Supplementary Information

Electrocatalytic Reductive Deuteration of (Hetero)Arenes

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Contents

1. Materials and method

Commercial Ruthenium(III) chloride ($RuCl_3$, 97%, Bide Pharmatech). Commercial platinum-carbon catalyst (Pt/C, 20 wt%, Macklin). Commercial palladium-carbon catalyst (Pd/C, 10 wt%, Innochem). Commercial palladium(II) acetate catalyst ($Pd(OAc)_2$, 99.95%, HWRK Chem). Unless otherwise stated, analytical grade solvents and commercially available reagents were used without further purification. All solvents were analytical reagents or better and were degassed prior to be used. The instrument for electrolysis is dual display potentiostat (DJS-292B) (made in China). The anode electrode is carbon felt (10 mm × 15 mm × 3.0 mm) and the cathode electrode is prepared N doped carbon felt supported Ru electrode (10 mm × 15 mm × 3.0 mm). Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel in petroleum ether (bp. 60−90 ºC).

The surface morphologies were observed by transmission electron microscopy (TEM, JEOL plus-2100, Japan). Scanning transmission electron microscopy (STEM) imaging and energy-dispersive X-ray spectroscopy (EDX) mapping were acquired on a JEOL JEM-ARM200F microscope operated at 80 kV with a Schottky cold-field emission gun in Wuhan University. The EDX elemental mapping was carried using the JEOL SDD-detector with two 100 mm^2 X-ray sensor. X-ray photoelectron spectroscopy (XPS) was collected on a Thermo Scientific K-Alpha with a monochromatic A1 Kα X-ray source. The metal loading contents were determined using an inductively coupled plasma-optical emission spectrum (ICP-OES, Agilent 5110, USA). The crystal structure of the products was determined by powder X-ray diffraction (XRD, Smartlab SE, Japan). GC yields were recorded with a Shimadzu GC-2014 gas chromatograph instrument with an FID detector and biphenyl was added as an internal standard. ^1H and ^{13}C NMR data were recorded with Bruker Advanced II (400 MHz) spectrometers. All chemical shifts (δ) were reported in ppm and coupling constants (*J*) in Hz. All chemical shifts are reported relative to *d*-solvent peaks (7.27 ppm for ^1H, 77.23 ppm for ^{13}C, $CDCl_3$). High resolution mass spectra (HRMS) were measured with a Orbitrap Elite LTQ XL.

Determination of deuterium incorporation. The positions and percentage of deuterium incorporation were determined by ^1H NMR. The equation below was used to determine the degree of deuterium incorporation; peaks were calibrated against a signal corresponding to an unlabelled position. The labelling position was determined by ^1H NMR according to the chemical shifts and peak multiplicity. In addition, deuterium incorporations were confirmed using high-resolution MS

by comparison of all the labelled and unlabelled compounds (note that high-resolution MS serves here to substantiate the results of quantitative NMR analysis).

$$\% \text{ deuteration} = 100 - \left[\left(\frac{\text{residual integral}}{\text{number of labelling sites}} \times 100 \right) \right]$$

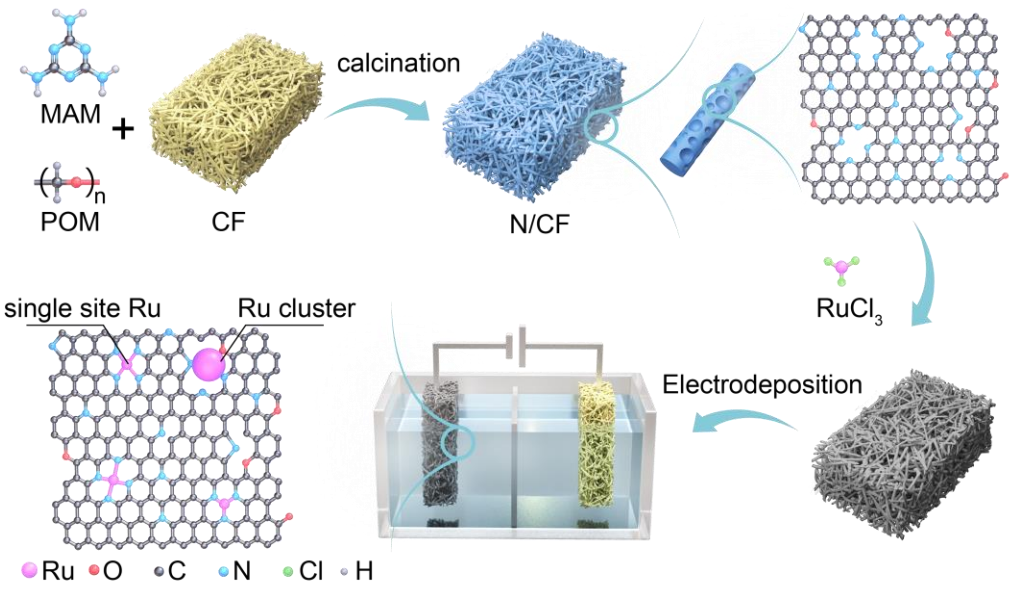
2. Catalyst preparation

Preparation of N/CF

About 330 mg carbon felt (CF, 30.0 mm × 20.0 mm × 3.0 mm) was reflux in EtOH with 660 mg melamine (MAM) for 24 h in a 50 mL PE tube equipped with reflux condenser to get MAM@CF. The resulted MAM@CF was washed twice with EtOH and dried at 80 ^{o}C. Then 2.90 g MAM was added into 12 mL DMSO in a 100 mL beaker, heated at 50 ^{o}C and stirred until melamine was fully dispersed in DMSO. Then 1.25 g paraformaldehyde and MAM@CF were added in turn. The obtained mixture was heat at 120 ^{o}C for 1 h and 170 ^{o}C for 72 h for polymerization. Then, the obtained solid was calcinated at 900 ^{o}C for 1 h under Ar atmosphere with heating rate of 4 ^{o}C/min to get N-doped carbon felt (N/CF). The prepared N/CF was cut into three pieces, the size of each piece was 10.0 mm × 20.0 mm × 3.0 mm.

Preparation of Ru-N/CF

The prepared N/CF (10.0 mm × 20.0 mm × 3.0 mm) was immersed with 20 mM $RuCl_3$ in 12 mL H_2O in a 50 mL PE tube for 24 h. Then impregnated $RuCl_3$@N/CF was taken out, washed three times with H_2O and was dried at 80 ^{o}C under vacuum. The dried $RuCl_3$@N/CF was placed into a divided cell as cathode electrode with 0.08 M Et_4NF in $^{t}BuOH/H_2O$ cathode solution and CF was used as anode electrode with 0.08 M NaF in H_2O anode solution for electrodeposition, which was operated at 10 mA for 3 h to obtain the electrode Ru-N/CF. Besides, the residual Ru-containing solution was recovery and could be reused.

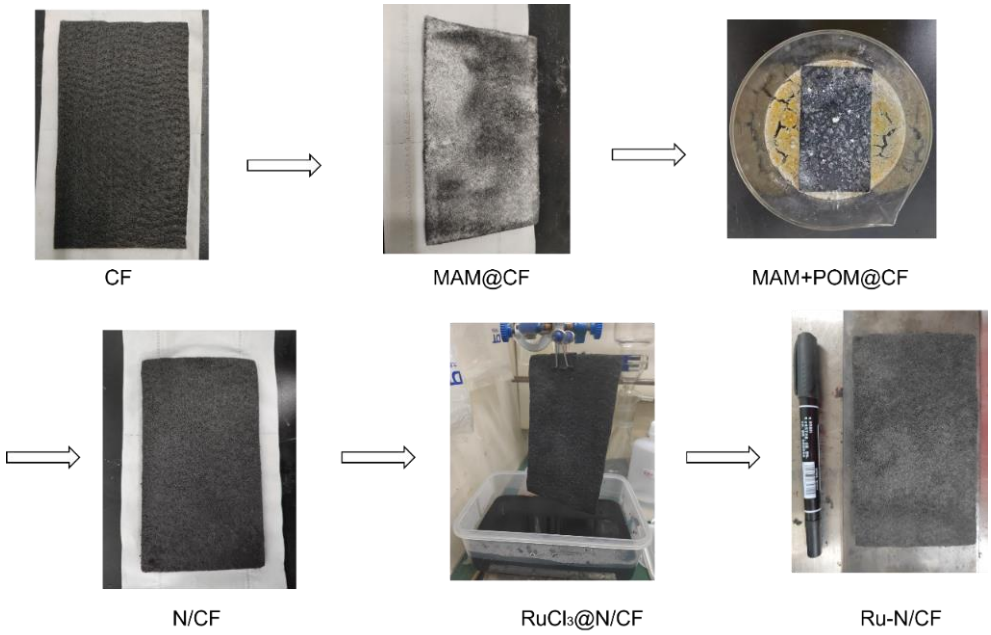


Supplementary Figure S1. Preparation of Ru-N/CF electrode.

Preparation of Ru-N/CF used in electrochemical flow device

About 5.57 g carbon felt (CF, 135.0 mm × 75.0 mm × 3.0 mm) was reflux in EtOH with 11.14 g melamine (MAM) for 24 h to get MAM@CF. The resulted MAM@CF was washed twice with EtOH and dried at 80 ^{o}C. Then 48.95 g MAM was added into 200 mL DMSO in a water bath, heated at 50 ^{o}C and stirred until melamine was fully dispersed in DMSO. Then 21.13 g paraformaldehyde and MAM@CF were added in turn. The obtained mixture was heat at 120 ^{o}C for 1 h and 170 ^{o}C for 72 h for polymerization. Then, the obtained solid was calcinated at 900 ^{o}C for 1 h under Ar atmosphere with heating rate of 4 ^{o}C/min to get N-doped carbon felt (N/CF).

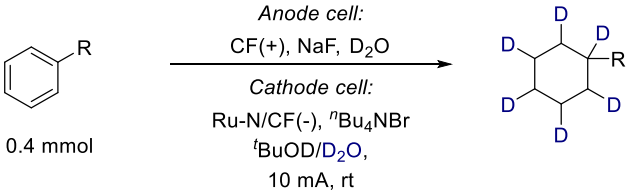
The prepared N/CF (135.0 mm × 75.0 mm × 3.0 mm) was immersed with 40 mM $RuCl_3$ in 230 mL H_2O in a cuboid PE box for 24 h. Then impregnated $RuCl_3$@N/CF was taken out, washed three times with H_2O and was dried at 80 ^{o}C under vacuum. The dried $RuCl_3$@N/CF was calcinated at 300 ^{o}C for 1 h under 10% H_2 atmosphere with heating rate of 2 ^{o}C/min to obtain electrode Ru-N/CF. Besides, the residual Ru-containing solution was recovery and could be reused.



Supplementary Figure S2. Preparation of Ru-N/CF used in electrochemical flow device.

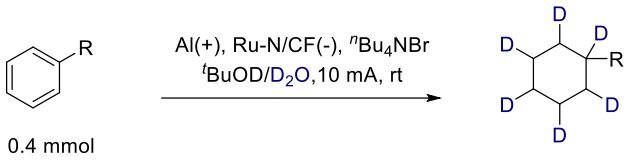
3. General procedure for the electro-reductive deuteration reactions

Method 1: Electro-reductive deuteration reactions in a divided cell



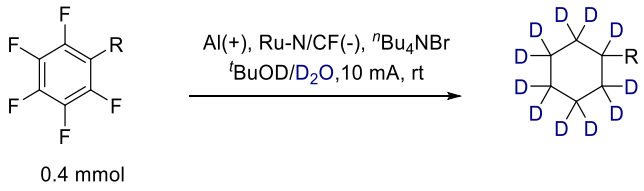
In an oven-dried divided cell, the arene (0.4 mmol, 1 equiv.) and $^{n}Bu_4NBr$ (0.8 mmol) were placed in the cathode cell, and NaF (0.8 mmol) was placed in the anode cell. The cell was equipped with a stir bar, a carbon felt anode (10 mm × 15 mm × 3.0 mm) and N doped carbon felt supported Ru cathode (10 mm × 15 mm × 3.0 mm). The cell was flushed with Ar. Degased $^{t}BuOD$ (5.0 mL) and D_2O (5.0 mL) were added in the cathode cell. D_2O (10 mL) was added in the anode cell. The reaction mixture was stirred and electrolyzed at a constant current of 10 mA at room temperature until the reaction was complete monitored by TLC and GC-MS. The reaction time is generally between 8 h and 20 h. After completion of the reaction, the reaction mixture was extracted three times with ethyl acetate and the combined organic phase was removed under reduced pressure by an aspirator and dried by Na_2SO_4, then the pure product was obtained by flash column chromatography on silica gel.

Method 2: Electro-reductive deuteration reactions in an undivided cell



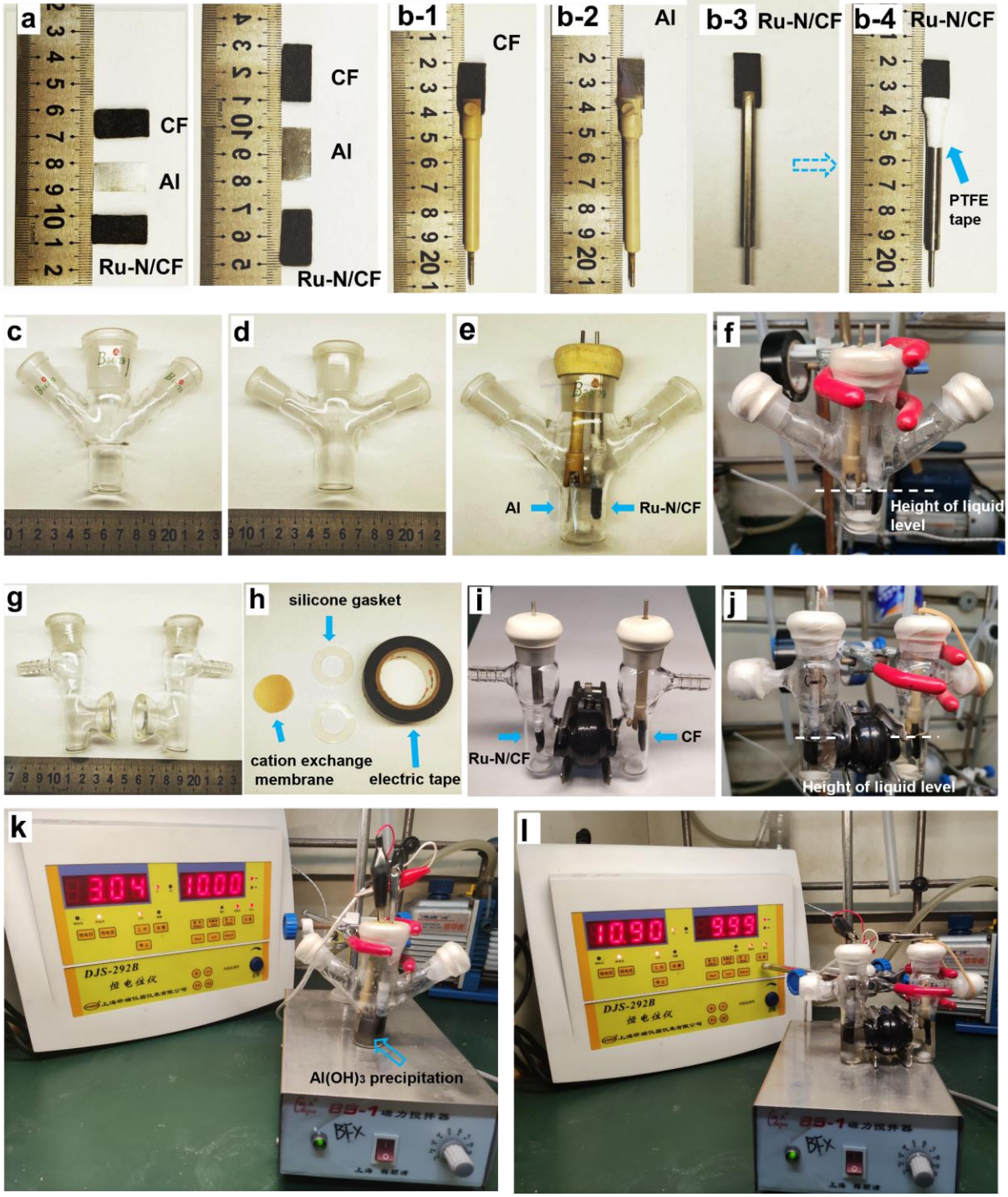
The arene (0.4 mmol, 1 equiv.) and $^{n}Bu_4NBr$ (0.4 mmol) were placed in an oven-dried undivided three-necked bottle (25 mL). The bottle was equipped with a stir bar, an aluminum sheet (10 mm × 15 mm × 0.3 mm) anode and N doped carbon felt supported Ru cathode (10 mm × 15 mm × 3.0 mm). The bottle was flushed with Ar. Degased $^{t}BuOD$ (2.5 mL) and degased D_2O (2.5 mL) were added. The reaction mixture was stirred and electrolyzed at a constant current of 10 mA at room temperature until the reaction was complete monitored by TLC and GC-MS. The reaction time is generally between 8 h and 20 h. After completion of the reaction, the reaction mixture was extracted three times with ethyl acetate and the combined organic phase was removed under reduced pressure by an aspirator, then the pure product was obtained by flash column chromatography on silica gel.

Method 3: Electro-reductive deuteration reactions of polyfluoro arene compounds.



The arene (0.4 mmol, 1 equiv.) and $^{n}Bu_4NBr$ (0.8 mmol) were placed in an oven-dried undivided three-necked bottle (25 mL). The bottle was equipped with a stir bar, an aluminum sheet (10 mm × 15 mm × 0.3 mm) anode and N doped carbon felt supported Ru cathode (10 mm × 15 mm × 3.0 mm). The bottle was flushed with Ar. Degased $^{t}BuOD$ (5.0 mL) and degased D_2O (5.0 mL) were added. The reaction mixture was stirred and electrolyzed at a constant current of 10 mA at room temperature until the reaction was complete monitored by TLC and GC-MS. The reaction time is generally between 36 h and 48 h. After completion of the reaction, the reaction mixture was extracted three times with ethyl acetate and the combined organic phase was removed under reduced pressure by an aspirator, then the pure product was obtained by flash column chromatography on silica gel.

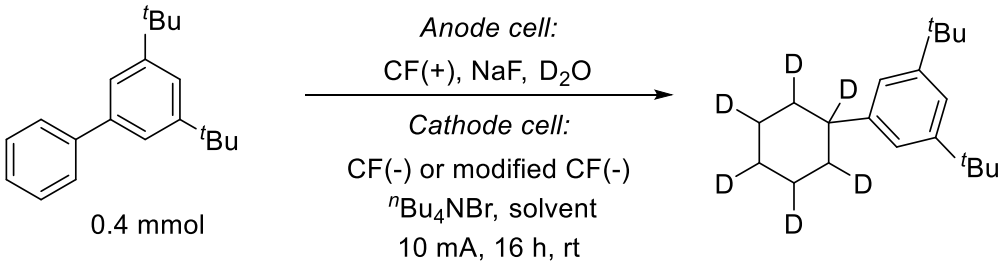
Graphic guide for setting up electro-reductive deuteration reactions



Supplementary Figure S3. Images of electrochemical reaction devices. (a) CF, Al sheet and Ru-N/CF electrodes and their original dimensions of length and width (1.0 cm * 2.0 cm). (b) Assembly of electrodes and electrode clamps and the effective electrode area was 1.0 cm * 1.5 cm. (c) Three-necked bottle used to hold 5 ml solvent. (d) Three-necked bottle used to hold 10 ml

solvent. (e) Assembly of electrodes and reaction bottle. (f) Setting up reaction in an undivided cell. (g) Divided cell. (h) Assembly accessories for divided cell. (i) Assembly of electrodes and divided cell. (j) Setting up reaction in a divided cell. (k) Connect the cathode and anode in an undivided cell to a DC power supply. (l) Connect the cathode and anode in a divided cell to a DC power supply.

4. Reaction development and optimization



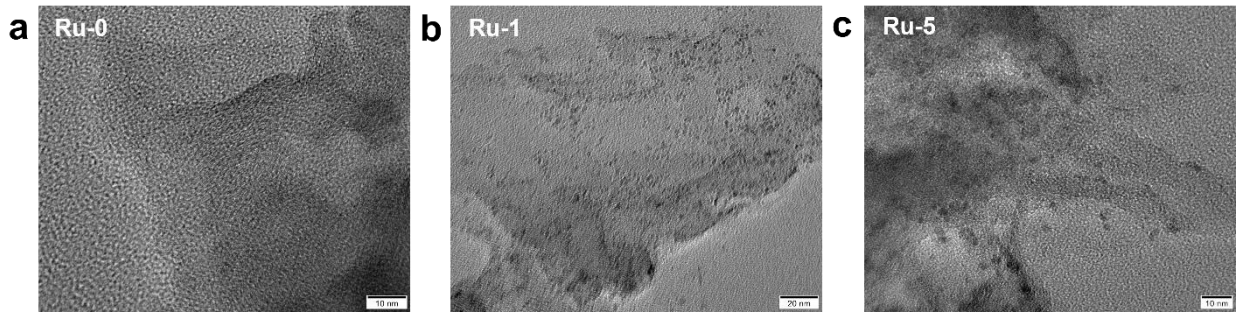
Entry	Catalyst or modified cathode	Solvent	Yield	D Total/molecule
1	Pd/C	^{t}BuOH/H_2O	n.d.	-
2	Ir/C	^{t}BuOH/H_2O	n.d.	-
3	Pt/C	^{t}BuOH/H_2O	trace	-
4	Rh/C	^{t}BuOH/H_2O	trace	-
5	Ru/C	^{t}BuOH/H_2O	trace	-
6	Ru-N/CF	^{t}BuOH/H_2O	99%[a]	-
7[b]	Ru-N/CF	^{t}BuOD/D_2O	99%[a]	7.5
8[b]	N/CF	^{t}BuOD/D_2O	n.d.	-
9[b,c]	Ru-N/CF	^{t}BuOH/H_2O	n.d.	-

Supplementary Table S1. Reaction conditions: Anode cell, CF (+), NaF 0.8 mmol, H_2O 10 mL; cathode cell, CF or modified cathode (-), arene 0.4 mmol, $^{n}Bu_4NBr$ 0.8 mmol, ^{t}BuOH/H_2O = 5/5 mL, 10 mA, 16 h, room temperature, Ar atmosphere. [a]Isolated yield. [b]t = 9 h. [c]Reaction was carried out without electrolysis under 1 atm H_2 atmosphere. n.d. = not detected.

5. Characterization of Ru-N/CF

In order to understand the detailed structure of the most active material (Ru-N/CF), characterization of modified cathode Ru-N/CF was performed with high-angle annular dark-field scanning transmission electron microscopy (HAADF-STEM), X-ray photoelectron spectroscopy (XPS), powder X-ray diffraction (XRD) and X-ray absorption spectroscopy (XAS). These results showed that the Ru species on freshly Ru-N/CF were supported as single atom/site and cluster and the ratio of Ru^{3+}/Ru^{0} was 0.73. The Ru species were partially reduced to Ru^{0} during reaction to form Ru nanoparticles with size of 1-5 nm and the ratio of Ru^{3+}/Ru^{0} was change to 0.09 after 5 cycle reaction, which indicated N/CF supported Ru nanoparticles might be the catalytic active species (for details see Supplementary Figures S4-8).

TEM spectrums of Ru-N/CF

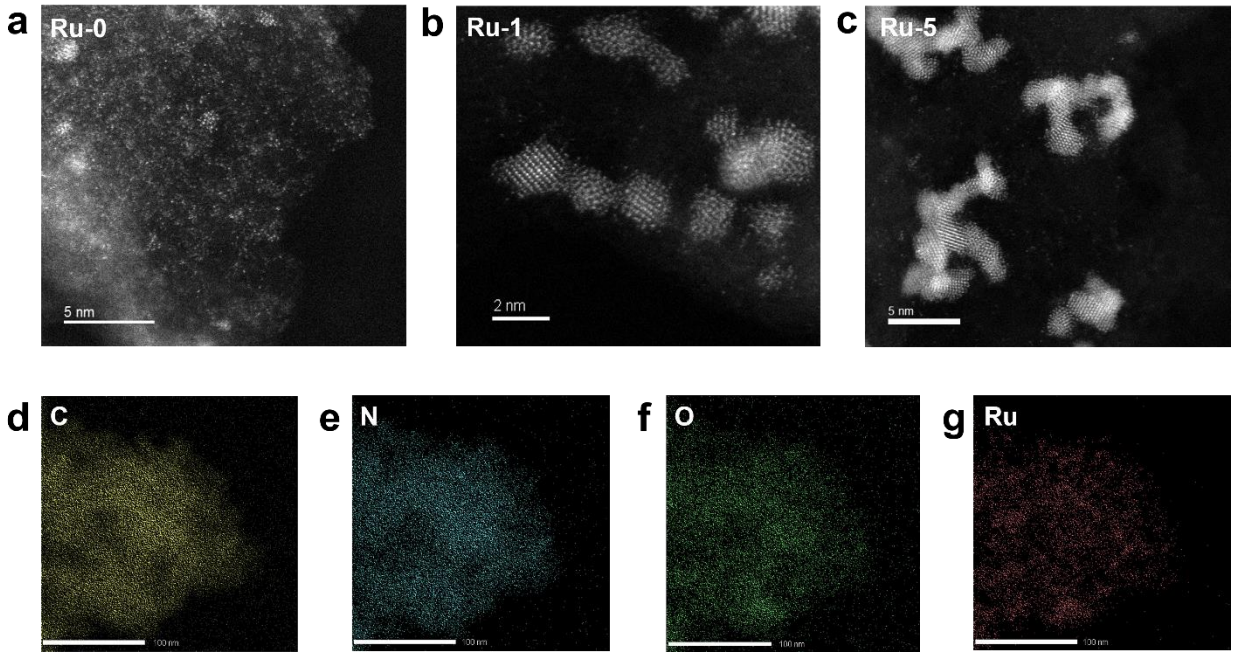


Supplementary Figure S4. (a) TEM spectrum of fresh Ru-N/CF. (b) TEM spectrum of Ru-N/CF after reaction. (c) TEM spectrum of Ru-N/CF after 5 cycle reactions.

The fresh Ru-N/CF was marked as Ru-0. The Ru-N/CF after 1 cycling was marked as Ru-1. The Ru-N/CF after 5 cycling was marked as Ru-5.

TEM spectrum of Ru-0 showed that none of nanoparticles was observed (Supplementary Figure S4a). TEM spectrum of Ru-1 showed that many nanoparticles were formed and the size of nanoparticles was about 2 nm after reaction (Supplementary Figure S4b). TEM spectrum of Ru-5 showed that a slight agglomeration of nano particles was observed after 5 cycling reactions (Supplementary Figure S4c).

STEM and EDS mapping spectrums of Ru-N/CF

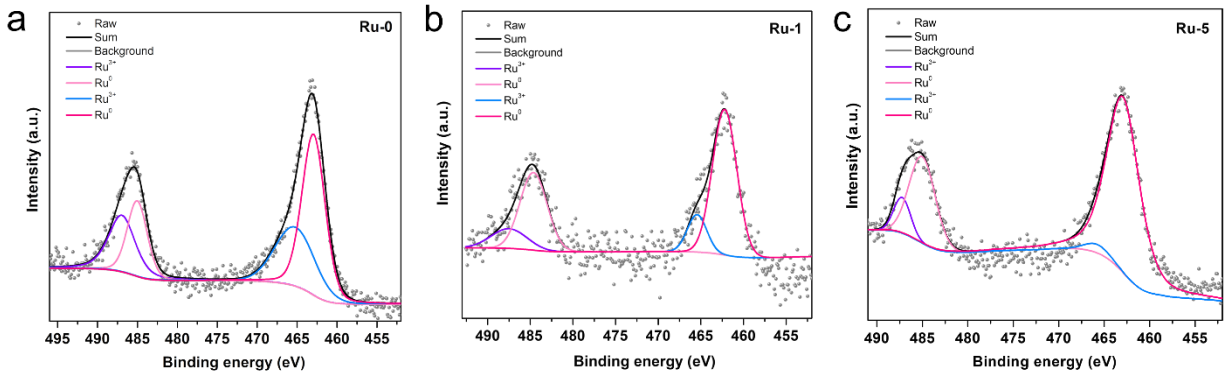


Supplementary Figure S5. (a) STEM spectrum of fresh Ru-N/CF. (b) STEM spectrum of Ru-N/CF after reaction. (c) STEM spectrum of Ru-N/CF after 5 cycle reactions. (d-g) EDS mapping spectrum of Ru-N/CF after reaction.

STEM spectrum of Ru-0 showed that Ru species were mainly dispersed on the carrier in the form of single atom/site (Supplementary Figure S5a). Besides, there were a few Ru clusters and the size was < 1 nm. STEM spectrum of Ru-1 showed that many nanoparticles with the size of around 2 nm were formed after electroreduction (Supplementary Figure S5b). STEM spectrum of Ru-5 showed that nanoparticles were agglomerated to a certain extent and the size was around 5 nm after 5 cycle reactions (Supplementary Figure S5c).

EDS mapping spectrum of Ru-1 showed that there were C, N, O and Ru elements on the electrode and all of these elements were dispersed randomly (Supplementary Figure S5d-g).

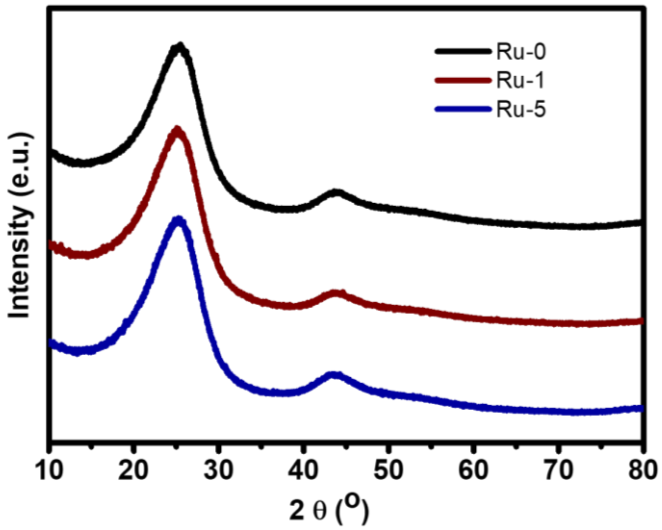
XPS spectra of Ru-N/CF.



Supplementary Figure S6. Ru 3p XPS spectra of (a) fresh Ru-N/CF, (b) Ru-N/CF after reaction, (c) Ru-N/CF after 5 cycle reactions.

XPS analysis of fresh Ru-N/CF showed that both $Ru^{3+}$and Ru^{0} existed on the surface of the electrode and the ratio of Ru^{3+}/Ru^{0} was 0.73 (Supplementary Figure S6a). XPS spectrum of Ru-N/CF after reaction showed that both Ru^{3+} and Ru^{0} existed and the ratio of Ru^{3+}/Ru^{0} was 0.25 (Supplementary Figure S6b). XPS analysis of Ru-N/CF after 5 cycle reactions showed that both Ru^{3+} and Ru^{0} existed and the ratio of Ru^{3+}/Ru^{0} was 0.09 (Supplementary Figure S6c). Above results indicated that as the reaction proceeded, the ratio of Ru^{0} species increased. The reaction yield and D-incorporation were not decreased for 6^{th} cycle reaction catalyzed by Ru-5 (Supplementary Figure S10), which might indicate the Ru^{0} was the active specie for reductive deuteration of arene in consideration that the ratio of Ru^{3+}/Ru^{0} was 0.09 for Ru-5.

XRD spectra of Ru-N/CF.



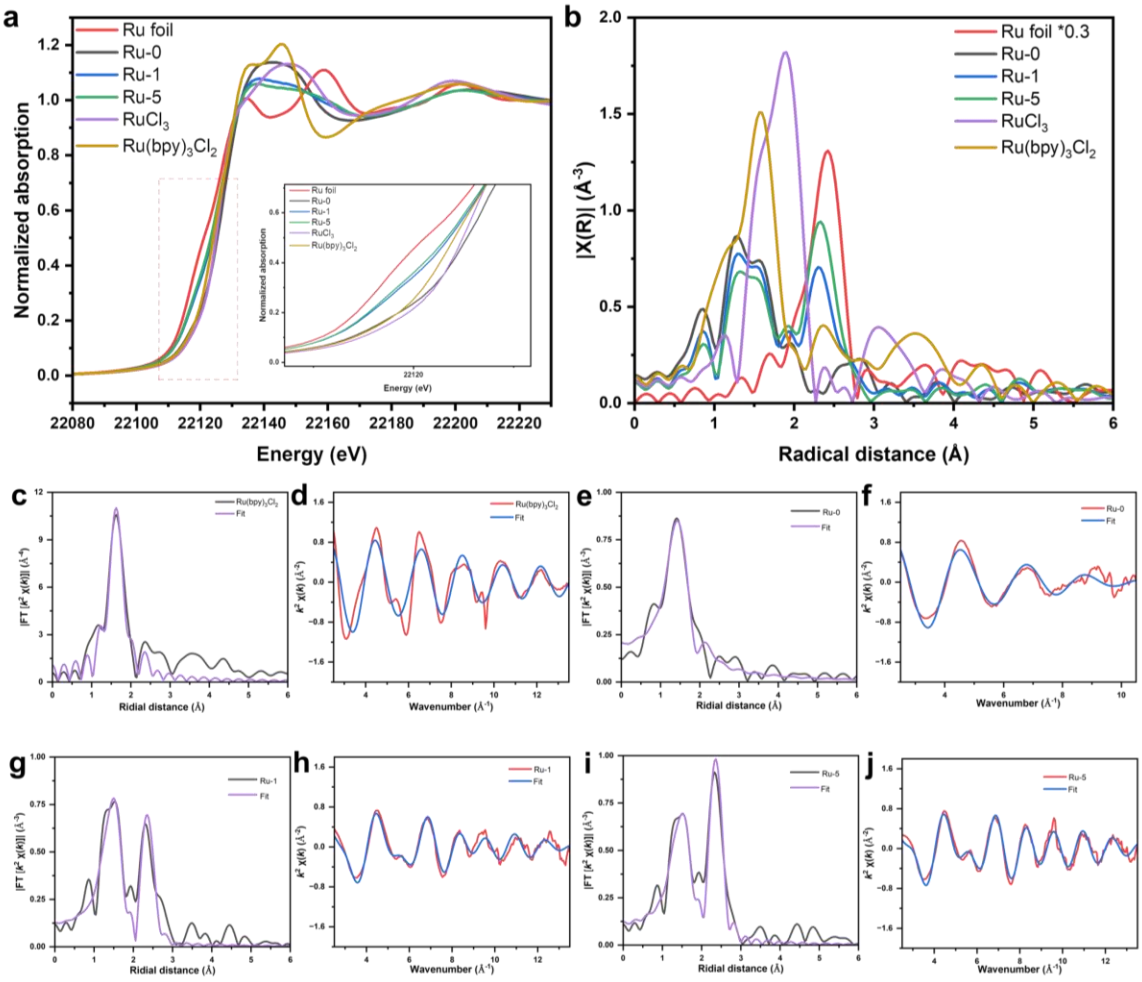
Supplementary Figure S7. XRD spectra of fresh Ru-N/CF, Ru-N/CF after reaction and Ru-N/CF after 5 cycle reactions.

XRD spectra showed that no peak of Ru NPs was detected.

ICP result

The mass of the electrode Ru-N/CF (10 mm × 15 mm × 3.0 mm) was 117 mg. Besides, ICP analysis of Ru-N/CF showed that the loading of Ru was 1.0 wt%.

XANES and EXAFS spectra of Ru-N/CF.



Supplementary Figure S8. (a) XANES, (b) EXAFS spectrum of Ru-N/CF with respect to the reference samples. Fitting data of (c, d) standard sample $Ru(bpy)_3Cl_2$, (e, f) Ru-0 electrode, (g, h) Ru-1 electrode and (i, j) Ru-5 electrode.

XANES spectrum of fresh Ru-N/CF (Ru-0) showed that the edge energy of Ru on the fresh Ru-N/CF was higher than that of $Ru(bpy)_3Cl_2$ and close to that of $RuCl_3$, which was consistent with XPS results. XANES analysis of Ru-1 and Ru-5 indicated that the average valence of Ru species on the Ru-1 and Ru-5 were both between Ru^0 and Ru^{2+}. EXAFS analysis of Ru-0 showed that Ru-Ru bond was hardly observed and the Ru species on the Ru-0 mainly existed in the form of single site. EXAFS analysis of Ru-1 and Ru-5 showed that there were both Ru-Ru bond and Ru-N/O or Ru-Cl bond, which indicated that both Ru NPs and single site Ru were existed on the Ru-1 and Ru-5.

Sample	Path	Amp	CN	DW factor ($Å^2$)	deltaE (eV)	R (Å)	k-range ($Å^{-1}$)	R-range (Å)	R factor
$Ru(bpy)_3Cl_2$	Ru-N	0.84(8)	<u>6</u>	0.0018 (9)	1.1 (5)	2.062 (6)	3.0 - 13.5	1.1 - 2.1	0.042
Ru-0	Ru-N/O	<u>0.84</u>	6.2 (6)	0.010 (3)	-2.0 (7)	2.017 (8)	3.0 - 10.0	1.1 - 1.9	0.00368
Ru-1	Ru-N/O	<u>0.84</u>	4.2 (7)	0.006 (1)	-4.6 (6)	1.997 (4)	3.0 - 13.5	1.0 – 3.0	0.071
	Ru-Ru		2.7 (7)	0.007 (1)		2.674 (5)			
Ru-5	Ru-N/O	<u>0.84</u>	4.0 (9)	0.007 (2)	-4.8 (5)	2.00 (1)	3.0 - 13.5	1.0 – 3.0	0.043
	Ru-Ru		3.5 (7)	0.006 (2)		2.672 (9)			

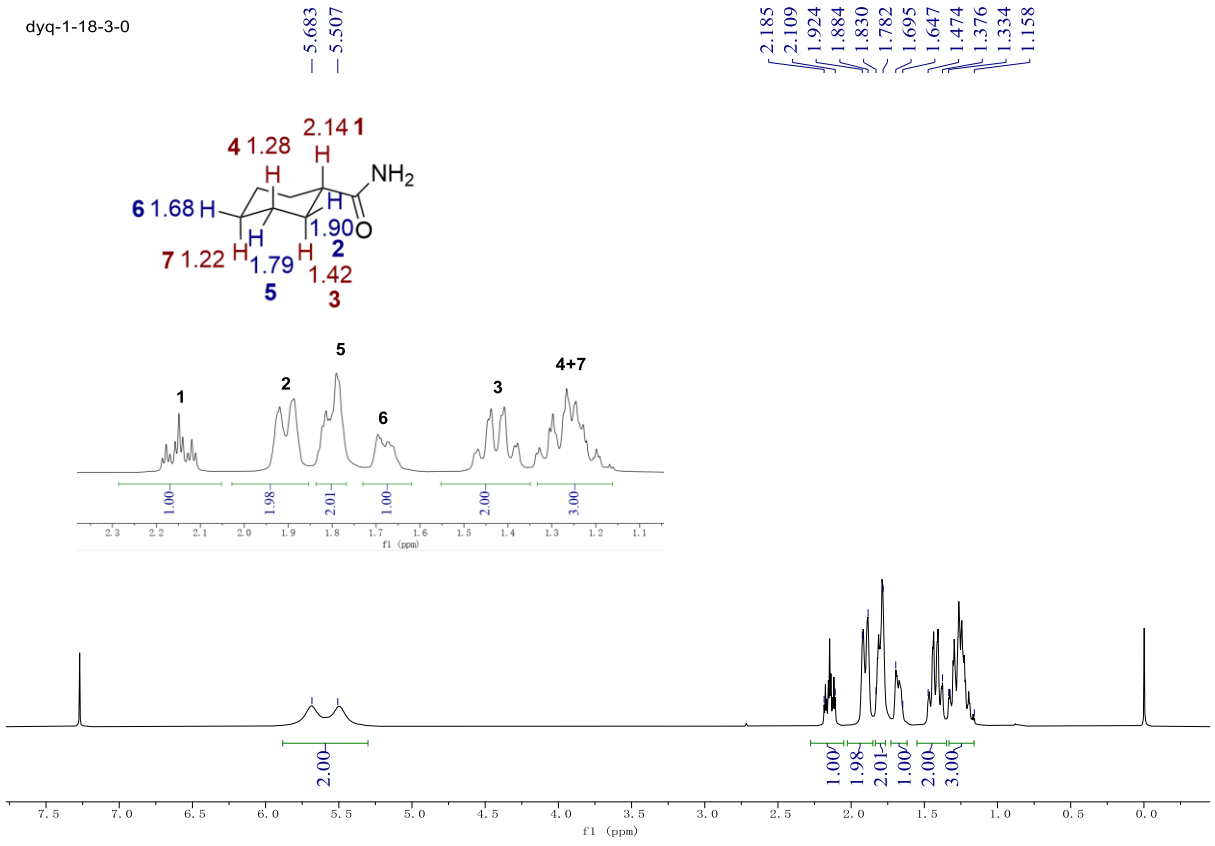
Supplementary Table S2. EXAFS Fitting results. Amp = Amplitude reduction factor, DW = Debye-Waller factor, numbers in parentheses are fitting errors, numbers underline are fixed values in fitting.

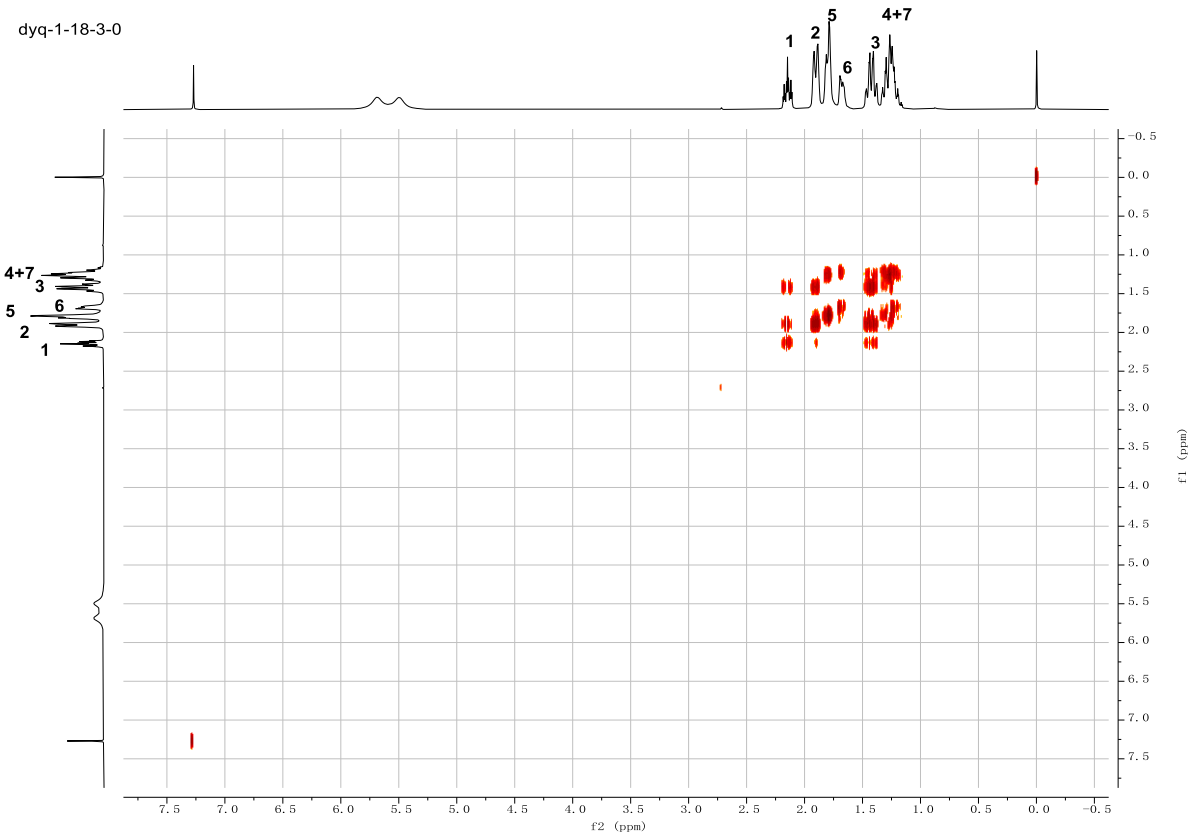
6. ^{1}H NMR and HRMS spectrum analysis of selected examples

a-1. Cyclohexyl formamide.

The ^{1}H NMR spectrum and ^{1}H, ^{1}H COSY spectrum of cyclohexyl formamide were shown as follows. The chemical shift of two active H on -NH_2 was 5.60 ppm. The chemical shift of the hydrogen on the α position of amide was 2.14 ppm and the H was marked as **H1**. It could be obtained from ^{1}H, ^{1}H COSY spectrum, the **H1** was correlated with the hydrogens at 1.90 and 1.42 ppm chemical shifts (marked as **H2** and **H3**, respectively). Thus, **H2** and **H3** were the hydrogens on the β site of amide. Based on the same principle, **H4** and **H5** were the hydrogens on the γ site of amide. **H6** and **H7** were the hydrogens on the δ site of amide. However, **H4** and **H7** were difficult to be distinguished from ^{1}H NMR (400 MHz) and ^{1}H, ^{1}H COSY spectrum.

Then ^{1}H NMR (800 MHz) spectrum of cyclohexyl formamide was tested to distinguish **H4** and **H7**. The integral number of the hydrogen peak at 1.29 ppm was 2, and the integral number of the hydrogen peak at 1.23 ppm was 1. Thus, the hydrogen peak at 1.29 ppm corresponded to **H4** and the hydrogen peak at 1.23 ppm corresponded to **H7**.

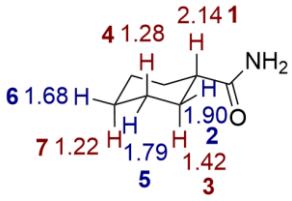


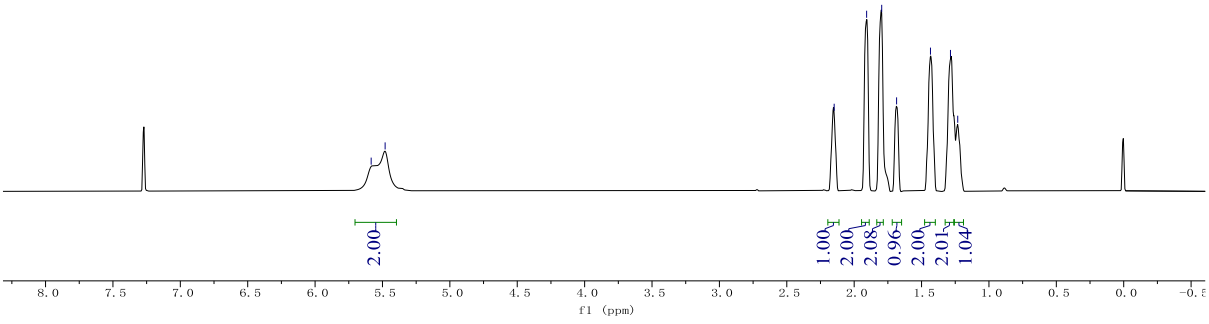


leiaiwen-00006 (d-18-3-H)
800 MHz

5.584
5.480

2.148
1.908
1.796
1.685
1.434
1.285
1.232

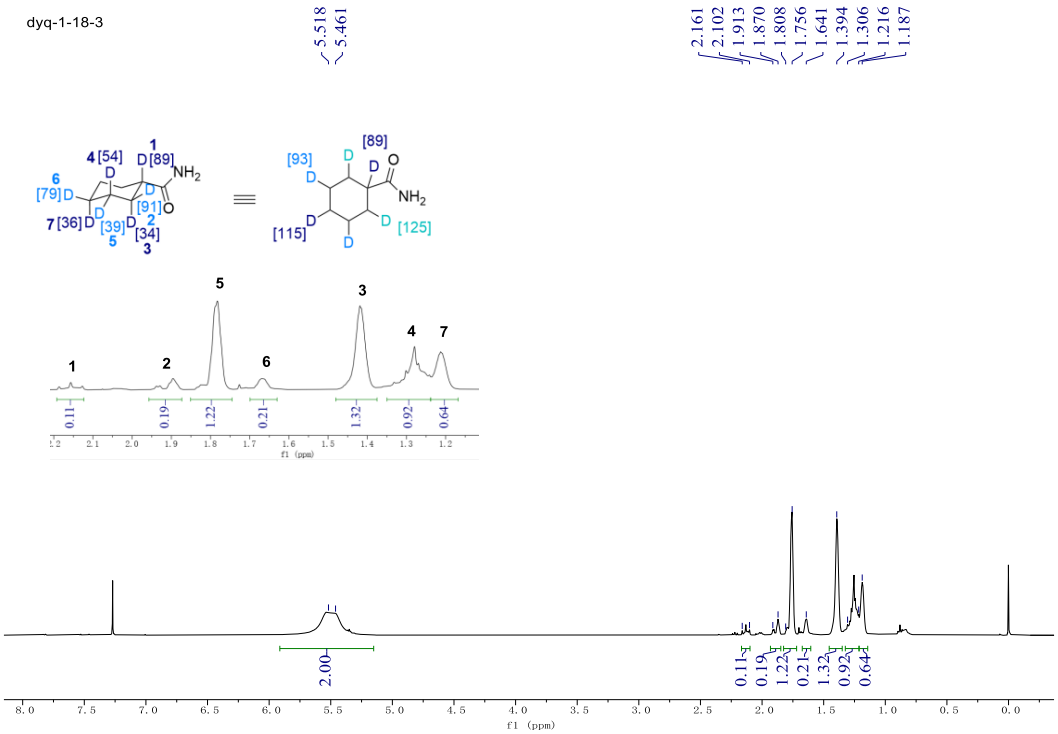




a-2. Cyclohexyl formamide-d_6

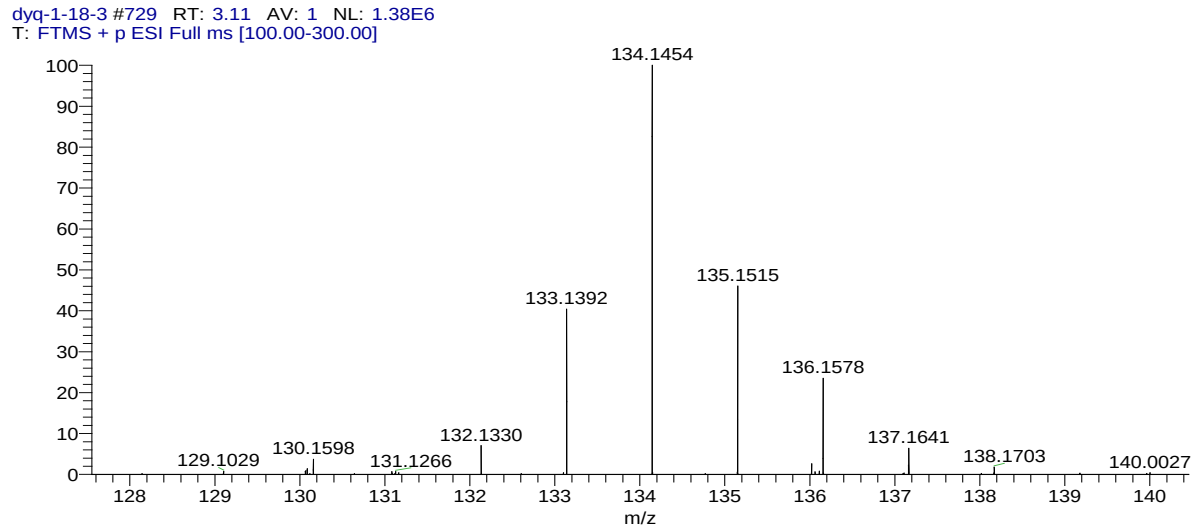
Based on above analytic results in a-1. The spectrum of electrochemical reductive deuteration product, cyclohexyl formamide-d_6, was analyzed as follows. The hydrogen peak at 5.49 ppm corresponded to active hydrogen of amide and was integrated into 2. The hydrogen peak at 2.13 ppm corresponded to **H1** which was at α position of amide. The D-incorporation of this site was (1-0.11)/1 * 100% = 89%. The hydrogen peak at 1.89 ppm corresponded to **H2** which was at β position of amide. The D-incorporation of this site was (2-0.19)/2 * 100% = 91%. The hydrogen peak at 1.78 ppm corresponded to **H5** which was at γ position of amide. The D-incorporation of this site was (2-1.22)/2 * 100% = 39%. The hydrogen peak at 1.64 ppm corresponded to **H6** which was at δ position of amide. The D-incorporation of this site was (1-0.21)/1 * 100% = 79%. The hydrogen peak at 1.39 ppm corresponded to **H3** which was at β position of amide. The D-incorporation of this site was (2-1.32)/2 * 100% = 34%. The hydrogen peak at 1.26 ppm corresponded to **H4** which was at γ position of amide. The D-incorporation of this site was (2-0.92)/2 * 100% = 54%. The hydrogen peak at 1.19 ppm corresponded to **H7** which was at δ position of amide. The D-incorporation of this site was (1-0.64)/1 * 36% = 64%.

Thus, the D-incorporation of α site of amide was 89%. The total D-incorporation of β site of amide was 125%. The total D-incorporation of γ site of amide was 93%. The total D-incorporation of δ site of amide was 115%.



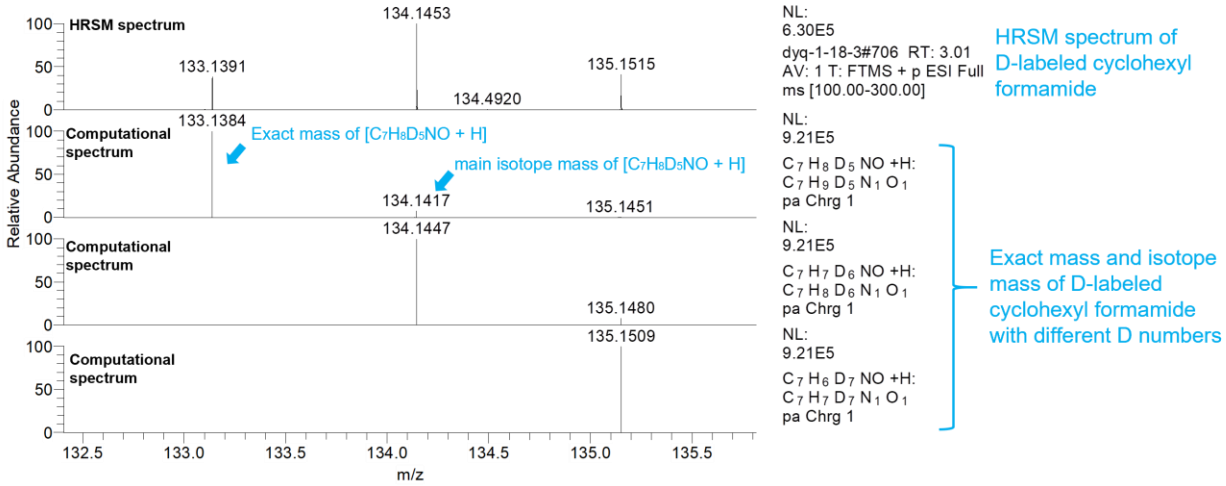
a-3. HRMS analysis of Cyclohexyl formamide-d_6

The full HRMS spectrum of D-labeled cyclohexyl formamide was as follows.



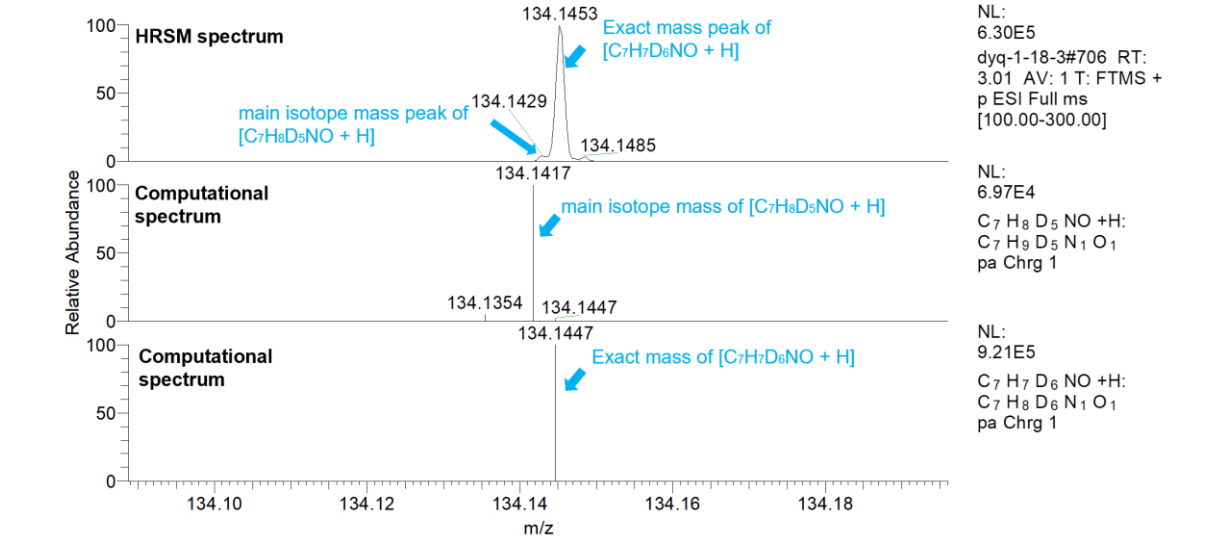
Any compound with definite element composition, including deuterium element, has exact mass and isotope masses. For example, the exact HRMS mass of cyclohexyl formamide labeled with 5 deuterium atoms ($C_7H_8D_5NO$ + H, marked as **amide-d_5**) is 133.1384 and the main isotope mass of that is 134.1417 (see below figure). And the exact HRMS mass of cyclohexyl formamide labeled with 6 deuterium atoms ($C_7H_7D_6NO$ + H, marked as **amide-d_6**) is 134.1447 and the main isotope mass of that is 135.1480.

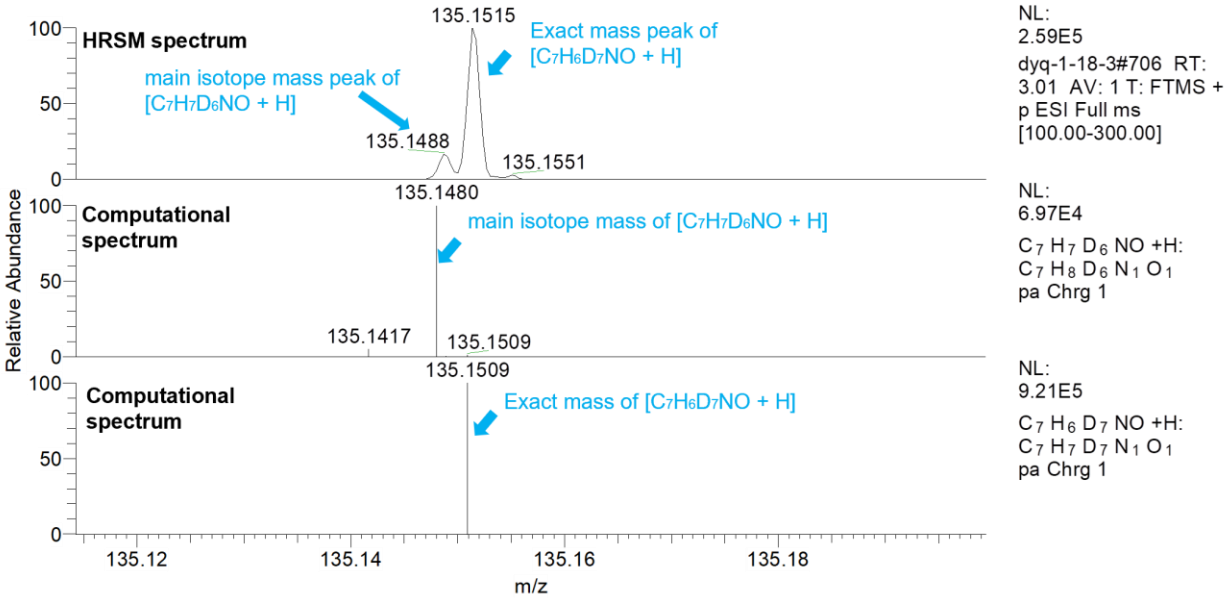
The main isotope mass of **amide-d_5** was close to exact mass of **amide-d_6**, which must be considerate and distinguished for calculating D-incorporation.



By using the HRMS device Orbitrap Elite LTQ XL and setting some parameters, the isotope mass peak of **amide-d_{n-1}** and exact mass peak of **amide-d_n** could be distinguished. For example,

the isotope mass peak of **amide-*d*$_5$** (mass peak of 134.1429) and exact mass peak of **amide-*d*$_6$** (mass peak of 134.1453) could be distinguished (see below figures). And the isotope mass peak of **amide-*d*$_6$** (mass peak of 135.1488) and exact mass peak of **amide-*d*$_7$** (mass peak of 135.1515) could be distinguished.



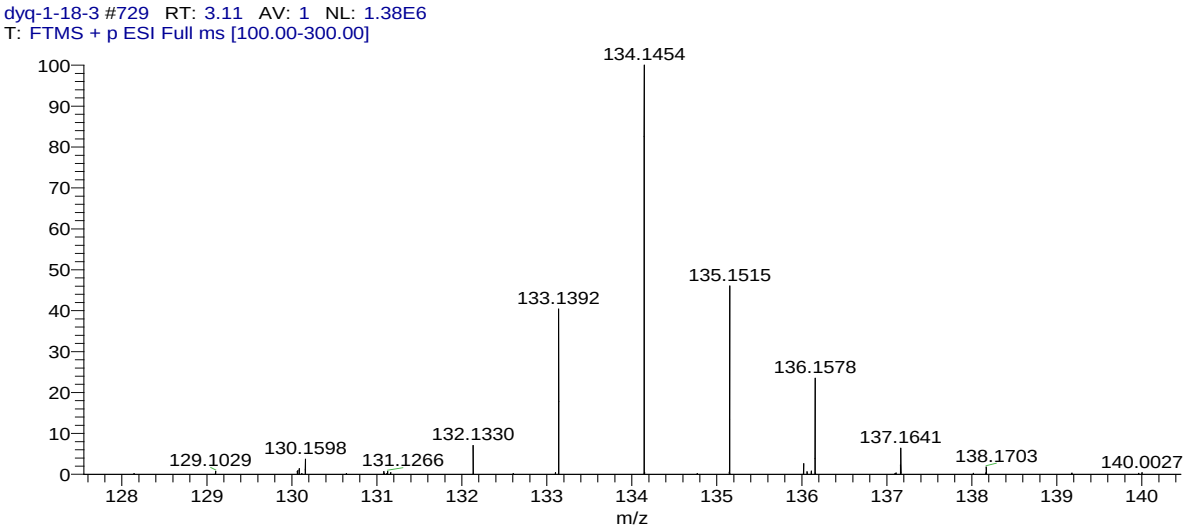


Thus, calculation of total D number could directly use exact mass peak areas of different D number labeled cyclohexyl formamide. And the calculated formula was as follows. (n represents the D number, A_n represents the exact mass peak area of **amide-*d*$_n$**, R_n represents the proportion of exact mass peak area of **amide-*d*$_n$**)

$$\text{Total D number} = \frac{A_1 * 1 + A_2 * 2 + A_3 * 3 + ... + A_n * n}{A_1 + A_2 + A_3 + ... + A_n}$$

$$= R_1 * 1 + R_2 * 2 + R_3 * 3 + ... + R_n * n$$

The proportion area of various mass peak was shown as follows.

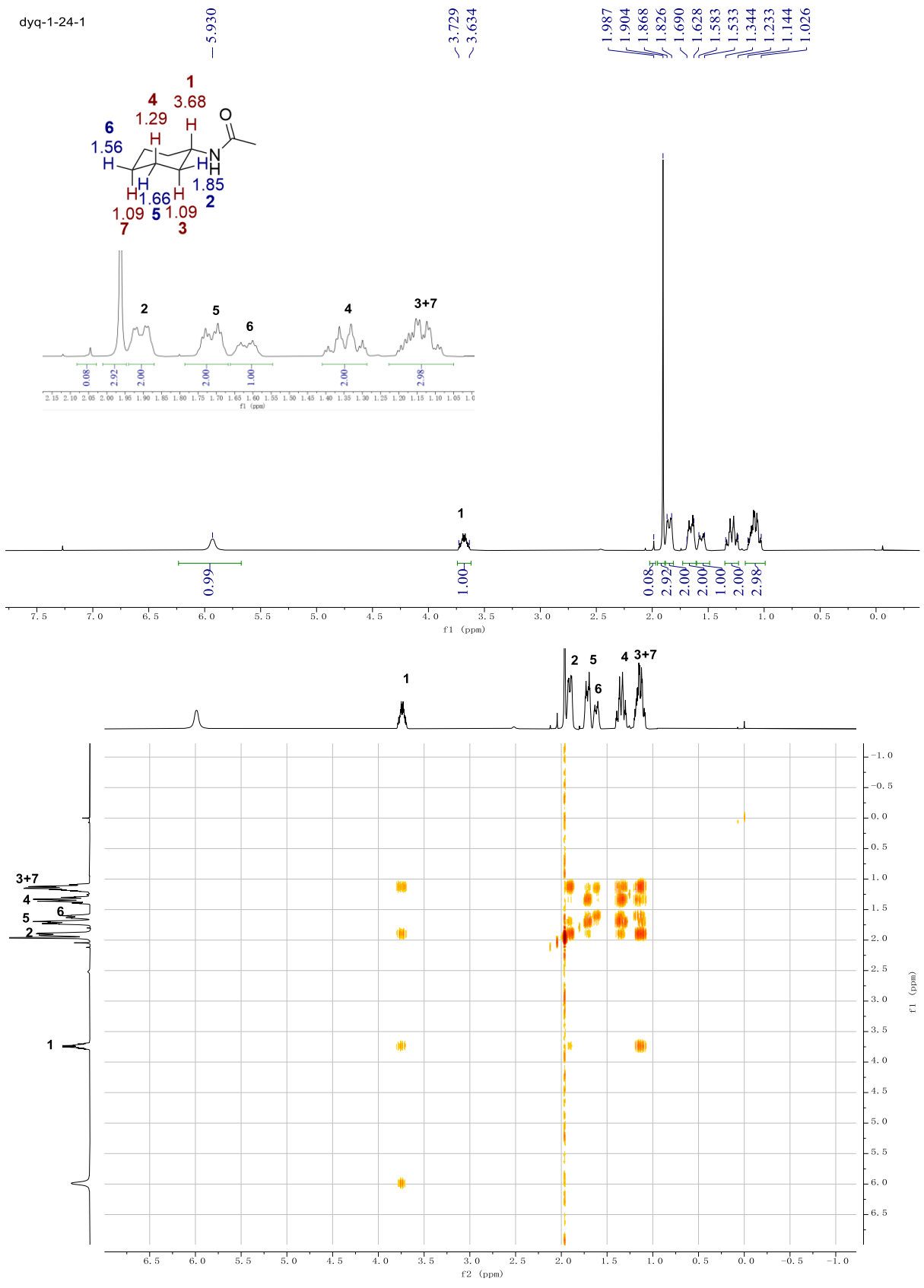


132.1328 ($C_7H_9D_4NO + H^+$, 3%), 133.1391 ($C_7H_8D_5NO + H^+$, 18%), 134.1453 ($C_7H_7D_6NO + H^+$, 47%), 135.1515 ($C_7H_6D_7NO + H^+$, 20%), 136.1578 ($C_7H_5D_8NO + H^+$, 9%), 137.1641 ($C_7H_4D_9NO + H^+$, 3%), 138.1704 ($C_7H_3D_{10}NO + H^+$, 1%).

Thus, the total number of D-labeled cyclohexyl formamide was = 6.3/molecule.

b-1. *N*-Cyclohexylacetamide.

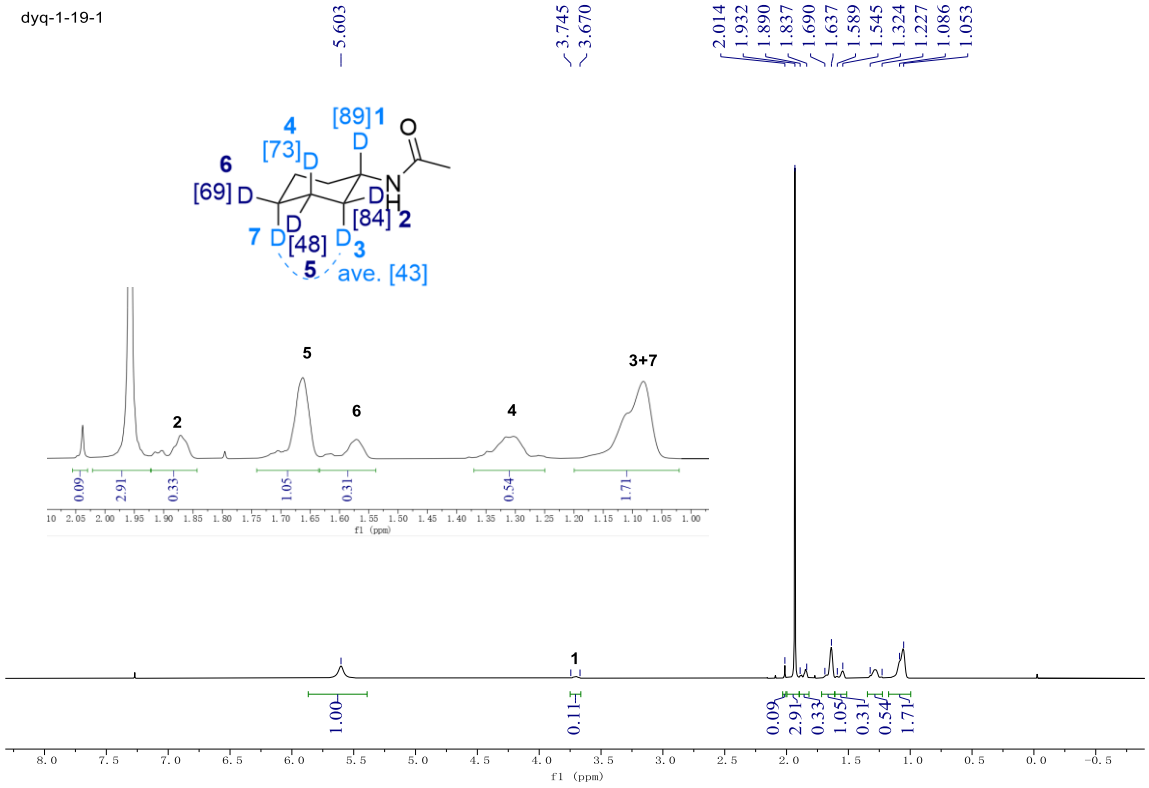
The ^1H NMR spectrum and ^1H, ^1H COSY spectrum of *N*-cyclohexylacetamide were shown as follows. The chemical shift of active H on -NHAc was 5.93 ppm. The chemical shift of the hydrogen on the α position of amine was 3.68 ppm and the H was marked as **H1**. It could be obtained from ^1H, ^1H COSY spectrum that the **H1** was correlated with the hydrogens at 1.85 and 1.09 ppm chemical shifts (marked as **H2** and **H3**, respectively). Thus, **H2** and **H3** were the hydrogens on the β site of amine. Based on the same principle, **H4** and **H5** were the hydrogens on the γ site of amine. **H6** and **H7** were the hydrogens on the δ site of amine. However, **H3** and **H7** were difficult to distinguish from ^1H NMR (400 MHz) and ^1H, ^1H COSY spectrum.


dyq-1-24-1
5.930
3.729
3.634
1.987
1.904
1.868
1.826
1.690
1.628
1.583
1.533
1.344
1.233
1.144
1.026
1
4
3.68
1.29
6
1.56
1.66
1.09
1.09
1.85
7
5
3
2
2
5
6
4
3+7
0.08
2.92
2.00
2.00
1.00
2.00
2.98
0.99
1.00
0.08
2.92
2.00
2.00
1.00
2.00
2.98
f1 (ppm)
f2 (ppm)

b-2. *N*-Cyclohexylacetamide-d_7.

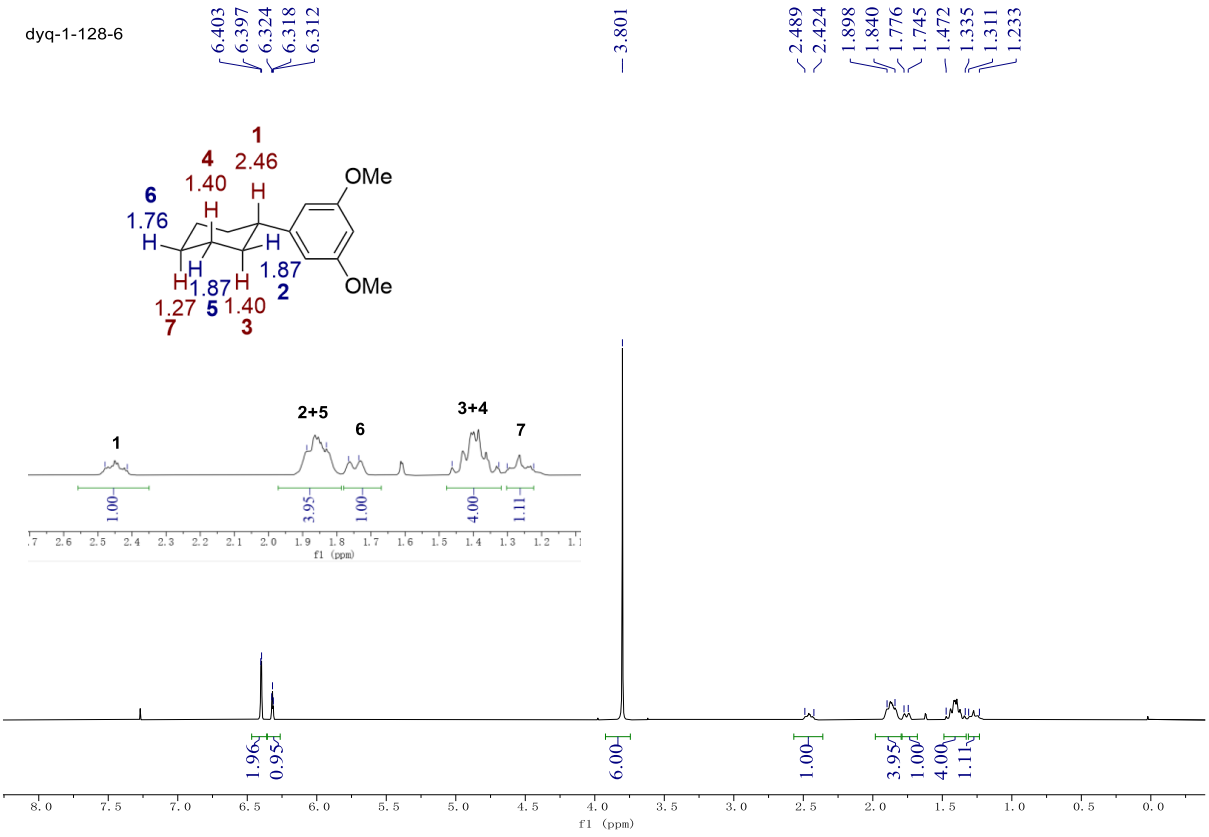
Based on above analytic results in b-1. The spectrum of electrochemical reductive deuteration product, *N*-cyclohexylacetamide-d_7, was analyzed as follows. The hydrogen peak at 5.60 ppm corresponded to active hydrogen of amide and was integrated into 1. The hydrogen peak at 3.71 ppm corresponded to **H1** which was at α position of amide. The D-incorporation of this site was (1-0.11)/1 * 100% = 89%. The hydrogen peak at 1.89-1.84 ppm corresponded to **H2** which was at β position of amide. The D-incorporation of this site was (2-0.33)/2 * 100% = 84%. The hydrogen peak at 1.69-1.64 ppm corresponded to **H5** which was at γ position of amide. The D-incorporation of this site was (2-1.05)/2 * 100% = 48%. The hydrogen peak at 1.59-1.55 ppm corresponded to **H6** which was at δ position of amide. The D-incorporation of this site was (1-0.31)/1 * 100% = 69%. The hydrogen peak at 1.32-1.23 ppm corresponded to **H4** which was at γ position of amide. The D-incorporation of this site was (2-0.54)/2 * 100% = 73%. The hydrogen peak at 1.09-1.05 ppm corresponded to **H3** and **H7** which were at β and δ position of amide. The average D-incorporation of these sites was (3-1.71)/3 * 100% = 43%.

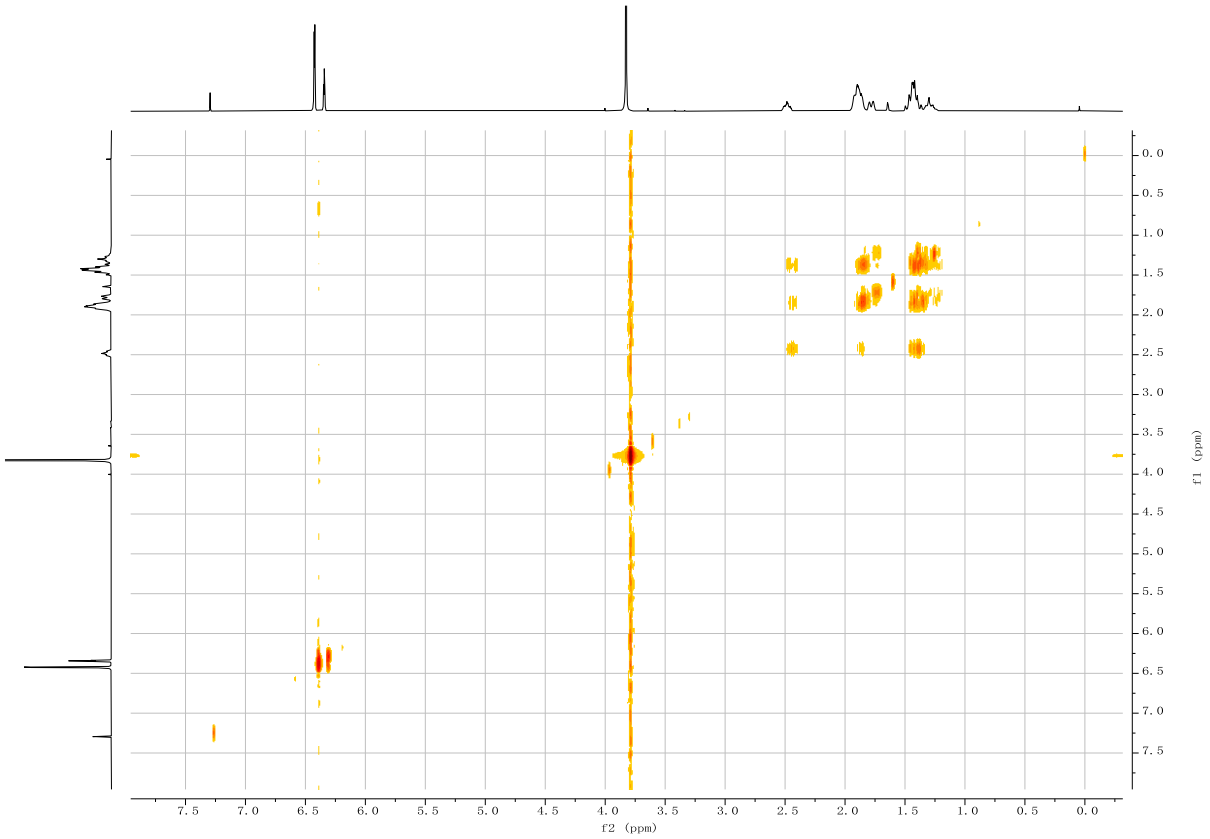
Thus, the D-incorporation of α site of amide was 89%. The total average D-incorporation of β and δ sites of amide was (84*2 + 43*3 + 69)/3 = 122%. The total D-incorporation of γ site of amide was 121%.



c-1. 1-Cyclohexyl-3,5-dimethoxybenzene.

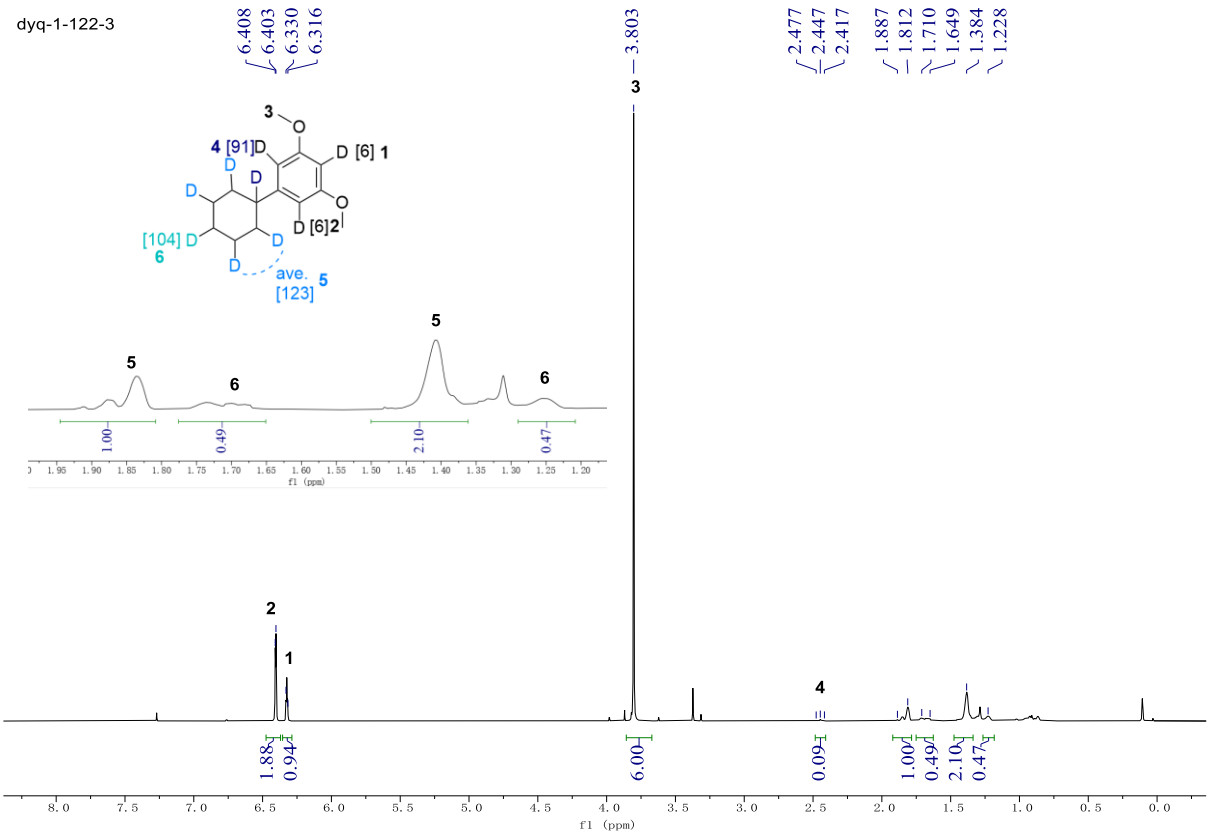
The ^{1}H NMR spectrum and ^{1}H, ^{1}H COSY spectrum of 1-cyclohexyl-3,5-dimethoxybenzene were shown as follows. The chemical shift of the hydrogen on the α position of aromatic ring was 2.46 ppm and the H was marked as **H1**. It could be obtained from ^{1}H, ^{1}H COSY spectrum that the **H1** was correlated with the hydrogens at 1.87 and 1.40 ppm chemical shifts (marked as **H2** and **H3**, respectively). The integral numbers of hydrogen peaks at 1.87 and 1.40 ppm were 4 and 4, respectively. Besides, the integral numbers of hydrogen peaks at 1.76 and 1.27 ppm were 1 and 1, respectively. Thus, chemical shifts of the hydrogens at γ site of aromatic ring (**H4**, **H5**) were also 1.87 and 1.40 ppm. Chemical shifts of the hydrogens at δ site of aromatic ring (**H6**, **H7**) were 1.76 and 1.27 ppm.





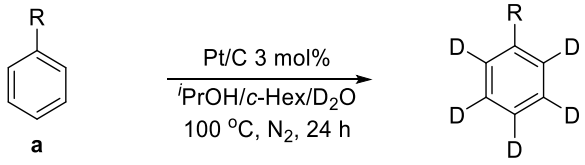
c-2. 1-Cyclohexyl-3,5-dimethoxybenzene-d_7

Based on above analytic results in c-1. The spectrum of electrochemical reductive deuteration product, 1-cyclohexyl-3,5-dimethoxybenzene-d_7, was analyzed as follows. The hydrogen peak at 3.80 ppm corresponded to hydrogens of -OCH_3 and was integrated into 6.00. The hydrogen peak at 2.45 ppm corresponded to the hydrogen at α site of aromatic ring. The D-incorporation of this site was (1-0.09)/1 * 100% = 91%. The hydrogen peaks at 1.85 and 1.38 ppm were correspond to hydrogens at β and γ site of aromatic ring. The average D-incorporation of these sites was (8-1.00-2.10)/4 * 100% = 123%. The hydrogen peaks at 1.68 and 1.23 ppm corresponded to δ site of aromatic ring. The D-incorporation of this site was (2-0.49-0.47)/2 * 100% = 104%.



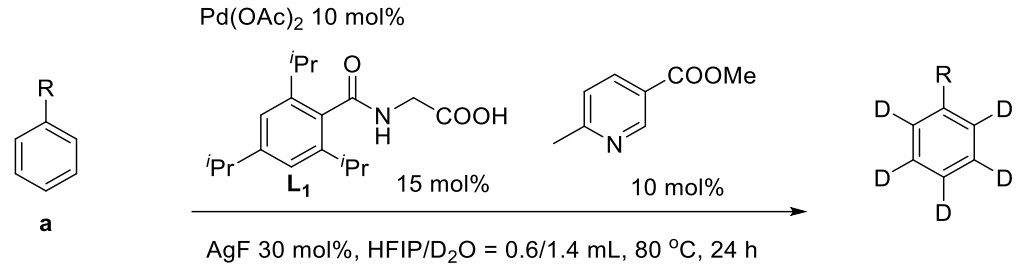
7. Procedure for H/D exchange of arenes

Procedure 1:



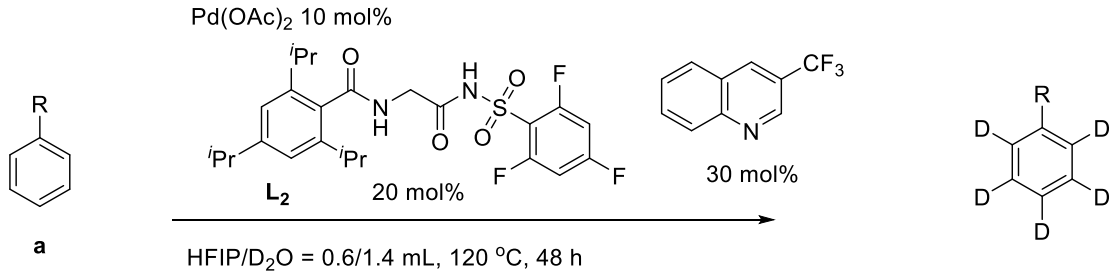
The method was modified from Sajiki's work[1]. In an over dried schlenk tube, substrate **a** 0.4 mmol and Pt/C (20 wt%) 3 mol% were added. After the tube was flushed with N_2 3 times, ^{i}PrOH/c-Hex/D_2O = 0.1/0.9/2 mL were added. Then, the tube was placed into an oil bath and heated to 100 ^{o}C for 24 h. After completion of reaction, the reaction solution was filtered with Na_2SO_4, washed with DCM (3 times) and concentrated by rotary evaporation. The residue was directly used in the followed electro-reductive deuteration reactions without further purification. Substrate **1c** and **2c** were deuterated with this H/D exchange method.

Procedure 2:



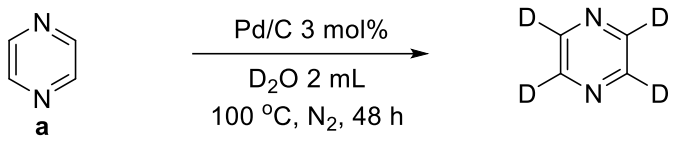
The method was modified from Gemmeren's work[2]. In an over dried schlenk tube, substrate **a** 0.4 mmol, **L₁** 15 mol%, methyl 6-methylnicotinate 10 mol% and AgF 30 mol% were added. After the tube was flushed with N_2 3 times, HFIP/D_2O = 0.6/1.4 mL were added. Then, the tube was placed into an oil bath and heated to 80 °C for 24 h. After completion of reaction, the reaction solution was filtered with Na_2SO_4, washed with DCM (3 times) and concentrated by rotary evaporation. The residue was directly used in the followed electro-reductive deuteration reactions without further purification. Substrate **3-6c**, **8c** and **9c** were deuterated with this H/D exchange method.

Procedure 3:



The method was also modified from Gemmeren's work[2]. In an over dried schlenk tube, substrate **a** 0.4 mmol, **L₂** 20 mol% and 3-(trifluoromethyl)quinoline 30 mol% were added. After the tube was flushed with N_2 3 times, HFIP/D_2O = 0.6/1.4 mL were added. Then, the tube was placed into an oil bath and heated to 120 °C for 48 h. After completion of reaction, the reaction solution was filtered with Na_2SO_4, washed with DCM (3 times) and concentrated by rotary evaporation. The residue was directly used in the followed electro-reductive deuteration reactions without further purification. Substrate **7c** was deuterated with this H/D exchange method.

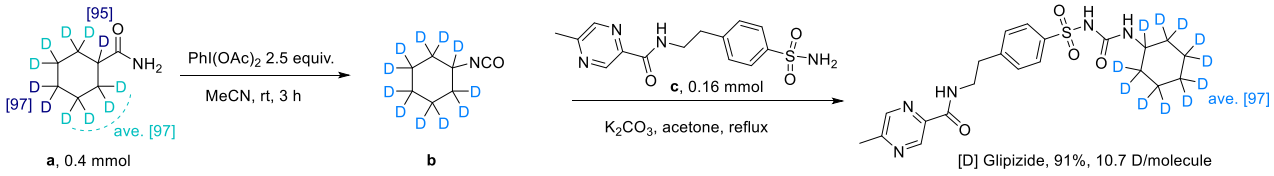
Procedure 4:



In an over dried schlenk tube, substrate **a** 0.4 mmol and Pd/C (10 wt%) 3 mol% were added. After the tube was flushed with N_2 3 times, D_2O 2 mL was added. Then, the tube was placed into an oil bath and heated to 120 °C for 48 h. After completion of reaction, the reaction solution was filtered and the filtrate was directly used in the followed electro-reductive deuteration reactions without further purification. Substrate **10c** was deuterated with this H/D exchange method.

8. Procedure for the synthesis of D-labeling drugs

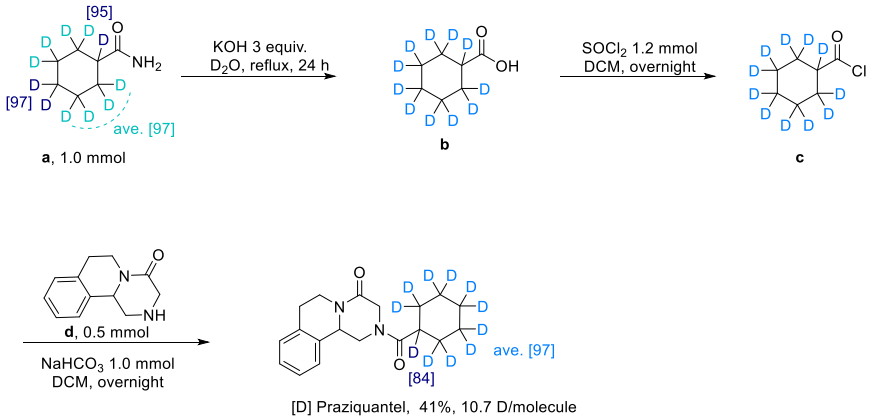
Procedure for synthesis of [D] Glipizide:



Step 1: In an over dried schlenk tube, cyclohexane-d_{11}-1-carboxamide **a** (0.4 mmol) and $PhI(OAc)_2$ (1.0 mmol) were added in MeCN (2 mL). After stirring the solution at room temperature for 3 h, the solution was concentrated and the product **b** was obtained by flash column chromatography on silica gel.

Step 2: In an over dried schlenk tube, substrate **c** (0.16 mmol) and K_2CO_3 (0.30 mmol) were added in acetone (2 mL). After stirring the solution at 61 °C for 7 h, the product obtained in step 1 was added. Then reaction mixture was stirred at 61 °C for another 7 h, followed by at room temperature for 1 h. Then, the reaction solution was concentrated and the product [D] Glipizide was obtained by flash column chromatography on silica gel.

Procedure for synthesis of [D] Praziquantel:

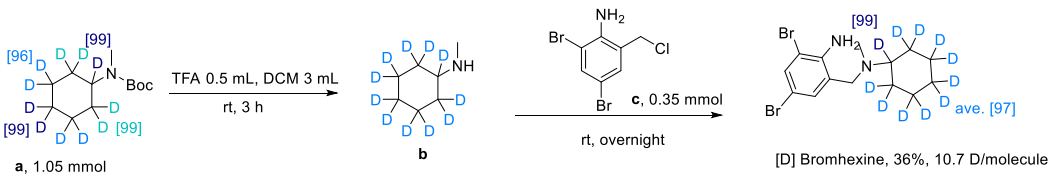


Step 1: In an over dried schlenk tube, cyclohexane-d_{11}-1-carboxamide **a** (1.0 mmol) and KOH (3.0 mmol) were added in D_2O (4 mL). After stirring at 100 ^oC for 3 h, the solution was acidified by HCl and DCM (20 mL) was added. The organic phase was separated and aqueous solution was extracted by DCM 2 times. The combined organic phase was dried by Na_2SO_4 and concentrated under reduced pressure by an aspirator and the crude product **b** was obtained directly using in the following step.

Step 2: In an over dried schlenk tube, product **b** obtained in the step 1 was added in DCM (2 mL). Then $SOCl_2$ (1.2 mmol) was added dropwise. After the reaction mixture was stirred at room temperature overnight, the solution was concentrated under reduced pressure by an aspirator and the crude product **c** was obtained directly using in the following step.

Step 3: In an over dried schlenk tube, amine **d** (0.5 mmol) and $NaHCO_3$ (1.0 mmol) were added in DCM (2 mL). Then product **c** obtained in step 2 was added slowly. After stirring at room temperature overnight, the reaction solution was concentrated under reduced pressure by an aspirator and the pure product [D] Praziquantel was obtained by flash column chromatography on silica gel.

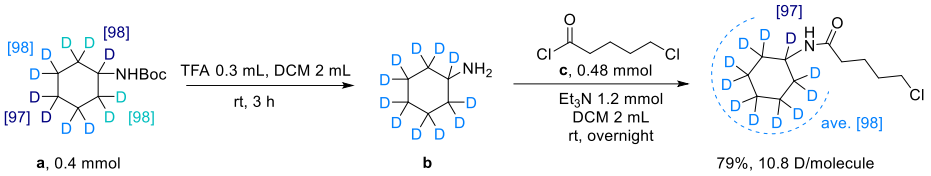
Procedure for synthesis of [D] Bromhexine:



In an over dried schlenk tube, tert-butyl (cyclohexyl-d_{11})(methyl)carbamate **a** 1.05 mmol was added. Then, TFA 0.5 mL and DCM 3 mL were added. The solution was stirred at room

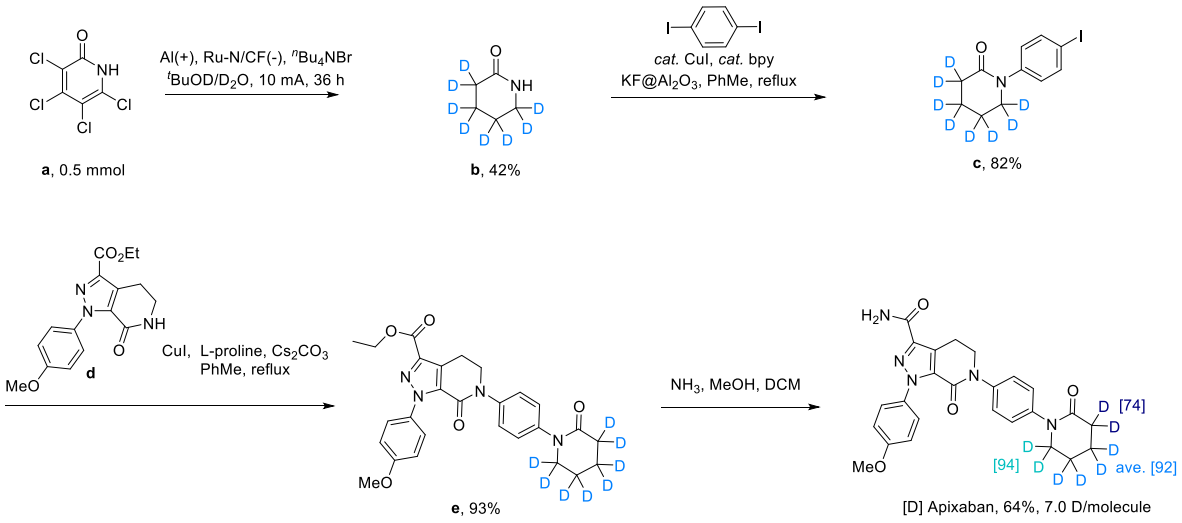
temperature for 3 h. After completion of reaction, NaOH aqueous was added adjusting pH to 14, and then the solution was extracted with DCM (3 times). The combined organic phase was dried by Na_2SO_4, concentrated to 3 mL and then 0.35 mmol **c** was added. After stirring overnight at rt, the reaction mixture was concentrated under reduced pressure by an aspirator, then the pure product was obtained by flash column chromatography on silica gel.

Procedure for synthesis of 5-chloro-N-(cyclohexyl-d_{11})pentanamide:



In an over dried schlenk tube, tert-butyl (cyclohexyl-d_{11})carbamate **a** 0.4 mmol was added. Then, TFA 0.3 mL and DCM 2 mL were added. The solution was stirred at room temperature for 3 h. After completion of reaction, NaOH aqueous was added adjusting pH to 14, and then the solution was extracted with DCM (3 times). The combined organic phase was concentrated to 3 mL and then 0.48 mmol **c**, 1.2 mmol Et_3N were added. After stirring overnight at rt, the reaction mixture was dried by Na_2SO_4, concentrated under reduced pressure by an aspirator, then the pure product was obtained by flash column chromatography on silica gel.

Procedure for synthesis of [D] Apixaban:



Step1: The 3,4,5,6-tetrachloropyridin-2(1*H*)-one **a** (0.5 mmol) and $^nBu_4NBr$ (0.8 mmol) were placed in an oven-dried undivided three-necked bottle (25 mL). The bottle was equipped with a

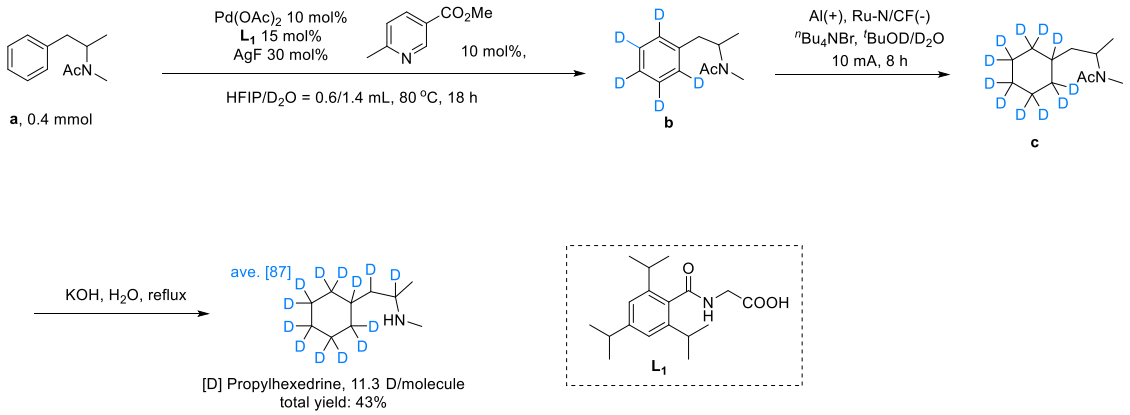
stir bar, an aluminum sheet (10 mm × 15 mm × 0.3 mm) anode and N doped carbon felt supported Ru cathode (10 mm × 15 mm × 3.0 mm). The bottle was flushed with Ar. Degassed ^{t}BuOD (5.0 mL) and degassed D_2O (5.0 mL) were added. The reaction mixture was stirred and electrolyzed at a constant current of 10 mA at room temperature for 36 h. After completion of the reaction, the reaction mixture was concentrated under reduced pressure by an aspirator, then the product **b** was obtained by flash column chromatography on silica gel.

Step 2: This method was adapted from Hosseinzadeh's work[3]. In an over dried schlenk tube, intermediate **b** (0.5 mmol), 1,4-diiodobenzene (2.5 mmol), KF@Al_2O_3 (2.5 mmol), CuI (0.2 mmol) and 1,10-phenanthroline (0.2 mmol) were added. After the tube was flushed with N_2 3 times, 3 mL toluene were added. Then, reaction solution was refluxed for 18 h. After completion of reaction, the reaction solution was concentrated by rotary evaporation and separated by flash column chromatography on silica gel to obtain the product **c**.

Step 3: In an over dried schlenk tube, substrate **d** (0.3 mmol), intermediate **c** (0.41 mmol), Cs_2CO_3 (1.35 mmol), CuI (0.15 mmol) and L-proline (0.15 mmol) were added. After the tube was flushed with N_2 3 times, 3 mL toluene were added. Then, reaction solution was refluxed for 24 h. After completion of reaction, the reaction solution was concentrated by rotary evaporation and separated by flash column chromatography on silica gel to obtain the product **e**.

Step 4: In an over dried schlenk tube, intermediate **e** (0.28 mmol) was added in 2 mL DCM. Then 7.5 mL NH_3 in MeOH solution (7 M) was added. After the reaction was stirred at room temperature for 72 h, the reaction solution was concentrated by rotary evaporation and separated by flash column chromatography on silica gel to obtain the product [D] Apixaban.

Procedure for synthesis of [D] Propylhexedrine:

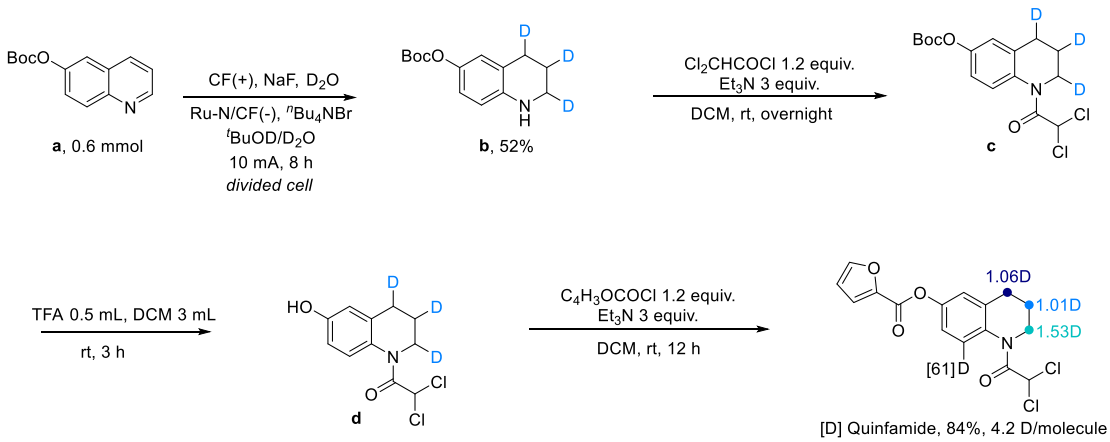


Step 1: In an over dried schlenk tube, substrate **a** 0.4 mmol, **L**$_1$ 15 mol%, methyl 6-methylnicotinate 10 mol% and AgF 30 mol% were added. After the tube was flushed with N_2 3 times, HFIP/D_2O = 0.6/1.4 mL were added. Then, the reaction tube was placed into an oil bath and heated to 80 ^oC for 18 h. After completion of reaction, the reaction solution was filtered with Na_2SO_4, washed with DCM (3 times) and concentrated by rotary evaporation. The residue (intermediate **b**) was directly used in the followed electro-reductive deuteration reactions without further purification.

Step 2: The obtained intermediate **b** and $^nBu_4NBr$ (0.4 mmol) were placed in an oven-dried undivided three-necked bottle (25 mL). The bottle was equipped with a stir bar, an aluminum sheet (10 mm × 15 mm × 0.3 mm) anode and N doped carbon felt supported Ru cathode (10 mm × 15 mm × 3.0 mm). The bottle was flushed with Ar. Degased ^tBuOD (2.5 mL) and degased D_2O (2.5 mL) were added. The reaction mixture was stirred and electrolyzed at a constant current of 10 mA at room temperature for 8 h. After completion of the reaction, the reaction mixture was concentrated under reduced pressure by an aspirator, then the product **c** was obtained by flash column chromatography on silica gel.

Step 3: In an over dried schlenk tube, intermediate **c** and KOH (2 mmol) were added into H_2O (3 mL). After refluxing the solution for 24 h, the solution was extracted with DCM (3 times). The combined organic phase was concentrated under reduced pressure by an aspirator to obtain the [D] Propylhexedrine.

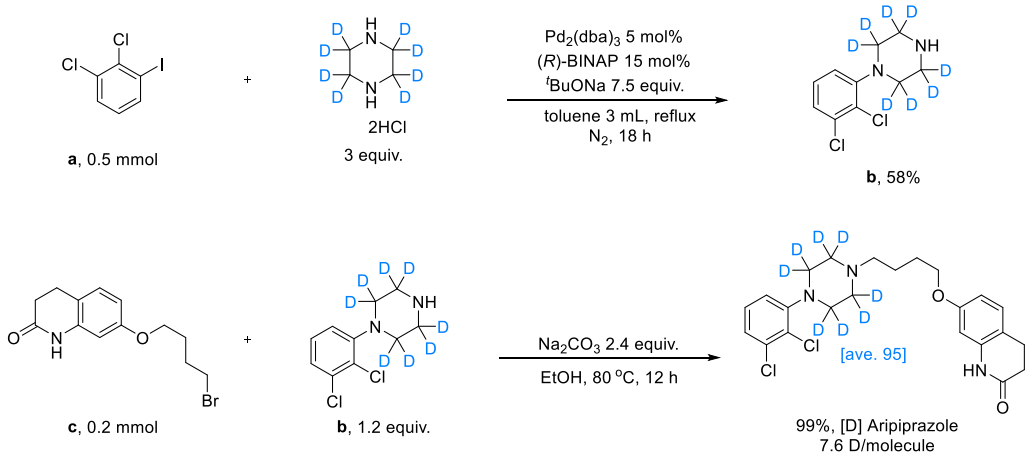
Procedure for synthesis of [D] Quinfamide:



Step 1: In an oven-dried divided cell, the *tert*-butyl quinolin-6-yl carbonate **a** (0.6 mmol) and $^{n}Bu_4NBr$ (0.8 mmol) were placed in the cathode cell, and NaF (0.8 mmol) was placed in the anode cell. The cell was equipped with a stir bar, a carbon felt anode (10 mm × 15 mm × 3.0 mm) and N doped carbon felt supported Ru cathode (10 mm × 15 mm × 3.0 mm). The cell was flushed with Ar. Degased $^{t}BuOD$ (5.0 mL) and D_2O (5.0 mL) were added in the cathode cell. D_2O (10 mL) was added in the anode cell. The reaction mixture was stirred and electrolyzed at a constant current of 10 mA at room temperature for 8 h. After completion of the reaction, the reaction mixture was extracted three times with ethyl acetate and the combined organic phase was removed under reduced pressure by an aspirator, then the pure product **b** was obtained by flash column chromatography on silica gel.

Step 2: In an over dried schlenk tube, intermediate **b** (1.26 mmol) was added. Then, $Cl_2CHCOCl$ (1.2 equiv.), Et_3N (3 equiv.) and DCM 3 mL were added. The solution was stirred at room temperature overnight. After completion of reaction, the reaction mixture was extracted with DCM (3 times). The combined organic phase was dried by Na_2SO_4, concentrated under reduced pressure by an aspirator and then TFA 0.5 mL and DCM 3 mL were added. After stirring the solution at room temperature for 3 h, NaOH aqueous was added to adjust pH to 14, and then the solution was extracted with DCM (3 times). The combined organic phase was concentrated to 3 mL and then 2-furoyl chloride (1.2 equiv.) and Et_3N (3 equiv.) were added. After stirring overnight at rt, the reaction mixture was concentrated under reduced pressure by an aspirator, then the pure product was obtained by flash column chromatography on silica gel.

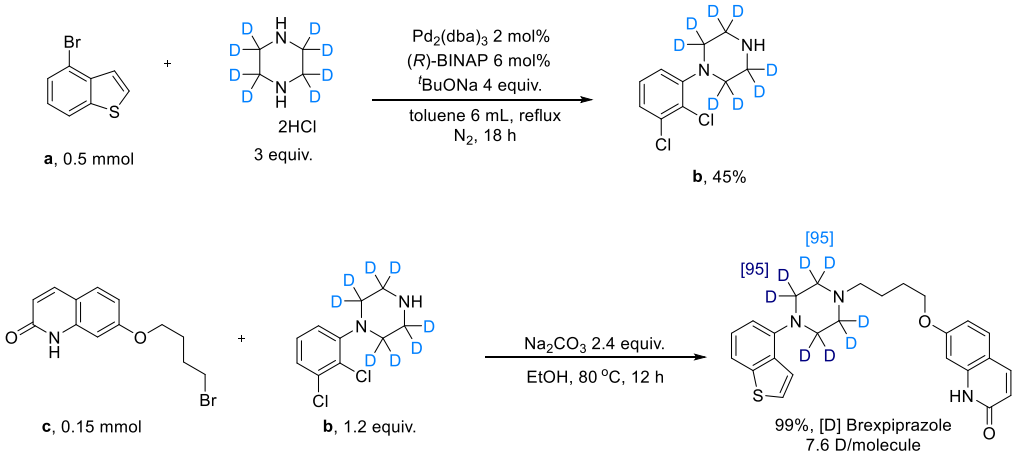
Procedure for synthesis of [D] Aripiprazole:



Step 1: In an over dried schlenk tube, substrate **a** (0.5 mmol), piperazine hydrochloride-d_8 (1.5 mmol), $Pd_2(dba)_3$ (5 mol%), (*R*)-BINAP (15 mol%), ^{t}BuONa (3.75 mmol) were added. After the tube was flushed with N_2 3 times, 3 mL toluene were added. Then, reaction solution was refluxed for 18 h. After completion of reaction, the reaction solution was concentrated by rotary evaporation and separated by flash column chromatography on silica gel to obtain the product **b**.

Step 2: In an over dried schlenk tube, substrate **c** (0.2 mmol), intermediate product **b** (0.24 mmol), Na_2CO_3 (0.48 mmol) were added into 2 mL EtOH. Then, reaction solution was heated at 80 ^{o}C for 12 h. After completion of reaction, the reaction solution was concentrated by rotary evaporation and separated by flash column chromatography on silica gel to obtain the product [D] Aripiprazole.

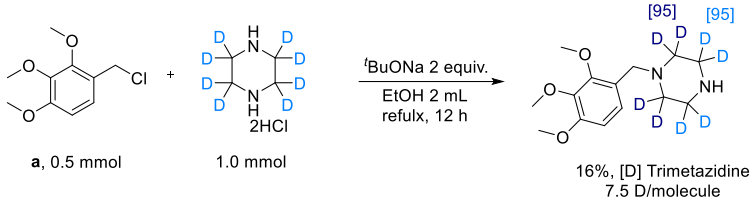
Procedure for synthesis of [D] Brexpiprazole:



Step 1: In an over dried schlenk tube, substrate **a** (0.5 mmol), piperazine hydrochloride-d_8 (1.5 mmol), $Pd_2(dba)_3$ (2 mol%), (*R*)-BINAP (6 mol%), ^{t}BuONa (2.0 mmol) were added. After the tube was flushed with N_2 3 times, 6 mL toluene was added. Then, reaction solution was refluxed for 18 h. After completion of reaction, the reaction solution was concentrated by rotary evaporation and separated by flash column chromatography on silica gel to obtain the product **b**.

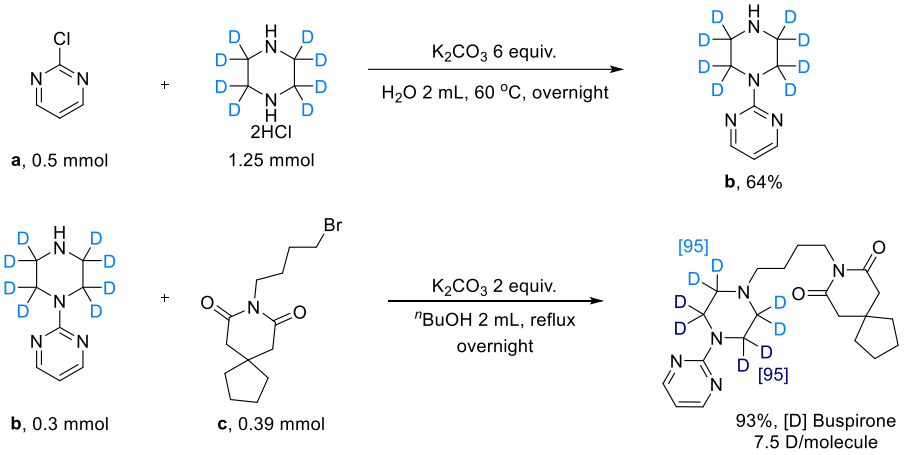
Step 2: In an over dried schlenk tube, substrate **c** (0.15 mmol), intermediate product **b** (0.18 mmol) and Na_2CO_3 (0.36 mmol) were added into 2 mL EtOH. Then, reaction solution was heated at 80 ^{o}C for 12 h. After completion of reaction, the reaction solution was concentrated by rotary evaporation and separated by flash column chromatography on silica gel to obtain the product [D] Brexpiprazole.

Procedure for synthesis of [D] Trimetazidine:



In an over dried schlenk tube, substrate **a** (0.5 mmol), piperazine hydrochloride-d_8 (1.0 mmol), ^{t}BuONa (1.0 mmol) were added into 2 mL EtOH. Then, reaction solution was refluxed for 12 h. After completion of reaction, the reaction solution was concentrated by rotary evaporation and separated by flash column chromatography on silica gel to obtain the product [D] Trimetazidine.

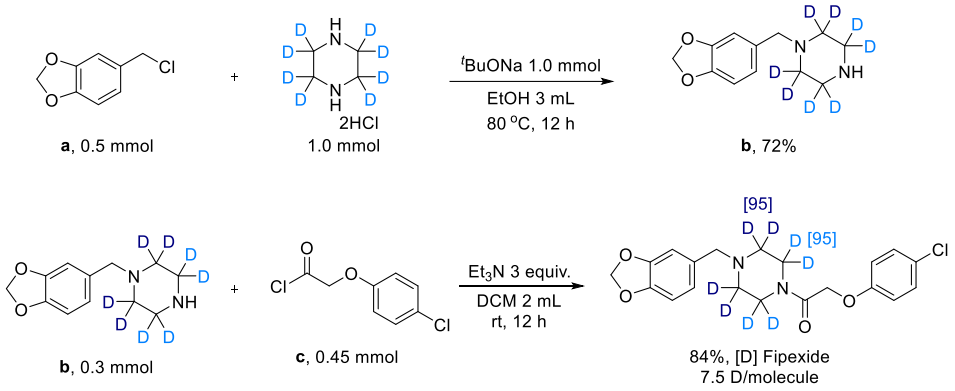
Procedure for synthesis of [D] Buspirone:



Step 1: In an over dried schlenk tube, substrate **a** (0.5 mmol), piperazine hydrochloride-d_8 (1.25 mmol) and K_2CO_3 (3.0 mmol) were added into 2 mL H_2O. Then, reaction solution was heated overnight at 60 °C. After completion of reaction, the reaction solution was concentrated by rotary evaporation and separated by flash column chromatography on silica gel to obtain the product **b**.

Step 2: In an over dried schlenk tube, intermediate product **b** (0.3 mmol), bromide **c** (0.39 mmol) and K_2CO_3 (0.6 mmol) were added into 2 mL ^{n}BuOH. Then, reaction was refluxed overnight. After completion of reaction, the reaction solution was concentrated by rotary evaporation and separated by flash column chromatography on silica gel to obtain the product [D] Buspirone.

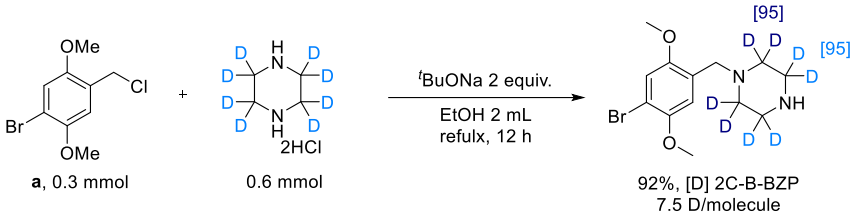
Procedure for synthesis of [D] Fipexide:



Step 1: In an over dried schlenk tube, chloride **a** (0.5 mmol), piperazine hydrochloride-d_8 (1.0 mmol) and ^{t}BuONa (1.0 mmol) were added into 3 mL EtOH. Then, the tube was placed into an oil bath and heated to 80 ^{o}C for 12 h. After completion of reaction, the reaction solution was concentrated by rotary evaporation and separated by flash column chromatography on silica gel to obtain the product **b**.

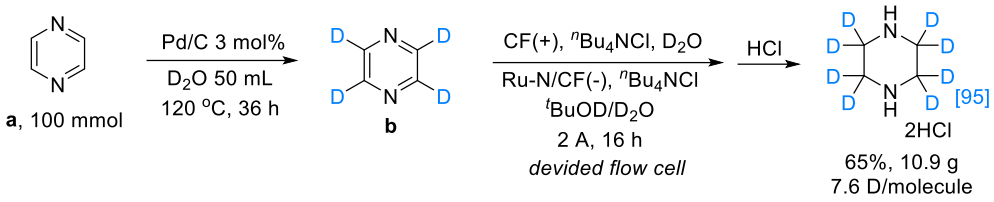
Step 2: In an over dried schlenk tube, intermediate product **b** (0.3 mmol), acyl chloride **c** (0.45 mmol), Et_3N (0.9 mmol) were added into 2 mL DCM. Then, reaction solution was stirred at room temperature for 12 h. After completion of reaction, the reaction solution was concentrated by rotary evaporation and separated by flash column chromatography on silica gel to obtain the product [D] Fipexide.

Procedure for synthesis of [D] 2C-B-BZP:



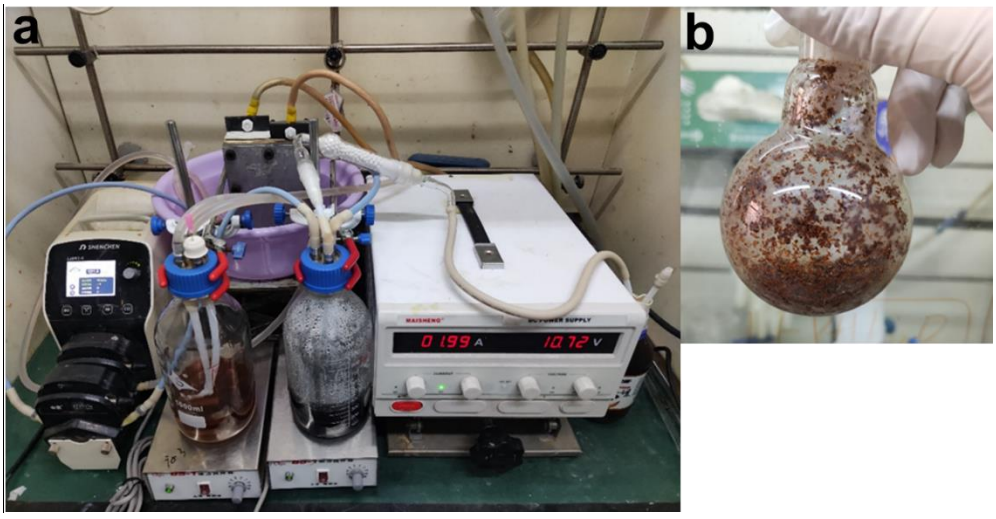
In an over dried schlenk tube, chloride **a** (0.3 mmol), piperazine hydrochloride-d_8 (0.6 mmol), ^{t}BuONa (0.6 mmol) were added into 2 mL EtOH. Then, reaction was refluxed for 12 h. After completion of reaction, the reaction solution was concentrated by rotary evaporation and separated by flash column chromatography on silica gel to obtain the product [D] 2C-B-BZP.

9. Procedure for the synthesis of 10 g scale deuterated piperazine hydrochloride



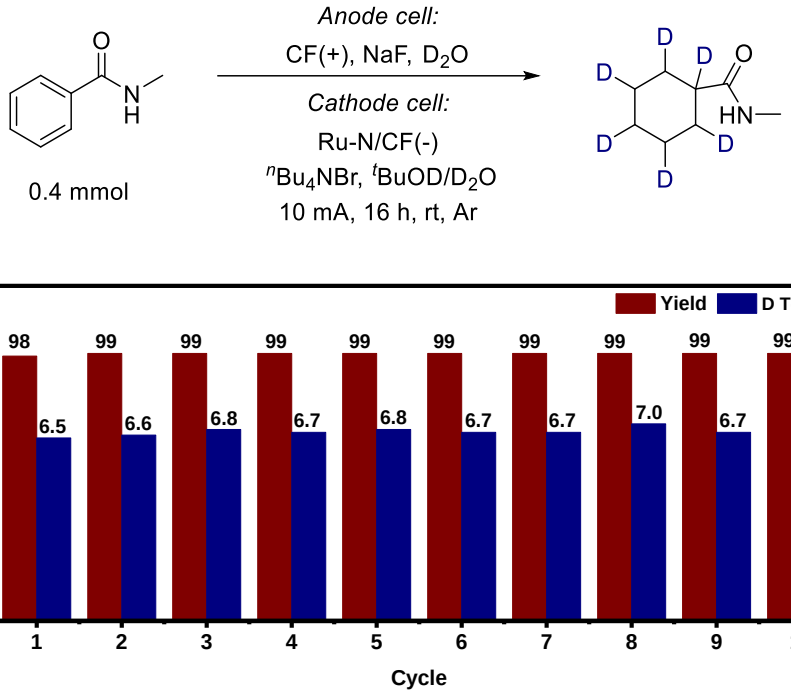
Step 1: In an over dried sealed tube, pyrazine **a** (100 mmol) and Pd/C (3 mol%) were added. After the tube was flushed with N_2 3 times, D_2O 50 mL was added. Then, reaction was heated at 120 °C for 36 h. After completion of reaction, the reaction solution was filtered to filter out Pd/C. The filtrate was directly used in the followed step.

Step 2: As shown in Supplementary Figure S9a, the filtrate in step 1, 250 mL D_2O, 300 mL ^{t}BuOD and ^{n}Bu$_4$NCl (0.2 M) were placed in a bottle connected to cathode cell. ^{n}Bu$_4$NCl (0.2 M) and 400 mL D_2O were placed in a bottle connected to anode cell. The two cell was separated by an anion exchange membrane. One peristaltic pump was used to circulate the liquid in the anode and cathode reaction cell, respectively. A carbon felt (135 mm × 75 mm × 3.0 mm) was used as anode and N doped carbon felt supported Ru electrode (135 mm × 75 mm × 3.0 mm) was used as cathode. After two bottle was bubbled with N_2 for 30 min. The reaction mixture was electrolyzed at a constant current of 2 A at room temperature for 16 h. After completion of the reaction, the cathode solution was acidified by HCl. The piperazine hydrochloride-d_8 was obtained by recrystallization (2 times) with water and ethanol (Supplementary Figure S9b).



Supplementary Figure S9. (a) Electrochemical flow device. (b) Obtained piperazine hydrochloride-d_8.

10. Recycling experiment

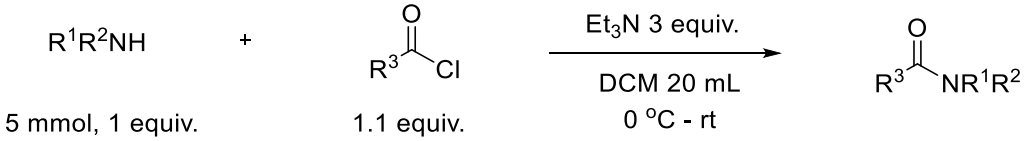


Supplementary Figure S10. Recycle experiment of electrochemical reductive deuteration of N-methylbenzamide catalyzed by Ru-N/CF.

The yield and total D number had almost no change in 10 cycles of arene electroreduction, which indicated that the activity of the Ru-N/CF was very stable.

11. Procedure for the synthesis of starting materials

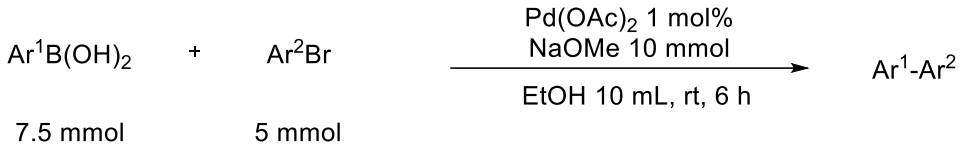
General procedure 1: procedure for the synthesis of amides



Amine (5 mmol, 1 equiv.) was dissolved in 20 mL DCM, followed by adding Et_3N (15 mmol, 3 equiv.). Then the solution was placed on an ice bath. Acyl chloride (5.5 mmol, 1.1 equiv.) was added dropwise to the reaction mixture over 5 mins. The reaction was then allowed to heat to room temperature and stirred overnight. After completion of the reaction, 30 mL H_2O was added and the solution was extracted with DCM (3 times). Then combined organic phase was dried over

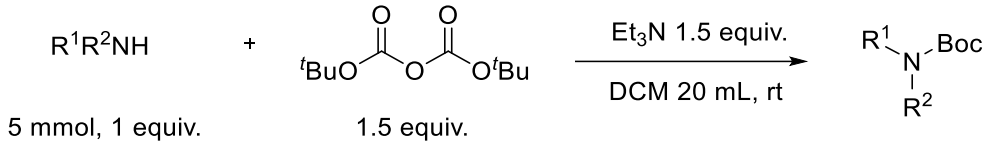
anhydrous Na_2SO_4 and concentrated in vacuo. The product was purified the product by flash column chromatography (eluent: EA) to obtain the corresponding product.

General procedure 2: procedure for the synthesis of biaryl substrates



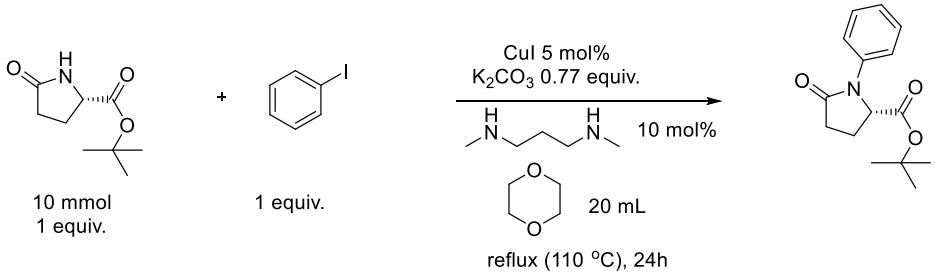
The method was modified from Li's work[4]. A mixture of aryl halide (5.0 mmol), arylboronic acid (7.5 mmol), $Pd(OAc)_2$ (1 mol%), NaOMe (10 mol) and EtOH (10 mL) were stirred at room temperature for 6 h. After the mixture had been filtered and concentrated, the residue was then purified by flash column chromatography to afford the corresponding coupled product.

Produce for the synthesis of Boc-amine



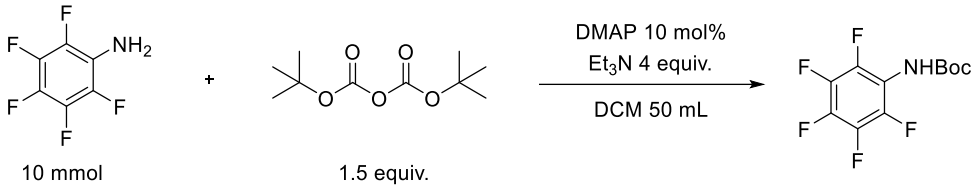
Amine (5 mmol, 1 equiv.), Et_3N (7.5 mmol, 1.5 equiv.) and $O(Boc)_2$ (7.5 mmol, 1.5 equiv.) were dissolved in 20 mL DCM and stirred overnight at room temperature. After completion of the reaction, 30 mL H_2O was added and the solution was extracted with DCM (3 times). Then combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The product was purified the product by flash column chromatography (eluent: DCM) to obtain the corresponding product.

Produce for the synthesis of N-aryl-2- pyrrolidinone

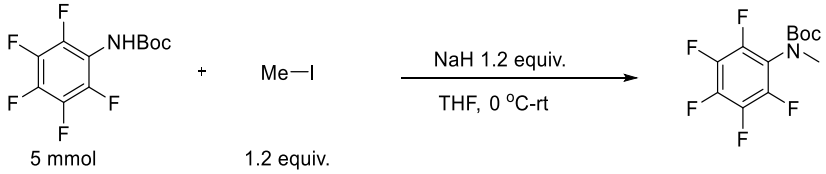


The method was modified from Lacour's work[5]. 2-pyrrolidinone (1 equiv.), iodobenzene (1 equiv.), anhydrous K_2CO_3 (0.77 equiv.), CuI (5 mol%) and *N*, *N*′-dimethyl-1,3-propanediamine (10 mol%) were dissolved in dry 1,4- dioxane (0.65 M) and the mixture was refluxed for 24 h. Then, the reaction mixture was cooled at room temperature and extracted with ethyl acetate (3 times). The combined organic parts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Eventually, the crude reaction mixture was purified by usual silica gel column chromatography (eluent: PE/EA = 2/1) to afford the desired *N*-aryl-2-pyrrolidinone.

Produce for the synthesis of pentafluoro-*N*-methyl-Boc-aniline

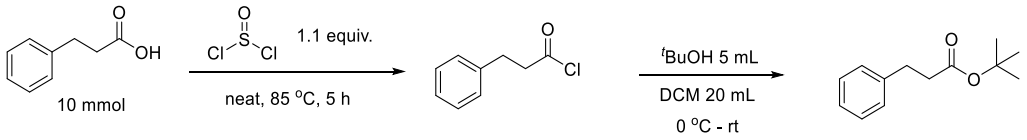


Amine (10 mmol, 1 equiv.), Et_3N (40 mmol, 4.0 equiv.), DMAP (1 mmol, 10 mol%) and $O(Boc)_2$ (15 mmol, 1.5 equiv.) were dissolved in 50 mL DCM and the mixture was stirred overnight at room temperature. After completion of the reaction, 50 mL H_2O was added and the solution was extracted with DCM (3 times). Then combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The product was purified the product by flash column chromatography (eluent: DCM) to obtain *N*-Boc-2,3,4,5,6-pentafluoroaniline.



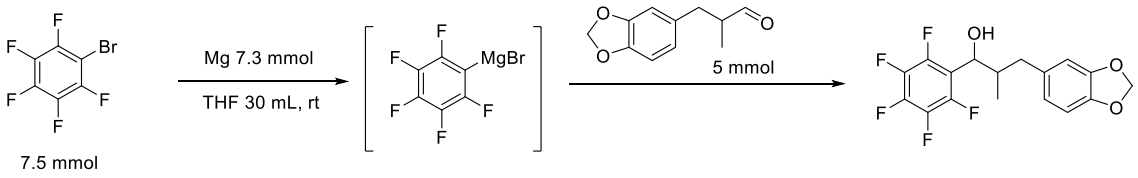
To a solution of *N*-Boc-pentafluoroaniline (5 mmol, 1.0 equiv.) in THF (1.2 M), NaH (1.2 equiv.) and MeI (1.2 equiv.) were added at 0 °C. After being stirred at room temperature for 12 h, the reaction mixture was poured into water and then the solution was extracted with CH_2Cl_2 (3 times), dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography (eluent: DCM) on silica gel to give the corresponding product.

Produce for the synthesis of tert-butyl 3-phenylpropanoate



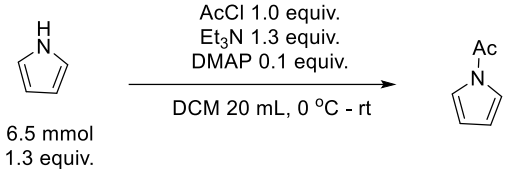
Dissolve the acid (10 mmol, 1 equiv.) in thionyl chloride (11 mmol, 1.1 equiv.) and reflux for 5 h. After reaction, thionyl chloride was distilled under reduced pressure. The obtained crude acyl chloride product was then dissolved in 20 mL DCM and placed on an ice bath. ^{t}BuOH (5 mL) was added dropwise to the reaction mixture over 5 mins. Then the reaction was allowed to heat to room temperature and stirred overnight. After completion of reaction, the reaction solution was concentrated under vacuo. The residue was purified by column chromatography (eluent: DCM) on silica gel to give the corresponding product.

Produce for the synthesis of alcohols



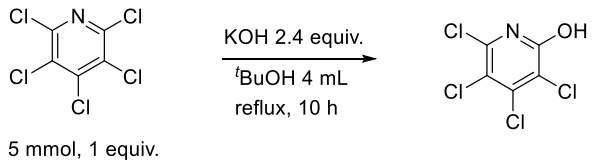
The method was modified from Filhol's work[6]. Magnesium turnings (7.3 mmol, 175.2 mg) were placed in a 100 mL three necked flask equipped with a magnetic stir bar and a dropping funnel. Place the setup under an inert atmosphere of N_2. Cover the magnesium turnings with 30 mL of THF. Charge the dropping funnel with a portion of 1-bromo-2,3,4,5,6-pentafluorobenzene (7.5 mmol) via a syringe. Add a few drops of bromopentafluorobenzene to the flask to initiate the formation of the magnesium derivative. Add the left solution dropwise to the flask. The reaction was stirred at room temperature until the magnesium turnings disappear. Then aldehyde (5 mmol) was injected into the dropping funnel and added dropwise to the reaction mixture. After stirred for 12 h, the reaction was quenched by 50 mL water. The reaction solution was extracted by DCM (3 times), dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography (eluent: PE/EA) on silica gel to give the corresponding product.

