Electron Transfer Reduction of Carboxylic Acids Using SmI_2–H_2O–Et_3N

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Supplementary Information

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List of Known Compounds

All compounds used in this study have been described in the literature or are commercially available. Carboxylic acids were purchased from commercial suppliers at the highest quality and used without further purification. Samarium(II) iodide was purchased from Alfa Aesar, Strem or ABCR or prepared by standard methods and titrated prior to use.[1-4] Tetrahydrofuran (THF) was purchased from Fisher Scientific or Sigma Aldrich and used as received or purified by passing through activated alumina columns.

Experimental Procedures and Characterization Data

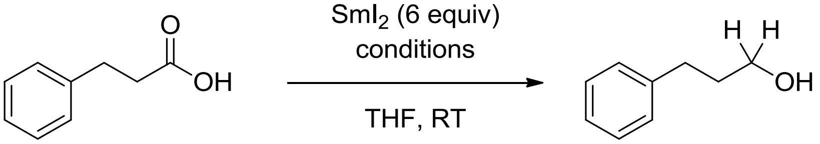
General procedure for the reduction of carboxylic acids with SmI_2–H_2O–Et_3N. *Method A:* (Stock solutions of SmI_2 were used in Method A). To acid (neat), samarium(II) iodide (THF solution, typically, 6 equiv) was added, followed by amine (typically, 18 or 36 equiv) and water (typically, 18 or 36 equiv) under inert atmosphere at room temperature and stirred vigorously. After the specified time (typically, 2-5 h), the excess of SmI_2 was oxidized by bubbling air through the reaction mixture. The reaction mixture was diluted with CH_2Cl_2 (30 mL) and HCl (1 *N*, 30 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), organic layers were combined, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography using a short plug of silica gel. All yields refer to isolated yields unless stated otherwise.

Method B: (*In situ* prepared solutions of SmI_2 were used in Method B). To a solution of samarium(II) iodide (THF solution, typically, 6 equiv), carboxylic acid was added (in 1.0 mL of THF), followed by amine (typically, 18 or 36 equiv) and water (typically, 18 or 36 equiv) under inert atmosphere at room temperature and stirred vigorously. Work-up and purification proceed as described in Method A.

Note: in terms of substrate scope or efficiency of the reaction, there are no differences between Methods A and B. Method B was developed for experimental convenience when preparation of stock solutions of SmI_2 is not desirable.

Note: we have noticed marginal differences in reactivity between systems employing SmI_2–H_2O–amine in 6-18-18 ratio and SmI_2–H_2O–amine in 6-36-36 ratio. Due to a slightly higher reactivity, the latter system has been typically preferred. For the reduction of more sterically-demanding acids, systems employing SmI_2–H_2O–amine in 8-48-48 ratio have been typically preferred over the systems employing 6 equivalents of SmI_2, however conversions higher than 95% have been routinely observed even with limiting number of equivalents of the reductant. The amount of samarium(II) iodide used (typically, 6-8 equiv) is consistent with the proposed four-electron mechanism: a 1.5-2-fold excess of the reagent was used to ensure that the reactions were complete. Note that related systems routinely used for reduction of carboxylic acid derivatives are less selective and require much larger excess of electron transfer reagent.[5]

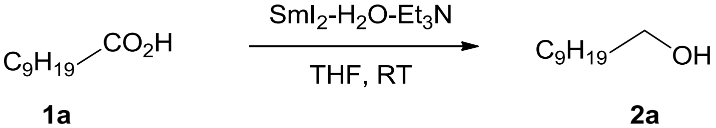
Table SI-1. Optimization of reduction of hydrocinnamic methyl ester with SmI_2.[a]



entry	proton source	amine	proton source (equiv)	amine (equiv)	time (h)	conversion[b] (%)	yield[b] (%)
1	-	Et_3N	-	18	18	<5	<5
2	H_2O	-	18	-	18	<5	<5
3	H_2O	-	800	-	18	<5	<5
4	H_2O	Et_3N	18	18	2	>95	99
5	MeOH	Et_3N	18	18	18	15	15
6	*t*-BuOH	Et_3N	18	18	18	11	11
7	$(HOCH_2)_2$	Et_3N	9	18	18	45	25
8	H_2O	*n*-$BuNH_2$	18	18	2	86	86
9	H_2O	*i*-Pr_2NH	18	18	2	97	96
10	H_2O	pyrrolidine	18	18	2	96	67
11	H_2O	morpholine	18	18	2	98	88
12	H_2O	piperidine	18	18	2	95	53
13	H_2O	Et_3N	6	18	18	51	48
14	H_2O	Et_3N	18	6	18	28	28
15	H_2O	Et_3N	12	12	18	78	78

[a] All reactions carried out using standard Schlenk techniques for handling air-sensitive reagents. [b] Determined by GC or ^{1}H NMR.

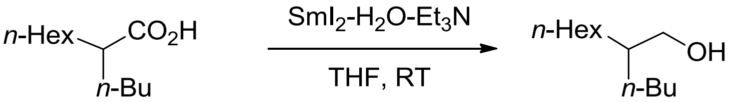
Decan-1-ol (Table 2, entry 1)



1a **2a**

According to the general procedure *Method A*, the reaction of decanoic acid (0.10 mmol), samarium(II) iodide (0.6 mmol), water (3.6 mmol) and triethylamine (3.6 mmol) for 3 h at rt, afforded after chromatography (1/10-1/4 EtOAc/hexanes) the title compound in 98% yield. Oil (R_f = 0.54, 1/4 EtOAc/hexanes). ^1H NMR (500 MHz, $CDCl_3$) δ 0.81 (t, *J* = 6.9 Hz, 3H), 1.15-1.33 (m, 15H), 1.47-1.53 (m, 2H), 3.57 (t, *J* = 6.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 22.7, 25.8, 29.3, 29.5, 29.6, 29.7, 31.9, 32.8, 63.1.

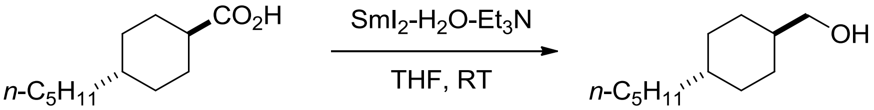
2-Butyloctan-1-ol (Table 2, entry 2)



1b **2b**

According to the general procedure *Method A*, the reaction of 2-butyloctanoic acid (0.10 mmol), samarium(II) iodide (0.6 mmol), water (4.8 mmol) and triethylamine (4.8 mmol) for 18 h at rt, afforded after chromatography (1/10-1/4 EtOAc/hexanes-EtOAc) the title compound in 94% yield. Oil. ^1H NMR (500 MHz, $CDCl_3$) δ 0.79-0.85 (m, 6H), 1.09-1.14 (br, 1H), 1.16-1.29 (m, 16H), 1.35-1.42 (m, 1H), 3.47 (t, *J* = 5.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.7, 23.1, 26.9, 29.1, 29.8, 30.6, 30.9, 31.9, 40.5, 65.8.

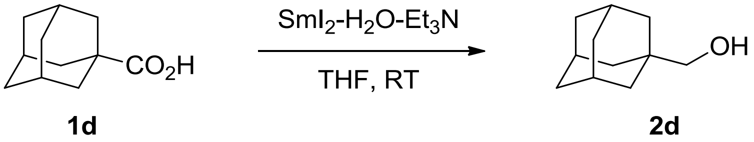
***trans*-4-(Pentylcyclohexyl)methanol** (Table 2, entry 3)



1c **2c**

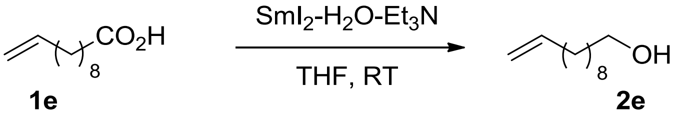
According to the general procedure *Method A*, the reaction of *trans*-4-pentylcyclohexanecarboxylic acid (0.10 mmol), samarium(II) iodide (0.6 mmol), water (3.6 mmol) and triethylamine (3.6 mmol) for 18 h at rt, afforded after chromatography (1/10-1/4 EtOAc/hexanes) the title compound in 96% yield. Oil (R_f = 0.60, 1/4 EtOAc/hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 0.75-0.91 (m, 7H), 1.02-1.27 (m, 10H), 1.38 (br, 1H), 1.71 (d, *J* = 8.7 Hz, 4H), 3.37 (d, *J* = 6.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.7, 26.6, 29.5, 32.2, 32.7, 37.4, 37.8, 40.7, 68.8.

1-Adamantanemethanol (Table 2, entry 4)



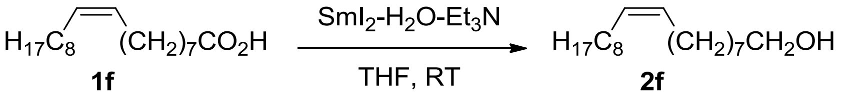
According to the general procedure *Method A*, the reaction of adamantane-1-carboxylic acid (0.10 mmol), samarium(II) iodide (0.80 mmol), water (2.4 mmol) and triethylamine (2.4 mmol) for 3 h at rt, afforded after chromatography (1/10-1/4 EtOAc/hexanes) the title compound in 94% yield. Solid (R_f = 0.48, 1/4 EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (br, 1H), 1.44 (d, *J* = 2.4 Hz, 6H), 1.55-1.70 (m, 6H), 1.90-1.95 (m, 3H), 3.13 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.2, 34.5, 37.2, 39.0, 73.9.

Undec-10-en-1-ol (Table 2, entry 5)



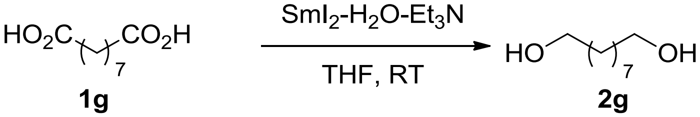
According to the general procedure *Method A*, the reaction of undec-10-enoic acid (0.10 mmol), samarium(II) iodide (0.4 mmol), water (2.4 mmol) and triethylamine (2.4 mmol) for 2 h at rt, afforded after chromatography (1/10-4/1 EtOAc/hexanes) the title compound in 90% yield. Oil (R_f = 0.50, 1/4 EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.06-1.36 (m, 13H), 1.44-1.55 (m, 2H), 1.92-2.01 (m, 2H), 3.57 (t, *J* = 6.6 Hz, 2H), 4.83-4.96 (m, 2H), 5.67-5.82 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.7, 28.9, 29.1, 29.4, 29.6, 32.8, 33.8, 63.1, 114.1, 139.2.

(*Z*)-Octadec-9-en-1-ol (Table 2, entry 6)



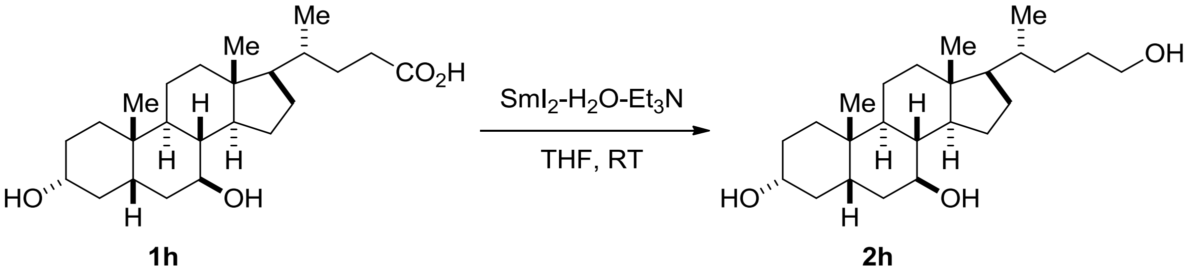
According to the general procedure *Method A*, the reaction of oleic acid (0.10 mmol), samarium(II) iodide (0.6 mmol), water (3.6 mmol) and triethylamine (3.6 mmol) for 2 h at rt, afforded after chromatography (100/3-4/1 EtOAc/hexanes) the title compound in 97% yield. Oil (R_f = 0.46, 1/4 EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81 (t, *J* = 7.2 Hz, 3H), 1.16-1.32 (m, 23H), 1.45-1.53 (m, 2H), 1.91-1.97 (m, 4H), 3.57 (t, *J* = 6.8 Hz, 2H), 5.23-5.33 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.7, 25.7, 27.2, 27.2, 29.3, 29.3, 29.4, 29.5, 29.5, 29.8, 29.8, 31.9, 32.8, 63.1, 129.8, 130.0.

Nonane-1,9-diol (Table 2, entry 7)



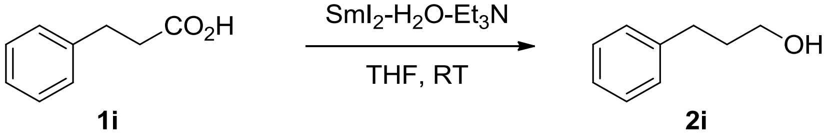
According to the general procedure *Method A*, the reaction of azelaic acid (0.10 mmol), samarium(II) iodide (1.2 mmol), water (7.2 mmol) and triethylamine (7.2 mmol) for 18 h at rt, afforded after chromatography (1/10-1/1 EtOAc/hexanes) the title compound in 88% yield. Solid (R_f = 0.55, EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.20-1.32 (m, 10H), 1.43-1.55 (m, 4H), 1.74 (br, 2H), 3.56 (t, *J* = 6.6 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.7, 29.3, 29.5, 32.7, 63.0.

(3*R*, 5*S*, 7*S*, 8*R*, 9*S*, 10*S*, 13*R*, 14*S*, 17*R*)-17-((*R*)-5-Hydroxypentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,7-diol (Table 2, entry 8)[6-7]



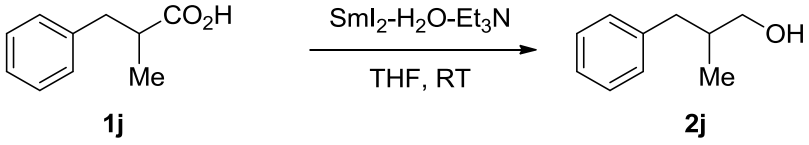
According to the general procedure *Method B*, the reaction of ursodeoxycholic acid (CAS: 128-12-2) (0.25 mmol), samarium(II) iodide (1.5 mmol), water (9.0 mmol) and triethylamine (9.0 mmol) for 4 h at rt, afforded after chromatography (1/10-1/1 EtOAc/hexanes-EtOAc) the title compound in 94% yield. Solid (R_f = 0.33, EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.61 (s, 3H), 0.88 (s, 6H), 0.91-1.11 (m, 4H), 1.13-1.27 (m, 4H), 1.29-1.46 (m, 11H), 1.49-1.63 (m, 5H), 1.68-1.76 (m, 3H), 1.77-1.86 (m, 1H), 1.94 (dt, *J* = 3.2, 12.5 Hz, 1H), 348-3.59 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.1, 18.8, 21.2, 23.4, 26.9, 28.8, 29.4, 30.3, 31.9, 34.1, 34.9, 35.5, 36.8, 37.2, 39.2, 40.2, 42.4, 43.8, 43.8, 55.1, 55.7, 63.6, 71.4, 71.5.

3-Phenylpropan-1-ol (Table 2, entry 9)



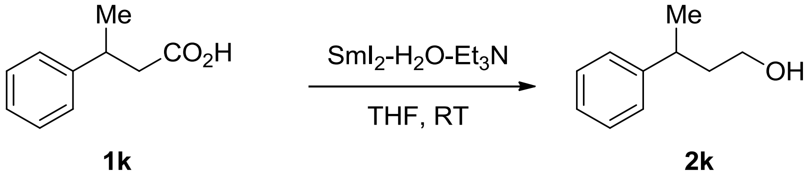
According to the general procedure *Method A*, the reaction of methyl 3-phenylpropanoic acid (0.10 mmol), samarium(II) iodide (0.6 mmol), water (1.8 mmol) and triethylamine (1.8 mmol) for 3 h at rt, afforded after chromatography (1/10-1/1 EtOAc/hexanes) the title compound in 92% yield. Oil (R_f = 0.56, 1/1 EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (br, 1H), 1.79-1.87 (m, 2H), 2.64 (t, *J* = 7.6 Hz, 2H), 3.61 (t, *J* = 6.4 Hz, 2H), 7.09-7.24 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.1, 34.3, 62.3, 125.9, 128.4, 128.5, 141.8.

2-Methyl-3-phenylpropan-1-ol (Table 2, entry 10)



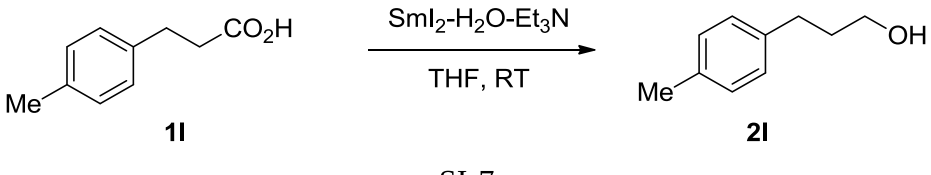
According to the general procedure *Method A*, the reaction of 2-methyl-3-phenylpropanoic acid (0.10 mmol), samarium(II) iodide (0.6 mmol), water (3.6 mmol) and triethylamine (3.6 mmol) for 16 h at rt, afforded after chromatography (1/10-4/1 EtOAc/hexanes) the title compound in 97% yield. Oil (R_f = 0.37, 1/4 EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85 (d, *J* = 6.9 Hz, 3H), 1.33 (br, 1H), 1.79-1.94 (m, 1H), 2.36 (dd, *J* = 8.0, 13.5 Hz, 1H), 2.69 (dd, *J* = 6.2, 13.4 Hz, 1H), 3.37-3.50 (m, 2H), 7.07-7.25 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.5, 37.8, 39.7, 67.7, 125.9, 128.3, 129.2, 140.6.

3-Phenylbutan-1-ol (Table 2, entry 11)



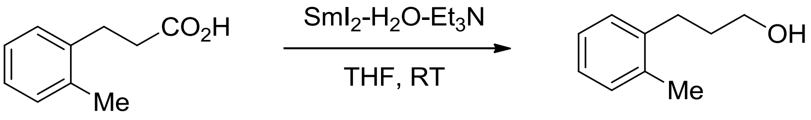
According to the general procedure *Method B*, the reaction of 3-phenylbutanoic acid (0.25 mmol), samarium(II) iodide (1.5 mmol), water (9.0 mmol) and triethylamine (9.0 mmol) for 3 h at rt, afforded after chromatography (1/10-1/1 EtOAc/hexanes) the title compound in 88% yield. Oil (R_f = 0.60, 1/1 EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.21 (d, *J* = 7.0 Hz, 3H), 1.24 (br, 1H), 1.75-1.82 (m, 2H), 2.77-2.85 (m, 1H), 3.43-3.54 (m, 2H), 7.10-7.25 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.4, 36.5, 41.0, 61.2, 126.1, 127.0, 128.5, 146.8.

3-(*p*-Tolyl)propan-1-ol (Table 2, entry 12)



According to the general procedure *Method A*, the reaction of 3-(*p*-tolyl)propanoic acid (0.10 mmol), samarium(II) iodide (0.6 mmol), water (3.6 mmol) and triethylamine (3.6 mmol) for 18 h at rt, afforded after chromatography (1/10-1/1 EtOAc/hexanes) the title compound in 95% yield. Oil (R_f = 0.31, 1/4 EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (br, 1H), 1.75-1.86 (m, 2H), 2.25 (s, 3H), 2.60 (t, *J* = 7.5 Hz, 2H), 3.60 (t, *J* = 6.4 Hz, 2H), 7.02 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0, 31.7, 34.4, 62.4, 128.3, 129.1, 135.3, 138.7.

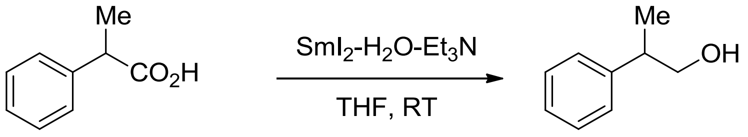
3-(*o*-Tolyl)propan-1-ol (Table 2, entry 13)



1m **2m**

According to the general procedure *Method A*, the reaction of 3-(*o*-tolyl)propanoic acid (0.10 mmol), samarium(II) iodide (0.6 mmol), water (3.6 mmol) and triethylamine (3.6 mmol) for 18 h at rt, afforded after chromatography (1/10-1/4 EtOAc/hexanes) the title compound in 98% yield. Oil (R_f = 0.36, 1/4 EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (br, 1H), 1.73-1.84 (m, 2H), 2.25 (s, 3H), 2.59-2.66 (m, 2H), 3.64 (t, *J* = 6.6 Hz, 2H), 7.00-7.11 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.3, 29.5, 33.1, 62.6, 126.0, 126.0, 128.8, 130.3, 136.0, 140.0.

