Late-Stage Carbon Isotope Exchange of Aryl Nitriles through Ni-Catalyzed C–CN Bond Activation

Supporting Information

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General Experimental Details

Reagents and common substrates were purchased from commercial suppliers and used as received. Non-commercially available substrates were procured from Merck's building block collection and used as received. $Zn(^{14}CN)_2$ was purchased from ViTrax. NMR chemical shifts are reported in ppm and referenced to residual solvent peaks. Coupling constants are reported in hertz (Hz).

HPLC MS analyses were performed on an Agilent 1100 HPLC-MSD instrument in API-ES positive ionization mode using an Ascentis® Express C18 column. Isotope incorporation was determined based on the mass distribution using Isopat. software.[1] Carbon-14 reagents and compounds were handled by experimentalist uniquely trained in working with radioactive materials and operating in specialized laboratories. C-14 radioactivity was measured in PerkinElmer Ultra Gold liquid scintillation cocktail with either a PerkinElmer 3110TR liquid scintillation analyzer. RadioHPLC and HPLC-UV comparison was conducted with an Agilent 1100 series HPLC connected in series to a PerkinElmer Radiomatic 625TR Flow Scintillation Analyzer.

Representative Reaction Procedure: The following setup was conducted in a glovebox under a N_2 atmosphere: To an 8 mL screw-cap vial with a stir bar was added NiCOD(DQ) (0.1 mmol), 1 mL of NMP, and phosphine ligand (0.2 mmol). The solution was then allowed to stir for ~5 minutes at room temperature. Next, aryl nitrile (0.5 mmol), BPh_3 (0.4 mmol), and $Zn(^{13}CN)_2$ (0.6 mmol) were added directly to the stirring solution, followed by an additional 1 mL of NMP. For ^{14}C labeling reactions, $Zn(^{13}CN)_2$ was replaced with $Zn(^{14}CN)_2$, and all other conditions were kept the same.

The reaction vial was then sealed, taken out of the glovebox, to be placed in an oil bath and heated at 80 ^oC for 18 hours. After which, the reaction vial was taken out of the oil bath, and then allowed to cool to room temp. Then ~5 mL of MeOH was slowly added to the crude reaction mixture, and followed by filtration of the solution on a disposable 20 mL medium frit filter funnel. The frit was washed with an additional 20 mL of MeOH, and then the solvent from the collected filtered reaction mixture was removed under reduced pressure. The crude product was then purified by silica gel chromatography.

NOTES: Although an air-stable Ni(COD)(DQ) complex is employed, reactions were generally set up in a glovebox due to the use of moderately air-sensitive phosphine ligand solutions and moisture-sensitive BPh_3. The use of Ni(COD)(DQ) was preferred over $Ni(COD)_2$ due to the known thermal stability issues of $Ni(COD)_2$, even under an N_2 atmosphere.

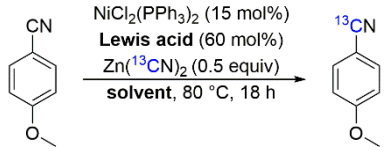
In several cases, mostly with method **A**, moderate yields were obtained due to methyl cross-coupling, homocoupling, protodecyanation of the ArCN substrates, and other unidentified decomposition pathways. At extended reaction times or higher temperatures, greater decomposition of the substrate was observed.

Mass Spectral Data and IsoPat Analysis: Percent ^{13}C and ^{14}C incorporation was determined by comparison of the mass spectral patterns of the labeled product versus authentic starting material using the IsoPat2 spreadsheet.[1] The mass spectra were tabulated for abundance vs. *m/z*, and these data were inputted to the Isopat2 spreadsheet (included below), which uses its programmed algorithm to determine the relative percentage of each labeled species differentiated in the number of incorporated isotopes. Sum of these percentages give rise to the overall isotope enrichment. For the ^{14}C labeled compound, specific activity (SA) is the radioactivity per quantity of a radionuclide, expressed as Ci/mmol in this work. ^{14}C has a

maximum theoretical SA of 62.4 mCi per mmol, which refers to 100% of the molecules contain one ^{14}C label.

Initial Optimization Studies

Solvent and Lewis Acid Screen: As shown in Table S1, polar solvents were found to be most optimal, with the highest ^{13}C enrichment achieved in NMP (entry 10). No CIE was observed when replacing $Zn(^{13}CN)_2$ with $Cu^{13}CN$ or $K^{13}CN$.

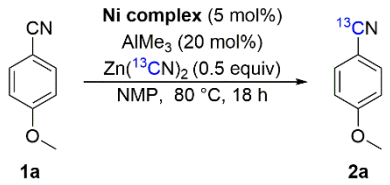


1a **2a**

Table S1

Reaction	Solvent	Lewis acid	LCMS Yield (%)	%^{13}C Enrichment
1	toluene	$AlMe_3$	<10	12
2	trifluorotoluene	$AlMe_3$	<10	9
3	1,2-dichloroethane	$AlMe_3$	<10	<1
4	MTBE	$AlMe_3$	<10	27
5	DMAC	$AlMe_3$	85	45
6	dioxane	$AlMe_3$	31	30
7	DME	$AlMe_3$	<10	28
8	DMAC	$AlMe_3$	89	42
9	DMF	$AlMe_3$	64	50
11	DMAC	$AlMe_3$	94	4
10	**NMP**	$AlMe_3$	**80**	**53**
13	NMP	$Al(CH_3)_2Cl$	42	37
14	NMP	$AlEt_3$	9	45
15	NMP	$Al(Et_2)Cl$	56	34
16	NMP	$AlCl_3$	>95	<3
17	NMP	Al^tBu_3	>95	31
18	NMP	$B(Ph)_3$	>95	`<3
19	NMP	BEt_3	89	<3
20	NMP	$BF_3{\cdot}O(C_2H_5)_2$	50	<3
21	NMP	$Ho(OTf)_3$	>95	<3
22	NMP	$Zn(OTf)_2$	78	<3
23	NMP	TMSOTf	86	<3
24	NMP	TFAA	62	<3

Ni Complex Screen: Using the optimized conditions from Table S1 (entry 10), we then examined an array of Ni complexes to determine which complex provided the highest amount of ^{13}C enrichment (Table S2). Although $NiCl_2(PMe_3)_2$ was found to be the most optimal Ni complex in this screen (entry 28), comparable ^{13}C enrichment values were also observed with other alkyl phosphine (entry 29 and 31) and NNN pincer (entry 35) Ni (II) systems.

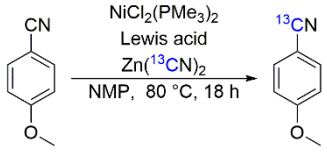


1a **2a**

Table S2

Reaction	Ni Complex	LCMS Yield (%)	%^{13}C Enrichment
25	$NiCl_2(PPh_3)_2$	96	37
26	$NiCl_2$ glyme	>97	12
27	$NiCl_2$(dppp)	95	27
28	**$NiCl_2(PMe_3)_2$**	**82**	**50**
29	$NiCl_2(PBu_3)_2$	92	48
30	$NiCl_2$(dppe)	93	37
31	*trans*-$(PCy_2Ph)_2Ni$(*o*-tolyl)Cl	92	45
32	$NiCl_2(PCy_3)_2$	91	36
36	$NiCl_2$(dppf)	92	22
33	*bis(methyl methacrylate)(1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene)nickel*	93	32
34	*Chloro(4-cyanophenyl)[(R)-1-[(S)-2-(dicyclohexylphosphino)ferrocenyl]ethyldiphenylphosphine]nickel*	95	25
35	*bis[(2-dimethylamino)phenyl]amine nickel chloride*	92	45

Loading Optimization for $Zn(^{13}CN)_2$, $NiCl_2(PMe_3)_2$, and Lewis Acid: Optimal loading ratios for $Zn(^{13}CN)_2$, $NiCl_2(PMe_3)_2$, and $AlMe_3$ were identified through systematic reaction studies (Table S3). Maximum ^{13}C enrichment for **2a** was obtained using the conditions shown in entry 39. It should be noted that no appreciable increase in ^{13}C enrichment for **2a** was observed when running entry 39 conditions at 100 °C. Decreasing the reaction temperature to 60 °C, using the conditions from entry 39, led to a reduction in **2a** enrichment.



1a **2a**

Table S3

Reaction	$Zn(^{13}CN)_2$ (equiv)	$NiCl_2(PMe_3)_2$ (mol%)	Lewis acid (mol%)	LCMS Yield (%)	%^{13}C Enrichment
37	2.0	20	$AlMe_3$ (80 mol%)	66	77
38	1.5	20	$AlMe_3$ (80 mol%)	66	73
39	**1.2**	**20**	**$AlMe_3$ (80 mol%)**	**60**	**73**
40	1.2	20	DABAL-Me_3 (40 mol%) [2 $AlMe_3$ molecules per DABAL-Me_3]	77	54
41	1.1	20	$AlMe_3$ (80 mol%)	61	72
42	1.1	15	$AlMe_3$ (80 mol%)	83	57
43	1.1	10	$AlMe_3$ (80 mol%)	87	50
44	0.6	20	$AlMe_3$ (80 mol%)	63	52
45	0.3	20	$AlMe_3$ (80 mol%)	47	39
46	1.1	20	$AlMe_3$ (60 mol%)	80	64
47	1.1	20	$AlMe_3$ (40 mol%)	88	54
48	1.1	20	$AlMe_3$ (20 mol%)	91	11

Computational Methods, Cartesian Coordinates, and Energies

The quantum chemical calculations were performed using the Gaussian 16 electronic structure program.[2] Geometry optimization and frequency calculations were performed at the B3LYP-D3/basis-I level of theory,[3-7] where basis-I stands for the 6-31+G* basis set for the non-metal atoms and the LANL2DZ[8] basis set and effective core potential for Ni. Pure d-type angular momentum functions were used for all systems. An "ultrafine" integration grid and a two-electron integral accuracy of 10^{-14} (`int=(Acc2E=14,ultrafine)`) were used. The natures of all stationary points were verified by calculating vibrational frequencies at the same level of theory. The thermal corrections for Gibbs energies were calculated for 298.15 K and 1 atm using the quasi-harmonic approximation proposed by Cramer and Truhlar[9], in which all of the real vibrational frequencies lower than 100 cm^{-1} were set to 100 cm^{-1} before their contributions to the vibrational entropy were computed with the usual harmonic oscillator model. For a best estimate of Gibbs energies, single-point electronic energies were computed for the B3LYP-D3/basis-I geometries using the M06[10] density functional and the def2-TZVPD[11] basis for all atoms. The def2-TZVPD basis set specifications were obtained from the EMSL Basis Set Exchange website.[12] Solvation corrections were computed for all optimized structures using the PCM solvation model[13] with the dielectric constant of NMP, ε = 32.0.

Structure: 5

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Charge =  0, Multiplicity = 1
SCF Energy:         -1416.111318 hartree
SCF Energy + ZPVE:  -1415.780853 hartree
Enthalpy:           -1415.756214 hartree
Free Energy:        -1415.835640 hartree
Free Energy with quasiharmonic correction:  -1415.829944 hartree
SCF Energy (SP): -2754.81488208 hartree
DeltaG (solv)                              (kcal/mol) =      -7.27
Ni          0.61575       -0.19761        0.02743
P           2.66402       -1.08200        0.04492
C           4.26866       -0.15052        0.07539
H           5.13110       -0.82908        0.07845
H           4.33578        0.50301       -0.80093
H           4.31305        0.47837        0.97159
C           2.88165       -2.23444        1.47427
H           3.81251       -2.81080        1.40039
H           2.88361       -1.66570        2.41038
H           2.02384       -2.91383        1.48965
C           2.92887       -2.22384       -1.38542
H           3.85792       -2.79925       -1.28570
H           2.07415       -2.90577       -1.43260
H           2.95985       -1.64923       -2.31744
P           0.58697        1.97689       -0.08634
C           2.17354        2.84792       -0.49859
H           2.04134        3.93598       -0.55048
H           2.92719        2.61466        0.26035
H           2.54440        2.48817       -1.46438
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C	-0.53458	2.72635	-1.35823
H	-0.49712	3.82294	-1.33859
H	-0.23109	2.37596	-2.35058
H	-1.56254	2.39344	-1.18818
C	0.09573	2.90706	1.44216
H	0.10503	3.99168	1.27575
H	-0.90523	2.60128	1.76136
H	0.79286	2.66331	2.25090
C	-1.10977	-0.97311	0.05410
N	-0.30769	-1.90564	0.04795
C	-2.56052	-0.78000	0.04597
C	-3.12086	0.44911	0.42274
C	-4.50539	0.63088	0.41909
C	-5.34647	-0.41541	0.02631
C	-4.79553	-1.64624	-0.35286
C	-3.41312	-1.83184	-0.33773
H	-2.45841	1.25231	0.72822
H	-4.92764	1.58652	0.72021
H	-5.44653	-2.46269	-0.65607
H	-2.97480	-2.78342	-0.62393
H	-6.42436	-0.27432	0.01591

Structure: TS6

Charge = 0, Multiplicity = 1

SCF Energy: -1416.077911 hartree

SCF Energy + ZPVE: -1415.749787 hartree

Enthalpy: -1415.725337 hartree

Free Energy: -1415.802854 hartree

Free Energy with quasiharmonic correction: -1415.798475 hartree

SCF Energy (SP): -2754.77894931 hartree

DeltaG (solv) (kcal/mol) = -9.84

C	-4.15440	-0.99072	0.34521
C	-3.28896	-1.24256	1.41678
C	-1.91667	-1.36627	1.19992
C	-1.37850	-1.22300	-0.09813
C	-2.26421	-0.99457	-1.17578
C	-3.63351	-0.87305	-0.95230
Ni	0.37094	-0.15724	-0.02292
P	-0.43060	1.94566	-0.02690
C	-0.99536	2.49058	-1.70532
C	0.04774	-1.96219	-0.39986
N	0.40364	-3.04379	-0.74689
P	2.56335	-0.37376	0.11806
C	3.11126	-1.62899	1.35872
C	3.30846	-1.04109	-1.43428
C	3.67996	1.05630	0.50036
C	0.62114	3.38619	0.48018
C	-1.95983	2.23536	0.97263
H	-1.85984	-0.92197	-2.18131
H	-1.24577	-1.58024	2.02715
H	-4.30178	-0.68842	-1.79051
H	-5.22429	-0.90240	0.51458

H	-3.68668	-1.34762	2.42360
H	-2.72295	1.51175	0.67124
H	-1.74324	2.07146	2.03348
H	-2.34465	3.25373	0.83695
H	-1.43559	3.49505	-1.67789
H	-0.14888	2.48815	-2.40017
H	-1.74337	1.78122	-2.07340
H	0.94396	3.25663	1.51891
H	0.08131	4.33731	0.39139
H	4.73305	0.75048	0.53492
H	3.56165	1.82950	-0.26648
H	2.83488	-1.30210	2.36684
H	2.59013	-2.56649	1.14085
H	4.19530	-1.79222	1.31763
H	4.37734	-1.25369	-1.31022
H	3.17624	-0.32128	-2.24916
H	2.77557	-1.96171	-1.69275
H	3.40480	1.49224	1.46683
H	1.51688	3.42547	-0.14860

Structure: 7

Charge = 0, Multiplicity = 1
SCF Energy: -1416.101669 hartree
SCF Energy + ZPVE: -1415.771577 hartree
Enthalpy: -1415.746791 hartree
Free Energy: -1415.825129 hartree
Free Energy with quasiharmonic correction: -1415.820468 hartree
SCF Energy (SP): -2754.80235905 hartree
DeltaG (solv) (kcal/mol) = -15.28

C	4.45944	-0.96425	-0.00082
C	3.74091	-1.02108	-1.20092
C	2.35036	-0.86651	-1.19777
C	1.64927	-0.64145	-0.00228
C	2.37674	-0.62307	1.19735
C	3.76991	-0.77468	1.20092
Ni	-0.25779	-0.33592	-0.02714
P	0.24214	1.86698	-0.04392
C	0.61515	2.47569	1.65859
C	-0.37745	-2.20463	0.04973
N	-0.54138	-3.36400	0.09174
P	-2.56752	-0.40871	-0.00867
C	-3.21736	-1.39143	-1.42753
C	-3.20041	-1.32540	1.46145
C	-3.70227	1.05710	-0.02989
C	-0.98240	3.12862	-0.62836
C	1.74514	2.38415	-0.97892
H	1.85419	-0.50269	2.14452
H	1.80614	-0.92401	-2.13822
H	4.31377	-0.75450	2.14352
H	5.54008	-1.08478	-0.00115
H	4.26398	-1.19232	-2.13988
H	2.62126	1.86565	-0.58354

H	1.64021	2.10805	-2.03282
H	1.88474	3.46838	-0.89916
H	0.87818	3.53978	1.64556
H	-0.25466	2.32698	2.30677
H	1.45336	1.90208	2.06336
H	-1.30771	2.89286	-1.64701
H	-0.53447	4.12906	-0.62361
H	-4.74753	0.72618	-0.01361
H	-3.52538	1.68807	0.84747
H	-2.98924	-0.87777	-2.36759
H	-2.71879	-2.36420	-1.43109
H	-4.30206	-1.52806	-1.34571
H	-4.28686	-1.45883	1.40022
H	-2.95723	-0.77134	2.37448
H	-2.70665	-2.29948	1.50296
H	-3.53888	1.65631	-0.93046
H	-1.85995	3.13603	0.02221

Structure: 8

Charge = 0, Multiplicity = 1
SCF Energy: -2136.030664 hartree
SCF Energy + ZPVE: -2135.418898 hartree
Enthalpy: -2135.378838 hartree
Free Energy: -2135.491089 hartree
Free Energy with quasiharmonic correction: -2135.481998 hartree
SCF Energy (SP): -3474.35132546 hartree
DeltaG (solv) (kcal/mol) = -10.80

Ni	1.57470	0.38402	-0.15342
P	2.59536	-1.63590	0.06550
C	3.48752	-2.20744	-1.45294
H	4.04415	-3.13234	-1.26001
H	2.74793	-2.39902	-2.23725
H	4.18002	-1.43954	-1.80857
C	3.92900	-1.64937	1.35196
H	4.44076	-2.61864	1.38511
H	4.66703	-0.86444	1.16005
H	3.47085	-1.45952	2.32858
C	1.67543	-3.16317	0.52465
H	2.34973	-4.02746	0.48129
H	1.27150	-3.06547	1.53455
H	0.83921	-3.31437	-0.16106
P	3.21706	1.83631	-0.35278
C	4.80387	1.30936	-1.15145
H	5.51628	2.14197	-1.19117
H	5.25939	0.48251	-0.59904
H	4.60178	0.97028	-2.17275
C	2.83164	3.33706	-1.35833
H	3.68376	4.02678	-1.38771
H	2.58608	3.02621	-2.37931
H	1.95934	3.85033	-0.94629
C	3.83696	2.55875	1.23400
H	4.63072	3.29412	1.05594

H	3.01263	3.04324	1.76583
H	4.22513	1.75780	1.87169
C	-0.01726	1.37063	-0.17397
N	-0.32463	0.17407	-0.16630
C	-0.67610	2.67262	-0.15886
C	-0.16129	3.69227	0.65797
C	-0.79443	4.93383	0.71903
C	-1.93216	5.17502	-0.05949
C	-2.43966	4.16601	-0.88541
C	-1.82190	2.91666	-0.93373
H	0.71961	3.49116	1.26135
H	-0.40230	5.71106	1.37002
H	-3.33290	4.34214	-1.47828
H	-2.23506	2.12187	-1.54365
B	-1.45330	-0.92368	0.03276
C	-0.47754	-2.86329	3.98017
C	-1.25881	-3.52992	3.03038
C	-1.55896	-2.91989	1.80840
C	-1.09786	-1.63236	1.47470
C	-0.33022	-0.98048	2.46083
C	-0.01851	-1.57571	3.68870
H	-0.23684	-3.33609	4.92966
H	-1.62946	-4.53195	3.23777
H	-2.14828	-3.48036	1.08984
H	0.05506	0.01759	2.26532
H	0.58180	-1.03207	4.41668
C	-1.23320	-3.80400	-3.40695
C	-0.26641	-2.80497	-3.26794
C	-0.33839	-1.89904	-2.20311
C	-1.35999	-1.94865	-1.23545
C	-2.33872	-2.94669	-1.42655
C	-2.27956	-3.86358	-2.48008
H	-1.18325	-4.51257	-4.23059
H	0.54154	-2.72472	-3.99399
H	0.42154	-1.12437	-2.13054
H	-3.18704	-2.99148	-0.74704
H	-3.05655	-4.61849	-2.58384
C	-5.22985	1.48991	0.18512
C	-4.90253	0.77543	-0.97105
C	-3.74231	-0.00764	-1.00843
C	-2.87520	-0.11168	0.09611
C	-3.23895	0.61002	1.24960
C	-4.38982	1.40131	1.30035
H	-6.12897	2.10146	0.21968
H	-5.54878	0.82771	-1.84563
H	-3.50458	-0.54497	-1.92342
H	-2.60359	0.55394	2.13098
H	-4.63155	1.94953	2.20900
H	-2.42443	6.14323	-0.01728

Structure: TS9
Charge = 0, Multiplicity = 1

SCF Energy: -2135.988802 hartree
SCF Energy + ZPVE: -2135.380954 hartree
Enthalpy: -2135.340221 hartree
Free Energy: -2135.457086 hartree
Free Energy with quasiharmonic correction: -2135.444347 hartree
SCF Energy (SP): -3474.31241521 hartree
DeltaG (solv) (kcal/mol) = -12.67

C	1.72027	-4.16422	-0.79773
C	1.79063	-3.37962	-1.95510
C	1.53766	-2.00893	-1.88583
C	1.23368	-1.40579	-0.65003
C	1.14603	-2.20408	0.50948
C	1.38996	-3.57366	0.42994
Ni	2.06203	0.48764	-0.56053
P	4.11972	-0.04566	0.22363
C	4.03965	-0.36551	2.04318
C	0.32793	-0.01332	-0.67044
N	-0.83151	0.17514	-0.48133
P	1.65740	2.65228	-0.75562
C	0.73650	3.11750	-2.28386
C	0.53890	3.26077	0.57624
C	3.04074	3.88058	-0.72500
C	5.56793	1.09994	0.09995
C	4.82179	-1.63091	-0.41233
H	0.85128	-1.75211	1.45123
H	1.56029	-1.39831	-2.78454
H	1.30659	-4.18353	1.32568
H	1.90112	-5.23441	-0.85516
H	2.02804	-3.83834	-2.91176
H	4.07993	-2.42503	-0.28608
H	5.03643	-1.53715	-1.48192
H	5.74294	-1.90214	0.11722
H	5.00374	-0.71381	2.43268
H	3.74939	0.55084	2.56754
H	3.27578	-1.12444	2.23845
H	5.78821	1.30431	-0.95328
H	6.46033	0.67313	0.57344
H	2.66682	4.90393	-0.84913
H	3.56989	3.81294	0.23138
H	1.34537	2.90591	-3.16892
H	-0.17416	2.51375	-2.33072
H	0.46325	4.17910	-2.27583
H	0.31906	4.32697	0.44901
H	1.00278	3.09960	1.55479
H	-0.39964	2.70024	0.53504
H	3.75312	3.66107	-1.52718
H	5.32881	2.05077	0.58703
B	-2.24926	-0.03468	0.16935
C	-0.84887	-1.98604	3.95876
C	-1.65667	-2.69603	3.06676
C	-2.13876	-2.07863	1.90419
C	-1.83754	-0.74194	1.59458

C	-1.03571	-0.04445	2.52264
C	-0.54332	-0.64608	3.68309
H	-0.47020	-2.46278	4.86043
H	-1.90878	-3.73511	3.27063
H	-2.74957	-2.65610	1.21523
H	-0.78215	0.99476	2.32084
H	0.07386	-0.07446	4.37454
C	-4.07371	4.04054	0.49465
C	-3.48292	3.60614	-0.69885
C	-2.92128	2.32930	-0.77264
C	-2.91670	1.44504	0.32445
C	-3.52651	1.90302	1.50438
C	-4.09835	3.17956	1.59509
H	-4.51467	5.03285	0.56127
H	-3.46869	4.26010	-1.56930
H	-2.47878	1.99872	-1.71168
H	-3.55144	1.25092	2.37477
H	-4.56177	3.50042	2.52626
C	-4.63909	-2.80264	-2.40144
C	-5.26684	-1.77348	-1.69250
C	-4.50869	-0.89307	-0.91197
C	-3.11138	-1.01064	-0.80515
C	-2.50529	-2.05701	-1.52791
C	-3.24935	-2.94073	-2.31623
H	-5.22394	-3.48694	-3.01242
H	-6.34701	-1.65287	-1.75080
H	-5.01408	-0.09255	-0.37572
H	-1.42705	-2.19186	-1.46722
H	-2.74604	-3.73780	-2.86101

Structure: 10

Charge = 0, Multiplicity = 1

SCF Energy: -2136.010106 hartree

SCF Energy + ZPVE: -2135.400471 hartree

Enthalpy: -2135.359406 hartree

Free Energy: -2135.477745 hartree

Free Energy with quasiharmonic correction: -2135.463743 hartree

SCF Energy (SP): -3474.33353103 hartree

DeltaG (solv) (kcal/mol) = -16.05

Ni	2.15659	-0.23154	0.03364
P	4.40008	-0.10678	0.01673
C	5.43502	-1.62869	-0.16764
H	5.20336	-2.12801	-1.11349
H	6.49926	-1.36681	-0.16010
H	5.23793	-2.32592	0.65070
P	1.62621	-2.49683	0.03504
C	0.46010	-2.92788	1.39672
C	0.68944	-2.94643	-1.48429
C	2.85734	-3.87262	0.15906
H	0.93674	-2.75230	2.36685
H	-0.43419	-2.30402	1.33129
H	0.16391	-3.98031	1.32418

H	-0.19678	-2.31284	-1.57367
H	1.31901	-2.79599	-2.36763
H	0.36458	-3.99164	-1.44442
H	3.41642	-3.80217	1.09749
H	2.33705	-4.83716	0.13477
H	3.56457	-3.83576	-0.67397
C	2.00110	3.83636	-1.15438
C	2.01627	4.53573	0.05708
C	2.08608	3.82582	1.25987
C	2.14906	2.42653	1.24812
C	2.15873	1.71583	0.03879
C	2.06436	2.43811	-1.16041
H	1.92097	4.37693	-2.09498
H	2.07419	4.35798	2.20867
H	2.17284	1.88790	2.19355
H	2.02436	1.90806	-2.10973
C	0.32509	0.02253	0.02953
N	-0.83242	0.11464	0.01803
C	5.09544	0.62836	1.55686
C	5.10714	0.96122	-1.30793
H	6.18748	0.69290	1.49192
H	4.67728	1.62794	1.69785
H	4.82271	0.01161	2.41955
H	6.20085	0.97445	-1.24080
H	4.81214	0.57719	-2.29005
H	4.71703	1.97615	-1.20650
C	-2.89529	1.47271	-0.69764
C	-4.14841	1.56220	-1.33169
C	-2.13356	2.65442	-0.62821
C	-4.62558	2.76562	-1.86142
H	-4.76050	0.66700	-1.42648
C	-2.59587	3.86340	-1.15860
H	-1.15436	2.63498	-0.15341
C	-3.84882	3.92597	-1.77693
H	-5.60034	2.79638	-2.34486
H	-1.97628	4.75569	-1.08791
H	-4.21356	4.86384	-2.19041
C	-2.69714	-1.25649	-0.92687
C	-2.93935	-2.51520	-0.34657
C	-2.59371	-1.21666	-2.33139
C	-3.06799	-3.67574	-1.11972
H	-3.03701	-2.58789	0.73447
C	-2.71999	-2.36720	-3.11704
H	-2.41205	-0.26021	-2.81756
C	-2.95579	-3.60722	-2.51186
H	-3.26227	-4.63131	-0.63536
H	-2.63875	-2.29702	-4.20026
H	-3.06023	-4.50459	-3.11809
C	-2.91967	-0.06188	1.51360
C	-4.30238	-0.18438	1.75494
C	-2.08099	-0.07838	2.64117
C	-4.82098	-0.32187	3.04417

H	-4.98857	-0.17184	0.91060
C	-2.58631	-0.21310	3.94139
H	-1.00534	0.02549	2.51144
C	-3.96155	-0.33815	4.14981
H	-5.89572	-0.41379	3.18897
H	-1.90414	-0.21657	4.79011
H	-4.36051	-0.44263	5.15636
B	-2.39404	0.08013	-0.02384
H	1.95557	5.62105	0.06411

Structure: BPh_3

Charge = 0, Multiplicity = 1
SCF Energy: -719.870417 hartree
SCF Energy + ZPVE: -719.592462 hartree
Enthalpy: -719.576534 hartree
Free Energy: -719.635932 hartree
Free Energy with quasiharmonic correction: -719.633492 hartree
SCF Energy (SP): -719.497004600 hartree
DeltaG (solv) (kcal/mol) = -3.30

B	-0.10300	1.16614	5.90134
C	2.52529	2.60731	2.67584
C	1.17454	2.34906	2.41820
C	0.34811	1.87786	3.44043
C	0.83257	1.67930	4.75298
C	2.19720	1.96333	4.98547
C	3.03780	2.40606	3.96207
H	3.17446	2.96317	1.87923
H	0.76997	2.50806	1.42139
H	-0.69711	1.67074	3.22480
H	2.60517	1.82115	5.98308
H	4.08790	2.60097	4.16676
C	0.54511	2.52411	10.03949
C	0.07674	1.22937	9.79073
C	-0.14168	0.80795	8.47747
C	0.12759	1.64945	7.37460
C	0.61398	2.94574	7.65744
C	0.80671	3.38572	8.96863
H	0.70524	2.85953	11.06150
H	-0.12394	0.55408	10.61915
H	-0.51590	-0.19683	8.29794
H	0.83116	3.62120	6.83376
H	1.16664	4.39455	9.15648
C	-3.37721	-1.63277	4.98782
C	-3.53009	-0.68020	6.00115
C	-2.48362	0.19556	6.29759
C	-1.26868	0.16975	5.57630
C	-1.15019	-0.79340	4.54903
C	-2.18018	-1.69280	4.26595
H	-4.18585	-2.32401	4.76213
H	-4.46001	-0.62623	6.56232
H	-2.61106	0.92410	7.09437
H	-0.22911	-0.84340	3.97374

H	-2.05435	-2.43413	3.48035

Structure: $[NCBPh_3]^-$

Charge = -1, Multiplicity = 1

SCF Energy: -812.812123 hartree

SCF Energy + ZPVE: -812.528058 hartree

Enthalpy: -812.509480 hartree

Free Energy: -812.577315 hartree

Free Energy with quasiharmonic correction: -812.571127 hartree

SCF Energy (SP): -812.409747679 hartree

DeltaG (solv) (kcal/mol) = -43.66

B	-0.00043	0.00048	0.69064
C	1.57020	-3.93993	-0.79876
C	0.49962	-3.31632	-1.44654
C	-0.00899	-2.10438	-0.96082
C	0.52629	-1.46845	0.17501
C	1.60312	-2.12252	0.80742
C	2.12042	-3.33347	0.33743
H	1.96773	-4.88367	-1.16921
H	0.05526	-3.77479	-2.32952
H	-0.84701	-1.64158	-1.47780
H	2.04394	-1.66898	1.69356
H	2.95236	-3.80664	0.85806
C	-4.19648	0.60957	-0.80454
C	-3.95098	-0.14691	0.34800
C	-2.64416	-0.30439	0.82005
C	-1.53551	0.27839	0.17348
C	-1.81408	1.03720	-0.97910
C	-3.11705	1.20228	-1.46687
H	-5.21195	0.73702	-1.17666
H	-4.77972	-0.61286	0.88014
H	-2.47574	-0.89455	1.71926
H	-0.99106	1.51380	-1.50752
H	-3.28837	1.79825	-2.36286
C	2.62692	3.32833	-0.80514
C	2.61243	2.09198	-1.45808
C	1.81713	1.04655	-0.97054
C	1.00816	1.19043	0.17249
C	1.04596	2.44718	0.80978
C	1.83628	3.49974	0.33791
H	3.24571	4.14362	-1.17702
H	3.22419	1.93793	-2.34656
H	1.82795	0.09136	-1.49138
H	0.44041	2.60090	1.70140
H	1.83778	4.45458	0.86272
C	0.00037	0.00203	2.30380
N	0.00038	0.00277	3.47147

Structure: $[CNBPh_3]^-$

Charge = -1, Multiplicity = 1

SCF Energy: -812.802979 hartree

SCF Energy + ZPVE: -812.519018 hartree

Enthalpy: -812.500493 hartree
Free Energy: -812.567093 hartree
Free Energy with quasiharmonic correction: -812.561982 hartree
SCF Energy (SP): -812.399945622 hartree
DeltaG (solv) (kcal/mol) = -42.70

C	0.00069	-0.00115	3.41139
N	0.00066	-0.00016	2.23792
B	0.00082	0.00072	0.68752
C	4.07852	1.19742	-0.77445
C	3.29440	0.30816	-1.51606
C	2.03662	-0.08537	-1.04165
C	1.51103	0.39106	0.17445
C	2.32529	1.28176	0.90103
C	3.58505	1.68143	0.44319
H	5.05919	1.50408	-1.13525
H	3.66420	-0.08610	-2.46223
H	1.45111	-0.78908	-1.63009
H	1.96161	1.66464	1.85241
H	4.18426	2.37060	1.03759
C	-1.00033	-4.12890	-0.77556
C	-0.32411	-3.94376	0.43649
C	-0.04097	-2.65294	0.89449
C	-0.41604	-1.50222	0.17368
C	-1.10132	-1.71893	-1.03683
C	-1.38905	-3.00508	-1.51135
H	-1.22470	-5.13157	-1.13645
H	-0.01842	-4.80749	1.02627
H	0.48061	-2.52940	1.84143
H	-1.42624	-0.85993	-1.62068
H	-1.92333	-3.12814	-2.45307
C	-3.08013	2.93019	-0.76985
C	-1.91005	2.71228	-1.50385
C	-0.93815	1.82102	-1.03123
C	-1.09355	1.11298	0.17553
C	-2.28020	1.35631	0.89474
C	-3.25843	2.24573	0.43863
H	-3.83783	3.62489	-1.12931
H	-1.74897	3.24143	-2.44273
H	-0.03005	1.67878	-1.61379
H	-2.43455	0.83786	1.83888
H	-4.16124	2.40702	1.02704

Structure: CN^-
Charge = -1, Multiplicity = 1
SCF Energy: -92.862909 hartree
SCF Energy + ZPVE: -92.858072 hartree
Enthalpy: -92.854767 hartree
Free Energy: -92.877124 hartree
Free Energy with quasiharmonic correction: -92.877124 hartree
SCF Energy (SP): -92.8259120404 hartree
DeltaG (solv) (kcal/mol) = -64.42

N	1.43942	-1.06383	0.00000

C 0.25593 -1.06383 0.00000

Structure: 11
Charge = 1, Multiplicity = 1
SCF Energy: -1649.062553 hartree
SCF Energy + ZPVE: -1648.598782 hartree
Enthalpy: -1648.567886 hartree
Free Energy: -1648.661959 hartree
Free Energy with quasiharmonic correction: -1648.653561 hartree
SCF Energy (SP): -2987.66464099 hartree
DeltaG (solv) (kcal/mol) = -36.92

Ni	0.26004	-0.02520	-0.27353
P	0.41805	-2.27384	-0.29150
C	1.58489	-2.96183	-1.53404
C	0.95335	-3.05538	1.28519
C	-1.16530	-3.13802	-0.68006
H	2.59303	-2.59469	-1.32609
H	1.29454	-2.63303	-2.53705
H	1.57934	-4.05678	-1.50018
H	0.26478	-2.78098	2.09129
H	0.97292	-4.14636	1.18795
H	1.95129	-2.69439	1.54699
H	-1.90874	-2.92593	0.09496
H	-1.01500	-4.22170	-0.73584
H	-1.55459	-2.77537	-1.63570
P	0.34014	2.23057	-0.33326
C	-1.31208	3.05303	-0.34980
C	1.23731	3.10318	1.01239
C	1.13752	2.86426	-1.86516
H	-1.84749	2.83797	0.58109
H	-1.90335	2.66795	-1.18531
H	-1.20724	4.13880	-0.45028
H	2.28293	2.78559	1.01818
H	1.18234	4.18766	0.86775
H	0.79889	2.84794	1.98255
H	2.17653	2.52556	-1.89602
H	1.11387	3.95935	-1.88829
H	0.61437	2.47483	-2.74425
C	-3.86436	0.30988	2.11428
C	-2.46397	-0.07382	1.60081
C	-2.61072	-0.03646	0.09306
N	-3.91014	-0.00377	-0.22887
C	-4.79743	-0.06145	0.94171
O	-1.67844	-0.05668	-0.74485
H	-3.91294	1.38821	2.29787
H	-4.14032	-0.20053	3.03946
H	-5.21339	-1.07371	1.03749
H	-5.62983	0.63736	0.81468
C	4.45231	0.12320	-0.54398
C	3.08977	0.07064	-0.86789
C	2.11089	0.01291	0.13665
C	2.53155	0.00497	1.47667

C	3.89167	0.05591	1.80556
C	4.85707	0.11690	0.79452
H	5.19465	0.16763	-1.33751
H	2.79312	0.06844	-1.91506
H	1.79453	-0.03710	2.27705
H	4.19625	0.04964	2.84959
H	5.91289	0.15784	1.04749
H	-1.65589	0.58806	1.92596
H	-2.17506	-1.09441	1.88669
C	-4.42385	-0.07616	-1.58807
H	-4.96060	-1.02009	-1.73950
H	-5.11243	0.75532	-1.77052
H	-3.58658	-0.01924	-2.28540

Structure: NMP

Charge = 0, Multiplicity = 1

SCF Energy: -325.963318 hartree

SCF Energy + ZPVE: -325.823943 hartree

Enthalpy: -325.816072 hartree

Free Energy: -325.854864 hartree

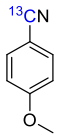
Free Energy with quasiharmonic correction: -325.854864 hartree

SCF Energy (SP): -325.845611481 hartree

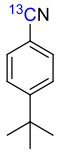
DeltaG (solv) (kcal/mol) = -6.21

C	0.53917	-1.38114	0.13227
N	-0.56078	-0.44541	-0.06332
C	-0.17918	0.87154	-0.00666
C	1.34284	0.90421	0.13482
C	1.78807	-0.53198	-0.19023
O	-0.93357	1.83713	-0.04067
C	-1.94332	-0.86913	-0.01161
H	0.54954	-1.75239	1.17057
H	0.43008	-2.24841	-0.53018
H	1.77130	1.67091	-0.51593
H	1.57415	1.18553	1.17089
H	2.66567	-0.85780	0.37553
H	2.02337	-0.61943	-1.25694
H	-2.57622	0.00725	-0.16864
H	-2.14592	-1.61159	-0.79328
H	-2.18341	-1.31430	0.96507

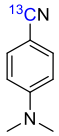
Compound Characterization



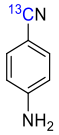
2a was purified on silica gel with a gradient of 0-60% EtOAC in hexanes, and obtained as a white solid in 60% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 7.75 (m, 2H), 7.09 (d, *J* = 8.8 Hz, 2H), 3.83 (s, 3H). **^{13}C NMR (126 MHz, DMSO-*d*$_6$)** δ 13C NMR (126 MHz, DMSO) δ 162.68, 134.13, 119.10, 115.09, 102.80, 55.63. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 72.9%.



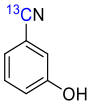
2b was purified on silica gel with a gradient of 0-60% EtOAC in hexanes, and obtained as a clear liquid in 42% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 7.76 – 7.71 (m, 2H), 7.58 (d, *J* = 8.3 Hz, 2H), 1.28 (s, 9H). **^{13}C NMR (126 MHz, DMSO-*d*$_6$)** δ ^{13}C NMR (126 MHz, DMSO) δ 156.36, 131.96, 126.33, 118.91, 108.40, 34.96, 30.53. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 72.1%.



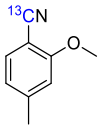
2c was purified on silica gel with a gradient of 0-60% EtOAC in hexanes, and obtained as a light white solid in 78% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 7.53 – 7.50 (m, 2H), 6.73 (d, *J* = 8.9 Hz, 2H), 2.98 (s, 6H). **^{13}C NMR (126 MHz, DMSO-*d*$_6$)** δ ^{13}C NMR (126 MHz, DMSO) δ 152.44, 133.08, 120.47, 111.59, 95.75, 39.41. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 65.5%.



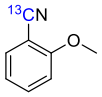
2d was purified on silica gel with a gradient of 0-100% EtOAC in hexanes, and obtained as an off-white solid in 90% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 7.38 (dq, *J* = 6.7, 2.2 Hz, 2H), 6.61 (d, *J* = 8.6 Hz, 2H), 6.11 (s, 2H). **^{13}C NMR (126 MHz, DMSO-*d*$_6$)** δ 152.99, 133.42, 120.66, 113.45, 95.56. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 58.2%.



2e was purified on silica gel with a gradient of 0-100% EtOAC in hexanes, and obtained as an off-white solid in 77% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 10.18 (s, 1H), 7.40 – 7.34 (m, 1H), 7.22 (m, 1H), 7.10 (m, 2H). **^{13}C NMR (126 MHz, DMSO)** δ 157.79, 130.86, 122.77, 120.74, 118.80, 118.20, 112.02. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 73.6%.

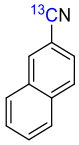


2f was purified on silica gel with a gradient of 0-60% EtOAC in hexanes, and obtained as a light-white solid in 81% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 7.60 – 7.53 (m, 1H), 7.07 (s, 1H), 6.90 (d, *J* = 7.8 Hz, 1H), 3.89 (s, 3H), 2.37 (s, 3H). **^{13}C NMR (126 MHz, DMSO)** δ 160.76, 146.09, 133.22, 121.75, 116.65, 112.72, 97.35, 56.05, 21.68. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 62.7%.

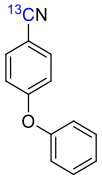


2g was purified on silica gel with a gradient of 0-60% EtOAC in hexanes, and obtained as a clear oil in 52% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 7.75 – 7.69 (m, 1H), 7.69 – 7.63 (m, 1H), 7.23 (d, *J* = 8.6 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 3.91 (s, 3H). **^{13}C NMR (126 MHz, DMSO)** δ 160.80, 135.09, 133.60, 120.98, 116.40, 112.17, 100.27, 56.17. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 67.0%.

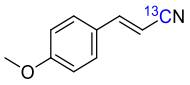
2h was purified on silica gel with a gradient of 0-60% EtOAC in hexanes, and obtained as a clear oil in 67% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 7.77 – 7.72 (m, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 2.47 (s, 3H). **^{13}C NMR (126 MHz, DMSO)** δ 134.32, 134.27, 131.88, 129.34, 129.27, 128.47, 127.99, 127.74, 126.27, 119.14, 108.39. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 83.7%.



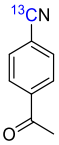
2i was purified on silica gel with a gradient of 0-60% EtOAC in hexanes, and obtained as a white solid in 40% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 8.60 – 8.56 (m, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 8.06 (t, *J* = 8.0 Hz, 2H), 7.81 – 7.76 (m, 1H), 7.76 – 7.70 (m, 1H), 7.68 (t, *J* = 7.5 Hz, 1H). **^{13}C NMR (126 MHz, DMSO)** δ 141.43, 133.08, 132.43, 130.30, 126.56, 117.90, 111.71, 19.85. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 71.2%.



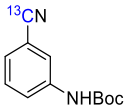
2j was purified on silica gel with a gradient of 0-60% EtOAC in hexanes, and obtained as a crystalline semi-solid in 50% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 7.83 (dq, *J* = 6.7, 2.2 Hz, 4H), 7.47 (t, *J* = 7.9 Hz, 4H), 7.27 (t, *J* = 7.4 Hz, 2H), 7.14 (d, *J* = 7.8 Hz, 4H), 7.08 (d, *J* = 8.7 Hz, 4H). **^{13}C NMR (126 MHz, DMSO)** δ 161.09, 154.40, 134.60, 130.41, 125.14, 120.22, 118.67, 117.98, 105.04. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 68.7%.



2k (isolated as mixture of *cis* and *trans*) was purified on silica gel with a gradient of 0-60% EtOAC in hexanes, and obtained as a clear viscous oil in 54% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 7.81 (d, *J* = 8.7 Hz, 1H), 7.60 (d, *J* = 8.7 Hz, 2H), 7.56 (dt, *J* = 16.7, 4.4 Hz, 1H), 7.30 (dt, *J* = 11.9, 8.0 Hz, 1H), 7.06 (d, *J* = 8.8 Hz, 1H), 6.99 (d, *J* = 8.7 Hz, 2H), 6.26 (d, *J* = 16.7 Hz, 1H), 5.67 (d, *J* = 12.1 Hz, 1H), 3.81 (s, 2H), 3.80 (s, 3H). **^{13}C NMR (126 MHz, DMSO)** δ 161.54, 161.18, 150.10, 148.21, 130.58, 129.52, 126.49, 120.23, 119.21, 118.30, 114.39, 93.62, 92.15, 55.36. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 45.6%.

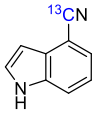


2l was purified on silica gel with a gradient of 0-40% EtOAC in hexanes, and obtained as a light white solid in 60% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 8.09 (d, *J* = 8.2 Hz, 2H), 8.00 (dq, *J* = 6.2, 2.3 Hz, 2H), 2.63 (s, 3H). **^{13}C NMR (126 MHz, DMSO)** δ 197.32, 139.84, 132.74, 128.74, 118.14, 115.13, 26.96. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 60.4%.

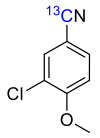


2m was purified on silica gel with a gradient of 0-60% EtOAC in hexanes, and obtained as a light-white solid in 46% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 9.73 (s, 1H), 7.88 (s, 1H), 7.71 (d, *J* = 8.2 Hz, 1H), 7.46 (t, *J* = 7.9 Hz, 1H), 7.44 – 7.36 (m, 1H), 1.48 (s, 9H). **^{13}C NMR (126 MHz, DMSO)** δ 152.61, 140.45, 130.09, 125.49, 122.60, 120.46, 118.77, 111.50, 27.99. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 40.4%.

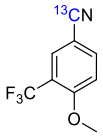
2o was purified on silica gel with a gradient of 0-100% EtOAC in hexanes, and obtained as a light tan solid in 71% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 9.09 (d, *J* = 3.6 Hz, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 8.14 – 8.05 (m, 2H), 7.97 – 7.90 (m, 1H), 7.87 – 7.81 (m, 1H). **^{13}C NMR (126 MHz, DMSO)** δ 150.22, 147.22, 131.23, 129.91, 129.45, 125.83, 124.80, 124.38, 117.34, 115.53. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 51.0%.



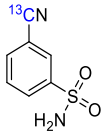
2p was purified on silica gel with a gradient of 0-100% EtOAC in hexanes, and obtained as a light tan solid in 58% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 11.73 (s, 1H), 7.77 (d, *J* = 8.2 Hz, 1H), 7.65 (t, *J* = 2.7 Hz, 1H), 7.55 – 7.49 (m, 1H), 7.24 (t, *J* = 7.8 Hz, 1H), 6.59 (s, 1H). **^{13}C NMR (126 MHz, DMSO)** δ 135.62, 128.87, 128.50, 124.52, 120.94, 118.83, 116.88, 101.07, 99.40. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 53.7%.



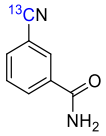
2q was purified on silica gel with a gradient of 0-60% EtOAC in hexanes, and obtained as an off-white solid in 47% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 8.03 – 7.95 (m, 1H), 7.82 (dd, *J* = 5.8, 2.8 Hz, 1H), 7.31 (d, *J* = 8.6 Hz, 1H), 3.95 (s, 3H). **^{13}C NMR (126 MHz, DMSO)** δ 158.23, 133.31, 121.93, 119.10, 117.89, 113.52, 103.68, 56.73. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 59.5%.



