Supplementary Information

For

Alkane Solvent-Derived Acylation Reaction Driven by Electric Fields

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1 REACTION CONDITIONS

1.1 SAMPLE PREPARATION

1.1.1 General experimental considerations

Unless otherwise specified, all commercial chemicals were used as supplied without additional purification. New compounds were synthesized as described in Section 3. All sample preparations were conducted under ambient conditions.

1.1.2 General reaction solution preparation

To prepare solutions: reagents with a desired final concentration of less than 10 mM in the reaction solution were first made as a separate solution of 100x concentration and added to the reaction mixture with serial dilution; reagents with a desired final concentration of more than 10 mM in the reaction solution were added directly. Following the addition of all reagents, the reaction mixture was topped up to the desired volume (1 mL) in a volumetric flask.

1.2 STM-BJ SETUP

STM-BJ measurements were made using a custom-built scanning tunneling microscope.[1] The electric field was applied between a 0.25 mm gold wire (99.998%, Alfa Aesar) as a gold STM-tip and a gold-coated (99.999%, Alfa Aesar) steel puck as a gold substrate, while the strength of the field was modulated either by changing the bias applied or the distance between tip and substrate.[2] Conductance measurements were performed in dilute solutions (1 mM) of reaction mixtures in different solvents as indicated in the main text. In polar solvents, the insulated tips were created by driving a mechanically cut gold tip through Apiezon wax. A commercially available z-axis piezoelectric positioner (P-840.10, PI) was used to drive the tip in and out of contact with the substrate at a speed of 20 nm/s in a dilute solution of the target molecule under ambient conditions. The junction current (I) was recorded as a function of tip-substrate displacement at a fixed applied bias voltage (with a 100 kΩ resistor in series). The current, voltage across the junction, and electrode position data are all collected at a 40 kHz acquisition rate using custom Igor Pro (Wavemetric, Inc.). All the measurements are performed using fresh solutions, without any exposure to light, and in a dark acoustic box.

2 REACTION ANALYSIS

2.1 STM-BJ CONDUCTANCE

Conductance ($G=I/V$) was determined as a function of displacement and analyzed further using one-dimensional (1D) conductance and two-dimensional (2D) conductance-displacement histograms. A gold point-contact is first formed with a conductance close to 1 G_0 (= $2e^2/h$, conductance quantum) and then followed by a molecular conductance plateau below 1 G_0. The measured conductance traces were then collected and compiled into logarithmically binned 1D histograms (100/decade), and 2D histograms along the conductance axis (100/decade) and linear bins (1000/nm) along the displacement axis without data selection. Authentic standards of the +6, 9, and 10 C products (**2a, 2b, 2c**) were synthesized as described in SI section 3.3.

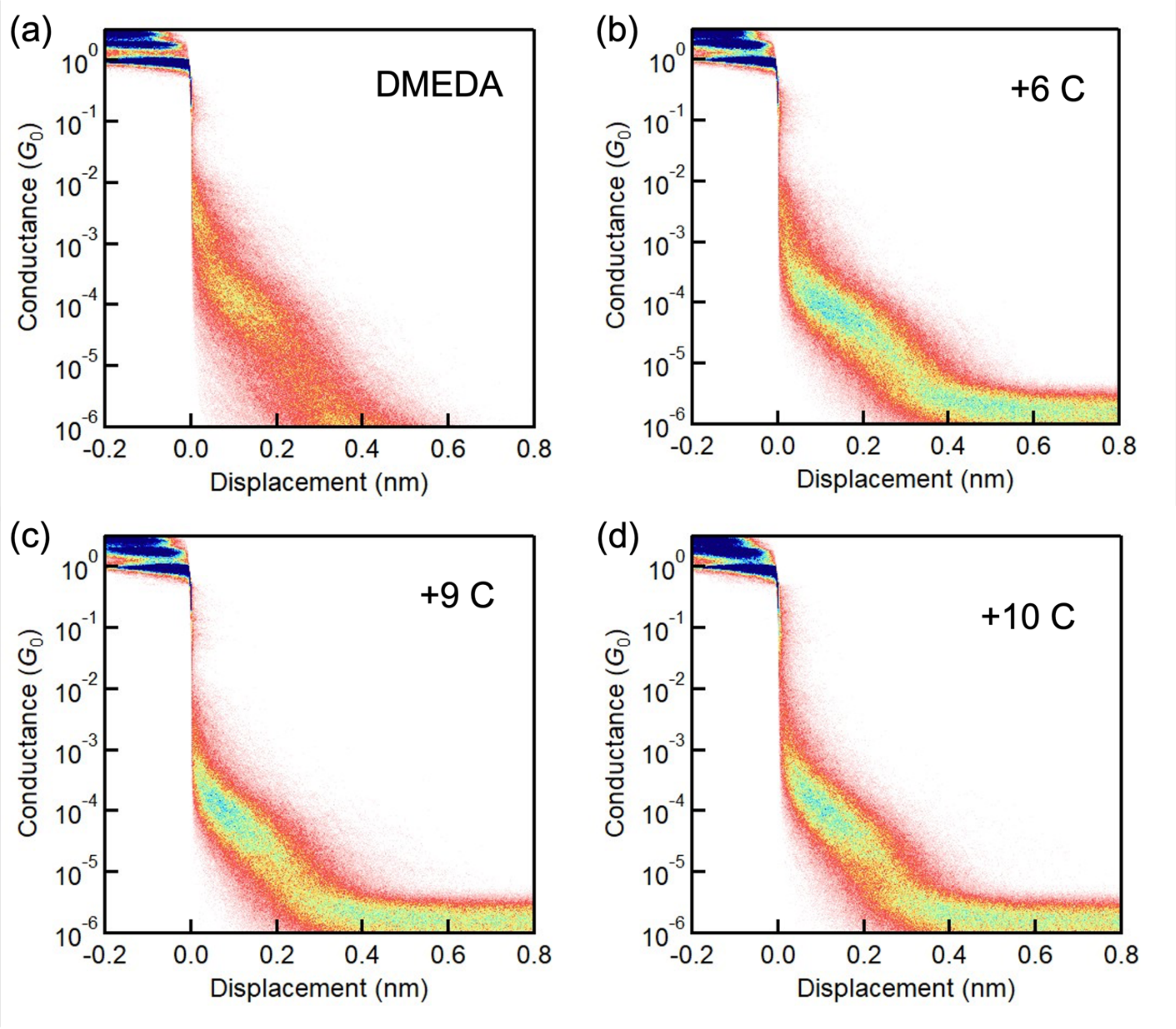


Figure 2-1 Logarithm-binned 2D conductance-displacement histograms of conductance traces measured with ***DMEDA*** *and ex-situ synthesized products, compiled from thousands of measured traces without data selection. All measurements were performed using ~1 mM in tetradecane at room temperature.*

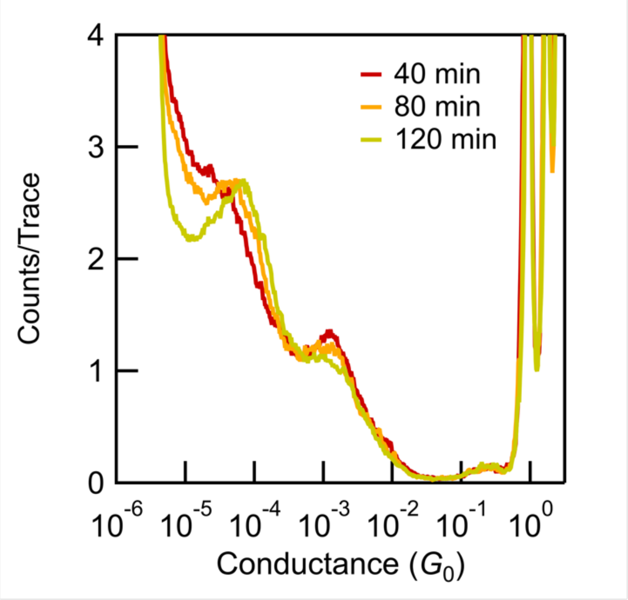


Figure 2-2 Logarithm-binned 1D conductance-displacement histograms of conductance traces measured with DMEDA over time, compiled from thousands of measured traces without data selection. All measurements were performed using 1 mM in tetradecane at room temperature.

2.2 GOLD-ONLY SCALE-UP EXPERIMENT

2.2.1 Au substrate synthesis

To fabricate the scale-up Au substrate, we first used degenerately doped silicon wafer with a 285 nm thermal silicon oxide layer as the bottom substrate. Next, we coated the bottom substrate with gold (99.999%, Alfa Aesar) as the scale up Au substrate.

2.2.2 Isolation and purification procedure

1 mL of 1 mM DMEDA in TD was placed on the large Au substrate, and removed after 24 h. An additional 1 mL 1 mM DMEDA in TD was added and allowed to react on Au for 24 h and removed until 10 mL of combined product mixture was collected. The reaction was extracted with 1 M aqueous HCl (3 x 10 mL), and the combined aqueous layer was washed with hexanes (10 mL) to remove organics, and concentrated *in vacuo* to afford a mixture of products as their HCl salts.

2.2.3 Preparative HPLC-MS analysis

The combined product HCl salts were resuspended in 1 mL H_2O and purified using preparative HPLC-MS: 10-90% MeCN in H_2O with 0.1 % formic acid over 12 min, 100 uL injection volume, XBridge Prep C18 5 µm OBD 19x100 mm column, 20 mL/min flow rate, with Waters 3100 mass detector in ES+ mode. Fractions with $[C_4H_{13}N_2+CO+(CH_2)_{4-11}]^+$, corresponding to $[DMEDA+CO+(CH_2)_{4-11}+H]^+$, or +5-12 C products were collected.

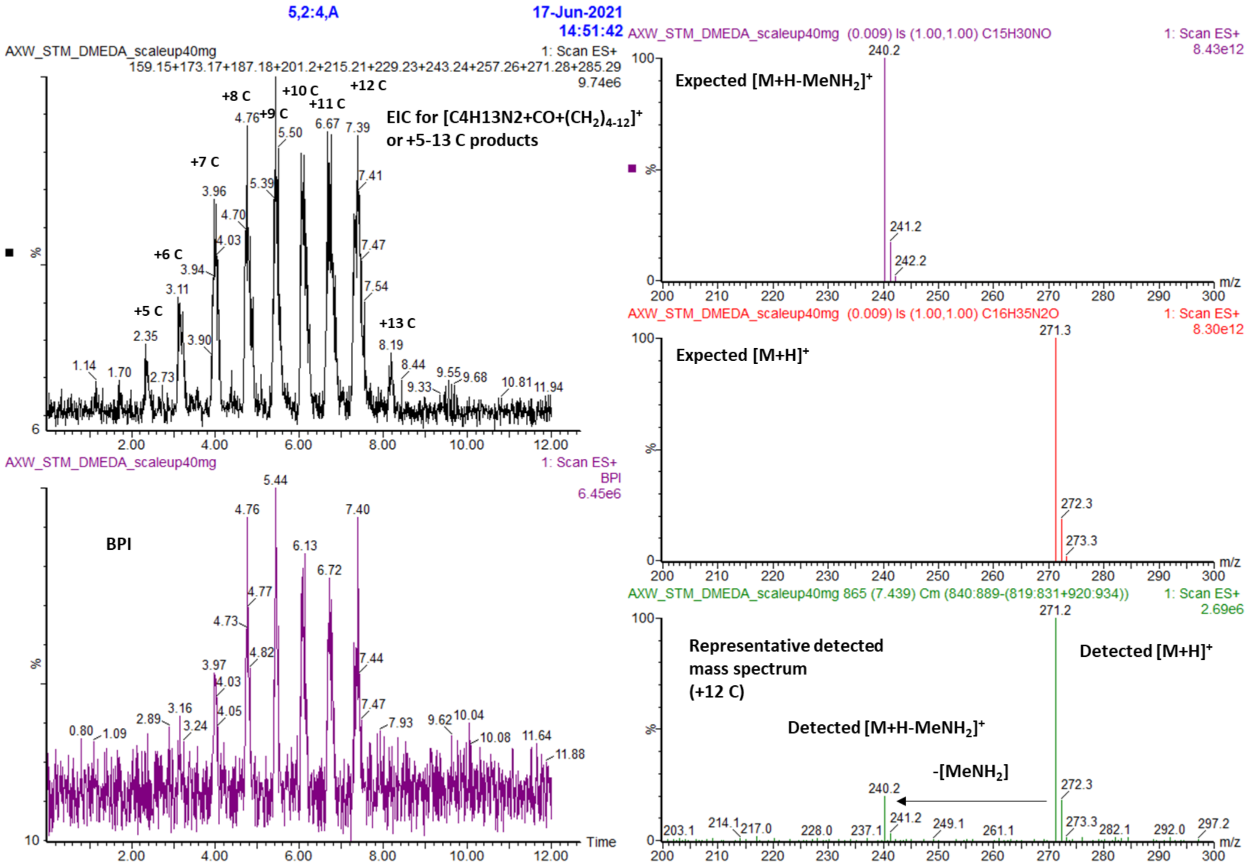

5,2:4,A
17-Jun-2021
14:51:42
AXW_STM_DMEDA_scaleup40mg
1: Scan ES+
159.15+173.17+187.18+201.2+215.21+229.23+243.24+257.26+271.28+285.29
9.74e6
EIC for [C4H13N2+CO+(CH2)4-12]+
or +5-13 C products
+5 C
+6 C
+7 C
+8 C
+9 C
+10 C
+11 C
+12 C
+13 C
1.14
1.70
2.35
2.73
3.11
3.90
3.94
3.96
4.03
4.70
4.76
5.39
5.50
6.67
7.39
7.41
7.47
7.54
8.19
8.44
9.33
9.55
9.68
10.81
11.94
%
6
2.00
4.00
6.00
8.00
10.00
12.00
AXW_STM_DMEDA_scaleup40mg
1: Scan ES+
BPI
6.45e6
BPI
0.80
1.09
2.89
3.16
3.24
3.97
4.03
4.05
4.73
4.76
4.77
4.82
5.44
6.13
6.72
7.40
7.44
7.47
7.93
9.62
10.04
10.08
11.64
11.88
10
Time
AXW_STM_DMEDA_scaleup40mg (0.009) Is (1.00,1.00) C15H30NO
1: Scan ES+
8.43e12
Expected [M+H-MeNH2]+
240.2
241.2
242.2
AXW_STM_DMEDA_scaleup40mg (0.009) Is (1.00,1.00) C16H35N2O
1: Scan ES+
8.30e12
Expected [M+H]+
271.3
272.3
273.3
AXW_STM_DMEDA_scaleup40mg 865 (7.439) Cm (840:889-(819:831+920:934))
1: Scan ES+
2.69e6
Representative detected
mass spectrum
(+12 C)
Detected [M+H]+
Detected [M+H-MeNH2]+
-[MeNH2]
271.2
240.2
241.2
272.3
273.3
203.1
214.1
217.0
228.0
237.1
249.1
261.1
282.1
292.0
297.2
100
0
m/z
200
210
220
230
240
250
260
270
280
290
300

Figure 2-3

2.3 NMR ANALYSIS

Although preparative HPLC (section 2.2.3) did not isolate products of sufficient quantity and analytical purity for characterization purposes, structural assignments could be achieved from ^{1}H NMR, COSY, HSQC, and HRMS data.

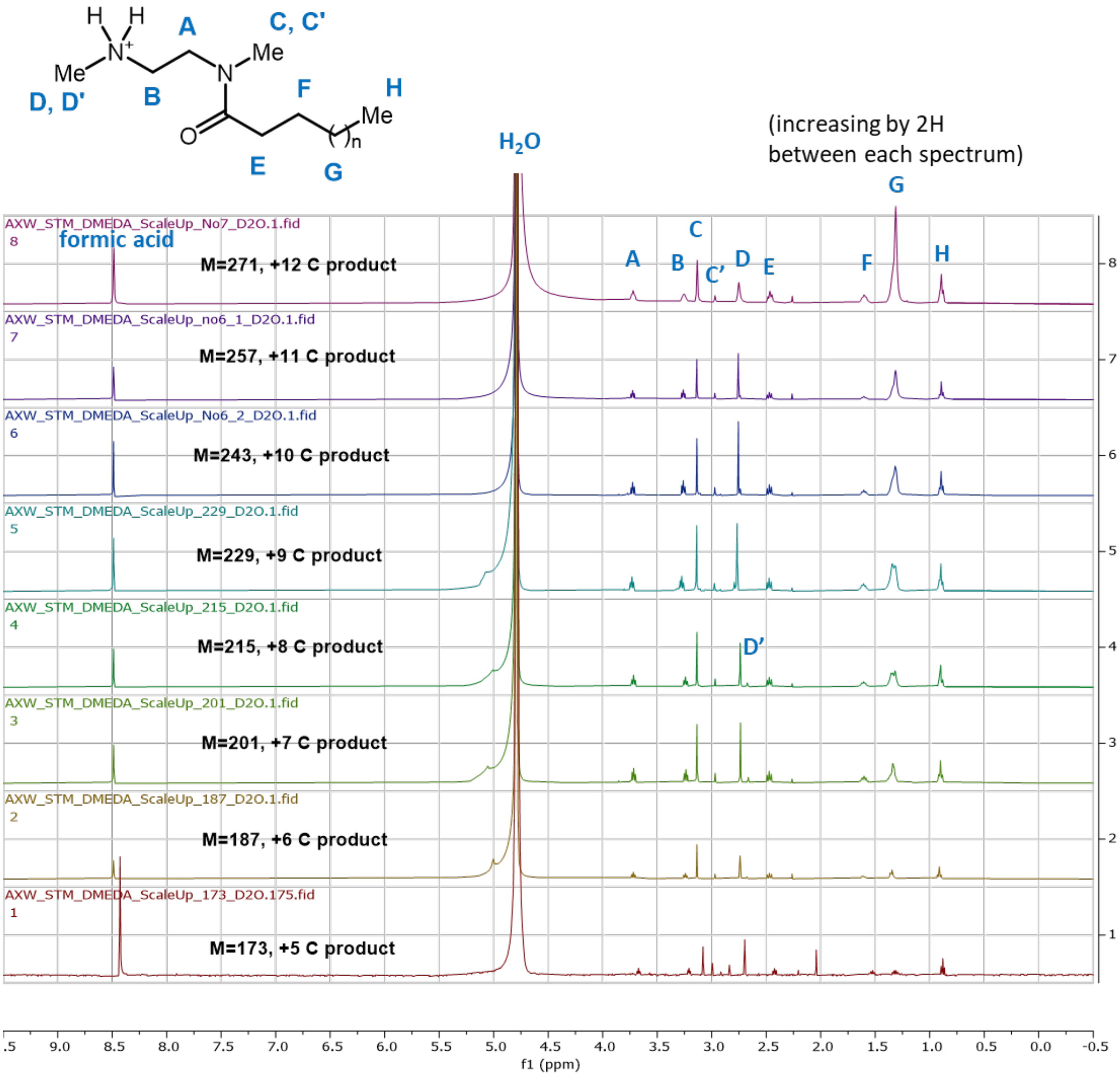
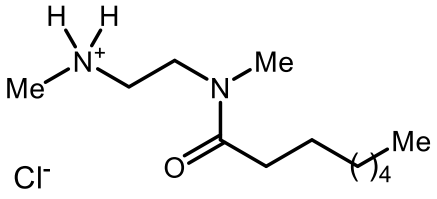


Figure 2-4

Representative product compound +8 C:



2g

N-methyl-2-(N-methyloctanamido)ethan-1-aminium chloride (2g), mixture of rotamers (A:B=4.5:1) in D_2O. ^{1}**H NMR** (400 MHz, D_2O) δ 3.72 (t, *J* = 6.0 Hz, 2H), 3.24 (t, *J* = 5.9 Hz, 2H), 3.14 (rotamer A, s, 3H), 2.97 (rotamer B, s, 3H), 2.74 (rotamer A, s, 3H), 2.67 (rotamer B, s, 3H), 2.54 – 2.39 (m, 2H), 1.69 – 1.55 (m, 2H), 1.45 – 1.27 (m, 8H), 0.98 – 0.84 (m, 3H).

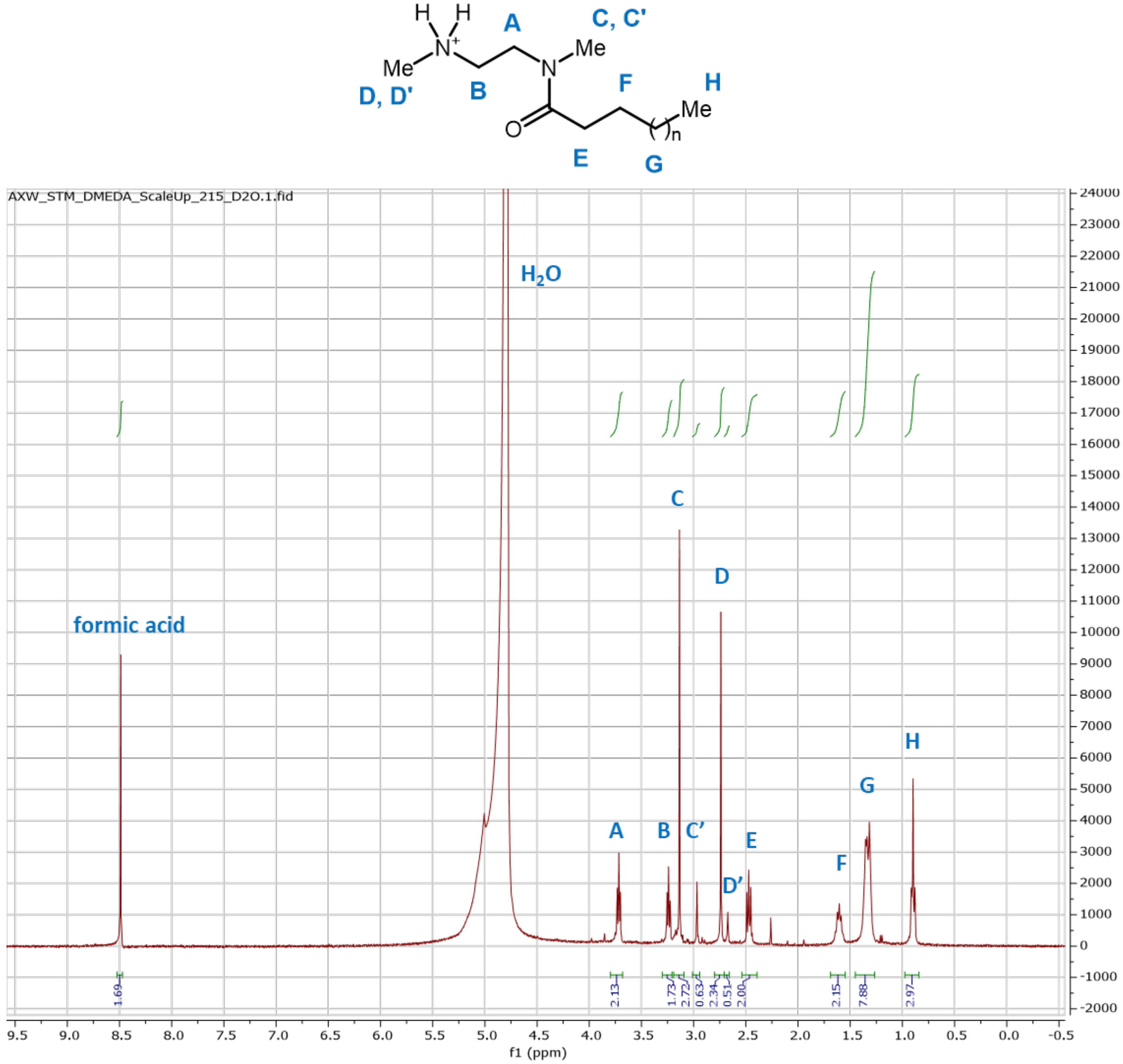


Figure 2-5

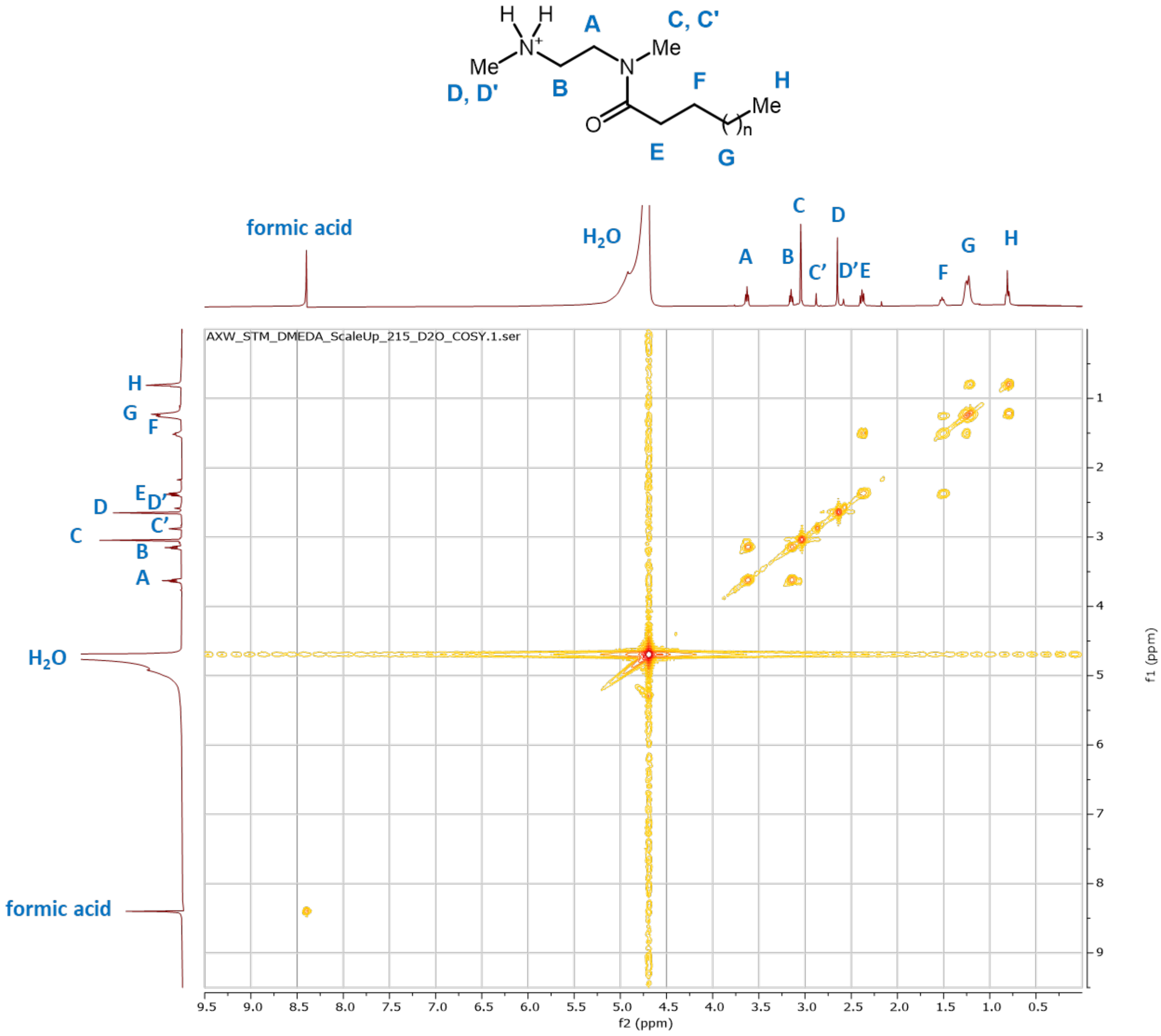
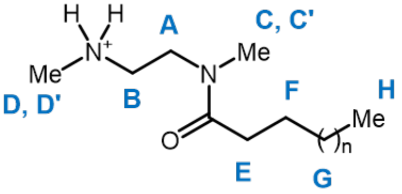

H
H
N+
Me
D, D'
B
A
N
Me
C, C'
F
H
Me
O
E
G
n
formic acid
H2O
C
D
A
B
C'
D'E
F
G
H
AXW_STM_DMEDA_ScaleUp_215_D2O_COSY.1.ser
H
G
F
E
D'
D
C'
C
B
A
H2O
formic acid
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f2 (ppm)
1
2
3
4
5
6
7
8
9
f1 (ppm)

Figure 2-6


H
H
N+
Me
D, D'
B
A
N
Me
C, C'
F
H
Me
O
E
G
n

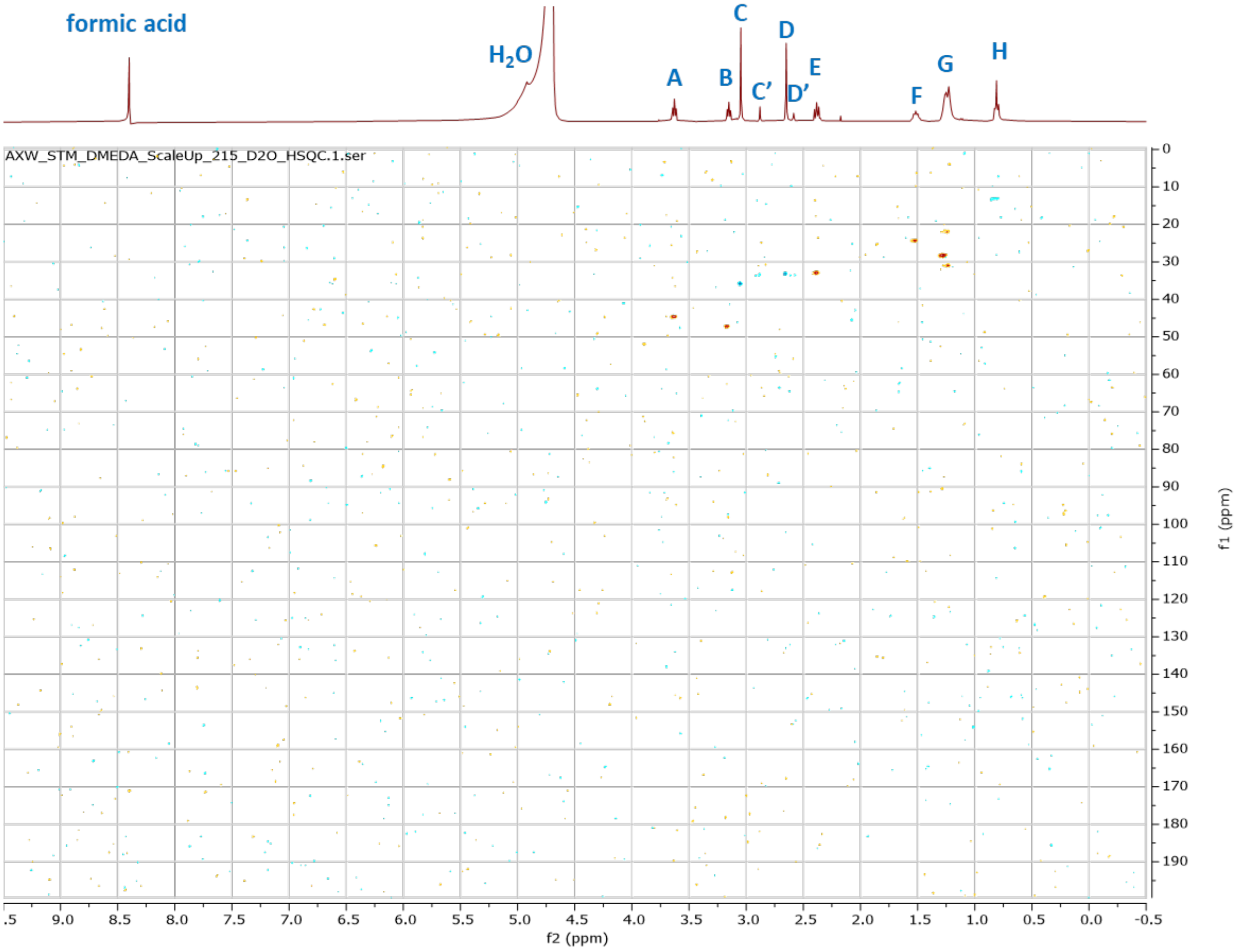

formic acid
H2O
A
B
C
C'
D
D'
E
F
G
H
AXW_STM_DMEDA_ScaleUp_215_D2O_HSQC.1.ser
f2 (ppm)
f1 (ppm)

Figure 2-7

2.4 LC-MS AND MS^E ANALYSIS

2.4.1 LC sample preparation, method, and analysis

50 µL of a TD solution containing 1 mM DMEDA is subjected to the STM-BJ conditions (described in SI section 1.2) at 100 mV for 24 h. 50 µL of the reaction mixture was diluted with 50 µL isopropanol, and analyzed by LC-MS or LC-MS^E. When visualization of DMEDA was required, an additional 50 µL of propionic anhydride was added; this allowed DMEDA and the mono-acylated products to be detected as their +propionate [+C_3H_4O] adduct.

Chromatographic separation was performed on Acquity UPLC H-Class system (Waters Corporation, Milford, MA, USA) using an Acquity UPLC BEH C18 column (2.1 mm × 100 mm, 1.7 µm). Mobile phase A consisted of water with 0.1% formic acid and mobile phase B consisted of MeOH/IPA (4:1; v/v). The chromatographic gradient was set as follows: 80% A, and 20% B, 0-2 min 20% A and 80% B, 2-4 min 20% A and 80% B, 4-5 min 80% A. The flow rate was set to 0.35 mL/min and the column temperature was set at 40 °C. The UPLC was coupled to a Xevo G2 XS Q-ToF MS (Waters Corporation, Milford, MA, USA), and operated in positive electrospray ionization mode. The capillary voltage and sampling cone voltage of 3 kV and 30 V were used in the positive mode. The source and desolvation temperatures were 120 °C and 500 °C, respectively. The desolvation gas flow (N2) was set to 650 L/hr. The samples were also acquired in data independent MSE mode for the structural assignment of the compounds. The low collision energy was set to 4 eV, and the trap collision energy was ramping from 15-40 eV. All data were analyzed in MassLynx software (Waters, Version 4.1).

For quantitative analysis, the samples ran in triplicates, and integrations of each product compound were then averaged. When no internal standard is used, quantification was based on the raw integration values; experiments were only compared relatively if all samples came from the same stock solution. When an internal standard (1-methyl-2-phenylindole at 50 µM) is used, all product quantifications were normalized to the internal standard integration (yield reported as the ratio of integral values of product/internal standard, or A/IS). The quantification of the data was performed in QuanLynx software.