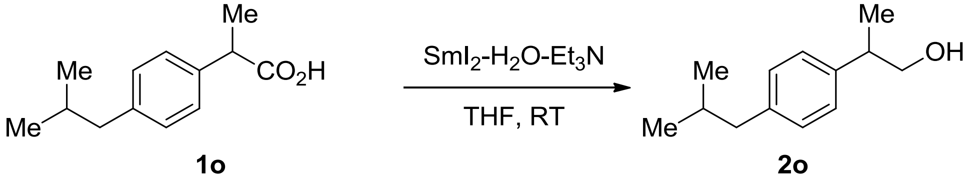
2-Phenylpropan-1-ol (Table 2, entry 14)



1n **1n**

According to the general procedure *Method A*, the reaction of 2-phenylpropanoic acid (0.10 mmol), samarium(II) iodide (0.6 mmol), water (3.6 mmol) and triethylamine (3.6 mmol) for 16 h at rt, afforded the title compound in 94% yield (^{1}H NMR vs. internal standard). Note: the product is volatile. Spectroscopic properties matched those previously described.[11]

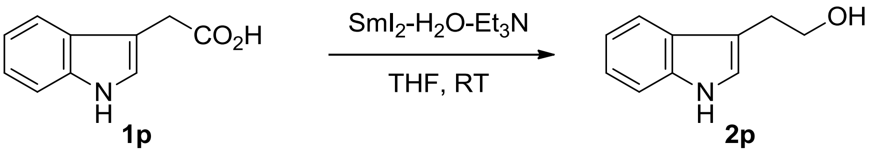
2-(4-Isobutylphenyl)propan-1-ol (Table 2, entry 15)



1o **2o**

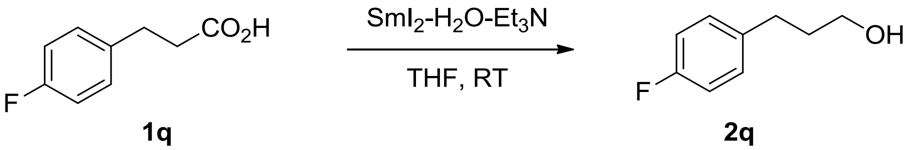
According to the general procedure *Method A*, the reaction of 2-(4-isobutylphenyl)propanoic acid (0.10 mmol), samarium(II) iodide (0.6 mmol), water (3.6 mmol) and triethylamine (3.6 mmol) for 16 h at rt, afforded after chromatography (1/10-1/4 EtOAc/hexanes) the title compound in 91% yield. Oil (R_f = 0.44, 1/4 EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.83 (d, *J* = 6.6 Hz, 6H), 1.19 (d, *J* = 7.2 Hz, 3H), 1.34 (br, 1H), 1.70-1.85 (m, 1H), 2.37 (d, *J* = 7.2 Hz, 2H), 2.79-2.92 (m, 1H), 3.61 (d, *J* = 6.9 Hz, 2H), 7.01-7.09 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.6, 22.4, 30.2, 42.1, 45.1, 68.8, 127.2, 129.4, 140.1, 140.7.

2-(1*H*-Indol-3-yl)ethanol (Table 2, entry 16)



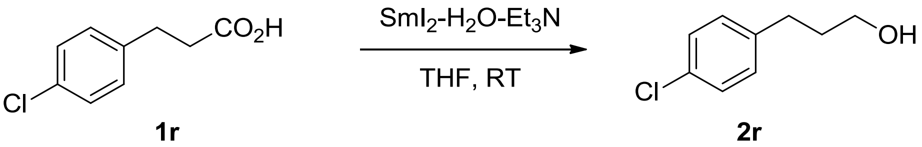
According to the general procedure *Method B*, the reaction of 2-(1*H*-indol-3-yl)acetic acid (0.25 mmol), samarium(II) iodide (1.12 mmol), water (6.0 mmol) and triethylamine (6.0 mmol) for 5 h at rt, afforded after purification by preparative thin layer chromatography (EtOAc) the title compound in 82% yield. Oil (R_f = 0.71, EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.57 (br, 1H), 2.96 (t, *J* = 6.6 Hz, 2H), 3.83 (t, *J* = 6.3 Hz, 2H), 6.98 (d, *J* = 2.4 Hz, 1H), 7.06 (td, *J* = 7.2, 1.2 Hz, 1H), 7.14 (td, *J* = 8.1, 0.9 Hz, 1H), 7.28 (d, *J* = 8.1 Hz, 1H), 7.55 (dd, *J* = 0.6, 7.8 Hz, 1H), 8.01 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.8, 62.6, 111.3, 112.3, 118.9, 119.5, 122.3, 122.5, 127.4, 136.5.

3-(4-Fluorophenyl)propan-1-ol (Table 3, entry 1)



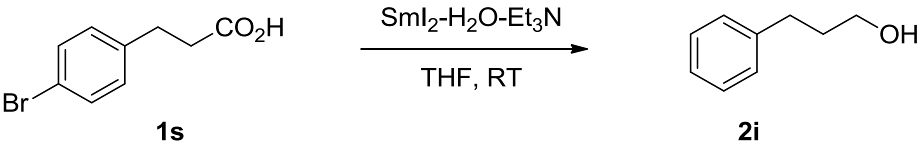
According to the general procedure *Method B*, the reaction of 3-(4-fluorophenyl)propanoic acid (0.25 mmol), samarium(II) iodide (1.5 mmol), water (9.0 mmol) and triethylamine (9.0 mmol) for 1 h at rt, afforded after chromatography (1/4-1/1 EtOAc/hexanes) the title compound in 93% yield. Oil (R_f = 0.53, 1/1 EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.47 (br, 1H), 1.74-1.84 (m, 2H), 2.61 (t, *J* = 7.8 Hz, 2H), 3.59 (t, *J* = 6.6 Hz, 2H), 6.84-6.93 (m, 2H), 7.03-7.11 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.2, 34.3, 62.1, 115.1 (d, J^2 = 21.0 Hz), 129.7 (d, J^3 = 8.3 Hz), 137.4 (d, J^4 = 3.0 Hz), 161.3 (d, J^1 = 241.5 Hz); ^{19}F (376 MHz, $CDCl_3$) δ -117.7.

3-(4-Chlorophenyl)propan-1-ol (Table 3, entry 2)



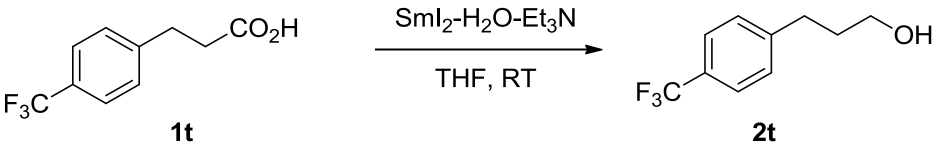
According to the general procedure *Method B*, the reaction of 3-(4-chlorophenyl)propanoic acid (0.25 mmol), samarium(II) iodide (2.5 mmol), water (15 mmol) and triethylamine (15 mmol) for 3 h at rt, afforded after chromatography (1/0-1/1 EtOAc/hexanes) the title compound in 86% yield. Oil (R_f = 0.59, 1/1 EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.59 (br, 1H), 1.83-1.93 (m, 2H), 2.70 (t, *J* = 7.5 Hz, 2H), 3.68 (t, *J* = 6.3 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.4, 34.1, 62.0, 125.9, 129.8, 131.6, 140.3.

3-Phenylpropan-1-ol (Table 3, entry 3)



According to the general procedure *Method B*, the reaction of 3-(4-bromophenyl)propanoic acid (0.25 mmol), samarium(II) iodide (2.0 mmol), water (12 mmol) and triethylamine (12 mmol) for 1 h at rt, afforded after chromatography (1/10-1/1 EtOAc/hexanes) the title compound in 86% yield. Oil (R_f = 0.48, 1/1 EtOAc/hexanes). Spectroscopic properties matched those previously described.

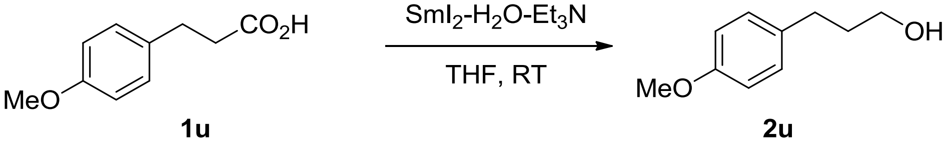
3-(4-(Trifluoromethyl)phenyl)propan-1-ol (Table 3, entry 4)



According to the general procedure *Method B*, the reaction of 3-(4-(trifluoromethyl)phenyl)propanoic acid (0.25 mmol), samarium(II) iodide (1.5 mmol), water (9.0 mmol) and triethylamine (9.0 mmol) for 5 h at rt, afforded after chromatography (1/4-1/1 EtOAc/hexanes) the title compound in 98% yield. Oil (R_f = 0.62, 60/40 EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.45 (br, 1H), 1.80-1.86 (m, 2H), 2.70 (t, *J* = 7.5 Hz, 2H), 3.61 (t, *J* = 6.3 Hz, 2H), 7.23 (d, *J* = 7.9 Hz, 2H), 7.47 (d, *J* = 7.9 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ

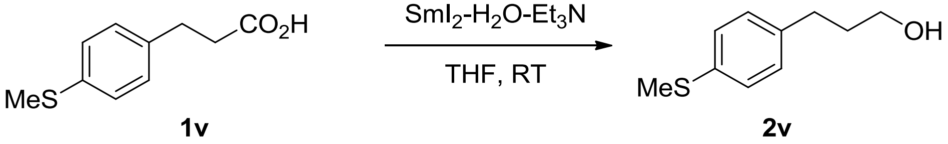
31.9, 33.9, 61.9, 123.3, 125.3 (q, J^3 = 3.6 Hz), 128.3 (q, J^2 = 32.5 Hz), 128.8, 146.0; ^{19}F (470 MHz, $CDCl_3$) δ -62.3.

3-(4-Methoxyphenyl)propan-1-ol (Table 3, entry 5)



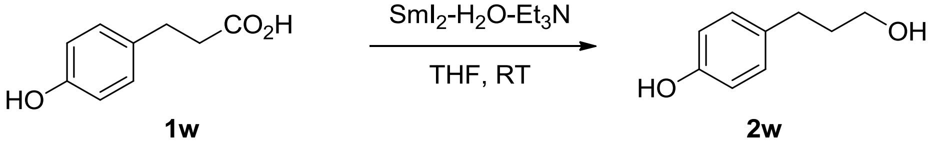
According to the general procedure *Method A*, the reaction of methyl 3-(4-methoxyphenyl)propanoic acid (2.5 mmol), samarium(II) iodide (12.5 mmol), water (75 mmol) and triethylamine (75 mmol) for 2 h at rt, afforded after chromatography (1/0-1/1 EtOAc/hexanes) the title compound in 94% yield. Oil (R_f = 0.52, 1/1 EtOAc/hexanes). Note: the following extraction procedure was used: 1 *N* HCl/CH_2Cl_2 (200 mL/200 mL, 4 x 50 mL). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (br, 1H), 1.74-1.84 (m, 2H), 2.58 (t, *J* = 7.5 Hz, 2H), 3.59 (t, *J* = 6.3 Hz, 2H), 3.72 (s, 3H), 6.76 (d, *J* = 8.7 Hz, 2H), 7.04 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.2, 34.5, 55.3, 62.3, 113.9, 129.3, 133.9, 157.8.

3-(4-(Methylthio)phenyl)propan-1-ol (Table 3, entry 6)



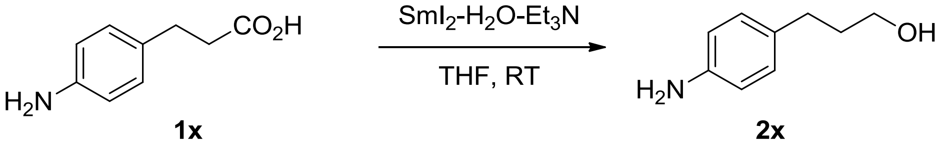
According to the general procedure *Method B*, the reaction of 3-(4-(methylthio)phenyl)propanoic acid (0.25 mmol), samarium(II) iodide (1.5 mmol), water (9.0 mmol) and triethylamine (9.0 mmol) for 1 h at rt, afforded after chromatography (1/0-1/1 EtOAc/hexanes) the title compound in 96% yield. Oil (R_f = 0.50, 1/1 EtOAc/hexanes). Note: the product is unstable. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.52 (br, 1H), 1.74-1.84 (m, 2H), 2.39 (s, 3H), 2.59 (t, *J* = 7.2 Hz, 2H), 3.58 (t, *J* = 6.3 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 2H), 7.13 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.4, 31.5, 34.2, 62.2, 127.3, 129.0, 135.4, 139.0.

4-(3-Hydroxypropyl)phenol (Table 3, entry 7)



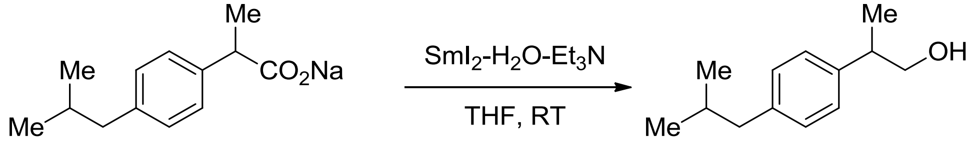
According to the general procedure *Method B*, the reaction of 3-(4-hydroxyphenyl)propanoic acid (0.25 mmol), samarium(II) iodide (1.5 mmol), water (9.0 mmol) and triethylamine (9.0 mmol) for 3 h at rt, afforded after chromatography (1/10-2/1 EtOAc/hexanes-EtOAc) the title compound and 4-(3-hydroxypropyl)cyclohex-3-enol in 71% yield. 4-(3-Hydroxypropyl)phenol: 48%, oil (R_f = 0.33, 1/1 EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.49 (br, 1H), 1.74-1.84 (m, 2H), 2.57 (t, *J* = 7.2 Hz, 2H), 3.61 (t, *J* = 6.6 Hz, 2H), 4.97 (br, 1H), 6.68 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.1, 34.4, 62.3, 115.3, 129.5, 133.9, 153.8. 4-(3-Hydroxypropyl)cyclohex-3-enol: 23%, oil (R_f = 0.13, 1/1 EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.45-1.67 (m, 5H), 1.74-1.84 (m, 1H), 1.87-2.07 (m, 5H), 2.21-2.34 (m, 1H), 3.57 (t, *J* = 6.6 Hz, 2H), 3.84-3.92 (m, 1H), 5.24-5.29 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.2, 30.6, 31.0, 33.8, 34.3, 62.8, 66.8, 118.1, 137.2. Note: to the best of our knowledge reductive dearomatization of simple aromatic compounds has not been reported previously with SmI_2 under mild conditions. Studies on elucidation of these processes are currently ongoing in our group.

3-(4-Aminophenyl)propan-1-ol (Table 3, entry 8)



According to the general procedure *Method B*, the reaction of 3-(4-aminophenyl)propanoic acid (0.25 mmol), samarium(II) iodide (1.5 mmol), water (9.0 mmol) and triethylamine (9.0 mmol) for 5 h at rt, afforded after chromatography (1/10-1/1 EtOAc/hexanes-EtOAc) the title compound in 73% yield. Oil (R_f = 0.60, EtOAc). Note: the following extraction procedure was used: 1 *N* NaOH/CH_2Cl_2 (50 mL/30 mL, 4 x 30 mL). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.71-1.81 (m, 2H), 2.52 (t, *J* = 7.2 Hz, 2H), 3.34 (br, 2H), 3.58 (t, *J* = 6.3 Hz, 2H), 6.56 (d, *J* = 8.4 Hz, 2H), 6.92 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.2, 34.5, 62.4, 115.4, 129.2, 131.9, 144.3.

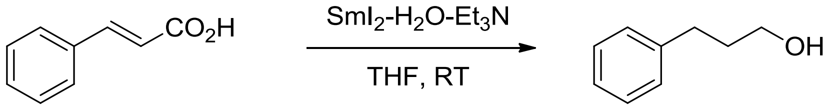
2-(4-Isobutylphenyl)propan-1-ol (Reduction of carboxylate salt – Scheme 1)



3 **2o**

According to the general procedure, the reaction of sodium 2-(4-isobutylphenyl)propanoate (0.10 mmol), samarium(II) iodide (0.6 mmol), water (7.2 mmol) and triethylamine (7.2 mmol) for 18 h at rt, afforded after chromatography (1/10-1/4 EtOAc/hexanes) the title compound in 97% yield. Oil (R_f = 0.15, 1/10 EtOAc/hexanes). Spectroscopic properties matched those previously described.

3-Phenylpropan-1-ol (Reduction of α,β-unsaturated acid – Scheme 2)

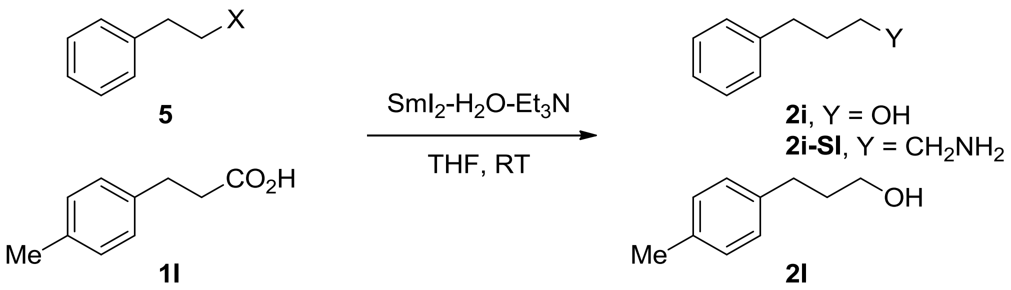


4 **2i**

According to the general procedure, the reaction of cinnamic acid (0.10 mmol), samarium(II) iodide (0.8 mmol), water (4.8 mmol) and triethylamine (4.8 mmol) for 2 h at rt, afforded after chromatography (1/4-4/1 EtOAc/hexanes) the title compound in 85% yield. Oil (R_f = 0.38, 1/4 EtOAc/hexanes). Spectroscopic properties matched those previously described.

Competition Experiments

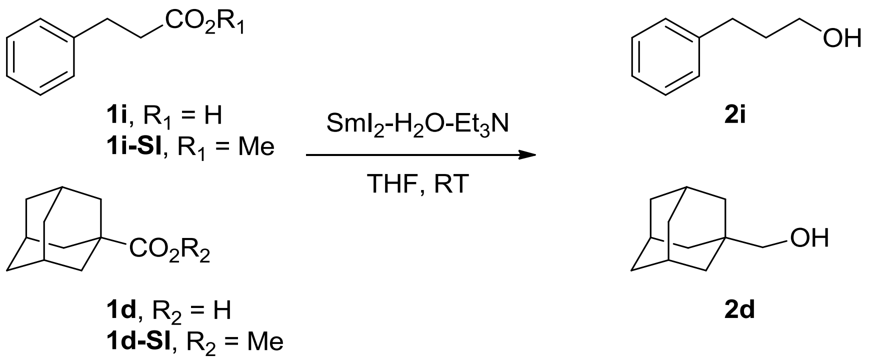
A) Competition between carboxylic acids and derivatives or equivalents of carboxylic acids



Entry	X	Y	**2i/2i-SI**	**2l**
1	CO_2Me	OH	62	38
2	CO_2Et	OH	53	47
3	CO_2*i*-Pr	OH	28	72
4	CO_2*t*-Bu	OH	11	89
5	$C(O)NH_2$	OH	95	5
6	CH_2CN	CH_2NH_2	91	9

According to the general procedure, the reaction of **5** (0.10 mmol) and 3-(*p*-tolyl)propanoic acid (0.10 mmol), samarium(II) iodide (0.4 mmol), water (2.4 mmol) and triethylamine (2.4 mmol) for 5 min at rt, afforded 3-phenylpropan-1-ol (**2i**) or 4-phenylbutan-1-amine (**2i-SI**) and 3-(*p*-tolyl)propan-1-ol (**2l**). The relative quantity of each product was determined by ^1H NMR (500 MHz, $CDCl_3$) and GC (GCTCM-5, 30 mm x 0.32 mm; mobile phase: helium; flow rate: 1.0 mL/min; 70 °C, 4 min; 70 °C to 220 °C, 10 °C/min; retention time: **2i**,11.27 min; **2l**, 12.71 min).