Produce for the synthesis of 1-(1*H*-pyrrol-1-yl)ethan-1-one



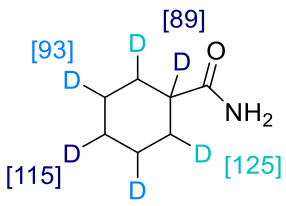
The method was modified from Wu's work[7]. Add benzoyl chloride (1.0 equiv.) dropwise to a stirred solution of pyrrole (1.3 equiv.), triethylamine (1.3 equiv.) and DMAP (0.1 equiv.) in CH_2Cl_2 (10 mL) at 0 °C. Then, the solution was warmed to room temperature. Stir the mixture till the end of the reaction. Then, the reaction mixture was diluted with ethyl acetate and washed with 1 M HCl (10 mL), saturated aqueous $NaHCO_3$ (10 mL) and brine (10 mL) in turn. Next, the residue was dried over Na_2SO_4, filtered, concentrated in vacuo and purified by column chromatography (eluent: PE/EA) on silica gel to give the corresponding product.

Produce for the synthesis of 3,4,5,6-tetrachloropyridin-2-ol



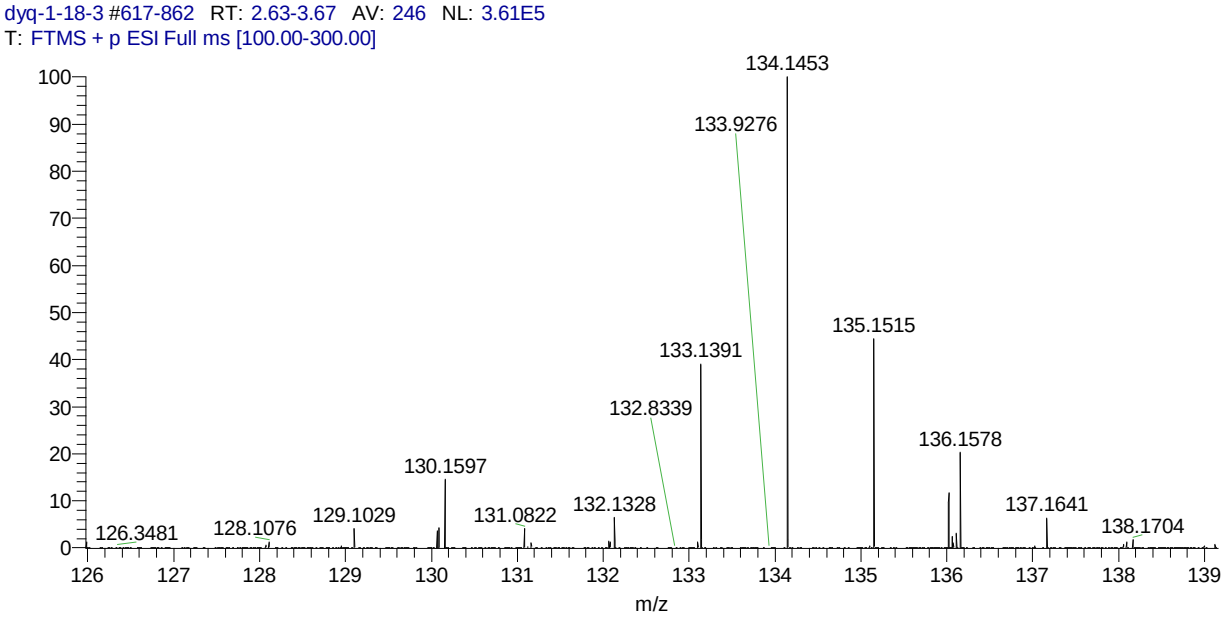
The method was modified from Bhalerao's work[8]. Perchloropyridine (1.26 g, 5 mmol) and potassium hydroxide (672 mg, 12 mmol) were refluxed in tertiary butanol (4 mL) for 10 h. The reaction mixture was cooled, solvent was removed under reduced pressure. The residue was dissolved in water (20 mL) and extracted with dichloromethane to remove the unreacted product. The aqueous layer was acidified with conc. hydrochloric acid and extracted with dichloromethane. Then, the organic layer was dried over Na_2SO_4, concentrated in vacuo and purified by column chromatography to afford the tetrachloropyridin-2-ol.

12. Characterization of products

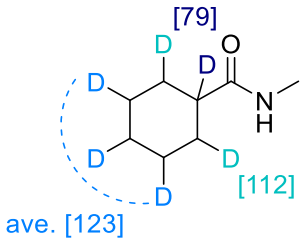


Cyclohexane-1,2,3,4,5,6-*d*$_6$-1-carboxamide (1b). The title product was obtained with 82% yield (50.3 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.49 (d, *J* = 23.2 Hz, 2.00H), 2.16-2.10 (m, 0.11H), 1.91-1.87 (m, 0.19H), 1.81-1.76 (m, 1.22H), 1.64 (s, 0.21H), 1.39 (s, 1.32H), 1.31-1.22 (m, 0.92H), 1.19 (s, 0.64H); ^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 177.46, 43.16 (m, labeled), 28.55 (m, labeled), 24.79 (m, labeled).

Deuterium incorporation: 6.4 D/molecule (^{1}H-NMR), 6.3 D/molecule [HRMS (ESI)].

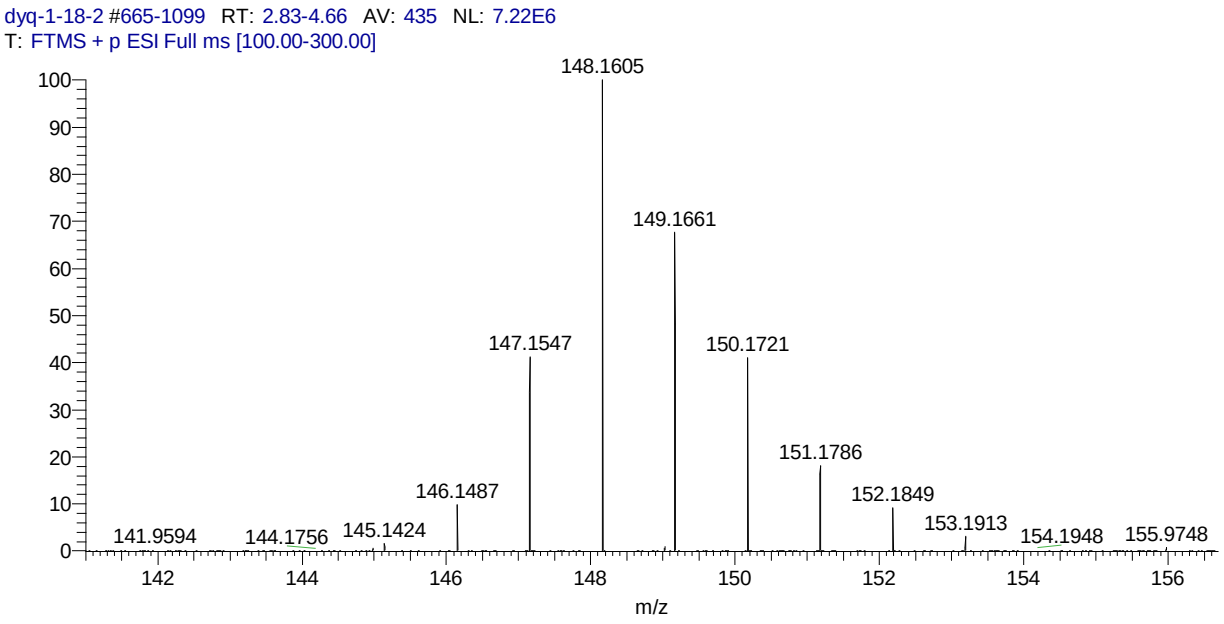


132.1328 ($C_7H_9D_4NO + H^+$, 3%), 133.1391 ($C_7H_8D_5NO + H^+$, 18%), 134.1453 ($C_7H_7D_6NO + H^+$, 47%), 135.1515 ($C_7H_6D_7NO + H^+$, 20%), 136.1578 ($C_7H_5D_8NO + H^+$, 9%), 137.1641 ($C_7H_4D_9NO + H^+$, 3%), 138.1704 ($C_7H_3D_{10}NO + H^+$, 1%).

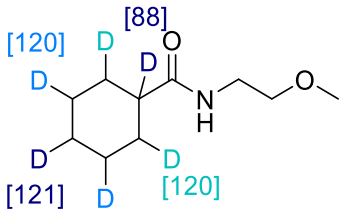


***N*-methylcyclohexane-1,2,3,4,5,6-*d*$_6$-1-carboxamide (2b)**, The title product was obtained with 98% yield (57.9 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.94 (s, 1.00H), 2.75 (d, *J* = 4.8 Hz, 3.00H), 2.07-2.01 (m, 0.21H), 1.81-1.77 (m, 0.30H), 1.74-1.70 (m, 1.09H), 1.63-1.59 (m, 0.26H), 1.36 (s, 1.46H), 1.18-1.13 (m, 0.97H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.01, 45.12 (m, labeled), 29.50 (m, labeled), 26.39, 25.31 (m, labeled).

Deuterium incorporation: 6.7 D/molecule (^{1}H-NMR), 6.7 D/molecule [HRMS (ESI)]

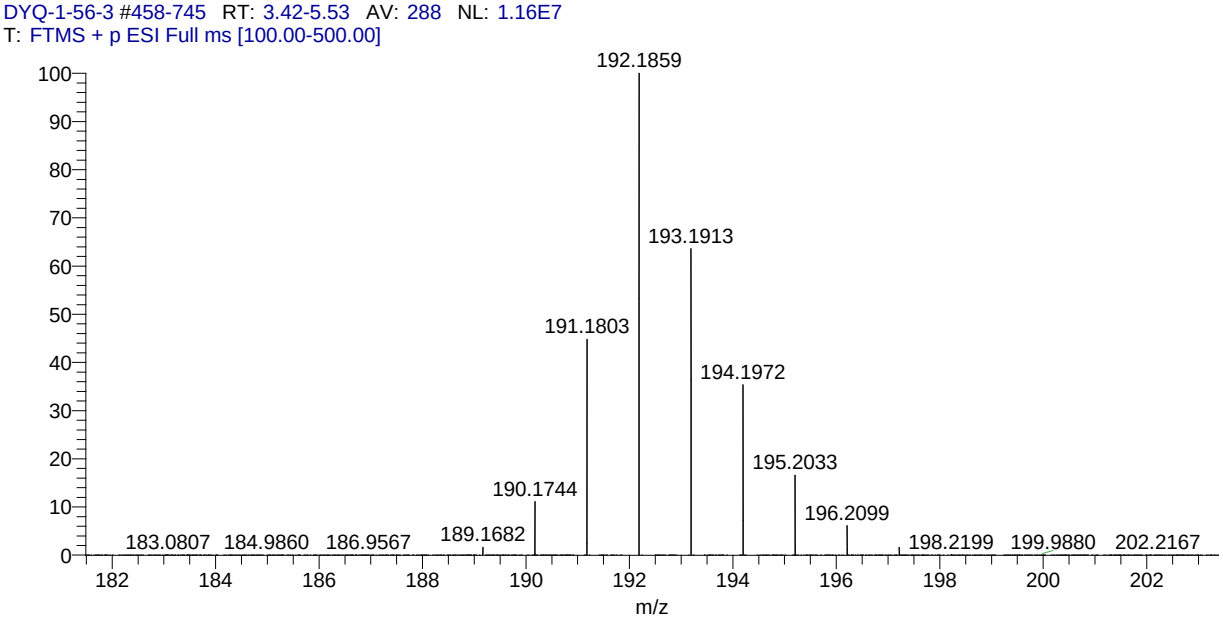


145.1424 ($C_8H_{12}D_3NO + H^+$, 1%), 146.1487 ($C_8H_{11}D_4NO + H^+$, 3%), 147.1547 ($C_8H_{10}D_5NO + H^+$, 12%), 148.1605 ($C_8H_9D_6NO + H^+$, 38%), 149.1661 ($C_8H_8D_7NO + H^+$, 22%), 150.1721 ($C_8H_7D_8NO + H^+$, 13%), 151.1786 ($C_8H_6D_9NO + H^+$, 7%), 152.1849 ($C_8H_5D_{10}NO + H^+$, 3%), 153.1913 ($C_8H_4D_{11}NO + H^+$, 1%).

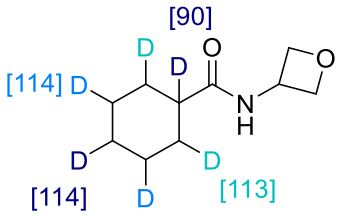


***N*-(2-methoxyethyl)cyclohexane-1,2,3,4,5,6-*d*$_6$-1-carboxamide (3b)**. The title product was obtained with 94% yield (72.0 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.89 (s, 0.98H), 3.43-3.41 (m, 4.00H), 3.35-3.32 (m, 2.99H), 2.08-2.02 (m, 0.12H), 1.83-1.80 (m, 0.21H), 1.72 (s, 1.74H), 1.60 (s, 0.25H), 1.38 (s, 1.46H), 1.23-1.16 (m, 1.20H); ^{1}H NMR (800 MHz, $CDCl_3$) δ 5.86 (s, 0.99H), 3.44-3.41 (m, 4.05H), 3.34 (s, 3.00H), 2.06-2.03 (m, 0.12H), 1.83-1.80 (m, 0.21H), 1.76-1.73 (m, 1.19H), 1.65-1.61 (m, 0.24H), 1.41-1.38 (m, 1.39H), 1.21-1.20 (m, 0.41H), 1.16 (s, 0.55H); ^{13}C NMR (201 MHz, $CDCl_3$) δ 176.38, 71.51, 58.92, 45.02 (m, labeled), 39.10, 29.19 (m, labeled), 25.25 (m, labeled).

Deuterium incorporation: 6.5 D/molecule (^{1}H-NMR, 400 MHz), 6.9 D/molecule (^{1}H-NMR, 800 MHz), 6.8 D/molecule [HRMS (ESI)].

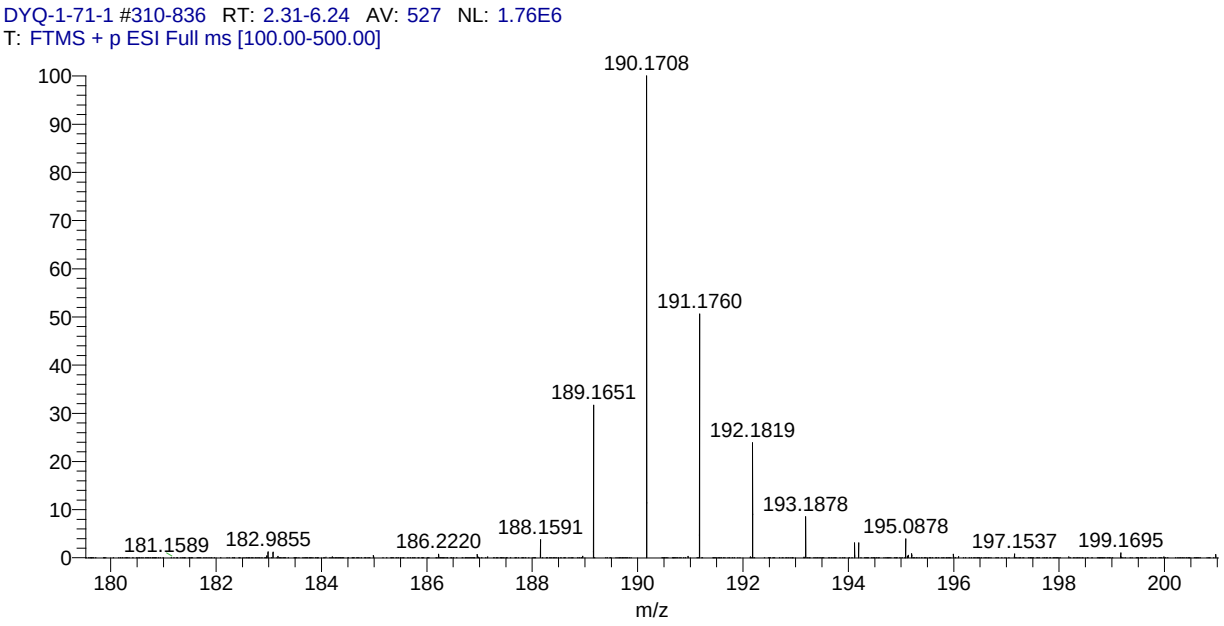


190.1744 ($C_{10}H_{15}D_4NO_2 + H^+$, 1%), 191.1803 ($C_{10}H_{14}D_5NO_2 + H^+$, 5%), 192.1859 ($C_{10}H_{13}D_6NO_2 + H^+$, 11%), 193.1913 ($C_{10}H_{12}D_7NO_2 + H^+$, 75%), 194.1972 ($C_{10}H_{11}D_8NO_2 + H^+$, 4%), 195.2033 ($C_{10}H_{10}D_9NO_2 + H^+$, 2%), 196.2099 ($C_{10}H_9D_{10}NO_2 + H^+$, 1%).

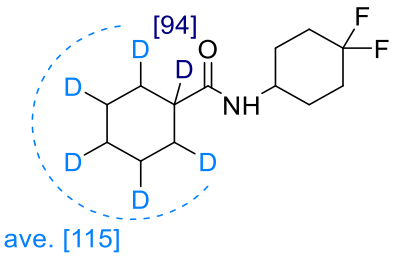


***N*-(oxetan-3-yl)cyclohexane-1,2,3,4,5,6-*d*$_6$-1-carboxamide (4b)**. The title product was obtained with 94% yield (66.8 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.54 (s, 1.00H), 5.07-4.98 (m, 1.00H), 4.89 (t, *J* = 7.0 Hz, 1.99H), 4.47 (t, *J* = 6.4 Hz, 2.00H), 2.07 (t, *J* = 11.8 Hz, 0.09H), 1.82-1.78 (m, 0.24H), 1.73 (s, 1.29H), 1.62 (s, 0.20H), 1.37 (s, 1.55H), 1.20-1.15 (m, 1.04H); ^{1}H NMR (800 MHz, $CDCl_3$) δ 6.35 (s, 1.00H), 5.04 (s, 0.98H), 4.91 (s, 2.00H), 4.47 (s, 2.00H), 2.09-2.06 (m, 0.10H), 1.83-1.80 (m, 0.20H), 1.74 (s, 1.33H), 1.66-1.63 (m, 0.22H), 1.39 (s, 1.55H), 1.21 (s, 0.40H), 1.17 (s, 0.64H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.18, 78.73, 44.65 (m, labeled), 44.59, 29.05 (m, labeled), 25.11 (m, labeled).

Deuterium incorporation: 6.6 D/molecule (^{1}H-NMR, 400 MHz), 6.6 D/molecule (^{1}H-NMR, 800 MHz), 6.6 D/molecule [HRMS (ESI)].

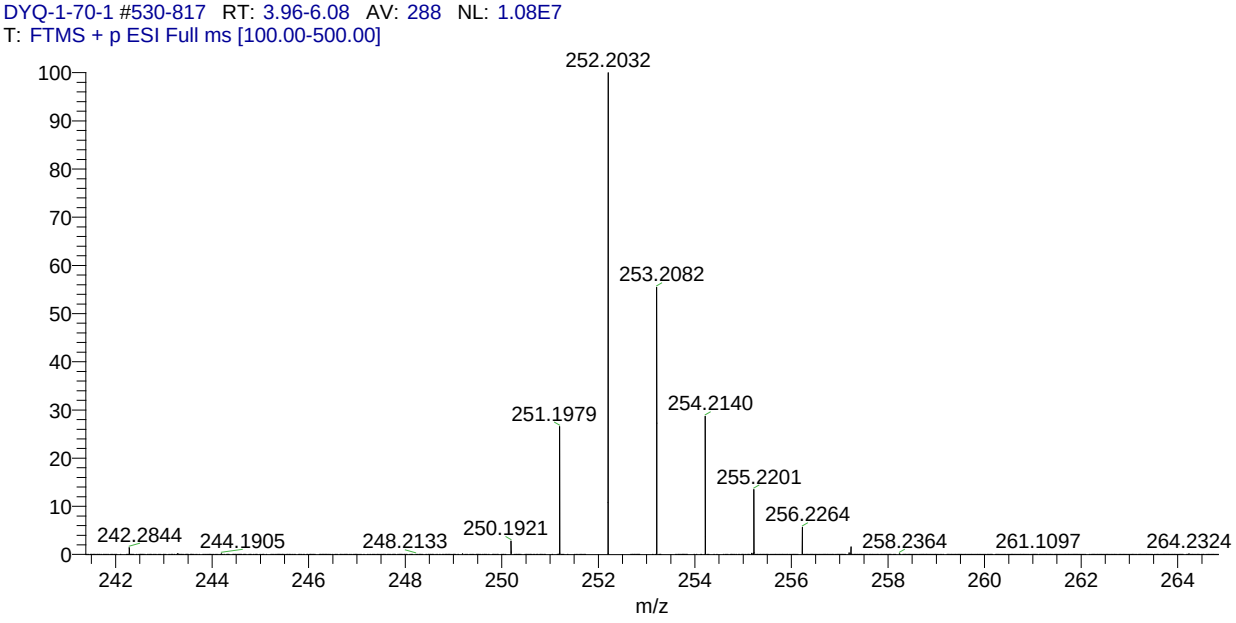


188.1591 ($C_{10}H_{13}D_4NO_2$ + H^+, 1%), 189.1651 ($C_{10}H_{12}D_5NO_2$ + H^+, 12%), 190.1708 ($C_{10}H_{11}D_6NO_2$ + H^+, 42%), 191.1760 ($C_{10}H_{10}D_7NO_2$ + H^+, 25%), 192.1819 ($C_{10}H_9D_8NO_2$ + H^+, 12%), 193.1878 ($C_{10}H_8D_9NO_2$ + H^+, 5%).

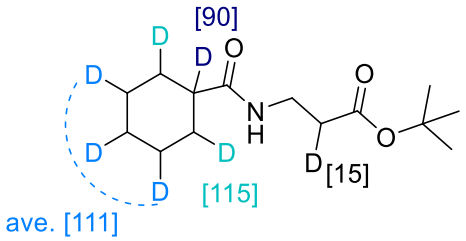


***N*-(4,4-difluorocyclohexyl)cyclohexane-1,2,3,4,5,6-d_6-1-carboxamide (5b)**. The title product was obtained with 99% yield (54.6 mg, 0.2 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (d, *J* = 7.2 Hz, 1.00H), 4.13 (q, *J* = 7.2 Hz, 0.11H), 3.94-3.85 (m, 0.88H), 2.23 (t, *J* = 7.4 Hz, 0.06H), 2.12-1.75 (m, 6.52H), 1.67-1.64 (m, 0.79H), 1.54-1.44 (m, 1.80H), 1.38 (s, 1.23H), 1.28-1.21 (m, 1.18H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.86, 125.11, 122.73, 120.32, 46.04, 32.70, 32.46, 32.21, 29.26 (m, labeled), 28.99, 28.89, 25.26 (m, labeled). ^{19}F NMR (377 MHz, $CDCl_3$) δ -94.48, -95.11, -101.08, -101.71.

Deuterium incorporation: 6.7 D/molecule (^{1}H-NMR), 6.7 D/molecule [HRMS (ESI)].

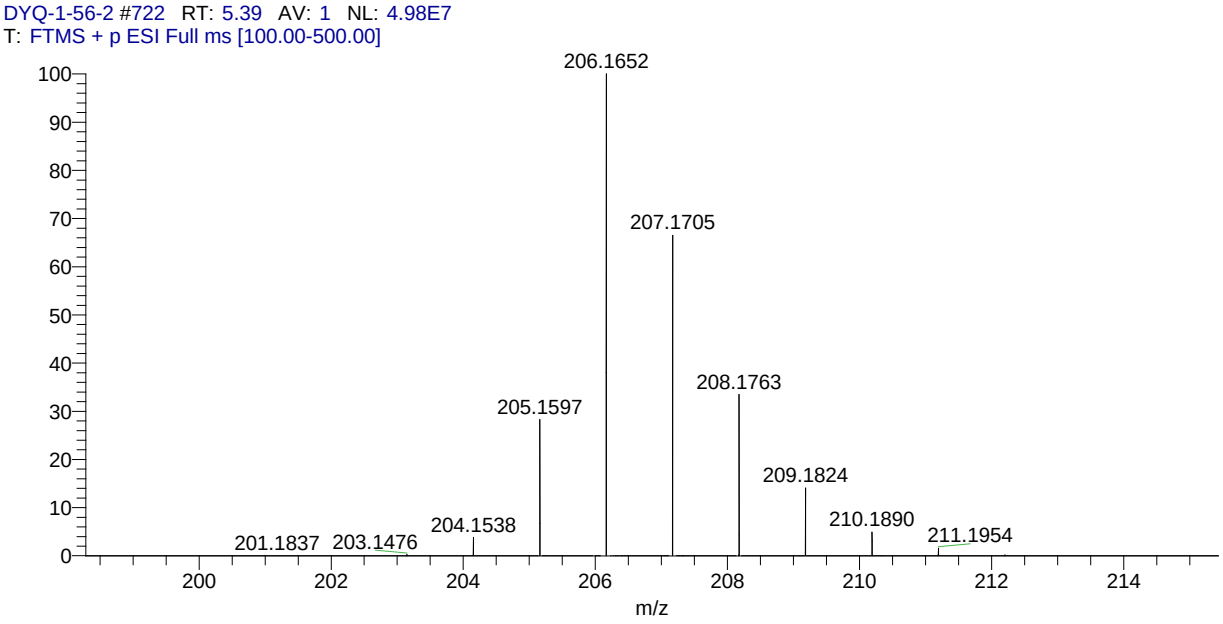


250.1921 ($C_{13}H_{17}D_4F_2NO$ + H^+, 1%), 251.1979 ($C_{13}H_{16}D_5F_2NO$ + H^+, 11%), 252.2032 ($C_{13}H_{15}D_6F_2NO$ + H^+, 43%), 253.2082 ($C_{13}H_{14}D_7F_2NO$ + H^+, 24%), 254.2140 ($C_{13}H_{13}D_8F_2NO$ + H^+, 12%), 255.2201 ($C_{13}H_{12}D_9F_2NO$ + H^+, 6%), 256.2264 ($C_{13}H_{11}D_{10}F_2NO$ + H^+, 2%).

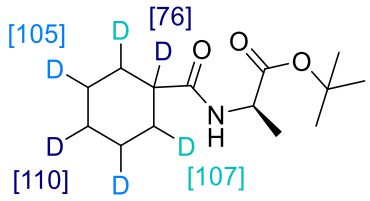


***tert*-Butyl 3-(cyclohexane-1-carboxamido-1,2,3,4,5,6-*d*$_6$)propanoate (6b)**. The title product was obtained with 99% yield (53.0 mg, 0.2 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.10 (s, 0.90H), 3.46 (q, *J* = 6.0, 12.0 Hz, 2.00H), 2.42 (t, *J* = 6.0 Hz, 1.85H), 2.03 (t, *J* = 12.0 Hz, 0.10H), 1.83-1.79 (m, 0.15H), 1.79-1.71 (m, 1.26H), 1.65-1.60(m, 0.29H), 1.45 (s, 9.02H), 1.36 (s, 1.56H), 1.21-1.16 (m, 1.13H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.29, 172.38, 81.22, 45.12 (m, labeled), 35.31, 34.97, 29.86, 29.16 (m, labeled), 28.27, 25.22 (m, labeled).

Deuterium incorporation: 6.7 D/molecule (^{1}H-NMR), 6.7 D/molecule [HRMS (ESI)]

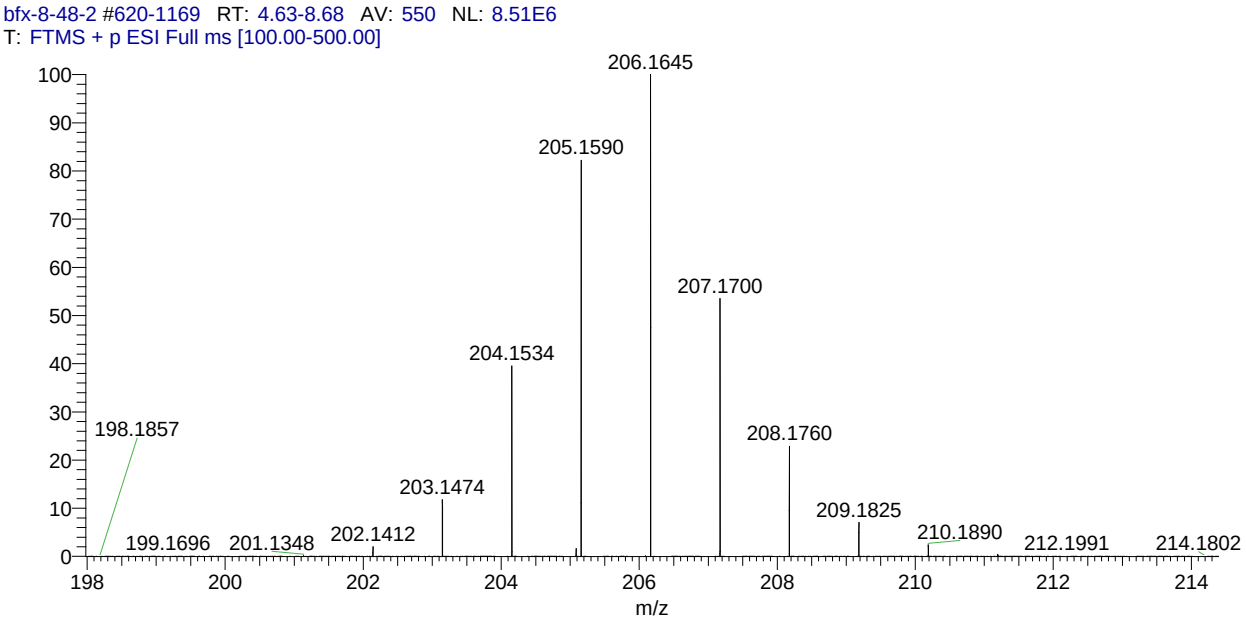


204.1538 ($C_{14}H_{21}D_4NO_3$ + H^+, 1%), 205.1597 ($C_{14}H_{20}D_5NO_3$ + H^+, 11%), 206.1652 ($C_{14}H_{19}D_6NO_3$ + H^+, 40%), 207.1705 ($C_{14}H_{18}D_7NO_3$ + H^+, 26%), 208.1763 ($C_{14}H_{17}D_8NO_3$ + H^+, 13%), 209.1824 ($C_{14}H_{16}D_9NO_3$ + H^+, 6%), 210.1890 ($C_{14}H_{15}D_{10}NO_3$ + H^+, 2%), 211.1954 ($C_{14}H_{14}D_{11}NO_3$ + H^+, 1%).

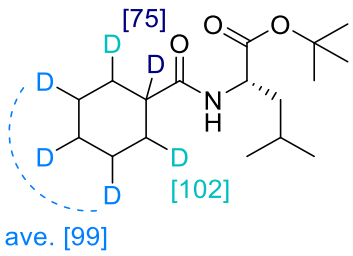


***tert*-Butyl (cyclohexane-1-carbonyl-1,2,3,4,5,6-d_6)-*D*-alaninate (7b)**. The title product was obtained with 81% yield (61.0 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.13 (d, *J* = 7.2 Hz, 1.00H), 4.46-4.39 (m, 1.00H), 2.08-2.03 (m, 0.24H), 1.86-1.79 (m, 0.36H), 1.75-1.66 (m, 1.58H), 1.63-1.58 (m, 0.33H), 1.46 (s, 0.30H), 1.42 (s, 8.73H), 1.36 (s, 1.49H), 1.31 (d, *J* = 7.2 Hz, 2.97H), 1.20-1.14 (m, 1.06H); ^{1}H NMR (800 MHz, $CDCl_3$) δ 6.09 (d, *J* = 7.2 Hz, 1.00H), 4.46-4.42 (m, 0.96H), 2.08-2.05 (m, 0.24H), 1.86-1.80 (m, 0.33H), 1.75-1.72 (m, 1.41H), 1.64-1.60 (m, 0.31H), 1.48 (s, 0.44H), 1.44 (s, 8.62H), 1.41-1.36 (m, 1.54H), 1.33 (d, *J* = 7.2 Hz, 2.97H), 1.21-1.20 (m, 0.49H), 1.15 (s, 0.59H); ^{13}C NMR (201 MHz, $CDCl_3$) δ 175.61, 172.80, 82.01, 48.41, 44.80 (m, labeled), 29.14 (m, labeled), 28.12, 25.19 (m, labeled), 18.96.

Deuterium incorporation: 6.1 D/molecule (^{1}H-NMR), 5.8 D/molecule [HRMS (ESI)].

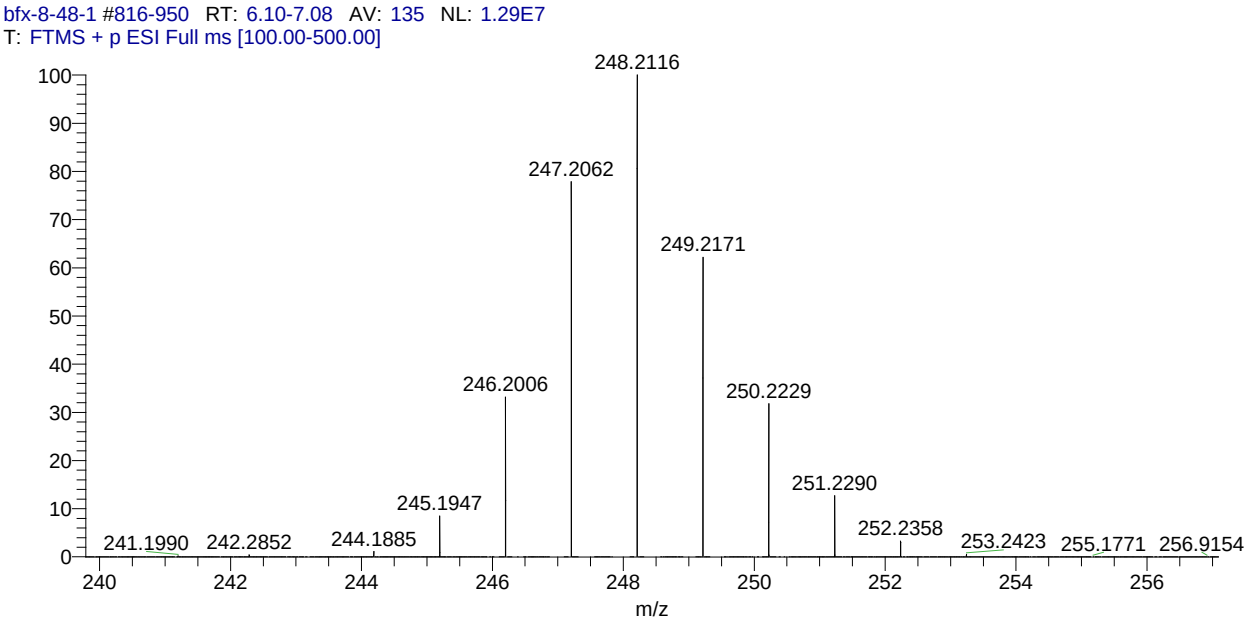


202.1412 ($C_{14}H_{23}D_2NO_3 + H^+$, 1%), 203.1474 ($C_{14}H_{22}D_3NO_3 + H^+$, 3%), 204.1534 ($C_{14}H_{21}D_4NO_3 + H^+$, 12%), 205.1590 ($C_{14}H_{20}D_5NO_3 + H^+$, 25%), 206.1645 ($C_{14}H_{19}D_6NO_3 + H^+$, 32%), 207.1700 ($C_{14}H_{18}D_7NO_3 + H^+$, 17%), 208.1760 ($C_{14}H_{17}D_8NO_3 + H^+$, 7%), 209.1825 ($C_{14}H_{16}D_9NO_3 + H^+$, 2%).

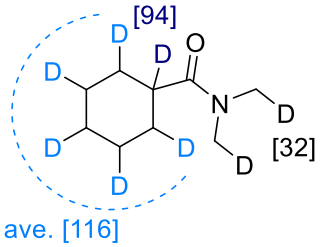


***tert*-Butyl (cyclohexane-1-carbonyl-1,2,3,4,5,6-*d*$_6$)-L-leucinate (8b)**. The title product was obtained with 99% yield (119.7 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.85 (d, *J* = 8.4 Hz, 1.00H), 4.55-4.49 (m, 1.00H), 2.10 (t, *J* = 11.6 Hz, 0.25H), 1.91-1.83 (m, 0.37H), 1.77-1.74 (m, 1.42H), 1.69-1.57 (m, 2.42H), 1.52-1.44 (m, 10.00H), 1.40 (s, 1.60H), 1.24-1.17 (m, 1.18H), 0.94 (dd, *J* = 1.6, 6.4 Hz, 6.00H); ^{1}H NMR (800 MHz, $CDCl_3$) δ 5.84 (d, *J* = 8.0 Hz, 1.00H), 4.53-4.50 (m, 0.99H), 2.11-2.08 (m, 0.22H), 1.87-1.82 (m, 0.31H), 1.78-1.74 (m, 1.33H), 1.67-1.59 (m, 2.26H), 1.49-1.46 (m, 10.06H), 1.43-1.38 (m, 1.64H), 1.24-1.23 (m, 0.53H), 1.18 (s, 0.55H), 0.95-0.94 (m, 6.03H); ^{13}C NMR (201 MHz, $CDCl_3$) δ 175.86, 172.81, 81.98, 51.14, 42.36, 29.84 (m, labeled), 29.19 (m, labeled), 28.22, 25.71 (m, labeled), 25.28 (m, labeled), 25.20, 23.05, 22.43.

Deuterium incorporation: 6.2 D/molecule (^{1}H-NMR), 6.0 D/molecule [HRMS (ESI)]

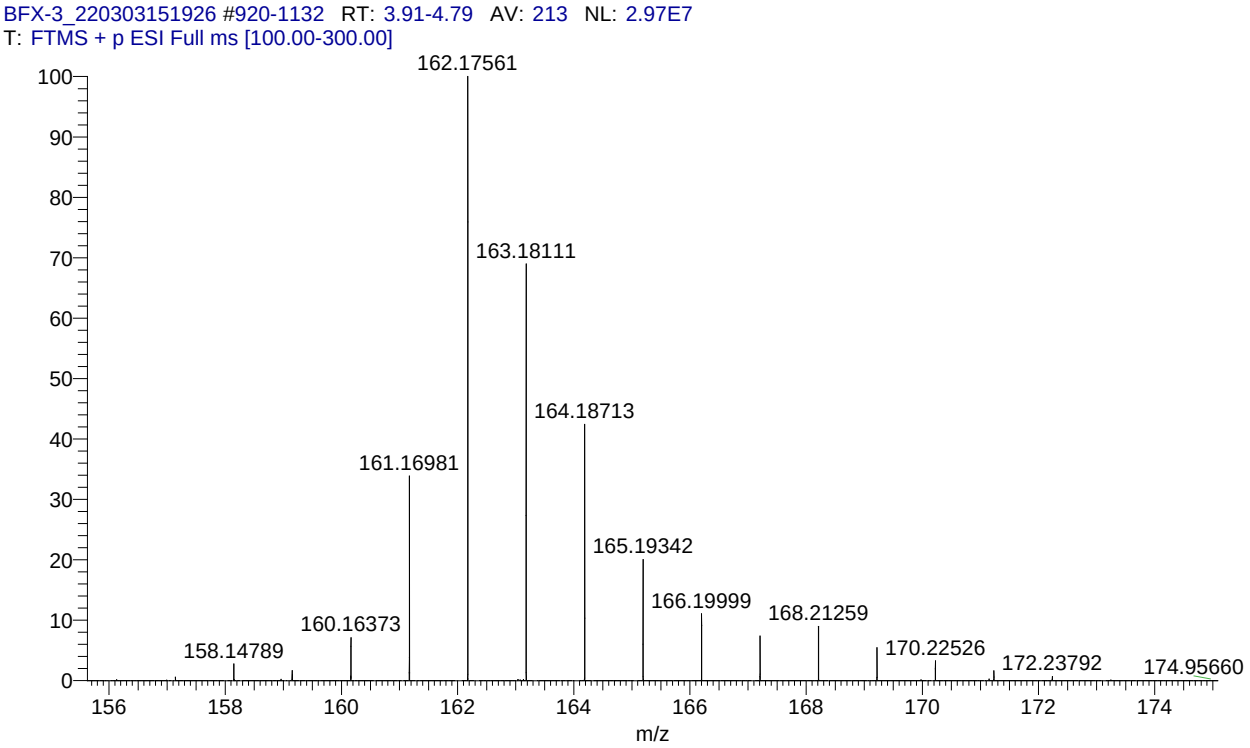


244.1885 ($C_{13}H_{21}D_2NO_3$ + H^+, < 1%), 245.1885 ($C_{13}H_{20}D_3NO_3$ + H^+, 3%), 246.2006 ($C_{13}H_{19}D_4NO_3$ + H^+, 10%), 247.2062 ($C_{13}H_{18}D_5NO_3$ + H^+, 24%), 248.2116 ($C_{13}H_{17}D_6NO_3$ + H^+, 30%), 249.2171 ($C_{13}H_{16}D_7NO_3$ + H^+, 19%), 250.2229 ($C_{13}H_{15}D_8NO_3$ + H^+, 9%), 251.2290 ($C_{13}H_{14}D_9NO_3$ + H^+, 4%), 252.2358 ($C_{13}H_{13}D_{10}NO_3$ + H^+, 1%),

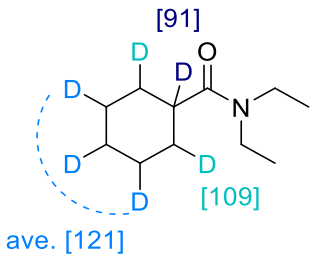


***N, N*-dimethylcyclohexane-1-carboxamide-1,2,3,4,5,6-d_6 (9b)**. The title product was obtained with 63% yield (40.6 mg, 0.4 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.00 (s, 2.74H), 2.88 (s, 2.63H), 2.42 (t, *J* = 12.0 Hz, 0.06H), 1.71 (s, 1.32H), 1.63-1.59(m, 0.37H), 1.41 (s, 1.53H), 1.19-1.16 (m, 0.98H); ^{13}C NMR (201 MHz, $CDCl_3$) δ 176.26, 40.10 (m, labeled), 37.12, 35.56, 28.62 (m, labeled), 25.30 (m, labeled).

Deuterium incorporation: 7.4 D/molecule (^{1}H-NMR), 7.2 D/molecule [HRMS (ESI)]

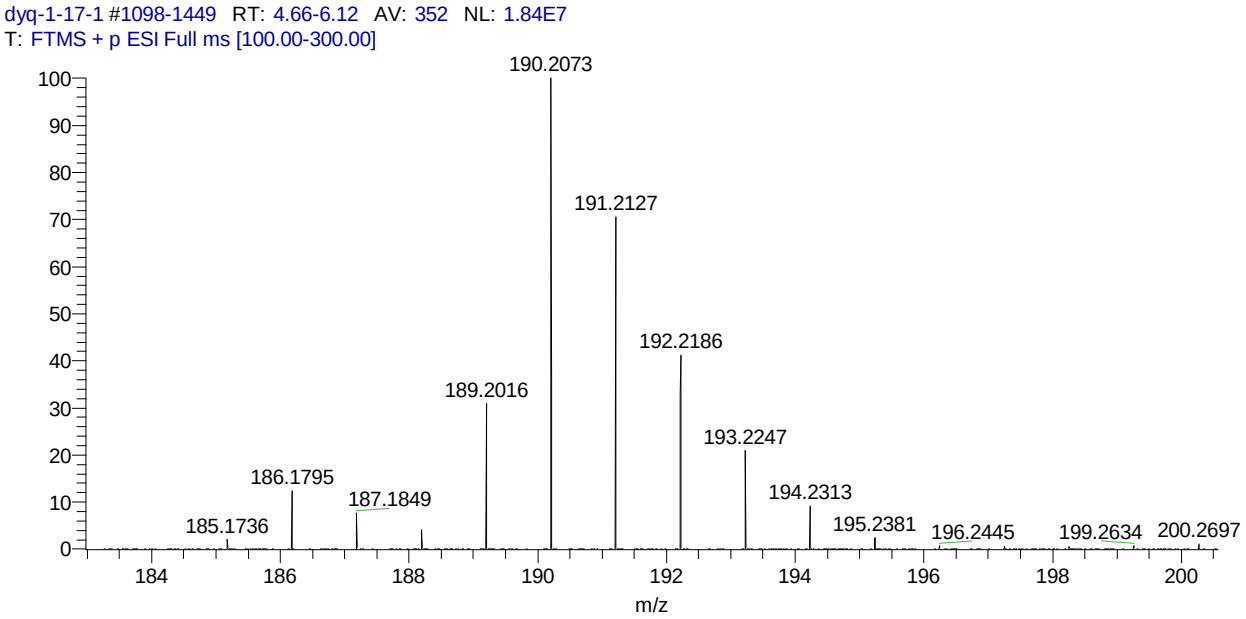


160.1637 ($C_9H_{13}D_4NO + H^+$, 2%), 161.1698 ($C_9H_{12}D_5NO + H^+$, 10%), 162.1756 ($C_9H_{11}D_6NO + H^+$, 32%), 163.1811 ($C_9H_{10}D_7NO + H^+$, 22%), 164.1871 ($C_9H_9D_8NO + H^+$, 14%), 165.1934 ($C_9H_8D_9NO + H^+$, 7%), 166.2000 ($C_9H_7D_{10}NO + H^+$, 4%), 167.2062 ($C_9H_6D_{11}NO + H^+$, 3%), 168.2126 ($C_9H_5D_{12}NO + H^+$, 3%), 169.2189 ($C_9H_4D_{13}NO + H^+$, 2%), 170.2253 ($C_9H_3D_{14}NO + H^+$, 1%).



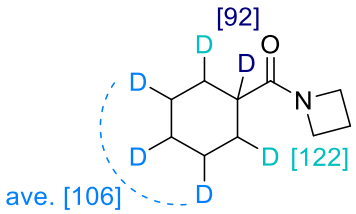
***N*-(2-Methoxyethyl)cyclohexane-1,2,3,4,5,6-*d*$_6$-1-carboxamide (10b)**. The title product was obtained with 99% yield (76.9 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.37-3.28 (m, 4.00H), 2.40-2.34 (m, 0.09H), 1.90 (s, 0.31H), 1.75 (s, 1.12H), 1.69-1.64 (m, 0.48H), 1.51 (s, 1.52H), 1.26-1.16 (m, 4.09H), 1.10-1.06 (m, 3.00H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.74, 41.83, 40.18, 29.17 (m, labeled), 25.42 (m, labeled), 15.21, 13.33.

Deuterium incorporation: 6.4 D/molecule (^{1}H-NMR), 6.4 D/molecule [HRMS (ESI)]



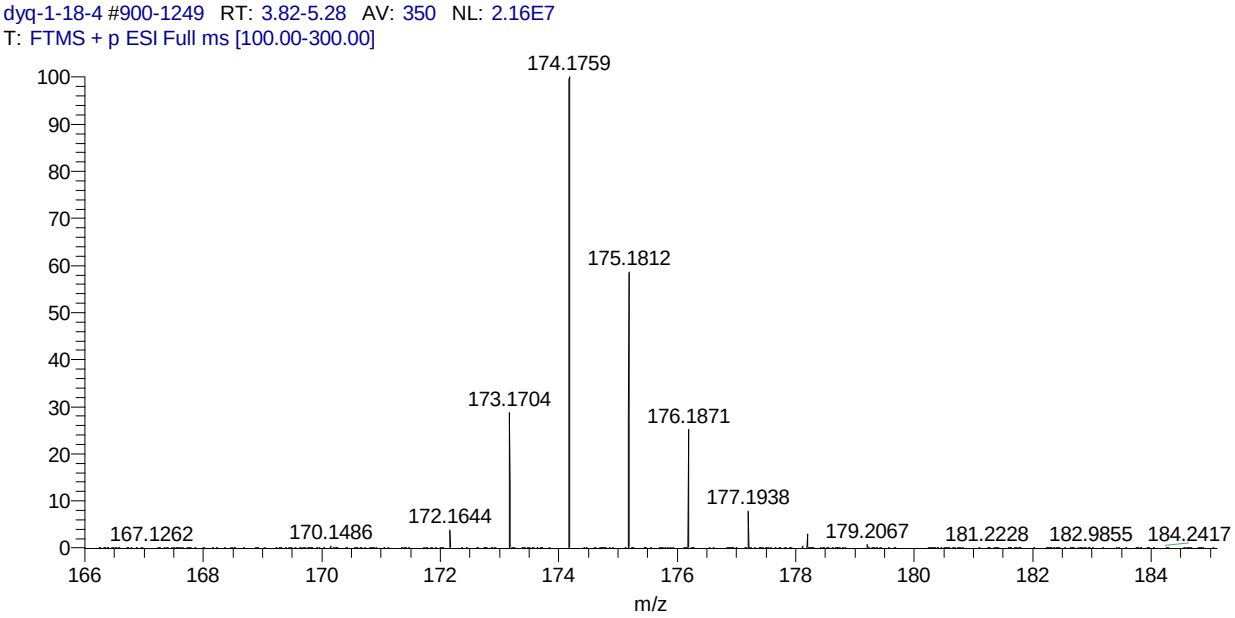
185.1736 ($C_{11}H_{20}DNO + H^+$, 1%), 186.1795 ($C_{11}H_{19}D_2NO + H^+$, 5%), 187.1849 ($C_{11}H_{18}D_3NO + H^+$, 4%), 188.1957 ($C_{11}H_{17}D_4NO + H^+$, 3%), 189.2016 ($C_{11}H_{16}D_5NO + H^+$, 11%), 190.2073

($C_{11}H_{15}D_6NO + H^+$, 30%), 191.2127 ($C_{11}H_{14}D_7NO + H^+$, 23%), 192.2186 ($C_{11}H_{13}D_8NO + H^+$, 13%), 193.2247 ($C_{11}H_{12}D_9NO + H^+$, 7%), 194.2313 ($C_{11}H_{11}D_{10}NO + H^+$, 3%), 195.2381 ($C_{11}H_{10}D_{11}NO + H^+$, 1%).

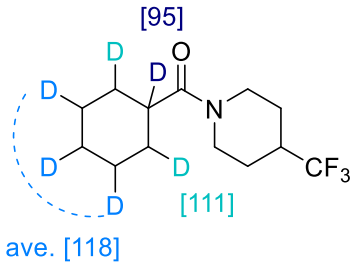


Azetidin-1-yl(cyclohexyl-1,2,3,4,5,6-*d*$_6$)methanone (11b). The title product was obtained with 89% yield (61.8 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.13 (t, *J* = 7.6 Hz, 2.00H), 3.97 (t, *J* = 7.6 Hz, 1.99H), 2.27-2.19 (m, 2.01H), 2.11-2.05 (m, 0.08H), 2.02-1.96 (m, 0.03H), 1.72 (s, 1.32H), 1.66-1.60 (m, 0.45H), 1.41 (s, 1.53H), 1.17 (s, 1.05H); ^{13}C NMR (201 MHz, $CDCl_3$) δ 176.28, 50.16, 47.79, 28.08 (m, labeled), 25.16 (m, labeled), 15.24.

Deuterium incorporation: 6.5 D/molecule (^{1}H-NMR), 6.5 D/molecule [HRMS (ESI)].

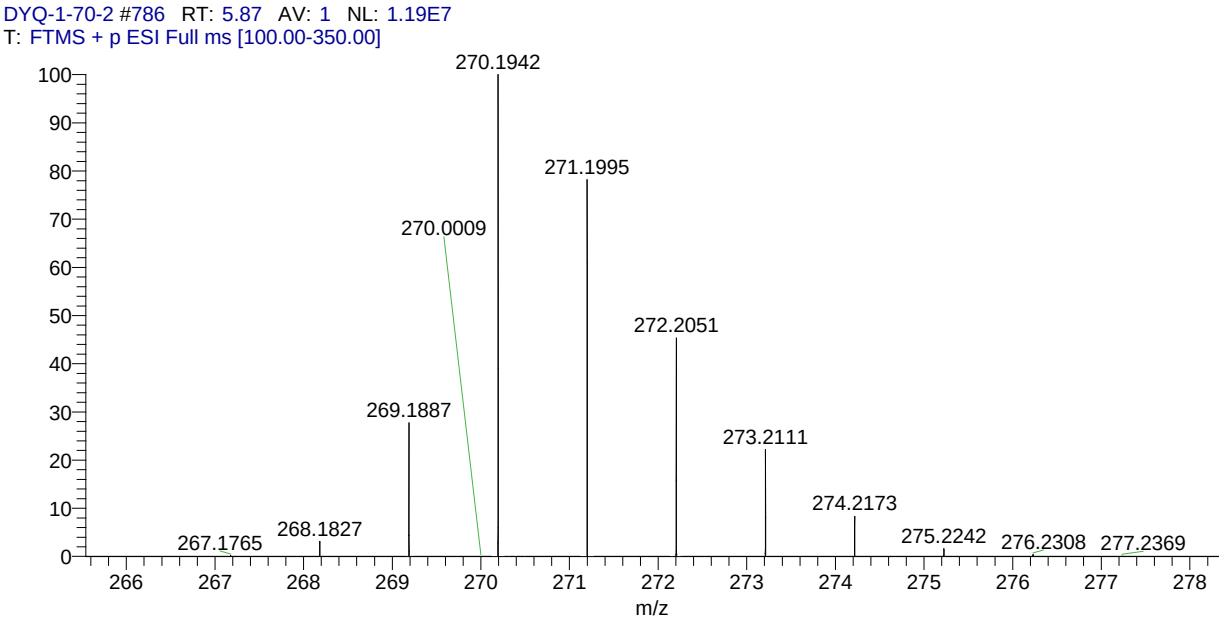


172.1644 ($C_{10}H_{13}D_4NO + H^+$, 2%), 173.1704 ($C_{10}H_{12}D_5NO + H^+$, 12%), 174.1759 ($C_{10}H_{11}D_6NO + H^+$, 44%), 175.1812 ($C_{10}H_{10}D_7NO + H^+$, 25%), 176.1871 ($C_{10}H_9D_8NO + H^+$, 12%), 177.1938 ($C_{10}H_8D_9NO + H^+$, 3%).

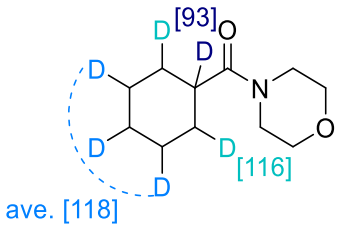


(Cyclohexyl-1,2,3,4,5,6-*d*$_6$)(4-(trifluoromethyl)piperidin-1-yl)methanone (12b). The title product was obtained with 79% yield (85.0 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.75 (d, *J* = 13.2 Hz, 1.00H), 4.01 (d, *J* = 13.6 Hz, 1.00H), 3.00 (t, *J* = 13.0 Hz, 1.00H), 2.52-2.40 (m, 1.05H), 2.33-2.18 (m, 1.01H), 1.95-1.87 (m, 2.24H), 1.75 (s, 1.23H), 1.67-1.64 (m, 0.36H), 1.53-1.40 (m, 3.55H), 1.21 (s, 0.87H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.79, 127.14 (q, *J* = 279.30 Hz), 44.34, 41.28, 41.00, 40.73, 40.65, 40.46, 40.01 (m, labeled), 28.98 (m, labeled), 25.64, 25.32 (m, labeled), 24.48. ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.89.

Deuterium incorporation: 6.7 D/molecule (^{1}H-NMR), 6.9 D/molecule [HRMS (ESI)].

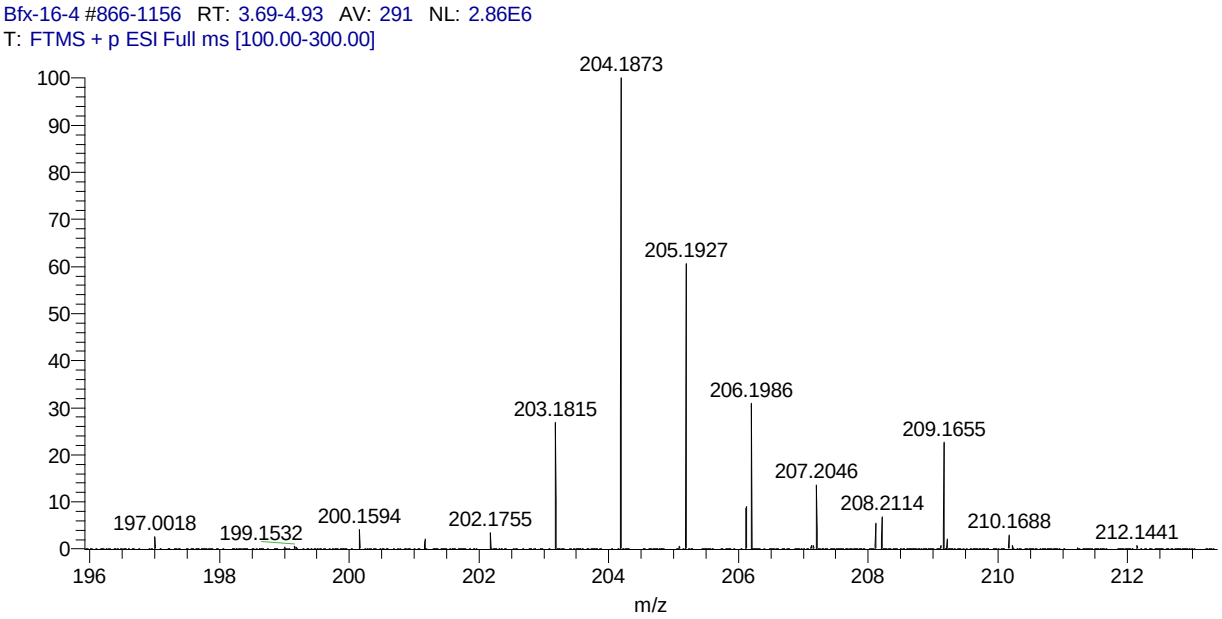


268.1827 ($C_{13}H_{16}D_4F_3NO$ + H^+, 1%), 269.1887 ($C_{13}H_{15}D_5F_3NO$ + H^+, 9%), 270.1942 ($C_{13}H_{14}D_6F_3NO$ + H^+, 34%), 271.1995 ($C_{13}H_{13}D_7F_3NO$ + H^+, 27%), 272.2051 ($C_{13}H_{12}D_8F_3NO$ + H^+, 16%), 273.2111 ($C_{13}H_{11}D_9F_3NO$ + H^+, 8%), 274.2173 ($C_{13}H_{10}D_{10}F_3NO$ + H^+, 3%), 275.2242 ($C_{13}H_9D_{11}F_3NO$ + H^+, 1%).

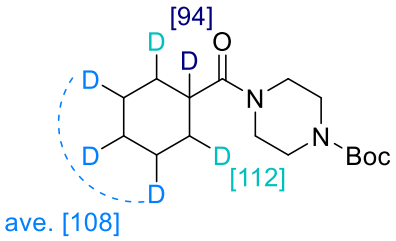


(Cyclohexyl-1,2,3,4,5,6-*d*$_6$)(morpholino)methanone (13b). The title product was obtained with 86% yield (70.1 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66-3.47 (m, 8.00H), 2.42-2.37 (m, 0.07H), 2.02-1.90 (m, 0.16H), 1.75 (s, 1.22H), 1.70-1.63 (m, 0.38H), 1.48 (s, 1.52H), 1.20 (s, 0.87H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.92, 67.17, 67.04, 46.00, 42.00, 39.89 (m, labeled), 28.80 (m, labeled), 25.28 (m, labeled).

Deuterium incorporation: 6.8 D/molecule (^{1}H-NMR), 6.8 D/molecule [HRMS (ESI)]

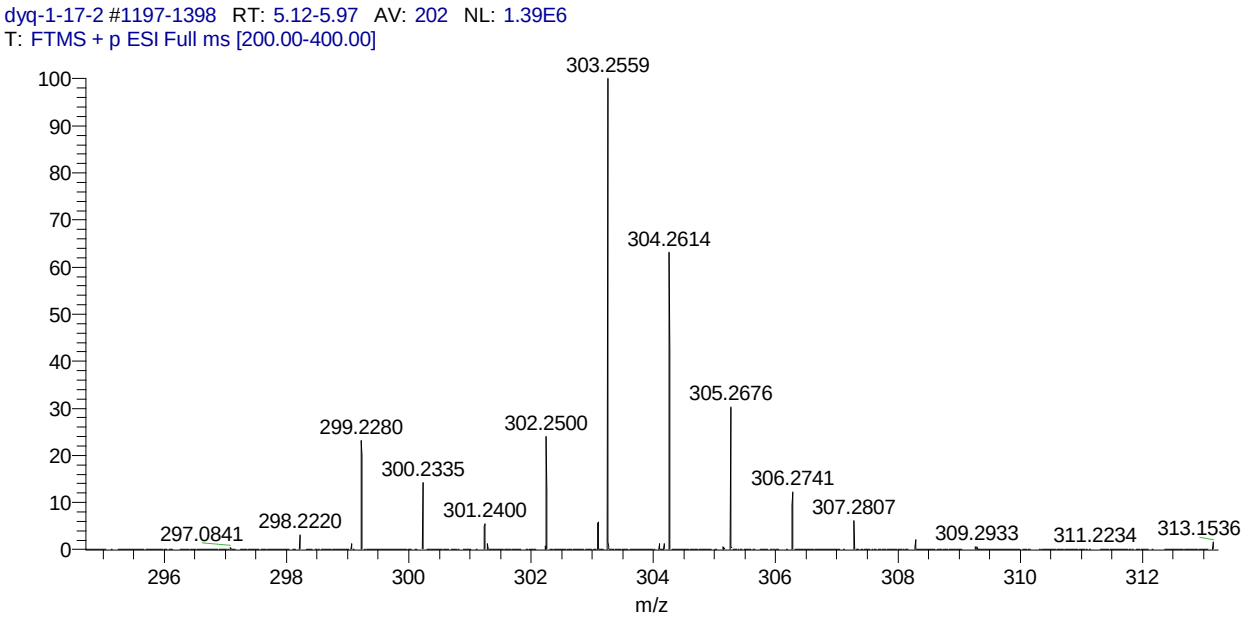


202.1755 ($C_{11}H_{15}D_4NO_2$ + H^+, 1%), 203.1815 ($C_{11}H_{14}D_5NO_2$ + H^+, 10%), 204.1873 ($C_{11}H_{13}D_6NO_2$ + H^+, 39%), 205.1927 ($C_{11}H_{12}D_7NO_2$ + H^+, 26%), 206.1986 ($C_{11}H_{11}D_8NO_2$ + H^+, 13%), 207.2046 ($C_{11}H_{10}D_9NO_2$ + H^+, 6%), 208.2114 ($C_{11}H_9D_{10}NO_2$ + H^+, 3%).

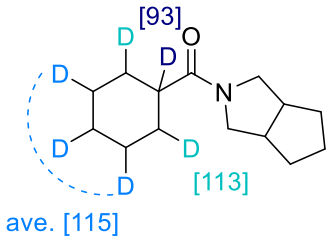


***tert*-Butyl 4-(cyclohexane-1-carbonyl-1,2,3,4,5,6-*d*$_6$)piperazine-1-carboxylate (14b)**, The title product was obtained with 86% yield (106.6 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.58-3.56 (m, 2.00H), 3.44-3.37 (m, 6.00H), 2.42 (t, *J* = 11.6 Hz, 0.06H), 1.75 (s, 1.28H), 1.70-1.63 (m, 0.42H), 1.49-1.46 (m, 10.76H), 1.20 (s, 1.05H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.02, 154.78, 80.41, 45.35, 43.70 (m, labeled), 41.52, 28.92 (m, labeled), 28.56, 25.32 (m, labeled).

Deuterium incorporation: 6.5 D/molecule (^{1}H-NMR), 6.2 D/molecule [HRMS (ESI)].

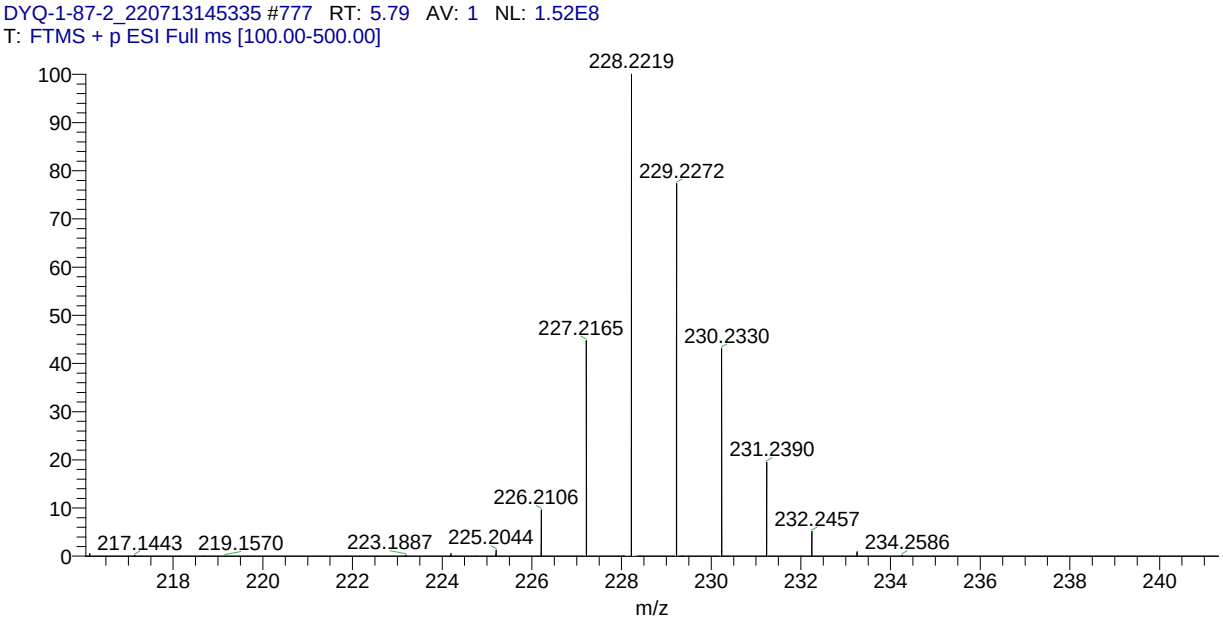


298.2220 ($C_{16}H_{27}DN_2O_3$ + H^+, 1%), 299.2280 ($C_{16}H_{26}D_2N_2O_3$ + H^+, 8%), 300.2335 ($C_{16}H_{25}D_3N_2O_3$ + H^+, 13%), 301.2400 ($C_{16}H_{24}D_4N_2O_3$ + H^+, <1%), 302.2500 ($C_{16}H_{23}D_5N_2O_3$ + H^+, 9%), 303.2559 ($C_{16}H_{22}D_6N_2O_3$ + H^+, 37%), 304.2614 ($C_{16}H_{21}D_7N_2O_3$ + H^+, 24%), 305.2676 ($C_{16}H_{20}D_8N_2O_3$ + H^+, 11%), 306.2741 ($C_{16}H_{19}D_9N_2O_3$ + H^+, 5%), 307.2807 ($C_{16}H_{18}D_{10}N_2O_3$ + H^+, 2%).

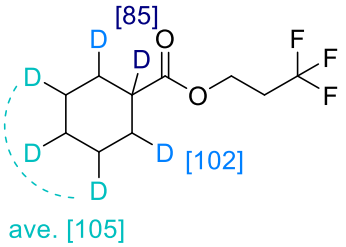


(Cyclohexyl-1,2,3,4,5,6-*d*$_6$)(hexahydrocyclopenta[*c*]pyrrol-2(1*H*)-yl)methanone (15b). The title product was obtained with 98% yield (89.0 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.86-3.41 (m, 2.02H), 3.26-2.98 (m, 1.99H), 2.71-2.53 (m, 2.00H), 2.26 (t, *J* = 11.6 Hz, 0.08H), 1.86-1.53 (m, 5.70H), 1.45-1.39 (m, 3.57H), 1.18 (s, 0.93H); ^{1}H NMR (800 MHz, $CDCl_3$) δ 3.67-3.62 (m, 2.00H), 3.28-3.22 (m, 2.00H), 2.71-2.67 (m, 1.00H), 2.62-2.58 (m, 1.00H), 2.30-2.27 (m, 0.07H), 1.93-1.92 (m, 0.21H), 1.86-1.79 (m, 2.01H), 1.76-1.67 (m, 2.47H), 1.63-1.58 (m, 1.17H), 1.47-1.41 (m, 3.54H), 1.20 (s, 0.92H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.84, 52.51, 51.62, 43.80, 42.16 (m, labeled), 41.78, 32.16, 32.14, 28.42 (m, labeled), 25.59, 25.30 (m, labeled).

Deuterium incorporation: 6.7 D/molecule (^{1}H-NMR, 400 MHz), 6.6 D/molecule (^{1}H-NMR, 800 MHz), 6.6 D/molecule [HRMS (ESI)].

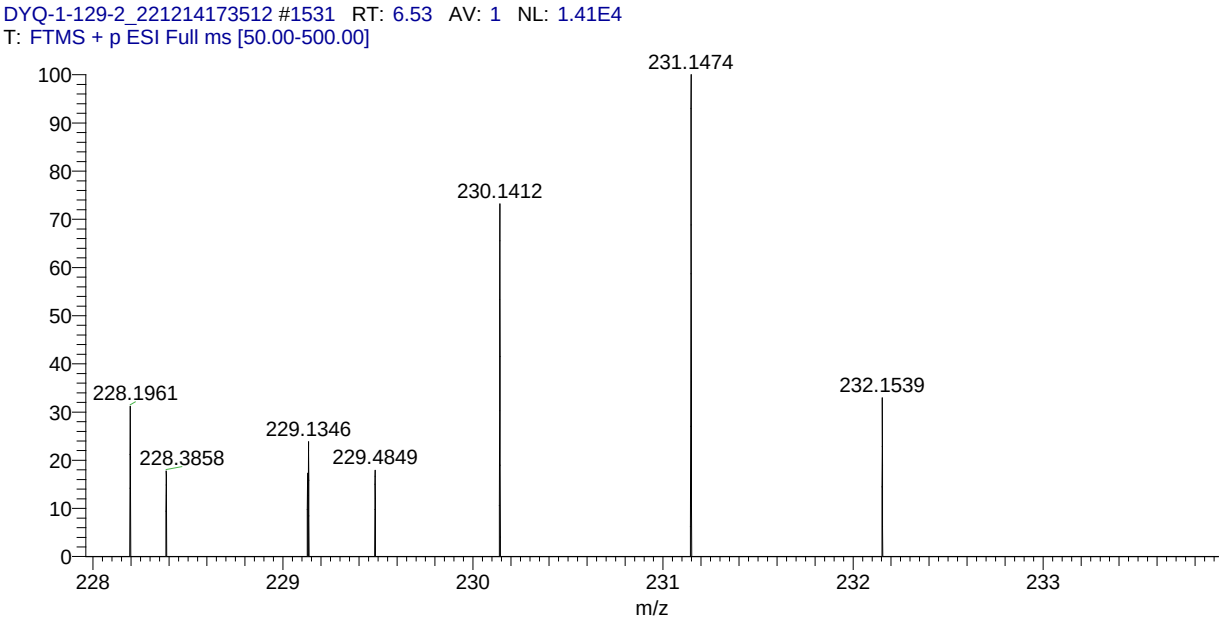


226.2106 ($C_{14}H_{19}D_4NO$ + H+, 3%), 227.2165 ($C_{14}H_{18}D_5NO$ + H+, 14%), 228.2219 ($C_{14}H_{17}D_6NO$ + H+, 33%), 229.2272 ($C_{14}H_{16}D_7NO$ + H+, 25%), 230.2330 ($C_{14}H_{15}D_8NO$ + H+, 15%), 231.2390 ($C_{14}H_{14}D_9NO$ + H+, 7%), 232.2457 ($C_{14}H_{13}D_{10}NO$ + H+, 2%).

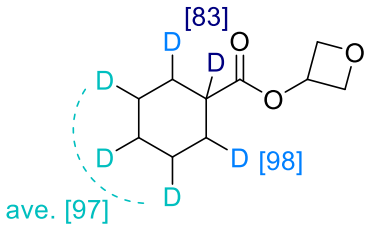


3,3,3-Trifluoropropyl cyclohexane-1-carboxylate-1,2,3,4,5,6-*d*$_6$ (16b). The title product was obtained with 82% yield (75.5 mg, 0.4 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.29 (t, *J* = 6.2 Hz, 2.00H), 2.52-2.41 (m, 2.01H), 2.32-2.27 (m, 0.15H), 1.91-1.86 (m, 0.29H), 1.77-1.71 (m, 1.32H), 1.66-1.61 (m, 0.32H), 1.43-1.40 (m, 1.68H), 1.19 (s, 1.21H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.97, 126.05 (q, *J* = 277.8 Hz), 57.06 (q, *J* = 3.7 Hz), 43.00 (m, labeled), 33.60 (q, *J* = 29.3 Hz), 28.22 (m, labeled), 24.73 (m, labeled).

Deuterium incorporation: 6.0 D/molecule (^{1}H-NMR), 5.8 D/molecule [HRMS (ESI)].

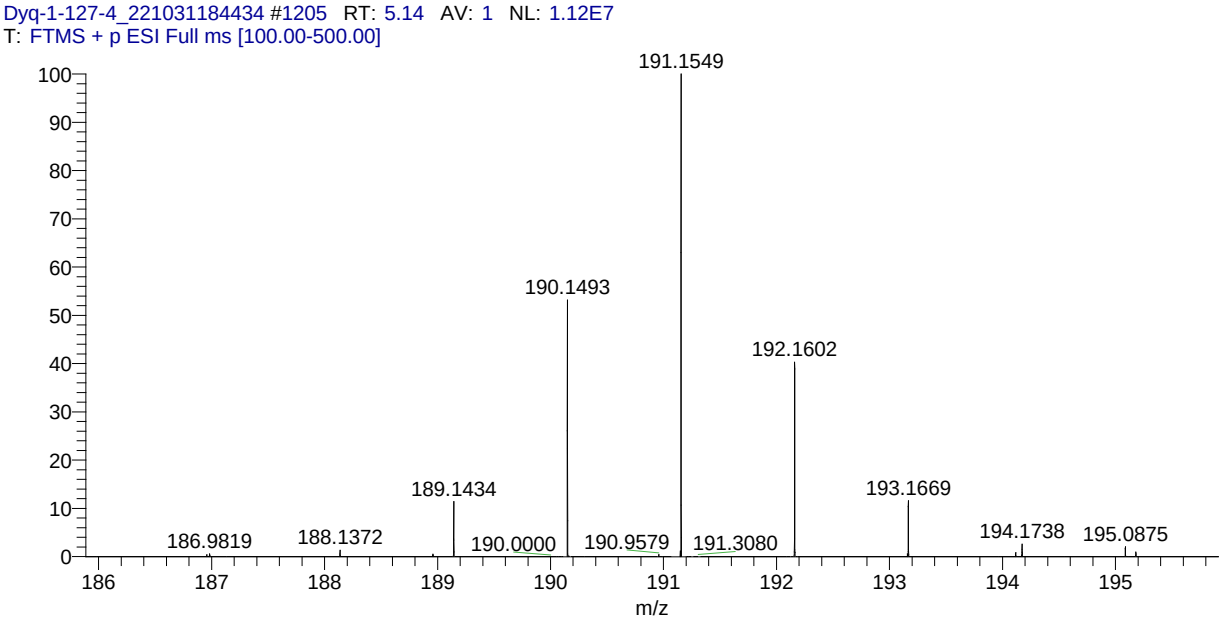


229.1346 ($C_{10}H_{11}D_4F_3O_2$ + H^+, 1%), 230.1412 ($C_{10}H_{10}D_5F_3O_2$ + H^+, 32%), 231.1474 ($C_{10}H_9D_6F_3O_2$ + H^+, 54%), 232.1539 ($C_{10}H_8D_7F_3O_2$ + H^+, 12%).

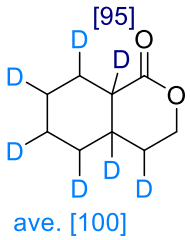


Oxetan-3-yl cyclohexane-1-carboxylate-1,2,3,4,5,6-*d*$_6$ (17b). The title product was obtained with 60% yield (45.6 mg, 0.4 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.45-5.39 (m, 0.99H), 4.90 (t, *J* = 7.4 Hz, 2.00H), 4.62 (dd, *J* = 6.4, 8.4 Hz, 2.00H), 2.36-2.30 (m, 0.17H), 1.93-1.89 (m, 0.27H), 1.78-1.72 (m, 1.49H), 1.67-1.63 (m, 0.71H), 1.42 (s, 1.77H), 1.20 (s, 0.88H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.69, 77.92, 67.75, 43.60 (m, labeled), 28.43 (m, labeled), 24.97 (m, labeled).

Deuterium incorporation: 5.7 D/molecule (^{1}H-NMR), 6.0 D/molecule [HRMS (ESI)].

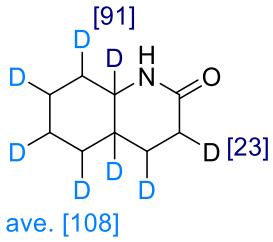


188.1372 ($C_{10}H_{13}D_3O_3 + H^+$, 1%), 189.1434 ($C_{10}H_{12}D_4O_3 + H^+$, 5%), 190.1493 ($C_{10}H_{11}D_5O_3 + H^+$, 23%), 191.1549 ($C_{10}H_{10}D_6O_3 + H^+$, 47%), 192.1602 ($C_{10}H_9D_7O_3 + H^+$, 17%), 193.1669 ($C_{10}H_8D_8O_3 + H^+$, 5%), 194.1738 ($C_{10}H_7D_9O_3 + H^+$, 1%).



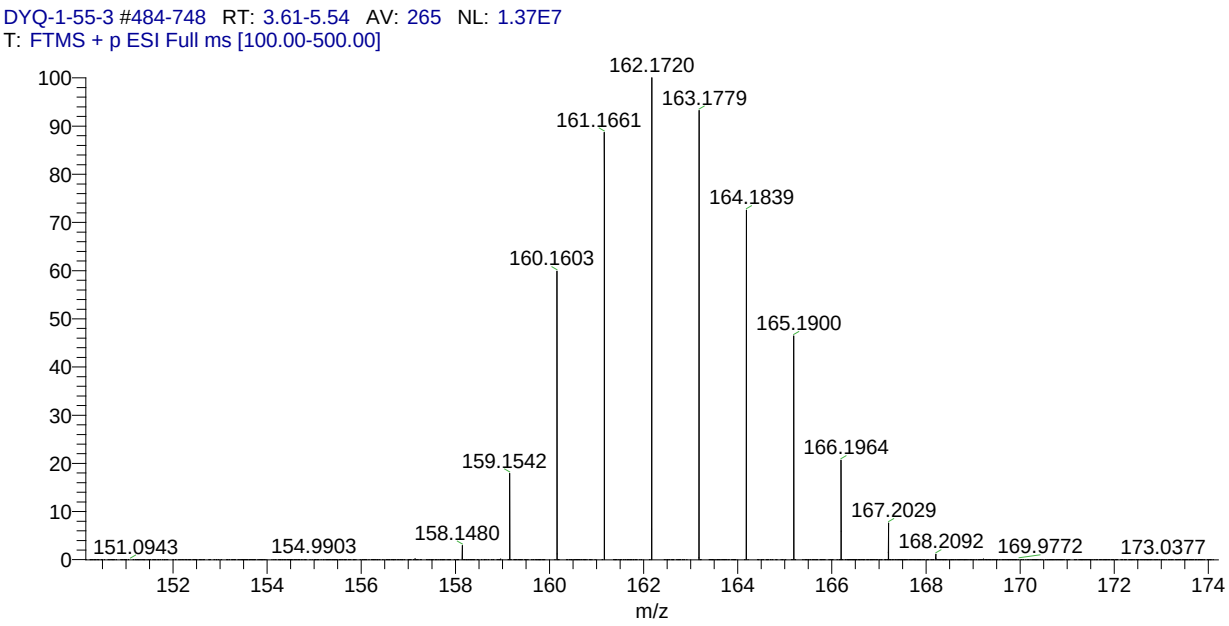
Octahydro-1*H*-isochromen-1-one-4,4a,5,6,7,8,8a-*d*$_7$ (18b). The title product was obtained with 84% yield (54.0 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.39-4.22 (m, 2.00H), 2.69-2.67 (m, 0.05H), 2.32-2.16 (m, 2.20H), 2.03-1.97 (m, 0.15H), 1.79 (s, 0.15H), 1.72-1.62 (m, 2.00H), 1.45 (s, 0.34H), 1.20 (s, 0.19H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.83, 151.64, 124.30, 66.93, 66.88, 65.60, 65.55, 65.50, 30.11 (m, labeled), 29.30, 28.95 (m, labeled), 23.13 (m, labeled), 21.39 (m, labeled).

Deuterium incorporation: 6.9 D/molecule (^{1}H-NMR).

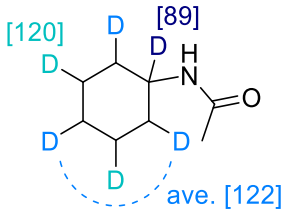


Octahydroquinolin-2(1H)-one-4,4a,5,6,7,8,8a-*d*$_7$ (19b). The title product was obtained with 96% yield (61.4 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.61 (s, 1.00H), 3.46 (s, 0.09H), 2.40-2.25 (m, 1.77H), 1.90-1.77 (m, 0.64H), 1.70-1.63 (m, 0.48H), 1.59-1.40 (m, 2.64H), 1.34-1.28 (m, 0.44H); ^{13}C NMR (201 MHz, $CDCl_3$) δ 172.94, 51.94 (m, labeled), 32.30 (m, labeled), 30.79 (m, labeled), 28.88 (m, labeled), 26.09 (m, labeled), 23.99 (m, labeled), 22.75 (m, labeled), 20.81 (m, labeled).

Deuterium incorporation: 7.9 D/molecule (^{1}H-NMR), 8.5 D/molecule [HRMS (ESI)]

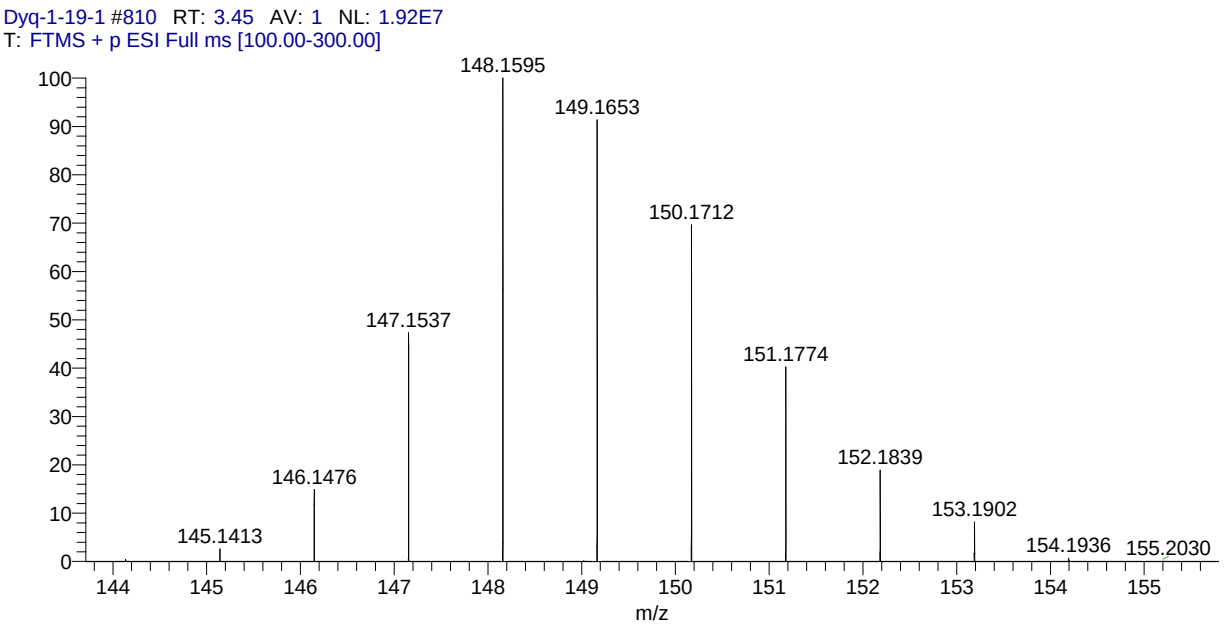


158.1480 ($C_9H_{11}D_4NO + H^+$, 1%), 159.1542 ($C_9H_{10}D_5NO + H^+$, 3%), 160.1603 ($C_9H_9D_6NO + H^+$, 12%), 161.1661 ($C_9H_8D_7NO + H^+$, 17%), 162.1720 ($C_9H_7D_8NO + H^+$, 20%), 163.1779 ($C_9H_6D_9NO + H^+$, 18%), 164.1839 ($C_9H_5D_{10}NO + H^+$, 14%), 165.1900 ($C_9H_4D_{11}NO + H^+$, 9%), 166.1964 ($C_9H_3D_{12}NO + H^+$, 4%), 167.2029 ($C_9H_2D_{13}NO + H^+$, 2%).

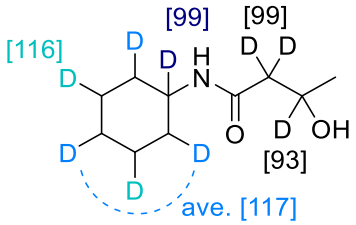


***N*-(cyclohexyl-1,2,3,4,5,6-*d*$_6$)acetamide (20b)**. The title product was obtained with 89% yield (50.5 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.60 (s, 1.00H), 3.75-3.67 (m, 0.11H), 2.01 (s, 0.10H), 1.93 (s, 2.88H), 1.89-1.84 (m, 0.33H), 1.69-1.64 (m, 1.05H), 1.59-1.55 (m, 0.31H), 1.35-1.23 (m, 0.55H), 1.14-1.06 (m, 1.69H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.27, 32.67 (m, labeled), 29.77 (m, labeled), 24.87 (m, labeled), 23.84.

Deuterium incorporation: 7.0 D/molecule (^{1}H-NMR), 7.1 D/molecule [HRMS (ESI)].

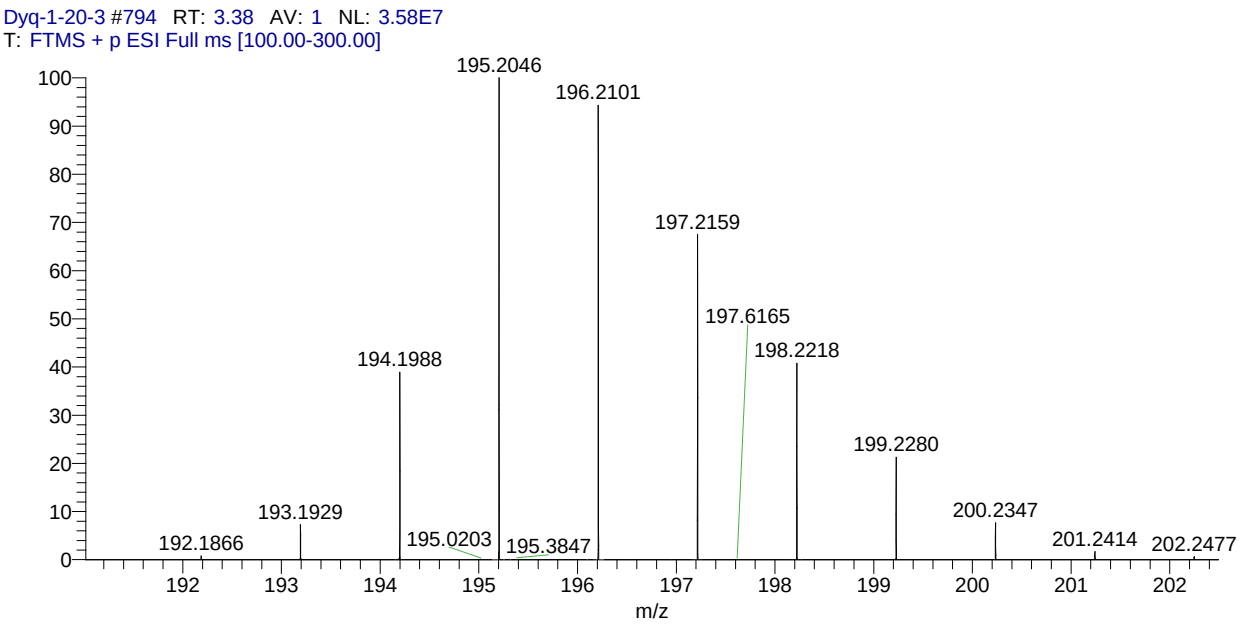


145.1413 ($C_8H_{12}D_3NO + H^+$, 1%), 146.1476 ($C_8H_{11}D_4NO + H^+$, 5%), 147.1537 ($C_8H_{10}D_5NO + H^+$, 17%), 148.1595 ($C_8H_9D_6NO + H^+$, 37%), 149.1653 ($C_8H_8D_7NO + H^+$, 36%), 150.1712 ($C_8H_7D_8NO + H^+$, 27%), 151.1774 ($C_8H_6D_9NO + H^+$, 17%), 152.1839 ($C_8H_5D_{10}NO + H^+$, 9%), 153. 1902 ($C_8H_4D_{11}NO + H^+$, 4%).

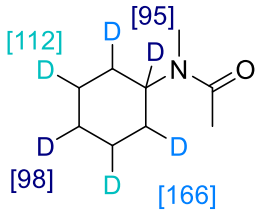


***N*-(cyclohexyl-1,2,3,4,5,6-*d*$_6$)-3-hydroxybutanamide (21b)**. The title product was obtained with 71% yield (60.1 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.91 (s, 1.00H), 4.09-4.05 (s, 1.00H), 3.77-3.70 (m, 0.07H), 2.24 (d, *J* = 29.2 Hz, 0.03H), 1.89-1.84 (m, 0.28H), 1.65 (s, 1.17H), 1.60-1.56 (m, 0.35H), 1.34-1.29 (m, 0.51H), 1.26-1.17 (m, 2.95H), 1.10 (s, 1.85H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.66, 64.67 (m, labeled), 47.76 (m, labeled), 43.30 (m, labeled), 32.59 (m, labeled), 24.66 (m, labeled), 22.77, 22.38 (m, labeled).

Deuterium incorporation: 9.7 D/molecule (^{1}H-NMR), 10.2 D/molecule [HRMS (ESI)].

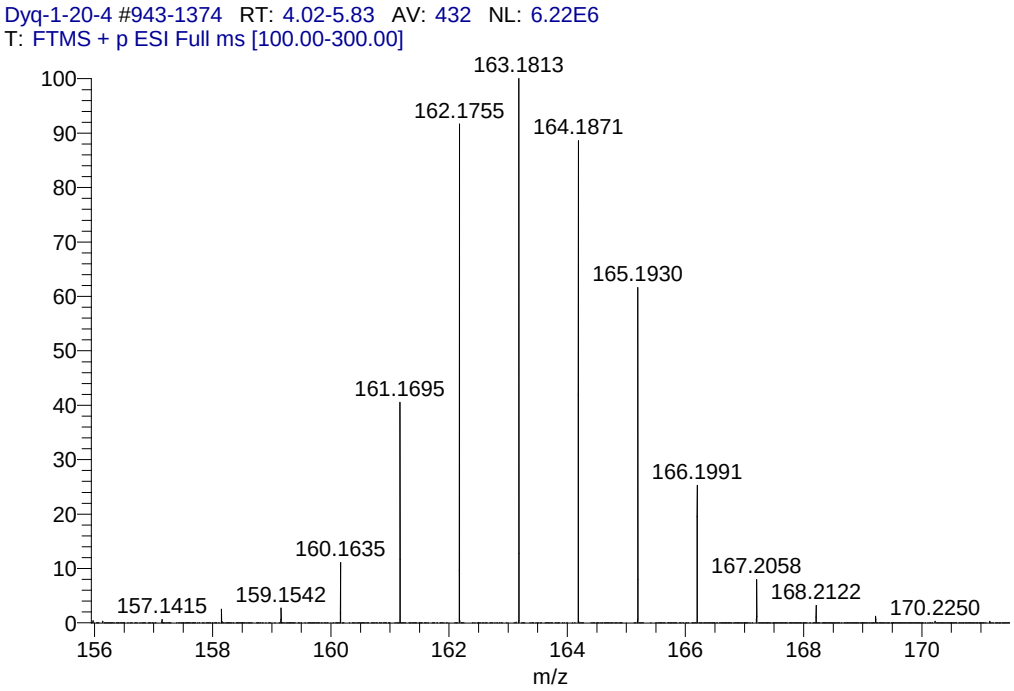


193.1932 ($C_{10}H_{12}D_7NO_2$ + H^+, 2%), 194.1992 ($C_{10}H_{11}D_8NO_2$ + H^+, 14%), 195.2050 ($C_{10}H_{10}D_9NO_2$ + H^+, 39%), 196.2105 ($C_{10}H_9D_{10}NO_2$ + H^+, 36%), 197.2163 ($C_{10}H_8D_{11}NO_2$ + H^+, 26%), 198.2222 ($C_{10}H_7D_{12}NO_2$ + H^+, 16%), 199.2283 ($C_{10}H_6D_{13}NO_2$ + H^+, 8%), 200.2350 ($C_{10}H_5D_{14}NO_2$ + H^+, 4%), 201.2416 ($C_{10}H_4D_{15}NO_2$ + H^+, 1%).

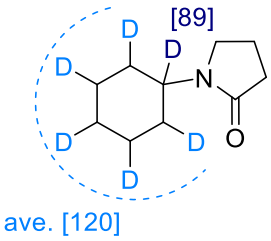


***N*-(cyclohexyl-1,2,3,4,5,6-*d*$_6$)-*N*-methylacetamide (22b)**. The title product was obtained with 70% yield (45.2 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.47-3.41 (m, 0.05H), 2.78 (d, *J* = 12.8 Hz, 3.00H), 2.06 (d, *J* = 15.6 Hz, 2.98H), 1.78 (s, 0.54H), 1.71 (s, 0.56H), 1.44 (s, 0.80H), 1.27 (s, 1.26H), 1.03-1.00 (m, 0.52H); ^{1}H NMR (800 MHz, $CDCl_3$) δ 3.43 (s, 0.05H), 2.77 (d, *J* = 14.8 Hz, 3.00H), 2.05 (d, *J* = 16.8 Hz, 2.99H), 1.78 (s, 0.51H), 1.70 (s, 0.56H), 1.44 (s, 0.77H), 1.26 (s, 1.26H), 1.03 (s, 0.25H), 1.00 (s, 0.23H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.21, 170.11, 57.27 (m, labeled), 51.60 (m, labeled), 30.31 (m, labeled), 30.29, 29.48 (m, labeled), 27.01, 24.99 (m, labeled), 22.66, 21.76.

Deuterium incorporation: 7.3 D/molecule (^{1}H-NMR-400MHz), 7.4 D/molecule (^{1}H-NMR-800MHz), 7.3 D/molecule [HRMS (ESI)].

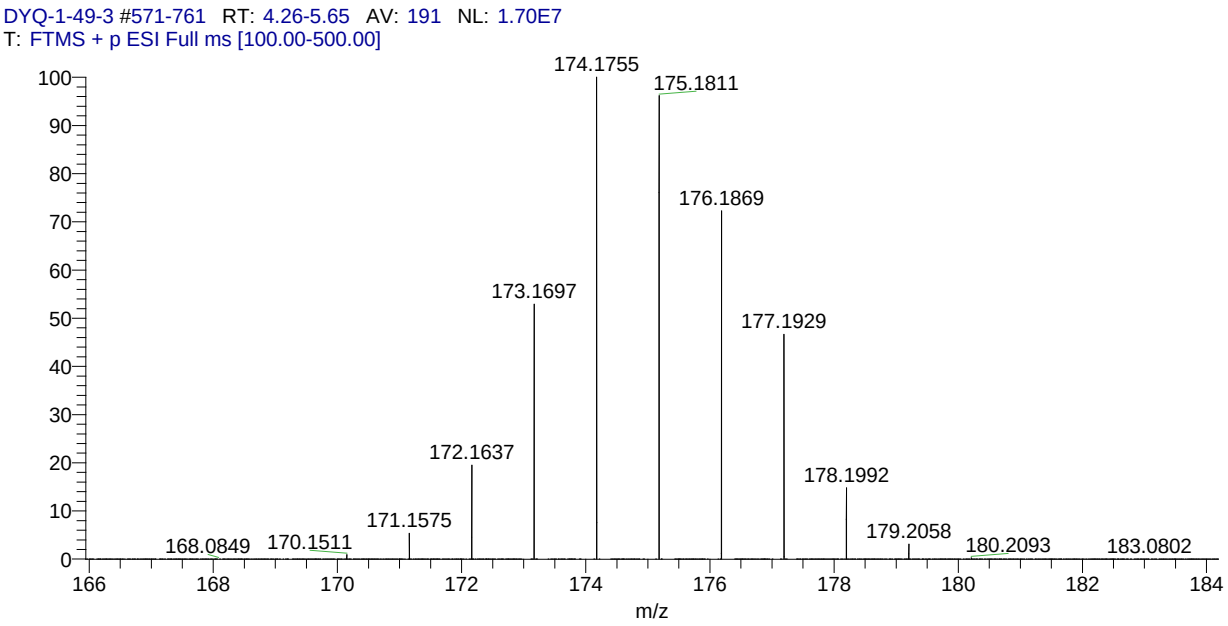


160.1635 ($C_9H_{13}D_4NO + H^+$, 2%), 161.1695 ($C_9H_{12}D_5NO + H^+$, 9%), 162.1755 ($C_9H_{11}D_6NO + H^+$, 21%), 163.1813 ($C_9H_{10}D_7NO + H^+$, 23%), 164.1871 ($C_9H_9D_8NO + H^+$, 21%), 165.1930 ($C_9H_8D_9NO + H^+$, 14%), 166.1991 ($C_9H_7D_{10}NO + H^+$, 6%), 167.2058 ($C_9H_6D_{11}NO + H^+$, 2%), 168.2122 ($C_9H_5D_{12}NO + H^+$, 1%).

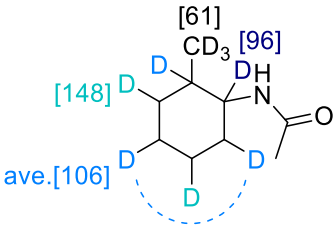


1-(Cyclohexyl-1,2,3,4,5,6-*d*$_6$)pyrrolidin-2-one (23b). The title product was obtained with 89% yield (61.7 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.90-3.83 (m, 0.11H), 3.29 (t, *J* = 7.0 Hz, 2.00H), 2.33 (t, *J* = 8.0 Hz, 1.99H), 1.97-1.89 (m, 1.99H), 1.69 (s, 0.92H), 1.64-1.57 (m, 0.62H), 1.28 (s, 2.02H), 1.01 (s, 0.43H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.30, 50.07 (m, labeled), 42.90, 31.71, 29.75 (m, labeled), 24.87 (m, labeled), 18.23.

Deuterium incorporation: 6.9 D/molecule (^{1}H-NMR), 6.9 D/molecule [HRMS (ESI)].

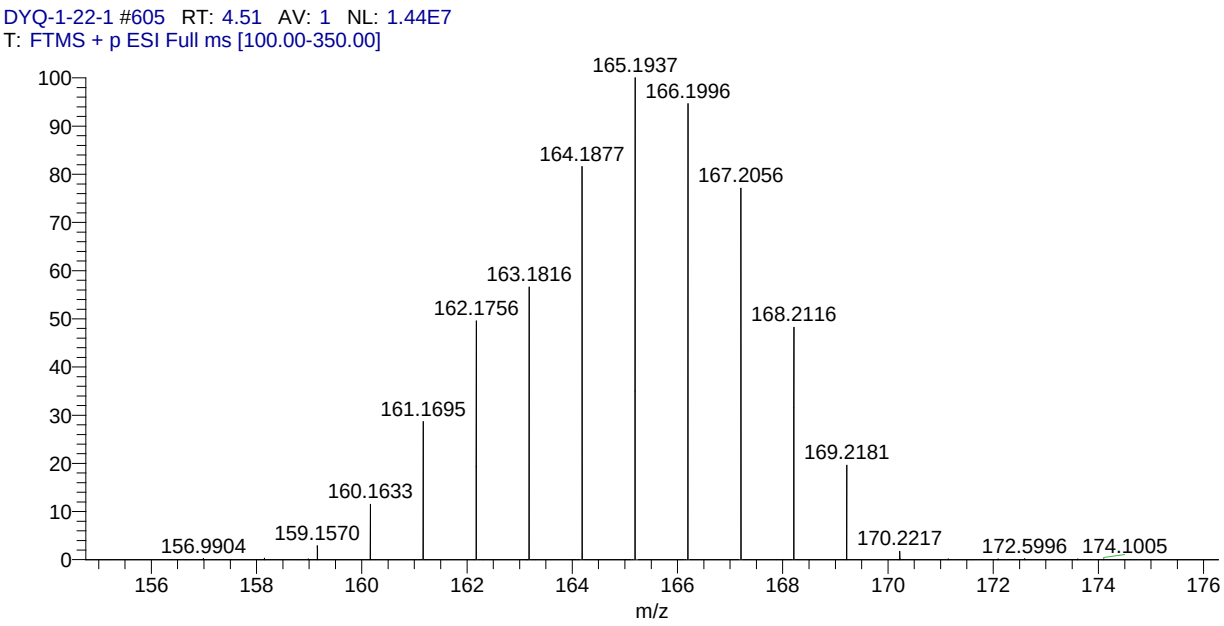


171.1575 ($C_{10}H_{14}D_3NO + H^+$, 1%), 172.1637 ($C_{10}H_{13}D_4NO + H^+$, 4%), 173.1697 ($C_{10}H_{12}D_5NO + H^+$, 12%), 174.1755 ($C_{10}H_{11}D_6NO + H^+$, 25%), 175.1811 ($C_{10}H_{10}D_7NO + H^+$, 24%), 176.1869 ($C_{10}H_9D_8NO + H^+$, 18%), 177.1929 ($C_{10}H_8D_9NO + H^+$, 4%), 178.1992 ($C_{10}H_7D_{10}NO + H^+$, 1%).

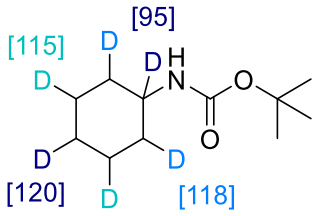


***N*-(2-(methyl-*d*$_3$)cyclohexyl-1,2,3,4,5,6-*d*$_6$)acetamide (24b)**. The title product was obtained with 85% yield (67.6 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.66 (d, *J* = 36.8 Hz, 0.59H), 1.95 (d, *J* = 10.0 Hz, 3.00H), 1.70-1.55 (m, 0.78H), 1.49-1.45 (m, 0.52H), 1.42-1.35 (m, 0.65H), 1.15 (s, 0.52H), 1.00 (s, 0.39H), 0.94-0.79 (m, 1.17H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.66, 169.61, 169.57, 169.52, 53.43 (m, labeled), 49.28 (m, labeled), 33.21 (m, labeled), 29.36 (m, labeled), 25.05 (m, labeled), 23.67, 23.62, 23.59, 23.54, 22.84 (m, labeled), 21.88 (m, labeled), 15.64 (m, labeled).

Deuterium incorporation: 8.9 D/molecule (^{1}H-NMR), 8.9 D/molecule [HRMS (ESI)].

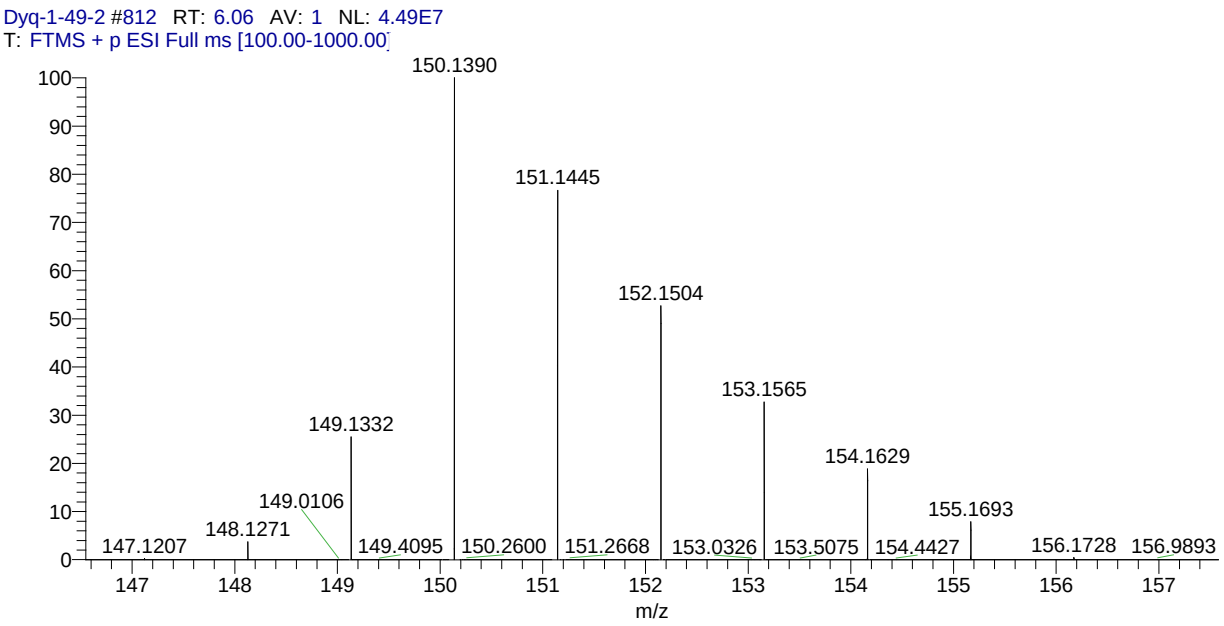


160.1633 ($C_9H_{13}D_4NO + H^+$, 2%), 161.1695 ($C_9H_{12}D_5NO + H^+$, 5%), 162.1756 ($C_9H_{11}D_6NO + H^+$, 8%), 163.1816 ($C_9H_{10}D_7NO + H^+$, 11%), 164.1877 ($C_9H_9D_8NO + H^+$, 13%), 165.1937 ($C_9H_8D_9NO + H^+$, 18%), 166.1996 ($C_9H_7D_{10}NO + H^+$, 17%), 167.2056 ($C_9H_6D_{11}NO + H^+$, 13%), 168.2116 ($C_9H_5D_{12}NO + H^+$, 9%), 169.2181 ($C_9H_4D_{13}NO + H^+$, 3%).

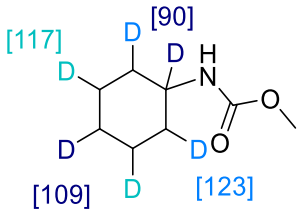


***tert*-Butyl (cyclohexyl-1,2,3,4,5,6-*d*$_6$)carbamate (25b)**. The title product was obtained with 90% yield (75.0 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.43 (s, 0.98H), 3.39 (s, 0.05H), 1.91-1.84 (m, 0.34H), 1.64 (s, 1.09H), 1.53 (s, 0.25H), 1.43 (s, 9.00H), 1.27 (s, 0.61H), 1.09 (s, 0.55H), 1.05 (s, 1.30H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.39, 79.10, 49.03 (m, labeled), 33.08 (m, labeled), 29.87, 28.61, 24.76 (m, labeled).

Deuterium incorporation: 6.8 D/molecule (^{1}H-NMR), 7.1 D/molecule [HRMS (ESI)].

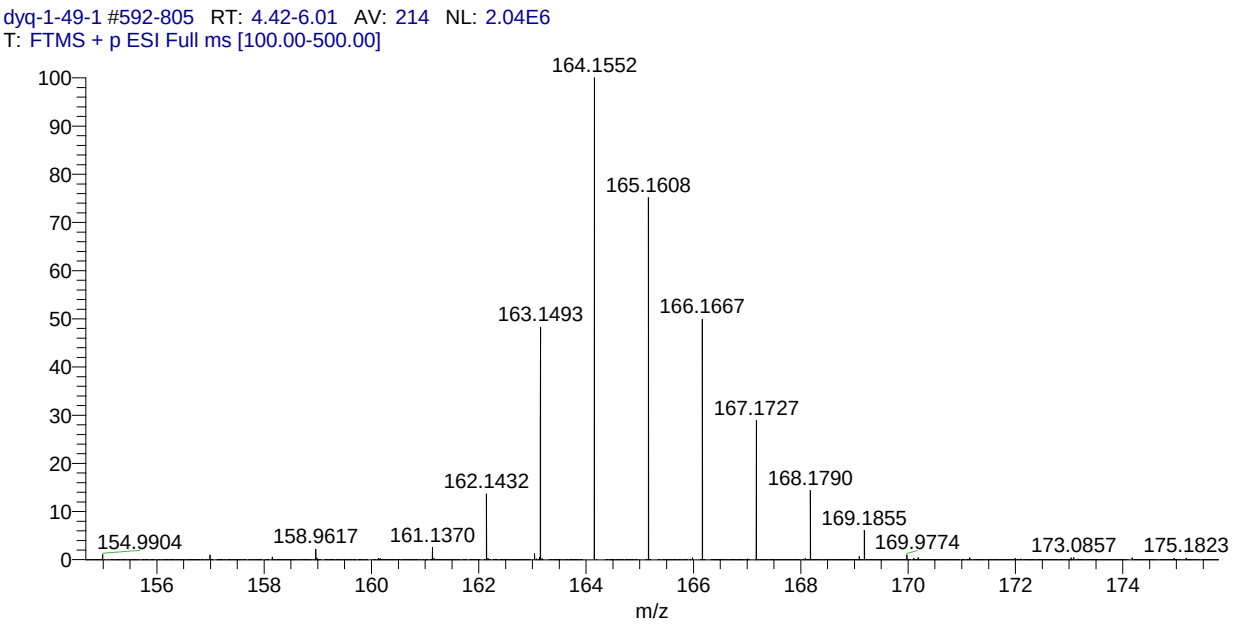


148.1271 ($C_{11}H_{17}D_4NO_2 + H^+$, 1%), 149.1332 ($C_{11}H_{16}D_5NO_2 + H^+$, 8%), 150.1390 ($C_{11}H_{15}D_6NO_2 + H^+$, 32%), 151.1445 ($C_{11}H_{14}D_7NO_2 + H^+$, 24%), 152.1504 ($C_{11}H_{13}D_8NO_2 + H^+$, 17%), 153.1565 ($C_{11}H_{12}D_9NO_2 + H^+$, 10%), 154.1629 ($C_{11}H_{11}D_{10}NO_2 + H^+$, 6%), 155.1693 ($C_{11}H_{10}D_{11}NO_2 + H^+$, 2%).

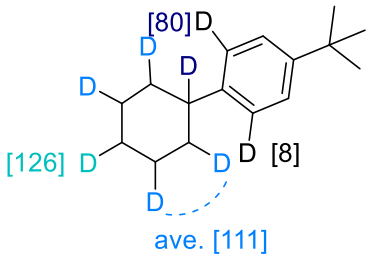


Methyl (cyclohexyl-1,2,3,4,5,6-*d*$_6$)carbamate (26b). The title product was obtained with 90% yield (55.6 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.59 (s, 1.00H), 3.64 (s, 3.00H), 3.45 (s, 0.11H), 1.92-1.87 (m, 0.30H), 1.69-1.64 (m, 1.04H), 1.60-1.54 (0.29H), 1.34-1.25 (m, 0.56H), 1.11-1.08 (m, 1.84H); ^{1}H NMR (800 MHz, $CDCl_3$) δ 4.58-4.43 (m, 1.00H), 3.64 (s, 3.02H), 3.46 (s, 0.10H), 1.88 (s, 0.32H), 1.66 (s, 1.10H), 1.55 (s, 0.29H), 1.30 (s, 0.56H), 1.12 (s, 0.62H), 1.09 (s, 1.22H); ^{13}C NMR (201 MHz, $CDCl_3$) δ 156.41, 52.38 (m, labeled), 51.96, 49.82 (m, labeled), 49.39 (m, labeled), 32.96 (m, labeled), 24.93 (m, labeled), 24.33 (m, labeled).

Deuterium incorporation: 6.9 D/molecule (^{1}H-NMR), 6.9 D/molecule [HRMS (ESI)]

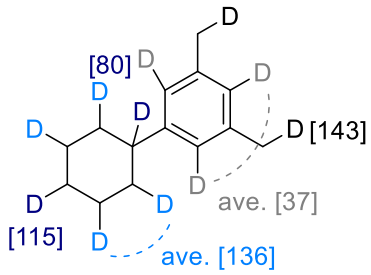


161.1370 ($C_8H_{12}D_3NO_2 + H^+$, 1%), 162.1432 ($C_8H_{11}D_4NO_2 + H^+$, 4%), 163.1493 ($C_8H_{10}D_5NO_2 + H^+$, 13%), 164.1552 ($C_8H_9D_6NO_2 + H^+$, 28%), 165.1608 ($C_8H_8D_7NO_2 + H^+$, 23%), 166.1667 ($C_8H_7D_8NO_2 + H^+$, 16%), 167.1727 ($C_8H_6D_9NO_2 + H^+$, 9%), 168.1790 ($C_8H_5D_{10}NO_2 + H^+$, 5%), 169.1855 ($C_8H_4D_{11}NO_2 + H^+$, 2%).



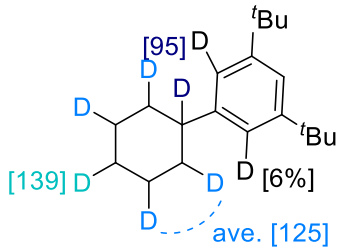
1-(*tert*-Butyl)-4-(cyclohexyl-1,2,3,4,5,6-d_6)benzene (27b). The title product was obtained with 62% yield (34.1 mg, 0.2 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.4 Hz, 1.94H), 7.18 (d, *J* = 8.4 Hz, 1.84H), 2.50 (t, *J* = 12.0 Hz, 0.20H), 1.91-1.83 (m, 1.27H), 1.77-1.74 (m, 0.25H), 1.41 (s, 2.28H), 1.35 (s, 9.00H), 1.25 (s, 0.49H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.59, 145.23, 126.60, 125.32, 44.00 (m, labeled), 34.53, 33.68 (m, labeled), 31.65, 26.56 (m, labeled).

Deuterium incorporation: 6.7 D/molecule (^{1}H-NMR).



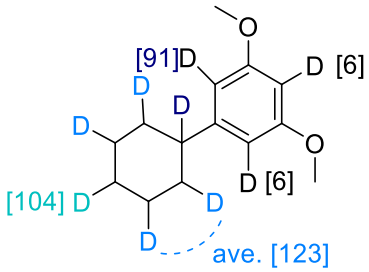
1-(Cyclohexyl-1,2,3,4,5,6-*d*$_6$)-3,5-bis(methyl-*d*)benzene (28b). The title product was obtained with 30% yield (24.0 mg, 0.2 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (s, 1.89H), 2.48-2.40 (m, 0.20H), 2.32 (s, 3.15H), 1.87-1.81 (m, 1.89H), 1.76-1.69 (m, 0.31H), 1.39 (s, 1.66H), 1.23 (s, 0.54H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.35, 137.87, 127.65, 124.87, 44.52 (m, labeled), 34.18 (m, labeled), 26.43 (m, labeled), 21.57.

Deuterium incorporation: 11.4 D/molecule (^{1}H-NMR).



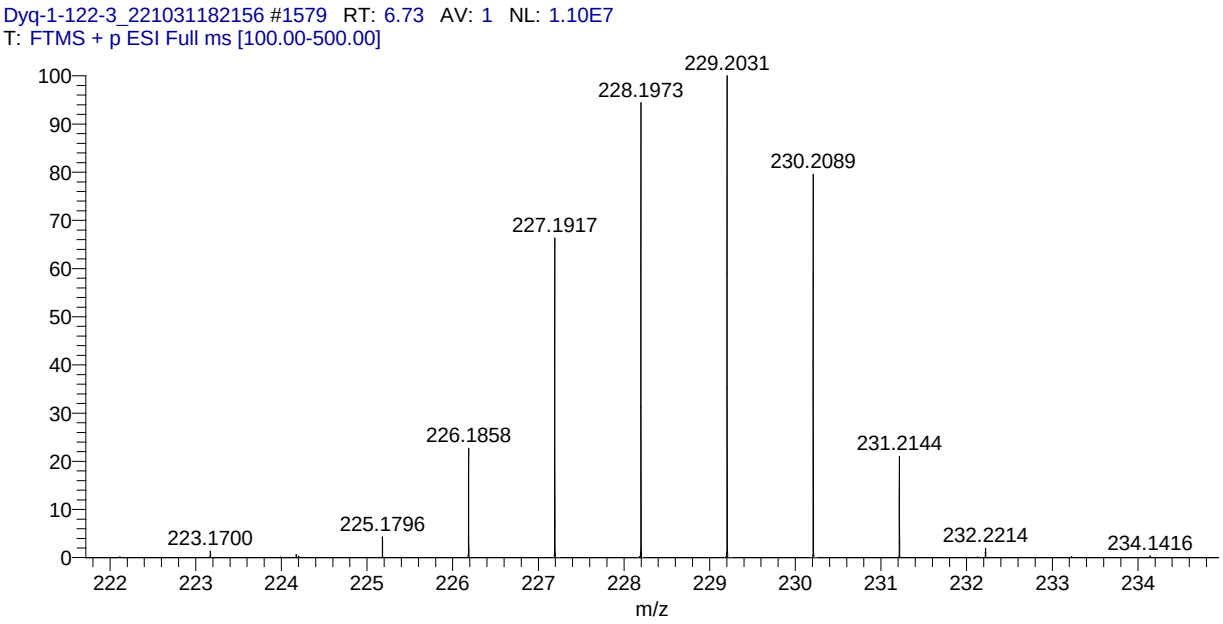
1,3-Di-*tert*-butyl-5-(cyclohexyl-1,2,3,4,5,6-*d*$_6$)benzene (29b). The title product was obtained with 86% yield (40.0 mg, 0.2 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, *J* = 2.0 Hz, 0.98H), 7.10 (d, *J* = 2.0 Hz, 1.88H), 2.52 (t, *J* = 12.0 Hz, 0.05H), 1.94-1.83 (m, 1.15H), 1.74 (s, 0.13H), 1.44 (s, 1.85H), 1.37 (s, 18.00H), 1.27 (s, 0.48H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.54, 147.34, 121.25, 120.08, 44.67 (m, labeled), 35.09, 34.21 (m, labeled), 31.80, 26.58 (m, labeled).

Deuterium incorporation: 7.5 D/molecule (^{1}H-NMR).

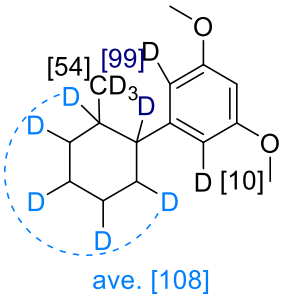


1-(Cyclohexyl-1,2,3,4,5,6-*d*$_6$)-3,5-dimethoxybenzene (30b). The title product was obtained with 78% yield (70.8 mg, 0.4 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.41 (d, *J* = 2.0 Hz, 1.88H), 6.32 (m, 0.94H), 3.80 (s, 6.00H), 2.45 (t, *J* = 12.0, 0.09H), 1.89-1.81 (m, 1.00H), 1.71-1.65 (m, 0.49H), 1.38 (s, 2.10H), 1.23 (s, 0.47H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.87, 150.88, 105.18, 97.75, 55.38, 44.62 (m, labeled), 33.84 (m, labeled), 29.44 (m, labeled), 26.36 (m, labeled), 25.61 (m, labeled).

Deuterium incorporation: 7.1 D/molecule (^{1}H-NMR), 7.4 D/molecule (HRMS (ESI)).

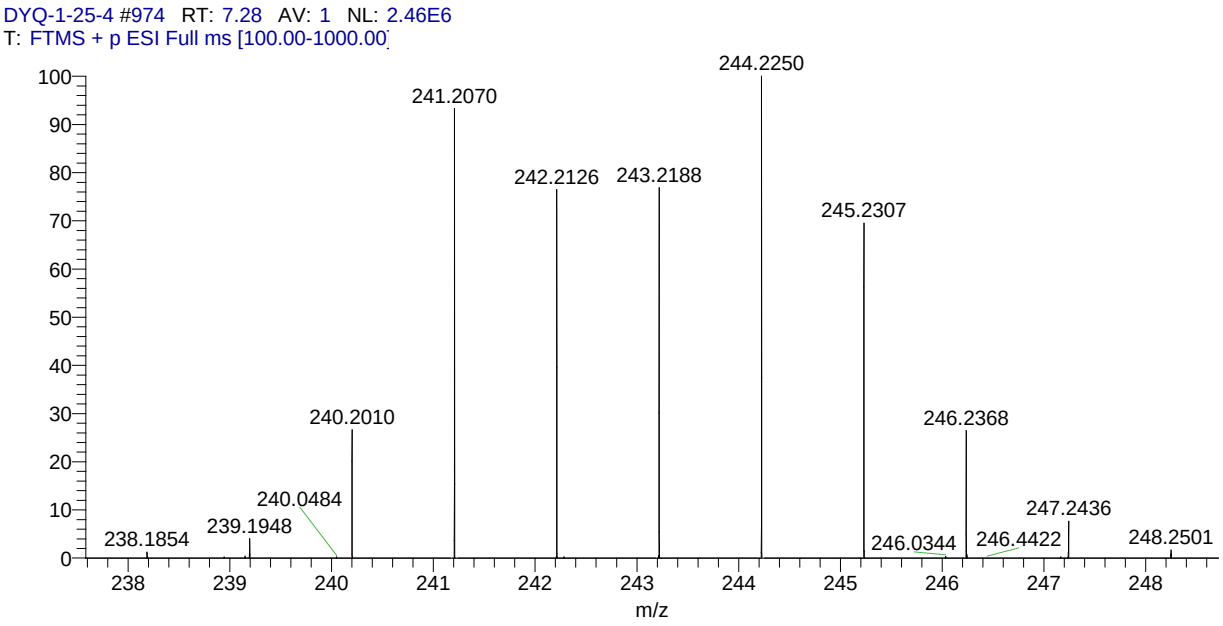


225.1796 ($C_{14}H_{16}D_4O_2 + H^+$, 1%), 226.1858 ($C_{14}H_{15}D_5O_2 + H^+$, 4%), 227.1917 ($C_{14}H_{14}D_6O_2 + H^+$, 13%), 228.1973 ($C_{14}H_{13}D_7O_2 + H^+$, 43%), 229.2031 ($C_{14}H_{12}D_8O_2 + H^+$, 20%), 230.2089 ($C_{14}H_{11}D_9O_2 + H^+$, 15%), 231.2144 ($C_{14}H_{10}D_{10}O_2 + H^+$, 4%).

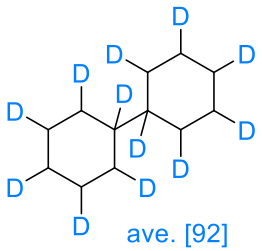


1,3-Dimethoxy-5-(2-(methyl-*d*$_2$)cyclohexyl-1,3,4,5,6-*d*$_5$)benzene (31b). The title product was obtained with 76% yield (73.6 mg, 0.4 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.36-6.34 (m, 1.80H), 6.32-6.31 (m, 0.98H), 3.80 (s, 6.00H), 1.82 (s, 0.61H), 1.75 (s, 0.88H), 1.66-1.59 (m, 1.38H), 1.46 (s, 0.74H), 0.72-0.67 (m, 1.37H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.62, 149.18, 106.03, 97.42, 55.41, 33.13 (m, labeled), 26.29 (m, labeled), 24.26 (m, labeled), 19.90 (m, labeled), 12.51.

Deuterium incorporation: 8.2 D/molecule (^{1}H-NMR) , 8.0 D/molecule (HRMS (ESI)).

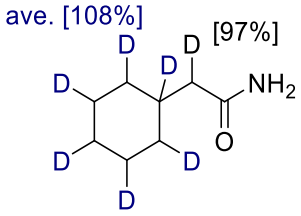


239.1948 ($C_{15}H_{18}D_4O_2 + H^+$, 1%), 240.2010 ($C_{15}H_{17}D_5O_2 + H^+$, 6%), 241.2070 ($C_{15}H_{16}D_6O_2 + H^+$, 20%), 242.2126 ($C_{15}H_{15}D_7O_2 + H^+$, 15%), 243.2188 ($C_{15}H_{14}D_8O_2 + H^+$, 15%), 244.2250 ($C_{15}H_{13}D_9O_2 + H^+$, 21%), 245.2307 ($C_{15}H_{12}D_{10}O_2 + H^+$, 14%), 246.2368 ($C_{15}H_{11}D_{11}O_2 + H^+$, 6%), 247.2436 ($C_{15}H_{10}D_{12}O_2 + H^+$, 1%).



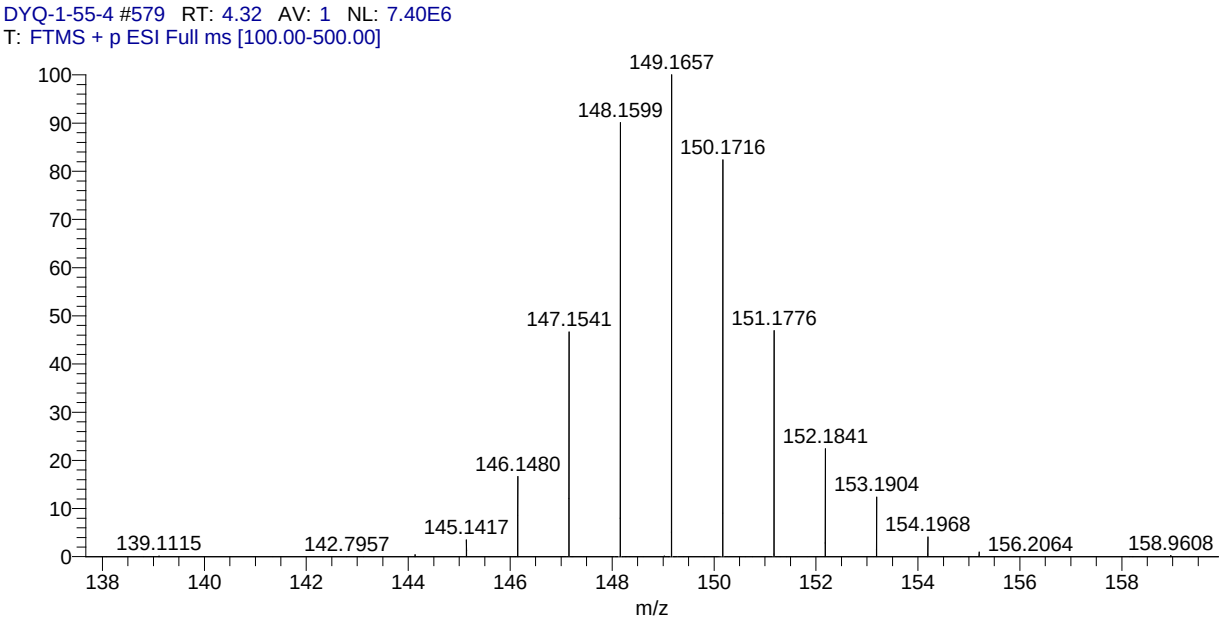
1,1'-Bi(cyclohexane)-1,1',2,2',3,3',4,4',5,5',6,6'-*d*$_{12}$ (32b). The title product was obtained with 68% yield (48.9 mg, 0.4 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.71-1.58 (m, 3.82H), 1.15-0.90 (m, 7.11H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 29.75 (m, labeled), 26.42 (m, labeled).

Deuterium incorporation: 11.1 D/molecule (^{1}H-NMR).

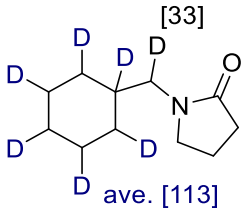


2-(Cyclohexyl-1,2,3,4,5,6-*d*$_6$)acetamide-2-*d* (33b). The title product was obtained with 83% yield (48.7 mg, 0.4 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.43 (d, *J* = 25.6 Hz, 2.00H), 2.10-2.07 (m, 1.03H), 1.78-1.62 (m, 1.68H), 1.38-1.22 (m, 0.95H), 1.11 (s, 0.57), 0.93 (s, 1.34); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.18, 44.10, 32.64 (m, labeled), 29.91 (m, labeled), 25.57 (m, labeled).

Deuterium incorporation: 7.4 D/molecule (^{1}H-NMR), 7.2 D/molecule [HRMS (ESI)]

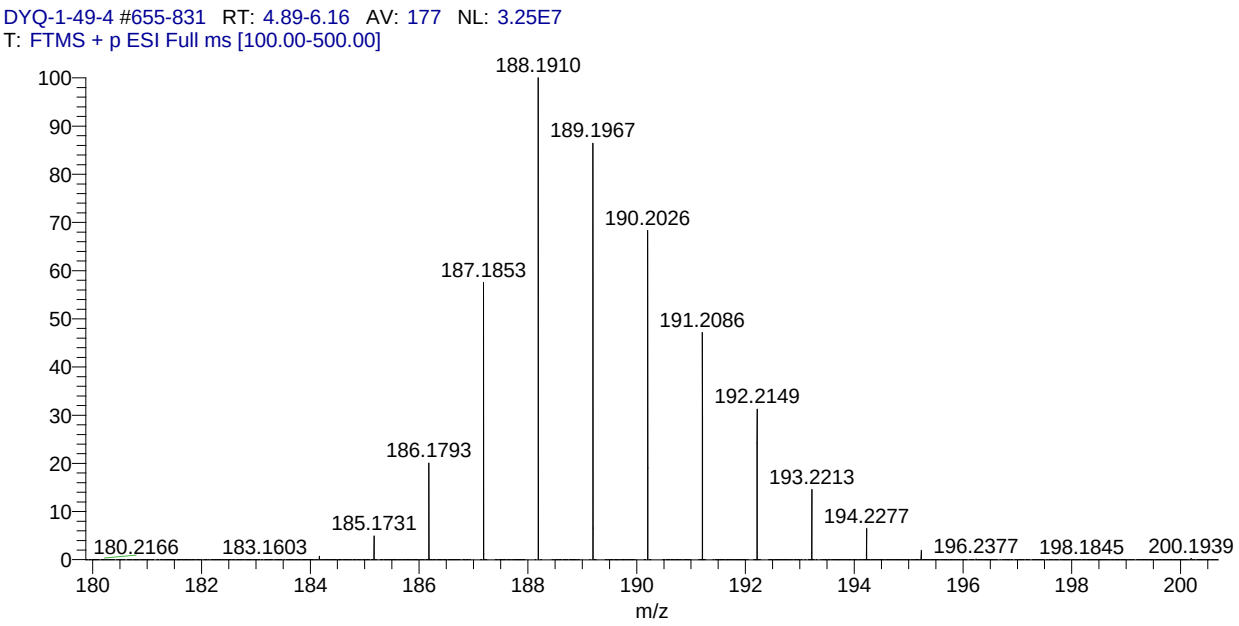


145.1417 ($C_8H_{12}D_3NO + H^+$, 1%), 146.1480 ($C_8H_{11}D_4NO + H^+$, 4%), 147.1541 ($C_8H_{10}D_5NO + H^+$, 12%), 148.1599 ($C_8H_9D_6NO + H^+$, 21%), 149.1657 ($C_8H_8D_7NO + H^+$, 23%), 150.1716 ($C_8H_7D_8NO + H^+$, 19%), 151.1776 ($C_8H_6D_9NO + H^+$, 11%), 152.1841 ($C_8H_5D_{10}NO + H^+$, 6%), 153.1904 ($C_8H_4D_{11}NO + H^+$, 3%), 154.1968 ($C_8H_3D_{12}NO + H^+$, 1%).

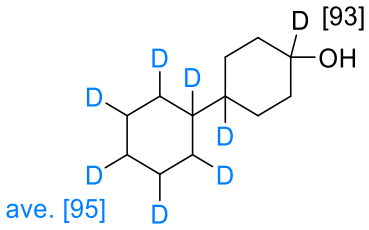


1-((Cyclohexyl-1,2,3,4,5,6-*d*$_6$)methyl-*d*)pyrrolidin-2-one (34b). The title product was obtained with 89% yield (66.5 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.29 (t, *J* = 7.2 Hz, 2.00H), 3.03-2.99 (m, 1.67H), 2.30 (t, *J* = 8.0 Hz, 2.00H), 1.97-1.89 (m, 2.01H), 1.63-1.52 (m, 1.78H), 1.12-1.04 (m, 0.88H), 0.83 (s, 1.55H); ^{13}C NMR (201 MHz, $CDCl_3$) δ 175.27, 49.03, 48.94, 48.62 (m, labeled), 48.06, 48.03, 47.99, 35.31 (m, labeled), 31.20, 30.20 (m, labeled), 25.79 (m, labeled), 25.22 (m, labeled), 18.19.

Deuterium incorporation: 7.1D/molecule (^{1}H-NMR), 7.1 D/molecule [HRMS (ESI)]

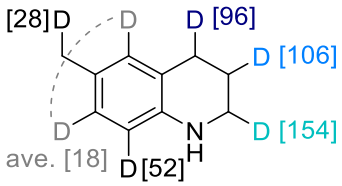


185.1731 ($C_{11}H_{16}D_3NO + H^+$, 1%), 186.1793, ($C_{11}H_{15}D_4NO + H^+$, 4%), 187.1853 ($C_{11}H_{14}D_5NO + H^+$, 12%), 188.1910 ($C_{11}H_{13}D_6NO + H^+$, 22%), 189.1967 ($C_{11}H_{12}D_7NO + H^+$, 21%), 190.2026 ($C_{11}H_{11}D_8NO + H^+$, 17%), 191.2086 ($C_{11}H_{10}D_9NO + H^+$, 11%), 192.2149 ($C_{11}H_9D_{10}NO + H^+$, 7%), 193.2213 ($C_{11}H_8D_{11}NO + H^+$, 2%), 194.2277 ($C_{11}H_7D_{12}NO + H^+$, 1%).