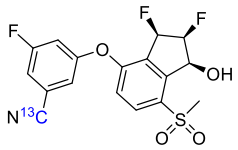
2r was purified on silica gel with a gradient of 0-60% EtOAC in hexanes, and obtained as a white solid in 79% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 8.16 – 8.09 (m, 2H), 7.45 (d, *J* = 8.6 Hz, 1H), 3.99 (s, 3H). **^{13}C NMR (126 MHz, DMSO)** δ 160.28, 138.80, 131.21, 123.69, 119.36, 117.86, 114.17, 102.97, 56.91. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 60.9%.



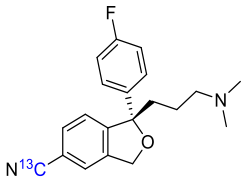
2s was purified on silica gel with a gradient of 0-100% EtOAC in hexanes, and obtained as a white solid in 42% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 8.22 (s, 1H), 8.14 – 8.07 (m, 2H), 7.81 (t, *J* = 7.9 Hz, 1H), 7.62 (s, 2H). **^{13}C NMR (126 MHz, DMSO)** δ 145.24, 135.43, 130.58, 130.14, 129.20, 117.66, 112.10. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 54.5%.



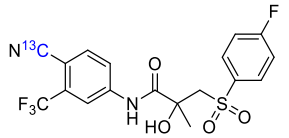
2t was purified on silica gel with a gradient of 0-100% EtOAC in hexanes, and obtained as a white solid in 74% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 8.28 (s, 1H), 8.17 (d, *J* = 8.1 Hz, 2H), 7.99 (d, *J* = 7.7 Hz, 1H), 7.71 – 7.58 (m, 2H). **^{13}C NMR (126 MHz, DMSO)** δ 165.97, 135.30, 134.70, 132.21, 131.06, 129.70, 118.37, 111.45. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 44.4%.



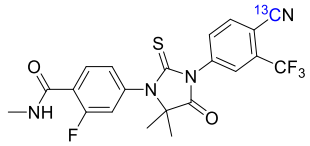
4a was purified on silica gel with a gradient of 20-100% EtOAC in hexanes. The obtained solid was washed with CH_2Cl_2, and then redissolved in acetone. Solvent was removed under reduced pressure, affording a white solid in 89% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 8.03 (d, *J* = 8.6 Hz, 1H), 7.80 (d, *J* = 7.3 Hz, 1H), 7.62 (s, 1H), 7.58 (d, *J* = 9.7 Hz, 1H), 7.25 (d, *J* = 8.7 Hz, 1H), 6.19 (d, *J* = 5.9 Hz, 1H), 5.98 (dd, *J* = 56.2, 4.6 Hz, 1H), 5.60 (s, 1H), 5.20 (ddt, *J* = 47.9, 16.9, 4.9 Hz, 1H), 3.36 (s, 3H). **^{13}C NMR (126 MHz, DMSO)** δ 163.56, 161.58, 157.49, 156.42, 144.28, 134.42, 133.33, 128.74, 120.05, 118.56, 116.41, 114.34, 113.45, 89.57, 87.99, 87.10, 85.74, 69.34, 44.98. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 47.1%.



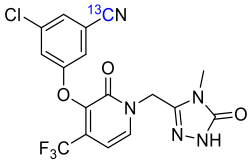
4b was purified on a reversed-phase C18 column, eluting with 60% acetonitrile/40% water solution (50 mM TEAA pH 11), and obtained as a clear viscous oil in 41% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 7.80 – 7.72 (m, 3H), 7.58 (dd, *J* = 8.7, 5.5 Hz, 2H), 7.14 (t, *J* = 8.8 Hz, 2H), 5.21 – 5.09 (m, 2H), 2.15 (dt, *J* = 14.0, 6.1 Hz, 4H), 2.01 (s, 6H), 1.28 (dq, *J* = 11.7, 6.0 Hz, 1H), 1.19 (dq, *J* = 13.2, 6.0 Hz, 1H). **^{13}C NMR (126 MHz, DMSO)** δ 162.18, 149.43, 140.47, 139.86, 131.95, 126.94, 125.60, 123.11, 118.77, 115.11, 110.75, 90.59, 70.98, 58.73, 44.93, 38.22, 21.76. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 56.9%.



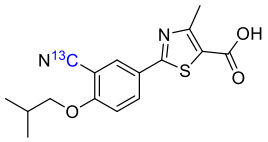
4c was purified on silica gel with a gradient of 0-10% MeOH in CH_2Cl_2, and obtained as a white solid in 57% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 10.38 (s, 1H), 8.43 (s, 1H), 8.22 (d, *J* = 8.6 Hz, 1H), 8.08 (d, *J* = 8.6 Hz, 1H), 7.93 (dd, *J* = 8.7, 5.2 Hz, 2H), 7.37 (t, *J* = 8.8 Hz, 2H), 6.40 (s, 1H), 3.96 (d, *J* = 14.8 Hz, 1H), 3.72 (d, *J* = 14.9 Hz, 1H), 1.42 (s, 3H). **^{13}C NMR (126 MHz, DMSO)** δ 173.72, 163.87, 143.16, 137.16, 136.16, 131.34, 123.60, 122.86, 117.55, 116.13, 115.81, 101.97, 73.14, 63.48, 27.16. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 48.7%.



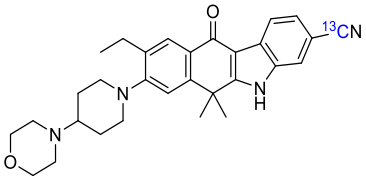
4d was purified on a reversed-phase C18 column, eluting with a gradient of 10-80% acetonitrile in water, and obtained as a white solid in 13% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 8.43 (d, *J* = 4.4 Hz, 1H), 8.40 (d, *J* = 8.3 Hz, 1H), 8.30 – 8.28 (m, 1H), 8.08 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.79 (t, *J* = 8.1 Hz, 1H), 7.43 (dd, *J* = 10.7, 1.5 Hz, 1H), 7.33 (dd, *J* = 8.2, 1.7 Hz, 1H), 2.80 (d, *J* = 4.5 Hz, 3H), 1.54 (s, 6H). **^{13}C NMR (126 MHz, DMSO)** δ 180.05, 174.70, 163.39, 157.89, 138.21, 137.91, 136.26, 133.94, 130.97, 130.85, 127.96, 126.08, 121.10, 118.10, 117.90, 114.98, 108.70, 66.57, 26.25, 22.93. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 13.5%.



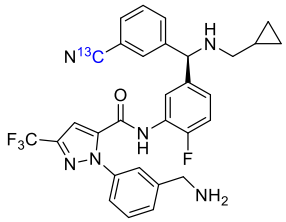
4e was purified on a reversed-phase C18 column, eluting with 40% acetonitrile solution (0.1 % (v/v) formic acid)/ 60% water solution (0.1 % (v/v) formic acid), and obtained as a white solid in 28% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 11.73 (s, 1H), 7.88 (d, *J* = 7.3 Hz, 1H), 7.76 – 7.72 (m, 1H), 7.63 – 7.59 (m, 1H), 7.53 (d, *J* = 1.9 Hz, 1H), 6.66 (d, *J* = 7.3 Hz, 1H), 5.17 (s, 2H), 3.11 (s, 3H). **^{13}C NMR (126 MHz, DMSO)** δ 157.23, 156.04, 155.01, 143.24, 140.09, 137.33, 134.95, 129.97, 126.51, 122.74, 120.56, 118.42, 116.90, 113.64, 100.17, 43.34, 26.70. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 68.0%.



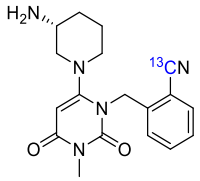
4f was purified on silica gel with a gradient of 0-10% MeOH in CH_2Cl_2, and obtained as a white solid in 54% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 13.37 (s, 1H), 8.23 (t, *J* = 2.6 Hz, 1H), 8.18 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.33 (d, *J* = 9.0 Hz, 1H), 3.98 (d, *J* = 6.5 Hz, 2H), 2.64 (s, 3H), 2.08 (dt, *J* = 13.3, 6.6 Hz, 1H), 1.02 (s, 3H), 1.01 (s, 3H). **^{13}C NMR (126 MHz, DMSO)** δ 166.15, 162.78, 162.01, 159.50, 132.98, 131.46, 125.32, 122.84, 115.33, 113.81, 101.52, 75.10, 27.57, 18.68, 17.00. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 45.1%.



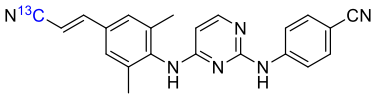
4g was purified on a reversed-phase C18 column, eluting with 60% acetonitrile solution (0.1 % (v/v) formic acid)/ 40% water solution (0.1 % (v/v) formic acid), and obtained as a white solid in 58% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 12.68 (s, 1H), 8.32 (d, *J* = 8.1 Hz, 1H), 8.04 (s, 1H), 7.99 (s, 1H), 7.63 – 7.57 (m, 1H), 7.33 (s, 1H), 3.63 – 3.57 (m, 4H), 3.21 (d, *J* = 11.8 Hz, 2H), 2.76 (t, *J* = 11.4 Hz, 2H), 2.70 (q, *J* = 7.5 Hz, 2H), 2.52 (s, 4H), 2.36 – 2.29 (m, 1H), 1.91 (d, *J* = 11.6 Hz, 2H), 1.75 (s, 6H), 1.63 – 1.55 (m, 2H), 1.27 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR (126 MHz, DMSO)** δ 179.14, 159.98, 155.46, 146.70, 136.21, 135.61, 127.68, 126.00, 125.83, 124.73, 121.59, 120.06, 116.38, 116.32, 109.35, 104.52, 66.56, 61.10, 51.59, 49.46, 36.40, 30.04, 28.43, 22.59, 14.33. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 55.9%.



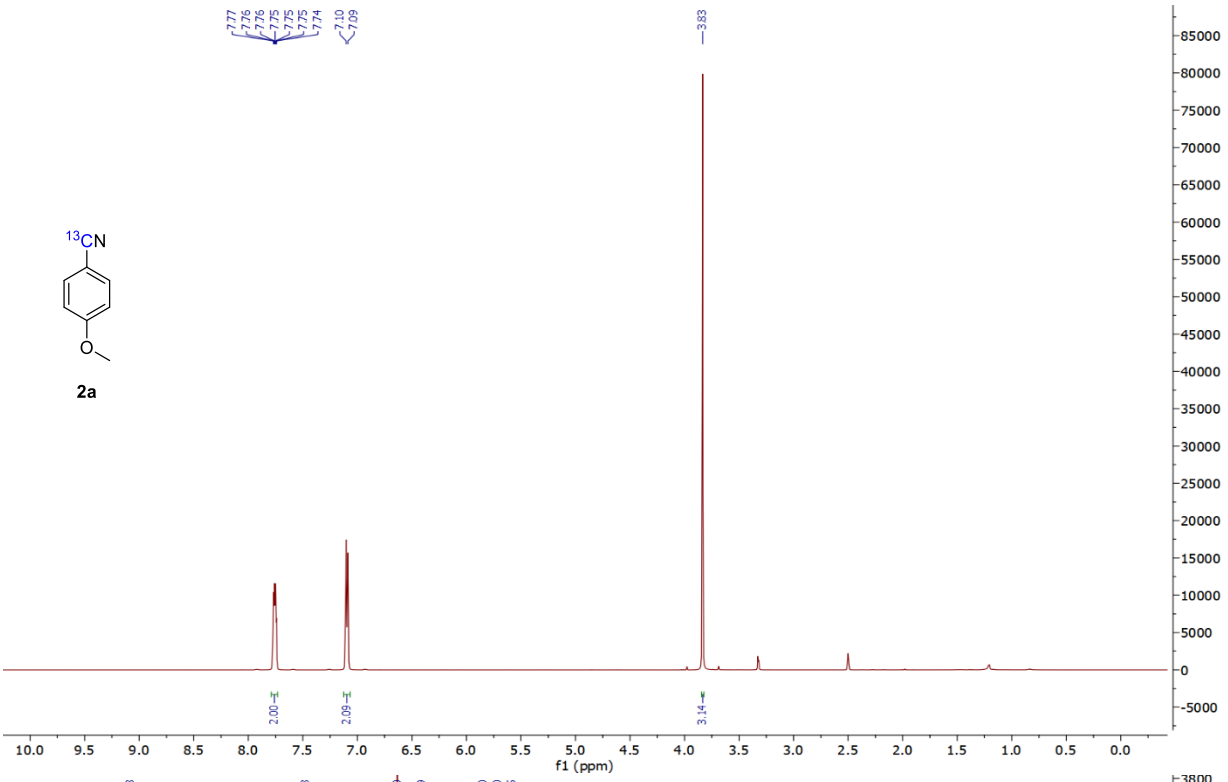
4h was purified on silica gel with a gradient of 0-1000% MeOH in CH_2Cl_2, and obtained as a white solid in 43% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 10.32 (s, 1H), 7.88 (s, 1H), 7.73 (d, *J* = 7.0 Hz, 1H), 7.65 (dt, *J* = 13.6, 7.6 Hz, 2H), 7.58 (d, *J* = 8.5 Hz, 1H), 7.52 (dt, *J* = 15.6, 7.3 Hz, 2H), 7.44 (d, *J* = 6.9 Hz, 2H), 7.38 – 7.32 (m, 2H), 7.22 (t, *J* = 9.3 Hz, 1H), 4.94 (d, *J* = 4.4 Hz, 1H), 3.81 (s, 2H), 2.92 (s, 3H), 2.31 – 2.22 (m, 2H), 0.95 – 0.86 (m, 1H), 0.42 – 0.35 (m, 2H), 0.09 – 0.02 (m, 2H). **^{13}C NMR (126 MHz, DMSO)** δ 156.79, 155.15, 153.19, 146.11, 144.87, 140.95, 140.23, 138.97, 138.55, 132.04, 130.62, 130.48, 129.61, 128.60, 127.76, 125.89, 124.58, 124.23, 123.43, 122.80, 122.11, 119.97, 118.86, 115.92, 115.77, 111.29, 107.47, 64.22, 51.94, 44.76, 10.96, 3.34, 3.32. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 67.2%.



4i was purified on a reversed-phase C18 column, eluting with 40% acetonitrile solution (0.1 % (v/v) formic acid)/ 60% water solution (0.1 % (v/v) formic acid). The white solid was redissolved in in CH_2Cl_2, and the solvent was removed under reduced pressure to the title compound in 58% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 7.85 – 7.81 (m, 1H), 7.65 (t, *J* = 7.7 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 7.9 Hz, 1H), 5.32 (s, 1H), 5.17 (s, 2H), 3.09 (s, 3H), 3.04 (d, *J* = 11.0 Hz, 1H), 2.94 (d, *J* = 12.1 Hz, 1H), 2.70 (t, *J* = 9.0 Hz, 1H), 2.59 (t, *J* = 10.4 Hz, 1H), 2.40 – 2.31 (m, 1H), 1.80 – 1.74 (m, 1H), 1.66 (dd, *J* = 9.7, 3.8 Hz, 1H), 1.48 – 1.37 (m, 1H), 1.11 (q, *J* = 9.6 Hz, 1H). **^{13}C NMR (126 MHz, DMSO)** δ 162.17, 159.75, 151.99, 141.20, 133.53, 133.03, 127.87, 126.91, 117.22, 117.12, 109.92, 58.82, 50.98, 48.56, 47.11, 45.81, 32.59, 27.33, 22.91. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 68.9%.

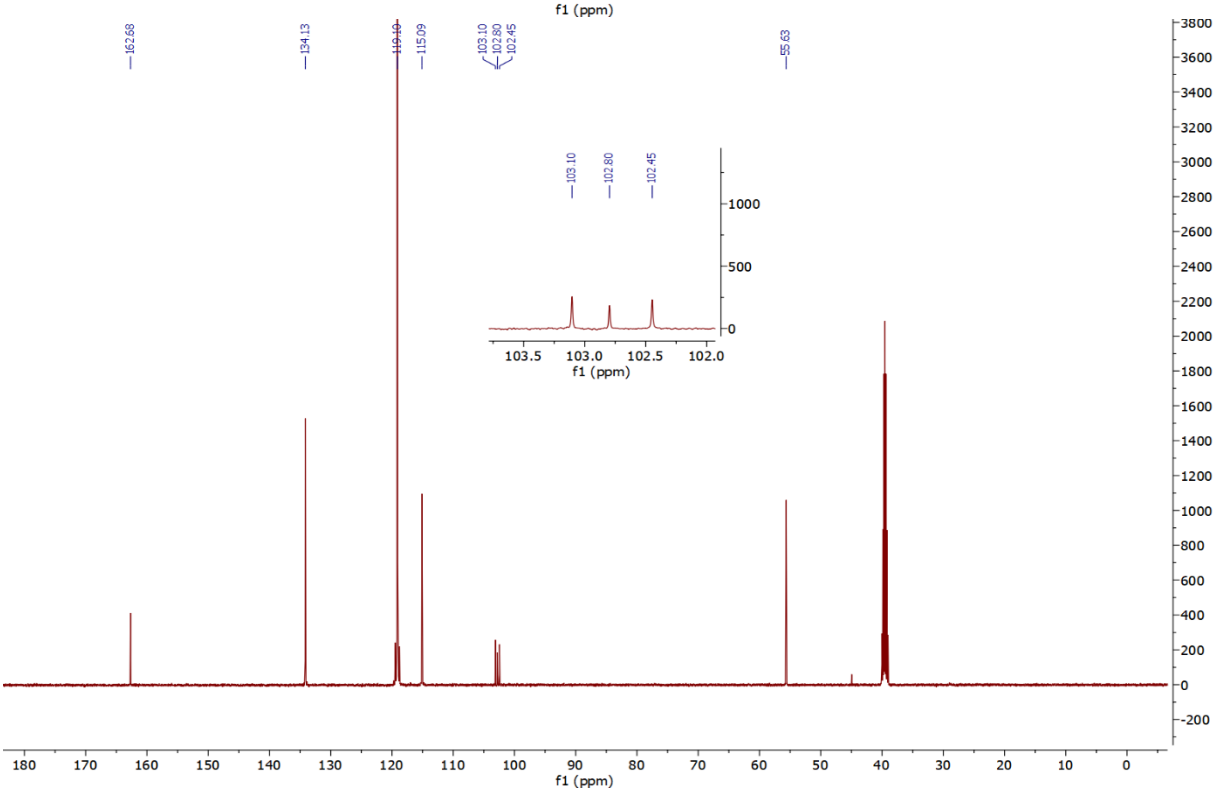


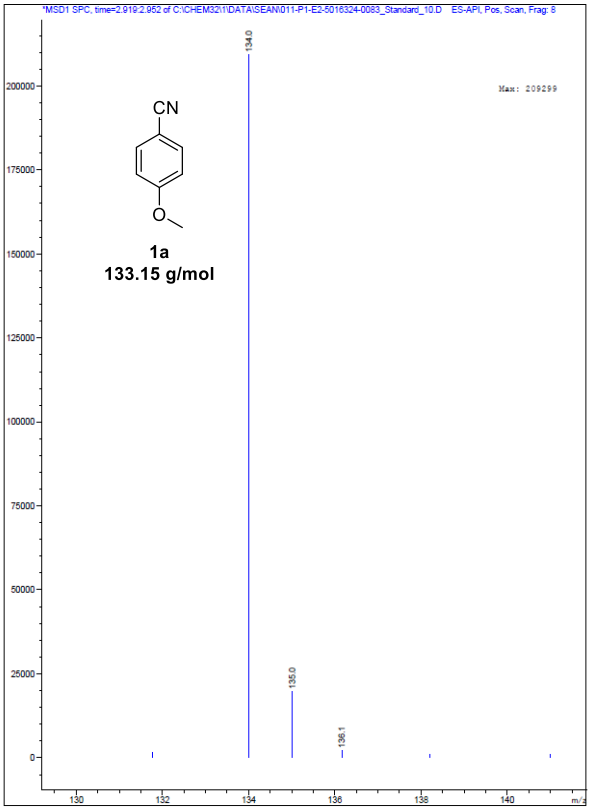
4j was purified on silica gel with a gradient of 0-10% MeOH in CH_2Cl_2, and obtained as a white solid in 50% yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ 9.59 (s, 1H), 8.92 (s, 1H), 8.01 (d, *J* = 5.3 Hz, 1H), 7.63 (dq, *J* = 12.8, 4.2 Hz, 2H), 7.48 (s, 4H), 6.45 (d, *J* = 16.7 Hz, 1H), 6.33 (s, 1H), 2.17 (s, 6H). **^{13}C NMR (126 MHz, DMSO) δ ^{13}C NMR** (126 MHz, DMSO) δ 161.70, 159.19, 155.97, 150.30, 145.50, 139.13, 136.50, 132.50, 131.80, 127.42, 119.68, 118.97, 117.93, 117.86, 101.36, 98.61, 96.13, 18.24. Mass spectral data was obtained under ESI positive ionization mode and the ^{13}C isotope incorporation was determined to be 53.3%.

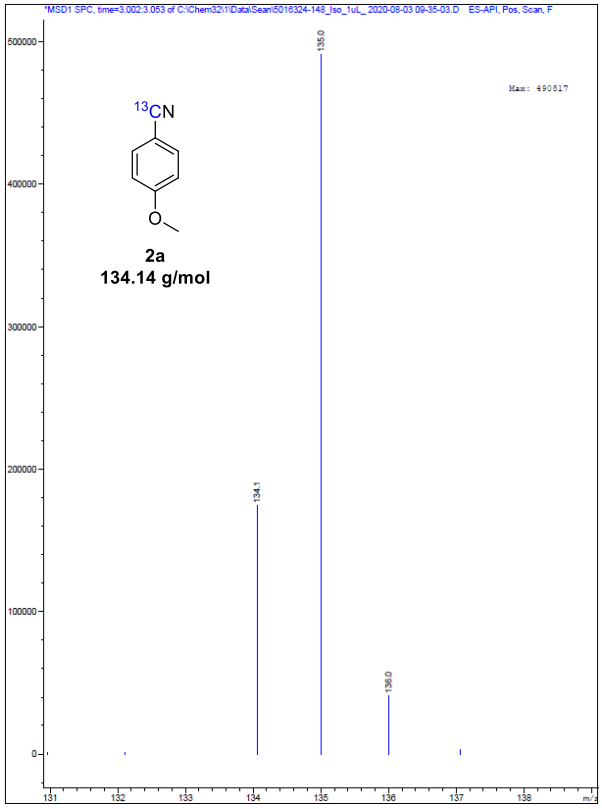

7.77
7.76
7.76
7.75
7.75
7.75
7.74
7.10
7.09
3.83
2.00
2.09
3.14
f1 (ppm)

13CN
O

2a


162.68
134.13
119.10
115.09
103.10
102.80
102.45
55.63
f1 (ppm)





Unlabeled compound	Abundance
M1+0	209299
M1+1	19676
M1+2	0
M1+3	0
M1+4	0
M1+5	0
M1+6	0
M1+7	0
M1+8	0
M1+9	0
M1+10	0
M1+11	0
M1+12	0
M1+13	0
M1+14	0
M1+15	0
M1+16	0
M1+17	0
M1+18	0
M1+19	0

Analyte	Abundance
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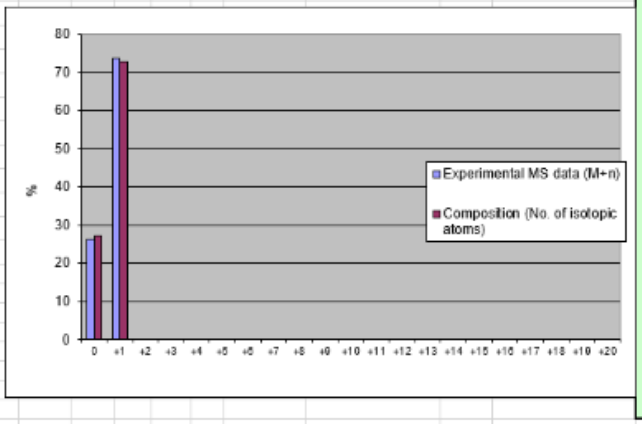
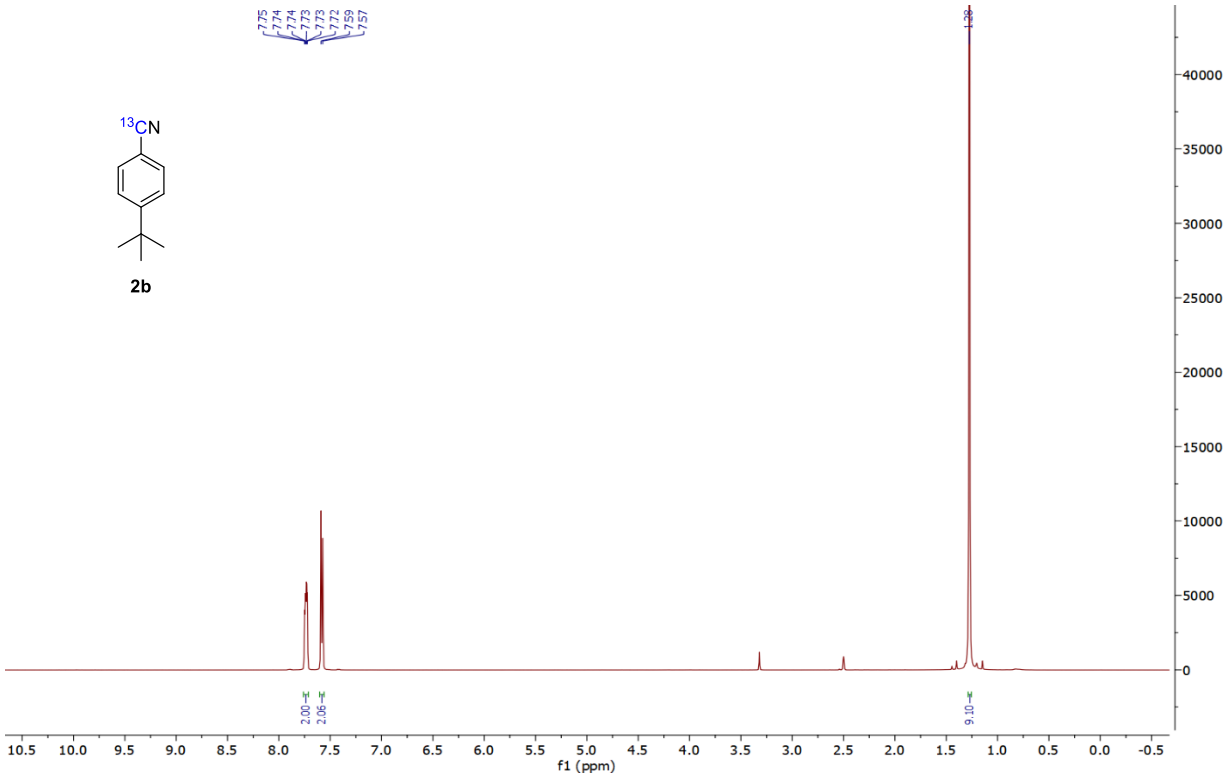
	490817
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0

Expected derivatives: 2 (Must be <2
Calculate
Labelled atoms 1
Atom% 72.9

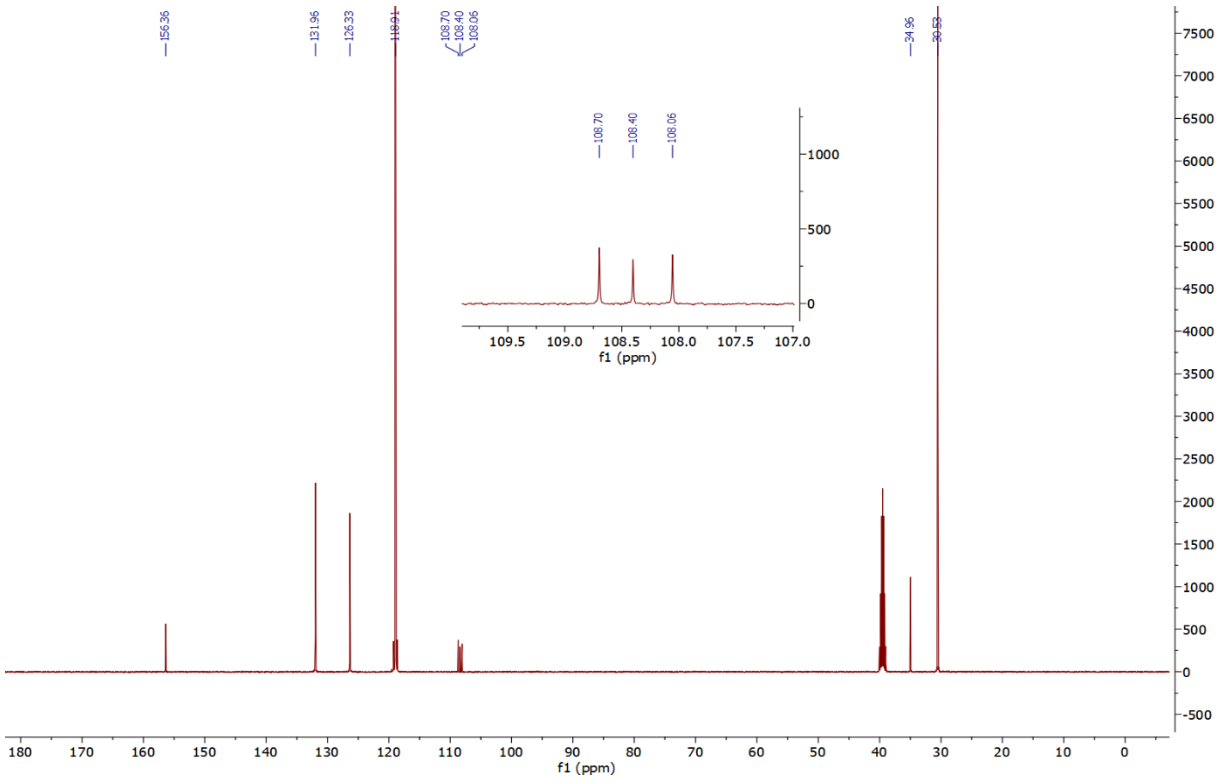


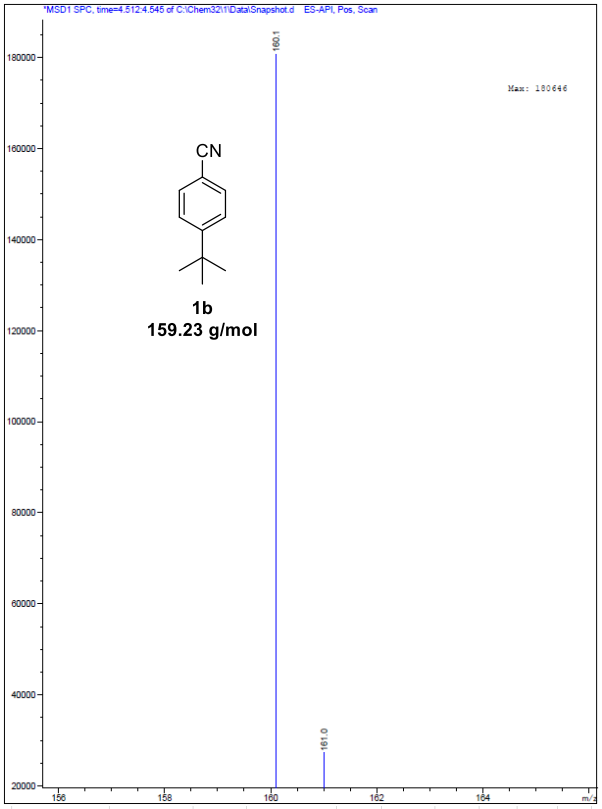
Results
Relative amounts [%]
unlabeled 27.1
1-label 72.9

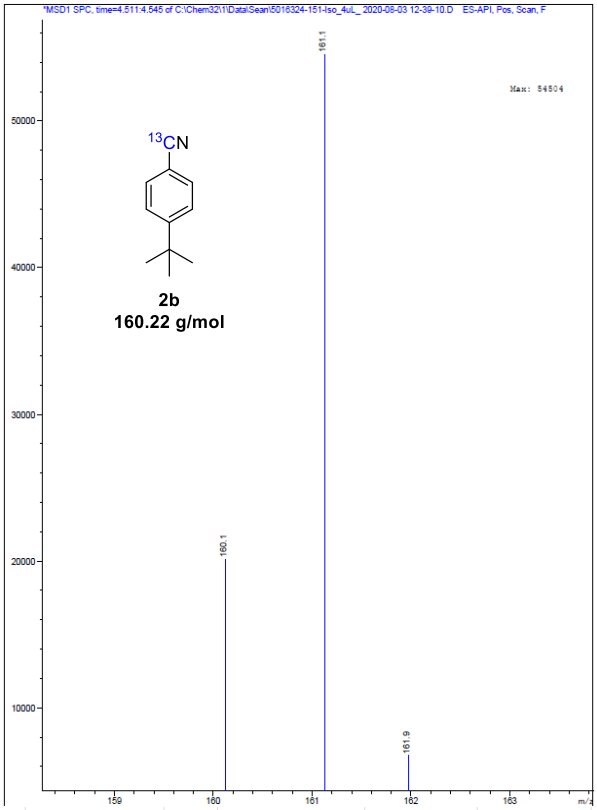

7.75
7.74
7.74
7.73
7.73
7.72
7.59
7.57
1.38
2.00
2.06
9.10
f1 (ppm)

^{13}CN

2b


156.36
131.96
126.33
118.91
108.70
108.40
108.06
34.96
30.82
f1 (ppm)





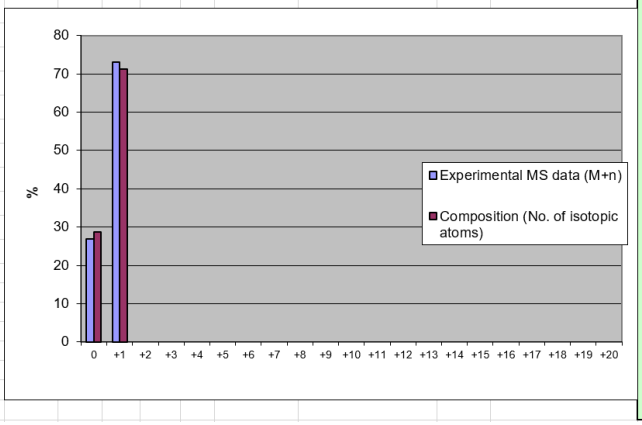
Unlabeled compound	Abundance	Analyte	Abundance
M1+0	180646		20145.7
M1+1	27211		54503.7
M1+2	0		0
M1+3	0		0
M1+4	0		0
M1+5	0		0
M1+6	0		0
M1+7	0		0
M1+8	0		0
M1+9	0		0
M1+10	0		0
M1+11	0		0
M1+12	0		0
M1+13	0		0
M1+14	0		0
M1+15	0		0
M1+16	0		0
M1+17	0		0
M1+18	0		0
M1+19	0		0

Expected derivatives: 2 (Must be <2

Calculate

Labelled atoms 1

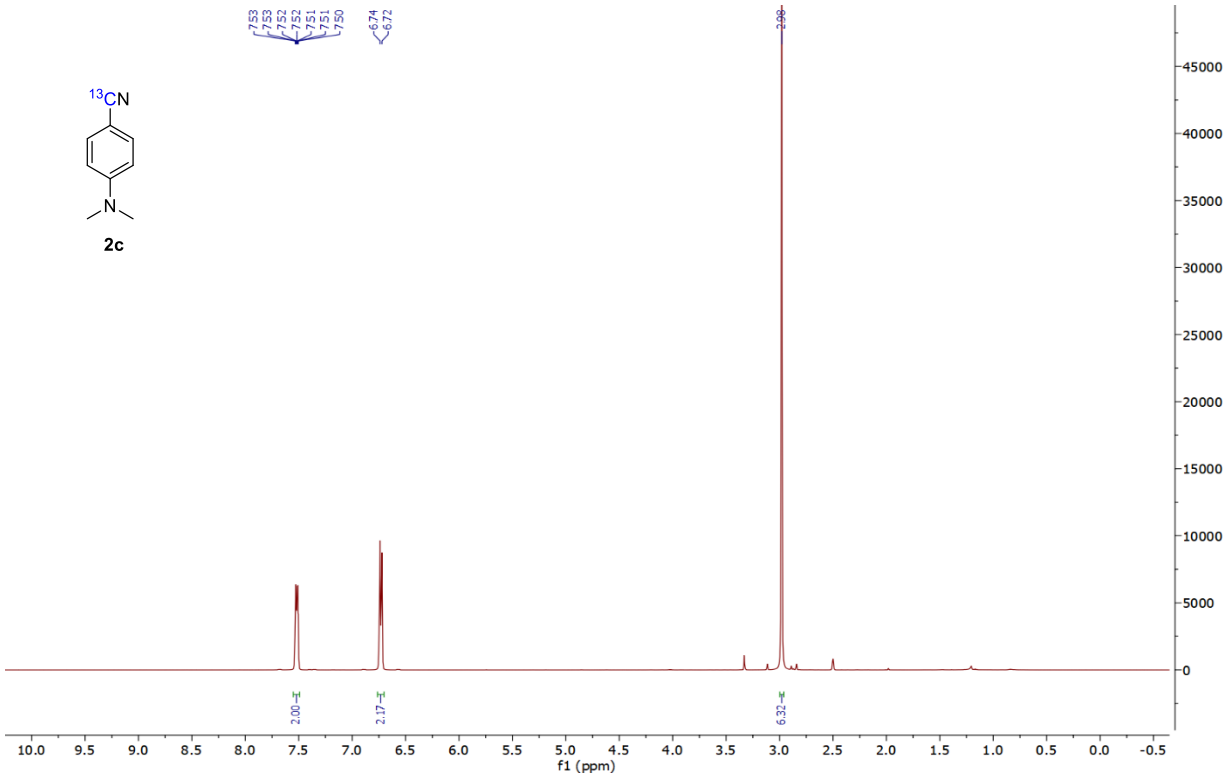
Atom% 71.2



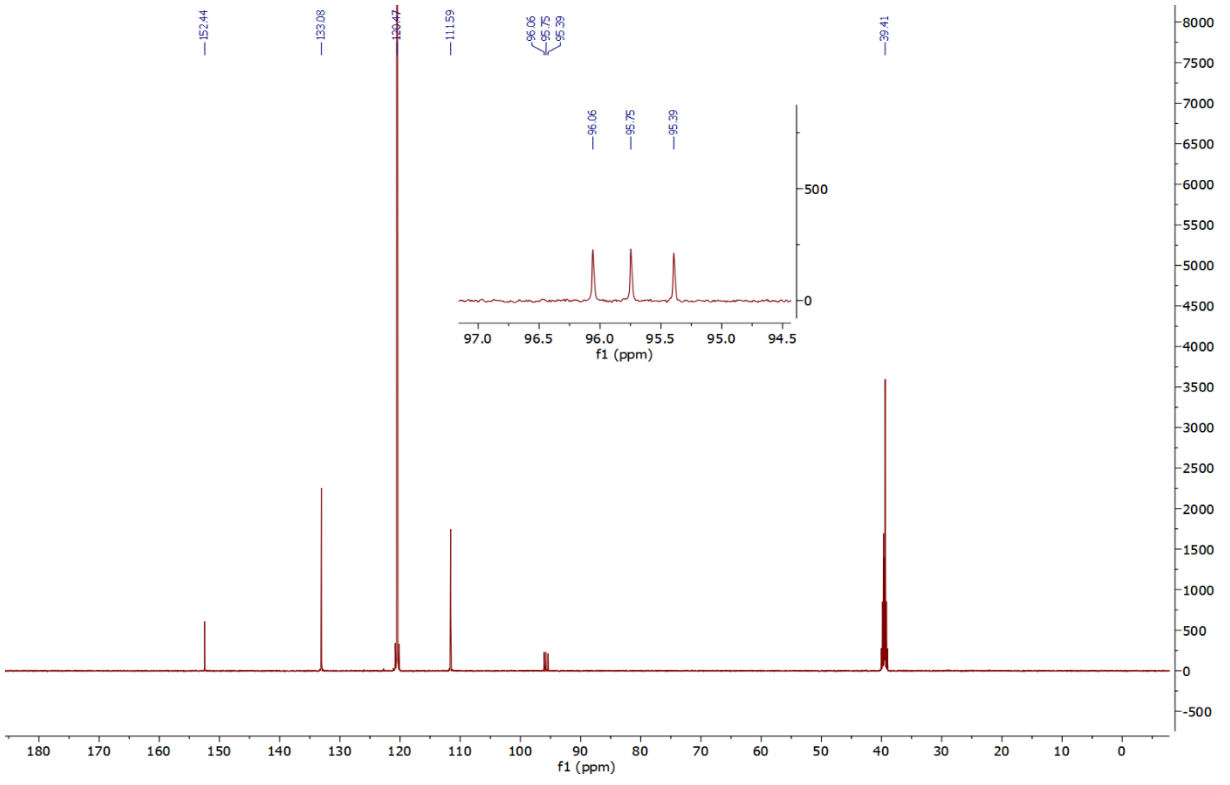
Results

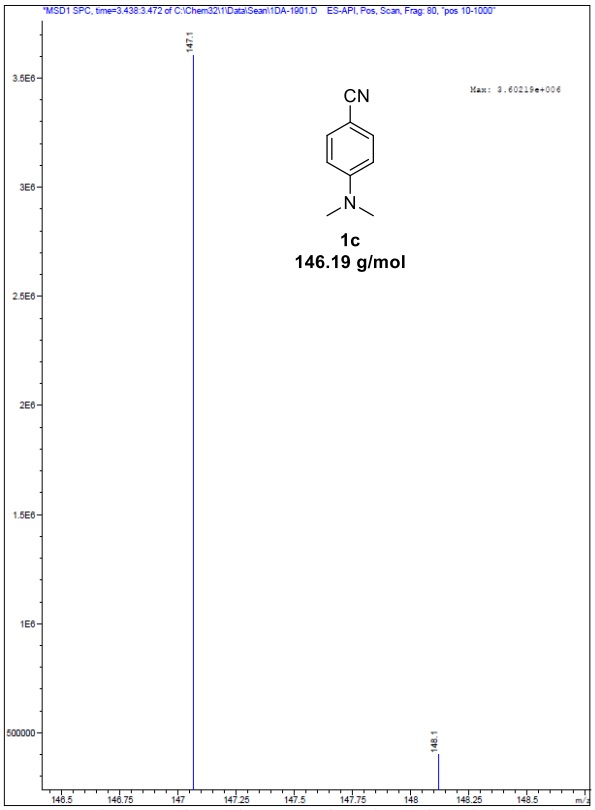
Relative amounts [%]

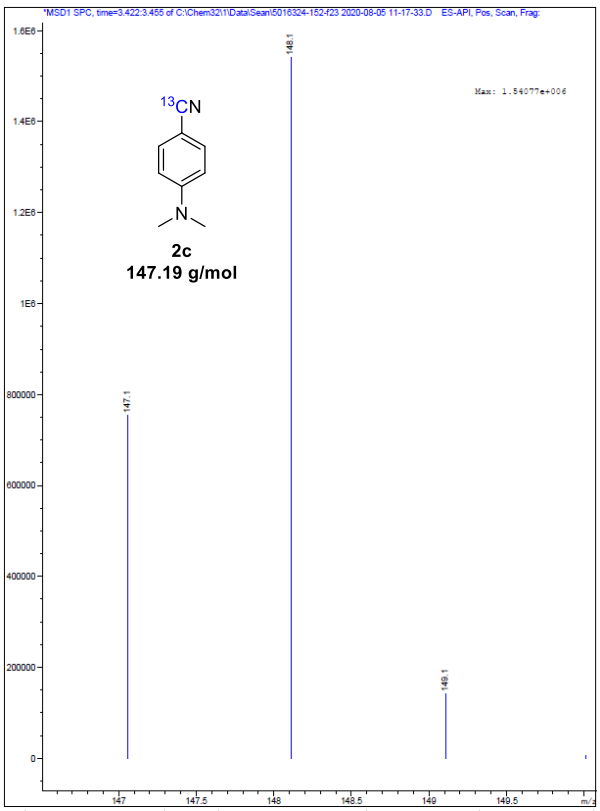
unlabeled	28.8
1-label	71.2


7.53
7.53
7.52
7.52
7.51
7.51
7.50
6.74
6.72
2.98
2.00
2.17
6.32
f1 (ppm)

2c


152.44
133.08
120.47
111.59
96.06
95.75
95.39
39.41
f1 (ppm)





Unlabeled compound	Abundance	Analyte	Abundance
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M1+1	398624		1540769
M1+2	0		0
M1+3	0		0
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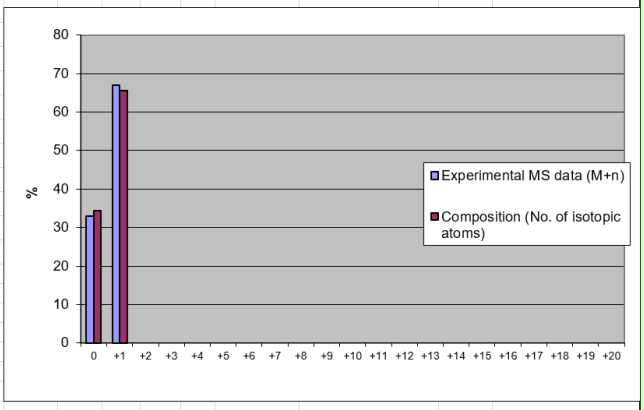
M1+7	0		0
M1+8	0		0
M1+9	0		0
M1+10	0		0
M1+11	0		0
M1+12	0		0
M1+13	0		0
M1+14	0		0
M1+15	0		0
M1+16	0		0
M1+17	0		0
M1+18	0		0
M1+19	0		0