B) Competition between carboxylic acids and sterically-hindered esters and acids

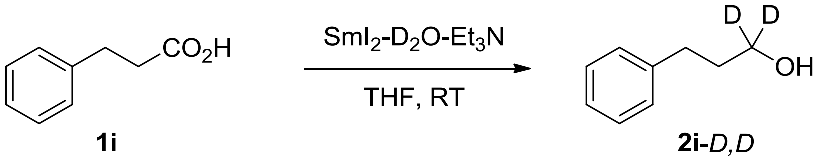


Entry	R_1	R_2	**2i**	**2d**
1	H	H	74	26
2	H	Me	81	19
3	Me	H	76	24

According to the general procedure, the reaction of **1i** or **1i-SI** (0.10 mmol) and **1d** or **1d-SI** (0.10 mmol), samarium(II) iodide (0.4 mmol), water (2.4 mmol) and triethylamine (2.4 mmol) for 5 min at rt, afforded 3-phenylpropan-1-ol (**2i**) and adamantan-1-ylmethanol (**2d**). The relative quantity of each product was determined by ^{1}H NMR (500 MHz, $CDCl_3$).

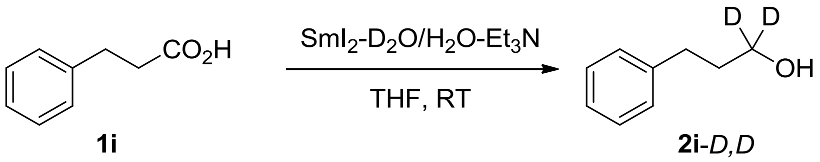
Mechanistic Studies

A) Deuterium incorporation



According to the general procedure, the reaction of methyl 3-phenylpropanoic acid (0.10 mmol), samarium(II) iodide (0.6 mmol), deuterium oxide (1.8 mmol) and triethylamine (1.2 mmol) for 2 h at rt, afforded 1,1-*D*,*D*-3-phenylpropan-1-ol (96% deuterium incorporation). Yield 80% (^{1}H NMR vs. internal standard). Purification by preparative thin layer chromatography (60/40 EtOAc/hexanes) afforded the title product (R_f = 0.58, 1/1 EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (br, 1H), 1.82 (t, *J* = 7.6 Hz, 2H), 2.64 (t, *J* = 7.6 Hz, 2H), 7.10-7.24 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.0, 34.0, 61.6 (t, J^1 = 21.1 Hz), 125.9, 128.4, 128.4, 141.8.

B) Determination of primary kinetic isotope effect[8-11]



According to the general procedure, the reaction of 3-phenylpropanoic acid (0.10 mmol), samarium(II) iodide (0.6 mmol), deuterium oxide/water (1:1, 1.8 mmol) and triethylamine (1.2 mmol) for 2 h at rt, afforded 1,1-*D*,*D*-3-phenylpropan-1-ol and 3-phenylpropan-1-ol. The amount of each species was determined by ^{1}H NMR (500 MHz, $CDCl_3$,). Kinetic isotope effect, k_H/k_D = 1.1.

