Supplementary Information

for

Weak, bidentate chelating group assisted cross-coupling of C(sp^3)–H bonds in aliphatic acid derivatives with aryltrifluoroborates

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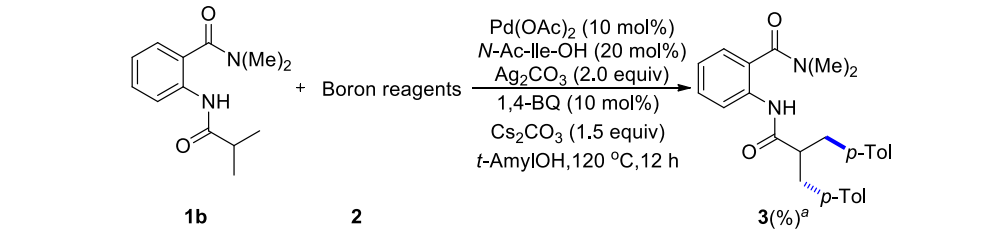
1. General Information

Unless otherwise noted, commercial available reagents were purchased from commercial suppliers (such as Adamas, Strem, J&K Chemical Co., Energy Chemical. etc), and used as received. Solvents were generally dried over 4 Å molecular sieves. The reaction vessels used for C–H functionalization were 15 mL sealed tube with a Teflon cap (Synthware). Purification of products was performed by flash chromatography (FC) using silica gel or preparative thin layer chromatography. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AVANCE III spectrometer (400 MHz and 101 MHz, respectively) and JEOL ECZ600S (600 MHz and 151 MHz, respectively). Chemical shifts are reported parts per million (ppm) referenced to $CDCl_3$ (δ 7.26 ppm), tetramethylsilane (TMS, δ 0.00 ppm), DMSO-d_6 (δ 3.30 ppm) for ^{1}H NMR; $CDCl_3$ (δ 77.16 ppm), DMSO-d_6 (δ 39.52 ppm) for ^{13}C NMR. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, hept = heptaplet, m = multiplet, and br = broad. High-resolution mass spectra (HRMS) were obtained on an Impact II UHR-TOF mass spectrometry equipped with an ESI source from Bruker at Fujian Institute of Research on the Structure of Matter. Enantiomeric excess was determined by HPLC analysis using Chiralpak AD-H column (Daicel Chemical Industries, LTD) on Shimadzu LC-20A.

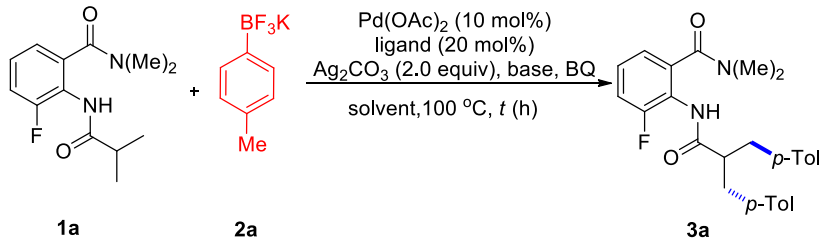
2. Optimization of the reaction

2.1 Screening of the boron reagents:



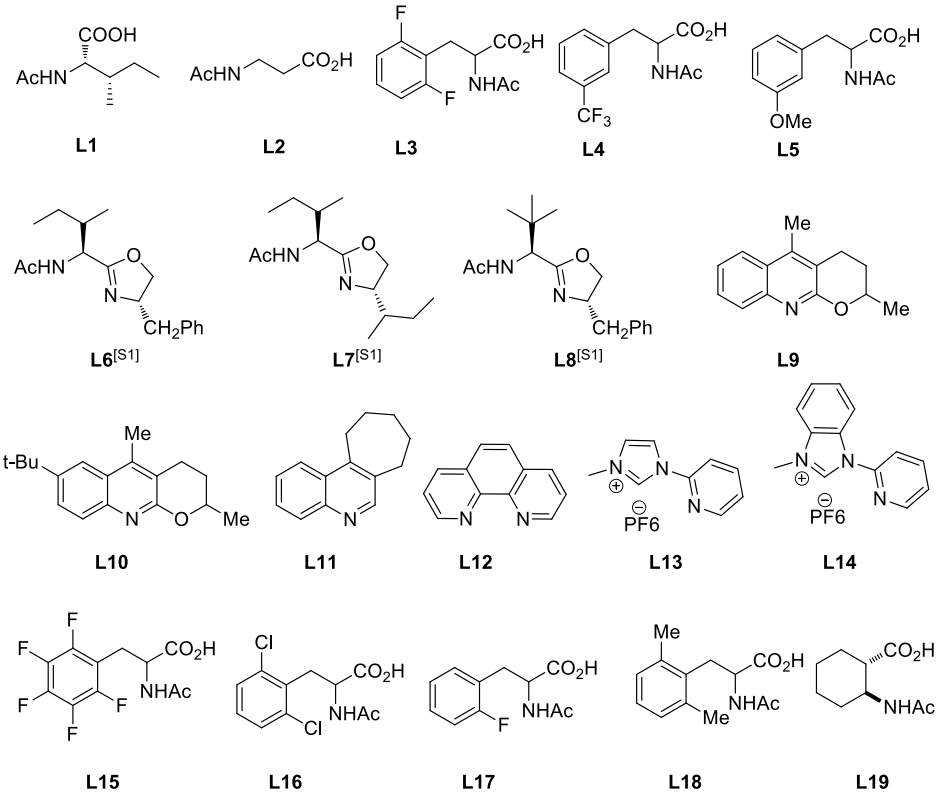
[a] ^{1}H NMR yields using CH_2Br_2 as internal standard.

2.2 Optimization of reaction conditions:[a]



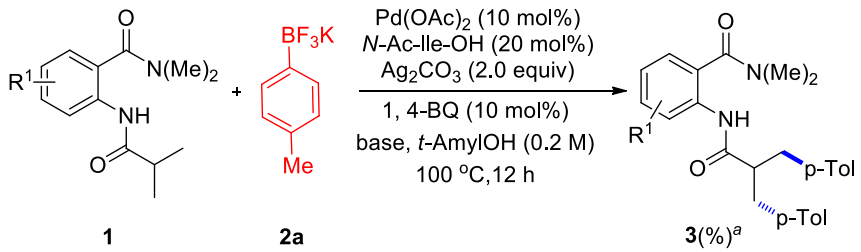
entry	ligand	base (equiv)	BQ	solvent (M)	*t* (h)	yield[b] (**mono**:**di**)
1	**L1**	Cs_2CO_3 (0.75)	BQ-1	*t*-AmylOH (0.1)	12	49 (3.5:1)
2	**L1**	Cs_2CO_3 (0.5)	BQ-1	*t*-AmylOH (0.1)	12	48 (3.8:1)
3	**L1**	Cs_2CO_3 (0.3)	BQ-1	*t*-AmylOH (0.1)	12	22 (10:1)
4	**L1**	Cs_2CO_3 (0.5)	BQ-1	*t*-AmylOH (0.1)	24	49 (3.5:1)
5	**L1**	Cs_2CO_3 (0.5)	BQ-1	*t*-AmylOH (0.1)	6	34 (3.9:1)
9	**L1**	Cs_2CO_3 (0.5)	BQ-2	*t*-AmylOH (0.1)	12	43 (5.1:1)
10	**L1**	Cs_2CO_3 (0.5)	BQ-3	*t*-AmylOH (0.1)	12	4 (4:0)
11	**L1**	Cs_2CO_3 (0.5)	-	*t*-AmylOH (0.1)	12	5 (5:0)
11	-	Cs_2CO_3 (0.5)	BQ-1	*t*-AmylOH (0.1)	12	4 (4:0)
12	**L1**	Cs_2CO_3 (0.5)	BQ-1	*t*-AmylOH (0.2)	12	54 (3.5:1)
13	**L1**	Cs_2CO_3 (0.5)	BQ-1	*t*-AmylOH (0.4)	12	48 (3.8:1)
14	**L1**	Cs_2CO_3 (0.5)	BQ-1	*t*-AmylOH (0.05)	12	35 (6:1)
15[c]	**L1**	Cs_2CO_3 (0.5)	BQ-1	*t*-AmylOH (0.2)	12	22 (6.3:1)
16[d]	**L1**	Cs_2CO_3 (0.5)	BQ-1	*t*-AmylOH (0.2)	12	48 (3:1)
17[e]	**L1**	Cs_2CO_3 (0.5)	BQ-1	*t*-AmylOH (0.2)	12	7 (7:0)
18	**L1**	K_3PO_4 (0.5)	BQ-1	*t*-AmylOH (0.2)	12	36 (5:1)
19	**L1**	K_2HPO_4 (0.5)	BQ-1	*t*-AmylOH (0.2)	12	11 (11:0)
20	**L1**	K_2CO_3 (0.5)	BQ-1	*t*-AmylOH (0.2)	12	44 (4.5:1)
21	**L1**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	58 (2.6:1)
22	**L1**	KOAc (2.0)	BQ-1	*t*-AmylOH (0.2)	12	11 (11:0)
23[f]	**L1**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	41 (5.8:1)
24[g]	**L1**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	49 (3.9:1)
25	**L1**	K_2CO_3 (2.0)	BQ-1	DMF (0.2)	12	5 (4:1)
26	**L1**	K_2CO_3 (2.0)	BQ-1	EA (0.2)	12	29 (4.8:1)
27	**L1**	K_2CO_3 (2.0)	BQ-1	2-Heptanol (0.2)	12	31 (9.3:1)
28	**L1**	K_2CO_3 (2.0)	BQ-1	3-Methyl-3-Petanol (0.2)	12	34 (7.5:1)
29	**L1**	K_2CO_3 (2.0)	BQ-1	4-Methyl-2-Petanol (0.2)	12	43 (7.6:1)
30	**L1**	K_2CO_3 (2.0)	BQ-1	DCM (0.2)	12	2 (2:0)
31	**L1**	K_2CO_3 (2.0)	BQ-1	Acetone (0.2)	12	7 (7:0)
32	**L2**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	39 (3.9:1)
33	**L3**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	59 (2.5:1)
34	**L4**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	55 (2.7:1)
35	**L5**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	42 (4.2:1)
36	**L6**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	52 (3.3:1)
37	**L7**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	54 (2.9:1)
38	**L8**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	61 (2.2:1)
39	**L8**	**K_2CO_3 (2.0)**	**BQ-1**	***t*-AmylOH (0.2)**	**24**	**65 (2.1:1)** **62 (2.3:1)**[h]
40	**L9**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	28 (13:1)
41	**L10**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	31 (9.3:1)
42	**L11**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	35 (4:1)
43	**L12**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	0 (0:0)

entry	ligand	base (equiv)	BQ	solvent (M)	*t* (h)	**mono**/**di**[b]
44	**L13**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	4 (4/0)
45	**L14**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	20 (20:0)
46	**L15**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	35 (6:1)
47	**L16**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	23 (10.5:1)
48	**L17**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	47 (2.9:1)
49	**L18**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	0 (0:0)
50	**L19**	K_2CO_3 (2.0)	BQ-1	*t*-AmylOH (0.2)	12	41 (3.1:1)



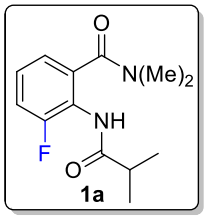
[a]Reaction conditions: **1f** (0.1 mmol), **2a** (0.2 mmol). [b]^{1}H NMR yield using CH_2Br_2 as internal standard. [c]10 mol% $Pd_2(dba)_3$ as catalyst. [d]10 mol% $Pd(TFA)_2$ as catalyst. [e]10 mol% $Pd(MeCN)_2(BF_4)_2$ as catalyst. [f]90 °C. [g]100 °C. [h]Isolated yield. BQ-1 = 1,4-benzochinon; BQ-2 = 2-methylcyclohexa-2,5-diene-1,4-dione; BQ-3 = 2,3,5,6- tetra-methylcyclohexa-2,5-diene-1,4-dione.

2.3 Directing group screening:



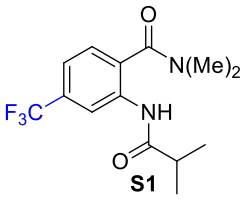
1 **2a** **3**(%)[a]

0.5 equiv of Cs_2CO_3 as the base:



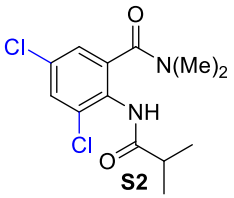
1a

mono+di=42+12



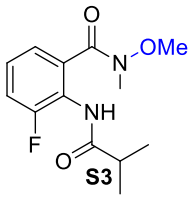
S1

mono+di=33+7



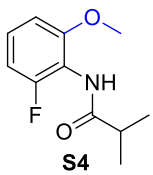
S2

mono+di=31+8



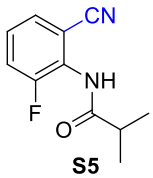
S3

mono+di=34+6



S4

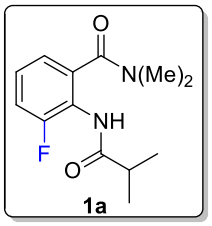
mono+di=21+0



S5

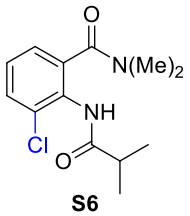
mono+di=15+0

2.0 equiv of K_2CO_3 as the base:



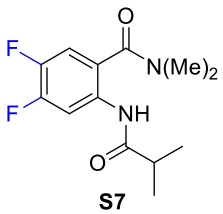
1a

mono+di=42+16



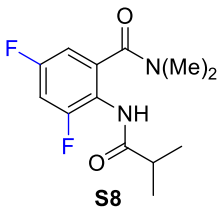
S6

mono+di=33+5



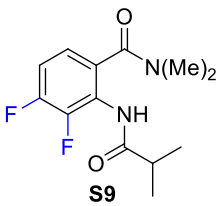
S7

mono+di=36+10



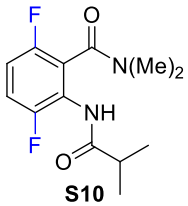
S8

mono+di=39+7



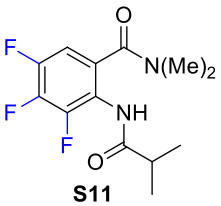
S9

mono+di=44+14



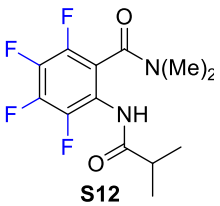
S10

mono+di=23+15



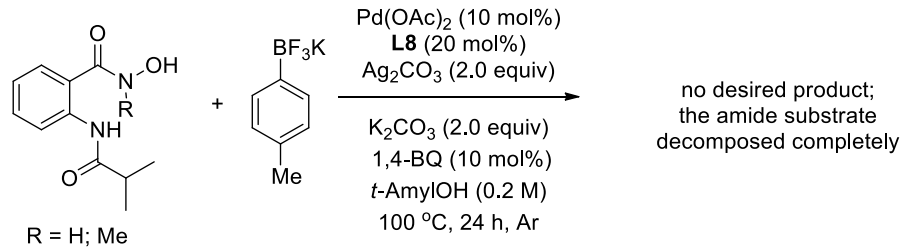
S11

mono+di=40+14



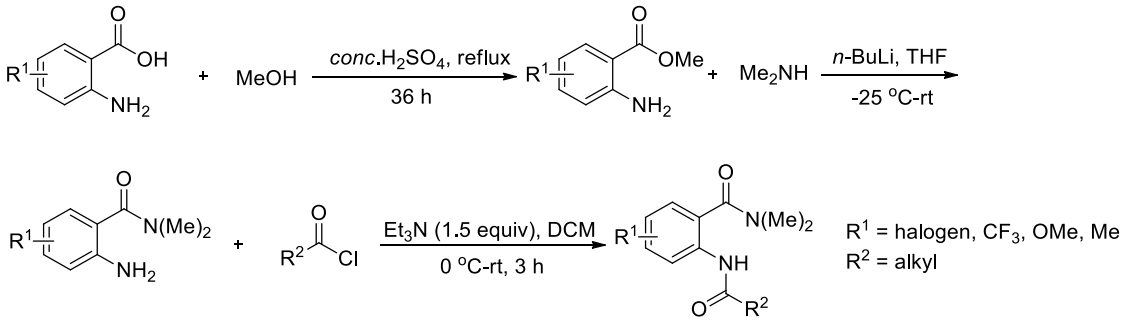
S12

mono+di=22+9



3. Experimental Section

3.1 General procedure for synthesis of substrates:



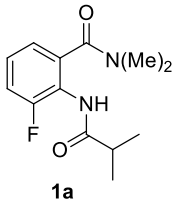
To a 100 mL three-neck bottom flask equipped with a reflux-condenser was added 2-amino benzoic acid (10 mmol), 20 mL MeOH and 2.0 mL *conc.*H_2SO_4. The mixture was then stirred at refluxing temperature for 36 h in an oil bath. After completion of the reaction, cooled down to room temperature, most of MeOH was evaporated under vacuum and then the residue was diluted by 100 mL EtOAc. The mixture was next washed with H_2O (3×30 mL), the remaining organic phase was dried over anhydrous Na_2SO_4, concentrated under vacuum then purified through flash silica-gel chromatography to obtain corresponding ester (eluents: PE : EtOAc = 10 : 1).

To a 50 mL dried Schlenk tube protected by a nitrogen balloon was successively added Me_2NH (2.0 M in THF, 4.0 mL) and 10 mL anhydrous THF, then the solution was cooled to -20 °C. *n*-BuLi (2.5 M in THF, 3.2 mL) was added via a syringe slowly and the mixture was continued reacted at this temperature for 0.5 h to give the in-situ fresh Me_2NLi. To a new 50 mL dried Schlenk tube protected by a nitrogen balloon was successively added ester (4.0 mmol) and 10 mL anhydrous THF, then the solution was cooled to -20 °C. The above prepared Me_2NLi (8.0 mmol) was added via a syringe slowly and then the stirring was continued when the temperature was recovered to room temperature spontaneously. After completion of the reaction, it was quenched by H_2O in an ice-cold bath and then diluted by 100 mL EtOAc. The mixture was next washed with brine (3 × 30 mL), the remaining organic phase was dried over anhydrous Na_2SO_4, concentrated under vacuum then purified through flash silica-gel chromatography to obtain corresponding aminobenzamide (eluents: PE : EtOAc = 2:1).

To a 50 mL dried bottom flask protected by a nitrogen balloon was successively added aminobenzamide (3 mmol), 15 mL DCM and 0.62 mL Et_3N, then the solution was cooled to 0 °C. Acyl chloride (3.6 mmol) was added via a syringe slowly and the mixture was reacted at room temperature for 2-3 h. The reaction solution was then diluted by 100 mL EtOAc. The mixture was

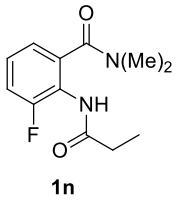
next washed with H_2O (2 × 20 mL), the remaining organic phase was dried over anhydrous Na_2SO_4, concentrated under vacuum then purified through flash silica-gel chromatography to give the target substrate (eluents: PE : EtOAc = 2:1-1:1).

3.2 Characterization of substrates:



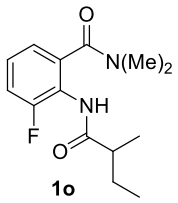
1a

3-fluoro-2-isobutyramido-*N*,*N*-dimethylbenzamide: prepared from the general procedure: white solid; 665 mg; yield: 88%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.25-7.16 (m, 1H), 7.15-7.07 (m, 1H), 7.03 (d, J = 7.6 Hz, 1H), 3.07 (s, 3H), 2.96 (s, 3H), 2.64-2.49 (m, 1H), 1.22 (d, J = 6.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.3, 168.8, 157.4 (d, J = 251.7 Hz), 135.0, 126.9 (d, J = 7.6 Hz), 122.9 (d, J = 14.5 Hz), 122.1, 116.8(d, J = 20.6 Hz), 39.4, 35.3, 35.0, 19.4. HRMS (m/z, ESI-TOF): Calcd for $C_{13}H_{17}FN_2NaO_2^+$ $[M+Na]^+$ 275.1166, found 275.1166.



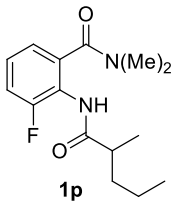
1n

3-fluoro-*N*,*N*-dimethyl-2-propionamidobenzamide: prepared from the general procedure: white solid; 656 mg; yield: 92%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.23-7.14 (m, 1H), 7.10-7.04 (m, 1H), 7.02 (d, J = 7.6 Hz, 1H), 3.08 (s, 3H), 2.98 (s, 3H), 2.38 (q, J = 7.6 Hz, 2H), 1.20 (t, J = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0, 169.1, 157.2(d, J = 251.3 Hz), 134.5, 126.7 (d, J = 7.9 Hz), 123.0 (d, J = 14.4 Hz), 122.3 (d, J = 3.7 Hz), 116.8 (d, J = 20.8 Hz), 39.5, 35.0, 29.6, 9.8. HRMS (m/z, ESI-TOF): Calcd for $C_{12}H_{15}FN_2NaO_2^+$ $[M+Na]^+$ 261.1010, found 261.1011.



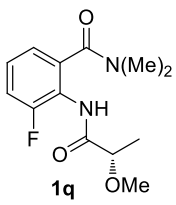
1o

3-fluoro-*N*,*N*-dimethyl-2-(2-methylbutanamido)benzamide: prepared from the general procedure: white solid; 718 mg; yield: 90%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.25-7.18 (m, 1H), 7.16-7.08 (m, 1H), 7.03 (d, J = 7.6 Hz, 1H), 3.07 (s, 3H), 2.96 (s, 3H), 2.41-2.28 (m, 1H), 1.78-1.66 (m, 1H), 1.57-1.44 (m, 1H), 1.21 (d, J = 6.8 Hz, 3H), 0.96 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.0, 168.8, 157.5 (d, J = 251.8 Hz), 135.4, 126.9 (d, J = 8.2 Hz), 122.8 (d, J = 14.7 Hz), 122.0 (d, J = 3.0 Hz), 116.7 (d, J = 20.8 Hz), 42.6, 39.3, 34.9, 27.2, 17.4, 11.7. HRMS (m/z, ESI-TOF): Calcd for $C_{14}H_{19}FN_2NaO_2^+$ $[M+Na]^+$ 289.1323, found 289.1324.



1p

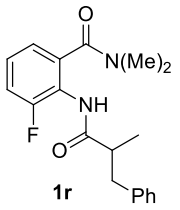
3-fluoro-*N*,*N*-dimethyl-2-(2-methylpentanamido)benzamide: prepared from the general procedure: white solid; 680 mg; yield: 81%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (br s, 1H), 7.24-7.11 (m, 1H), 7.08-6.93 (m, 2H), 3.06 (s, 3H), 2.94 (s, 3H), 2.53-2.40 (m, 1H), 1.75-1.60 (m, 1H), 1.44-1.31 (m, 3H), 1.17 (dd, J = 6.8, 2.4 Hz, 3H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.8, 168.8, 157.6(d, J = 251.9 Hz), 135.2, 127.1 (d, J = 8.1 Hz), 122.8 (d, J = 14.6 Hz), 122.0 (d, J = 3.0 Hz), 116.8 (d, J = 20.9 Hz), 41.1, 39.4, 36.4, 34.9, 20.4, 17.8, 14.1. HRMS (m/z, ESI-TOF): Calcd for $C_{15}H_{21}FN_2NaO_2^+$ $[M+Na]^+$ 303.1479, found 303.1478.



1q

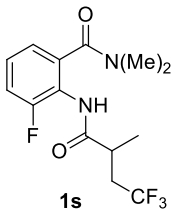
(S)-3-fluoro-2-(2-methoxypropanamido)-*N*,*N*-dimethylbenzamide: prepared from the general procedure: white solid; 627 mg; yield: 78%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.26-7.21 (m, 1H), 7.17 (t, J = 9.2 Hz, 1H), 7.07 (d, J = 7.6 Hz, 1H), 3.87 (q, J = 6.8 Hz, 1H), 3.47 (s, 3H), 3.06 (s, 3H), 2.98 (s, 3H),

1.45 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.2, 168.5 (d, *J* = 3.0 Hz), 157.2 (d, *J* = 251.4 Hz), 134.8, 127.3 (d, *J* = 8.2 Hz), 122.5 (d, *J* = 3.7 Hz), 121.9 (d, *J* = 14.1 Hz), 116.8(d, *J* = 20.5 Hz), 78.5, 57.8, 39.4, 35.0, 18.3. HRMS (m/z, ESI-TOF): Calcd for $C_{13}H_{17}FN_2NaO_3^+$ $[M+Na]^+$ 291.1115, found 291.1115.



1r

3-fluoro-*N*,*N*-dimethyl-2-(2-methyl-3-phenylpropanamido)benzamide: prepared from the general procedure: white solid; 824 mg; yield: 84%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.29-7.25 (m, 2H), 7.24-7.14 (m, 4H), 7.04 (t, *J* = 9.6 Hz, 1H), 6.97 (d, *J* = 7.6 Hz, 1H), 3.10 (dd, *J* = 12.8, 6.8 Hz, 1H), 3.00 (s, 3H), 2.85 (s, 3H), 2.78-2.62 (m, 2H), 1.21 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.8, 168.7, 157.5 (d, *J* = 252.6 Hz), 139.7, 134.8, 129.2, 128.3, 127.2 (d, *J* = 8.0 Hz), 126.2, 122.6 (d, *J* = 14.6 Hz), 122.1 (d, *J* = 3.0 Hz), 116.9 (d, *J* = 20.7 Hz), 43.2, 39.8, 39.2, 34.9, 17.6. HRMS (m/z, ESI-TOF): Calcd for $C_{19}H_{21}FN_2NaO_2^+$ $[M+Na]^+$ 351.1479, found 351.1479.

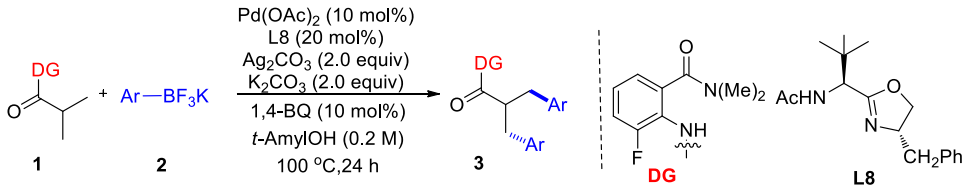


1s

3-fluoro-N,N-dimethyl-2-(4,4,4-trifluoro-2-methylbutanamido)benzamide: prepared from the general procedure: white solid; 796 mg; yield: 83%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (s, 1H), 7.23-7.14 (m, 1H), 7.03-6.91 (m, 2H), 3.05 (s, 3H), 2.90 (s, 3H), 2.89-2.79 (m, 1H), 2.78-2.63 (m, 1H), 2.21-2.03 (m, 1H), 1.29 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 168.7 (d, *J* = 3.0 Hz), 157.6 (d, *J* = 252.8 Hz), 135.3, 127.6 (d, *J* = 8.1 Hz), 126.5 (q, *J* = 278.2 Hz), 122.3 (q, *J* = 14.7 Hz), 121.9 (d, *J* = 3.7 Hz), 116.9 (d, *J* = 20.7 Hz), 39.2, 37.0 (q, *J* = 28.6 Hz), 35.07, 35.05, 34.9, 18.5. HRMS (m/z, ESI-TOF): Calcd for $C_{14}H_{16}F_4N_2NaO_2^+$ $[M+Na]^+$ 343.1040, found 343.1040.

3.3 General procedure and characterization of products.

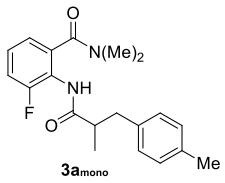
3.3.1 General procedure for C-H bond activation and cross-coupling:



1 2 3

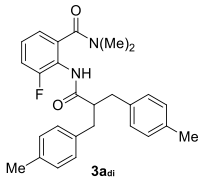
To an oven-dried 15 mL sealed tube equipped with a magnetic stir bar was added **1** (0.1 mmol), boron reagents (0.2 mmol), Ag_2CO_3 (55 mg, 0.2 mmol), K_2CO_3 (27.6 mg, 0.2 mmol), APAO (5.8 mg, 0.02 mol), $Pd(OAc)_2$ (2.2 mg, 0.01 mol) 1,4-BQ (1.1 mg, 0.01 mmol) and dried *t*-AmylOH (0.5 mL) successively. The tube was reacted in a preheated oil bath (100 °C) for 12 or 24 h and then cooled to room temperature. The reaction was diluted with EtOAc (20 mL) and filtered through a short pad of Celite. The tube and Celite pad were washed with an additional 10 mL of EtOAc. The filtrate was concentrated in vacuo, and purified by preparative thin layer chromatography using petroleum ether/EtOAc (1/1) as the eluent.

3.3.2 Characterization of products:



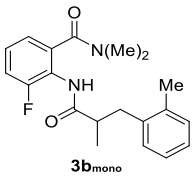
3amono

3-fluoro-*N*,*N*-dimethyl-2-(2-methyl-3-(p-tolyl)propanamido)benzamide: yellow oil; 14.7 mg; yield: 43%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, J = 12.0 Hz, 1H), 7.17-7.06 (m, 5H), 7.00-6.94 (m, 2H), 3.05 (dd, J = 13.6, 6.8 Hz, 1H), 3.00 (s, 3H), 2.83 (s, 3H), 2.79-2.70 (m, 1H), 2.60 (dd, J = 13.6, 7.6 Hz, 1H), 2.31 (s, 3H), 1.16 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1, 168.8, 157.5 (d, J = 252.7 Hz), 136.7, 135.5, 134.9, 129.0, 128.9, 127.1 (d, J = 8.2 Hz), 122.6 (d, J = 14.5 Hz), 122.0 (d, J = 3.5 Hz), 116.9, (d, J = 20.7 Hz), 43.1, 39.4, 39.2, 34.9, 21.0, 17.4. HRMS (m/z, ESI-TOF): Calcd for $C_{20}H_{23}FN_2NaO_2^+$ $[M+Na]^+$ 365.1636, found 365.1636. Enantiomeric excess was determined by HPLC analysis, *ee* = 45% (Chiralpak column AD-H, λ = 254 nm, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min, 30 °C, t_R(minor) = 13.216 min, t_R(major) =15.109 min.



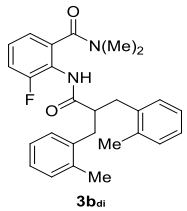
3adi

3-fluoro-*N*,*N*-dimethyl-2-(2-(4-methylbenzyl)-3-(p-tolyl)propanamido)benzamide: yellow oil; 8.2 mg; yield: 19%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.17-7.01 (m, 10H), 6.88 (d, J = 7.6 Hz, 1H), 3.02 (dd, J = 13.2, 8.4 Hz, 2H), 2.90-2.80 (m, 4H), 2.74 (dd, J = 13.6, 6.0 Hz, 2H), 2.62 (s, 3H), 2.30 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 168.5 (d, J = 2.9 Hz), 157.5 (d, J = 254.8 Hz), 136.5, 135.6, 134.3, 129.07, 129.04, 127.3 (d, J = 8.1 Hz), 122.3 (d, J = 14.5 Hz), 121.8 (d, J = 3.6 Hz), 117.2 (d, J = 20.7 Hz), 51.8, 38.9, 38.1, 34.7, 21.1. HRMS (m/z, ESI-TOF): Calcd for $C_{27}H_{29}FN_2NaO_2^+$ $[M+Na]^+$ 455.2105, found 455.2104.



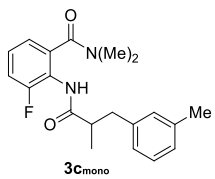
3bmono

3-fluoro-*N*,*N*-dimethyl-2-(2-methyl-3-(o-tolyl)propanamido)benzamide: yellow oil; 15.7 mg; yield: 46%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (br s, 1H), 7.19-7.09 (m, 5H), 6.97-6.91 (m, 2H), 3.08 (dd, J = 13.6, 6.8 Hz, 1H), 2.97 (s, 3H), 2.86-2.73 (m, 4H), 2.66 (dd, J = 13.6, 7.2 Hz, 1H), 2.34 (s, 3H), 1.19 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.2, 168.8, 157.5 (d, J = 252.9 Hz), 138.0, 136.4, 135.0, 130.2, 129.86, 129.84, 127.2 (d, J = 8.1 Hz), 126.2, 125.8, 122.6 (d, J = 14.7 Hz), 122.0 (d, J = 3.4 Hz), 116.9, (d, J = 20.7 Hz), 41.7, 39.1, 36.8, 34.9, 19.6, 17.7. HRMS (m/z, ESI-TOF): Calcd for $C_{20}H_{23}FN_2NaO_2^+$ $[M+Na]^+$ 365.1636, found 365.1637.



3bdi

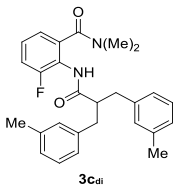
3-fluoro-*N*,*N*-dimethyl-2-(2-(2-methylbenzyl)-3-(o-tolyl)propanamido)benzamide: yellow solid; 4.7 mg; yield: 11%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.21-7.07 (m, 9H), 7.07-7.01 (m, 1H), 6.84 (d, J = 7.6 Hz, 1H), 3.15-3.05 (m, 2H), 2.87-2.78 (m, 6H), 2.65 (s, 3H), 2.25 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0, 168.4, 157.5 (d, J = 255.0 Hz), 137.7, 136.3, 134.1, 130.3, 130.1, 127.3 (d, J = 8.2 Hz), 126.5, 125.9, 122.3(d, J = 14.5 Hz), 121.9 (d, J = 3.7 Hz), 117.2 (d, J = 20.8 Hz), 49.3, 39.0, 35.7, 34.8, 19.4. HRMS (m/z, ESI-TOF): Calcd for $C_{27}H_{29}FN_2NaO_2^+$ $[M+Na]^+$ 455.2105, found 455.2105.



3cmono

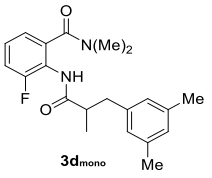
3-fluoro-*N*,*N*-dimethyl-2-(2-methyl-3-(m-tolyl)propanamido)benzamide: yellow solid; 13.7 mg; yield: 40%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 7.17-7.11 (m, 2H), 7.05-6.93 (m, 5H), 3.06 (dd, J = 13.2, 6.8 Hz, 1H),

3.00 (s, 3H), 2.82 (s, 3H), 2.80-2.73 (m, 1H), 2.59 (dd, *J* = 13.2, 7.6 Hz, 1H), 2.31 (s, 3H), 1.16 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.2, 168.8, 157.5 (d, *J* = 252.8 Hz), 139.7, 137.8, 135.0, 129.9, 128.2, 127.2 (d, *J* = 8.0 Hz), 126.9, 126.2, 122.6 (d, *J* = 14.6 Hz), 122.0 (d, *J* = 3.5 Hz), 116.9, (d, *J* = 20.7 Hz), 42.9, 39.8, 39.2, 34.9, 21.4, 17.4. HRMS (m/z, ESI-TOF): Calcd for $C_{20}H_{23}FN_2NaO_2^+$ $[M+Na]^+$ 365.1636, found 365.1636.



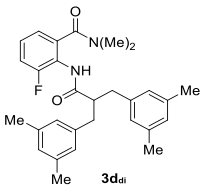
3c$_{di}$

3-fluoro-*N*,*N*-dimethyl-2-(2-(3-methylbenzyl)-3-(m-tolyl)propanamido)benzamide: yellow oil; 5.2 mg; yield: 12%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.19-7.10 (m, 3H), 7.08-6.97(m, 7H), 6.89 (d, *J* = 7.6 Hz, 1H), 3.03 (dd, *J* = 13.2, 8.4 Hz, 2H), 2.90-2.82 (m, 4H), 2.75 (dd, *J* = 13.2, 5.6 Hz, 2H), 2.62 (s, 3H), 2.31 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 168.4, 157.5 (d, *J* = 254.7 Hz), 139.4, 137.9, 134.3, 130.0, 128.3, 127.3 (d, *J* = 8.2 Hz), 127.0, 126.1, 122.3 (d, *J* = 14.5 Hz), 121.9 (d, *J* = 3.6 Hz), 117.2 (d, *J* = 20.7 Hz), 51.8, 38.9, 38.6, 34.8, 21.4. HRMS (m/z, ESI-TOF): Calcd for $C_{27}H_{29}FN_2NaO_2^+$ $[M+Na]^+$ 455.2105, found 455.2105.



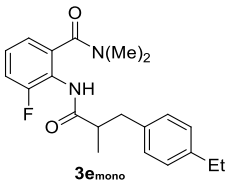
3d$_{mono}$

2-(3-(3,5-dimethylphenyl)-2-methylpropanamido)-3-fluoro-*N*,*N*-dimethylbenzamide: yellow solid; 15.7 mg; yield: 44%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 0.33H), 8.52 (s, 0.65H), 7.16-7.11 (m, 1H), 6.98-6.93 (m, 2H), 6.85 (s, 2H), 6.83 (s, 1H), 3.04 (dd, *J* = 13.6, 8.0 Hz, 1H), 3.01 (s, 3H), 2.83 (s, 3H), 2.79-2.74 (m, 1H), 2.55 (dd, *J* = 13.6, 6.8 Hz, 1H), 2.27 (s, 6H), 1.15 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.2, 168.8, 157.5 (d, *J* = 252.6 Hz), 139.6, 137.7, 135.1, 127.8, 127.1 (d, *J* = 8.0 Hz), 127.0, 122.6 (d, *J* = 14.6 Hz), 122.0 (d, *J* = 3.7 Hz), 116.9 (d, *J* = 20.7 Hz), 42.9, 39.7, 39.2, 34.9, 21.3, 17.4. HRMS (m/z, ESI-TOF): Calcd for $C_{21}H_{25}FN_2NaO_2^+$ $[M+Na]^+$ 379.1792, found 379.1792.



3d$_{di}$

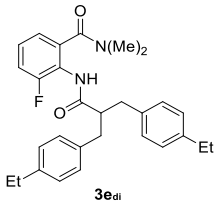
2-(2-(3,5-dimethylbenzyl)-3-(3,5-dimethylphenyl)propanamido)-3-fluoro-*N*,*N*-dimethylbenzamide: yellow oil; 5.0 mg; yield: 11%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (br s, 1H), 7.18-7.11 (m, 1H), 7.05 (td, *J* = 9.6, 1.6 Hz, 1H), 6.89 (d, *J* = 7.6 Hz, 1H), 6.83 (s, 6H), 2.98 (dd, *J* = 13.2, 8.4 Hz, 2H), 2.88-2.79 (m, 4H), 2.71 (dd, *J* = 13.2, 5.6 Hz, 2H), 2.60 (s, 3H), 2.26 (s, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0, 168.5, 157.5 (d, *J* = 254.8 Hz), 139.4, 137.7, 134.6, 127.9, 127.4 (d, *J* = 8.2 Hz), 127.0, 122.1(d, *J* = 14.6 Hz), 121.8 (d, *J* = 3.7 Hz), 117.1 (d, *J* = 20.7 Hz), 51.7, 38.7, 38.5, 34.6, 21.3. HRMS (m/z, ESI-TOF): Calcd for $C_{29}H_{33}FN_2NaO_2^+$ $[M+Na]^+$ 483.2418, found 483.2416.



3e$_{mono}$

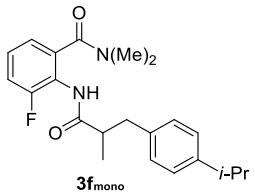
2-(3-(4-ethylphenyl)-2-methylpropanamido)-3-fluoro-*N*,*N*-dimethylbenzamide: yellow oil; 15.7 mg; yield: 44%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.20-7.09 (m, 5H), 7.06-7.01 (m, 1H), 6.97 (d, *J* = 7.6 Hz, 1H), 3.06 (dd, *J* = 13.2, 6.8 Hz, 1H), 3.00 (s, 3H), 2.84 (s, 3H), 2.78-2.68 (m, 1H), 2.65-2.59 (m, 3H), 1.25-1.15 (m, 6H) ; ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.9, 168.7, 157.5 (d, *J* = 252.8 Hz), 142.0, 136.8, 134.8, 129.1, 127.8, 127.2 (d, *J* = 8.2 Hz), 122.6 (d, *J* = 14.5 Hz), 122.1 (d, *J* = 3.7 Hz), 116.9, (d, *J* = 20.4 Hz), 43.2, 39.4, 39.2, 34.9, 28.5, 17.5, 15.6. HRMS (m/z, ESI-TOF): Calcd for $C_{21}H_{25}FN_2NaO_2^+$ $[M+Na]^+$

379.1792, found 379.1792.



