

Supporting Information

Structure-Activity Relationships and Evaluation of 2-(Heteroaryl-Cycloalkyl)-1*H*-Indoles as Tauopathy Positron Emission Tomography Radiotracers

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Scheme S1. Synthesis of compounds 29 – 36

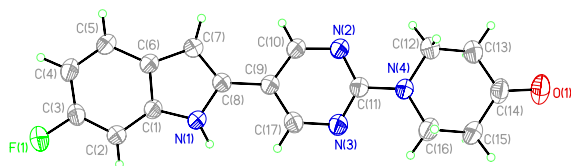
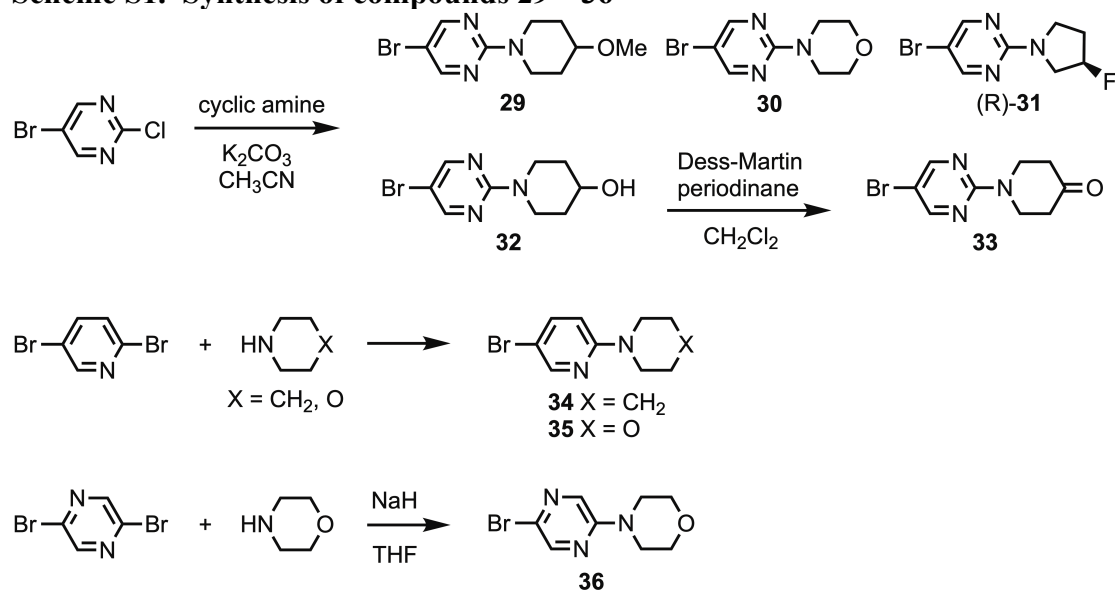
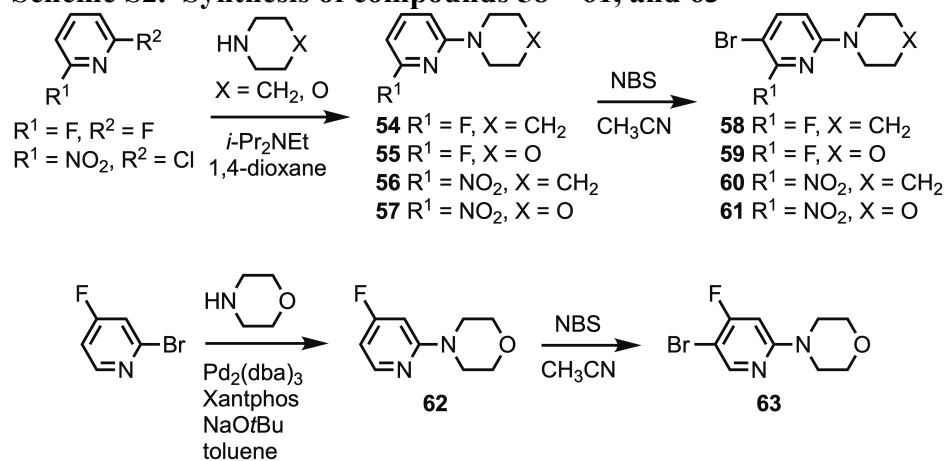


Figure S1. X-ray crystal structure of **44** (CCDC Deposition Number 2403956).

Scheme S2. Synthesis of compounds 58 – 61, and 63



Scheme S3. Synthesis of compounds 64 – 68

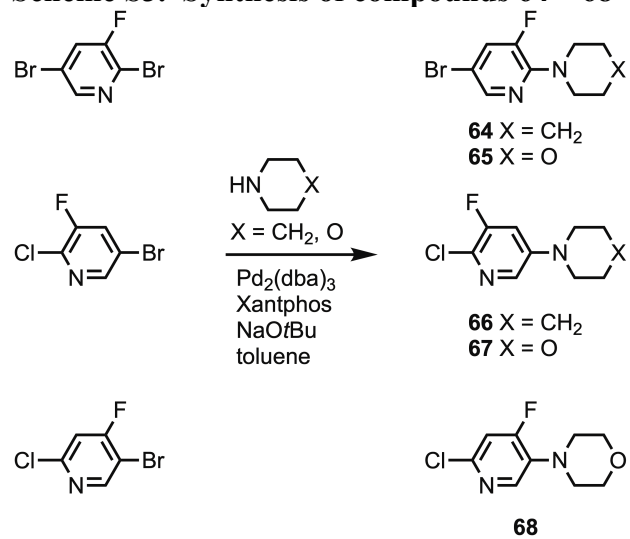
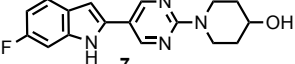
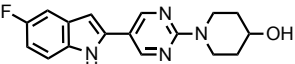
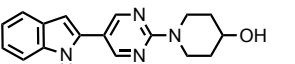
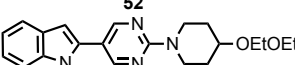
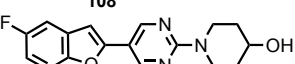


Table S1. Inhibition Constant (K_i) Values of Candidate Ligands versus [^3H]7, [^3H]8, and [^3H]3 in AD, PSP, and CBD Brain Tissue Homogenates.^a

Cmpd	[^3H]7			[^3H]8			[^3H]3		
	AD	K_i (nM)	CBD	AD	K_i (nM)	CBD	AD	K_i (nM)	CBD
tissue	tissue	tissue	tissue	tissue	tissue	tissue	tissue	tissue	tissue
7	12±7.3 ^b	24	22±12 ^b	6.7	15	14	18 ^e	20 ^e	22 ^e
8	8.4	13	11	7.7±0.6 ^c	8.5±1.2 ^d	11±1.3 ^d	22 ^e	18 ^e	19 ^e
9	11	8.9	8.9	10	11	15	33	37	40
21	3.5	6.2	6.3	7.7	9.2	12	27	26	28
22	11	14	11	14	18	15	35	37	47
23	37	23	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
24	120	129	n.d.	74	76	n.d.	n.d.	n.d.	n.d.
27	9.4	8.9	9.0	11	13	10	26	33	38
28	39	32	n.d.	34	31	n.d.	n.d.	n.d.	n.d.
42	5.0	10	8.2	9.5	10	14	24	19	22
(R)-43	16	14	15	17	23	20	48	41	46
44	12	13	17	17	14	15	35	31	36
45	4.6	4.6	6.2	4.9	5.2	5.9	25	28	27
46	9.5	7.9	11	13	11	12	25	24	26
49	45	91	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
52	11	24	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
53	21	20	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
74	8.0	6.6	6.4	7.8	7.7	7.8	29	30	33
75	9.2	10	13	6.5	10	11	22	28	30
78	n.d.	n.d.	n.d.	9.2	9.5	10	n.d.	n.d.	n.d.
79	n.d.	n.d.	n.d.	5.0	6.3	7.7	n.d.	n.d.	n.d.
81	n.d.	n.d.	n.d.	29	34	26	n.d.	n.d.	n.d.
87	n.d.	n.d.	n.d.	8.0	7.3	8.2	n.d.	n.d.	n.d.
88	n.d.	n.d.	n.d.	11	12	11	n.d.	n.d.	n.d.
89	n.d.	n.d.	n.d.	7.5	7.8	8.7	n.d.	n.d.	n.d.
90	n.d.	n.d.	n.d.	24	20	18	n.d.	n.d.	n.d.
94	n.d.	n.d.	n.d.	13	15	12	n.d.	n.d.	n.d.
95	n.d.	n.d.	n.d.	16	17	14	n.d.	n.d.	n.d.
96	n.d.	n.d.	n.d.	7.9	8.6	9.5	n.d.	n.d.	n.d.
98	n.d.	n.d.	n.d.	15	20	16	n.d.	n.d.	n.d.
103	n.d.	n.d.	n.d.	21	25	22	n.d.	n.d.	n.d.
104	n.d.	n.d.	n.d.	17	20	20	n.d.	n.d.	n.d.
105	n.d.	n.d.	n.d.	50	44	49	n.d.	n.d.	n.d.
106	n.d.	n.d.	n.d.	115	65	56	n.d.	n.d.	n.d.
108	19	20	39	20	23	30	n.d.	n.d.	n.d.
109	22	32	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

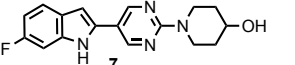
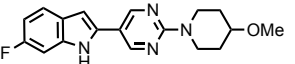
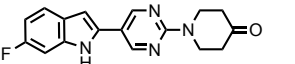
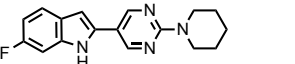
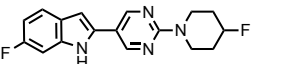
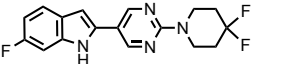
^{a)} $n = 1$, except where noted. n.d. = not determined. ^{b)} $n = 2$. ^{c)} $n = 5$. ^{d)} $n = 4$. ^{e)} Data from reference 46.

Table S2. Comparison of Inhibition Constant (K_i) Values of Pyrimidine-4-Hydroxypiperidine Compounds in AD, PSP, and CBD Brain Tissue Homogenates.^a

Compound	^[3H] 7			^[3H] 8		
	K_i (nM)			K_i (nM)		
	AD tissue	PSP tissue	CBD tissue	AD tissue	PSP tissue	CBD tissue
 7	12±7.3 (<i>n</i> = 2)	24	22±12 (<i>n</i> = 2)	6.7	15	14
 53	21	20	n.d.	n.d.	n.d.	n.d.
 52	11	24	n.d.	n.d.	n.d.	n.d.
 108	19	20	39	20	23	30
 49	45	91	n.d.	n.d.	n.d.	n.d.

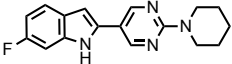
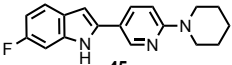
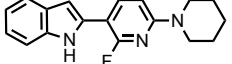
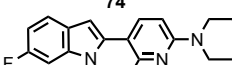
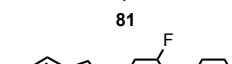
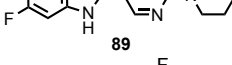
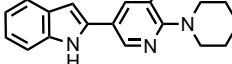
^a) *n* = 1, except where noted. n.d. = not determined.

Table S3. Comparison of Inhibition Constant (K_i) Values of Compounds Where Substituents on the Piperidine Ring Are Varied in AD, PSP, and CBD Brain Tissue Homogenates.^a

Compound	^[3H] 7			^[3H] 8			^[3H] 3		
	K_i (nM)			K_i (nM)			K_i (nM)		
	AD tissue	PSP tissue	CBD tissue	AD tissue	PSP tissue	CBD tissue	AD tissue	PSP tissue	CBD tissue
 7	12±7.3 (<i>n</i> = 2)	24	22±12 (<i>n</i> = 2)	6.7	15	14	18	20	22
 42	5.0	10	8.2	9.5	10	14	24	19	22
 44	12	13	17	17	14	15	35	31	36
 21	3.5	6.2	6.3	7.7	9.2	12	27	26	28
 22	11	14	11	14	18	15	35	37	47
 23	37	23	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

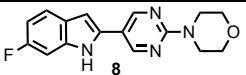
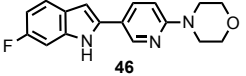
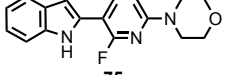
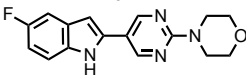
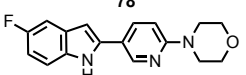
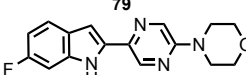
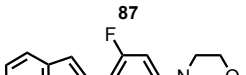
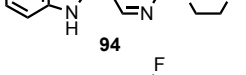
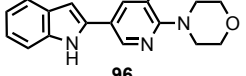
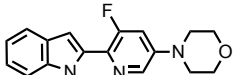
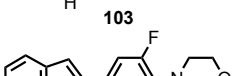
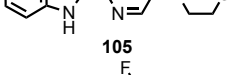
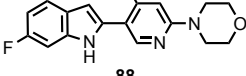
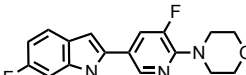
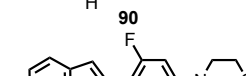
^a) *n* = 1, except where noted. n.d. = not determined.

Table S4. Comparison of Inhibition Constant (K_i) Values of Piperidine-Substituted Compounds in AD, PSP, and CBD Brain Tissue Homogenates.^a

Compound	^[3H] 7			^[3H] 8			^[3H] 3		
	AD tissue	PSP tissue	CBD tissue	AD tissue	PSP tissue	CBD tissue	AD tissue	PSP tissue	CBD tissue
 21	3.5	6.2	6.3	7.7	9.2	12	27	26	28
 45	4.6	4.6	6.2	4.9	5.2	5.9	25	28	27
 74	8.0	6.6	6.4	7.8	7.7	7.8	29	30	33
 81	n.d.	n.d.	n.d.	29	34	26	n.d.	n.d.	n.d.
 89	n.d.	n.d.	n.d.	7.5	7.8	8.7	n.d.	n.d.	n.d.
 95	n.d.	n.d.	n.d.	16	17	14	n.d.	n.d.	n.d.
 98	n.d.	n.d.	n.d.	15	20	16	n.d.	n.d.	n.d.

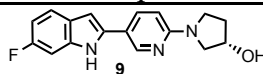
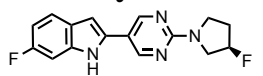
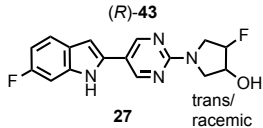
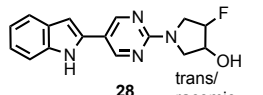
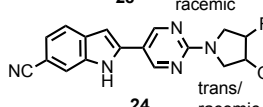
^a) $n = 1$. n.d. = not determined.

Table S5. Comparison of Inhibition Constant (K_i) Values of Morpholine-Substituted Compounds in AD, PSP, and CBD Brain Tissue Homogenates.^a

Compound	^{[3]H} 7			^{[3]H} 8			^{[3]H} 3		
	AD tissue	PSP tissue	CBD tissue	AD tissue	PSP tissue	CBD tissue	AD tissue	PSP tissue	CBD tissue
	8.4	13	11	7.7±0.6 (n = 5)	8.5±1.2 (n = 4)	11±1.3 (n = 4)	22	18	19
	9.5	7.9	11	13	11	12	25	24	26
	9.2	10	13	6.5	10	11	22	28	30
	n.d.	n.d.	n.d.	9.2	9.5	10	n.d.	n.d.	n.d.
	n.d.	n.d.	n.d.	5.0	6.3	7.7	n.d.	n.d.	n.d.
	n.d.	n.d.	n.d.	8.0	7.3	8.2	n.d.	n.d.	n.d.
	n.d.	n.d.	n.d.	13	15	12	n.d.	n.d.	n.d.
	n.d.	n.d.	n.d.	7.9	8.6	9.5	n.d.	n.d.	n.d.
	n.d.	n.d.	n.d.	21	25	22	n.d.	n.d.	n.d.
	n.d.	n.d.	n.d.	50	44	49	n.d.	n.d.	n.d.
	n.d.	n.d.	n.d.	11	12	11	n.d.	n.d.	n.d.
	n.d.	n.d.	n.d.	24	20	18	n.d.	n.d.	n.d.
	n.d.	n.d.	n.d.	17	20	20	n.d.	n.d.	n.d.
	n.d.	n.d.	n.d.	115	65	56	n.d.	n.d.	n.d.
	22	32	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

^a) n = 1, except where noted. n.d. = not determined.

Table S6. Comparison of Inhibition Constant (K_i) Values of Pyrrolidine-Substituted Compounds in AD, PSP, and CBD Brain Tissue Homogenates.^a

Compound	^[3H] 7			^[3H] 8			^[3H] 3		
	AD tissue	PSP tissue	CBD tissue	AD tissue	PSP tissue	CBD tissue	AD tissue	PSP tissue	CBD tissue
 9	11	8.9	8.9	10	11	15	33	37	40
 (R)-43	16	14	15	17	23	20	48	41	46
 27	9.4	8.9	9.0	11	13	10	26	33	38
 28	39	32	n.d.	34	31	n.d.	n.d.	n.d.	n.d.
 24	120	129	n.d.	74	76	n.d.	n.d.	n.d.	n.d.

^a) $n = 1$. n.d. = not determined.

Table S7. Inhibition Constant (K_i) Values of Selected Ligands versus ^[3H]5 in AD, PSP, and CBD Brain Tissue Homogenates, and versus ^[3H]PiB in AD Brain Tissue Homogenates.^a

Compound	^[3H] 5			^[3H] PiB
	AD tissue	PSP tissue	CBD tissue	AD tissue
21	182	185	189	49
27	214	219	273	n.d.
45	188	218	221	70
46	185	227	229	53
74	221	203	222	n.d.
75	203	335	360	61 ± 3 ^b

^a) $n = 1$, except where noted. ^b) $n = 3$. n.d. = not determined.

Table S8. Analytical HPLC data of compounds screened in the *in vitro* binding assays, ordered by k' values for each solvent ratio.^a

Compound	Purity (%)	solvent ratio	t_R (min)	k'
109	99.23	55:45	6.403	5.97
22	99.59	55:45	8.411	8.15
45	98.58	55:45	10.673	10.61
23	99.79	55:45	11.218	11.21
21	99.76	55:45	12.547	12.65
96	97.05	55:45	18.157	18.65
74	99.42	55:45	19.562	20.29
98	97.19	55:45	19.923	20.56
89	99.90	55:45	21.576	22.35
81	99.29	55:45	23.439	24.50
79	99.67	45:55	7.386	7.12
46	97.67	45:55	7.537	7.20
78	97.28	45:55	7.511	7.25
(R)-43	98.74	45:55	7.660	7.34
8	98.38	45:55	8.296	8.03
87	98.34	45:55	8.457	8.29
94	98.82	45:55	9.834	9.81
105	99.38	45:55	10.006	10.00
96	99.56	45:55	11.047	11.14
103	97.54	45:55	12.172	12.38
88	99.10	45:55	12.224	12.43
106	99.88	45:55	12.489	12.72
75	99.78	45:55	12.682	12.80
42	97.82	45:55	13.011	13.16
90	98.74	45:55	13.522	13.86
104	96.46	45:55	15.361	15.88
45	99.35	45:55	22.511	23.50
21	99.75	45:55	30.419	32.10
44	99.88	40:60	11.356	11.36
46	97.48	40:60	12.943	13.08
24	95.59	35:65	6.549	6.13
28	98.70	35:65	7.188	6.82
27	98.49	35:65	9.904	9.78
52	99.82	35:65	8.170	7.89
53	99.97	35:65	10.369	10.28
108	99.79	35:65	19.259	19.96
49	96.55	35:65	20.565	21.38
8	99.46	35:65	26.067	27.36

^a) Phenomenex Gemini, 5 μ m, NX-C18 110Å, 100 x 4.6 mm; (solvent ratio) v/v CH₃CN/0.1 M NH₄HCO₂ pH 4.2; 1 mL/min; 254 nm. k' = (retention time - void time)/void time. Void time was measured by injection of a sample of thiourea.

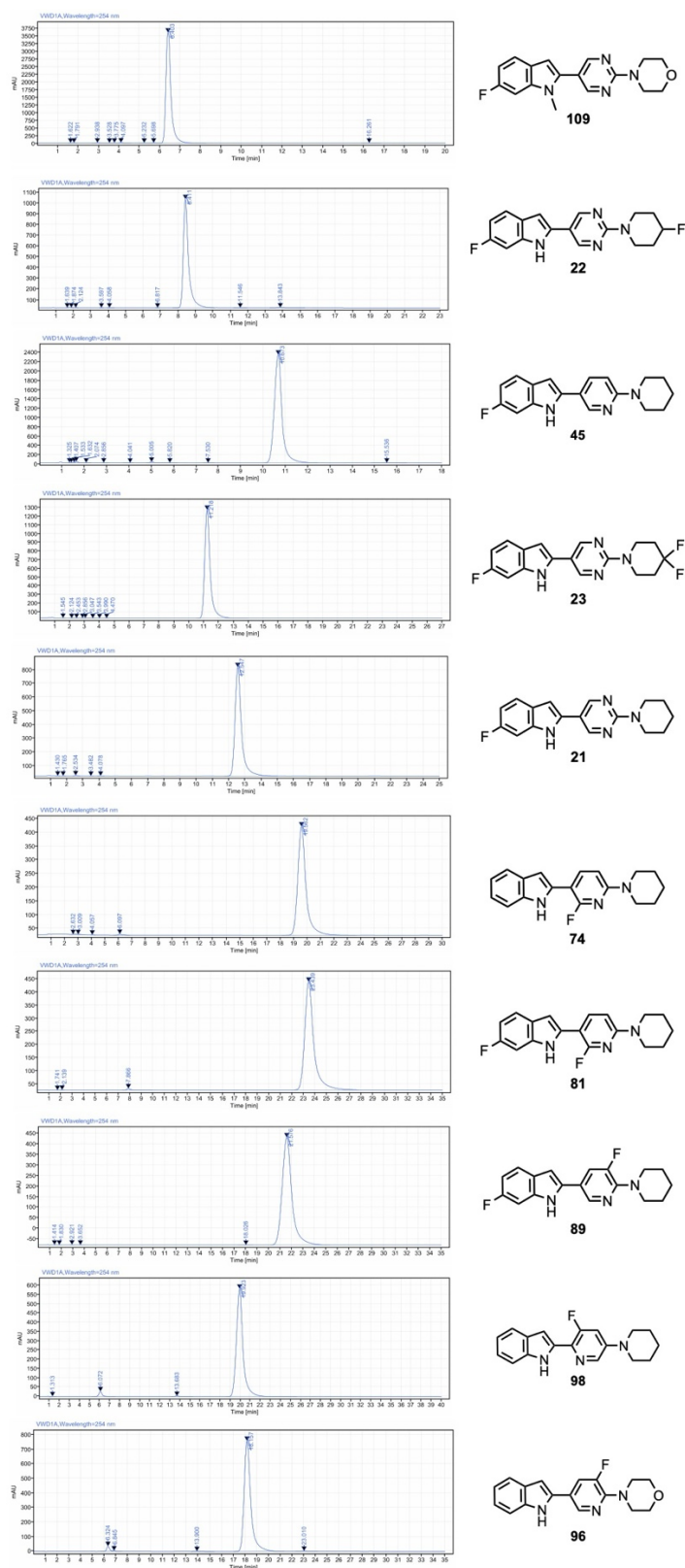


Figure S2. Analytical HPLC chromatograms of compounds **109**, **22**, **45**, **23**, **21**, **74**, **81**, **89**, **98**, and **96** (Phenomenex Gemini, 5 μ m, NX-C18 110Å, 100 x 4.6 mm; 55:45 v/v CH₃CN/0.1 M NH₄HCO₂ pH 4.2; 1 mL/min; 254 nm).

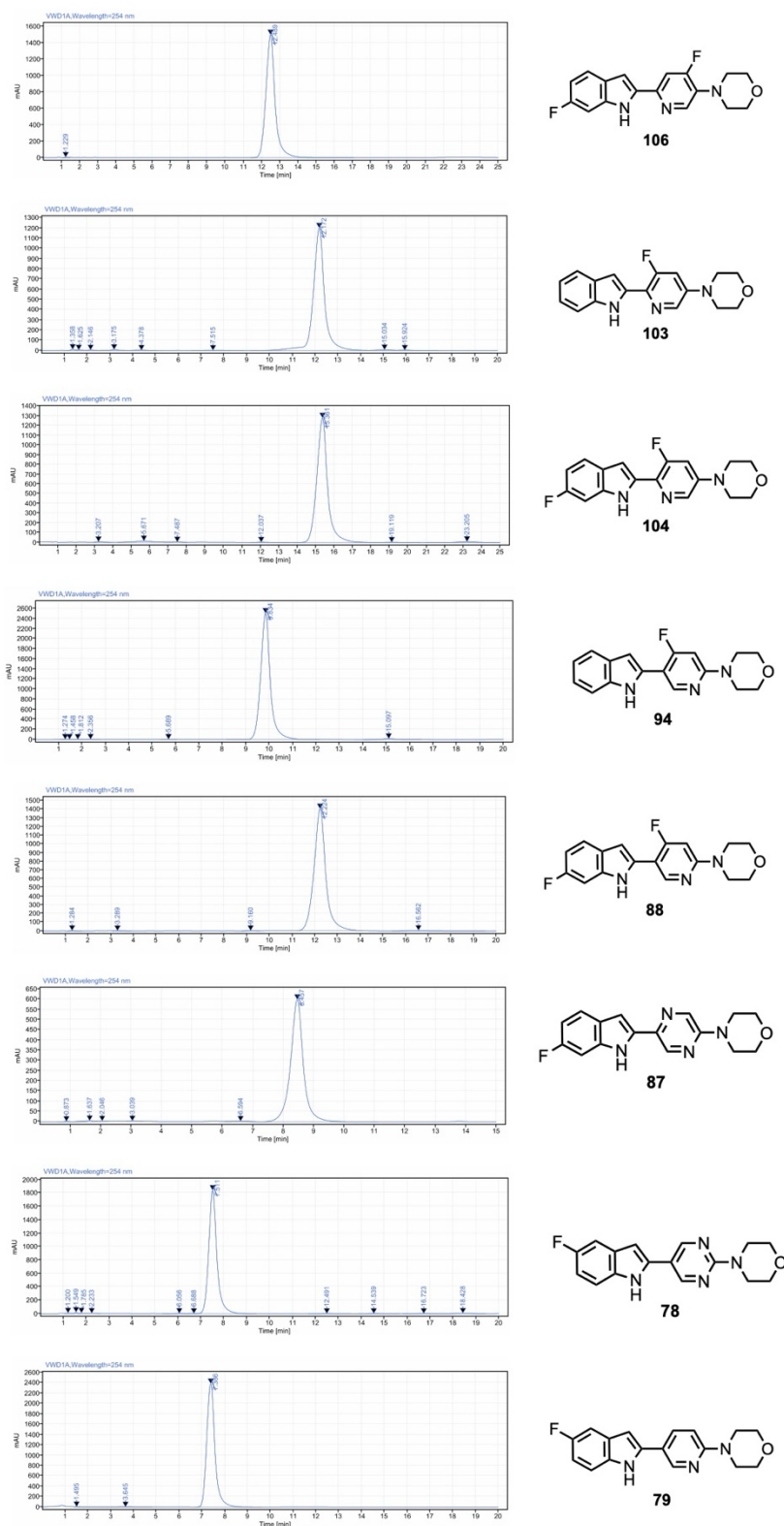


Figure S4. Analytical HPLC chromatograms of compounds **106**, **103**, **104**, **94**, **88**, **87**, **78**, and **79** (Phenomenex Gemini, 5 μ m, NX-C18 110Å, 100 x 4.6 mm; 45:55 v/v CH₃CN/0.1 M NH₄HCO₂ pH 4.2; 1 mL/min; 254 nm).

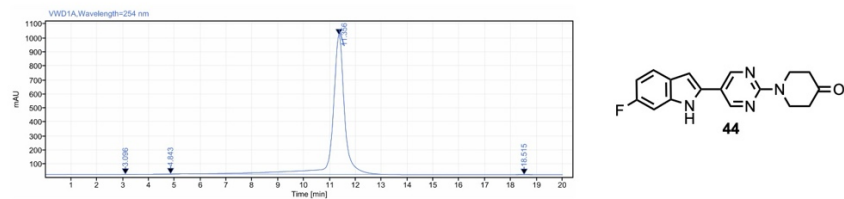


Figure S5. Analytical HPLC chromatogram of compound **44** (Phenomenex Gemini, 5 μ m, NX-C18 110Å, 100 x 4.6 mm; 40:60 v/v CH₃CN/0.1 M NH₄HCO₂ pH 4.2; 1 mL/min; 254 nm).

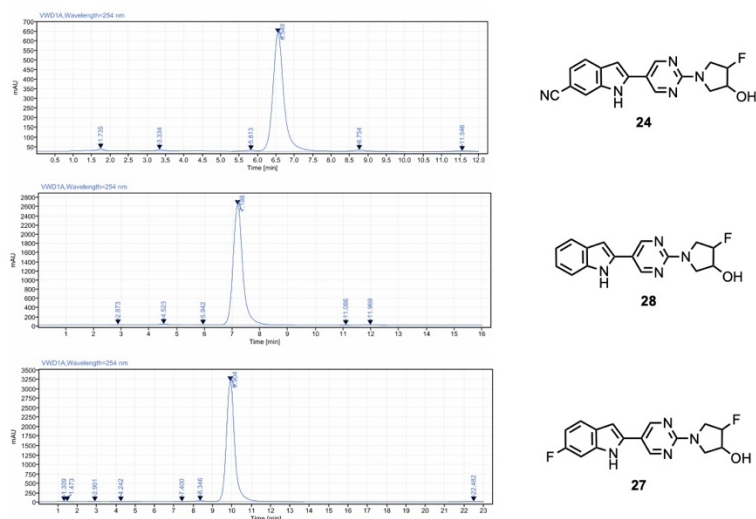


Figure S6. Analytical HPLC chromatograms of compounds **24**, **28**, and **27** (Phenomenex Gemini, 5 μ m, NX-C18 110Å, 100 x 4.6 mm; 35:65 v/v CH₃CN/0.1 M NH₄HCO₂ pH 4.2; 1 mL/min; 254 nm).

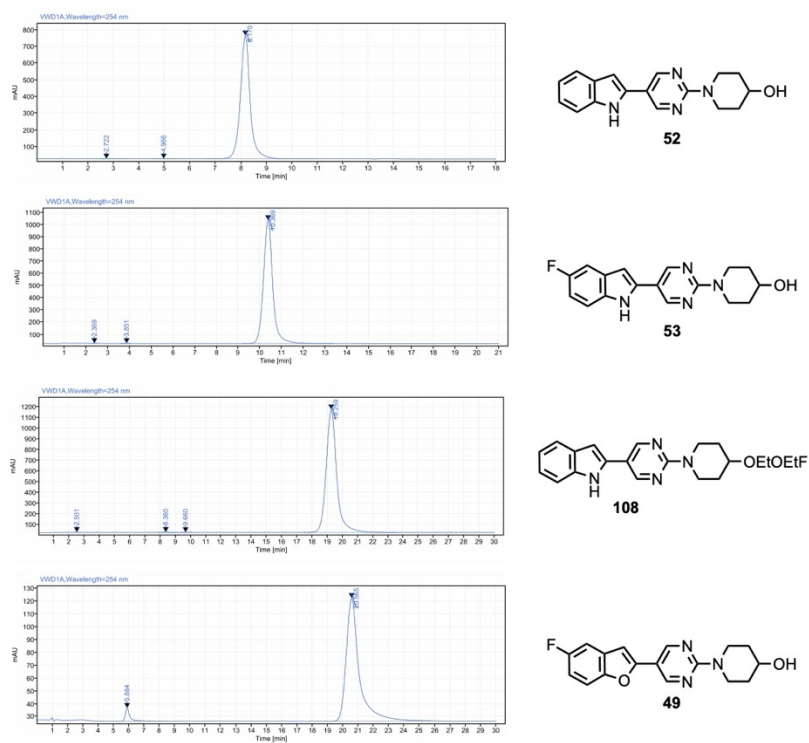
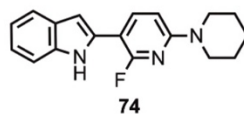


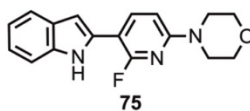
Figure S7. Analytical HPLC chromatograms of compounds **52**, **53**, **108**, and **49** (Phenomenex Gemini, 5 μ m, NX-C18 110Å, 100 x 4.6 mm; 35:65 v/v CH₃CN/0.1 M NH₄HCO₂ pH 4.2; 1 mL/min; 254 nm).



CNS MPO and PET MPO			
Property	Value	CNS MPO	CNS PET MPO
ClogP	3.86	0.570	0.117
ClogD	4.51	0.000	0.000
TPSA	31.92	0.596	0.000
MW	295.36	1.000	1.000
HBD	1	0.833	1.000
pKa	14.49	0.000	0.000
Total Score		3.0	2.1

BBB Score Calculator		
Property	Value	T ₀
Number of Aromatic Rings (Aro_R)	2	1.00
Number of Heavy Atoms (HA)	22	0.98
Molecular Weight (MW)	295.36	
Number of Hydrogen Bond Acceptor (HBA)	3	
Number of Hydrogen Bond Donor (HBD)	1	
MWHBN [MWHBN = (MW ^{-0.5})*HBN], where HBN=HBA+HBD]	0.23	0.98
Topological Polar Surface Area(TPSA)	31.92	0.78
pKa	14.49	0.00
BBB SCORE		5.01

Figure S8. MPO and BBB Score results for **74** (software used to calculate properties: SwissADME – ClogP (consensus Log $P_{o/w}$ value used), TPSA; ChemAxon – ClogD; Marvin – pK_a).



CNS MPO and PET MPO			
Property	Value	CNS MPO	CNS PET MPO
ClogP	3.07	0.965	0.775
ClogD	3.44	0.280	0.000
TPSA	41.15	1.000	0.708
MW	297.3334	1.000	1.000
HBD	1	0.833	1.000
pKa	14.49	0.000	0.000
Total Score		4.1	3.5

Property	Value	T ₀
Number of Aromatic Rings (Aro_R)	2	1.00
Number of Heavy Atoms (HA)	22	0.98
Molecular Weight (MW)	297.33	
Number of Hydrogen Bond Acceptor (HBA)	4	
Number of Hydrogen Bond Donor (HBD)	1	
MWHBN [MWHBN = (MW ^{-0.5})*HBN], where HBN=HBA+HBD]	0.29	0.87
Topological Polar Surface Area(TPSA)	41.15	0.71
pKa	14.49	0.00
BBB SCORE		4.71

Figure S9. MPO and BBB Score results for **75** (software used to calculate properties: SwissADME – ClogP (consensus Log $P_{o/w}$ value used), TPSA; ChemAxon – ClogD; Marvin – pK_a).

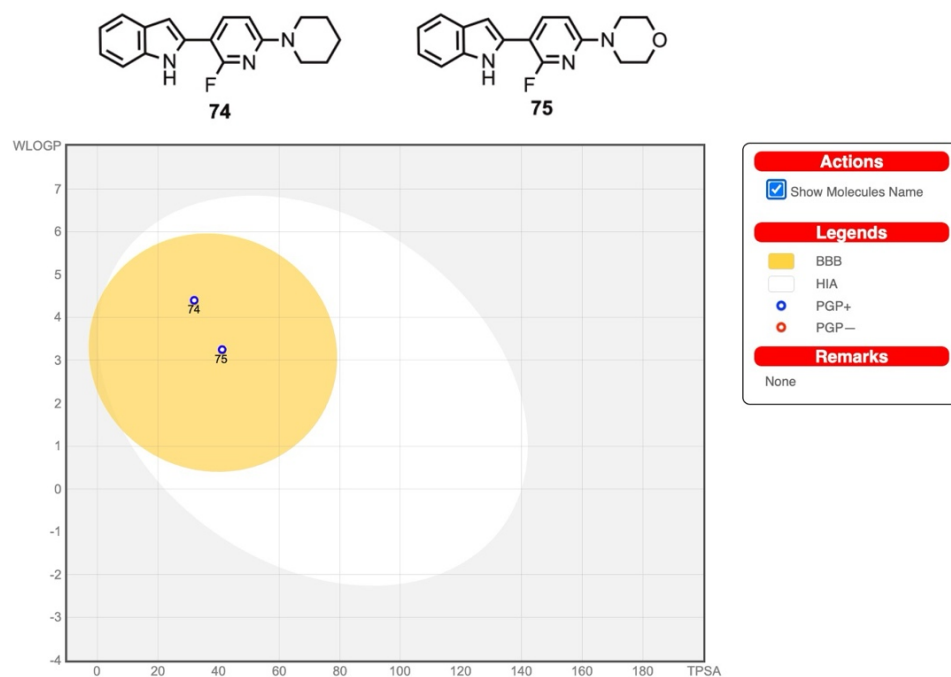


Figure S10. SwissADME BOILED-Egg plot of **74** and **75**.

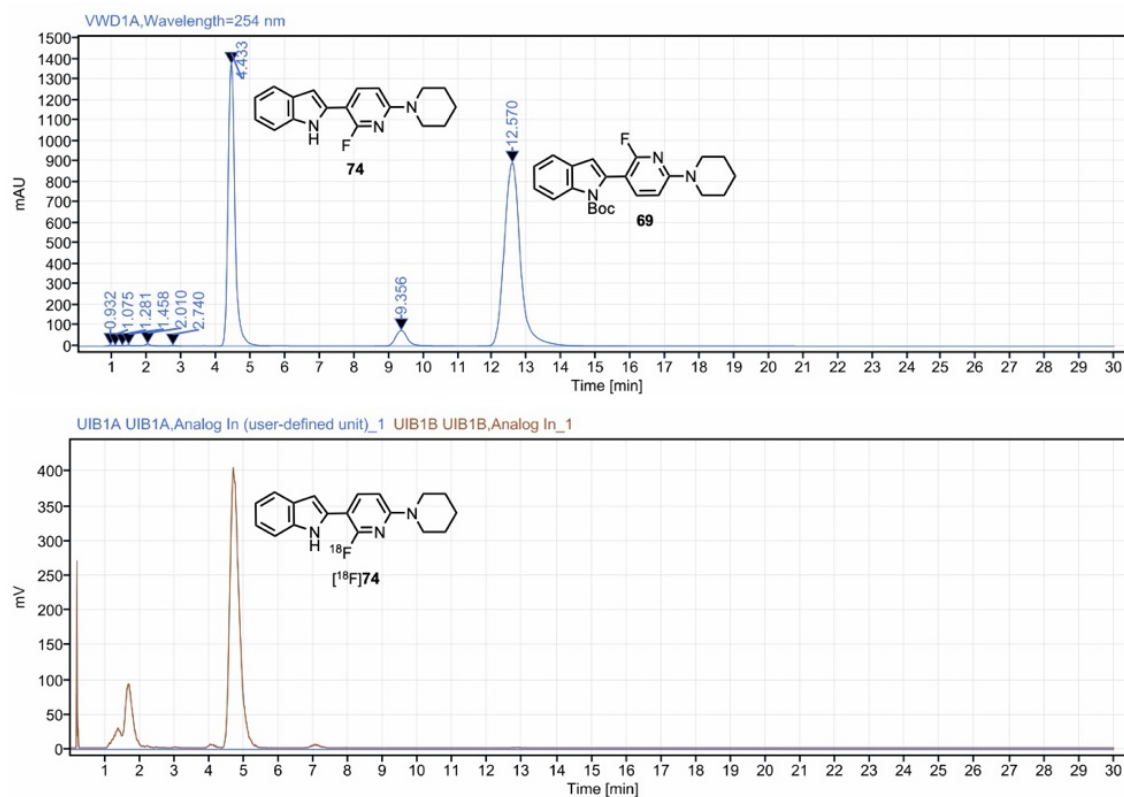


Figure S11. Analytical HPLC chromatograms of the $[^{18}\text{F}]\mathbf{74}$ crude reaction mixture after 45 min at $\sim 140^\circ\text{C}$, co-injected with compounds **69** and **74** (Phenomenex Gemini, 5 μm , NX-C18 110 $\text{\AA}$, 100 x 4.6 mm; 75:25 v/v $\text{CH}_3\text{CN}/0.1\text{ M NH}_4\text{HCO}_2$ pH 4.2; 1 mL/min; 254 nm). Note: the UV impurity at 9.36 min was in the sample of **69**.

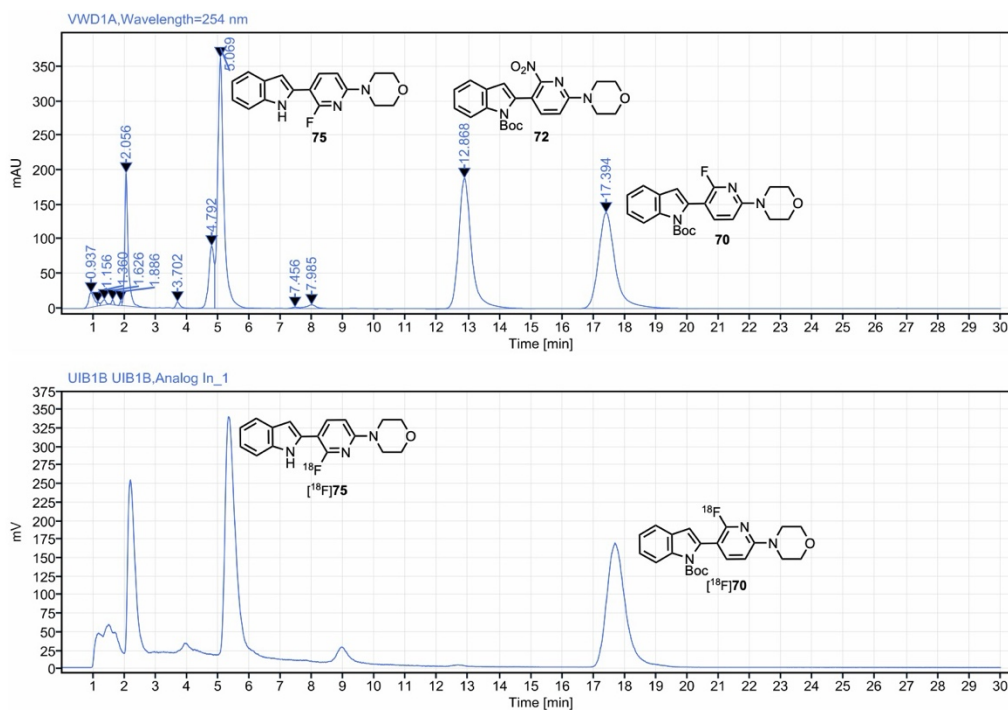


Figure S12. Analytical HPLC chromatograms of the [^{18}F]75 crude reaction mixture after 15 min at $\sim 140^\circ\text{C}$, co-injected with compounds **70**, **72**, and **75** (Phenomenex Gemini, 5 μm , NX-C18 110Å, 100 x 4.6 mm; 55:45 v/v $\text{CH}_3\text{CN}/0.1\text{ M NH}_4\text{HCO}_2$ pH 4.2; 1 mL/min; 254 nm).

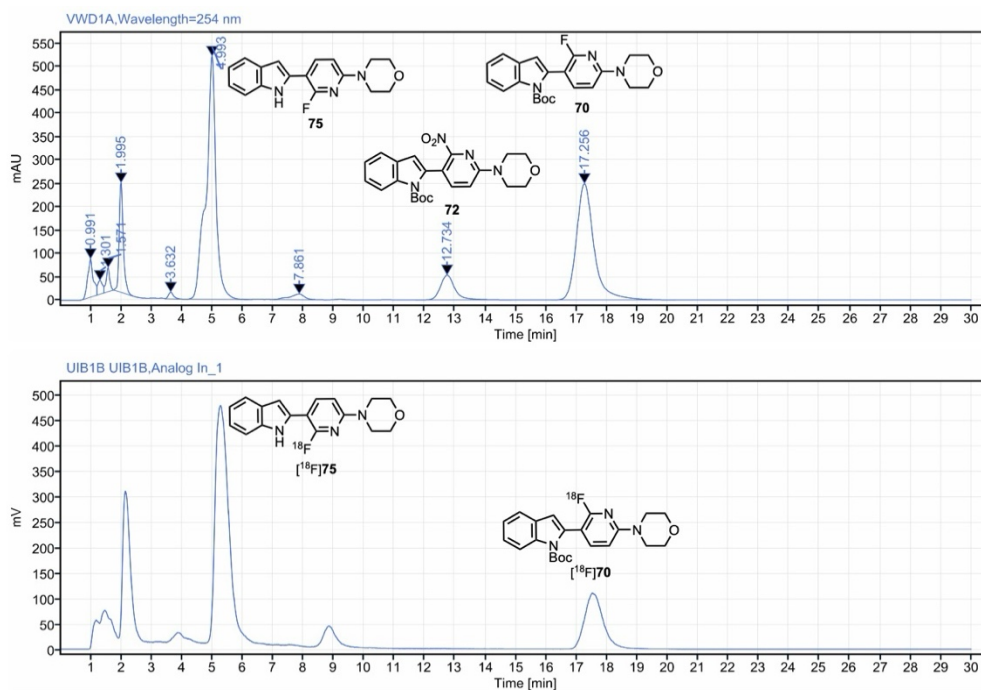


Figure S13. Analytical HPLC chromatograms of the [^{18}F]75 crude reaction mixture after 30 min at $\sim 140^\circ\text{C}$, co-injected with compounds **70**, **72**, and **75** (Phenomenex Gemini, 5 μm , NX-C18 110Å, 100 x 4.6 mm; 55:45 v/v $\text{CH}_3\text{CN}/0.1\text{ M NH}_4\text{HCO}_2$ pH 4.2; 1 mL/min; 254 nm).

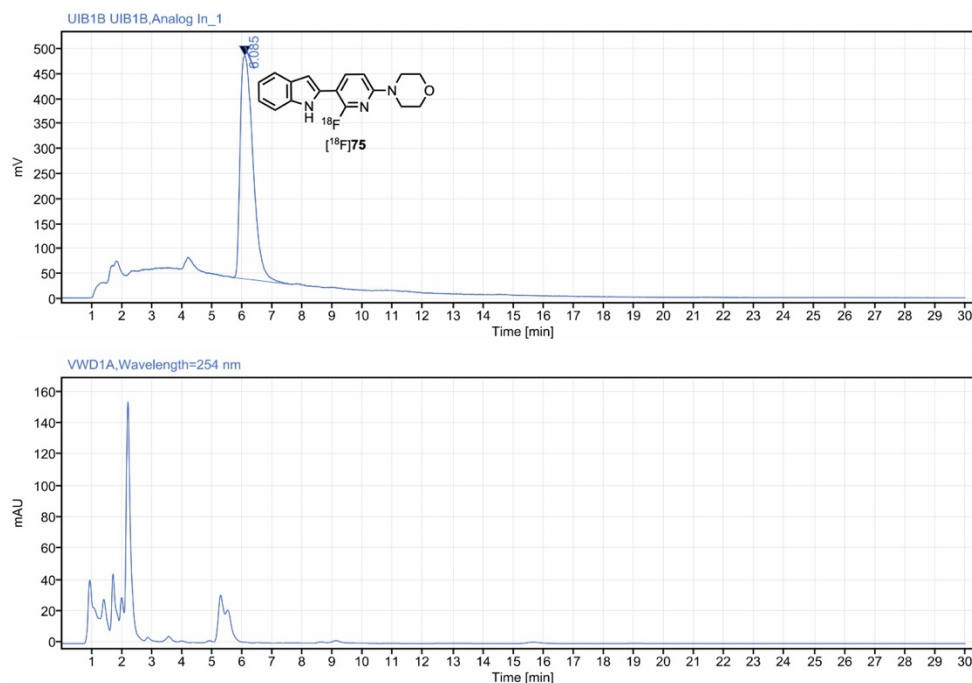


Figure S14. Analytical HPLC chromatograms of the $[^{18}\text{F}]\mathbf{75}$ crude reaction mixture after 45 min at $\sim 140^\circ\text{C}$ (Phenomenex Gemini, 5 μm , NX-C18 110Å, 100 x 4.6 mm; 55:45 v/v $\text{CH}_3\text{CN}/0.1\text{ M NH}_4\text{HCO}_2$ pH 4.2; 1 mL/min; 254 nm).

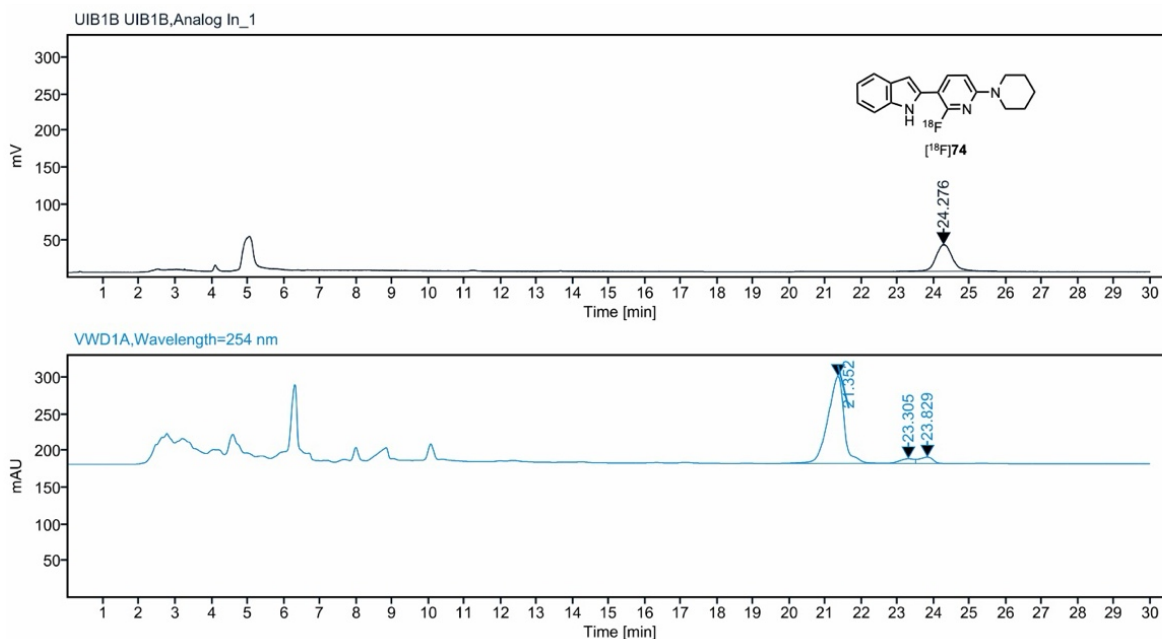


Figure S15. Semi-preparatory HPLC chromatogram of the purification of $[^{18}\text{F}]\mathbf{74}$ (Phenomenex Gemini 250 x 10 mm + guard; 55:45 v/v $\text{CH}_3\text{CN}/0.1\text{ M NH}_4\text{HCO}_2$ pH 4.2; 5 mL/min for 6 min, then 10 mL/min).

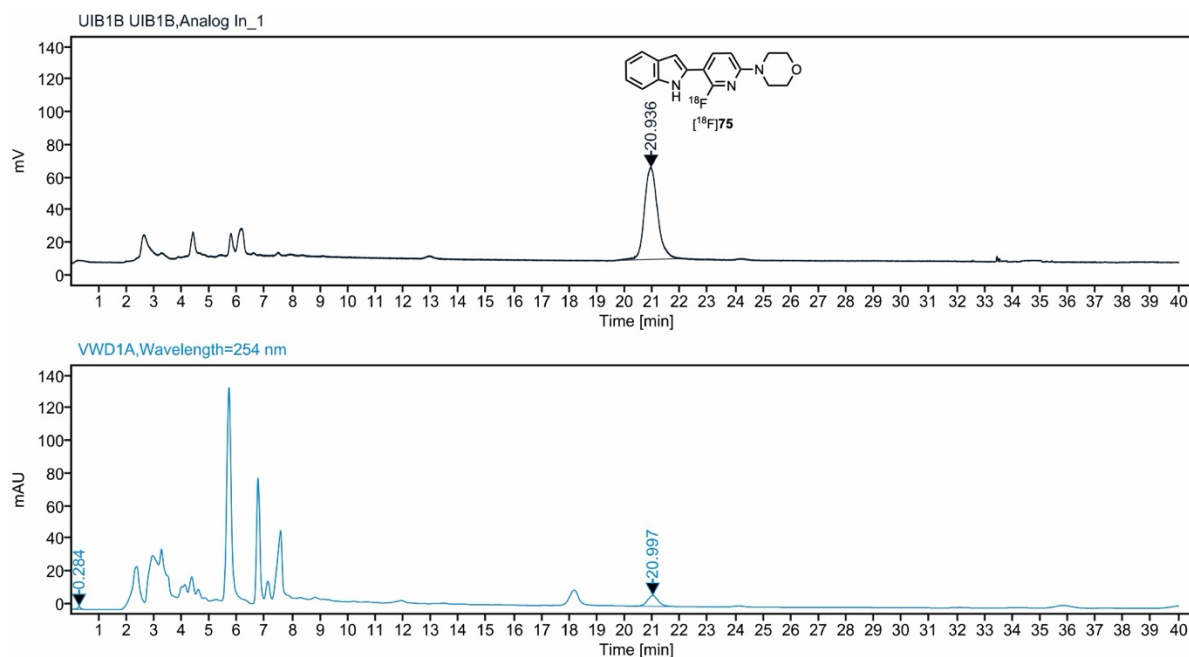


Figure S16. Semi-preparatory HPLC chromatogram of the purification of $[^{18}\text{F}]\mathbf{75}$ (Phenomenex Gemini 250 x 10 mm + guard; 45:55 v/v $\text{CH}_3\text{CN}/0.1 \text{ M NH}_4\text{HCO}_2$ pH 4.2; 5 mL/min for 6 min, then 8 mL/min).