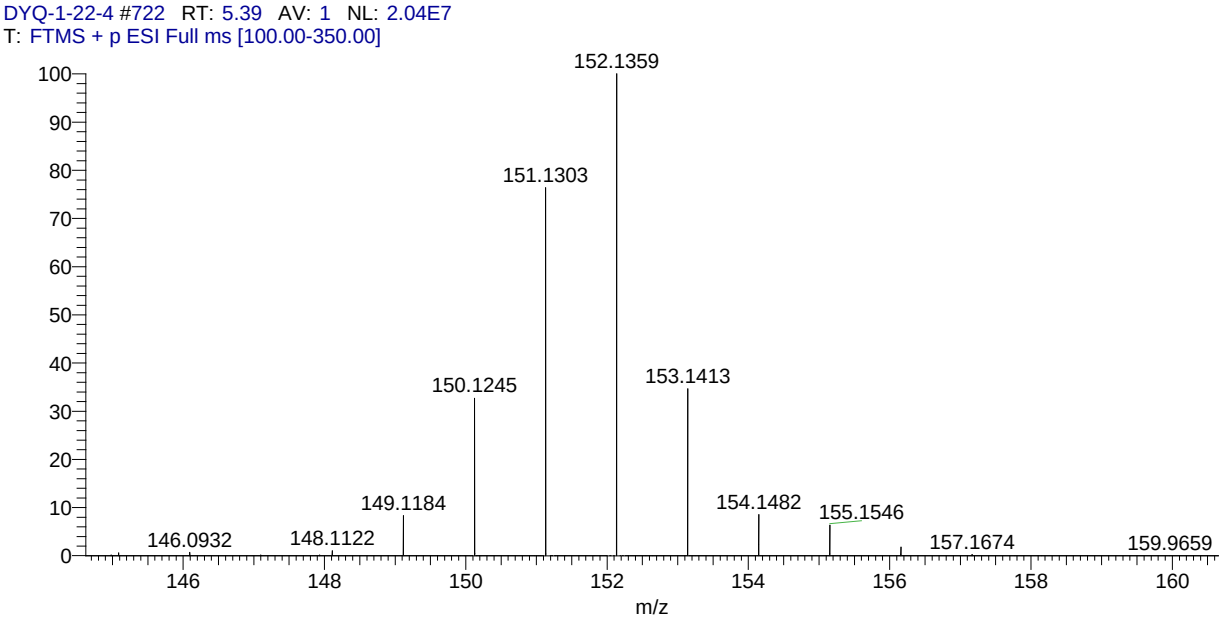
[1,1'-Bi(cyclohexan)]-1,1',2',3',4,4',5',6'-*d*$_8$-4-ol (35b). The title product was obtained with 99% yield (77.2 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.56-3.48 (m, 0.07H), 1.97 (d, *J* = 15.6 Hz, 1.00H), 1.74-1.68 (m, 3.01H), 1.60 (s, 0.38H), 1.55-0.91 (m, 9.07H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 71.01 (m, labeled), 42.43, 41.70 (m, labeled), 36.01, 35.73 (m, labeled), 32.85, 32.65 (m, labeled), 29.84 (m, labeled), 28.22, 28.11, 28.01, 26.27 (m, labeled), 23.96, 23.86, 23.77.

Deuterium incorporation: 7.5 D/molecule (^{1}H-NMR).

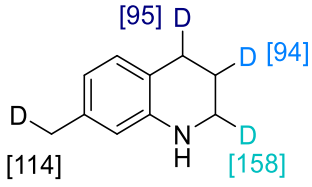


6-Methyl-1,2,3,4-tetrahydroquinoline-2,2,3,4,8-*d*$_5$ (36b). The title product was obtained with 82% yield (49.1 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84-6.83 (m, 1.64H), 6.47-6.45 (m, 0.48H), 3.69 (s, 1.00H), 3.31-3.28 (m, 0.46H), 2.80-2.75 (m, 1.04H), 2.26 (s, 2.72H), 1.98-1.93 (m, 0.94H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.64, 130.28, 127.44, 126.44, 121.77, 114.65, 42.27 (m, labeled), 27.03 (m, labeled), 21.83 (m, labeled), 20.60.

Deuterium incorporation: 4.7 D/molecule (^{1}H-NMR), 4.7 D/molecule [HRMS (ESI)].

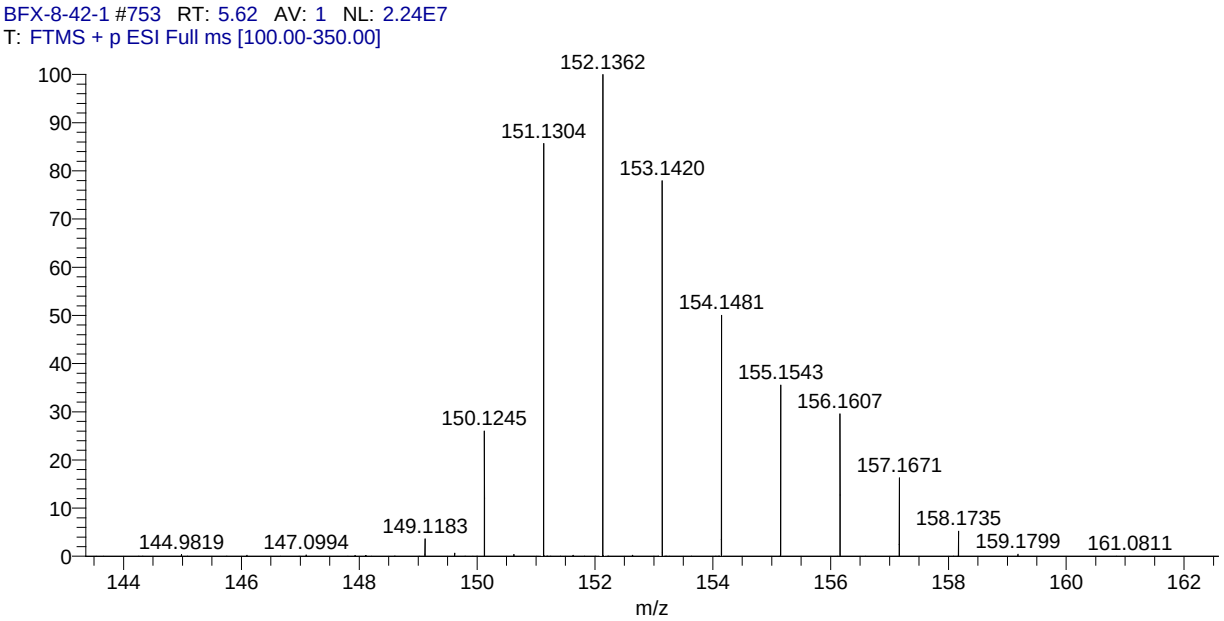


149.1184 ($C_{10}H_{12}DN + H^+$, 3%), 150.1245 ($C_{10}H_{11}D_2N + H^+$, 12%), 151.1303 ($C_{10}H_{10}D_3N + H^+$, 29%), 152.1359 ($C_{10}H_9D_4N + H^+$, 40%), 153.1413 ($C_{10}H_8D_5N + H^+$, 14%).

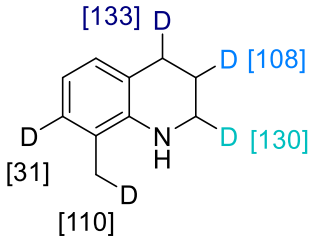


7-Methyl-1,2,3,4-tetrahydroquinoline-2,3,4-*d*$_3$ (37b). The title product was obtained with 81% yield (48.6 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (d, *J* = 7.6 Hz, 1.00H), 6.45 (dd, *J* = 1.6, 7.6 Hz, 1.00H), 6.33 (s, 1.00H), 3.29-3.26 (m, 0.42H), 2.74-2.71 (m, 1.05H), 2.23 (s, 2.86H), 1.94-1.89 (m, 1.06H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.81, 136.57, 129.59, 118.72, 118.11, 114.97, 41.78 (m, labeled), 29.91, 26.36 (m, labeled), 22.01 (m, labeled), 21.32.

Deuterium incorporation: 4.6 D/molecule (^{1}H-NMR), 4.7 D/molecule [HRMS (ESI)]

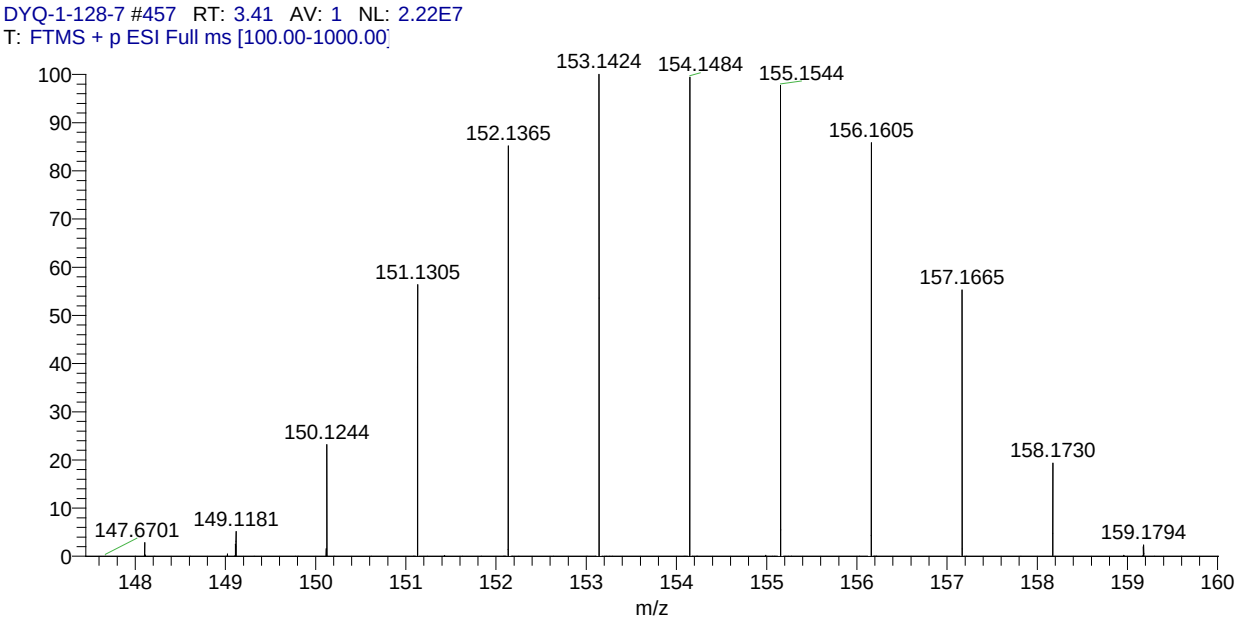


149.1183 ($C_{10}H_{12}D_1N + H^+$, 1%), 150.1245 ($C_{10}H_{11}D_2N + H^+$, 6%), 151.1304 ($C_{10}H_{10}D_3N + H^+$, 20%), 152.1362 ($C_{10}H_9D_4N + H^+$, 25%), 153.1420 ($C_{10}H_8D_5N + H^+$, 18%), 154.1481 ($C_{10}H_7D_6N + H^+$, 12%), 155.1543 ($C_{10}H_6D_7N + H^+$, 9%), 156.1607 ($C_{10}H_5D_8N + H^+$, 8%), 157.1671 ($C_{10}H_4D_9N + H^+$, 1%).

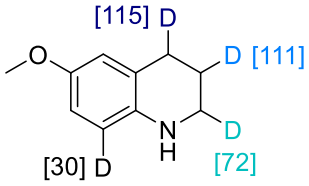


8-(Methyl-*d*)-1,2,3,4-tetrahydroquinoline-2,3,4-*d*$_3$ (38b). The title product was obtained with 74% yield (44.8 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.92-6.87 (m, 2.00H), 6.61-6.57 (m, 0.69H), 3.57-3.37 (m, 1.70H), 2.87-2.79 (m, 0.67H), 2.11-2.08 (m, 1.90H), 1.97-1.92 (m, 0.92H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.91, 128.02, 127.91, 127.56, 127.45, 121.38, 121.29, 121.01, 120.95, 116.58, 42.08 (m, labeled), 27.01 (m, labeled), 21.82 (m, labeled), 17.36, 17.08 (m, labeled).

Deuterium incorporation: 5.1D/molecule (^{1}H-NMR), 6.1 D/molecule [HRMS (ESI)].

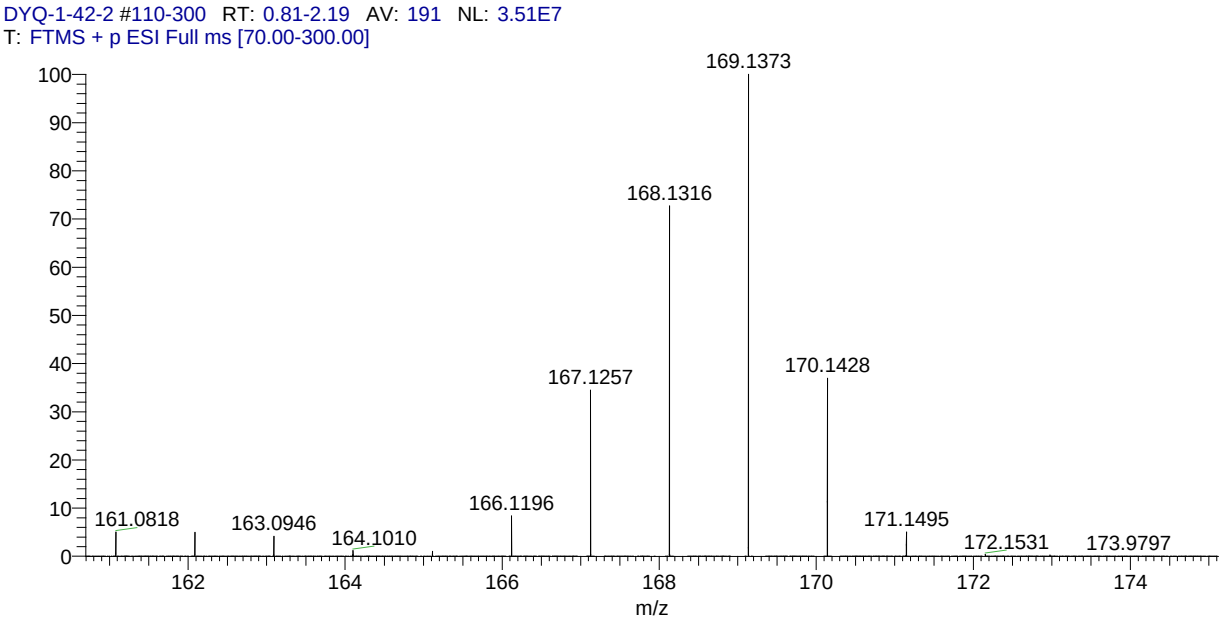


149.1181 ($C_{10}H_{12}DN + H^+$, 1%), 150.1244 ($C_{10}H_{11}D_2N + H^+$, 3%), 151.1305 ($C_{10}H_{10}D_3N + H^+$, 8%), 152.1365 ($C_{10}H_9D_4N + H^+$, 13%), 153.1424 ($C_{10}H_8D_5N + H^+$, 15%), 154.1484 ($C_{10}H_7D_6N + H^+$, 16%), 155.1544 ($C_{10}H_6D_7N + H^+$, 16%), 156.1605 ($C_{10}H_5D_8N + H^+$, 15%), 157.1665 ($C_{10}H_4D_9N + H^+$, 10%), 158.1730 ($C_{10}H_3D_{10}N + H^+$, 4%).

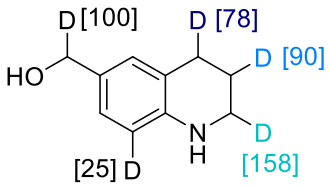


6-Methoxy-1,2,3,4-tetrahydroquinoline-2,2,3,4-*d*$_4$ (39b). The title product was obtained with 52% yield (35.0 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.62-6.57 (m, 1.98H), 6.47 (d, *J* = 8.4 Hz, 0.70H), 3.74 (s, 3.00H), 3.26-3.24 (m, 0.28H), 2.89-2.74 (m, 1.85H), 1.94-1.89 (m, 0.89H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.93, 151.99, 139.07, 130.97, 128.99, 123.05, 122.53, 115.77, 115.07, 113.07, 112.98, 105.29, 105.24, 56.00, 55.73, 41.93 (m, labeled), 38.90, 30.54, 29.11, 26.91 (m, labeled), 23.92, 23.19, 22.01 (m, labeled).

Deuterium incorporation: 4.3 D/molecule (^{1}H-NMR), 4.5 D/molecule [HRMS (ESI)]

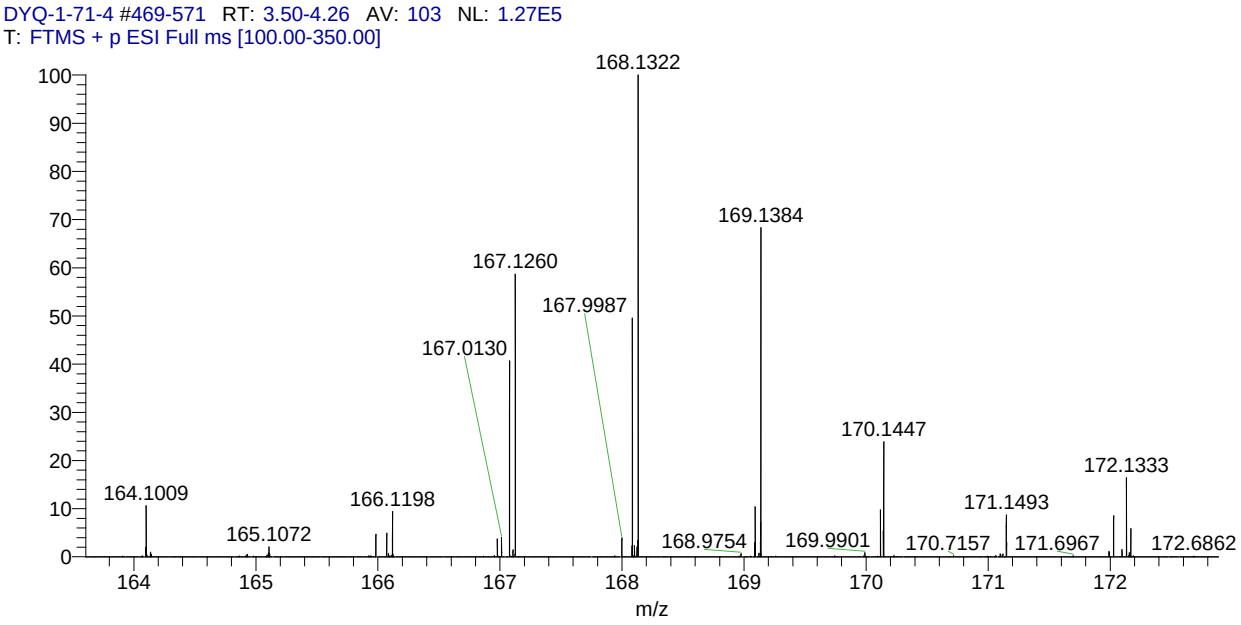


166.1196 ($C_{10}H_{11}D_2NO + H^+$, 3%), 167.1257 ($C_{10}H_{10}D_3NO + H^+$, 13%), 168.1316 ($C_{10}H_9D_4NO + H^+$, 28%), 169.1373 ($C_{10}H_8D_5NO + H^+$, 38%), 170.1428 ($C_{10}H_7D_6NO + H^+$, 15%), 171.1495 ($C_{10}H_6D_7NO + H^+$, 2%).

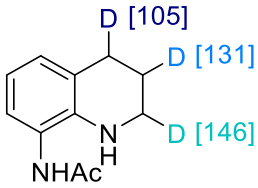


(1,2,3,4-Tetrahydroquinolin-6-yl-2,3,4-*d*$_3$)methan-*d*-ol (40b). The title product was obtained with 70% yield (46.5 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00-6.98 (m, 1.00H), 6.88-6.86 (m, 1.01H), 6.60-6.54 (m, 0.38H), 6.48-6.43 (m, 0.37H), 4.52-4.51 (m, 0.88H), 4.32 (d, *J* = 18.0 Hz, 1.00H), 3.34-3.28 (m, 0.42H), 2.78-2.71 (m, 1.22H), 1.95-1.91 (m, 1.10H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.91, 145.19, 144.73, 143.83, 129.49, 129.31, 128.82, 128.20, 128.10, 127.88, 127.72, 127.60, 127.34, 126.98, 126.87, 126.56, 126.45, 125.82, 125.71, 125.60, 125.46, 125.37, 125.26, 122.49, 122.35, 122.30, 121.81, 121.55, 114.56, 114.30, 111.30, 111.07, 65.75, 55.09, 54.95, 54.79, 54.65, 49.05 (m, labeled), 41.58 (m, labeled), 27.94 (m, labeled), 26.59 (m, labeled), 21.84 (m, labeled).

Deuterium incorporation: 4.5 D/molecule (^{1}H-NMR), 4.2 D/molecule [HRMS (ESI)].

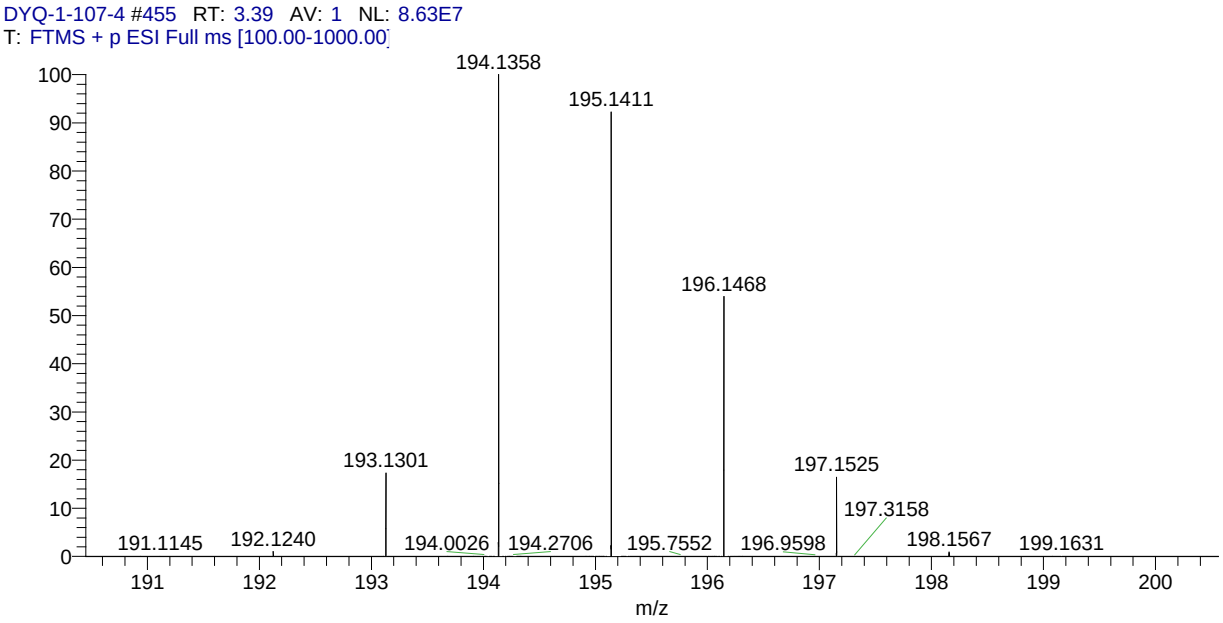


166.1198 ($C_{10}H_{11}D_2NO + H^+$, 5%), 167.1260 ($C_{10}H_{10}D_3NO + H^+$, 22%), 168.1322 ($C_{10}H_9D_4NO + H^+$, 36%), 169.1384 ($C_{10}H_8D_5NO + H^+$, 25%), 170.1447 ($C_{10}H_7D_6NO + H^+$, 9%), 171.1493 ($C_{10}H_6D_7NO + H^+$, 2%).

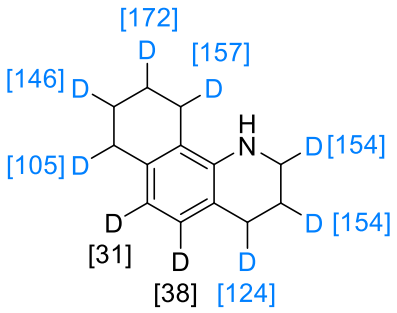


***N*-(1,2,3,4-tetrahydroquinolin-8-yl-2,3,4-*d*$_3$)acetamide (41b)**. The title product was obtained with 91% yield (70.4 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (s, 0.70H), 7.01-6.92 (m, 1.27H), 6.86 (d, *J* = 6.0 Hz, 0.70H), 6.82 (d, *J* = 6.8 Hz, 0.30H), 6.62 (t, *J* = 7.6 Hz, 0.70H), 6.55 (t, *J* = 7.6 Hz, 0.30H), 3.48-3.25 (m, 1.54H), 2.77-2.73 (m, 0.95H), 2.15 (s, 2.11H), 1.89 (s, 0.90H), 1.85-1.82 (m, 0.69H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.68, 169.52, 141.53, 139.39, 129.27, 127.83, 126.58, 124.14, 123.58, 123.34, 122.59, 121.57, 117.29, 115.89, 41.68 (m, labeled), 26.93 (m, labeled), 23.80, 21.32 (m, labeled), 20.57.

Deuterium incorporation: 3.8 D/molecule (^{1}H-NMR), 3.8 D/molecule [HRMS (ESI)].

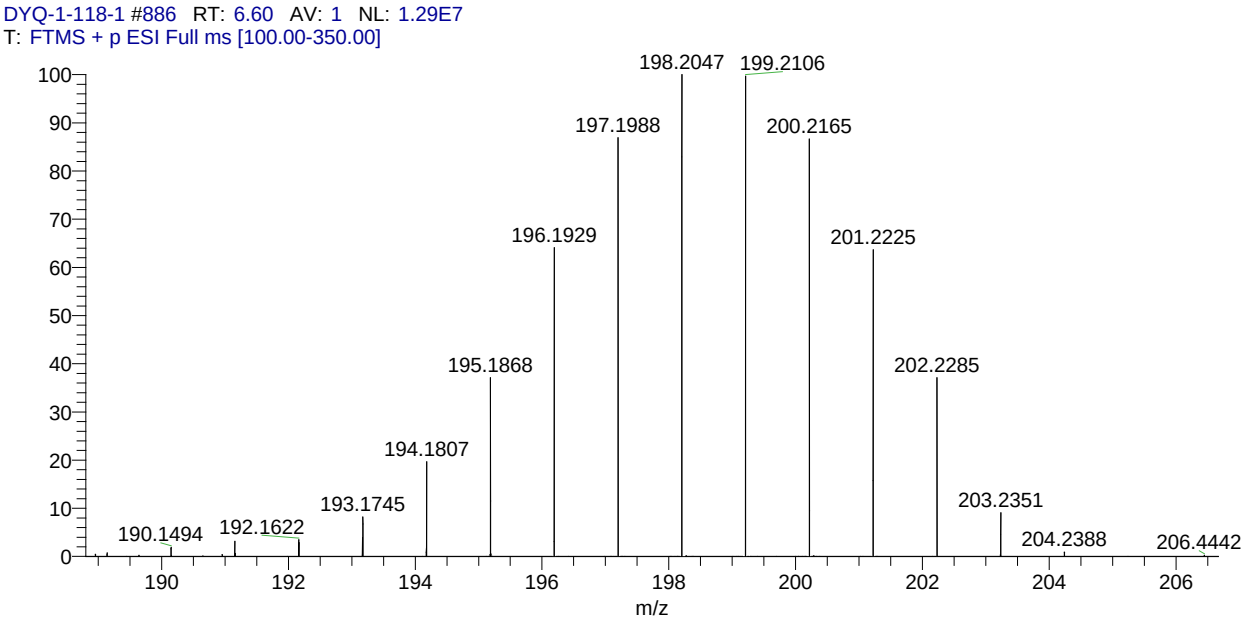


193.1301 ($C_{11}H_{12}D_2N_2O$ + H^+, 7%), 194.1358 ($C_{11}H_{11}D_3N_2O$ + H^+, 35%), 195.1411 ($C_{11}H_{10}D_4N_2O$ + H^+, 32%), 196.1468 ($C_{11}H_9D_5N_2O$ + H^+, 20%), 197.1525 ($C_{11}H_8D_6N_2O$ + H^+, 6%).

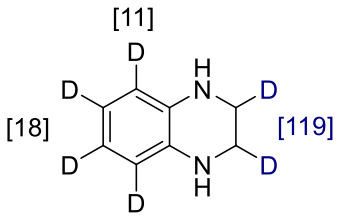


1,2,3,4,7,8,9,10-Octahydrobenzo[h]quinoline-2,2,3,3,4,7,8,9,9,10,10-*d*$_{11}$ (42b). The title product was obtained with 76% yield (60.4 mg, 0.4 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85-6.83 (m, 0.62H), 6.49-6.47 (m, 0.69H), 3.68 (s, 0.88H), 3.43-3.39 (m, 0.46H), 2.83-2.79 (m, 0.76H), 2.77-2.73 (m, 0.95H), 2.40-2.36 (m, 0.43H), 2.01-1.94 (m, 0.46H), 1.90-1.87 (m, 0.28H), 1.80-1.75 (m, 0.54H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.31, 135.36, 126.61, 126.50, 120.41, 120.36, 118.96 (m, labeled), 117.60, 117.49, 41.89 (m, labeled), 29.53 (m, labeled), 26.84 (m, labeled), 22.43 (m, labeled), 19.21.

Deuterium incorporation: 10.8 D/molecule (^{1}H-NMR), 10.7 D/molecule [HRMS (ESI)].

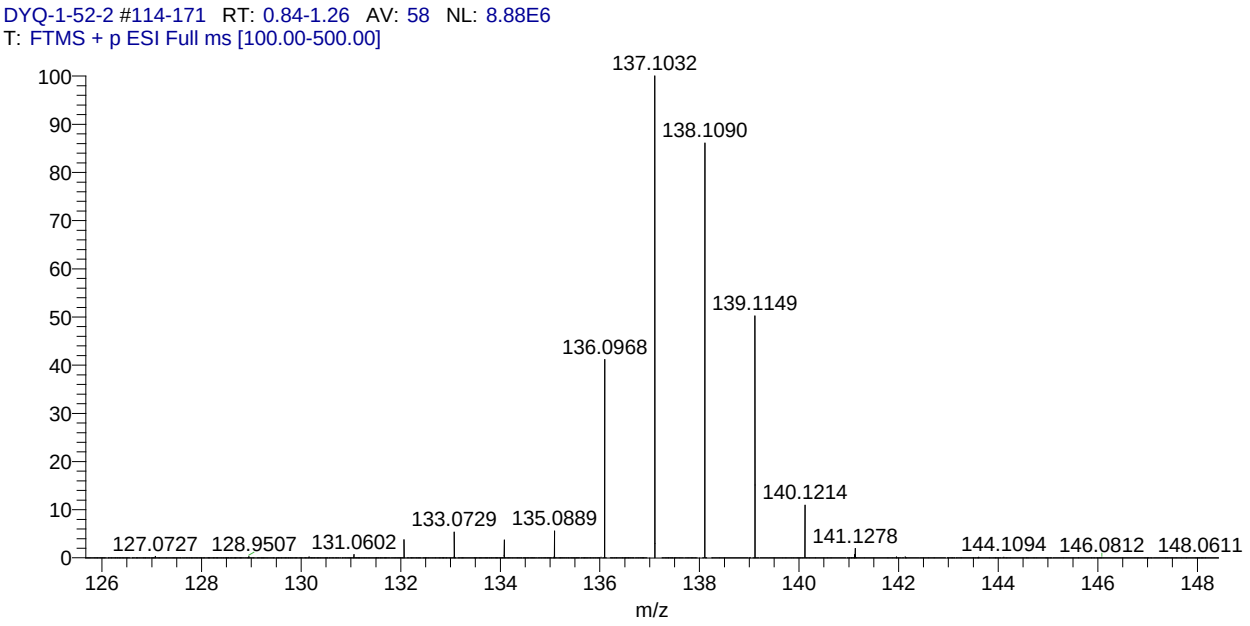


193.1745 ($C_{13}H_{12}D_5N + H^+$, 1%), 194.1807 ($C_{13}H_{11}D_6N + H^+$, 3%), 195.1868 ($C_{13}H_{10}D_7N + H^+$, 6%), 196.1929 ($C_{13}H_9D_8N + H^+$, 9%), 197.1988 ($C_{13}H_8D_9N + H^+$, 12%), 198.2047 ($C_{13}H_7D_{10}N + H^+$, 15%), 199.2106 ($C_{13}H_6D_{11}N + H^+$, 16%), 200.2165 ($C_{13}H_5D_{12}N + H^+$, 15%), 201.2225 ($C_{13}H_4D_{13}N + H^+$, 12%), 202.2285 ($C_{13}H_3D_{14}N + H^+$, 8%), 203.2351 ($C_{13}H_2D_{15}N + H^+$, 3%).

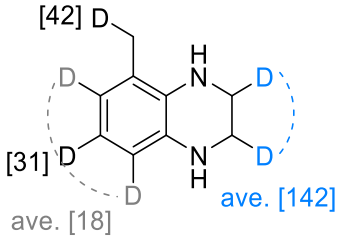


1,2,3,4-Tetrahydroquinoxaline-2,3-*d*$_2$ (43b). The title product was obtained with 76% yield (41.2 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.62-6.58 (m, 1.78H), 6.53-6.49 (m, 1.65H), 3.66 (s, 2.00H), 3.43-3.40 (m, 1.63H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.80, 118.99, 114.95, 41.19 (m, labeled).

Deuterium incorporation: 2.9D/molecule (^{1}H-NMR), 2.8 D/molecule [HRMS (ESI)]



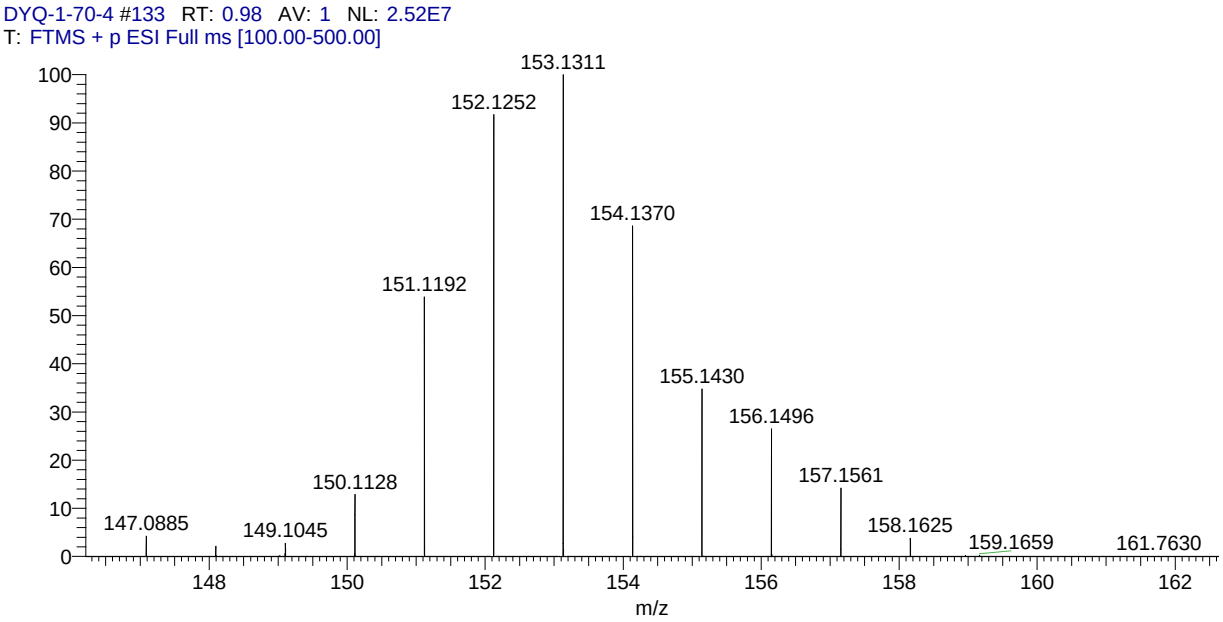
135.0889 ($C_8H_{10}N_2 + H^+$, 1%), 136.0968 ($C_8H_9D_1N_2 + H^+$, 12%), 137.1032 ($C_8H_8D_2N_2 + H^+$, 30%), 138.1090 ($C_8H_7D_3N_2 + H^+$, 33%), 139.1149 ($C_8H_6D_4N_2 + H^+$, 19%), 140.1214 ($C_8H_5D_5N_2 + H^+$, 4%), 141.1278 ($C_8H_4D_6N_2 + H^+$, 1%).



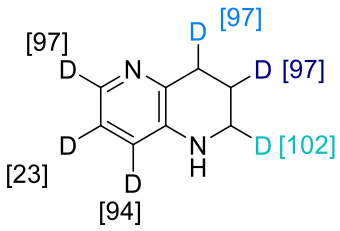
5-Methyl-1,2,3,4-tetrahydroquinoxaline-2,3-*d*$_2$ (44b). The title product was obtained with 60% yield (36.0 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.56-6.51 (m, 1.64H), 6.44-6.41 (m, 0.69H), 3.47-3.39 (m, 3.16H), 2.19-2.10 (m, 2.58H); ^{13}C NMR (101 MHz, $CDCl_3$)

δ 133.20, 131.82, 126.02, 124.43, 122.80, 122.38, 120.70, 120.58, 118.20, 118.08, 113.17, 41.21 (m, labeled), 17.68, 17.48, 17.11.

Deuterium incorporation: 3.9 D/molecule (^{1}H-NMR), 4.1 D/molecule [HRMS (ESI)]

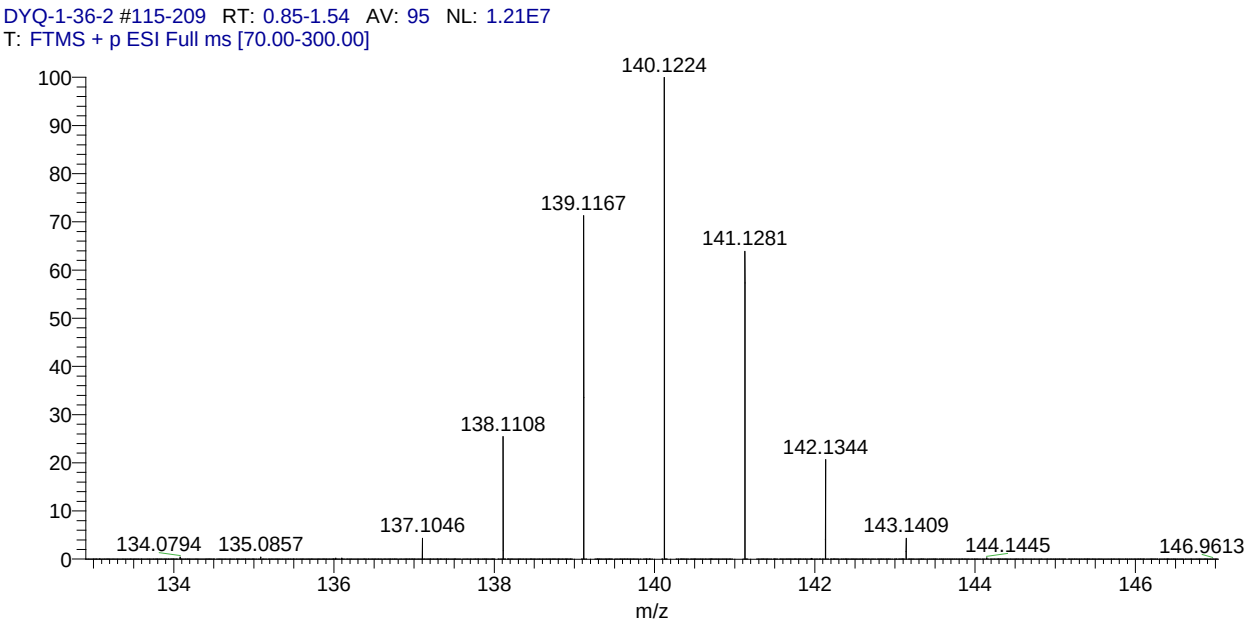


150.1128 ($C_9H_{11}DN_2 + H^+$, 3%), 151.1192 ($C_9H_{10}D_2N_2 + H^+$, 13%), 152.1252 ($C_9H_9D_3N_2 + H^+$, 23%), 153.1311 ($C_9H_8D_4N_2 + H^+$, 25%), 154.1370 ($C_9H_7D_5N_2 + H^+$, 16%), 155.1430 ($C_9H_6D_6N_2 + H^+$, 9%), 156.1496 ($C_9H_5D_7N_2 + H^+$, 6%), 157.1561 ($C_9H_4D_8N_2 + H^+$, 4%), 158.1625 ($C_9H_3D_9N_2 + H^+$, 1%).

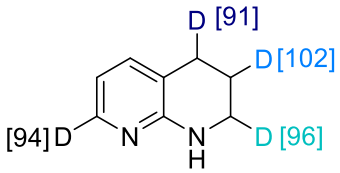


1,2,3,4-Tetrahydro-1,5-naphthyridine-2,3,4,6,7,8-*d*$_6$ (45b). The title product was obtained with 72% yield (39.1 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 4.8 Hz, 0.03H), 6.89 (s, 0.77H), 6.74 (d, *J* = 8.0 Hz, 0.06H), 3.91 (s, 1.00H), 3.31-3.26 (m, 0.98H), 2.96-2.90 (m, 1.03H), 2.04-1.97 (m, 1.03H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.51, 141.25, 137.30 (m, labeled), 121.92, 120.31 (m, labeled), 41.14 (m, labeled), 29.72 (m, labeled), 21.21 (m, labeled).

Deuterium incorporation: 5.1 D/molecule (^{1}H-NMR), 5.0 D/molecule [HRMS (ESI)]

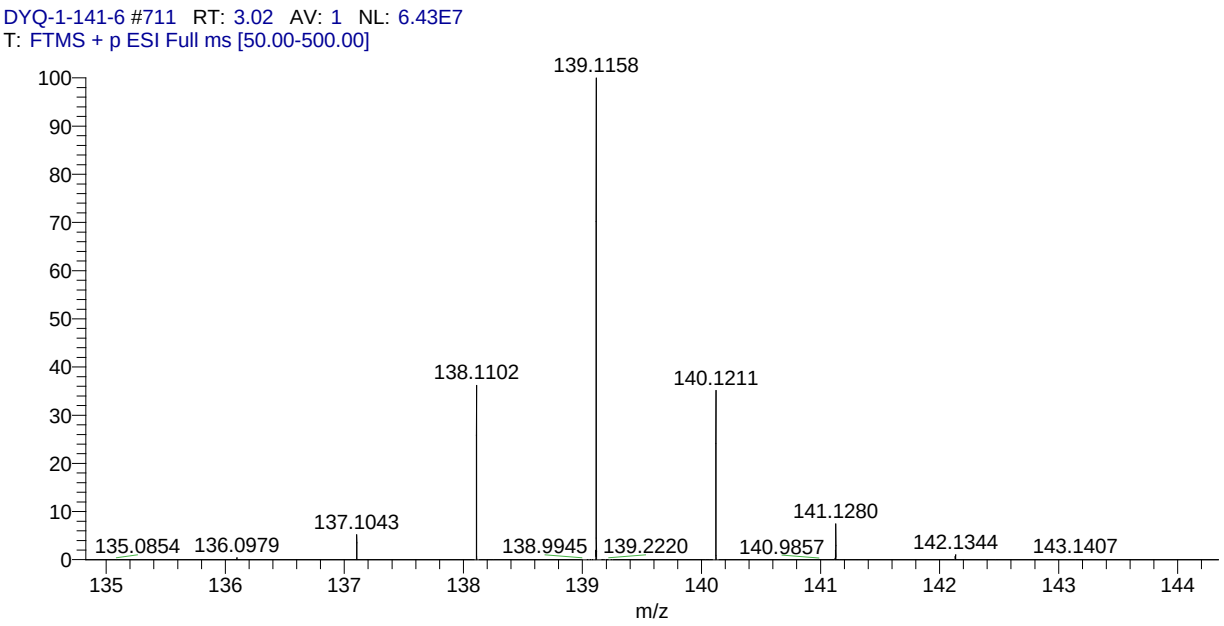


137.1046 ($C_8H_8D_2N_2 + H^+$, 1%), 138.1108 ($C_8H_7D_3N_2 + H^+$, 8%), 139.1167 ($C_8H_6D_4N_2 + H^+$, 23%), 140.1224 ($C_8H_5D_5N_2 + H^+$, 35%), 141.1281 ($C_8H_4D_6N_2 + H^+$, 23%), 142.1344 ($C_8H_3D_7N_2 + H^+$, 8%), 143.1409 ($C_8H_2D_8N_2 + H^+$, 2%).

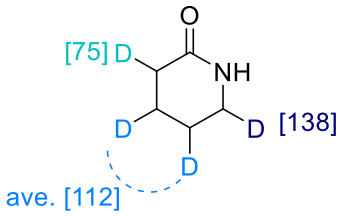


1,2,3,4-Tetrahydro-1,8-naphthyridine-2,3,4,7-*d*$_4$ (46b). The title product was obtained with 73% yield (40.3 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 5.6 Hz, 0.06H), 7.10 (d, *J* = 7.6 Hz, 0.97H), 6.46-6.43 (m, 0.97H), 5.20 (s, 1.00H), 3.35 (s, 1.04H), 2.67 (s, 1.09H), 1.85 (s, 0.98H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.49, 156.49, 145.97, 145.91, 145.65, 145.38, 136.23, 116.16, 116.11, 112.55, 112.41, 41.25 (m, labeled), 26.39 (m, labeled), 20.84 (m, labeled).

Deuterium incorporation: 3.8 D/molecule (^{1}H-NMR), 4.0 D/molecule [HRMS (ESI)].

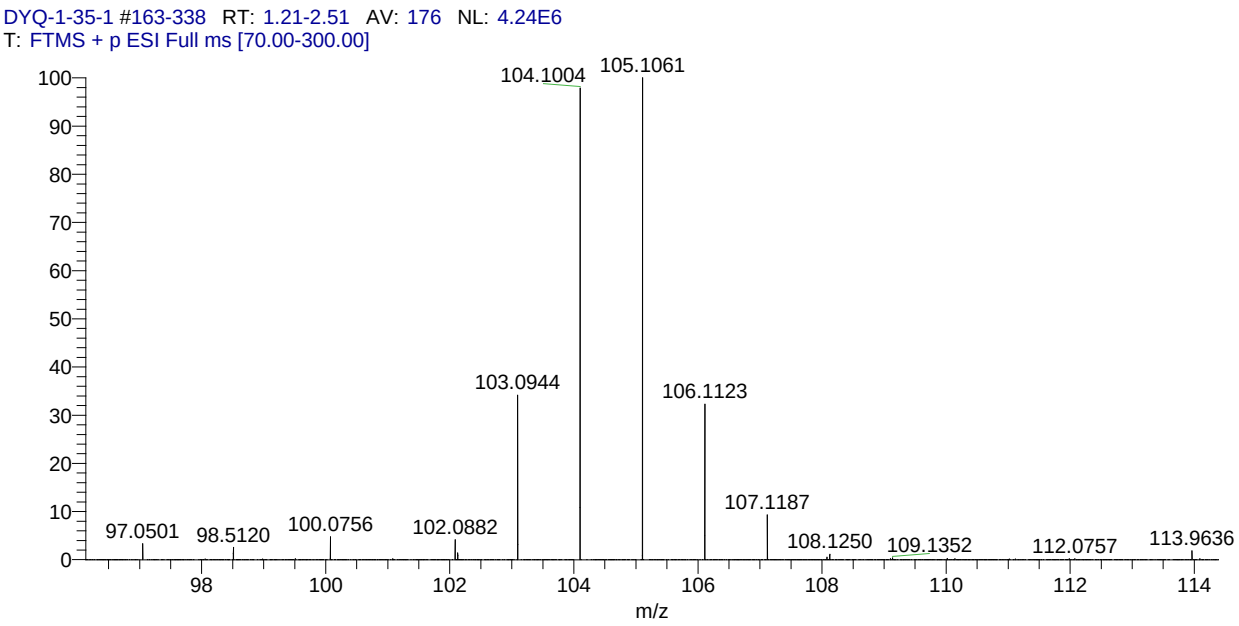


137.1043 ($C_8H_8D_2N_2 + H^+$, 3%), 138.1102 ($C_8H_7D_3N_2 + H^+$, 20%), 139.1158 ($C_8H_6D_4N_2 + H^+$, 58%), 140.1211 ($C_8H_5D_5N_2 + H^+$, 20%), 141.1280 ($C_8H_4D_6N_2 + H^+$, 2%).

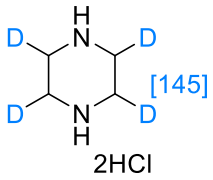


Piperidin-2-one-3,4,5,6-*d*$_4$ (47b). The title product was obtained with 98% yield (41.5 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 (s, 1.00H), 3.28-3.25 (m, 0.62H), 2.33-2.30 (m, 1.25H), 1.78-1.69 (m, 1.77H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.94, 41.96 (m, labeled), 31.23 (m, labeled), 21.71 (m, labeled), 20.37 (m, labeled).

Deuterium incorporation: 4.4 D/molecule (^{1}H-NMR), 4.5 D/molecule [HRMS (ESI)].

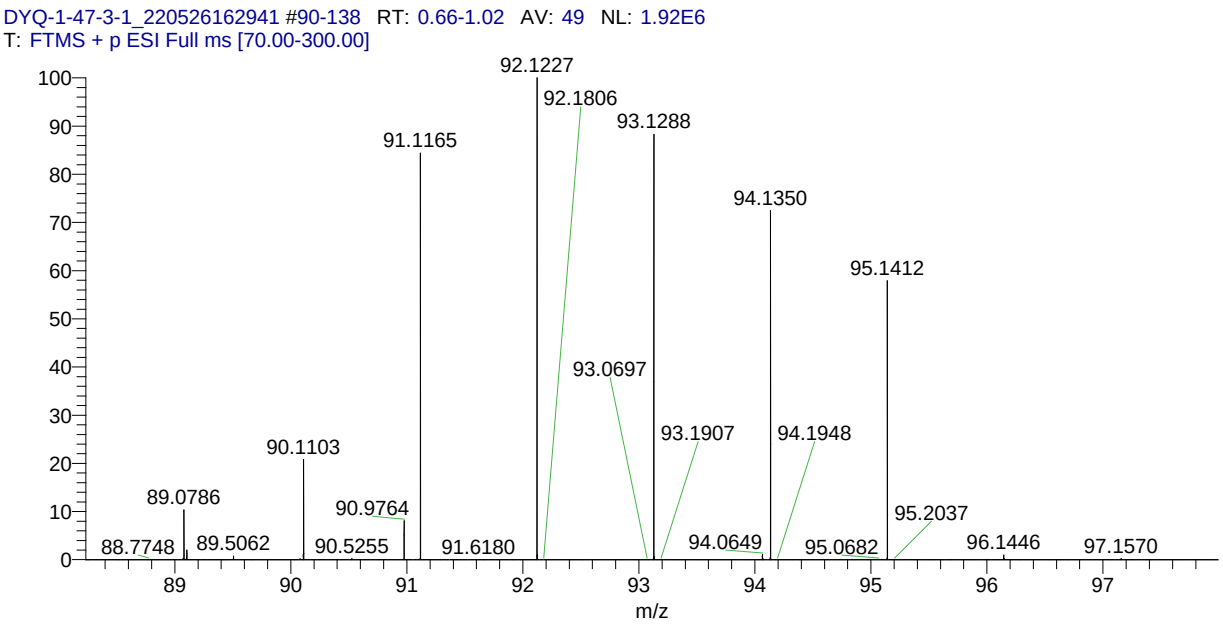


102.0882 ($C_5H_7D_2NO + H^+$, 2%), 103.0944 ($C_5H_6D_3NO + H^+$, 13%), 104.1004 ($C_5H_5D_4NO + H^+$, 45%), 105.1061 ($C_5H_4D_5NO + H^+$, 18%), 106.1123 ($C_5H_3D_6NO + H^+$, 17%), 107.1187 ($C_5H_2D_7NO + H^+$, 4%), 108.1250 ($C_5H_1D_8NO + H^+$, 1%).

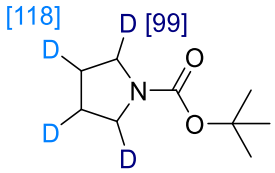


Piperazine-2,3,5,6-*d*$_4$ (48b). The title product was obtained with 78% yield (50.6 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, D_2O) δ 3.57-3.38 (m); ^{13}C NMR (101 MHz, D_2O) δ 39.91 (m, labeled).

Deuterium incorporation: 5.8 D/molecule [HRMS (ESI)].

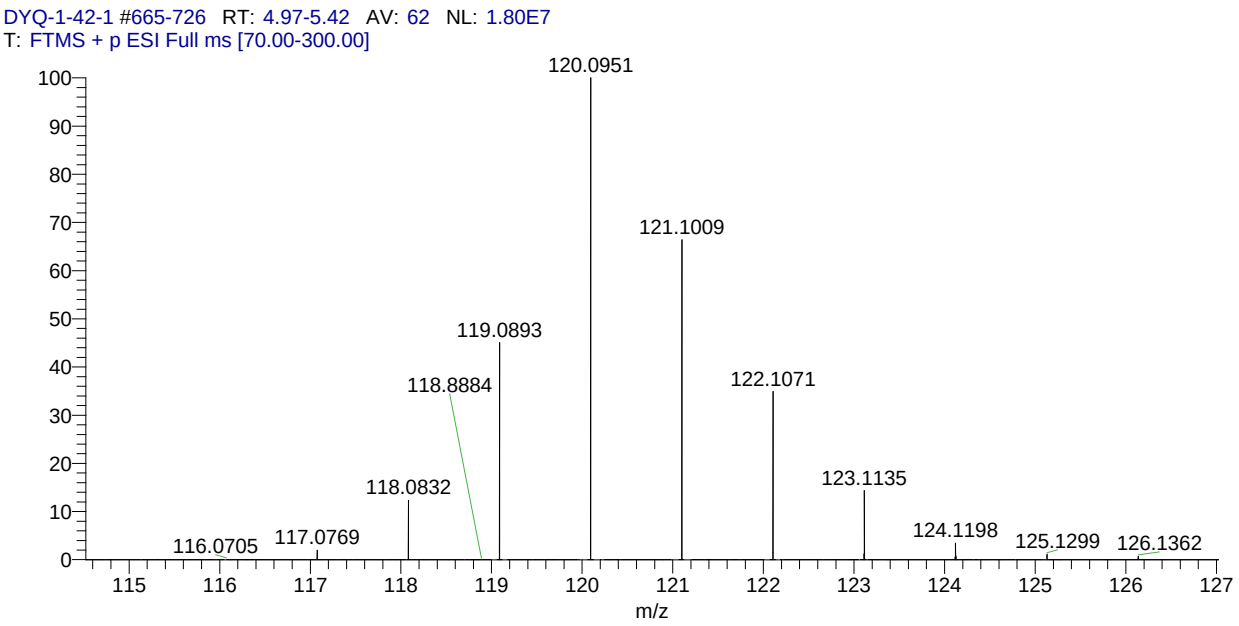


90.1103 ($C_4H_7D_3N_2 + H^+$, 4%), 91.1165 ($C_4H_6D_4N_2 + H^+$, 18%), 92.1227 ($C_4H_5D_5N_2 + H^+$, 21%), 93.1288 ($C_4H_4D_6N_2 + H^+$, 22%), 94.1350 ($C_4H_3D_7N_2 + H^+$, 19%), 95.1412 ($C_4H_2D_8N_2 + H^+$, 15%).

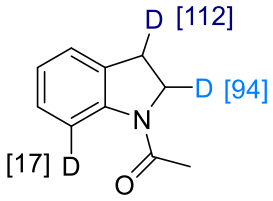


***tert*-Butyl pyrrolidine-1-carboxylate-2,3,4,5-*d*$_4$ (49b)**. The title product was obtained with 56% yield (47.7 mg, 0.4 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.30-3.23 (m, 2.03H), 1.79 (s, 1.64H), 1.44 (s, 9.00H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.84, 78.96, 45.52 (m, labeled), 28.67, 24.51 (m, labeled).

Deuterium incorporation: 4.3 D/molecule (^{1}H-NMR), 4.5 D/molecule [HRMS (ESI)].

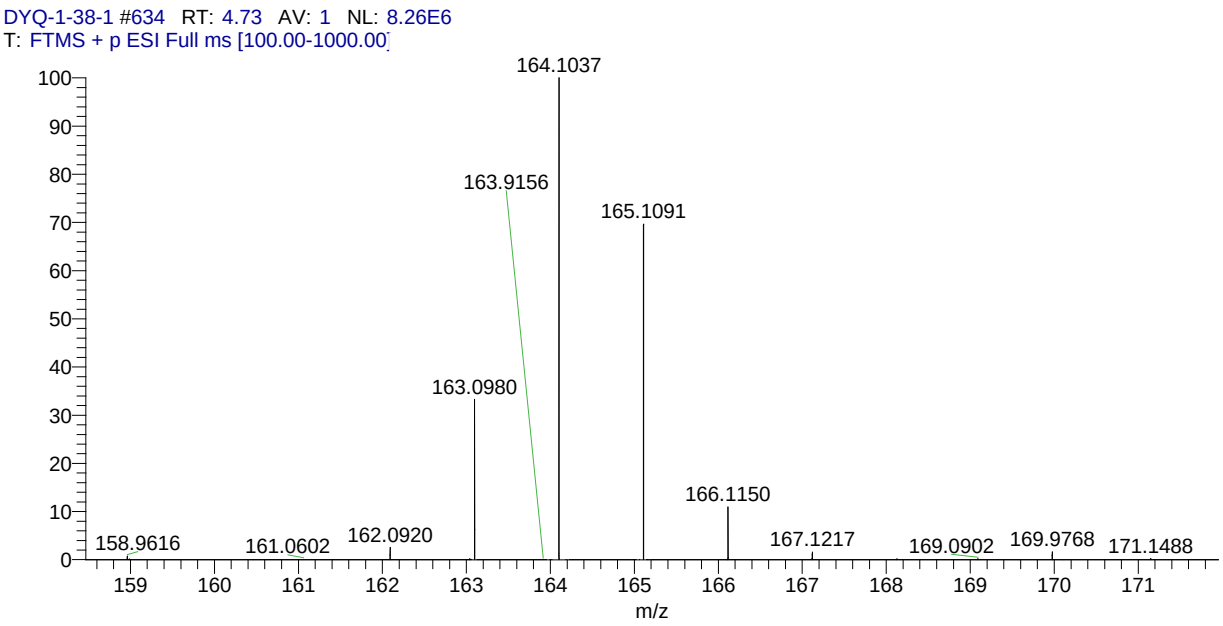


117.0769 ($C_9H_{16}DNO_2 + H^+$, 1%), 118.0832 ($C_9H_{15}D_2NO_2 + H^+$, 4%), 119.0893 ($C_9H_{14}D_3NO_2 + H^+$, 15%), 120.0951 ($C_9H_{13}D_4NO_2 + H^+$, 36%), 121.1009 ($C_9H_{12}D_5NO_2 + H^+$, 25%), 122.1071 ($C_9H_{11}D_6NO_2 + H^+$, 13%), 123.1135 ($C_9H_{10}D_7NO_2 + H^+$, 5%), 124.1198 ($C_9H_9D_8NO_2 + H^+$, 1%).

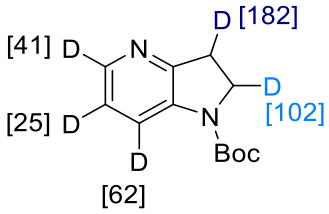


1-(Indolin-1-yl-2,3-*d*$_2$)ethan-1-one (50b). The title product was obtained with 80% yield (51.9 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.4 Hz, 0.83H), 7.26-7.12 (m, 2.02H), 7.01 (t, *J* = 7.4 Hz, 1.00H), 4.11-3.96 (m, 1.06H), 3.20-3.04 (m, 0.88H), 2.44-2.22 (m, 3.00H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.88, 143.11, 131.20, 127.71, 126.07, 124.72, 123.73, 123.30, 117.11, 48.50 (m, labeled), 27.80 (m, labeled), 24.83, 24.41.

Deuterium incorporation: 2.2 D/molecule (^{1}H-NMR), 2.2 D/molecule [HRMS (ESI)].

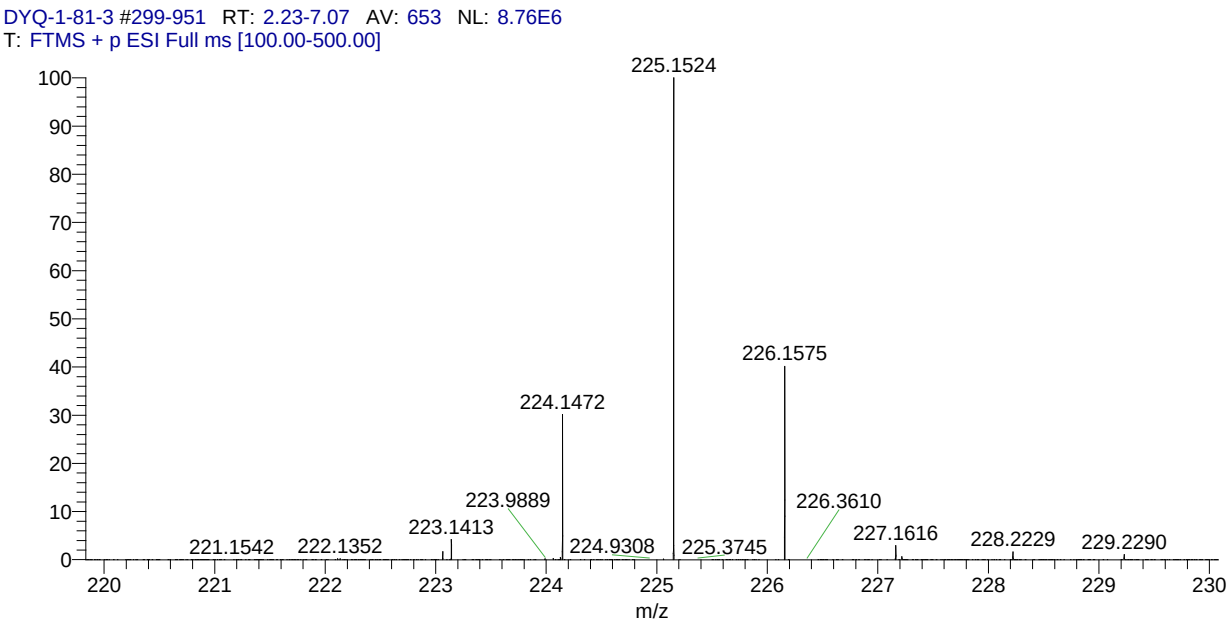


162.0902 ($C_{10}H_{11}D_0NO + H^+$, 1%), 163.0980 ($C_{10}H_{10}D_1NO + H^+$, 15%), 164.1037 ($C_{10}H_9D_2NO + H^+$, 50%), 165.1091 ($C_{10}H_8D_3NO + H^+$, 33%), 166.1217 ($C_{10}H_7D_4NO + H^+$, 1%).

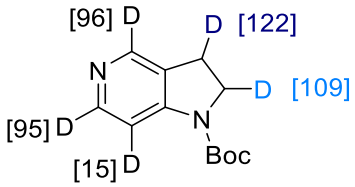


***tert*-Butyl 2,3-dihydro-1*H*-pyrrolo[3,2-*b*]pyridine-1-carboxylate-2,3,7-d_3 (51b)**. The title product was obtained with 79% yield (70.5 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 0.59H), 7.57 (s, 0.38H), 7.02 (d, J = 8.0 Hz, 0.75H), 3.95 (s, 0.98H), 3.19 (t, J = 8.0 Hz, 0.18H), 1.54 (s, 9.00H); ^{13}C NMR (201 MHz, $CDCl_3$) δ 154.01, 153.29, 152.80, 142.52, 142.26, 137.76, 136.74, 121.88, 120.97, 120.88, 82.30, 81.26, 45.54 (m, labeled), 29.01 (m, labeled), 28.54.

Deuterium incorporation: 4.1 D/molecule (^{1}H-NMR), 4.0 D/molecule [HRMS (ESI)]

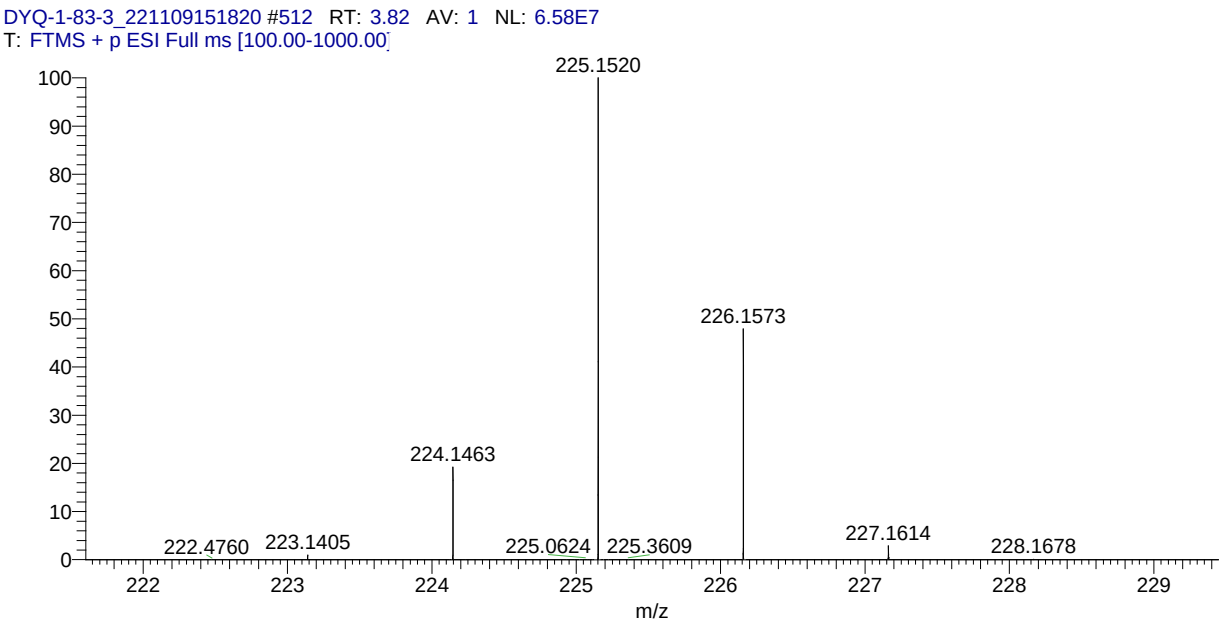


223.1413 ($C_{12}H_{14}D_2N_2O_2$ + H^+, 2%), 224.1472 ($C_{12}H_{13}D_3N_2O_2$ + H^+, 16%), 225.1524 ($C_{12}H_{12}D_4N_2O_2$ + H^+, 59%), 226.1575 ($C_{12}H_{11}D_5N_2O_2$ + H^+, 23%).

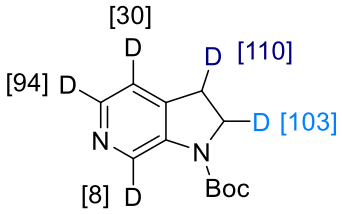


***tert*-Butyl 2,3-dihydro-1*H*-pyrrolo[3,2-*c*]pyridine-1-carboxylate-2,3,4,6-d_4 (52b)**. The title product was obtained with 69% yield (63.3 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) 7.95 (s, 0.04H), 7.85 (s, 0.05H), 7.60 (s, 0.85H), 3.95 (d, J = 10.0 Hz, 0.91H), 3.10-3.06 (m, 0.78H), 1.54 (s, 9.00H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.24, 149.01 (m, labeled), 145.30 (m, labeled), 126.96 (m), 109.44, 81.97 (m), 47.52 (m, labeled), 28.42, 24.59 (m, labeled).

Deuterium incorporation: 4.4 D/molecule (^{1}H-NMR), 4.2 D/molecule [HRMS (ESI)].

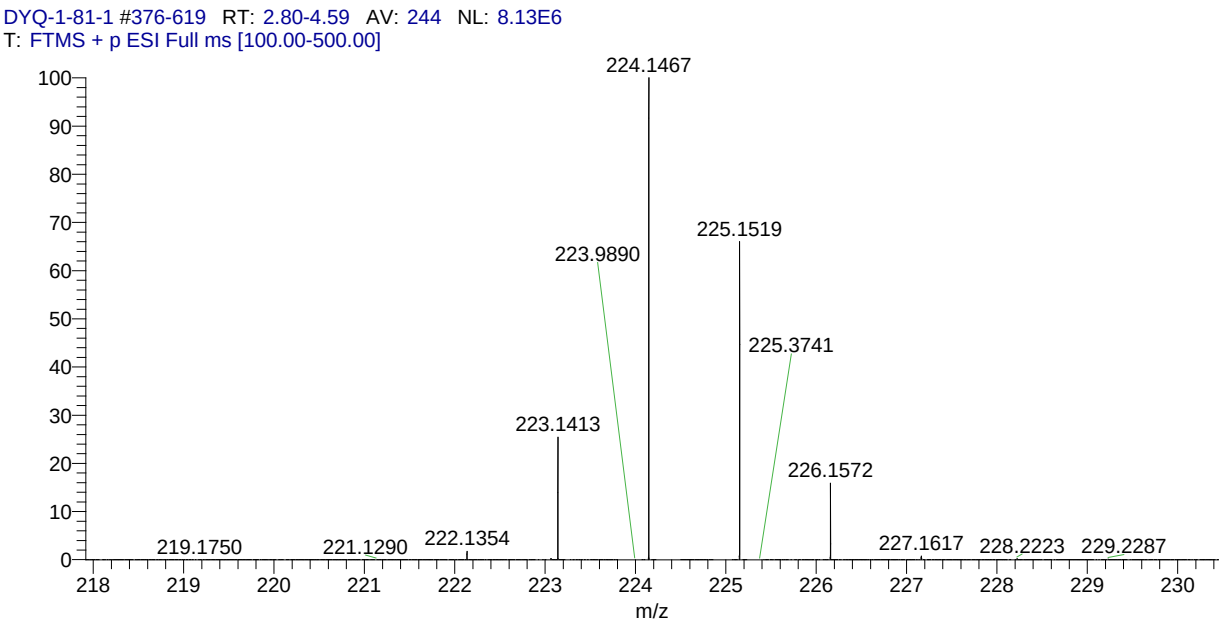


223.1405 ($C_{12}H_{14}D_2N_2O_2$ + H^+, 1%), 224.1463 ($C_{12}H_{13}D_3N_2O_2$ + H^+, 12%), 225.1520 ($C_{12}H_{12}D_4N_2O_2$ + H^+, 60%), 226.1573 ($C_{12}H_{11}D_5N_2O_2$ + H^+, 28%).

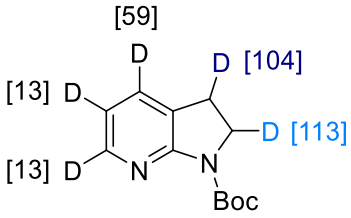


***tert*-Butyl 2,3-dihydro-1*H*-pyrrolo[2,3-*c*]pyridine-1-carboxylate-2,3,5-d_3 (53b)**. The title product was obtained with 73% yield (65.5 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (s, 0.44H), 8.67 (s, 0.48H), 8.17 (d, *J* = 4.4 Hz, 0.06H), 7.09 (s, 0.70H), 3.95 (d, *J* = 9.6 Hz, 0.97H), 3.11-3.06 (m, 0.90H), 1.57 (s, 9.00H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.38, 143.20 (m, labeled), 140.33 (m, labeled), 136.07, 120.07, 81.24 (m), 46.77 (m, labeled), 28.59, 27.15 (m, labeled).

Deuterium incorporation: 3.5 D/molecule (^{1}H-NMR), 3.3 D/molecule [HRMS (ESI)]

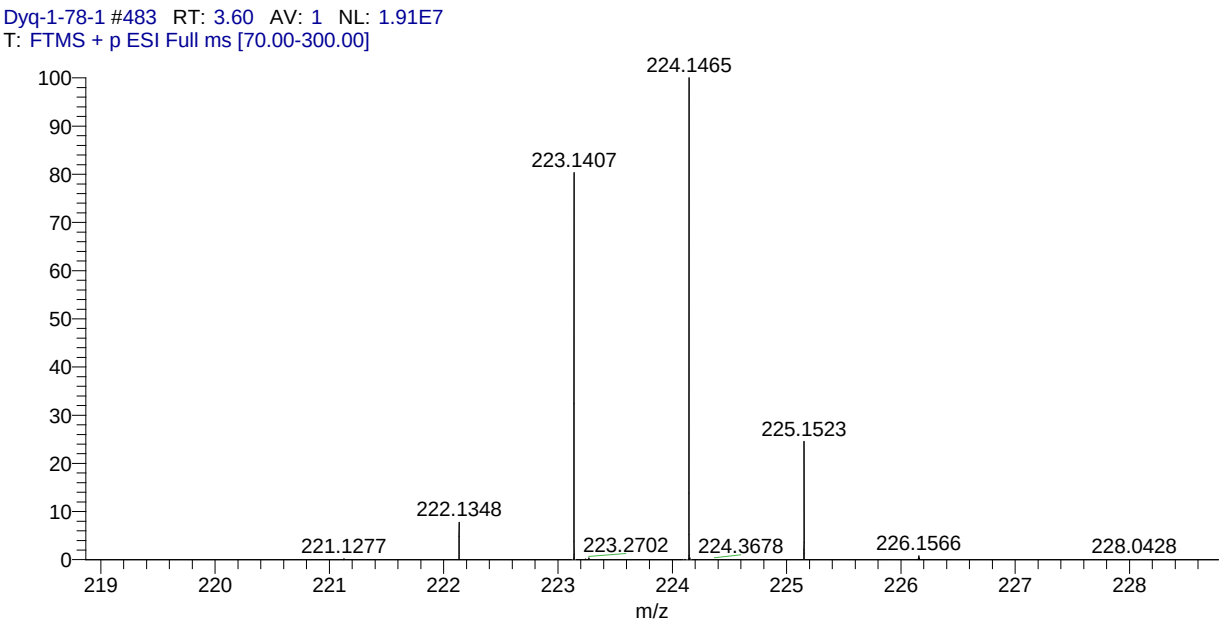


222.1354 ($C_{12}H_{15}DN_2O_2$ + H^+, 1%), 223.1413 ($C_{12}H_{14}D_2N_2O_2$ + H^+, 13%), 224.1467 ($C_{12}H_{13}D_3N_2O_2$ + H^+, 47%), 225.1519 ($C_{12}H_{12}D_4N_2O_2$ + H^+, 30%), 226.1572 ($C_{12}H_{11}D_5N_2O_2$ + H^+, 8%).

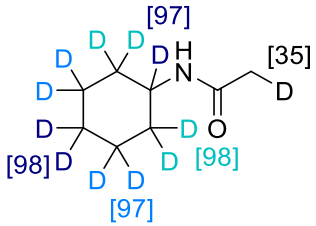


***tert*-Butyl 2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyridine-1-carboxylate-2,3,4-d_3 (54b)**. The title product was obtained with 63% yield (57.0 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 1.2, 5.2 Hz, 0.87H), 7.38 (dt, *J* = 1.4, 7.2 Hz, 0.41H), 6.81-6.78 (m, 0.87H), 3.97 (d, *J* = 10.4 Hz, 0.96H), 3.04-3.00 (m, 0.87H), 1.55 (s, 9.00H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.21, 151.20, 147.31, 132.81, 117.32, 117.22, 81.30, 46.22 (m, labeled), 28.51, 24.75 (m, labeled).

Deuterium incorporation: 3.0 D/molecule (^{1}H-NMR), 2.7 D/molecule [HRMS (ESI)]

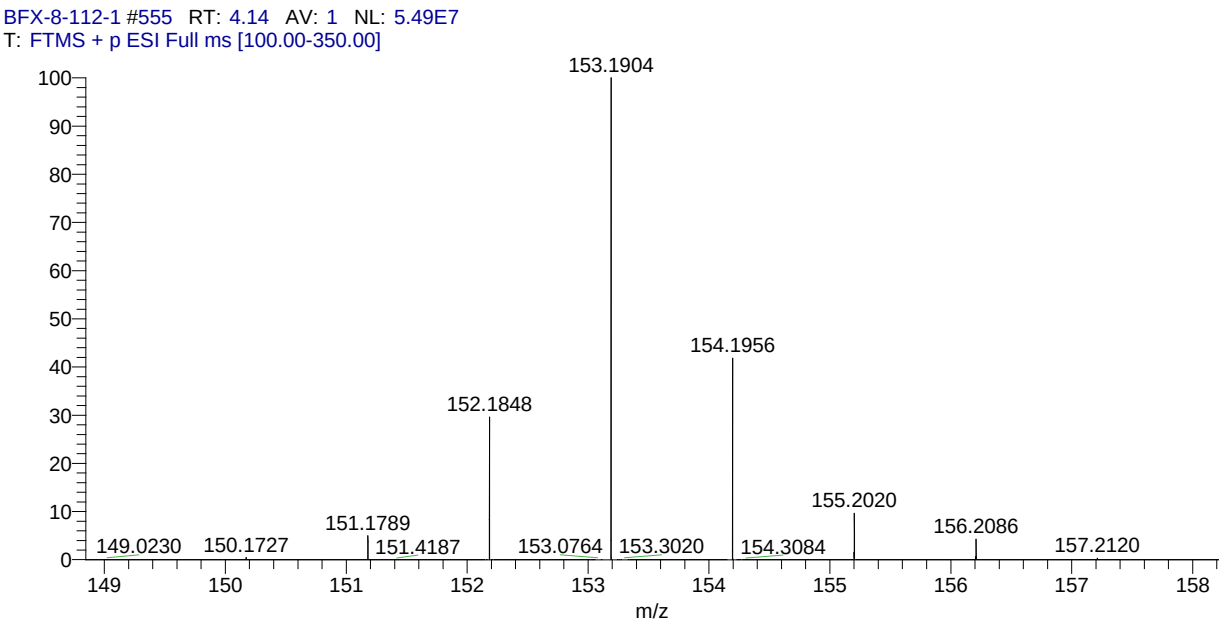


222.1348 ($C_{12}H_{15}D_1N_2O_2$ + H^+, 4%), 223.1407 ($C_{12}H_{14}D_2N_2O_2$ + H^+, 38%), 224.1465 ($C_{12}H_{13}D_3N_2O_2$ + H^+, 47%), ($C_{12}H_{12}D_4N_2O_2$ + H^+, 11%).

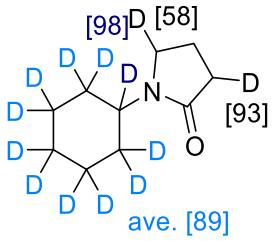


***N*-(cyclohexyl-*d*$_{11}$)acetamide (1d)**. The title product was obtained with 98% yield (59.4 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.48 (s, 1.00H), 2.21 (t, *J* = 7.6 Hz, 0.03H), 2.03-1.93 (m, 2.65H), 1.85 (s, 0.06H), 1.64 (s, 0.07H), 1.55 (s, 0.03H), 1.29 (s, 0.05H), 1.08 (s, 0.02H), 1.05 (s, 0.04H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.32, 47.77 (m, labeled), 32.24 (m, labeled), 29.71 (m, labeled), 23.94 (m, labeled), 23.74.

Deuterium incorporation: 11.1 D/molecule (^{1}H-NMR), 11.2 D/molecule [HRMS (ESI)].

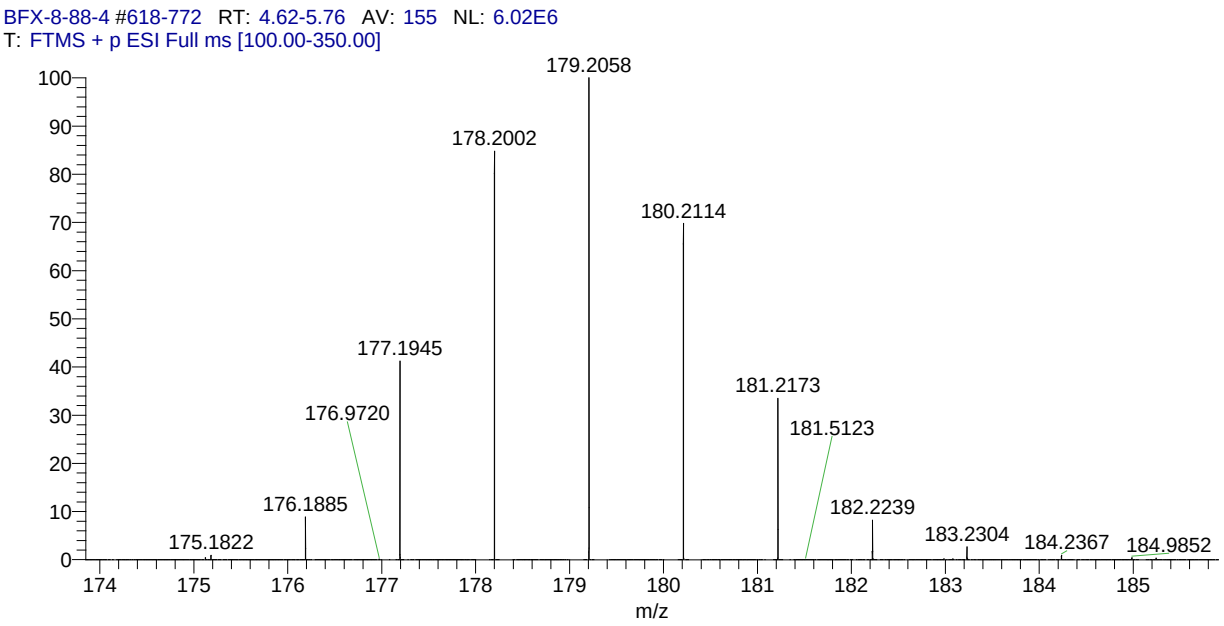


151.1789 ($C_8H_6D_9NO + H^+$, 3%), 152.1848 ($C_8H_5D_{10}NO + H^+$, 16%), 153.1904 ($C_8H_4D_{11}NO + H^+$, 52%), 154.1956 ($C_8H_3D_{12}NO + H^+$, 21%), 155.2020 ($C_8H_2D_{13}NO + H^+$, 5%), 156.2086 ($C_8H_1D_{14}NO + H^+$, 2%),

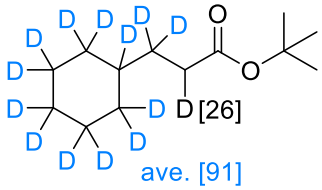


1-(Cyclohexyl-*d*$_{11}$)pyrrolidin-2-one-3,5-*d*$_2$ (2d). The title product was obtained with 75% yield (51.7 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.94-3.90 (m, 0.02H), 3.32 (t, *J* = 7.0 Hz, 1.42H), 2.39-2.33 (m, 1.07H), 2.01-1.94 (m, 2.00H), 1.72 (s, 0.05H), 1.67-1.60 (m, 0.17H), 1.30 (s, 0.89H), 1.02 (s, 0.03H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.42, 49.89 (m, labeled), 43.01, 31.83, 31.52 (m, labeled), 29.71 (m, labeled), 24.54 (m, labeled), 18.35, 18.25, 18.14.

Deuterium incorporation: 11.4 D/molecule (^{1}H-NMR), 11.0 D/molecule [HRMS (ESI)].

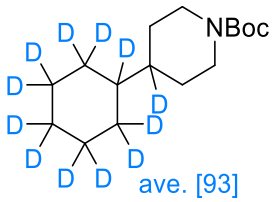


176.1885 ($C_{10}H_9D_8NO + H^+$, 2%), 177.1945 ($C_{10}H_8D_9NO + H^+$, 11%), 178.2002 ($C_{10}H_7D_{10}NO + H^+$, 24%), 179.2058 ($C_{10}H_6D_{11}NO + H^+$, 29%), 180.2114 ($C_{10}H_5D_{12}NO + H^+$, 20%), 181.2173 ($C_{10}H_4D_{13}NO + H^+$, 10%), 182.2239 ($C_{10}H_3D_{14}NO + H^+$, 2%), 183.2304 ($C_{10}H_2D_{15}NO + H^+$, 1%).



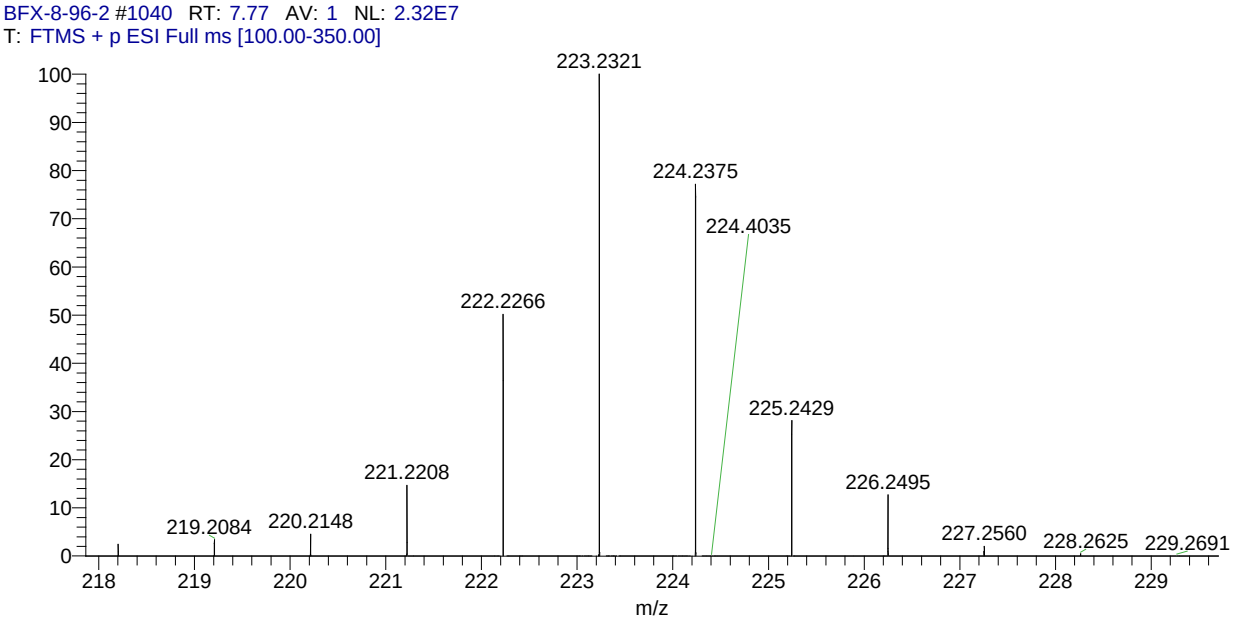
***tert*-Butyl 3-(cyclohexyl-d_{11})propanoate-3,3-d_2 (3d)**. The title product was obtained with 39% yield (35.0 mg, 0.4 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.23-2.17 (m, 1.74H), 1.68-1.64 (m, 0.59H), 1.60-1.58 (m, 0.09H), 1.48-1.46 (m, 0.53H), 1.44 (s, 9.00H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.95, 80.08, 33.30 (m, labeled), 32.14 (m, labeled), 29.92, 28.30, 25.68 (m, labeled).

Deuterium incorporation: 12.1 D/molecule (^{1}H-NMR).

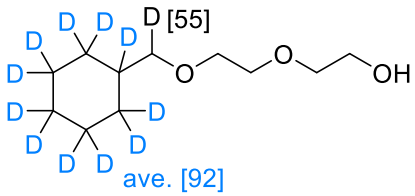


***tert*-Butyl 4-(cyclohexyl-d_{11})piperidine-1-carboxylate-4-*d* (4d)**. The title product was obtained with 42% yield (46.5 mg, 0.4 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.11 (s, 2.00H), 2.65-2.60 (m, 2.00H), 1.67-1.61 (m, 2.48H), 1.45 (s, 9.00H), 1.18-1.09 (m, 2.04H), 0.89 (s, 0.33H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.12, 79.30, 44.51 (m, labeled), 41.84, 41.16 (m, labeled), 29.44, 29.33, 28.70, 25.63 (m, labeled).

Deuterium incorporation: 11.2 D/molecule (^{1}H-NMR), 11.2 D/molecule [HRMS (ESI)].

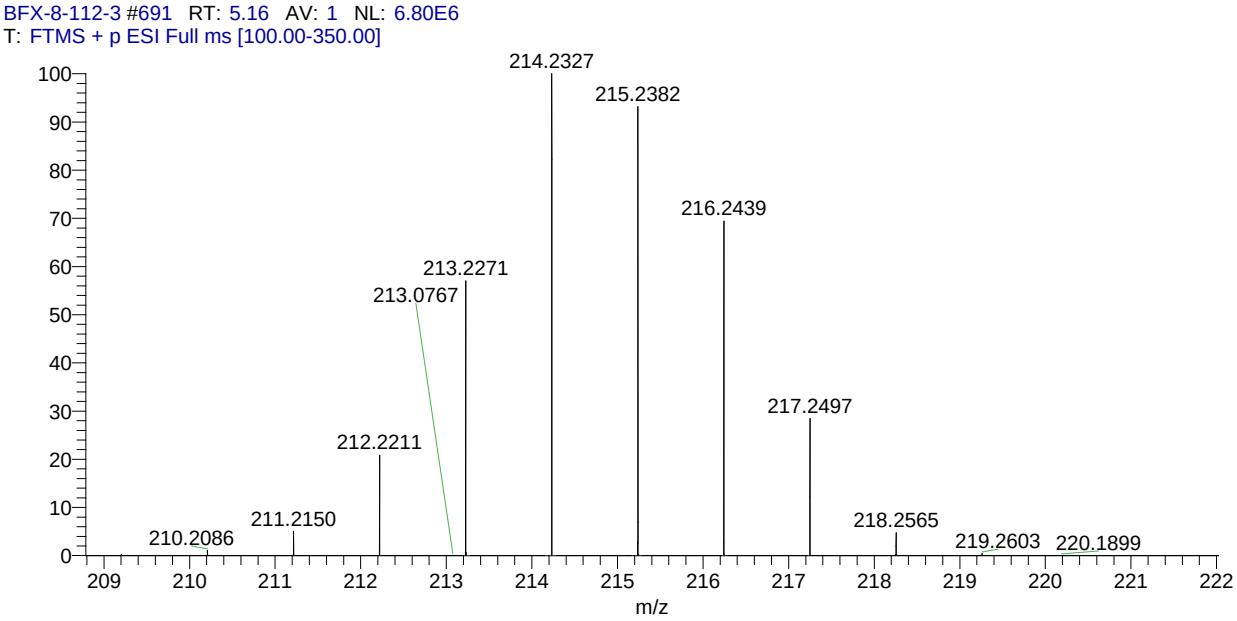


219.2084 ($C_{16}H_{22}D_7NO_2 - C_4H_7 + H^+$, 1%), 220.2148 ($C_{16}H_{21}D_8NO_2 - C_4H_7 + H^+$, 1%), 221.2208 ($C_{16}H_{20}D_9NO_2 - C_4H_7 + H^+$, 5%), 222.2266 ($C_{16}H_{19}D_{10}NO_2 - C_4H_7 + H^+$, 17%), 223.2321 ($C_{16}H_{18}D_{11}NO_2 - C_4H_7 + H^+$, 34%), 224.2375 ($C_{16}H_{17}D_{12}NO_2 - C_4H_7 + H^+$, 27%), 225.2429 ($C_{16}H_{16}D_{13}NO_2 - C_4H_7 + H^+$, 9%), 226.2495 ($C_{16}H_{15}D_{14}NO_2 - C_4H_7 + H^+$, 4%), 227.2560 ($C_{16}H_{14}D_{15}NO_2 - C_4H_7 + H^+$, 1%).

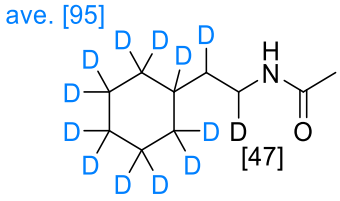


2-(2-((Cyclohexyl-*d*$_{11}$)methoxy-*d*)ethoxy)ethan-1-ol (5d). The title product was obtained with 72% yield (46.8 mg, 0.4 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.74-3.56 (m, 8.00H), 3.27-3.24 (m, 1.45H), 2.73 (s, 1.00H), 1.70-1.61 (m, 0.64H), 1.17 (s, 0.16H), 1.10 (s, 0.11H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 72.63, 72.57, 72.50, 70.62, 70.57, 70.53, 70.50, 62.03, 61.60 (m, labeled), 29.24 (m, labeled), 25.04 (m, labeled).

Deuterium incorporation: 10.6 D/molecule (^{1}H-NMR), 11.1 D/molecule [HRMS (ESI)].

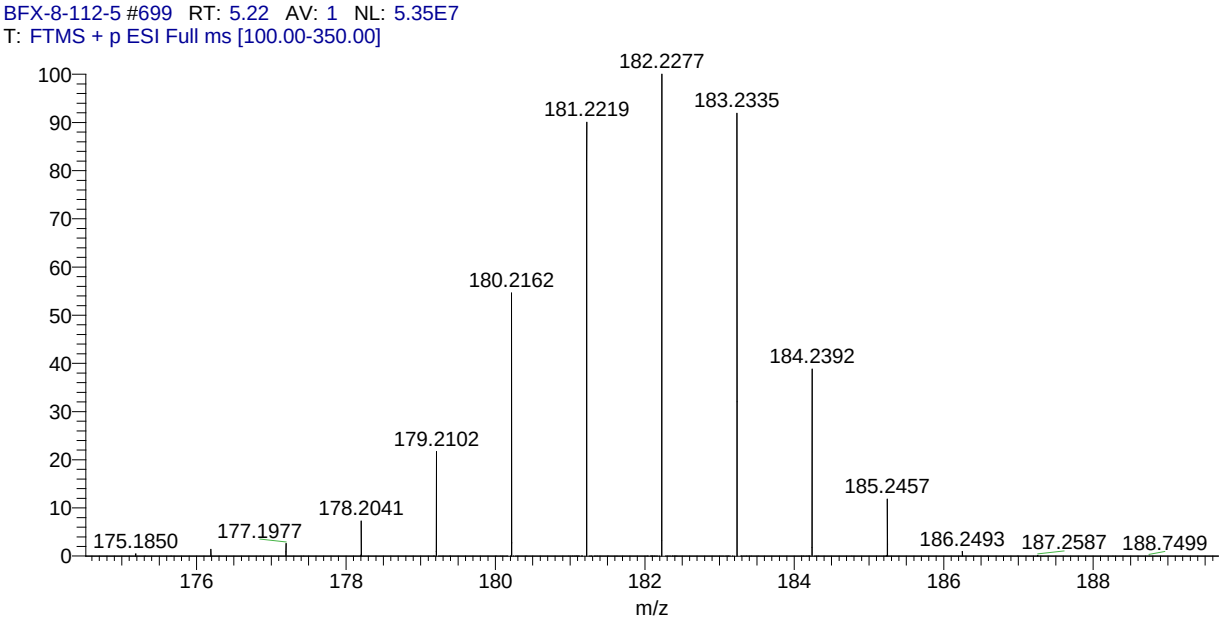


211.2150 ($C_{11}H_{14}D_8O_3$ + H^+, 2%), 212.2211 ($C_{11}H_{13}D_9O_3$ + H^+, 7%), 213.2271 ($C_{11}H_{12}D_{10}O_3$ + H^+, 20%), 214.2327 ($C_{11}H_{11}D_{11}O_3$ + H^+, 33%), 215.2382 ($C_{11}H_{10}D_{12}O_3$ + H^+, 29%), 216.2439 ($C_{11}H_9D_{13}O_3$ + H^+, 8%), 216.2439 ($C_{11}H_8D_{14}O_3$ + H^+, 2%).

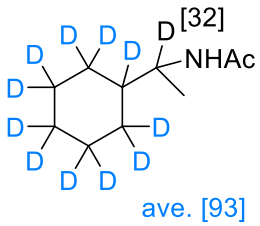


***N*-(2-(cyclohexyl-*d*$_{11}$)ethyl-2-*d*)acetamide (6d)**. The title product was obtained with 85% yield (61.0 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.65-5.34 (m, 0.99H), 3.27-3.15 (m, 1.53H), 2.05-1.93 (m, 3.00H), 1.64-1.57 (m, 0.35H), 1.38-1.24 (m, 1.06H), 1.14-1.07 (m, 0.21H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.19, 37.66, 37.60, 37.53, 37.06, 36.46 (m, labeled), 34.60 (m, labeled), 32.33 (m, labeled), 29.72 (m, labeled), 25.33 (m, labeled), 23.53.

Deuterium incorporation: 11.5 D/molecule (^{1}H-NMR), 10.8 D/molecule [HRMS (ESI)].



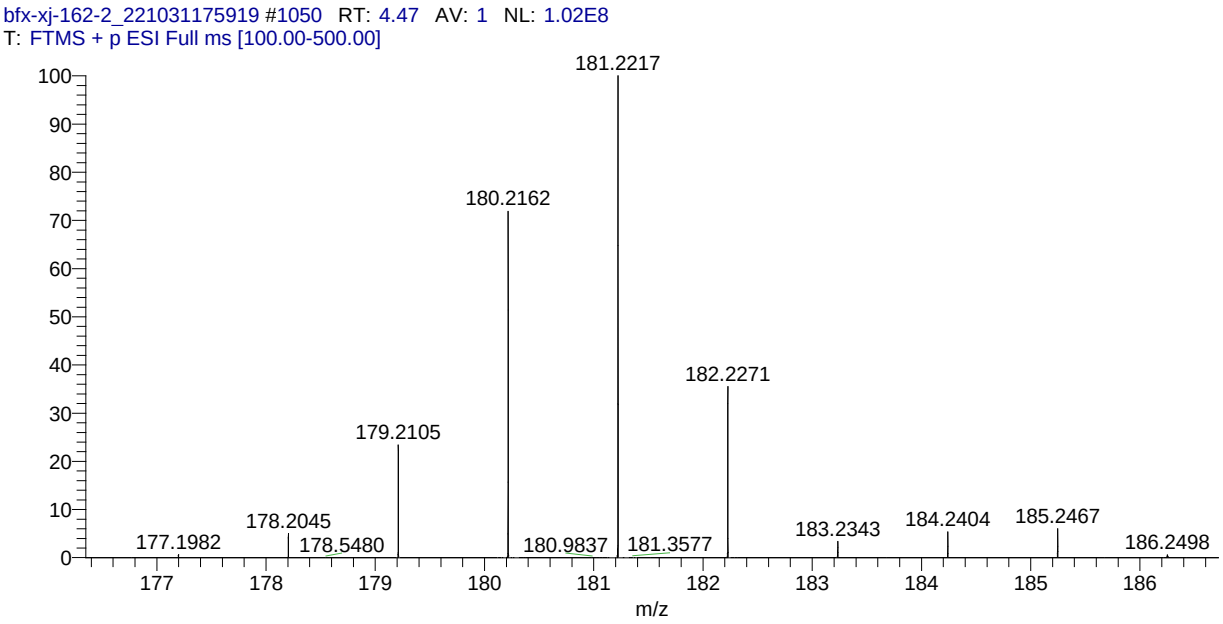
177.1977 ($C_{10}H_{12}D_7NO + H^+$, 1%), 178.2041 ($C_{10}H_{11}D_8NO + H^+$, 2%), 179.2102 ($C_{10}H_{10}D_9NO + H^+$, 5%), 180.2162 ($C_{10}H_9D_{10}NO + H^+$, 12%), 181.2219 ($C_{10}H_8D_{11}NO + H^+$, 21%), 182.2277 ($C_{10}H_7D_{12}NO + H^+$, 23%), 183.2335 ($C_{10}H_6D_{13}NO + H^+$, 23%), 184.2392 ($C_{10}H_5D_{14}NO + H^+$, 10%), 185.2457 ($C_{10}H_4D_{15}NO + H^+$, 3%).



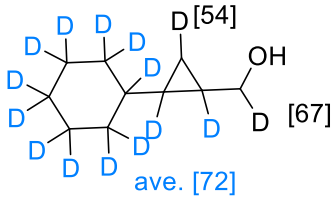
***N*-(1-(cyclohexyl-*d*$_{11}$)ethyl)acetamide (7d)**. The title product was obtained with 83% yield (44.9 mg, 0.3 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 (s, 0.05H), 5.35 (s, 0.95H), 3.87-3.80 (m, 0.68H), 2.02-1.97 (m, 3.00H), 1.84 (s, 0.56H), 1.69 (s, 0.10H), 1.61-1.59 (m, 0.10H),

1.49 (d, *J* = 7.2 Hz, 0.20H), 1.13 (d, *J* = 6.4 Hz, 0.20H), 1.06 (d, *J* = 6.8 Hz, 2.61H); ^{13}C NMR (101 MHz, $CDCl_3$) 169.50, 49.52, 42.43 (m, labeled), 29.89, 28.23 (m, labeled), 25.31 (m, labeled), 23.80, 18.06, 17.95.

Deuterium incorporation: 10.6 D/molecule (^{1}H-NMR), 10.7 D/molecule [HRMS (ESI)]



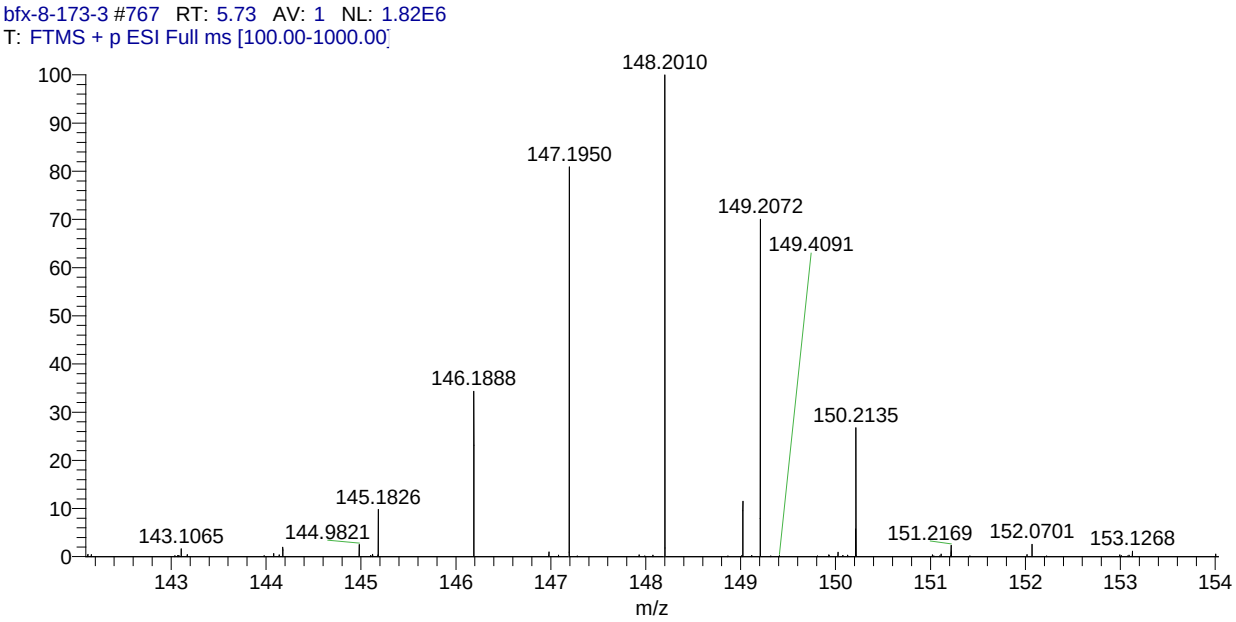
178.2045 ($C_{10}H_{11}D_8NO + H^+$, 2%), 179.2105 ($C_{10}H_{10}D_9NO + H^+$, 9%), 180.2162 ($C_{10}H_9D_{10}NO + H^+$, 29%), 181.2217 ($C_{10}H_8D_{11}NO + H^+$, 42%), 182.2271 ($C_{10}H_7D_{12}NO + H^+$, 14%), 183.2343 ($C_{10}H_6D_{13}NO + H^+$, 1%), 184.2404 ($C_{10}H_5D_{14}NO + H^+$, 2%).



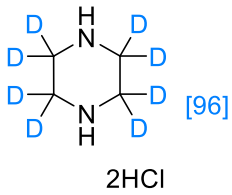
(2-(Cyclohexyl-*d*$_{11}$)cyclopropyl-1,2,3-*d*$_3$)methan-*d*-ol (8d). The title product was obtained with 37% yield (24.4 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.62-3.58 (m, 0.12H), 3.49-3.44 (m, 0.26H), 3.41-3.34 (m, 0.95H), 1.69-1.49 (m, 1.72H), 1.32-1.30 (m, 0.09H), 1.26-1.24 (m, 0.06H), 1.16-0.97 (m, 0.49H), 0.87-0.75 (m, 1.33H), 0.42-0.38 (m, 0.46H), 0.34-0.30 (m, 1.00H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 68.88, 68.47 (m, labeled), 67.46, 67.09 (m,

labeled), 40.88 (m, labeled), 32.34 (m, labeled), 25.51 (m, labeled), 24.01, 20.11, 20.02, 19.93, 16.64 (m, labeled), 8.85, 8.82.

Deuterium incorporation: 10.5 D/molecule (^{1}H-NMR), 10.0 D/molecule [HRMS (ESI)]

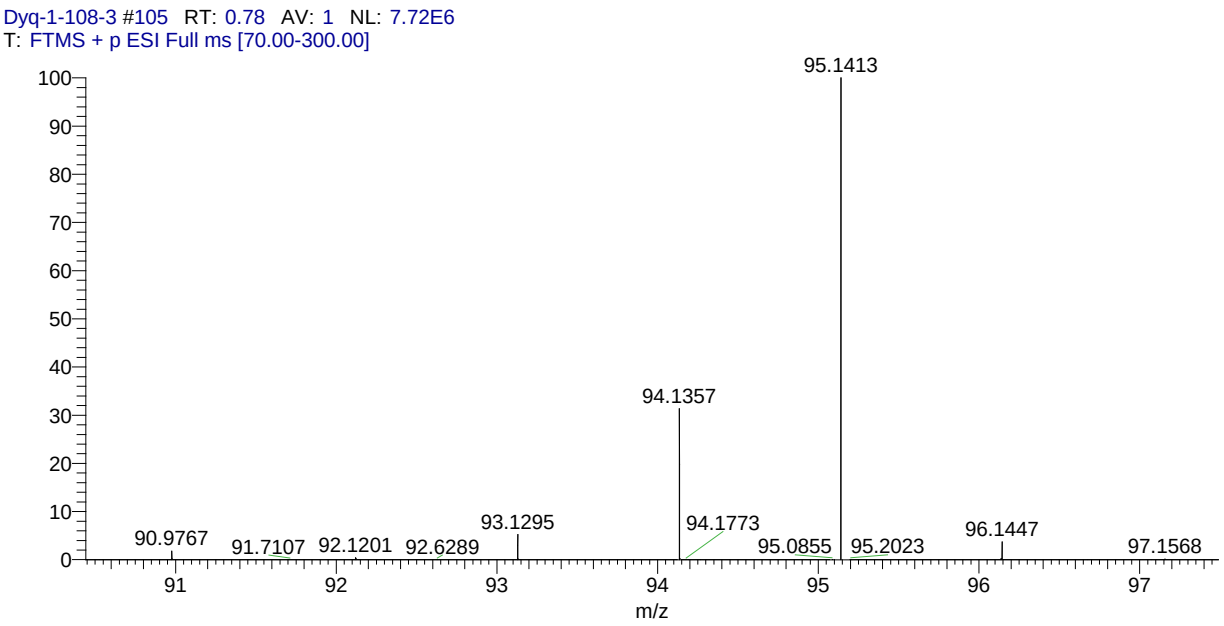


145.1826 ($C_{10}H_{10}D_8O$ – H_2O + H^+, 7%), 146.1888 ($C_{10}H_9D_9O$ – H_2O + H^+, 21%), 147.1950 ($C_{10}H_8D_{10}O$ – H_2O + H^+, 39%), 148.2010 ($C_{10}H_7D_{11}O$ – H_2O + H+, 23%), 149.2072 ($C_{10}H_6D_{12}O$ – H_2O + H+, 7%).

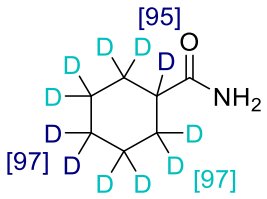


Piperazine-2,2,3,3,5,5,6,6-*d*$_8$ (10d). The title product was obtained with 80% yield (30.1 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, D_2O) δ 2.77 (s); ^{13}C NMR (101 MHz, D_2O) δ 34.68 (m, labeled).

Deuterium incorporation: 7.7 D/molecule [HRMS (ESI)]

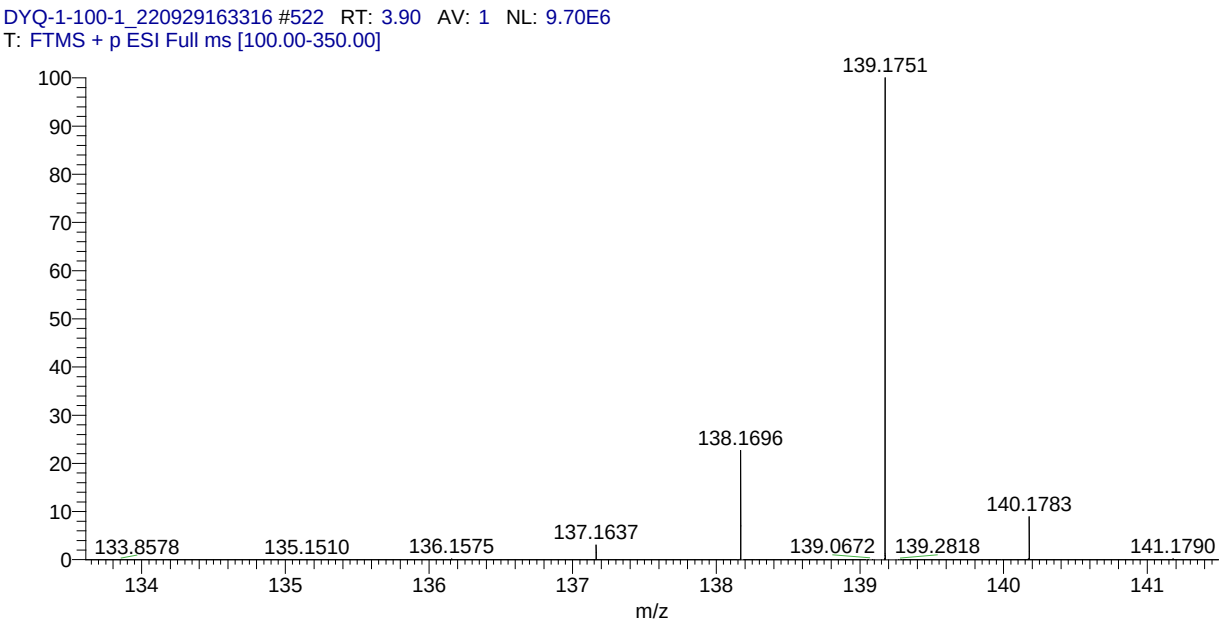


93.1295 ($C_4H_4D_6N_2 + H^+$, 4%), 94.1357 ($C_4H_3D_7N_2 + H^+$, 25%), 95.1413 ($C_4H_2D_8N_2 + H^+$, 71%).

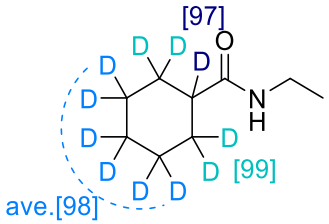


Cyclohexane-*d*$_{11}$-1-carboxamide (1f). The title product was obtained with 85% yield (46.9 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.14 (s, 0.98H), 6.63 (s, 1.00H), 2.01 (s, 0.05H), 1.62 (s, 0.14H), 1.53 (s, 0.03H), 1.13 (s, 0.07H), 1.06 (s, 0.03H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 177.50, 42.93 (m, labeled), 28.11 (m, labeled), 24.24 (m, labeled).

Deuterium incorporation: 10.7 D/molecule (^{1}H-NMR), 10.8 D/molecule [HRMS (ESI)]

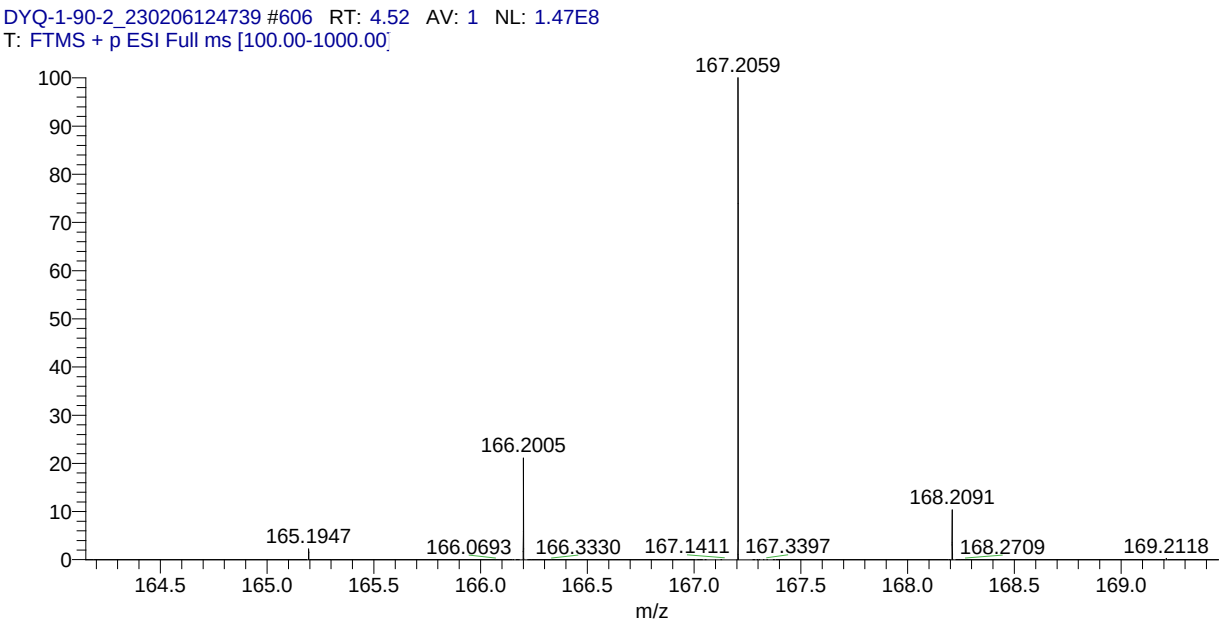


137.1637 ($C_7H_4D_9NO + H^+$, 2%), 138.1696 ($C_7H_3D_{10}NO + H^+$, 19%), 139.1751 ($C_7H_2D_{11}NO + H^+$, 78%).

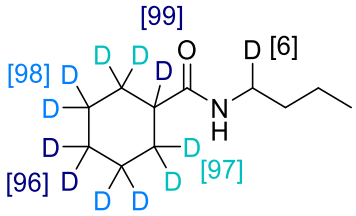


***N*-ethylcyclohexane-*d*$_{11}$-1-carboxamide (2f)**. The title product was obtained with 99% yield (33.2 mg, 0.2 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.52 (s, 0.99H), 3.30-3.23 (m, 3.00H), 2.01 (s, 0.03H), 1.79 (s, 0.02H), 1.72 (s, 0.05H), 1.60 (s, 0.02H), 1.37 (s, 0.04H), 1.19-1.18 (m, 0.05H), 1.12 (t, *J* = 7.2 Hz, 2.99H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.30, 44.94 (m, labeled), 34.27, 28.76 (m, labeled), 24.59 (m, labeled), 15.08.

Deuterium incorporation: 10.8 D/molecule (^{1}H-NMR), 10.8 D/molecule [HRMS (ESI)].

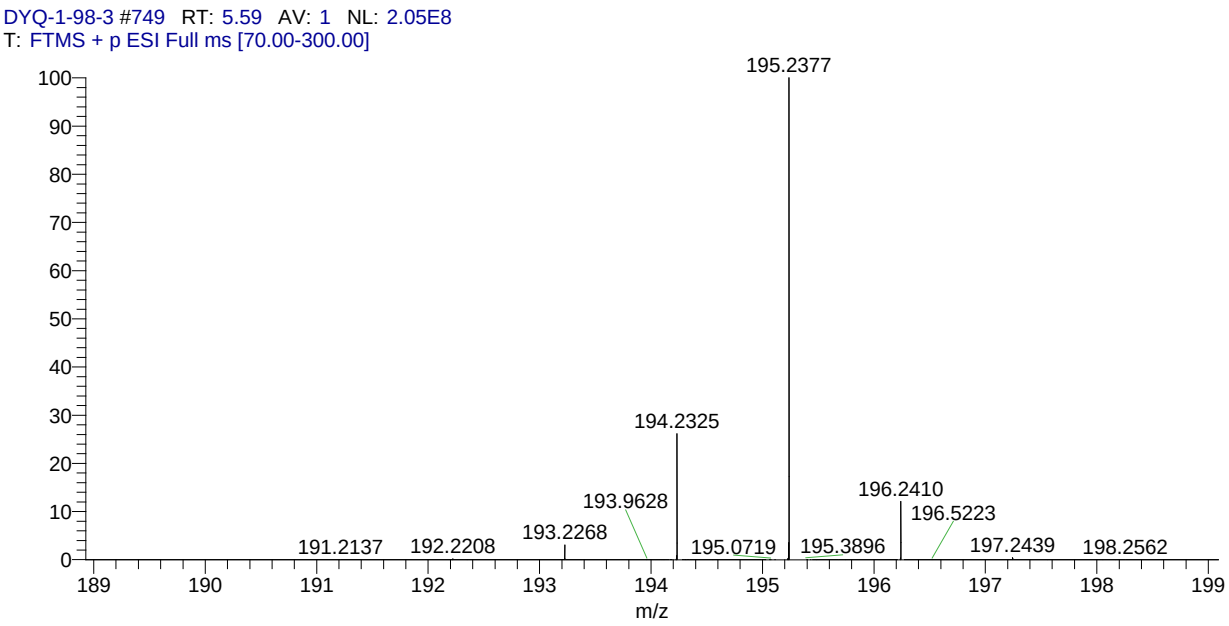


165.1947 ($C_9H_8D_9NO + H^+$, 2%), 166.2005 ($C_9H_7D_{10}NO + H^+$, 17%), 167.2059 ($C_9H_6D_{11}NO + H^+$, 81%).

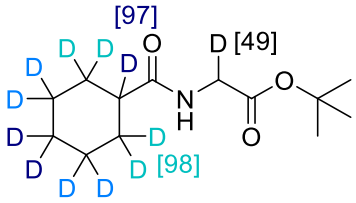


***N*-butylcyclohexane-*d*$_{11}$-1-carboxamide (3f)**. The title product was obtained with 99% yield (78.1 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.76 (s, 0.75H), 3.22-3.17 (m, 1.94H), 2.00 (s, 0.04H), 1.75 (s, 0.03H), 1.68 (s, 0.04H), 1.47-1.40 (m, 2.00H), 1.34-1.25 (m, 2.09H), 1.16 (s, 0.07H), 1.11 (s, 0.04H), 0.88 (t, *J* = 7.6 Hz, 3.00H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.36, 44.90 (m, labeled), 39.11, 38.97, 31.91, 31.89, 28.86 (m, labeled), 24.73 (m, labeled), 20.19, 13.88.

Deuterium incorporation: 10.7 D/molecule (^{1}H-NMR), 10.7 D/molecule [HRMS (ESI)]

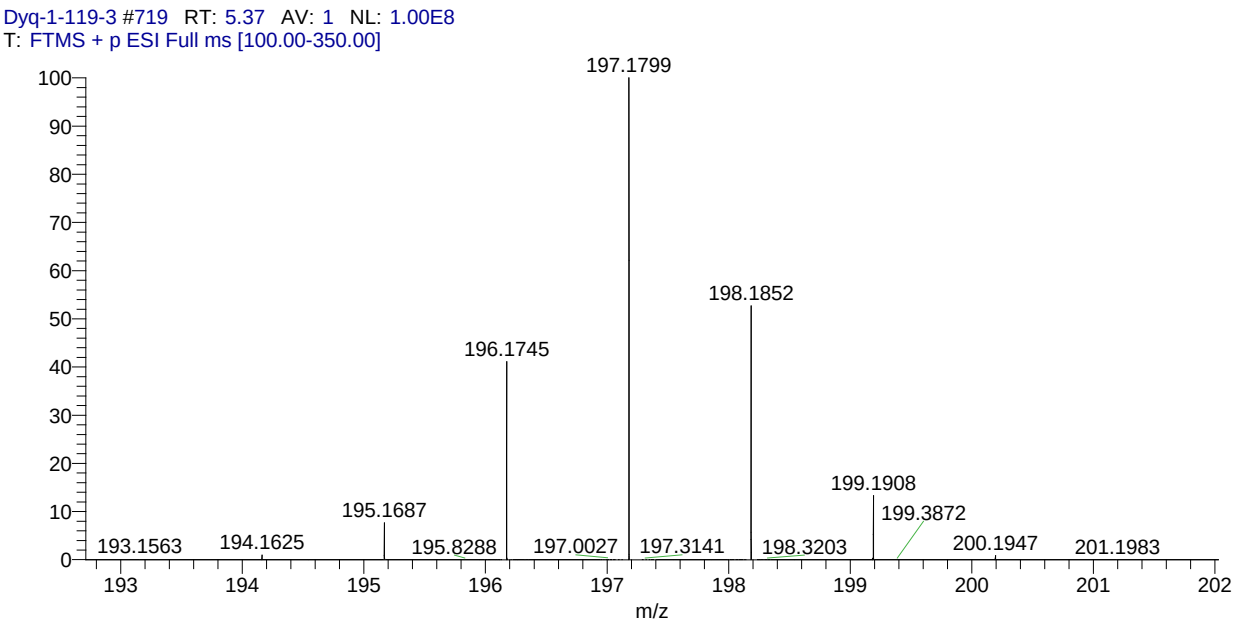


193.9628 ($C_{11}H_{12}D_9NO + H^+$, 2%), 194.2325 ($C_{11}H_{11}D_{10}NO + H^+$, 20%), 195.2377 ($C_{11}H_{10}D_{11}NO + H^+$, 77%).

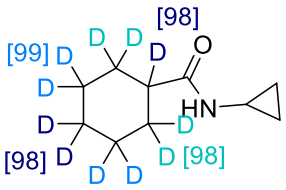


***tert*-Butyl (cyclohexane-1-carbonyl-*d*$_{11}$)glycinate (4f)**. The title product was obtained with 82% yield (83.1 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.08 (s, 0.96H), 3.89-3.86 (m, 1.51H), 1.98-1.95 (m, 0.03H), 1.80 (s, 0.05H), 1.69-1.67 (m, 0.11H), 1.59-1.58 (m, 0.08H), 1.47-1.36 (m, 9.00H), 1.28 (s, 0.05H), 1.18 (s, 0.05H), 1.12 (s, 0.02H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.35, 169.60, 82.41, 44.77, 42.05, 41.77 (m, labeled), 28.72 (m, labeled), 28.22, 24.68 (m, labeled).

Deuterium incorporation: 11.1 D/molecule (^{1}H-NMR), 11.1 D/molecule [HRMS (ESI)].

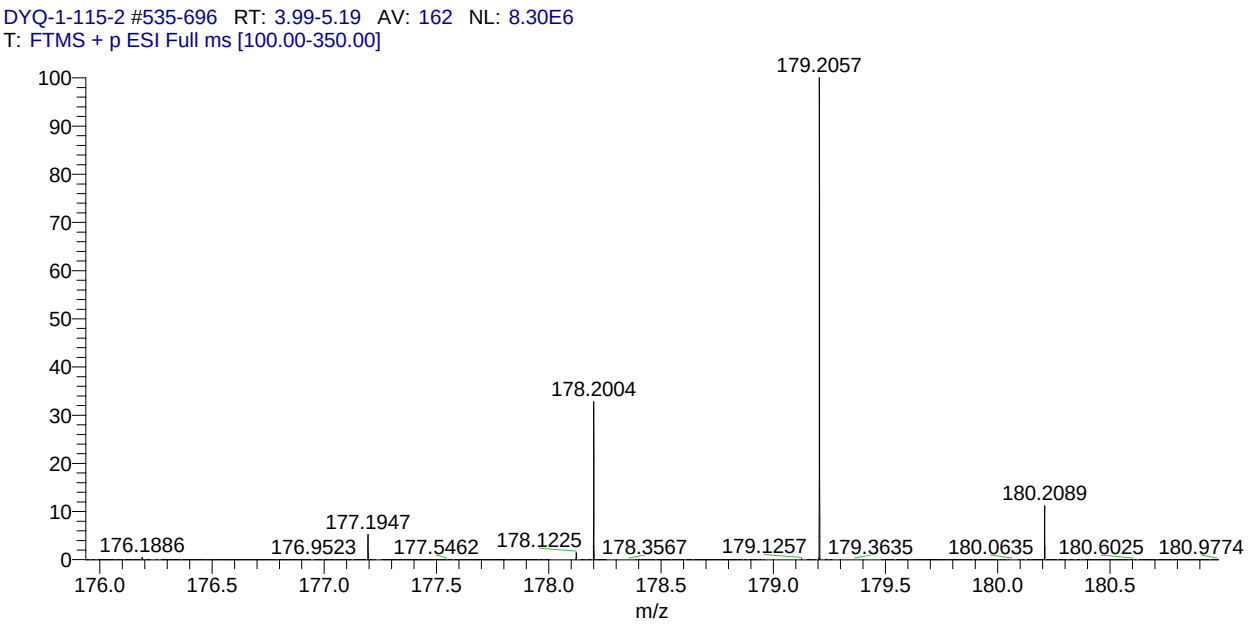


195.1687 ($C_{13}H_{14}D_9NO_3$ – C_4H_8 + H^+, 4%), 196.1745 ($C_{13}H_{13}D_{10}NO_3$ – C_4H_8 + H^+, 19%), 197.1799 ($C_{13}H_{12}D_{11}NO_3$ – C_4H_8 + H^+, 47%), 198.1852 ($C_{13}H_{11}D_{12}NO_3$ – C_4H_8 + H^+, 24%), 199.1908 ($C_{13}H_{10}D_{13}NO_3$ – C_4H_8 + H^+, 6%).

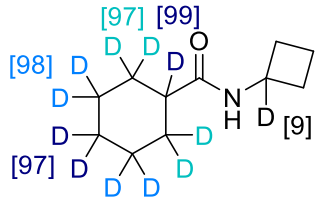


***N*-cyclopropylcyclohexane-*d*$_{11}$-1-carboxamide (5f)**. The title product was obtained with 99% yield (70.9 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.92 (s, 1.00H), 2.70-2.56 (m, 0.99H), 2.23 (s, 0.02H), 1.97 (s, 0.03H), 1.73 (s, 0.03H), 1.68 (s, 0.04H), 1.33 (s, 0.05H), 1.14 (s, 0.03H), 1.11 (s, 0.02H), 0.73-0.68 (m, 1.99H), 0.46-0.42 (m, 2.00H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.89, 44.61 (m, labeled), 28.57 (m, labeled), 24.56 (m, labeled), 22.62, 6.69.

Deuterium incorporation: 10.8 D/molecule (^{1}H-NMR), 10.7 D/molecule [HRMS (ESI)].

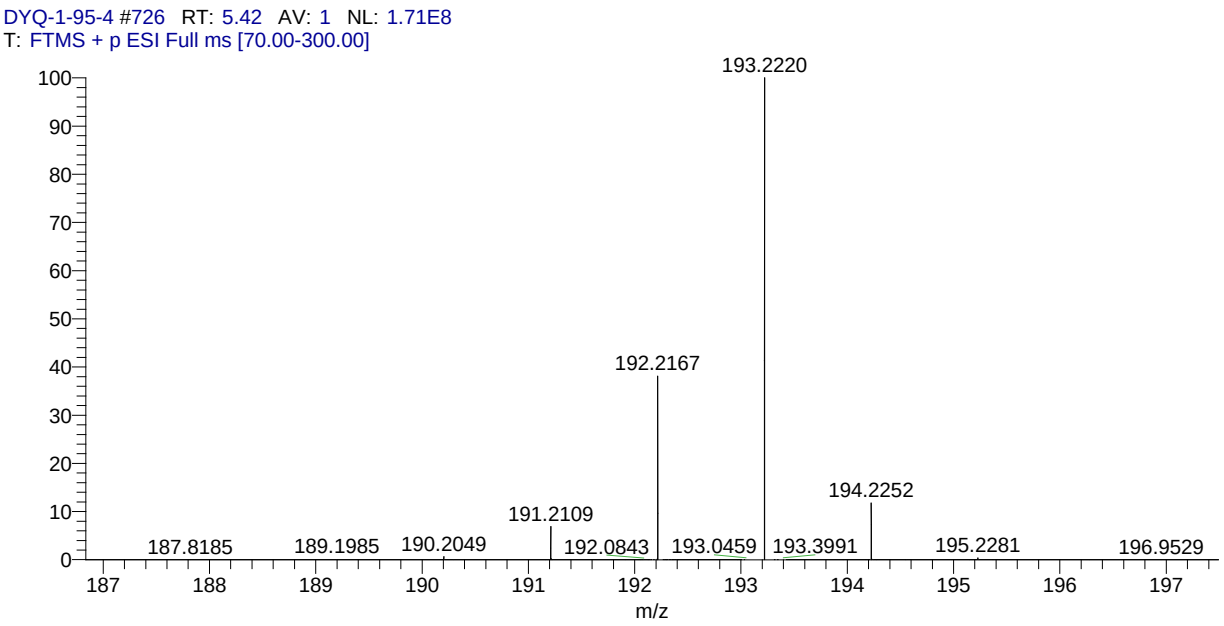


177.1947 ($C_{10}H_8D_9NO + H^+$, 3%), 178.2004 ($C_{10}H_7D_{10}NO + H^+$, 23%), 179.2057 ($C_{10}H_7D_{10}NO + H^+$, 73%).

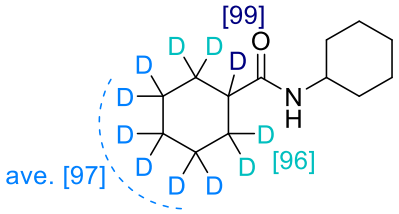


***N*-cyclobutylcyclohexane-d_{11}-1-carboxamide (6f)**. The title product was obtained with 95% yield (73.0 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.77 (d, J = 7.2 Hz, 0.74H), 4.43-4.32 (m, 0.91H), 2.34-2.27 (m, 2.00H), 2.00-1.97 (m, 0.06H), 1.86-1.76 (m, 2.05H), 1.72-1.62 (m, 2.05H), 1.35 (s, 0.07H), 1.17 (s, 0.05H), 1.13 (m, 0.02H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.44, 44.57, 44.44, 31.51, 31.49, 28.67 (m, labeled), 24.65 (m, labeled), 15.16.

Deuterium incorporation: 10.7 D/molecule (^{1}H-NMR), 10.6 D/molecule [HRMS (ESI)]

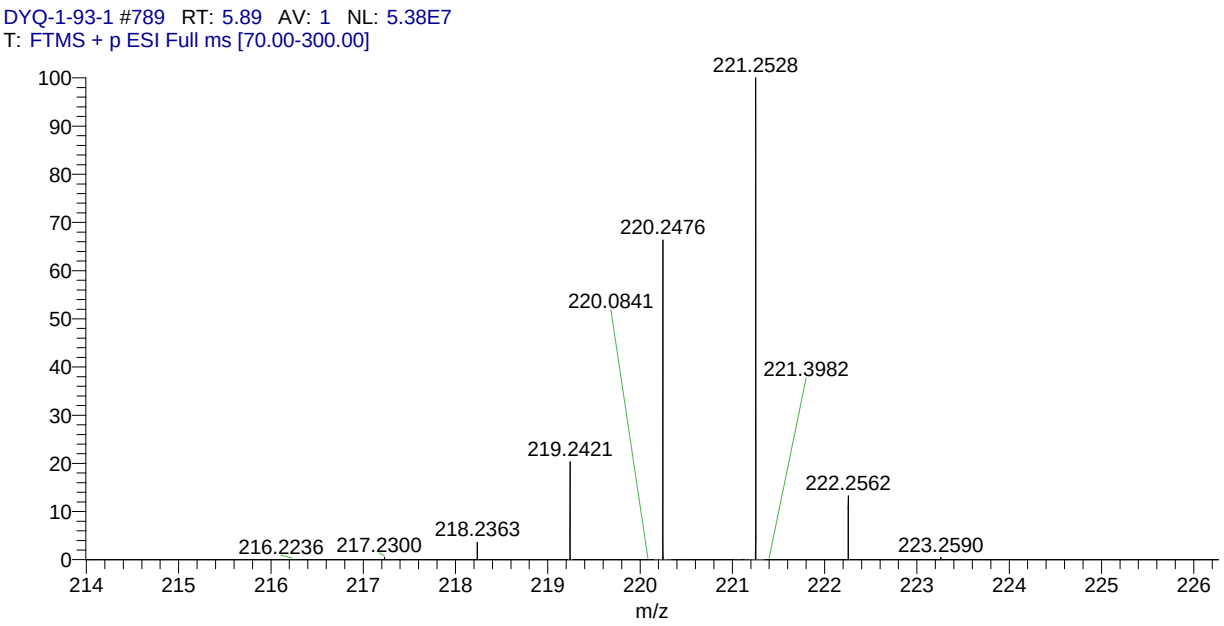


191.2109 ($C_{11}H_{10}D_9NO + H^+$, 5%), 192.2167 ($C_{11}H_9D_{10}NO + H^+$, 26%), 193.2220 ($C_{11}H_8D_{11}NO + H^+$, 68%).

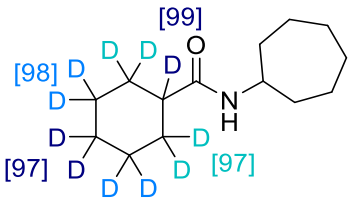


***N*-cyclohexylcyclohexane-*d*$_{11}$-1-carboxamide (7f)**. The title product was obtained with 87% yield (76.6 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.38 (d, *J* = 8.4 Hz, 0.98H), 3.78-3.69 (m, 0.98H), 2.21 (t, *J* = 8.0 Hz, 0.01H), 2.02-1.94 (m, 0.09H), 1.89-1.85 (m, 1.98H), 1.77 (s, 0.07H), 1.70-1.65 (m, 2.04H), 1.62-1.56 (m, 1.00H) 1.40-1.29 (m, 2.09H), 1.19-1.03 (m, 3.06H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.39, 47.84, 45.11 (m, labeled), 33.43, 28.92 (m, labeled), 25.75, 25.06, 24.50 (m, labeled).

Deuterium incorporation: 10.4 D/molecule (^{1}H-NMR), 10.4 D/molecule [HRMS (ESI)].