2.4.2 Mass list of products and their isotopologues

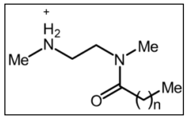
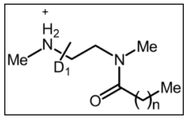
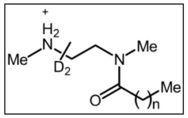
+ C	DMEDA major products	DMEDA-d1	DMEDA-d2	DMEDA-d3	DMEDA-d4	DMEDA-d5	DMEDA-d6	DMEDA-d7	DMEDA-d8	DMEDA-d9	DMEDA-d10	DMEDA-d11	DMEDA-d12	DMEDA-d13	DMEDA-d14
															
1	117.1022	118.1085	119.1148	120.1211	121.1274	122.1337	123.14	124.1463	125.1526	126.1589	127.1652	128.1715			
2	131.1179	132.1242	133.1305	134.1368	135.1431	136.1494	137.1557	138.162	139.1683	140.1746	141.1809	142.1872	143.1935	144.1998	
3	145.1336	146.1399	147.1462	148.1525	149.1588	150.1651	151.1714	152.1777	153.184	154.1903	155.1966	156.2029	157.2092	158.2155	159.2218
4	159.1493	160.1556	161.1619	162.1682	163.1745	164.1808	165.1871	166.1934	167.1997	168.206	169.2123	170.2186	171.2249	172.2312	173.2375
5	173.165	174.1713	175.1776	176.1839	177.1902	178.1965	179.2028	180.2091	181.2154	182.2217	183.228	184.2343	185.2406	186.2469	187.2532
6	187.1807	188.187	189.1933	190.1996	191.2059	192.2122	193.2185	194.2248	195.2311	196.2374	197.2437	198.25	199.2563	200.2626	201.2689
7	201.1964	202.2027	203.209	204.2153	205.2216	206.2279	207.2342	208.2405	209.2468	210.2531	211.2594	212.2657	213.272	214.2783	215.2846
8	215.2121	216.2184	217.2247	218.231	219.2373	220.2436	221.2499	222.2562	223.2625	224.2688	225.2751	226.2814	227.2877	228.294	229.3003
9	229.2278	230.2341	231.2404	232.2467	233.253	234.2593	235.2656	236.2719	237.2782	238.2845	239.2908	240.2971	241.3034	242.3097	243.316
10	243.2435	244.2498	245.2561	246.2624	247.2687	248.275	249.2813	250.2876	251.2939	252.3002	253.3065	254.3128	255.3191	256.3254	257.3317
11	257.2592	258.2655	259.2718	260.2781	261.2844	262.2907	263.297	264.3033	265.3096	266.3159	267.3222	268.3285	269.3348	270.3411	271.3474
12	271.2749	272.2812	273.2875	274.2938	275.3001	276.3064	277.3127	278.319	279.3253	280.3316	281.3379	282.3442	283.3505	284.3568	285.3631
13	285.2906	286.2969	287.3032	288.3095	289.3158	290.3221	291.3284	292.3347	293.341	294.3473	295.3536	296.3599	297.3662	298.3725	299.3788
14	299.3063	300.3126	301.3189	302.3252	303.3315	304.3378	305.3441	306.3504	307.3567	308.363	309.3693	310.3756	311.3819	312.3882	313.3945
15	313.322	314.3283	315.3346	316.3409	317.3472	318.3535	319.3598	320.3661	321.3724	322.3787	323.385	324.3913	325.3976	326.4039	327.4102

Figure 2-8

2.4.3 Representative extracted ion chromatograms and MS^E spectra

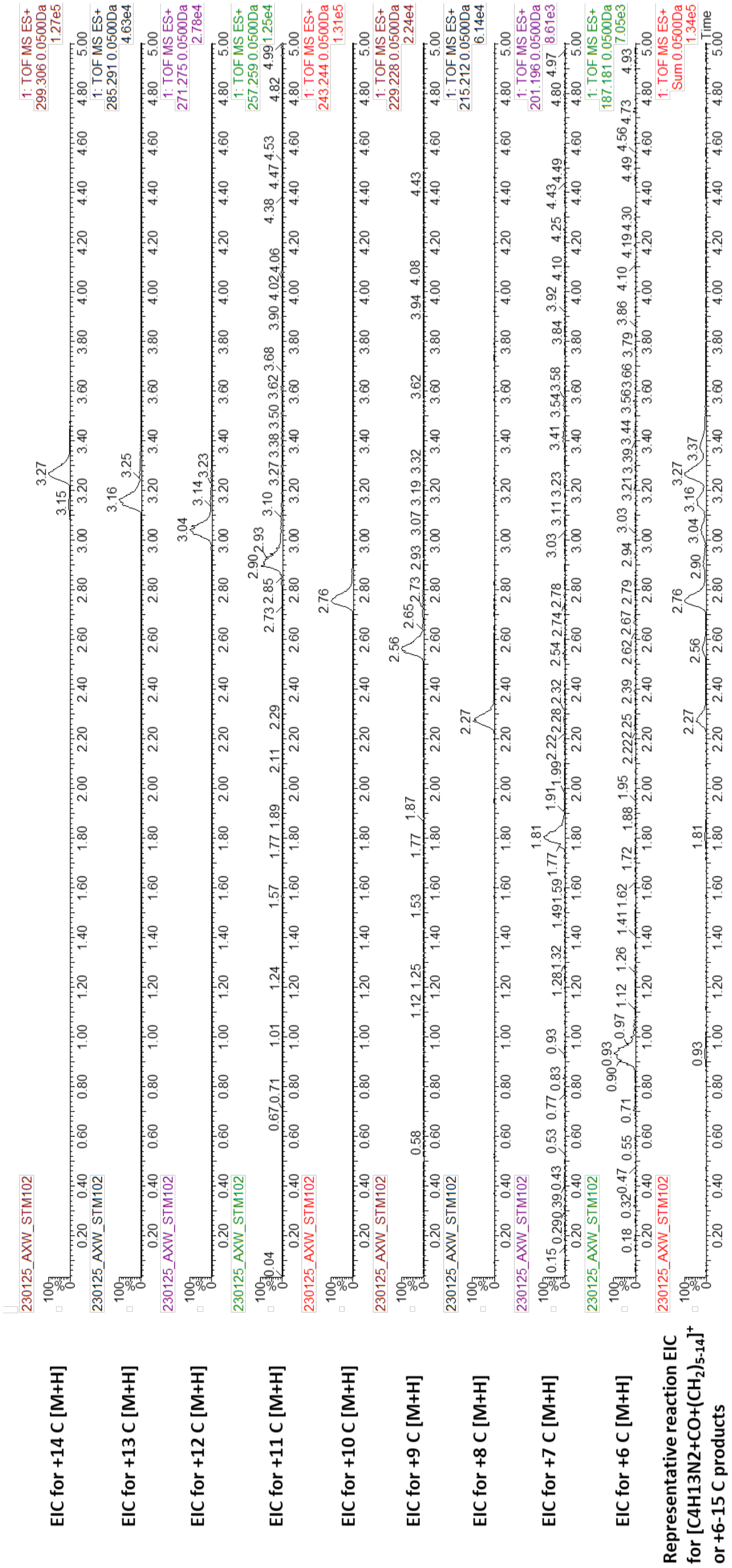


Figure 2-9

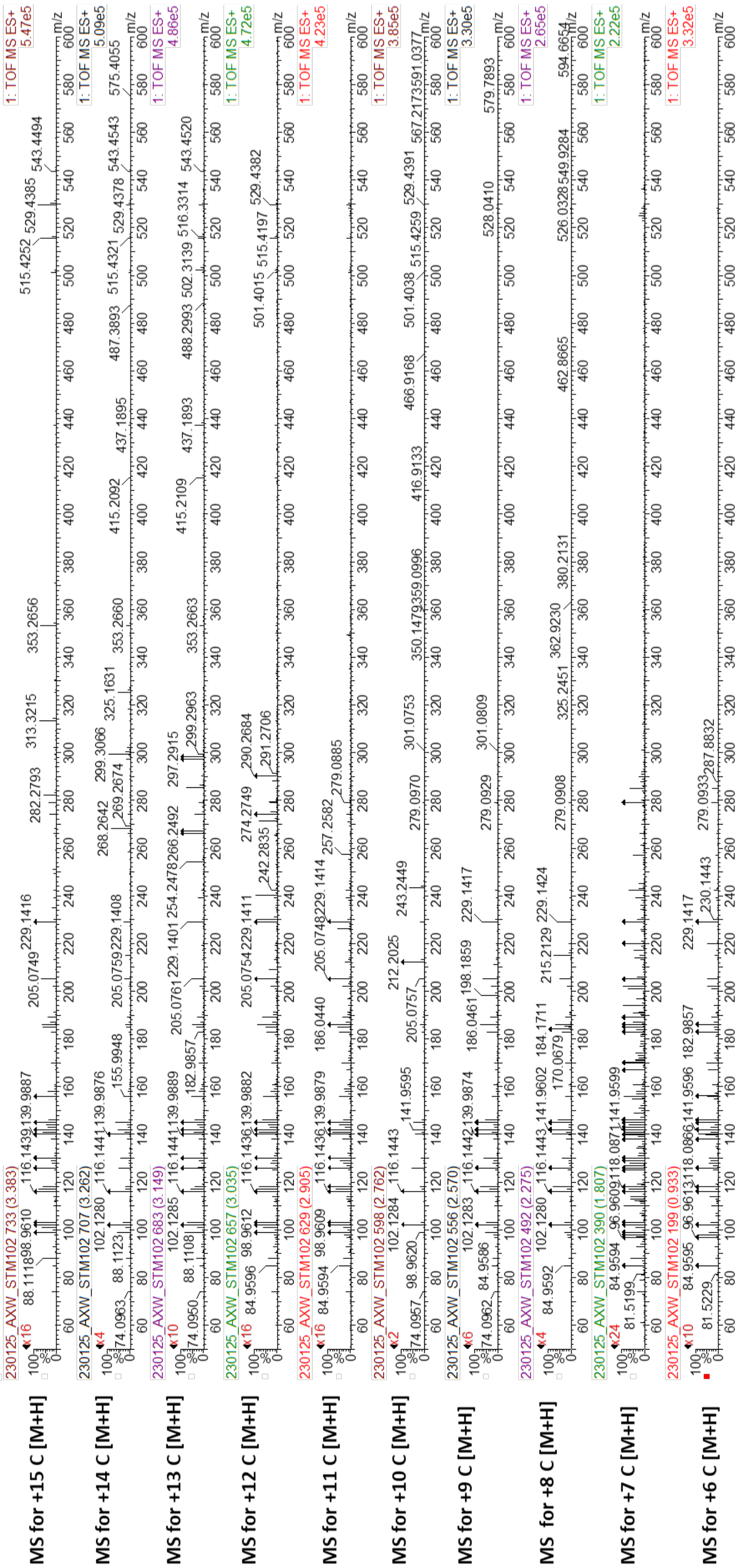

MS for +15 C [M+H]
230125_AXW_STM102 733 (3.383)
1: TOF MS ES+
5.47e5
x16
88.1118 98.9610 116.1439 139.9887 205.0749 229.1416 282.2793 313.3215 353.2656 515.4252 529.4385 543.4494
MS for +14 C [M+H]
230125_AXW_STM102 707 (3.262)
1: TOF MS ES+
5.09e5
x4
74.0963 88.1123 102.1280 116.1441 139.9876 155.9948 205.0759 229.1408 268.2642 269.2674 299.3066 325.1631 353.2660 415.2092 437.1895 487.3893 515.4321 529.4378 543.4543 575.4055
MS for +13 C [M+H]
230125_AXW_STM102 683 (3.149)
1: TOF MS ES+
4.86e5
x10
74.0950 88.1108 102.1285 116.1441 139.9889 182.9857 205.0761 229.1401 254.2478 266.2492 297.2915 299.2963 353.2663 415.2109 437.1893 488.2993 502.3139 516.3314 543.4520
MS for +12 C [M+H]
230125_AXW_STM102 657 (3.035)
1: TOF MS ES+
4.72e5
x16
84.9596 98.9612 116.1436 139.9882 205.0754 229.1411 242.2835 274.2749 290.2684 291.2706 501.4015 515.4197 529.4382
MS for +11 C [M+H]
230125_AXW_STM102 629 (2.905)
1: TOF MS ES+
4.23e5
x16
84.9594 98.9609 116.1436 139.9879 186.0440 205.0748 229.1414 257.2582 279.0885
MS for +10 C [M+H]
230125_AXW_STM102 598 (2.762)
1: TOF MS ES+
3.85e5
x2
74.0957 98.9620 102.1284 116.1443 141.9595 205.0757 212.2025 243.2449 279.0970 301.0753 350.1479 359.0996 416.9133 466.9168 501.4038 515.4259 529.4391 567.2173 591.0377
MS for +9 C [M+H]
230125_AXW_STM102 556 (2.570)
1: TOF MS ES+
3.30e5
x6
74.0962 84.9586 102.1283 116.1442 139.9874 186.0461 198.1859 229.1417 279.0929 301.0809 528.0410 579.7893
MS for +8 C [M+H]
230125_AXW_STM102 492 (2.275)
1: TOF MS ES+
2.65e5
x4
84.9592 102.1280 116.1443 141.9602 170.0679 184.1711 215.2129 229.1424 279.0908 325.2451 362.9230 380.2131 462.8665 526.0328 549.9284 594.6654
MS for +7 C [M+H]
230125_AXW_STM102 390 (1.807)
1: TOF MS ES+
2.22e5
x24
81.5199 84.9594 96.9609 118.0871 141.9599
MS for +6 C [M+H]
230125_AXW_STM102 199 (0.933)
1: TOF MS ES+
3.32e5
x10
81.5229 84.9595 96.9613 118.0866 141.9596 182.9857 229.1417 230.1443 279.0933 287.8832
100
%
0
60 80 100 120 140 160 180 200 220 240 260 280 300 320 340 360 380 400 420 440 460 480 500 520 540 560 580 600
m/z

Figure 2-10

MS for +6 C [M+H]

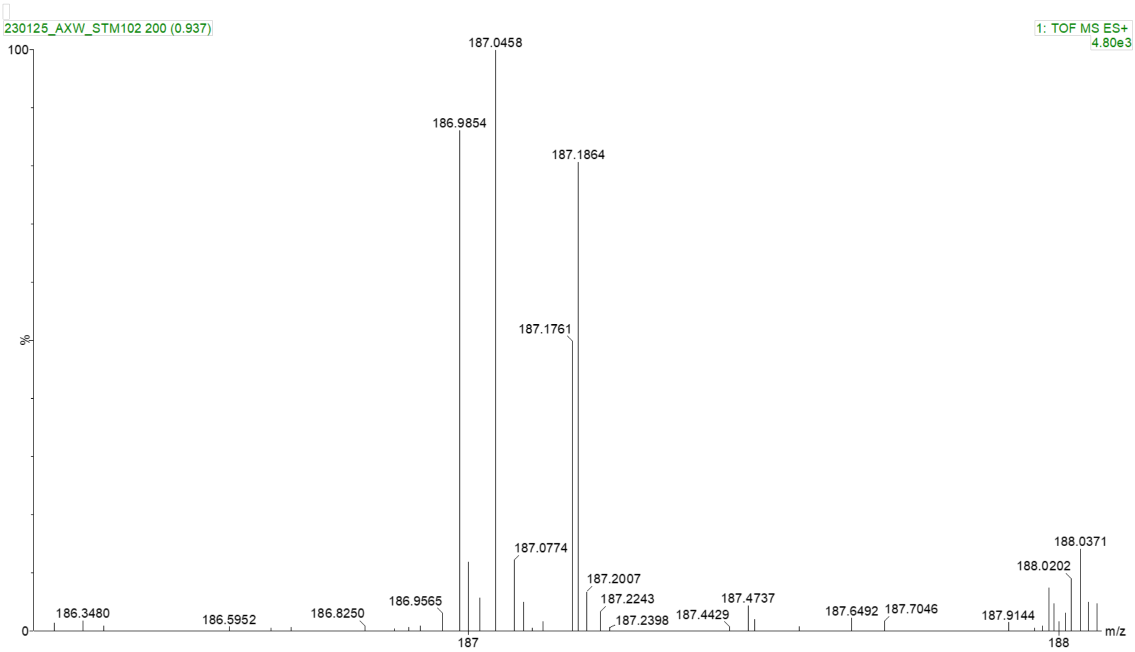


Figure 2-11

MS for +7 C [M+H]

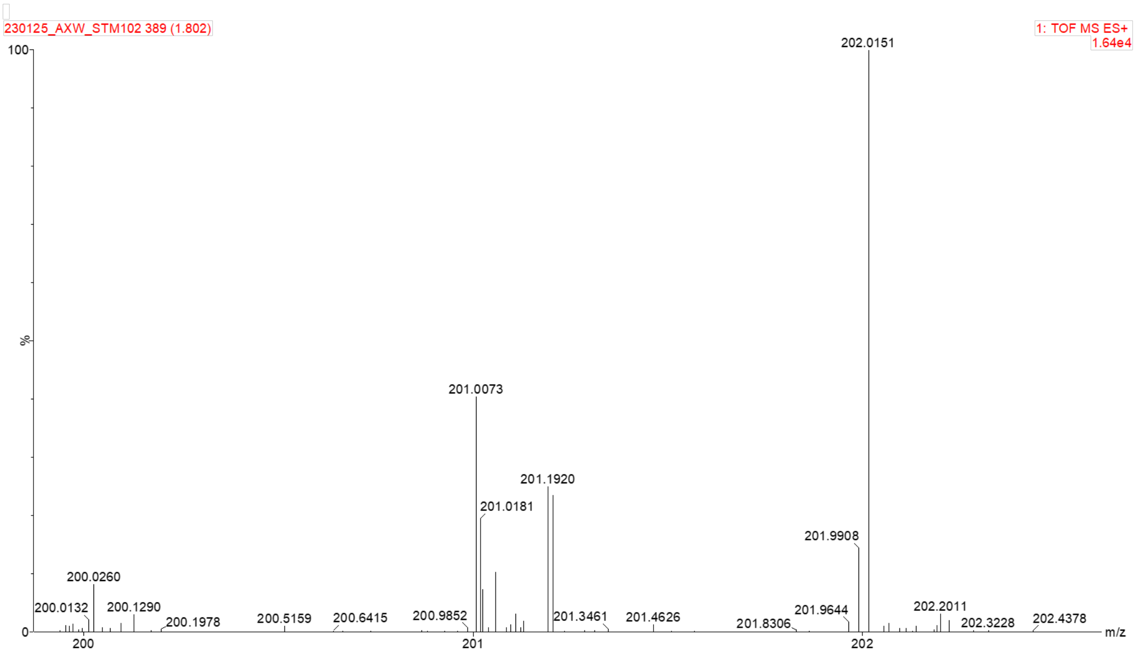


Figure 2-12

MS for +8 C [M+H]

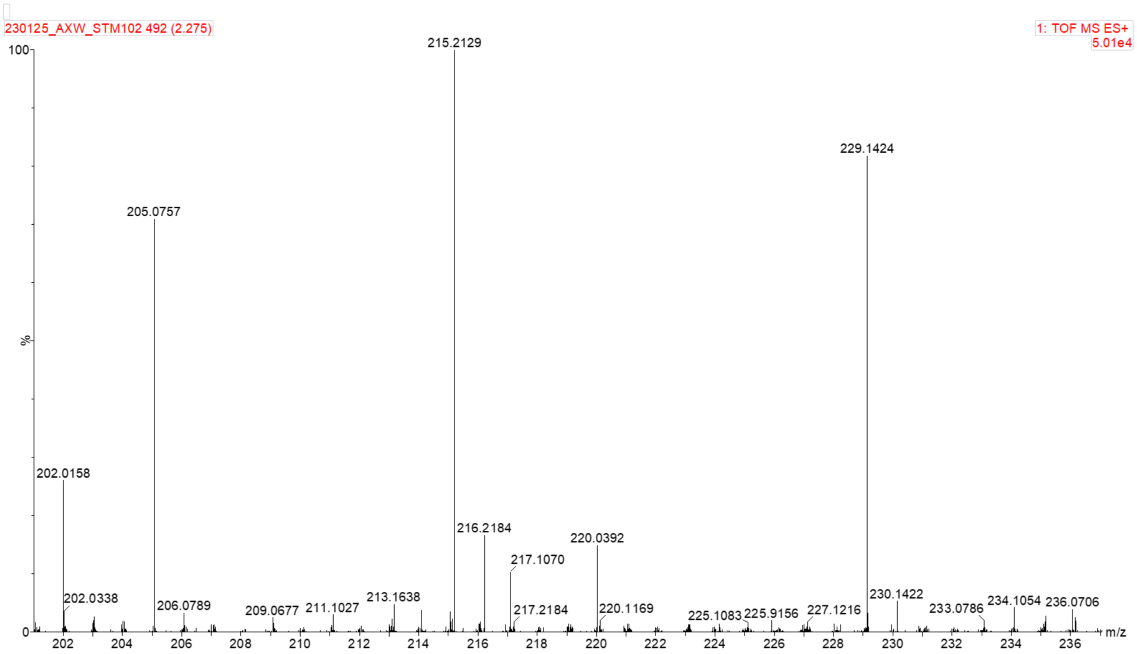


Figure 2-13

MS for +9 C [M+H]

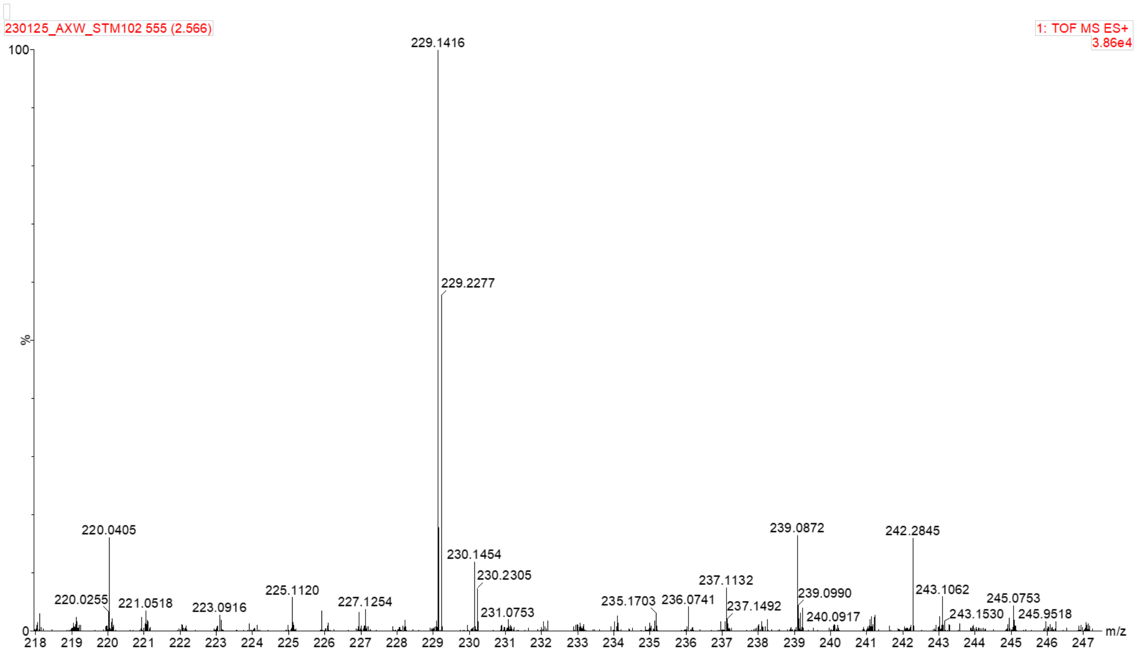


Figure 2-14

MS for +10 C [M+H]

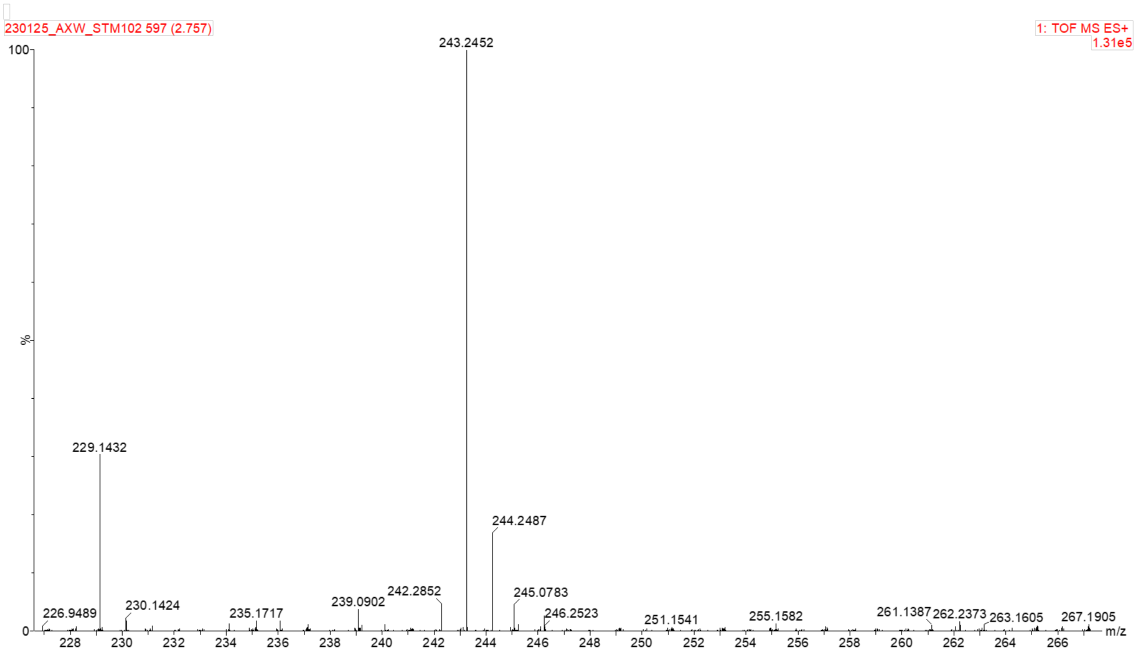


Figure 2-15

MS for +11 C [M+H]

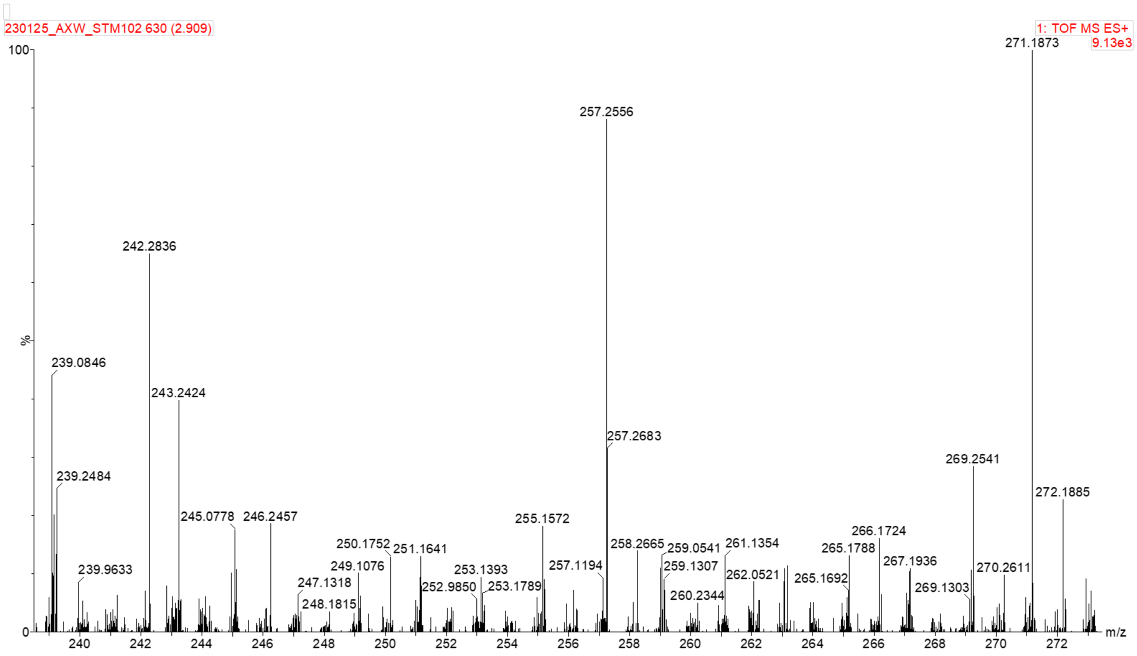


Figure 2-16

MS for +12 C [M+H]

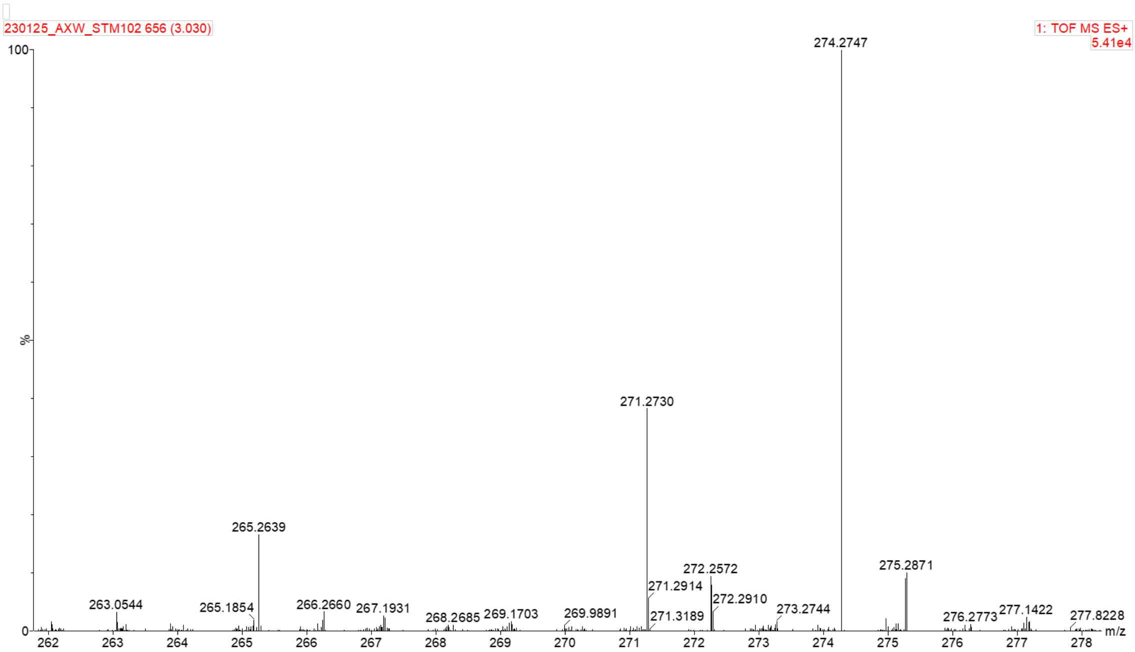


Figure 2-17

MS for +13 C [M+H]

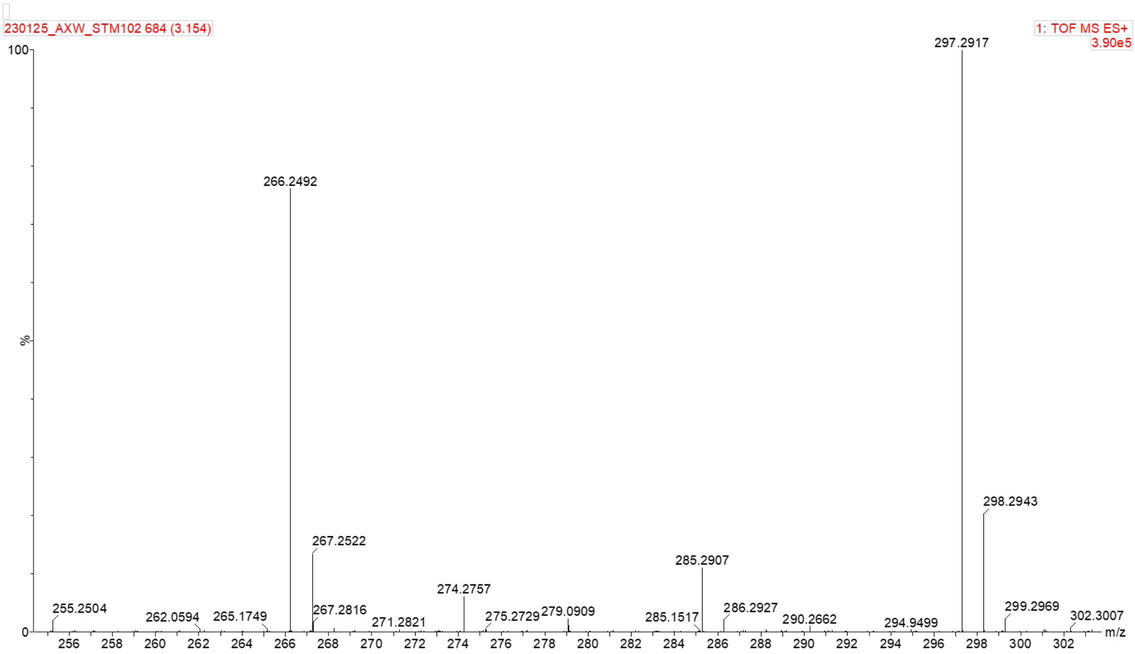


Figure 2-18

MS for +14 C [M+H]

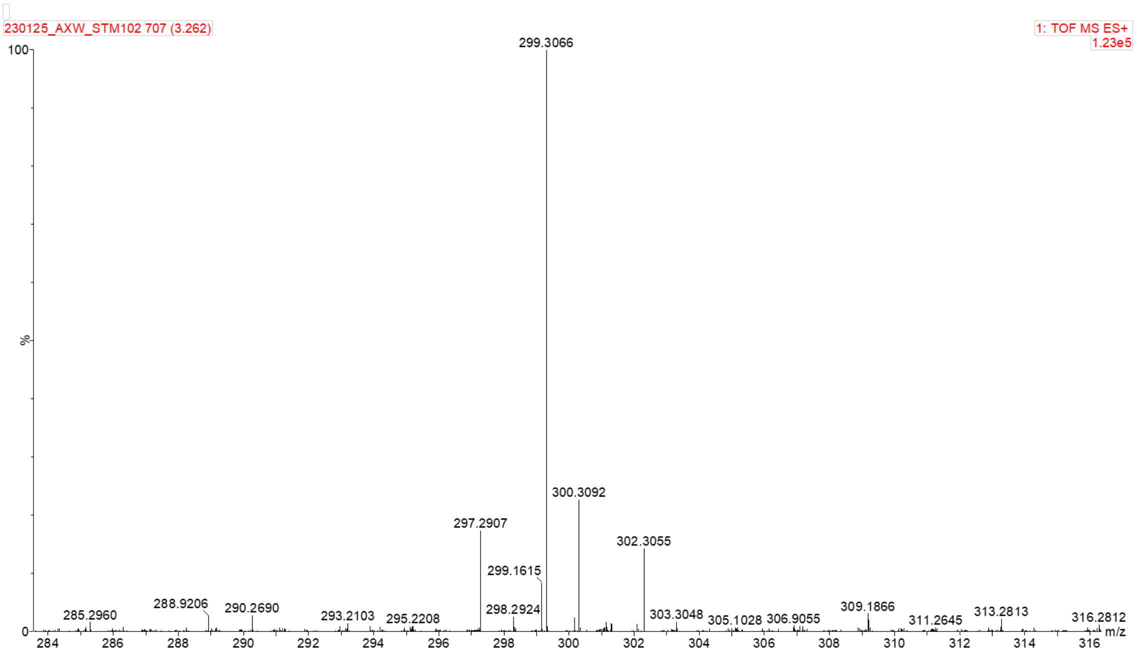


Figure 2-19

MS for +15 C [M+H]

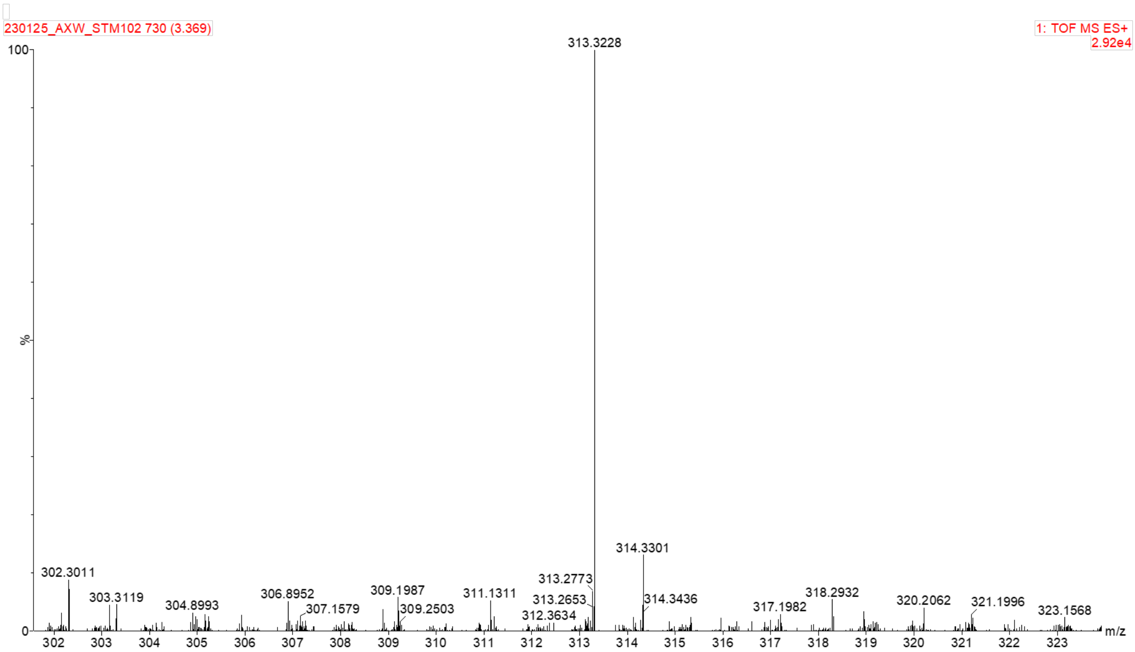
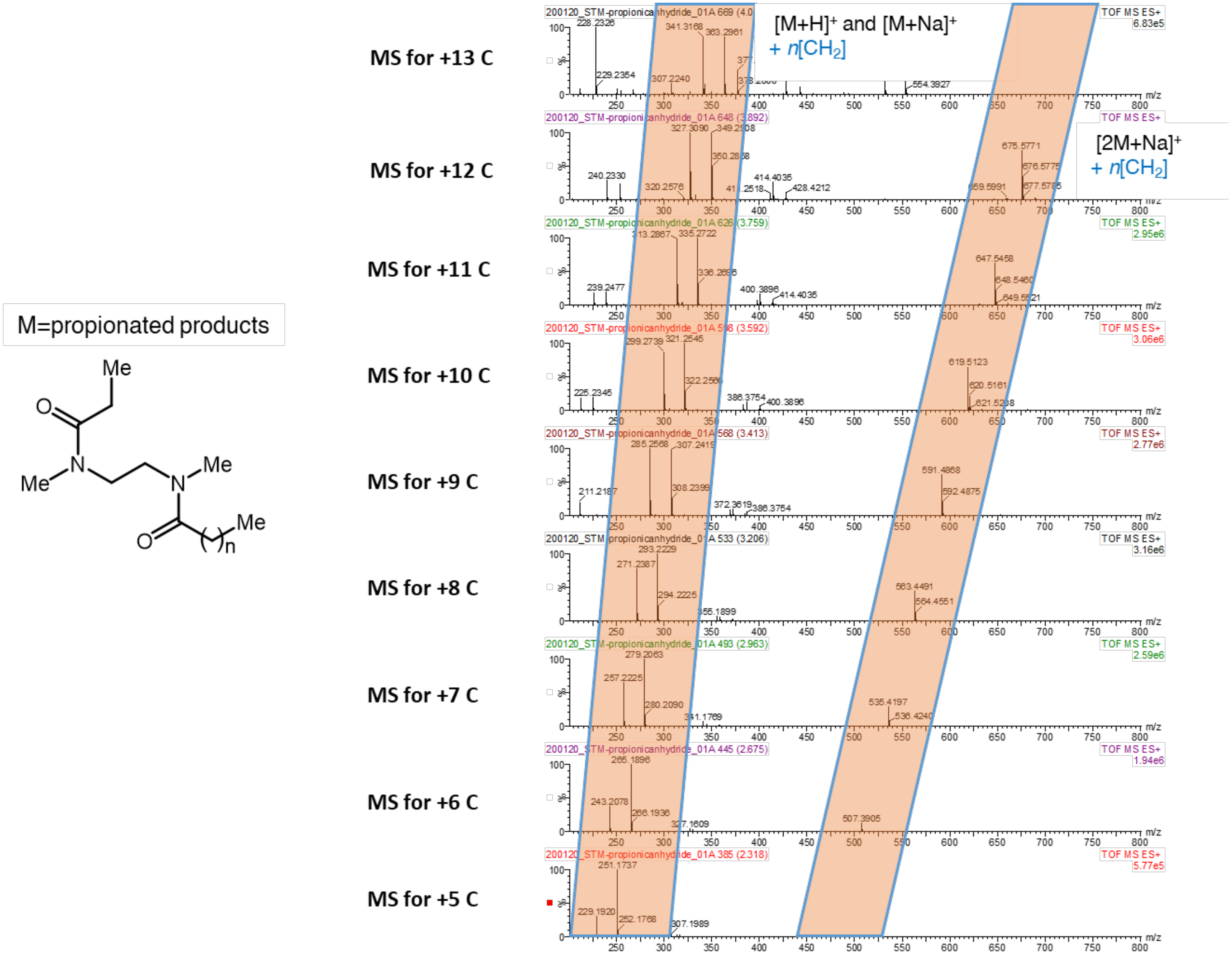


Figure 2-20

When derivatized with propionic anhydride (SI section 2.4.1), DMEDA and lighter amide products (+1-5 C) could be visualized.