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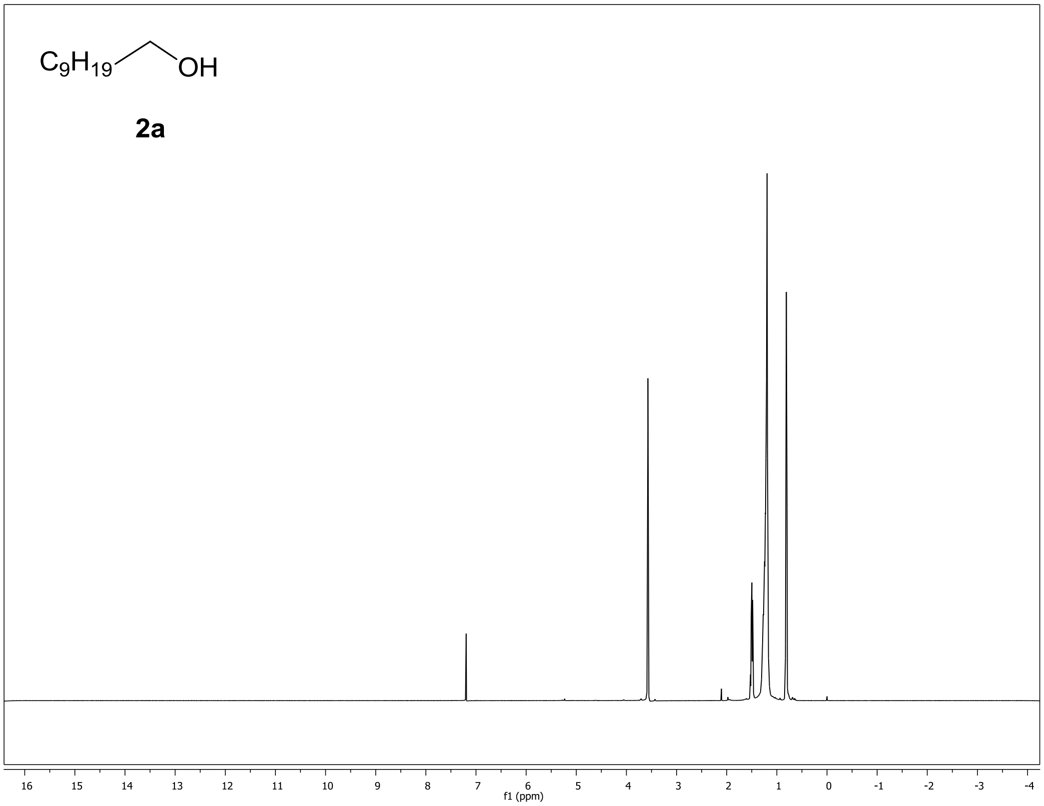
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13
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11
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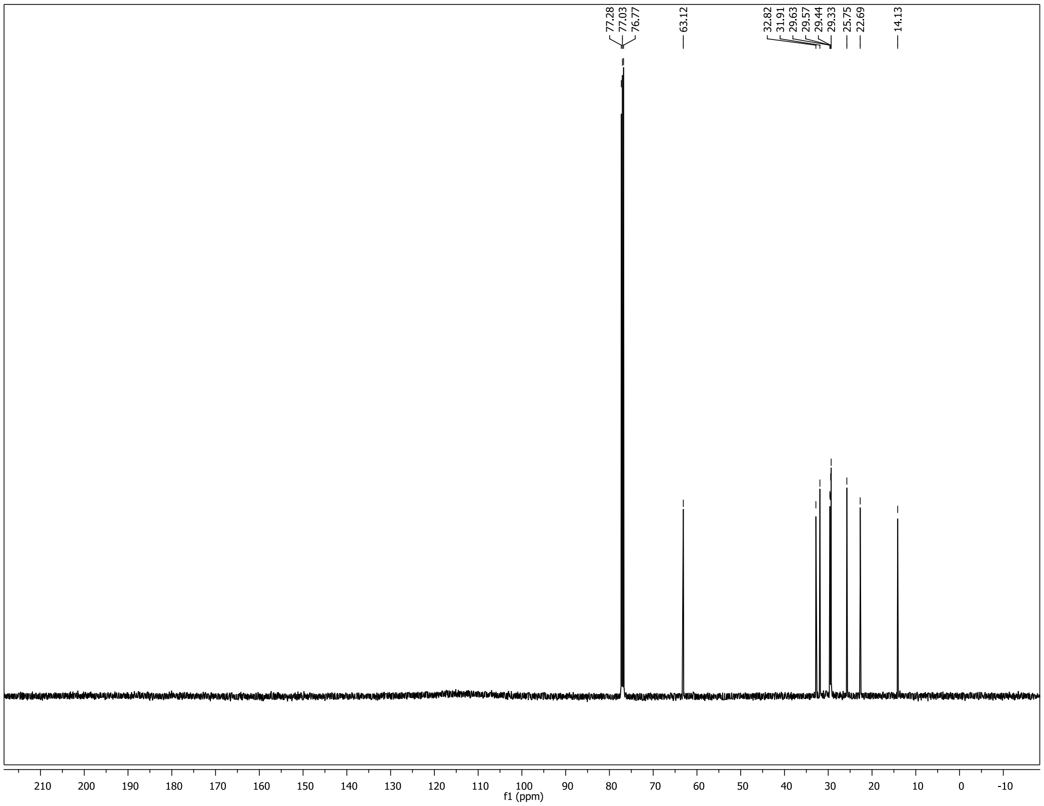
f1 (ppm)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200
190
180
170
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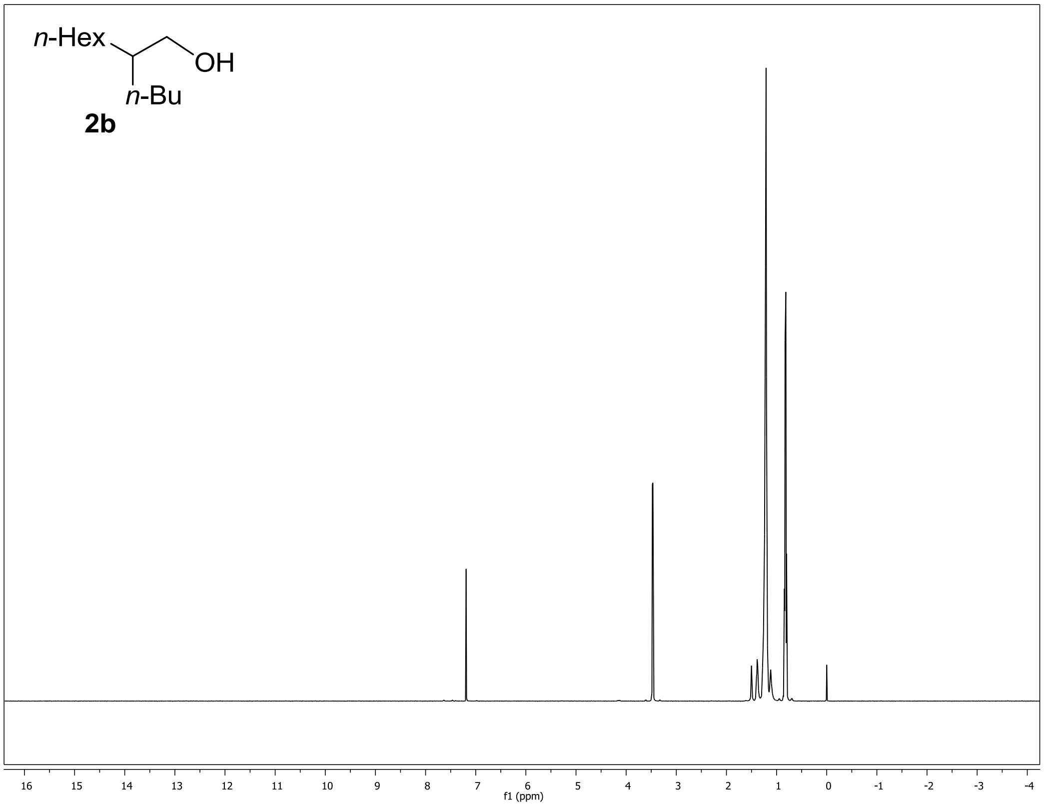
f1 (ppm)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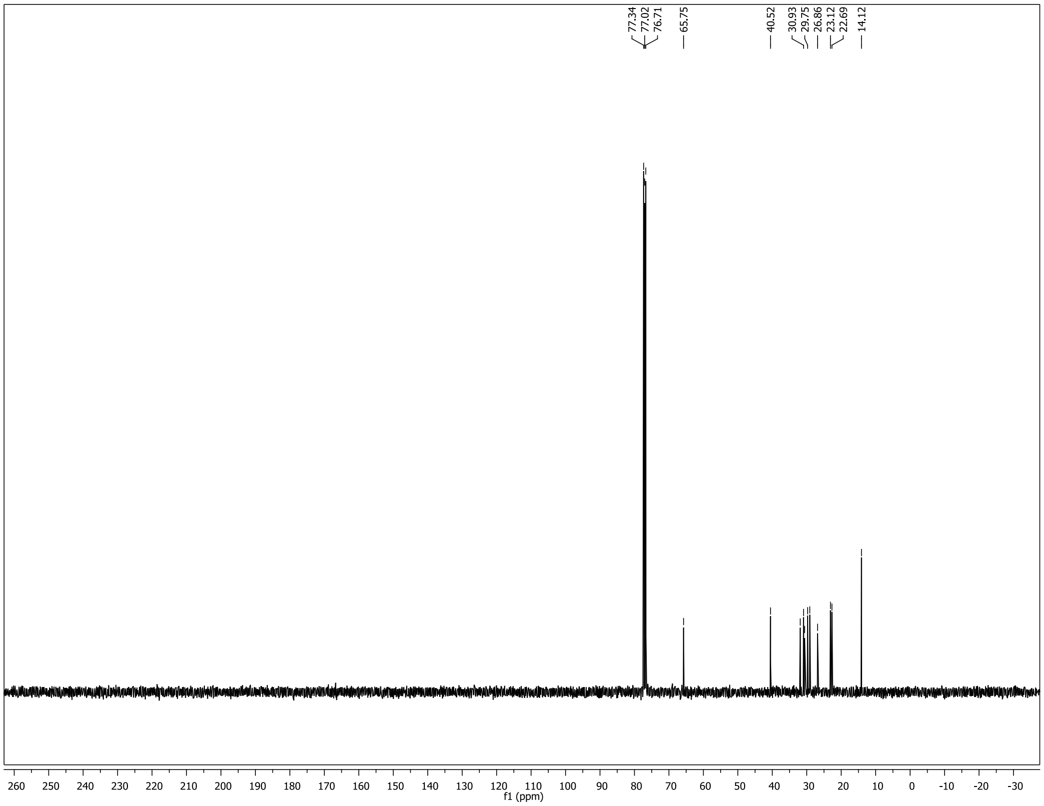
f1 (ppm)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200
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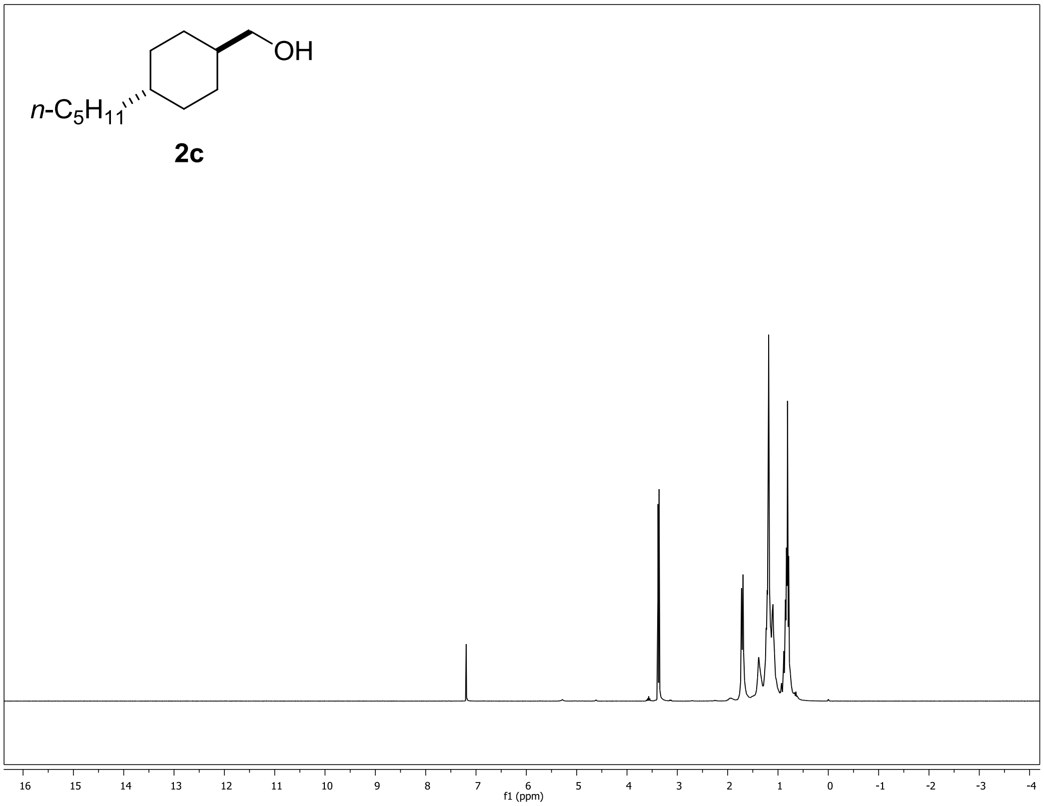
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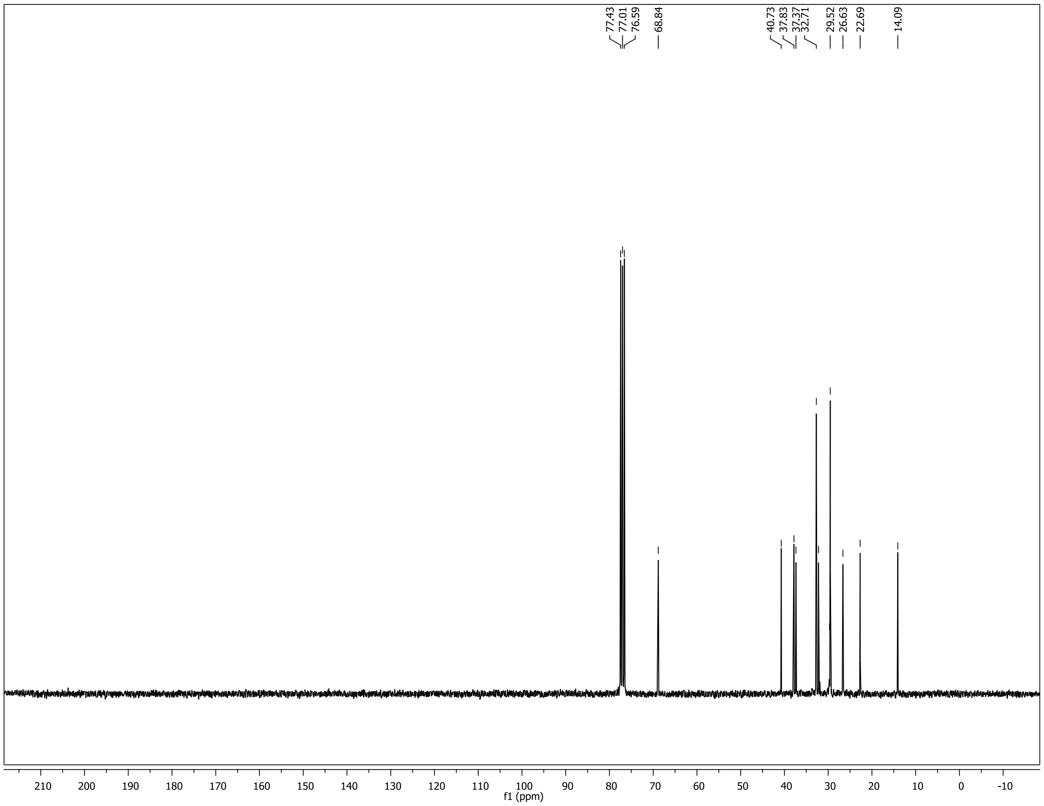
f1 (ppm)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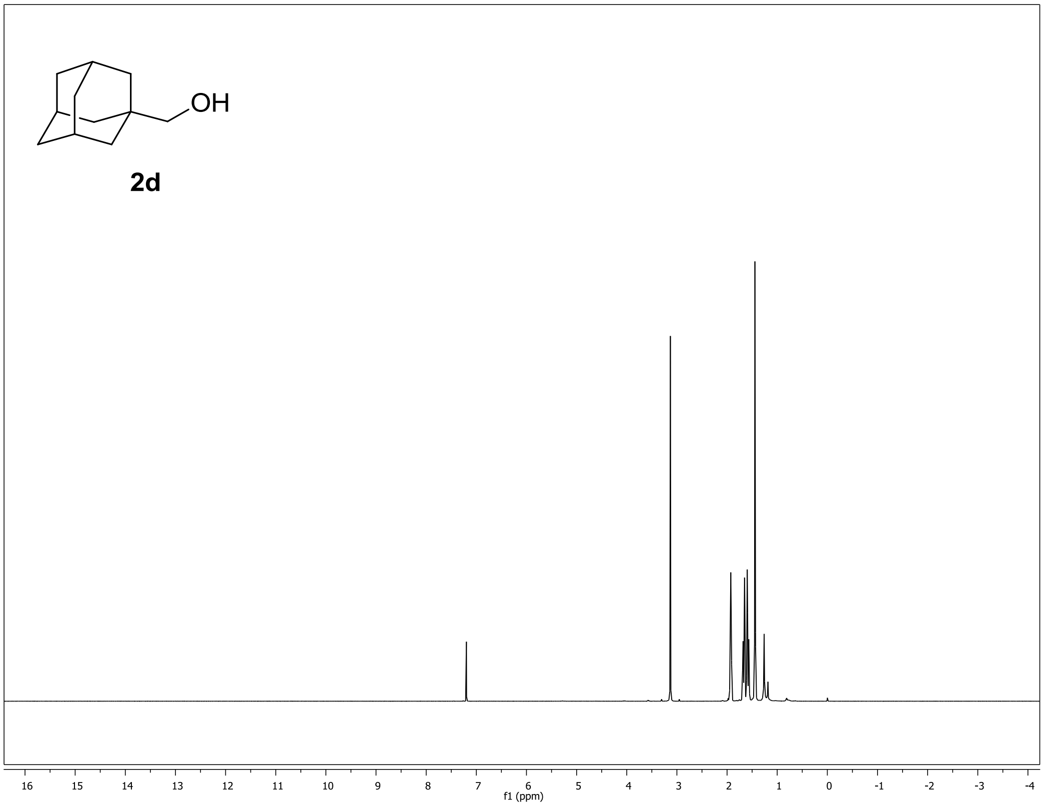
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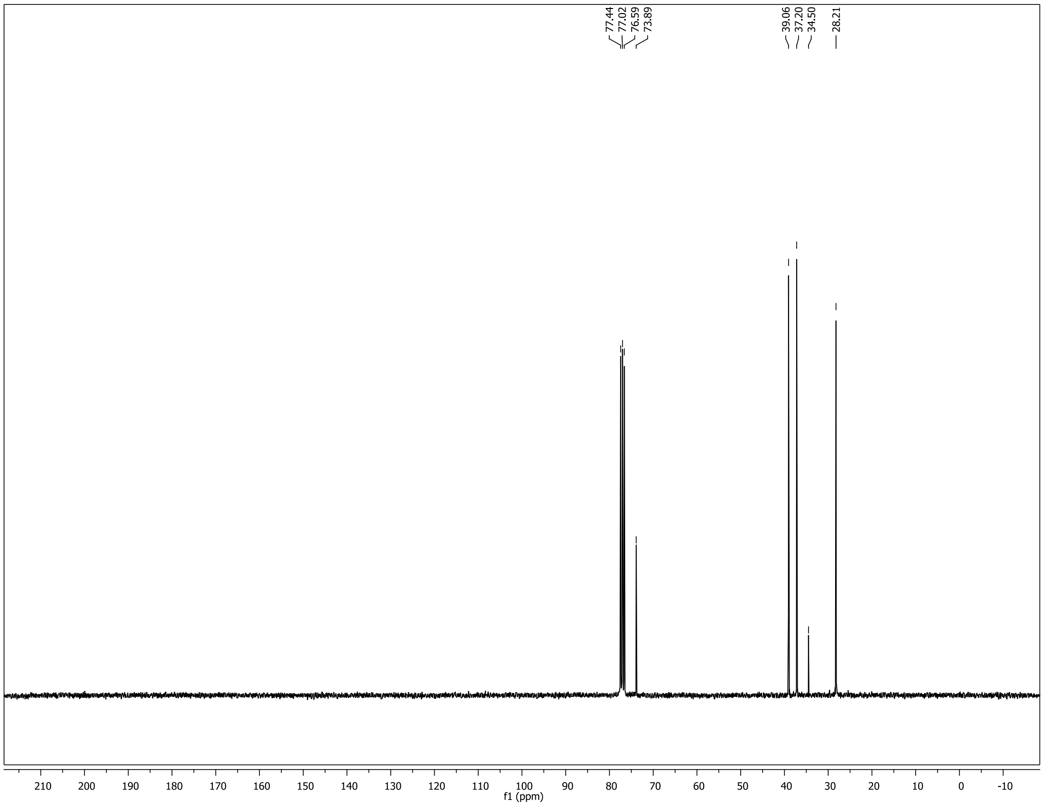
f1 (ppm)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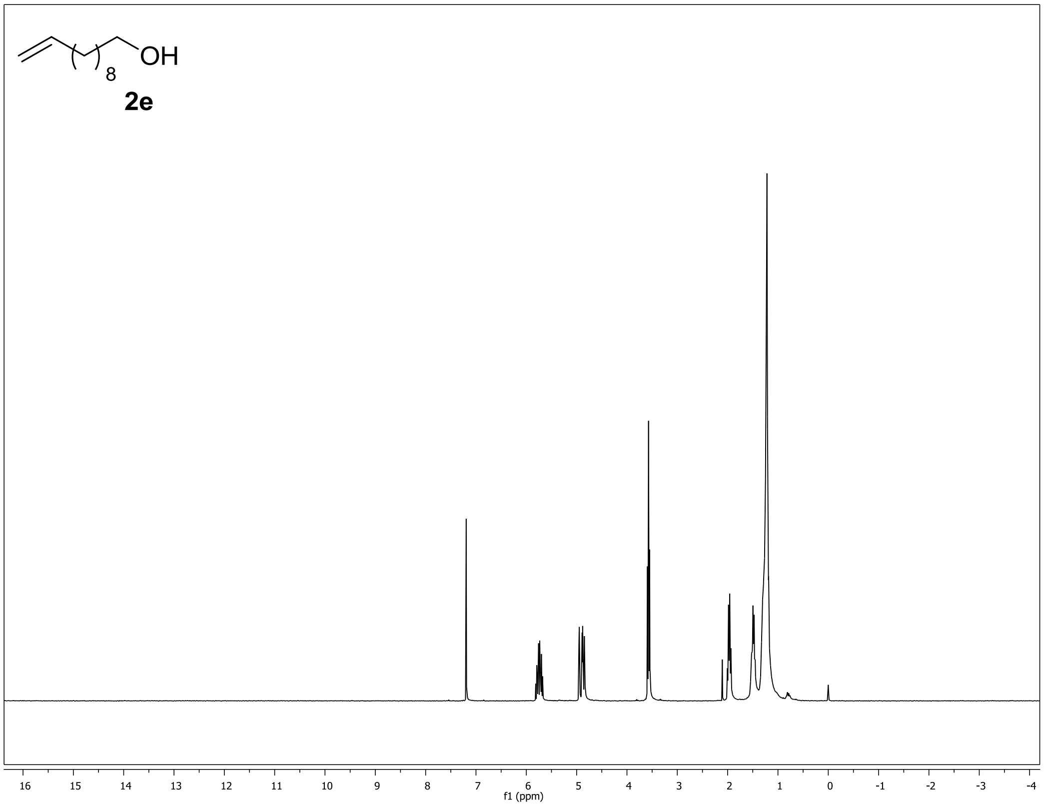
f1 (ppm)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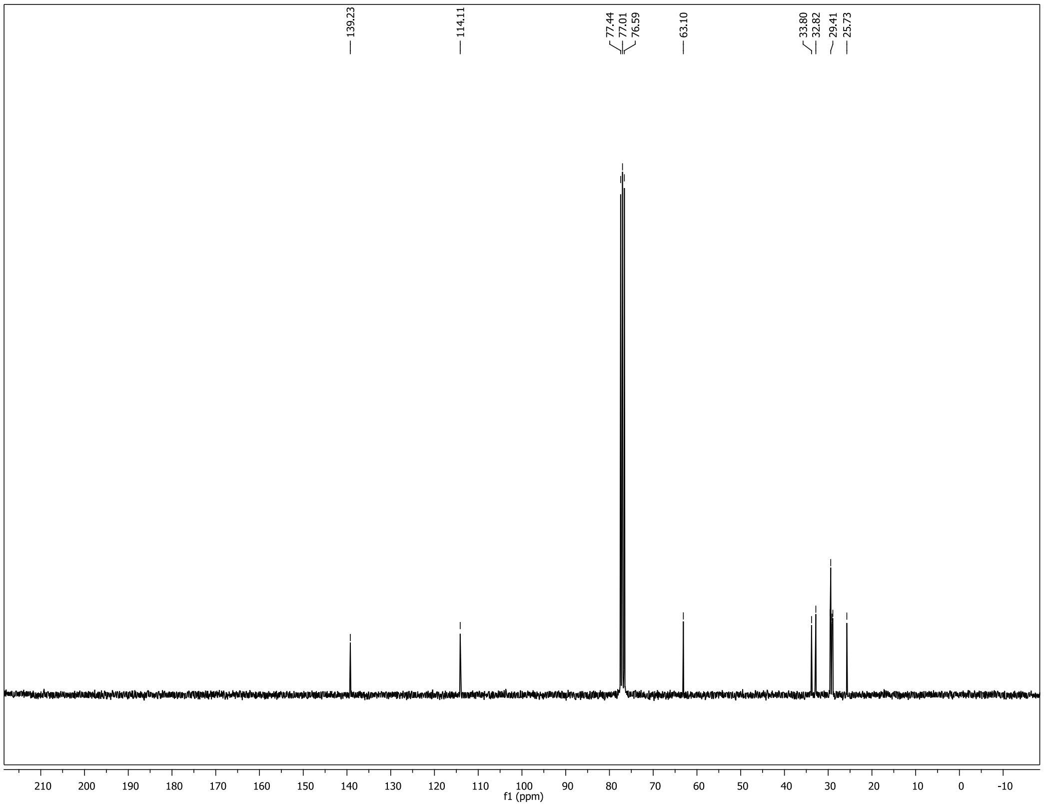
f1 (ppm)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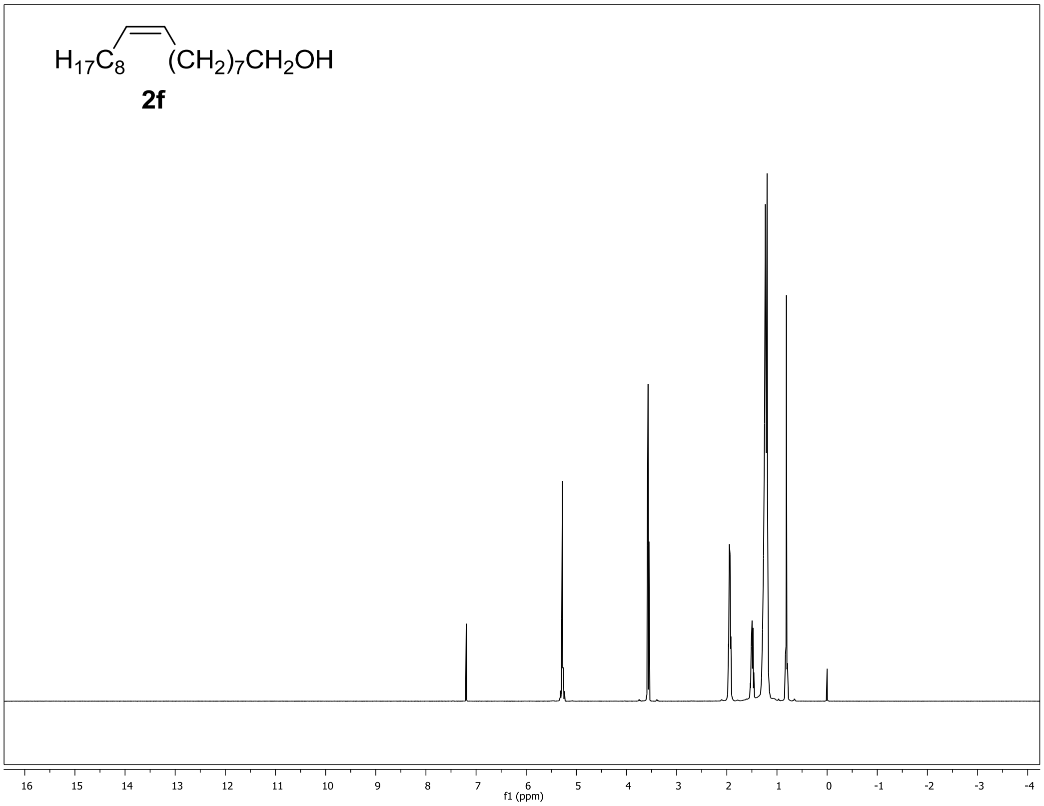
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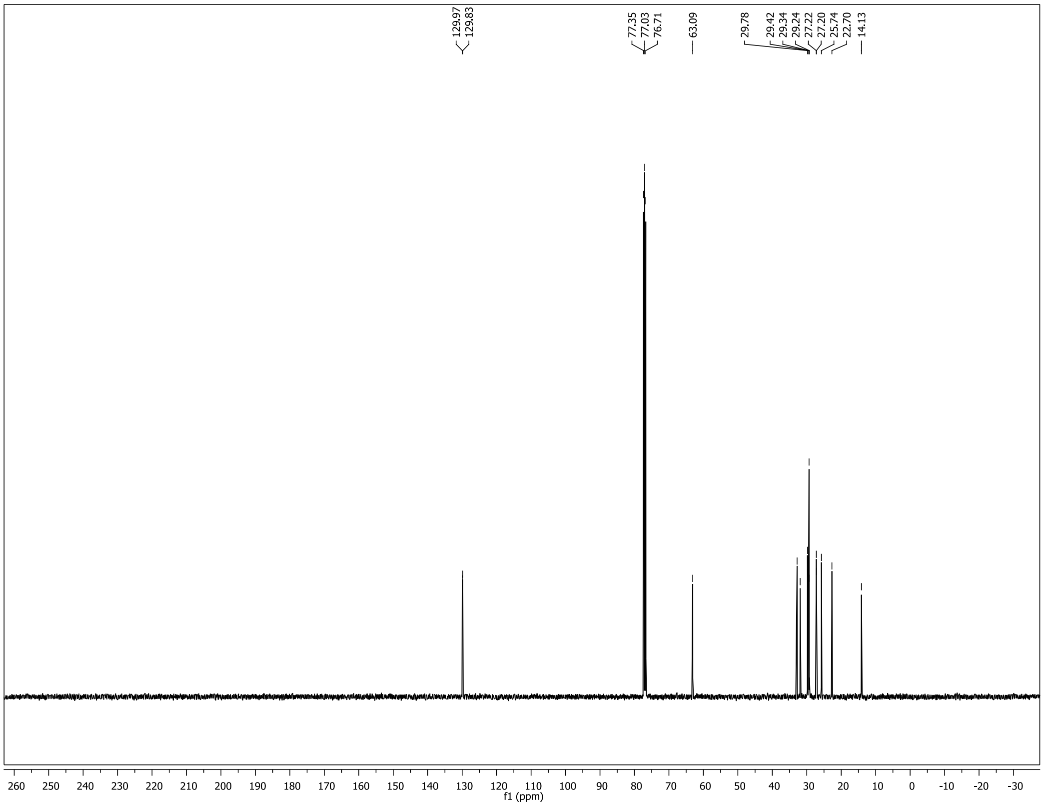
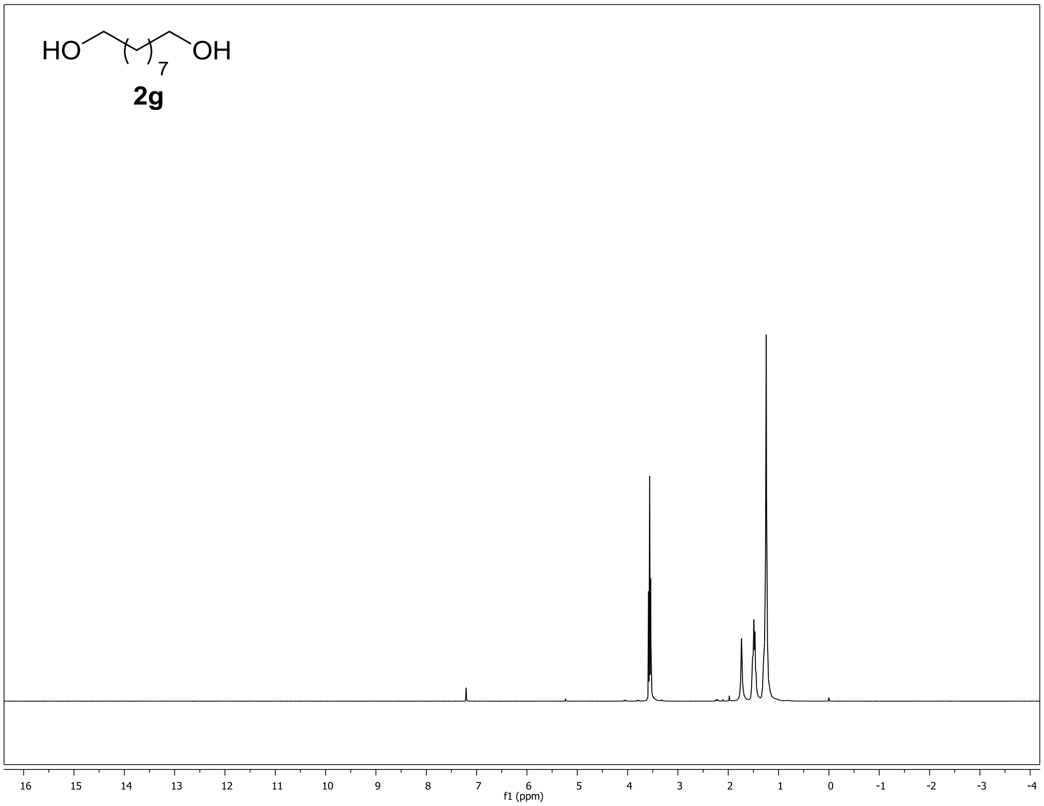
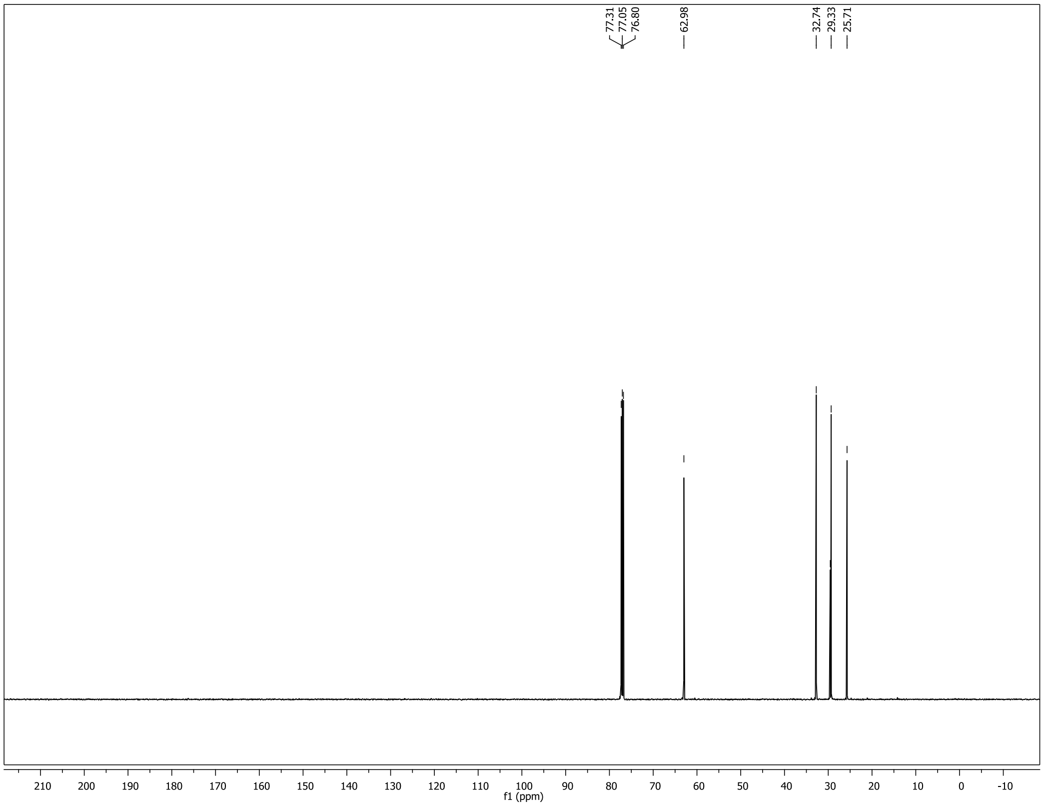
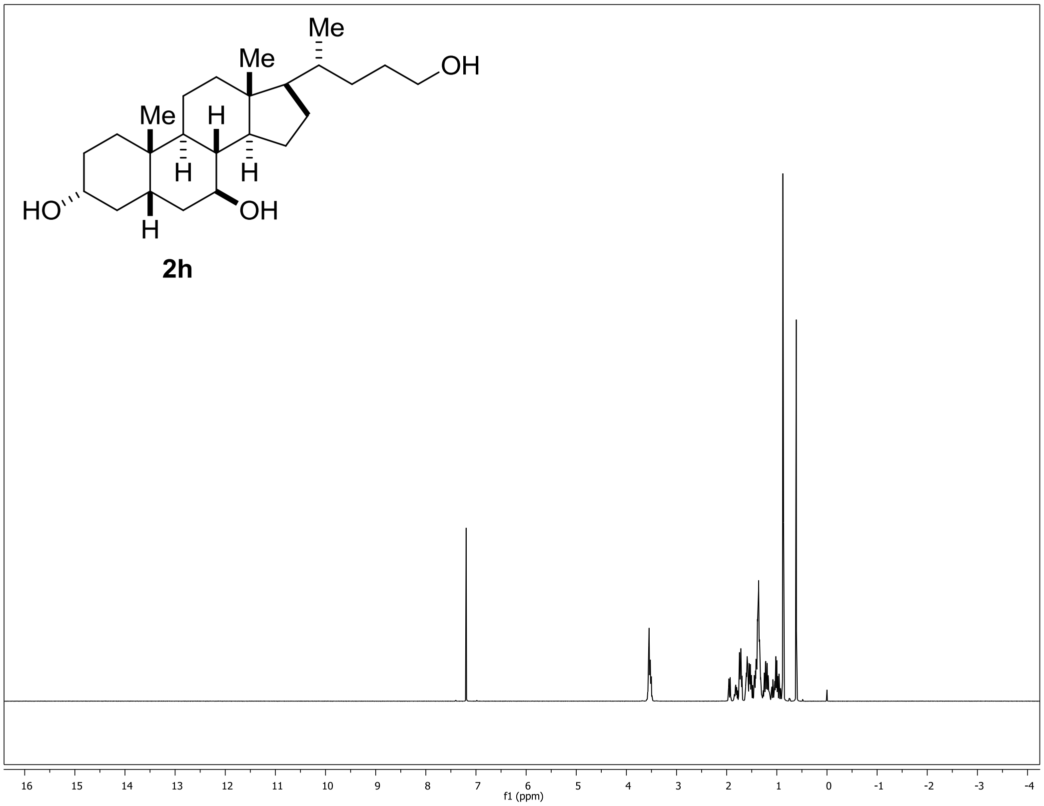
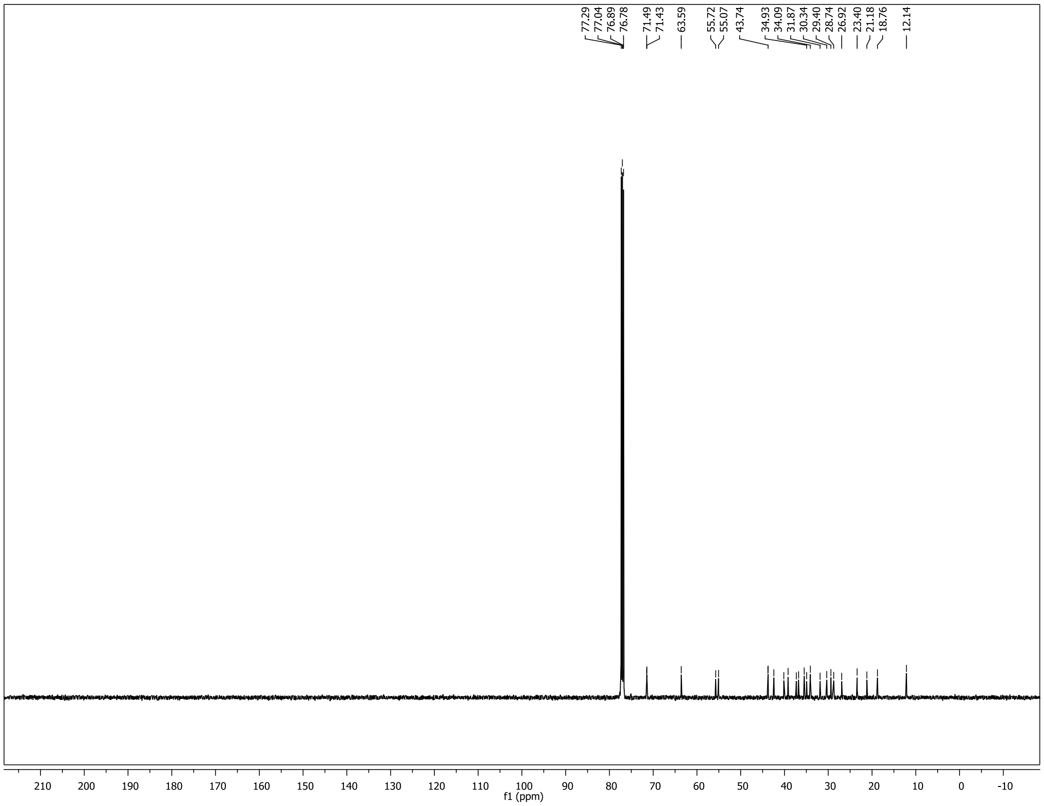
2
1
0
-1
-2
-3
-4
f1 (ppm)

