

- Supporting Information -

Catalyst-Free Site Selective Hydroxyalkylation of 5-phenylthiophen-2-amine with α -trifluoromethyl Ketones through Electrophilic Aromatic Substitution

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General Information

All reagents were purchased from commercial suppliers (Acros, Sigma Aldrich, Alfa Aeser and TCI) and were used without further purification. NMR spectra were recorded with a Bruker Avance 300 spectrometer (300 MHz and 75 MHz for ¹H and ¹³C NMR, respectively) and Bruker Avance 400 spectrometer (376.5 MHz for ¹⁹F). Chemical shifts (δ) and coupling constants (J) are given in ppm and Hz, respectively, using residual solvent signals as reference for the ¹H and ¹³C. The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, br s = broad signal, dd = doublet of doublets, dt = double of triplets, m = multiplet. High-resolution mass spectra (HRMS) were obtained by electrospray using a TOF analyzer Platform. IR spectra were obtained using a Jasco FT-IR 410 instrument as a thin film on NaCl disc as stated; only structurally important peaks ($\bar{\nu}$) are presented in cm^{-1} . Reactions were monitored with Merck Kieselgel 60F₂₅₄ precoated aluminum silica gel plates (0.25 mm thickness). Melting points were determined on a Stuart scientific SMP10 apparatus and are uncorrected. Flash chromatography was performed on a Grace Reveleris X2 using a 40 μm packed silica cartridge. HPLC analyses were obtained on the Waters Alliance 2795 using the following conditions: Thermo Hypersil C18 column (3 μm , 50 mm \times 2.1 mm), 20 °C column temperature, 0.2 mL/min flow rate, photodiodearray detection (210– 400 nm), mobile phase consistent of a gradient of water and acetonitrile (each containing 0.1% trifluoroacetic acid). UPLC analyses were obtained on the Waters Acquity H-Class using the following conditions: Waters Acquity BEH C18 column (1.7 μm , 50 \times 2.1 mm), 25 °C column temperature, 0.5 mL/min flow rate, photodiodearray detection (TUV – 214 nm), mobile phase consistent of a gradient of water and acetonitrile (each containing 0.1% of formic acid).

Spectra of compound 9 (^1H 300MHz, ^{13}C 75MHz, D₂O)

Figure S1 ^1H spectra of **9** in D₂O (singlet at 7.28 ppm; 300 MHz).

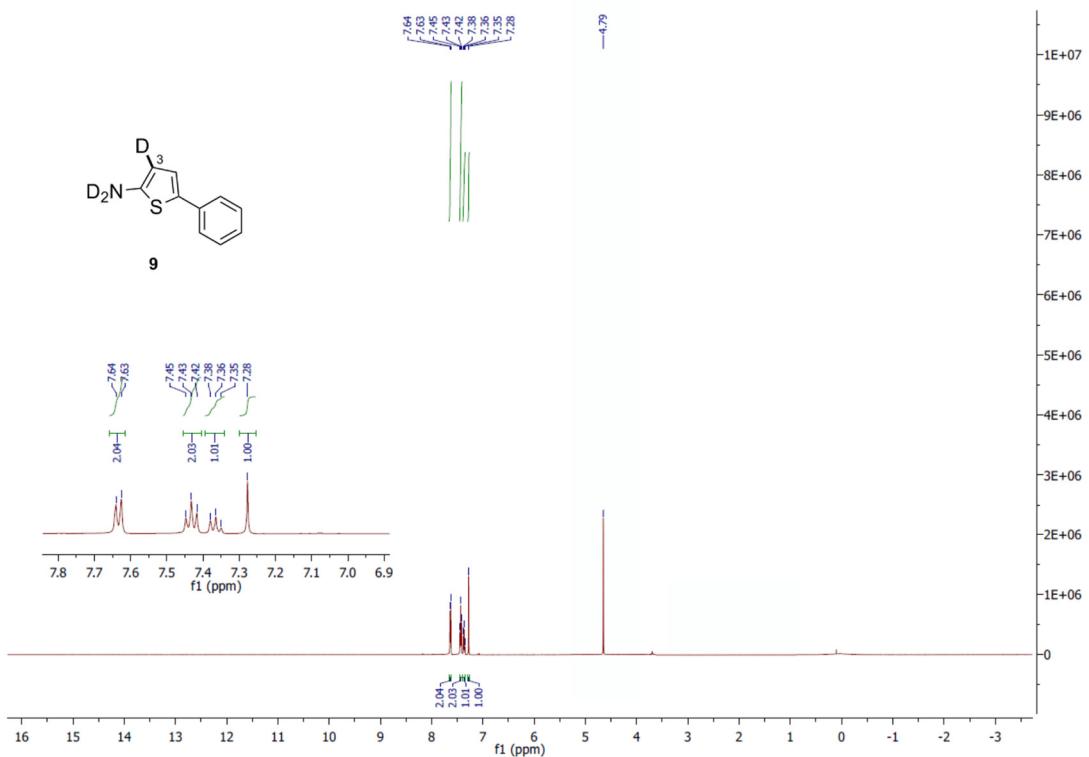
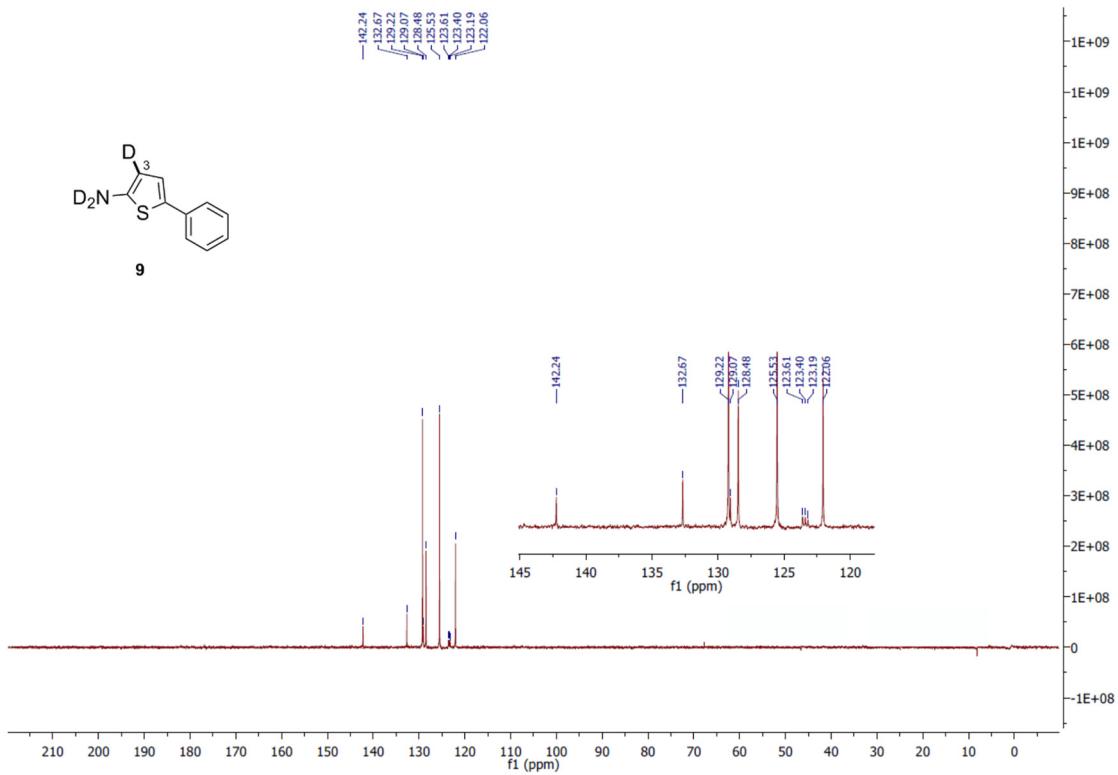
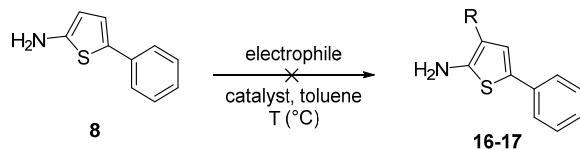


Figure. S2 ^{13}C spectra of **9** in D₂O (triplet at 123.40 ppm; 75 MHz).



Condition optimization on the synthesis of trifluorohydroxyalkyl-5-phenylthiophen-2-amine

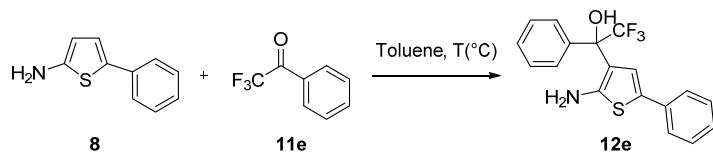
Table S1 Optimization attempts for the synthesis of 16-17



entry	Electrophile	catalyst	T(°C)	Yield ^b (%)
1	Acetophenone	None	120	/
2	Acetophenone	AlCl ₃ (0.1 eq)	120	/
3	Acetophenone	Sc(OTf) ₃ (0.1 eq)	120	/
4	p-anisaldehyde	None	120	/
5	p-anisaldehyde	AlCl ₃ (0.1 eq)	120	/
6	p-anisaldehyde	Sc(OTf) ₃ (0.1 eq)	120	/

^aGeneral conditions: **8** (0.57 mmol), electrophile (0.57 mmol), solvent (2mL), stirred at 120°C for 24 hours under argon atmosphere in round bottom flask. ^bOnly starting materials are recovered.

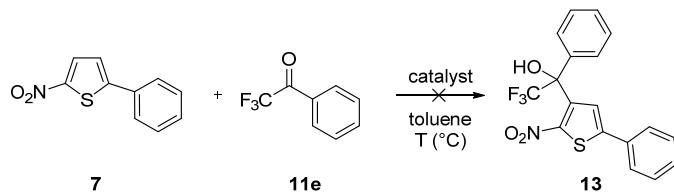
Table S2 Optimization studies for the synthesis of 12e



Entry	11e quantity	T(°C)	Yield (%) ^b
1 ^a	1 eq.	100	70%
2 ^a	1 eq.	120	83%
3 ^a	1 eq.	140	47%
4 ^a	1.5 eq.	120	82%
5 ^a	2 eq.	120	81%

^aGeneral conditions: **8** (0.57 mmol), electrophile **11e** (0.57 mmol), Toluene (2mL), stirred at 120°C for 4 hours under argon atmosphere in round bottom flask. ^bYields obtained after purification on flash chromatography.

Table S3 Optimization attempts for the synthesis of 13



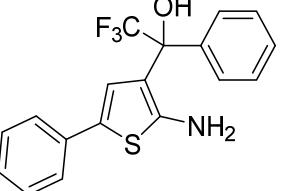
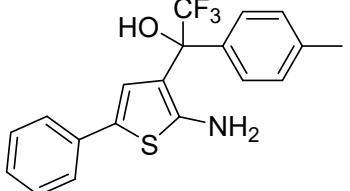
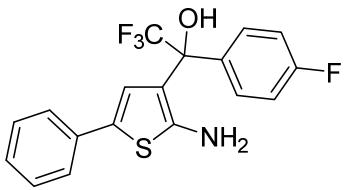
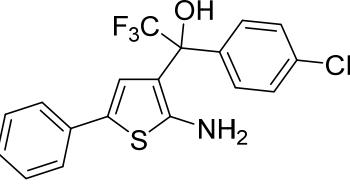
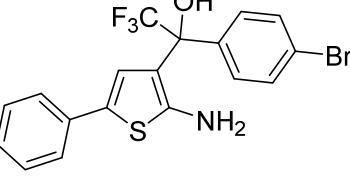
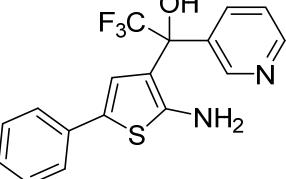
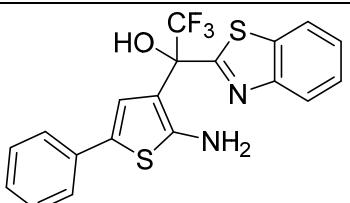
entry	catalyst	T(°C)	Yield (%)
1	None	120	/
2	AlCl ₃ (0.1 eq)	120	/
3	Sc(OTf) ₃ (0.1 eq)	120	/

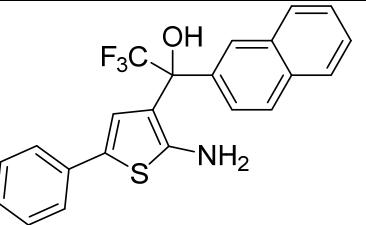
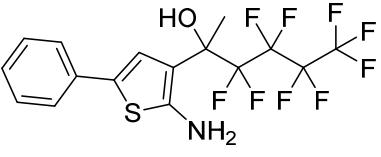
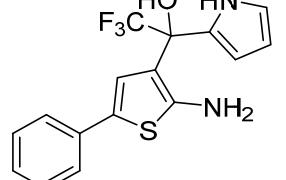
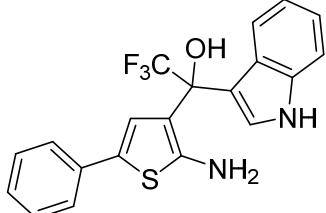
^aGeneral conditions: **7** (0.57 mmol), electrophile **11e** (0.57 mmol), toluene (2mL), stirred at 120°C for 24 hours under argon atmosphere in round bottom flask.

Kinetics studies

Table S4 Kinetics considerations following HPLC spectra

#	Structure	HPLC Yield ^a (%)	Starting material 8 remaining ^a (%)	Byproducts ^a (%)	Reactional time (h)
12a		92	0	8	3.5
12b		84	0	16	3
12c		80	7	13	3.5
12d		79	5	16	4.5

12e		93	0	7	3
12f		80	1	19	4
12g		85	1	14	2.5
12h		85	0	15	3
12i		86	0	14	3.5
12j		97	0	3	2
12k		84	0	16	3

12l		78	0	22	5
12m		0	/	/	/
12n		0	/	/	/
12o		0	/	/	/

^aDetermination realized *via* integration of peaks with DAD HPLC results.

X-ray crystallographic supporting data

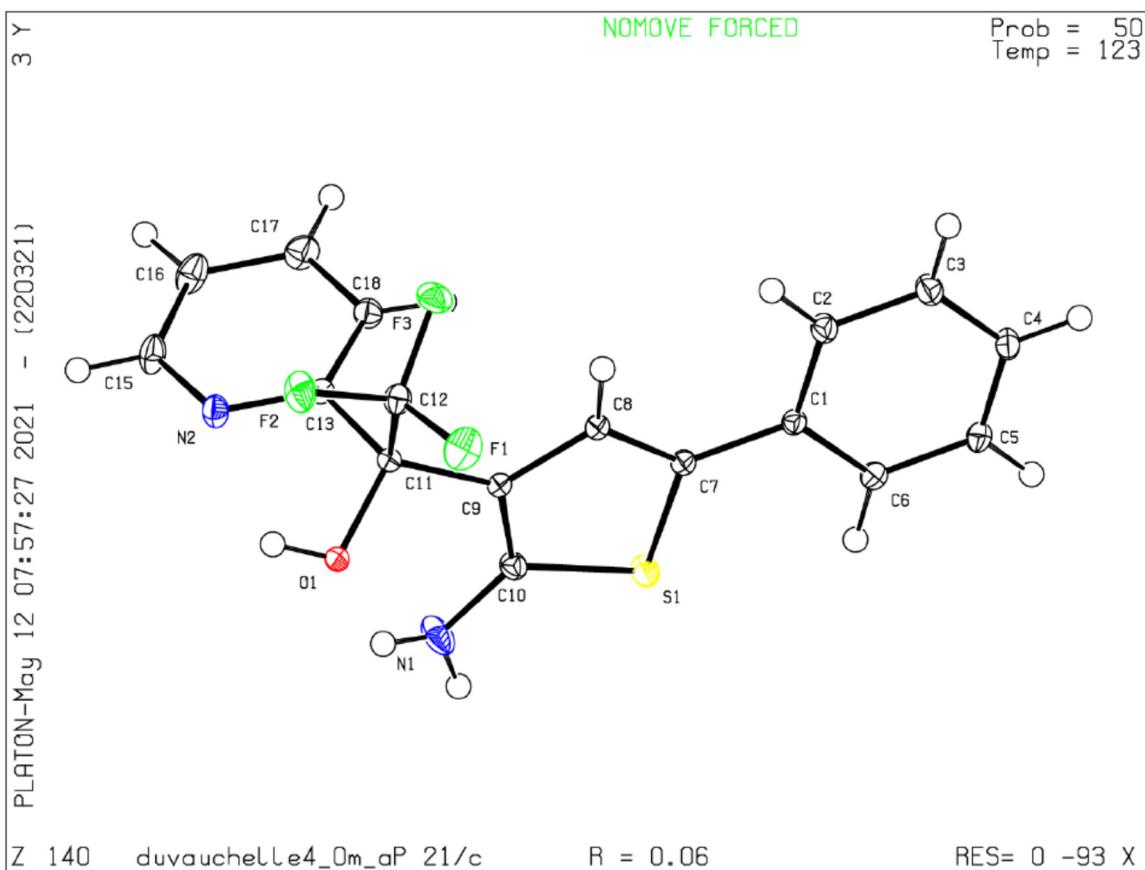


Figure S3 Crystal structure of compounds **12j**

The X-ray single crystal data of **12j**, were collected with monochromated Mo-K α radiation (0.71073 Å) on a Bruker Apex3 CCD Bruker diffractometer. Intensity data were collected at 123 K using θ -scan method. Data reduction of each compound was carried out using the Bruker SAINT software. Multi-scan absorption correction was applied to all intensity data using the SADABS 2016/2 program.² The structures were solved by a combination of direct methods with SHELXT-2014/5 and refined with full-matrix least-squares based on F^2 using SHELXL2018/3.³ The hydrogen atoms were treated by a mixture of independent and constrained refinement. Molecular and the crystal packing diagrams were drawn with Mercury software. Bruker SHELXTL has been used to prepare material for publication and realize molecular graphics. All of the crystal data are described in supporting information. The crystal structures were deposited with the Cambridge Crystallographic Database Centre (CCDC) and given the number CCDC 2083160.

A colorless plate-like specimen of compound **12j** ($C_{17}H_{13}F_3N_2OS$) with approximate dimensions 0.17 x 0.12 x 0.03 mm has been used. **12j** crystallized in the monoclinic crystal system using the space group $P\ 2_{1/c}$. Short contacts are apparent between two molecules in the solid state between sulfur atom of the thiophenyl and C₁ [C₁ ... S₁ 3.387 Å], F₃ atom of the trifluoride group and H₁₈ [C₁₂-F₃ ... H₁₈ 2.551 Å 143°] and between oxygen from the hydroxyl group and aromatics hydrogens, carbon and nitrogen [C₅-H₅ ... O₁ 2.495 Å 160°; C₁₃-H₁₃ ... O₁ 2.715 Å 146°; C₁₅-H₁₅ ... O₁ 2.691 Å 108°; O₁ ... N₂ 2.237 Å] (Fig. S4AB).

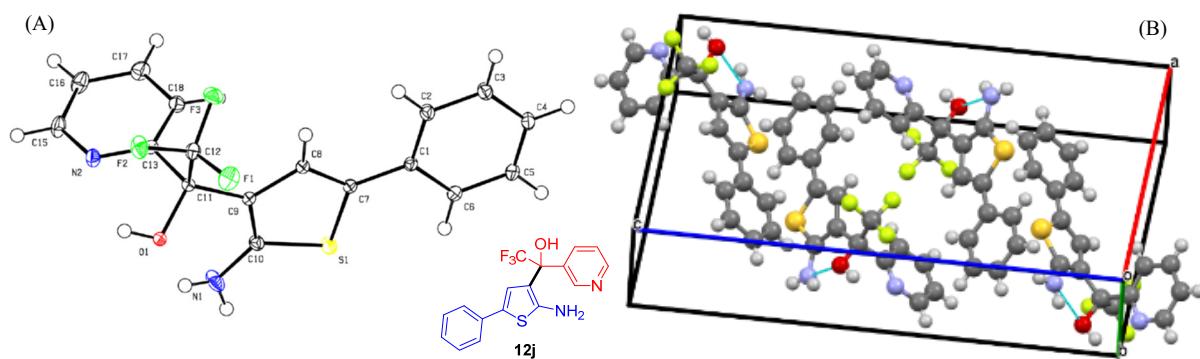


Figure S4 (A) XP diagram of compound **12j** with atomic numbering scheme; (B) Expansion of the packing diagram of compound **12j** within the crystal mesh through intra and intermolecular hydrogen bonds

Table S5 Crystal data and structure refinement details for **12j**

Identification code	12j
Formula	C ₁₇ H ₁₃ F ₃ N ₂ OS
M.W. (g.mol ⁻¹)	350.3592
Crystal system, space group	Monoclinic, P21/c
<i>d</i> _{calcd} (g.cm ⁻³)	1.525
Temperature (K)	123
<i>a</i> , <i>b</i> , <i>c</i> (Å)	10.5726(6), 6.8807(3), 21.0661(11)
α (°)	90
β (°)	95.232(2)
γ (°)	90
V (Å ³)	1526.11 (14)
Z	4
Radiation type	Mo <i>K</i> α
<i>μ</i> (mm ⁻¹)	0.25
Crystal size (mm)	0.17 × 0.12 × 0.03
<i>R</i> _{int}	0.054
(sin θ/λ)max (Å ⁻¹)	0.913
<i>R</i> [<i>F</i> 2 > 2σ(<i>F</i> 2)], <i>wR</i> (<i>F</i> 2), <i>S</i>	0.056, 0.125, 1.10
Δ <i>ρ</i> _{max} , Δ <i>ρ</i> _{min} (e Å ⁻³)	0.69, -0.43
Packing coefficient	0.707
F0000	720
CCDC number	2083160

Table S6 Bond lengths for **12j** (Å).

S1-C10	1.461(1)	C7-C1	1.461(1)
S1-C7	1.405(1)	C1-C2	1.405(1)
F3-C12	1.403(1)	C1-C6	1.403(1)
F1-C12	0.95	C5-H5	0.95
F2-C12	1.389(1)	C5-C6	1.389(1)
O1-C11	0.95	C18-H18	0.95
O1-H1C	1.393(1)	C18-C13	1.393(1)
N2-C13	1.387(1)	C18-C17	1.387(1)
N2-C15	1.537(1)	C13-C11	1.537(1)
N1-C10	1.543(1)	C11-C12	1.543(1)
N1-H1A	0.95	C2-H2	0.95
N1-H1B	0.95	C2-C3	1.389(1)
C9-C8	1.389(1)	C3-H3	0.95
C9-C10	0.95	C6-H6	0.95
C9-C11	0.95	C17-H17	0.95
C8-H8	0.95	C17-C16	1.387(2)
C8-C7	1.387(2)	C15-H15	0.95
C4-H4	0.95	C15-C16	1.385(2)
C4-C5	1.385(2)	C16-H16	0.95
C4-C3	0.95		

Table S7 Bond angles for **12j** (°).

C10-S1-C7	92.33(5)	C18-C13-C11	121.60(8)
C11-O1-H1C	106(1)	O1-C11-C9	108.21(7)
C13-N2-C15	117.57(9)	O1-C11-C13	110.80(7)
C10-N1-H1A	114(1)	O1-C11-C12	106.00(7)
C10-N1-H1B	119(1)	C9-C11-C13	111.65(7)
H1A-N1-H1B	120(2)	C9-C11-C12	111.83(7)
C8-C9-C10	111.73(8)	C13-C11-C12	108.21(7)
C8-C9-C11	126.86(8)	C1-C2-H2	119.66
C10-C9-C11	121.22(8)	C1-C2-C3	120.68(9)
C9-C8-H8	122.88	H2-C2-C3	119.7
C9-C8-C7	114.24(8)	C4-C3-C2	120.62(9)
H8-C8-C7	122.88	C4-C3-H3	119.7
H4-C4-C5	120.4	C2-C3-H3	119.7
H4-C4-C3	120.4	F3-C12-F1	107.14(8)
C5-C4-C3	119.22(9)	F3-C12-F2	106.78(8)
S1-C10-N1	119.66(8)	F3-C12-C11	112.32(8)
S1-C10-C9	111.51(7)	F1-C12-F2	107.65(8)
N1-C10-C9	128.79(9)	F1-C12-C11	112.38(8)
S1-C7-C8	110.18(6)	F2-C12-C11	110.28(8)
S1-C7-C1	120.12(6)	C1-C6-C5	121.11(9)
C8-C7-C1	129.70(8)	C1-C6-H6	119.4
C7-C1-C2	120.98(8)	C5-C6-H6	119.4
C7-C1-C6	121.05(8)	C18-C17-H17	120.5
C2-C1-C6	117.97(8)	C18-C17-C16	118.9(1)
C4-C5-H5	119.8	H17-C17-C16	120.5
C4-C5-C6	120.39(9)	N2-C15-H15	118.3
H5-C5-C6	119.8	N2-C15-C16	123.3(1)
H18-C18-C13	120.67	H15-C15-C16	118.4
H18-C18-C17	120.7	C17-C16-C15	118.5(1)
C13-C18-C17	118.64(9)	C17-C16-H16	120.8
N2-C13-C18	123.02(8)	C15-C16-H16	120.8
N2-C13-C11	115.37(8)		

Table S8 Torsion angles for **12j** (°).

C7-S1-C10-N1	177.08(9)	C7-C1-C2-C3	-179.71(9)
C7-S1-C10-C9	-0.98(8)	C6-C1-C2-H2	-179.63
C10-S1-C7-C8	1.03(7)	C6-C1-C2-C3	0.4(1)
C10-S1-C7-C1	-178.40(7)	C7-C1-C6-C5	179.72(9)
H1C-O1-C11-C9	-167(1)	C7-C1-C6-H6	-0.3
H1C-O1-C11-C13	-44(1)	C2-C1-C6-C5	-0.4(1)
H1C-O1-C11-C12	73(1)	C2-C1-C6-H6	179.65
C15-N2-C13-C18	2.0(1)	C4-C5-C6-C1	0.4(2)
C15-N2-C13-C11	-178.87(8)	C4-C5-C6-H6	-179.7
C13-N2-C15-H15	177.02	H5-C5-C6-C1	-179.65
C13-N2-C15-C16	-3.0(2)	H5-C5-C6-H6	0.3
H1A-N1-C10-S1	160(1)	H18-C18-C13-N2	-179.6
H1A-N1-C10-C9	-23(1)	H18-C18-C13-C11	1.3
H1B-N1-C10-S1	9(2)	C17-C18-C13-N2	0.4(1)
H1B-N1-C10-C9	-174(2)	C17-C18-C13-C11	-178.71(9)
C10-C9-C8-H8	-179.87	H18-C18-C17-H17	-1.9
C10-C9-C8-C7	0.1(1)	H18-C18-C17-C16	178.1
C11-C9-C8-H8	5.2	C13-C18-C17-H17	178.1
C11-C9-C8-C7	-174.79(8)	C13-C18-C17-C16	-1.8(2)
C8-C9-C10-S1	0.7(1)	N2-C13-C11-O1	25.3(1)
C8-C9-C10-N1	-177.2(1)	N2-C13-C11-C9	145.98(8)
C11-C9-C10-S1	175.91(7)	N2-C13-C11-C12	-90.52(9)
C11-C9-C10-N1	-1.9(2)	C18-C13-C11-O1	-155.56(8)
C8-C9-C11-O1	-142.52(9)	C18-C13-C11-C9	-34.9(1)
C8-C9-C11-C13	95.3(1)	C18-C13-C11-C12	88.6(1)
C8-C9-C11-C12	-26.1(1)	O1-C11-C12-F3	-172.68(7)
C10-C9-C11-O1	43.0(1)	O1-C11-C12-F1	66.4(1)
C10-C9-C11-C13	-79.2(1)	O1-C11-C12-F2	-53.7(1)
C10-C9-C11-C12	159.40(8)	C9-C11-C12-F3	69.6(1)
C9-C8-C7-S1	-0.8(1)	C9-C11-C12-F1	-51.3(1)
C9-C8-C7-C1	178.52(9)	C9-C11-C12-F2	-171.42(8)
H8-C8-C7-S1	179.15	C13-C11-C12-F3	-53.8(1)
H8-C8-C7-C1	-1.5	C13-C11-C12-F1	-174.69(8)
H4-C4-C5-H5	-0.3	C13-C11-C12-F2	65.2(1)
H4-C4-C5-C6	179.7	C1-C2-C3-C4	-0.4(2)
C3-C4-C5-H5	179.7	C1-C2-C3-H3	179.62
C3-C4-C5-C6	-0.4(2)	H2-C2-C3-C4	179.6
H4-C4-C3-C2	-179.6	H2-C2-C3-H3	-0.4
H4-C4-C3-H3	0.3	C18-C17-C16-C15	0.9(2)
C5-C4-C3-C2	0.4(2)	C18-C17-C16-H16	-179.1
C5-C4-C3-H3	-179.6	H17-C17-C16-C15	-179
S1-C7-C1-C2	173.72(7)	H17-C17-C16-H16	0.9

S1-C7-C1-C6	-6.4(1)	N2-C15-C16-C17	1.5(2)
C8-C7-C1-C2	-5.6(1)	N2-C15-C16-H16	-178.5
C8-C7-C1-C6	174.33(9)	H15-C15-C16-C17	-178.5
C7-C1-C2-H2	0.3	H15-C15-C16-H16	1.5

Table S9 Hydrogen bond distances (\AA) and angles for **12j** ($^{\circ}$).