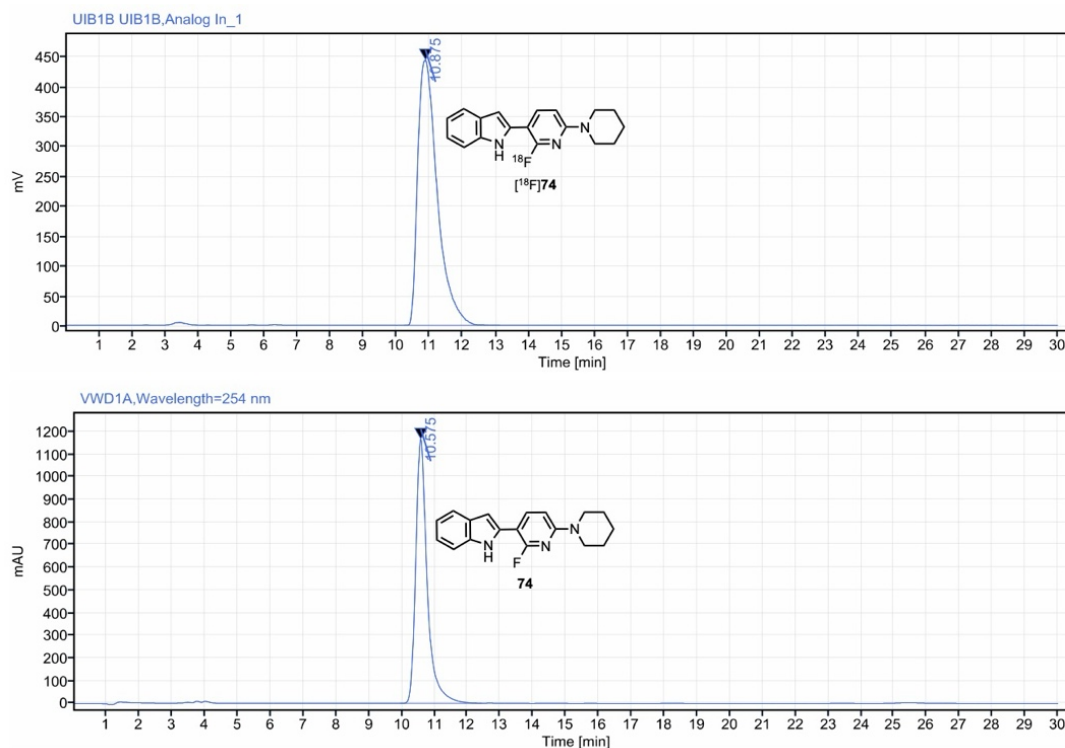


Figure S17. Analytical HPLC chromatograms of the $[^{18}\text{F}]\mathbf{74}$ final product co-injected with $\mathbf{74}$ (Phenomenex Gemini, 5 μm , NX-C18 110Å, 100 x 4.6 mm; 60:40 v/v $\text{CH}_3\text{CN}/0.1 \text{ M NH}_4\text{HCO}_2$ pH 4.2; 1 mL/min; 254 nm).

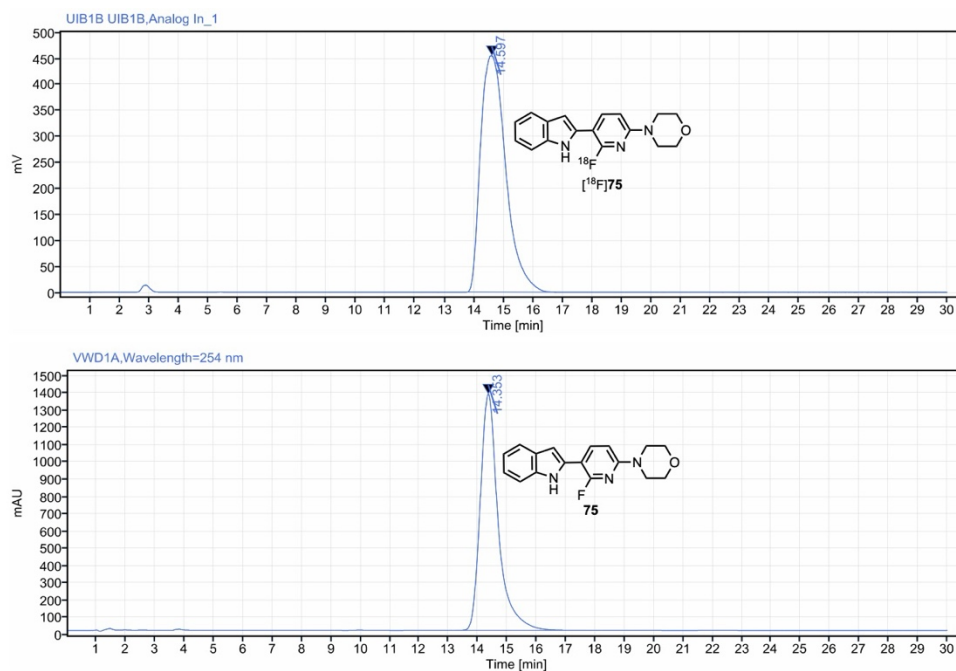


Figure S18. Analytical HPLC chromatograms of the $[^{18}\text{F}]\mathbf{75}$ final product co-injected with $\mathbf{75}$ (Phenomenex Gemini, 5 μm , NX-C18 110Å, 100 x 4.6 mm; 45:55 v/v $\text{CH}_3\text{CN}/0.1 \text{ M NH}_4\text{HCO}_2$ pH 4.2; 1 mL/min; 254 nm).

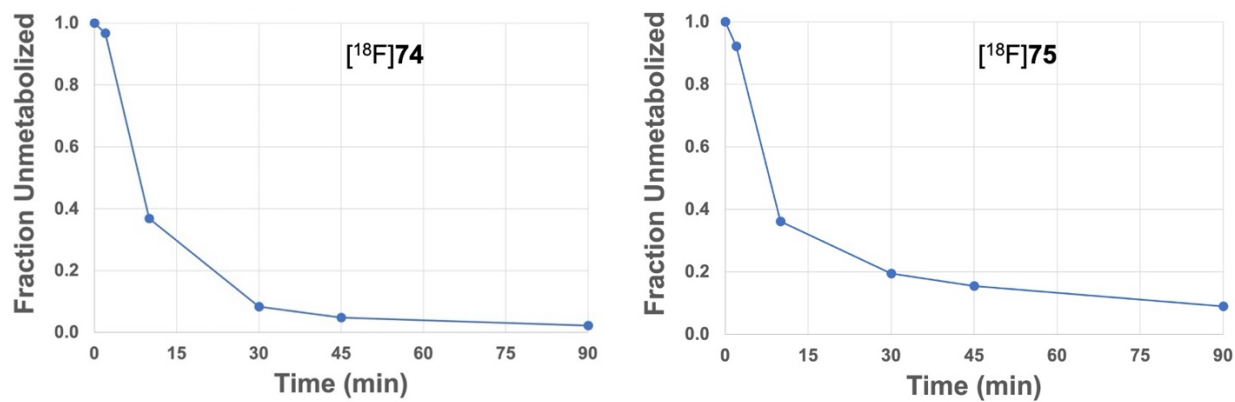
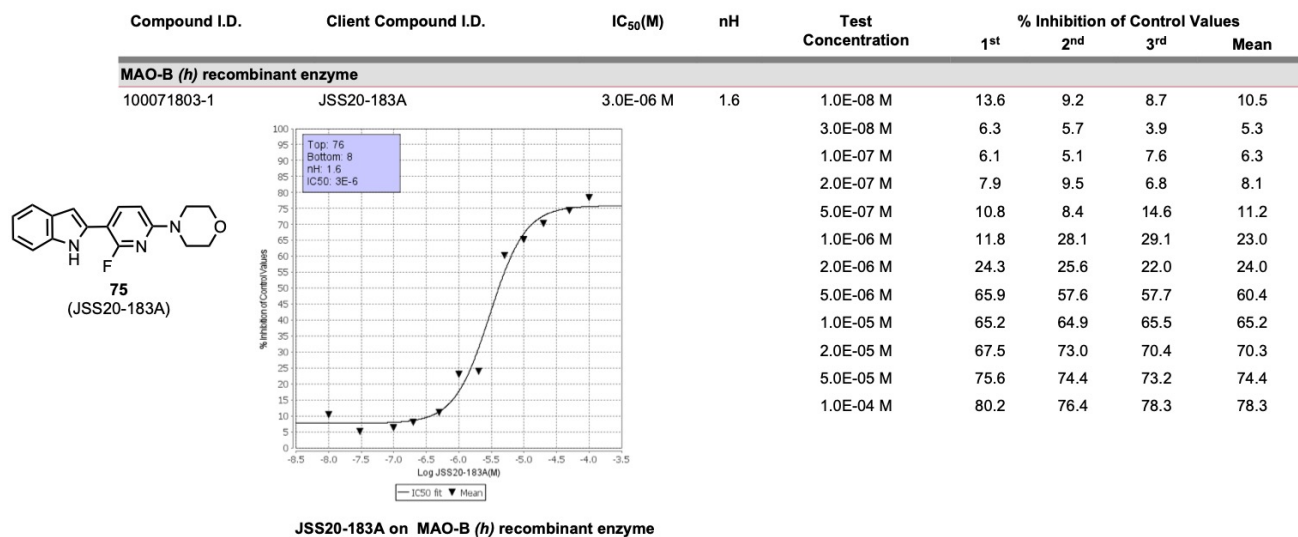


Figure S19. Unmetabolized venous fraction of $[^{18}\text{F}]\mathbf{74}$ (left) and $[^{18}\text{F}]\mathbf{75}$ (right) in male rhesus macaques.



Reference Compound Results

Compound I.D.	IC ₅₀ (M)	nH
MAO-B (h) recombinant enzyme		
deprenyl	5.0E-08 M	1.4

Figure S20. Results of Eurofins IC₅₀ determination of **75** (JSS20-183A) at human MAO-B.

Table S9. Selected demographics of cases used for autoradiography and immunohistochemistry.

Case patient (P)/(C)	Gender (M/F)	Age of onset (Years)	Age at death (Years)	Tau	A β	α -syn	TDP-43	Region used	Diagnosis
P	F		80	3+	2+	0	0	Parietal	PSP
P	M		86	3+	0	0	0	Frontal	CBD
P	F		70	3+	3+	0	0	Parietal	AD
C	M		66	0	0	0	0	Cingulate gyrus	CT

Table S10. Primary antibody selected for immunohistochemistry.

Primary Antibodies	Source/Cat No	Host and clonality	Antibody dilution used	Incubation time
Phospho-Tau (Ser202, Thr205) Monoclonal Antibody (AT8)	Thermo Fisher Scientific #MN1020	Mouse monoclonal	1:500	Overnight at 4 °C
Anti-beta Amyloid antibody [mOC23]	Abcam/ab205340	Rabbit monoclonal	1:500	Overnight at 4 °C

Table S11. Secondary antibody selected for immunohistochemistry.

Secondary Antibody	Source/Cat No	Host and clonality	Antibody dilution used	Incubation time
Goat Anti-Mouse IgG H&L	Abcam/ab205719	Goat polyclonal	1:10000	1 h at ambient temperature
Goat Anti-Rabbit IgG H&L	Ab97051	Goat polyclonal	1:10000	1h at ambient temperature

Table S12. Sample and crystal data for **44** (CCDC Deposition Number 2403956).

Identification code	JSS20-116A	
Chemical formula	C ₁₇ H ₁₅ FN ₄ O	
Formula weight	310.33 g/mol	
Temperature	296(2) K	
Wavelength	1.54178 Å	
Crystal size	0.003 x 0.120 x 0.200 mm	
Crystal habit	clear colorless plate	
Crystal system	monoclinic	
Space group	P 1 21/n 1	
Unit cell dimensions	a = 12.5190(4) Å	$\alpha = 90^\circ$
	b = 7.8750(4) Å	$\beta = 90.611(3)^\circ$
	c = 15.0667(5) Å	$\gamma = 90^\circ$
Volume	1485.30(10) Å ³	
Z	4	
Density (calculated)	1.388 g/cm ³	
Absorption coefficient	0.817 mm ⁻¹	
F(000)	648	

Table S13. Sample and crystal data for **71** (CCDC Deposition Number 2403955).

Identification code	JSS21-021B	
Chemical formula	C ₂₃ H ₂₆ N ₄ O ₄	
Formula weight	422.48 g/mol	
Temperature	296(2) K	
Wavelength	1.54178 Å	
Crystal size	0.050 x 0.120 x 0.190 mm	
Crystal habit	clear yellow Chunk	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 10.3939(2) Å	$\alpha = 90^\circ$
	b = 12.8366(3) Å	$\beta = 90^\circ$
	c = 16.0313(4) Å	$\gamma = 90^\circ$
Volume	2138.93(8) Å ³	
Z	4	
Density (calculated)	1.312 g/cm ³	
Absorption coefficient	0.747 mm ⁻¹	
F(000)	896	

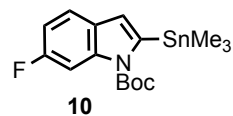
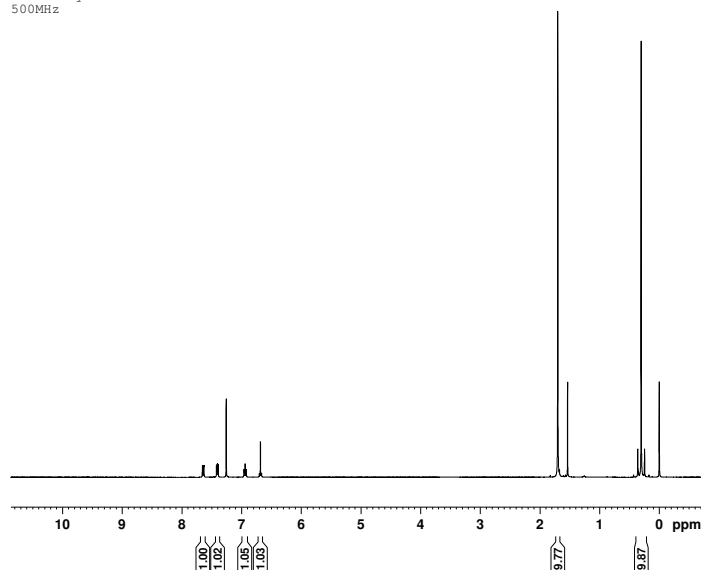
Table S14. Sample and crystal data for **72** (CCDC Deposition Number 2403957).

Identification code	JSS21-033A
Chemical formula	C ₂₂ H ₂₄ N ₄ O ₅
Formula weight	424.45 g/mol
Temperature	150(2) K
Wavelength	1.54178 Å
Crystal size	0.004 x 0.120 x 0.200 mm
Crystal system	monoclinic
Space group	P 1 21/c 1
Unit cell dimensions	a = 8.68420(10) Å α = 90° b = 12.4480(2) Å β = 91.5310(10)° c = 19.3489(3) Å γ = 90°
Volume	2090.89(5) Å ³
Z	4
Density (calculated)	1.348 g/cm ³
Absorption coefficient	0.805 mm ⁻¹
F(000)	896

Table S15. Sample and crystal data for **75** (CCDC Deposition Number 2403958).

Identification code	JSS20-183A
Chemical formula	C ₁₇ H ₁₆ FN ₃ O
Formula weight	297.33 g/mol
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal size	0.050 x 0.120 x 0.170 mm
Crystal habit	clear colorless block
Crystal system	monoclinic
Space group	P 1 21/c 1
Unit cell dimensions	a = 16.3426(5) Å α = 90° b = 5.9494(2) Å β = 105.0520(10)° c = 14.4881(4) Å γ = 90°
Volume	1360.33(7) Å ³
Z	4
Density (calculated)	1.452 g/cm ³
Absorption coefficient	0.102 mm ⁻¹
F(000)	624

white crystalline solid
500MHz



JSS20-139A
CDCl3, 100MHz

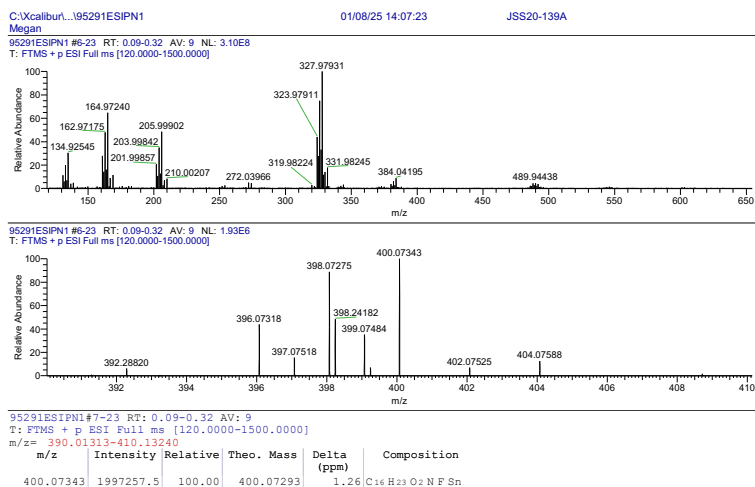
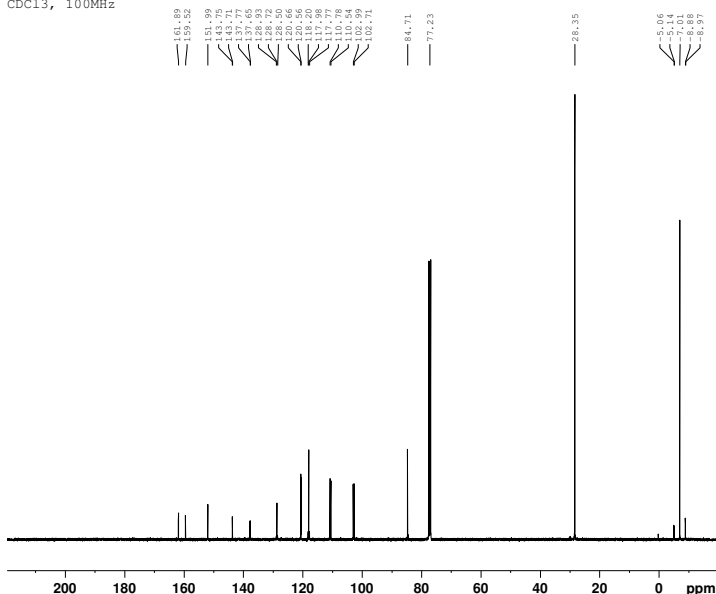
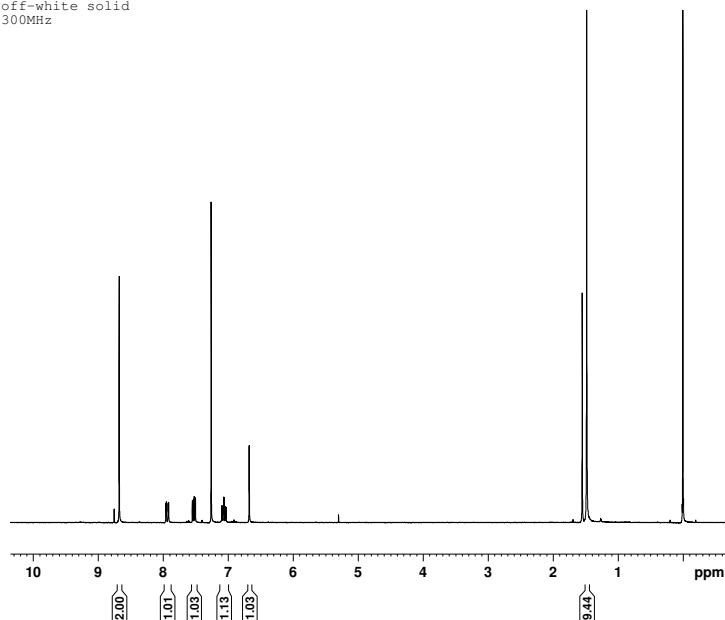


Figure S21. Compound **10** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

off-white solid
300MHz



Current Data Parameters
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PROCNO 1

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DE 13.19 usec
TE 295.4 K
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TD0 1
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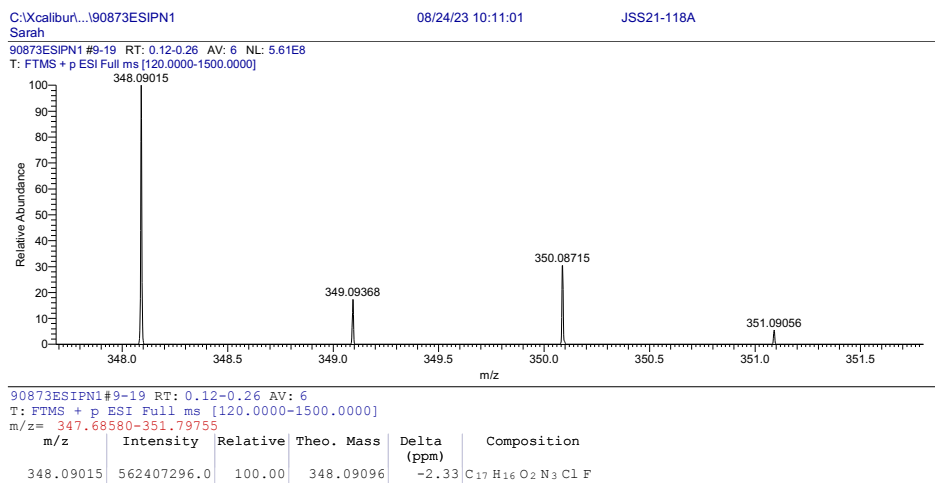
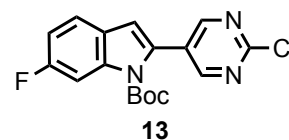
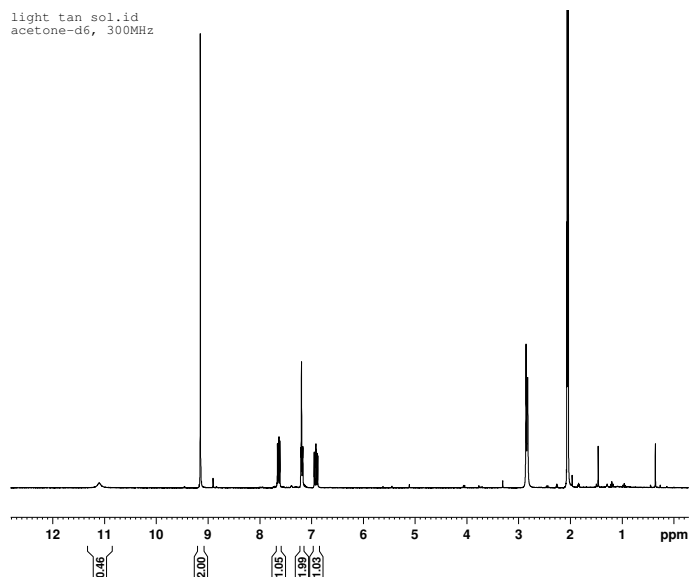
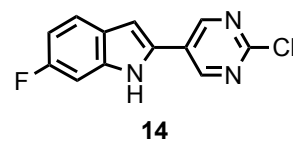


Figure S22. Compound **13** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

light tan solid
acetone-d6, 300MHz

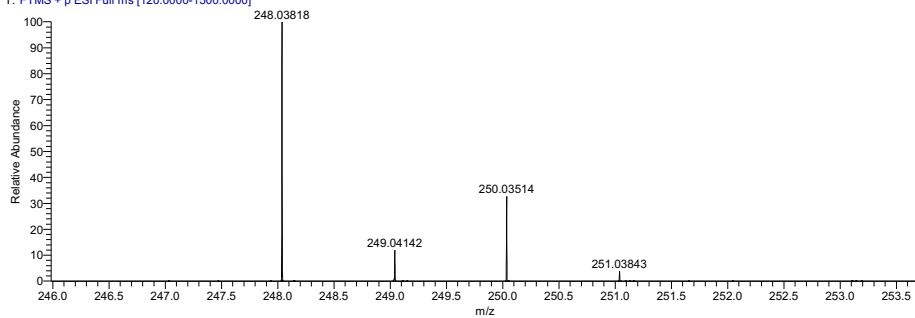


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PLW1 18.00000000 W
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C:\Xcalibur\...90872ESIPN1 08/24/23 10:04:12 JSS21-118B
Sarah

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T: FTMS + p ESI Full ms [120.0000-1500.0000]



90872ESIPN1#9-17 RT: 0.12-0.24 AV: 5

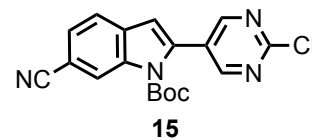
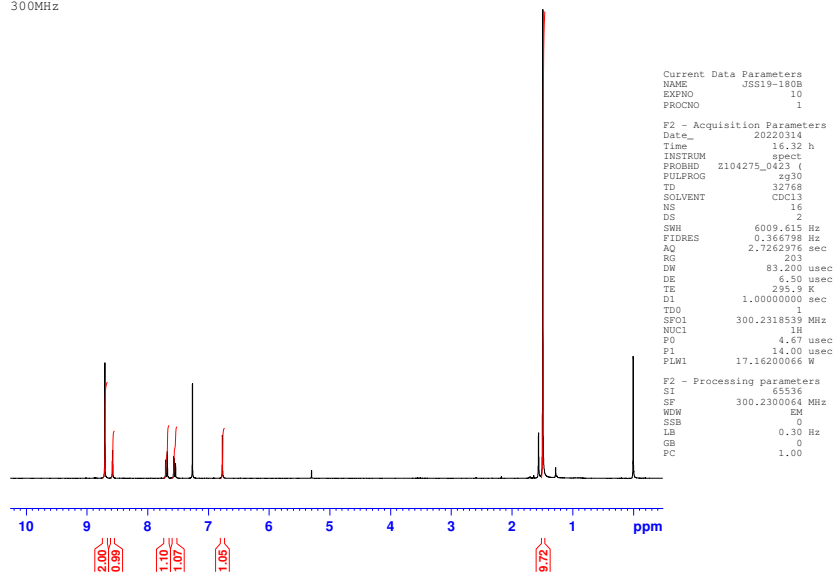
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z = 245.98475-253.70373

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
248.03818	474728576.0	100.00	248.03853	-1.41	C ₁₂ H ₈ N ₃ ClF

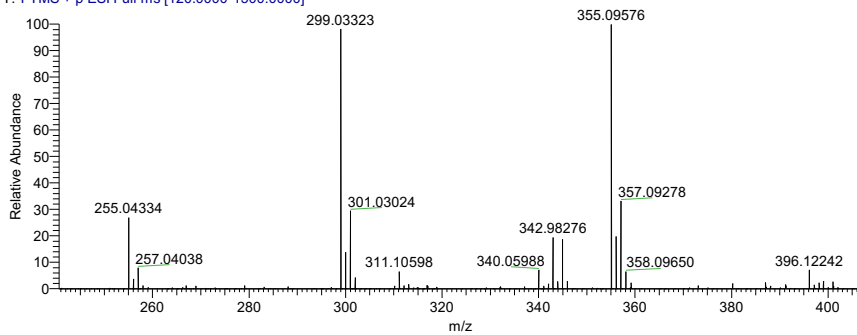
Figure S23. Compound **14** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

white solid
300MHz

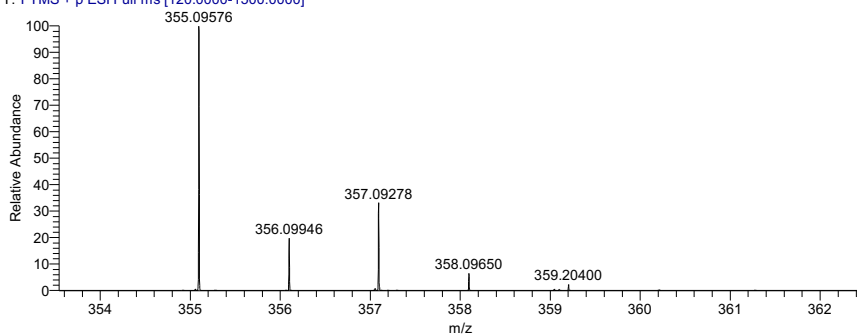


C:\Xcalibur\data\MSfacility\88128ESIPN1 07/29/22 09:42:53 JSS19-180B
Sarah

88128ESIPN1 #9-20 RT: 0.12-0.26 AV: 6 SB: 169 0.01-0.09, 0.33-4.96 NL: 1.48E8
T: FTMS + p ESI Full ms [120.0000-1500.0000]



88128ESIPN1 #9-20 RT: 0.12-0.26 AV: 6 SB: 169 0.01-0.09, 0.33-4.96 NL: 1.48E8
T: FTMS + p ESI Full ms [120.0000-1500.0000]

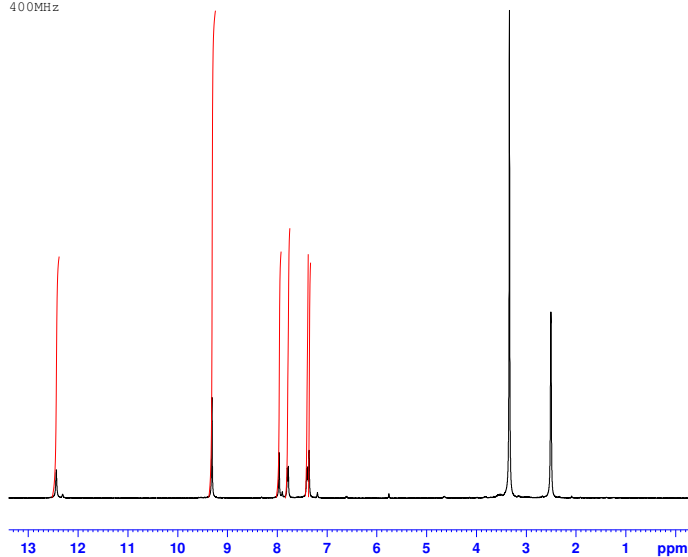


88128ESIPN1 #9-19 RT: 0.12-0.26 AV: 6
SB: 169 0.01-0.09, 0.33-4.96
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z = 353.54046-362.46545

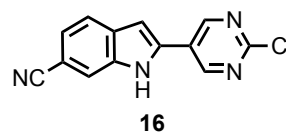
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
355.09576	151910704.0	100.00	355.09563	0.13	C ₁₈ H ₁₆ O ₂ N ₄ Cl

Figure S24. Compound **15** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

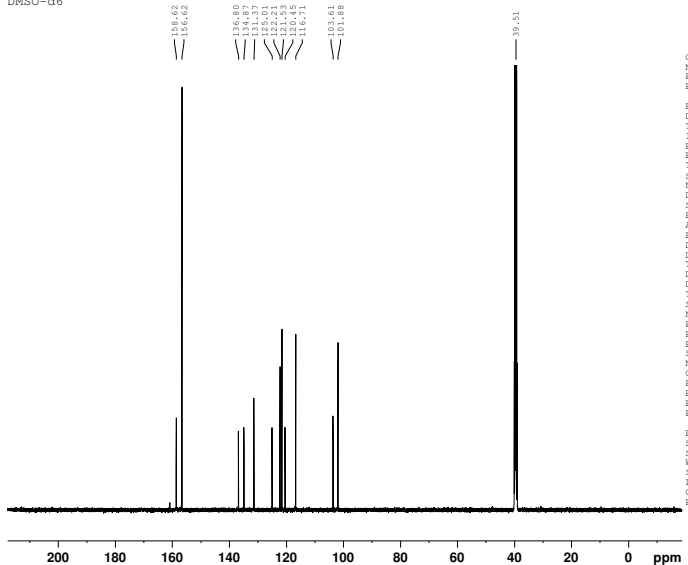
yellow/orange solid
400MHz



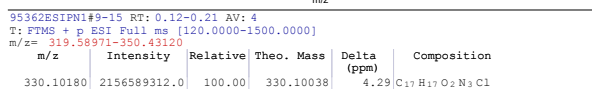
Current Data Parameters
NAME JSS19-160A
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220301
Time 10.36 h
INSTRUM spect
PROBHD Z108618_0240 ()
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 144
DW 62.400 usec
DE 6.50 usec
TE 89.3 K
D1 1.00000000 sec
TD0 1
SFO1 400.1324708 MHz
NUC1 1H
FO 4.83 usec
P1 14.50 usec
PLW1 12.00000000 W
F2 - Processing parameters
SI 65536
SF 400.1300034 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



BXXXII-159
DMSO-d6

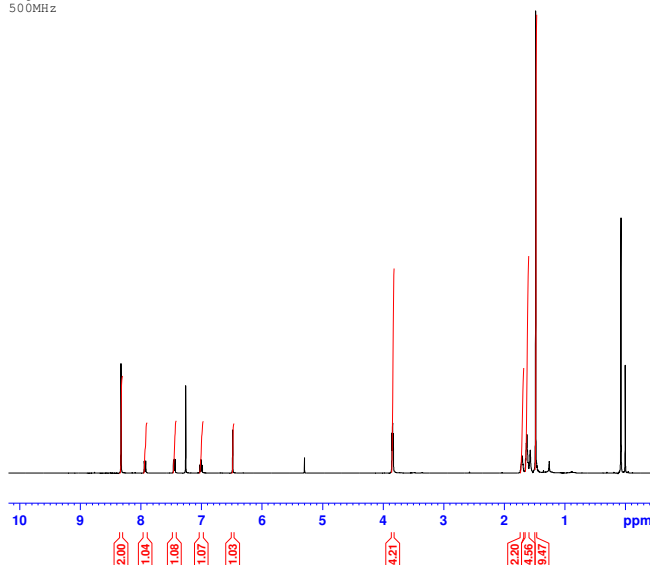


17



S31

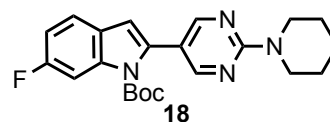
light tan solid
500MHz



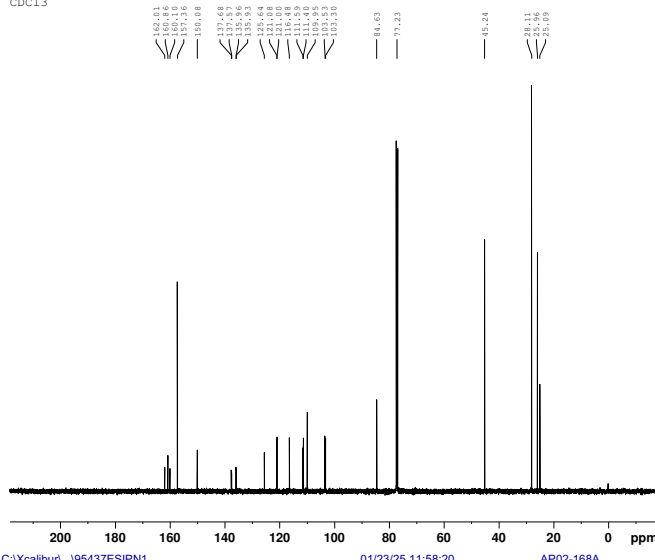
Current Data Parameters
NAME JSS20-037A
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20220518
Time 10:10 h
INSTRUM spect
PROBHD z113652_0064 (4
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 10000.000 Hz
FIDRES 0.305176 Hz
AQ 3.2767999 sec
RG 128
DW 50.000 usec
DE 13.64 usec
TE 299.8 K
D1 1.00000000 sec
TD0 1
SFO1 500.1630885 MHz
NUC1 1H
P0 3.83 usec
P1 11.50 usec
PLW1 18.00000000 W

F2 - Processing parameters
SI 65536
SF 500.1600123 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



AP02-168A
CDCl3



Current Data Parameters
NAME AP02-168A 13C
EXPNO 22
PROCNO 1

F2 - Acquisition Parameters
Date_ 20220512
Time 16:27 h
INSTRUM spect
PROBHD z113652_0064 (4
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 192
DS 4
SWH 29761.904 Hz
FIDRES 0.908261 Hz
AQ 1.1010248 sec
RG 203
DW 16.800 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 125.7779086 MHz
NUC1 13C
P0 3.47 usec
P1 10.40 usec
PLW1 110.00000000 W
SFO2 500.1620006 MHz
NUC2 1H
CPDPRG2 waltz165
PCPD2 80.00 usec
PLW2 18.00000000 W
PLW12 0.37195000 W
PLW13 0.18708999 W

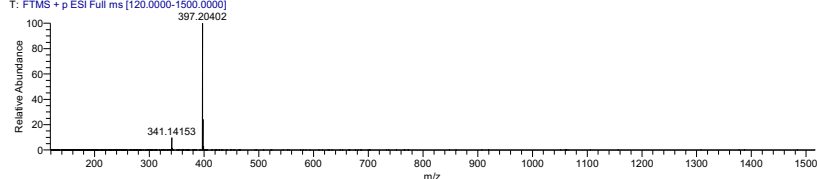
F2 - Processing parameters
SI 32768
SF 125.7653078 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

C:\Xcalibur\...95437ESIPN1
Mike

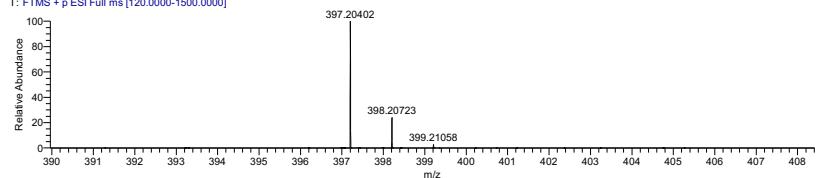
01/23/25 11:58:20

AP02-168A

95437ESIPN1 #9-14 RT: 0.12-0.18 AV: 3 SB: 22 1.06-1.55, 0.01-0.09 NL: 3.67E9
T: FTMS + p ESI Full ms [120.0000-1500.0000]



95437ESIPN1 #9-14 RT: 0.12-0.18 AV: 3 SB: 22 1.06-1.55, 0.01-0.09 NL: 3.67E9
T: FTMS + p ESI Full ms [120.0000-1500.0000]



95437ESIPN1#9-13 RT: 0.12-0.18 AV: 3

SB: 22 1.06-1.55, 0.01-0.09

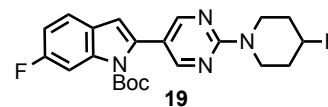
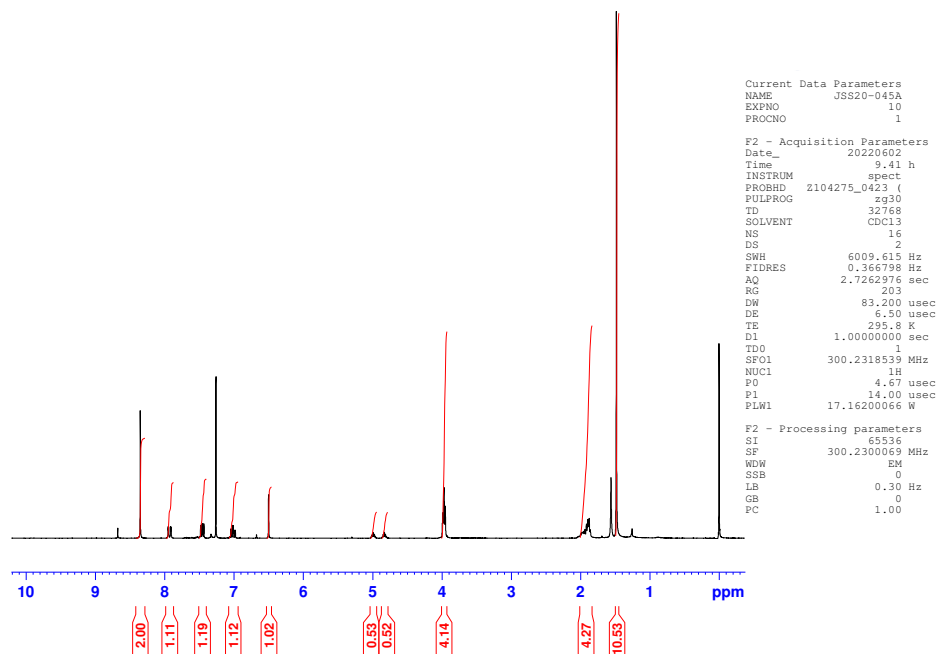
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z = 389.95883-408.40457

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
397.20402	3760296448.0	100.00	397.20343	1.49	C ₂₂ H ₂₆ O ₂ N ₄ F

Figure S27. Compound **18** ^1H NMR spectrum (top), ^{13}C NMR spectrum (middle), high-resolution mass spectrum (bottom).

white foam

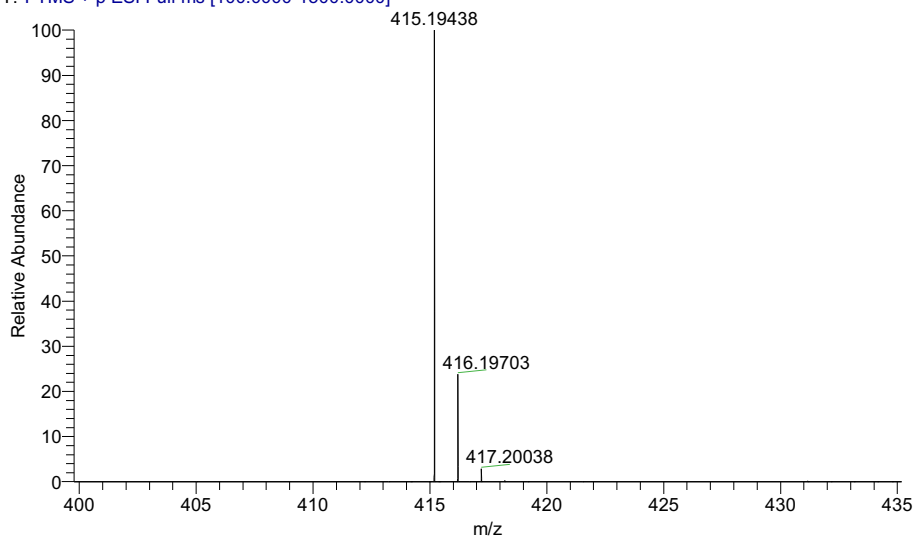


C:\Xcalibur\data\MSfacility\87807ESIPN1
Megan

06/10/22 14:04:38

JSS20-045A

87807ESIPN1#7-18 RT: 0.09-0.23 AV: 6 NL: 8.34E9
T: FTMS + p ESI Full ms [100.0000-1500.0000]



87807ESIPN1#7-17 RT: 0.09-0.23 AV: 6

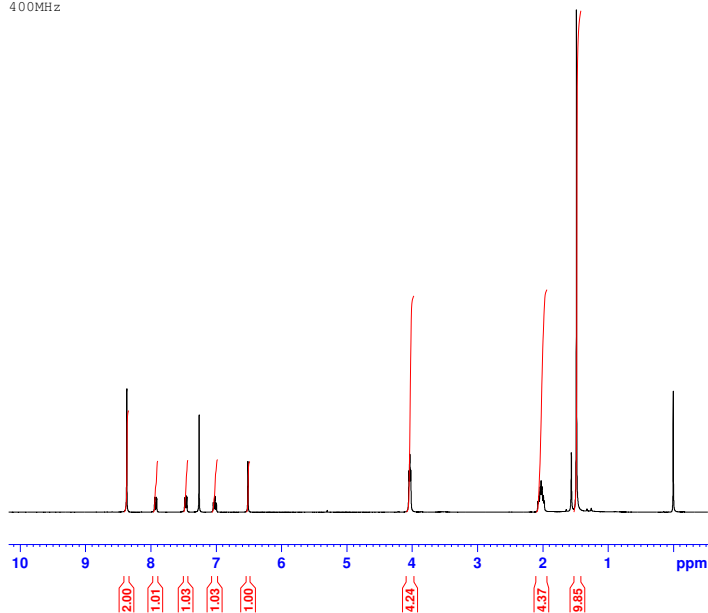
T: FTMS + p ESI Full ms [100.0000-1500.0000]

m/z = 399.76971-435.17407

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
415.19438	8486300160.0	100.00	415.19401	0.88	C ₂₂ H ₂₅ O ₂ N ₄ F ₂

Figure S28. Compound **19** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

white solid
400MHz



```

Current Data Parameters
NAME      JSS20-089A
EXPNO     10
PROCNO    1

F2 - Acquisition Parameters
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Time      9:29 h
INSTRUM   spect
PROBHD    Z108618_0240 (
PULPROG   zg30
TD         65536
SOLVENT   CDCl3
NS         16
DS         2
SWH        8012.820 Hz
FIDRES     0.244552 Hz
AQ         4.0894465 sec
RG         144
DW         62.400 usec
DE         6.50 usec
TE         102.6 K
D1         1.00000000 sec
TD0        1
SFO1       400.1324708 MHz
NUC1       1H
FO         4.83 usec
P1         14.50 usec
PLW1       12.00000000 W

F2 - Processing parameters
SI         65536
SF         400.1300094 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00

```

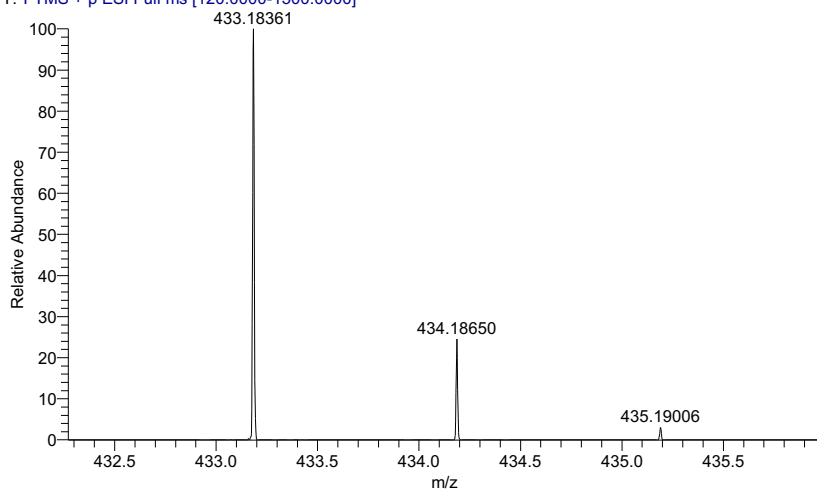


C:\Xcalibur\data\MSfacility\88264ESIPN1
Sarah

08/12/22 12:02:47

JSS20-089A

88264ESIPN1#9-16 RT: 0.12-0.21 AV: 4 NL: 9.17E9
T: FTMS + p ESI Full ms [120.0000-1500.0000]



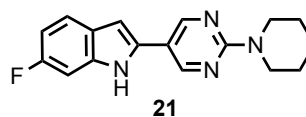
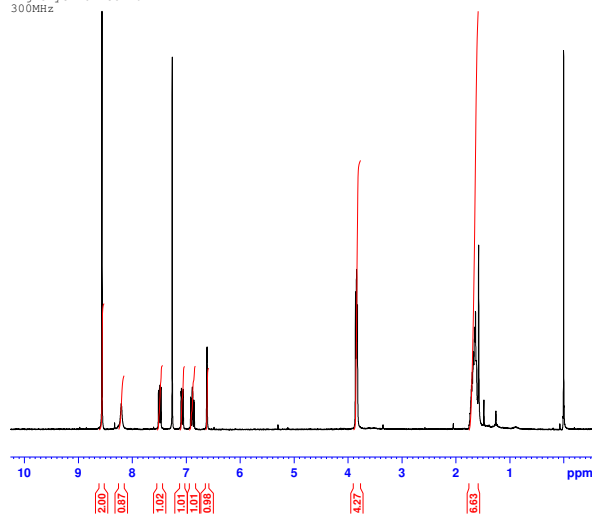
88264ESIPN1#9-15 RT: 0.12-0.21 AV: 4
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z = 432.27043-435.98292

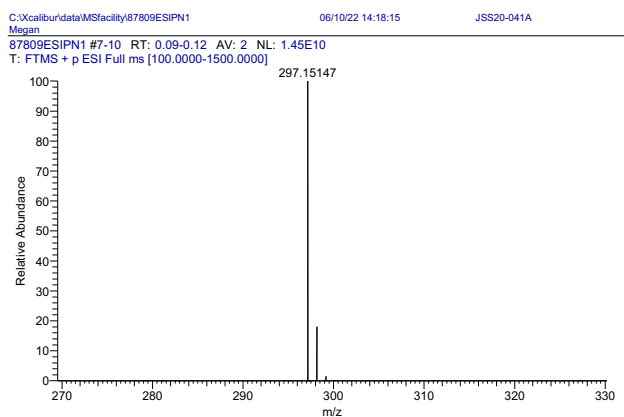
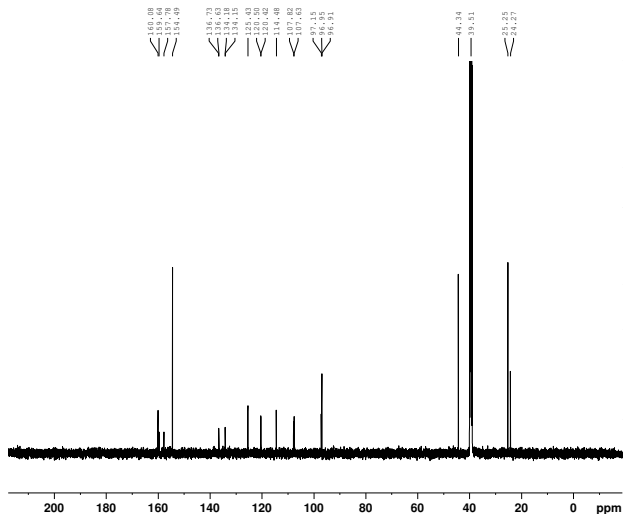
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
433.18361	9352170496.0	100.00	433.18459	-2.25	C ₂₂ H ₂₄ O ₂ N ₄ F ₃

Figure S29. Compound **20** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

light yellow solid
300MHz

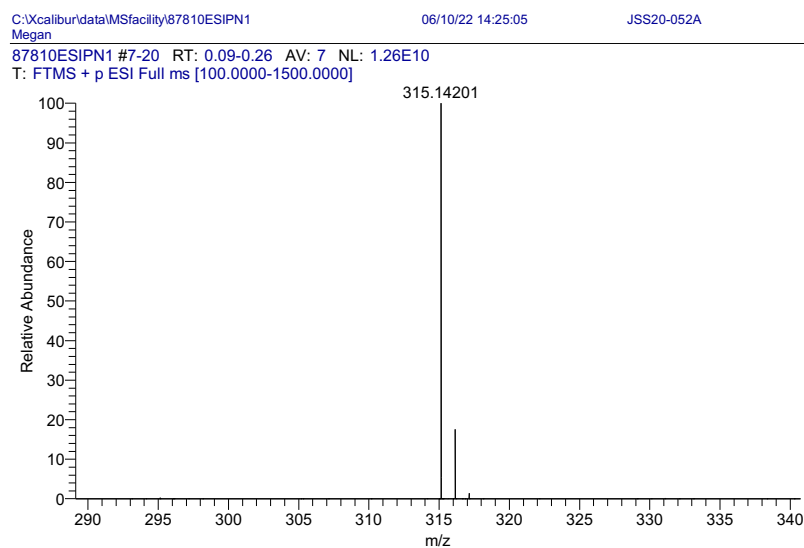
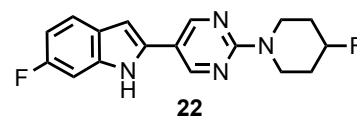
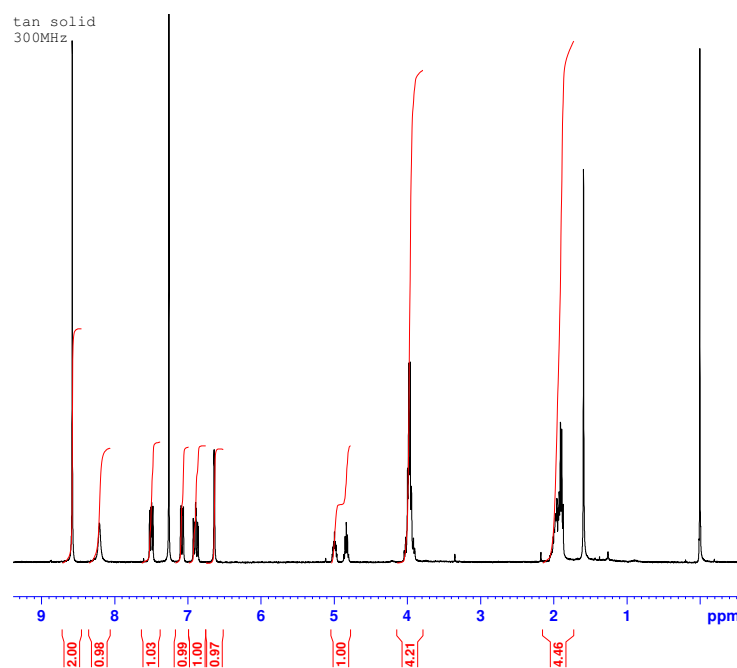


JSS20-041A



m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
297.15147	14697496576.0	100.00	297.15100	1.59	C ₁₇ H ₁₈ N ₄ F

Figure S30. Compound **21** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).