Expected derivatives: 2 (Must be <2

Labelled atoms 1

Atom% 65.5

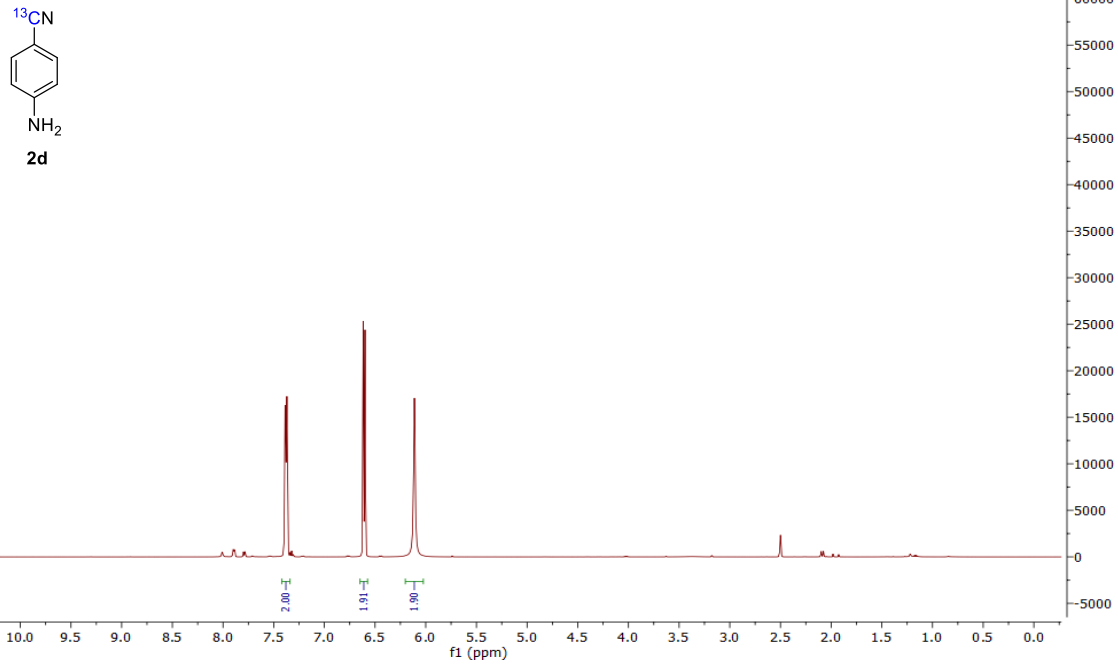
Calculate



Results

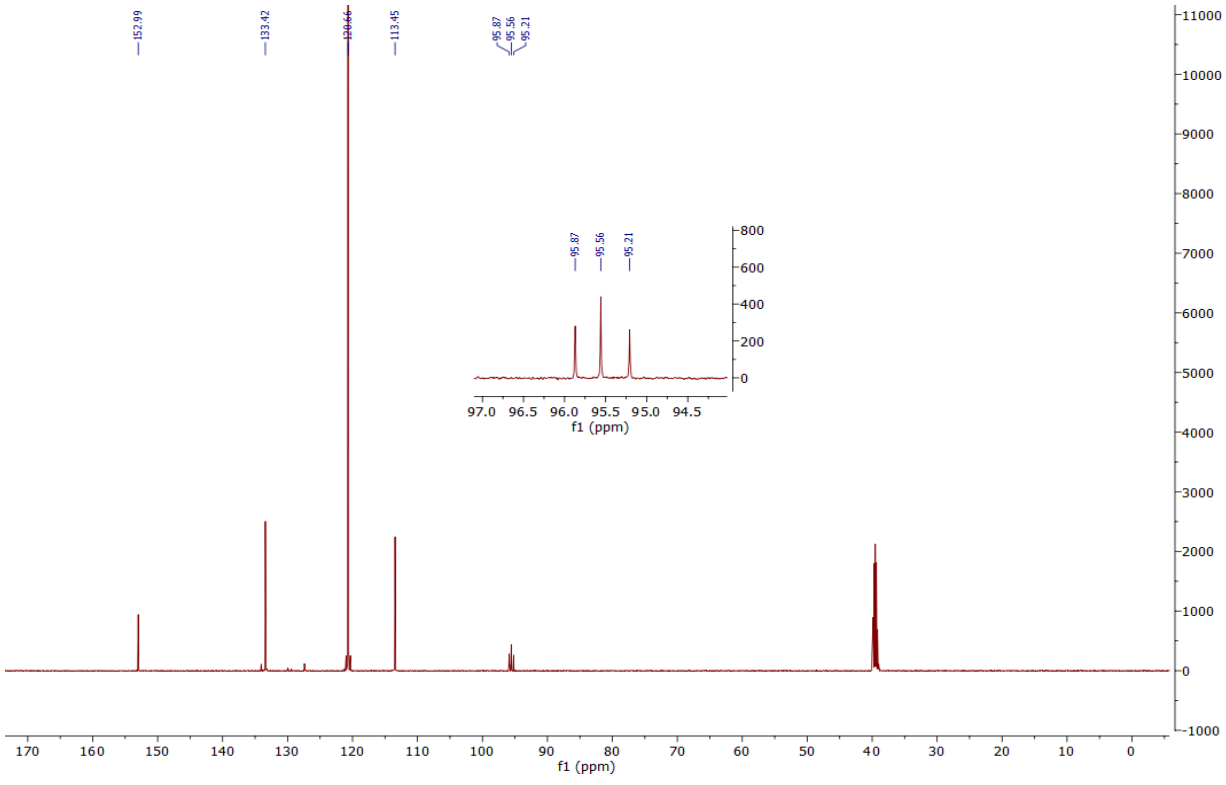
Relative amounts [%]

unlabeled	34.5
1-label	65.5


7.39
7.39
7.38
7.38
7.37
7.37
7.37
6.62
6.60
6.11
2.00
1.91
1.90
f1 (ppm)

^{13}CN
NH$_2$

2d


152.99
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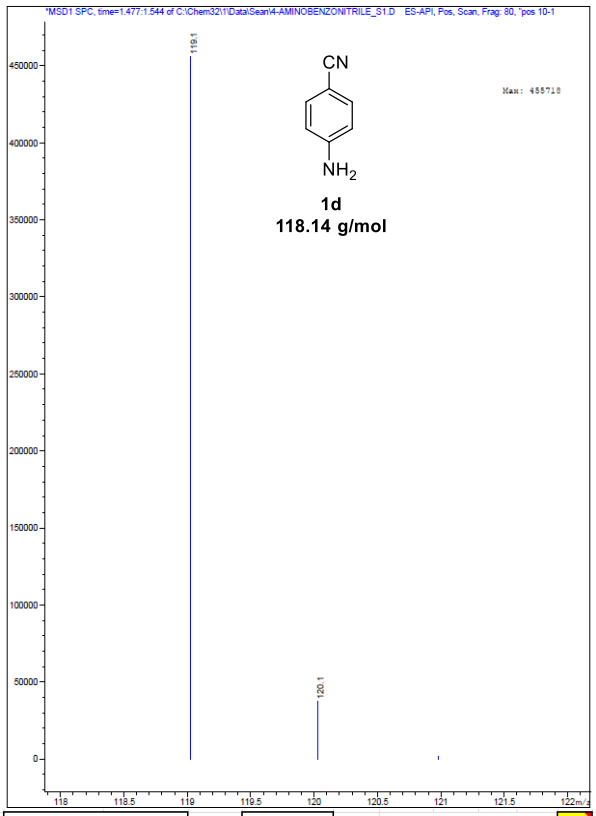
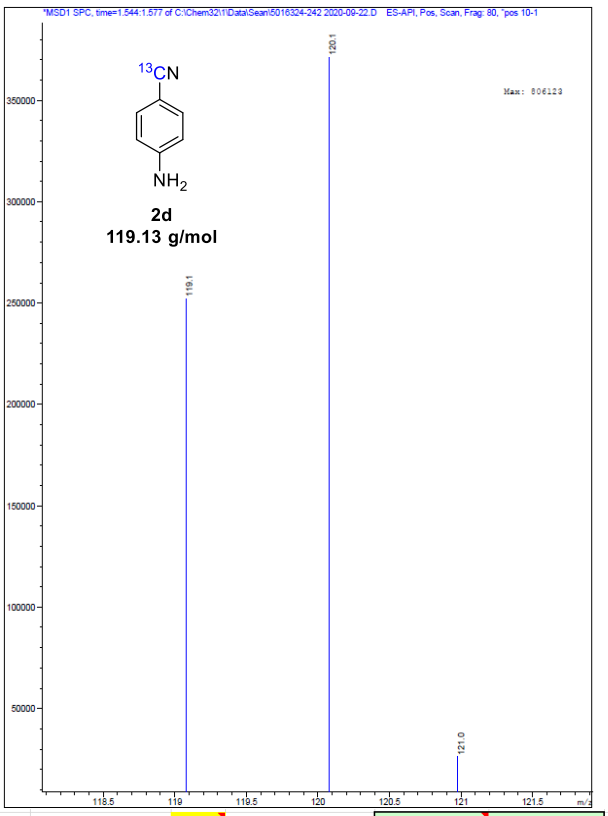
113.45
95.87
95.56
95.21
f1 (ppm)





Unlabeled compound	Abundance	Analyte	Abundance
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M1+1	37702		337968
M1+2	0		0
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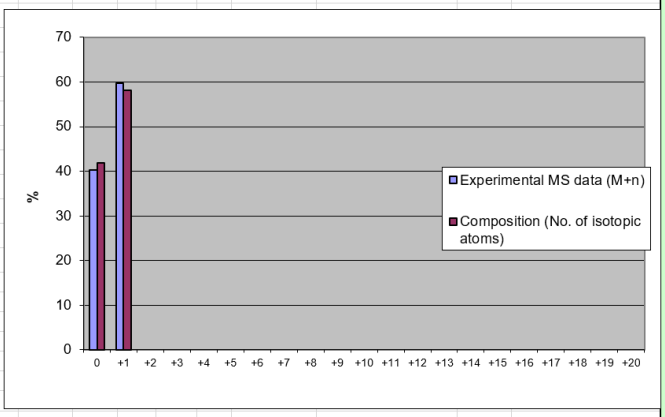
M1+5	0		0
M1+6	0		0
M1+7	0		0
M1+8	0		0
M1+9	0		0
M1+10	0		0
M1+11	0		0
M1+12	0		0
M1+13	0		0
M1+14	0		0
M1+15	0		0
M1+16	0		0
M1+17	0		0
M1+18	0		0
M1+19	0		0

Expected derivatives: 2 (Must be <2

Labelled atoms 1

Atom% 58.2

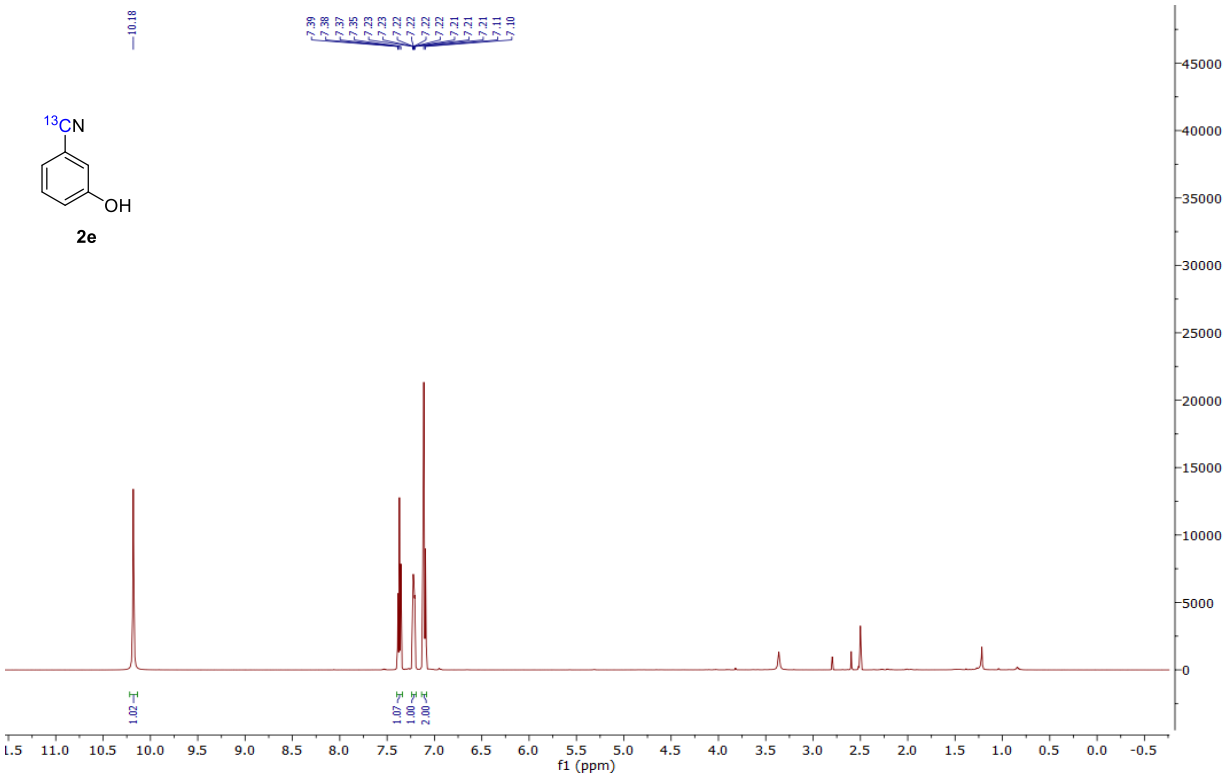
Calculate



Results

Relative amounts [%]

unlabeled	41.8
1-label	58.2


10.18
7.39
7.38
7.37
7.35
7.23
7.23
7.22
7.22
7.22
7.22
7.21
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OH
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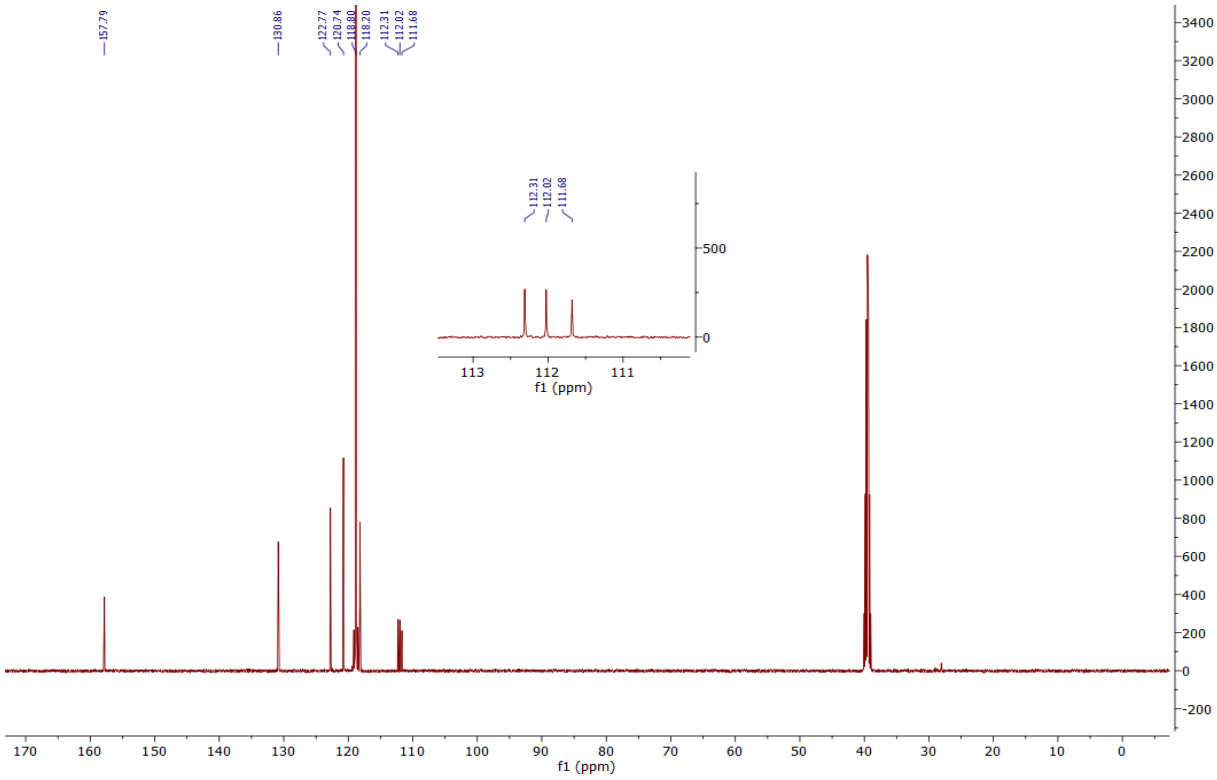
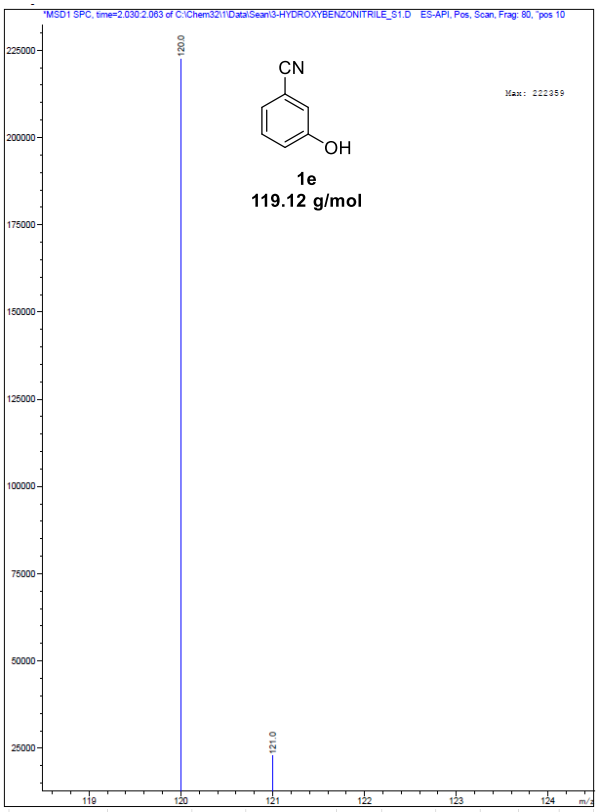
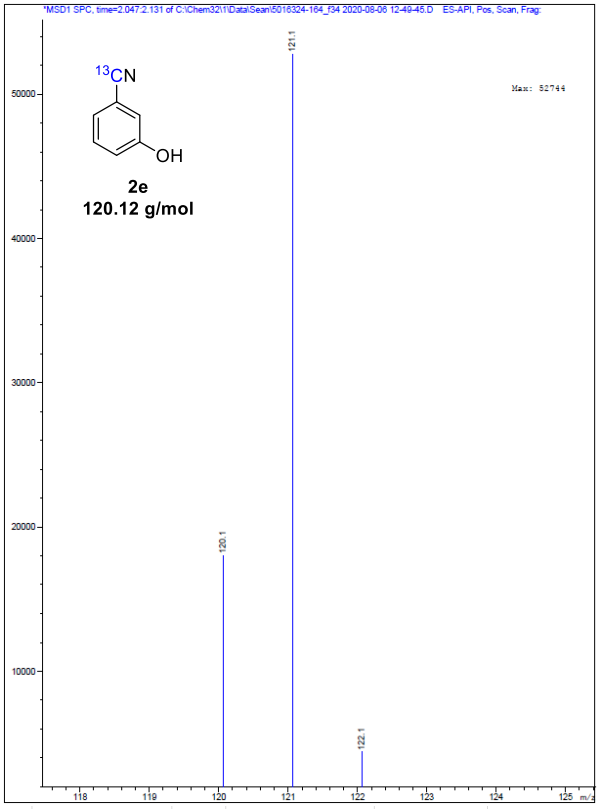
1.02
1.07
1.00
2.00
f1 (ppm)


157.79
130.86
122.77
120.74
118.80
118.20
112.31
112.02
111.68
f1 (ppm)





Unlabeled compound	Abundance
M1+0	222359
M1+1	22718
M1+2	0
M1+3	0
M1+4	0
M1+5	0
M1+6	0
M1+7	0
M1+8	0
M1+9	0
M1+10	0
M1+11	0
M1+12	0
M1+13	0
M1+14	0
M1+15	0
M1+16	0
M1+17	0
M1+18	0
M1+19	0

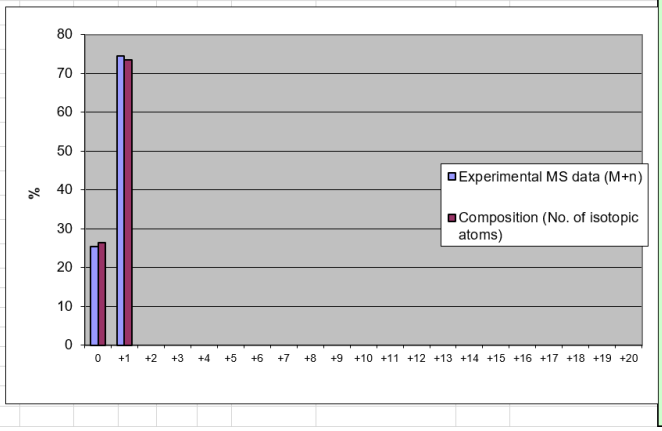
Analyte	Abundance
M1+0	18022.7
M1+1	52743.7
M1+2	0
M1+3	0
M1+4	0
M1+5	0
M1+6	0
M1+7	0
M1+8	0
M1+9	0
M1+10	0
M1+11	0
M1+12	0
M1+13	0
M1+14	0
M1+15	0
M1+16	0
M1+17	0
M1+18	0
M1+19	0

Expected derivatives: 2 (Must be <2

Calculate

Labelled atoms 1

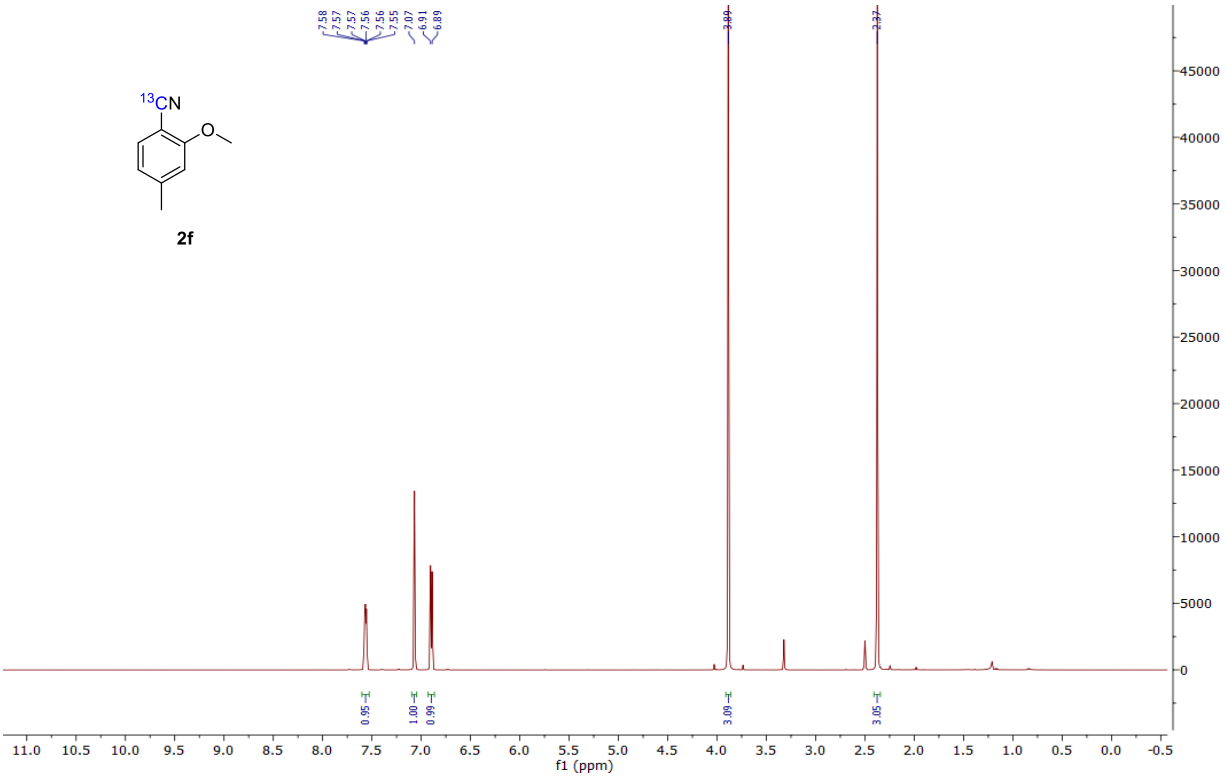
Atom% 73.6

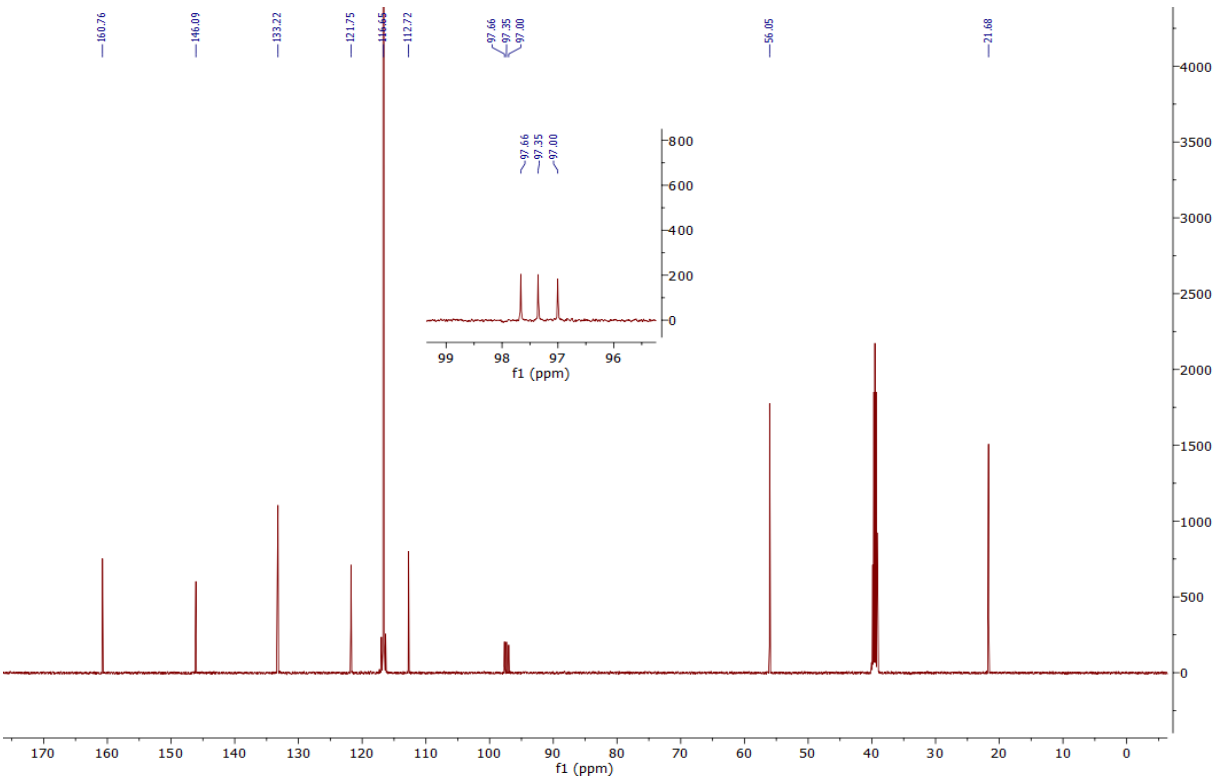


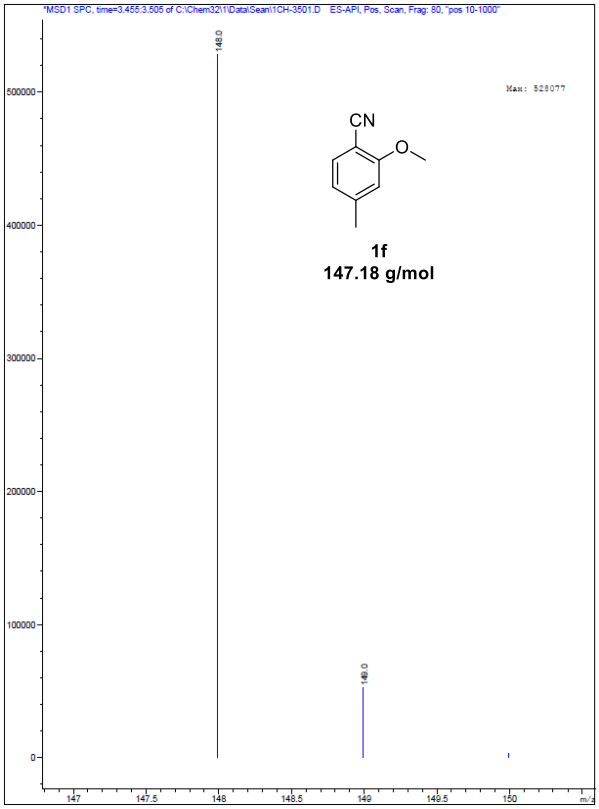
Results

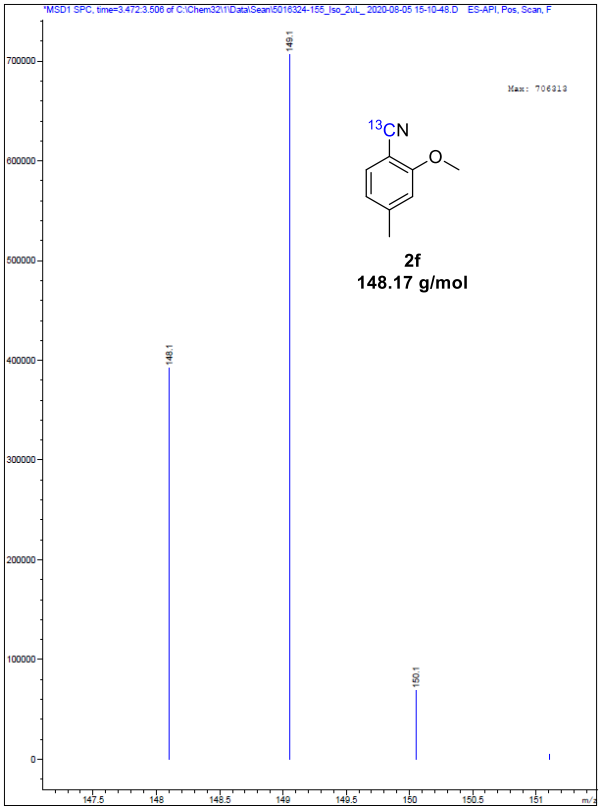
Relative amounts [%]

unlabeled	26.4
1-label	73.6


7.58
7.57
7.57
7.56
7.56
7.55
7.07
6.91
6.89
3.809
2.337
0.95
1.00
0.99
3.09
3.05
f1 (ppm)


160.76
146.09
133.22
121.75
116.65
112.72
97.66
97.35
97.00
56.05
21.68
f1 (ppm)





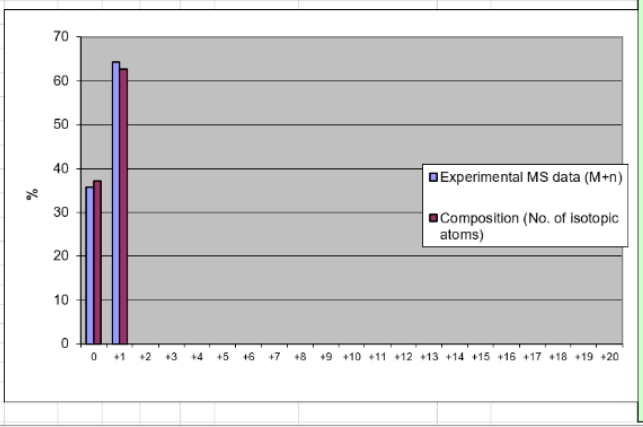
Unlabeled compound	Abundance	Analyte	Abundance
M1+0	528077		391886.7
M1+1	52218		706313
M1+2	0		0
M1+3	0		0
M1+4	0		0
M1+5	0		0
M1+6	0		0
M1+7	0		0
M1+8	0		0
M1+9	0		0
M1+10	0		0
M1+11	0		0
M1+12	0		0
M1+13	0		0
M1+14	0		0
M1+15	0		0
M1+16	0		0
M1+17	0		0
M1+18	0		0
M1+19	0		0

Expected derivatives: 2 (Must be <2

Calculate

Labelled atoms 1

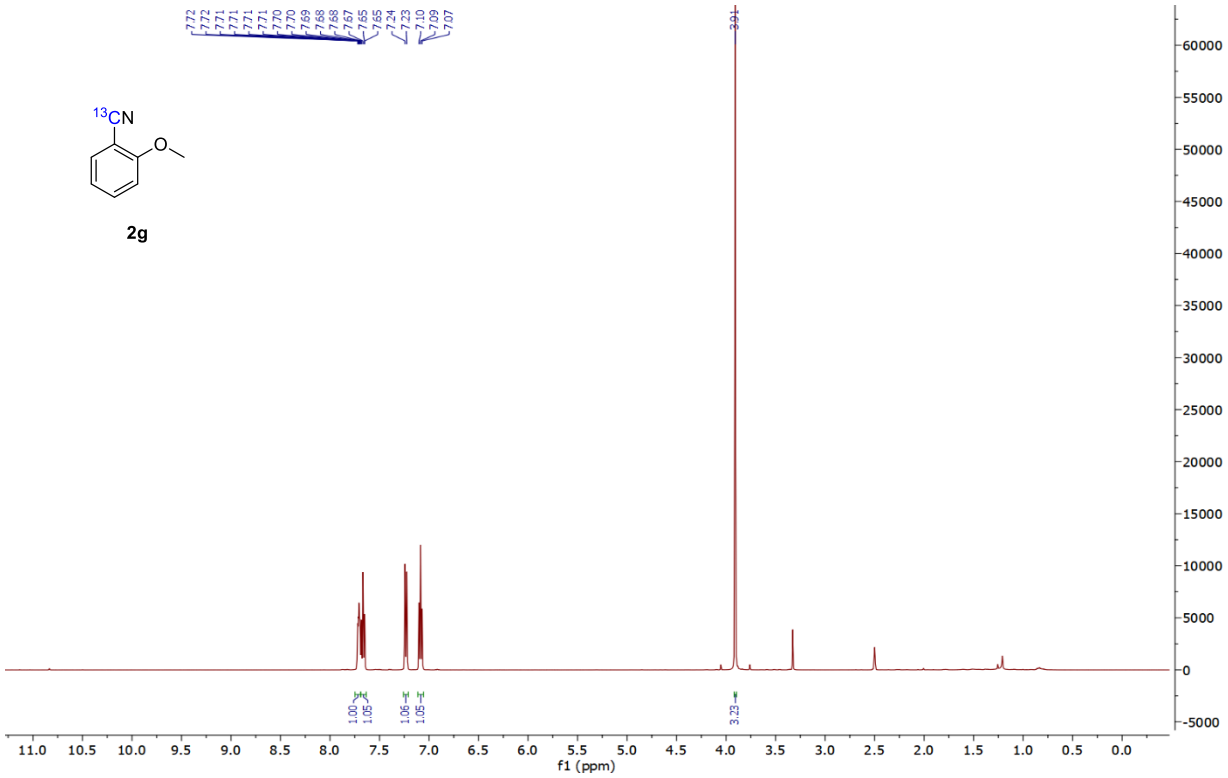
Atom% 62.7

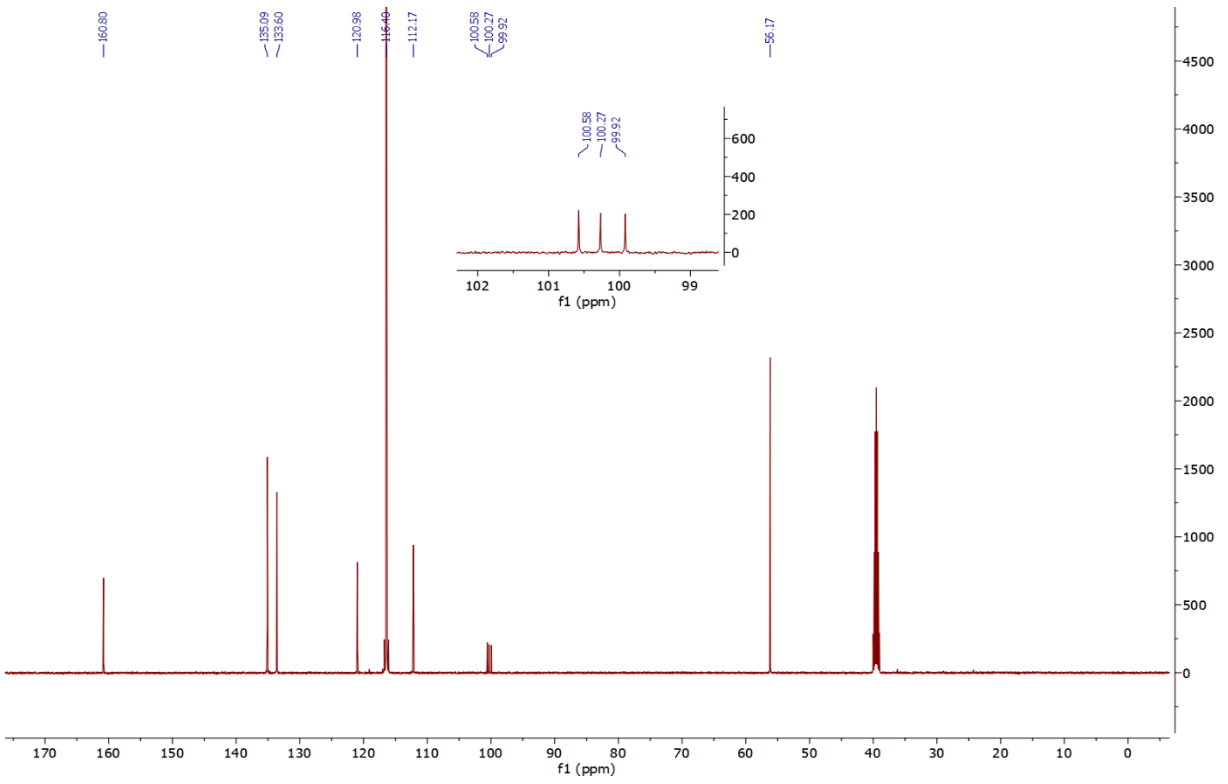


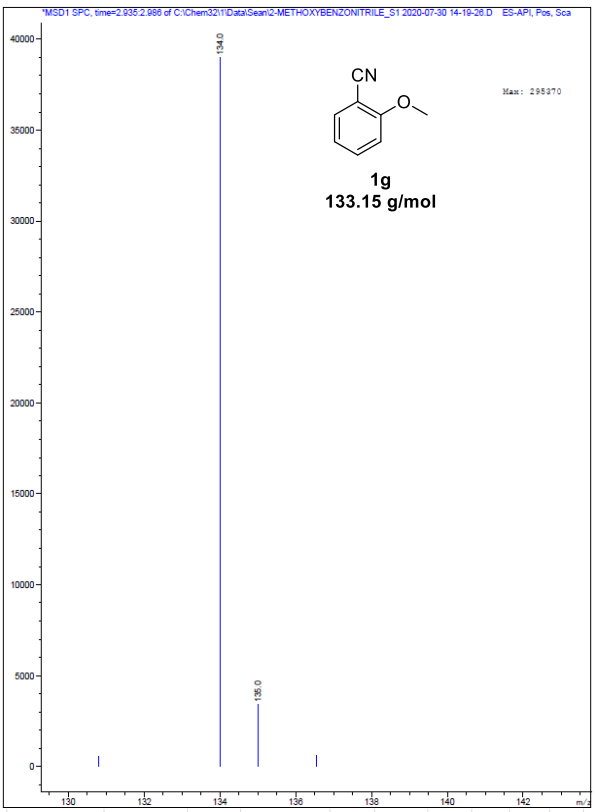
Results

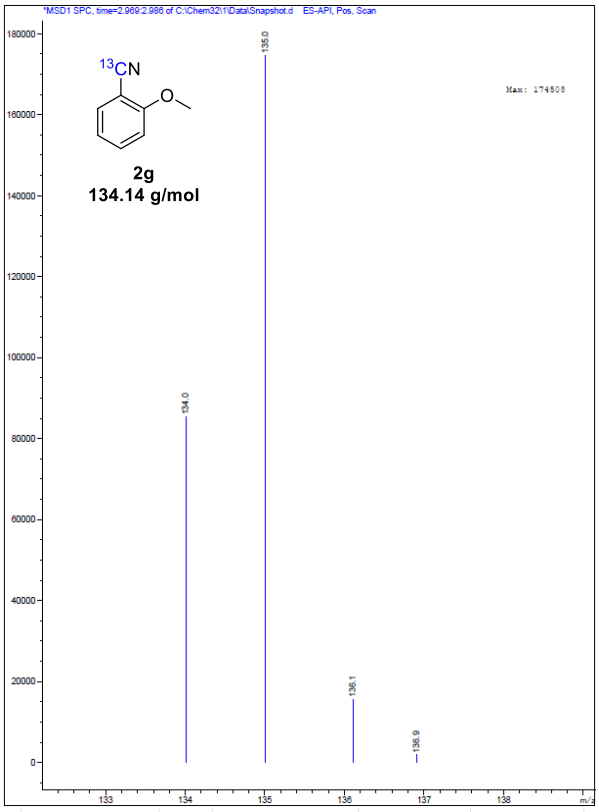
Relative amounts [%]

unlabeled	37.3
1-label	62.7


7.72
7.72
7.71
7.71
7.71
7.71
7.70
7.70
7.69
7.68
7.68
7.67
7.65
7.65
7.24
7.23
7.10
7.09
7.07
3.91
13CN
O
2g
1.00
1.05
1.06
1.05
3.23
f1 (ppm)


160.80
135.09
133.60
120.98
116.40
112.17
100.58
100.27
99.92
56.17
f1 (ppm)





Unlabeled compound	Abundance
M1+0	38982
M1+1	589
M1+2	0
M1+3	0
M1+4	0
M1+5	0
M1+6	0
M1+7	0
M1+8	0
M1+9	0
M1+10	0
M1+11	0
M1+12	0
M1+13	0
M1+14	0
M1+15	0
M1+16	0
M1+17	0
M1+18	0
M1+19	0

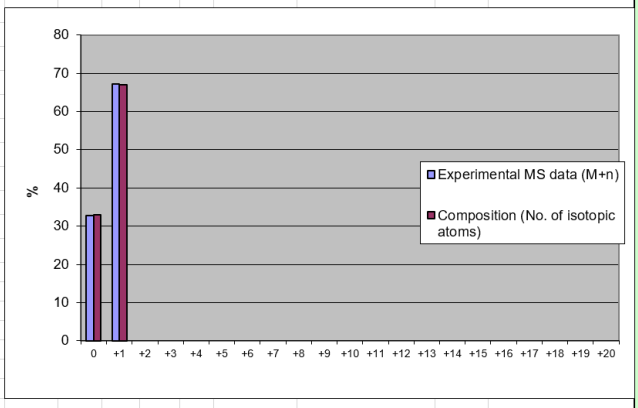
Analyte	Abundance
	85235
	174508
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0

Expected derivatives: 2 (Must be <2

Calculate

Labelled atoms 1

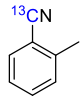
Atom% 67.0



Results

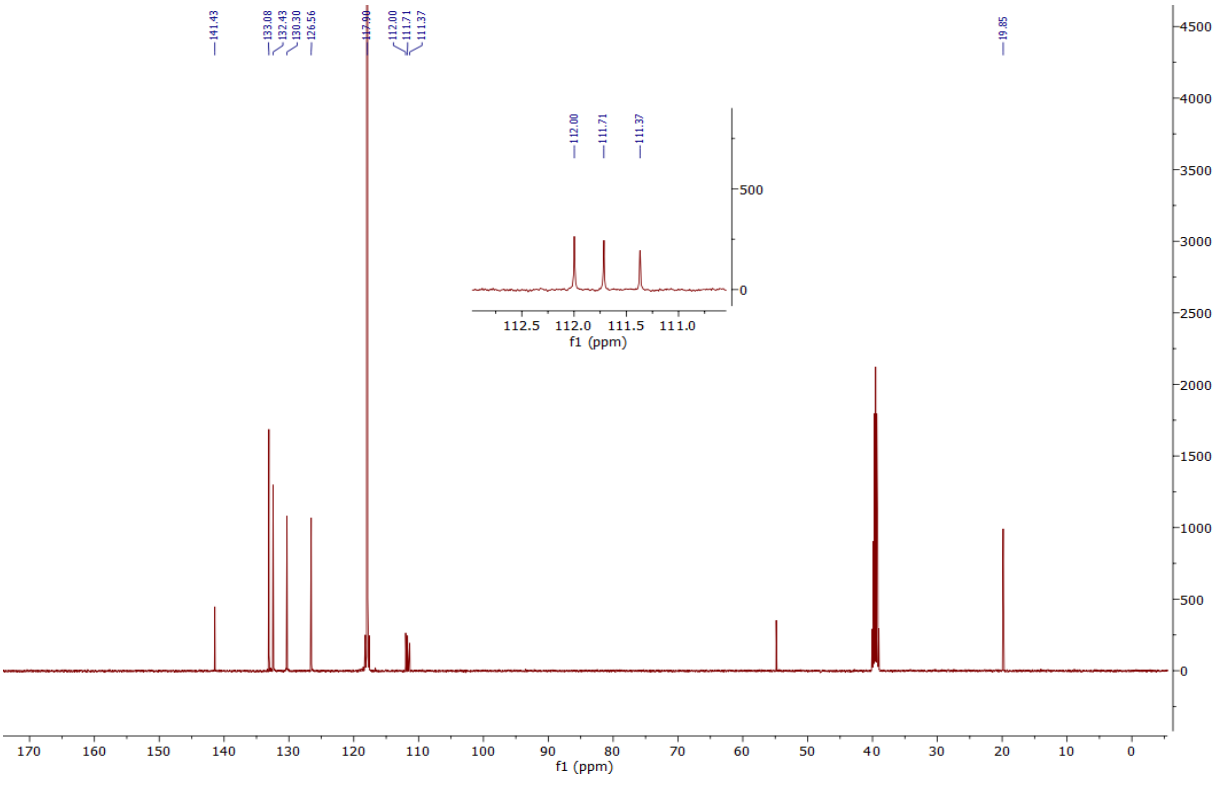
Relative amounts [%]

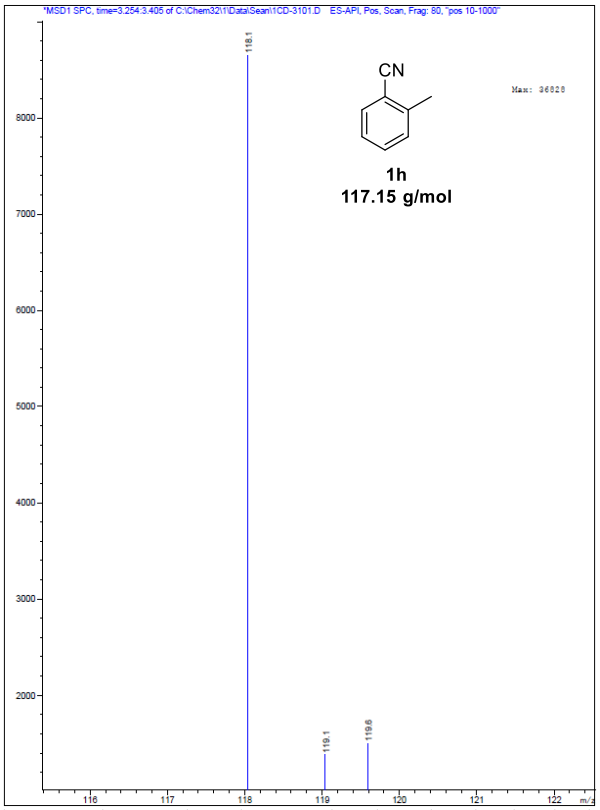
unlabeled	33.0
1-label	67.0

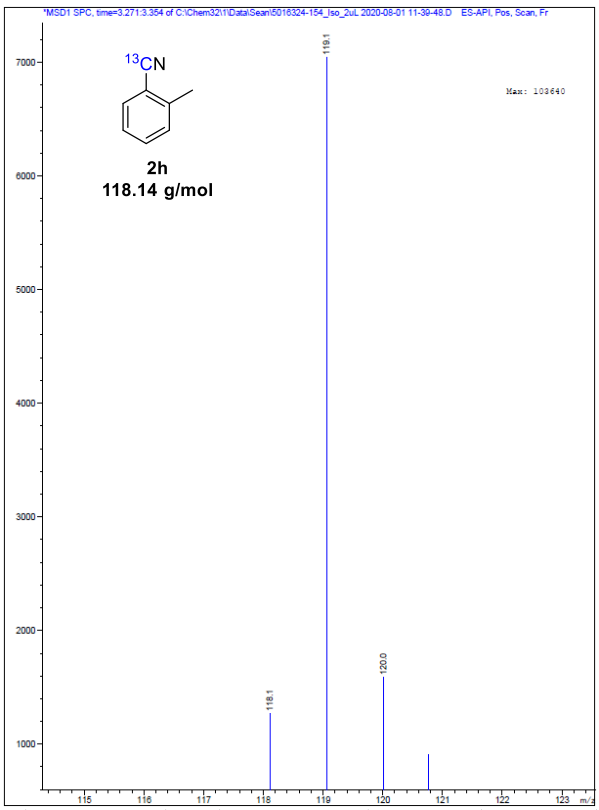

^{13}CN

2h

7.74
7.74
7.73
7.73
7.61
7.59
7.58
7.45
7.44
7.38
7.36
7.35
2.47
0.97
1.00
0.99
1.00
3.09
f1 (ppm)


141.43
133.08
132.43
130.30
126.56
117.00
112.00
111.71
111.37
19.85
112.00
111.71
111.37
f1 (ppm)
f1 (ppm)





