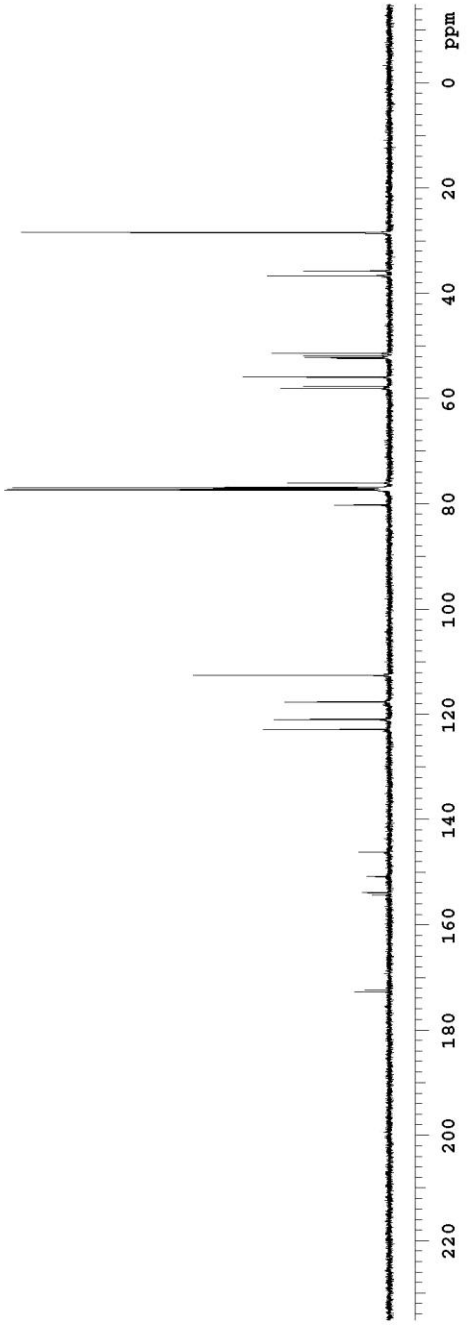
3d



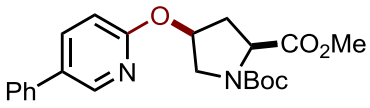
^{13}C NMR of **3d** ($CDCl_3$, 125 MHz, 23 ℃)



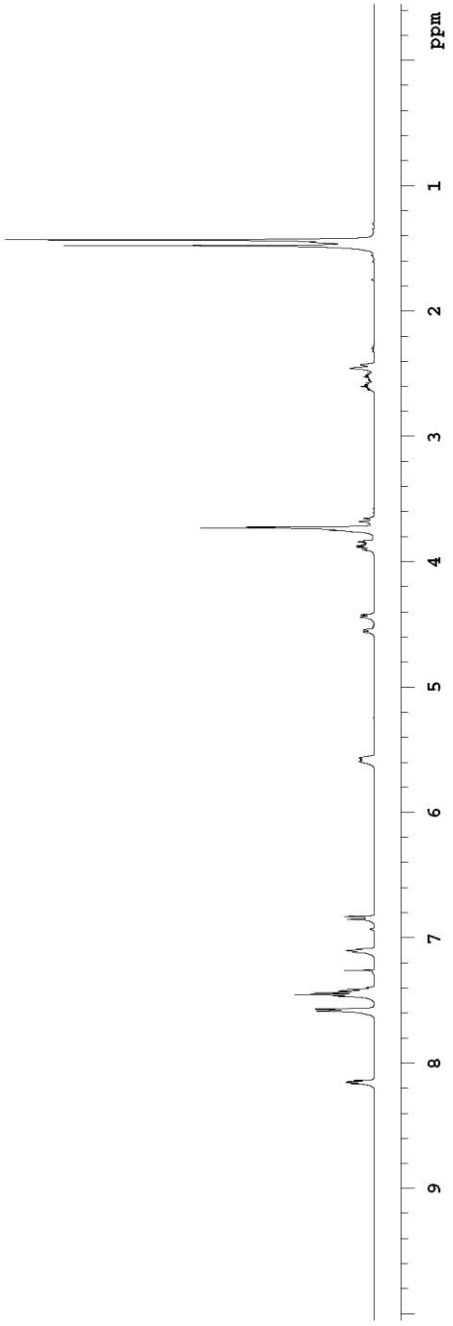
3d



^{1}H NMR of **3e** ($CDCl_3$, 500 MHz, 23 ℃)



3e



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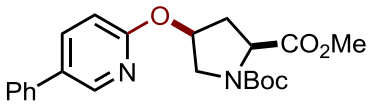
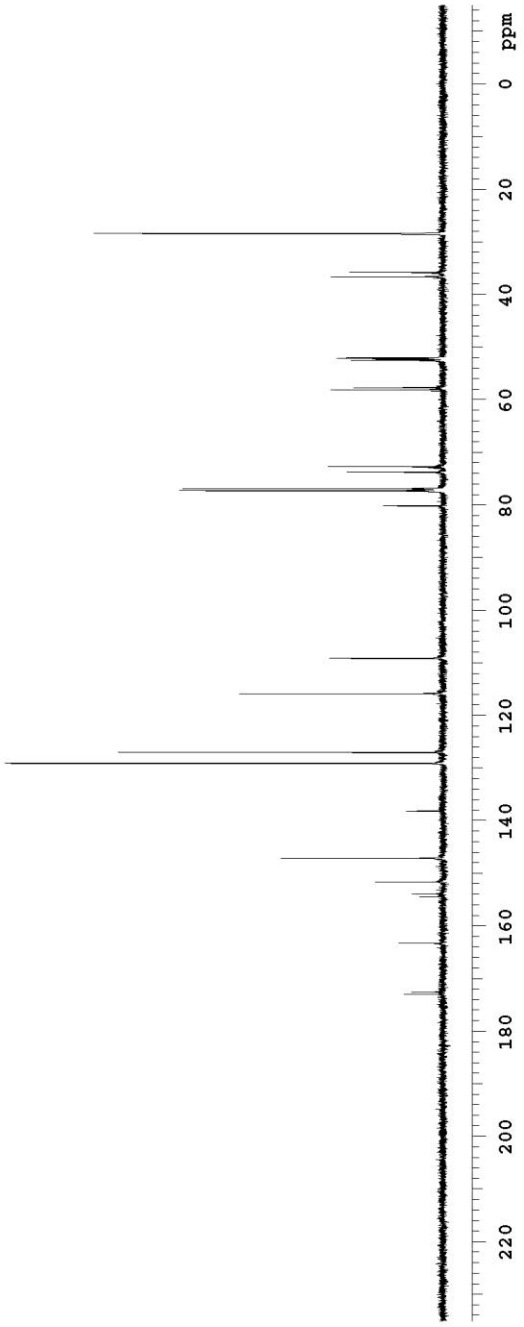
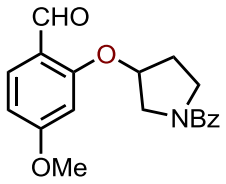


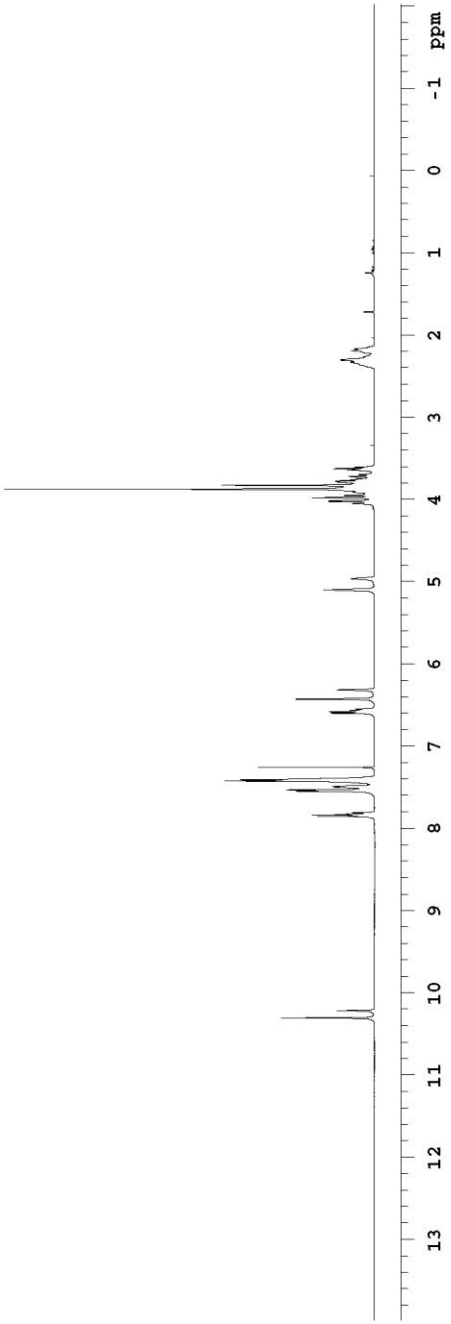
3e



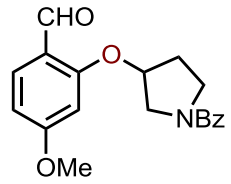
^{1}H NMR of (±)-**3f** ($CDCl_3$, 500 MHz, 23 ℃)



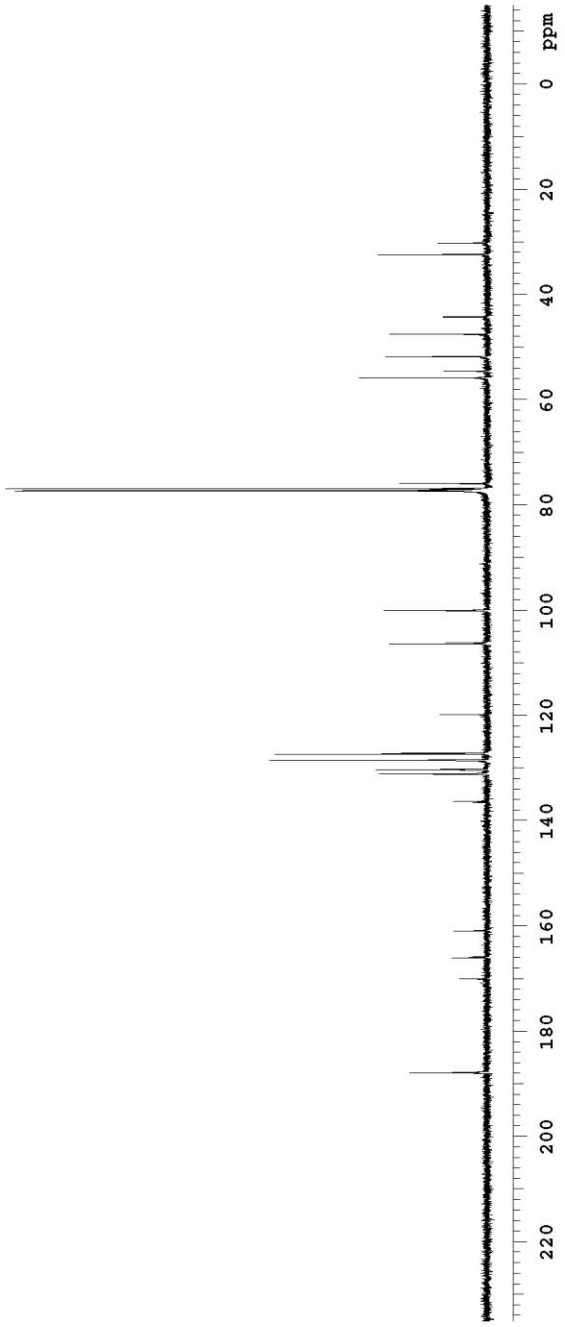
(±)-**3f**



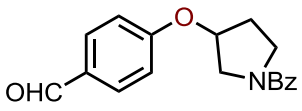
^{13}C NMR of (±)-**3f** ($CDCl_3$, 125 MHz, 23 ℃)



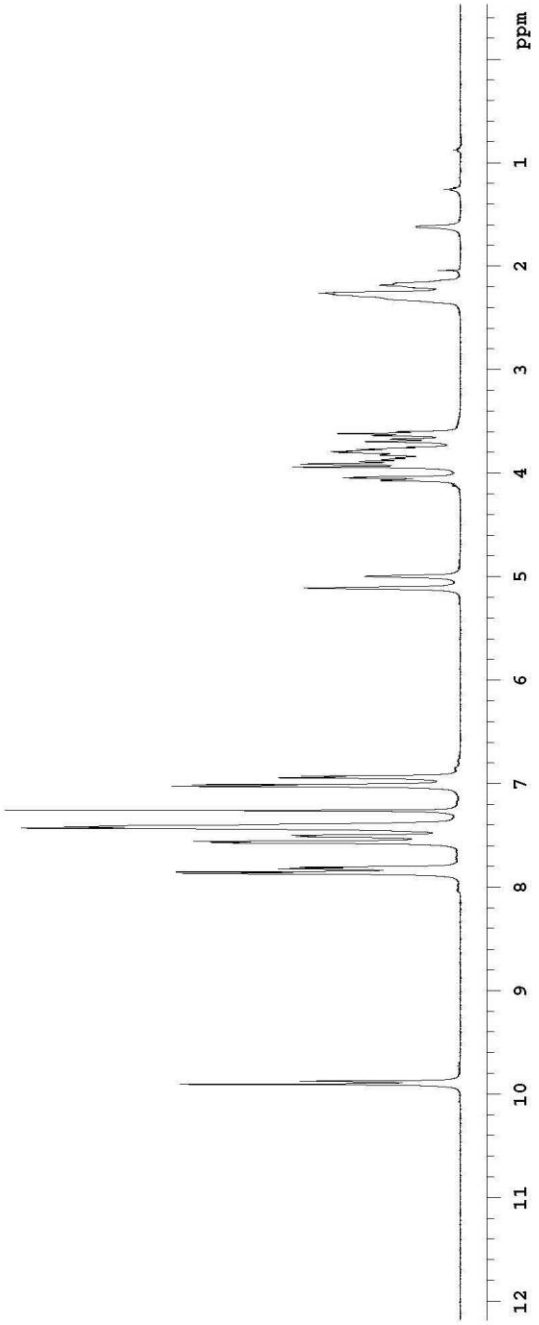
(±)-**3f**



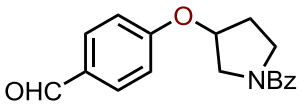
^{1}H NMR of (±)-**3g** ($CDCl_3$, 500 MHz, 23 ℃)



