

Synthesis and Biological Evaluation of Selective Survivin Inhibitors Derived from the MX 106 Scaffold

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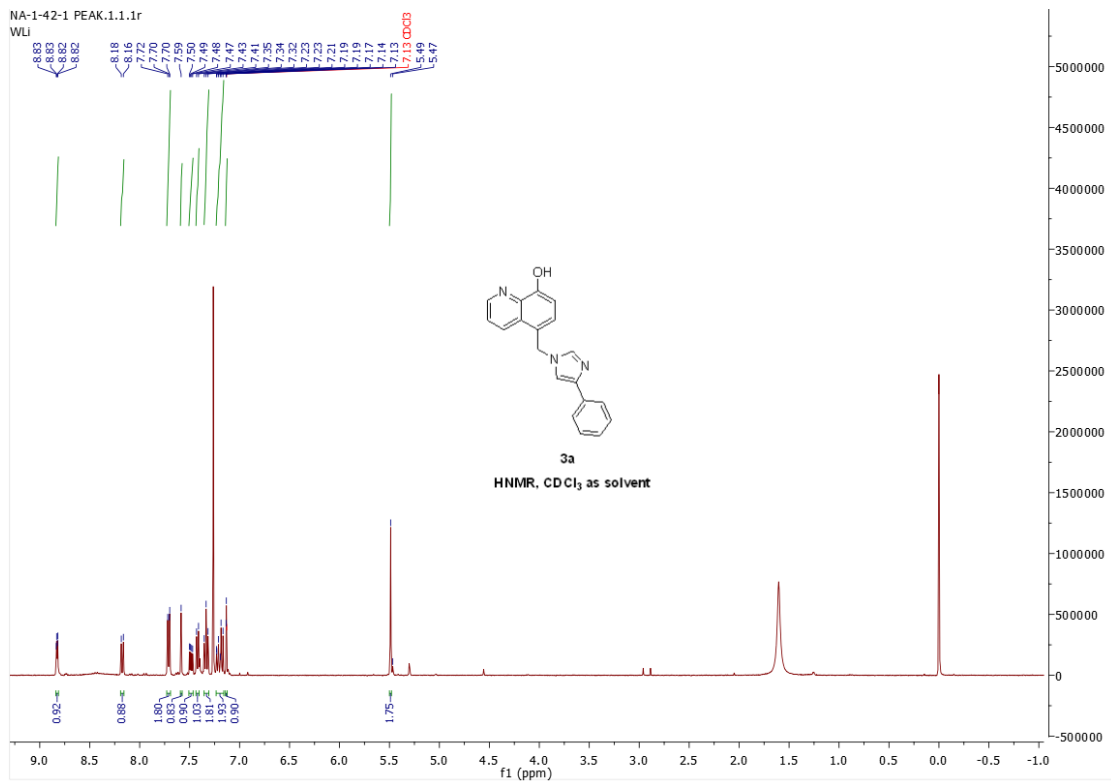
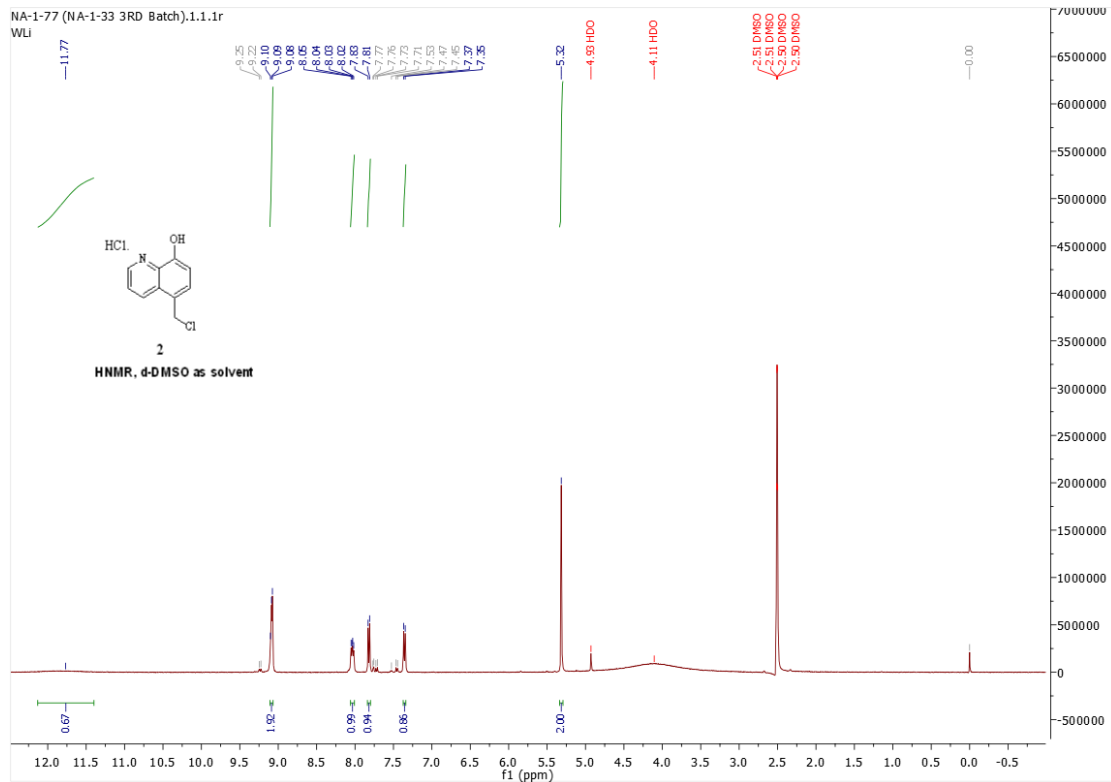
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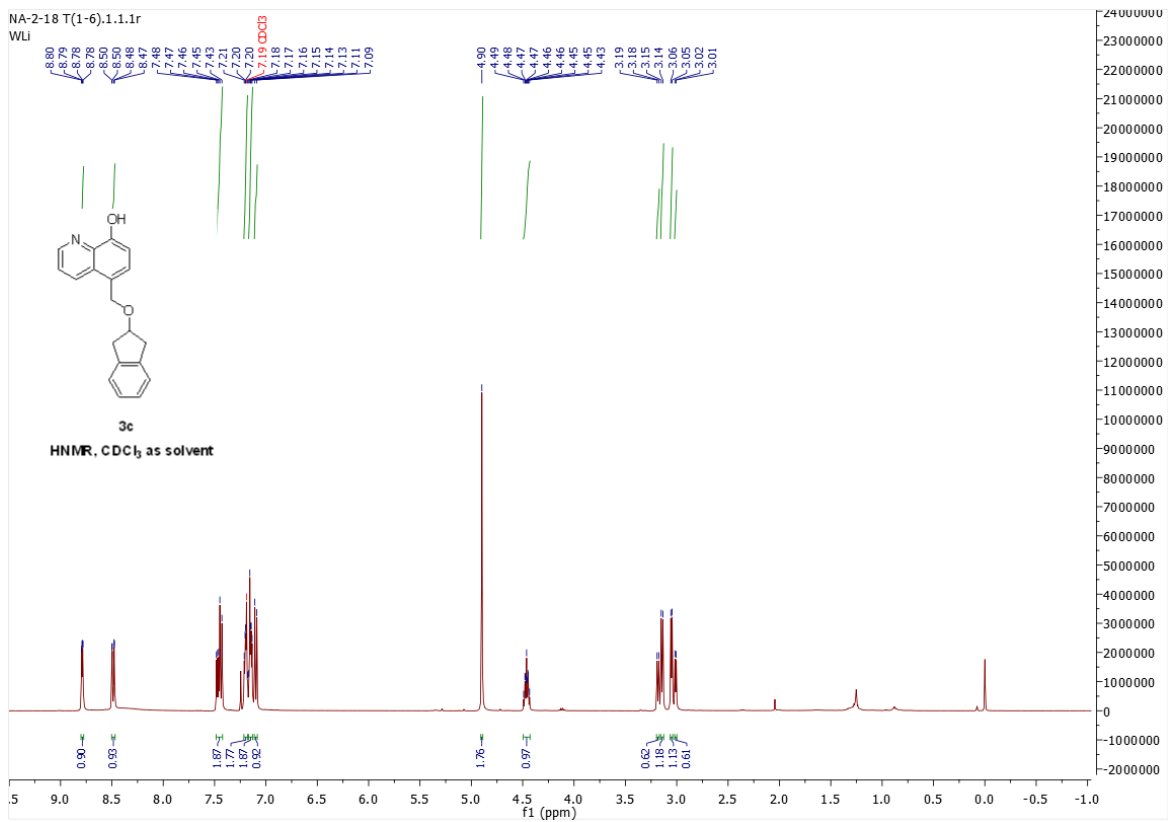
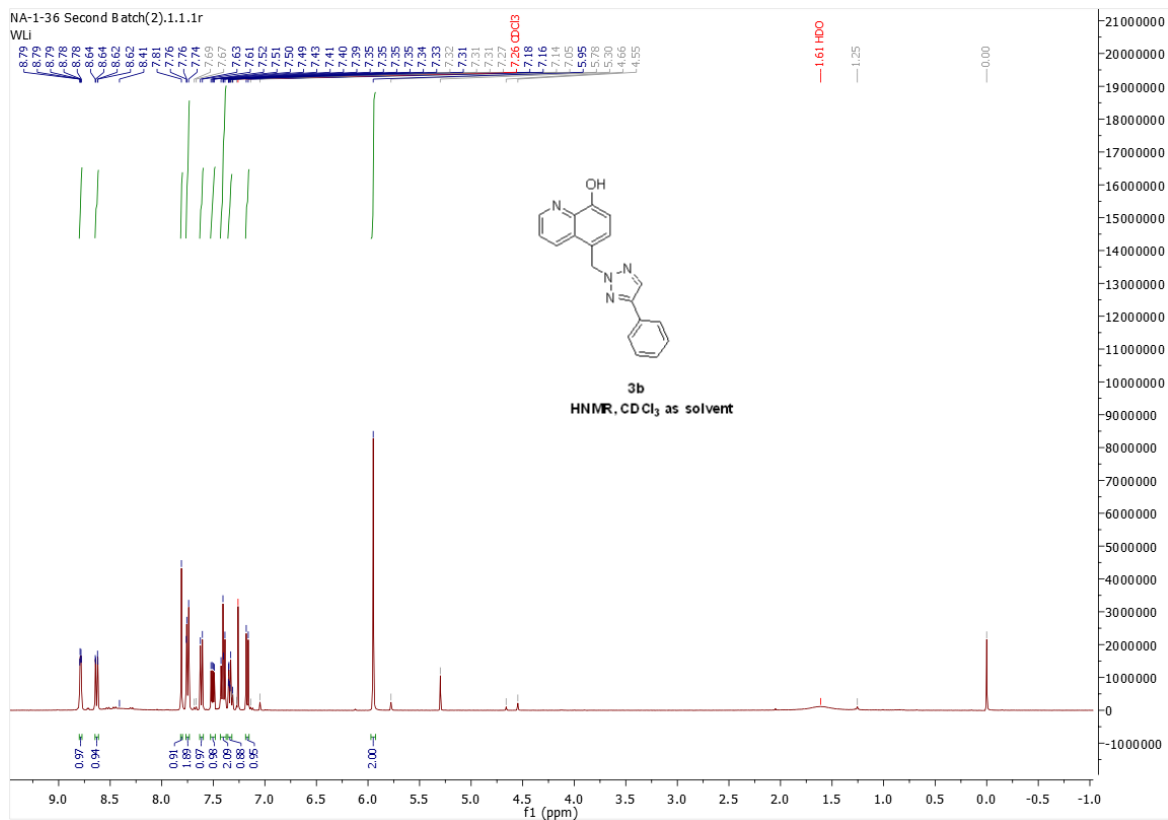
Supporting Information

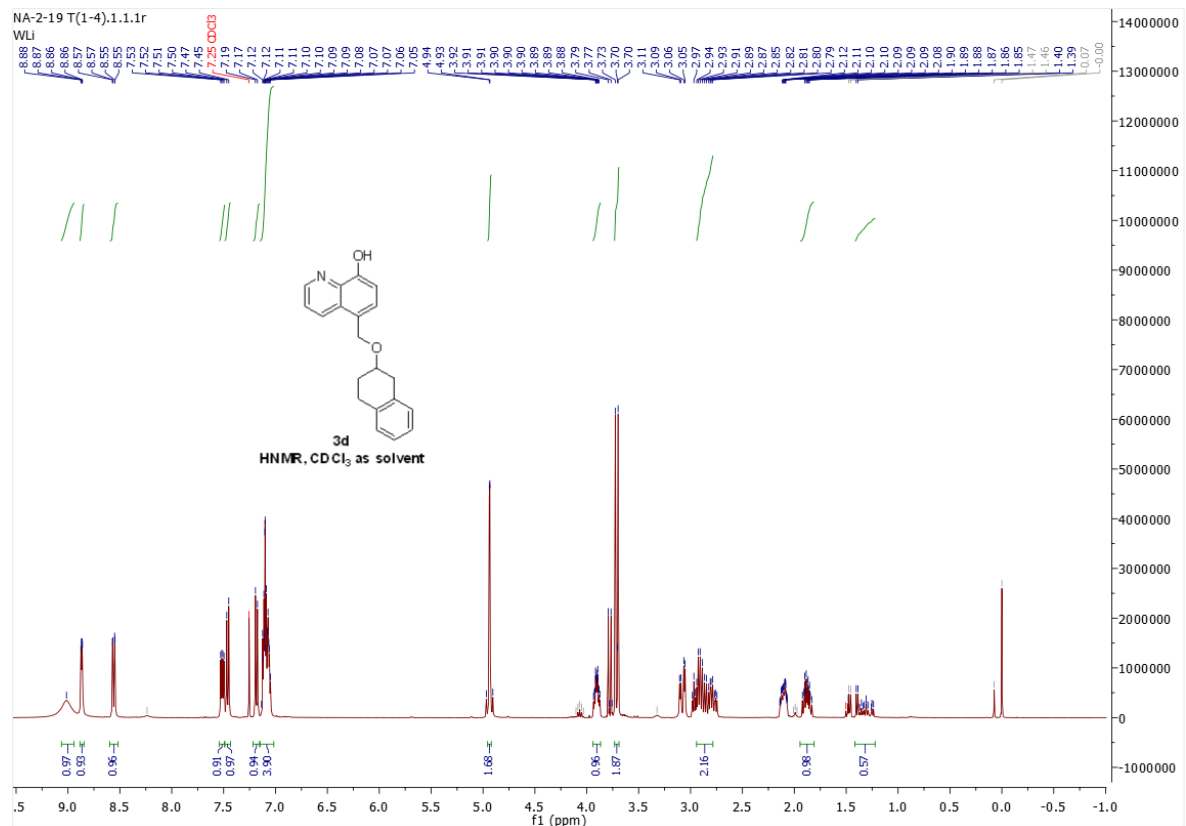
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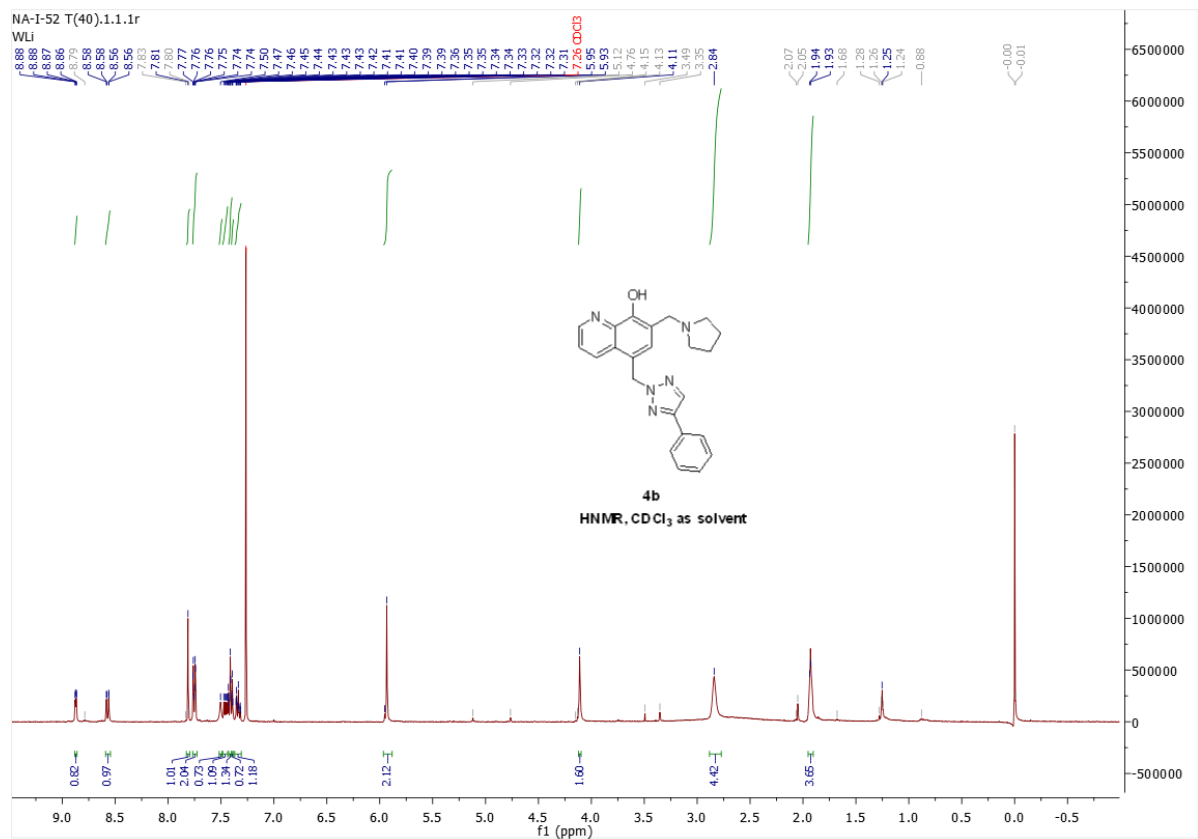
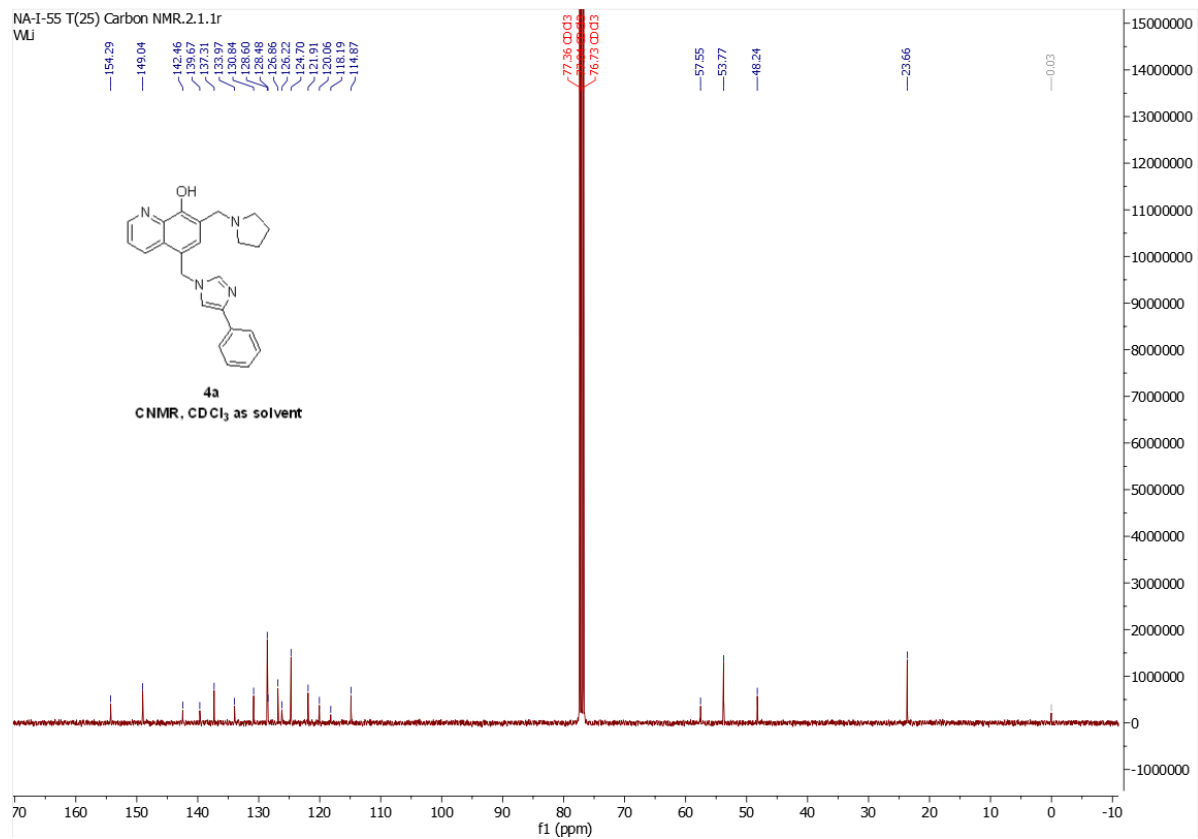
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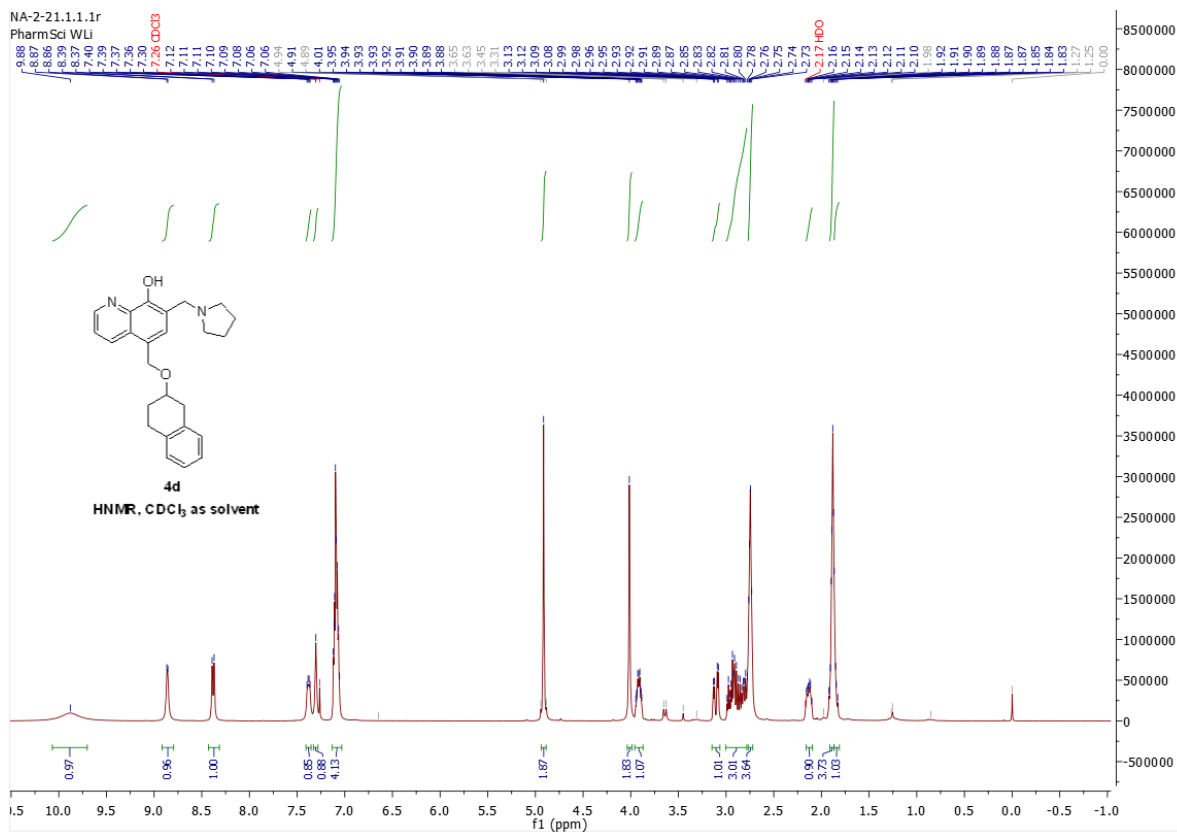
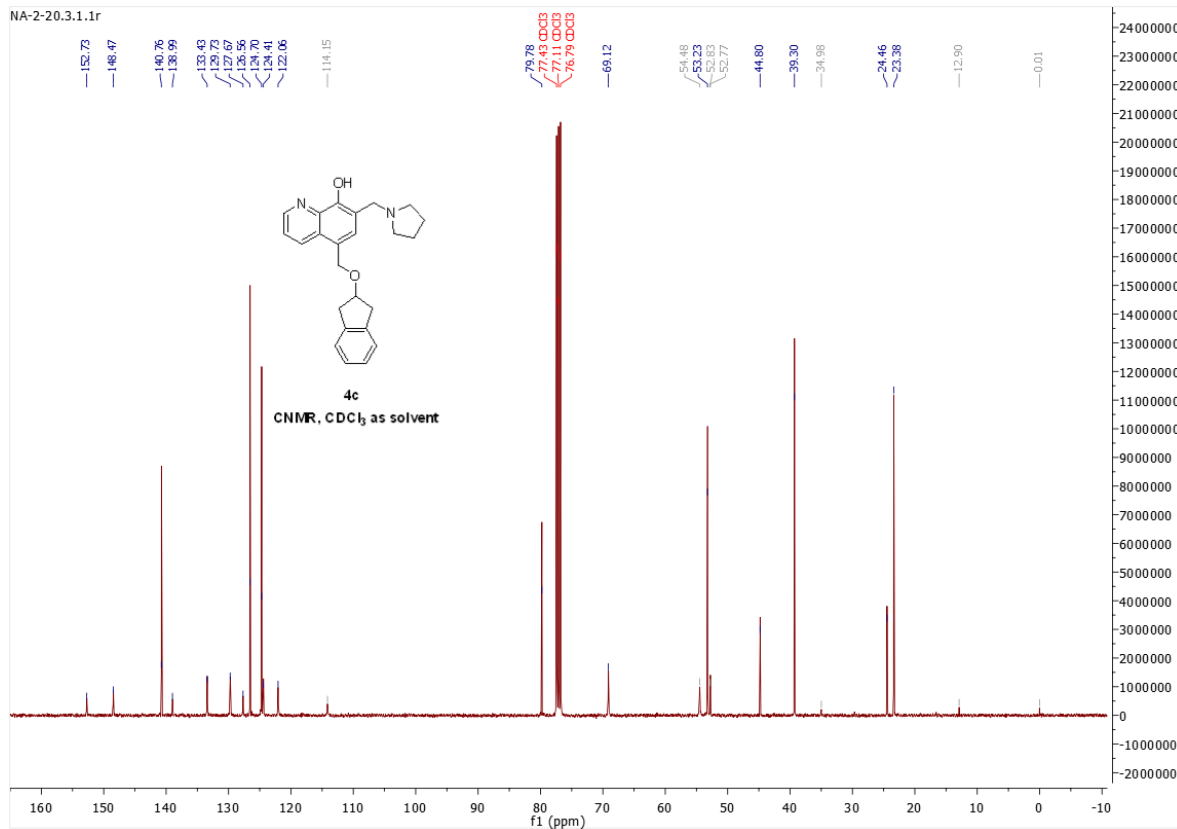
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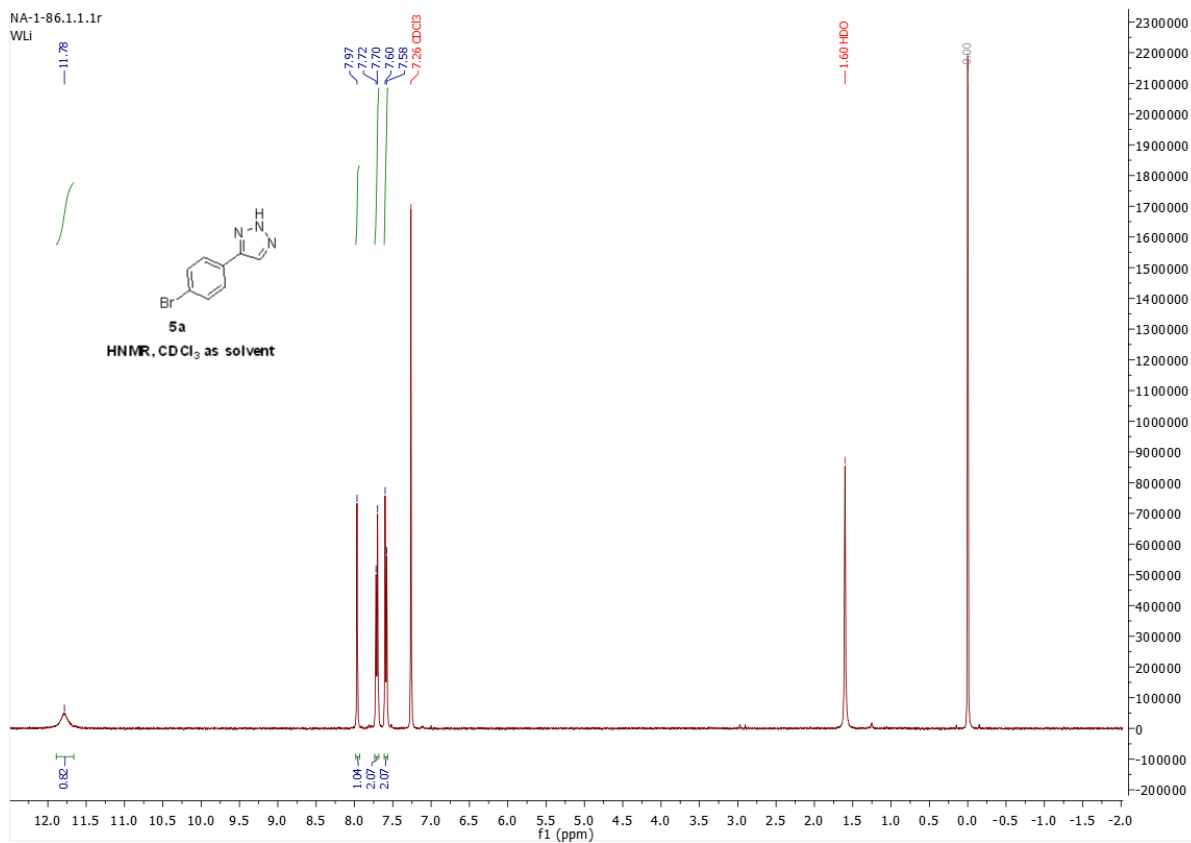
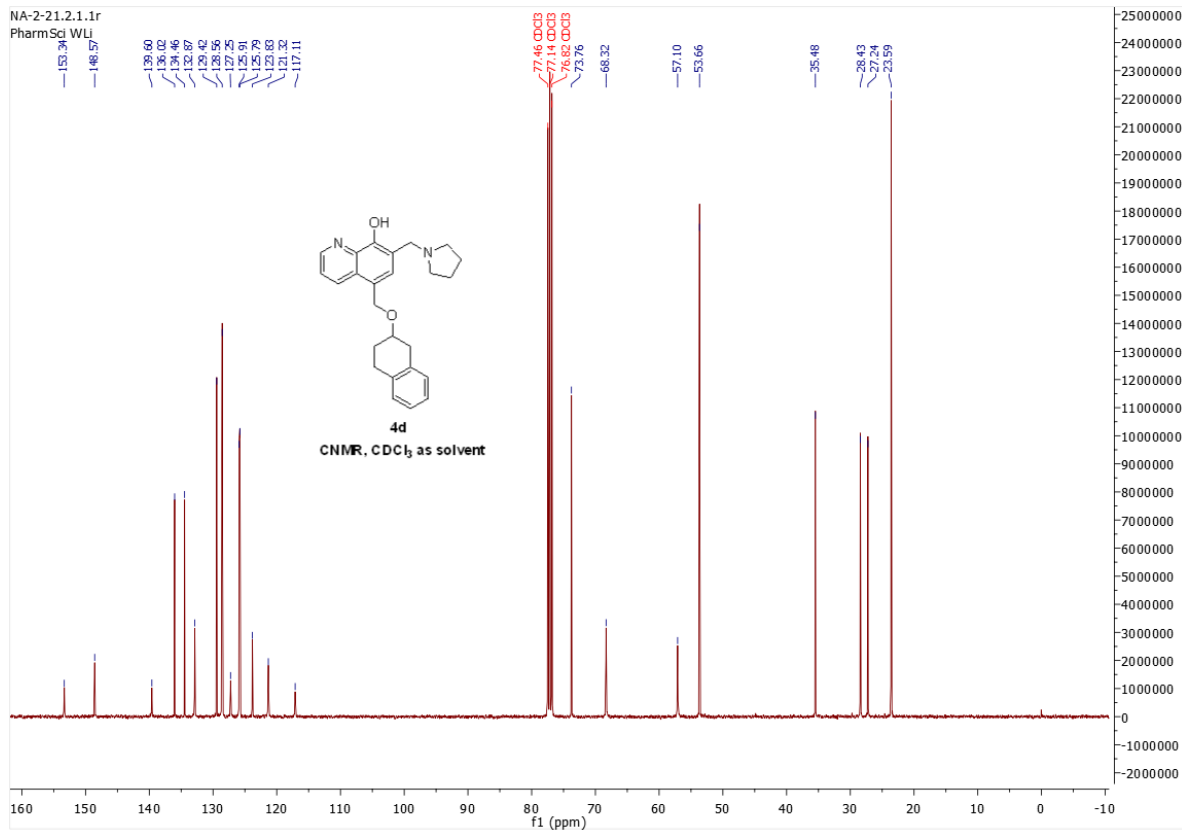


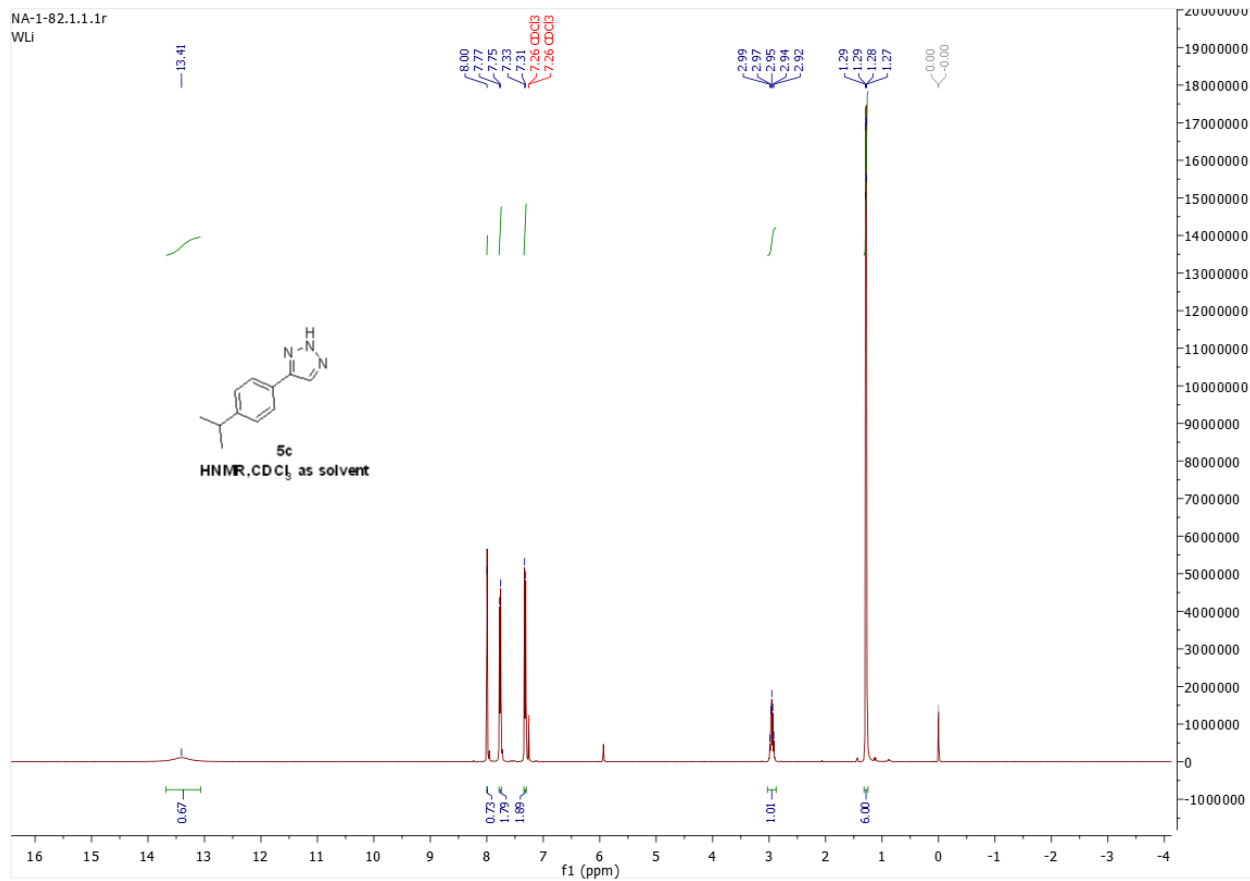
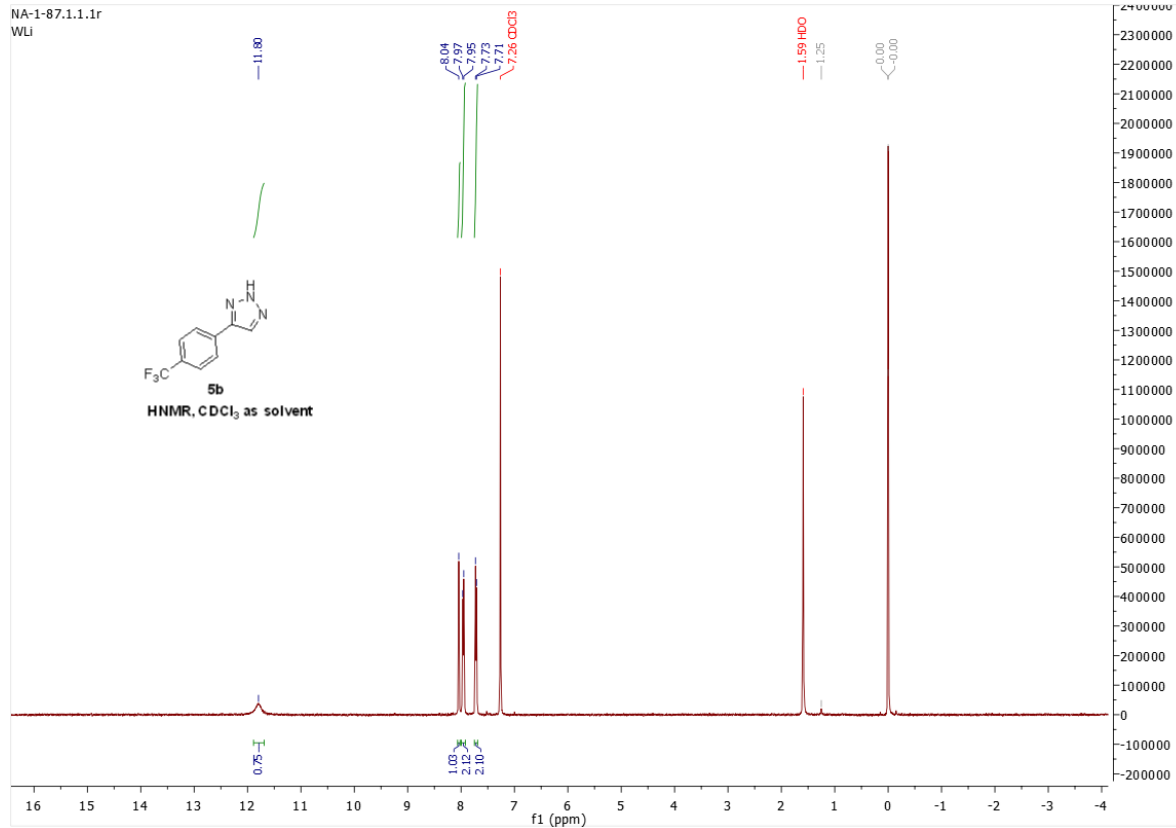


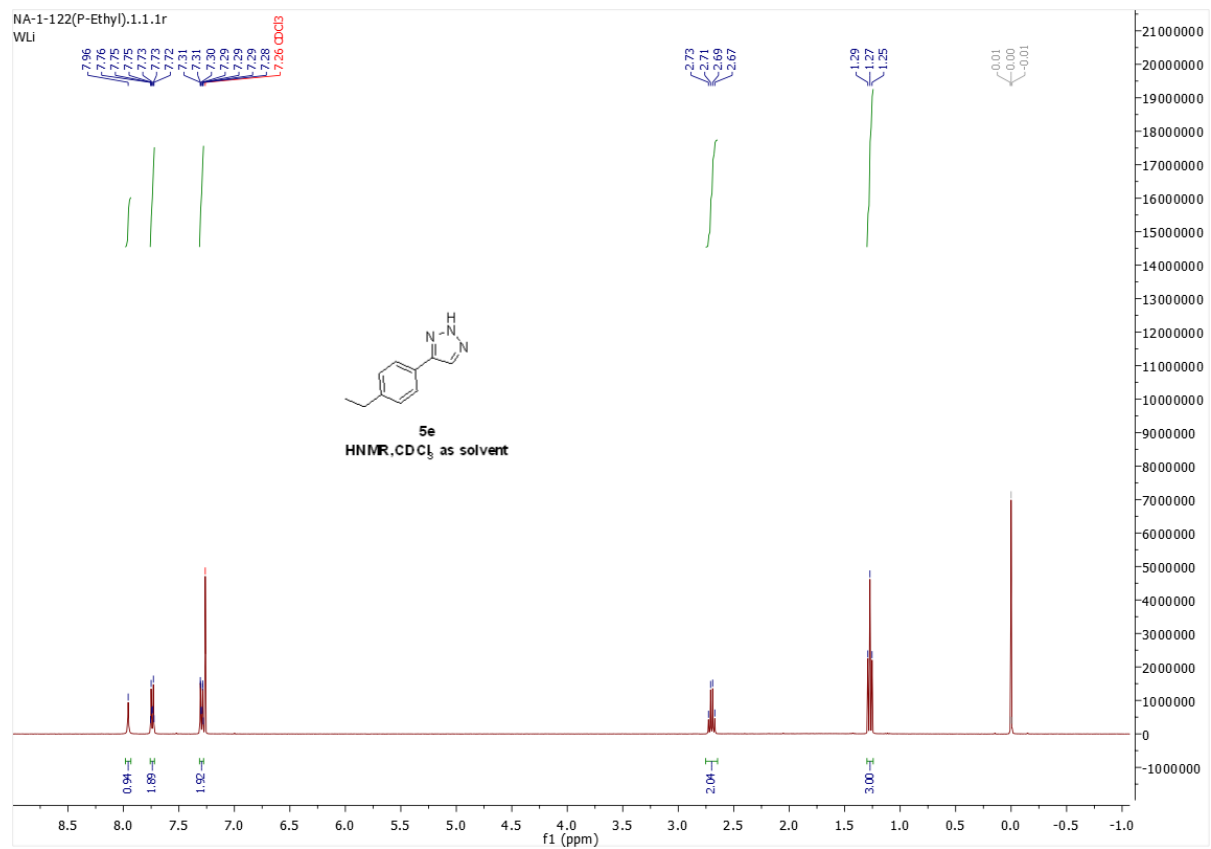
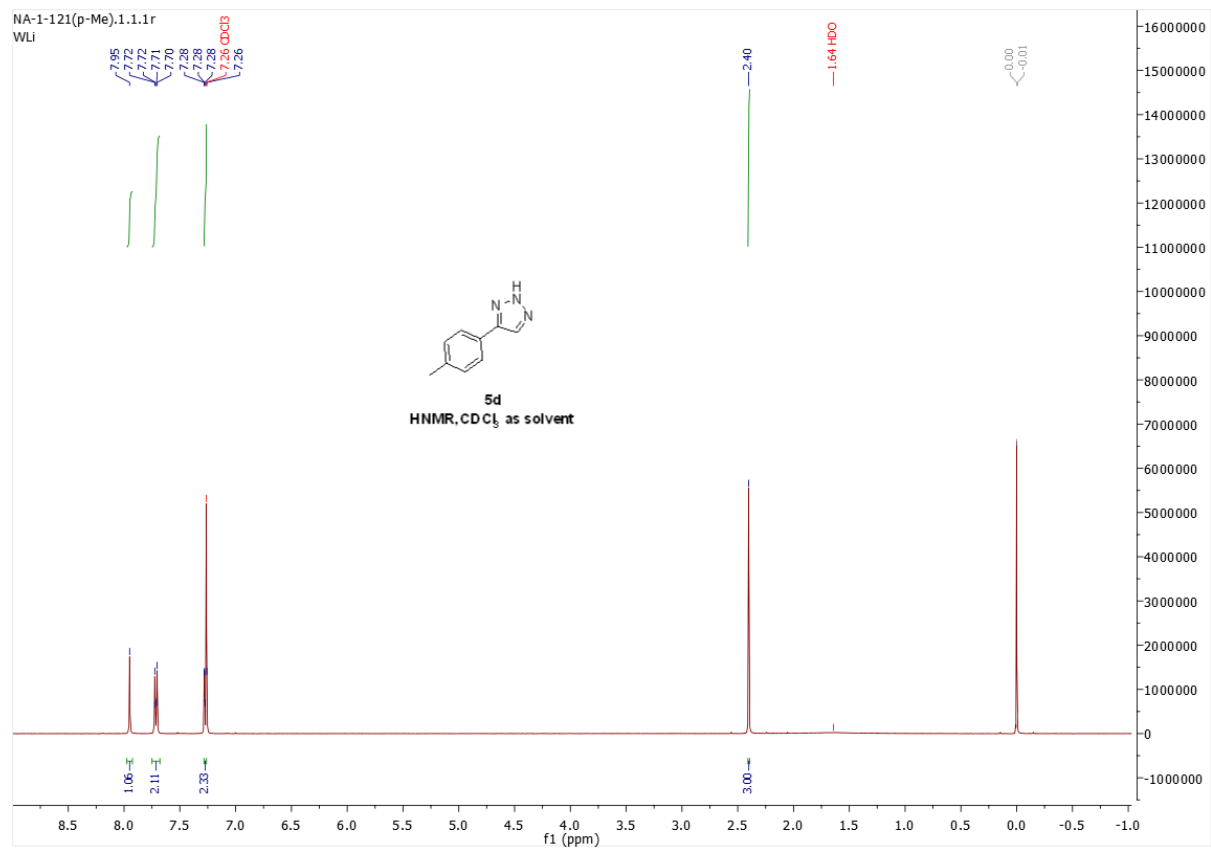