Figure 2-21


M=propionated products
Me
O
N
Me
N
Me
O
n
Me
MS for +13 C
MS for +12 C
MS for +11 C
MS for +10 C
MS for +9 C
MS for +8 C
MS for +7 C
MS for +6 C
MS for +5 C
[M+H]+ and [M+Na]+ + n[CH2]
[2M+Na]+ + n[CH2]
200120_STM-propionicanhydride_01A 669 (4.0
TOF MS ES+ 6.83e5
228.2326
229.2354
307.2240
341.3168
363.2961
554.3927
200120_STM-propionicanhydride_01A 648 (3.892)
TOF MS ES+
240.2330
320.2576
327.3090
349.2908
350.2868
414.4035
428.4212
659.5991
675.5771
676.5775
677.5785
200120_STM-propionicanhydride_01A 626 (3.759)
TOF MS ES+ 2.95e6
239.2477
313.2867
335.2722
336.2696
400.3896
414.4035
647.5458
648.5460
649.5521
200120_STM-propionicanhydride_01A 598 (3.592)
TOF MS ES+ 3.06e6
225.2345
299.2739
321.2545
322.2566
386.3754
400.3896
619.5123
620.5161
621.5208
200120_STM-propionicanhydride_01A 568 (3.413)
TOF MS ES+ 2.77e6
211.2187
285.2568
307.2415
308.2399
372.3619
386.3754
591.4868
592.4875
200120_STM-propionicanhydride_01A 533 (3.206)
TOF MS ES+ 3.16e6
271.2387
293.2229
294.2225
355.1899
563.4491
564.4551
200120_STM-propionicanhydride_01A 493 (2.963)
TOF MS ES+ 2.59e6
257.2225
279.2063
280.2090
341.1769
535.4197
536.4240
200120_STM-propionicanhydride_01A 445 (2.675)
TOF MS ES+ 1.94e6
243.2078
265.1896
266.1936
327.1609
507.3905
200120_STM-propionicanhydride_01A 385 (2.318)
TOF MS ES+ 5.77e5
229.1920
251.1737
252.1768
307.1989
100
%
0
250
300
350
400
450
500
550
600
650
700
750
800
m/z

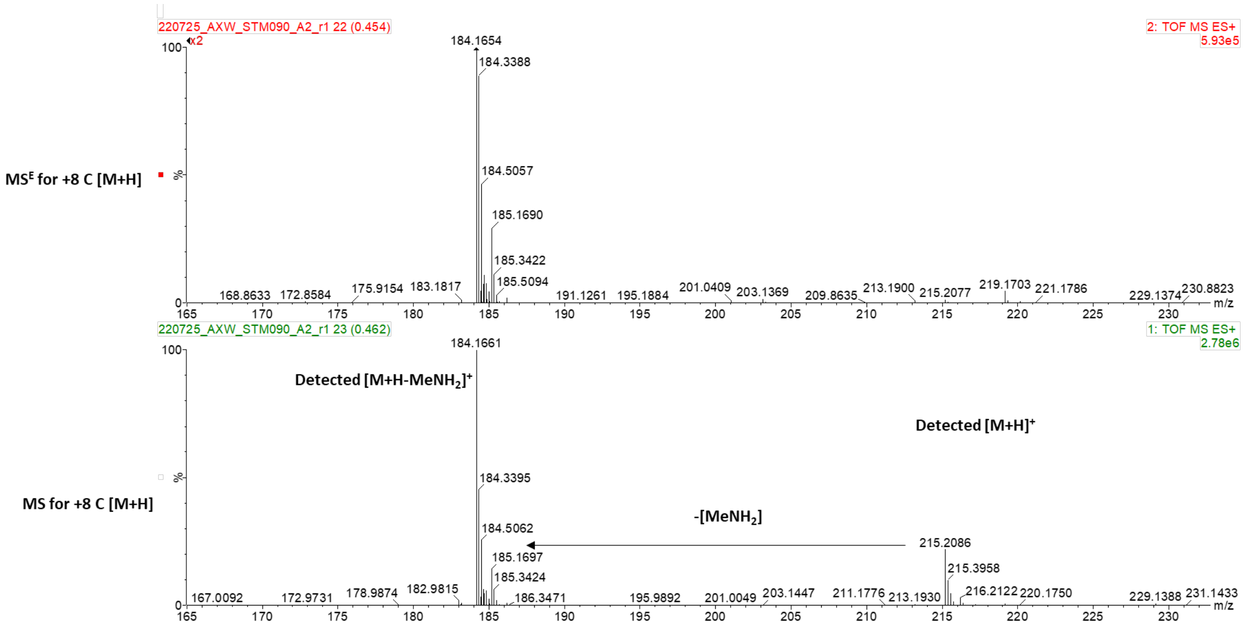


Figure 2-22

2.4.4 LC matching of reaction products and synthesized standards

Authentic standards of the +6, 9, and 10 C products (**2a, 2b, 2c**) were synthesized as described in SI section 3.3. 0.5 mM solutions in isopropanol of these 3 standards were compared to the STM reaction mixture using the LC method described in SI section 2.4.1

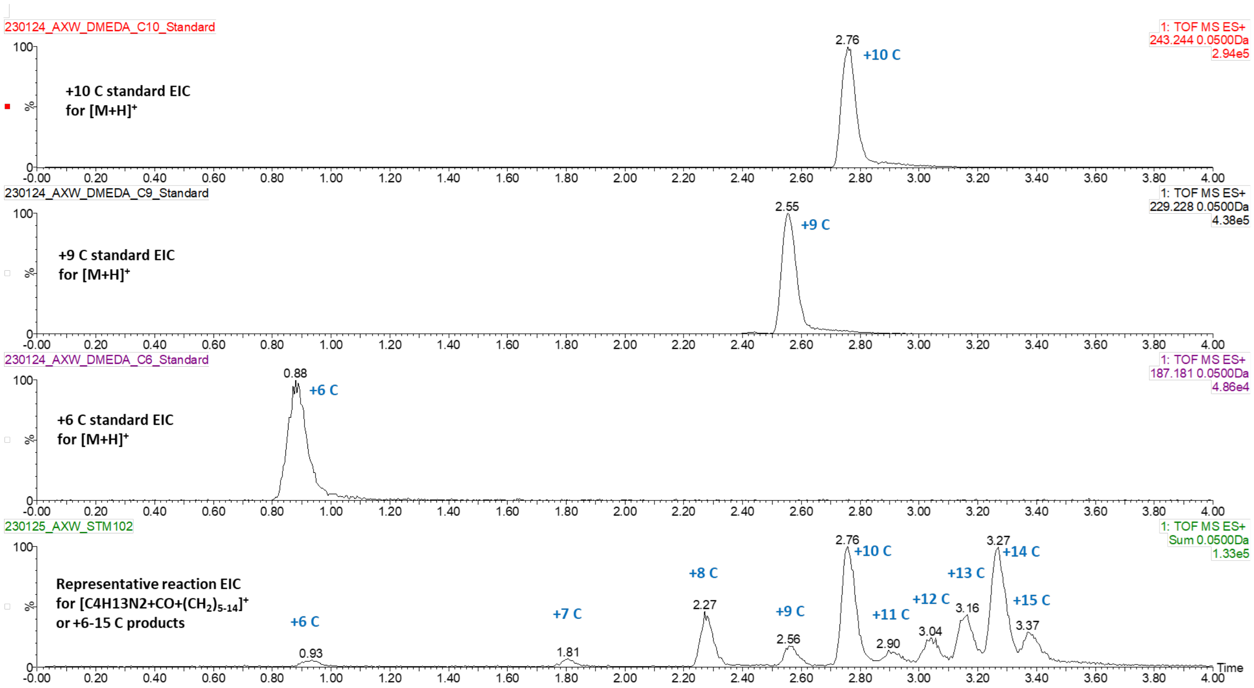


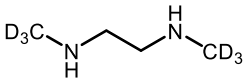
Figure 2-23

3 SYNTHETIC PROCEDURES AND CHARACTERIZATION OF NEW COMPOUNDS

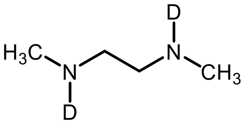
3.1 GENERAL EXPERIMENTAL CONSIDERATIONS

Unless otherwise specified, all commercial chemicals were used as supplied without additional purification; all reactions were conducted under ambient conditions with magnetic stirring. Thin layer chromatography was performed on SiliCycle® 250 µm, 60 Å plates. Visualization was accomplished with 254 nm UV light, cerium ammonium molybdate (CAM), KMnO$_4$, ninhydrin, or I$_2$. Chromatographic purification was accomplished by flash column chromatography on SiliCycle® Silica Flash® 40-63 µm silica gel, 60 Å or Redi*Sep*® Silver Silica Gel Disposable Flash Columns, 40–60 micron. ^{1}H NMR spectra were recorded on Bruker 300, 400, or 500 MHz spectrometers at ambient temperature and reported in ppm using tetramethylsilane (0.00 ppm) as an internal standard. Chemical shift is reported with multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet) and coupling constants (Hz) where appropriate. Proton-decoupled ^{13}C NMR spectra were recorded on Bruker 400 or 500 MHz spectrometers (^{13}C Larmor frequency at 101 or 126 MHz) at ambient temperature and reported in ppm using tetramethylsilane (0.00 ppm) as an internal standard. ^{2}H NMR spectra were recorded on Bruker 400 MHz spectrometers (^{2}H Larmor frequency at 61 MHz) at ambient temperature and reported in ppm using CDCl$_3$ (7.26 ppm) as an internal standard. Infrared spectra were recorded on a Perkin Elmer Spectrum Two FT-IR spectrometer in ATR mode. Low-resolution mass spectra (LRMS) were recorded on an Agilent 7890B GC System 5977B MSD GCMS with EI ionization. High-resolution mass spectra (HRMS) were obtained from the Columbia University Chemistry Department Mass Spectrometry Facility on a Waters XEVO G2-XS QToF mass spectrometer equipped with a UPC^2 SFC inlet and a LockSpray source with one of three probes: electrospray ionization (ESI) probe, atmospheric pressure chemical ionization (APCI) probe, or atmospheric pressure solids analysis probe (ASAP). All compounds were judged to be homogeneous (>95% purity) by ^{1}H and ^{13}C NMR spectroscopy.

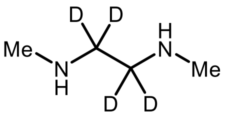
3.2 DMEDA AND ITS ISOTOPOLOGUES



1b

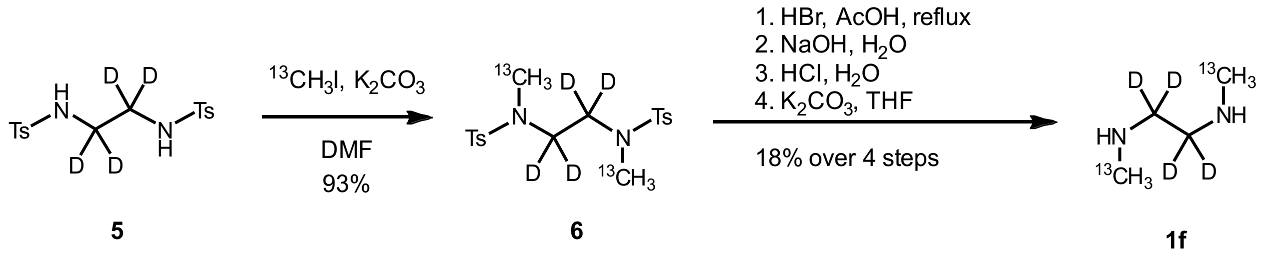


1c

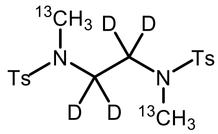


1d

N1,N2-bis(methyl-d3)ethane-1,2-diamine (1b)[3], **N1,N2-dimethylethane-1,2-diamine-d2 (1c)**[4,5], **and N1,N2-dimethylethane-d4-1,2-diamine (1d)**[3] were synthesized according to literature procedures and spectral data were in agreement with reported characterization.

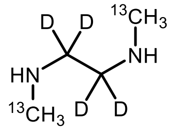


N,N'-(ethane-1,2-diyl-d4)bis(4-methylbenzenesulfonamide) (5) was synthesized according to literature procedures and spectral data were in agreement with reported characterization.[3]



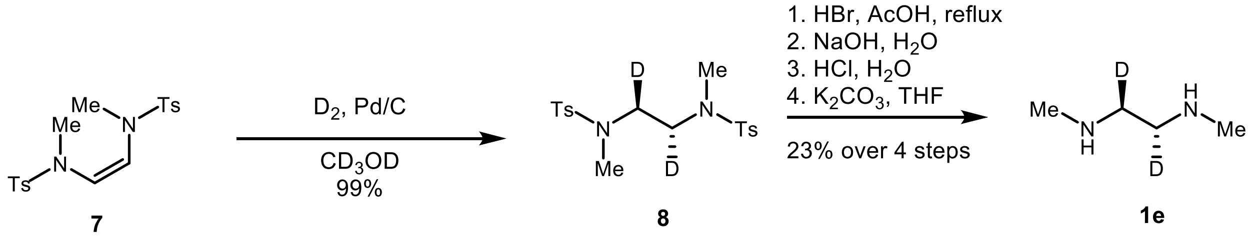
6

N,N'-(ethane-1,2-diyl-d4)bis(4-methyl-N-(methyl-13C)benzenesulfonamide) (6). A round bottom flask charged was charged with sulfonamide **5** (1.042 g, 2.80 mmol, 1 equiv), K_2CO_3 (1.160 g, 8.40 mmol, 3 equiv), N,N-dimethylformamide (20 mL) sequentially, and cooled to 0 °C. $^{13}CH_3I$ (1.000 g, 7.00 mmol, 2.5 equiv) was added and the suspension was allowed to warm up to room temperature, and stirred for 21 h. The suspension was poured into deionized water (100 mL) and filtered. The solid residue was washed with deionized water (2x50 mL) and dissolved in CH_2Cl_2 (100 mL). The solution was dried with anhydrous Na_2SO_4 and concentrated *in vacuo* to afford sulfonamide **6** as a white powder (1.040 g, 93% yield; >99% CD_2, >99% $^{13}CH_3$ by ^{1}H NMR). **TLC** (20% ethyl acetate in hexanes) R_f 0.11 (UV); **IR** (film) 2023, 2965, 2918, 2875, 2803, 1596, 1452, 1335, 1153 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.71 – 7.62 (m, 4H), 7.37 – 7.29 (m, 4H), 2.81 (d, J = 139.5 Hz, 6H), 2.44 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$, referenced to residual $CHCl_3$, minor decoupling sidebands observed due to ^{13}C labeling) δ 143.58, 134.26, 129.76, 127.31, 35.62, 21.45; **HRMS** (ESI+/qToF) m/z: [M+Na]$^+$ Calculated for C24H48N2O2Na$^+$ 419.3614; found 419.3629; **^{2}H NMR** (61 MHz, $CHCl_3$) δ 3.19.

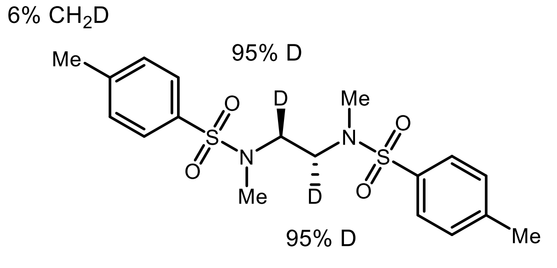


1f

N1,N2-di(methyl-13C)ethane-d4-1,2-diamine (1f). A round bottom flask was charged with N,N'-(ethane-1,2-diyl-d4)bis(4-methyl-N-(methyl-13C)benzenesulfonamide) **6** (1.000 g, 2.48 mmol, 1 equiv), 48 wt% HBr (6.0 mL), and acetic acid (3 mL), and stirred under reflux for 3 h. The solution was cooled to room temperature, concentrated, and redissolved in deionized water (10 mL). The solution was basified with NaOH (400 mg, 9.94 mmol, 4 equiv) until pH was verified to be >11. The solution was completely distilled (bath temperature 160 °C) into 1 M HCl (50 mL) and additional water (2x10 mL) was added to the solids and distilled over. The combined distillate pH was verified to be <1, and concentrated *in vacuo.* The salt was dried by azeotropic distillation with toluene (3x50 mL). The resulting solid was transferred to a flame-dried round bottom flask, to which K_2CO_3 (3.433 g, 25.0 mmol, 10 equiv) was added. The reaction vessel was evacuated and backfilled with argon (3x), and anhydrous tetrahydrofuran (10 mL) was added. The suspension was stirred for 18 h and filtered through a pad of celite, and the filtrate was cooled and slowly concentrated *in vacuo* at 0 °C; concentration progress was monitored by ^{1}H NMR of an aliquot, and deemed complete when tetrahydrofuran was completely removed, affording N^1,N^2-dimethylethane-1,2-d2-1,2-diamine **1f** as a yellow liquid (42 mg, 18% yield, 99% CHD by ^{1}H NMR). **IR** (film) 3301, 2957, 2836, 2780, 2187, 2064, 1473, 1448, 1429, 1146 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 2.43 (d, J = 132.9 Hz, 6H), 1.16 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 36.53; **LRMS** (GC/EI+) m/z: $[M]^+$ Calculated for $C_2{}^{13}C_2H_8D_4N_2{}^+$ 94.1 found 94.0; **^{2}H NMR** (61 MHz, $CHCl_3$) δ 2.66.

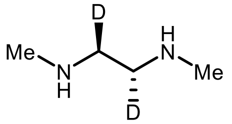


(Z)-N,N'-(ethene-1,2-diyl)bis(N,4-dimethylbenzenesulfonamide) (7) was synthesized according to literature procedures and spectral data were in agreement with reported characterization.[6]



8

N,N'-((1R,2S)-ethane-1,2-diyl-1,2-d2)bis(N,4-dimethylbenzenesulfonamide) (8). A flame-dried round bottom flask charged was charged with sulfonamide **7** (1.000 g, 2.54 mmol, 1 equiv), 10 wt% palladium on carbon (269 mg, 254 μmol, 0.1 equiv), and CD_3OD (20 mL). The reaction mixture was purged with D_2 for 1 min, and stirred under 1 atm D_2 for 22 h. The suspension was filtered through a pad of celite, washed with CH_2Cl_2 (3x50 mL), and concentrated *in vacuo* to afford sulfonamide **8** as a white powder (1.001 g, 99% yield; 95% CHD, 6% $SO_2C_6H_4CH_2D$ by ^{1}H NMR). **TLC** (20% ethyl acetate in hexanes) R_f 0.10 (UV); **IR** (film) 3033, 2168, 1596, 1494, 1453, 1384, 1339, 1306, 1156, 1089 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 – 7.63 (m, 4H), 7.36 – 7.30 (m, 4H), 3.19 (m, 2H), 2.82 (s, 6H), 2.44 (s, 6H).; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.61, 134.30, 129.79, 127.36, 48.68, 48.38 (t, J=21.1 Hz), 35.76, 21.49; **HRMS** (ESI+/qToF) m/z: $[M+H]^+$ Calculated for $C_{18}H_{22}D_2N_2O_4S_2$ 399.1381; found 399.1380; **^{2}H NMR** (61 MHz, $CHCl_3$) δ 3.22, 2.42.

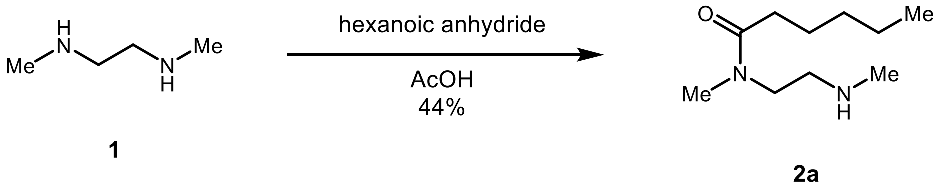


1e

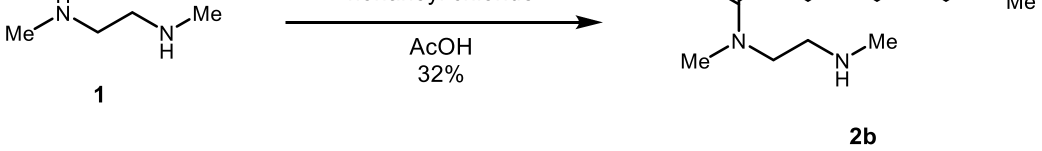
N^1,N^2-dimethylethane-1,2-d2-1,2-diamine (1e). A round bottom flask was charged with N,N'-(ethane-1,2-diyl-1,2-d2)bis(N,4-dimethylbenzenesulfonamide) **8** (996 mg, 2.50 mmol, 1 equiv), 48 wt% HBr (6.0

mL), and acetic acid (3 mL), and stirred under reflux for 3 h. The solution was cooled to room temperature, concentrated, and redissolved in deionized water (10 mL). The solution was basified with NaOH (400 mg, 10.0 mmol, 4 equiv) until pH was verified to be >11. The solution was completely distilled (bath temperature 160 °C) into 1 M HCl (50 mL) and additional water (2x10 mL) was added to the solids and distilled over. The combined distillate pH was verified to be <1, and concentrated *in vacuo*. The salt was dried by azeotropic distillation with toluene (3x50 mL). The resulting solid was transferred to a flame-dried round bottom flask, to which K_2CO_3 (3.450 g, 25.0 mmol, 10 equiv) was added. The reaction vessel was evacuated and backfilled with argon (3x), and anhydrous tetrahydrofuran (10 mL) was added. The suspension was stirred for 18 h and filtered through a pad of celite, and the filtrate was cooled and slowly concentrated *in vacuo* at 0 °C; concentration progress was monitored by ^{1}H NMR of an aliquot, and deemed complete when tetrahydrofuran was completely removed, affording N^1,N^2-dimethylethane-1,2-d2-1,2-diamine **1e** as a colorless liquid (52 mg, 23% yield, 99% CHD by ^{1}H NMR). **IR** (solution in $CDCl_3$) 3280, 2949, 2856, 2796, 1539, 1454, 1375, 1313 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$, referenced to residual $CHCl_3$) δ 2.70 – 2.63 (m, 2H), 2.43 (s, 6H), 1.45 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$, referenced to $CDCl_3$) δ 51.42, 51.02 (t, *J* = 20.5 Hz), 36.58; **^{2}H NMR** (61 MHz, $CHCl_3$) δ 2.68.

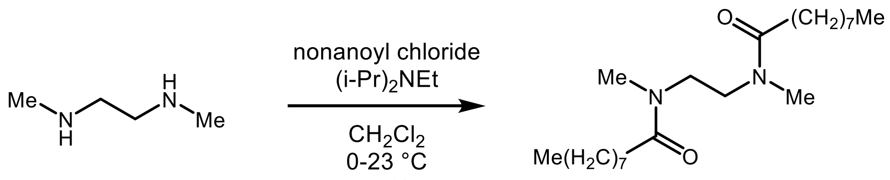
3.3 ACYLATED DMEDA DERIVATIVES



N-methyl-N-(2-(methylamino)ethyl)hexanamide (2a). A round bottom flask charged with acetic acid (20 mL) was placed in a room temperature (23 °C) water bath. N,N′-Dimethylethylenediamine (409 mg, 4.65 mmol, 2 equiv) and hexanoic anhydride (498 mg, 2.32 mmol, 1 equiv) were sequentially added dropwise to the reaction flask. The reaction was stirred for 2 h and poured into 60 mL 3 M aqueous NaOH, and the pH was verified to be >11. The resulting suspension was extracted with ethyl acetate (3x100 mL), dried with anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (gradient elution: 5-10% methanol in CH_2Cl_2+ 2% triethylamine) to afford amide **2a** as a yellow oil (190 mg, 44% yield, mixture of rotamer in $CDCl_3$ A:B=1.4:1): **TLC** (10% methanol in CH_2Cl_2 + 2% triethylamine), R_f 0.33 (ninhydrin); IR (film) 3627, 2929, 2857, 1638, 1466, 1457 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.50 (rotamer A, t, *J* = 6.6 Hz, 2H), 3.42 (rotamer B, t, *J* = 6.8 Hz, 2H), 3.02 (rotamer A, s, 3H), 2.94 (rotamer B, s, 3H), 2.76 (m, 2H), 2.47 (rotamer B, s, 3H), 2.45 (rotamer A: s, 3H), 2.33 (m, 2H), 1.70 – 1.56 (m, 2H), 1.43 (s, 1H), 1.38 – 1.27 (m, 4H), 0.94 – 0.84 (m, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.43, 173.38, 49.92, 49.74, 49.46, 47.47, 36.59, 36.32, 36.01, 33.57, 33.50, 33.01, 31.69, 31.66, 25.16, 24.75, 22.53, 13.98.; **HRMS** (ESI+/qToF) m/z: [M+H]$^+$ Calculated for C10H23N2O$^+$ 187.1810; found 187.1804. Equilibration between rotamers was observed by magnetization transfer via NOESY.

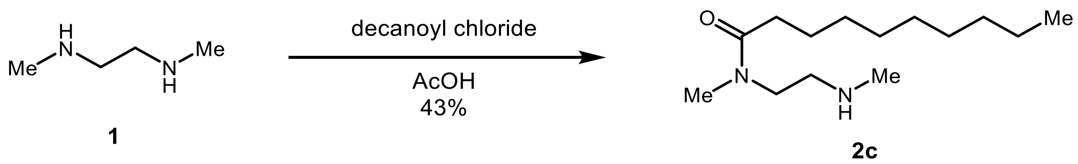


N-methyl-N-(2-(methylamino)ethyl)nonanamide (2b). A round bottom flask charged with acetic acid (20 mL) was placed in a room temperature (23 °C) water bath. N,N′-Dimethylethylenediamine (950 mg, 10.8 mmol, 2 equiv) and nonanoyl chloride (941 mg, 5.32 mmol, 1 equiv) were sequentially added dropwise to the reaction flask. The reaction was stirred for 2 h and poured into 120 mL 3 M aqueous NaOH, and the pH was verified to be >11. The resulting suspension was extracted with ethyl acetate (3x200 mL), dried with anhydrous Na_2SO_4, and concentrated *in vacuo*. The solid residue was triturated with CH_2Cl_2 (3x50 mL), filtered through a pad of celite, concentrated *in vacuo*, and the residue was purified by flash column chromatography on silica gel deactivated by 5 column volume of 10% methanol in CH_2Cl_2 + 2% triethylamine (gradient elution: 10-20% methanol in CH_2Cl_2) to afford amide **2b** as a colorless oil (392 mg, 32% yield, mixture of rotamer in $CDCl_3$ A:B=1.4:1): **TLC** (10% methanol in CH_2Cl_2 + 2% triethylamine), R_f 0.36 (ninhydrin); IR (film) 3313, 2923, 2852, 2793, 1636, 1464, 1401, 1147, 1111 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.49 (rotamer A, t, *J* = 6.6 Hz, 2H), 3.41 (rotamer B, t, *J* = 6.8 Hz, 2H), 3.02 (rotamer A, s, 3H), 2.94 (rotamer B, s, 3H), 2.75 (m, 2H), 2.47 (rotamer B, s, 3H), 2.44 (rotamer A: s, 3H), 2.33 (m, 2H), 1.69 – 1.56 (m, 2H), 1.39 – 1.18 (m, 10H), 1.13 (s, 1H), 0.92 – 0.84 (m, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.28, 50.01, 49.77, 49.59, 47.52, 36.61, 36.40, 35.98, 33.58, 33.45, 33.02, 31.88, 29.54, 29.49, 29.22, 25.48, 25.09, 22.68, 14.10; **HRMS** (ESI+/qToF) m/z: $[M+H]^+$ Calculated for $C13H29N2O^+$ 229.2280; found 229.2299; Equilibration between rotamers was observed by magnetization transfer via NOESY.

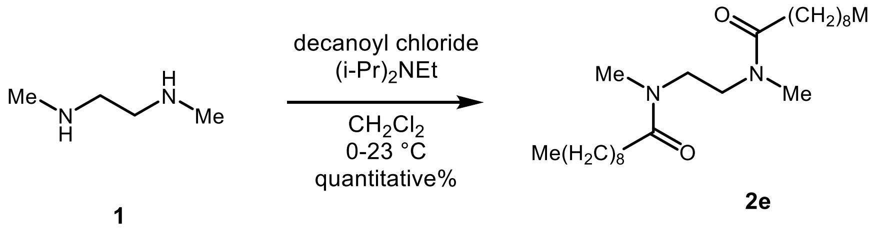


1 **2d**

N,N'-(ethane-1,2-diyl)bis(N-methylnonanamide) (2d). A round bottom flask was sequentially charged with N,N′-dimethylethylenediamine (409 mg, 4.65 mmol, 1 equiv) and *N*,*N*-diisopropylethylamine (1.50 g, 11.6 mmol, 2.5 equiv), and cooled to 0 °C. Nonanoyl chloride (1.81 g, 10.2 mmol, 2.2 equiv) was added dropwise to the mixture, and the reaction was stirred until the reaction warmed up to room temperature. The reaction mixture was partitioned between 50 mL CH_2Cl_2 and 50 mL 1 M aqueous NaOH solution. The organic layer was collected, and the aqueous layer was extracted with CH_2Cl_2 (2x 50 mL). The combined organic fractions were concentrated *in vacuo* to 50 mL volume, and washed with 50 mL 1 M aqueous HCl. The organic layer was collected, and the acidic aqueous layer was extracted with CH_2Cl_2 (2x 50 mL). The combined organic fractions were washed with saturated aqueous NaCl, dried with anhydrous Na_2SO_4, and concentrated *in vacuo* to afford amide **2d** as a yellow solid (1.54 g, 90% yield, mixture of rotamer in $CDCl_3$ A:B:C=3.5:1:1.2): **TLC** (50% ethyl acetate in hexanes), R_f 0.15 (CAM); IR (film) 2953, 2917, 2849, 1640, 1467, 1406, 1281, 1170 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.53 (rotamer A, s, 4H), 3.46 (rotamer B and C, s, 4H), 3.02 (rotamer A, s, 6H), 3.01 (rotamer B, s, 6H), 2.96 (rotamer C, s, 6H), 2.37 – 2.20 (m, 4H), 1.68-1.55 (m, 4H), 1.34 – 1.22 (m, 20H), 0.90 – 0.85 (m, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.37, 173.30, 173.23, 47.31, 46.99, 44.55, 36.94, 35.57, 33.53, 32.66, 31.92, 29.60, 29.58, 29.53, 29.27, 29.23, 25.55, 25.08, 24.96, 22.70, 14.11.; **HRMS** (ESI+/qToF) m/z: [M+Na]+ Calcd for C22H44N2O2Na 391.3300; found 391.3319; Equilibration between rotamers was observed by magnetization transfer via NOESY.



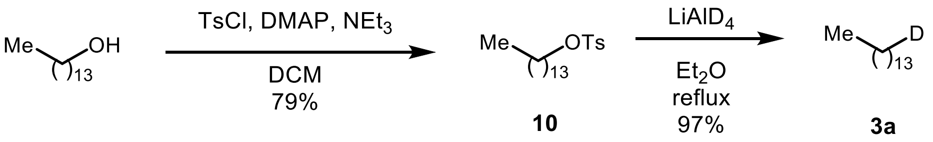
N-methyl-N-(2-(methylamino)ethyl)decanamide (2c). A round bottom flask charged with acetic acid (20 mL) was placed in a room temperature (23 °C) water bath. N,N′-Dimethylethylenediamine (832 mg, 9.44 mmol, 2 equiv) and decanoyl chloride (901 mg, 4.72 mmol, 1 equiv) were sequentially added dropwise to the reaction flask. The reaction was stirred for 2 h and poured into 120 mL 3 M aqueous NaOH, and the pH was verified to be >11. The resulting suspension was extracted with ethyl acetate (3x200 mL), dried with anhydrous Na_2SO_4, and concentrated *in vacuo*. The solid residue was triturated with CH_2Cl_2 (3x50 mL), filtered through a pad of celite, concentrated *in vacuo*, and the residue was purified by flash column chromatography on silica gel deactivated by 5 column volume of 10% methanol in CH_2Cl_2 + 2% triethylamine (gradient elution: 10-20% methanol in CH_2Cl_2) to afford amide **2c** as a colorless oil (486 mg, 43% yield, mixture of rotamer in $CDCl_3$ A:B=1.5:1): **TLC** (10% methanol in CH_2Cl_2 + 2% triethylamine), R_f 0.36 (ninhydrin); **IR** (film) 3312, 2922, 2852, 2794, 1637, 1463, 1401, 1147, 1109 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.50 (rotamer A, t, *J* = 6.5 Hz, 2H), 3.41 (rotamer B, t, *J* = 6.7 Hz, 2H), 3.02 (rotamer A, s, 3H), 2.94 (rotamer B, s, 3H), 2.76 (m, 2H), 2.46 (rotamer B, s, 3H), 2.45 (rotamer A: s, 3H), 2.38-2.20 (m, 2H), 1.70 – 1.55 (m, 2H), 1.38-1.19 (m, 12H), 1.13 (s, 1H), 0.87 (m, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.39, 173.26, 49.71, 49.53, 49.11, 47.15, 36.37, 35.92, 35.85, 33.46, 33.34, 32.92, 31.74, 29.34, 29.14, 25.33, 24.90, 22.51, 13.95; **HRMS** (ESI+/qToF) m/z: $[M+H]^+$ Calculated for $C_{14}H_{31}N_2O^+$ 243.2436; found 243.2463; Equilibration between rotamers was observed by magnetization transfer via NOESY.

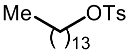


N,N'-(ethane-1,2-diyl)bis(N-methyldecanamide) (2e). A round bottom flask was sequentially charged with N,N′-dimethylethylenediamine (409 mg, 4.65 mmol, 1 equiv) and *N*,*N*-diisopropylethylamine (1.50 g, 11.6 mmol, 2.5 equiv), and cooled to 0 °C. Decanoyl chloride (1.95 g, 10.2 mmol, 2.2 equiv) was added dropwise to the mixture, and the reaction was stirred until the reaction warmed up to room temperature. The reaction mixture was partitioned between 50 mL CH_2Cl_2 and 50 mL 1 M aqueous NaOH solution. The organic layer was collected, and the aqueous layer was extracted with CH_2Cl_2 (2x 50 mL). The combined organic fractions were concentrated *in vacuo* to 50 mL volume, and washed with 50 mL 1 M aqueous HCl. The organic layer was collected, and the acidic aqueous layer was extracted with CH_2Cl_2 (2x 50 mL). The combined organic fractions were washed with saturated aqueous NaCl, dried with anhydrous Na_2SO_4, and concentrated *in vacuo* to afford amide **2e** as a yellow solid (1.84 g, quantitative yield, mixture of rotamer in $CDCl_3$ A:B:C=3.3:1:1.1): **TLC** (50% ethyl acetate in hexanes), R_f 0.15 (CAM); IR (film) 2954, 2917, 2849, 1628, 1468, 1407, 1285, 1170 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.53 (rotamer A, s, 4H), 3.47 (rotamer B and C, s, 4H), 3.02 (rotamer A, s, 6H), 3.01 (rotamer B, s, 6H), 2.96 (rotamer C, s, 6H), 2.39 – 2.19 (m, 4H), 1.67 – 1.52 (m, 4H), 1.35-1.22 (m, 24H), 0.91 – 0.84 (m, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.45, 173.33, 47.33, 47.00, 44.56, 36.94, 35.57, 34.26, 33.54, 32.65, 31.98, 29.61, 29.40, 25.58, 25.10, 24.98, 22.74, 14.13; **HRMS** (ESI+/qToF) m/z: [M+Na]+

Calcd for C24H48N2O2Na 419.3614; found 419.3629. Equilibration between rotamers was observed by magnetization transfer via NOESY.

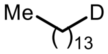
3.4 DEUTERATED *N*-ALKANES AND THEIR HYDROPEROXIDES





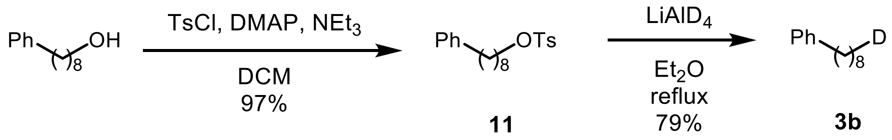
10

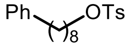
Tetradecyl 4-methylbenzenesulfonate (10). A round bottom flask was sequentially charged with tetradecan-1-ol (2.000 g, 9.329 mmol, 1 equiv), 4-dimethylaminopyridine (22.8 mg, 187 µmol, 0.02 equiv), triethylamine (2.360 g, 3.25 mL, 2.5 equiv, 23.32 mmol), and CH_2Cl_2 (100 mL). p-toluenesulfonyl chloride (2.668 g, 1.5 equiv, 13.99 mmol) was added to the solution, and the reaction was stirred for 15 h. The reaction mixture was poured into saturated $NaHCO_3$ (100 mL), the organic layer was removed, and the aqueous layer was extracted with CH_2Cl_2 (2 x 100 mL). The combined organic layer was dried with anhydrous Na_2SO_4, concentrated *in vacuo*, and the resulting residue was purified by flash column chromatography (gradient elution: 10-50% CH_2Cl_2 in hexanes) to afford tetradecyl 4-methylbenzenesulfonate **10** as a white solid (2.703 g, 79% yield): **TLC** (20% CH_2Cl_2 in hexanes), R_f 0.14 (CAM); **IR** (film) 2917, 2850, 1599, 1471, 1356, 1172 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.83 – 7.75 (m, 2H), 7.37 – 7.31 (m, 2H), 4.02 (t, J = 6.5 Hz, 2H), 2.45 (s, 3H), 1.63 (m, 2H), 1.34 – 1.19 (m, 22H), 0.92 – 0.84 (m, 3H); ^{13}**C NMR** (101 MHz, $CDCl_3$) δ 144.73, 133.48, 129.93, 128.04, 70.85, 32.07, 29.82, 29.80, 29.75, 29.65, 29.54, 29.50, 29.08, 28.98, 25.48, 22.84, 21.77, 14.26; **HRMS** (ESI+/qToF) m/z: $[M+Na]^+$ Calculated for $C21H36O3NaS^+$ 391.2283; found 391.2299.



3a

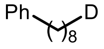
Tetradecane-1-d (3a). A flame-dried flask evacuated and backfilled with N_2 was charged with lithium aluminum deuteride (125.3 mg, 1.1 equiv, 2.984 mmol) and anhydrous Et_2O (30 mL) under N_2 sequentially, and cooled to 0 °C. A solution of tetradecyl 4-methylbenzenesulfonate (1.000 g, 1 equiv, 2.713 mmol) in anhydrous Et_2O was added to the reaction dropwise. The suspension was refluxed for 20 h. The reaction mixture was partitioned between 1 M HCl (50 mL) and hexanes (50 mL), and the organic layer was removed. The aqueous layer was extracted with hexanes (2 x 50 mL), and the combined organic layer was dried with anhydrous Na_2SO_4, and concentrated *in vacuo*. The resulting residue was purified by flash column chromatography (isocratic elution: hexanes) to afford tetradecane-1-d **3a** as a colorless oil (470 mg, 97% yield, 100% D by inverse-gated ^{13}C NMR): **TLC** (hexanes), R_f 0.74 (I_2); **IR** (film) 2922,2853, 2175, 1466, 1377 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 1.36-1.16 (m, 24H), 0.92-0.82 (m, 3H); ^{13}**C NMR** (101 MHz, $CDCl_3$) δ 32.27, 32.24, 30.06, 30.01, 29.72, 23.00, 22.91, 14.31, 14.01 (t, J=19.1 Hz); **LRMS** (GC/EI+) m/z: $[M]^+$ Calculated for $C14H29D^+$ 199.2 found 199.3; ^{2}**H NMR** (61 MHz, $CDCl_3$) δ 0.89.





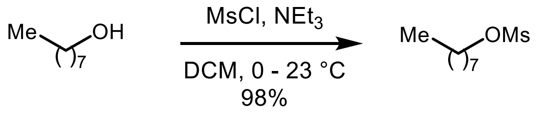
11

8-phenyloctyl 4-methylbenzenesulfonate (11). A round bottom flask was sequentially charged with 8-phenyloctan-1-ol (900 mg, 1 equiv, 4.36 mmol), 4-Dimethylaminopyridine (10.7 mg, 0.02 equiv, 87.2 µmol), triethylamine (1.10 g, 1.52 mL, 2.5 equiv, 10.9 mmol), and CH_2Cl_2 (50 mL). p-toluenesulfonyl chloride (1.25 g, 1.5 equiv, 6.54 mmol) was added to the solution, and the reaction was stirred for 15 h. The reaction mixture was poured into saturated $NaHCO_3$ (50 mL), the organic layer was removed, and the aqueous layer was extracted with CH_2Cl_2 (2 x 50 mL). The combined organic layer was dried with an anhydrous Na_2SO_4, concentrated *in vacuo*, and the resulting residue was purified by flash column chromatography (gradient elution: 20-50% CH_2Cl_2 in hexanes) to afford 8-phenyloctyl 4-methylbenzenesulfonate **11** as a colorless oil (1.57 g, 97% yield): **TLC** (20% CH_2Cl_2 in hexanes), R_f 0.38 (UV/CAM); **IR** (film) 2917, 2850, 1599, 1471, 1356, 1190, 1172, 1097 cm^{-1}; **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.82 – 7.75 (m, 2H), 7.33 (d, J = 8.1 Hz, 2H), 7.31 – 7.23 (m, 2H), 7.17 (td, J = 5.4, 2.9 Hz, 3H), 4.01 (t, J = 6.5 Hz, 2H), 2.63 – 2.54 (m, 2H), 2.44 (s, 3H), 1.59 (m, 4H), 1.26 (m, 8H).; **^{13}C NMR** (101 MHz, CDCl$_3$) δ 144.74, 142.91, 133.43, 129.92, 128.51, 128.37, 128.02, 125.73, 70.79, 70.71, 36.05, 31.53, 29.36, 29.24, 28.97, 28.94, 25.44, 21.75; **HRMS** (ESI+/qToF) m/z: [M+Na]$^+$ Calculated for C21H28O3NaS$^+$ 383.1657; found 383.1669.



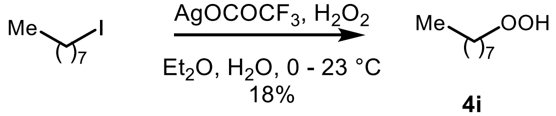
3b

(Octyl-8-*d*)benzene (3b). A flame-dried flask evacuated and backfilled with N_2 was charged with lithium aluminum deuteride (128.1 mg, 1.1 equiv, 3.051 mmol) and anhydrous Et_2O (55 mL) under N_2 sequentially, and cooled to 0 °C. A solution of 8-phenyloctyl 4-methylbenzenesulfonate (1.000 g, 1 equiv, 2.774 mmol) in anhydrous Et_2O (20 mL) was added to the reaction dropwise. The suspension was refluxed for 20 h. The reaction mixture was partitioned between 1 M HCl (50 mL) and hexanes (50 mL), and the organic layer was removed. The aqueous layer was extracted with hexanes (2 x 50 mL), and the combined organic layer was dried with anhydrous Na_2SO_4, and concentrated *in vacuo*. The resulting residue was purified by flash column chromatography (isocratic elution: hexanes) to afford (octyl-8-d)benzene **3b** as a colorless oil (420 mg, 79% yield, 100% D by ^{1}H NMR): **TLC** (hexanes), R_f 0.49 (UV/$KMnO_4$); **IR** (film) 3085, 3063, 3027, 2926, 2855, 2173, 1605, 1496, 1453 cm^{-1}; **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.33 – 7.25 (m, 2H), 7.18 (d, J = 7.3 Hz, 3H), 2.61 (t, J = 7.7 Hz, 2H), 1.78 – 1.54 (m, 2H), 1.50 – 1.20 (m, 10H), 0.87 (m, 2H).; **^{13}C NMR** (101 MHz, CDCl$_3$) δ 143.06, 128.54, 128.36, 125.69, 77.48, 77.16, 76.84, 36.19, 32.07, 31.73, 29.69, 29.55, 29.48, 22.78, 13.96 (t, *J* = 19.1 Hz); **LRMS** (GC/EI+) m/z: [M]$^+$ Calculated for C14H21D$^+$ 191.2; found 191.2; **^{2}H NMR** (61 MHz, CDCl$_3$) δ 0.89.