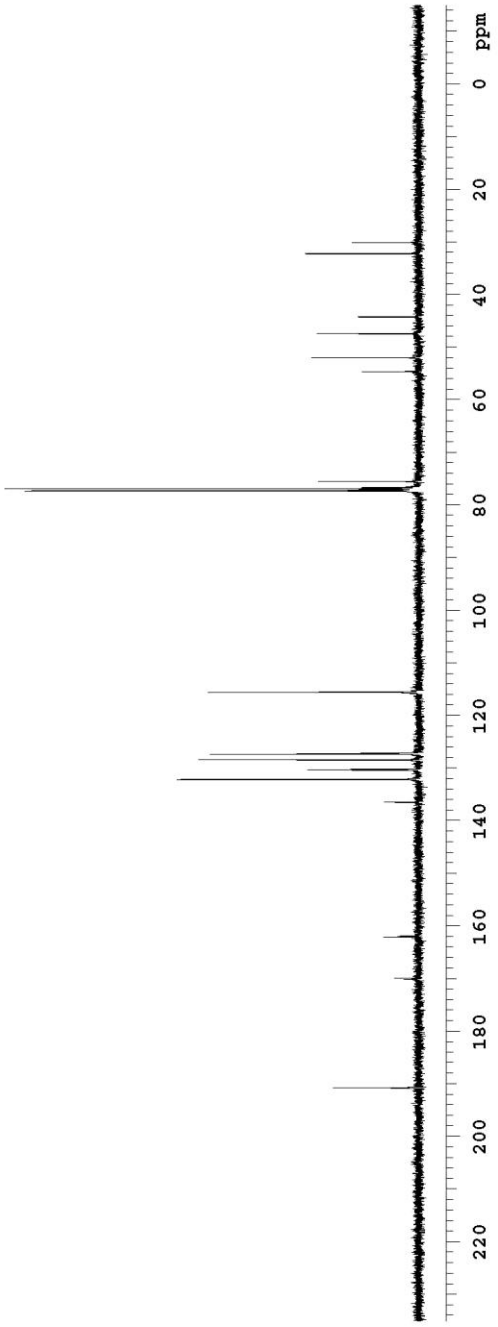
(±)-**3g**



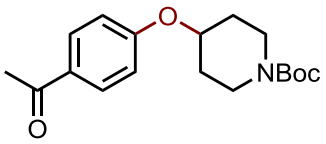
^{13}C NMR of (±)-**3g** ($CDCl_3$, 125 MHz, 23 ℃)



(±)-**3g**

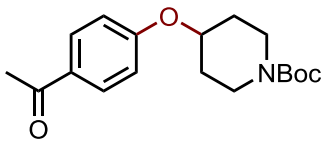


^{1}H NMR of **3h** ($CDCl_3$, 500 MHz, 23 ℃)

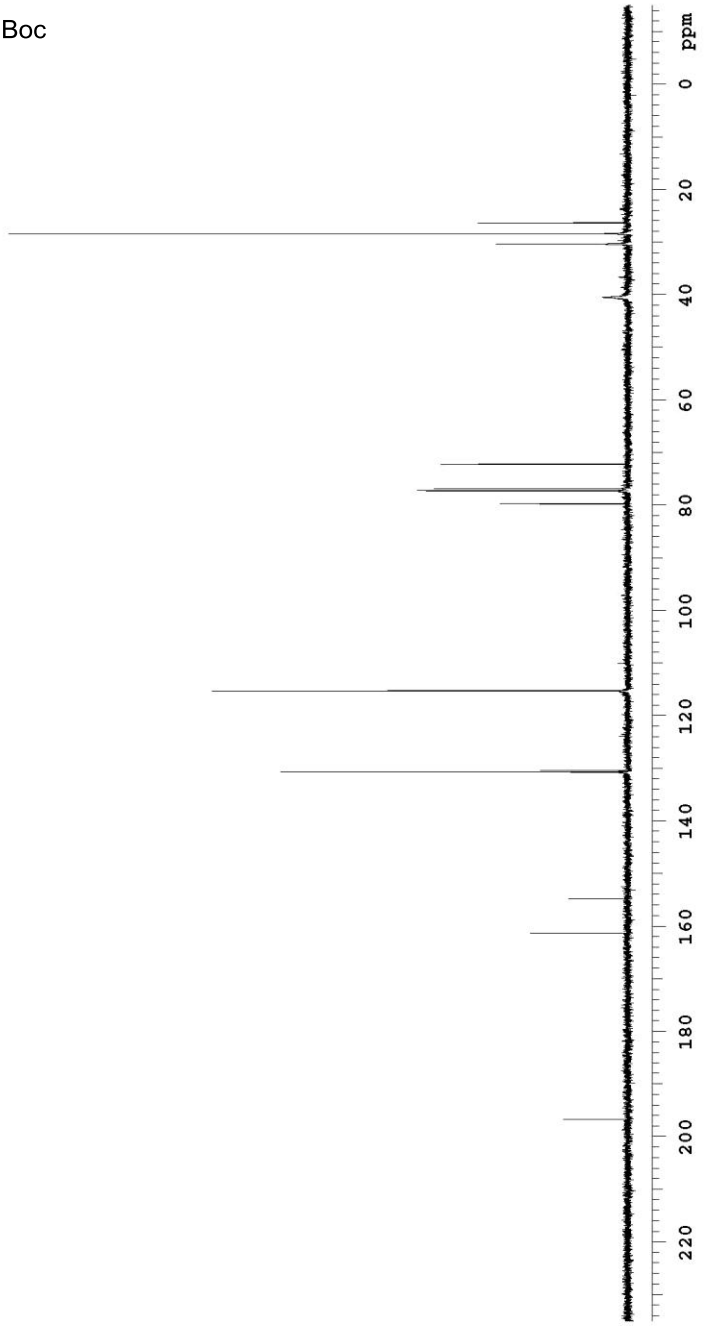


3h

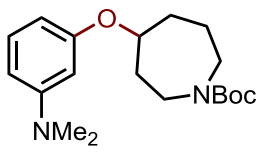
^{13}C NMR of **3h** ($CDCl_3$, 125 MHz, 23 ℃)



3h

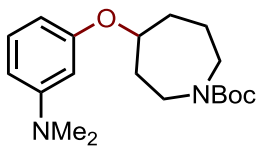


^{1}H NMR of (±)-**3i** ($CDCl_3$, 500 MHz, 23 ℃)

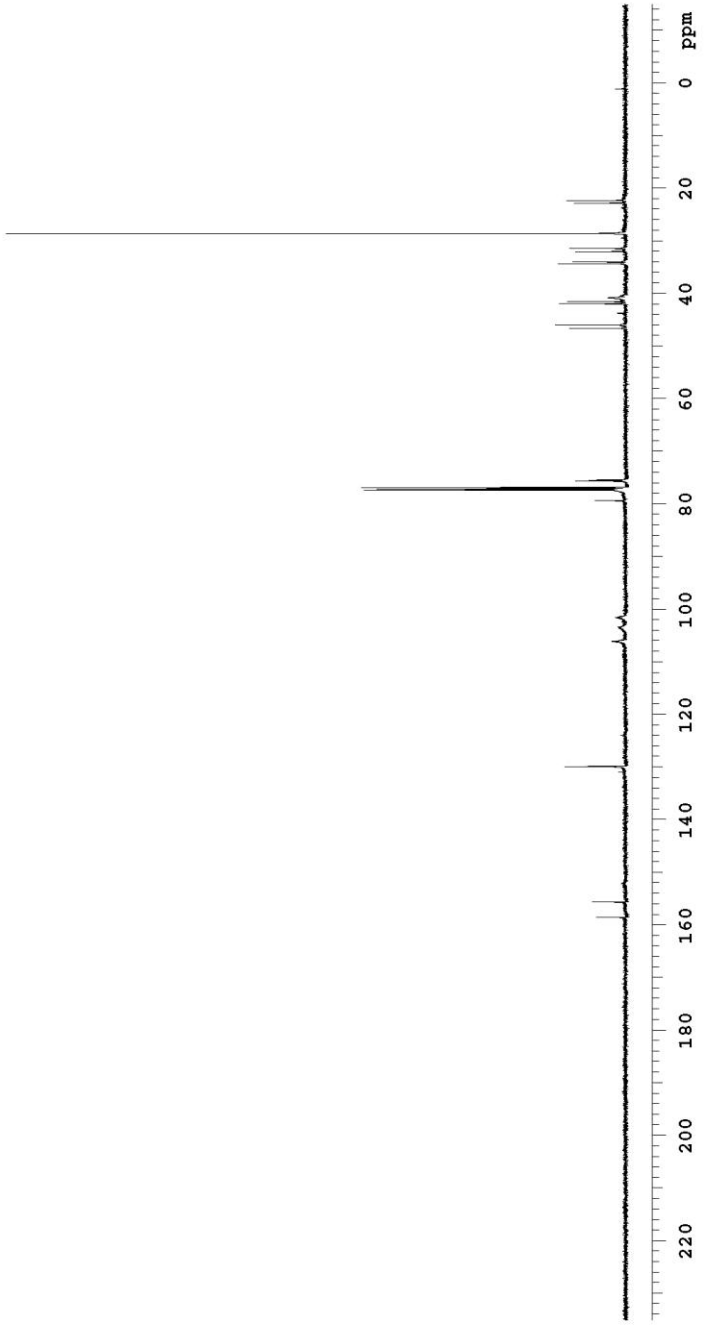


(±)-**3i**

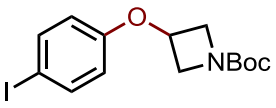
^{13}C NMR of (±)-**3i** ($CDCl_3$, 125 MHz, 23 ℃)



(±)-**3i**

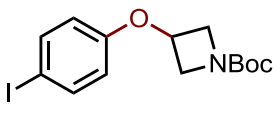


^{1}H NMR of **3j** ($CDCl_3$, 500 MHz, 23 ℃)



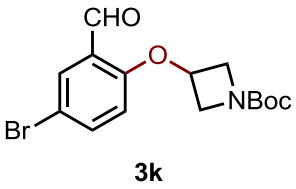
3j

^{13}C NMR of **3j** ($CDCl_3$, 125 MHz, 23 ℃)



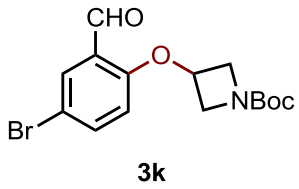
3j

^{1}H NMR of **3k** ($CDCl_3$, 500 MHz, 23 ℃)

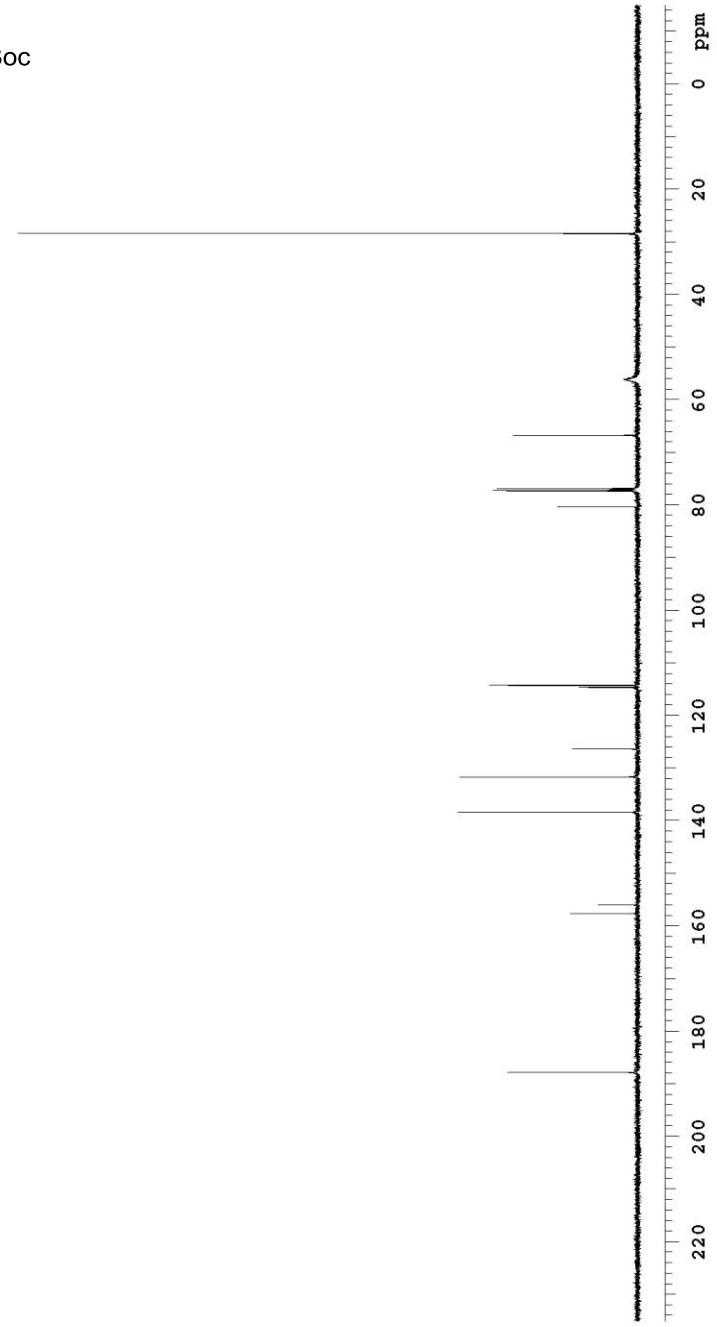


3k

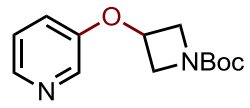
^{13}C NMR of **3k** ($CDCl_3$, 125 MHz, 23 ℃)