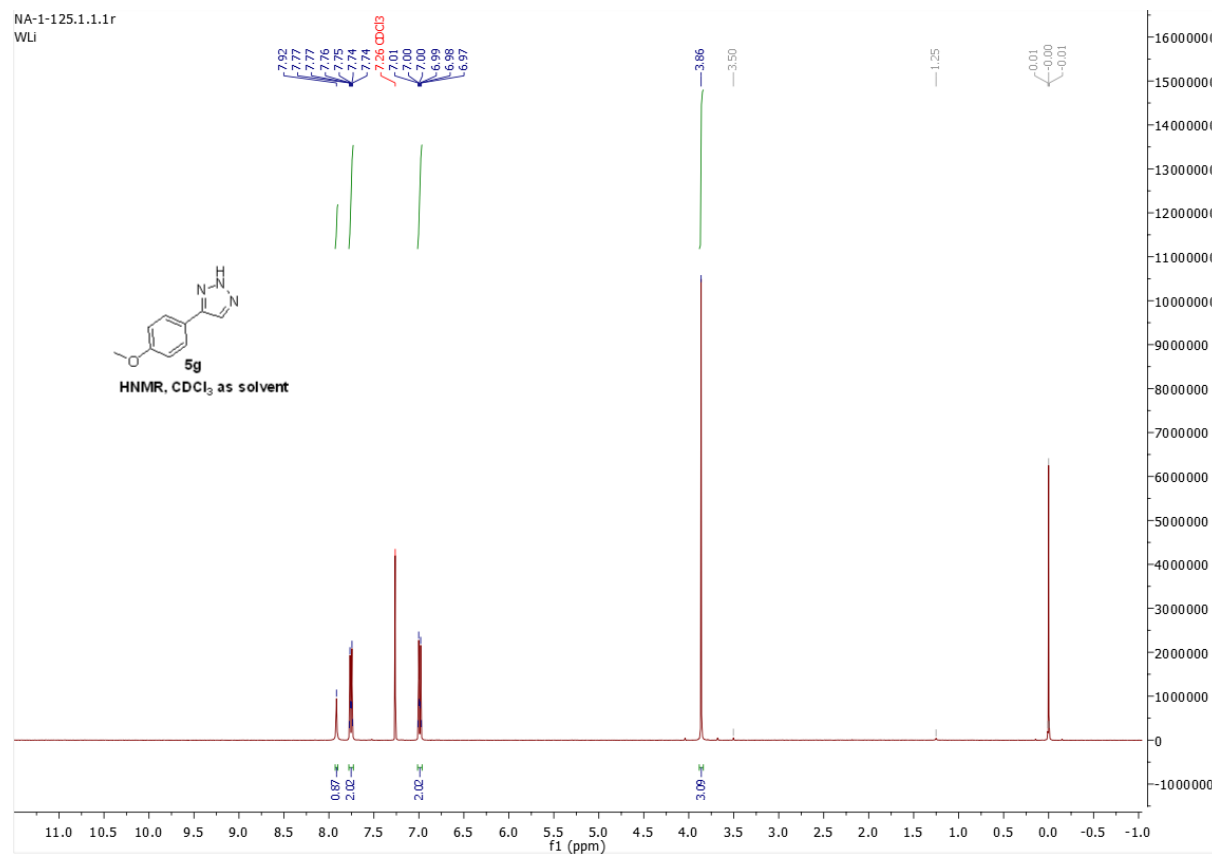
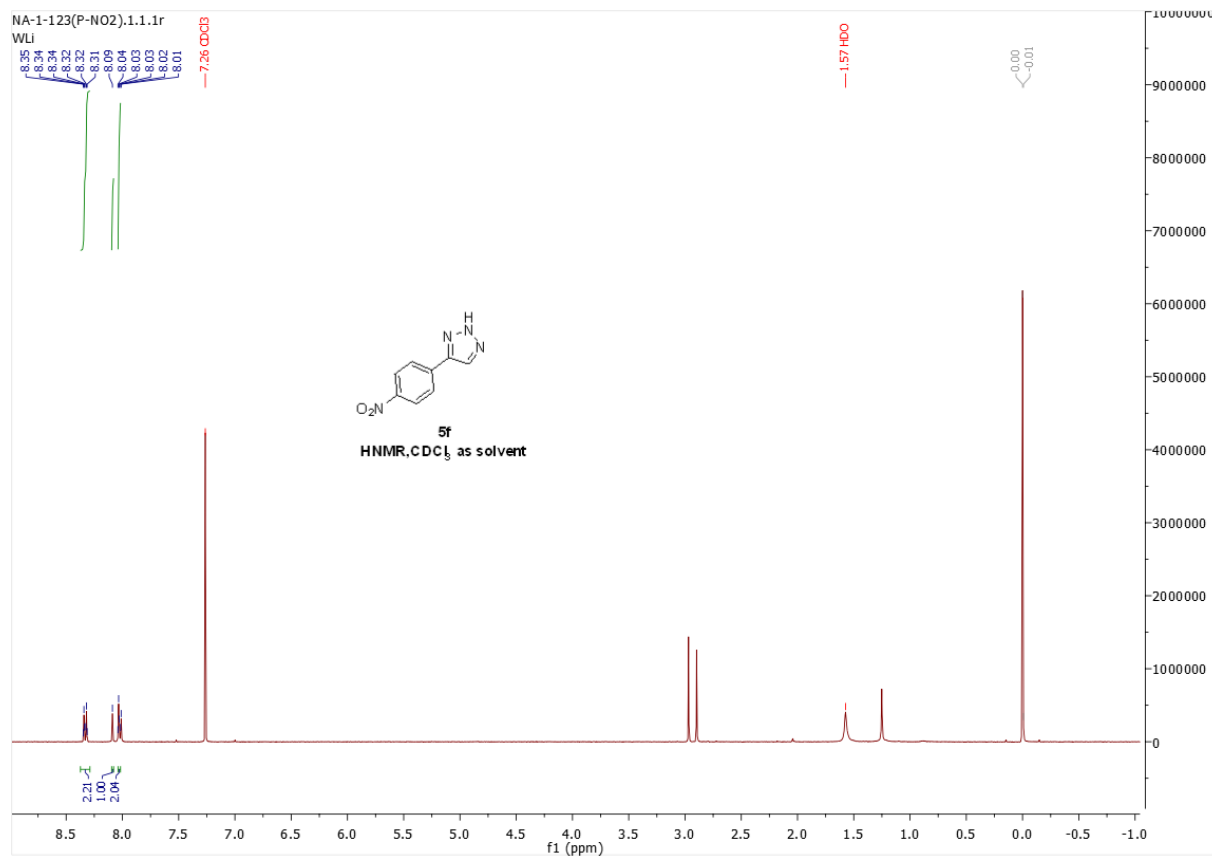


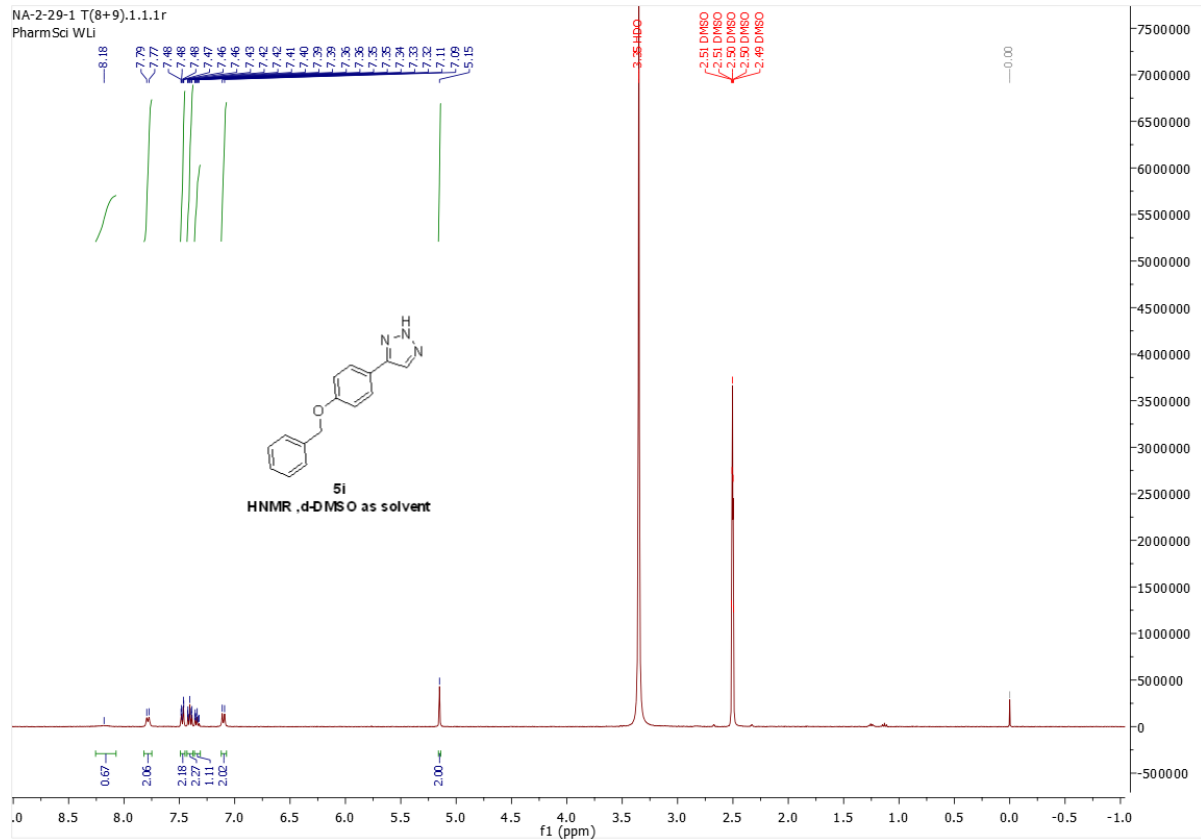
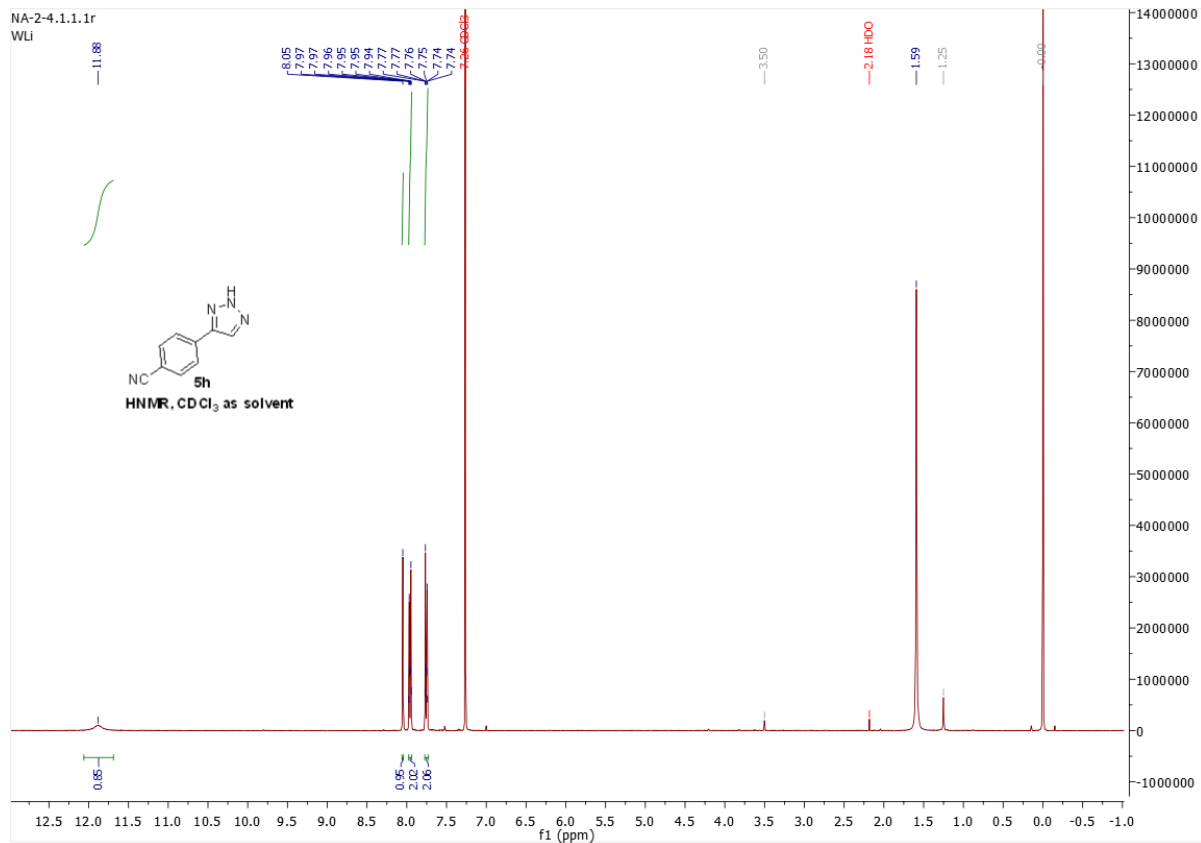


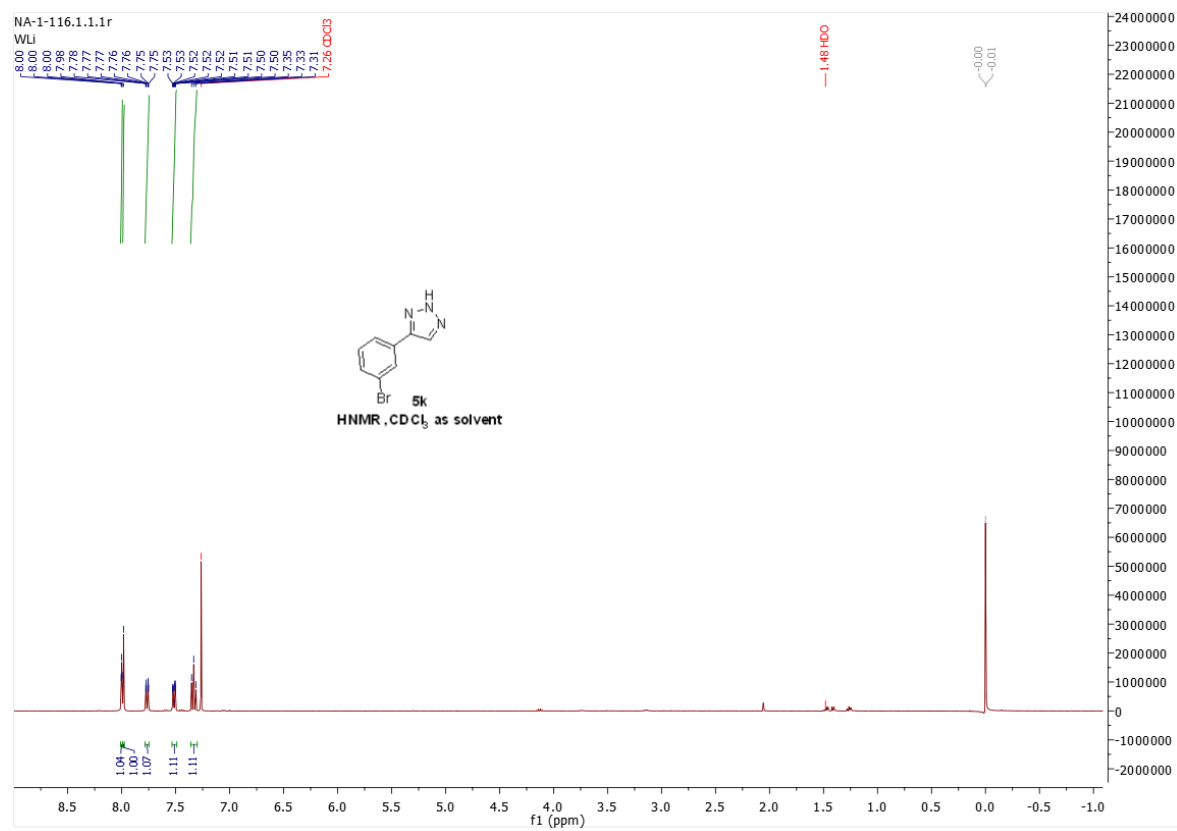
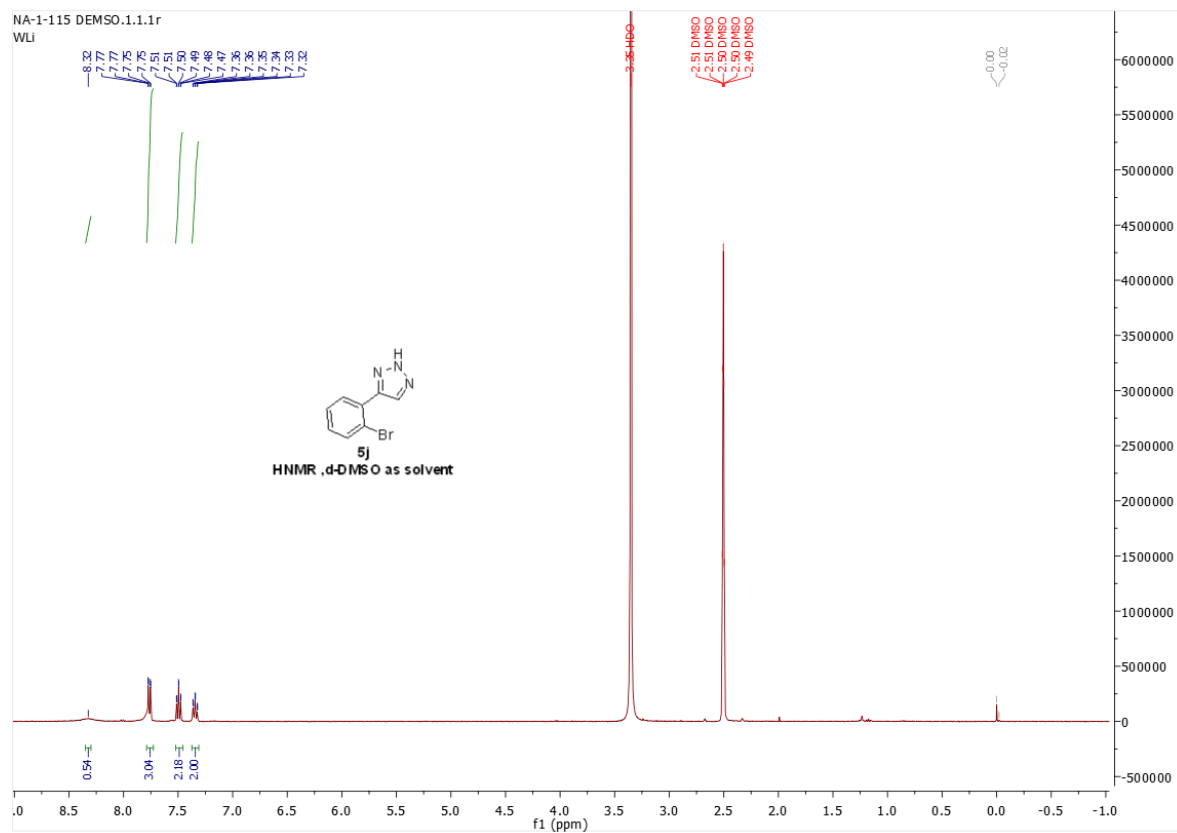


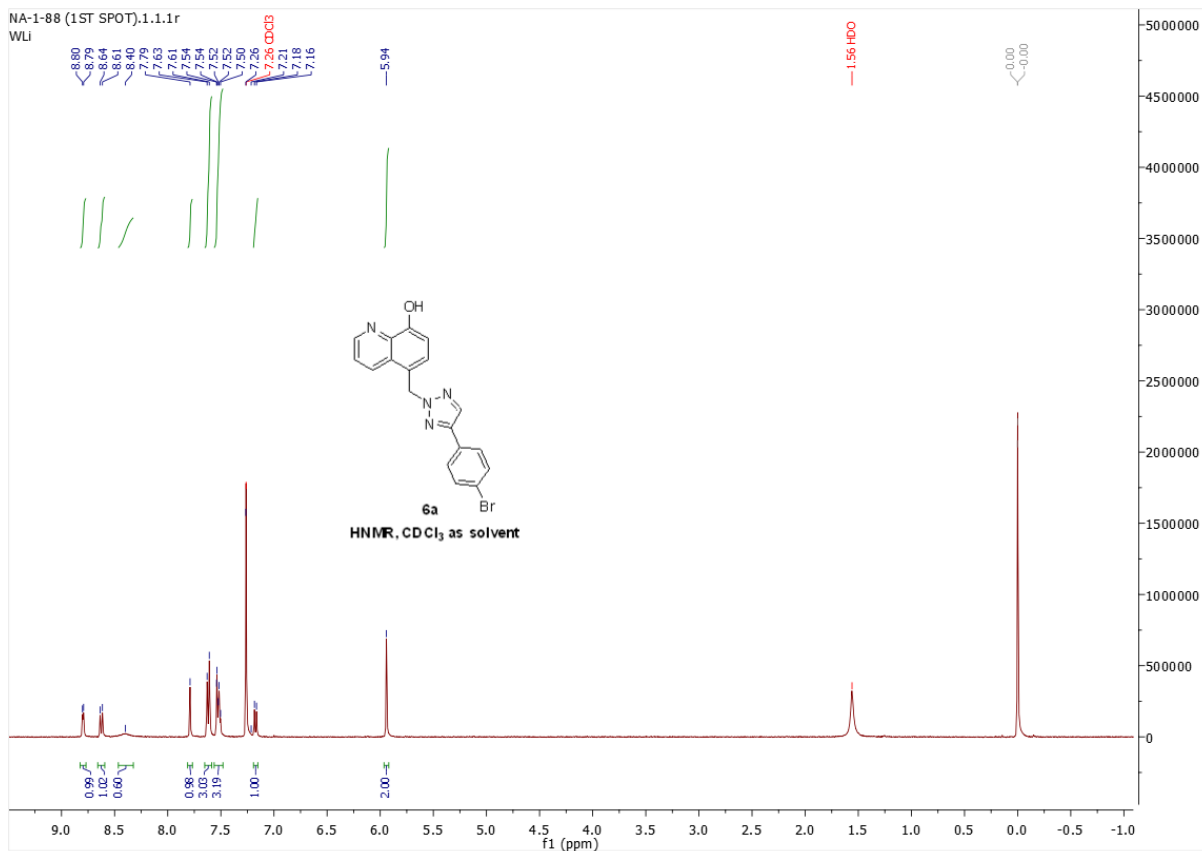
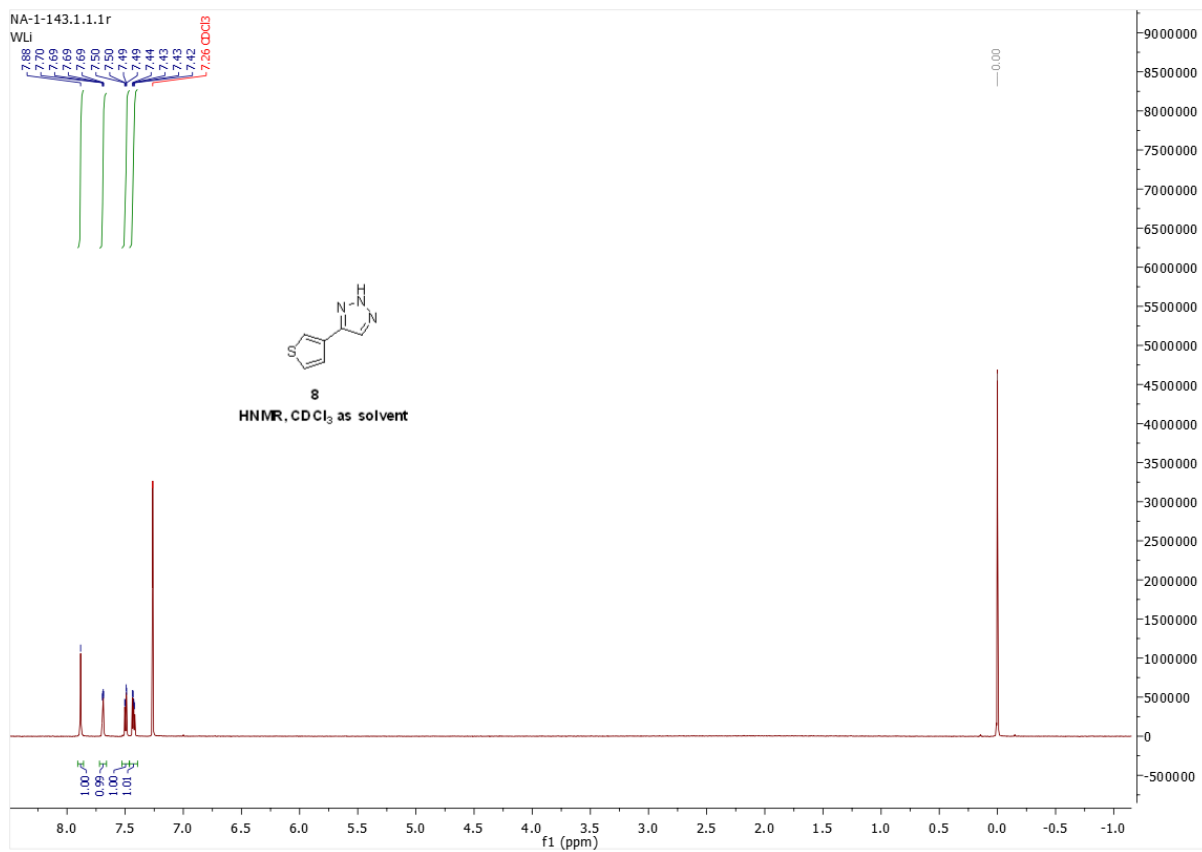


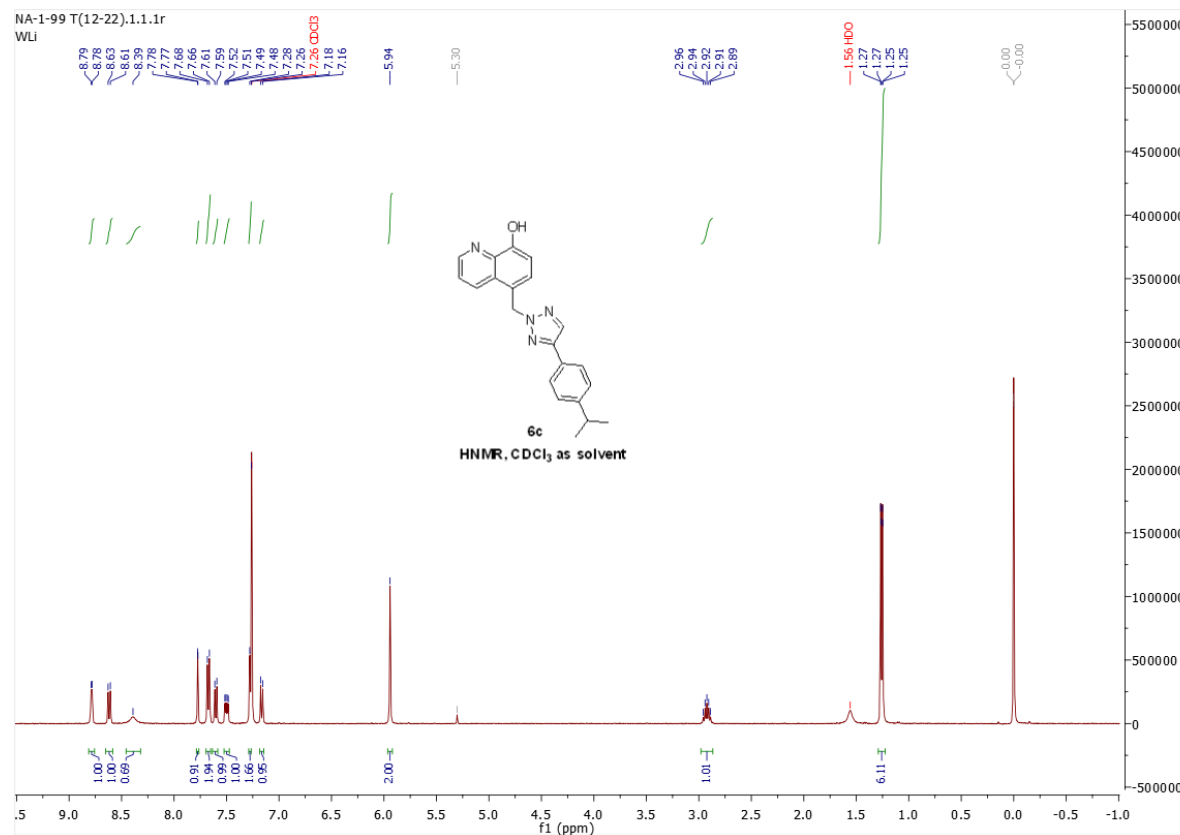
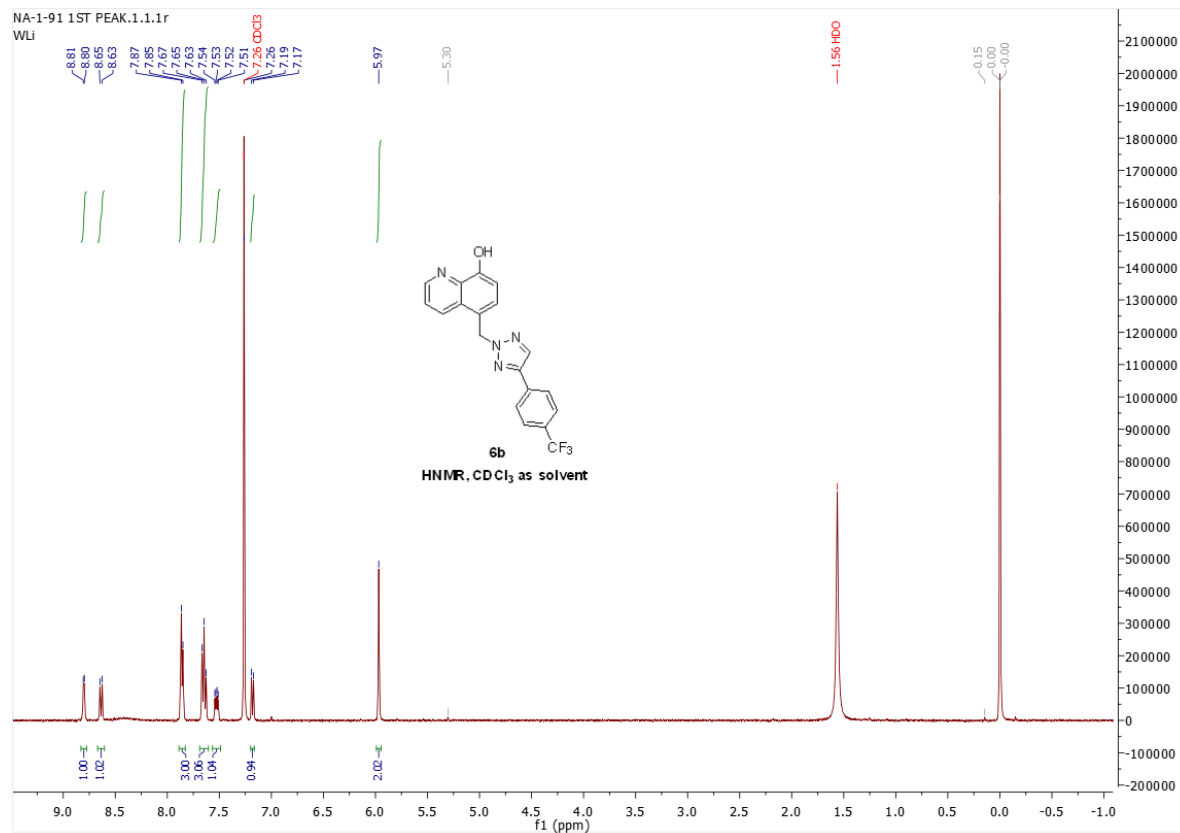


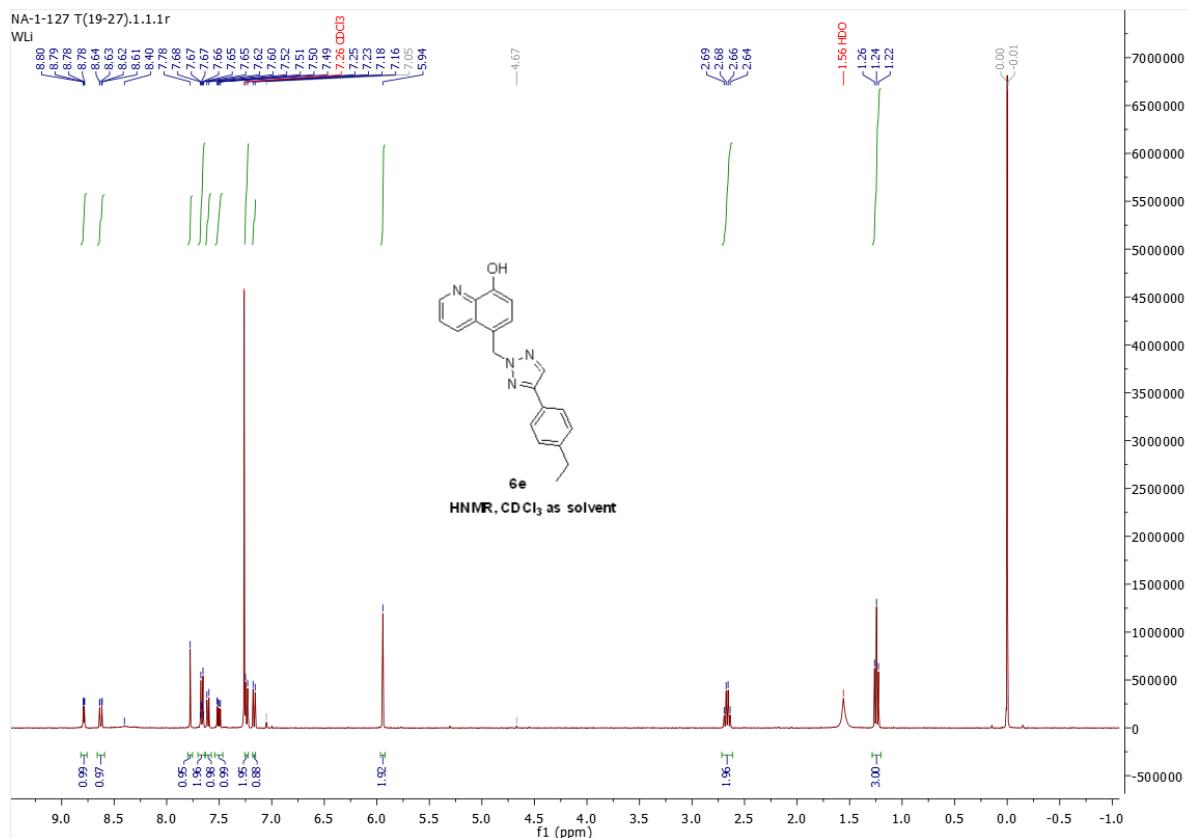
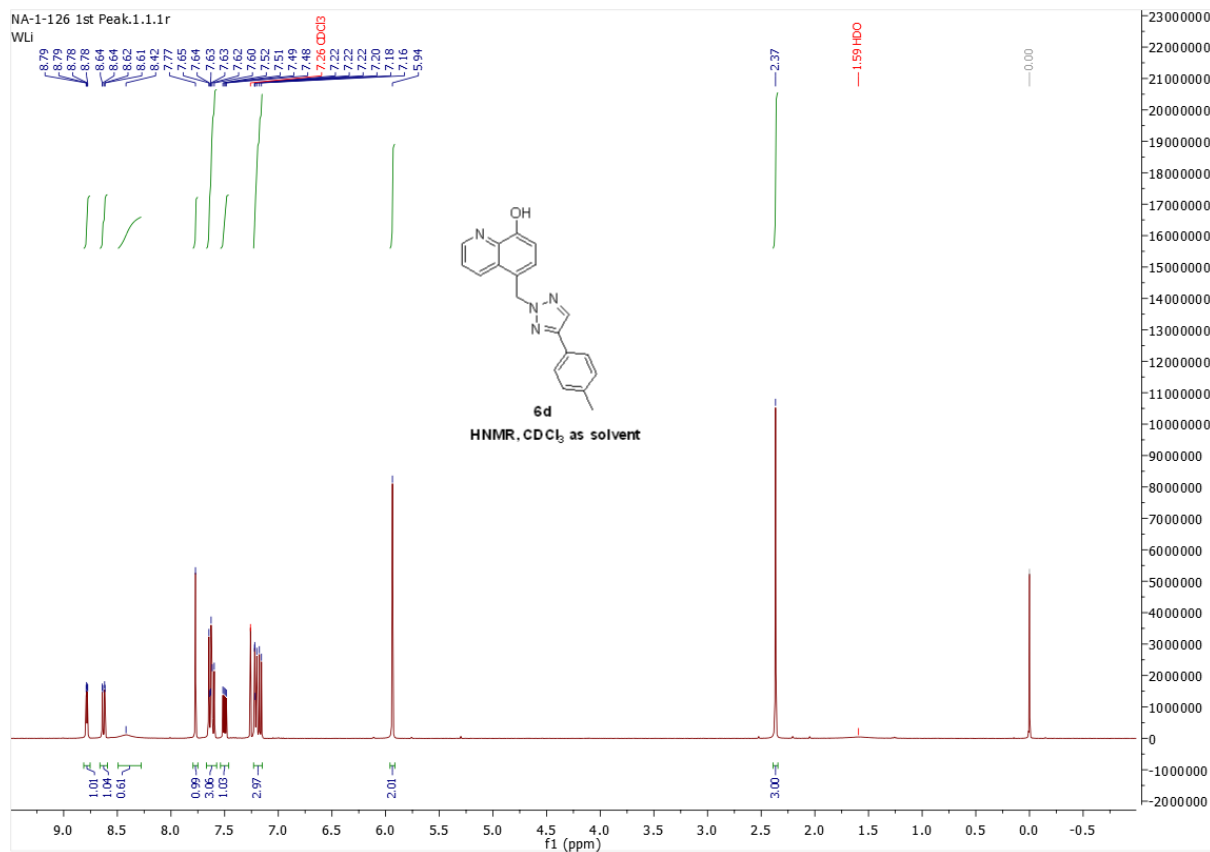


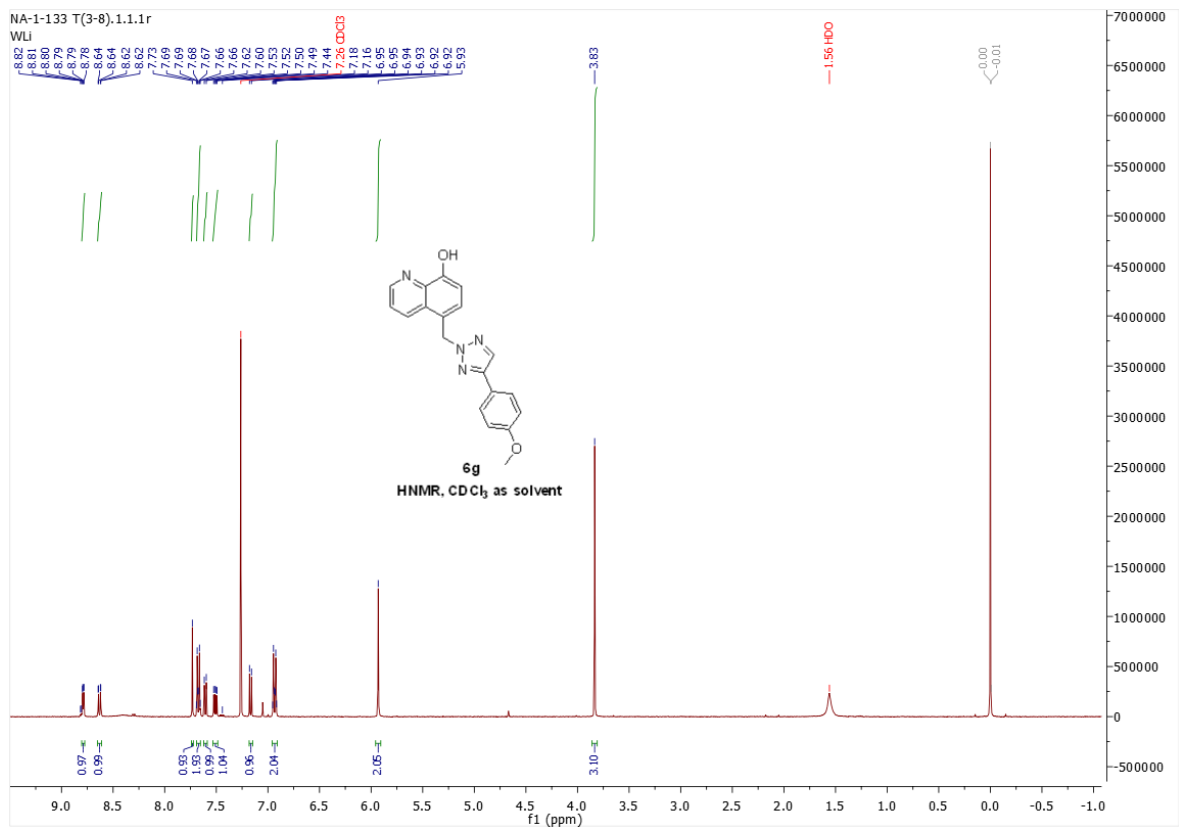
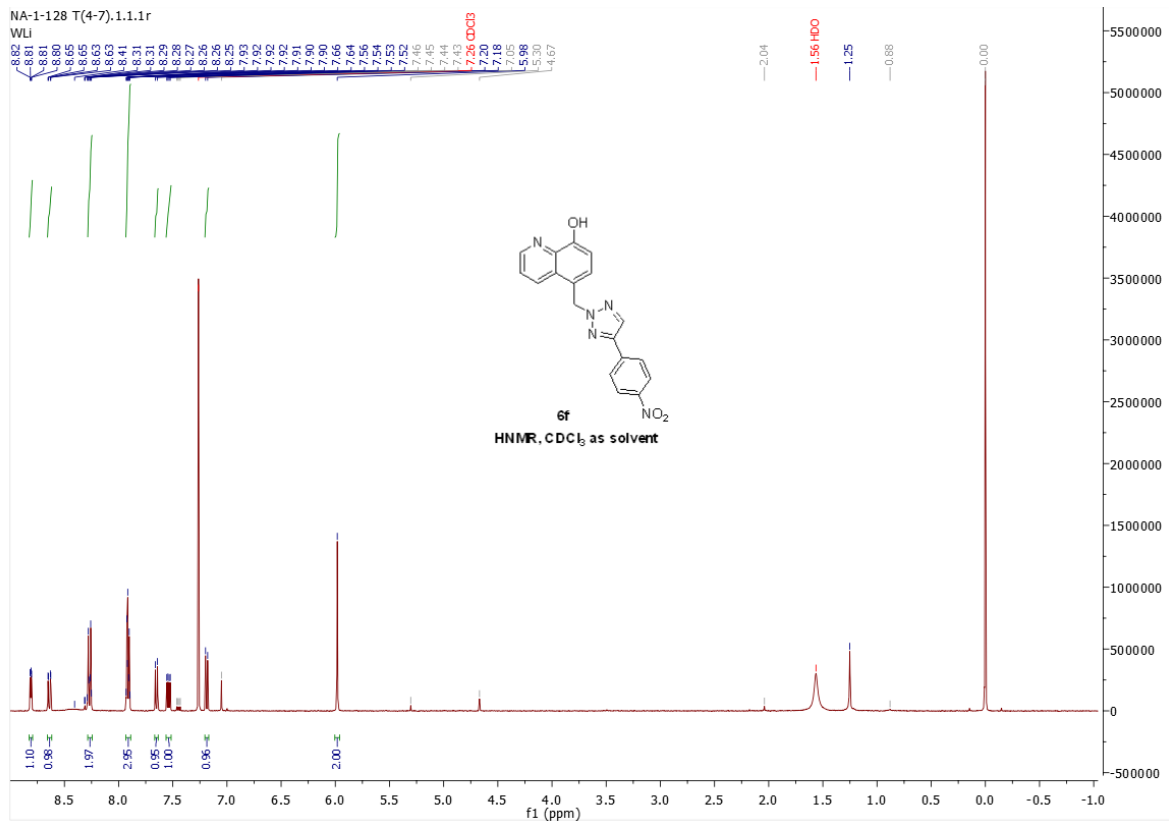


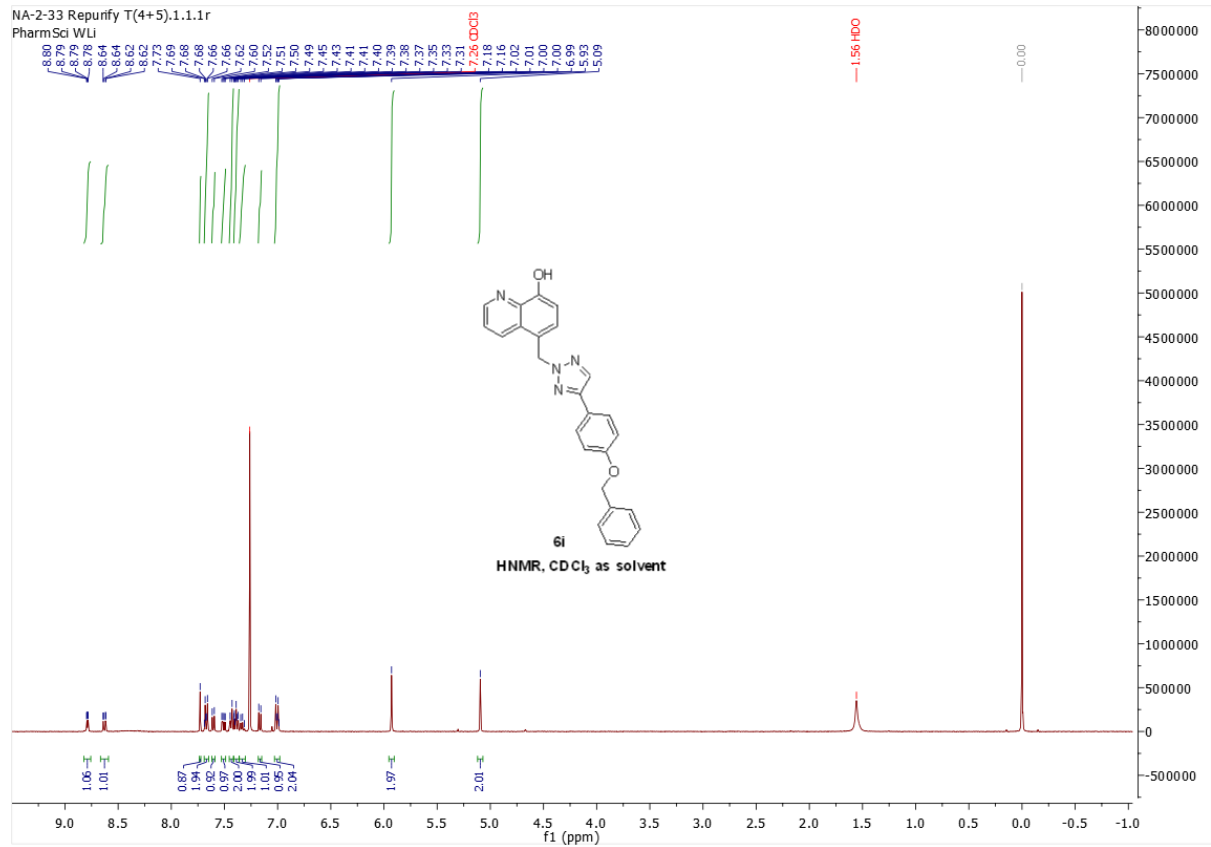
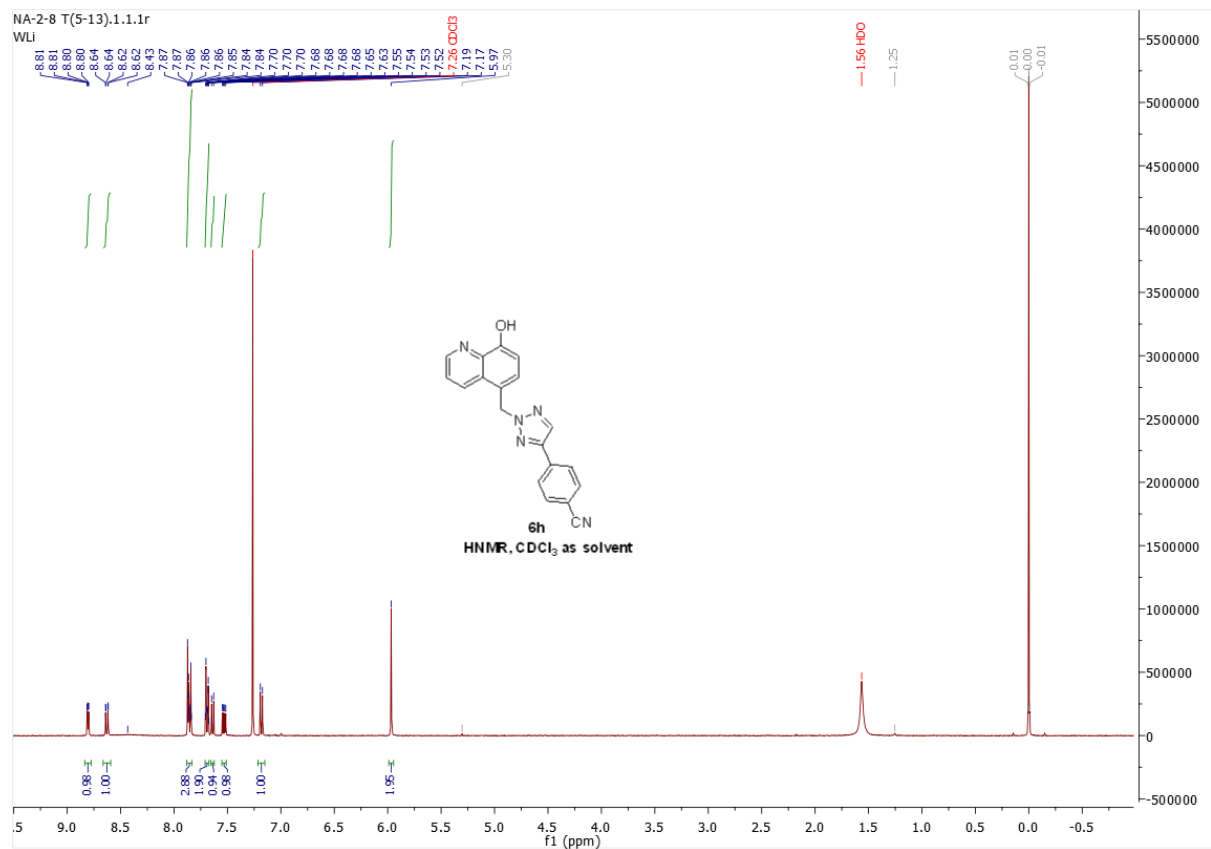