	Donor-H	Acceptor-H	Donor-Acceptor	Angle
N1-H1A…O1 ^a	0.843	2.187	2.800	129
O1-H1C…N2 ^b	0.830	2.237	2.899	137

^aintramolecular interaction

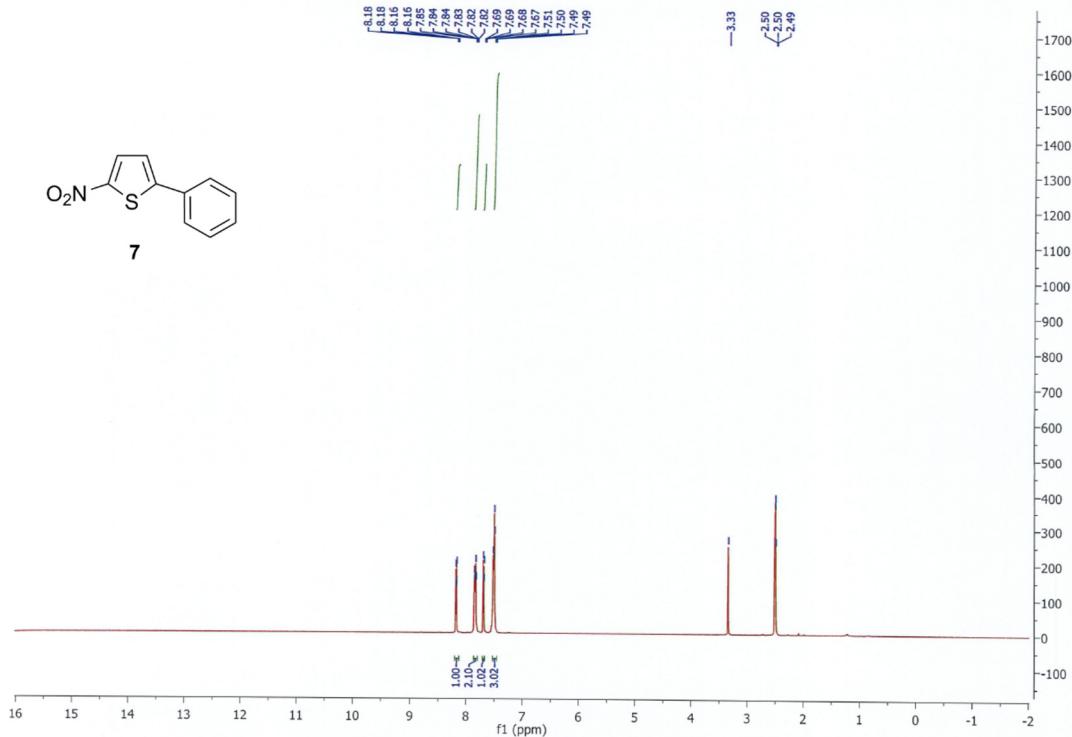
^bintermolecular interaction

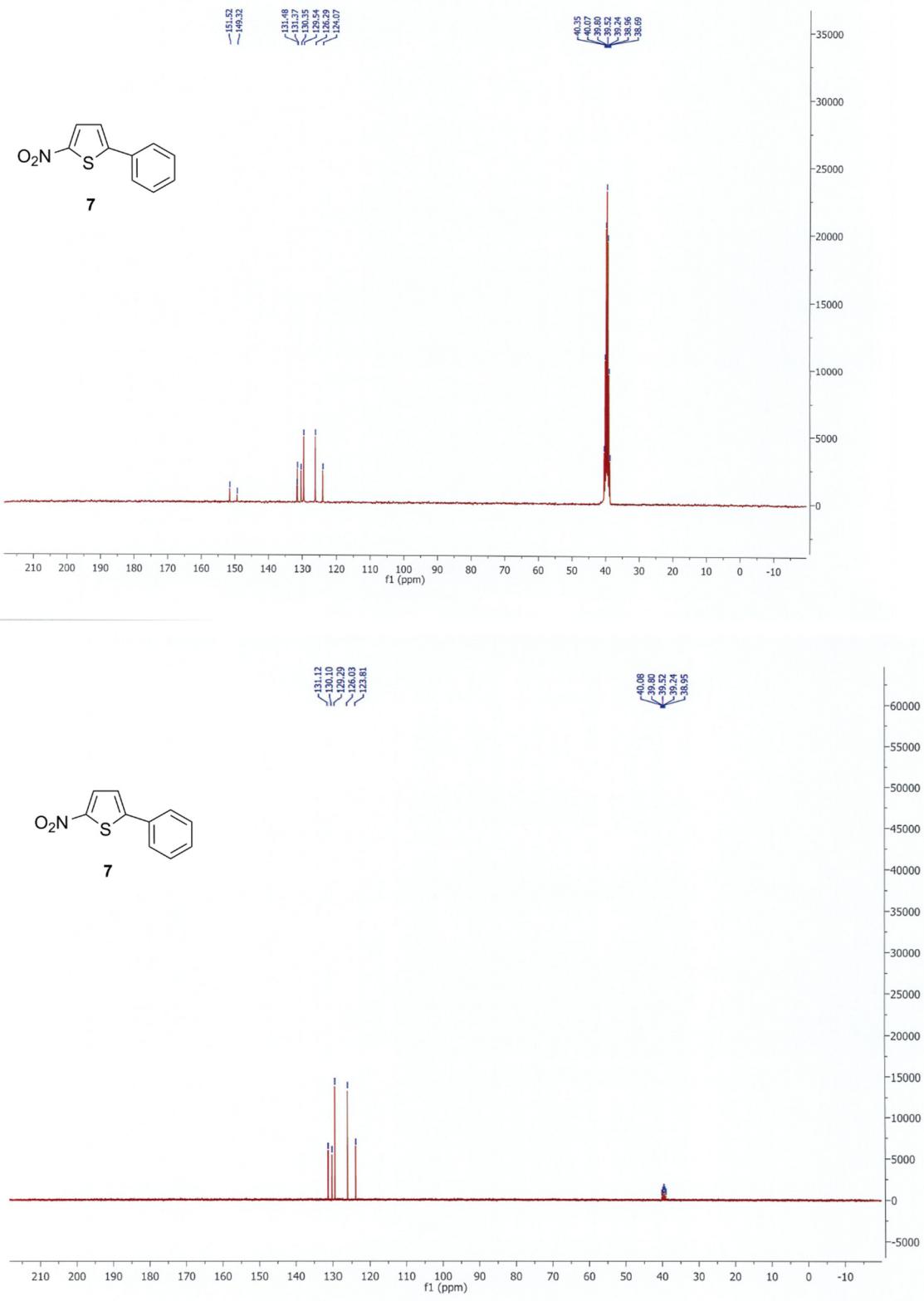
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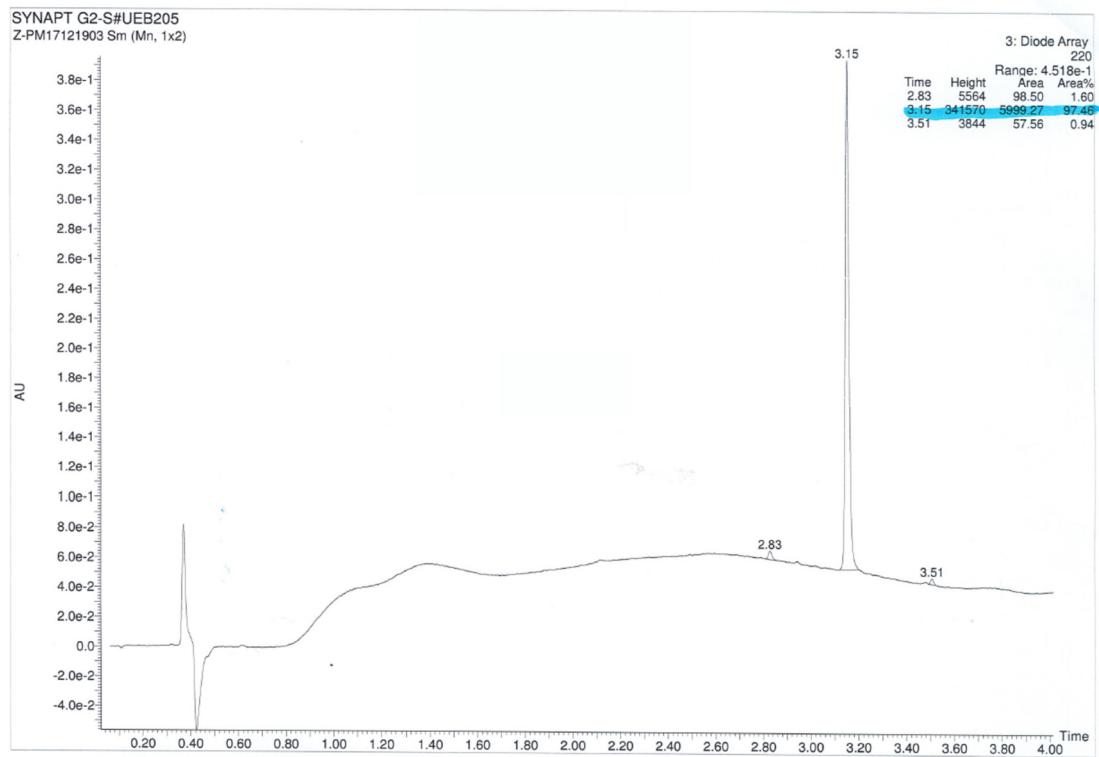
1. Boibessot, T.; Zschiedrich, C. P.; Dunyach-Rémy, C.; Lebeau, A.; Bénimèlis, D.; Dunyach-Rémy, C.; Lavigne, J.-P.; Szurmant, H.; Benfodda, Z.; Meffre, P. The Rational Design, Synthesis, and Antimicrobial Properties of Thiophene Derivatives That Inhibit Bacterial Histidine Kinases. *J. Med. Chem.* **2016**, *59* (19), 8830–8847.
<https://doi.org/10.1021/acs.jmedchem.6b00580>.
2. Nguyen, T.; Gamage, T. F.; Decker, A. M.; Barrus, D.; Langston, T. L.; Li, J. X.; Thomas, B. F.; Zhang, Y. Synthesis and Pharmacological Evaluation of 1-Phenyl-3-Thiophenylurea Derivatives as Cannabinoid Type-1 Receptor Allosteric Modulators. *J. Med. Chem.* **2019**, *62* (21), 9806–9823. <https://doi.org/10.1021/acs.jmedchem.9b01161>.
3. Krause, L.; Herbst-Irmer, R.; Sheldrick, G. M.; Stalke, D. SADABS Version 2016/2. 2015, pp 3–10.
4. Sheldrick, G. Crystal Structure Refinement with SHELXL. *Acta Crystallogr. Sect. C* **2015**, *71*.
<https://doi.org/10.1107/S2053229614024218>.

Characterization of compounds (^1H 300MHz, ^{13}C 75MHz, ^{19}F NMR 376 MHz, DEPT-135 in DMSO-d₆; HRMS, HPLC)

2-nitro-5-phenylthiophene (7)







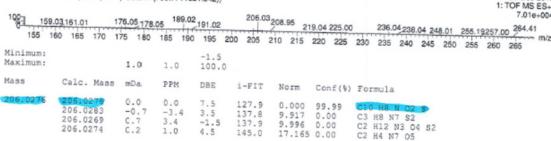
Elemental Composition Report

Page 1

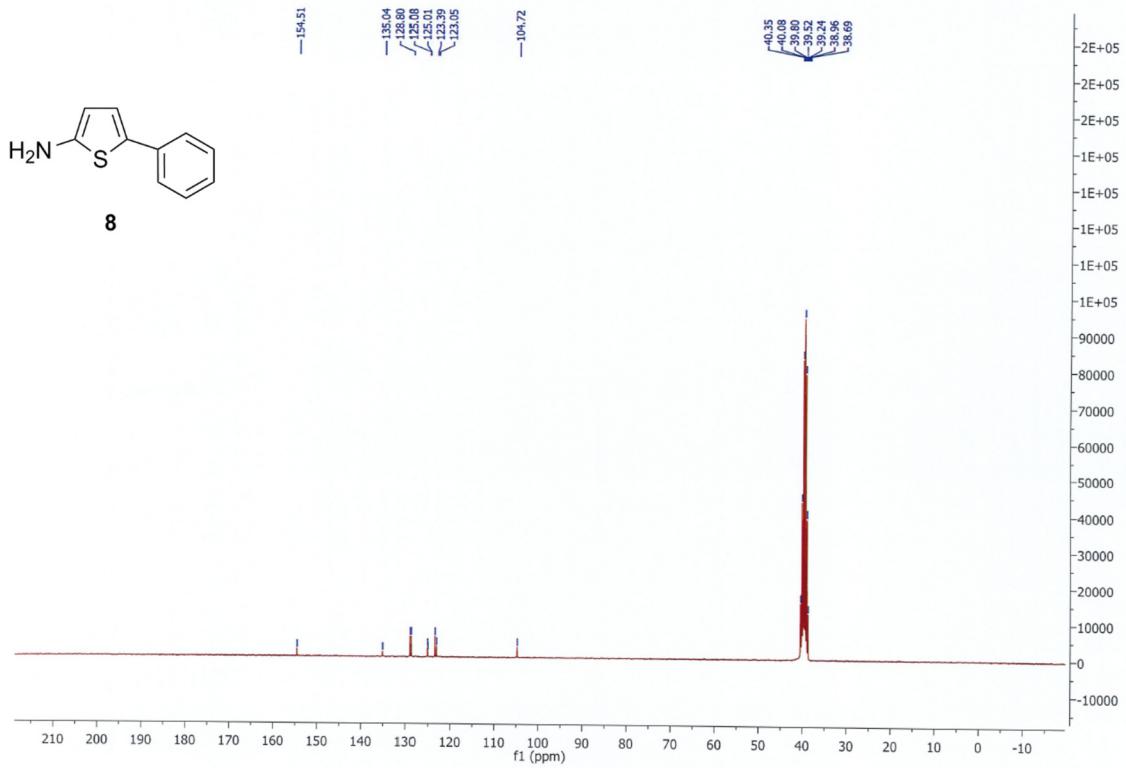
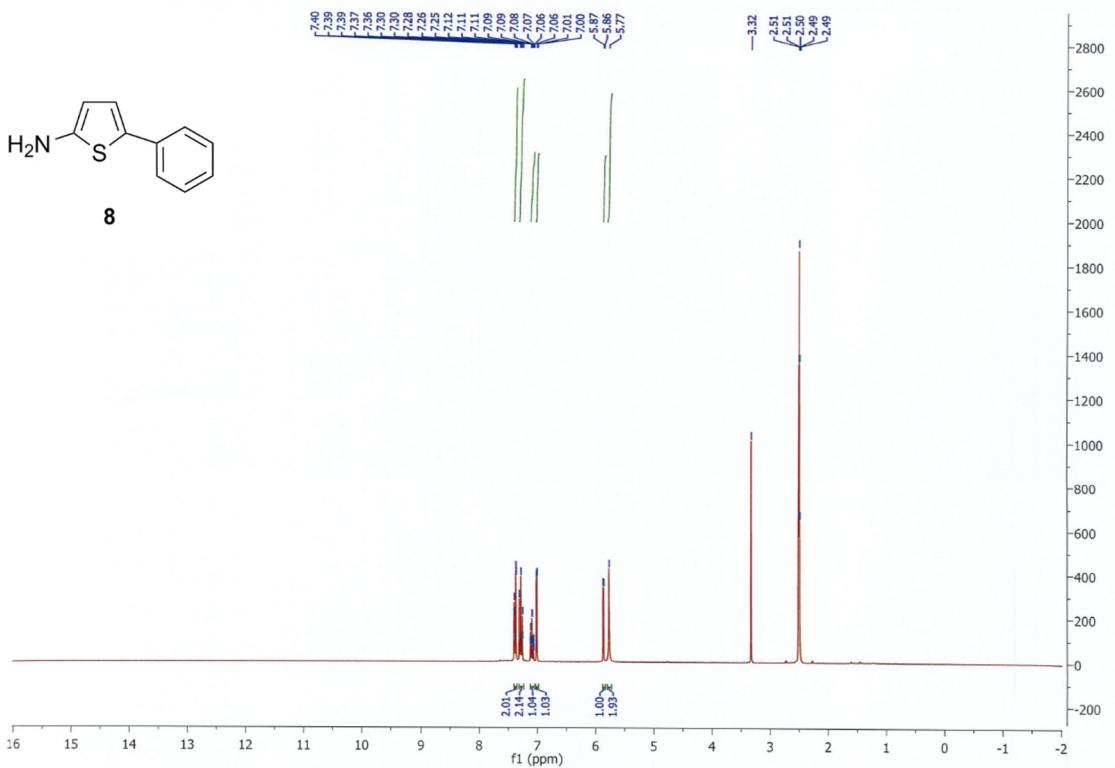
Single Mass Analysis
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Element prediction: Off
Number of isotope peaks used for I-FIT = 3

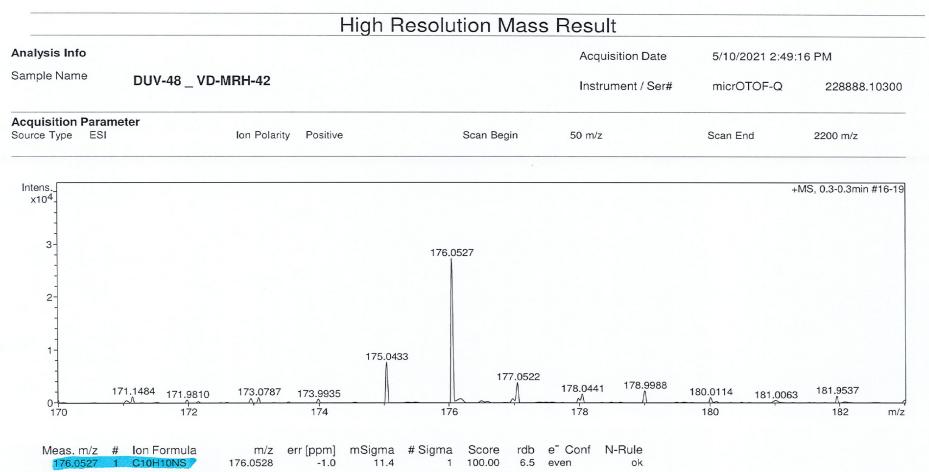
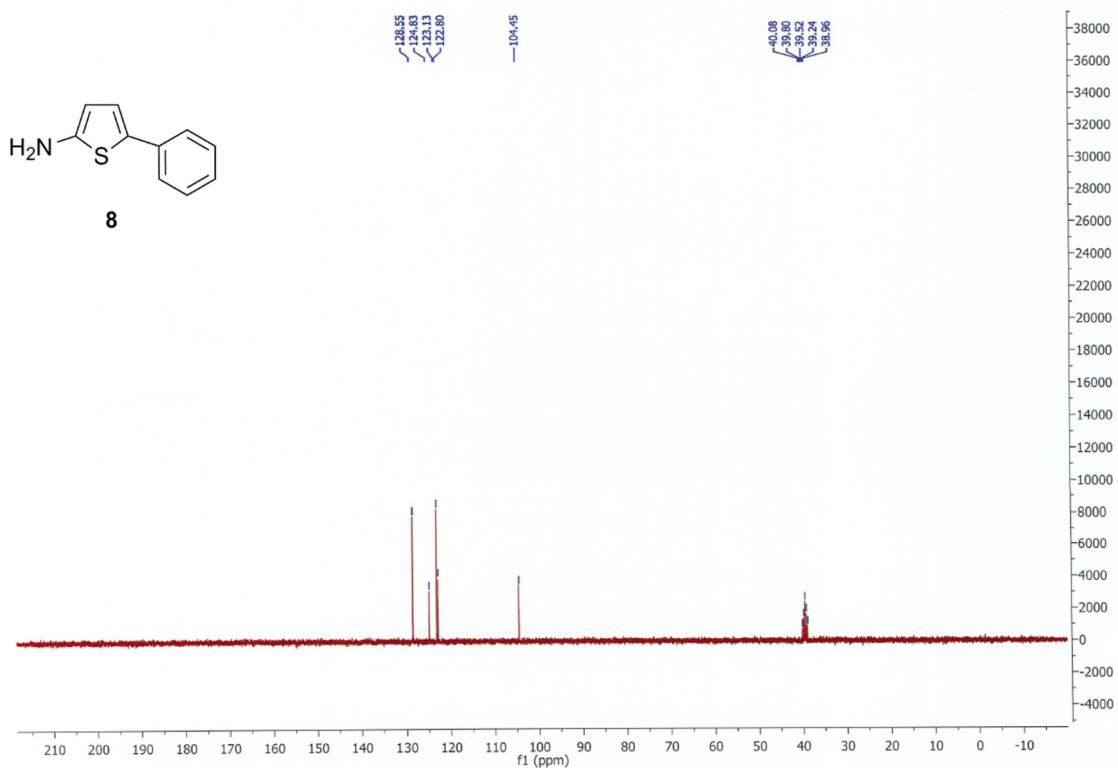
Monoisotopic Mass, Even Electron Ions
468 formula(s) evaluated with 4 results within limits (up to 50 best isotopic matches for each mass)
Element prediction: Off
C: 0-100 H: 0-100 N: 0-20 O: 0-20 S: 0-2
SYNAPT G2-S#UEB205
Z-PM17121903 Sm (Mn, 1x2) Cm (796.811-(756.771+821.842))

29-Dec-2017
1:TOF MS ES-
7.01e-004

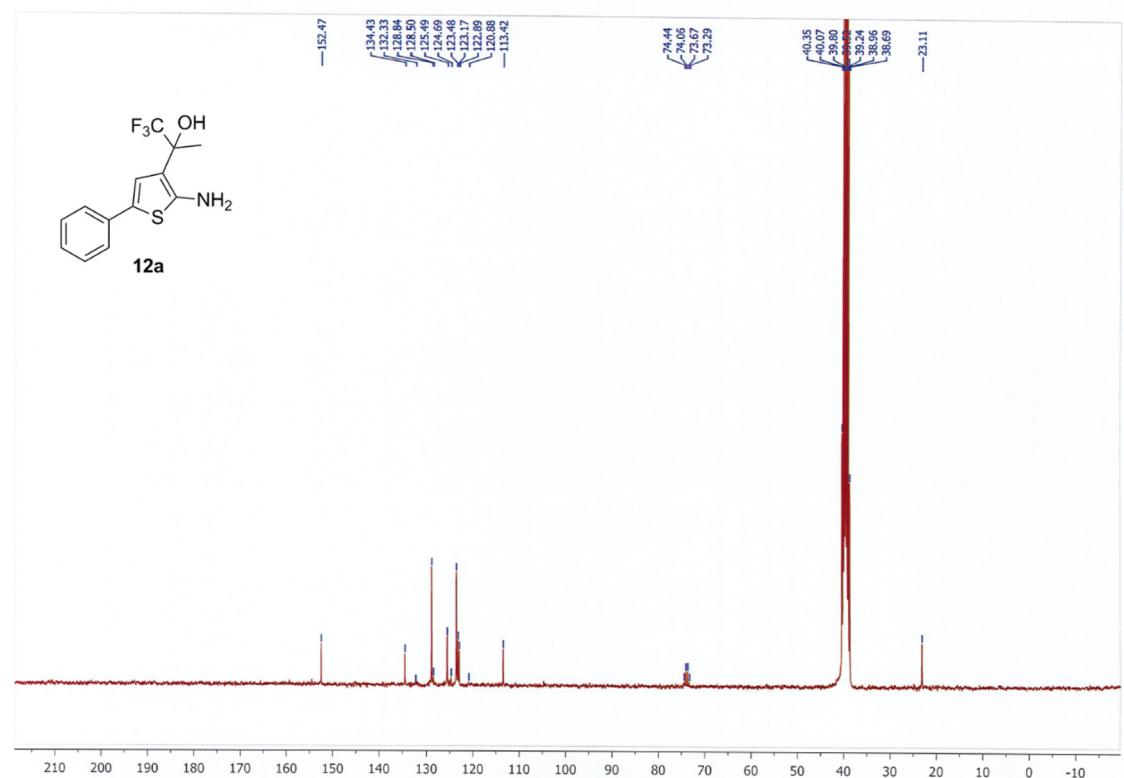
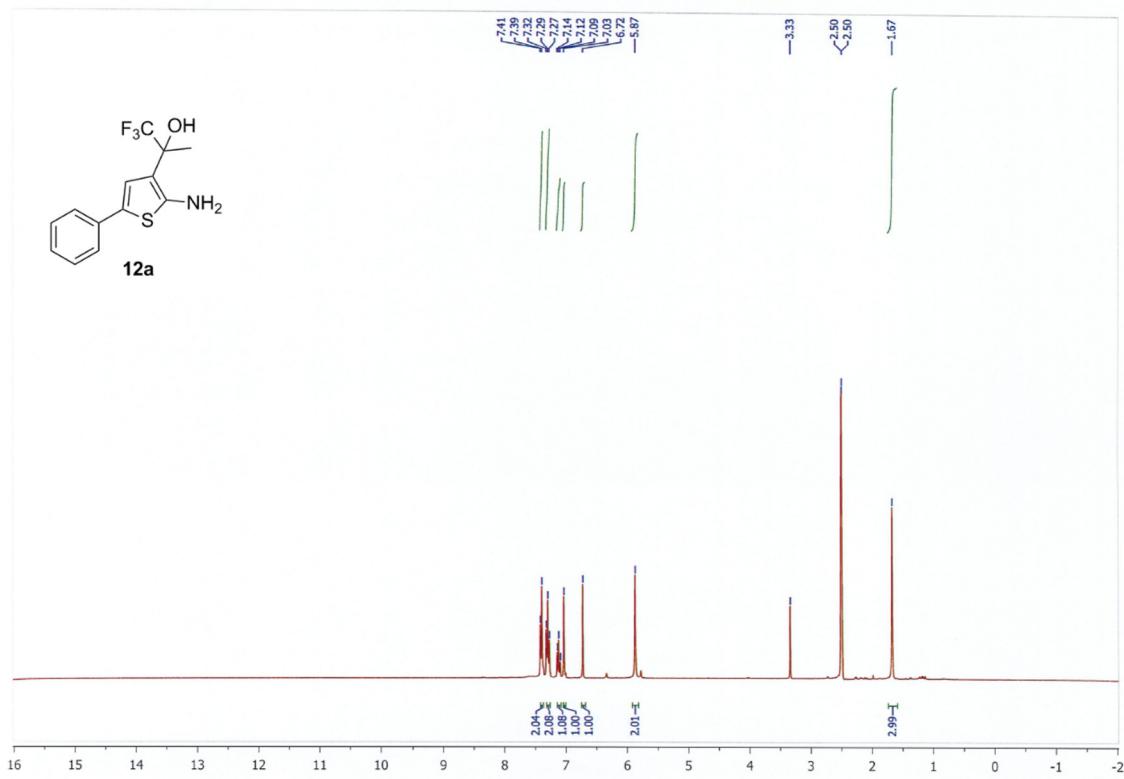