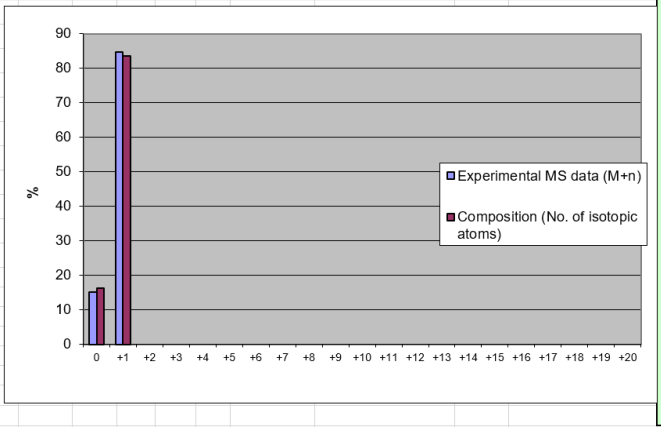
Unlabeled compound	Abundance	Analyte	Abundance
M1+0	8646		1268.8
M1+1	1379		7042
M1+2	0		0
M1+3	0		0
M1+4	0		0
M1+5	0		0
M1+6	0		0
M1+7	0		0
M1+8	0		0
M1+9	0		0
M1+10	0		0
M1+11	0		0
M1+12	0		0
M1+13	0		0
M1+14	0		0
M1+15	0		0
M1+16	0		0
M1+17	0		0
M1+18	0		0
M1+19	0		0

Expected derivatives: 2 (Must be <2

Labelled atoms 1

Atom% 83.7

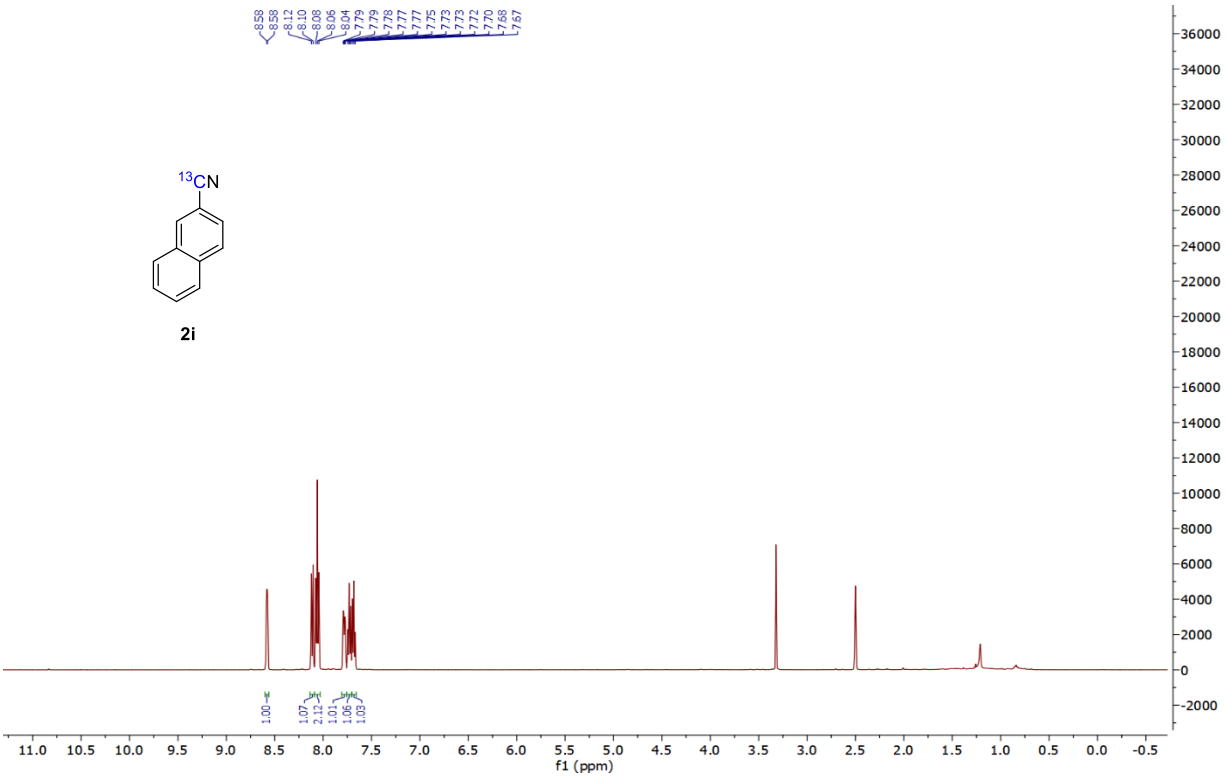
Calculate



Results

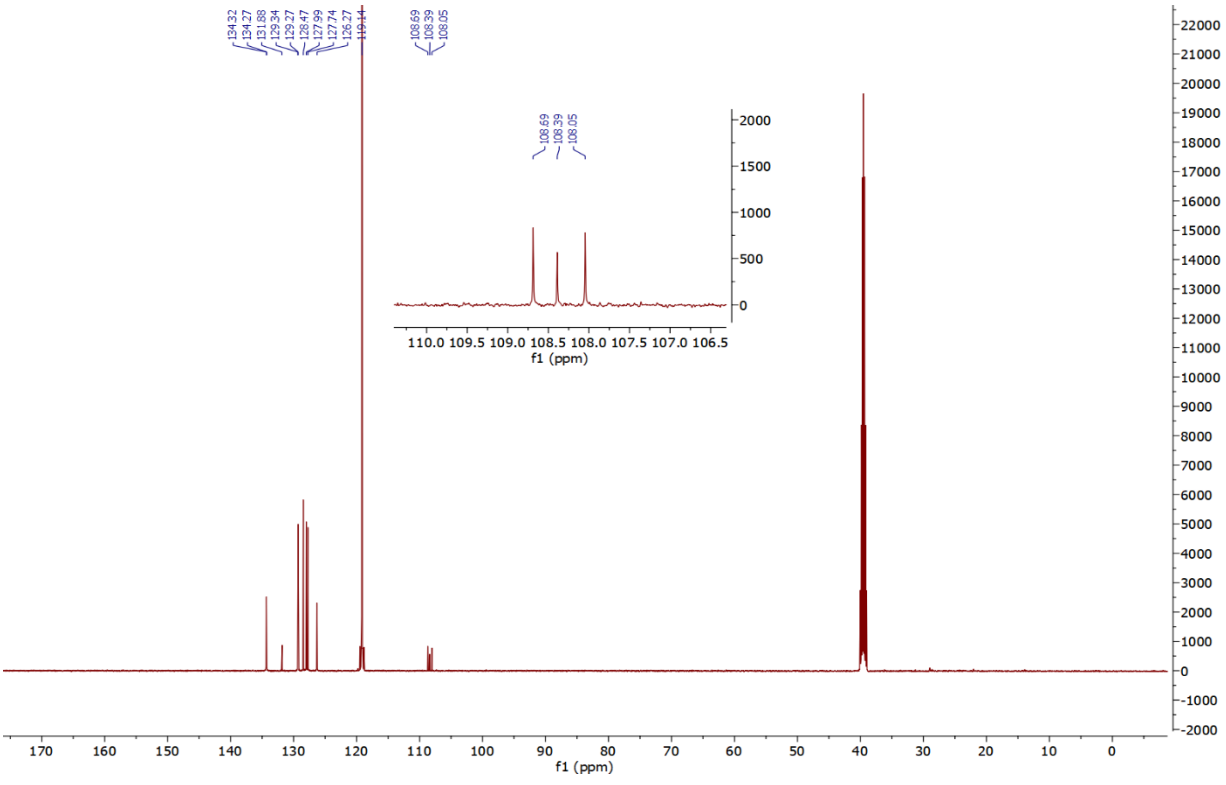
Relative amounts [%]

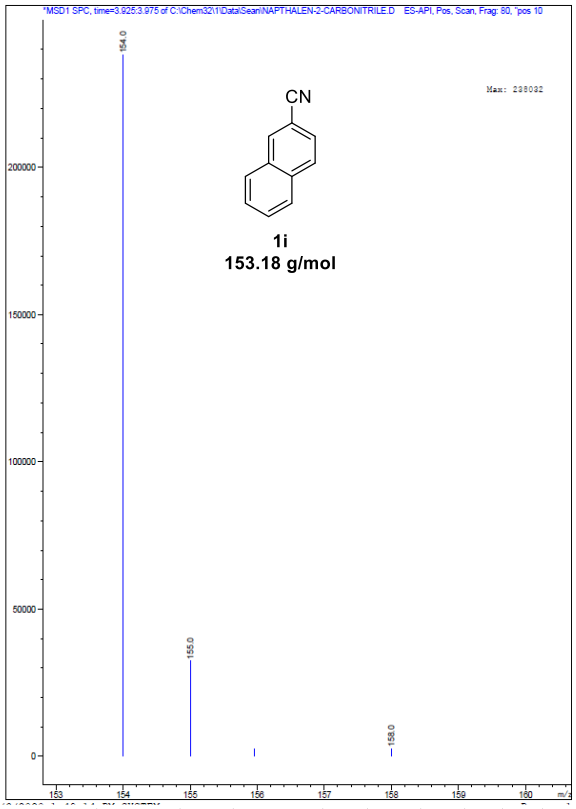
unlabeled	16.3
1-label	83.7

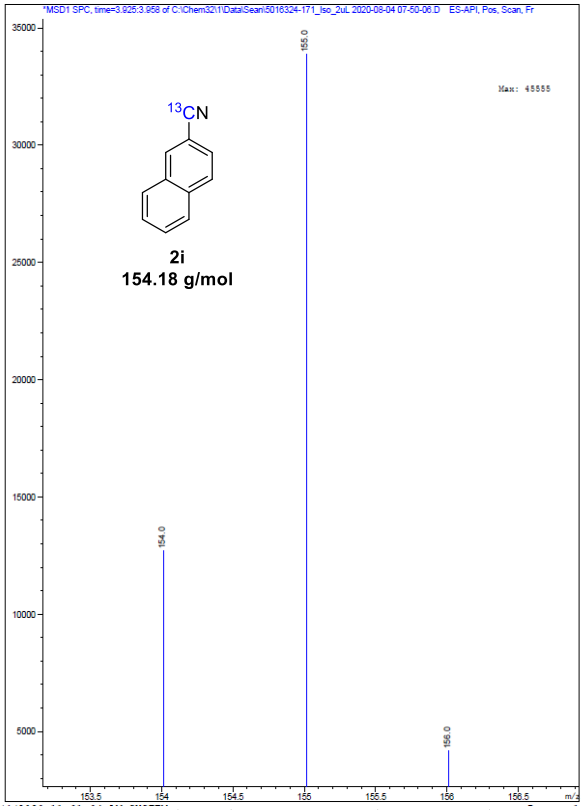

8.59
8.58
8.12
8.10
8.08
8.06
8.04
7.79
7.79
7.78
7.77
7.77
7.75
7.73
7.73
7.72
7.70
7.68
7.67
1.00
1.07
2.12
1.01
1.06
1.03
f1 (ppm)

13CN

2i


134.32
134.27
131.88
129.54
129.27
128.47
127.99
127.74
126.27
119.14
108.69
108.39
108.05
f1 (ppm)





Unlabeled compound	Abundance
M1+0	238032
M1+1	32358
M1+2	0
M1+3	0
M1+4	0
M1+5	0
M1+6	0
M1+7	0
M1+8	0
M1+9	0
M1+10	0
M1+11	0
M1+12	0
M1+13	0
M1+14	0
M1+15	0
M1+16	0
M1+17	0
M1+18	0
M1+19	0

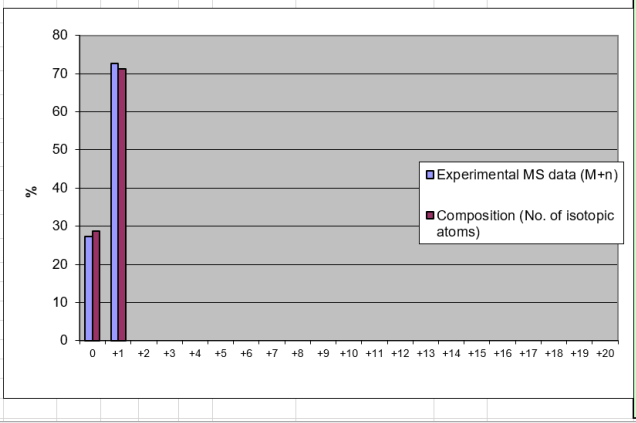
Analyte	Abundance
	12694
	33861.7
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0

Expected derivatives: 2 (Must be <2

Calculate

Labelled atoms 1

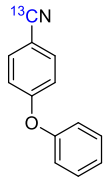
Atom% 71.2



Results

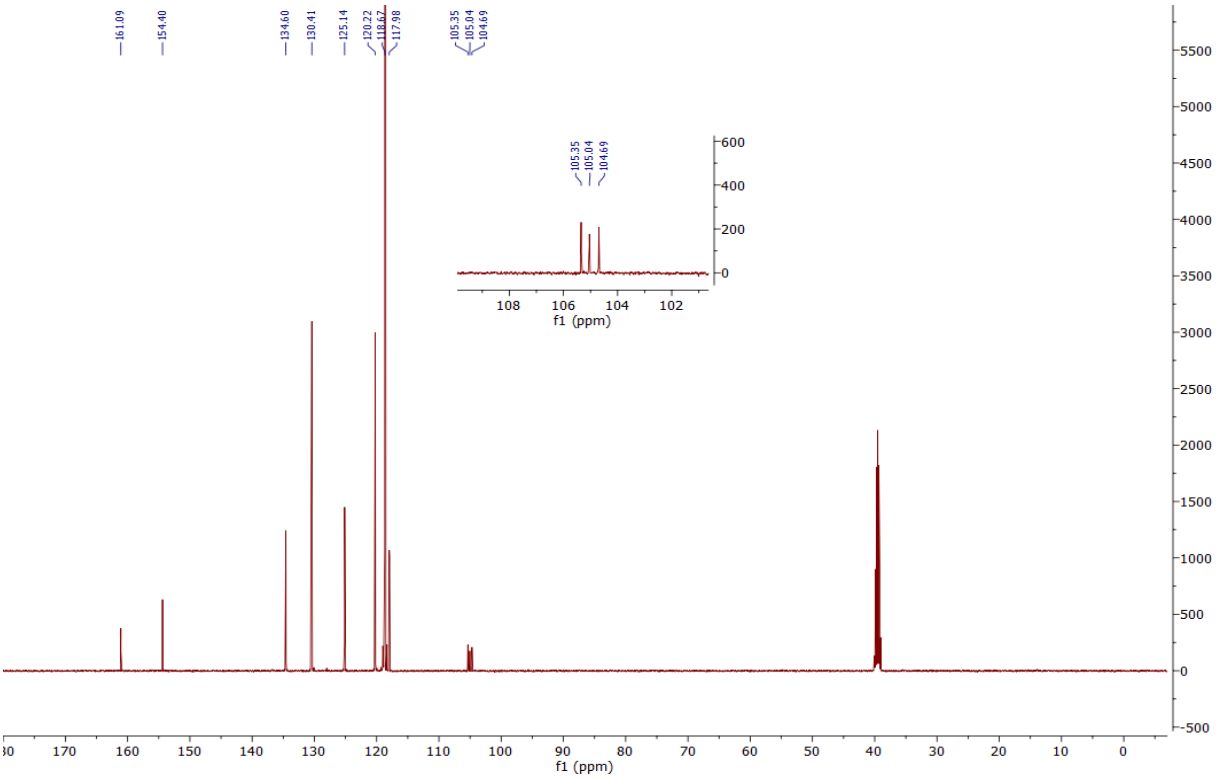
Relative amounts [%]

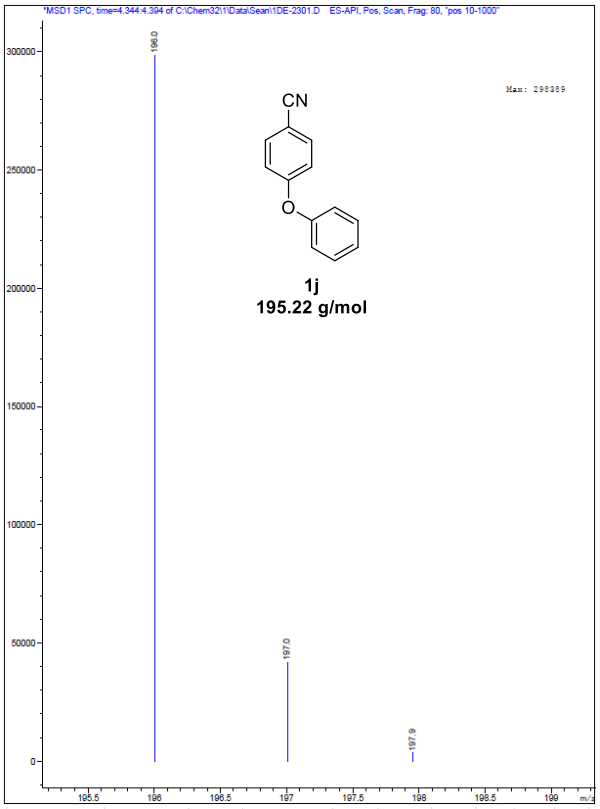
unlabeled	28.8
1-label	71.2

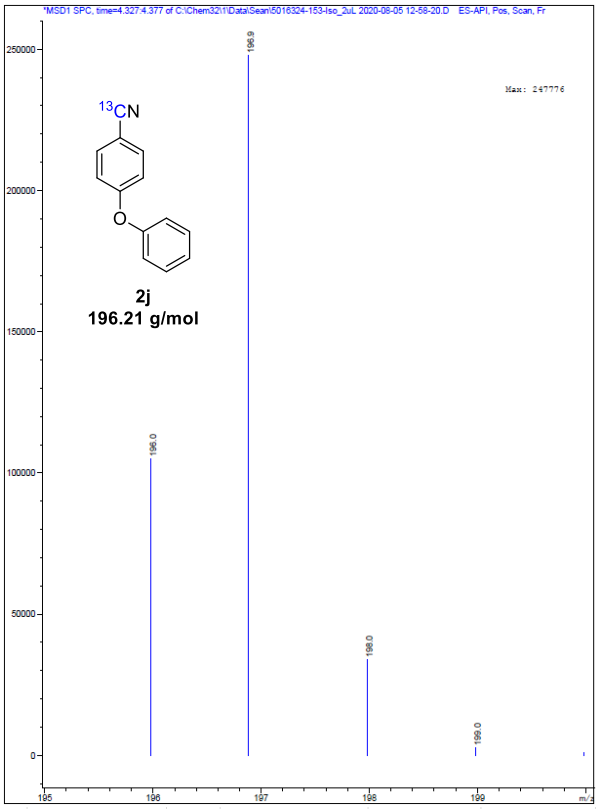

13CN
O

2j

7.84
7.83
7.83
7.83
7.82
7.82
7.81
7.49
7.47
7.46
7.28
7.27
7.26
7.15
7.13
7.09
7.07
3.99
4.03
2.00
3.99
4.09
f1 (ppm)


161.09
154.40
134.60
130.41
125.14
120.22
118.67
117.98
105.35
105.04
104.69
f1 (ppm)





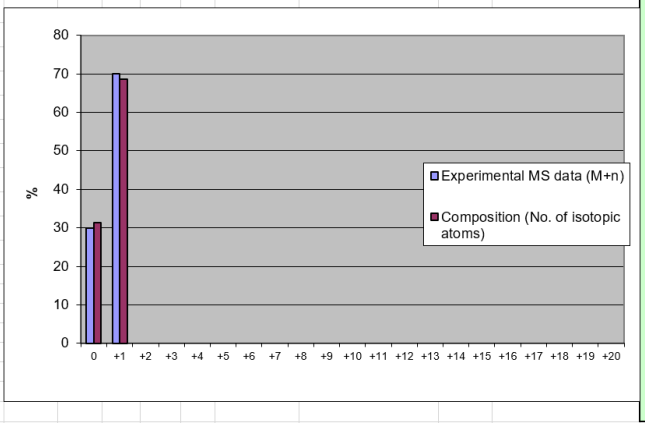
Unlabeled compound	Abundance	Analyte	Abundance
M1+0	3602192		86788.7
M1+1	398624		202761.7
M1+2	0		0
M1+3	0		0
M1+4	0		0
M1+5	0		0
M1+6	0		0
M1+7	0		0
M1+8	0		0
M1+9	0		0
M1+10	0		0
M1+11	0		0
M1+12	0		0
M1+13	0		0
M1+14	0		0
M1+15	0		0
M1+16	0		0
M1+17	0		0
M1+18	0		0
M1+19	0		0

Expected derivatives: 2 (Must be <2

Calculate

Labelled atoms 1

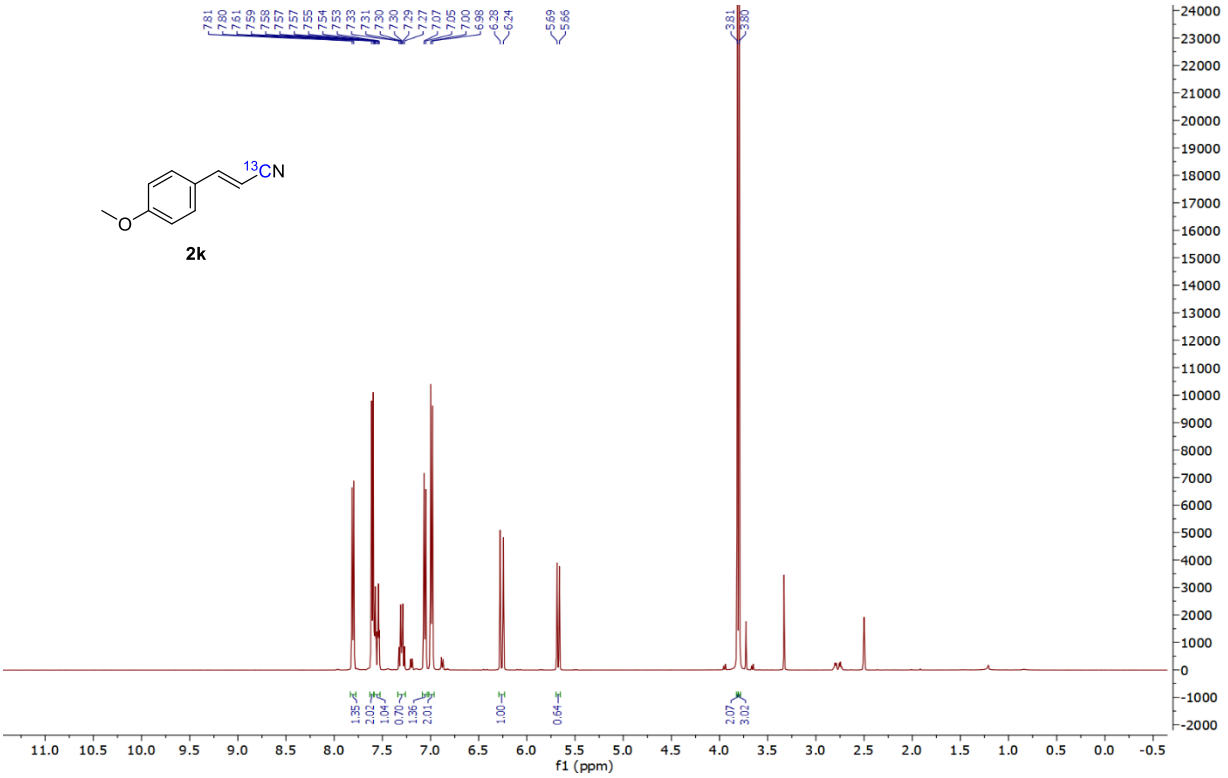
Atom% 68.7

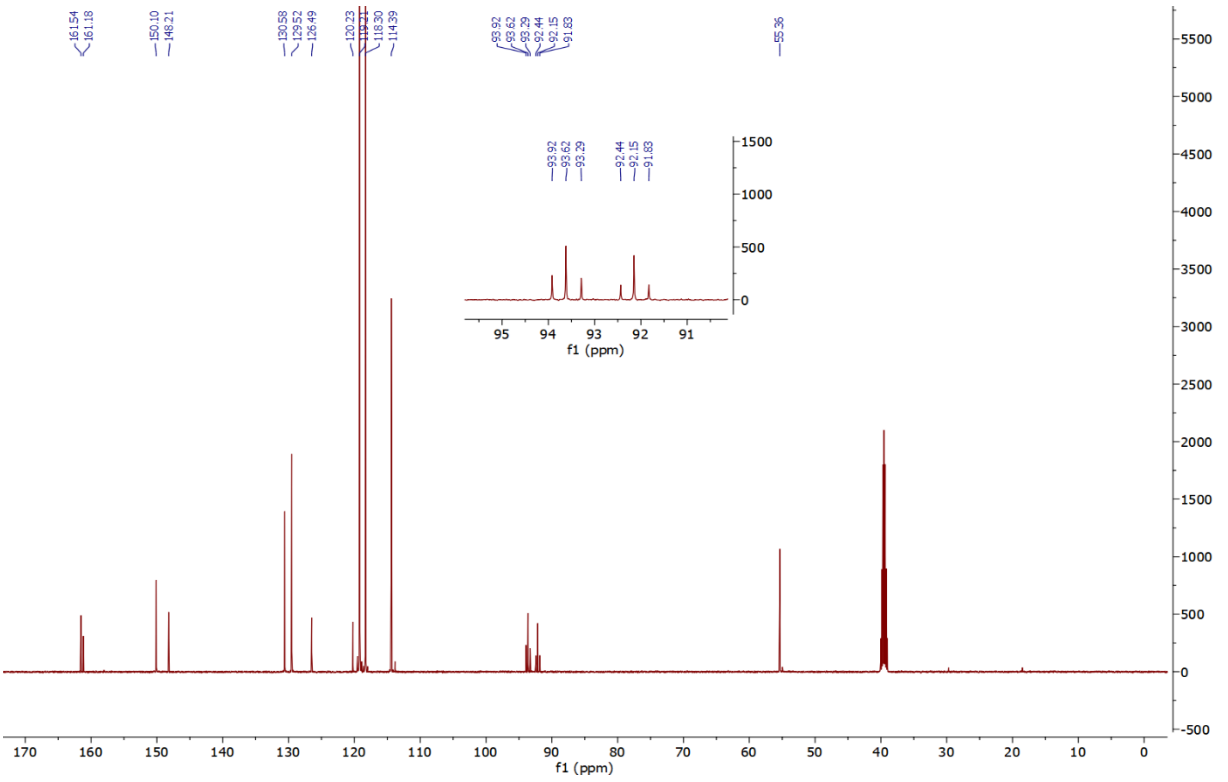


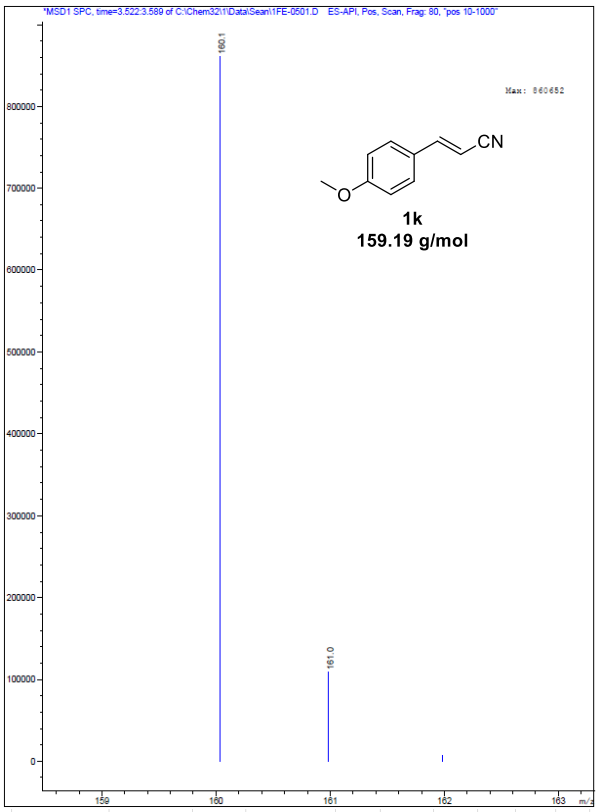
Results

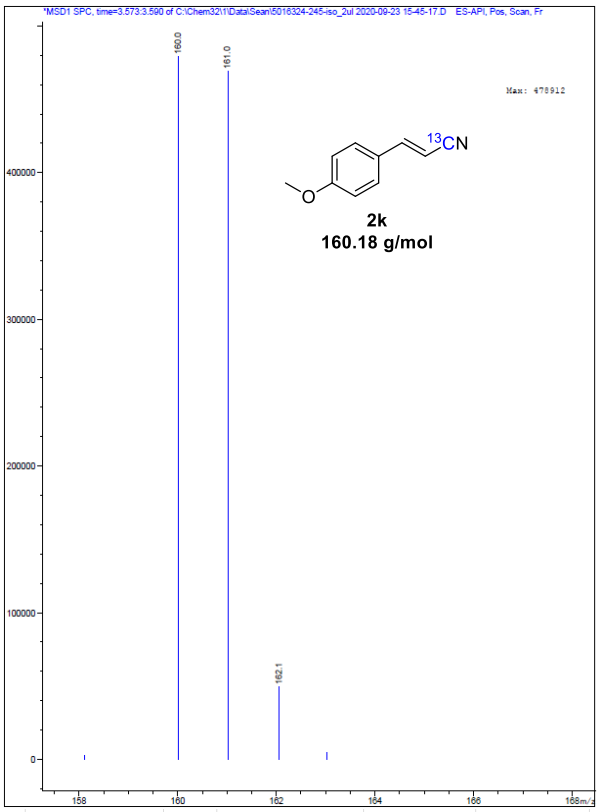
Relative amounts [%]

unlabeled	31.3
1-label	68.7


7.81
7.80
7.61
7.59
7.58
7.57
7.57
7.55
7.54
7.53
7.33
7.31
7.30
7.30
7.29
7.27
7.07
7.05
7.00
6.98
6.28
6.24
5.69
5.66
3.81
3.80
13CN
O
2k
1.35
2.02
1.04
0.70
1.36
2.01
1.00
0.64
2.07
3.01
f1 (ppm)


161.54
161.18
150.10
148.21
130.58
129.52
126.49
120.23
119.21
118.30
114.39
93.92
93.62
93.29
92.44
92.15
91.83
55.36
f1 (ppm)





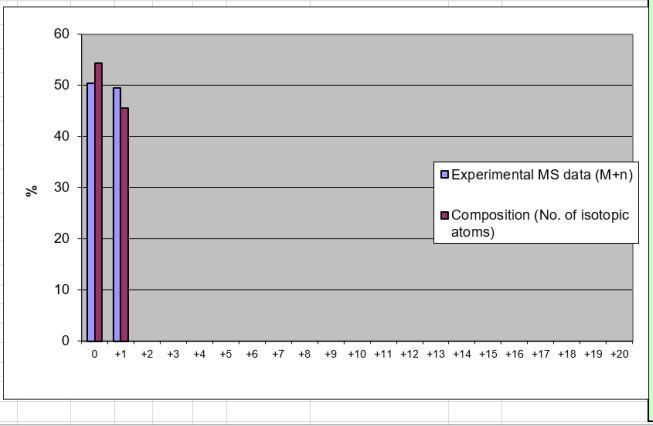
Unlabeled compound	Abundance	Analyte	Abundance
M1+0	860652		478912
M1+1	109562		469376
M1+2	0		0
M1+3	0		0
M1+4	0		0
M1+5	0		0
M1+6	0		0
M1+7	0		0
M1+8	0		0
M1+9	0		0
M1+10	0		0
M1+11	0		0
M1+12	0		0
M1+13	0		0
M1+14	0		0
M1+15	0		0
M1+16	0		0
M1+17	0		0
M1+18	0		0
M1+19	0		0

Expected derivatives: 2 (Must be <2

Labelled atoms 1

Atom% 45.6

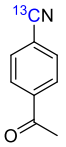
Calculate



Results

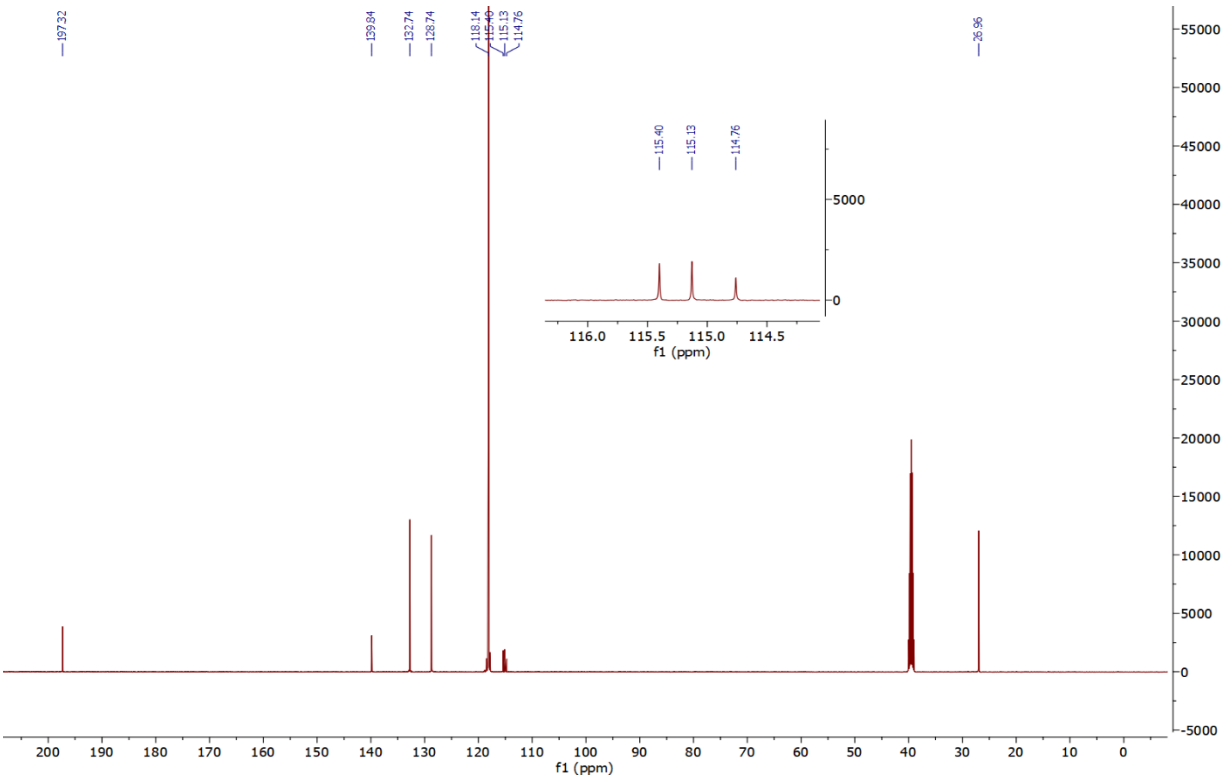
Relative amounts [%]

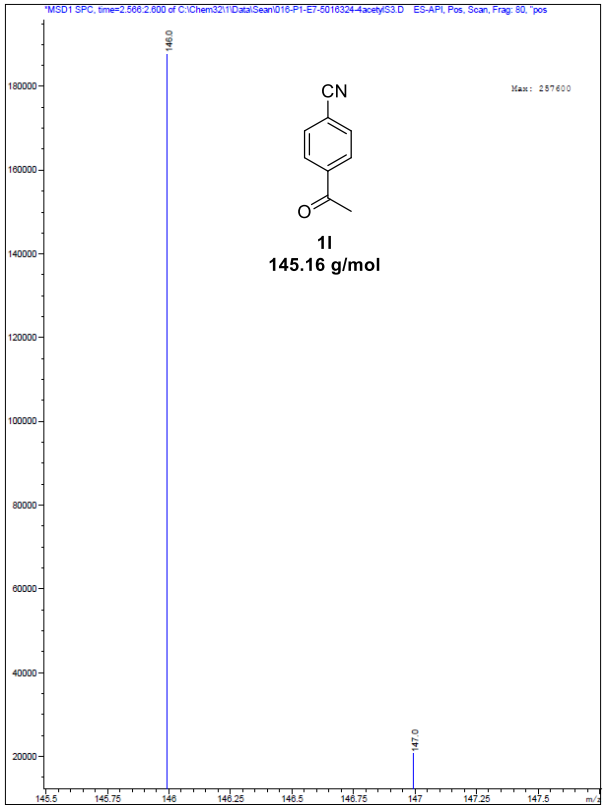
unlabeled	54.4
1-label	45.6

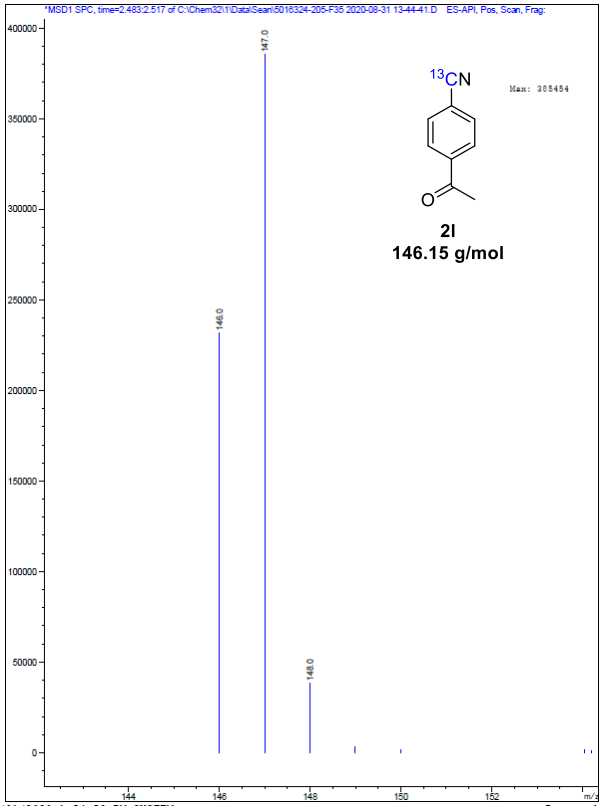

13CN
O

2l

8.10
8.08
8.01
8.01
8.00
8.00
8.00
8.00
7.99
7.99
2.63
2.07
2.00
3.09
f1 (ppm)


197.32
139.84
132.74
128.74
118.14
115.40
115.13
114.76
26.96
115.40
115.13
114.76
5000
0
116.0
115.5
115.0
114.5
f1 (ppm)
f1 (ppm)





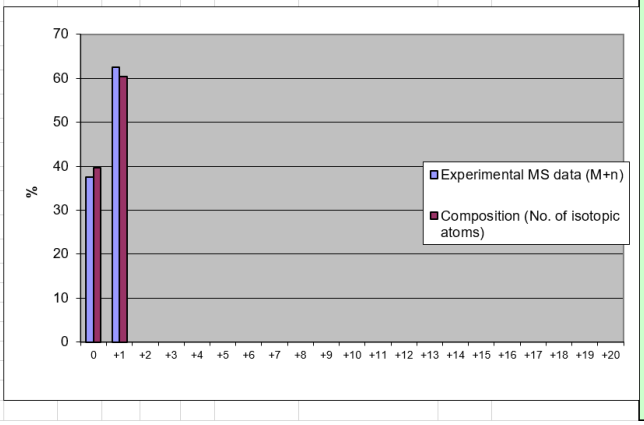
Unlabeled compound	Abundance	Analyte	Abundance
M1+0	158312		231772.7
M1+1	18035		385454
M1+2	0		0
M1+3	0		0
M1+4	0		0
M1+5	0		0
M1+6	0		0
M1+7	0		0
M1+8	0		0
M1+9	0		0
M1+10	0		0
M1+11	0		0
M1+12	0		0
M1+13	0		0
M1+14	0		0
M1+15	0		0
M1+16	0		0
M1+17	0		0
M1+18	0		0
M1+19	0		0

Expected derivatives: 2 (Must be <2

Labelled atoms 1

Atom% 60.4

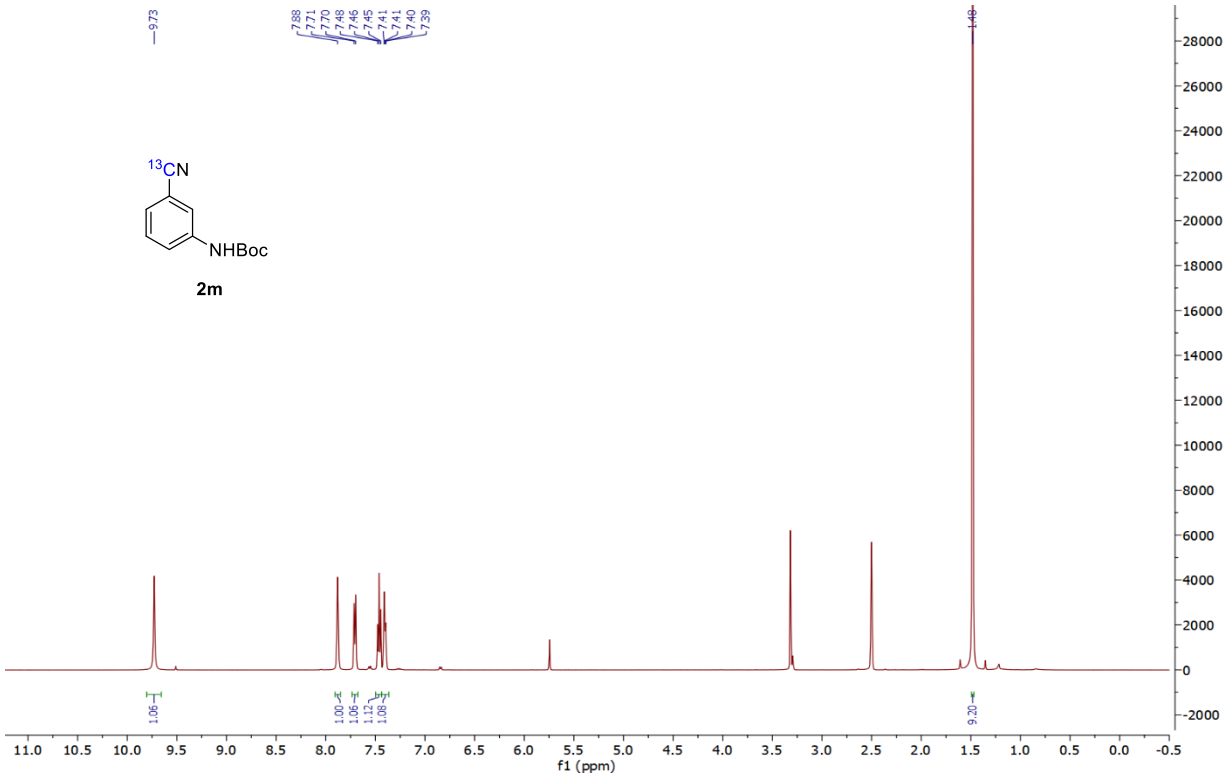
Calculate

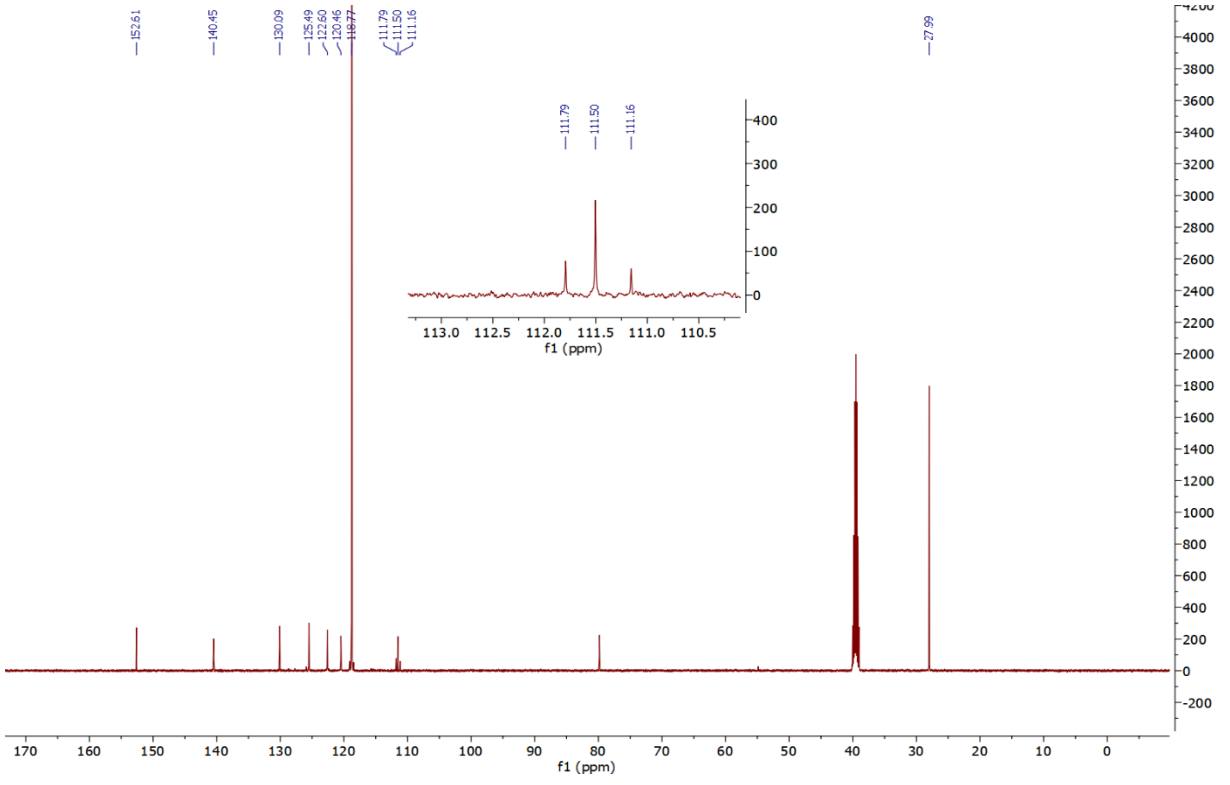


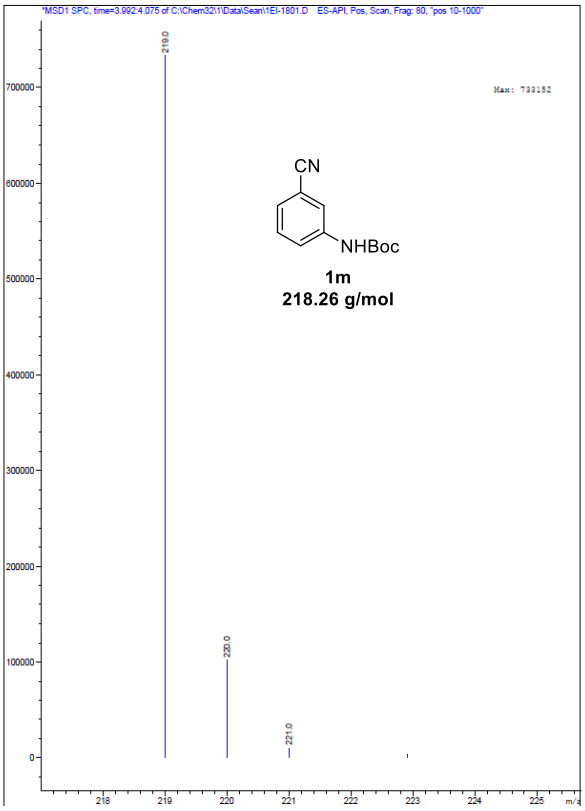
Results

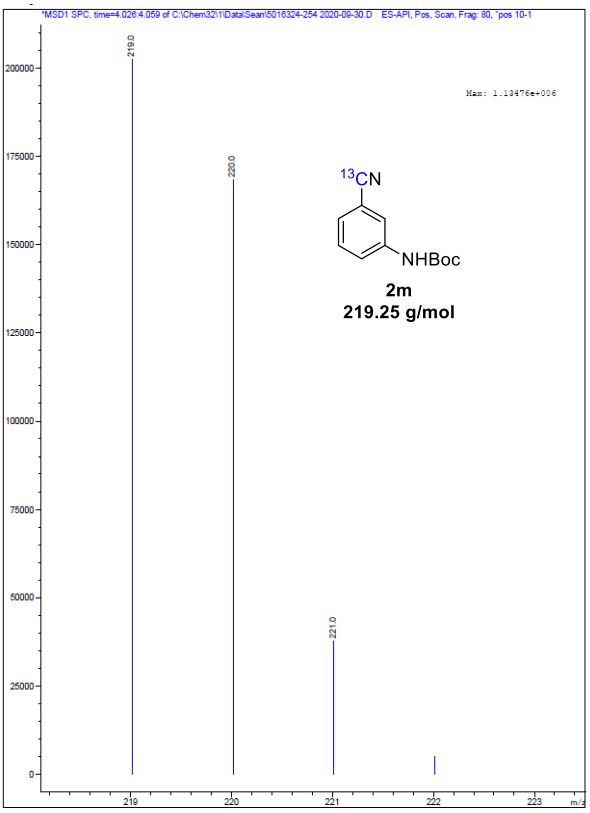
Relative amounts [%]

unlabeled	39.6
1-label	60.4


9.73
7.88
7.71
7.70
7.48
7.46
7.45
7.41
7.41
7.40
7.39
1.49
13CN
NHBoc
2m
1.06
1.00
1.06
1.12
1.08
9.20
f1 (ppm)