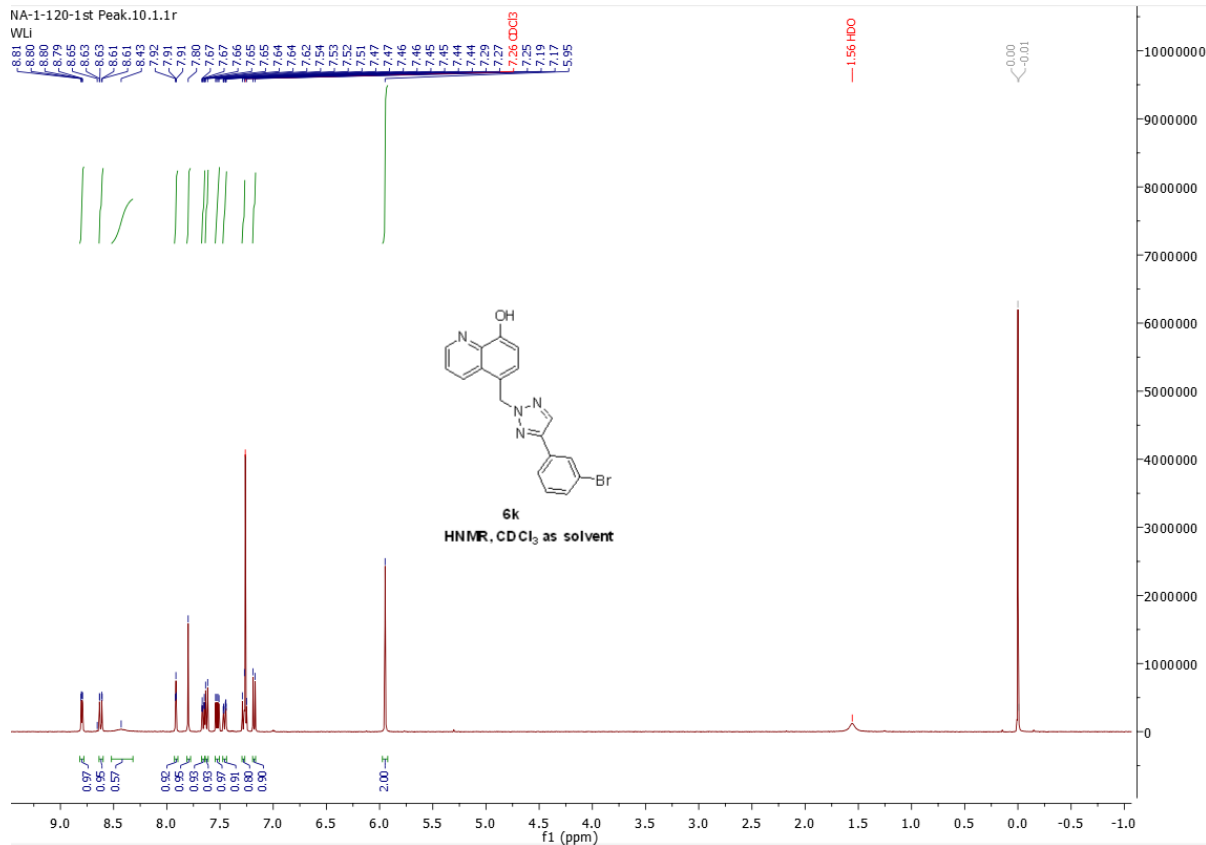
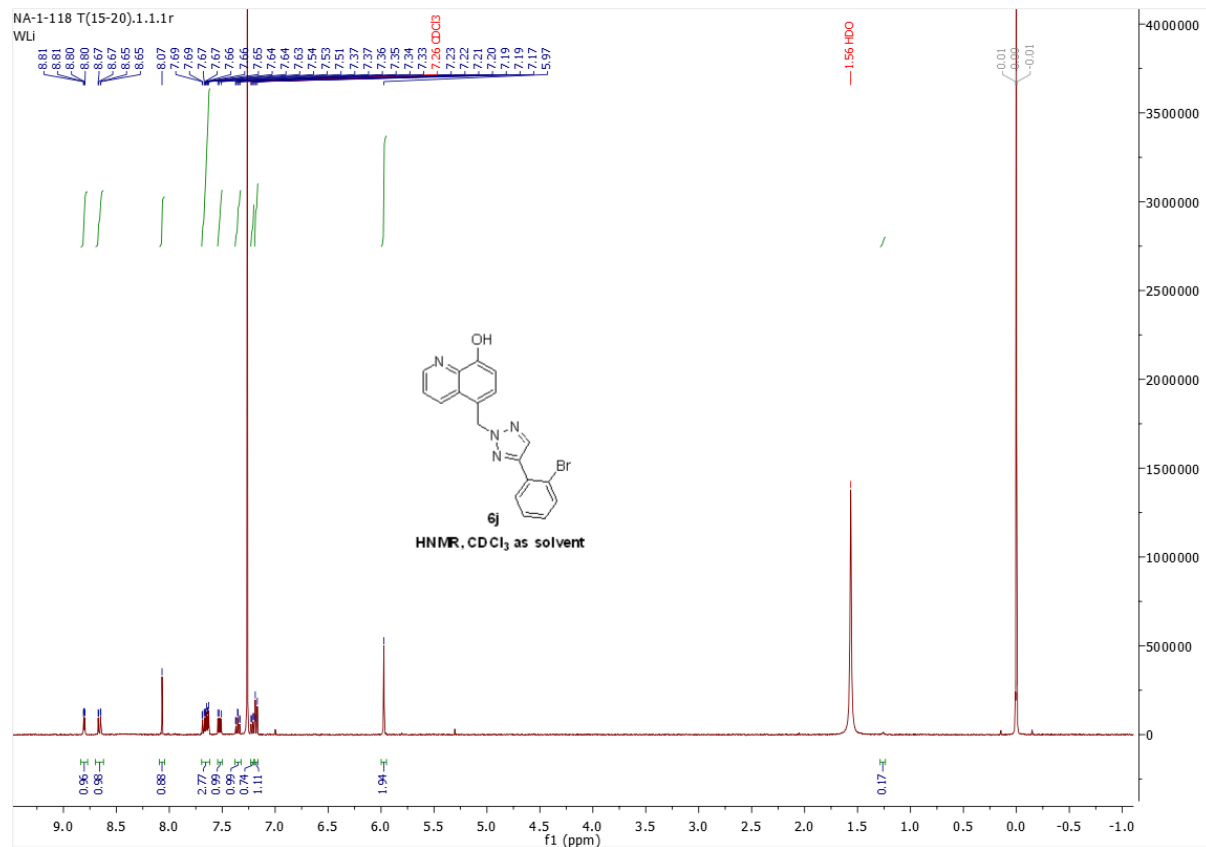


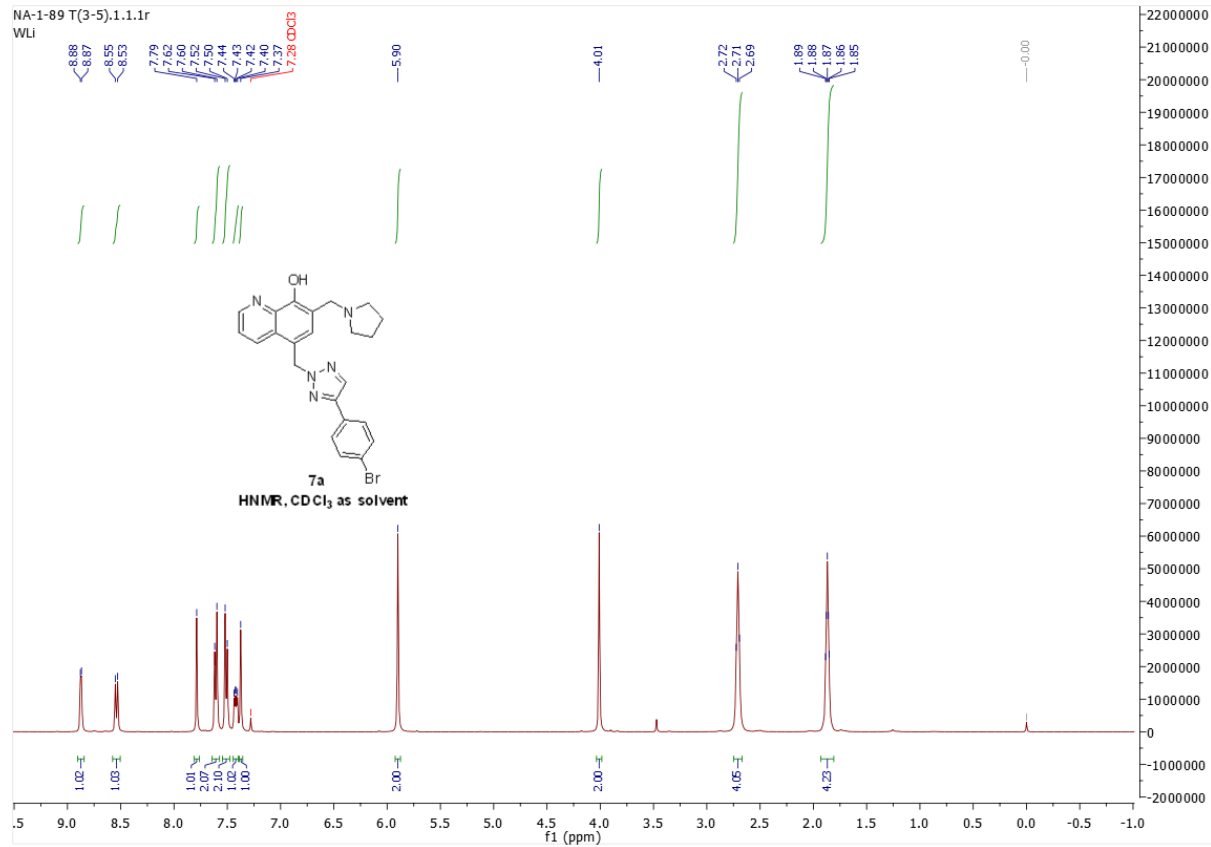
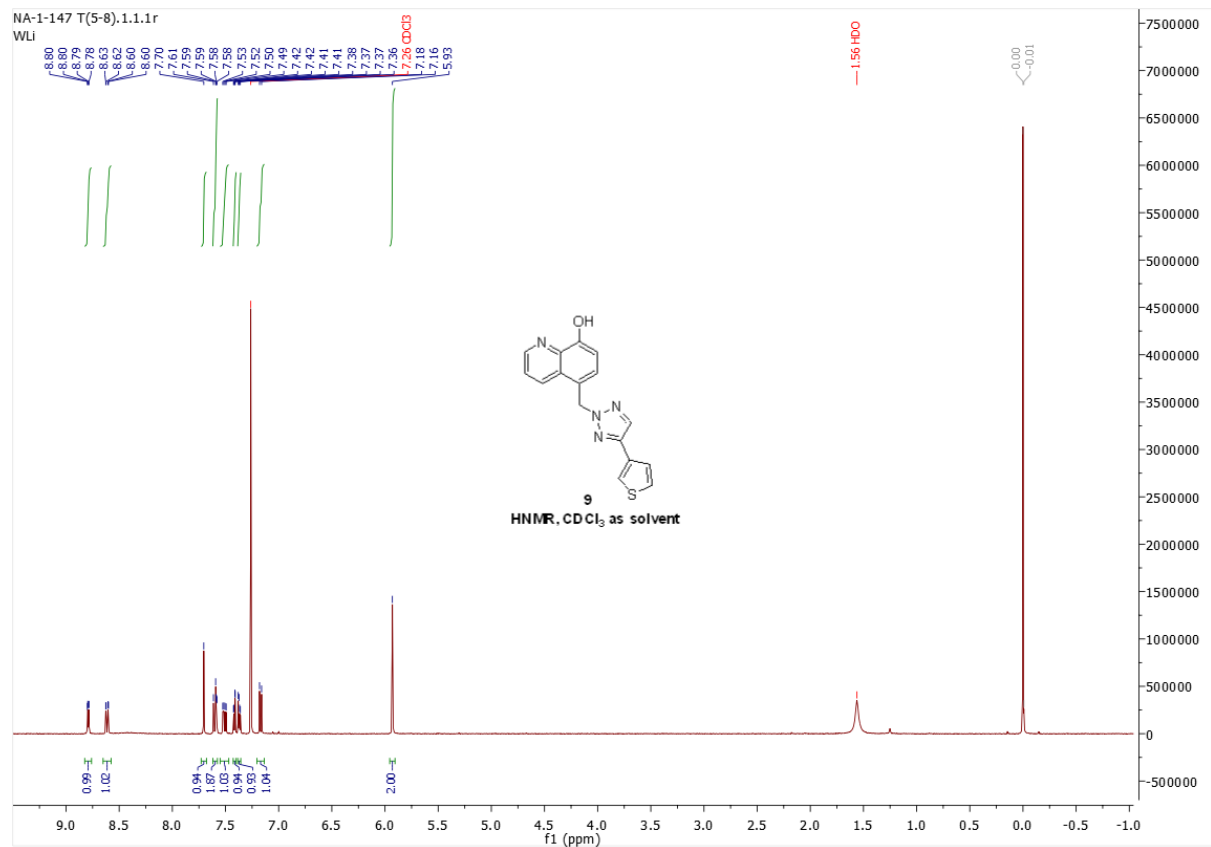


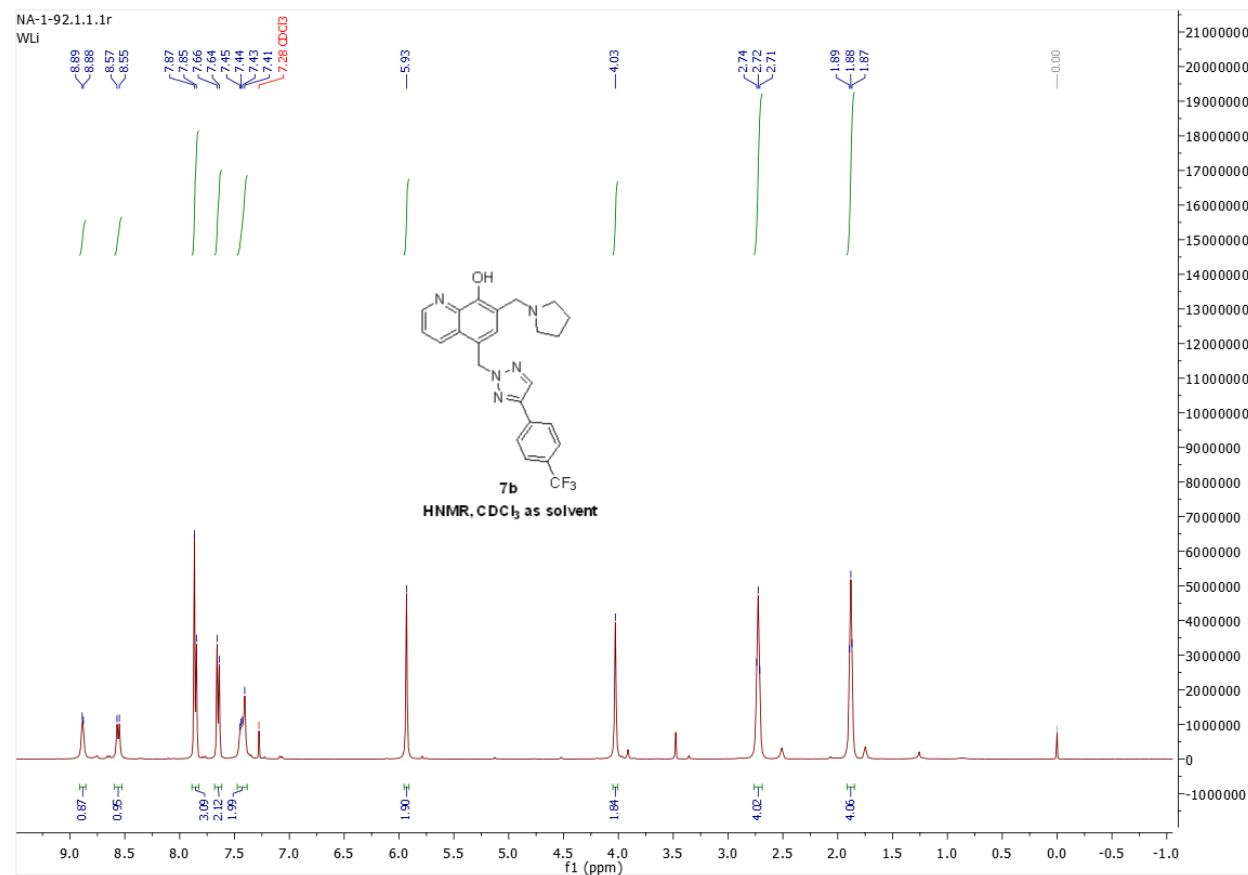
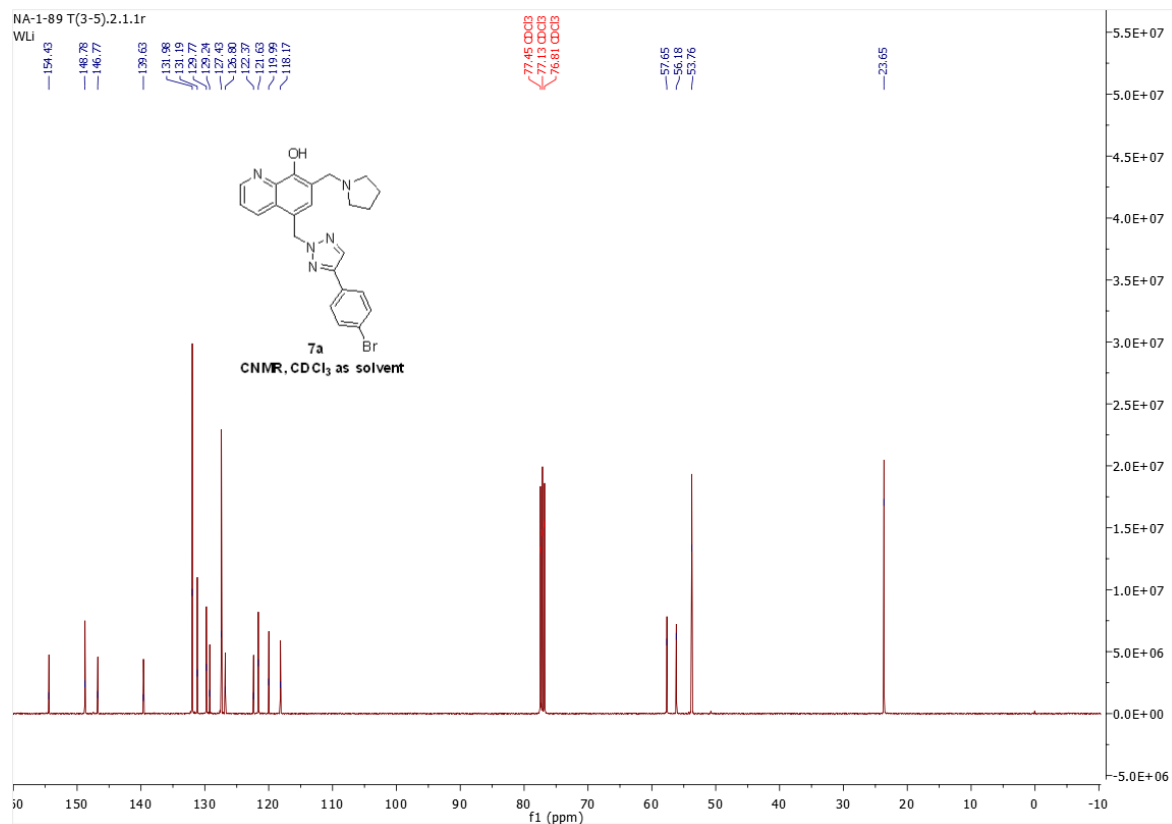


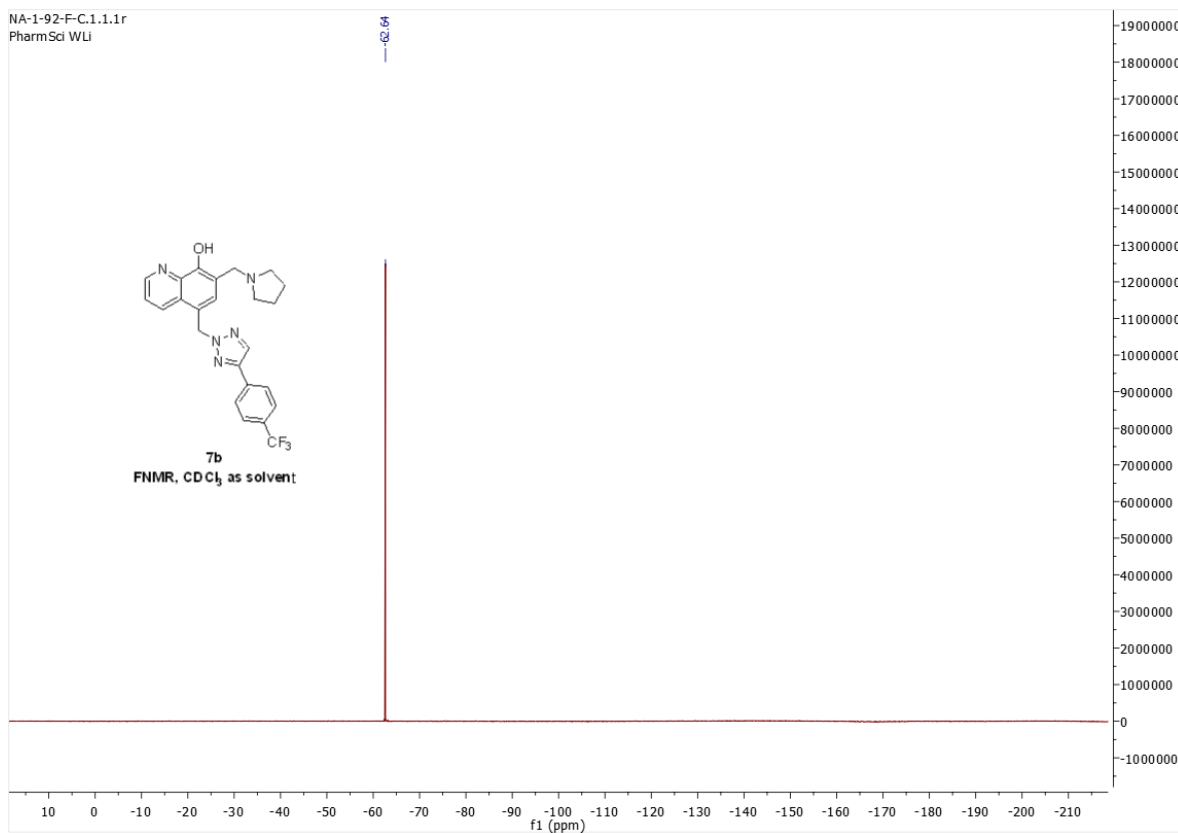
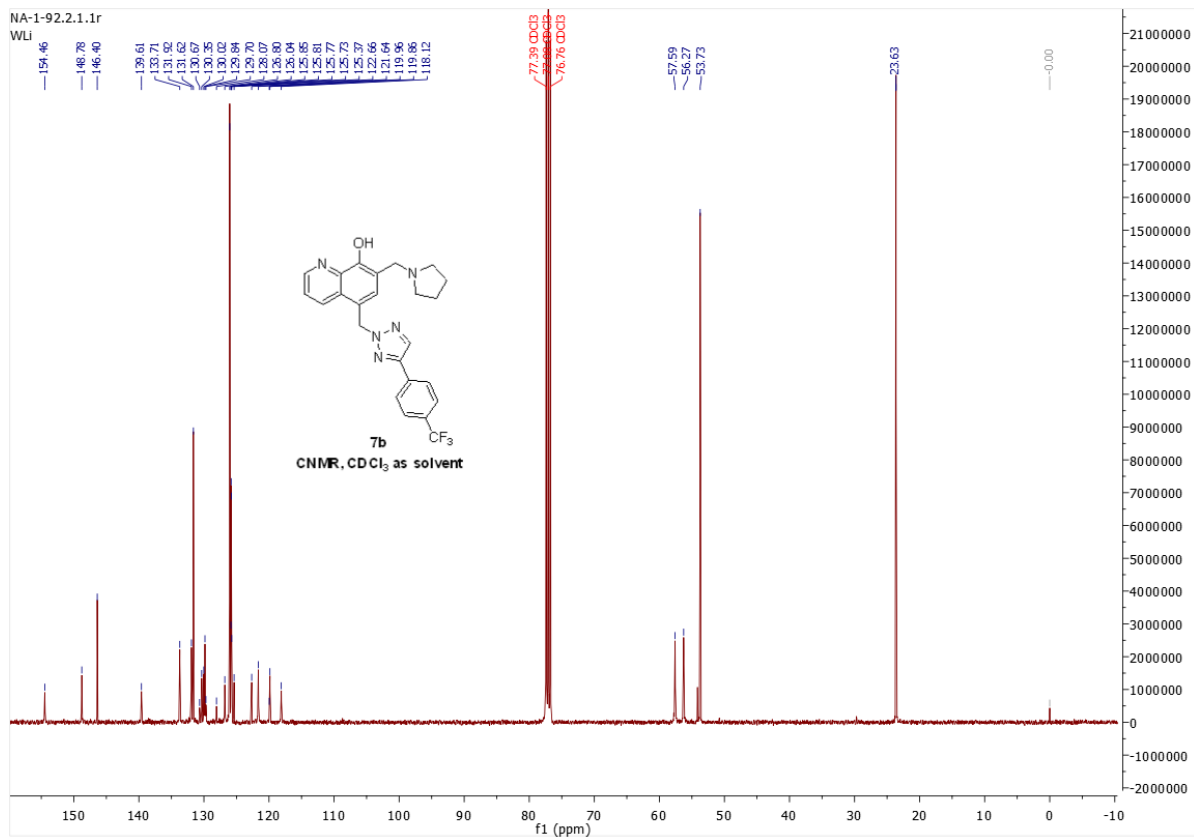


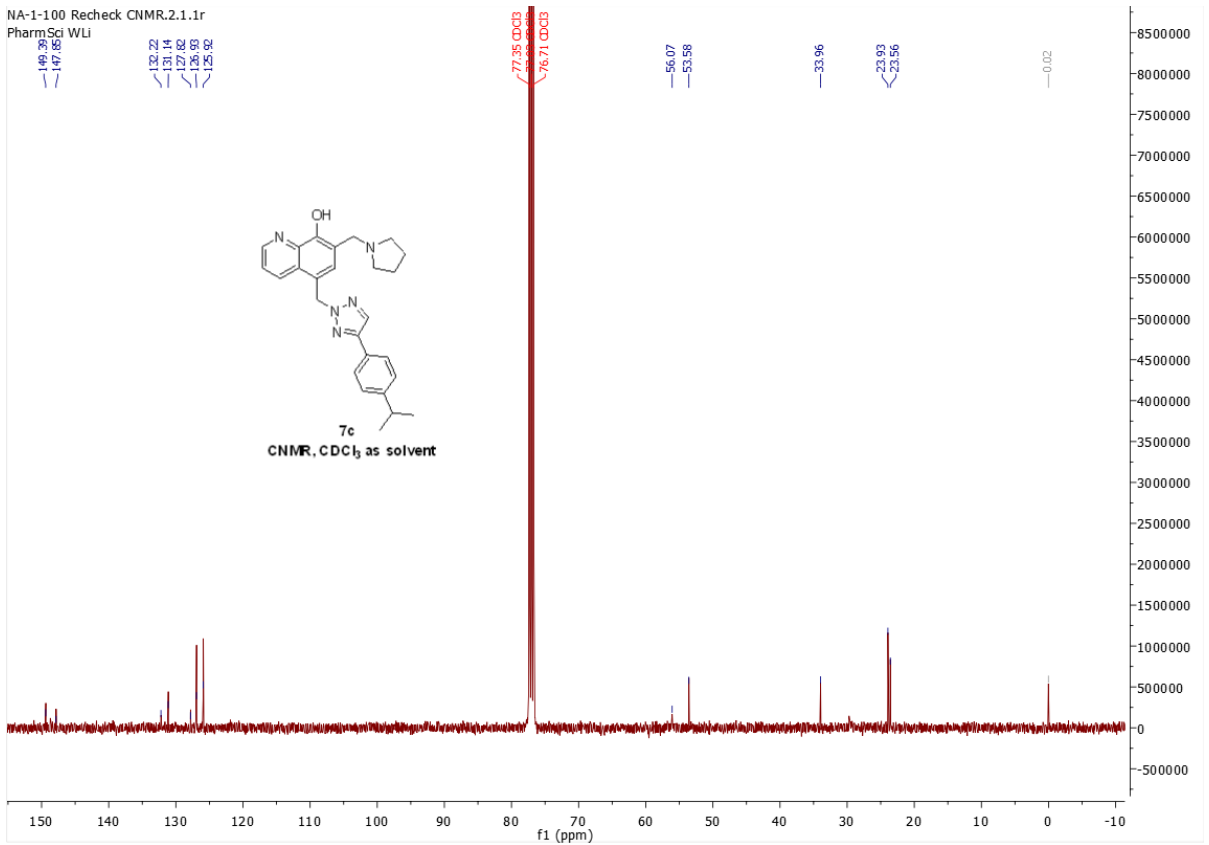
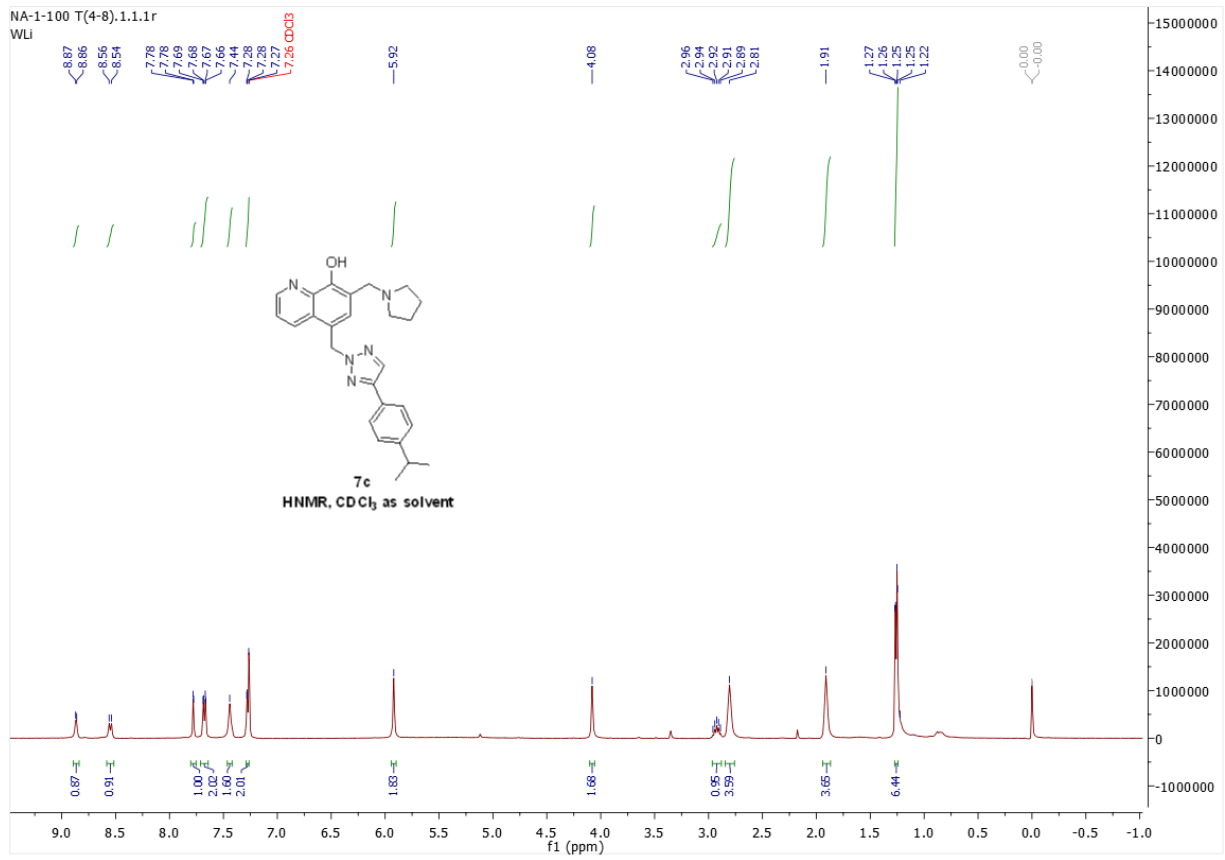


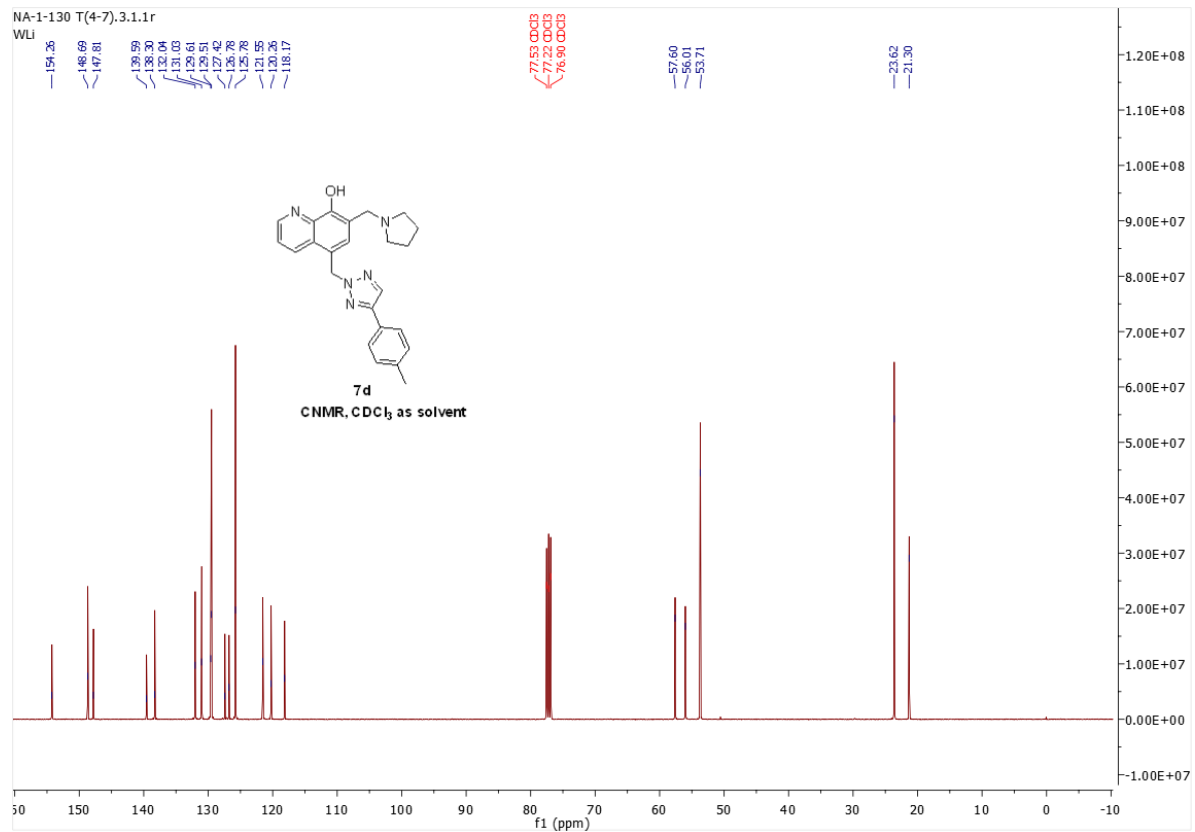
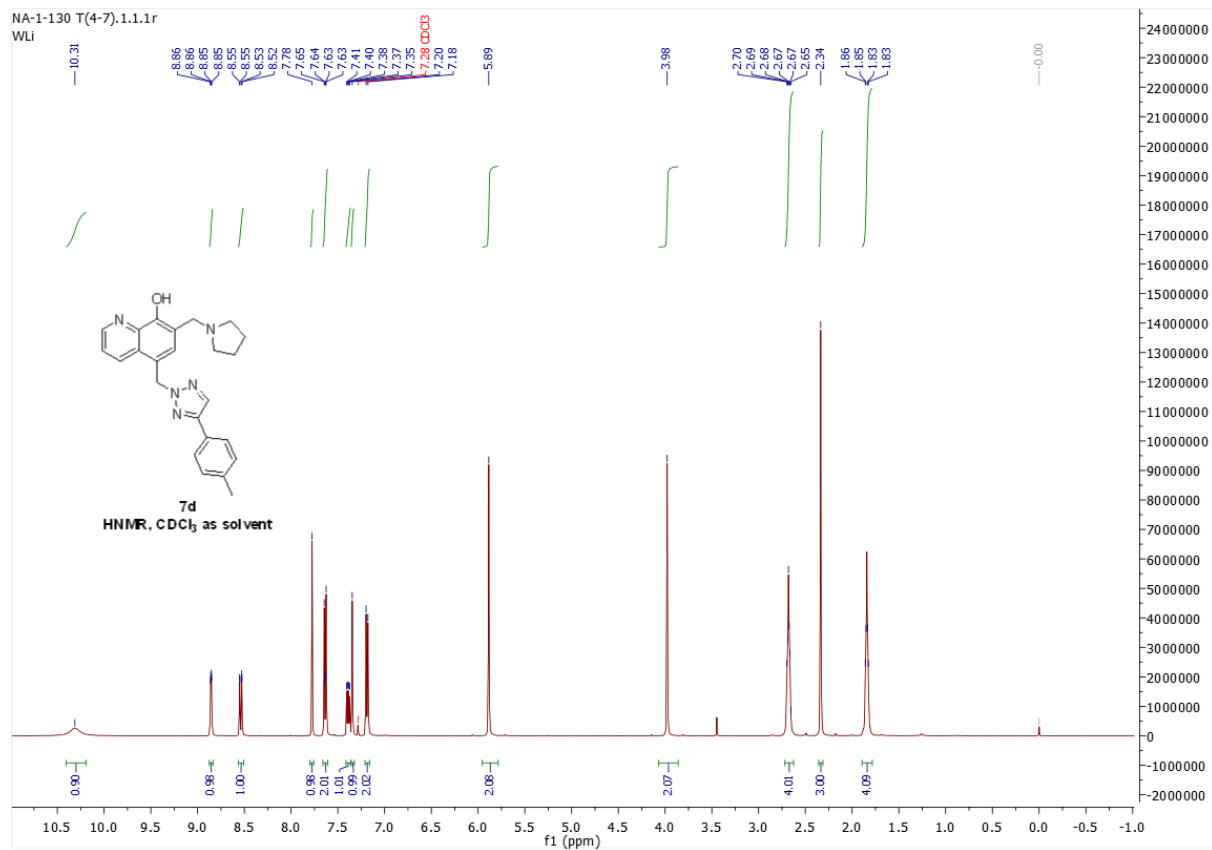


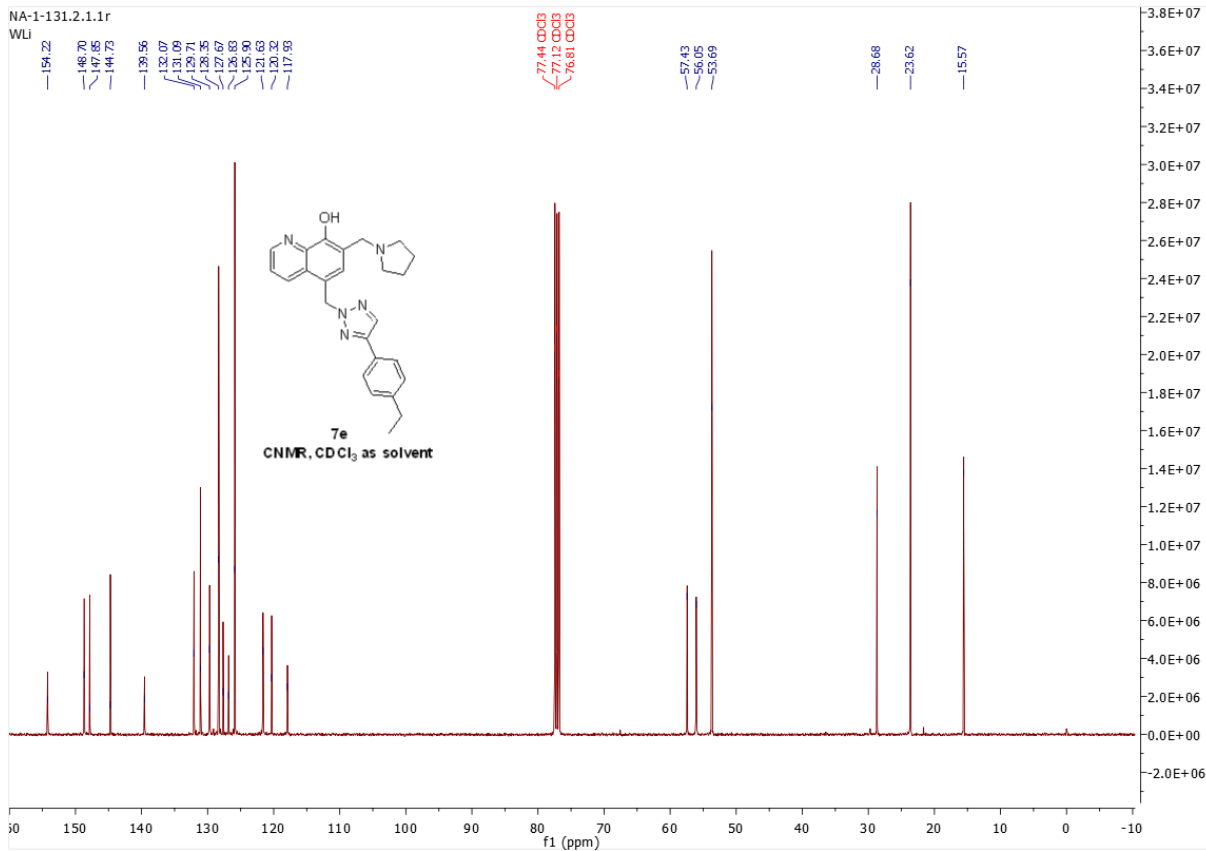
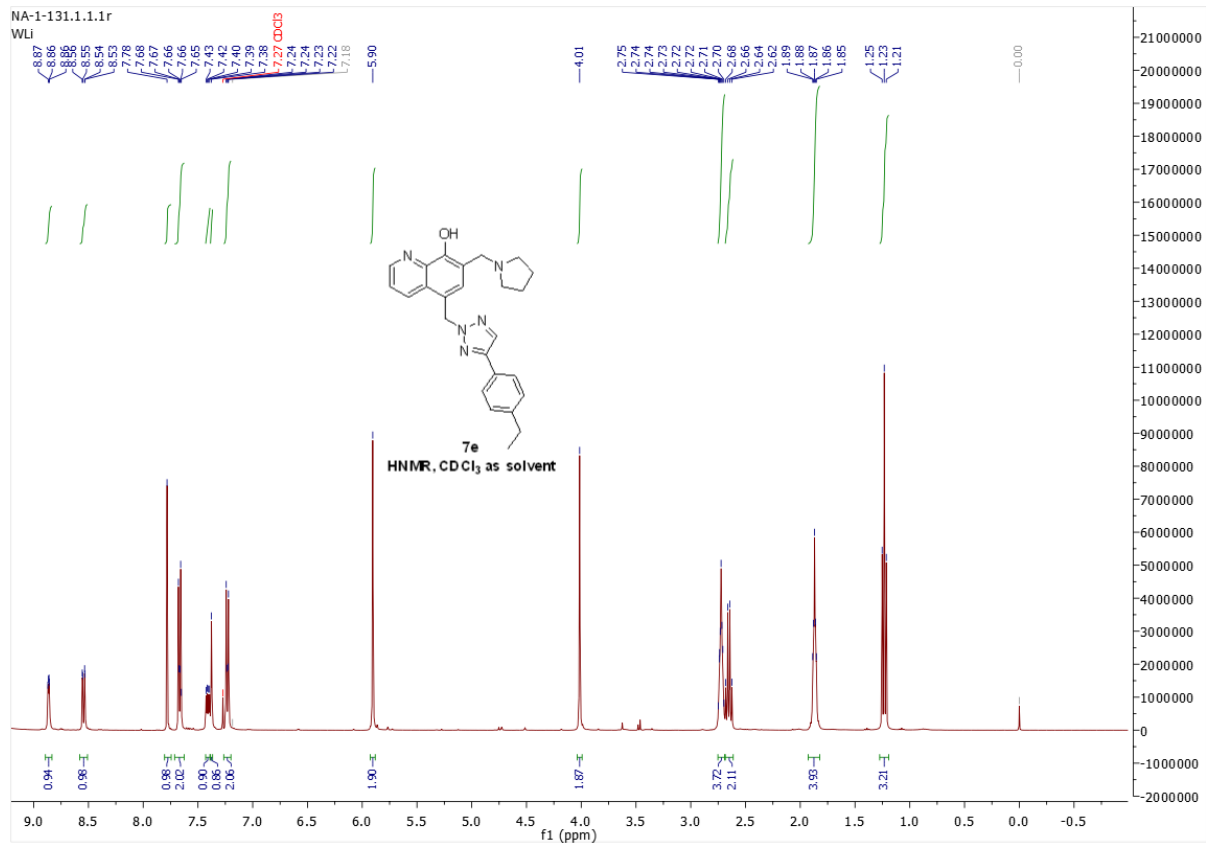