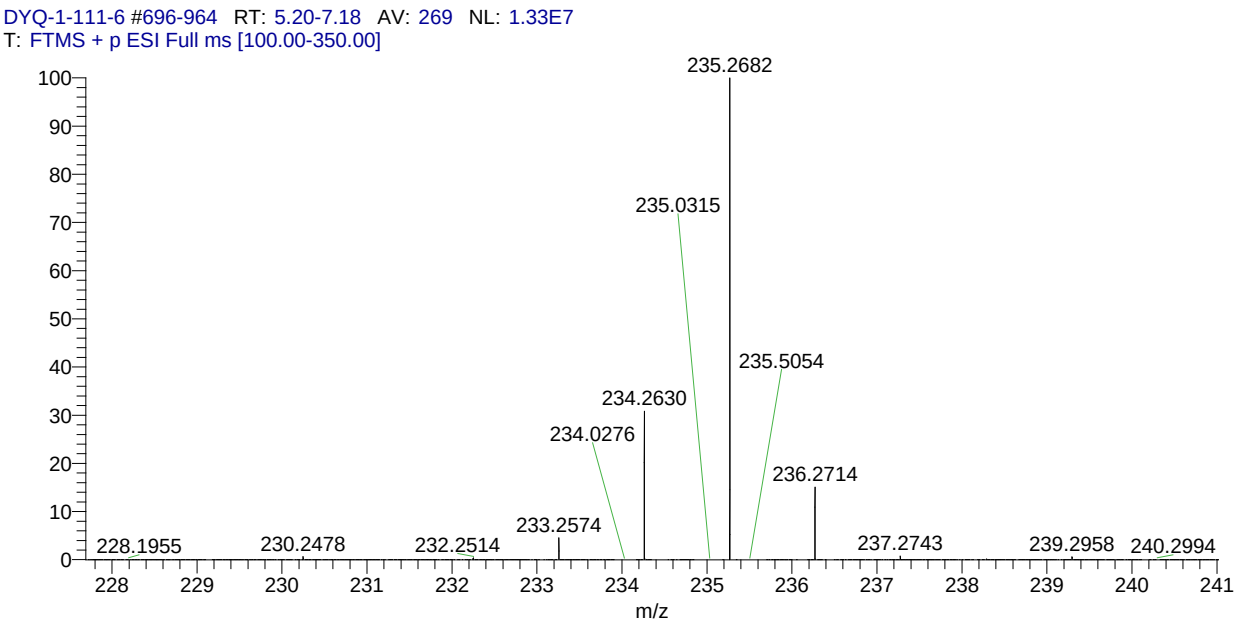


218.2363 ($C_{13}H_{15}D_8NO + H^+$, 2%), 219.2421 ($C_{13}H_{14}D_9NO + H^+$, 11%), 220.0841 ($C_{13}H_{13}D_{10}NO + H^+$, 34%), 221.3982 ($C_{13}H_{12}D_{11}NO + H^+$, 53%).

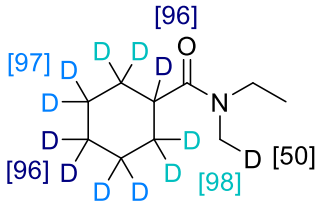


***N*-cycloheptylcyclohexane-*d*$_{11}$-1-carboxamide (8f)**. The title product was obtained with 99% yield (96.2 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.62 (d, *J* = 8.4 Hz, 0.25H), 3.93-3.84 (m, 1.00H), 1.95 (s, 0.05H), 1.87-1.81 (m, 2.00H), 1.72 (s, 0.02H), 1.66 (s, 0.05H), 1.57-1.32 (m, 10.06H), 1.14 (s, 0.06H), 1.10 (s, 0.02H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.06, 174.98, 50.01, 49.90, 44.84 (m, labeled), 35.23, 35.19, 28.80 (m, labeled), 28.08, 24.63 (m, labeled), 24.23.

Deuterium incorporation: 10.7 D/molecule (^{1}H-NMR), 10.7 D/molecule [HRMS (ESI)].

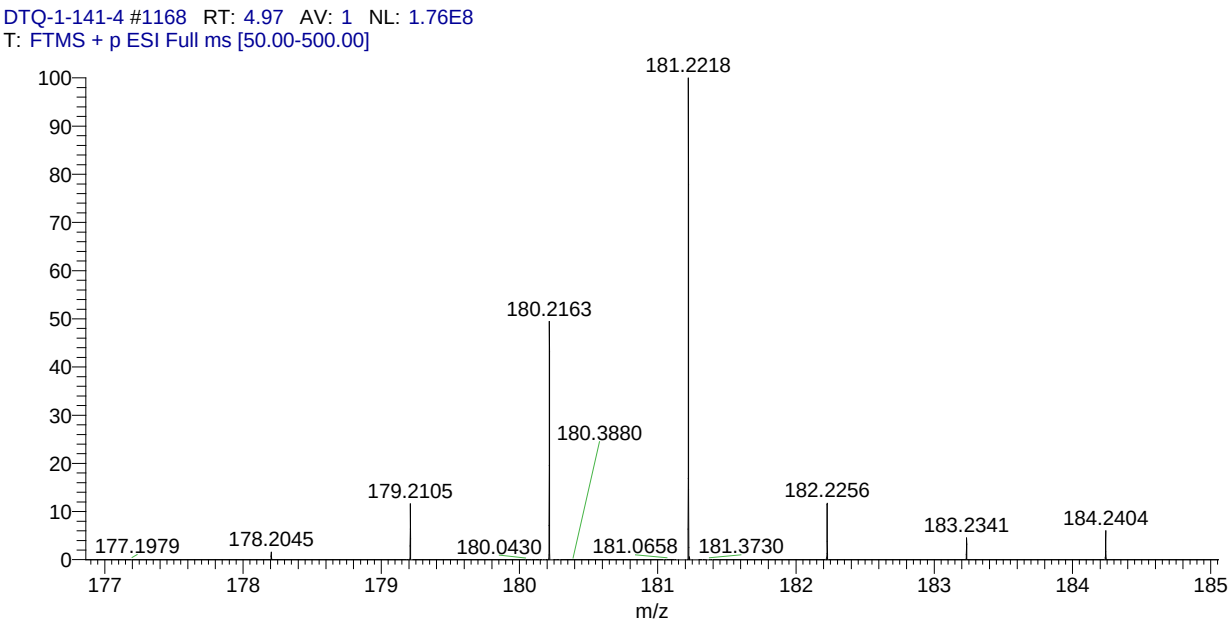


233.2574 ($C_{14}H_{16}D_9NO + H^+$, 3%), 234.2630 ($C_{14}H_{15}D_{10}NO + H^+$, 23%), 234.2682 ($C_{14}H_{14}D_{11}NO + H^+$, 74%).

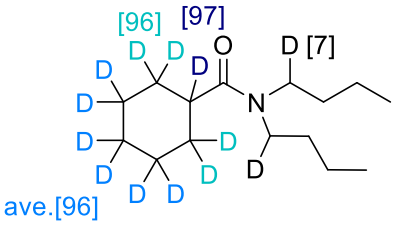


***N*-ethyl-*N*-(methyl-*d*)cyclohexane-1-carboxamide-d_{11} (9f)**. The title product was obtained with 83% yield (60.0 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.43-3.33 (m, 2.00H), 3.00 (s, 1.20H), 2.90 (s, 1.30H), 2.41 (s, 0.04H), 1.75 (s, 0.04H), 1.64 (s, 0.06H), 1.51 (s, 0.05H), 1.46 (s, 0.05H), 1.18 (t, *J* = 7.0 Hz, 1.50H), 1.15 (s, 0.05H), 1.13 (s, 0.04H), 1.08 (t, *J* = 7.2 Hz, 1.31H), 1.02 (t, *J* = 7.2 Hz, 0.06H), 0.88 (t, *J* = 6.6 Hz, 0.13H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 44.38, 42.48, 34.63, 33.07, 14.40, 12.53.

Deuterium incorporation: 11.2 D/molecule (^{1}H-NMR), 10.7 D/molecule [HRMS (ESI)].

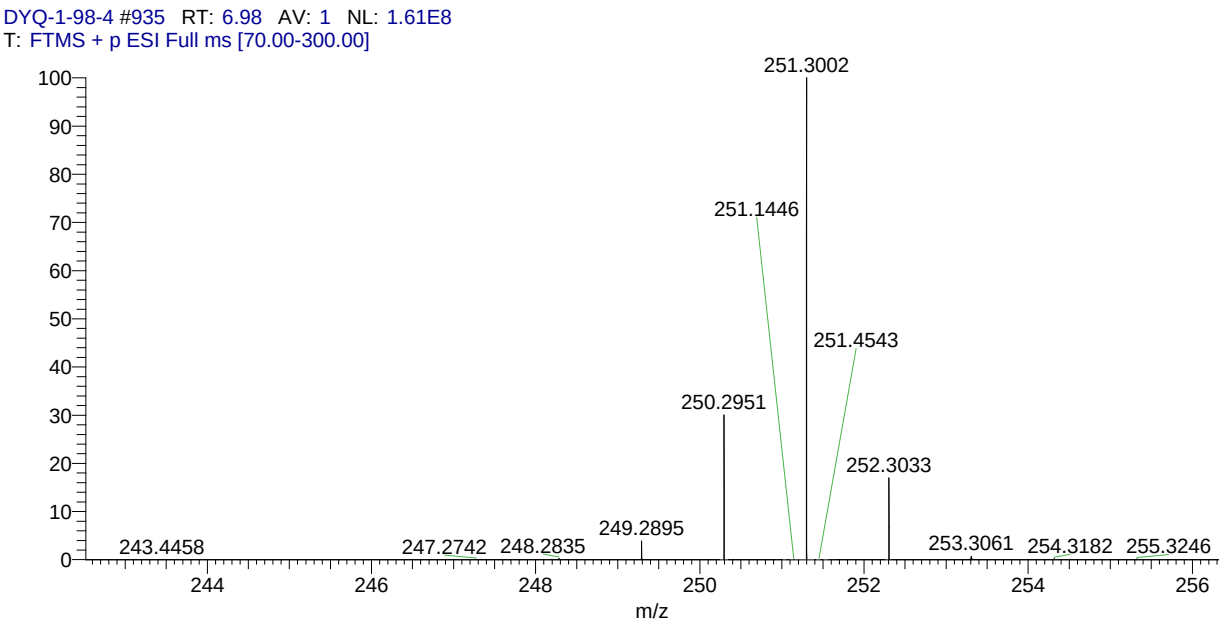


178.2045 ($C_{10}H_{11}D_8NO + H^+$, 1%), 179.2105 ($C_{10}H_{10}D_9NO + H^+$, 7%), 180.2163 ($C_{10}H_9D_{10}NO + H^+$, 30%), 181.2218 ($C_{10}H_8D_{11}NO + H^+$, 62%), 183.2341 ($C_{10}H_7D_{12}NO + H^+$, 3%), 184.2404 ($C_{10}H_{11}D_8NO + H^+$, 4%).

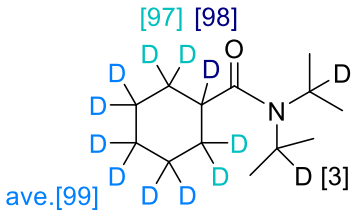


***N, N*-dibutylcyclohexane-1-carboxamide-*d*$_{11}$ (10f)**. The title product was obtained with 76% yield (76.2 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.25 (t, *J* = 7.6 Hz, 1.92H), 3.18 (t, *J* = 7.6 Hz, 1.94H), 2.34 (s, 0.03H), 1.99 (s, 0.01H), 1.70 (s, 0.04H), 1.63-1.59 (m, 0.10H), 1.54-1.40 (m, 4.00H), 1.35-1.20 (m, 4.21H), 1.17 (s, 0.10H), 0.92 (t, *J* = 7.2 Hz, 3.00H), 0.88 (t, *J* = 7.2 Hz, 3.00H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.95, 47.34, 45.53, 39.97 (m, labeled), 31.81, 29.95, 28.21 (m, labeled), 24.61 (m, labeled), 20.18, 20.03, 13.87, 13.82.

Deuterium incorporation: 10.6 D/molecule (^{1}H-NMR), 10.7 D/molecule [HRMS (ESI)]

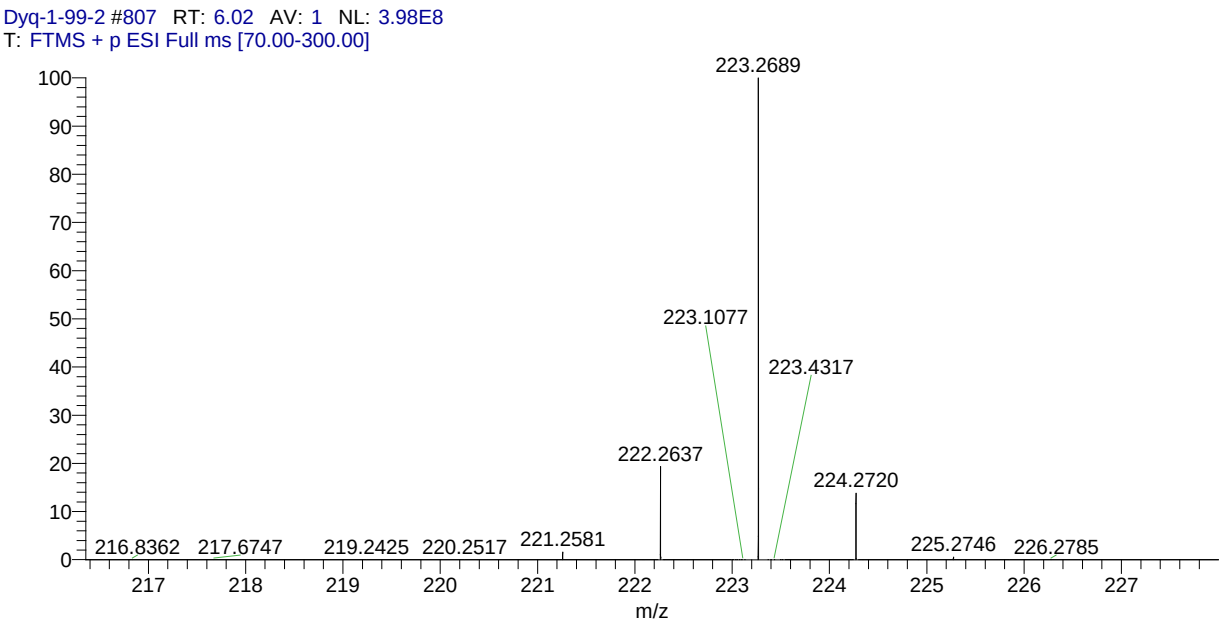


249.2895 ($C_{15}H_{20}D_9NO + H^+$, 3%), 250.2951 ($C_{15}H_{19}D_{10}NO + H^+$, 22%), 251.3002 ($C_{15}H_{18}D_{11}NO + H^+$, 75%).

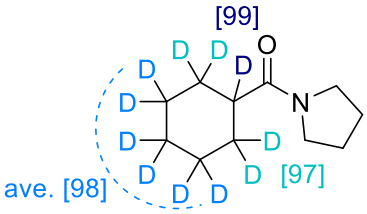


***N*, *N*-diisopropylcyclohexane-1-carboxamide-*d*$_{11}$ (11f)**. The title product was obtained with 84% yield (74.9 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.93-3.54 (m, 1.94H), 2.22-2.18 (m, 0.02H), 1.98 (s, 0.02H), 1.70 (s, 0.02H), 1.60 (s, 0.04H), 1.45 (s, 0.09H), 1.31-1.17 (m, 12.00H), 1.03-1.01 (s, 0.03H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.58, 47.49, 45.50, 41.81 (m, labeled), 29.82, 28.61 (m, labeled), 24.88 (m, labeled), 21.63, 20.88.

Deuterium incorporation: 10.8 D/molecule (^{1}H-NMR), 10.8 D/molecule [HRMS (ESI)]

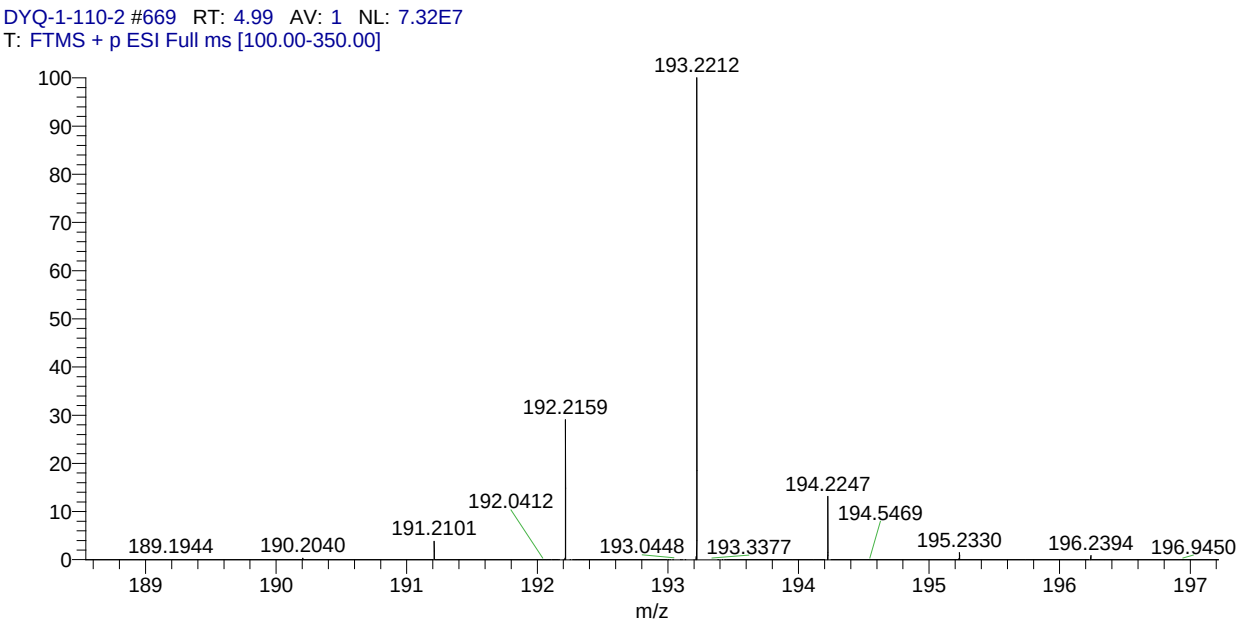


221.2581 ($C_{13}H_{16}D_9NO + H^+$, 1%), 222.2637 ($C_{13}H_{15}D_{10}NO + H^+$, 16%), 223.2689 ($C_{13}H_{14}D_{11}NO + H^+$, 82%).

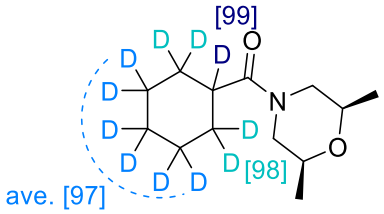


(Cyclohexyl-*d*$_{11}$)(pyrrolidin-1-yl)methanone (12f). The title product was obtained with 99% yield (80.6 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.62 (t, *J* = 7.0 Hz, 0.18H), 3.41 (q, *J* = 7.2 Hz, 3.65H), 3.28 (t, *J* = 6.6 Hz, 0.14H), 1.96-1.77 (m, 4.0H), 1.70 (s, 0.05H), 1.65 (s, 0.04H), 1.58 (s, 0.02H), 1.44 (s, 0.06H), 1.16 (s, 0.06H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.98, 46.35, 45.71, 42.25 (m, labeled), 27.91 (m, labeled), 26.26, 24.78 (m, labeled), 24.38.

Deuterium incorporation: 10.8 D/molecule (^{1}H-NMR), 10.7 D/molecule [HRMS (ESI)].

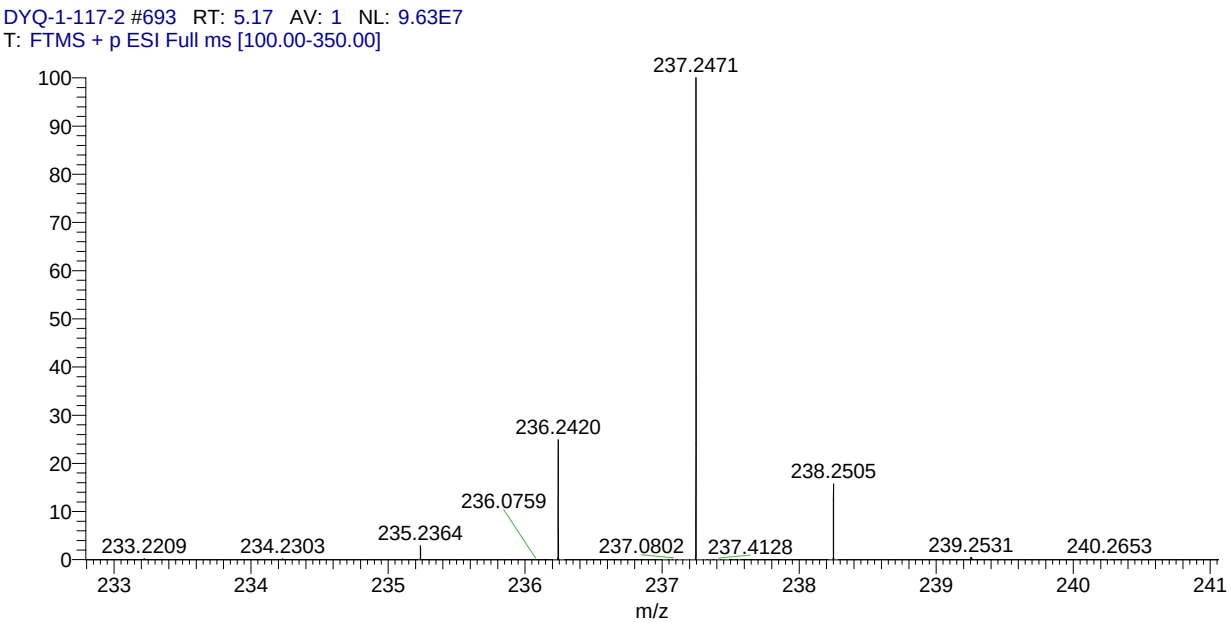


191.2101 ($C_{11}H_{10}D_9NO + H^+$, 3%), 192.2159 ($C_{11}H_9D_{10}NO + H^+$, 21%), 193.2212 ($C_{11}H_8D_{11}NO + H^+$, 75%).

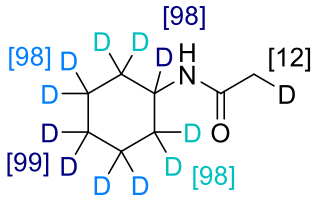


(Cyclohexyl-*d*$_{11}$)((2*S*,6*R*)-2,6-dimethylmorpholino)methanone (13f). The title product was obtained with 75% yield (70.5 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.45 (d, *J* = 13.2 Hz, 0.99H), 3.64 (d, *J* = 13.6 Hz, 1.00H), 3.55-3.45 (m, 2.00H), 2.76 (dd, *J* = 10.6, 13.0 Hz, 1.00H), 2.26 (dd, *J* = 10.8, 12.8 Hz, 0.97H), 1.92 (s, 0.08H), 1.73 (s, 0.04H), 1.62 (s, 0.08H), 1.49 (s, 0.02H), 1.25-1.16 (m, 6.08H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.68, 72.17, 72.10, 51.24, 47.13, 39.63 (m, labeled), 28.50 (m, labeled), 24.74 (m, labeled), 18.92.

Deuterium incorporation: 10.7 D/molecule (^{1}H-NMR), 10.8 D/molecule [HRMS (ESI)].

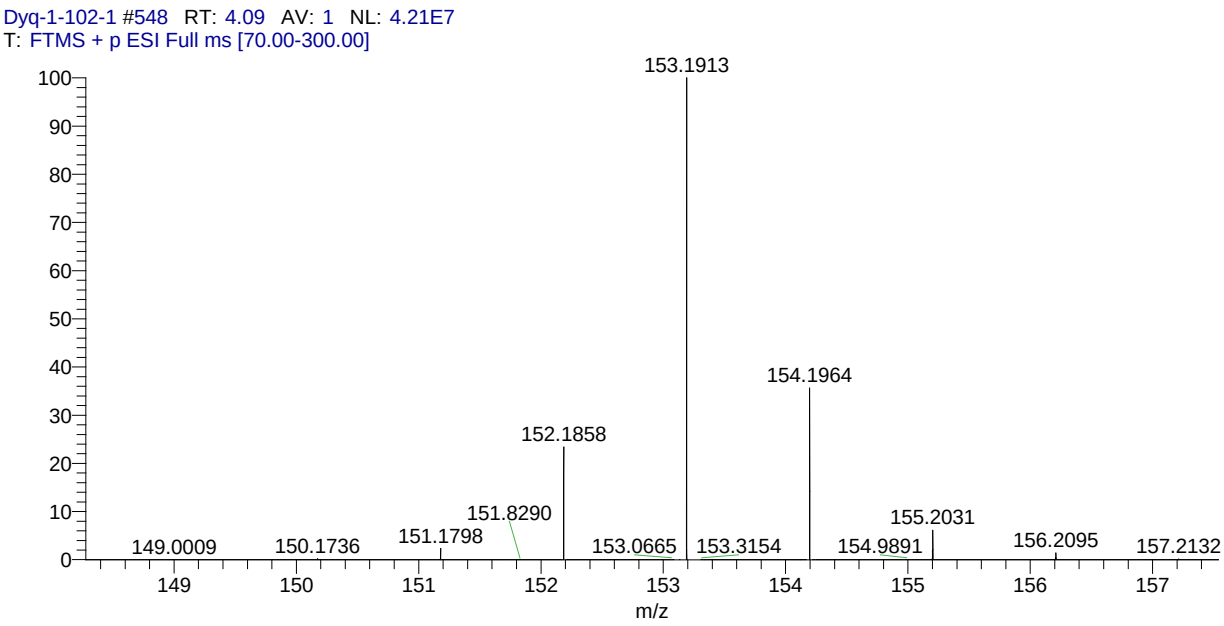


235.2364 ($C_{13}H_{14}D_9NO_2$ + H^+, 2%), 236.2420 ($C_{13}H_{13}D_{10}NO_2$ + H^+, 19%), 237.2471 ($C_{13}H_{12}D_{11}NO_2$ + H^+, 78%).

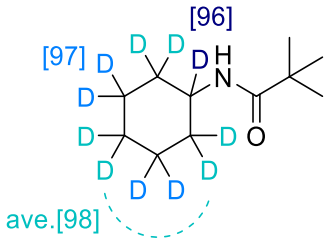


***N*-(cyclohexyl-*d*$_{11}$)acetamide (14f)**. The title product was obtained with 78% yield (47.2 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.47 (s, 1.00H), 3.71 (d, *J* = 8.9 Hz, 0.02H), 2.02-1.92 (m, 2.88H), 1.85 (s, 0.03H), 1.63 (s, 0.03H), 1.55 (s, 0.01H), 1.29 (s, 0.04H), 1.08 (s, 0.02H), 1.05 (s, 0.04H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.31, 47.72 (m, labeled), 32.16 (m, labeled), 23.84 (m, labeled), 23.77.

Deuterium incorporation: 10.9 D/molecule (^{1}H-NMR), 11.1 D/molecule [HRMS (ESI)].

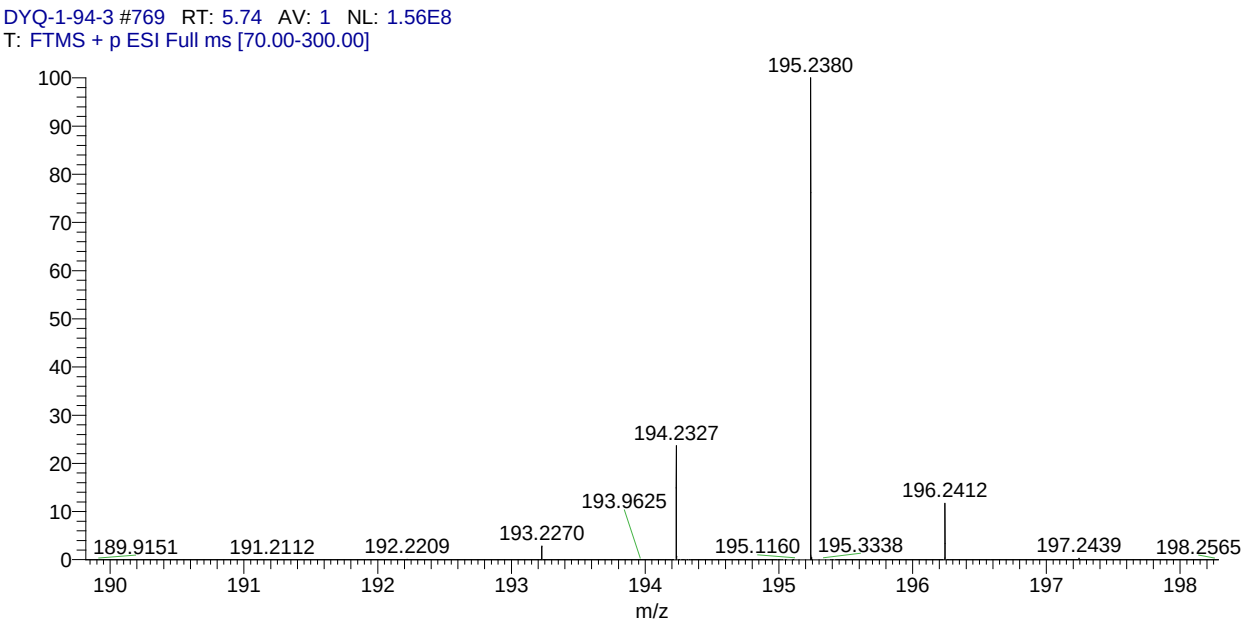


151.1798 ($C_8H_6D_9NO + H^+$, 1%), 152.1858 ($C_8H_5D_{10}NO + H^+$, 13%), 153.1913 ($C_8H_4D_{11}NO + H^+$, 62%), 154.1964 ($C_8H_3D_{12}NO + H^+$, 19%), 155.2031 ($C_8H_2D_{13}NO + H^+$, 3%), 156.2095 ($C_8H_1D_{14}NO + H^+$, 1%).

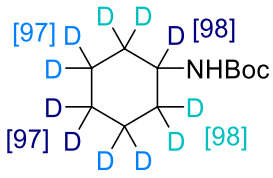


***N*-(cyclohexyl-*d*$_{11}$)pivalamide (15f)**. The title product was obtained with 93% yield (72.0 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.43 (s, 1.00H), 3.72 (d, *J* = 7.2 Hz, 0.04H), 1.84 (s, 0.04H), 1.64 (s, 0.06H), 1.56 (s, 0.03H), 1.26 (s, 0.33H), 1.18 (s, 8.72H), 1.06 (s, 0.07H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.67, 47.13 (m, labeled), 38.72, 32.24 (m, labeled), 29.66 (m, labeled), 27.81, 24.09 (m, labeled).

Deuterium incorporation: 10.8 D/molecule (^{1}H-NMR), 10.8 D/molecule [HRMS (ESI)]

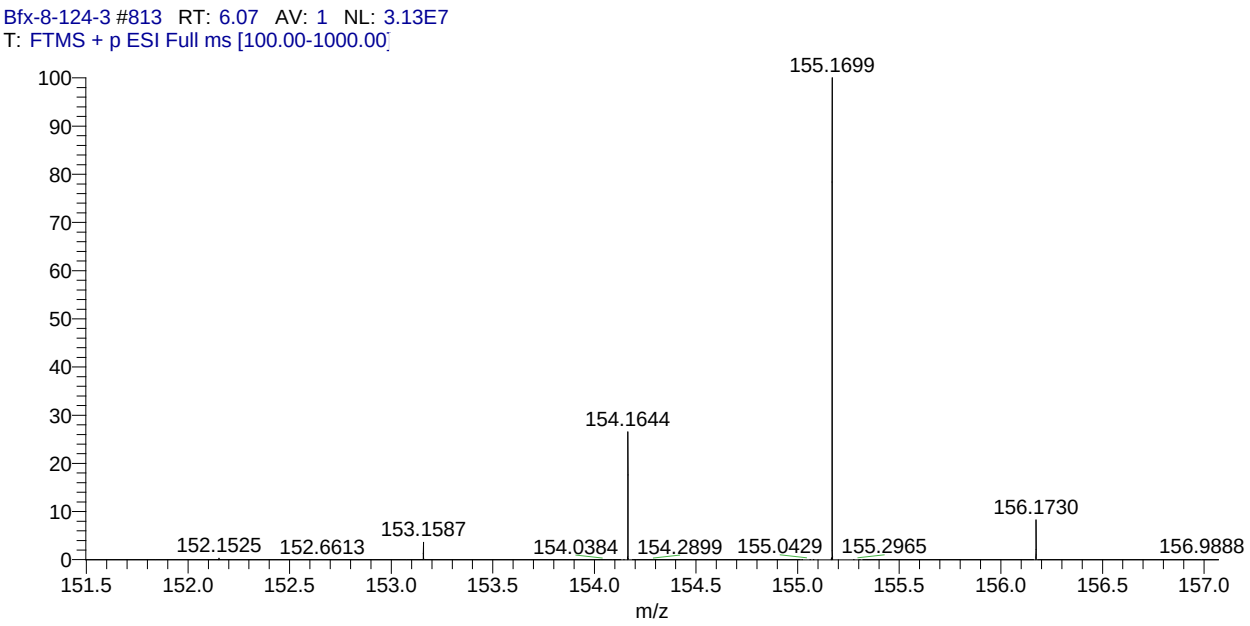


193.2270 ($C_{11}H_{12}D_9NO + H^+$, 2%), 194.2327 ($C_{11}H_{11}D_{10}NO + H^+$, 19%), 195.2380 ($C_{11}H_{10}D_{11}NO + H^+$, 76%).

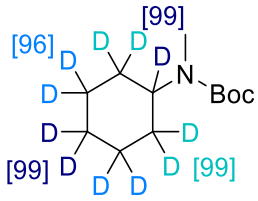


***tert*-Butyl (cyclohexyl-d_{11})carbamate (16f)**. The title product was obtained with 91% yield (76.4 mg, 0.4 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.42 (s, 1.00H), 3.39 (s, 0.02H), 1.86 (s, 0.04H), 1.77 (s, 0.23H), 1.63 (s, 0.04H), 1.59 (s, 0.03H), 1.44 (s, 8.80H), 1.28 (s, 0.07H), 1.08 (s, 0.03H), 1.04 (s, 0.06H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.42, 79.13, 48.96 (m, labeled), 32.48 (m, labeled), 28.63, 24.06 (m, labeled).

Deuterium incorporation: 10.7 D/molecule (^{1}H-NMR), 10.7 D/molecule [HRMS (ESI)].

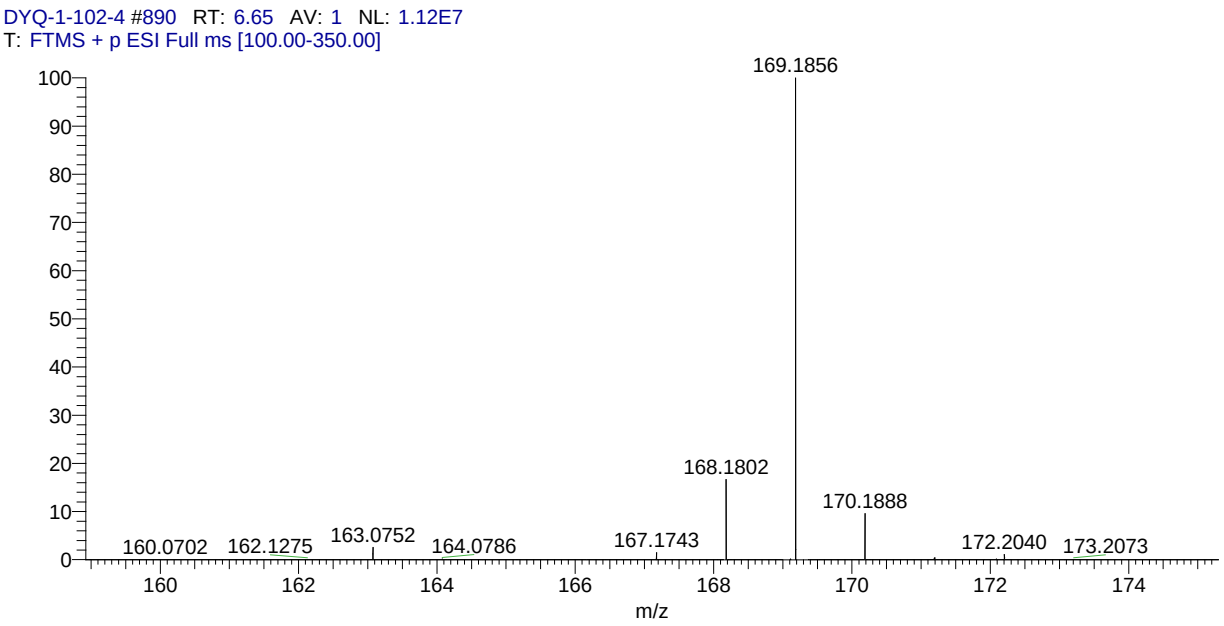


153.1587 ($C_{11}H_{12}D_9NO_2$ – C_4H_8 + H^+, 3%), 154.1644 ($C_{11}H_{11}D_{10}NO_2$ – C_4H_8 + H^+, 21%), 155.1699 ($C_{11}H_{10}D_{11}NO_2$ – C_4H_8 + H^+, 76%).

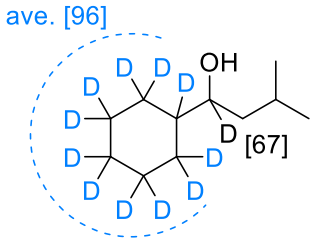


***tert*-Butyl (cyclohexyl-*d*$_{11}$)(methyl)carbamate (17f)**. The title product was obtained with 99% yield (89.8 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.70 (s, 3.00H), 2.05-1.98 (m, 0.05H), 1.81 (s, 0.12H), 1.72 (s, 0.03H), 1.45 (s, 9.02H), 1.29 (s, 0.03H), 0.99 (s, 0.01H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.86, 79.17, 29.87 (m, labeled), 29.65 (m, labeled), 29.48 (m, labeled), 28.68, 28.35, 24.77 (m, labeled).

Deuterium incorporation: 10.8 D/molecule (^{1}H-NMR), 10.8 D/molecule [HRMS (ESI)].

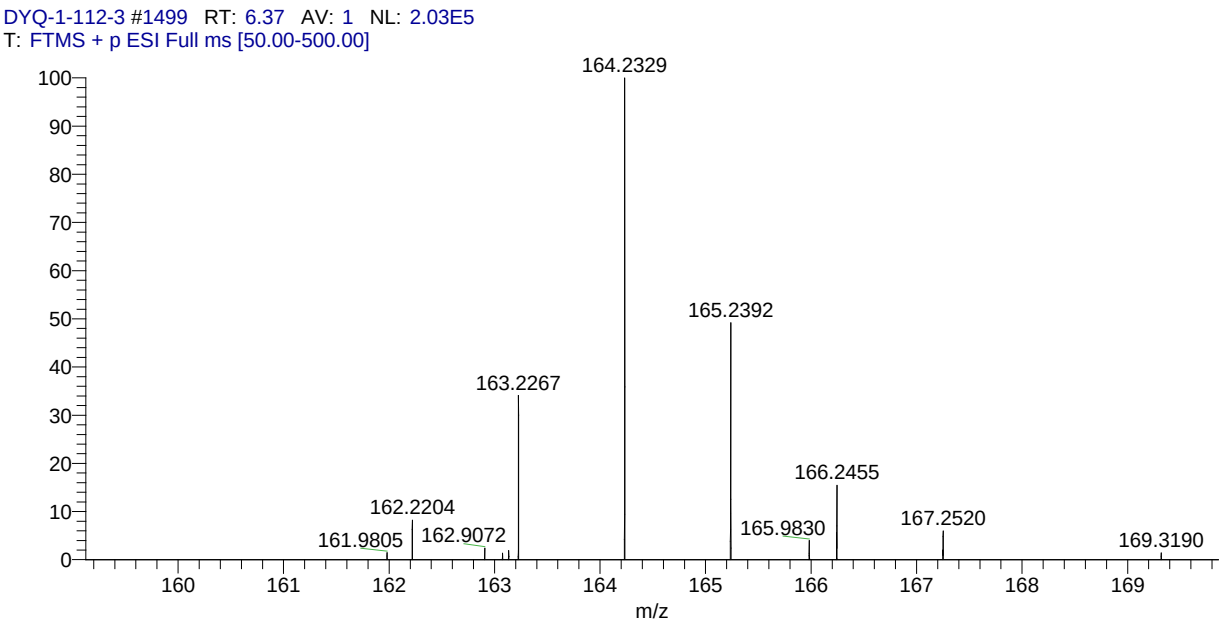


167.1743 ($C_{12}H_{14}D_9NO_2$ – C_4H_8 + H^+, 1%), 168.1802 ($C_{12}H_{13}D_{10}NO_2$ – C_4H_8 + H^+, 15%), 169.1856 ($C_{12}H_{12}D_{11}NO_2$ – C_4H_8 + H^+, 84%).

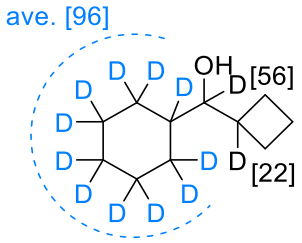


1-(Cyclohexyl-*d*$_{11}$)-3-methylbutan-1-*d*-1-ol (18f). The title product was obtained with 99% yield (72.8 mg, 0.4 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.39-3.31 (m, 1.33H), 1.77-1.54 (m, 1.72H), 1.45-1.39 (m,1.52H), 1.32-1.13 (m,1.34H), 0.97-0.82 (m, 4.84H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 73.43, 58.69, 43.10, 43.00, 27.81 (m, labeled), 26.48 (m, labeled), 24.81 (m, labeled), 24.32, 23.93, 23.58, 21.50, 19.50, 13.46.

Deuterium incorporation: 11.2 D/molecule (^{1}H-NMR), 11.2 D/molecule [HRMS (ESI)].

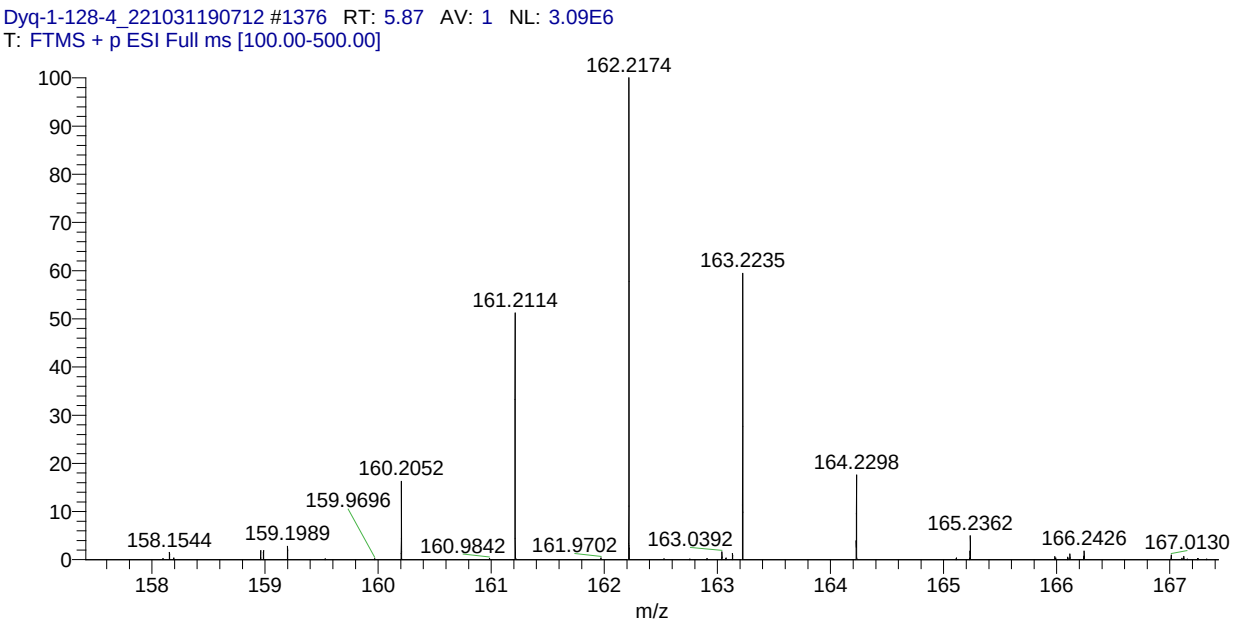


162.2204 ($C_{11}H_{13}D_9O$ - H_2O + H^+, 4%), 163.2267 ($C_{11}H_{12}D_{10}O$ - H_2O + H^+, 17%), 164.2329 ($C_{11}H_{11}D_{11}O$ - H_2O + H^+, 45%), 165.2392 ($C_{11}H_{10}D_{12}O$ - H_2O + H^+, 25%), 166.2455 ($C_{11}H_9D_{13}O$ - H_2O + H^+, 6%), 167.2520 ($C_{11}H_8D_{14}O$ - H_2O + H^+, 3%).

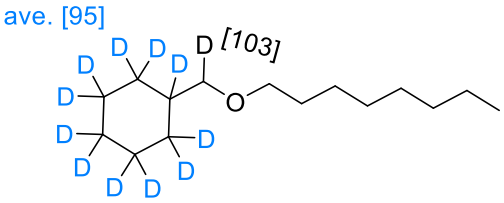


Cyclobutyl(cyclohexyl-*d*$_{11}$)methan-*d*-ol (19f). The title product was obtained with 99% yield (72.2 mg, 0.4 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.26 (d, *J* = 8.0 Hz, 0.44H), 2.53-2.43 (m, 0.78H), 2.02-1.53 (m, 6.28H), 1.39 (s, 1.00H), 1.16-1.06 (m, 0.17H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 80.15, 79.70 (m, labeled), 40.80 (m, labeled), 39.10, 39.01, 28.72 (m, labeled), 25.57 (m, labeled), 25.33, 25.31, 25.17, 24.98, 24.96, 24.80, 18.44.

Deuterium incorporation: 11.3 D/molecule (^{1}H-NMR), 11.1 D/molecule [HRMS (ESI)].

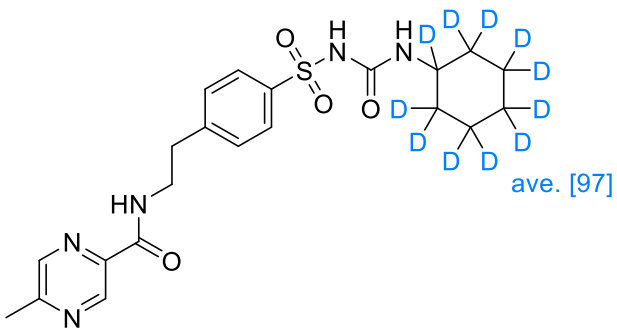


159.1989 ($C_{11}H_{12}D_8O + H^+ - H_2O$, 1%), 160.2052 ($C_{11}H_{11}D_9O + H^+ - H_2O$, 6%), 161.2114 ($C_{11}H_{10}D_{10}O + H^+ - H_2O$, 20%), 162.2174 ($C_{11}H_9D_{11}O + H^+ - H_2O$, 40%), 163.2235 ($C_{11}H_8D_{12}O + H^+ - H_2O$, 24%), 164.2298 ($C_{11}H_7D_{13}O + H^+ - H_2O$, 7%), 165.2362 ($C_{11}H_6D_{14}O + H^+ - H_2O$, 2%).



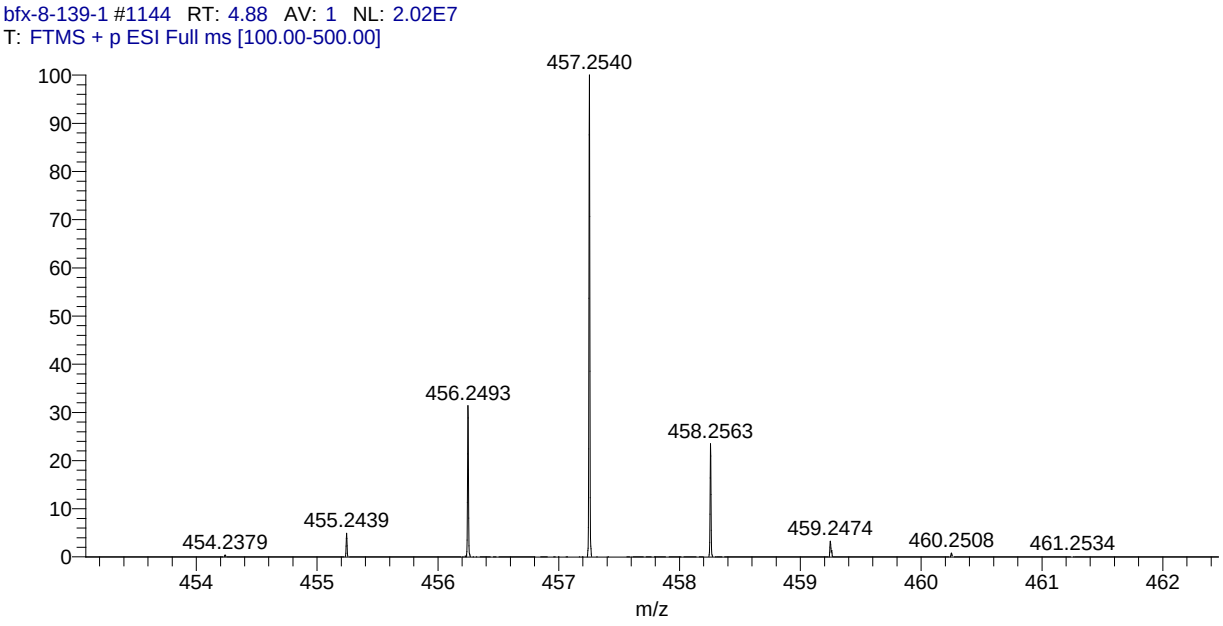
1-((Octyloxy)methyl-*d*)cyclohexane-1,2,3,4,5,6-d_6 (20f). The title product was obtained with 99% yield (89.3 mg, 0.4 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.37 (t, *J* = 6.8 Hz, 2.00H), 3.23-3.17 (m, 0.97H), 1.82-1.75 (m, 0.10H), 1.70 (s, 0.06H), 1.65 (s, 0.07H), 1.59-1.52 (m, 1.97H), 1.34-1.26 (m, 10.07H), 1.18-1.08 (m, 0.18H), 0.89-0.86 (m, 3.13H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 76.96, 76.54 (m, labeled), 71.35, 71.31, 71.28, 37.20 (m, labeled), 32.05, 29.96, 29.68, 29.49, 26.40, 25.17 (m, labeled), 22.86, 14.27.

Deuterium incorporation: 11.5 D/molecule (^{1}H-NMR).

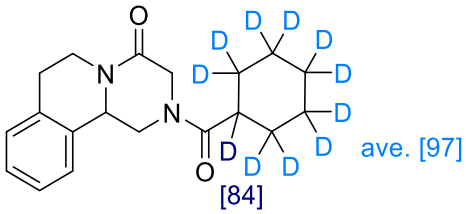


Glipizide-*d*$_{11}$ ([D]1h). The title product was obtained with 91% yield (66.8 mg, 0.16 mmol scale) as yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.02 (d, J = 1.6 Hz, 0.93H), 8.96 (t, J = 6.2 Hz, 1.01H), 8.59 (d, J = 1.2 Hz, 1.00H), 7.79 (d, J = 8.4 Hz, 1.93H), 7.44 (d, J = 8.4 Hz, 1.97H), 6.38 (s, 0.89H), 3.57 (q, J = 6.9 Hz, 2.00H), 2.96 (t, J = 7.2 Hz, 2.00H), 2.58 (s, 3.00H), 1.57 (s, 0.03H), 1.53-1.51 (m, 0.09H), 1.35 (s, 0.03H), 1.14 (s, 0.06H), 1.05-1.04 (m, 0.07H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.69, 157.17, 144.77, 142.93, 142.74, 142.61, 141.65, 129.35, 127.51, 40.07, 35.43, 31.90 (m, labeled), 29.27 (m, labeled), 23.44 (m, labeled), 21.40.

Deuterium incorporation: 10.7 D/molecule (^{1}H-NMR), 10.7 D/molecule [HRMS (ESI)].

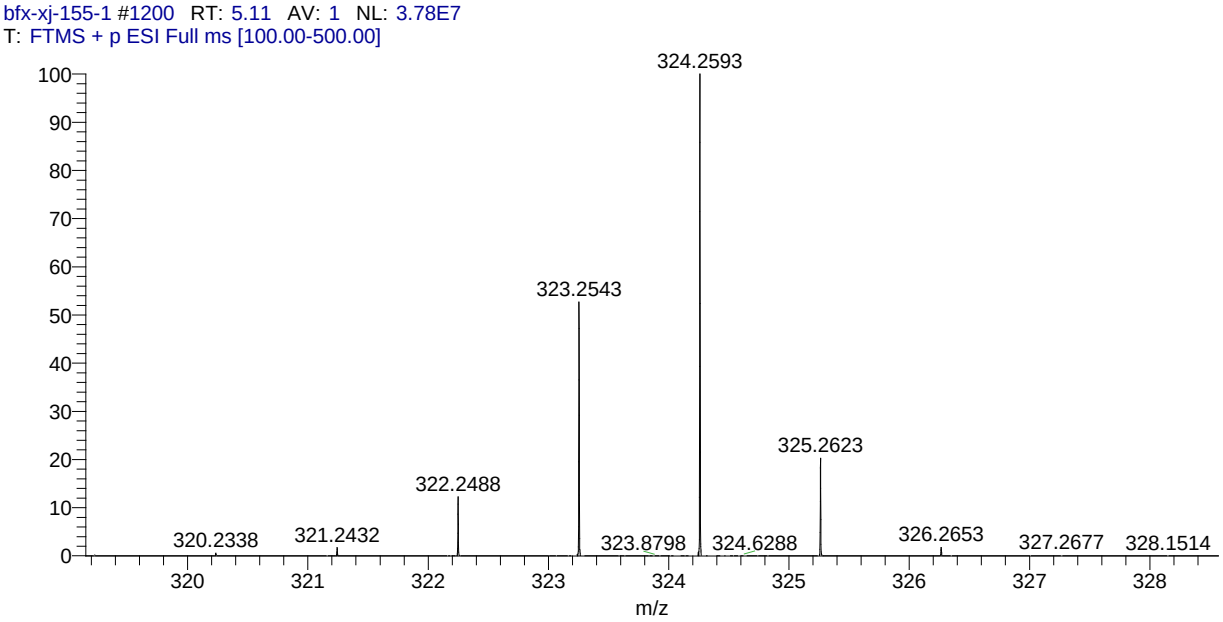


455.2439 ($C_{21}H_{18}D_9N_5O_4S$ + H^+, 3%), 456.2493 ($C_{21}H_{17}D_{10}N_5O_4S$ + H^+, 23%), 457.2540 ($C_{21}H_{16}D_{11}N_5O_4S$ + H^+, 73%).

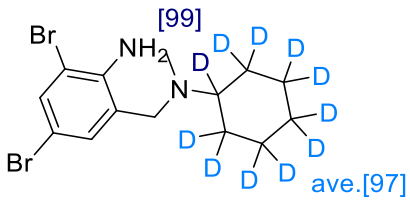


Praziquantel-*d*$_{11}$ ([D]2h). The title product was obtained with 41% yield (66.3 mg, 0.5 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.17 (m, 4.00H), 5.16 (dd, *J* = 2.6, 13.4 Hz, 0.70H), 4.99-4.77 (m, 2.22H), 4.46 (d, *J* = 17.6 Hz, 0.73H), 4.38-4.31 (m, 0.29H), 4.07 (d, *J* = 17.2 Hz, 0.78H), 3.85 (d, *J* = 18.4 Hz, 0.22H), 3.30-3.22 (m, 0.35H), 3.02-2.76 (m, 3.68H), 2.53-2.43 (m, 0.16H), 1.76-1.65 (m, 0.16H), 1.50-1.42 (m, 0.08H), 1.22-1.20 (m, 0.09H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.02, 165.71, 164.56, 135.66, 134.87, 132.91, 129.82, 129.44, 128.97, 128.79, 127.85, 127.69, 127.59, 127.12, 125.62, 125.32, 55.93, 55.10, 49.67, 49.14, 46.44, 45.27, 40.50, 40.11 (m, labeled), 39.24, 38.79, 28.86, 28.33 (m, labeled), 24.72 (m, labeled).

Deuterium incorporation: 10.5 D/molecule (^{1}H-NMR), 10.5 D/molecule [HRMS (ESI)].

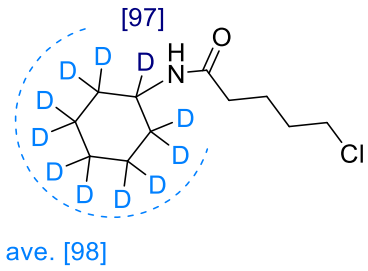


321.2432 ($C_{19}H_{16}D_8N_2O_2$ + H^+, 1%), 322.2488 ($C_{19}H_{15}D_9N_2O_2$ + H^+, 8%), 323.2543 ($C_{19}H_{14}D_{10}N_2O_2$ + H^+, 32%), 324.2593 ($C_{19}H_{13}D_{11}N_2O_2$ + H^+, 60%).



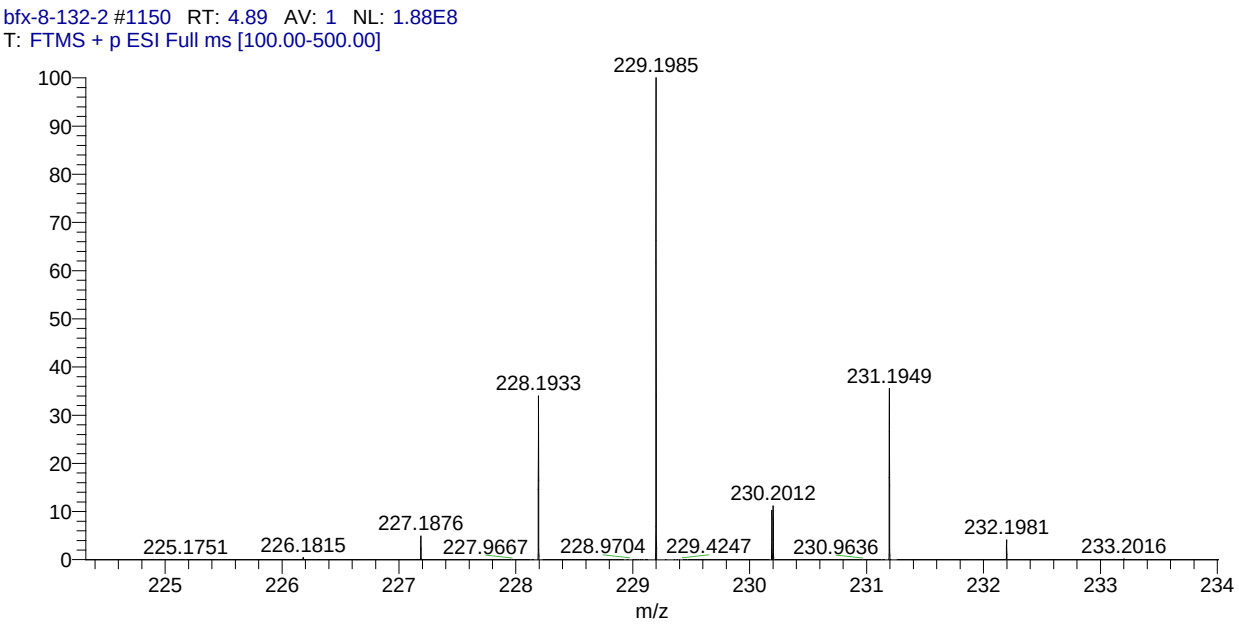
Bromhexine-*d*$_{11}$ ([D]3h). The title product was obtained with 36% yield (48.7 mg, 0.35 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54-7.49 (m, 0.63H), 7.18-7.14 (m, 0.96H), 5.30-5.02 (m, 2.00H), 4.22-4.05 (m, 2.04H), 2.77-2.59 (m, 3.01H), 1.69 (t, *J* = 1.2 Hz, 0.02H), 1.59-1.56 (m, 0.13H), 1.43-1.36 (m, 0.13H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.76, 143.60, 143.57, 134.26, 134.14, 134.06, 133.94, 132.28, 132.26, 124.02, 123.82, 123.55, 123.36, 110.53, 110.38, 108.52, 108.48, 108.32, 58.61, 58.41, 41.42, 41.03.

Deuterium incorporation: 10.7 D/molecule (^{1}H-NMR).

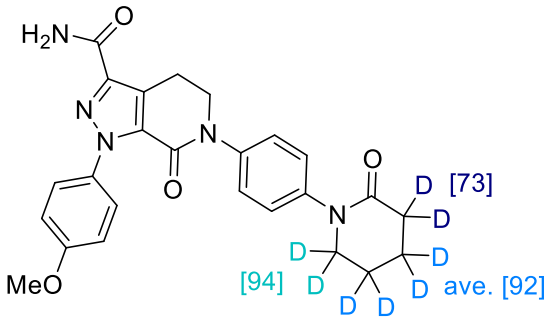


5-Chloro-N-(cyclohexyl-*d*$_{11}$)pentanamide (4h). The title product was obtained with 79% yield (108.1 mg, 0.4 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.52 (s, 0.68H), 5.64 (s, 0.32H), 3.55-3.51 (m, 2.00H), 3.38-3.27 (m, 0.03H), 2.56-2.17 (m, 2.01H), 1.90-1.63 (m, 4.13H), 1.32-1.27 (m, 0.06H), 1.11-1.05 (m, 0.04H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.50, 172.30, 47.81 (m, labeled), 44.73, 44.57, 36.02, 33.34, 32.13 (m, labeled), 32.03, 31.88, 24.09 (m, labeled), 23.25, 22.18.

Deuterium incorporation: 10.7 D/molecule (^{1}H-NMR), 10.7 D/molecule [HRMS (ESI)].

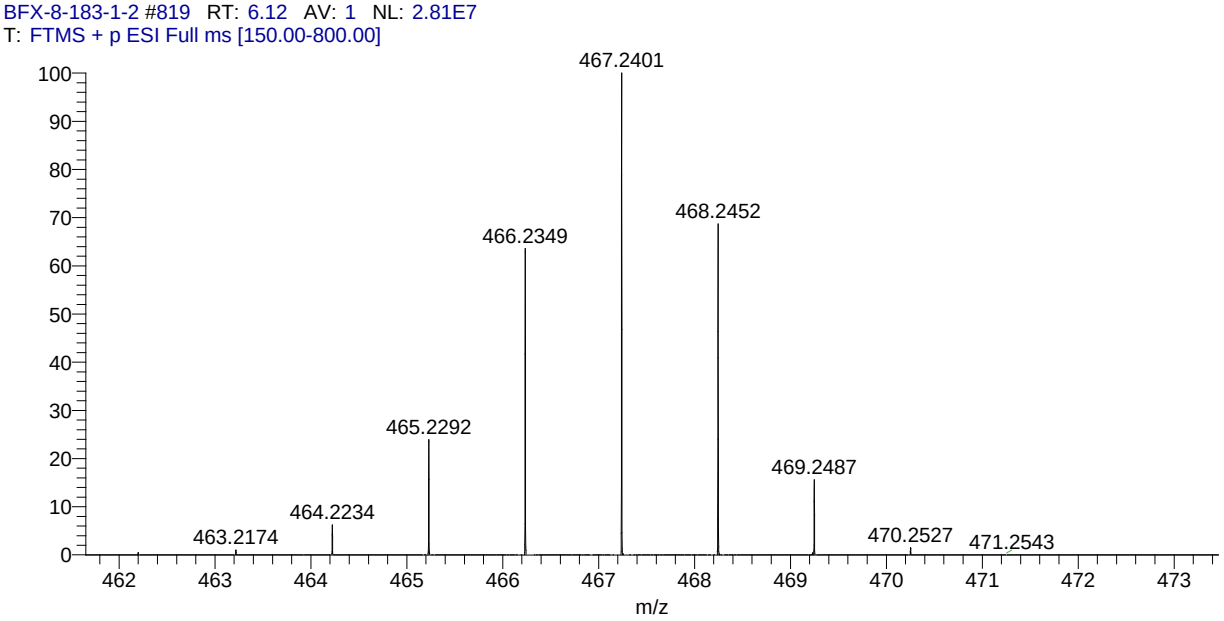


227.1876 ($C_{11}H_{11}D_9ClNO + H^+$, 4%), 228.1933 ($C_{11}H_{10}D_{10}ClNO + H^+$, 23%), 229.1985 ($C_{11}H_9D_{11}ClNO + H^+$, 73%).

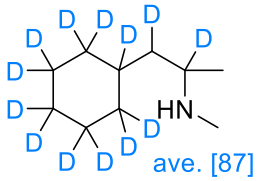


Apixaban-*d*$_7$ ([D]5h). The title product was obtained with 59% yield (82.8 mg, 0.3 mmol scale) as white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.78 (m, 0.98H), 7.53-7.48 (m, 3.60H), 7.42 (d, J = 8.8 Hz, 0.61H), 7.34 (d, J = 8.8 Hz, 1.40H), 7.27 (d, J = 8.8 Hz, 1.42H), 7.02-6.98 (m, 2.00H), 4.11-4.03 (m, 2.00H), 3.79 (s, 3.00H), 3.55 (s, 0.13H), 3.24-3.18 (m, 2.00H), 2.35 (d, J = 8.0 Hz, 0.54H), 1.82-1.75 (m, 0.31H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.97, 163.23, 161.25, 159.14, 156.72, 156.67, 141.78, 141.53, 141.50, 141.36, 139.81, 138.26, 133.00, 132.90, 132.57, 132.55, 126.94, 126.88, 126.85, 126.34, 126.29, 126.03, 125.40, 125.27, 113.43, 113.41, 55.51, 50.96, 50.93, 32.04 (m, labeled), 28.95 (m, labeled), 21.85 (m, labeled), 21.09.

Deuterium incorporation: 7.0 D/molecule (^{1}H-NMR), 6.8 D/molecule [HRMS (ESI)].

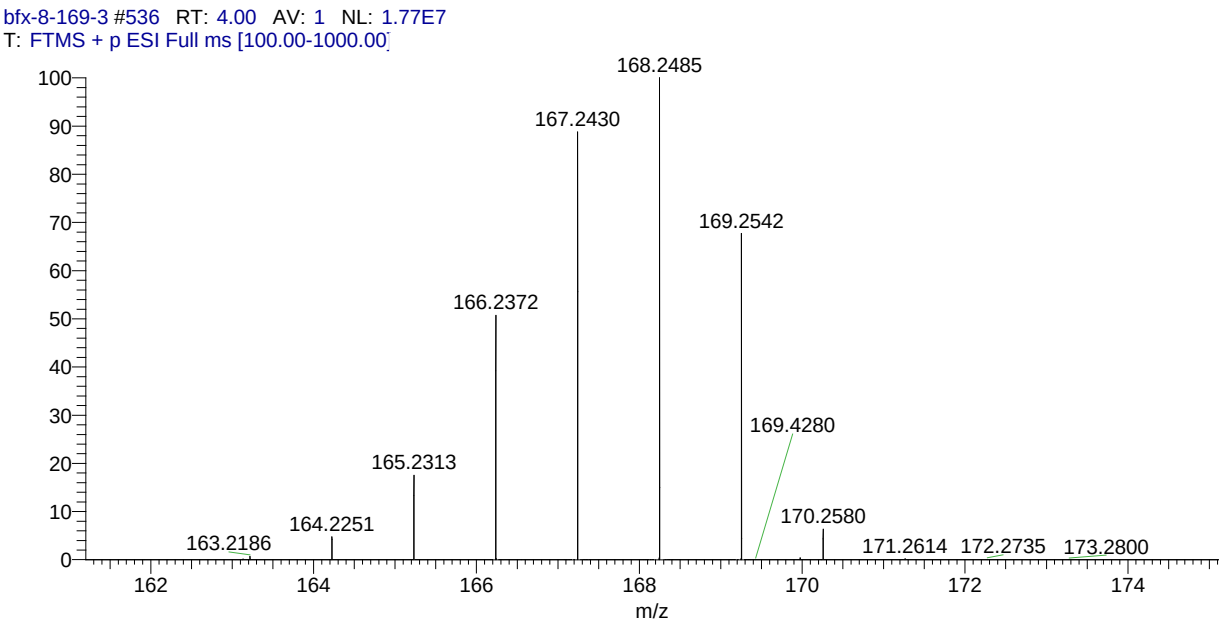


464.2234 ($C_{25}H_{21}D_4N_5O_4$ + H^+, 2%), 465.2292 ($C_{25}H_{20}D_5N_5O_4$ + H^+, 9%), 466.2349 ($C_{25}H_{19}D_6N_5O_4$ + H^+, 25%), 467.2401 ($C_{25}H_{18}D_7N_5O_4$ + H^+, 37%), 468.2452 ($C_{25}H_{17}D_8N_5O_4$ + H^+, 27%).

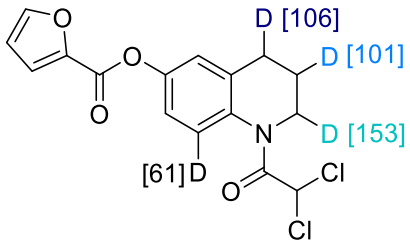


Propylhexedrine-*d*$_{11}$ ([D]6h). The title product was obtained with 43% yield (28.8 mg, 0.4 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.13 (q, *J* = 8.0 Hz, 3.00H), 2.77-2.64 (m, 0.20H), 2.33 (t, *J* = 7.6 Hz, 0.08H), 2.23 (t, *J* = 7.6 Hz, 0.17H), 2.01 (q, *J* = 6.4 Hz, 0.38H), 1.64-1.39 (m, 4.84H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 46.06, 29.90 (m, labeled), 29.53 (m, labeled), 8.82.

Deuterium incorporation: 11.3 D/molecule (^{1}H-NMR), 11.4 D/molecule [HRMS (ESI)].

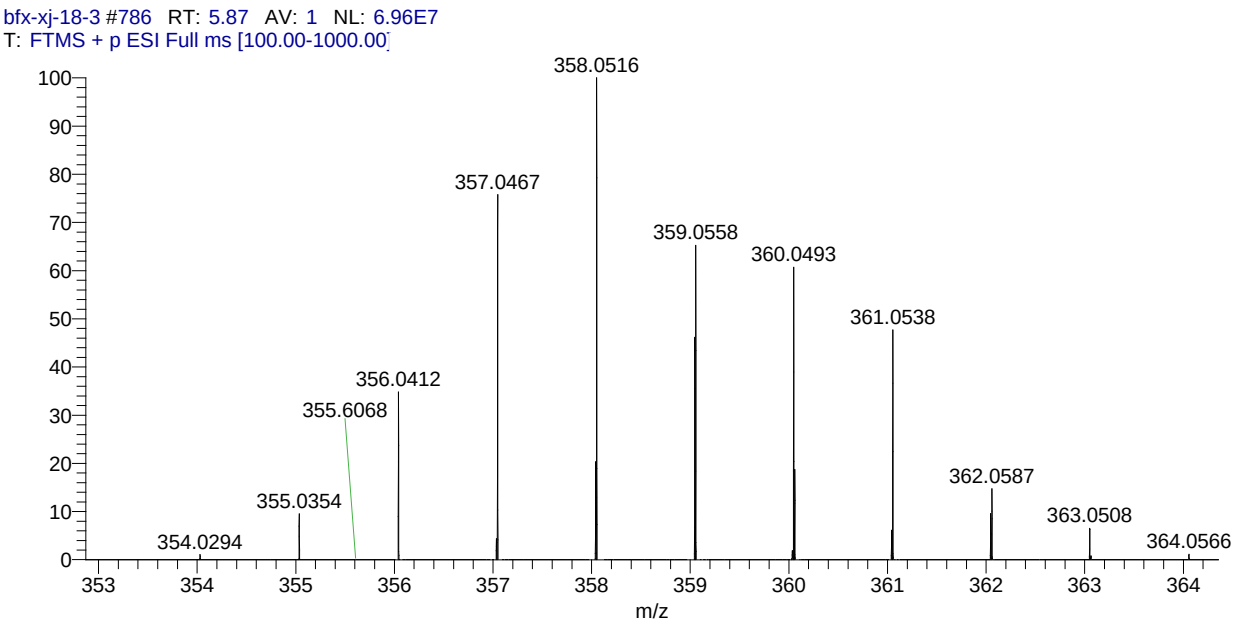


164.2251 ($C_{10}H_{13}D_8N + H^+$, 1%), 165.2313 ($C_{10}H_{12}D_9N + H^+$, 5%), 166.2372 ($C_{10}H_{11}D_{10}N + H^+$, 15%), 167.2430 ($C_{10}H_{10}D_{11}N + H^+$, 28%), 168.2485 ($C_{10}H_9D_{12}N + H^+$, 30%), 169.2542 ($C_{10}H_8D_{13}N + H^+$, 20%).

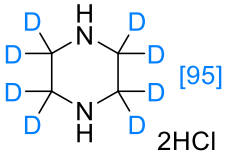


Quinfamide-*d*$_4$ ([D]7h). The title product was obtained with 84% yield (371.6 mg, 1.24 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1.00H), 7.40 (d, *J* = 3.6 Hz, 1.02H), 7.25 (d, *J* = 8.0 Hz, 0.39H), 7.14-7.03 (m, 2.00H), 6.62 (s, 1.00H), 6.48 (s, 0.99H), 3.85 (s, 0.47H), 2.74 (s, 0.94H), 2.00 (s, 0.99H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.07, 156.80, 148.55, 147.61, 143.53, 136.31, 135.35, 135.27, 123.90, 122.32, 120.33, 120.06, 112.44, 63.96, 43.75 (m, labeled), 26.09 (m, labeled), 22.79 (m, labeled).

Deuterium incorporation: 4.2 D/molecule (^{1}H-NMR), 3.8 D/molecule [HRMS (ESI)].

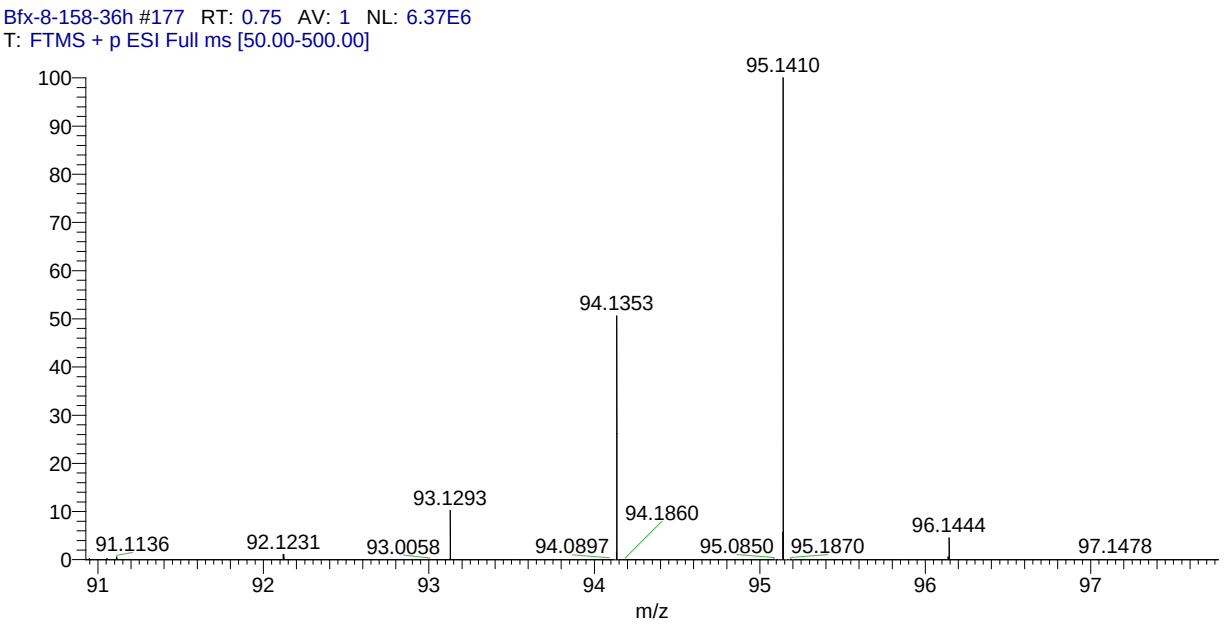


355.0354 ($C_{16}H_{12}D_1Cl_2NO_4$ + H^+, 3%), 356.0412 ($C_{16}H_{11}D_2Cl_2NO_4$ + H^+, 11%), 357.0467 ($C_{16}H_{10}D_3Cl_2NO_4$ + H^+, 24%), 358.0516 ($C_{16}H_9D_4Cl_2NO_4$ + H^+, 33%), 359.0558 ($C_{16}H_8D_5Cl_2NO_4$ + H^+, 23%), 360.0601 ($C_{16}H_7D_6Cl_2NO_4$ + H^+, 6%).

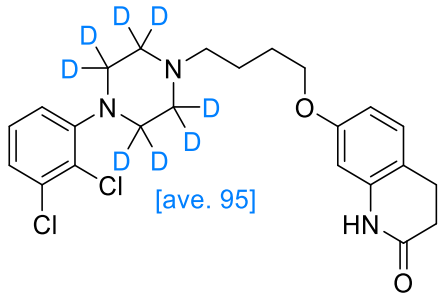


Piperazine-2,2,3,3,5,5,6,6-*d*$_8$ hydrochloride (10d'). The title product was obtained with 65% yield (10.9 g, 100 mmol scale) as white solid. ^{1}H NMR (400 MHz, D_2O) δ 3.49 (s); ^{13}C NMR (101 MHz, D_2O) δ 39.60 (m, labeled).

Deuterium incorporation: 7.6 D/molecule [HRMS (ESI)].

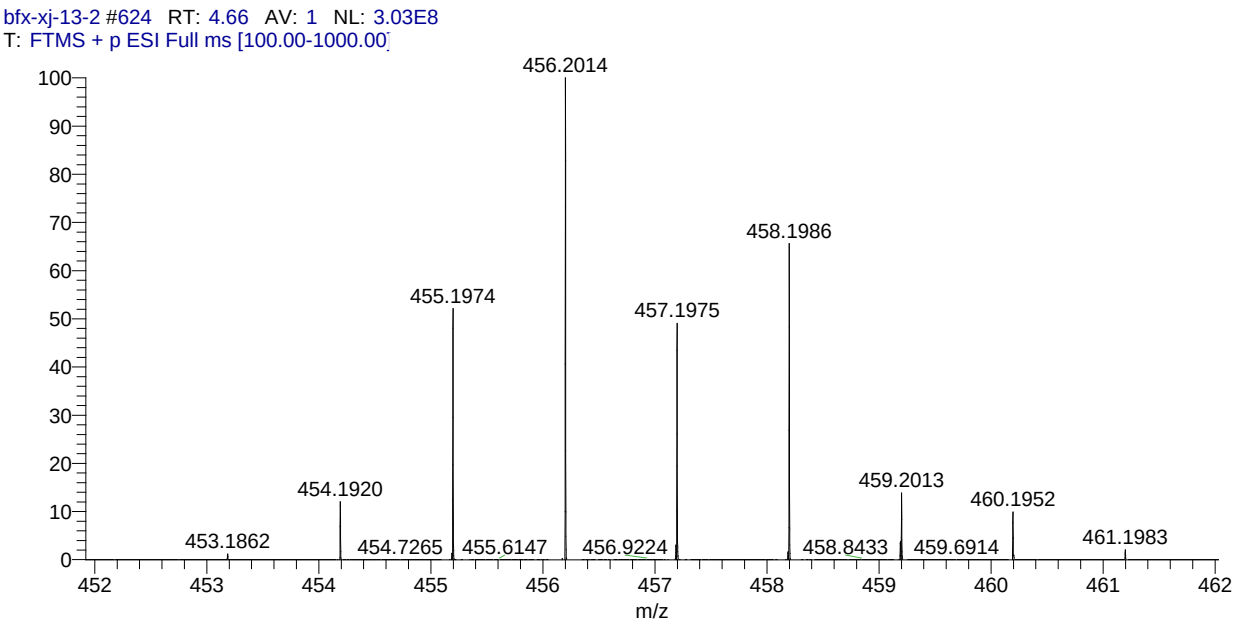


93.1293 ($C_4H_4D_6N_2 + H^+$, 6%), 94.1353 ($C_4H_3D_7N_2 + H^+$, 30%), 95.1410 ($C_4H_2D_8N_2 + H^+$, 64%).

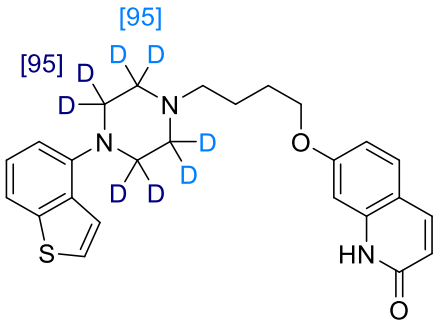


Aripiprazole-*d*$_8$ ([D]8h). The title product was obtained with 99% yield (91.3 mg, 0.2 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1.00H), 7.15 (s, 1.98H), 7.04 (d, *J* = 8.4 Hz, 0.99H), 6.96 (s, 0.98H), 6.52 (d, *J* = 8.4 Hz, 1.00H), 6.39 (s, 1.00H), 3.96 (s, 1.97H), 3.04 (s, 0.40H), 2.89 (t, *J* = 7.6 Hz, 2.01H), 2.62 (t, *J* = 7.6 Hz, 2.01H), 2.49 (t, *J* = 7.6 Hz, 2.01H), 1.85-1.67 (m, 4.00H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.52, 158.78, 151.41, 138.34, 134.13, 128.75, 127.63, 127.52, 124.66, 118.69, 115.79, 108.83, 102.38, 67.97, 58.29, 52.61 (m, labeled), 50.57 (m, labeled), 31.23, 29.87, 27.41, 24.70, 23.56.

Deuterium incorporation: 7.6 D/molecule (^{1}H-NMR), 7.5 D/molecule [HRMS (ESI)].

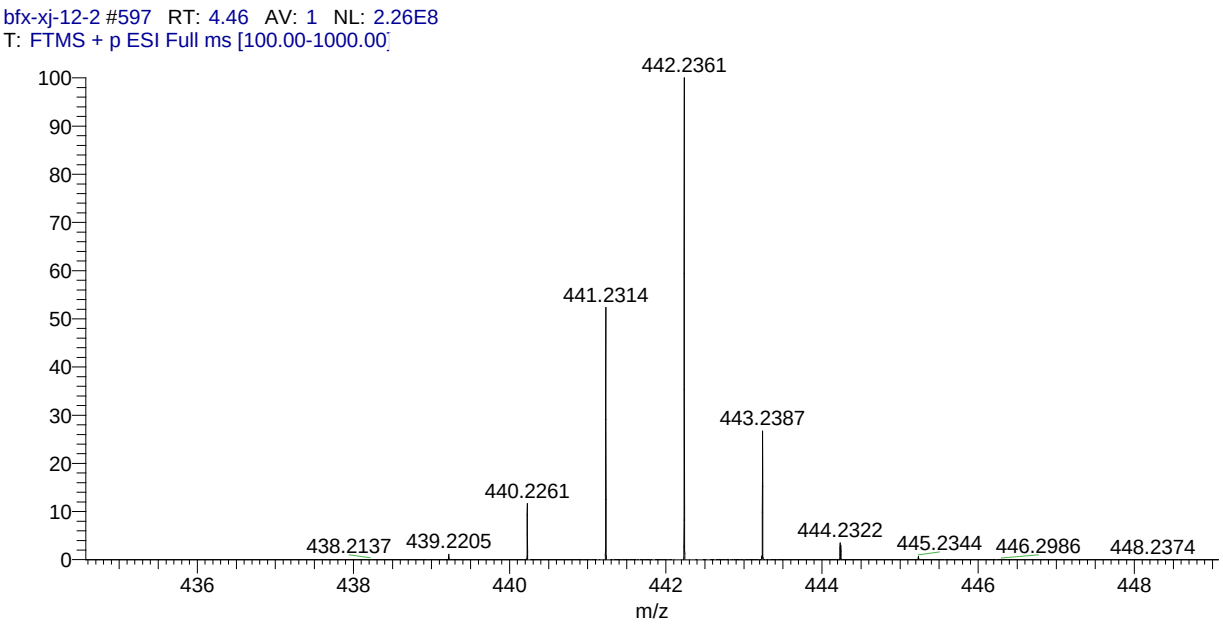


453.1862 ($C_{23}H_{22}D_5Cl_2N_3O_2$ + H^+, 1%), 454.1920 ($C_{23}H_{21}D_6Cl_2N_3O_2$ + H^+, 7%), 455.1974 ($C_{23}H_{20}D_7Cl_2N_3O_2$ + H^+, 31%), 456.2014 ($C_{23}H_{19}D_8Cl_2N_3O_2$ + H^+, 61%).

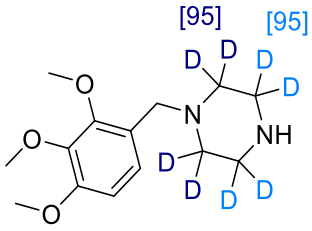


Brexpiprazole-*d*$_8$ ([D]9h). The title product was obtained with 71% yield (47.2 mg, 0.15 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.84 (s, 1.00H), 7.74 (d, *J* = 9.2 Hz, 1.00H), 7.55 (d, *J* = 8.0 Hz, 0.99H), 7.45-7.38 (m, 3.00H), 7.27 (t, *J* = 7.8 Hz, 1.18H), 6.90-6.88 (m, 1.99H), 6.82 (dd, *J* = 2.4, 8.8 Hz, 1.00H), 6.57 (d, *J* = 9.2 Hz, 1.00H), 4.11 (t, *J* = 6.2 Hz, 2.00H), 3.17 (s, 0.21H), 2.67 (s, 0.21H), 2.54 (t, *J* = 7.6 Hz, 1.96H), 1.92-1.73 (m, 4.00H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.43, 161.55, 148.61, 141.23, 141.10, 140.59, 134.13, 129.16, 125.19, 125.13, 122.05, 117.92, 117.09, 114.33, 112.94, 112.25, 99.08, 68.25, 58.38, 52.69 (m, labeled), 51.36 (m, labeled), 27.35, 23.59.

Deuterium incorporation: 7.6 D/molecule (^{1}H-NMR), 7.5 D/molecule [HRMS (ESI)].

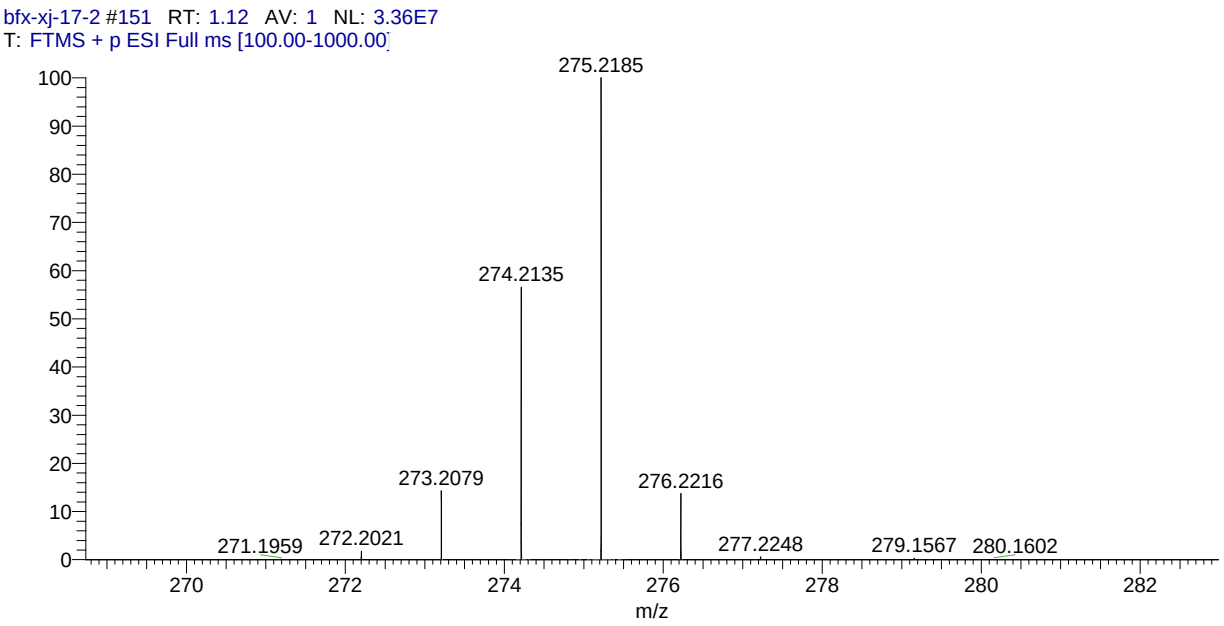


439.2205 ($C_{25}H_{22}D_5N_3O_2S$ + H^+, 1%), 440.2261 ($C_{25}H_{21}D_6N_3O_2S$ + H^+, 7%), 441.2314 ($C_{25}H_{20}D_7N_3O_2S$ + H^+, 31%), 442.2361 ($C_{25}H_{19}D_8N_3O_2S$ + H^+, 61%).

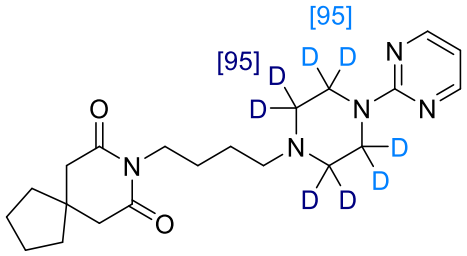


Trimetazidine-*d*$_8$ ([D]10h). The title product was obtained with 16% yield (21.3 mg, 0.5 mmol scale) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (d, *J* = 8.0 Hz, 1.01H), 6.65-6.49 (m, 2.98H), 3.86-3.85 (m, 9.00H), 3.51 (s, 1.99H), 3.11 (s, 0.21H), 2.67 (s, 0.21H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.45, 152.83, 142.45, 125.35, 122.92, 107.11, 61.45, 61.00, 56.48, 56.13, 49.33 (m, labeled), 43.57 (m, labeled).

Deuterium incorporation: 7.6 D/molecule (^{1}H-NMR), 7.5 D/molecule [HRMS (ESI)].

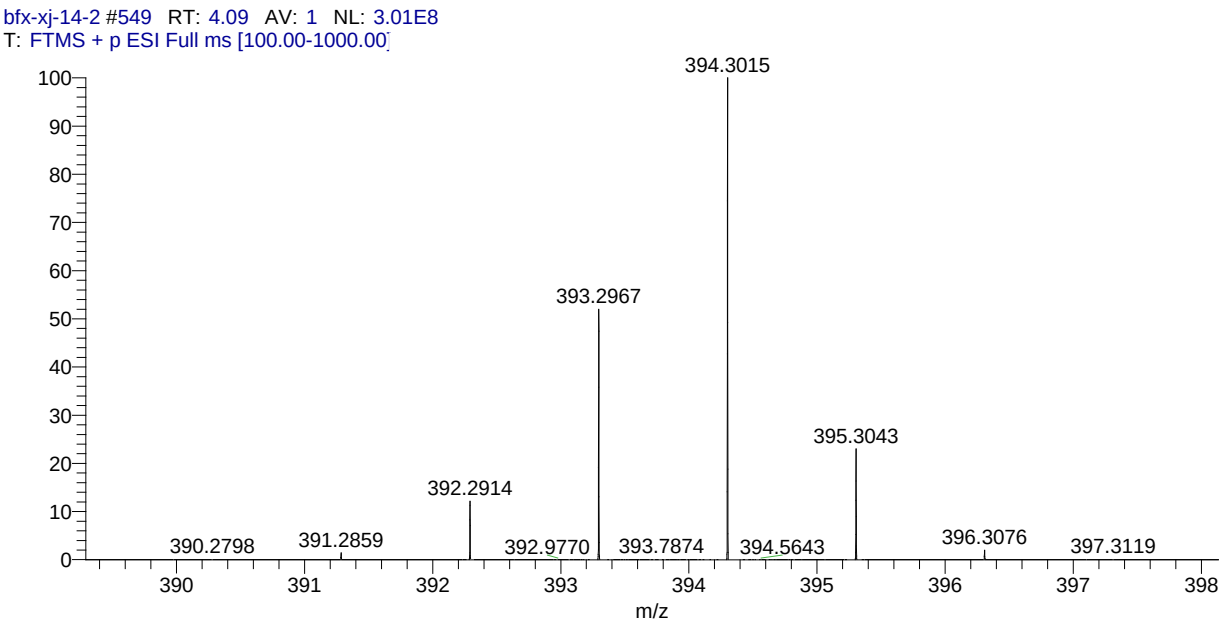


272.2021 ($C_{14}H_{17}D_5N_2O_3$ + H^+, 1%), 273.2079 ($C_{14}H_{16}D_6N_2O_3$ + H^+, 8%), 274.2135 ($C_{14}H_{15}D_7N_2O_3$ + H^+, 33%), 275.2185 ($C_{14}H_{14}D_8N_2O_3$ + H^+, 59%).

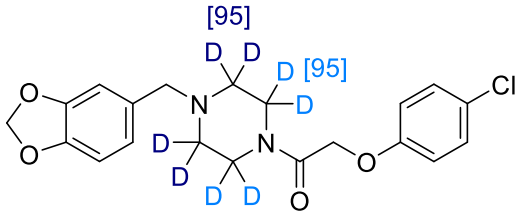


Buspirone-*d*$_8$ ([D]11h). The title product was obtained with 93% yield (109.8 mg, 0.3 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 4.4 Hz, 1.98H), 6.42 (t, *J* = 4.8 Hz, 1.00H), 3.75-3.71 (m, 2.21H), 2.53 (s, 4.01H), 2.39 (d, *J* = 7.6 Hz, 0.21H), 2.33 (t, *J* = 7.0 Hz, 1.98H), 1.67-1.64 (m, 4.01H) 1.49-1.42 (m, 8.00H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.29, 161.68, 157.77, 109.80, 58.35, 52.33 (m, labeled), 44.93, 42.94 (m, labeled), 39.54, 39.42, 37.59, 26.09, 24.31, 24.23.

Deuterium incorporation: 7.6 D/molecule (^{1}H-NMR), 7.6 D/molecule [HRMS (ESI)].

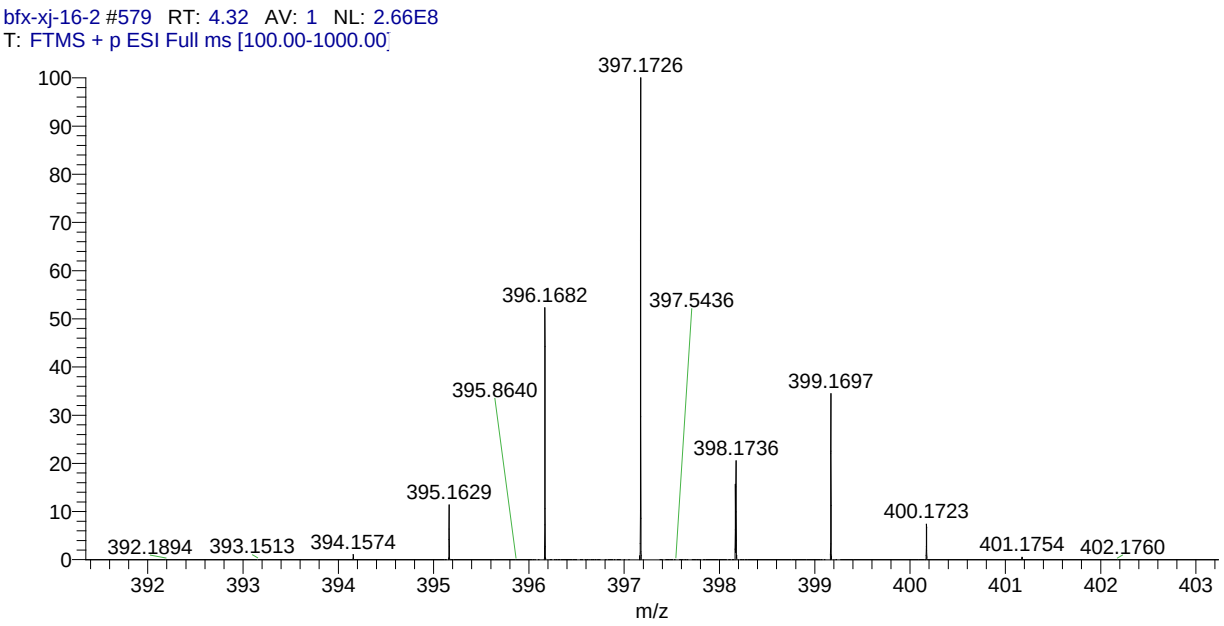


391.2859 ($C_{21}H_{26}D_5N_5O_2$ + H^+, 1%), 392.2914 ($C_{21}H_{25}D_6N_5O_2$ + H^+, 5%), 393.2967 ($C_{21}H_{24}D_7N_5O_2$ + H^+, 32%), 394.3015 ($C_{21}H_{23}D_8N_5O_2$ + H^+, 62%).

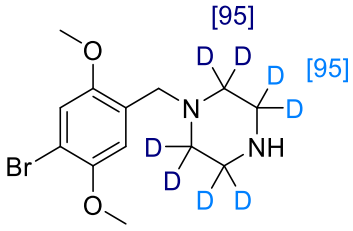


Fipexide-*d*$_8$ ([D]12h). The title product was obtained with 84% yield (119.0 mg, 0.3 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.8 Hz, 1.98H), 6.88-6.83 (m, 3.00H), 6.75-6.70 (m, 2.00H), 5.94 (s, 2.00H), 4.65 (s, 2.01H), 3.53 (d, *J* = 27.2 Hz, 0.21H), 3.40 (s, 1.97H), 2.34 (d, *J* = 4.8 Hz, 0.21H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.09, 156.56, 147.82, 146.86, 131.51, 129.59, 126.60, 122.28, 116.04, 109.42, 108.04, 101.08, 67.83, 62.53, 51.93 (m, labeled), 44.69 (m, labeled).

Deuterium incorporation: 7.6 D/molecule (^{1}H-NMR), 7.5 D/molecule [HRMS (ESI)].

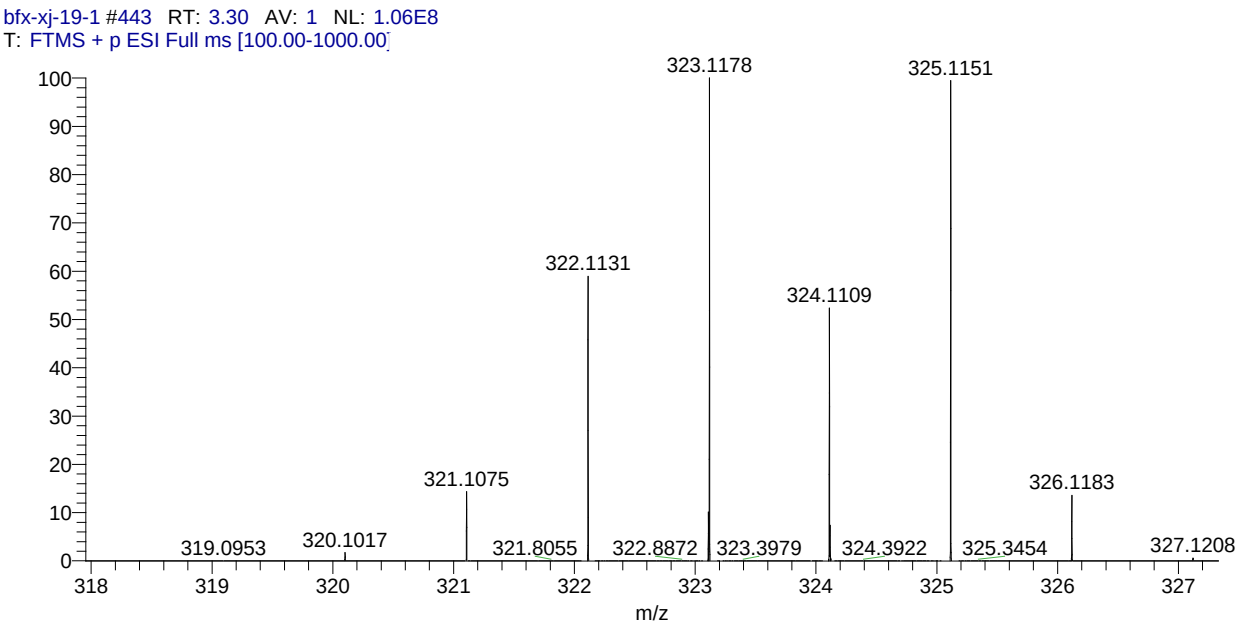


394.1574 ($C_{20}H_{16}D_5ClN_2O_4$ + H^+, 1%), 395.1629 ($C_{20}H_{15}D_6ClN_2O_4$ + H^+, 7%), 396.1682 ($C_{20}H_{14}D_7ClN_2O_4$ + H^+, 32%), 397.1726 ($C_{20}H_{13}D_8ClN_2O_4$ + H^+, 60%).



2C-B-BZP-*d*$_8$ ([D]13h). The title product was obtained with 92% yield (89.2 mg, 0.3 mmol scale) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 2.01H), 7.02 (s, 1.00H), 6.91 (s, 0.99H), 3.82 (s, 3.00H), 3.73 (s, 3.02H), 3.51 (s, 2.00H), 3.12 (s, 0.21H), 2.67 (s, 0.21H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.22, 150.07, 125.46, 116.22, 114.34, 110.35, 56.99, 56.33, 55.40, 49.26 (m, labeled), 43.25 (m, labeled).

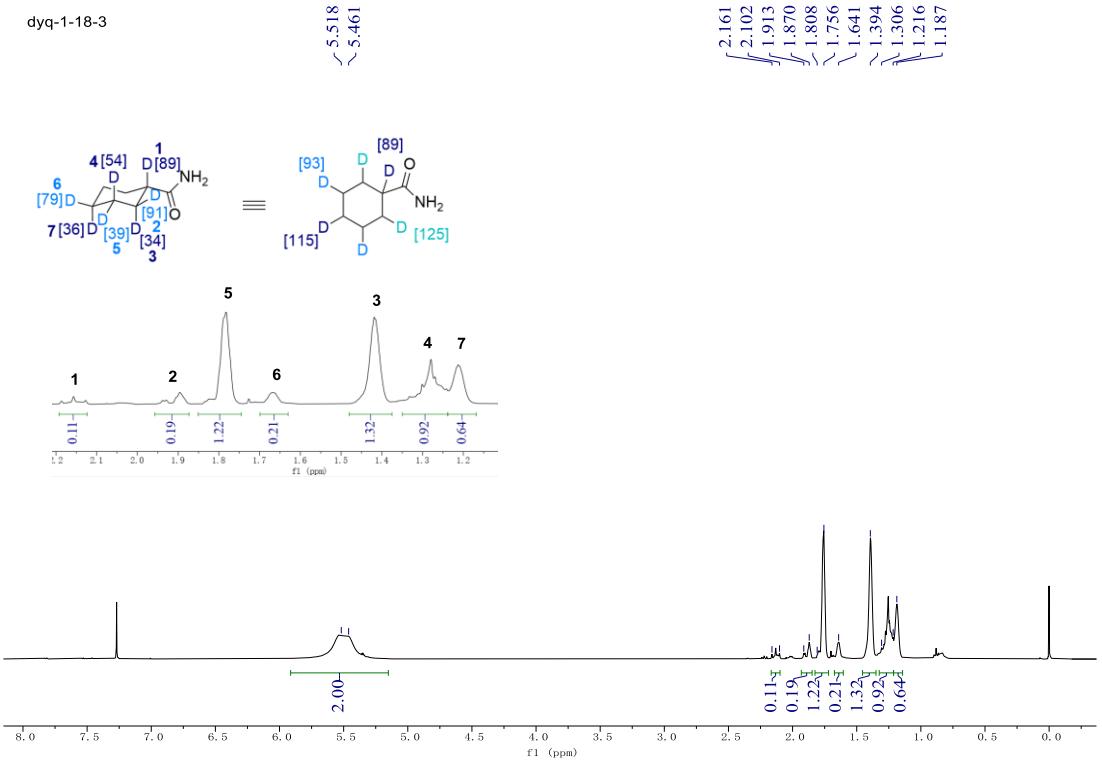
Deuterium incorporation: 7.6 D/molecule (^{1}H-NMR), 7.5 D/molecule [HRMS (ESI)].



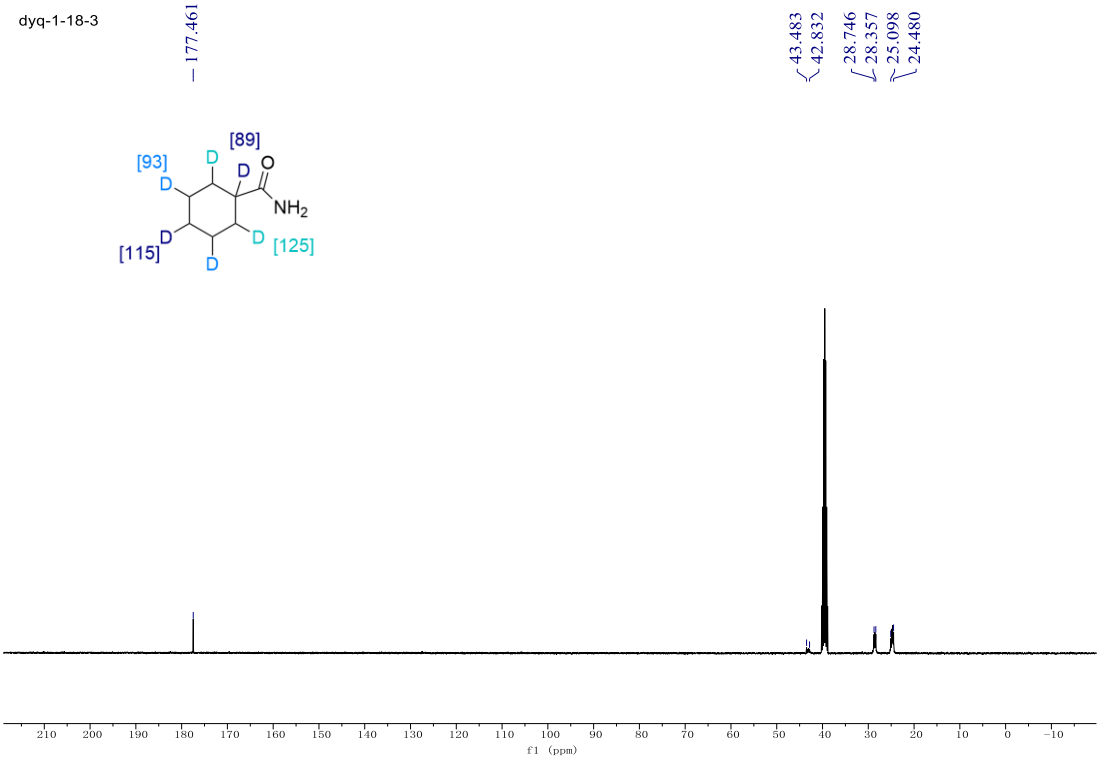
320.1017 ($C_{13}H_{14}D_5BrN_2O_2 + H^+$, 1%), 321.1075 ($C_{13}H_{13}D_6BrN_2O_2 + H^+$, 8%), 322.1131 ($C_{13}H_{12}D_7BrN_2O_2 + H^+$, 33%), 323.1178 ($C_{13}H_{11}D_8BrN_2O_2 + H^+$, 59%).

13. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra for products

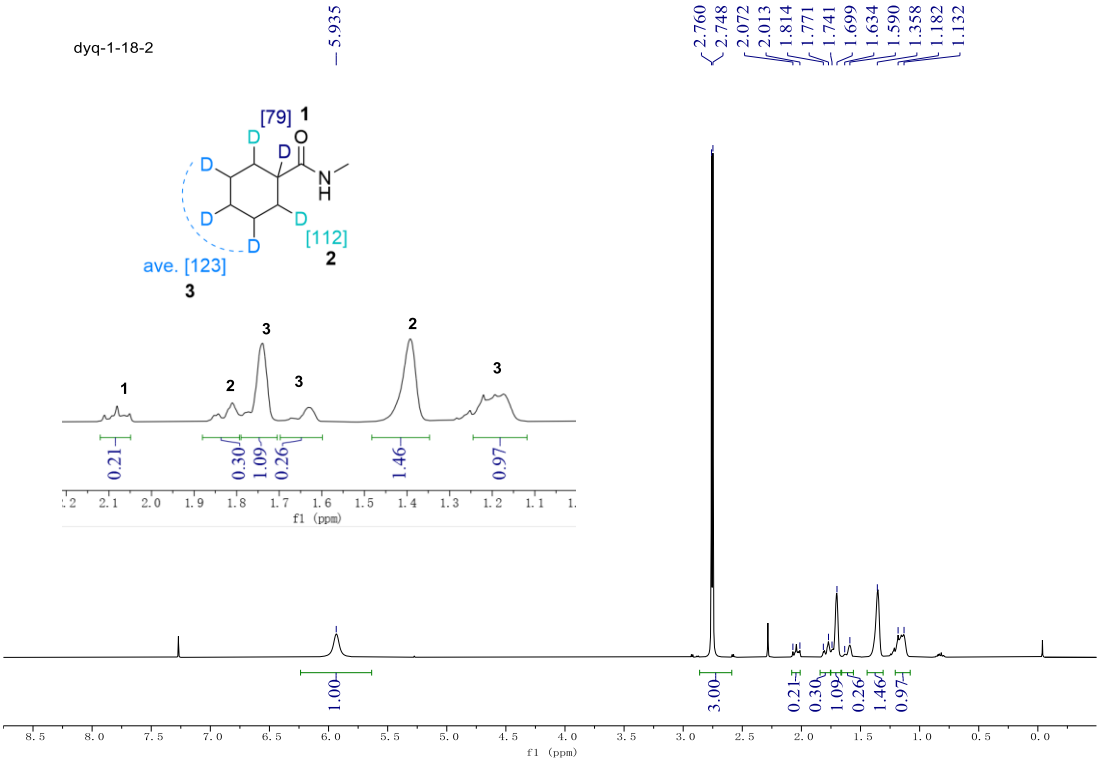
^{1}H NMR for 1b



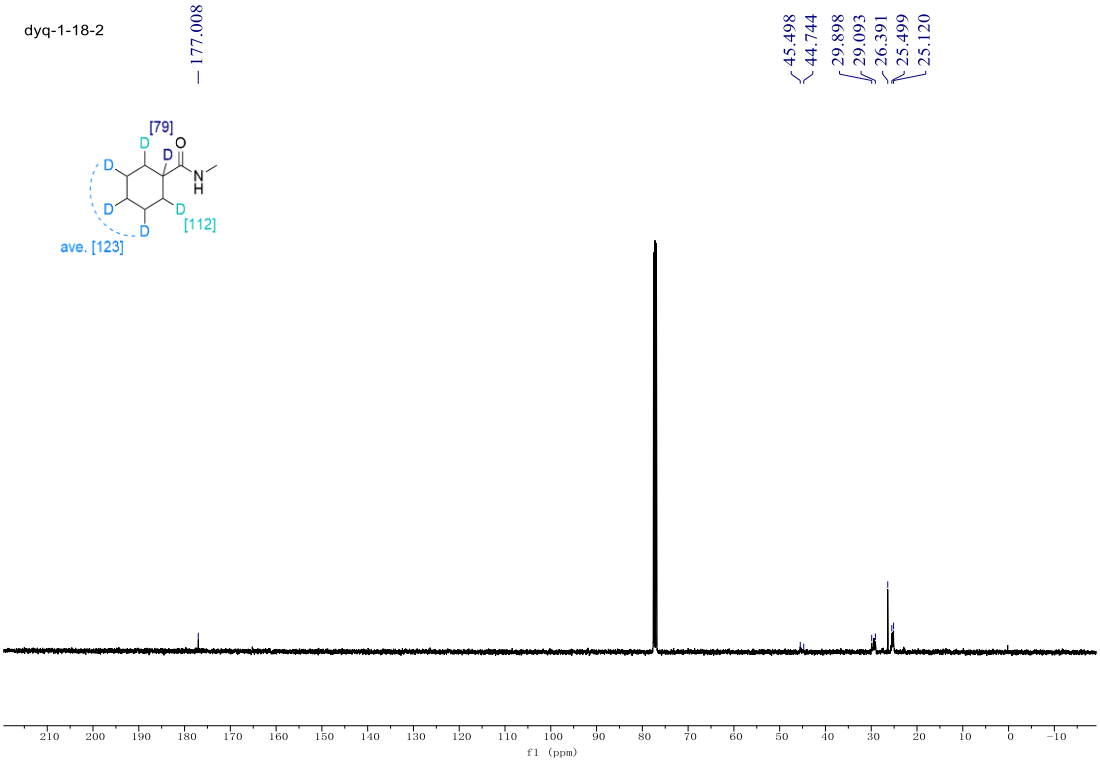
^{13}C NMR for 1b



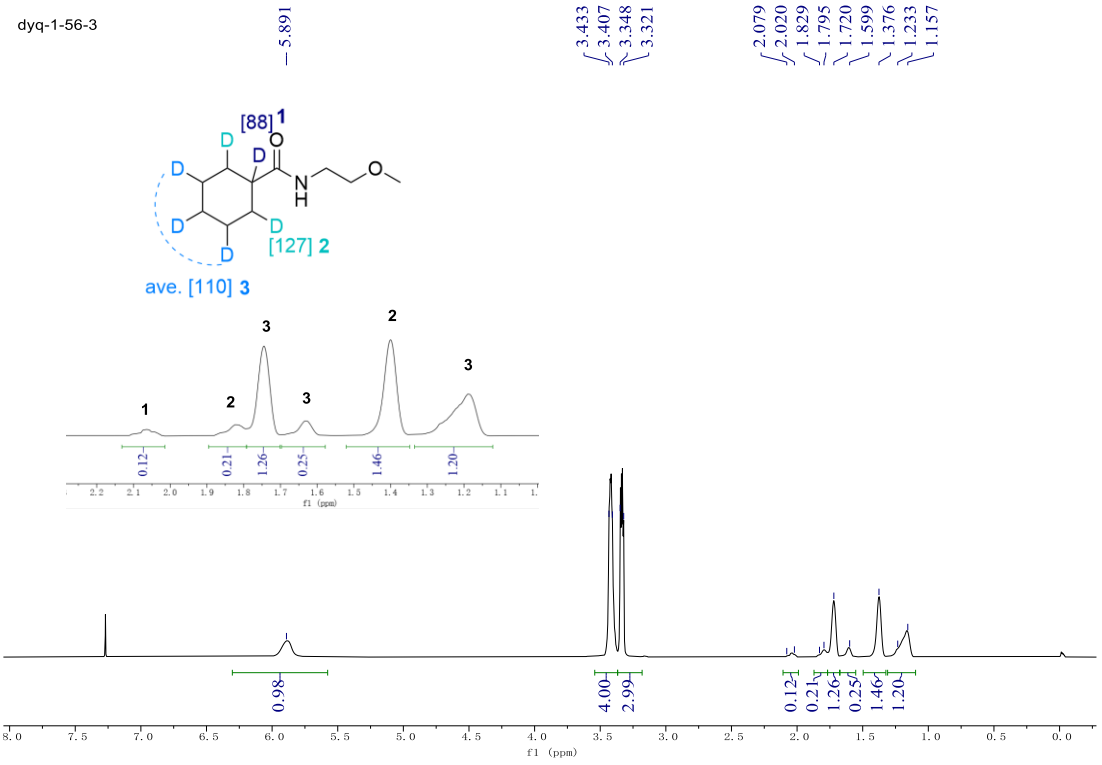
^{1}H NMR for 2b



^{13}C NMR for 2b



^{1}H NMR for 3b


dyq-1-56-3
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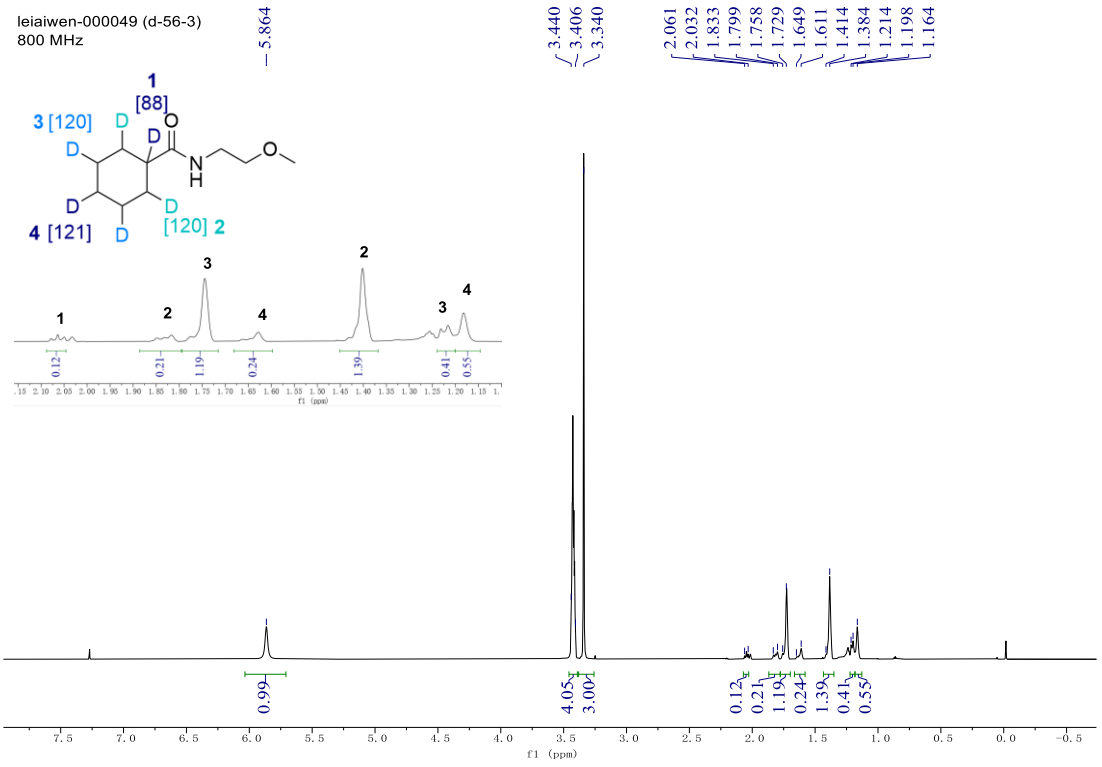
3.433
3.407
3.348
3.321
2.079
2.020
1.829
1.795
1.720
1.599
1.376
1.233
1.157
[88] 1
[127] 2
ave. [110] 3
0.98
4.00
2.99
0.12
0.21
1.26
0.25
1.46
1.20
f1 (ppm)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3.440
3.406
3.340
2.061
2.032
1.833
1.799
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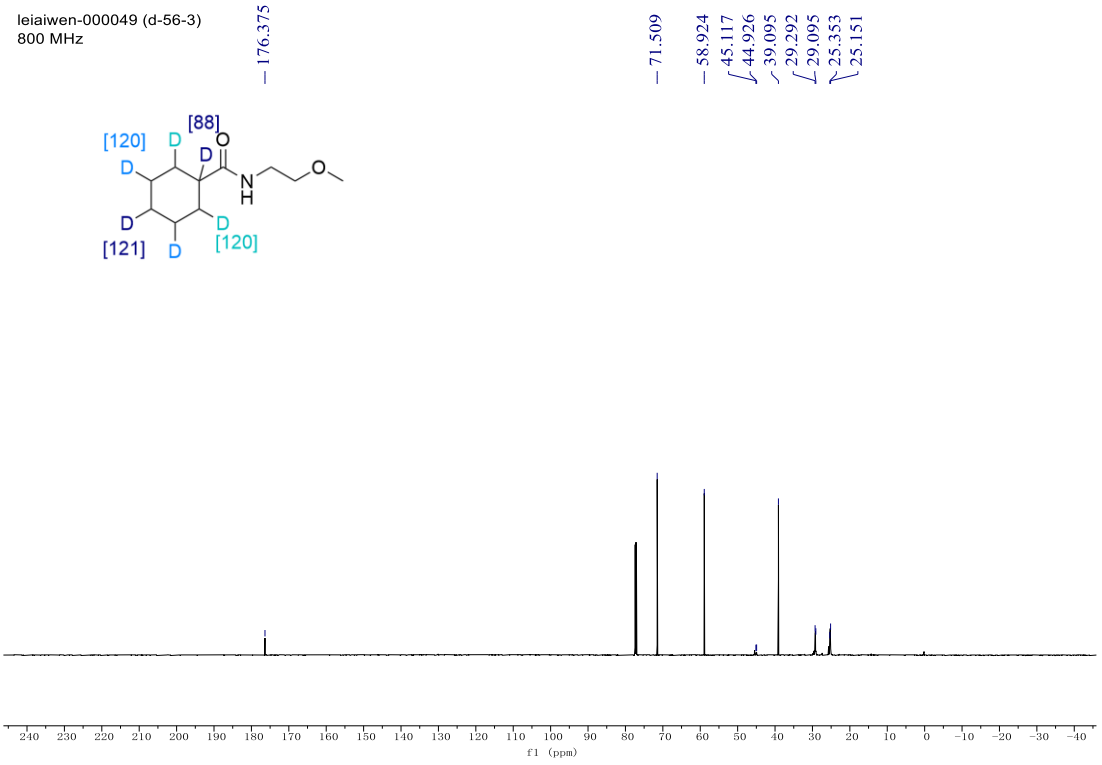
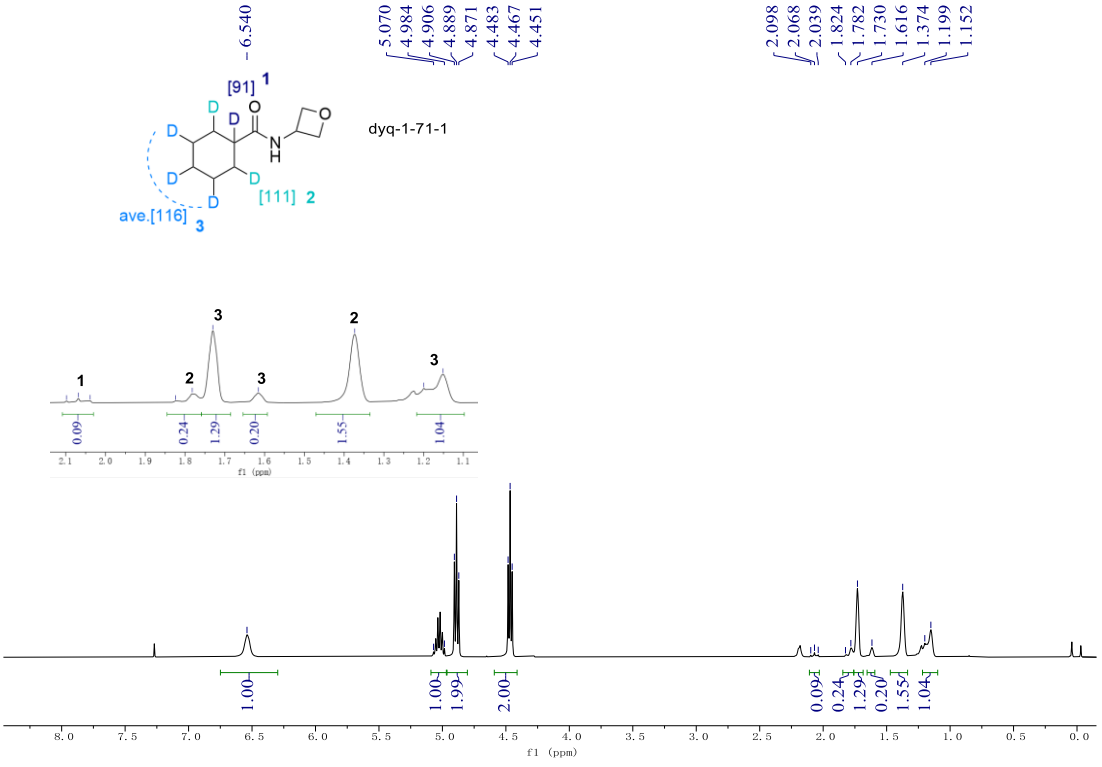
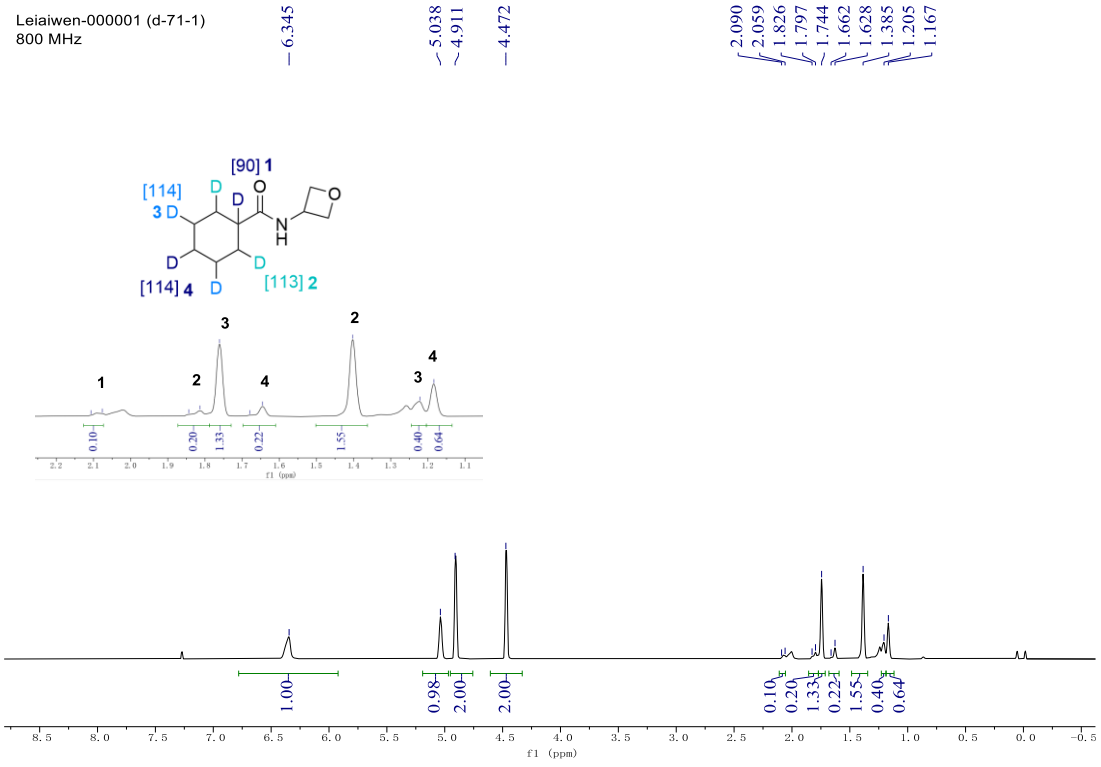
1.649
1.611
1.414
1.384
1.214
1.198
1.164
1
[88]
3 [120]
4 [121]
[120] 2
0.99
4.05
3.00
0.12
0.21
1.19
0.24
1.39
0.41
0.55
f1 (ppm)