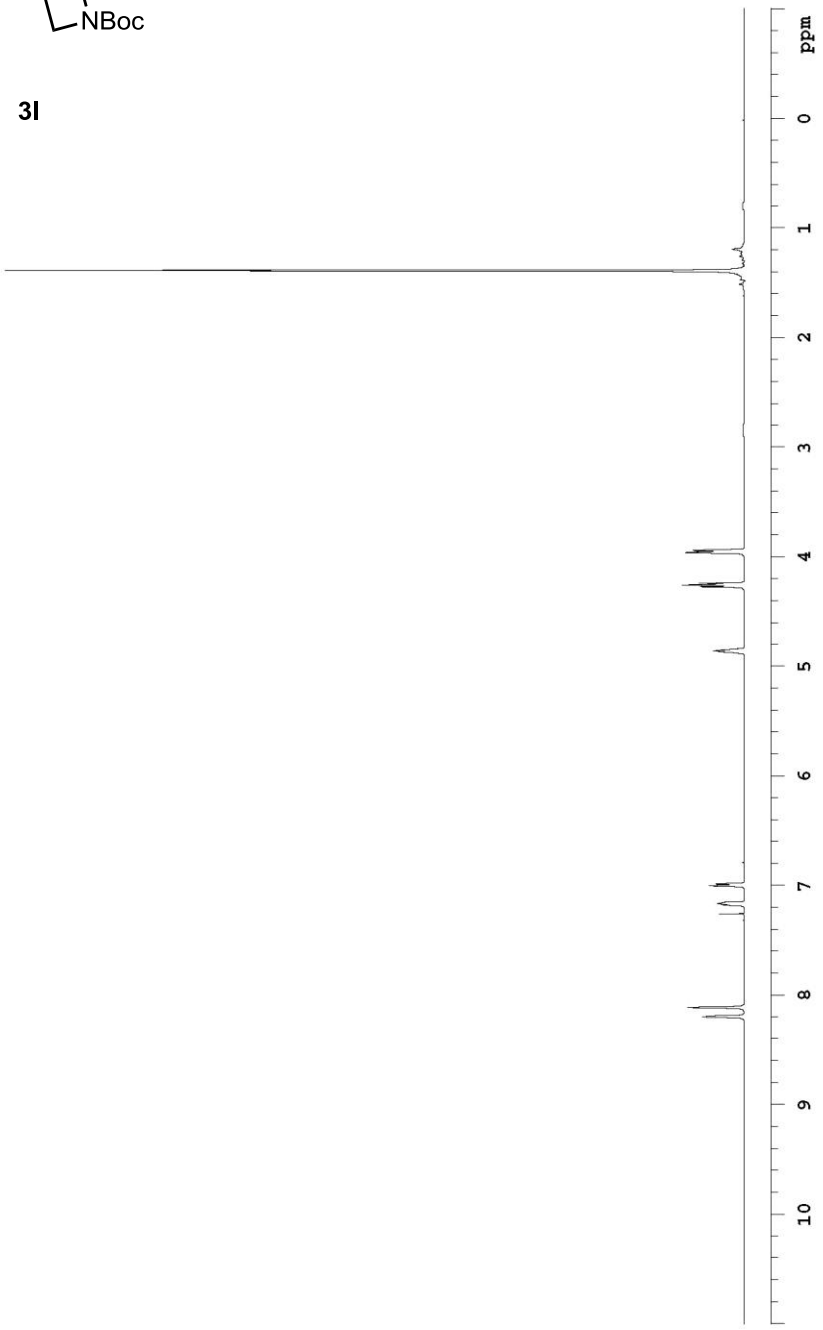
3k



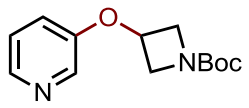
^{1}H NMR of **3l** ($CDCl_3$, 500 MHz, 23 ℃)



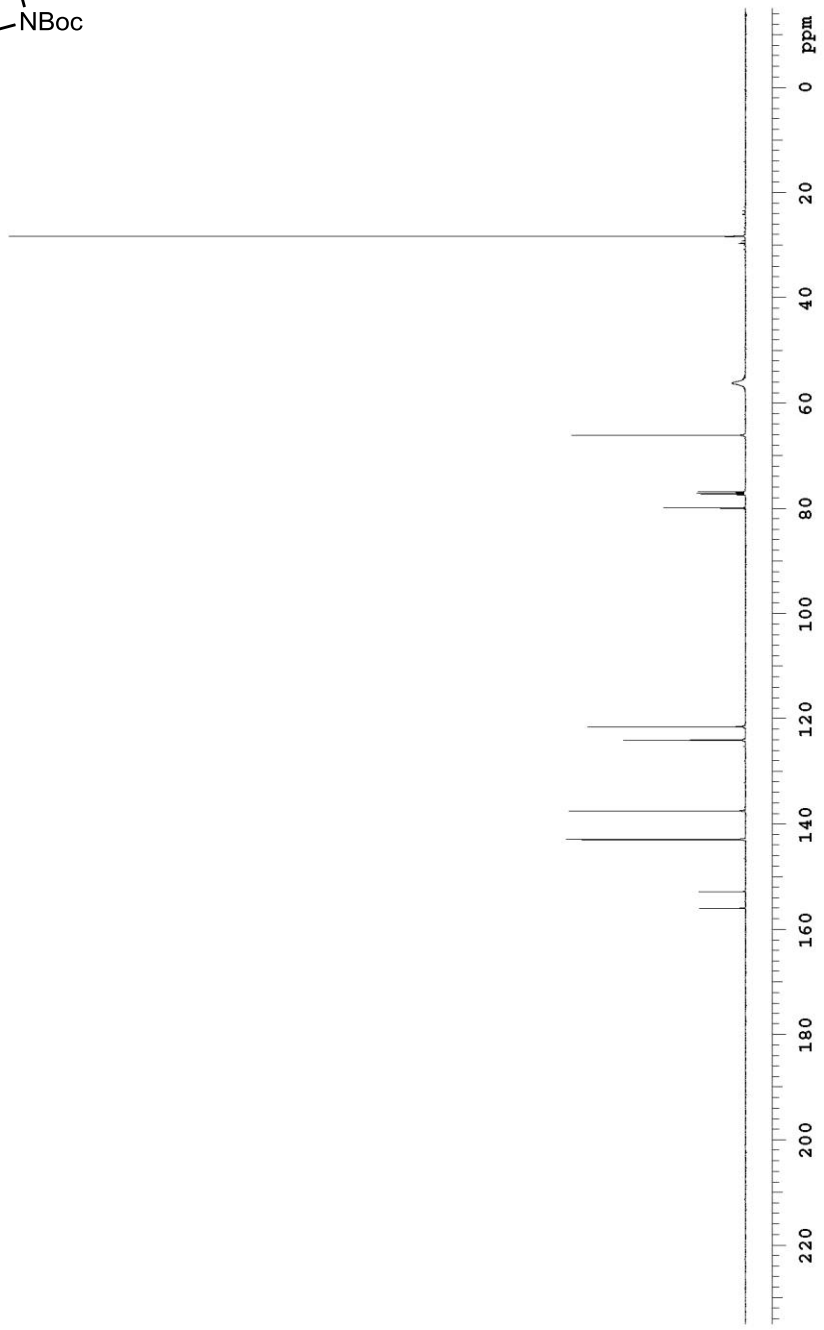
3l



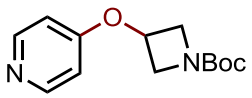
^{13}C NMR of **3l** ($CDCl_3$, 125 MHz, 23 ℃)



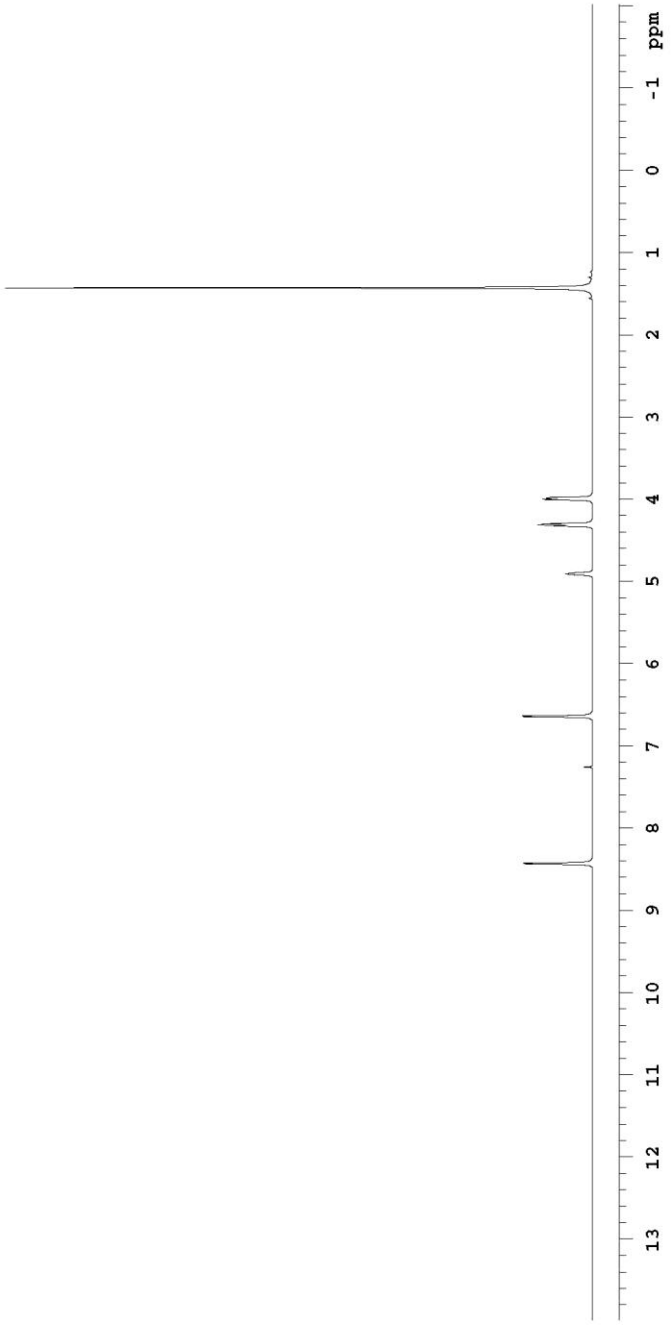
3l



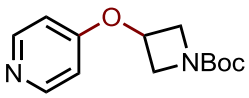
^{1}H NMR of **3m** ($CDCl_3$, 500 MHz, 23 ℃)



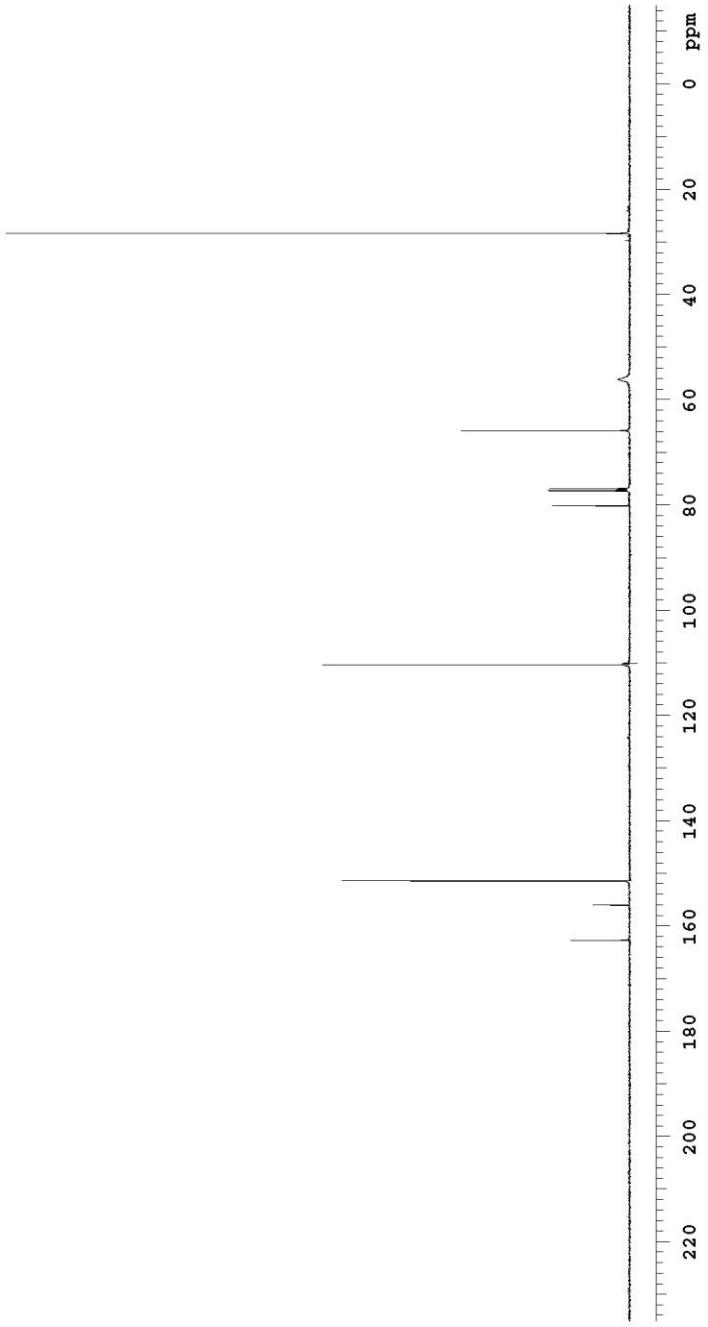
3m



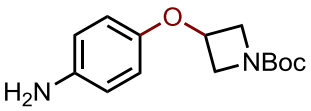
^{13}C NMR of **3m** ($CDCl_3$, 125 MHz, 23 ℃)



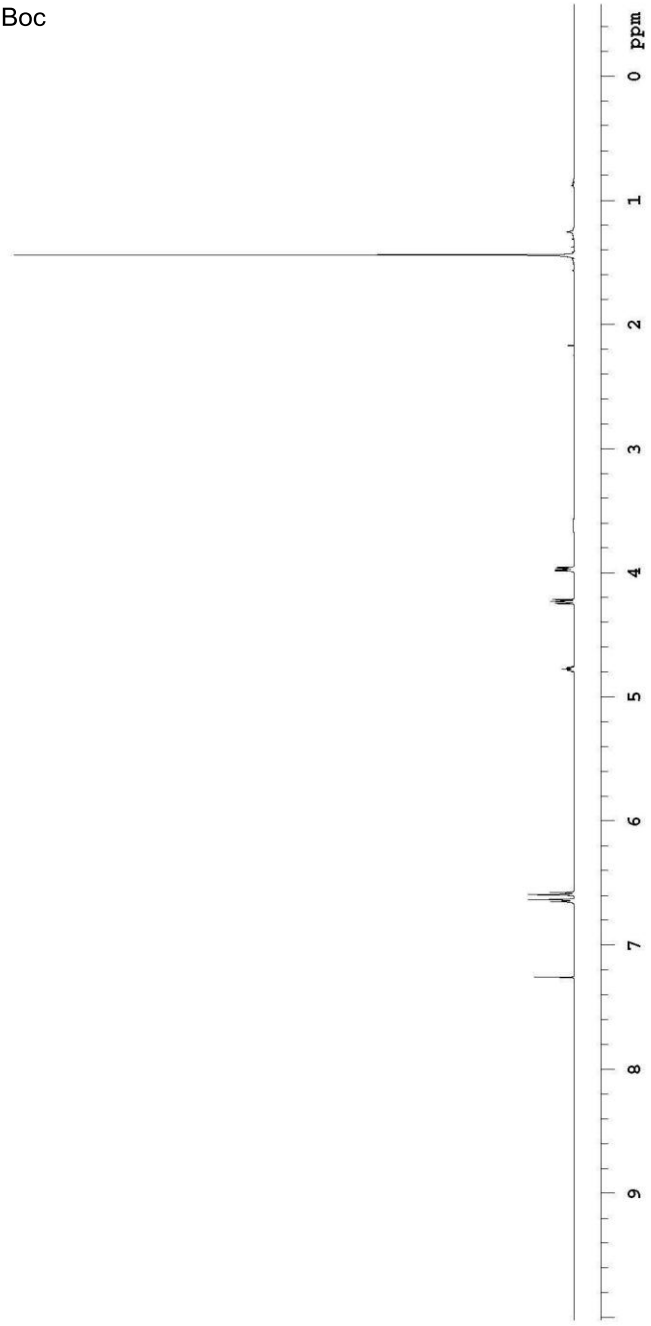
3m



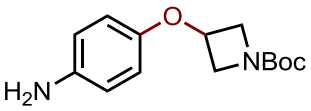
^{1}H NMR of **3n** ($CDCl_3$, 500 MHz, 23 ℃)