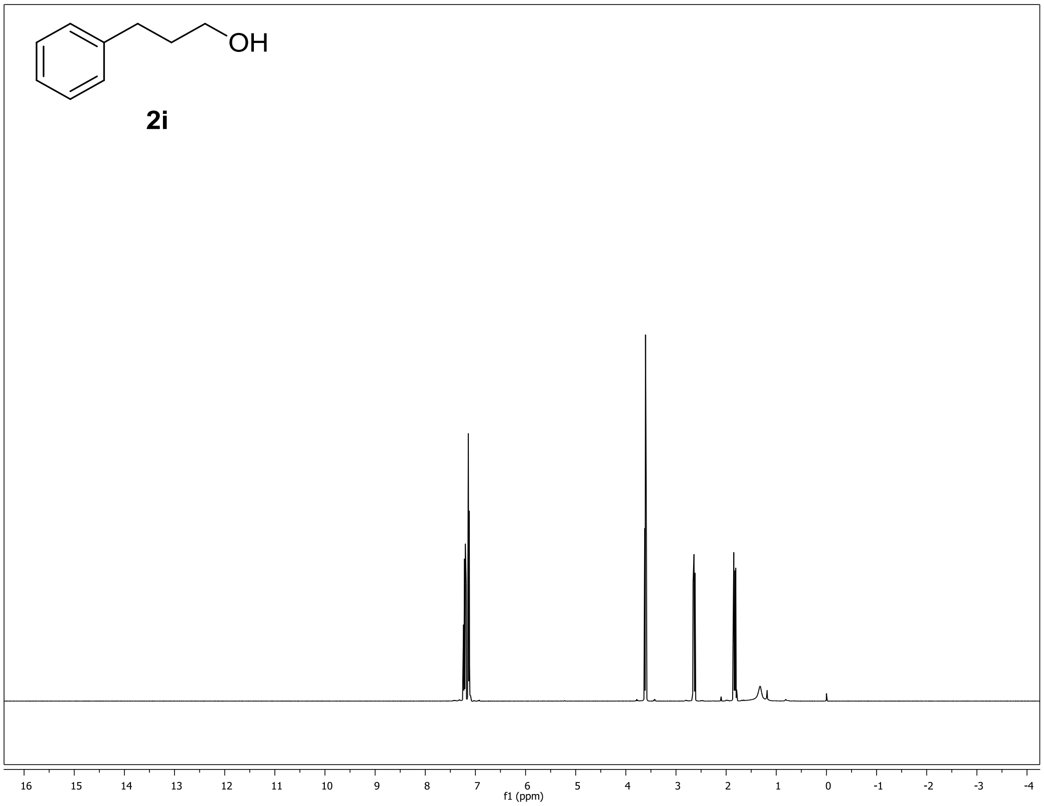

129.97
129.83
77.35
77.03
76.71
63.09
29.78
29.42
29.34
29.24
27.22
27.20
25.74
22.70
14.13
260
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
f1 (ppm)


HO
OH
7
2g
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)

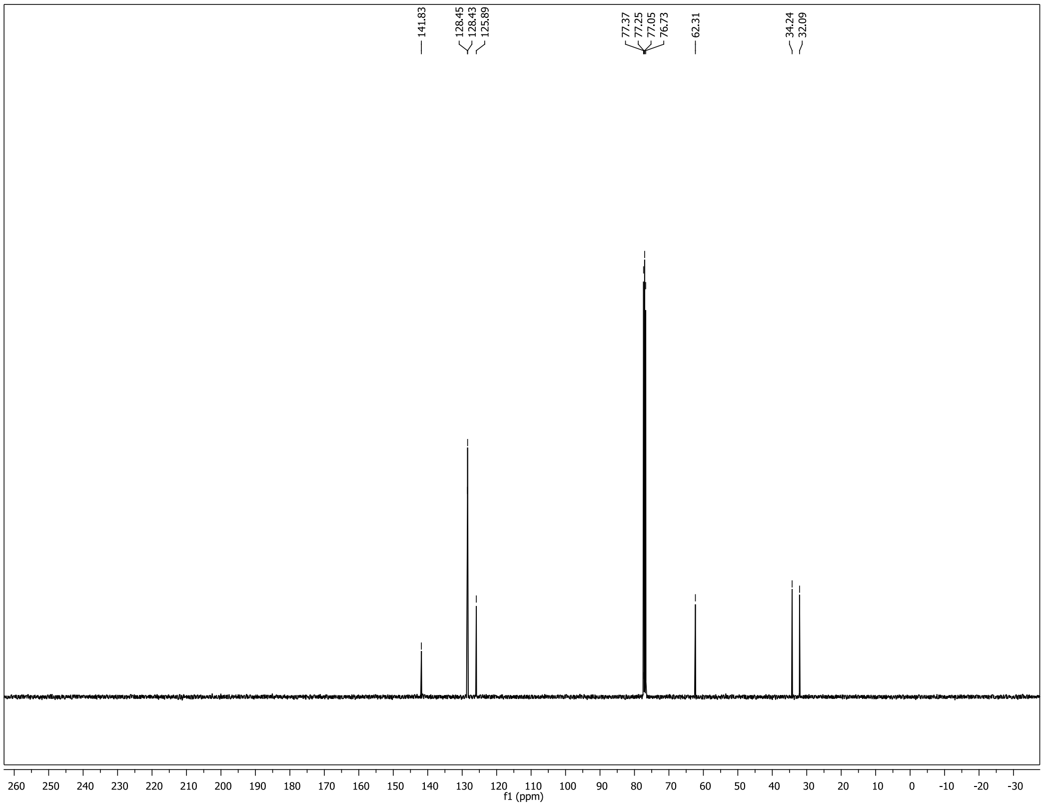

77.31
77.05
76.80
62.98
32.74
29.33
25.71
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

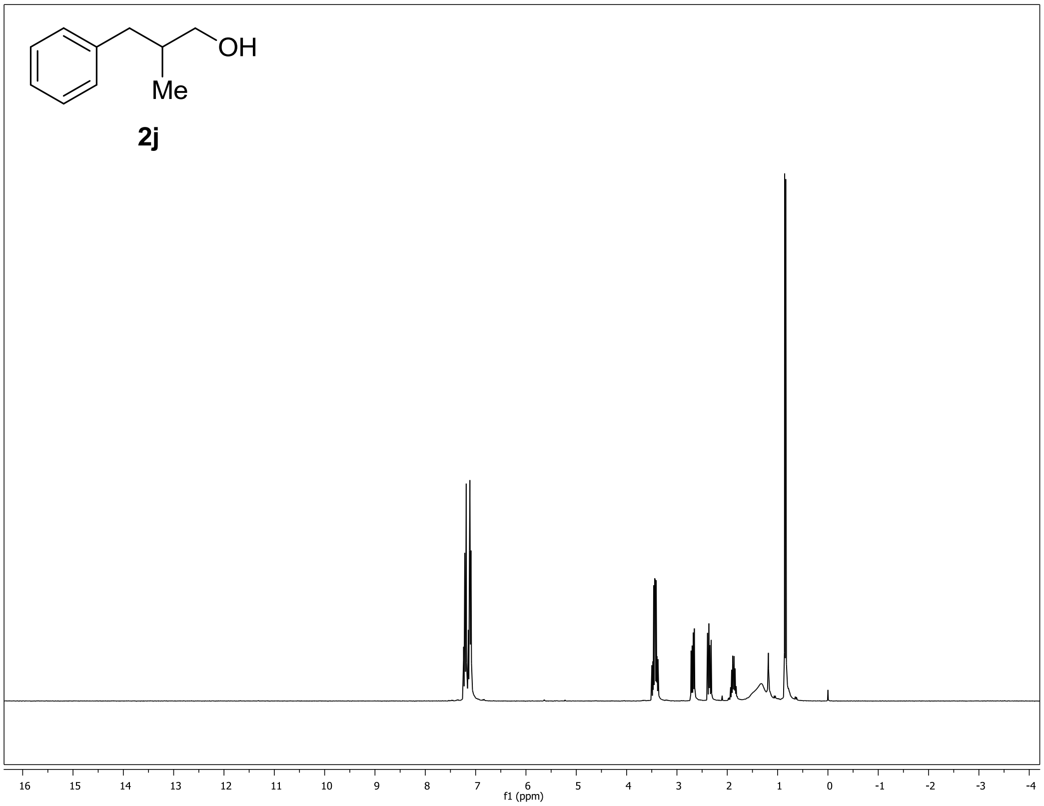

Me
Me
OH
Me
H
H
H
HO
H
OH
2h
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)


77.29
77.04
76.89
76.78
71.49
71.43
63.59
55.72
55.07
43.74
34.93
34.09
31.87
30.34
29.40
28.74
26.92
23.40
21.18
18.76
12.14
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

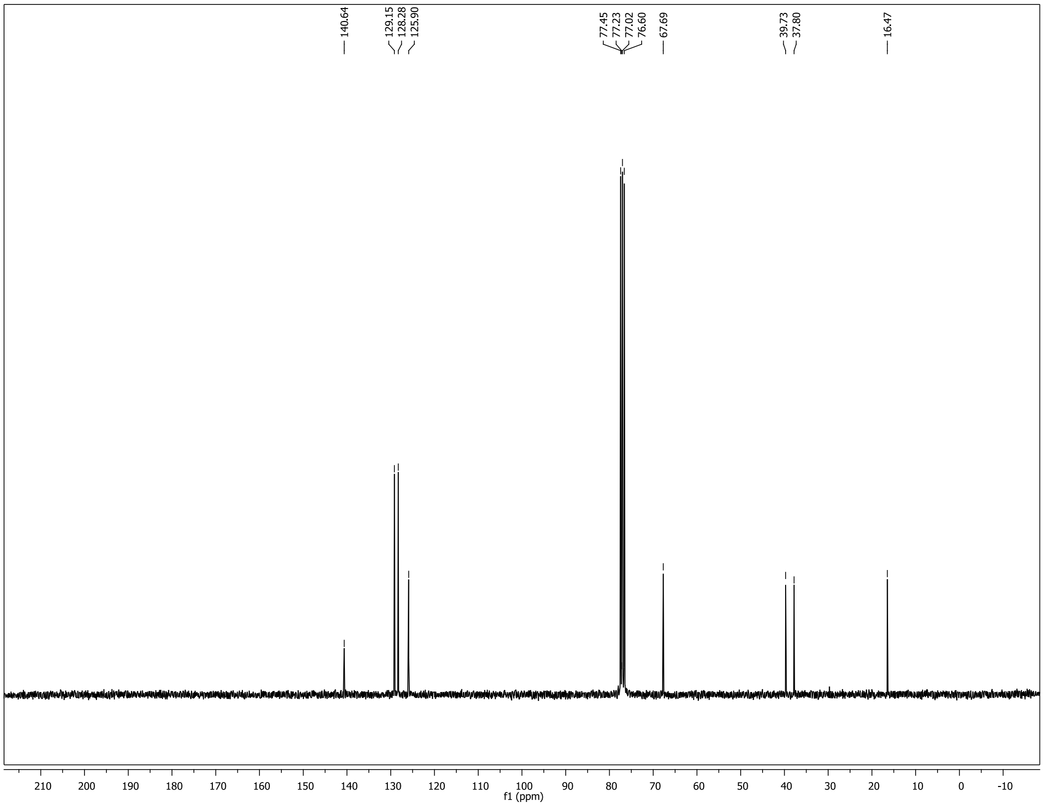

2i

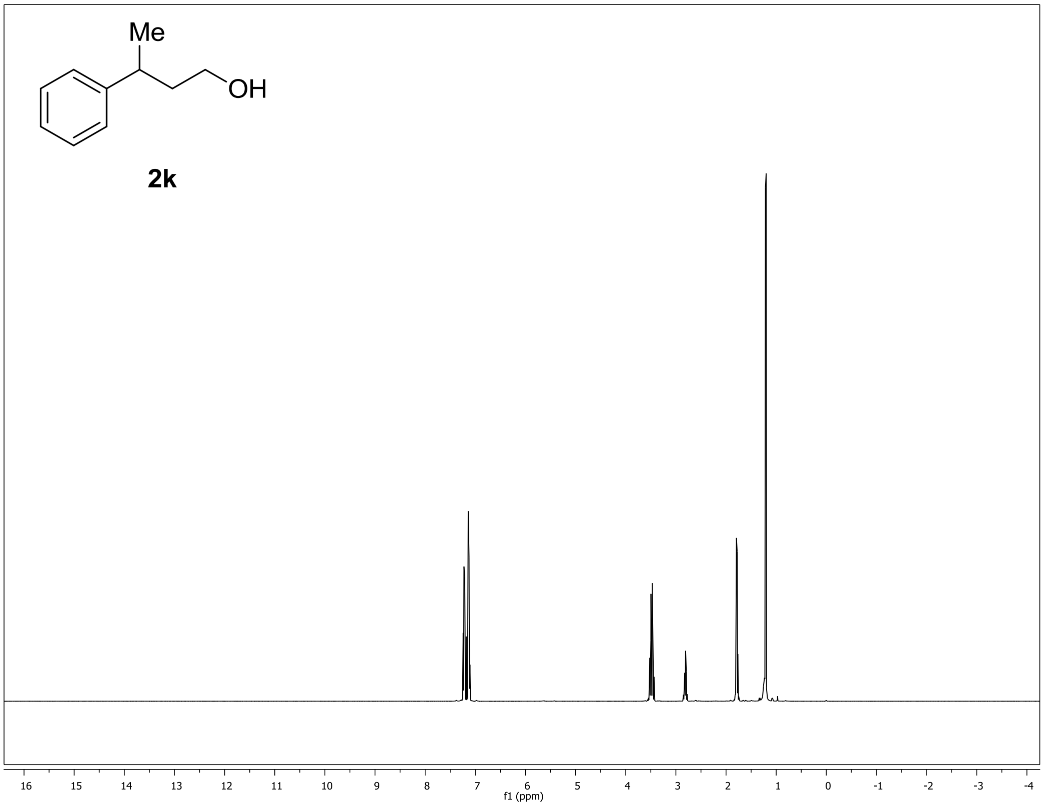
OH
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)