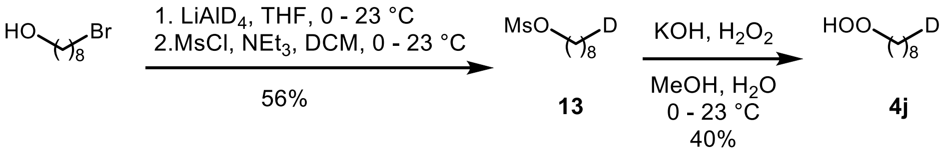
12

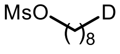
Octyl methanesulfonate (12). A round bottom flask was charged with octan-1-ol (5.000 g, 6.05 mL, 1 equiv, 38.39 mmol), CH_2Cl_2 (100 mL), methanesulfonyl chloride (4.837 g, 3.291 mL, 1.1 equiv, 42.23 mmol) sequentially and cooled to 0 °C. Triethylamine (4.662 g, 6.42 mL, 1.2 equiv, 46.07 mmol) was added to the reaction mixture dropwise, and the reaction was warmed to room temperature, and stirred for 24 h. The reaction was poured into 1 M HCl (100 mL), and the organic layer was removed. The aqueous layer was extracted with CH_2Cl_2 (2 x 100 mL), and the combined organic layer was washed with saturated $NaHCO_3$ (100 mL), dried with anhydrous Na_2SO_4, and concentrated *in vacuo*. The solid residue was triturated with hexanes (100 mL), filtered through a pad of celite, and concentrated *in vacuo* to afford octyl methanesulfonate **X** as a yellow oil (7.8438 g, 98% yield): **TLC** (10% ethyl acetate/hexanes), R_f 0.13 (CAM); **IR** (film) 3028, 2927, 2857, 1468, 1353, 1173 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.96 (t, *J* = 6.6 Hz, 2H), 2.74 (s, 3H), 1.55 – 1.43 (m, 2H), 1.20 – 0.96 (m, 10H), 0.67 – 0.58 (m, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 70.34, 37.47, 37.45, 31.81, 29.24, 29.18, 29.09, 25.53, 22.71, 14.16; **LRMS** (GC/EI+) m/z: $[M]^+$ Calculated for $C9H20O3S^+$ 208.1 found 208.1.



4i

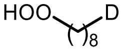
1-hydroperoxyoctane (4i). An oven-dried 3-dram vial was charged with 1-iodooctane (1.000 g, 752 µL, 1 equiv, 4.164 mmol) and dry Et_2O (4 mL) sequentially, and cooled to 0 °C. Silver trifluoroacetate (1.104 g, 1.2 equiv, 4.997 mmol) was added to the reaction in small portions, followed by hydrogen peroxide dropwise (708.2 mg, 638.0 µL, 30% Wt, 1.5 equiv, 6.247 mmol). The reaction was warmed to room temperature and stirred for 3 h. The reaction was filtered through a pad of celite, and the filtrate was added to saturated $NaHCO_3$ (10 mL). The organic layer was removed and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic layer was dried with anhydrous Na_2SO_4, and concentrated *in vacuo*. The solid residue was purified by flash column chromatography on silica gel (gradient elution: 0-40% ethyl acetate in hexanes) to afford 1-hydroperoxyoctane **4i** as a colorless oil (111 mg, 18% yield): **TLC** (15% ethyl acetate/hexanes), R_f 0.37 (KMnO4); **IR** (film) 3384, 2924, 2855, 1655, 1467, 1378 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ7.77 (s, 1H), 4.02 (t, J = 6.6 Hz, 2H), 1.63 (m, 2H), 1.42 – 1.18 (m, 10H), 0.95 – 0.82 (m, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 77.38, 31.93, 29.53, 29.33, 27.70, 26.05, 22.78, 14.21; **LRMS** (GC/EI+) m/z: $[M]^+$ Calculated for $C8H18O2^+$ 146.1 found 146.0.





13

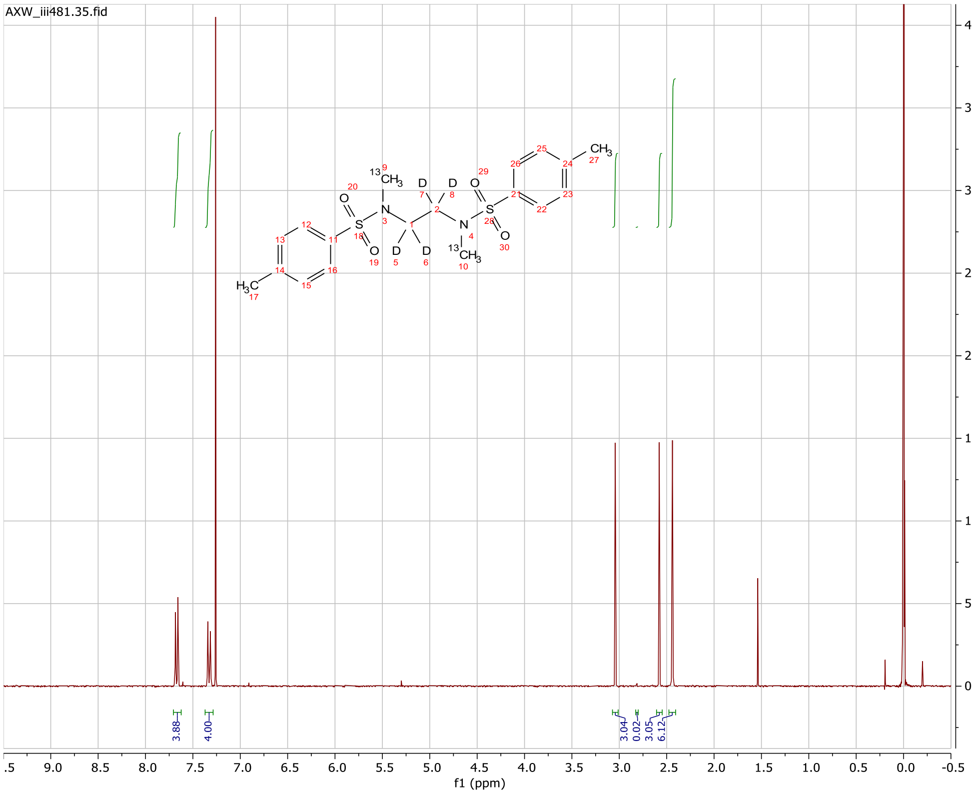
Octyl-8-d methanesulfonate (13). A flame-dried round bottom flask was charged with 8-bromooctan-1-ol (1.66 g, 1.36 mL, 1 equiv, 7.94 mmol), and dry THF (40 mL) sequentially, and cooled to 0 °C. LiAlD4 (500 mg, 1.50 Eq, 11.9 mmol) was added to the reaction in portions, and the reaction was warmed to room temperature and stirred for 18 h. The reaction was partitioned between saturated NH_4Cl (50 mL) and Et_2O (50 mL), and the organic layer was removed. The aqueous layer was extracted with Et_2O (2 x 50 mL), and the combined organic layer was dried with anhydrous Na_2SO_4, and concentrated *in vacuo* to afford the crude reduced n-octanol-d1 (790 mg), which was used without purification. The solid residue was transferred to a round bottom flask. To the reaction vessel CH_2Cl_2 (15 mL), and methanesulfonyl chloride (758.7 mg, 516.1 µL, 1.1 equiv, 6.624 mmol) was added sequentially, and cooled to 0 °C. Triethylamine (731.2 mg, 1.01 mL, 1.2 Eq, 7.226 mmol) was added dropwise to the reaction. The reaction was warmed to room temperature, and stirred for 24 h. 1 M HCl (50 mL) was added to the reaction, and the organic layer was removed. The aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL), and the combined organic layer was washed with $NaHCO_3$ (50 mL), dried with anhydrous Na_2SO_4, and concentrated *in vacuo*. The solid residue was triturated with hexanes (50 mL), filtered through a pad of celite, concentrated *in vacuo,* and the residue was purified by flash column chromatography on silica gel (gradient elution: 0-40% ethyl acetate in hexanes) to afford octyl-8-d methanesulfonate **13** as a colorless oil (925 mg, 56% yield over 2 steps): **TLC** (25% ethyl acetate/hexanes), R_f 0.38 (CAM); **IR** (film) 3031, 2928, 2857, 2174, 1467, 1352, 1173 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.22 (t, J = 6.6 Hz, 2H), 3.00 (s, 3H), 1.75 (m, J = 7.7, 6.6 Hz, 2H), 1.47 – 1.18 (m, 10H), 0.86 (m, J = 4.1, 1.9 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 70.34, 37.48, 31.80, 29.25, 29.20, 29.10, 25.54, 22.63, 14.06, 13.87, 13.68; **LRMS** (GC/EI+) m/z: $[M]^+$ Calculated for $C9H19DO3S^+$ 209.1 found 208.9; **^{2}H NMR** (61 MHz, $CDCl_3$) δ 0.88.

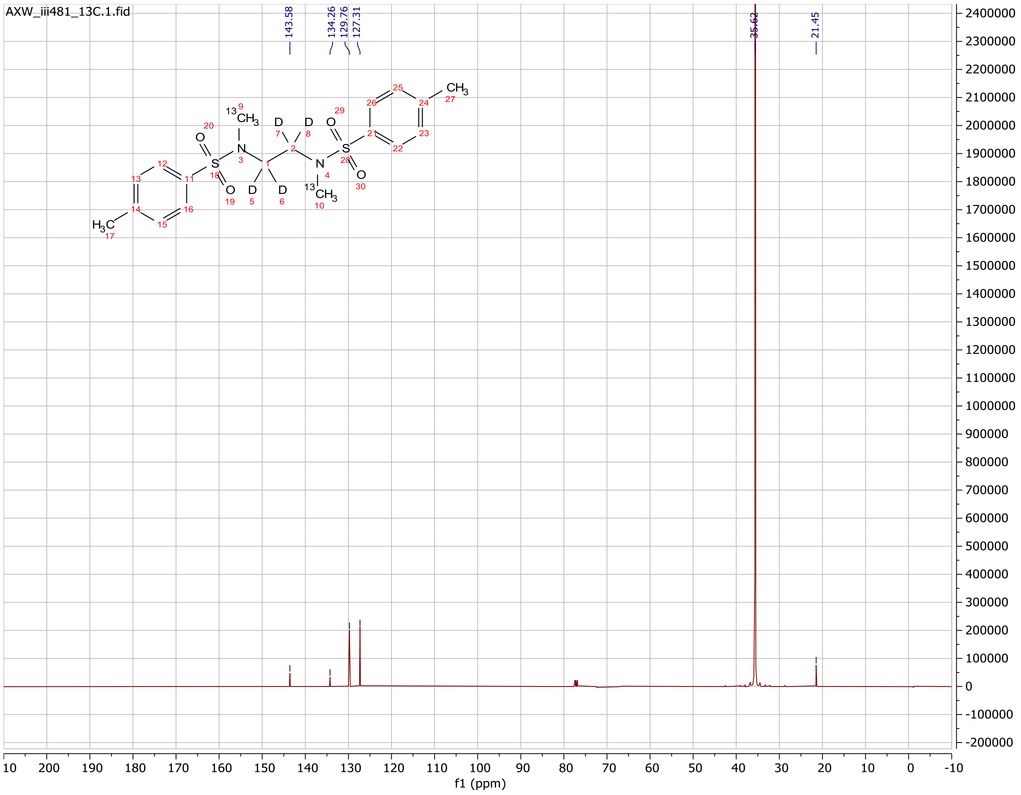


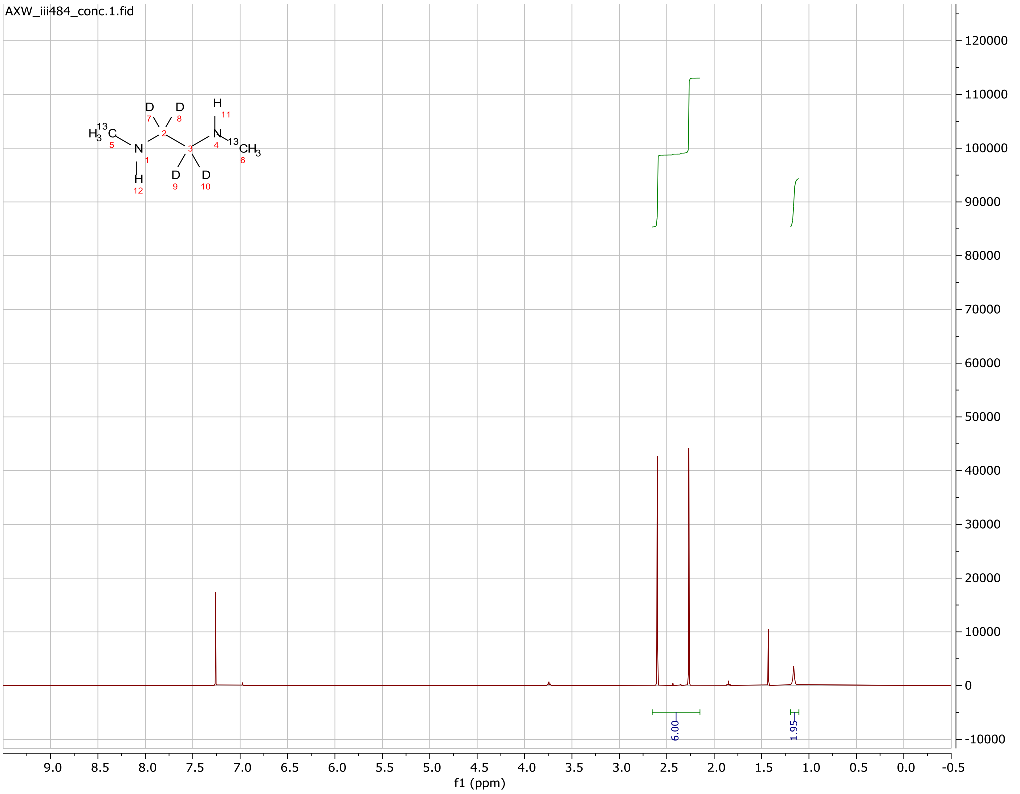
4j

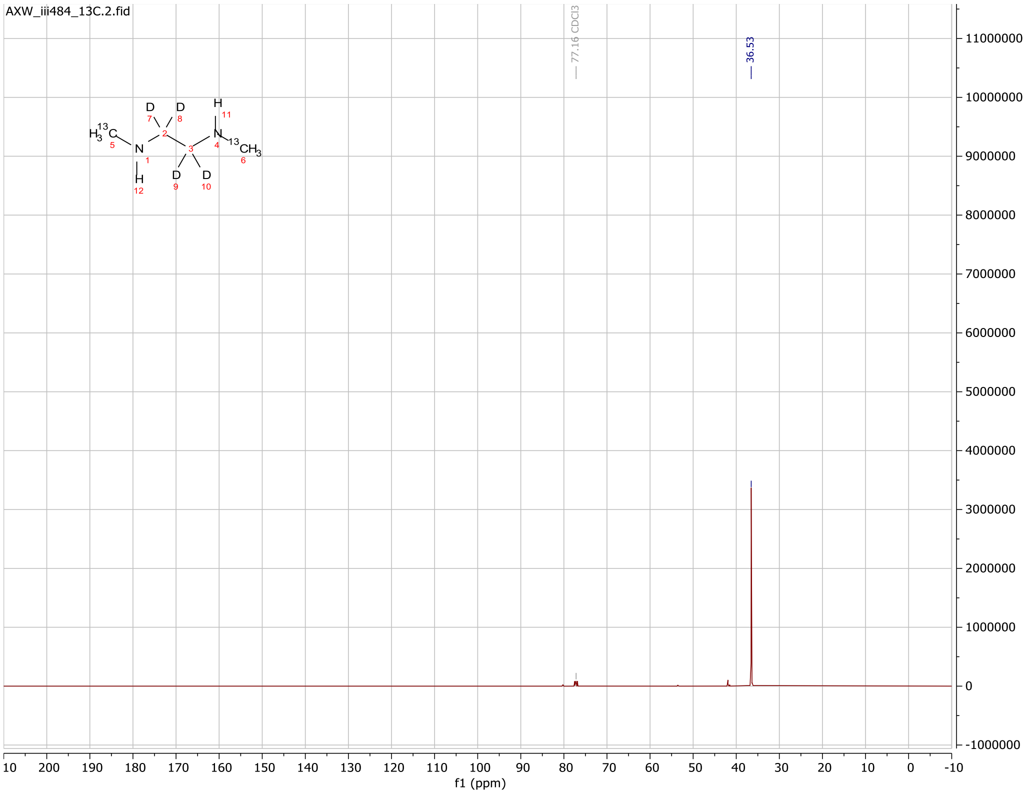
1-hydroperoxyoctane-8-*d* (**4j**). A round bottom flask was charged with octyl-8-d methanesulfonate (500 mg, 1 equiv, 2.39 mmol), methanol (7.2 mL), water (0.8 mL), hydrogen peroxide (1.08 g, 976 µL, 30% Wt, 4 Eq, 9.55 mmol) sequentially, and cooled to 0 °C. A solution of potassium hydroxide (298 mg, 90% Wt, 2 Eq, 4.78 mmol) in water (0.5 mL) was added to the reaction dropwise, and the reaction was warmed to room temperature and stirred for 20 h. The reaction was partitioned between Et_2O (50 mL) and H_2O (50 mL), and the organic layer was removed. The aqueous layer was extracted with Et_2O (3 x 50 mL), and the combined organic layer was dried with anhydrous Na_2SO_4, and concentrated *in vacuo*. The solid residue was purified by flash column chromatography on silica gel (gradient elution: 0-40% ethyl acetate in hexanes) to afford 1-hydroperoxyoctane-8-*d* **4j** (colorless liquid, 142 mg, 40% yield). **TLC** (15% ethyl acetate/hexanes), R_f 0.37 (KMnO4); **IR** (film) 3378, 2926, 2856, 2174, 1650, 1465, 1374 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 4.02 (t, J = 6.6 Hz, 2H), 1.71 – 1.58 (m, 2H), 1.44 – 1.20 (m, 10H), 0.94 – 0.78 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 31.76, 29.40, 29.20, 27.57, 25.91, 22.56, 13.94, 13.79, 13.64; **LRMS** (GC/EI+) m/z: $[M]^+$ Calculated for $C8H17DO2^+$ 147.1 found 146.8; **^{2}H NMR** (61 MHz, $CDCl_3$) δ 0.89.

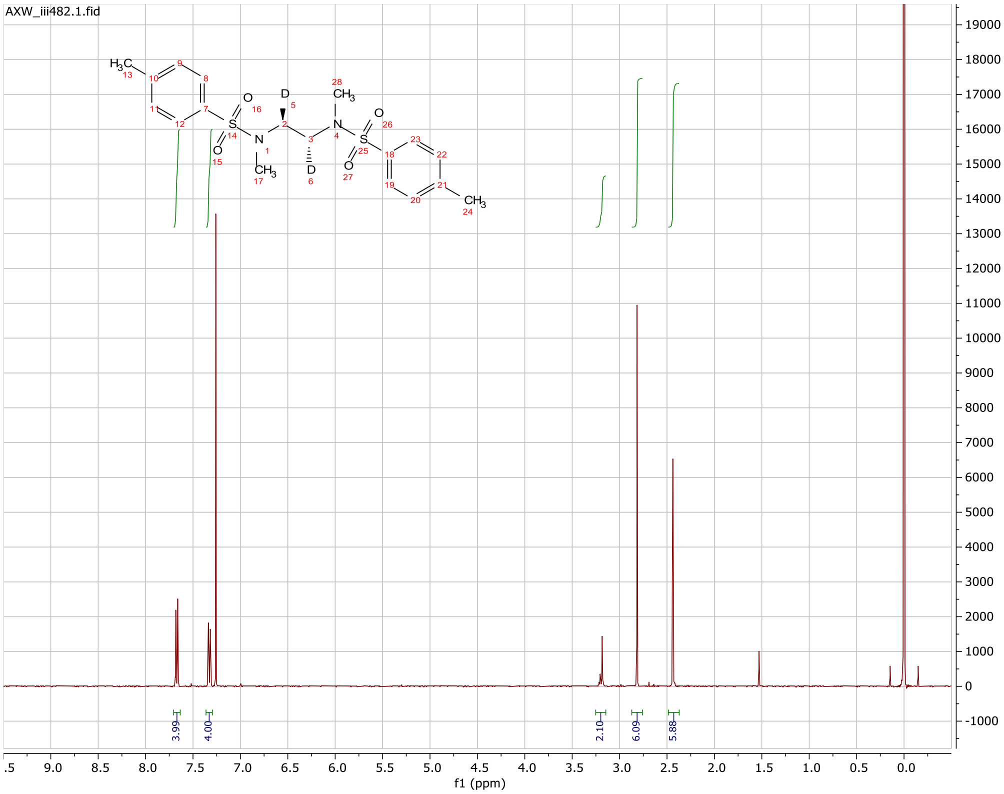
3.5 ^{1}H AND ^{13}C NMR SPECTRA OF NEW COMPOUNDS

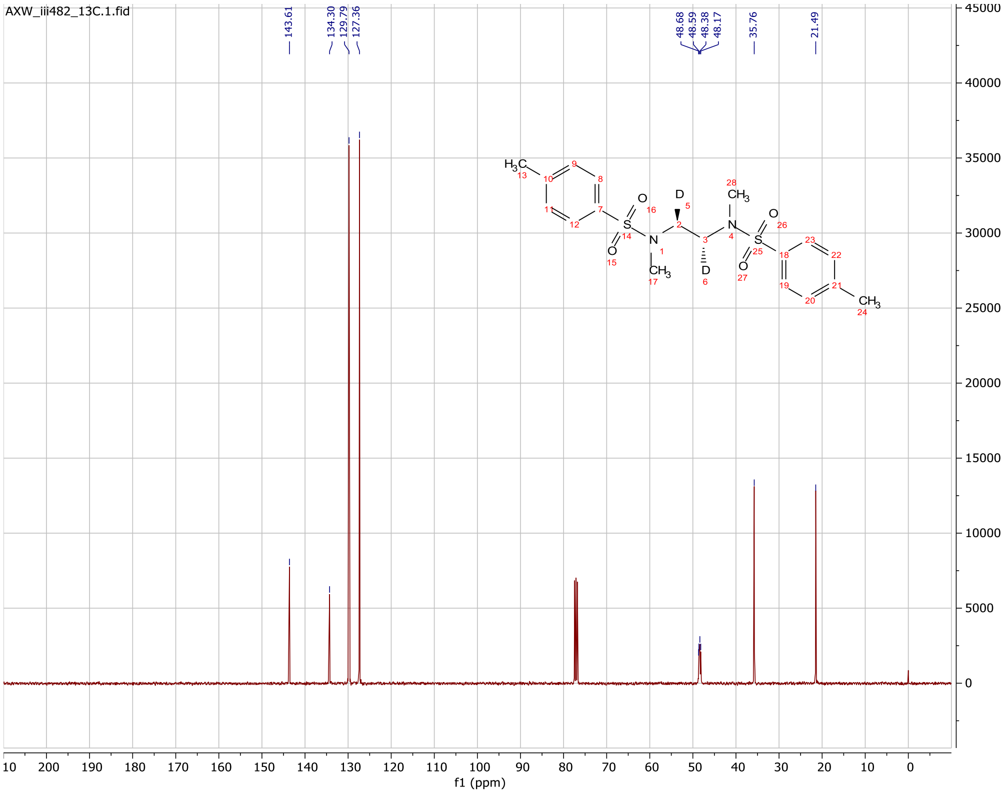


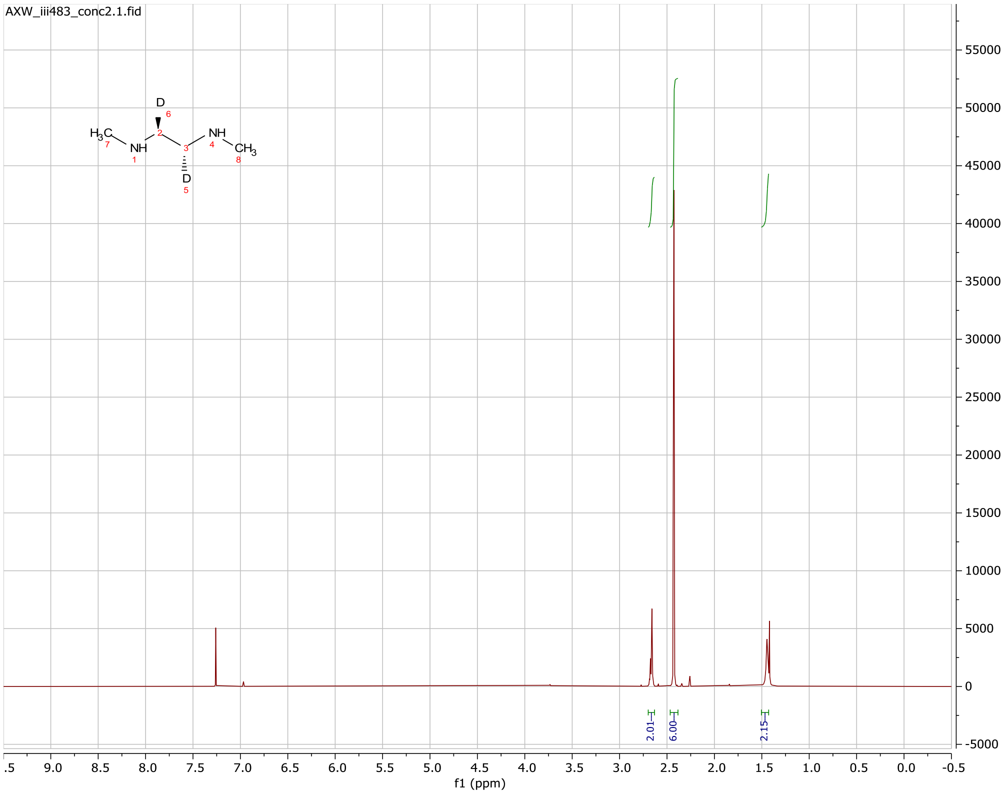



AXW_iii484_conc.1.fid
H3 13C 5 N 1 H 12 D 7 D 8 2 3 D 9 D 10 N 4 H 11 13CH3 6
6.00
1.95
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

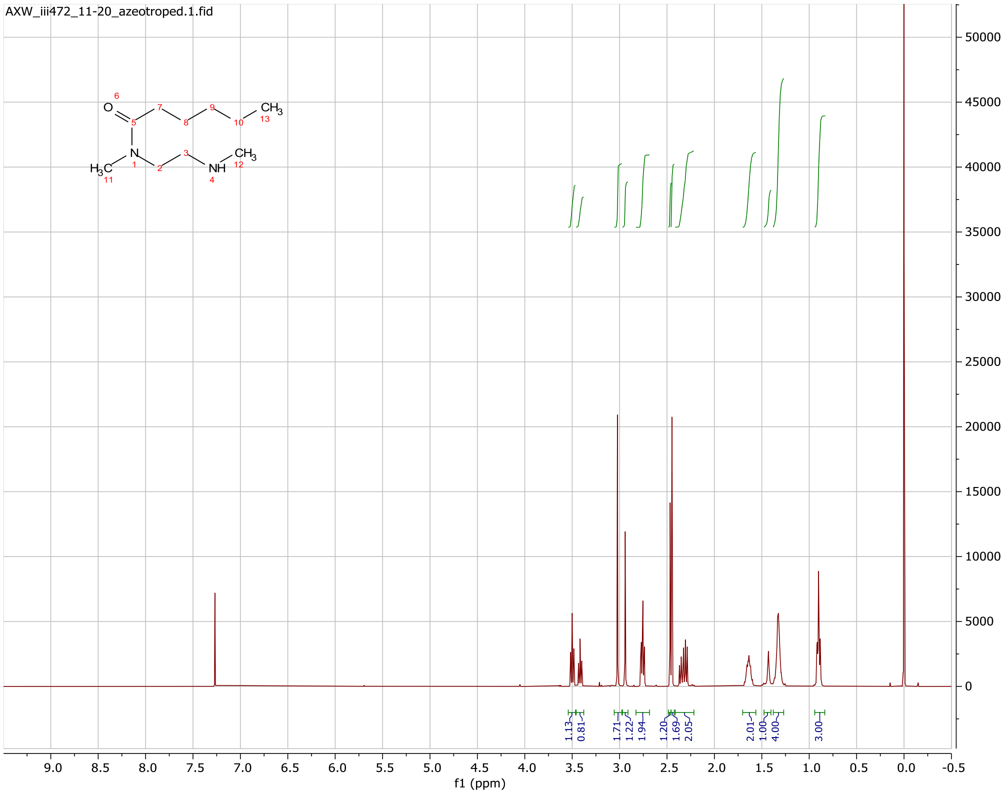

AXW_iii484_13C.2.fid
77.16 CDCl3
36.53
H3 13C 5 N 1 H 12 D 7 D 8 2 3 D 9 D 10 N 4 H 11 13CH3 6
11000000
10000000
9000000
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
-1000000
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

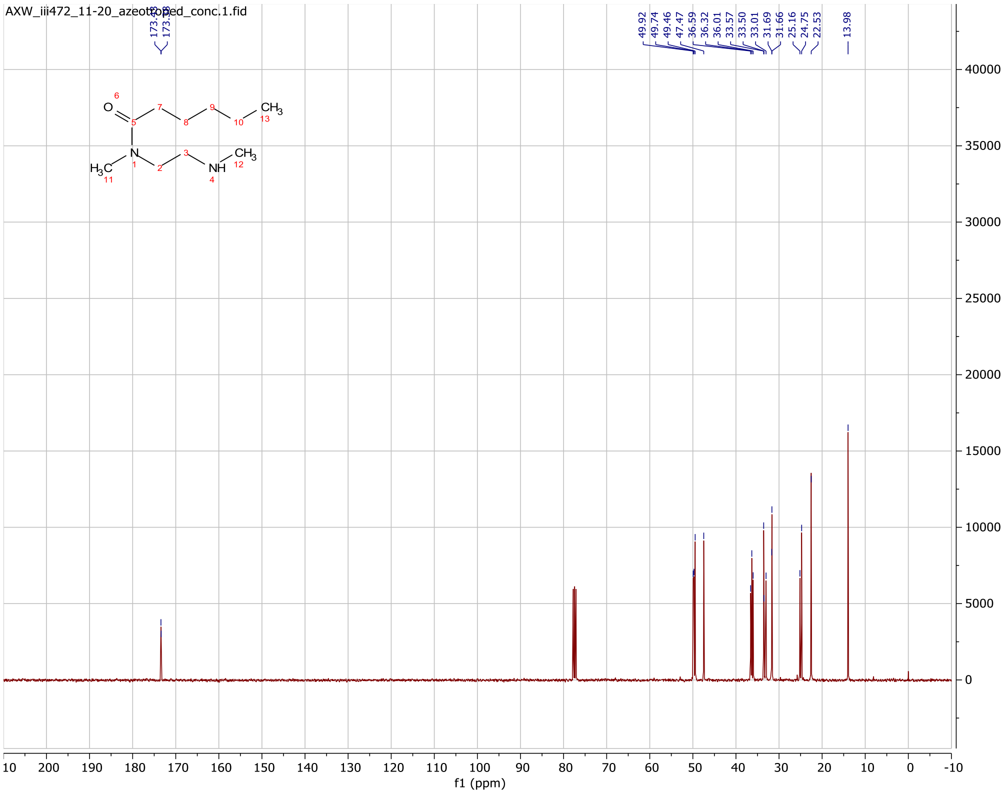

AXW_iii482.1.fid
3.99
4.00
2.10
6.09
5.88
f1 (ppm)

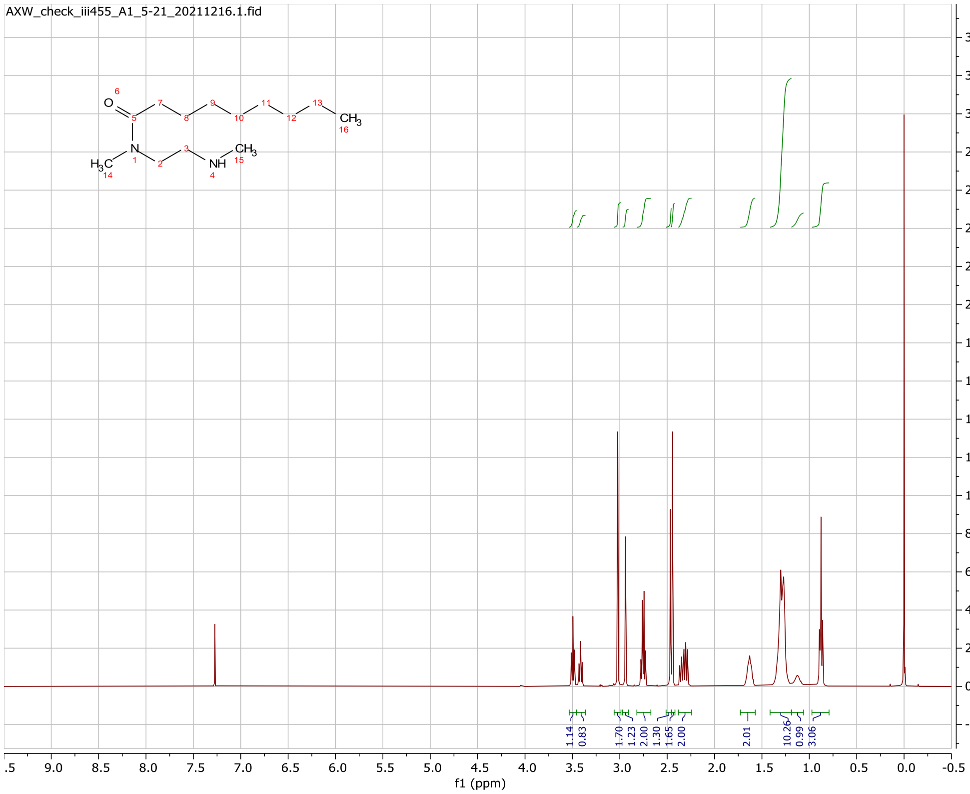

AXW_iii482_13C.1.fid
143.61
134.30
129.79
127.36
48.68
48.59
48.38
48.17
35.76
21.49
f1 (ppm)

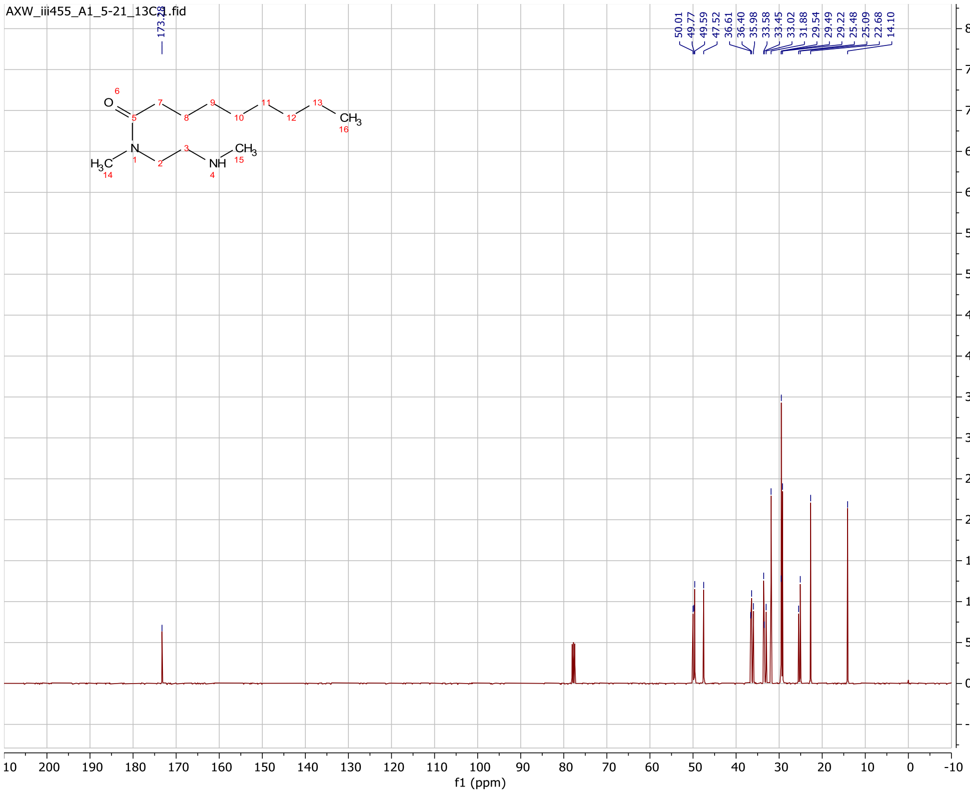

AXW_iii483_conc2.1.fid
D
6
H3C
7
NH
1
2
3
NH
4
CH3
8
D
5
2.01
6.00
2.15
f1 (ppm)

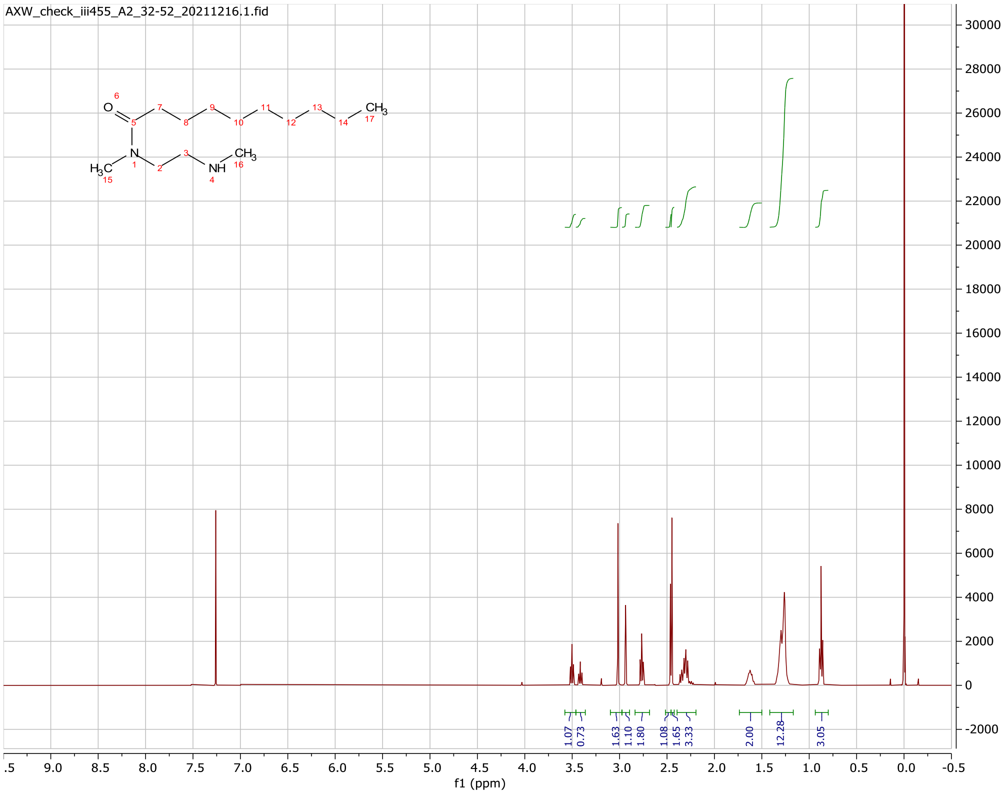

AXW_iii483_conc2_13C.5.fid
Carbon CPD decoupled
51.42
51.02
36.58
D
6
H3C
7
NH
1
2
3
NH
4
CH3
8
D
5
f1 (ppm)