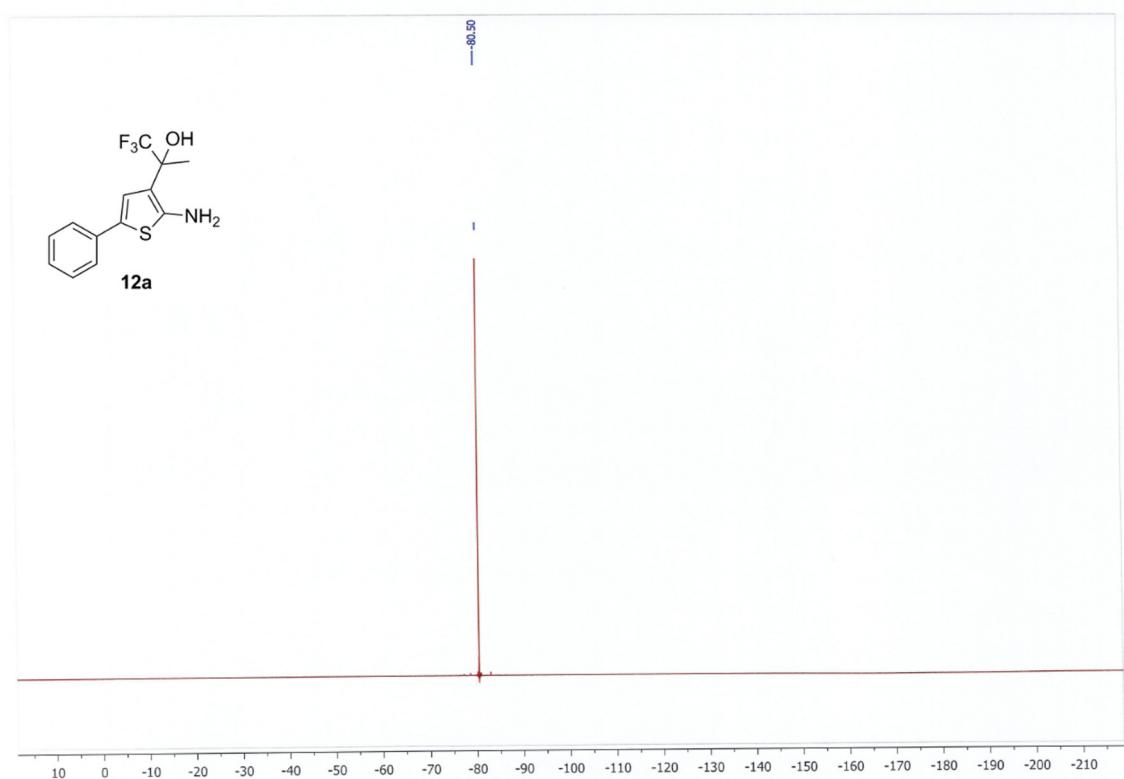
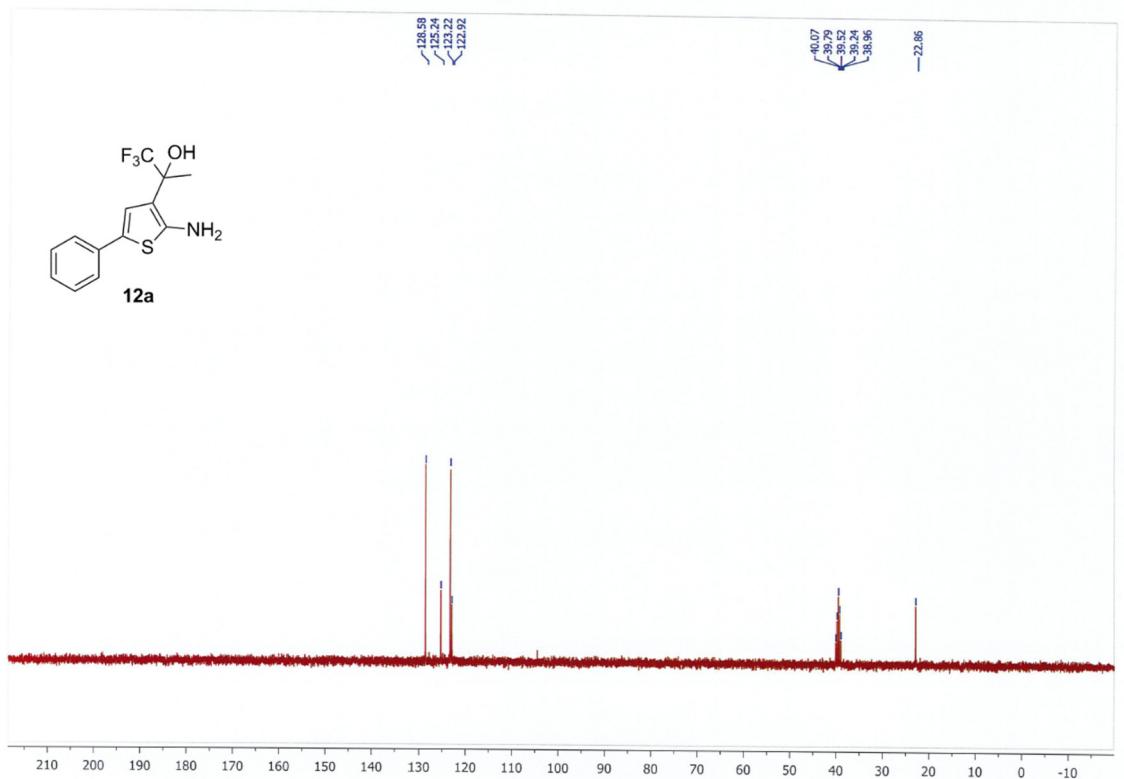
5-phenylthiophen-2-amine (8)

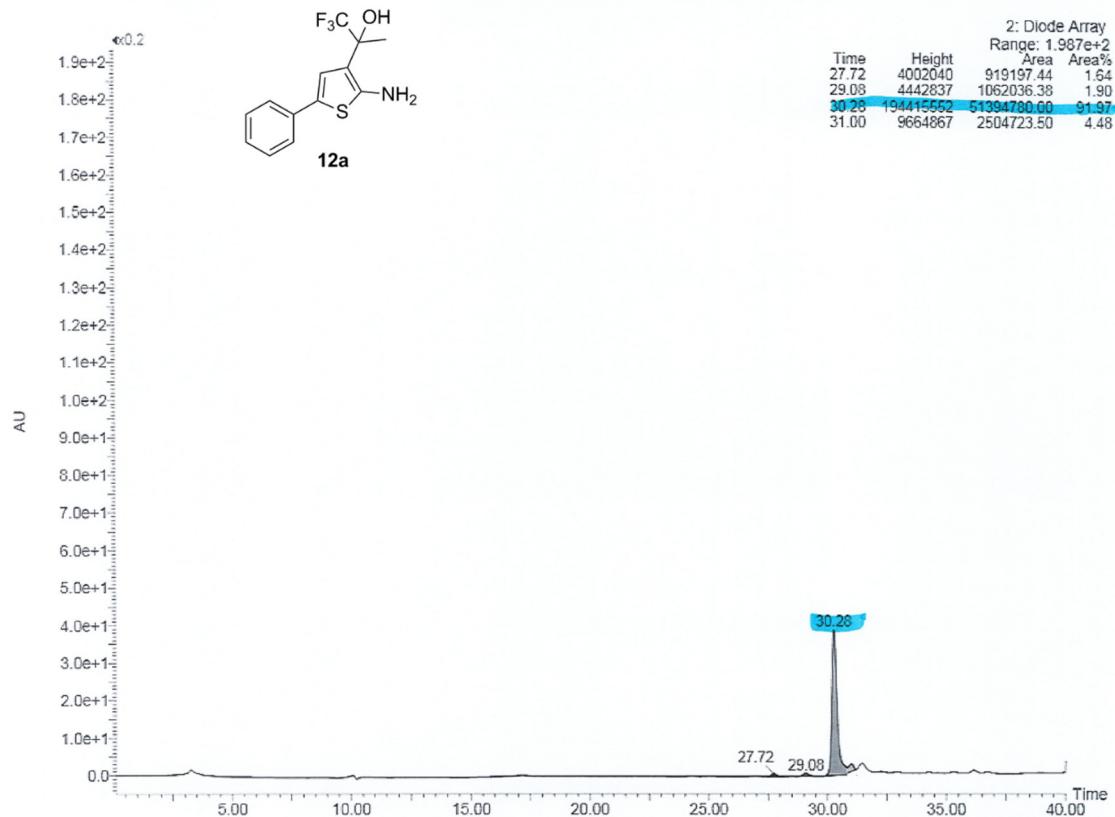




2-(2-amino-5-phenylthiophen-3-yl)-1,1,1-trifluoropropan-2-ol (12a)







Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 3.0 mDa / DBE: min = -1.0, max = 100.0

Element prediction: Off

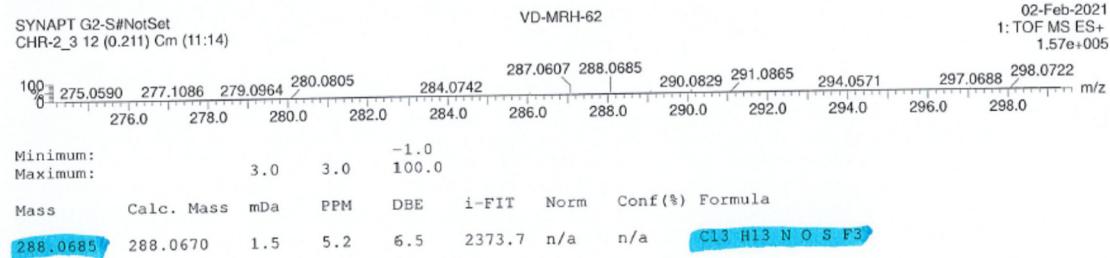
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

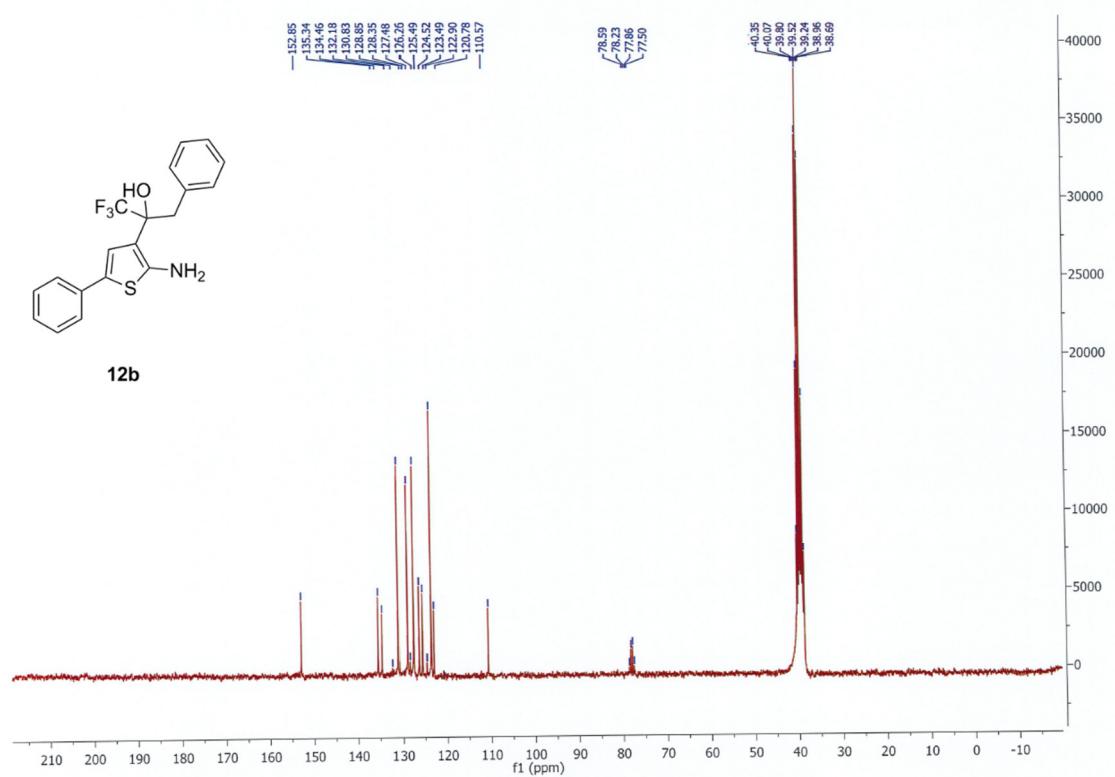
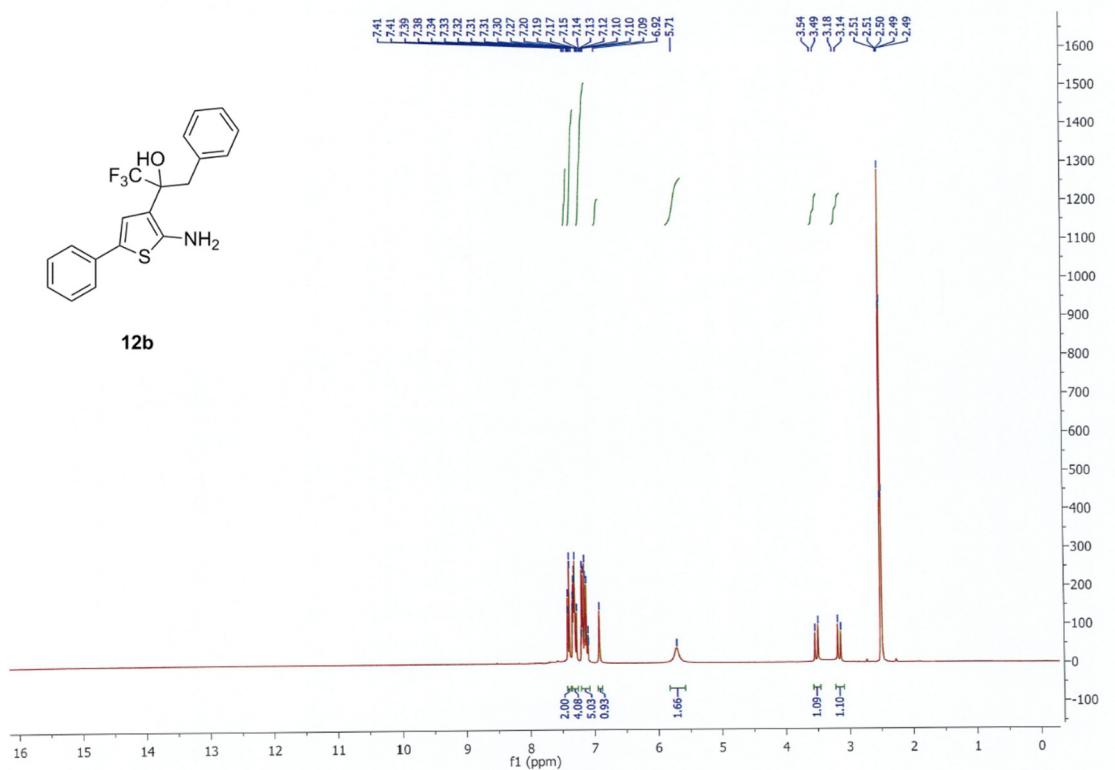
196 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

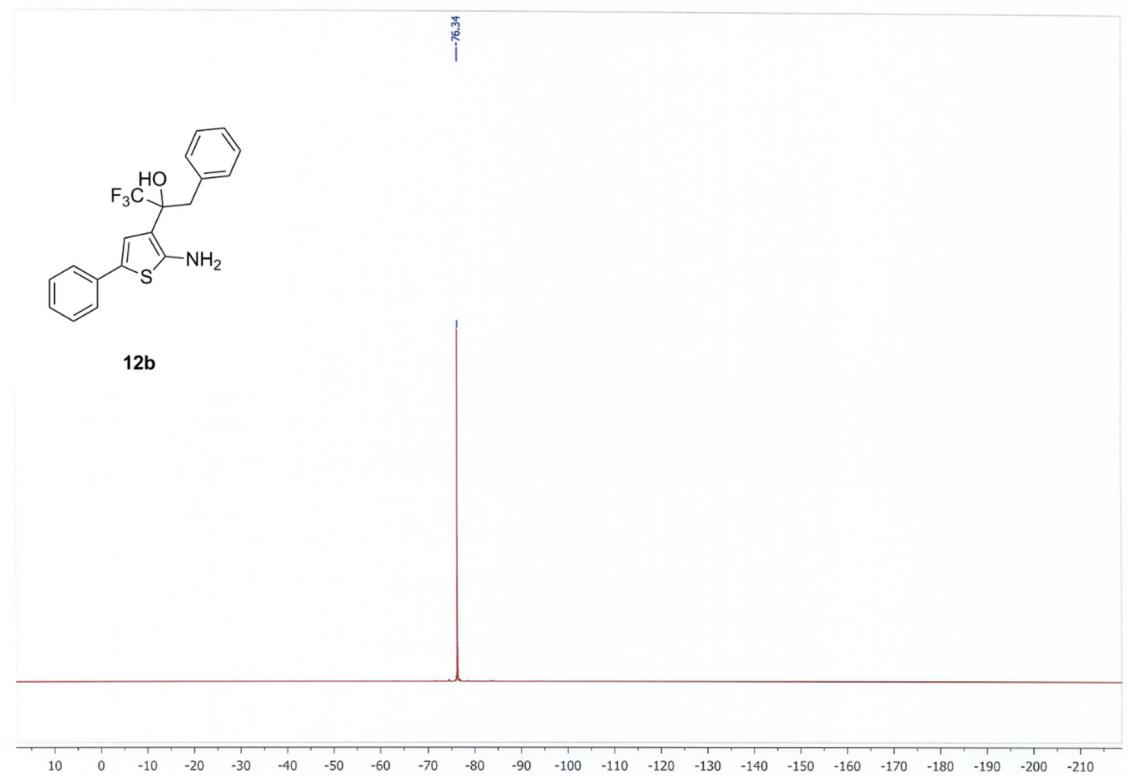
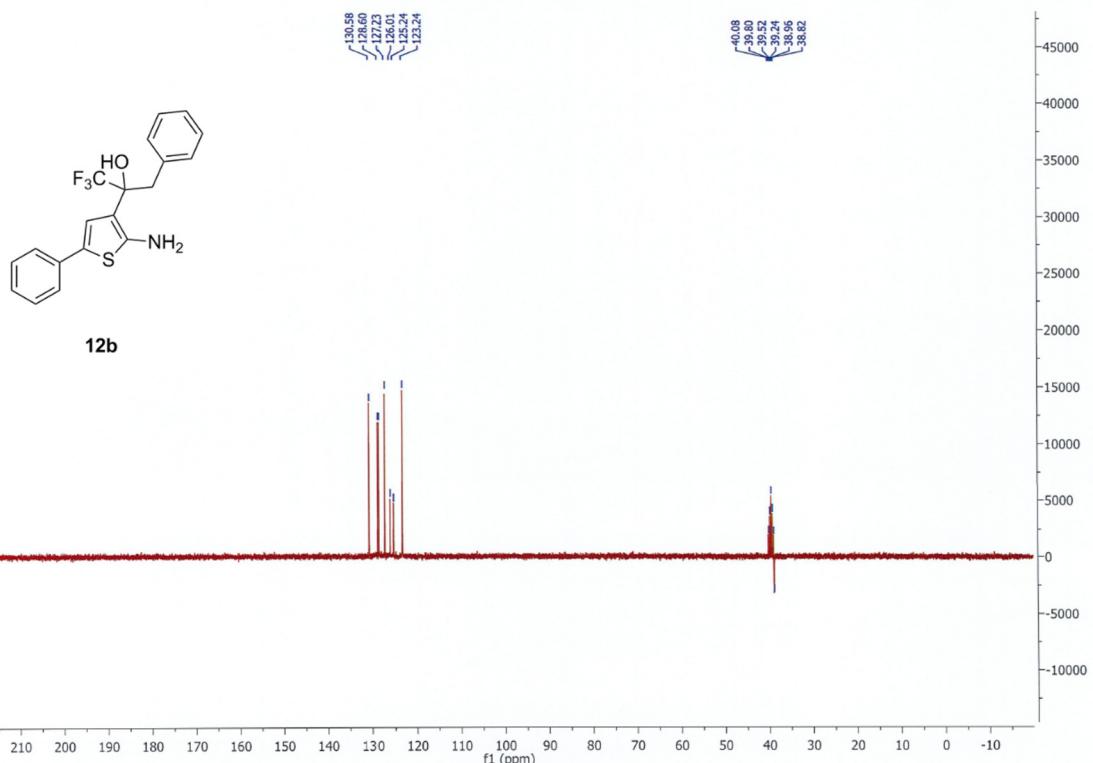
Elements Used:

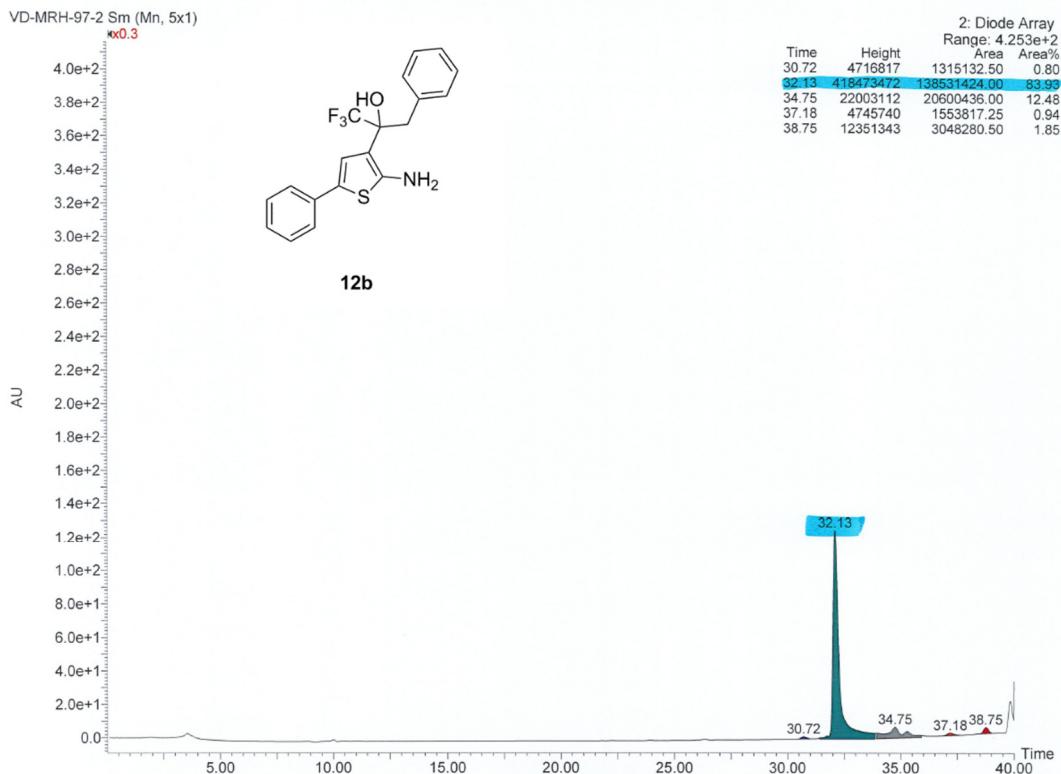
C: 0-100 H: 0-100 N: 0-20 O: 0-30 S: 1-1 F: 3-3



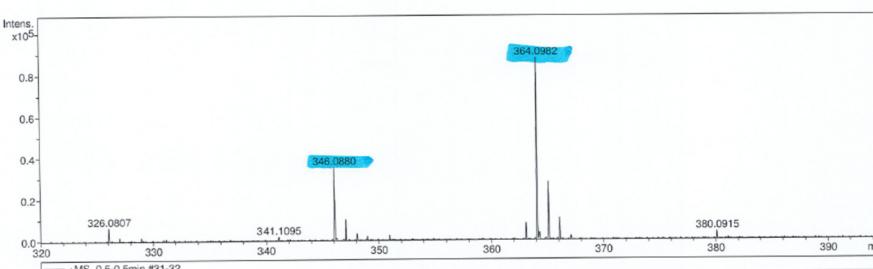
*2-(2-amino-5-phenylthiophen-3-yl)-1,1,1-trifluoro-3-phenylpropan-2-ol (**12b**)*