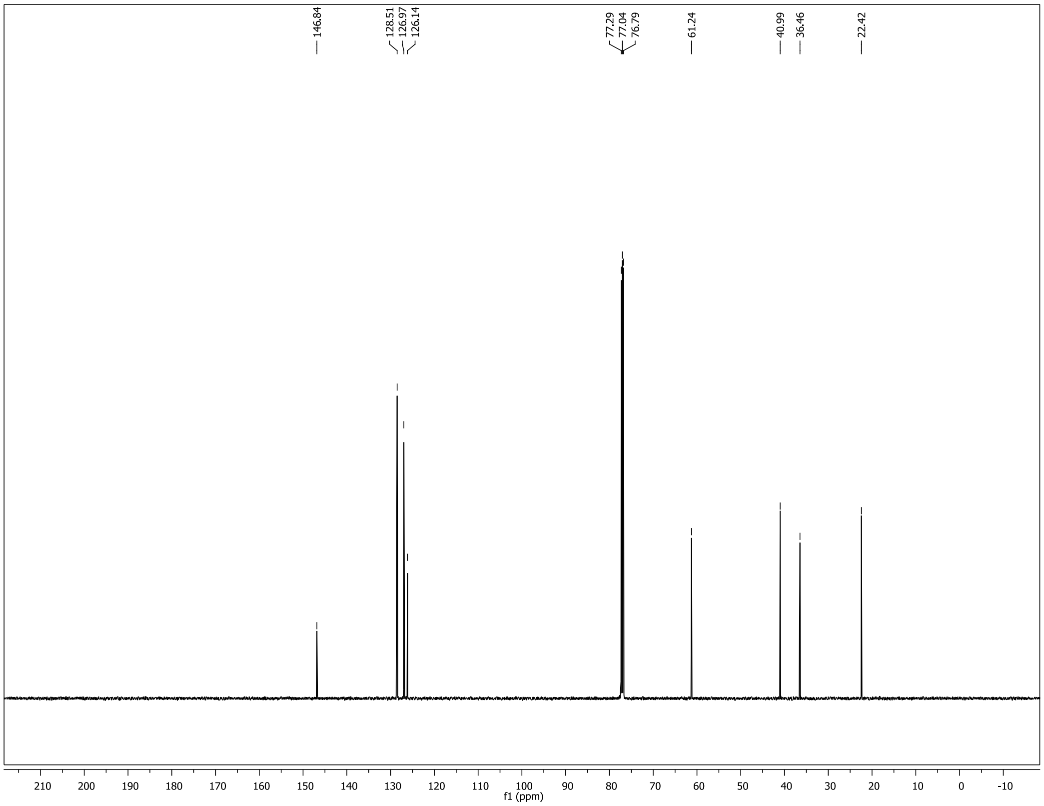

141.83
128.45
128.43
125.89
77.37
77.25
77.05
76.73
62.31
34.24
32.09
260
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
f1 (ppm)

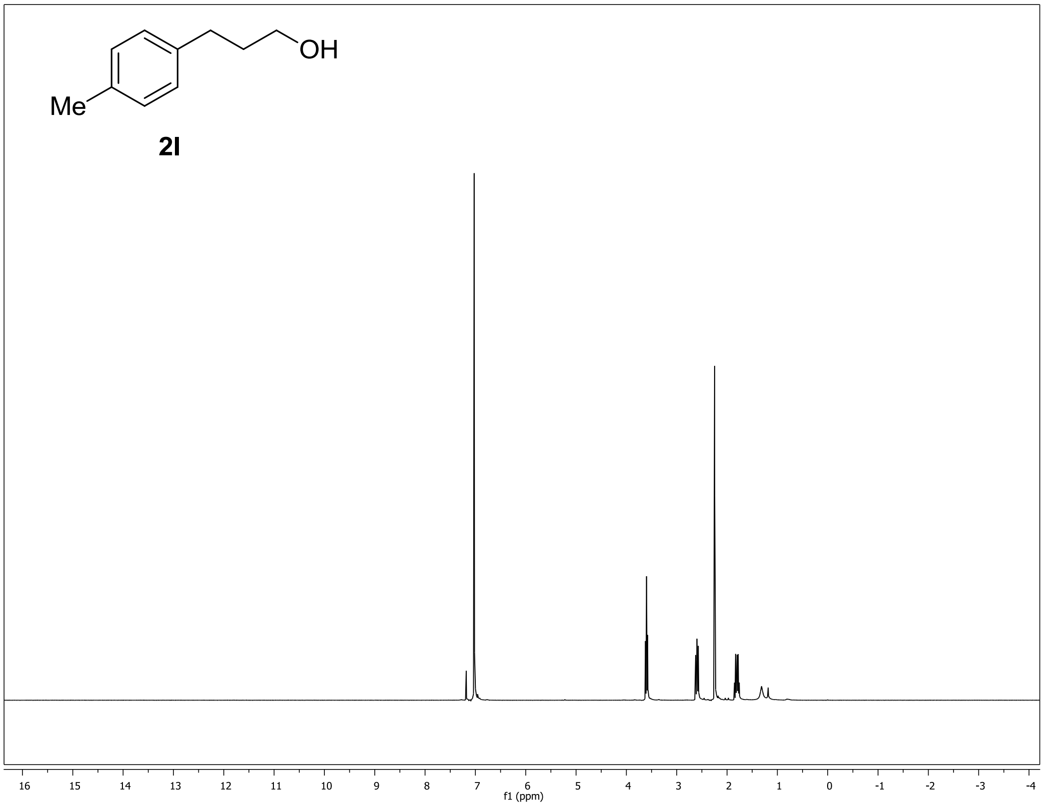

OH
Me
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)

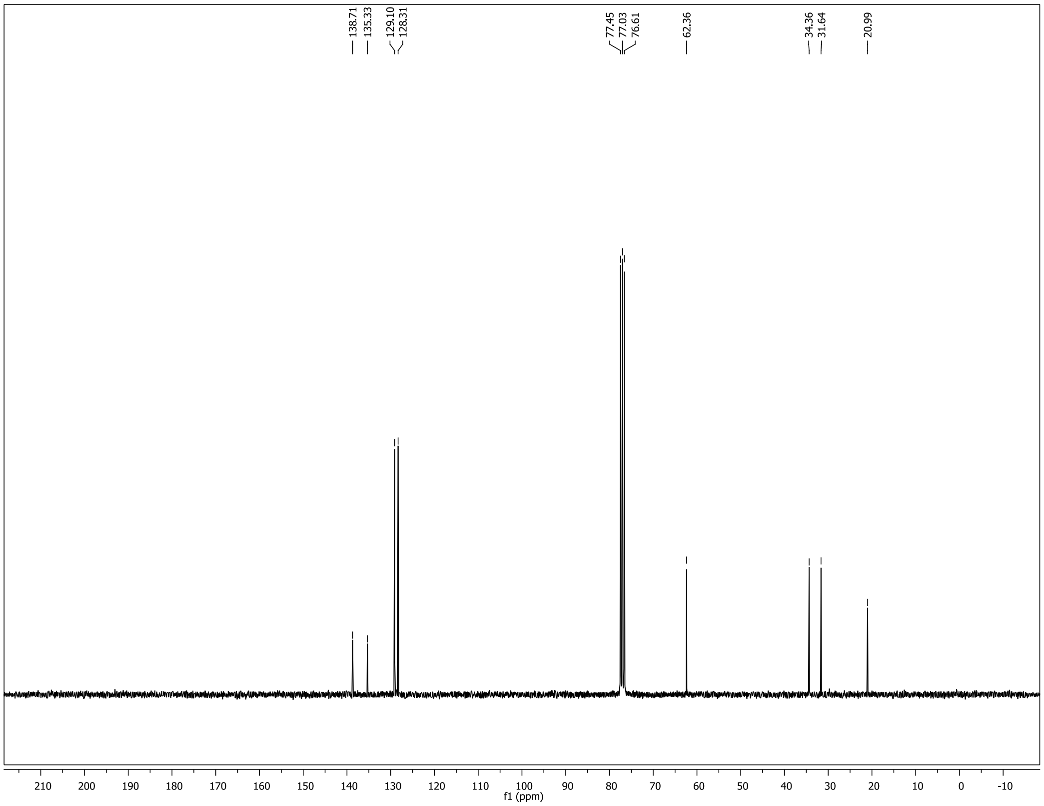
2j

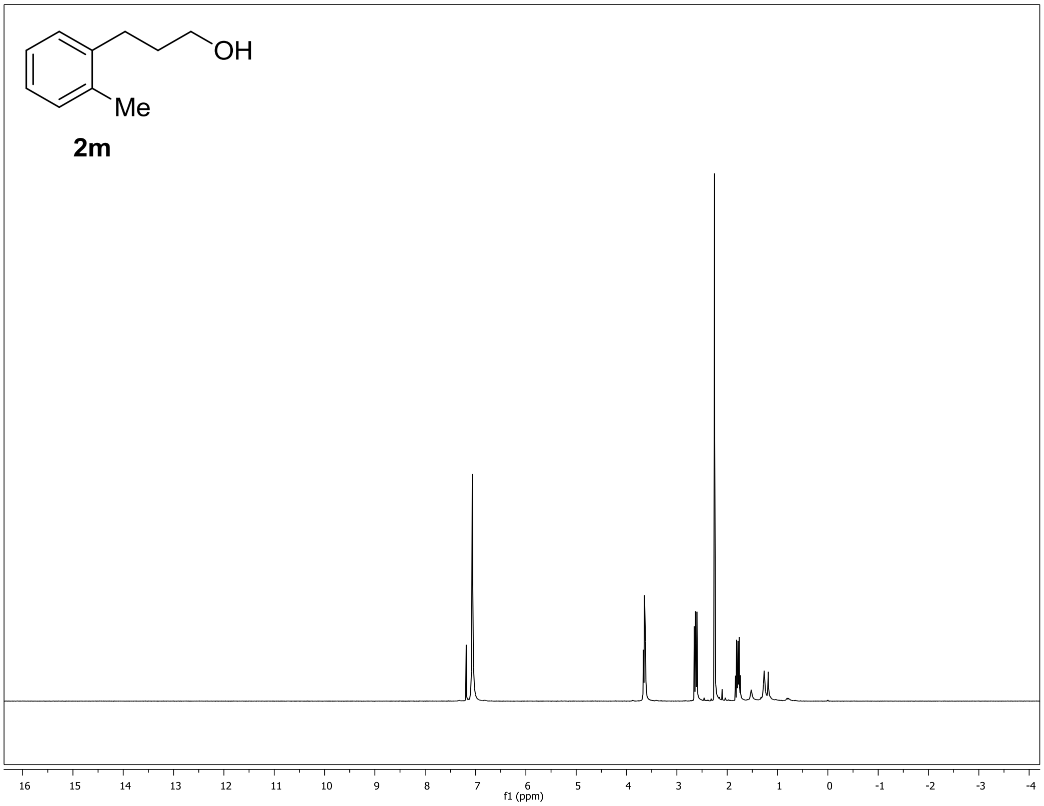

140.64
129.15
128.28
125.90
77.45
77.23
77.02
76.60
67.69
39.73
37.80
16.47
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Me
OH
2k
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)

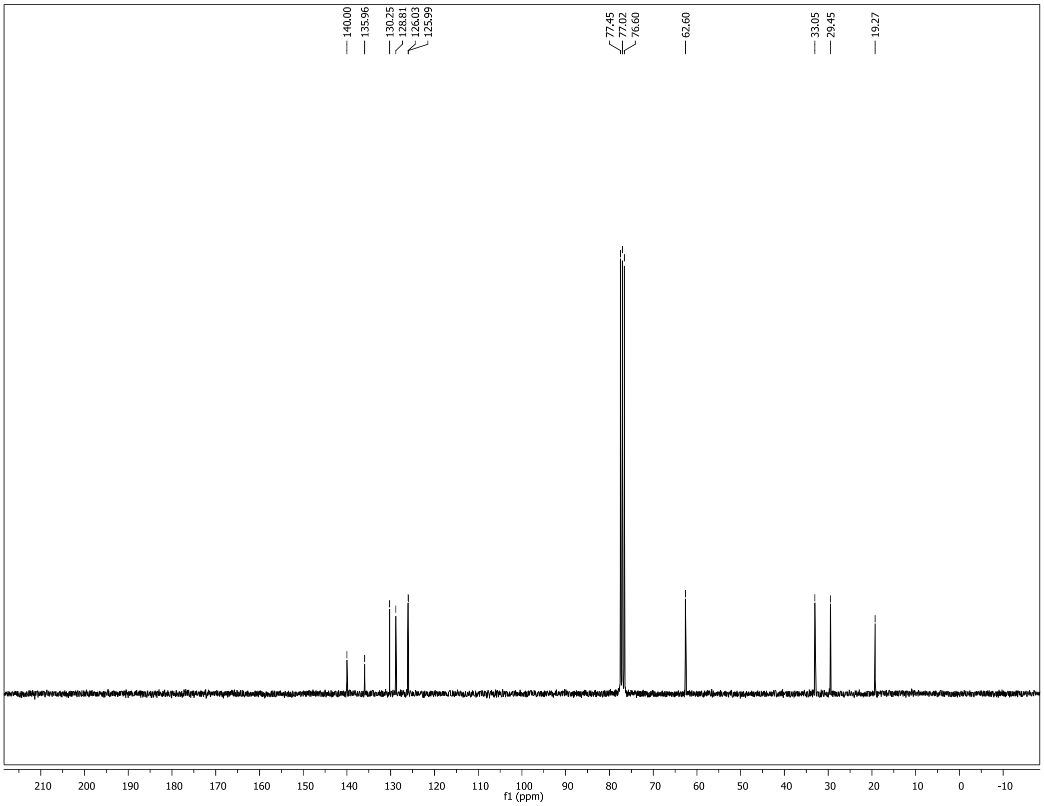

146.84
128.51
126.97
126.14
77.29
77.04
76.79
61.24
40.99
36.46
22.42
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

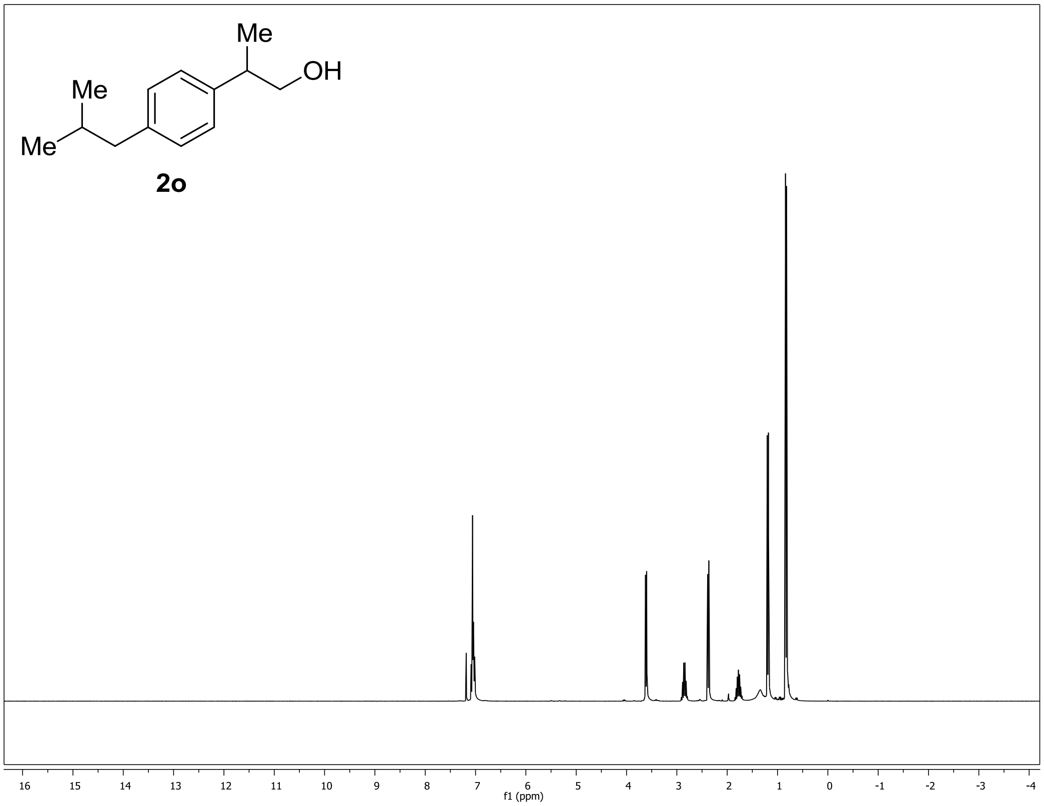

OH
Me
2l
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

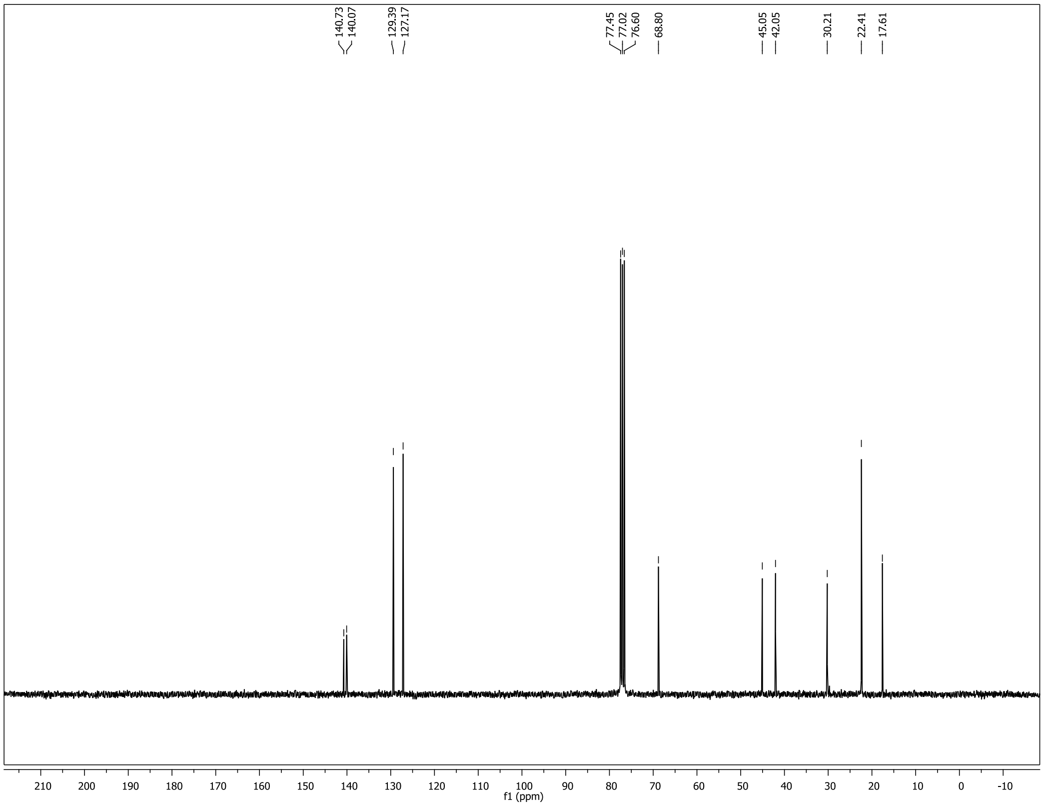

138.71
135.33
129.10
128.31
77.45
77.03
76.61
62.36
34.36
31.64
20.99
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