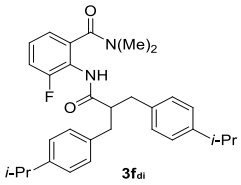
3e$_{di}$

2-(2-(4-ethylbenzyl)-3-(4-ethylphenyl)propanamido)-3-fluoro-*N*,*N*-dimethylbenzamide: yellow oil; 8.3 mg; yield: 18%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.19-7.05 (m, 9H), 7.04-6.98 (m, 1H), 6.87 (d, J = 7.6 Hz, 1H), 3.04 (dd, J = 13.6, 8.4 Hz, 2H), 2.96-2.87 (m, 1H), 2.85 (s, 3H), 2.73 (dd, J = 13.6, 6.0 Hz, 2H), 2.60 (q, J = 7.6 Hz, 4H), 2.56 (s, 3H), 1.21 (t, J = 7.6 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 168.5 (d, J = 2.9 Hz), 157.5(d, J = 254.7 Hz), 142.0, 136.8, 134.7, 129.1, 127.9, 127.4 (d, J = 8.1 Hz), 122.2 (d, J = 14.5 Hz), 121.8 (d, J = 3.7 Hz), 117.0 (d, J = 20.7 Hz), 51.4, 38.8, 38.0, 34.7, 28.5, 15.6. HRMS (m/z, ESI-TOF): Calcd for $C_{29}H_{33}FN_2NaO_2^+$ $[M+Na]^+$ 483.2418, found 483.2418.



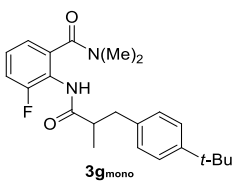
3f$_{mono}$

3-fluoro-2-(3-(4-isopropylphenyl)-2-methylpropanamido)-*N*,*N*-dimethylbenzamide: yellow oil; 15 mg; yield: 41%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.20-7.11 (m, 5H), 7.05-7.01 (m, 1H), 6.97 (d, J = 7.6 Hz, 1H), 3.07 (dd, J = 13.6, 7.2 Hz, 1H), 3.00 (s, 3H), 2.90-2.83 (m, 1H), 2.82 (s, 3H), 2.78-2.68 (m, 1H), 2.62 (dd, J = 13.2, 7.2 Hz, 1H), 1.23 (d, J = 7.2 Hz, 6H), 1.20 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.9, 168.7, 157.5 (d, J = 252.8 Hz), 146.7, 136.9, 134.9, 129.1, 127.2 (d, J = 8.1 Hz), 126.4, 122.5 (d, J = 14.5 Hz), 122.1 (d, J = 3.7 Hz), 117.0, (d, J = 20.7 Hz), 43.1, 39.4, 39.2, 34.9, 33.7, 24.1, 17.6. HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{27}FN_2NaO_2^+$ $[M+Na]^+$ 393.1949, found 393.1949.



3f$_{di}$

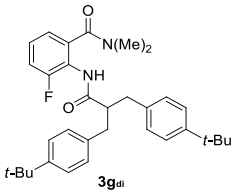
3-fluoro-2-(2-(4-isopropylbenzyl)-3-(4-isopropylphenyl)propanamido)-*N*,*N*-dimethylbenzamide: yellow oil; 6.8 mg; yield: 14%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (br s, 1H), 7.18-7.08 (m, 9H), 7.00 (t, J = 9.6 Hz, 1H), 6.89 (d, J = 7.2 Hz, 1H), 3.04 (dd, J = 13.6, 8.0 Hz, 2H), 2.99-2.91 (m, 1H), 2.90-2.82 (m, 5H), 2.73 (dd, J = 13.6, 6.0 Hz, 2H), 2.54 (s, 3H), 1.22 (d, J = 6.8 Hz, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 168.6, 157.5 (d, J = 254.4 Hz), 146.7, 136.9, 134.9, 129.1, 127.5 (d, J = 8.1 Hz), 126.4, 122.1 (d, J = 14.4 Hz), 121.8 (d, J = 3.7 Hz), 117.0 (d, J = 20.7 Hz), 51.0, 38.7, 37.9, 34.7, 33.7, 24.1. HRMS (m/z, ESI-TOF): Calcd for $C_{31}H_{37}FN_2NaO_2^+$ $[M+Na]^+$ 511.2731, found 511.2731.



3g$_{mono}$

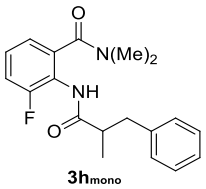
2-(3-(4-(tert-butyl)phenyl)-2-methylpropanamido)-3-fluoro-*N*,*N*-dimethylbenzamide: yellow oil; 12.7 mg; yield: 33%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.29 (d, J = 8.0 Hz, 2H), 7.24-7.14 (m, 3H), 7.07-7.03 (m, 1H), 6.98 (d, J = 7.6 Hz, 1H), 3.07 (dd, J = 13.2, 6.8 Hz, 1H), 3.00 (s, 3H), 2.83 (s, 3H), 2.79-2.68 (m , 1H), 2.63 (dd, J = 13.6, 7.6 Hz, 1H), 1.31 (s, 9H), 1.21 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.9, 168.7, 157.5 (d, J = 252.8 Hz), 148.9, 136.6, 134.9, 128.8, 127.3 (d, J = 8.2 Hz), 125.2, 122.5 (d, J = 14.5 Hz),

122.1 (d, *J* = 3.6 Hz), 116.9 (d, *J* = 20.7 Hz), 43.1, 39.24, 39.20, 34.9, 34.4, 31.4, 17.6. HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{29}FN_2NaO_2^+$ $[M+Na]^+$ 407.2105, found 407.2105.



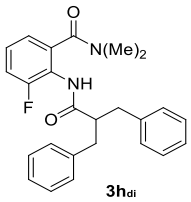
3g$_{di}$

2-(2-(4-(tert-butyl)benzyl)-3-(4-(tert-butyl)phenyl)propanamido)-3-fluoro-*N*,*N*-dimethylbenzamide: yellow solid; 2.6 mg; yield: 5%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.27 (t, *J* = 6.6 Hz, 4H), 7.21-7.08 (m, 5H), 7.03 (t, *J* = 8.4 Hz, 1H), 6.91 (d, *J* = 7.6 Hz, 1H), 3.05 (dd, *J* = 13.6, 8.0 Hz, 2H), 2.98-2.90 (m, 1H), 2.86 (s, 3H), 2.75 (dd, *J* = 13.6, 6.0 Hz, 2H), 2.57 (s, 3H), 1.29 (s, 16H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 168.5, 157.4 (d, *J* = 254.2 Hz), 149.0, 136.4, 134.8, 128.8, 127.5 (d, *J* = 8.1 Hz), 125.3, 122.0 (d, *J* = 14.3 Hz), 121.9 (d, *J* = 3.6 Hz), 116.9 (d, *J* = 20.7 Hz), 51.0, 38.8, 37.9, 34.8, 34.4, 31.4. HRMS (m/z, ESI-TOF): Calcd for $C_{33}H_{41}FN_2NaO_2^+$ $[M+Na]^+$ 539.3044, found 539.3044.



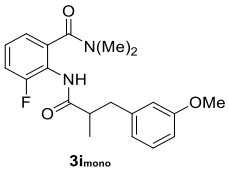
3h$_{mono}$

3-fluoro-*N*,*N*-dimethyl-2-(2-methyl-3-phenylpropanamido)benzamide: yellow oil; 11.8 mg; yield: 36%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.28-7.12 (m, 6H), 7.00-6.94 (m, 2H), 3.09 (dd, *J* = 13.6, 7.2 Hz, 1H), 2.99 (s, 3H), 2.82 (s, 3H), 2.80-2.75 (m, 1H), 2.64 (dd, *J* = 13.6, 7.6 Hz, 1H), 1.18 (dd, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.0, 168.8 (d, *J* = 2.9 Hz), 157.5 (d, *J* = 252.7 Hz), 139.8, 134.9, 129.2, 128.3, 127.2 (d, *J* = 8.2 Hz), 126.1, 122.6 (d, *J* = 14.6 Hz), 122.0 (d, *J* = 3.5 Hz), 116.9, (d, *J* = 20.7 Hz), 43.0, 39.8, 39.2, 34.9, 17.5. HRMS (m/z, ESI-TOF): Calcd for $C_{19}H_{21}FN_2NaO_2^+$ $[M+Na]^+$ 351.1479, found 351.1479.



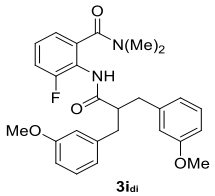
3h$_{di}$

2-(2-benzyl-3-phenylpropanamido)-3-fluoro-*N*,*N*-dimethylbenzamide: pale yellow oil; 3.2 mg; yield: 8%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.28-7.11 (m, 11H), 7.08-7.02 (m, 1H), 6.89 (d, *J* = 7.6 Hz, 1H), 3.08 (dd, *J* = 13.2, 8.8 Hz, 2H), 2.94-2.87 (m, 1H), 2.86 (s, 3H), 2.80 (dd, *J* = 13.2, 5.6 Hz, 2H), 2.65 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 168.4, 157.5 (d, *J* = 254.8 Hz), 139.5, 134.1, 129.2, 128.4, 127.2 (d, *J* = 8.3 Hz), 126.3, 122.3 (d, *J* = 14.3 Hz), 121.9 (d, *J* = 3.6 Hz), 117.2 (d, *J* = 20.8 Hz), 51.8, 39.0, 38.6, 34.9. HRMS (m/z, ESI-TOF): Calcd for $C_{25}H_{25}FN_2NaO_2^+$ $[M+Na]^+$ 427.1792, found 427.1791.



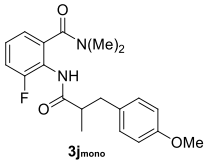
3i$_{mono}$

3-fluoro-2-(3-(3-methoxyphenyl)-2-methylpropanamido)-*N*,*N*-dimethylbenzamide: yellow solid; 14.3 mg; yield: 40%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 7.20-7.12 (m, 2H), 7.00-6.94 (m, 2H), 6.82-6.73 (m, 3H), 3.78 (s, 3H), 3.07 (dd, *J* = 13.6, 7.2 Hz, 1H), 3.00 (s, 3H), 2.82 (s, 3H), 281-2.74 (m, 1H), 2.62 (dd, *J* = 13.2, 6.0 Hz, 1H), 1.18 (dd, *J* = 6.8, 2.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 168.8 (d, *J* = 2.8 Hz), 159.6, 157.5 (d, *J* = 252.7 Hz), 141.4, 134.9, 129.2, 127.2 (d, *J* = 8.2 Hz), 122.6 (d, *J* = 14.6 Hz), 122.0 (d, *J* = 3.5 Hz), 121.6, 116.9 (d, *J* = 20.7 Hz), 114.7, 111.7, 55.1, 42.9, 39.9, 39.2, 34.9, 17.5. HRMS (m/z, ESI-TOF): Calcd for $C_{20}H_{23}FN_2NaO_3^+$ $[M+Na]^+$ 381.1585, found 381.1585.



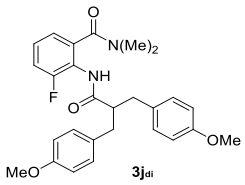
3i$_{di}$

3-fluoro-2-(2-(3-methoxybenzyl)-3-(3-methoxyphenyl)propanamido)-*N*,*N*-dimethylbenzamide: yellow oil; 7.0 mg; yield: 15%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.21-7.11 (m, 3H), 7.08-7.01 (m, 1H), 6.90 (d, J = 7.6 Hz, 1H), 6.81 (d, J = 7.6 Hz, 2H), 6.78-6.69 (m, 4H), 3.77 (s, 6H), 3.05 (dd, J = 13.2, 8.4 Hz, 2H), 2.94-2.83 (m, 4H), 2.77 (dd, J = 13.2, 6.0 Hz, 2H), 2.65 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 168.4, 159.6, 157.4 (d, J = 254.7 Hz), 141.1, 134.1, 129.4, 127.2 (d, J = 8.1 Hz), 122.3 (d, J = 14.6 Hz), 122.0 (d, J = 3.6 Hz), 121.5, 117.2 (d, J = 20.7Hz), 114.6, 112.0, 55.1, 51.5, 38.9, 38.6, 34.8. HRMS (m/z, ESI-TOF): Calcd for $C_{27}H_{29}FN_2NaO_4^+$ $[M+Na]^+$ 487.2004, found 487.2004.



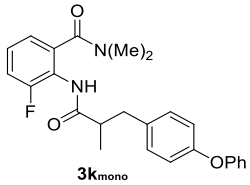
3j$_{mono}$

3-fluoro-2-(3-(4-methoxyphenyl)-2-methylpropanamido)-*N*,*N*-dimethylbenzamide: yellow oil; 14.3 mg; yield: 40%; ^{1}H NMR (400 MHz, d_6-DMSO) δ 9.57 (s, 1H), 7.36-7.26 (m, 2H), 7.14 (d, J = 8.4 Hz, 2H), 7.08 (d, J = 7.2 Hz, 1H), 6.85 (d, J = 8.4 Hz, 2H), 3.73 (s, 3H), 2.90 (dd, J = 13.6, 7.2 Hz, 1H), 2.87 (s, 3H), 2.83-2.74 (m, 1H), 2.67 (s, 3H), 2.47 (dd, J = 13.6, 7.2 Hz, 1H), 1.03 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, d_6-DMSO) δ 175.1, 167.5 (d, J = 2.9 Hz), 158.0, 157.8 (d, J = 250.3 Hz), 137.5, 132.3, 130.3, 128.3 (d, J = 8.2 Hz), 122.9, 122.8 (d, J = 10.6 Hz), 116.5 (d, J = 20.7 Hz), 114.0, 55.4, 41.9, 38.63, 38.60, 34.6, 17.8. HRMS (m/z, ESI-TOF): Calcd for $C_{20}H_{23}FN_2NaO_3^+$ $[M+Na]^+$ 381.1585, found 381.1585.



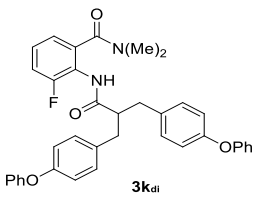
3j$_{di}$

3-fluoro-2-(2-(4-methoxybenzyl)-3-(4-methoxyphenyl)propanamido)-*N*,*N*-dimethylbenzamide: pale yellow oil; 3.7 mg; yield: 8%; ^{1}H NMR (400 MHz, d_6-DMSO) δ 9.63 (s, 1H), 7.35-7.23 (m, 2H), 7.10 (d, J = 8.8 Hz, 4H), 7.08-7.02 (m, 1H), 6.84 (d, J = 8.8 Hz, 4H), 3.72 (s, 6H), 3.09-3.00 (m, 1H), 2.88 (dd, J = 13.6, 7.6 Hz, 2H), 2.79 (s, 3H), 2.53 (s, 3H), 2.46 (dd, J = 13.6, 6.8 Hz, 2H). ^{13}C NMR (101 MHz, d_6-DMSO) δ 173.8, 167.4, 158.0, 137.3, 132.1, 130.2, 128.4 (d, J = 9.7 Hz), 122.8(d, J = 3.3 Hz), 122.7(d, J = 14.6 Hz), 116.5(d, J = 20.6 Hz), 114.1, 55.4, 49.5, 38.4, 36.7, 34.5. HRMS (m/z, ESI-TOF): Calcd for $C_{27}H_{29}FN_2NaO_4^+$ $[M+Na]^+$ 487.2004, found 487.2004.



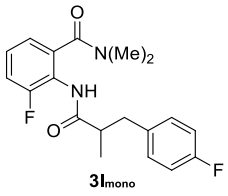
3k$_{mono}$

3-fluoro-*N*,*N*-dimethyl-2-(2-methyl-3-(4-phenoxyphenyl)propanamido)benzamide: yellow oil; 16 mg; yield: 38%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 7.31 (t, J = 7.2 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 7.16-7.06 (m, 2H), 6.99-6.91 (m, 6H), 3.06 (dd, J = 13.6, 7.2 Hz, 1H), 3.02 (s, 3H), 2.88 (s, 3H), 2.80-2.74 (m, 1H), 2.63 (dd, J = 13.6, 7.2 Hz, 1H), 1.18 (dd, J = 6.8, 2.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.0, 168.8 (d, J = 2.8 Hz), 157.6, 157.4 (d, J = 252.6 Hz), 155.4, 134.9, 134.8, 130.4, 129.7, 127.0 (d, J = 8.2 Hz), 123.0, 122.7(d, J = 14.5 Hz), 122.1 (d, J = 3.6 Hz), 119.0, 118.5, 116.9 (d, J = 20.8 Hz), 43.1, 39.3, 39.2, 35.0, 17.4. HRMS (m/z, ESI-TOF): Calcd for $C_{25}H_{25}FN_2NaO_3^+$ $[M+Na]^+$ 443.1741, found 443.1740.



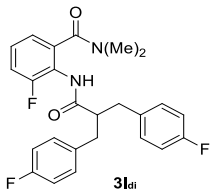
3k$_{di}$

3-fluoro-*N*,*N*-dimethyl-2-(2-(4-phenoxybenzyl)-3-(4-phenoxyphenyl)propanamido)benzamide: yellow oil; 5.3 mg; yield: 9%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.34-7.27 (m, 4H), 7.21-7.12 (m, 5H), 7.10-7.00 (m, 3H), 7.00-6.89 (m, 9H), 3.06 (dd, J = 13.2, 8.4 Hz, 2H), 2.95 (s, 3H), 2.91-2.84 (m, 1H), 2.84-2.74 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 168.4, 157.5, 157.4 (d, J = 254.3 Hz), 155.5, 134.4, 133.8, 130.4, 129.7, 127.1 (d, J = 8.0 Hz), 123.1, 122.5 (d, J = 14.4 Hz), 122.1 (d, J = 3.8 Hz), 119.0, 118.6, 117.3 (d, J = 20.8 Hz), 52.0, 39.2, 37.9, 34.9. HRMS (m/z, ESI-TOF): Calcd for $C_{37}H_{33}FN_2NaO_4^+$ $[M+Na]^+$ 611.2317, found 611.2317.



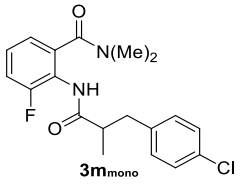
3l$_{mono}$

3-fluoro-2-(3-(4-fluorophenyl)-2-methylpropanamido)-*N*,*N*-dimethylbenzamide: pale yellow solid; 13 mg; yield: 38%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 14.8 Hz, 1H), 7.19-7.11 (m, 3H), 6.98-6.92 (m, 4H), 3.05 (dd, J = 13.6, 7.6 Hz, 1H), 3.00 (s, 3H), 2.85 (s, 3H), 2.78-2.70 (m, 1H), 2.62 (dd, J = 13.6, 7.2 Hz, 1H), 1.17 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.8, 168.8, 161.4 (d, J = 226.3 Hz), 157.4 (d, J = 252.6 Hz), 135.5 (d, J = 3.0 Hz), 134.8, 130.5 (d, J = 7.8 Hz), 127.1 (d, J = 8.2 Hz), 122.6 (d, J = 14.6 Hz), 122.1 (d, J = 3.5 Hz), 116.9 (d, J = 20.7 Hz), 114.9 (d, J = 21.1 Hz), 43.2, 39.2, 39.0, 34.9, 17.5. HRMS (m/z, ESI-TOF): Calcd for $C_{19}H_{20}F_2N_2NaO_2^+$ $[M+Na]^+$ 369.1385, found 369.1385.



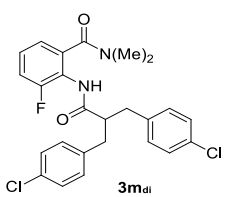
3l$_{di}$

3-fluoro-2-(2-(4-fluorobenzyl)-3-(4-fluorophenyl)propanamido)-*N*,*N*-dimethylbenzamide: yellow solid; 8.4 mg; yield: 19%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.21-7.09 (m, 5H), 7.07-6.99 (m, 1H), 6.98-6.91 (m, 4H), 6.88 (d, J = 7.6 Hz, 1H), 3.03 (dd, J = 13.2, 8.4 Hz, 2H), 2.90 (s, 3H), 2.84-2.70 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 168.4, 161.5 (d, J = 244.9 Hz), 157.4 (d, J = 254.7 Hz), 135.0 (d, J = 3.2 Hz), 133.5, 130.6 (d, J = 7.9 Hz), 127.0 (d, J = 8.2 Hz), 122.5 (d, J = 14.5 Hz), 122.1 (d, J = 3.6 Hz), 117.4 (d, J = 20.8 Hz), 115.1 (d, J = 21.1 Hz), 52.2, 39.2, 37.8, 34.9. HRMS (m/z, ESI-TOF): Calcd for $C_{25}H_{23}F_3N_2NaO_2^+$ $[M+Na]^+$ 463.1604, found 463.1604.



3m$_{mono}$

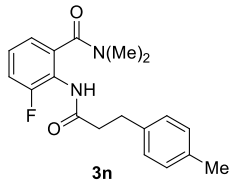
2-(3-(4-chlorophenyl)-2-methylpropanamido)-3-fluoro-*N*,*N*-dimethylbenzamide: yellow oil; 14 mg; yield: 39%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 7.23-7.11 (m, 5H), 6.96-6.92 (m, 2H), 3.04 (dd, J = 13.6, 7.6 Hz, 1H), 3.00 (s, 3H), 2.83 (s, 3H), 2.79-2.71 (m, 1H), 2.60 (dd, J = 13.6, 7.2 Hz, 1H), 1.16 (dd, J = 6.8, 2.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.7, 168.8 (d, J = 2.7 Hz), 157.4 (d, J = 252.7 Hz), 138.4, 134.8, 131.8, 130.5, 128.3, 127.1 (d, J = 8.1 Hz), 122.5 (d, J = 14.6 Hz), 122.0 (d, J = 3.7 Hz), 117.0 (d, J = 20.8 Hz), 42.9, 39.2, 39.1, 34.9, 17.6. HRMS (m/z, ESI-TOF): Calcd for $C_{19}H_{20}ClFN_2NaO_2^+$ $[M+Na]^+$ 385.1090, found 385.1090.



3m$_{di}$

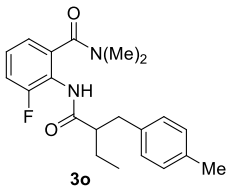
2-(2-(4-chlorobenzyl)-3-(4-chlorophenyl)propanamido)-3-fluoro-*N*,*N*-dimethylbenzamide: yellow solid; 5.7 mg; yield: 12%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.25-7.18 (m, 4H), 7.18-7.11 (m, 5H), 7.05-6.97 (m,

1H), 6.86 (d, *J* = 7.6 Hz, 1H), 3.03 (dd, *J* = 13.2, 8.8 Hz, 2H), 2.90 (s, 3H), 2.88-2.80 (m, 1H), 2.75-2.68 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 168.5, 157.4 (d, *J* = 254.8 Hz), 137.8, 133.7, 132.1, 130.6, 128.5, 127.2 (d, *J* = 8.1 Hz), 122.3 (d, *J* = 14.6 Hz), 122.0 (d, *J* = 3.6 Hz), 117.4(d, *J* = 20.8 Hz), 51.5, 39.1, 37.9, 34.8. HRMS (m/z, ESI-TOF): Calcd for $C_{25}H_{23}Cl_2FN_2NaO_2^+$ $[M+Na]^+$ 495.1013, found 495.1010.



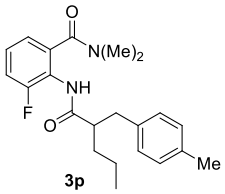
3n

3-fluoro-N,N-dimethyl-2-(3-(p-tolyl)propanamido)benzamide: yellow solid; 13 mg; yield: 40%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.20-6.97 (m, 7H), 3.02 (s, 3H), 2.96 (t, *J* = 7.6 Hz, 2H), 2.90 (s, 3H), 2.64 (t, *J* = 8.4 Hz, 2H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 168.8, 157.3 (d, *J* = 254.4 Hz), 137.6, 135.6, 134.5, 129.1, 128.3, 127.0 (d, *J* = 8.9 Hz), 122.7 (d, *J* = 14.3 Hz), 122.2 (d, *J* = 3.7 Hz), 116.9 (d, *J* = 20.8 Hz), 39.4, 38.3, 35.0, 31.1, 21.0. HRMS (m/z, ESI-TOF): Calcd for $C_{19}H_{21}FN_2NaO_2^+$ $[M+Na]^+$ 351.1479, found 351.1480.



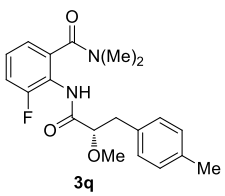
3o

3-fluoro-N,N-dimethyl-2-(2-(4-methylbenzyl)butanamido)benzamide: yellow solid; 17 mg; yield: 47%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.21-7.14 (m, 1H), 7.12-7.02 (m, 5H), 6.95 (d, *J* = 7.6 Hz, 1H), 3.03-2.95 (m, 4H), 2.82 (s, 3H), 2.68 (dd, *J* = 13.6, 6.4 Hz, 1H), 2.55-2.46 (m, 1H), 2.31 (s, 3H), 1.75-1.65 (m, 1H), 1.62-1.50 (m, 1H), 0.95 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.0, 168.6, 157.6 (d, *J* = 253.5 Hz), 136.7, 135.5, 134.8, 129.0, 127.2 (d, *J* = 8.2 Hz), 122.5 (d, *J* = 14.7 Hz), 121.9 (d, *J* = 3.7 Hz), 117.0 (d, *J* = 20.8 Hz), 51.3, 39.2, 38.2, 34.8, 25.7, 21.0, 11.7. HRMS (m/z, ESI-TOF): Calcd for $C_{21}H_{25}FN_2NaO_2^+$ $[M+Na]^+$ 379.1792, found 379.1792.



3p

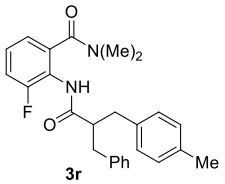
3-fluoro-N,N-dimethyl-2-(2-(4-methylbenzyl)pentanamido)benzamide: yellow oil; 18.5 mg; yield: 50%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.20-7.14 (m, 1H), 7.12-7.02 (m, 5H), 6.94 (d, *J* = 7.6 Hz, 1H), 3.03-2.95 (m, 4H), 2.82 (s, 3H), 2.67 (dd, *J* = 13.6, 6.4 Hz, 1H), 2.63-2.54 (m, 1H), 2.31 (s, 3H), 1.74-1.64 (m, 1H), 1.53-1.22 (m, 4H), 0.90 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 168.6 (d, *J* = 2.9 Hz), 157.7 (d, *J* = 253.6 Hz), 136.7, 135.5, 134.8, 129.0, 128.9, 127.2 (d, *J* = 8.2 Hz), 122.5 (d, *J* = 14.6 Hz), 121.9 (d, *J* = 3.7 Hz), 117.0 (d, *J* = 20.8 Hz), 49.5, 39.2, 38.5, 34.8, 21.1, 20.5, 14.1. HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{27}FN_2NaO_2^+$ $[M+Na]^+$ 393.1949, found 393.1947.



3q

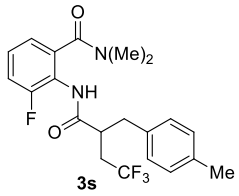
3-fluoro-N,N-dimethyl-2-(3-(p-tolyl)propanamido)benzamide: yellow oil; 14 mg; yield: 38%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.26-7.21 (m, 1H), 7.19-7.08 (m, 5H), 7.05 (d, *J* = 7.6 Hz, 1H), 3.94 (dd, *J* = 8.4, 3.6 Hz, 1H), 3.39 (s, 3H), 3.13 (dd, *J* = 14.0, 3.6 Hz, 1H), 3.04 (s, 3H), 2.95 (s, 3H), 2.93 (dd, *J* = 14.0, 8.4 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 168.5 (d, *J* = 2.8 Hz), 157.2 (d, *J* = 252.0 Hz), 136.0, 134.6, 134.1, 129.4, 129.0,

127.3 (d, *J* = 8.2 Hz), 122.5 (d, *J* = 3.7 Hz), 121.9 (d, *J* = 14.1 Hz), 116.8 (d, *J* = 20.5 Hz), 83.7, 59.0, 39.4, 38.6, 35.0, 21.1. HRMS (m/z, ESI-TOF): Calcd for $C_{20}H_{23}FN_2NaO_3^+$ $[M+Na]^+$ 381.1585, found 381.1585.



3r

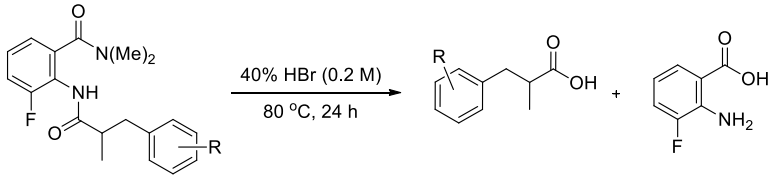
2-(2-benzyl-3-(p-tolyl)propanamido)-3-fluoro-N,N-dimethylbenzamide: yellow oil; 16 mg; yield: 39%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09 (br s, 1H), 7.26-7.19 (m, 4H), 7.17 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.14-7.05 (m, 5H), 7.00 (tt, *J* = 8.4, 1.2 Hz, 1H), 6.86 (d, *J* = 7.8 Hz, 1H), 3.09-3.02 (m, 2H), 2.95-2.88 (m, 1H), 2.85 (s, 3H), 2.78-2.71 (m, 2H), 2.58 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0, 168.5, 157.5 (d, *J* = 254.7 Hz), 139.8, 136.5, 135.6, 134.5, 129.2, 129.1, 129.0, 128.3, 127.4 (d, *J* = 7.9 Hz), 126.2, 122.2 (d, *J* = 14.6 Hz), 121.8 (d, *J* = 3.5 Hz), 117.1 (d, *J* = 20.7 Hz), 51.4, 38.8, 38.2, 38.1, 34.7, 21.1. HRMS (m/z, ESI-TOF): Calcd for $C_{26}H_{27}FN_2NaO_2^+$ $[M+Na]^+$ 441.1949, found 441.1946.



3s

3-fluoro-N,N-dimethyl-2-(4,4,4-trifluoro-2-(4-methylbenzyl)butanamido)benzamide: yellow oil; 17 mg; yield: 42%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.85 (br s, 1H), 7.21-7.08 (m, 5H), 6.99 (t, *J* = 9.0 Hz, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 3.11 (dd, *J* = 13.8, 6.6 Hz, 1H), 3.08-2.98 (m, 4H), 2.83 (s, 3H), 2.76-2.62 (m, 2H), 2.32 (s, 3H), 2.15-2.05 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.1, 167.6, 156.7 (d, *J* = 253.5 Hz), 135.3, 134.2, 133.7, 128.3, 128.0, 126.7 (d, *J* = 8.0 Hz), 125.5 (q, *J* = 277.1 Hz), 121.0 (d, *J* = 14.6 Hz), 120.7, 116.1 (d, *J* = 20.2 Hz), 41.5, 38.1, 37.4, 33.8, 33.6 (q, *J* = 26.6 Hz), 20.0. HRMS (m/z, ESI-TOF): Calcd for $C_{21}H_{22}F_4N_2NaO_2^+$ $[M+Na]^+$ 433.1510, found 433.1510.

3.4 Removal of directing group[S2]



3h$_{mono}$: R = H
3i$_{mono}$: R = 3-OMe
3l$_{mono}$: R = 4-F
3m$_{mono}$: R = 4-Cl

4h: R = H, 87% **5**, 86%
4i: R = 3-OH, 82% **5**, 82%
4l: R = 4-F, 91% **5**, 90%
4m: R = 4-Cl,, 92% **5**, 90%

To an oven-dried 15 mL sealed tube equipped with a magnetic stir bar was added **3** (0.3 mmol) and 40% HBr solution (1.5 mL). The tube was reacted in a preheated oil bath (80 °C) for 24 h and then cooled to room temperature. The reaction was diluted with H_2O (20 mL) and extracted by EtOAc (3 × 20 mL). The combined organic phase was dried over anhydrous Na_2SO_4, concentrated under vacuum then purified through flash silica-gel chromatography to obtain corresponding **4** (eluents: PE : EtOAc = 2 : 1).

2-methyl-3-phenylpropanoic acid (4h) (known compound[S3]): white solid; 46 mg, yield: 87%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2H), 7.23-7.17 (m, 3H), 3.08 (dd, *J* = 13.8, 6.6 Hz, 1H), 2.80-2.73 (m, 1H), 2.67 (dd, *J* = 13.8, 8.4 Hz, 1H), 1.17 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.2, 139.2, 129.1, 128.5, 126.5, 41.3, 39.4, 16.6.

3-(3-hydroxyphenyl)-2-methylpropanoic acid (4i) (known compound[S4]): colourless oil; 44 mg, yield: 82%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (t, J = 8.0 Hz, 1H), 7.77-6.66 (m, 3H), 2.97 (dd, J = 14.0, 6.8 Hz, 1H), 2.81-2.70 (m, 1H), 2.64 (dd, J = 13.2, 7.2 Hz, 1H), 1.18 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.2, 155.5, 140.8, 129.7, 121.5, 115.9, 113.5, 41.2, 39.2, 16.7.

3-(4-fluorophenyl)-2-methylpropanoic acid (4l) (known compound[S5]): colourless oil; 49 mg, yield: 91%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.34 (br s, 1H), 7.17-7.10 (m, 2H), 7.00-6.93 (m, 2H), 3.02 (dd, J = 13.2, 6.4 Hz, 1H), 2.78-2.68 (m, 1H), 2.65 (dd, J = 13.2, 8.0 Hz, 1H), 1.17 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.7, 161.6 (d, J = 245.2 Hz), 134.6 (d, J = 3.1 Hz), 130.4 (d, J = 7.8 Hz), 115.2 (d, J = 21.1 Hz), 41.4, 38.4, 16.5.

3-(4-chlorophenyl)-2-methylpropanoic acid (4m) (known compound[S5]): colourless oil; 54 mg, yield: 92%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.34 (br s, 1H), 7.28-7.22 (m, 2H), 7.14-7.08 (m, 2H), 3.01 (dd, J = 13.2, 6.4 Hz, 1H), 2.78-2.68 (m, 1H), 2.64 (dd, J = 13.2, 7.6 Hz, 1H), 1.17 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.5, 137.5, 132.3, 130.4, 128.6, 41.2, 38.6, 16.6.

3.5 Reference

[S1] (a) J.-Y. Lee, J. J. Miller, S. S. Hamilton and M. S. Sigman, *Org. Lett*., 2005, **7**, 1837. (b) Q.-F. Wu, P.-X. Shen, J. He, X.-B. Wang, F. Zhang, Q. Shao, R.-Y. Zhu, C. Mapelli, J. X. Qiao, M. A. Poss and J.-Q. Yu, *Science.,* 2017, **355**, 499. (c) J. He, Q. Shao, Q.-F. Wu and J.-Q. Yu, *J. Am. Chem. Soc*., 2017, **139**, 3344. (d) Q. Shao, J. He, Q.-F. Wu and J.-Q. Yu, *ACS Catalysis.*, 2017, **7**, 7777.

[S2] Y. Pang, M. Guan, R. Zeng and Y. Zhao, *Org. Chem. Front*., 2017, **4, 2408.**

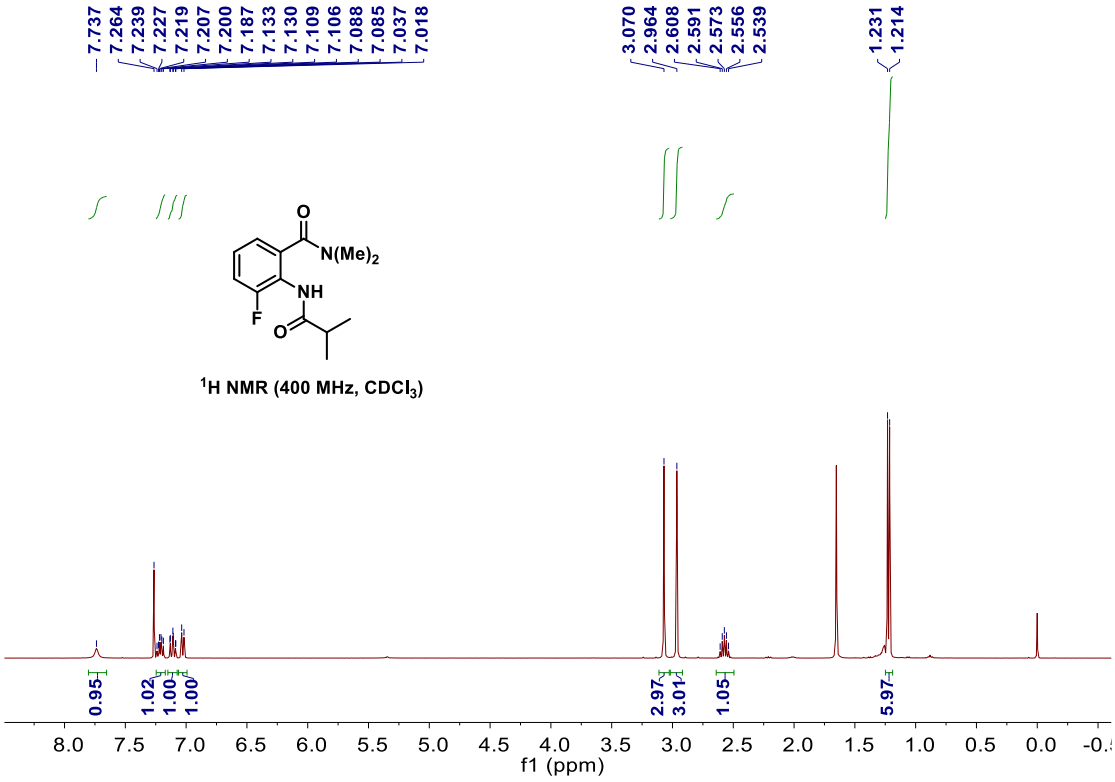
[S3] H. Seo, A. Liu, and T. F. Jamison, *J. Am. Chem. Soc*., 2017, **139**, 13969.

[S4] S. Vickers, E. K. Stuart, H. B. Hucker, and W. J. A. VandenHeuvel, *J. Med. Chem*., 1975, **18**, 134.

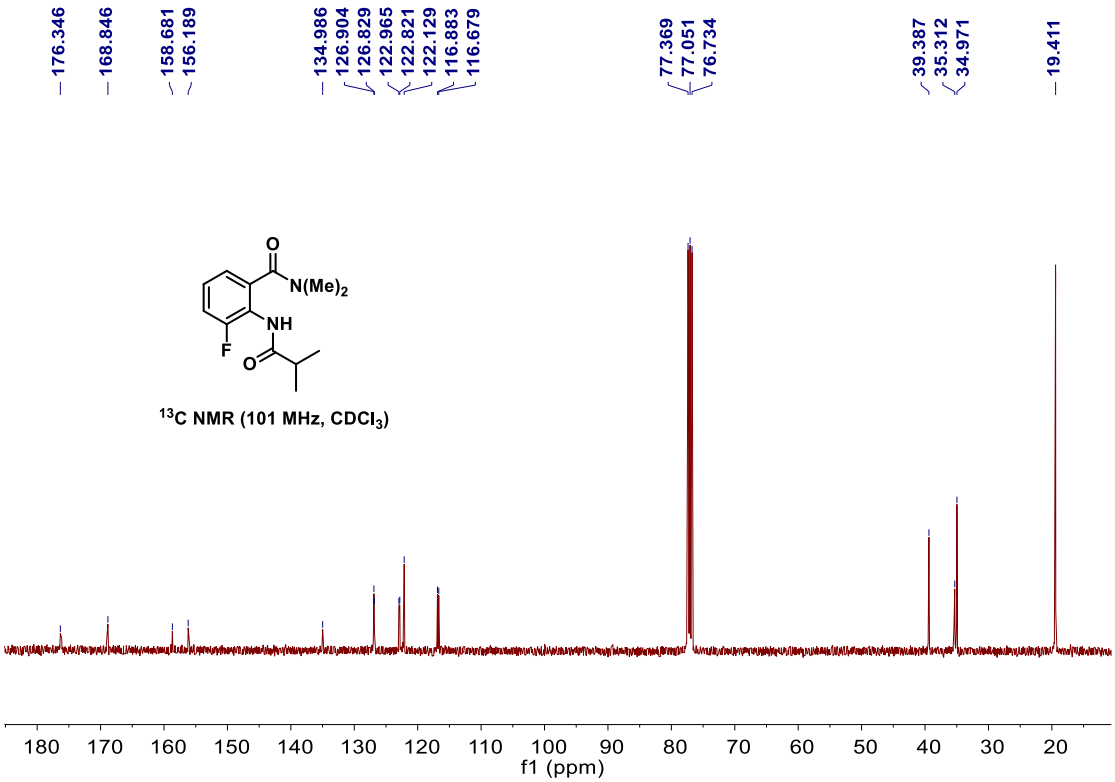
[S5] Z.-G. Wang, Li. Chen, J. Chen, J.-F. Zheng, W. Gao, Z. Zeng, H. Zhou, X.-K. Zhang,; P.-Q Huang and Y. Su, *Eur. J. Med. Chem.,* 2013, **62**, 632.