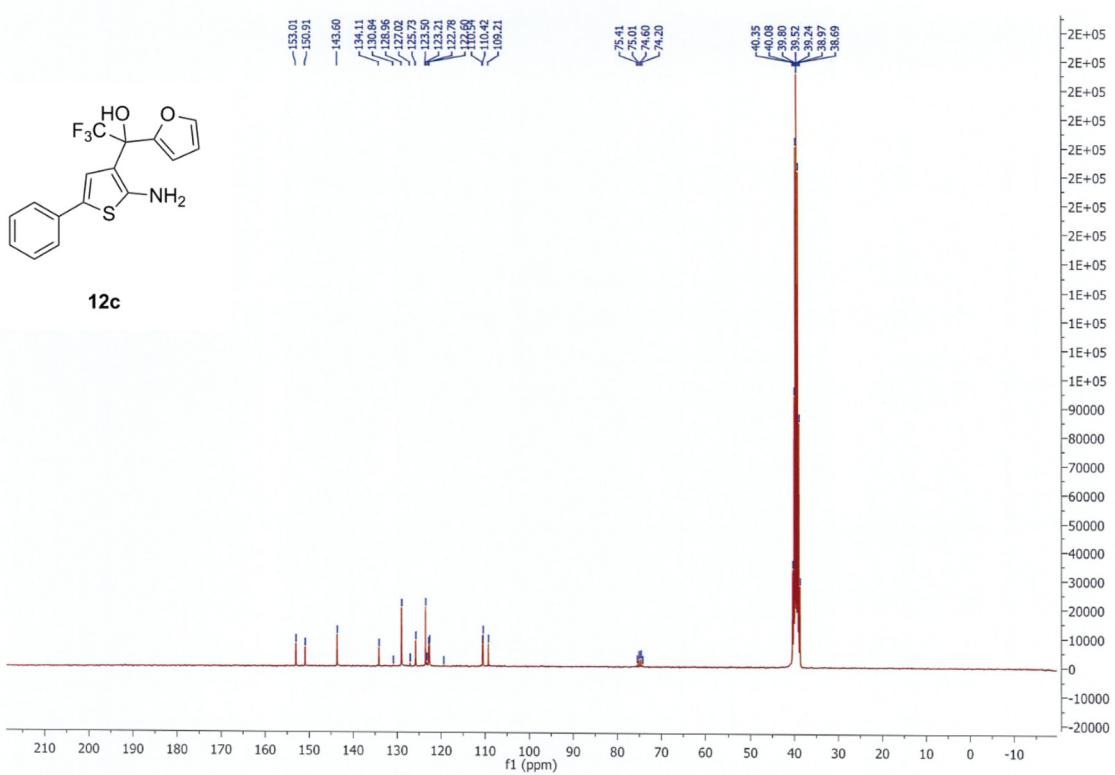
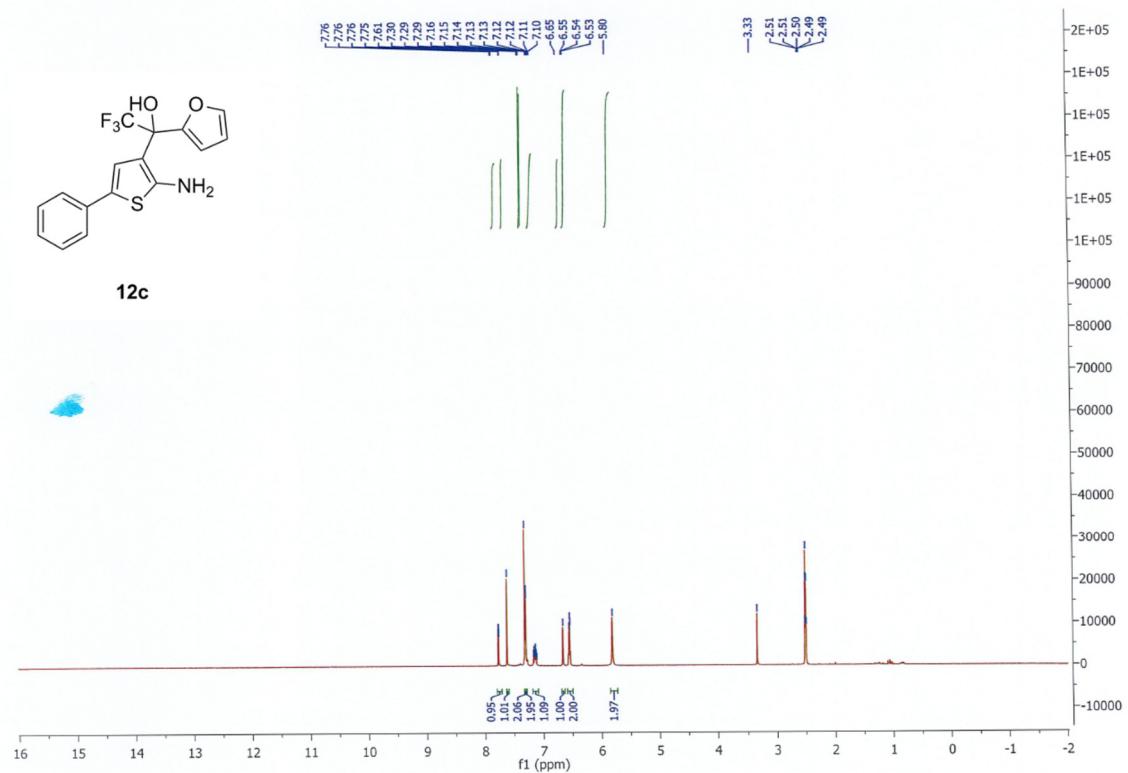


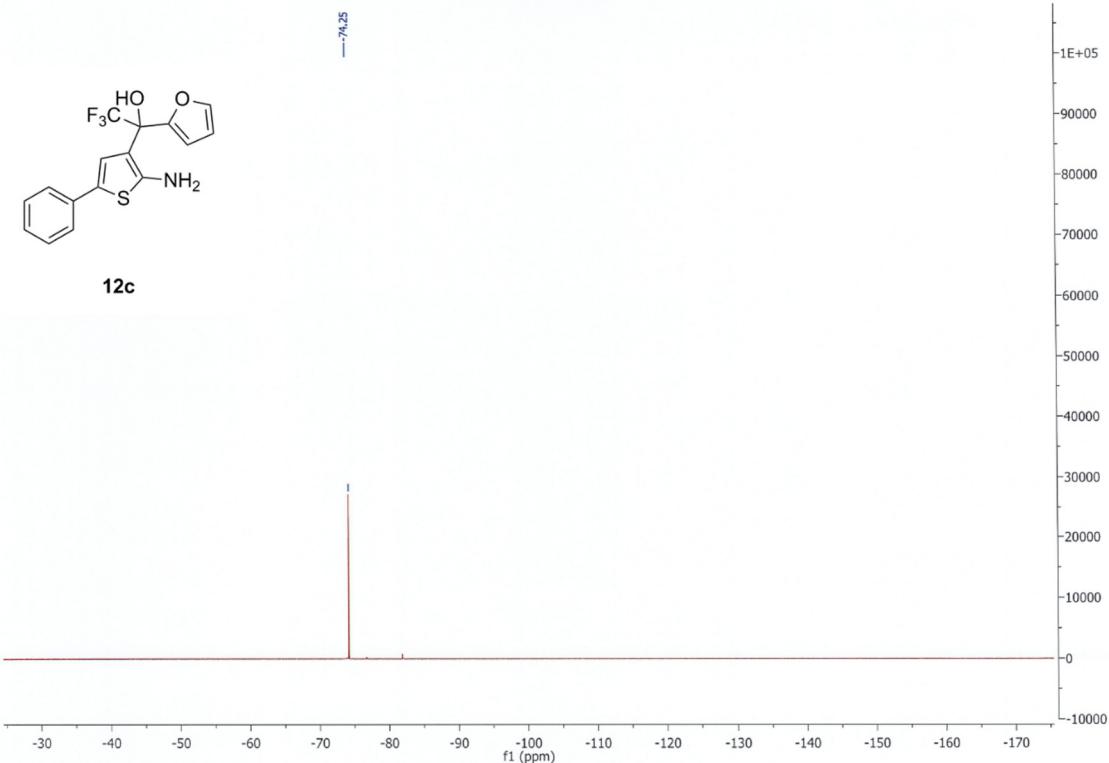
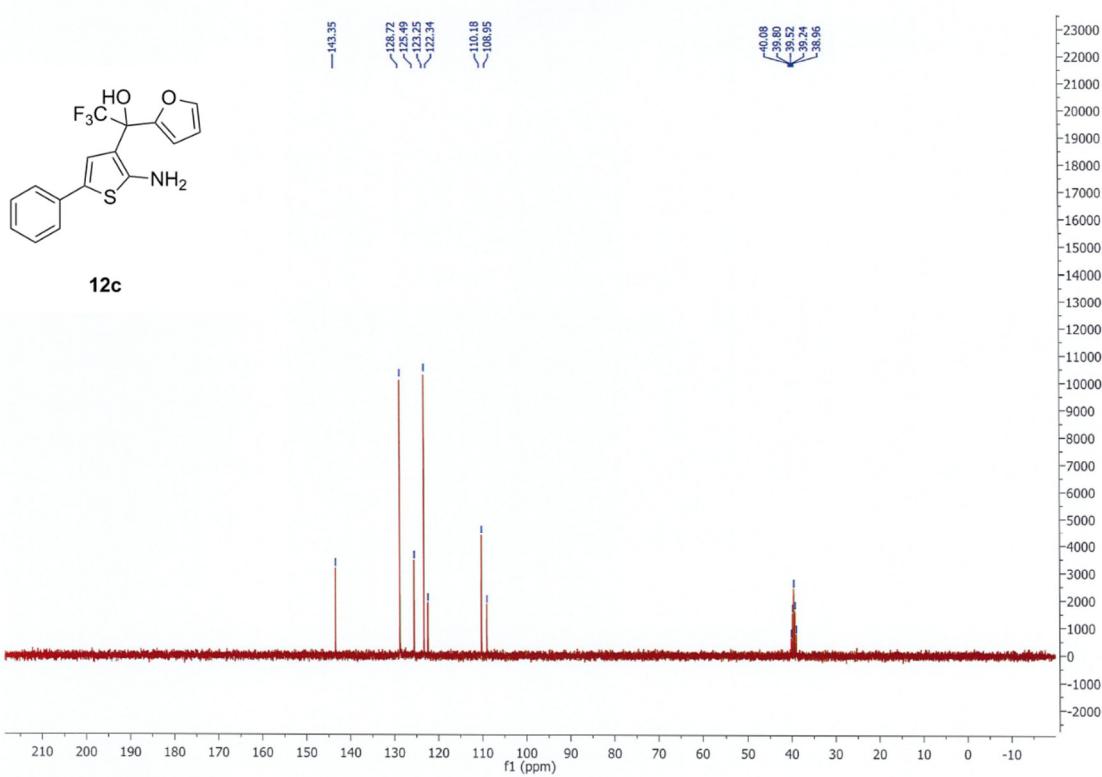


High Resolution Mass Result

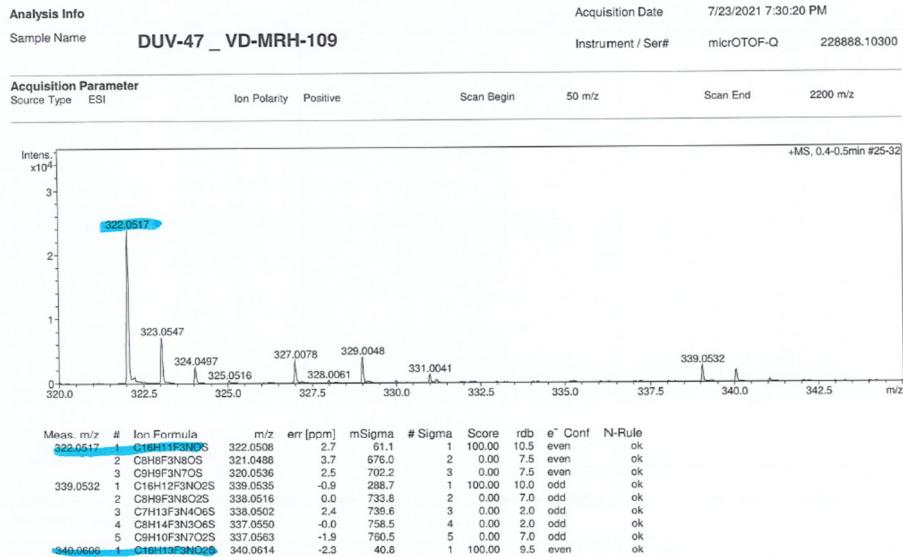
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Sample Name	VD-MRH-97	5/10/2021 2:55:21 PM	
Acquisition Parameter		Instrument / Ser#	
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		2200 m/z	
			
Meas. m/z # Ion Formula m/z err [ppm] mSigma # Sigma Score rdb e- Conf N-Rule 346.0982 1 C19H15F3NOS 346.0872 -2.3 38.7 1 100.00 11.5 even ok 346.0982 1 C19H17F3NOS 364.0977 -1.2 55.9 1 100.00 10.5 even ok 2 C8H17F3N7O4S 364.1009 -7.6 102.2 2 3.12 2.5 even ok 3 C7H21F3N3O6S 364.0996 3.9 112.7 3 5.25 -2.5 even ok			

1-(2-amino-5-phenylthiophen-3-yl)-2,2,2-trifluoro-1-(furan-2-yl)ethan-1-ol (12c)

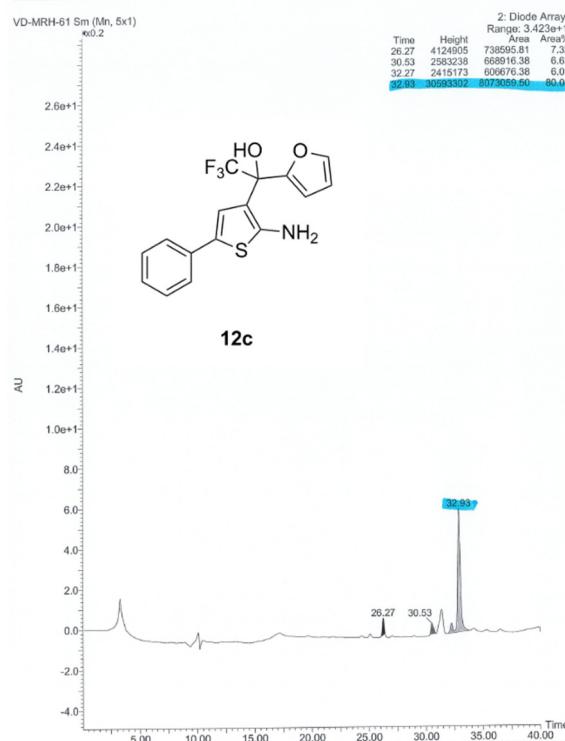




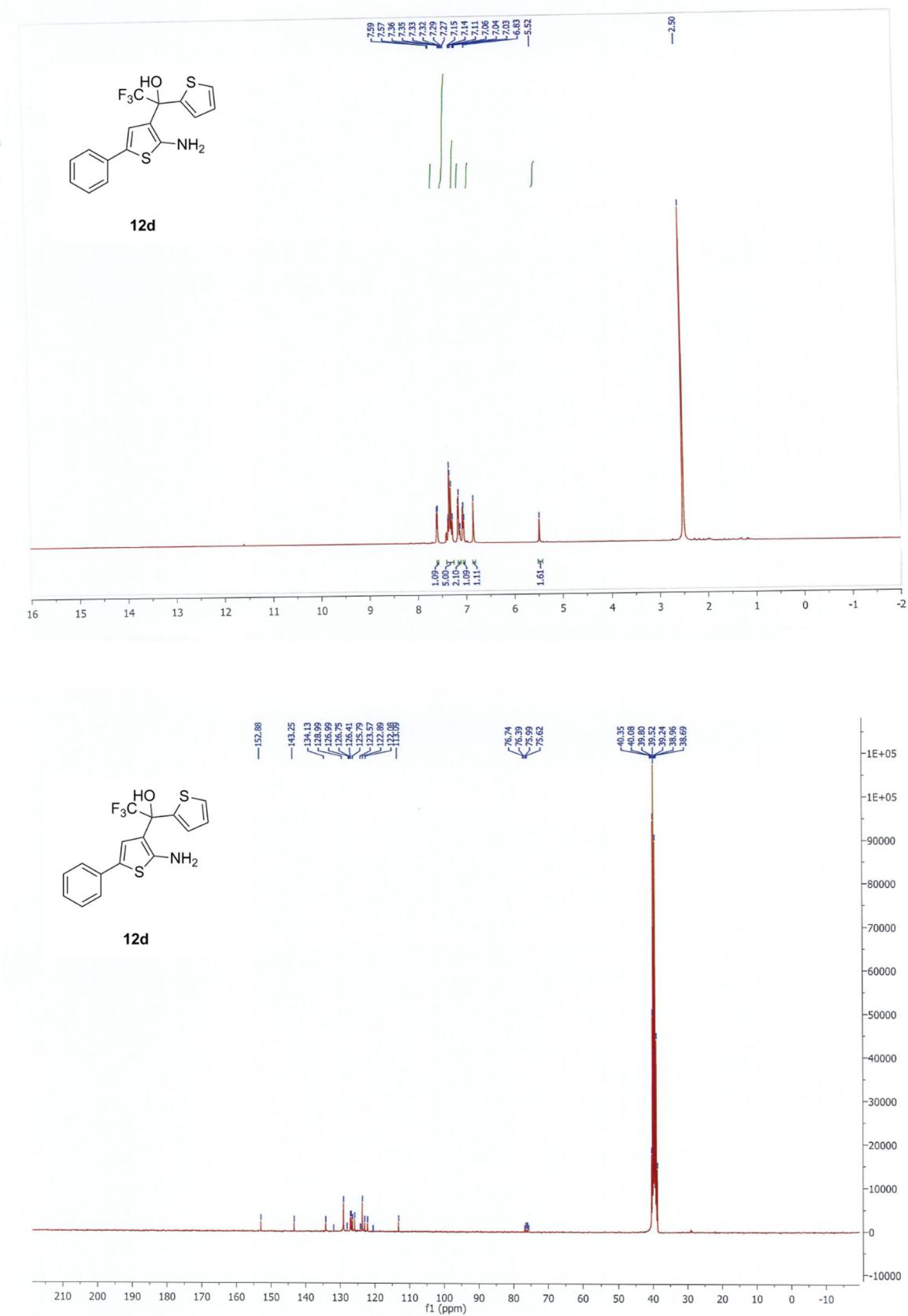
High Resolution Mass Result

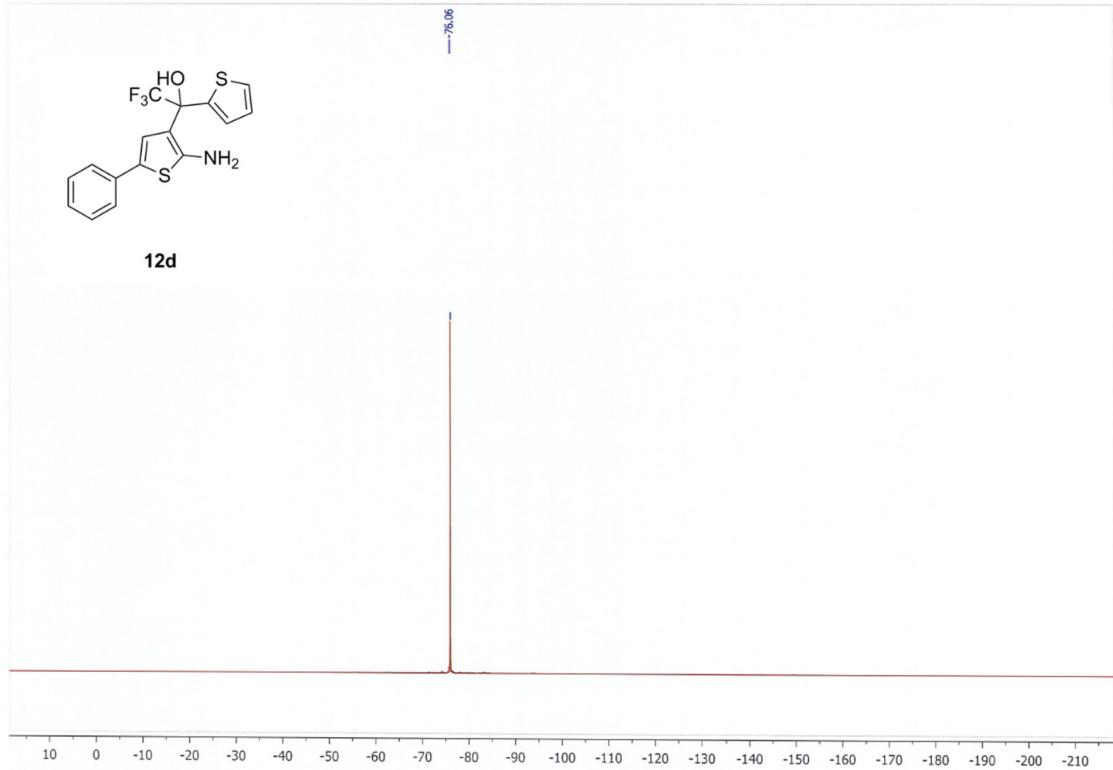
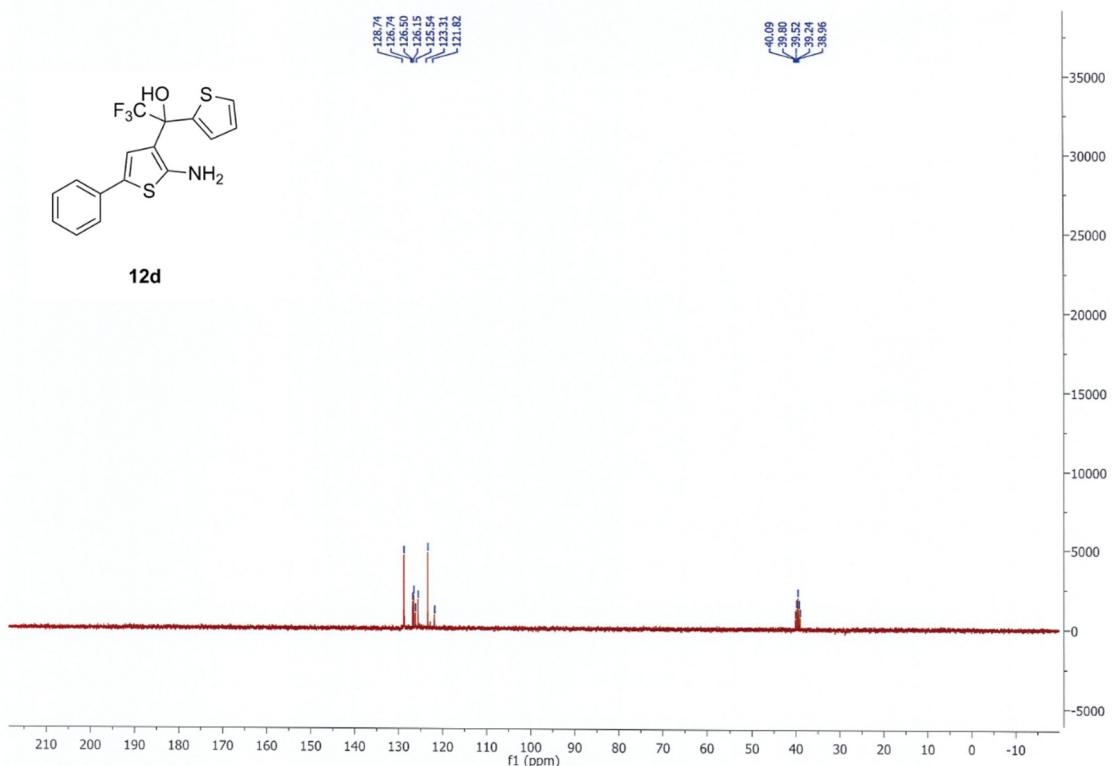


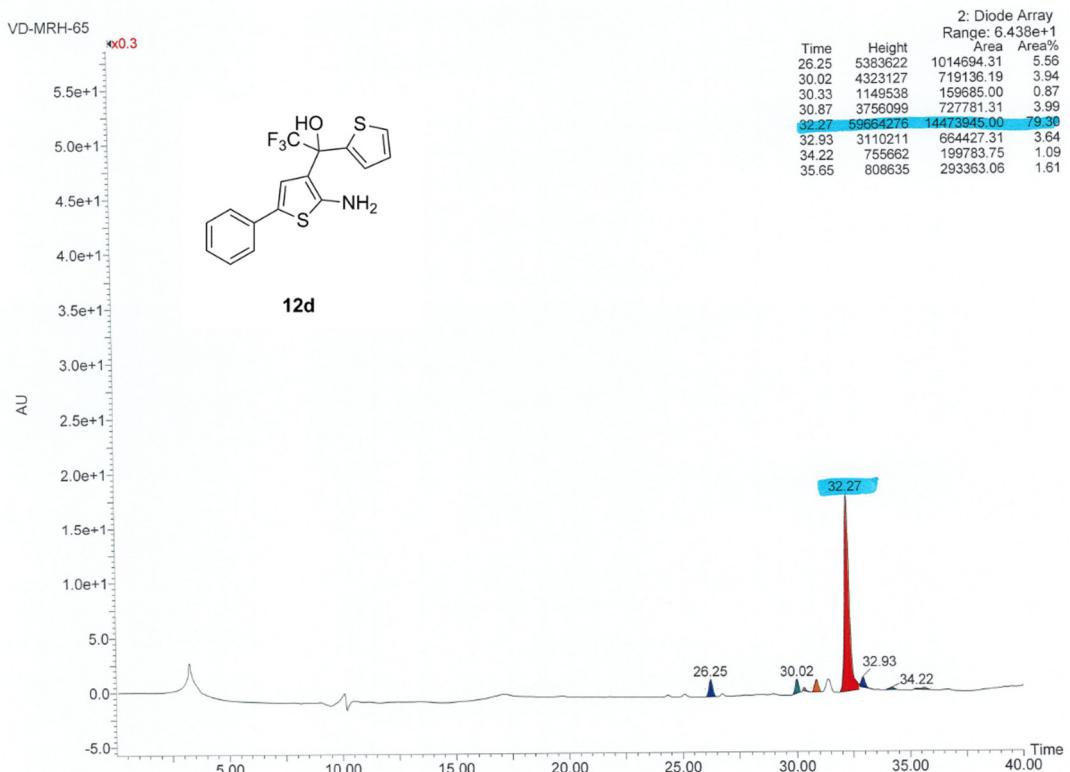
Bruker Compass DataAnalysis 4.1 printed: 7/26/2021 10:32:48 AM Page 1 of 1



1-(2-amino-5-phenylthiophen-3-yl)-2,2,2-trifluoro-1-(thiophen-2-yl)ethan-1-ol (12d)