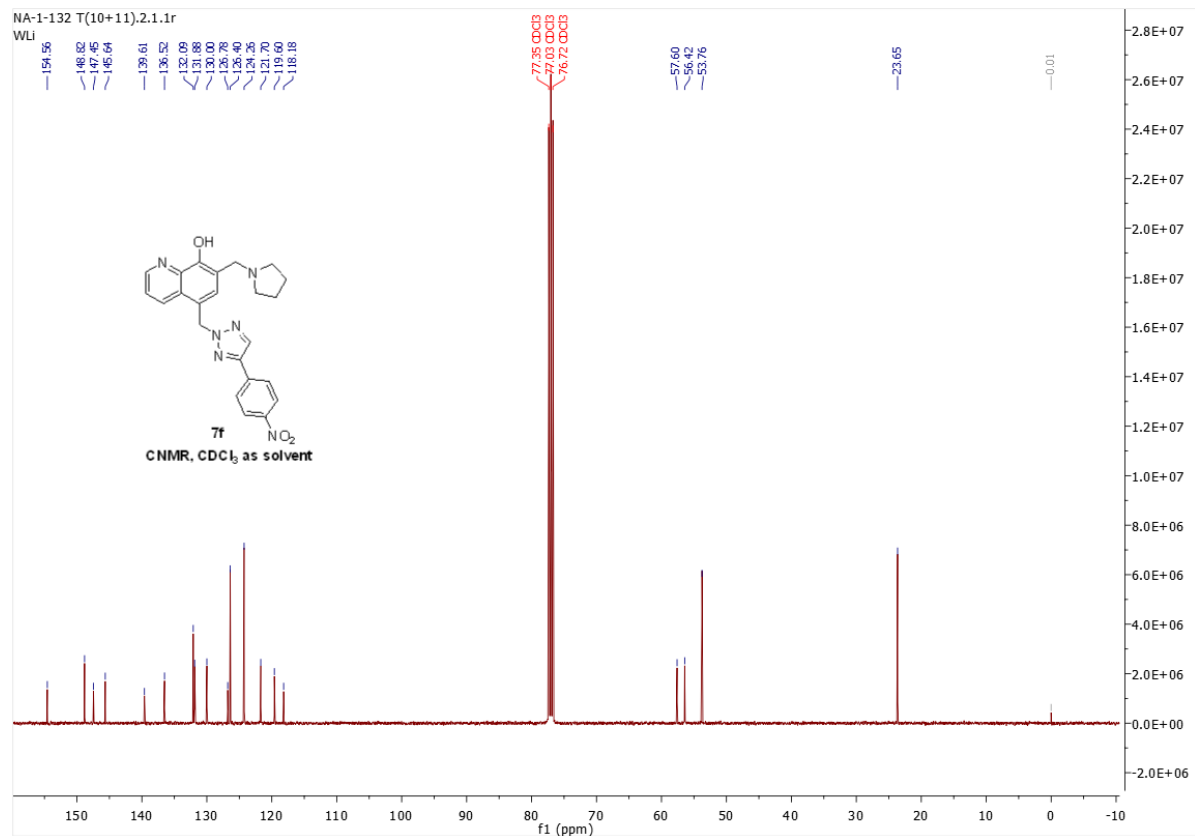
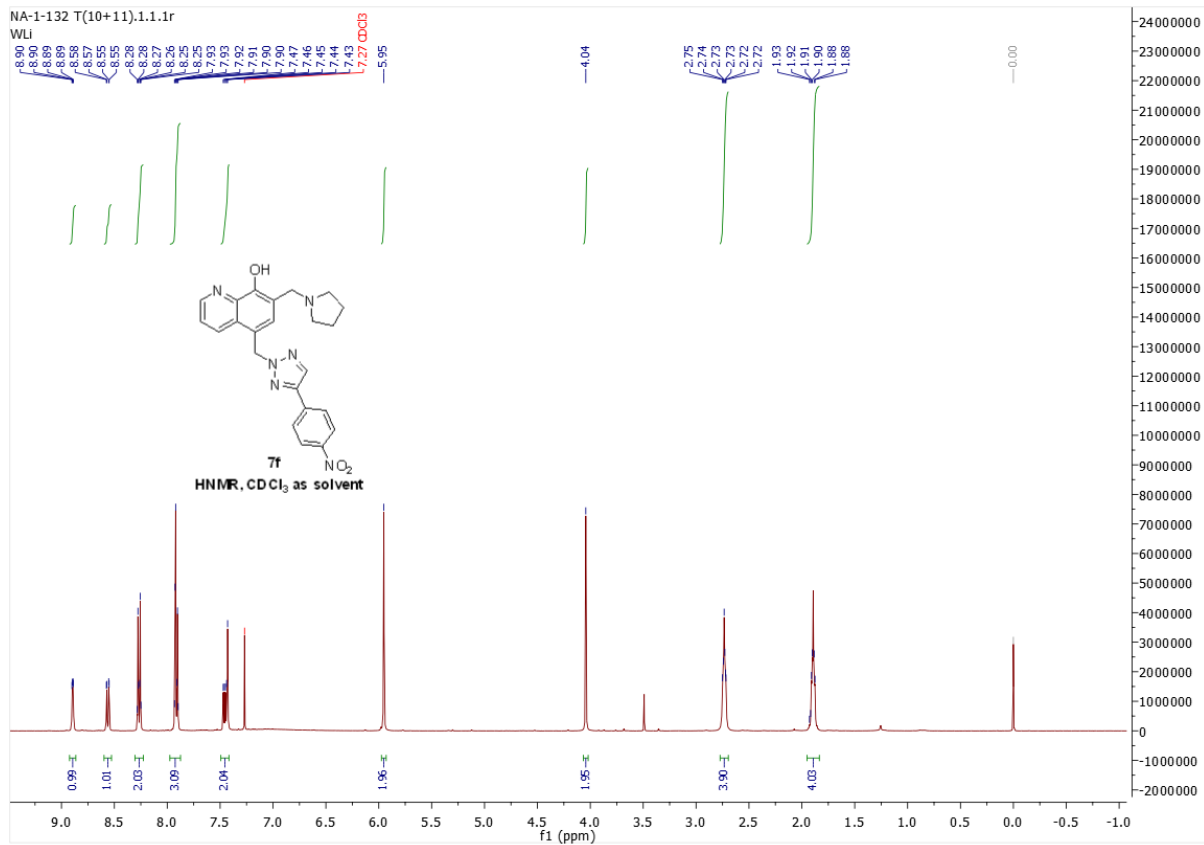


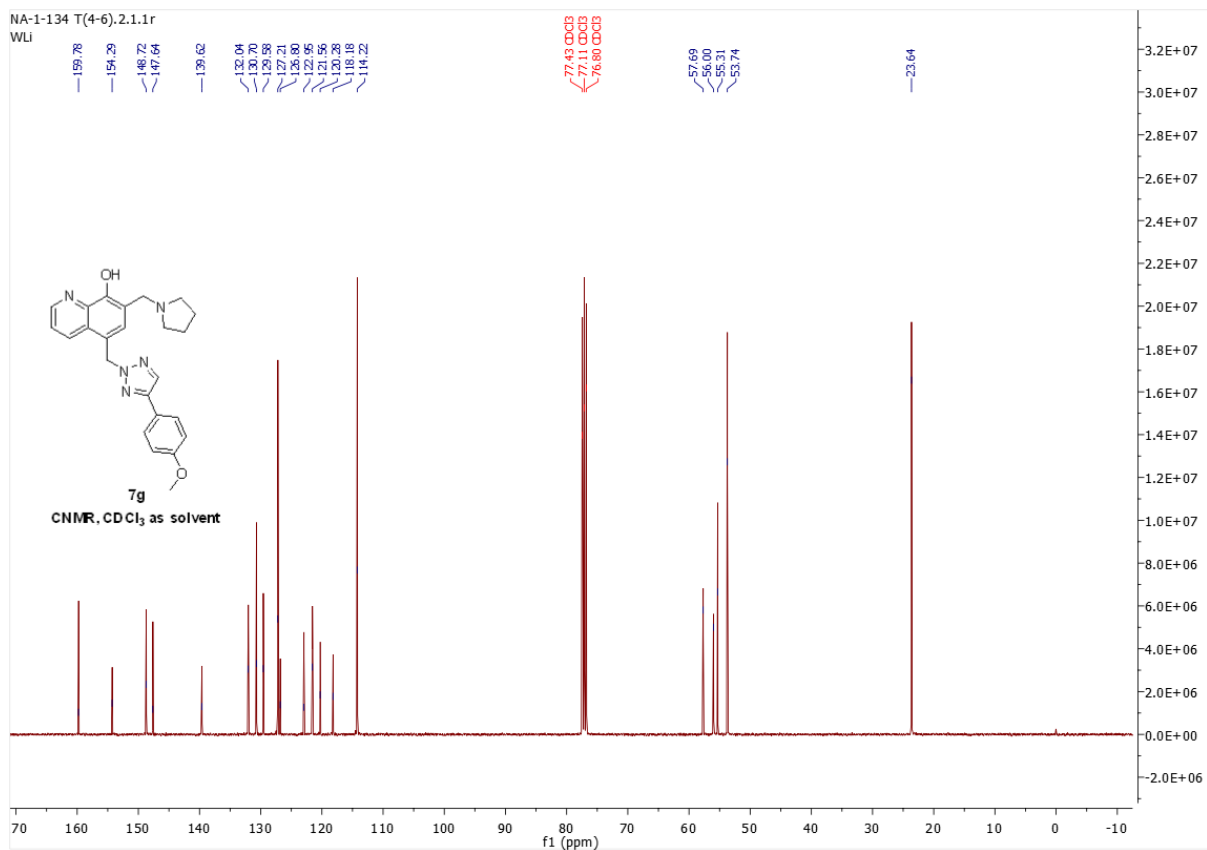
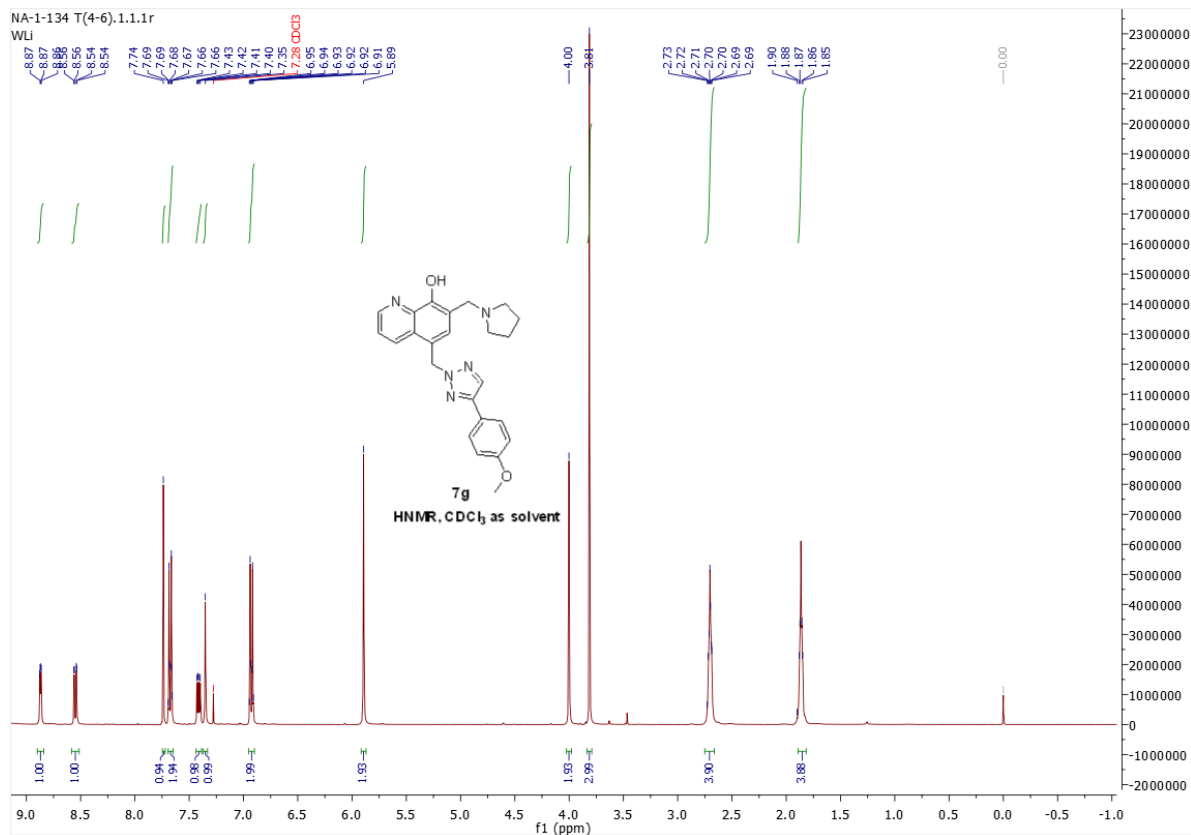


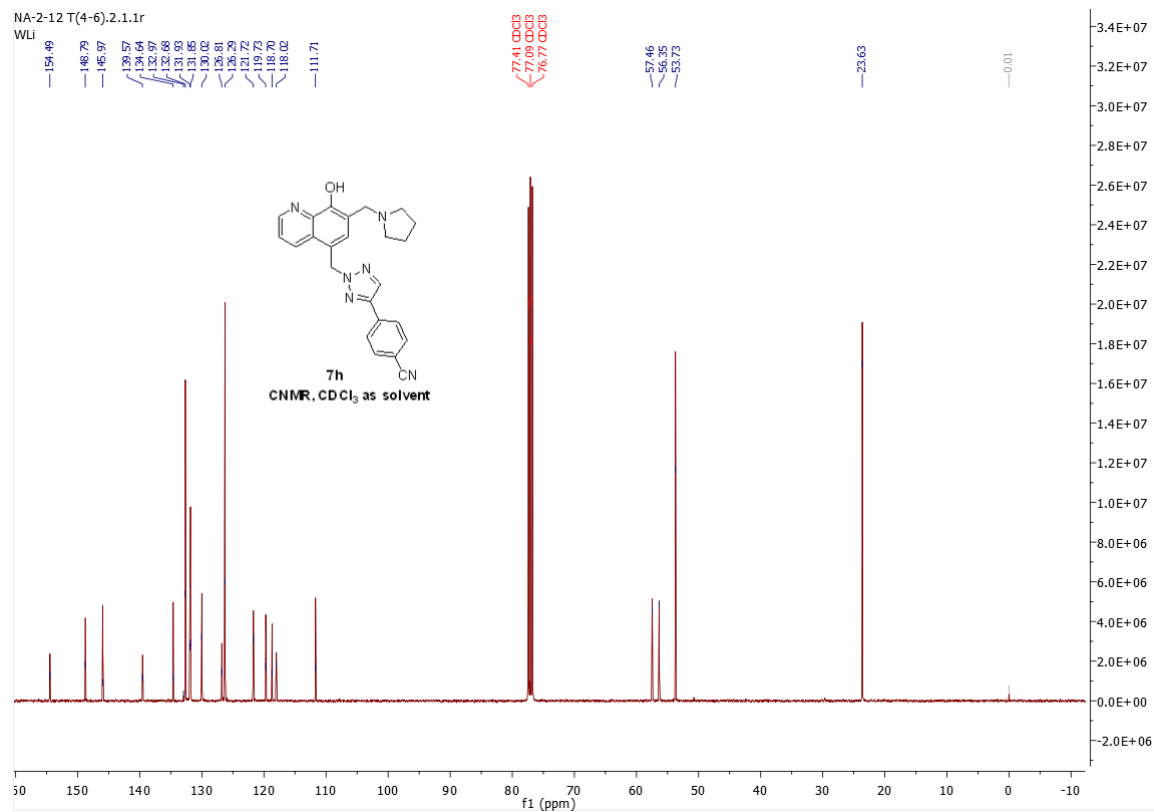
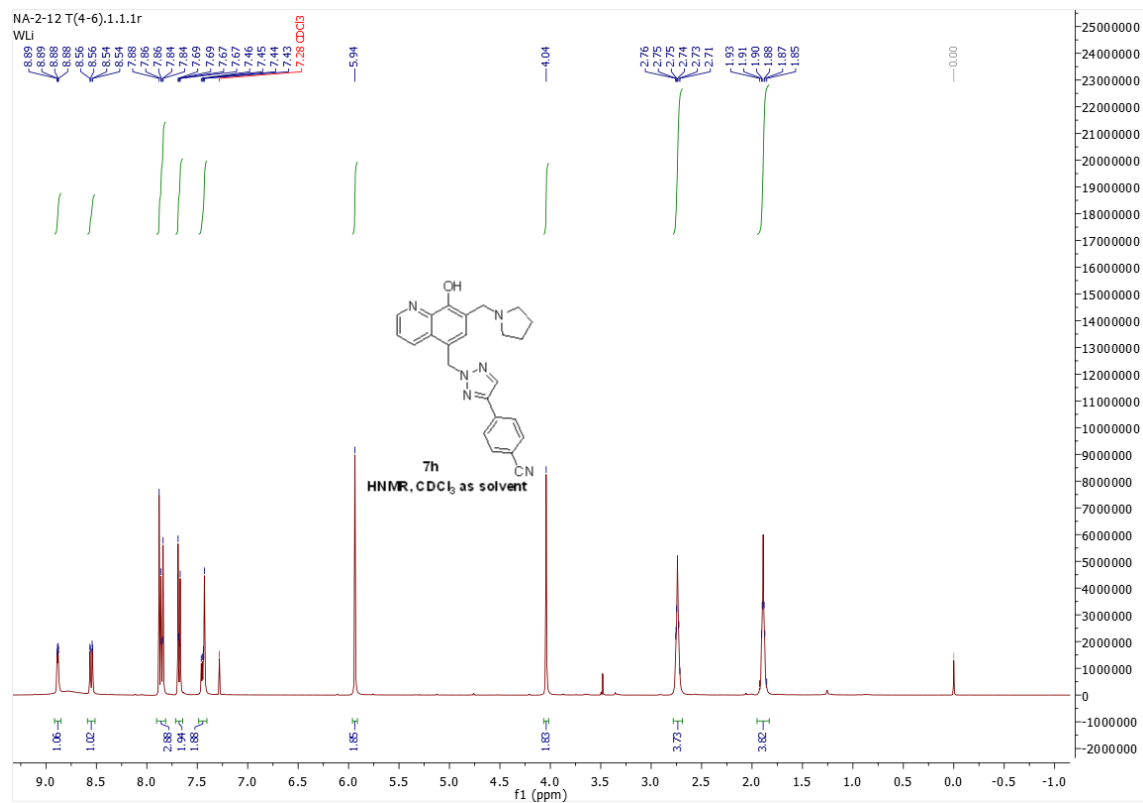


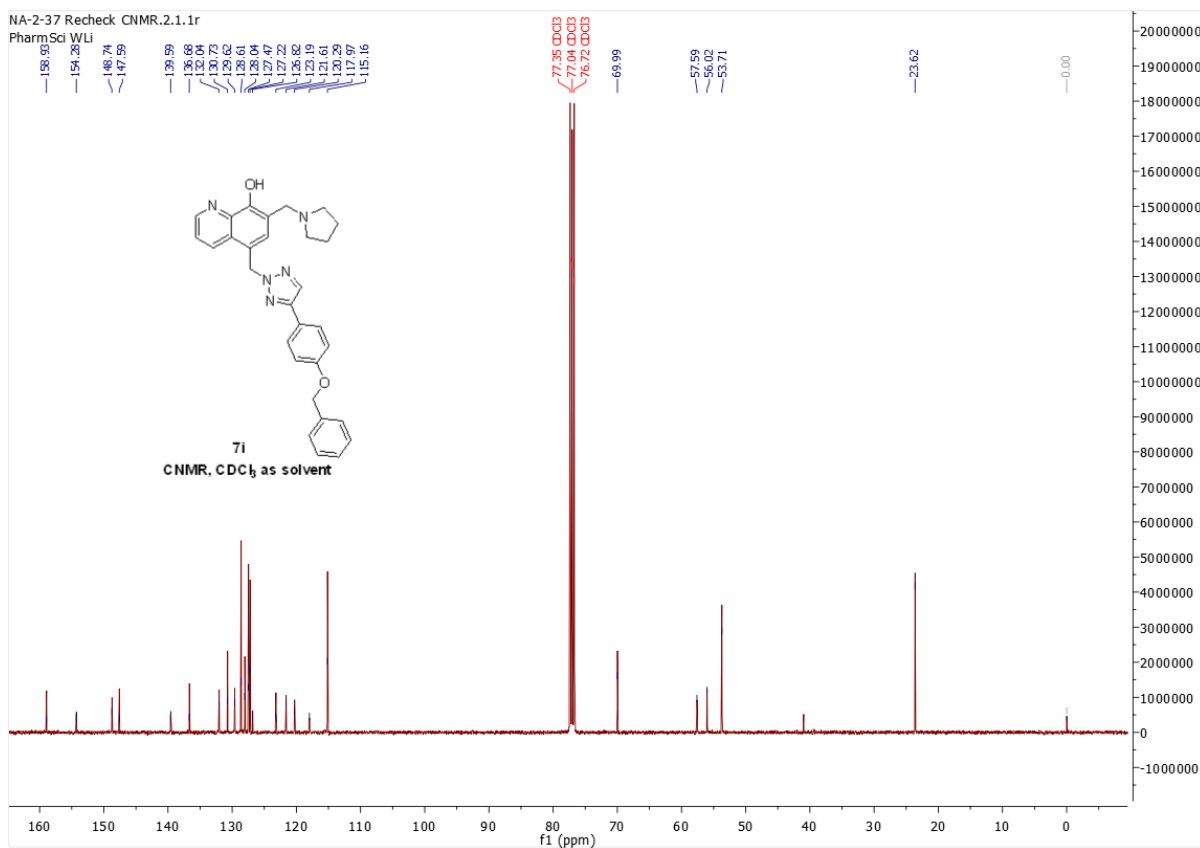
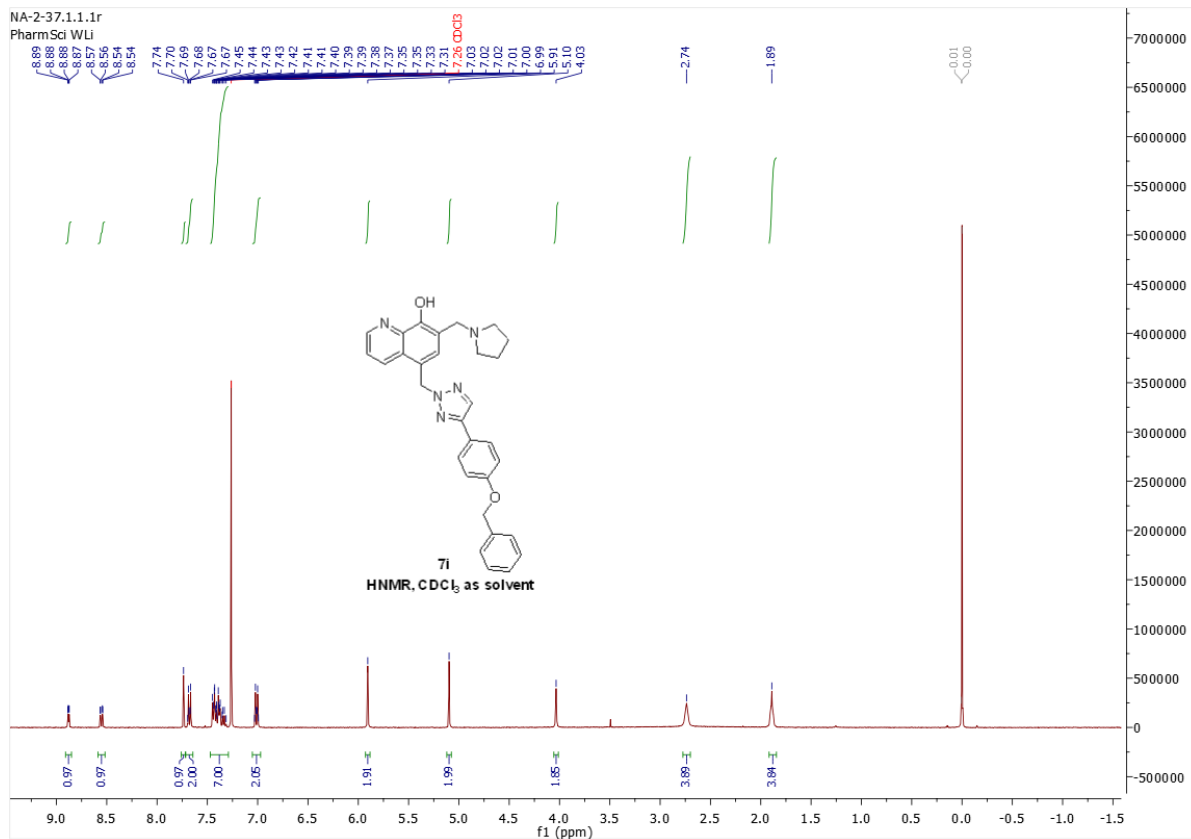


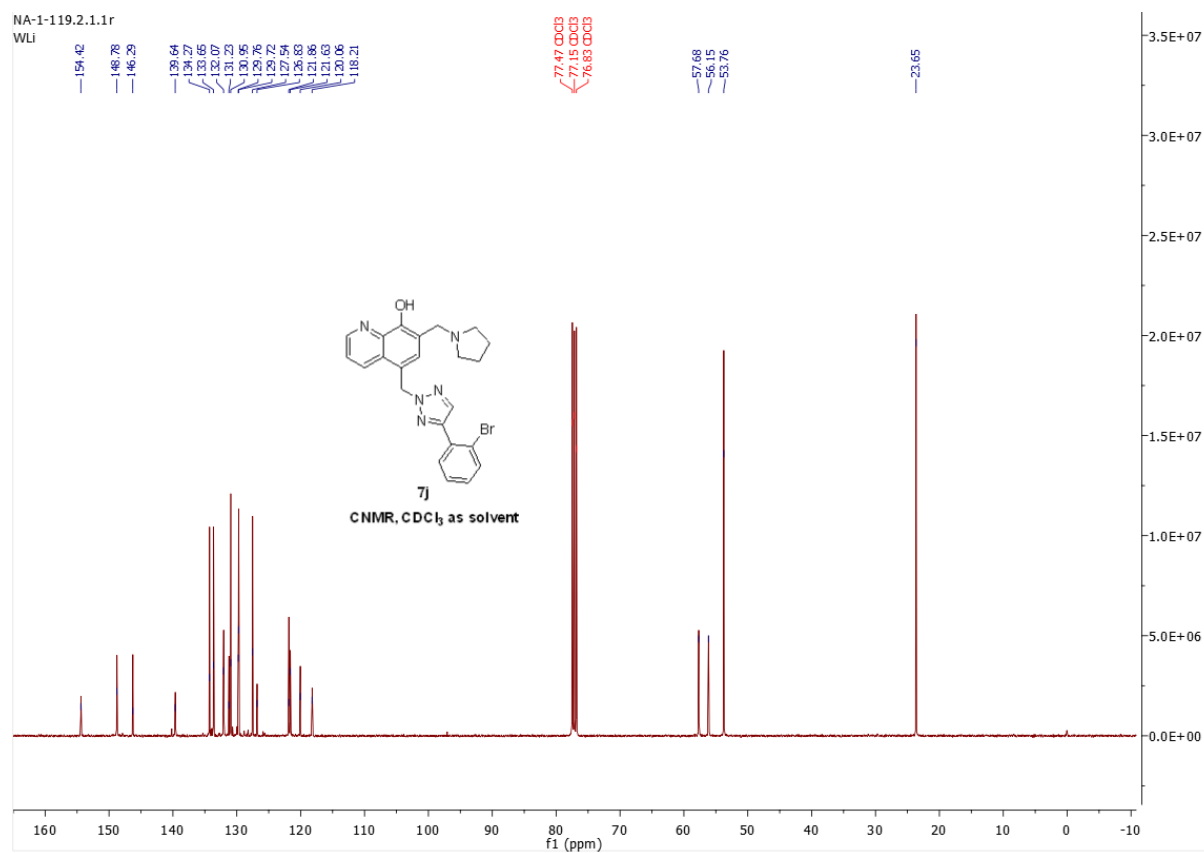
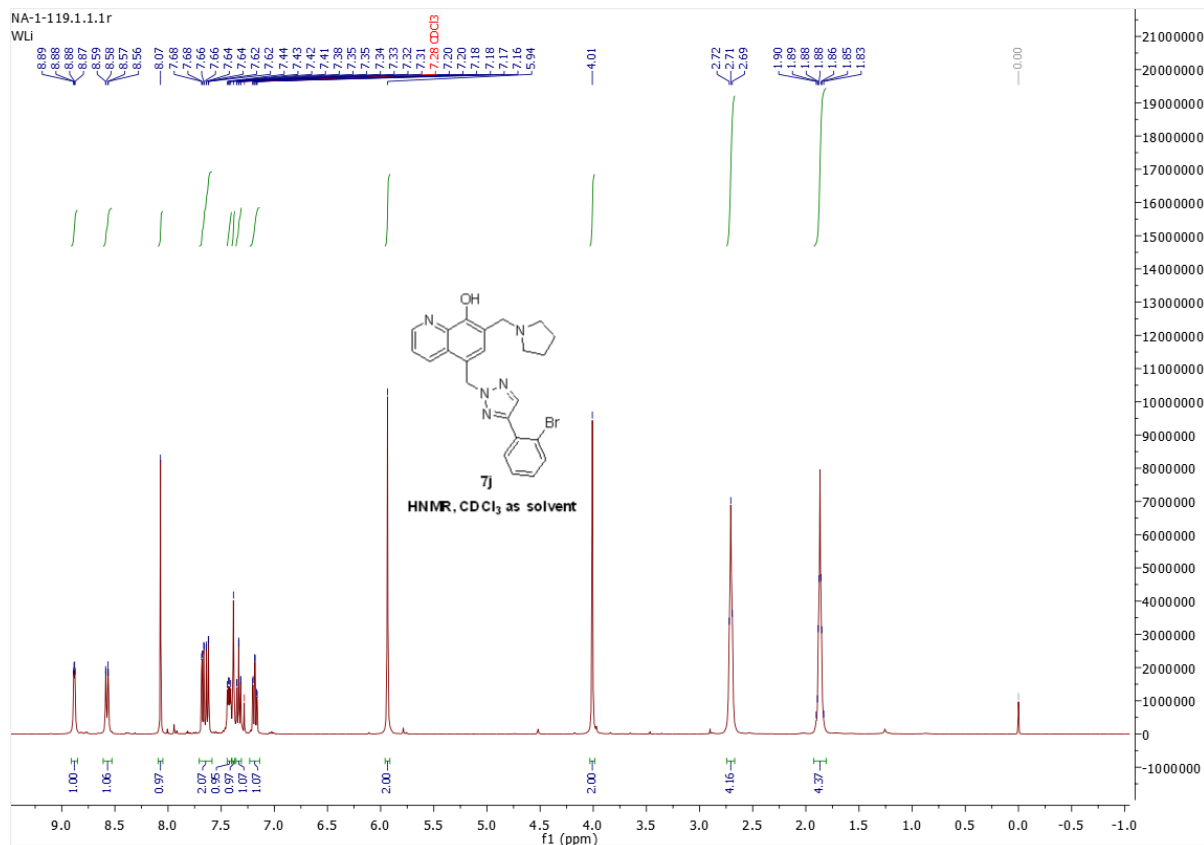


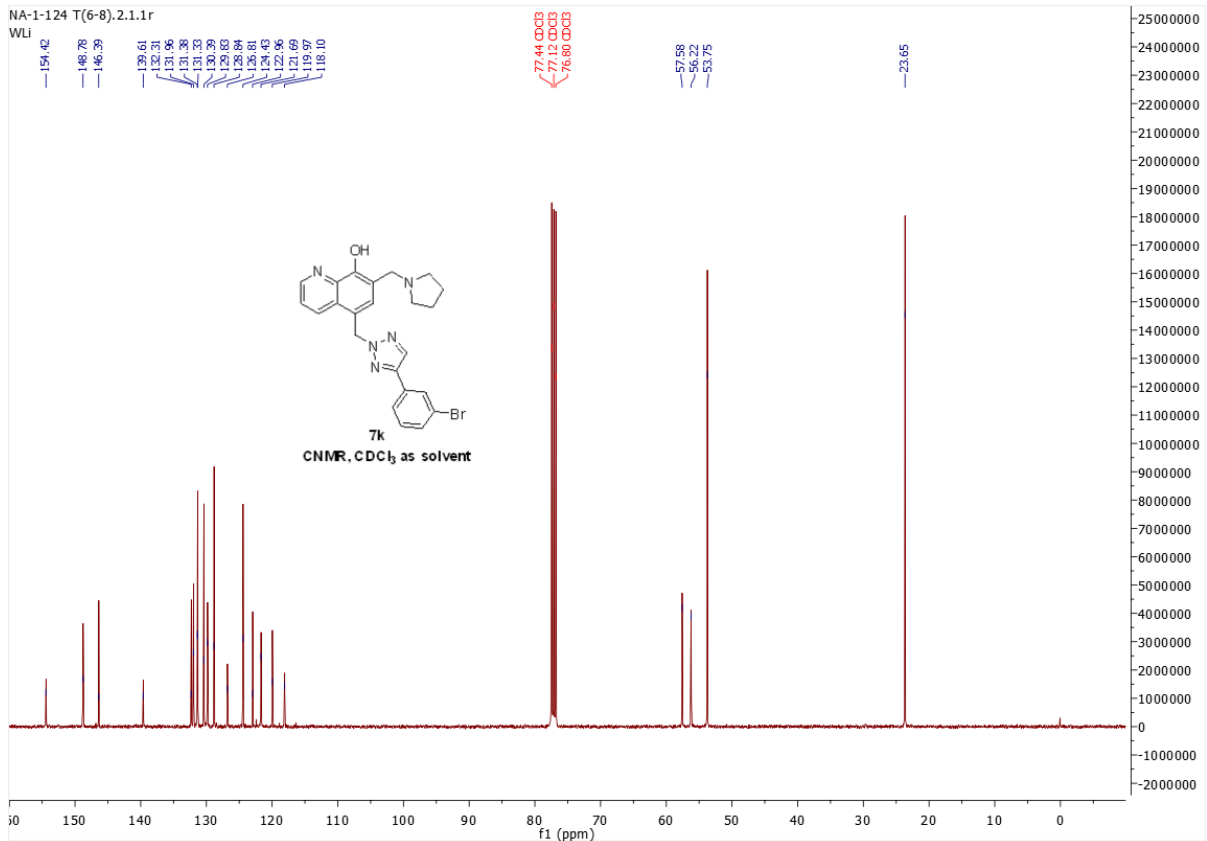
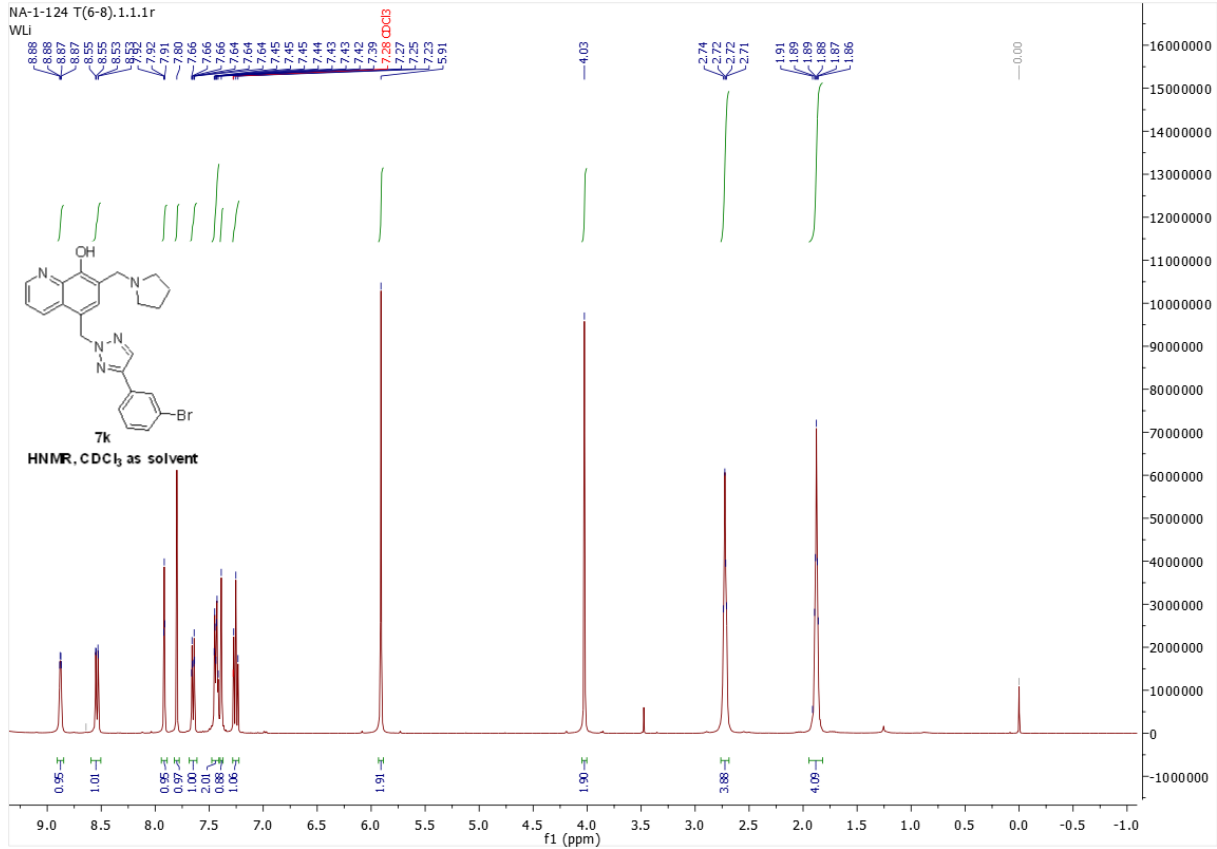


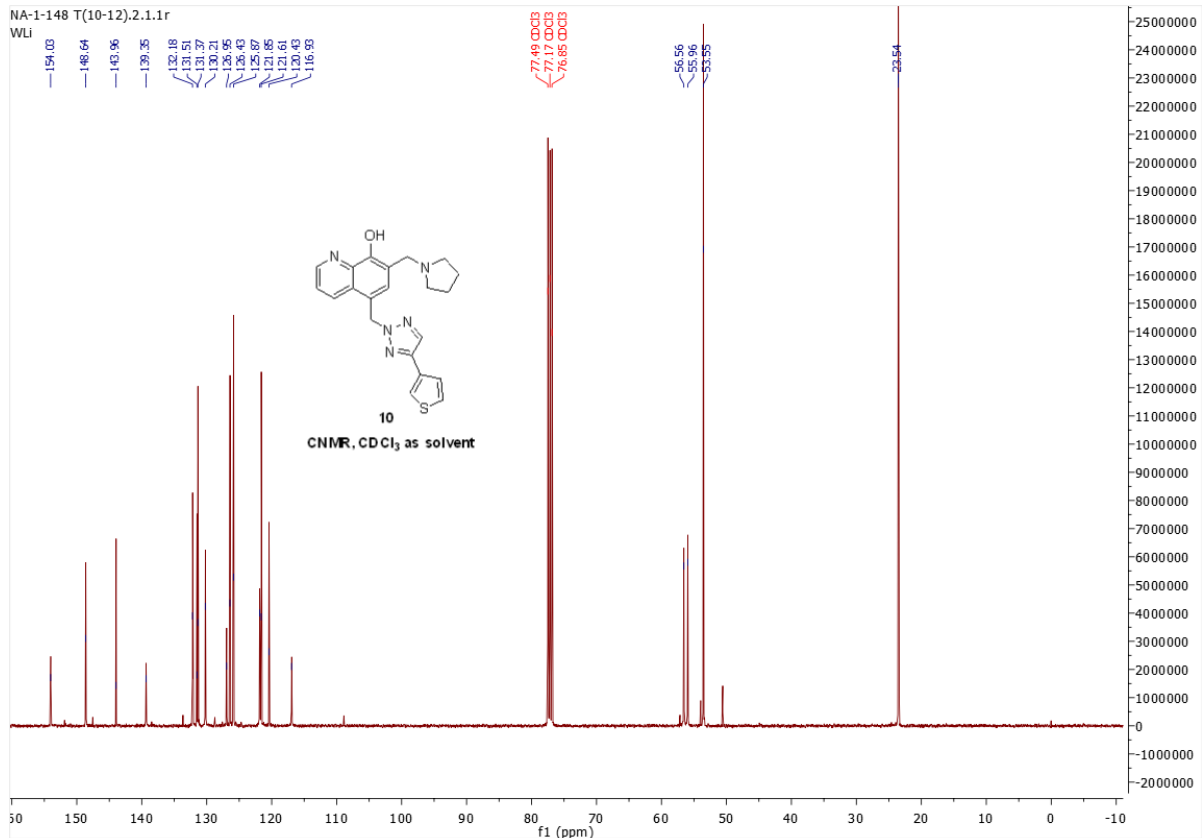
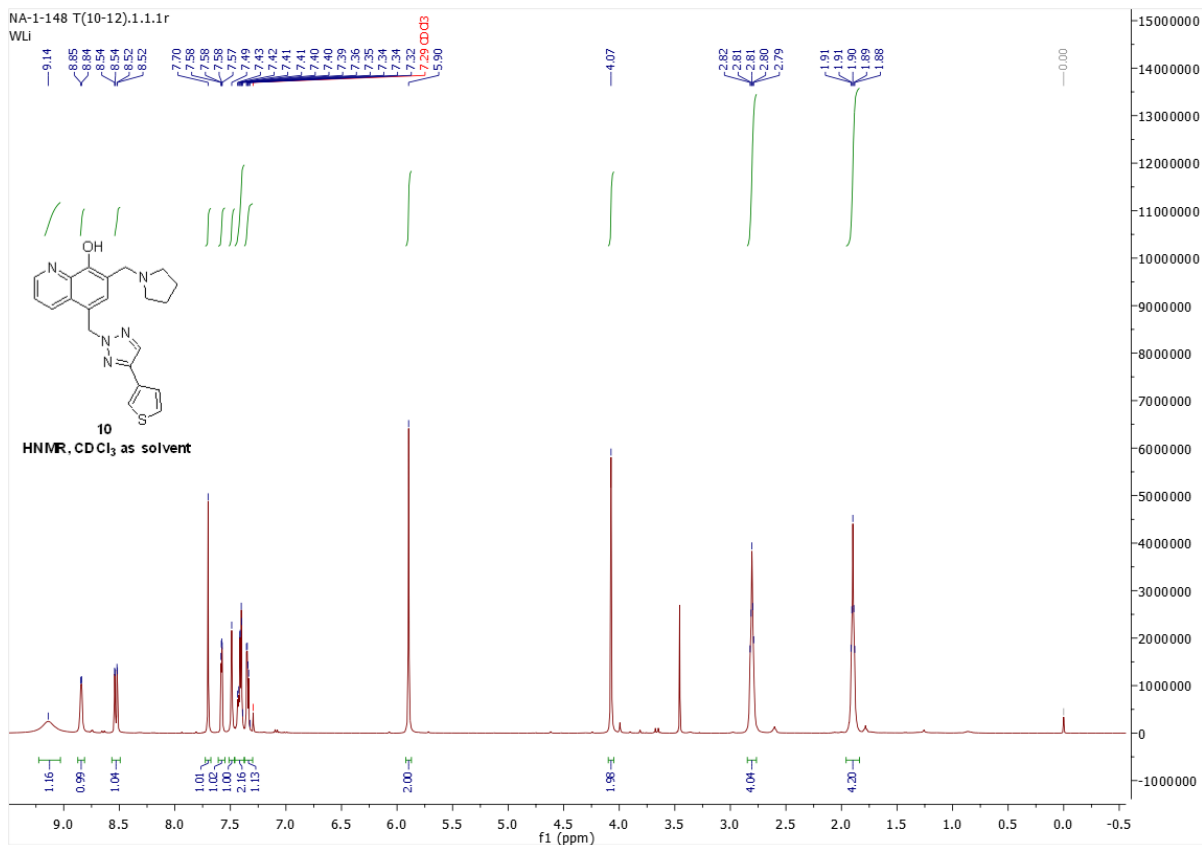


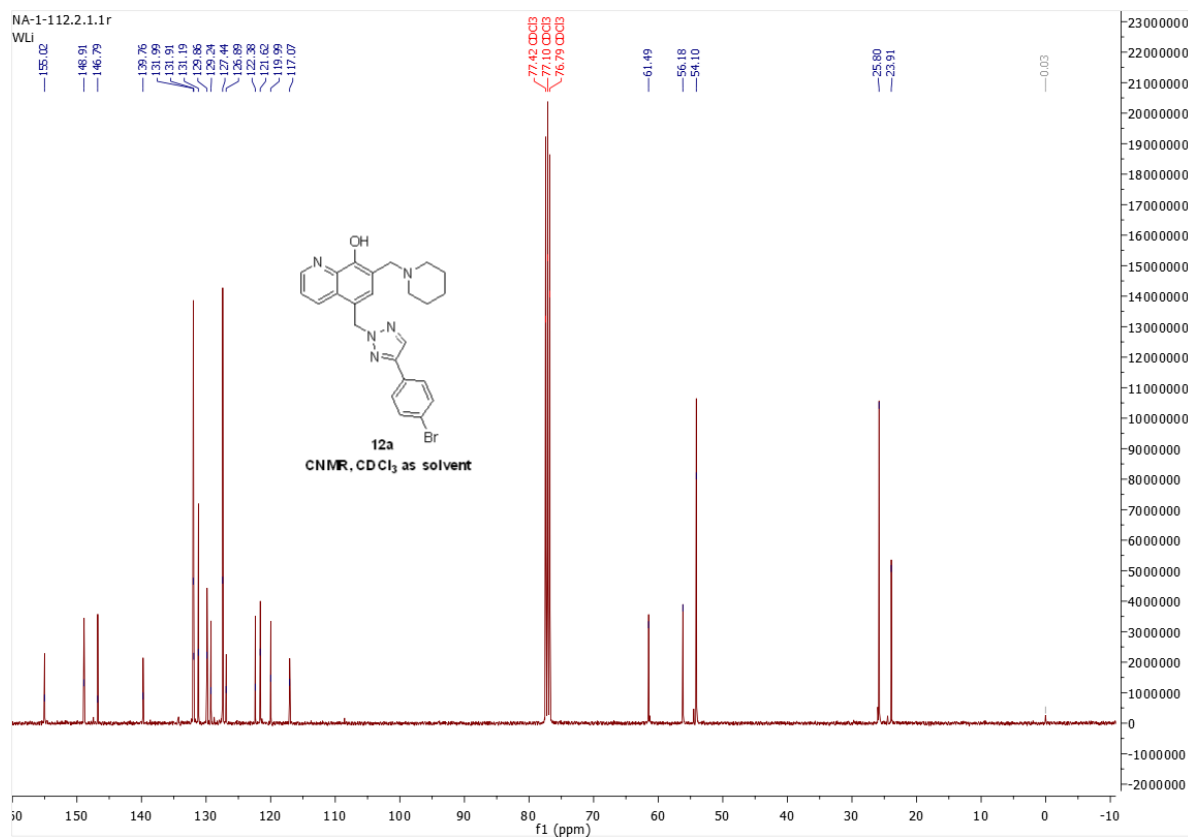
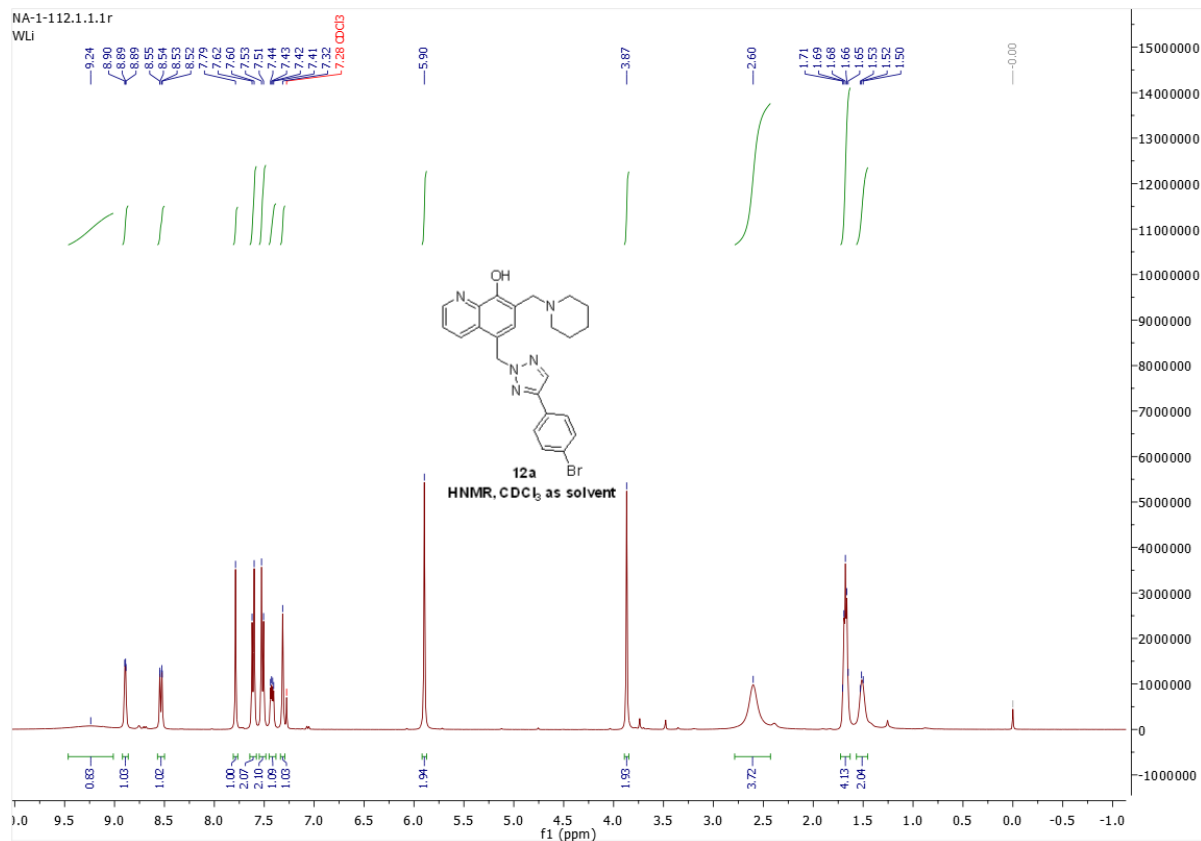