87810ESIPN1#7-19 RT: 0.09-0.26 AV: 7
T: FTMS + p ESI Full ms [100.0000-1500.0000]
m/z= 289.10871-340.72683

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
315.14201	12641028096.0	100.00	315.14158	1.35	C ₁₇ H ₁₇ N ₄ F ₂

Figure S31. Compound **22** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

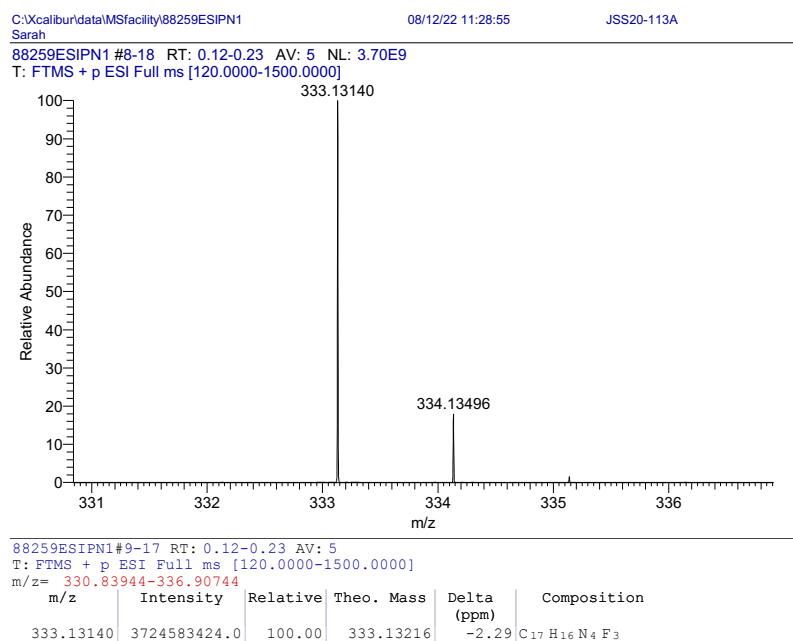
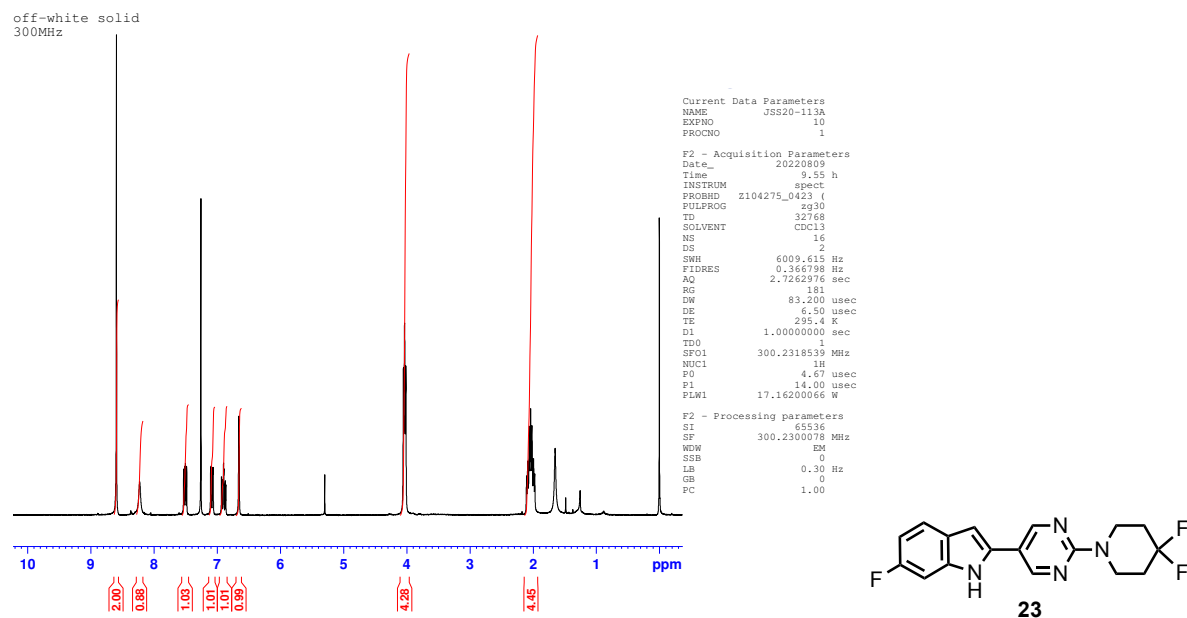
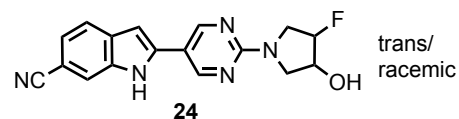
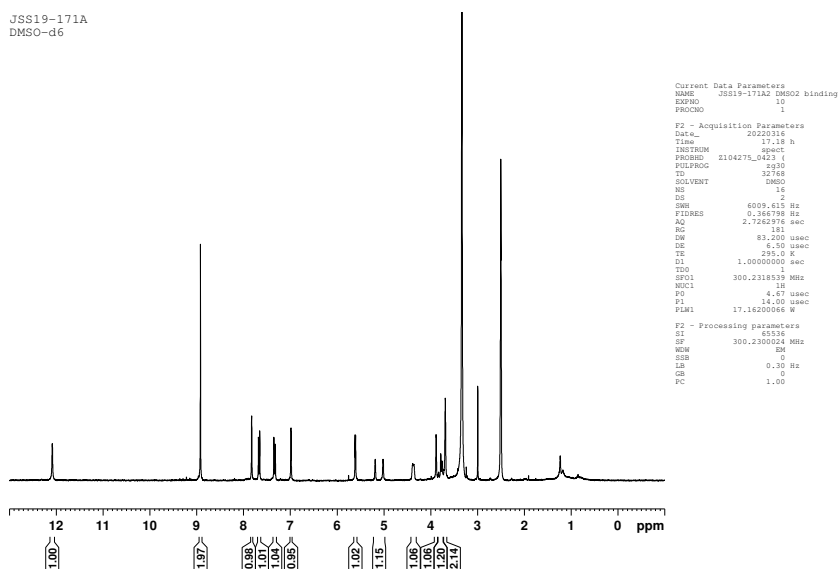


Figure S32. Compound **23** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

JSS19-171A
DMSO-d6



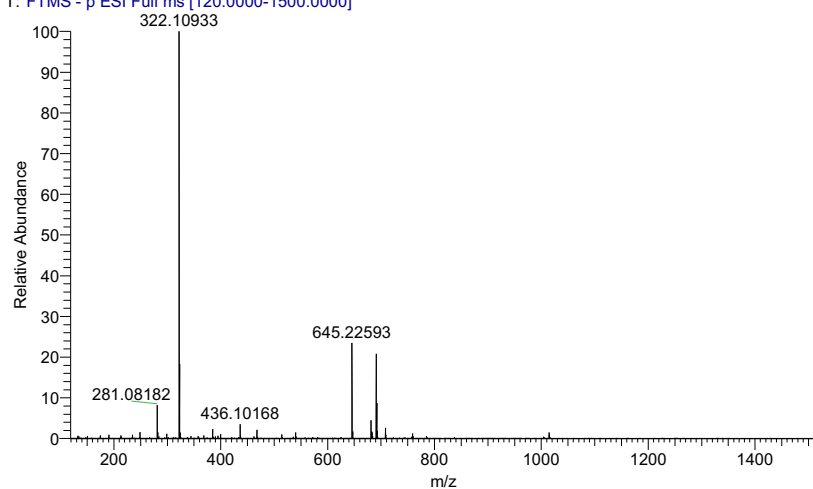
C:\Xcalibur\data\MSfacility\87429ESIPN1

03/21/22 12:05:52

JSS19-171A

87429ESIPN1#8-21 RT: 0.13-0.31 AV: 7 NL: 3.03E8

T: FTMS - p ESI Full ms [120.0000-1500.0000]



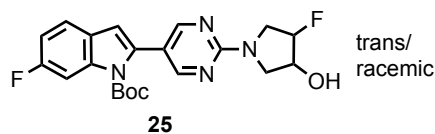
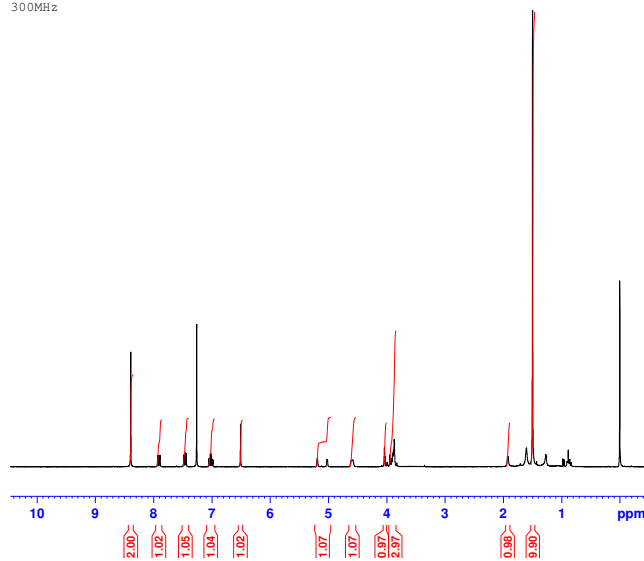
87429ESIPN1#8-20 RT: 0.13-0.31 AV: 7

T: FTMS - p ESI Full ms [120.0000-1500.0000]

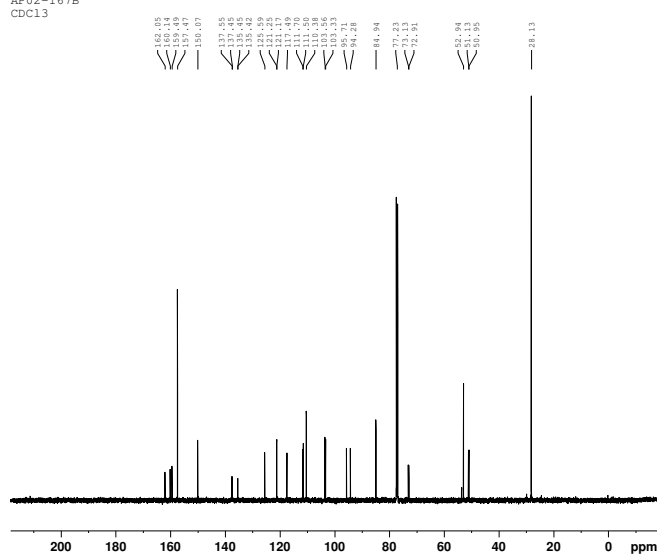
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
322.10933	303485024.0	100.00	322.10986	-0.53	C ₁₇ H ₁₃ O N ₅ F

Figure S33. Compound **24** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

off-white solid
300MHz

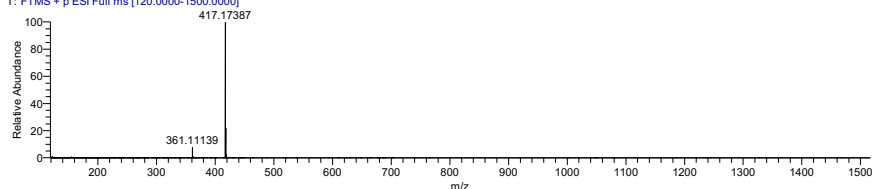


AP02-167B
CDC13

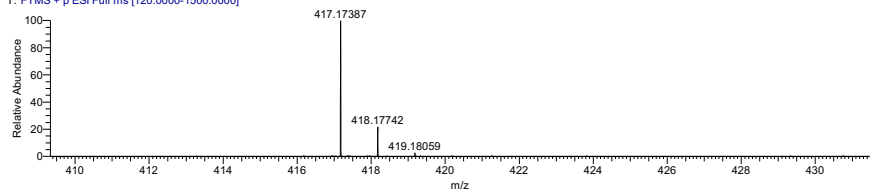


C:\Xcalibur\...95436ESIPN1 01/23/25 11:51:16 AP02-167B

95436ESIPN1 #10-14 RT: 0.15-0.18 AV: 2 SB: 10 0.39-0.59, 0.04-0.09 NL: 1.96E8
T: FTMS + p ESI Full ms [120.0000-1500.0000]



95436ESIPN1 #10-14 RT: 0.15-0.18 AV: 2 SB: 10 0.39-0.59, 0.04-0.09 NL: 1.96E8
T: FTMS + p ESI Full ms [120.0000-1500.0000]



95436ESIPN1 #11-13 RT: 0.15-0.18 AV: 2

SB: 10 0.39-0.59, 0.04-0.09

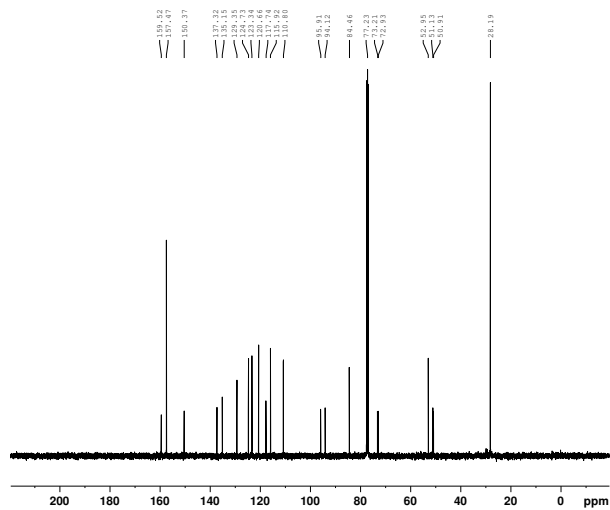
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z= 409.32826-431.46324

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
417.17387	203296880.0	100.00	417.17327	0.60	C ₂₁ H ₂₃ O ₃ N ₄ F ₂

Figure S34. Compound **25** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).


26 *trans*/
racemic

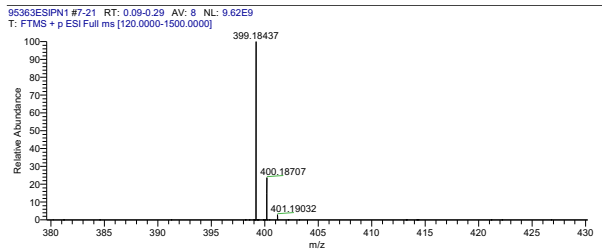
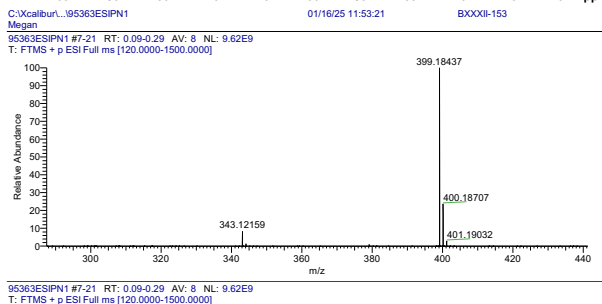


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PULPROG    zgpg30
PROCNO     1
DATE_      20250117
INSTRUM     spect
PROBHD      1H/5mmBBO-4
P1          12.00 usec
TD          65536
SOLVENT     CDCl3
NS          254
DS          4
AQ          24038.464 Hz
FIDRES      0.733698 Hz
RG           1.36358 Hz
RG2          203
DE           20.80 usec
TE          300.2 usec
AQ2          96.4 K
NUC1         1
NUC2         2
NUC3         2
D11          0.0300000 usec
TD1          65536
AQ1          100.4222298 MHz
F1           13C
P1           12.00 usec
F1M1         400.0000000 MHz
NUC1M1       13C
NUC2M1       1H
F2           125.00 MHz
F2M1         62.5000000 MHz
F2M2         15.0000000 MHz
F2M3         0.41666666 MHz
F1M1M        0.2095800 MHz

F2 - Processing parameters
SI          32768
SF           100.6181590 MHz
WDW          EM
SSB          0
LB           1.00 Hz
GB           0
PC           1.40 usec

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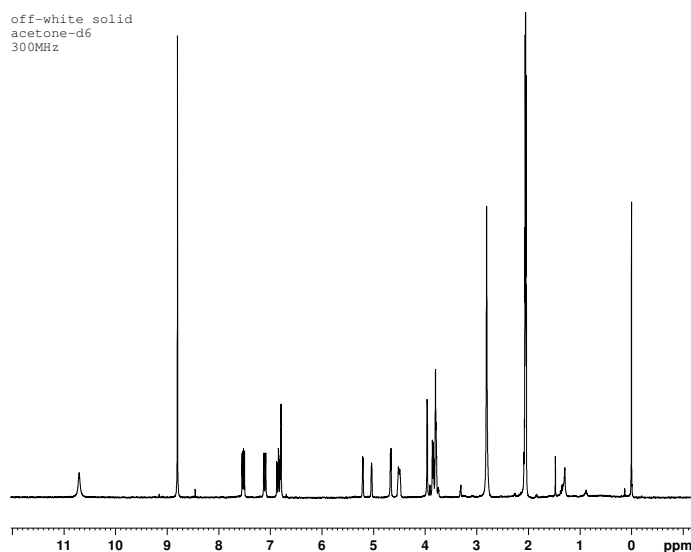


95363ESIPN1#7-21 RT: 0.09-0.29 AV: 8
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z= 379.59164-430.18535

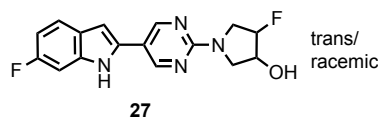
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
399.18437	9904142336.0	100.00	399.18270	4.21	C ₂₁ H ₂₄ O ₃ N ₄ F

S40

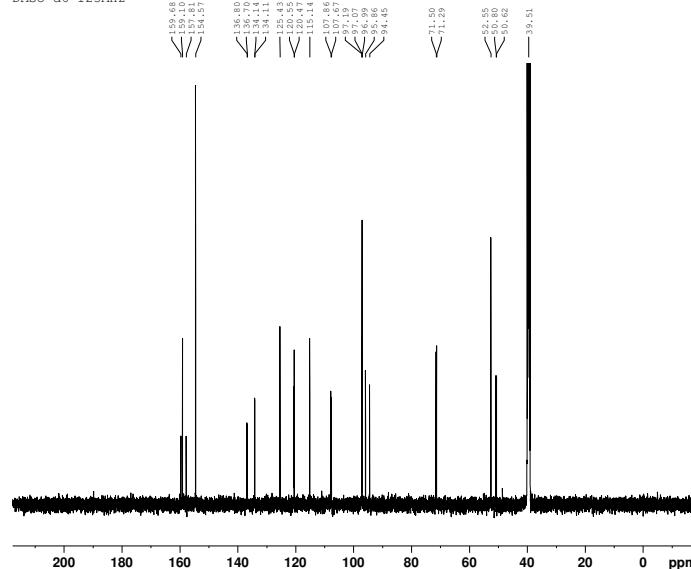
off-white solid
acetone-d6
300MHz



Current Data Parameters
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EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220224
Time 10.07 h
INSTRUM spect
PROBHD Z104275_0423 (
PULPROG zg30
TD 32768
SOLVENT Acetone
NS 16
DS 2
SWH 6009.615 Hz
FIDRES 0.366798 Hz
AQ 2.7262976 sec
RG 203
DW 83.200 usec
DE 6.50 usec
TE 297.7 K
D1 1.00000000 sec
TDO 1
SFO1 300.2318539 Mhz
NUC1 1H
PQ 4.67 usec
P1 14.00 usec
PLW1 17.16200066 W
F2 - Processing parameters
SI 65536
SF 300.2300045 Mhz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



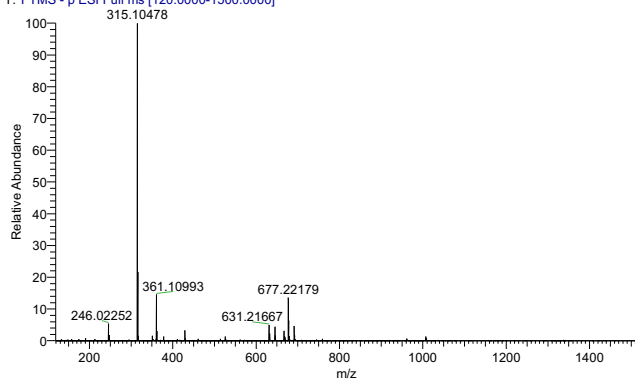
JSS19-188A light tan solid
DMSO-d6 125MHz



Current Data Parameters
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EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20231108
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INSTRUM spect
PROBHD Z113652_0064 (
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 1024
DS 4
SWH 29761.904 Hz
FIDRES 0.908261 Hz
AQ 1.1010048 sec
RG 203
DW 16.800 usec
DE 6.50 usec
TE -139.9 K
D1 2.00000000 sec
D11 0.03000000 sec
TDO 1
SFO1 125.7779086 Mhz
NUC1 13C
PQ 3.47 usec
P1 10.40 usec
PLW1 110.00000000 W
SFO2 500.1620006 Mhz
NUC2 1H
CPDPRG2 waltres
PCPD2 80.00 usec
PLW2 18.00000000 W
PLW12 0.37195000 W
PLW13 0.18708999 W
F2 - Processing parameters
SI 32768
SF 125.7653939 Mhz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

C:\xcalibur\data\MSfacility\87428ESIPN1 03/21/22 11:59:04 JSS19-159A

87428ESIPN1#6-26 RT: 0.10-0.40 AV: 11 NL: 4.65E8
T: FTMS - p ESI Full ms [120.0000-1500.0000]

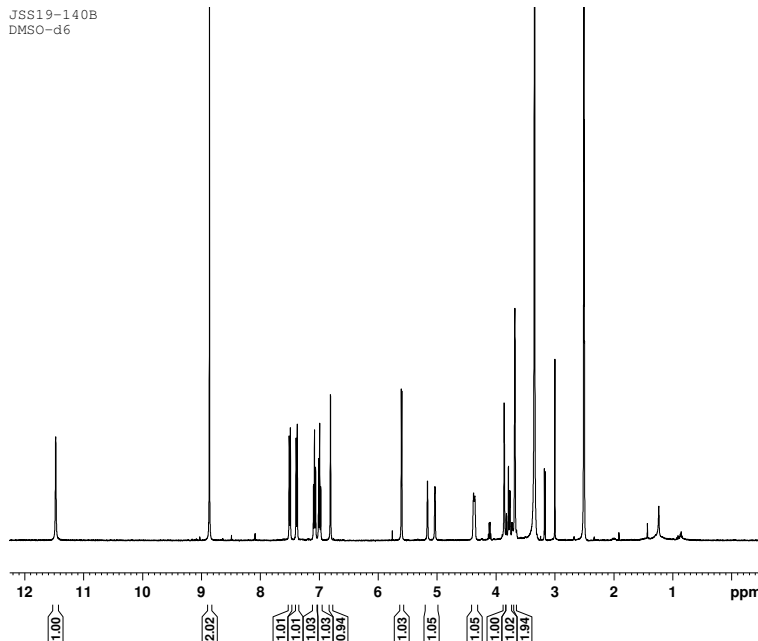


87428ESIPN1#6-26 RT: 0.10-0.40 AV: 11
T: FTMS - p ESI Full ms [120.0000-1500.0000]

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
315.10478	467651104.0	100.00	315.10519	-0.41	C ₁₆ H ₁₃ ON ₄ F ₂

Figure S36. Compound 27 ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

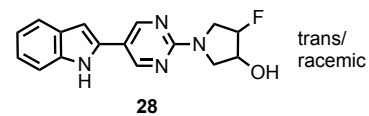
JSS19-140B
DMSO-d6



Current Data Parameters
NAME JSS19-140B2
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20220316
Time 16:57 h
INSTRUM spect
PROBHD Z108618_0240 (
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 128
DW 62.400 usec
DE 8.50 usec
TE 87.7 K
D1 1.00000000 sec
TD0 1
SFO1 400.1324708 MHz
NUC1 1H
FO 4.83 usec
P1 14.50 usec
PLW1 12.00000000 W

F2 - Processing parameters
SI 65536
SF 400.1300032 MHz
WCHW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

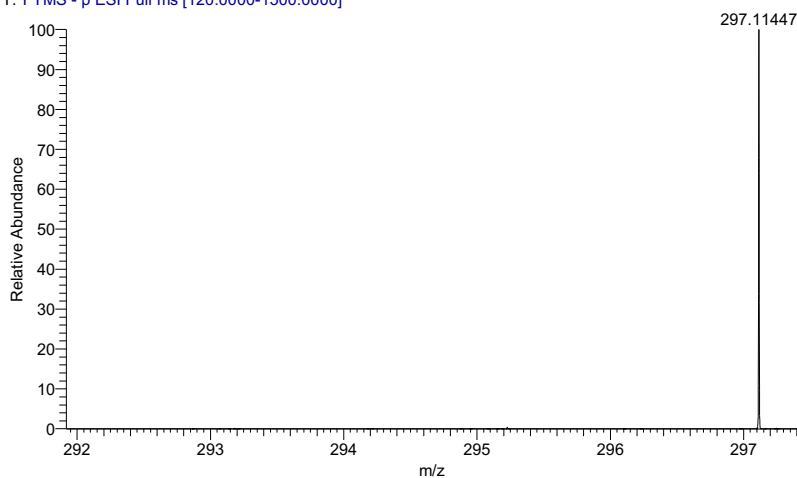


C:\Xcalibur\data\MSfacility\87427ESIPN1

03/21/22 11:52:17

JSS19-140B

87427ESIPN1#8-18 RT: 0.13-0.28 AV: 6 NL: 2.82E8
T: FTMS - p ESI Full ms [120.0000-1500.0000]



87427ESIPN1#8-18 RT: 0.13-0.28 AV: 6

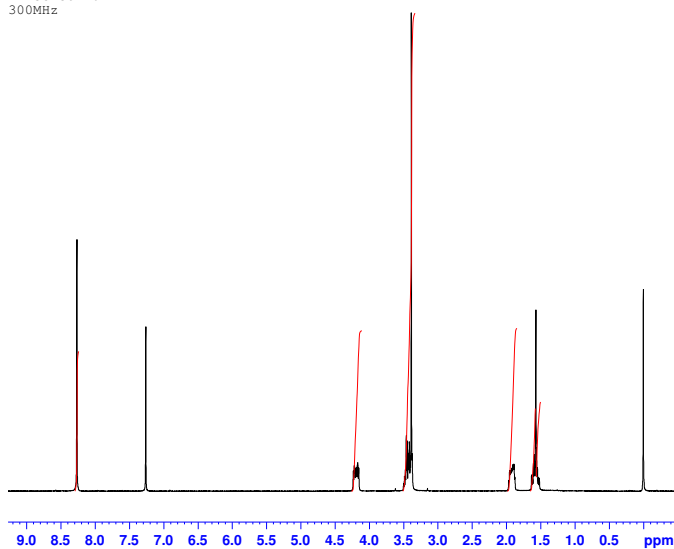
T: FTMS - p ESI Full ms [120.0000-1500.0000]

m/z = 291.91784-297.40755

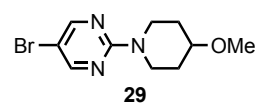
m/z	Intensity	Relative	Delta (ppm)	Composition
297.11447	292447040.0	100.00	-0.48	C ₁₆ H ₁₄ ON ₄ F

Figure S37. Compound **28** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

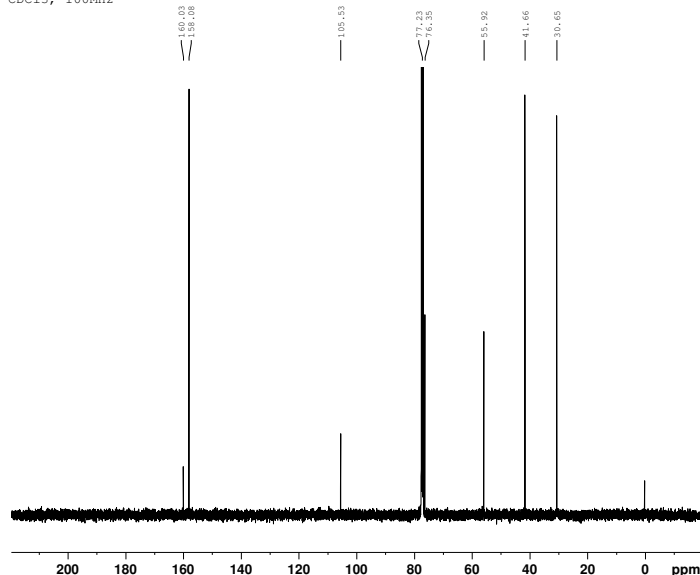
white solid
300MHz



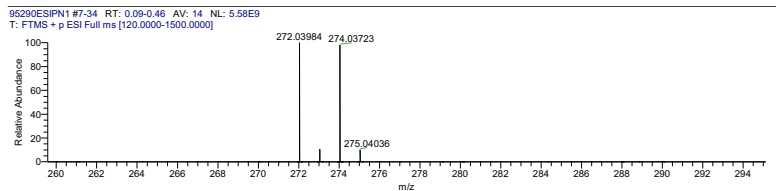
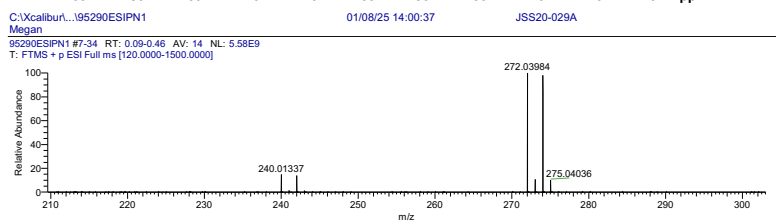
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EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220509
Time 9.11 h
INSTRUM spect
PROBHD Z104275_0423 (
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 6009.615 Hz
FIDRES 0.366798 Hz
AQ 2.7262976 sec
RG 181
DW 83.200 usec
DE 6.50 usec
TE 295.0 K
D1 1.00000000 sec
TDO 1
SFO1 300.2318539 MHz
NUC1 1H
P0 4.67 usec
P1 14.00 usec
PLW1 17.16200066 W
F2 - Processing parameters
SI 65536
SF 300.2300065 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



JSS20-029A
CDCl3, 100MHz



Current Data Parameters
NAME JSS20-029A 13C
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20250108
Time 3.32 h
INSTRUM spect
PROBHD Z108618_0240 (
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 24038.461 Hz
FIDRES 0.733596 Hz
AQ 1.3631488 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 96.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TDO 1
SFO1 100.6228238 MHz
NUC1 13C
P0 4.20 usec
P1 12.60 usec
PLW1 60.00000000 W
SFO2 400.1316005 MHz
NUC2 1H
CPDPRG2 waltz65
PCPD2 90.00 usec
PLW2 15.00000000 W
PLW12 0.41666999 W
PLW13 0.20956000 W
F2 - Processing parameters
SI 32768
SF 100.6127472 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

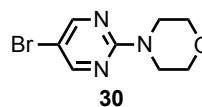
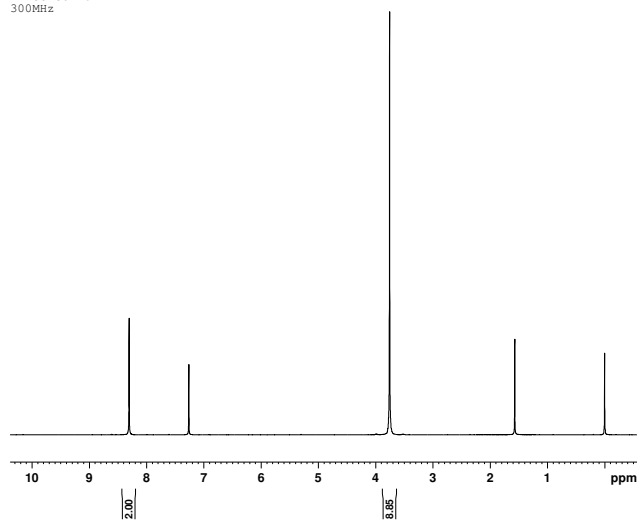


95290ESIPN1#7-33 RT: 0.09-0.46 AV: 14
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z = 259.57150-295.10509

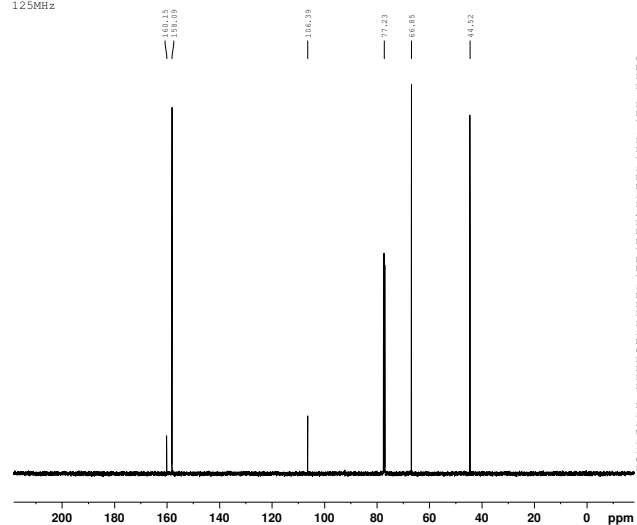
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
272.03984	5599183872.0	100.00	272.03930	2.00	C ₁₀ H ₁₅ O ₃ Br

Figure S38. Compound **29** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), high-resolution mass spectrum (bottom).

white solid
300MHz



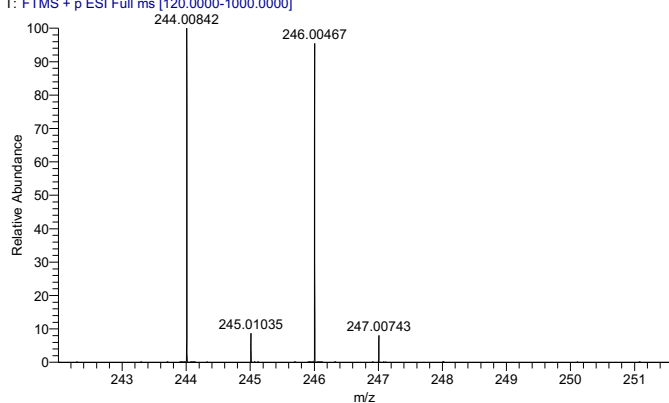
white solid
125MHz



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06/15/23 16:40:05

90344ESIP1#50-94 RT: 0.52-0.98 AV: 45 SB: 60 0.11-0.34, 1.39-1.77 NL: 7.69E9
T: FTMS + p ESI Full ms [120.0000-1000.0000]



90344ESIP1#50-94 RT: 0.52-0.98 AV: 45

SB: 60 0.11-0.34, 1.39-1.77

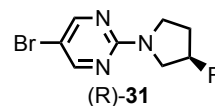
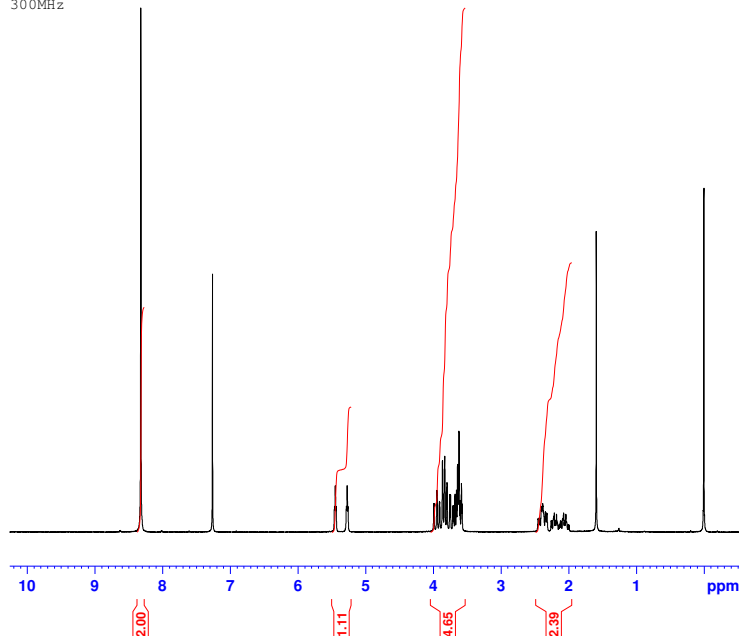
T: FTMS + p ESI Full ms [120.0000-1000.0000]

m/z= 242.00217-251.56310

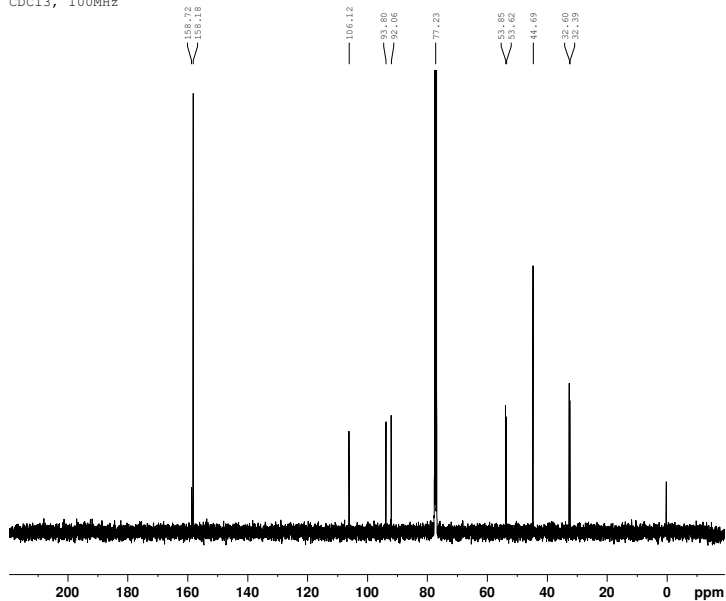
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
244.00842	7738014208.0	100.00	244.00800	1.72	C ₈ H ₁₁ ON ₃ Br

Figure S39. Compound **30** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), high-resolution mass spectrum (bottom).

off-white solid
300MHz



JSS20-088A
CDCl3, 100MHz

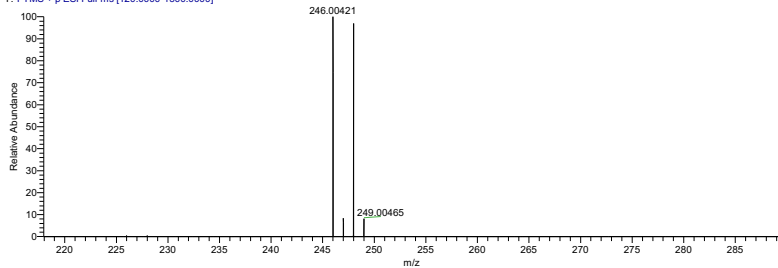


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Megan

95289ESIPN1 #7-29 RT: 0.09-0.41 AV: 12 NL: 4.89E9

T: FTMS + p ESI Full ms [120.0000-1500.0000]



95289ESIPN1#7-29 RT: 0.09-0.41 AV: 12

T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z = 217.95148-289.29780

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
246.00421	4901943808.0	100.00	246.00366	2.22	C ₈ H ₁₀ N ₃ BrF

Figure S40. Compound (R)-31 ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), high-resolution mass spectrum (bottom).

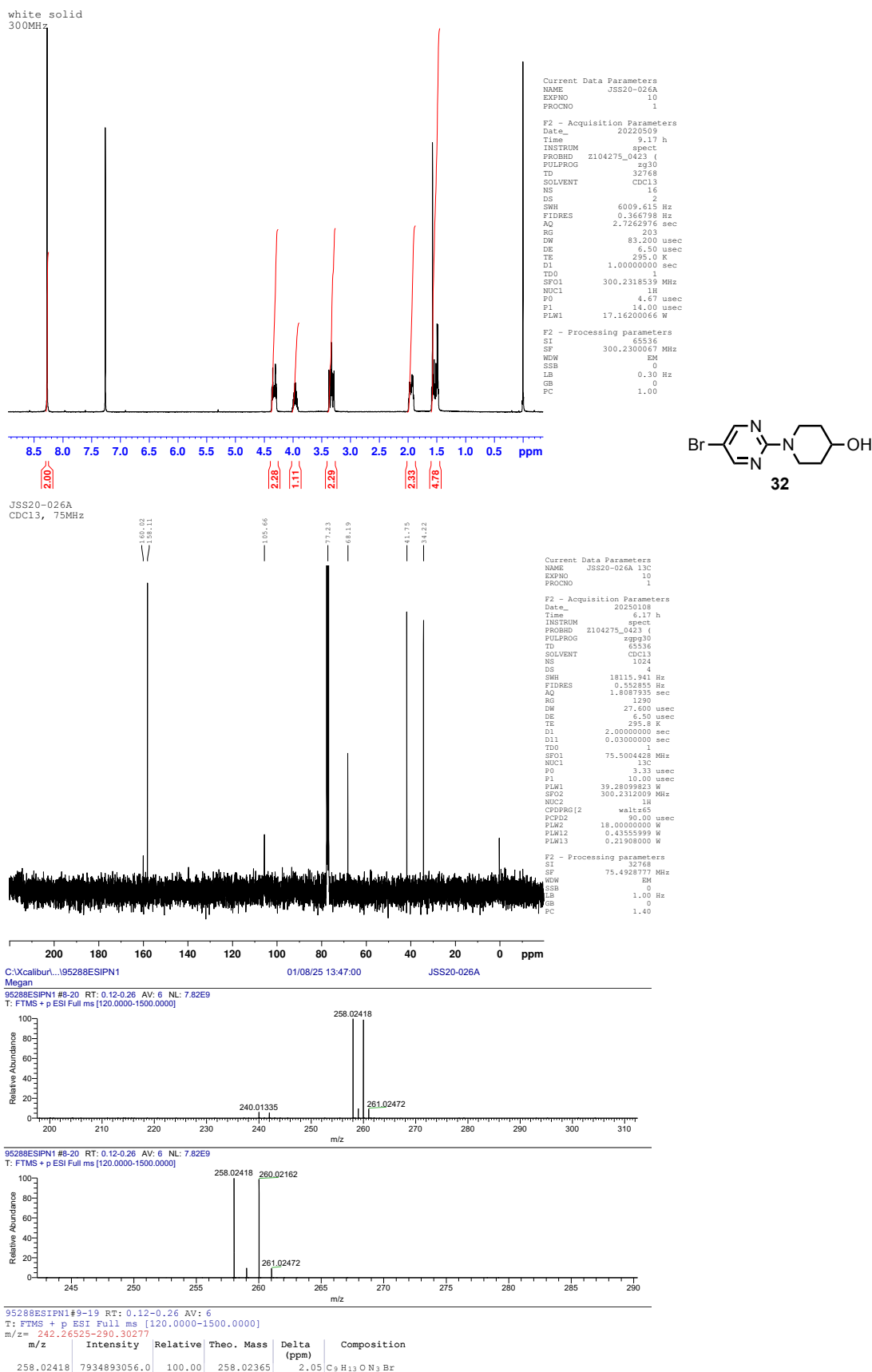
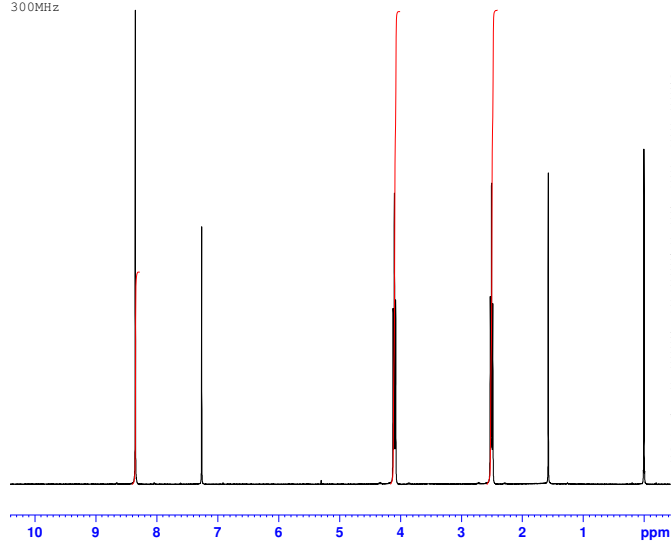


Figure S41. Compound **32** ^1H NMR spectrum (top), ^{13}C NMR spectrum (middle), high-resolution mass spectrum (bottom).

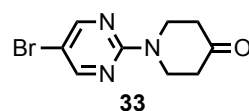
white solid
300MHz



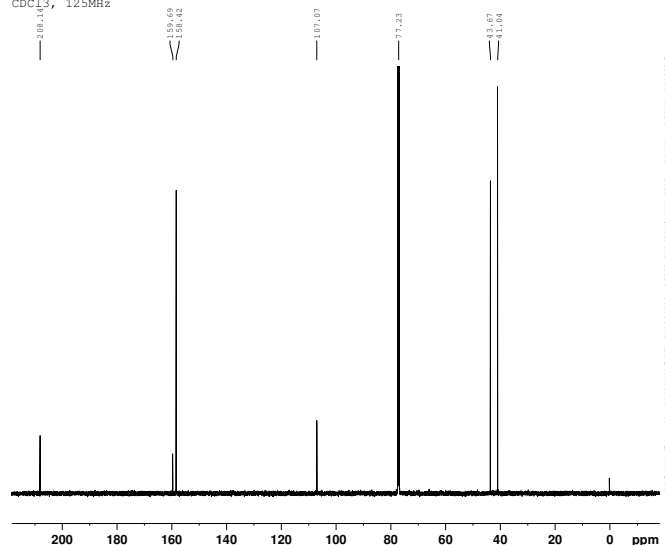
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EXPNO     10
PROCNO    1

F2 - Acquisition Parameters
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Time      9.43 h
INSTRUM   spect
PROBHD    Z104275_0423 (
PULPROG   zg30
TD         32768
SOLVENT   CDCl3
NS         16
DS         2
SWH        6009.615 Hz
FIDRES     0.366798 Hz
AQ         2.7262976 sec
RG         203
DW         83.200 usec
DE         6.50 usec
TE         295.8 K
D1         1.00000000 sec
TD0        1
SFO1       300.2318539 MHz
NUC1       1H
P0         4.67 usec
P1         14.00 usec
PLW1       17.16200066 W

F2 - Processing parameters
SI         65536
SF         300.2300066 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
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AP02-160B
CDCl3, 125MHz



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Current Data Parameters
NAME      AP02-160B-132MR
EXPNO     12
PROCNO    1

F2 - Acquisition Parameters
Date_     20230108
Time      23.57 h
INSTRUM   spect
PROBHD    Z113652_0064 (
PULPROG   zgpg30
TD         65536
SOLVENT   CDCl3
NS         1024
DS         4
SWH        29761.904 Hz
FIDRES     0.908261 Hz
AQ         1.1010048 sec
RG         203
DW         16.800 usec
DE         6.50 usec
TE         298.0 K
D1         2.00000000 sec
D11        0.03000000 sec
TD0        1
SFO1       125.7779086 MHz
NUC1       13C
P0         3.47 usec
P1         10.40 usec
PLW1       110.0000000 W
SFO2       500.1620006 MHz
NUC2       1H
CPDPRG2   waltz165
PCPD2     60.00 usec
PLW2       18.0000000 W
PLW12     0.3719500 W
PLW13     0.1870899 W