Page 1

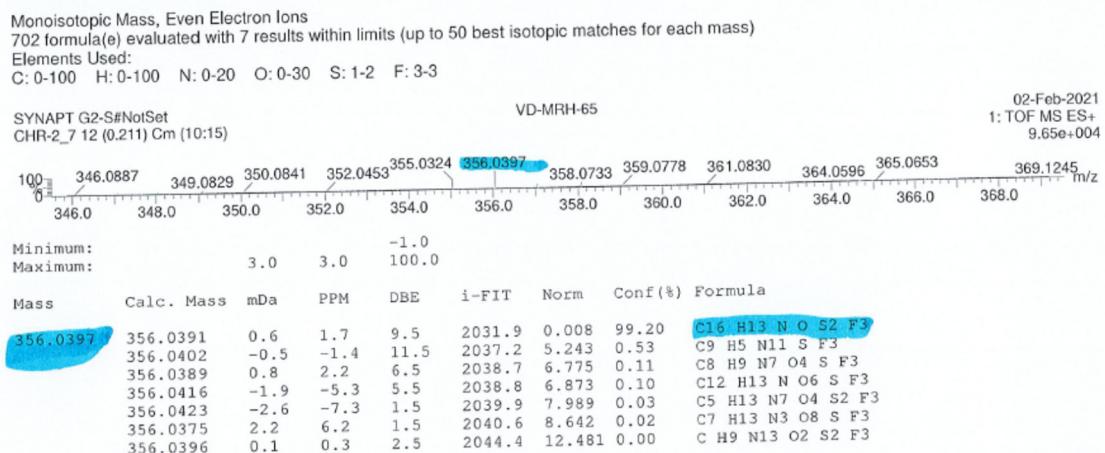
Elemental Composition Report

Single Mass Analysis

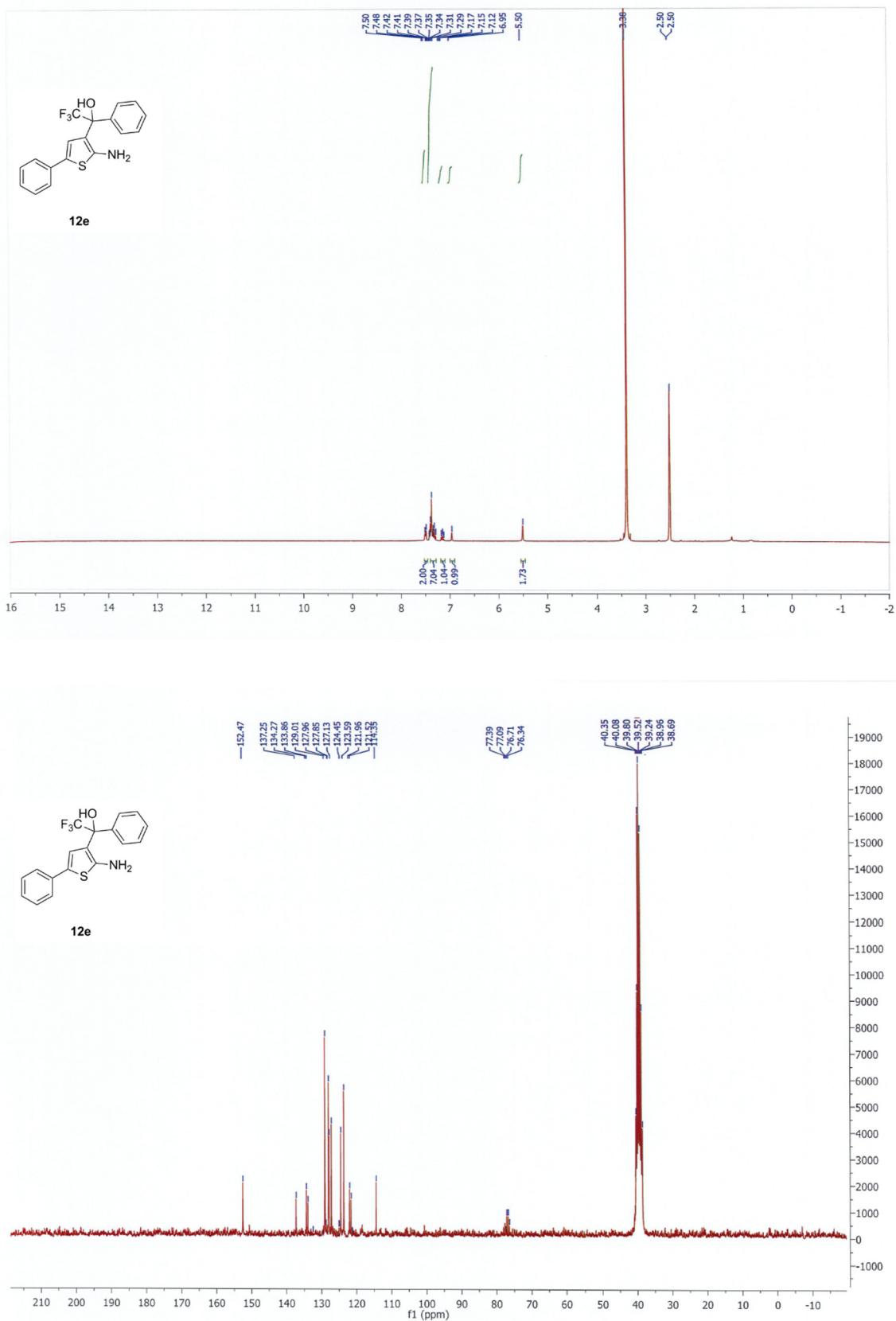
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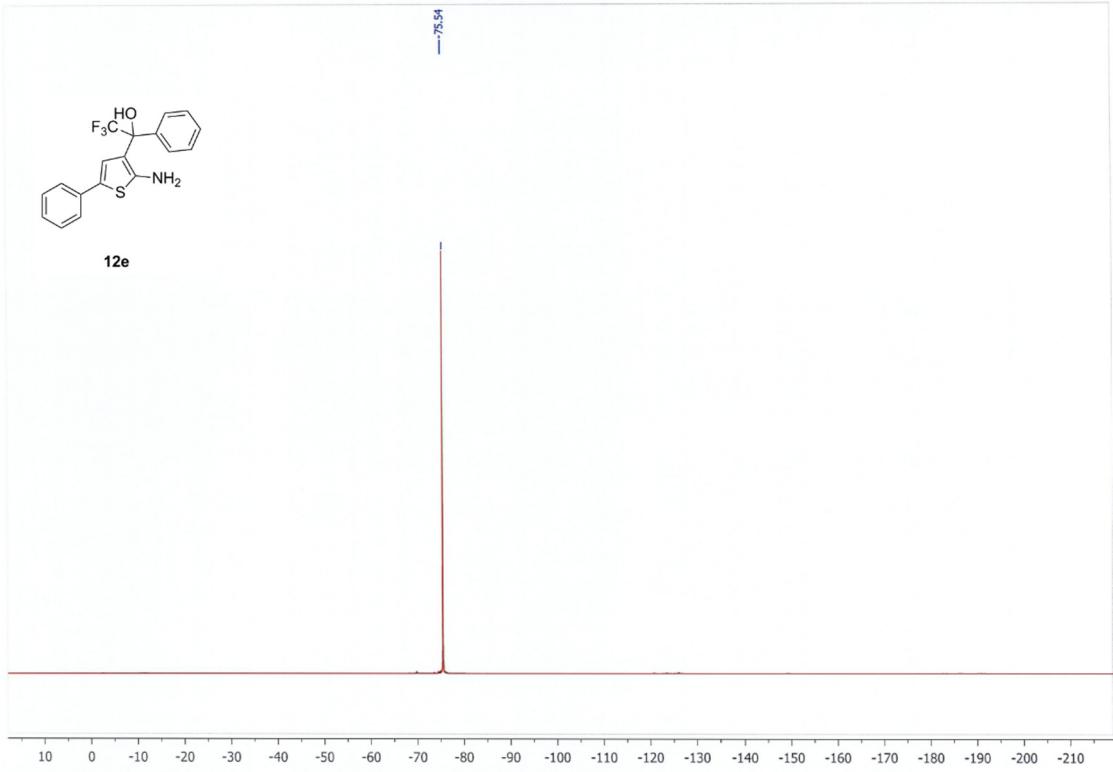
Element prediction: Off

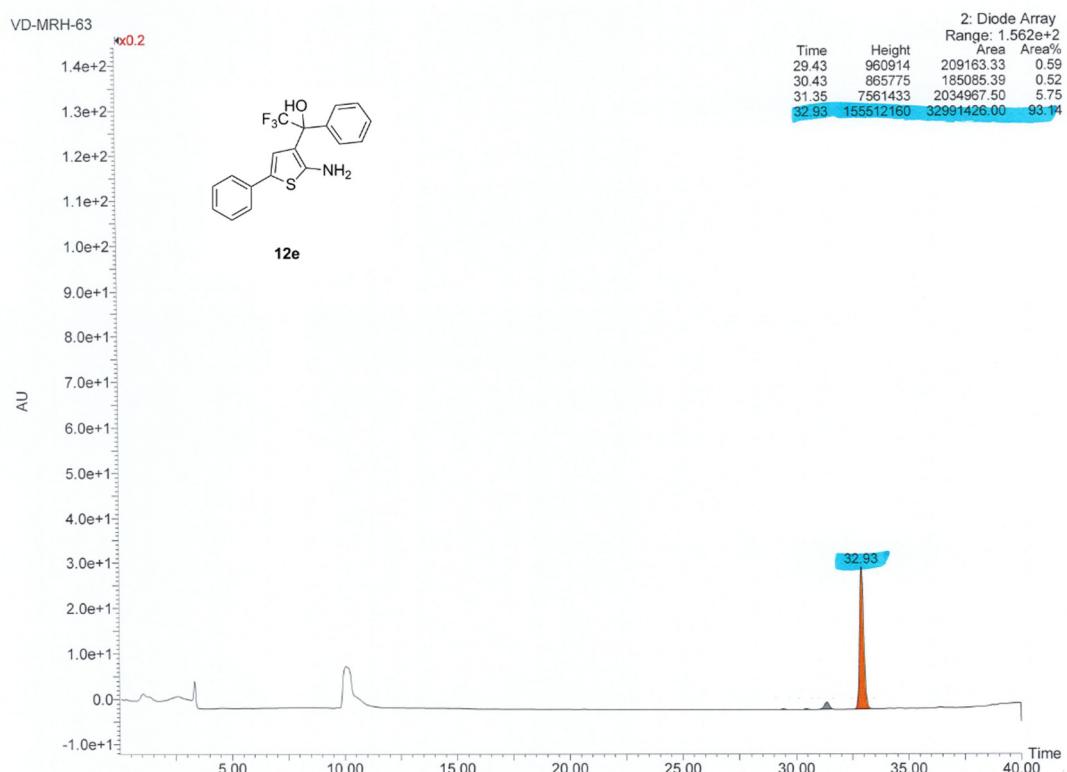
Number of isotope peaks used for i-FIT = 3



1-(2-amino-5-phenylthiophen-3-yl)-2,2,2-trifluoro-1-phenylethan-1-ol (12e)







Page 1

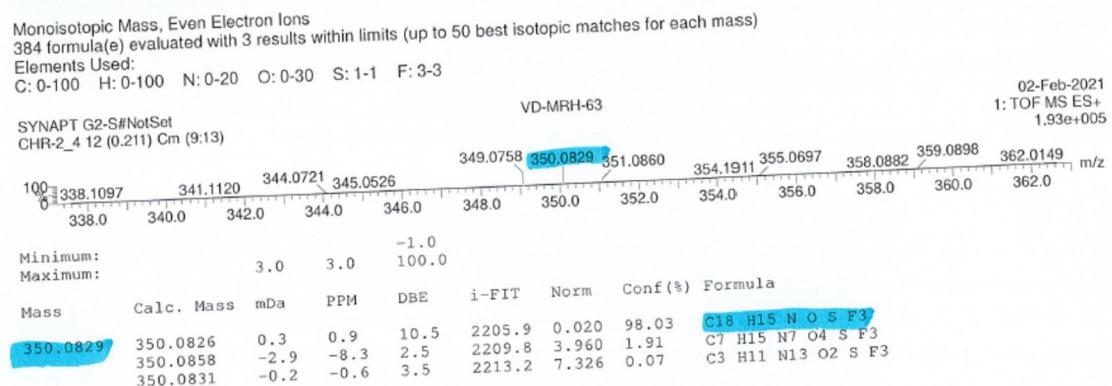
Elemental Composition Report

Single Mass Analysis

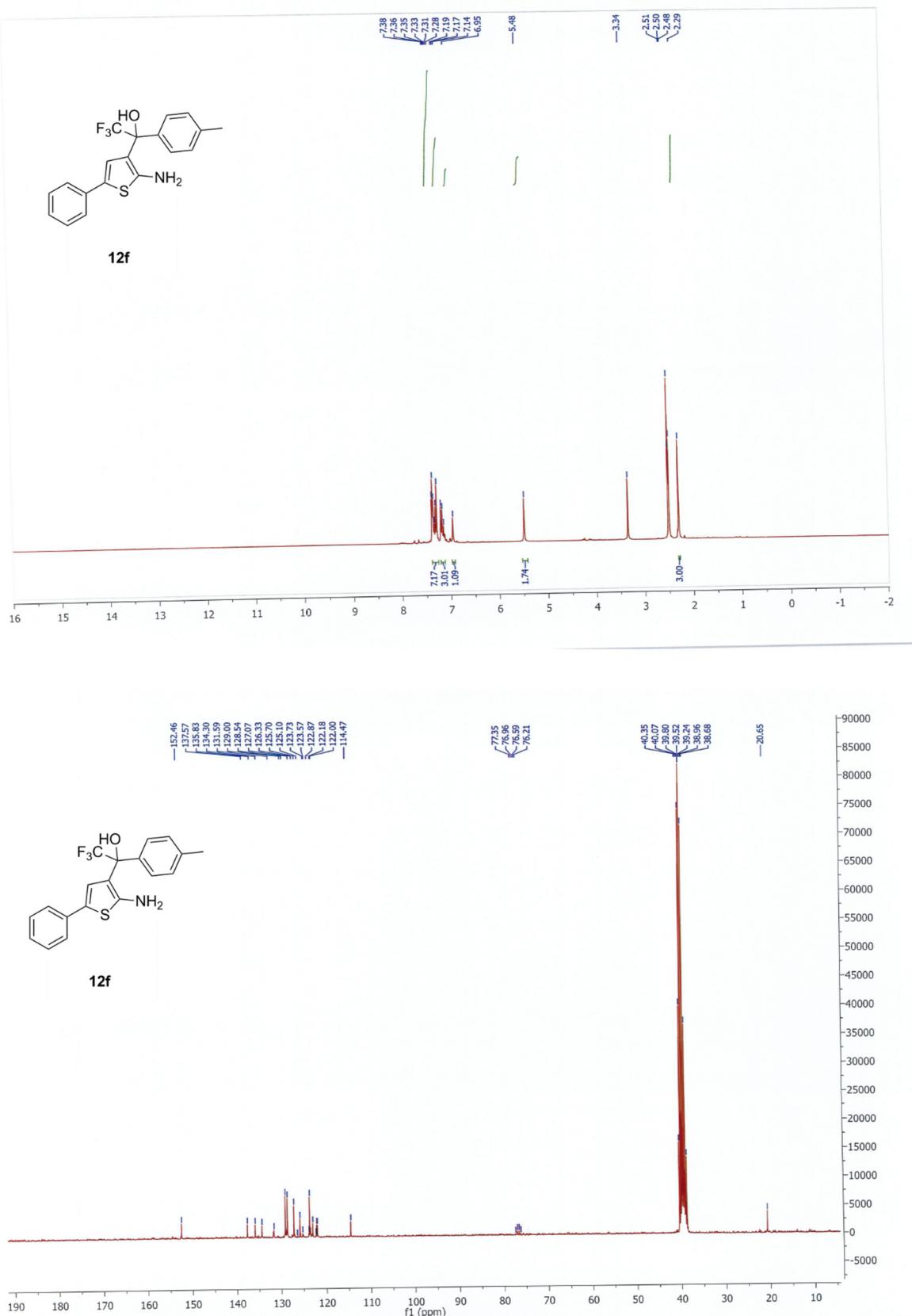
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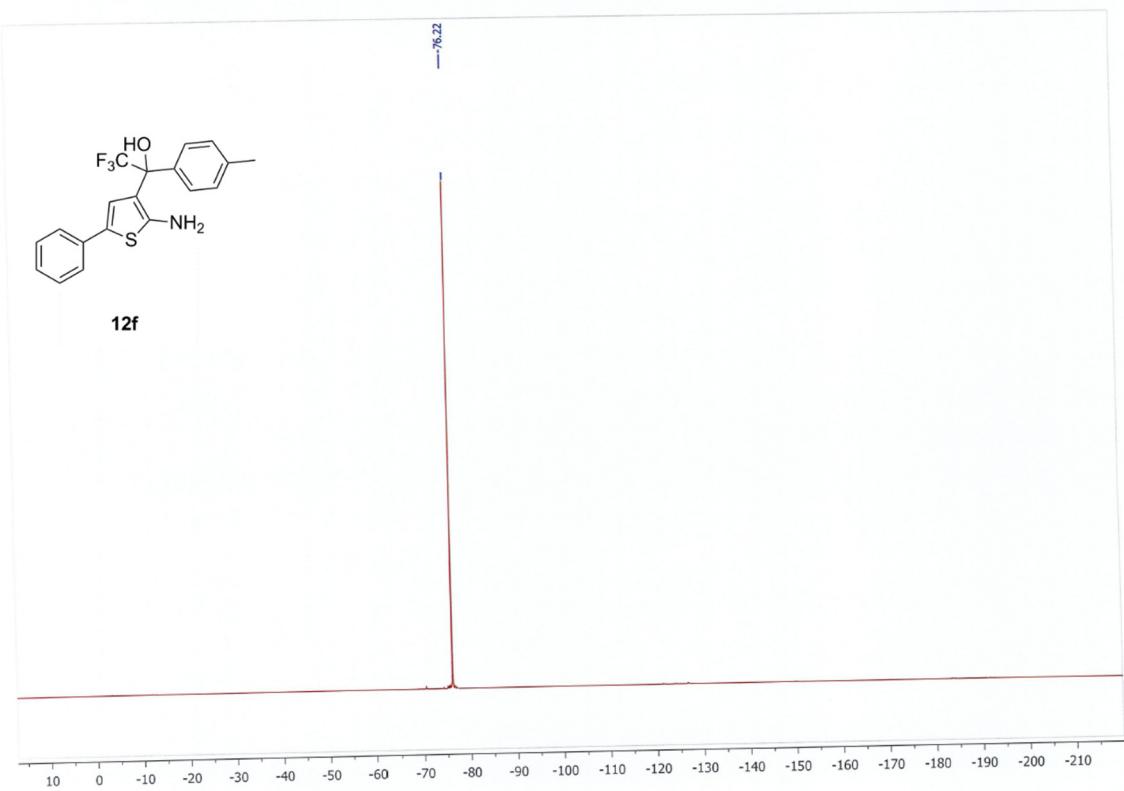
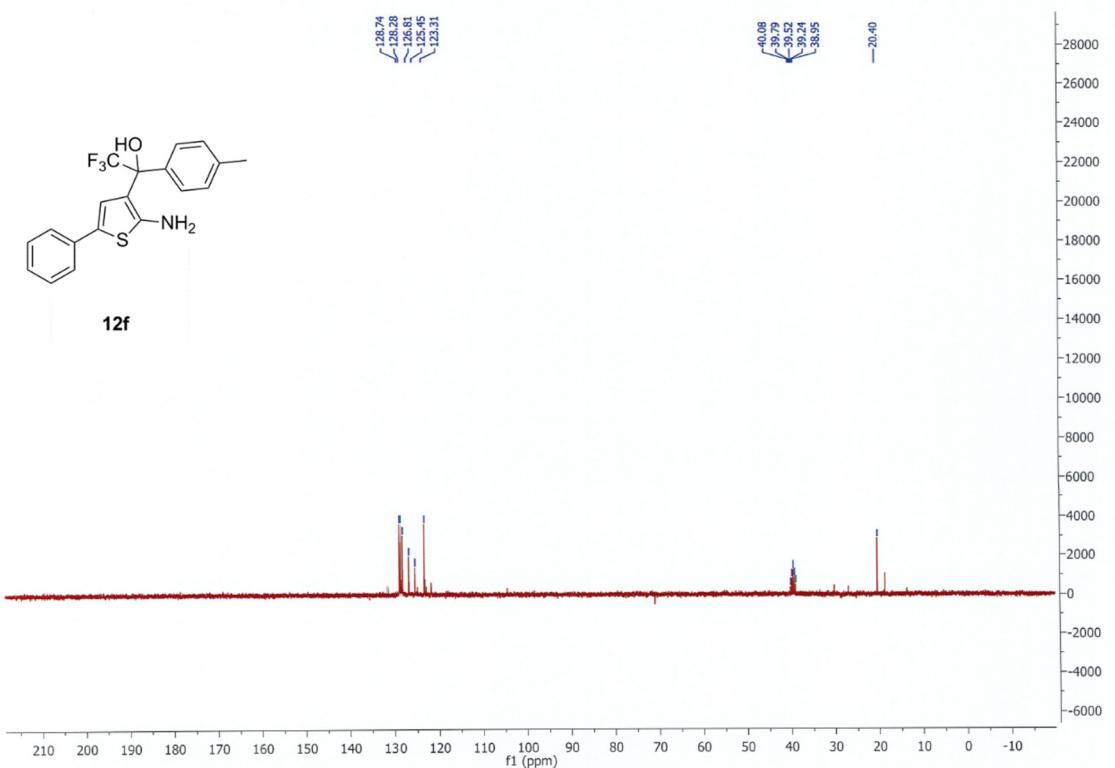
Element prediction: Off

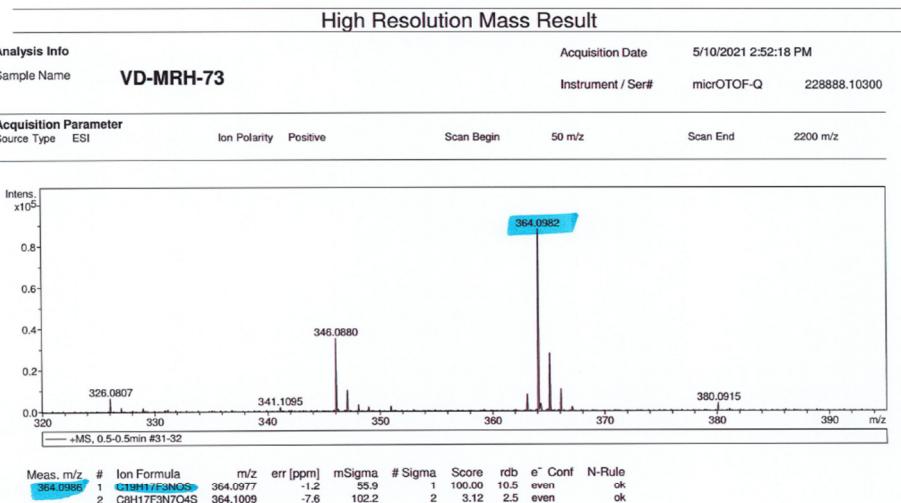
Number of isotope peaks used for i-FIT = 3



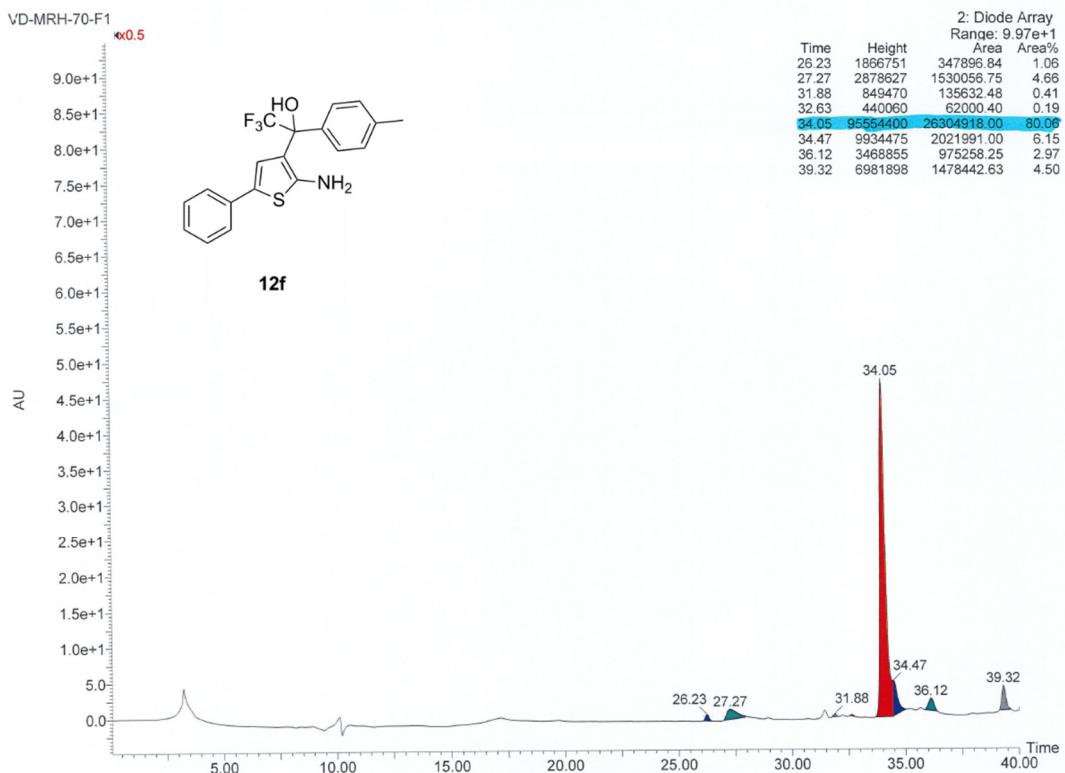
*1-(2-amino-5-phenylthiophen-3-yl)-2,2,2-trifluoro-1-(*p*-tolyl)ethan-1-ol (**12f**)*



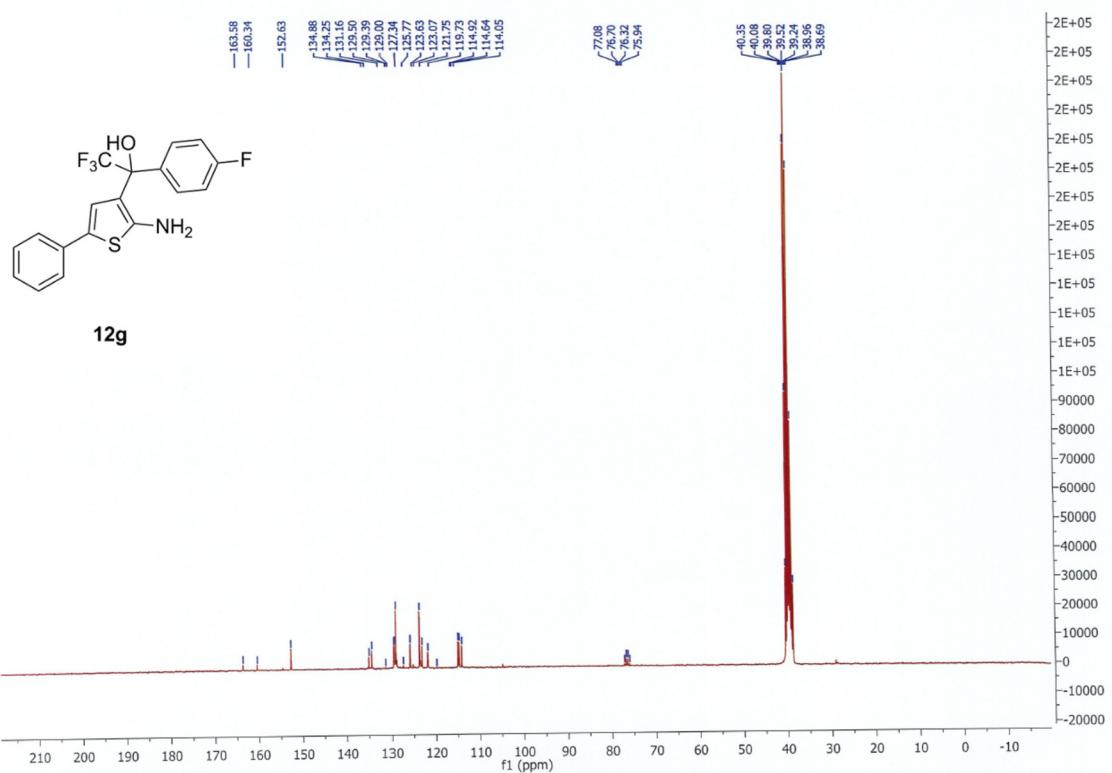
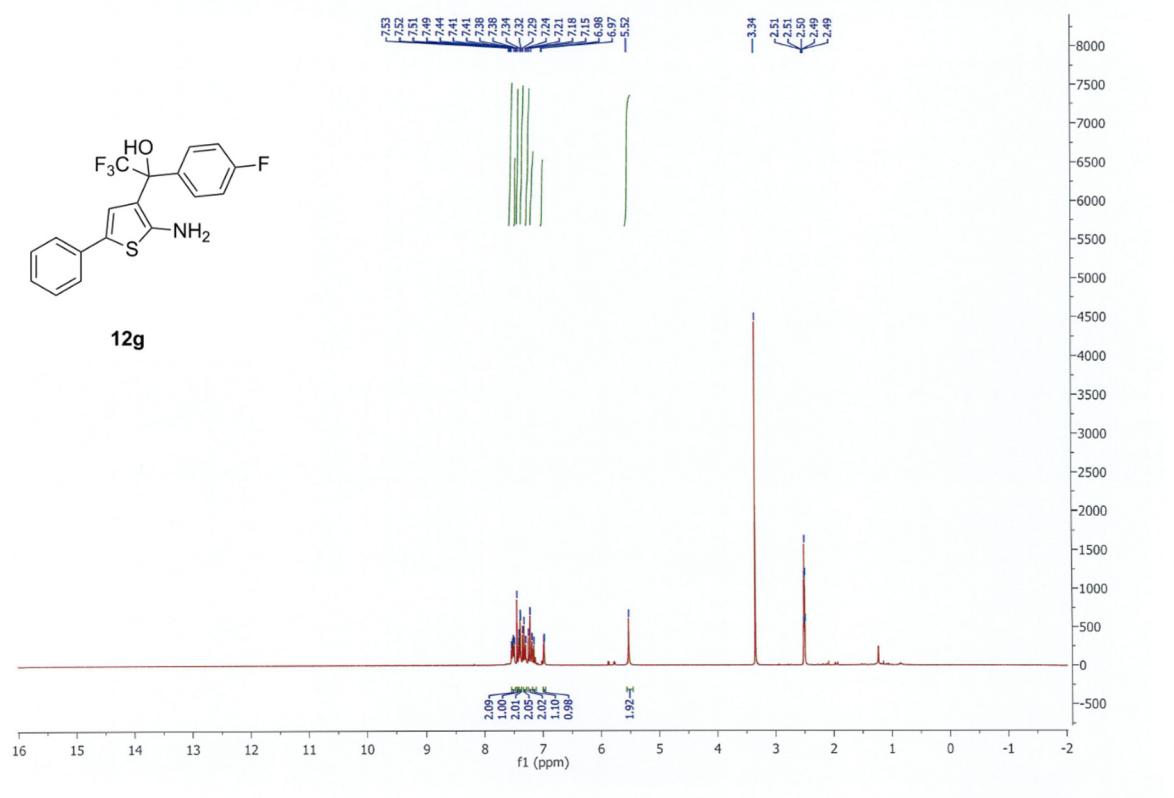