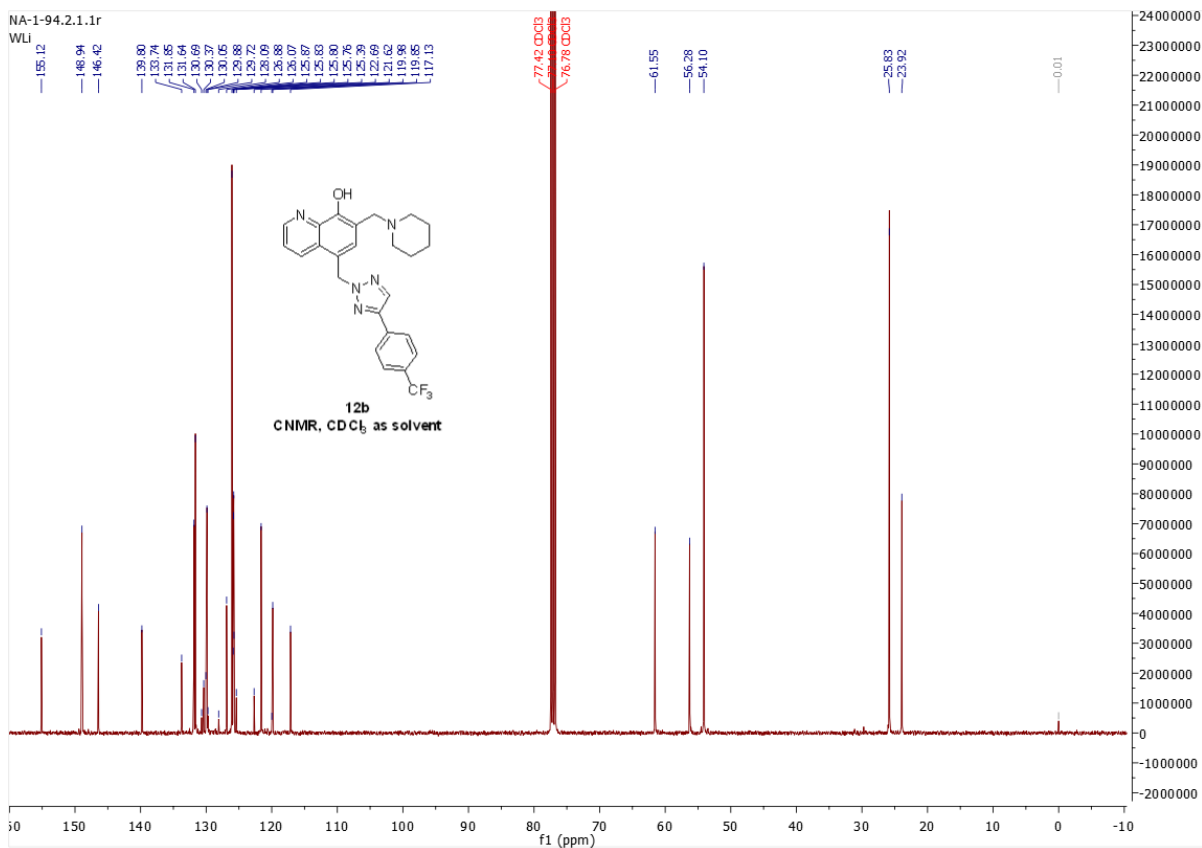
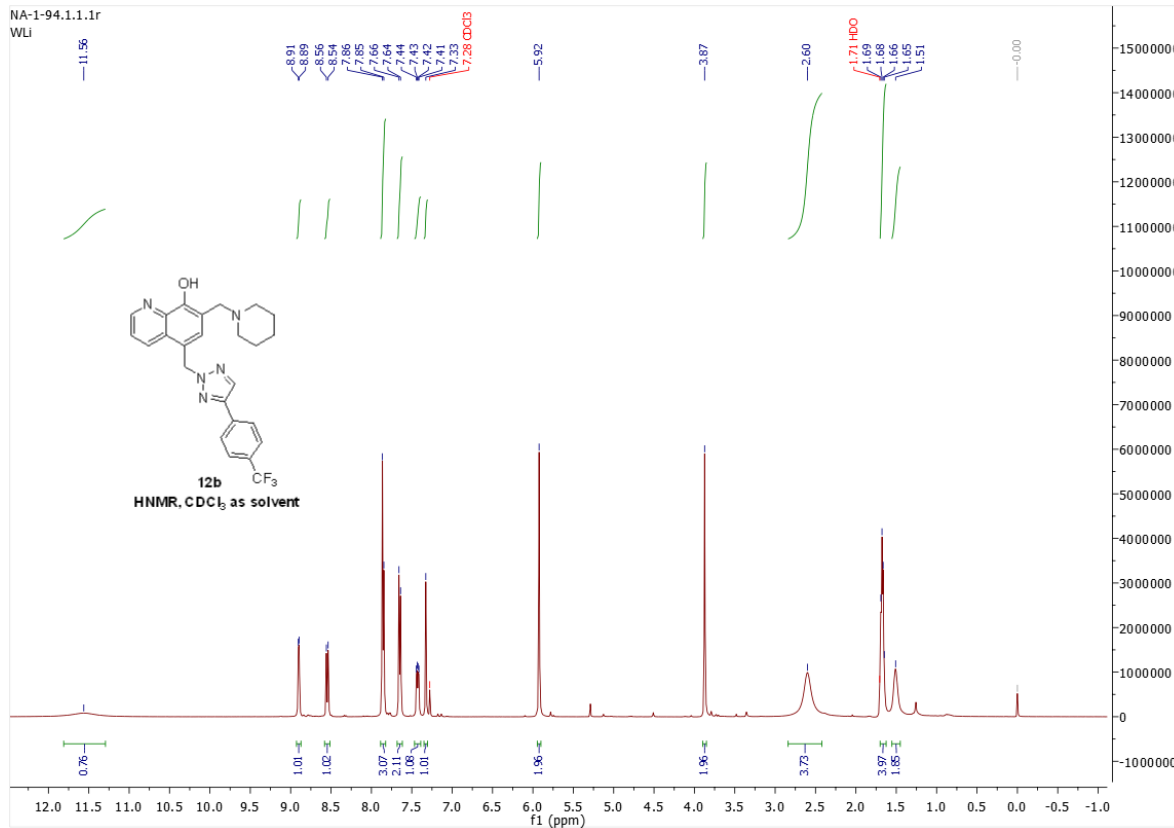


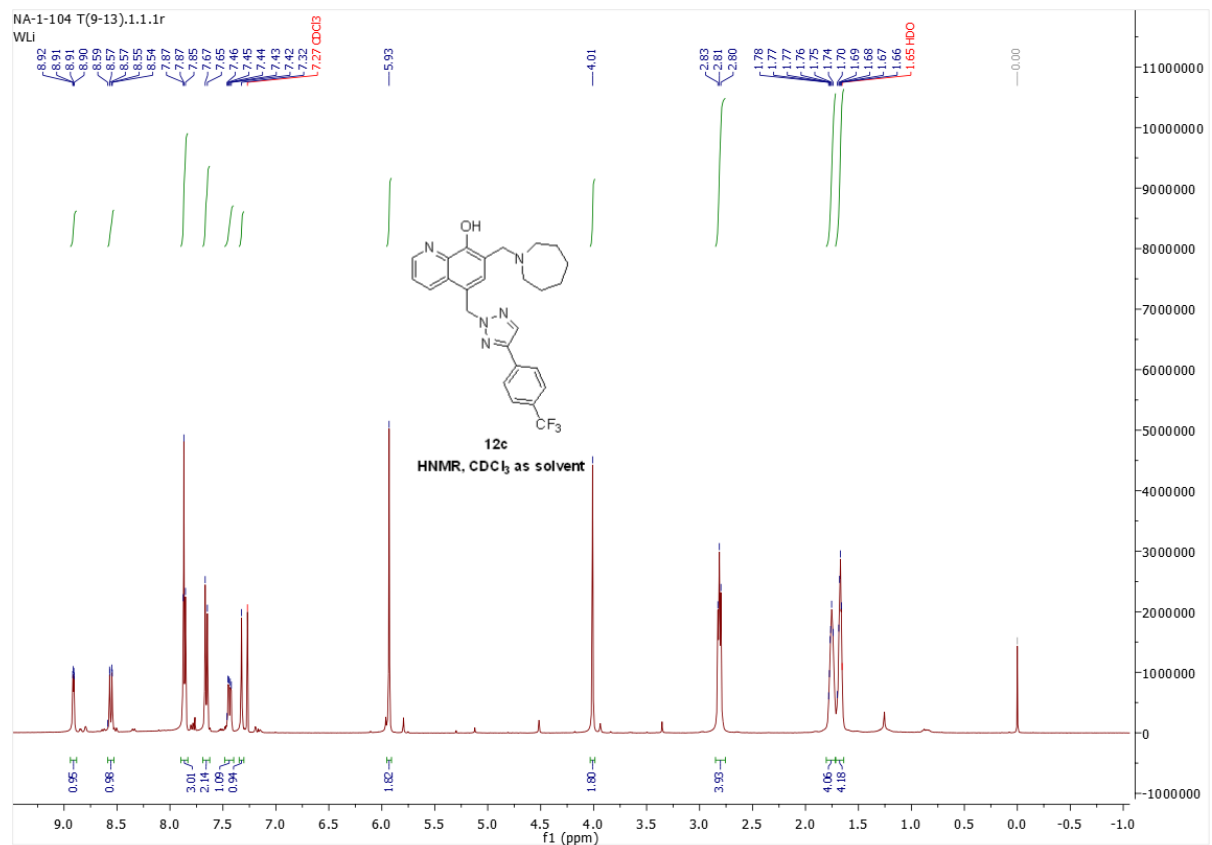
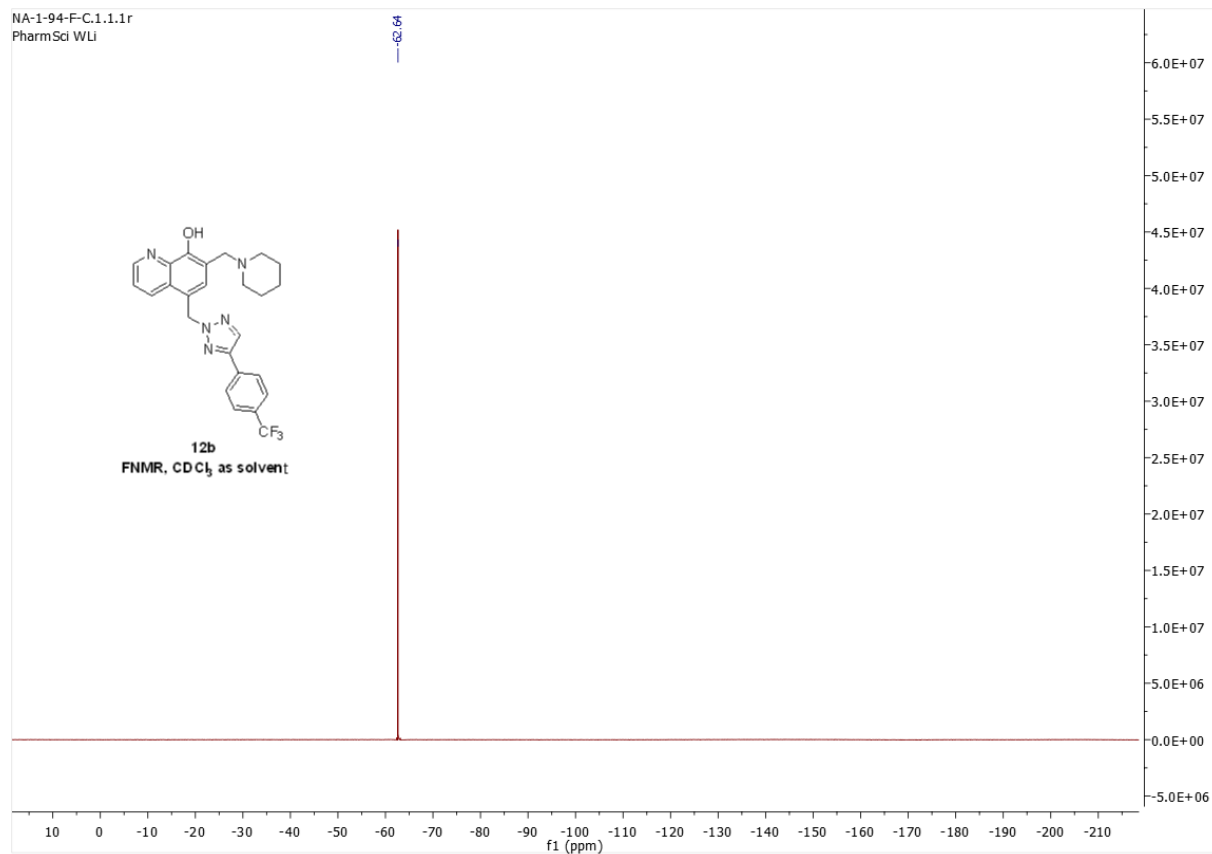


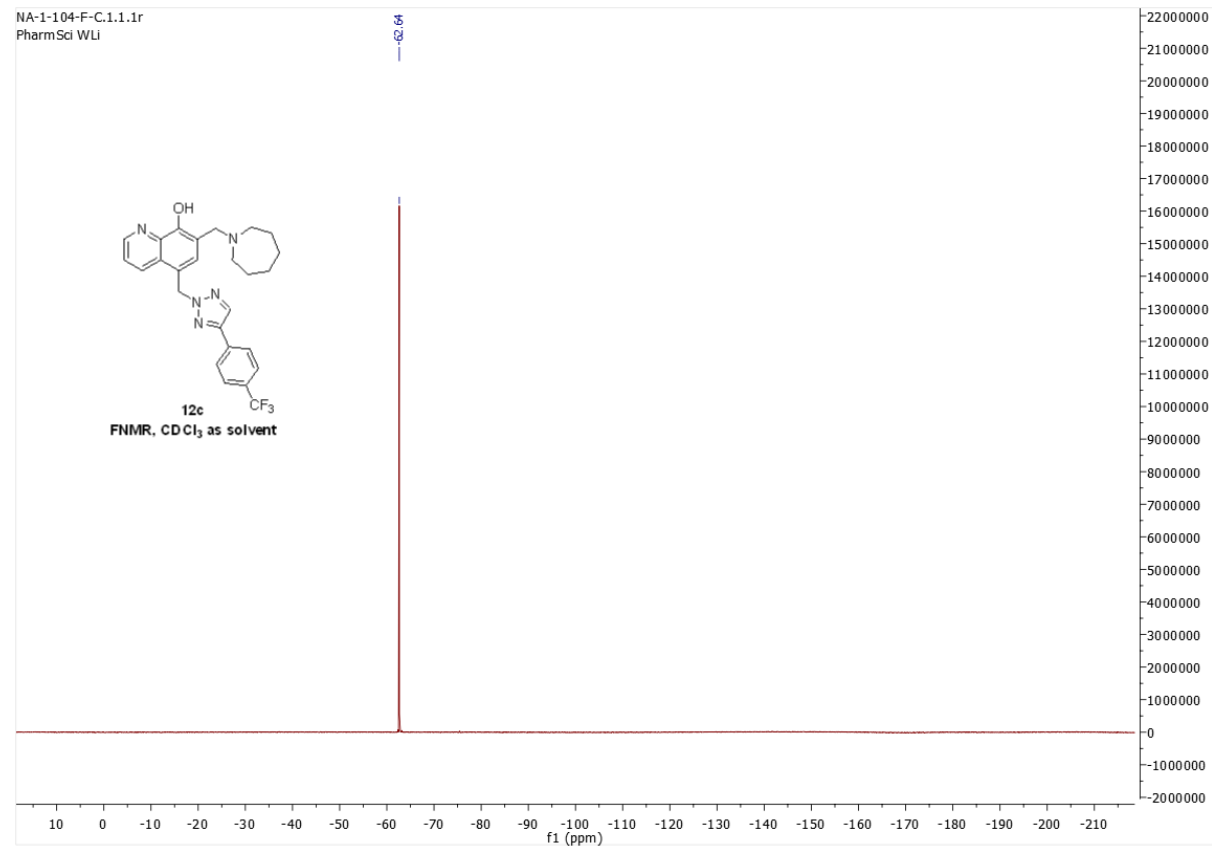
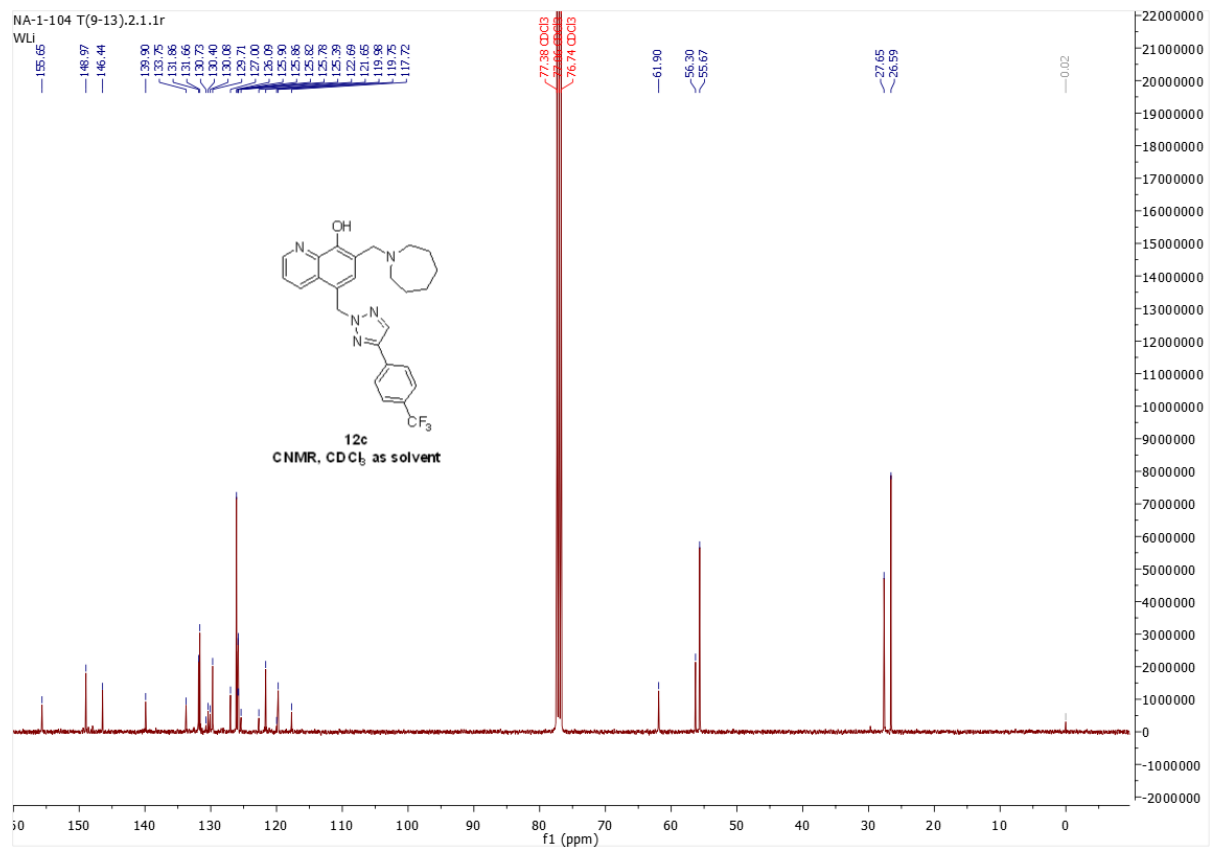


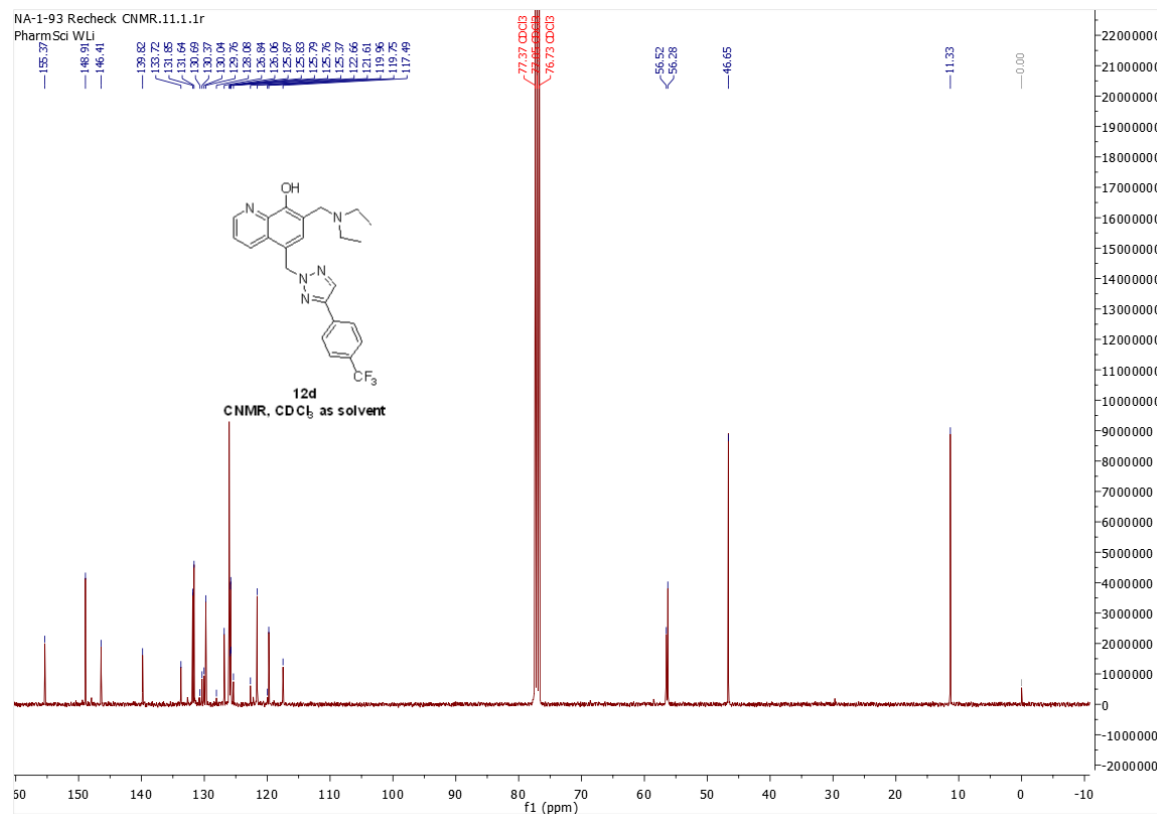
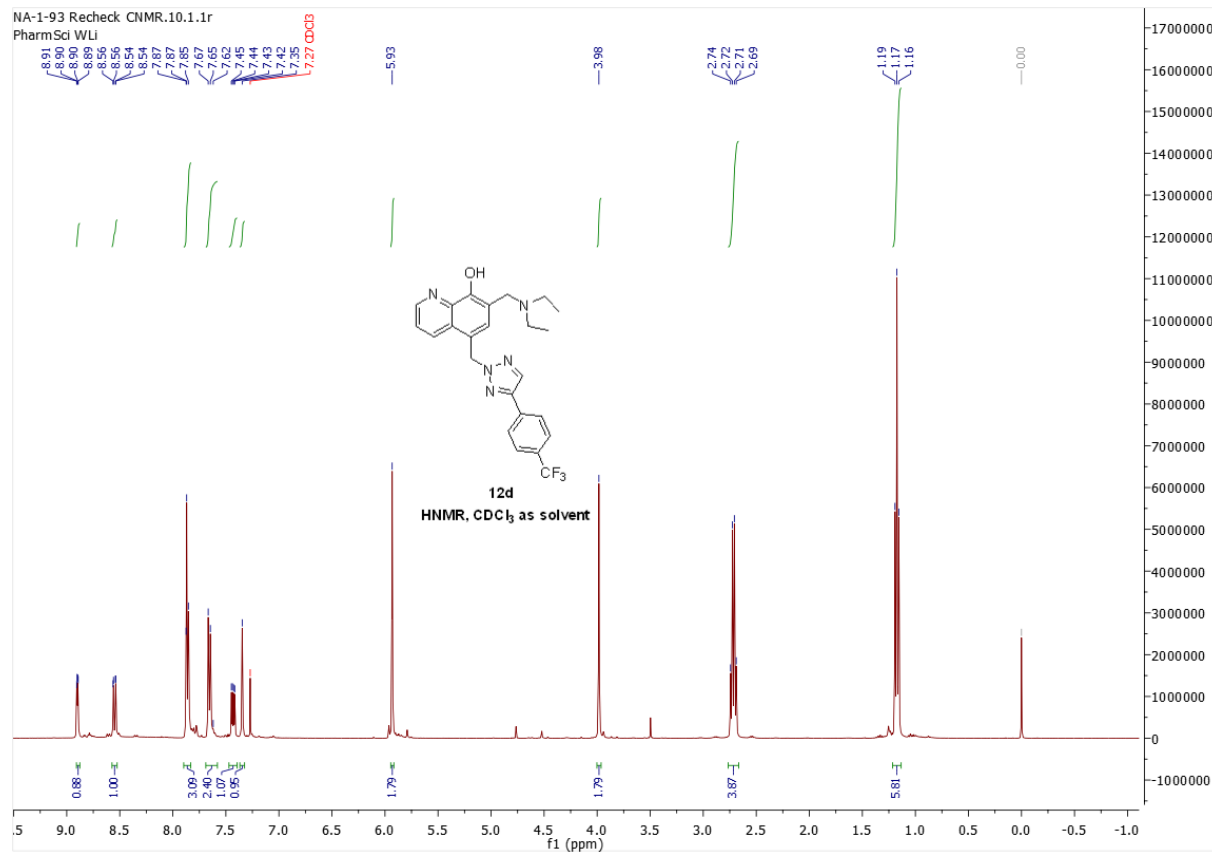


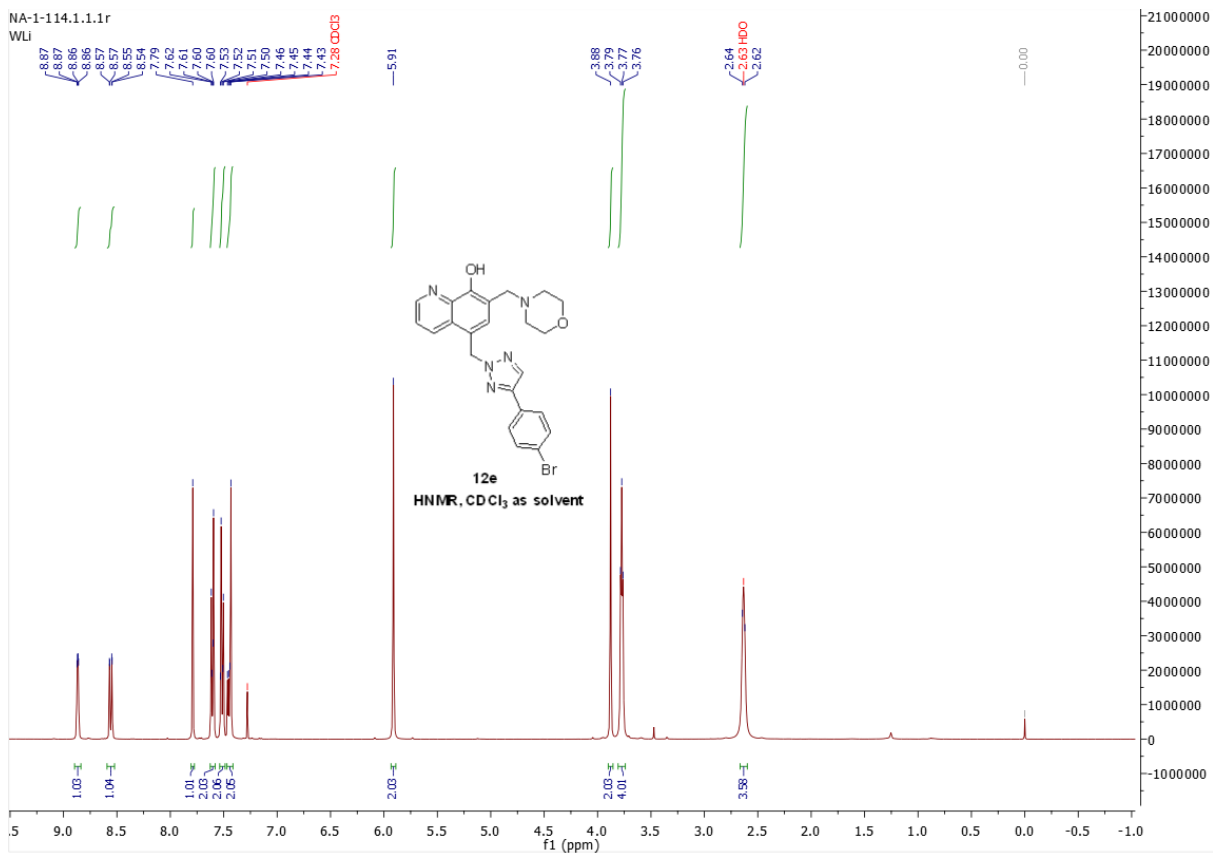
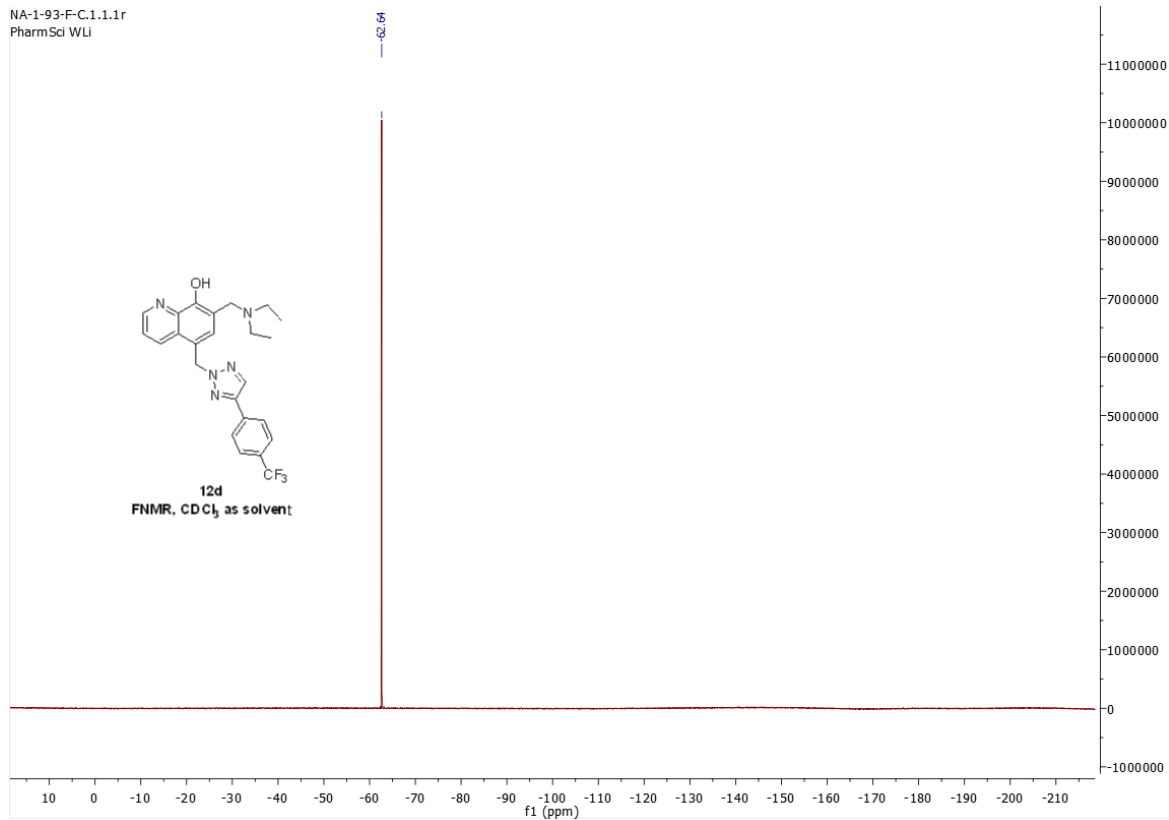


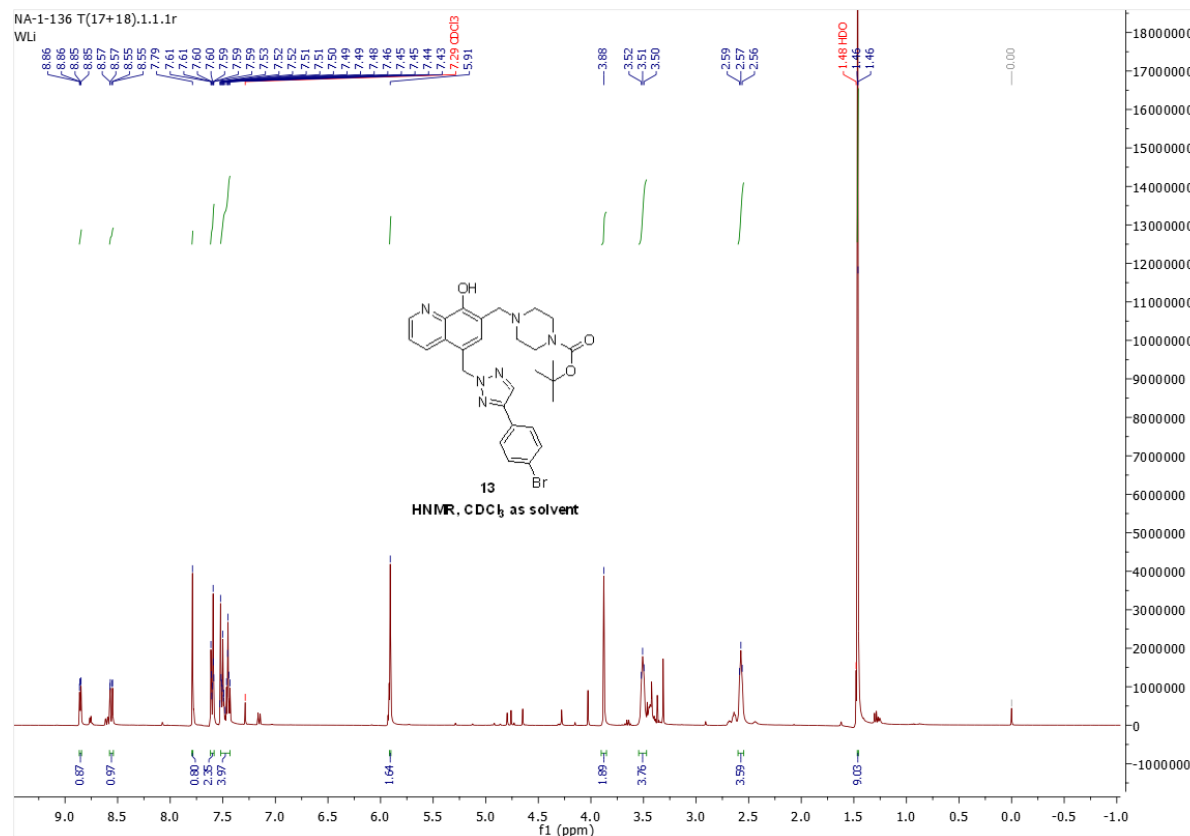
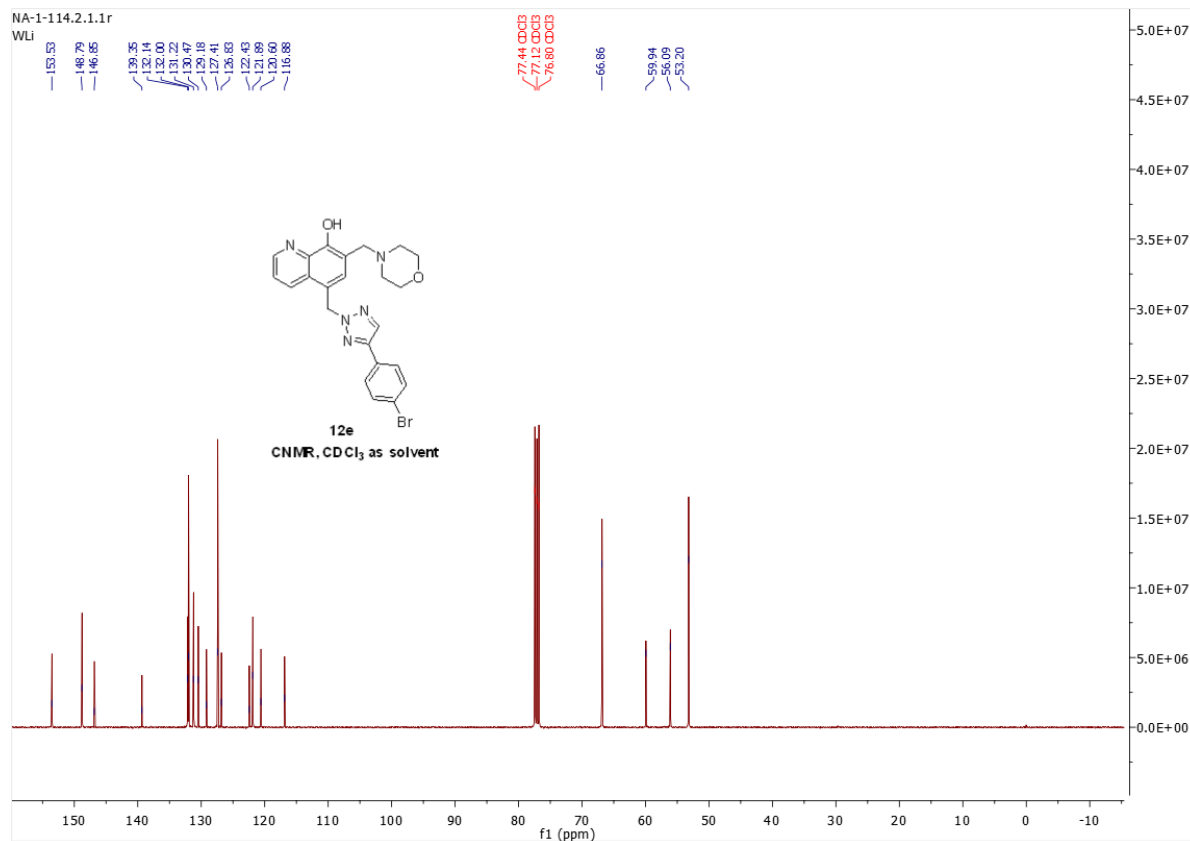


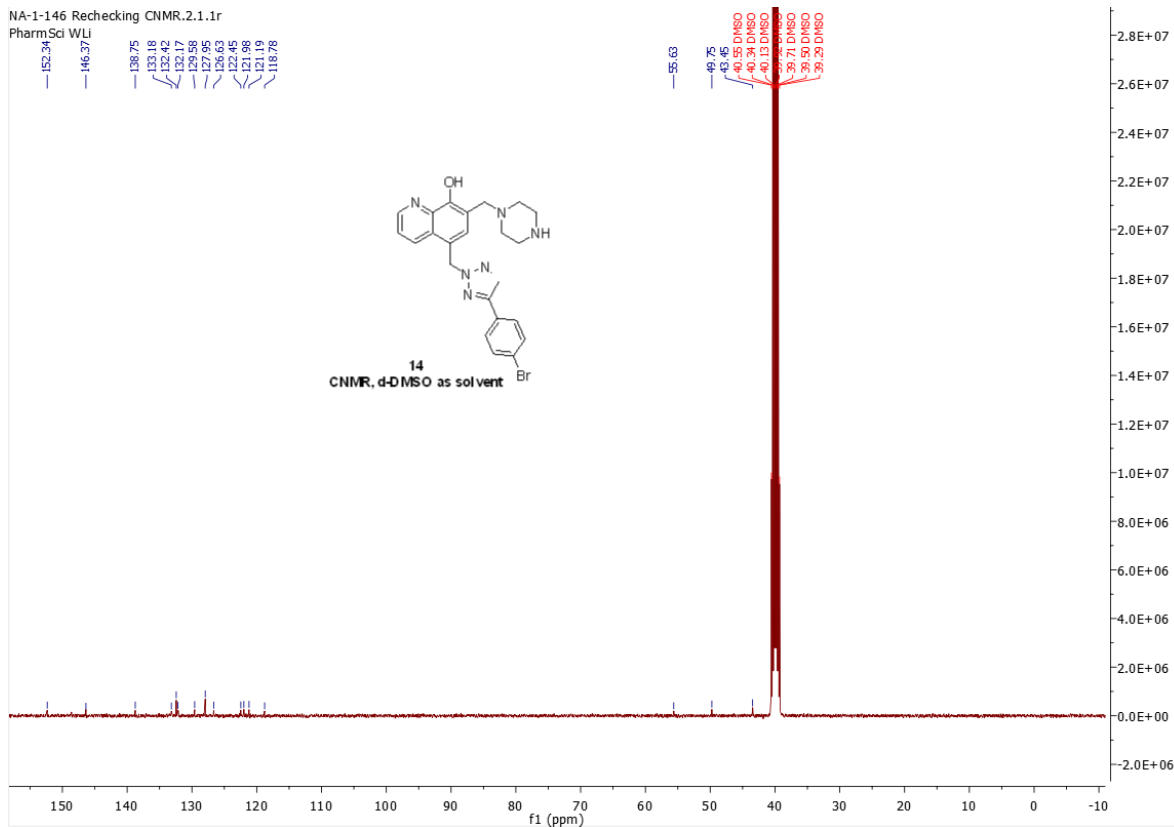
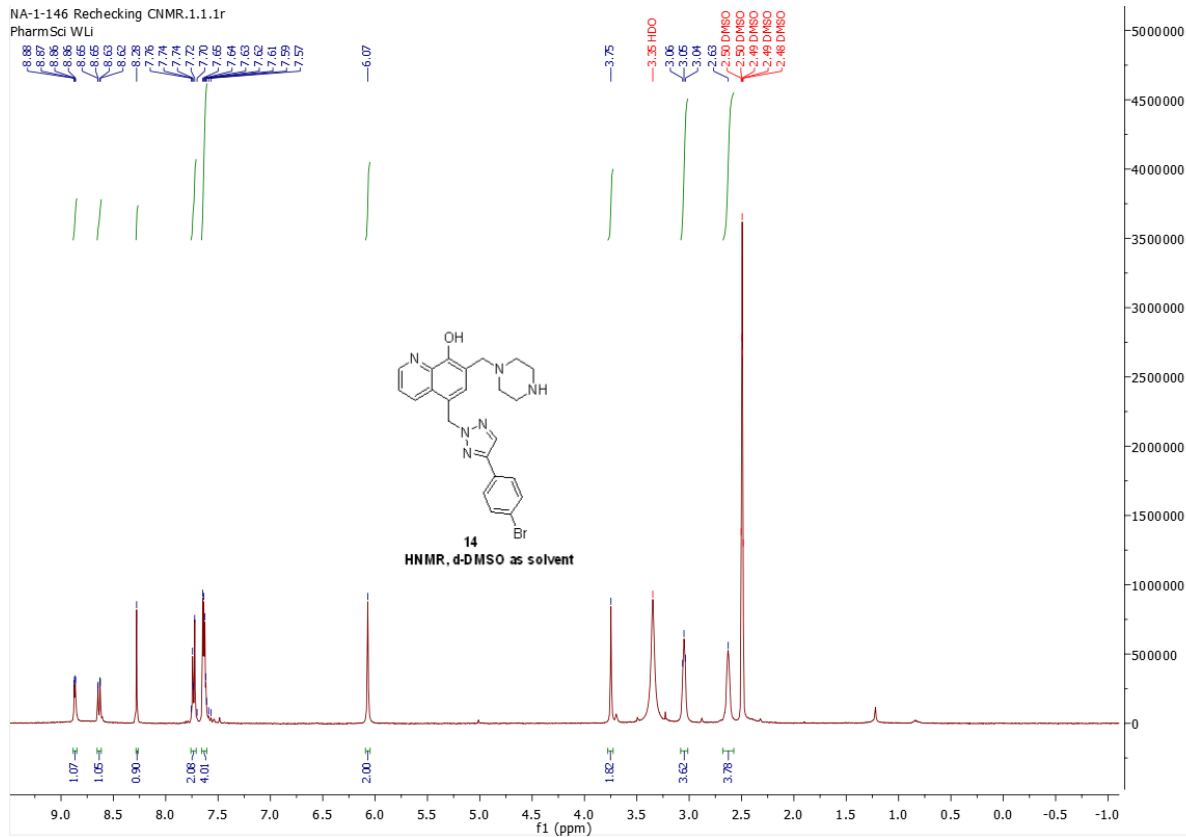