F2 - Processing parameters
SI         32768
SF         125.7653058 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         1.40
```

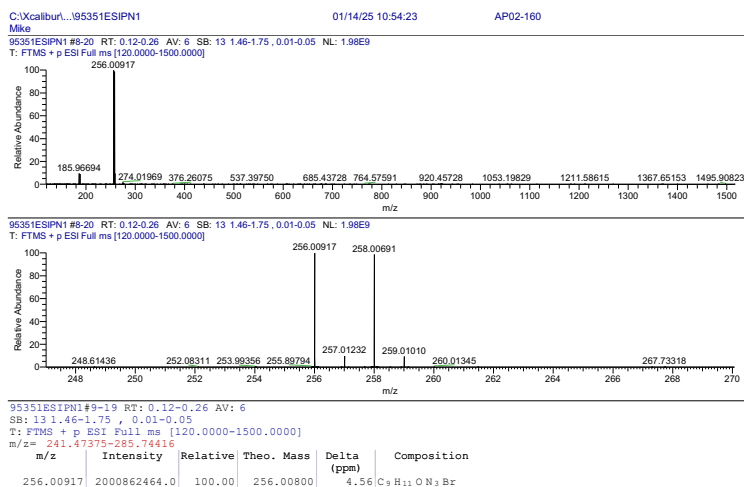
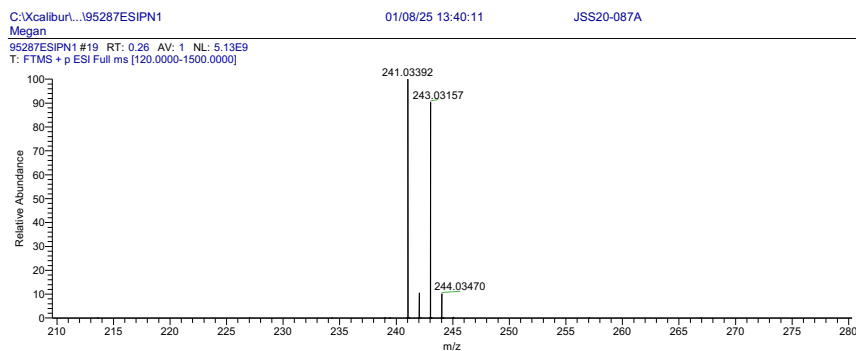
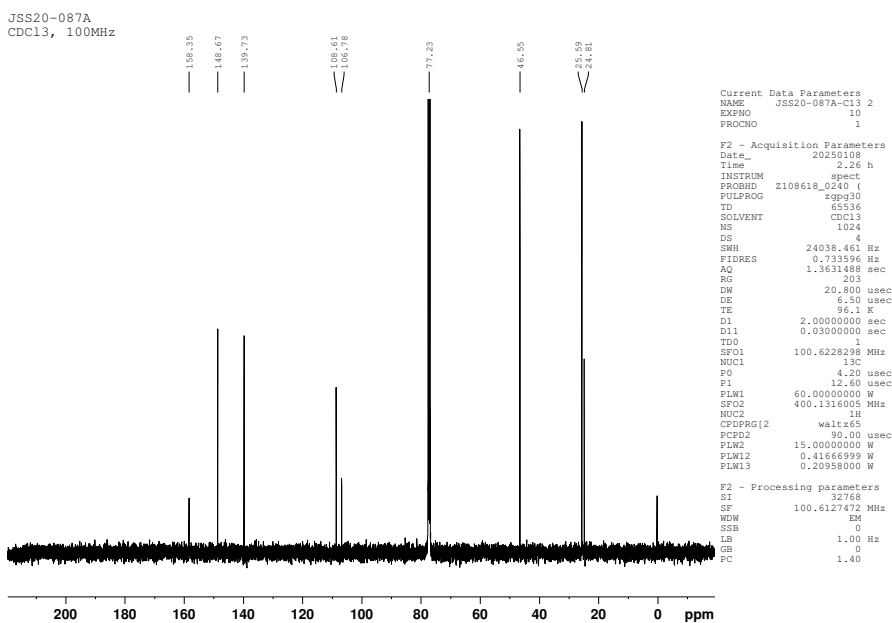
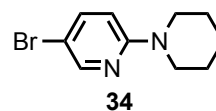
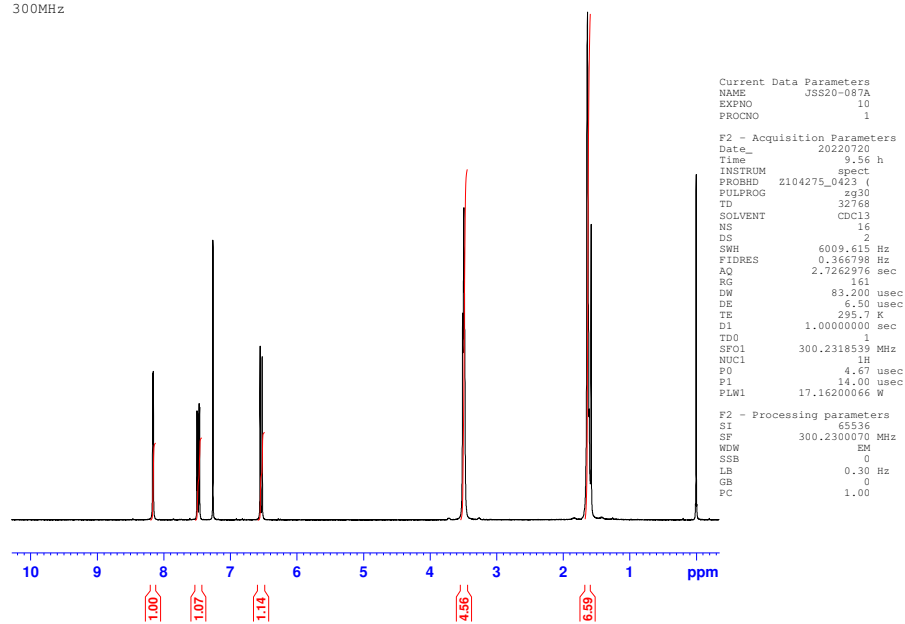


Figure S42. Compound **33** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), high-resolution mass spectrum (bottom).

colorless oil
300MHz

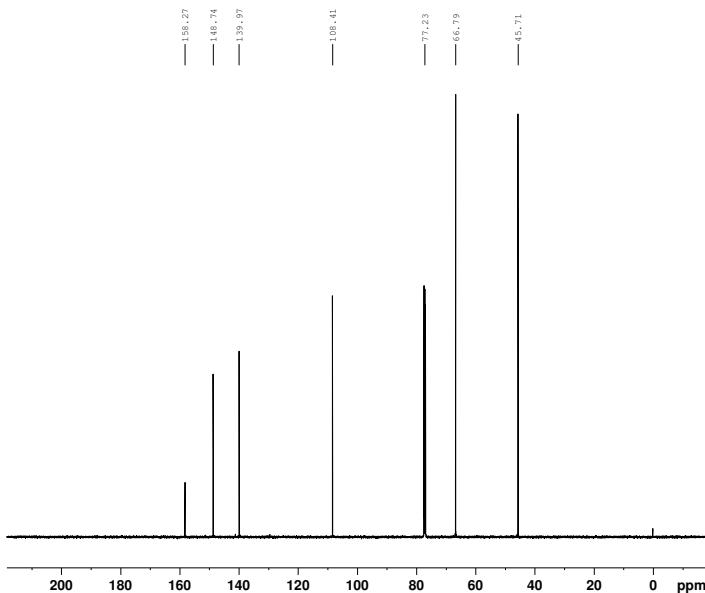
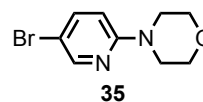
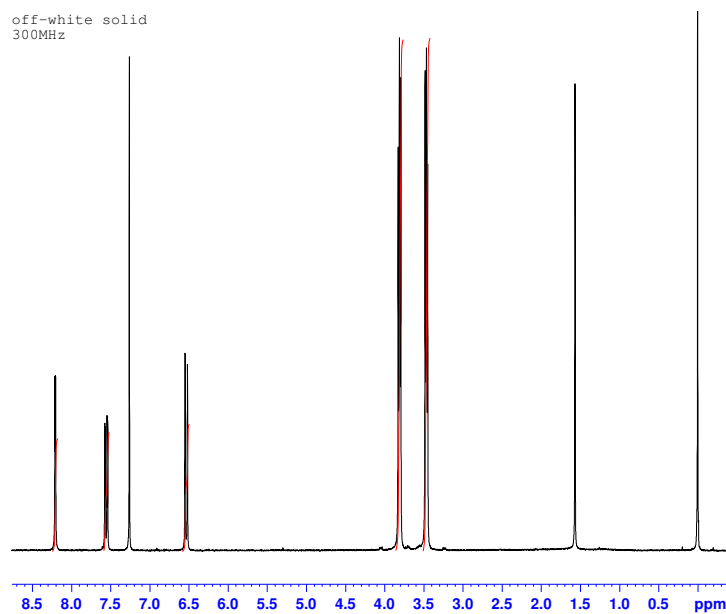


95287ESIPN1#19 RT: 0.26
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z= 209.58236-280.29005

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
241.03392	5135907328.0	100.00	241.03349	1.80	C ₁₀ H ₁₄ N ₂ Br

Figure S43. Compound **34** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), high-resolution mass spectrum (bottom).

off-white solid
300MHz



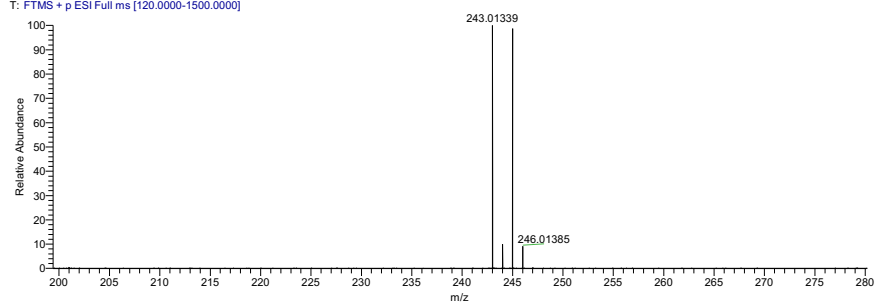
C:\Xcalibur\...95286ESIPN1
Megan

01/08/25 13:33:25

JSS20-086A

95286ESIPN1 #8-26 RT: 0.12-0.35 AV: 9 NL: 5.78E9

T: FTMS + p ESI Full ms [120.0000-1500.0000]



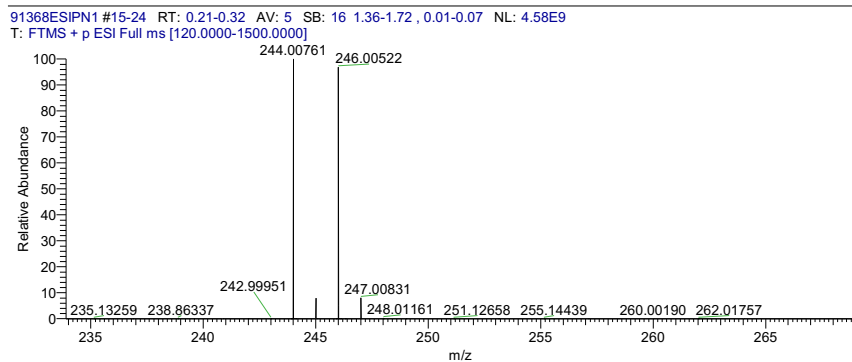
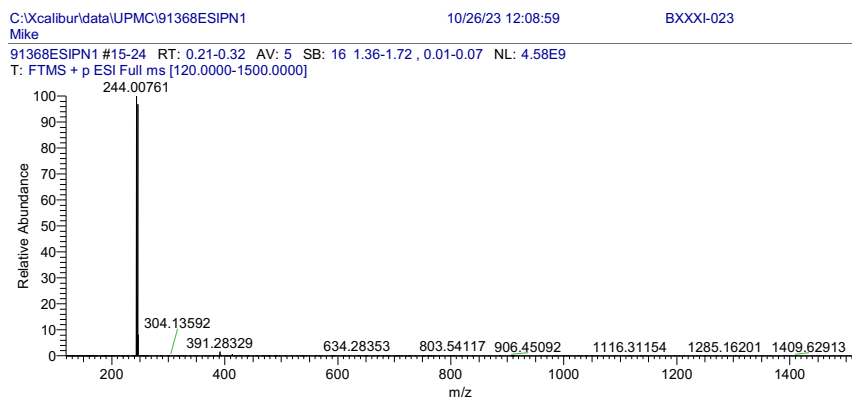
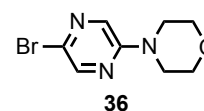
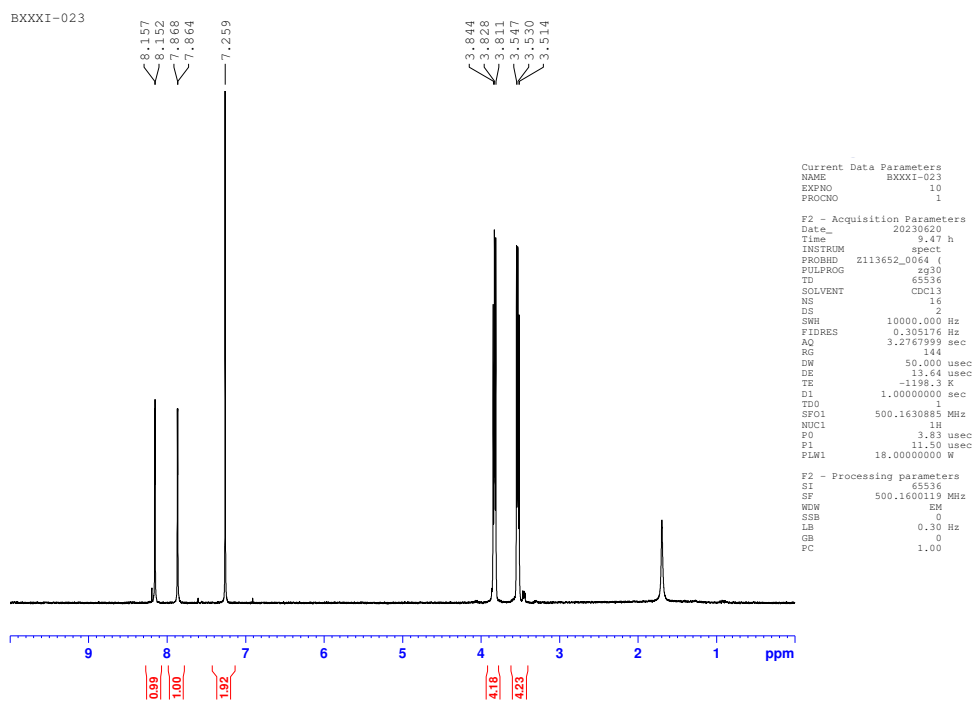
95286ESIPN1#9-25 RT: 0.12-0.35 AV: 9

T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z = 199.39356-280.11456

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
243.01339	5895931904.0	100.00	243.01275	2.64	C ₉ H ₁₂ O N ₂ Br

Figure S44. Compound **35** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), high-resolution mass spectrum (bottom).

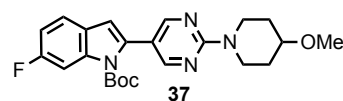
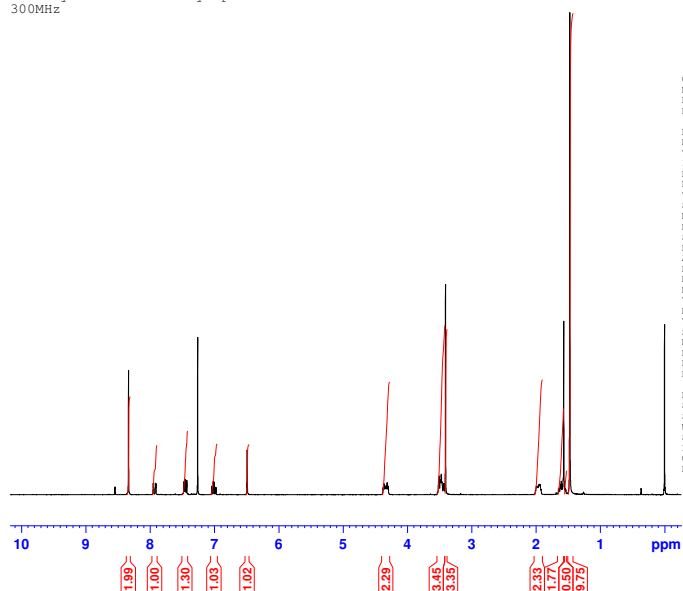


91368ESIPN1#15-23 RT: 0.21-0.32 AV: 5
SB: 16 1.36-1.72, 0.01-0.07
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z = 233.89190-268.96538

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
244.00761	4591328256.0	100.00	244.00800	-1.58	C ₈ H ₁₁ ON ₃ Br

Figure S45. Compound 36 ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

faint yellow viscous syrup
300MHz

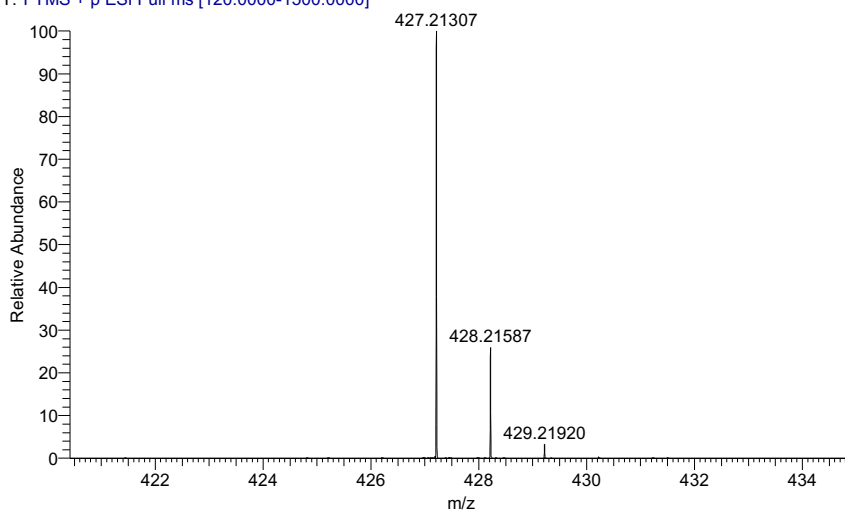


C:\Xcalibur\data\MSfacility\89008ESIPN1
Sarah

12/15/22 10:20:50

jss20-158A

89008ESIPN1 #7-20 RT: 0.09-0.26 AV: 7 NL: 9.05E9
T: FTMS + p ESI Full ms [120.0000-1500.0000]

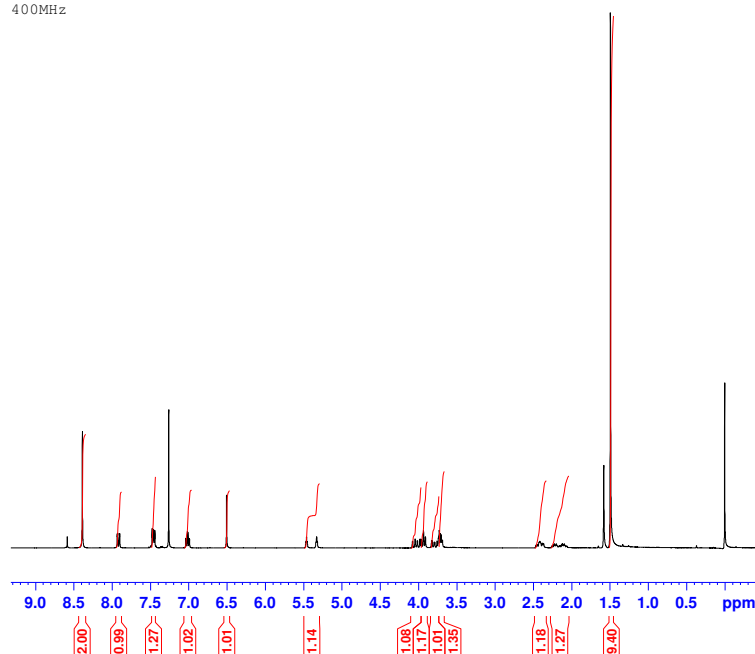


89008ESIPN1#7-19 RT: 0.09-0.26 AV: 7
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z= 420.41587-434.93539

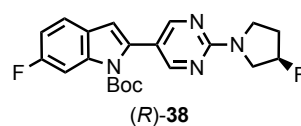
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
427.21307	9255216128.0	100.00	427.21400	-2.16	C ₂₃ H ₂₈ O ₃ N ₄ F

Figure S46. Compound **37** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

off-white solid
400MHz

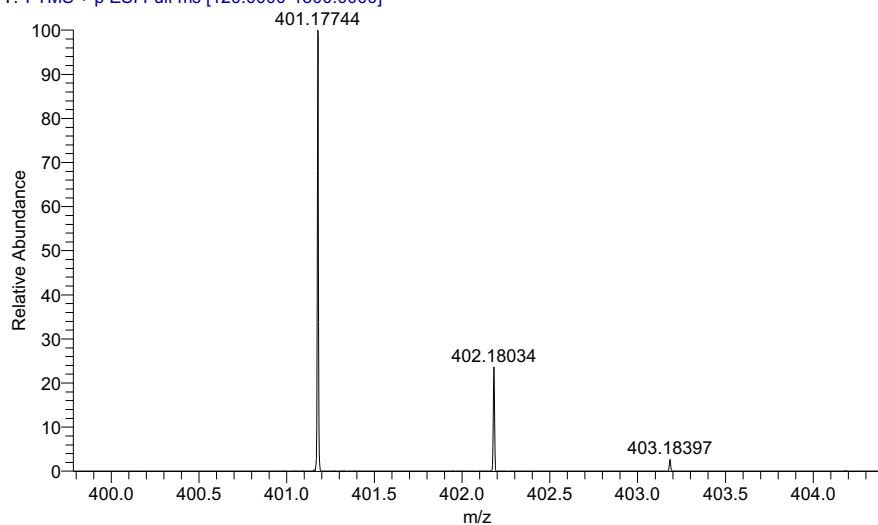


Current Data Parameters
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EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220803
Time 9.42 h
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PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 144
DW 62.400 usec
DE 6.50 usec
TE 104.5 K
D1 1.00000000 sec
TDO 1
SFO1 400.1324708 MHz
NUC1 1H
P0 4.83 usec
P1 14.50 usec
PLW1 12.00000000 W
F2 - Processing parameters
SI 65536
SF 400.1300093 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



C:\Xcalibur\data\MSfacility\88262ESIPN1
Sarah 08/12/22 11:49:14 JSS20-100B

88262ESIPN1#10-16 RT: 0.15-0.21 AV: 3 NL: 1.00E10
T: FTMS + p ESI Full ms [120.0000-1500.0000]

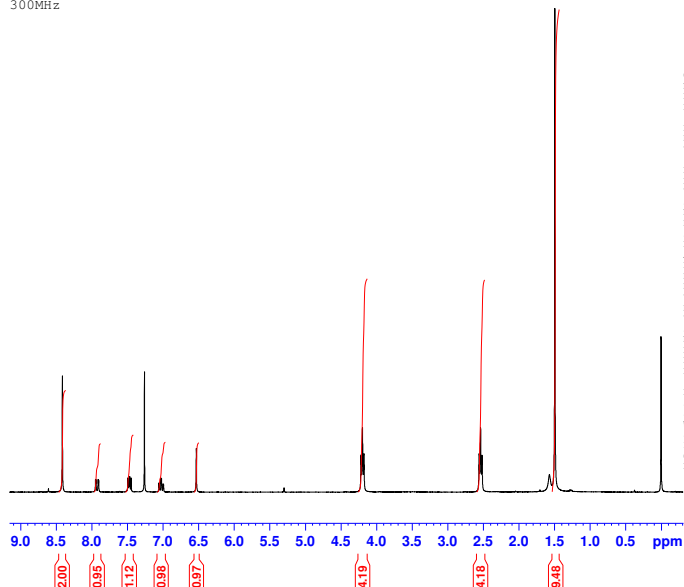


88262ESIPN1#11-15 RT: 0.15-0.21 AV: 3
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z= 399.78301-404.38922

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
401.17744	10368265216.0	100.00	401.17836	-2.29	C ₂₁ H ₂₃ O ₂ N ₄ F ₂

Figure S47. Compound (R)-38 ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

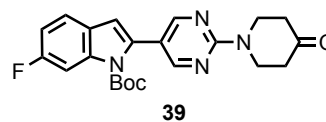
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300MHz



Current Data Parameters
NAME JSS20-109A
EXPNO 10
PROCNO 1

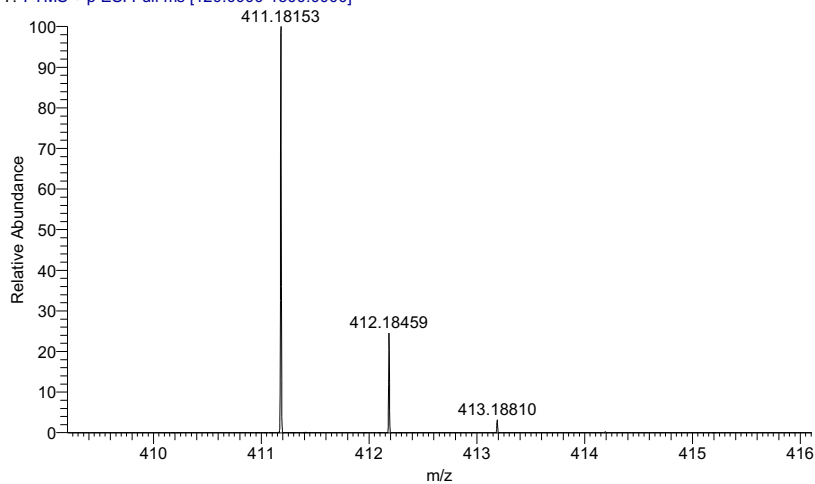
F2 - Acquisition Parameters
Date_ 20220804
Time 9.52 h
INSTRUM spect
PROBHD Z104275_0423 (
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 6009.615 Hz
FIDRES 0.366798 Hz
AQ 2.7262976 sec
RG 203
DW 83.200 usec
DE 6.50 usec
TE 295.9 K
D1 1.00000000 sec
TD0 1
SFO1 300.2318539 MHz
NUC1 1H
PQ 4.67 usec
P1 14.00 usec
PLW1 17.16200066 W

F2 - Processing parameters
SI 65536
SF 300.2300071 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



C:\Xcalibur\data\MSfacility\88260ESIPN1 08/12/22 11:35:41 JSS20-109A
Sarah

88260ESIPN1 #7-15 RT: 0.09-0.21 AV: 5 NL: 6.84E9
T: FTMS + p ESI Full ms [120.0000-1500.0000]

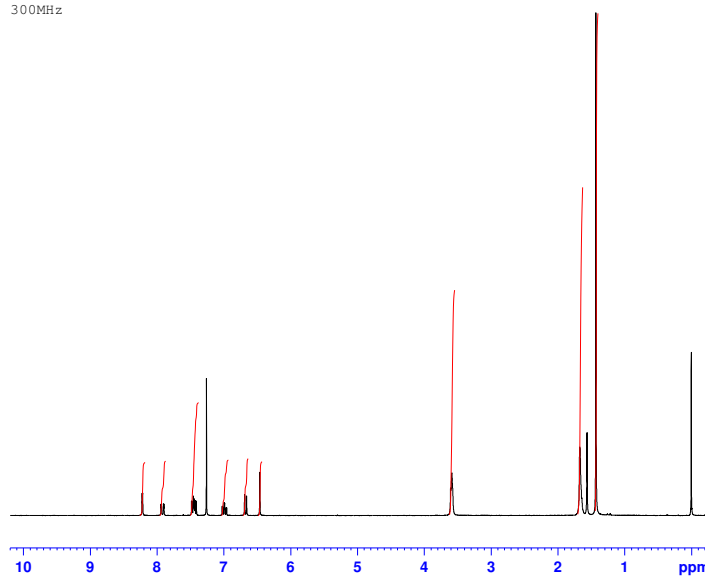


88260ESIPN1#7-15 RT: 0.09-0.21 AV: 5
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z= 399.11632-424.53643

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
411.18153	7059740160.0	100.00	411.18270	-2.84	C ₂₂ H ₂₄ O ₃ N ₄ F

Figure S48. Compound **39** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

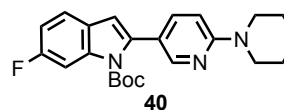
off-white solid
300MHz



Current Data Parameters
NAME JSS20-126B
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20220927
Time 9.03 h
INSTRUM spect
PROBHD Z104275_0423 (
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 6009.615 Hz
FIDRES 0.366798 Hz
AQ 2.7262976 sec
RG 203
DW 83.200 usec
DE 6.50 usec
TE 295.2 K
D1 1.00000000 sec
TD0 1
SFO1 300.2318539 MHz
NUC1 1H
FO 4.67 usec
P1 14.00 usec
PLW1 17.16200066 W

F2 - Processing parameters
SI 65536
SF 300.2300073 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



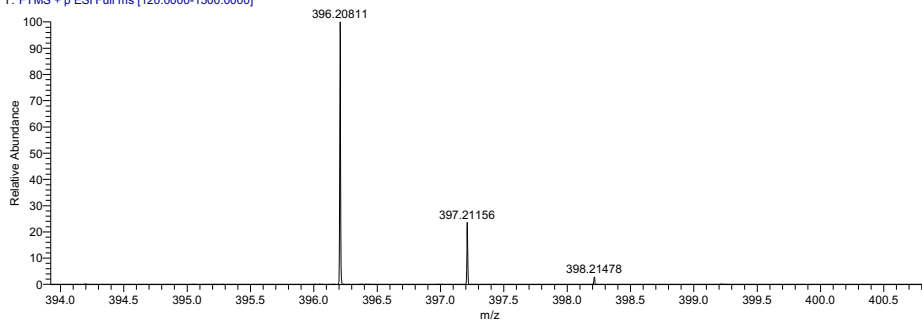
C:\Xcalibur\data\UPMC\88513ESIPN1

09/29/22 09:23:26

JSS20-126B

Sarah

88513ESIPN1#7-15 RT: 0.09-0.21 AV: 5 NL: 2.55E9
T: FTMS + p ESI Full ms [120.0000-1500.0000]



88513ESIPN1#7-15 RT: 0.09-0.21 AV: 5

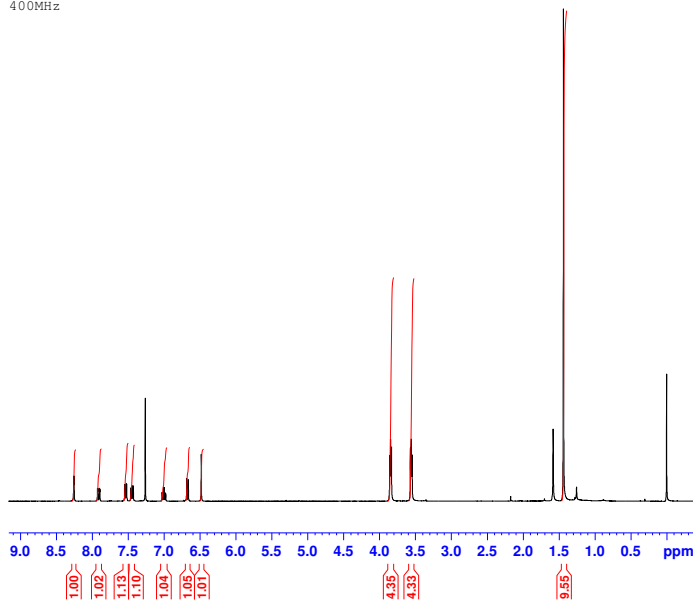
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z = 393.92201-400.85905

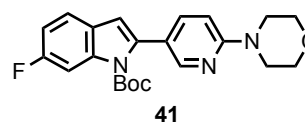
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
396.20811	2567506688.0	100.00	396.20818	-0.19	C ₂₃ H ₂₇ O ₂ N ₃ F

Figure S49. Compound **40** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

light yellow foam
400MHz



Current Data Parameters
NAME JSS20-099A
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220729
Time 9.07 h
INSTRUM spect
PROBHD z108618_0240 (4
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 144
DW 62.400 usec
DE 6.50 usec
TE 303.4 K
D1 1.00000000 sec
TD0 1
SFO1 400.1324708 MHz
NUC1 1H
P0 4.83 usec
P1 14.50 usec
PLW1 12.00000000 W
F2 - Processing parameters
SI 65536
SF 400.1300093 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



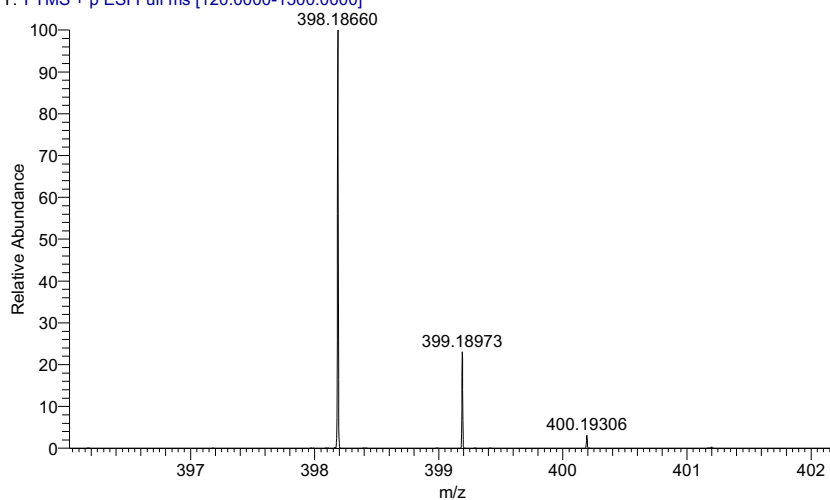
C:\Xcalibur\data\MSfacility\88263ESIPN1
Sarah

08/12/22 11:56:01

JSS20-099A

88263ESIPN1 #8-17 RT: 0.12-0.23 AV: 5 NL: 4.72E9

T: FTMS + p ESI Full ms [120.0000-1500.0000]



88263ESIPN1#9-17 RT: 0.12-0.23 AV: 5

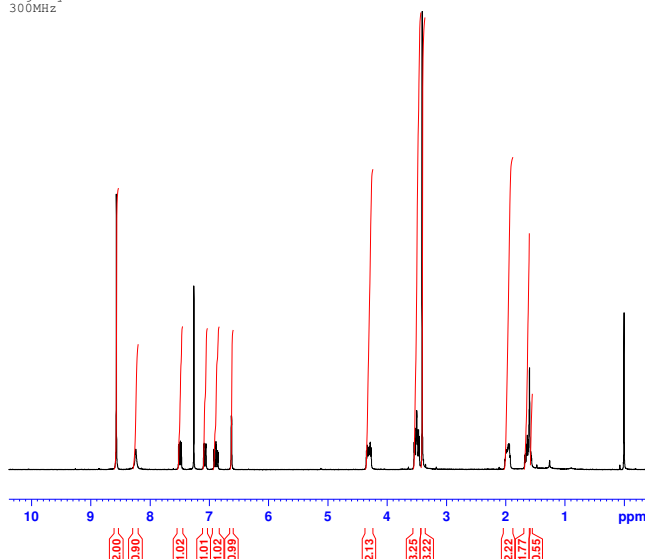
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z = 396.02327-402.19912

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
398.18660	4752931840.0	100.00	398.18745	-2.12	C ₂₂ H ₂₅ O ₃ N ₃ F

Figure S50. Compound **41** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

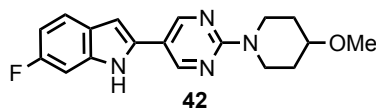
light yellow solid
300MHz



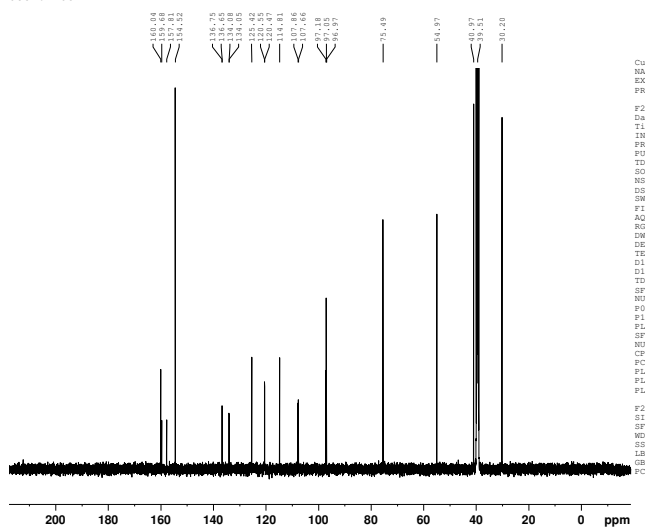
```
Current Data Parameters
NAME      JSS20-040A
EXPNO     20
PROCNO    1

F2 - Acquisition Parameters
Date_     20220518
Time      10.19 h
INSTRUM   spect
PROBHD    Z104275_0423 (
PULPROG   zg30
TD         32768
SOLVENT   CDCl3
NS         16
DS         2
SWH        6009.615 Hz
FIDRES     0.366798 Hz
AQ         2.7262776 sec
RG         181
DW         83.200 usec
DE         6.50 usec
TE         296.0 K
D1         1.00000000 sec
TD0        1
SF01       300.2318539 MHz
NUC1       1H
P0         4.67 usec
P1         14.00 usec
PLW1       17.16200066 W

F2 - Processing parameters
SI         65536
SF         300.2300073 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
```



JSS20-153B



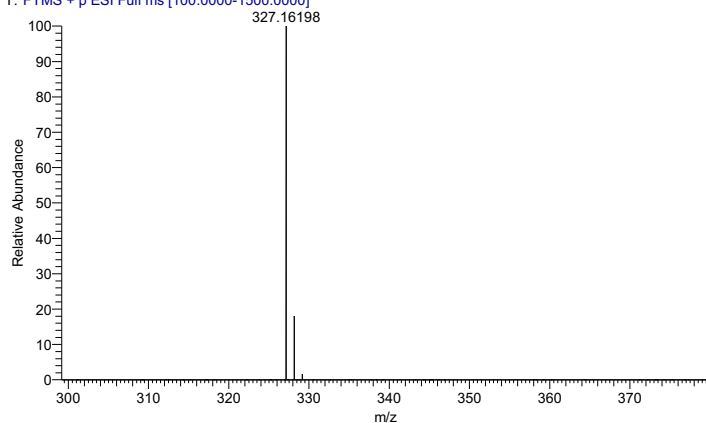
```
Current Data Parameters
NAME      JSS20-153B C13
EXPNO     10
PROCNO    1

F2 - Acquisition Parameters
Date_     20221107
Time      5.17 h
INSTRUM   spect
PROBHD    Z113652_0054 (
PULPROG   zgpg30
TD         65536
SOLVENT   DMSO
NS         1024
DS         4
SWH        29761.904 Hz
FIDRES     0.508261 Hz
AQ         1.1010048 sec
RG         203
DW         16.800 usec
DE         6.50 usec
TE         -1403.4 K
D1         2.00000000 sec
D11        0.03000000 sec
TD0        1
SF01       125.7779086 MHz
NUC1       13C
P0         3.47 usec
P1         10.40 usec
PLW1       110.00000000 W
SF02       500.1420006 MHz
NUC2       1H
CPDPRG2   waltz165
PCPD2      80.00 usec
PLM2       18.00000000 W
PLW2       0.37195000 W
PLM13      0.18708999 W

F2 - Processing parameters
SI         32768
SF         125.7653941 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         1.40
```

C:\calibur\data\MSfacility\87808ESI\PN1
Megan
06/10/22 14:11:26
JSS20-040A

87808ESI\PN1#7-17 RT: 0.09-0.23 AV: 6 NL: 3.12E9
T: FTMS + p ESI Full ms [100.0000-1500.0000]

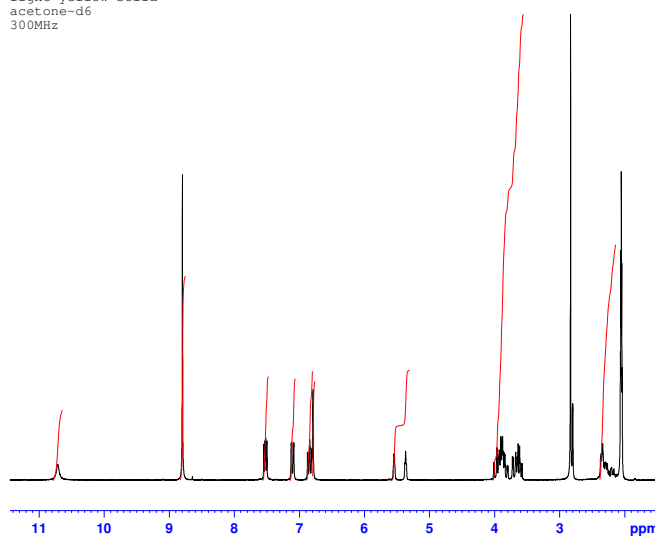


87808ESI\PN1#7-17 RT: 0.09-0.23 AV: 6
T: FTMS + p ESI Full ms [100.0000-1500.0000]
m/z = 299.15896-379.95799

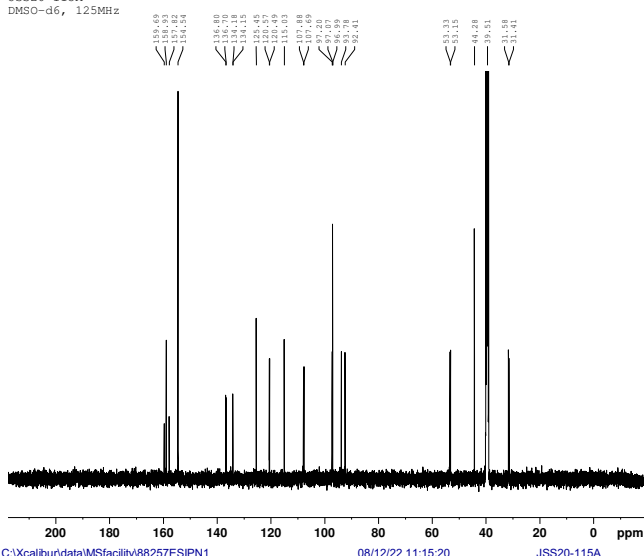
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
327.16198	3148229120.0	100.00	327.16157	1.26	C ₁₈ H ₂₀ ON ₄ F

Figure S51. Compound **42** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

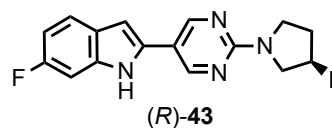
light yellow solid
acetone-d6
300MHz



JSS20-115A
DMSO-d6, 125MHz



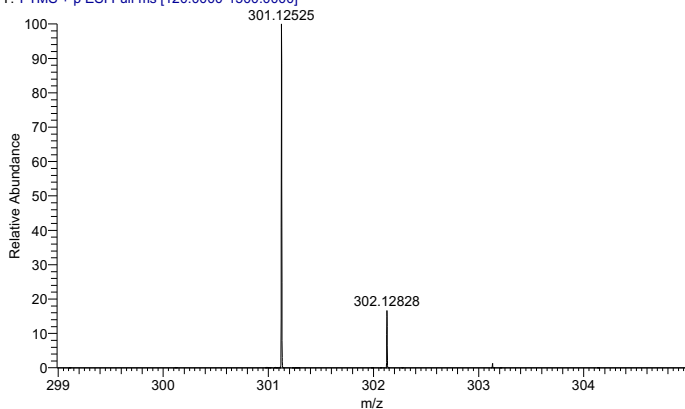
Current Data Parameters
NAME JSS20-115A
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220811
Time 10.13 h
INSTRUM spect
PROBHD Z104275_0423 ()
PULPROG zg30
TD 32768
SOLVENT Acetone
NS 16
DS 2
SWH 6009.615 Hz
FIDRES 0.366798 Hz
AQ 2.7262976 sec
RG 181
DW 83.200 usec
DE 6.50 usec
TE 295.8 K
D1 1.00000000 sec
TD0 1
SFO1 300.2318539 MHz
NUC1 1H
P0 4.67 usec
P1 14.00 usec
PLW1 17.1620066 W
F2 - Processing parameters
SI 65536
SF 300.2300051 MHz
WCM EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



Current Data Parameters
NAME JSS20-115A 13C
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20250204
Time 2.19 h
INSTRUM spect
PROBHD Z113652_0064 ()
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 1024
DS 4
SWH 29761.904 Hz
FIDRES 0.908261 Hz
AQ 1.1010348 sec
RG 203
DW 16.800 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 125.7779086 MHz
NUC1 13C
P0 3.47 usec
P1 10.40 usec
PLW1 110.0000000 W
SFO2 500.1620006 MHz
NUC2 1H
CPDPRG2 waltz65
PCPD2 80.00 usec
PLW2 18.0000000 W
PLW12 0.37195000 W
PLW13 0.18708999 W
F2 - Processing parameters
SI 32768
SF 125.7653919 MHz
WCM EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

C:\Xcalibur\data\MSfacility\88257ESIPN1
Sarah

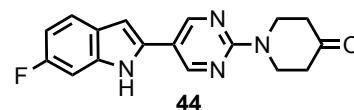
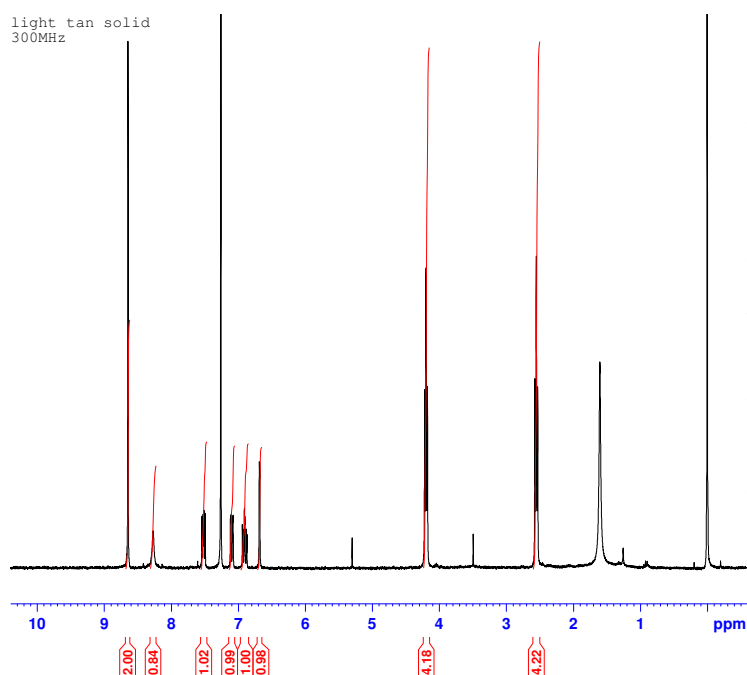
88257ESIPN1 #8-15 RT: 0.12-0.21 AV: 4 NL: 9.24E9
T: FTMS + p ESI Full ms [120.0000-1500.0000]



88257ESIPN1#9-15 RT: 0.12-0.21 AV: 4
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z= 298.98890-304.98208

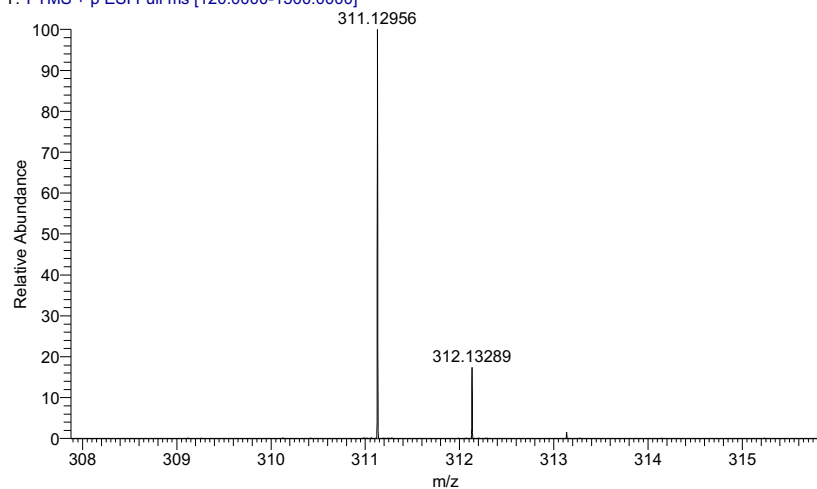
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
301.12525	9302198272.0	100.00	301.12593	-2.25	C ₁₆ H ₁₅ N ₄ F ₂

Figure S52. Compound (R)-43 ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).



C:\Xcalibur\data\MSfacility\88256ESIPN1 08/12/22 11:08:09 JSS20-116A
Sarah

88256ESIPN1 #7-15 RT: 0.09-0.21 AV: 5 NL: 3.11E9
T: FTMS + p ESI Full ms [120.0000-1500.0000]



88256ESIPN1 #7-15 RT: 0.09-0.21 AV: 5
T: FTMS + p ESI Full ms [120.0000-1500.0000]

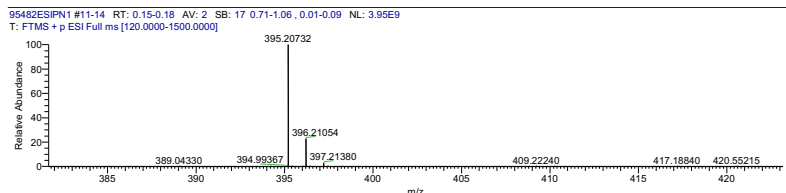
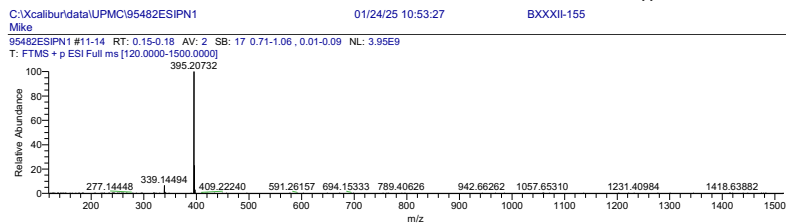
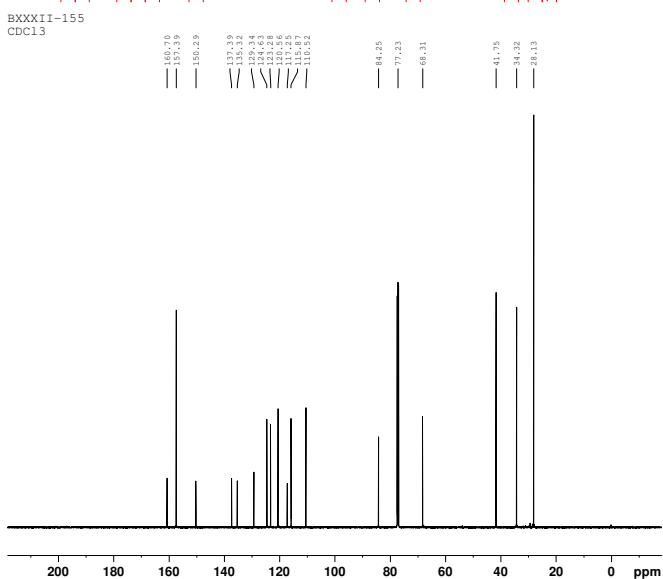
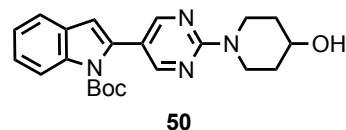
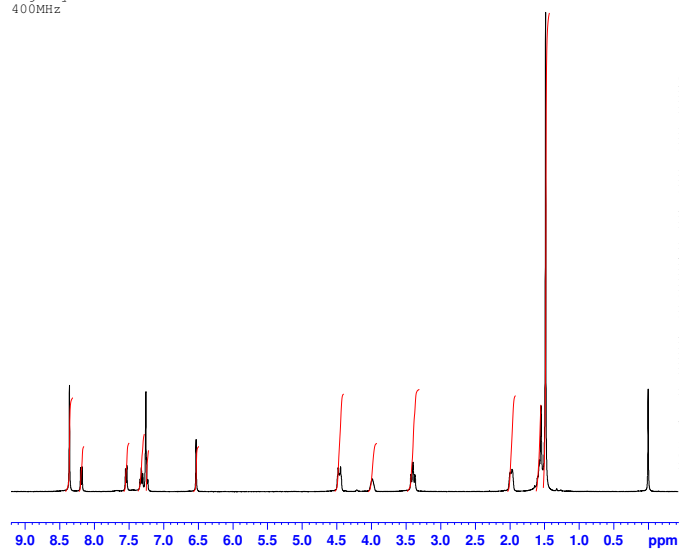
m/z = 307.87563-315.83032

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
311.12956	3116225280.0	100.00	311.13027	-2.27	C ₁₇ H ₁₆ O N ₄ F

Figure S53. Compound **44** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

S59

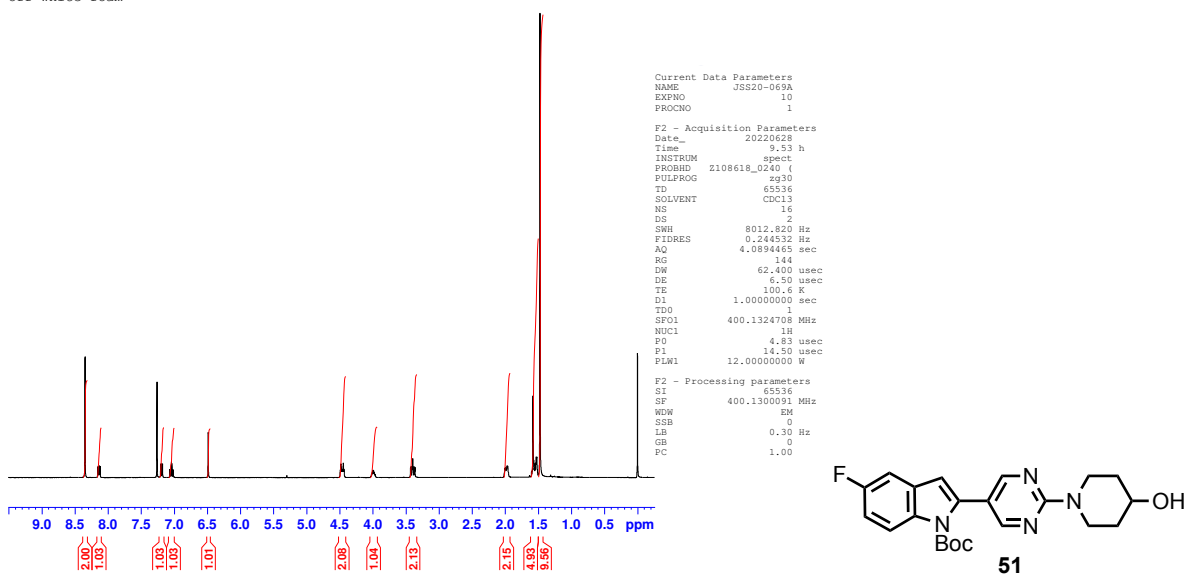
light yellow foam
400MHz



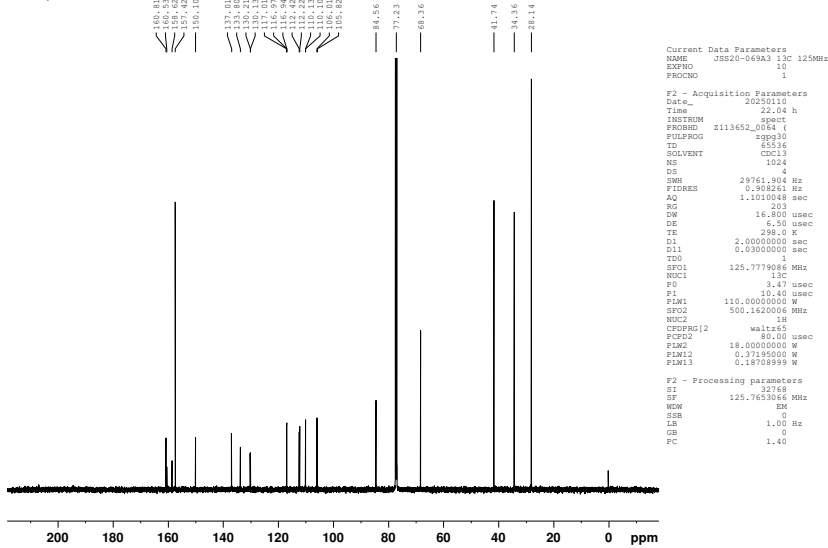
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
395.20732	3968109056.0	100.00	395.20777	-1.12	C ₂₂ H ₂₇ O ₃ N ₄

Figure S57. Compound **50** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

off-white foam

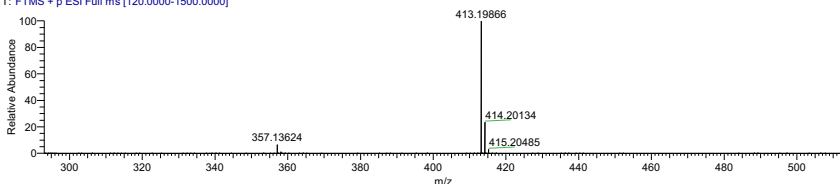


JSS20-069A
CDCl3, 125MHz

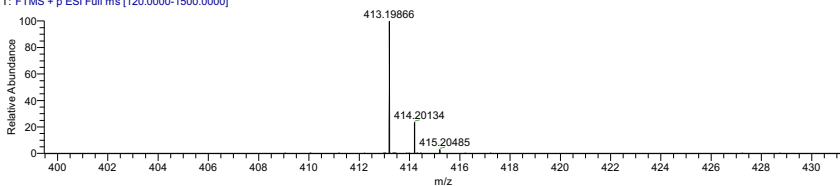


C:\Xcalibur\...95285ESIPN1
Megan
01/08/25 13:26:40 JSS20-069A

95285ESIPN1 #8-24 RT: 0.12-0.32 AV: 8 NL: 1.02E10
T: FTMS + p ESI Full ms [120.0000-1500.0000]



95285ESIPN1 #8-24 RT: 0.12-0.32 AV: 8 NL: 1.02E10
T: FTMS + p ESI Full ms [120.0000-1500.0000]

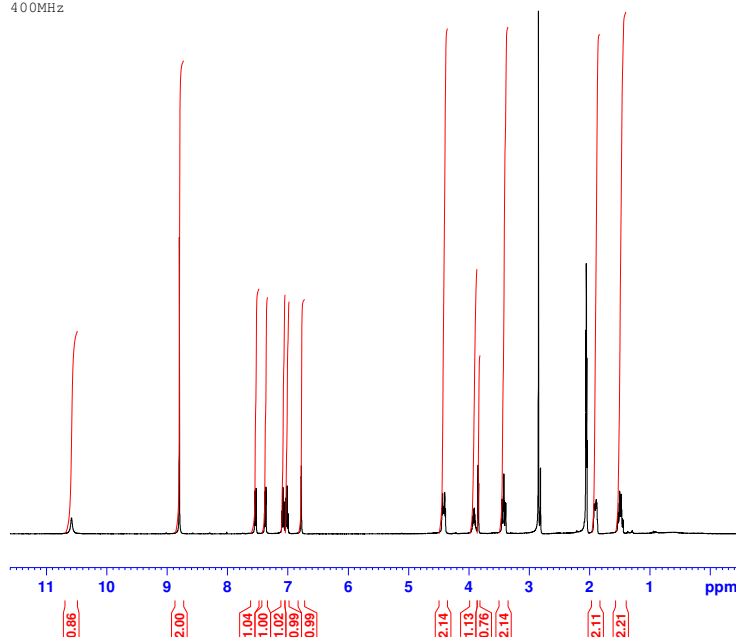


95285ESIPN1#9-23 RT: 0.12-0.32 AV: 8
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z= 399.46738-431.23229

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
413.19866	10230135808.0	100.00	413.19835	0.76	C ₂₂ H ₂₆ O ₃ N ₄ F

Figure S58. Compound **51** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

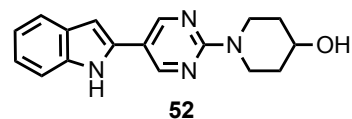
off-white solid
400MHz



```
Current Data Parameters
NAME      JSS20-064A2 acetone-d6
EXPNO     10
PROCNO    1

F2 - Acquisition Parameters
Date_     20220630
Time      10.55 h
INSTRUM   spect
PROBHD    z108618_0240 (
PULPROG   zg30
TD         65536
SOLVENT   Acetone
NS         16
DS         2
SWH        8012.820 Hz
FIDRES     0.244532 Hz
AQ         4.0894465 sec
RG         144
DW         62.400 usec
DE         6.50 usec
TE         100.5 K
D1         1.00000000 sec
TD0        1
SFO1       400.1324708 MHz
NUC1       1H
PC         4.83 usec
P1         14.50 usec
PLW1       12.00000000 W