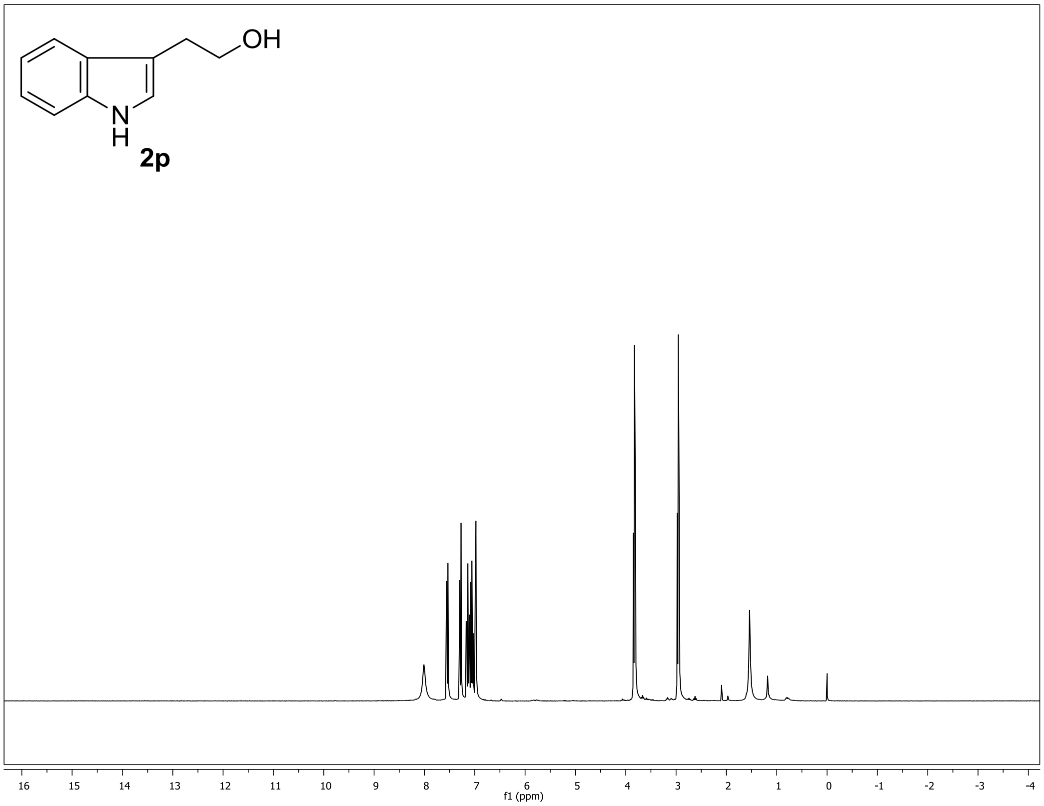

OH
Me
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)

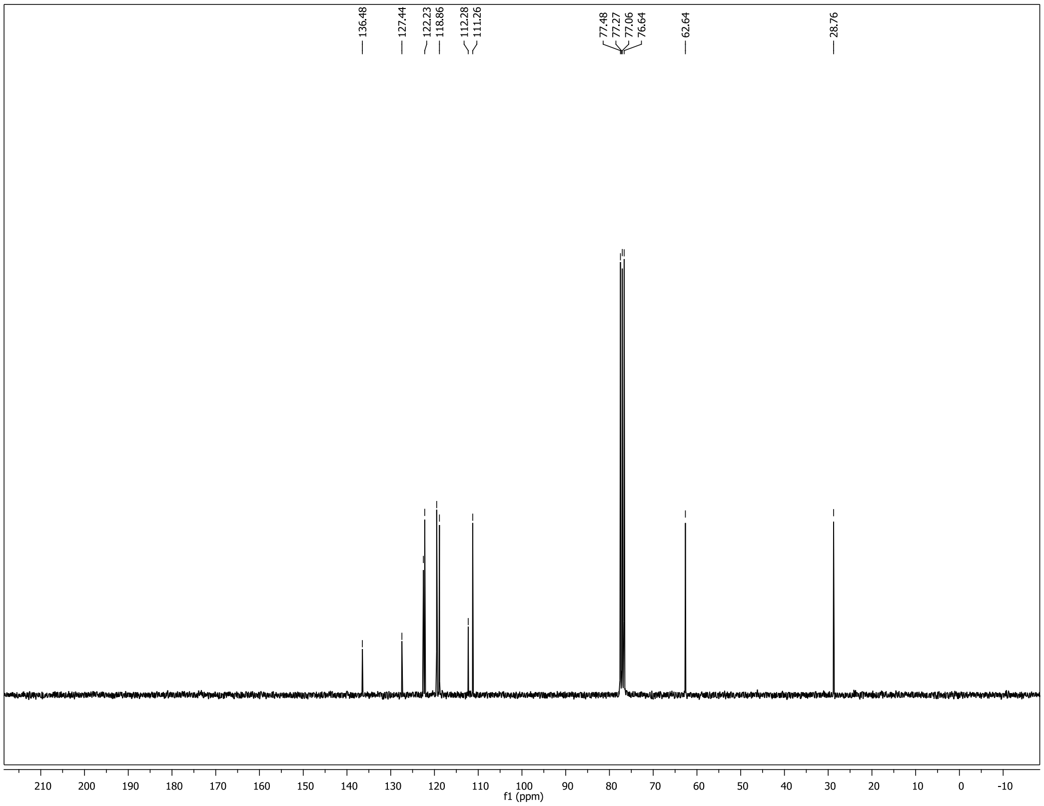
2m

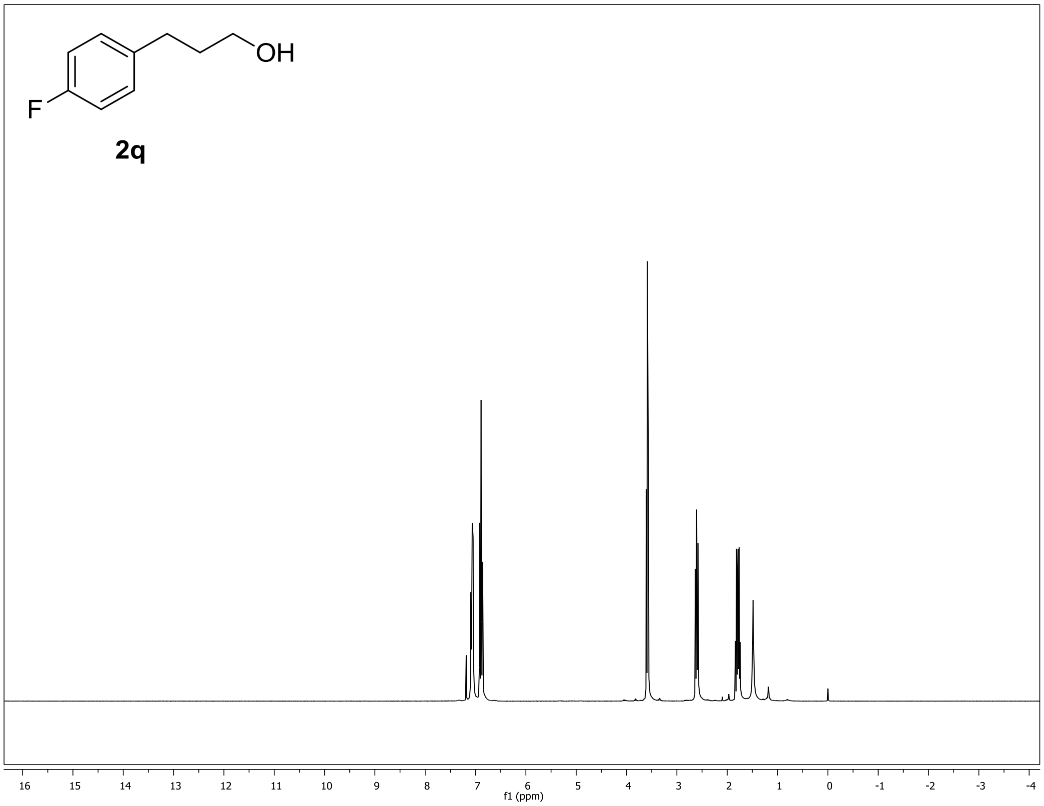

140.00
135.96
130.25
128.81
126.03
125.99
77.45
77.02
76.60
62.60
33.05
29.45
19.27
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Me
OH
Me
Me
2o
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)


140.73
140.07
129.39
127.17
77.45
77.02
76.60
68.80
45.05
42.05
30.21
22.41
17.61
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

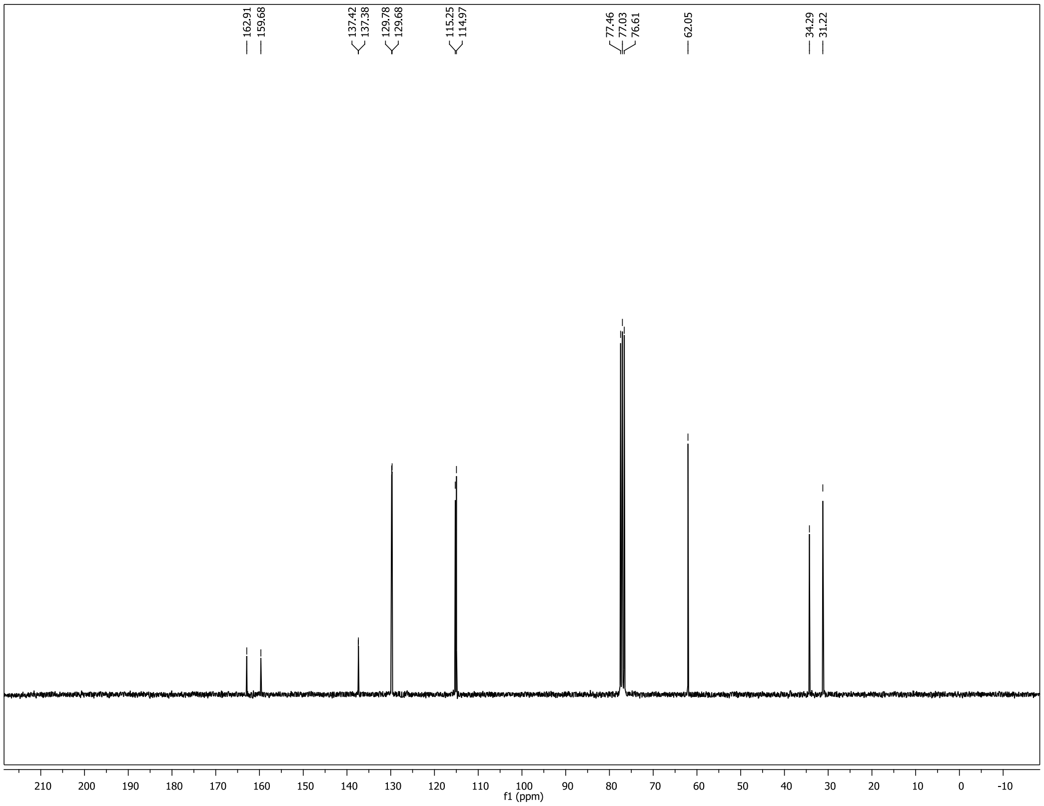

OH
N
H
2p
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


136.48
127.44
122.23
118.86
112.28
111.26
77.48
77.27
77.06
76.64
62.64
28.76
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

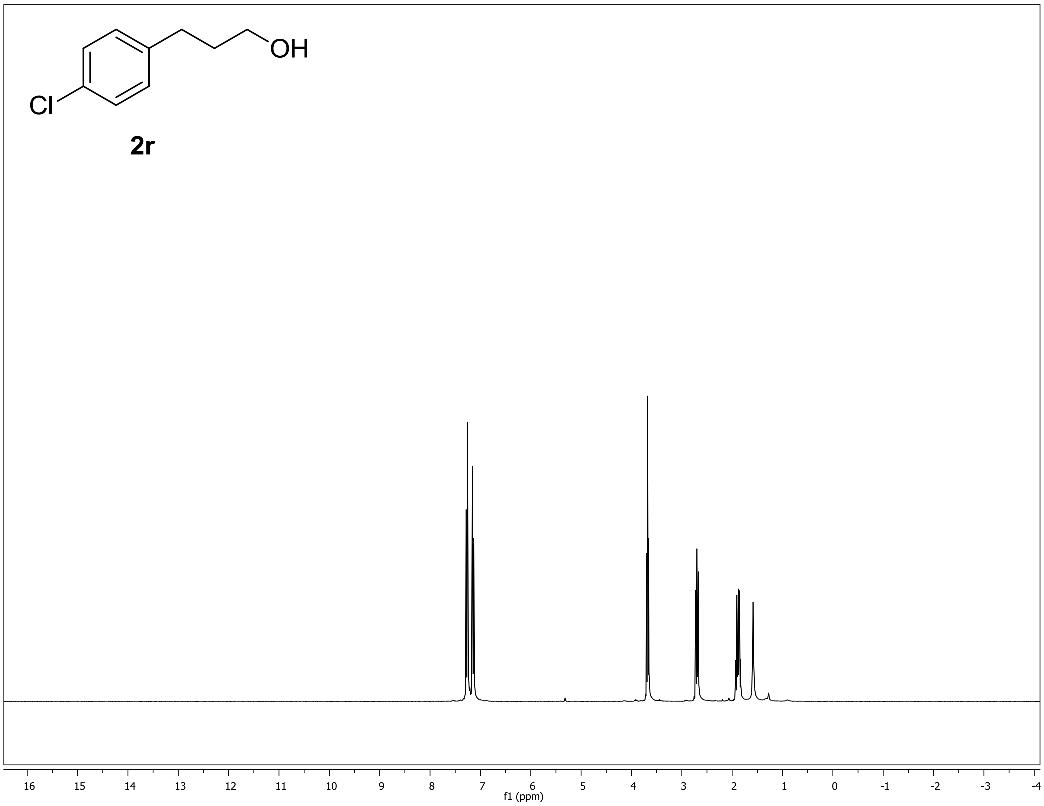


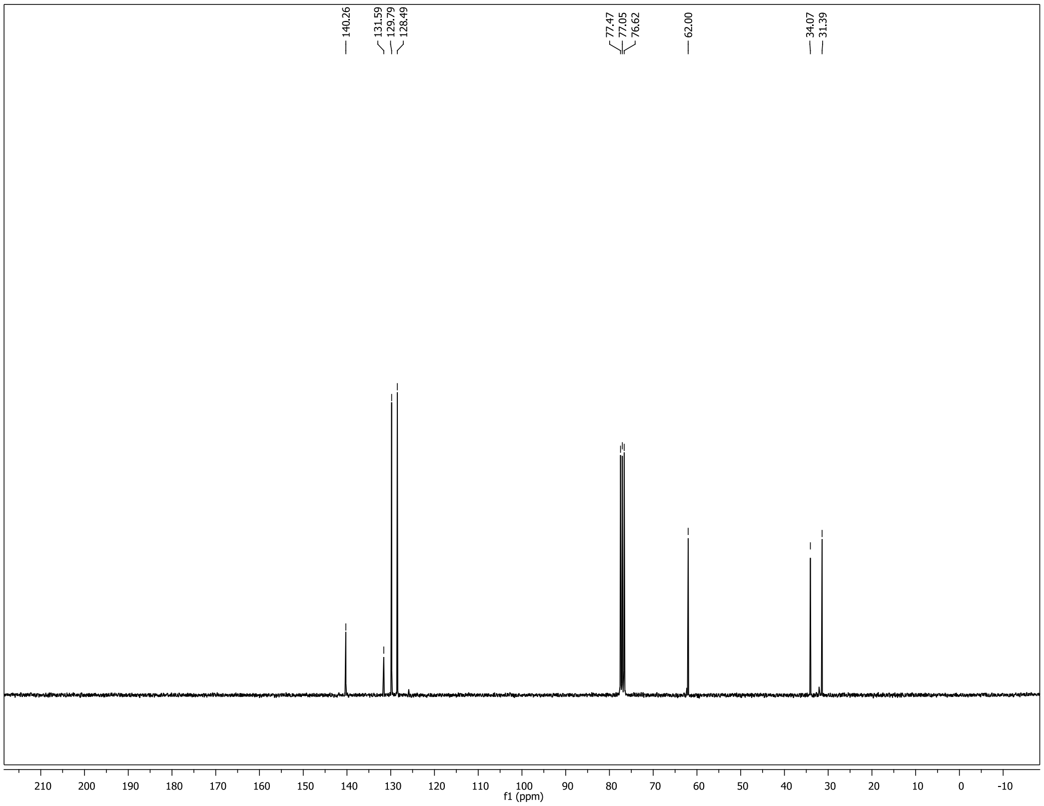
2q

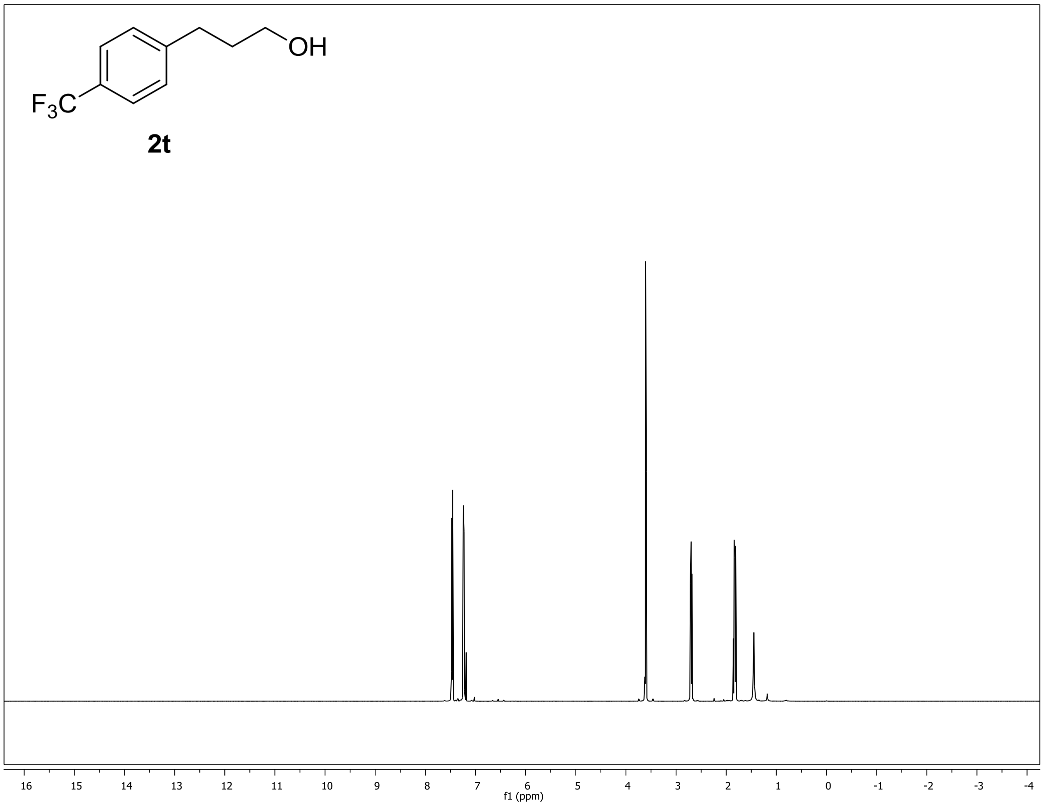
F
OH
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)



162.91
159.68
137.42
137.38
129.78
129.68
115.25
114.97
77.46
77.03
76.61
62.05
34.29
31.22
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

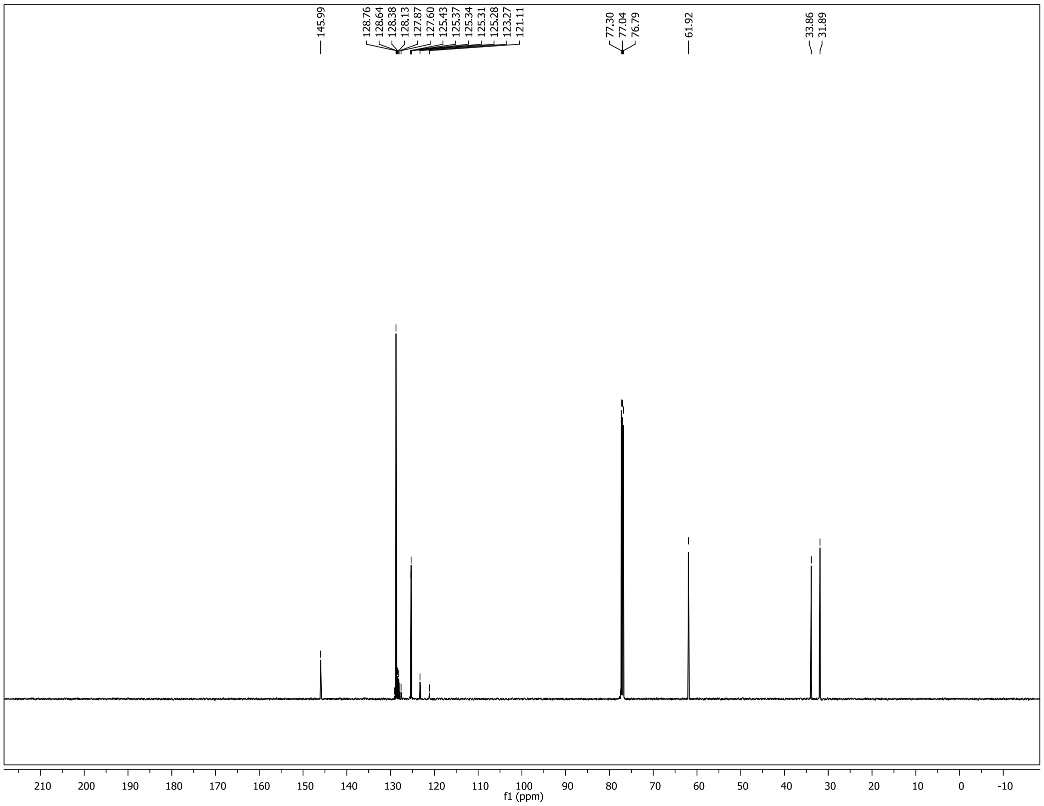

Cl
OH
2r
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)