4. NMR Spectra of Substrates and Products.

1a



^{1}H NMR (400 MHz, $CDCl_3$)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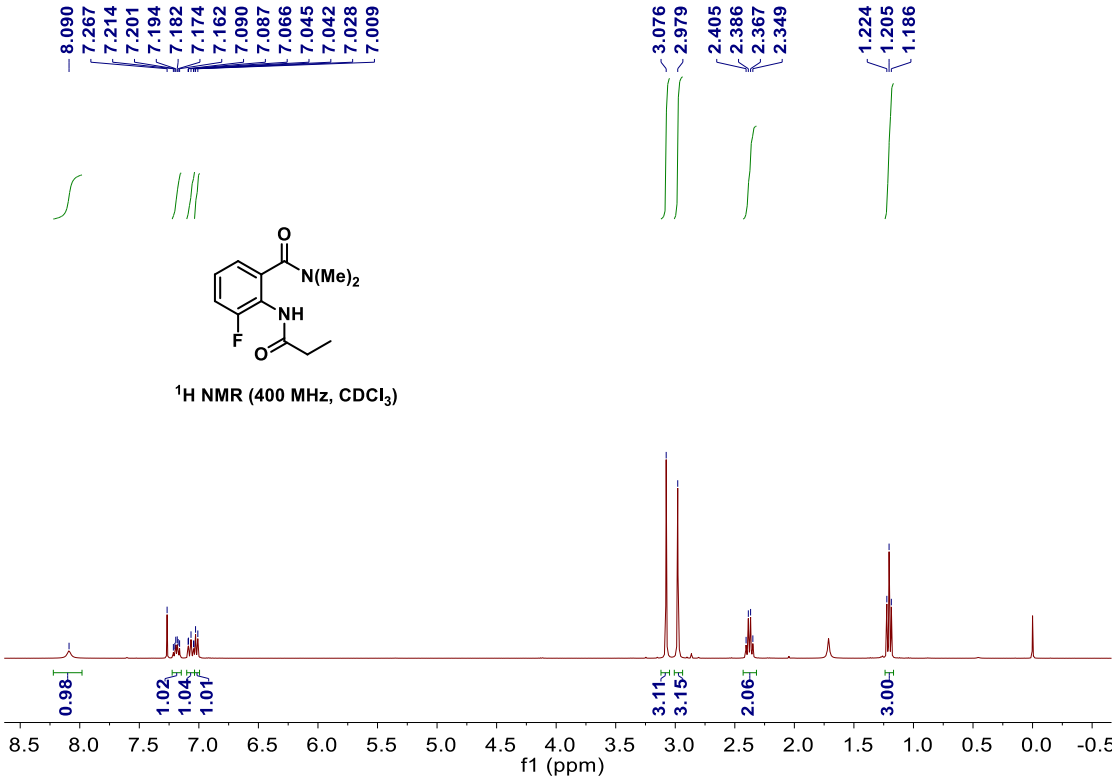
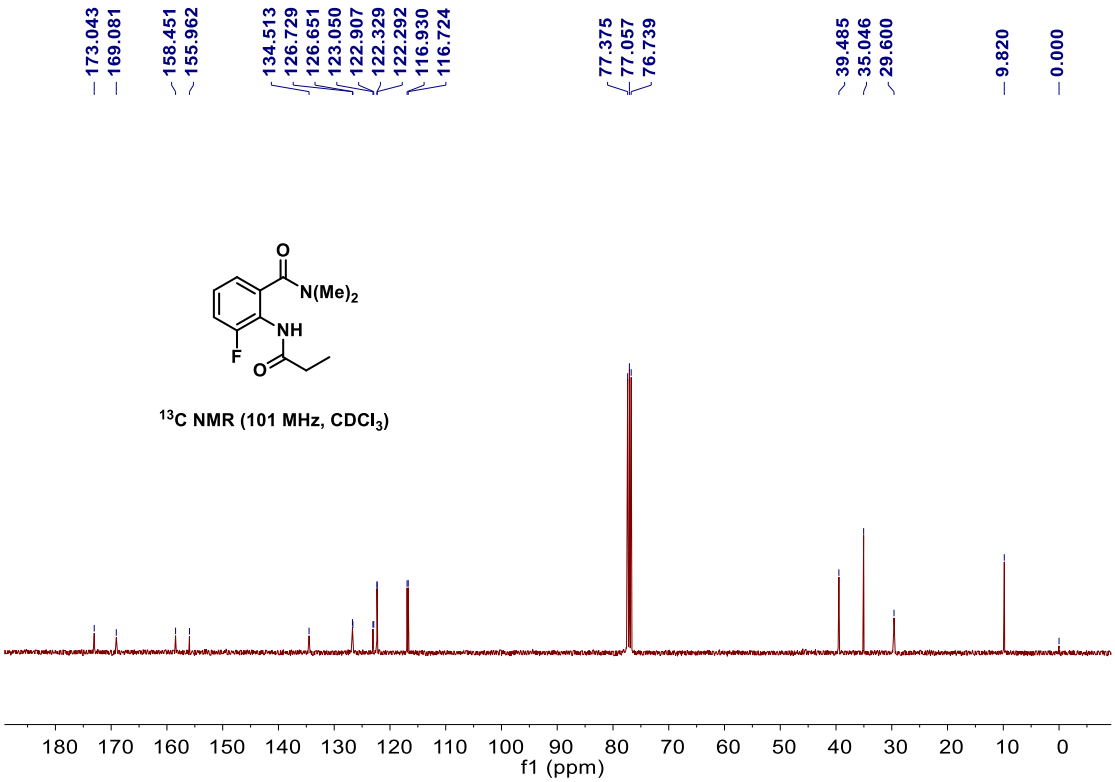
158.681
156.189
134.986
126.904
126.829
122.965
122.821
122.129
116.883
116.679
77.369
77.051
76.734
39.387
35.312
34.971
19.411
O
N(Me)2
NH
F
O
13C NMR (101 MHz, CDCl3)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)

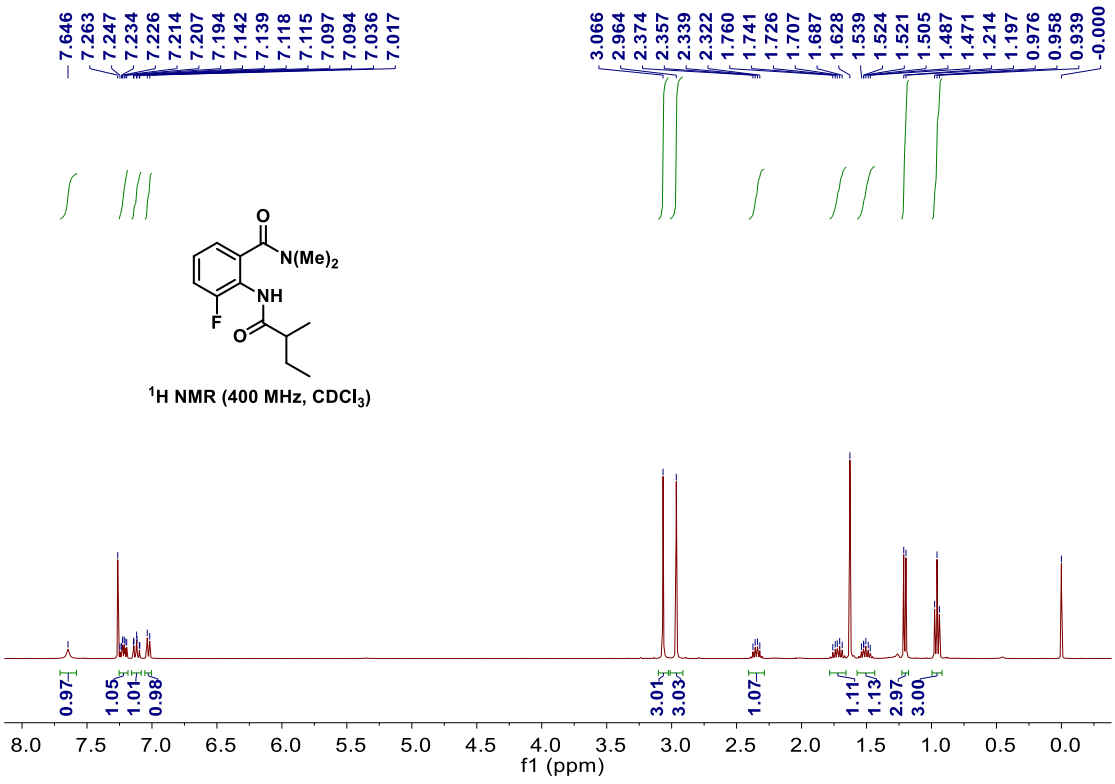
1n


8.090
7.267
7.214
7.201
7.194
7.182
7.174
7.162
7.090
7.087
7.066
7.045
7.042
7.028
7.009
3.076
2.979
2.405
2.386
2.367
2.349
1.224
1.205
1.186
O
N(Me)2
NH
F
O
1H NMR (400 MHz, CDCl3)
0.98
1.02
1.04
1.01
3.11
3.15
2.06
3.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

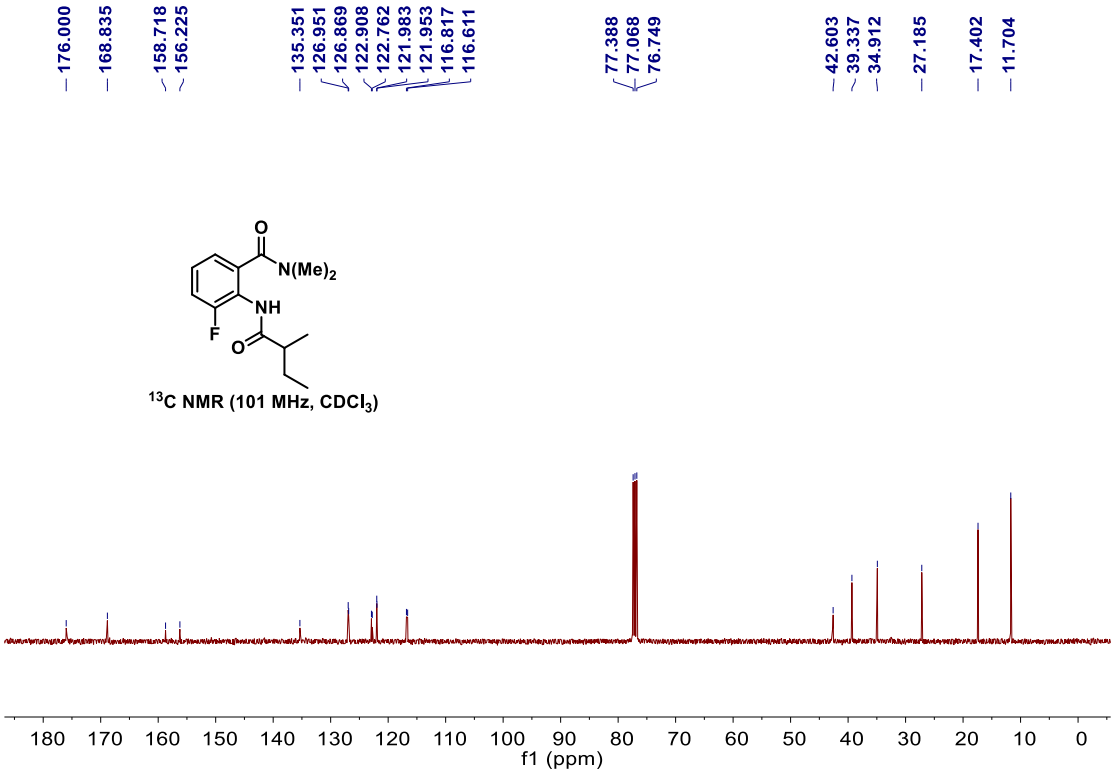


^{13}C NMR (101 MHz, $CDCl_3$)

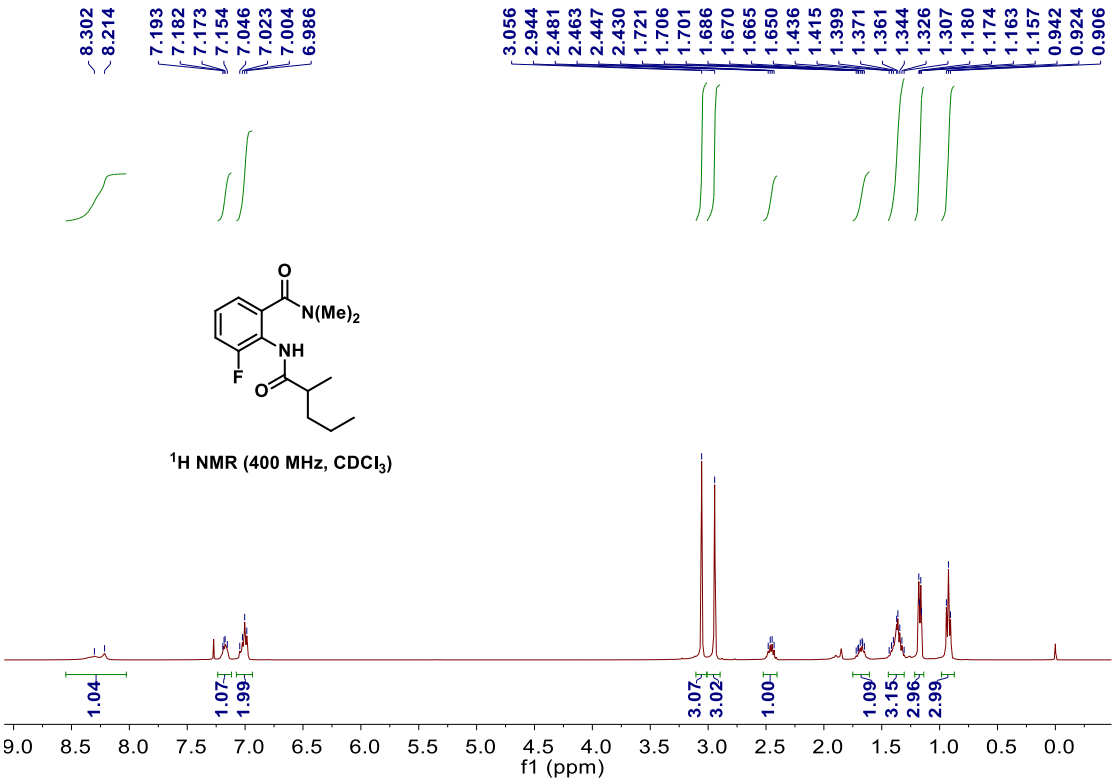
1o



^{1}H NMR (400 MHz, $CDCl_3$)


176.000
168.835
158.718
156.225
135.351
126.951
126.869
122.908
122.762
121.983
121.953
116.817
116.611
77.388
77.068
76.749
42.603
39.337
34.912
27.185
17.402
11.704
O
N(Me)2
NH
F
O
13C NMR (101 MHz, CDCl3)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

1p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8.214
7.193
7.182
7.173
7.154
7.046
7.023
7.004
6.986
3.056
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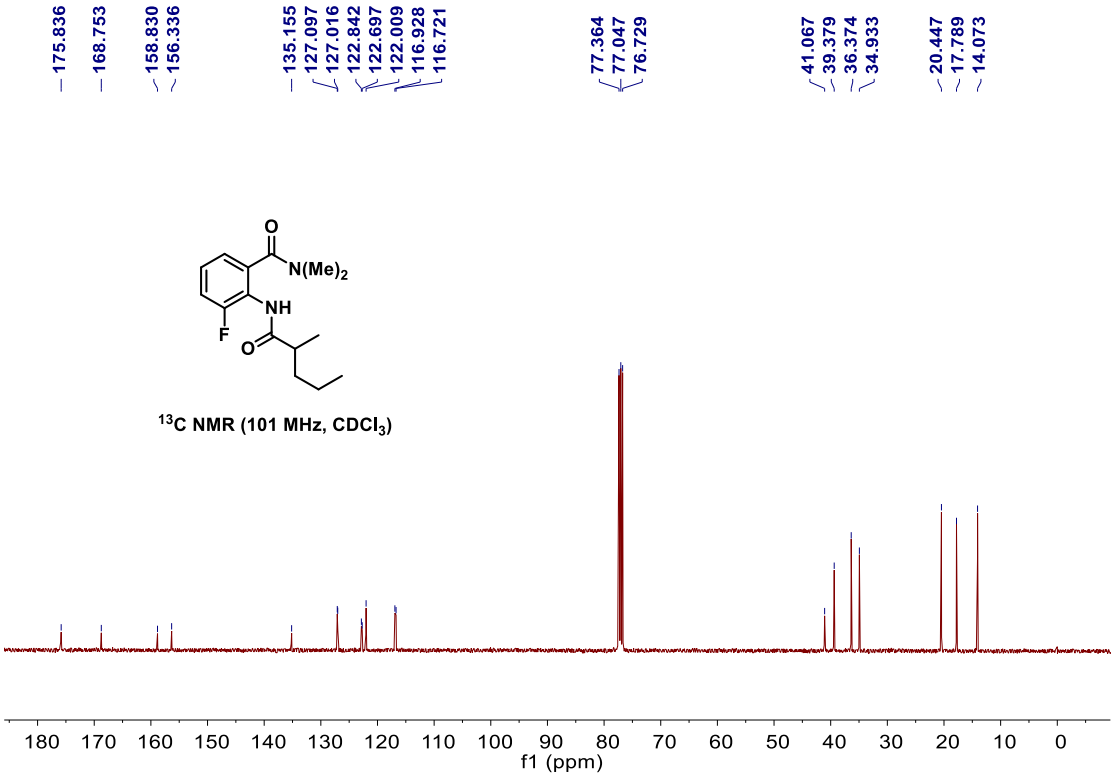
2.463
2.447
2.430
1.721
1.706
1.701
1.686
1.670
1.665
1.650
1.436
1.415
1.399
1.371
1.361
1.344
1.326
1.307
1.180
1.174
1.163
1.157
0.942
0.924
0.906
O
N(Me)2
NH
F
O
1H NMR (400 MHz, CDCl3)
1.04
1.07
1.99
3.07
3.02
1.00
1.09
3.15
2.96
2.99
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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168.753
158.830
156.336
135.155
127.097
127.016
122.842
122.697
122.009
116.928
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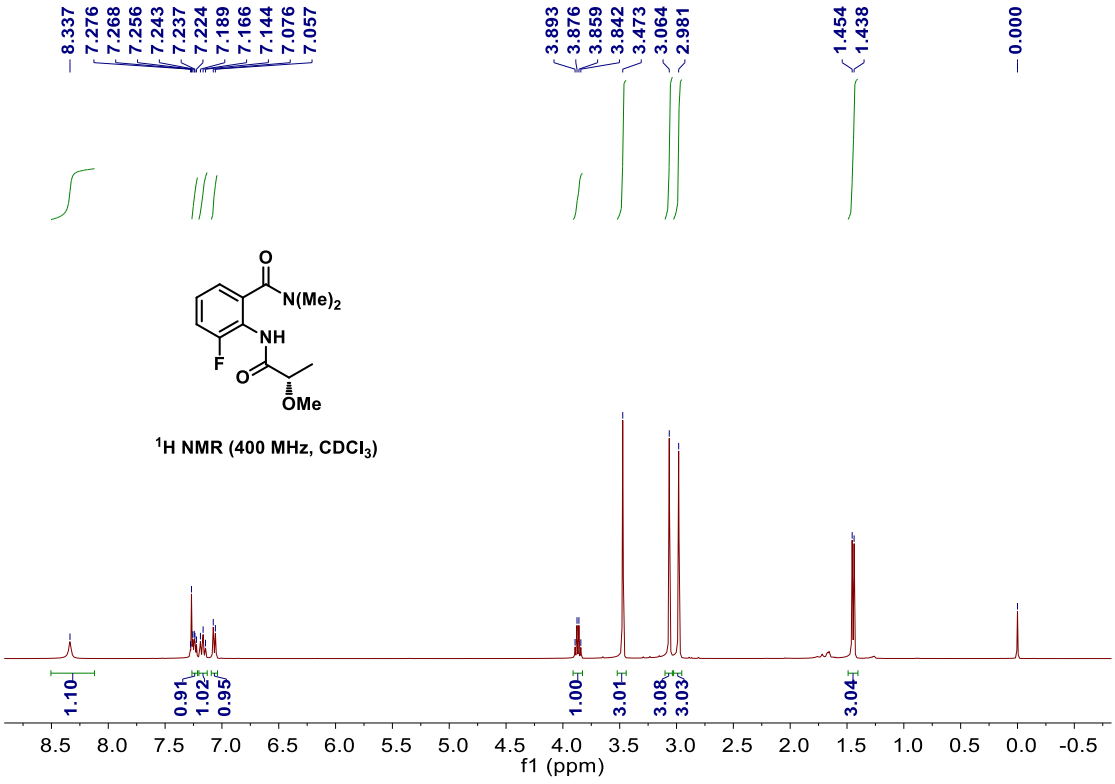
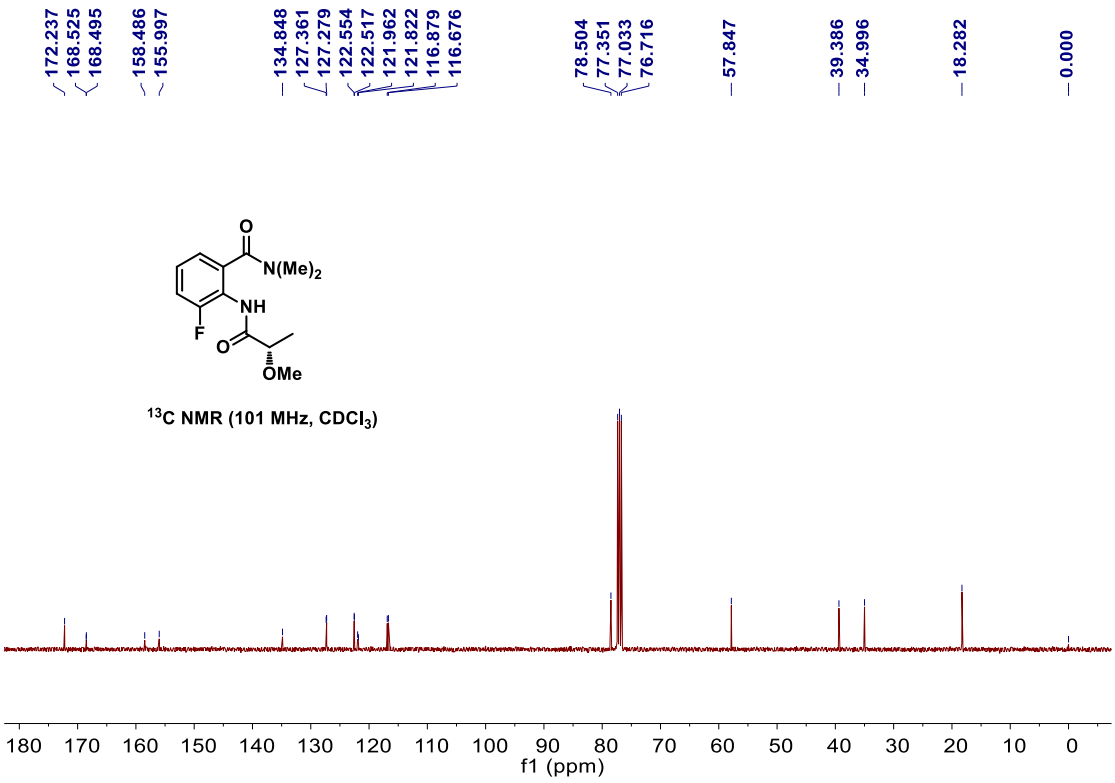
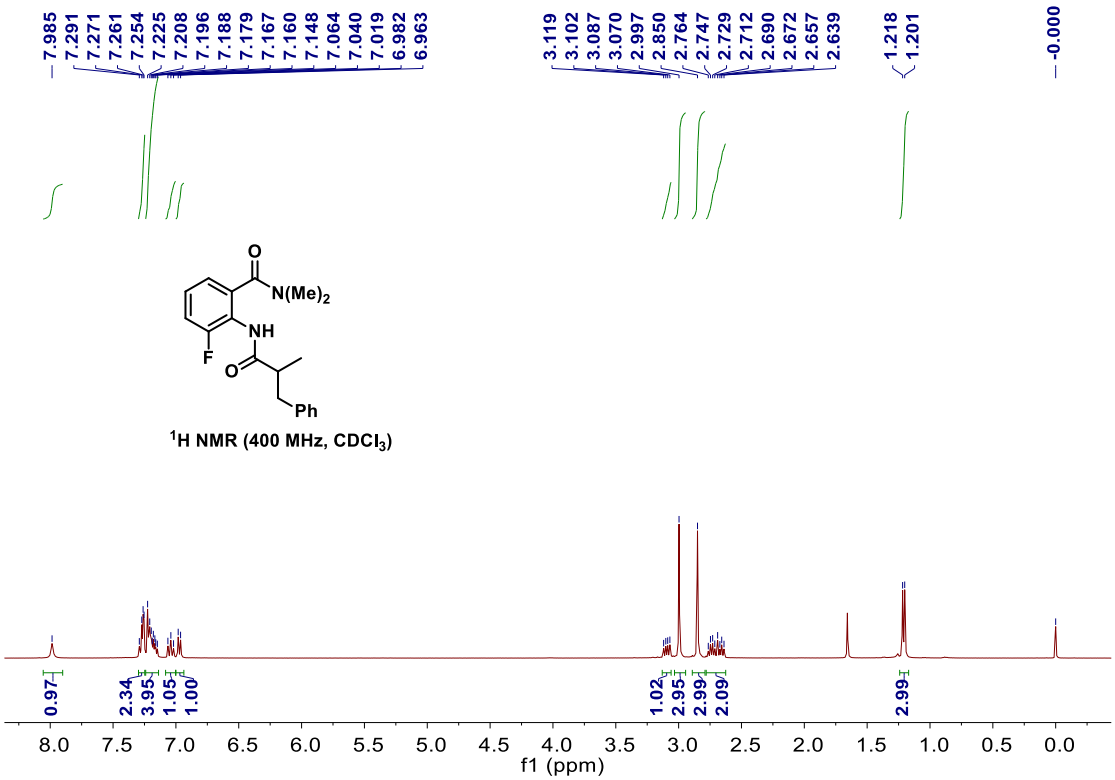
77.364
77.047
76.729
41.067
39.379
36.374
34.933
20.447
17.789
14.073
O
N(Me)2
NH
F
O
13C NMR (101 MHz, CDCl3)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

1q

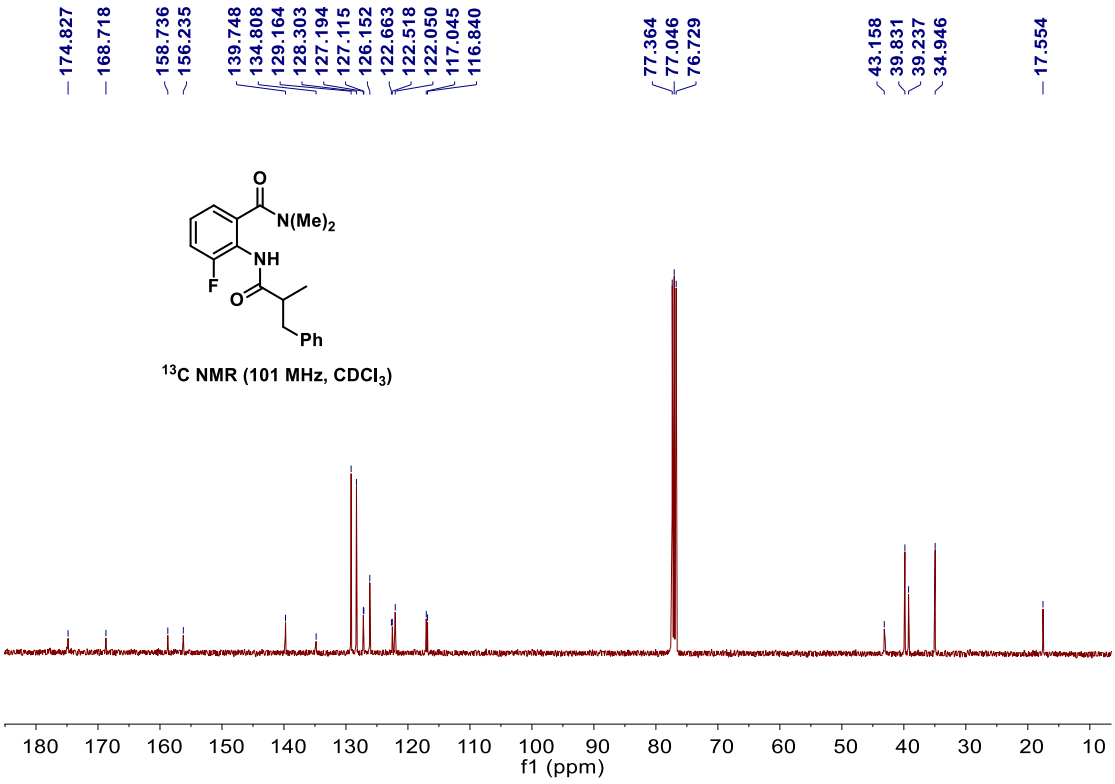

8.337
7.276
7.268
7.256
7.243
7.237
7.224
7.189
7.166
7.144
7.076
7.057
3.893
3.876
3.859
3.842
3.473
3.064
2.981
1.454
1.438
0.000
O
N(Me)2
NH
F
O
OMe
1H NMR (400 MHz, CDCl3)
1.10
0.91
1.02
0.95
1.00
3.01
3.08
3.03
3.04
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


172.237
168.525
168.495
158.486
155.997
134.848
127.361
127.279
122.554
122.517
121.962
121.822
116.879
116.676
78.504
77.351
77.033
76.716
57.847
39.386
34.996
18.282
0.000
O
N(Me)2
NH
F
O
OMe
13C NMR (101 MHz, CDCl3)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

1r

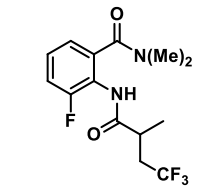


^{1}H NMR (400 MHz, $CDCl_3$)

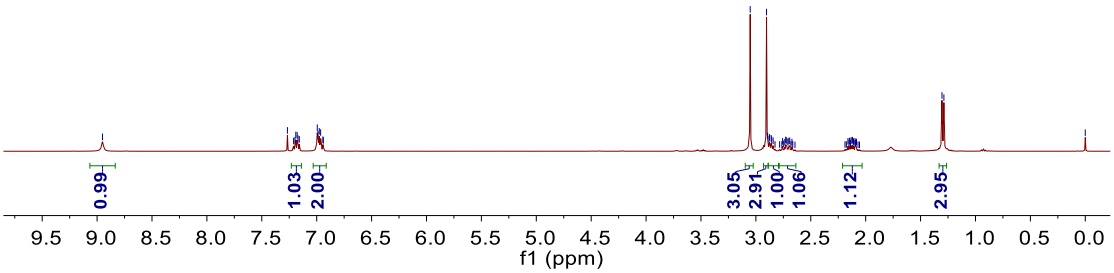


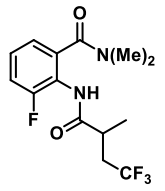
^{13}C NMR (101 MHz, $CDCl_3$)

1s

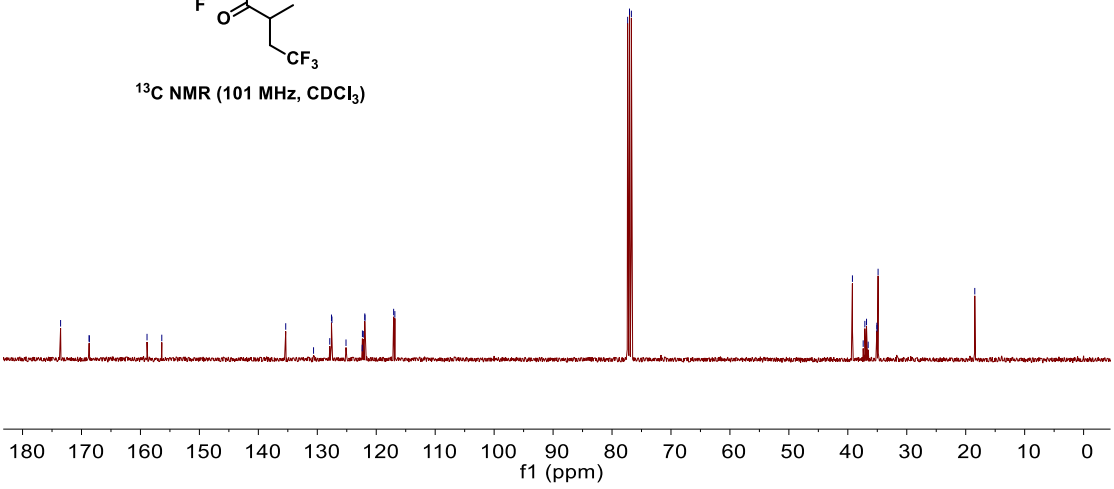


^{1}H NMR (400 MHz, $CDCl_3$)

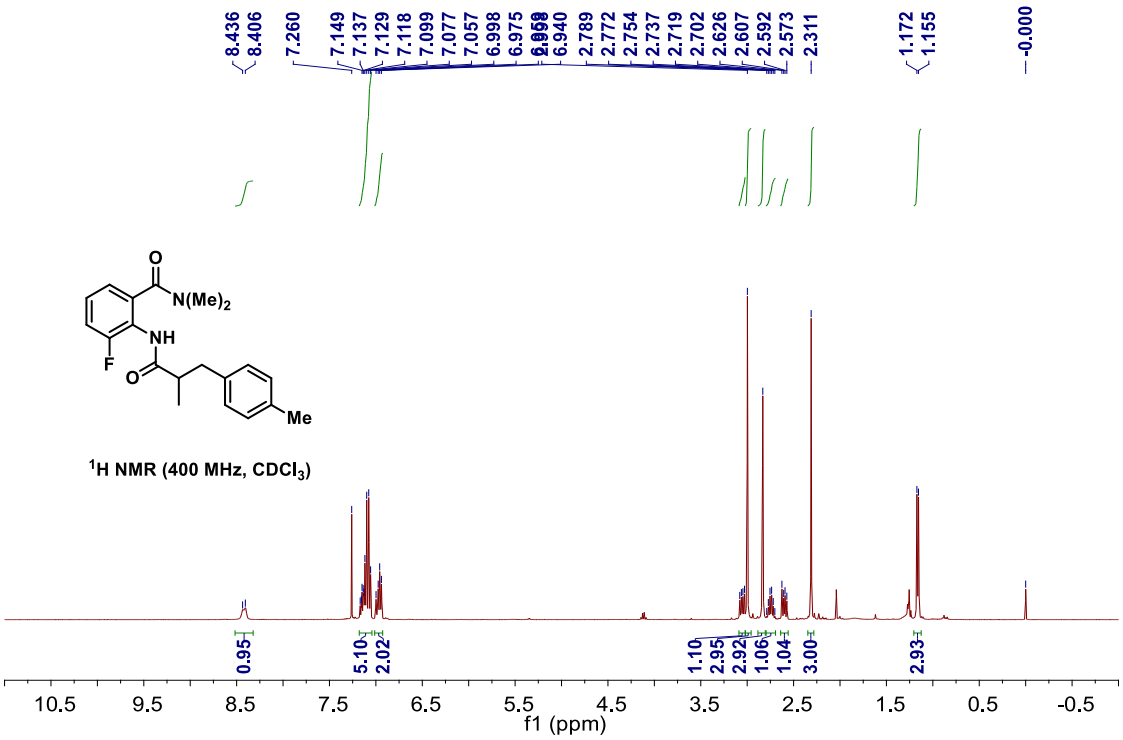


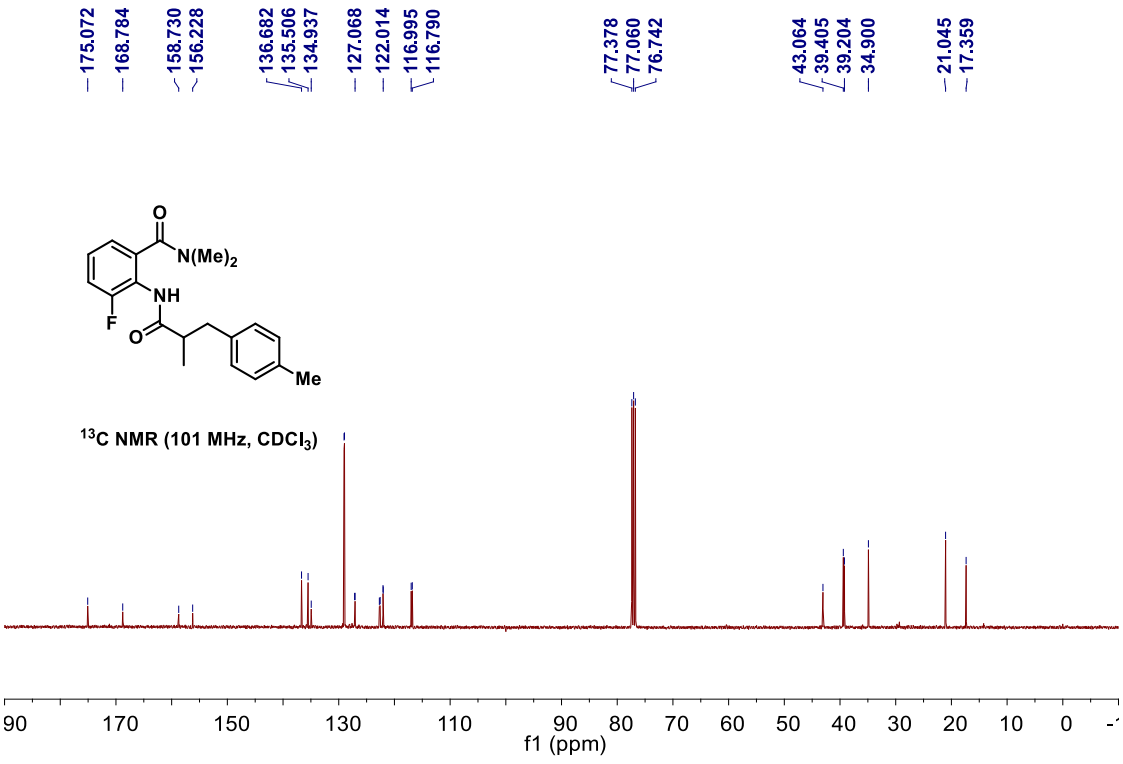


^{13}C NMR (101 MHz, $CDCl_3$)