F2 - Processing parameters
SI         65536
SF         400.1300068 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
```

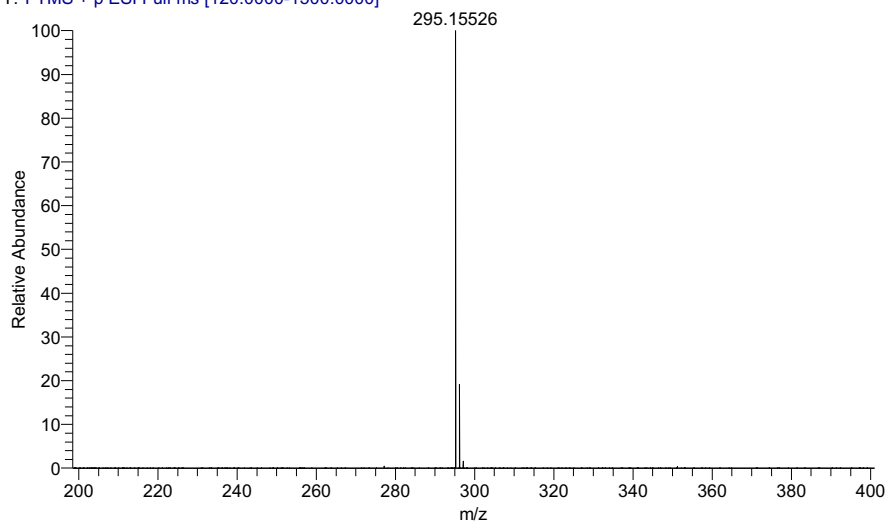


C:\Xcalibur\data\MSfacility\88053ESIPN1
Sarah

07/14/22 10:21:25

JSS20-064A

88053ESIPN1 #4-24 RT: 0.06-0.32 AV: 10 SB: 34 1.16-2.10 NL: 3.70E9
T: FTMS + p ESI Full ms [120.0000-1500.0000]



88053ESIPN1#5-23 RT: 0.06-0.32 AV: 10

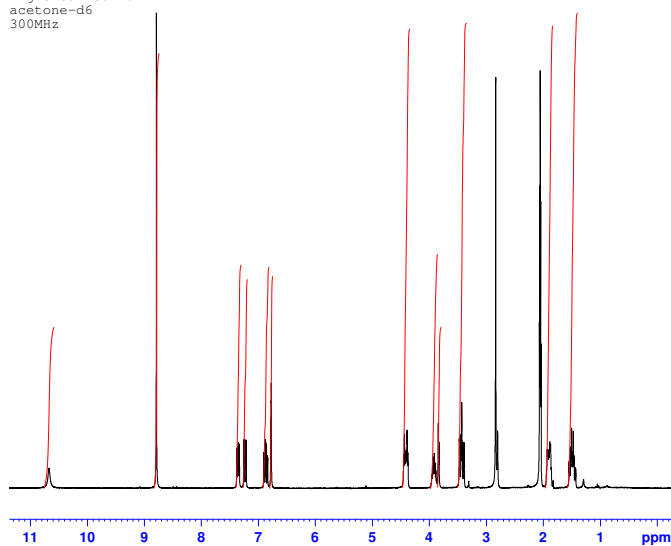
SB: 34 1.16-2.10

T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
295.15526	3837855744.0	100.00	295.15534	-0.26	C ₁₇ H ₁₉ ON ₄

Figure S59. Compound **52** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

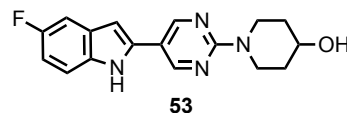
light tan solid
acetone-d6
300MHz



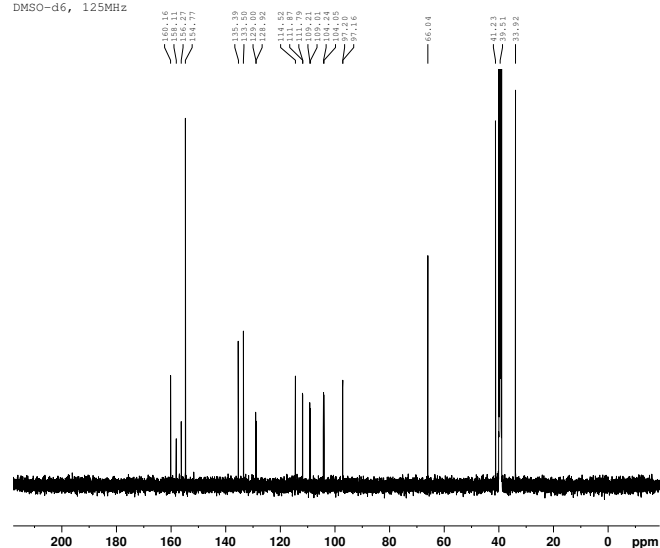
Current Data Parameters
NAME JSS20-073A2
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20220714
Time 10.09 h
INSTRUM spect
PROBHD Z104275_0423 ()
PULPROG zg30
TD 32768
SOLVENT Acetone
NS 16
DS 2
SWH 6009.615 Hz
FIDRES 0.366798 Hz
AQ 2.7262976 sec
RG 181
DW 83.200 usec
DE 6.50 usec
TE 295.7 K
D1 1.00000000 sec
TDO 1
SFO1 300.2318539 MHz
NUC1 1H
PQ 4.67 usec
PI 14.00 usec
PLW1 17.16200066 W

F2 - Processing parameters
SI 65536
SF 300.2300053 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



JSS20-073A
DMSO-d6, 125MHz



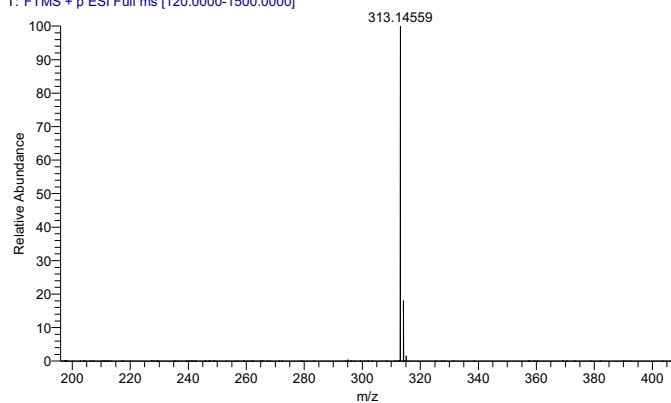
Current Data Parameters
NAME JSS20-073A.13C
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20250504
Time 1.11 h
INSTRUM spect
PROBHD Z113652_0064 ()
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 1024
DS 4
SWH 29761.904 Hz
FIDRES 0.598261 Hz
AQ 1.1010048 sec
RG 203
DW 16.800 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TDO 1
SFO1 125.7779086 MHz
NUC1 13C
PQ 3.47 usec
PI 10.40 usec
PLW1 110.00000000 W
PLW2 500.16200006 MHz
NUC2 1H
CPDPRG2 wait65
PCPD2 80.00 usec
PLW2 18.00000000 W
PLW2 0.37195000 W
PLW13 0.18708999 W

F2 - Processing parameters
SI 32768
SF 125.7653916 MHz
WDW EM
SSB 0
LB 0
GB 0
PC 1.40

C:\xcalibur\data\MSfacility\88054ESIPN1
Sarah

88054ESIPN1#8-20 RT: 0.12-0.26 AV: 6 SB: 34 1.16-2.10 NL: 6.16E9
T: FTMS + p ESI Full ms [120.0000-1500.0000]



88054ESIPN1#9-19 RT: 0.12-0.26 AV: 6

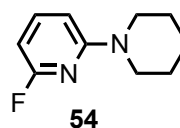
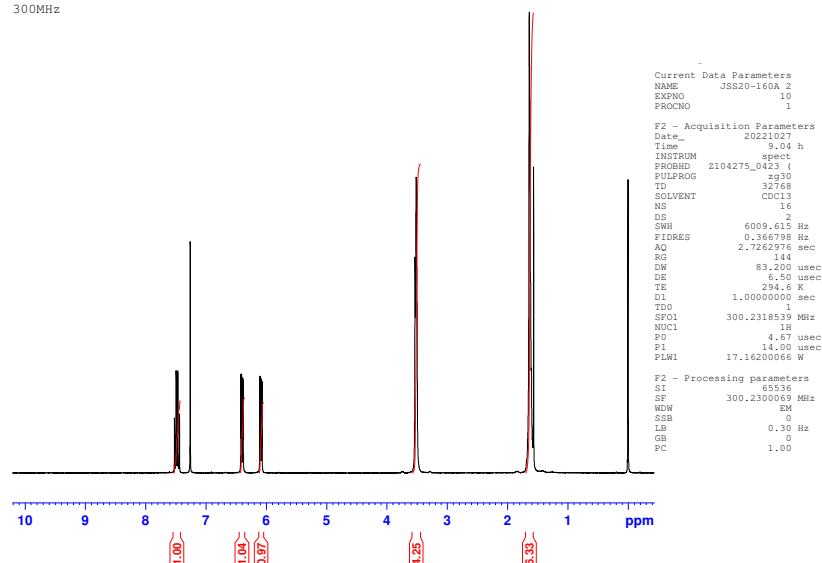
SB: 34 1.16-2.10

T: FTMS + p ESI Full ms [120.0000-1500.0000]

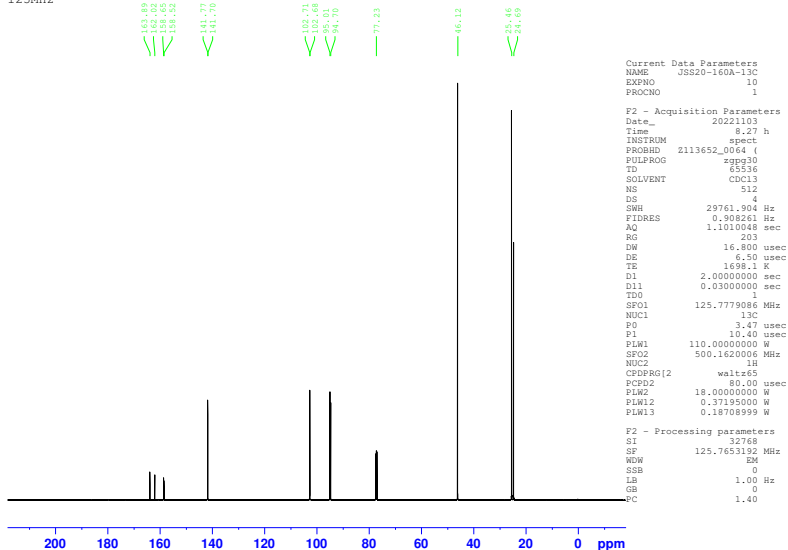
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
313.14559	6182631936.0	100.00	313.14592	-1.03	C ₁₇ H ₁₈ O N ₄ F

Figure S60. Compound **53** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

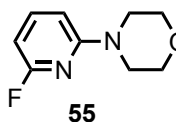
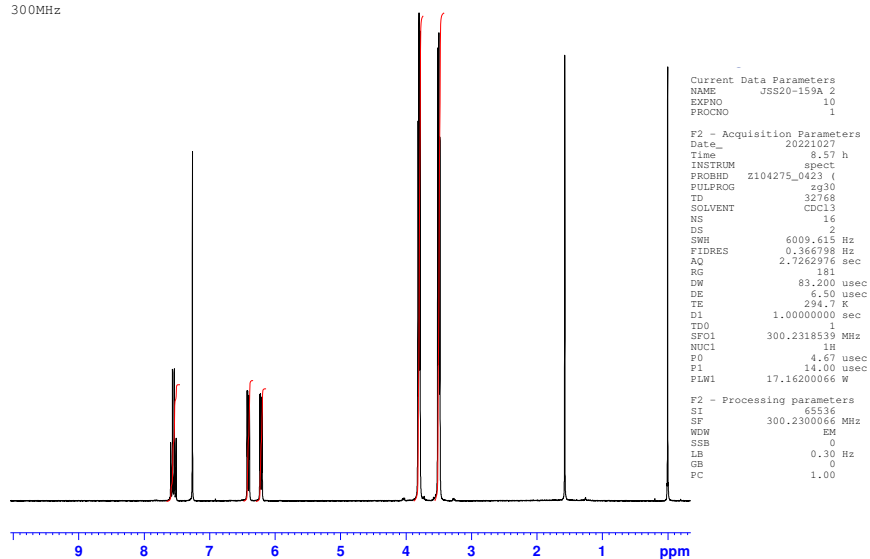
colorless oil
300MHz



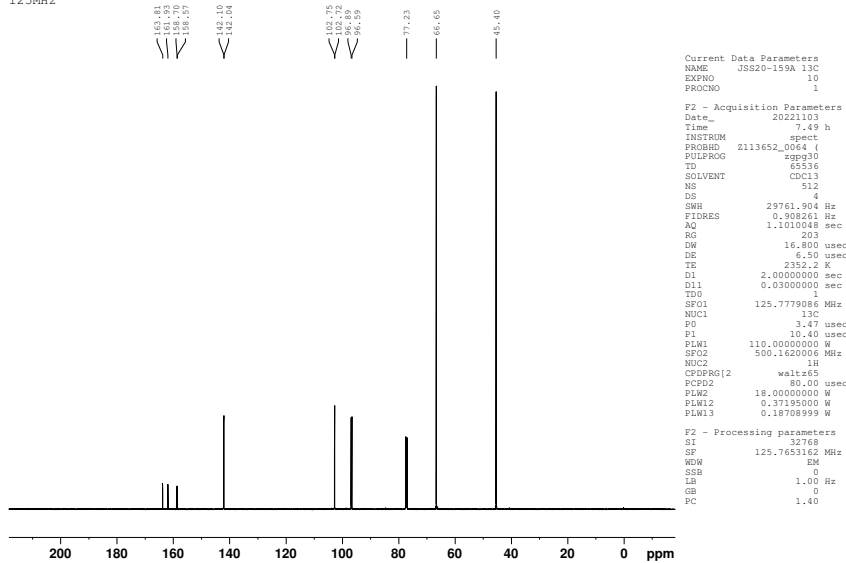
colorless oil
125MHz



colorless oil
300MHz



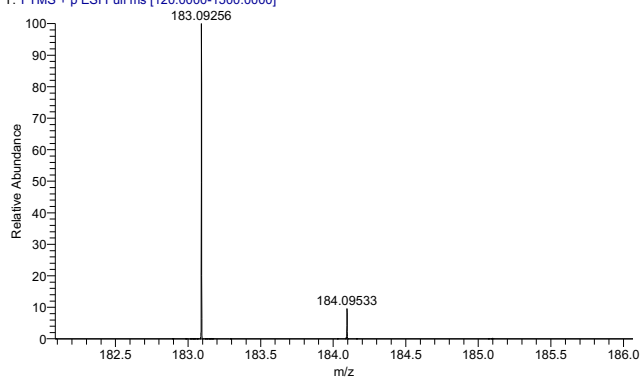
white solid
125MHz



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Sarah

88729ESIPN1 #10-18 RT: 0.15-0.23 AV: 4 NL: 1.63E10

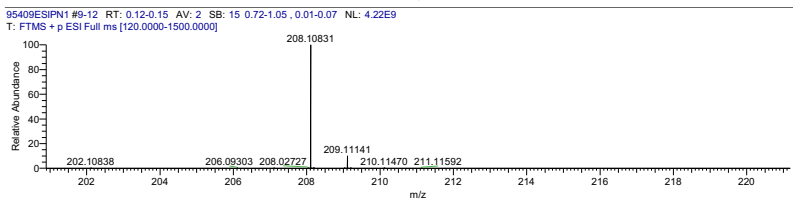
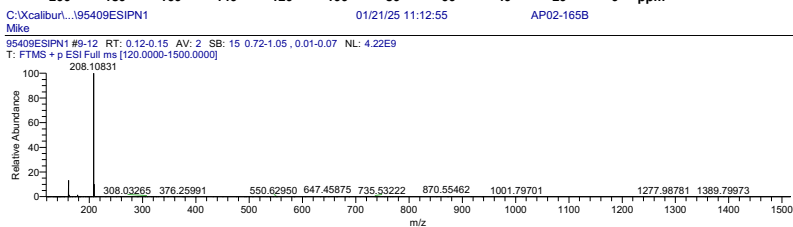
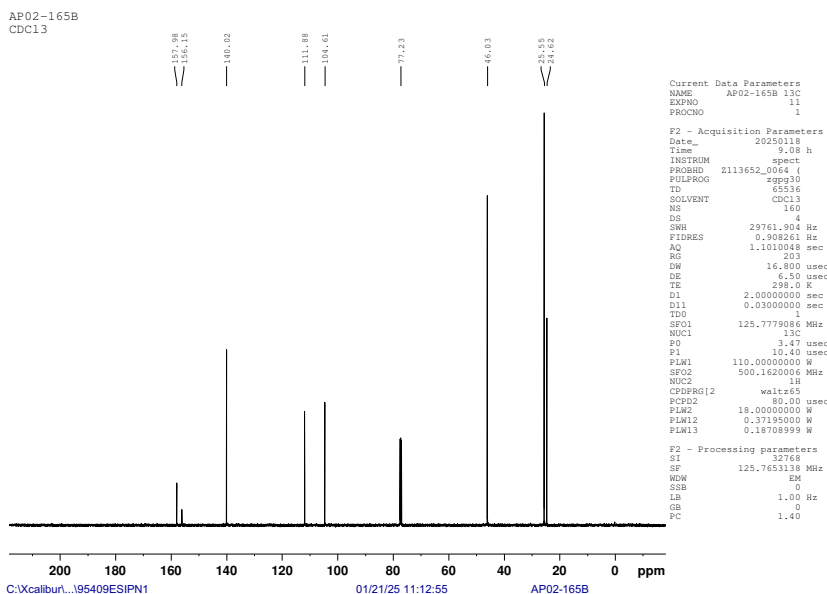
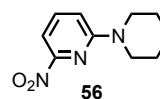
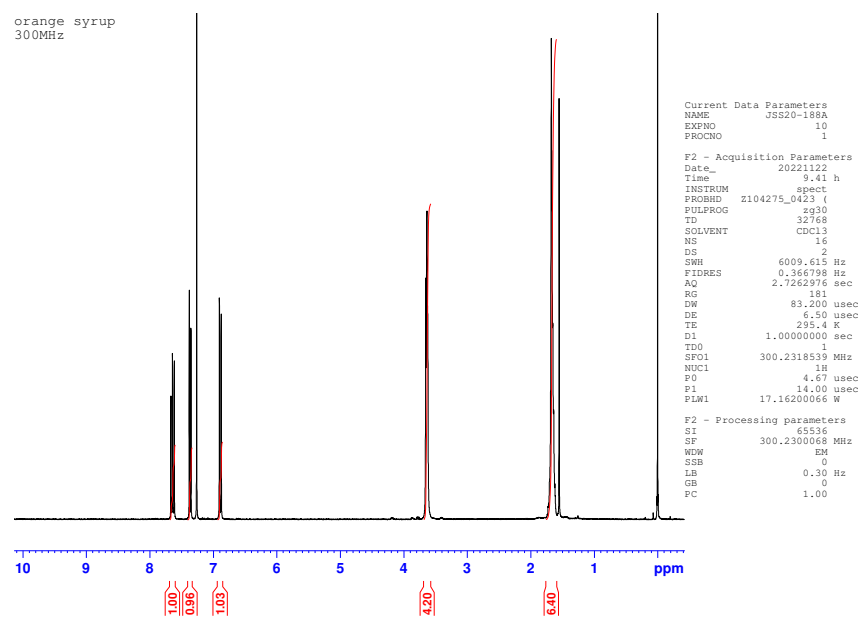
T: FTMS + p ESI Full ms [120.0000-1500.0000]



88729ESIPN1#11-17 RT: 0.15-0.23 AV: 4
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
183.09256	16264146944.0	100.00	183.09282	-1.38	C ₉ H ₁₂ ON ₂ F

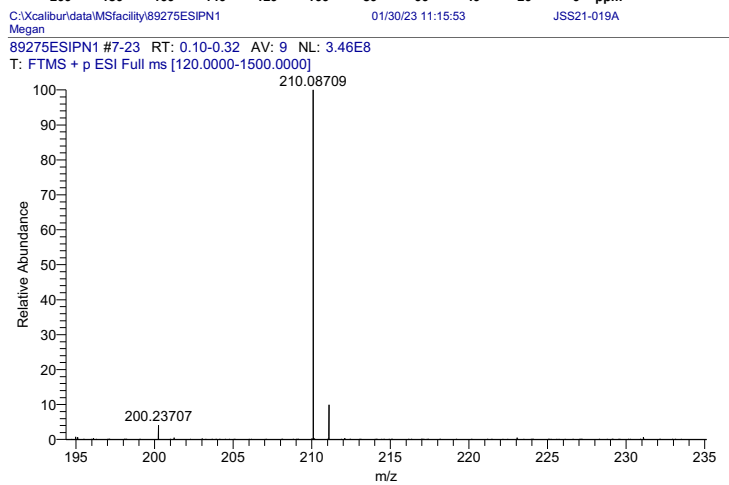
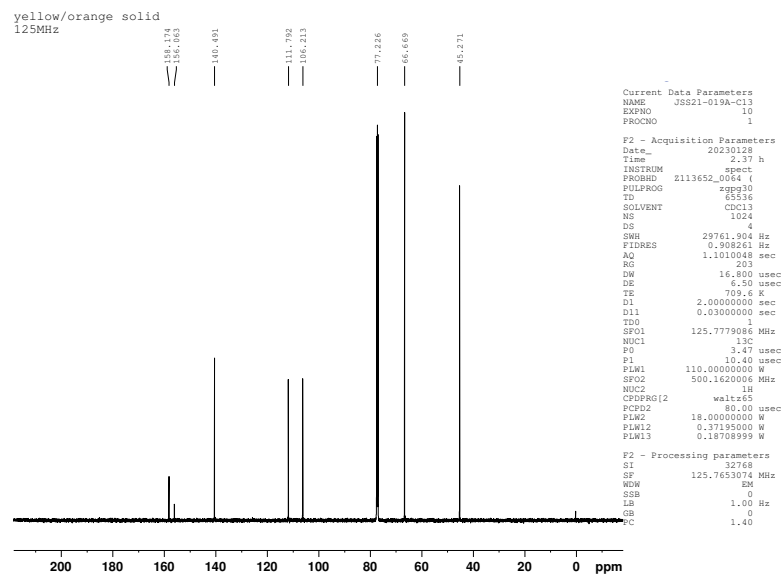
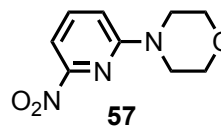
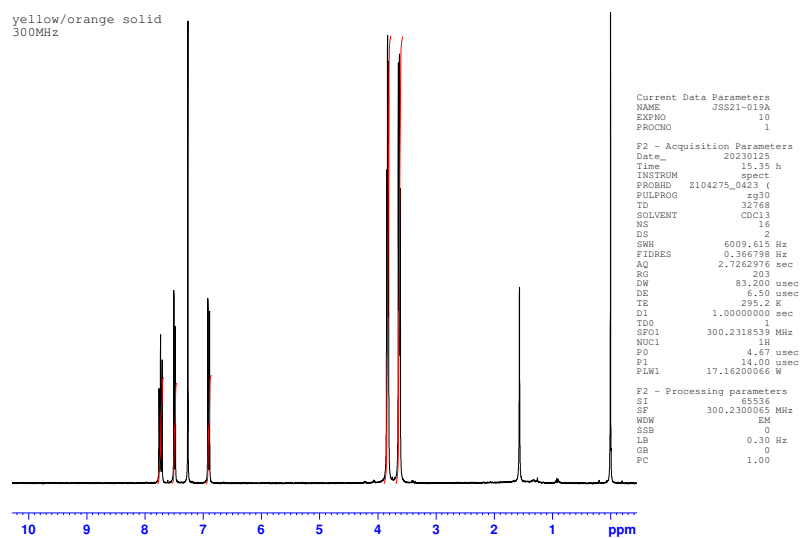
Figure S62. Compound **55** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).



95409ESIPN1 #9-11 RT: 0.12-0.15 AV: 2
SB: 15 0.72-1.05, 0.01-0.07
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z = 200.89233-221.18286

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
208.10831	4240568320.0	100.00	208.10805	1.23	C ₁₀ H ₁₄ O ₂ N ₃

Figure S63. Compound **56** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

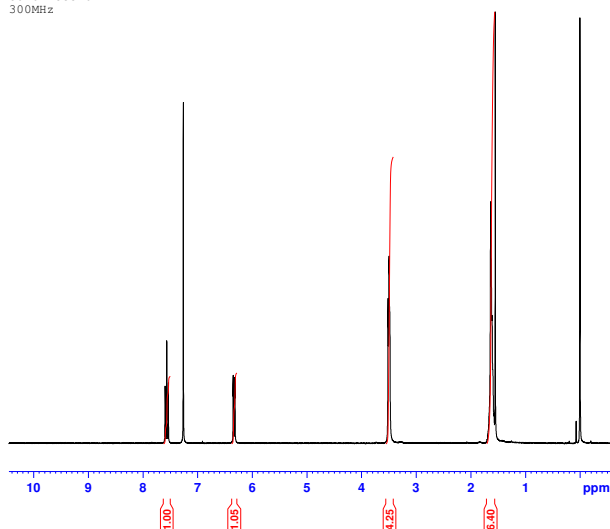


89275ESIPN1#7-23 RT: 0.10-0.32 AV: 9
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z= 194.35026-235.11148

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
210.08709	351968000.0	100.00	210.08732	-1.10	C ₉ H ₁₂ O ₃ N ₃

Figure S64. Compound **57** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

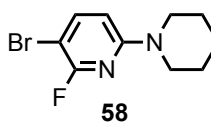
colorless oil
300MHz



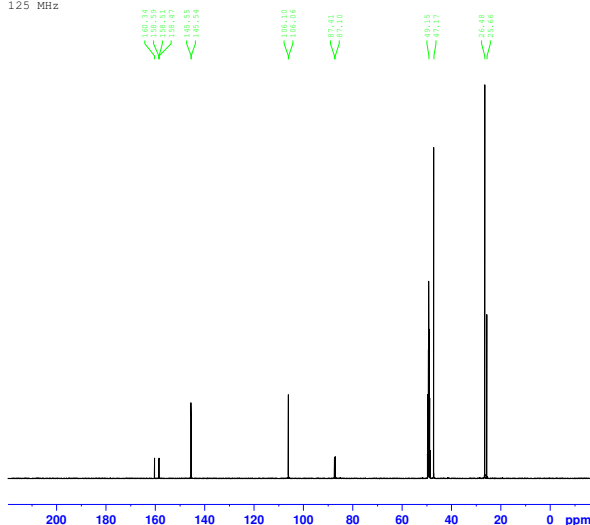
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Current Data Parameters
NAME      JSS20-170B
EXPNO     10
PROCNO    1

F2 - Acquisition Parameters
Date_     20221103
Time      16:31 h
INSTRUM    spect
PROBHD     Z104275_0423 (
PULPROG    zg30
TD         32768
SOLVENT    CDCl3
NS         16
DS         2
SWH         6009.615 Hz
FIDRES     0.366798 Hz
AQ         2.7262376 sec
RG         203
DW         83.200 usec
DE         6.50 usec
TE         300.2 K
D1         1.00000000 sec
TDO        300.2318539 MHz
SFO1       300.2318539 MHz
NUC1       1H
P1         4.67 usec
F1         14.00 usec
PL1        17.16200066 W

F2 - Processing parameters
SI         65536
SF         300.2300068 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
```



colorless oil
125 MHz



```
Current Data Parameters
NAME      JSS20-170B3-13C
EXPNO     10
PROCNO    1

F2 - Acquisition Parameters
Date_     20221118
Time      2:58 h
INSTRUM    spect
PROBHD     Z113652_0044 (
PULPROG    zgpg30
TD         65536
SOLVENT    MeCO
NS         1024
DS         4
SWH         29761.904 Hz
FIDRES     0.908261 Hz
AQ         1.1010048 sec
RG         203
DW         16.800 usec
DE         6.50 usec
TE         300.2 K
D1         2.00000000 sec
D11        0.03000000 sec
TDO        125.7779892 MHz
SFO1       125.7779892 MHz
NUC1       13C
P1         3.47 usec
F1         10.40 usec
PL1        110.00000000 W
PLM1       500.1620006 MHz
NUC2       1H
CPDPRG2    waltz165
PCPD2      80.00 usec
PLM2       18.00000000 W
PLM12      0.37195000 W
PLM13      0.18708999 W

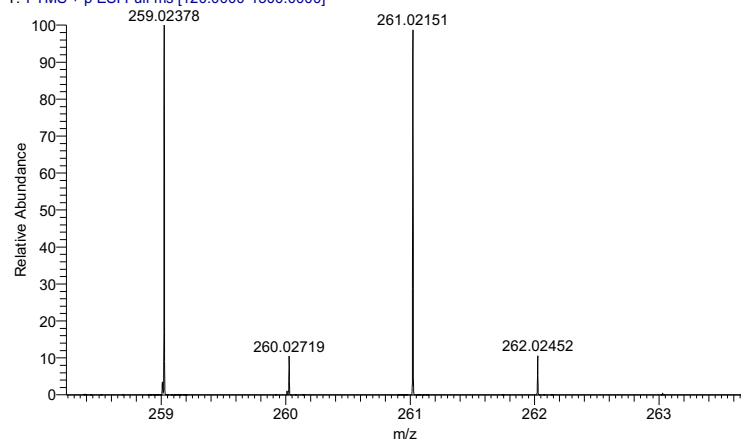
F2 - Processing parameters
SI         32768
SF         125.7651496 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         1.40
```

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Sarah

88732ESIPN1#8-20 RT: 0.12-0.26 AV: 6 SB: 118 0.01-0.07, 1.49-4.75 NL: 1.38E10

T: FTMS + p ESI Full ms [120.0000-1500.0000]



88732ESIPN1#9-19 RT: 0.12-0.26 AV: 6

SB: 118 0.01-0.07, 1.49-4.75

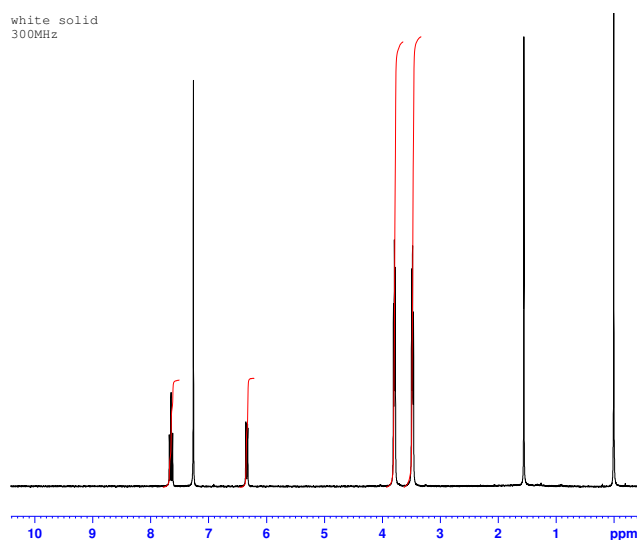
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z= 258.23689-263.68037

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
259.02378	13897758720.0	100.00	259.02407	-1.09	C ₁₀ H ₁₃ N ₂ BrF

Figure S65. Compound **58** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

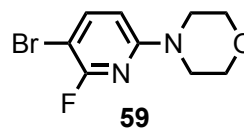
white solid
300MHz



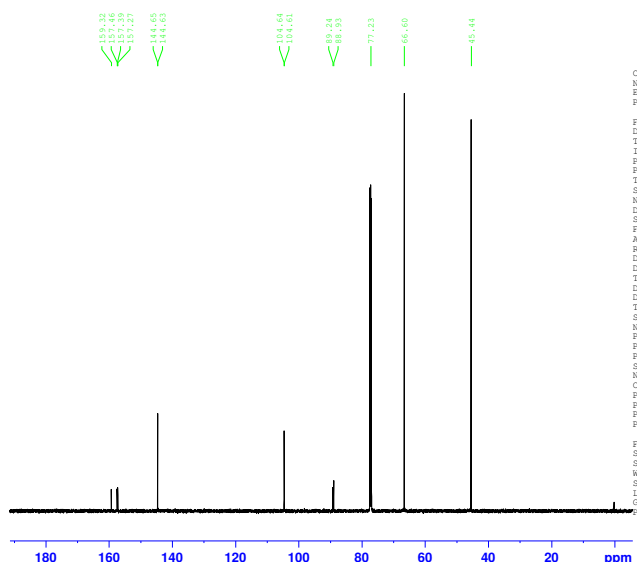
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Current Data Parameters
NAME      JSS20-169A
EXPNO     10
PROCNO    1

F2 - Acquisition Parameters
Date_     20221103
Time      16.25 h
INSTRUM   spect
PROBHD    Z104275_0423 (
PULPROG   zg30
TD         32768
SOLVENT   CDCl3
NS         16
DS         2
SWH        6009.615 Hz
FIDRES     0.366798 Hz
AQ         2.7262976 sec
RG         228
DW         83.200 usec
DE         6.50 usec
TE         294.1 K
D1         1.00000000 sec
TDO        1
SFO1      300.2318539 MHz
NUC1       1H
P0         4.57 usec
P1         14.00 usec
PLW1       17.16200066 W

F2 - Processing parameters
SI         65536
SF         300.2300068 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
```



white solid



```
Current Data Parameters
NAME      JSS20-169A-C13
EXPNO     10
PROCNO    1

F2 - Acquisition Parameters
Date_     20221105
Time      6.11 h
INSTRUM   spect
PROBHD    Z113652_0064 (
PULPROG   zgpg30
TD         65536
SOLVENT   CDCl3
NS         512
DS         2
SWH        29761.904 Hz
FIDRES     0.908261 Hz
AQ         1.1010048 sec
RG         203
DW         16.800 usec
DE         6.50 usec
TE         706.4 K
D1         2.00000000 sec
D11        0.03000000 sec
TDO        1
SFO1      125.7779086 MHz
NUC1       13C
P0         3.47 usec
P1         10.40 usec
PLW1       110.0000000 W
SFO2       500.1620006 MHz
NUC2       1H
CPDPRG2   waltz165
PCPD2      80.00 usec
PLW2       18.00000000 W
PLW12      0.37195000 W
PLW13      0.18708999 W