152.61
140.45
130.09
125.49
122.60
120.46
118.77
111.79
111.50
111.16
27.99
f1 (ppm)





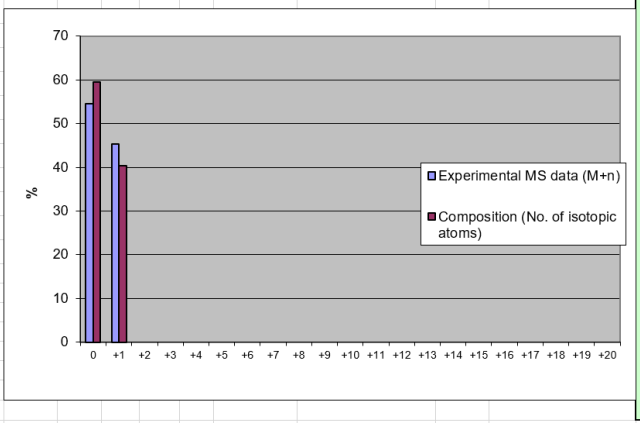
Unlabeled compound	Abundance	Analyte	Abundance
M1+0	733152		202352
M1+1	101659		168298.7
M1+2	0		0
M1+3	0		0
M1+4	0		0
M1+5	0		0
M1+6	0		0
M1+7	0		0
M1+8	0		0
M1+9	0		0
M1+10	0		0
M1+11	0		0
M1+12	0		0
M1+13	0		0
M1+14	0		0
M1+15	0		0
M1+16	0		0
M1+17	0		0
M1+18	0		0
M1+19	0		0

Expected derivatives: 2 (Must be <2

Labelled atoms 1

Atom% 40.4

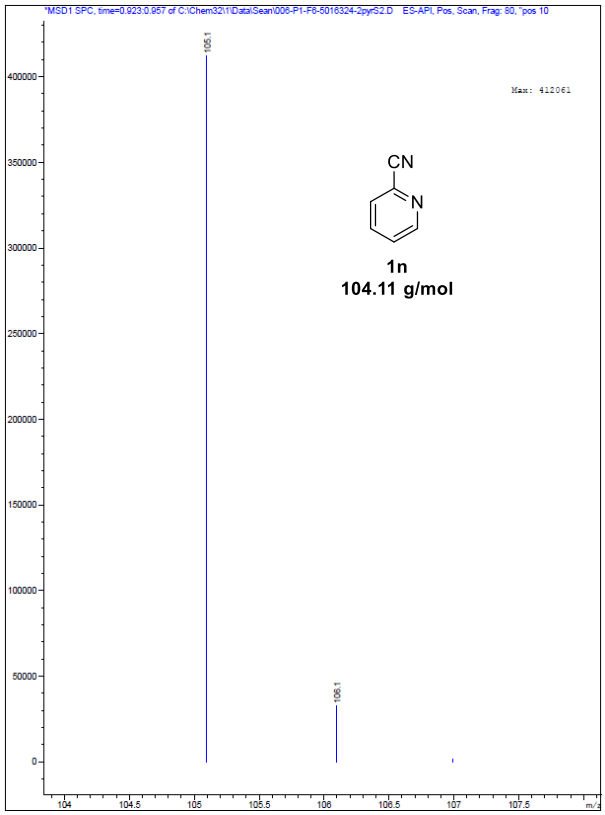
Calculate

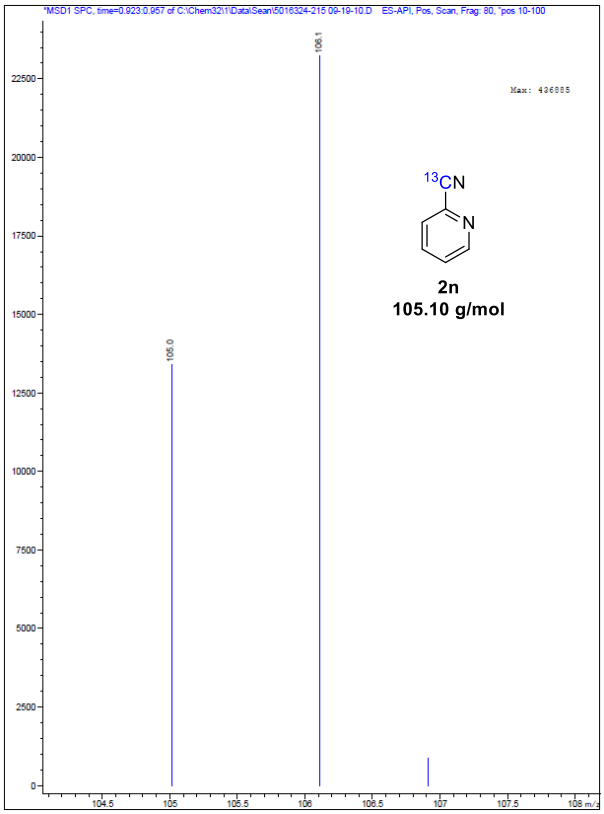


Results

Relative amounts [%]

unlabeled	59.6
1-label	40.4





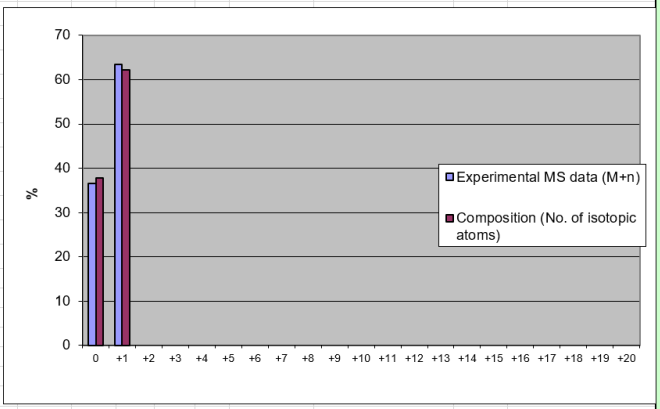
Unlabeled compound	Abundance	Analyte	Abundance
M1+0	412061		13413.7
M1+1	32743		23228.7
M1+2	0		0
M1+3	0		0
M1+4	0		0
M1+5	0		0
M1+6	0		0
M1+7	0		0
M1+8	0		0
M1+9	0		0
M1+10	0		0
M1+11	0		0
M1+12	0		0
M1+13	0		0
M1+14	0		0
M1+15	0		0
M1+16	0		0
M1+17	0		0
M1+18	0		0
M1+19	0		0

Expected derivatives: 2 (Must be <2

Labelled atoms 1

Atom% 62.1

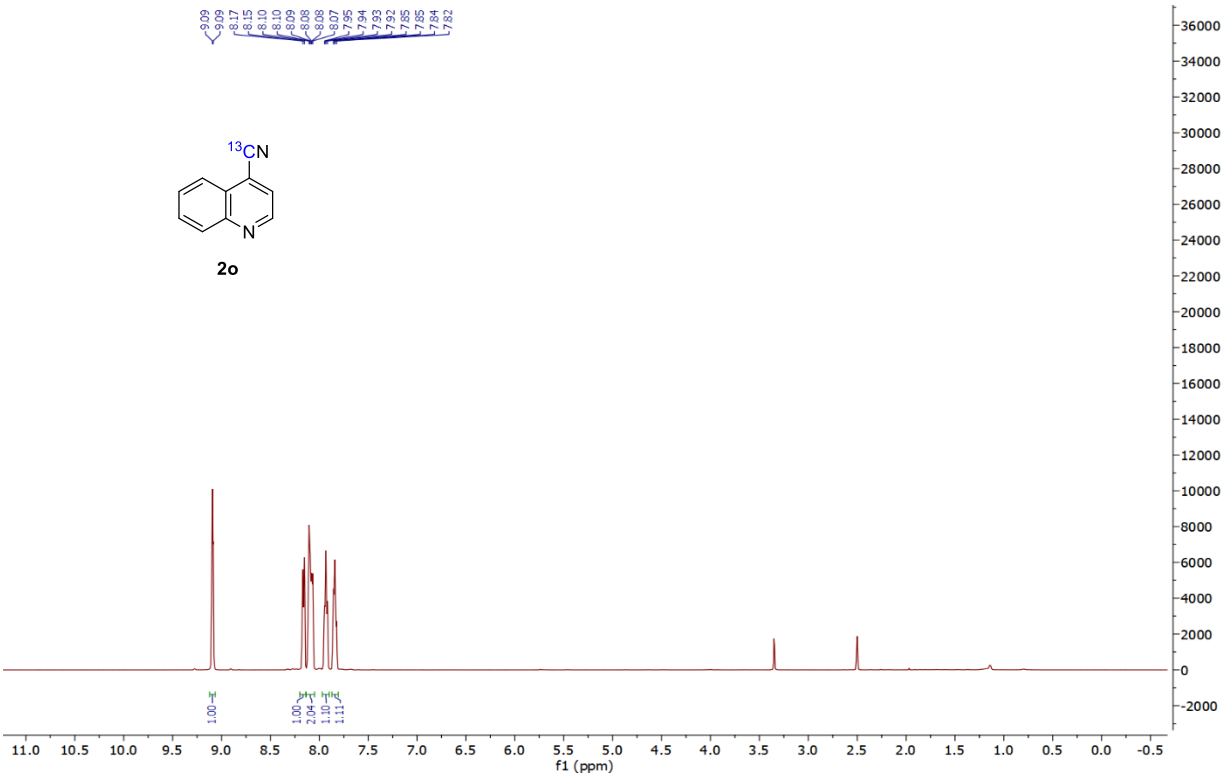
Calculate



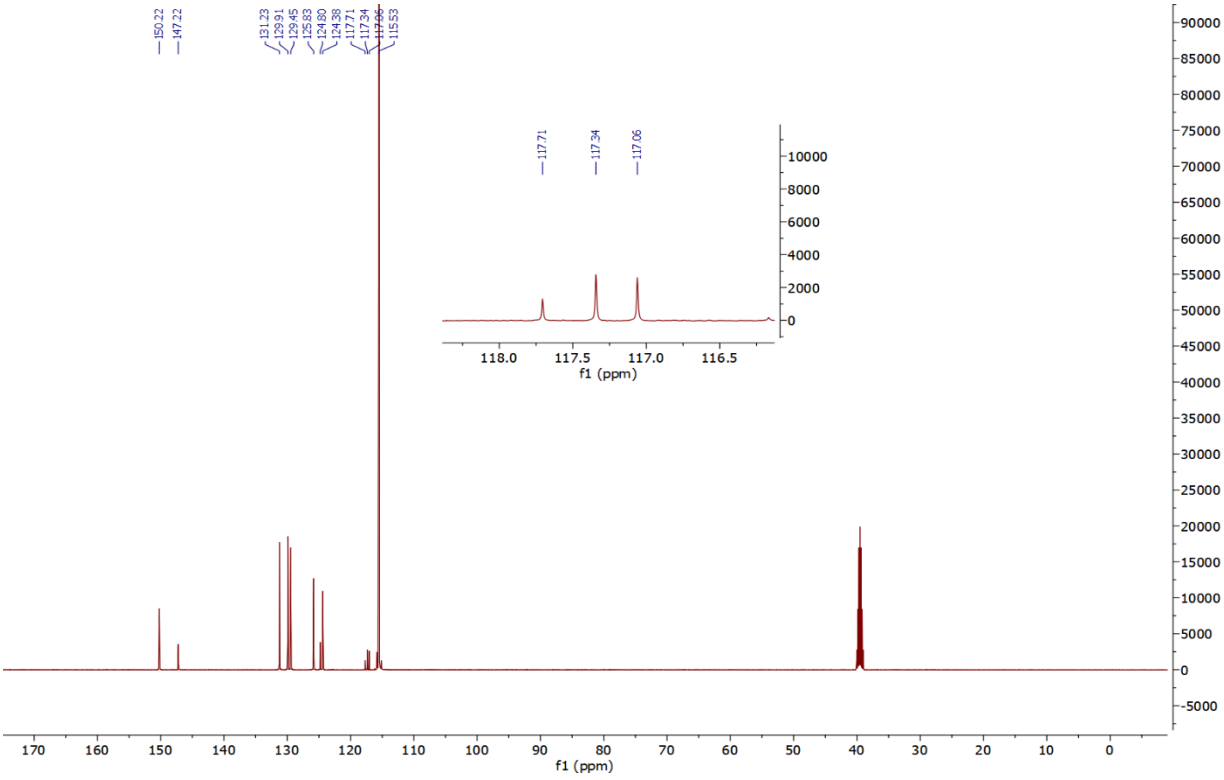
Results

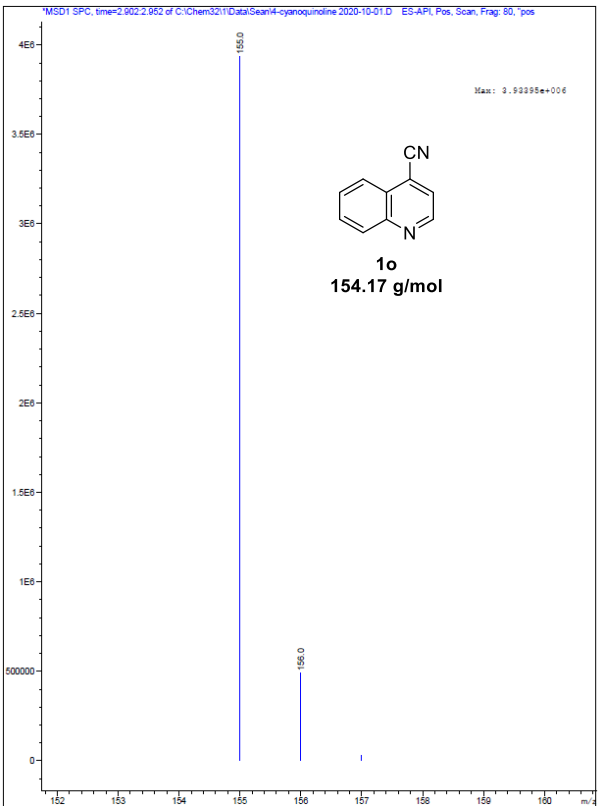
Relative amounts [%]

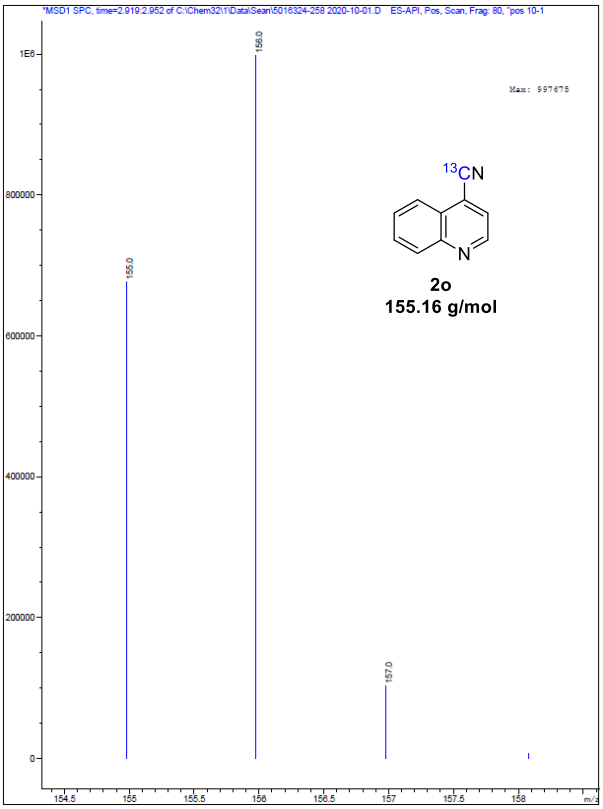
unlabeled	37.9
1-label	62.1
2-label	
3-label	
4-label	
5-label	
6-label	
…	
…	


9.09
9.09
8.17
8.15
8.10
8.10
8.09
8.08
8.08
8.07
7.95
7.94
7.93
7.92
7.85
7.85
7.84
7.82
13CN
N
1.00
1.00
2.04
1.10
1.11
f1 (ppm)

2o


150.22
147.22
131.23
129.91
129.45
125.83
124.80
124.38
117.71
117.34
117.06
115.53
117.71
117.34
117.06
f1 (ppm)
f1 (ppm)





Unlabeled compound	Abundance
M1+0	3933952
M1+1	491424
M1+2	0
M1+3	0
M1+4	0
M1+5	0
M1+6	0
M1+7	0
M1+8	0
M1+9	0
M1+10	0
M1+11	0
M1+12	0
M1+13	0
M1+14	0
M1+15	0
M1+16	0
M1+17	0
M1+18	0
M1+19	0

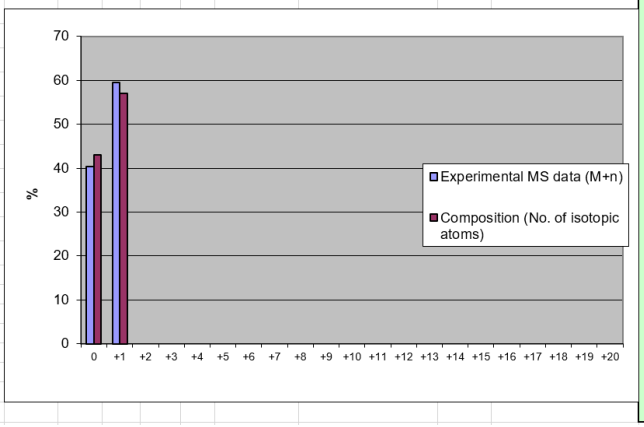
Analyte	Abundance
	676309.3
	997674.7
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0

Expected derivatives: 2 (Must be <2

Calculate

Labelled atoms 1

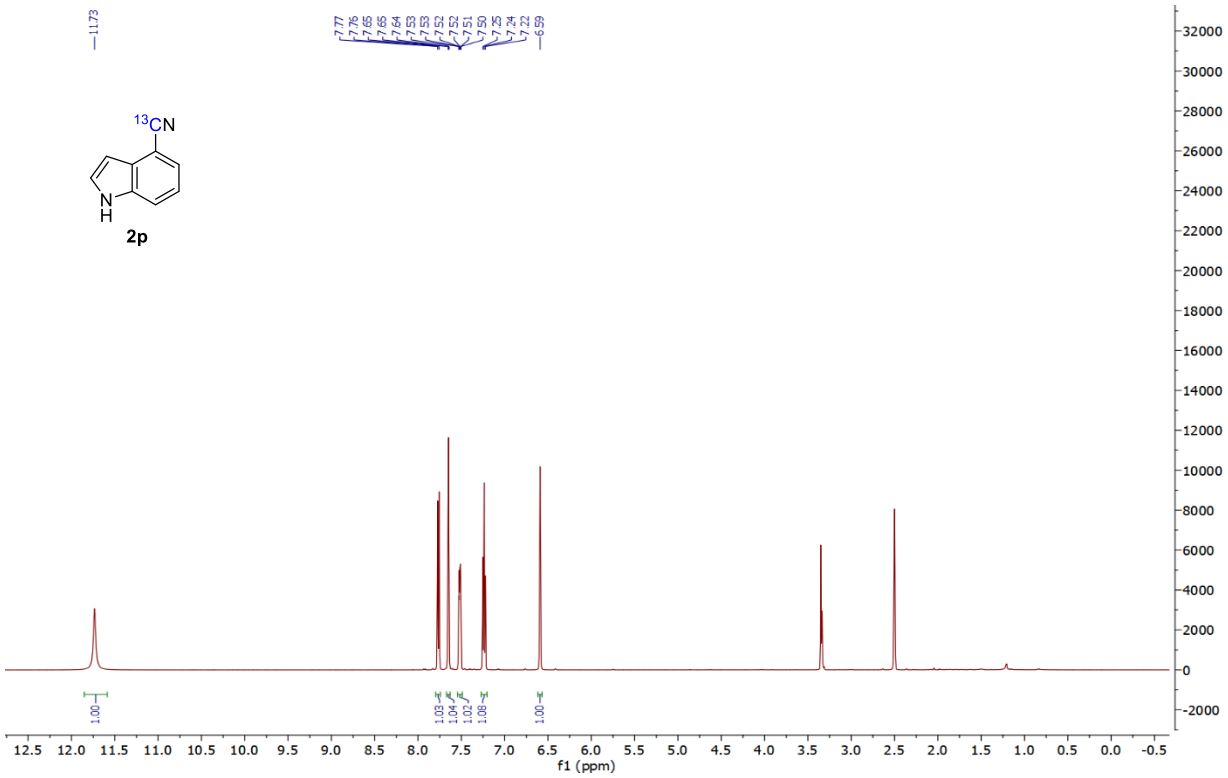
Atom% 57.0

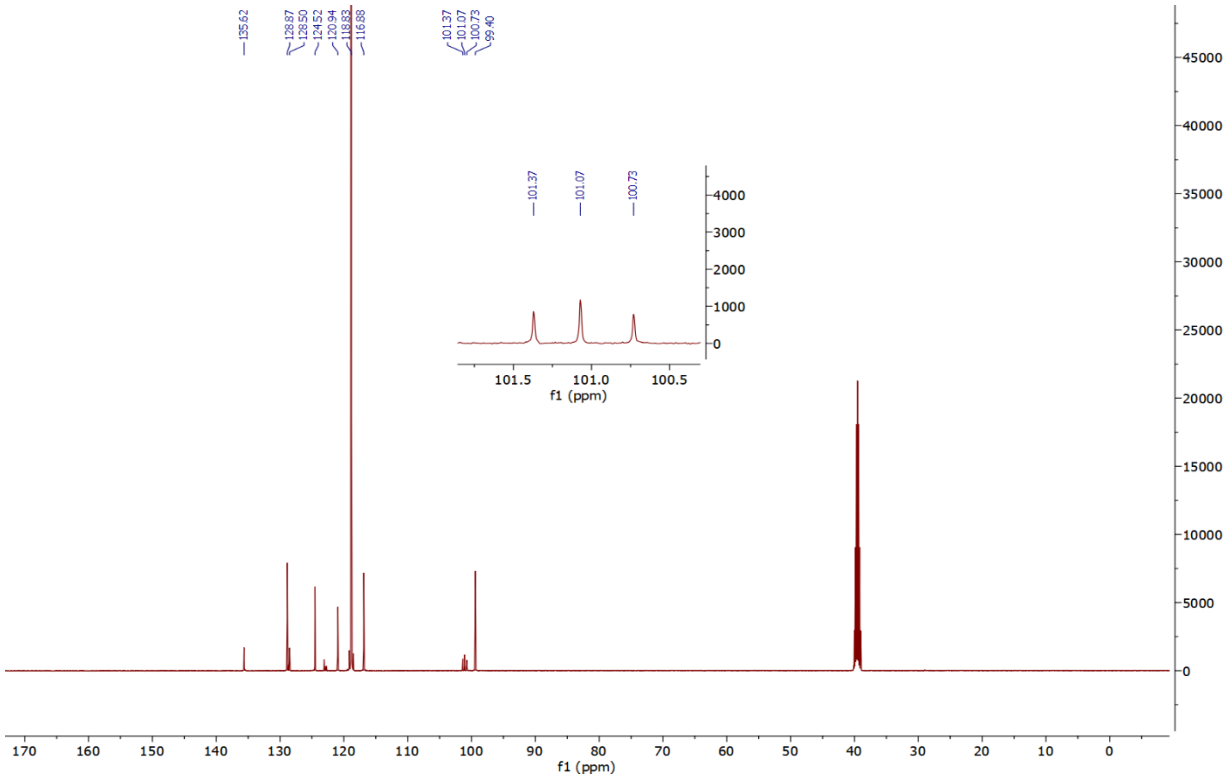


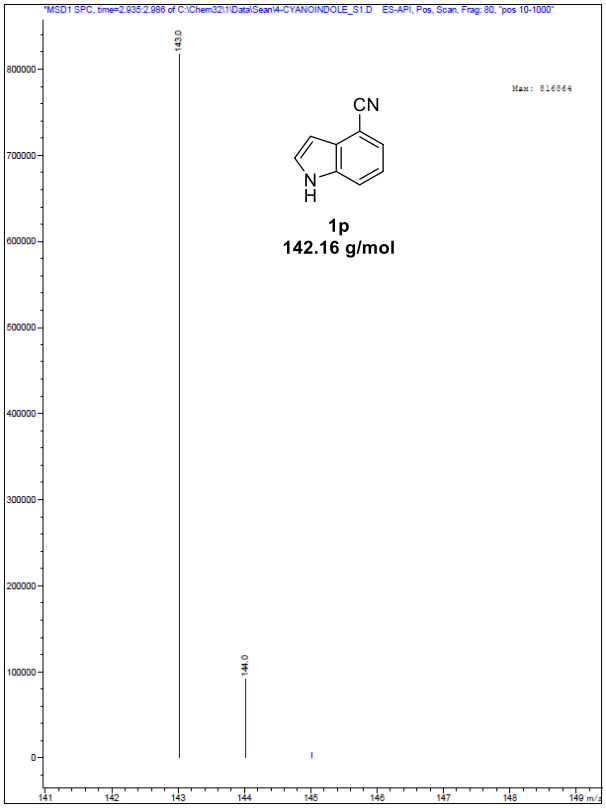
Results

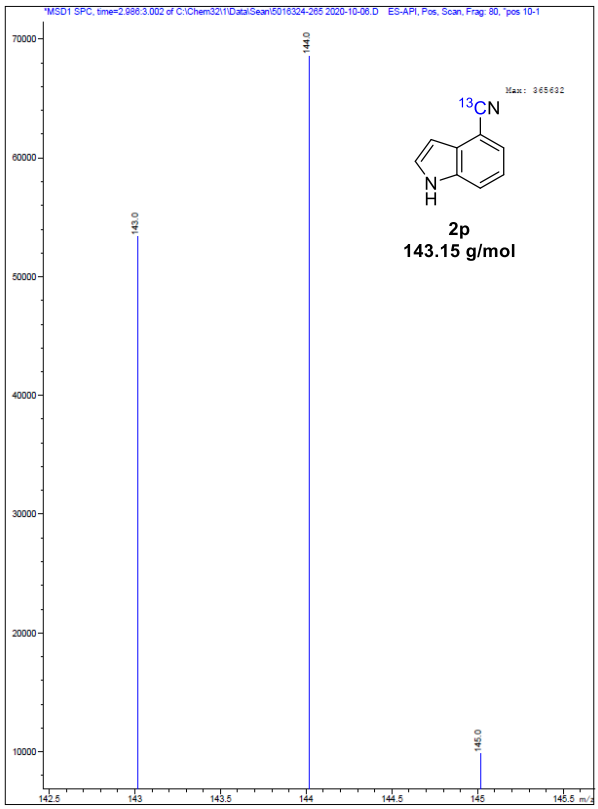
Relative amounts [%]

unlabeled	43.0
1-label	57.0


11.73
7.77
7.76
7.65
7.65
7.64
7.53
7.53
7.52
7.52
7.51
7.50
7.35
7.34
7.22
6.59
13CN
N
H
2p
1.00
1.03
1.04
1.02
1.08
1.00
f1 (ppm)


135.62
128.87
128.50
124.52
120.94
118.83
116.88
101.37
101.07
100.73
99.40
101.37
101.07
100.73
f1 (ppm)
f1 (ppm)





Unlabeled compound	Abundance
M1+0	816864
M1+1	91226
M1+2	0
M1+3	0
M1+4	0
M1+5	0
M1+6	0
M1+7	0
M1+8	0
M1+9	0
M1+10	0
M1+11	0
M1+12	0
M1+13	0
M1+14	0
M1+15	0
M1+16	0
M1+17	0
M1+18	0
M1+19	0

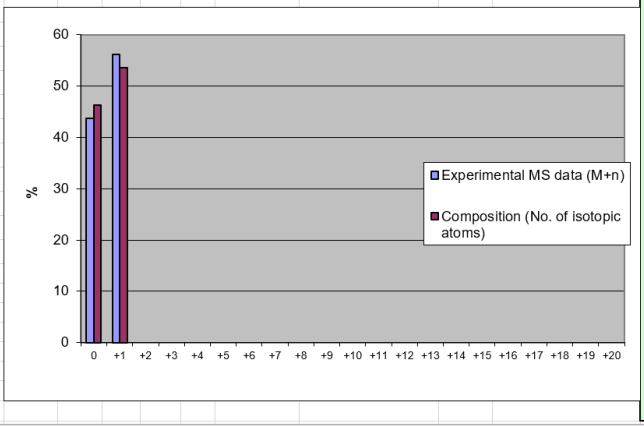
Analyte	Abundance
M1+0	53332
M1+1	68536
M1+2	0
M1+3	0
M1+4	0
M1+5	0
M1+6	0
M1+7	0
M1+8	0
M1+9	0
M1+10	0
M1+11	0
M1+12	0
M1+13	0
M1+14	0
M1+15	0
M1+16	0
M1+17	0
M1+18	0
M1+19	0

Expected derivatives: 2 (Must be <2

Labelled atoms 1

Atom% 53.6

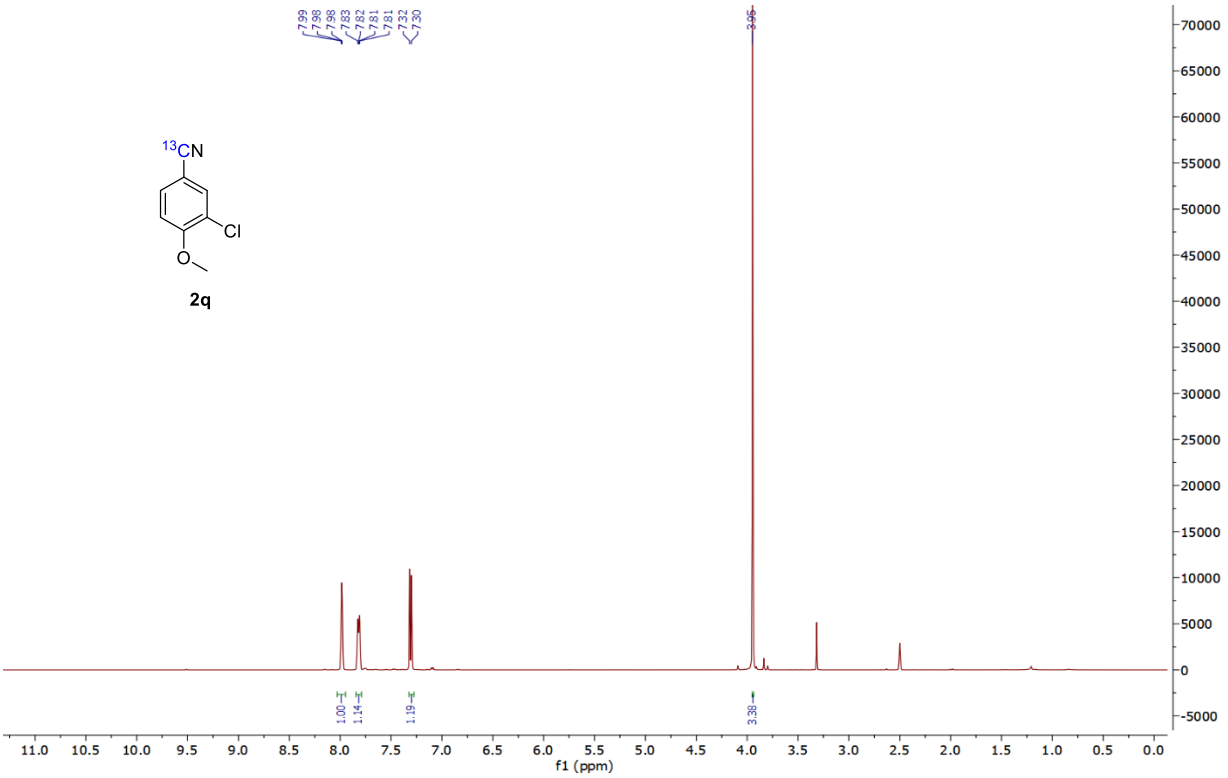
Calculate

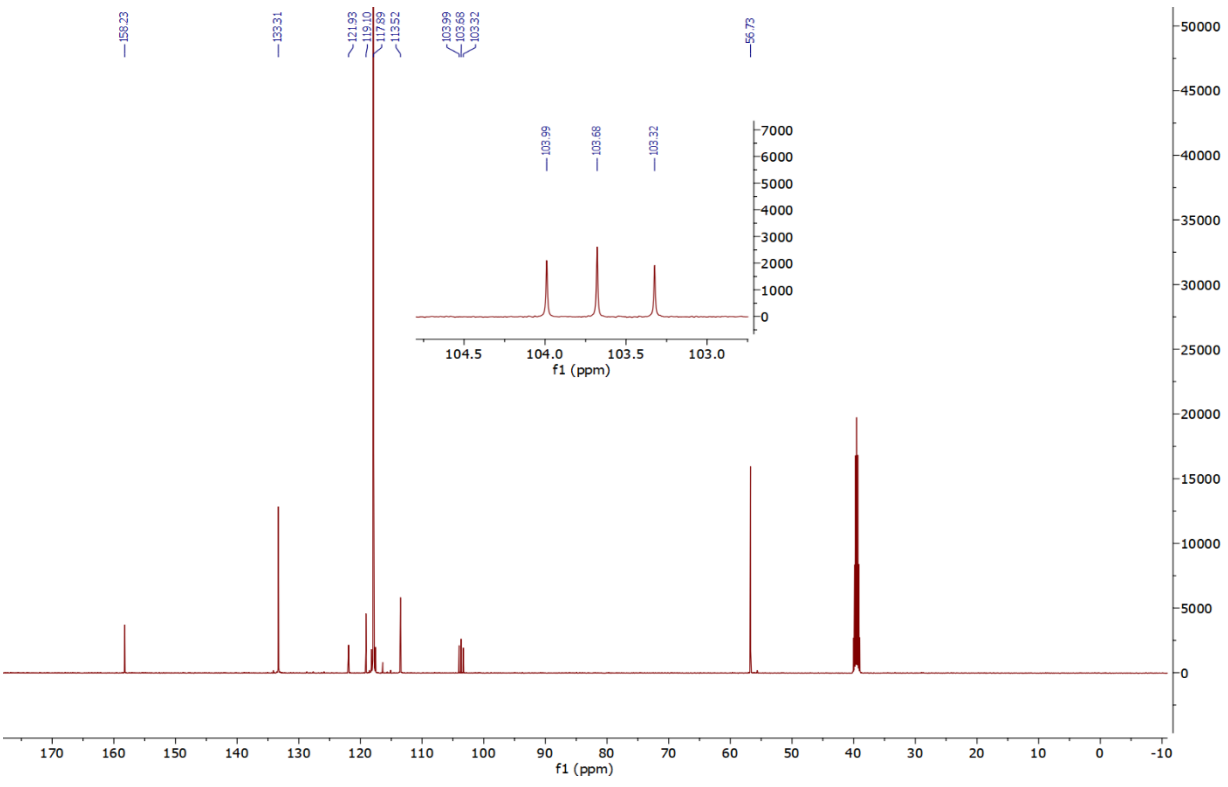


Results

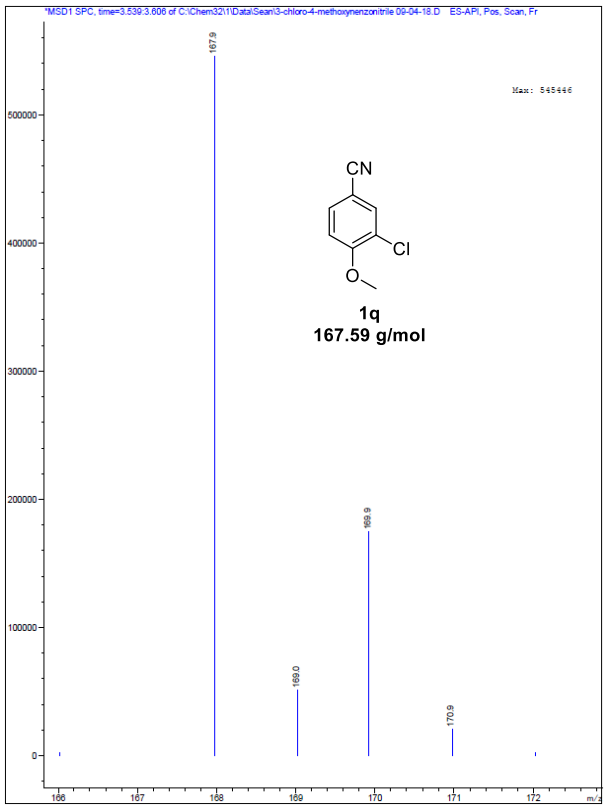
Relative amounts [%]

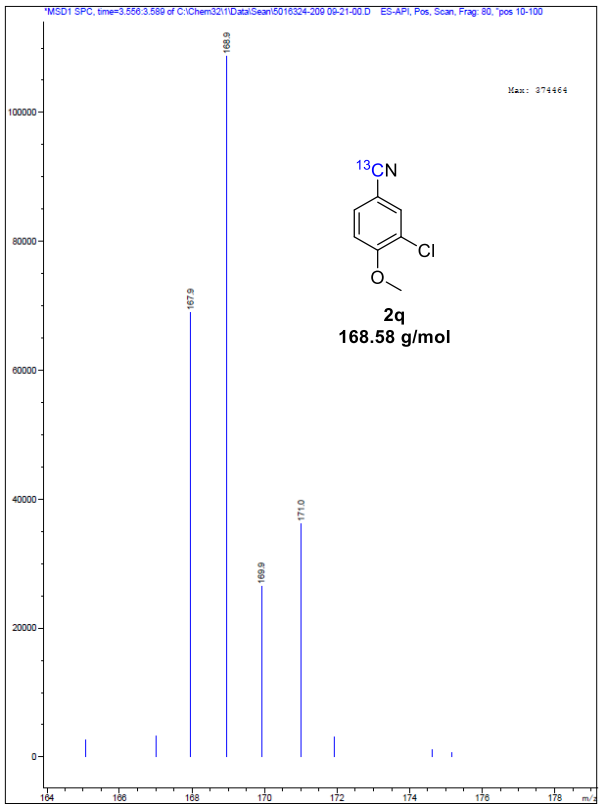
unlabeled	46.4
1-label	53.6


7.99
7.98
7.96
7.83
7.82
7.81
7.81
7.32
7.30
3.95
1.00
1.14
1.19
3.38
f1 (ppm)


158.23
133.31
121.93
119.10
117.89
113.52
103.99
103.68
103.32
56.73
f1 (ppm)

2q





Unlabeled compound	Abundance
M1+0	545446
M1+1	51031
M1+2	0
M1+3	0
M1+4	0
M1+5	0
M1+6	0
M1+7	0
M1+8	0
M1+9	0
M1+10	0
M1+11	0
M1+12	0
M1+13	0
M1+14	0
M1+15	0
M1+16	0
M1+17	0
M1+18	0
M1+19	0

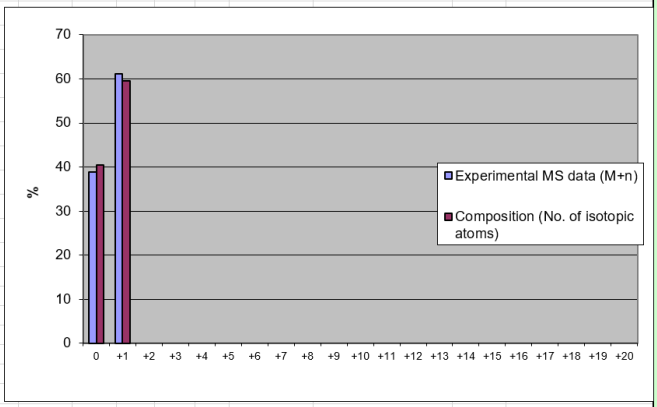
Analyte	Abundance
	68912
	108690.7
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0

Expected derivatives: 2 (Must be <2

Calculate

Labelled atoms 1

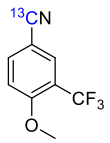
Atom% 59.5



Results

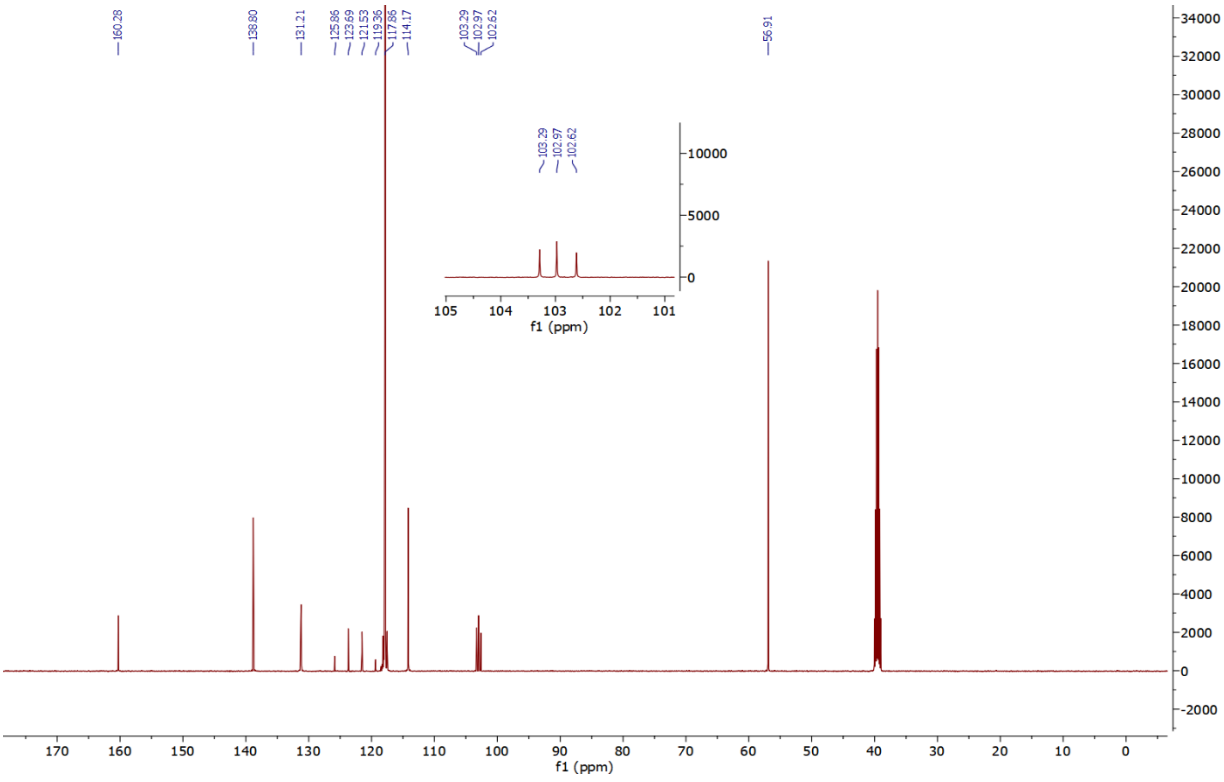
Relative amounts [%]

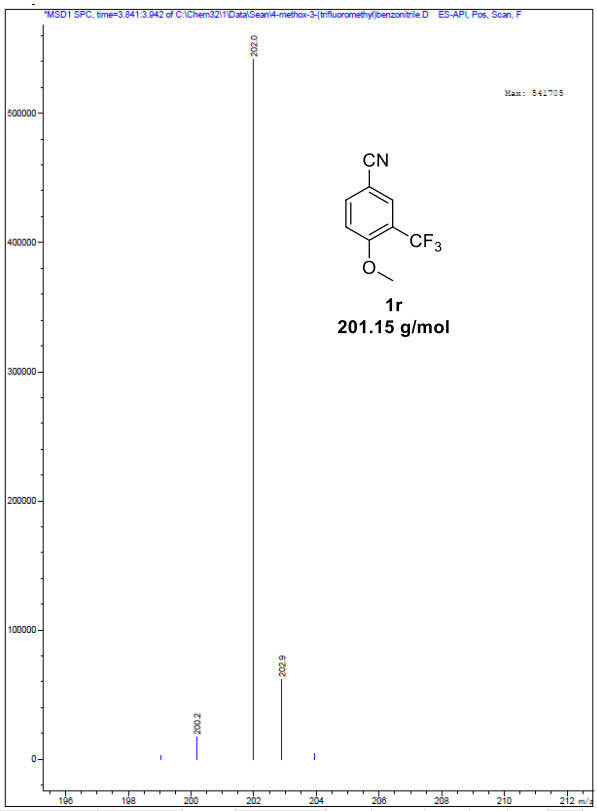
unlabeled	40.5
1-label	59.5

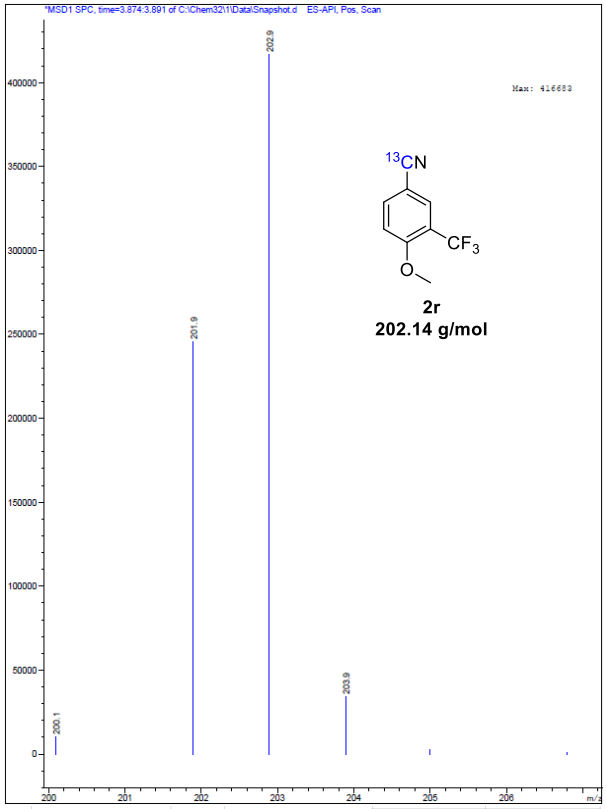

13CN
CF3
O

2r

8.14
8.14
8.13
8.12
7.46
7.44
3.99
2.00
1.06
3.19
f1 (ppm)


160.28
138.80
131.21
125.86
123.69
121.53
119.36
117.86
114.17
103.29
102.97
102.62
56.91
f1 (ppm)