^{13}C NMR for 3b

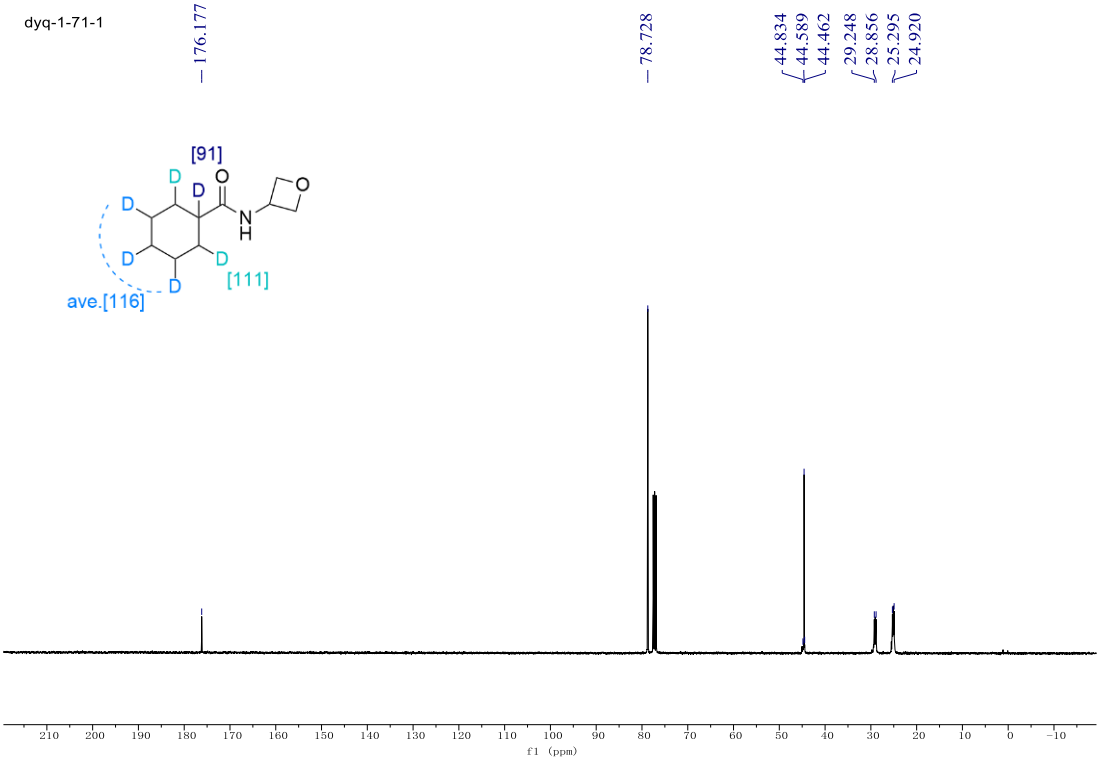


^{1}H NMR for 4b

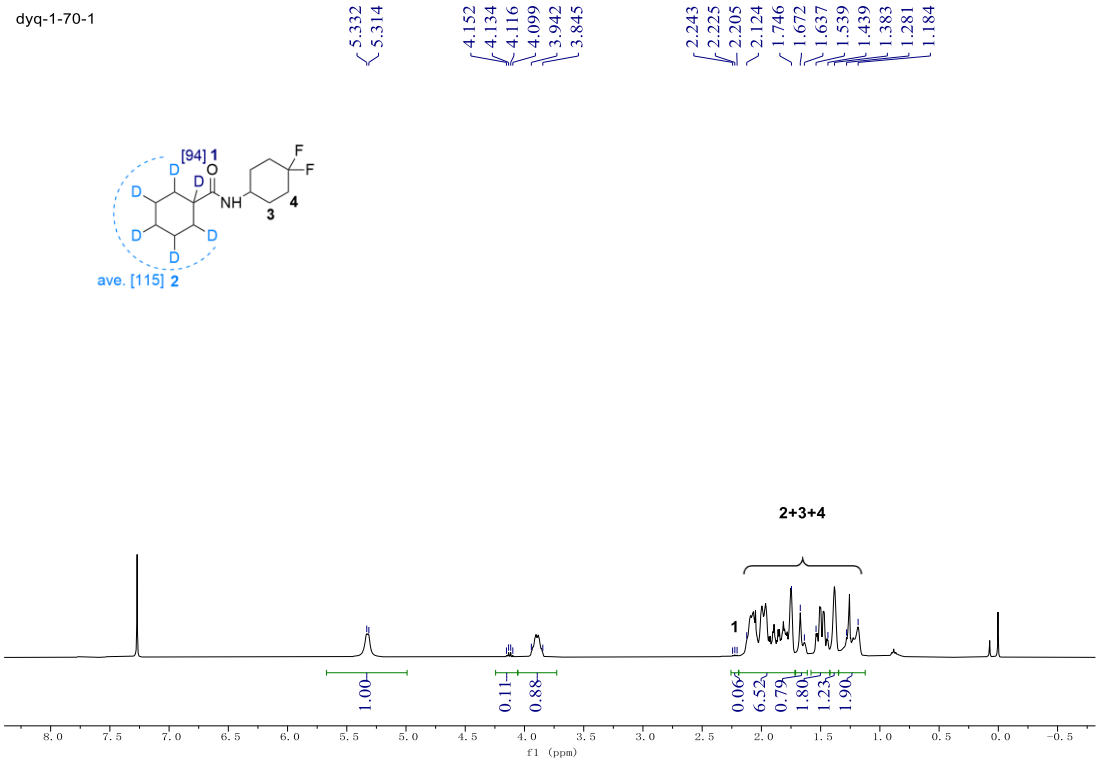




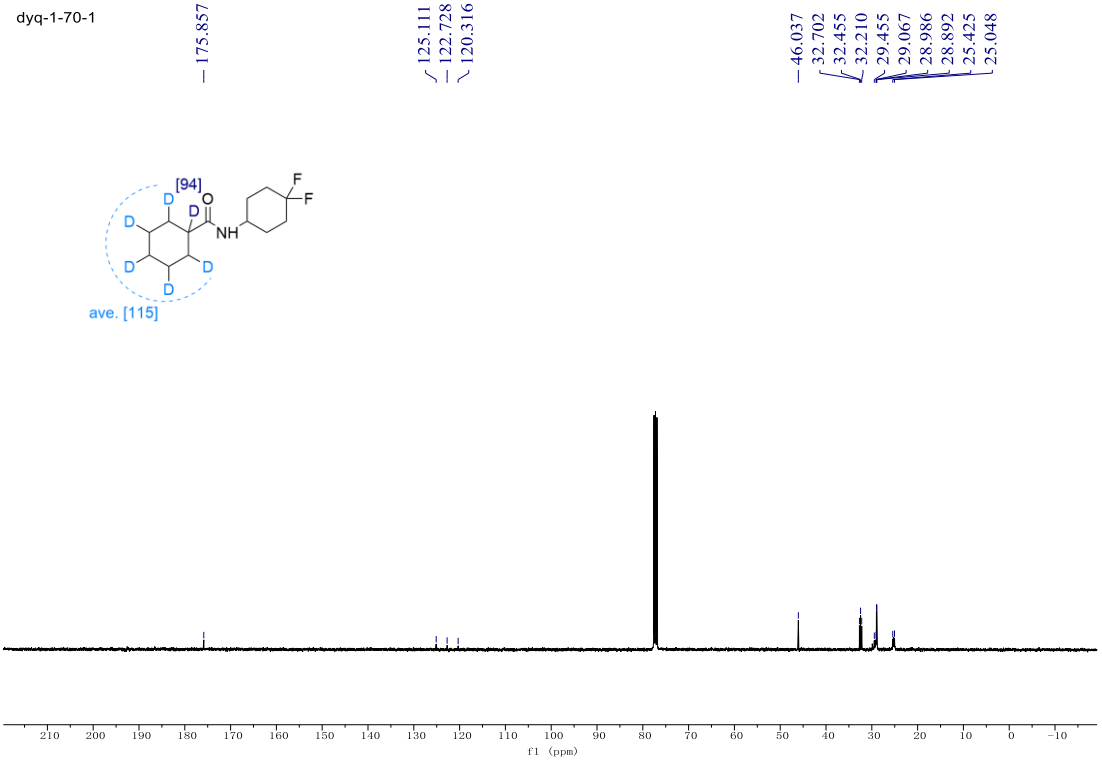
^{13}C NMR for 4b



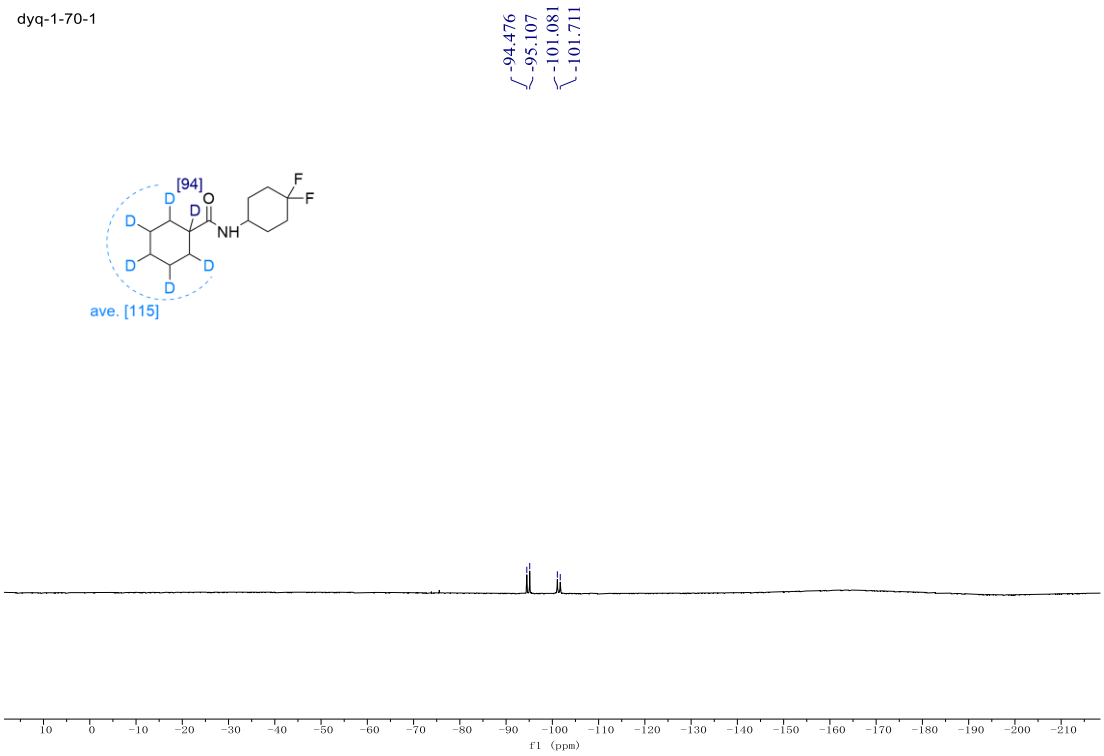
^{1}H NMR for 5b



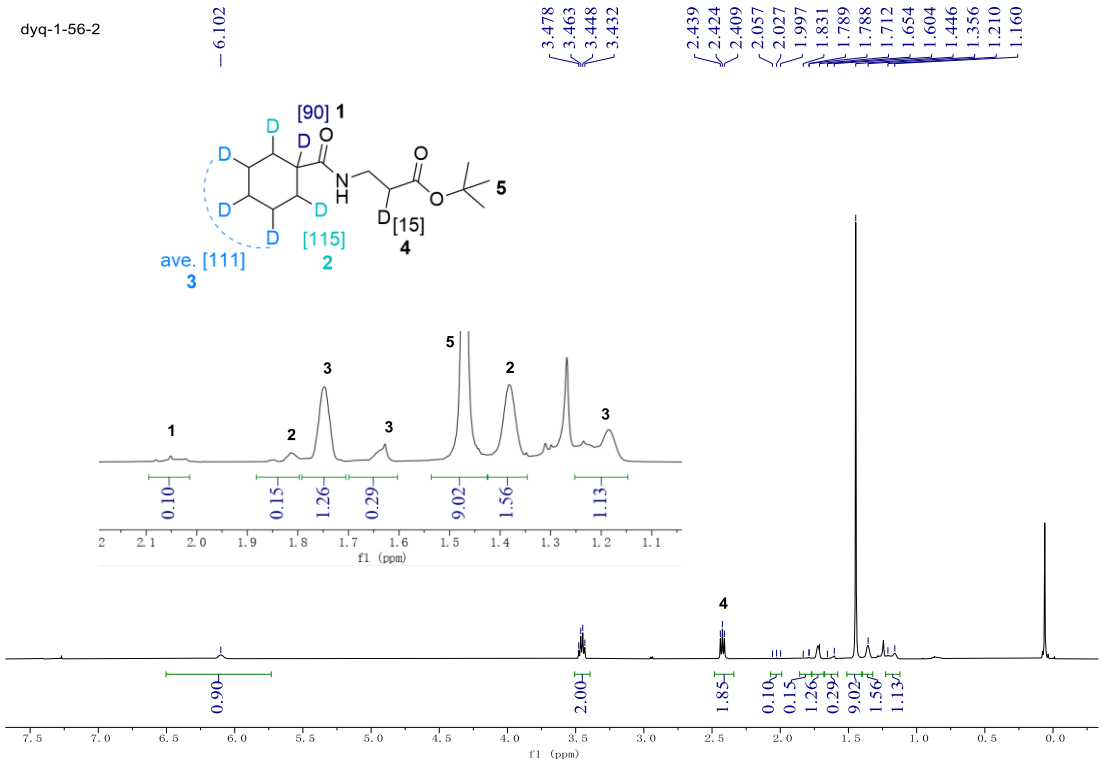
^{13}C NMR for 5b



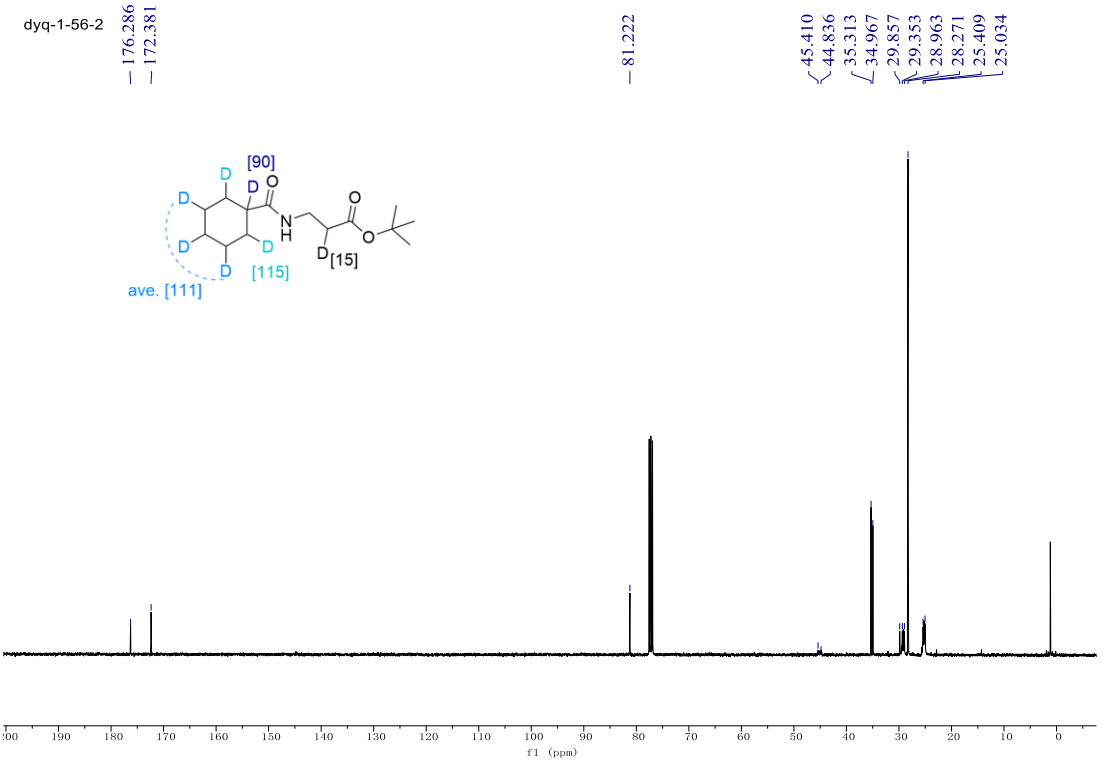
^{19}F NMR for 5b



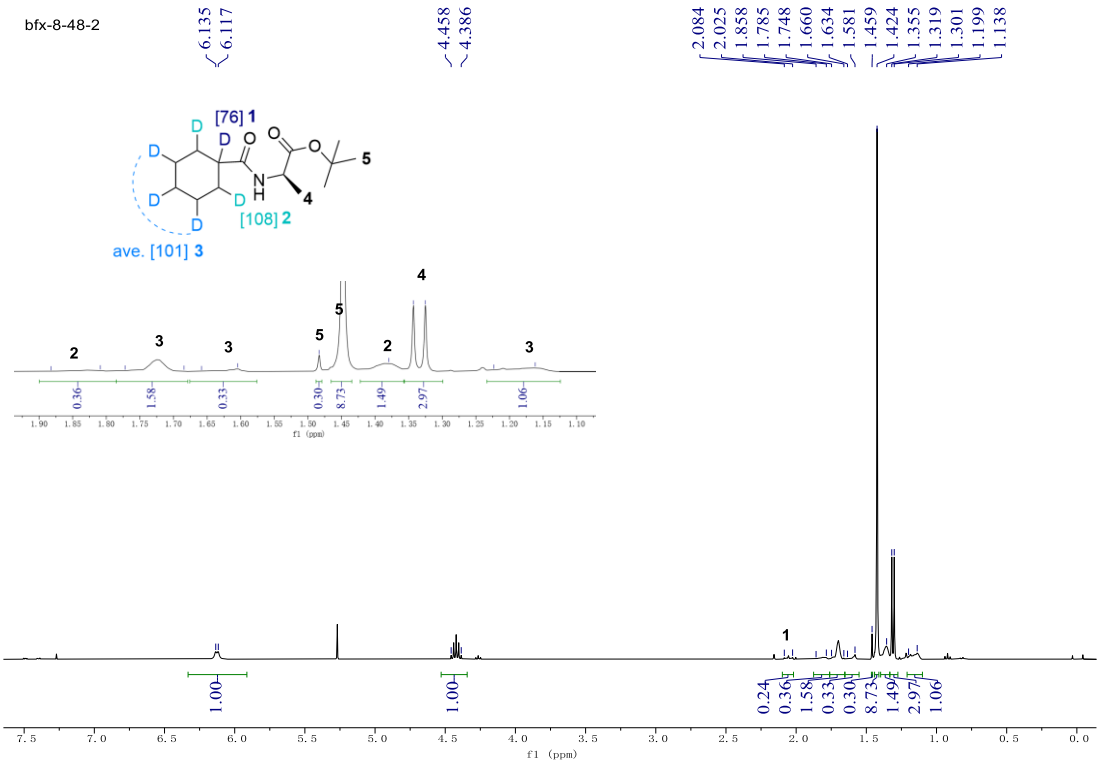
^{1}H NMR for 6b

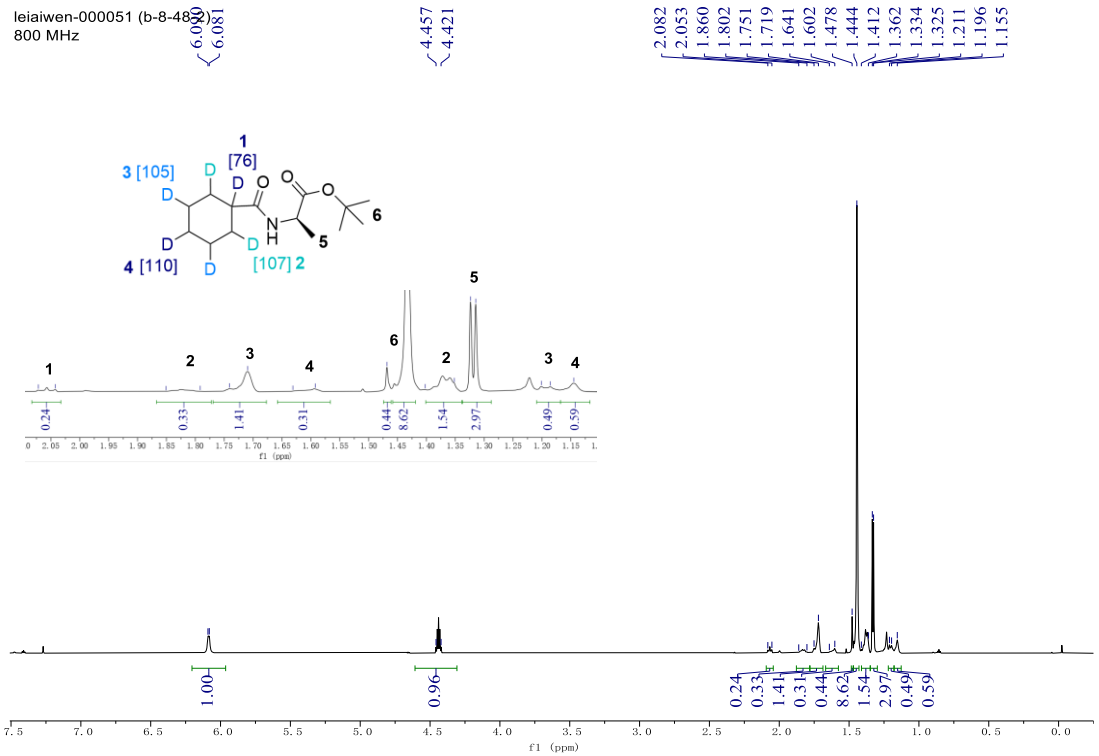


^{13}C NMR for 6b

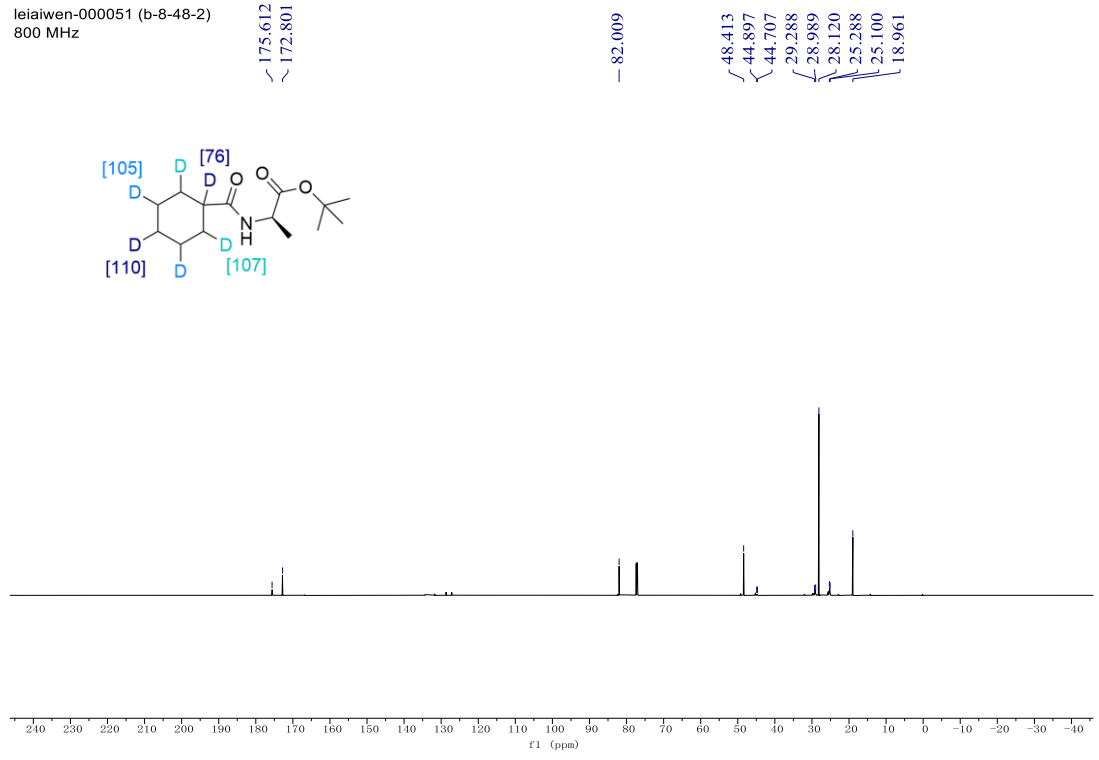


^{1}H NMR for 7b

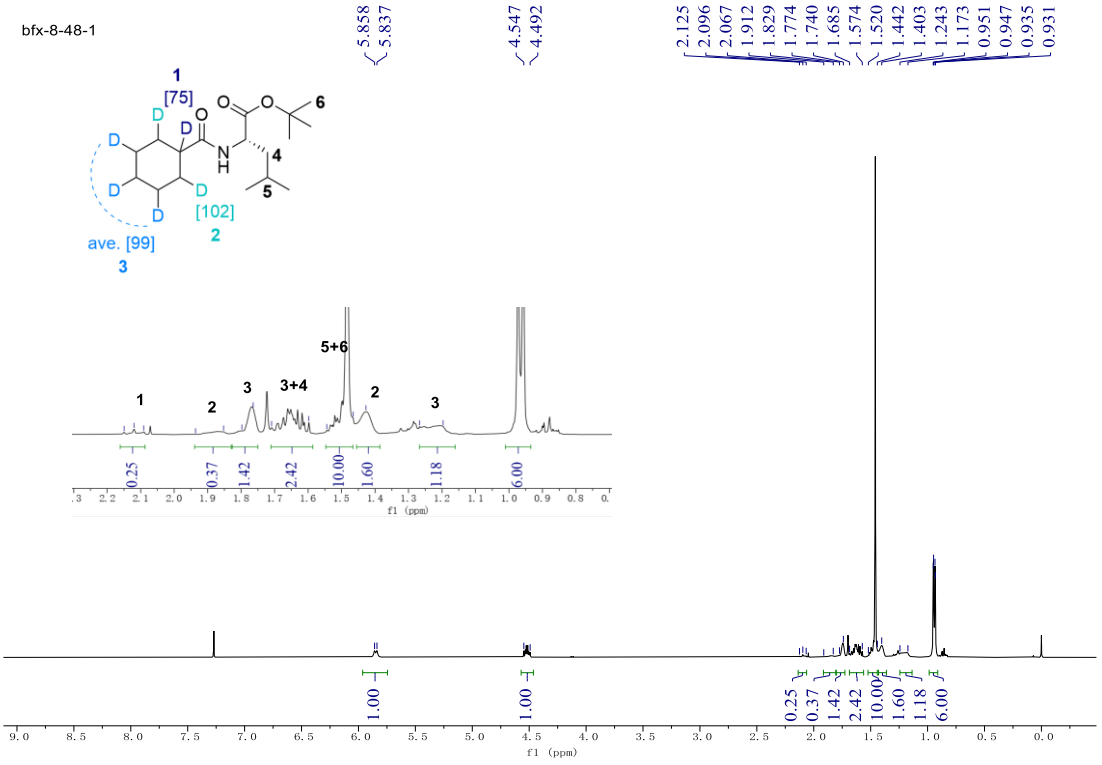


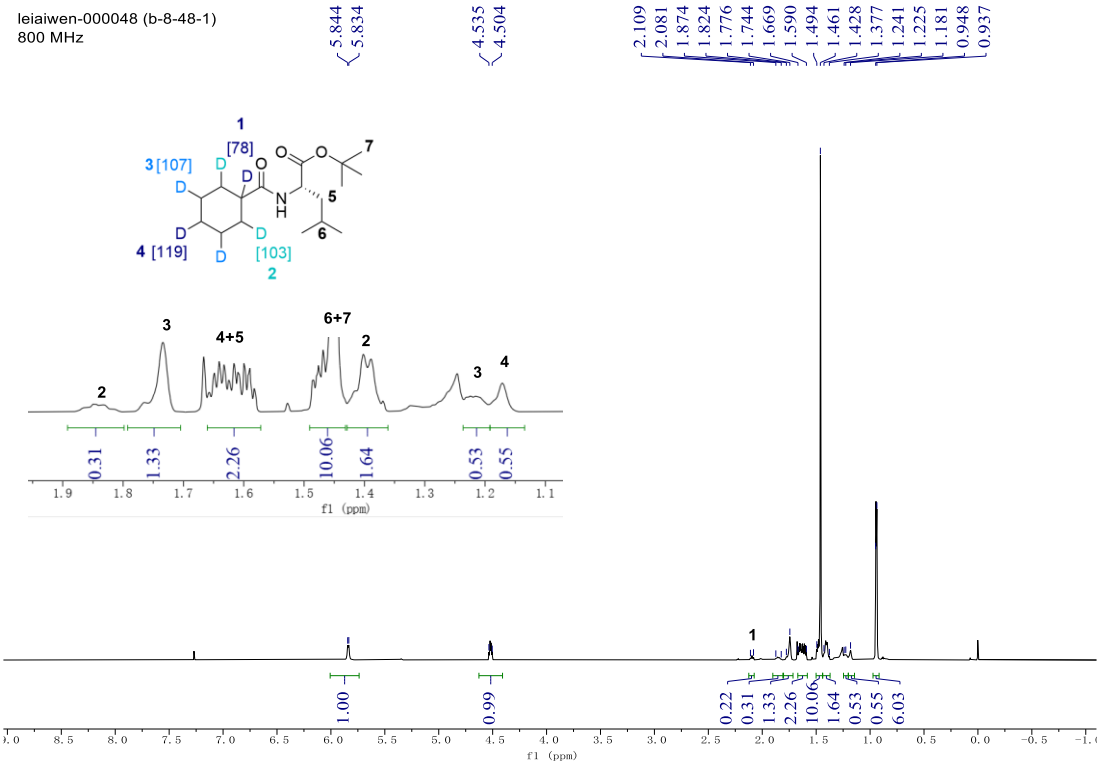


^{13}C NMR for 7b



^{1}H NMR for 8b


bfx-8-48-1
5.858
5.837
4.547
4.492
2.125
2.096
2.067
1.912
1.829
1.774
1.740
1.685
1.574
1.520
1.442
1.403
1.243
1.173
0.951
0.947
0.935
0.931
1
[75]
6
4
5
[102]
2
ave. [99]
3
5+6
3+4
1.00
1.00
0.25
0.37
1.42
2.42
10.00
1.60
1.18
6.00
f1 (ppm)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800 MHz
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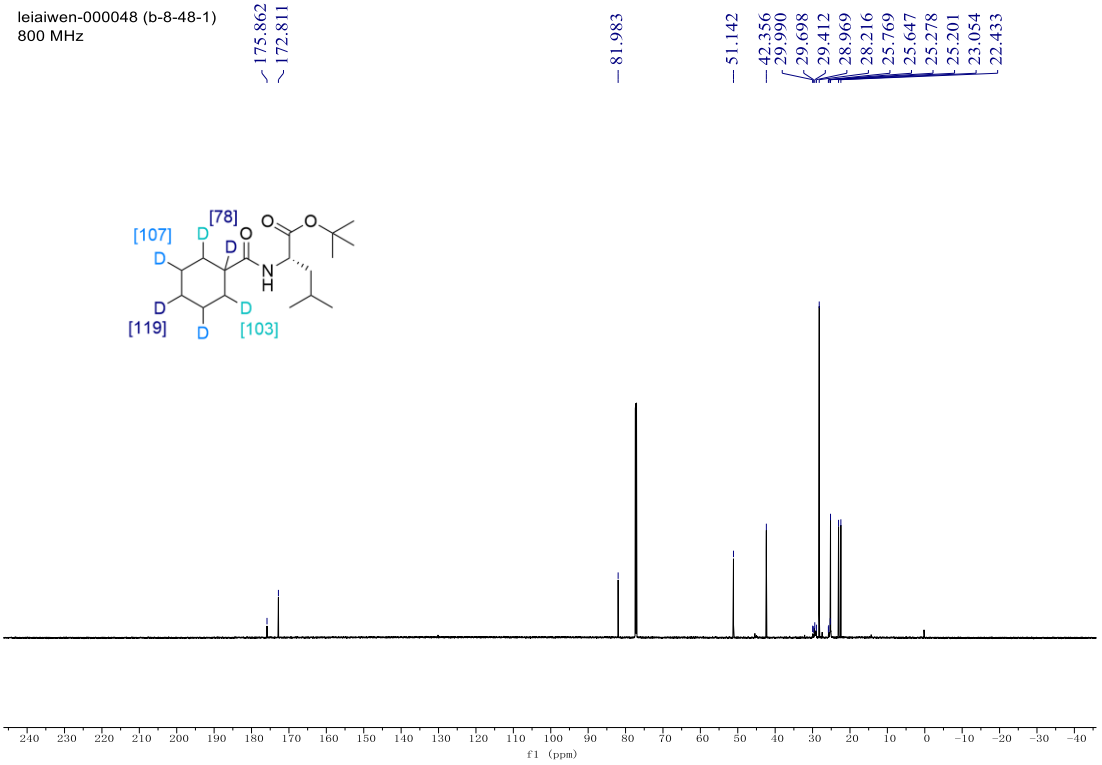
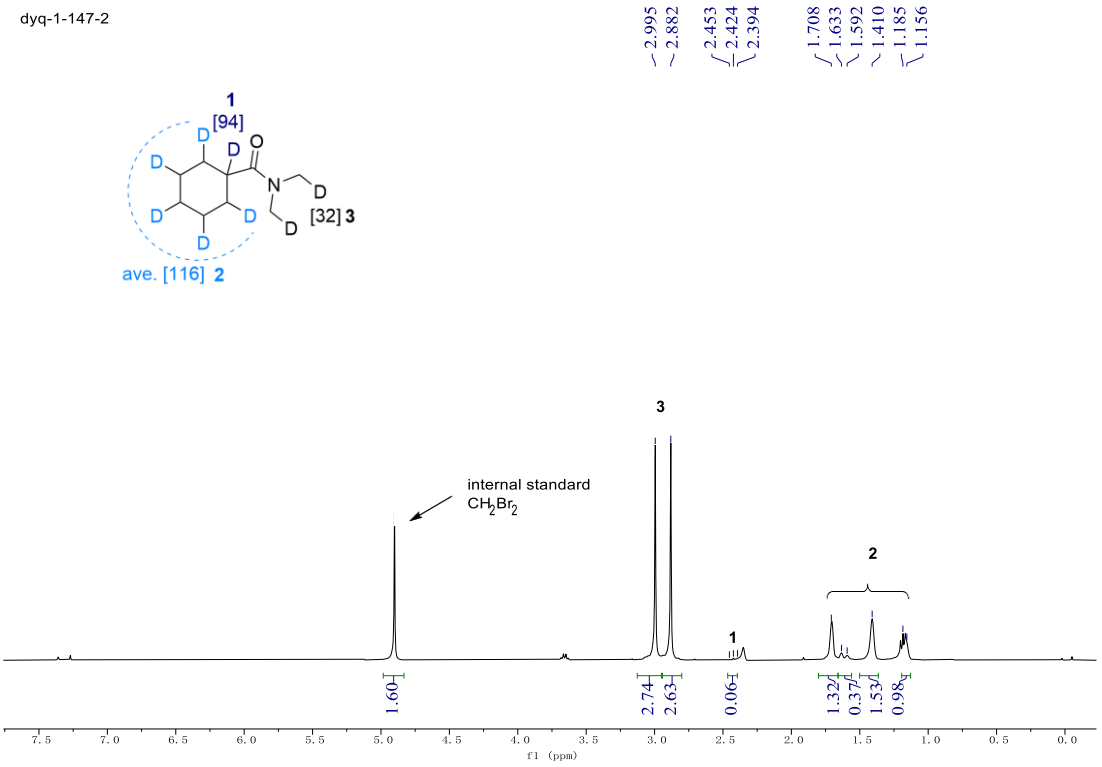
5.834
4.535
4.504
2.109
2.081
1.874
1.824
1.776
1.744
1.669
1.590
1.494
1.461
1.428
1.377
1.241
1.225
1.181
0.948
0.937
1
[78]
3 [107]
7
5
6
4 [119]
[103]
2
6+7
4+5
1.00
0.99
0.22
0.31
1.33
2.26
10.06
1.64
0.53
0.55
6.03
f1 (ppm)