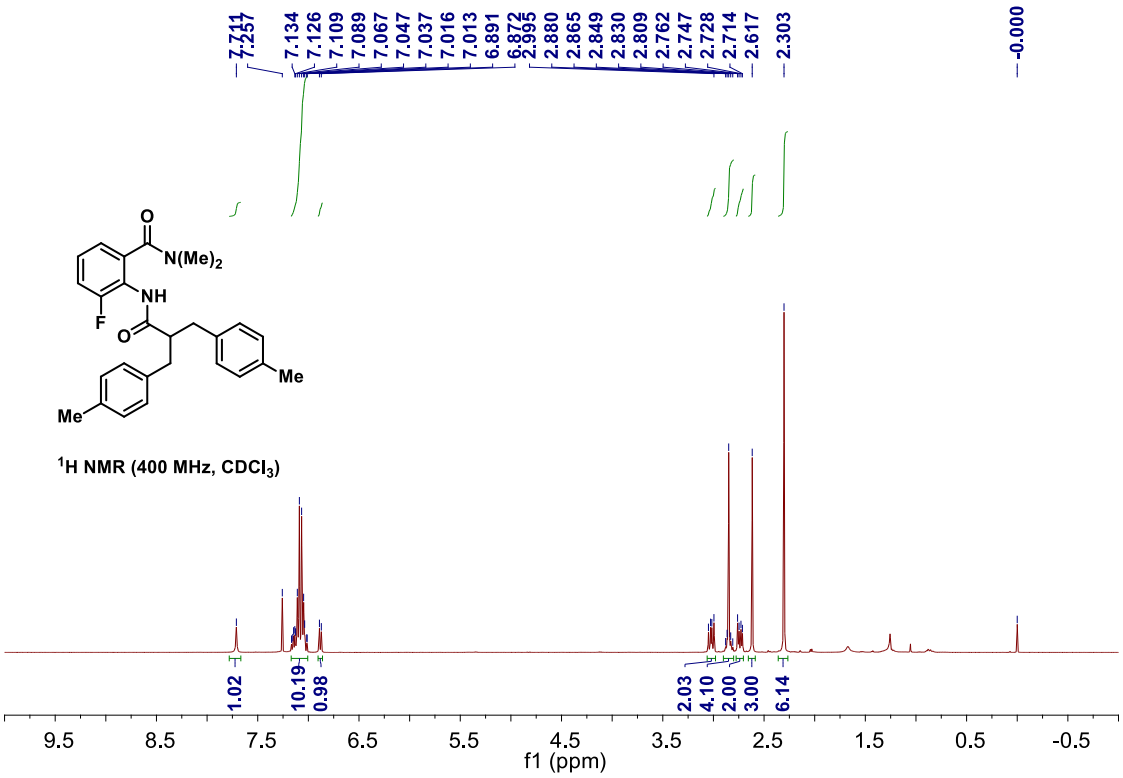


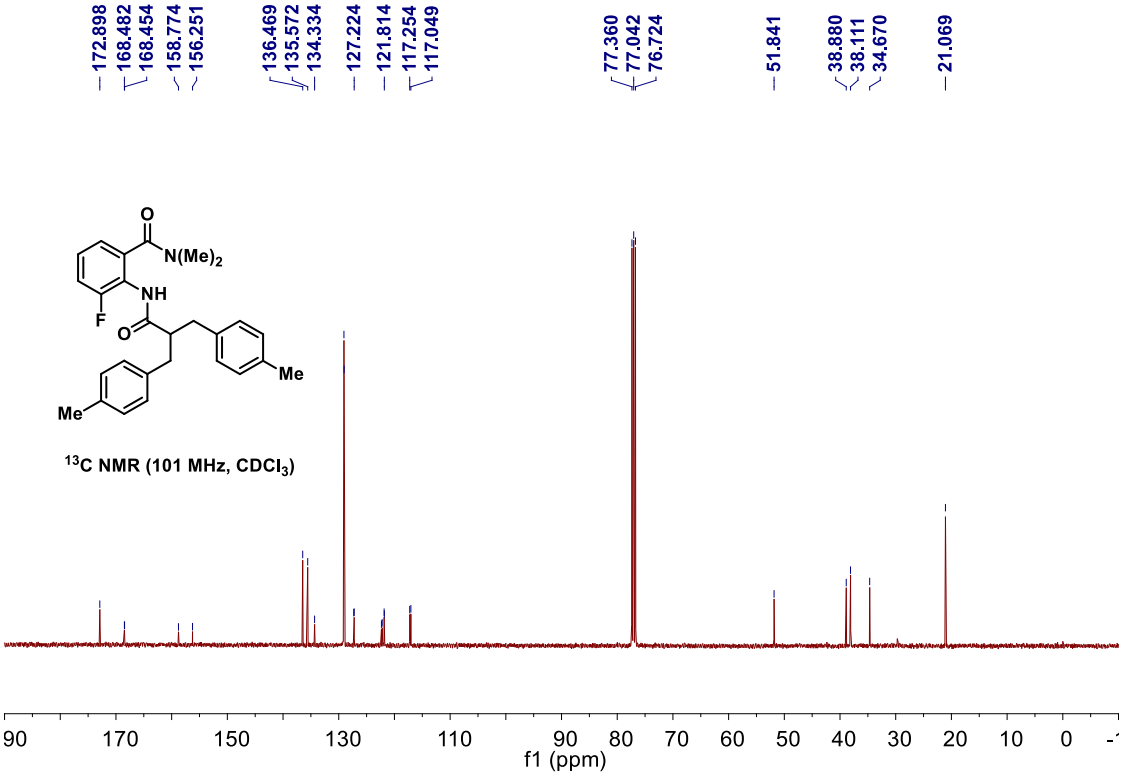
3a$_{mono}$


8.436
8.406
7.260
7.149
7.137
7.129
7.118
7.099
7.077
7.057
6.998
6.975
6.940
2.789
2.772
2.754
2.737
2.719
2.702
2.626
2.607
2.592
2.573
2.311
1.172
1.155
-0.000
O
N(Me)2
NH
F
O
Me
1H NMR (400 MHz, CDCl3)
0.95
5.10
2.02
1.10
2.95
2.92
1.06
1.04
3.00
2.93
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

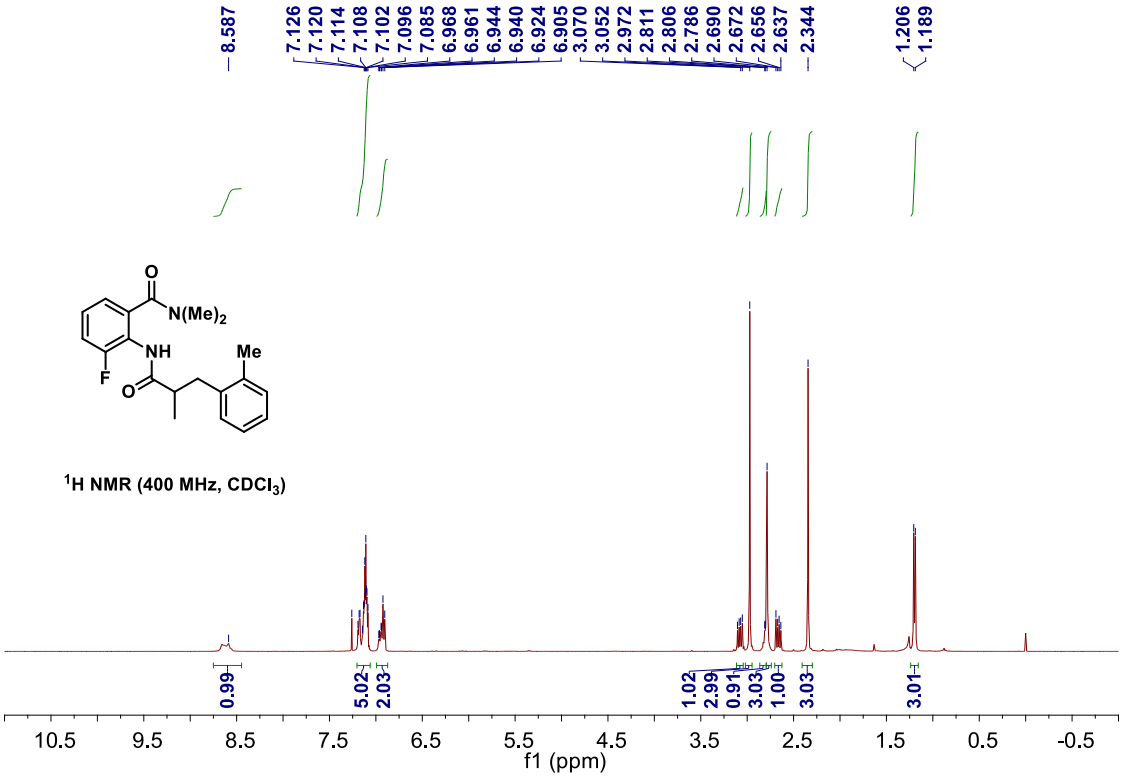

175.072
168.784
158.730
156.228
136.682
135.506
134.937
127.068
122.014
116.995
116.790
77.378
77.060
76.742
43.064
39.405
39.204
34.900
21.045
17.359
O
N(Me)2
NH
F
O
Me
13C NMR (101 MHz, CDCl3)
90
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

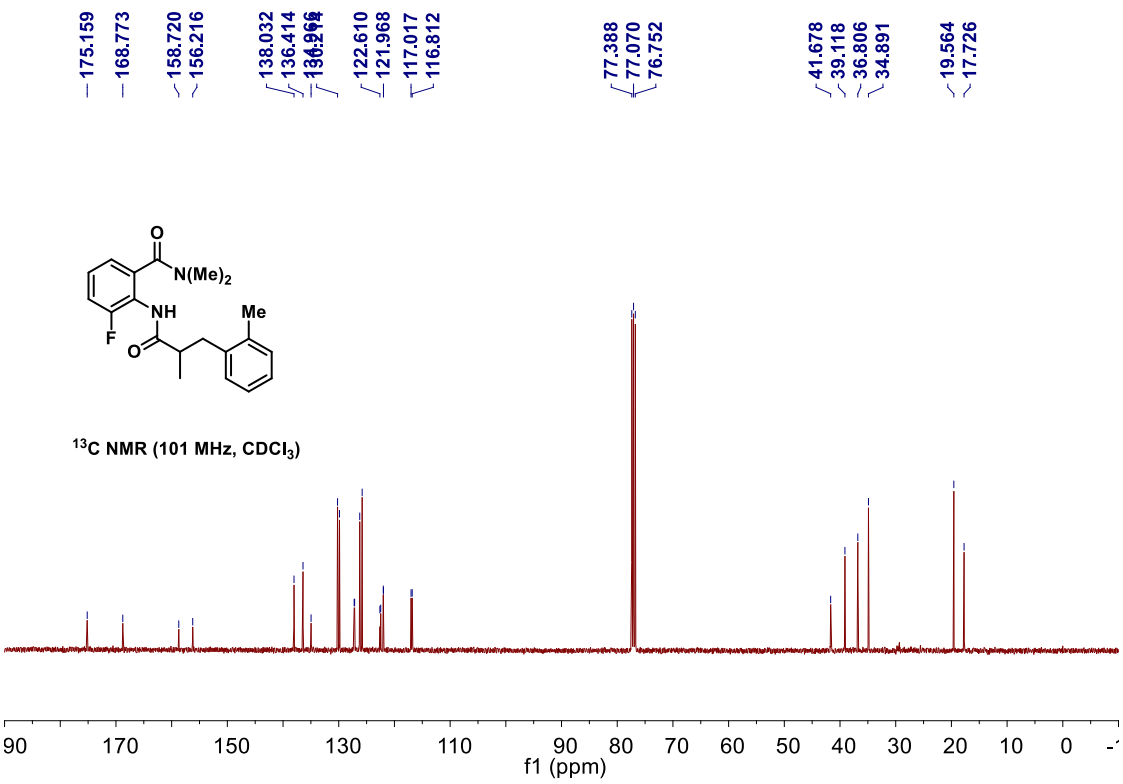
3a$_{di}$


7.711
7.257
7.134
7.126
7.109
7.089
7.067
7.047
7.037
7.016
7.013
6.891
6.872
2.995
2.880
2.865
2.849
2.830
2.809
2.762
2.747
2.728
2.714
2.617
2.303
-0.000
O
N(Me)2
NH
F
O
Me
Me
1H NMR (400 MHz, CDCl3)
1.02
10.19
0.98
2.03
4.10
2.00
3.00
6.14
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

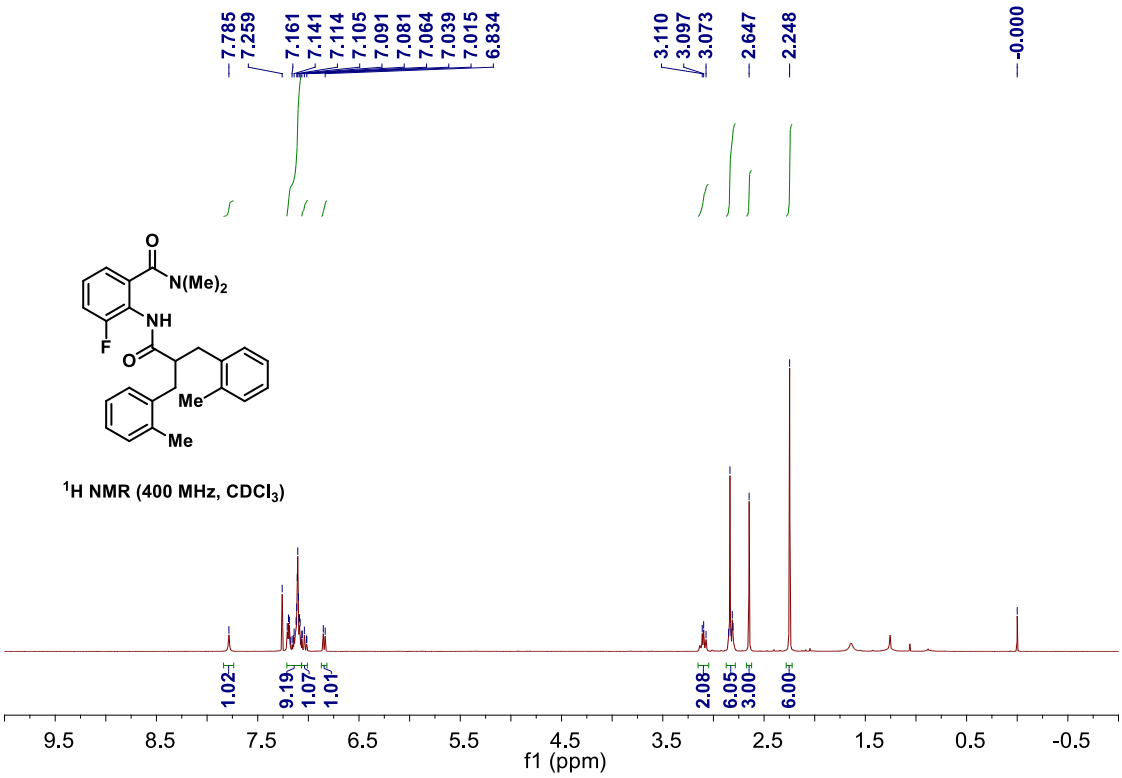

172.898
168.482
168.454
158.774
156.251
136.469
135.572
134.334
127.224
121.814
117.254
117.049
77.360
77.042
76.724
51.841
38.880
38.111
34.670
21.069
O
N(Me)2
NH
F
O
Me
Me
13C NMR (101 MHz, CDCl3)
90
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

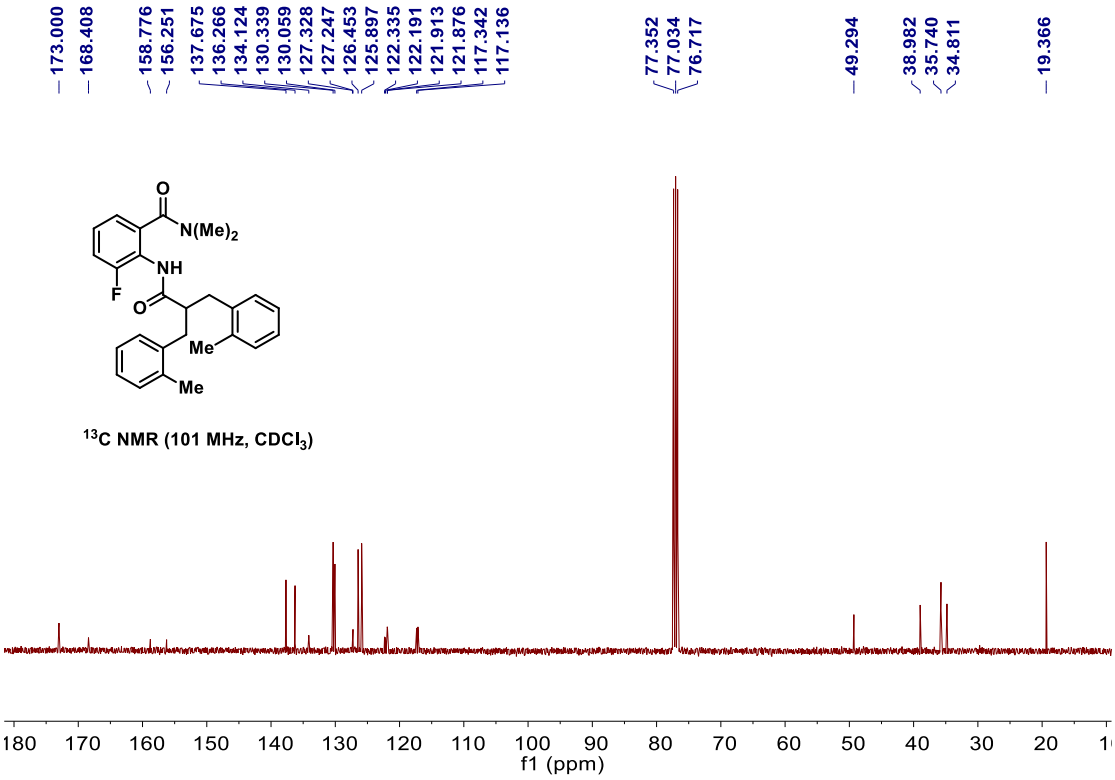
3b$_{mono}$


8.587
7.126
7.120
7.114
7.108
7.102
7.096
7.085
6.968
6.961
6.944
6.940
6.924
6.905
3.070
3.052
2.972
2.811
2.806
2.786
2.690
2.672
2.656
2.637
2.344
1.206
1.189
O
N(Me)2
NH
Me
F
O
1H NMR (400 MHz, CDCl3)
0.99
5.02
2.03
1.02
2.99
0.91
3.03
1.00
3.03
3.01
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

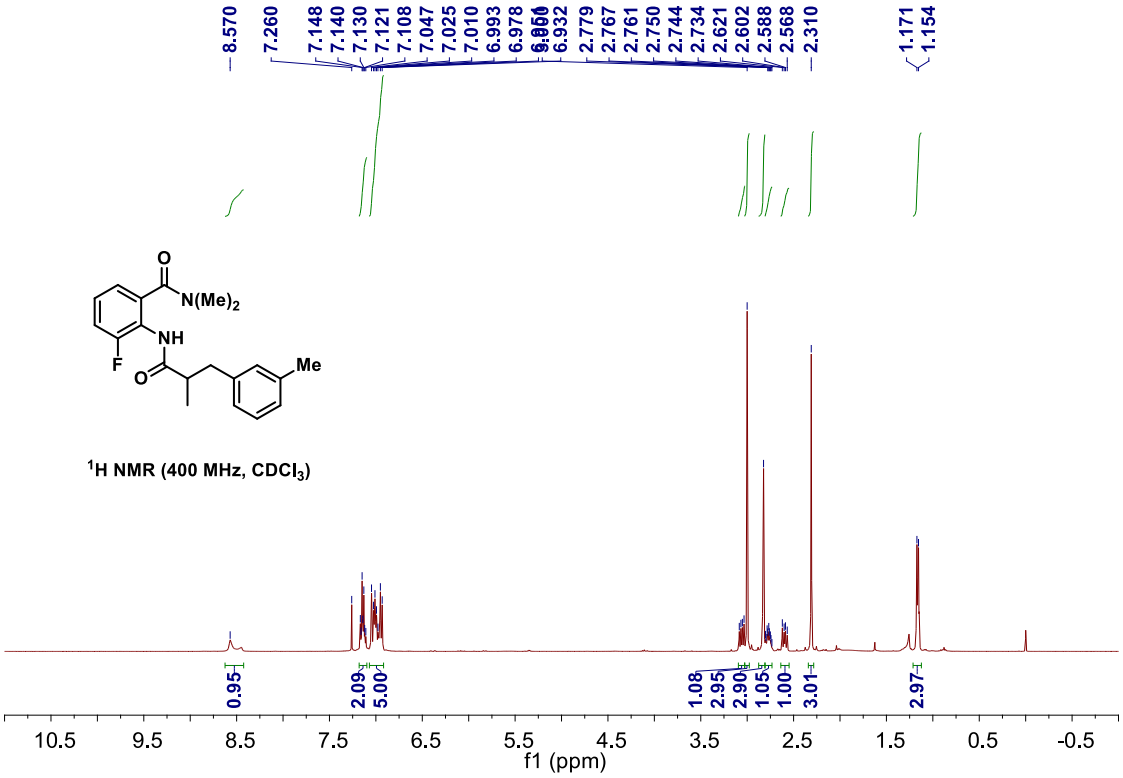

175.159
168.773
158.720
156.216
138.032
136.414
122.610
121.968
117.017
116.812
77.388
77.070
76.752
41.678
39.118
36.806
34.891
19.564
17.726
O
N(Me)2
NH
Me
F
O
13C NMR (101 MHz, CDCl3)
90
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

3b$_{di}$

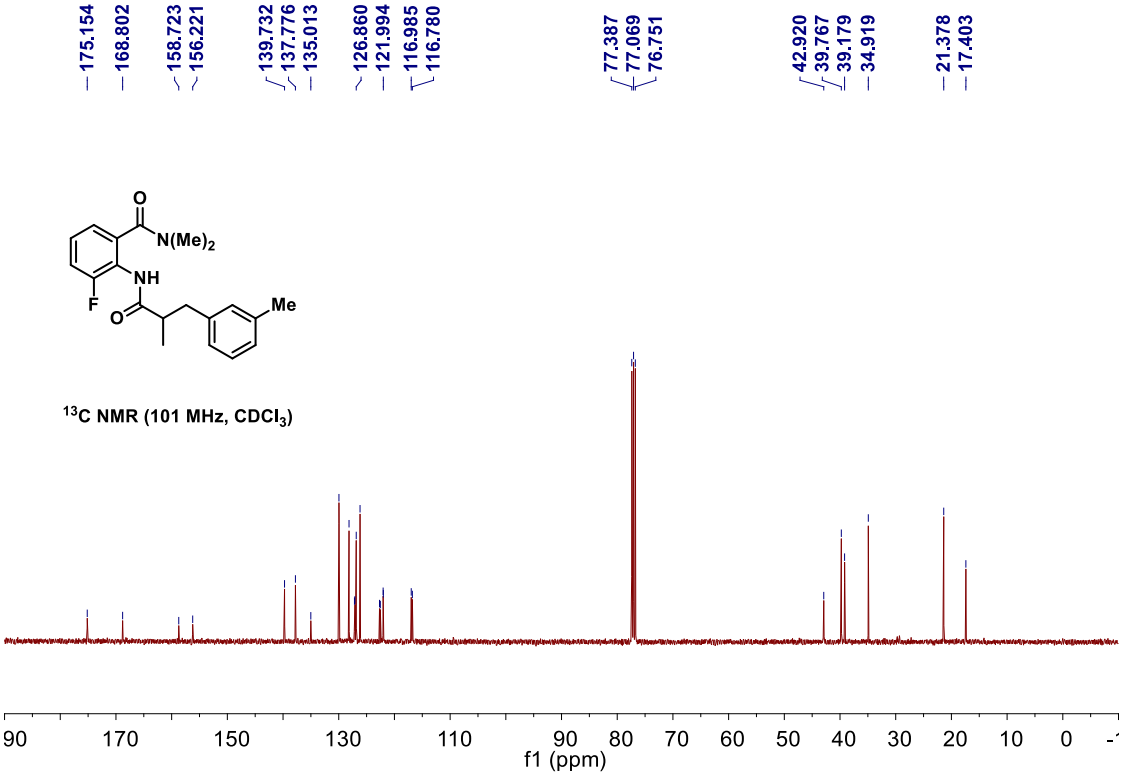

7.785
7.259
7.161
7.141
7.114
7.105
7.091
7.081
7.064
7.039
7.015
6.834
3.110
3.097
3.073
2.647
2.248
-0.000
O
N(Me)2
NH
F
O
Me
Me
1H NMR (400 MHz, CDCl3)
1.02
9.19
1.07
1.01
2.08
6.05
3.00
6.00
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)


173.000
168.408
158.776
156.251
137.675
136.266
134.124
130.339
130.059
127.328
127.247
126.453
125.897
122.335
122.191
121.913
121.876
117.342
117.136
77.352
77.034
76.717
49.294
38.982
35.740
34.811
19.366
O
N(Me)2
NH
F
O
Me
Me
13C NMR (101 MHz, CDCl3)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

3c$_{mono}$

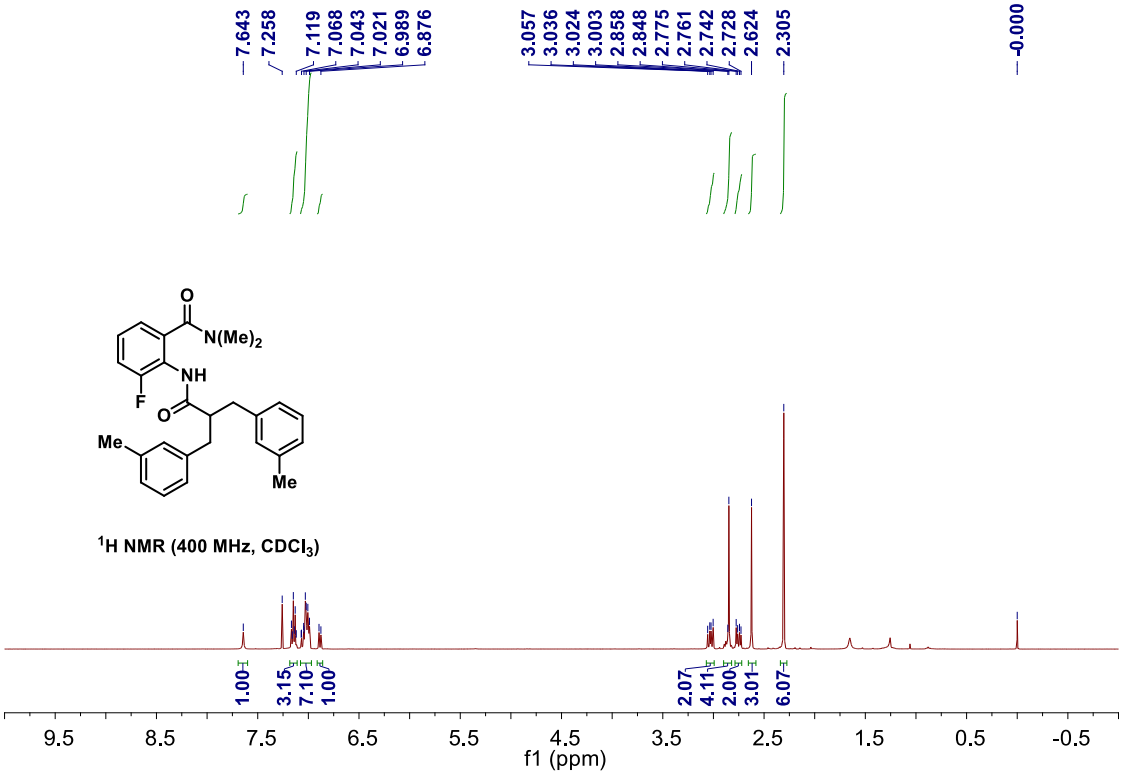


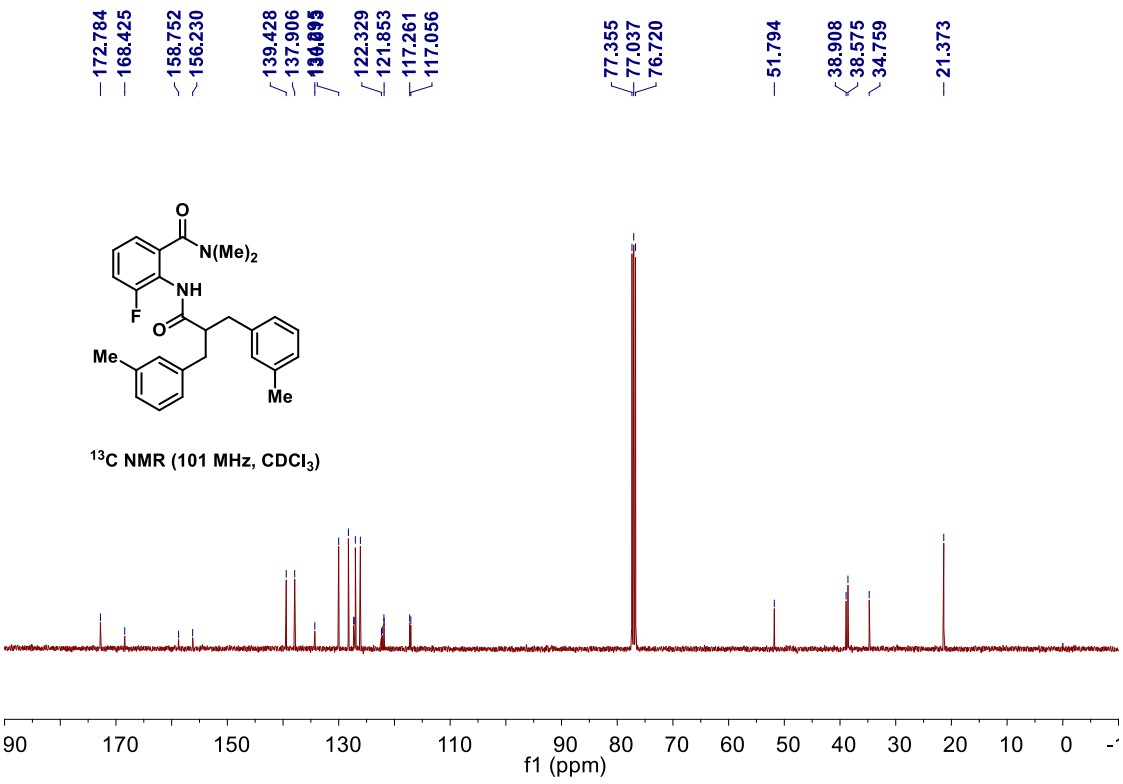
^{1}H NMR (400 MHz, $CDCl_3$)



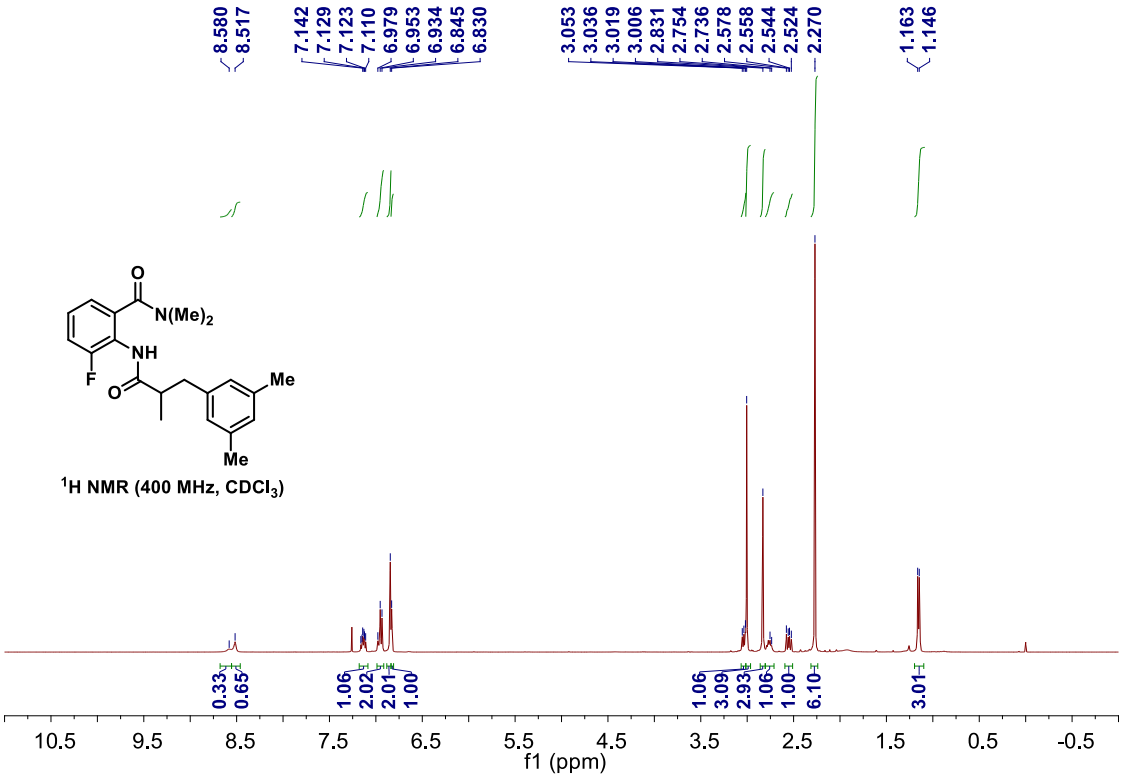
^{13}C NMR (101 MHz, $CDCl_3$)

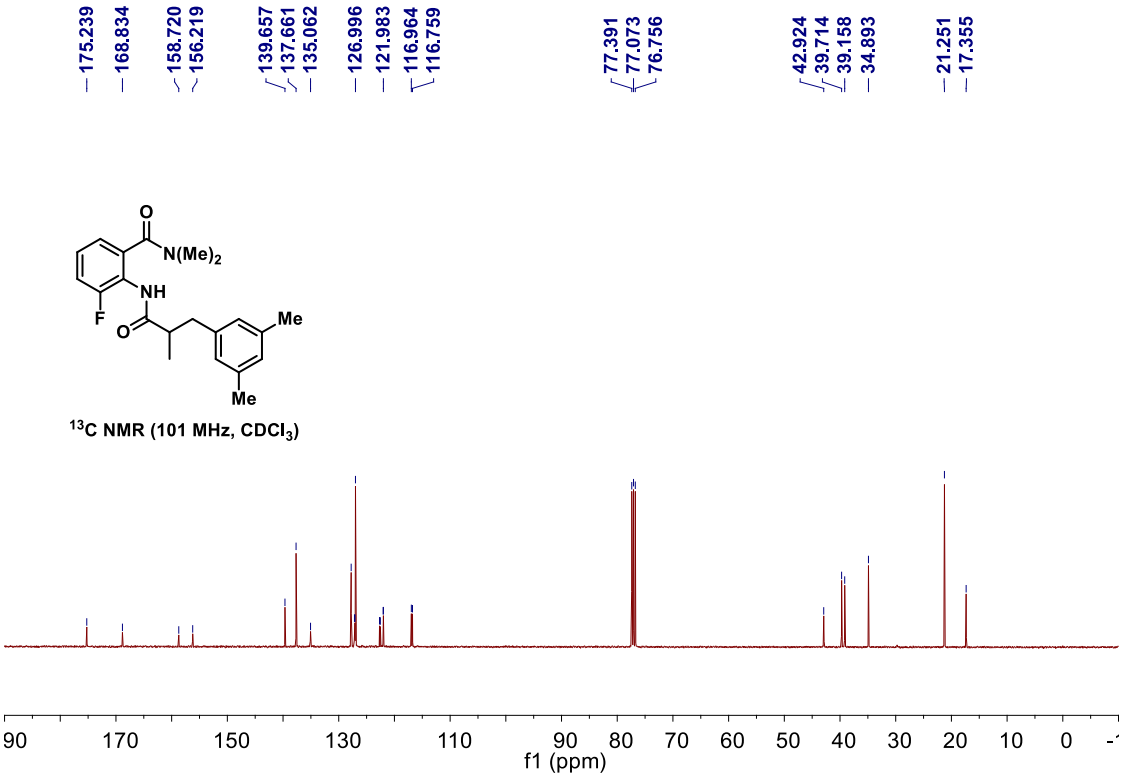
3c$_{di}$


7.643
7.258
7.119
7.068
7.043
7.021
6.989
6.876
3.057
3.036
3.024
3.003
2.858
2.848
2.775
2.761
2.742
2.728
2.624
2.305
-0.000
O
N(Me)2
NH
F
O
Me
Me
1H NMR (400 MHz, CDCl3)
1.00
3.15
7.10
1.00
2.07
4.11
2.00
3.01
6.07
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

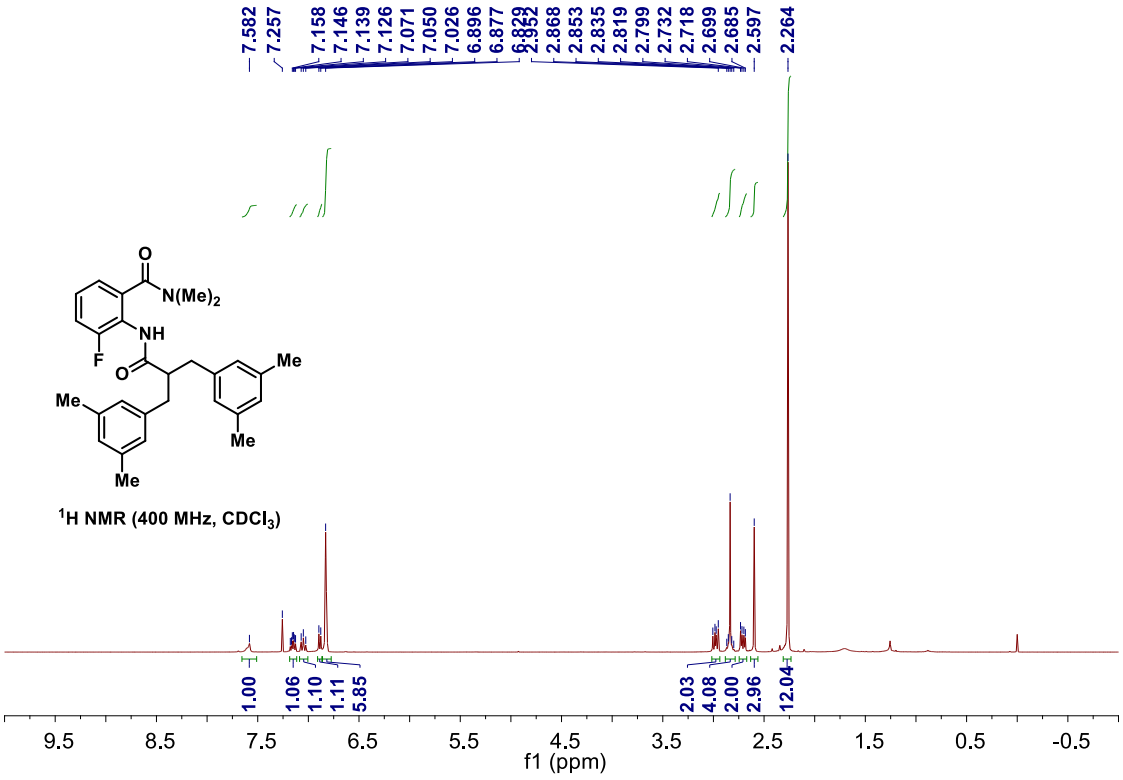

172.784
168.425
158.752
156.230
139.428
137.906
122.329
121.853
117.261
117.056
77.355
77.037
76.720
51.794
38.908
38.575
34.759
21.373
O
N(Me)2
NH
F
O
Me
Me
13C NMR (101 MHz, CDCl3)
90
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