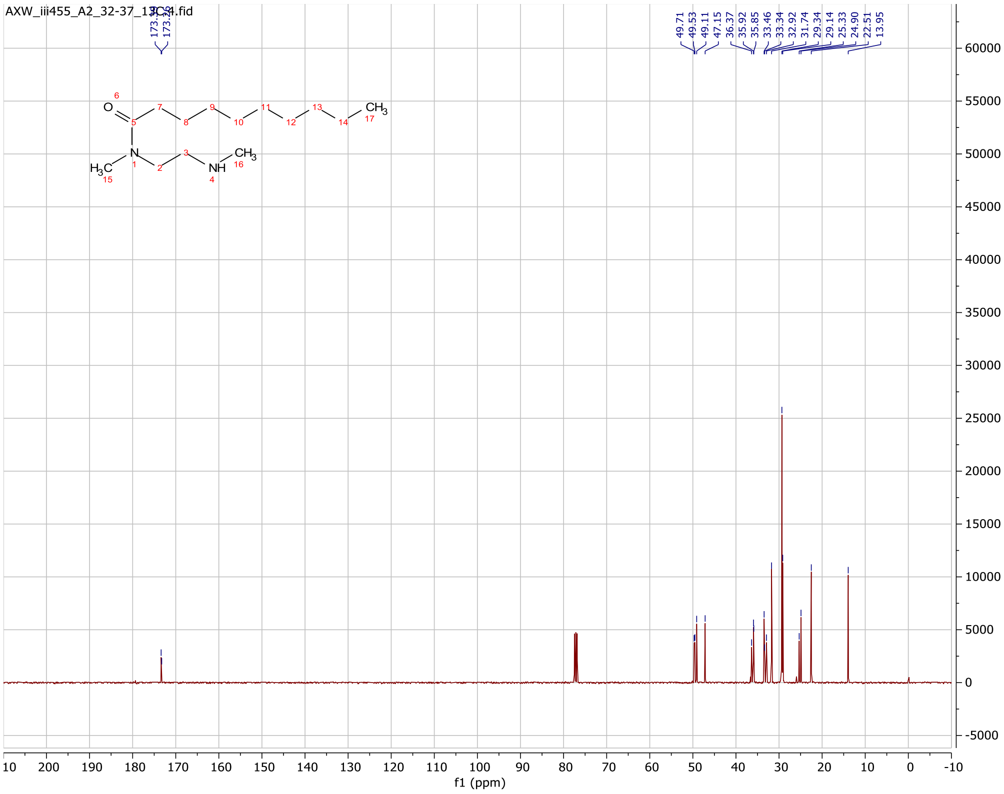

AXW_iii472_11-20_azeotroped.1.fid
O
6
5
7
8
9
10
CH3
13
N
1
H3C
11
2
3
NH
4
CH3
12
1.13
0.81
1.71
1.22
1.94
1.20
1.69
2.05
2.01
1.00
4.00
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0

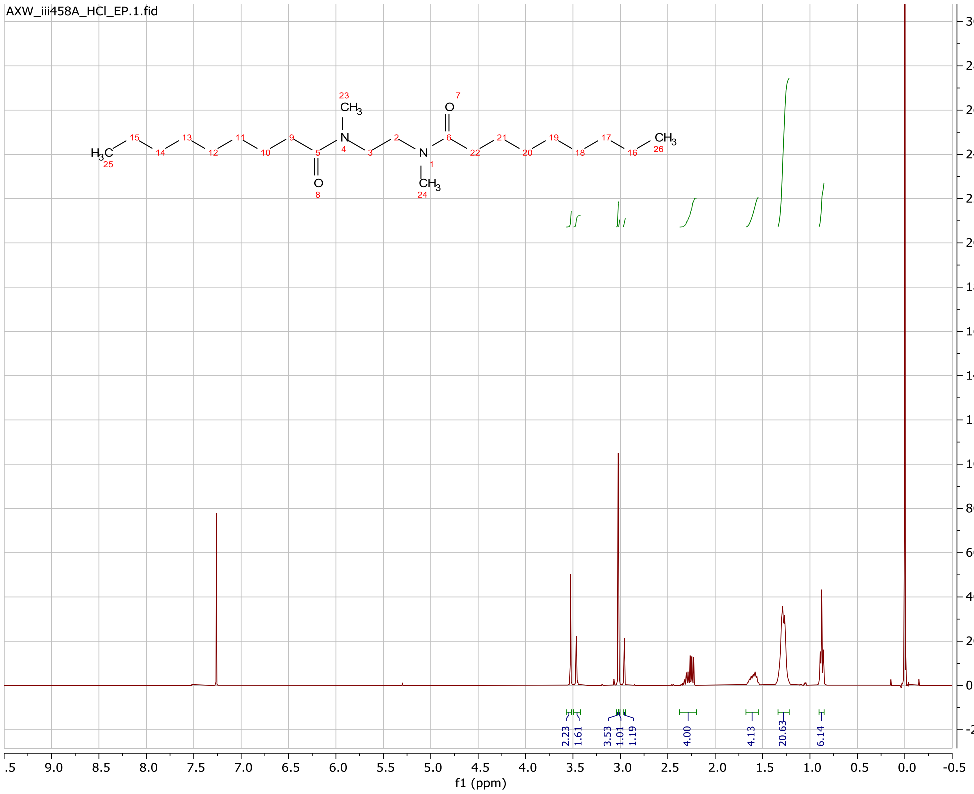

AXW_iii472_11-20_azeotroped_conc.1.fid
173.43
173.38
49.92
49.74
49.46
47.47
36.59
36.32
36.01
33.57
33.50
33.01
31.69
31.66
25.16
24.75
22.53
13.98
O
6
5
7
8
9
10
CH3
13
N
1
H3C
11
2
3
NH
4
CH3
12
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
40000
35000
30000
25000
20000
15000
10000
5000
0

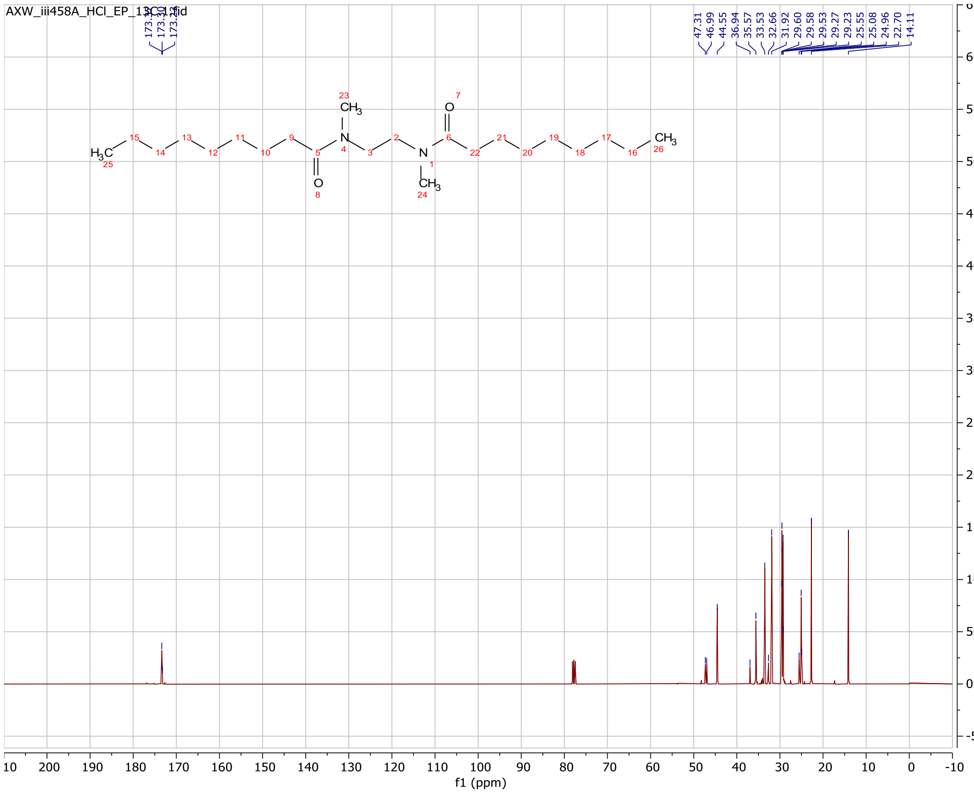

AXW_check_iii455_A1_5-21_20211216.1.fid
6
O
5
7
8
9
10
11
12
13
CH3
16
N
1
H3C
14
2
3
NH
4
CH3
15
1.14
0.83
1.70
1.23
2.00
1.30
1.65
2.00
2.01
10.26
0.99
3.06
34000
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

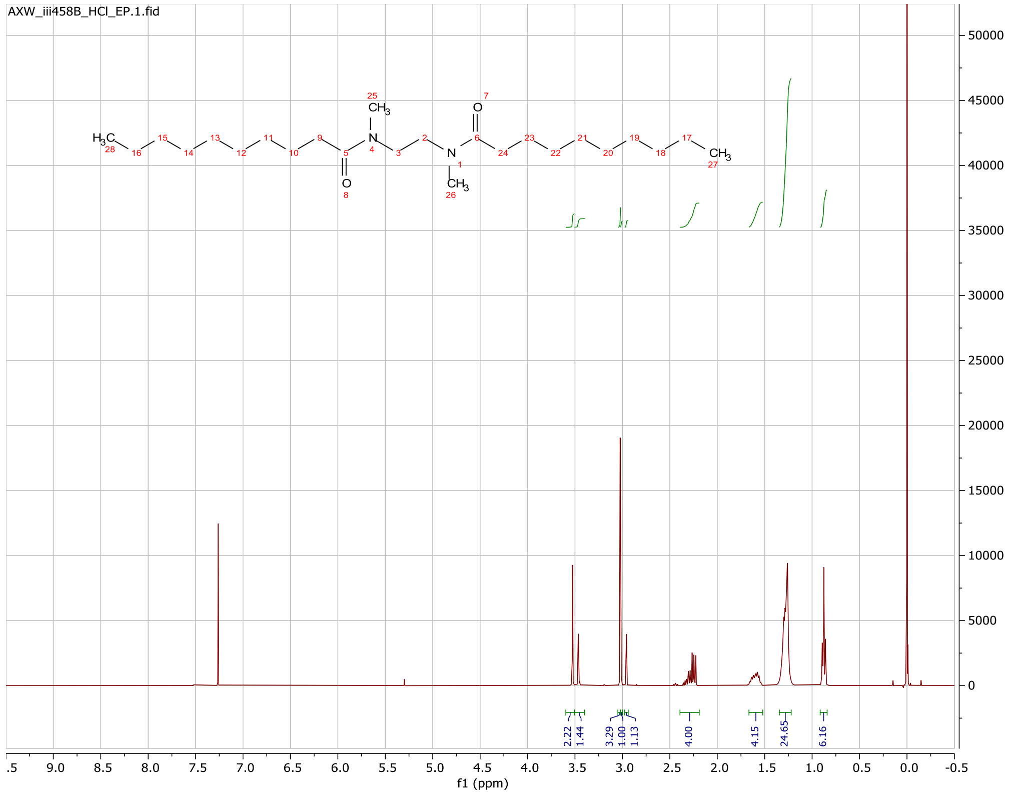

AXW_iii455_A1_5-21_13C-1.fid
173.28
50.01
49.77
49.59
47.52
36.61
36.40
35.98
33.58
33.45
33.02
31.88
29.54
29.49
29.22
25.48
25.09
22.68
14.10
6
O
5
7
8
9
10
11
12
13
CH3
16
N
1
H3C
14
2
3
NH
4
CH3
15
80000
75000
70000
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

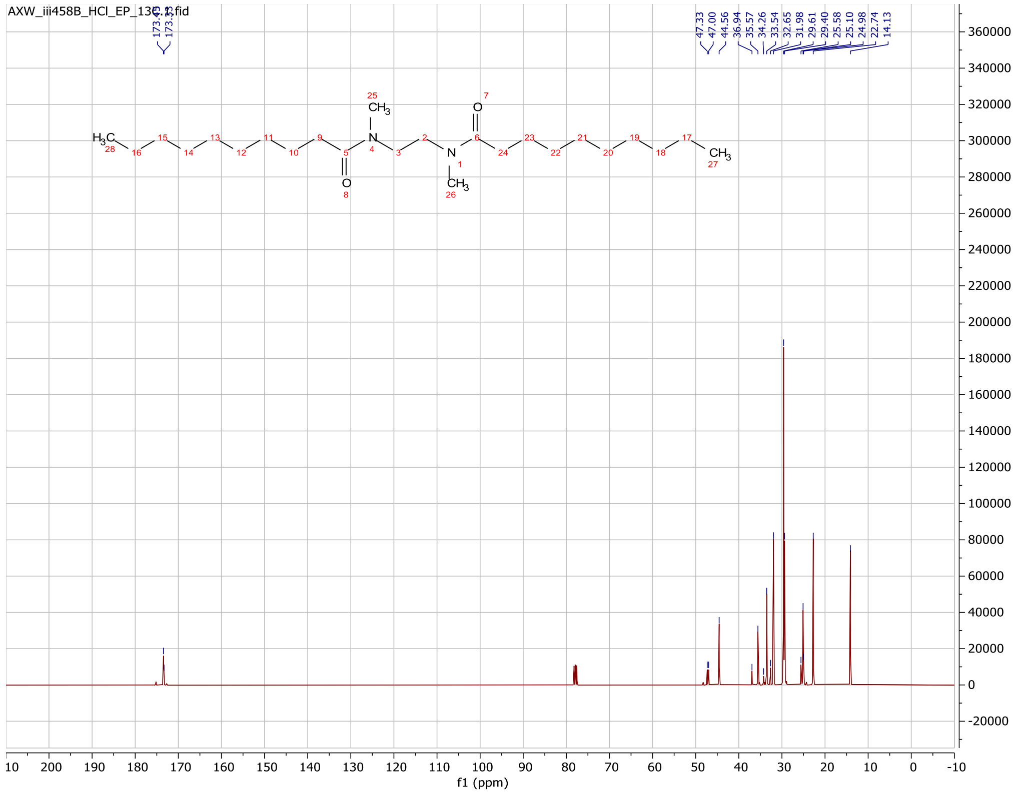

AXW_check_iii455_A2_32-52_20211216.1.fid
O 6, 5, 7, 8, 9, 10, 11, 12, 13, 14, CH3 17, N 1, H3C 15, 2, 3, NH 4, CH3 16
1.07
0.73
1.63
1.10
1.80
1.08
1.65
3.33
2.00
12.28
3.05
f1 (ppm)

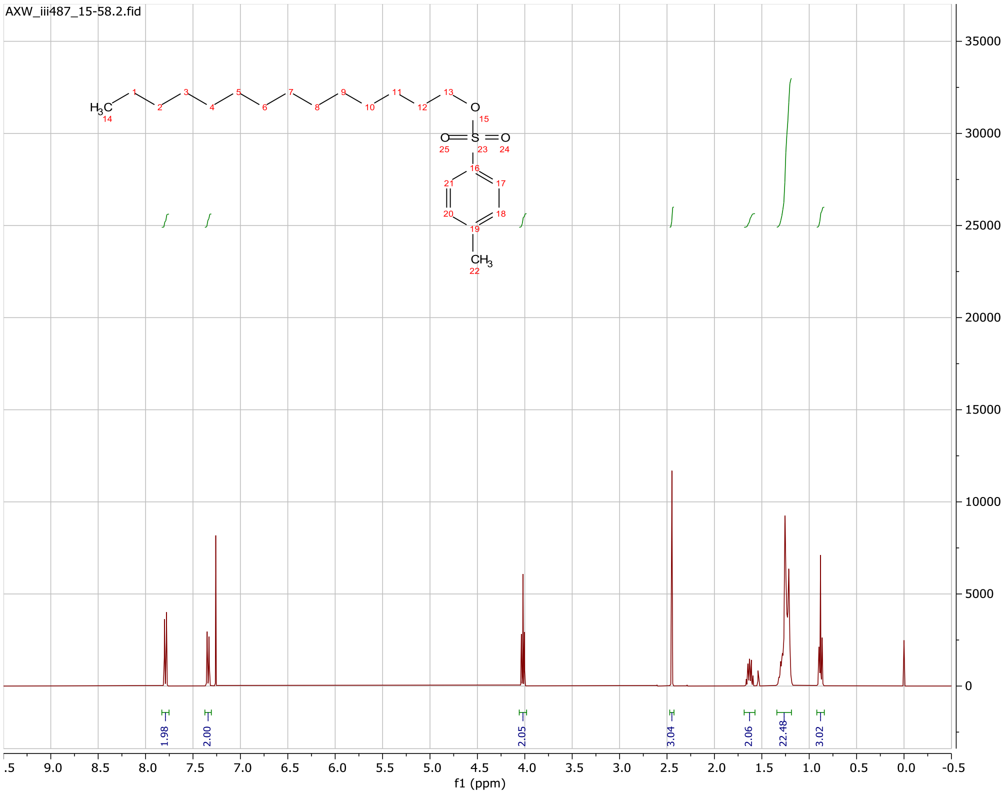

AXW_iii455_A2_32-37_13C.4.fid
173.39
173.26
49.71
49.53
49.11
47.15
36.37
35.92
35.85
33.46
33.34
32.92
31.74
29.34
29.14
25.33
24.90
22.51
13.95
O 6, 5, 7, 8, 9, 10, 11, 12, 13, 14, CH3 17, N 1, H3C 15, 2, 3, NH 4, CH3 16
f1 (ppm)

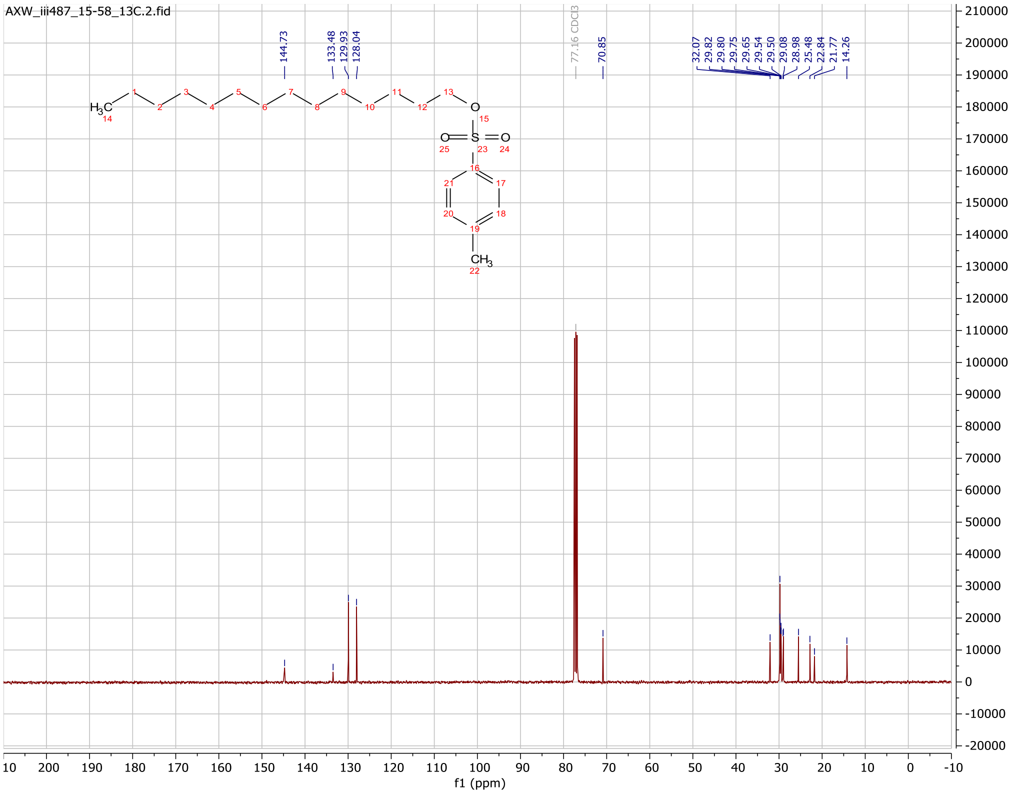

AXW_iii458A_HCl_EP.1.fid
H3C 25 15 14 13 12 11 10 9 5 O 8 N 4 CH3 23 3 2 N 1 CH3 24 6 O 7 22 21 20 19 18 17 16 CH3 26
2.23
1.61
3.53
1.01
1.19
4.00
4.13
20.63
6.14
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

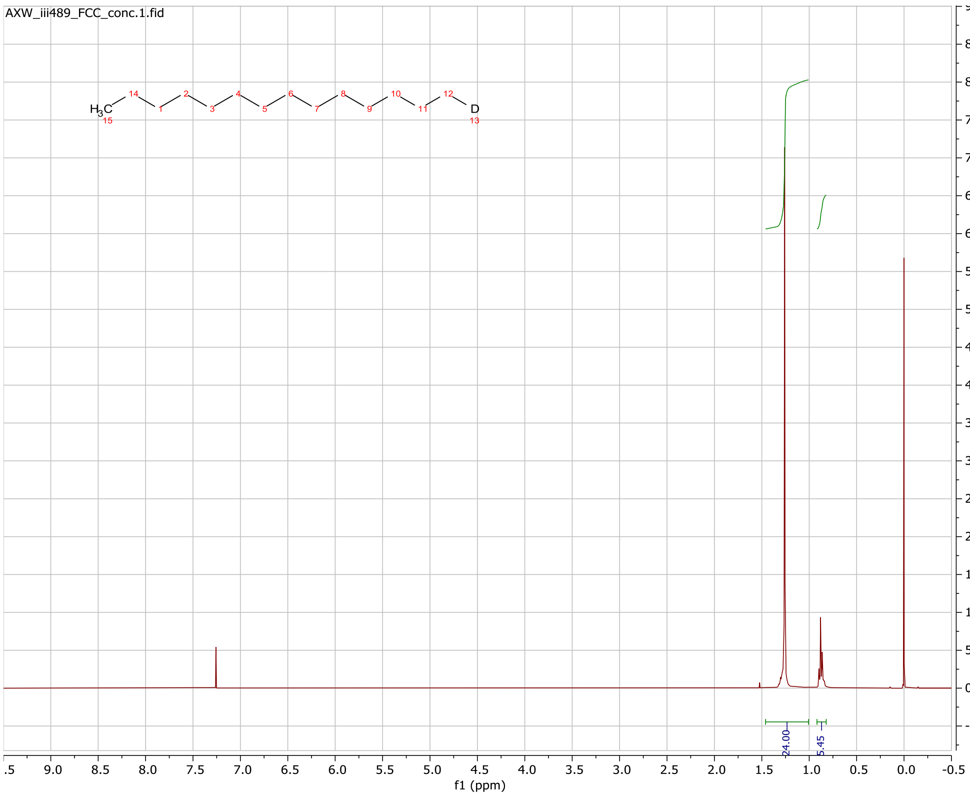

AXW_iii458A_HCl_EP_13C.1.fid
173.3
173.30
173.2
47.31
46.99
44.55
36.94
35.57
33.53
32.66
31.92
29.60
29.58
29.53
29.27
29.23
25.55
25.08
24.96
22.70
14.11
H3C 25 15 14 13 12 11 10 9 5 O 8 N 4 CH3 23 3 2 N 1 CH3 24 6 O 7 22 21 20 19 18 17 16 CH3 26
650000
600000
550000
500000
450000
400000
350000
300000
250000
200000
150000
100000
50000
0
-50000
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

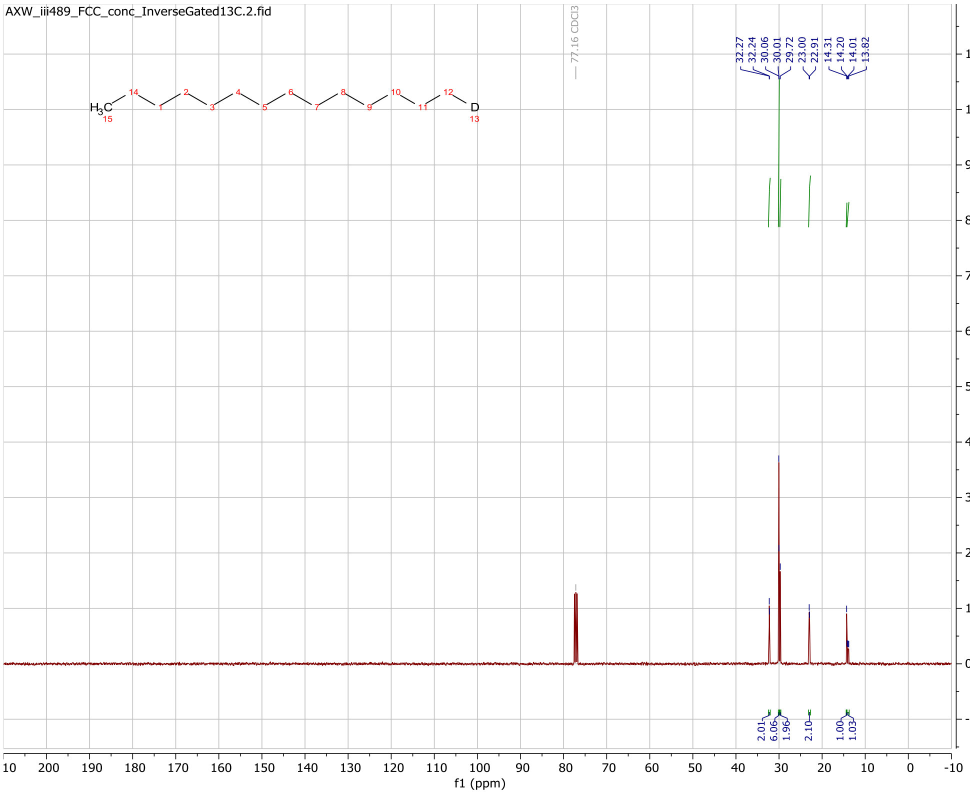

AXW_iii458B_HCl_EP.1.fid
25
CH3
7
O
H3C
28
16
15
14
13
12
11
10
9
5
O
8
N
4
3
2
N
1
CH3
26
6
24
23
22
21
20
19
18
17
CH3
27
2.22
1.44
3.29
1.00
1.13
4.00
4.15
24.65
6.16
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

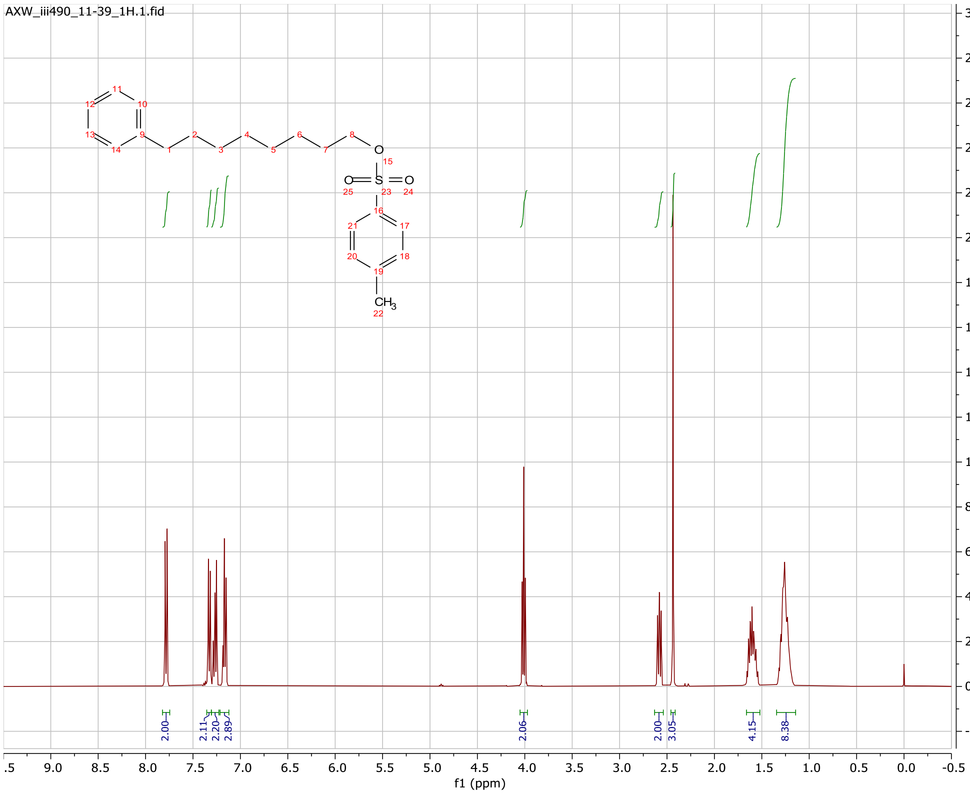

AXW_iii458B_HCl_EP_13C.1.fid
173.45
173.33
47.33
47.00
44.56
36.94
35.57
34.26
33.54
32.65
31.98
29.61
29.40
25.58
25.10
24.98
22.74
14.13
25
CH3
7
O
H3C
28
16
15
14
13
12
11
10
9
5
O
8
N
4
3
2
N
1
CH3
26
6
24
23
22
21
20
19
18
17
CH3
27
360000
340000
320000
300000
280000
260000
240000
220000
200000
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
-20000
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

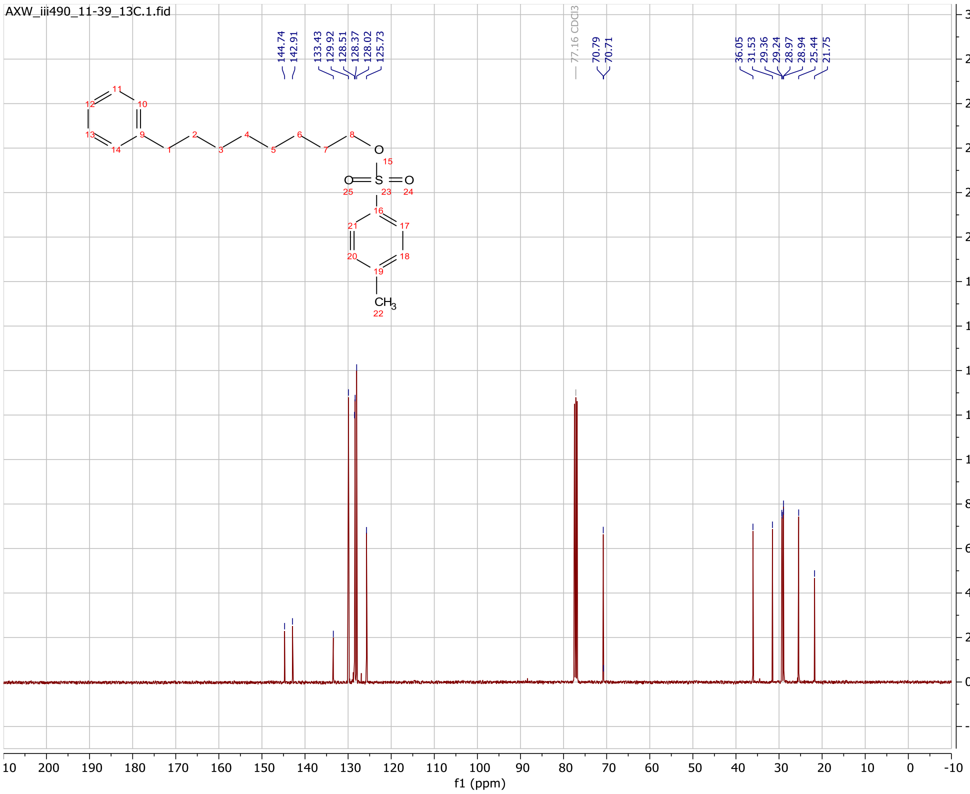

AXW_iii487_15-58.2.fid
1.98
2.00
2.05
3.04
2.06
22.48
3.02
f1 (ppm)

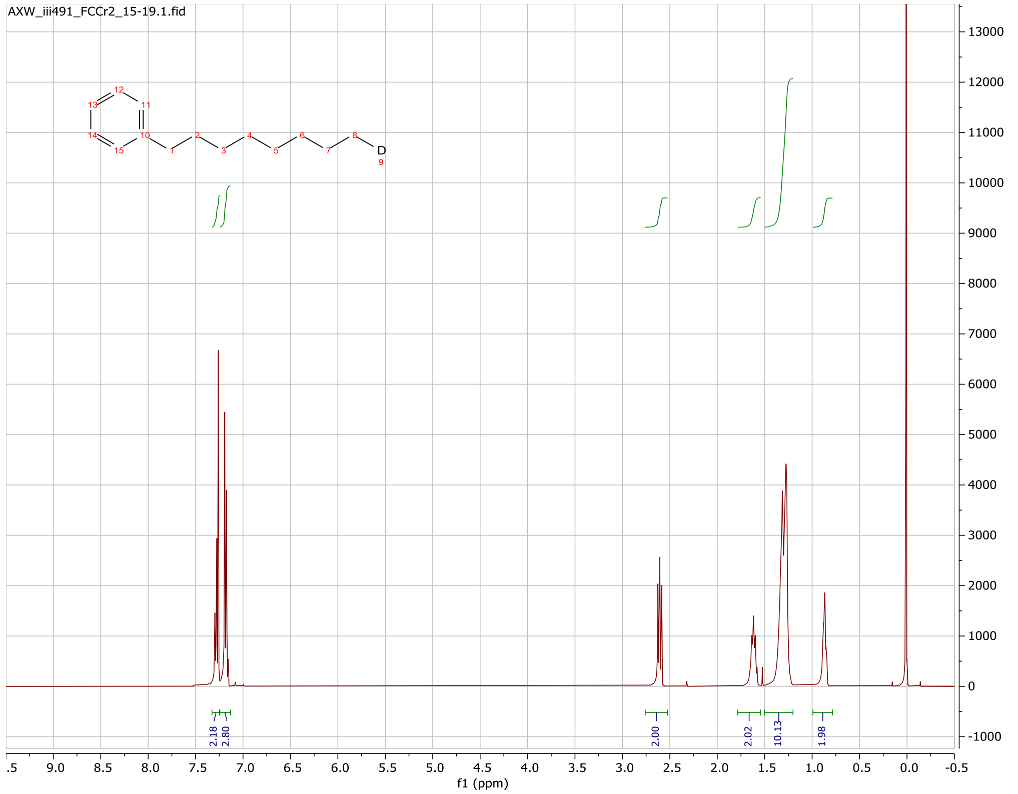

AXW_iii487_15-58_13C.2.fid
144.73
133.48
129.93
128.04
77.16 CDCl3
70.85
32.07
29.82
29.80
29.75
29.65
29.54
29.50
29.08
28.98
25.48
22.84
21.77
14.26
f1 (ppm)

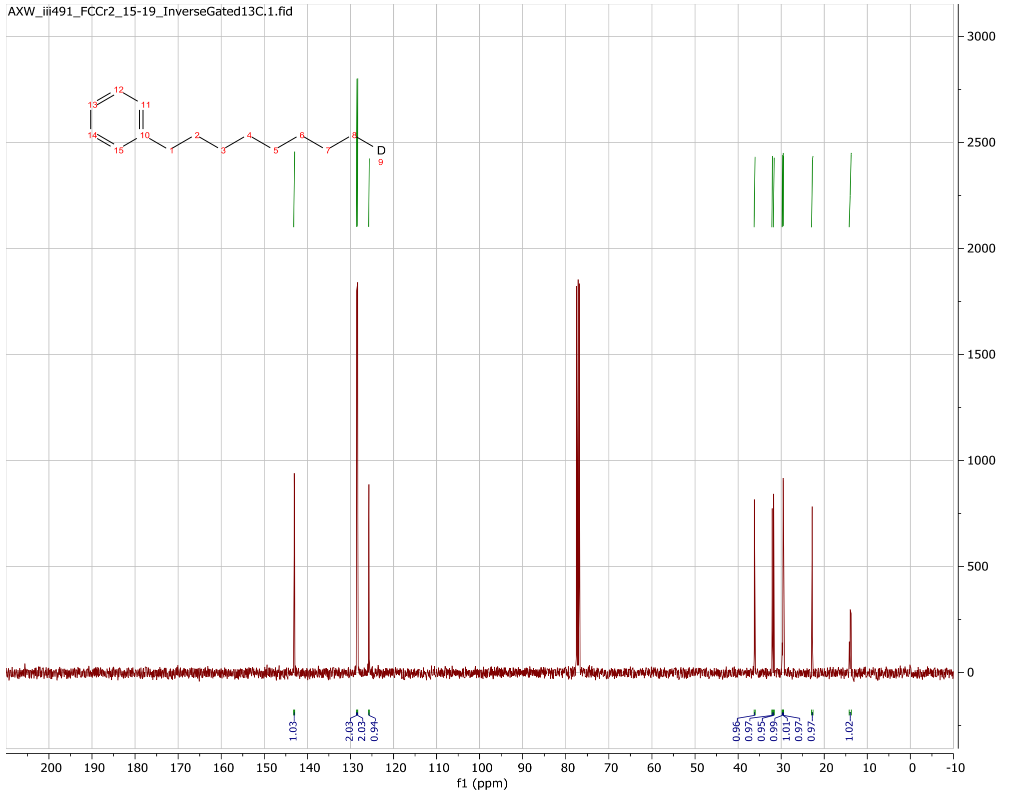

AXW_iii489_FCC_conc.1.fid
H_3C 15 14 1 2 3 4 5 6 7 8 9 10 11 12 D 13
24.00
5.45
f1 (ppm)

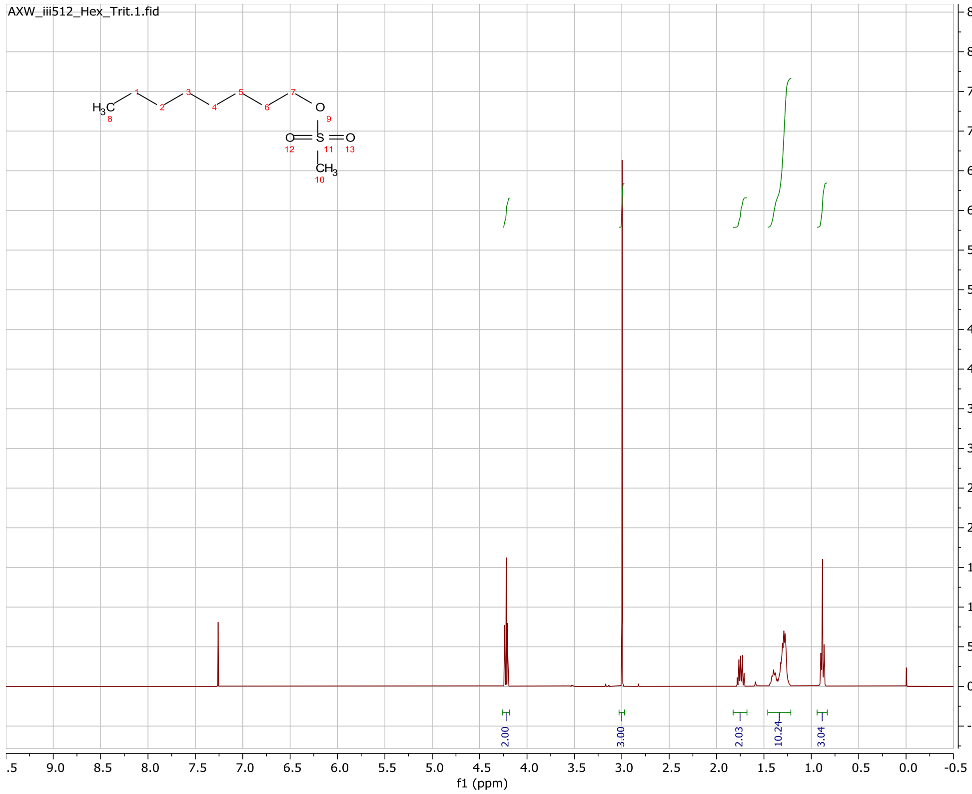

AXW_iii489_FCC_conc_InverseGated13C.2.fid
77.16 CDCl3
32.27
32.24
30.06
30.01
29.72
23.00
22.91
14.31
14.20
14.01
13.82
H_3C 15 14 1 2 3 4 5 6 7 8 9 10 11 12 D 13
2.01
6.06
1.96
2.10
1.00
1.03
f1 (ppm)