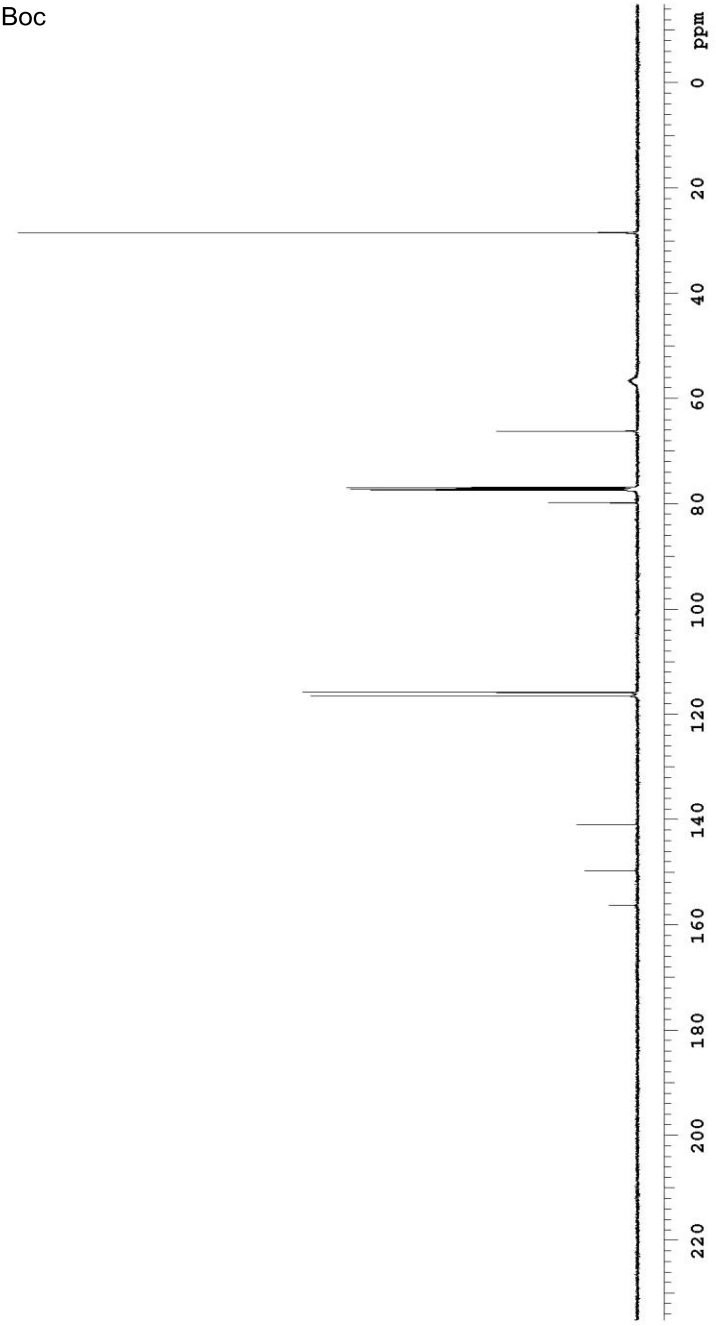
3n



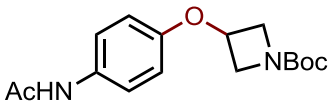
^{13}C NMR of **3n** ($CDCl_3$, 125 MHz, 23 ℃)



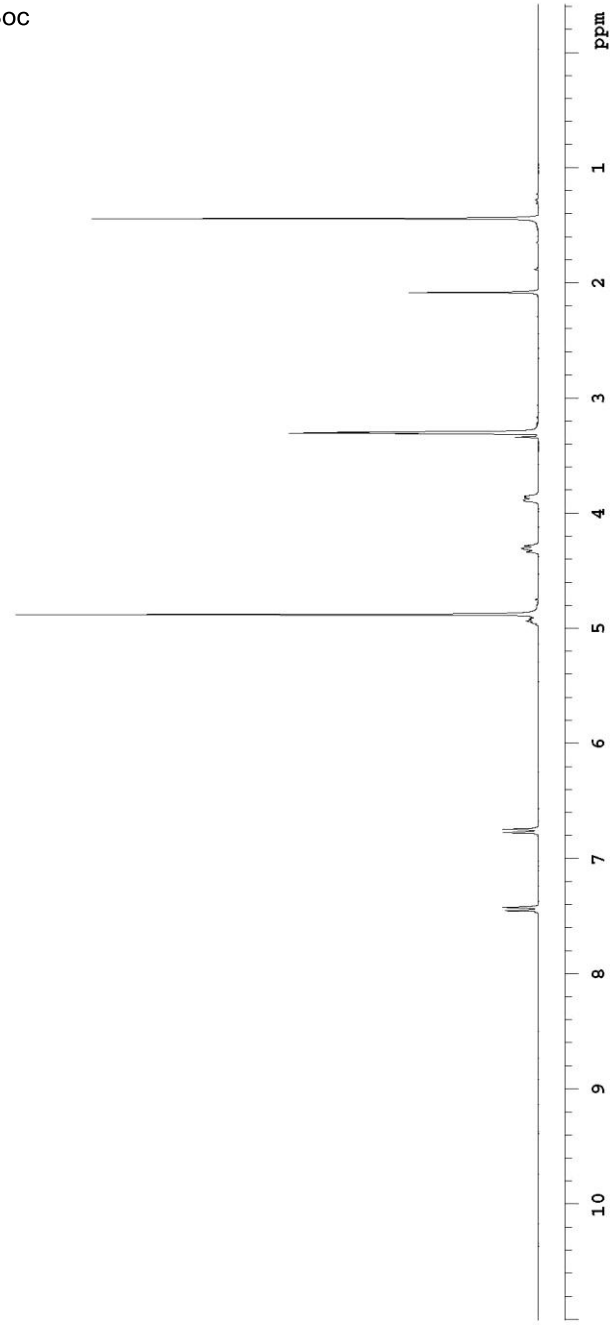
3n



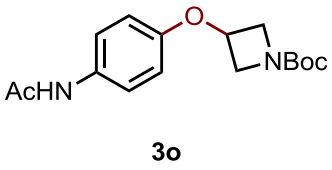
^{1}H NMR of **3o** (CD_3OD, 600 MHz, 23 ℃)



3o

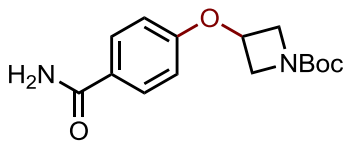


^{13}C NMR of **3o** (CD_3OD, 125 MHz, 23 ℃)

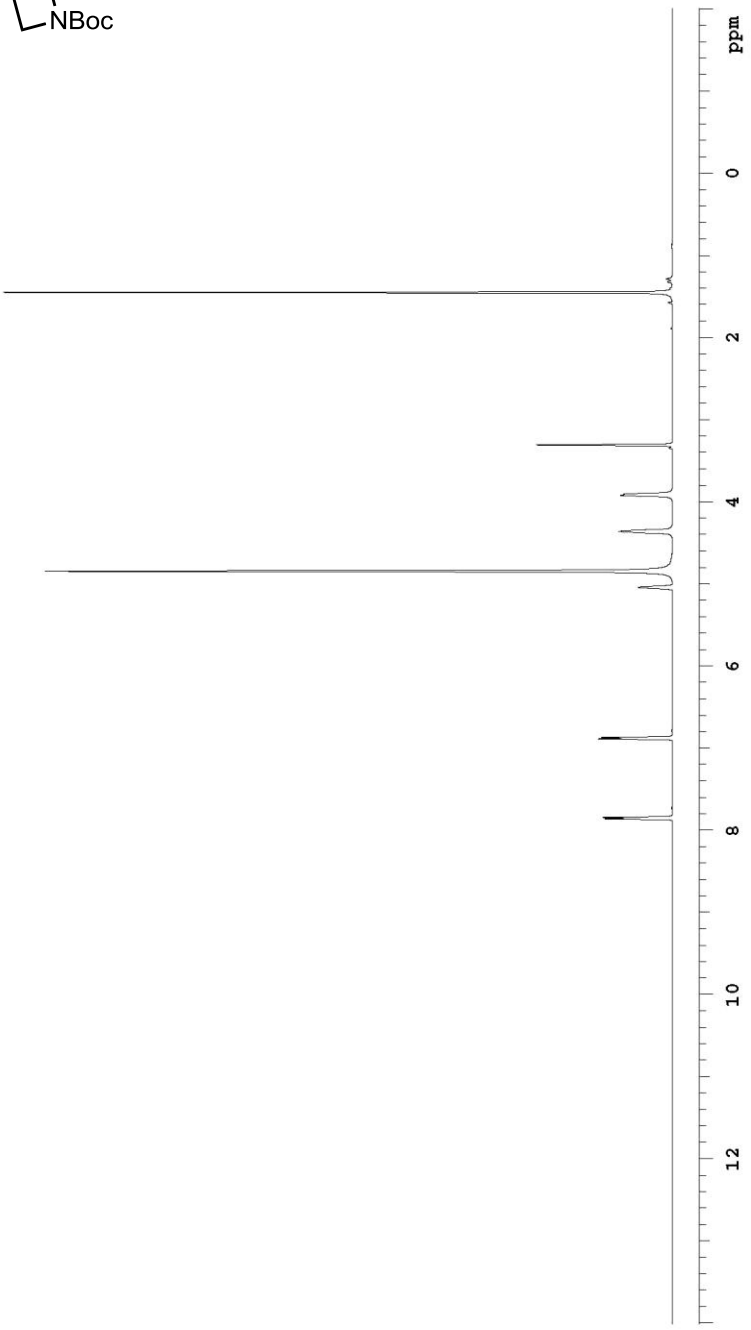


3o

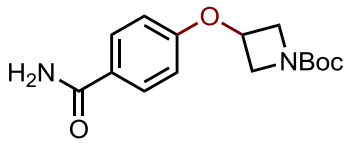
^{1}H NMR of **3p** ($CDCl_3$, 600 MHz, 23 ℃)



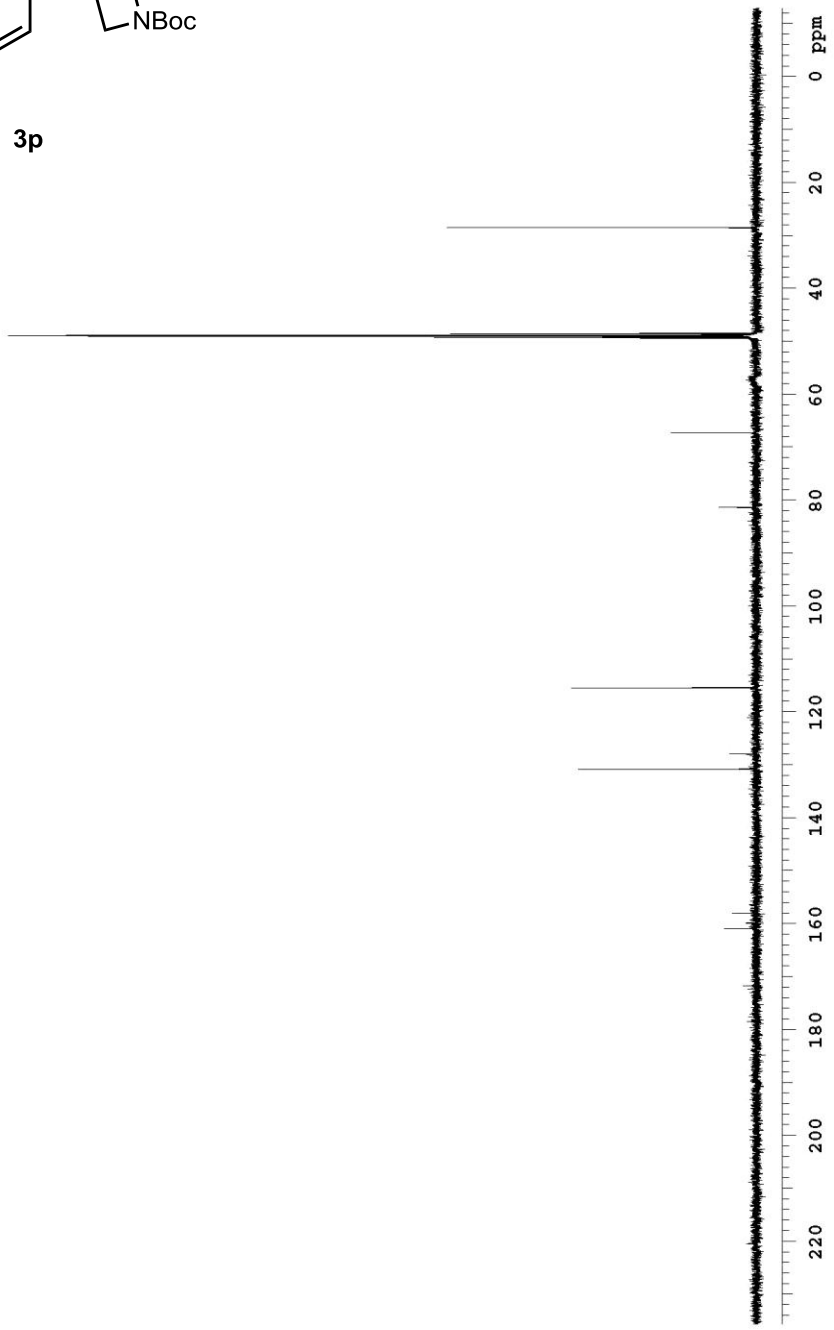
3p



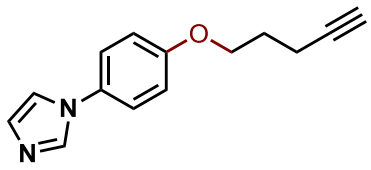
^{13}C NMR of **3p** ($CDCl_3$, 125 MHz, 23 ℃)