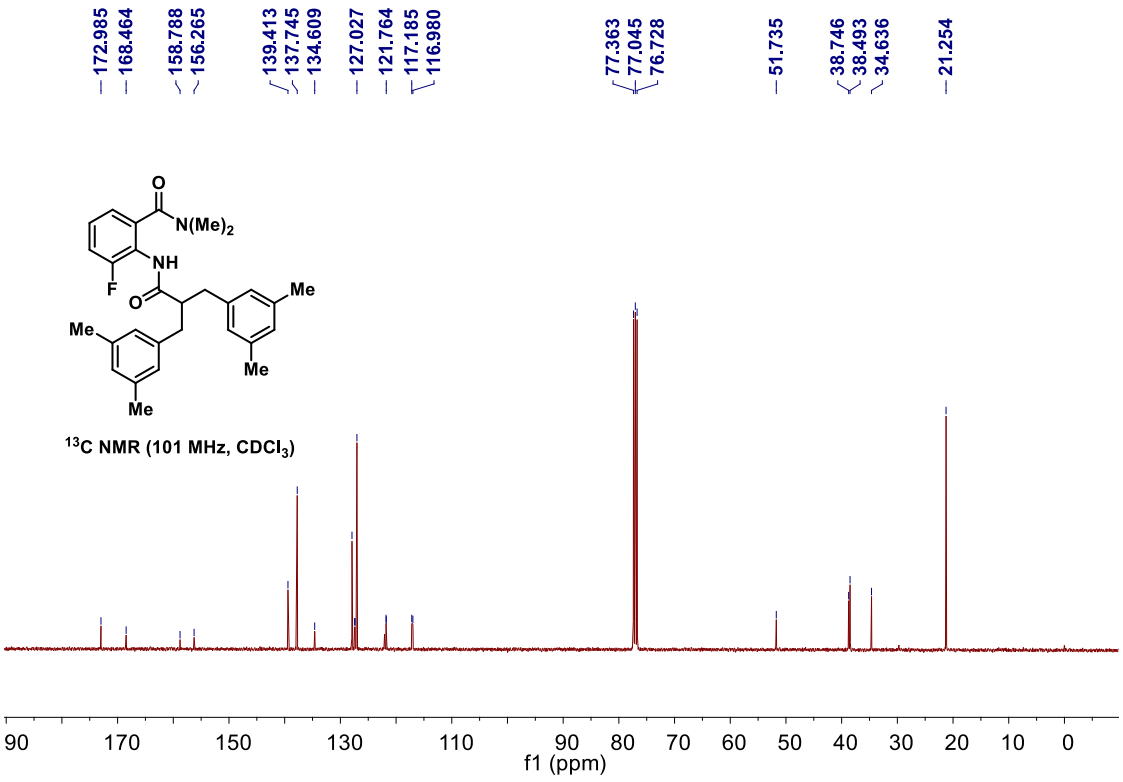
3d$_{mono}$


8.580
8.517
7.142
7.129
7.123
7.110
6.979
6.953
6.934
6.845
6.830
3.053
3.036
3.019
3.006
2.831
2.754
2.736
2.578
2.558
2.544
2.524
2.270
1.163
1.146
O
N(Me)2
NH
F
O
Me
Me
1H NMR (400 MHz, CDCl3)
0.33
0.65
1.06
2.02
2.01
1.00
1.06
3.09
2.93
1.06
1.00
6.10
3.01
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

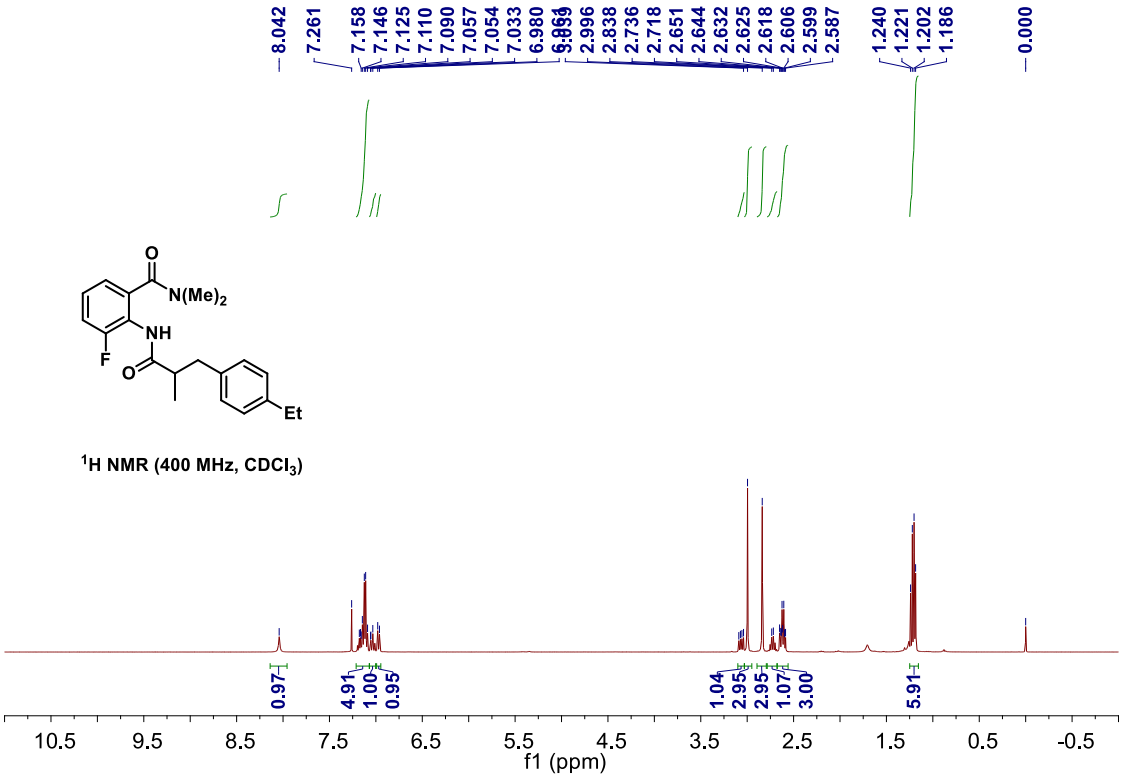

175.239
168.834
158.720
156.219
139.657
137.661
135.062
126.996
121.983
116.964
116.759
77.391
77.073
76.756
42.924
39.714
39.158
34.893
21.251
17.355
O
N(Me)2
NH
F
O
Me
Me
13C NMR (101 MHz, CDCl3)
90
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

3d$_{di}$

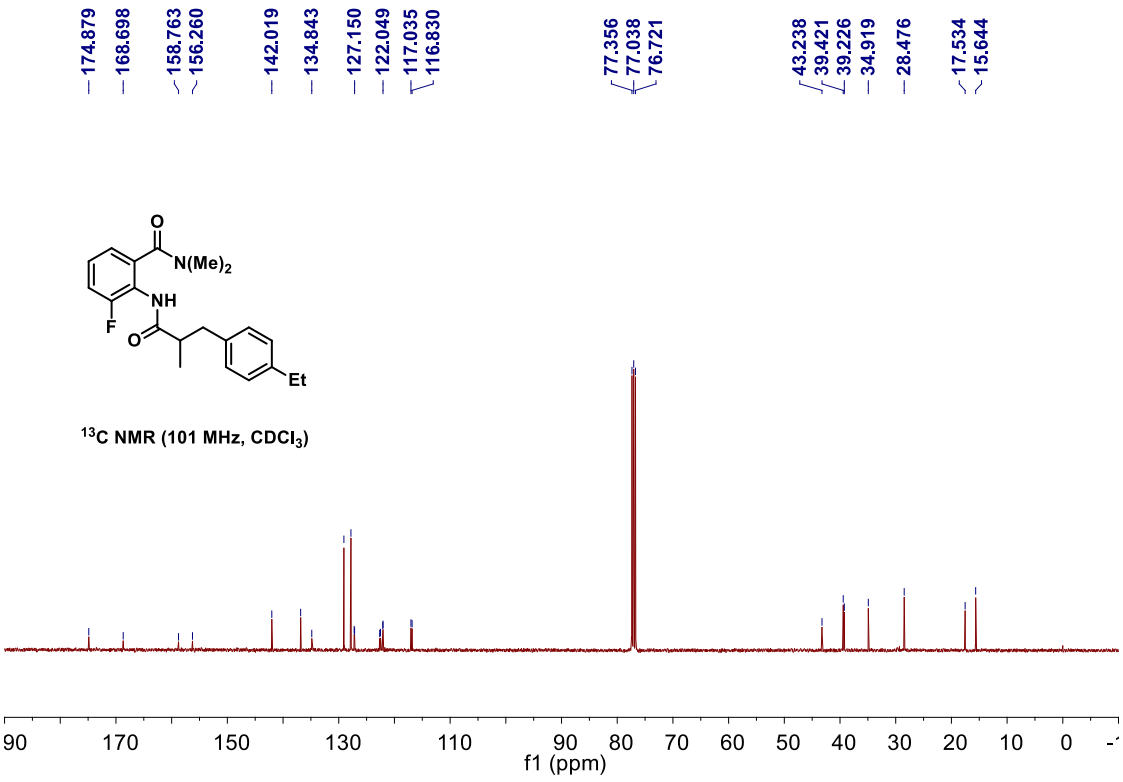

7.582
7.257
7.158
7.146
7.139
7.126
7.071
7.050
7.026
6.896
6.877
2.868
2.853
2.835
2.819
2.799
2.732
2.718
2.699
2.685
2.597
2.264
O
N(Me)2
NH
F
O
Me
Me
Me
Me
1H NMR (400 MHz, CDCl3)
1.00
1.06
1.10
1.11
5.85
2.03
4.08
2.00
2.96
12.04
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)


172.985
168.464
158.788
156.265
139.413
137.745
134.609
127.027
121.764
117.185
116.980
77.363
77.045
76.728
51.735
38.746
38.493
34.636
21.254
O
N(Me)2
NH
F
O
Me
Me
Me
Me
13C NMR (101 MHz, CDCl3)
90
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

3e$_{mono}$

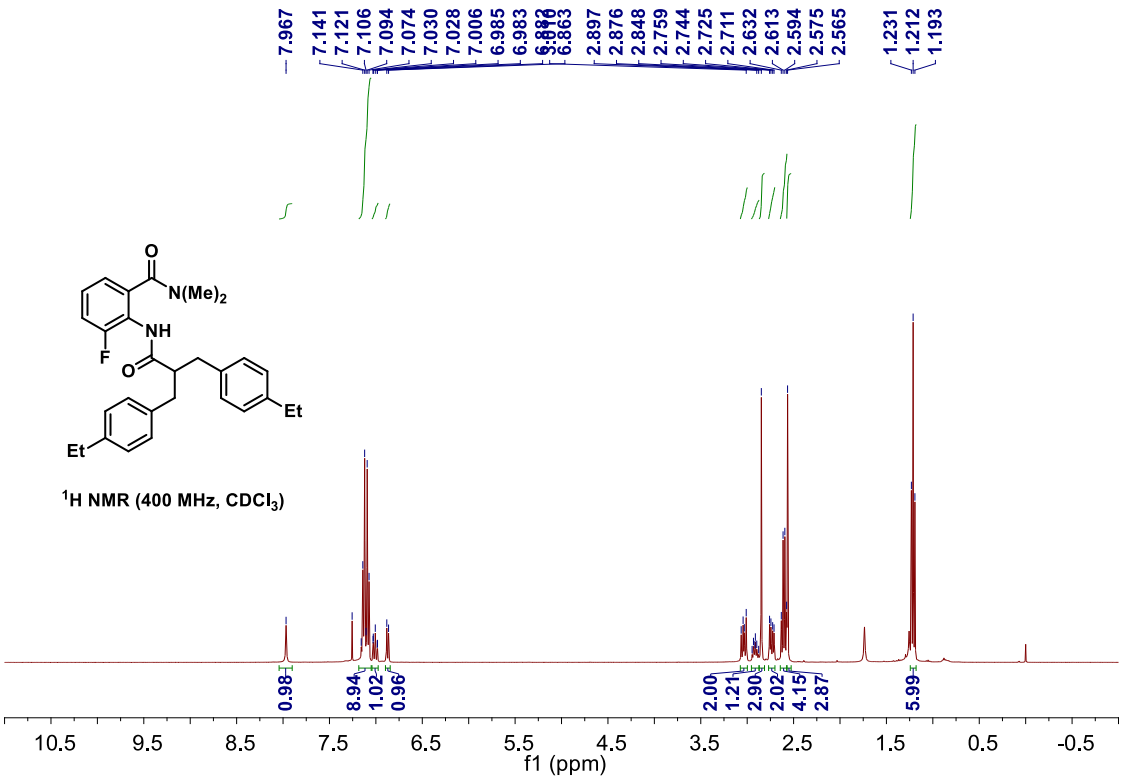


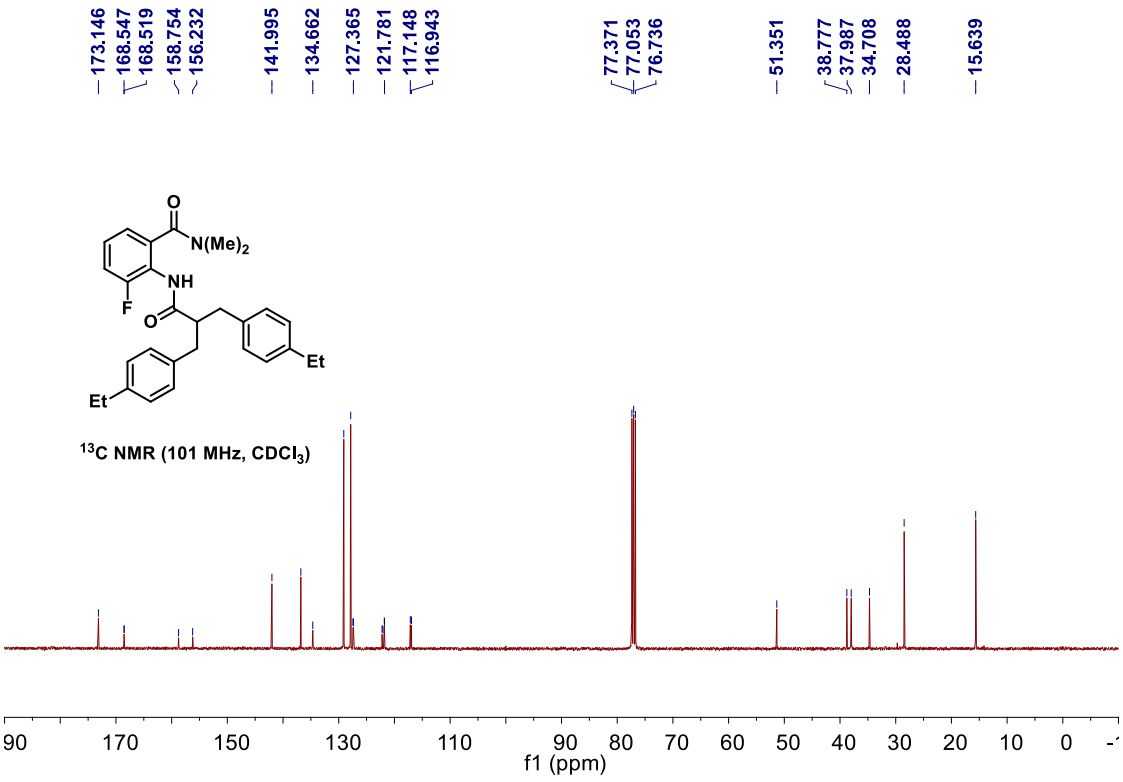
^{1}H NMR (400 MHz, $CDCl_3$)



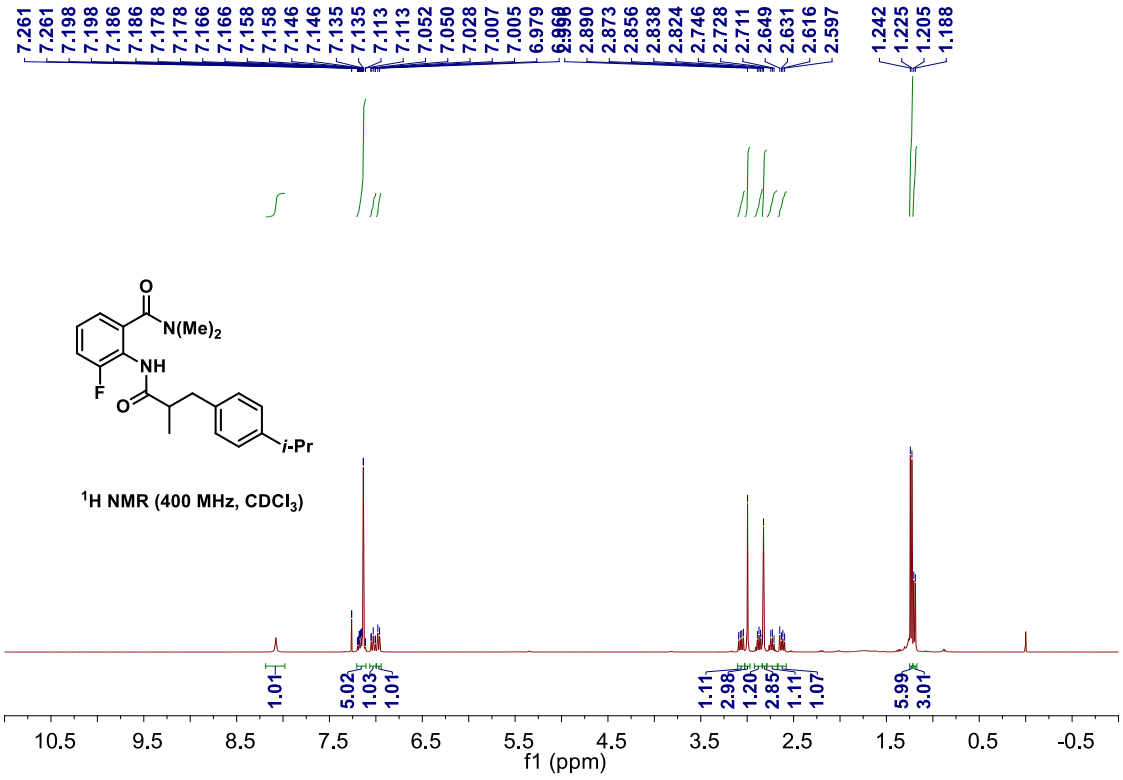
^{13}C NMR (101 MHz, $CDCl_3$)

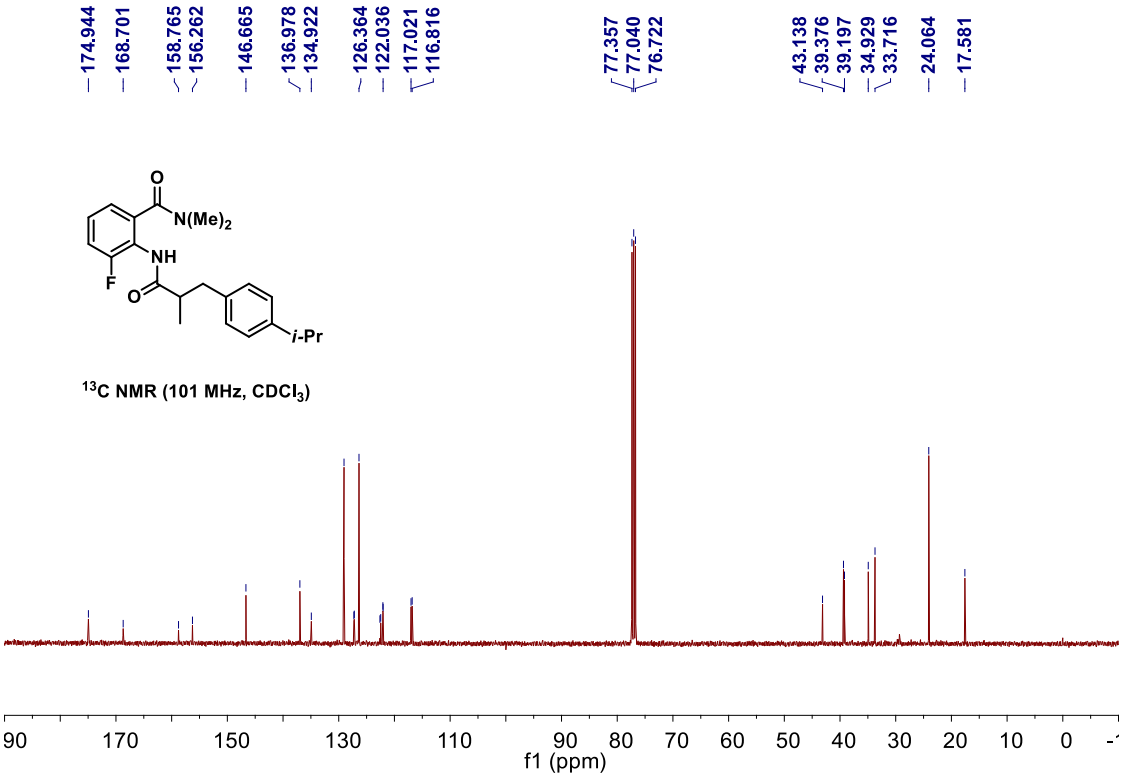
3e$_{di}$


7.967
7.141
7.121
7.106
7.094
7.074
7.030
7.028
7.006
6.985
6.983
6.863
2.897
2.876
2.848
2.759
2.744
2.725
2.711
2.632
2.613
2.594
2.575
2.565
1.231
1.212
1.193
O
N(Me)2
NH
F
O
Et
Et
1H NMR (400 MHz, CDCl3)
0.98
8.94
1.02
0.96
2.00
1.21
2.90
2.02
4.15
2.87
5.99
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

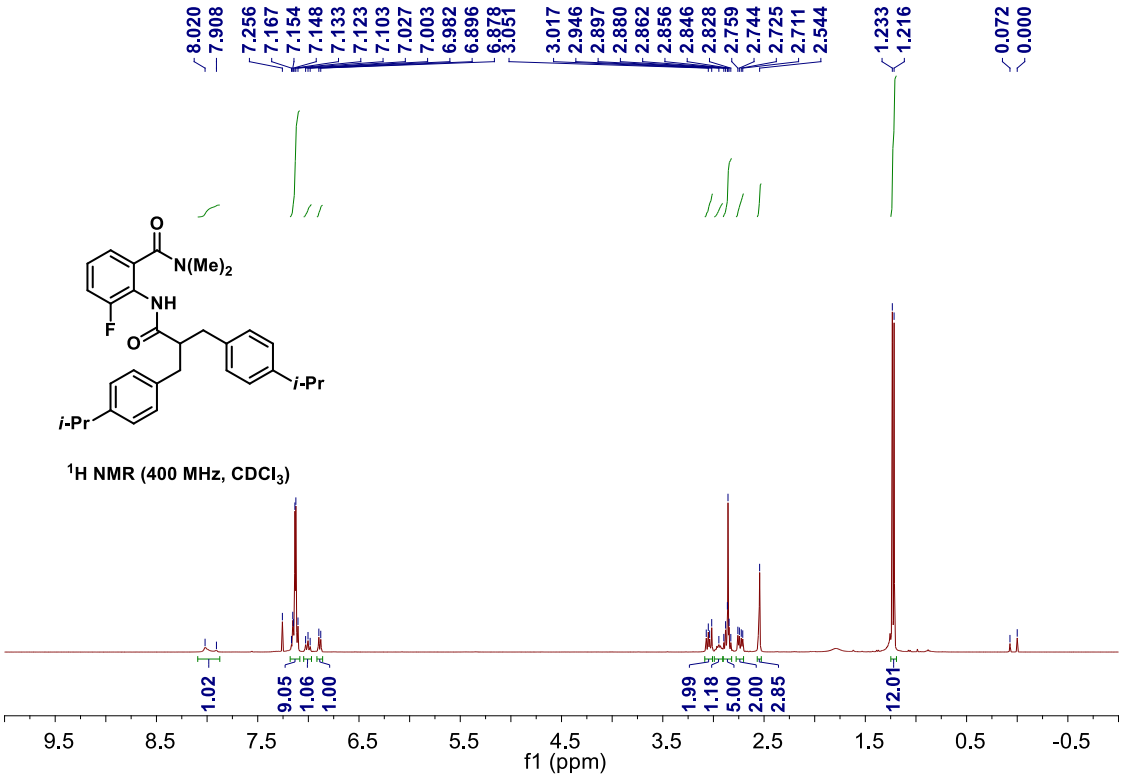

173.146
168.547
168.519
158.754
156.232
141.995
134.662
127.365
121.781
117.148
116.943
77.371
77.053
76.736
51.351
38.777
37.987
34.708
28.488
15.639
O
N(Me)2
NH
F
O
Et
Et
13C NMR (101 MHz, CDCl3)
90
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

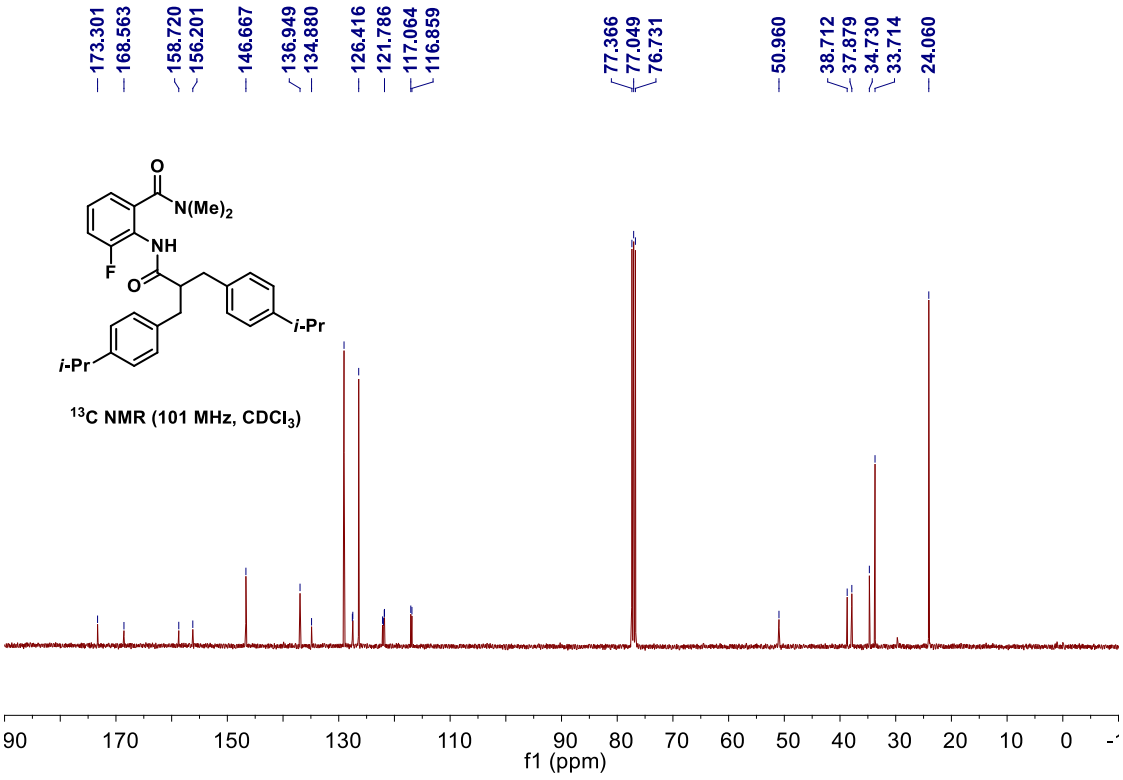
3f$_{mono}$


7.261
7.261
7.198
7.198
7.186
7.186
7.178
7.178
7.166
7.166
7.158
7.158
7.146
7.146
7.135
7.135
7.113
7.113
7.052
7.050
7.028
7.007
7.005
6.979
2.890
2.873
2.856
2.838
2.824
2.746
2.728
2.711
2.649
2.631
2.616
2.597
1.242
1.225
1.205
1.188
O
N(Me)2
NH
F
O
i-Pr
1H NMR (400 MHz, CDCl3)
1.01
5.02
1.03
1.01
1.11
2.98
1.20
2.85
1.11
1.07
5.99
3.01
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

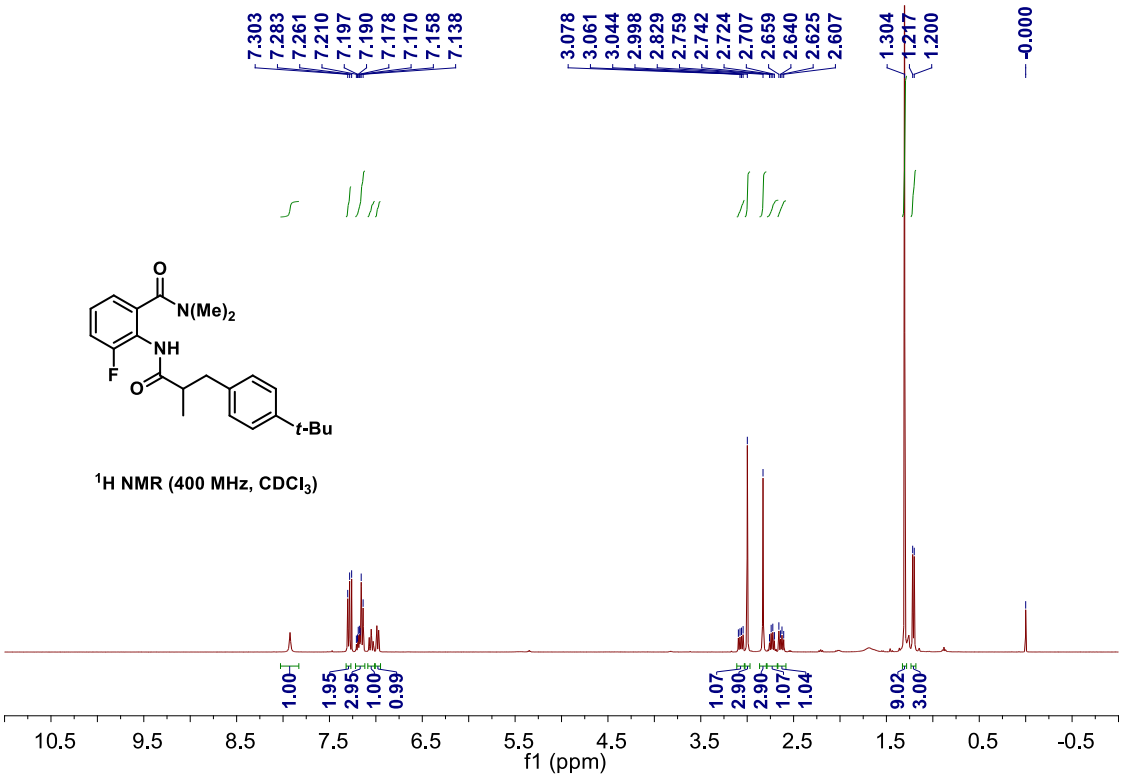

174.944
168.701
158.765
156.262
146.665
136.978
134.922
126.364
122.036
117.021
116.816
77.357
77.040
76.722
43.138
39.376
39.197
34.929
33.716
24.064
17.581
O
N(Me)2
NH
F
O
i-Pr
13C NMR (101 MHz, CDCl3)
90
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

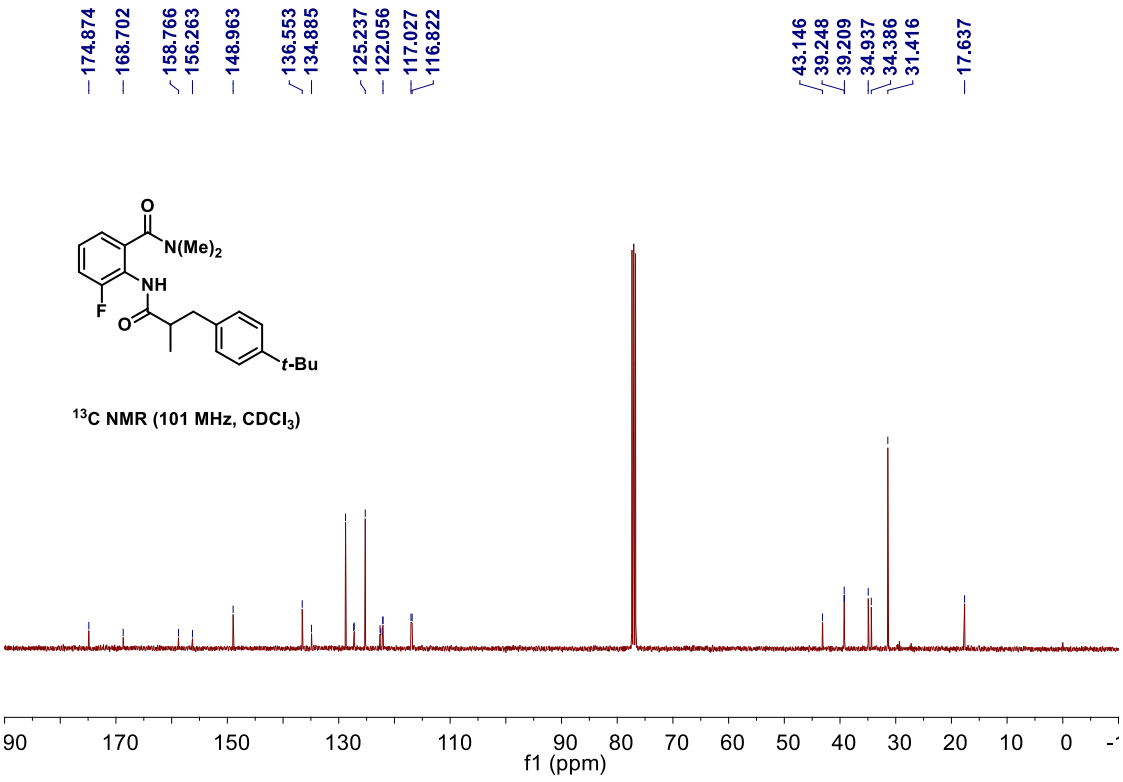
3f$_{di}$


8.020
7.908
7.256
7.167
7.154
7.148
7.133
7.123
7.103
7.027
7.003
6.982
6.896
6.878
6.851
3.017
2.946
2.897
2.880
2.862
2.856
2.846
2.828
2.759
2.744
2.725
2.711
2.544
1.233
1.216
0.072
0.000
N(Me)2
NH
F
O
i-Pr
i-Pr
1H NMR (400 MHz, CDCl3)
1.02
9.05
1.06
1.00
1.99
1.18
5.00
2.00
2.85
12.01
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

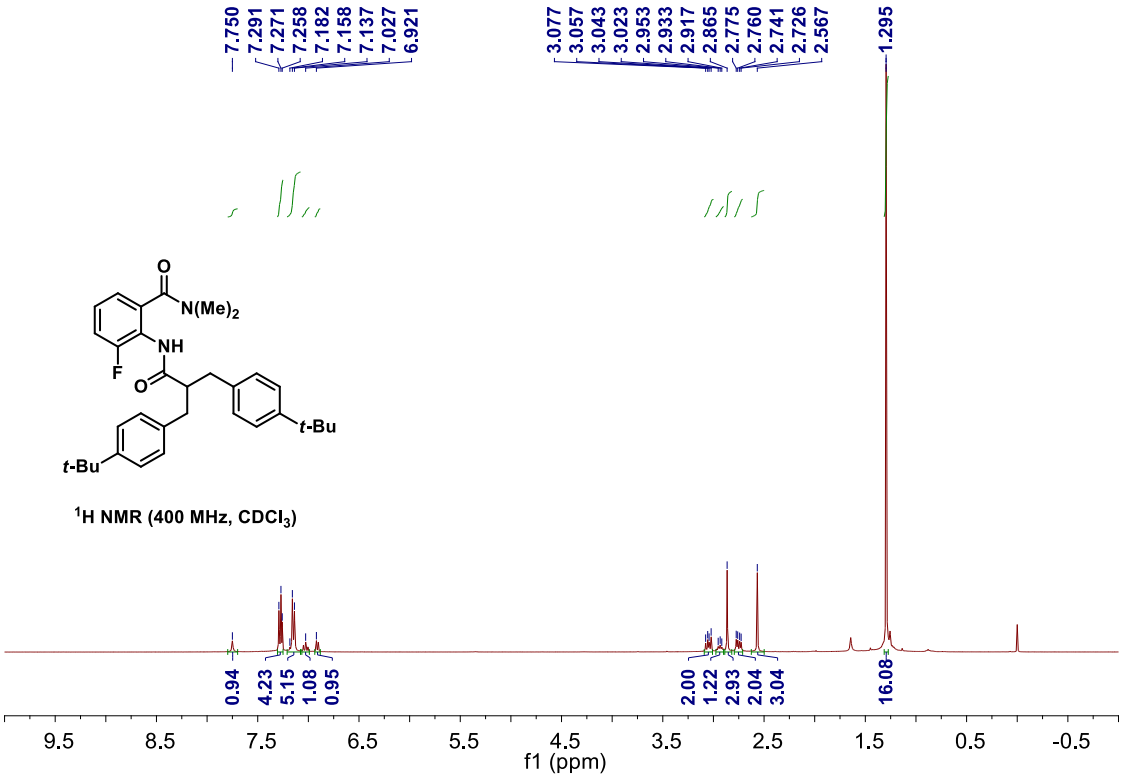

173.301
168.563
158.720
156.201
146.667
136.949
134.880
126.416
121.786
117.064
116.859
77.366
77.049
76.731
50.960
38.712
37.879
34.730
33.714
24.060
N(Me)2
NH
F
O
i-Pr
i-Pr
13C NMR (101 MHz, CDCl3)
90
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

3g$_{mono}$

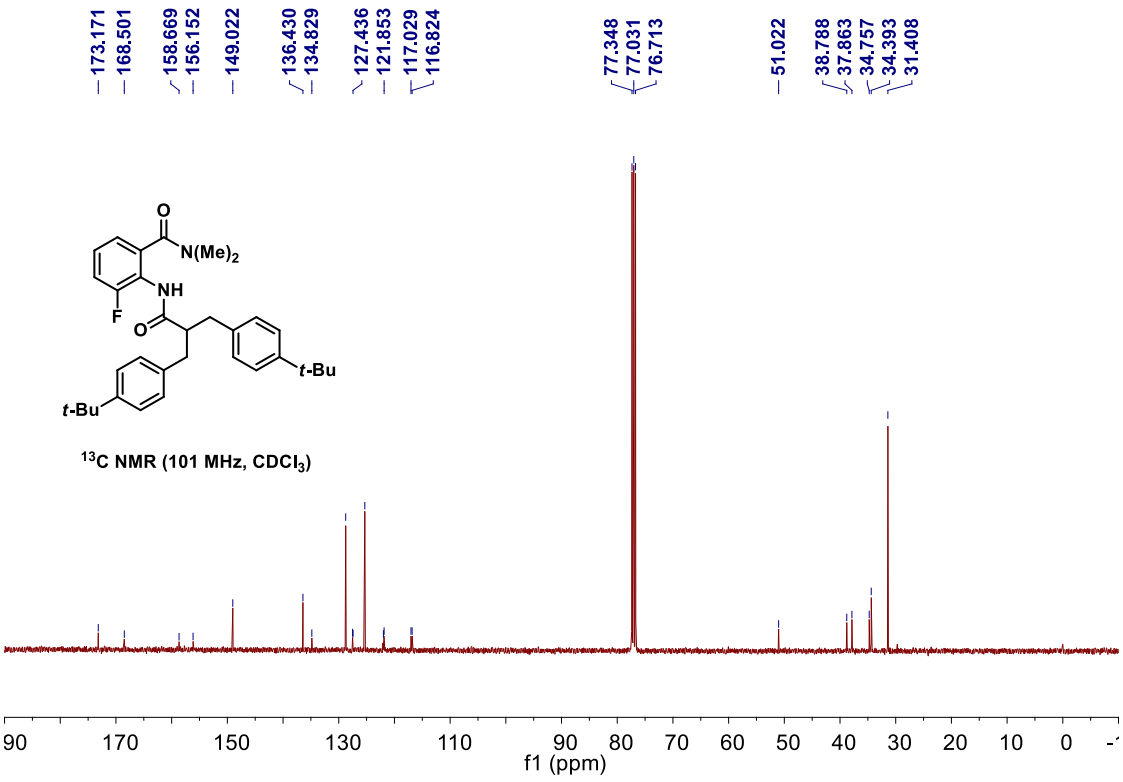

7.303
7.283
7.261
7.210
7.197
7.190
7.178
7.170
7.158
7.138
3.078
3.061
3.044
2.998
2.829
2.759
2.742
2.724
2.707
2.659
2.640
2.625
2.607
1.304
1.217
1.200
-0.000
O
N(Me)2
NH
F
O
t-Bu
1H NMR (400 MHz, CDCl3)
1.00
1.95
2.95
1.00
0.99
1.07
2.90
2.90
1.07
1.04
9.02
3.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)


174.874
168.702
158.766
156.263
148.963
136.553
134.885
125.237
122.056
117.027
116.822
43.146
39.248
39.209
34.937
34.386
31.416
17.637
O
N(Me)2
NH
F
O
t-Bu
13C NMR (101 MHz, CDCl3)
90
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