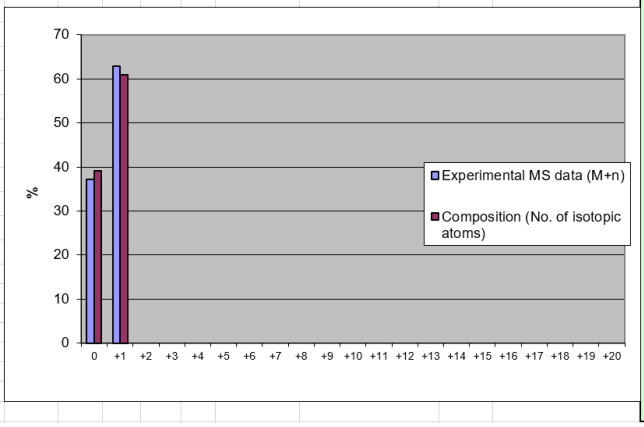
Unlabeled compound	Abundance	Analyte	Abundance
M1+0	541705		245861
M1+1	61570		416683
M1+2	0		0
M1+3	0		0
M1+4	0		0
M1+5	0		0
M1+6	0		0
M1+7	0		0
M1+8	0		0
M1+9	0		0
M1+10	0		0
M1+11	0		0
M1+12	0		0
M1+13	0		0
M1+14	0		0
M1+15	0		0
M1+16	0		0
M1+17	0		0
M1+18	0		0
M1+19	0		0

Expected derivatives: 2 (Must be <2

Labelled atoms 1

Atom% 60.9

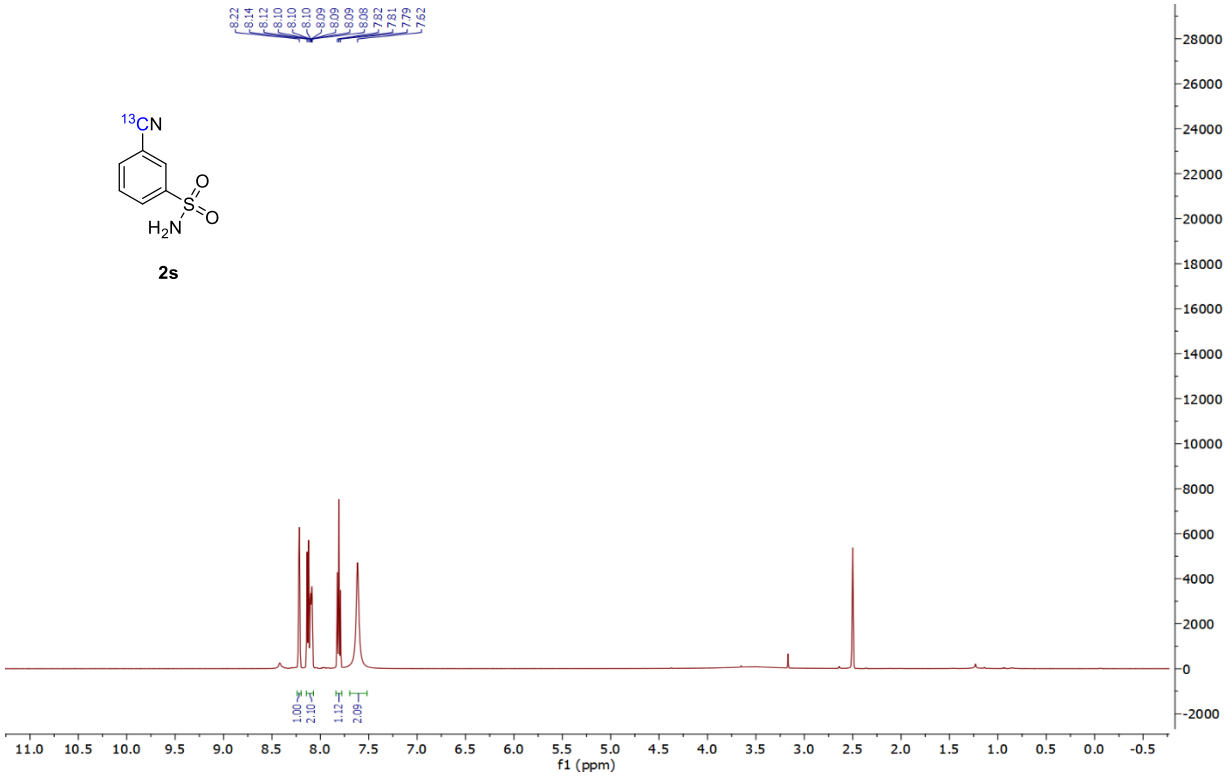
Calculate

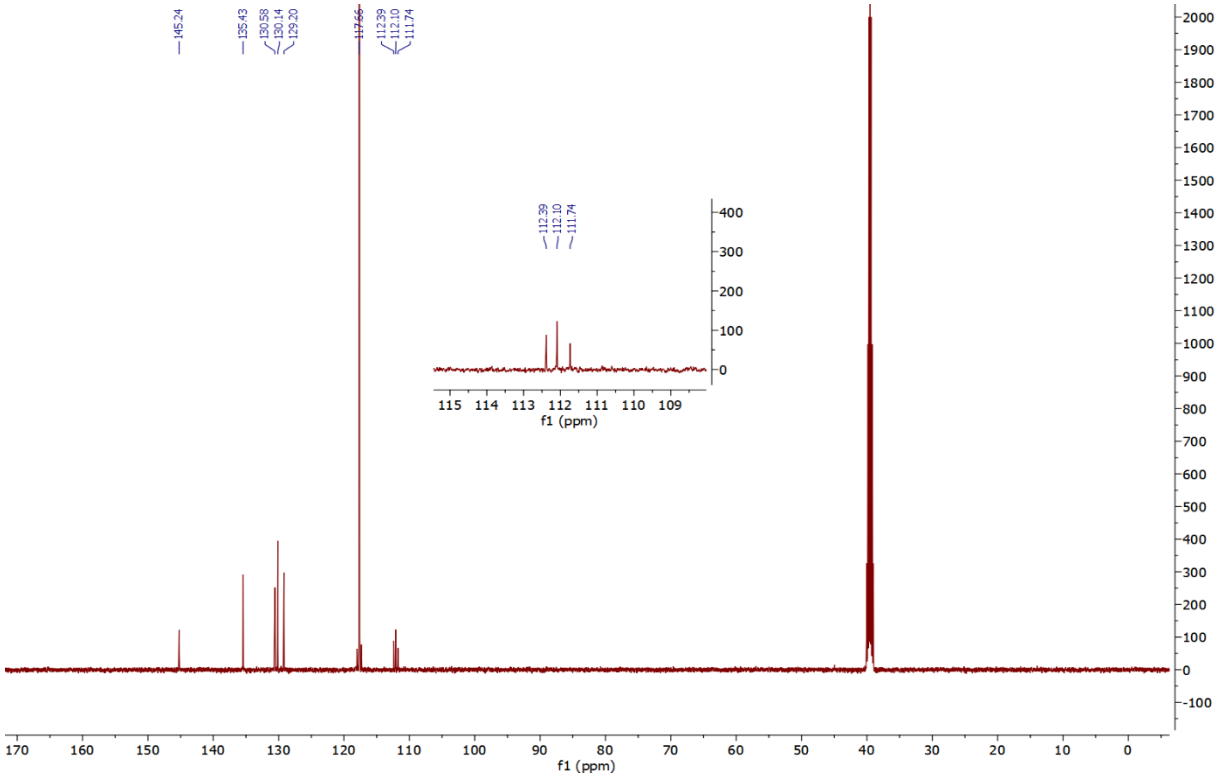


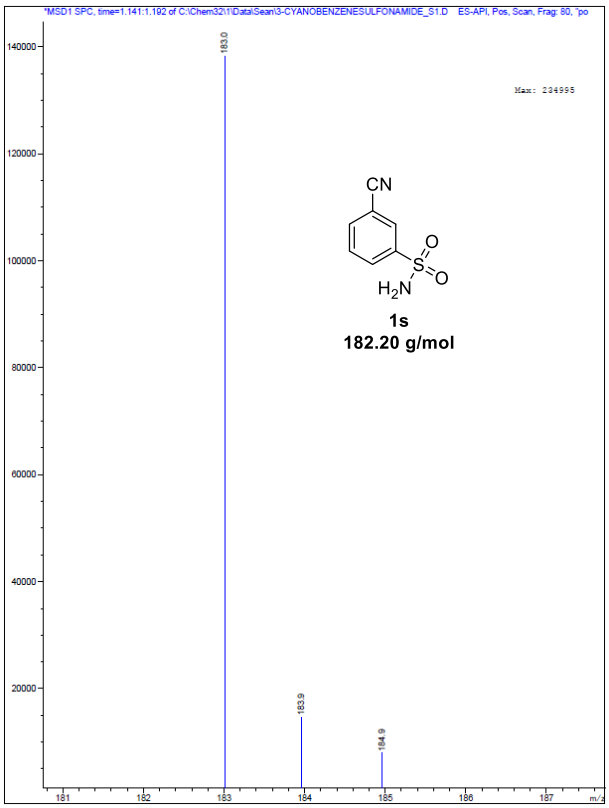
Results

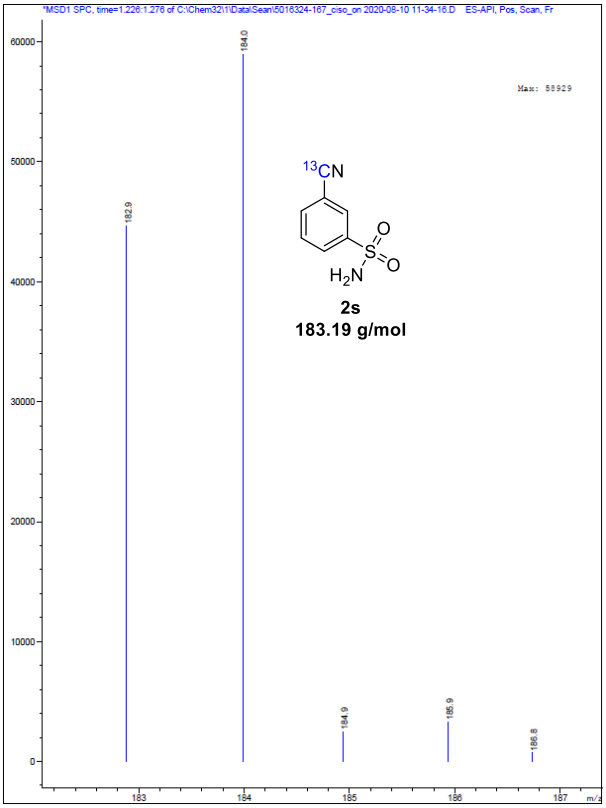
Relative amounts [%]

unlabeled	39.1
1-label	60.9


8.22
8.14
8.12
8.10
8.10
8.10
8.09
8.09
8.09
8.08
7.82
7.81
7.79
7.62
13CN
O
S
O
H2N
2s
1.00
2.10
1.12
2.09
f1 (ppm)


145.24
135.43
130.58
130.14
129.20
117.66
112.39
112.10
111.74
f1 (ppm)





Unlabeled compound	Abundance
M1+0	138168
M1+1	14624
M1+2	0
M1+3	0
M1+4	0
M1+5	0
M1+6	0
M1+7	0
M1+8	0
M1+9	0
M1+10	0
M1+11	0
M1+12	0
M1+13	0
M1+14	0
M1+15	0
M1+16	0
M1+17	0
M1+18	0
M1+19	0

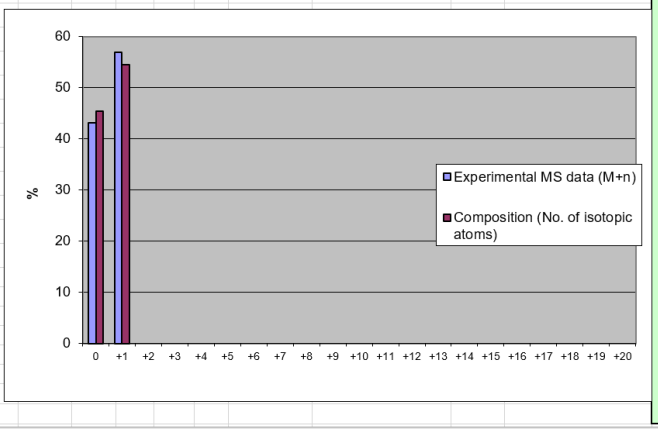
Analyte	Abundance
	44625
	58928.5
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0

Expected derivatives: 2 (Must be <2

Labelled atoms 1

Atom% 54.5

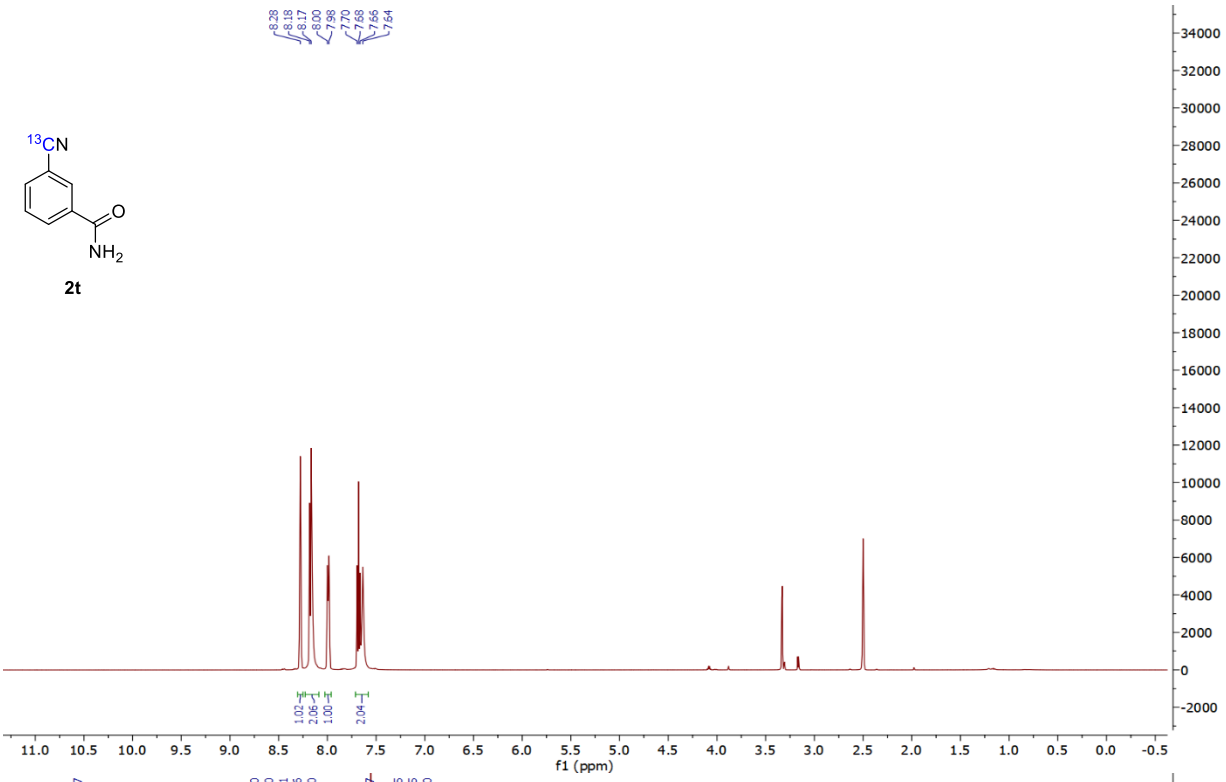
Calculate



Results

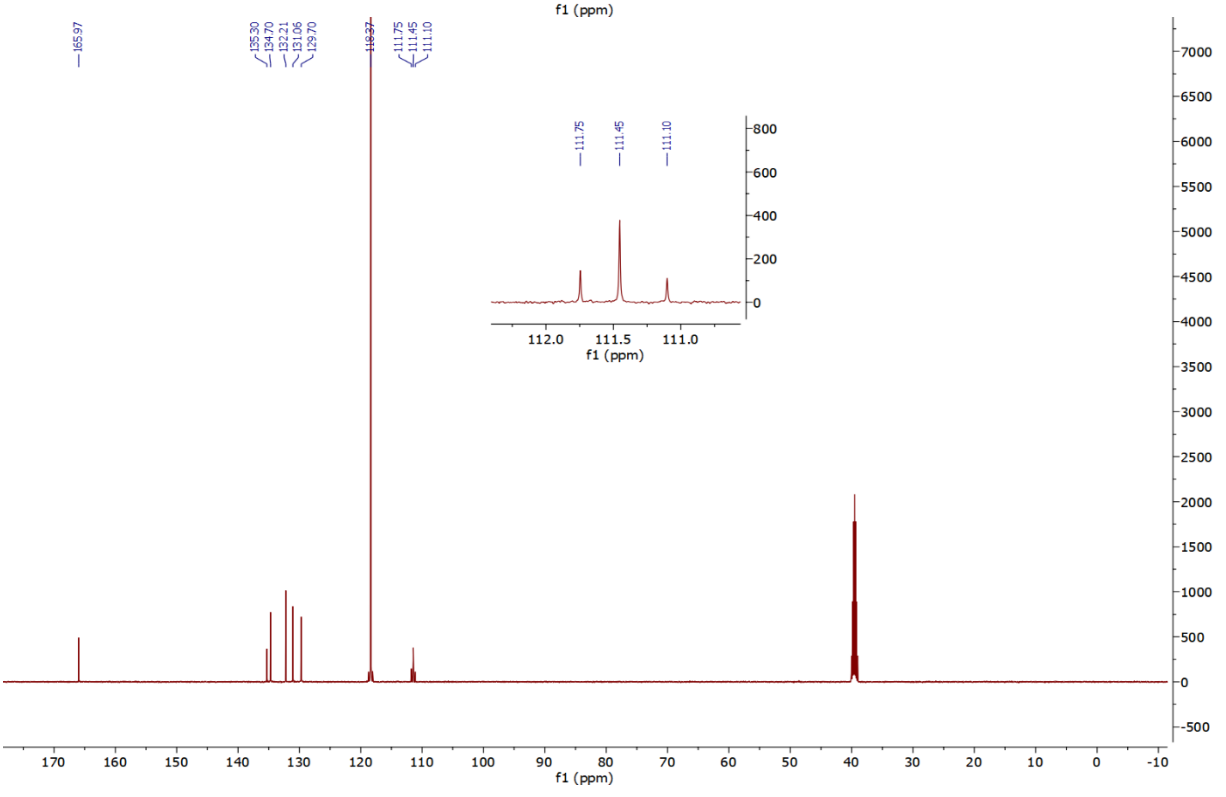
Relative amounts [%]

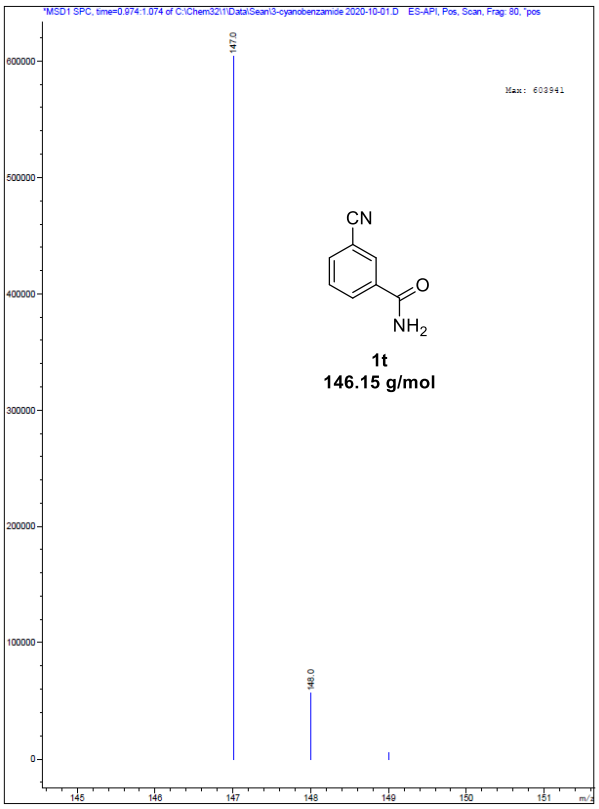
unlabeled	45.5
1-label	54.5

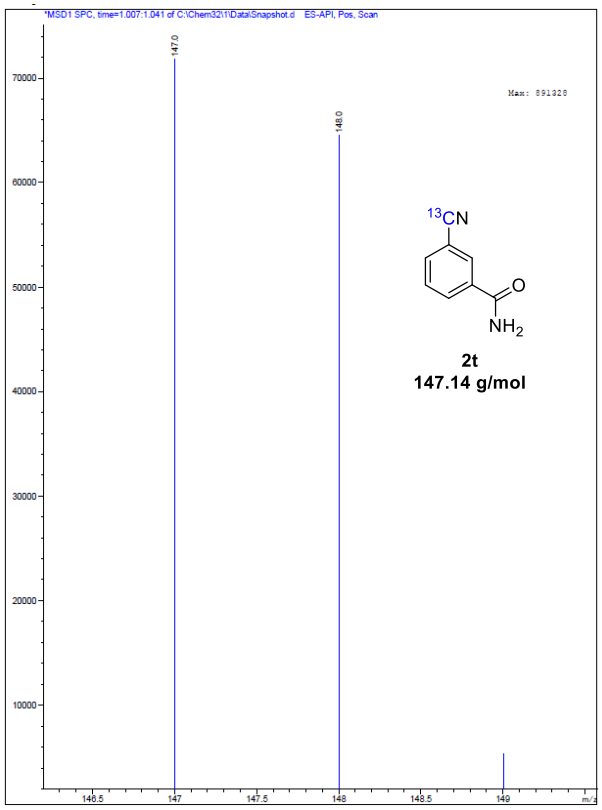

8.28
8.18
8.17
8.00
7.98
7.70
7.68
7.66
7.64
1.02
2.06
1.00
2.04
f1 (ppm)

13CN
O
NH2

2t


165.97
135.30
134.70
132.21
131.06
129.70
118.37
111.75
111.45
111.10
111.75
111.45
111.10
112.0
111.5
111.0
f1 (ppm)
f1 (ppm)





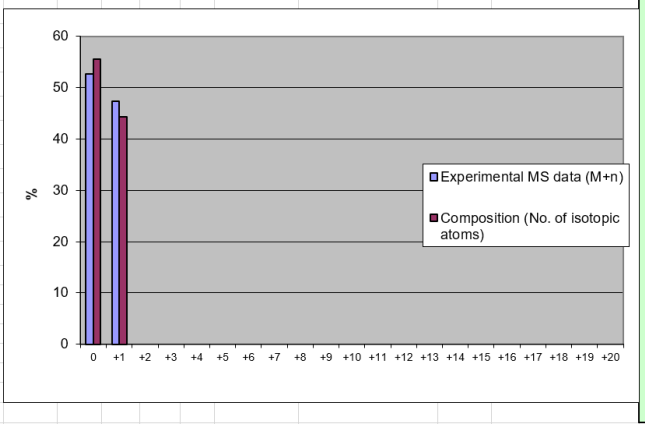
Unlabeled compound	Abundance	Analyte	Abundance
M1+0	603941		71792
M1+1	56406		64504
M1+2	0		0
M1+3	0		0
M1+4	0		0
M1+5	0		0
M1+6	0		0
M1+7	0		0
M1+8	0		0
M1+9	0		0
M1+10	0		0
M1+11	0		0
M1+12	0		0
M1+13	0		0
M1+14	0		0
M1+15	0		0
M1+16	0		0
M1+17	0		0
M1+18	0		0
M1+19	0		0

Expected derivatives: 2 (Must be <2

Labelled atoms 1

Atom% 44.4

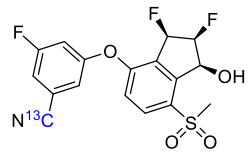
Calculate



Results

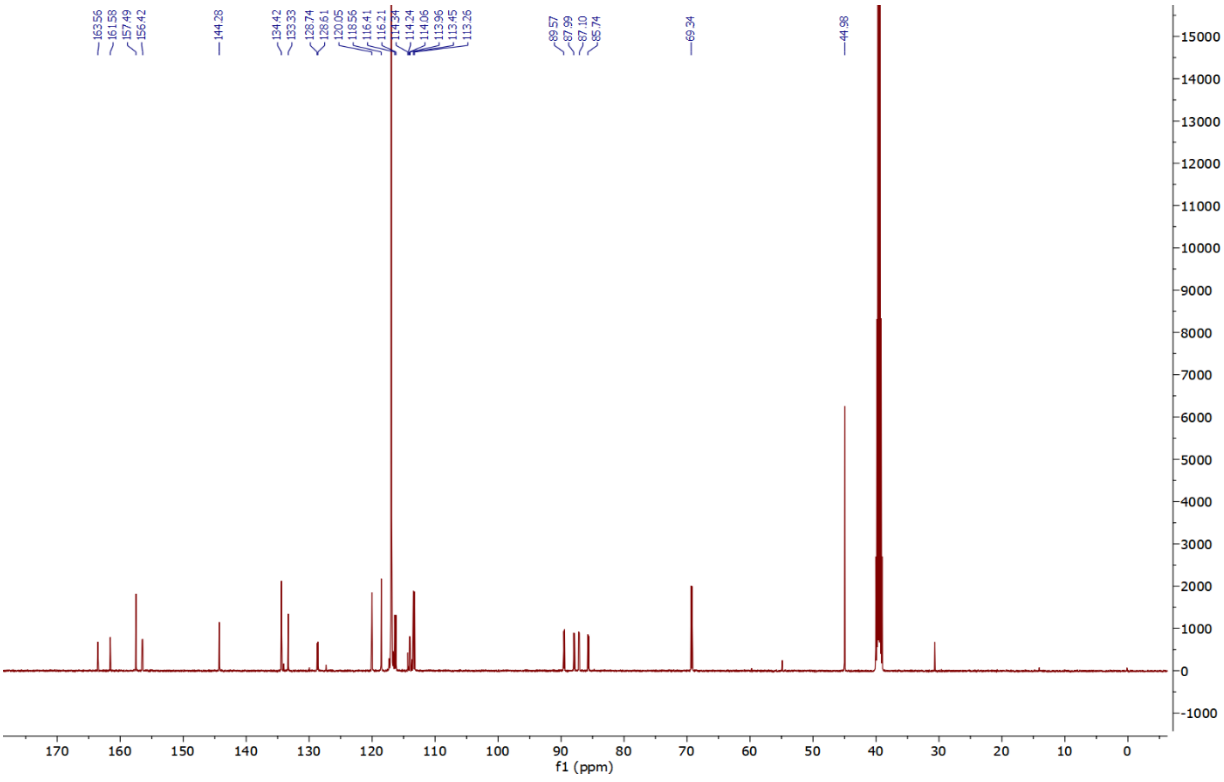
Relative amounts [%]

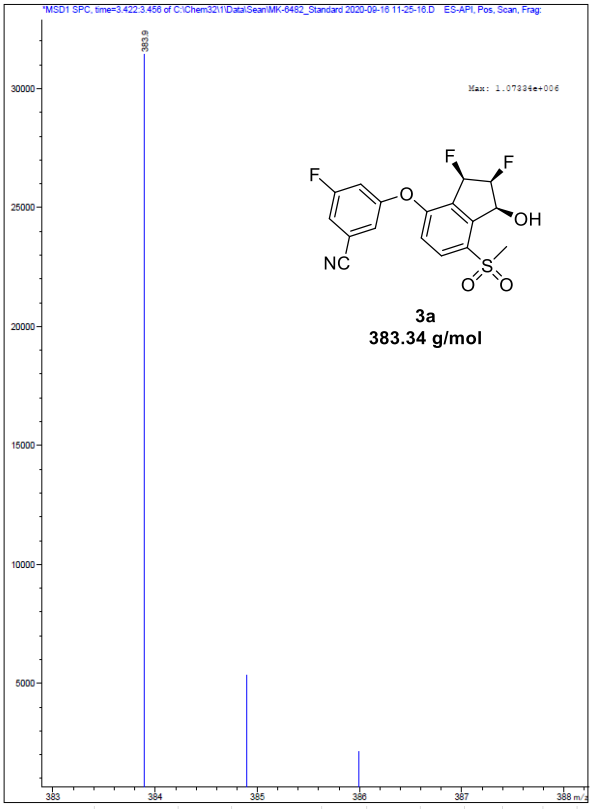
unlabeled	55.6
1-label	44.4


F
F
F
O
OH
N13C
S
O
O

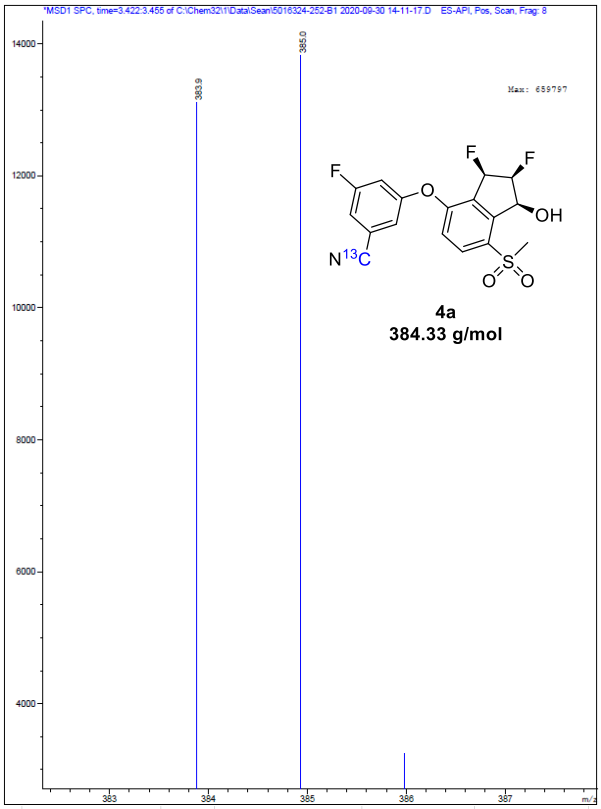
4a

8.04
8.02
7.81
7.79
7.76
7.59
7.57
7.26
7.24
6.19
6.18
6.04
6.03
5.93
5.92
5.60
5.27
5.26
5.25
5.24
5.23
5.22
5.18
5.17
5.16
5.14
5.13
5.12
3.36
1.04
1.03
1.00
1.04
1.06
1.08
1.09
1.07
1.10
3.09
f1 (ppm)


163.56
161.58
157.49
156.42
144.28
134.42
133.33
128.74
128.61
120.05
118.56
116.41
116.21
114.34
114.24
114.06
113.96
113.45
113.26
89.57
87.99
87.10
85.74
69.34
44.98
f1 (ppm)



3a
383.34 g/mol



4a
384.33 g/mol

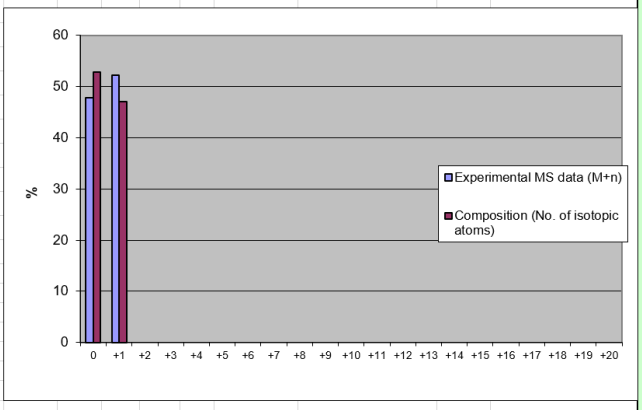
Unlabeled compound	Abundance	Analyte	Abundance
M1+0	31429		12056.5
M1+1	5354		13152
M1+2	0		0
M1+3	0		0
M1+4	0		0
M1+5	0		0
M1+6	0		0
M1+7	0		0
M1+8	0		0
M1+9	0		0
M1+10	0		0
M1+11	0		0
M1+12	0		0
M1+13	0		0
M1+14	0		0
M1+15	0		0
M1+16	0		0
M1+17	0		0
M1+18	0		0
M1+19	0		0

Expected derivatives: 2 (Must be <2

Calculate

Labelled atoms 1

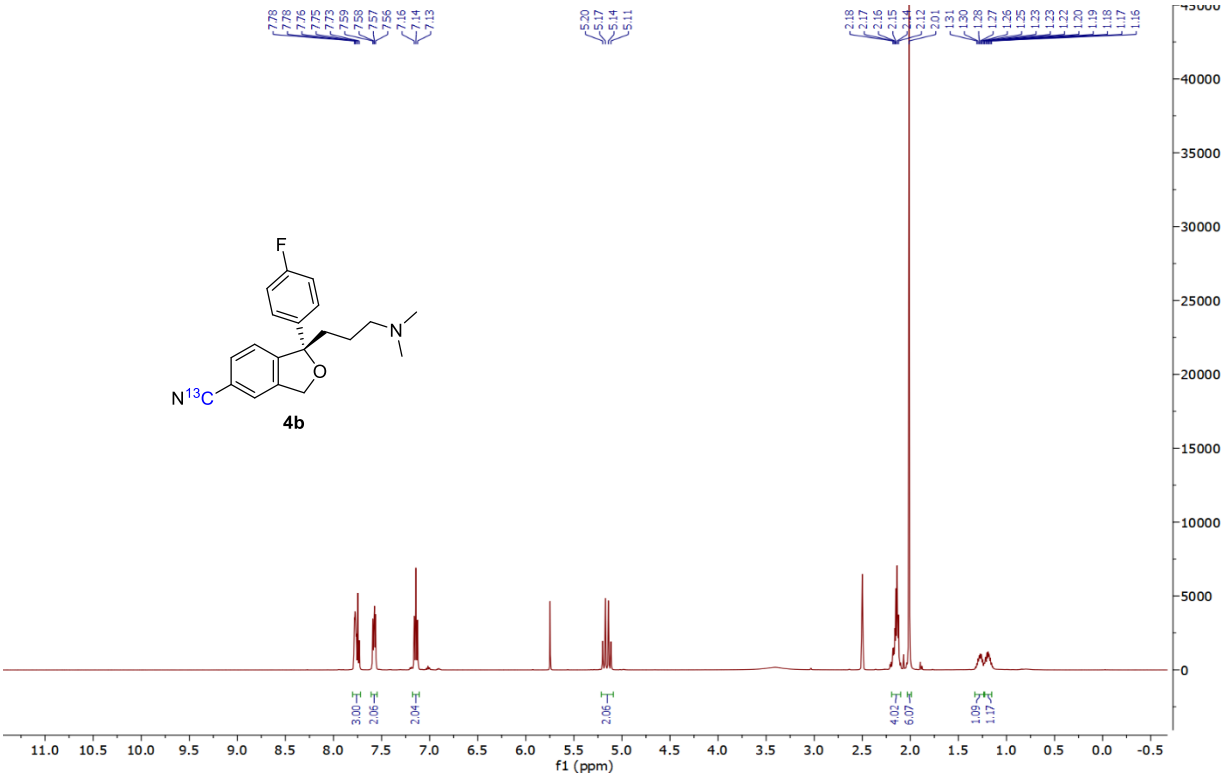
Atom% 47.1

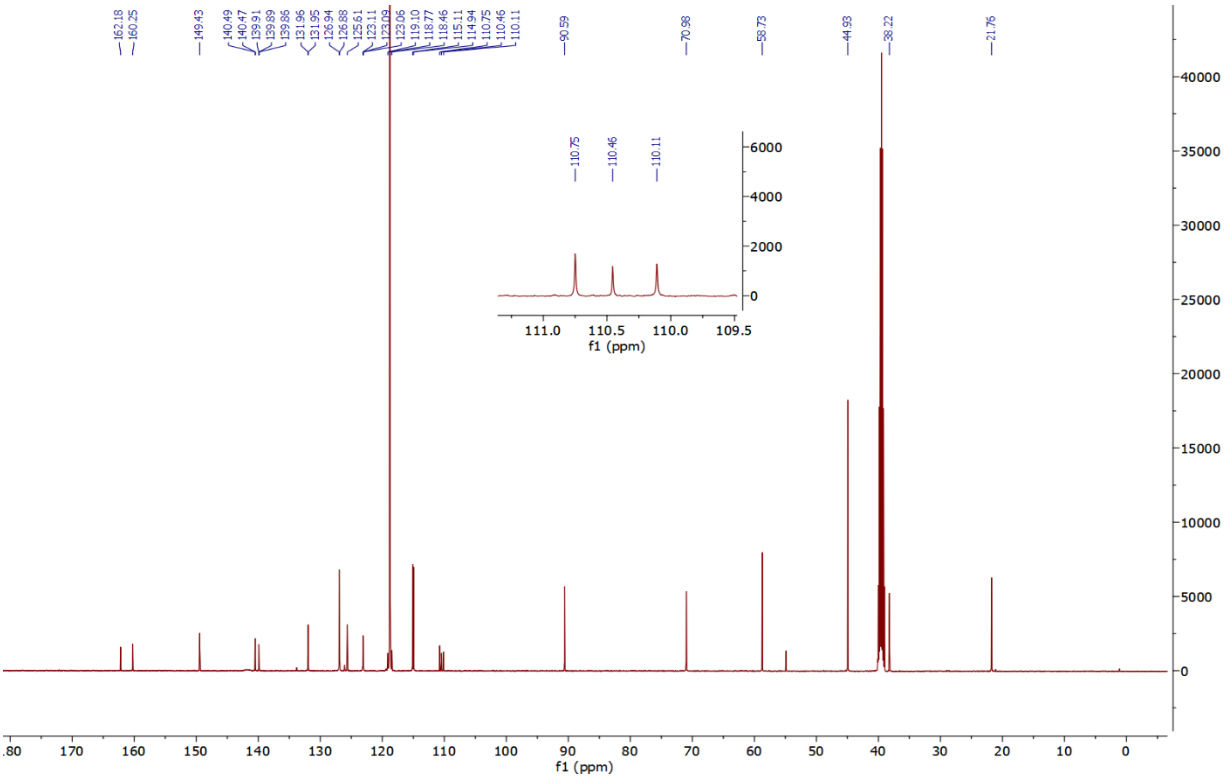


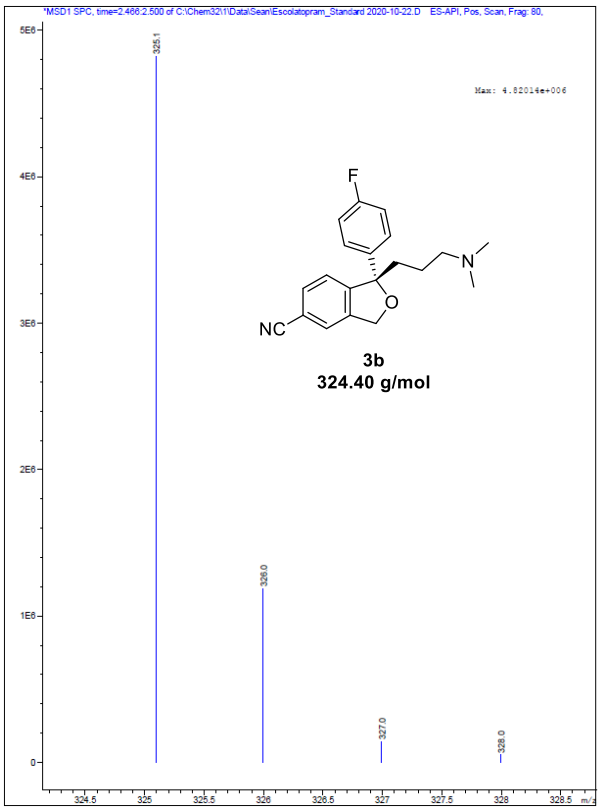
Results

Relative amounts [%]

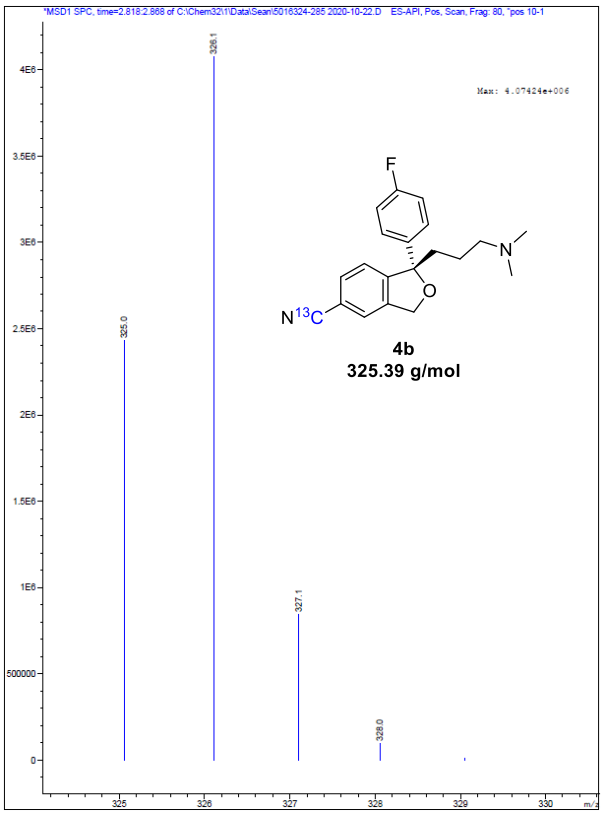
unlabeled	52.9
1-label	47.1
2-label	
3-label	
4-label	
5-label	
6-label	
…	
…	


F
N
O
N13C
4b
f1 (ppm)


f1 (ppm)



3b
324.40 g/mol



4b
325.39 g/mol

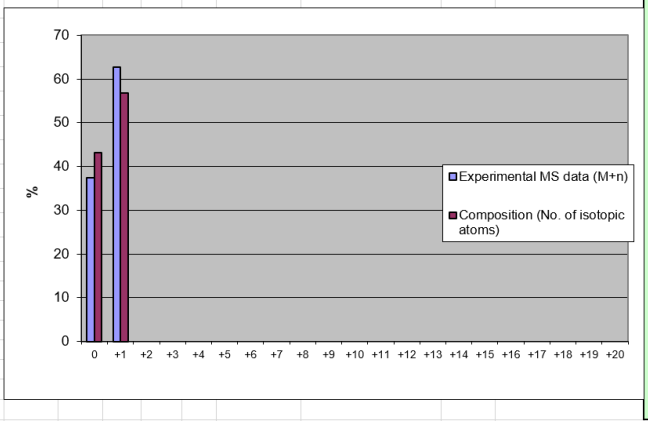
Unlabeled compound	Abundance	Analyte	Abundance
M1+0	4820139		2428928
M1+1	1184277		4074240
M1+2	0		0
M1+3	0		0
M1+4	0		0
M1+5	0		0
M1+6	0		0
M1+7	0		0
M1+8	0		0
M1+9	0		0
M1+10	0		0
M1+11	0		0
M1+12	0		0
M1+13	0		0
M1+14	0		0
M1+15	0		0
M1+16	0		0
M1+17	0		0
M1+18	0		0
M1+19	0		0

Expected derivatives: 2 (Must be <2

Labelled atoms 1

Atom% 56.9

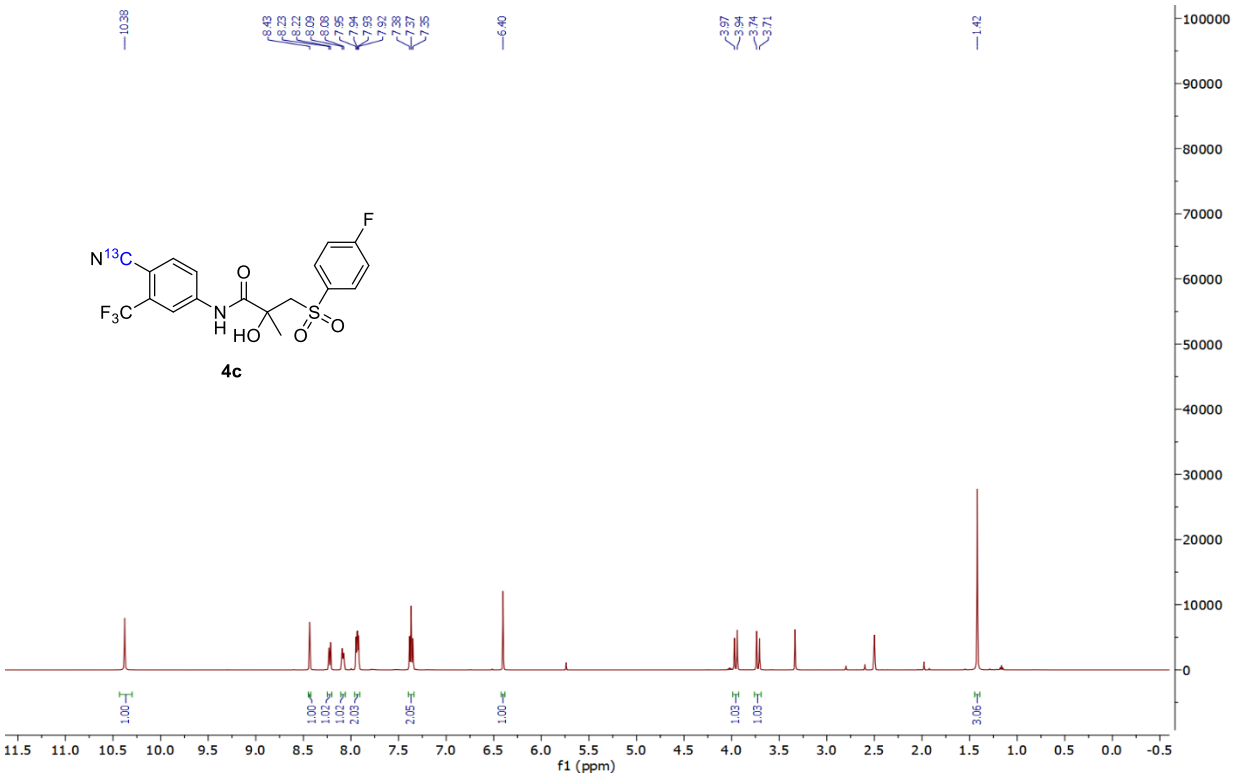
Calculate

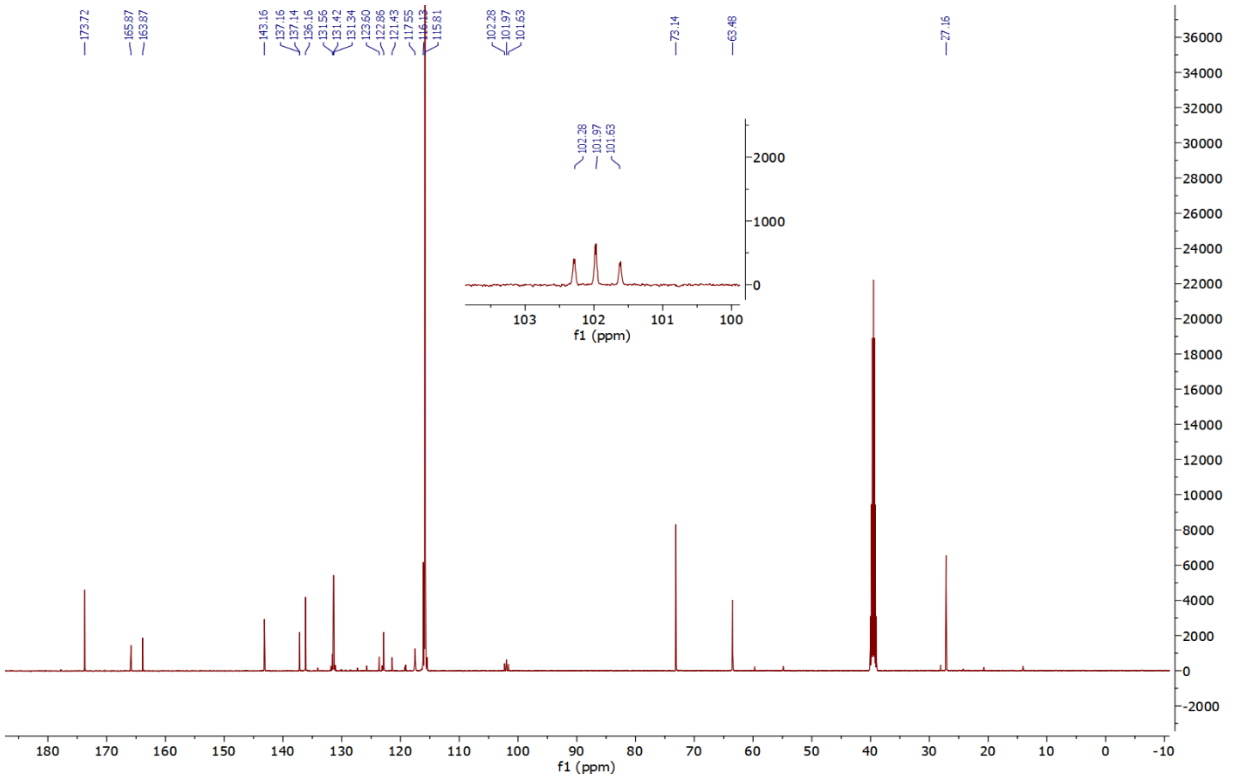


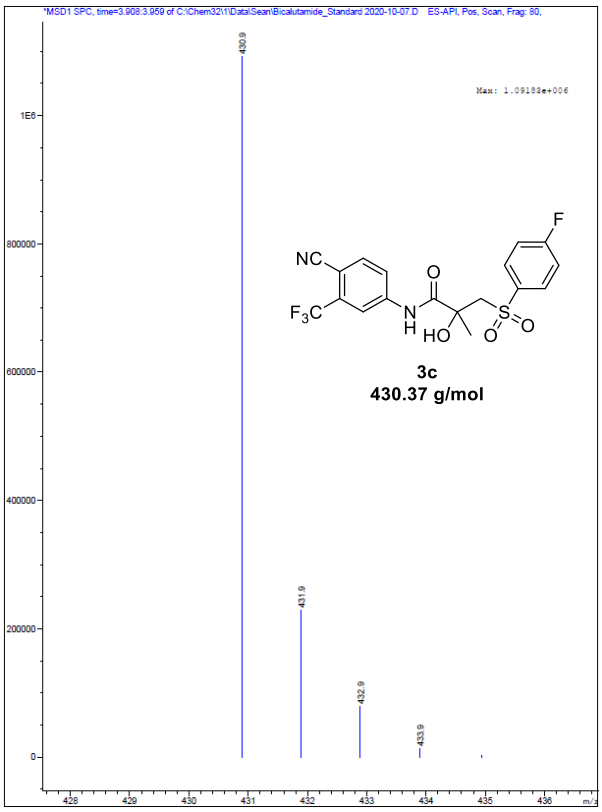
Results

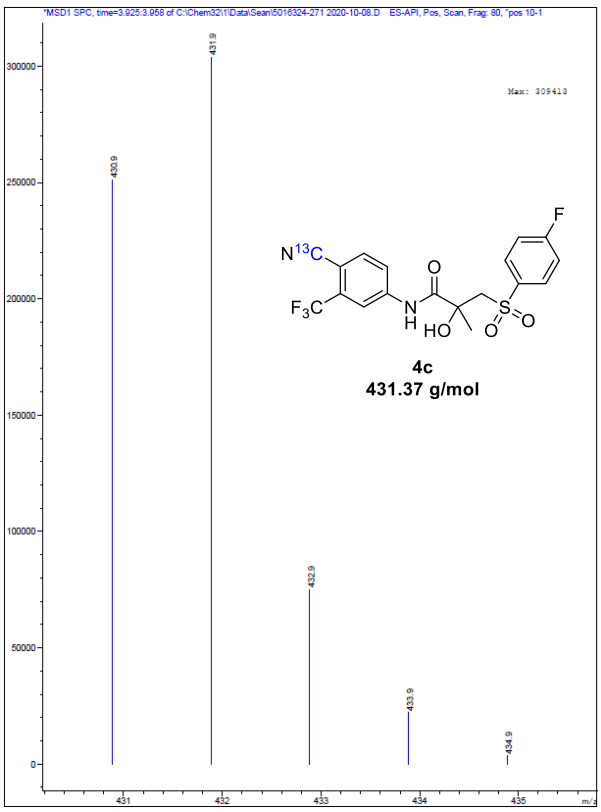
Relative amounts [%]

unlabeled	43.1
1-label	56.9
2-label	
3-label	
4-label	
5-label	
6-label	
…	
…	


10.38
8.43
8.23
8.22
8.09
8.08
7.95
7.94
7.93
7.92
7.38
7.37
7.35
6.40
3.97
3.94
3.74
3.71
1.42
F
N13C
O
F3C
N
H
HO
S
O
O
4c
f1 (ppm)