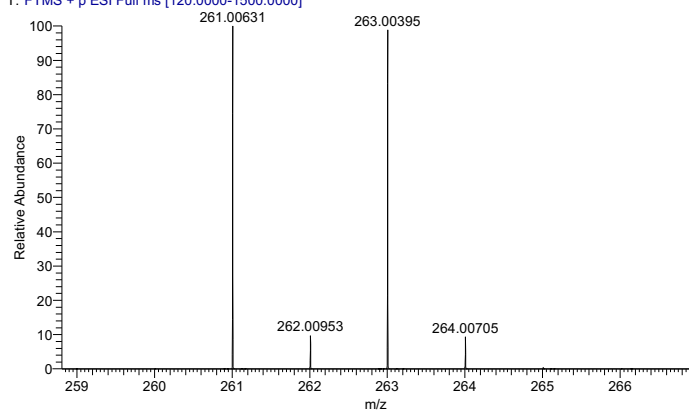
F2 - Processing parameters
SI         32768
SF         125.7653083 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         1.40
```

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Sarah

88795ESIPN4 #10-15 RT: 0.15-0.21 AV: 3 NL: 6.10E9

T: FTMS + p ESI Full ms [120.0000-1500.0000]



88795ESIPN4#11-15 RT: 0.15-0.21 AV: 3

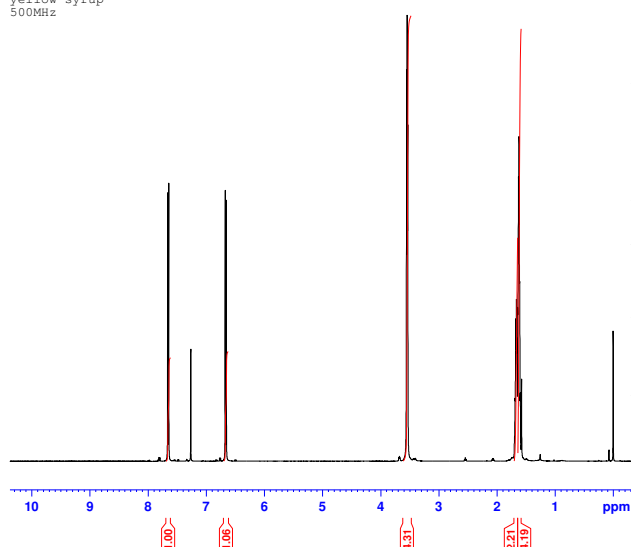
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z = 258.80333-266.90327

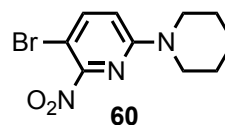
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
261.00631	6166740480.0	100.00	261.00333	2.98	C ₉ H ₁₁ ON ₂ BrF

Figure S66. Compound **59** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

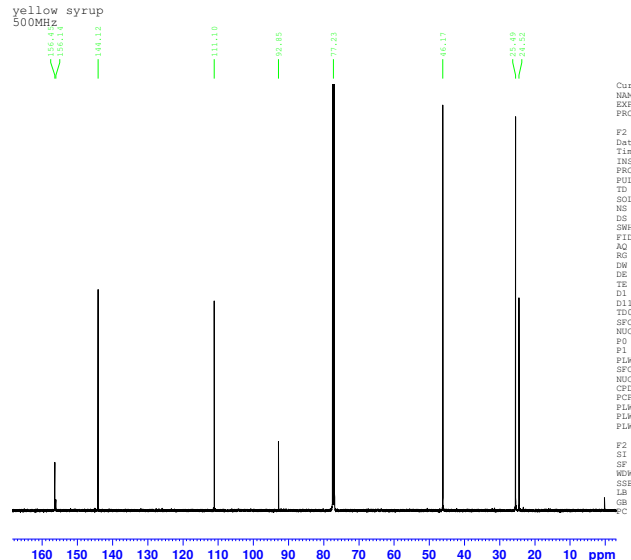
yellow syrup
500MHz



Current Data Parameters
NAME JSS21-006B2 2
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20221217
Time 4.26 h
INSTRUM spect
PROBHD Z113652_0064 (1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 10000.000 Hz
FIDRES 0.305176 Hz
AQ 3.2767999 sec
RG 80.6
DW 50.000 usec
DE 13.64 usec
TE 700.0 K
D1 1.00000000 sec
TD0 1
SFO1 500.1630885 MHz
NUC1 1H
P0 3.83 usec
P1 11.50 usec
PLW1 18.00000000 W
F2 - Processing Parameters
SI 65536
SF 500.1600093 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



yellow syrup
500MHz



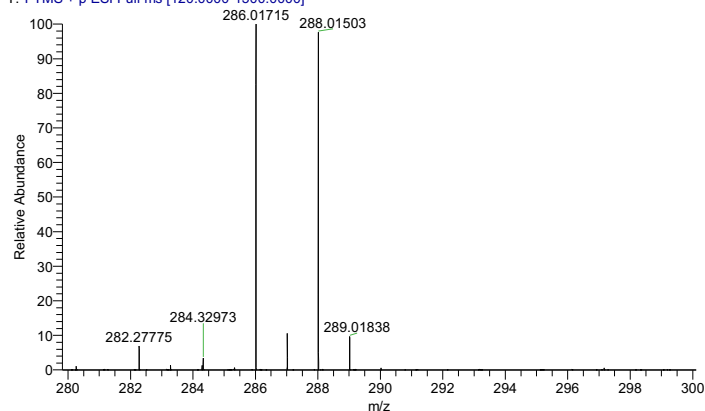
Current Data Parameters
NAME JSS21-006B2
EXPNO 11
PROCNO 1
F2 - Acquisition Parameters
Date_ 20221217
Time 5.22 h
INSTRUM spect
PROBHD Z113652_0064 (1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 29761.904 Hz
FIDRES 0.308261 Hz
AQ 1.1010048 sec
RG 203
DW 16.800 usec
DE 6.50 usec
TE 700.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 125.7779086 MHz
NUC1 13C
P0 3.47 usec
P1 10.40 usec
PLW1 110.00000000 W
SFO2 500.1620006 MHz
NUC2 1H
CPDPRG2 waltz165
PCPD2 80.00 usec
PLW2 18.00000000 W
PLW12 0.71595000 W
PLW13 0.18708999 W
F2 - Processing Parameters
SI 32768
SF 125.7653083 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

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Sarah

89028ESIPN1 #9-18 RT: 0.12-0.23 AV: 5 NL: 5.17E8

T: FTMS + p ESI Full ms [120.0000-1500.0000]



89028ESIPN1#9-17 RT: 0.12-0.23 AV: 5

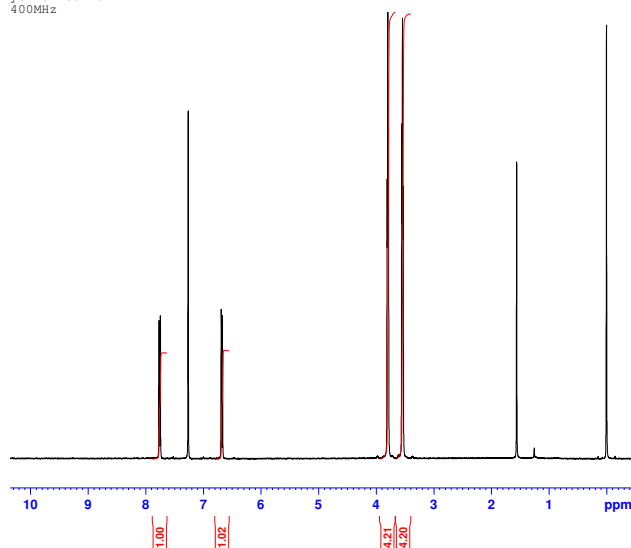
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z= 279.81619-300.10734

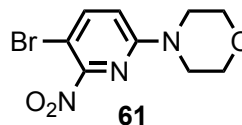
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
286.01715	517168608.0	100.00	286.01857	-4.93	C ₁₀ H ₁₃ O ₂ N ₃ Br

Figure S67. Compound **60** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

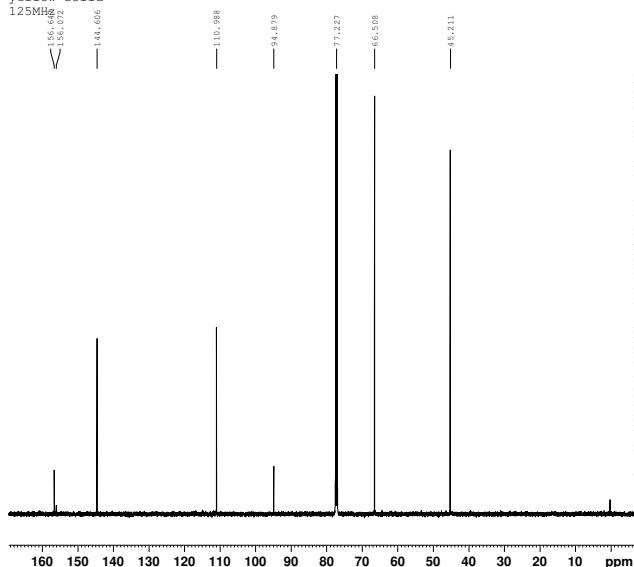
yellow solid
400MHz



Current Data Parameters
NAME JSS21-023A
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20230202
Time 16:29 h
INSTRUM spect
PROBHD 2108618_0240 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244530 Hz
AQ 4.0894465 sec
RG 144
DW 62.400 usec
DE 6.50 usec
TE 300.2 K
D1 1.00000000 sec
TD0 1
SFO1 400.1324708 MHz
NUC1 1H
FO 4.83 usec
P1 14.50 usec
PLW1 12.00000000 W
F2 - Processing parameters
SI 65536
SF 400.1300081 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



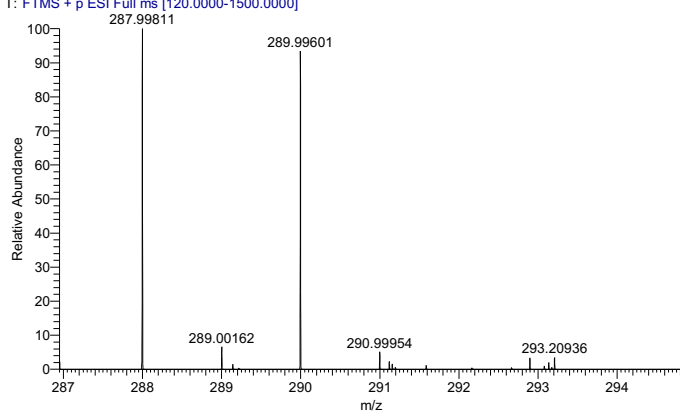
yellow solid
125MHz



Current Data Parameters
NAME JSS21-023A-C13
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20230207
Time 2:22 h
INSTRUM spect
PROBHD 2113652_0064 (
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 29761.904 Hz
FIDRES 0.908261 Hz
AQ 1.1010048 sec
RG 203
DW 16.800 usec
DE 6.50 usec
TE 711.3 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 125.7779086 MHz
NUC1 13C
FO 3.47 usec
P1 10.40 usec
PLW1 110.0000000 W
SFO2 500.1620006 MHz
NUC2 1H
CPDPRG2 waltz165
PCPD2 80.00 usec
PLW2 18.0000000 W
PLW12 0.3719500 W
PLW13 0.1870899 W
F2 - Processing parameters
SI 32768
SF 125.7653067 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

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Sarah

89321ESIPN1 #9-17 RT: 0.13-0.24 AV: 5 NL: 5.78E6
T: FTMS + p ESI Full ms [120.0000-1500.0000]



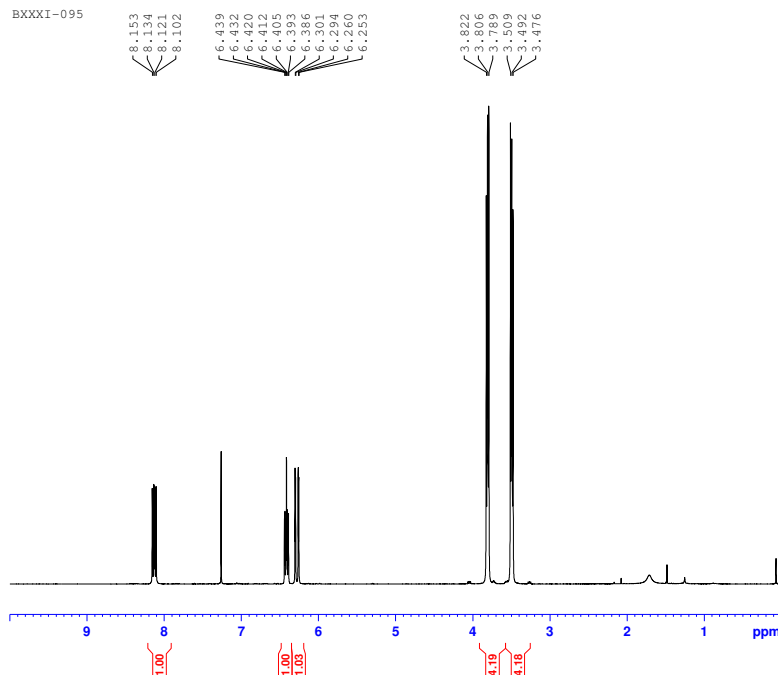
89321ESIPN1#9-17 RT: 0.13-0.24 AV: 5
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z= 286.94879-294.84087

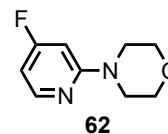
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
287.99811	5776413.0	100.00	287.99783	0.98	C ₉ H ₁₁ O ₃ N ₃ Br

Figure S68. Compound **61** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

BXXXI-095



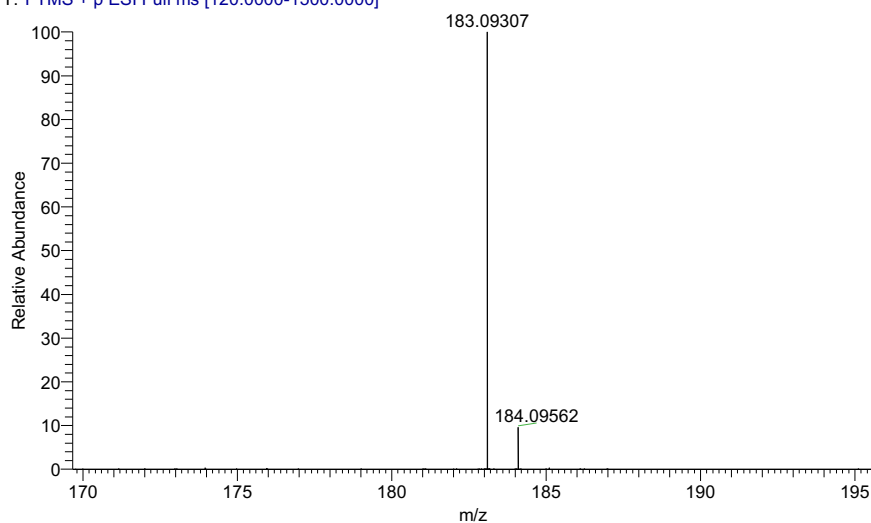
Current Data Parameters
 NAME BXXXI-095 (BXXXI-016)
 EXPNO 10
 PROCNO 1
 F2 - Acquisition Parameters
 Date_ 20231030
 Time 7.51 h
 INSTRUM spect
 PROBHD Z104275_0423 (4
 PULPROG zg30
 TD 65536
 SOLVENT CDCl3
 NS 16
 DS 2
 SWH 6009.615 Hz
 FIDRES 0.183359 Hz
 AQ 5.4525952 sec
 RG 114
 DW 83.200 usec
 DE 13.19 usec
 TE 295.2 K
 D1 1.00000000 sec
 TDO 1
 SFO1 300.2318539 MHz
 NUC1 1H
 PG 4.67 usec
 P1 14.00 usec
 PLW1 18.00000000 W
 F2 - Processing parameters
 SI 65536
 SF 300.2300074 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

C:\Xcalibur\data\UPMC\91429ESIPN1
Megan

10/31/23 12:37:54

BXXXI-016

91429ESIPN1 #7-36 RT: 0.09-0.49 AV: 15 NL: 1.46E10
 T: FTMS + p ESI Full ms [120.0000-1500.0000]



91429ESIPN1#7-35 RT: 0.09-0.49 AV: 15
 T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z = 169.65996-195.61581

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
183.09307	15064797184.0	100.00	183.09282	1.35	C ₉ H ₁₂ ON ₂ F

Figure S69. Compound **62** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

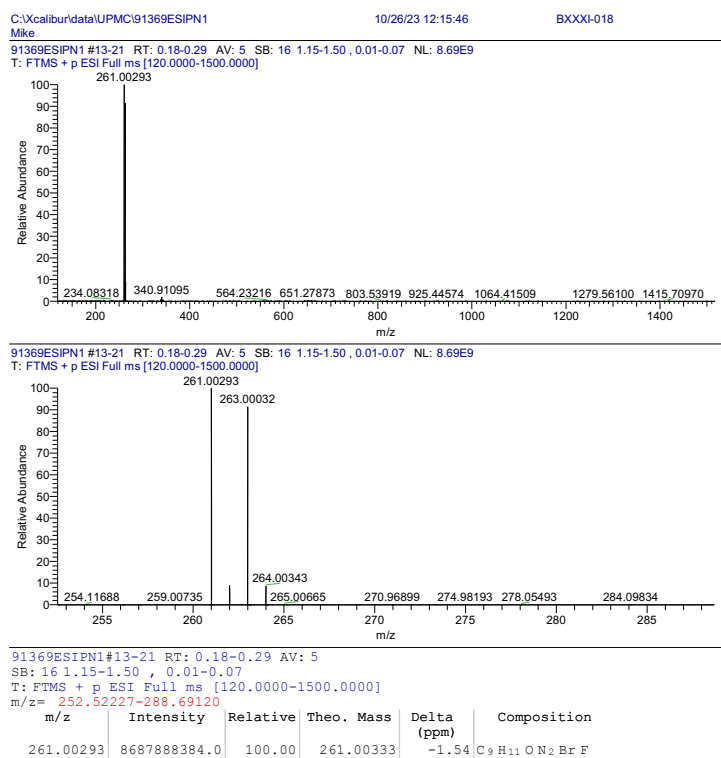
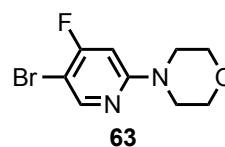
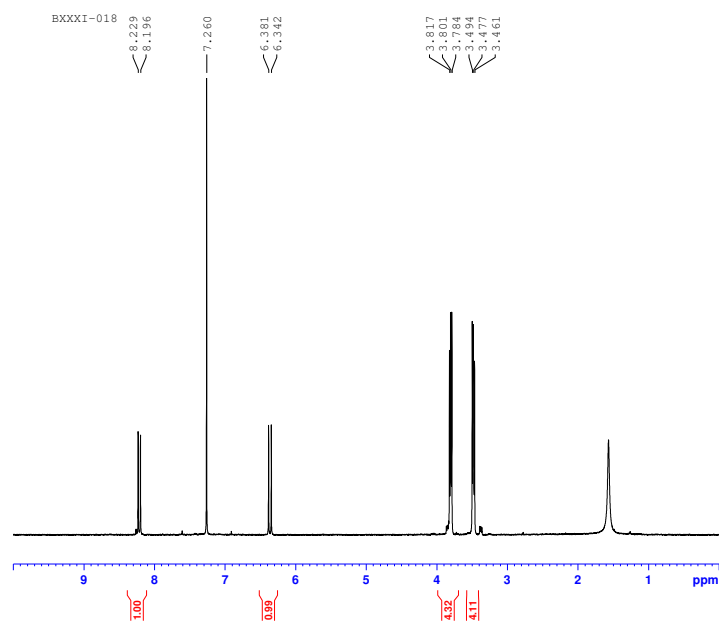


Figure S70. Compound **63** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

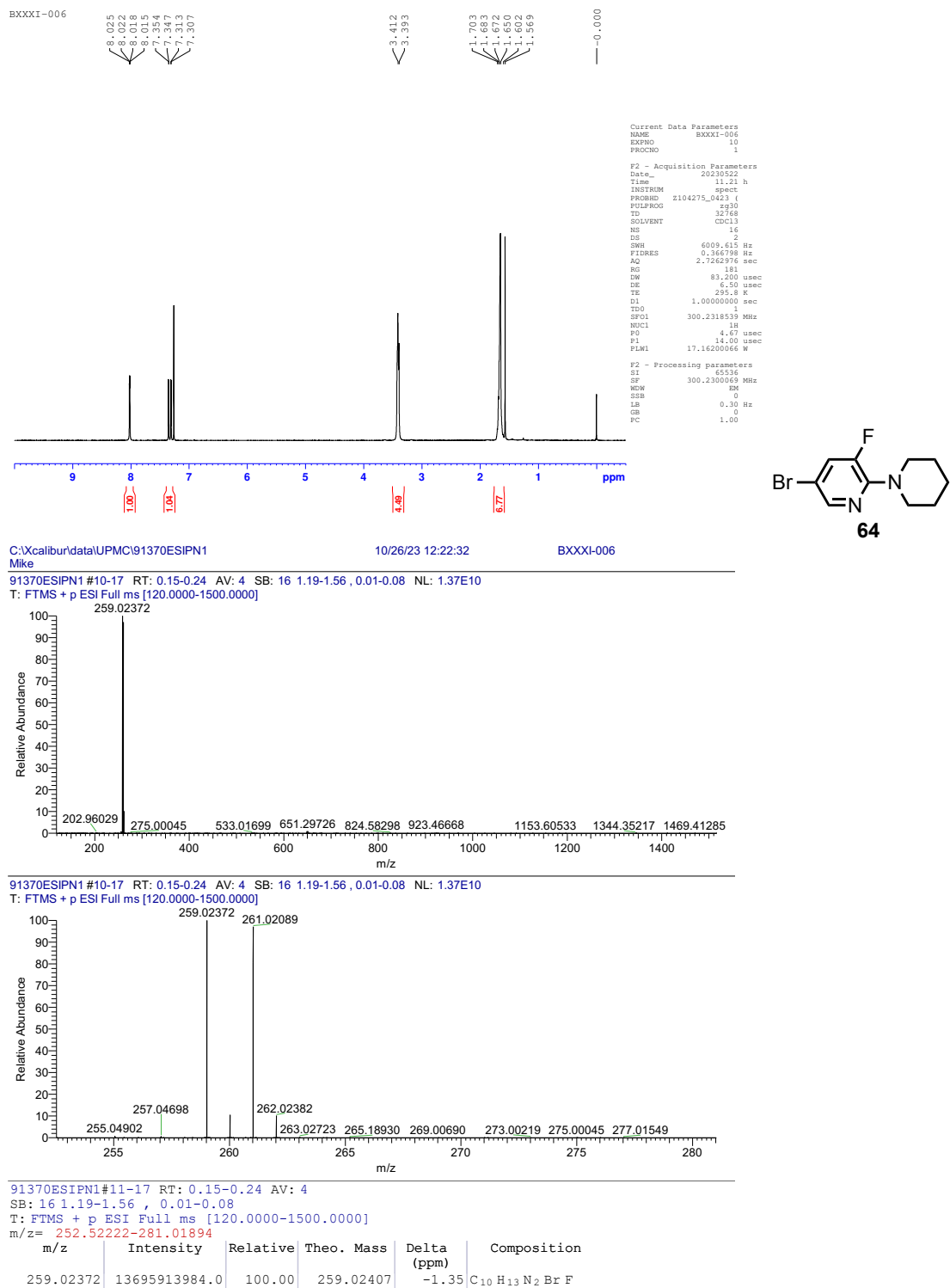


Figure S71. Compound **64** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

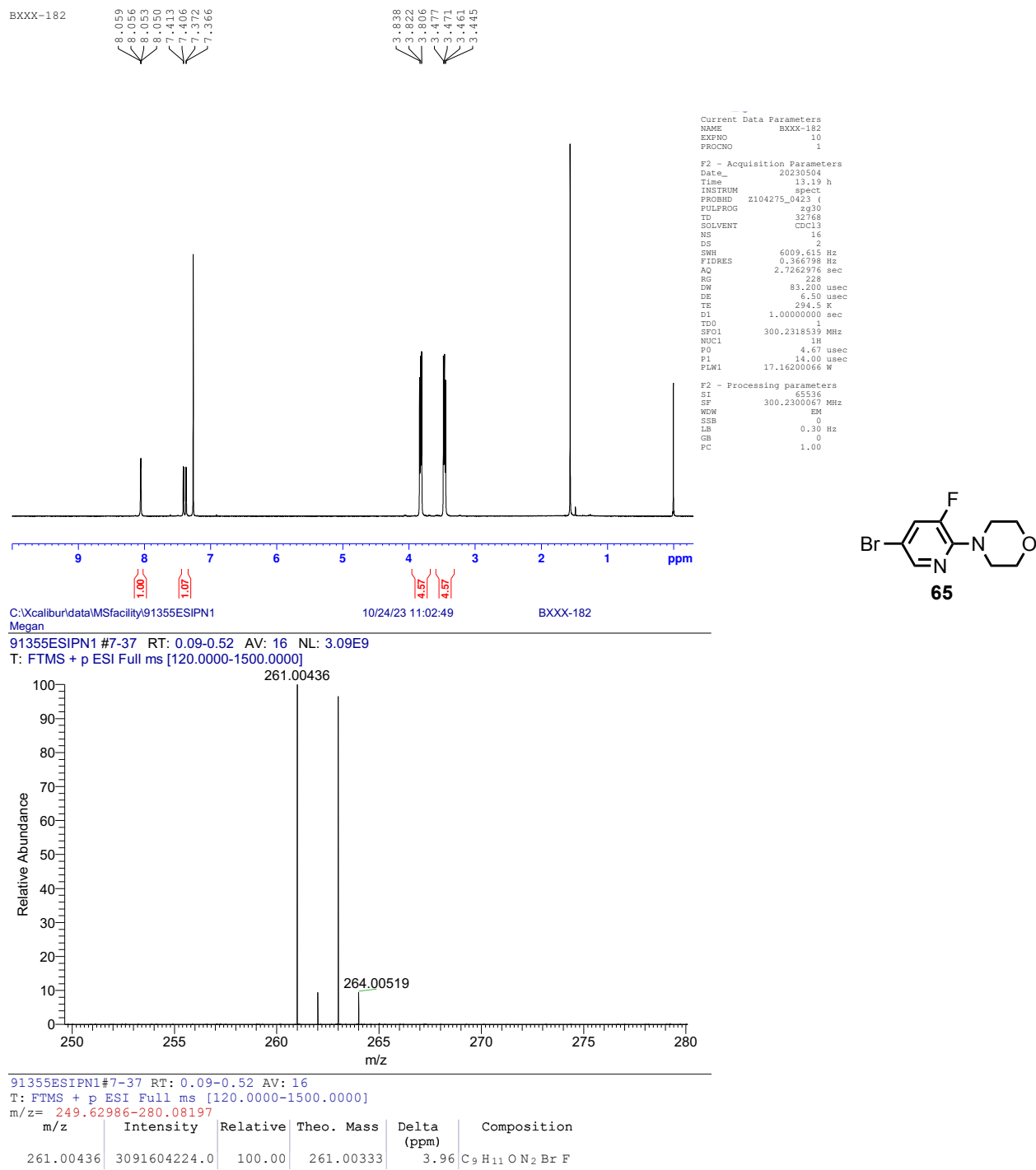


Figure S72. Compound **65** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

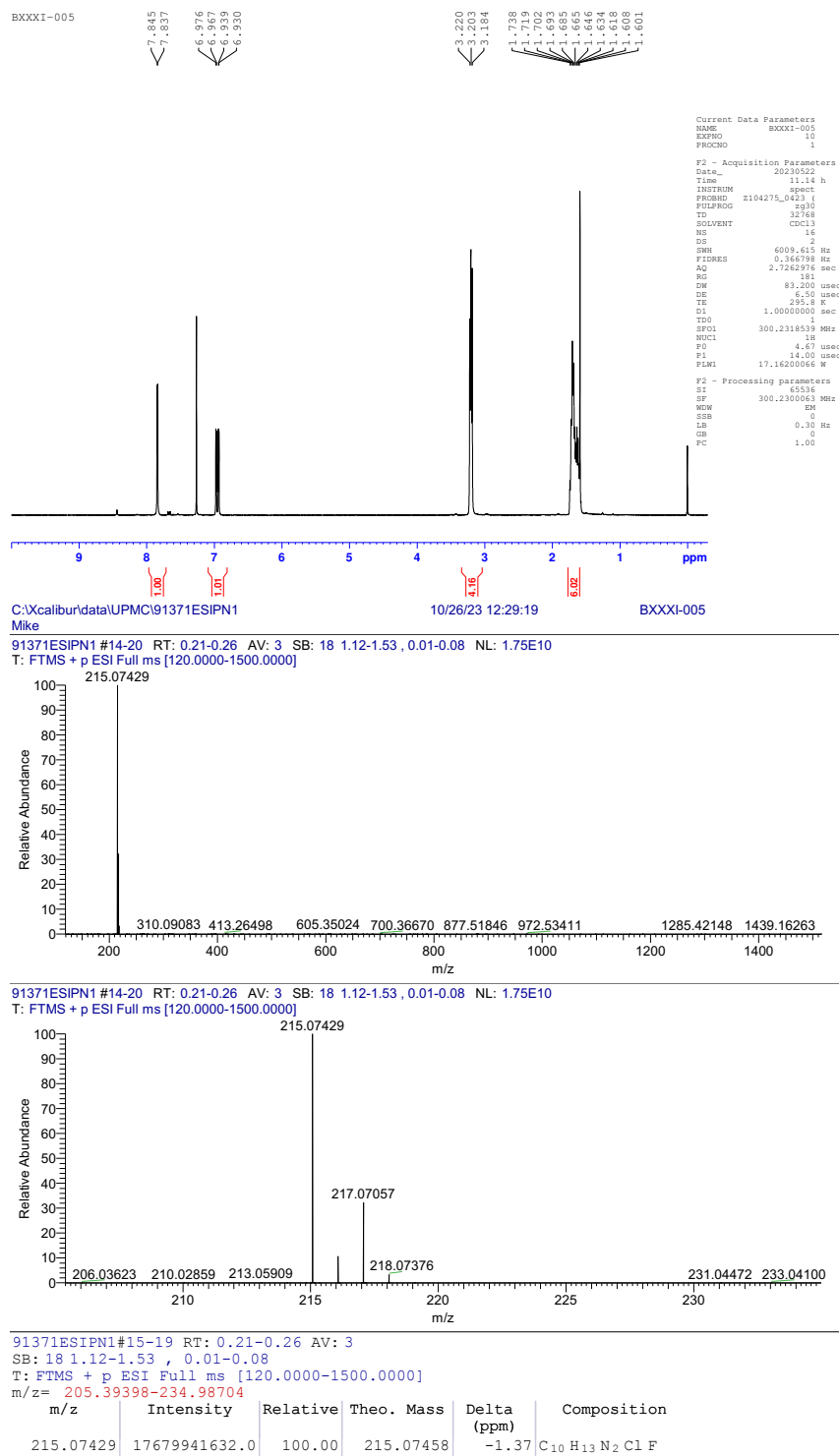
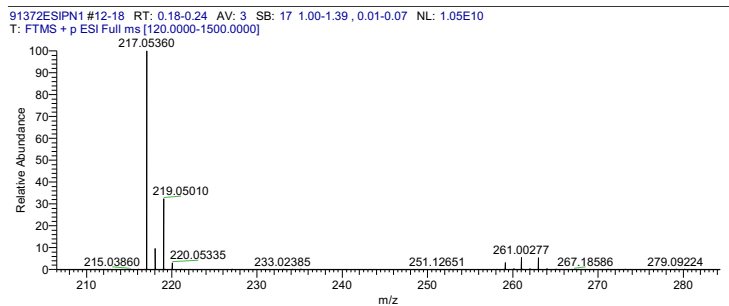
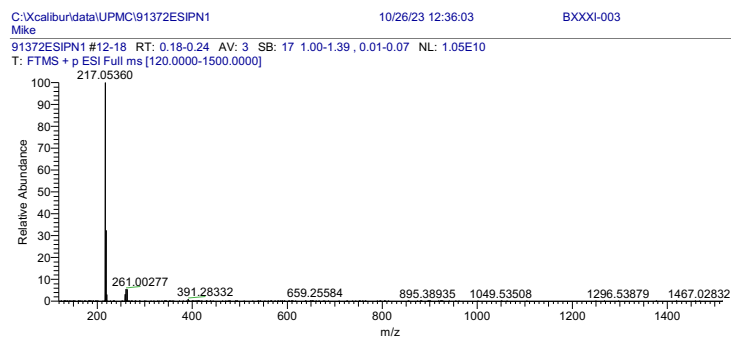
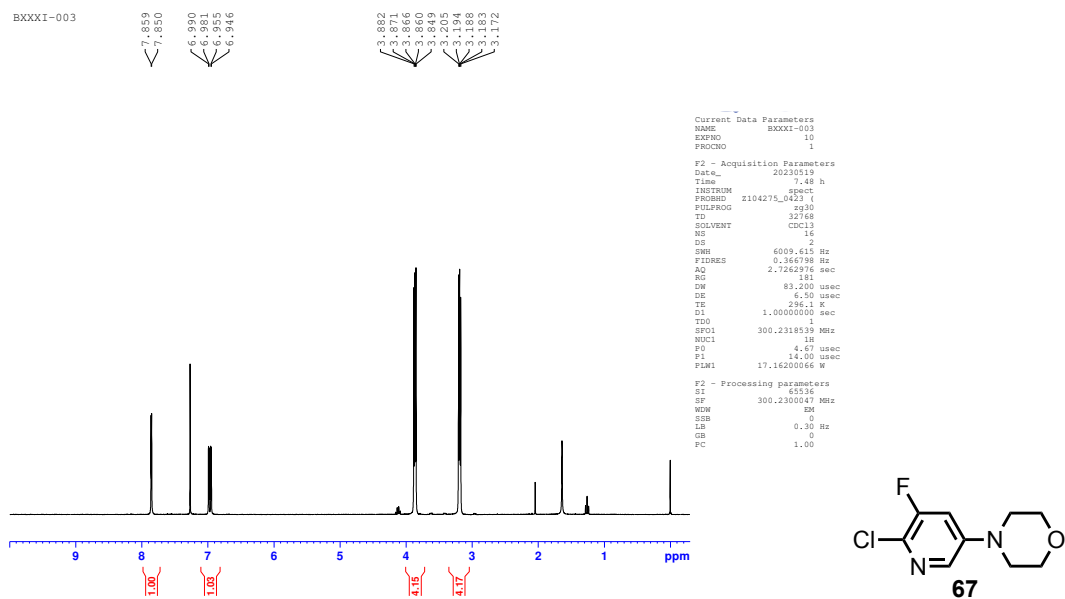


Figure S73. Compound **66** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).



91372ESIPN1#13-17 RT: 0.18-0.24 AV: 3
SB: 17 1.00-1.39, 0.01-0.07
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z= 206.48999-284.30877

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
217.05360	10581902336.0	100.00	217.05385	-1.14	C ₉ H ₁₁ ON ₂ ClF

Figure S74. Compound **67** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), high-resolution mass spectrum (bottom).

BXXX-180B

7.998
7.962

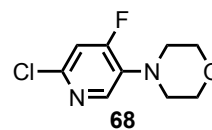
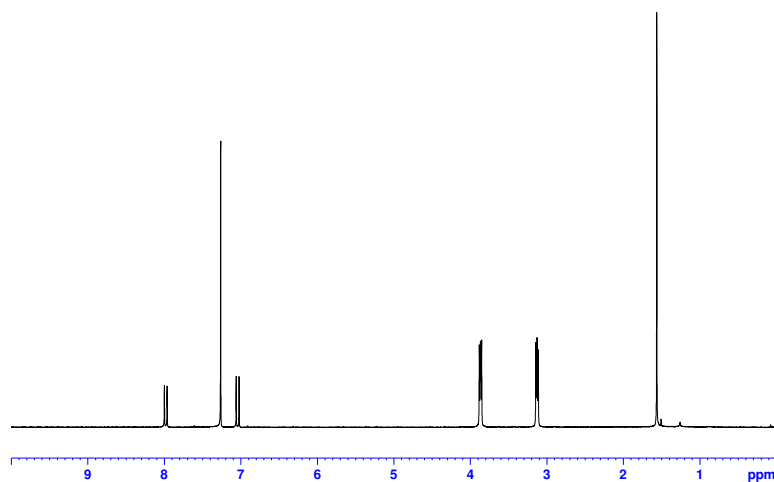
7.059
7.021

3.880
3.865
3.858
3.849
3.841
3.832
3.825
3.819
3.810

Current Data Parameters
NAME BXXX-180B
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20230428
Time 7.13 h
INSTRUM spect
PROBHD Z104275_0423 (
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 6009.615 Hz
FIDRES 0.366798 Hz
AQ 2.7262976 sec
RG 228
DW 83.200 usec
DE 6.50 usec
TE 294.9 K
D1 1.00000000 sec
TD0 1
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PO 4.67 usec
P1 14.00 usec
PLW1 17.1620066 W

F2 - Processing parameters
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SF 300.2300068 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



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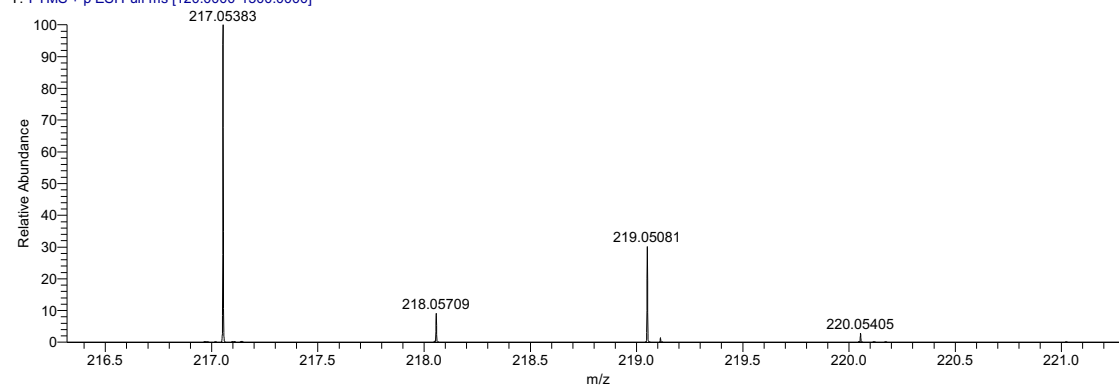