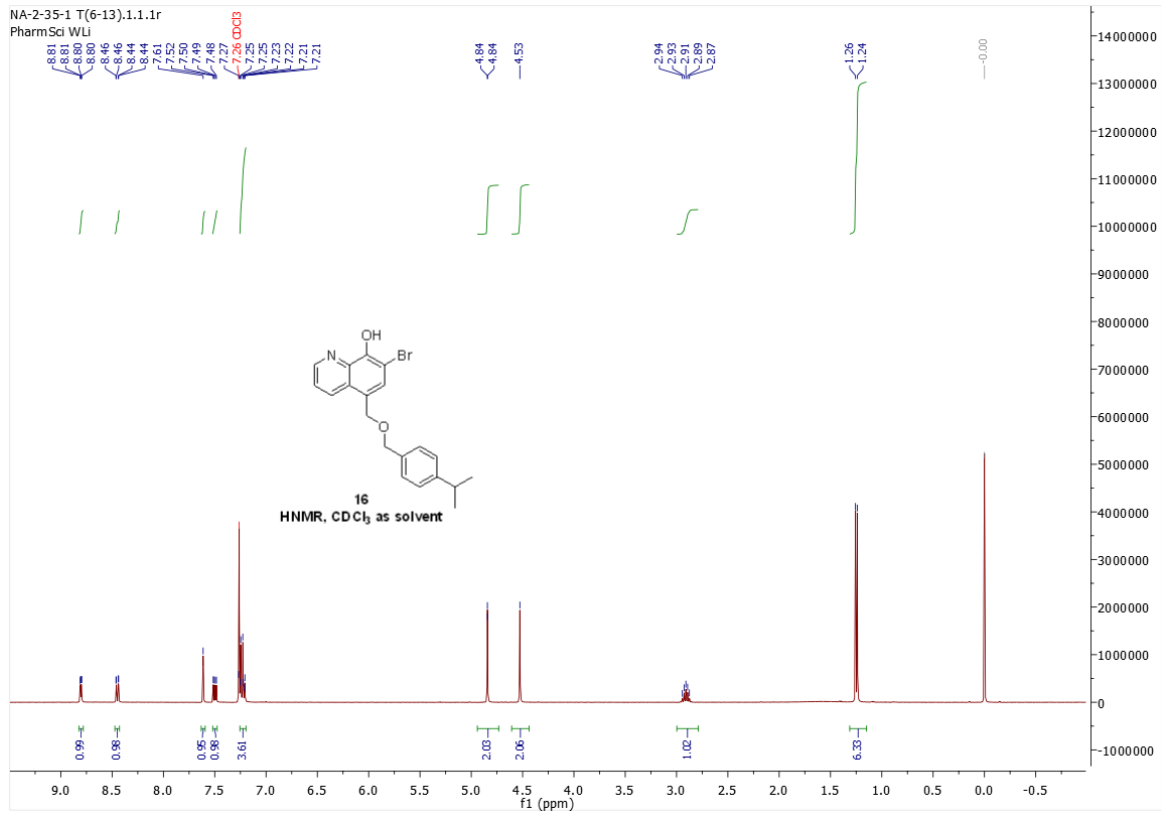
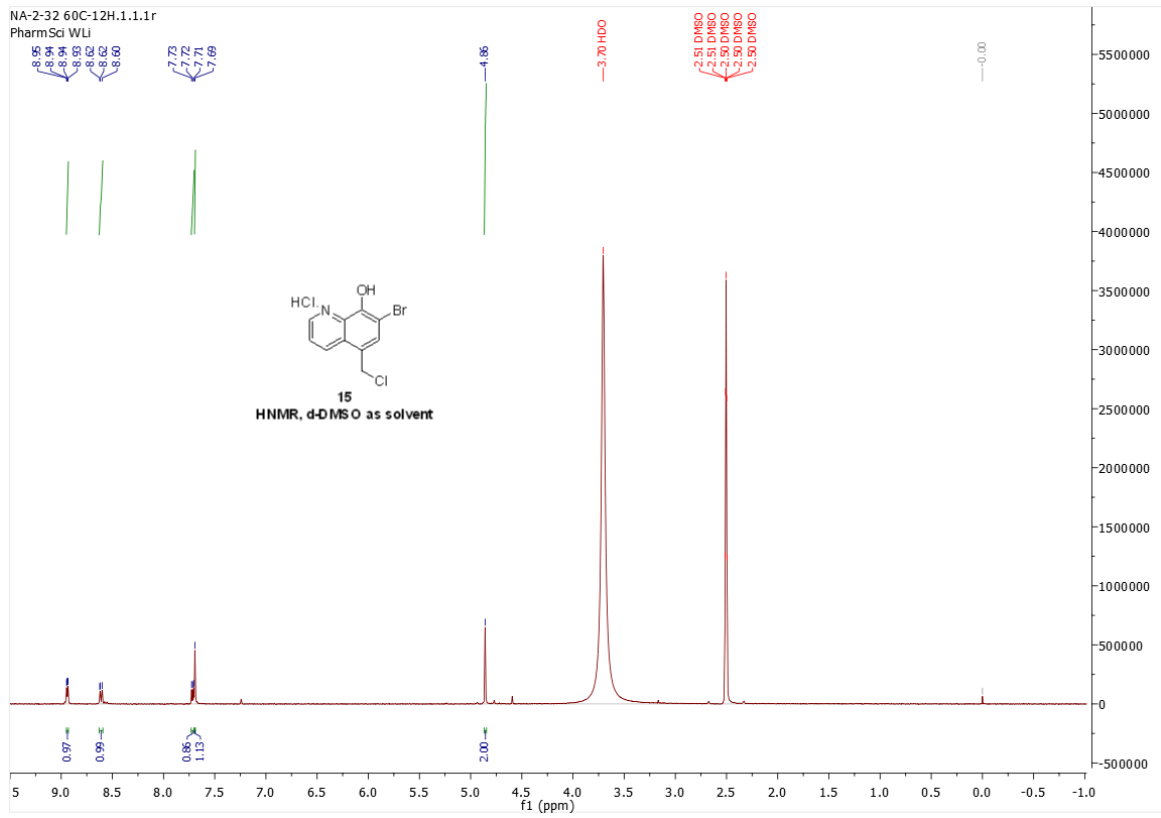


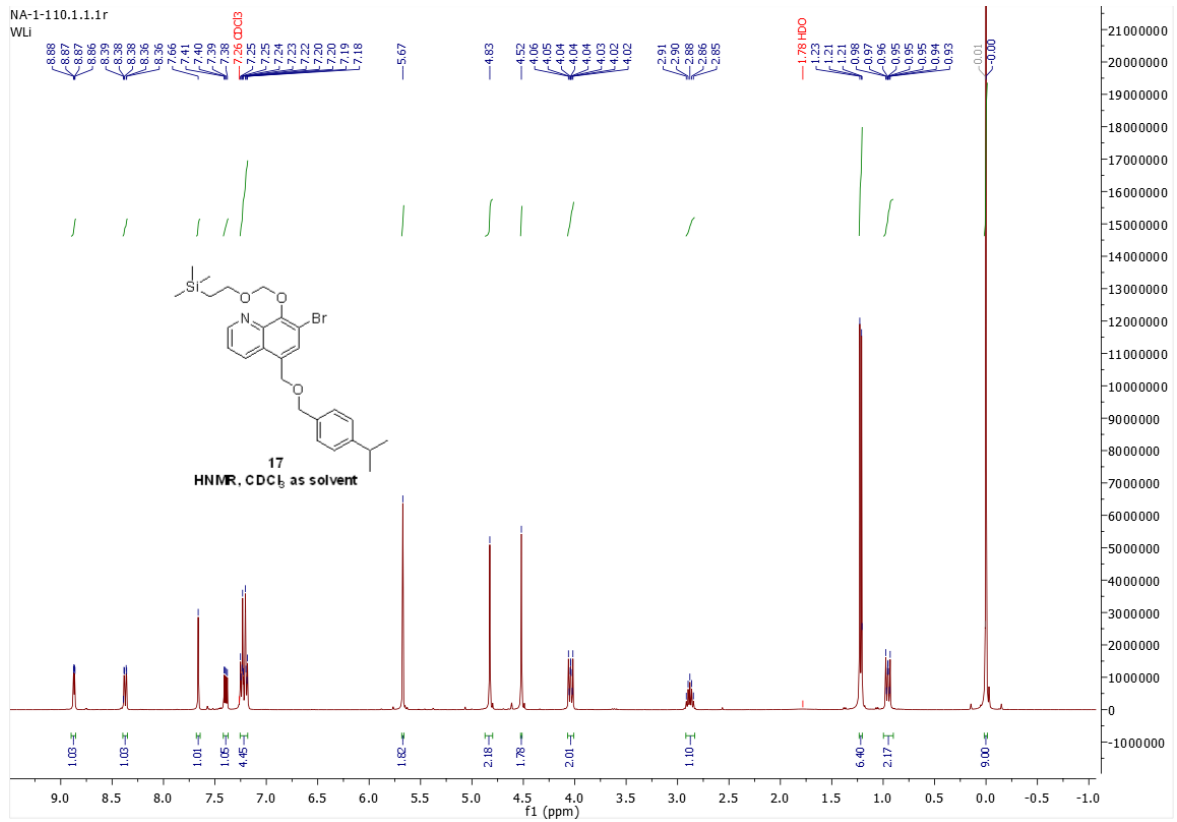
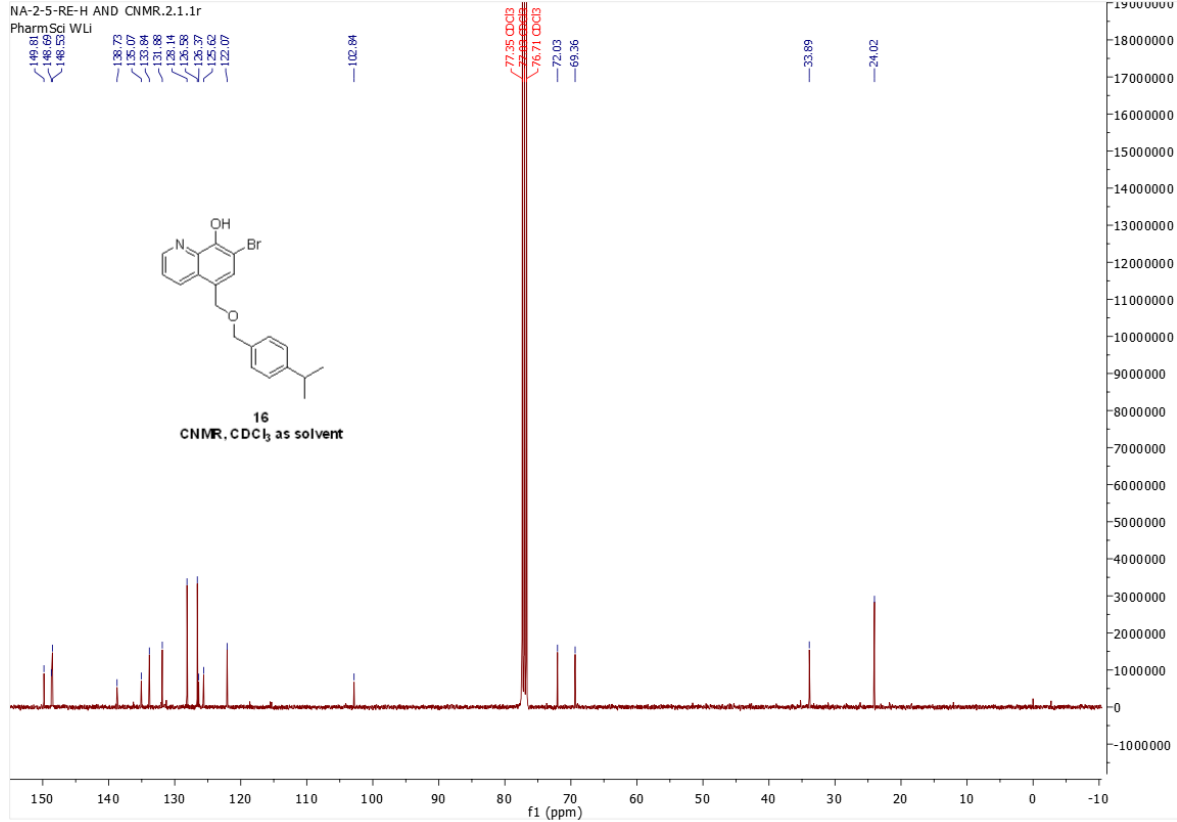


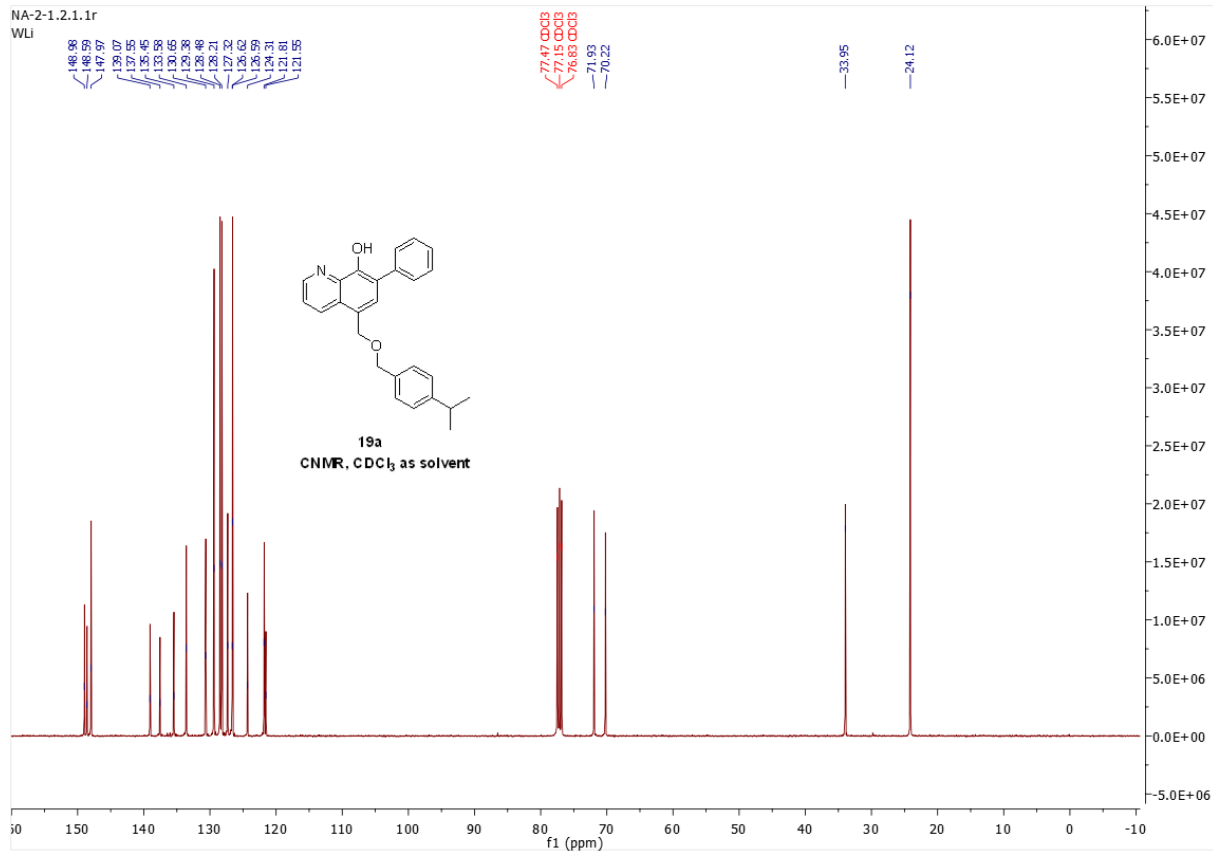
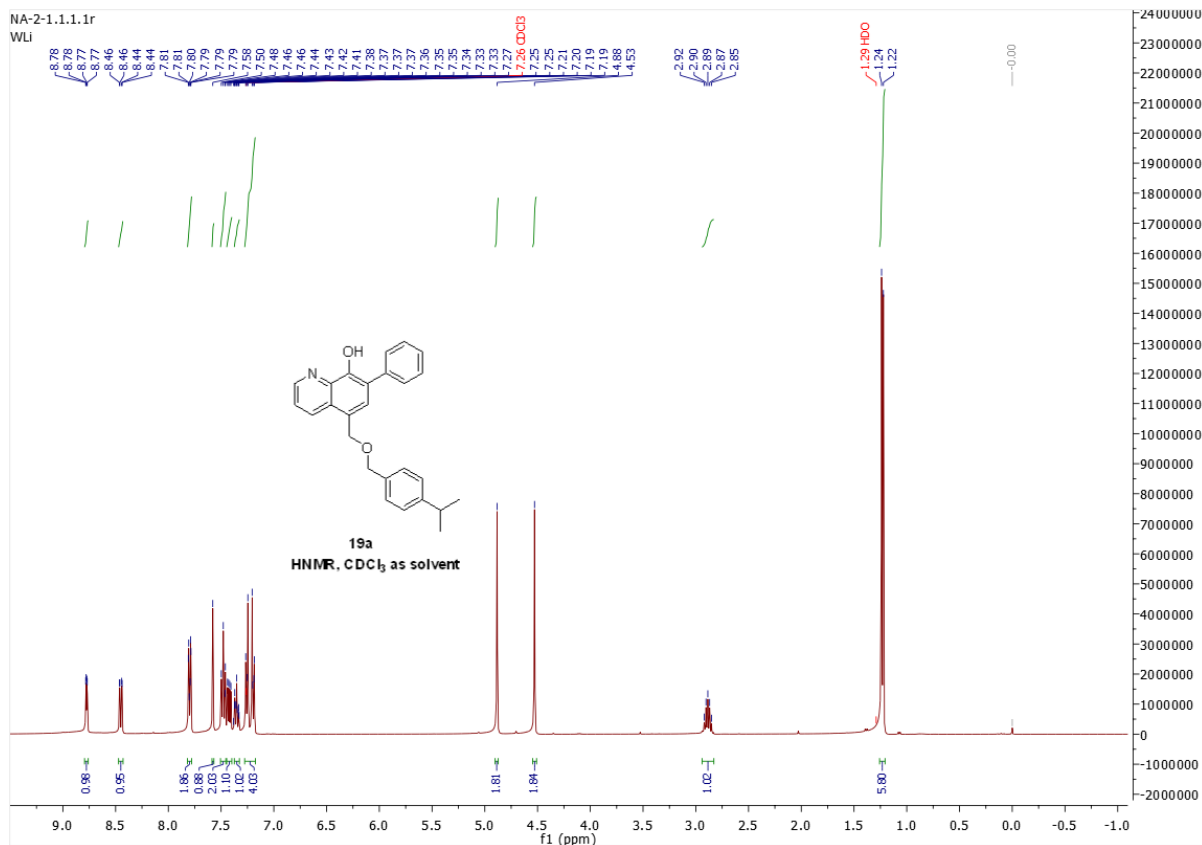


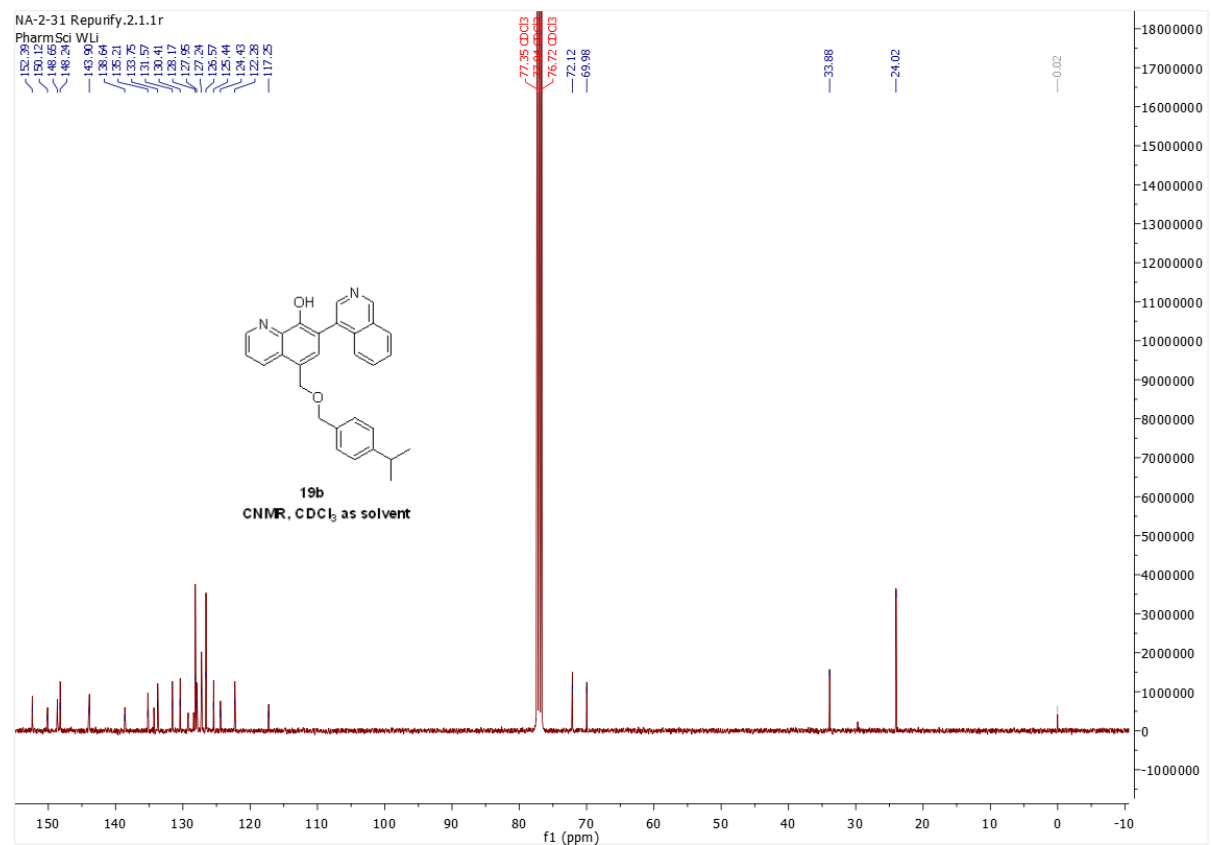
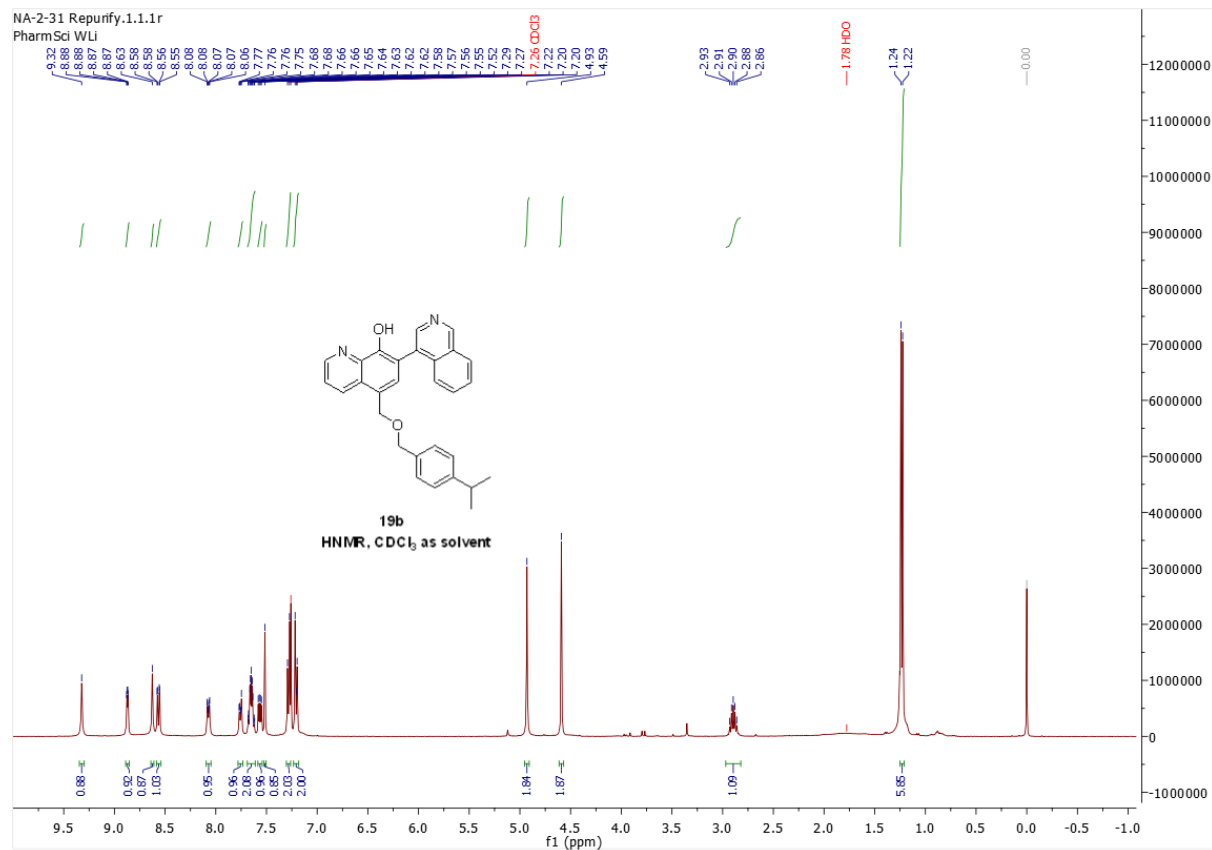


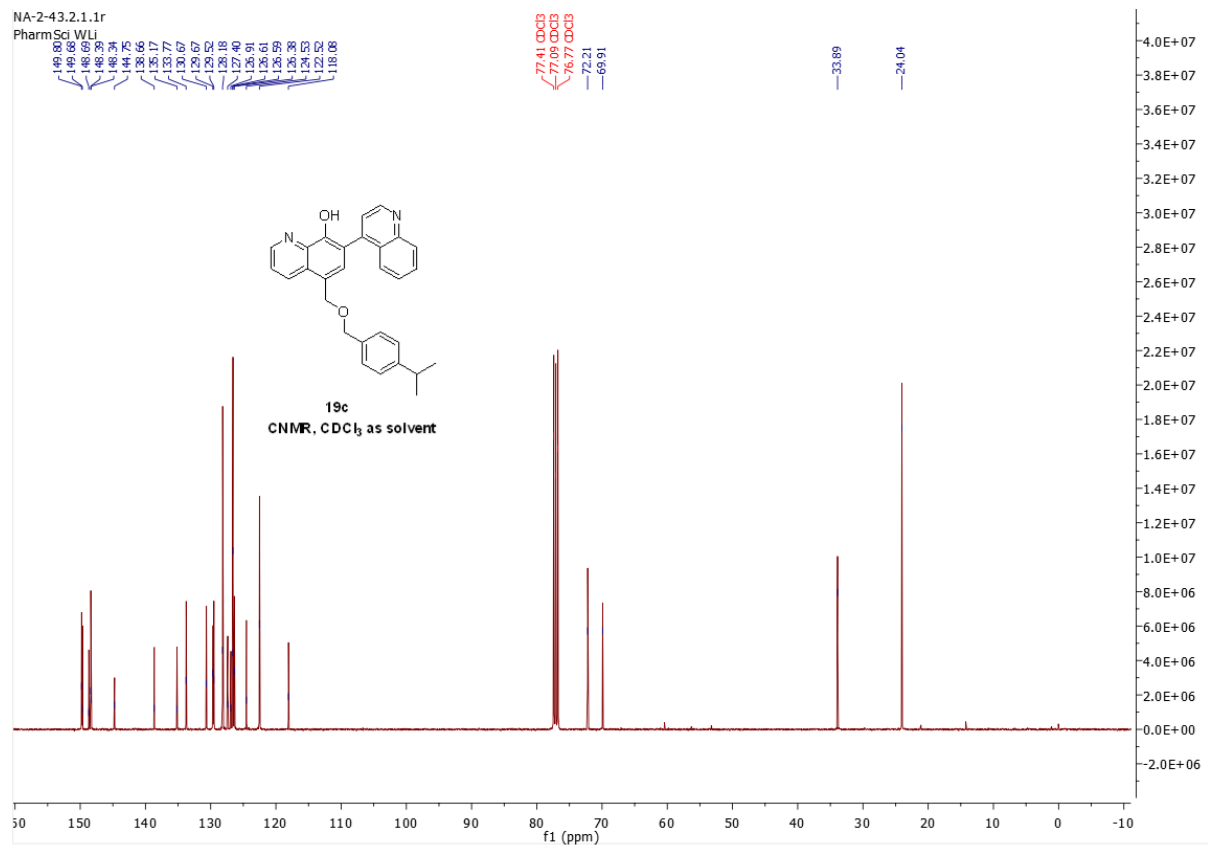
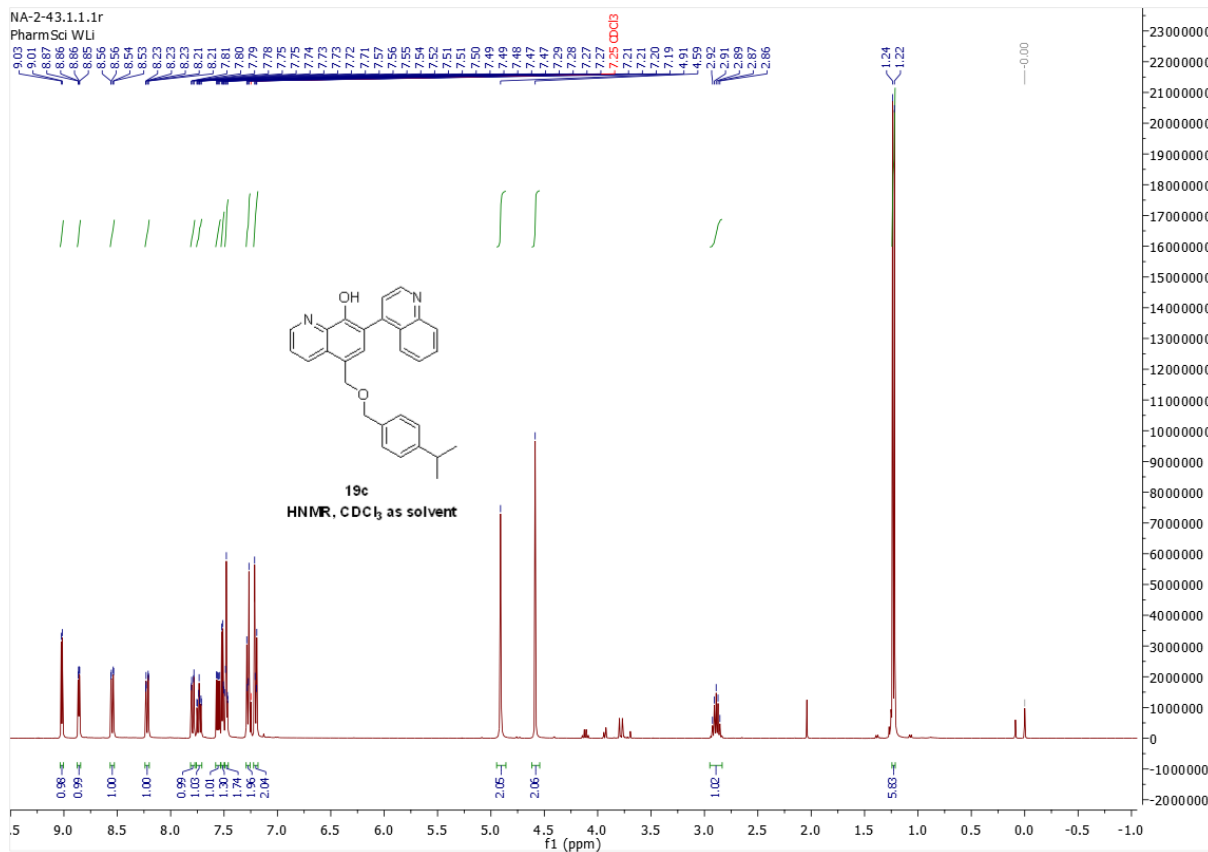


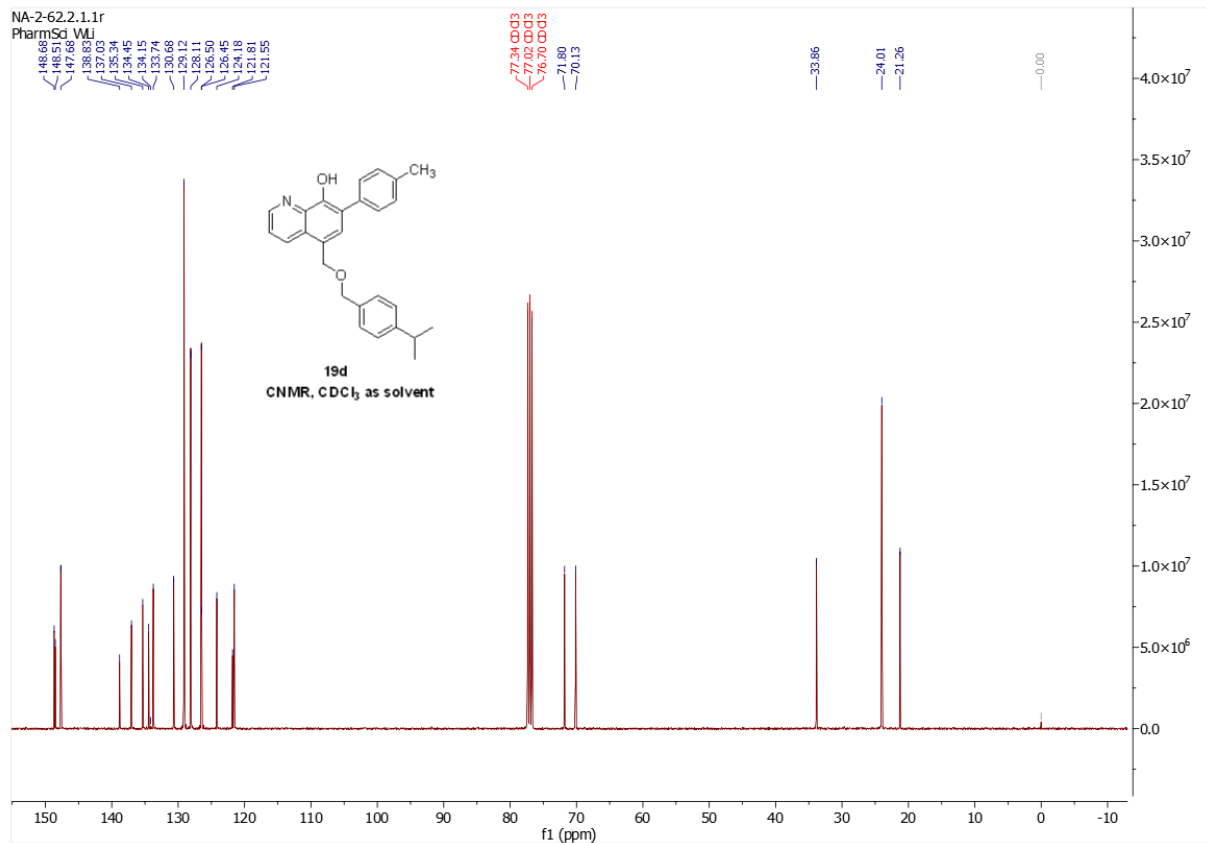
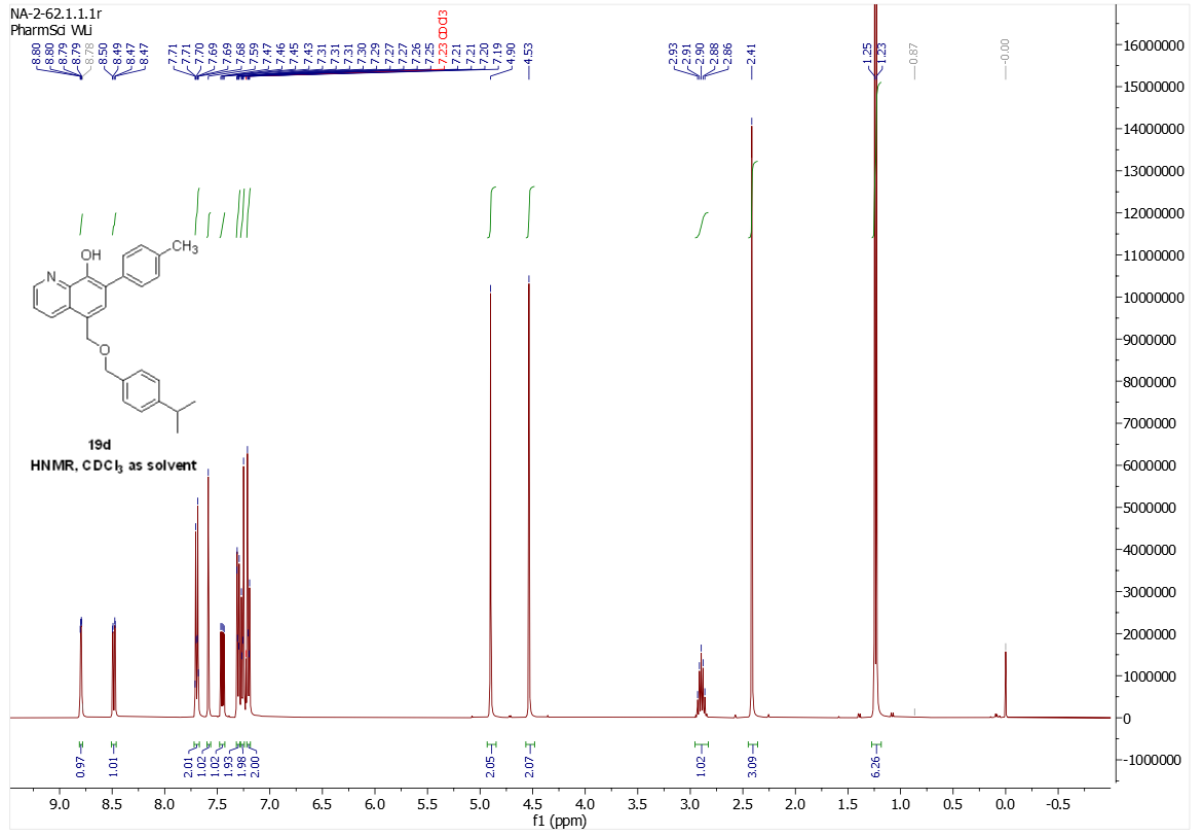


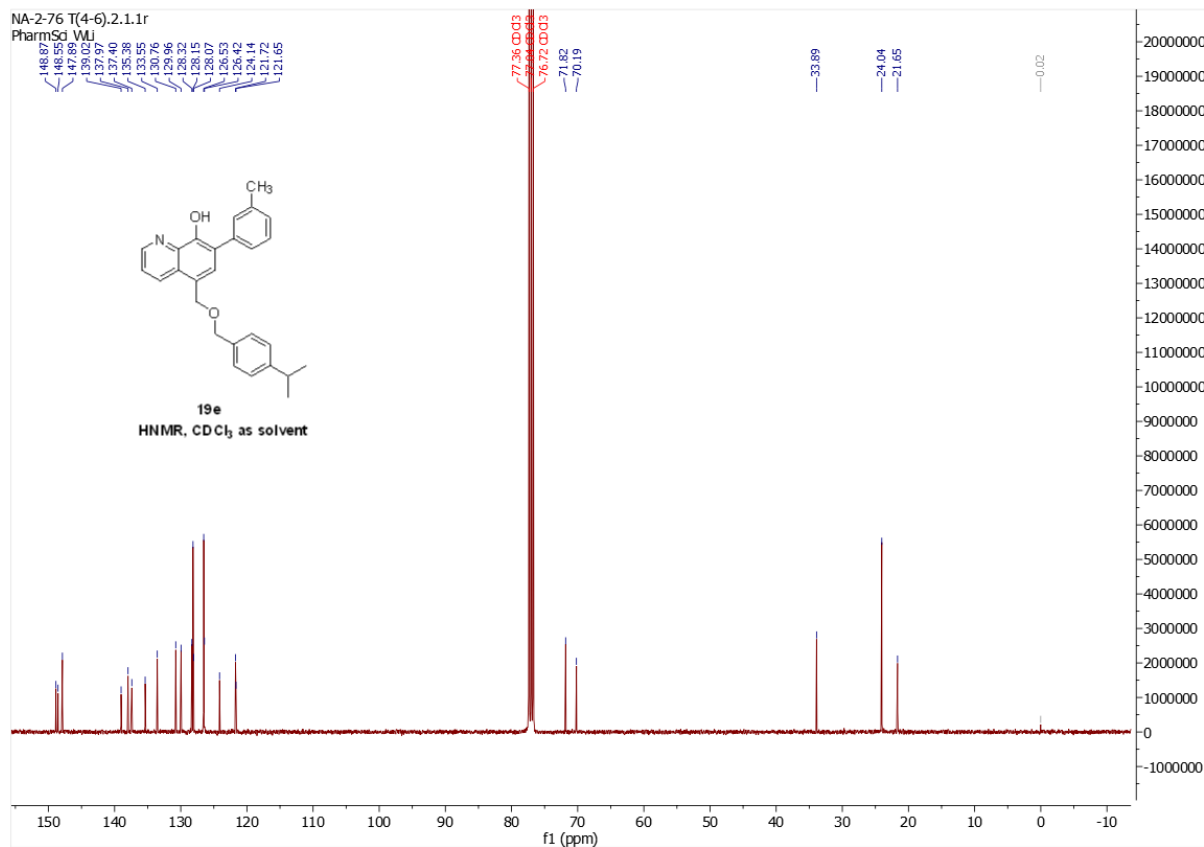
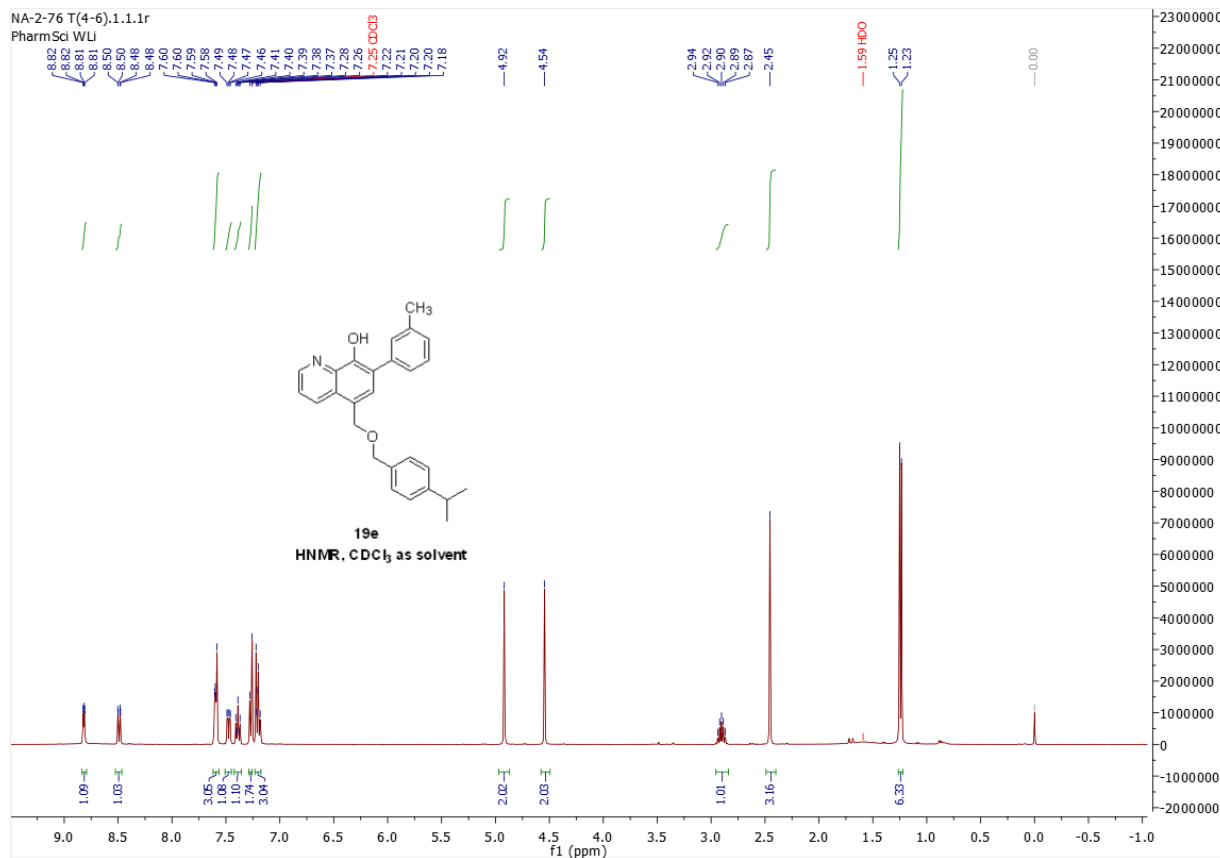


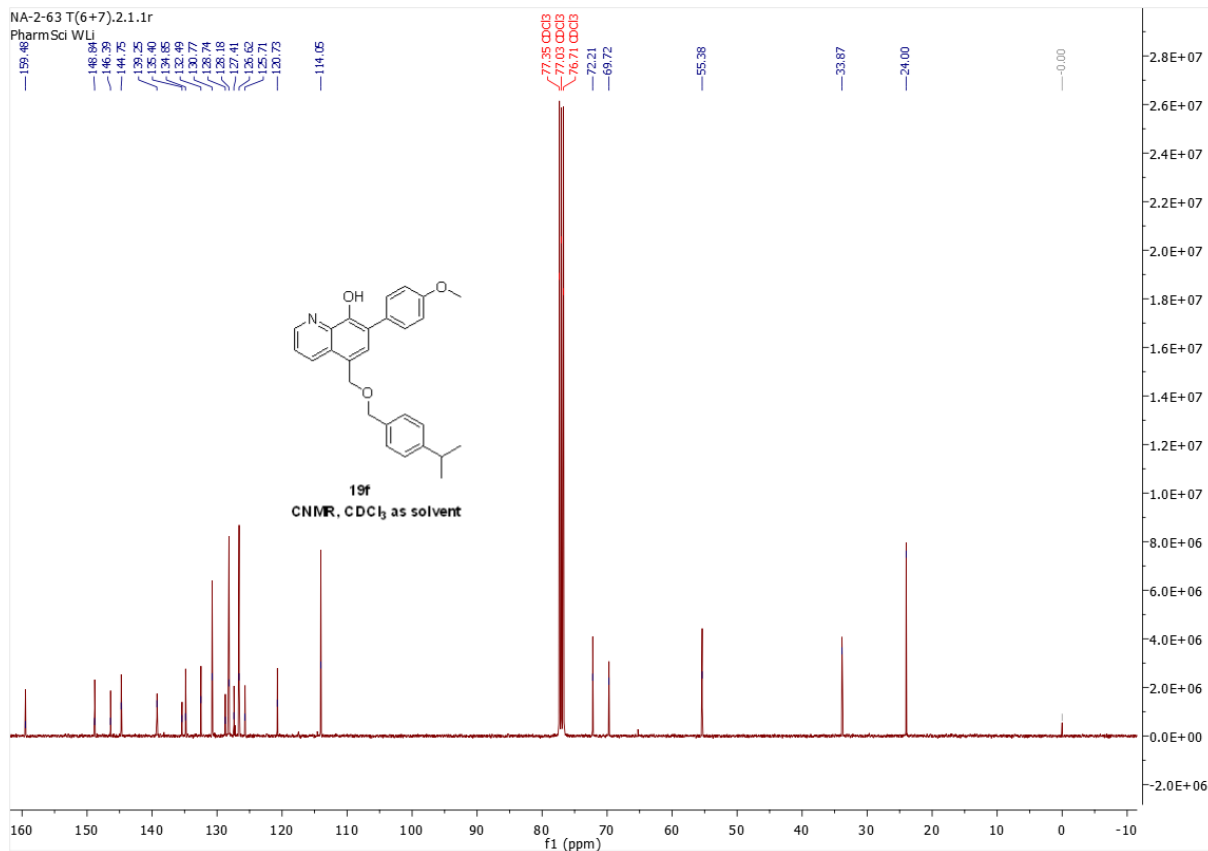
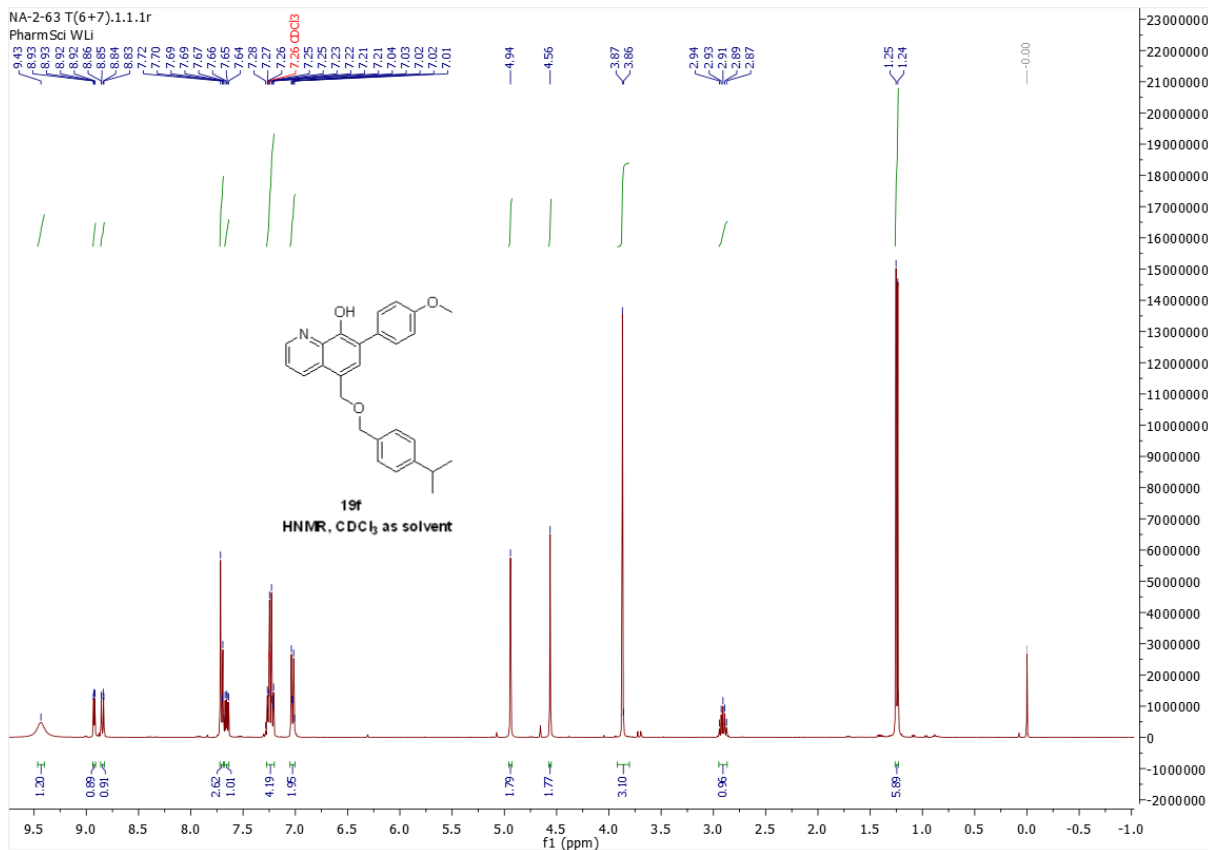