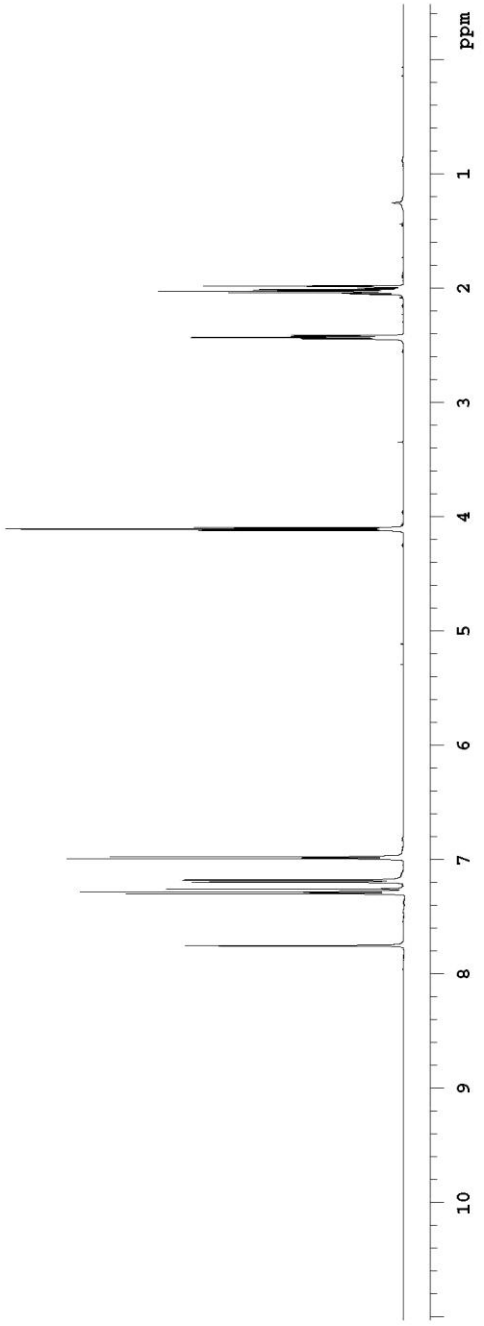
3p



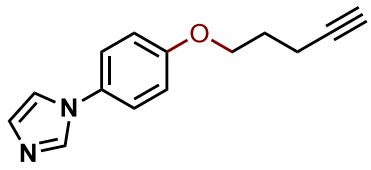
^{1}H NMR of **3q** ($CDCl_3$, 500 MHz, 23 ℃)



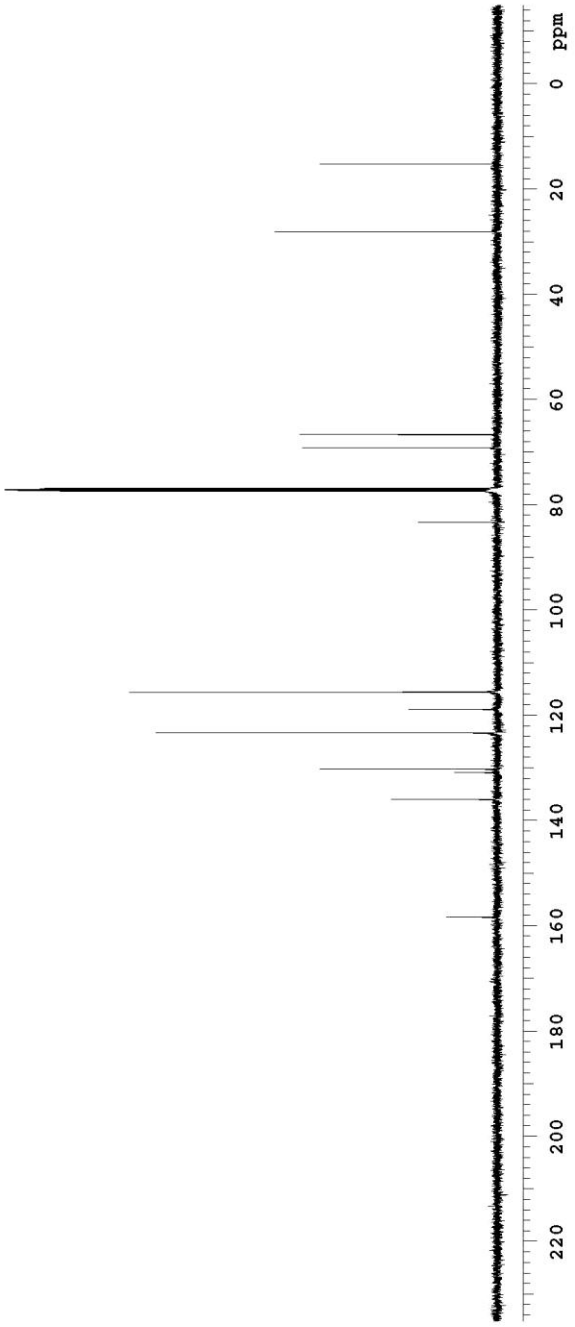
3q



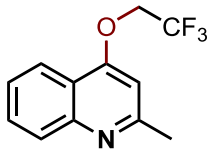
^{13}C NMR of **3q** ($CDCl_3$, 125 MHz, 23 ℃)



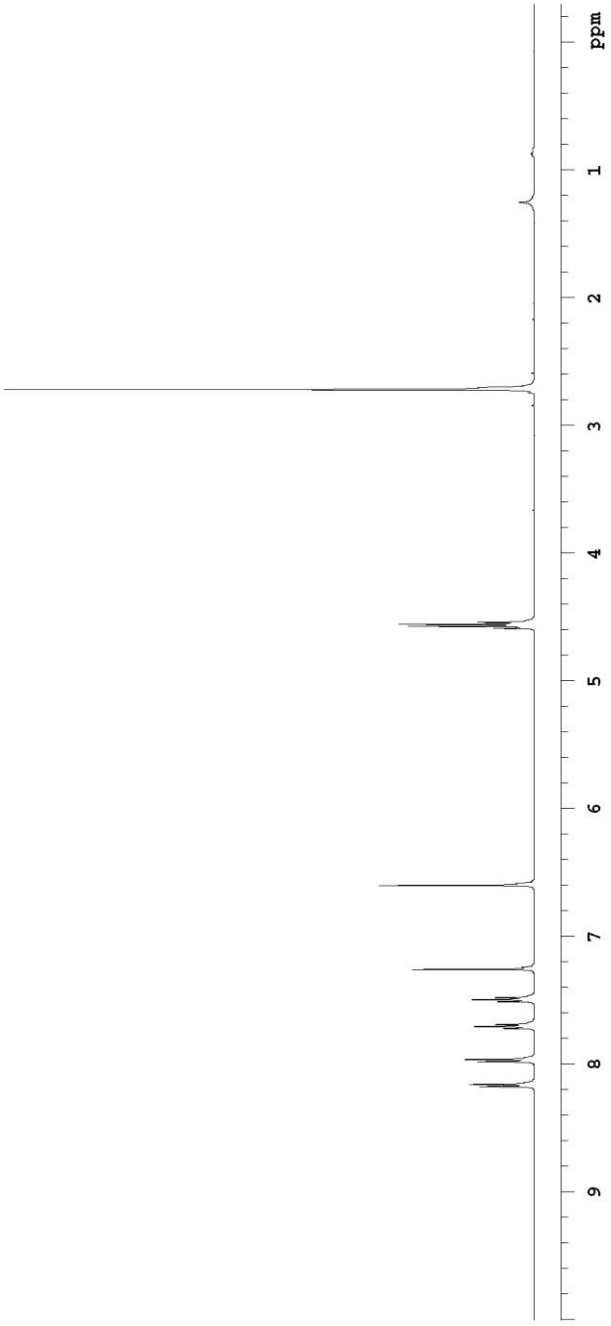
3q



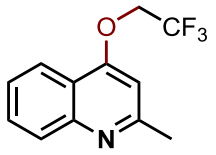
^{1}H NMR of **3r** ($CDCl_3$, 500 MHz, 23 ℃)



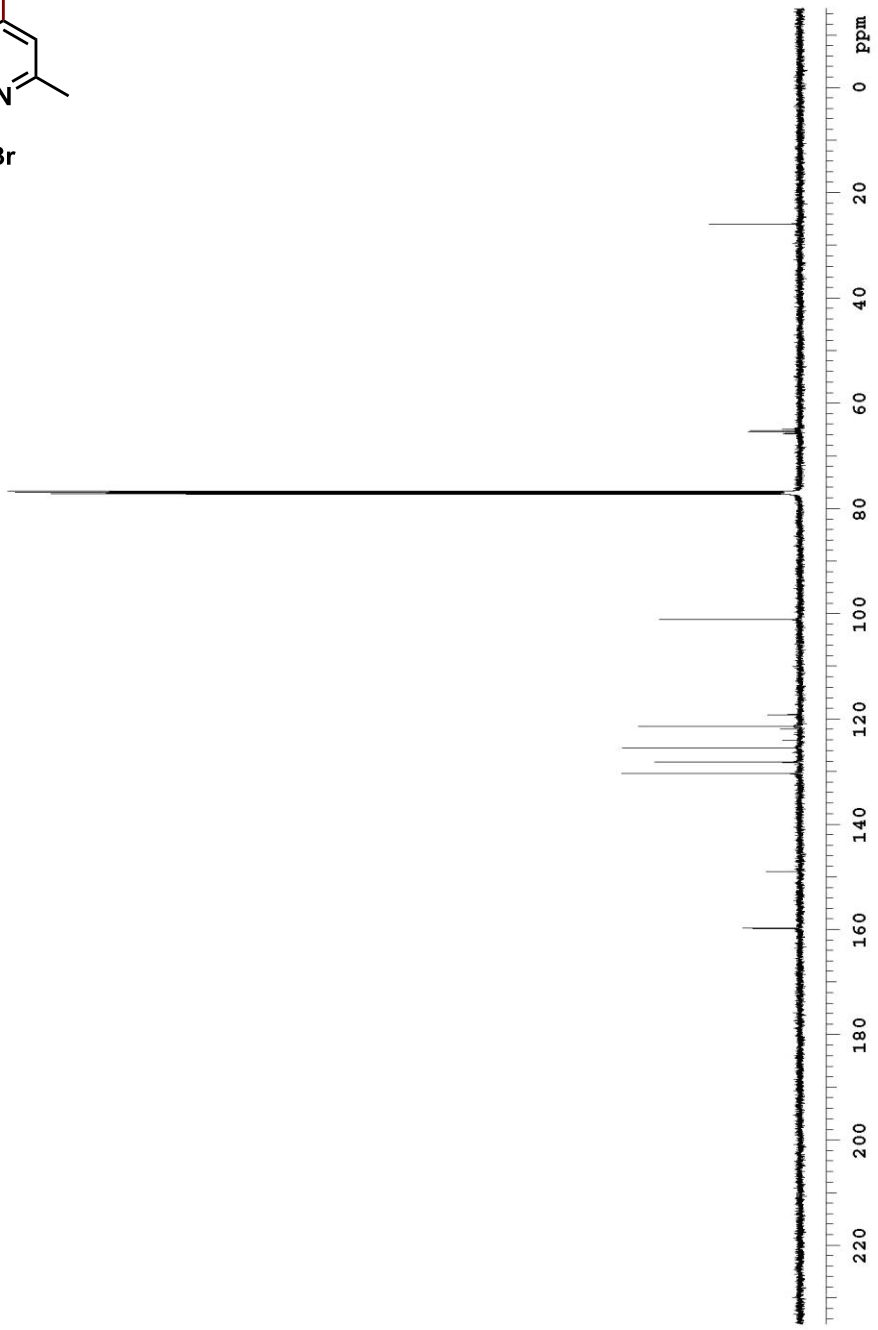
3r



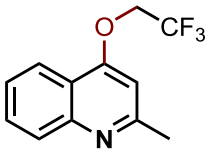
^{13}C NMR of **3r** ($CDCl_3$, 125 MHz, 23 ℃)



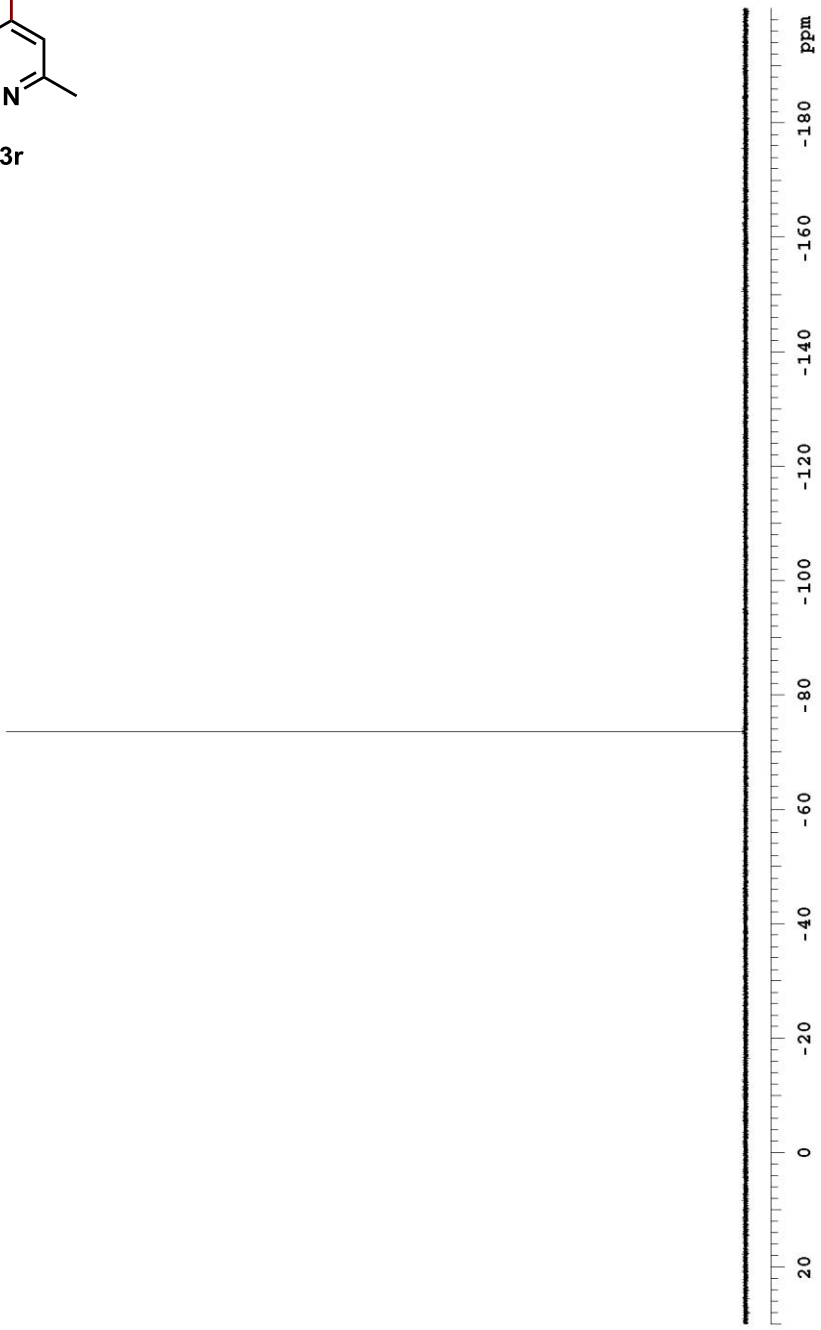
3r



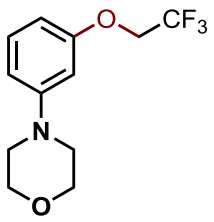
^{19}F NMR of **3r** ($CDCl_3$, 282 MHz, 23 ℃)