173.72
165.87
163.87
143.16
137.16
137.14
136.16
131.56
131.42
131.34
123.60
122.86
121.43
117.55
116.13
115.81
102.28
101.97
101.63
73.14
63.48
27.16
f1 (ppm)





Unlabeled compound	Abundance
M1+0	1092032
M1+1	229232
M1+2	0
M1+3	0
M1+4	0
M1+5	0
M1+6	0
M1+7	0
M1+8	0
M1+9	0
M1+10	0
M1+11	0
M1+12	0
M1+13	0
M1+14	0
M1+15	0
M1+16	0
M1+17	0
M1+18	0
M1+19	0

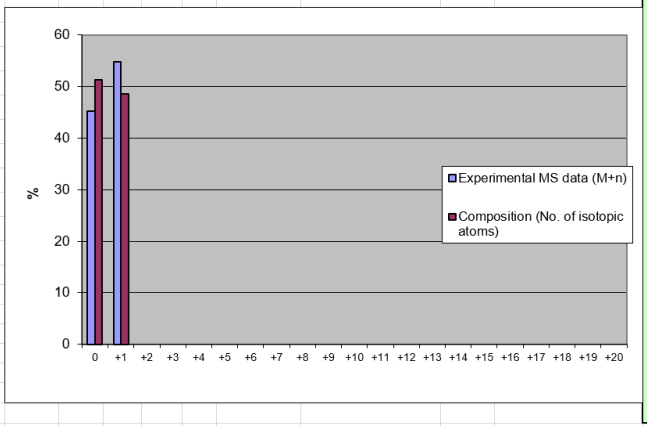
Analyte	Abundance
	250926.3
	303688
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0

Expected derivatives: 2 (Must be <2

Calculate

Labelled atoms 1

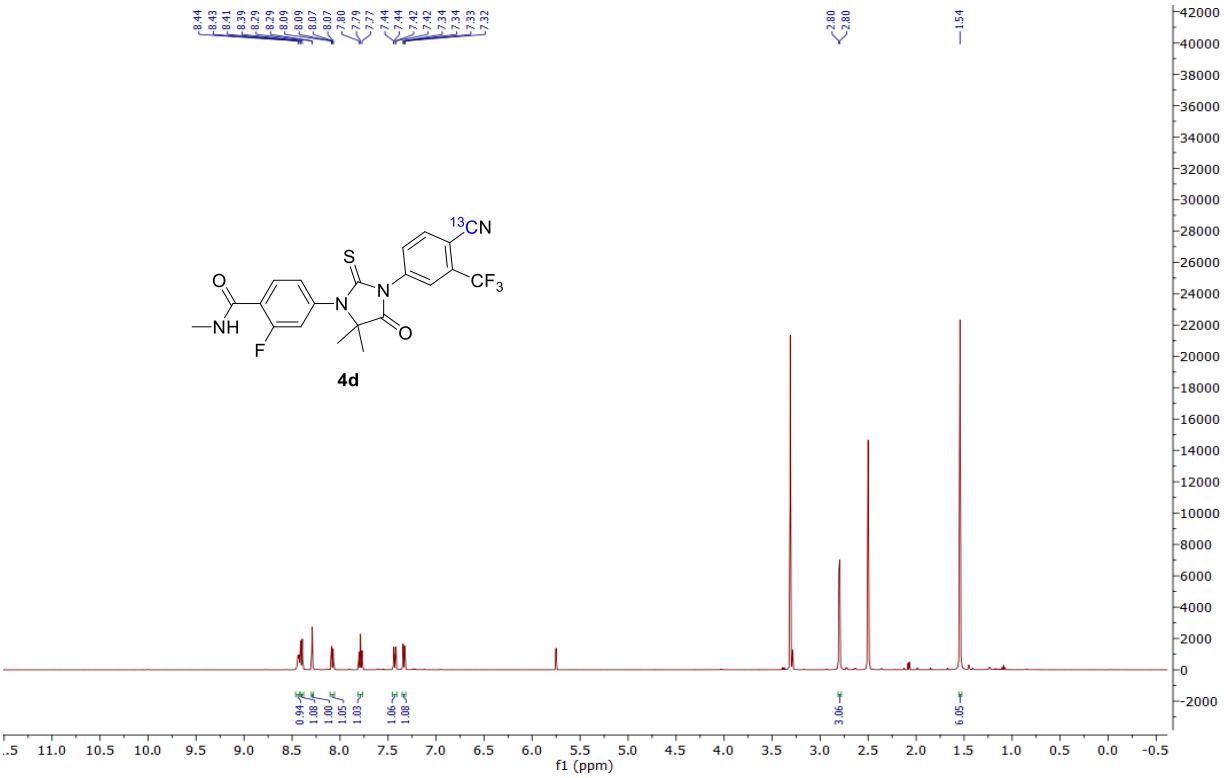
Atom% 48.7



Results

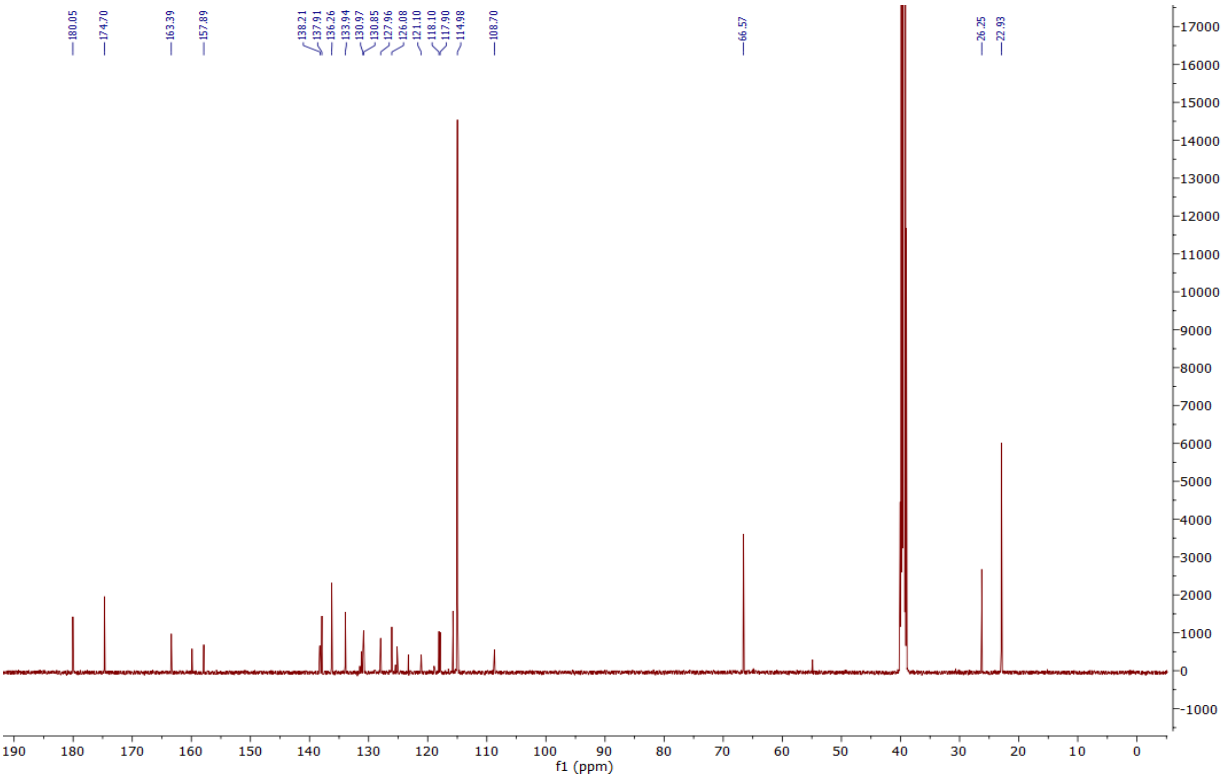
Relative amounts [%]

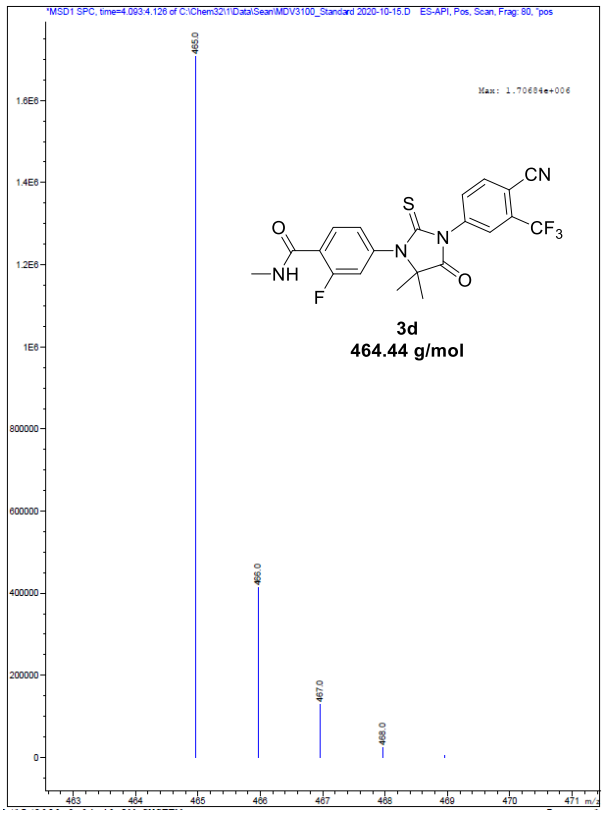
unlabeled	51.3
1-label	48.7
2-label	
3-label	
4-label	
5-label	
6-label	
…	
…	

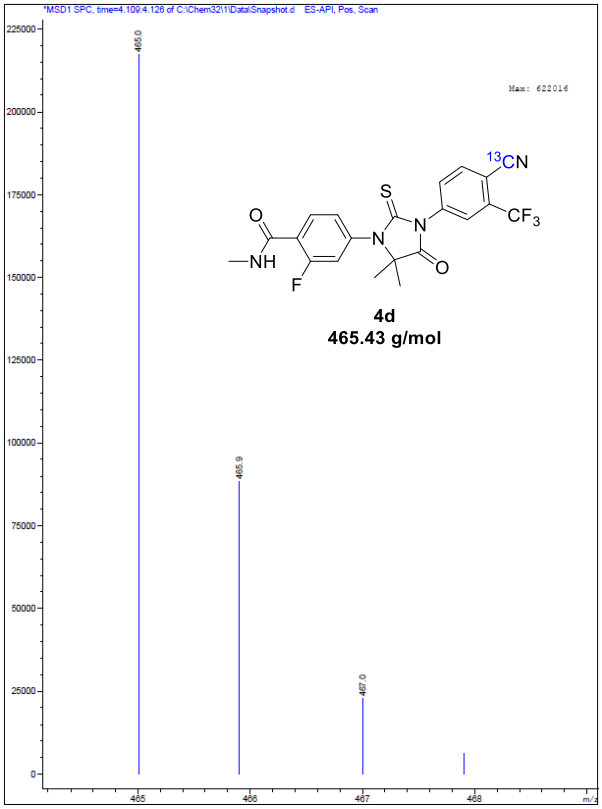

8.44
8.43
8.41
8.39
8.29
8.29
8.09
8.09
8.07
8.07
7.80
7.79
7.77
7.44
7.44
7.42
7.42
7.34
7.34
7.33
7.32
2.80
2.80
1.54
0.94
1.08
1.00
1.05
1.03
1.06
1.08
3.06
6.05
f1 (ppm)

13CN
S
O
N
N
CF3
NH
F
O

4d


180.05
174.70
163.39
157.89
138.21
137.91
136.26
133.94
130.97
130.85
127.96
126.08
121.10
118.10
117.90
114.98
108.70
66.57
26.25
22.93
f1 (ppm)





Unlabeled compound	Abundance
M1+0	1706837
M1+1	412416
M1+2	0
M1+3	0
M1+4	0
M1+5	0
M1+6	0
M1+7	0
M1+8	0
M1+9	0
M1+10	0
M1+11	0
M1+12	0
M1+13	0
M1+14	0
M1+15	0
M1+16	0
M1+17	0
M1+18	0
M1+19	0

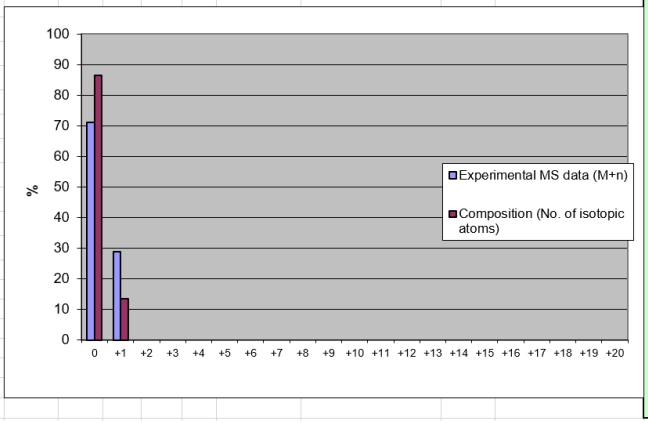
Analyte	Abundance
	217248
	88440
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0

Expected derivatives: 2 (Must be <2

Calculate

Labelled atoms 1

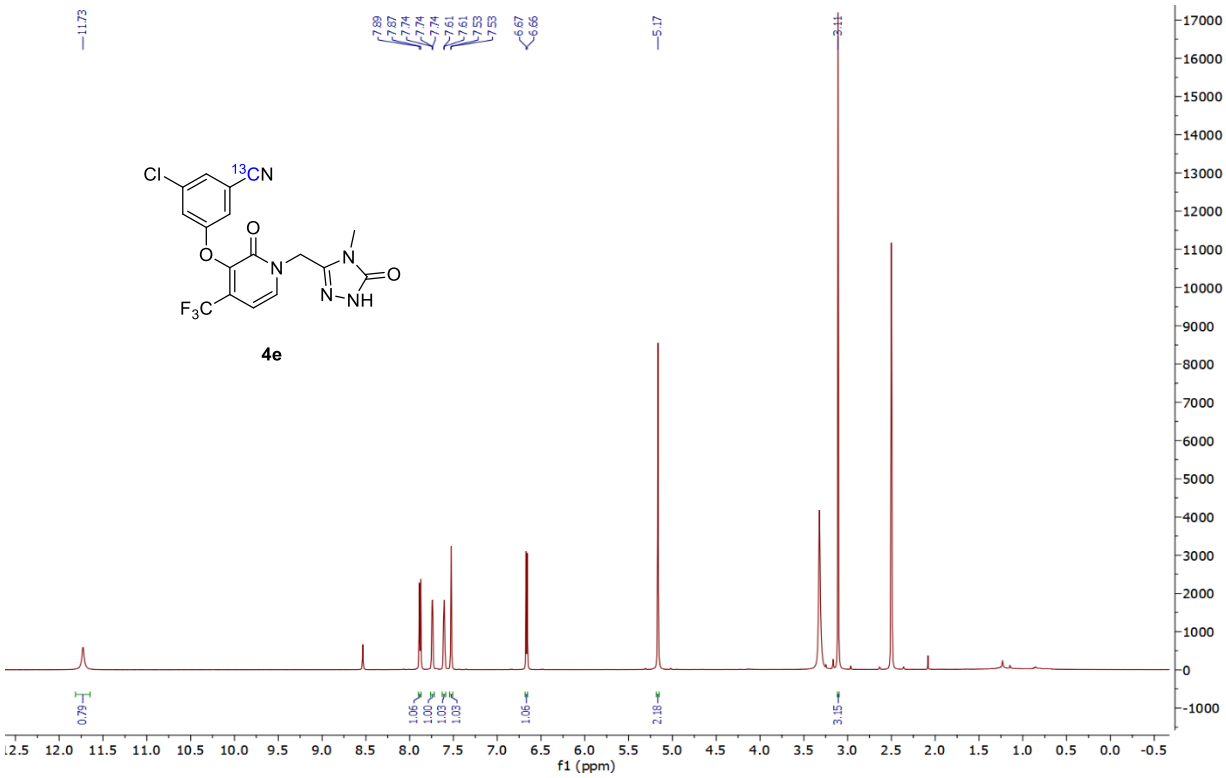
Atom% 13.5



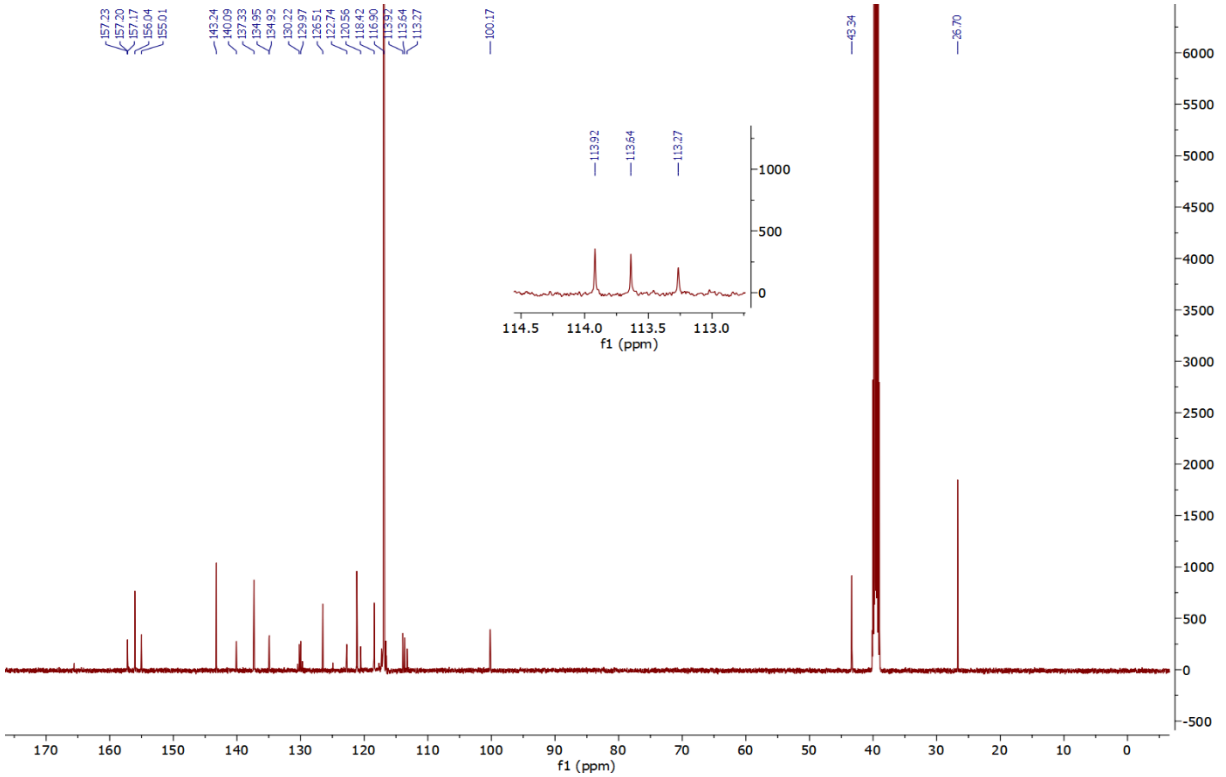
Results

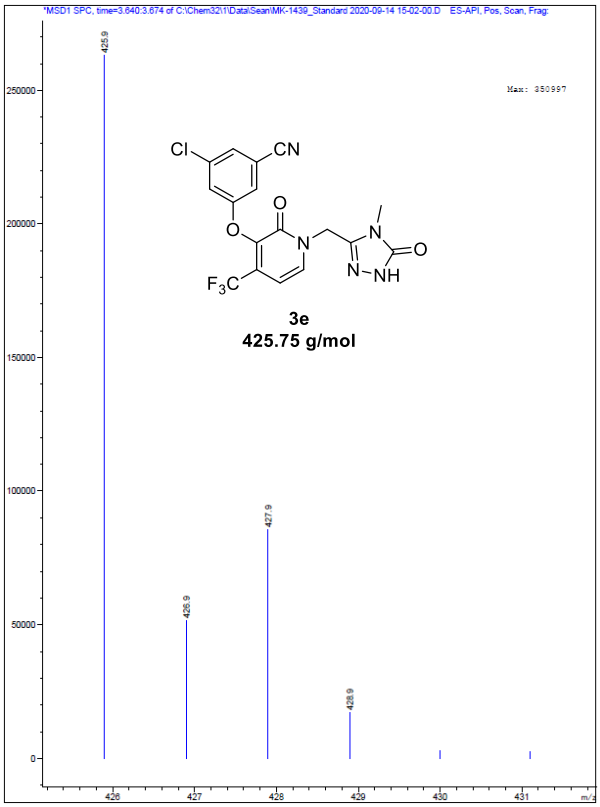
Relative amounts [%]

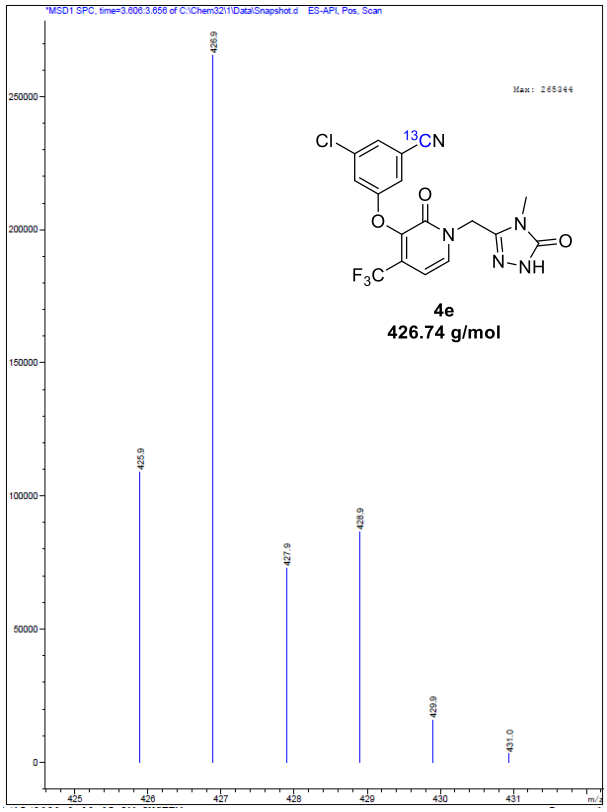
unlabeled	86.5
1-label	13.5
2-label	
3-label	
4-label	
5-label	
6-label	
…	
…	


11.73
7.89
7.87
7.74
7.74
7.74
7.61
7.61
7.53
7.53
6.67
6.66
5.17
3.11
Cl
13CN
O
O
N
N
N
O
N-NH
F3C
0.79
1.06
1.00
1.03
1.03
1.06
2.18
3.15
f1 (ppm)

4e


157.23
157.20
157.17
156.04
155.01
143.24
140.09
137.33
134.95
134.92
130.22
129.97
125.51
122.74
120.56
118.42
116.90
113.92
113.64
113.27
100.17
43.34
26.70
113.92
113.64
113.27
f1 (ppm)
f1 (ppm)





Unlabeled compound	Abundance
M1+0	262976
M1+1	51611
M1+2	0
M1+3	0
M1+4	0
M1+5	0
M1+6	0
M1+7	0
M1+8	0
M1+9	0
M1+10	0
M1+11	0
M1+12	0
M1+13	0
M1+14	0
M1+15	0
M1+16	0
M1+17	0
M1+18	0
M1+19	0

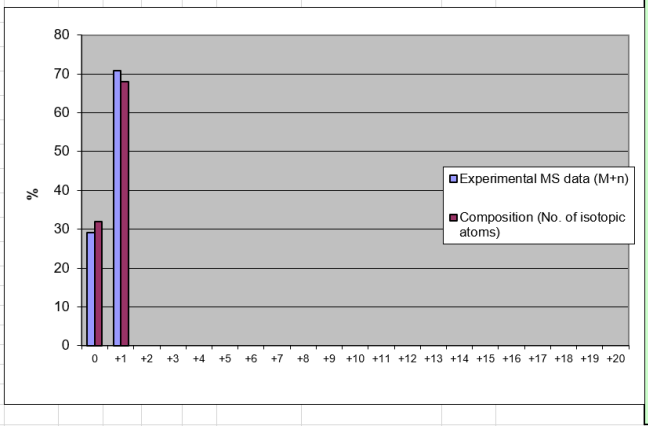
Analyte	Abundance
	108844
	265344
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0

Expected derivatives: 2 (Must be <2

Labelled atoms 1

Atom% 68.0

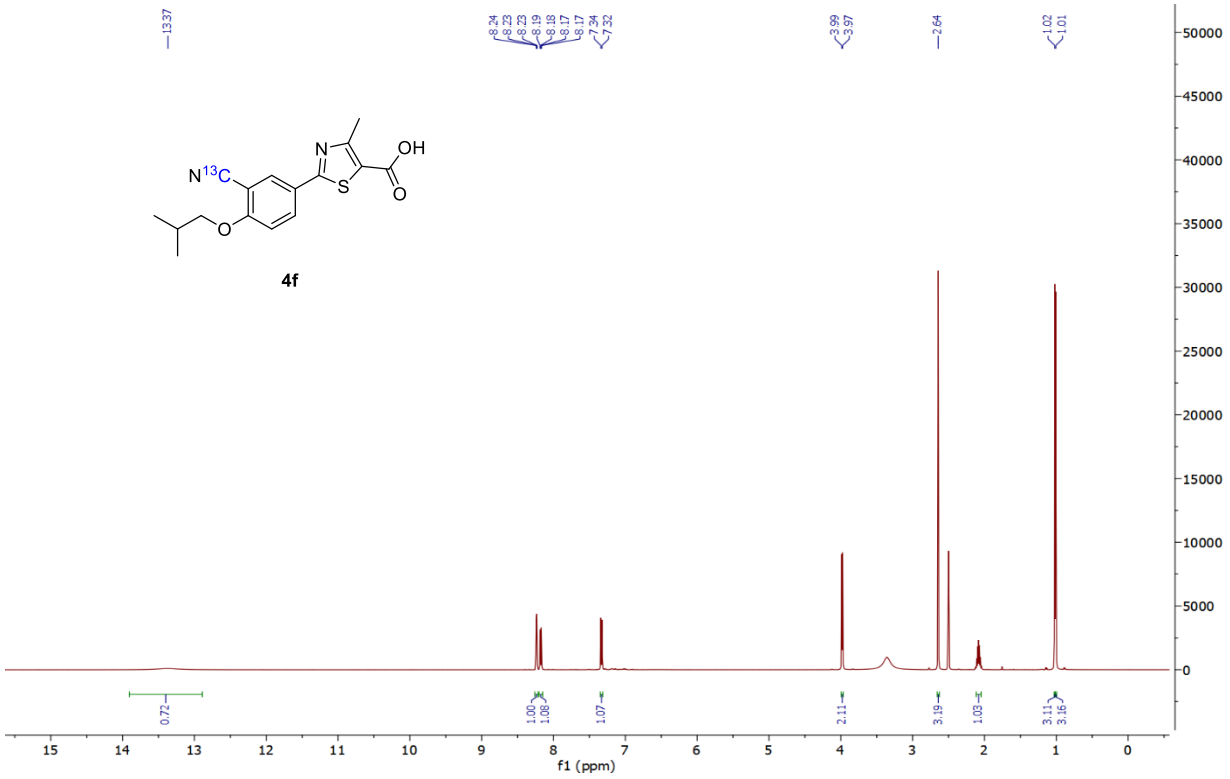
Calculate



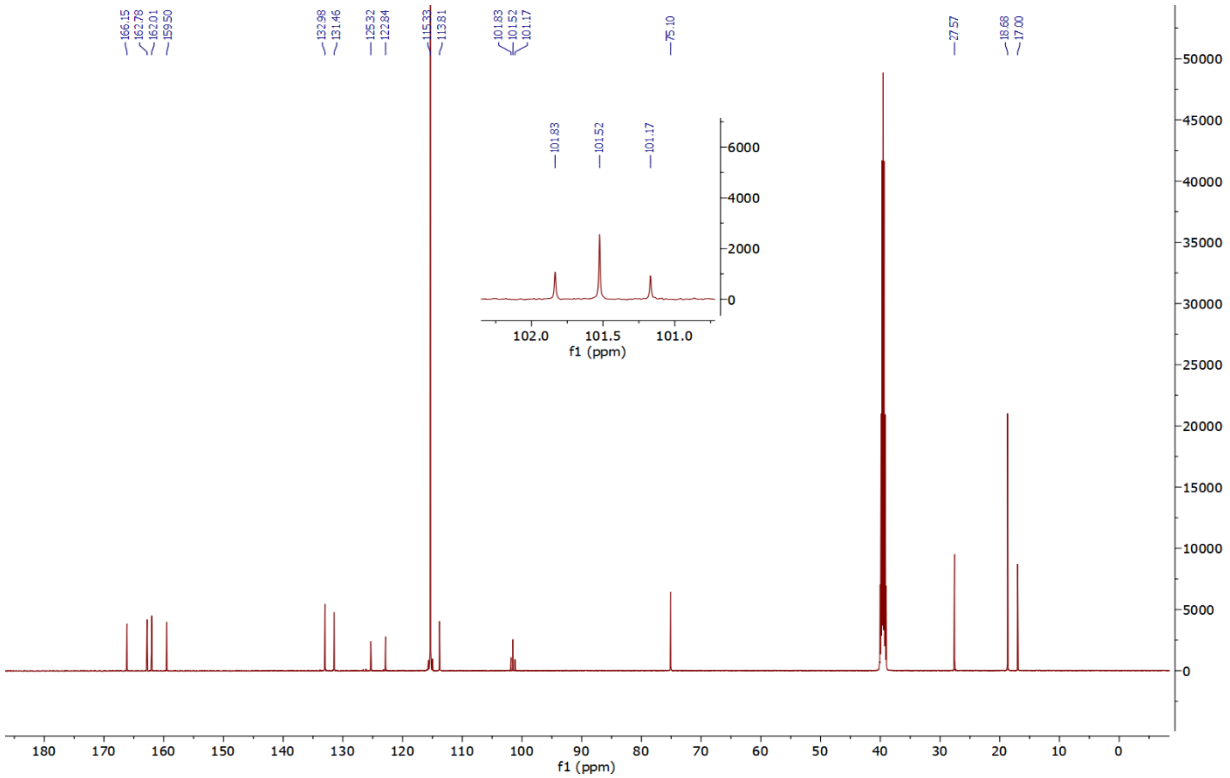
Results

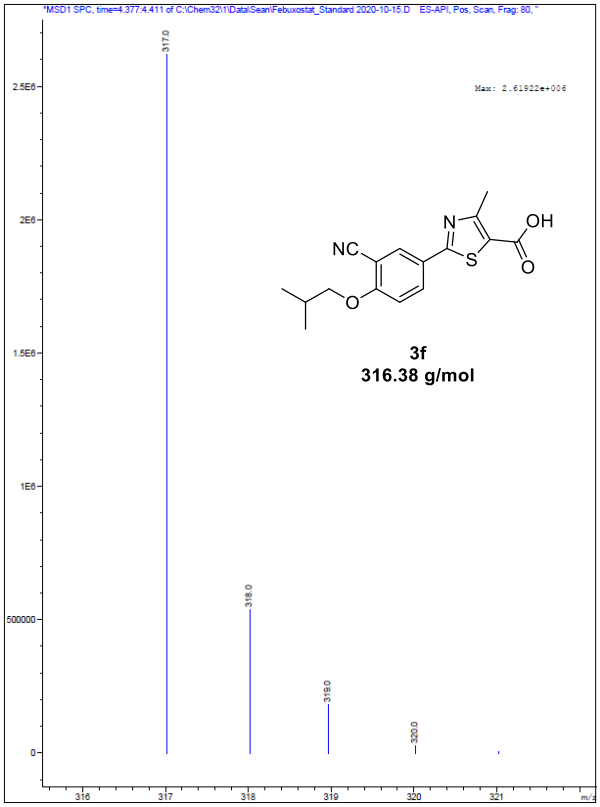
Relative amounts [%]

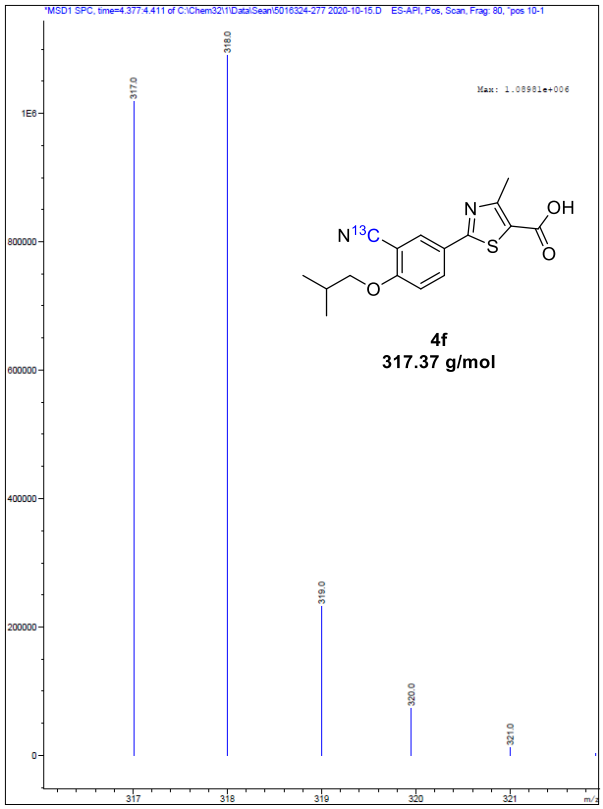
unlabeled	32.0
1-label	68.0
2-label	
3-label	
4-label	
5-label	
6-label	
…	
…	


13.37
8.24
8.23
8.23
8.19
8.18
8.17
8.17
7.34
7.32
3.99
3.97
2.64
1.02
1.01
OH
N
S
O
O
N13C
0.72
1.00
1.08
1.07
2.11
3.19
1.03
3.11
3.16
f1 (ppm)

4f


166.15
162.78
162.01
159.50
132.98
131.46
125.32
122.84
115.33
113.81
101.83
101.52
101.17
75.10
27.57
18.68
17.00
f1 (ppm)





Unlabeled compound	Abundance
M1+0	2619221
M1+1	538475
M1+2	0
M1+3	0
M1+4	0
M1+5	0
M1+6	0
M1+7	0
M1+8	0
M1+9	0
M1+10	0
M1+11	0
M1+12	0
M1+13	0
M1+14	0
M1+15	0
M1+16	0
M1+17	0
M1+18	0
M1+19	0

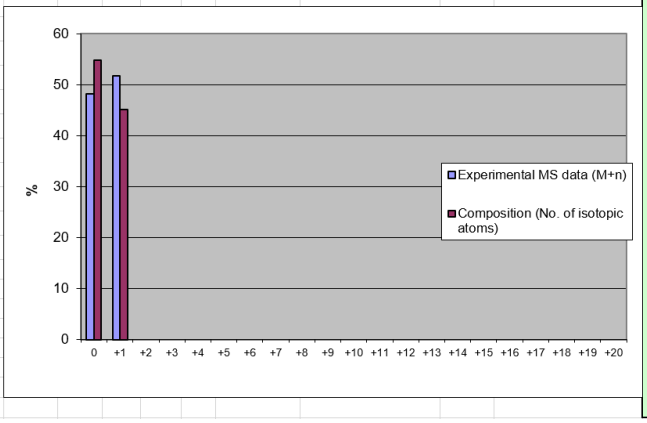
Analyte	Abundance
	1017835
	1089813
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0

Expected derivatives: 2 (Must be <2

Calculate

Labelled atoms 1

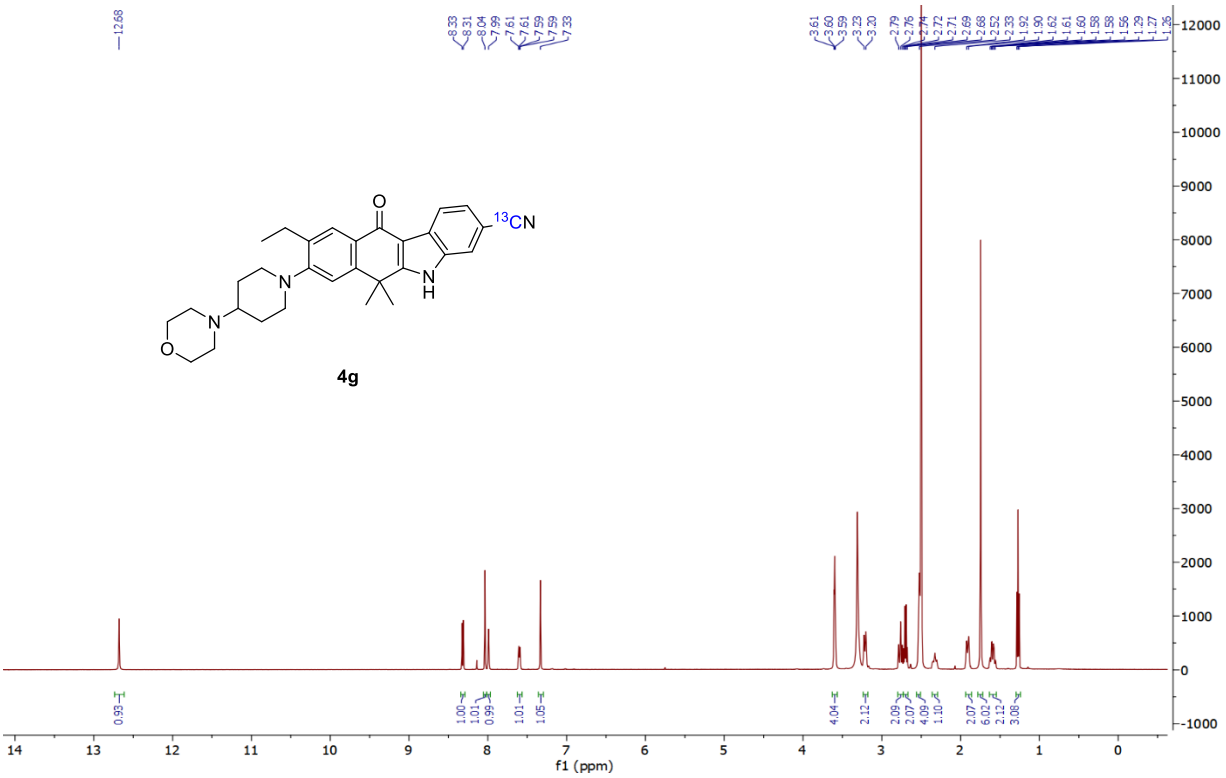
Atom% 45.1



Results

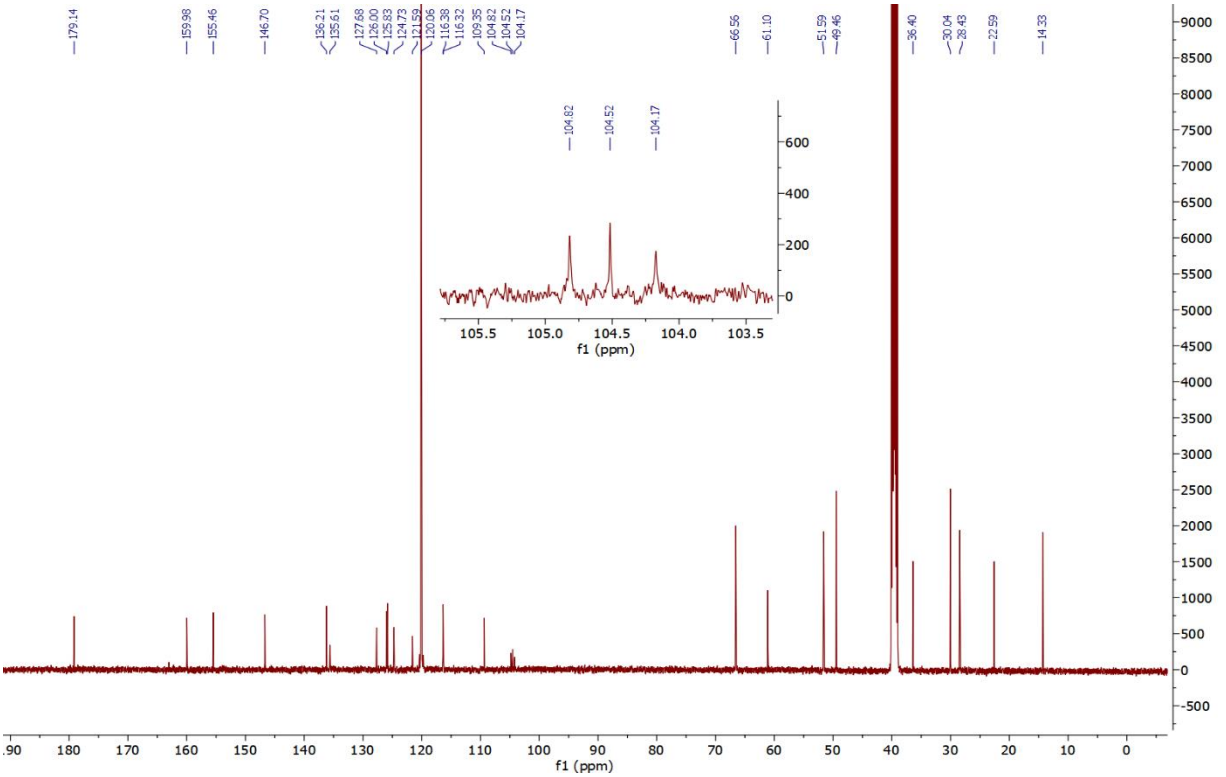
Relative amounts [%]

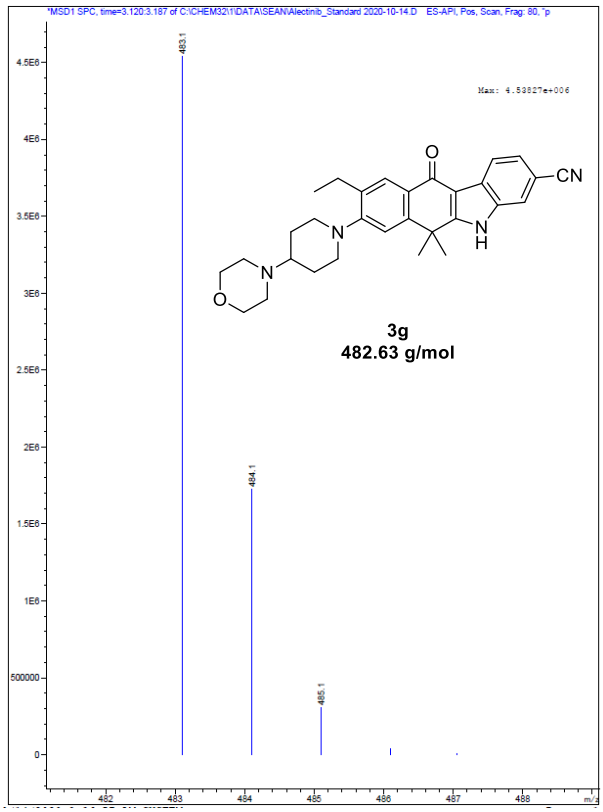
unlabeled	54.9
1-label	45.1
2-label	
3-label	
4-label	
5-label	
6-label	
…	
…	