3g$_{di}$

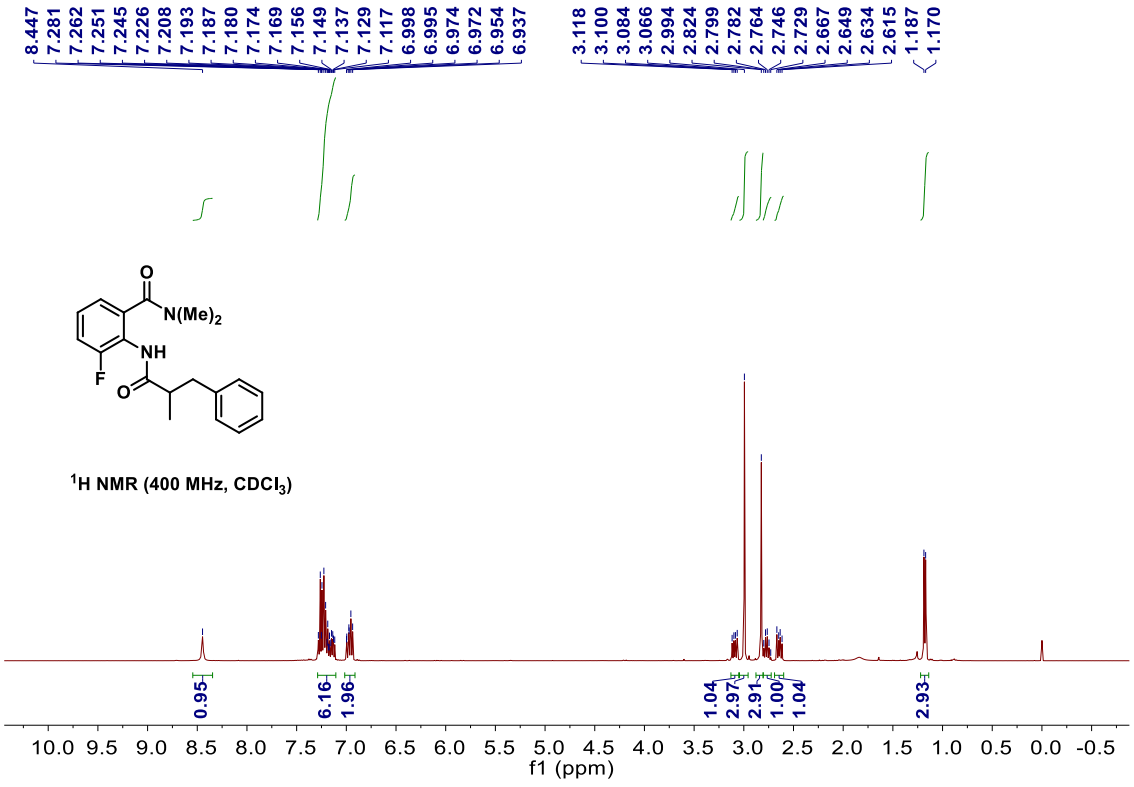


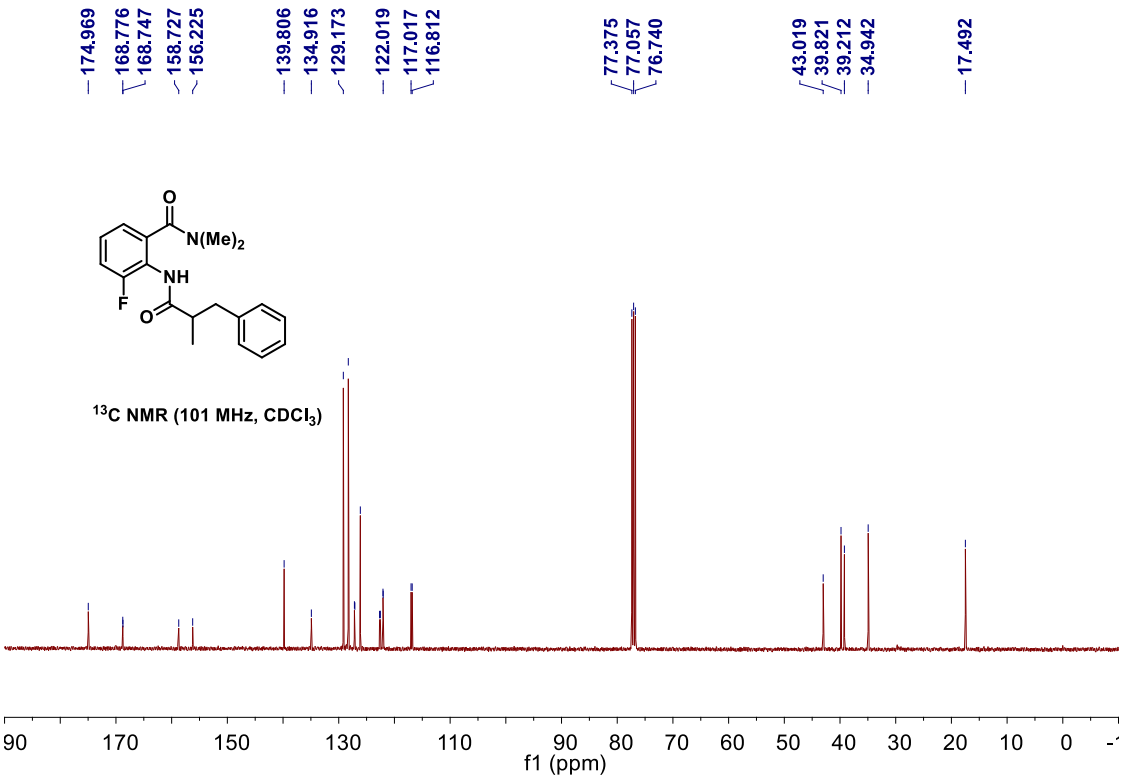
^{1}H NMR (400 MHz, $CDCl_3$)



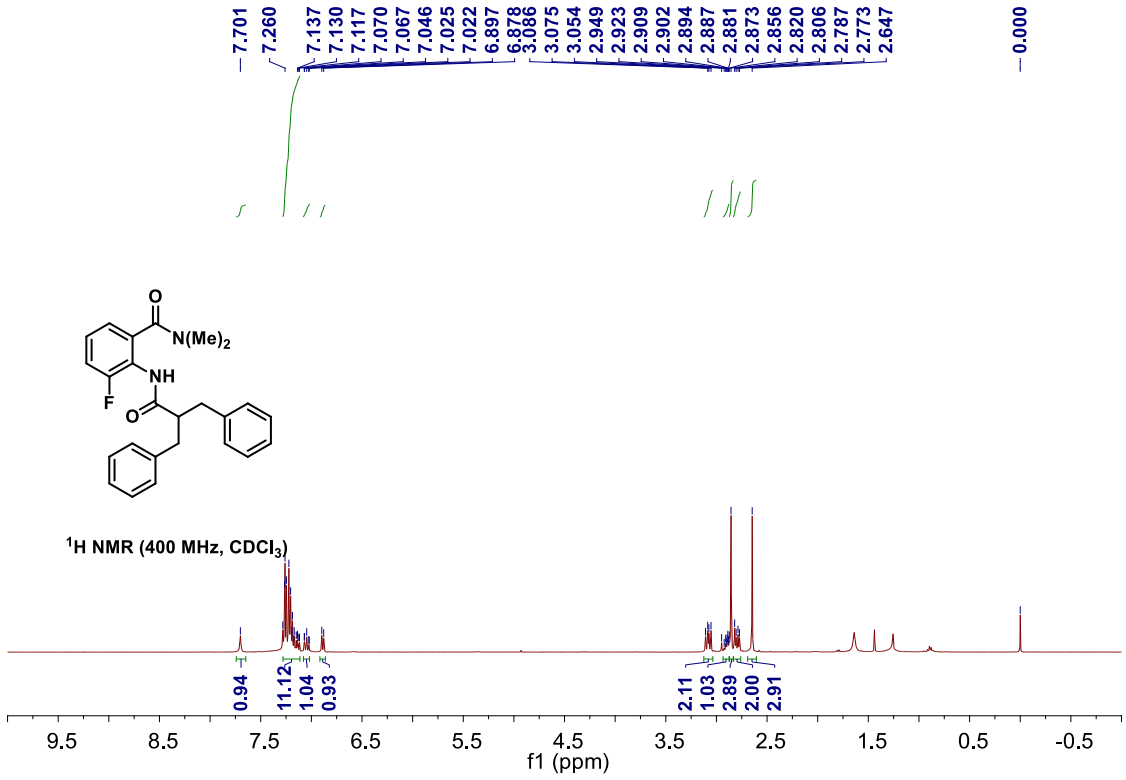
^{13}C NMR (101 MHz, $CDCl_3$)

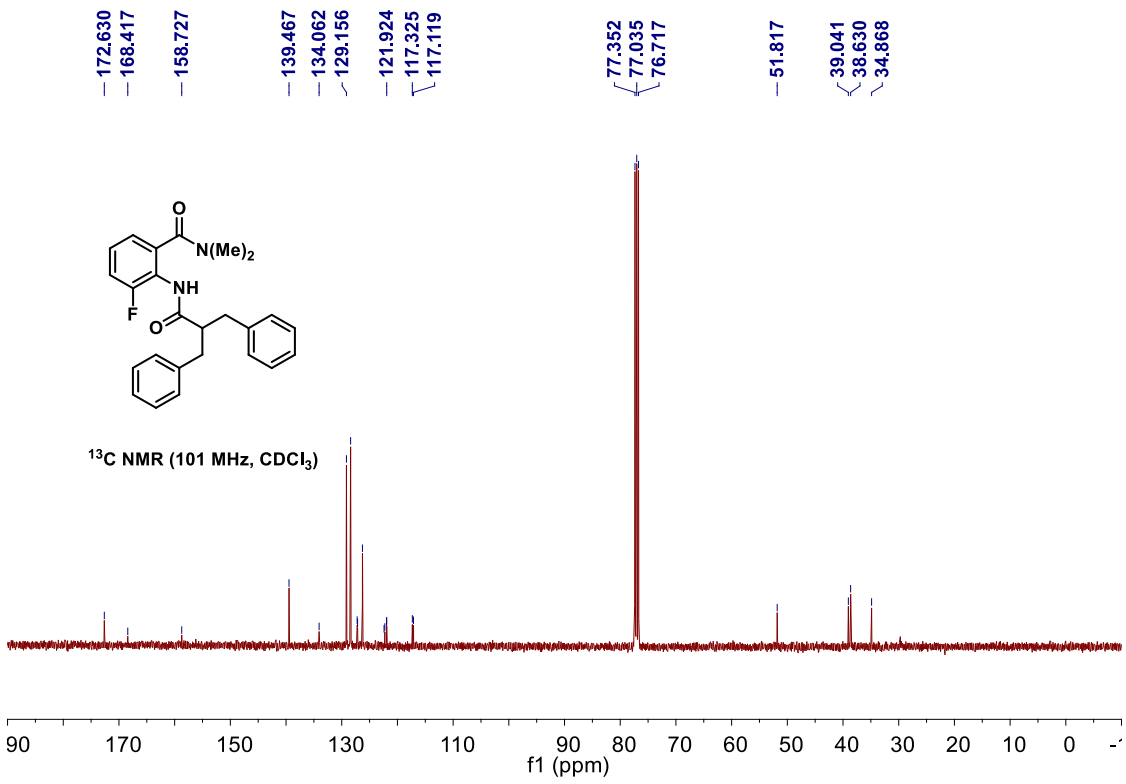
3h$_{mono}$


8.447
7.281
7.262
7.251
7.245
7.226
7.208
7.193
7.187
7.180
7.174
7.169
7.156
7.149
7.137
7.129
7.117
6.998
6.995
6.974
6.972
6.954
6.937
3.118
3.100
3.084
3.066
2.994
2.824
2.799
2.782
2.764
2.746
2.729
2.667
2.649
2.634
2.615
1.187
1.170
O
N(Me)2
NH
F
O
1H NMR (400 MHz, CDCl3)
0.95
6.16
1.96
1.04
2.97
2.91
1.00
1.04
2.93
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

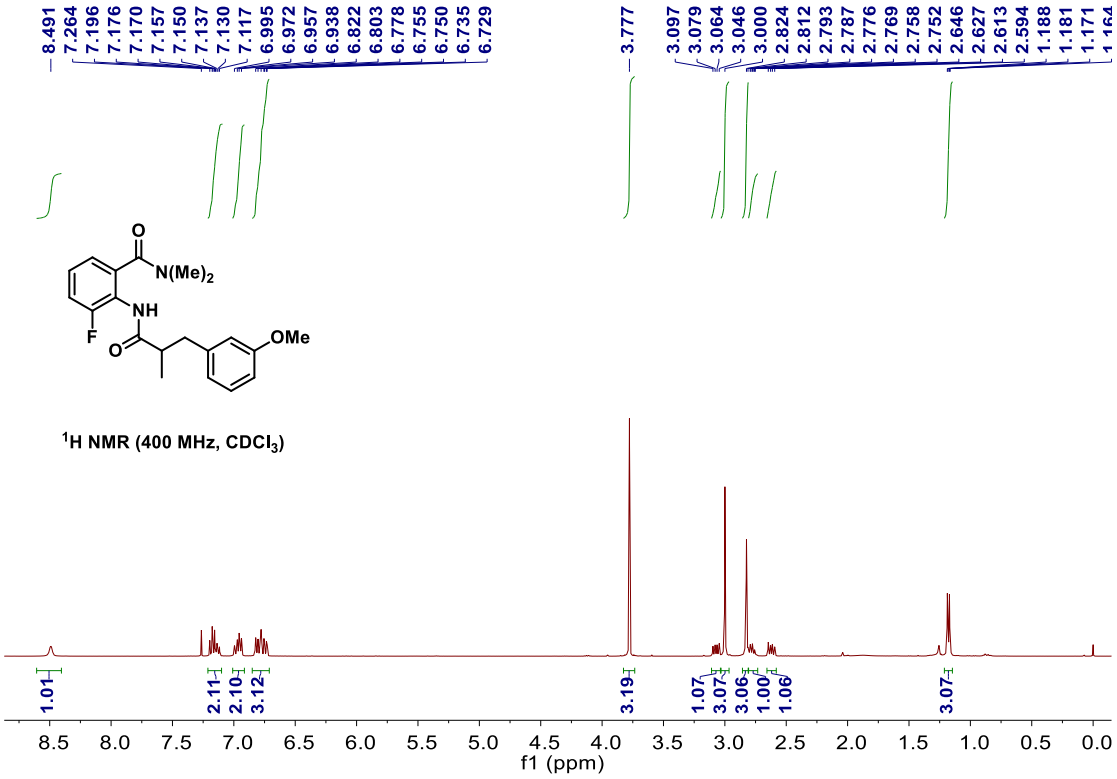

174.969
168.776
168.747
158.727
156.225
139.806
134.916
129.173
122.019
117.017
116.812
77.375
77.057
76.740
43.019
39.821
39.212
34.942
17.492
O
N(Me)2
NH
F
O
13C NMR (101 MHz, CDCl3)
90 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

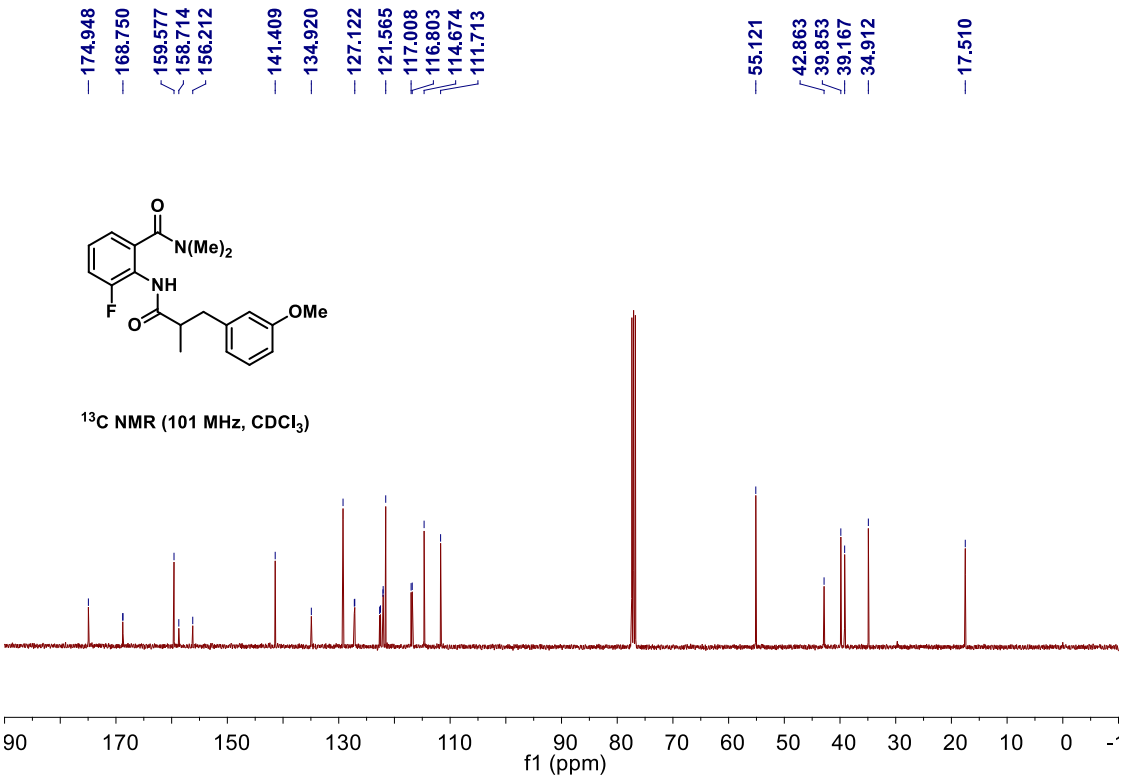
3h$_{di}$


7.701
7.260
7.137
7.130
7.117
7.070
7.067
7.046
7.025
7.022
6.897
6.878
3.086
3.075
3.054
2.949
2.923
2.909
2.902
2.894
2.887
2.881
2.873
2.856
2.820
2.806
2.787
2.773
2.647
0.000
N(Me)2
NH
F
O
1H NMR (400 MHz, CDCl3)
0.94
11.12
1.04
0.93
2.11
1.03
2.89
2.00
2.91
f1 (ppm)

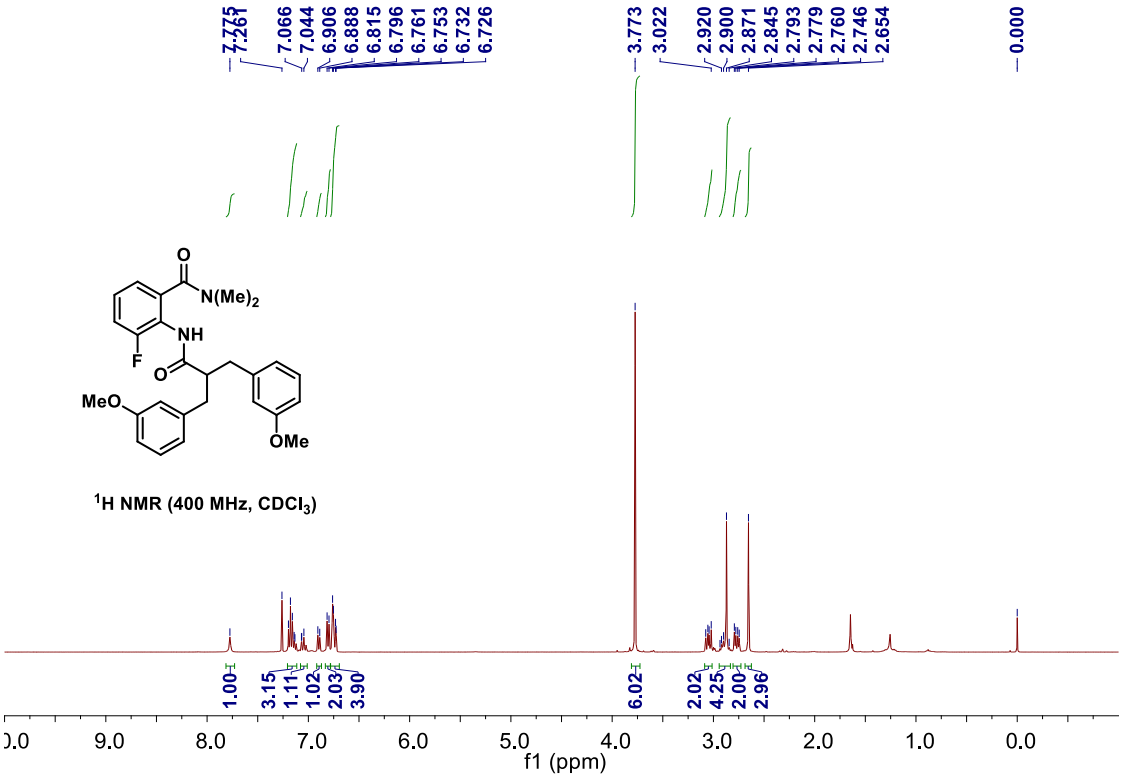

172.630
168.417
158.727
139.467
134.062
129.156
121.924
117.325
117.119
77.352
77.035
76.717
51.817
39.041
38.630
34.868
N(Me)2
NH
F
O
13C NMR (101 MHz, CDCl3)
f1 (ppm)

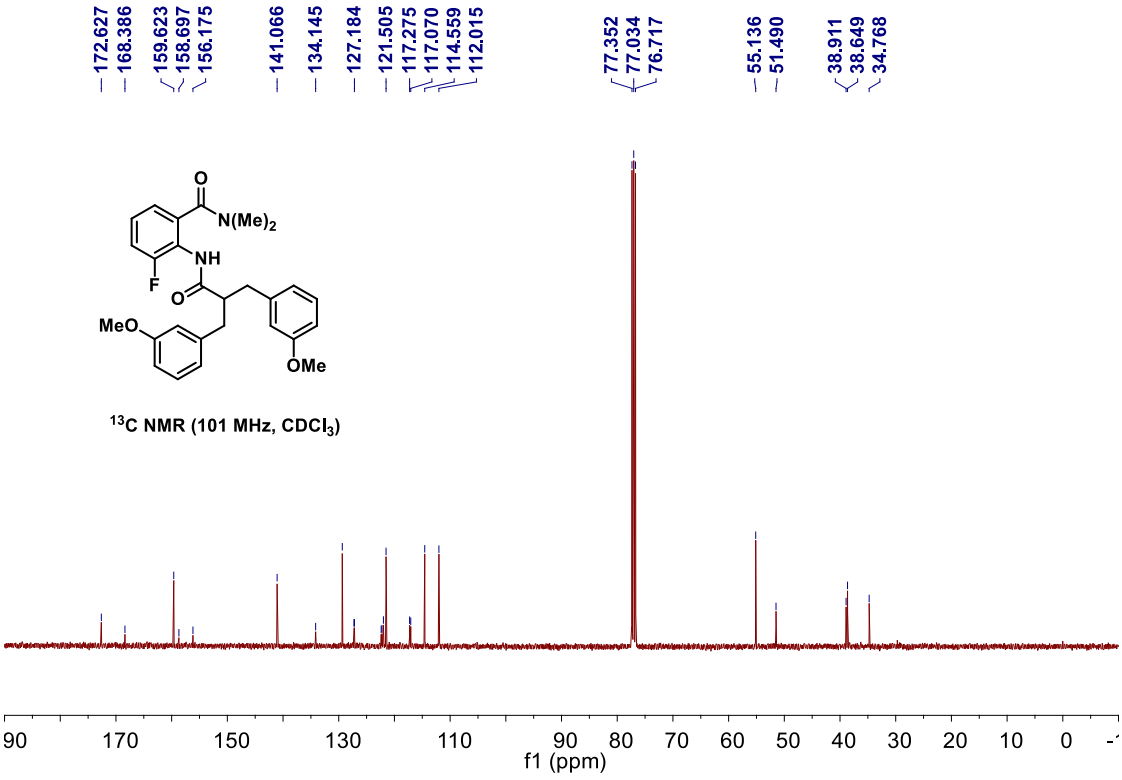
3i$_{mono}$


8.491
7.264
7.196
7.176
7.170
7.157
7.150
7.137
7.130
7.117
6.995
6.972
6.957
6.938
6.822
6.803
6.778
6.755
6.750
6.735
6.729
3.777
3.097
3.079
3.064
3.046
3.000
2.824
2.812
2.793
2.787
2.776
2.769
2.758
2.752
2.646
2.627
2.613
2.594
1.188
1.181
1.171
1.164
O
N(Me)2
NH
F
O
OMe
1H NMR (400 MHz, CDCl3)
1.01
2.11
2.10
3.12
3.19
1.07
3.07
3.06
1.00
1.06
3.07
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

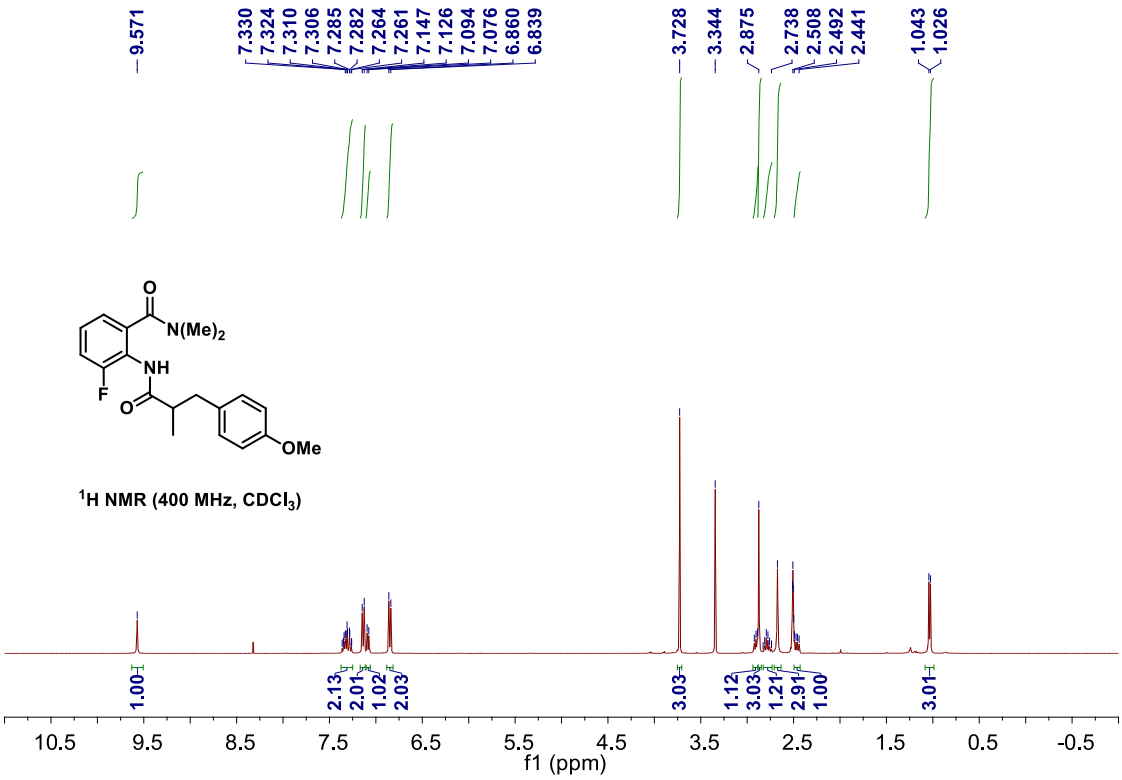

174.948
168.750
159.577
158.714
156.212
141.409
134.920
127.122
121.565
117.008
116.803
114.674
111.713
55.121
42.863
39.853
39.167
34.912
17.510
O
N(Me)2
NH
F
O
OMe
13C NMR (101 MHz, CDCl3)
90 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

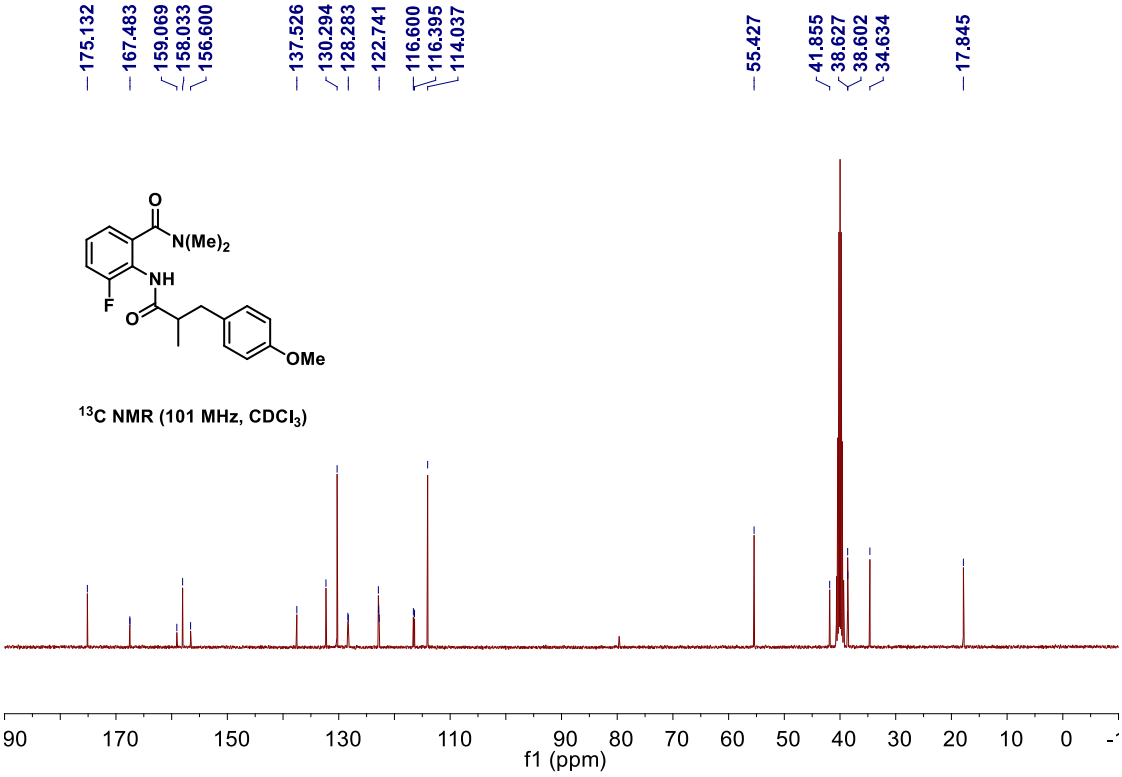
3i$_{di}$


7.775
7.261
7.066
7.044
6.906
6.888
6.815
6.796
6.761
6.753
6.732
6.726
3.773
3.022
2.920
2.900
2.871
2.845
2.793
2.779
2.760
2.746
2.654
0.000
O
N(Me)2
NH
F
O
MeO
OMe
1H NMR (400 MHz, CDCl3)
1.00
3.15
1.11
1.02
2.03
3.90
6.02
2.02
4.25
2.00
2.96
f1 (ppm)

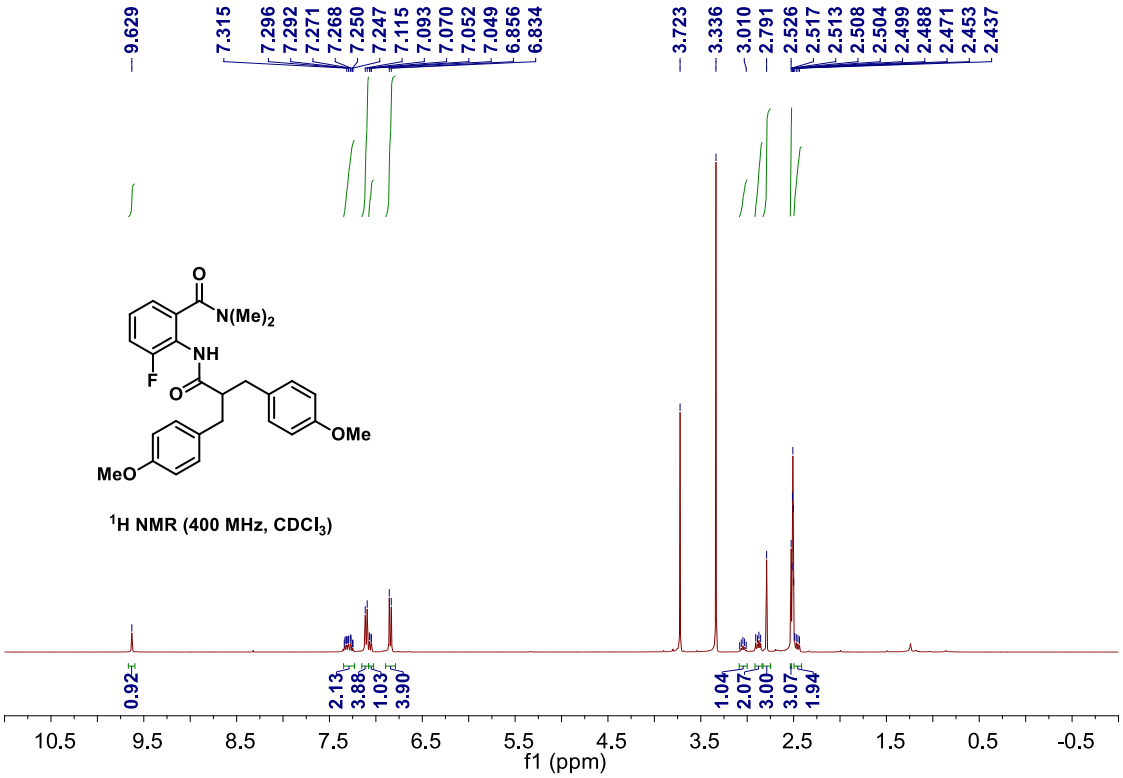

172.627
168.386
159.623
158.697
156.175
141.066
134.145
127.184
121.505
117.275
117.070
114.559
112.015
77.352
77.034
76.717
55.136
51.490
38.911
38.649
34.768
O
N(Me)2
NH
F
O
MeO
OMe
13C NMR (101 MHz, CDCl3)
f1 (ppm)

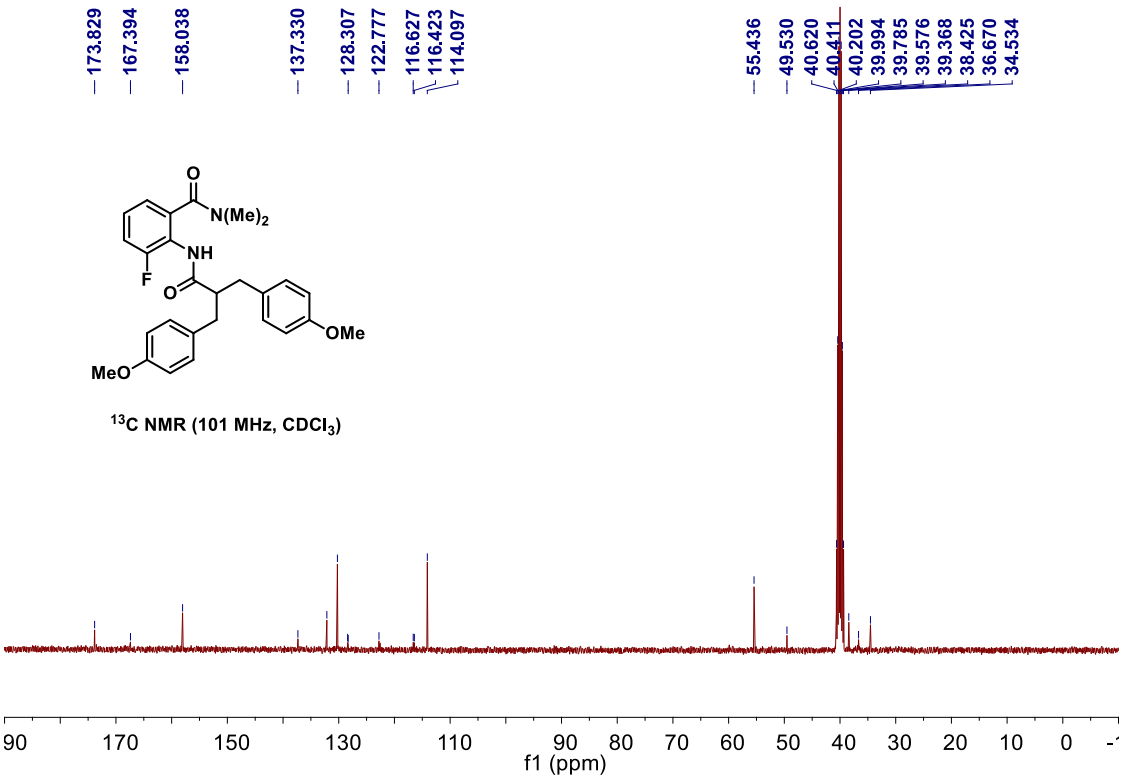
3j$_{mono}$


9.571
7.330
7.324
7.310
7.306
7.285
7.282
7.264
7.261
7.147
7.126
7.094
7.076
6.860
6.839
3.728
3.344
2.875
2.738
2.508
2.492
2.441
1.043
1.026
O
N(Me)2
NH
F
O
OMe
1H NMR (400 MHz, CDCl3)
1.00
2.13
2.01
1.02
2.03
3.03
1.12
3.03
1.21
2.91
1.00
3.01
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

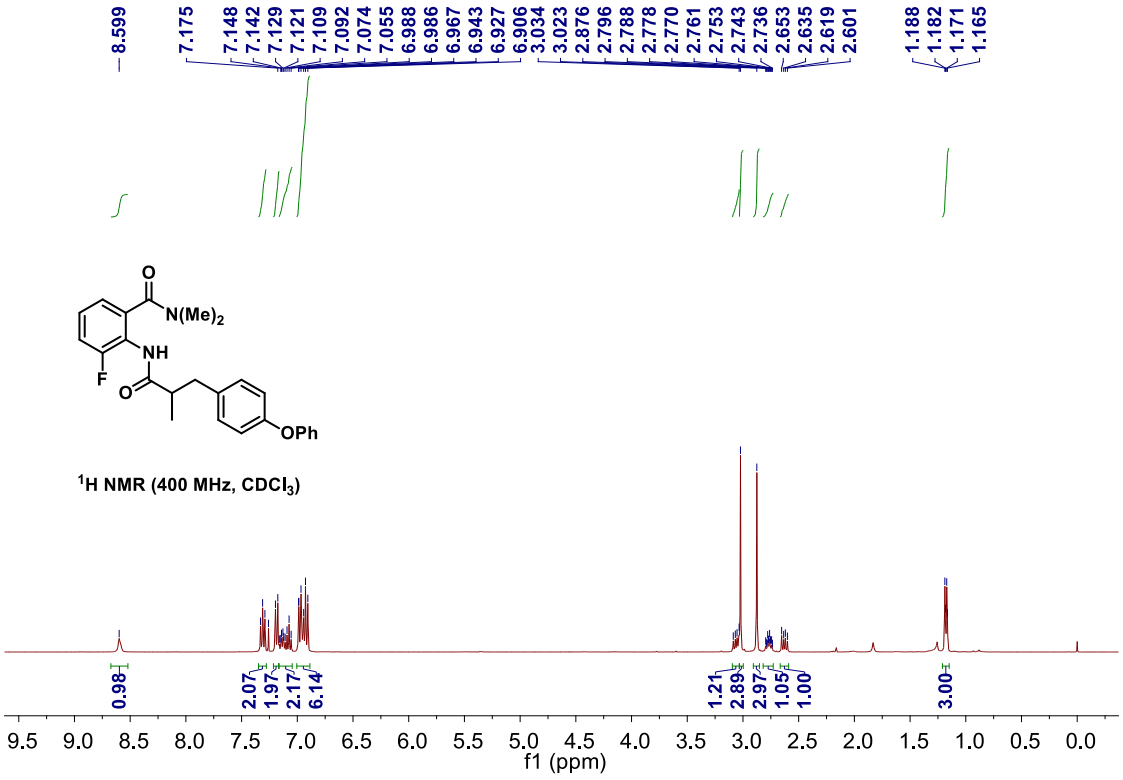

175.132
167.483
159.069
158.033
156.600
137.526
130.294
128.283
122.741
116.600
116.395
114.037
55.427
41.855
38.627
38.602
34.634
17.845
O
N(Me)2
NH
F
O
OMe
13C NMR (101 MHz, CDCl3)
90
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