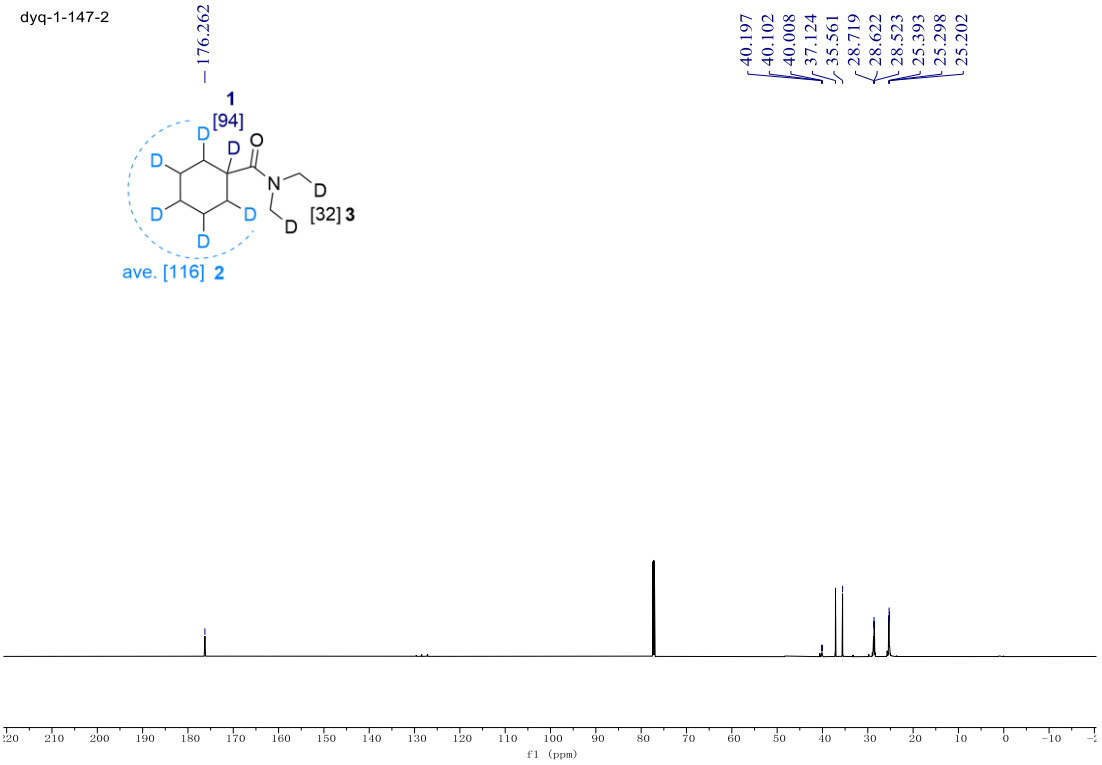
^{13}C NMR for 8b



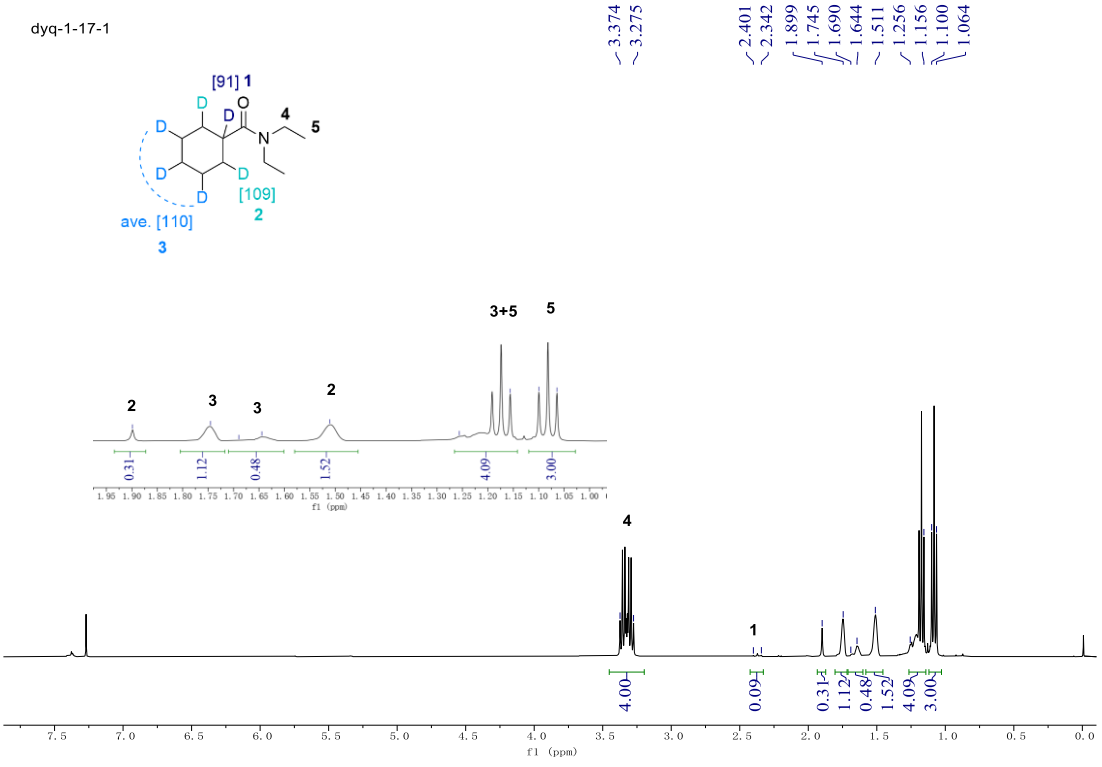
^{1}H NMR for 9b



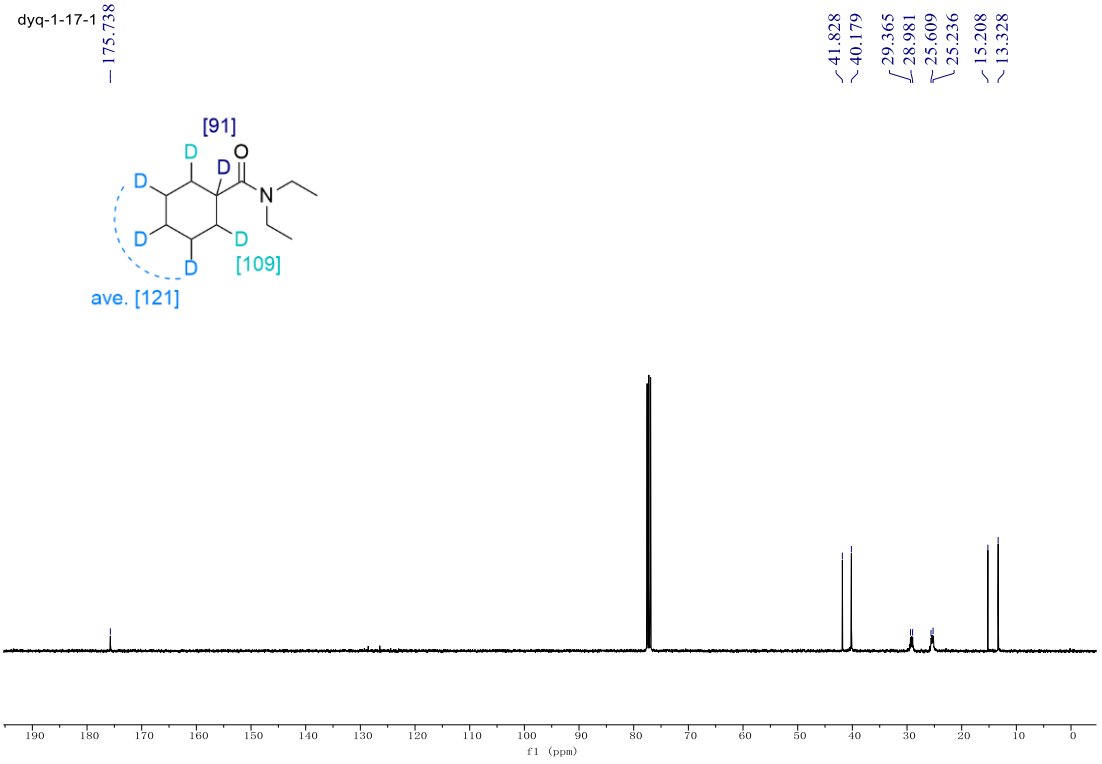
^{13}C NMR for 9b



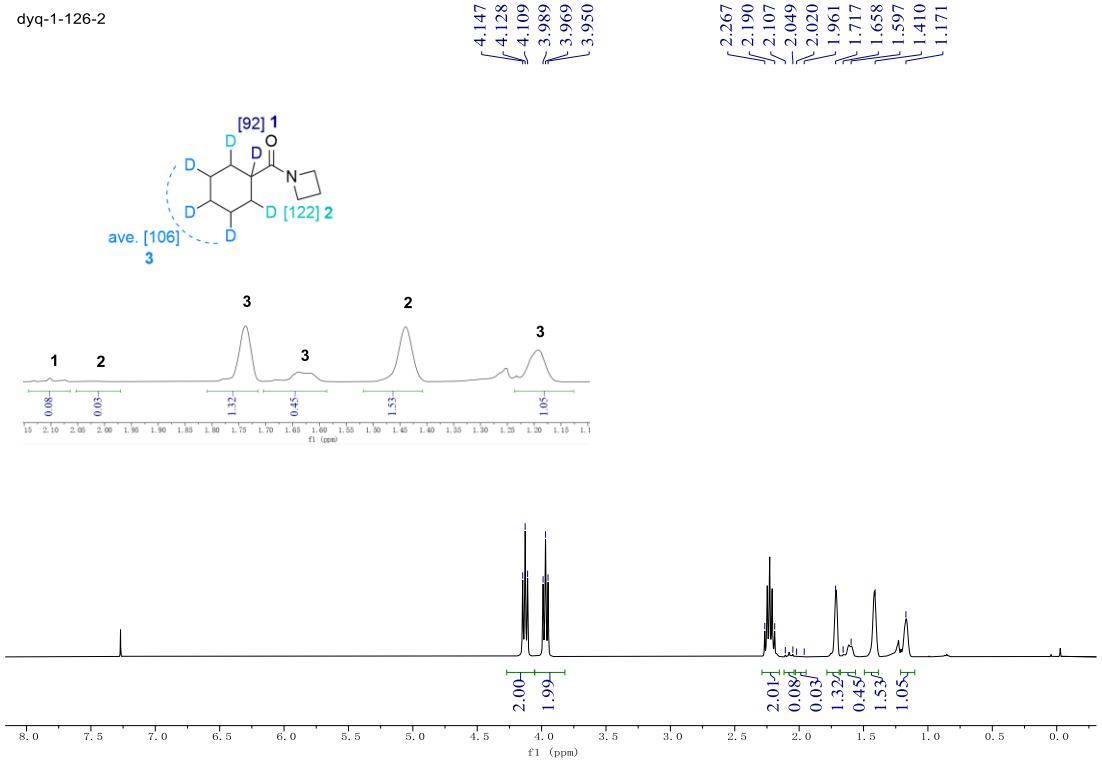
^{1}H NMR for 10b



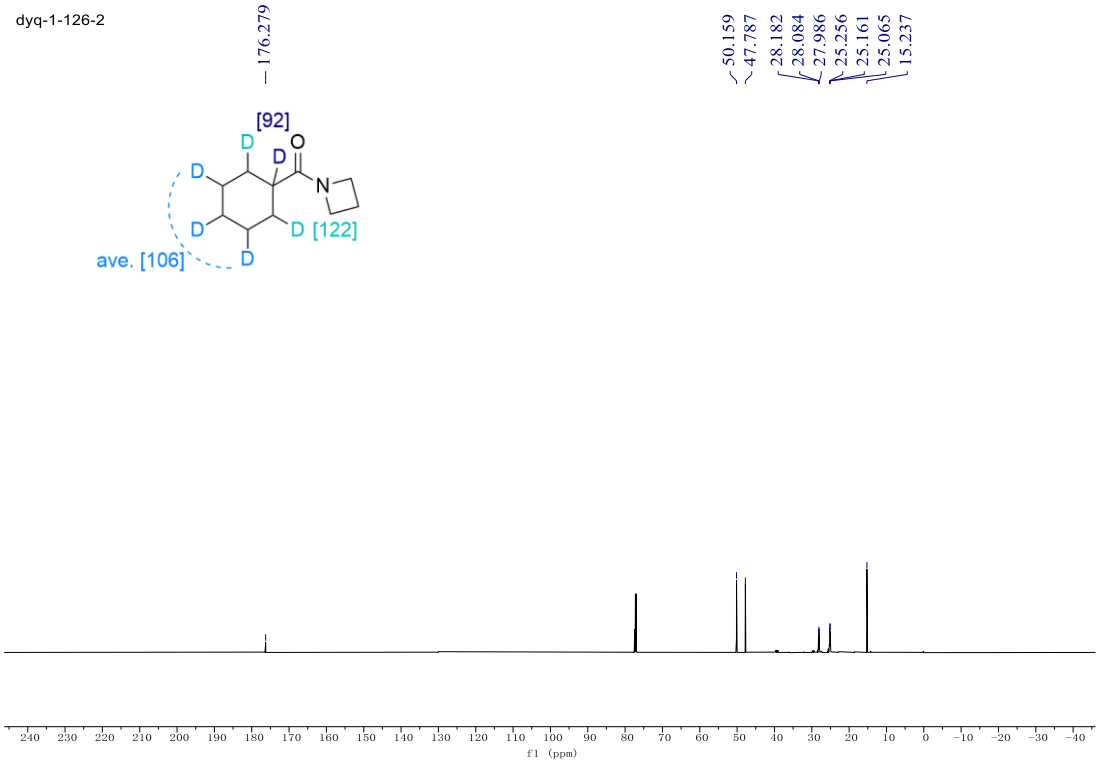
^{13}C NMR for 10b



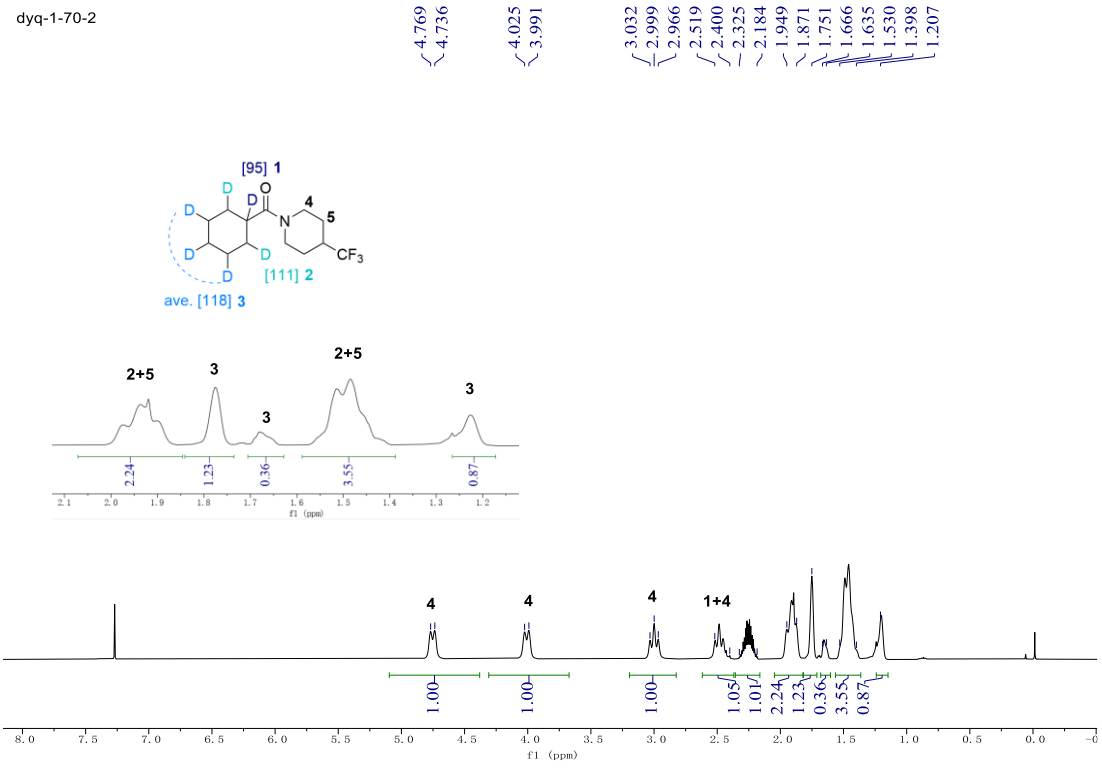
^{1}H NMR for 11b



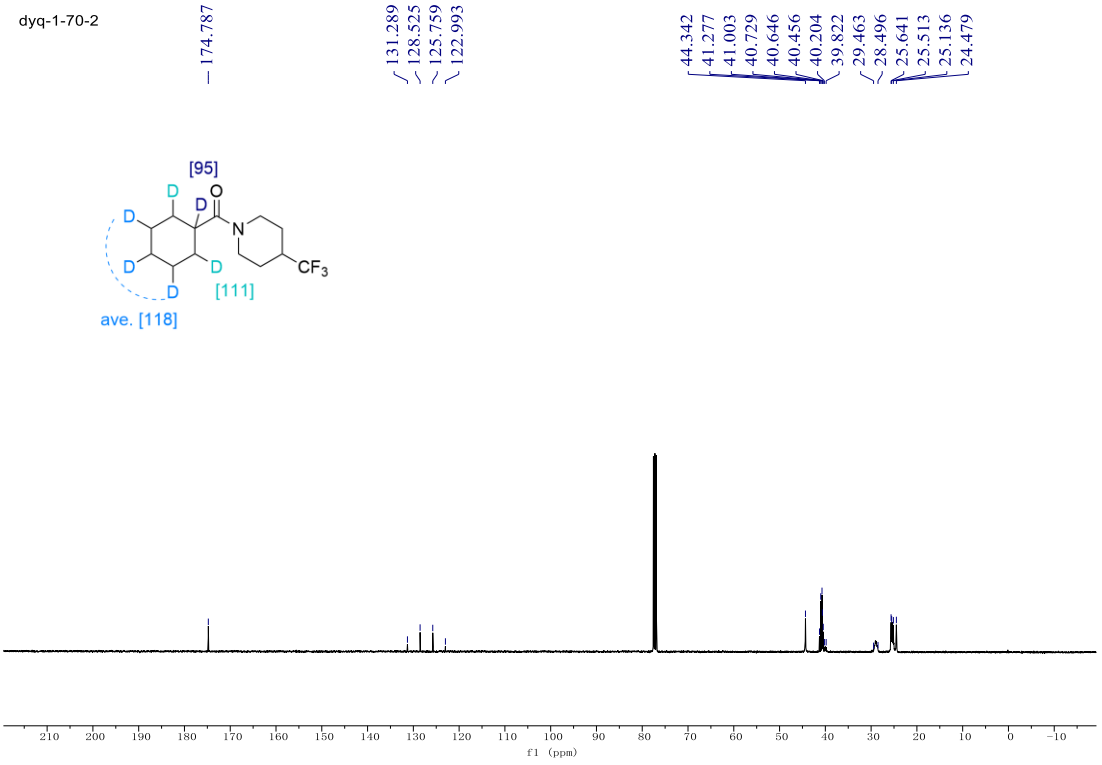
^{13}C NMR for 11b



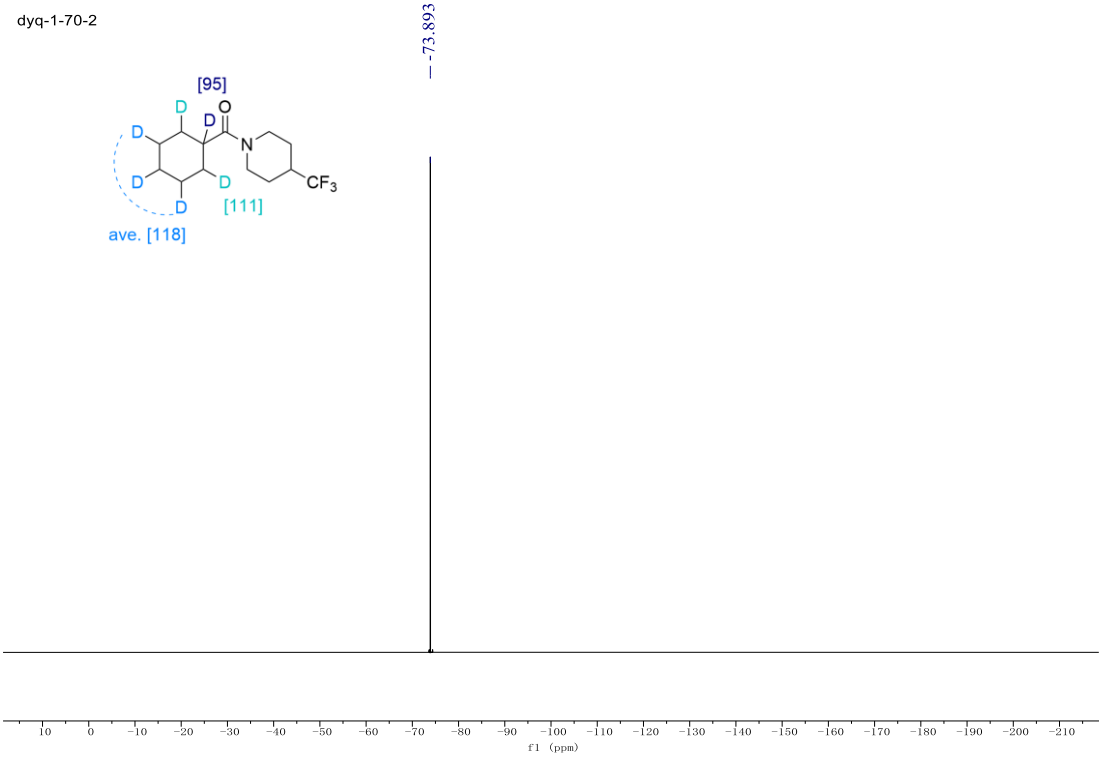
^{1}H NMR for 12b



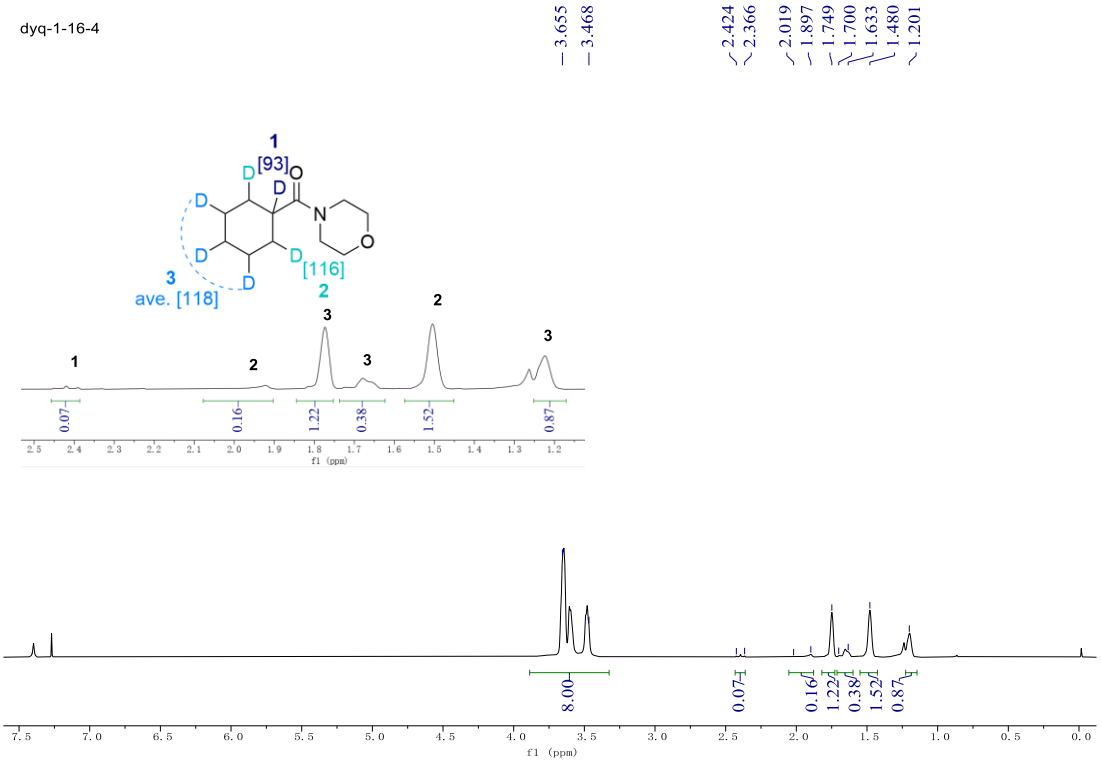
^{13}C NMR for 12b



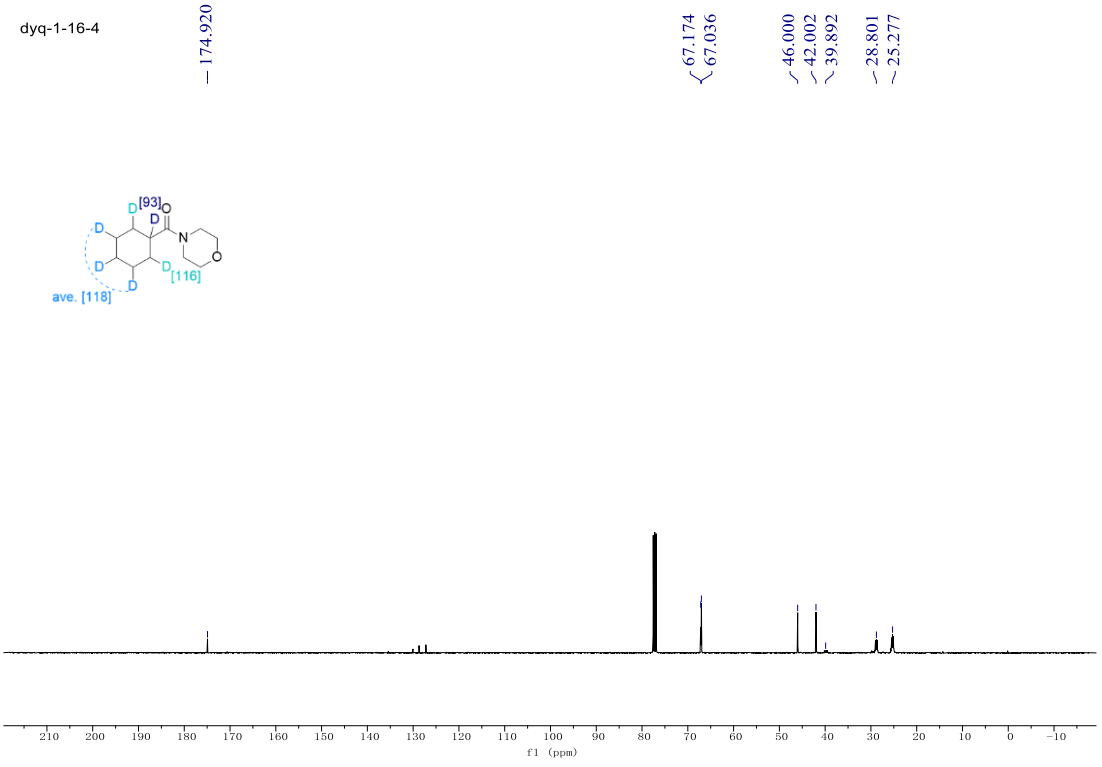
^{19}F NMR for 12b



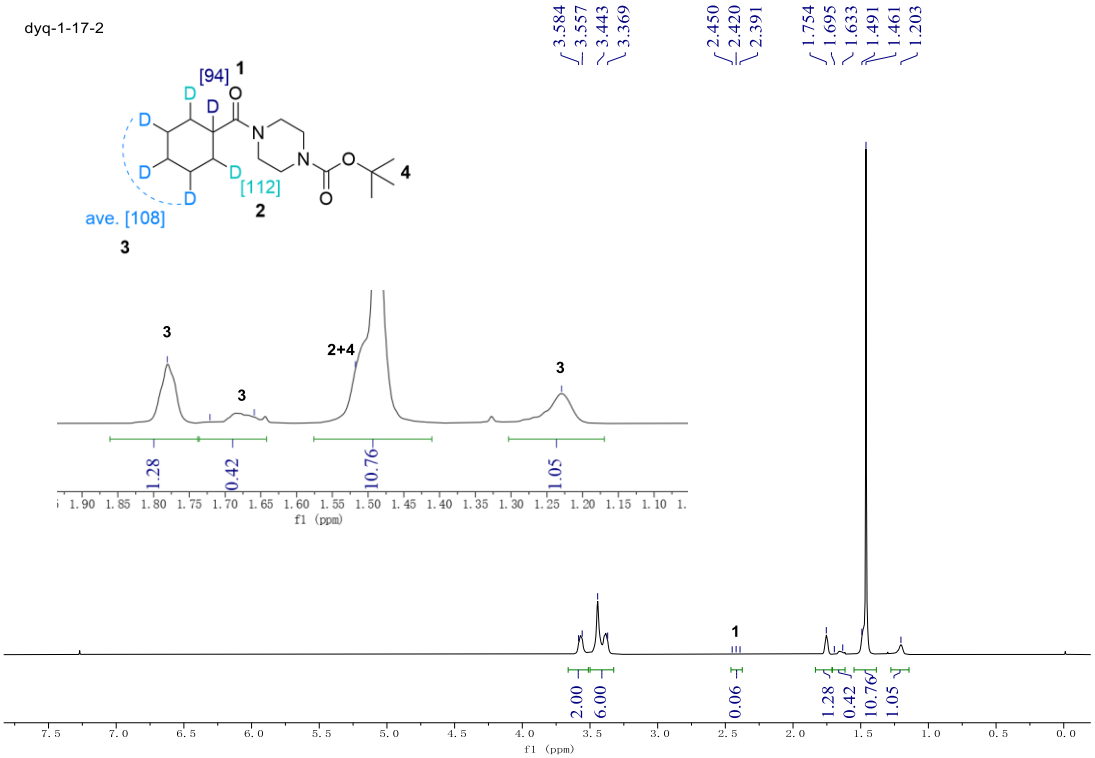
^{1}H NMR for 13b



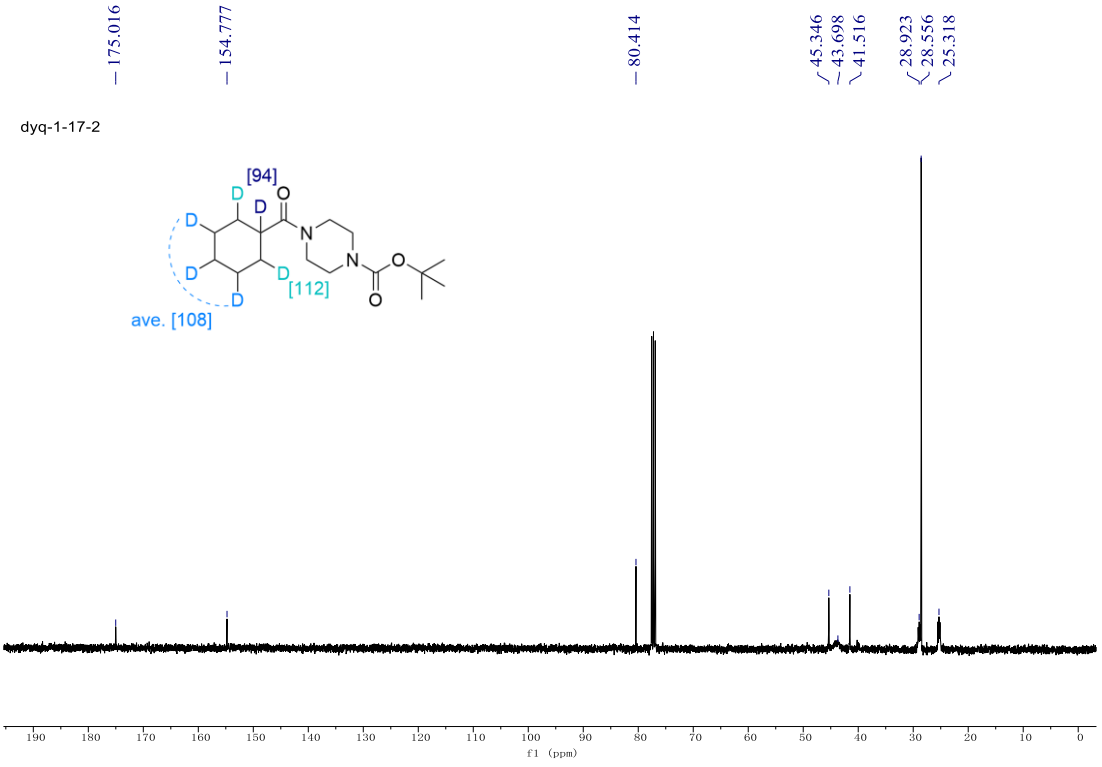
^{13}C NMR for 13b



^{1}H NMR for 14b

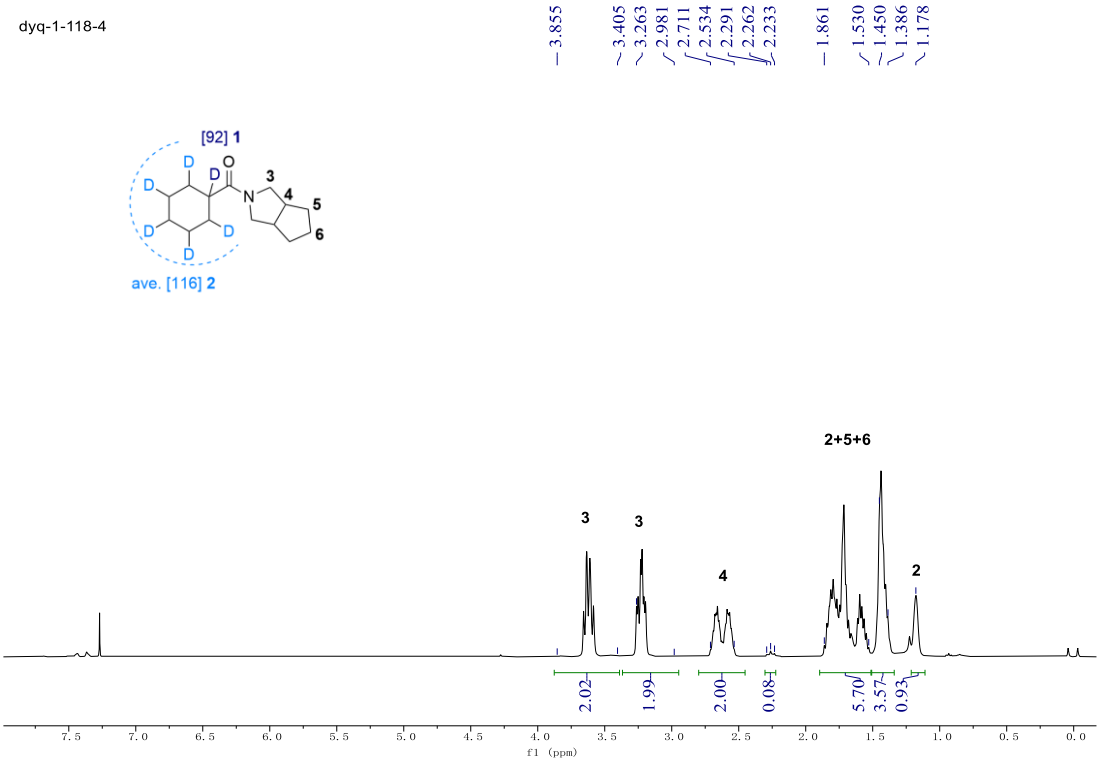


^{13}C NMR for 14b

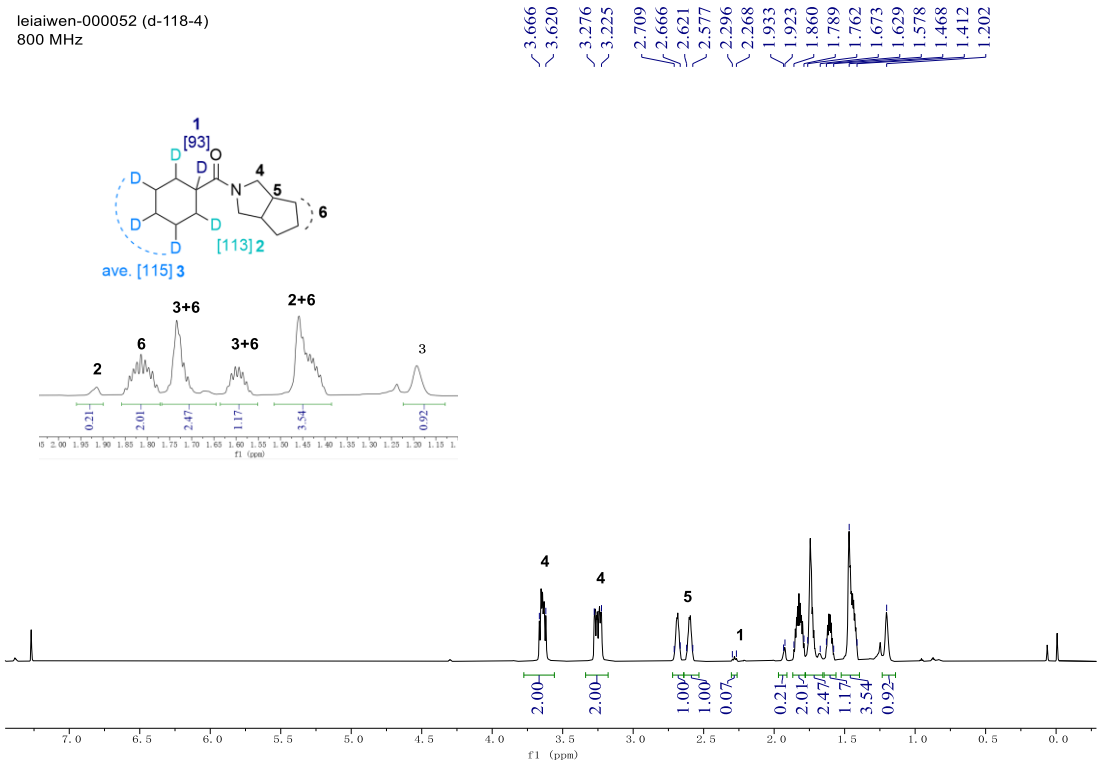


^{1}H NMR for 15b

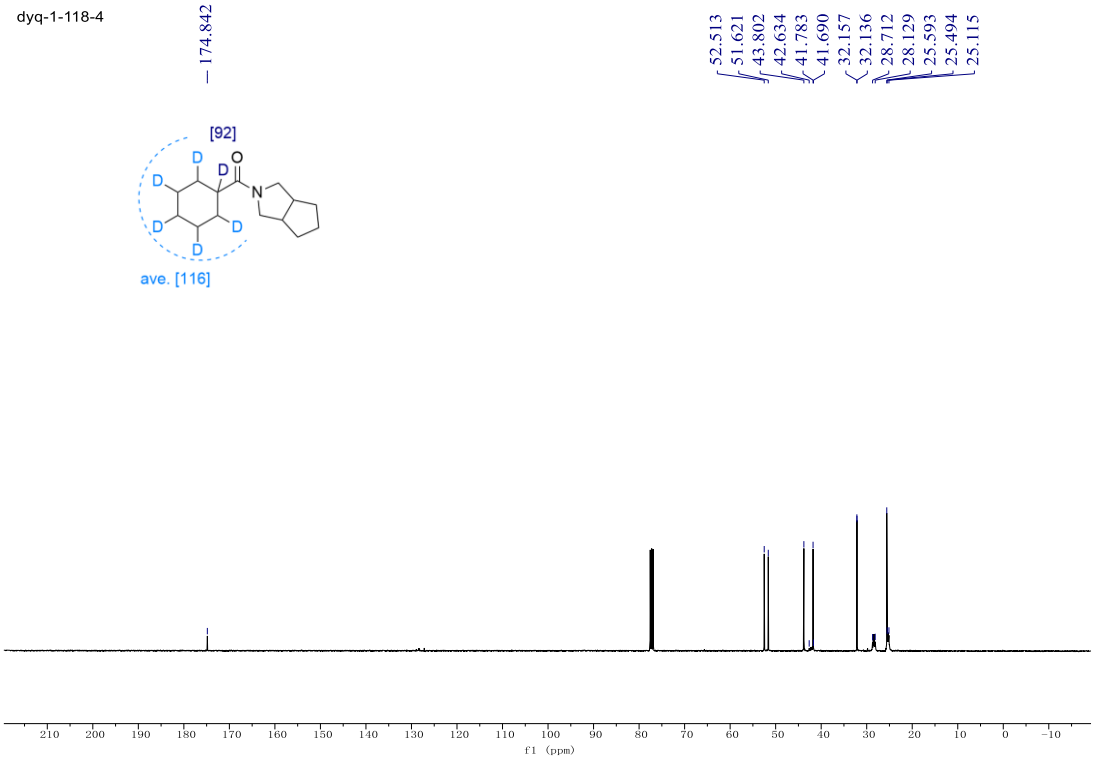
dyq-1-118-4



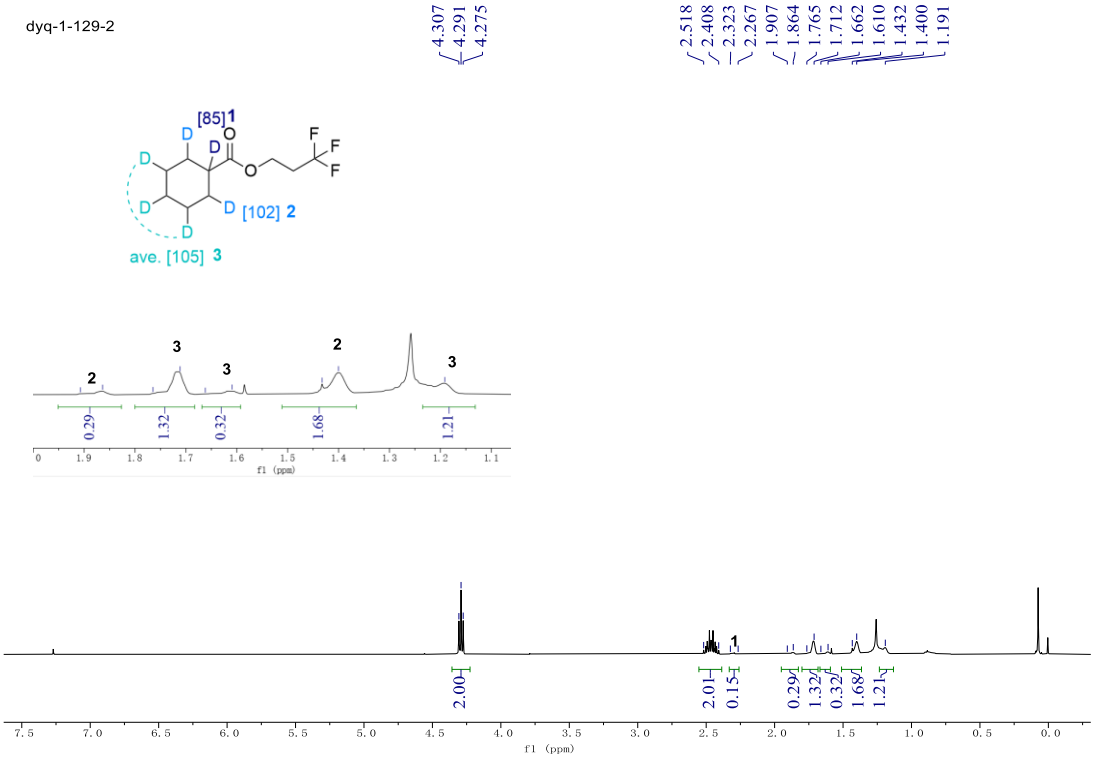
leiaiwen-000052 (d-118-4)
800 MHz



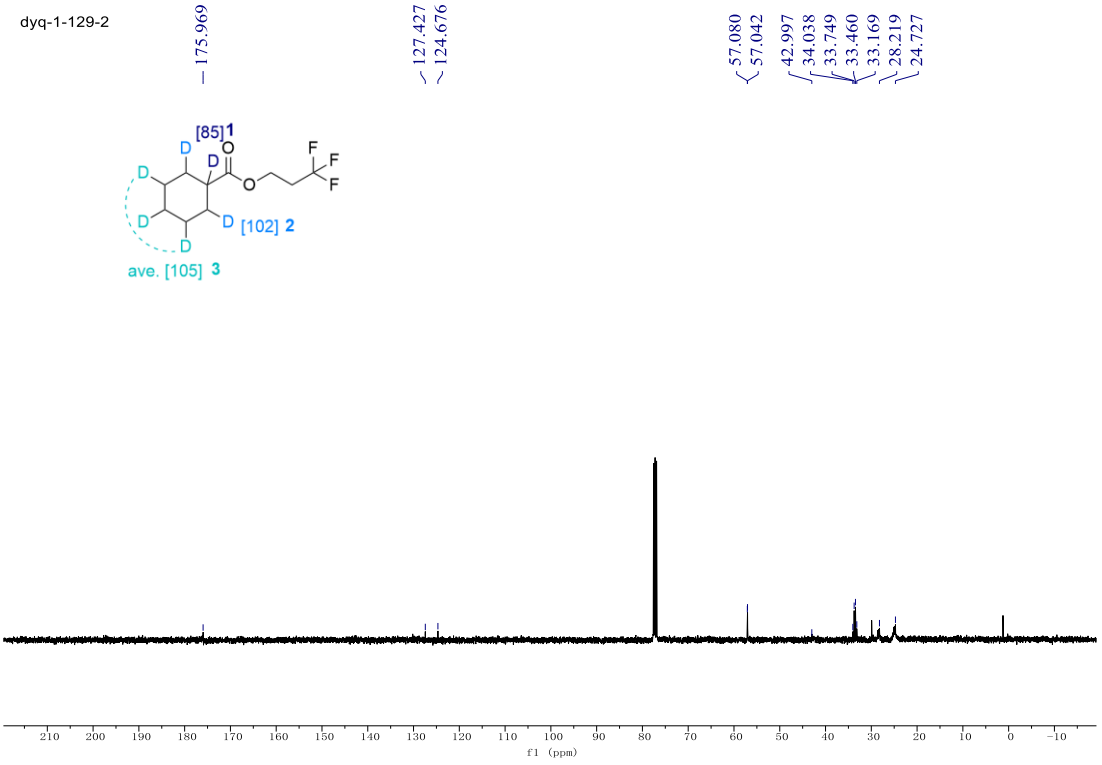
^{13}C NMR for 15b



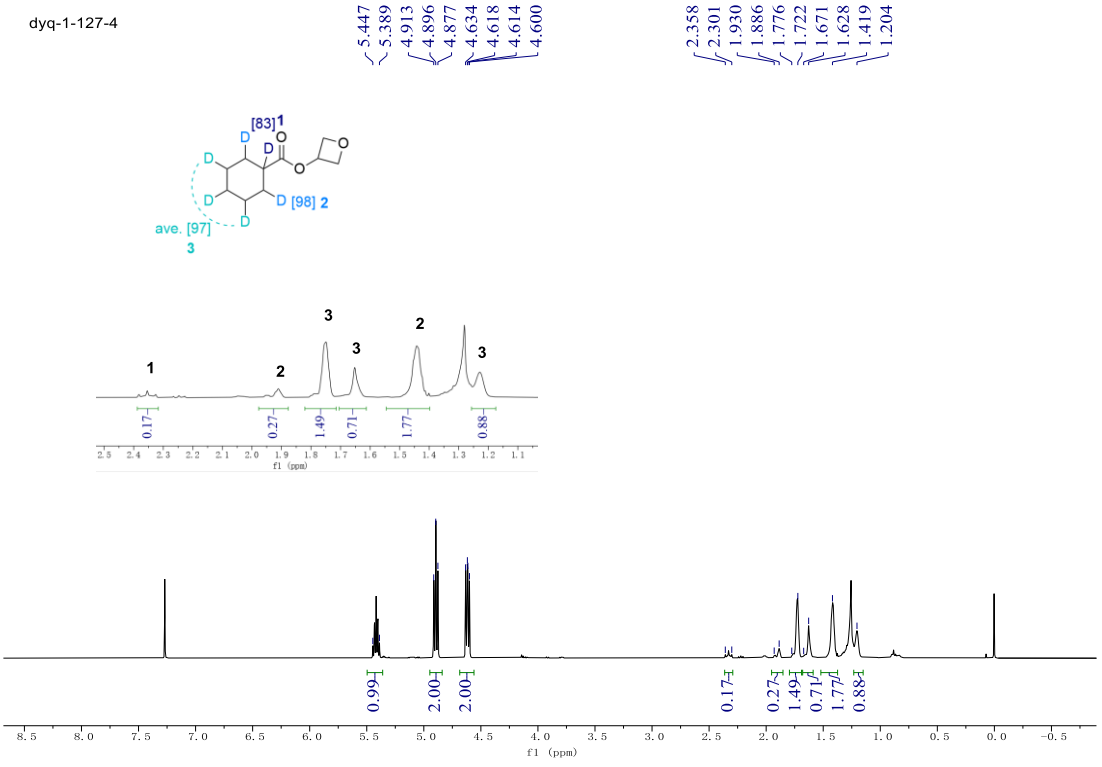
^{1}H NMR for 16b



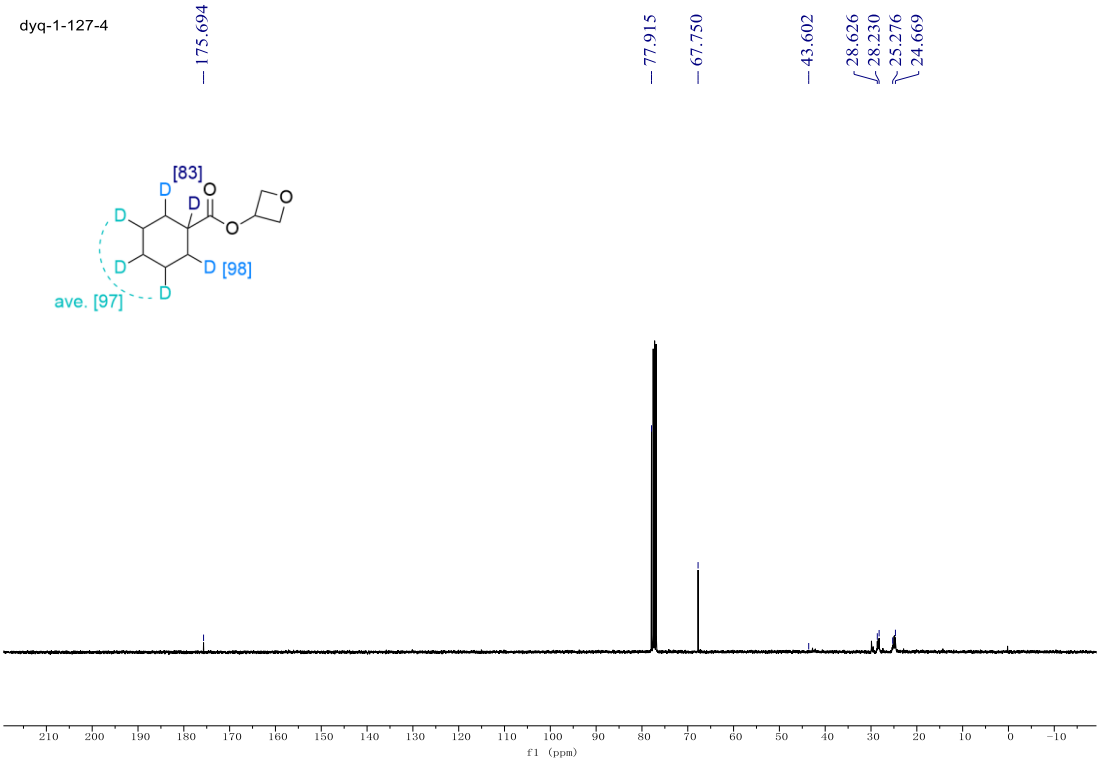
^{13}C NMR for 16b



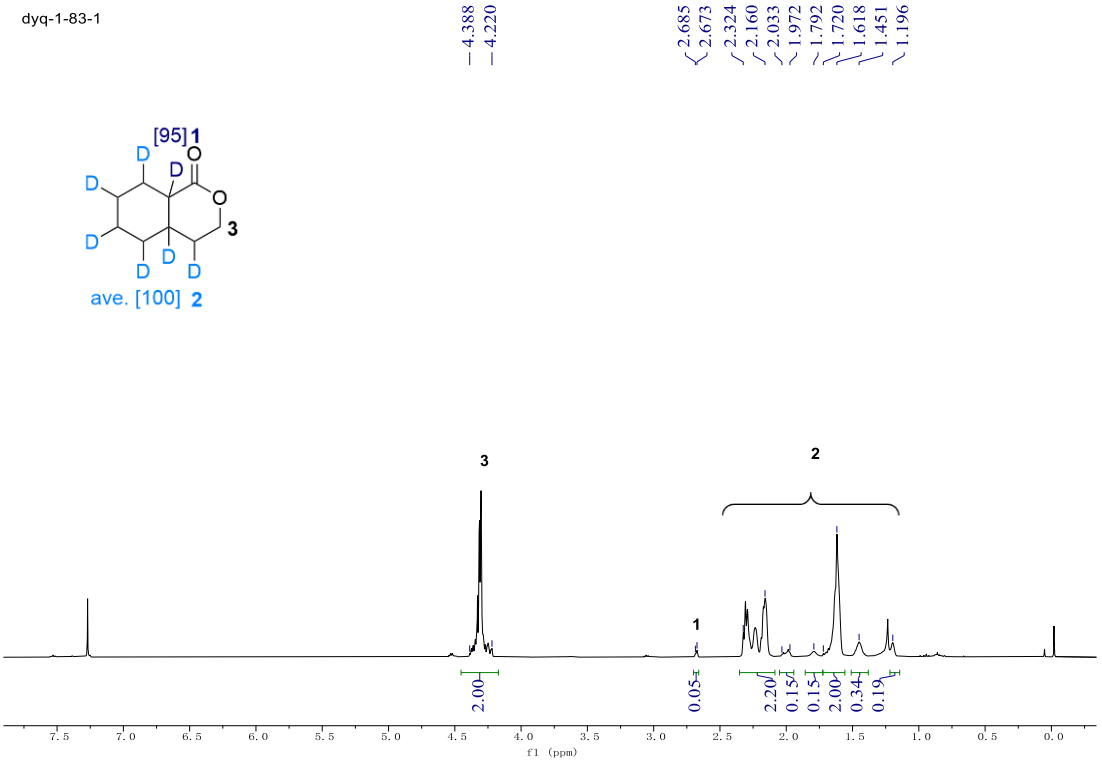
^{1}H NMR for 17b



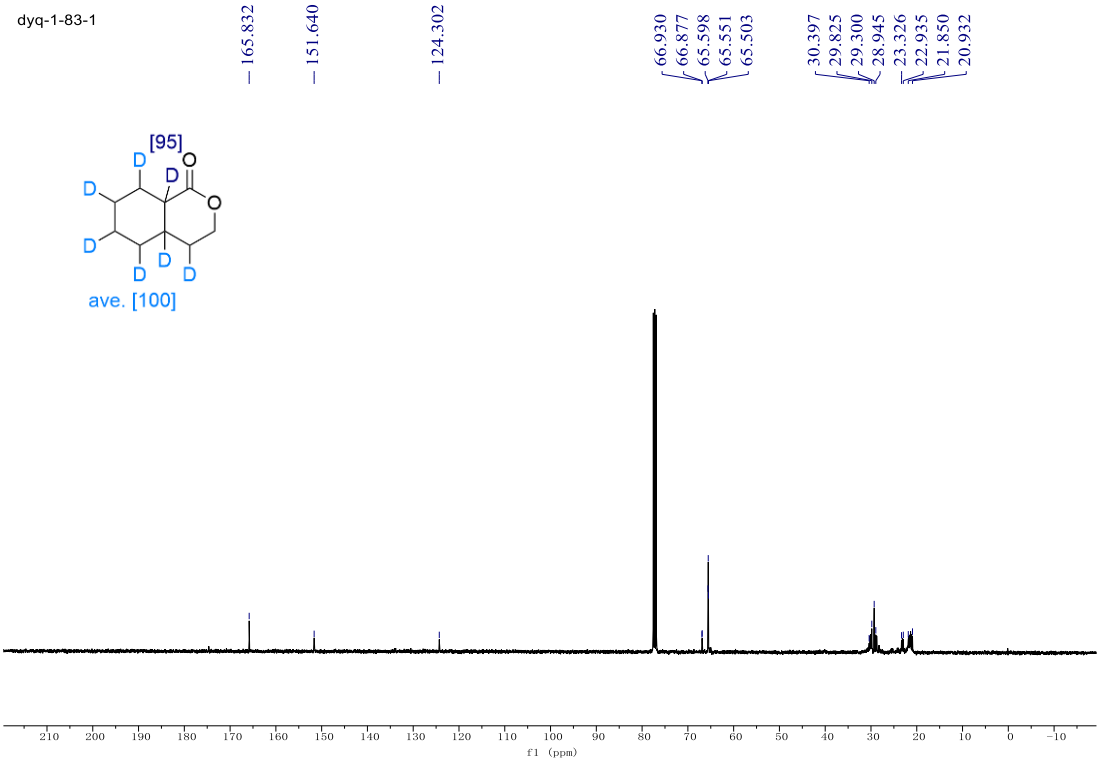
^{13}C NMR for 17b



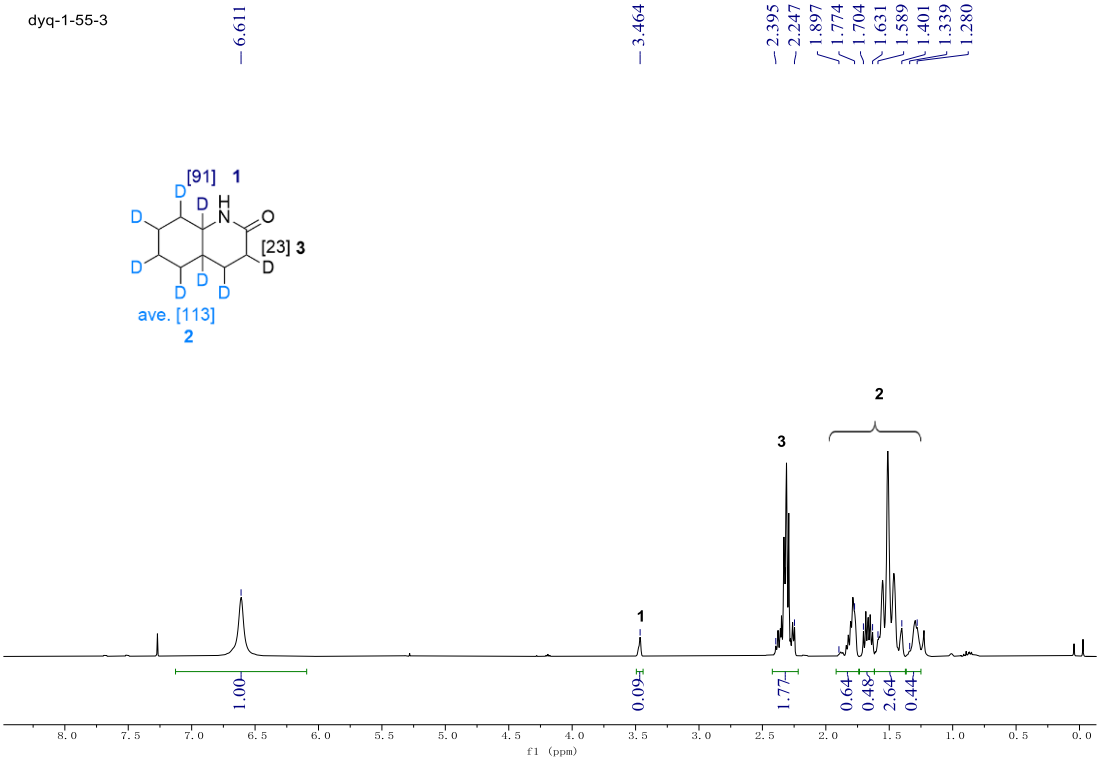
^{1}H NMR for 18b



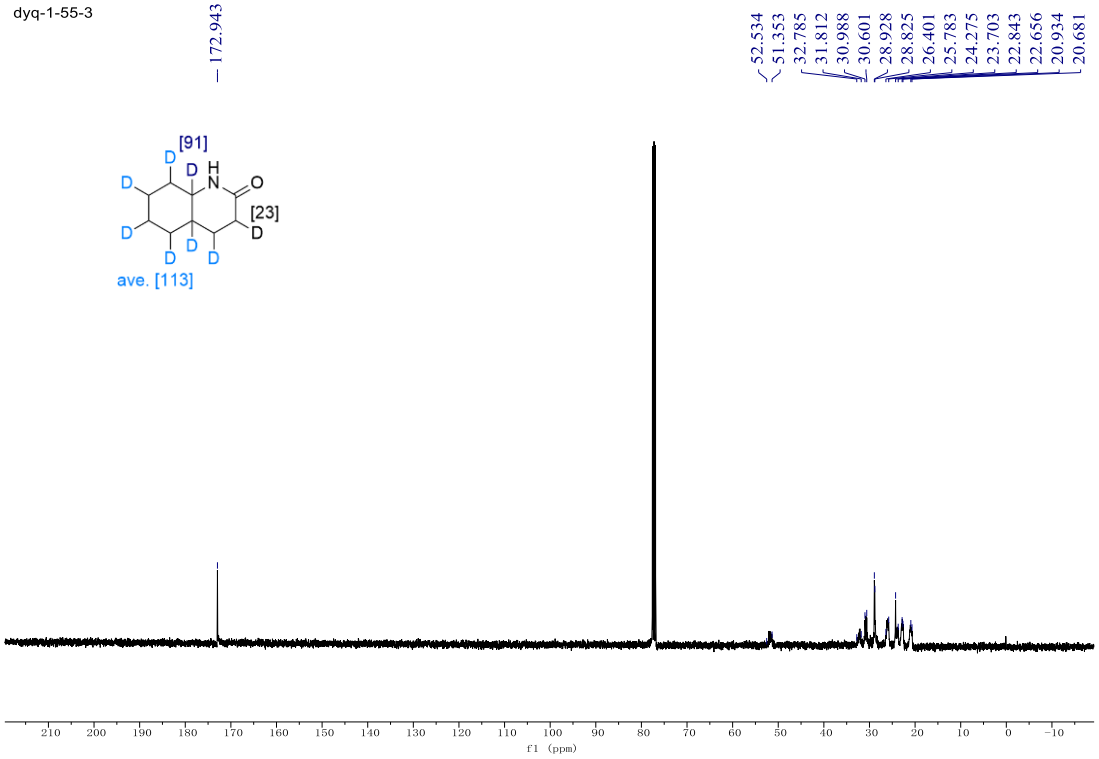
^{13}C NMR for 18b



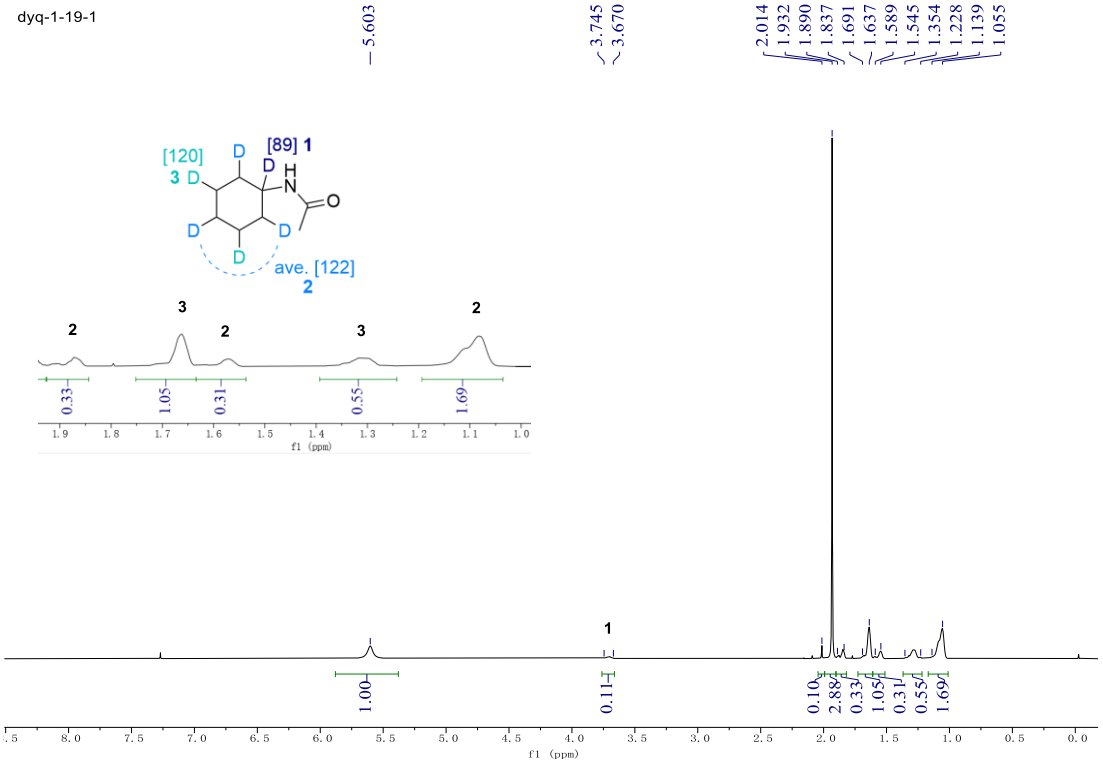
^{1}H NMR for 19b



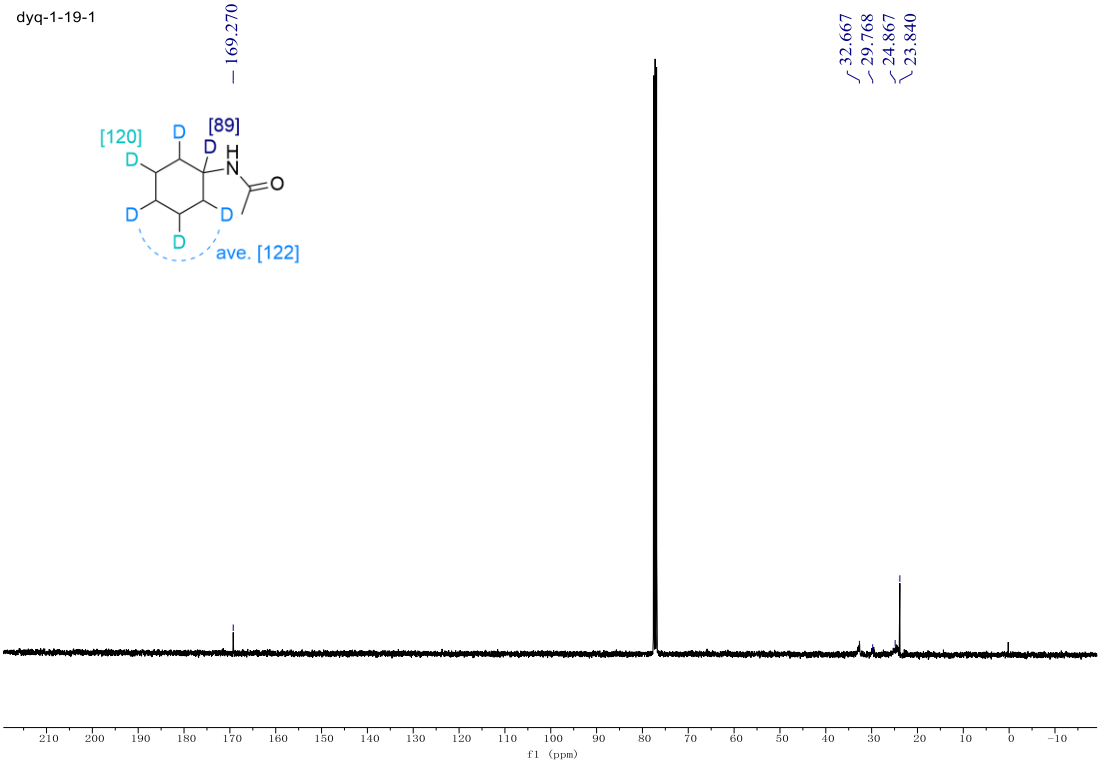
^{13}C NMR for 19b



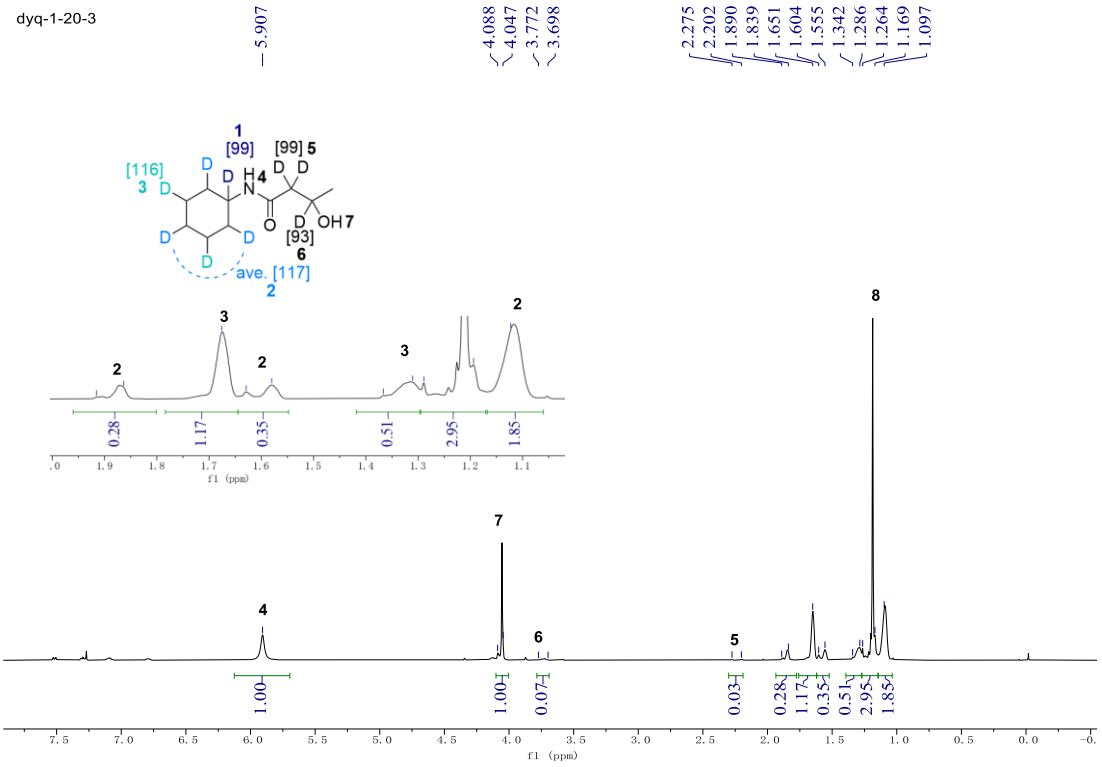
^{1}H NMR for 20b



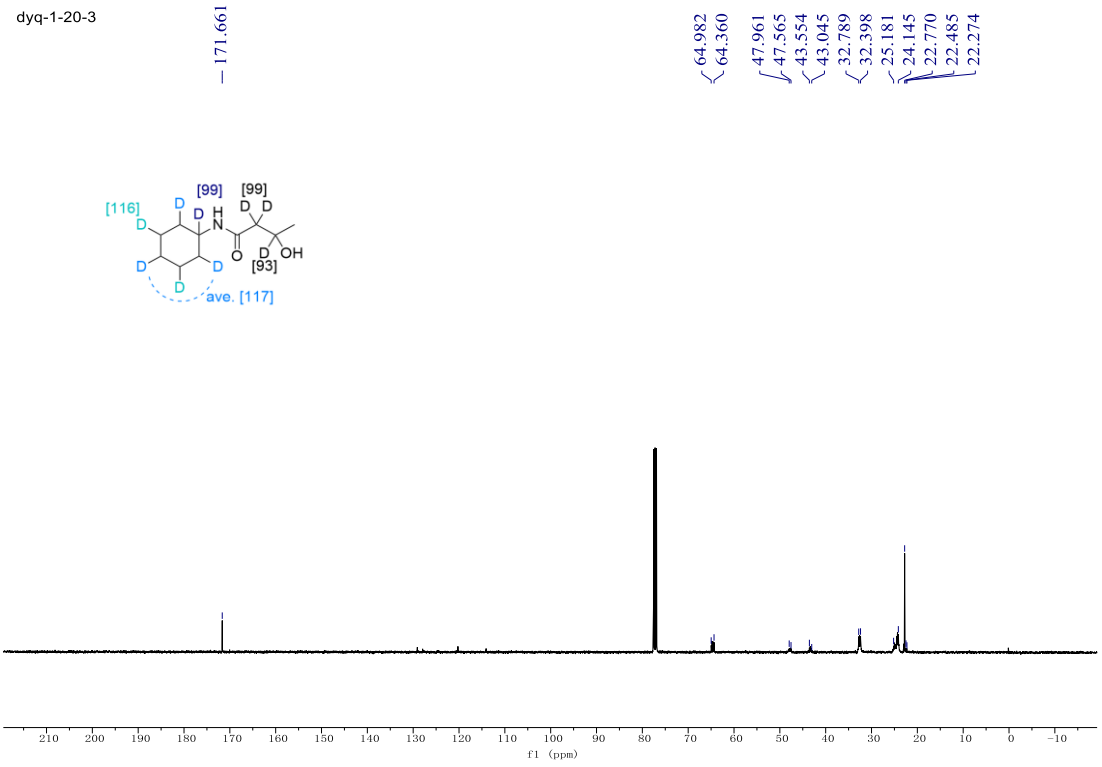
^{13}C NMR for 20b



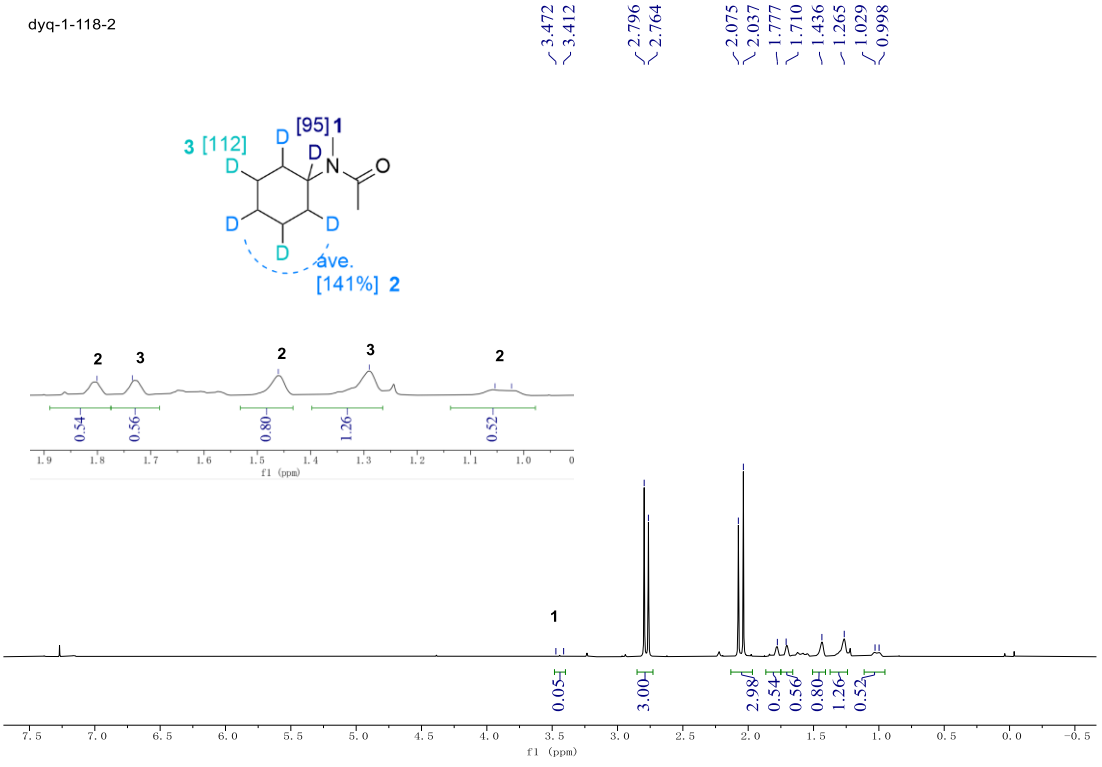
^{1}H NMR for 21b

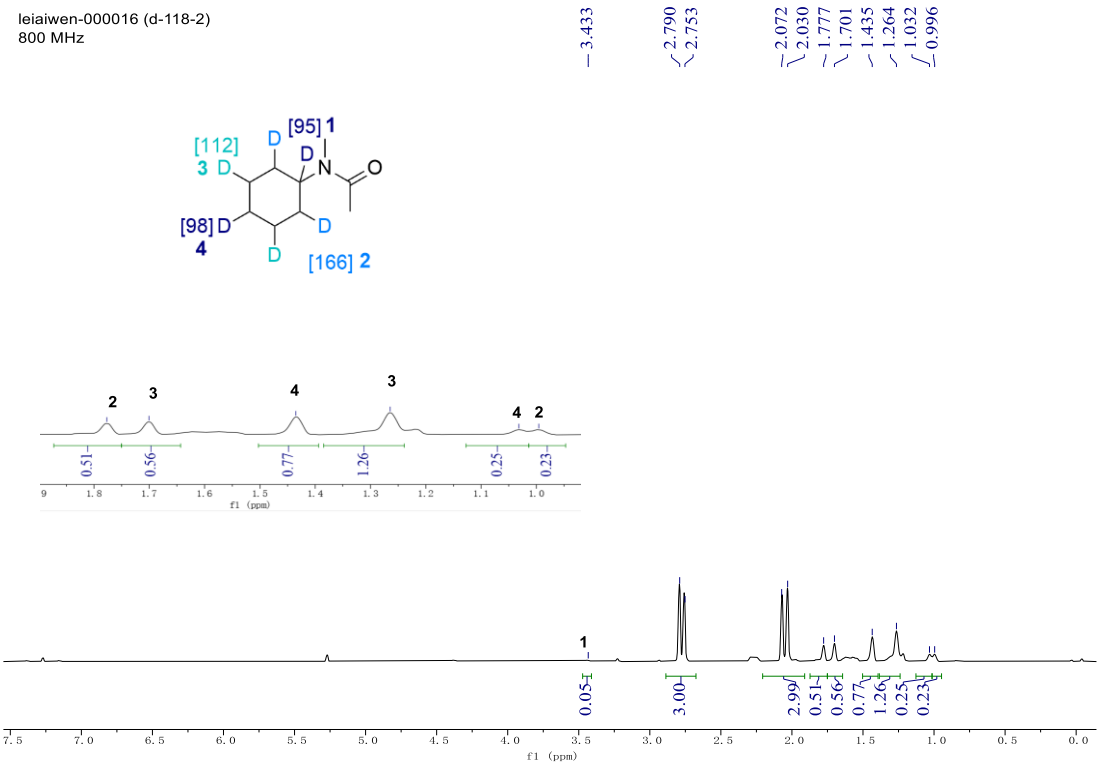


^{13}C NMR for 21b

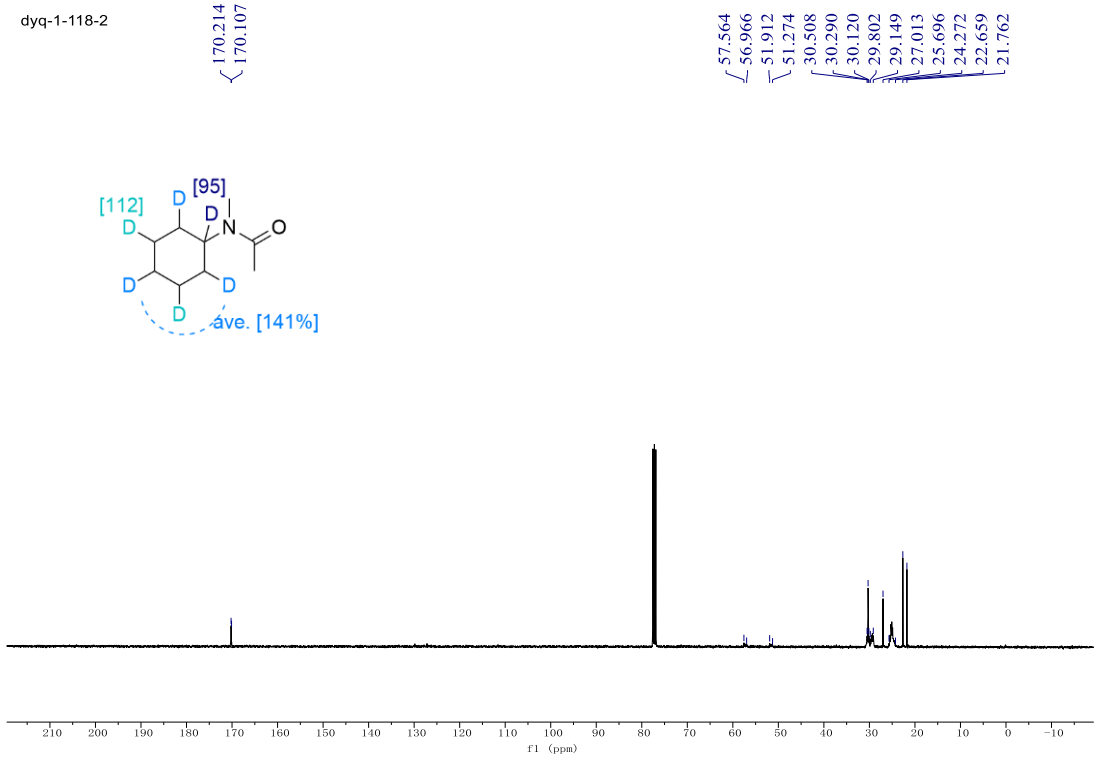


^{1}H NMR for 22b

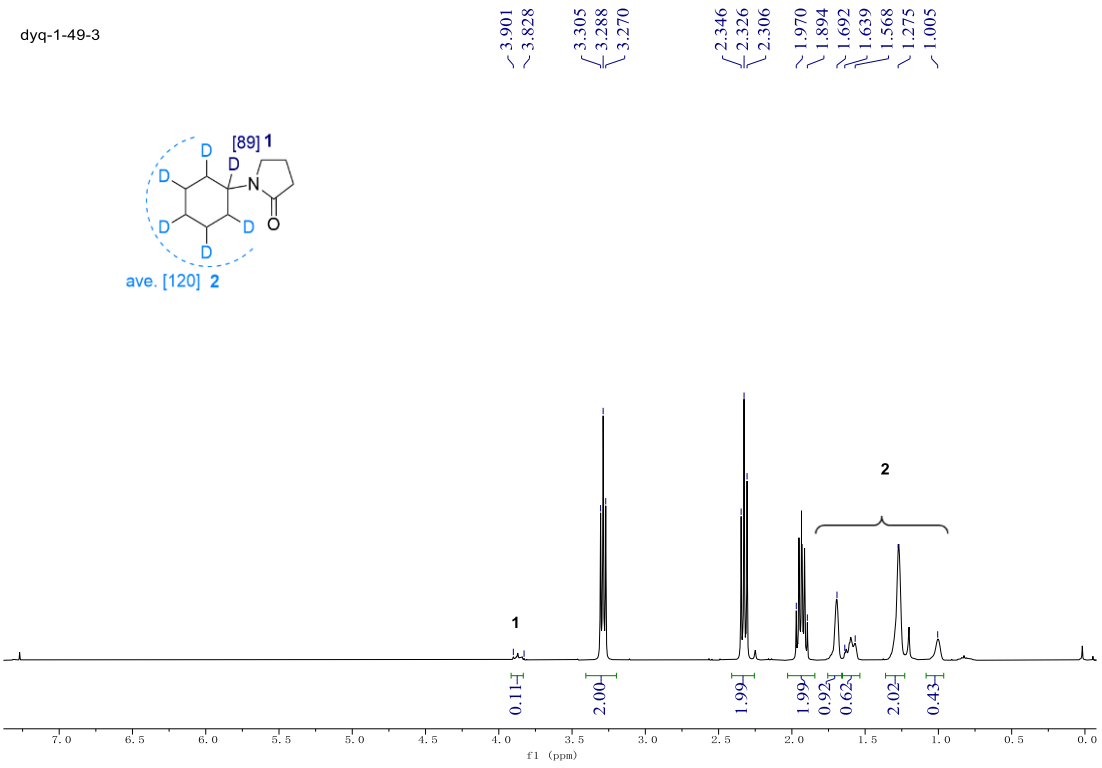




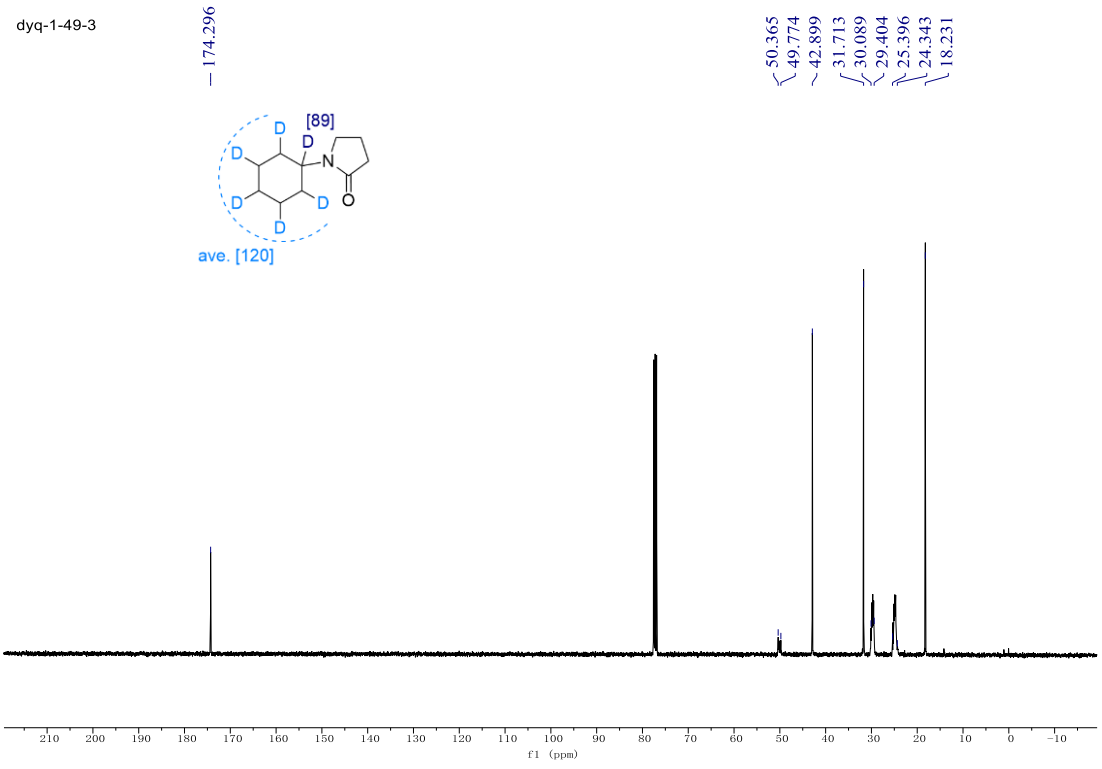
^{13}C NMR for 22b



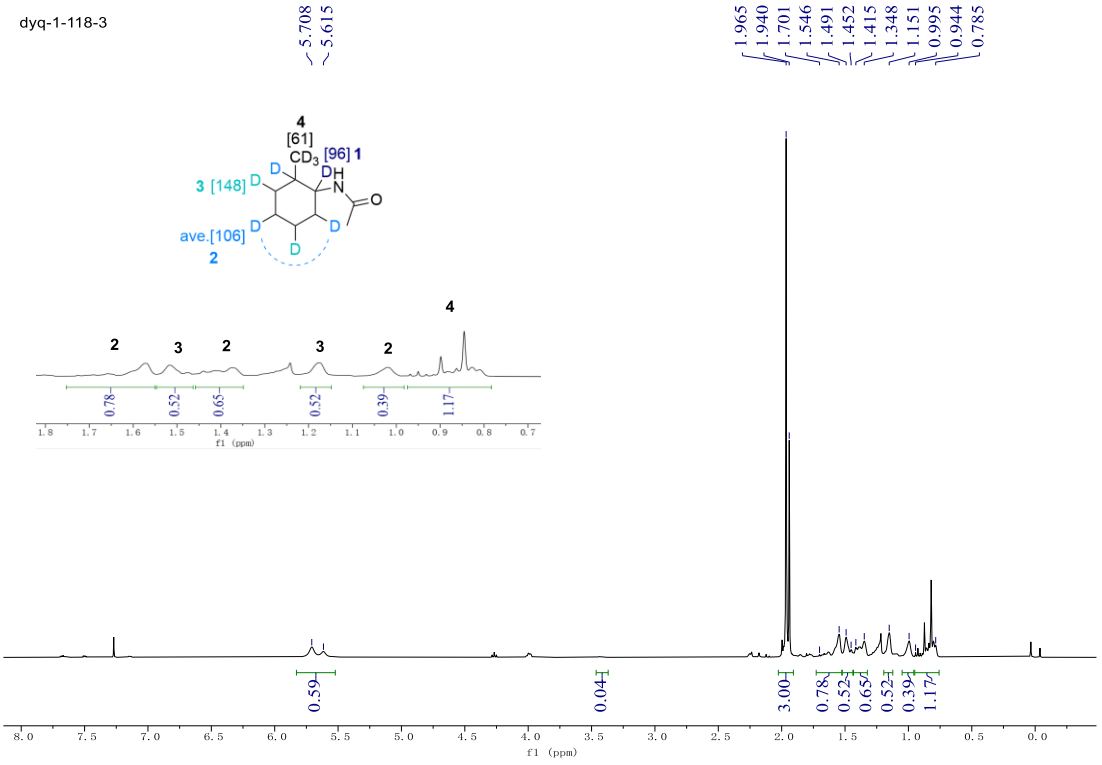
^{1}H NMR for 23b



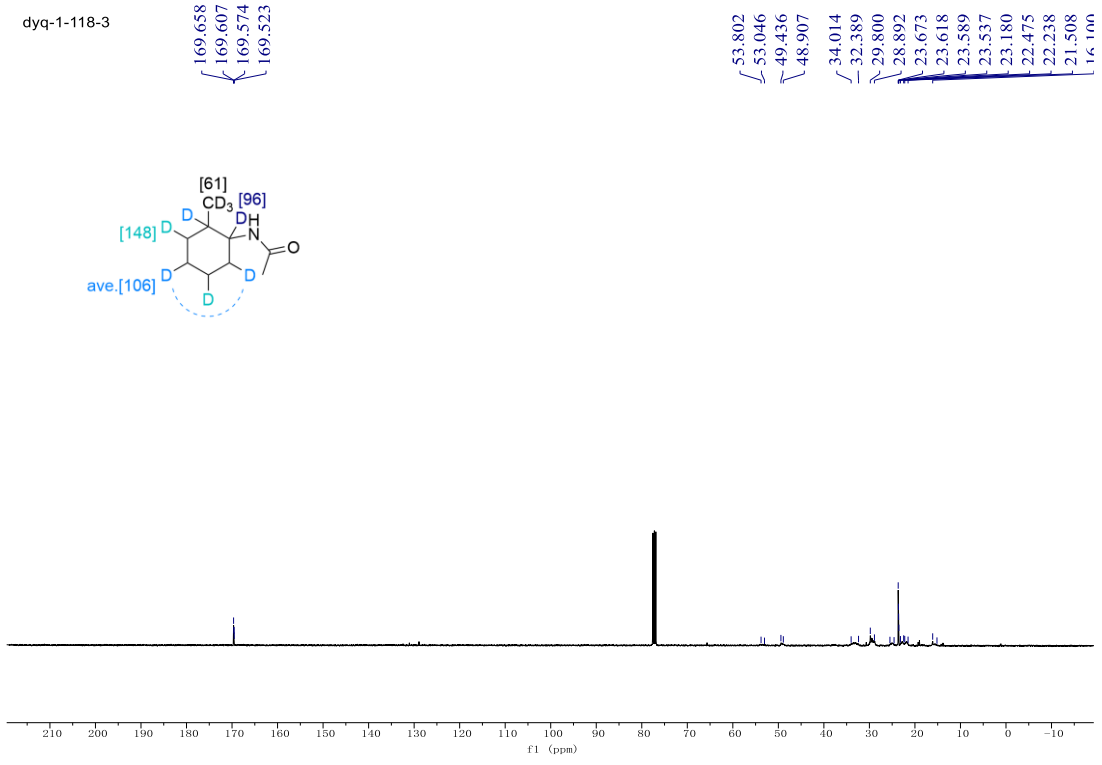
^{13}C NMR for 23b



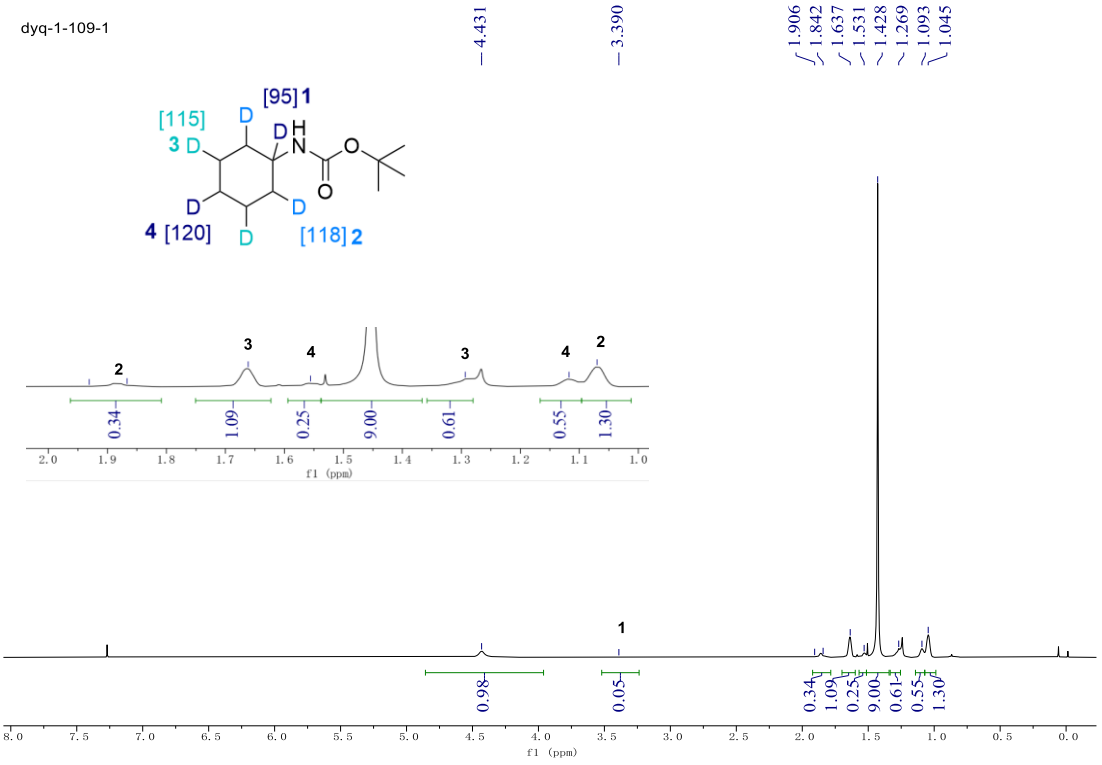
^{1}H NMR for 24b



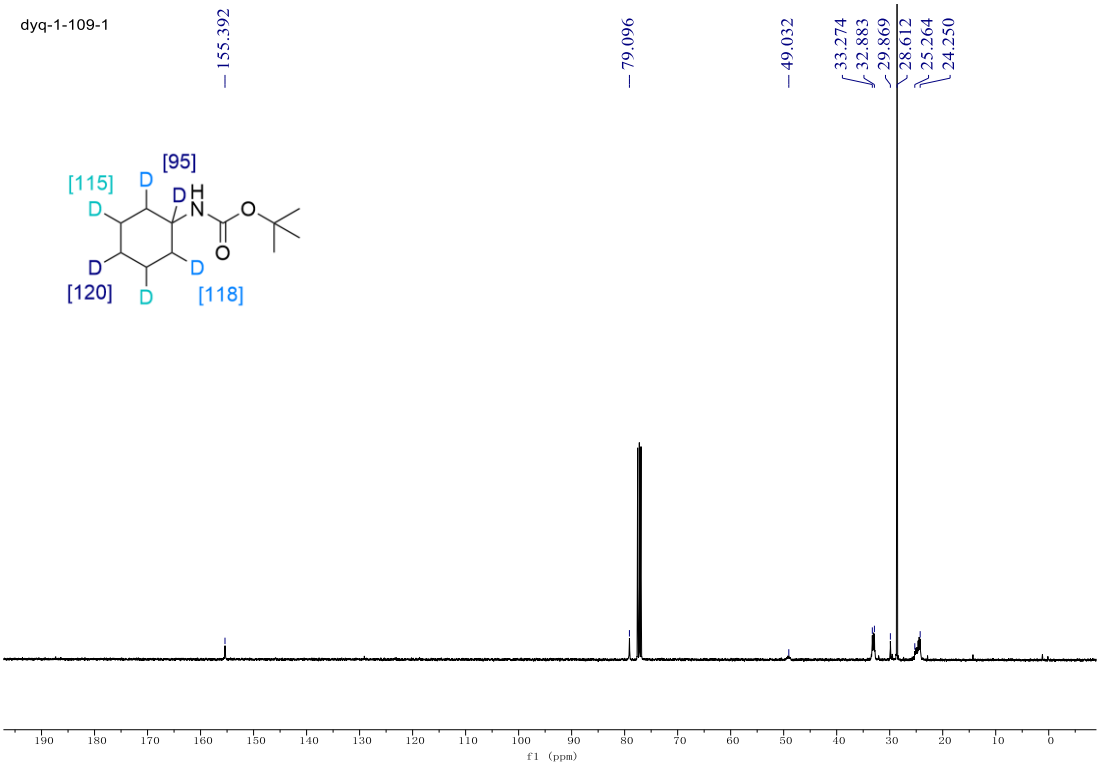
^{13}C NMR for 24b



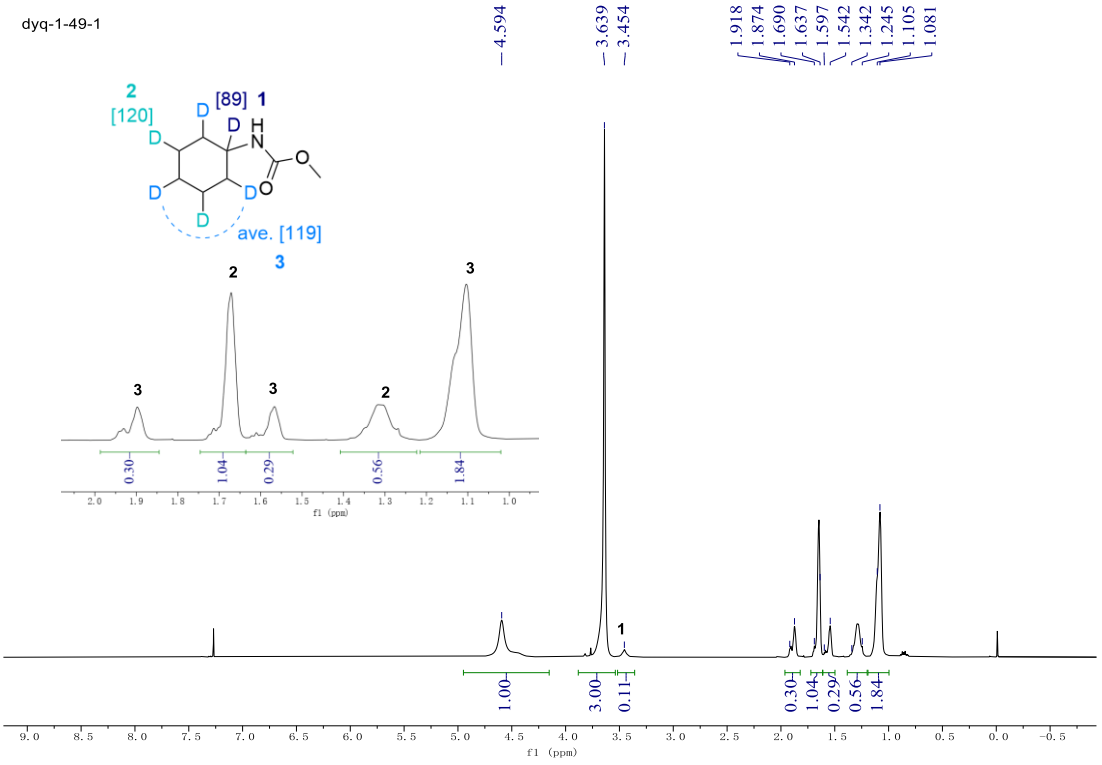
^{1}H NMR for 25b

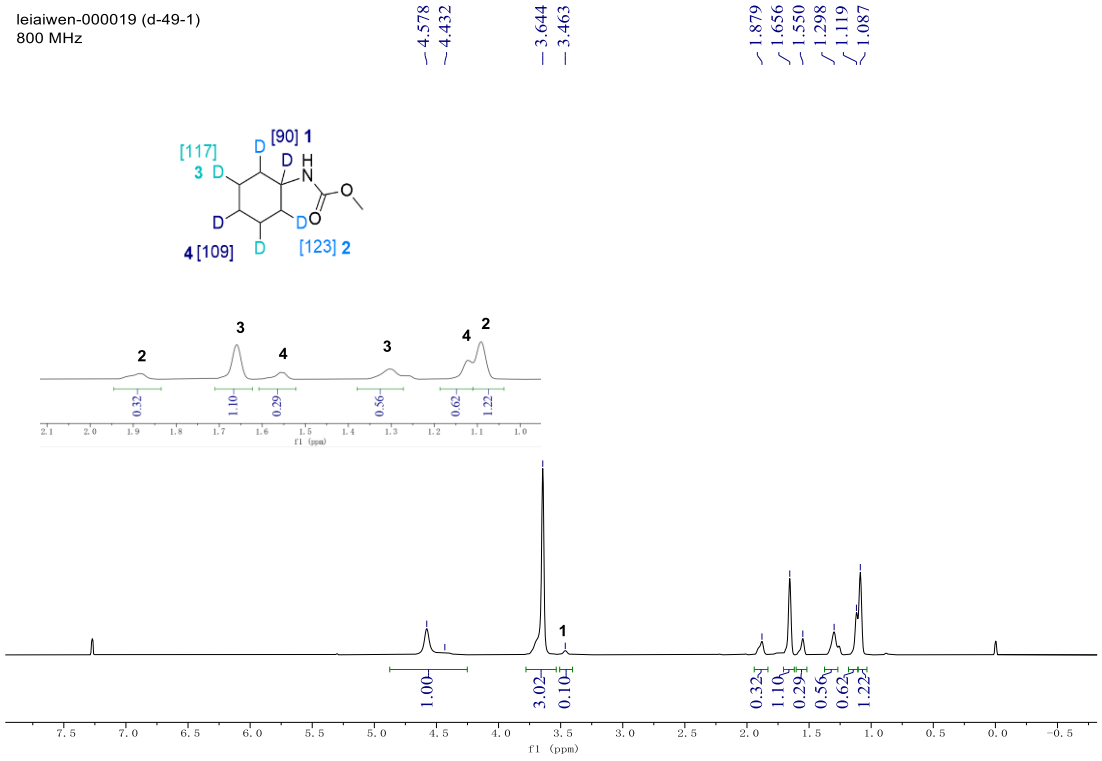


^{13}C NMR for 25b

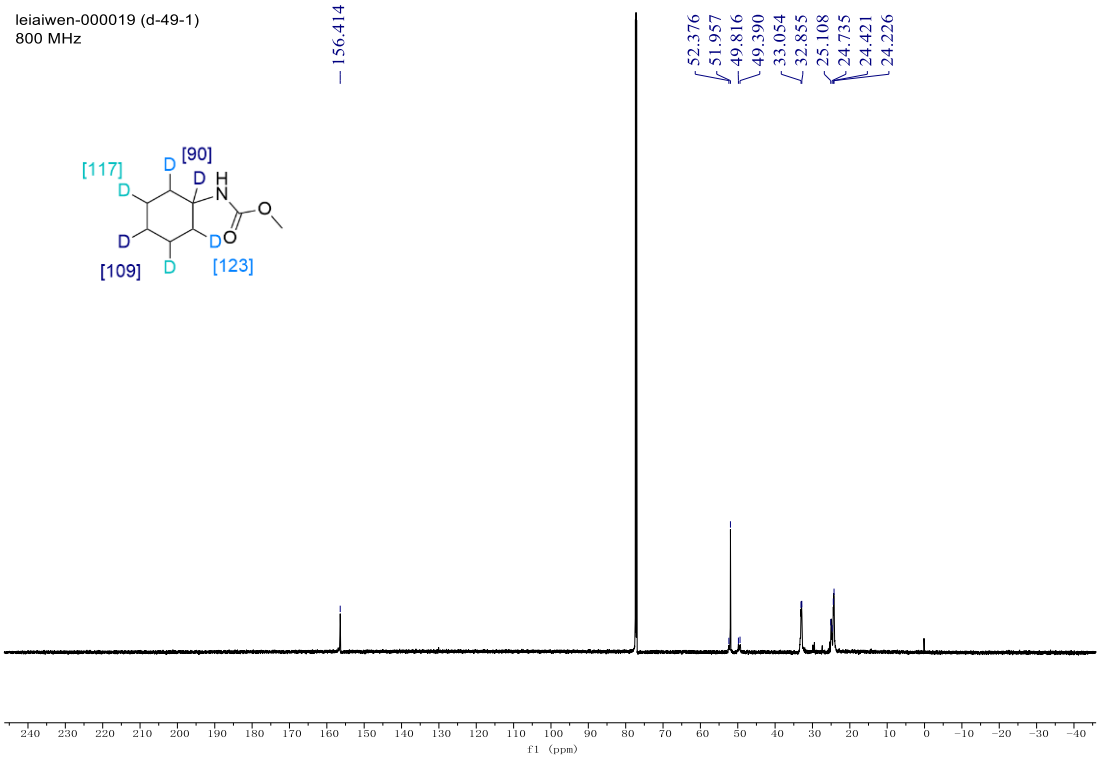


^{1}H NMR for 26b

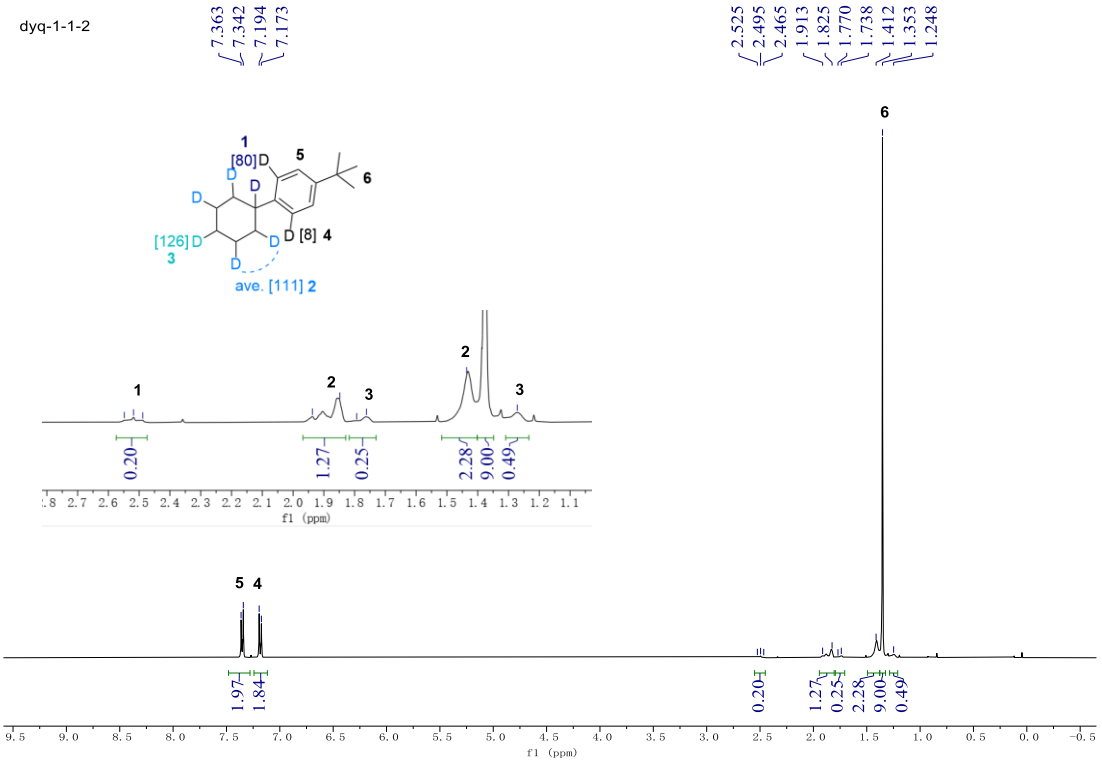




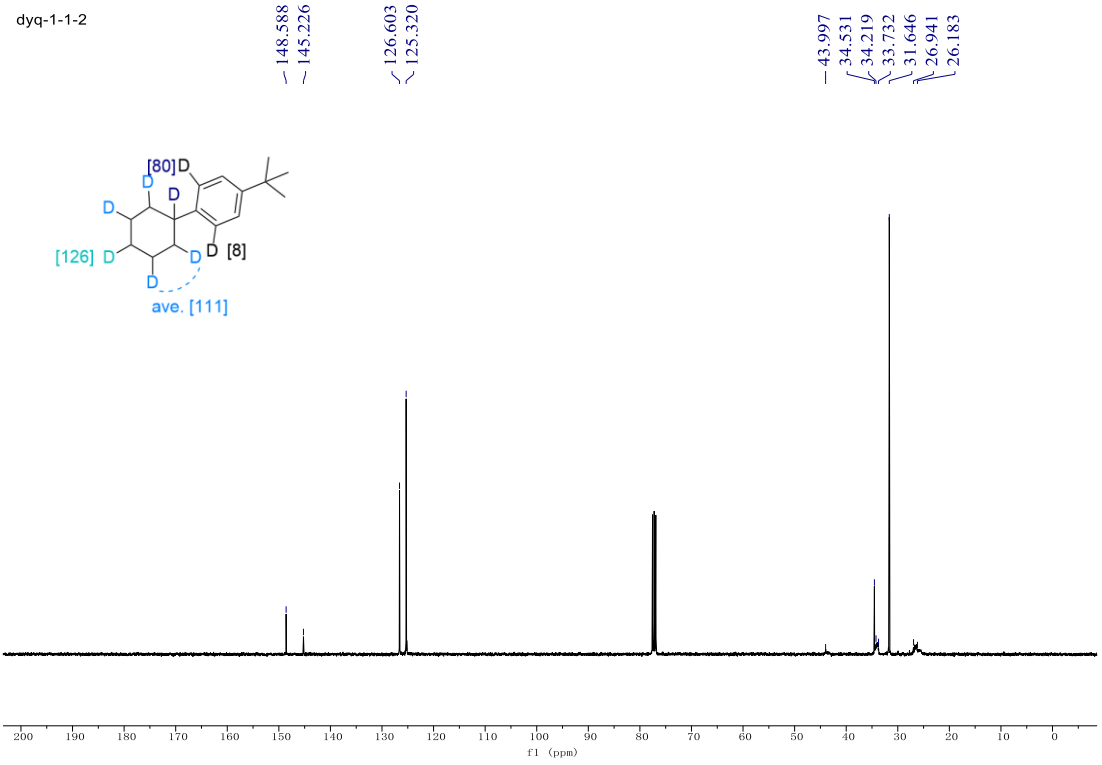
^{13}C NMR for 26b



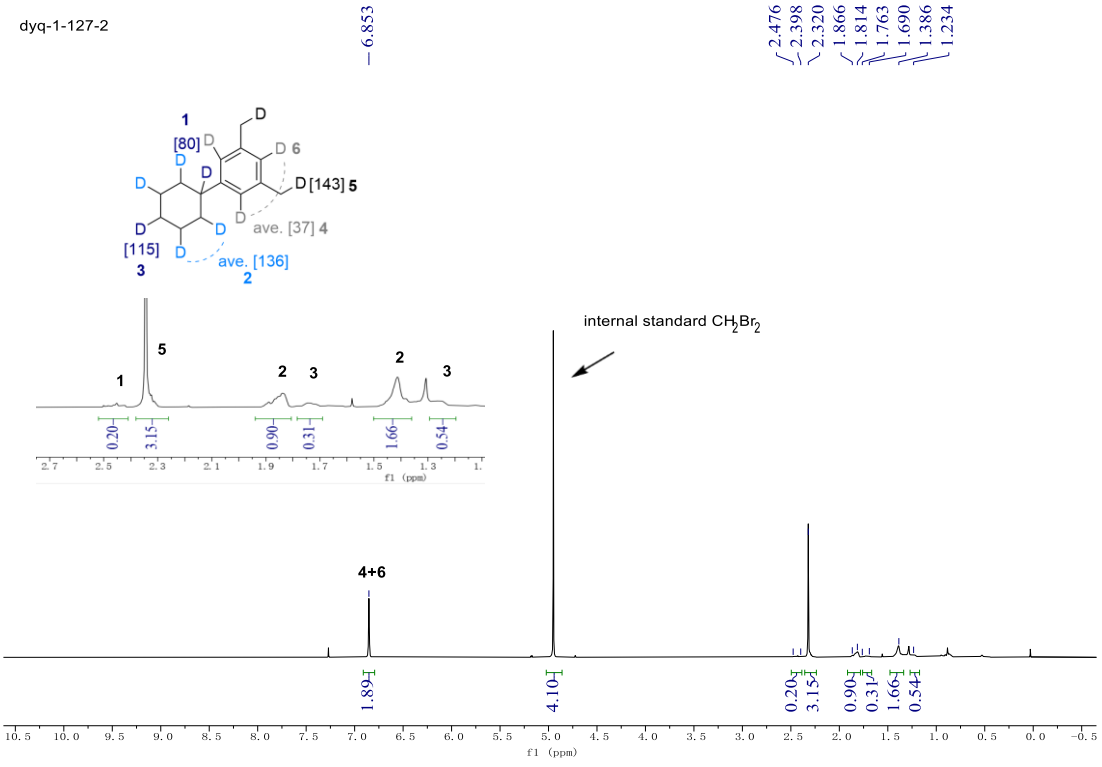
^{1}H NMR for 27b



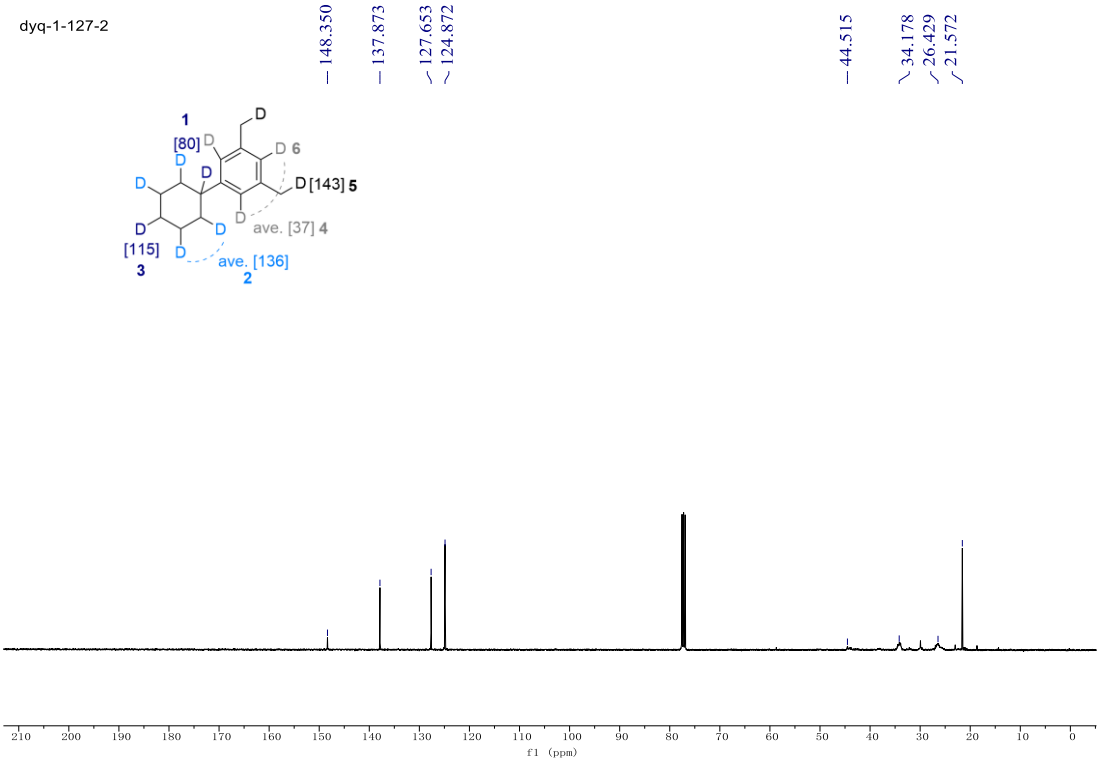
^{13}C NMR for 27b



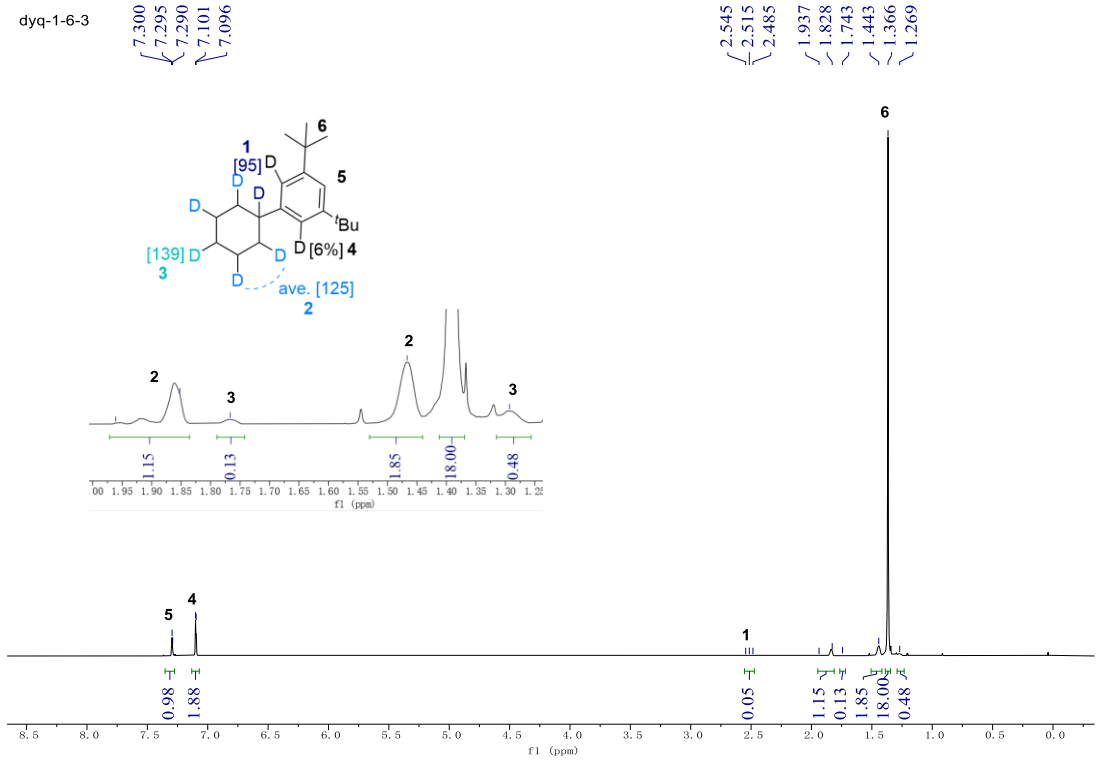
^{1}H NMR for 28b



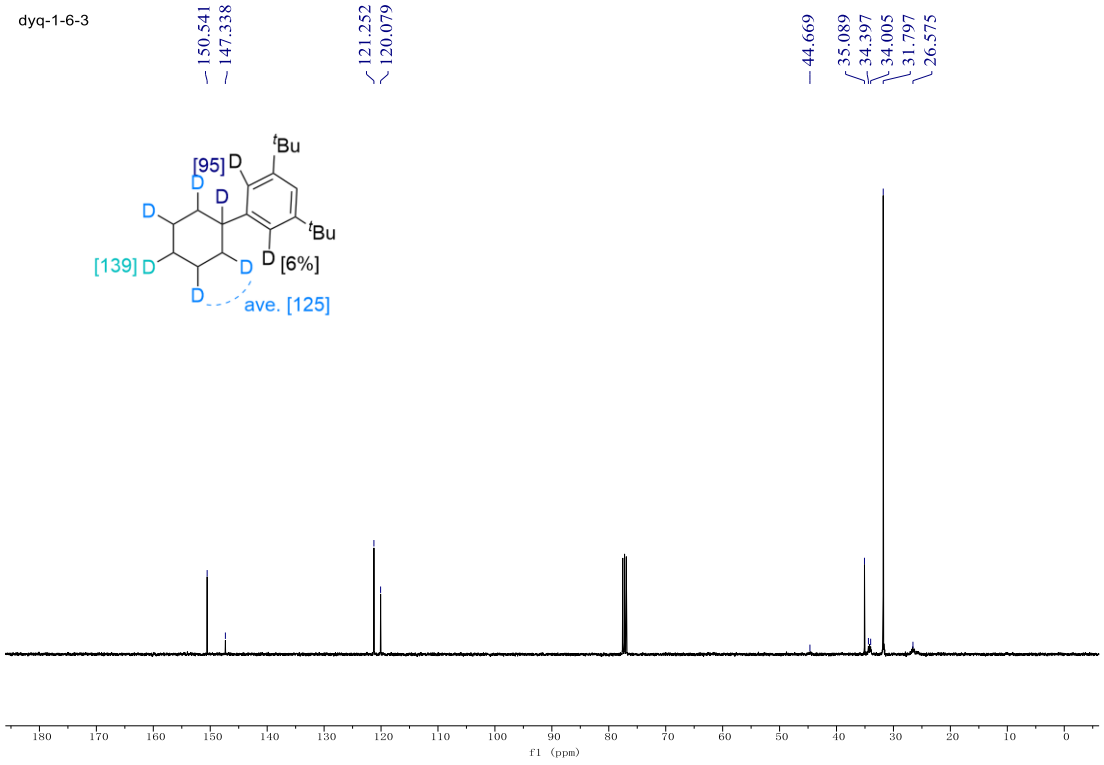
^{13}C NMR for 28b



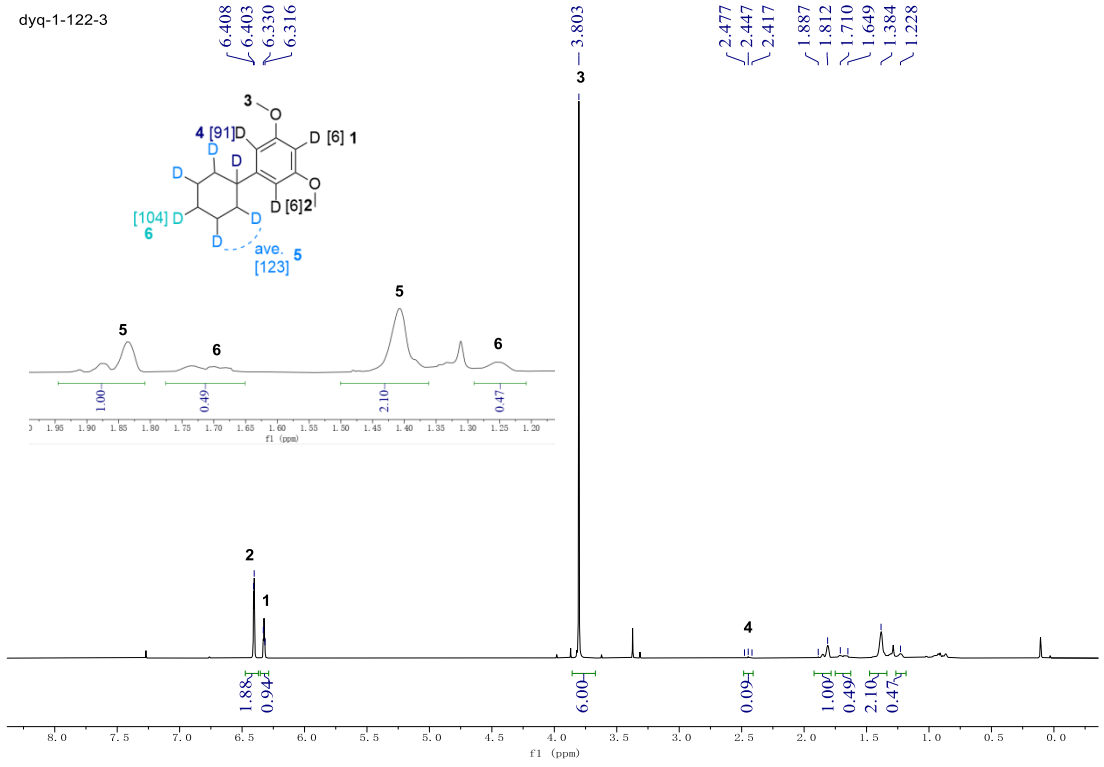
^{1}H NMR for 29b



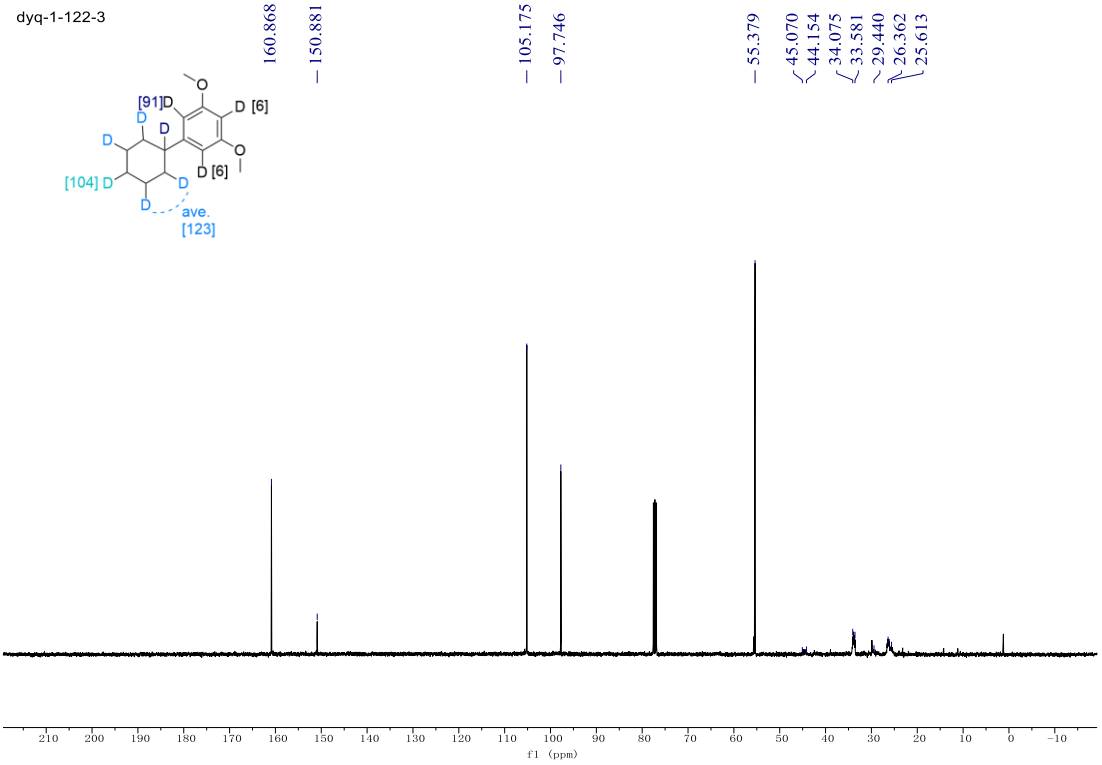
^{13}C NMR for 29b



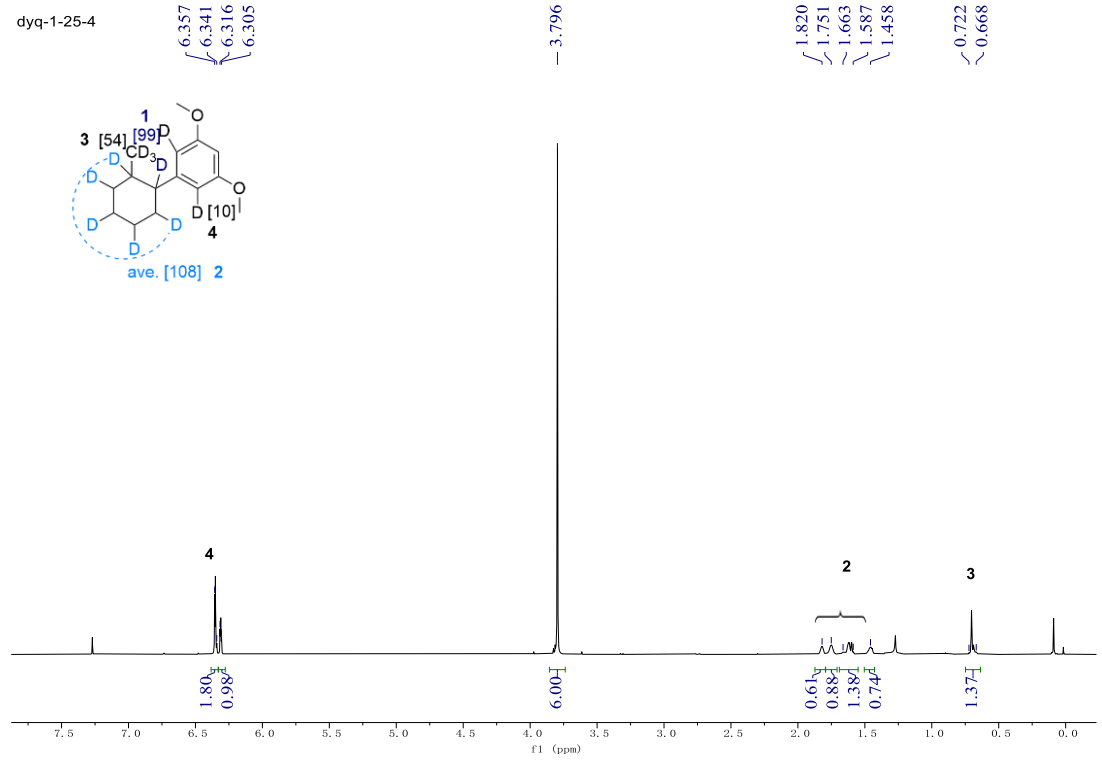
^{1}H NMR for 30b



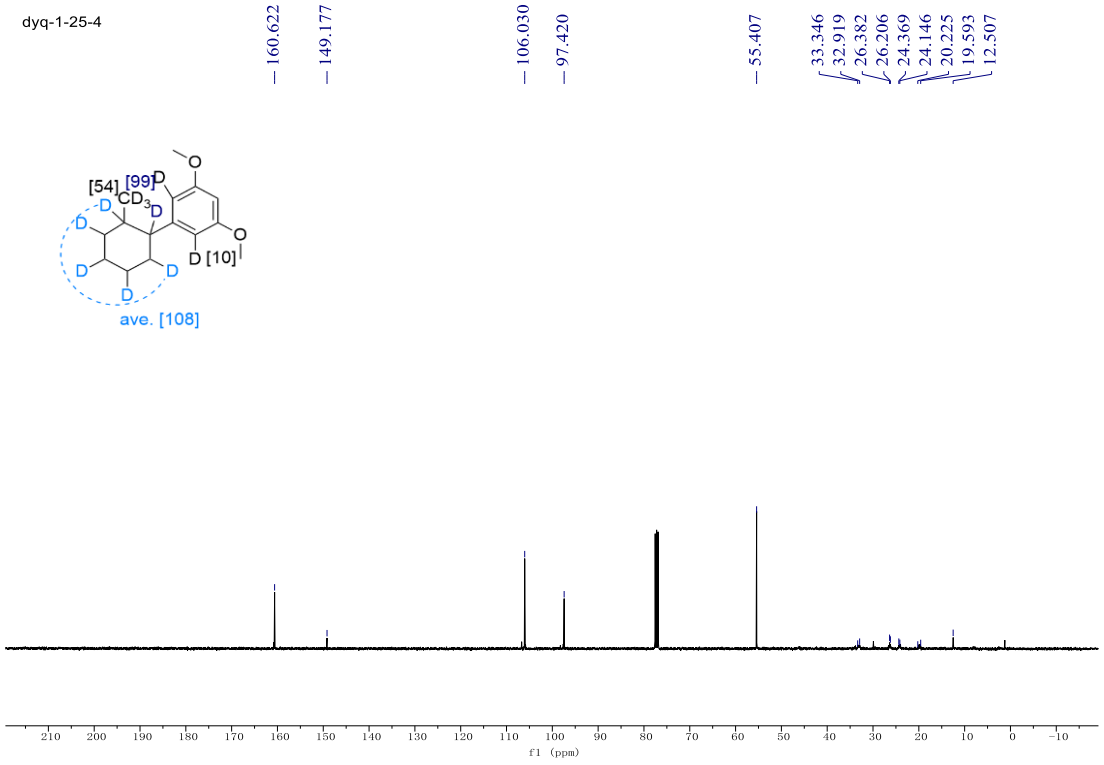
^{13}C NMR for 30b



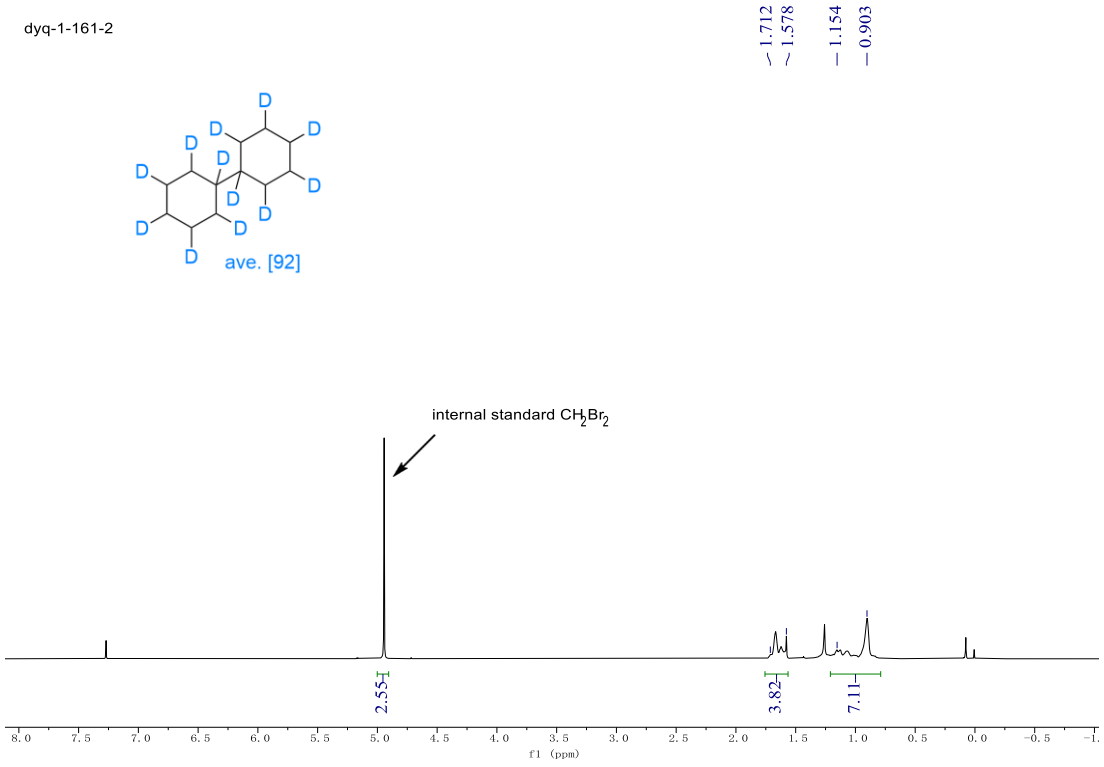
^{1}H NMR for 31b



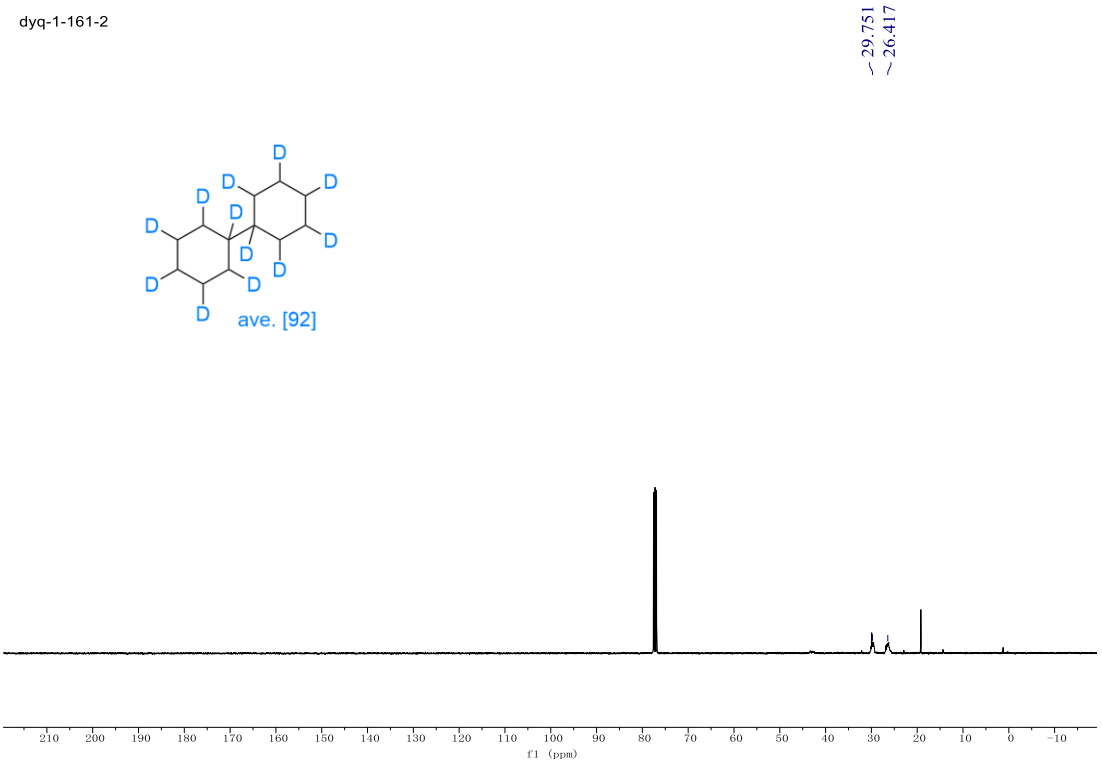
^{13}C NMR for 31b



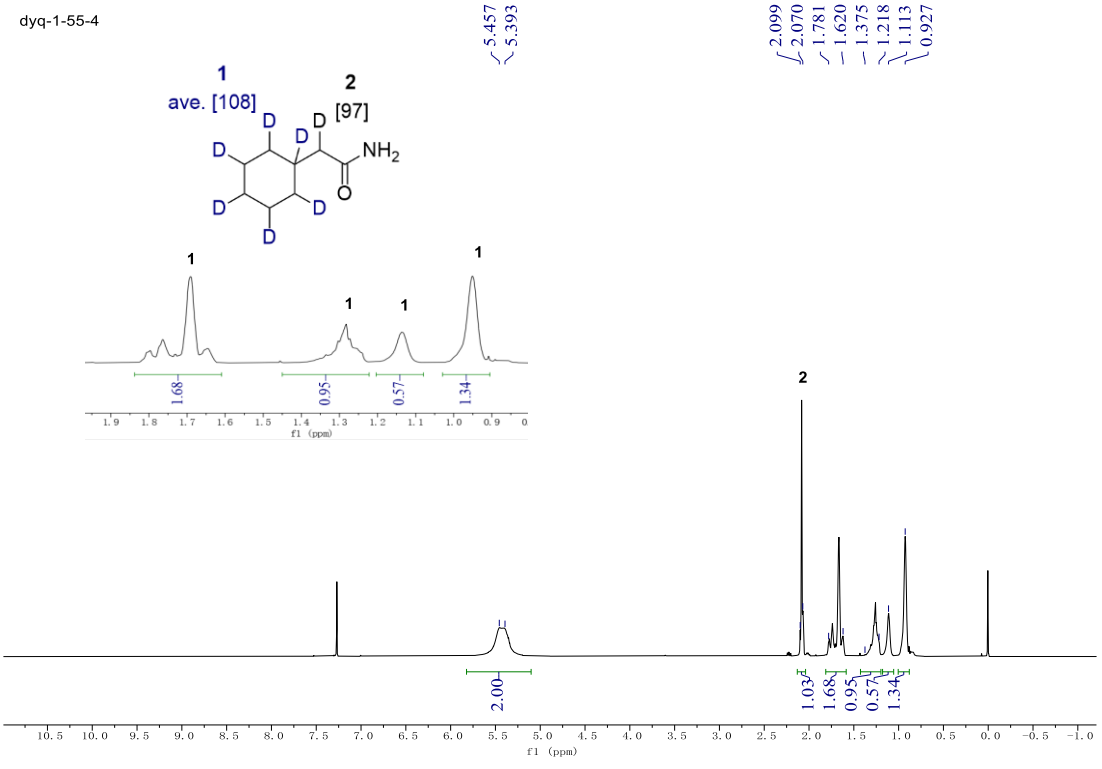
^{1}H NMR for 32b



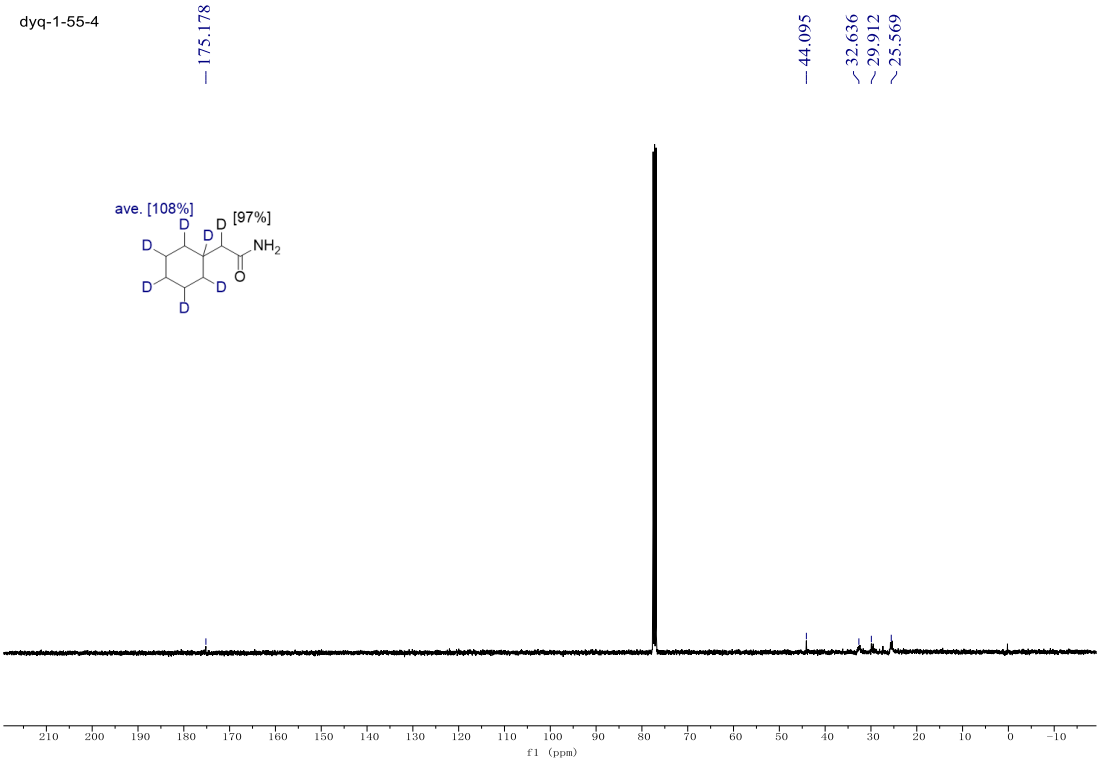
^{13}C NMR for 32b



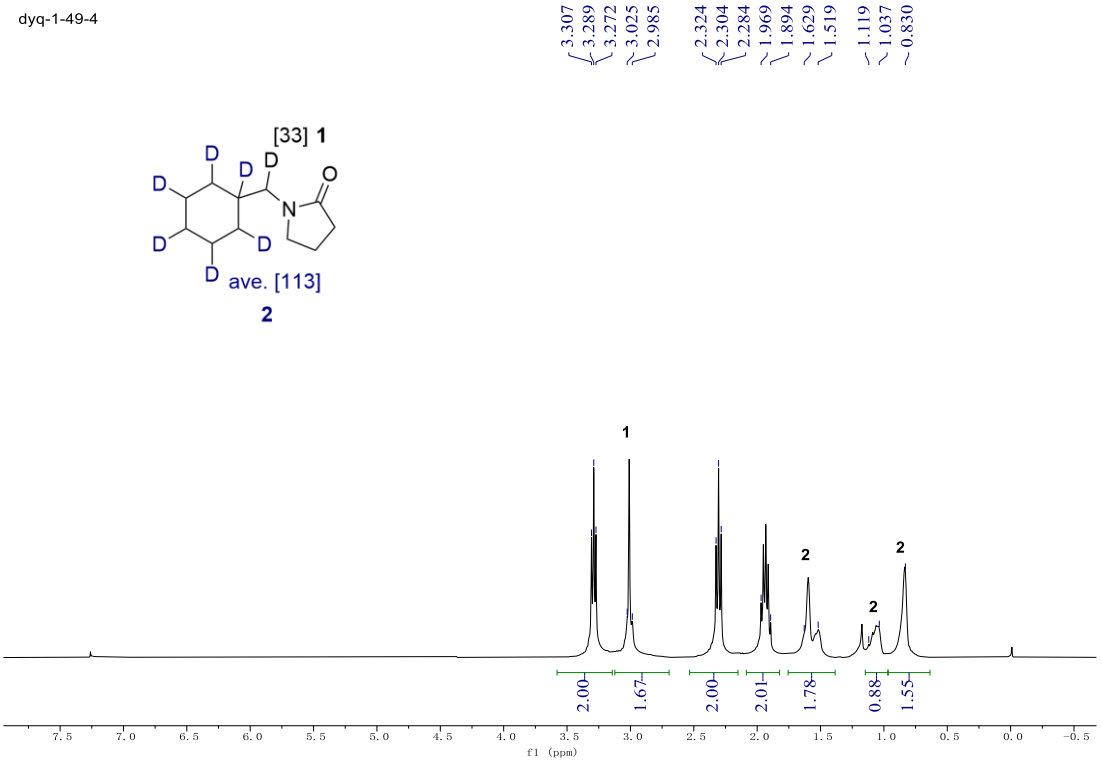
^{1}H NMR for 33b



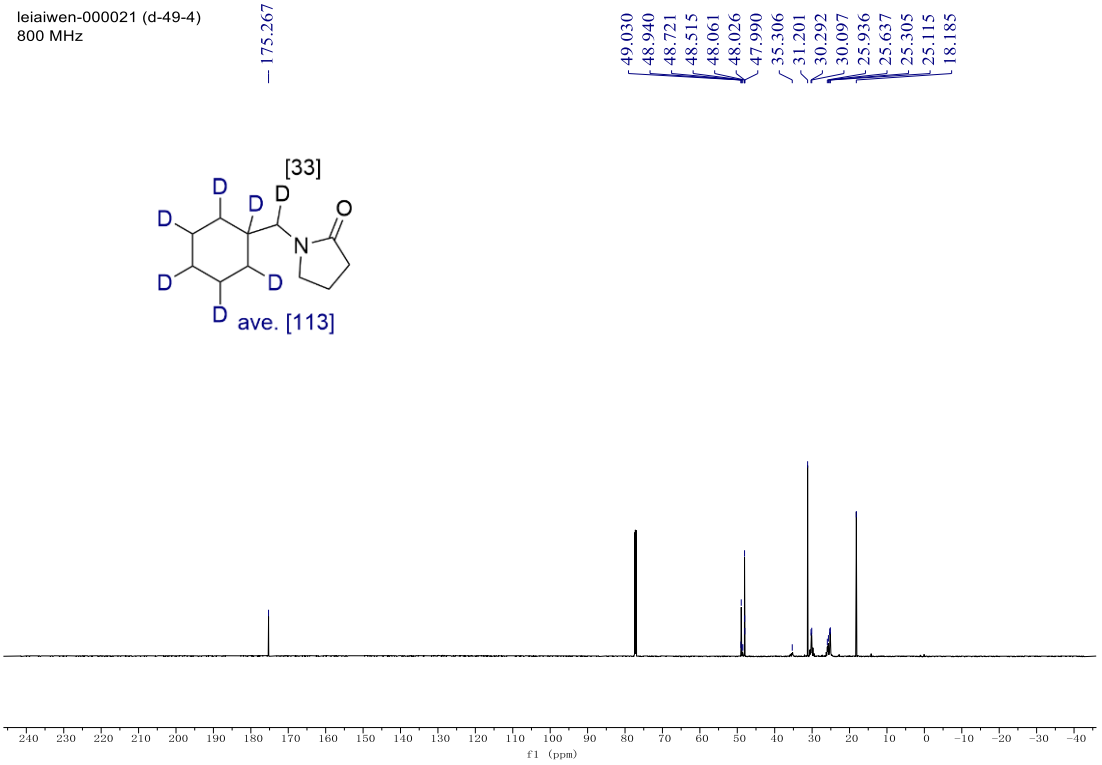
^{13}C NMR for 33b



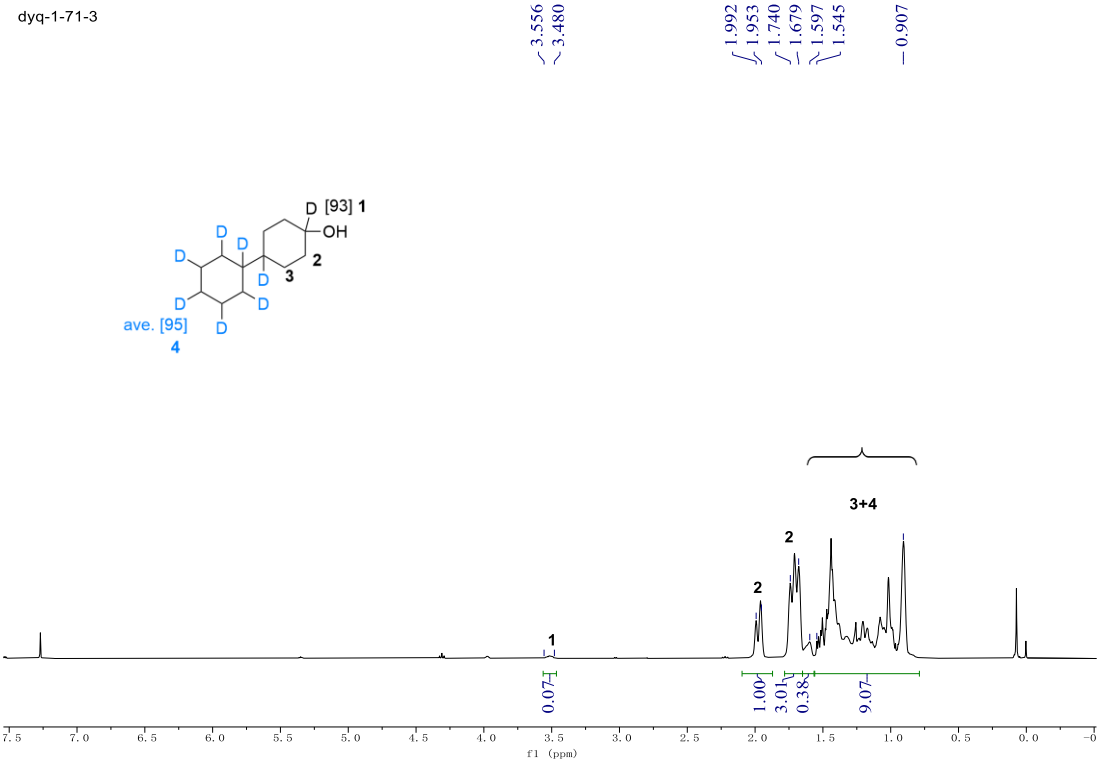
^{1}H NMR for 34b



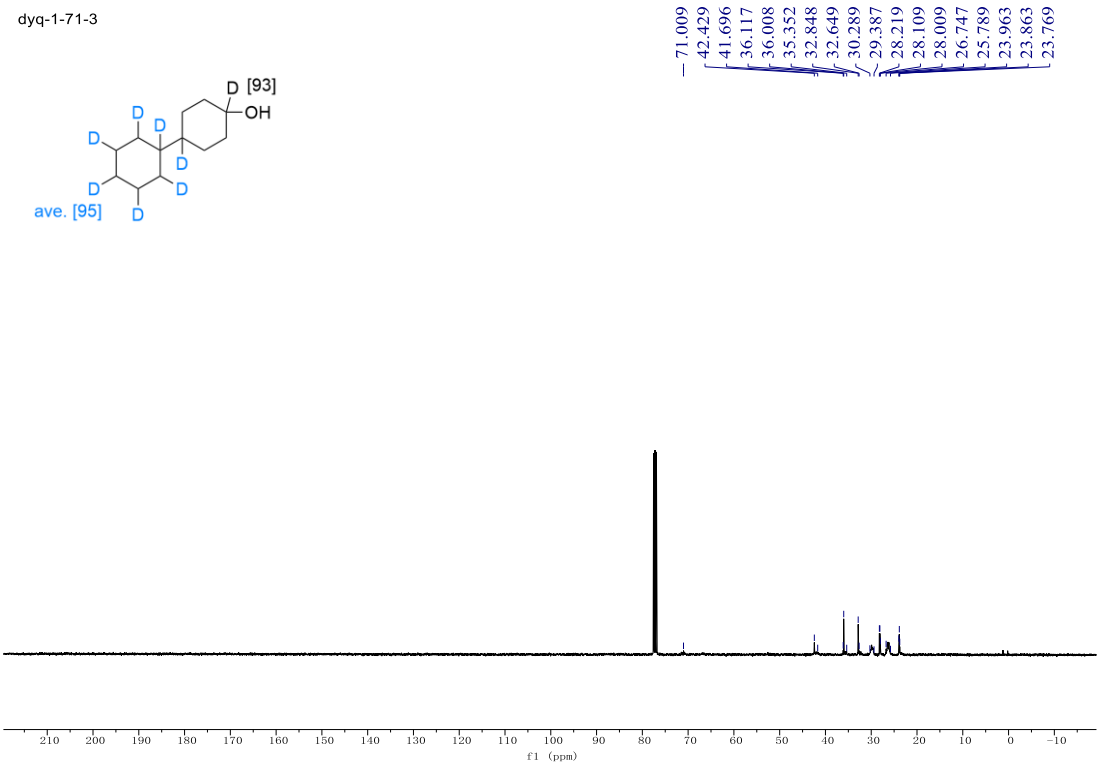
^{13}C NMR for 34b



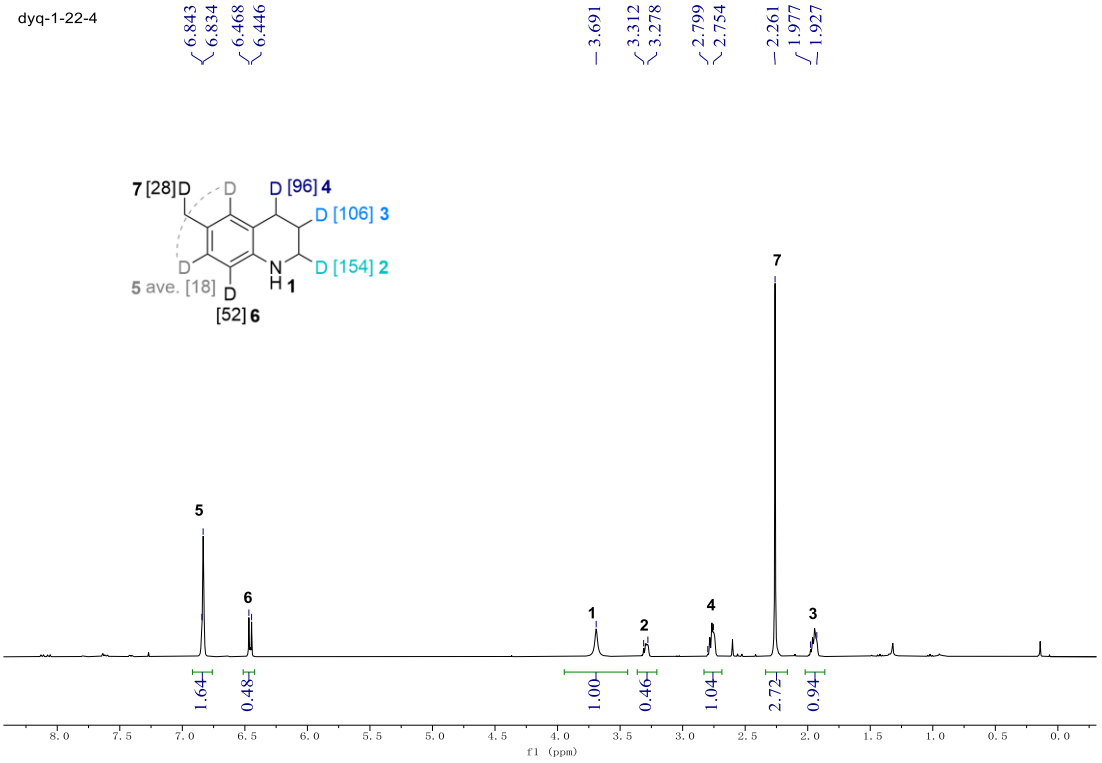
^{1}H NMR for 35b



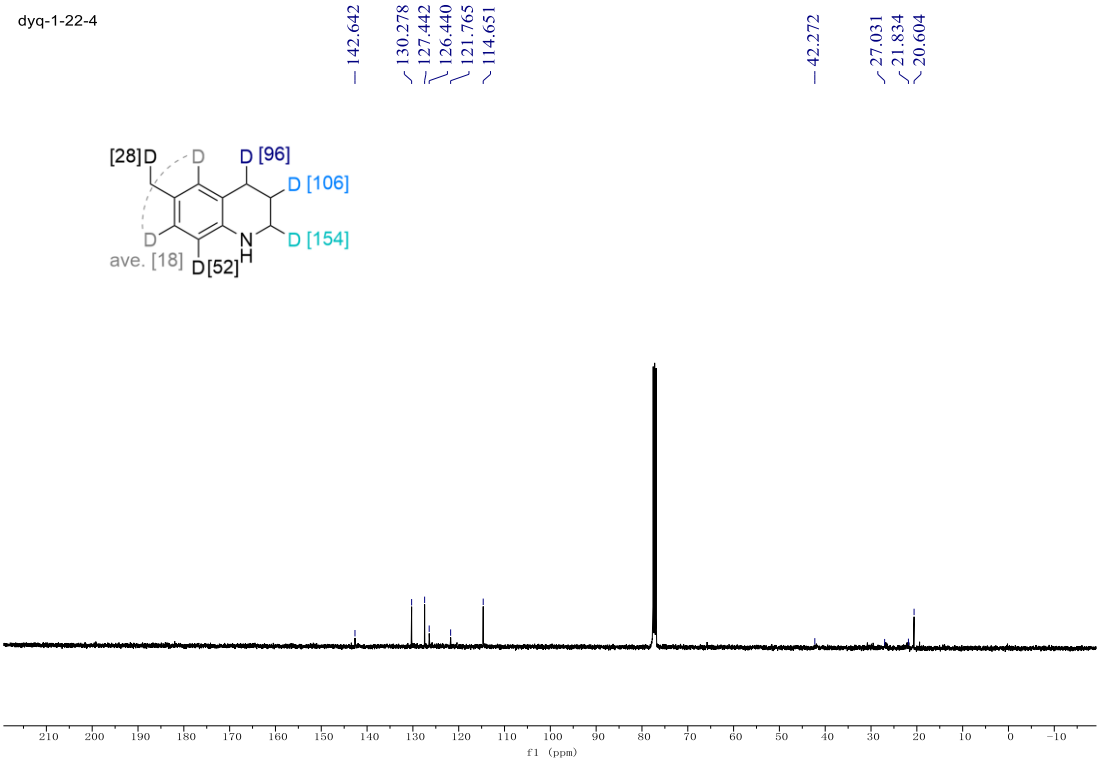
^{13}C NMR for 35b



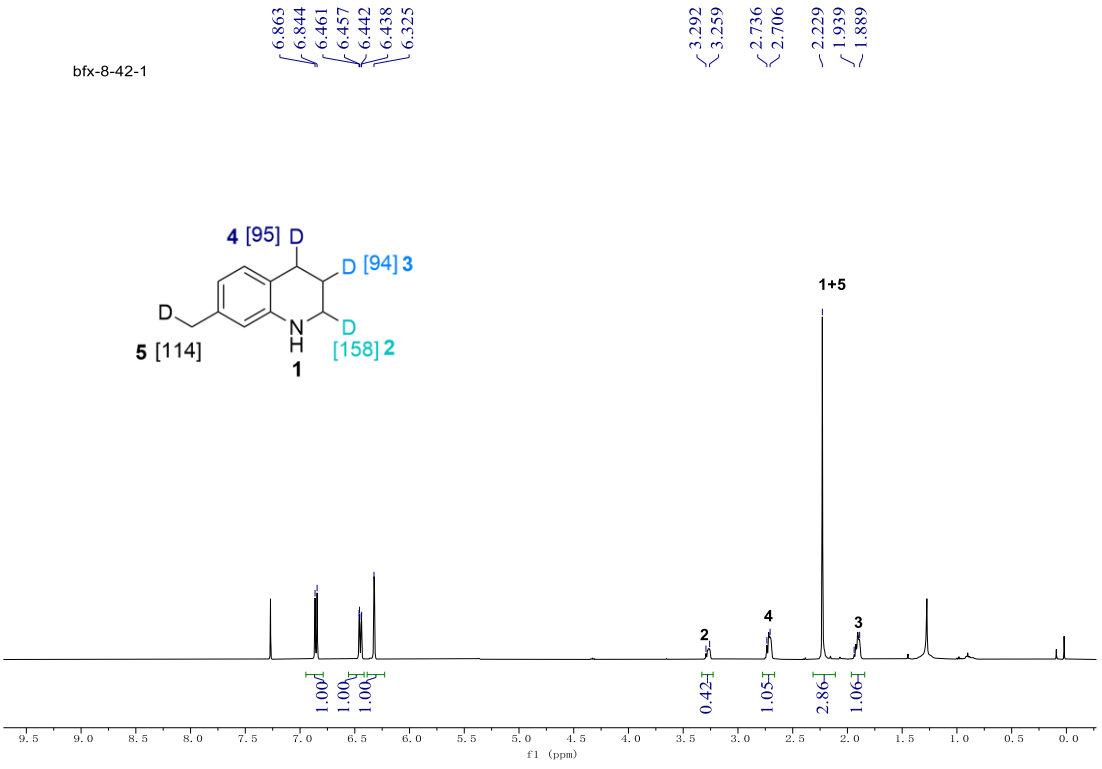
^{1}H NMR for 36b



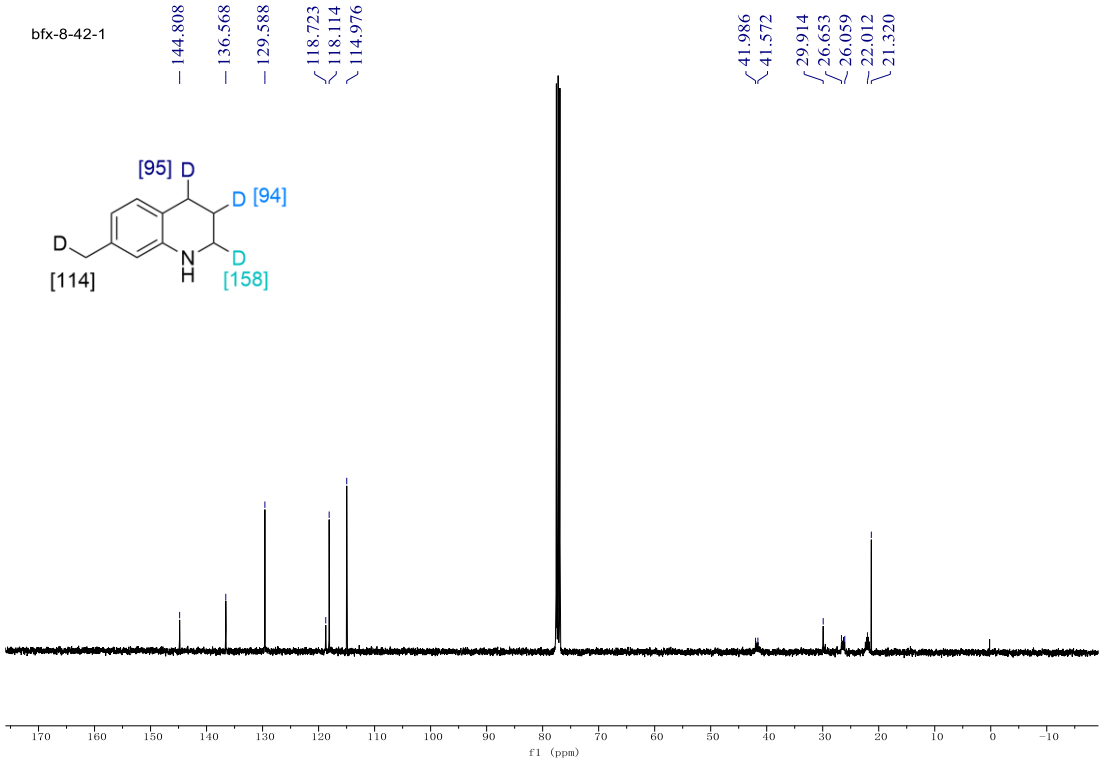
^{13}C NMR for 36b



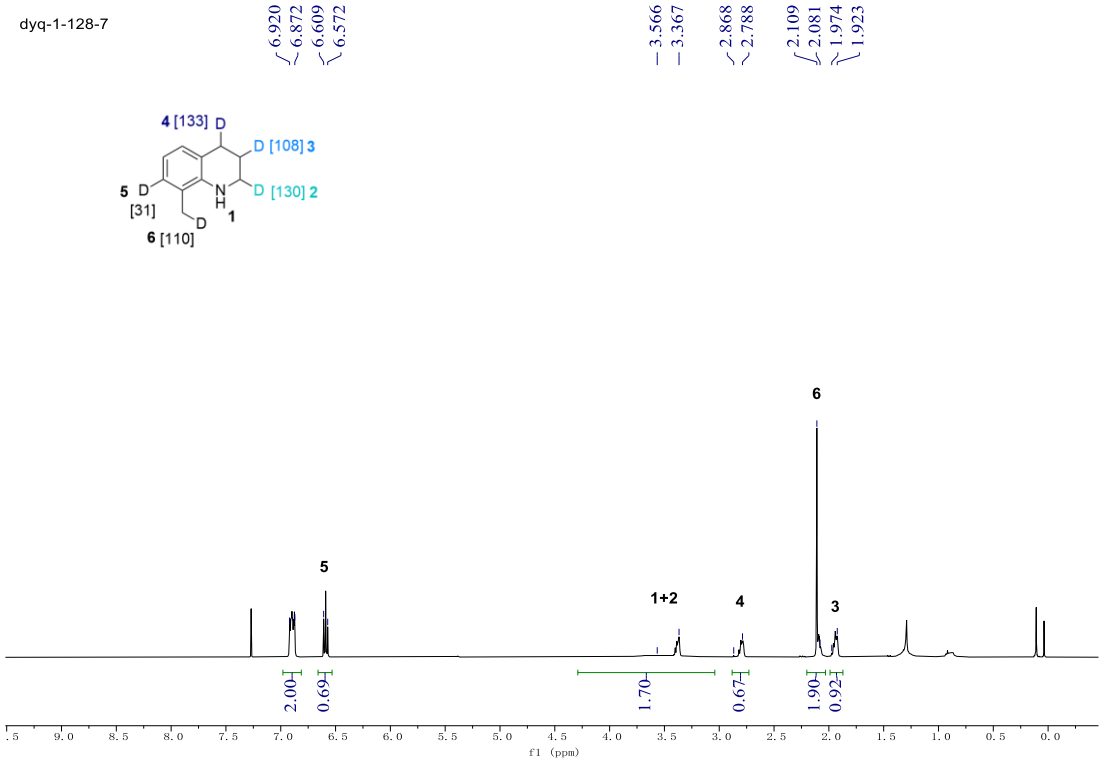
^{1}H NMR for 37b



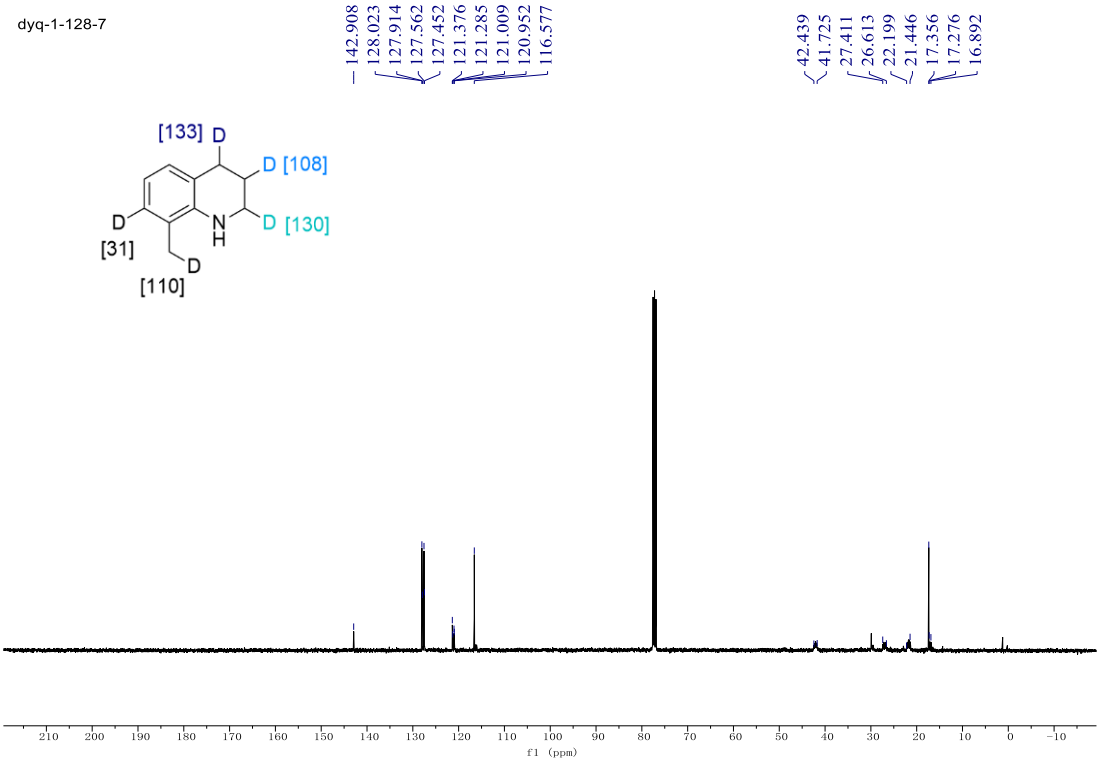
^{13}C NMR for 37b



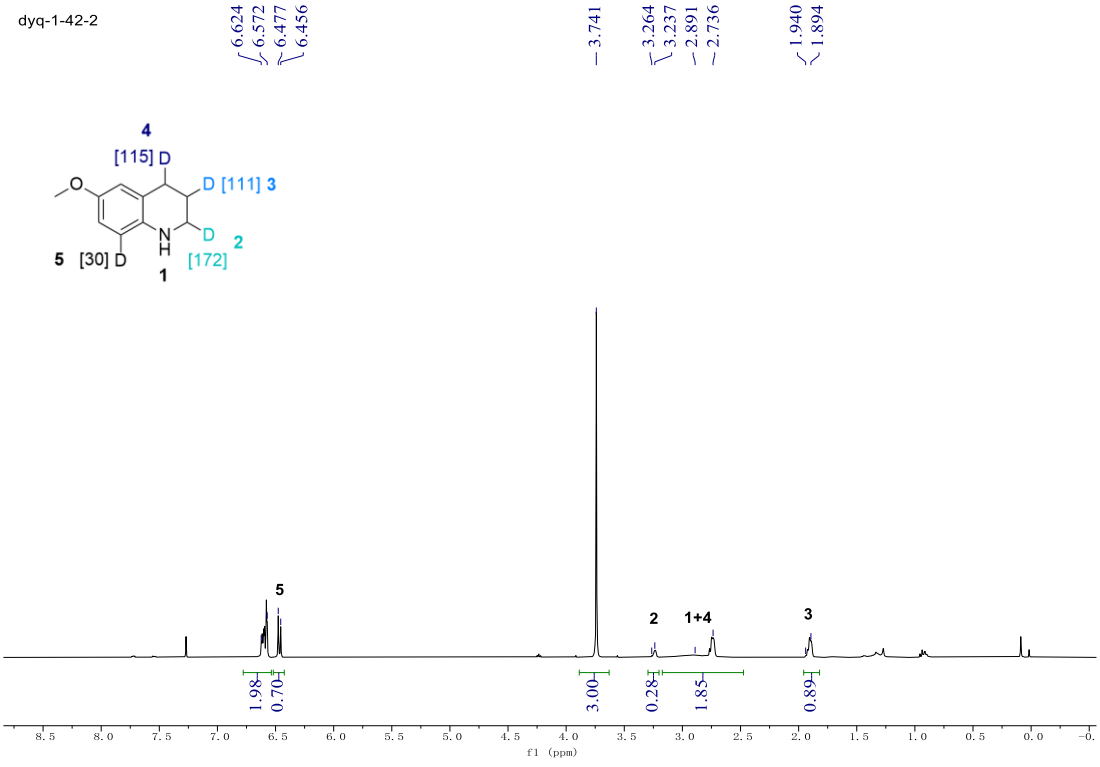
^{1}H NMR for 38b



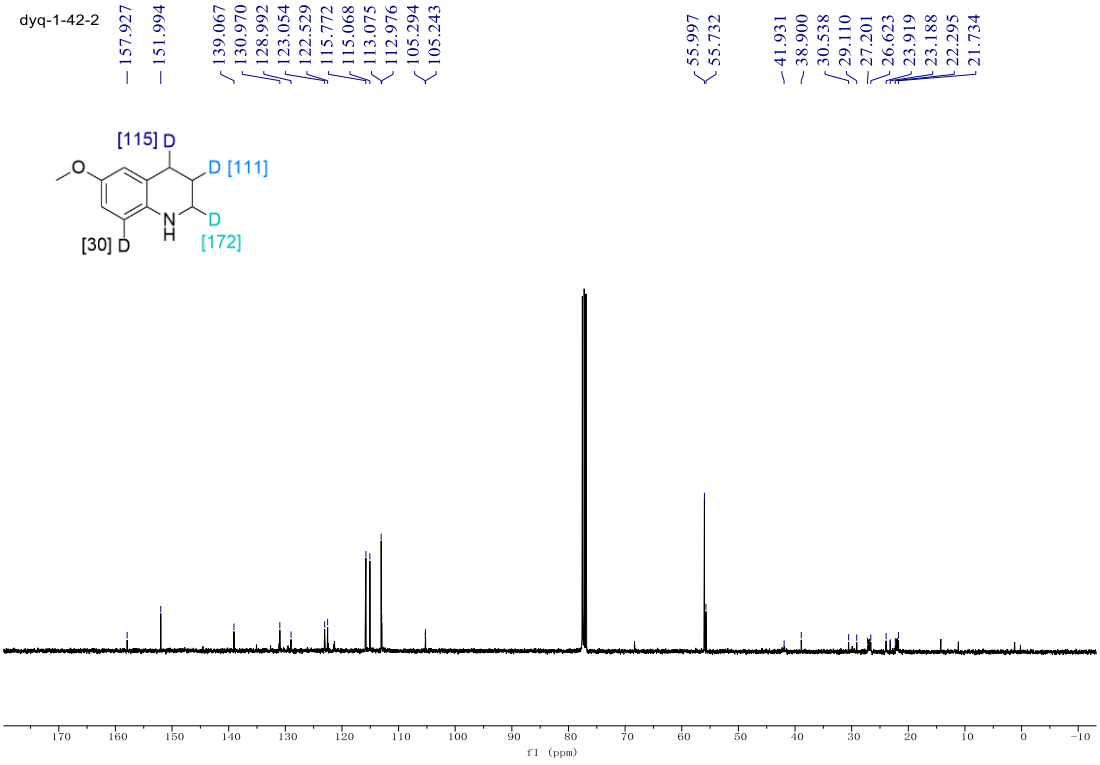
^{13}C NMR for 38b



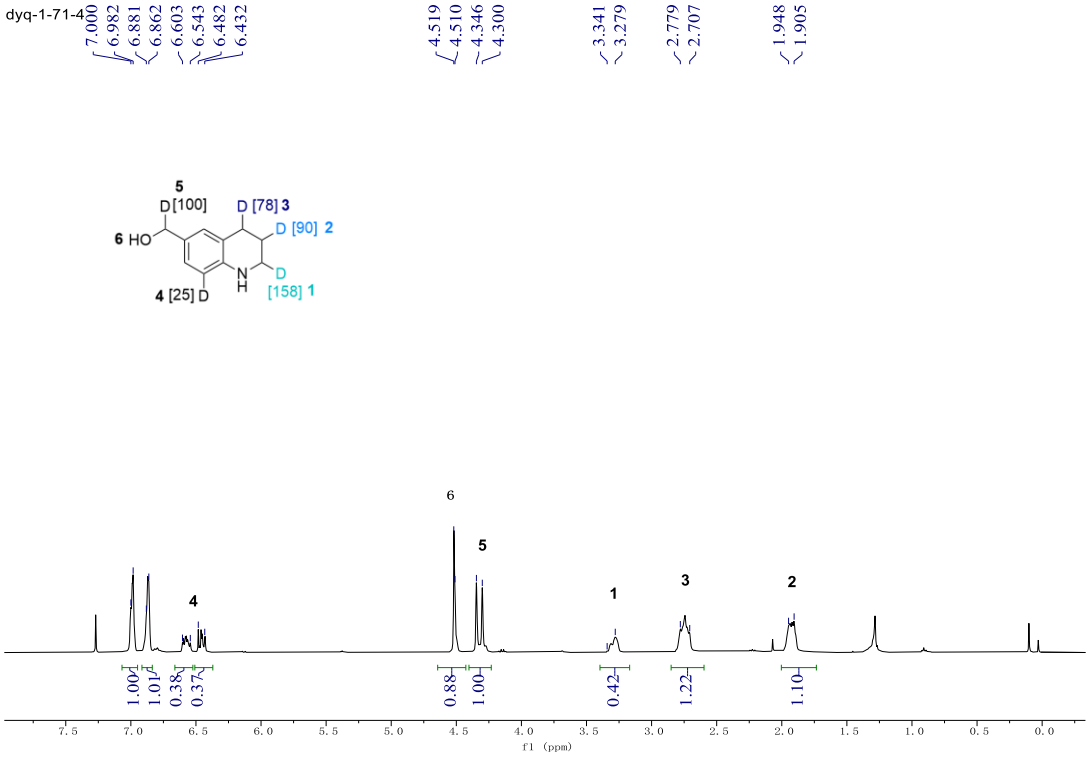
^{1}H NMR for 39b



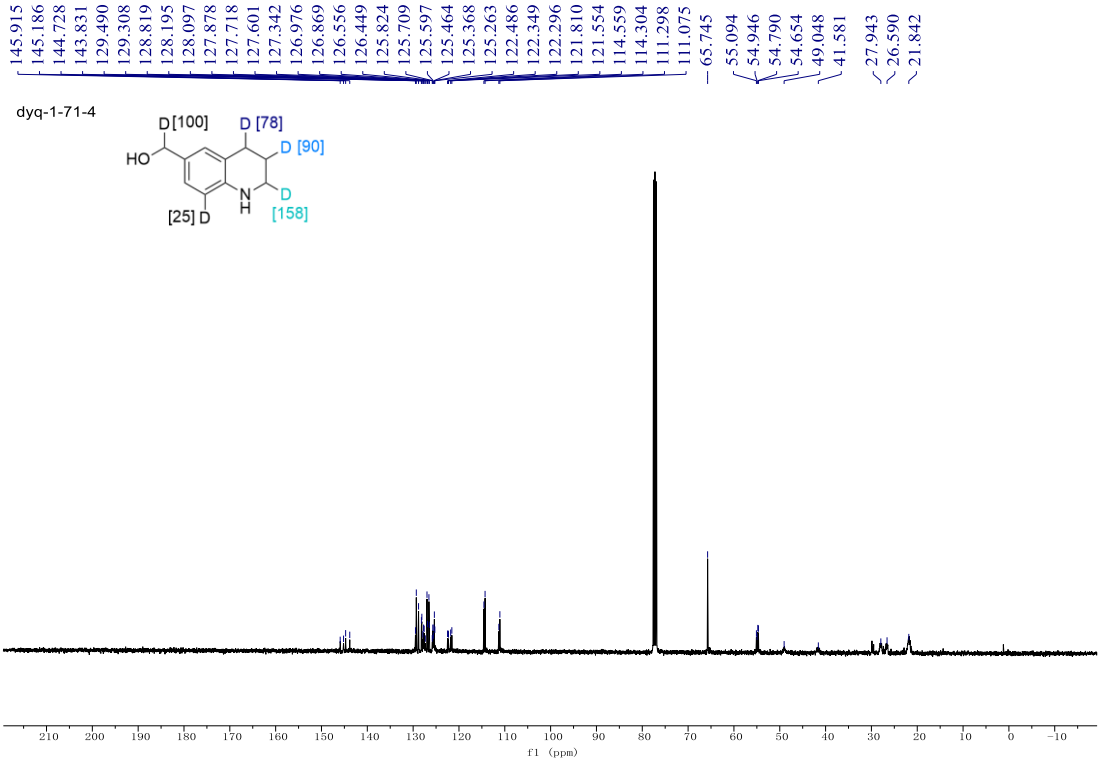
^{13}C NMR for 39b



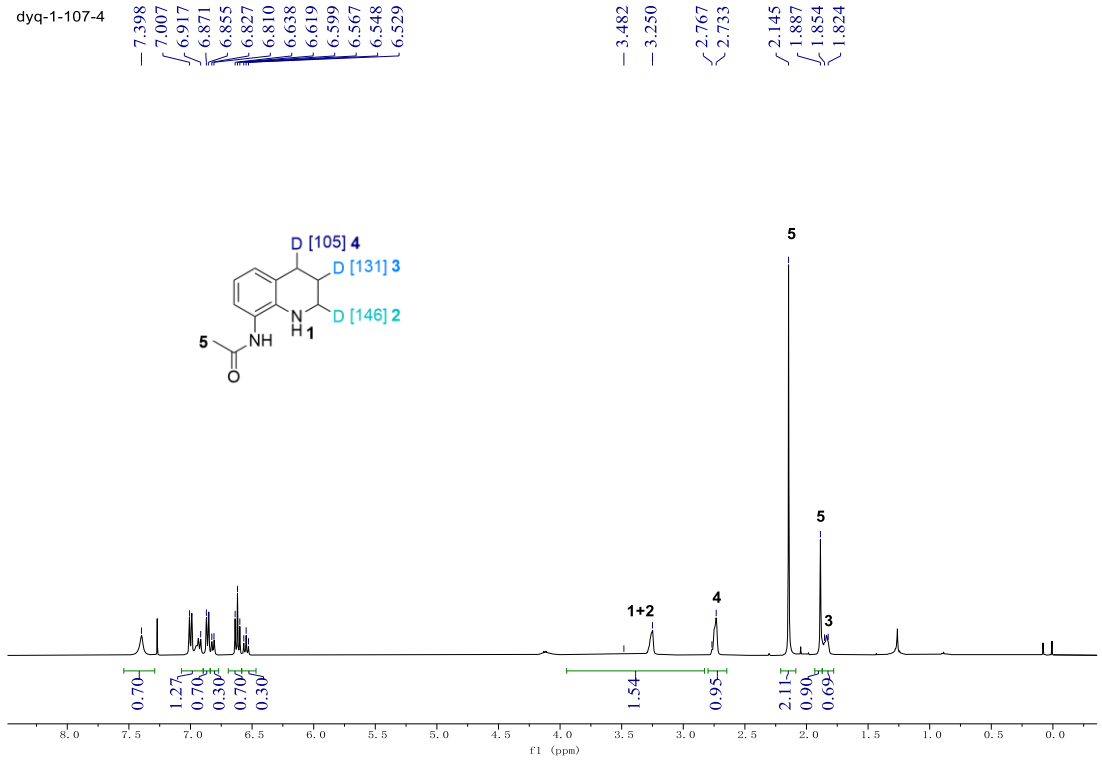
^{1}H NMR for 40b



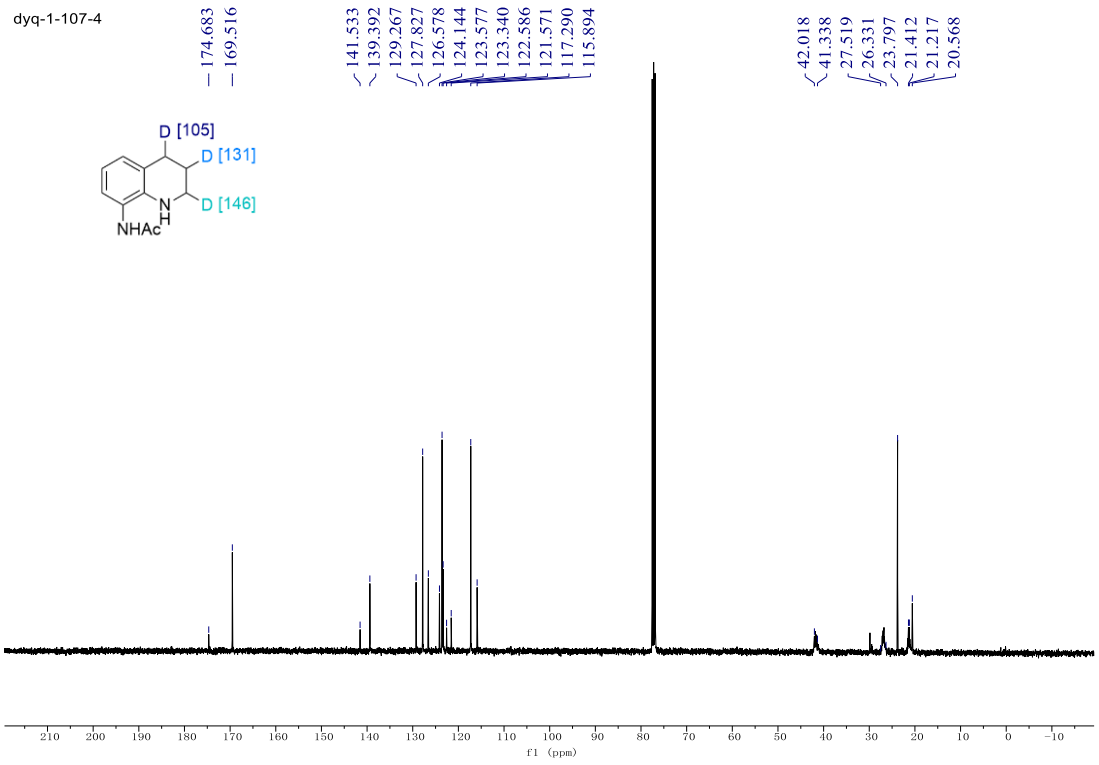
^{13}C NMR for 40b



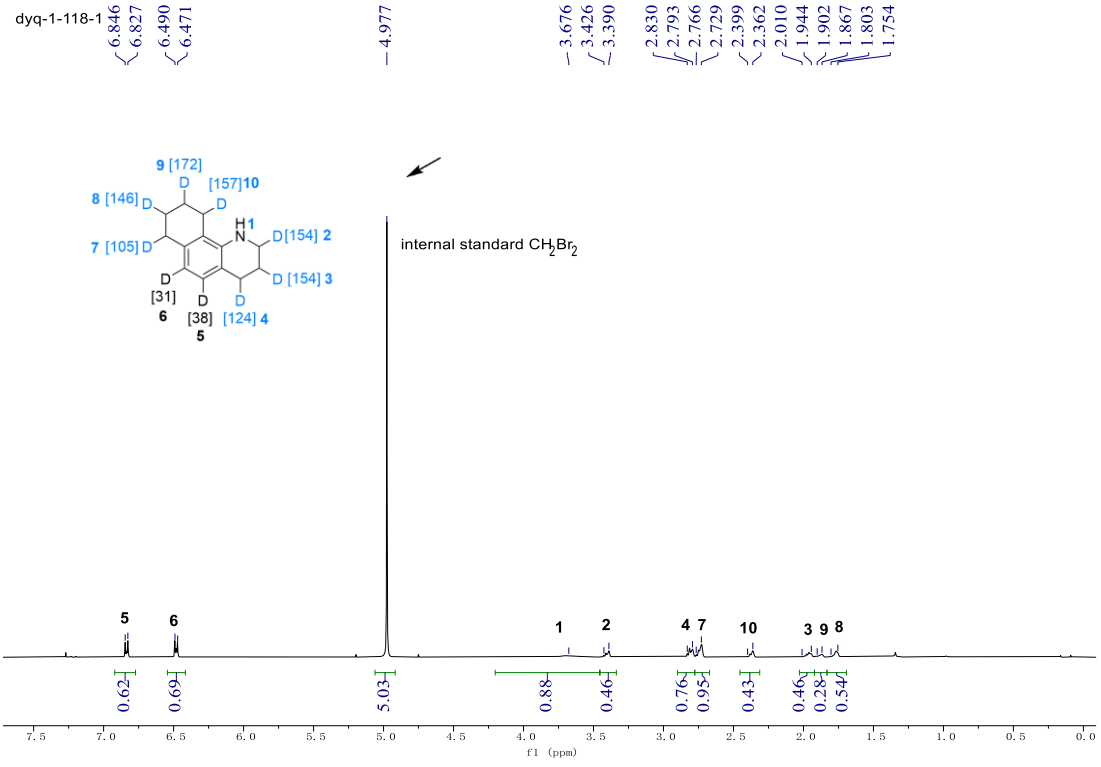
^{1}H NMR for 41b