140.26
131.59
129.79
128.49
77.47
77.05
76.62
62.00
34.07
31.39
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

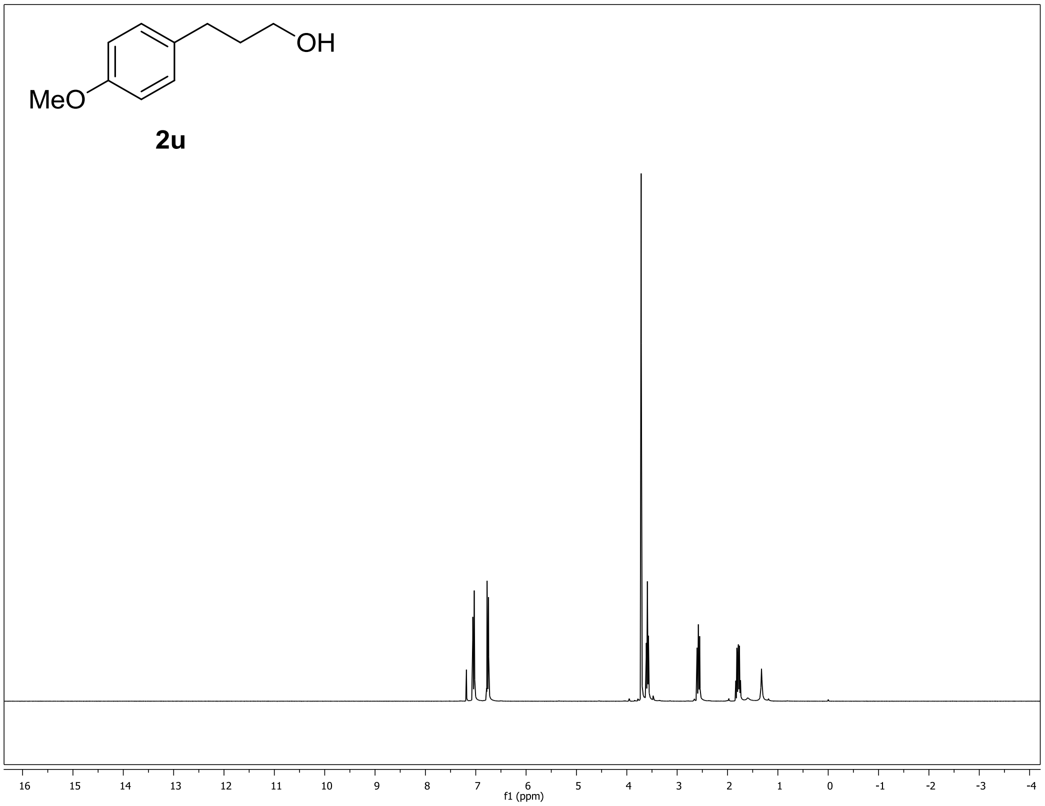


2t

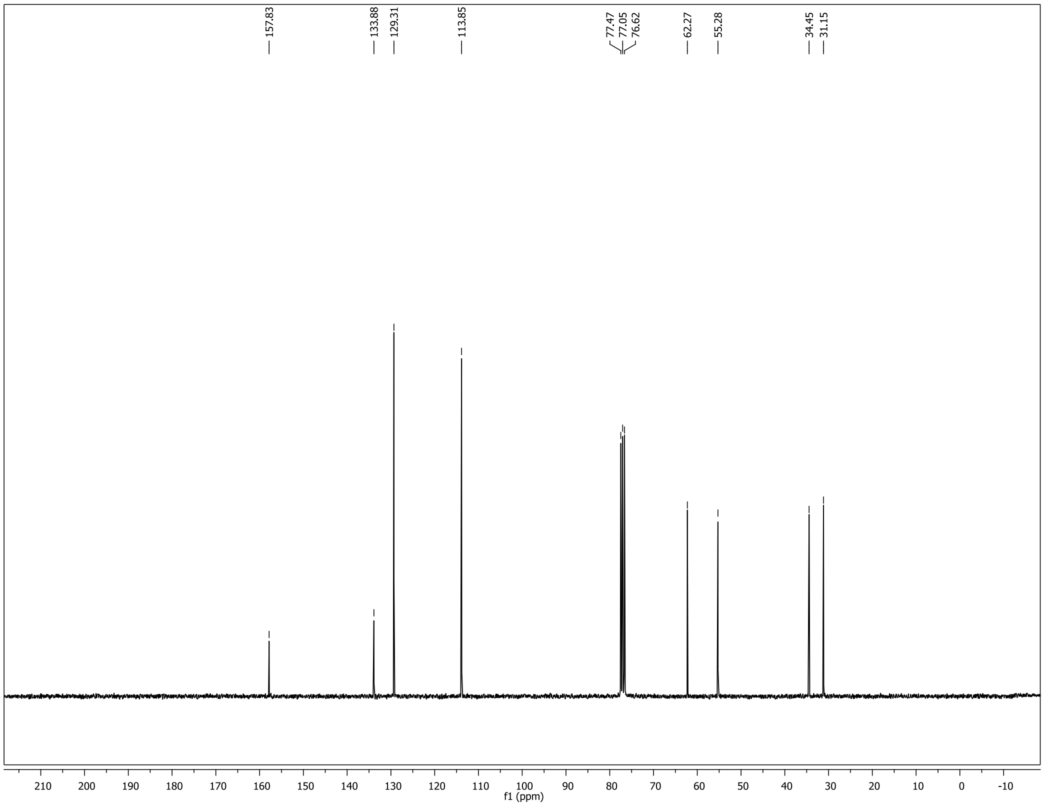
OH
F3C
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)

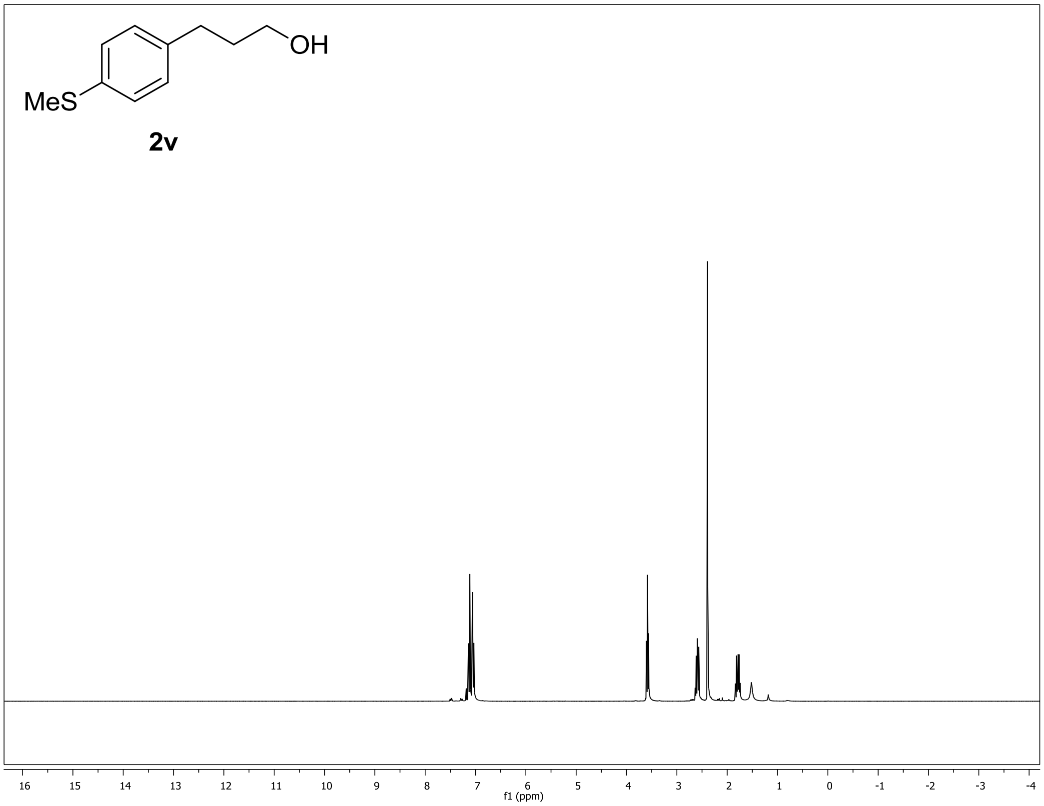


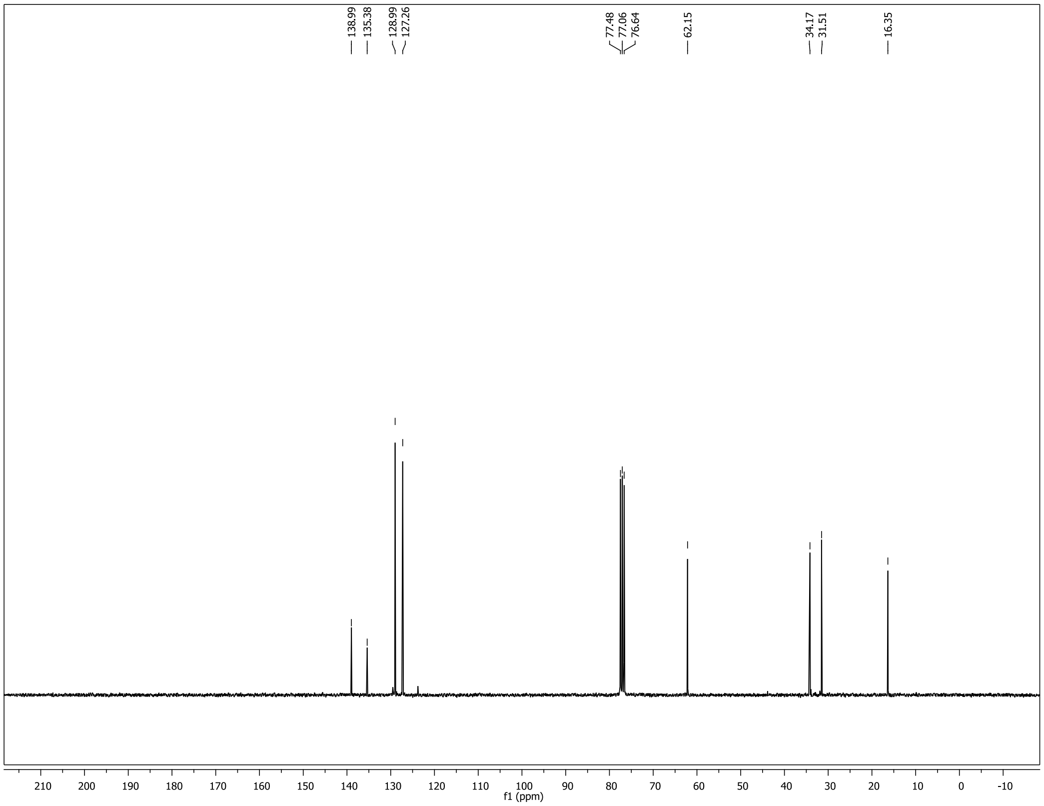
145.99
128.76
128.64
128.38
128.13
127.87
127.60
125.43
125.37
125.34
125.31
125.28
123.27
121.11
77.30
77.04
76.79
61.92
33.86
31.89
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


OH
MeO
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)

2u

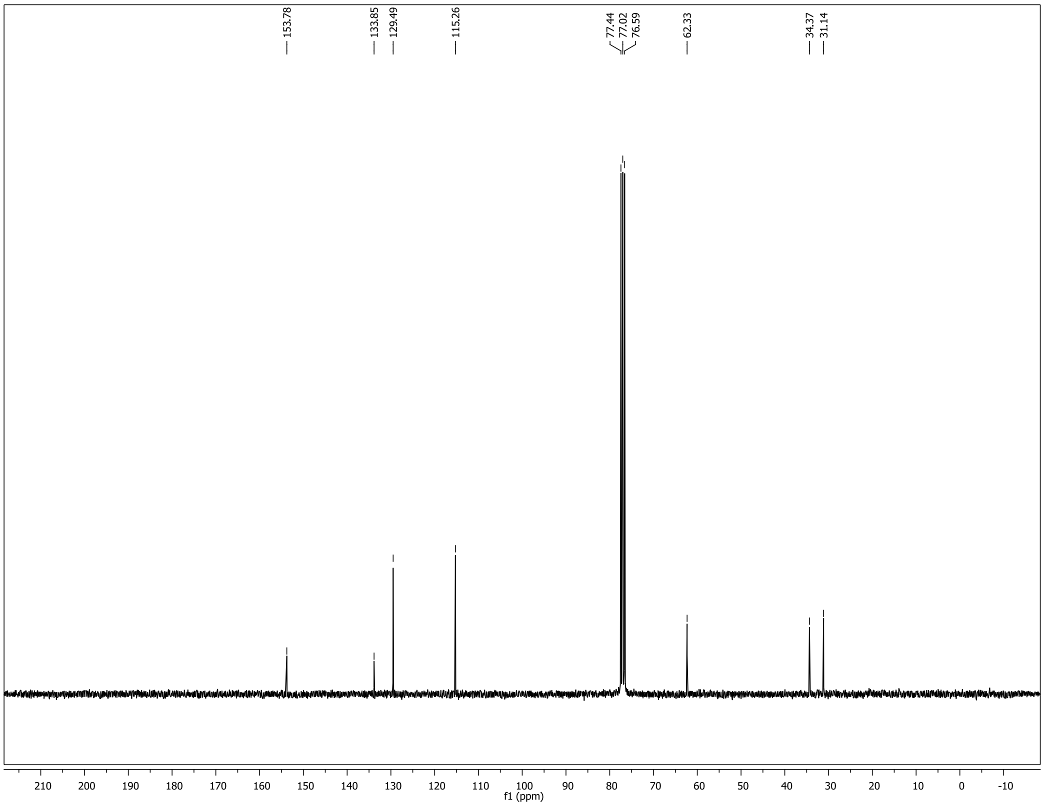

157.83
133.88
129.31
113.85
77.47
77.05
76.62
62.27
55.28
34.45
31.15
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

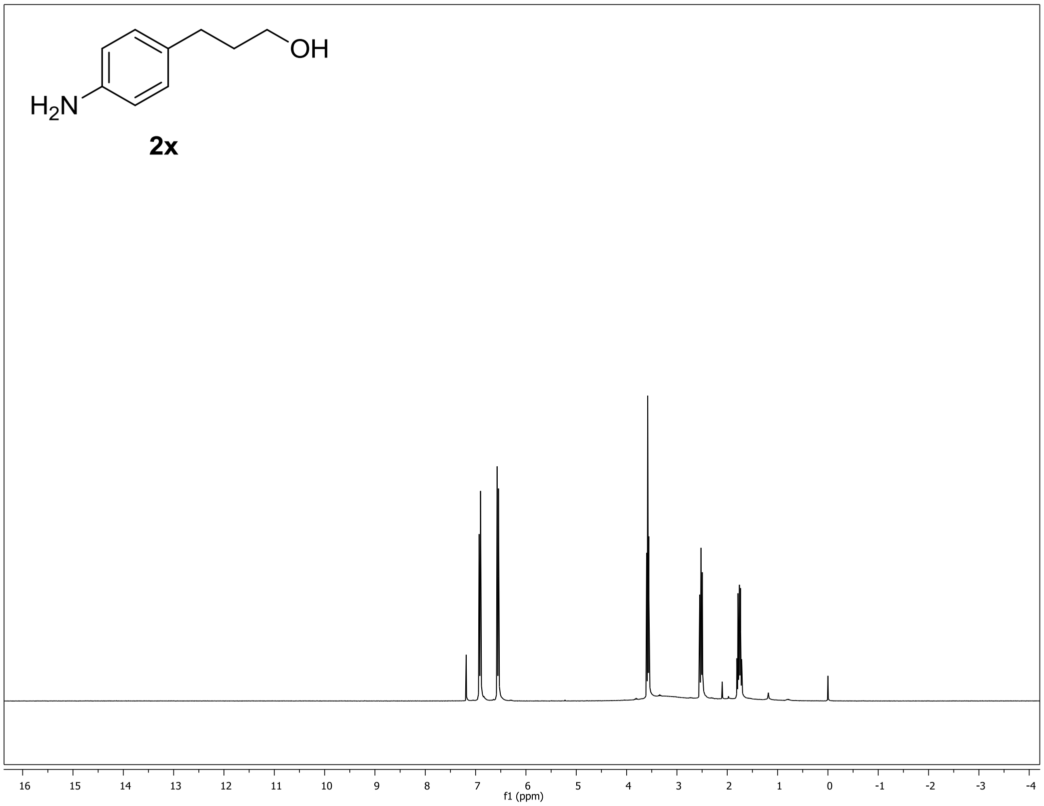

2v
MeS
OH
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)

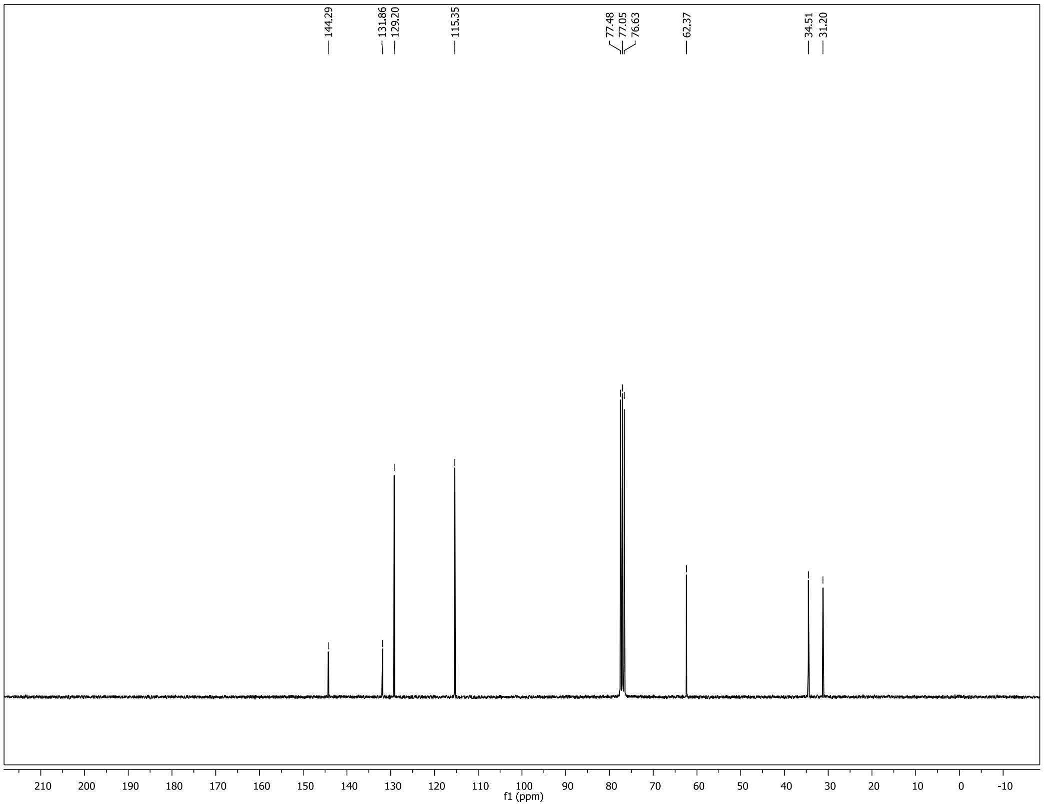

138.99
135.38
128.99
127.26
77.48
77.06
76.64
62.15
34.17
31.51
16.35
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


OH
HO
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)

2w


153.78
133.85
129.49
115.26
77.44
77.02
76.59
62.33
34.37
31.14
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


OH
H2N
2x
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)


144.29
131.86
129.20
115.35
77.48
77.05
76.63
62.37
34.51
31.20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)