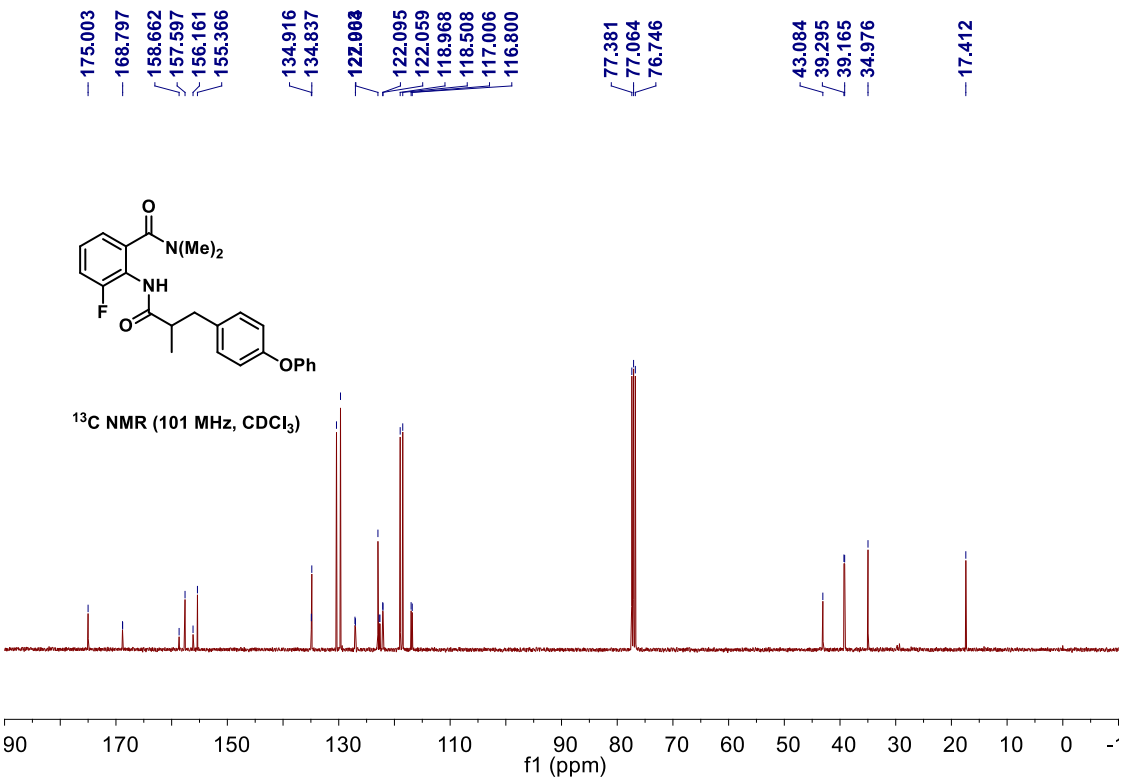
3j$_{di}$


9.629
7.315
7.296
7.292
7.271
7.268
7.250
7.247
7.115
7.093
7.070
7.052
7.049
6.856
6.834
3.723
3.336
3.010
2.791
2.526
2.517
2.513
2.508
2.504
2.499
2.488
2.471
2.453
2.437
O
N(Me)2
NH
F
O
OMe
MeO
1H NMR (400 MHz, CDCl3)
0.92
2.13
3.88
1.03
3.90
1.04
2.07
3.00
3.07
1.94
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

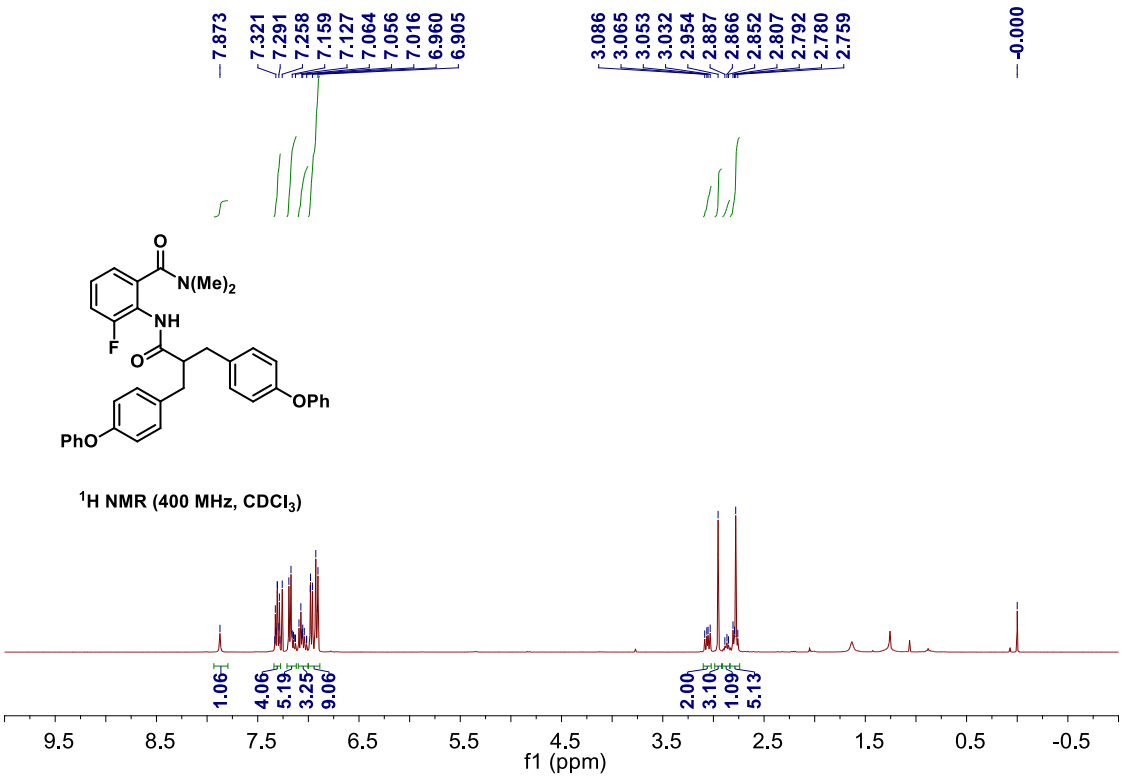

173.829
167.394
158.038
137.330
128.307
122.777
116.627
116.423
114.097
55.436
49.530
40.620
40.411
40.202
39.994
39.785
39.576
39.368
38.425
36.670
34.534
O
N(Me)2
NH
F
O
OMe
MeO
13C NMR (101 MHz, CDCl3)
90
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

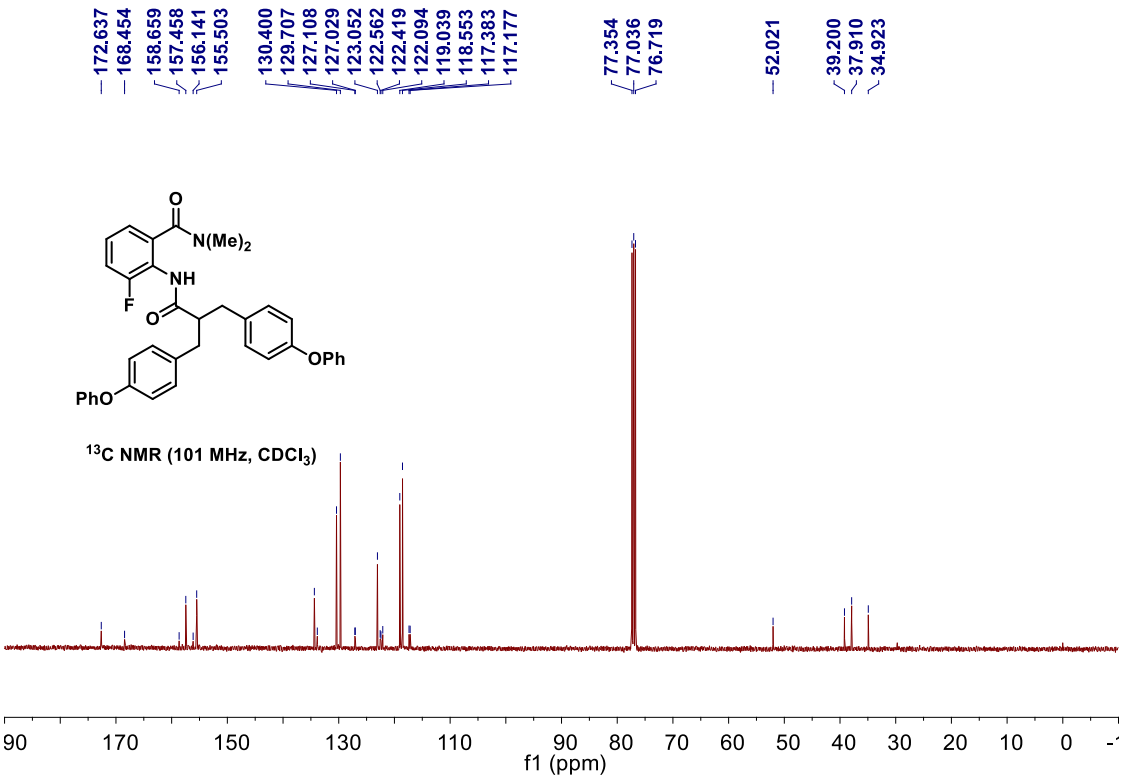
3k$_{mono}$


8.599
7.175
7.148
7.142
7.129
7.121
7.109
7.092
7.074
7.055
6.988
6.986
6.967
6.943
6.927
6.906
3.034
3.023
2.876
2.796
2.788
2.778
2.770
2.761
2.753
2.743
2.736
2.653
2.635
2.619
2.601
1.188
1.182
1.171
1.165
O
N(Me)2
NH
F
O
OPh
1H NMR (400 MHz, CDCl3)
0.98
2.07
1.97
2.17
6.14
1.21
2.89
2.97
1.05
1.00
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

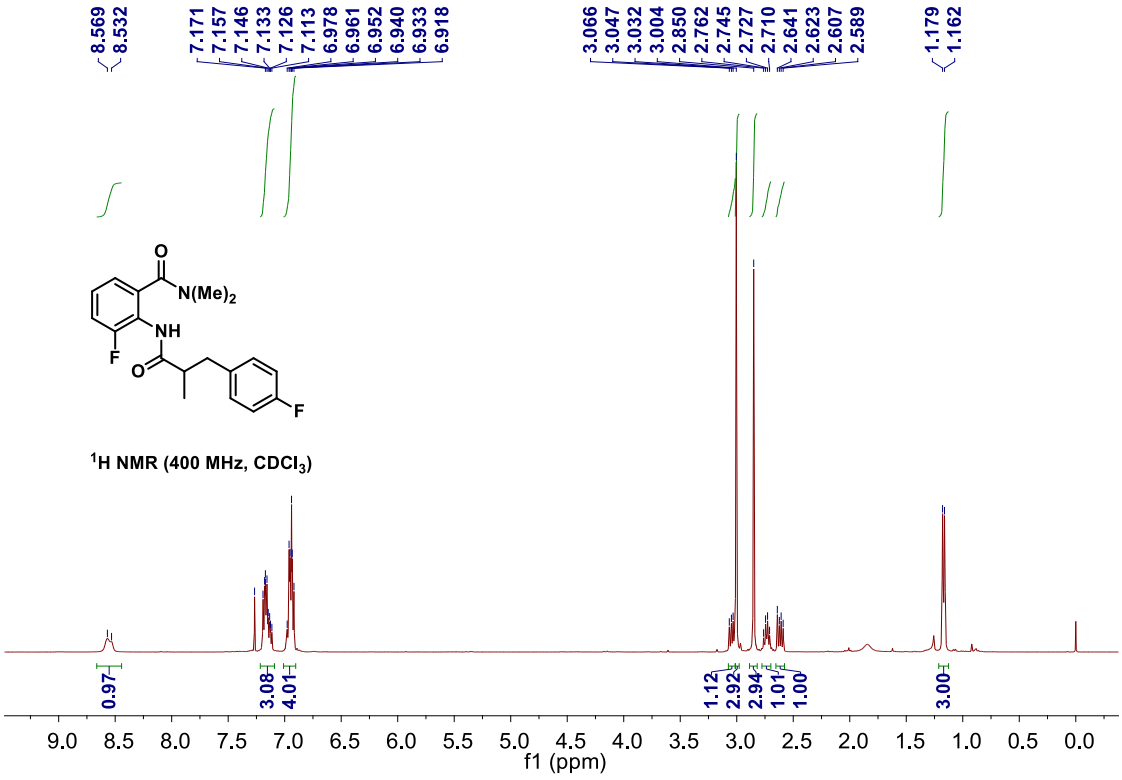

175.003
168.797
158.662
157.597
156.161
155.366
134.916
134.837
122.095
122.059
118.968
118.508
117.006
116.800
77.381
77.064
76.746
43.084
39.295
39.165
34.976
17.412
O
N(Me)2
NH
F
O
OPh
13C NMR (101 MHz, CDCl3)
90 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

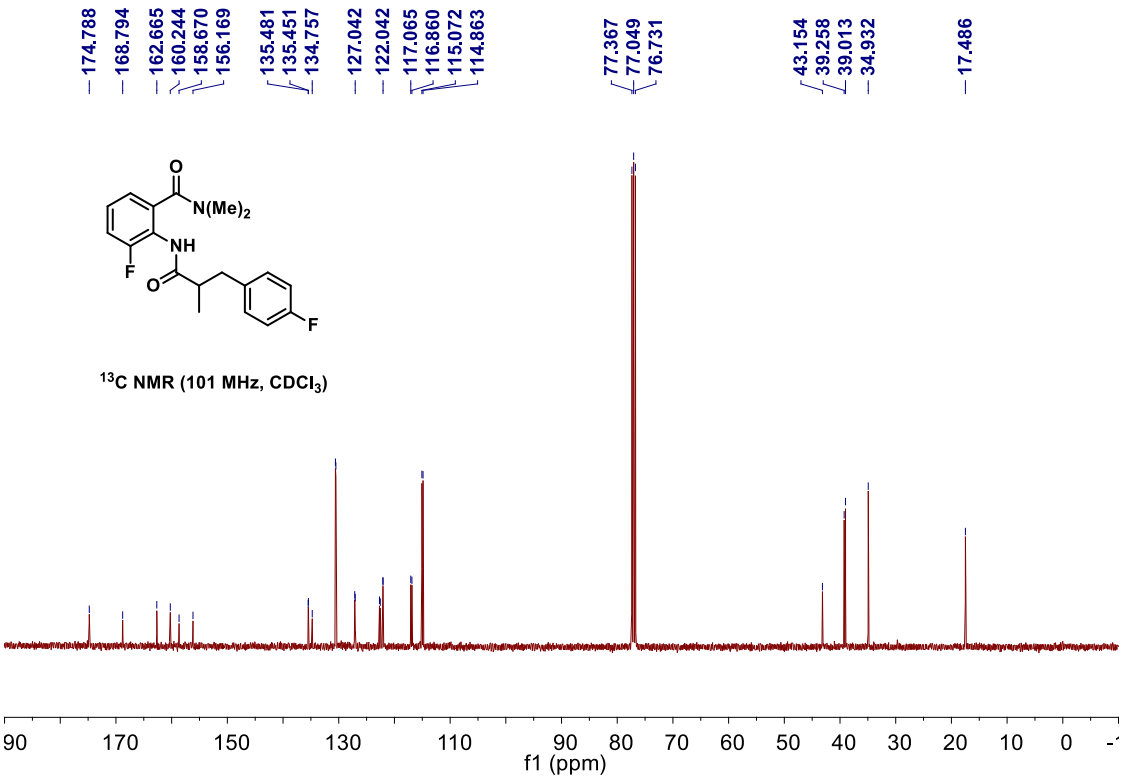
3k$_{di}$


7.873
7.321
7.291
7.258
7.159
7.127
7.064
7.056
7.016
6.960
6.905
3.086
3.065
3.053
3.032
2.954
2.887
2.866
2.852
2.807
2.792
2.780
2.759
-0.000
O
N(Me)2
NH
F
O
OPh
PhO
1H NMR (400 MHz, CDCl3)
1.06
4.06
5.19
3.25
9.06
2.00
3.10
1.09
5.13
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)


172.637
168.454
158.659
157.458
156.141
155.503
130.400
129.707
127.108
127.029
123.052
122.562
122.419
122.094
119.039
118.553
117.383
117.177
77.354
77.036
76.719
52.021
39.200
37.910
34.923
O
N(Me)2
NH
F
O
OPh
PhO
13C NMR (101 MHz, CDCl3)
90
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

3l$_{mono}$


8.569
8.532
7.171
7.157
7.146
7.133
7.126
7.113
6.978
6.961
6.952
6.940
6.933
6.918
3.066
3.047
3.032
3.004
2.850
2.762
2.745
2.727
2.710
2.641
2.623
2.607
2.589
1.179
1.162
N(Me)2
NH
F
O
F
1H NMR (400 MHz, CDCl3)
0.97
3.08
4.01
1.12
2.92
2.94
1.01
1.00
3.00
f1 (ppm)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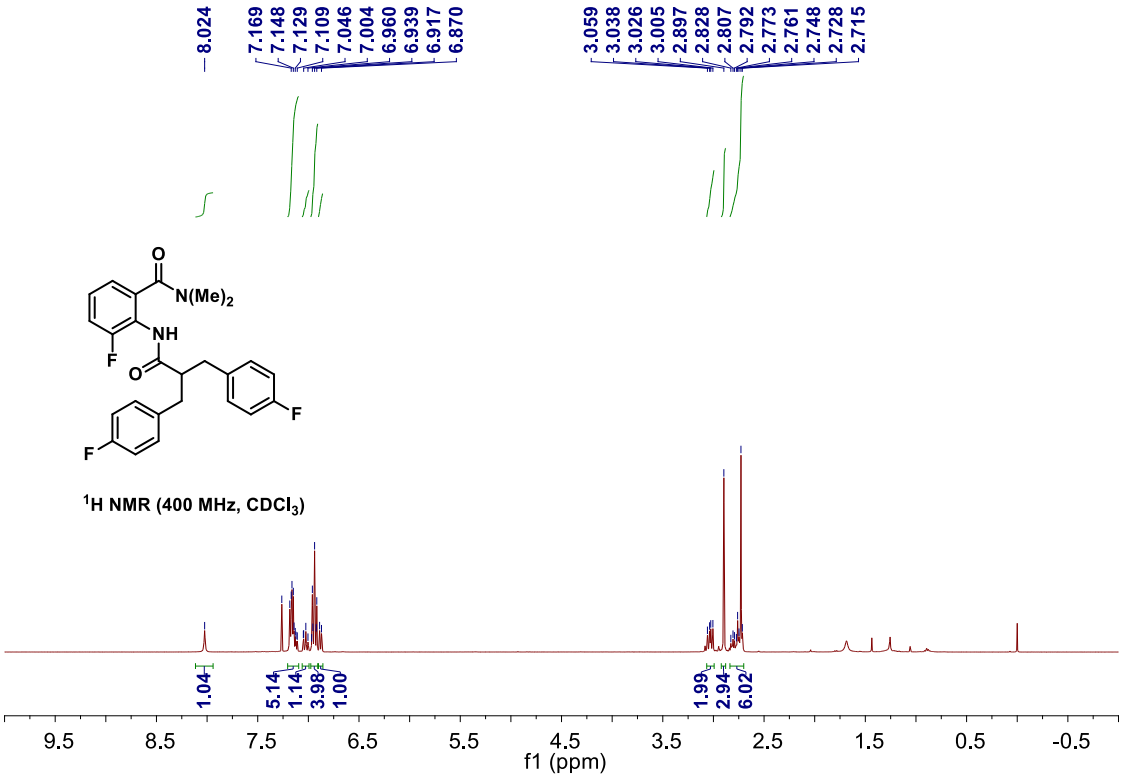
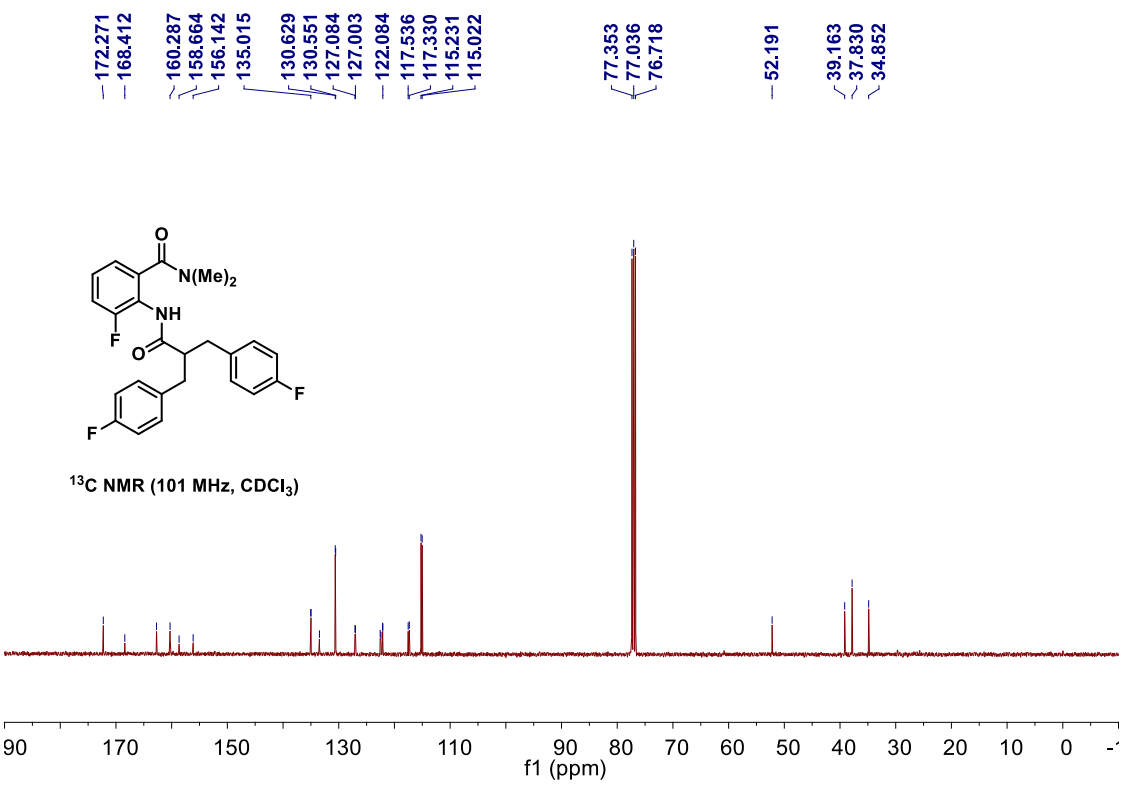
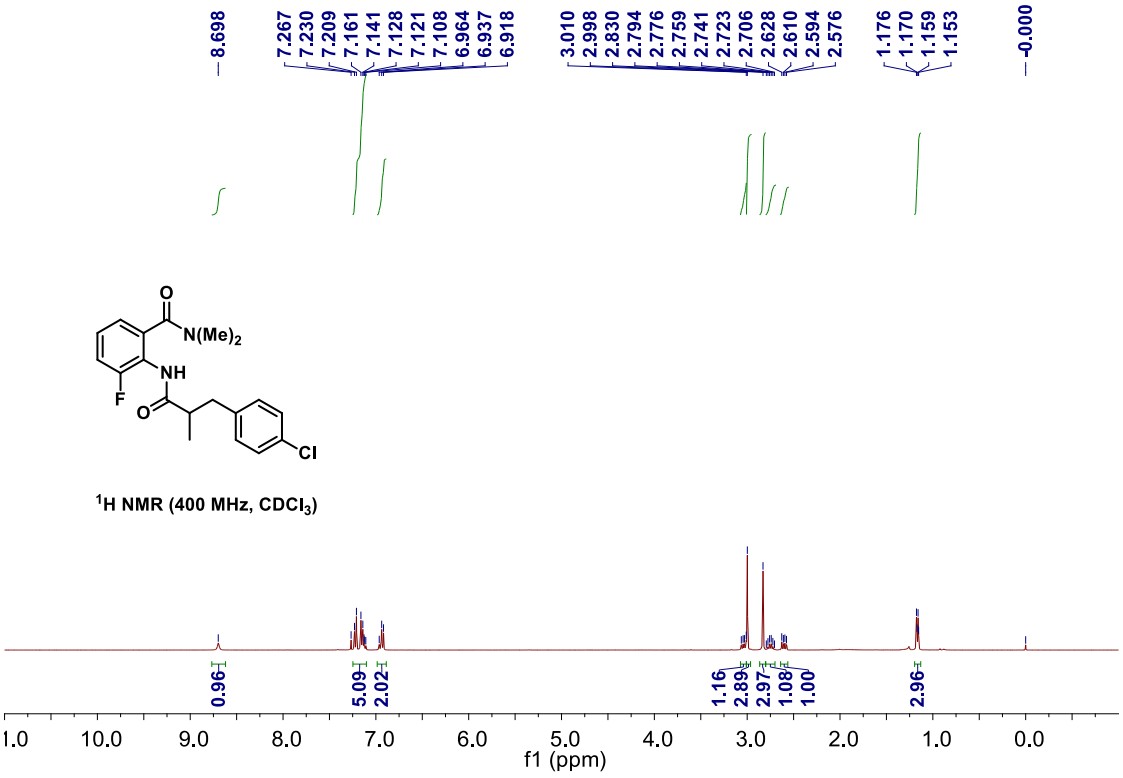
168.794
162.665
160.244
158.670
156.169
135.481
135.451
134.757
127.042
122.042
117.065
116.860
115.072
114.863
77.367
77.049
76.731
43.154
39.258
39.013
34.932
17.486
N(Me)2
NH
F
O
F
13C NMR (101 MHz, CDCl3)
f1 (ppm)

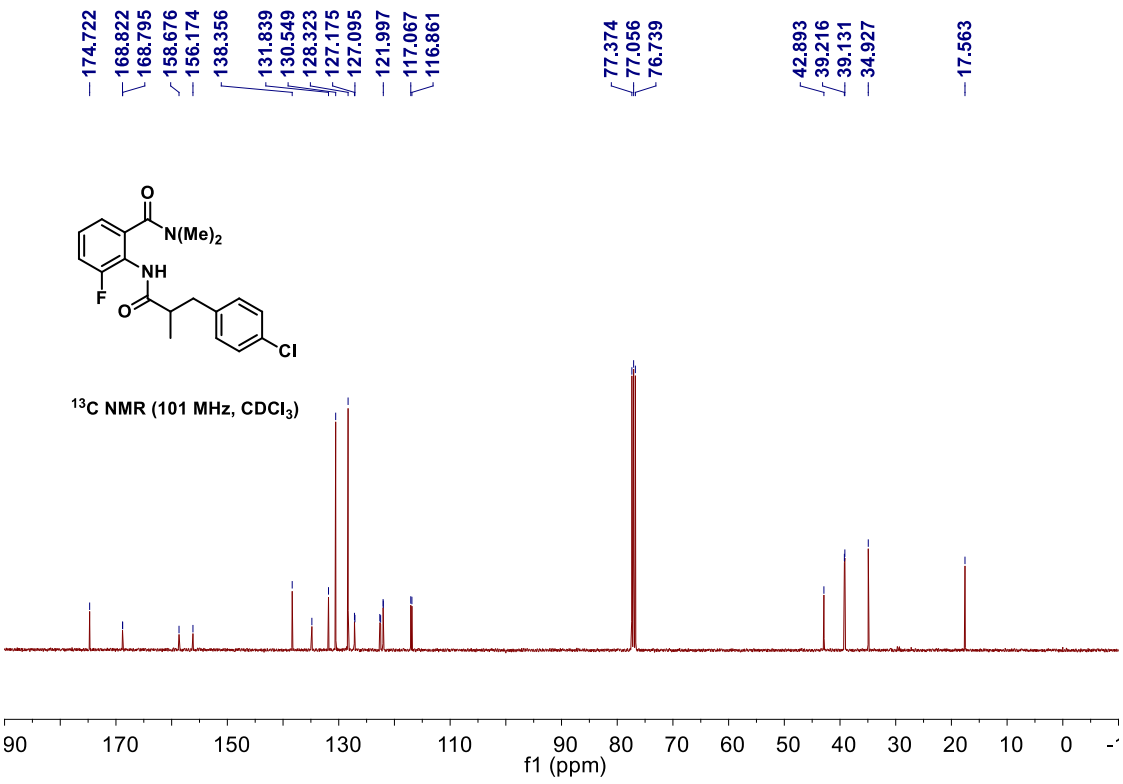
3l$_{di}$


8.024
7.169
7.148
7.129
7.109
7.046
7.004
6.960
6.939
6.917
6.870
3.059
3.038
3.026
3.005
2.897
2.828
2.807
2.792
2.773
2.761
2.748
2.728
2.715
O
N(Me)2
NH
F
O
F
F
1H NMR (400 MHz, CDCl3)
1.04
5.14
1.14
3.98
1.00
1.99
2.94
6.02
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

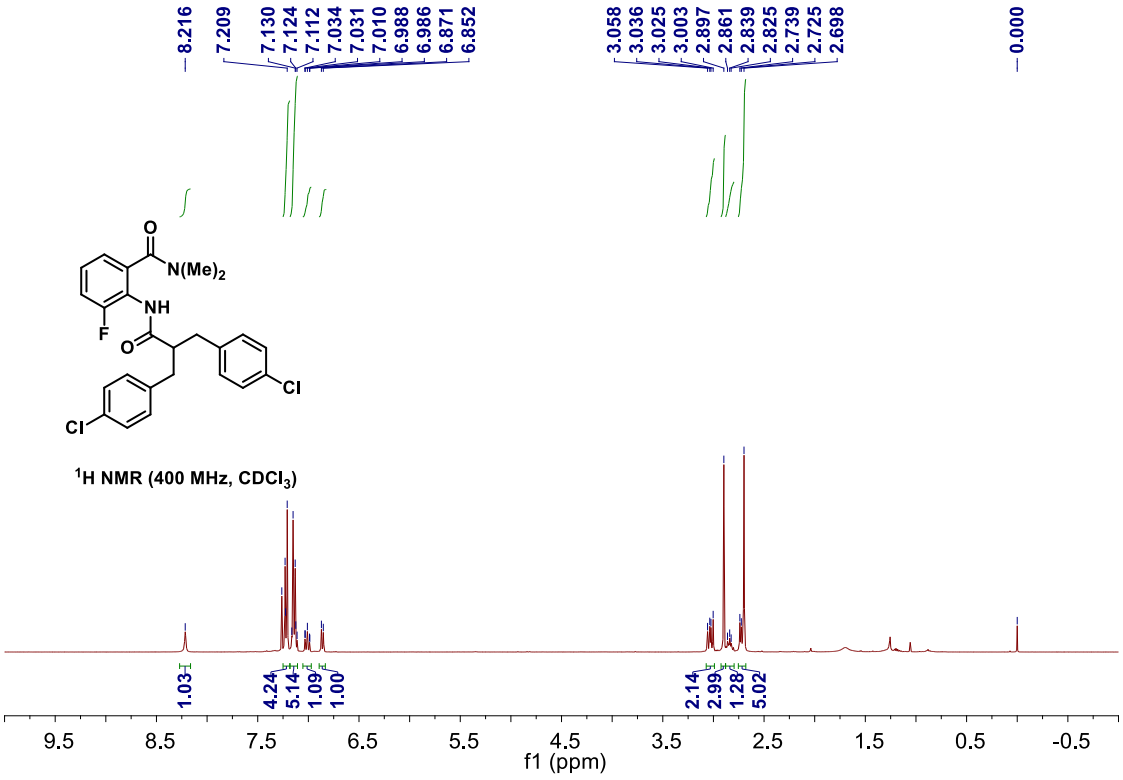

172.271
168.412
160.287
158.664
156.142
135.015
130.629
130.551
127.084
127.003
122.084
117.536
117.330
115.231
115.022
77.353
77.036
76.718
52.191
39.163
37.830
34.852
O
N(Me)2
NH
F
O
F
F
13C NMR (101 MHz, CDCl3)
90
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

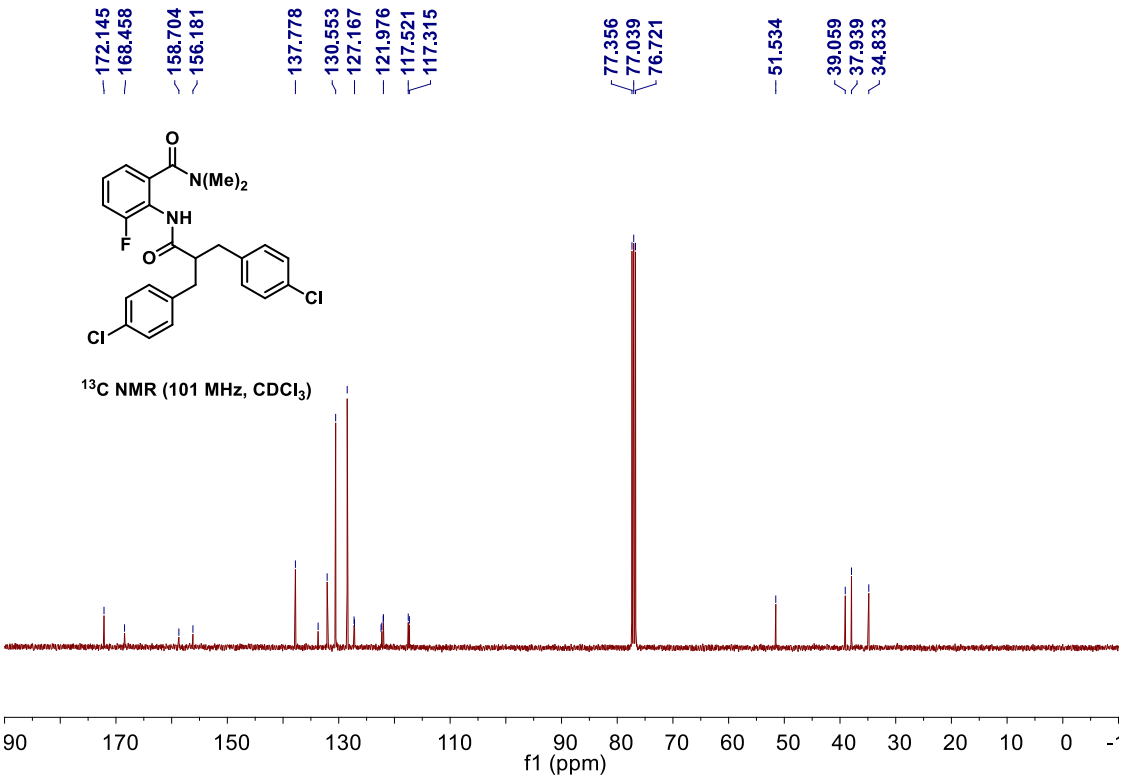
3m$_{mono}$


8.698
7.267
7.230
7.209
7.161
7.141
7.128
7.121
7.108
6.964
6.937
6.918
3.010
2.998
2.830
2.794
2.776
2.759
2.741
2.723
2.706
2.628
2.610
2.594
2.576
1.176
1.170
1.159
1.153
-0.000
O
N(Me)2
NH
F
O
Cl
1H NMR (400 MHz, CDCl3)
0.96
5.09
2.02
1.16
2.89
2.97
1.08
1.00
2.96
f1 (ppm)

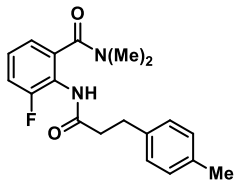

174.722
168.822
168.795
158.676
156.174
138.356
131.839
130.549
128.323
127.175
127.095
121.997
117.067
116.861
77.374
77.056
76.739
42.893
39.216
39.131
34.927
17.563
O
N(Me)2
NH
F
O
Cl
13C NMR (101 MHz, CDCl3)
f1 (ppm)

3m$_{di}$

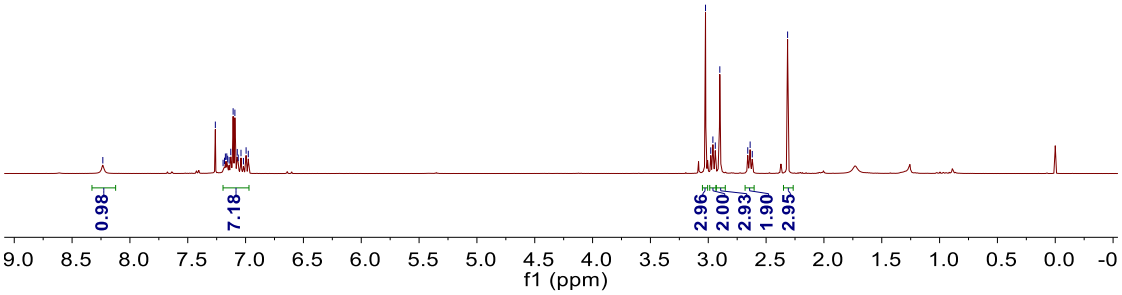

8.216
7.209
7.130
7.124
7.112
7.034
7.031
7.010
6.988
6.986
6.871
6.852
3.058
3.036
3.025
3.003
2.897
2.861
2.839
2.825
2.739
2.725
2.698
0.000
O
N(Me)2
NH
F
O
Cl
Cl
1H NMR (400 MHz, CDCl3)
1.03
4.24
5.14
1.09
1.00
2.14
2.99
1.28
5.02
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

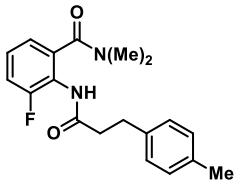

172.145
168.458
158.704
156.181
137.778
130.553
127.167
121.976
117.521
117.315
77.356
77.039
76.721
51.534
39.059
37.939
34.833
O
N(Me)2
NH
F
O
Cl
Cl
13C NMR (101 MHz, CDCl3)
90
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

3n

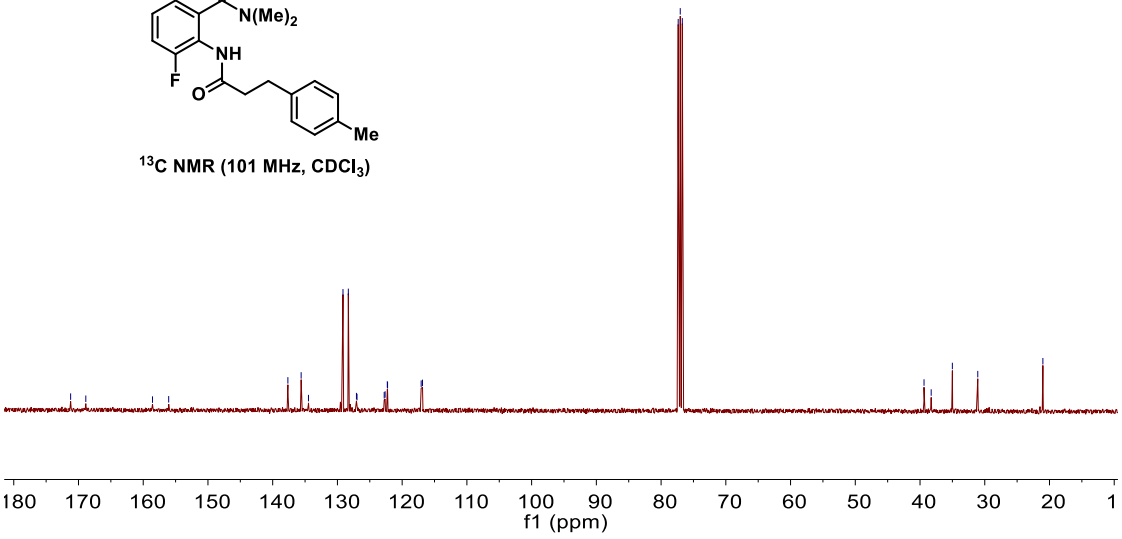


^{1}H NMR (400 MHz, $CDCl_3$)