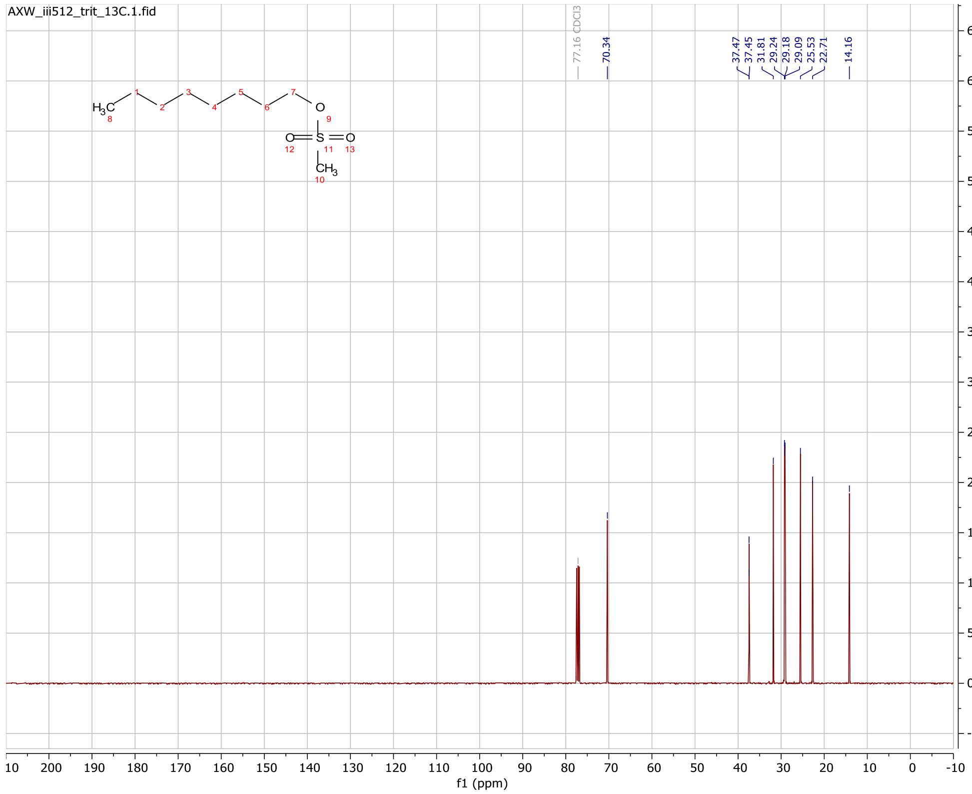

AXW_iii490_11-39_1H.1.fid
2.00
2.11
2.20
2.89
2.06
2.00
3.05
4.15
8.38
f1 (ppm)
CH3

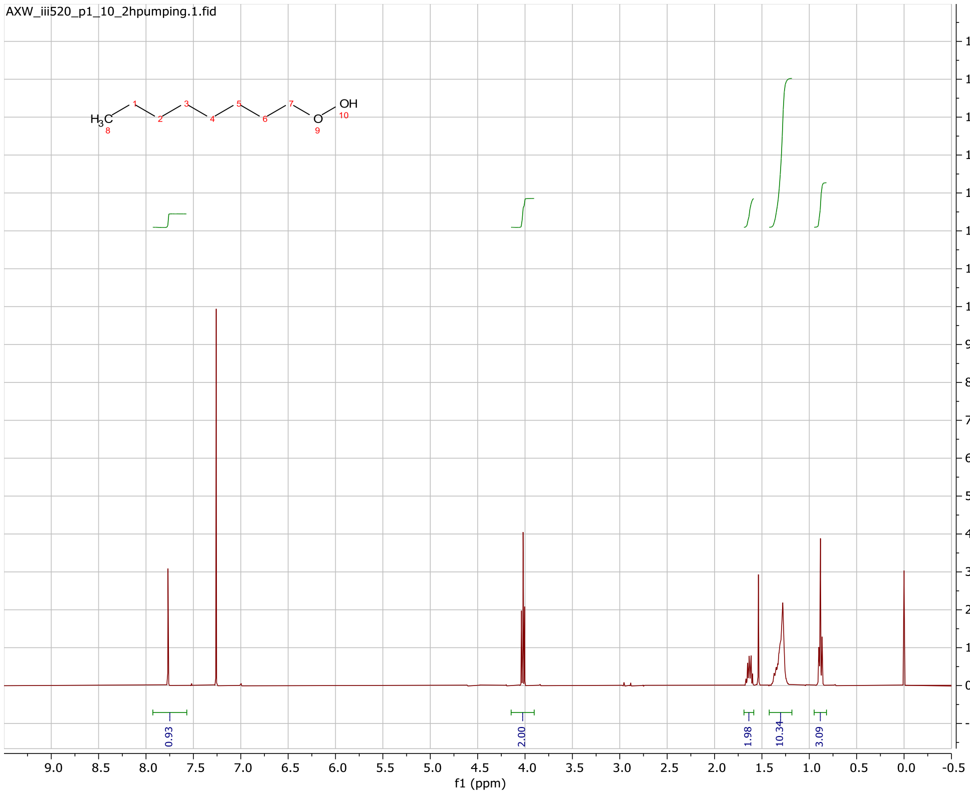

AXW_iii490_11-39_13C.1.fid
144.74
142.91
133.43
129.92
128.51
128.37
128.02
125.73
77.16 CDCl3
70.79
70.71
36.05
31.53
29.36
29.24
28.97
28.94
25.44
21.75
f1 (ppm)
CH3

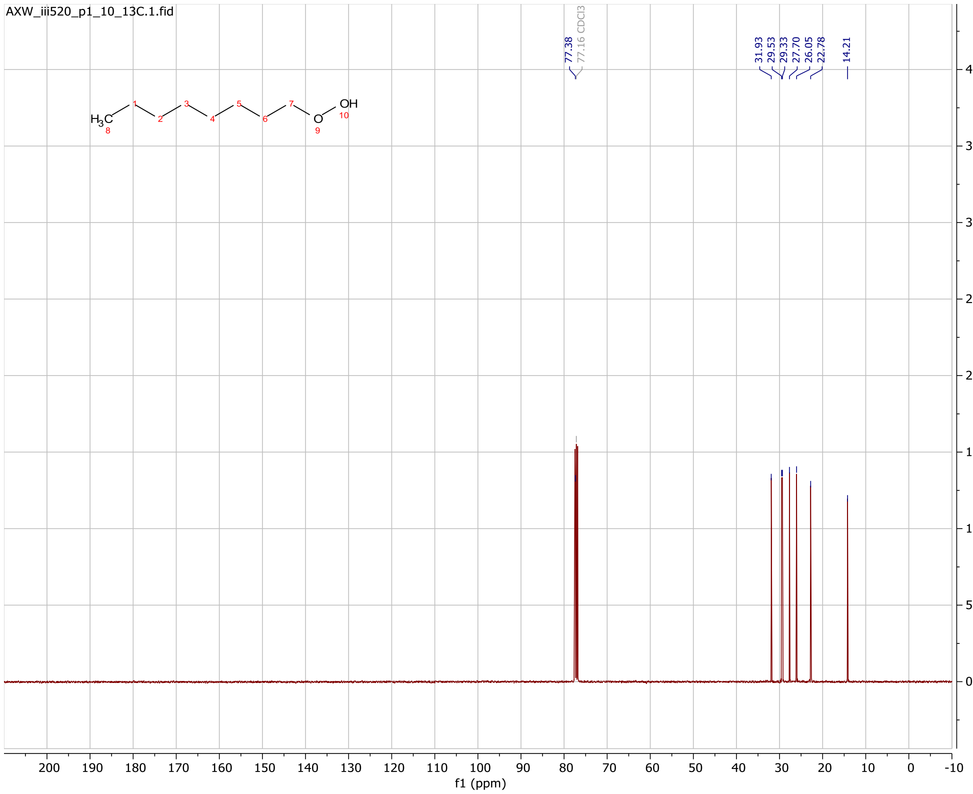

AXW_iii491_FCCr2_15-19.1.fid
12
11
13
10
14
15
1
2
3
4
5
6
7
8
D
9
2.18
2.80
2.00
2.02
10.13
1.98
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

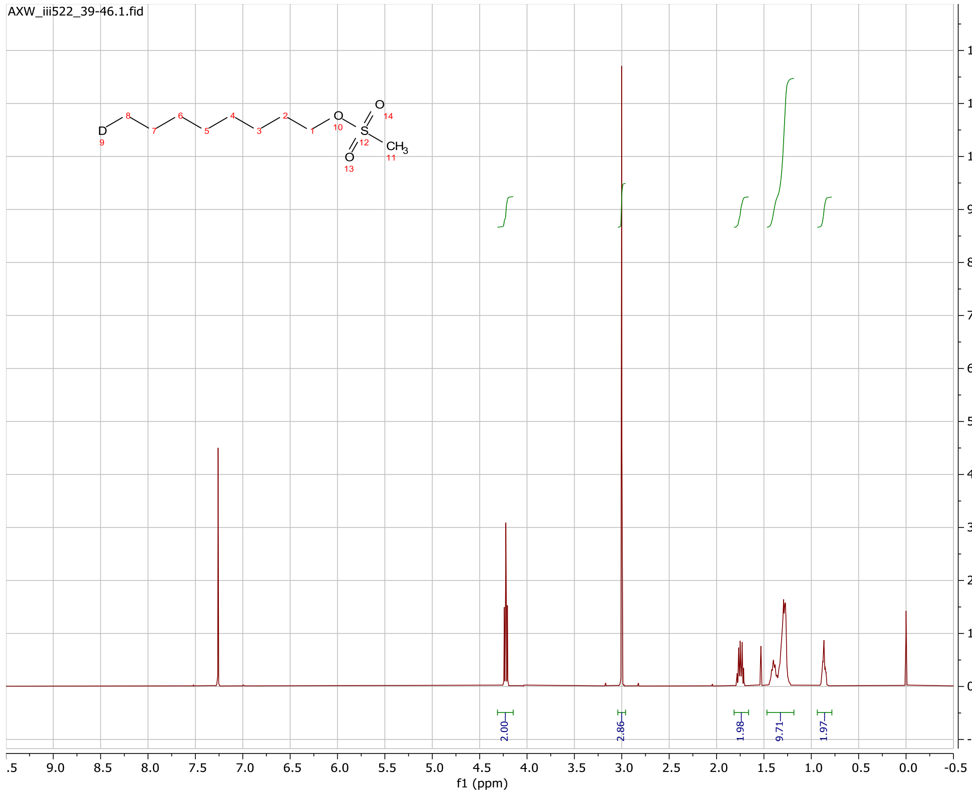

AXW_iii491_FCCr2_15-19_InverseGated13C.1.fid
12
11
13
10
14
15
1
2
3
4
5
6
7
8
D
9
1.03
2.03
2.03
0.94
0.96
0.97
0.95
0.99
1.01
0.97
0.97
1.02
3000
2500
2000
1500
1000
500
0
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

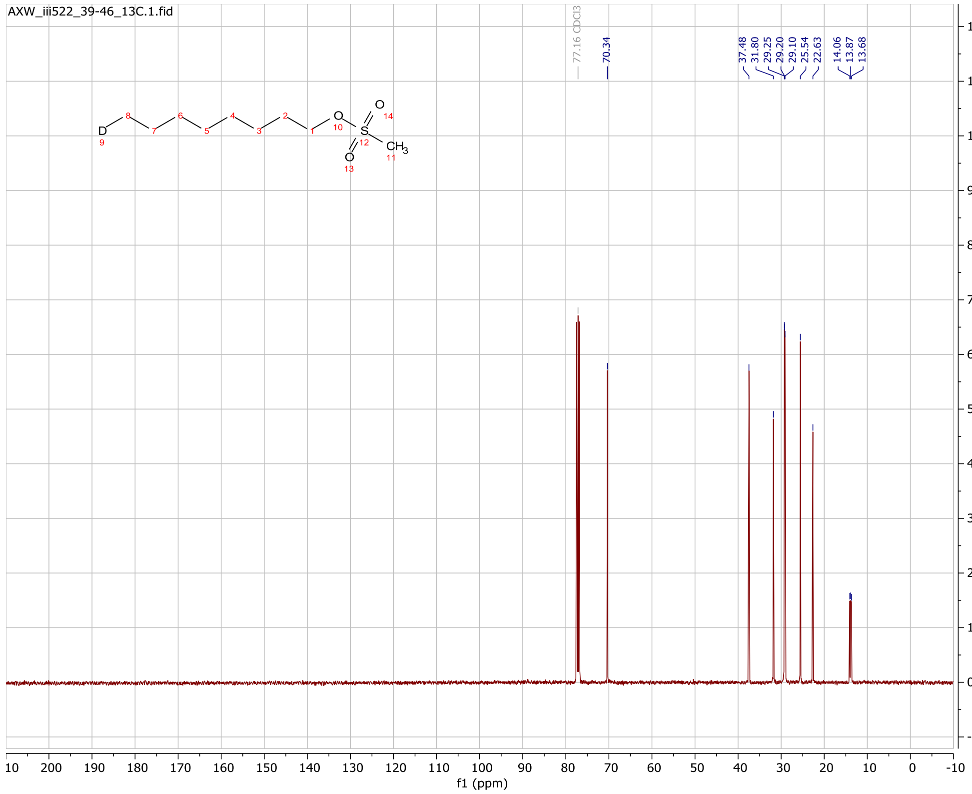

AXW_iii512_Hex_Trit.1.fid
H3C
8
1
2
3
4
5
6
7
O
9
O=S=O
12
11
13
CH3
10
2.00
3.00
2.03
10.24
3.04
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
85000
80000
75000
70000
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000

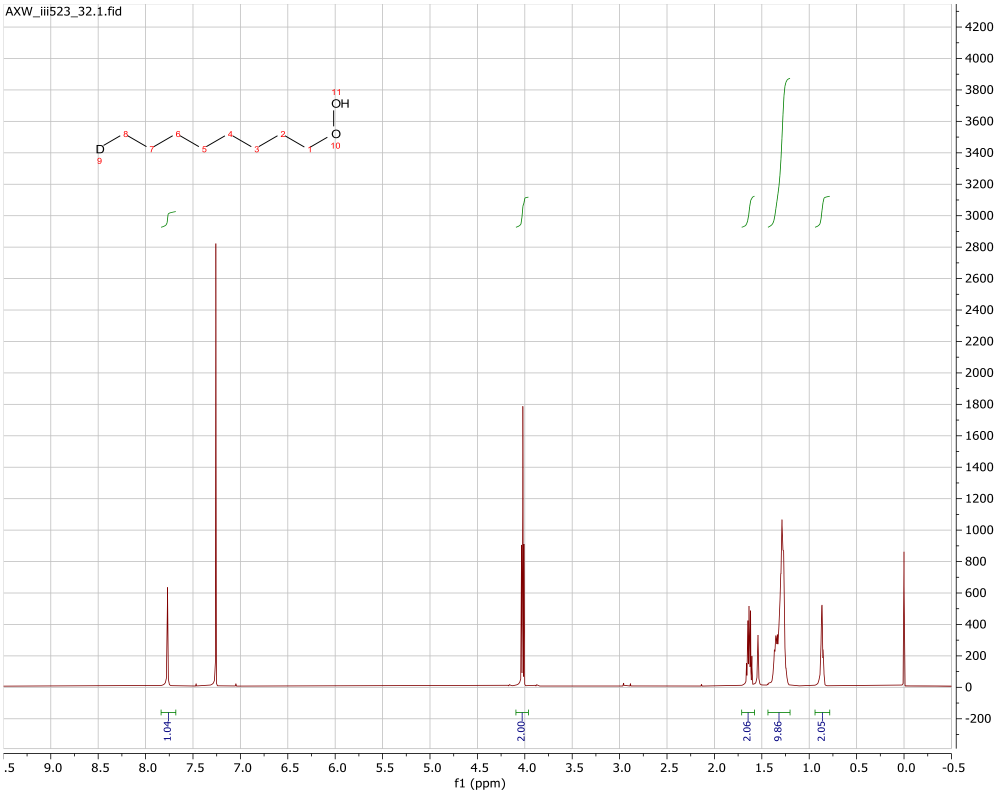

AXW_iii512_trit_13C.1.fid
77.16 CDCl3
70.34
37.47
37.45
31.81
29.24
29.18
29.09
25.53
22.71
14.16
H3C
8
1
2
3
4
5
6
7
O
9
O=S=O
12
11
13
CH3
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
650000
600000
550000
500000
450000
400000
350000
300000
250000
200000
150000
100000
50000
0
-50000

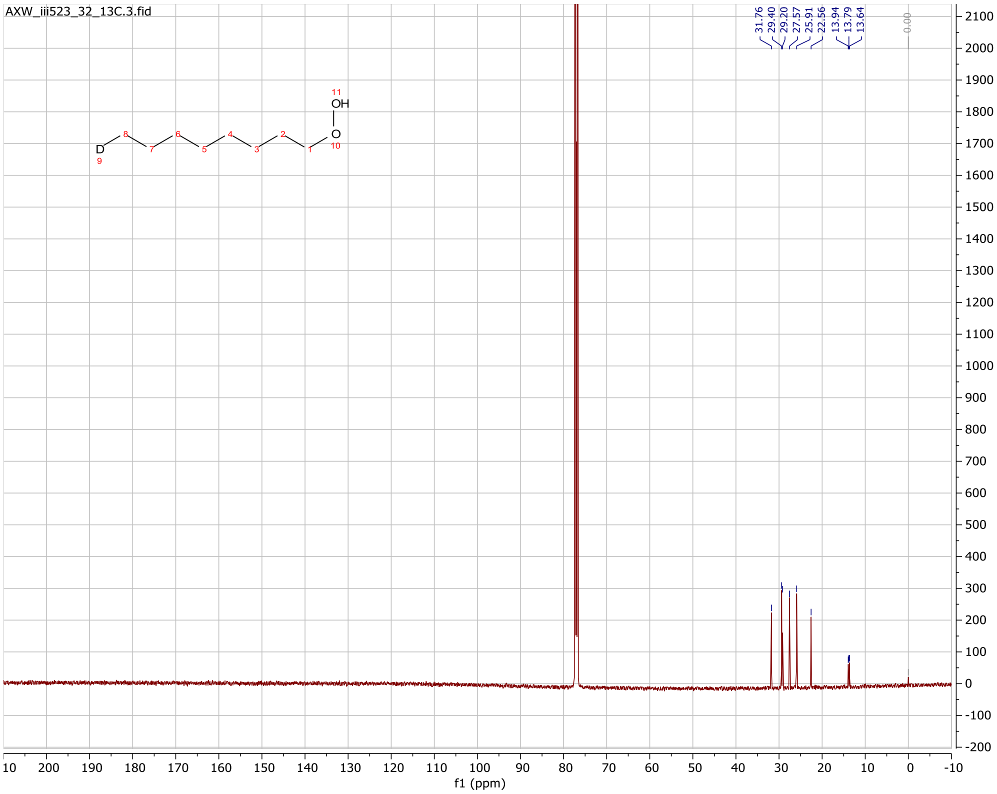

AXW_iii520_p1_10_2hpumping.1.fid
H3C
8
1
2
3
4
5
6
7
O
9
OH
10
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
0.93
2.00
1.98
10.34
3.09
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


AXW_iii520_p1_10_13C.1.fid
77.38
77.16 CDCl3
31.93
29.53
29.33
27.70
26.05
22.78
14.21
H3C
8
1
2
3
4
5
6
7
O
9
OH
10
400000
350000
300000
250000
200000
150000
100000
50000
0
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


AXW_iii522_39-46.1.fid
D
9
8
7
6
5
4
3
2
1
O
10
S
12
O
14
O
13
CH3
11
2.00
2.86
1.98
9.71
1.97
f1 (ppm)
.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000

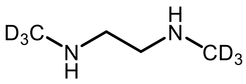

AXW_iii522_39-46_13C.1.fid
77.16 CDCl3
70.34
37.48
31.80
29.25
29.20
29.10
25.54
22.63
14.06
13.87
13.68
D
9
8
7
6
5
4
3
2
1
O
10
S
12
O
14
O
13
CH3
11
f1 (ppm)
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000


AXW_iii523_32.1.fid
OH
O
D
11
10
9
8
7
6
5
4
3
2
1
1.04
2.00
2.06
9.86
2.05
4200
4000
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

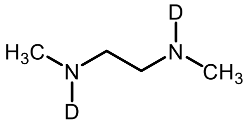

AXW_iii523_32_13C.3.fid
31.76
29.40
29.20
27.57
25.91
22.56
13.94
13.79
13.64
0.00
OH
O
D
11
10
9
8
7
6
5
4
3
2
1
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

4 MECHANISTIC INVESTIGATIONS

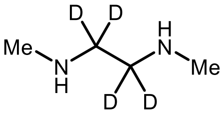
4.1 MEASUREMENT OF DEUTERIUM ISOTOPOLOGUES OF DMEDA



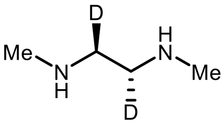
1b



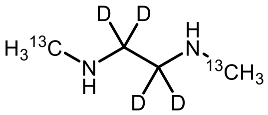
1c



1d



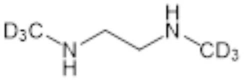
1e



1f

1b-f were synthesized as described in SI section 3.2. TD solutions containing 1 mM DMEDA or their isotopologues were subjected to STM conditions (SI section 1.2) and analyzed via LC-MS (SI section 2.4.1). A modified LC method was used from described in the general LC parameters: 20-80% methanol/isopropanol (4:1) in H_2O with 0.1% formic acid over 11.5 min, 1 uL injection volume, Acquity UPLC BEH C_{18} column (2.1 mm × 100 mm, 1.7 µm), 0.35 mL/min flow rate, with the mass detector in ES+ mode.


EIC for +14 C [M+H]
EIC for +13 C [M+H]
EIC for +12 C [M+H]
EIC for +11 C [M+H]
EIC for +10 C [M+H]
EIC for +9 C [M+H]
EIC for +8 C [M+H]
EIC for +7 C [M+H]
EIC for +6 C [M+H]
EIC for +6-15 C (-d6) products
220201_AXW_STM061B_r1
1: TOF MS ES+
305.344 0.0500Da
4.07e3
291.328 0.0500Da
9.36e3
277.313 0.0500Da
3.58e4
263.297 0.0500Da
1.69e4
249.281 0.0500Da
1.62e5
235.266 0.0500Da
2.39e5
221.25 0.0500Da
1.56e5
207.234 0.0500Da
4.00e4
193.219 0.0500Da
1.99e4
Sum 0.0500Da
2.40e5
100
%
0
Time
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
9.50



1b

Figure 4-1

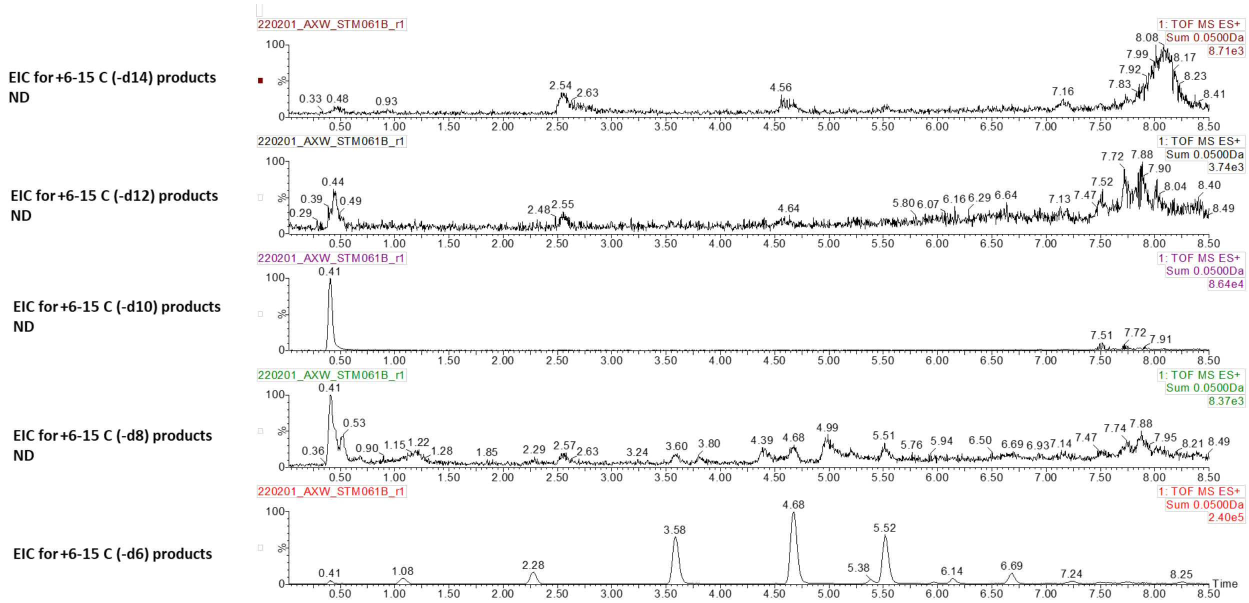


Figure 4-2

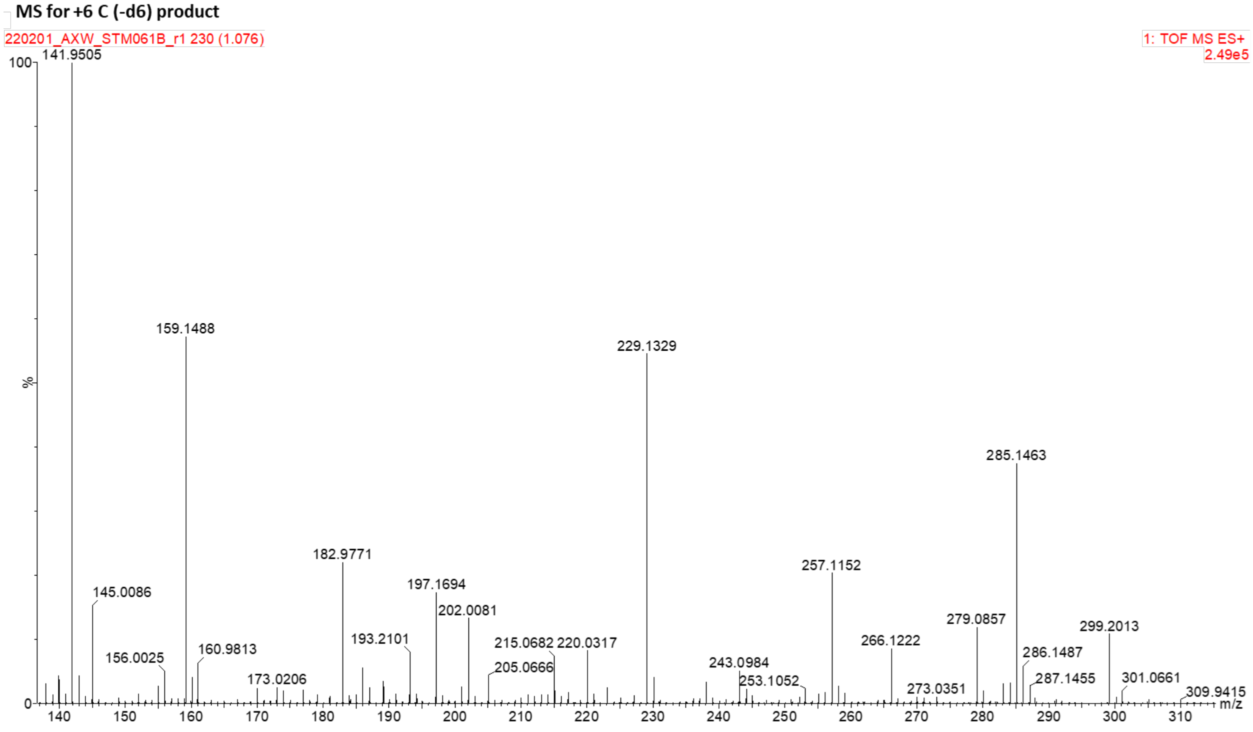
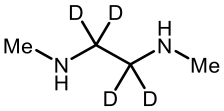
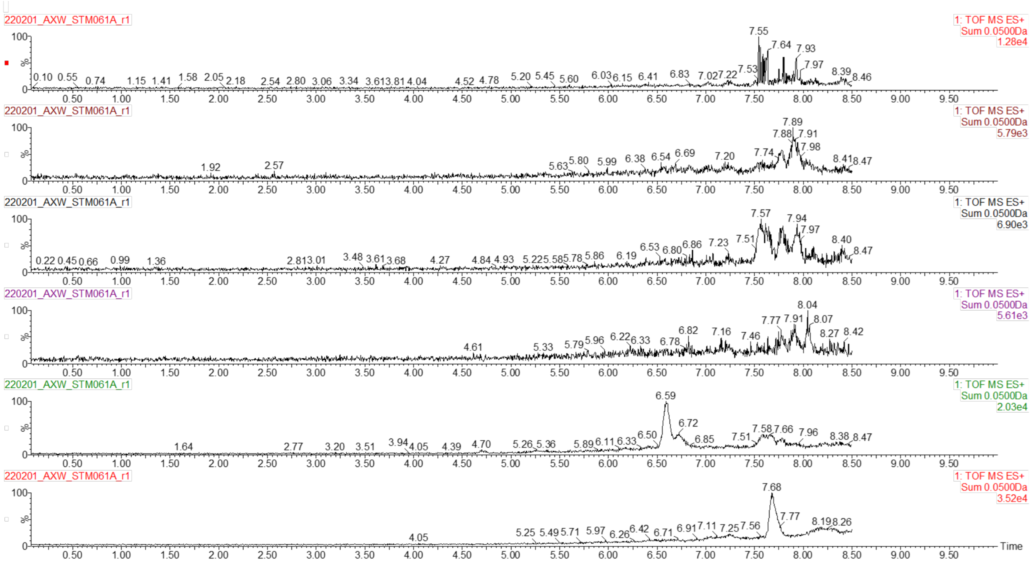


Figure 4-3

No deuterium incorporation on the alkyl chain in the product was detected.



1d



EIC for +6-15 C (-d10) products
ND

EIC for +6-15 C (-d8) products
ND

EIC for +6-15 C (-d6) products
ND

EIC for +6-15 C (-d4) products
ND

EIC for +6-15 C (-d2) products
ND

EIC for +6-15 C products
ND

Figure 4-4

MS at 1.08 min
(where +6 C product and any possible isotopologues should elute under LC conditions)
+6 C or isotopologues ND

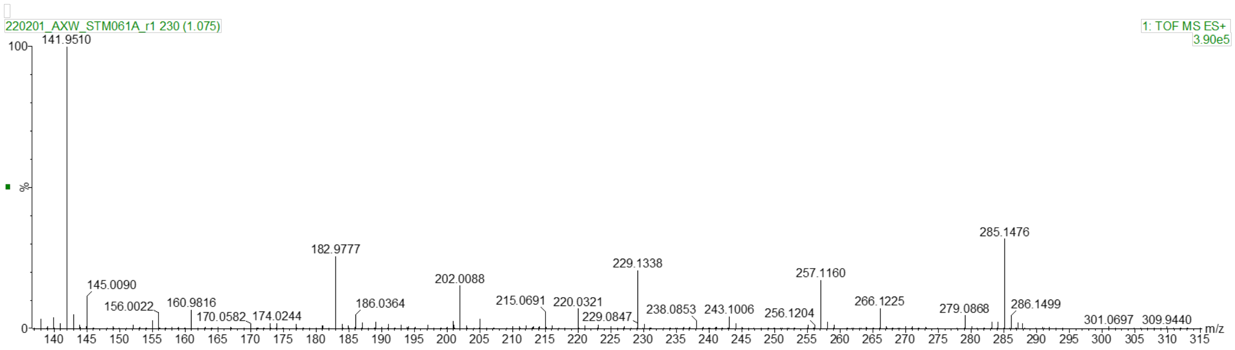
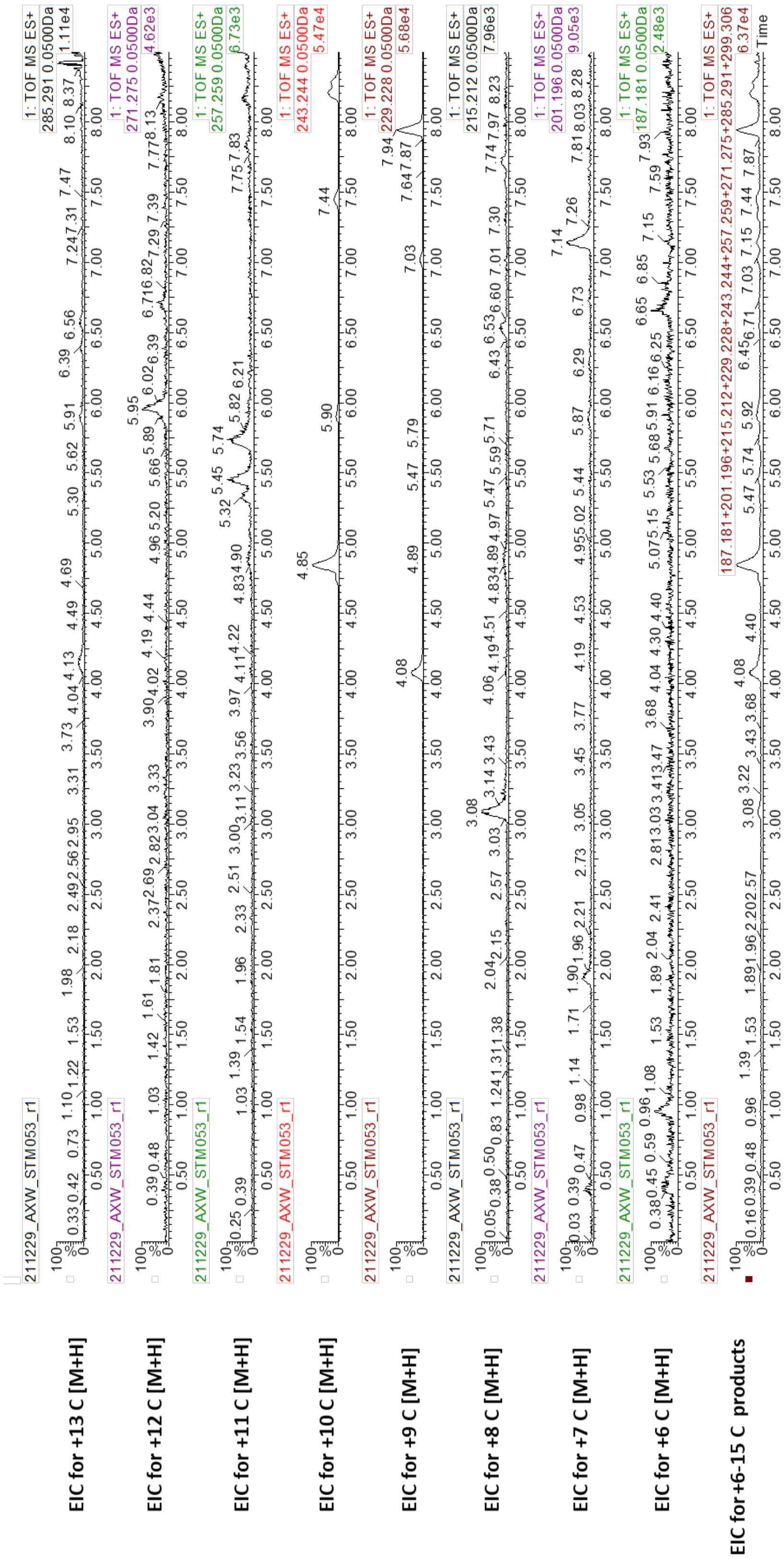
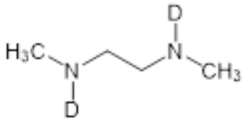


Figure 4-5

No products were detected.