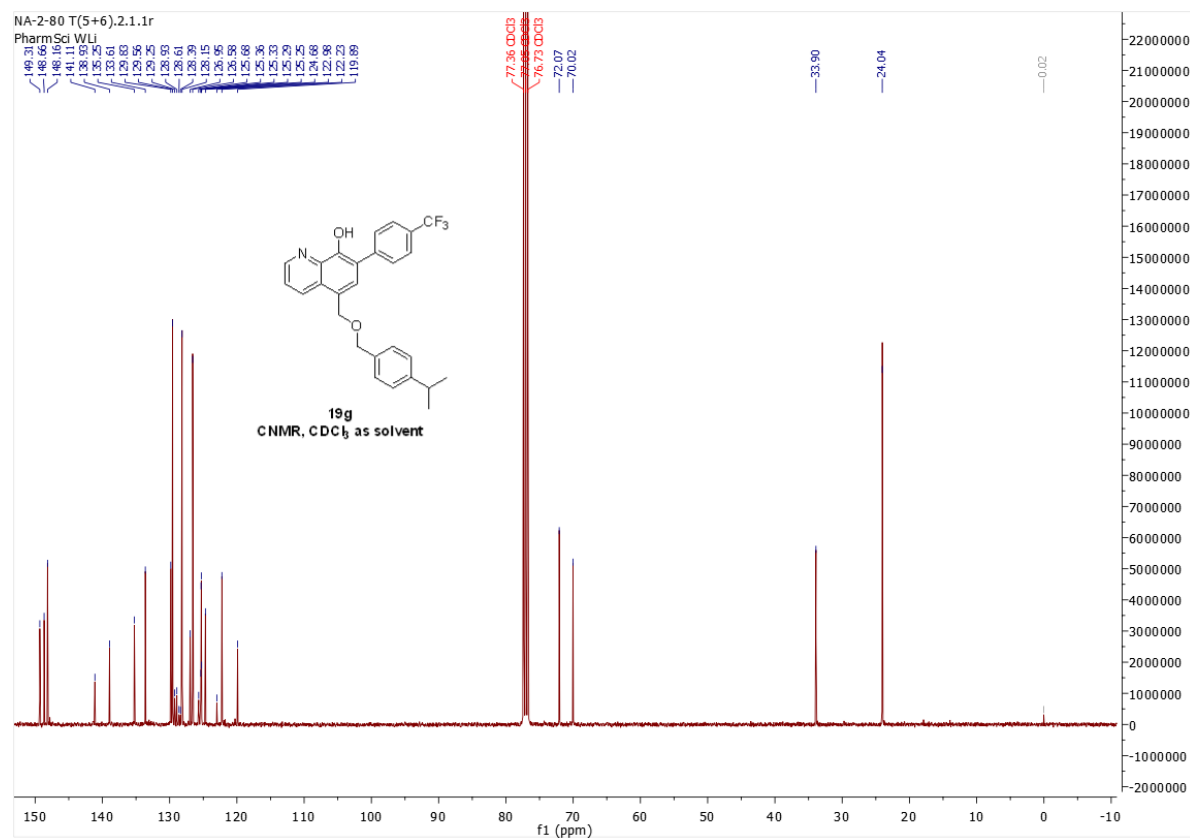
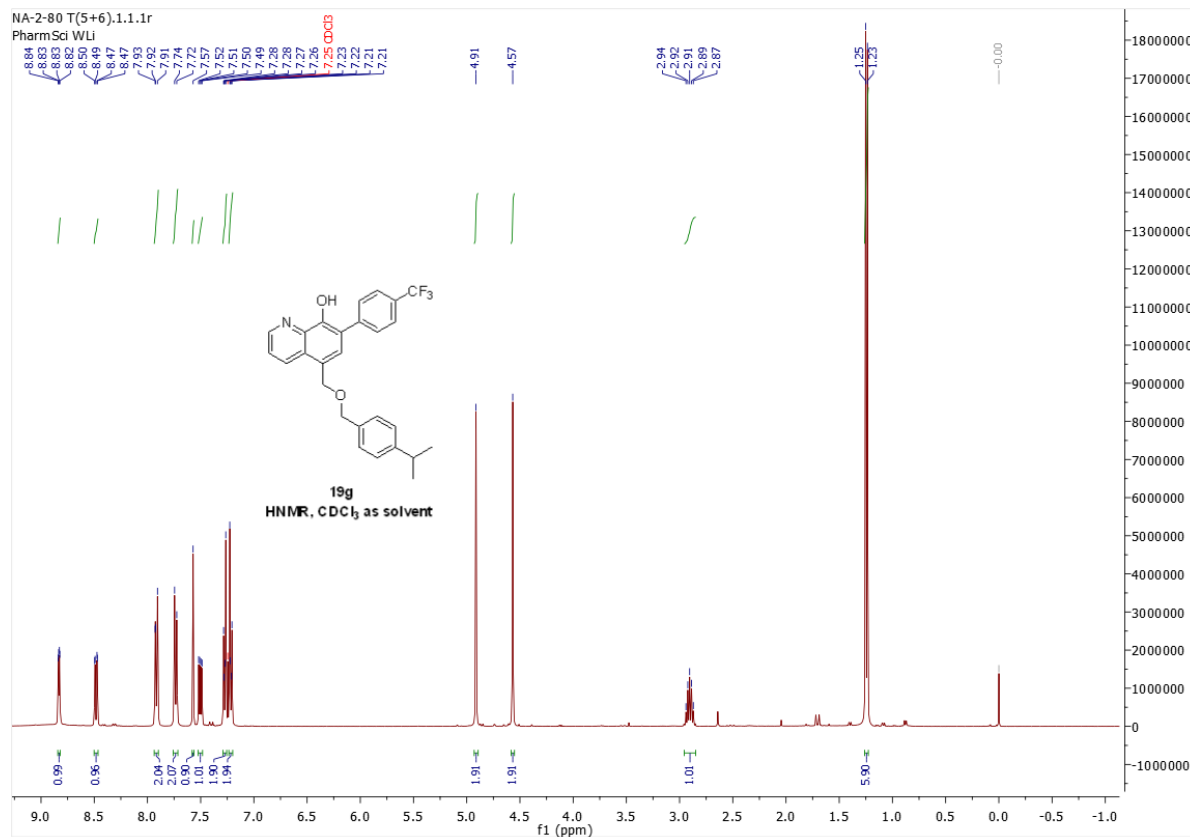


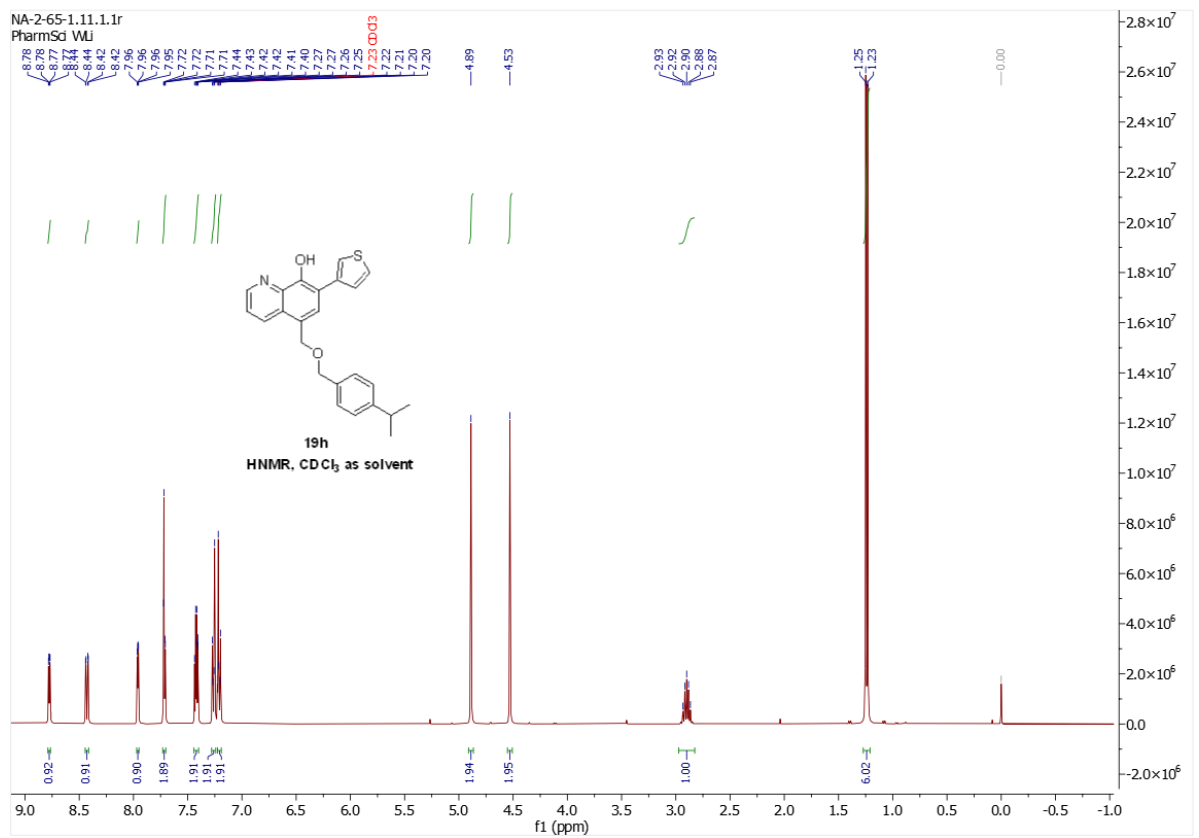
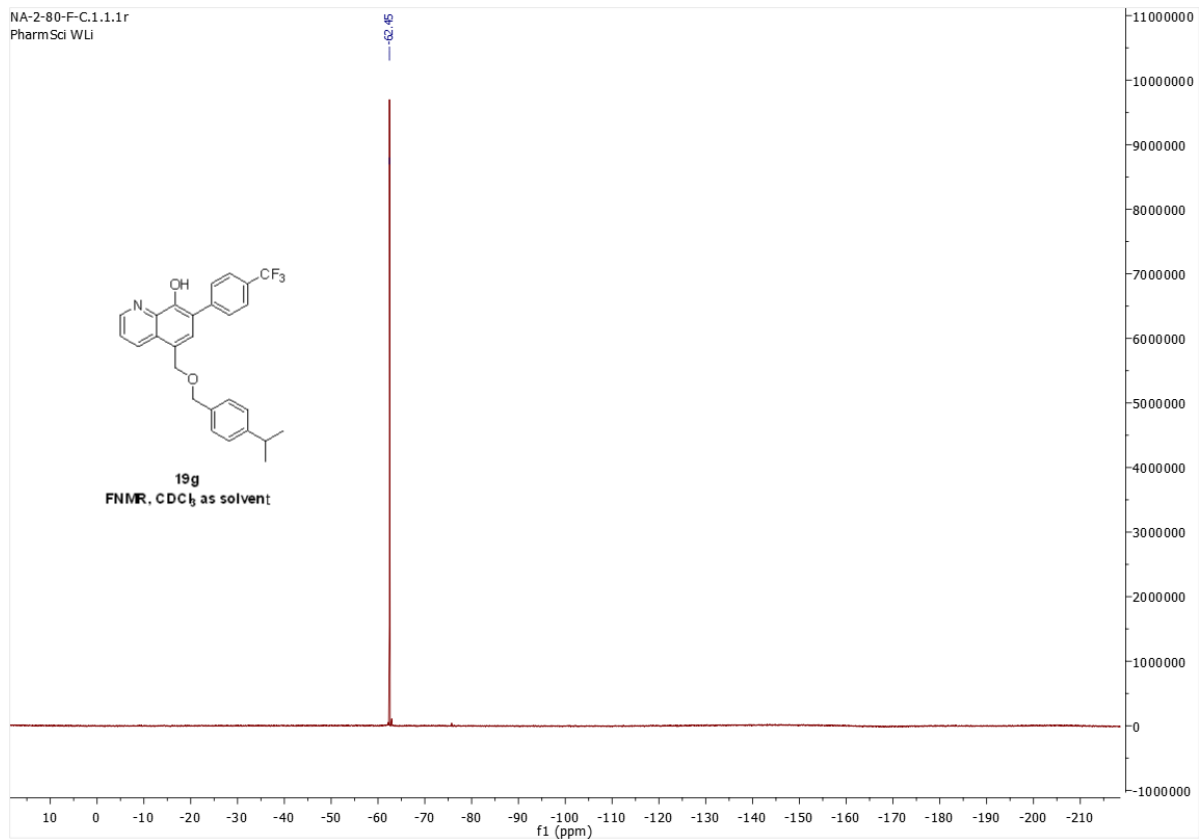


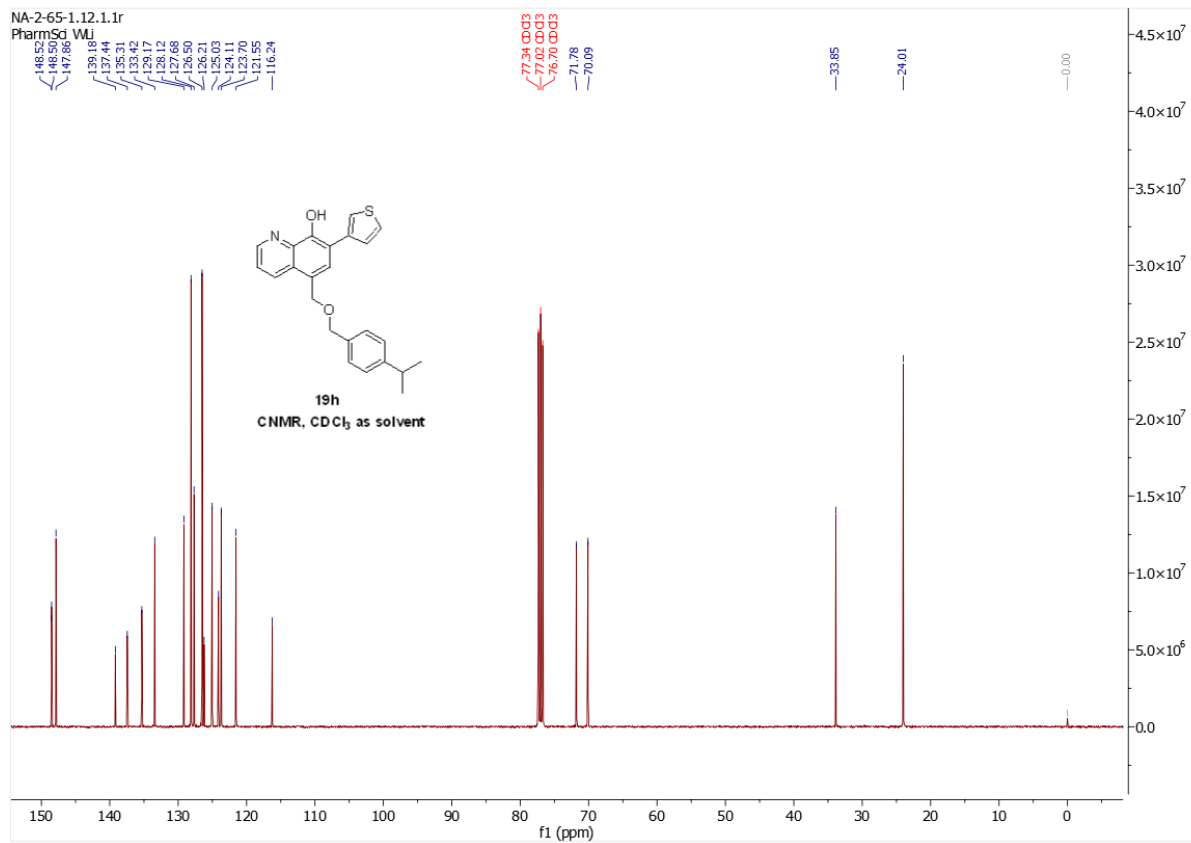






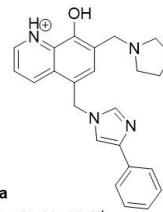
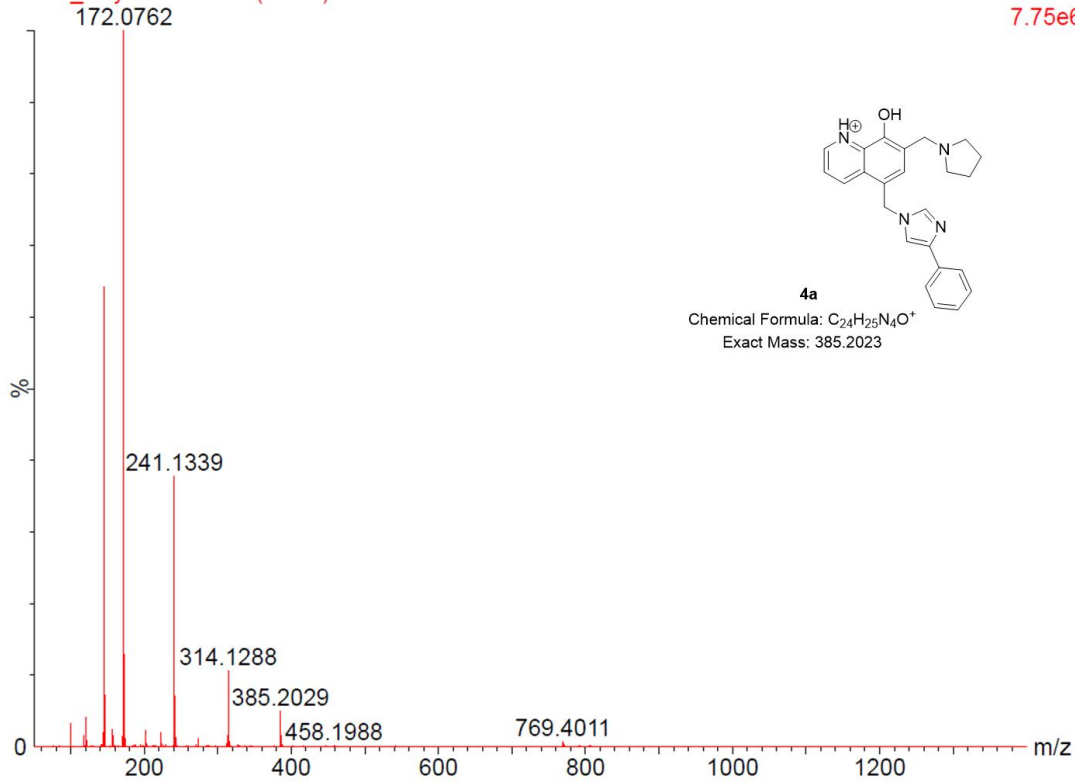






NA-1-55_July 27 2020 99 (1.749)

1: TOF MS ES+
7.75e6

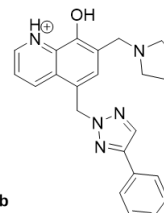
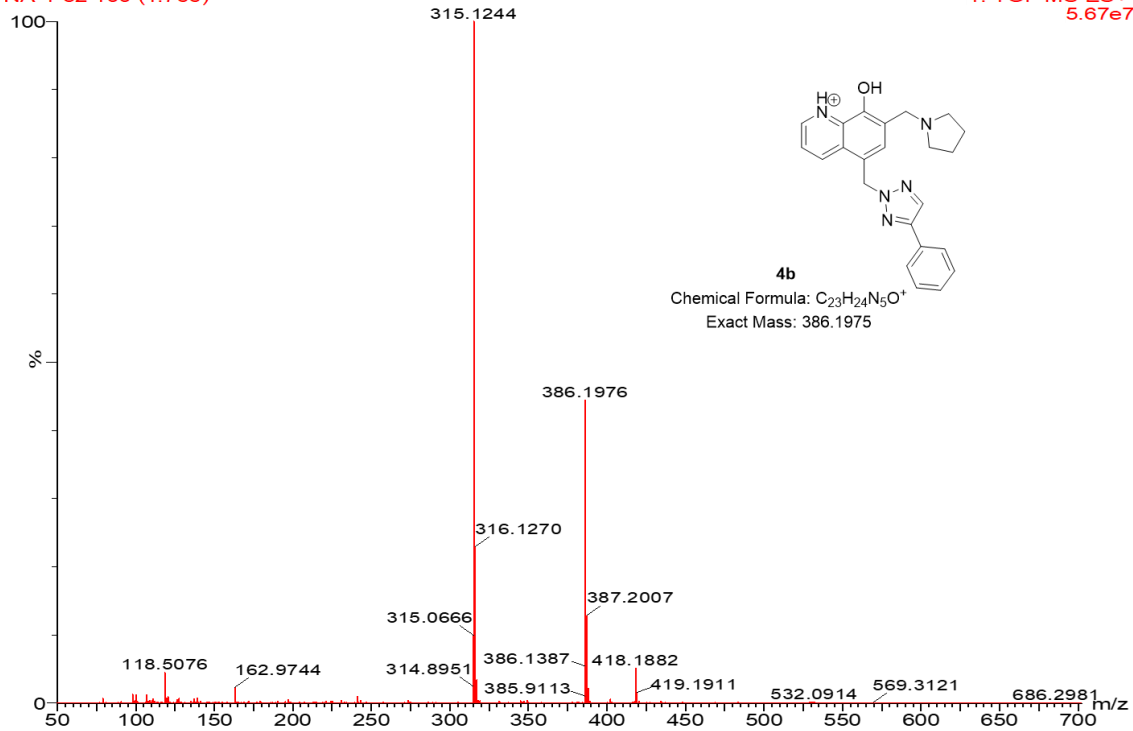


4a
Chemical Formula: C₂₄H₂₅N₄O⁺
Exact Mass: 385.2023

CE: 6.0
NA-1-52 100 (1.766)

XEVO-G2QTOF#YBA089
Acq MODE: CID

09-Jul-2020 09:54:43
Cone V: 40.0
1: TOF MS ES+
5.67e7

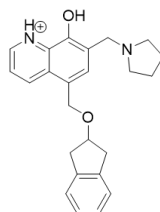
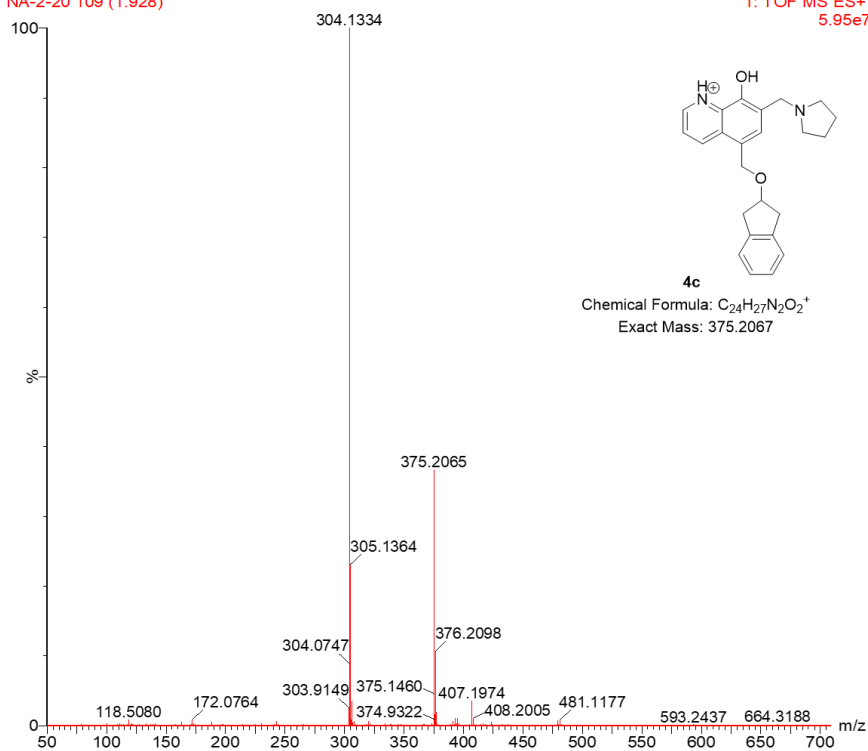


4b
Chemical Formula: C₂₃H₂₄N₅O⁺
Exact Mass: 386.1975

CE: 6.0
NA-2-20 109 (1.928)

XEVO-G2TOF#YBA089
Acq MODE: CID

09-Jul-2020 12:57:16
Cone V: 40.0
1: TOF MS ES+
5.95e7

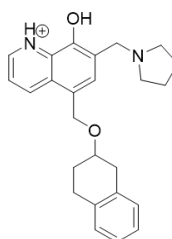
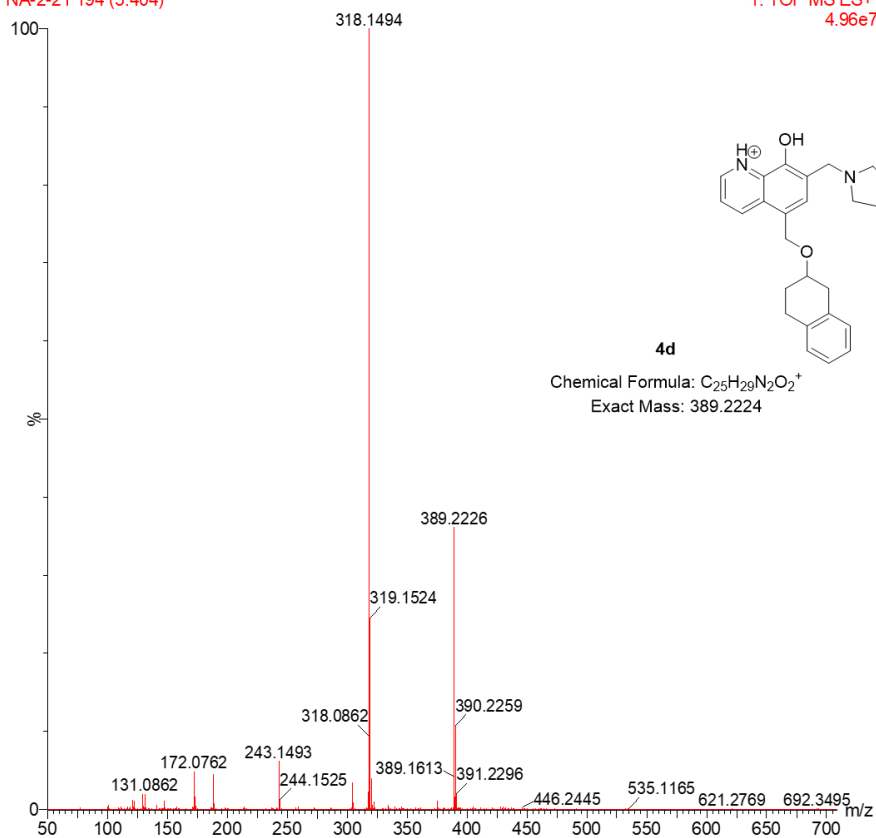


4c
Chemical Formula: C₂₄H₂₇N₂O₂⁺
Exact Mass: 375.2067

CE: 6.0
NA-2-21 194 (3.404)

XEVO-G2TOF#YBA089
Acq MODE: CID

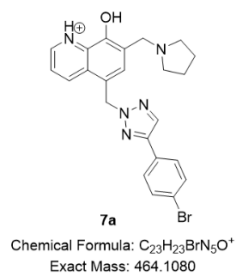
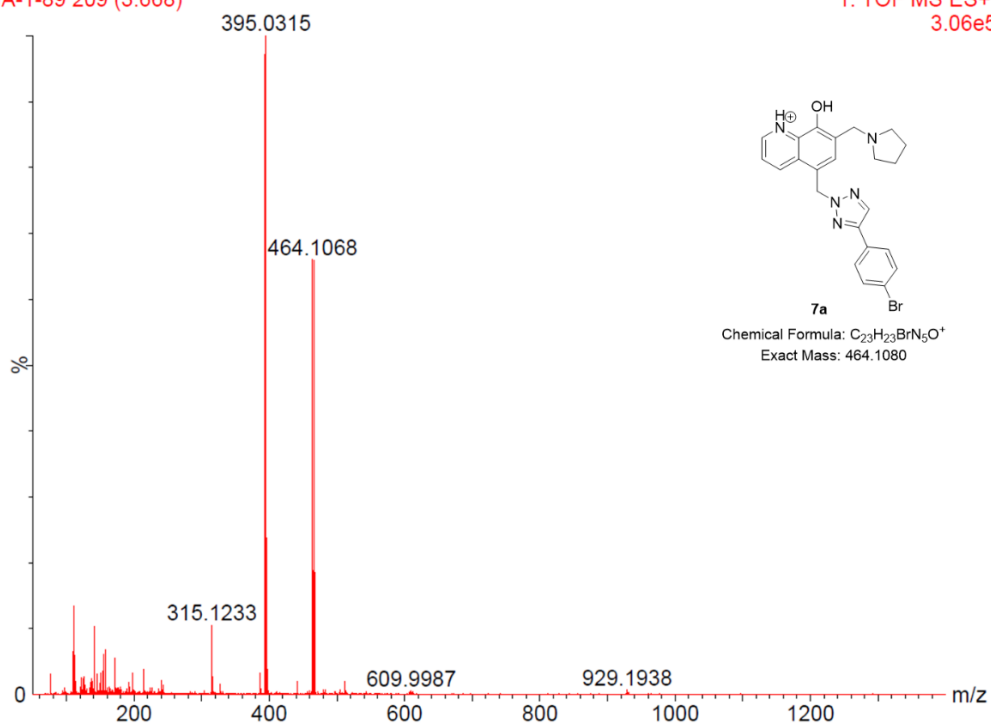
09-Jul-2020 12:08:15
Cone V: 40.0
1: TOF MS ES+
4.96e7



4d
Chemical Formula: C₂₅H₂₉N₂O₂⁺
Exact Mass: 389.2224

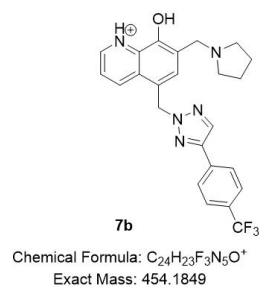
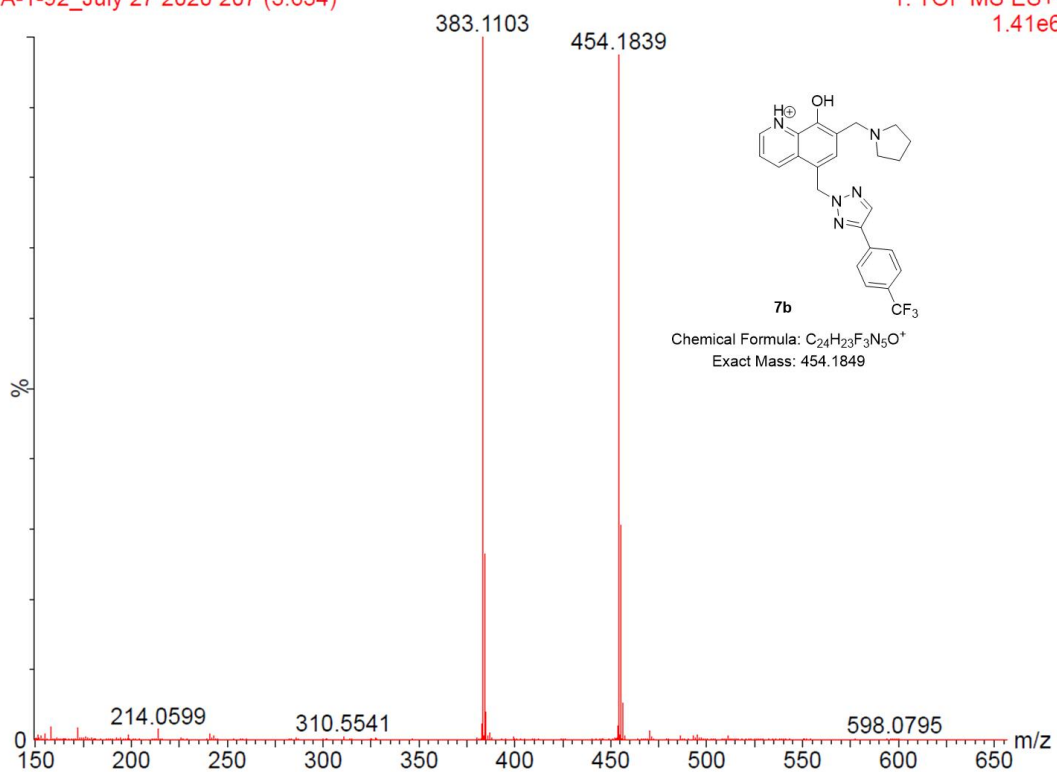
NA-1-89 209 (3.668)

1: TOF MS ES+
3.06e5



NA-1-92_July 27 2020 207 (3.634)

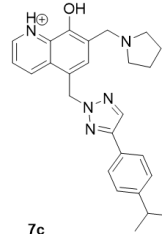
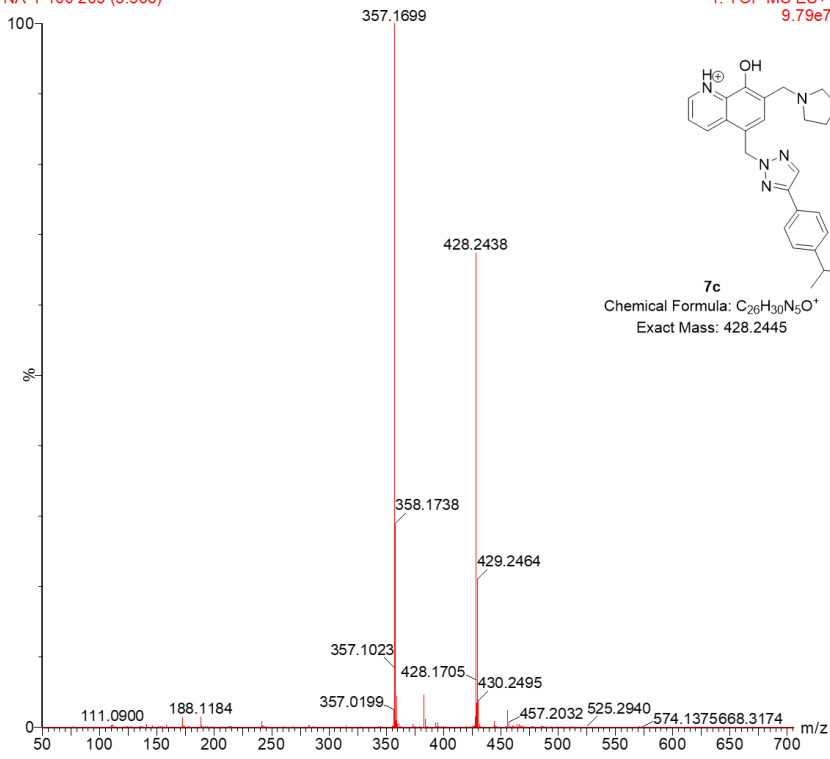
1: TOF MS ES+
1.41e6



CE: 6.0
NA-1-100 203 (3.566)

XEVO-G2QTOF#YBA089
Acq MODE: CID

09-Jul-2020 10:22:43
Cone V: 40.0
1: TOF MS ES+
9.79e7

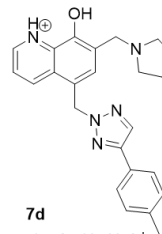
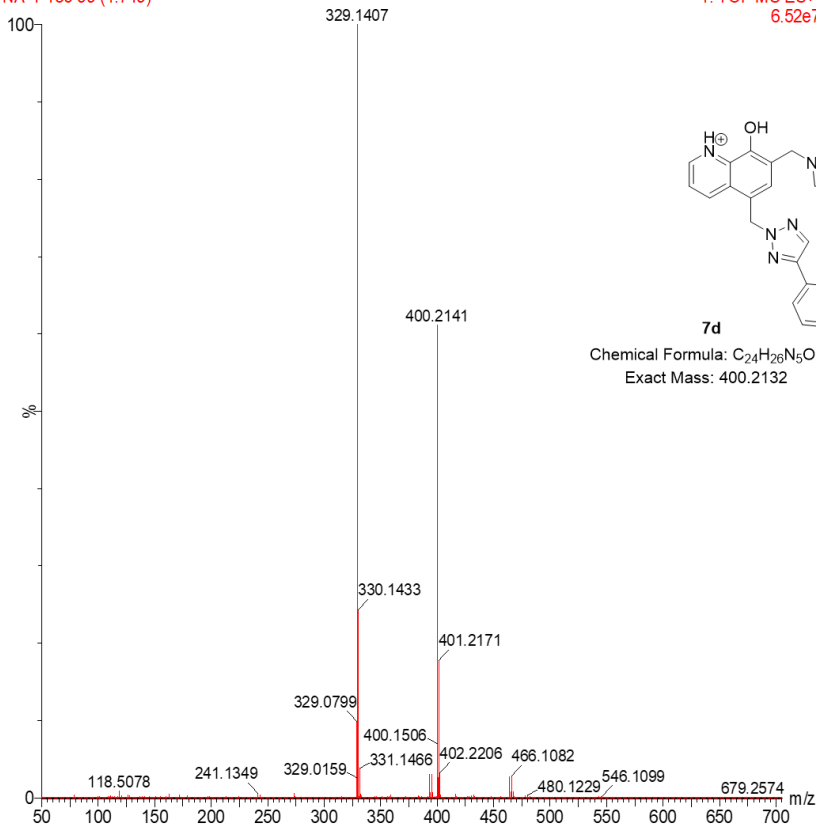


Chemical Formula: C₂₆H₃₀N₅O⁺
Exact Mass: 428.2445

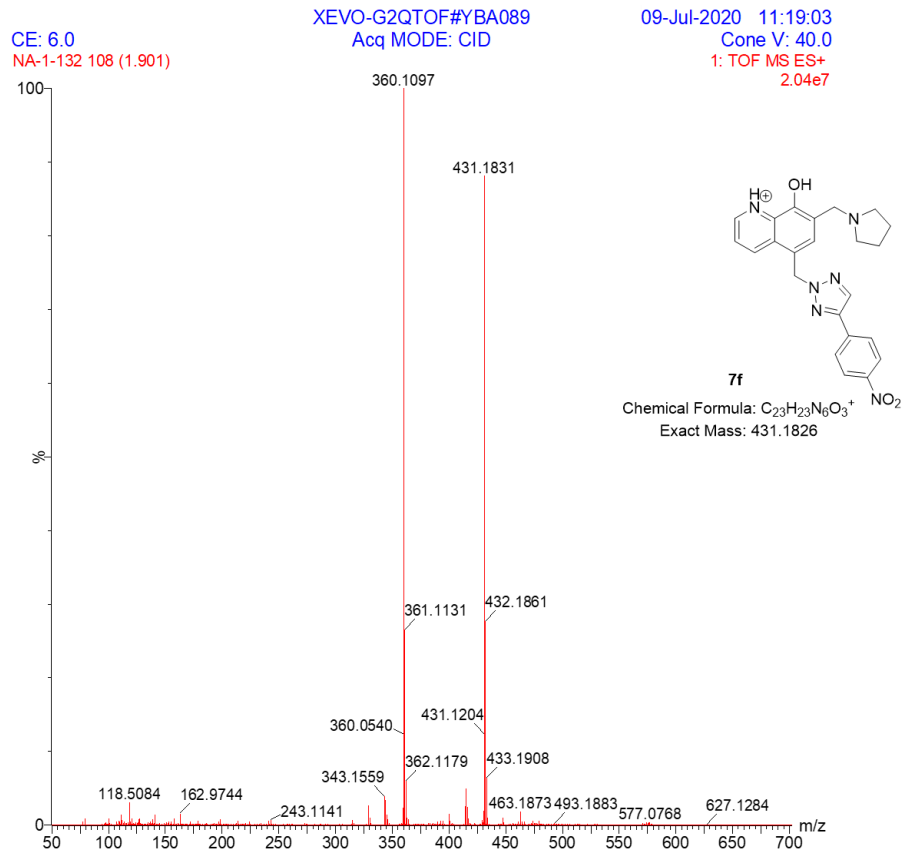
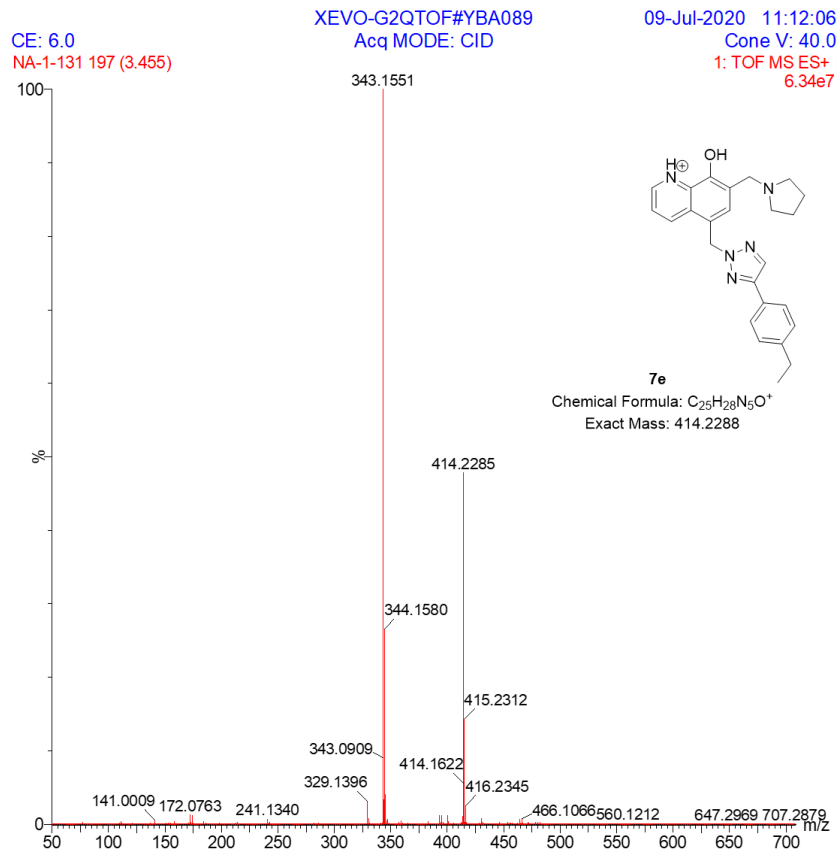
CE: 6.0
NA-1-130 99 (1.749)

XEVO-G2QTOF#YBA089
Acq MODE: CID

09-Jul-2020 11:05:02
Cone V: 40.0
1: TOF MS ES+
6.52e7



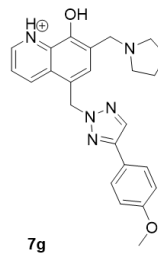
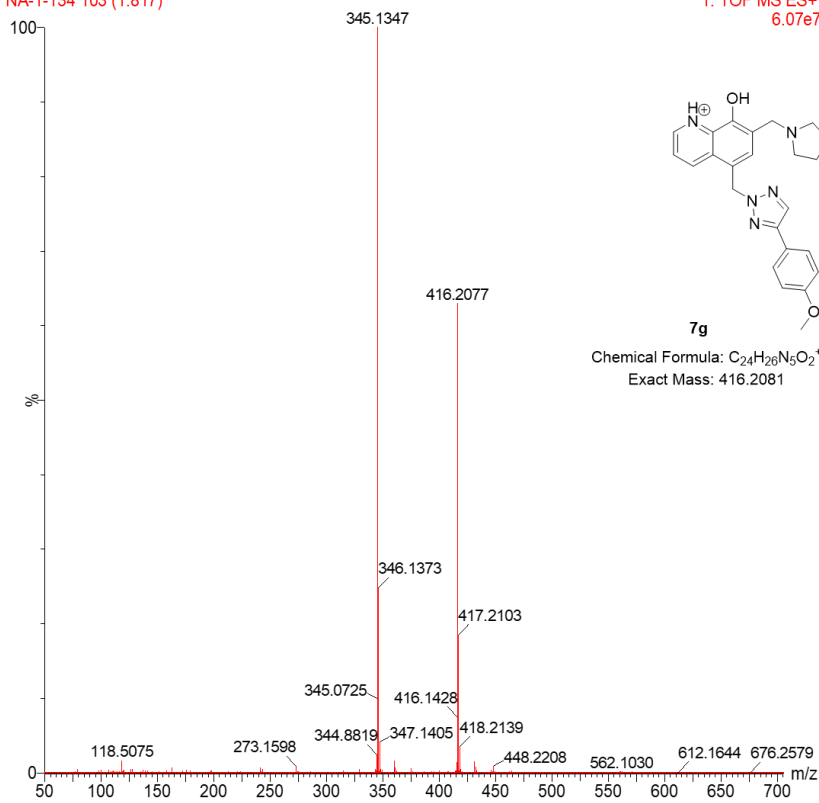
Chemical Formula: C₂₄H₂₆N₅O⁺
Exact Mass: 400.2132



CE: 6.0
NA-1-134 103 (1.817)

XEVO-G2QTOF#YBA089
Acq MODE: CID

09-Jul-2020 11:26:08
Cone V: 40.0
1: TOF MS ES+
6.07e7

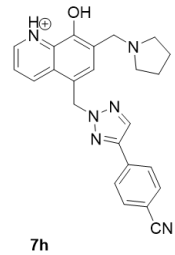
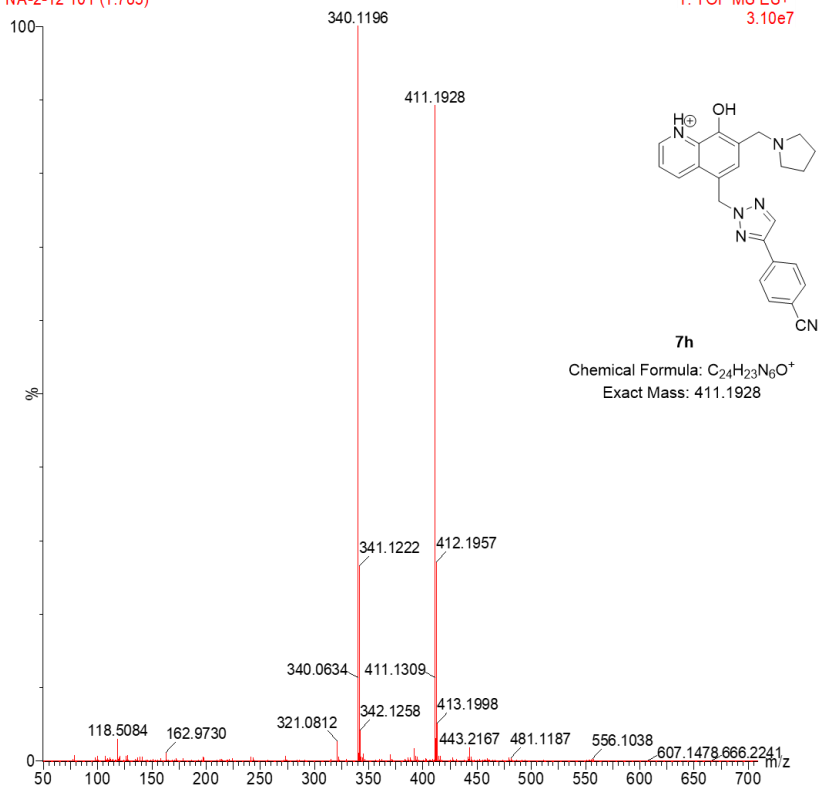


Chemical Formula: C₂₄H₂₆N₅O₂⁺
Exact Mass: 416.2081

CE: 6.0
NA-2-12 101 (1.783)