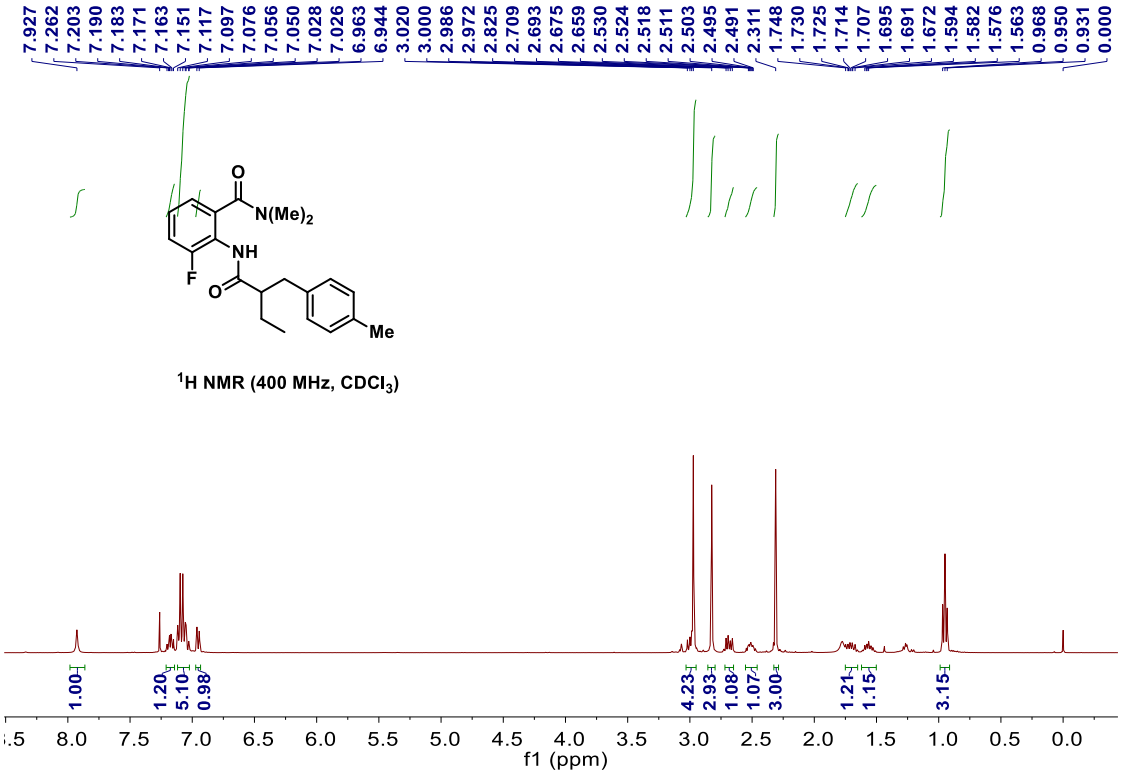




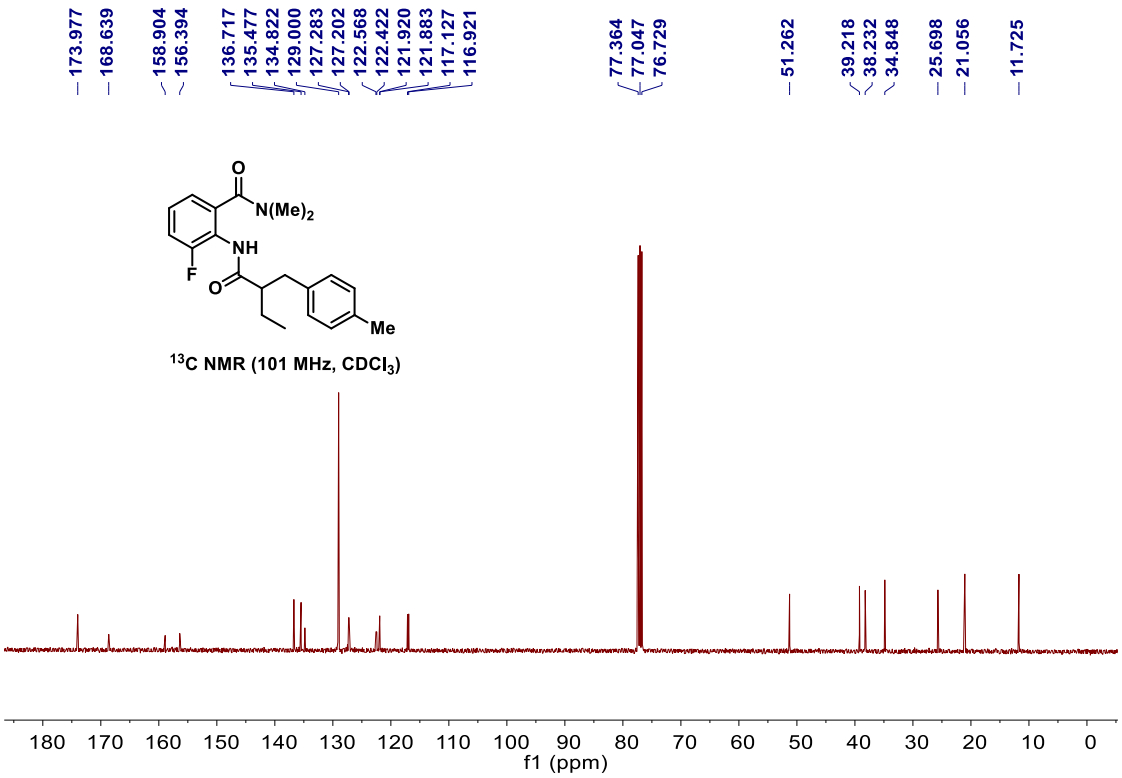
^{13}C NMR (101 MHz, $CDCl_3$)



3o

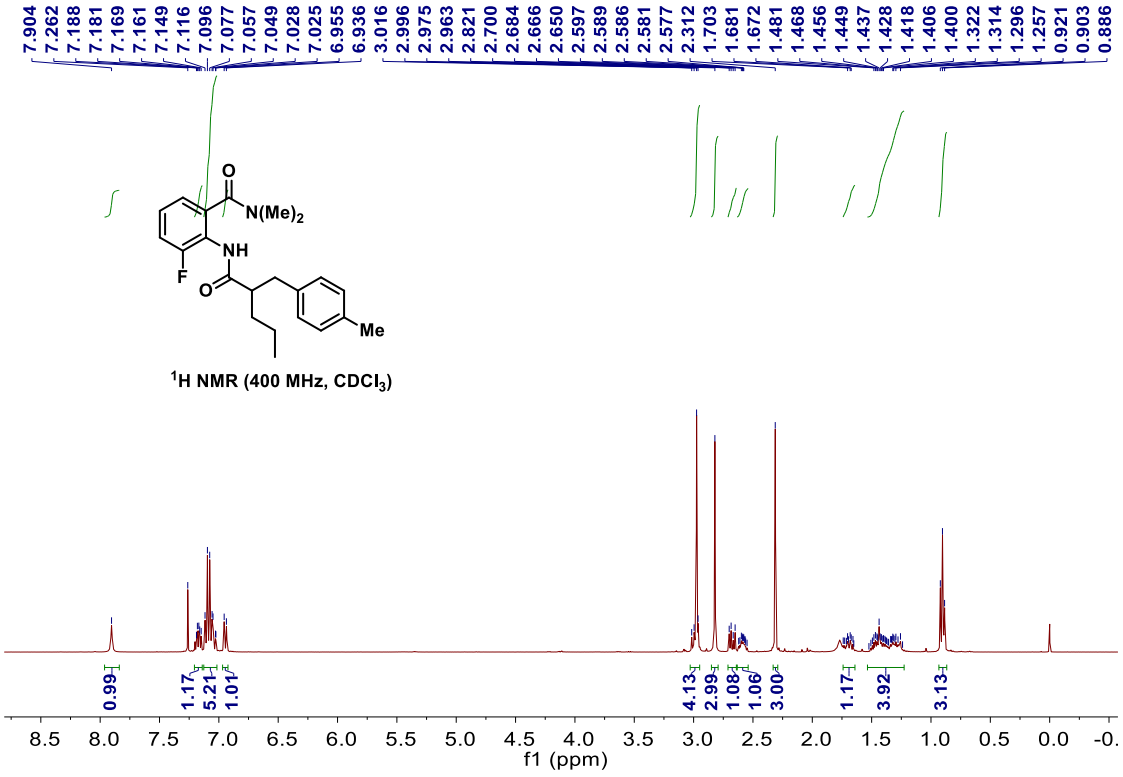


^{1}H NMR (400 MHz, $CDCl_3$)

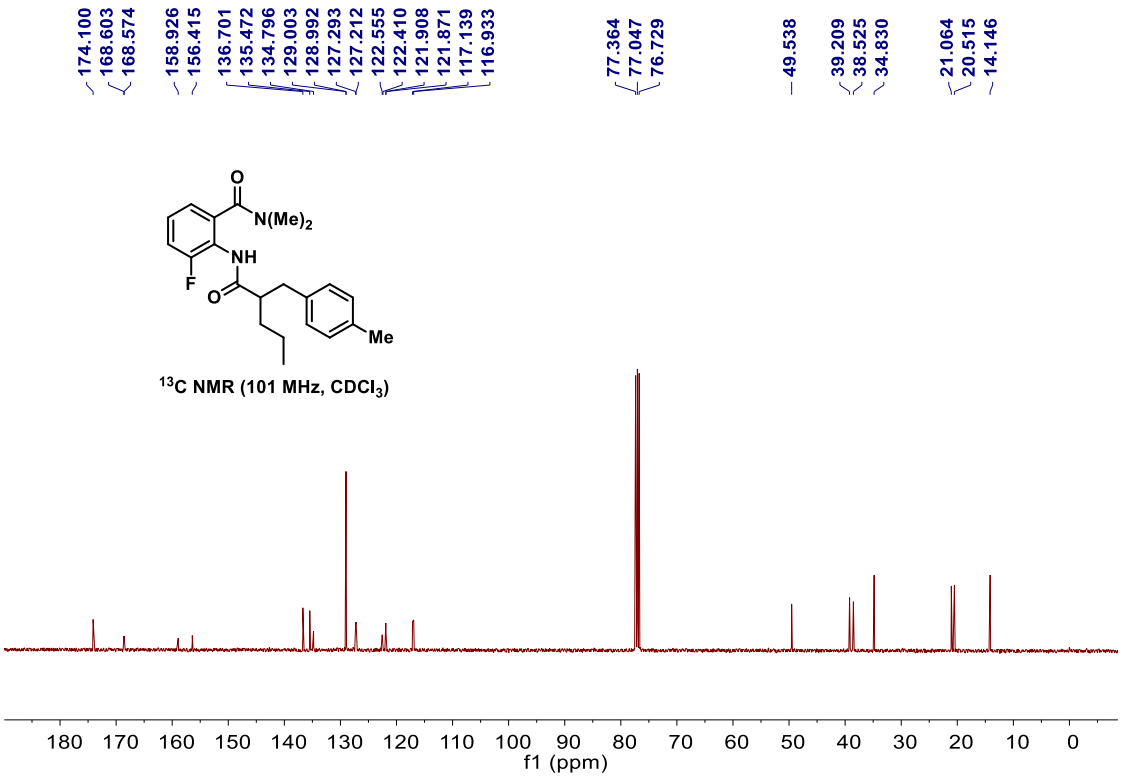


^{13}C NMR (101 MHz, $CDCl_3$)

3p

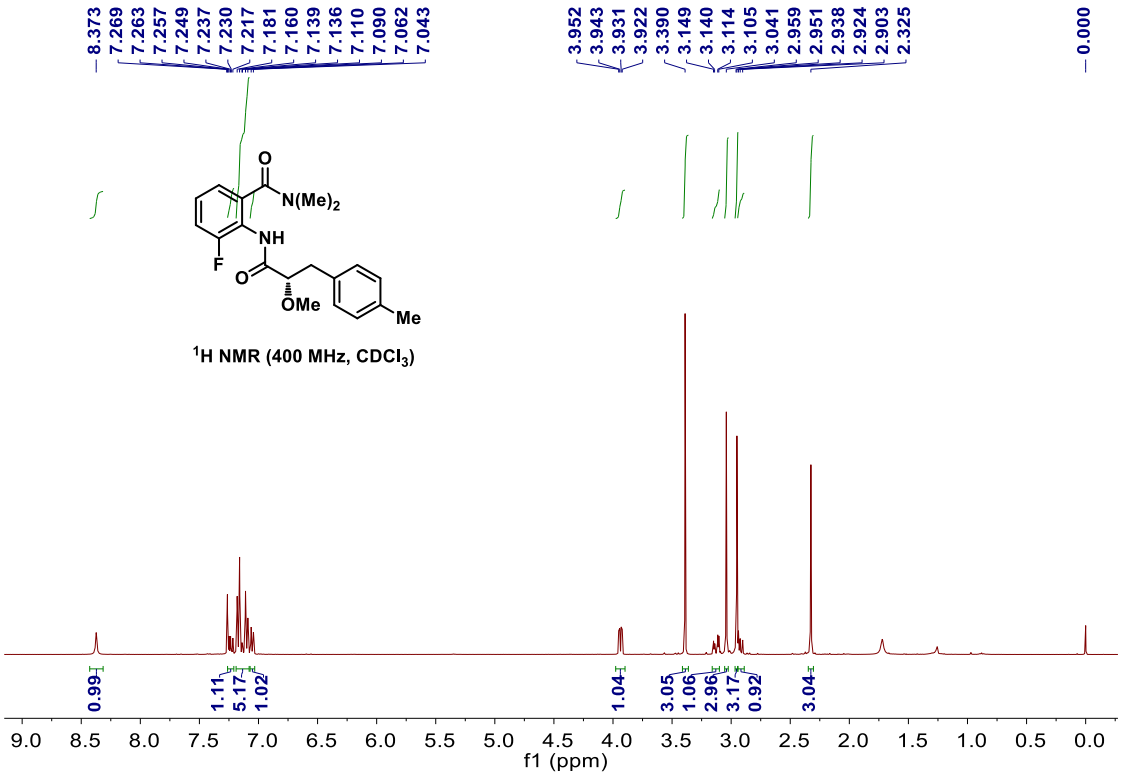


^{1}H NMR (400 MHz, $CDCl_3$)

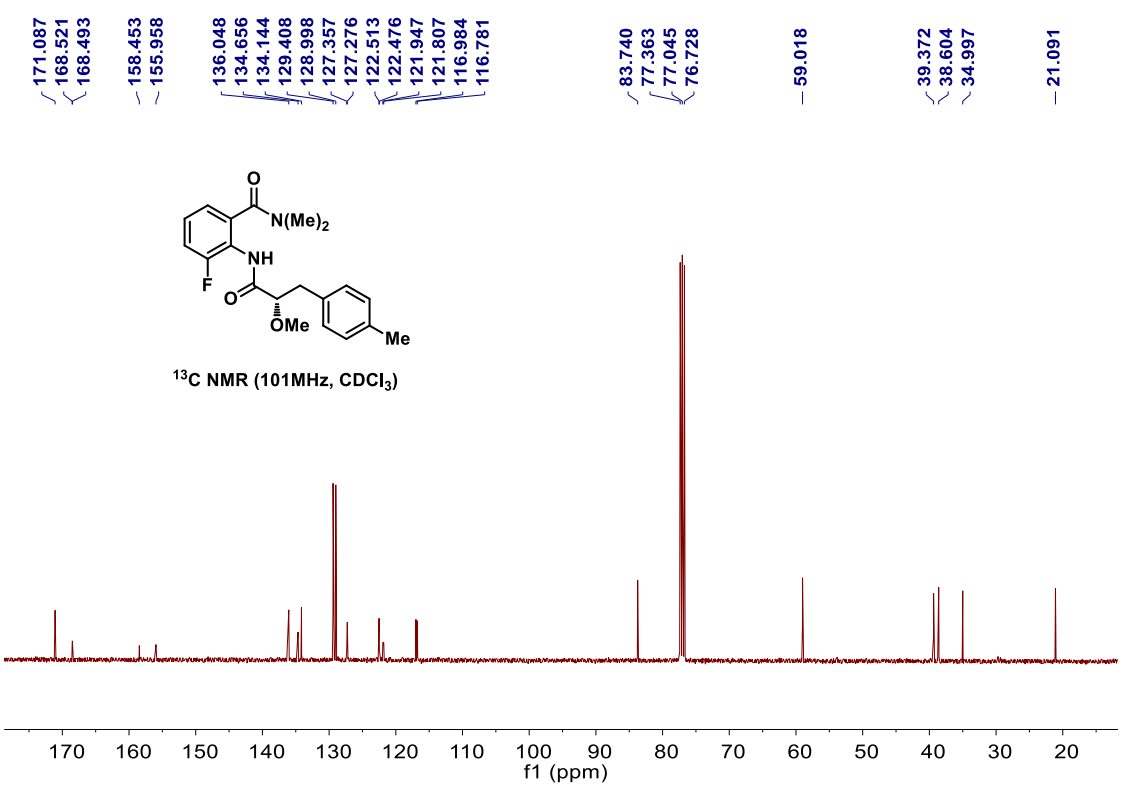


^{13}C NMR (101 MHz, $CDCl_3$)

3q

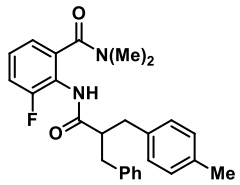


^{1}H NMR (400 MHz, $CDCl_3$)

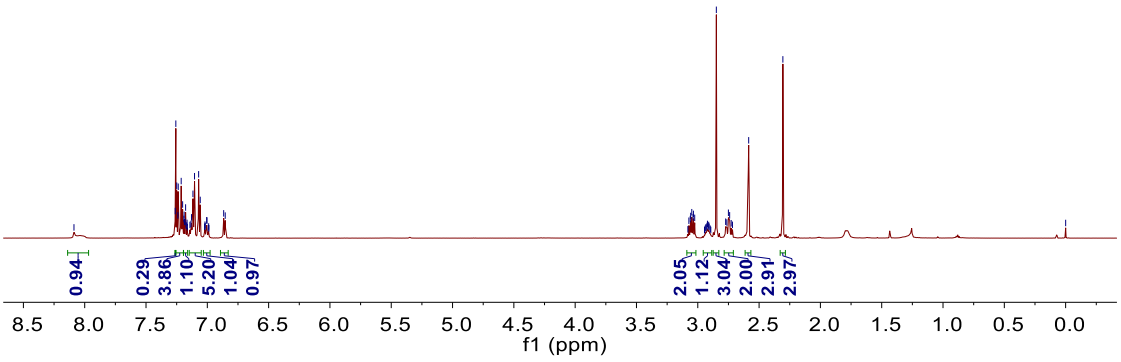


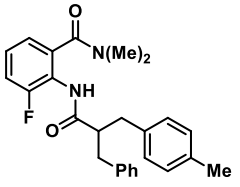
^{13}C NMR (101MHz, $CDCl_3$)

3r

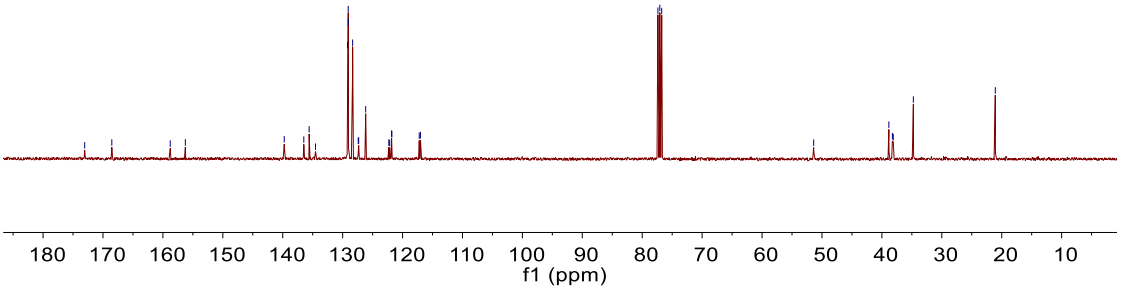


^{1}H NMR (600 MHz, $CDCl_3$)

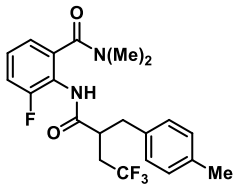




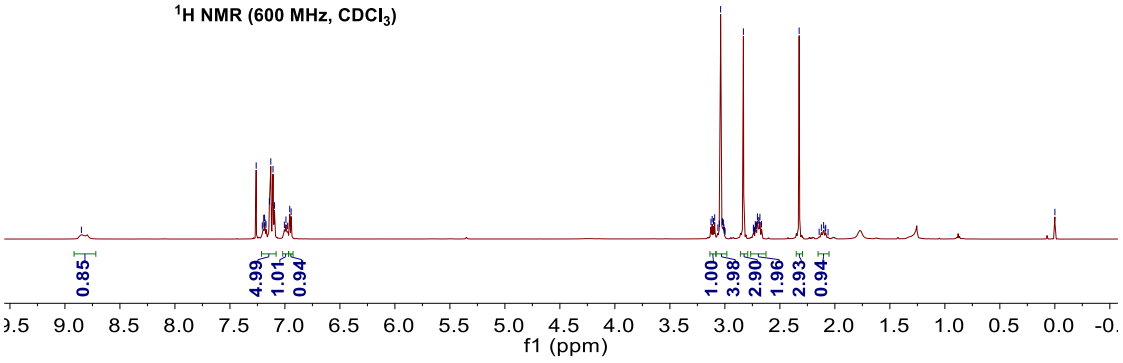
^{13}C NMR (101 MHz, $CDCl_3$)

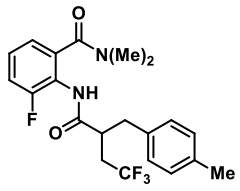


3s

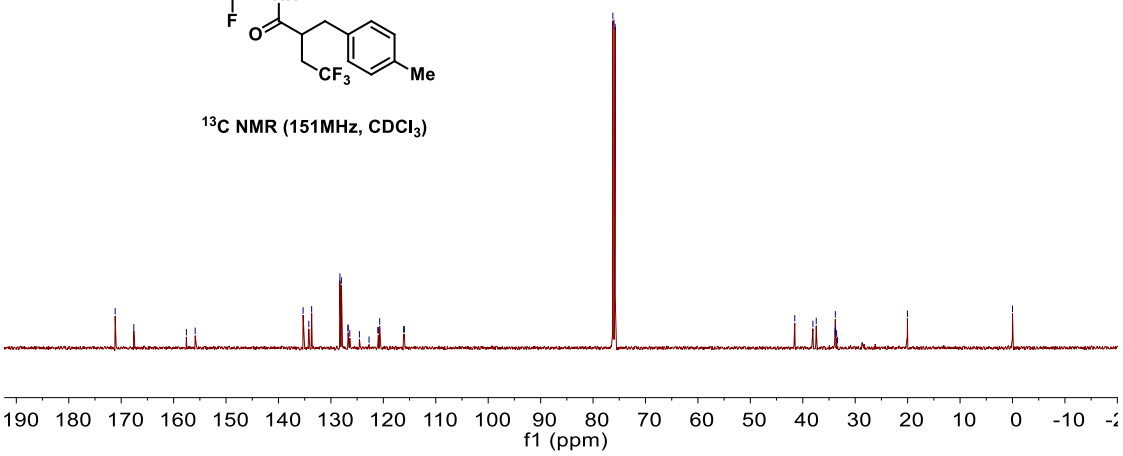


^{1}H NMR (600 MHz, $CDCl_3$)

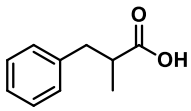




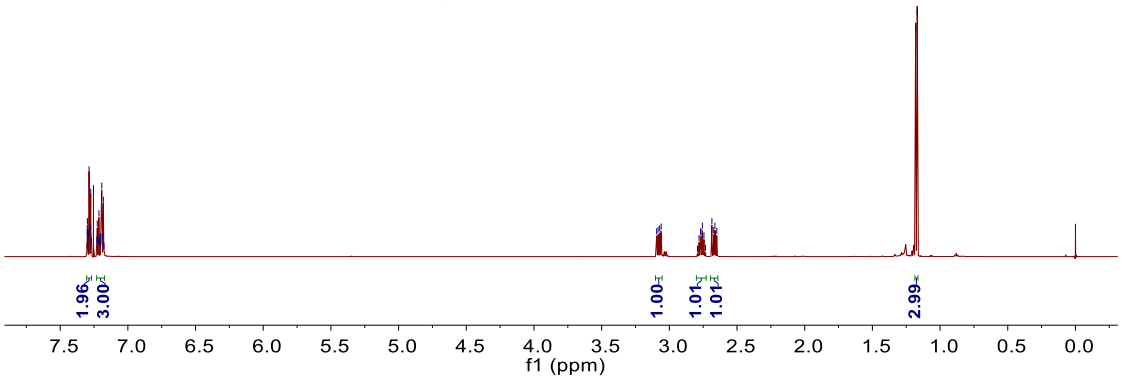
^{13}C NMR (151MHz, $CDCl_3$)

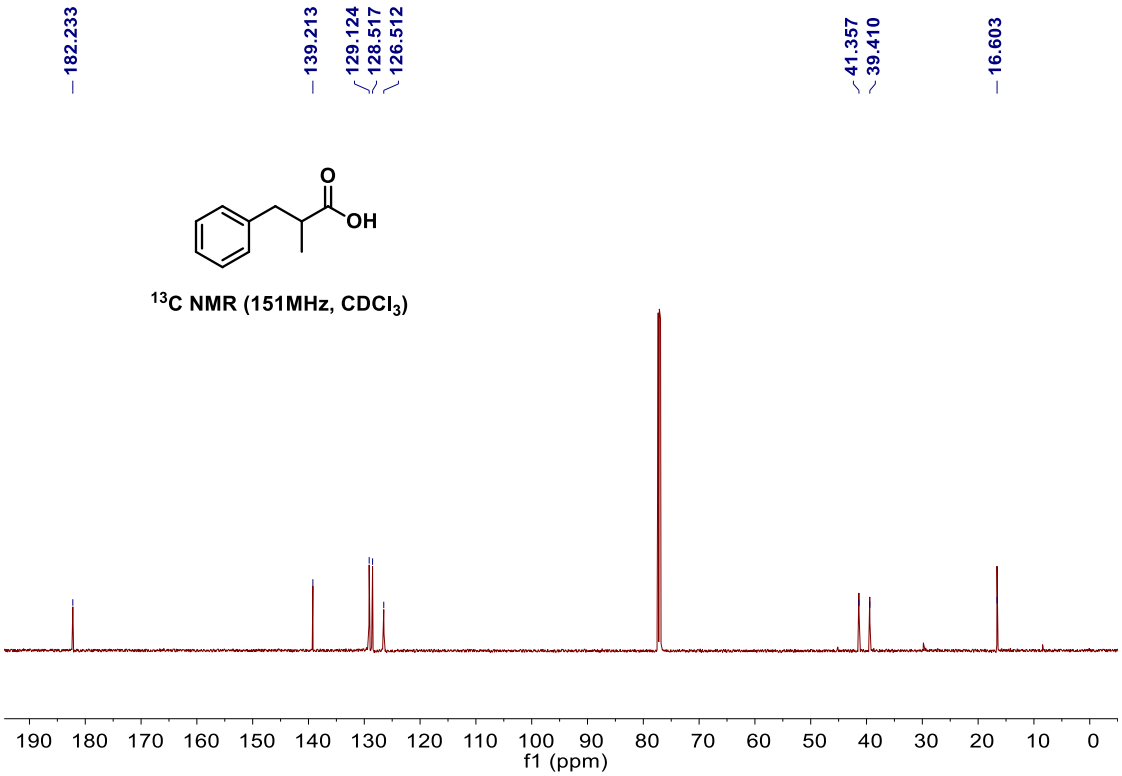


4h



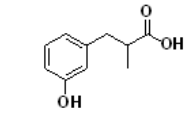
^{1}H NMR (600 MHz, $CDCl_3$)



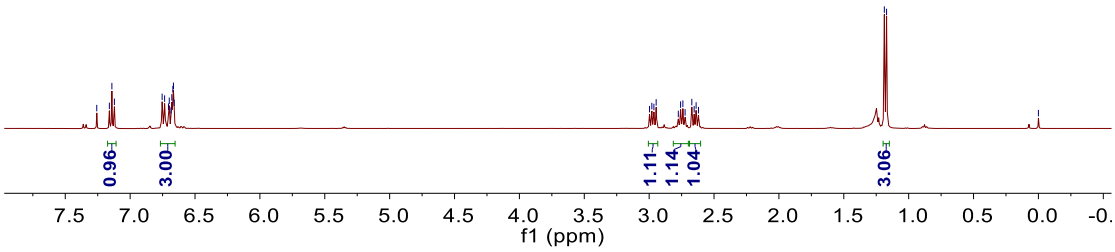


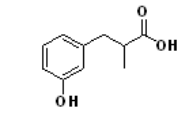
^{13}C NMR (151MHz, $CDCl_3$)

4i

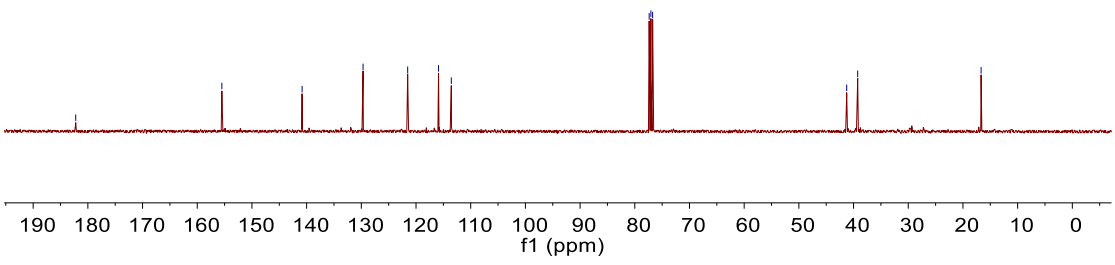


^{1}H NMR (400 MHz, $CDCl_3$)

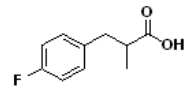




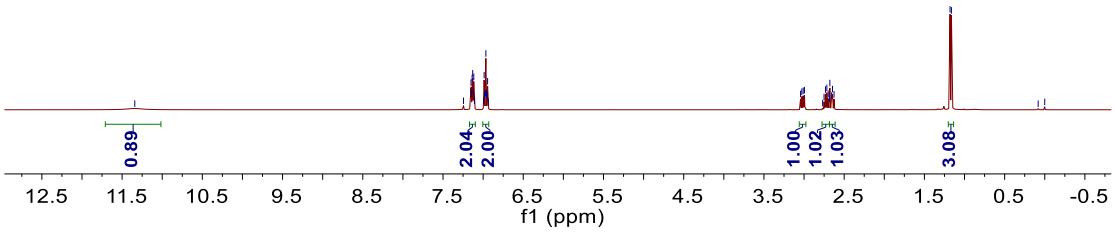
^{13}C NMR (101 MHz, $CDCl_3$)

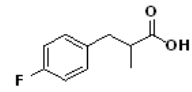


4l

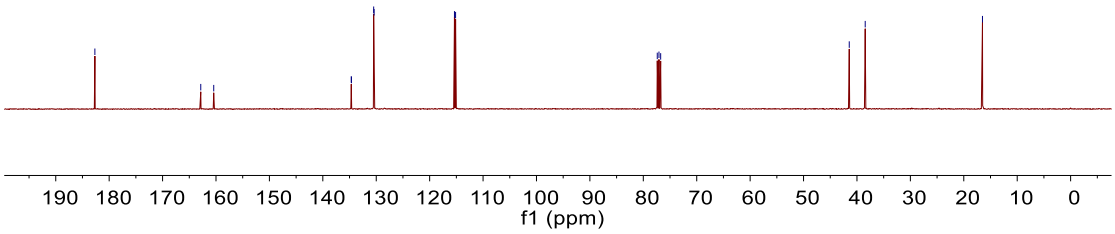


^{1}H NMR (400 MHz, CDCl$_3$)

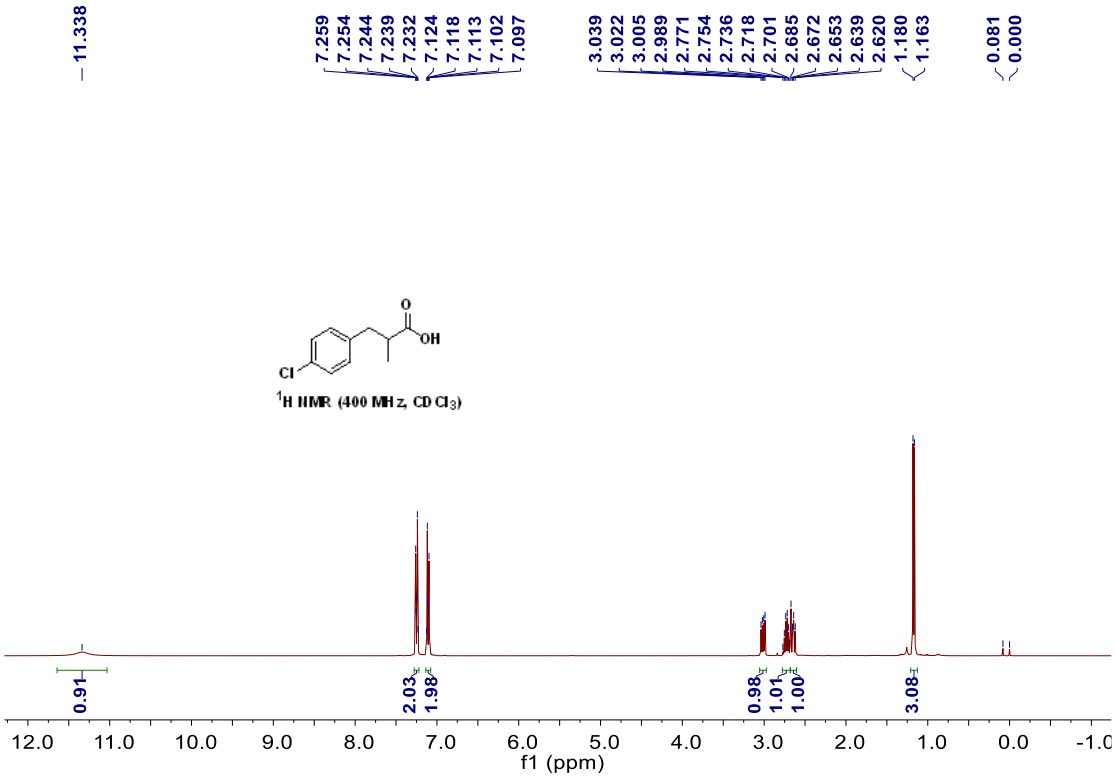


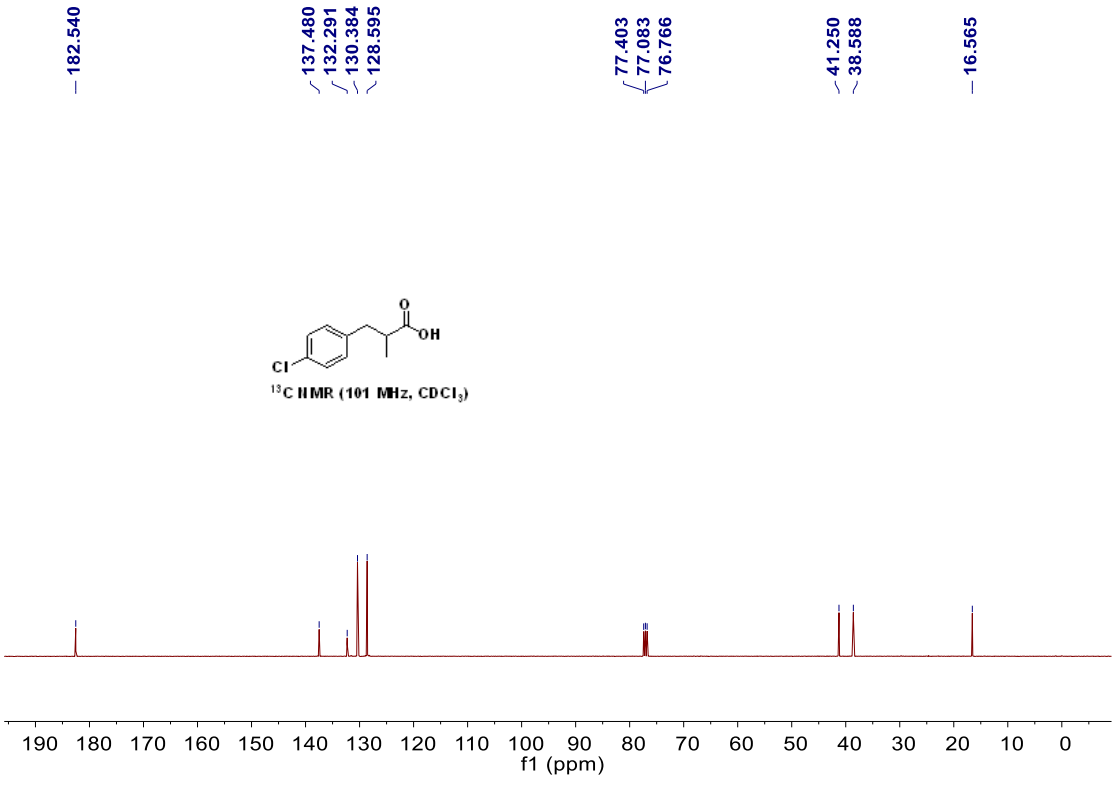


^{13}C NMR (101 MHz, CDCl$_3$)

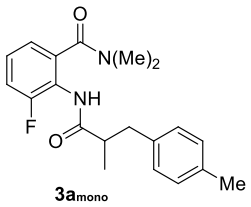


4m


11.338
7.259
7.254
7.244
7.239
7.232
7.124
7.118
7.113
7.102
7.097
3.039
3.022
3.005
2.989
2.771
2.754
2.736
2.718
2.701
2.685
2.672
2.653
2.639
2.620
1.180
1.163
0.081
0.000
Cl
OH
O
^{1}H NMR (400 MHz, CDCl$_3$)
0.91
2.03
1.98
0.98
1.01
1.00
3.08
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
f1 (ppm)

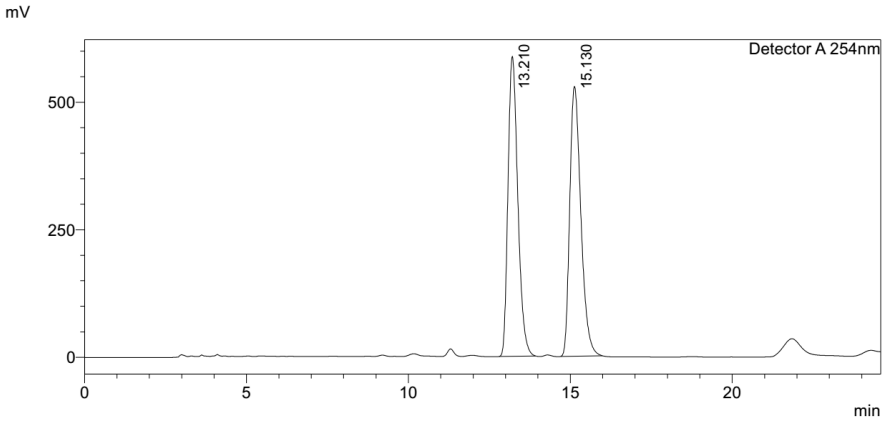

182.540
137.480
132.291
130.384
128.595
77.403
77.083
76.766
41.250
38.588
16.565
Cl
OH
O
^{13}C NMR (101 MHz, CDCl$_3$)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

5. HPLC traces on Chiral Stationary Phase



3a$_{mono}$

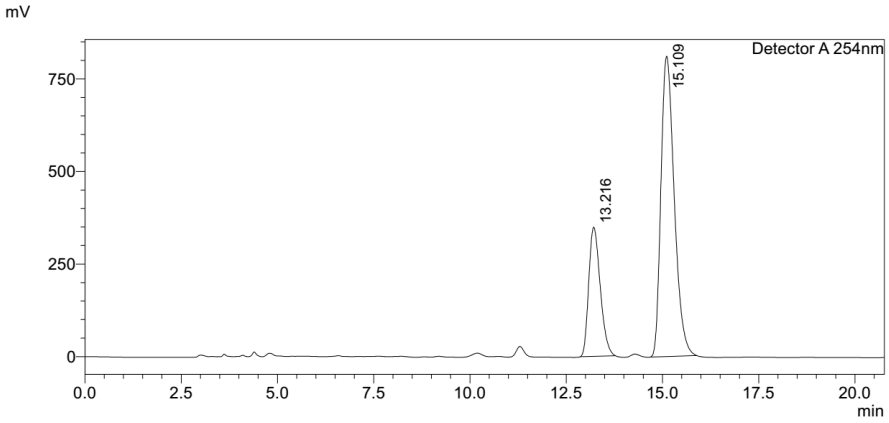
Racemic 3a$_{mono}$:



Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.
1	13.210	12395953	587380	49.619
2	15.130	12586401	528477	50.381
Total		24982354	1115857	

Chiral 3a$_{mono}$:



Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.
1	13.216	7251034	348600	27.116
2	15.109	19489880	811131	72.884
Total		26740914	1159731	