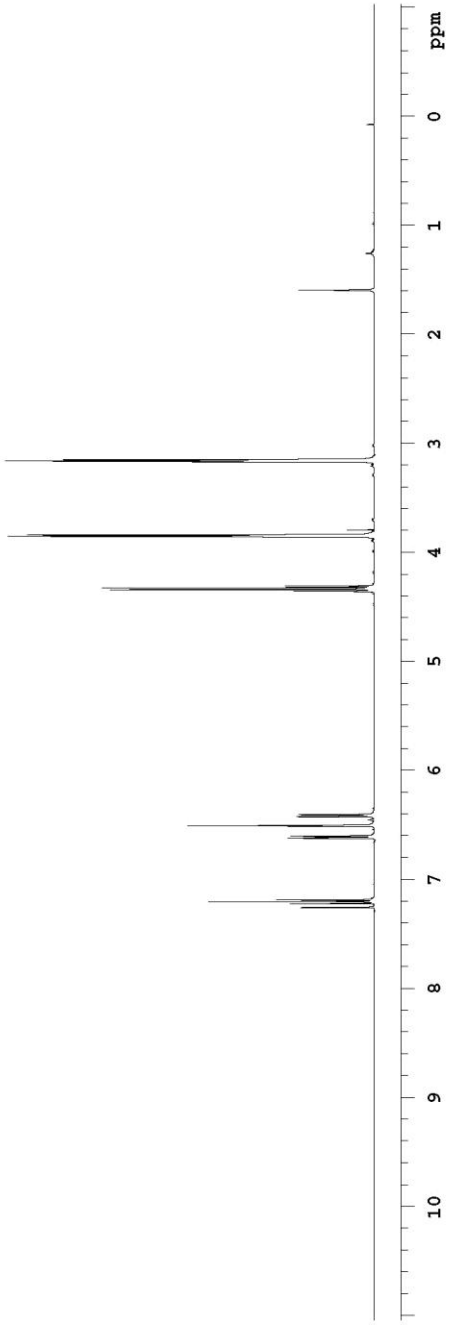
3r



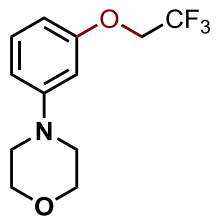
^{1}H NMR of **3s** ($CDCl_3$, 500 MHz, 23 ℃)



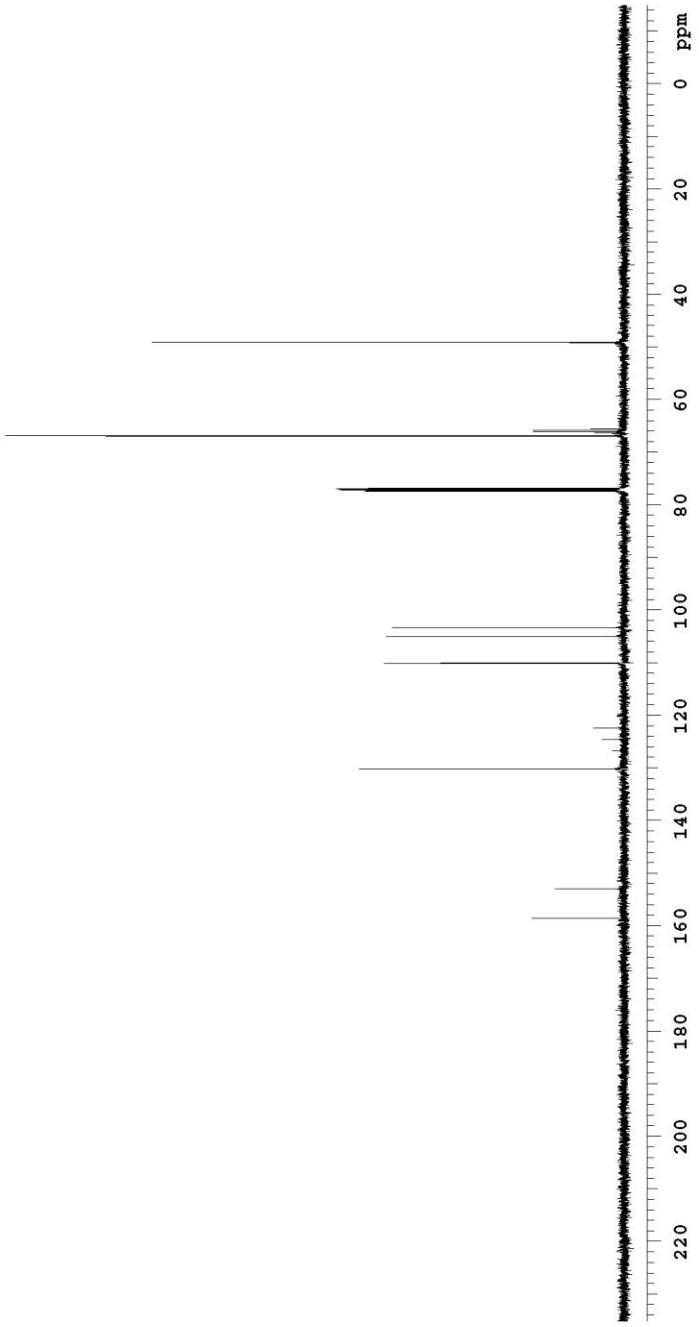
3s



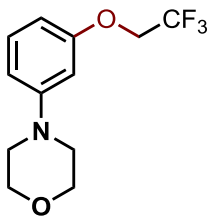
^{13}C NMR of **3s** ($CDCl_3$, 125 MHz, 23 ℃)



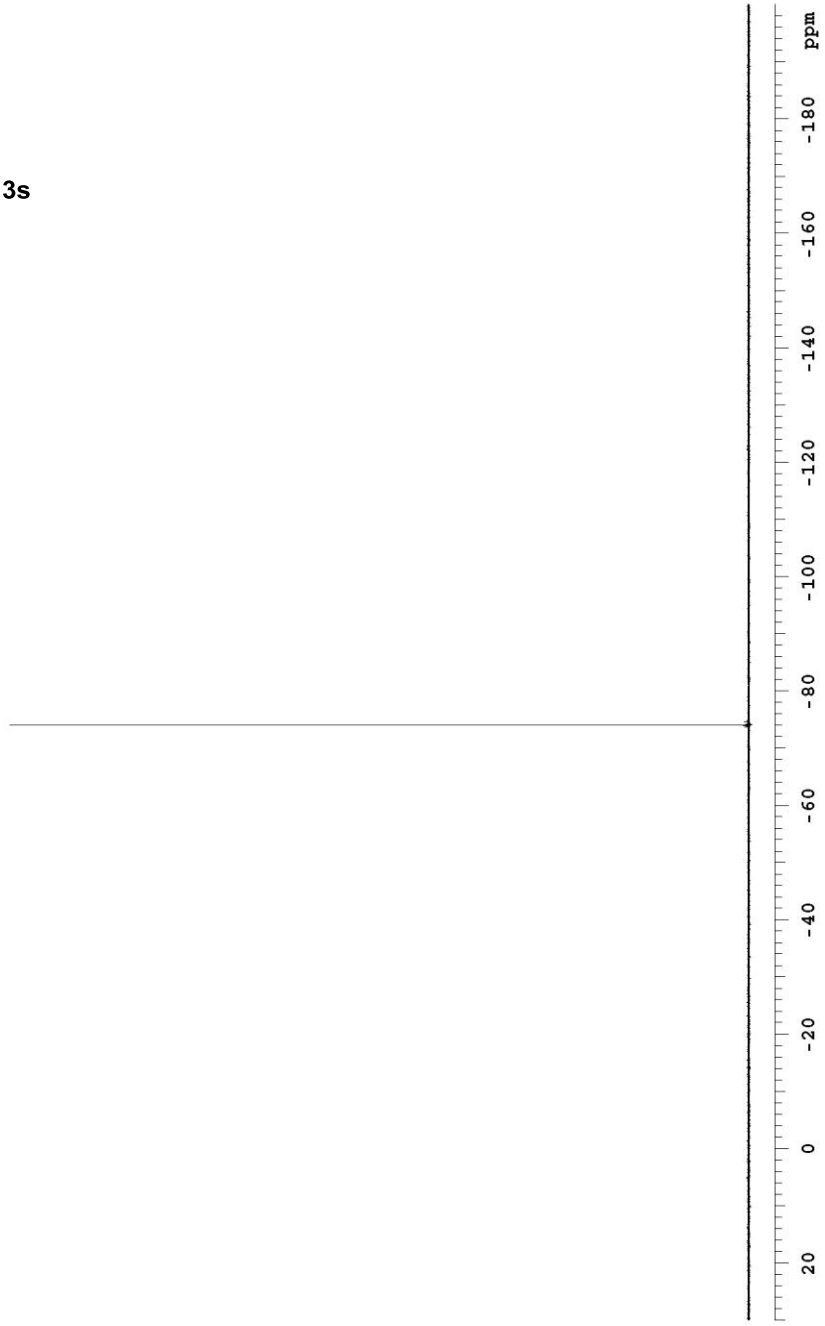
3s



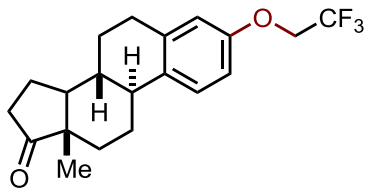
^{19}F NMR of **3s** ($CDCl_3$, 282 MHz, 23 ℃)



3s

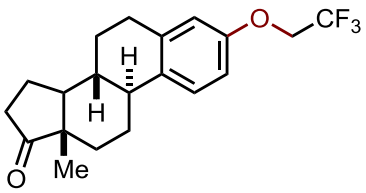


^{1}H NMR of **3t** ($CDCl_3$, 500 MHz, 23 ℃)

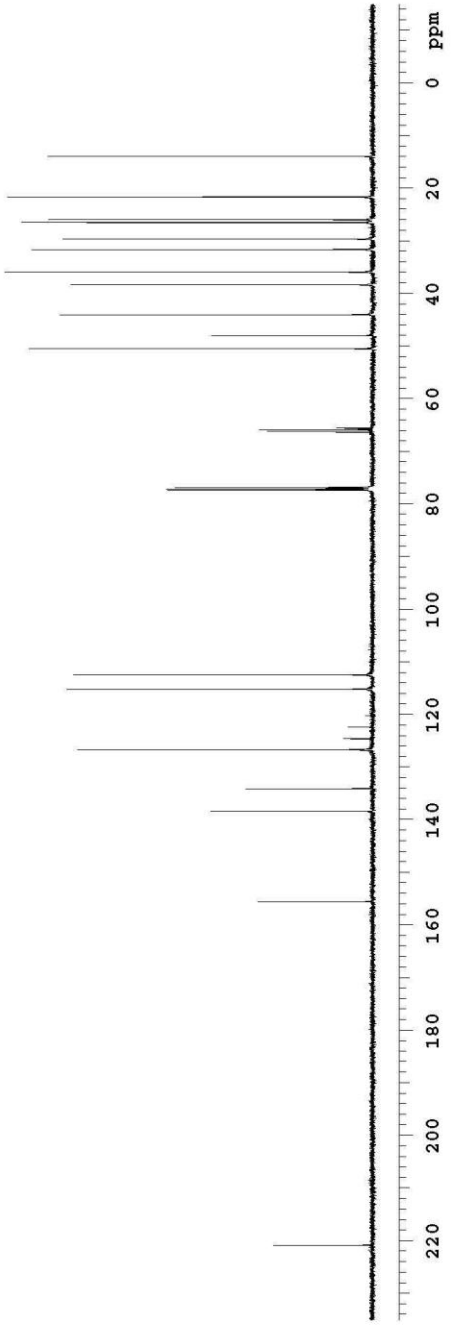


3t

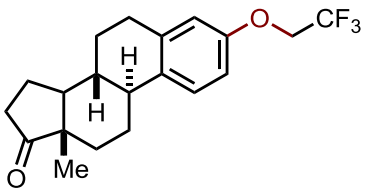
^{13}C NMR of **3t** ($CDCl_3$, 125 MHz, 23 ℃)



3t

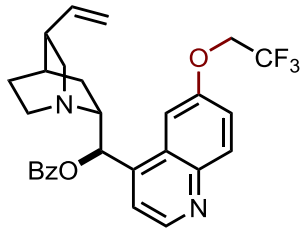


^{19}F NMR of **3t** ($CDCl_3$, 282 MHz, 23 ℃)