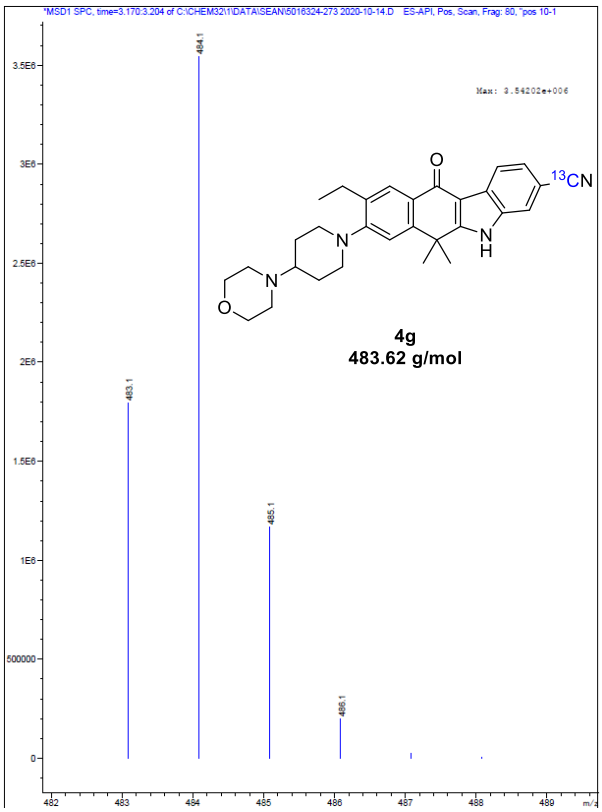

12.68
8.33
8.31
8.04
7.99
7.61
7.61
7.59
7.59
7.33
3.61
3.60
3.59
3.23
3.20
2.79
2.76
2.74
2.72
2.71
2.69
2.68
2.52
2.33
1.92
1.90
1.62
1.61
1.60
1.58
1.58
1.56
1.29
1.27
1.25
0.93
1.00
1.01
0.99
1.01
1.05
4.04
2.12
2.09
2.07
4.09
1.10
2.07
6.02
2.13
3.08
f1 (ppm)

O
13CN
N
N
H
N
O

4g


179.14
159.98
155.46
146.70
136.21
135.61
127.68
126.00
125.83
124.73
121.59
120.06
116.38
116.32
109.35
104.82
104.52
104.17
66.56
61.10
51.59
49.46
36.40
30.04
28.43
22.59
14.33
104.82
104.52
104.17
f1 (ppm)
f1 (ppm)





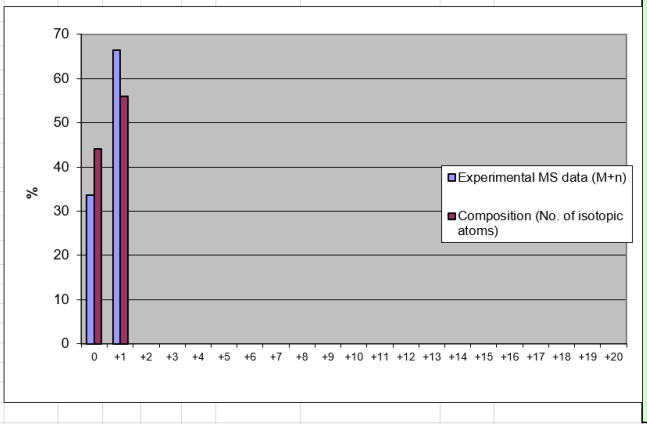
Unlabeled compound	Abundance	Analyte	Abundance
M1+0	4538266		1795925
M1+1	1729126		3542016
M1+2	0		0
M1+3	0		0
M1+4	0		0
M1+5	0		0
M1+6	0		0
M1+7	0		0
M1+8	0		0
M1+9	0		0
M1+10	0		0
M1+11	0		0
M1+12	0		0
M1+13	0		0
M1+14	0		0
M1+15	0		0
M1+16	0		0
M1+17	0		0
M1+18	0		0
M1+19	0		0

Expected derivatives: 2 (Must be <2

Calculate

Labelled atoms 1

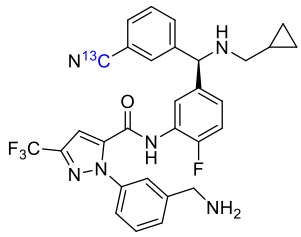
Atom% 55.9



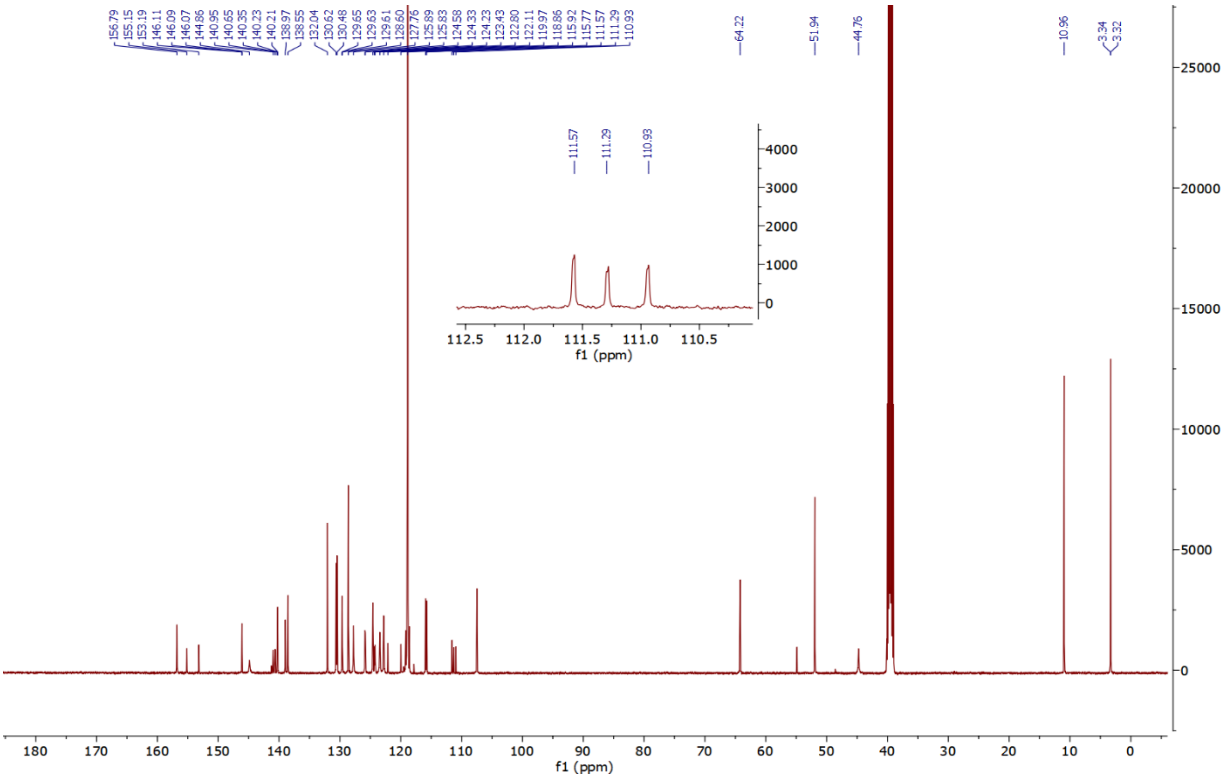
Results

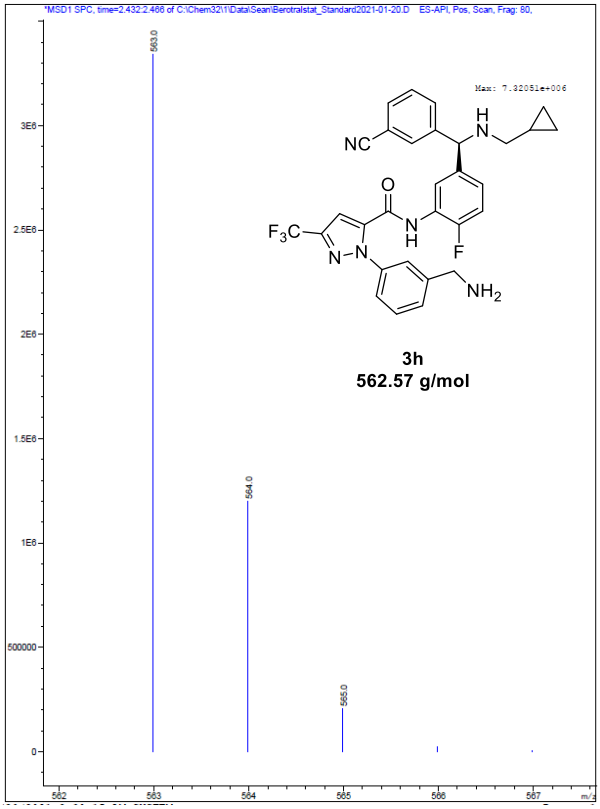
Relative amounts [%]

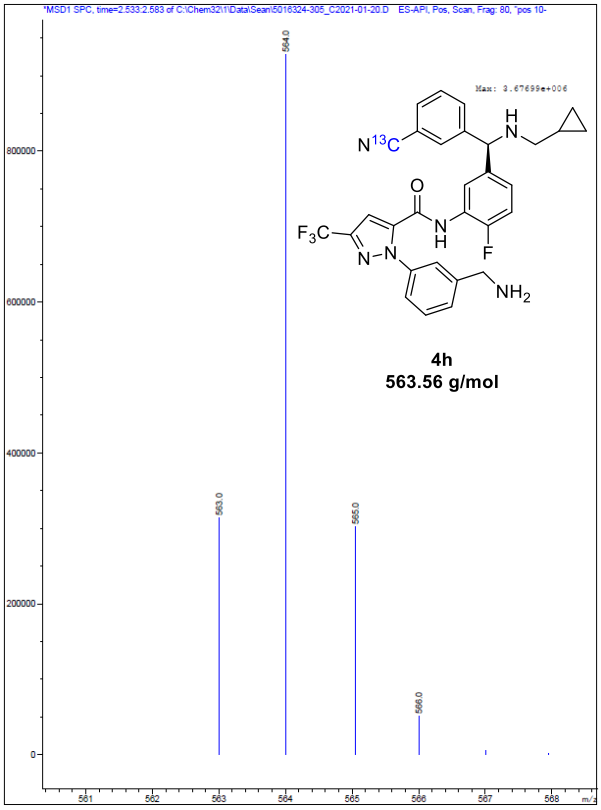
unlabeled	44.1
1-label	55.9
2-label	
3-label	
4-label	
5-label	
6-label	
…	
…	



4h







Unlabeled compound	Abundance
M1+0	3340258
M1+1	1201152
M1+2	0
M1+3	0
M1+4	0
M1+5	0
M1+6	0
M1+7	0
M1+8	0
M1+9	0
M1+10	0
M1+11	0
M1+12	0
M1+13	0
M1+14	0
M1+15	0
M1+16	0
M1+17	0
M1+18	0
M1+19	0

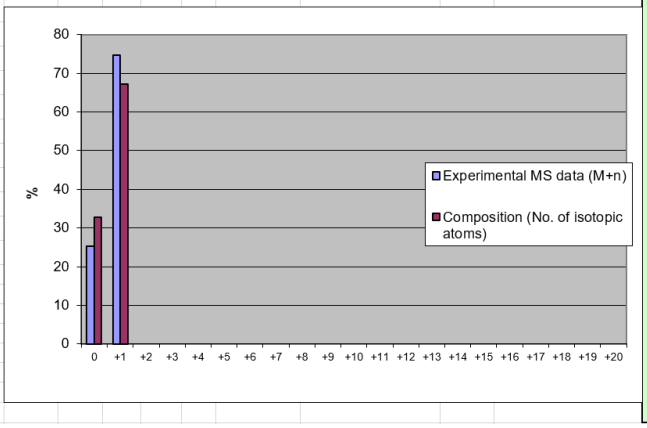
Analyte	Abundance
	314250.5
	927754.5
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0
	0

Expected derivatives: 2 (Must be <2

Labelled atoms 1

Atom% 67.2

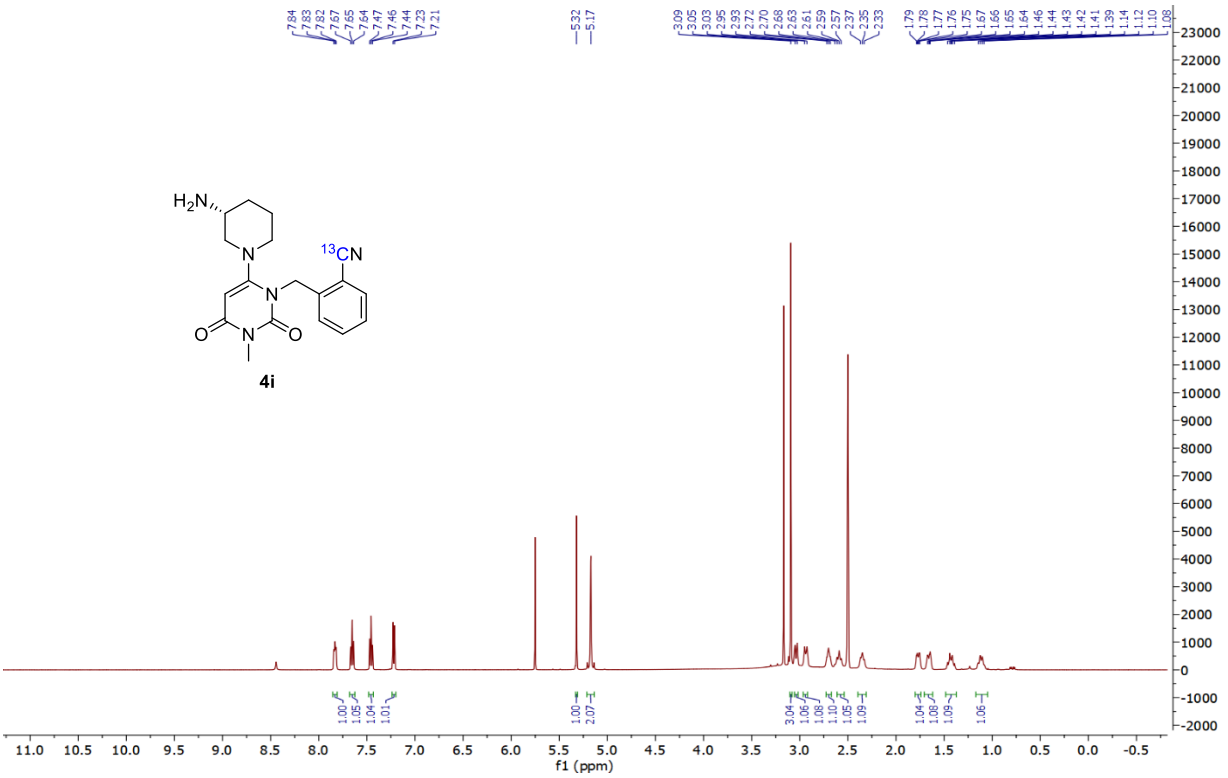
Calculate

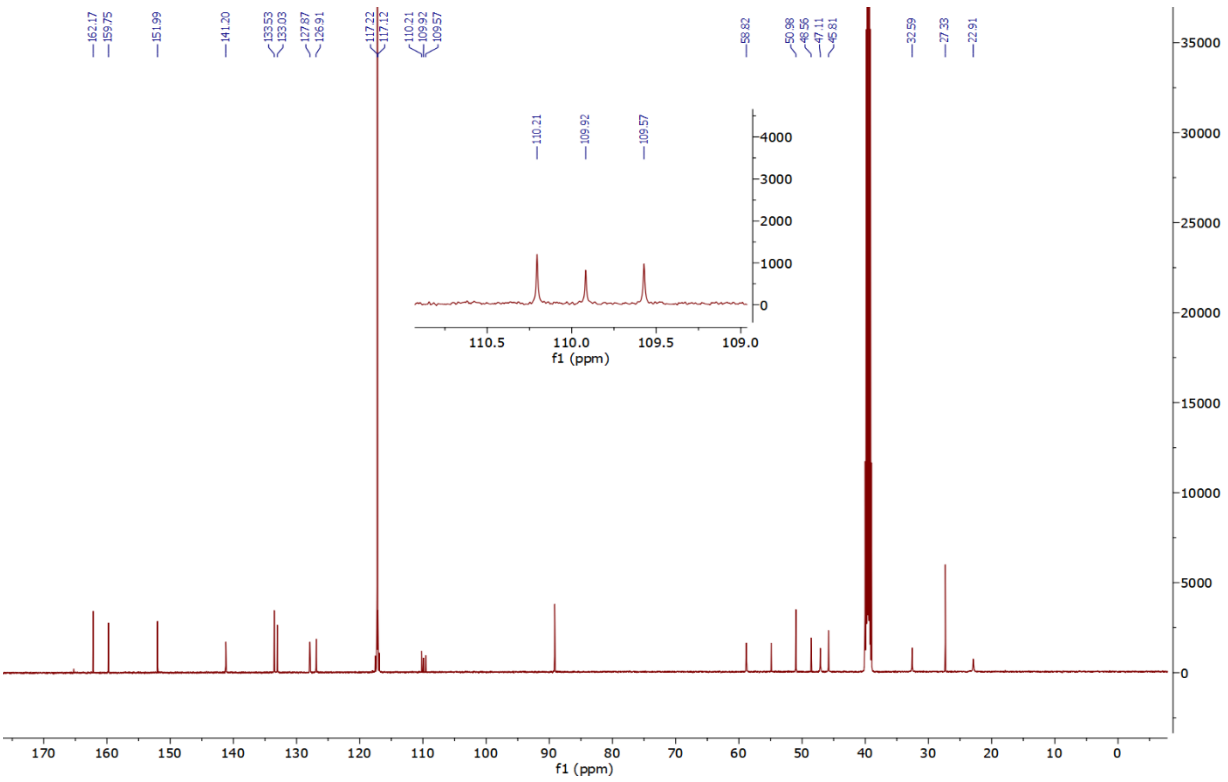


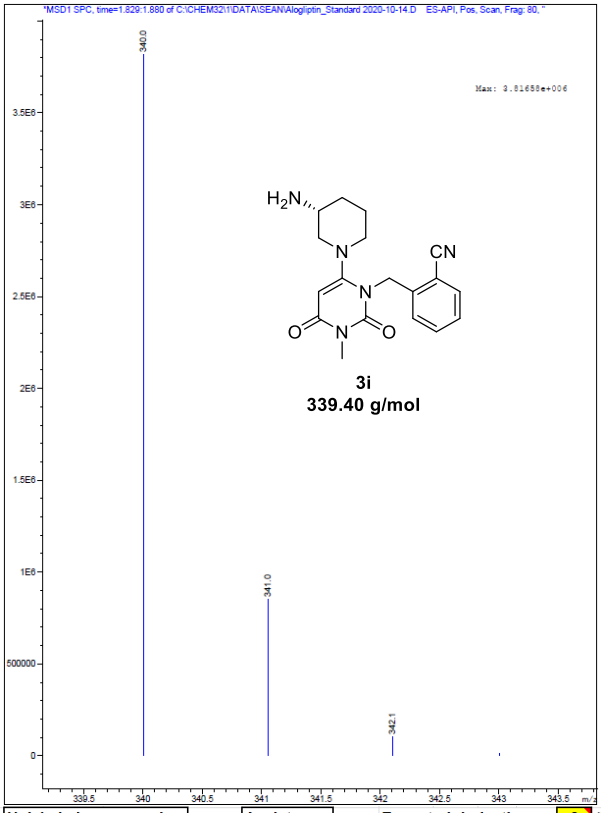
Results

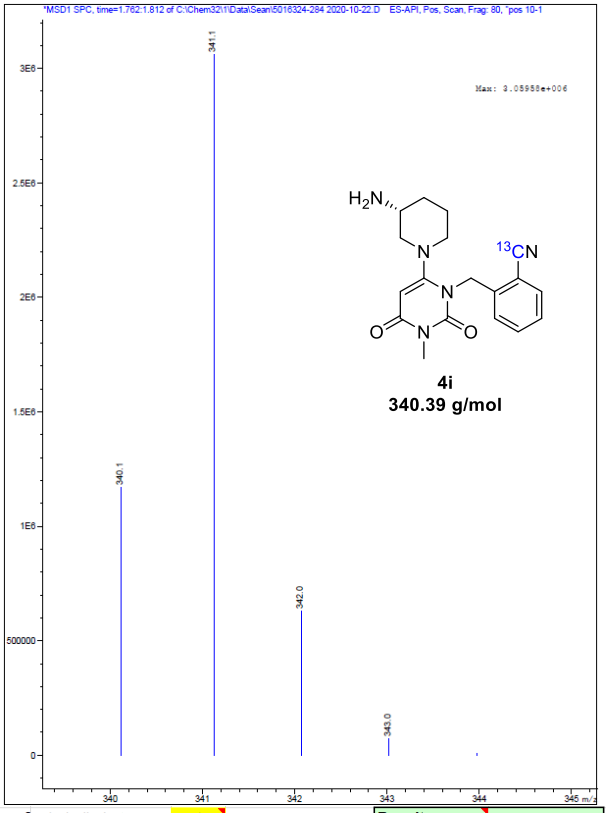
Relative amounts [%]

unlabeled	32.8
1-label	67.2


7.84
7.83
7.82
7.67
7.65
7.64
7.47
7.46
7.44
7.23
7.21
5.32
5.17
3.09
3.05
3.03
2.95
2.93
2.72
2.70
2.68
2.63
2.61
2.59
2.57
2.37
2.35
2.33
1.79
1.78
1.77
1.76
1.75
1.67
1.66
1.65
1.64
1.46
1.44
1.43
1.42
1.41
1.39
1.14
1.12
1.10
1.08
H_2N
N
^{13}CN
N
O
N
O
4i
1.00
1.05
1.04
1.01
1.00
2.07
3.04
1.06
1.06
1.02
1.05
1.09
1.04
1.08
1.09
1.06
f1 (ppm)


162.17
159.75
151.99
141.20
133.53
133.03
127.87
126.91
117.22
117.12
110.21
109.92
109.57
58.82
50.98
48.56
47.11
45.81
32.59
27.33
22.91
110.21
109.92
109.57
110.5
110.0
109.5
109.0
f1 (ppm)
f1 (ppm)





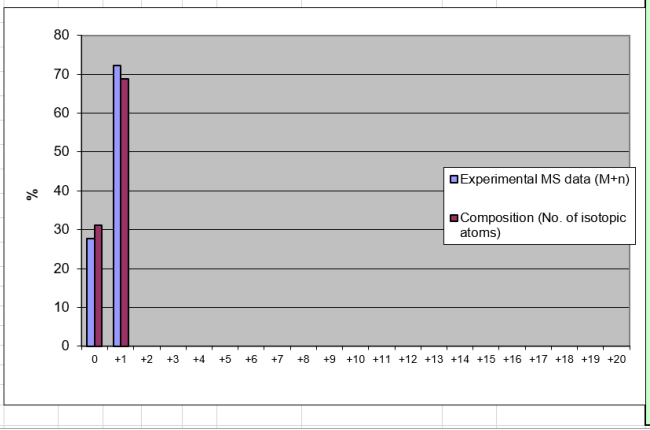
Unlabeled compound	Abundance	Analyte	Abundance
M1+0	3816576		1171264
M1+1	853600		3059584
M1+2	0		0
M1+3	0		0
M1+4	0		0
M1+5	0		0
M1+6	0		0
M1+7	0		0
M1+8	0		0
M1+9	0		0
M1+10	0		0
M1+11	0		0
M1+12	0		0
M1+13	0		0
M1+14	0		0
M1+15	0		0
M1+16	0		0
M1+17	0		0
M1+18	0		0
M1+19	0		0

Expected derivatives: 2 (Must be <2

Labelled atoms 1

Atom% 68.9

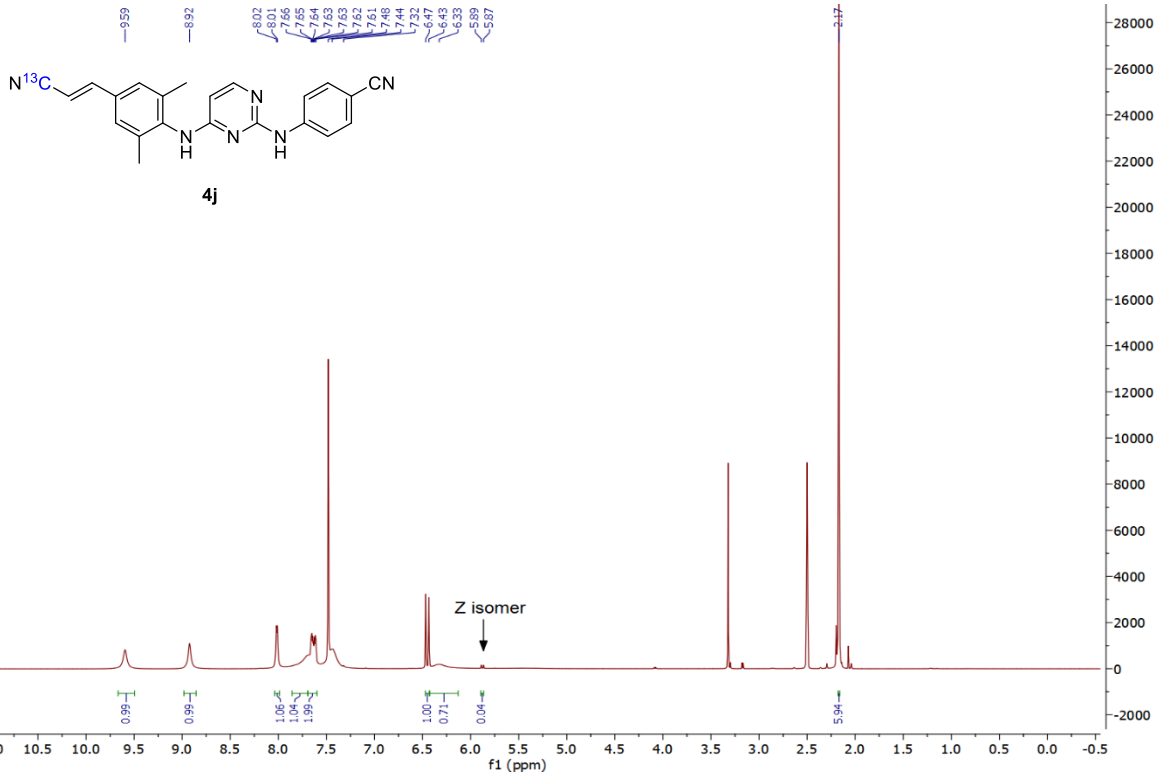
Calculate

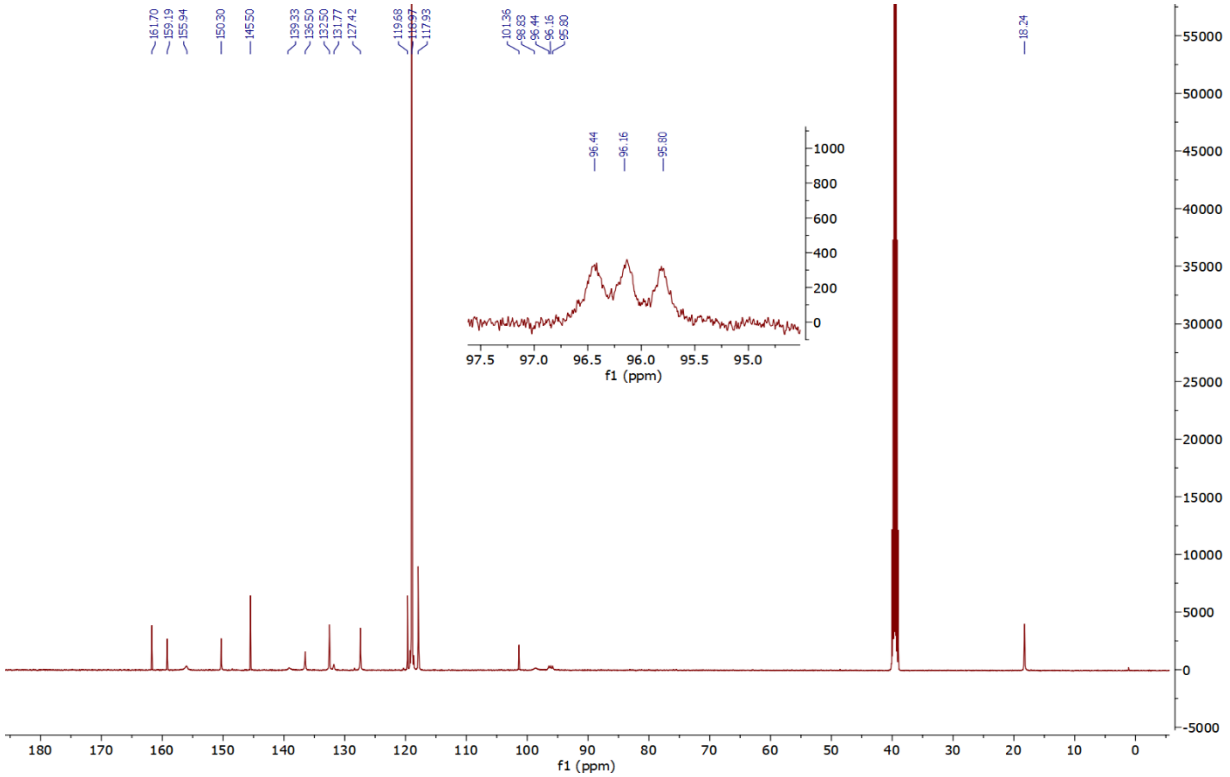


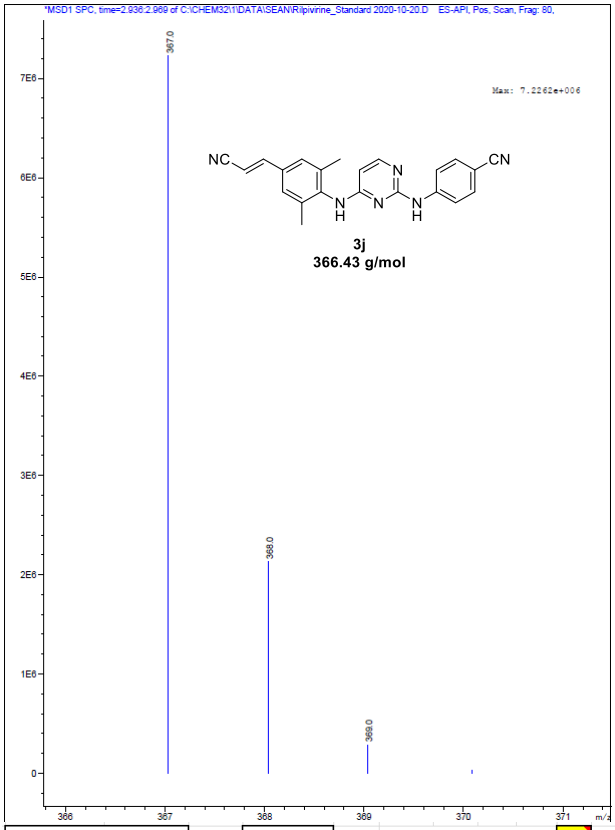
Results

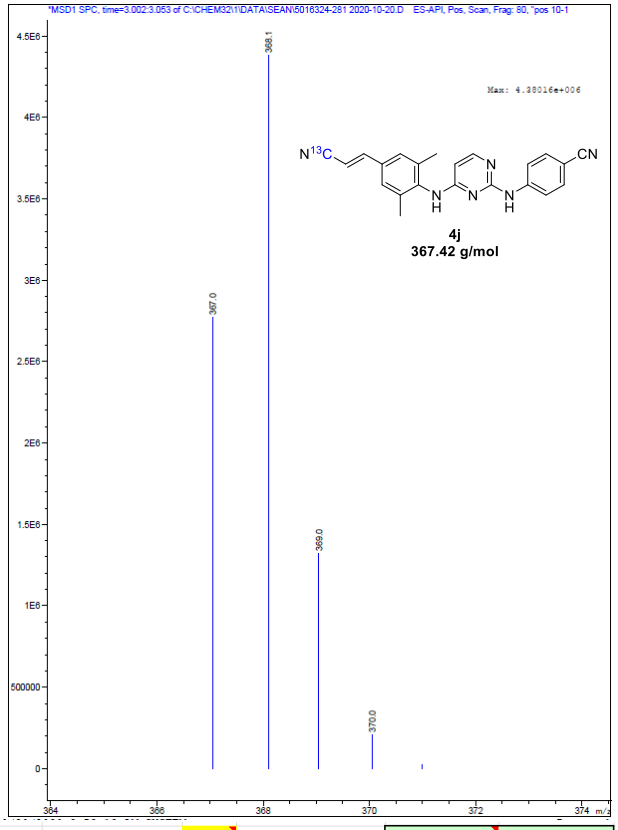
Relative amounts [%]

unlabeled	31.1
1-label	68.9
2-label	
3-label	
4-label	
5-label	
6-label	
…	
…	


9.59
8.92
8.02
8.01
7.66
7.65
7.54
7.53
7.52
7.51
7.48
7.44
7.32
6.47
6.43
6.33
5.89
5.87
2.17
N13C
CN
N
H
N
N
N
H
4j
Z isomer
0.99
0.99
1.06
1.04
1.99
1.00
0.71
0.04
5.94
f1 (ppm)


161.70
159.19
155.94
150.30
145.50
139.33
136.50
132.50
131.77
127.42
119.68
118.97
117.93
101.36
98.83
96.44
96.16
95.80
18.24
96.44
96.16
95.80
f1 (ppm)





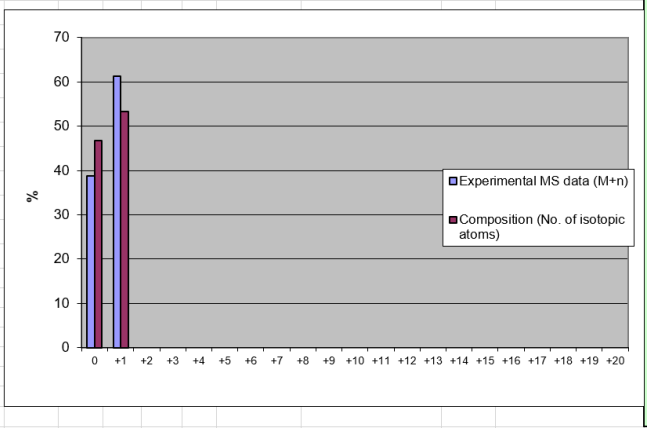
Unlabeled compound	Abundance	Analyte	Abundance
M1+0	7226197		2770304
M1+1	2130091		4380160
M1+2	0		0
M1+3	0		0
M1+4	0		0
M1+5	0		0
M1+6	0		0
M1+7	0		0
M1+8	0		0
M1+9	0		0
M1+10	0		0
M1+11	0		0
M1+12	0		0
M1+13	0		0
M1+14	0		0
M1+15	0		0
M1+16	0		0
M1+17	0		0
M1+18	0		0
M1+19	0		0

Expected derivatives: 2 (Must be <2

Labelled atoms 1

Atom% 53.3

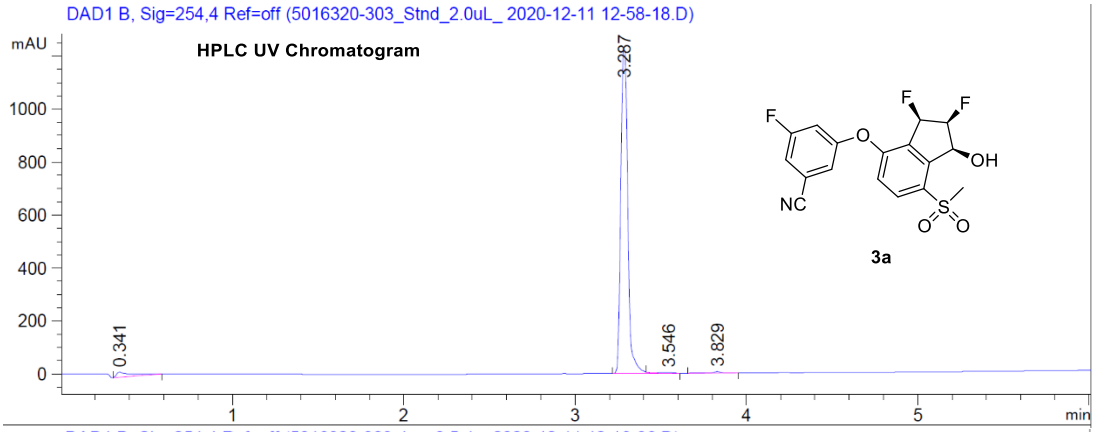
Calculate



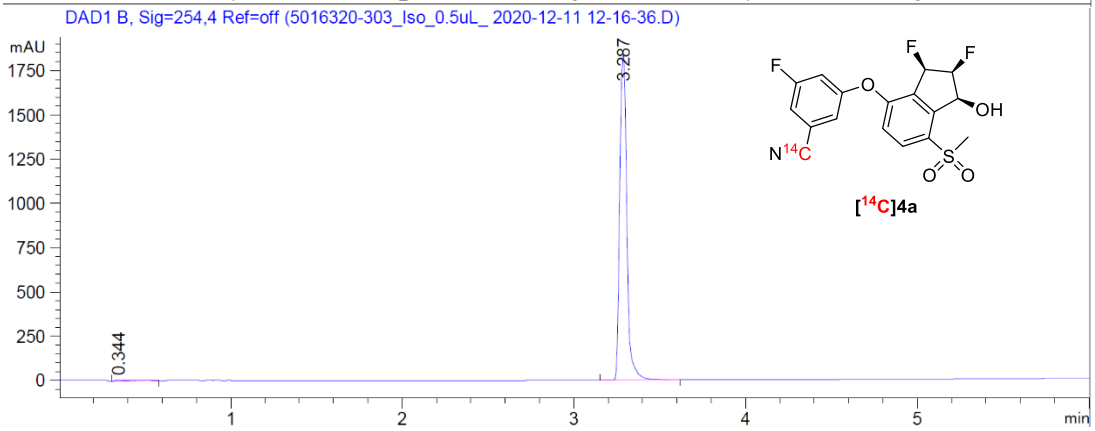
Results

Relative amounts [%]

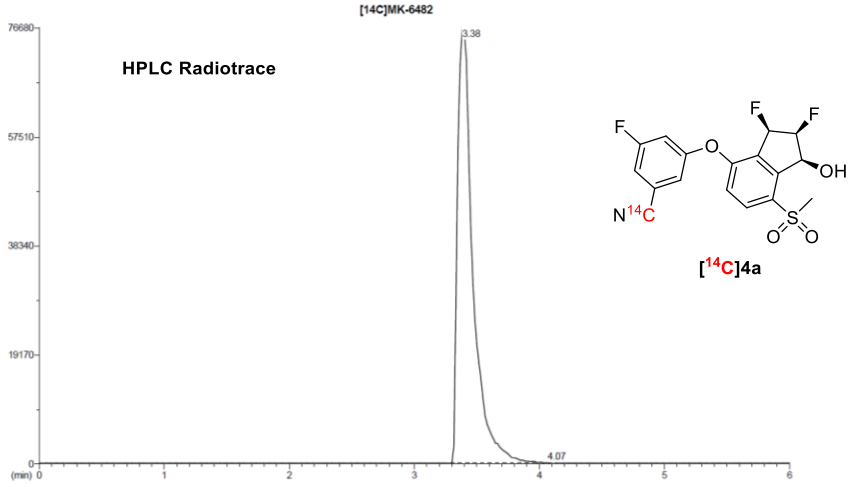
unlabeled	46.7
1-label	53.3
2-label	
3-label	
4-label	
5-label	
6-label	
…	
…	



3a



[^{14}C]4a



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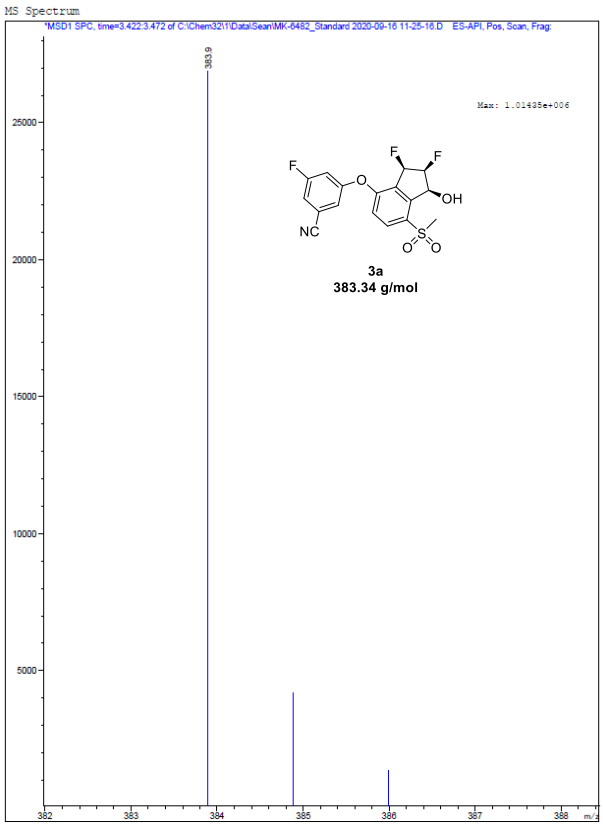

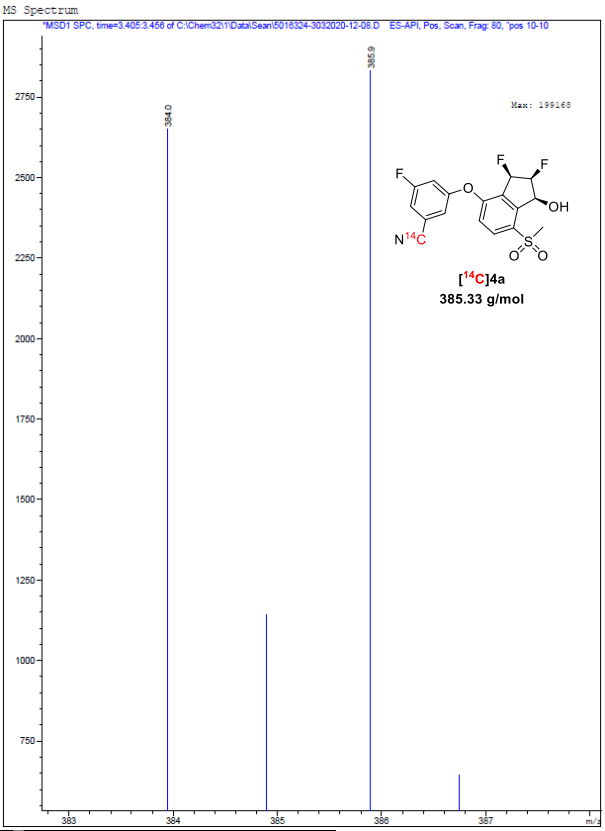

Carbon-14 Specific Activity From Mass Spectrometry						
SPACTCAL ver2.10						
[M-H] [M+H]	Reference	Percent of Parent	Percent of Total	Carbon-14 Labeled	Percent of Parent	Percent of Total
384	26,873	100.00%	82.895%	2,651	100.00%	36.475%
385	4,204	15.64%	12.968%	1,143	43.11%	15.724%
386	1,341	4.99%	4.138%	2,831	106.80%	38.956%
387	0	0.00%	0.000%	643	24.25%	8.844%
388	0	0.00%	0.000%	0	0.00%	0.000%
389	0	0.00%	0.000%	0	0.00%	0.000%
390	0	0.00%	0.000%	0	0.00%	0.000%
391	0	0.00%	0.000%	0	0.00%	0.000%
392	0	0.00%	0.000%	0	0.00%	0.000%
393	0	0.00%	0.000%	0	0.00%	0.000%
394	0	0.00%	0.000%	0	0.00%	0.000%
395	0	0.00%	0.000%	0	0.00%	0.000%
396	0	0.00%	0.000%	0	0.00%	0.000%
397	0	0.00%	0.000%	0	0.00%	0.000%
398	0	0.00%	0.000%	0	0.00%	0.000%
399	0	0.00%	0.000%	0	0.00%	0.000%
400	0	0.00%	0.000%	0	0.00%	0.000%
Total	32,418			7,268		

Molecular Weight	[M-H] [M+H]	# 14C Atoms	Tracer Intensity	Reference Ion Intensity	Net Tracer Intensity	Theoretical mCi/mmol	Measured mCi/mmol	Mol. Wt. Calculation	Tracer % of Total (corr)
383.340	384	0	2,651	100.00%	2,651	0.0	0.0000	189.95	49.55%
385.329	386	1	2,831	4.99%	2,699	62.4	31.4798	194.39	50.45%
387.318	388	2	0	0.00%	0	124.8	0.0000	0.00	0.00%
389.307	390	3	0	0.00%	0	187.2	0.0000	0.00	0.00%
391.296	392	4	0	0.00%	0	249.6	0.0000	0.00	0.00%
393.285	394	5	0	0.00%	0	312.0	0.0000	0.00	0.00%
395.274	396	6	0	0.00%	0	374.4	0.0000	0.00	0.00%
397.263	398	7	0	0.00%	0	436.8	0.0000	0.00	0.00%
399.252	400	8	0	0.00%	0	499.2	0.0000	0.00	0.00%
Total	Total		5,482		5,350		31.4798	384.343	
							mCi/mmol	31.480	
							Mol. Wt.	384.343	
							uCi/mg:	81.9054	
							mCi/mL:	0.71	
							mg/mL:	8.668535875	

References

1. Isotope distribution was calculated based on mass spectrometry data using IsoPat2. Excel-Worksheet for deconvolution of MS-patterns (D,^{17}O,^{13}C,^{15}N) © Christian C. Gruber, Wolfgang Kroutil 2006. Changes and additions to the original and excellent IsoPat2 have been made by W J S Lockley (Mod21) to facilitate its use by isotopic chemists. For details of the original spreadsheet see: Gruber, C.; Oberdorfer, G.; Voss, C.; Kremsner, J.; Kappe, C.; Kroutil, W. An Algorithm for the Deconvolution of Mass Spectroscopic Patterns in Isotope Labeling Studies. Evaluation for the Hydrogen−Deuterium Exchange Reaction in Ketones. *J. Org. Chem.* **2007**, 72, 5778.

2. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A., et al. *Gaussian 16*, Wallingford, CT, 2016.

3. Becke, A. D., Density-Functional Thermochemistry. III. The Role of Exact Exchange. *J. Chem. Phys.* **1993,** *98*, 5648-5652.

4. Lee, C.; Yang, W.; Parr, R. G., Development of the Colle-Salvetti Correlation-Energy Formula into a Functional of the Electron Density. *Phys. Rev. B* **1988,** *37*, 785-789.

5. Vosko, S. H.; Wilk, L.; Nusair, M., Accurate Spin-Dependent Electron Liquid Correlation Energies for Local Spin Density Calculations: A Critical Analysis. *Can. J. Phys.* **1980,** *58*, 1200-1211.

6. Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J., Ab Initio Calculation of Vibrational Absorption and Circular Dichroism Spectra Using Density Functional Force Fields. *J. Phys. Chem.* **1994,** *98*, 11623-11627.

7. Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H., A Consistent and Accurate *Ab Initio* Parametrization of Density Functional Dispersion Correction (DFT-D) for the 94 Elements H-Pu. *J. Chem. Phys.* **2010,** *132*, 154104.

8. Hay, P. J.; Wadt, W. R., Ab Initio Effective Core Potentials for Molecular Calculations. Potentials for the Transition Metal Atoms Sc to Hg. *J. Chem. Phys.* **1985,** *82*, 270-283.

9. Ribeiro, R. F.; Marenich, A. V.; Cramer, C. J.; Truhlar, D. G., Use of Solution-Phase Vibrational Frequencies in Continuum Models for the Free Energy of Solvation. *J. Phys. Chem. B* **2011,** *115*, 14556-14562.

10. Zhao, Y.; Truhlar, D. G., The M06 Suite of Density Functionals for Main Group Thermochemistry, Thermochemical Kinetics, Noncovalent Interactions, Excited States, and Transition Elements: Two New Functionals and Systematic Testing of Four M06-Class Functionals and 12 Other Tunctionals. *Theor. Chem. Acc.* **2008,** *120*, 215-241.

11. Rappoport, D.; Furche, F., Property-Optimized Gaussian Basis Sets for Molecular Response Calculations. *J. Chem. Phys.* **2010,** *133*, 134105.

12. Pritchard, B. P.; Altarawy, D.; Didier, B.; Gibson, T. D.; Windus, T. L., New Basis Set Exchange: An Open, Up-to-Date Resource for the Molecular Sciences Community. *J. Chem. Inf. Model.* **2019,** *59*, 4814-4820.

13. Tomasi, J.; Mennucci, B.; Cammi, R., Quantum Mechanical Continuum Solvation Models. *Chem. Rev.* **2005,** *105*, 2999-3094.