05/18/23 11:48:07

BXXXI-180

Sarah

90096ESIPN1#8-16 RT: 0.12-0.21 AV: 4 NL: 3.63E8

T: FTMS + p ESI Full ms [120.0000-1500.0000]



90096ESIPN1#9-15 RT: 0.12-0.21 AV: 4

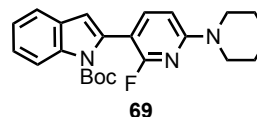
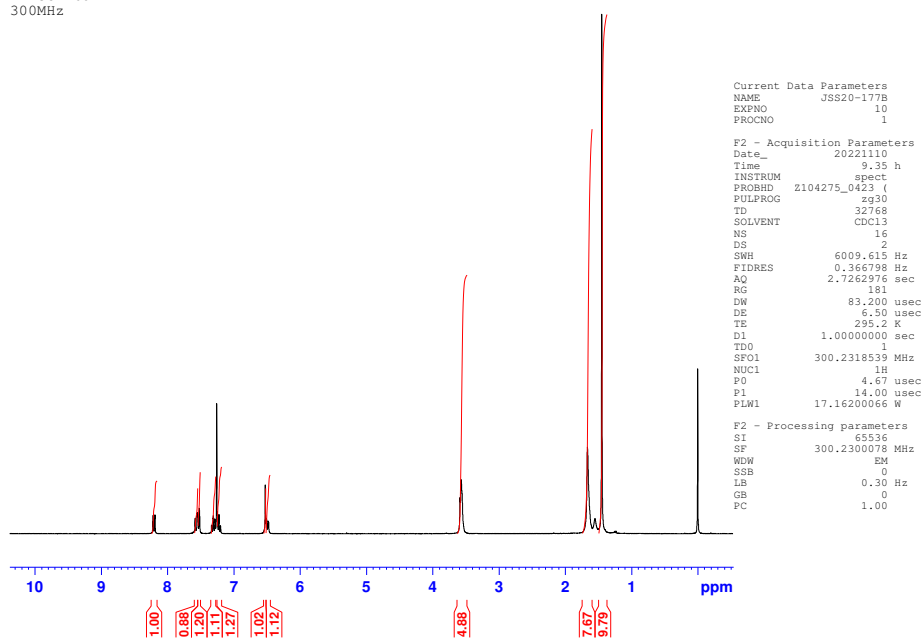
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z= 216.31866-221.32113

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
217.05383	370609952.0	100.00	217.05385	-0.07	C ₉ H ₁₁ ON ₂ ClF

Figure S75. Compound **68** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

white foam
300MHz



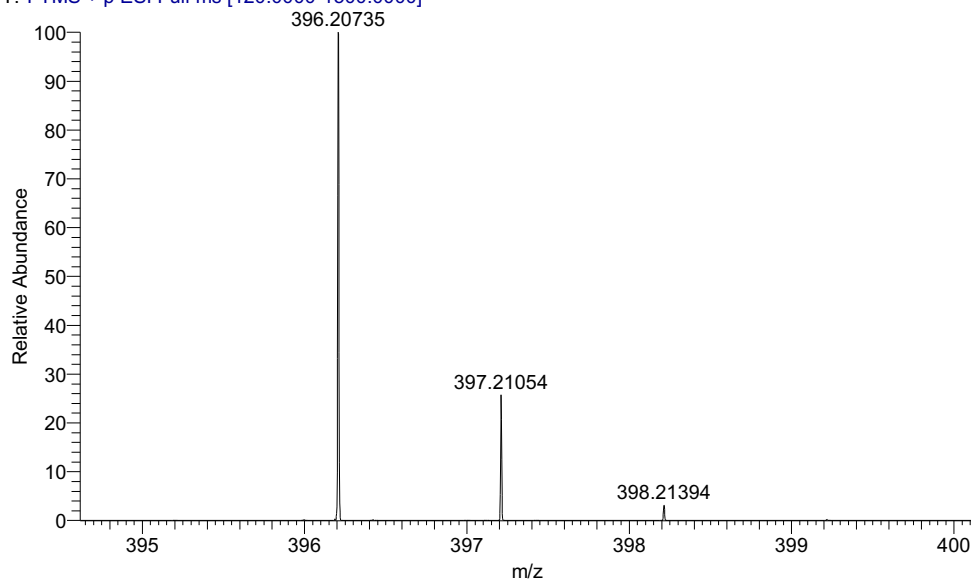
C:\Xcalibur\data\MSfacility\89007ESIPN1
Sarah

12/15/22 10:14:04

jss20-177B

89007ESIPN1 #9-19 RT: 0.12-0.26 AV: 6 NL: 5.94E9

T: FTMS + p ESI Full ms [120.0000-1500.0000]



89007ESIPN1#9-19 RT: 0.12-0.26 AV: 6

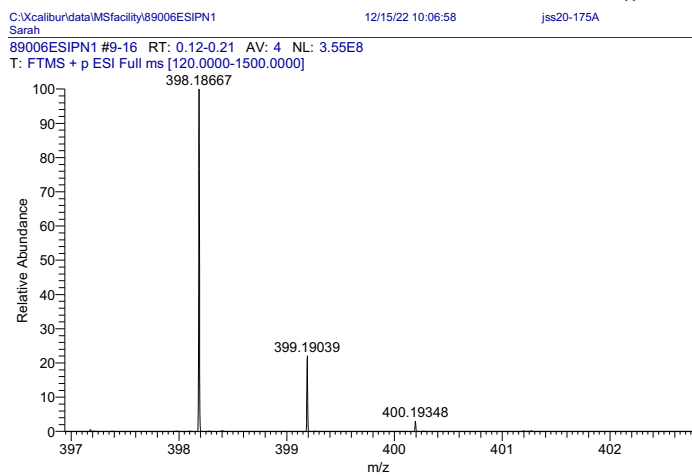
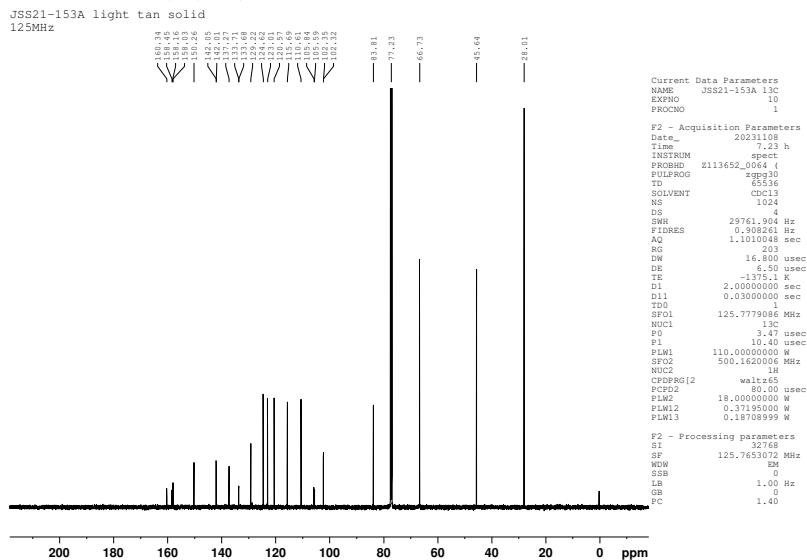
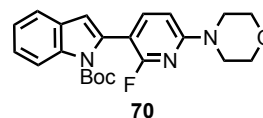
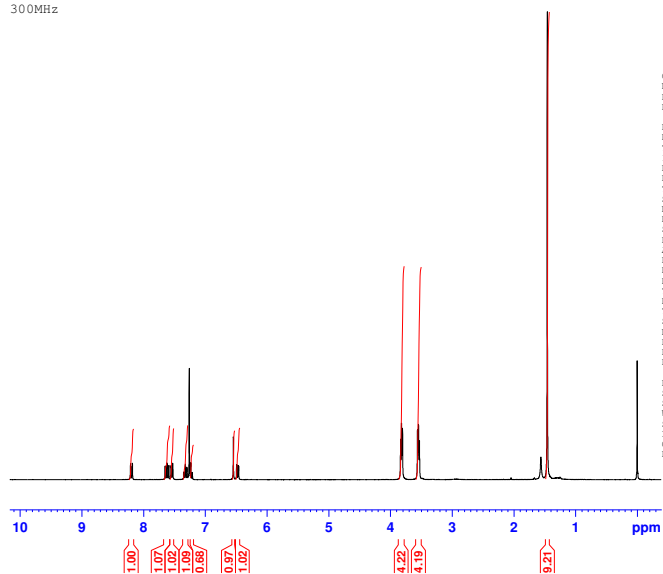
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z = 394.61629-400.12767

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
396.20735	6182650880.0	100.00	396.20818	-2.09	C ₂₃ H ₂₇ O ₂ N ₃ F

Figure S76. Compound **69** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

white foam
300MHz

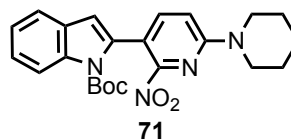
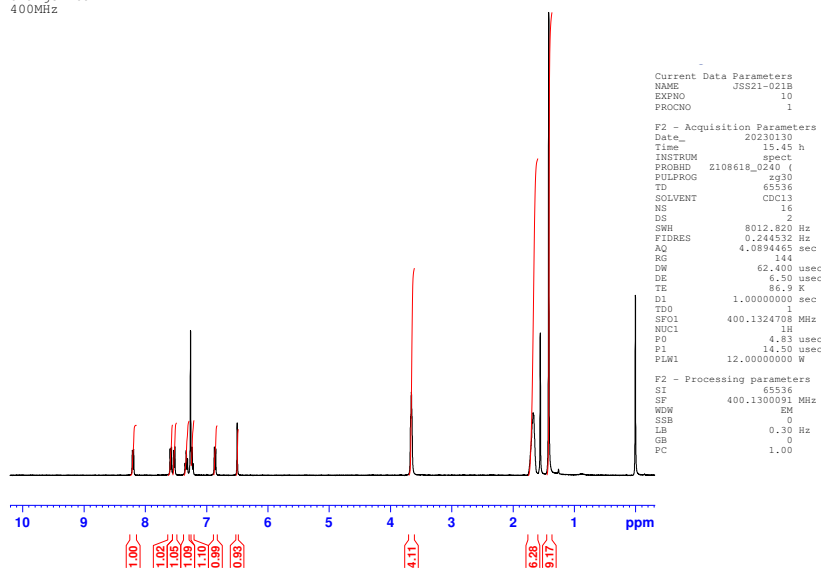


89006ESIPN1#9-15 RT: 0.12-0.21 AV: 4
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z= 396.94007-402.76113

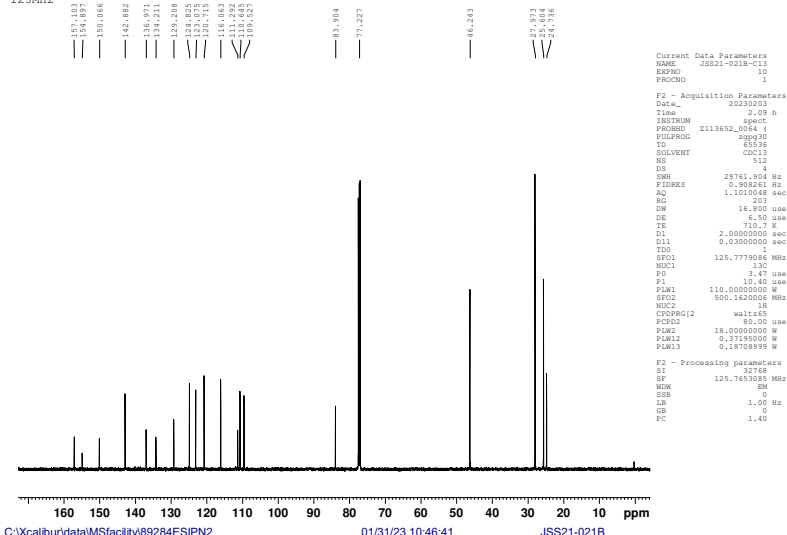
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
398.18667	355398112.0	100.00	398.18745	-1.94	C ₂₂ H ₂₅ O ₃ N ₃ F

Figure S77. Compound **70** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

orange foam
400MHz



yellow/orange foam
125MHz



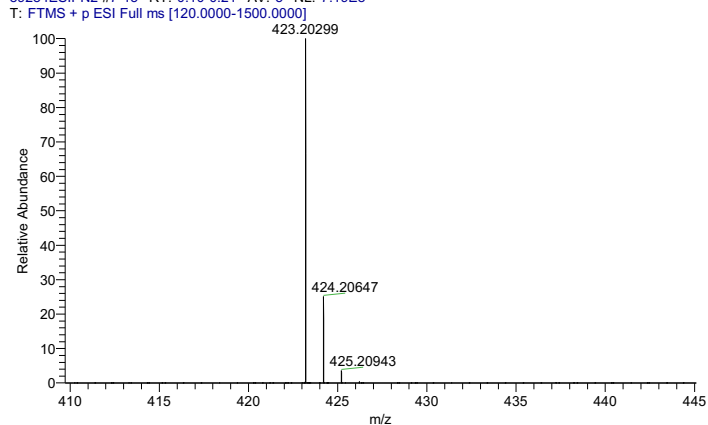
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01/31/23 10:46:41

JSS21-0218

89284ESI\IPN2 #7-15 RT: 0.10-0.21 AV: 5 NL: 7.19E8

T: FTMS + p ESI Full ms [120.0000-1500.0000]



89284ESI\IPN2 #7-15 RT: 0.10-0.21 AV: 5

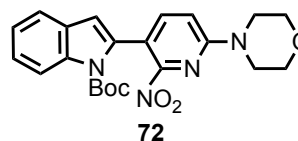
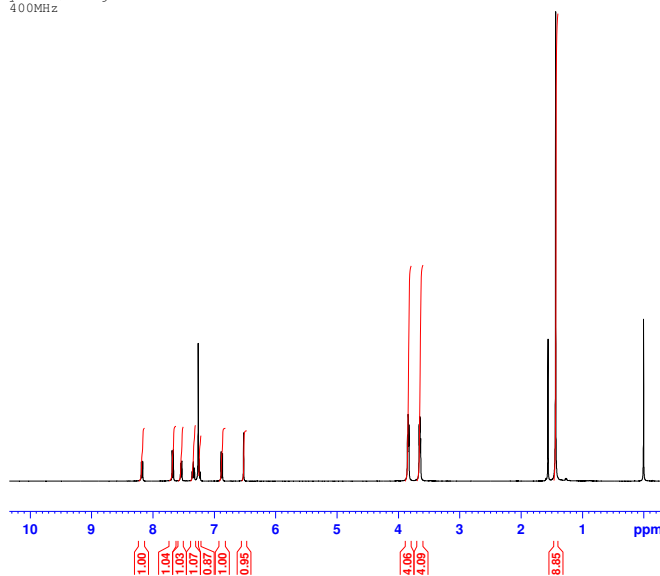
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z = 409.71417-445.09268

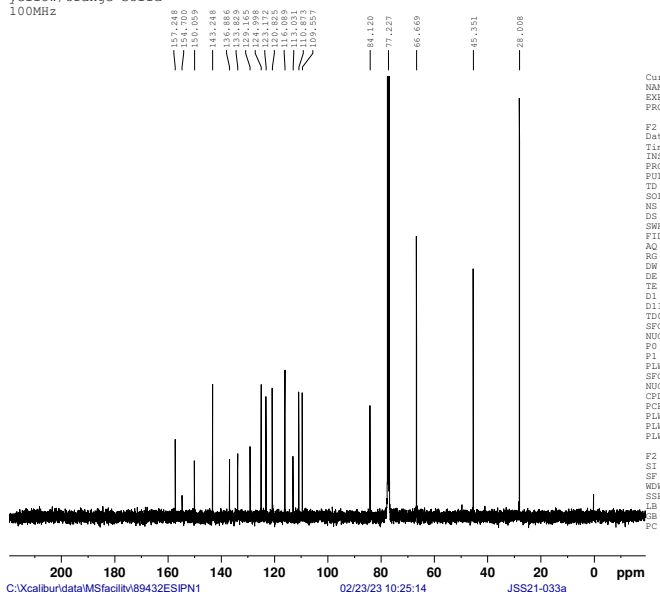
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
423.20299	742180096.0	100.00	423.20268	0.73	C ₂₃ H ₂₇ O ₄ N ₄

Figure S78. Compound **71** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

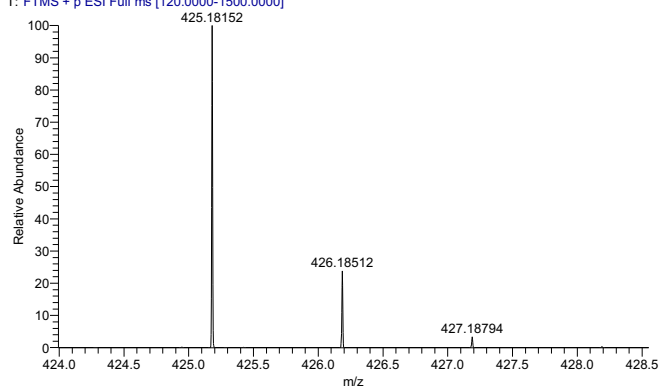
yellow/orange foam
400MHz



yellow/orange solid
100MHz



C:\xcalibur\data\MSfacility\89432ESIPN1
Sarah
89432ESIPN1 #12-19 RT: 0.18-0.27 AV: 4 NL: 7.57E8
T: FTMS + p ESI Full ms [120.0000-1500.0000]

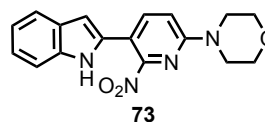
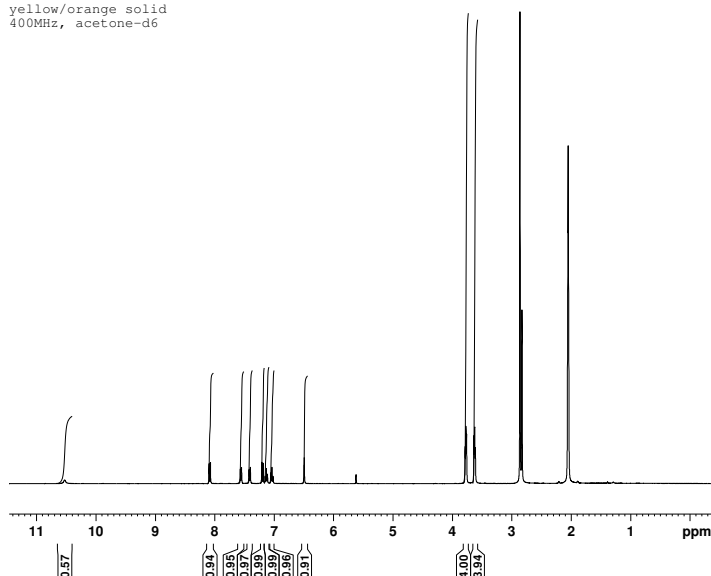


89432ESIPN1#13-19 RT: 0.18-0.27 AV: 4
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z= 423.99300-428.55014

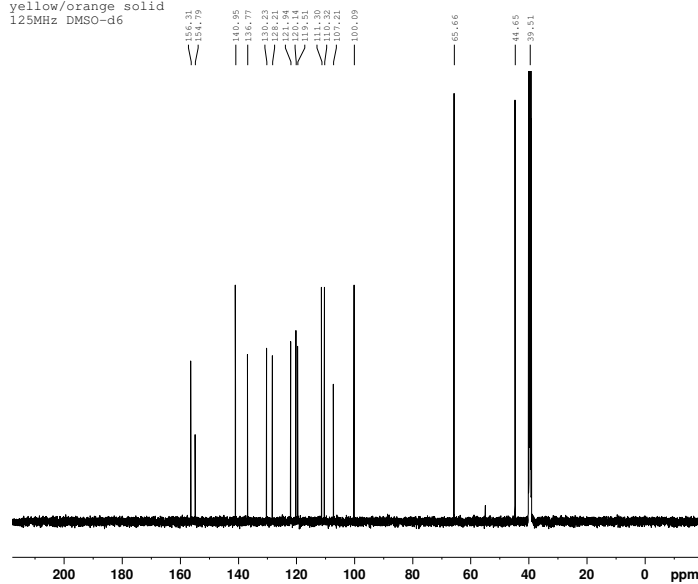
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
425.18152	758258752.0	100.00	425.18195	-1.00	C ₂₂ H ₂₅ O ₅ N ₄

Figure S79. Compound **72** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

JSS21-123B
yellow/orange solid
400MHz, acetone-d6



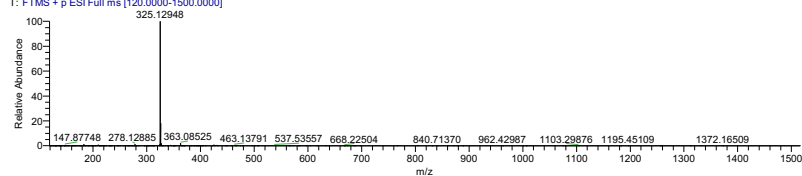
JSS21-123B
yellow/orange solid
125MHz DMSO-d6



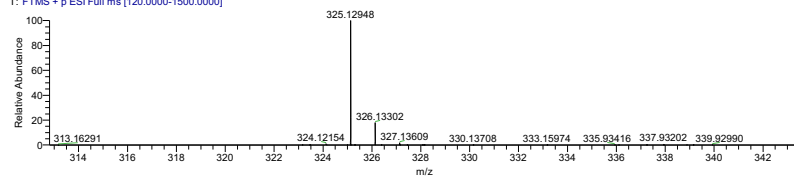
C:\Xcalibur\...91013ESIPN1

Mike

91013ESIPN1#12-17 RT: 0.18-0.24 AV: 3 NL: 7.84E8
T: FTMS + p ESI Full ms [120.0000-1500.0000]



91013ESIPN1#12-17 RT: 0.18-0.24 AV: 3 NL: 7.84E8
T: FTMS + p ESI Full ms [120.0000-1500.0000]



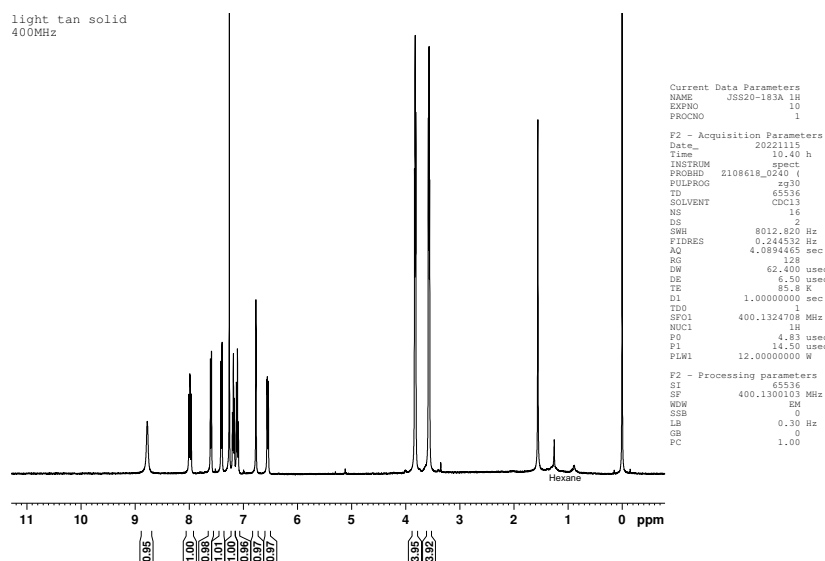
91013ESIPN1#13-17 RT: 0.18-0.24 AV: 3
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z = 312.80561-343.49456

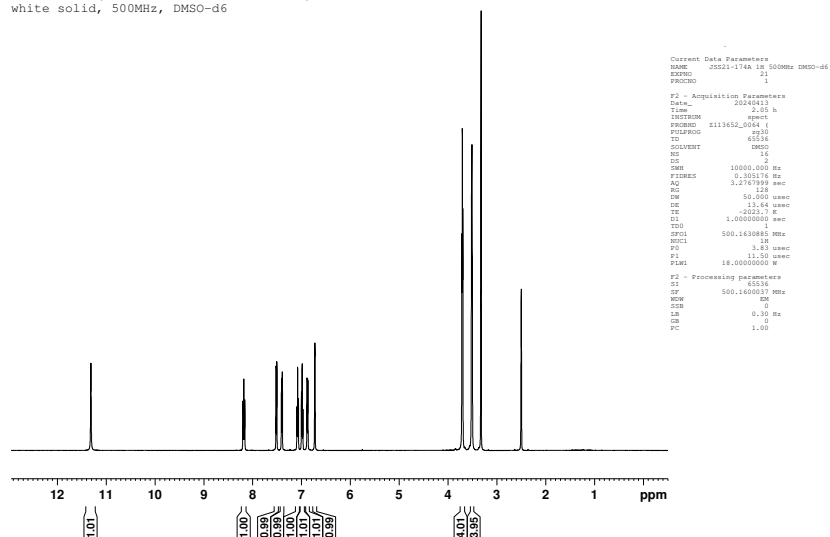
m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
325.12948	784773568.0	100.00	325.12952	-0.11	C ₁₇ H ₁₇ O ₃ N ₄

Figure S80. Compound **73** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

light tan solid
400MHz



JSS20-183A (batch# JSS21-174A-11-29-23)
white solid, 500MHz, DMSO-d6



JSS20-183A (batch# JSS22-047A-3-21-24)
tan solid, 500MHz, acetone-d6

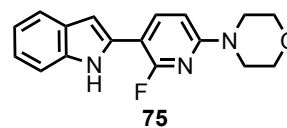
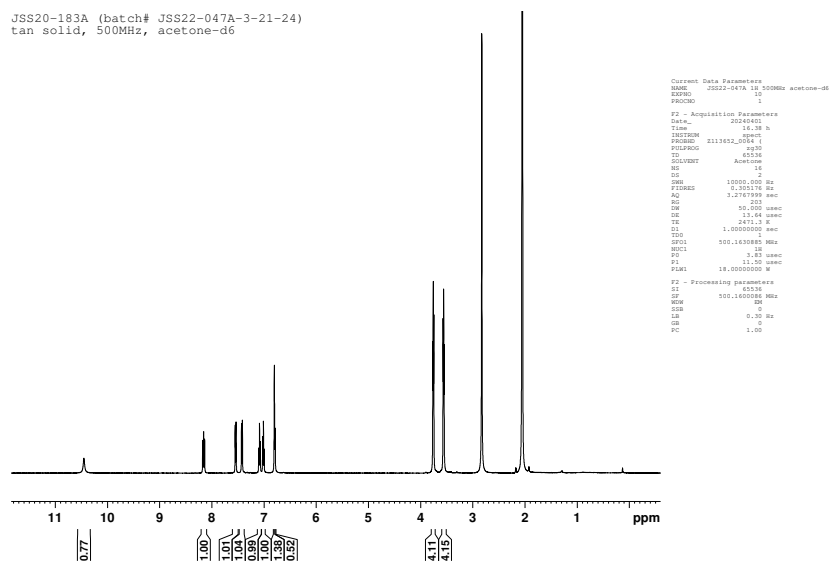
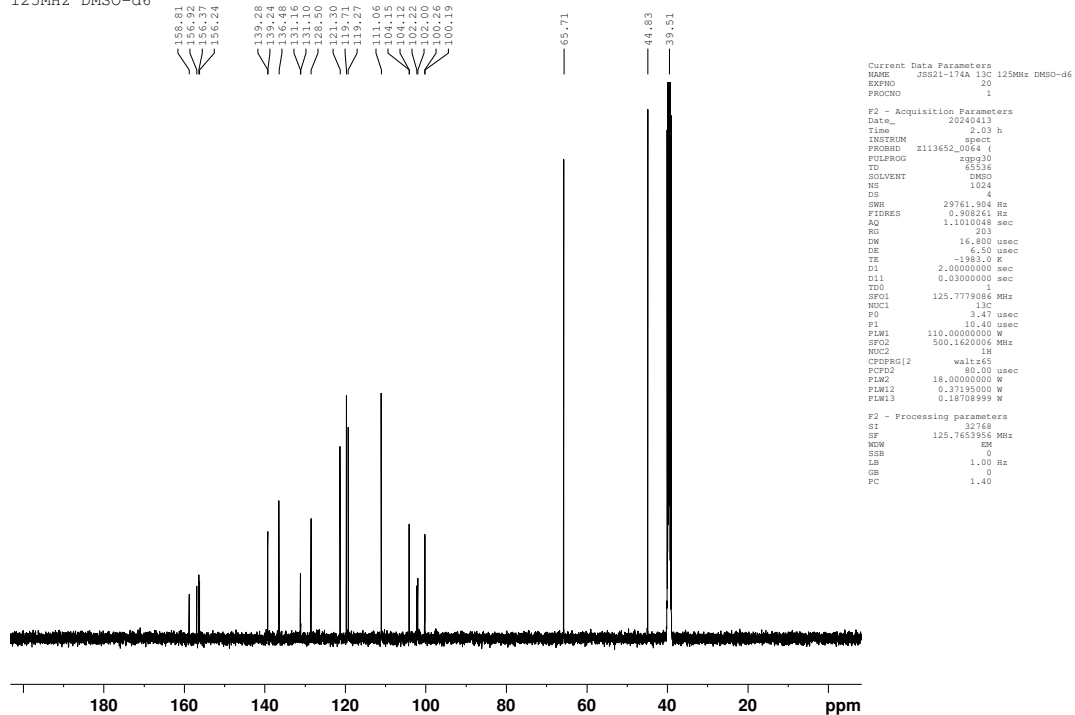


Figure S82. Compound **75** ^1H NMR spectra in CDCl_3 (top), $\text{DMSO}-d_6$ (middle), and $\text{acetone}-d_6$ (bottom).

JSS20-183A (batch# JSS21-174A)
125MHz DMSO-d6

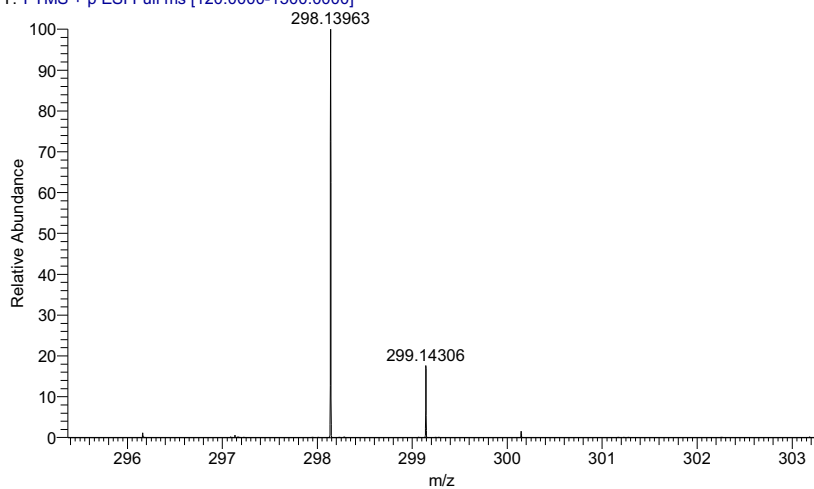


C:\Xcalibur\data\MSfacility\88809ESIPN4
Sarah

11/17/22 14:38:55

JSS20-183A

88809ESIPN4 #8-13 RT: 0.12-0.18 AV: 3 NL: 7.71E8
T: FTMS + p ESI Full ms [120.0000-1500.0000]



88809ESIPN4#9-13 RT: 0.12-0.18 AV: 3
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z = 295.37040-303.25121

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
298.13963	784189376.0	100.00	298.13502	4.61	C ₁₇ H ₁₇ ON ₃ F

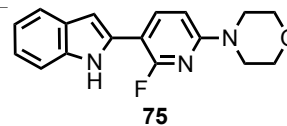
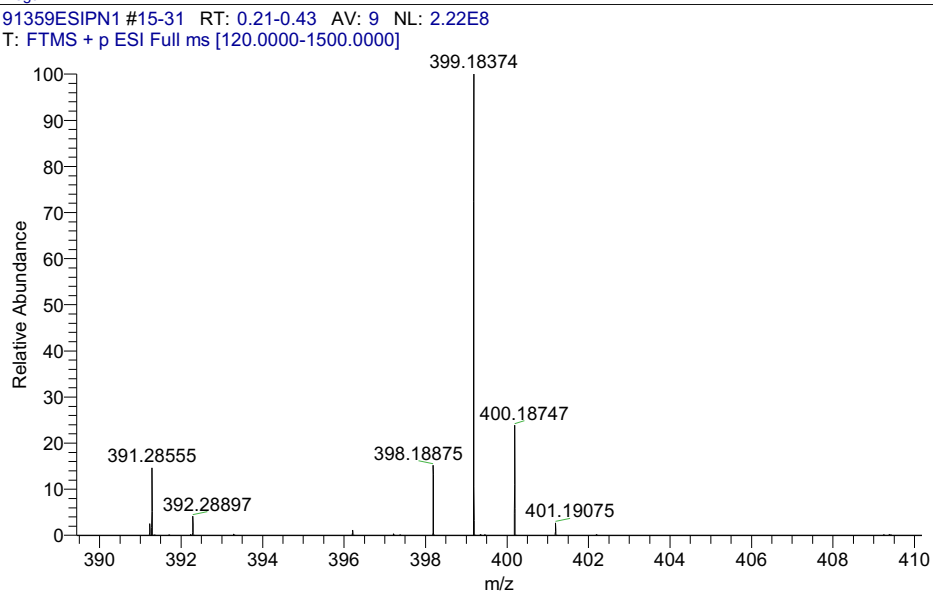
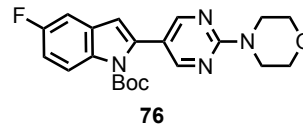
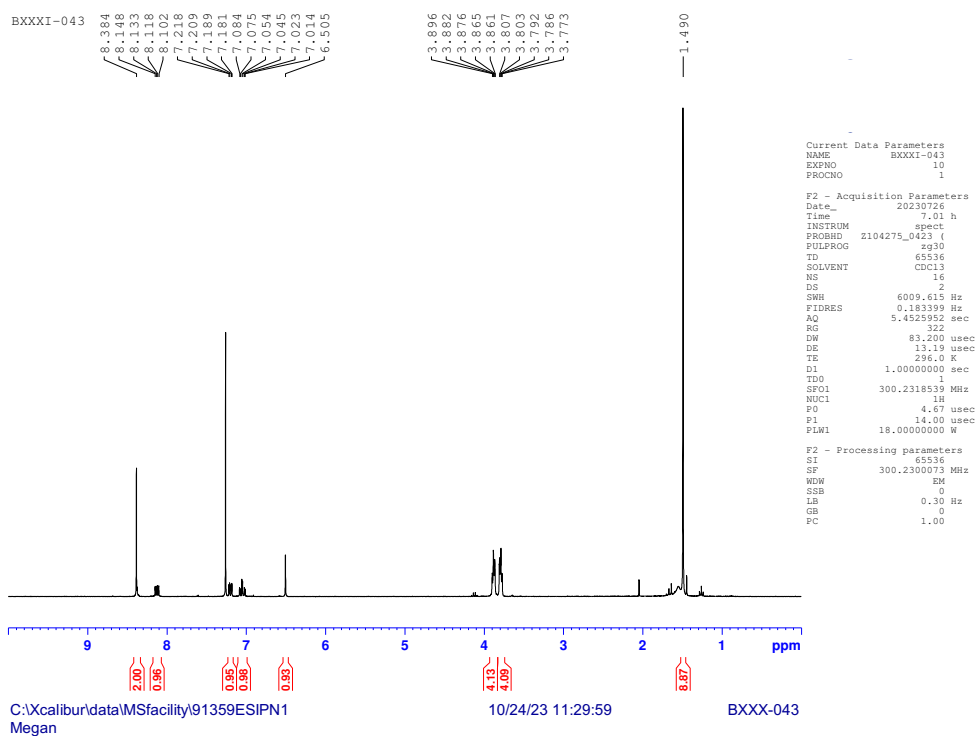


Figure S83. Compound **75** ¹³C NMR spectrum (top) and high-resolution mass spectrum (bottom).



91359ESIPN1#15-31 RT: 0.21-0.43 AV: 9
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z= 389.43346-410.17931

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
399.18374	225761696.0	100.00	399.18270	2.63	C ₂₁ H ₂₄ O ₃ N ₄ F

Figure S84. Compound **76** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

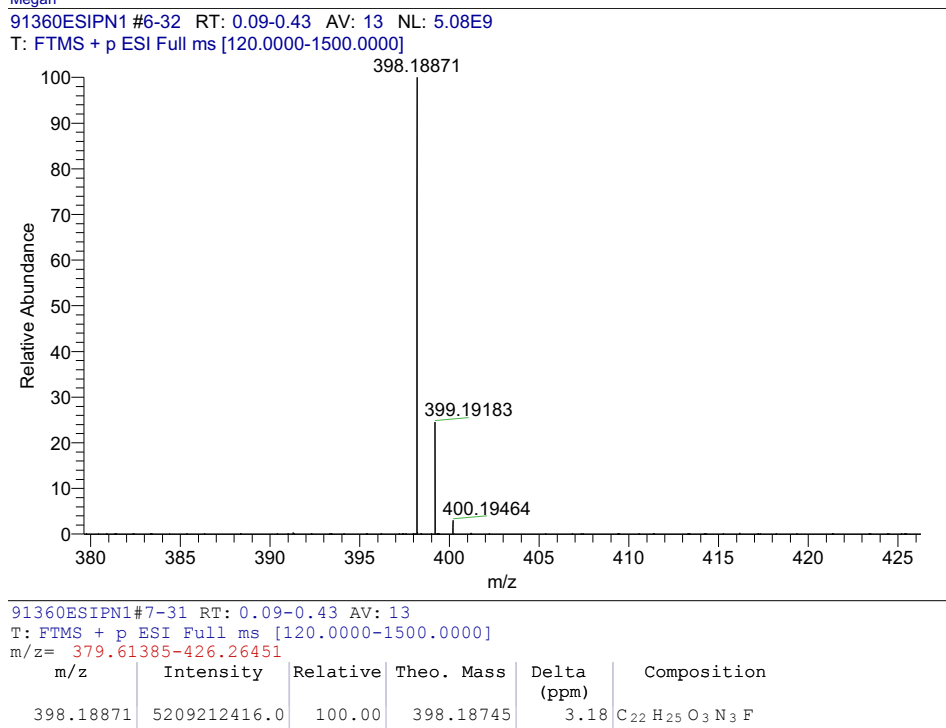
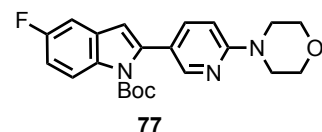
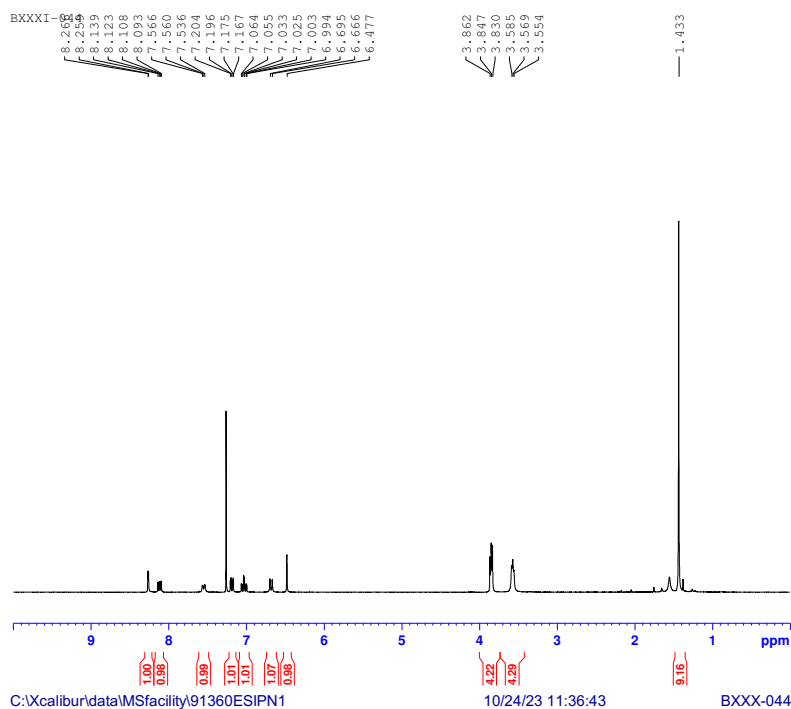
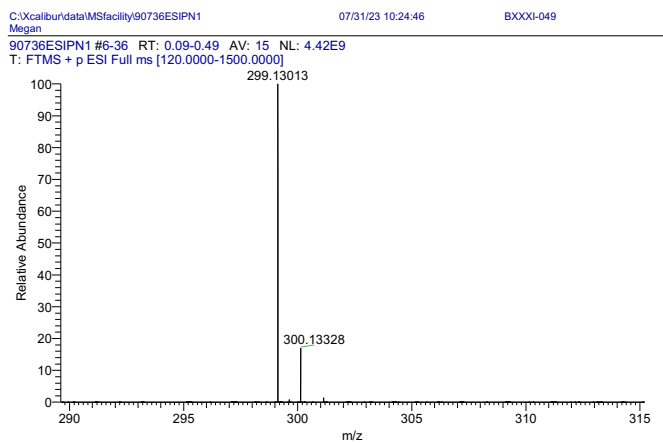
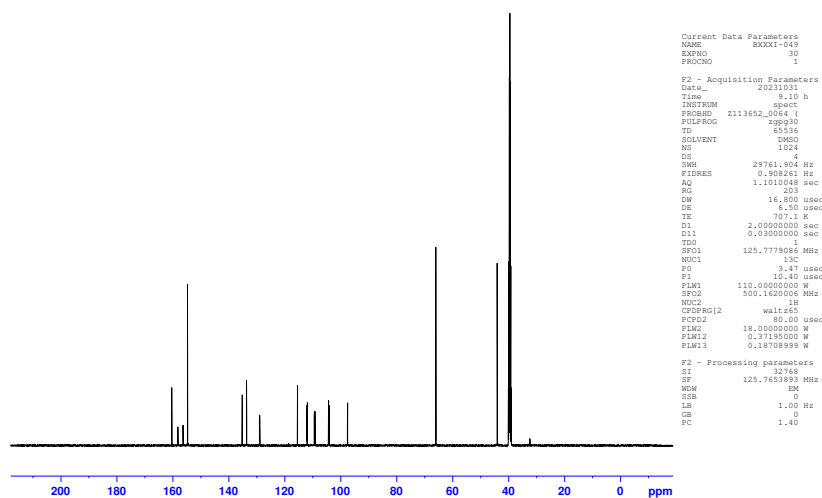
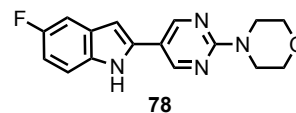
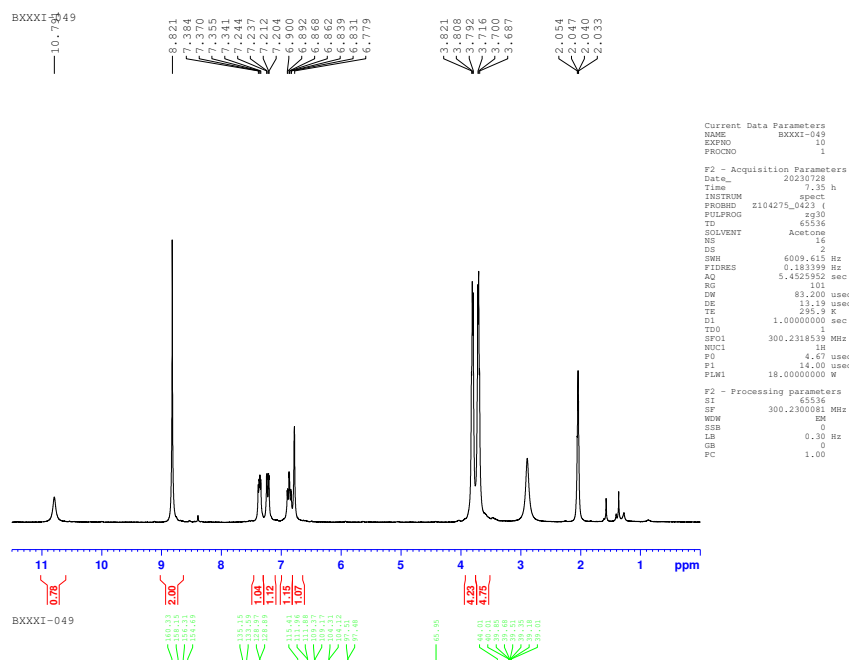


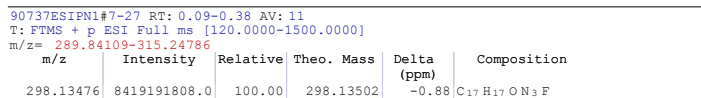
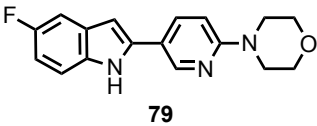
Figure S85. Compound **77** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).



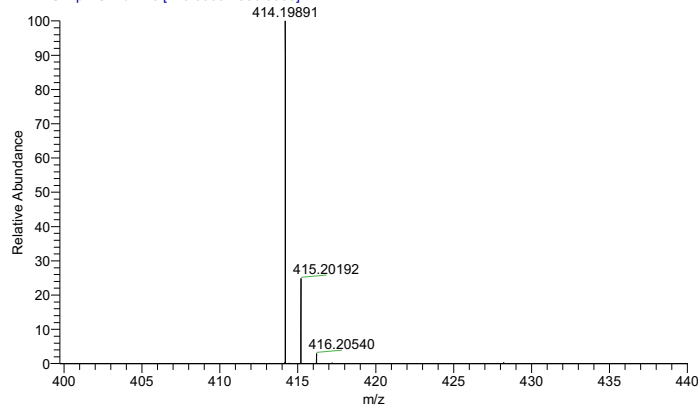
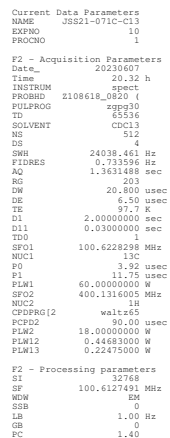
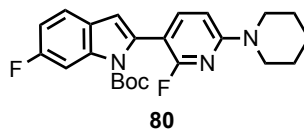
90736ESIPN1 #7-35 RT: 0.09-0.49 AV: 15
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
299.13013	4565434368.0	100.00	299.13027	-0.45	C ₁₆ H ₁₆ ON ₄ F

Figure S86. Compound **78** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), high-resolution mass spectrum (bottom).



S92



m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
414.19891	6151417344.0	100.00	414.19876	0.37	C ₂₃ H ₂₆ O ₂ N ₃ F ₂

Figure S88. Compound **80** ^1H NMR spectrum (top), ^{13}C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

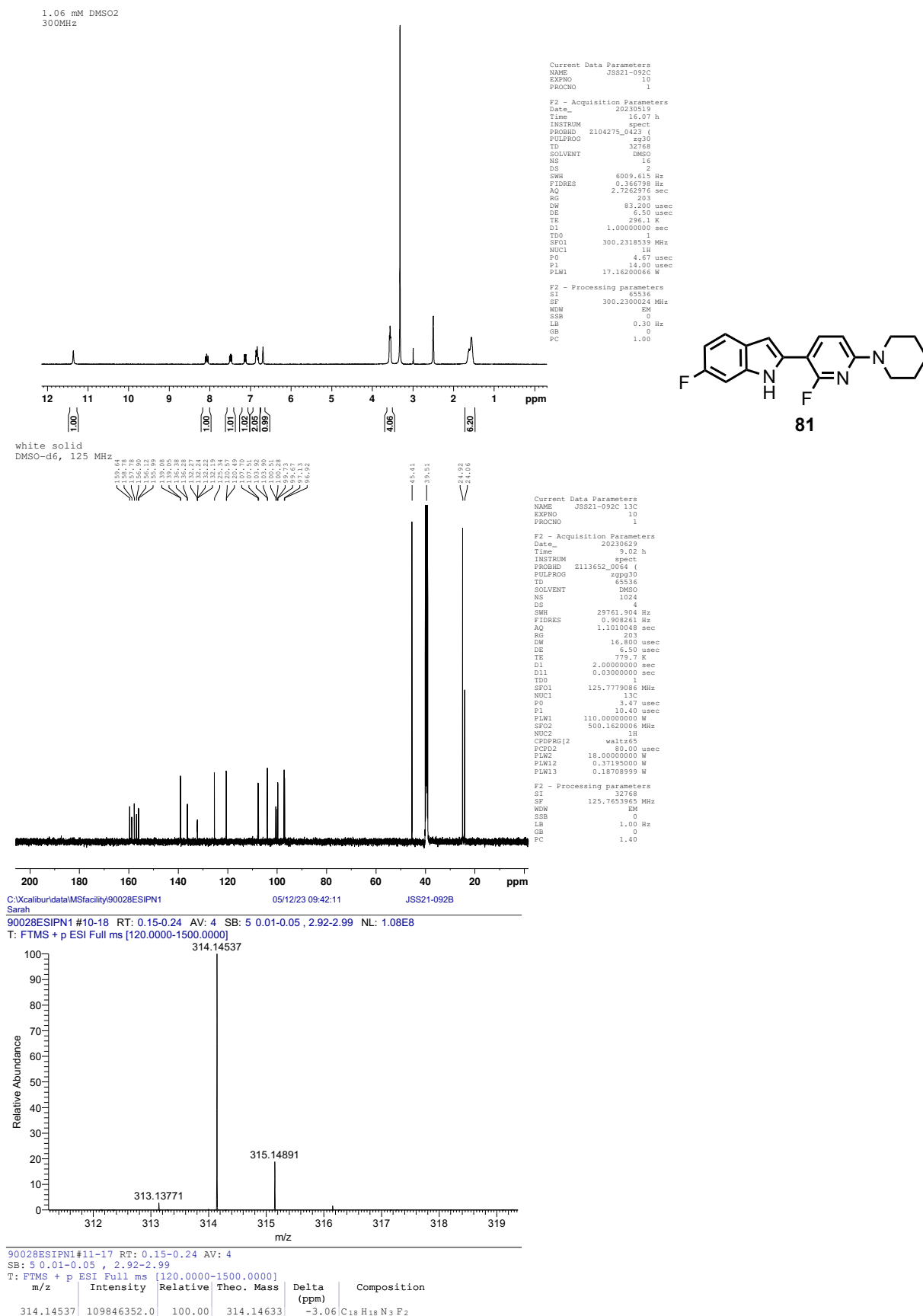


Figure S89. Compound **81** ^1H NMR spectrum (top), ^{13}C NMR spectrum (middle), and high-resolution mass spectrum (bottom).

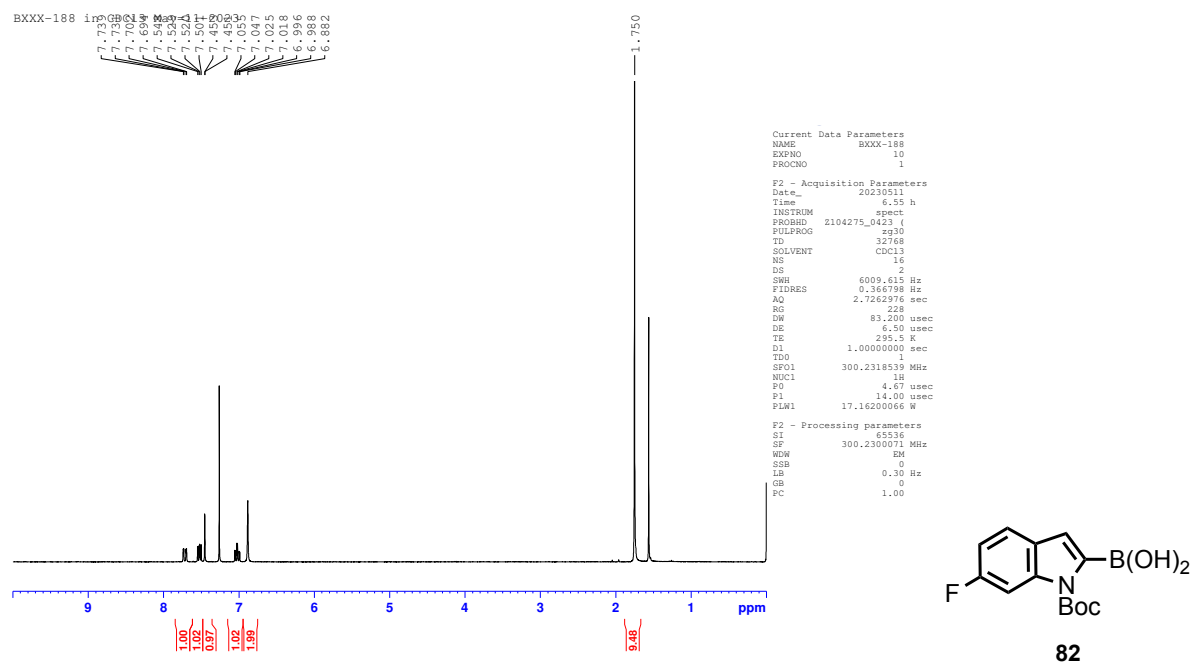
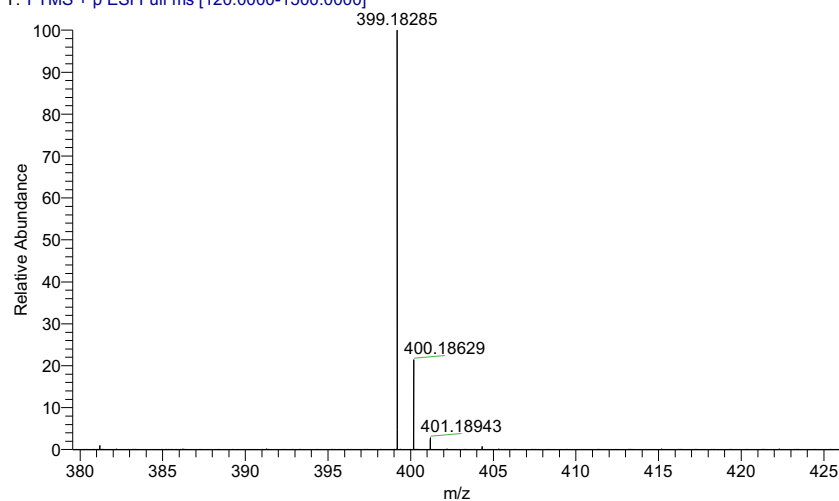
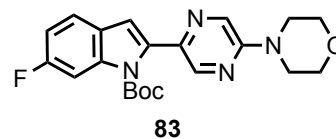
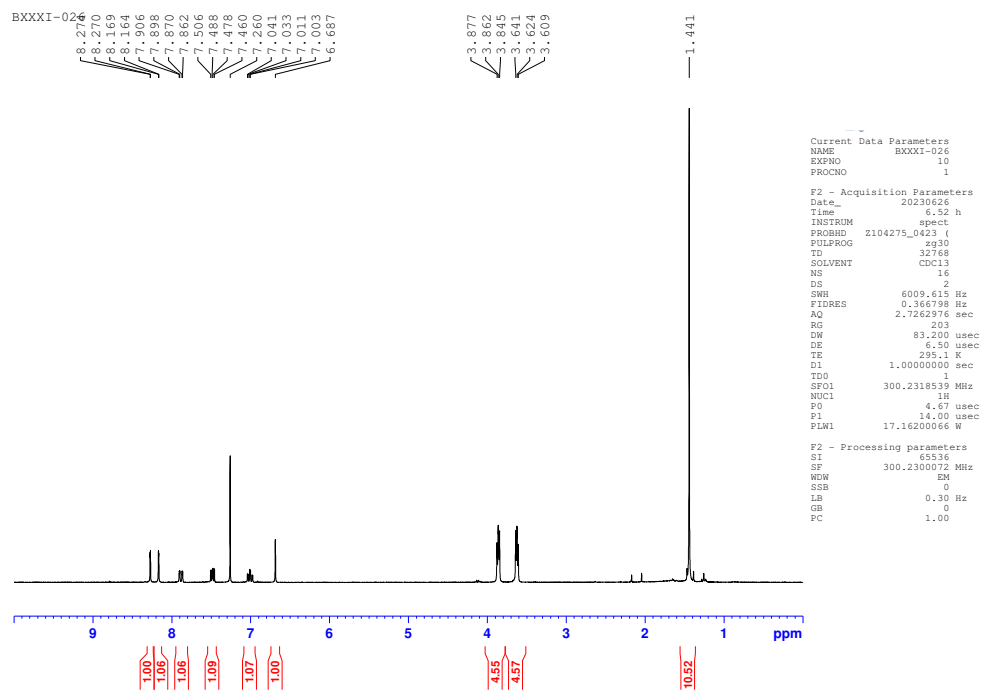


Figure S90. Compound **82** ^1H NMR spectrum.

Note: compound **82** decomposes in the mass spectrometer under both positive ion mode and negative ion mode.



91431ESIPN1#7-33 RT: 0.09-0.46 AV: 14
 T: FTMS + p ESI Full ms [120.0000-1500.0000]
 m/z = 379.54296-426.04479

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
399.18285	2647502592.0	100.00	399.18270	0.38	C ₂₁ H ₂₄ O ₃ N ₄ F

Figure S91. Compound **83** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

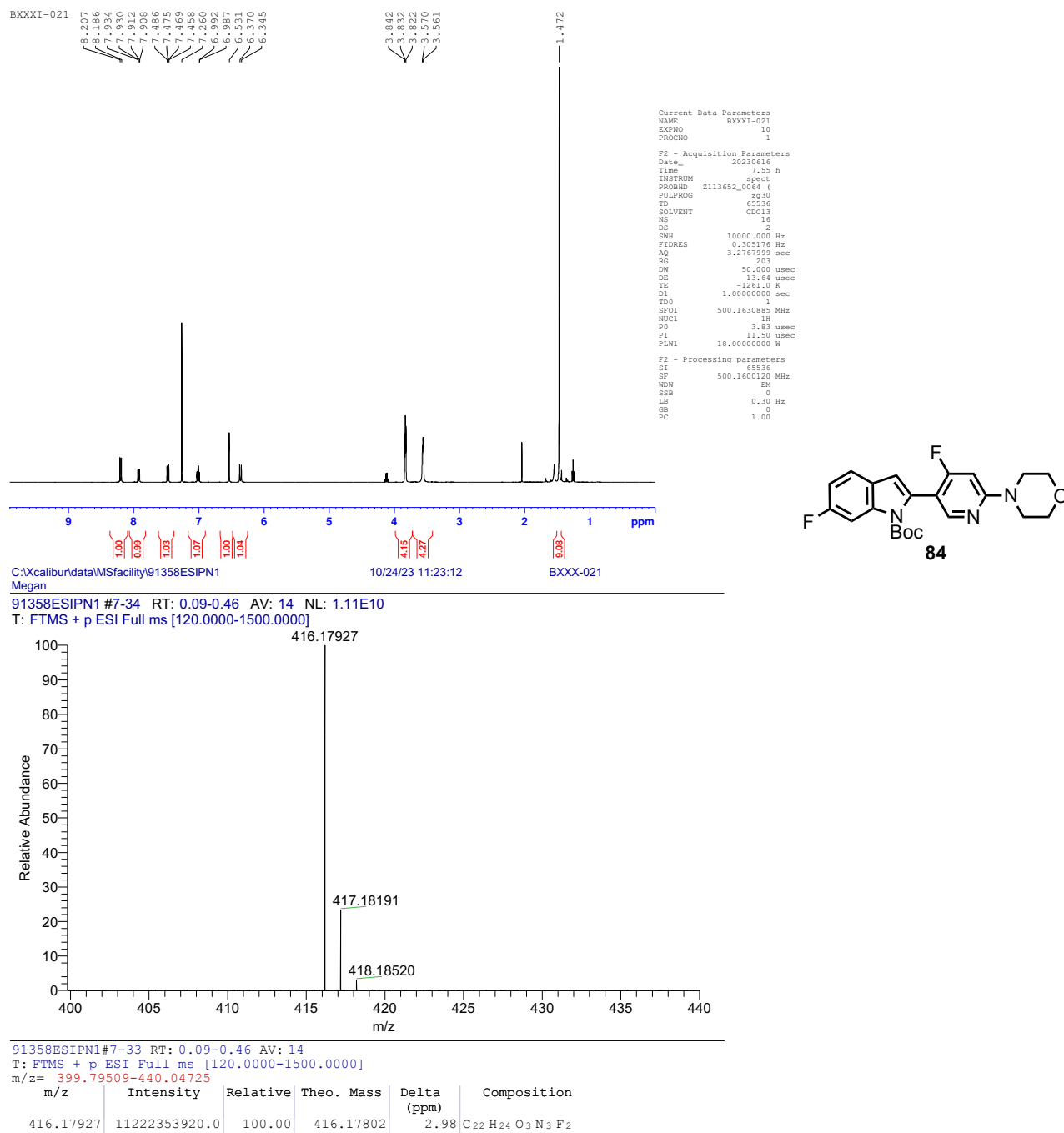


Figure S92. Compound **84** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