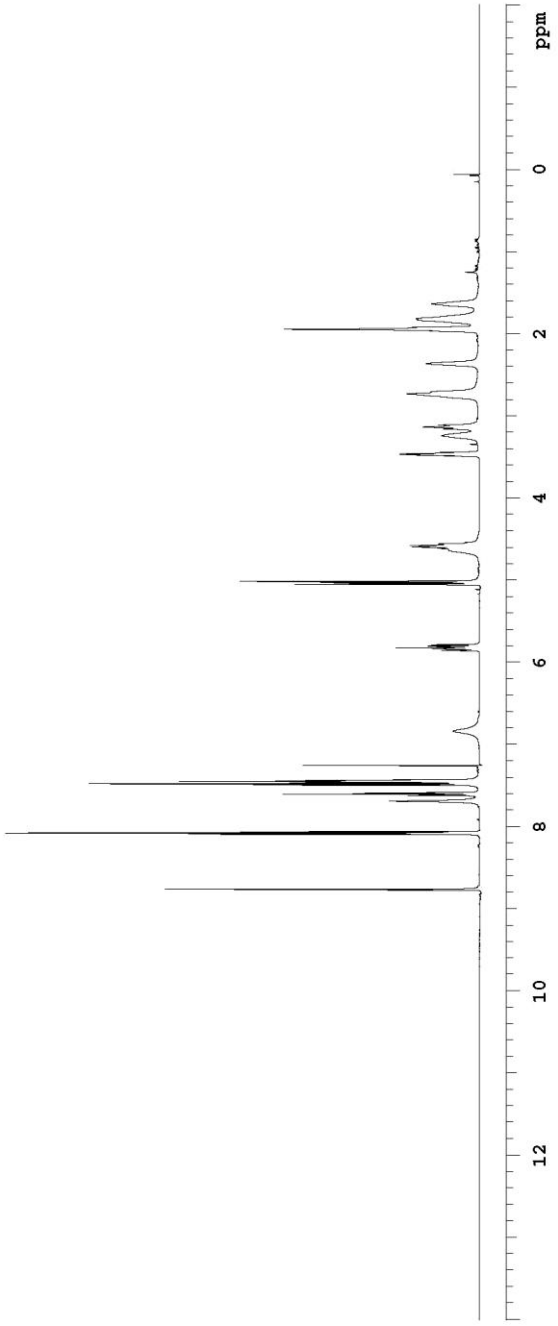


3t

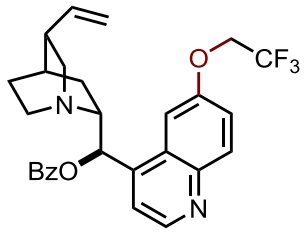
^{1}H NMR of **3u** ($CDCl_3$, 500 MHz, 23 ℃)



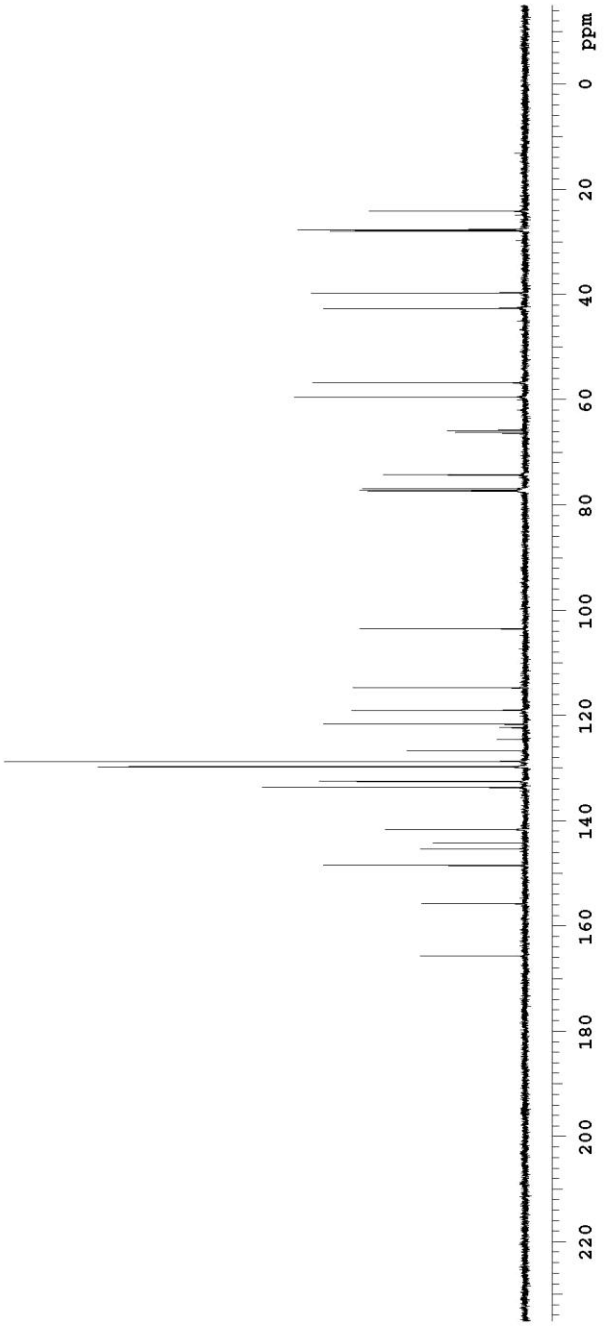
3u



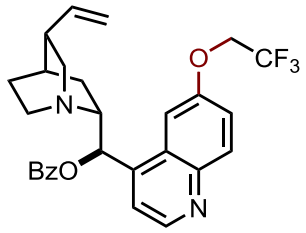
^{13}C NMR of **3u** ($CDCl_3$, 125 MHz, 23 ℃)



3u

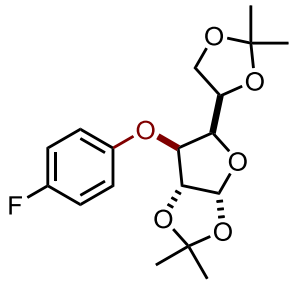


^{19}F NMR of **3u** ($CDCl_3$, 282 MHz, 23 ℃)

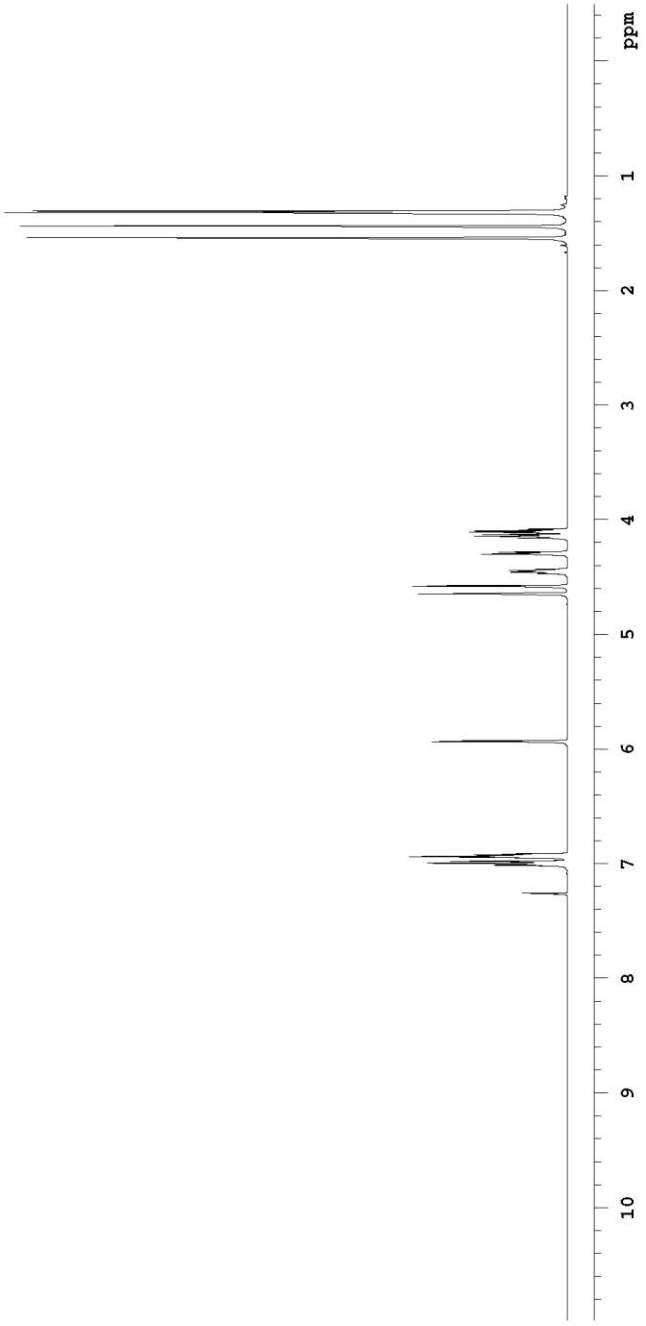


3u

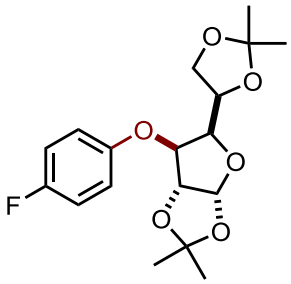
^{1}H NMR of **3v** ($CDCl_3$, 500 MHz, 23 ℃)



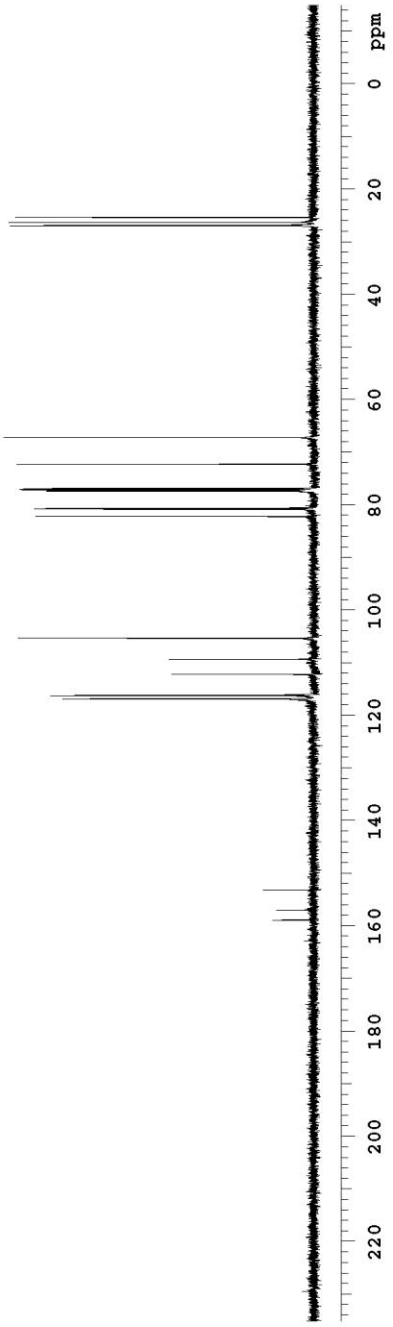
3v



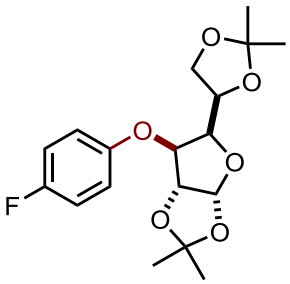
^{13}C NMR of **3v** ($CDCl_3$, 125 MHz, 23 ℃)



3v

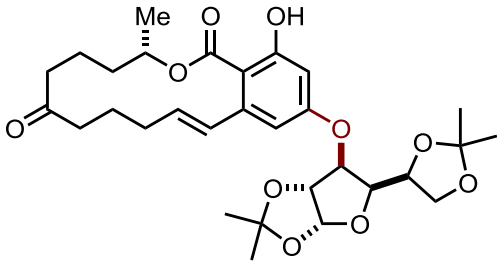


^{19}F NMR of **3v** ($CDCl_3$, 282 MHz, 23 ℃)

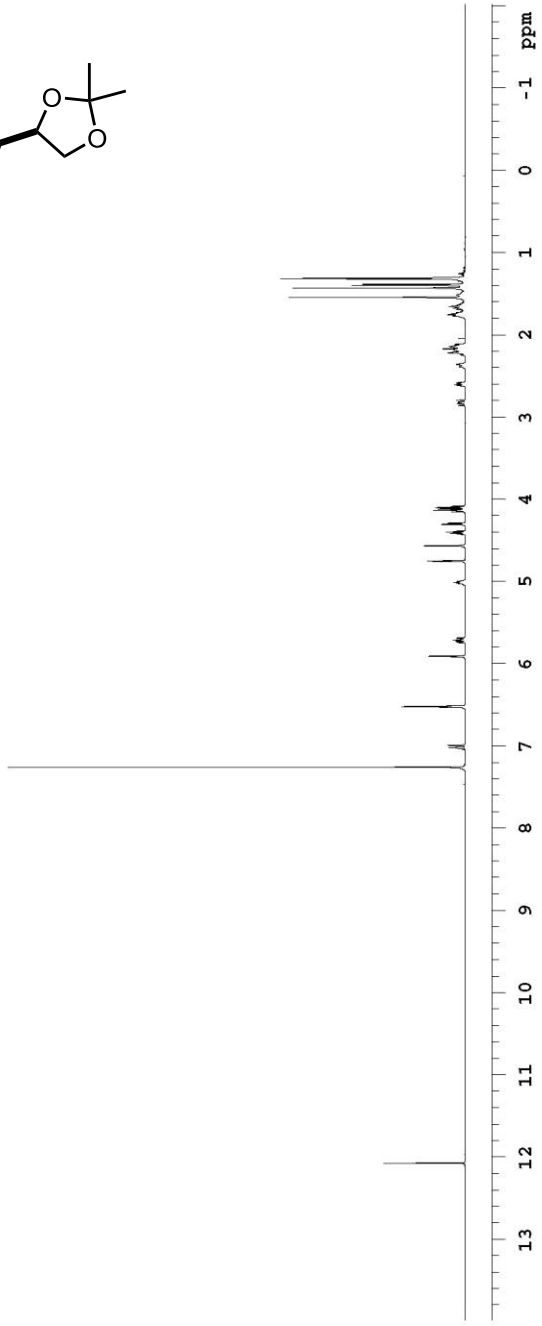


3v

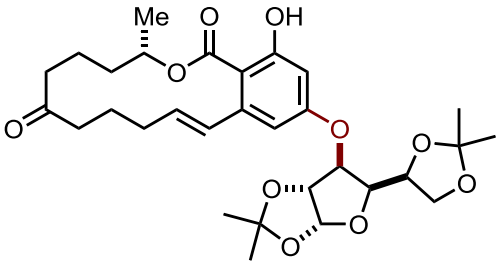
^{1}H NMR of **3w** ($CDCl_3$, 500 MHz, 23 ℃)