EIC for +13 C [M+H]
EIC for +12 C [M+H]
EIC for +11 C [M+H]
EIC for +10 C [M+H]
EIC for +9 C [M+H]
EIC for +8 C [M+H]
EIC for +7 C [M+H]
EIC for +6 C [M+H]
EIC for +6-15 C products
211229_AXW_STM053_r1
1: TOF MS ES+ 285.291 0.0500Da 1.11e4
1: TOF MS ES+ 271.275 0.0500Da 4.62e3
1: TOF MS ES+ 257.259 0.0500Da 6.73e3
1: TOF MS ES+ 243.244 0.0500Da 5.47e4
1: TOF MS ES+ 229.228 0.0500Da 5.68e4
1: TOF MS ES+ 215.212 0.0500Da 7.96e3
1: TOF MS ES+ 201.196 0.0500Da 9.05e3
1: TOF MS ES+ 187.181 0.0500Da 2.48e3
1: TOF MS ES+ 187.181+201.196+215.212+229.228+243.244+257.259+271.275+285.291+299.306 6.37e4
Time


H3C
N
D
D
N
CH3

1c

Figure 4-6

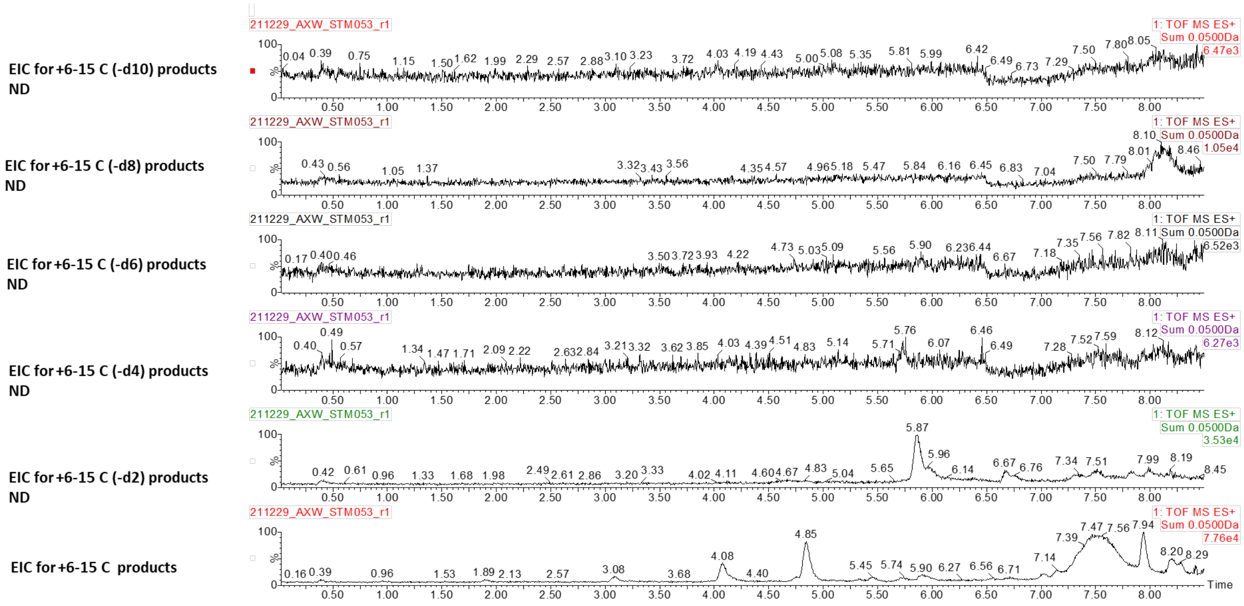


Figure 4-7

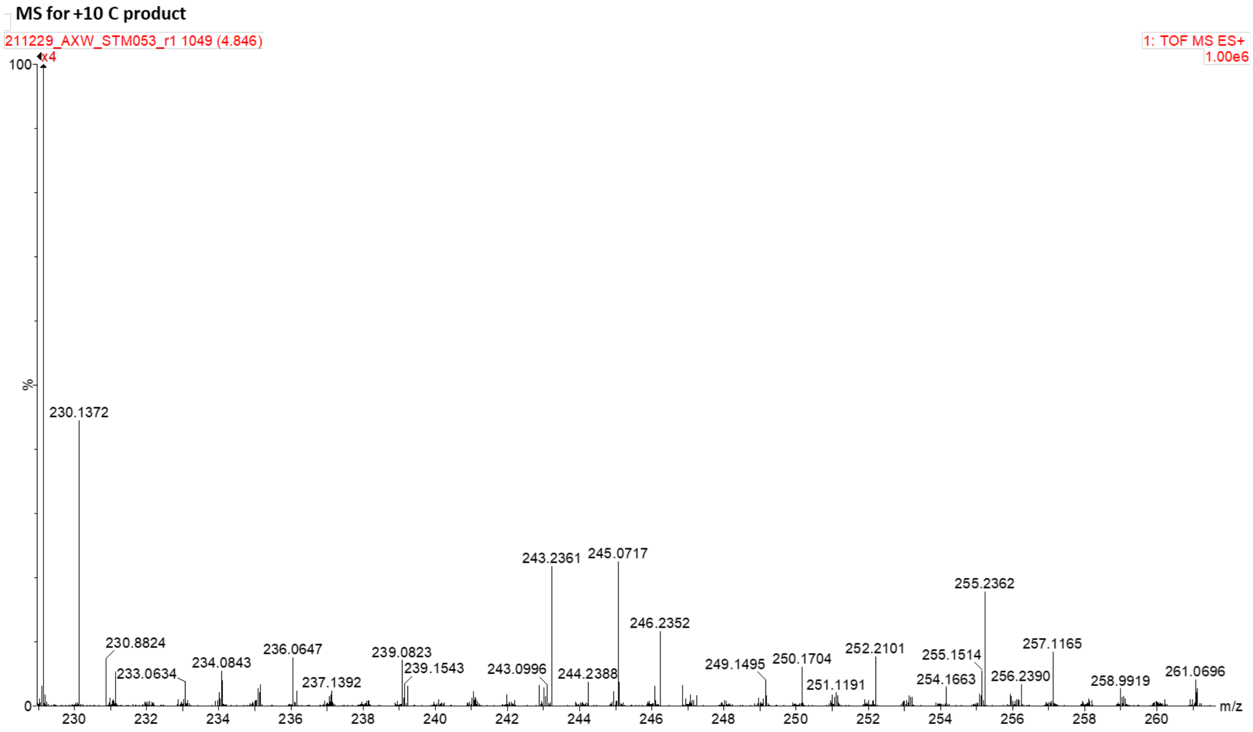
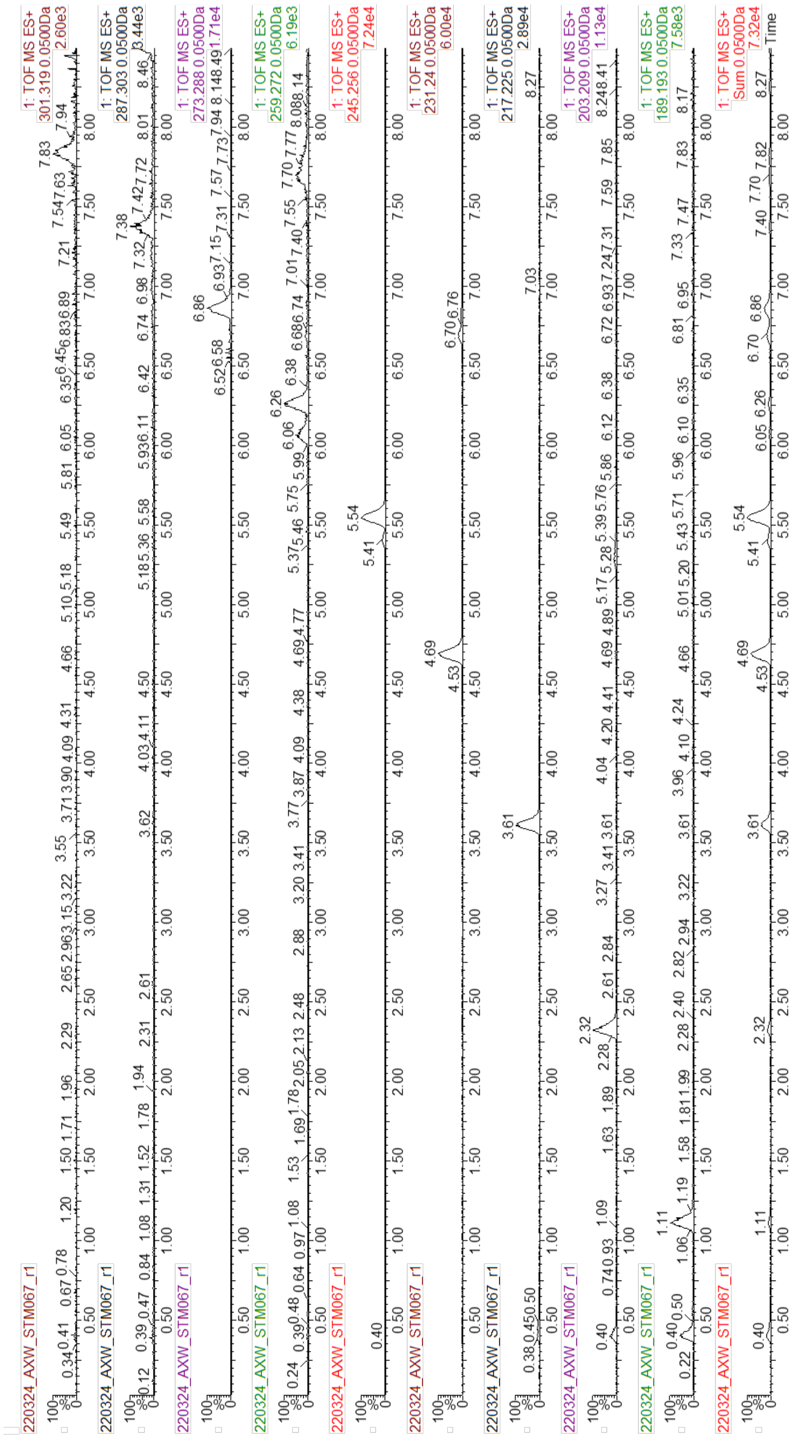


Figure 4-8

No deuterium incorporation on the alkyl chain in the product was detected.



EIC for +14 C [M+H]

EIC for +13 C [M+H]

EIC for +12 C [M+H]

EIC for +11 C [M+H]

EIC for +10 C [M+H]

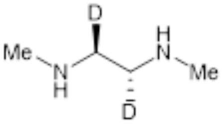
EIC for +9 C [M+H]

EIC for +8 C [M+H]

EIC for +7 C [M+H]

EIC for +6 C [M+H]

EIC for +6-15 C (-d2) products



1e

Figure 4-9

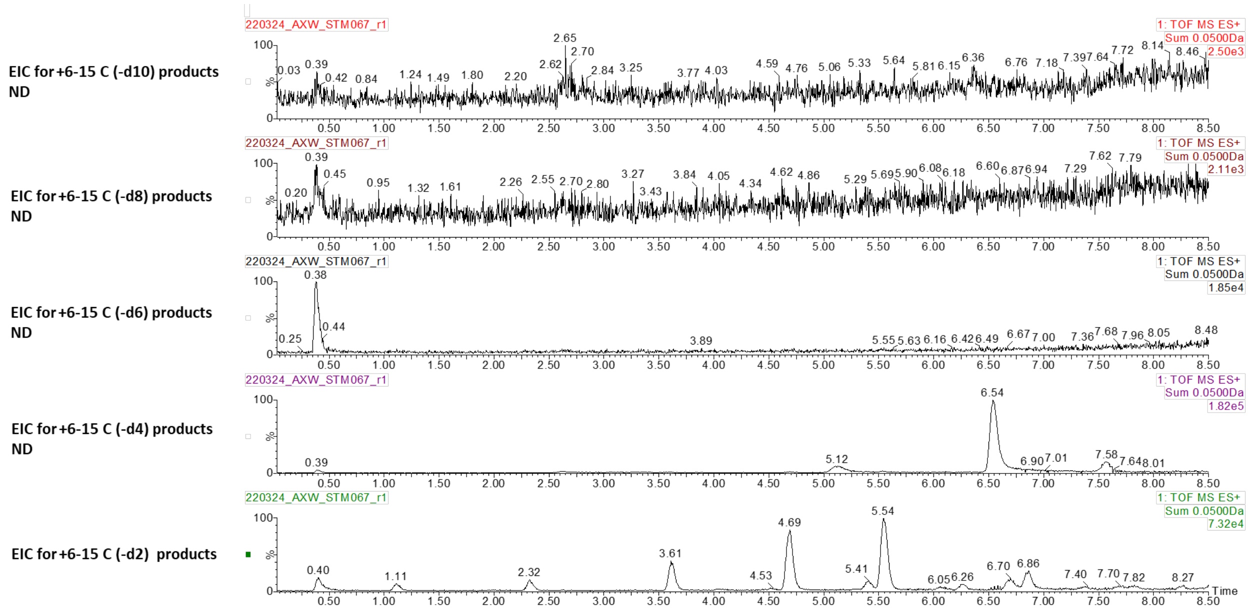


Figure 4-10

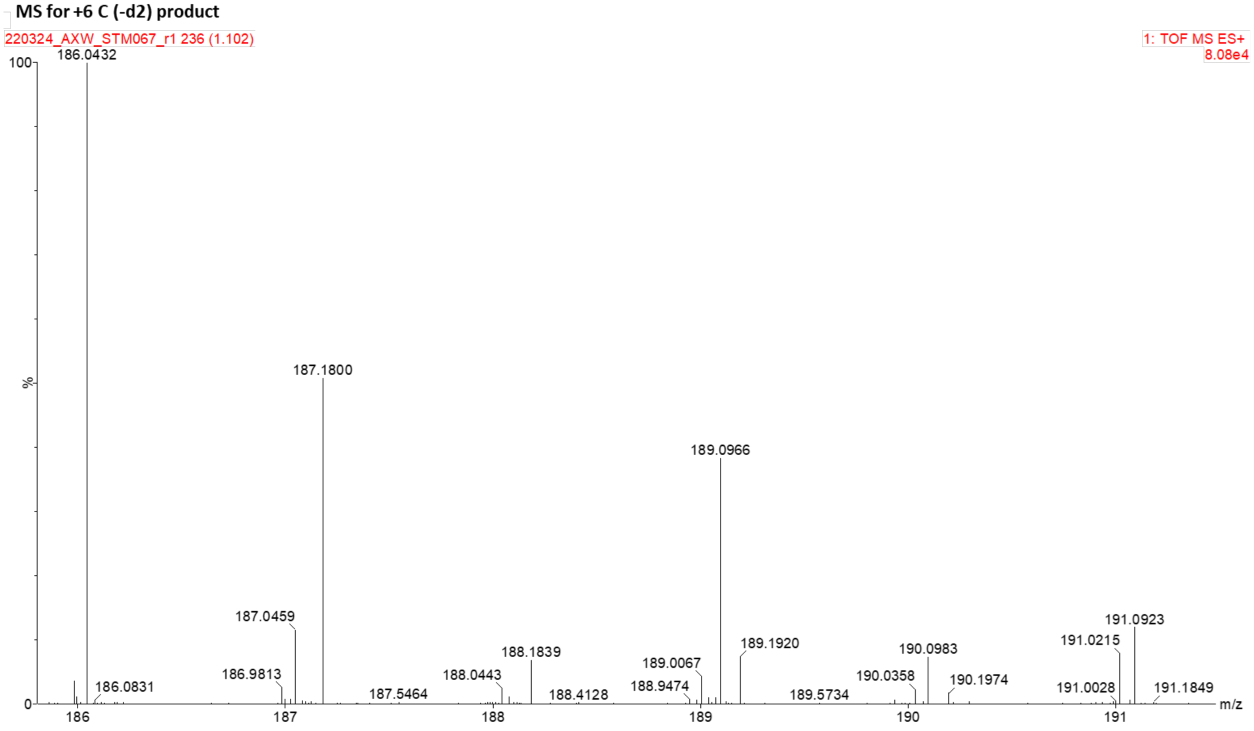
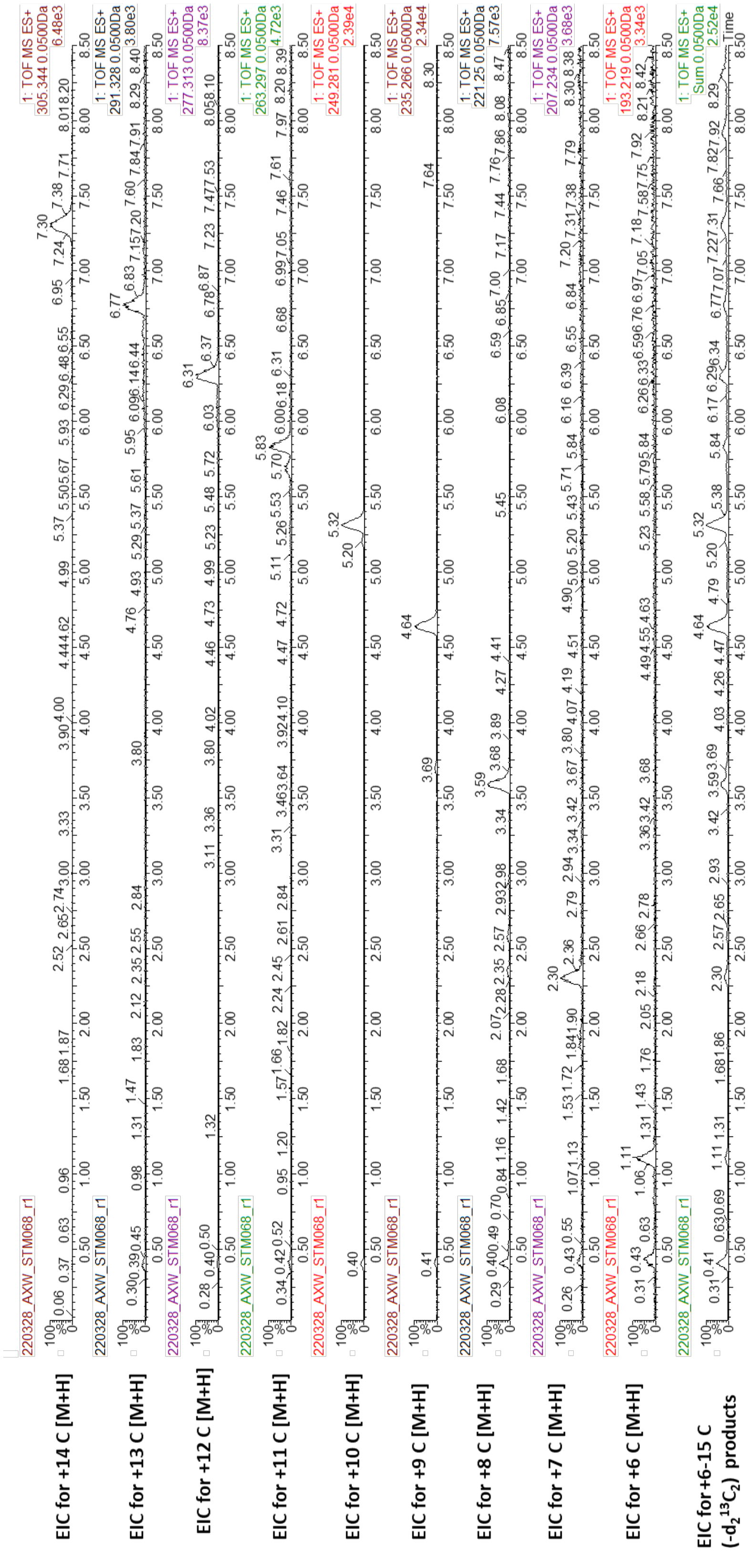
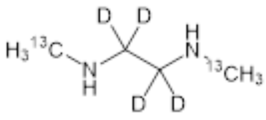


Figure 4-11

No deuterium incorporation on the alkyl chain in the product was detected.





1f

Figure 4-12

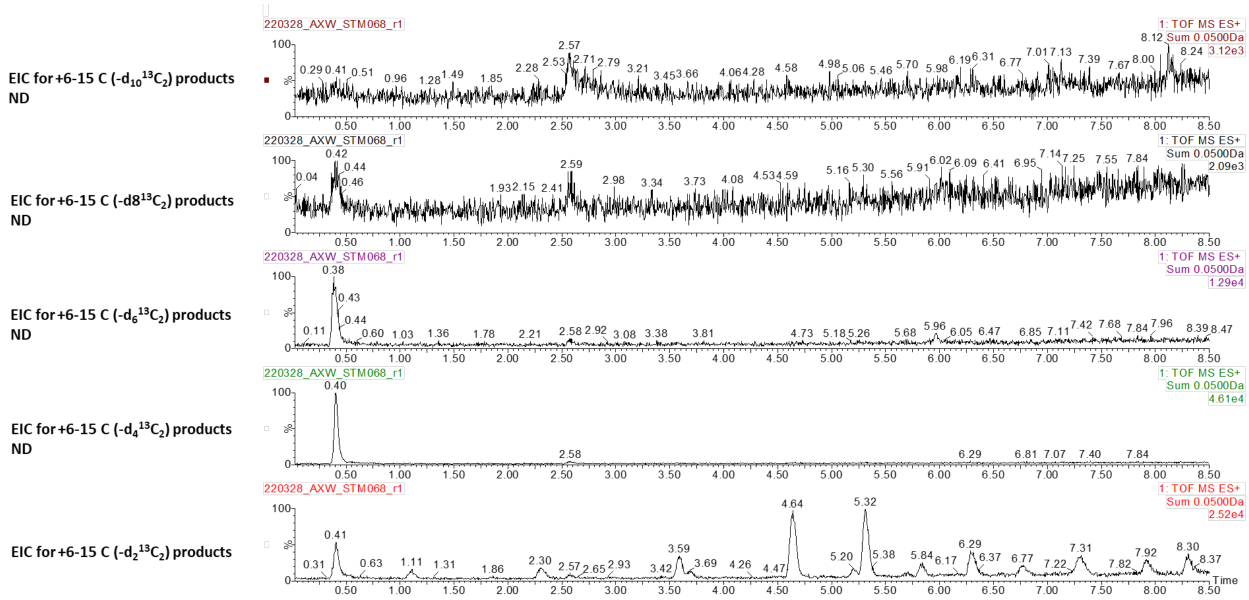


Figure 4-13

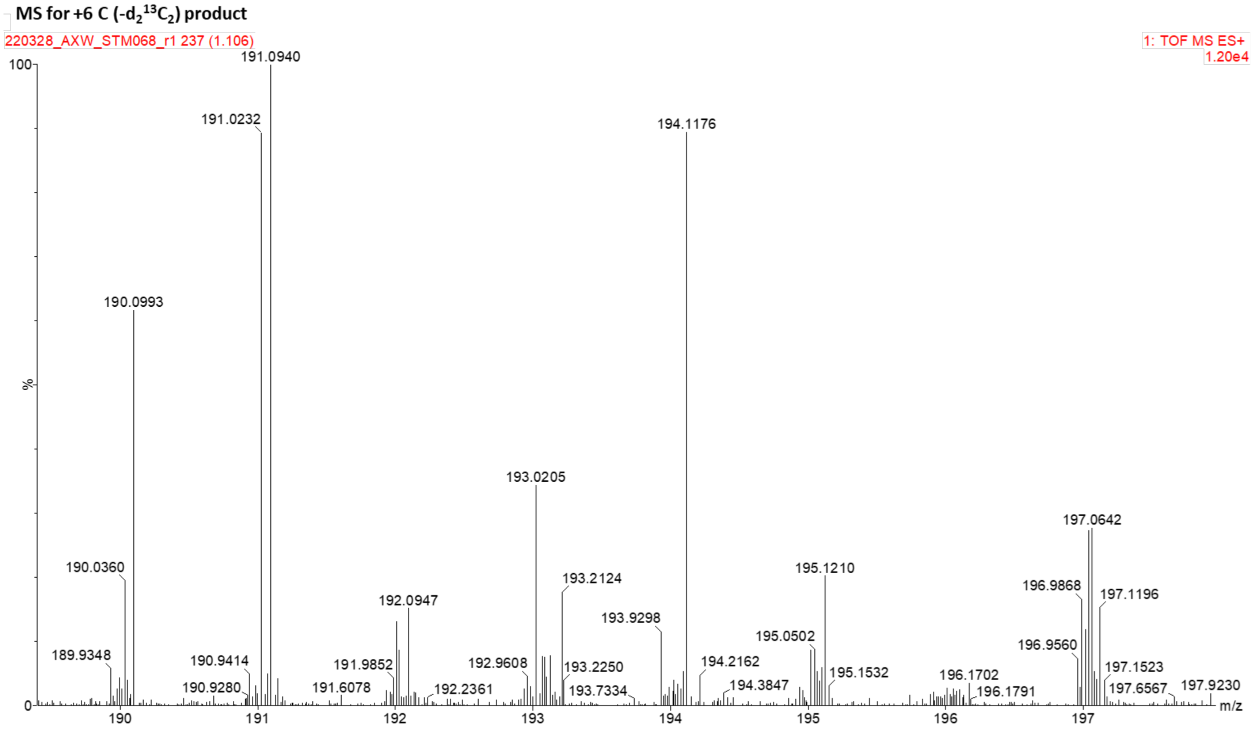
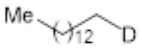


Figure 4-14

No deuterium or ^{13}C incorporation on the alkyl chain in the product was detected.

4.2 MEASUREMENT IN DEUTERATED SOLVENTS

Tetradecane-1-d (3a) and **(Octyl-8-*d*)benzene (3b)** were synthesized as described in SI section 3.4. Solutions in deuterated solvents **3a, 3b**, and tetradecane-d30 (**3c**) containing 1 mM DMEDA were subjected to STM conditions at 750 mV (SI section 1.2) and analyzed via LC-MS (SI section 2.4.1). A modified LC method was used from described in the general LC parameters (SI section 2.4.1): 10-100% methanol/isopropanol (4:1) in H_2O with 0.1% formic acid over 9.5 min, 0.5 uL injection volume, Acquity UPLC BEH C_{18} column (2.1 mm × 100 mm, 1.7 µm), 0.35 mL/min flow rate, with the mass detector in ES+ mode.



3a

Figure 4-15

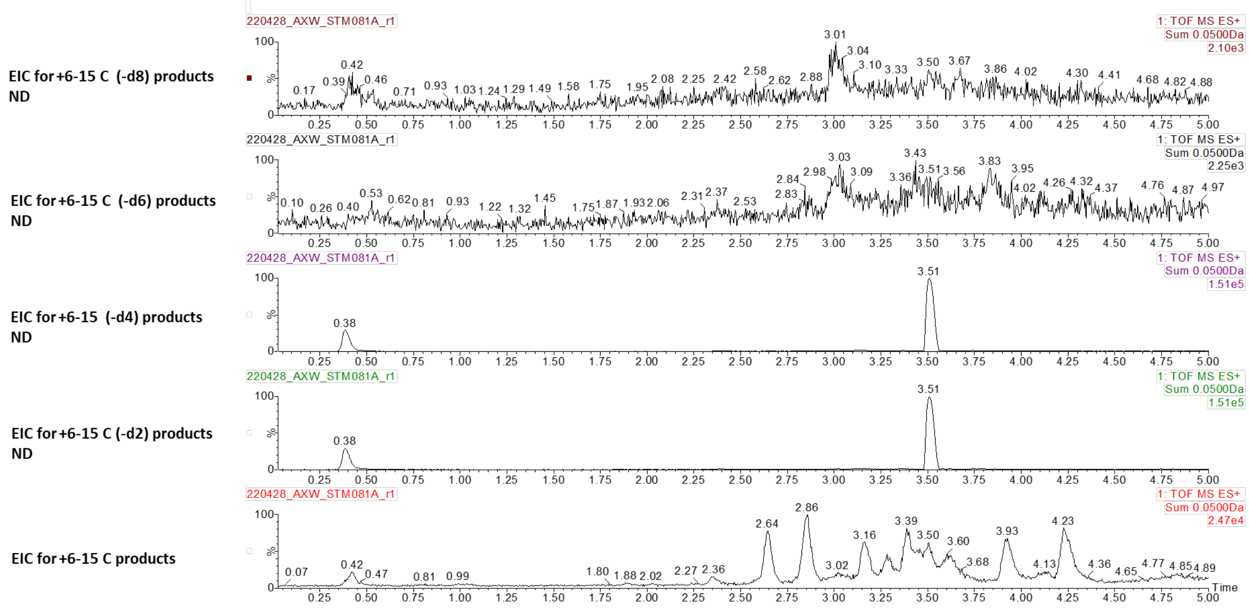


Figure 4-16

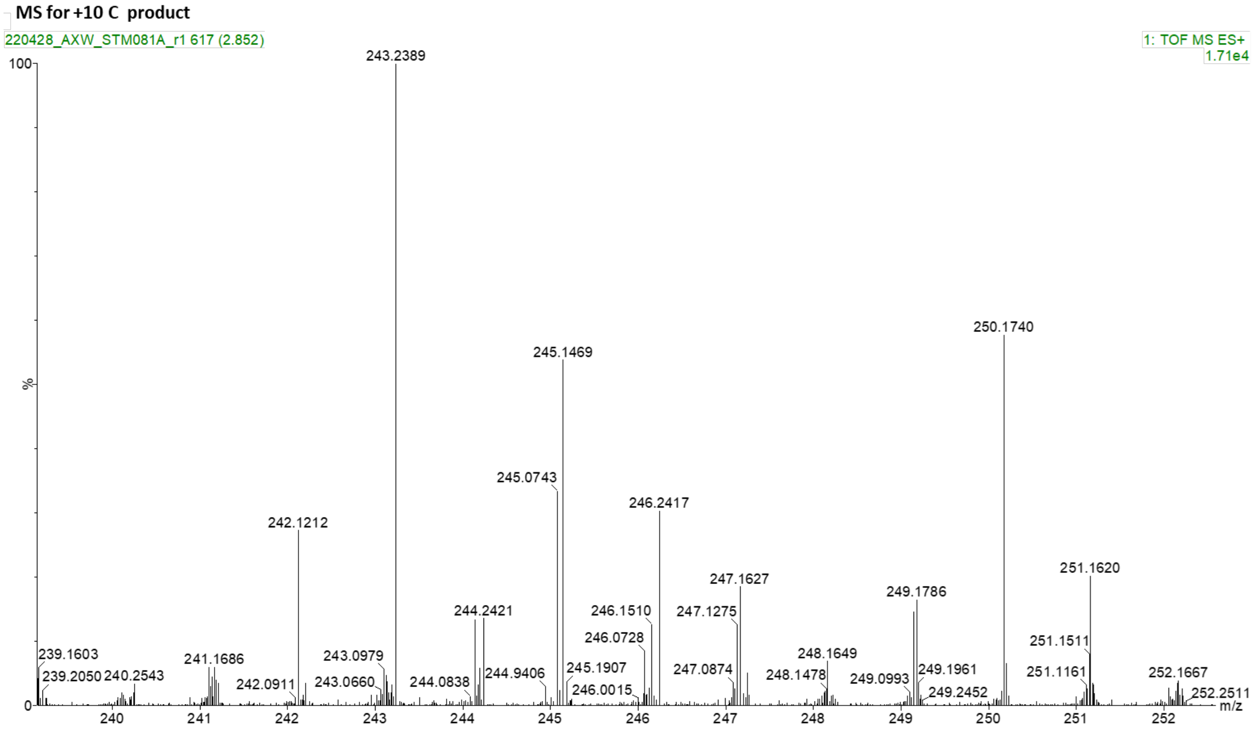
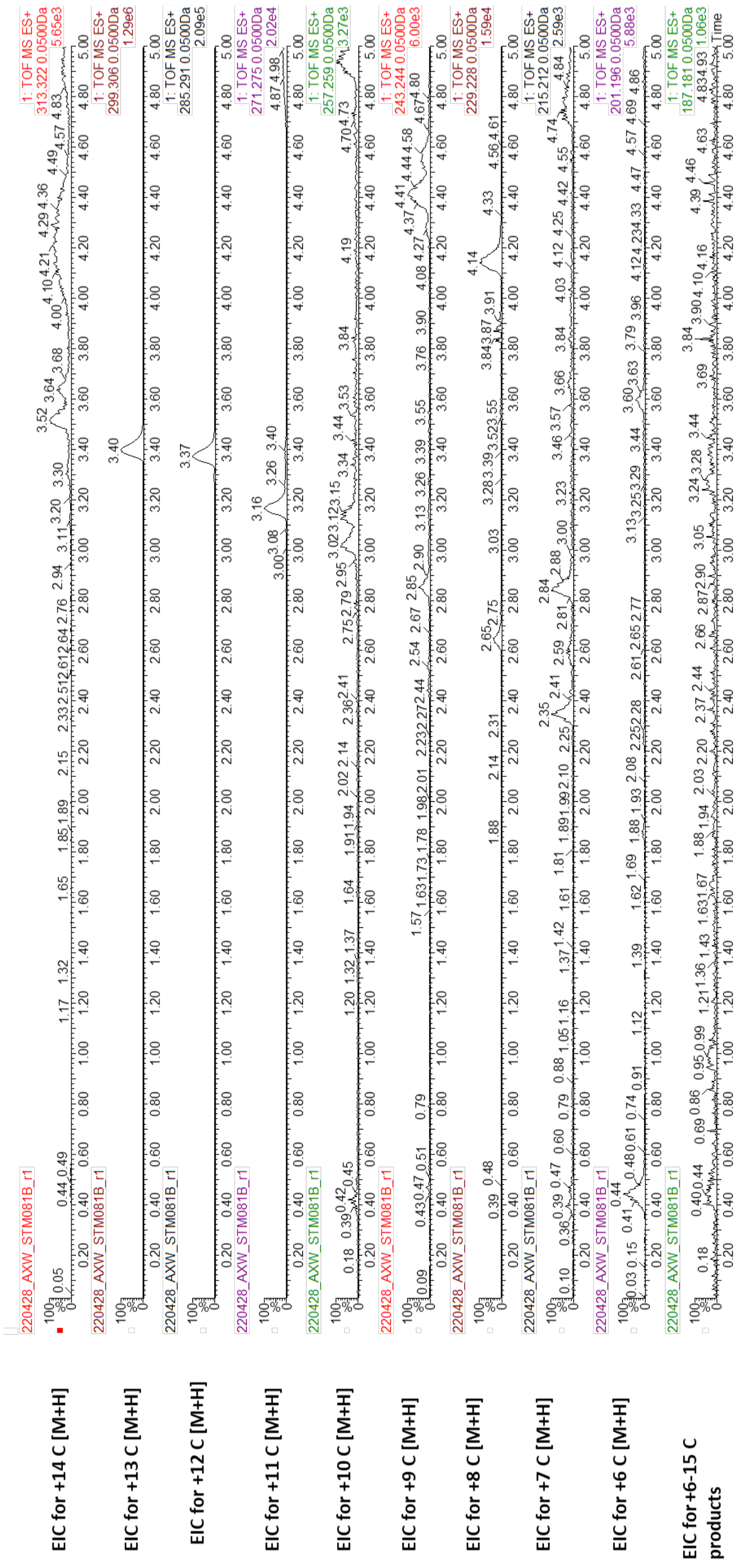
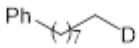


Figure 4-17

No deuterium incorporation on the alkyl chain in the product was detected.





3b

Figure 4-18

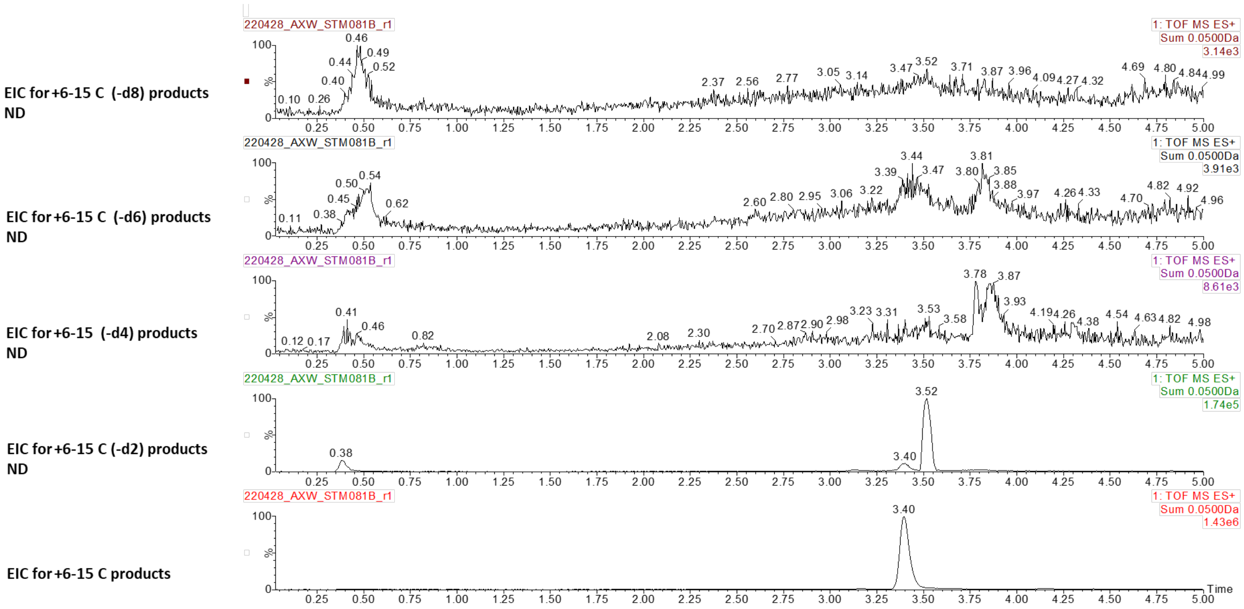


Figure 4-19

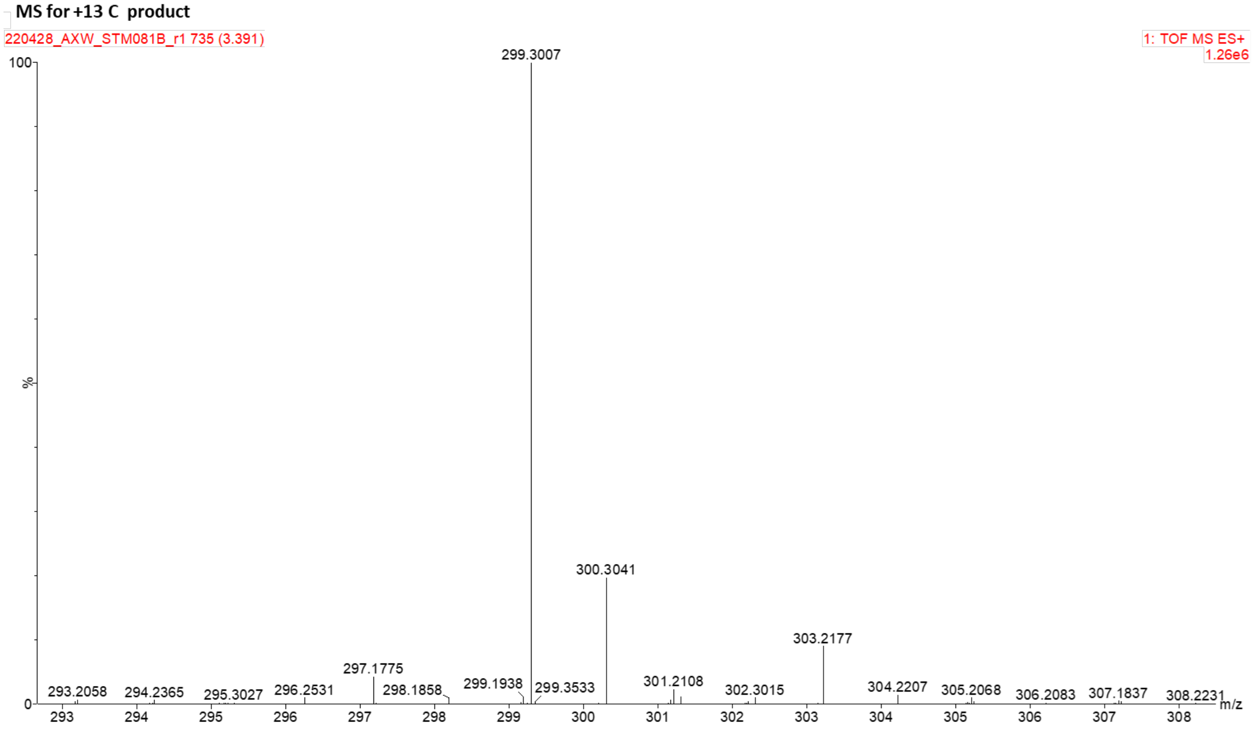


Figure 4-20

No deuterium incorporation on the alkyl chain in the product was detected.

tetradecane-d30 (**3c**)

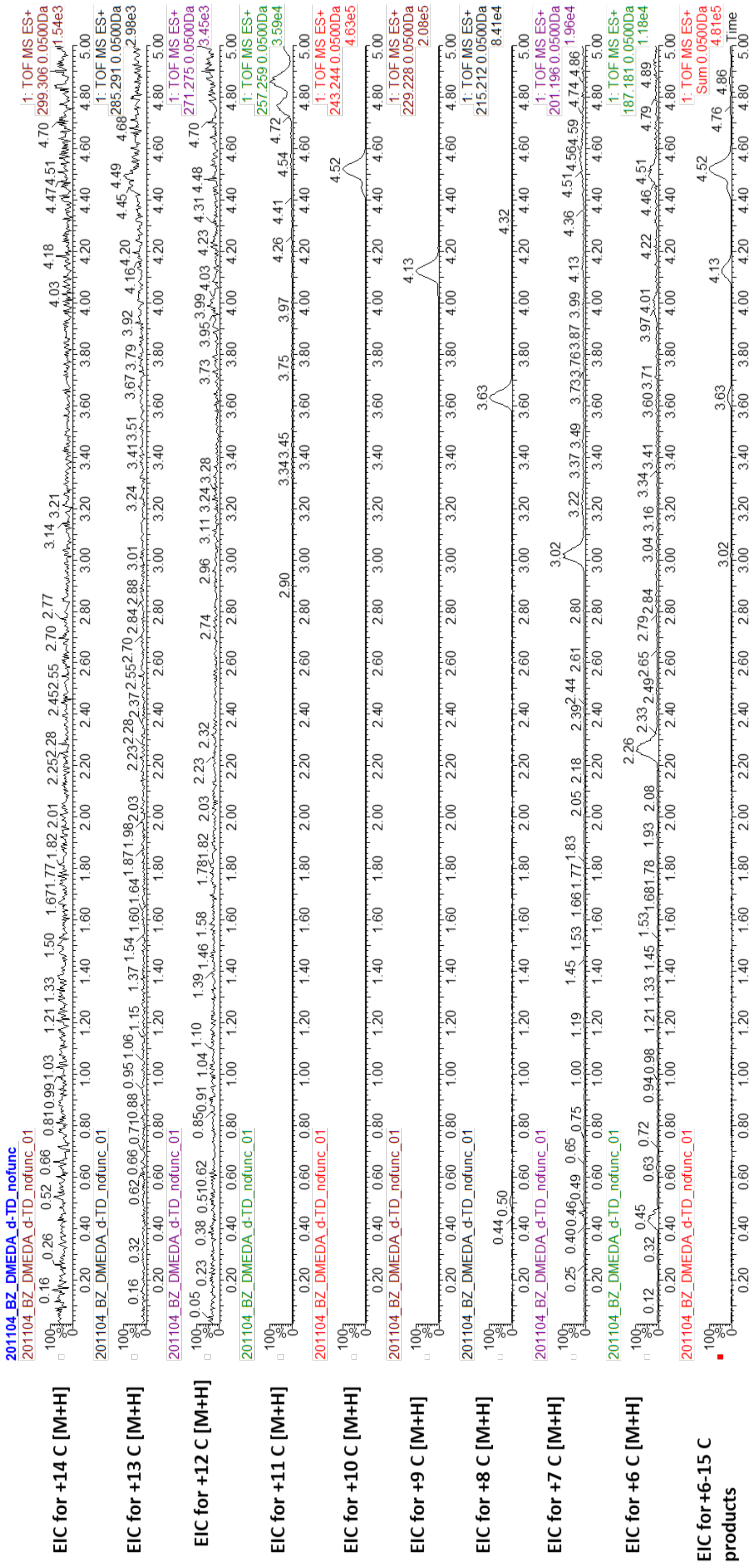


Figure 4-21

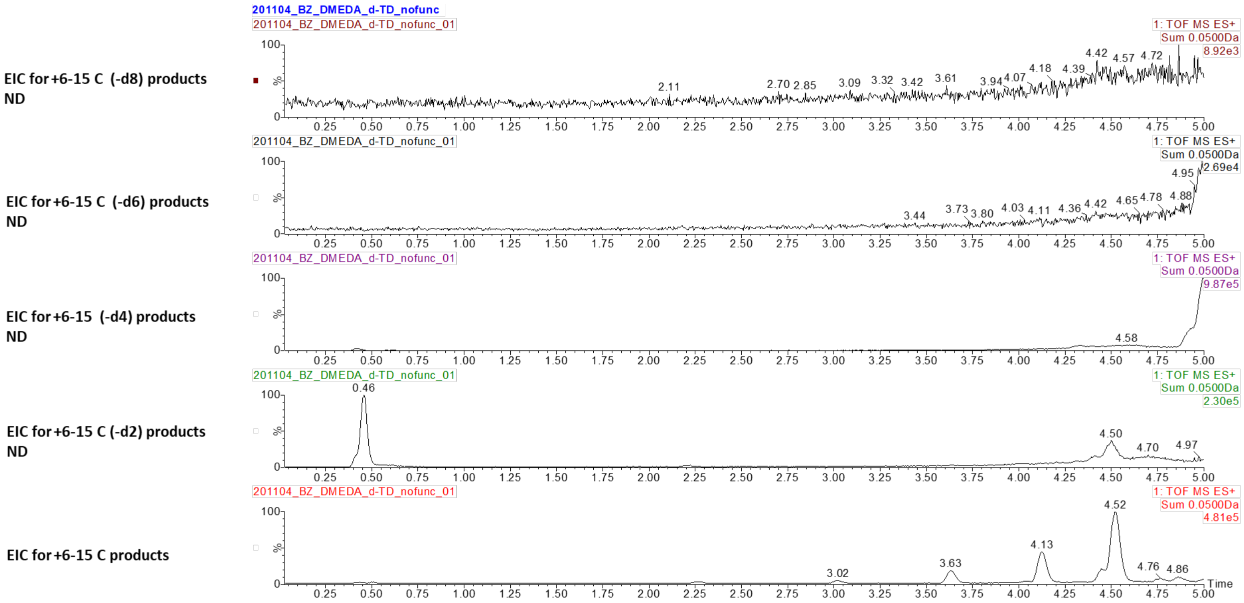


Figure 4-22

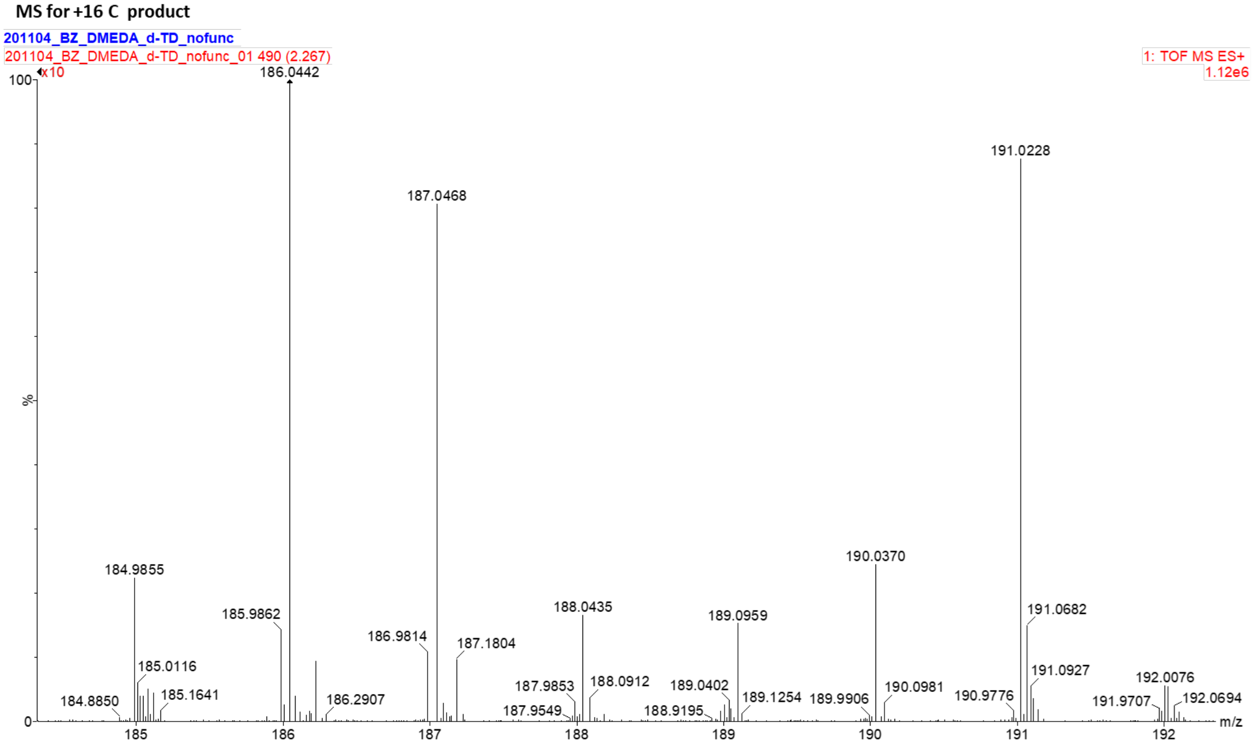


Figure 4-23

No deuterium incorporation on the alkyl chain in the product was detected.