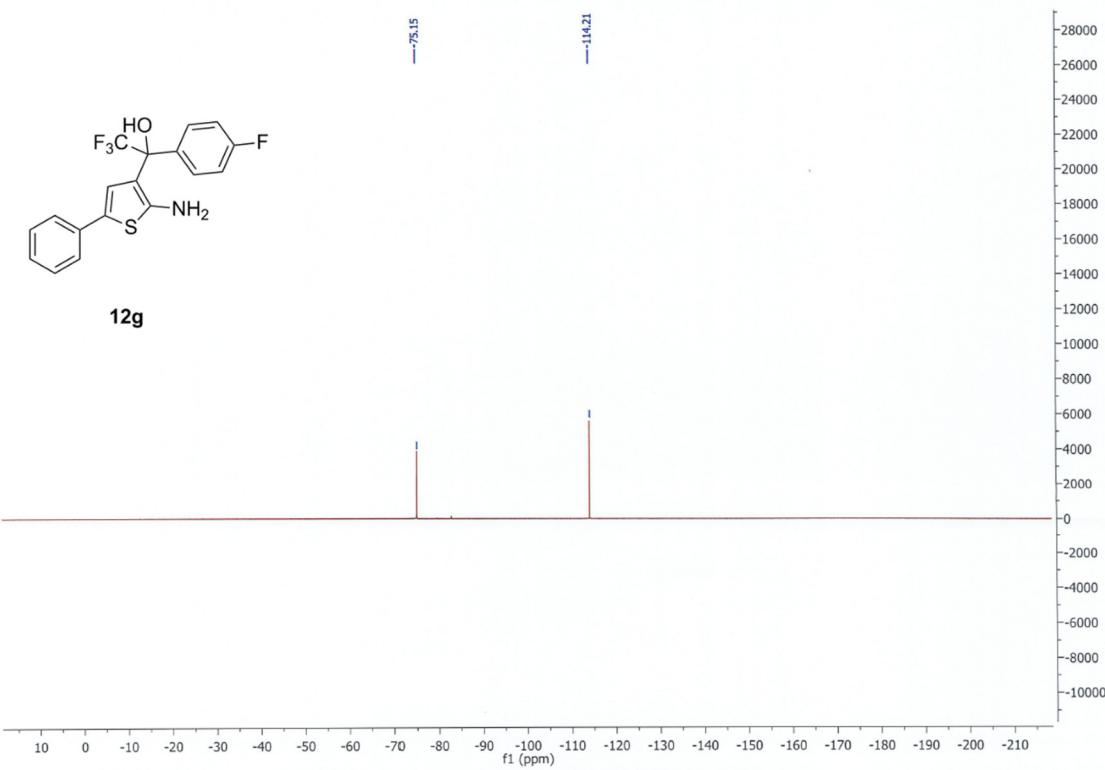
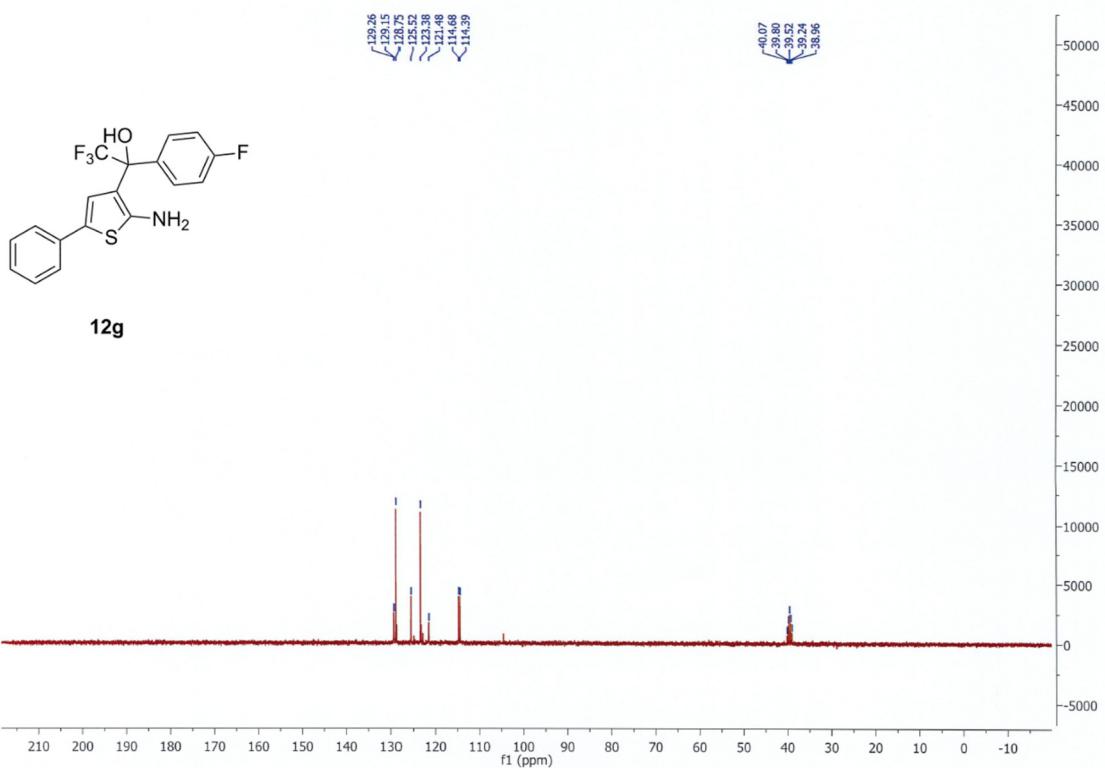


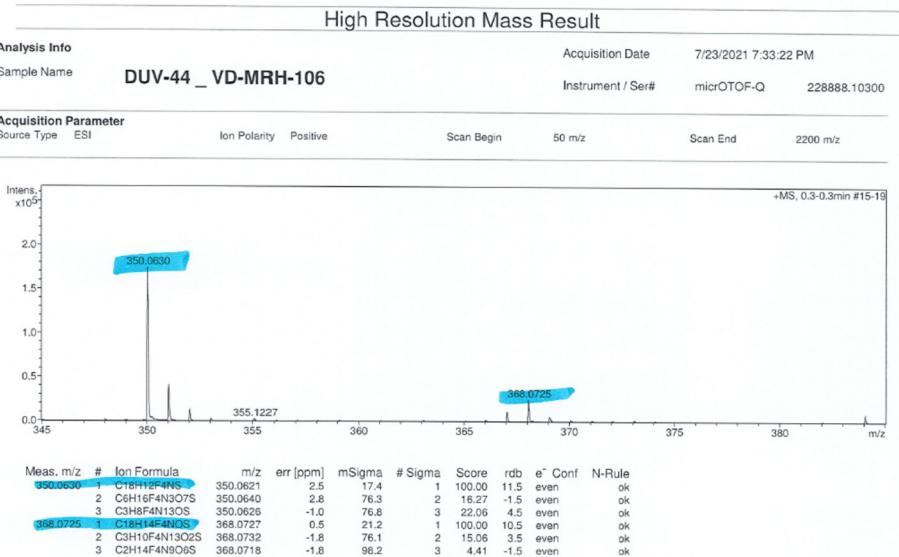
Bruker Compass DataAnalysis 4.1 printed: 5/10/2021 3:40:11 PM Page 1 of 1



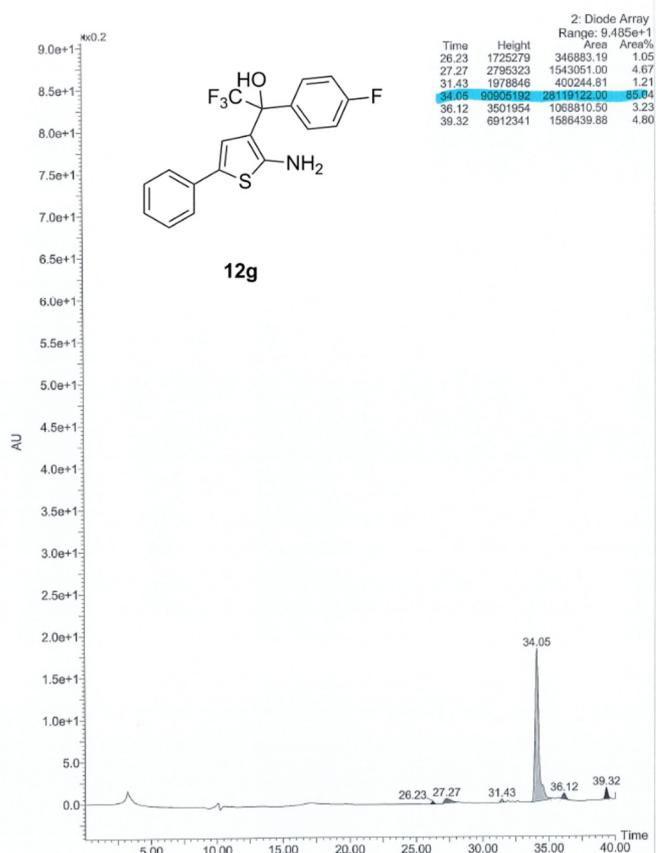
1-(2-amino-5-phenylthiophen-3-yl)-2,2,2-trifluoro-1-(4-fluorophenyl)ethan-1-ol (12g)



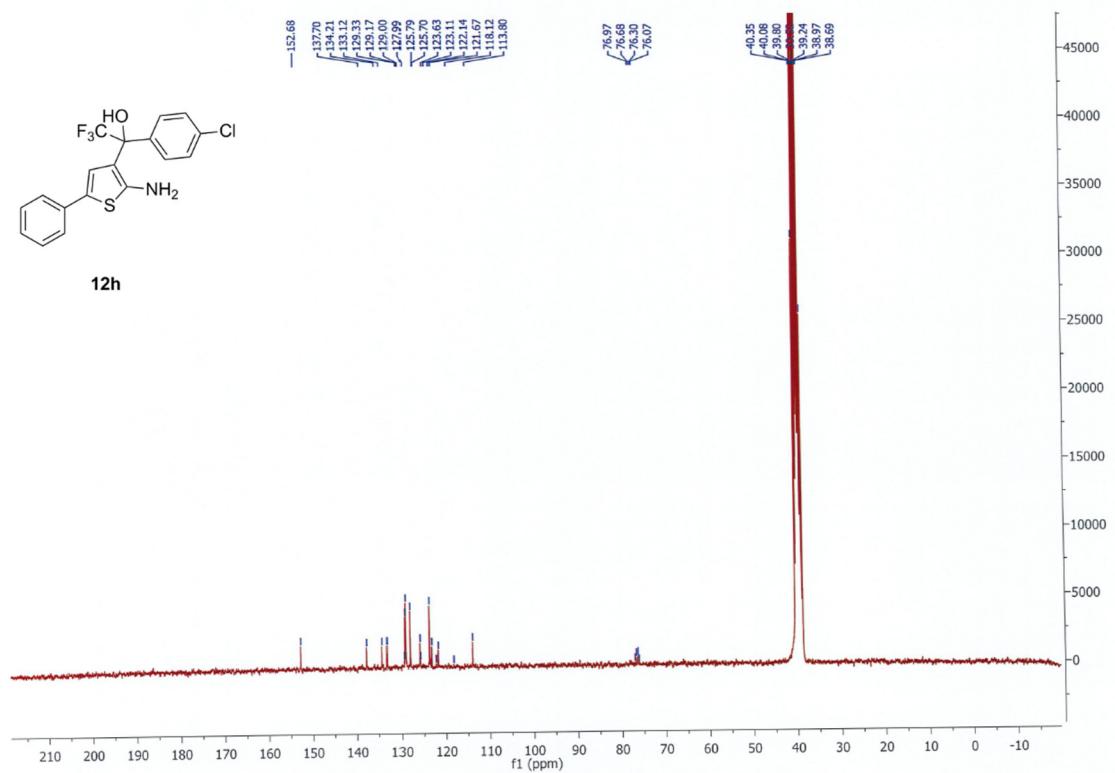
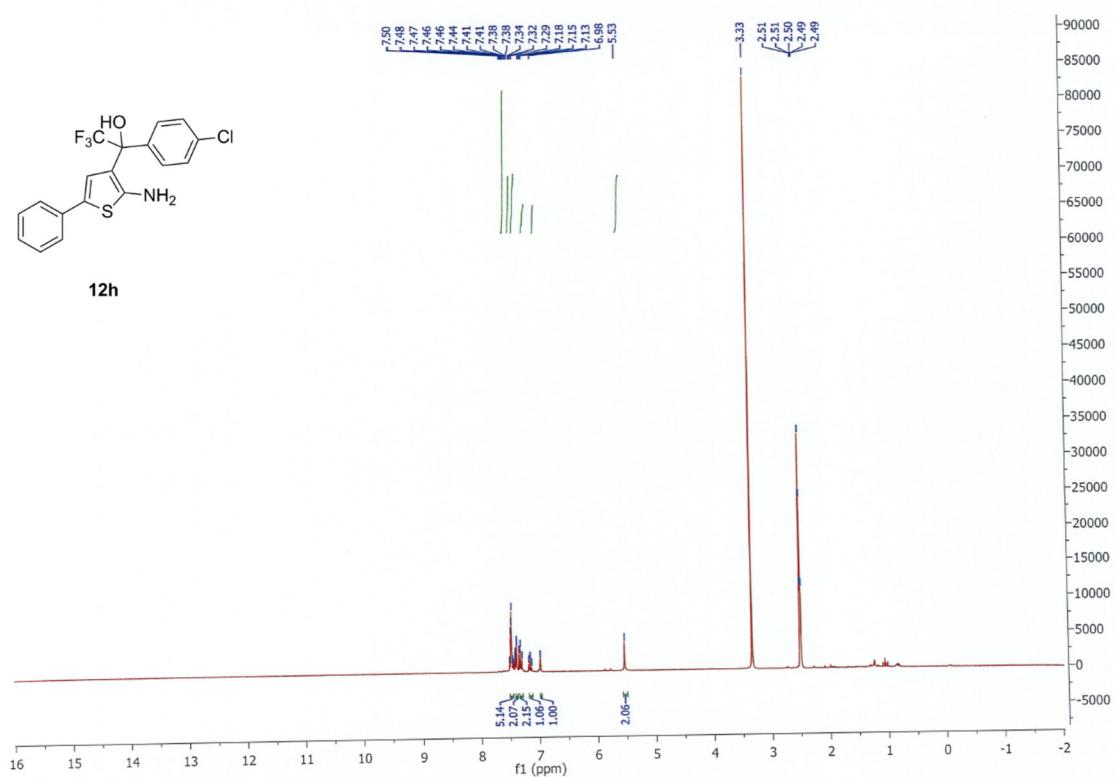


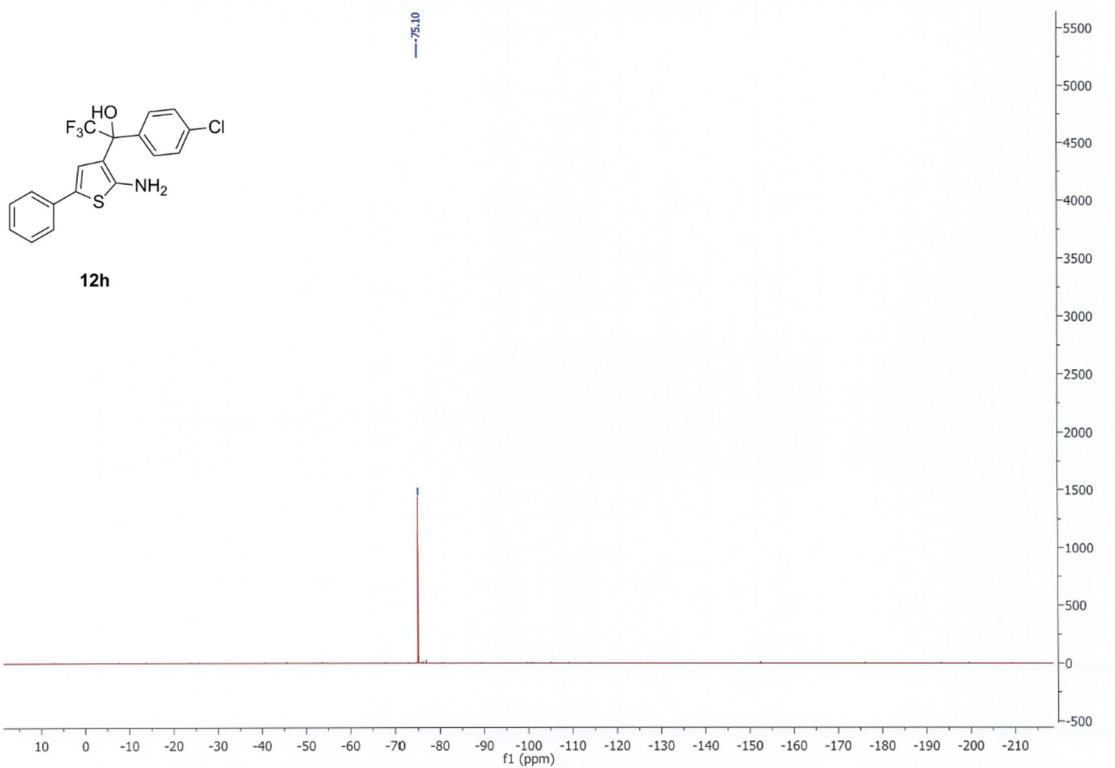
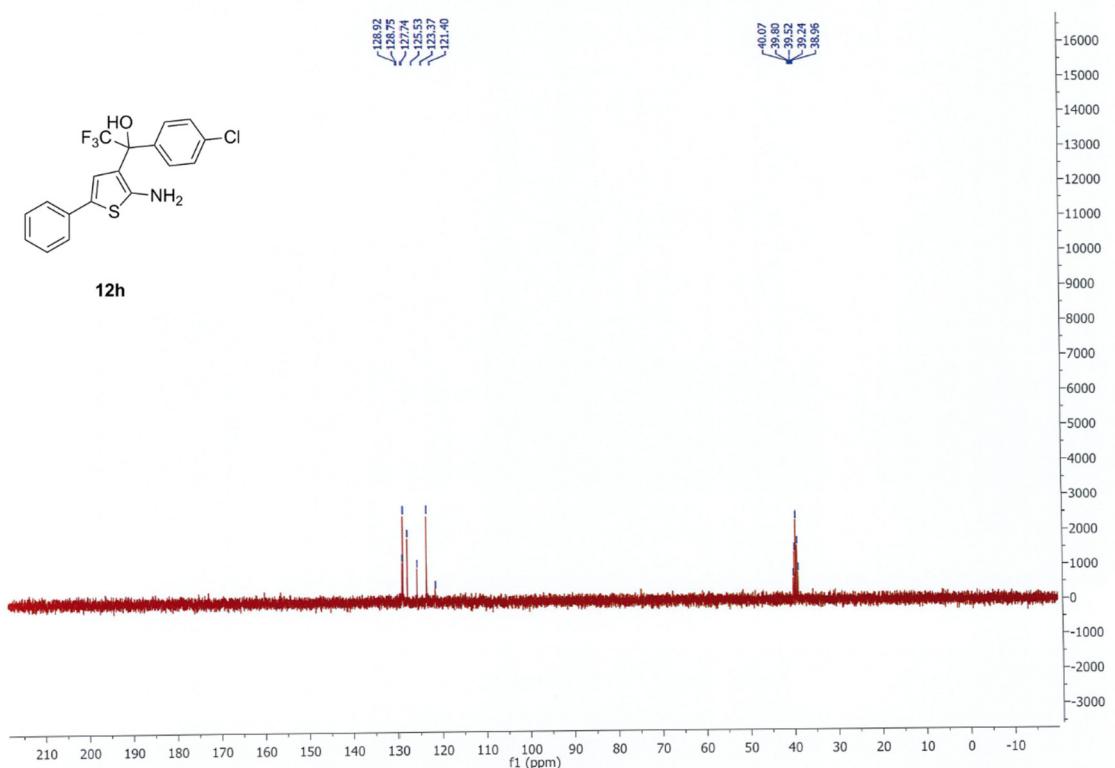


Bruker Compass DataAnalysis 4.1 printed: 7/26/2021 10:22:23 AM Page 1 of 1

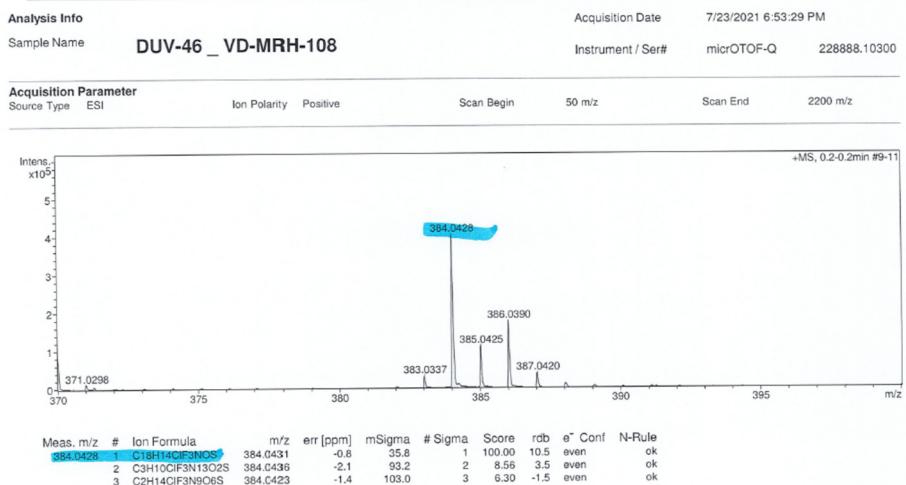


*1-(2-amino-5-phenylthiophen-3-yl)-1-(4-chlorophenyl)-2,2,2-trifluoroethan-1-ol (**12h**)*





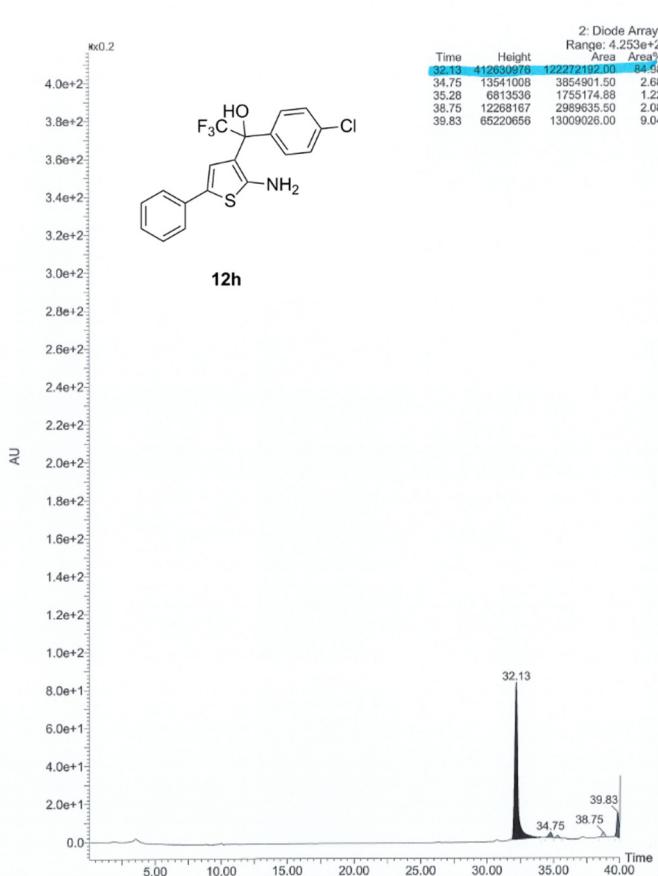
High Resolution Mass Result



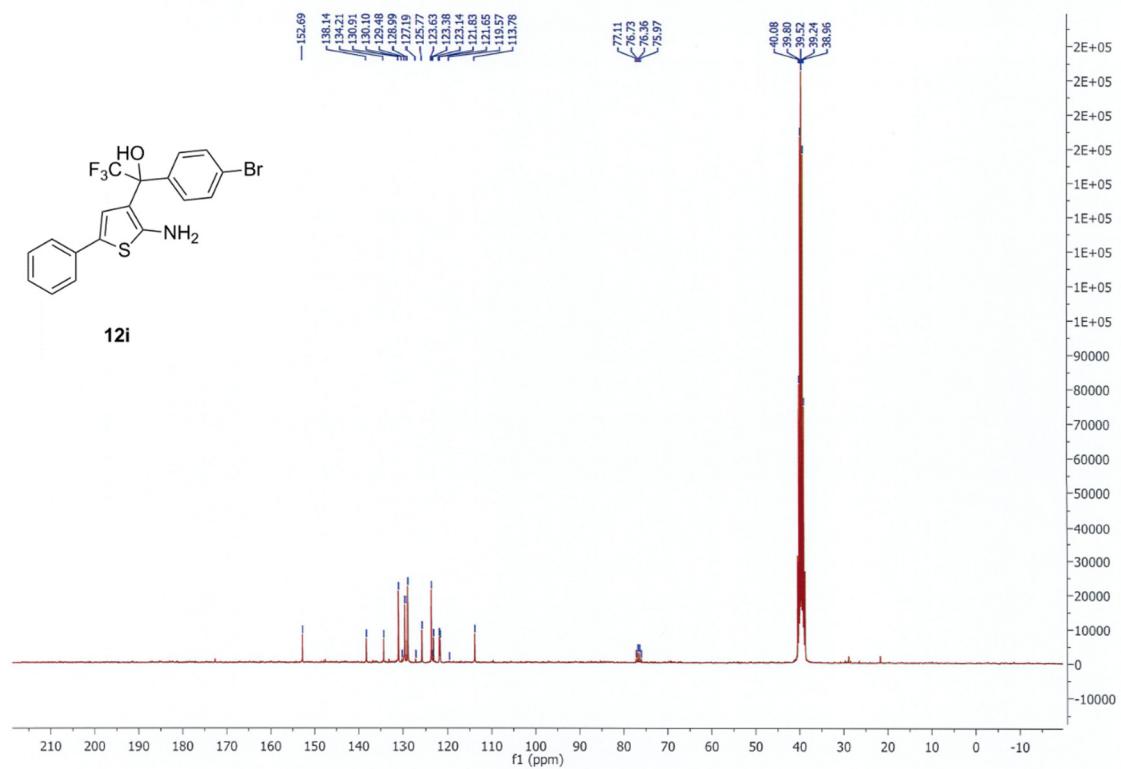
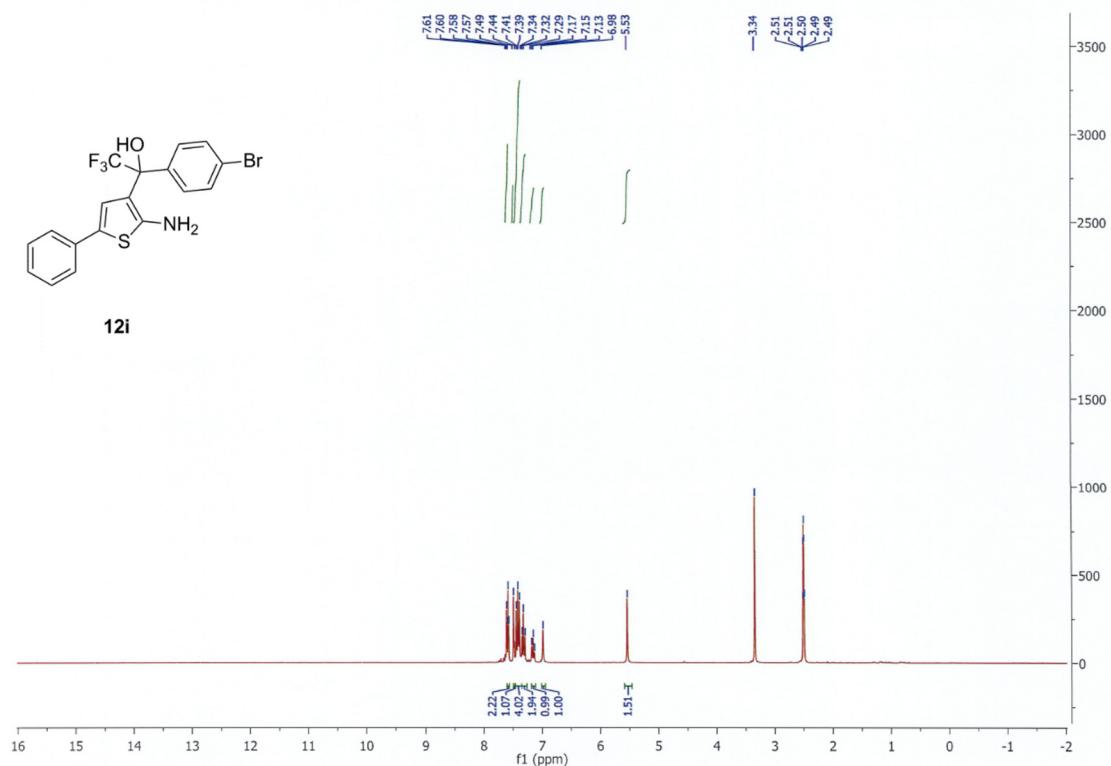
Bruker Compass DataAnalysis 4.1