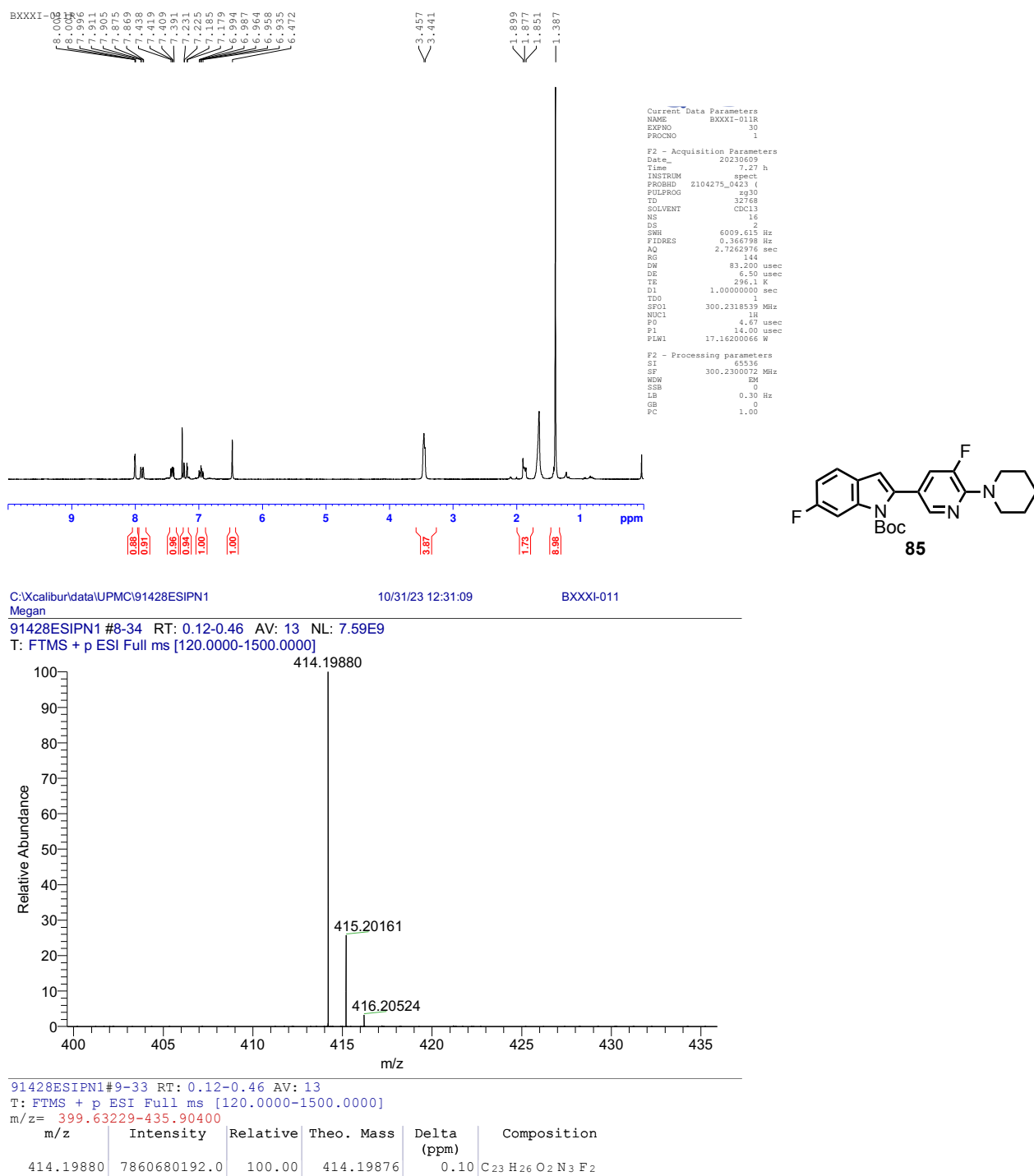


Figure S93. Compound **85** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

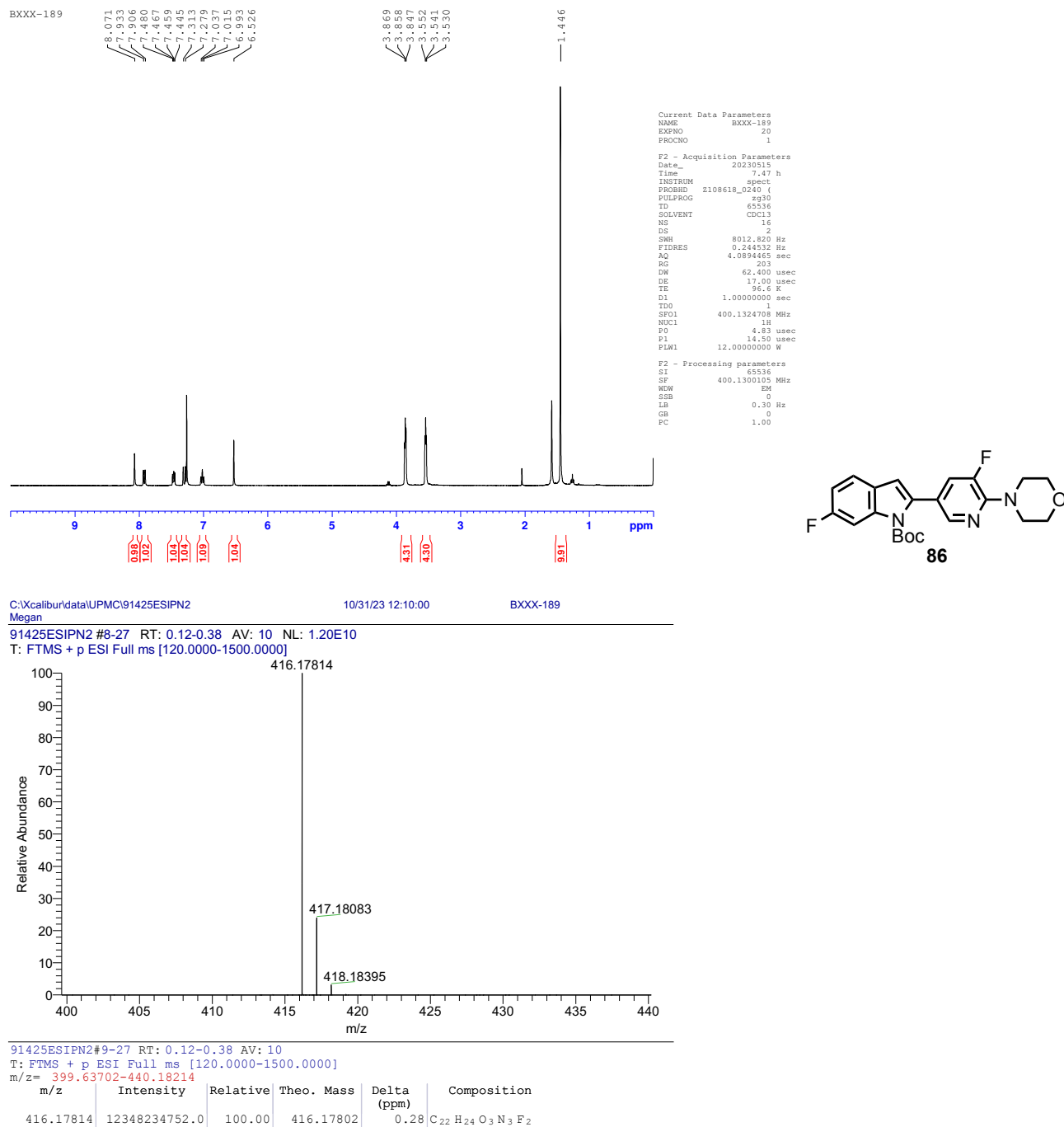


Figure S94. Compound **86** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

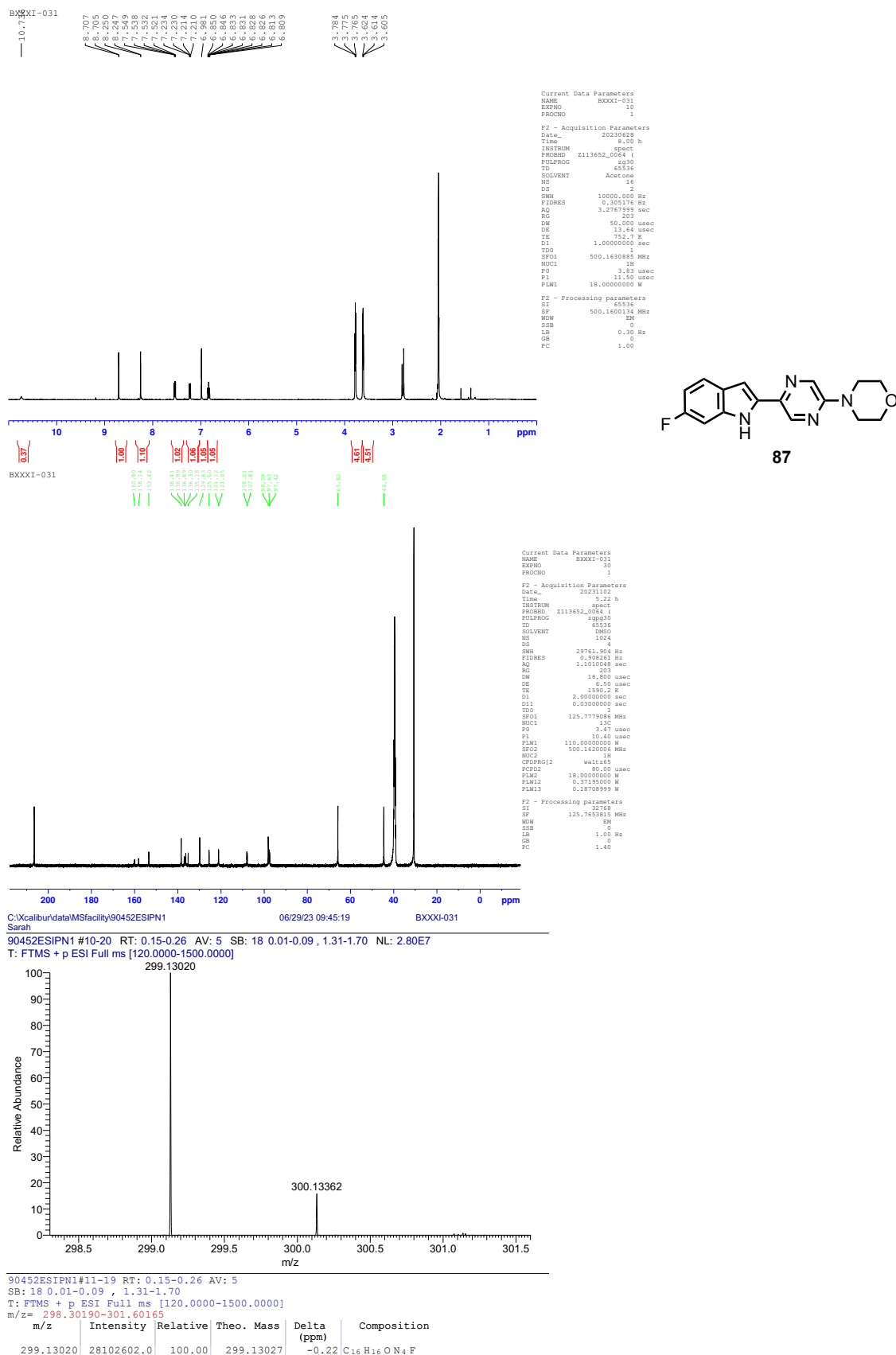
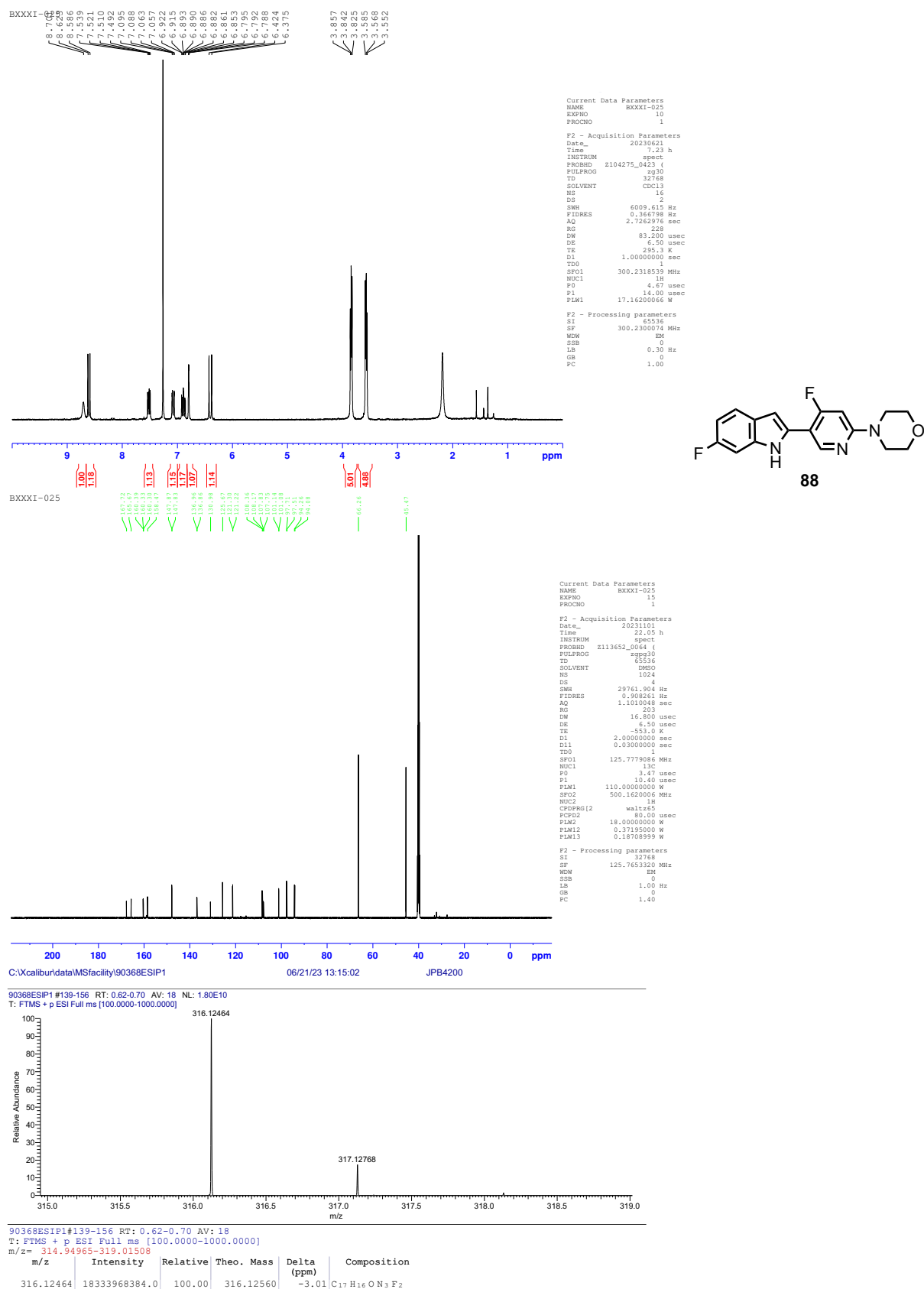
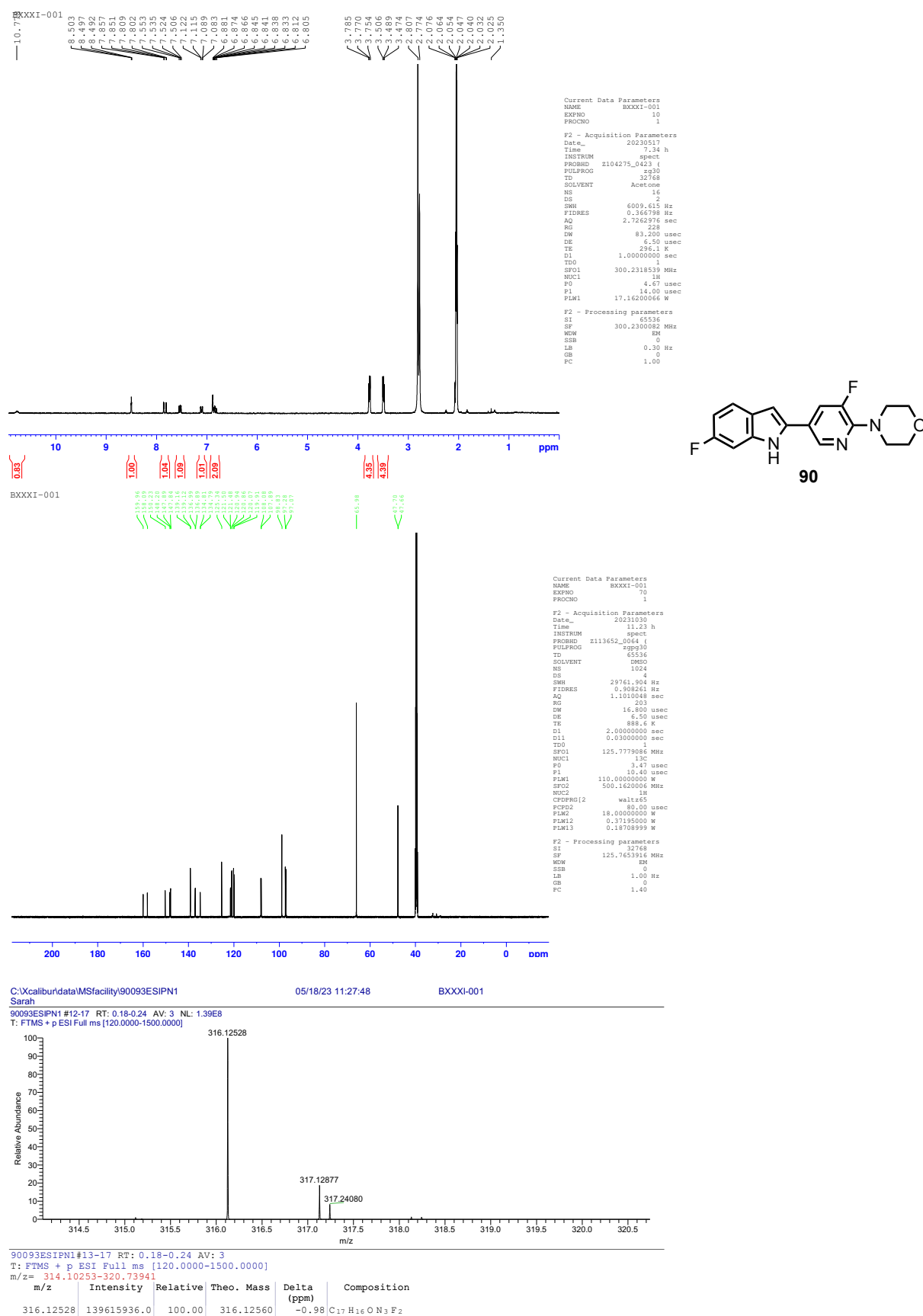
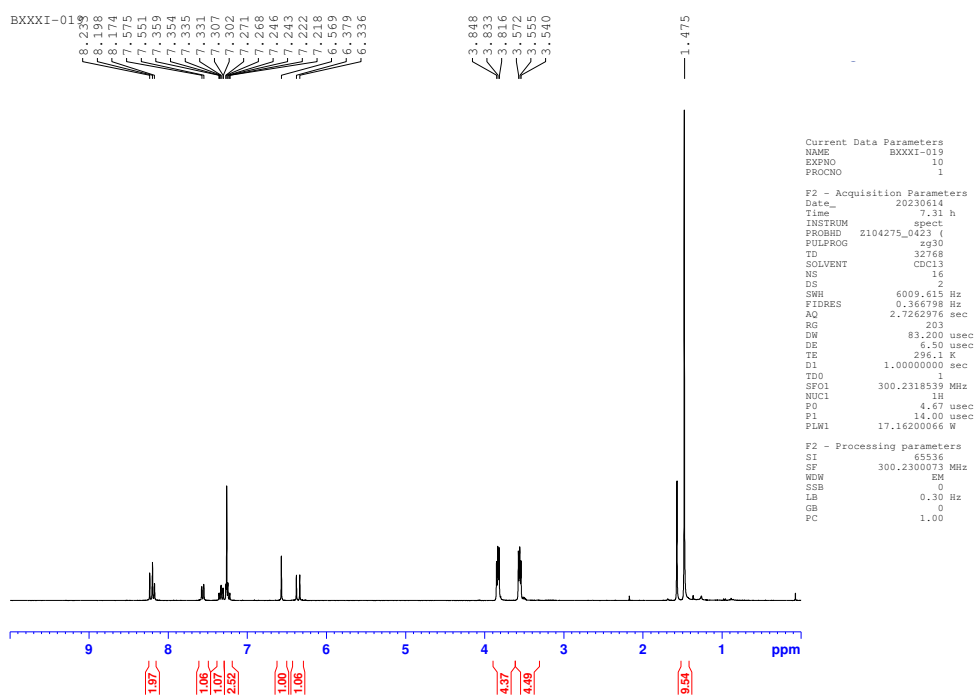


Figure S95. Compound **87** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), high-resolution mass spectrum (bottom).





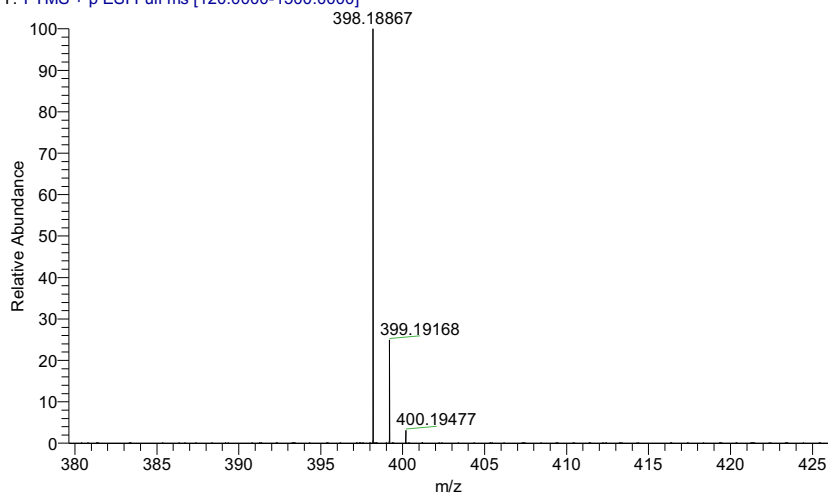


C:\Xcalibur\data\MSfacility\91357ESIPN1
Megan

10/24/23 11:16:26

BXXX-019

91357ESIPN1#7-32 RT: 0.09-0.44 AV: 13 NL: 7.36E9
T: FTMS + p ESI Full ms [120.0000-1500.0000]



91357ESIPN1#7-31 RT: 0.09-0.44 AV: 13
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z = 379.62237-425.96293

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
398.18867	7587728384.0	100.00	398.18745	3.06	C ₂₂ H ₂₅ O ₃ N ₃ F

Figure S99. Compound **91** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

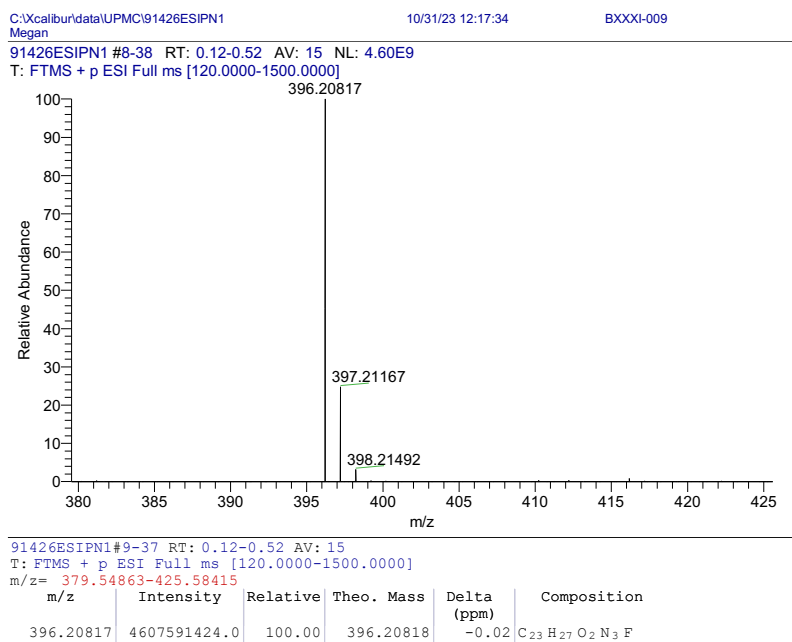
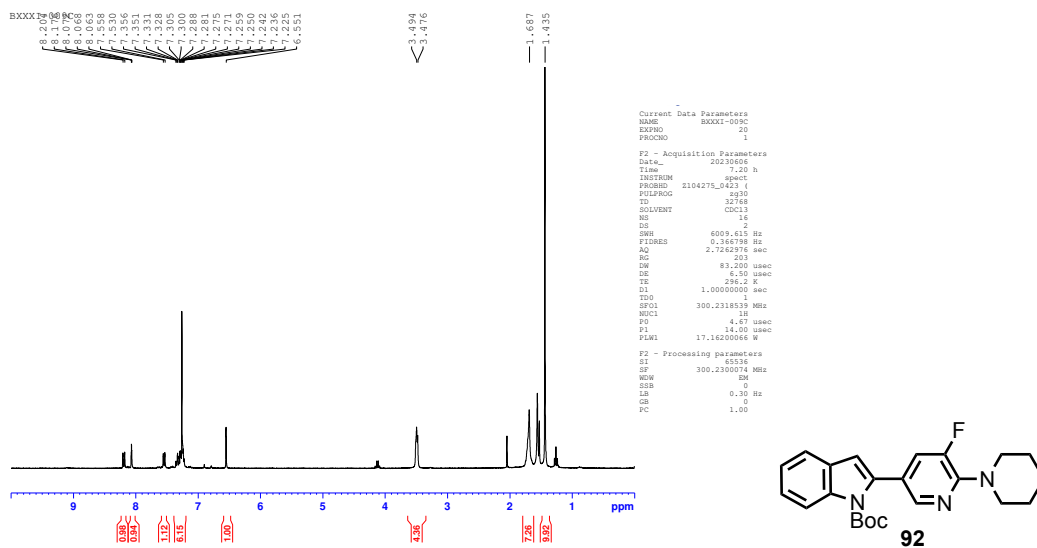


Figure S100. Compound **92** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

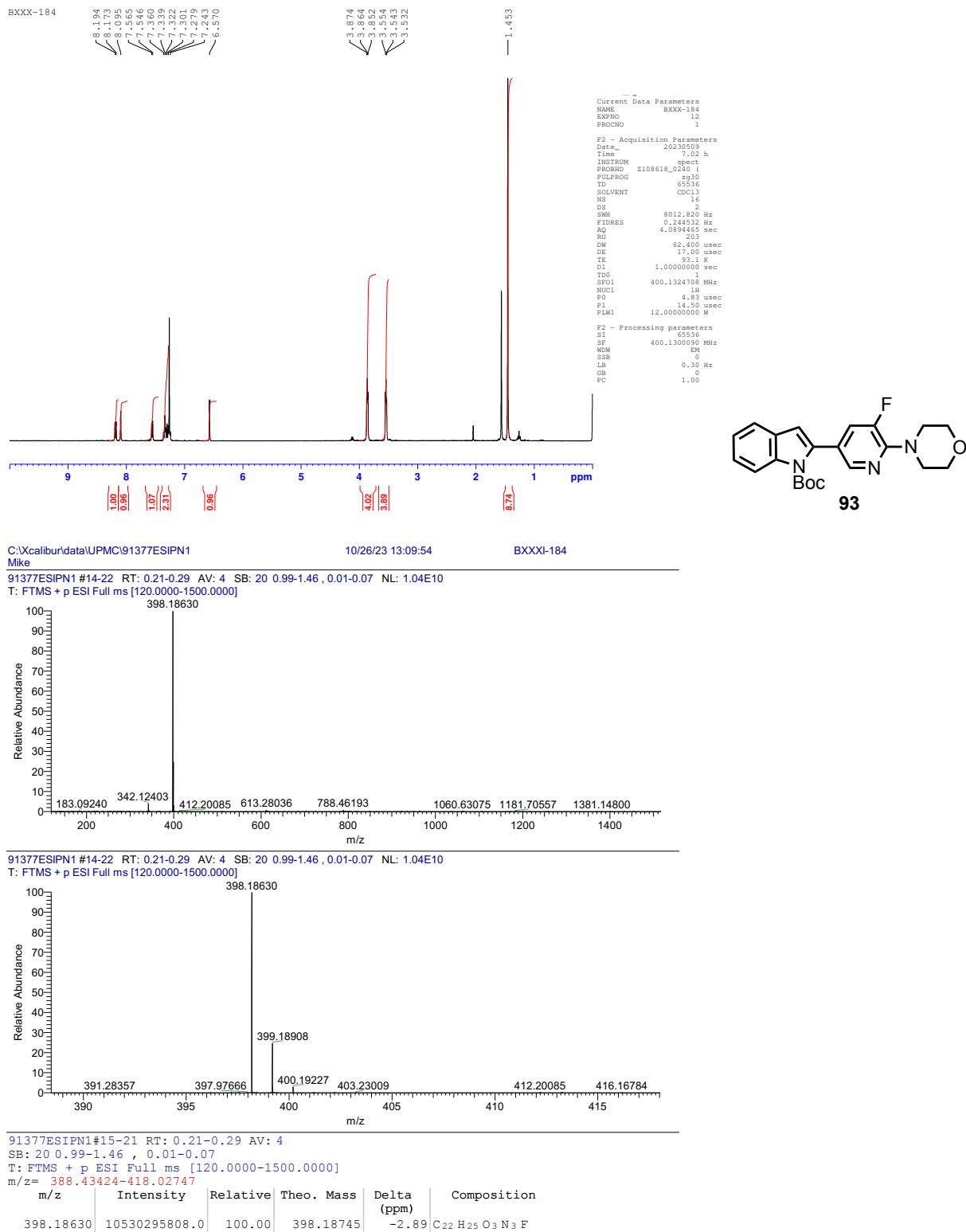


Figure S101. Compound **93** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

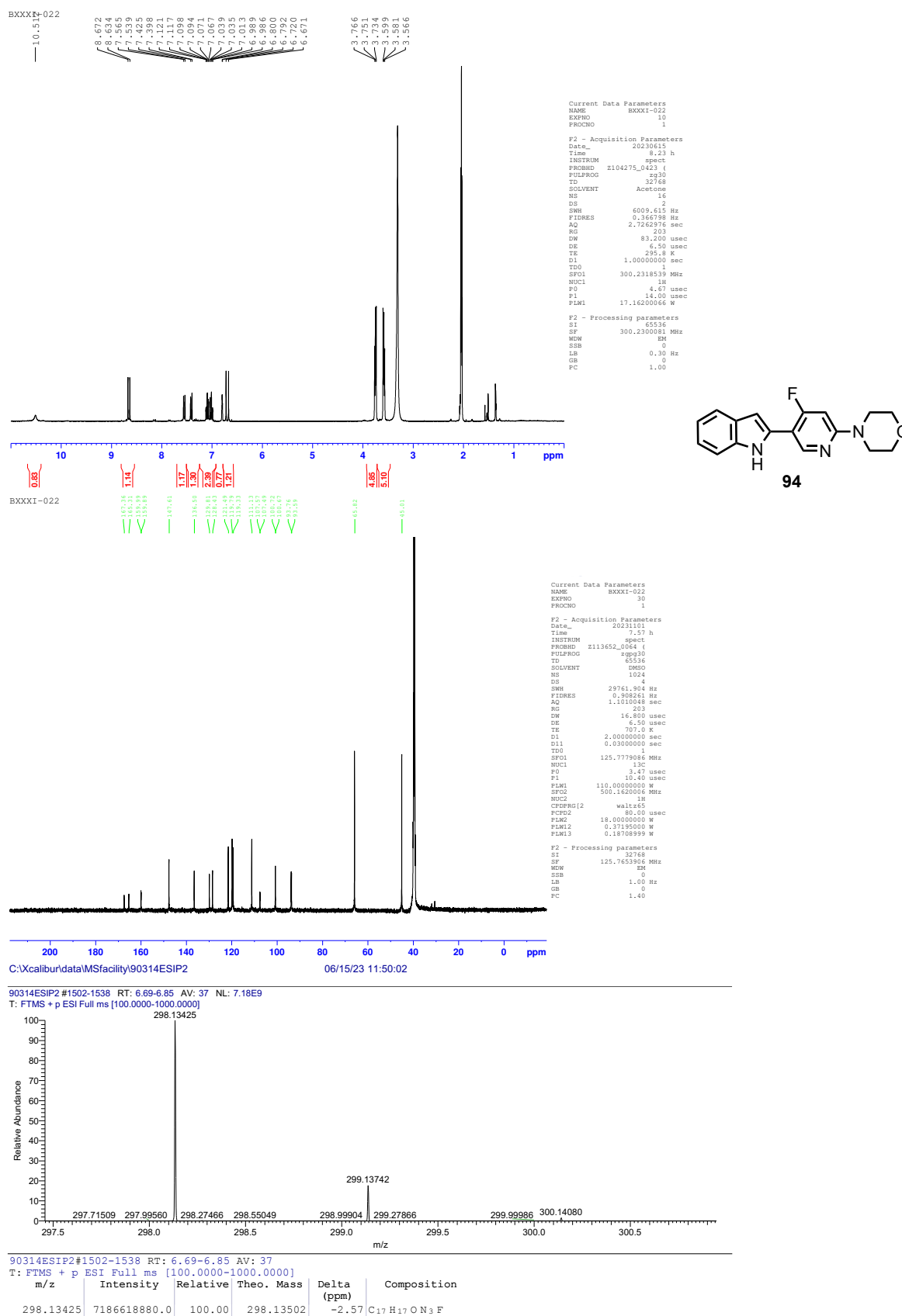
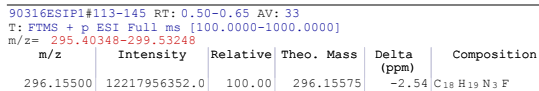
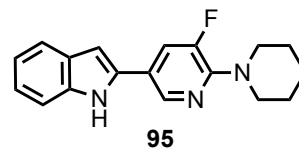
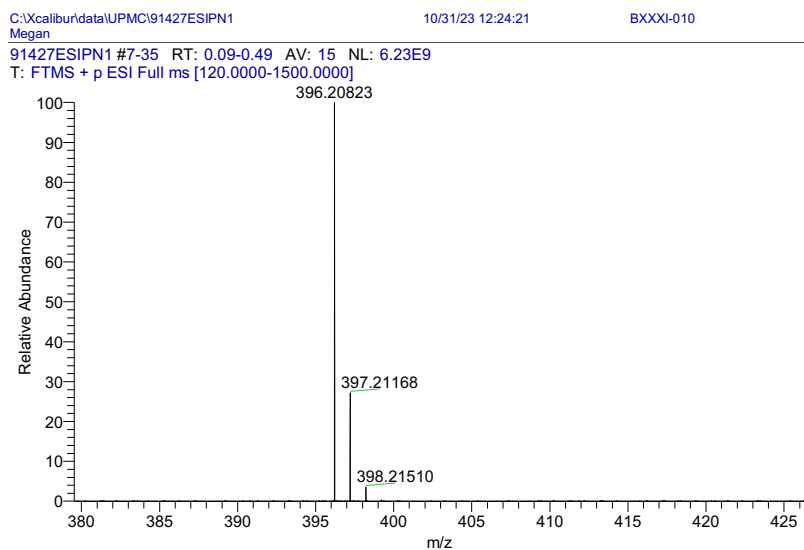
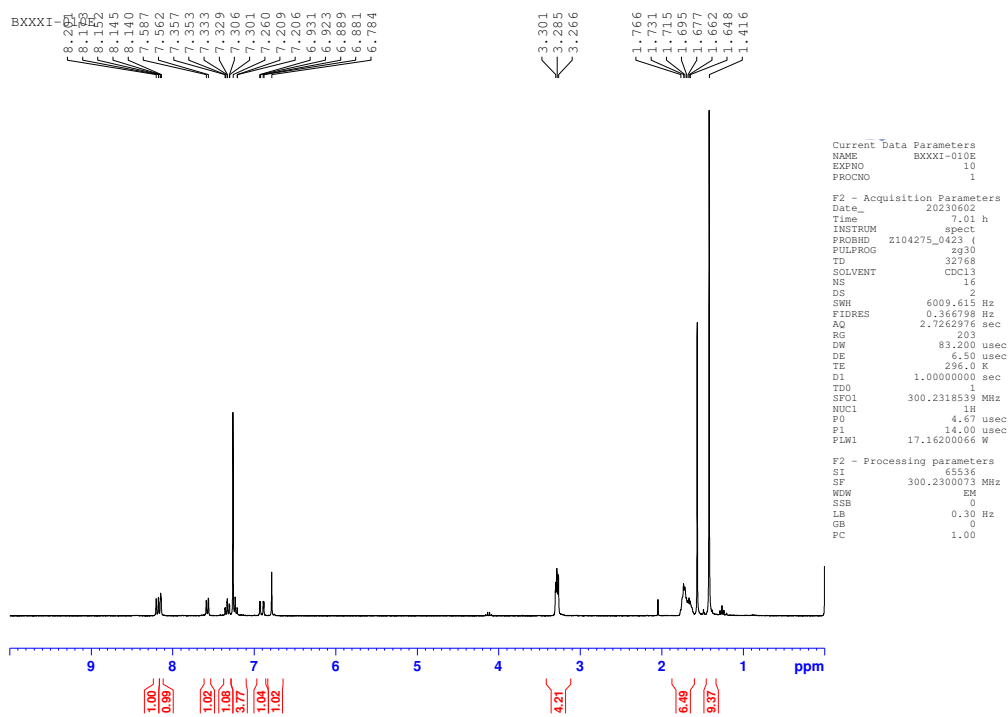


Figure S102. Compound **94** ^1H NMR spectrum (top), ^{13}C NMR spectrum (middle), high-resolution mass spectrum (bottom).

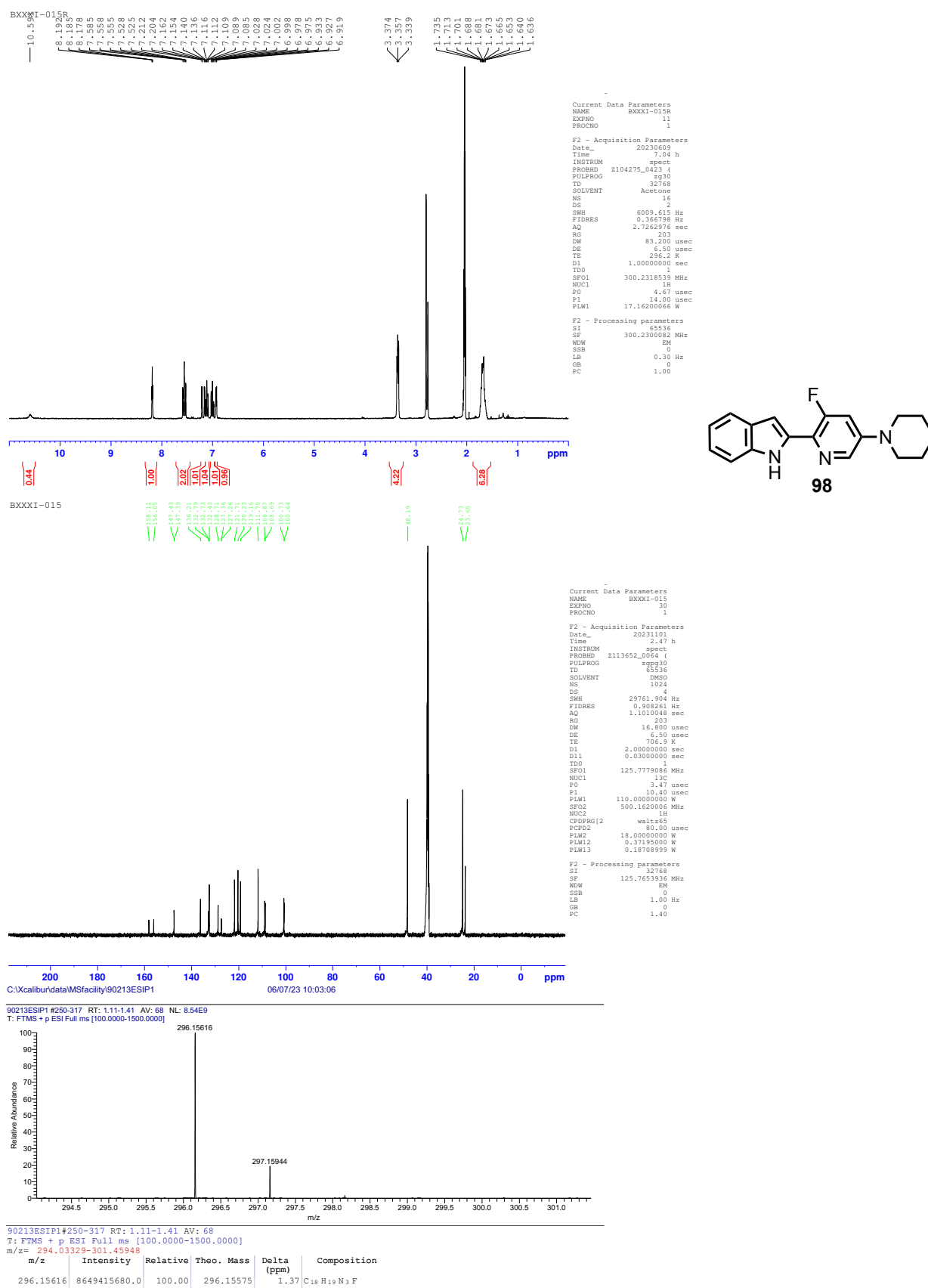


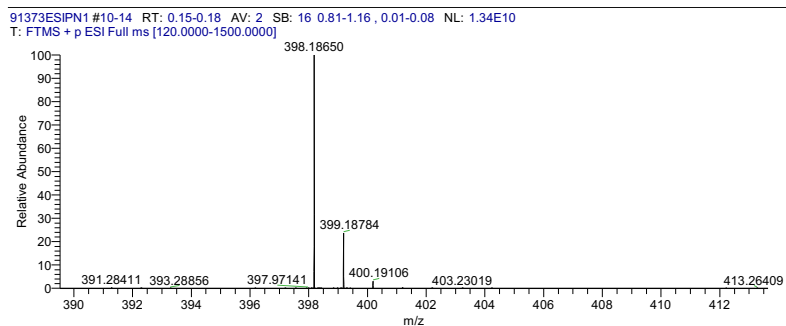
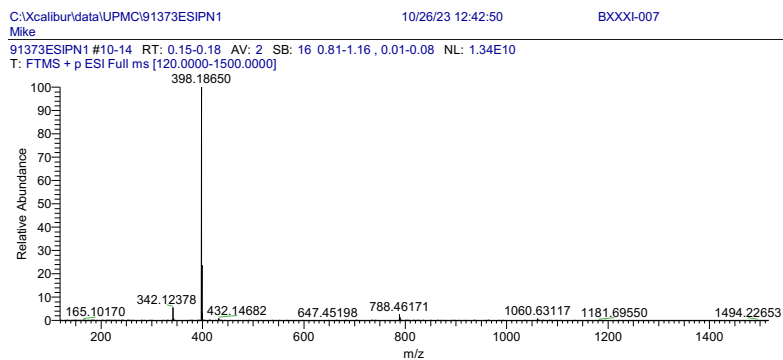
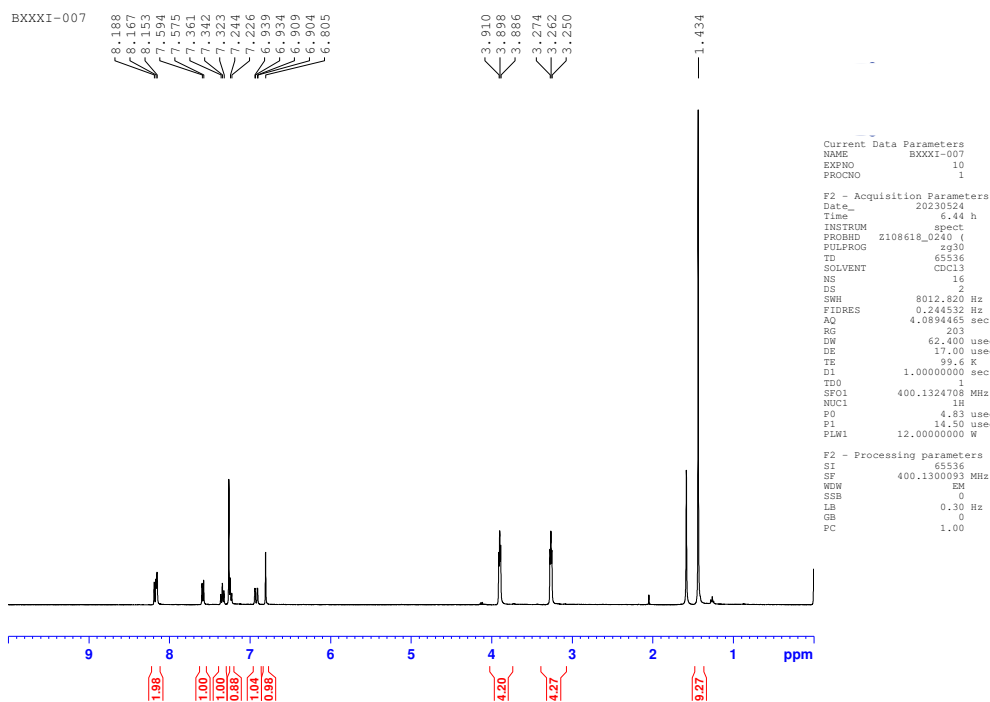


91427ESIPN1#7-35 RT: 0.09-0.49 AV: 15
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z= 379.52615-426.33063

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
396.20823	6236114432.0	100.00	396.20818	0.11	C ₂₃ H ₂₇ O ₂ N ₃ F

Figure S105. Compound **97** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).





91373ESIPN1#11-13 RT: 0.15-0.18 AV: 2
SB: 16 0.81-1.16, 0.01-0.08
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z= 389.52597-413.63861

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
398.18650	13625583616.0	100.00	398.18745	-2.38	C ₂₂ H ₂₅ O ₃ N ₃ F

Figure S107. Compound **99** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

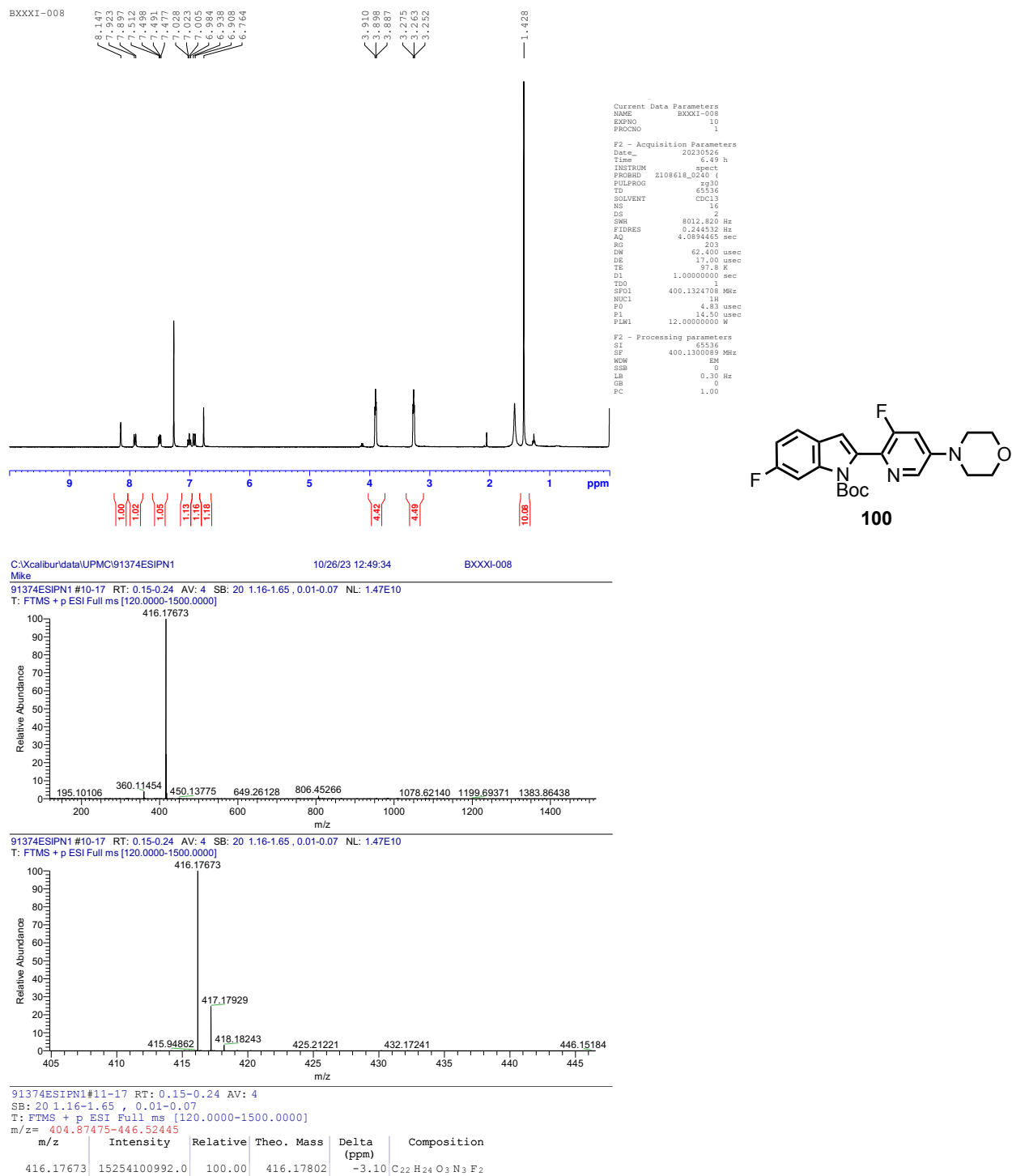


Figure S108. Compound **100** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

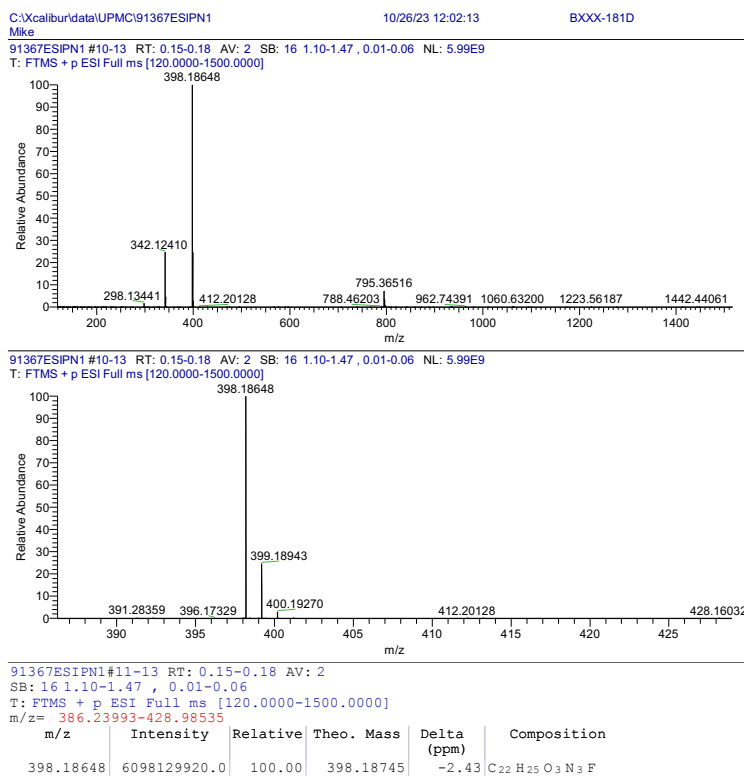
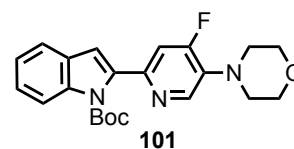
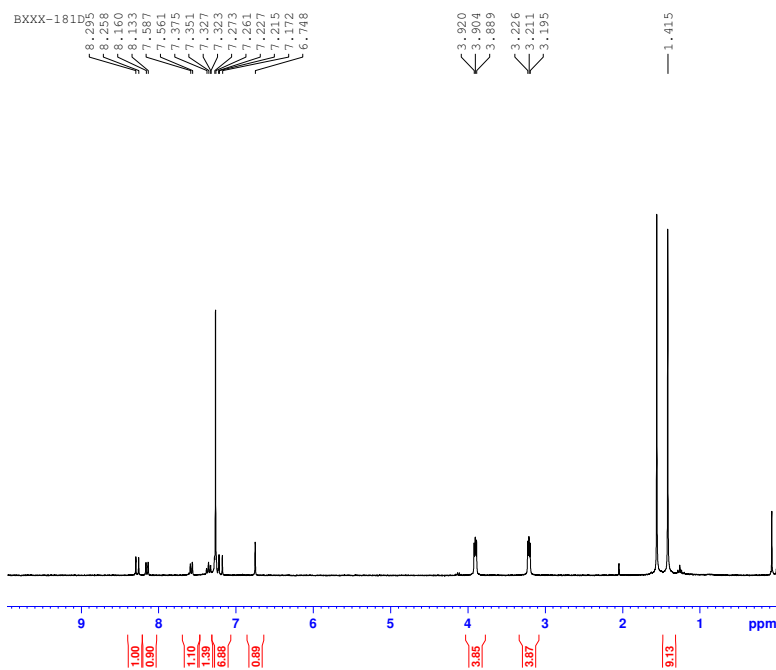


Figure S109. Compound **101** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

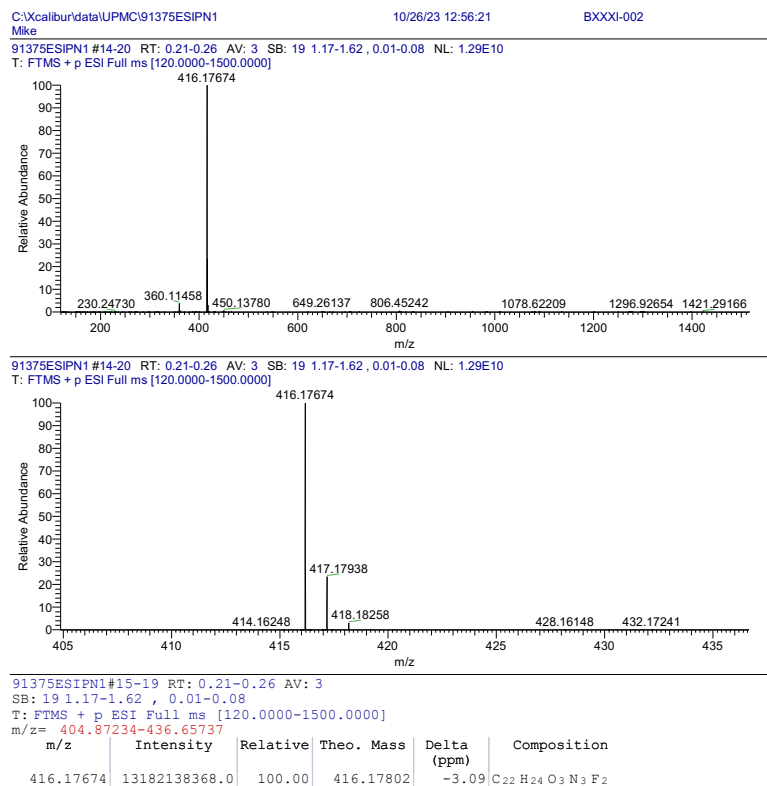
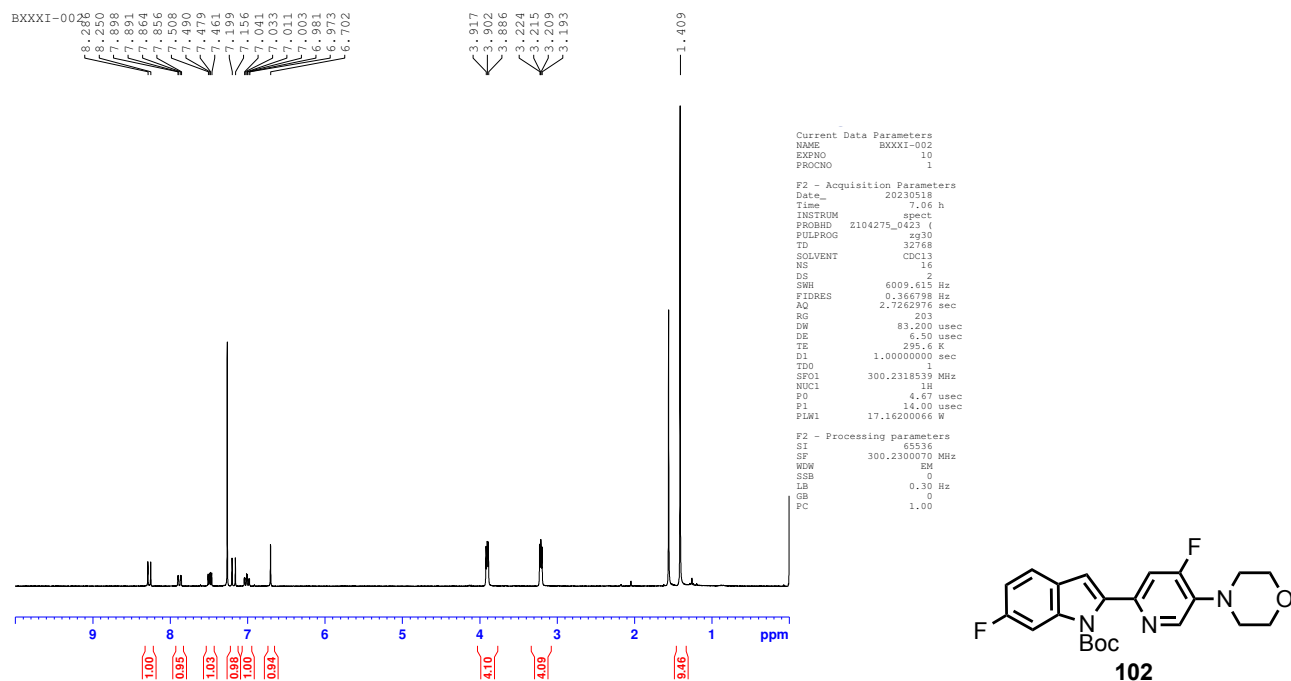
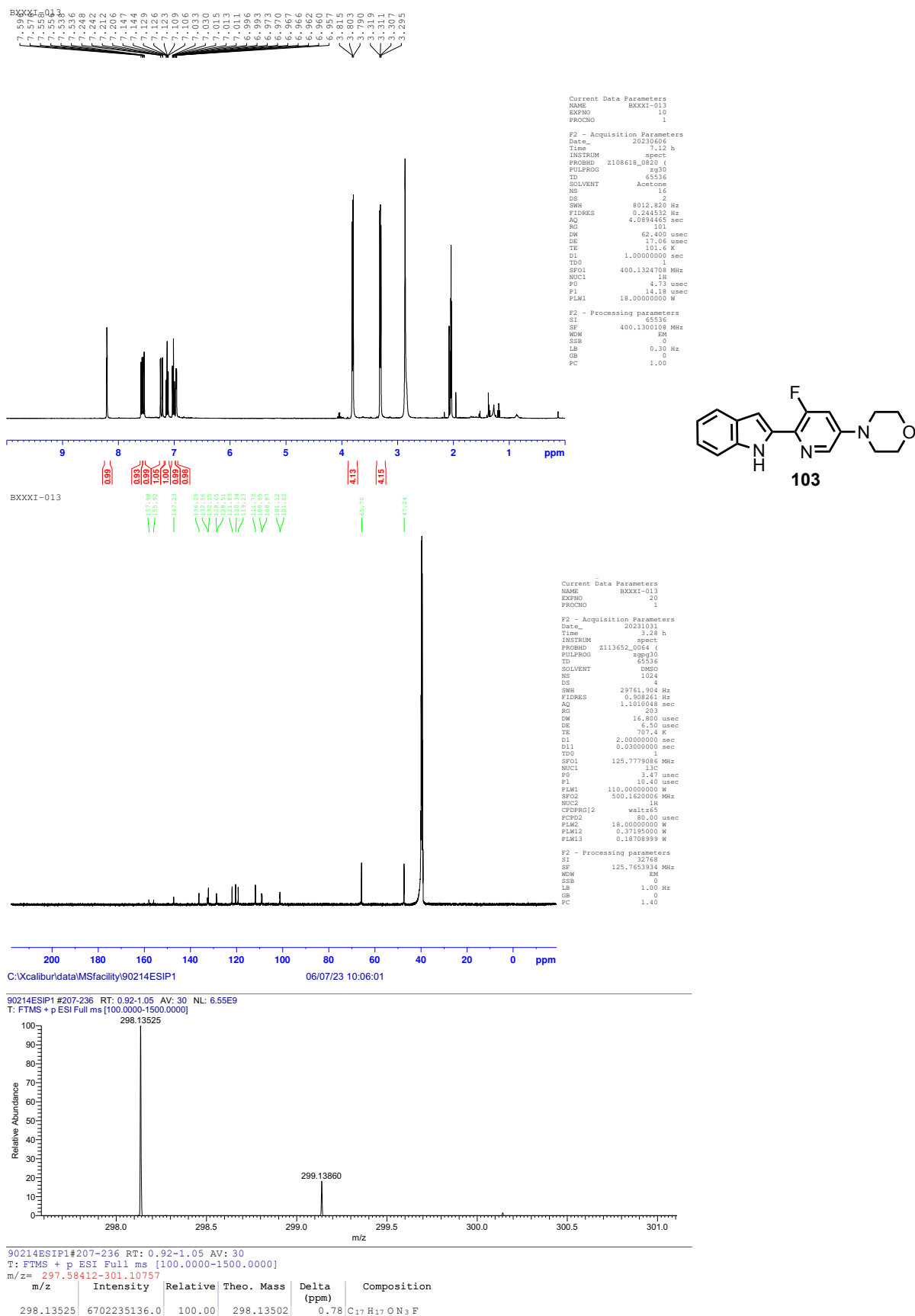
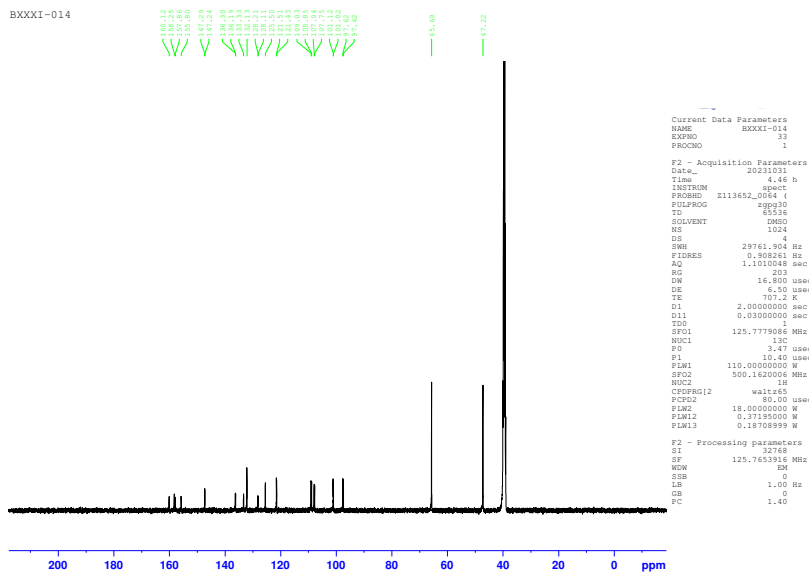
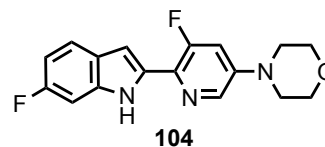
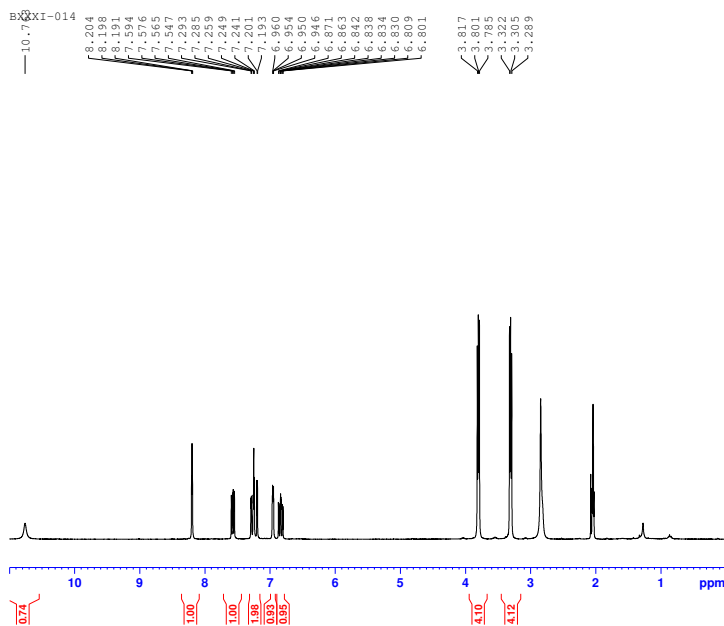


Figure S110. Compound **102** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

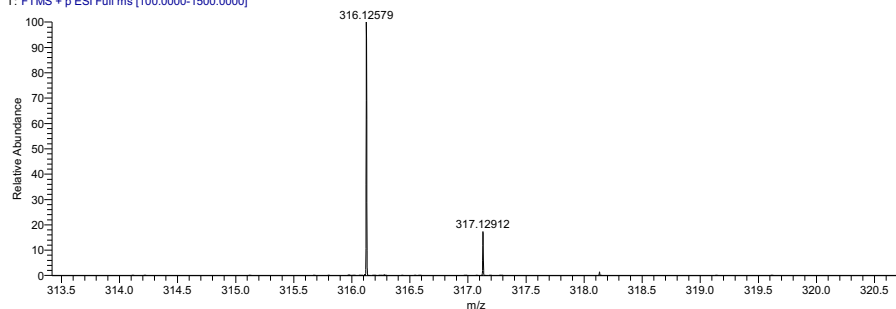




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06/07/23 10:09:37

90215ESI1#123-133 RT: 0.55-0.59 AV: 11 NL: 1.03E10
T: FTMS + p ESI Full ms [100.0000-1500.0000]



90215ESI1#123-133 RT: 0.55-0.59 AV: 11

T: FTMS + p ESI Full ms [100.0000-1500.0000]

m/z = 313.41787-320.72321

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
316.12579	10461192192.0	100.00	316.12560	0.63	C ₁₇ H ₁₆ O ₃ N ₃ F ₂

Figure S112. Compound **104** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), high-resolution mass spectrum (bottom).

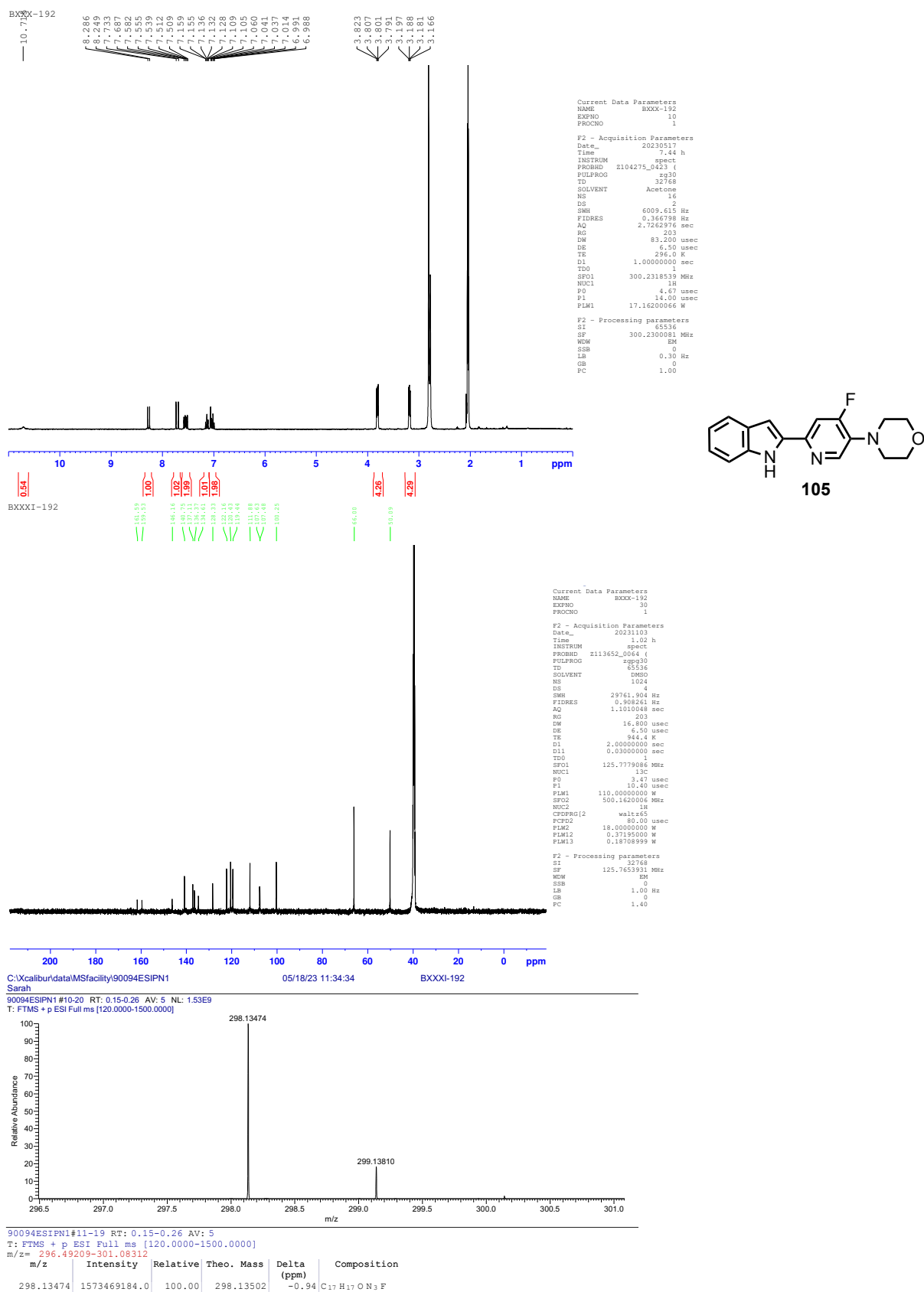
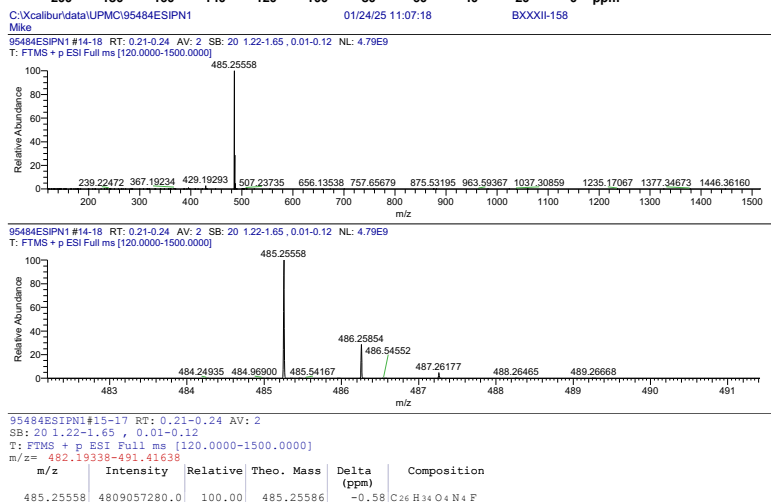


Figure S113. Compound **105** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), high-resolution mass spectrum (bottom).

CCOC(=O)C1CCN(C1)c2ncnc2C3=C(C=C4C=CC=CC=C4N3C(=O)OC(C)(C)C)C5=CC=CC=C6

107



S120

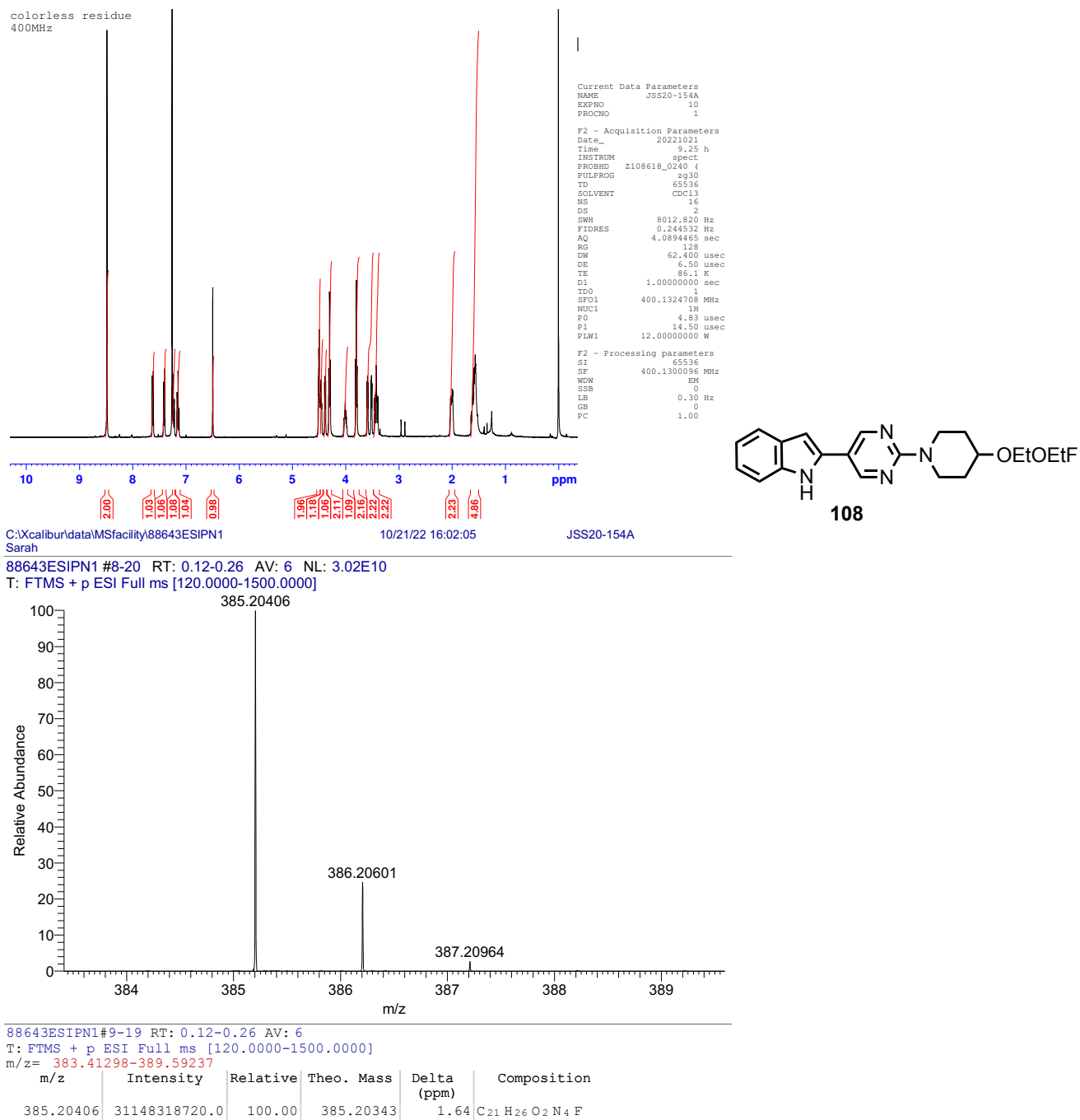
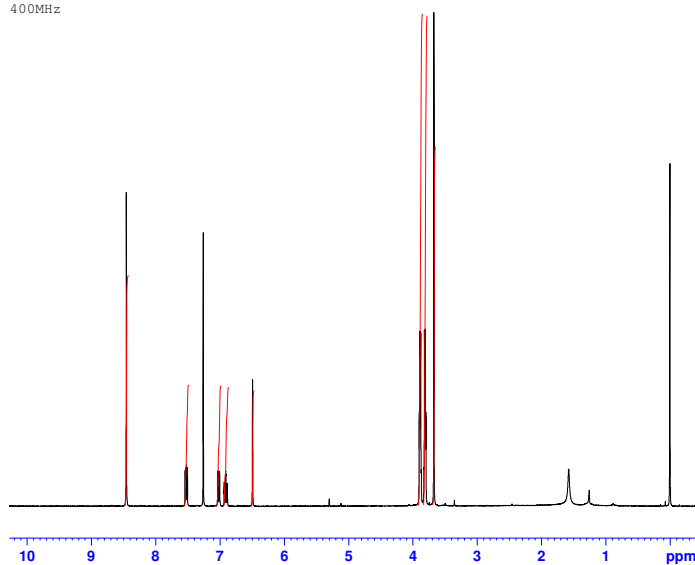


Figure S116. Compound **108** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

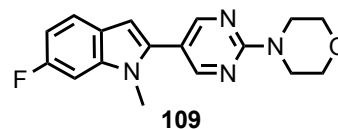
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EXPNO 10
PROCNO 1

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PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
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FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 144
DW 62.400 usec
DE 6.50 usec
TE 102.7 K
D1 1.00000000 sec
TD0 1
SFO1 400.1324708 MHz
NUC1 1H
PO 4.83 usec
PI 14.50 usec
PLW1 12.00000000 W

F2 - Processing parameters
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SF 400.1300096 MHz
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SSB 0
LB 0.30 Hz
GB 0
PC 1.00

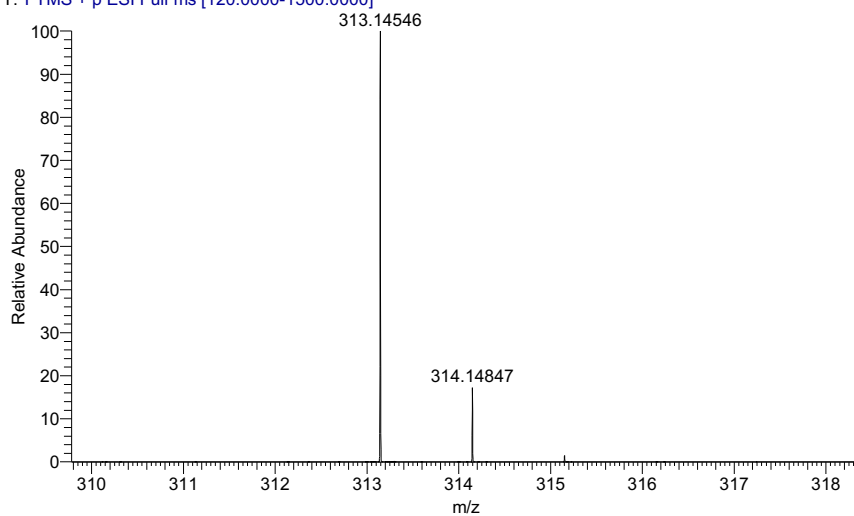


C:\Xcalibur\data\MSfacility\88181ESIPN1
Sarah

08/03/22 10:19:04

JSS20-090A

88181ESIPN1 #5-18 RT: 0.07-0.23 AV: 7 SB: 49 0.01-0.09 , 0.33-1.60 NL: 5.72E9
T: FTMS + p ESI Full ms [120.0000-1500.0000]



88181ESIPN1#5-17 RT: 0.07-0.23 AV: 7

SB: 49 0.01-0.09 , 0.33-1.60

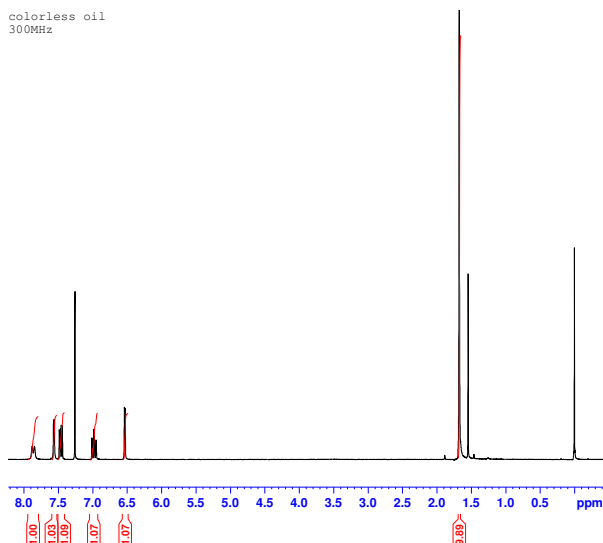
T: FTMS + p ESI Full ms [120.0000-1500.0000]

m/z= 309.78090-318.38191

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
313.14546	5724209152.0	100.00	313.14592	-1.47	C ₁₇ H ₁₈ ON ₄ F

Figure S117. Compound **109** ¹H NMR spectrum (top) and high-resolution mass spectrum (bottom).

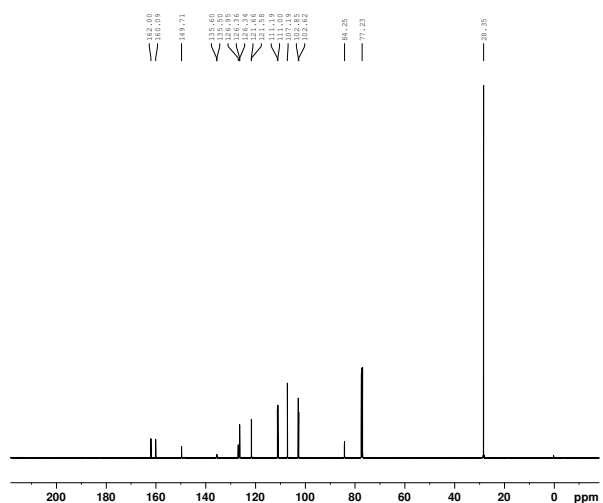
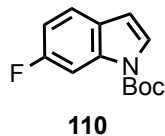
colorless oil
300MHz



Current Data Parameters
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EXPNO 10
PROCNO 1

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PULPROG zgpg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 6009.615 Hz
FIDRES 0.166796 Hz
AQ 2.1262976 sec
RG 181
DW 83.200 usec
DE 6.50 usec
TE 295.4 K
D1 1.00000000 sec
TD0 300.2318539 MHz
NUC1 1H
PQ 4.47 usec
P1 14.00 usec
PLW1 17.16200066 W

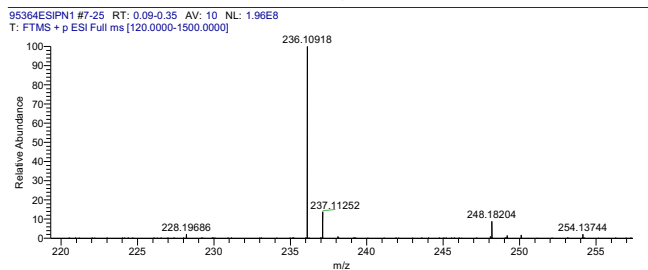
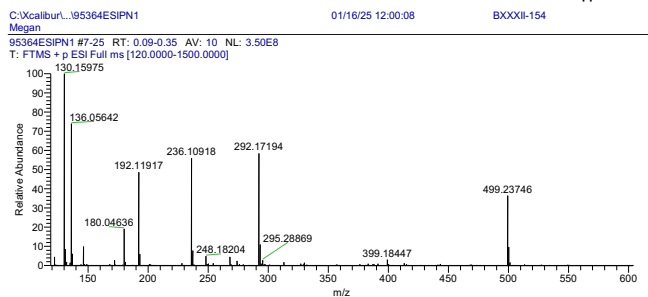
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WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



Current Data Parameters
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EXPNO 11
PROCNO 1

F2 - Acquisition Parameters
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Time 8:05 h
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PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 29761.904 Hz
FIDRES 0.909261 Hz
AQ 1.1010048 sec
RG 203
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DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 125.7779084 MHz
NUC1 13C
PQ 3.47 usec
P1 10.40 usec
PLW1 110.0000000 W
SP02 500.1620006 MHz
NUC2 1H
CPDPRG2 waltz165
PCPD2 80.00 usec
PLW2 18.0000000 W
PLW12 0.37195000 W
PLW13 0.18708999 W

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WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



95364ESIPN1 #7-25 RT: 0.09-0.35 AV: 10
T: FTMS + p ESI Full ms [120.0000-1500.0000]
m/z = 219.31316-257.40271

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	Composition
236.10918	196301616.0	100.00	236.10813	4.43	C ₁₃ H ₁₅ O ₂ NF

Figure S118. Compound **110** ¹H NMR spectrum (top), ¹³C NMR spectrum (middle), and high-resolution mass spectrum (bottom).