4.3 EVALUATION OF BIAS DEPENDENCY

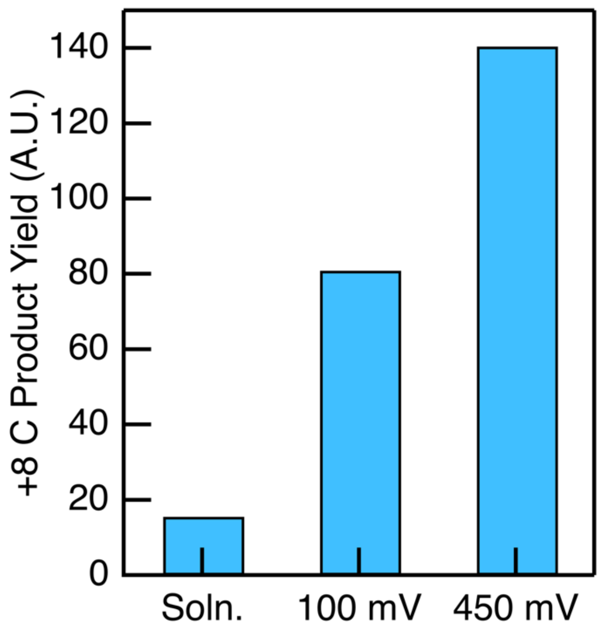


Figure 4-24 Reaction yields with added n-OctOOH (100 mM) in solution only, with field at 100 mV, and with field at 750 mV in the STM-BJ

4.4 EVALUATION OF REPRODUCIBILITY

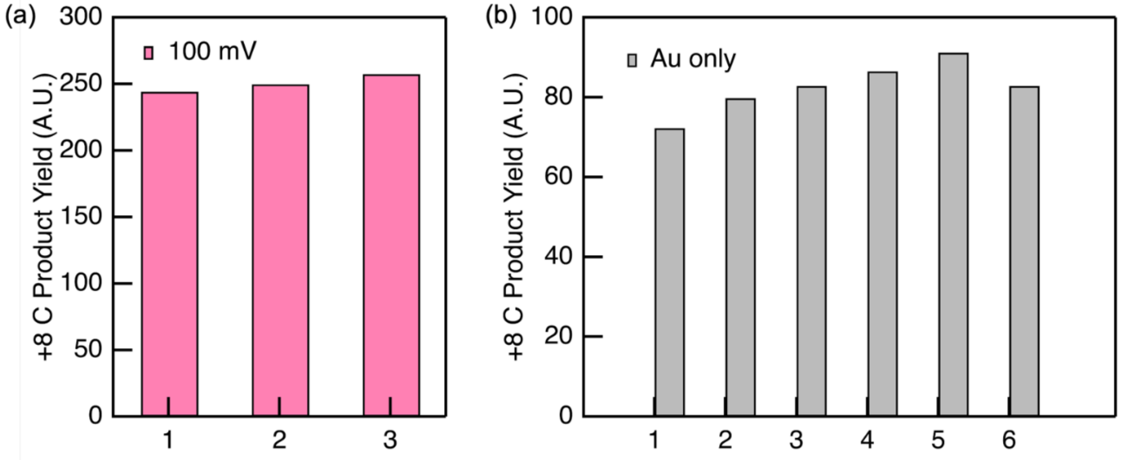


Figure 4-25 Reaction yields with added n-OctOOH (100 mM) in (a) 3 different gold-coated substrates coated with 100 mV applied bias and (b) 6 different gold-coated substrates coated without applying the field.

4.5 EVALUATION OF AIR COMPONENTS ON REACTIVITY

Solutions in TD containing 1 mM DMEDA and internal standard (1-methyl-2-phenylindole at 50 µM) were purged with air, Ar, O_2, or CO_2 at 1 atm for 5 min, then 50 µL of the solutions were deposited on Au substrates, left for 24 h, and analyzed by LC-MS (SI section 2.4.1).

+C	air	Ar	O2	CO2
6	0.00122213	0.001564	0.000935	0.000682
7	2.05308E-05	0.00015	0.000172	0.000121
8	0.000614761	0.000755	0.000706	0.000485
9	0.00093615	0.001929	0.001573	0.000887
10	0.001714229	0.001844	0.001554	0.001737
11	0.001297938	0.001243	0.000932	0.001005
12	0.002122961	0.002225	0.002134	0.002767
13	0.005020478	0.00464	0.005004	0.005056
14	0.009734664	0.00924	0.009812	0.0094
15	0.004355012	0.004441	0.004877	0.00459

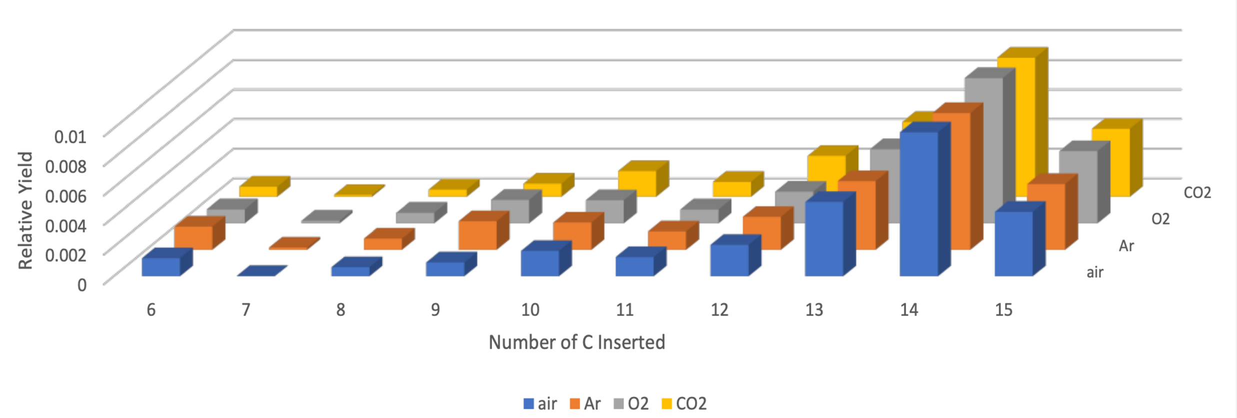


Figure 4-26

4.6 EVALUATION OF INTERNAL STANDARD ON REACTIVITY

50 µL of solutions in TD, TCB, and OB containing 1 mM DMEDA with or without internal standard (1-methyl-2-phenylindole at 50 µM) were deposited on Au substrates, left for 24 h, and analyzed by LC-MS (SI section 2.4.1).

+C	TD w IS	TD w/o IS	TCB w IS	TCB w/o IS	OB w IS	OB w/o Is	% w IS	% w/o IS	% TCB w IS	%TCB w/o IS	% OB w IS	% OB w/o Is
6	324.6053	191.34	148.0113	165.309333	21633.296	18567.9623	1.01264776	0.614207	4.7578937	3.520456181	12.43029	12.2118378
7	114.513	90.916	37.538	59.057	133068.031	117184.76	0.35723792	0.291843	1.2066766	1.257688096	76.45966	77.0704538
8	411.208	364.1447	131.6897	180.848	11604.8723	9635.193	1.28281583	1.168915	4.2332261	3.851370316	6.668053	6.33690503
9	1750.447	2109.392	2366.86	3240.95067	3388.20533	2549.901	5.46074175	6.771207	76.083835	69.01984647	1.946832	1.67702717
10	2258.715	2538.346	278.9273	816.346	560.559	552.402	7.04635072	8.148162	8.9662499	17.38504574	0.322092	0.36330554
11	1183.069	1321.044	24.27333	115.867	204.668667	266.857667	3.69073576	4.240589	0.7802777	2.467523691	0.117601	0.17550782
12	2947.434	3319.498	49.058	58.381	678.97	861.005333	9.19489545	10.65568	1.5769924	1.243291883	0.39013	0.56626878
13	4888.613	5183.407	15.742	33.686	698.037333	551.815333	15.2506521	16.63888	0.506034	0.717382888	0.401086	0.3629197
14	11431.03	8531.237	6.432	17.223	738.895333	632.326333	35.6605527	27.38551	0.2067597	0.36678399	0.424562	0.41587044
15	6745.475	7503.052	52.32633	8.01133333	1461.371	1246.65467	21.0433701	24.085	1.6820545	0.170610742	0.83969	0.81990389

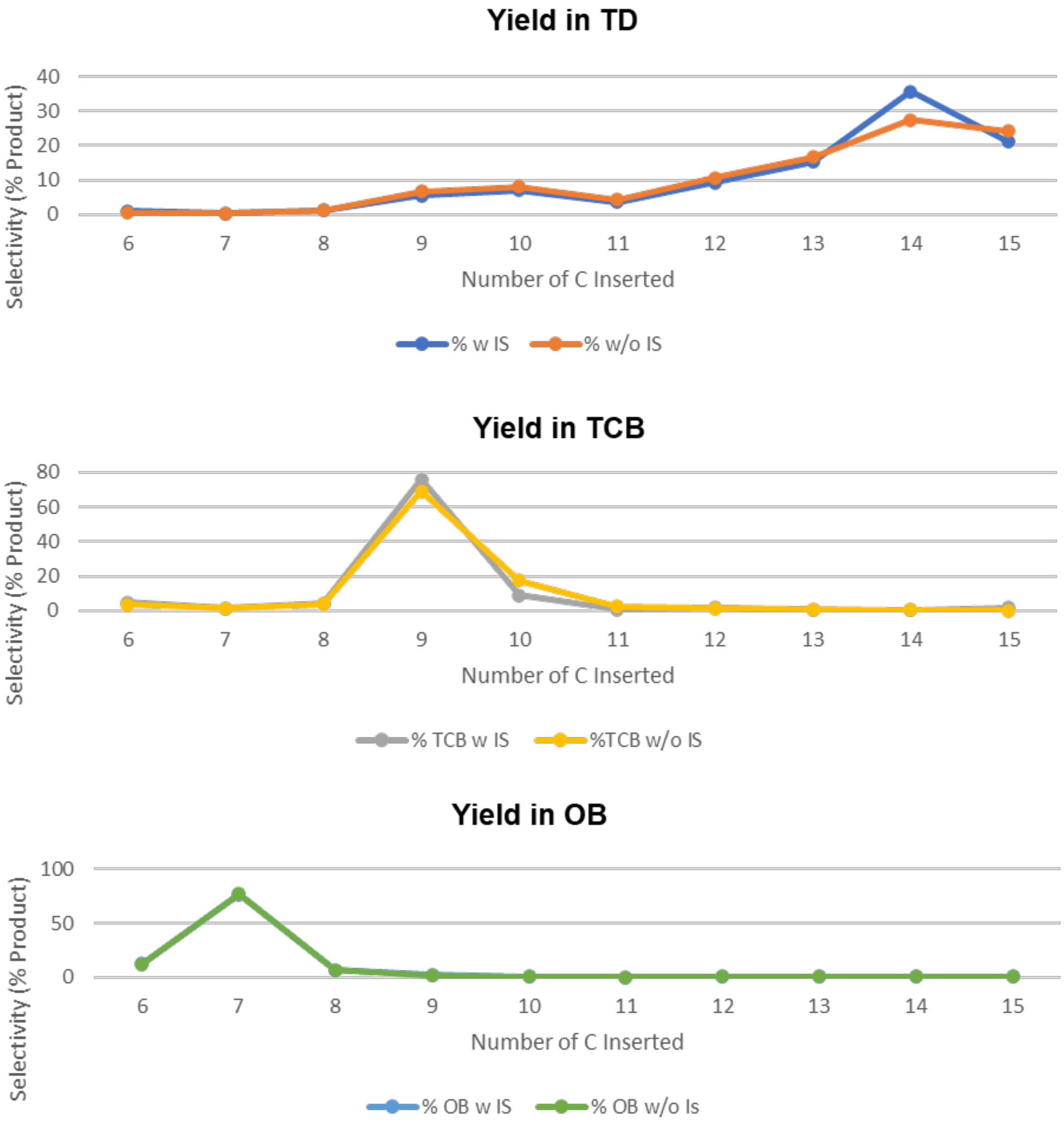

Yield in TD
Selectivity (% Product)
40
30
20
10
0
6
7
8
9
10
11
12
13
14
15
Number of C Inserted
% w IS
% w/o IS
Yield in TCB
Selectivity (% Product)
80
60
40
20
0
6
7
8
9
10
11
12
13
14
15
Number of C Inserted
% TCB w IS
%TCB w/o IS
Yield in OB
Selectivity (% Product)
100
50
0
6
7
8
9
10
11
12
13
14
15
Number of C Inserted
% OB w IS
% OB w/o Is

Figure 4-27

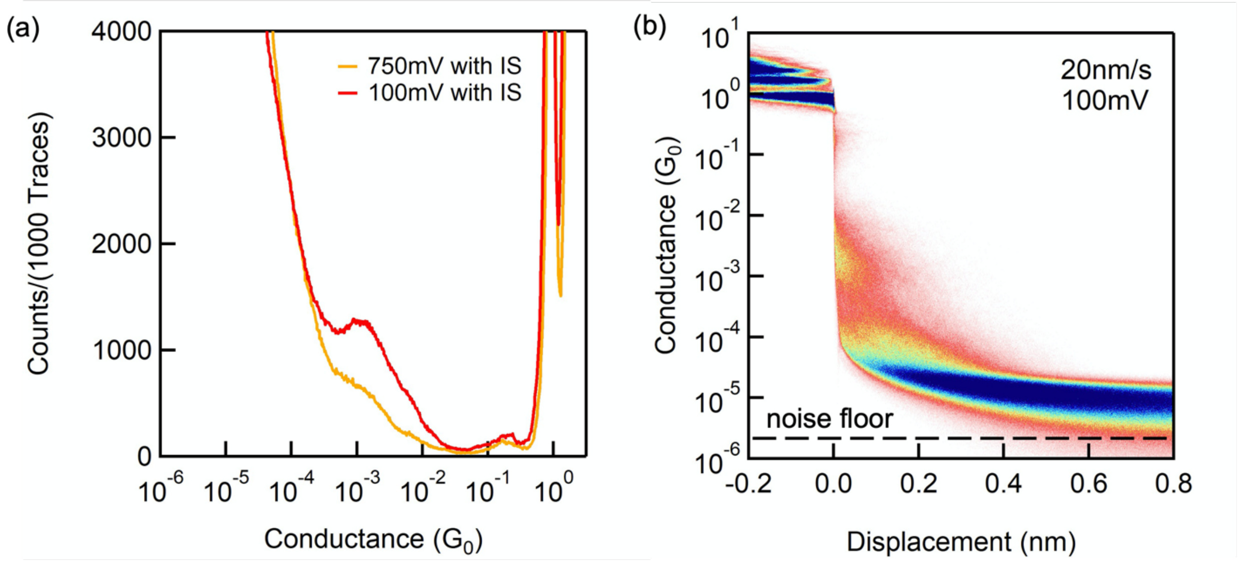


Figure 4-28 Logarithm-binned 1D and 2D conductance-displacement histograms of conductance traces measured with DMEDA and internal standard tributylamine, showing the tunneling current. The dash line shows the noise floor, indicating the current is above noise floor. All measurements were performed using 1 mM in tetradecane at room temperature.

4.7 REACTIVITY SOLVENT DEPENDENCE

50 µL of solutions in TD, or OB containing 1 mM DMEDA and internal standard (1-methyl-2-phenylindole at 50 µM) were deposited on Au substrates, left for 24 h, and analyzed by LC-MS (SI section 2.4.1).

Data with an older (more autoxidized) bottle of TD.

n=	TD	TD A/IS	OB	OB A/IS
6	392	0.141	618	0.229
7	1094	0.395	4329	1.606
8	2602	0.939	359	0.133
9	4068	1.468	122	0.045
10	6570	2.370	27	0.010
11	9463	3.414	19	0.007
12	11846	4.273	125	0.046
13	1713	0.618	92	0.034
14	62	0.022	55	0.020
15	trace	trace	84	0.031

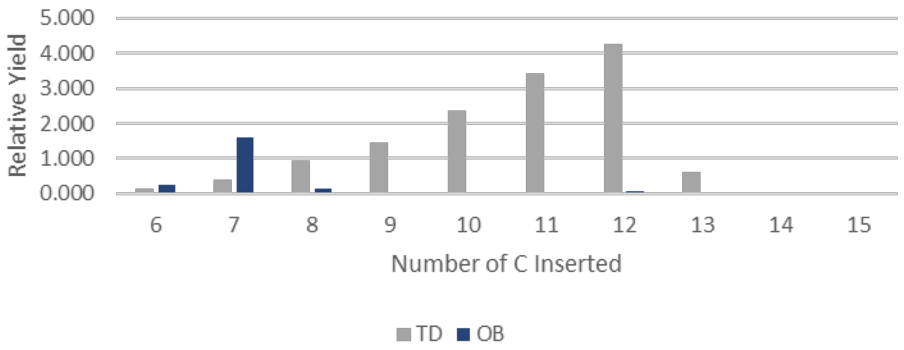


Figure 4-29

Data with a newer (less autoxidized) bottle of TD. For raw data see SI section 4.4.

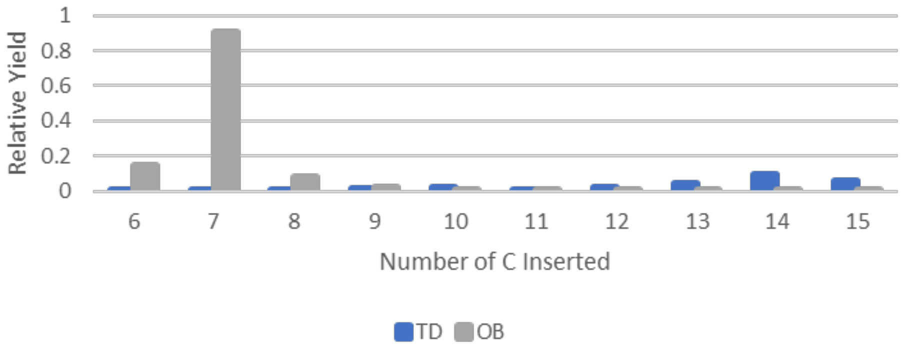
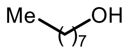
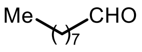


Figure 4-30

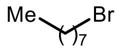
4.8 EVALUATION OF POSSIBLE ALKYL PRECURSORS



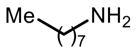
4a



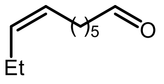
4b



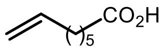
4c



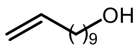
4d



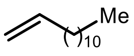
4e



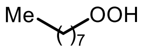
4f



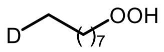
4g



4h



4i



4j

4i and **4j** were synthesized as described in SI section 3.4. 50 µL of solutions in TCB containing 1 mM DMEDA and 100 mM additives **4a-j** were deposited on Au substrates, left for 24 h, and analyzed by LC-MS (SI section 2.4.1). A modified LC method was used from described in the general LC parameters (SI section 2.4.1): 0-100% methanol/isopropanol (4:1) in H_2O with 0.1% formic acid over 5 min, 0.1 uL injection volume, Acquity UPLC BEH C_{18} column (2.1 mm × 100 mm, 1.7 µm), 0.35 mL/min flow rate, with the mass detector in ES+ mode.

4a-4g

EIC for or +6-15 C products

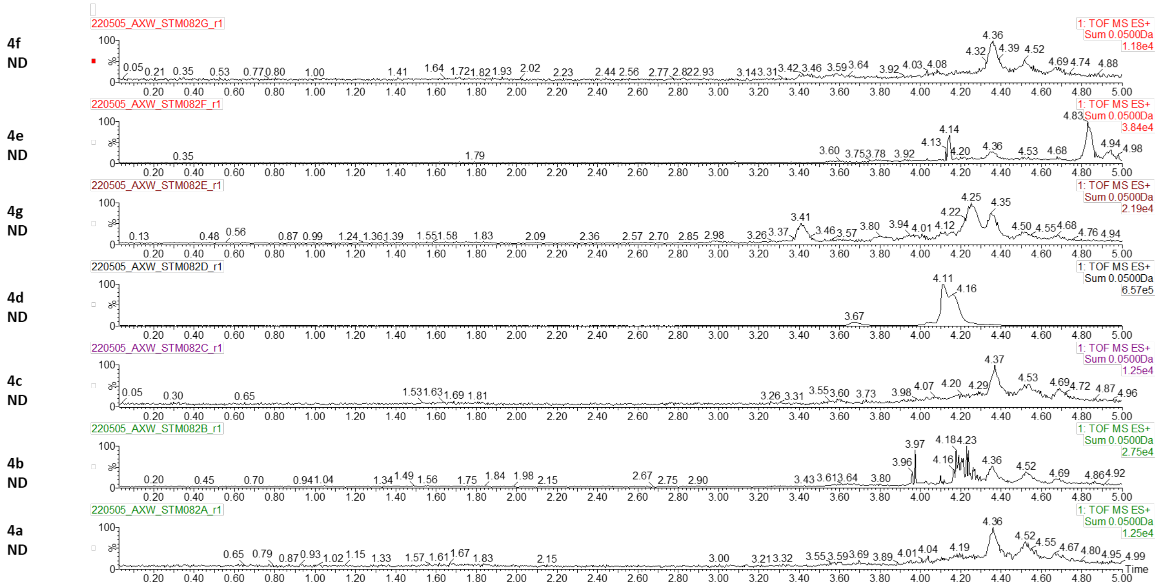
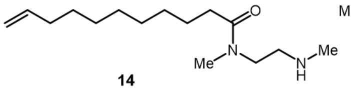
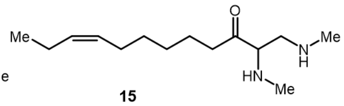


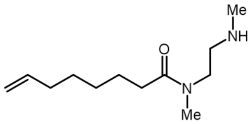
Figure 4-31



14



15



16

EIC for or expected adducts with DMEDA

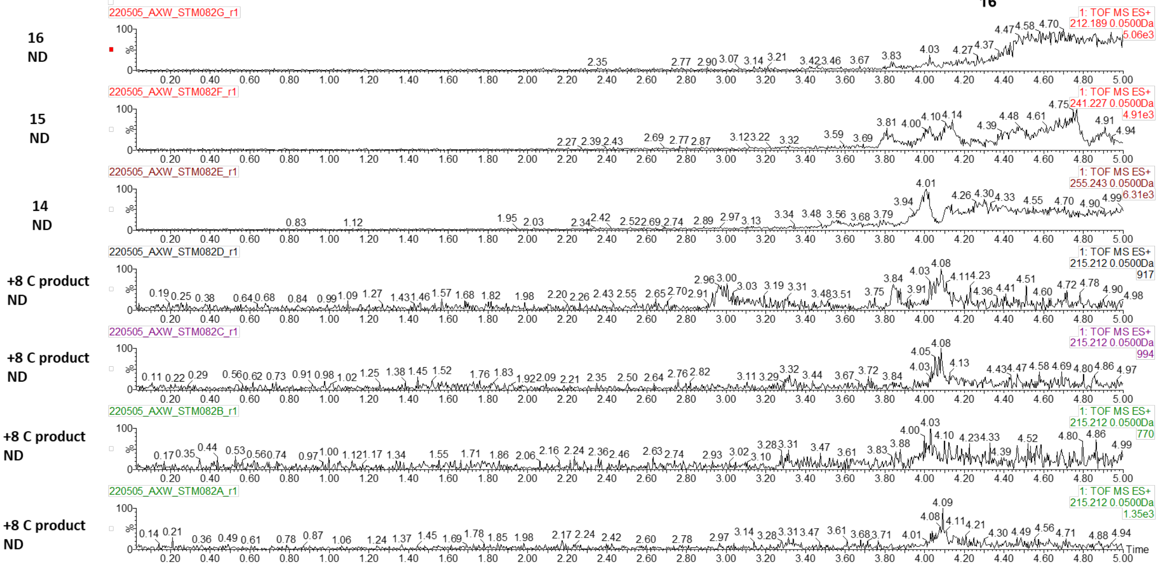


Figure 4-32

4a-4g are not alkyl sources since they inhibit reactivity.

4h

+C	TD
6	0
7	0.000148
8	0.001663
9	0.004388
10	0.008011
11	0.004232
12	0.012887
13	0.018637
14	0.041506
15	0.017755

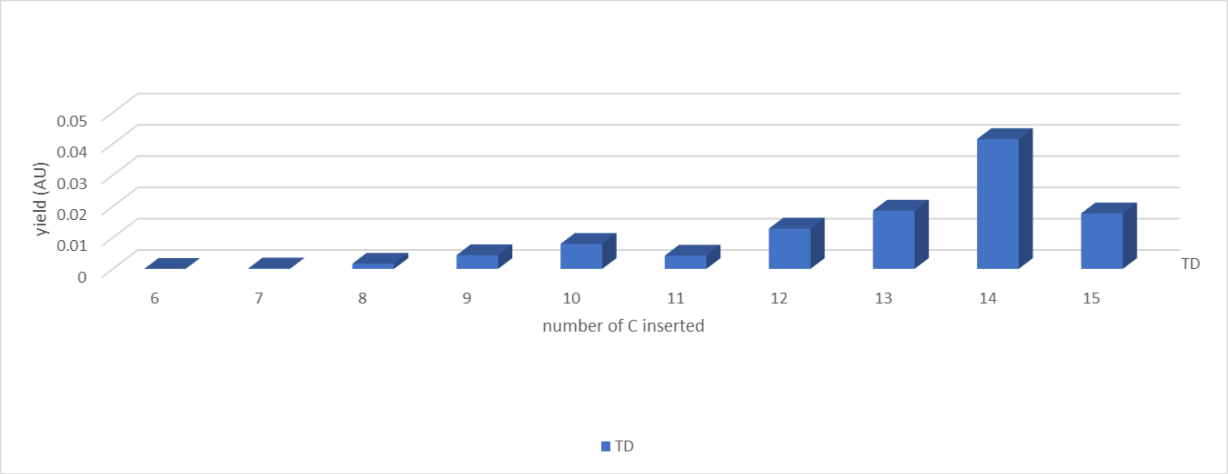
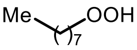


Figure 4-33

No significant increase in the +13 C product suggests **4h** is not the alkyl precursor.



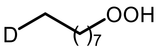
4i

	no Au	Au only	100 mV
avg A	48749.64	143121	181997

Yield vs. conditions is graphed in Fig. 4 in the main text. **4i** significantly increases +8 C product, this is consistent with it being the alkyl precursor.

An identical reaction was done with steel substrates instead, and the corresponding yield vs. conditions figure can be found in Fig. 4 in the main text.

	avg A
solution only	2984.55
steel only	4158.037
field	5328.432



4j

MS spectrum of the +C8 product is shown in Fig. 2d in the main text. **4j** is a competent alkyl transferring reagent under STM reaction conditions.

4.9 EVALUATION OF SURFACE FUNCTIONALIZATION

Experiment A: 50 µL of solution in TCB containing 1 mM DMEDA and 100 mM n-OctOOH (**4i**) is deposited on an Au substrate, removed after 10s, and frozen until analysis by LCMS. The substrate is then used in experiment C.

Experiment B: 50 µL of solution in TCB containing 1 mM DMEDA is deposited on an Au substrate, removed after 26 h, and frozen until analysis by LCMS.

Experiment C: Substrate from experiment A is washed with tetradecane and CH_2Cl_2 thoroughly (3x2 mL with each solvent), and an additional 50 µL of solution in TCB containing 1 mM DMEDA is deposited on the substrate, removed after 26 h, and frozen until analysis by LCMS.

Experiment D: 50 µL of solution in TCB containing 100 mM n-OctOOH (**4i**) is deposited on an Au substrate, removed after 10 s, and the substrate is then washed with tetradecane and CH_2Cl_2 thoroughly (3x2 mL with each solvent), and an additional 50 µL of solution in TCB containing 1 mM DMEDA is deposited on the substrate, removed after 26 h, and frozen until analysis by LCMS.

Upon thawing of the samples, they are prepared and analyzed by LCMS (SI section 2.4.1)

Experiment	**A**	**B**	**C**	**D**
Au	+	+	+, from A	OctOOH Functionalized
n-OctOOH	+	−	−	−
time	10 s	26 h	26 h	26 h
avg A	626.61433	0	32.067333	26.850667

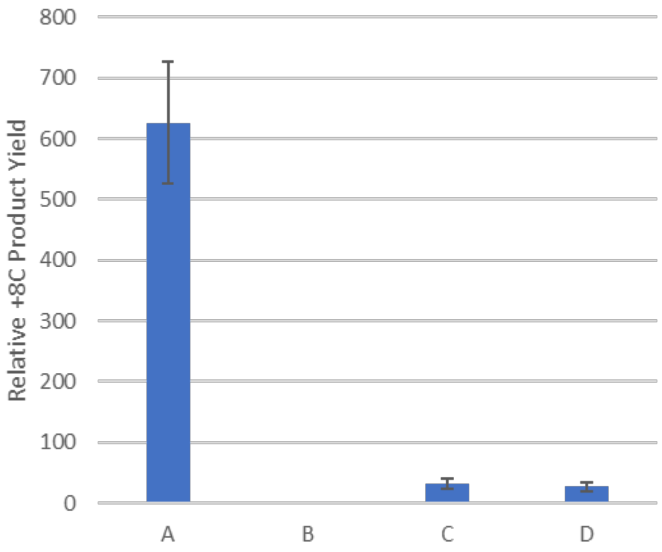


Figure 4-34

4.10 PLAUSIBLE MECHANISMS

4.10.1 Alkyl chain from alkyl hydroperoxides

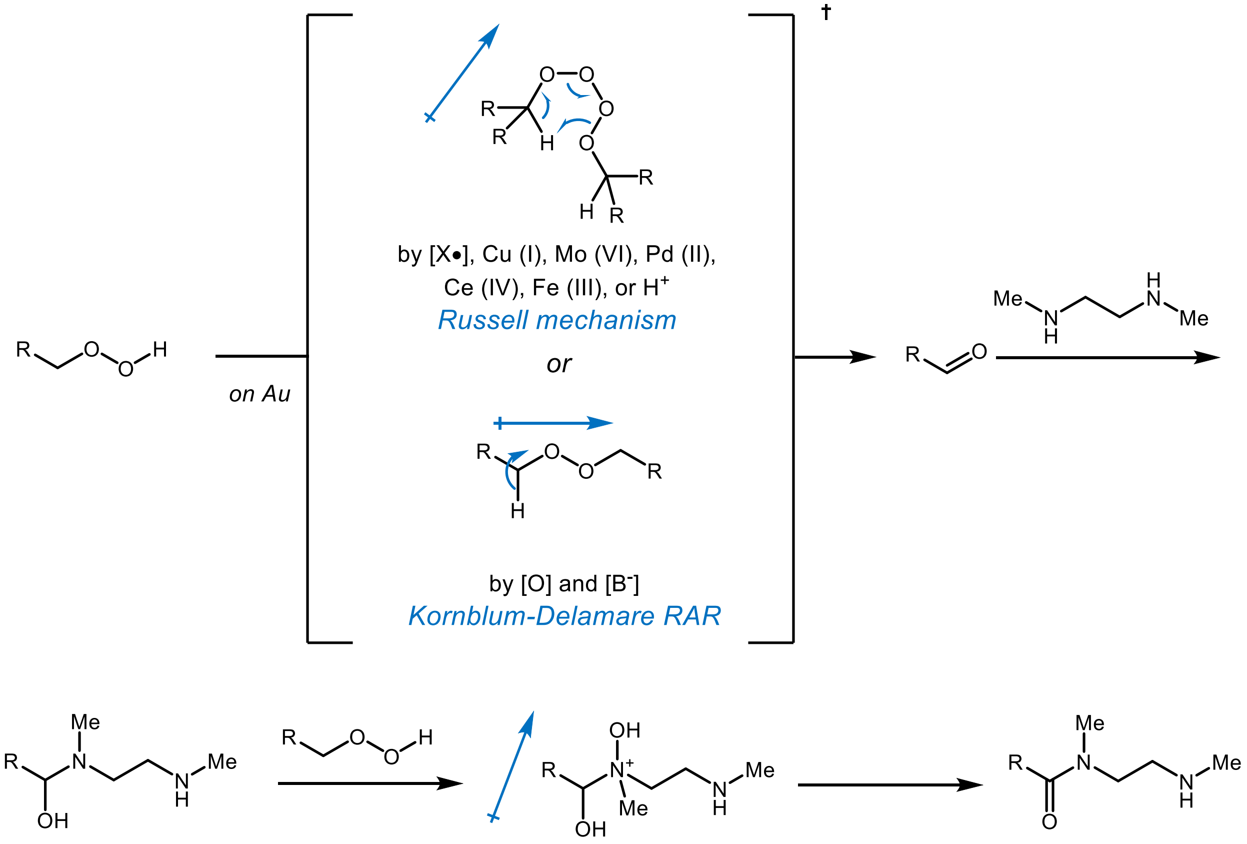


Figure 4-35

Alkyl hydroperoxides originating from autoxidation of alkanes are known to decompose to their corresponding aldehydes as a secondary autoxidation product under O_2 and high heat.[7–9] This process is known to be facilitated by radical initiators such as AIBN,[10] (t-BuO)$_2$,[11] or oxidants such as Cu (I),[12,13] Mo (VI),[14] Pd (II),[15] Ce (IV),[16] Fe (III),[17] or IBX.[18] This is thought to intercept the dimeric Russell intermediate which fragments to afford the aldehyde, along with the alcohol, and O_2.[10,16] Alternatively, upon oxidative dimerization of the hydroperoxide to the dialkyl peroxide, base catalyzed Kornblum-Delamare rearrangement could also afford the aldehyde.[19] Both of these reaction mechanisms intercept charge-separated intermediates (dipoles shown) that could be stabilized by the presence of the electric field; moreover, the catalytic effect of the Au surface on hydroperoxide functionalization is unprecedented in the literature. The novel Au-catalyzed disproportionation of the alkyl hydroperoxide can generate the corresponding aldehyde, which could be intercepted by DMEDA. The hydrophobicity of the reaction solvent (tetradecane) likely favors the formation of the hemiaminal, and could be oxidized by the hydroperoxide.[20] The reaction likely operates under diffusion control, as this novel mode of peroxide activation by the Au surface is at millimolar concentration, with the peroxide originating from solvent autoxidation likely similarly dilute. Alternatively, data from Figure 3b in the main text suggests some rapid functionalization and stabilization of the hydroperoxide or their fragmentation products may be implicated in this novel activation mode.

4.10.2 Alkyl chain truncation from alkyl hydroperoxides

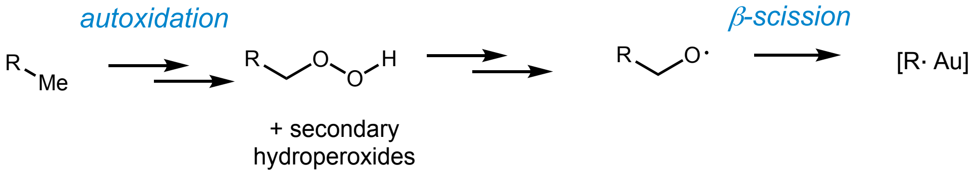


Figure 4-36

Following autoxidation of the alkane, the hydroperoxide products is known to fragment to shorter carbon-containing synthons via Hock RAR[19] or β-scission.[21] This mode of C-C cleavage mediated by a Au surface and electric field is unknown in the literature, but likely the stabilization of their corresponding charge-separated transition state by Au is integral to the electric field acceleration effect observed.

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