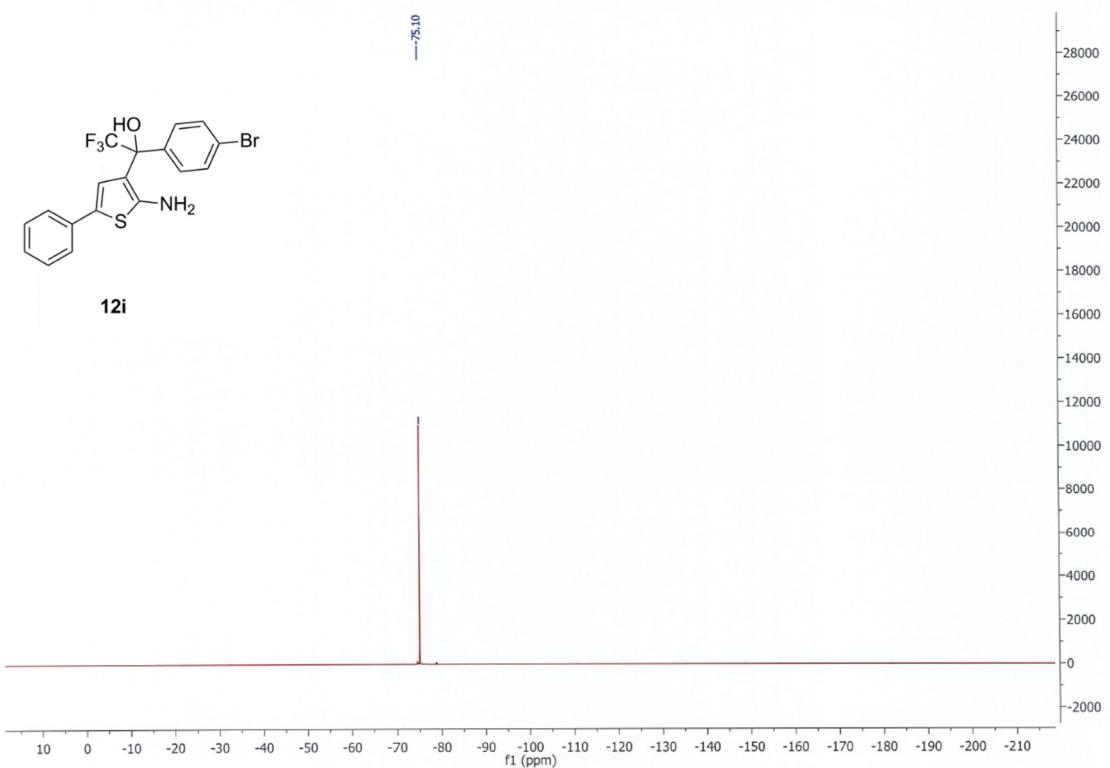
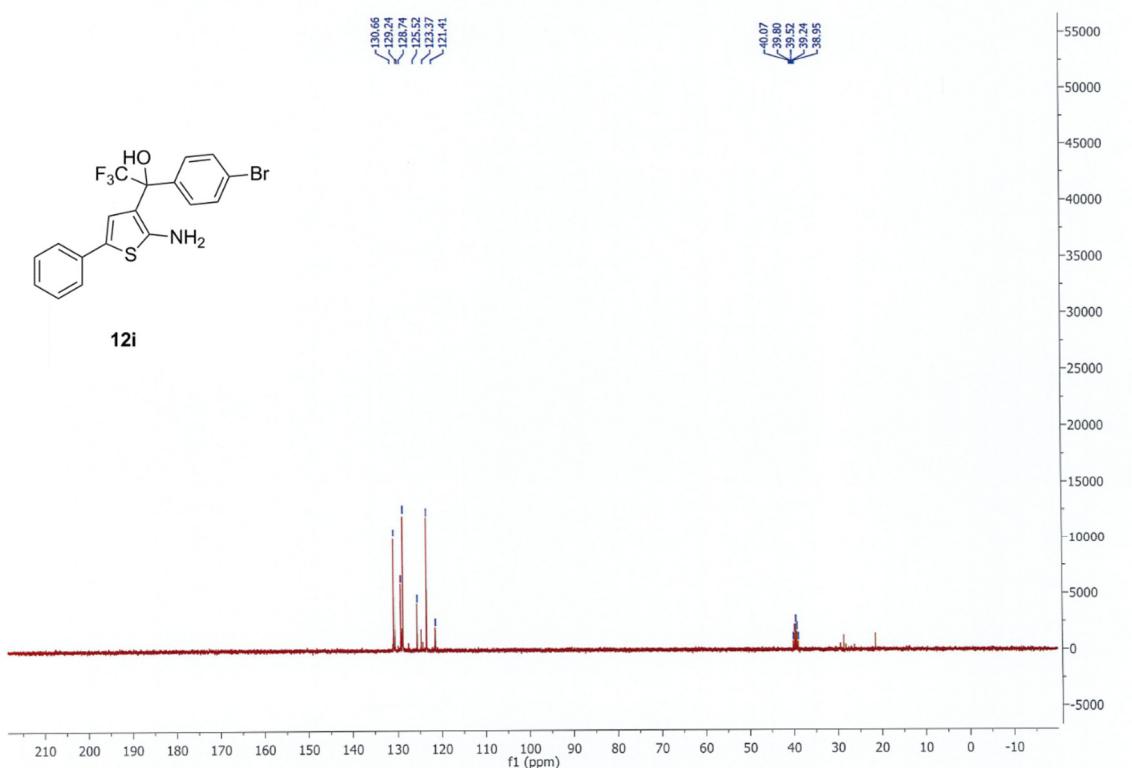
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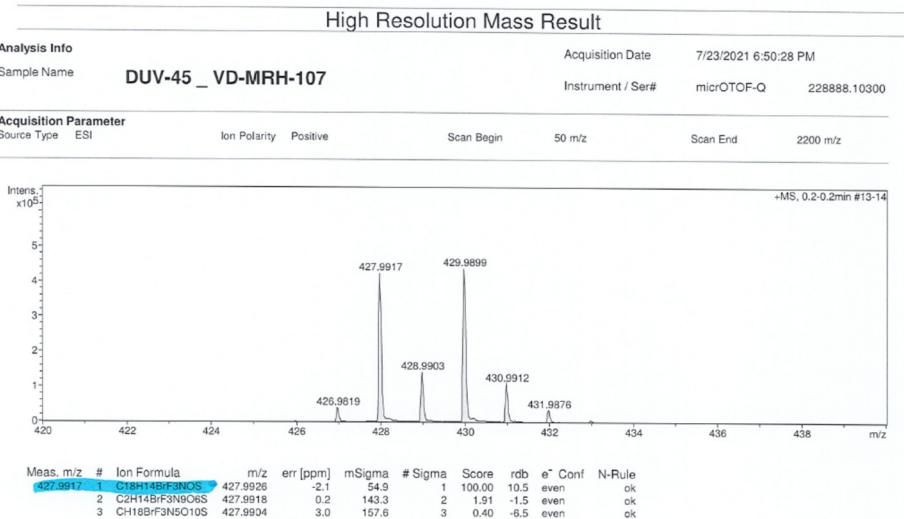
Page 1 of 1



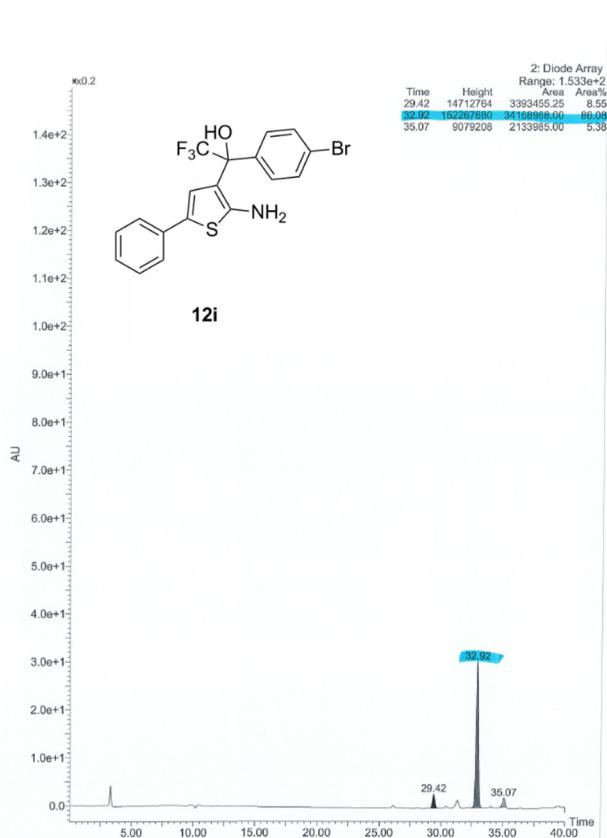
*1-(2-amino-5-phenylthiophen-3-yl)-1-(4-bromophenyl)-2,2,2-trifluoroethan-1-ol (**12i**)*



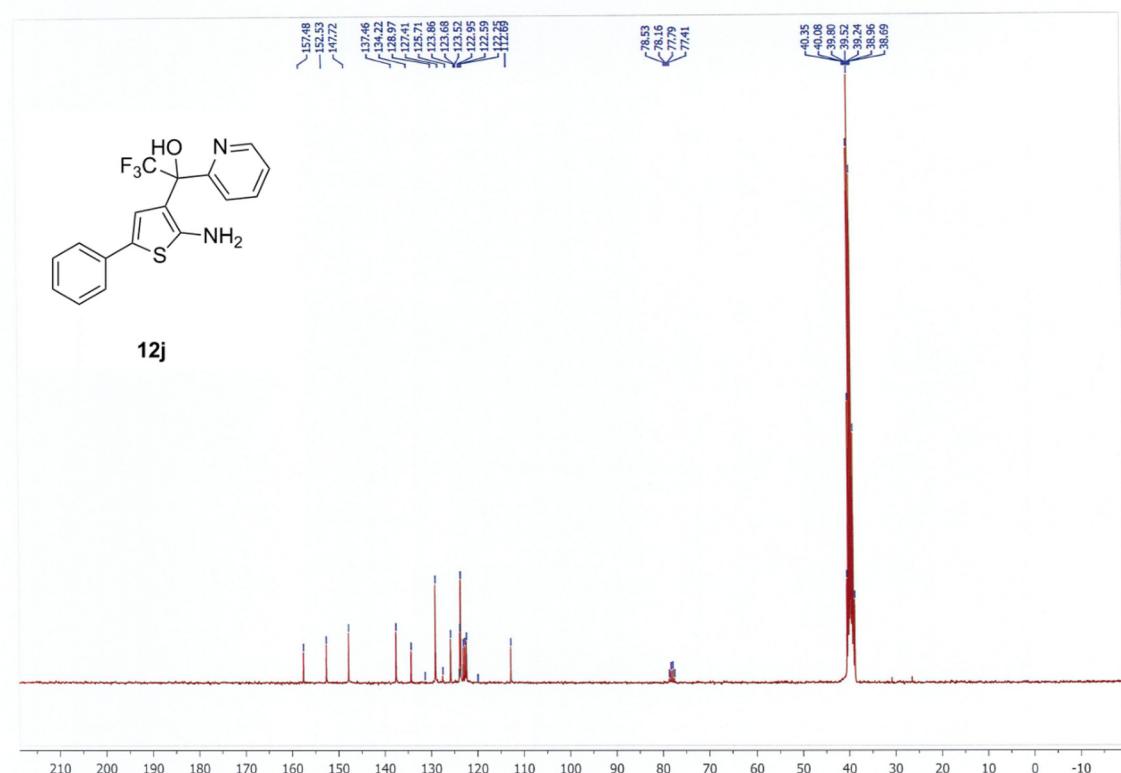
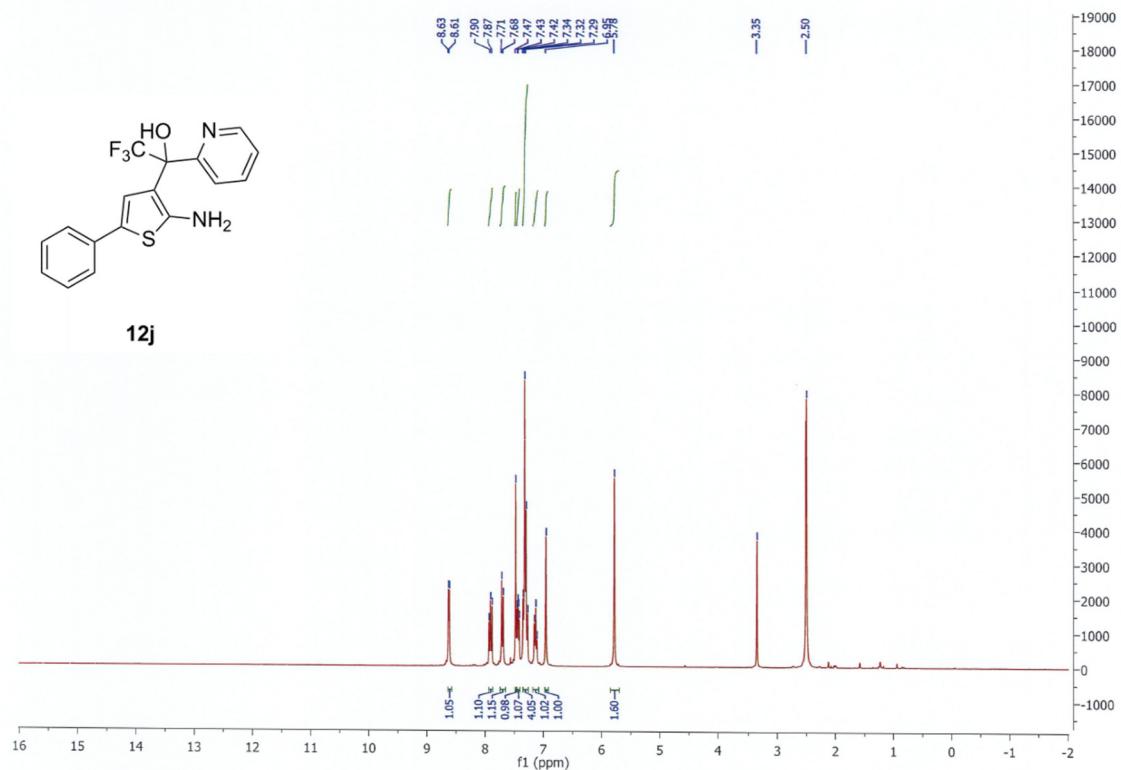


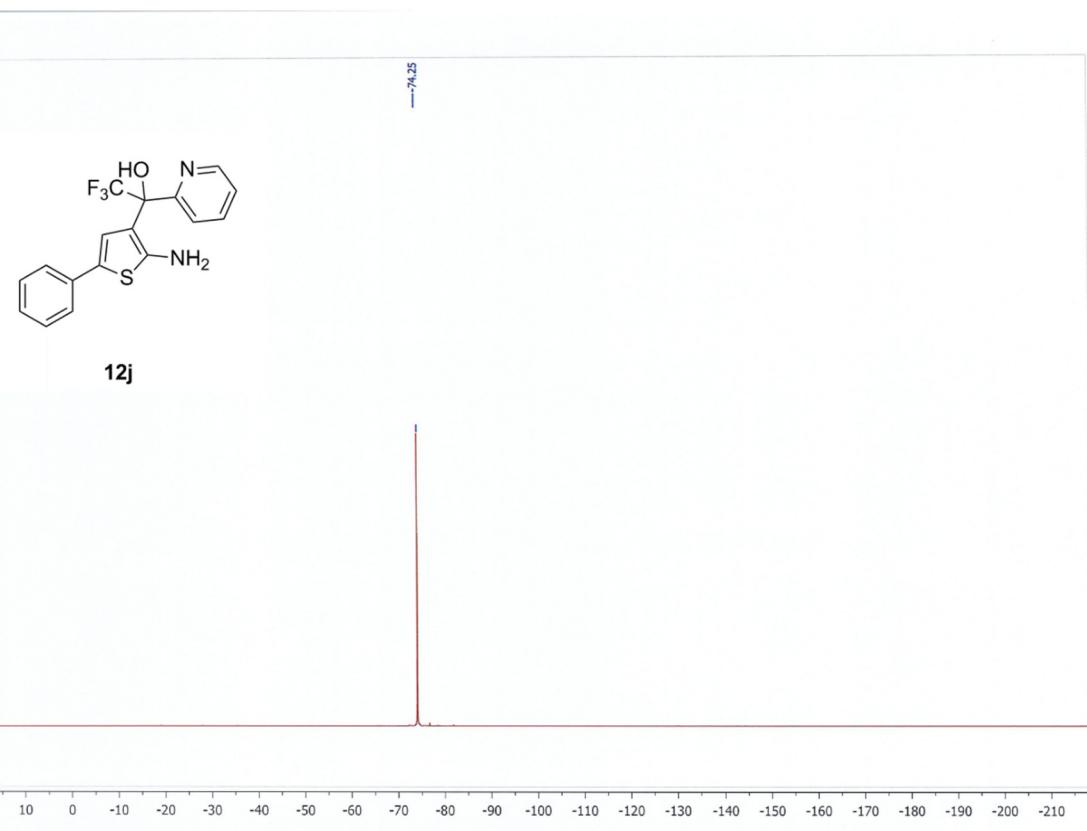
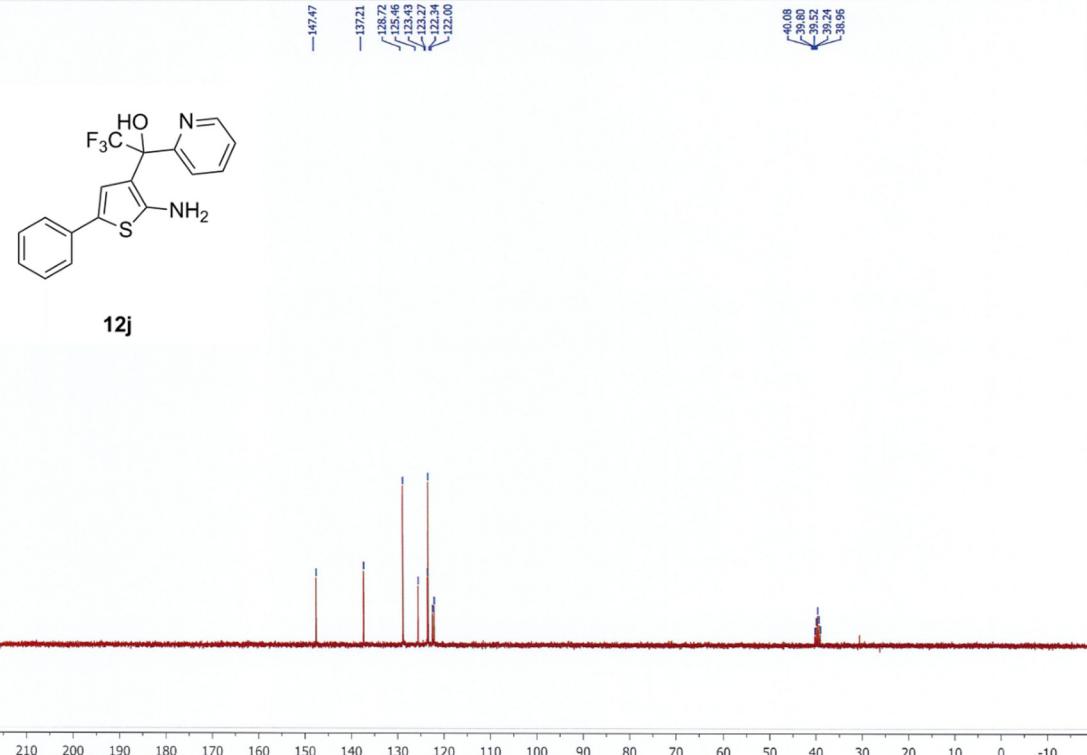


Bruker Compass DataAnalysis 4.1 printed: 7/23/2021 7:01:48 PM Page 1 of 1



*1-(2-amino-5-phenylthiophen-3-yl)-2,2,2-trifluoro-1-(pyridin-2-yl)ethan-1-ol (**12j**)*





Elemental Composition Report

Single Mass Analysis

Tolerance = 3.0 mDa / DBE: min = -1.0, max = 100.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

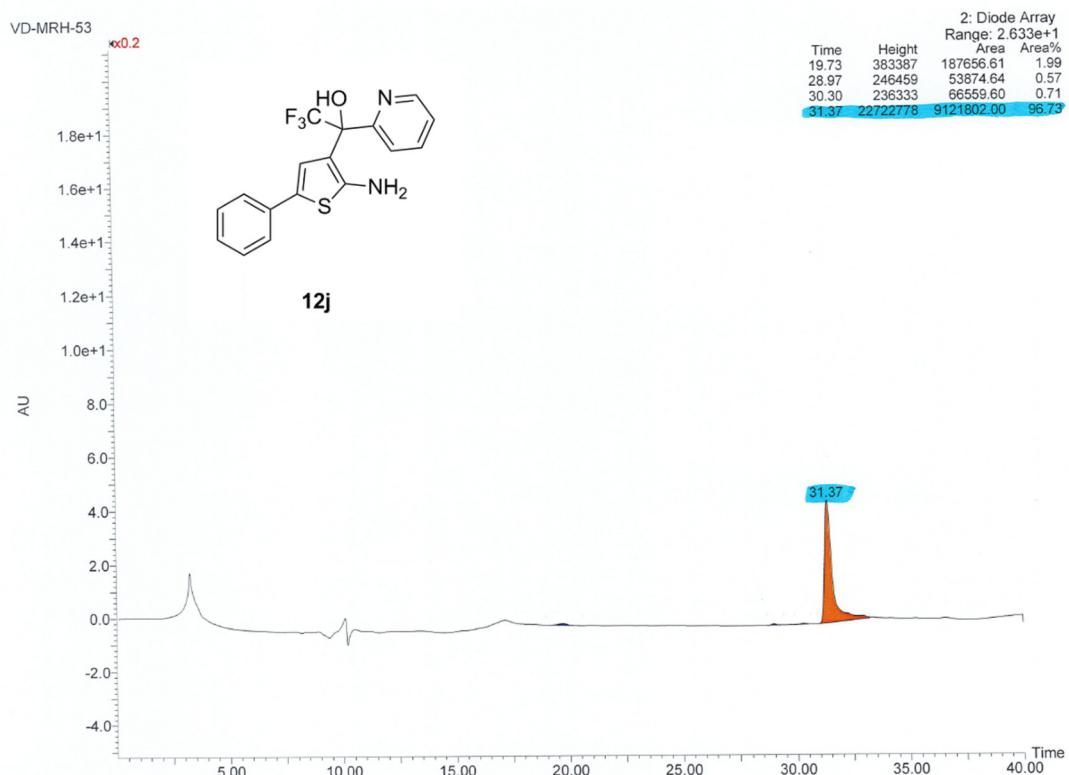
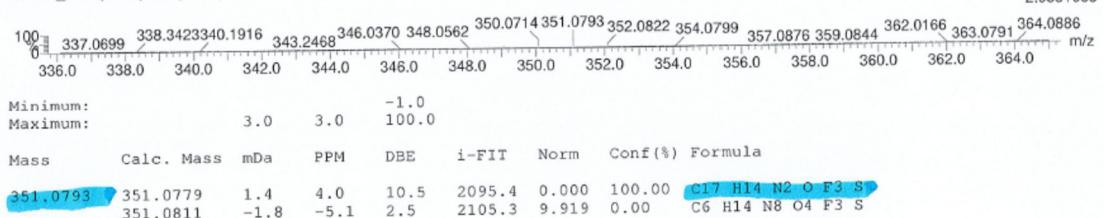
Monoisotopic Mass, Even Electron Ions

282 formula(e) evaluated with 2 results within limits (up to 50 best isotopic matches for each mass)