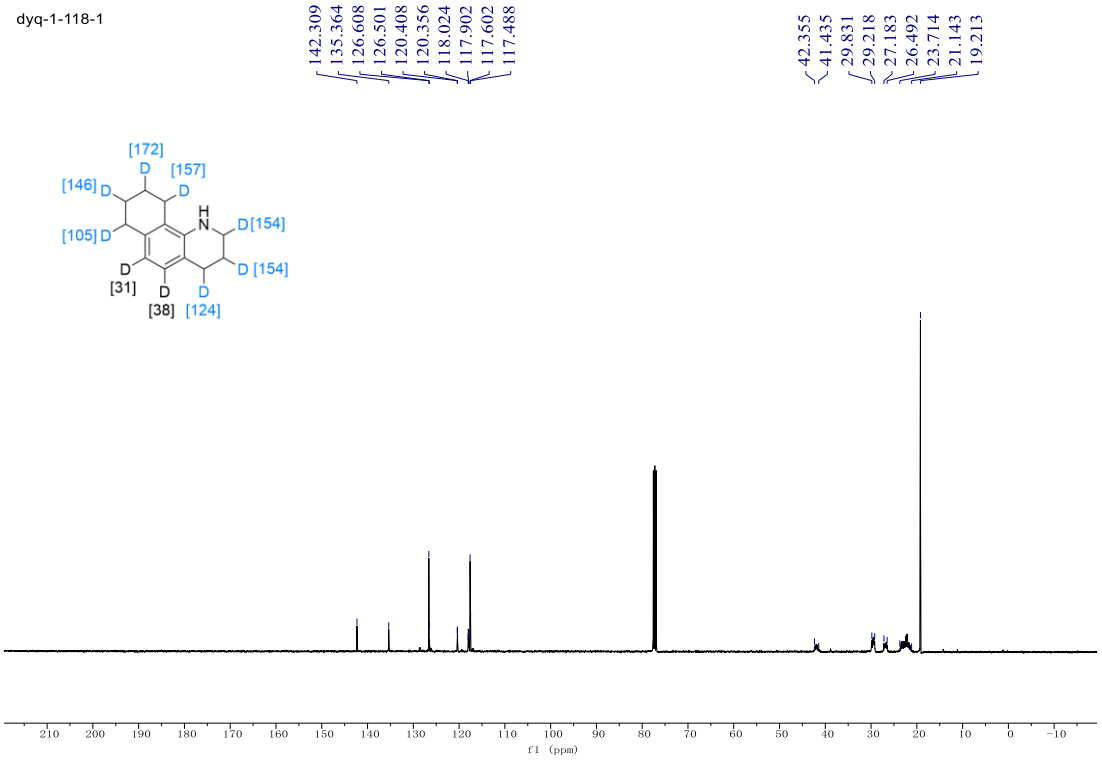
^{13}C NMR for 41b



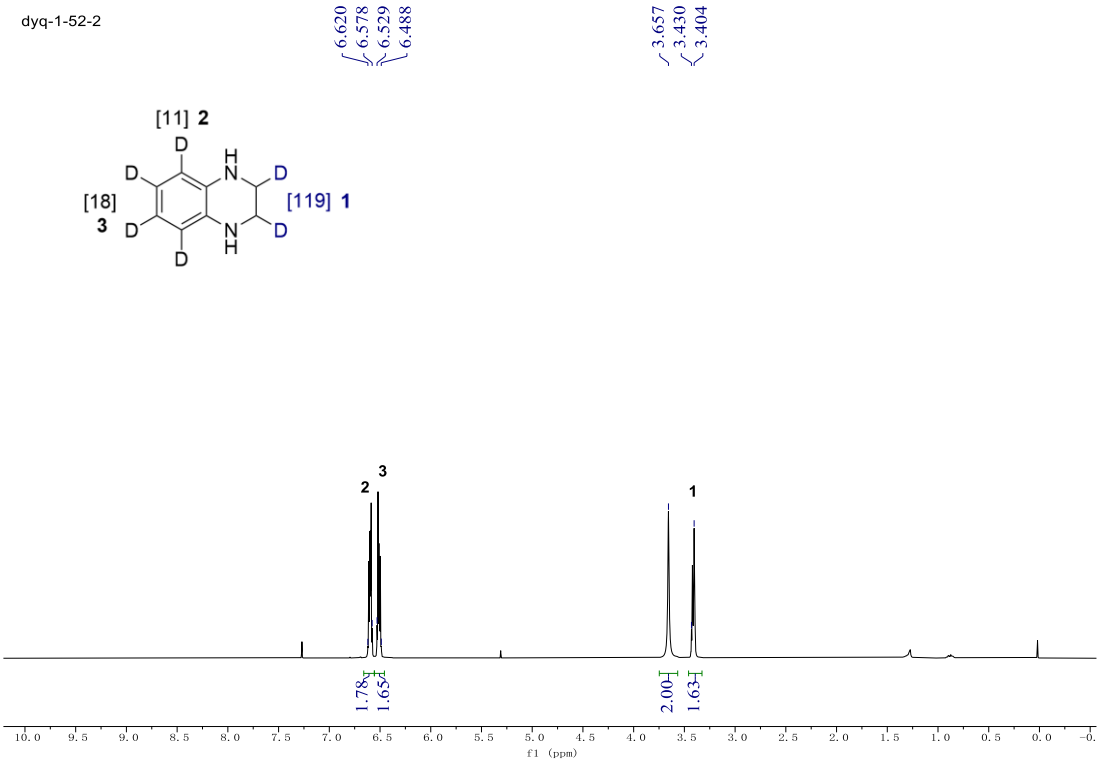
^{1}H NMR for 42b



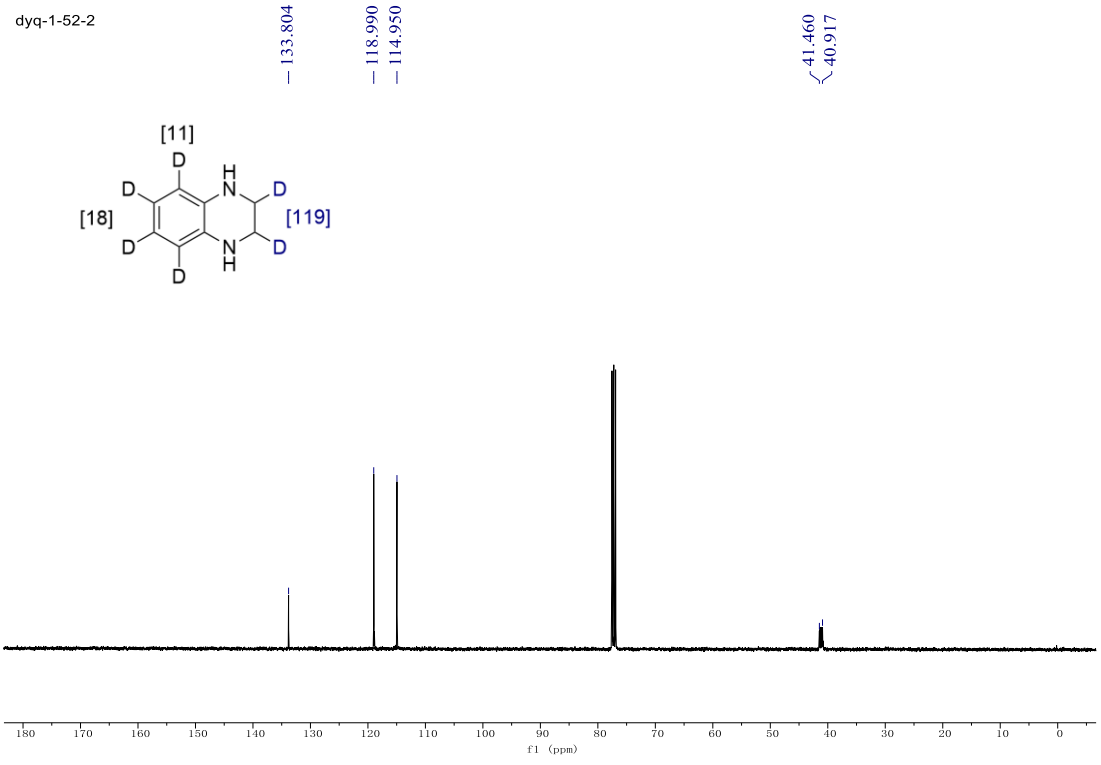
^{13}C NMR for 42b



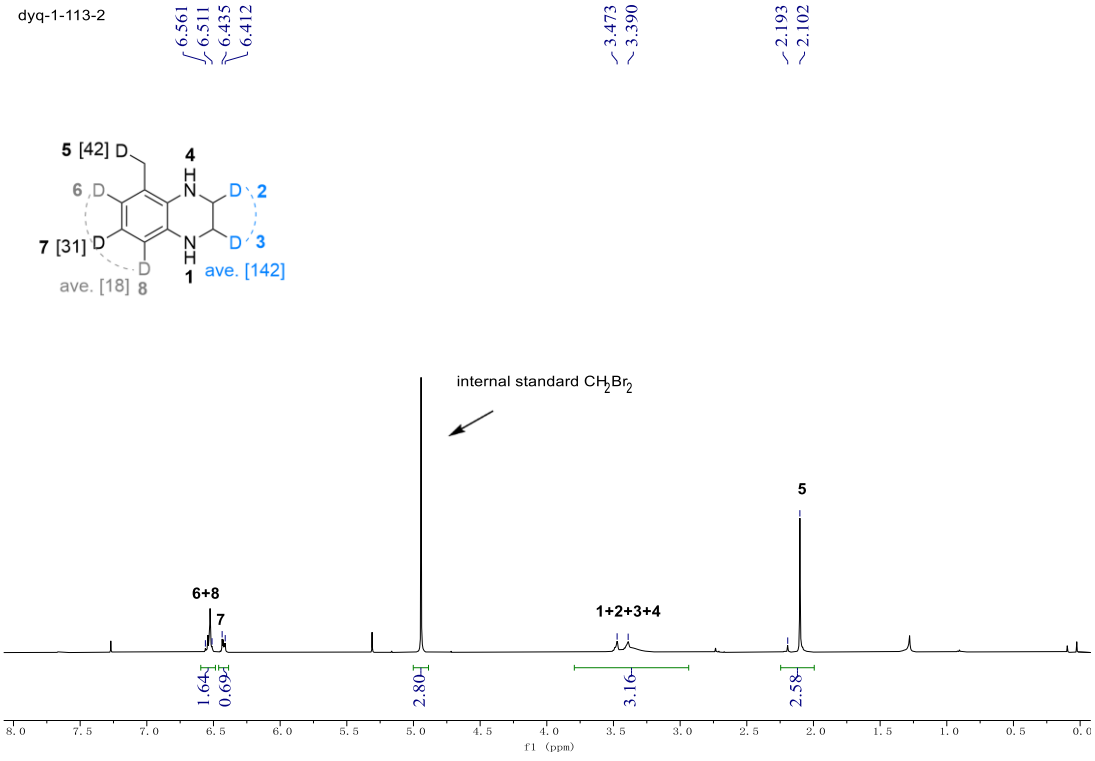
^{1}H NMR for 43b



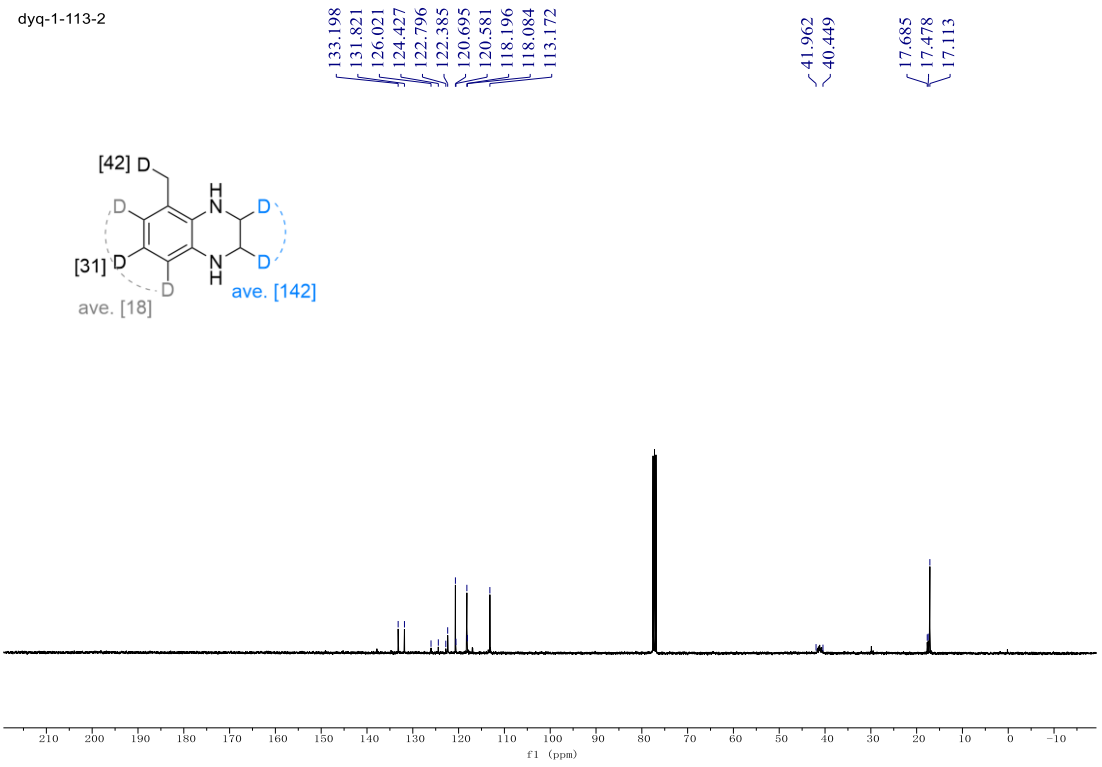
^{13}C NMR for 43b



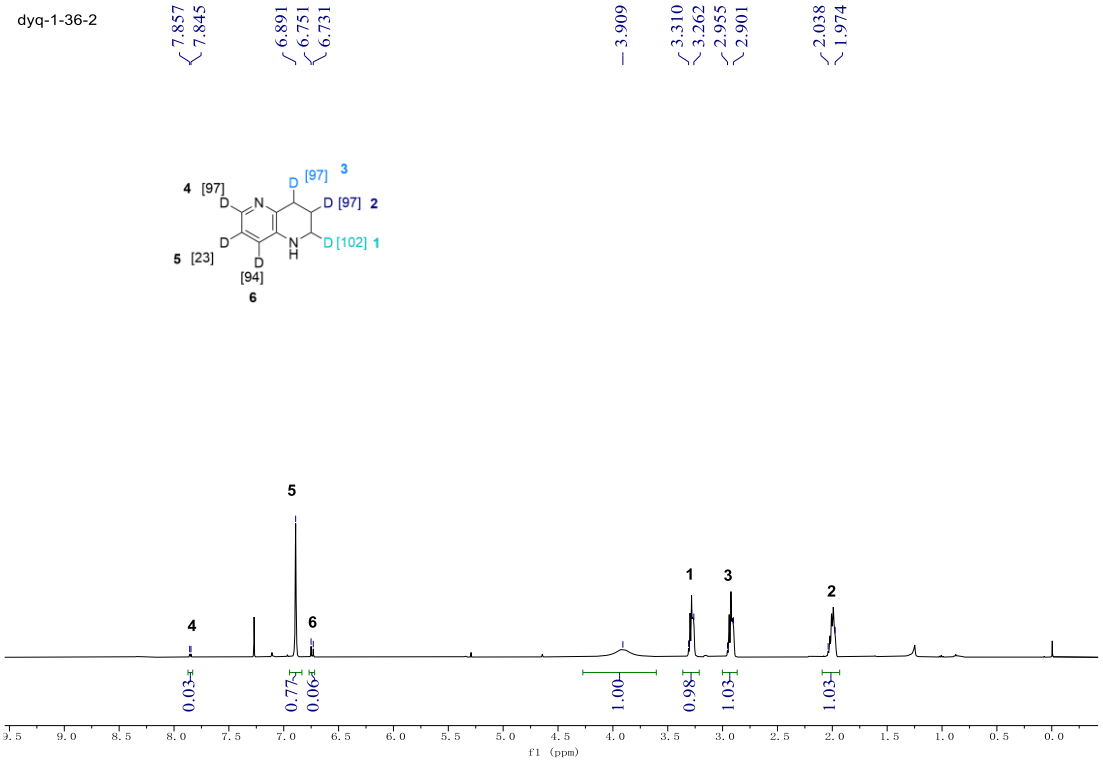
^{1}H NMR for 44b



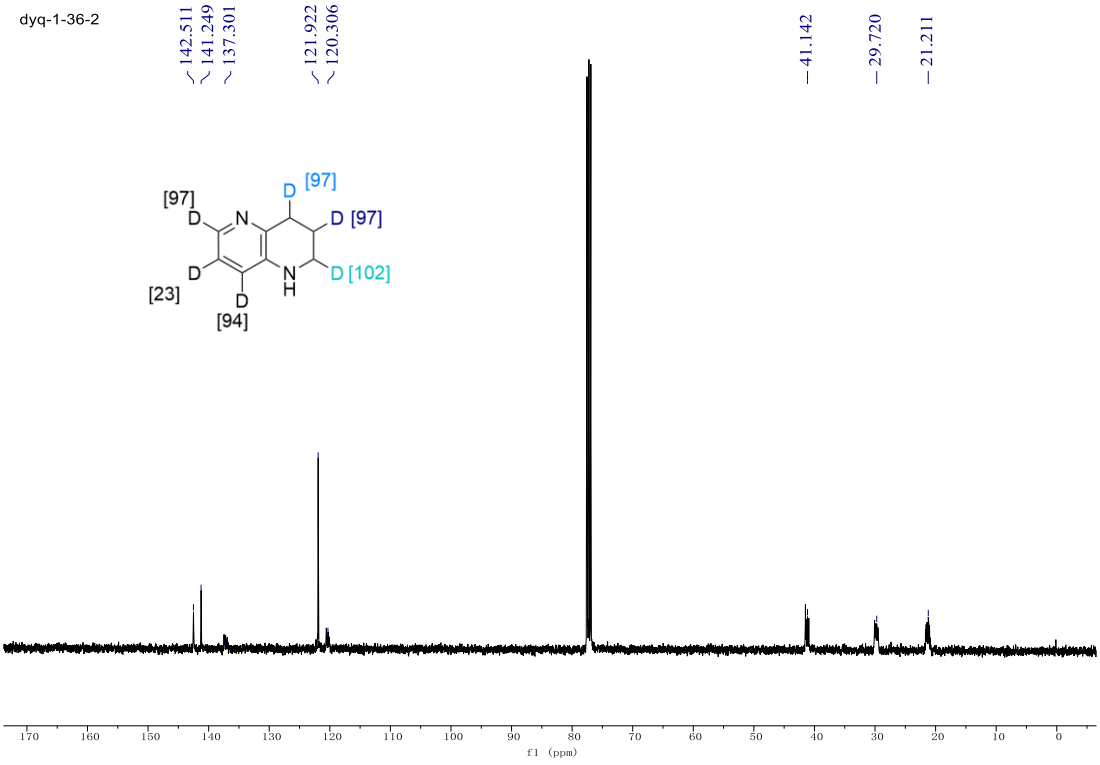
^{13}C NMR for 44b



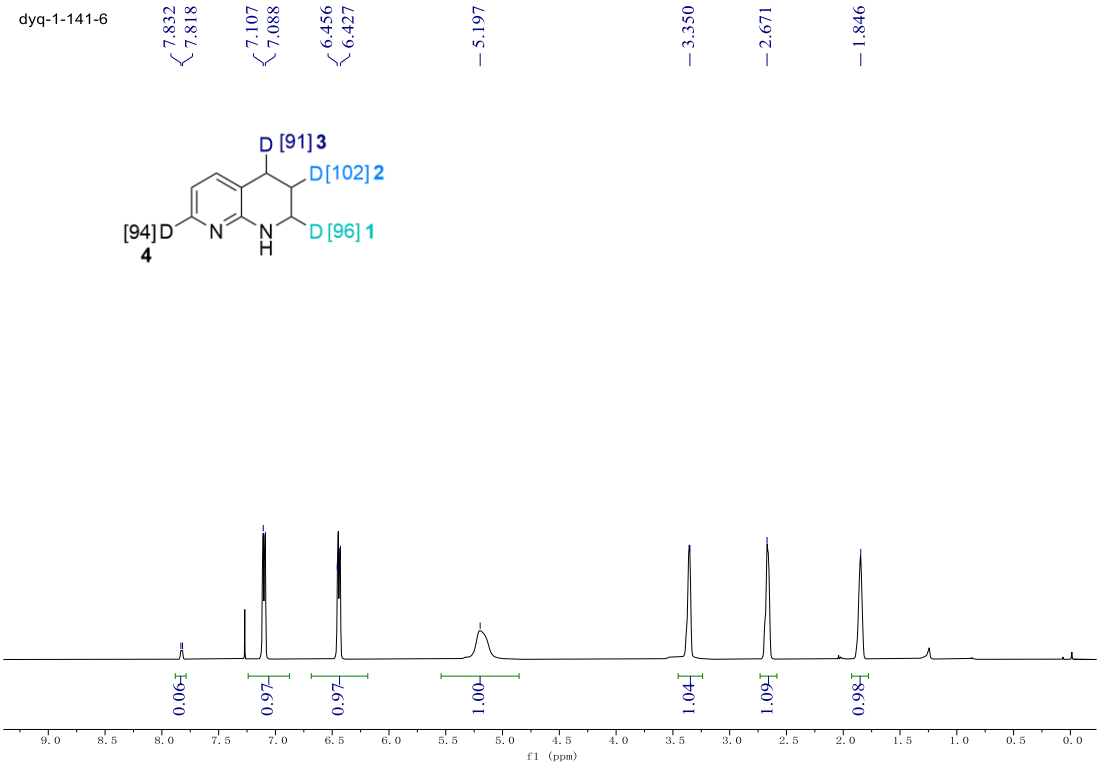
^{1}H NMR for 45b



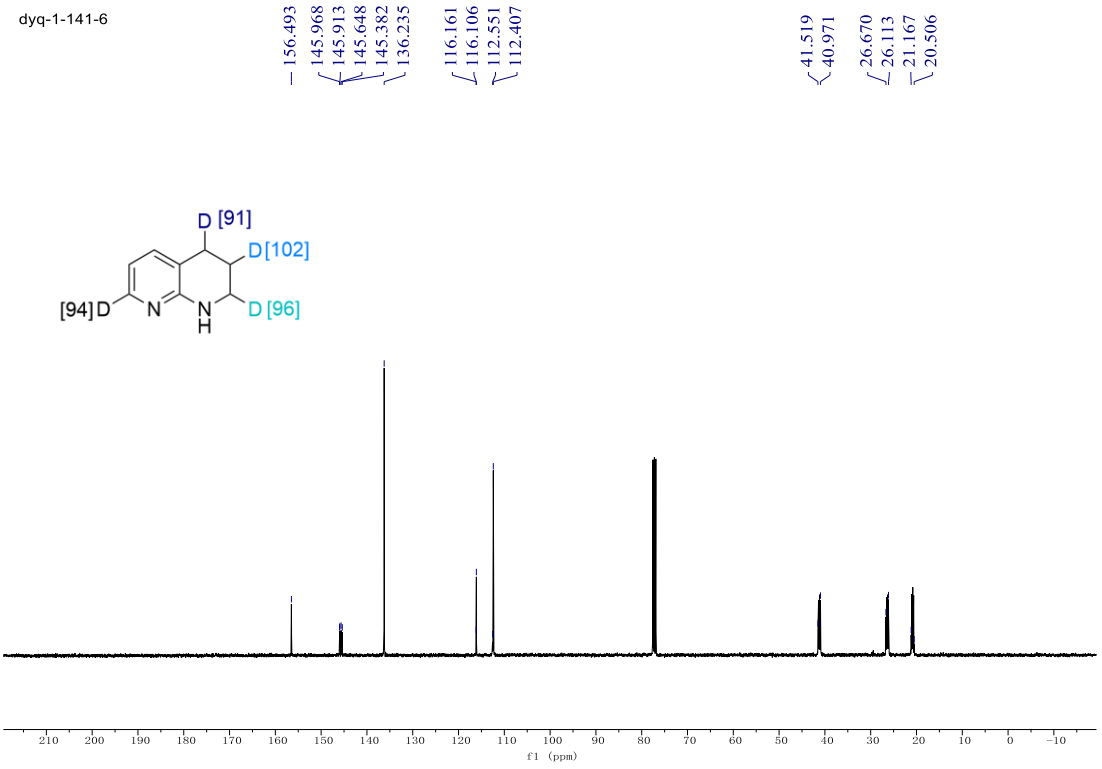
^{13}C NMR for 45b



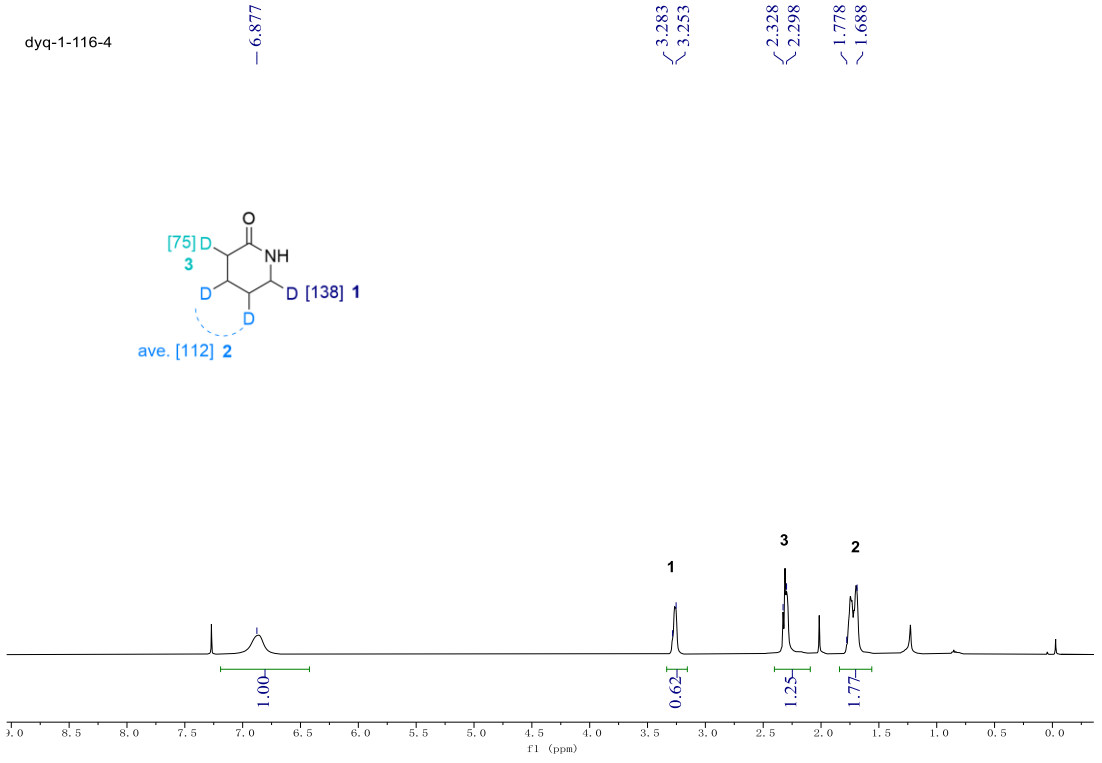
^{1}H NMR for 46b



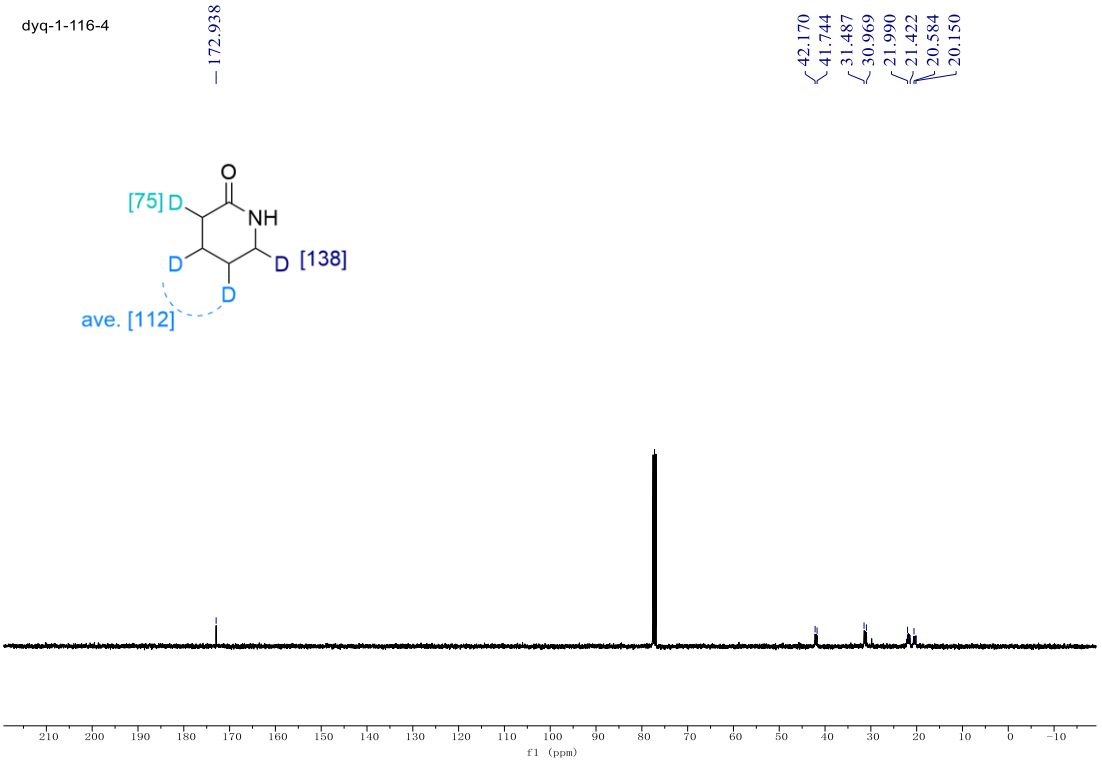
^{13}C NMR for 46b



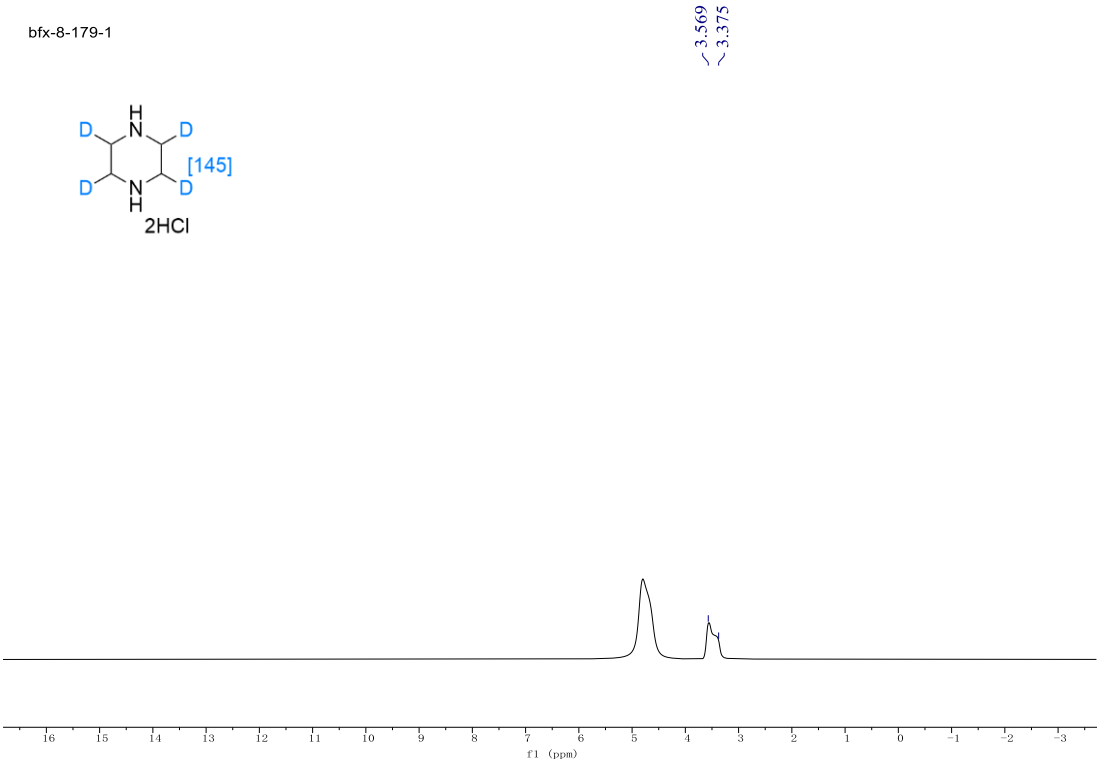
^{1}H NMR for 47b



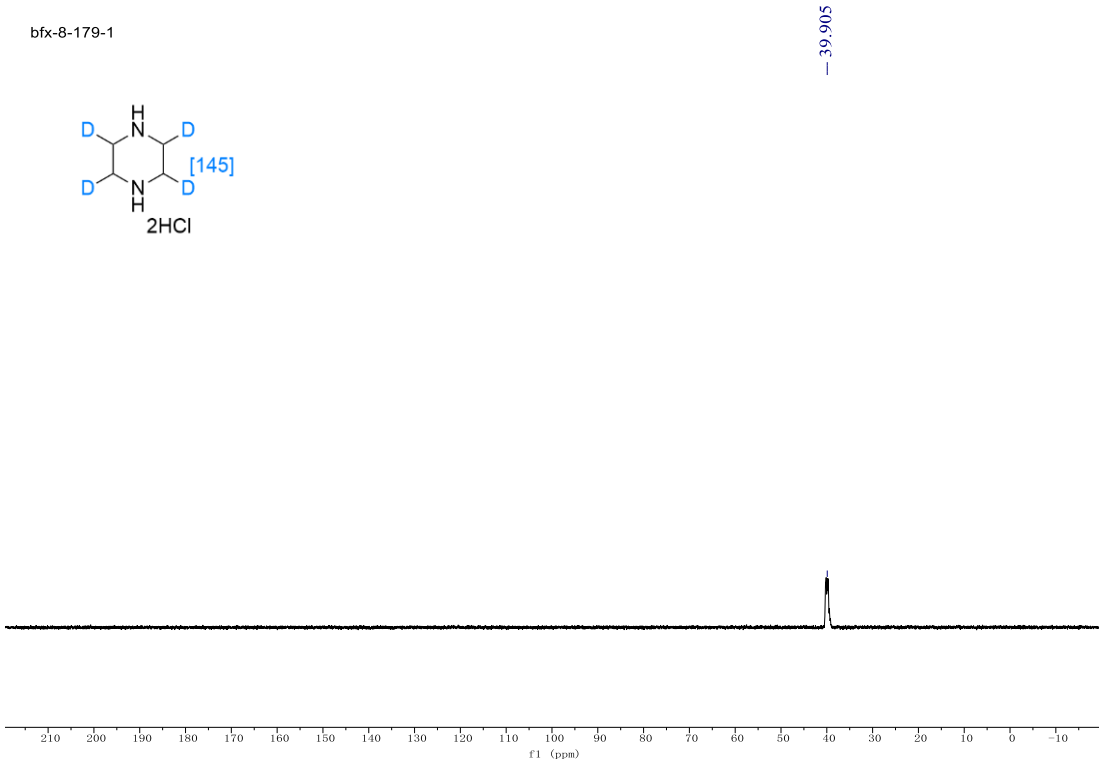
^{13}C NMR for 47b



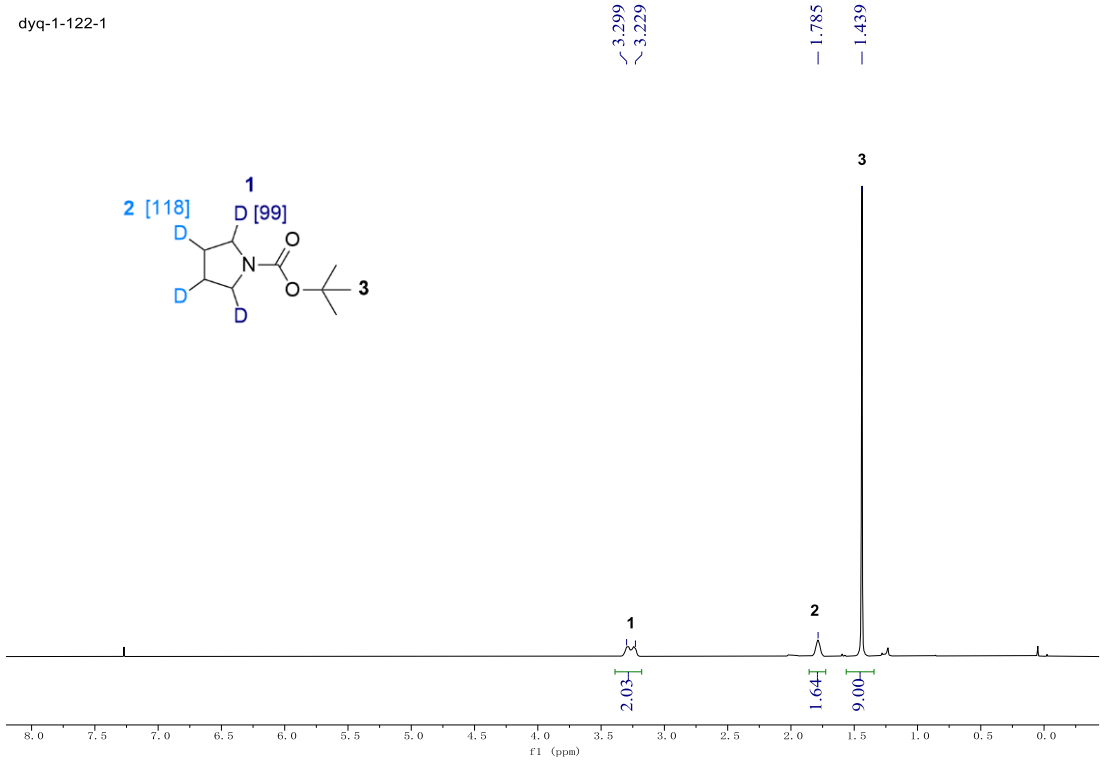
^{1}H NMR for 48b



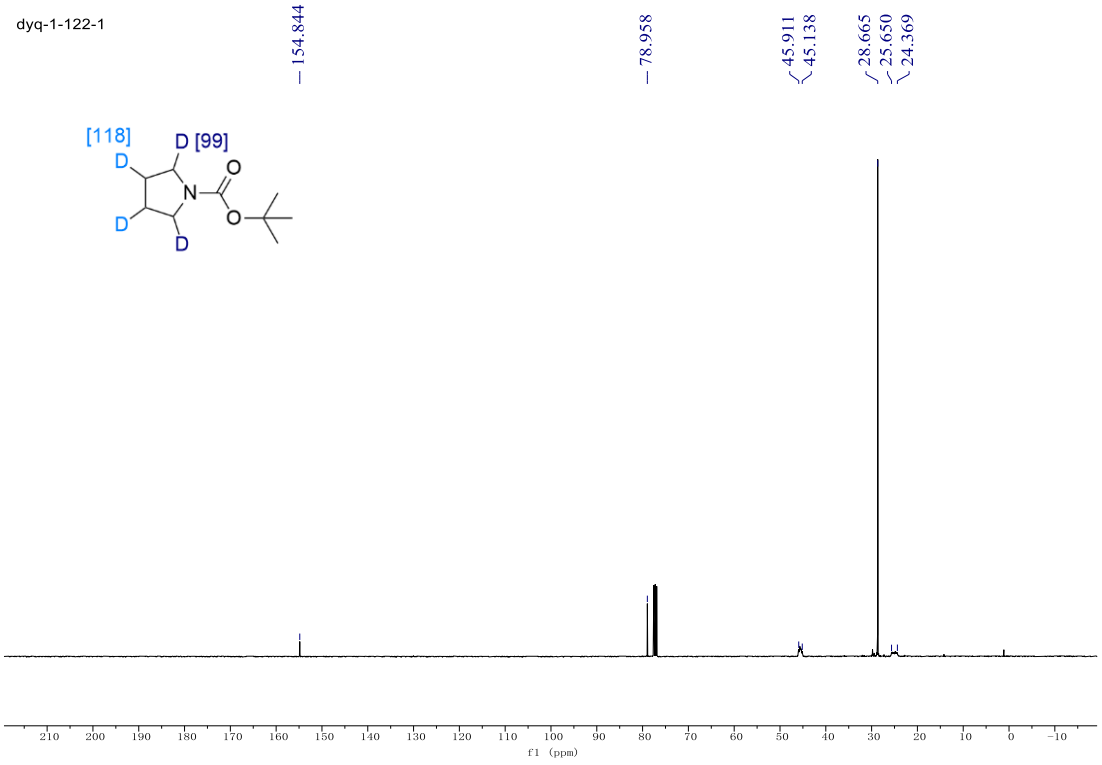
^{13}C NMR for 48b



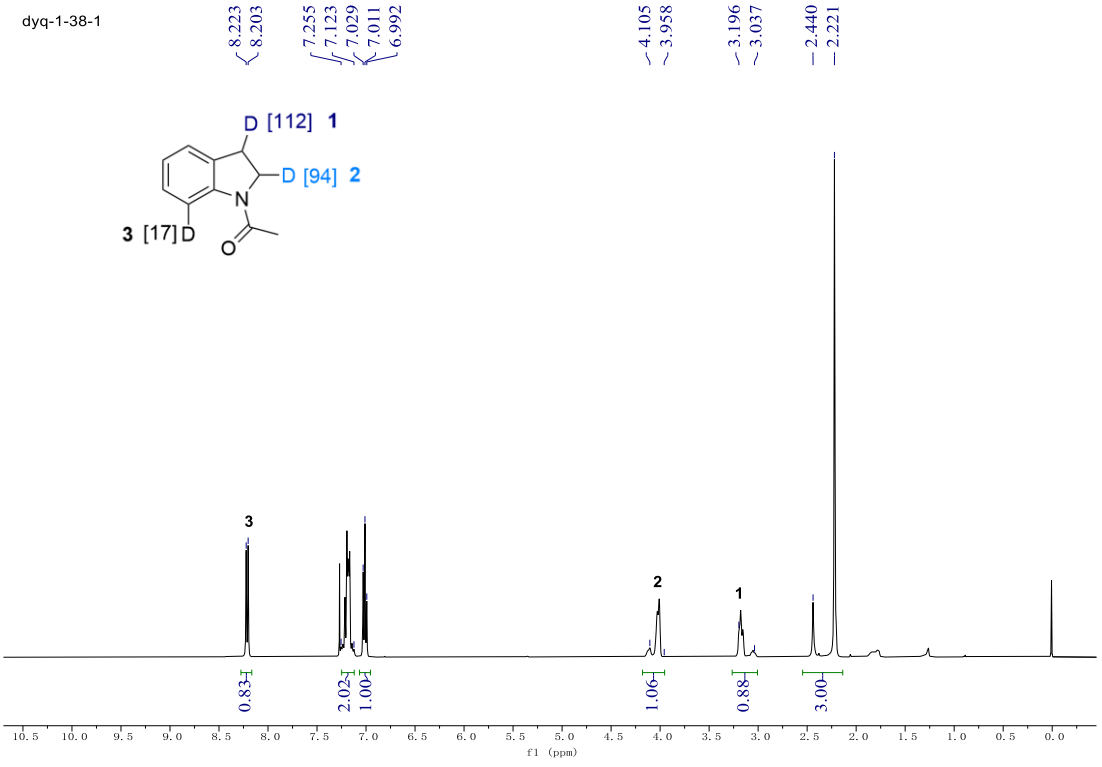
^{1}H NMR for 49b



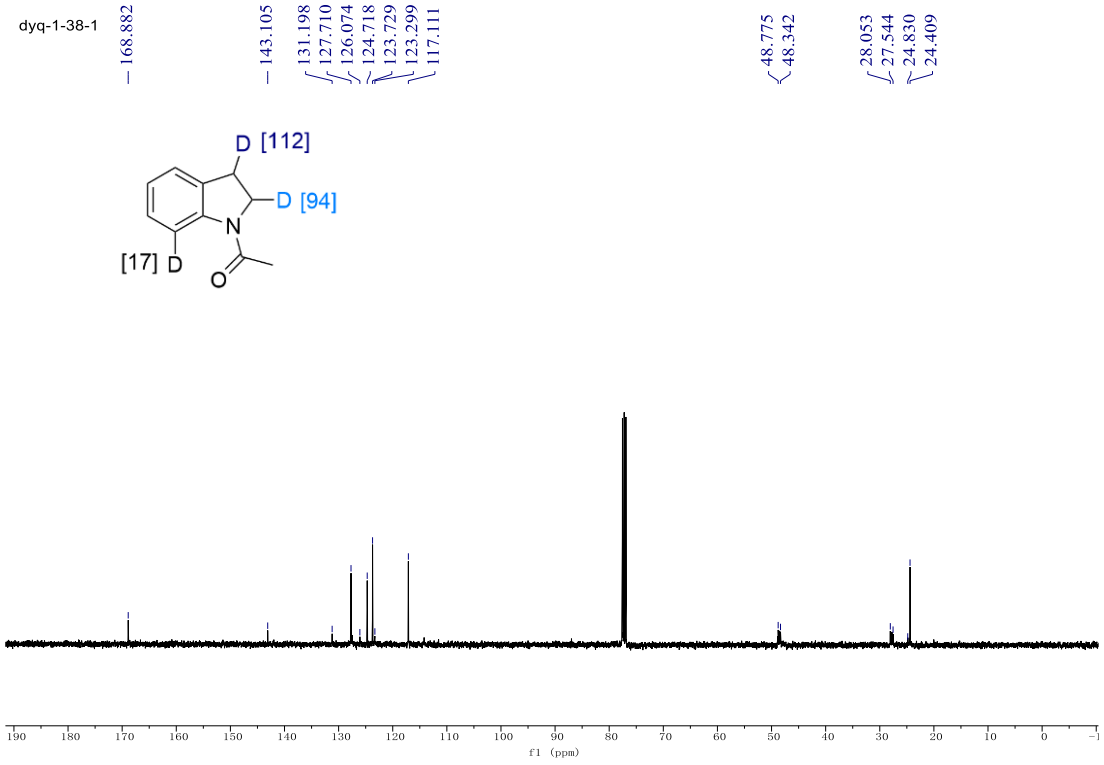
^{13}C NMR for 49b



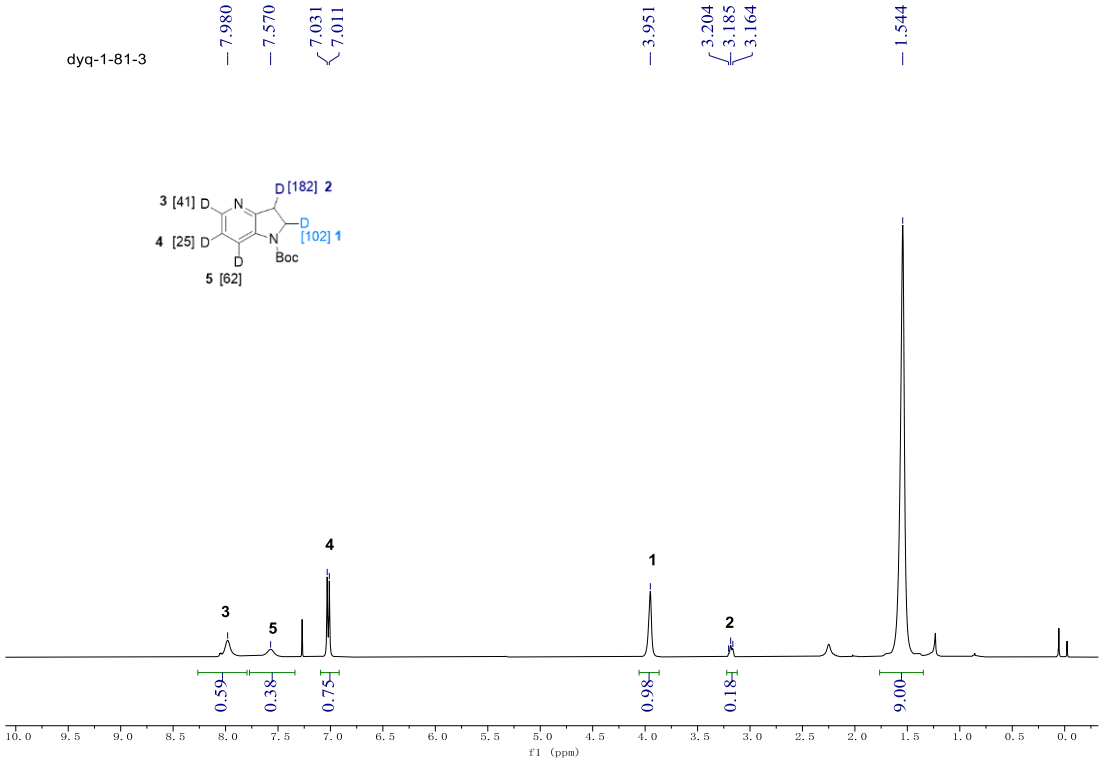
^{1}H NMR for 50b



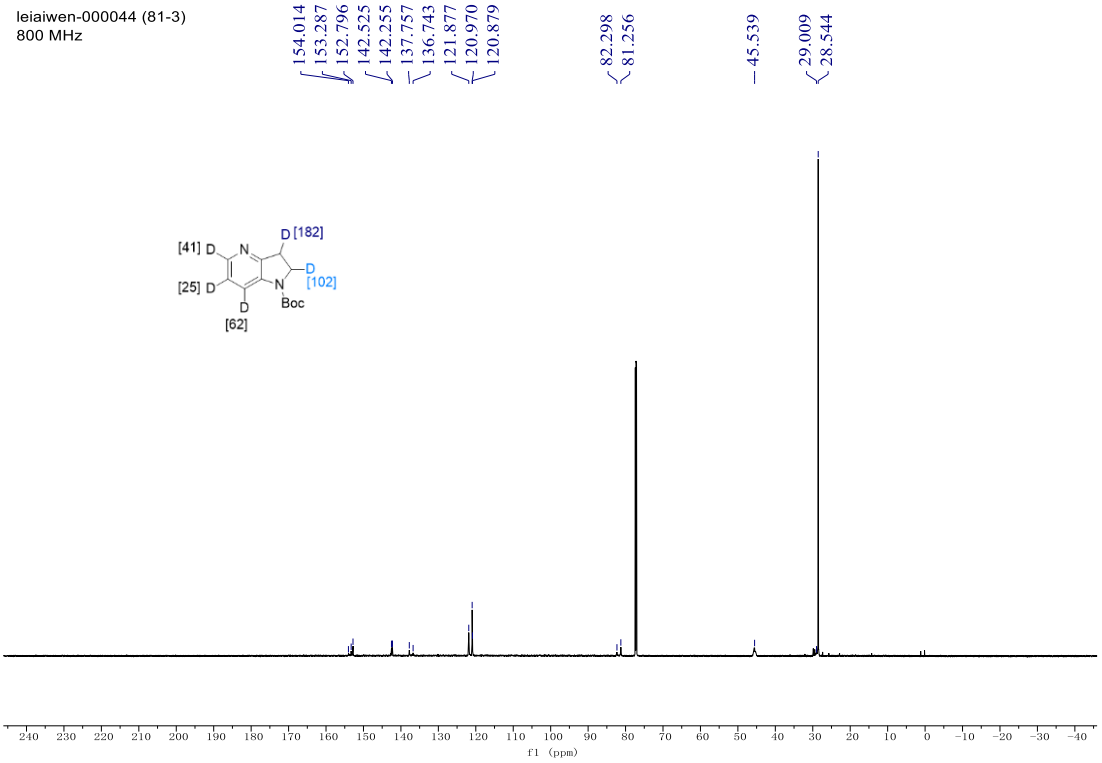
^{13}C NMR for 50b



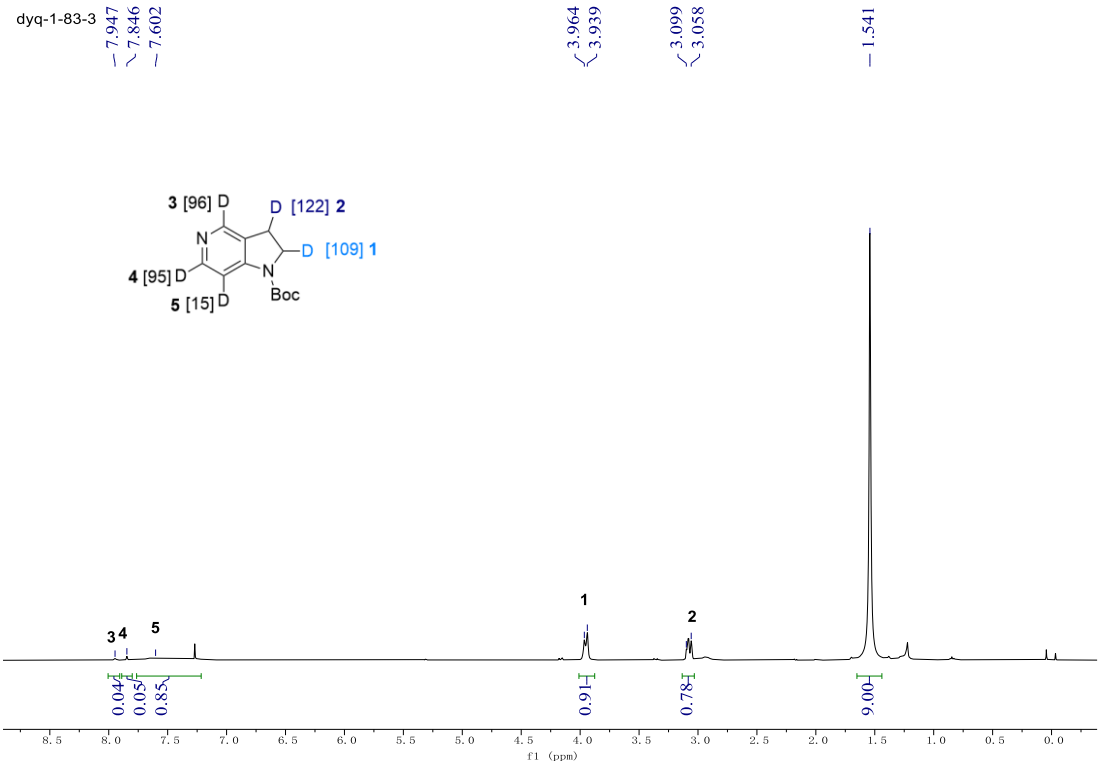
^{1}H NMR for 51b



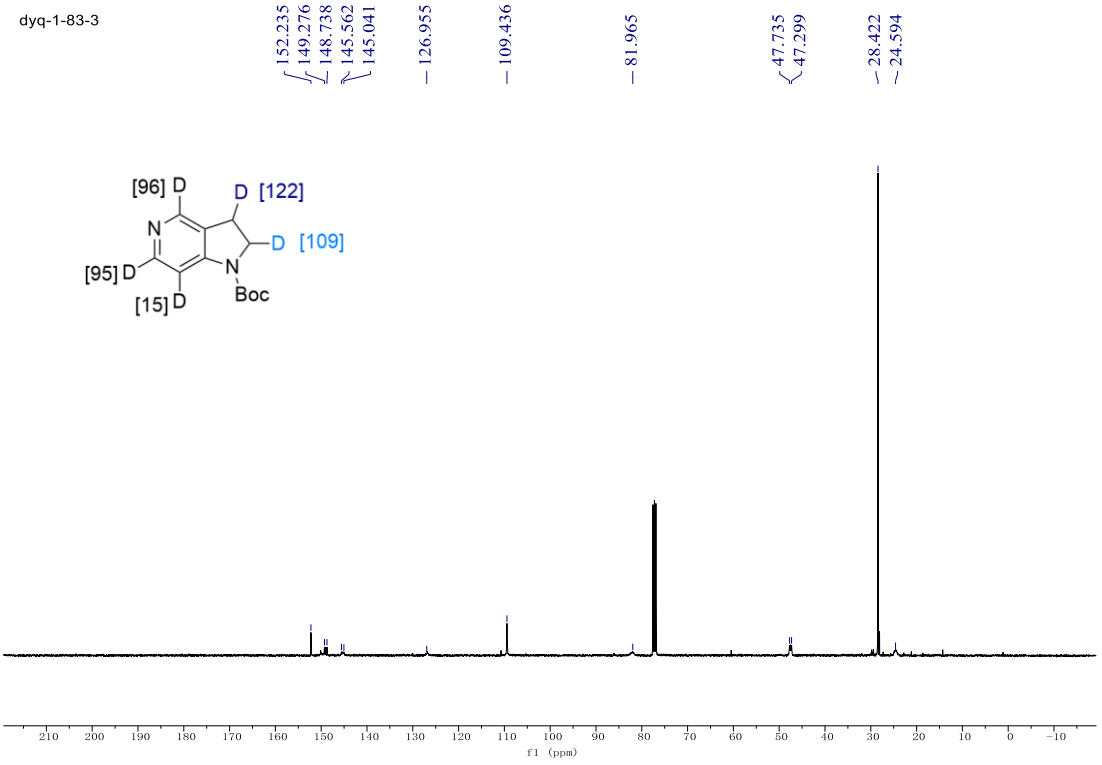
^{13}C NMR for 51b



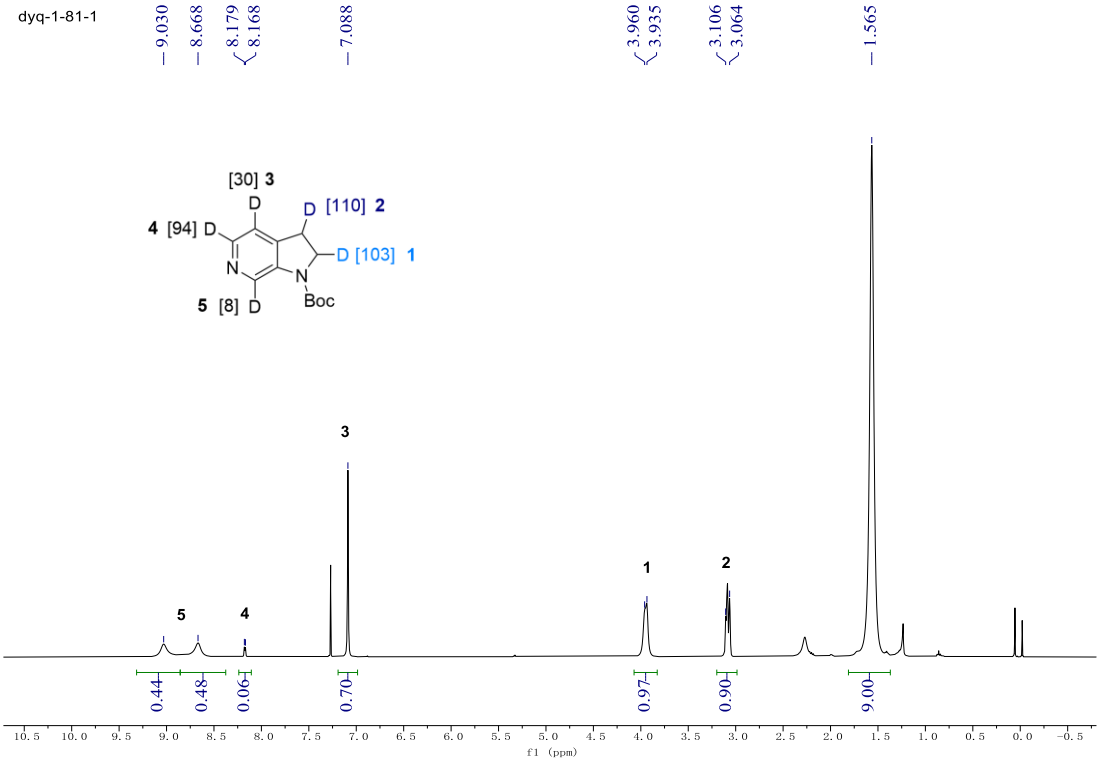
^{1}H NMR for 52b



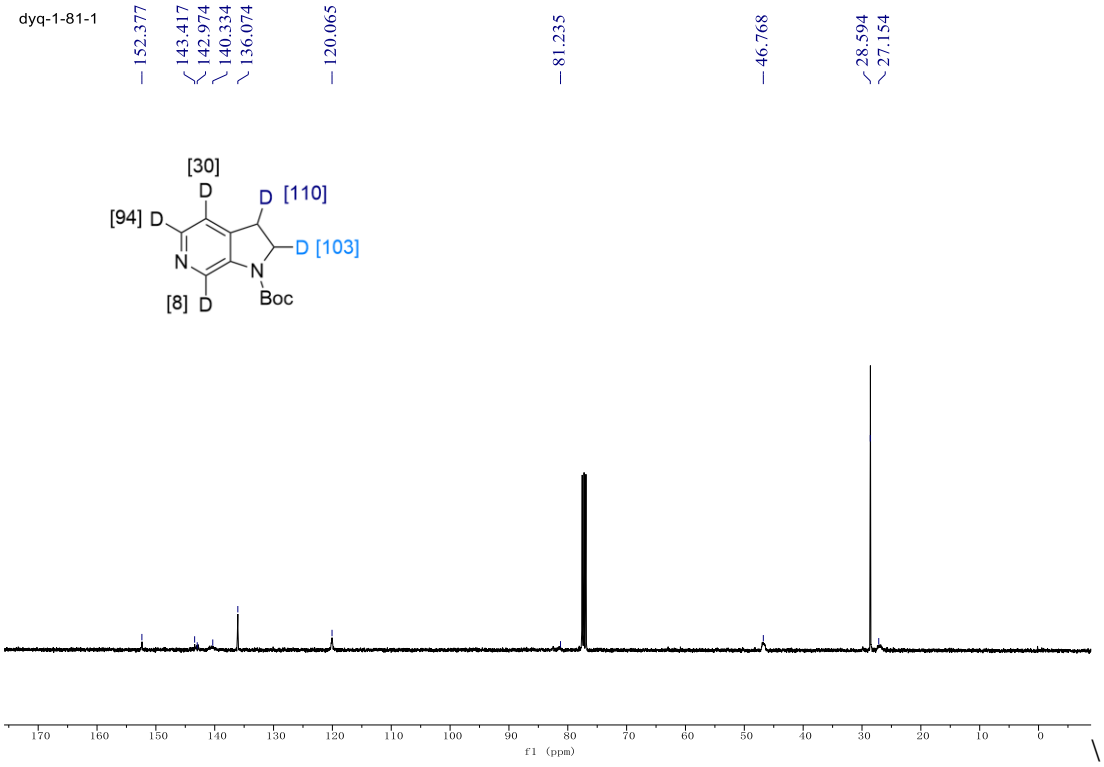
^{13}C NMR for 52b



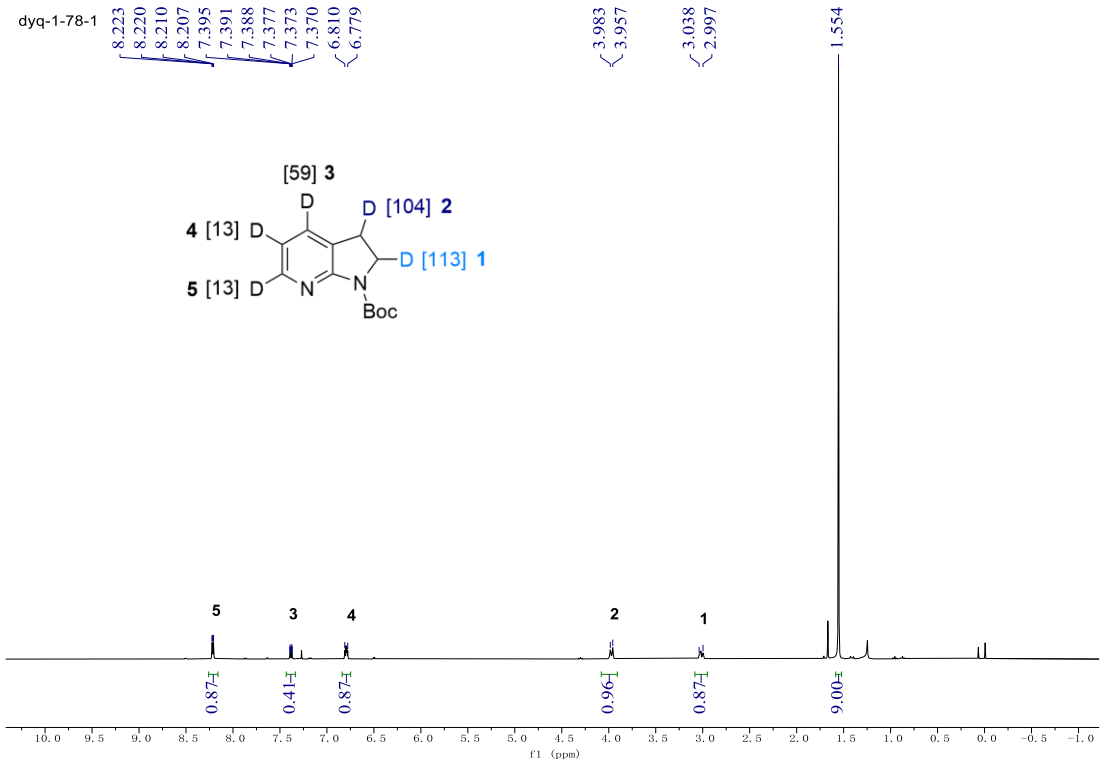
^{1}H NMR for 53b



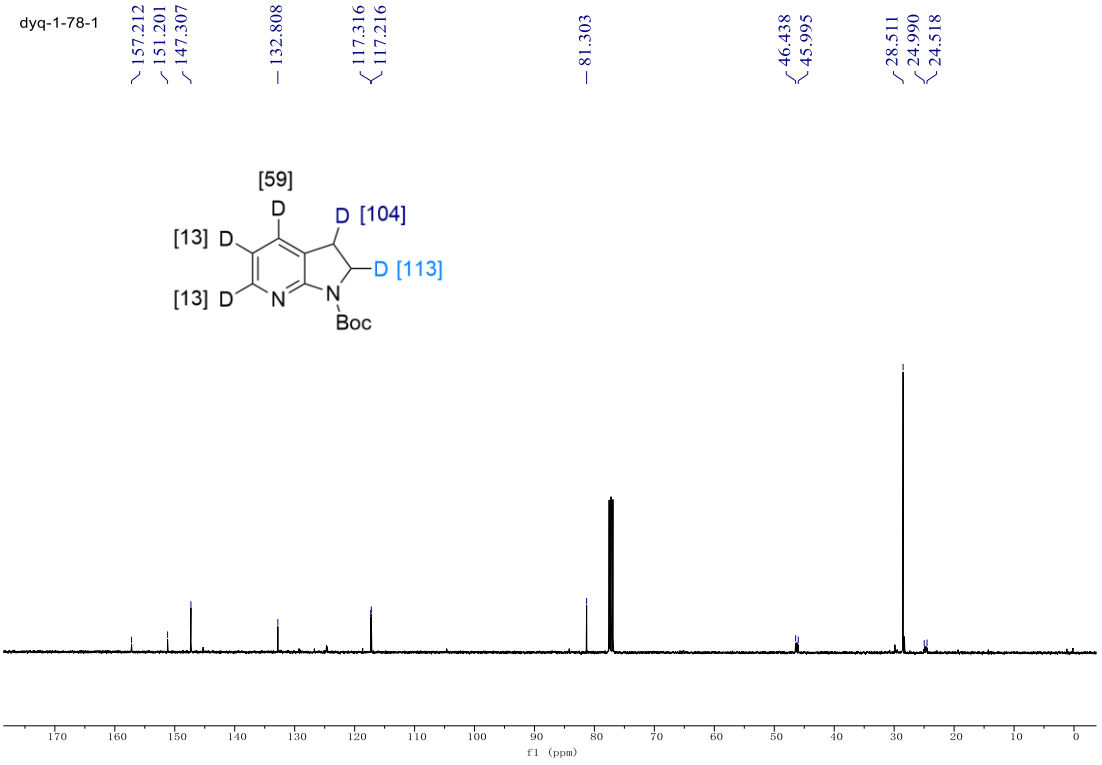
^{13}C NMR for 53b



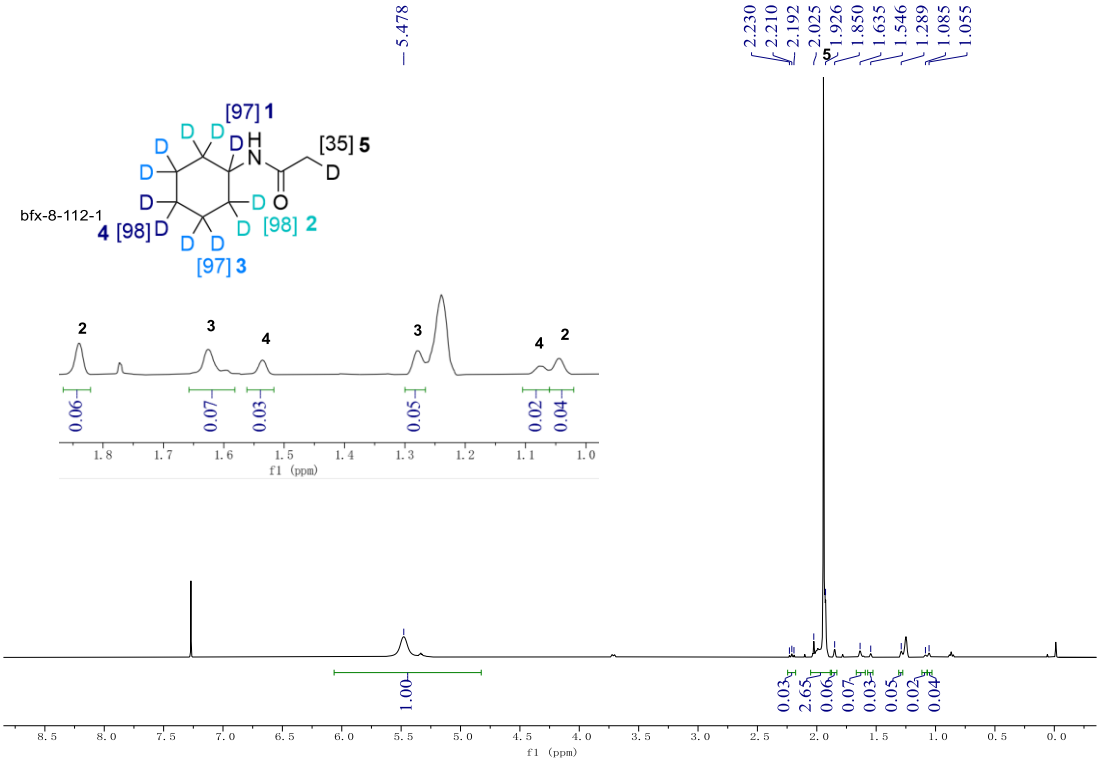
^{1}H NMR for 54b



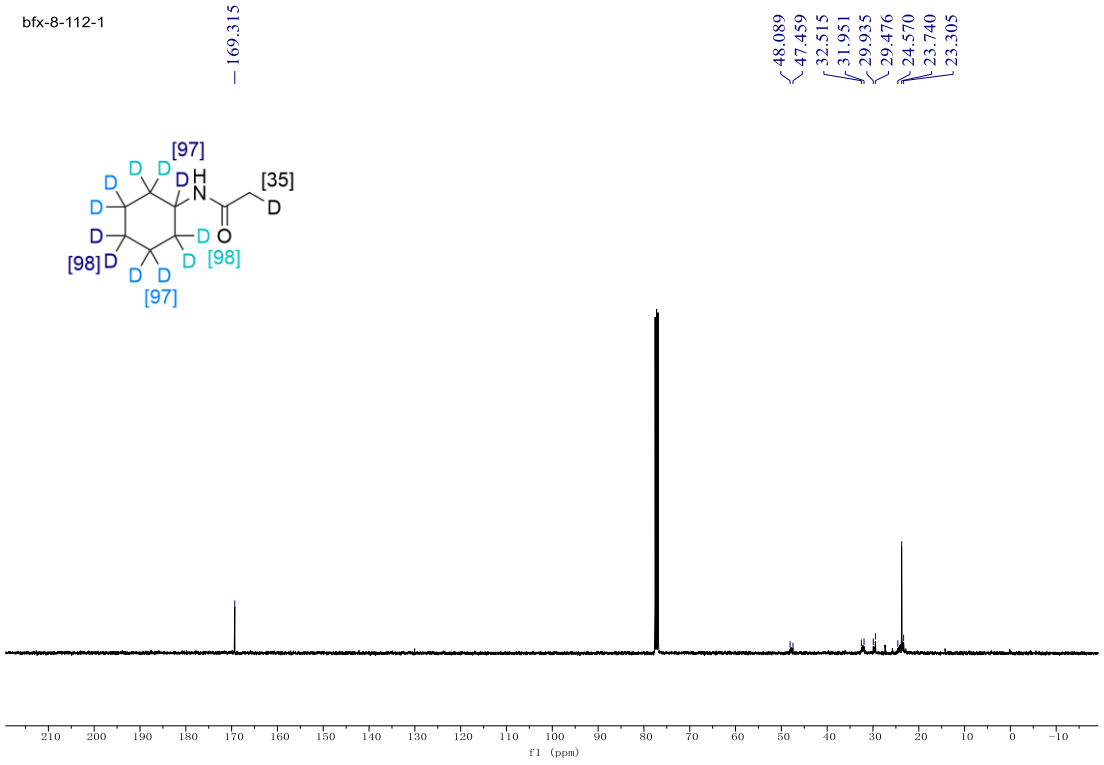
^{13}C NMR for 54b



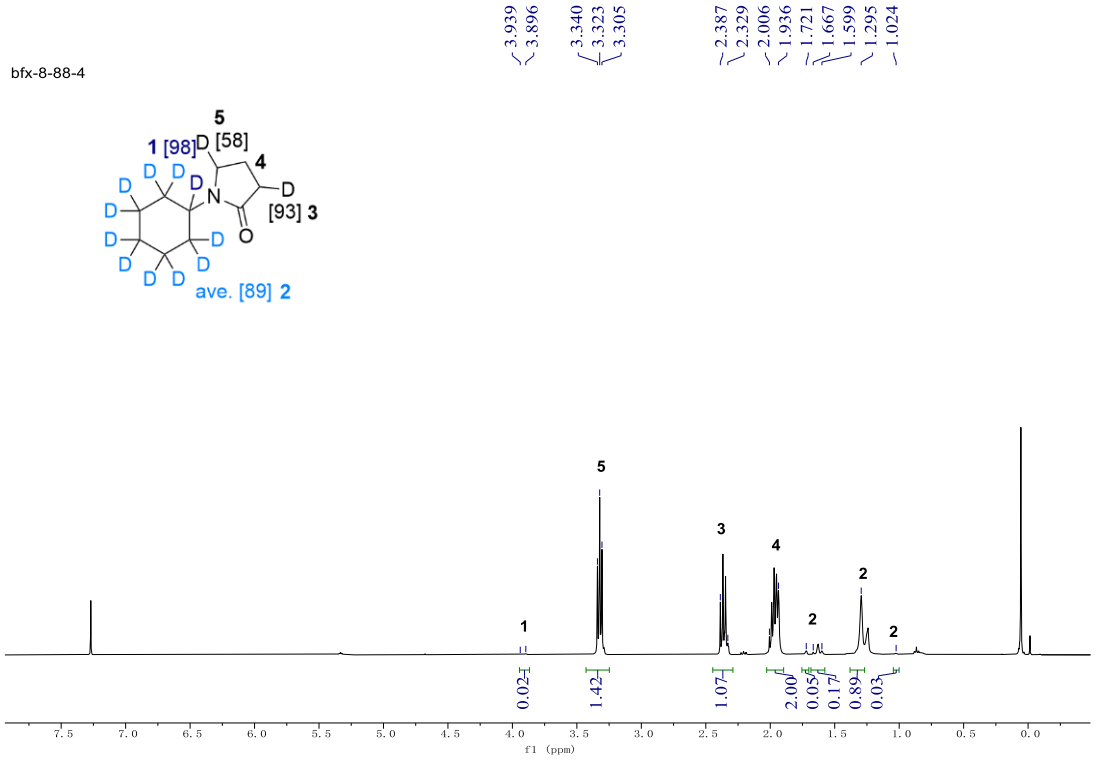
^{1}H NMR for 1d



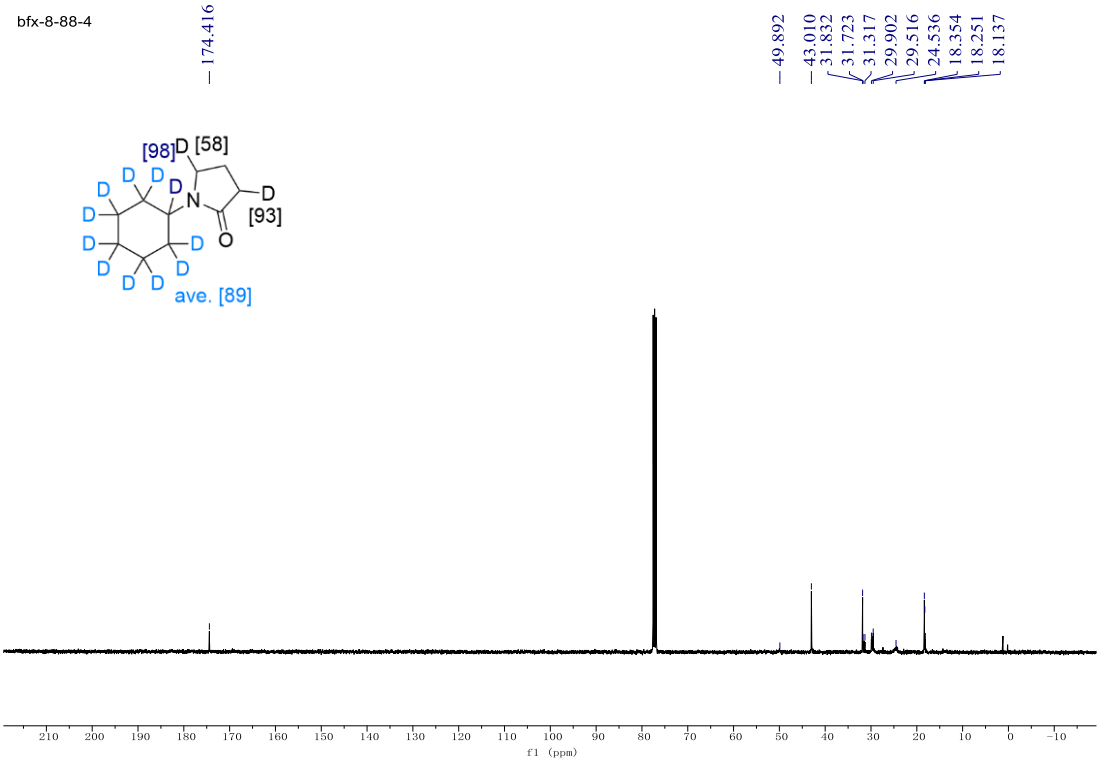
^{13}C NMR for 1d



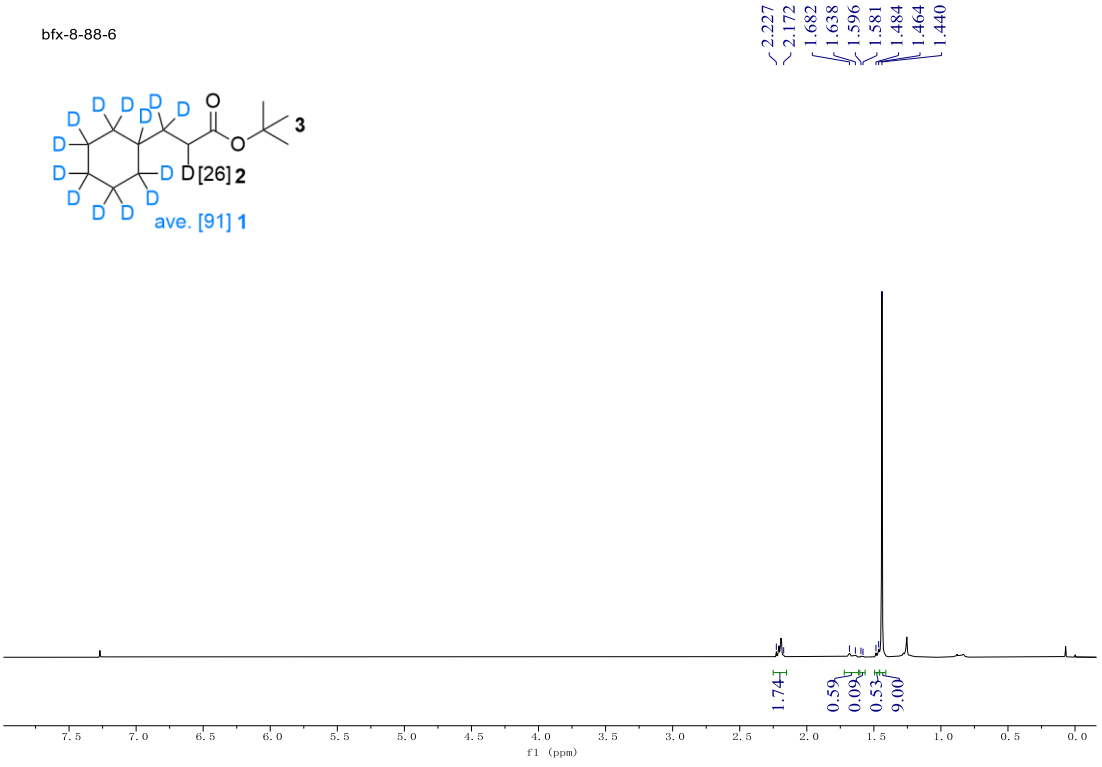
^{1}H NMR for 2d



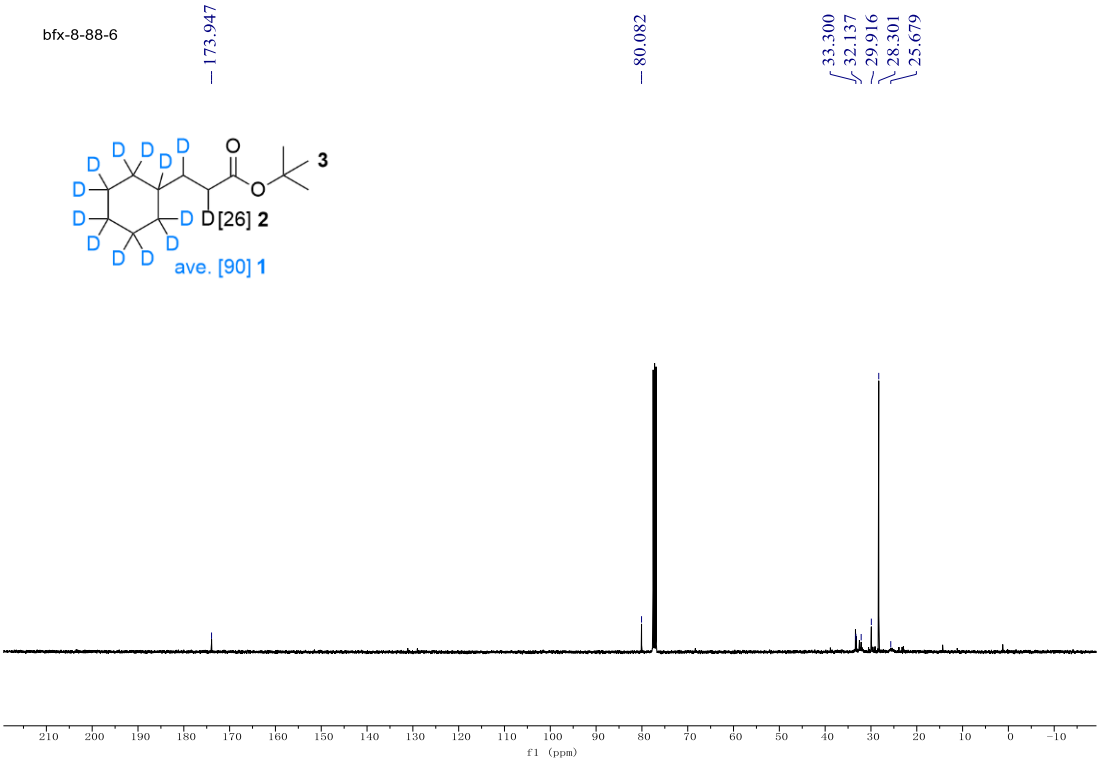
^{13}C NMR for 2d



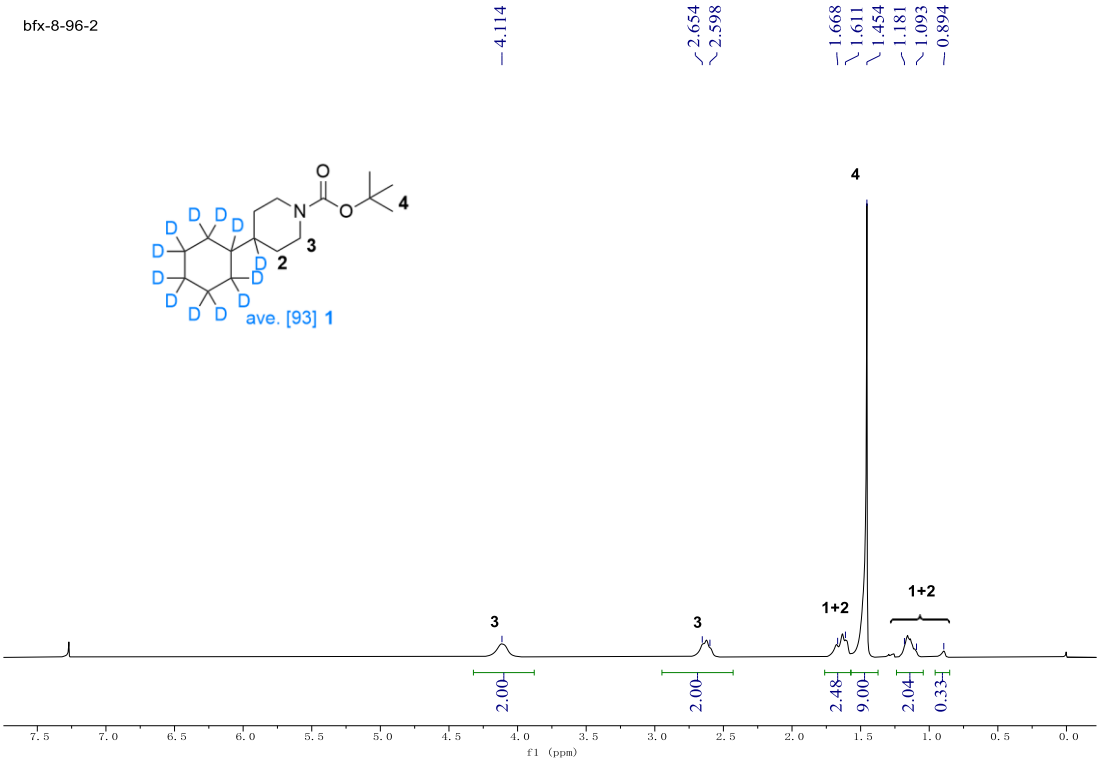
^{1}H NMR for 3d



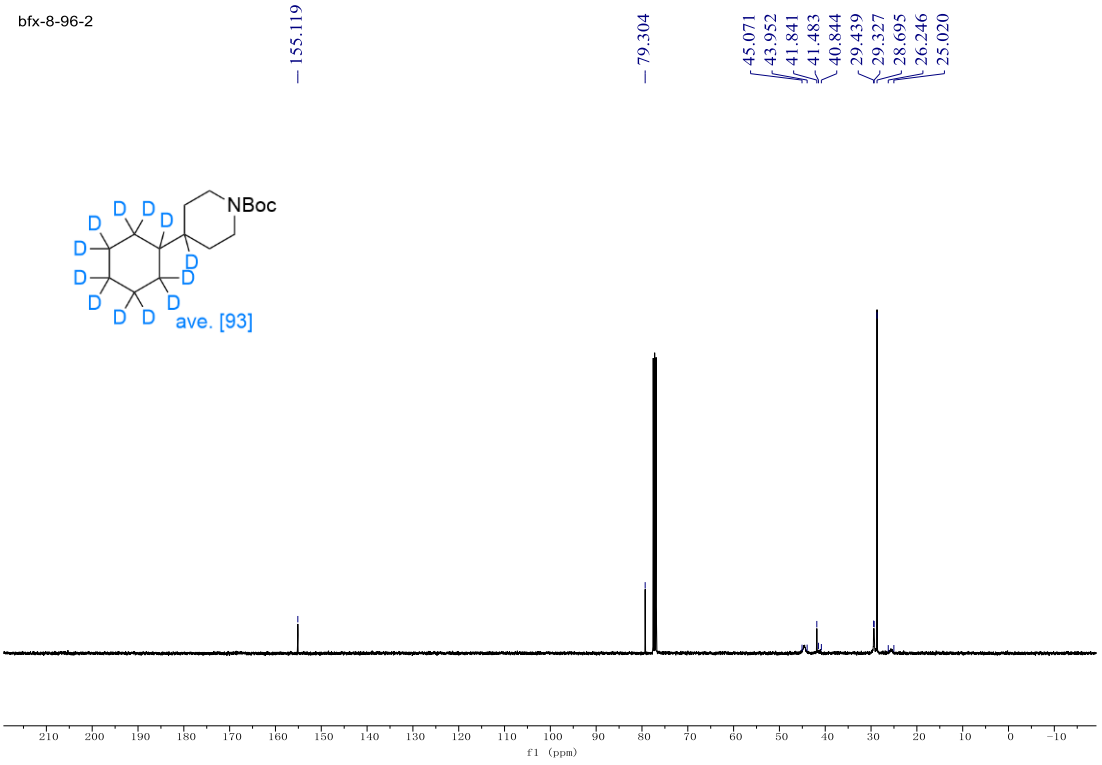
^{13}C NMR for 3d



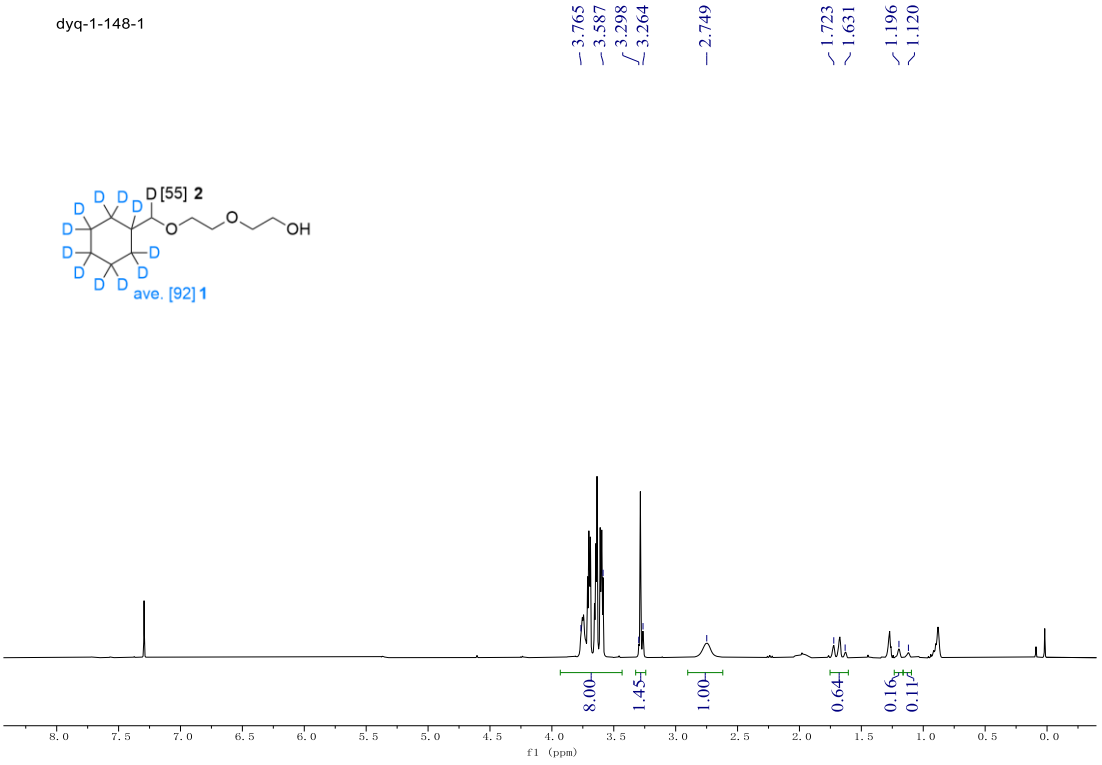
^{1}H NMR for 4d



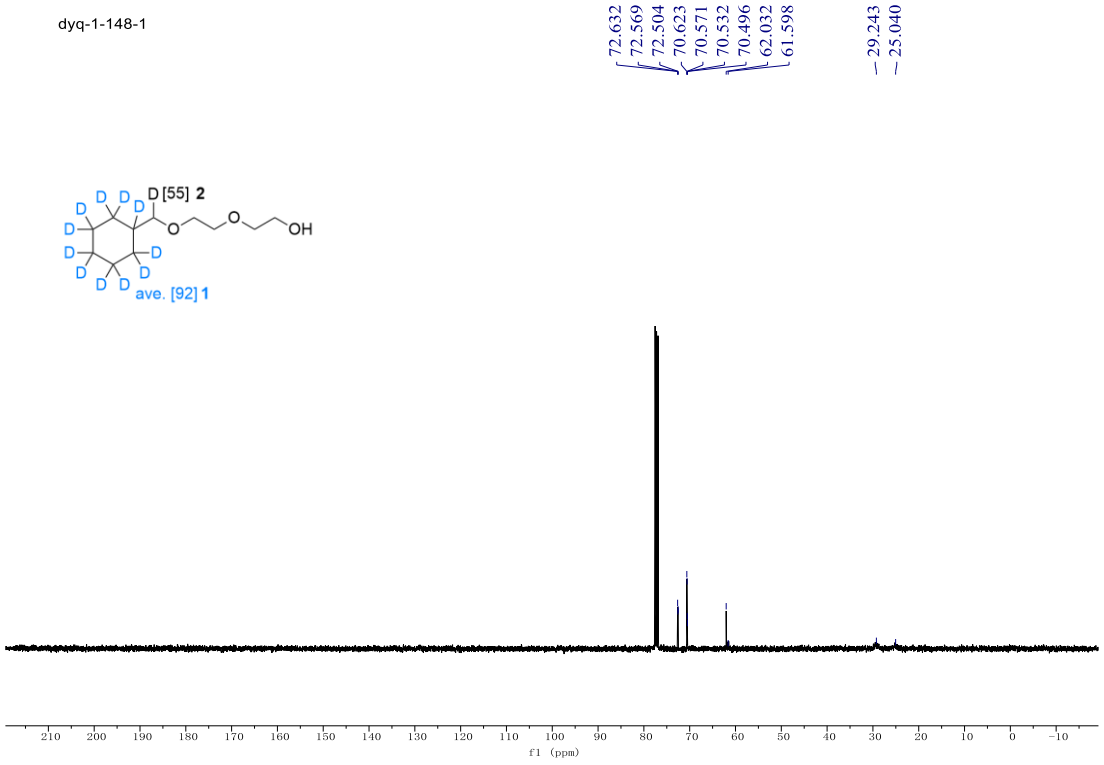
^{13}C NMR for 4d



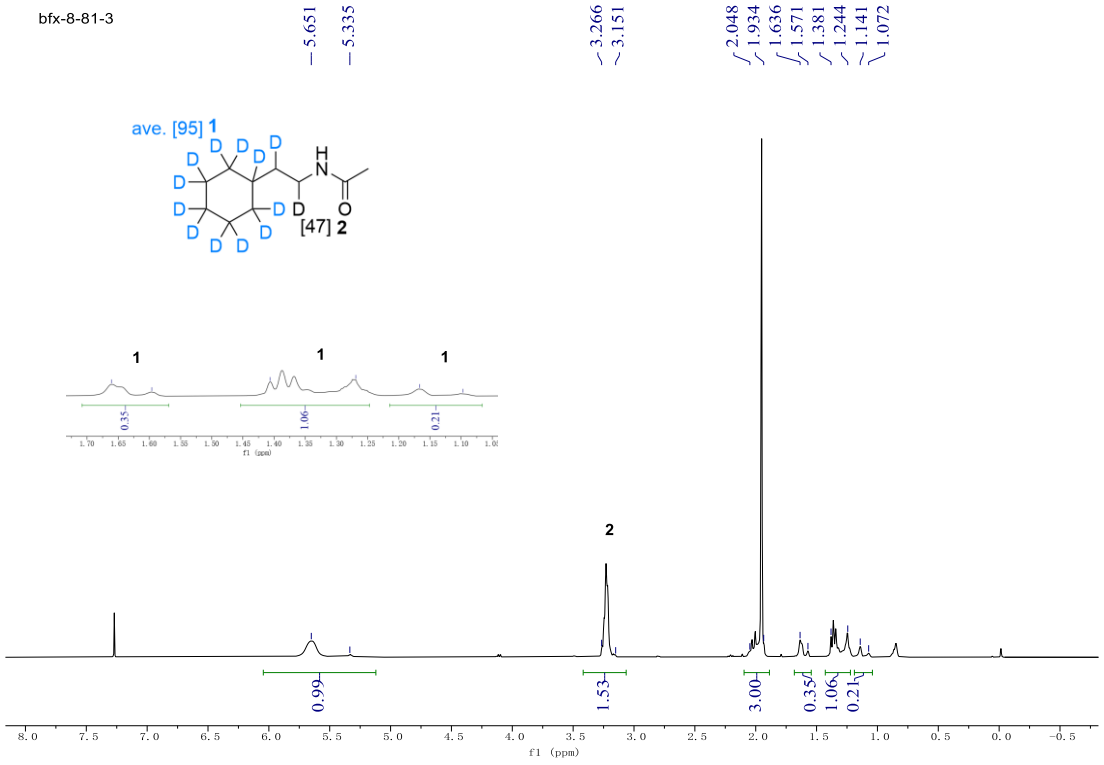
^{1}H NMR for 5d



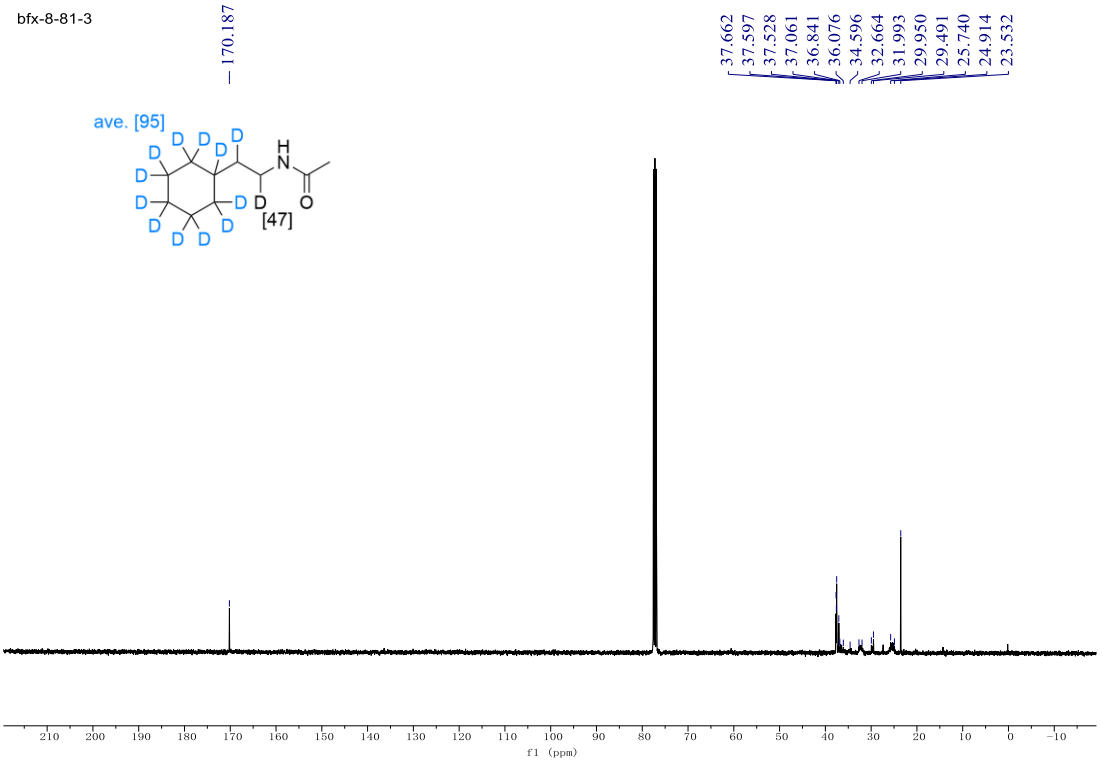
^{13}C NMR for 5d



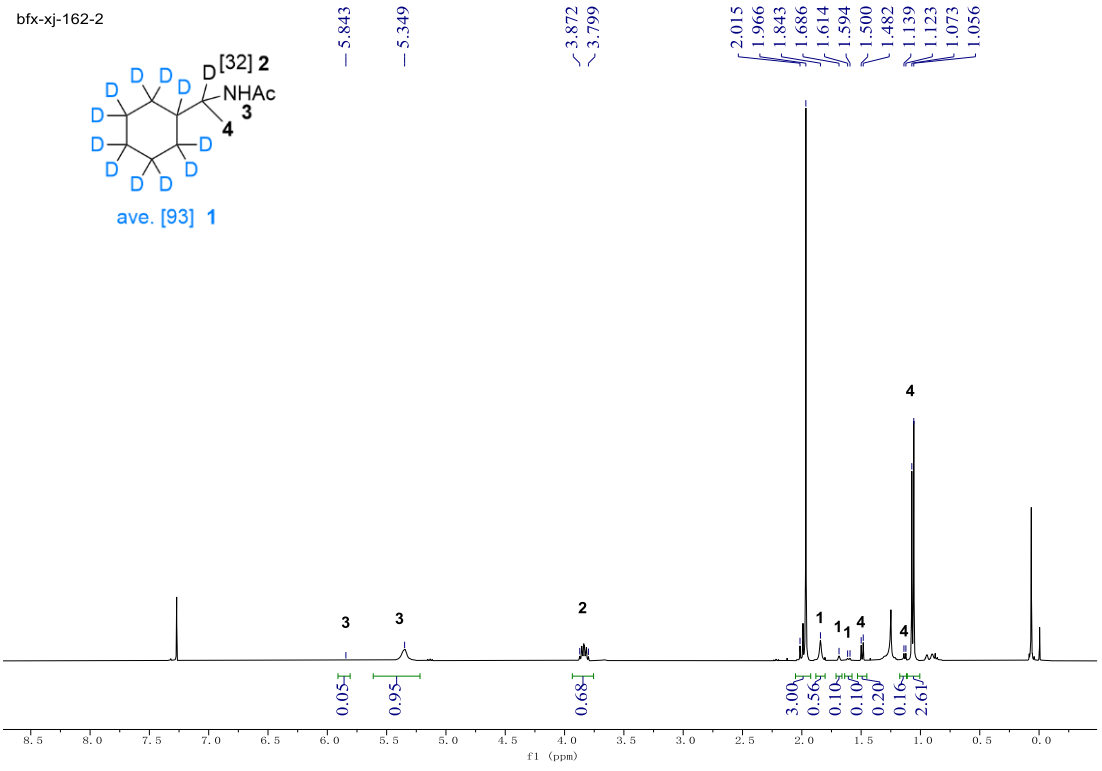
^{1}H NMR for 6d



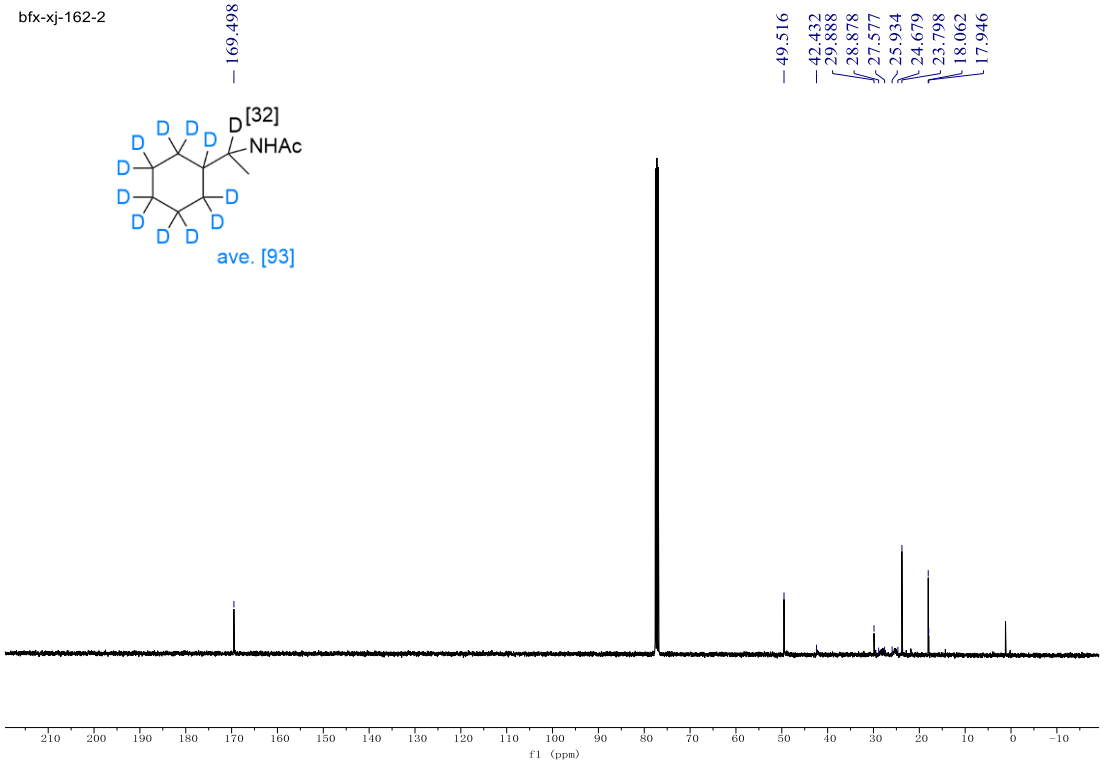
^{13}C NMR for 6d



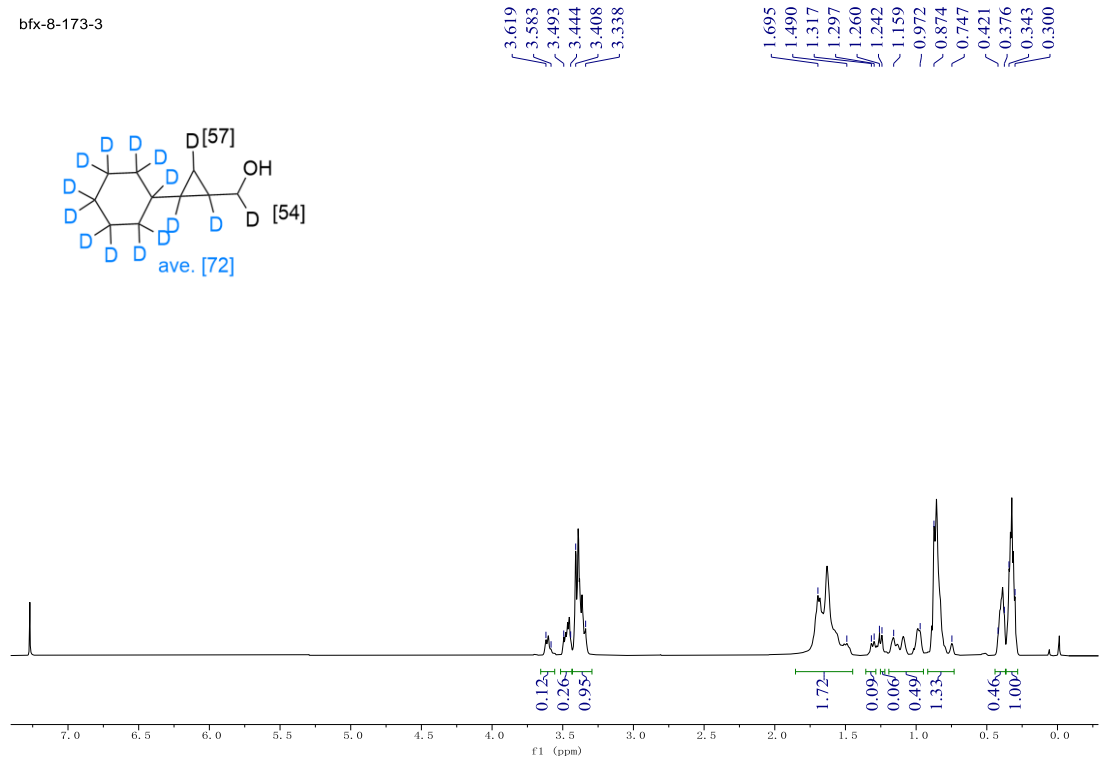
^{1}H NMR for 7d



^{13}C NMR for 7d

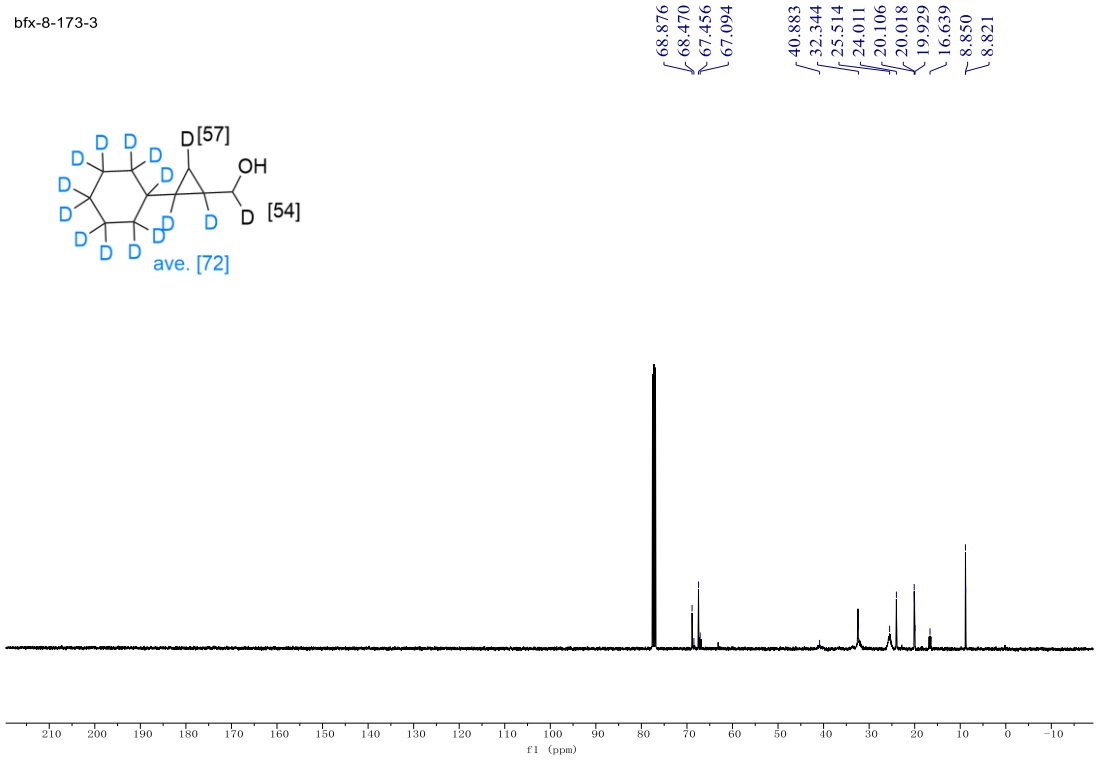


^{1}H NMR for 8d



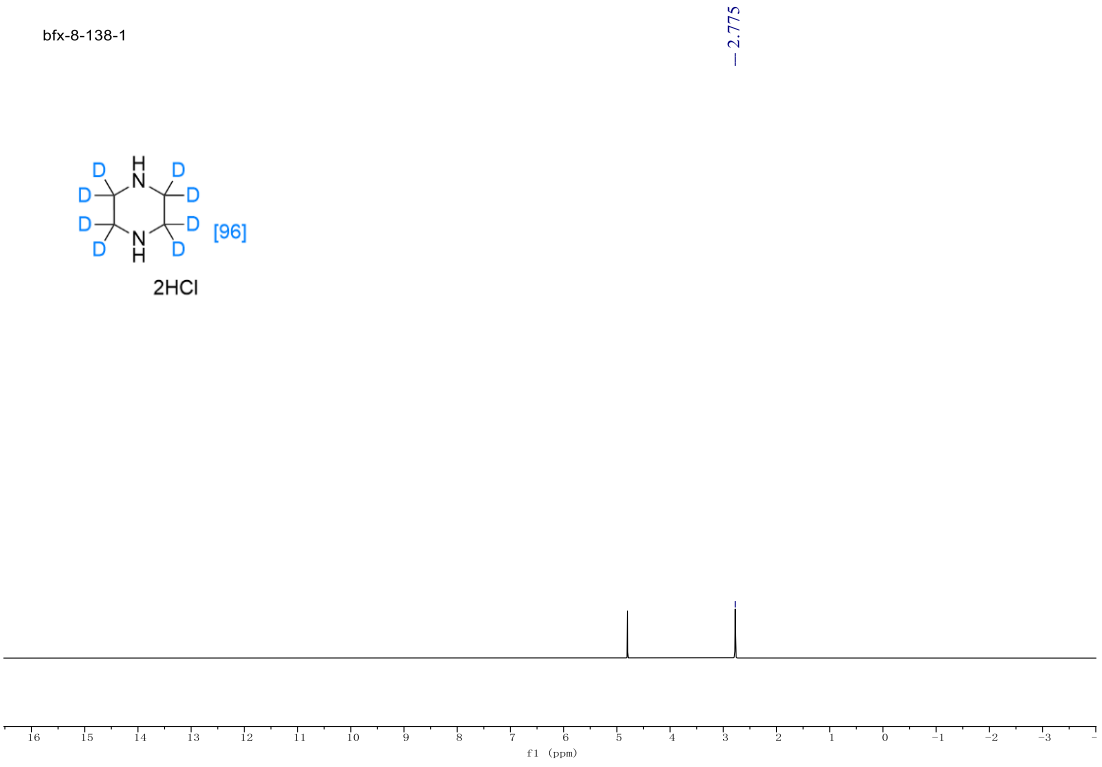
^{13}C NMR for 8d

bfx-8-173-3

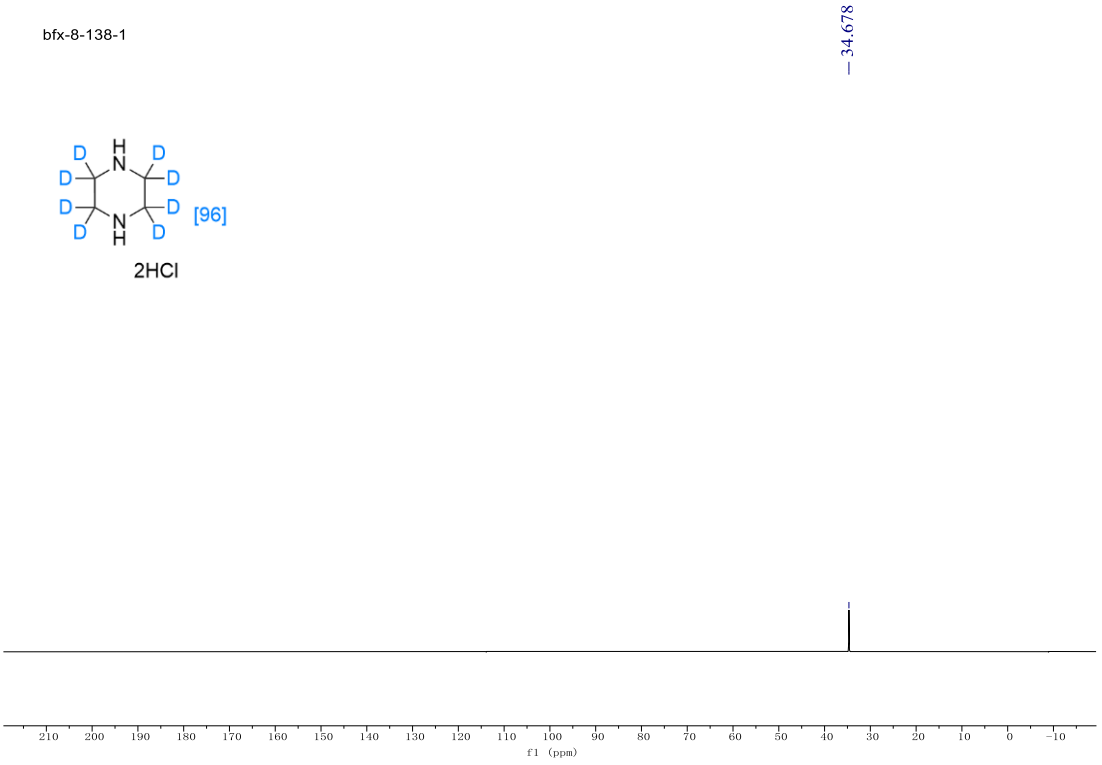


^{1}H NMR for 10d

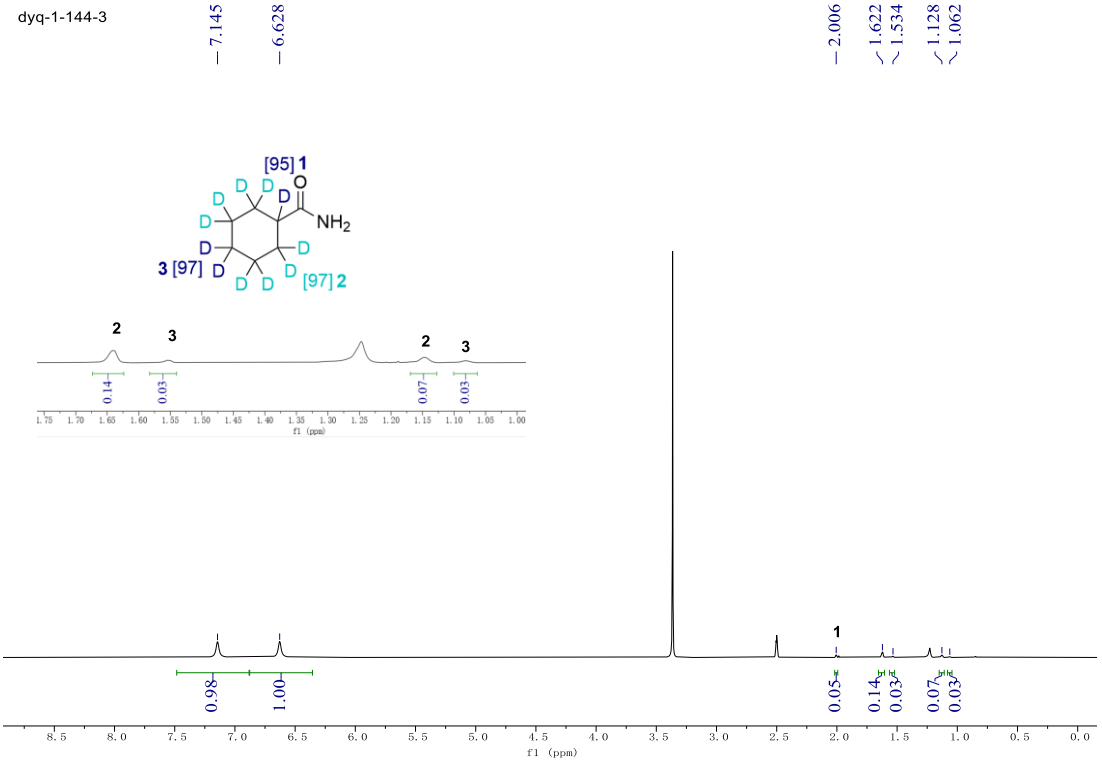
bfx-8-138-1



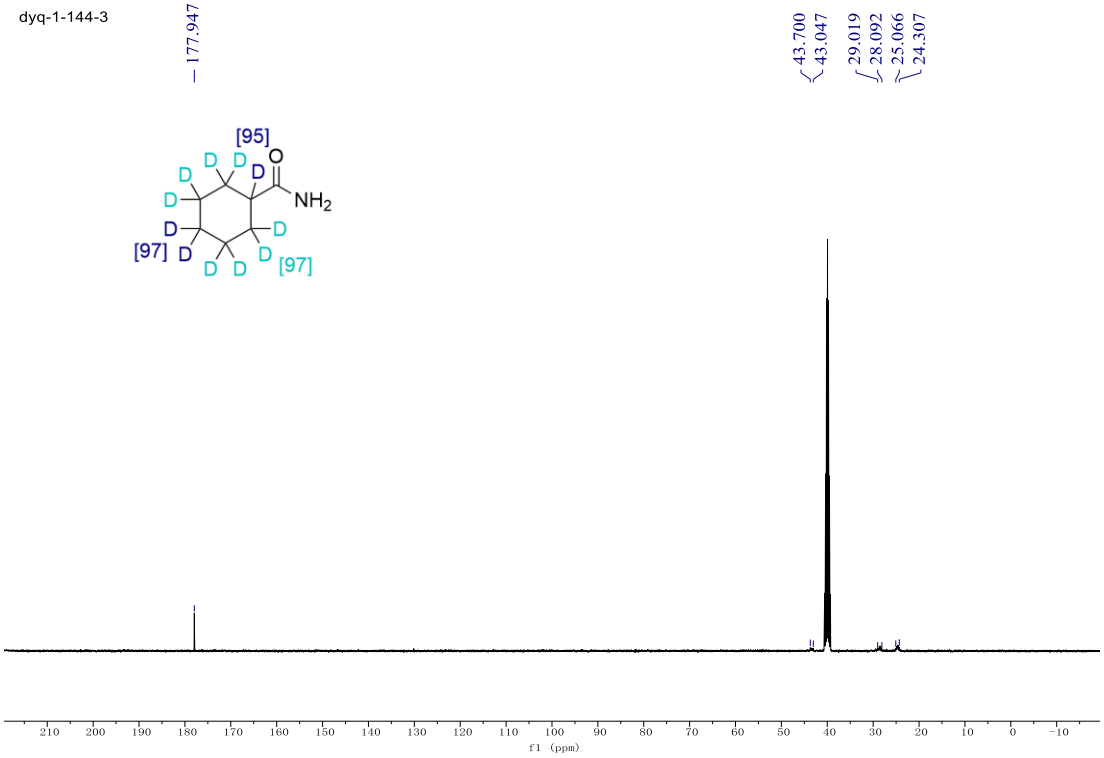
^{13}C NMR for 10d



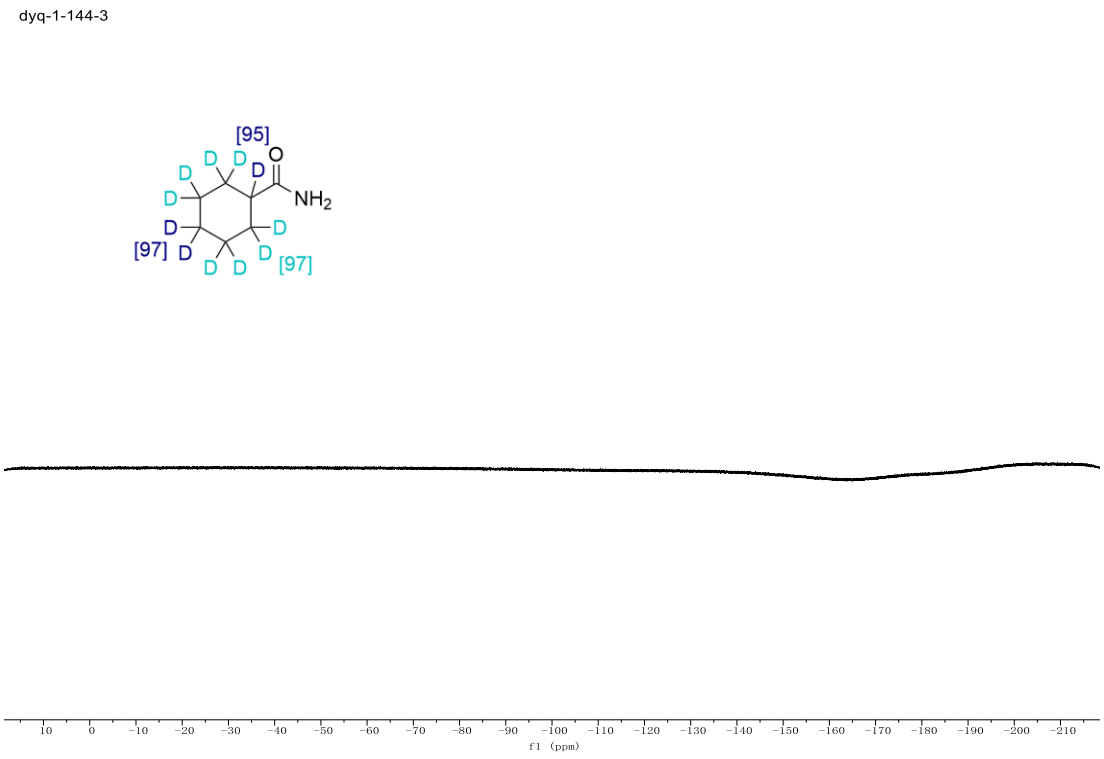
^{1}H NMR for 1f



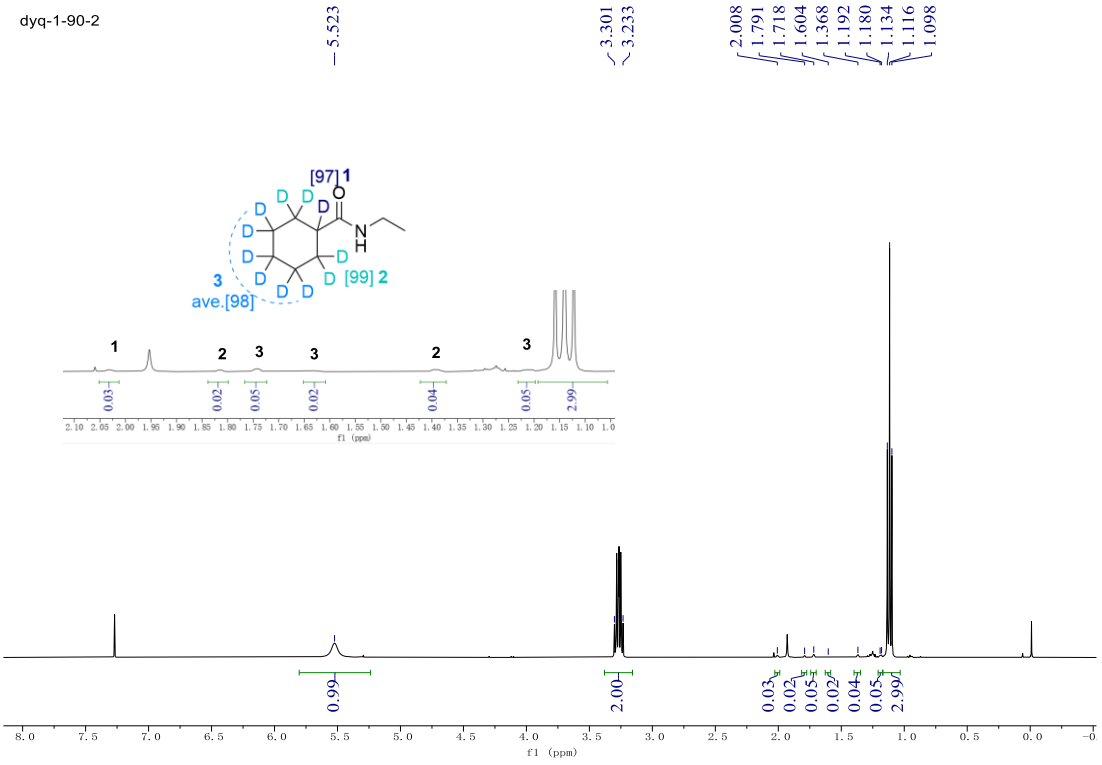
^{13}C NMR for 1f



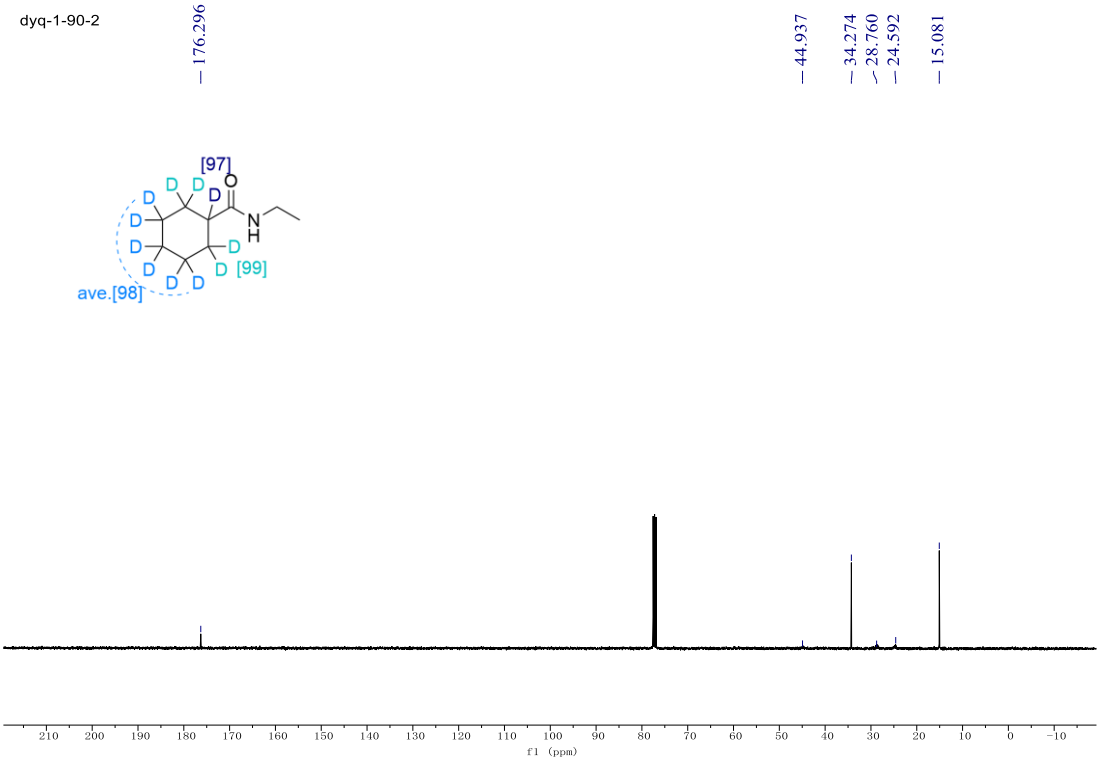
^{19}F NMR for 1f



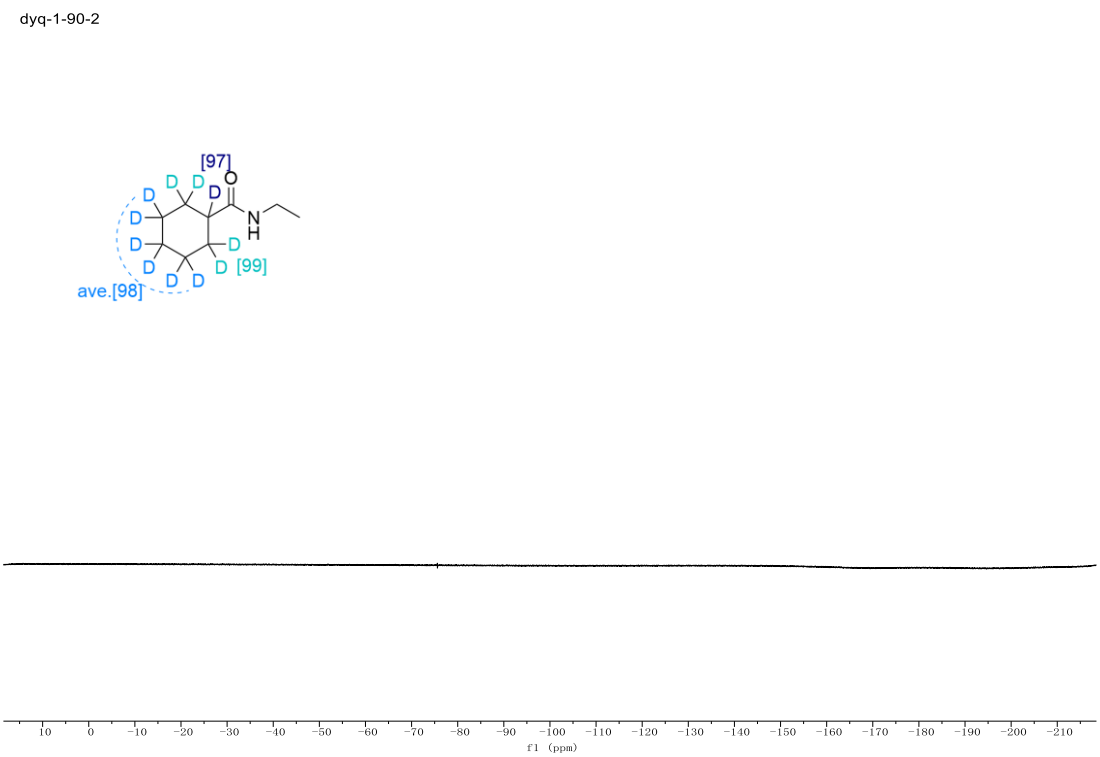
^{1}H NMR for 2f



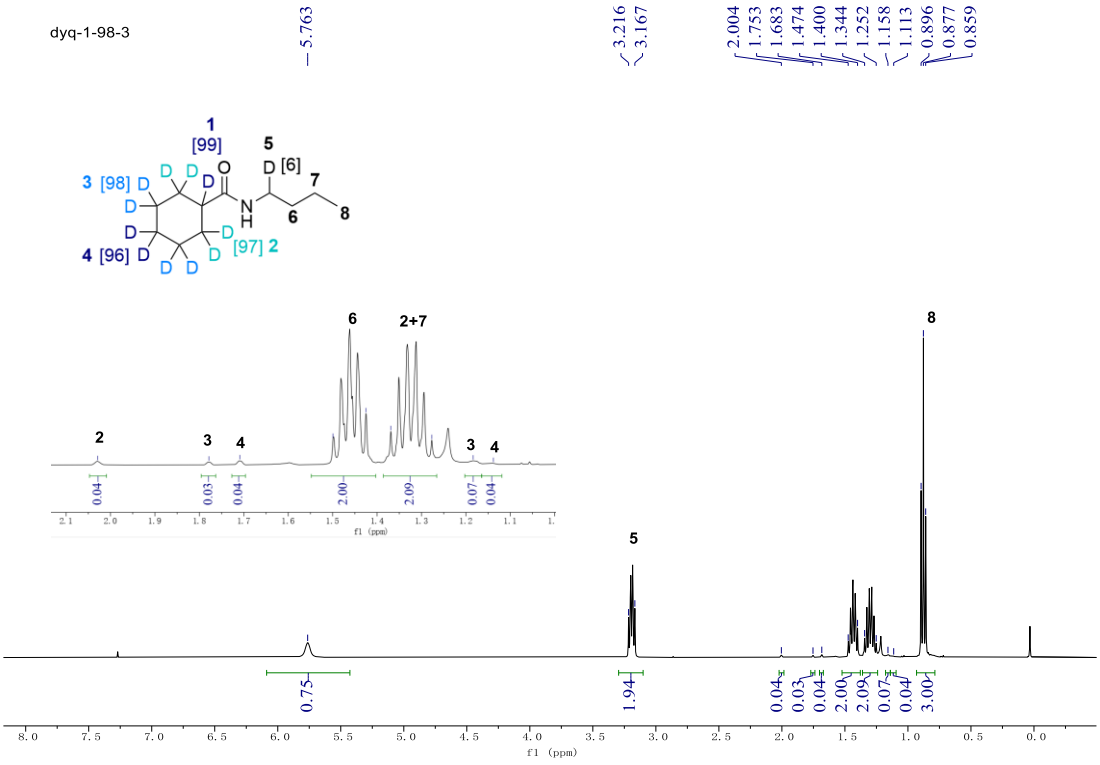
^{13}C NMR for 2f



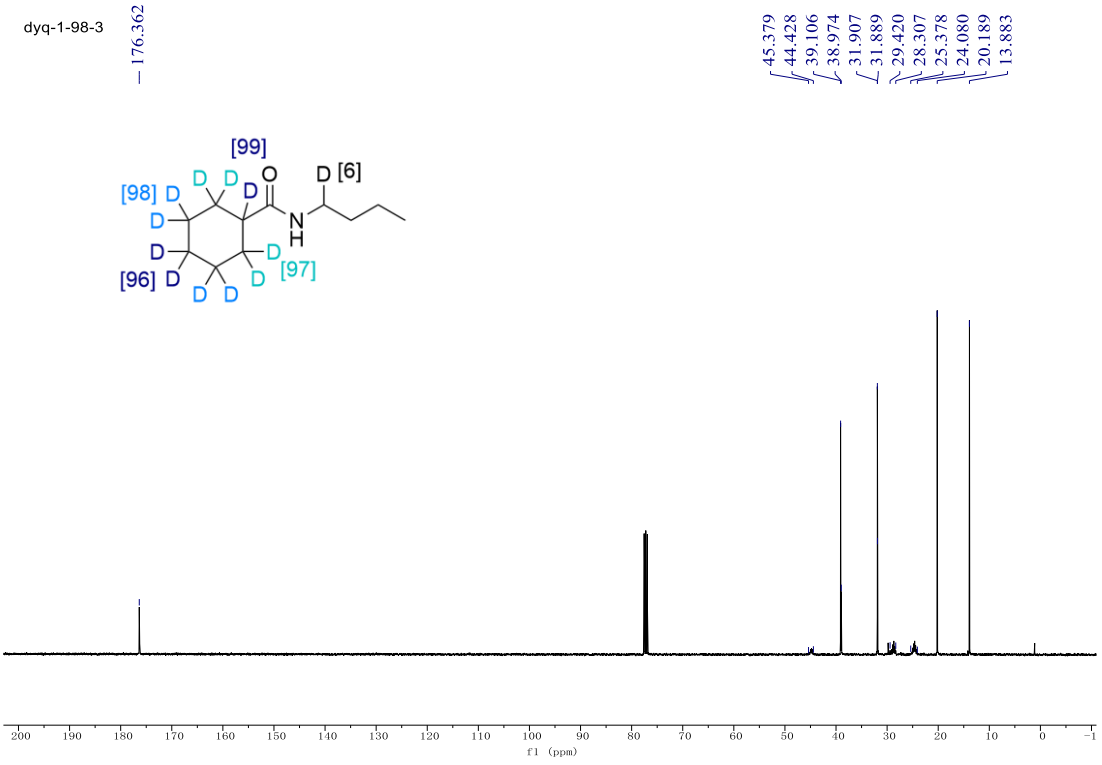
^{19}F NMR for 2f



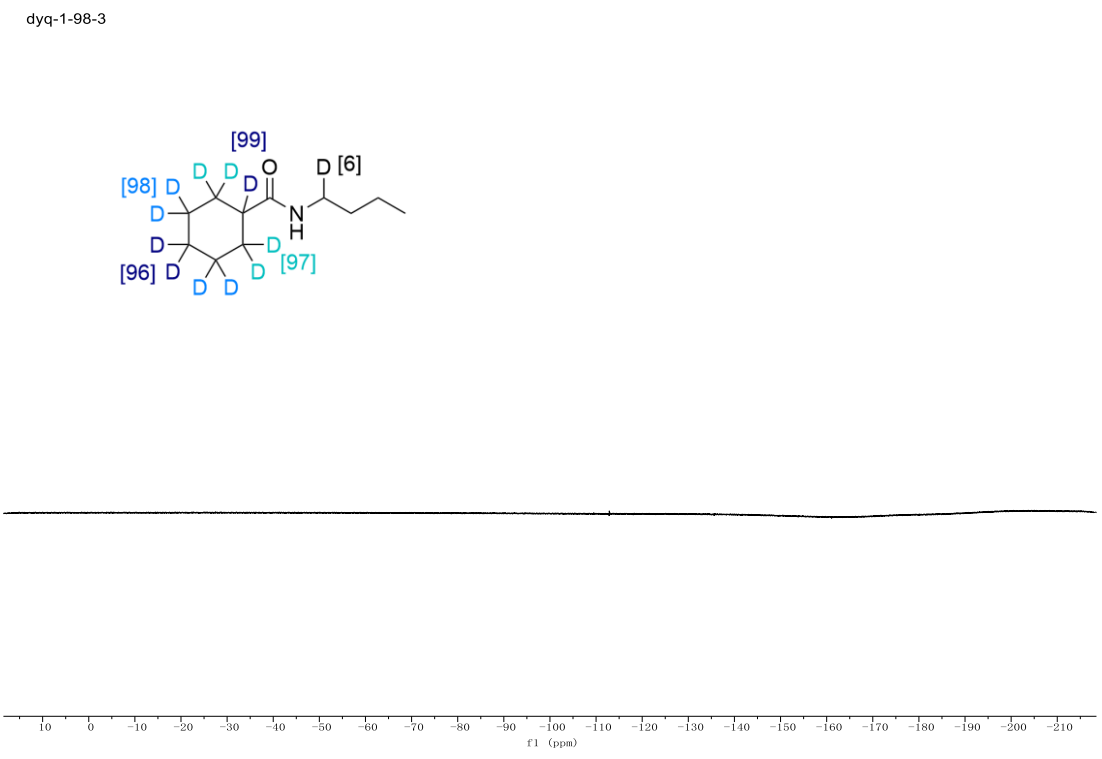
^{1}H NMR for 3f



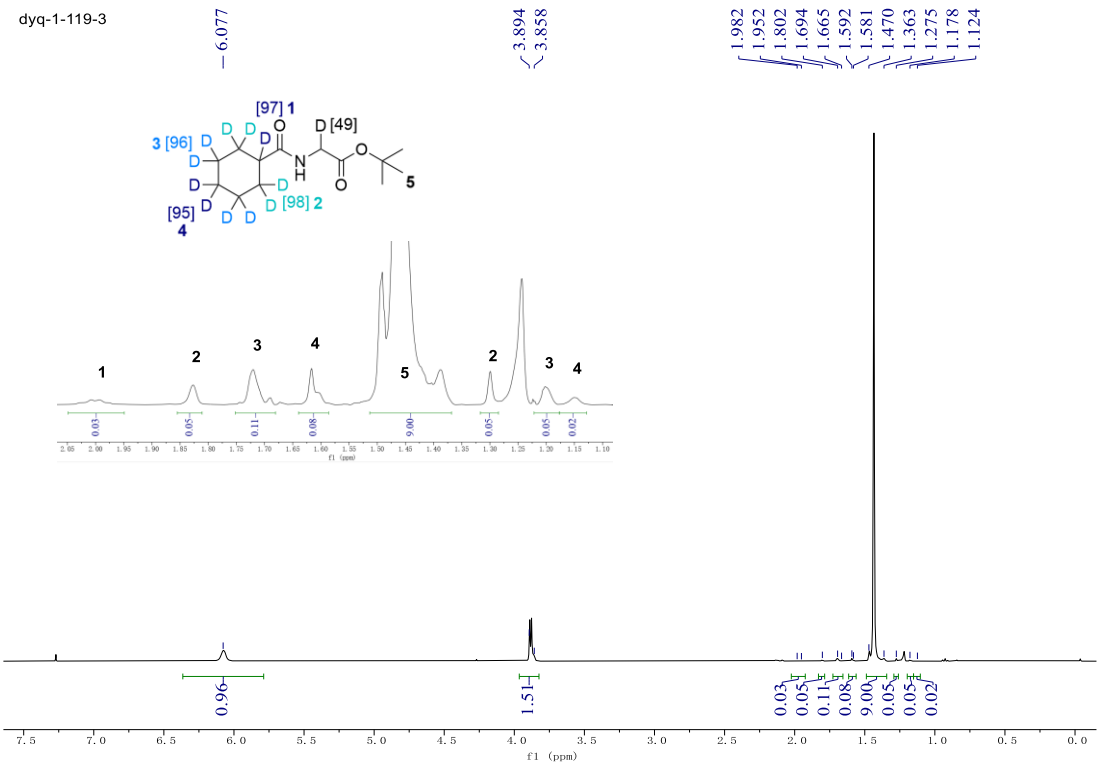
^{13}C NMR for 3f



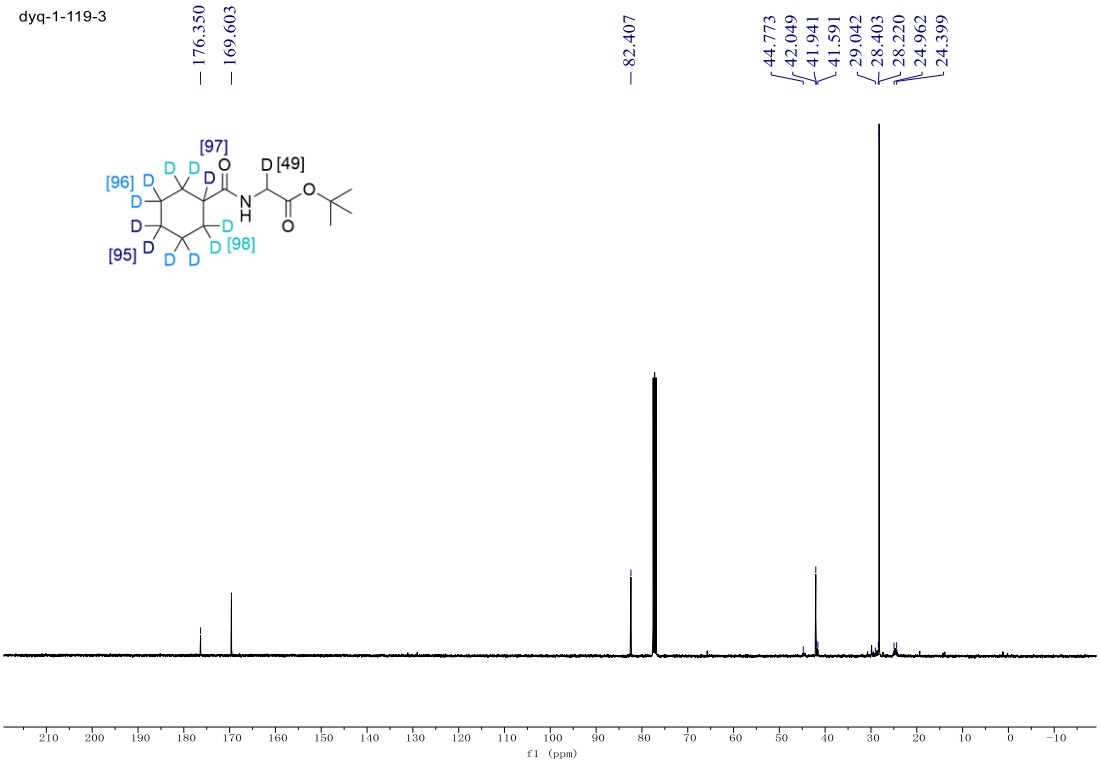
^{19}F NMR for 3f



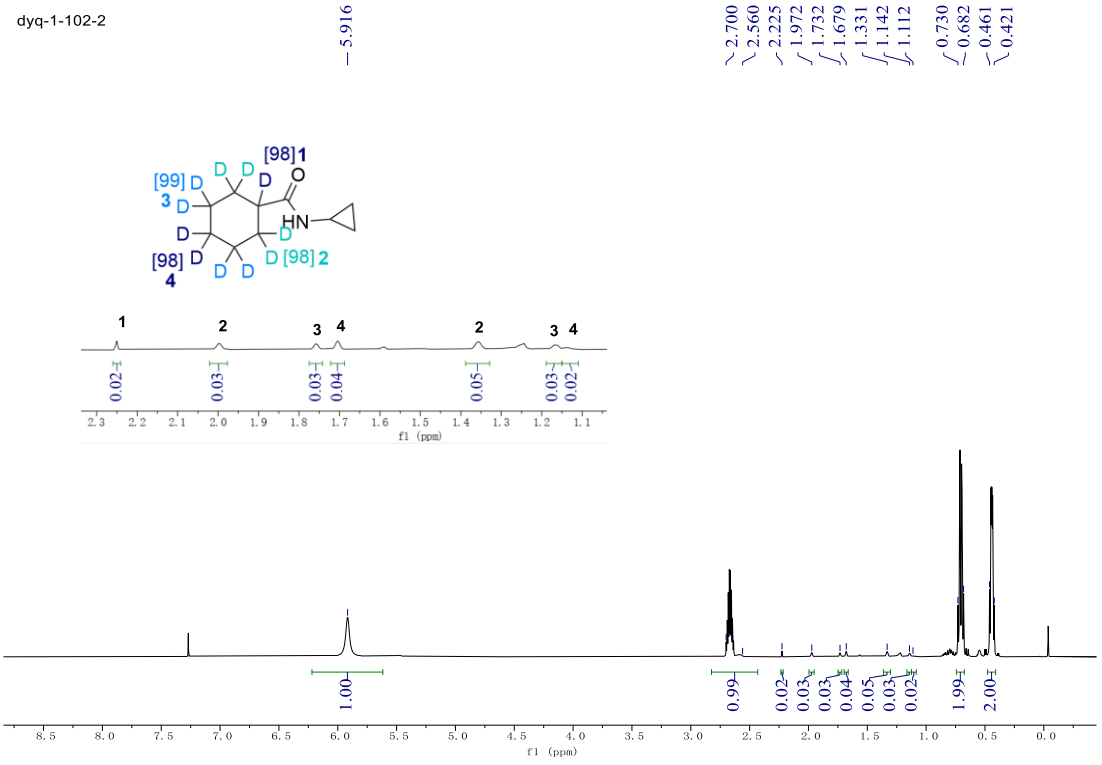
^{1}H NMR for 4f



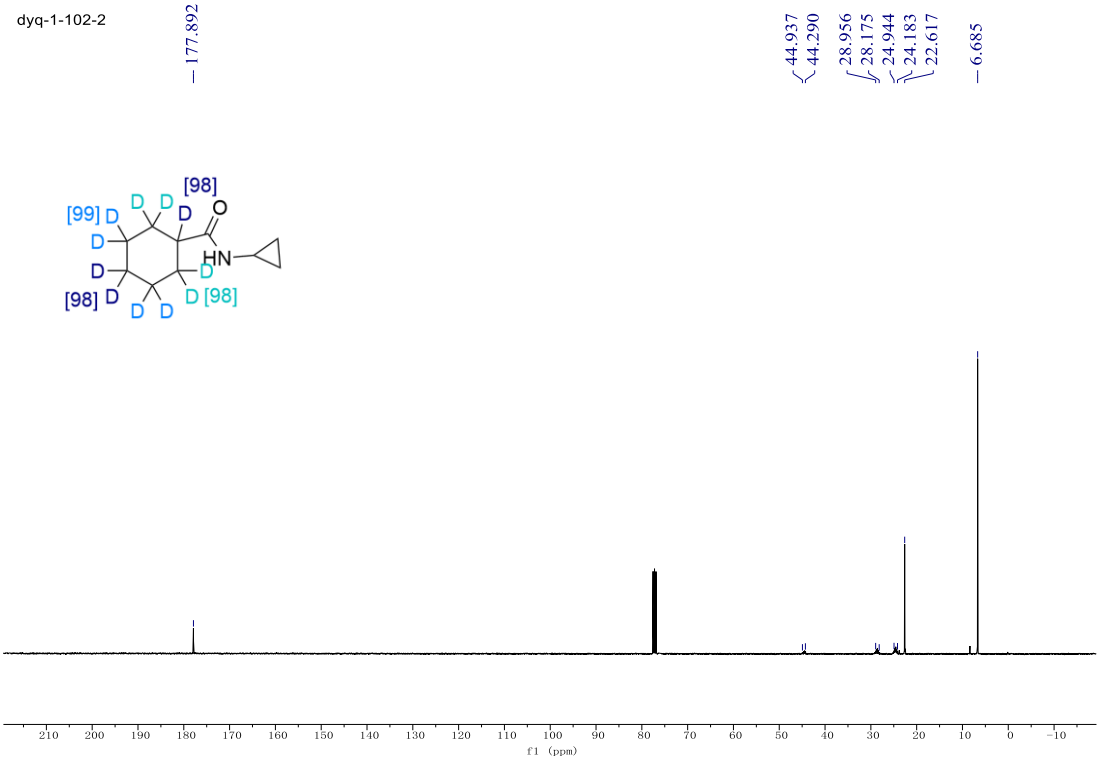
^{13}C NMR for 4f



^{1}H NMR for 5f

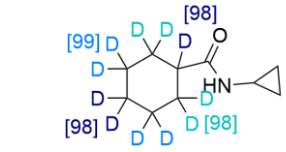


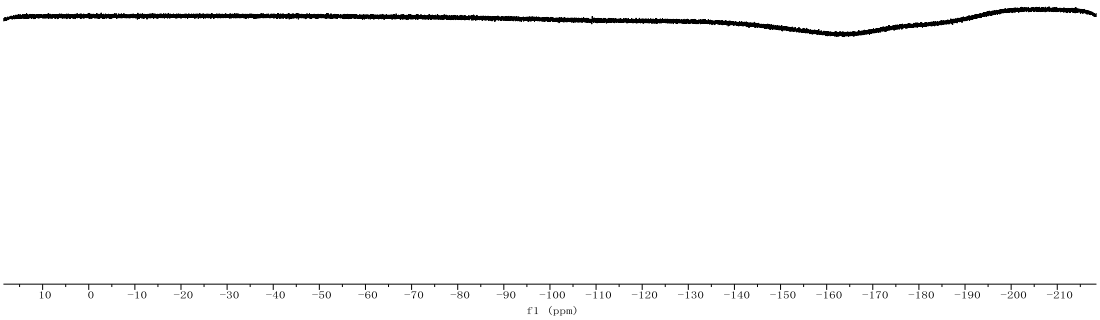
^{13}C NMR for 5f



^{19}F NMR for 5f

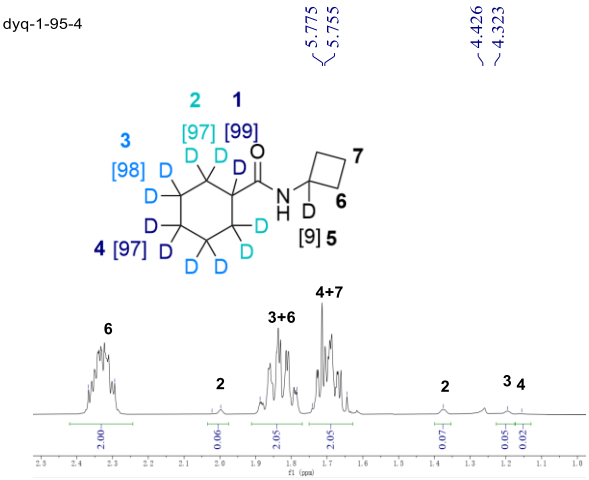
dyq-1-102-2



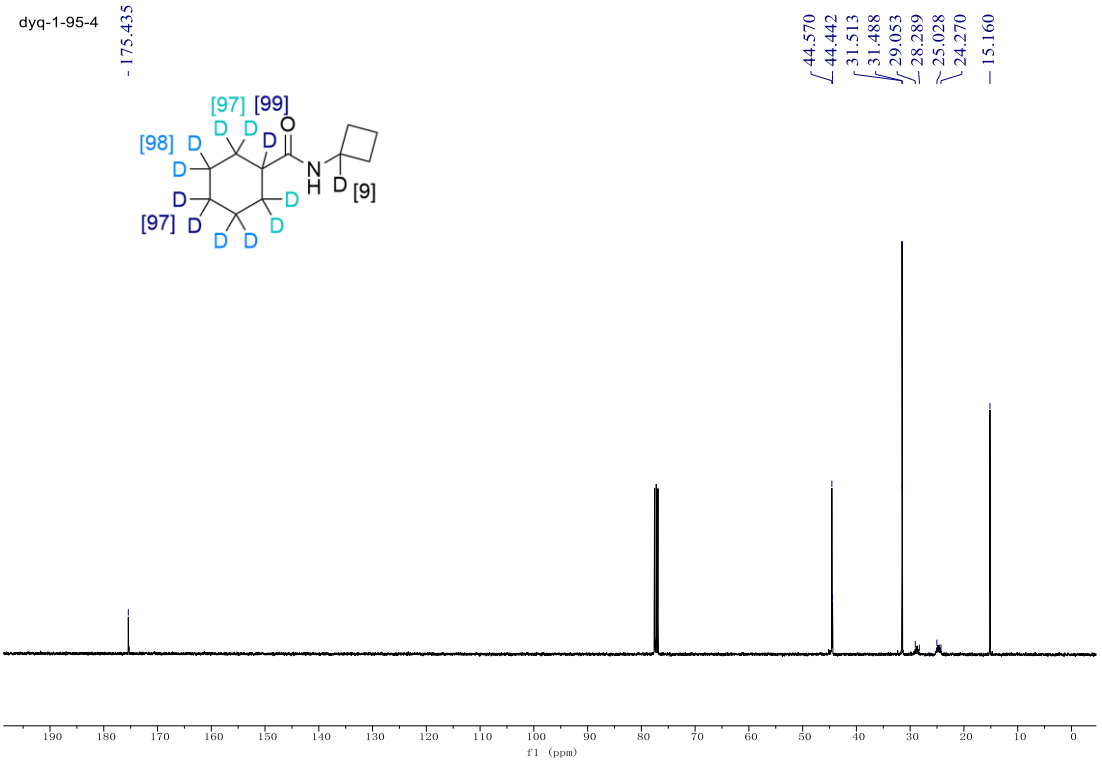


^{1}H NMR for 6f

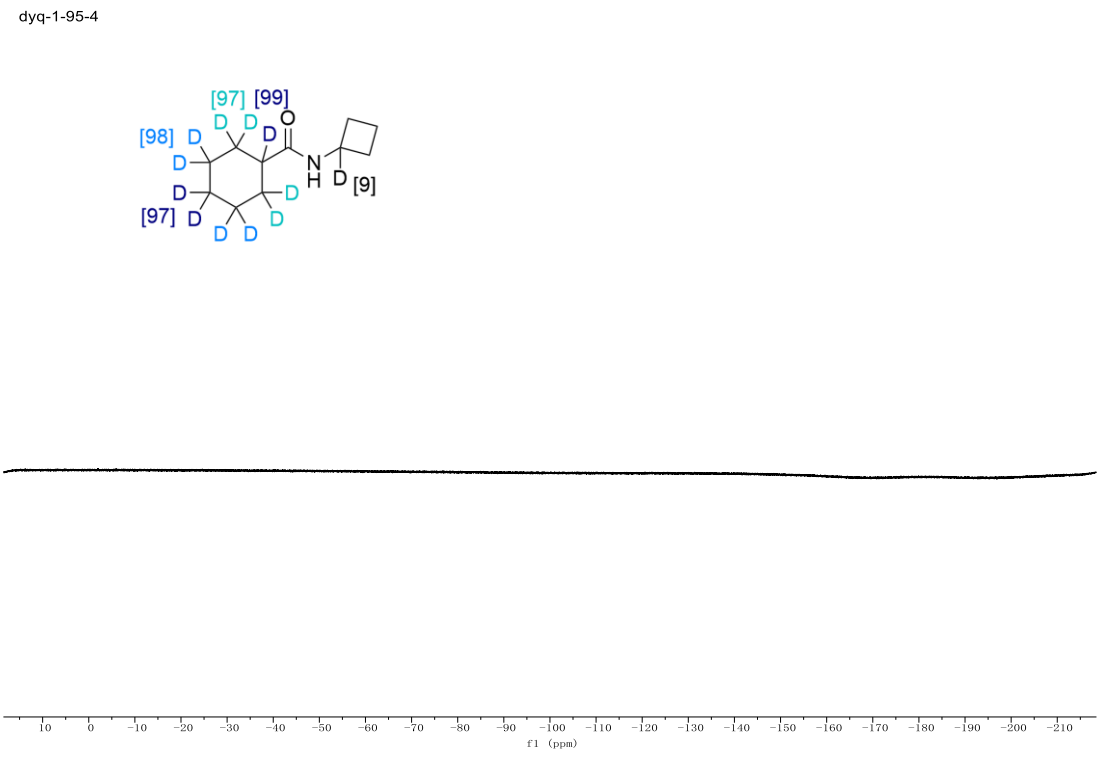
dyq-1-95-4



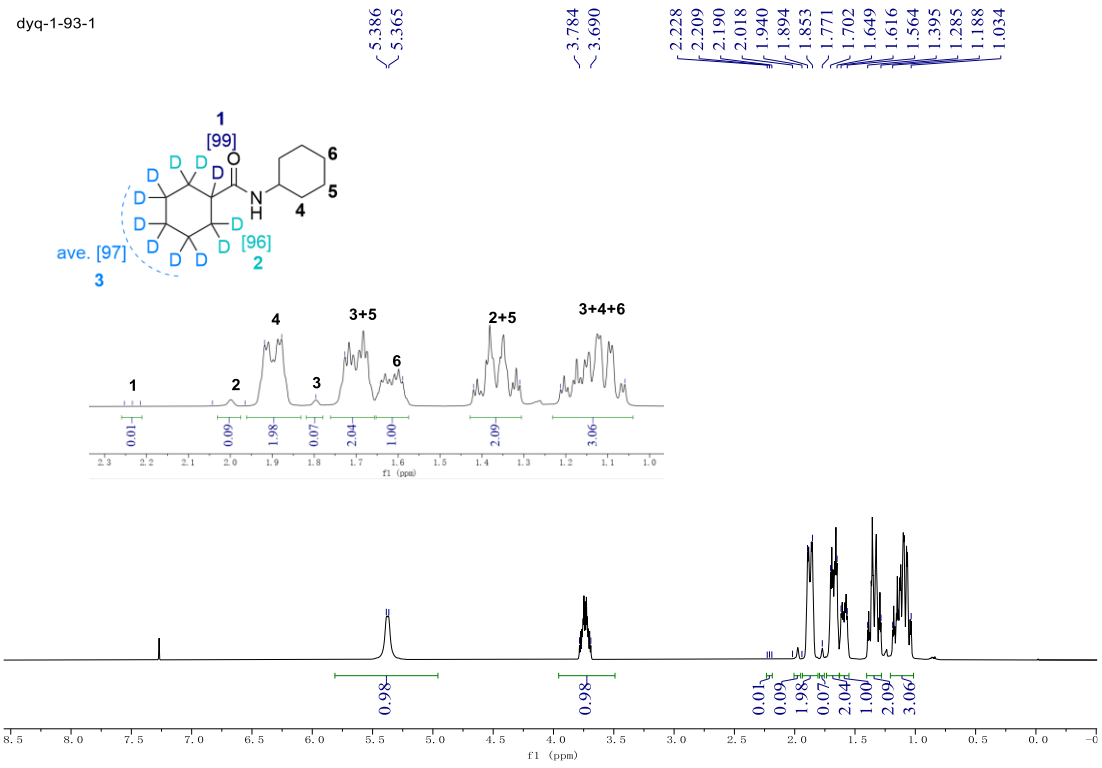
^{13}C NMR for 6f



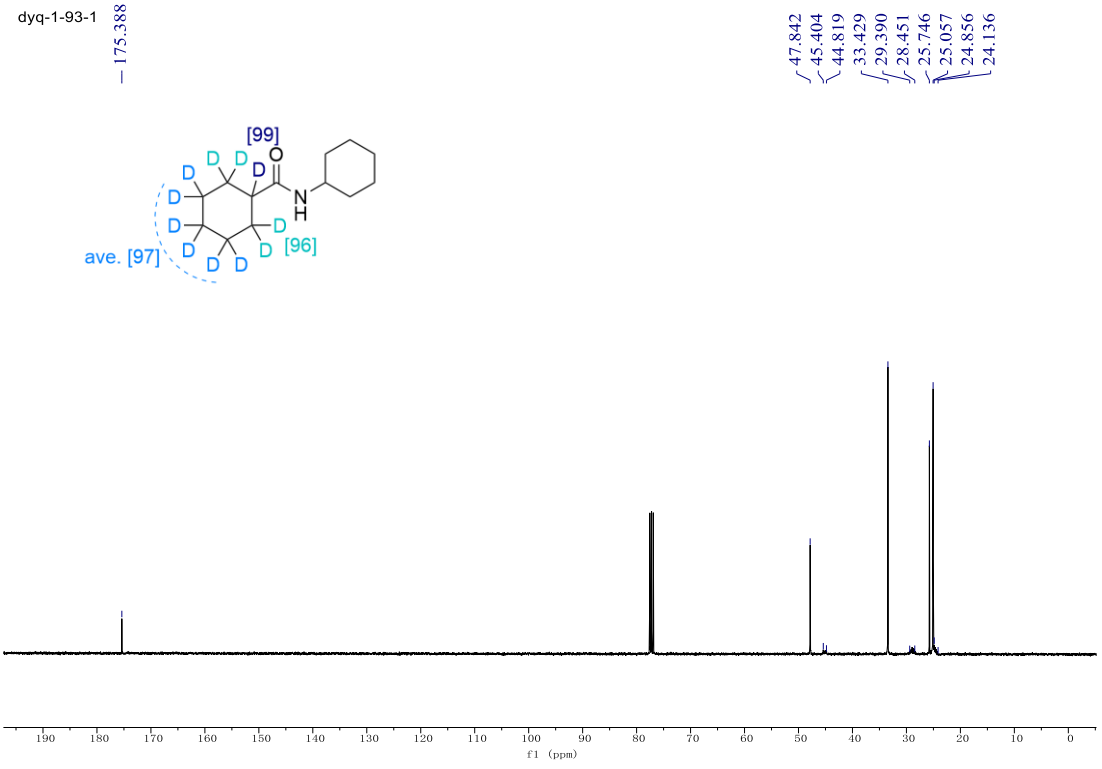
^{19}F NMR for 6f



^{1}H NMR for 7f

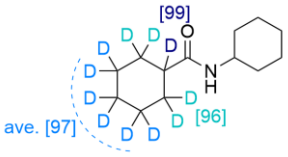


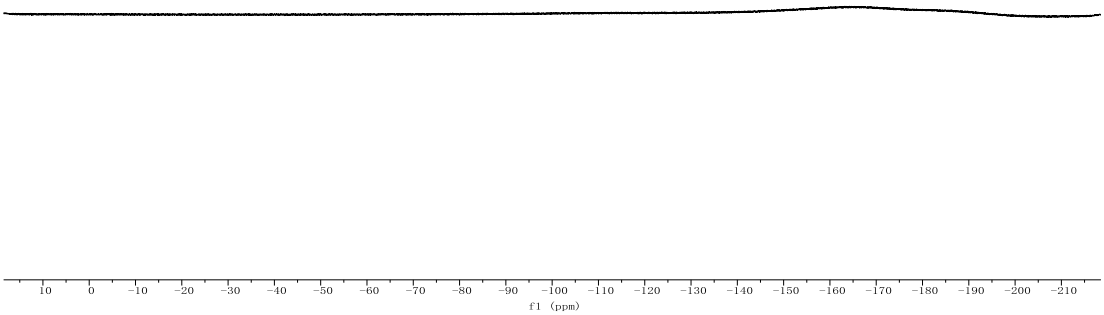
^{13}C NMR for 7f



^{19}F NMR for 7f

dyq-1-93-1

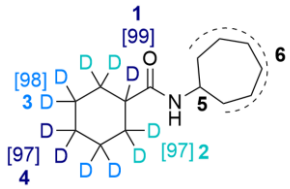


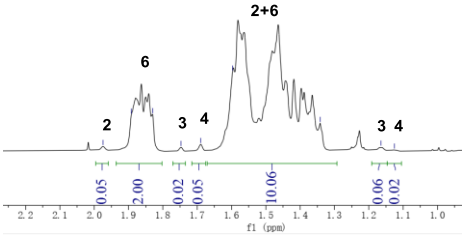


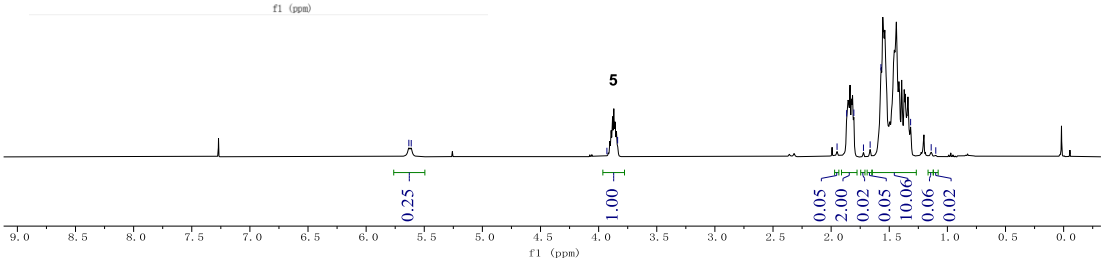
^{1}H NMR for 8f

dyq-1-111-6

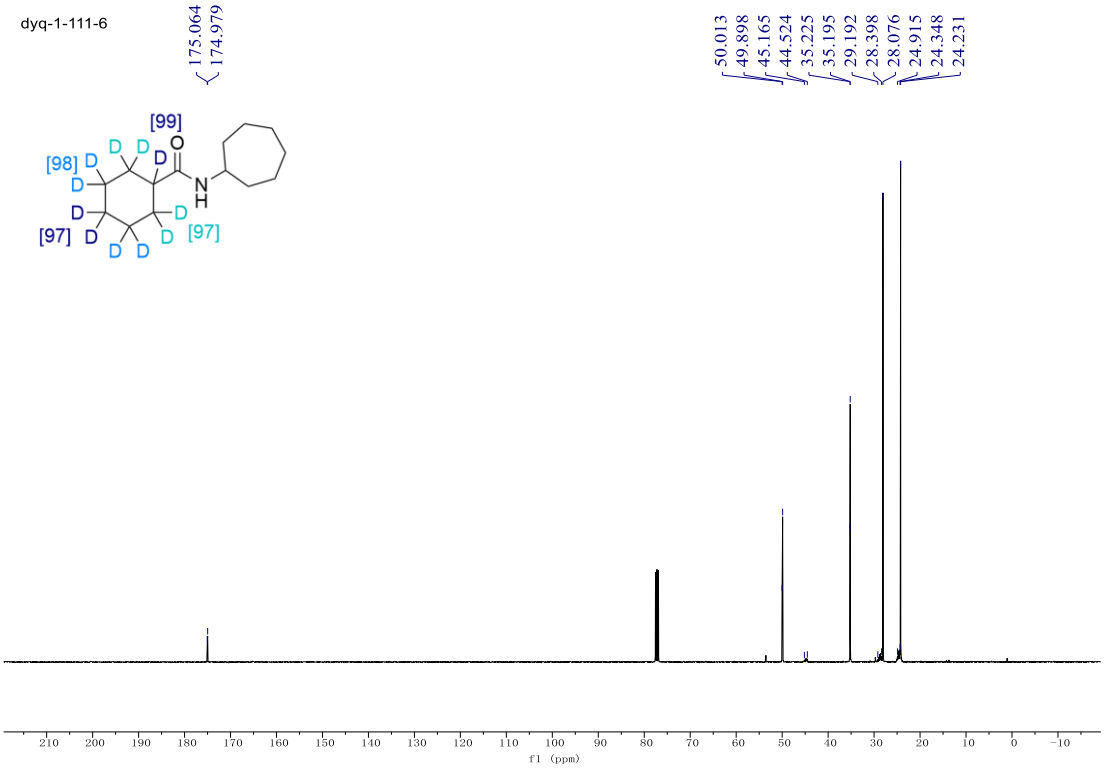
5.633
5.612
3.929
3.837
1.949
1.867
1.805
1.722
1.664
1.572
1.316
1.139
1.100