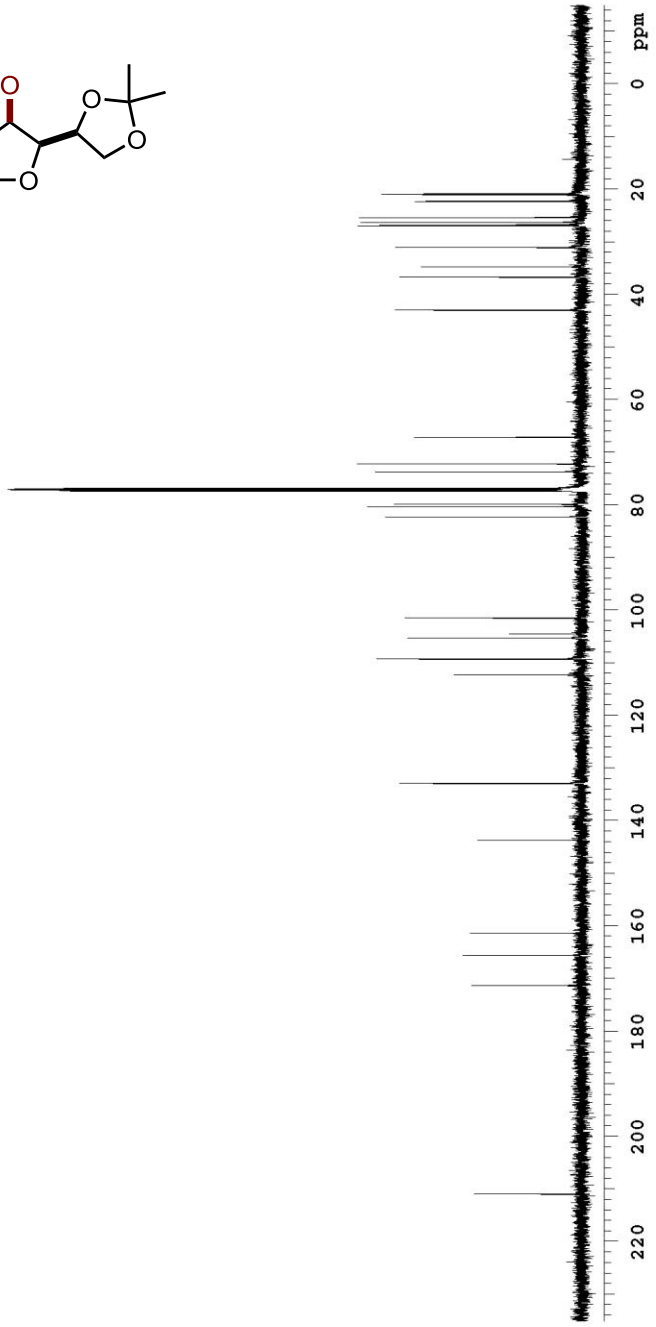
3w



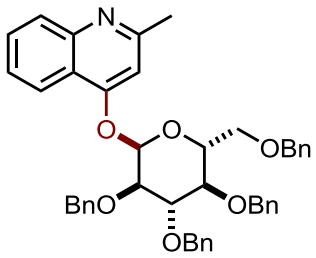
^{13}C NMR of **3w** ($CDCl_3$, 125 MHz, 23 ℃)



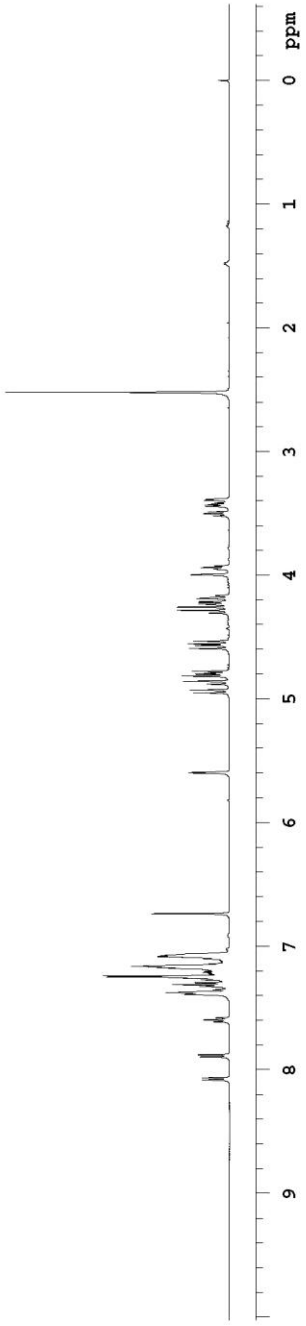
3w



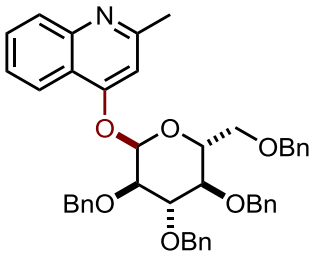
^{1}H NMR of **3x** ($CDCl_3$, 500 MHz, 23 ℃)



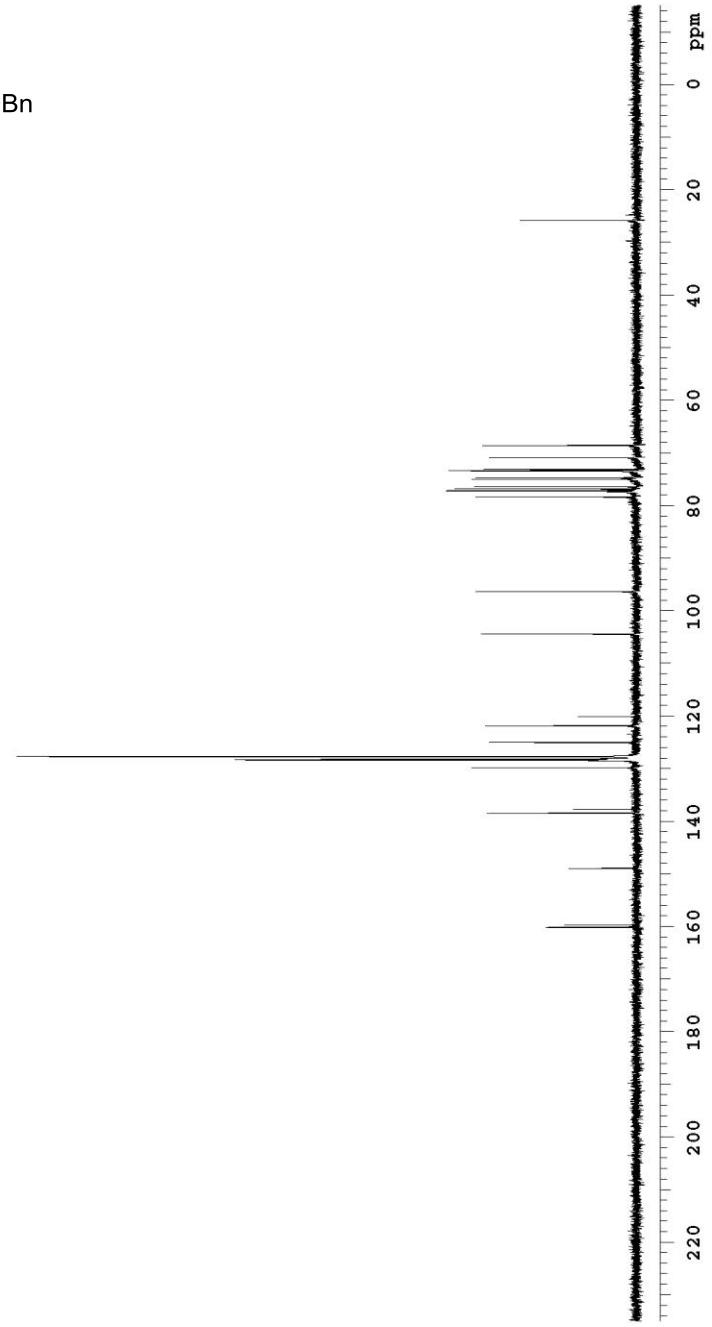
3x



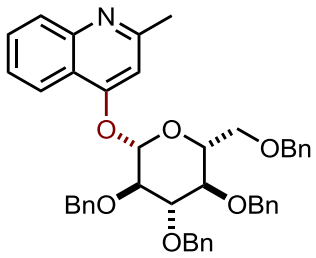
^{13}C NMR of **3x** ($CDCl_3$, 125 MHz, 23 ℃)



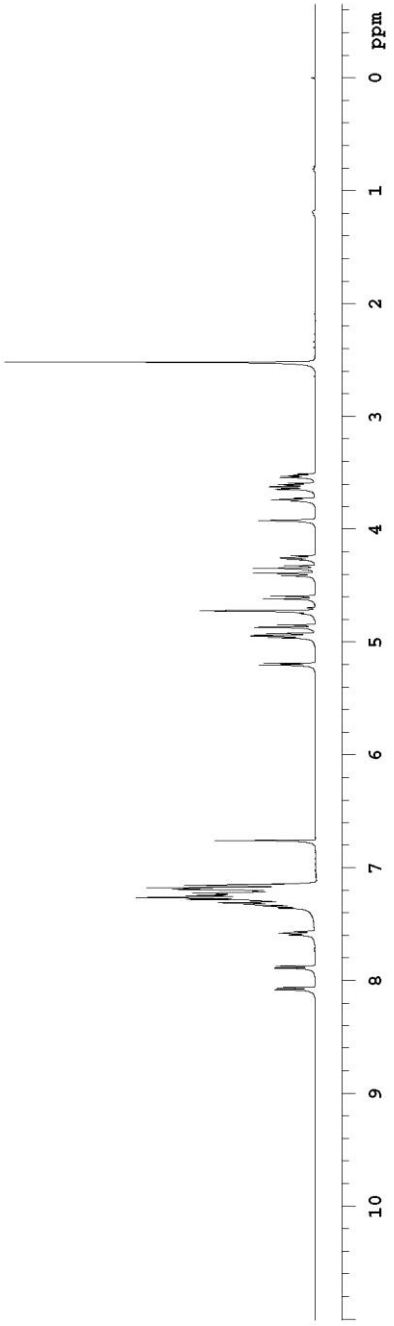
3x



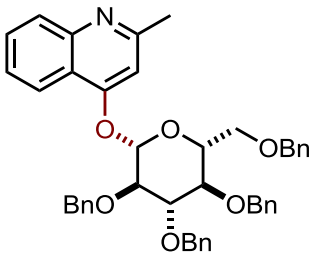
^{1}H NMR of **3x'** ($CDCl_3$, 500 MHz, 23 ℃)



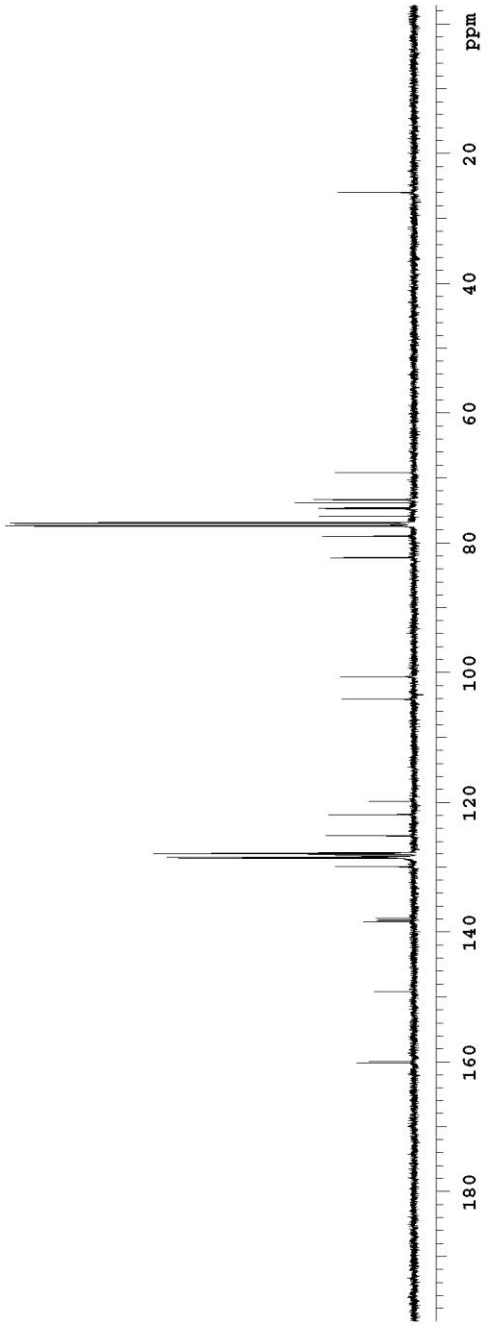
3x'



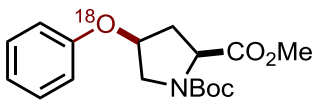
^{13}C NMR of **3x'** ($CDCl_3$, 125 MHz, 23 ℃)



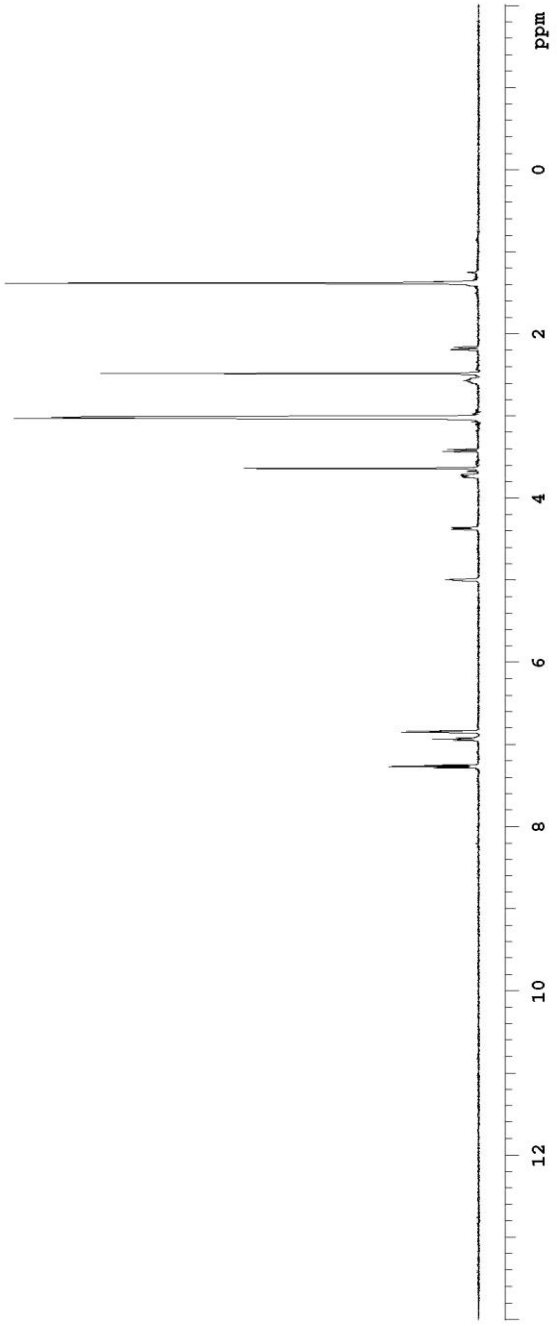
3x'



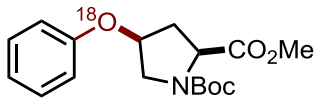
^{13}H NMR of **3y** (DMSO-*d6*, 500 MHz, 99 ℃)



3y



^{1}H NMR of **3y** (DMSO-*d6*, 500 MHz, 23 ℃)



3y