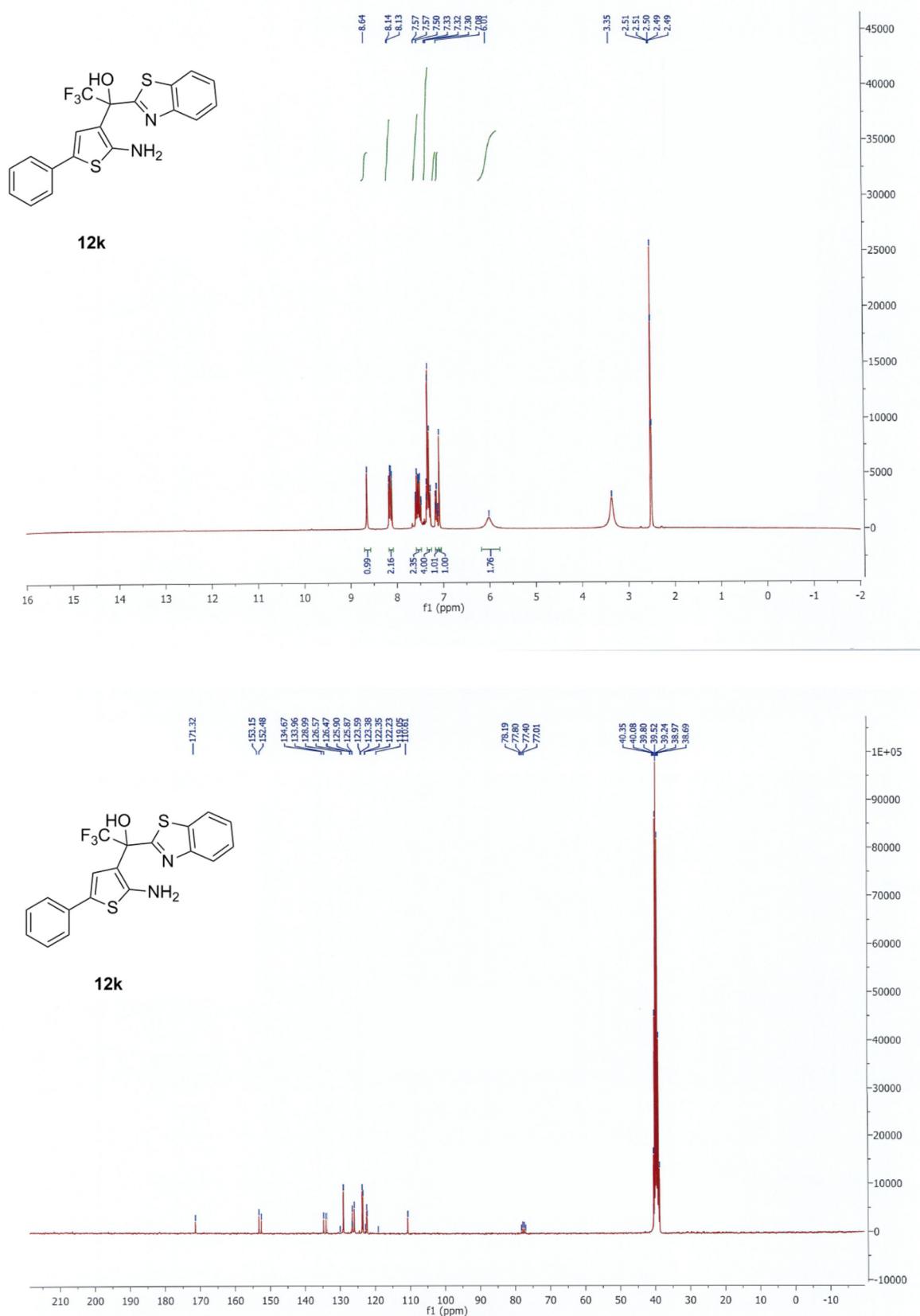
Elements Used:

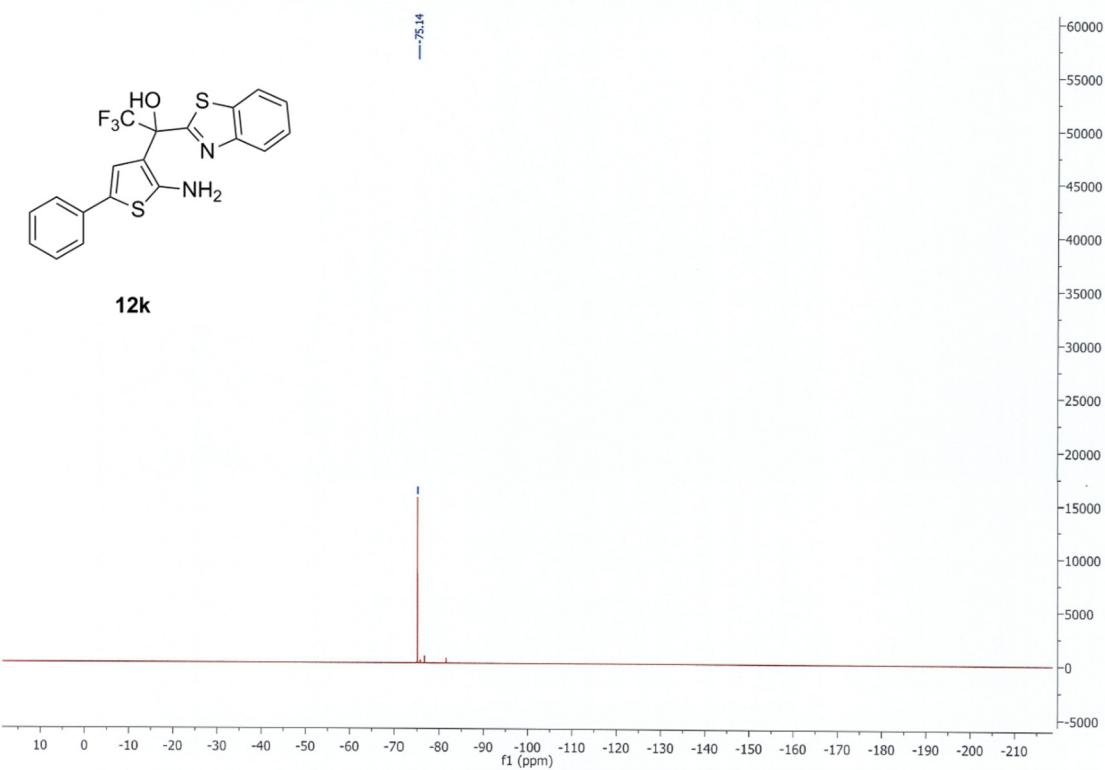
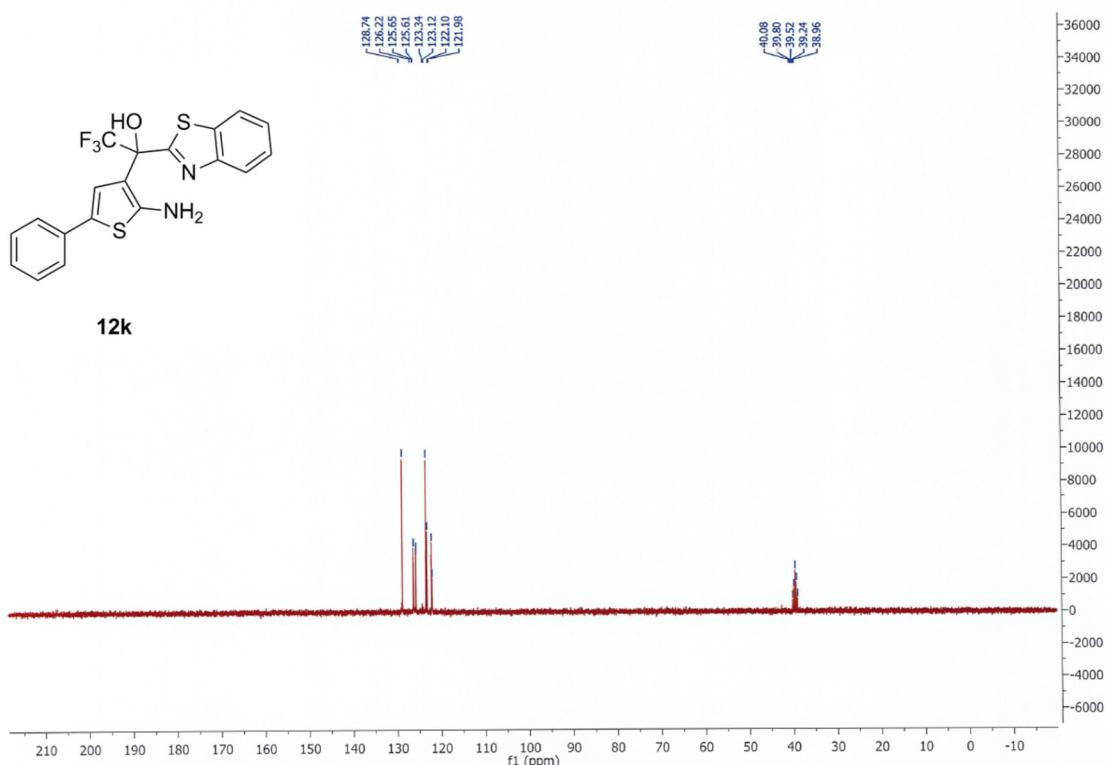
C: 0-100 H: 0-100 N: 0-10 O: 0-10 F: 3-3 S: 1-1

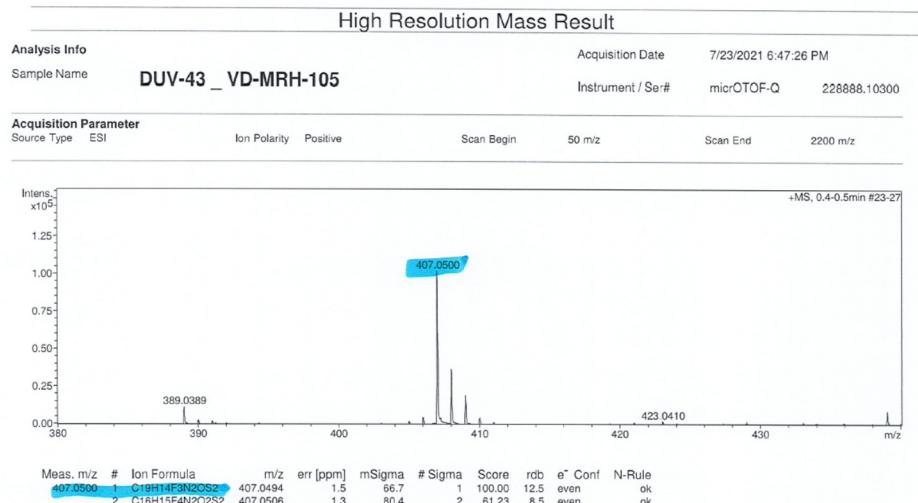
VD-MRH-53

02-Feb-2021
1: TOF MS ES+
2.98e+05SYNAPT G2-S⁺NotSet
CHR-2_1 12 (0.211) Cm (10:14)

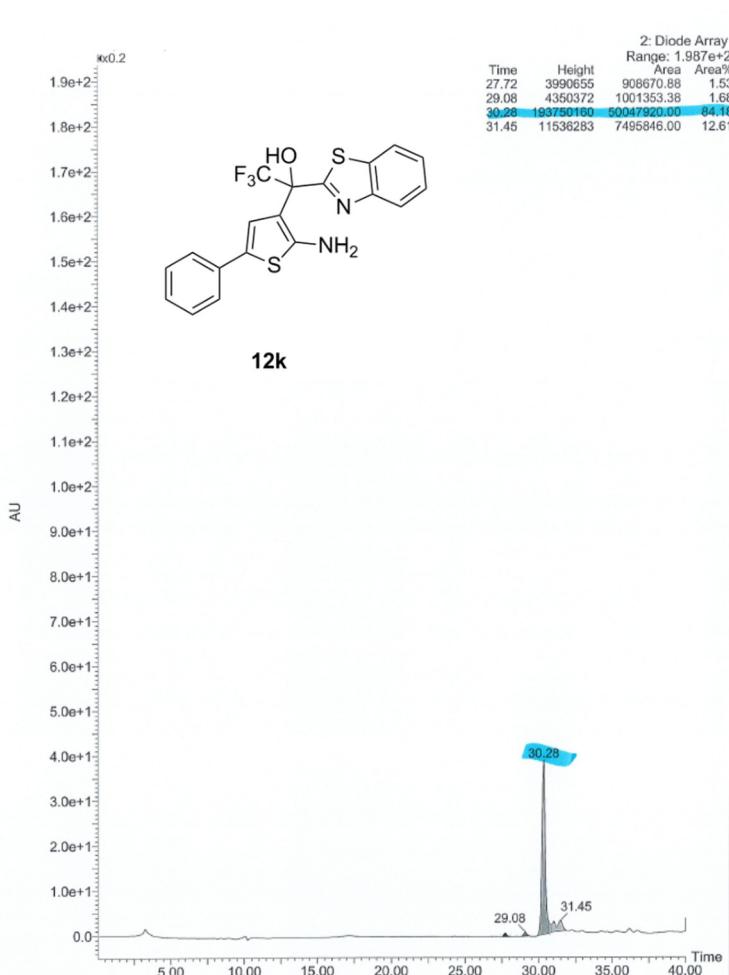
1-(2-amino-5-phenylthiophen-3-yl)-1-(benzo[d]thiazol-2-yl)-2,2,2-trifluoroethan-1-ol (12k)



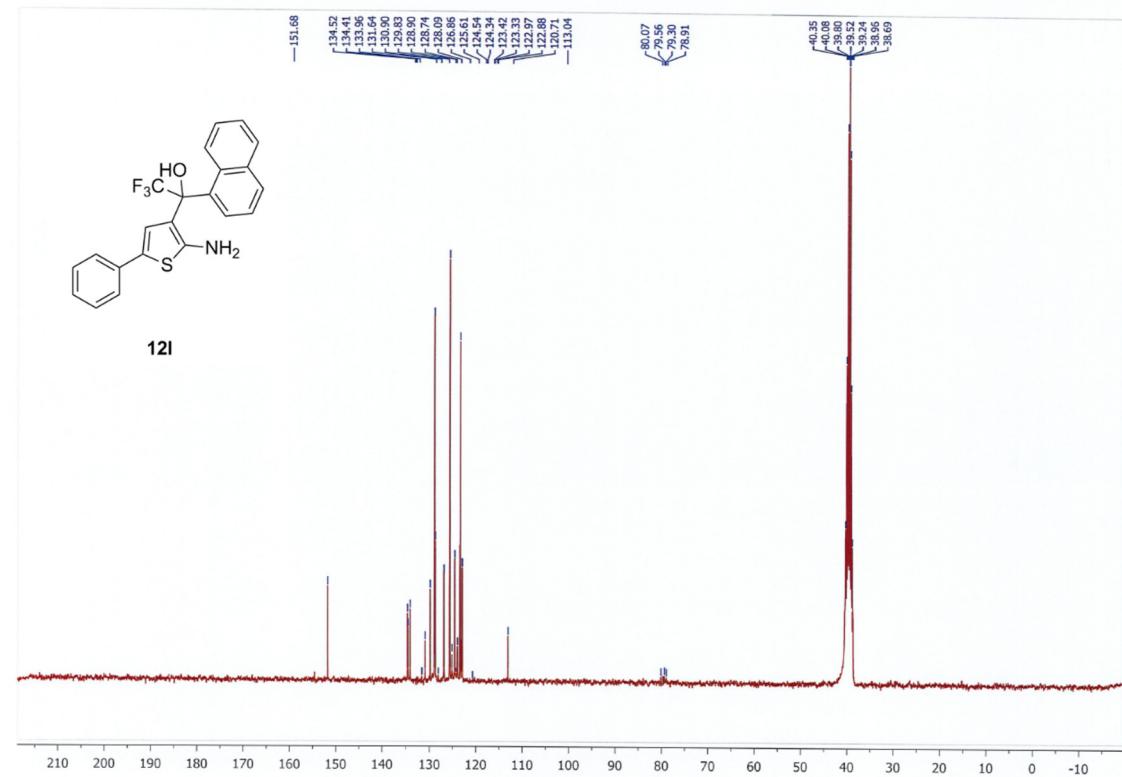
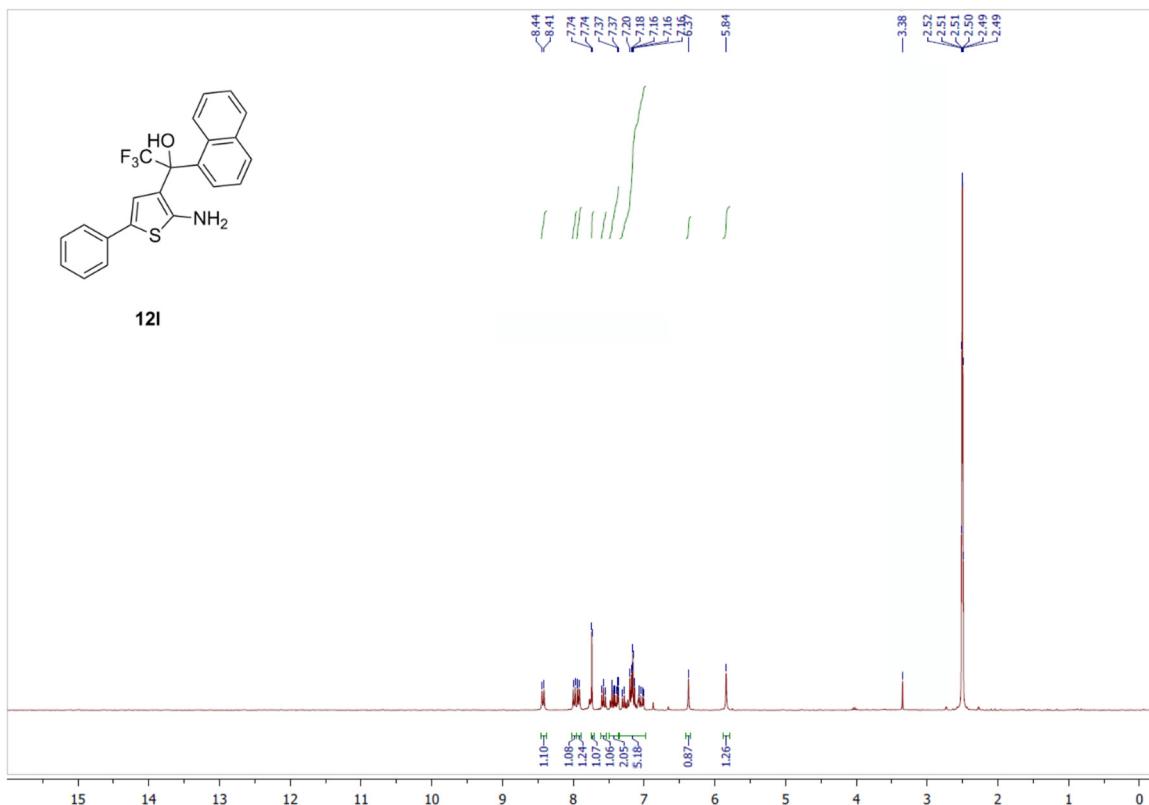


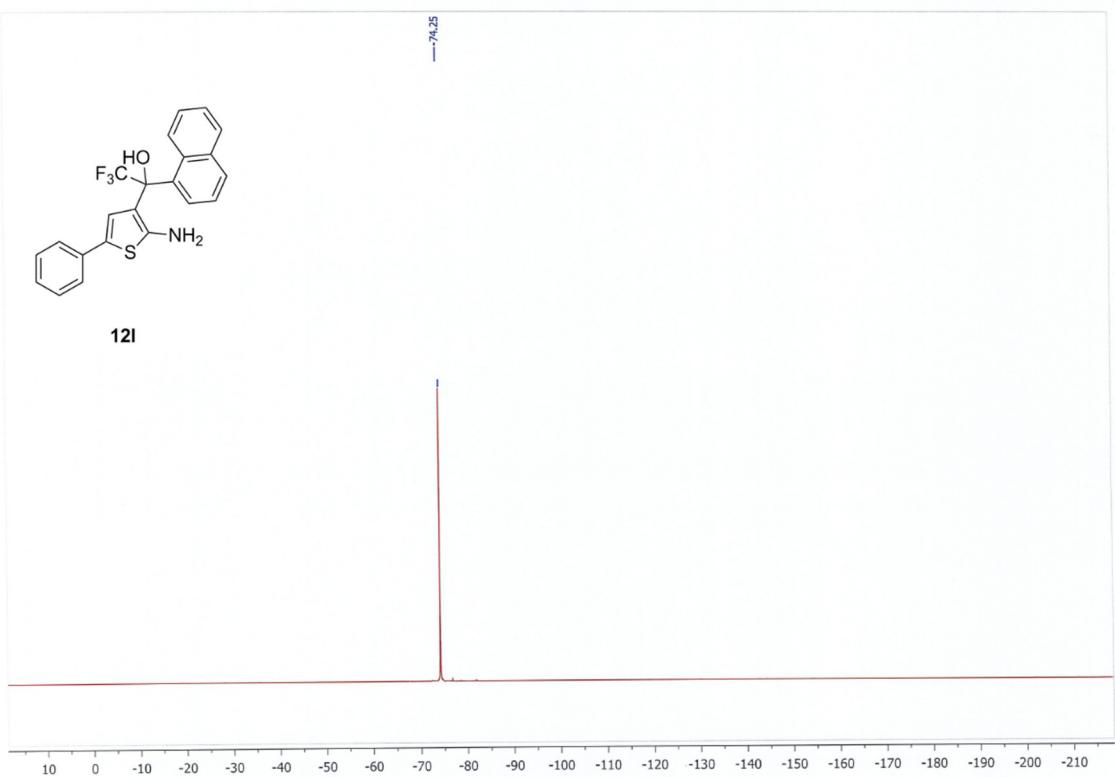
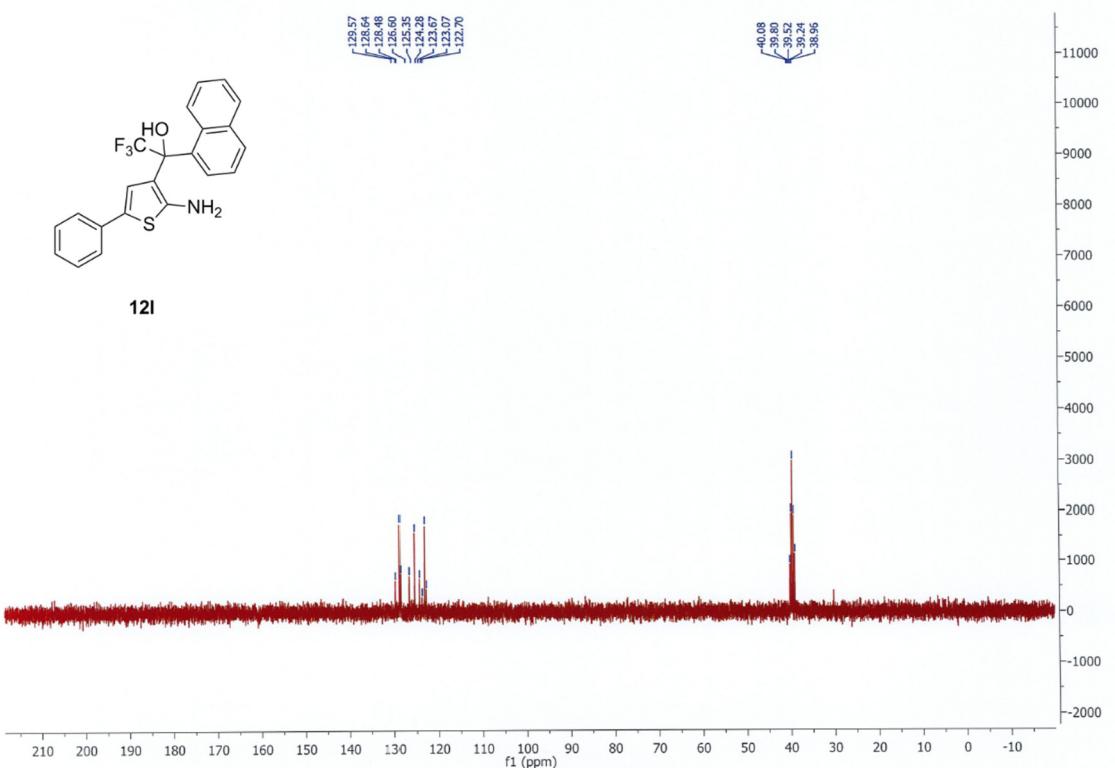


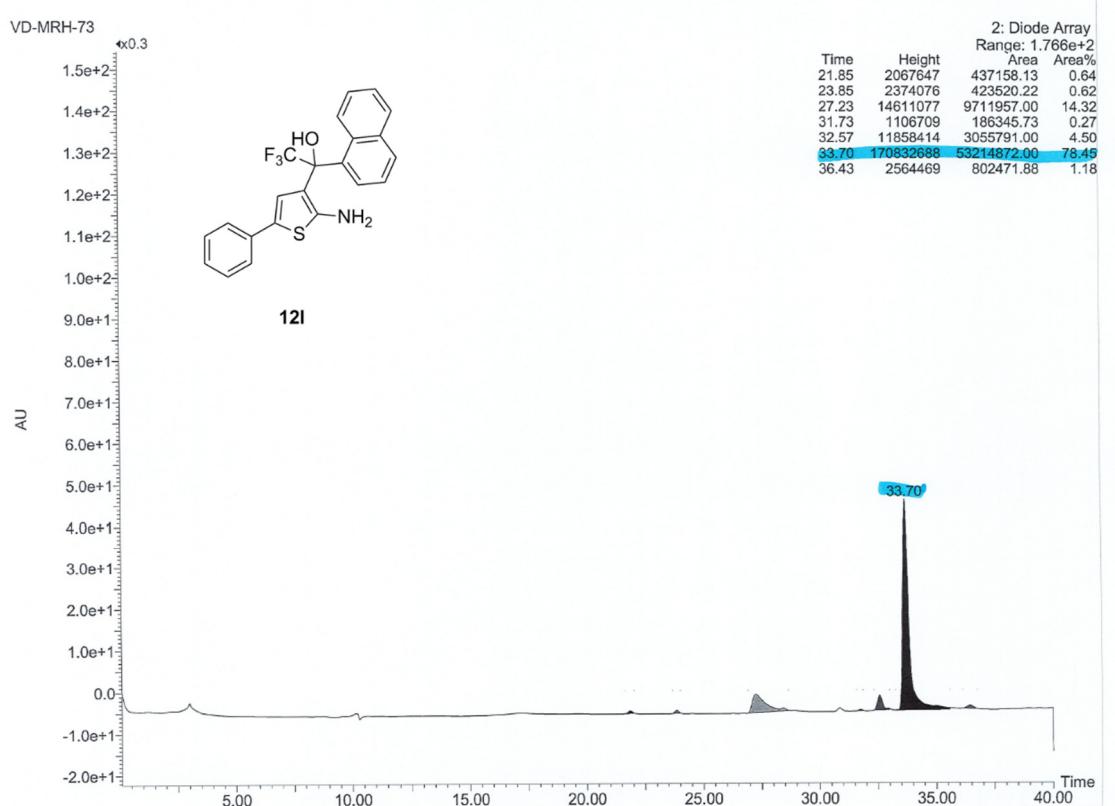
Bruker Compass DataAnalysis 4.1 printed: 7/23/2021 6:55:07 PM Page 1 of 1



*1-(2-amino-5-phenylthiophen-3-yl)-2,2,2-trifluoro-1-(naphthalen-1-yl)ethan-1-ol (**12l**)*



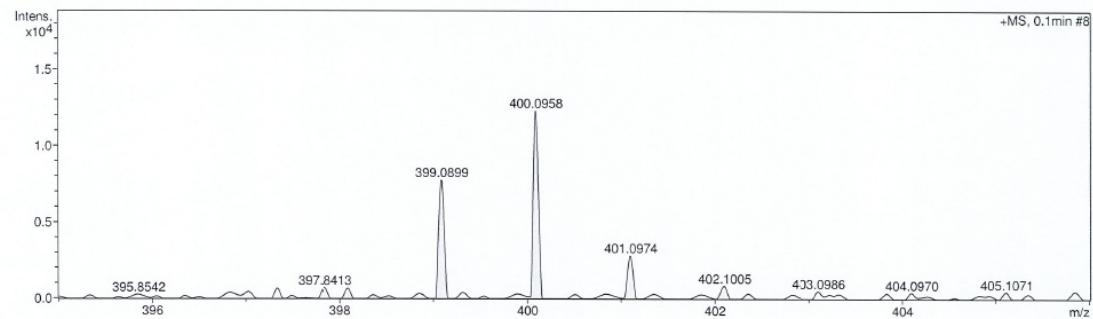




High Resolution Mass Result

Analysis Info		Acquisition Date	5/10/2021 2:52:18 PM
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Source Type	ESI						



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rb	e ⁻ Conf	N-Rule
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400.0958	1	C₂₂H₁₇F₃NO₃S	400.0977	4.9	18.7	1	100.00	13.5	even	ok
432.0871	1	C ₂₂ H ₁₇ F ₃ NO ₃ S	432.0876	1.1	13.5	1	100.00	13.5	even	ok
	2	C ₁₈ H ₁₃ F ₃ N ₇ O ₉ S	432.0849	-5.1	23.2	2	26.92	14.5	even	ok