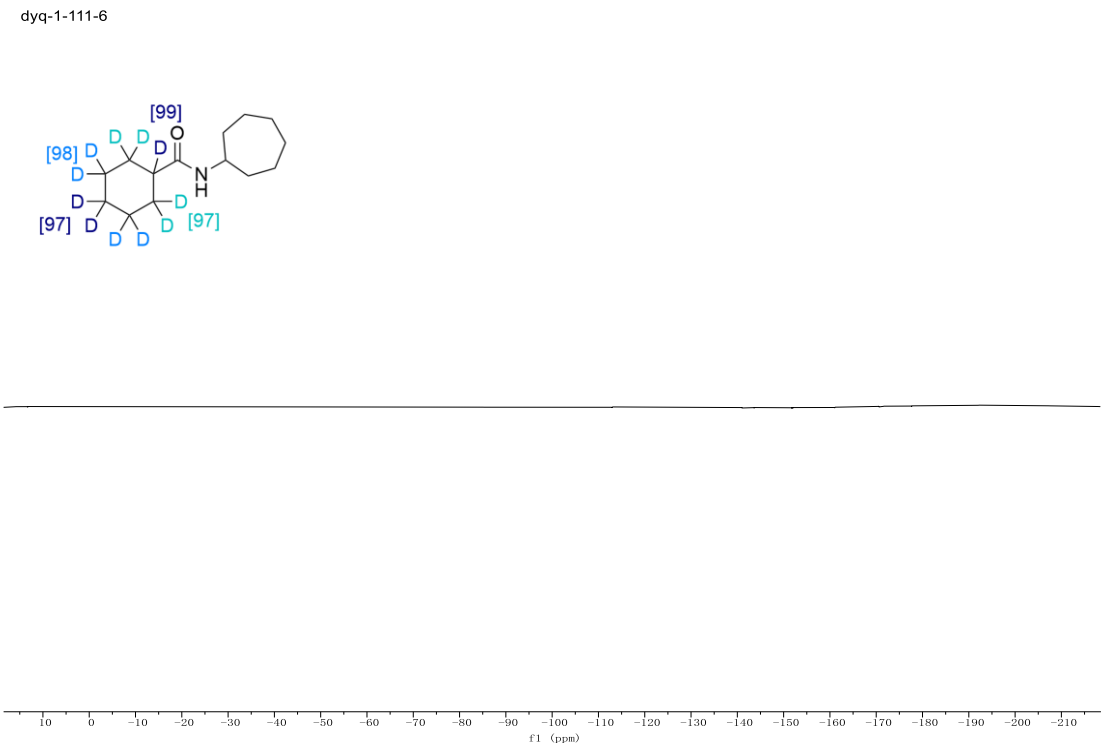




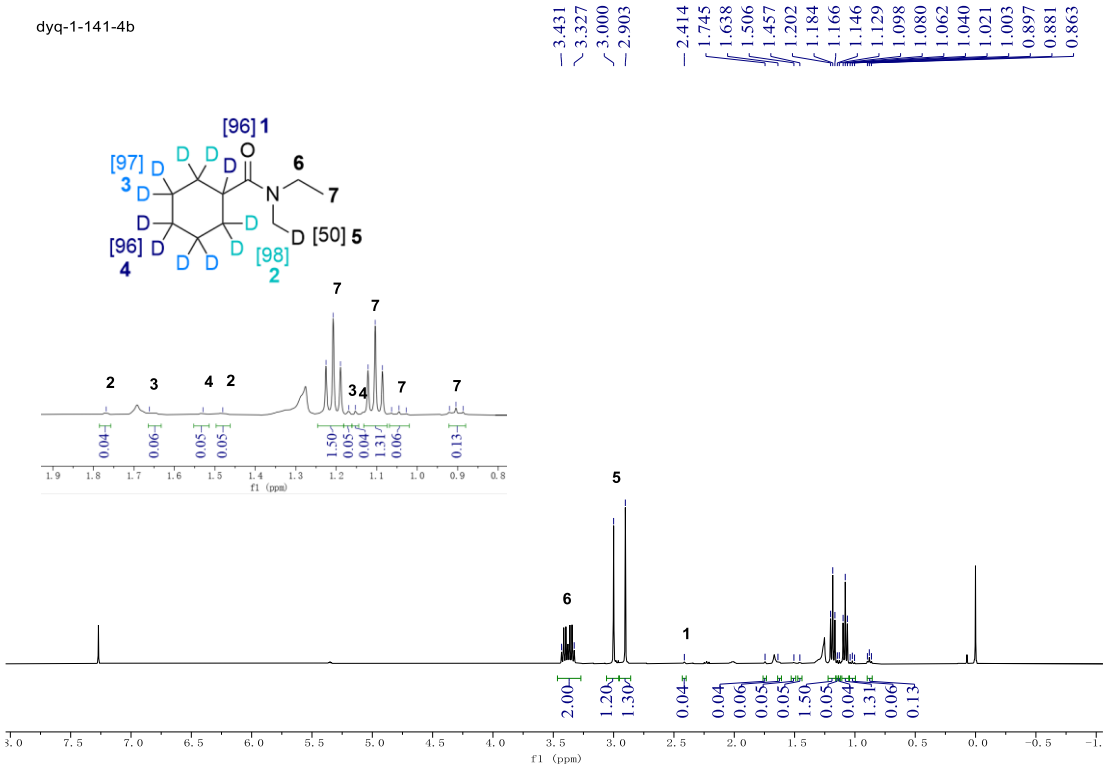
^{13}C NMR for 8f



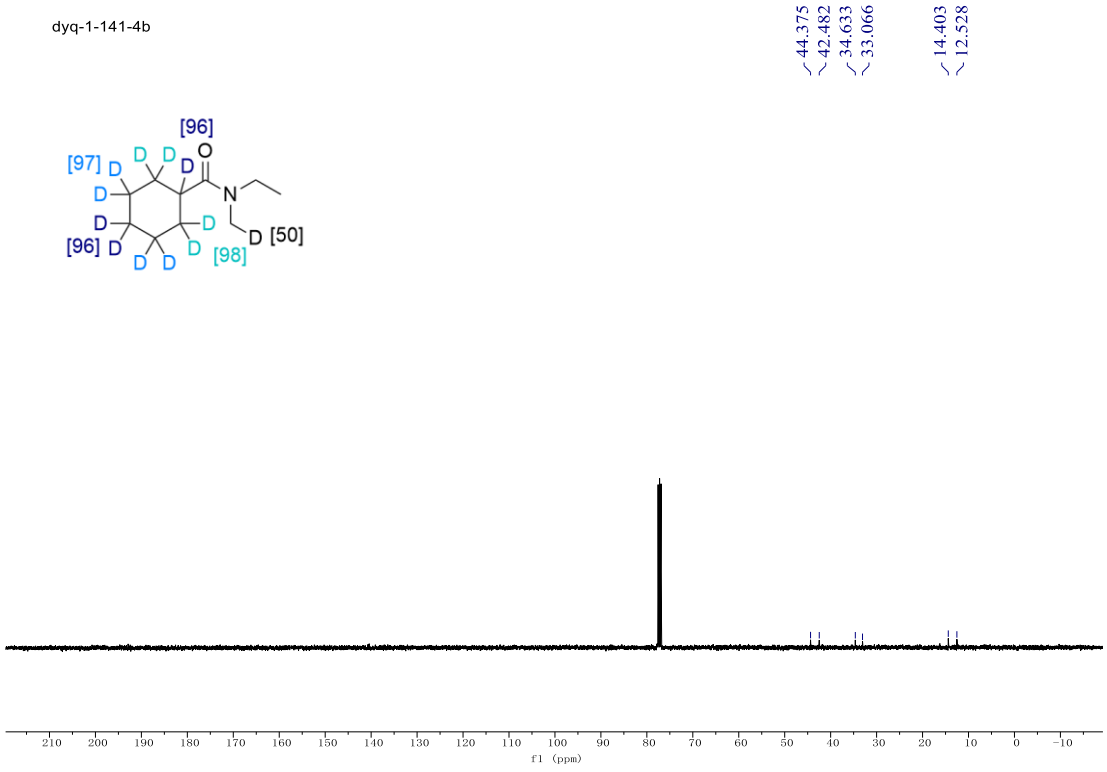
^{19}F NMR for 8f



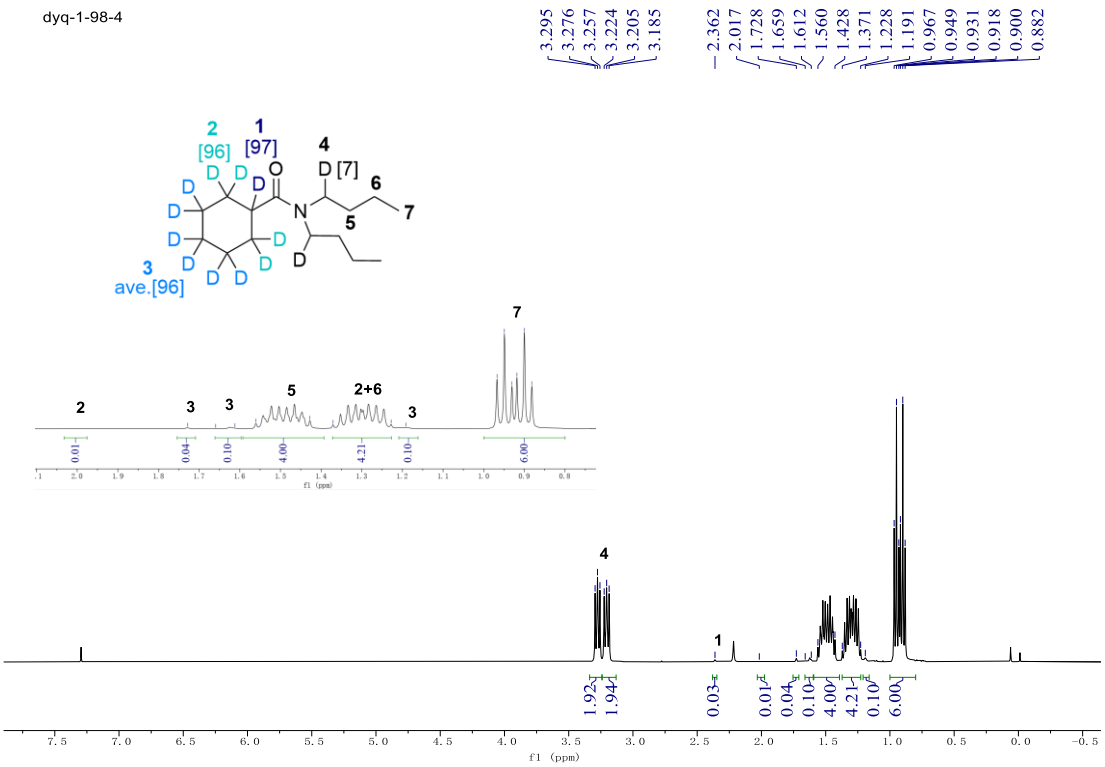
^{1}H NMR for 9f



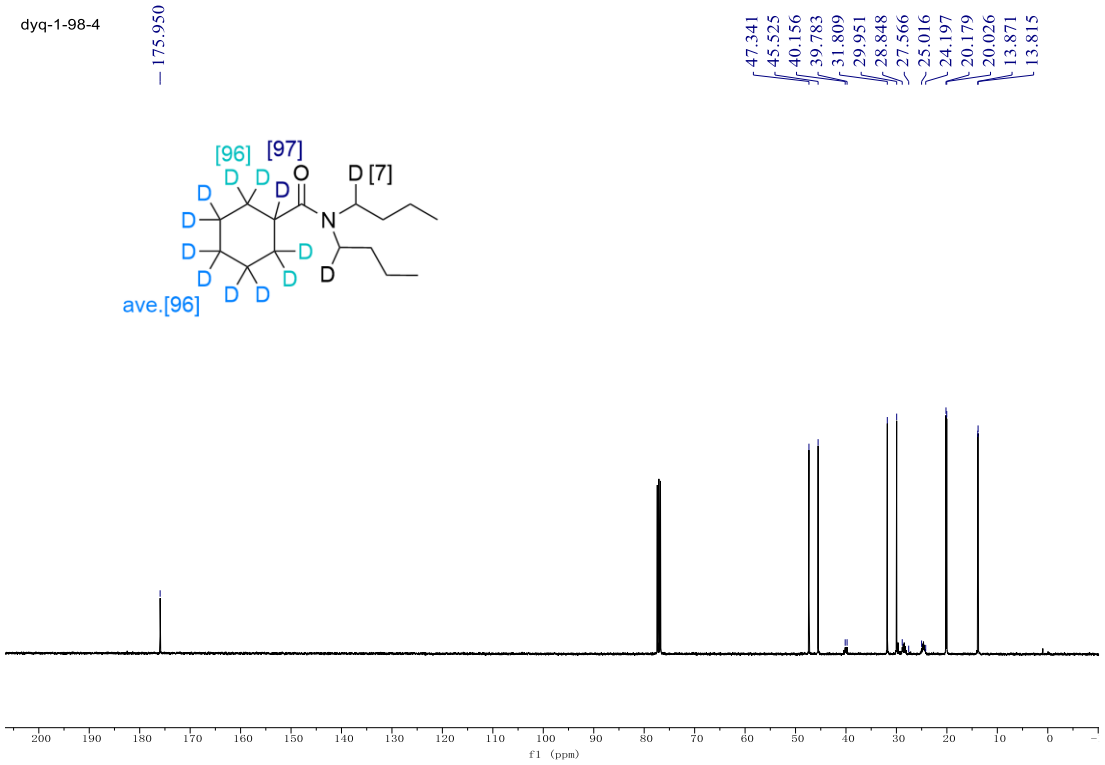
^{13}C NMR for 9f



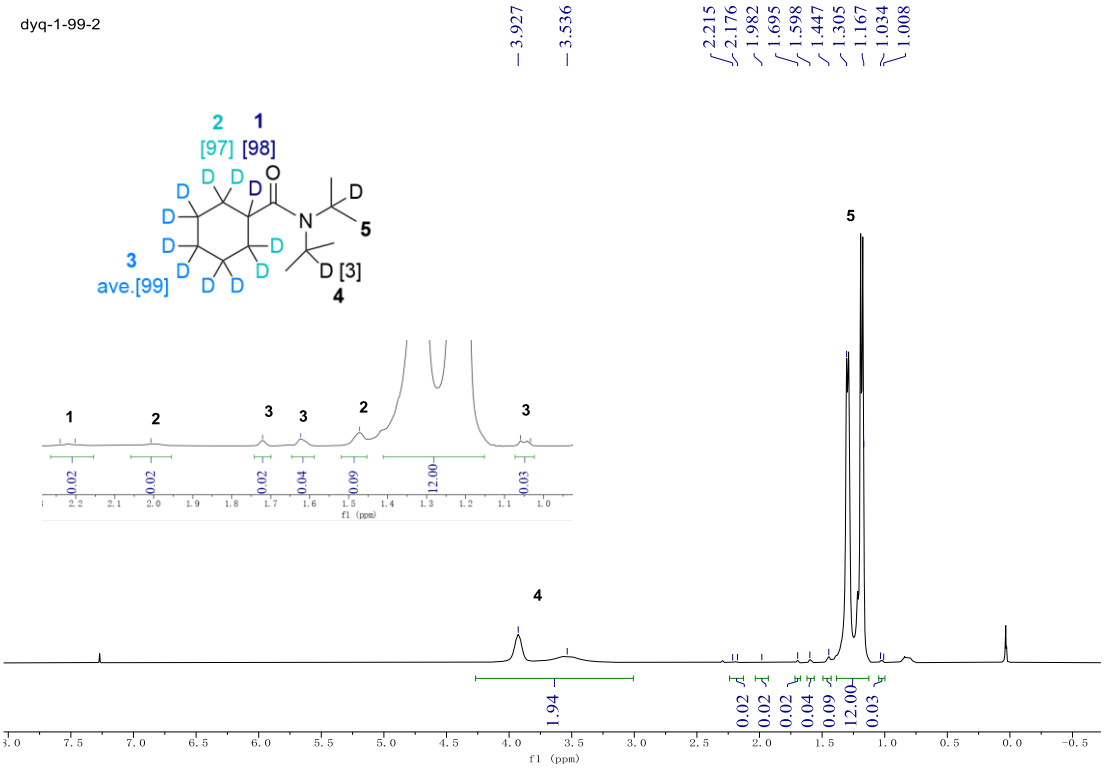
^{1}H NMR for 10f



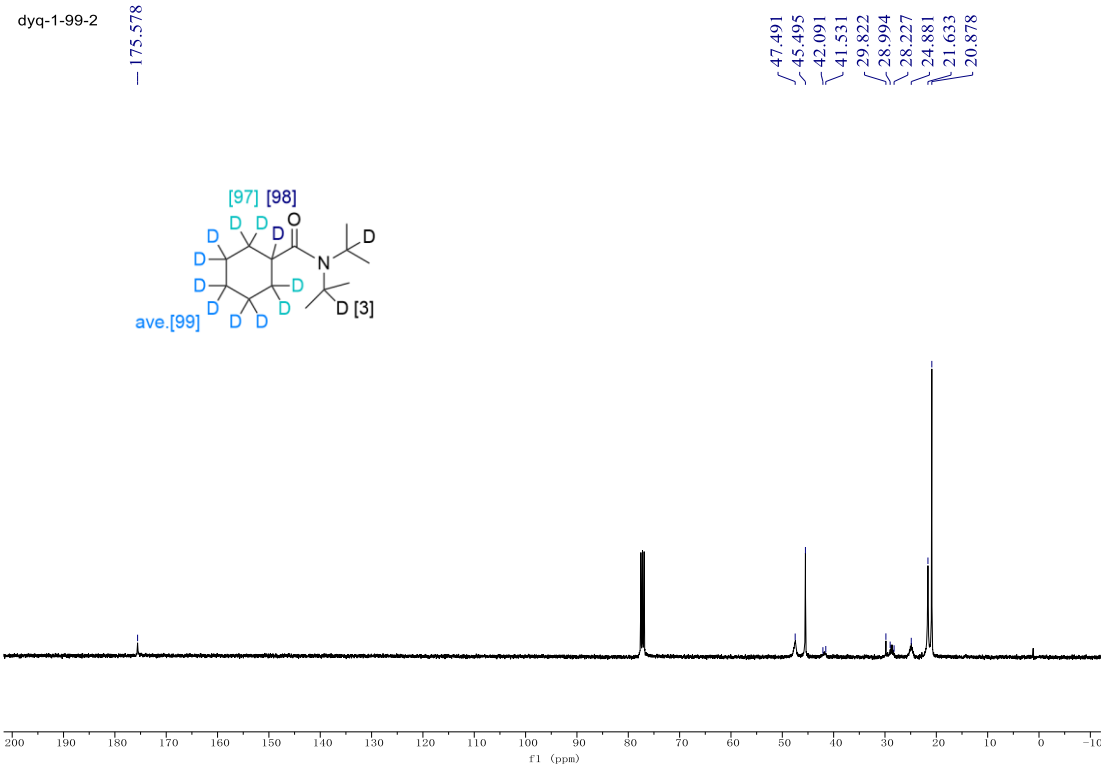
^{13}C NMR for 10f



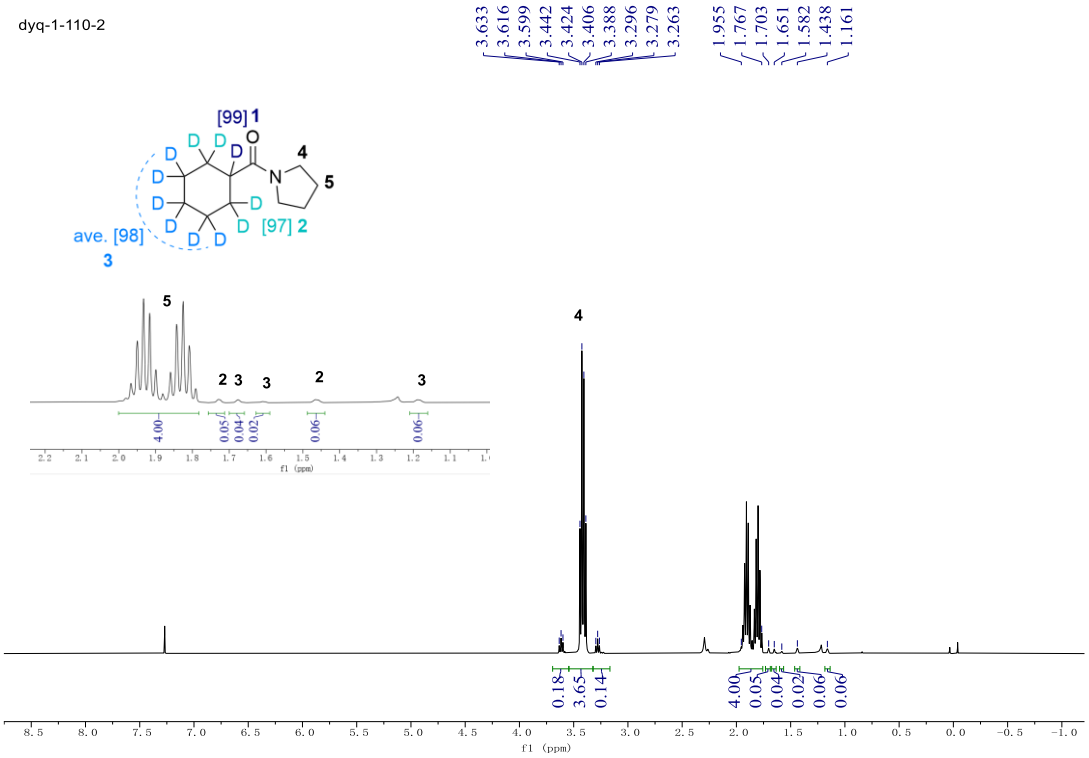
^{1}H NMR for 11f



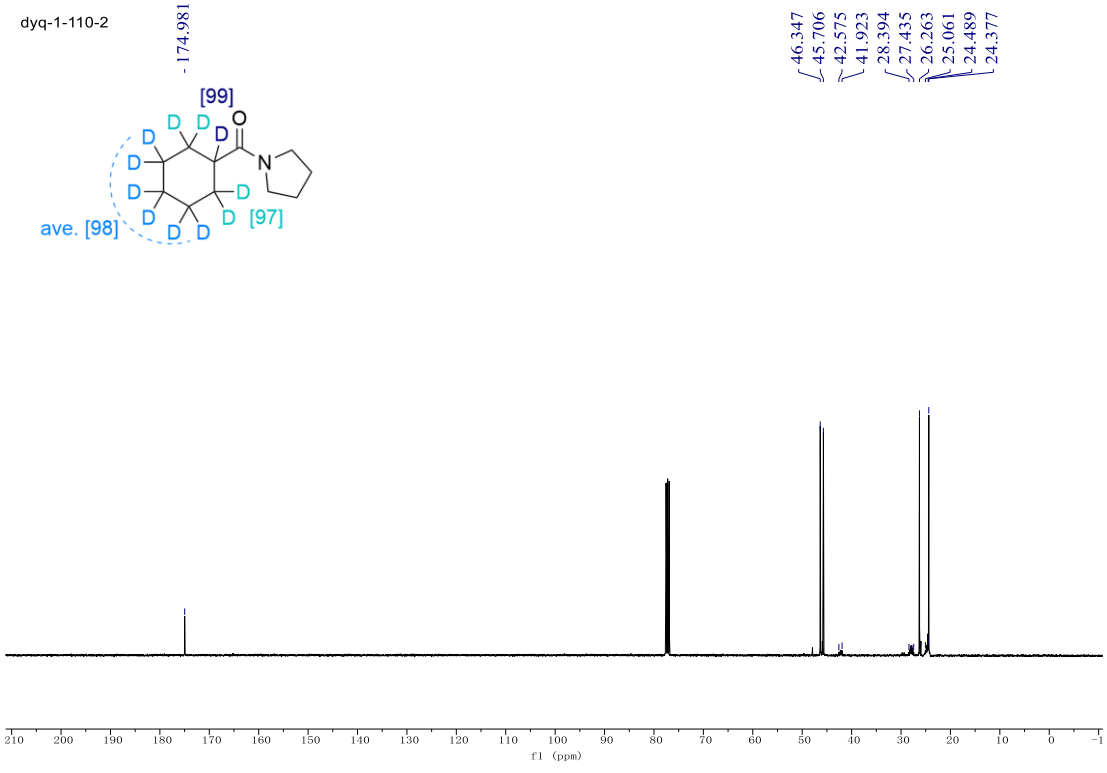
^{13}C NMR for 11f



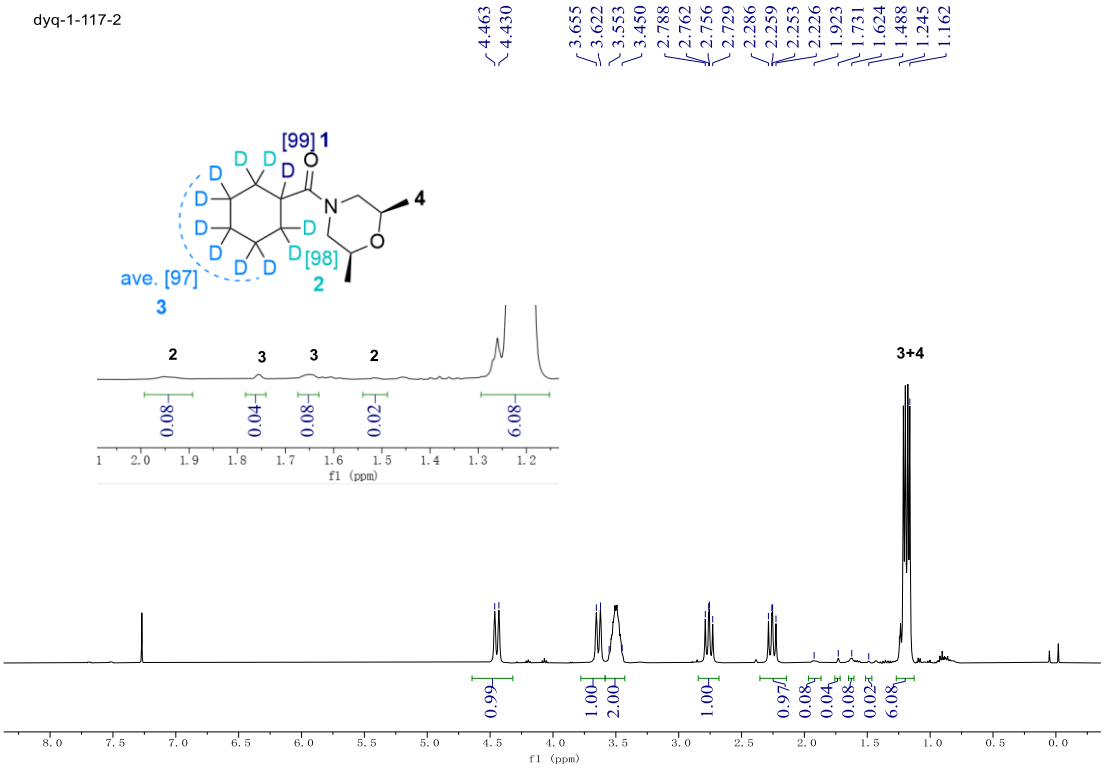
^{1}H NMR for 12f



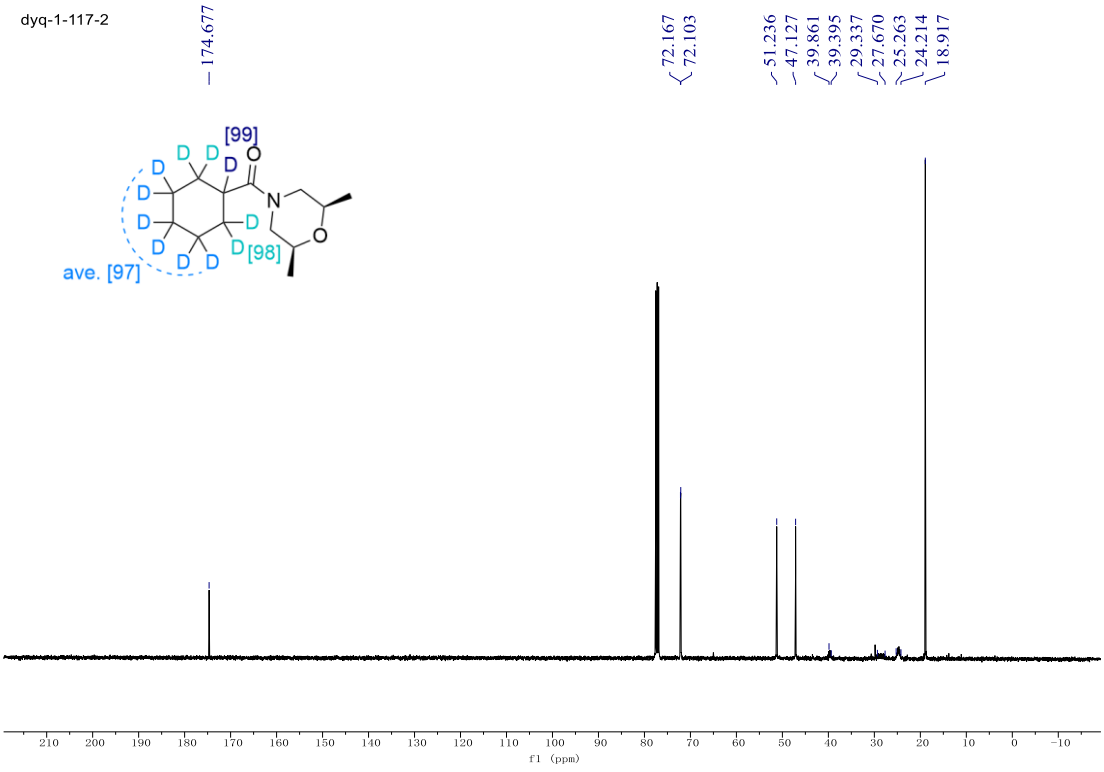
^{13}C NMR for 12f



^{1}H NMR for 13f

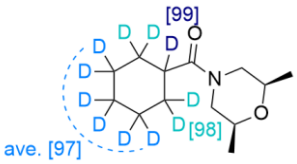


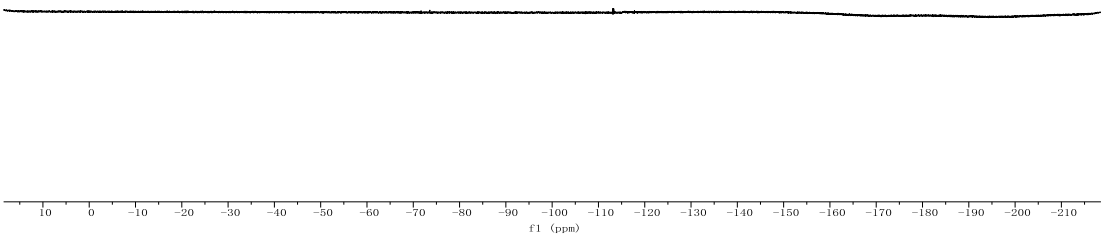
^{13}C NMR for 13f



^{19}F NMR for 13f

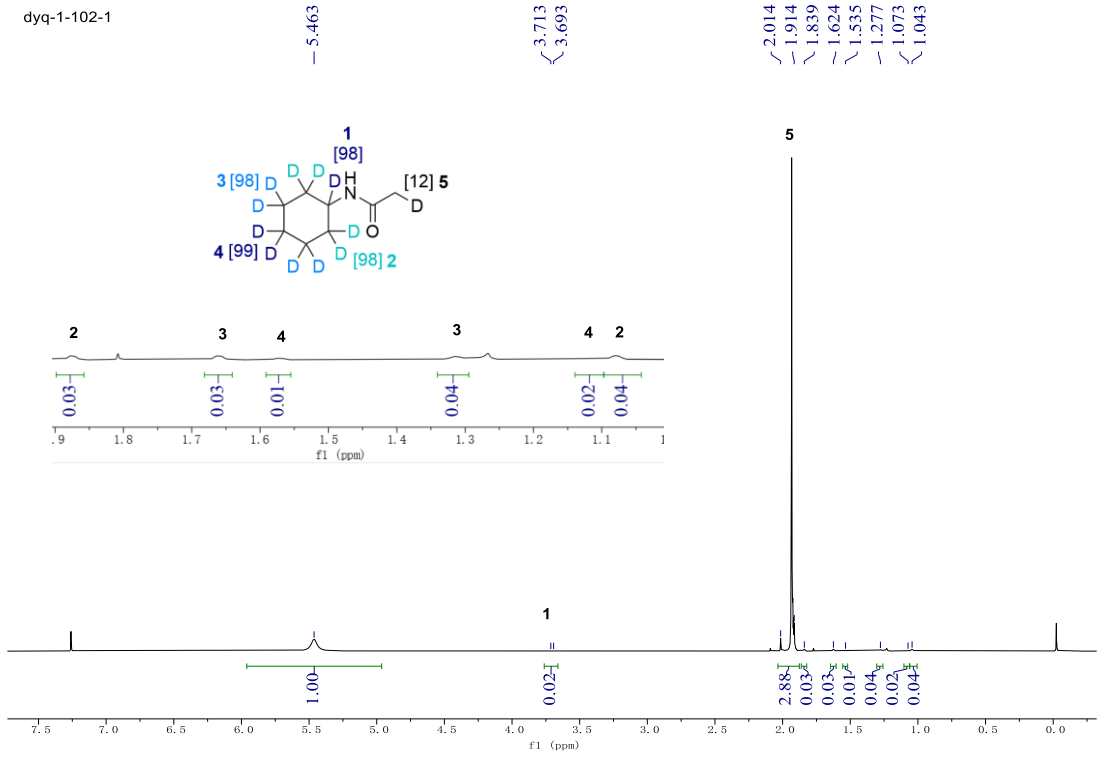
dyq-1-117-2



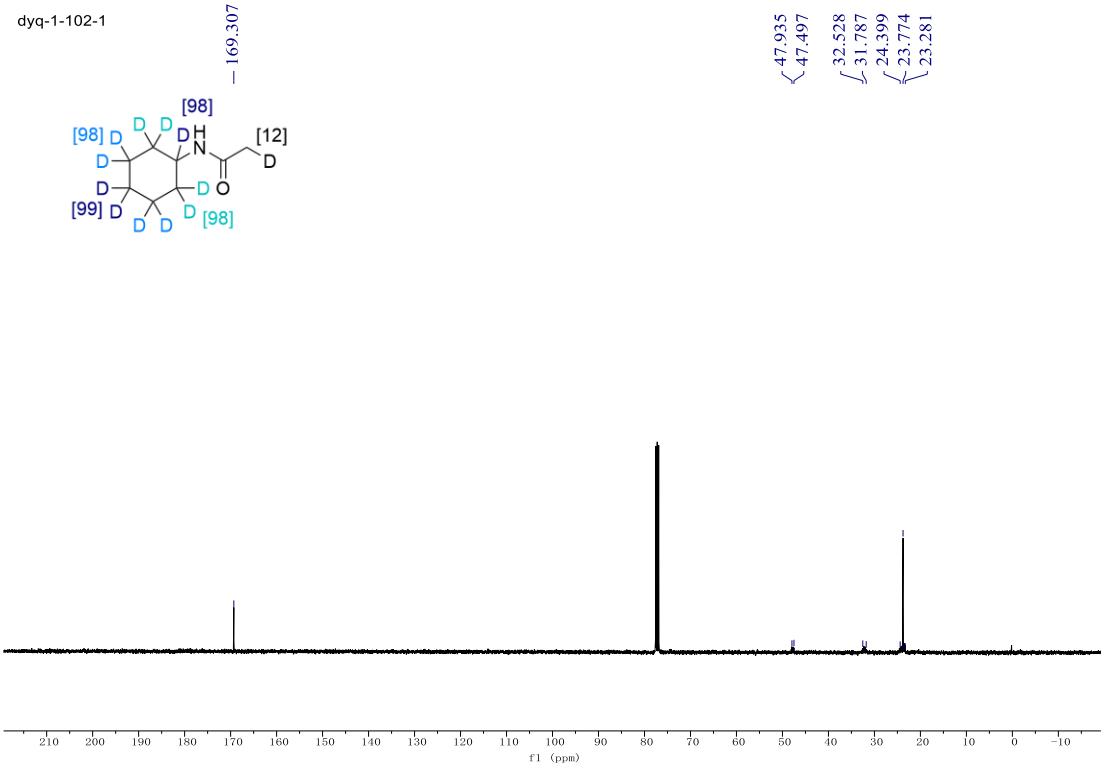


^{1}H NMR for 14f

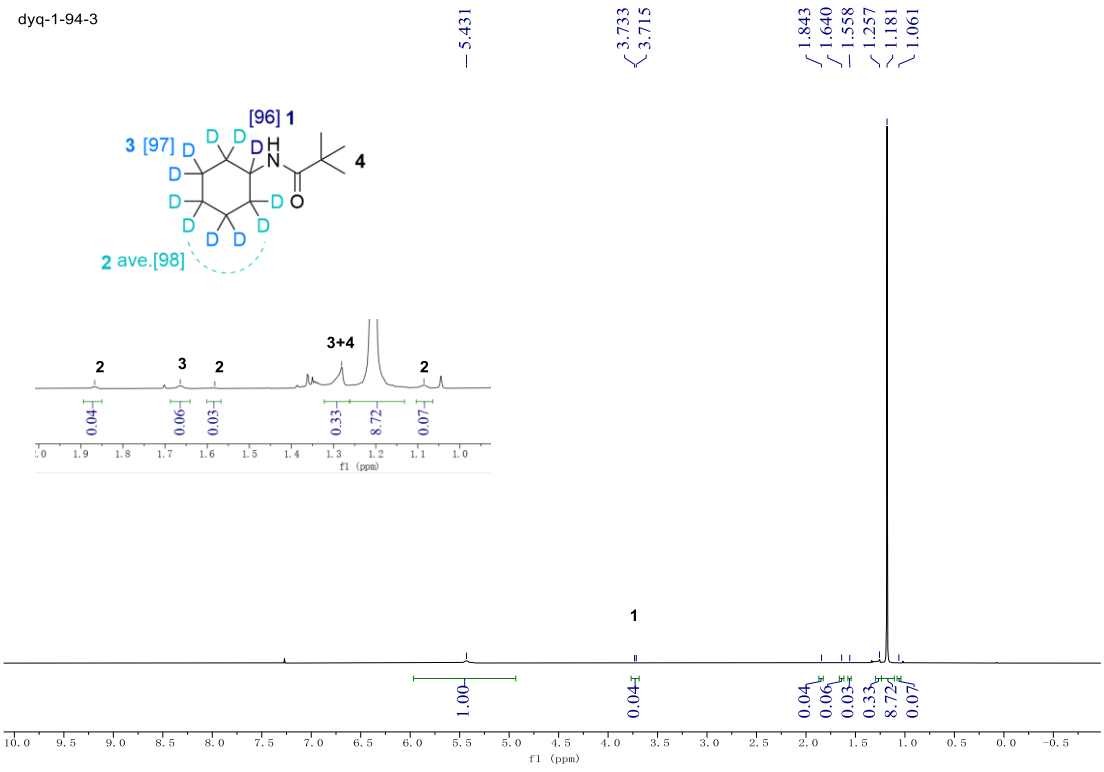
dyq-1-102-1



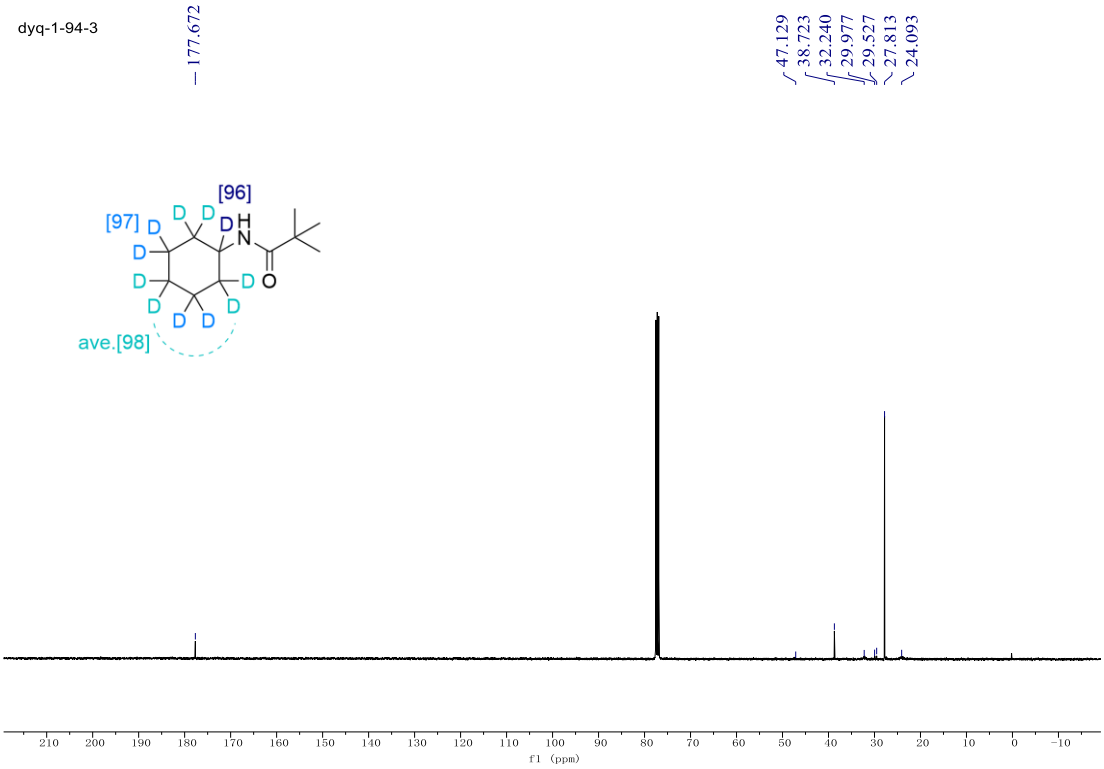
^{13}C NMR for 14f



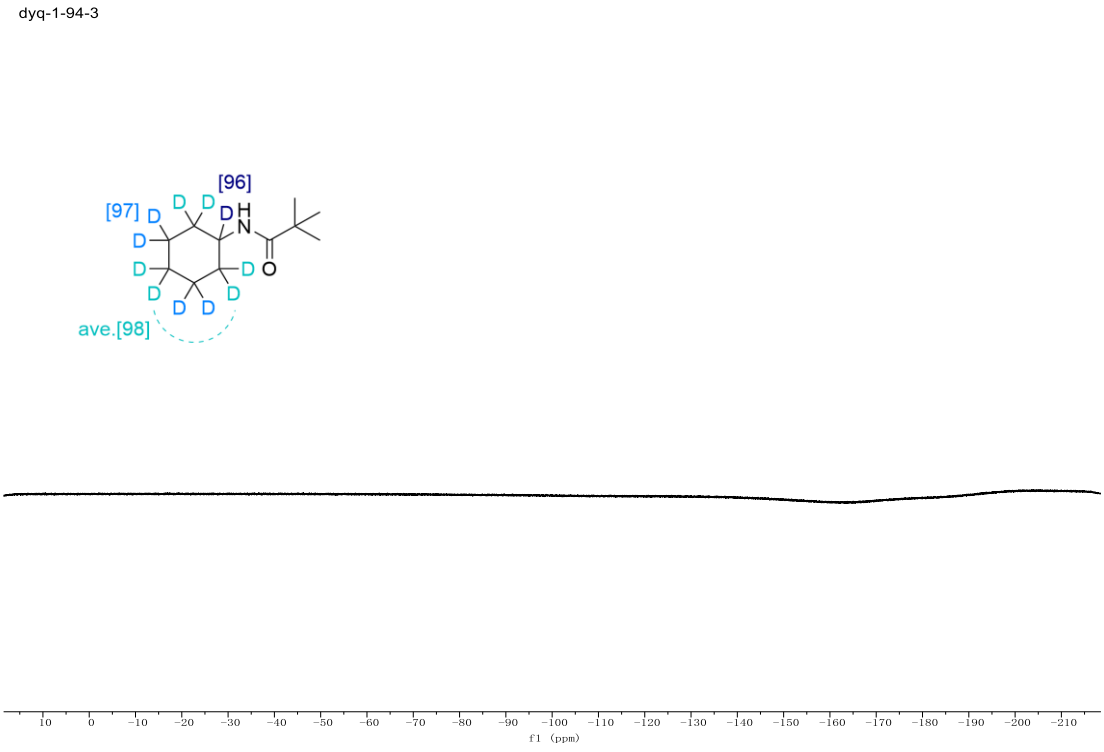
^{1}H NMR for 15f



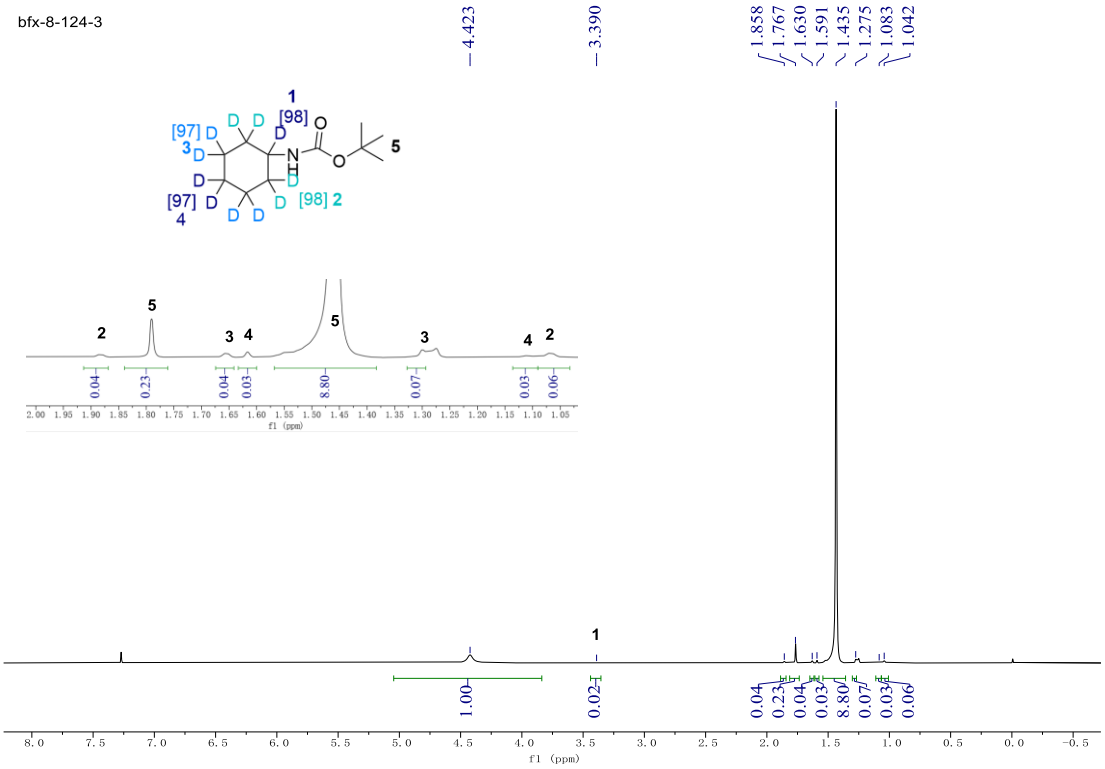
^{13}C NMR for 15f



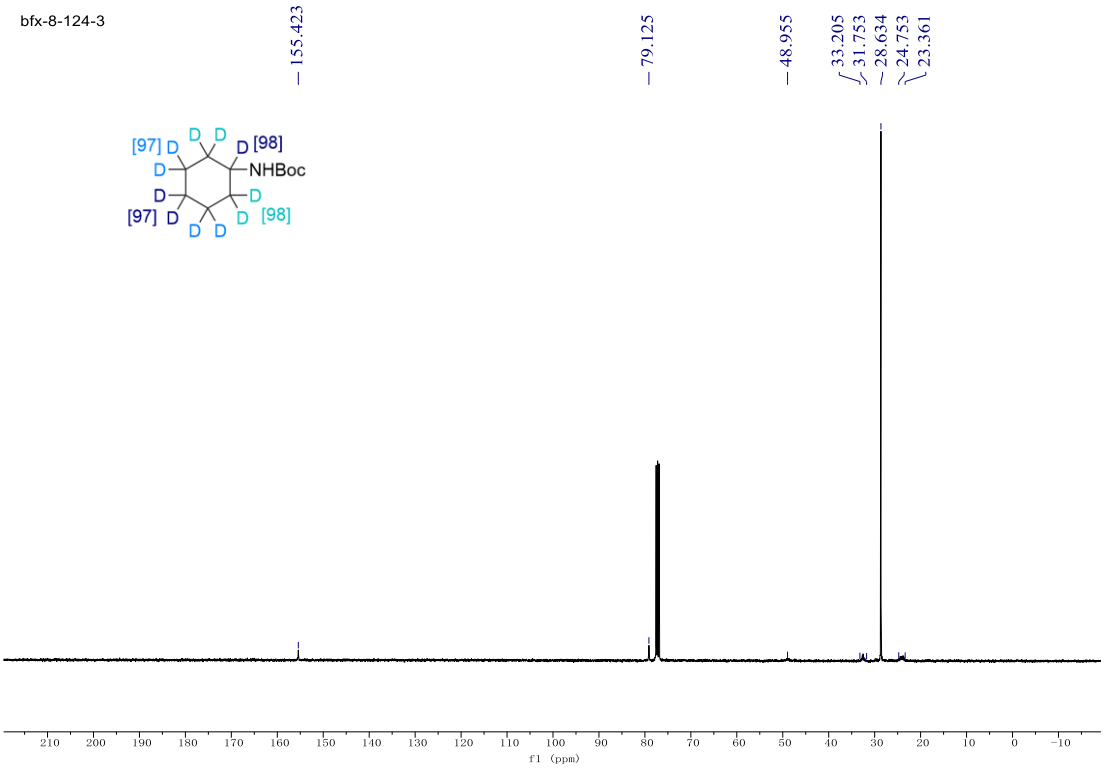
^{19}F NMR for 15f



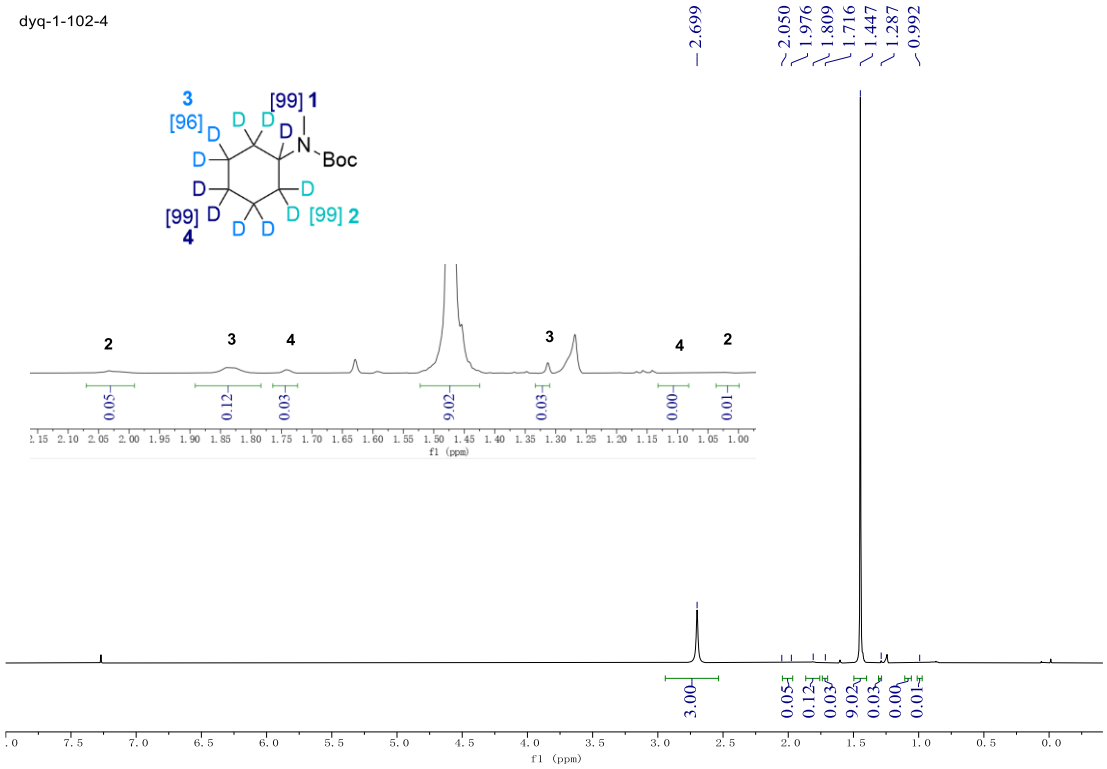
^{1}H NMR for 16f



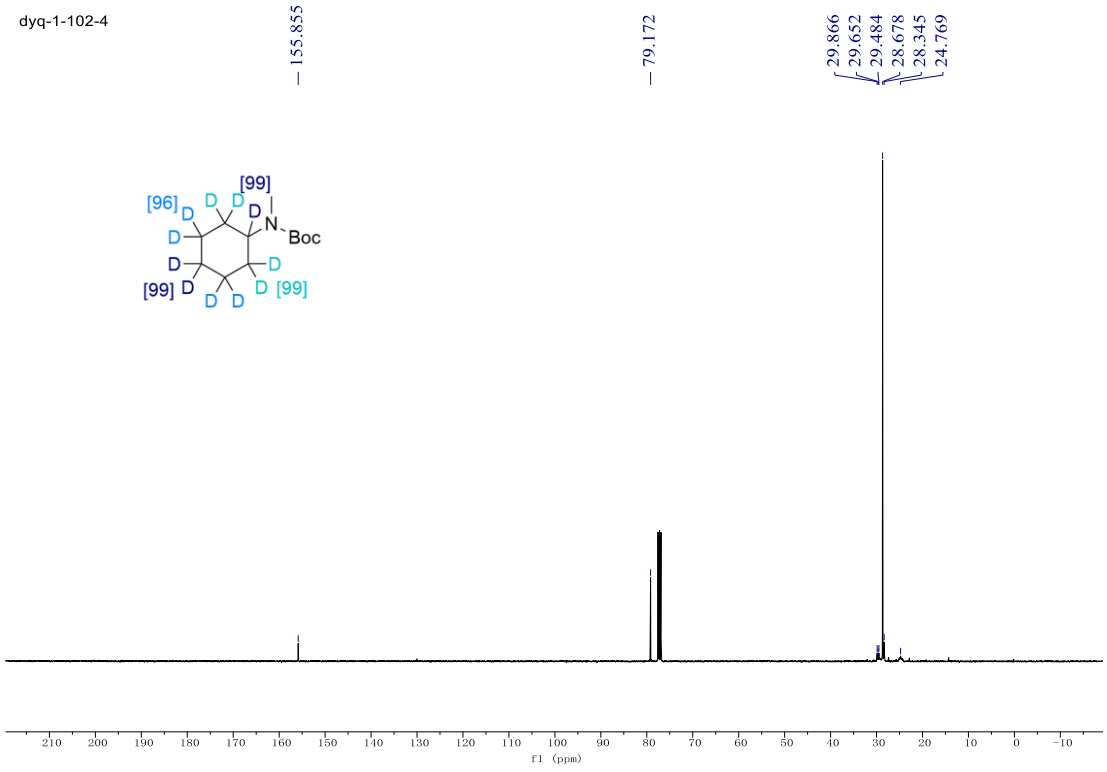
^{13}C NMR for 16f



^{1}H NMR for 17f

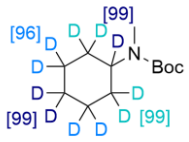


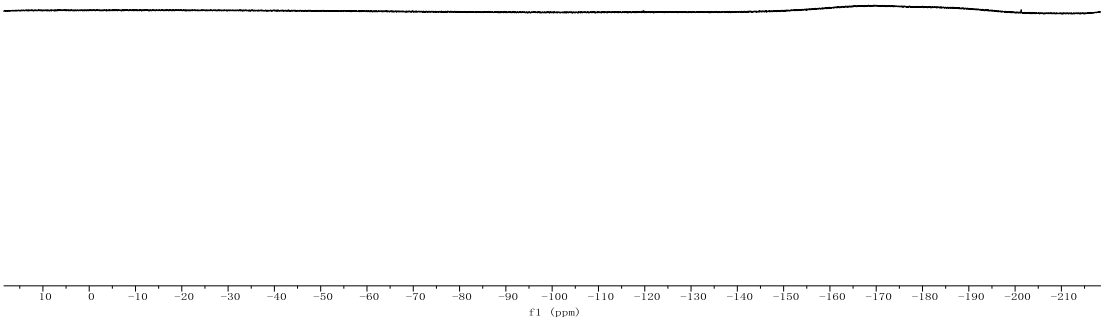
^{13}C NMR for 17f



^{19}F NMR for 17f

dyq-1-102-4

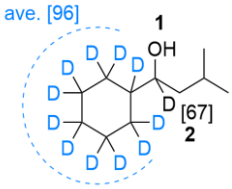


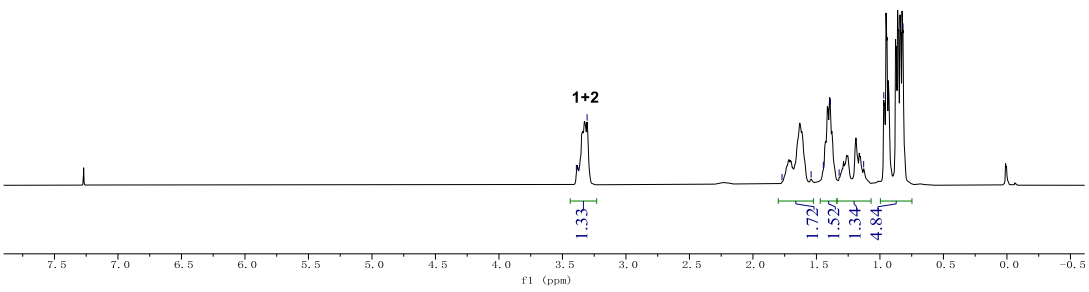


^{1}H NMR for 18f

dyq-1-112-3

3.390
3.306
1.771
1.542
1.446
1.390
1.321
1.128
0.970
0.818

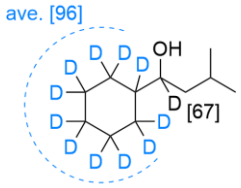


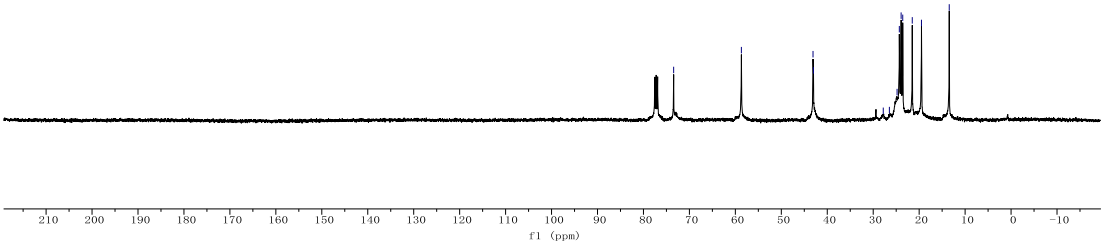


^{13}C NMR for 18f

dyq-1-112-3

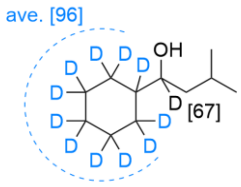
73.427
58.689
43.100
42.996
27.812
26.480
24.807
24.319
23.926
23.575
21.501
19.499
13.455

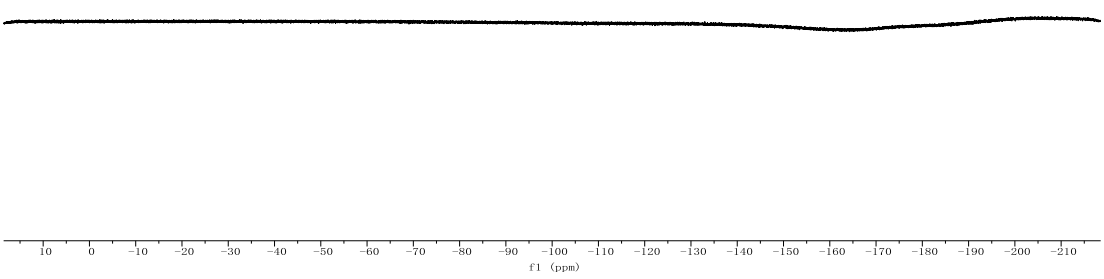




^{19}F NMR for 18f

dyq-1-112-3

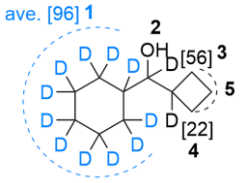


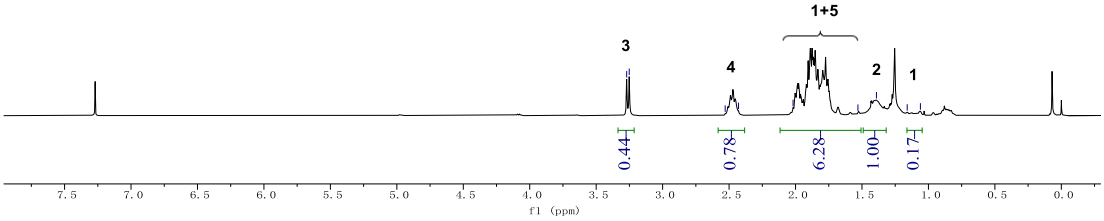


^{1}H NMR for 19f

dyq-1-128-4

3.271
3.251
2.529
2.429
2.019
1.530
1.391
1.160
1.060

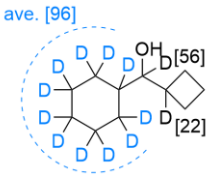


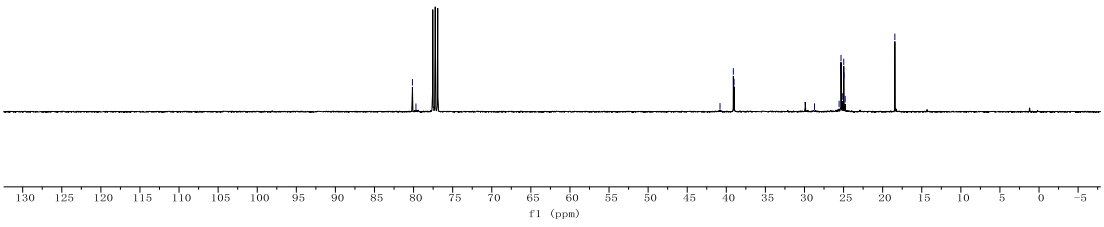


^{13}C NMR for 19f

dyq-1-128-4

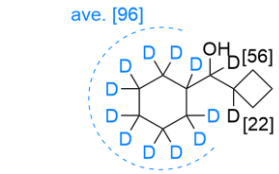
80.151
79.699
40.804
39.098
39.008
28.719
25.571
25.329
25.310
25.165
24.975
24.955
24.795
18.440

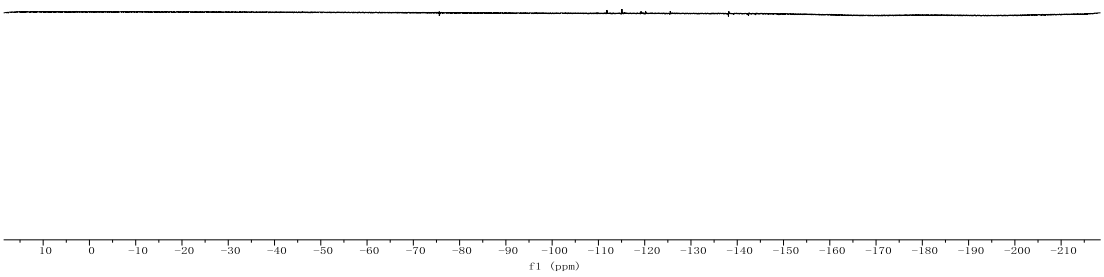




^{19}F NMR for 19f

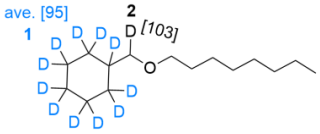
dyq-1-128-4

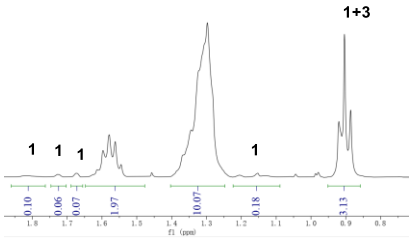


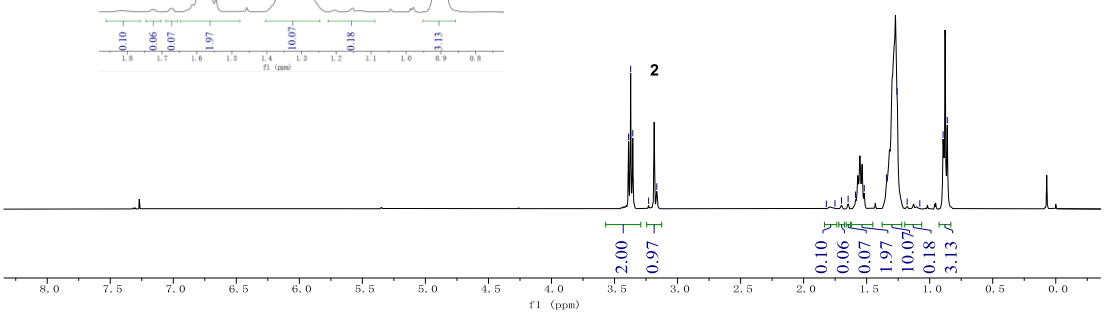


^{1}H NMR for 20f

dyq-1-113-1

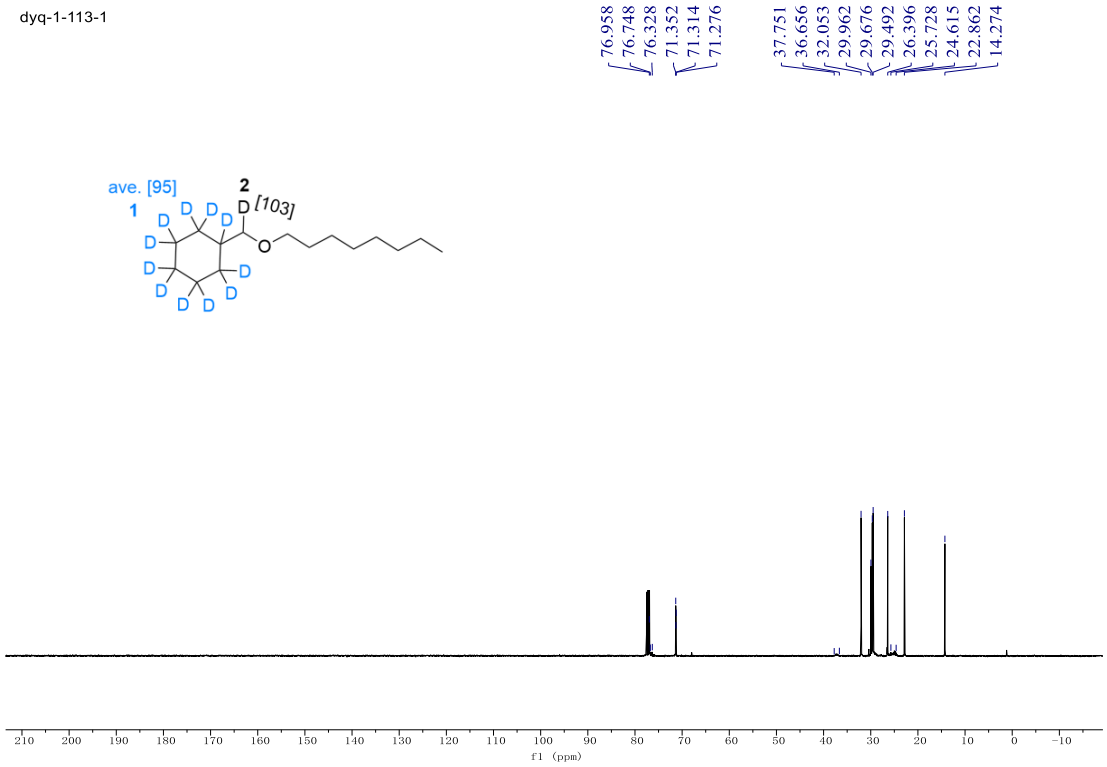






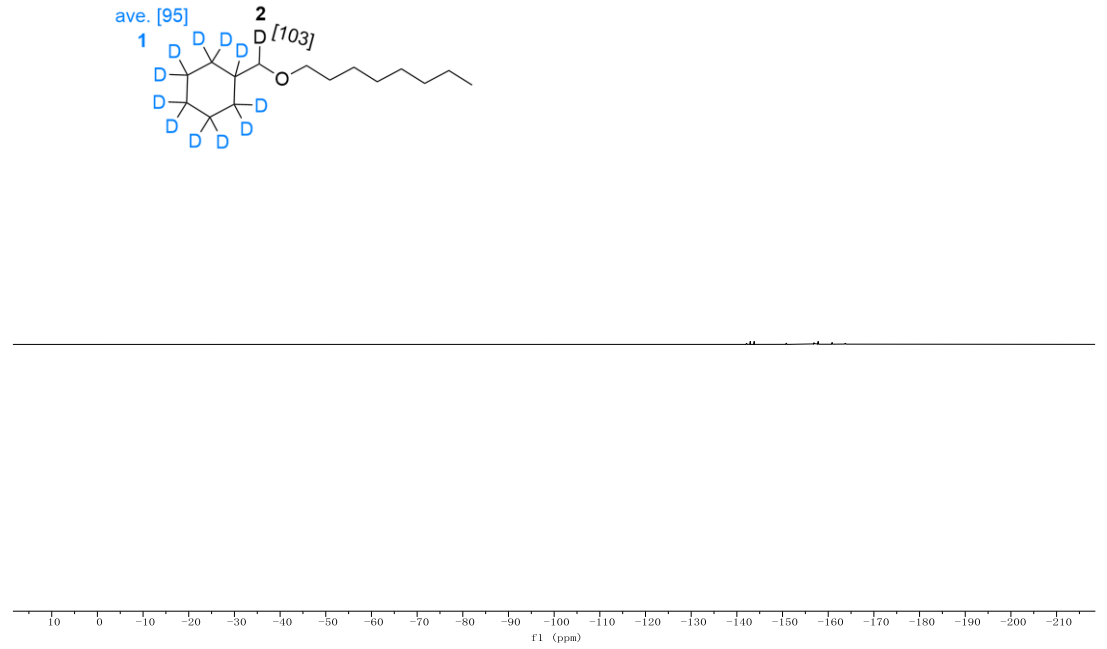
^{13}C NMR for 20f

dyq-1-113-1

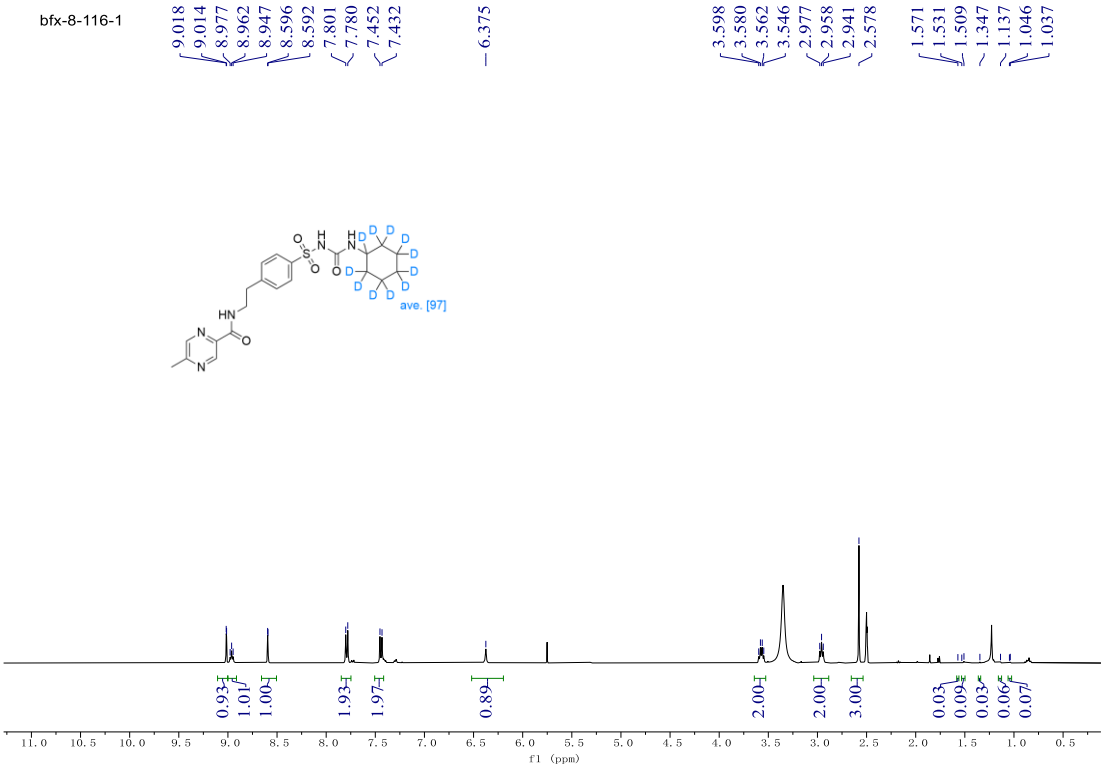


^{19}F NMR for 20f

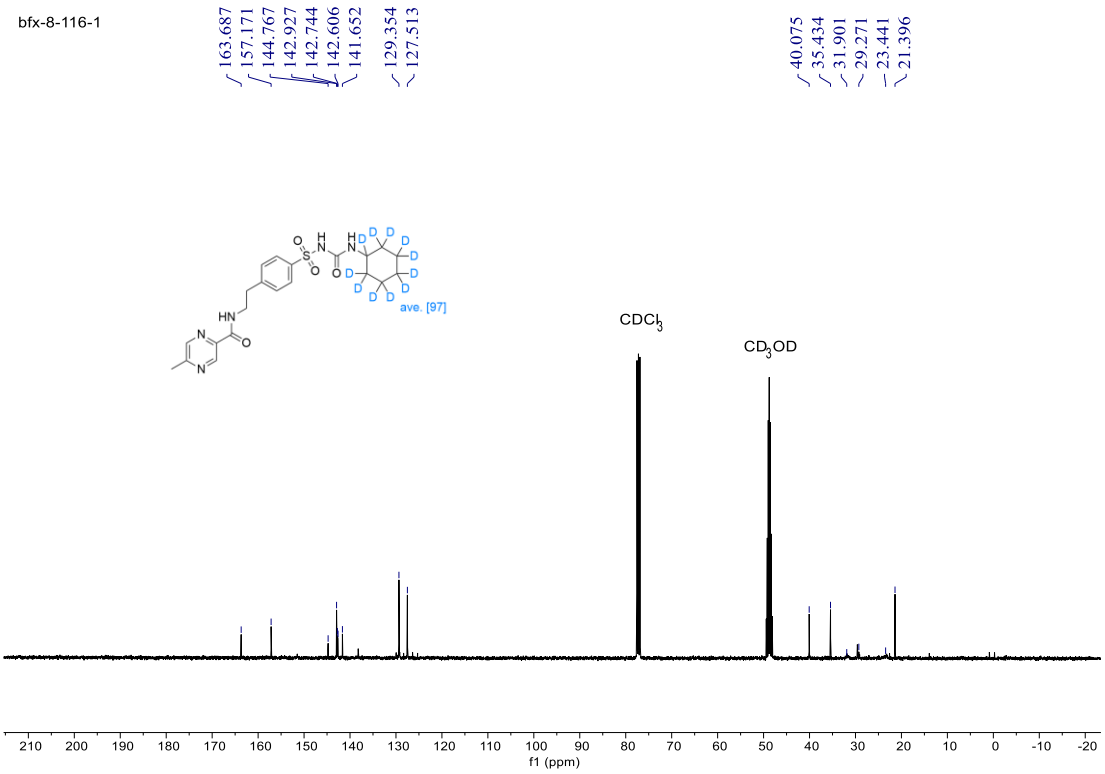
dyq-1-113-1



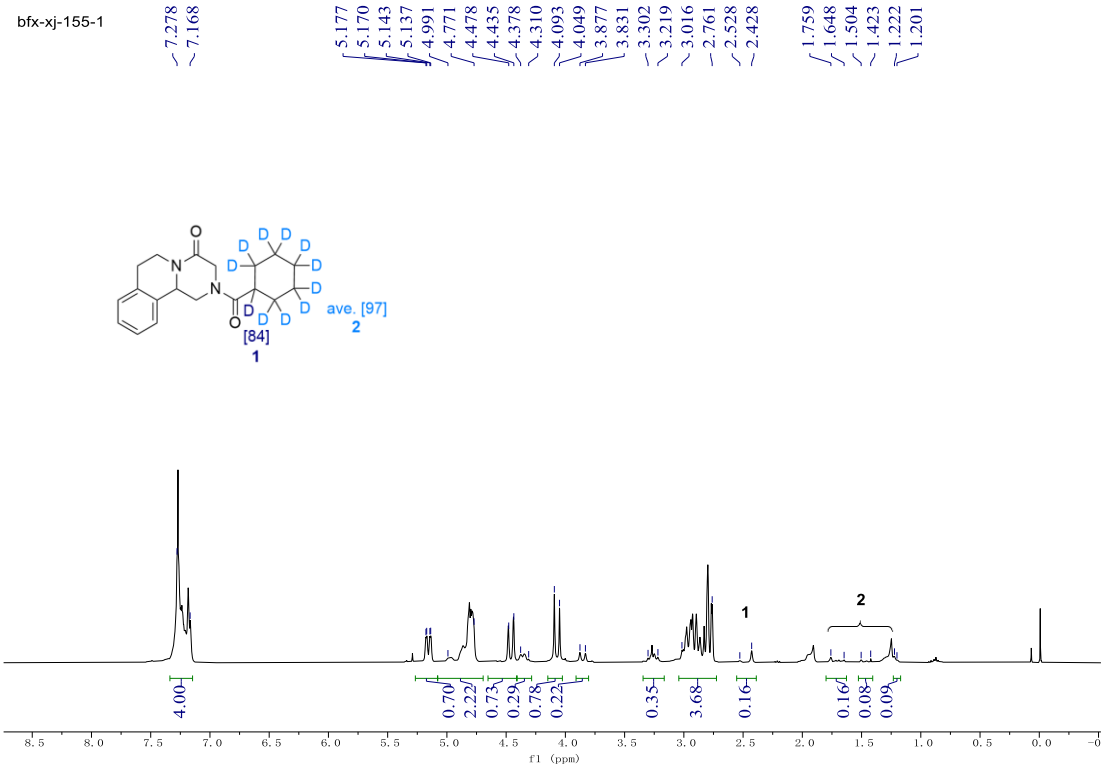
^{1}H NMR for [D]1h



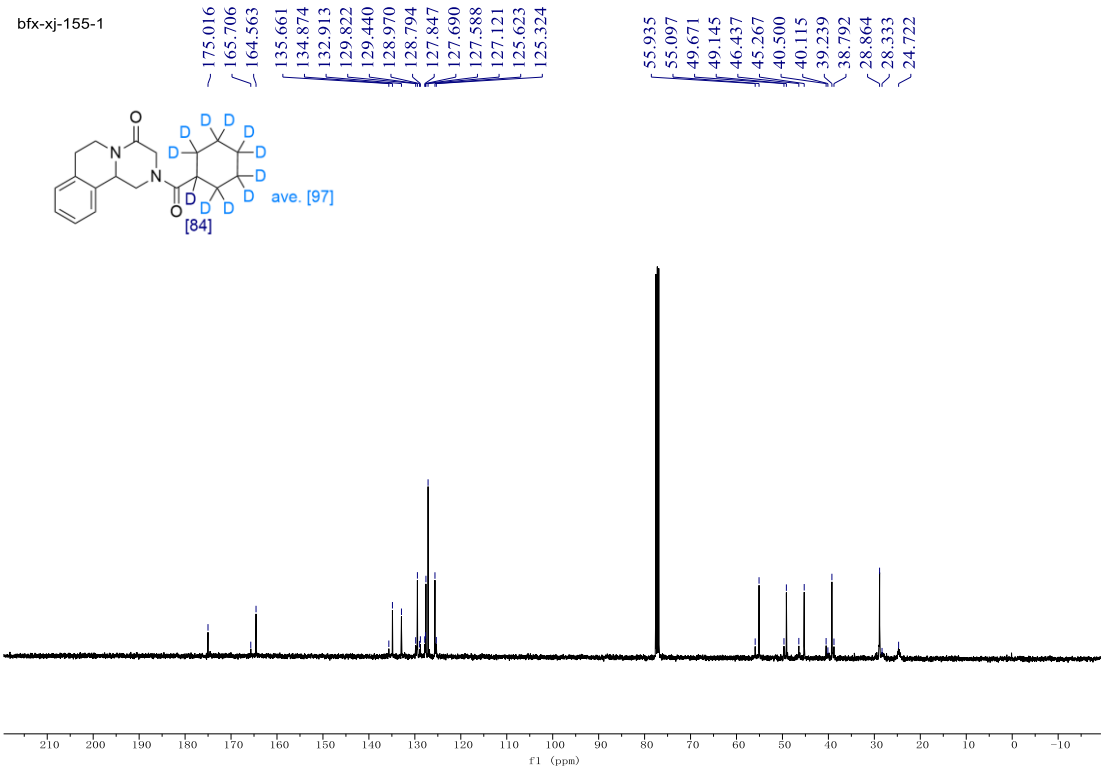
^{13}C NMR for [D]1h



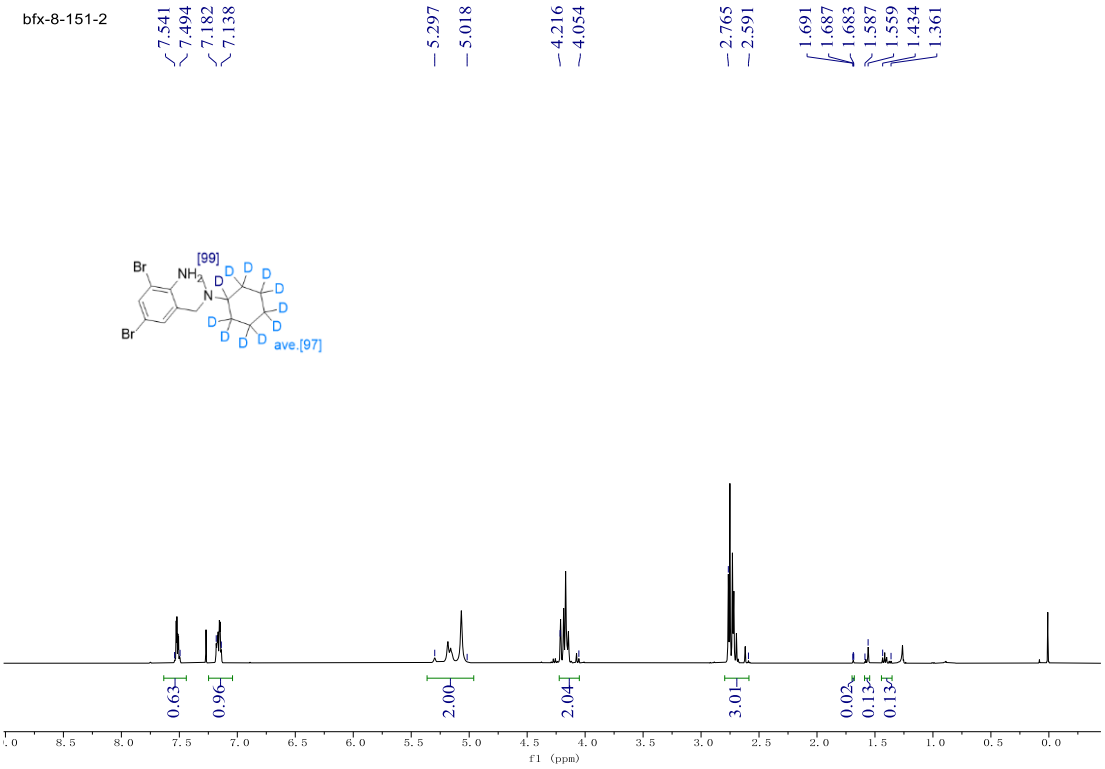
^{1}H NMR for [D]2h



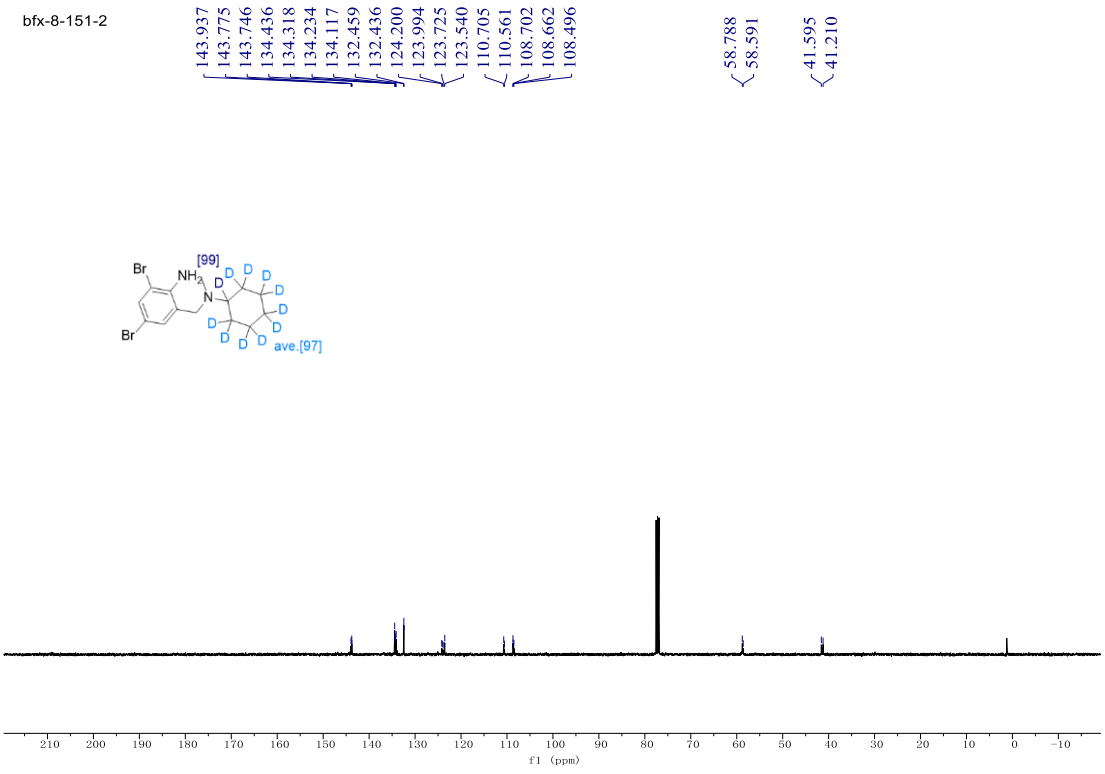
^{13}C NMR for [D]2h



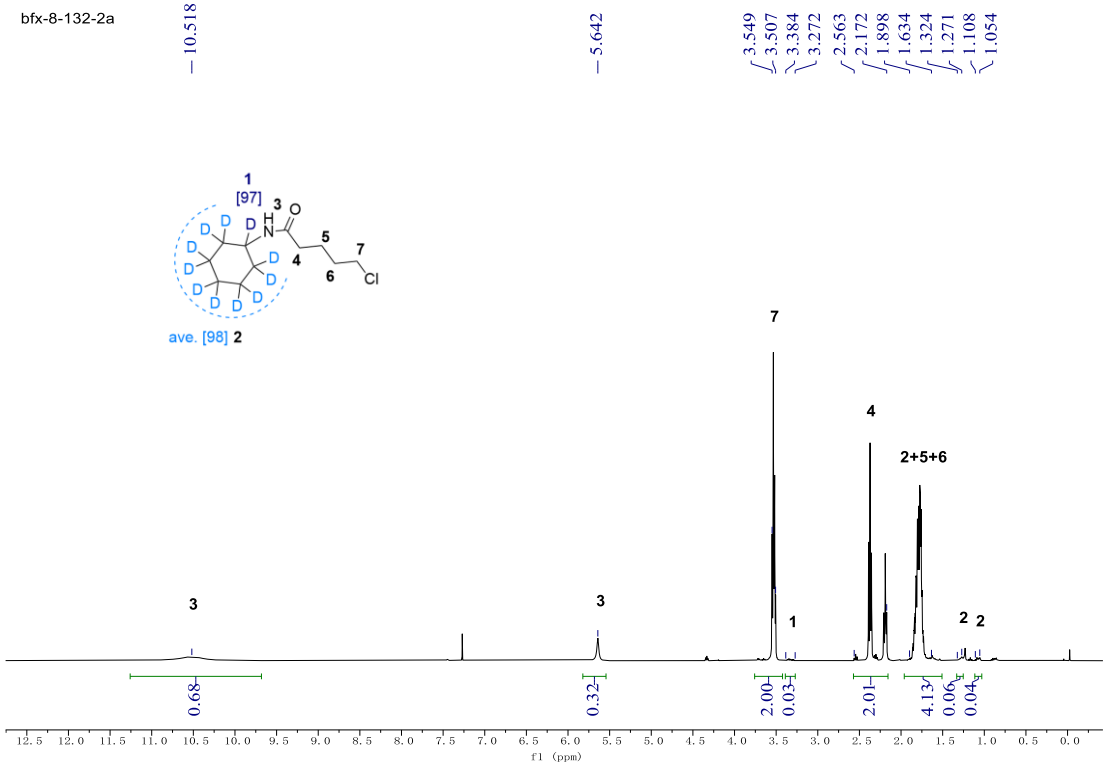
^{1}H NMR for [D]3h



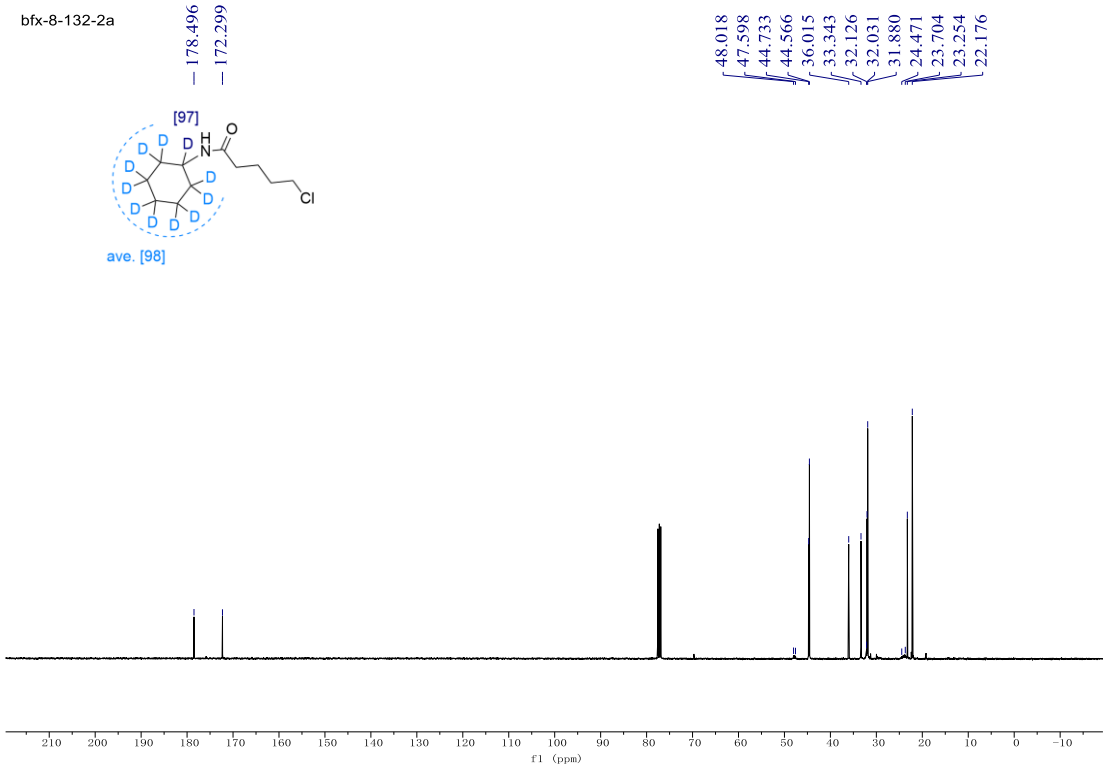
^{13}C NMR for [D]3h



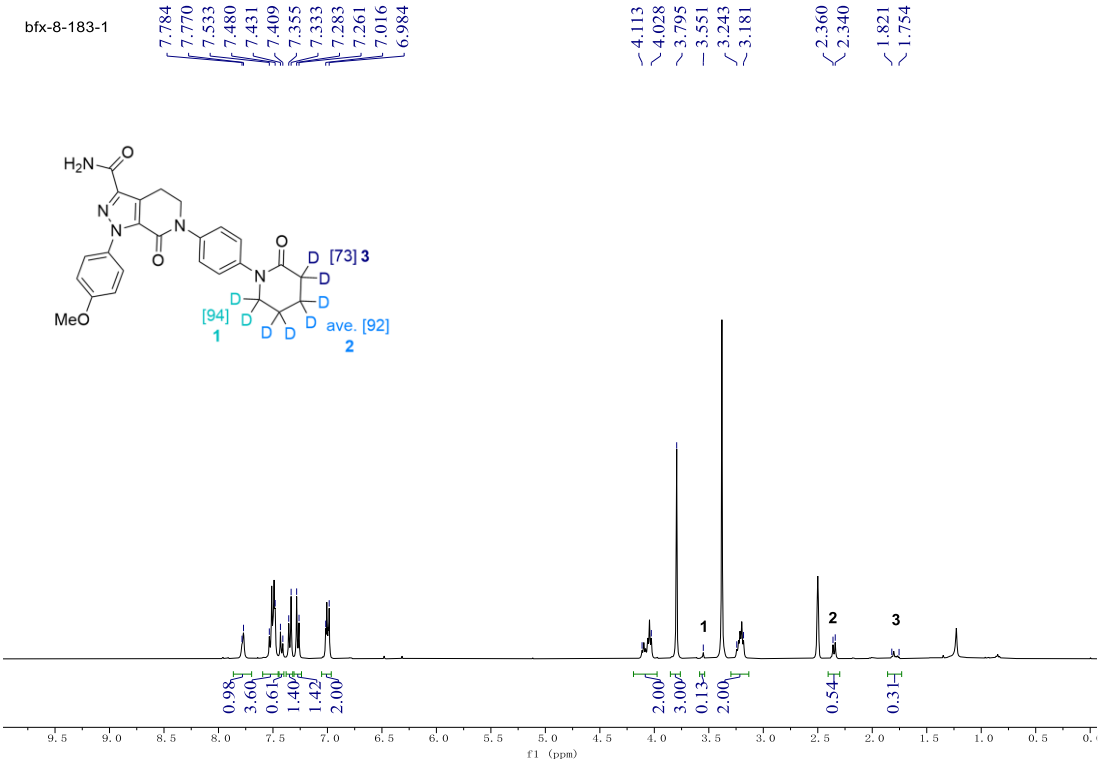
^{1}H NMR for 4h



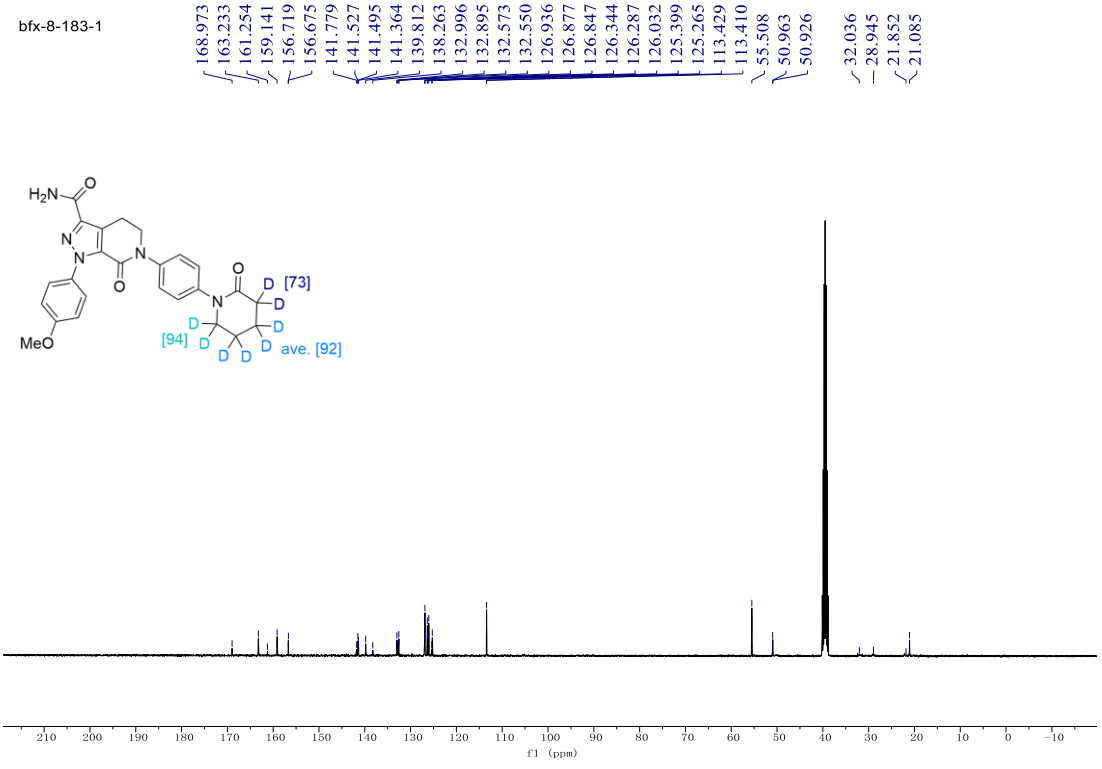
^{13}C NMR for 4h



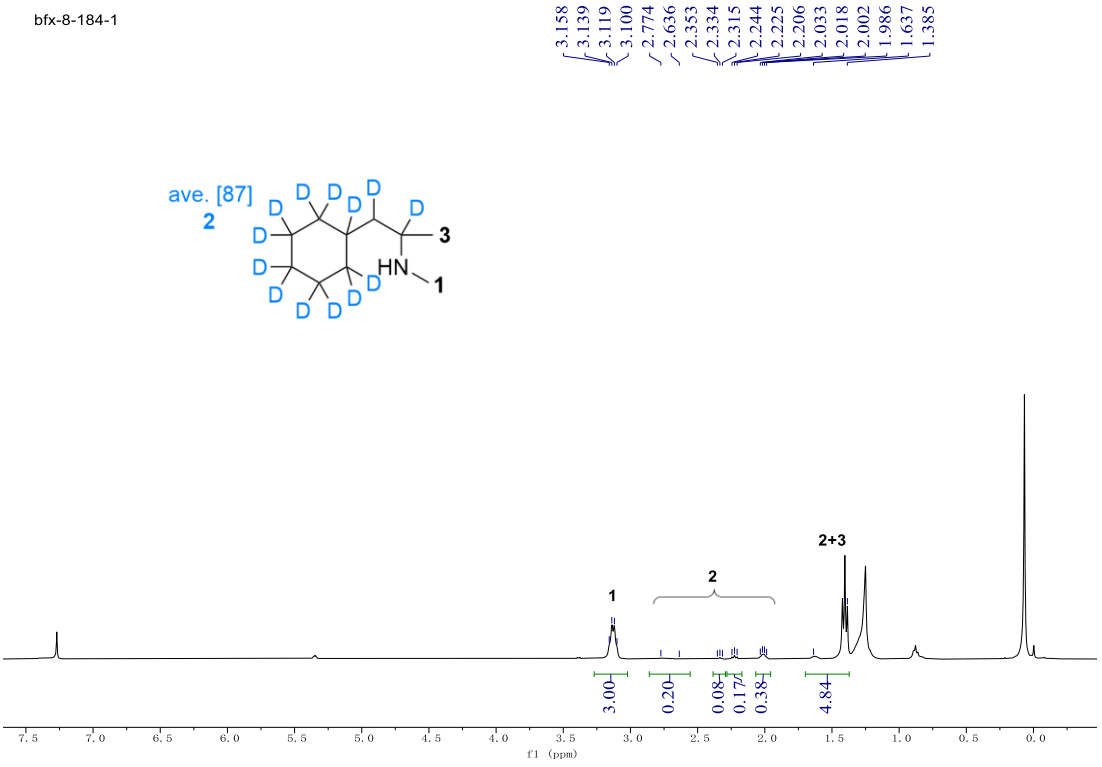
^{1}H NMR for [D]5h



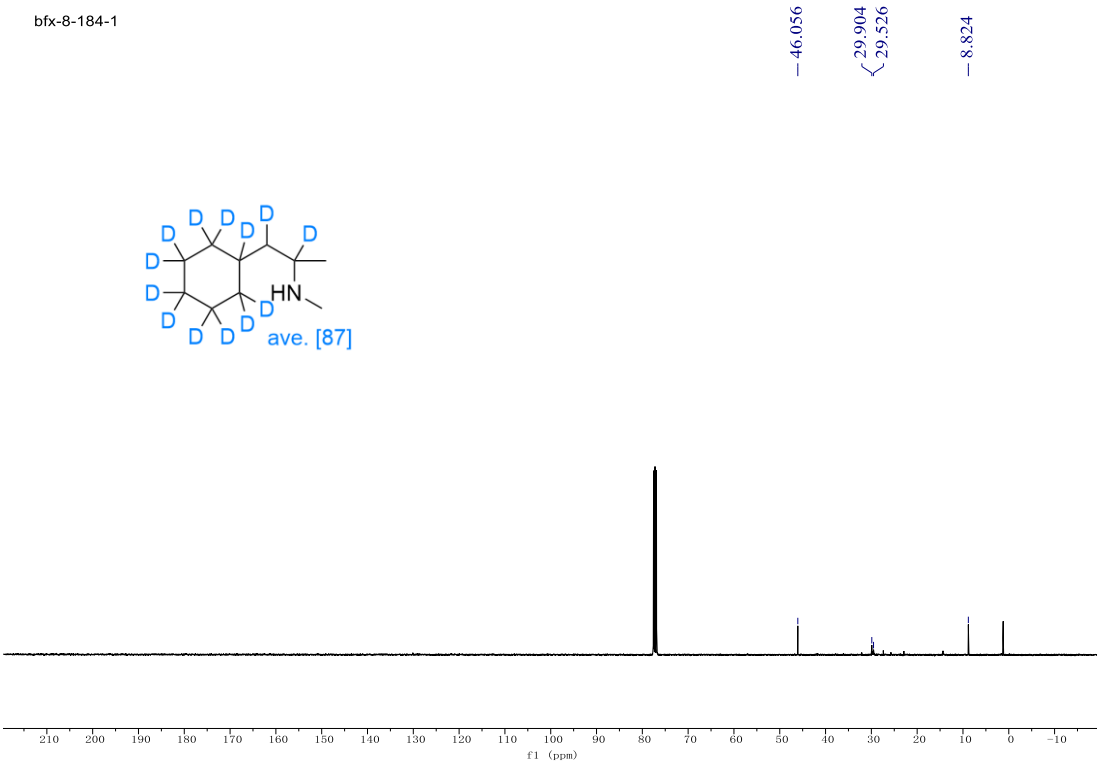
^{13}C NMR for [D]5h



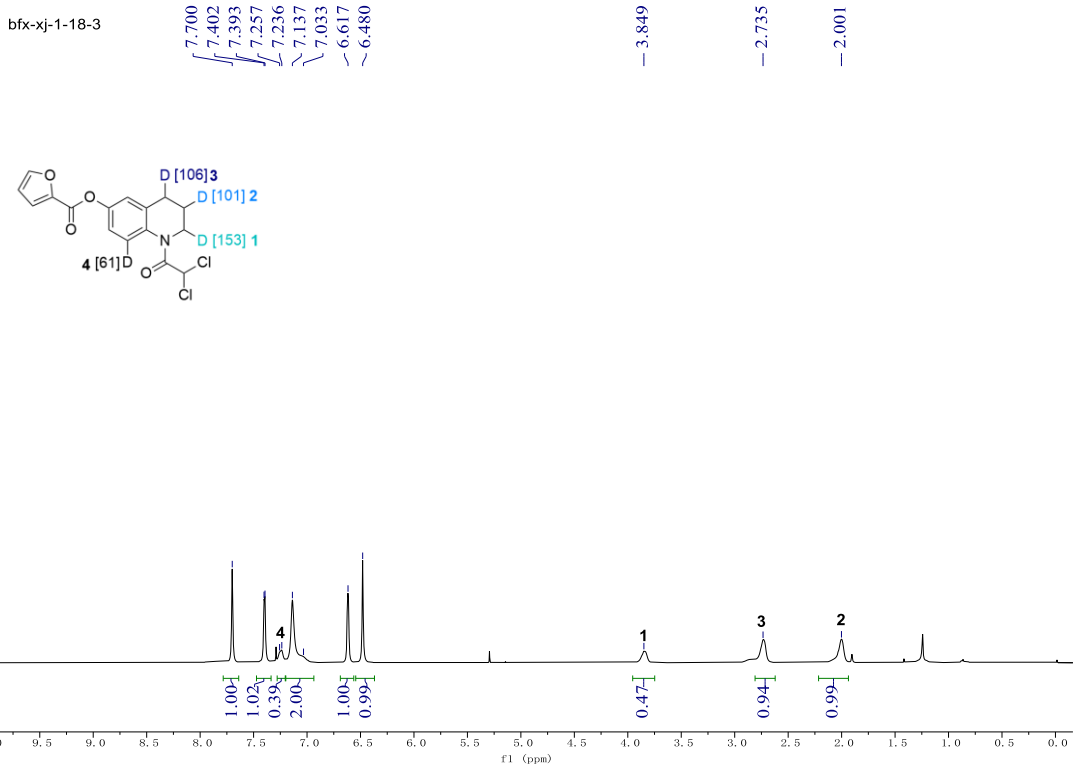
^{1}H NMR for [D]6h



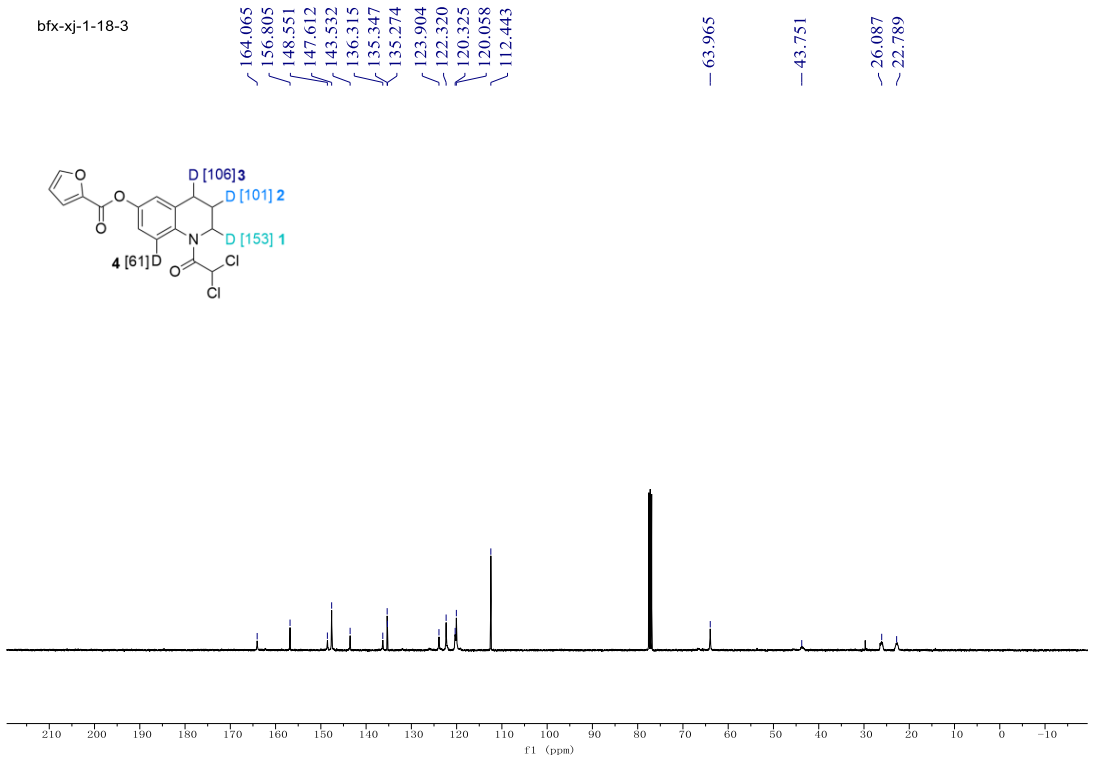
^{13}C NMR for [D]6h



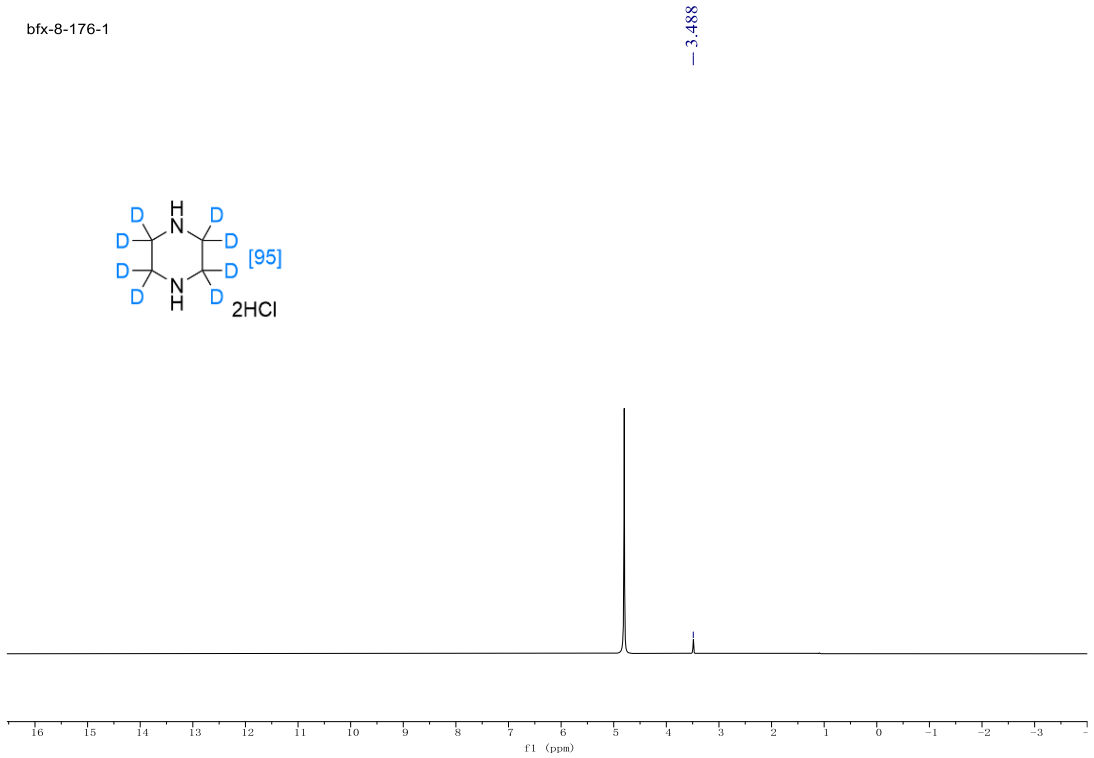
^{1}H NMR for [D]7h



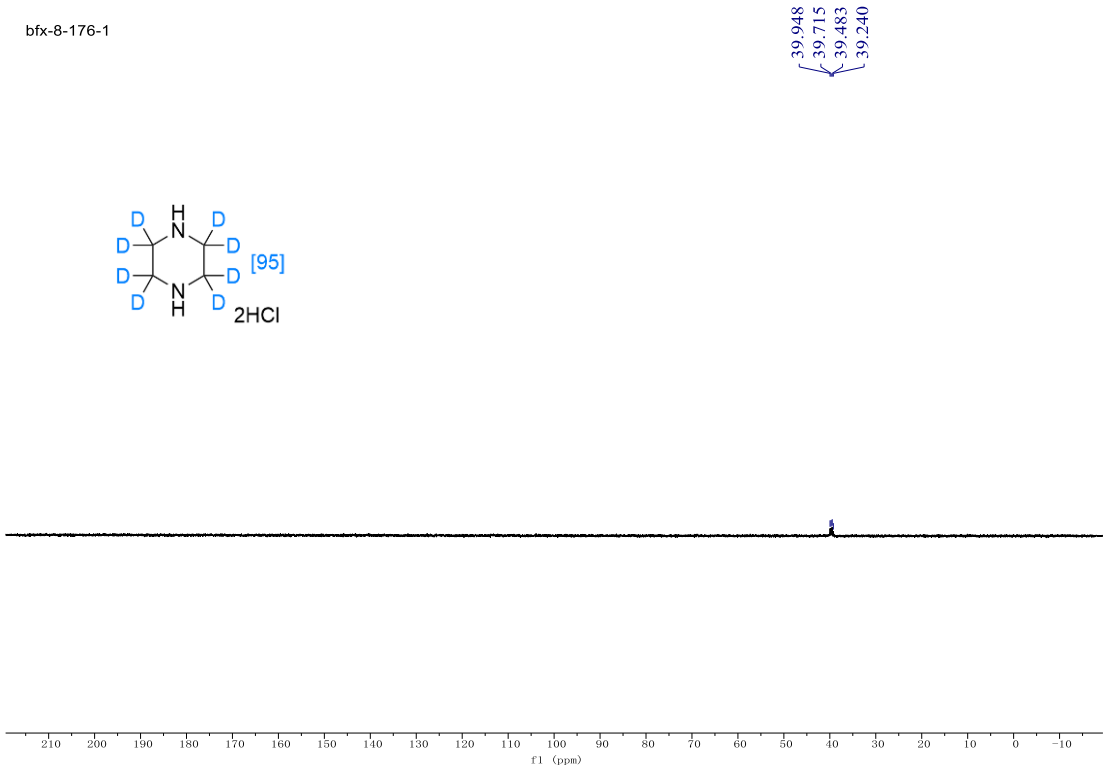
^{13}C NMR for [D]7h



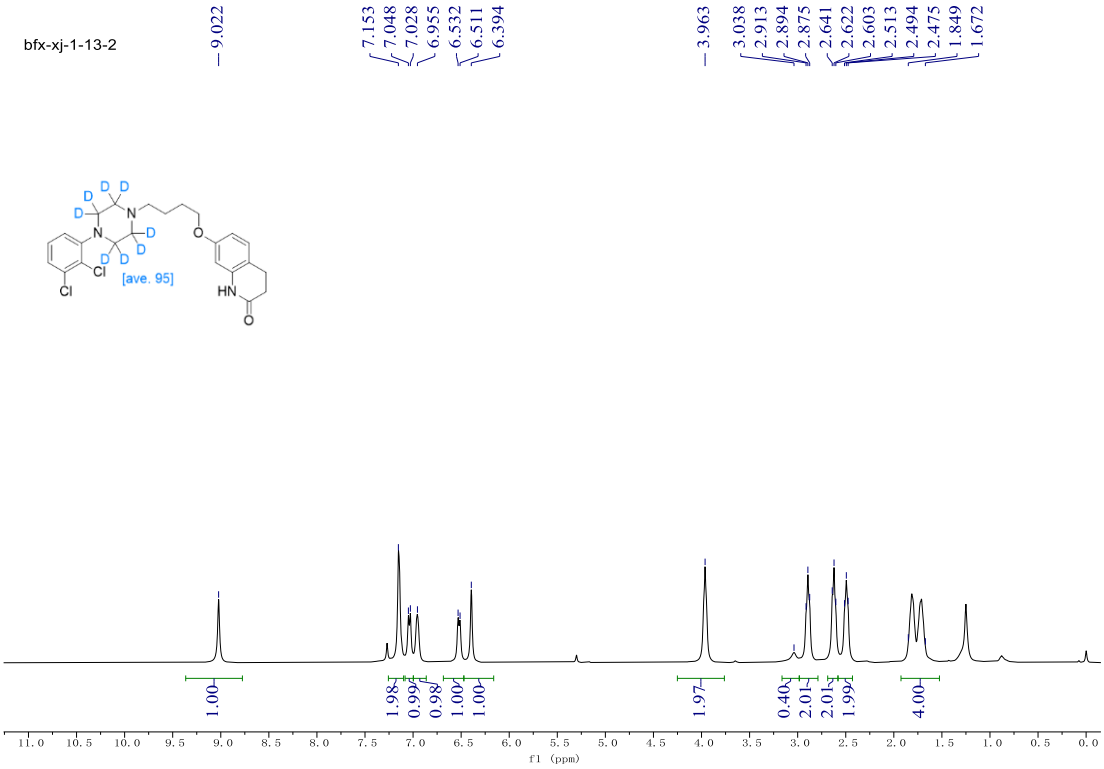
^{1}H NMR for 10d’



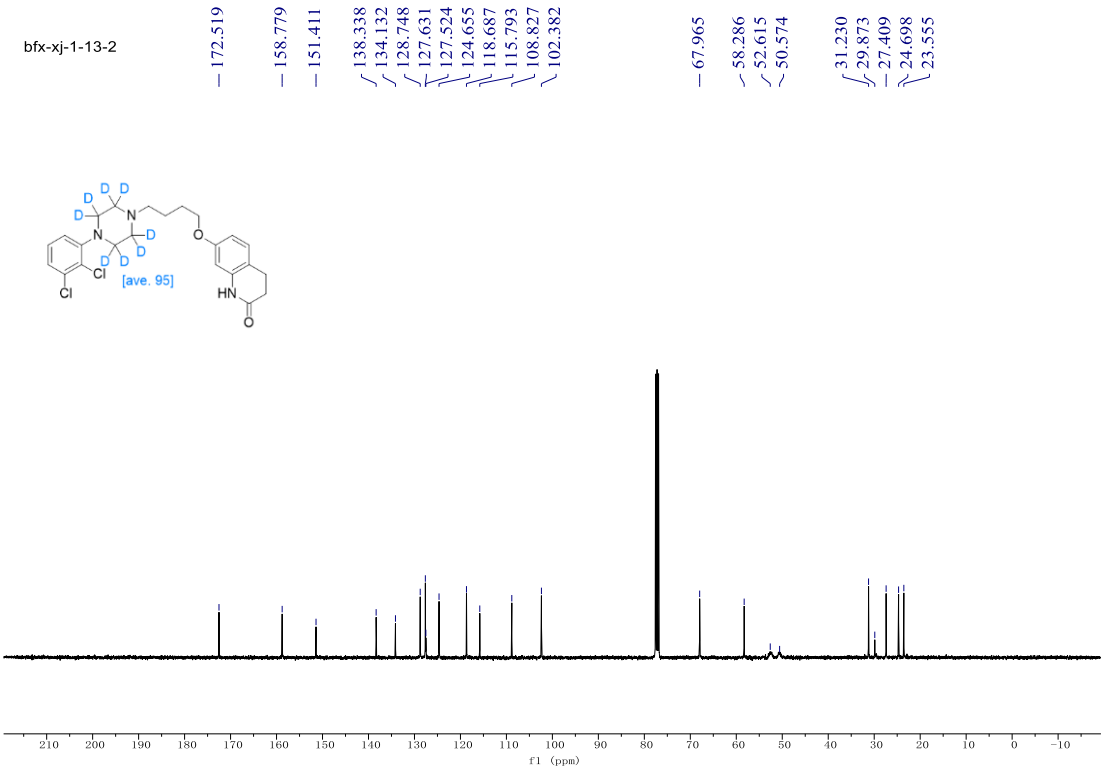
^{13}C NMR for 10d’



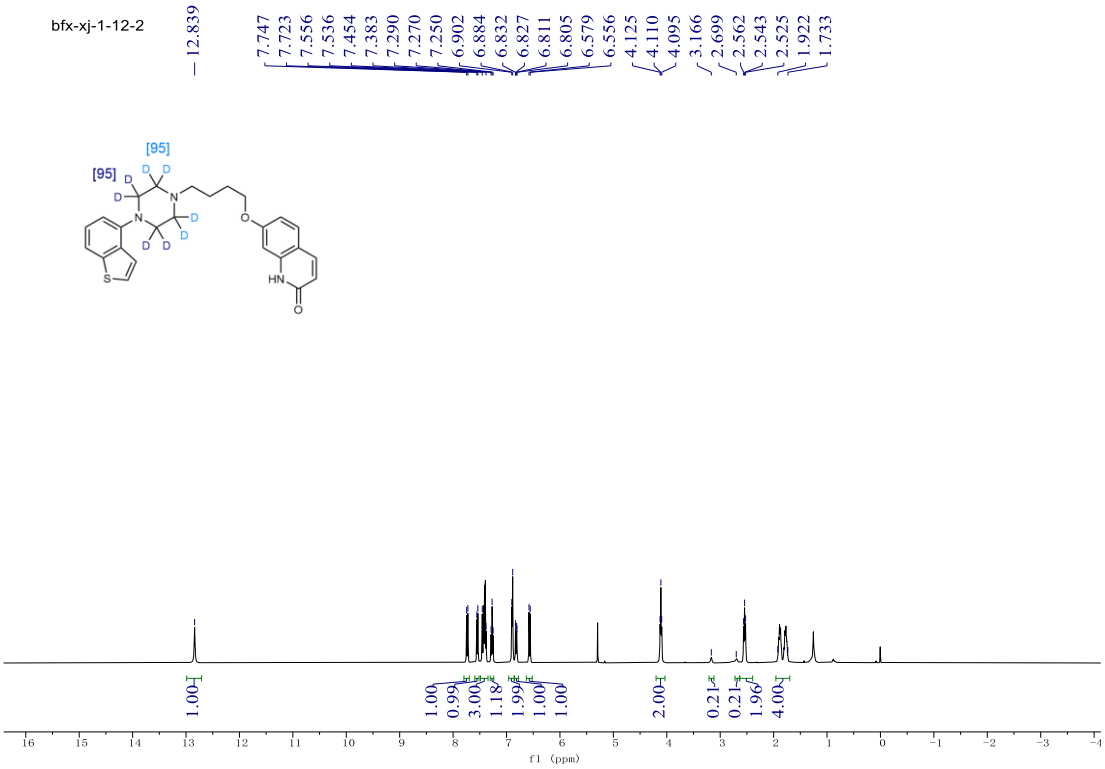
^{1}H NMR for [D]8h



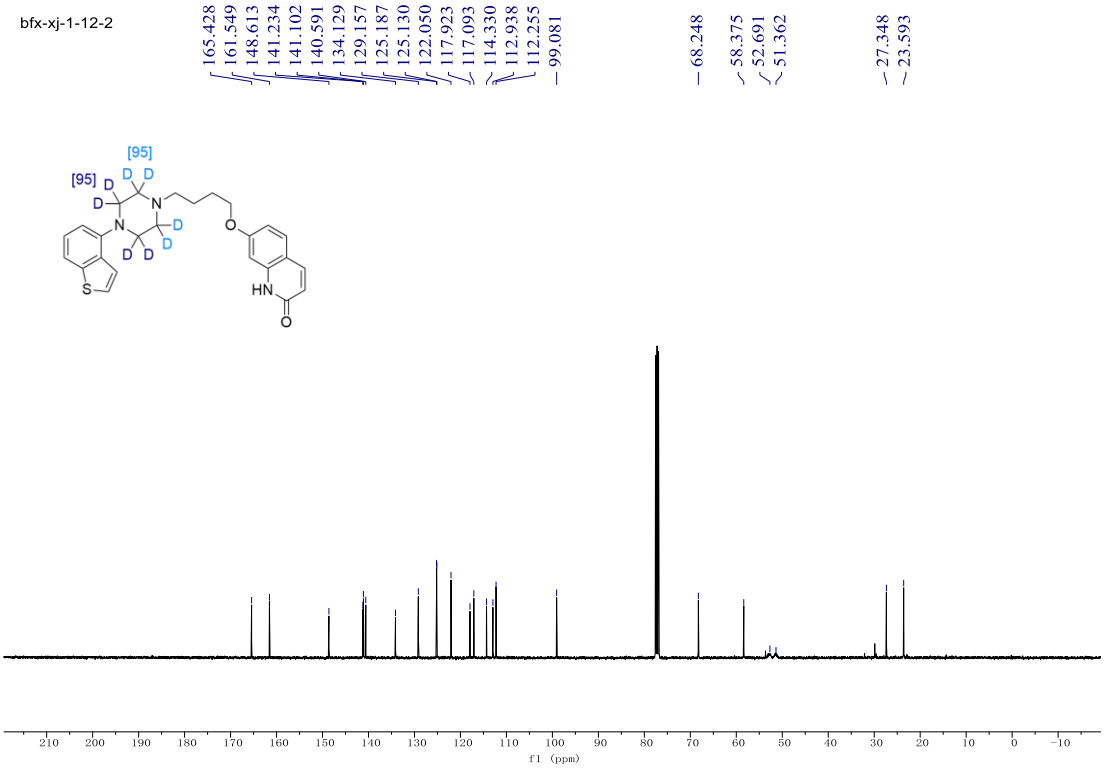
^{13}C NMR for [D]8h



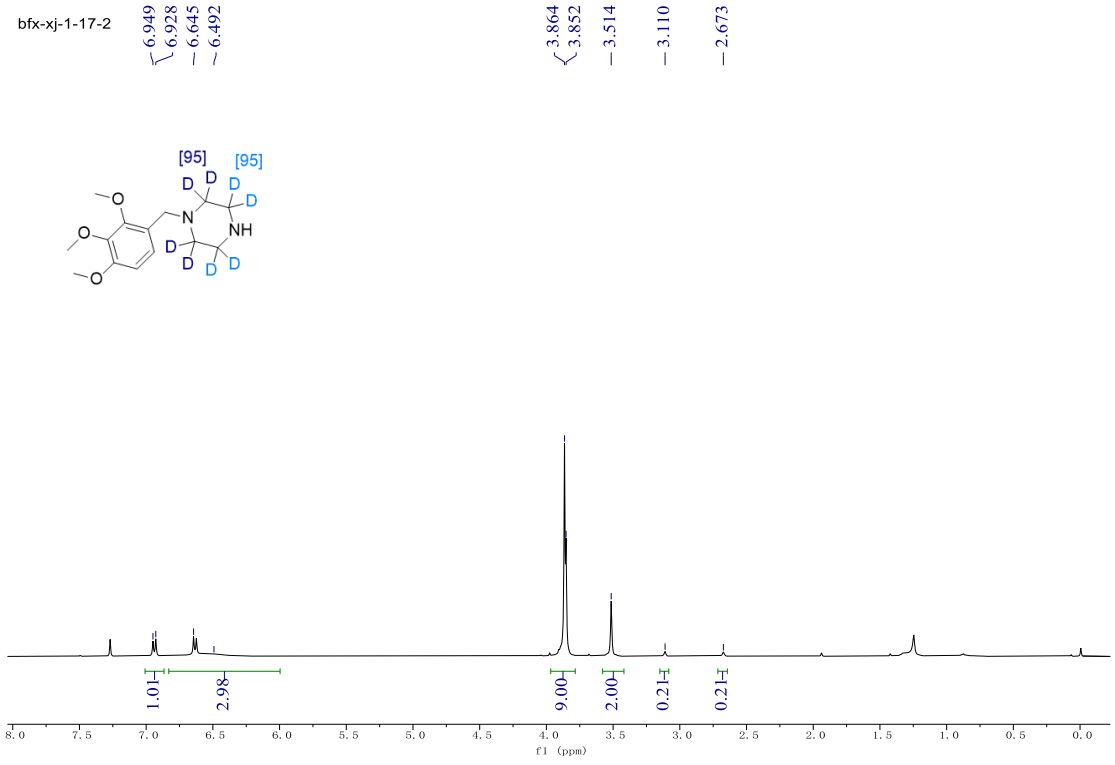
^{1}H NMR for [D]9h



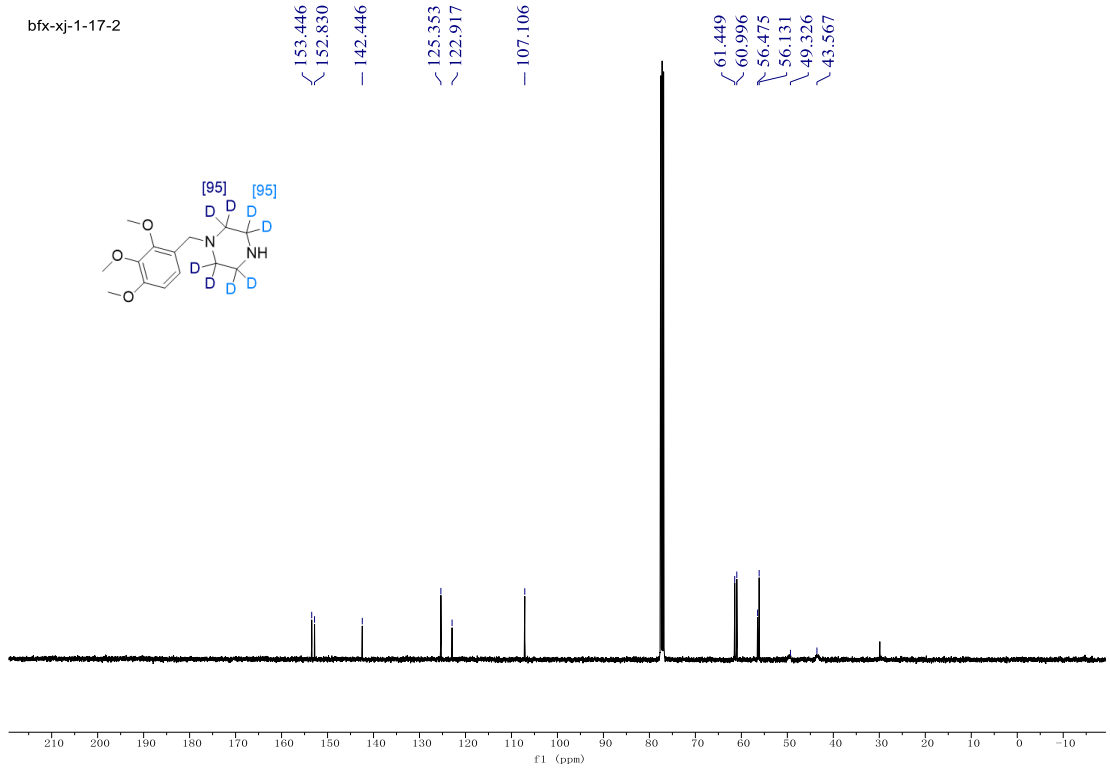
^{13}C NMR for [D]9h



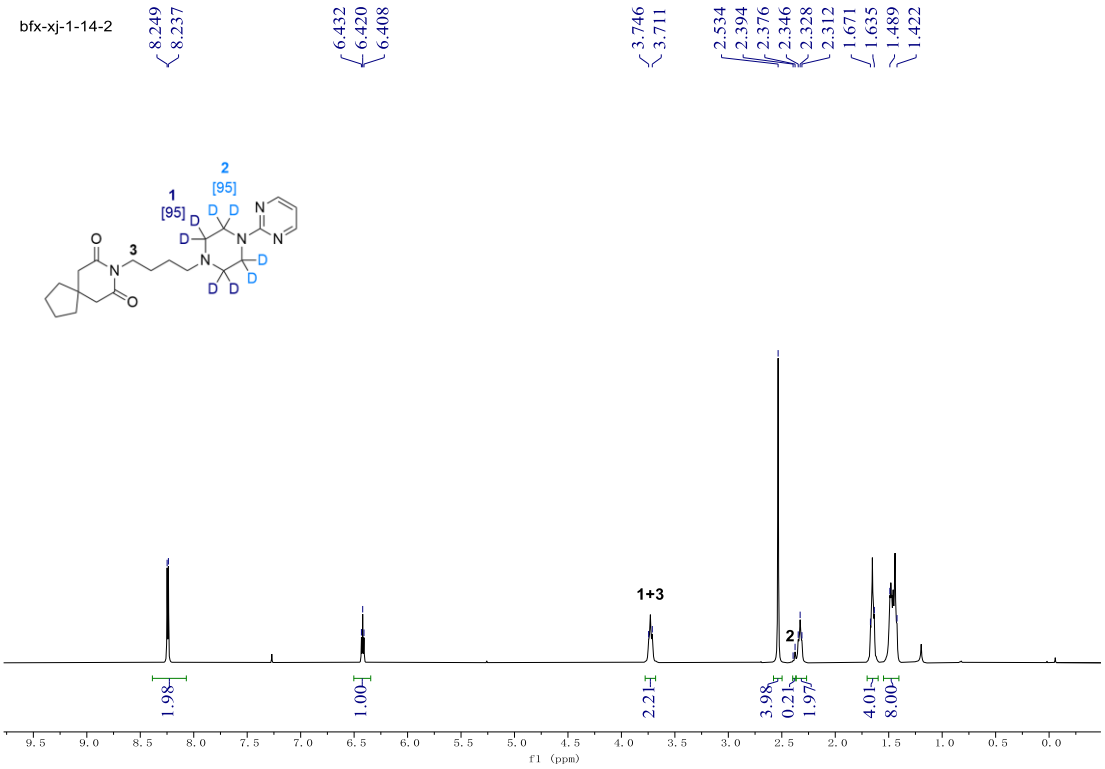
^{1}H NMR for [D]10h



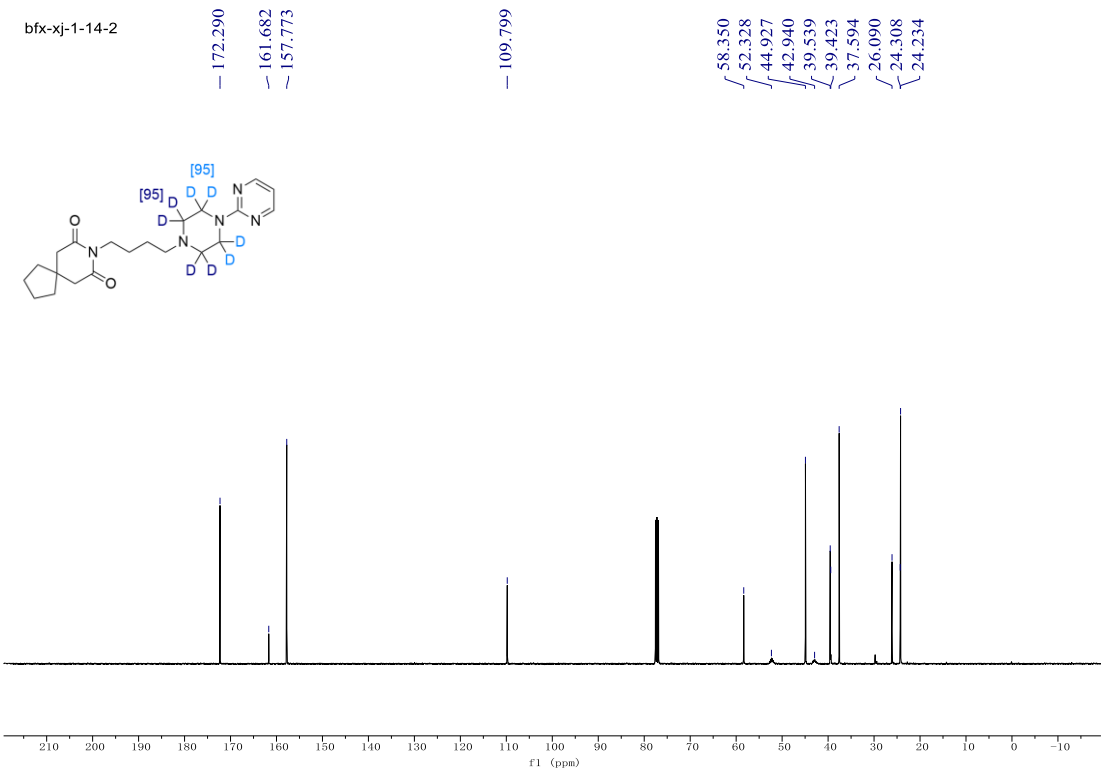
^{13}C NMR for [D]10h



^{1}H NMR for [D]11h



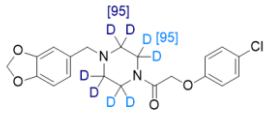
^{13}C NMR for [D]11h

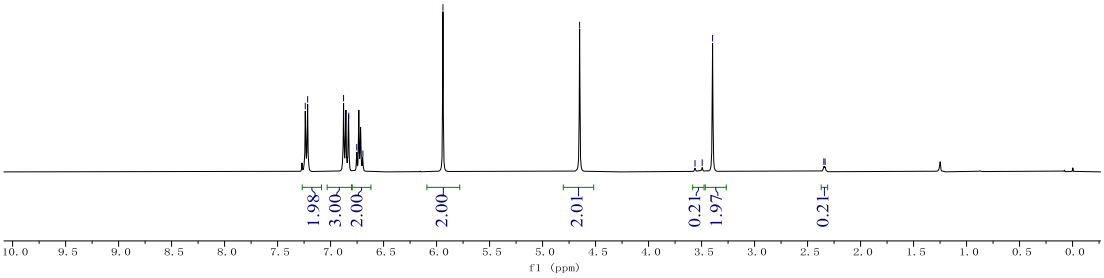


^{1}H NMR for [D]12h

bfx-xj-1-16-2

7.239
7.217
6.878
6.829
6.753
6.695
5.940
4.651
3.562
3.494
3.396
2.347
2.335

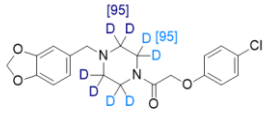


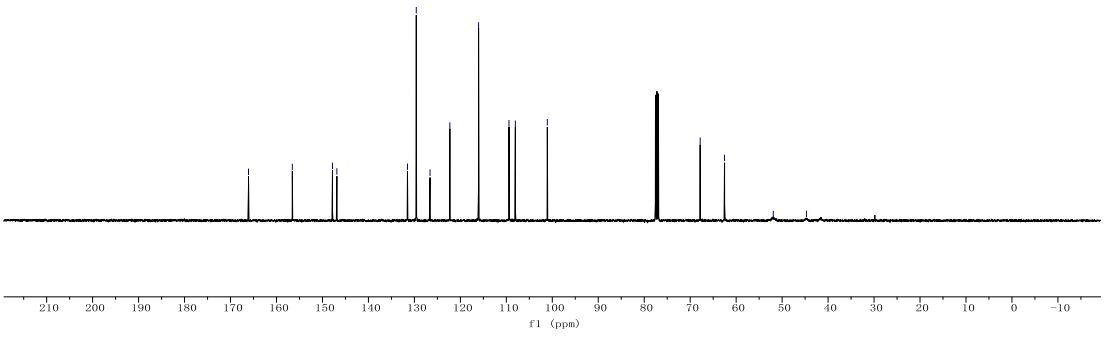


^{13}C NMR for [D]12h

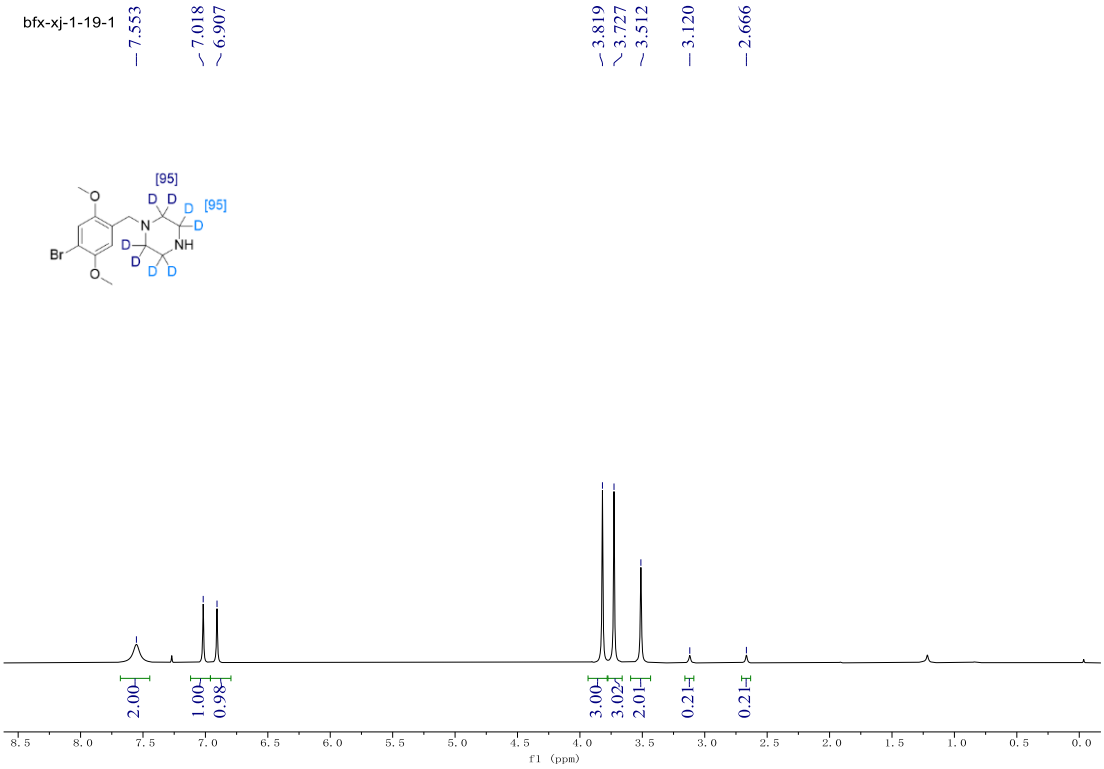
bfx-xj-1-16-2

166.091
156.556
147.819
146.864
131.507
129.591
126.596
122.284
116.038
109.421
108.037
101.082
67.833
62.527
51.926
44.692

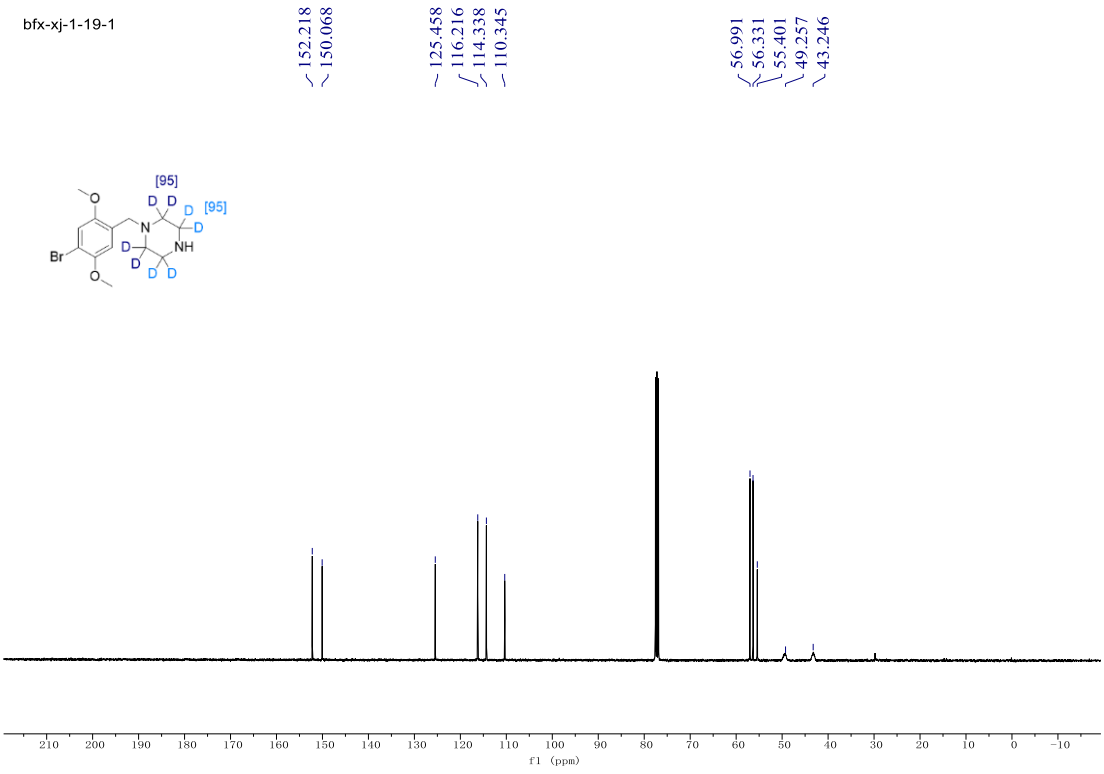




^{1}H NMR for [D]13h



^{13}C NMR for [D]13h



14. Reference

1. Sawama, Y., Yamada, T., Yabe, Y., Morita, K., Shibata, K., Shigetsura, M., Monguchi, Y. & Sajiki, H. Platinum on Carbon-Catalyzed H-D Exchange Reaction of Aromatic Nuclei due to Isopropyl Alcohol-Mediated Self- Activation of Platinum Metal in Deuterium Oxide. *Adv. Synth. Catal.* **355**, 1529-1534 (2013).

2. Farizyan, M., Mondal, A., Mal, S., Deufel, F. & van Gemmeren, M. Palladium-Catalyzed Nondirected Late-Stage C-H Deuteration of Arenes. *J. Am. Chem. Soc.* **143**, 16370-16376 (2021).

3. Hosseinzadeh, R., Tajbakhsh, M., Mohadjerani, M. & Mehdinejad, H. Copper-Catalyzed Amidation of Aryl Iodides Using KF/Al_2O_3: An Improved Protocol. *Synlett* **9**, 1517-1520 (2004).

4. Deng, C.-L., Guo, S.-M., Xie, Y.-X. & Li, J.-H. Mild and Ligand-Free Palladium-Catalyzed Cross-Couplings between Aryl Halides and Arylboronic Acids for the Synthesis of Biaryls and Heterocycle-Containing Biaryls. *Eur. J. Org. Chem.* **2007**, 1457-1462 (2007).

5. Goudedranche, S., Besnard, C., Egger, L. & Lacour, J. Synthesis of Pyrrolidines and Pyrrolizidines with α-Pseudoquaternary Centers by Copper-Catalyzed Condensation of α-Diazodicarbonyl Compounds and Aryl γ-Lactams. *Angew. Chem. In. Ed.* **55**, 13775-13779 (2016).

6. Dutremez, S. G., Dumail, X., Mallet-Ladeira, S., van der Lee, A., Granier, D., Masquelez, N. & Filhol, J.-S. Pentafluorophenylphosphonic Acid as a New Building Block for Molecular Crystal Fabrication. *Cryst. Growth Des.* **21**, 2028-2045 (2021).

7. Chen, W., Li, H.-J., Lu, W.-Y. & Wu, Y.-C. Ruthenium(II)-catalyzed Monohydroalkylation of α,β-Unsaturated Ketones with N-Acyl Pyrroles using a C-H Activation Strategy. *Asian J. Org. Chem.* **9**, 1602-1609 (2020).

8. Raju, B. C., Neelakantan, P. & Bhalerao, U. T. A Facile and Convenient Method for the Synthesis of Nitro Phenols and Chloropyridinols. *Synth. Commun.* **34**, 2903-2909 (2004).