XEVO-G2QTOF#YBA089
Acq MODE: CID

09-Jul-2020 11:54:20
Cone V: 40.0
1: TOF MS ES+
3.10e7

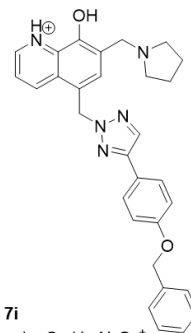
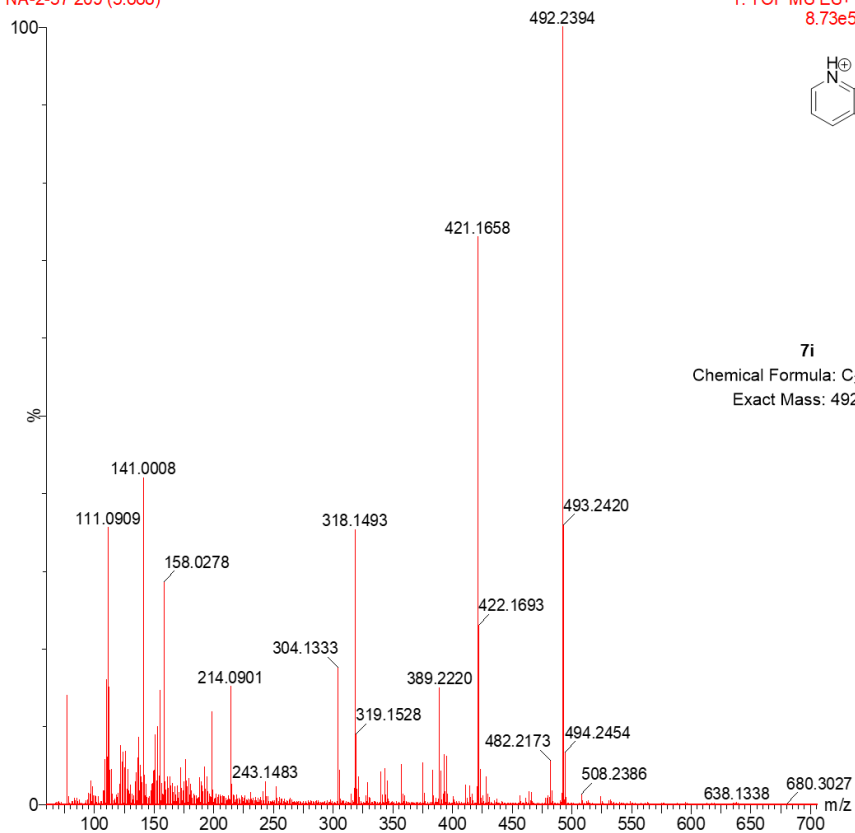


Chemical Formula: C₂₄H₂₃N₆O⁺
Exact Mass: 411.1928

CE: 6.0
NA-2-37 209 (3.668)

XEVO-G2QTOF#YBA089
Acq MODE: CID

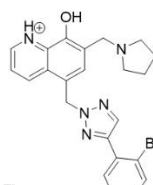
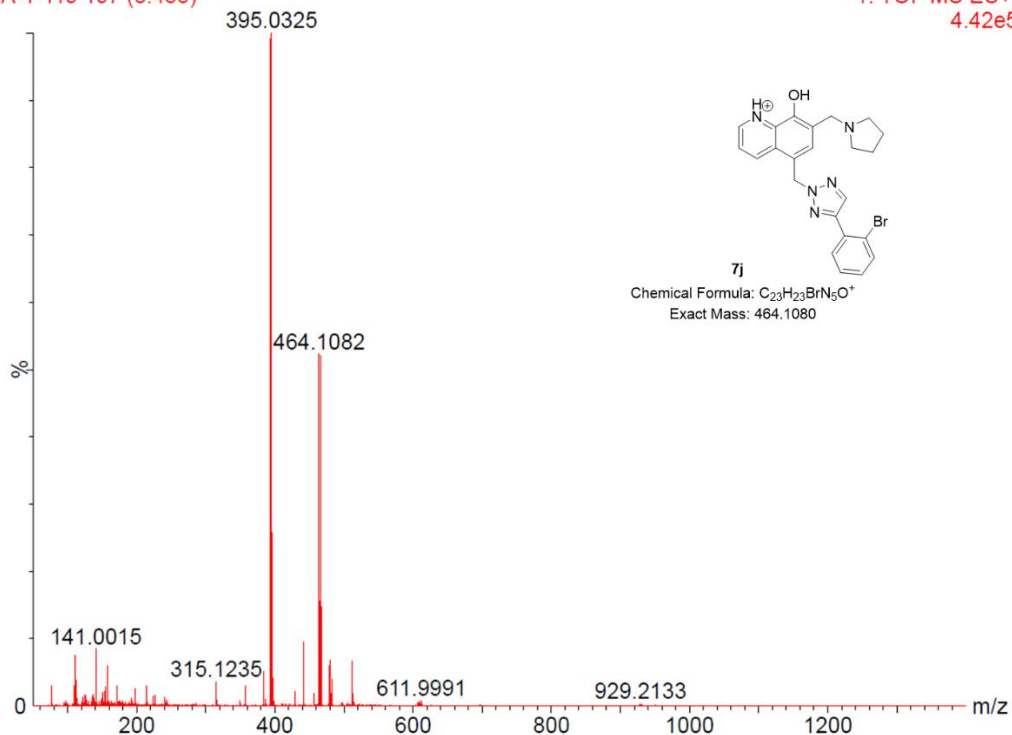
09-Jul-2020 12:22:18
Cone V: 40.0
1: TOF MS ES+
8.73e5



Chemical Formula: C₃₀H₃₀N₅O₂⁺
Exact Mass: 492.2394

NA-1-119 197 (3.455)

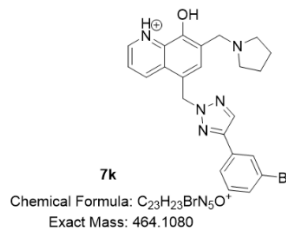
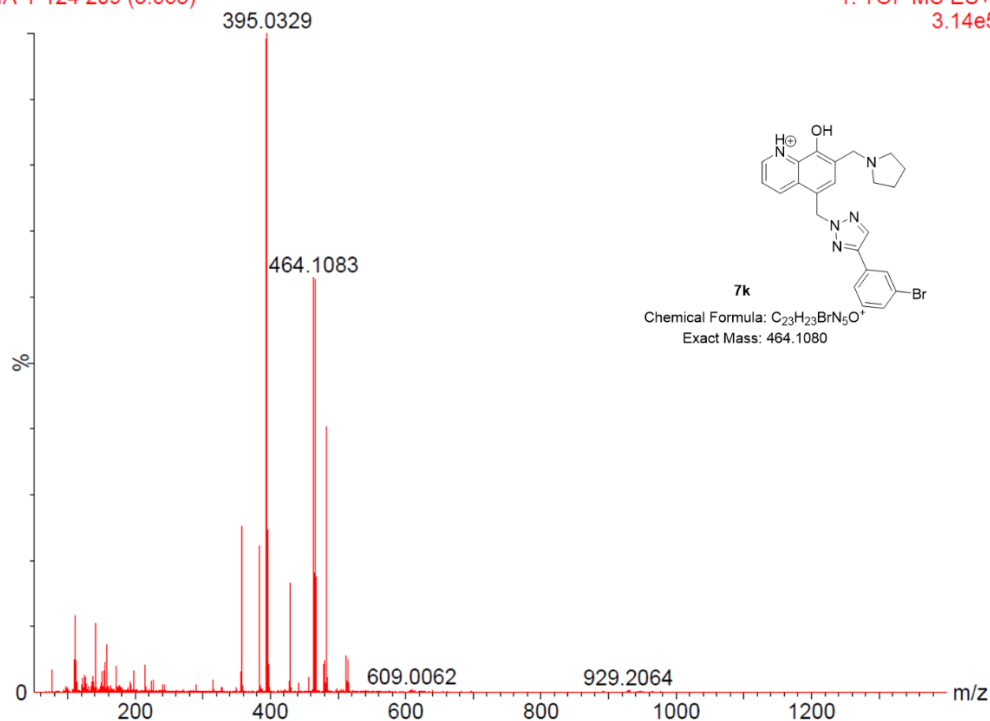
1: TOF MS ES+
4.42e5



Chemical Formula: C₂₃H₂₃BrN₅O⁺
Exact Mass: 464.1080

NA-1-124 209 (3.668)

1: TOF MS ES+
3.14e5



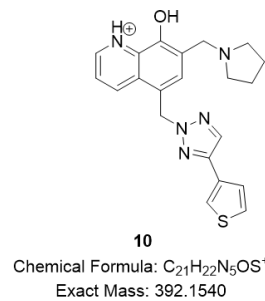
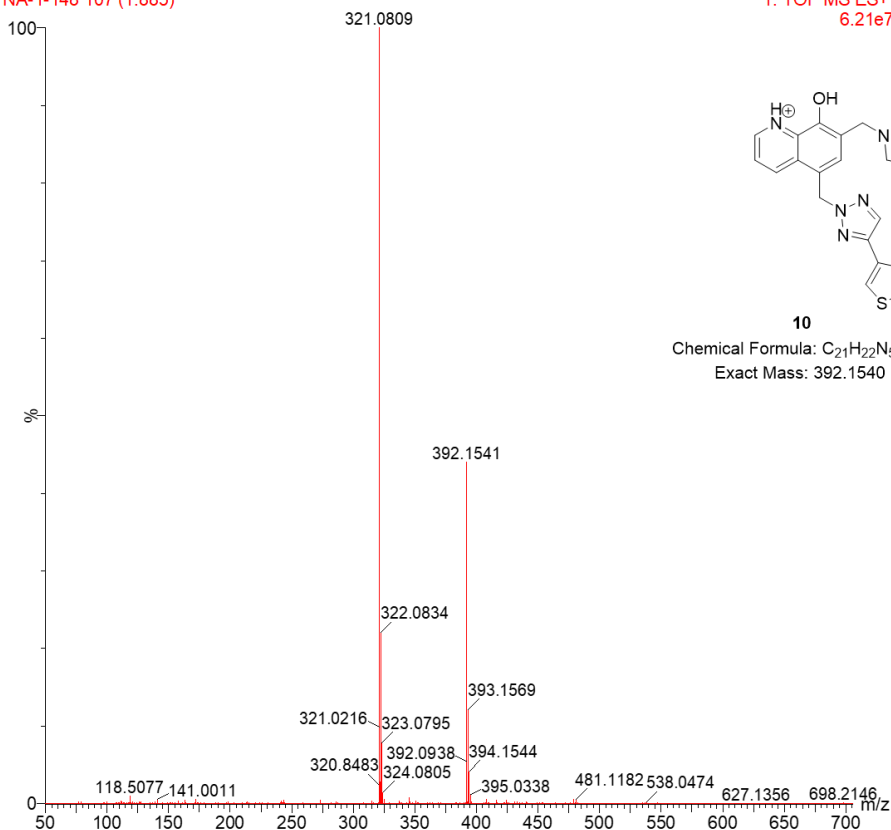
CE: 6.0

XEVO-G2QTOF#YBA089
Acq MODE: CID

09-Jul-2020 11:40:10
Cone V: 40.0

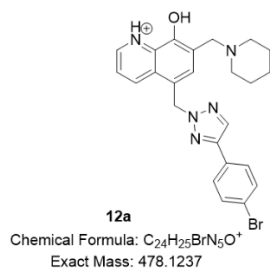
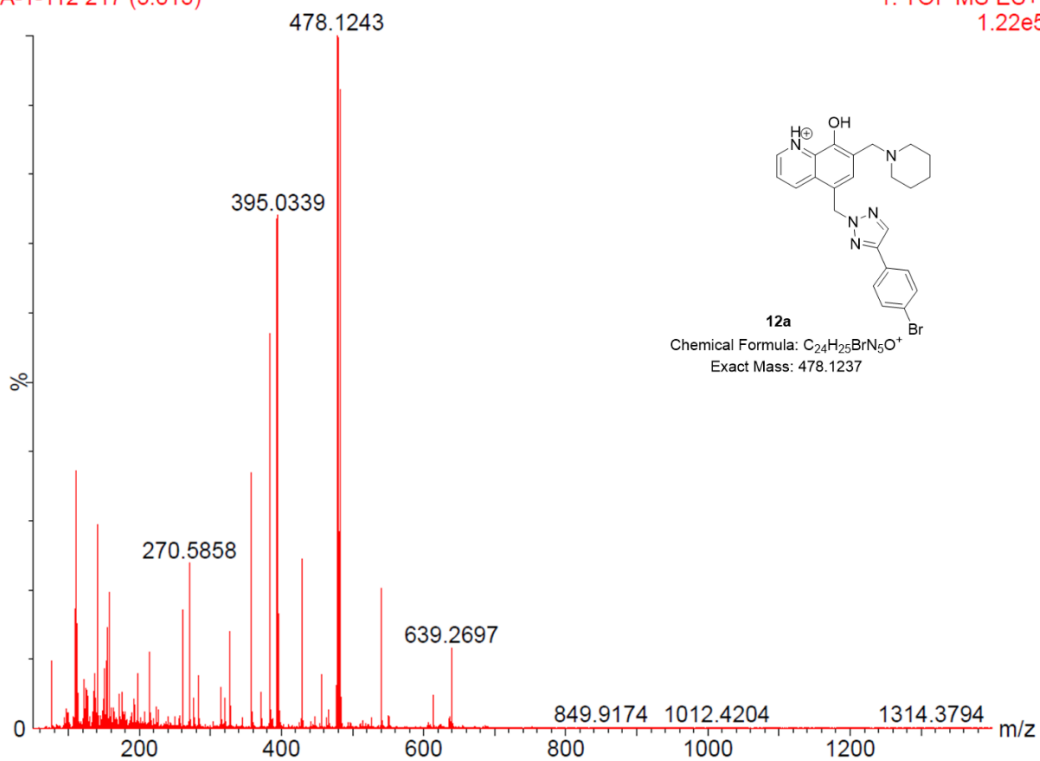
NA-1-148 107 (1.885)

1: TOF MS ES+
6.21e7



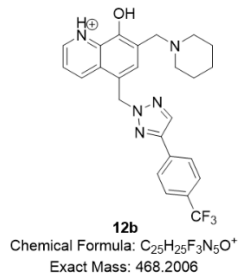
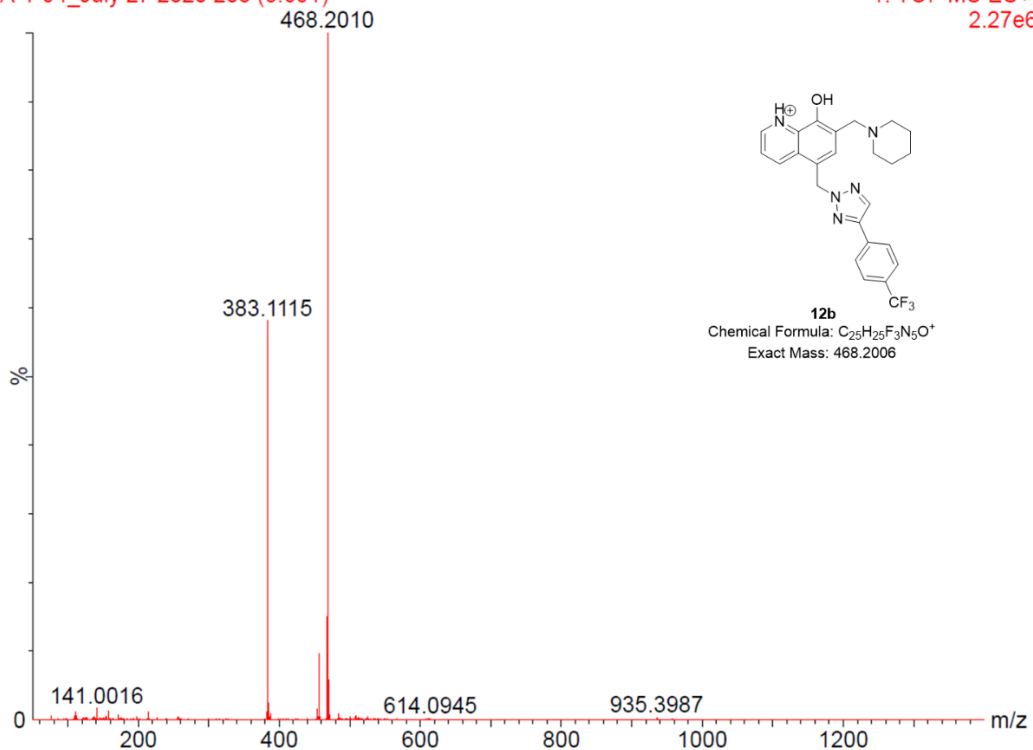
NA-1-112 217 (3.813)

1: TOF MS ES+
1.22e5



NA-1-94_July 27 2020 208 (3.651)

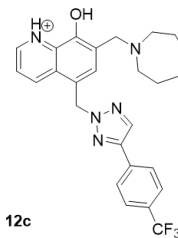
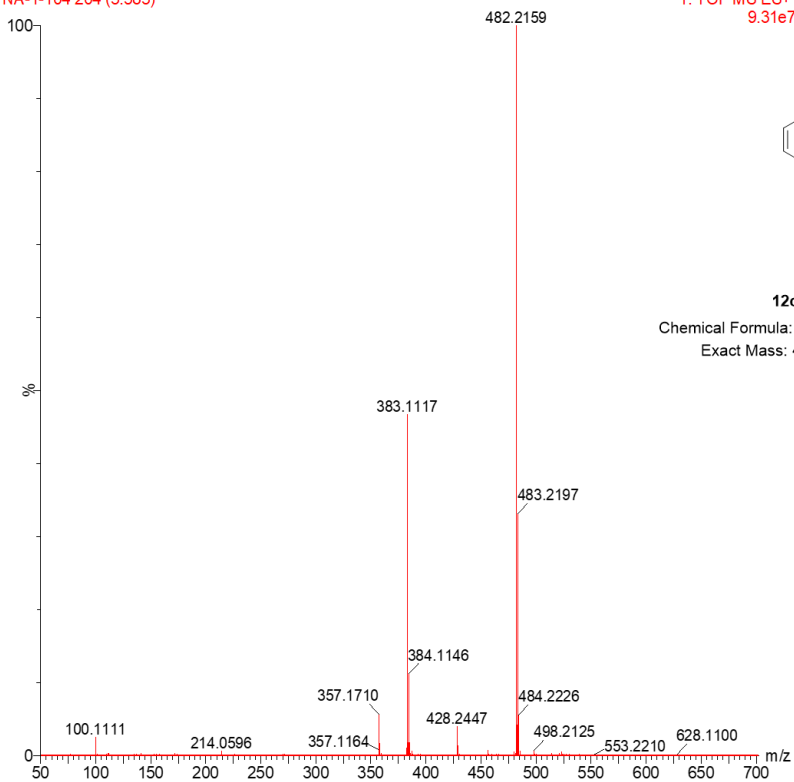
1: TOF MS ES+
2.27e6



CE: 6.0
NA-1-104 204 (3.583)

XEVO-G2QTOF#YBA089
Acq MODE: CID

09-Jul-2020 10:29:43
Cone V: 40.0
1: TOF MS ES+
9.31e7

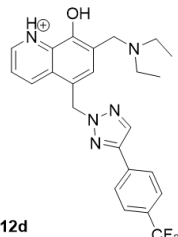
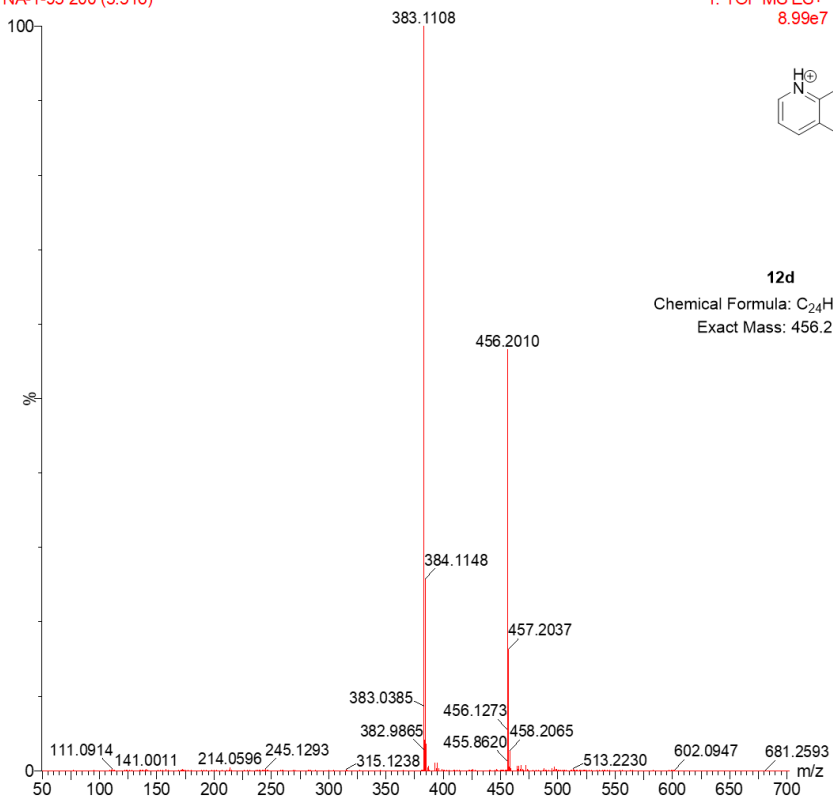


Chemical Formula: $C_{26}H_{27}F_3N_5O^+$
Exact Mass: 482.2162

CE: 6.0
NA-1-93 200 (3.516)

XEVO-G2QTOF#YBA089
Acq MODE: CID

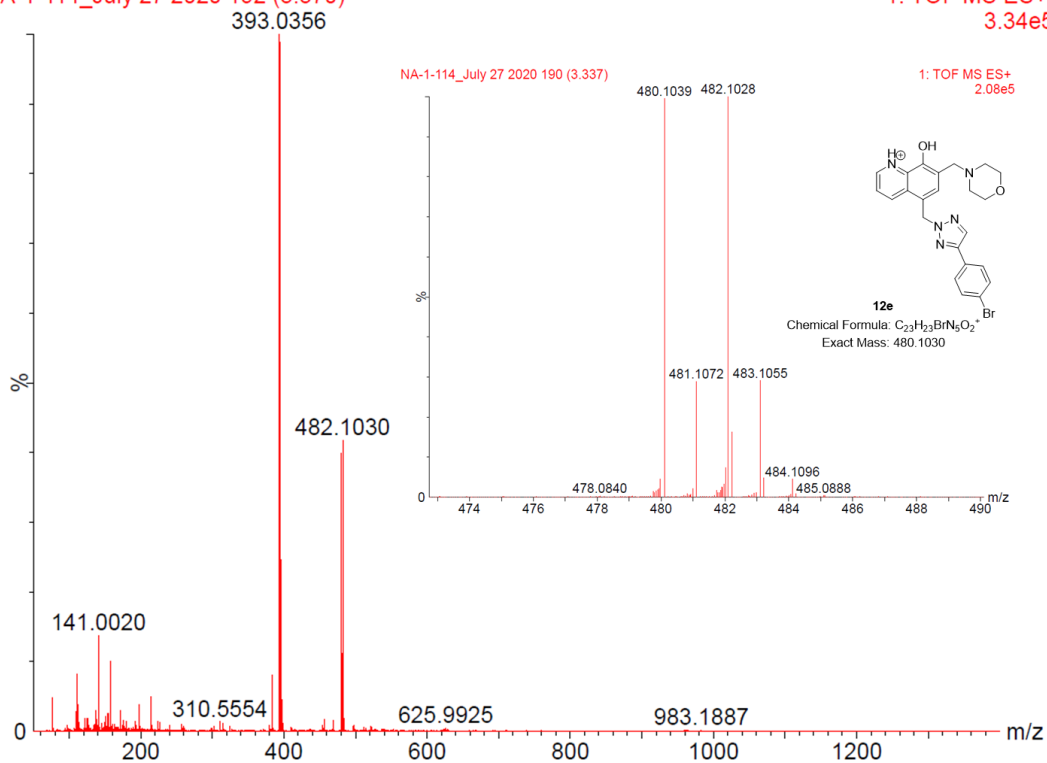
09-Jul-2020 10:15:45
Cone V: 40.0
1: TOF MS ES+
8.99e7



Chemical Formula: $C_{24}H_{25}F_3N_5O^+$
Exact Mass: 456.2006

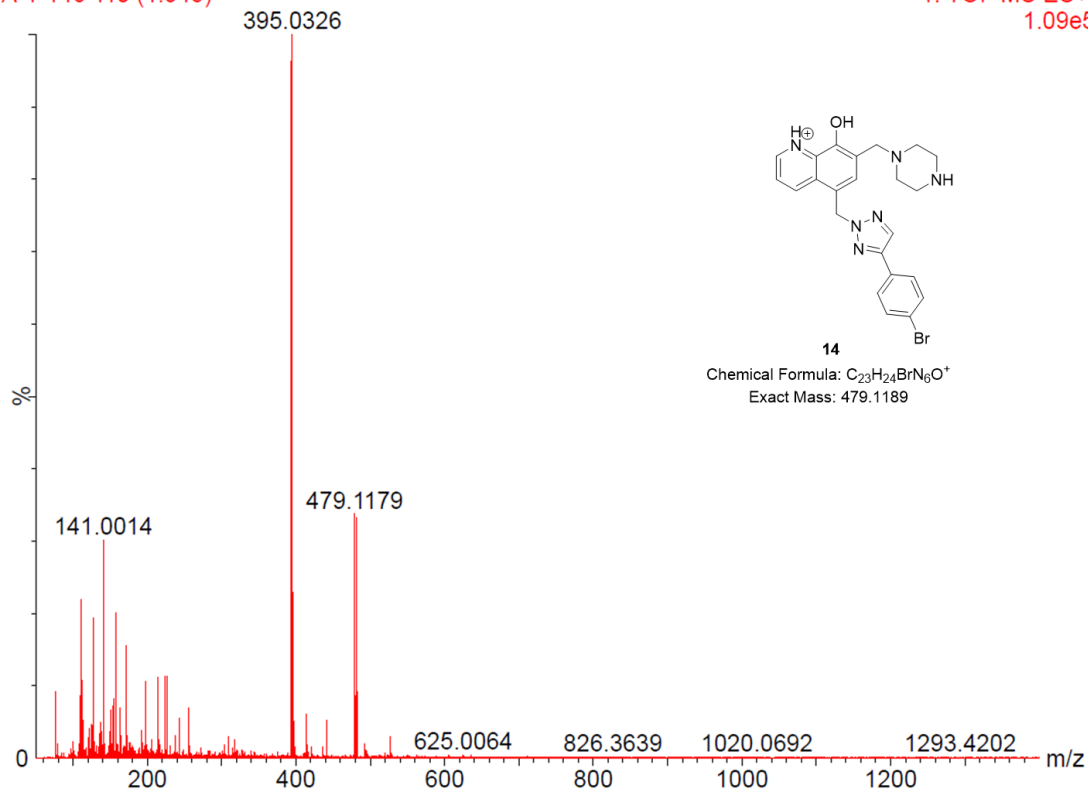
NA-1-114_July 27 2020 192 (3.370)

1: TOF MS ES+
3.34e5



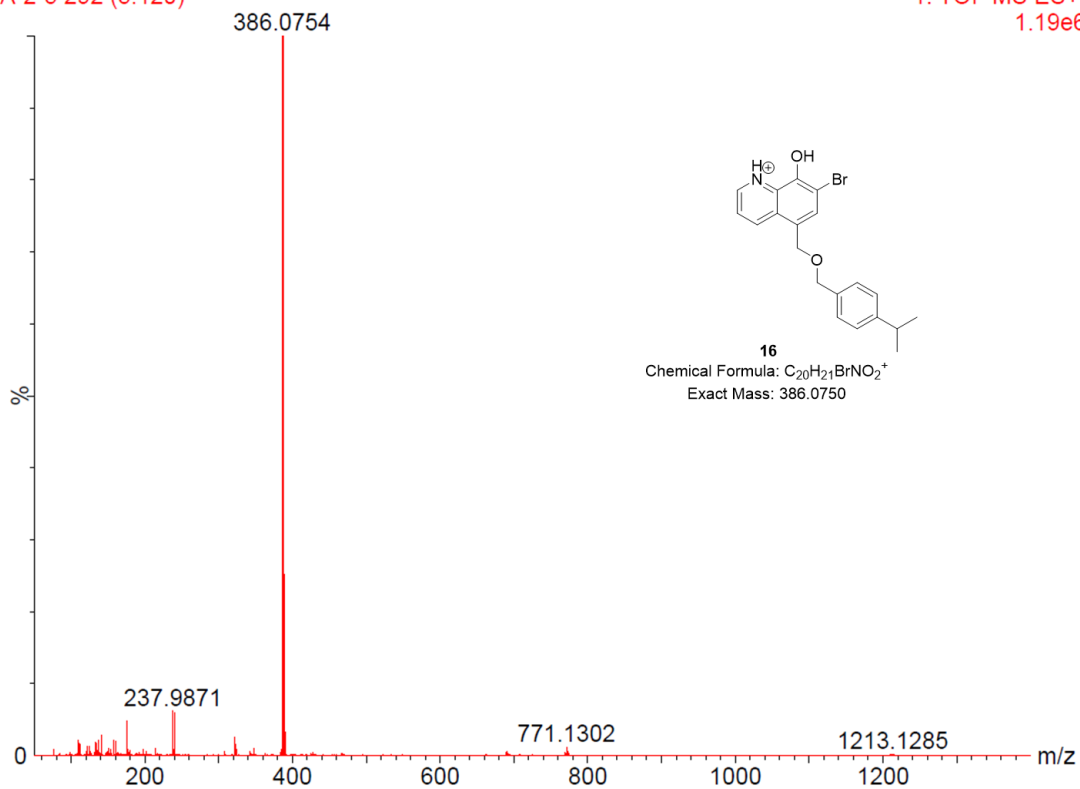
NA-1-146 110 (1.945)

1: TOF MS ES+
1.09e5



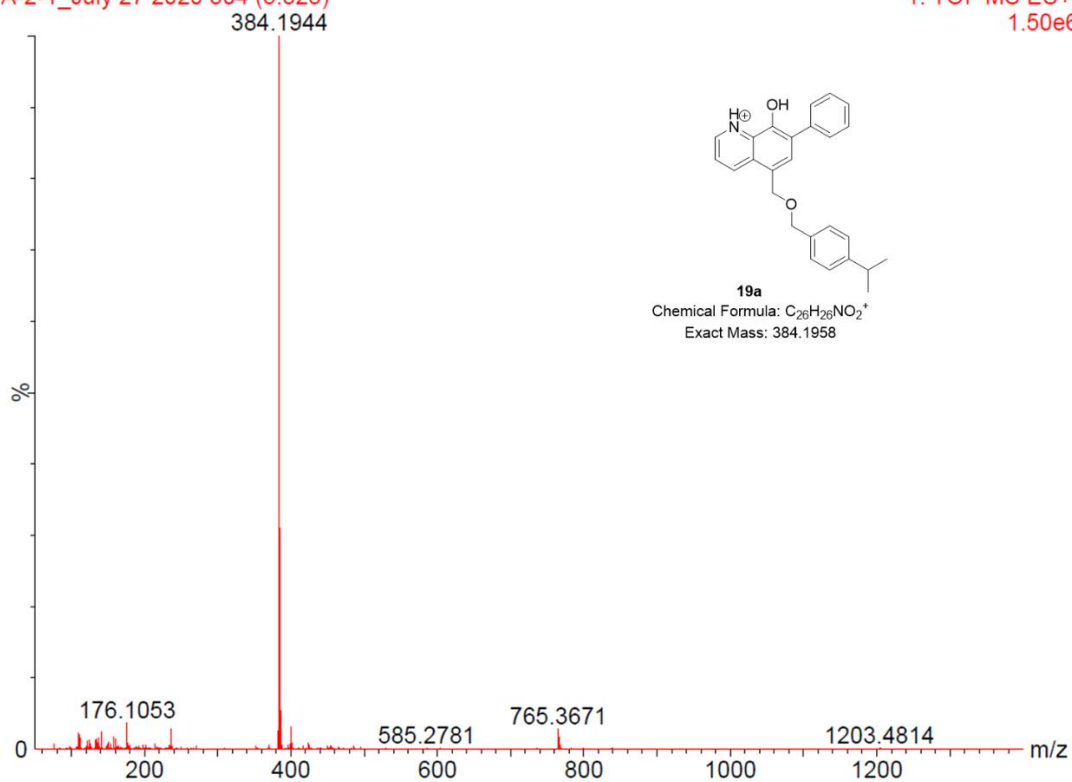
NA-2-5 292 (5.120)

1: TOF MS ES+
1.19e6



NA-2-1_July 27 2020 304 (5.323)

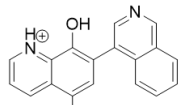
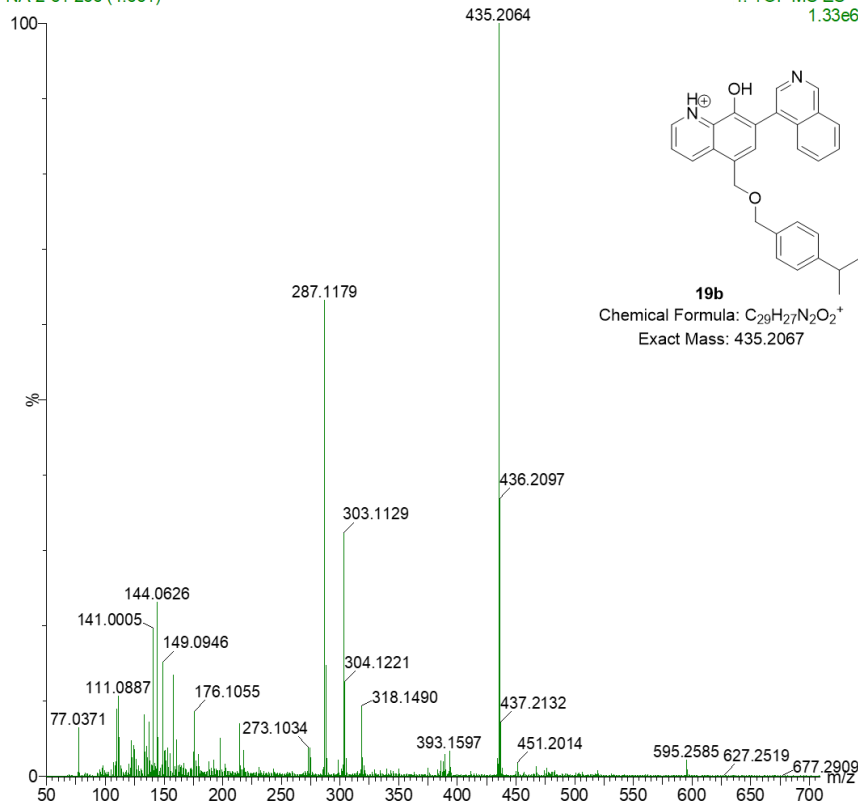
1: TOF MS ES+
1.50e6



CE: 6.0
NA-2-31 266 (4.661)

XEVO-G2QTOF#YBA089
Acq MODE: CID

09-Jul-2020 12:15:13
Cone V: 40.0
1: TOF MS ES+
1.33e6



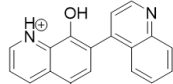
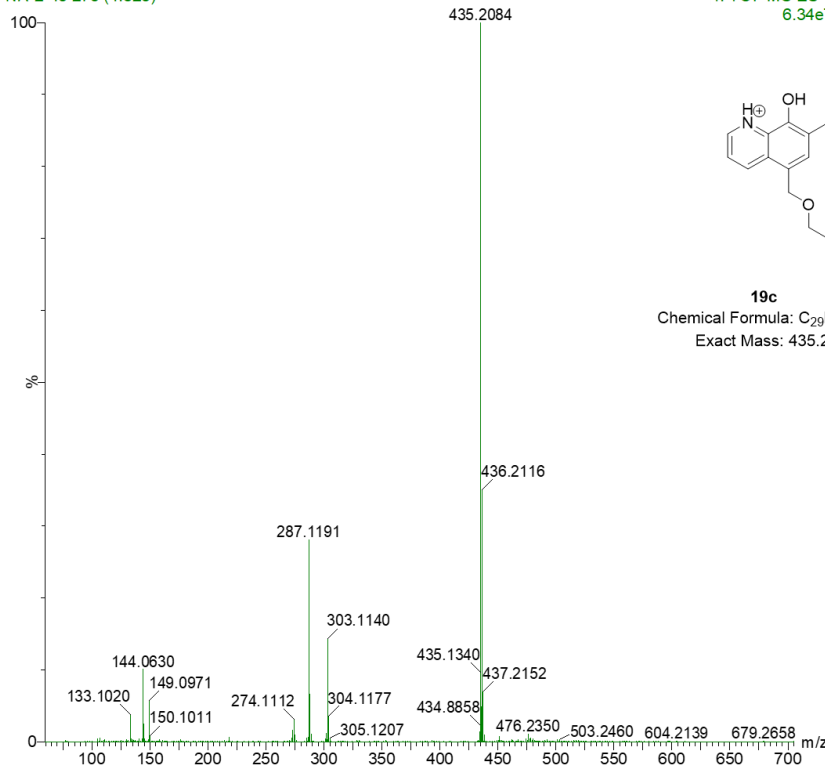
19b

Chemical Formula: $C_{29}H_{27}N_2O_2^+$
Exact Mass: 435.2067

CE: 6.0
NA-2-43 275 (4.823)

XEVO-G2QTOF#YBA089
Acq MODE: CID

09-Jul-2020 12:29:16
Cone V: 40.0
1: TOF MS ES+
6.34e7



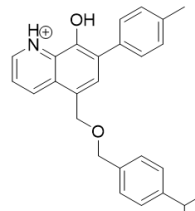
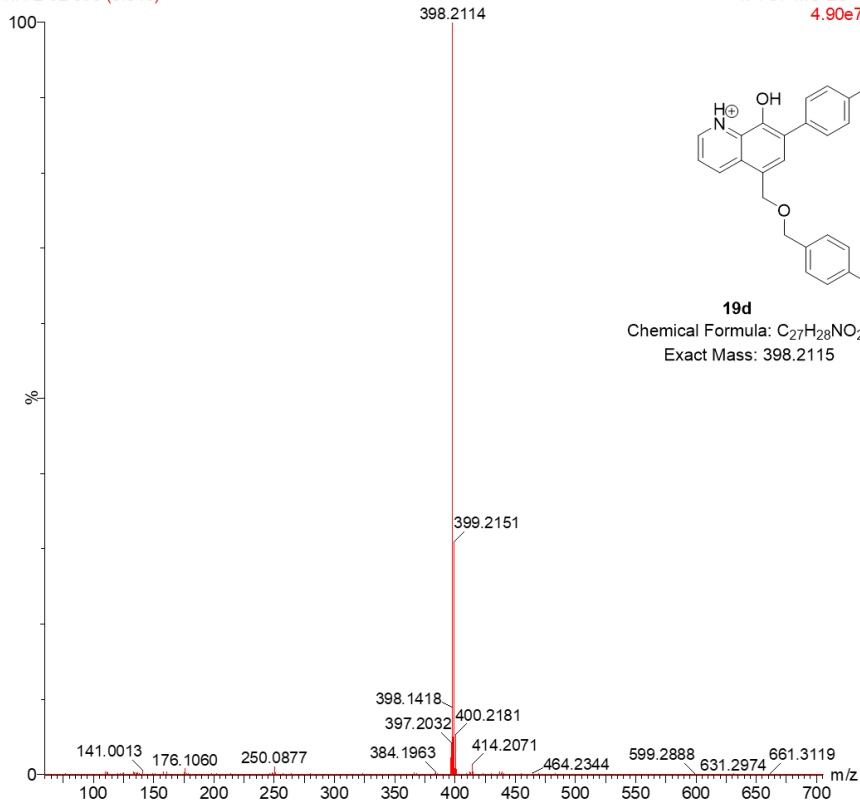
19c

Chemical Formula: $C_{29}H_{27}N_2O_2^+$
Exact Mass: 435.2067

CE: 6.0
NA-2-62 305 (5.340)

XEVO-G2QTOF#YBA089
Acq MODE: CID

09-Jul-2020 12:36:14
Cone V: 40.0
1: TOF MS ES+
4.90e7

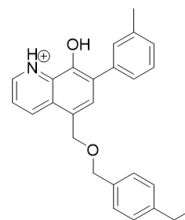
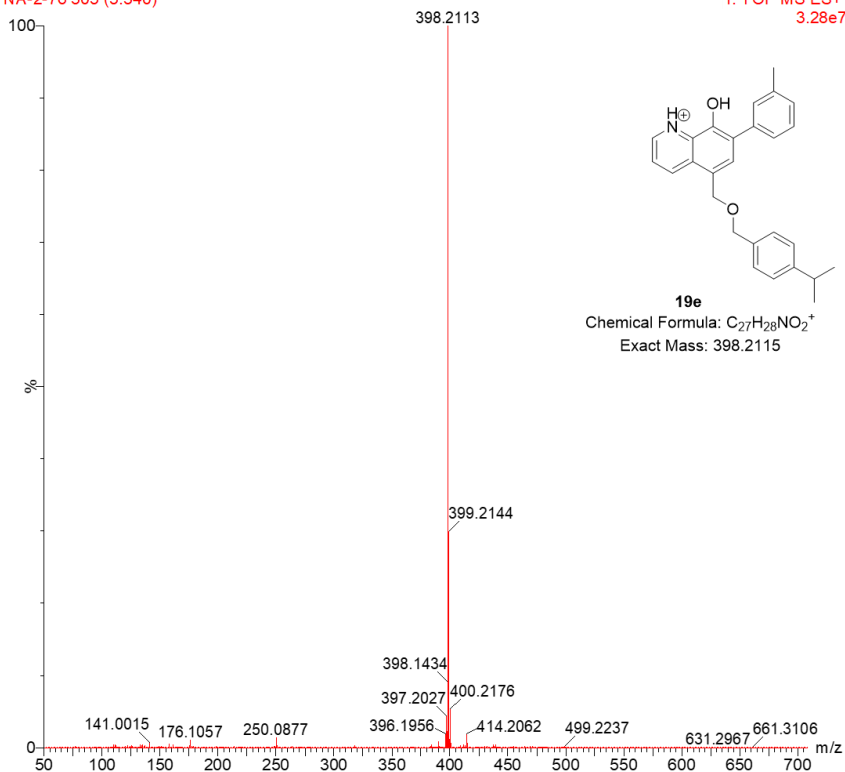


19d
Chemical Formula: C₂₇H₂₈NO₂⁺
Exact Mass: 398.2115

CE: 6.0
NA-2-76 305 (5.340)

XEVO-G2QTOF#YBA089
Acq MODE: CID

09-Jul-2020 13:18:21
Cone V: 40.0
1: TOF MS ES+
3.28e7

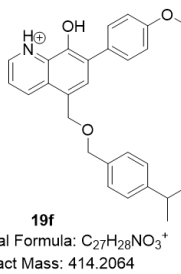
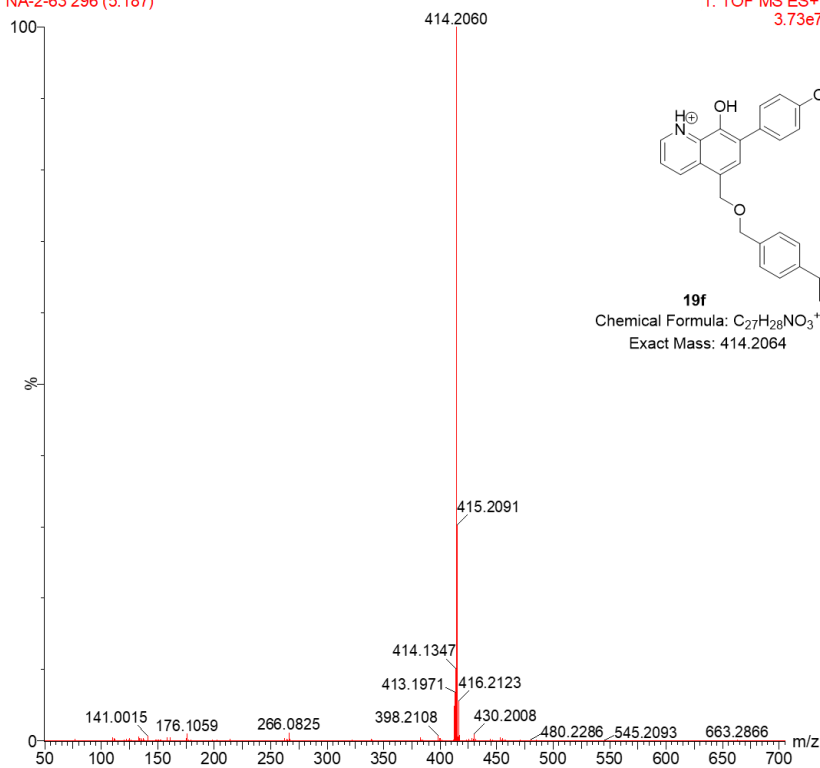


19e
Chemical Formula: C₂₇H₂₈NO₂⁺
Exact Mass: 398.2115

CE: 6.0
NA-2-63 296 (5.187)

XEVO-G2QTOF#YBA089
Acq MODE: CID

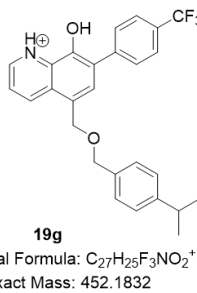
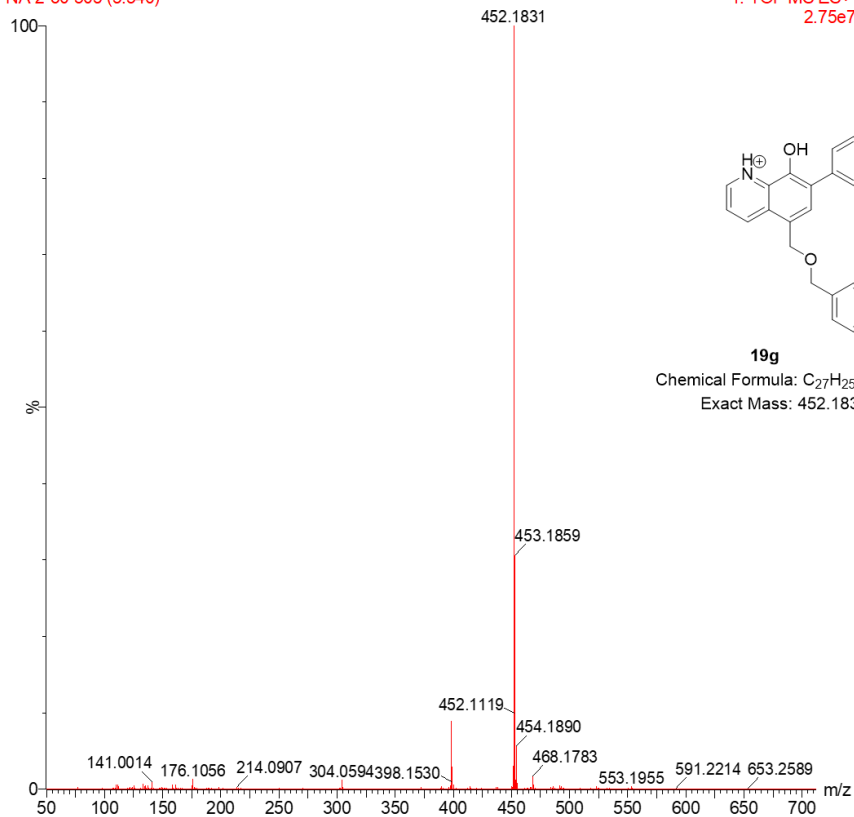
09-Jul-2020 12:43:11
Cone V: 40.0
1: TOF MS ES+
3.73e7



CE: 6.0
NA-2-80 305 (5.340)

XEVO-G2QTOF#YBA089
Acq MODE: CID

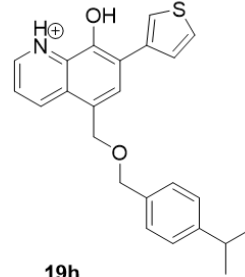
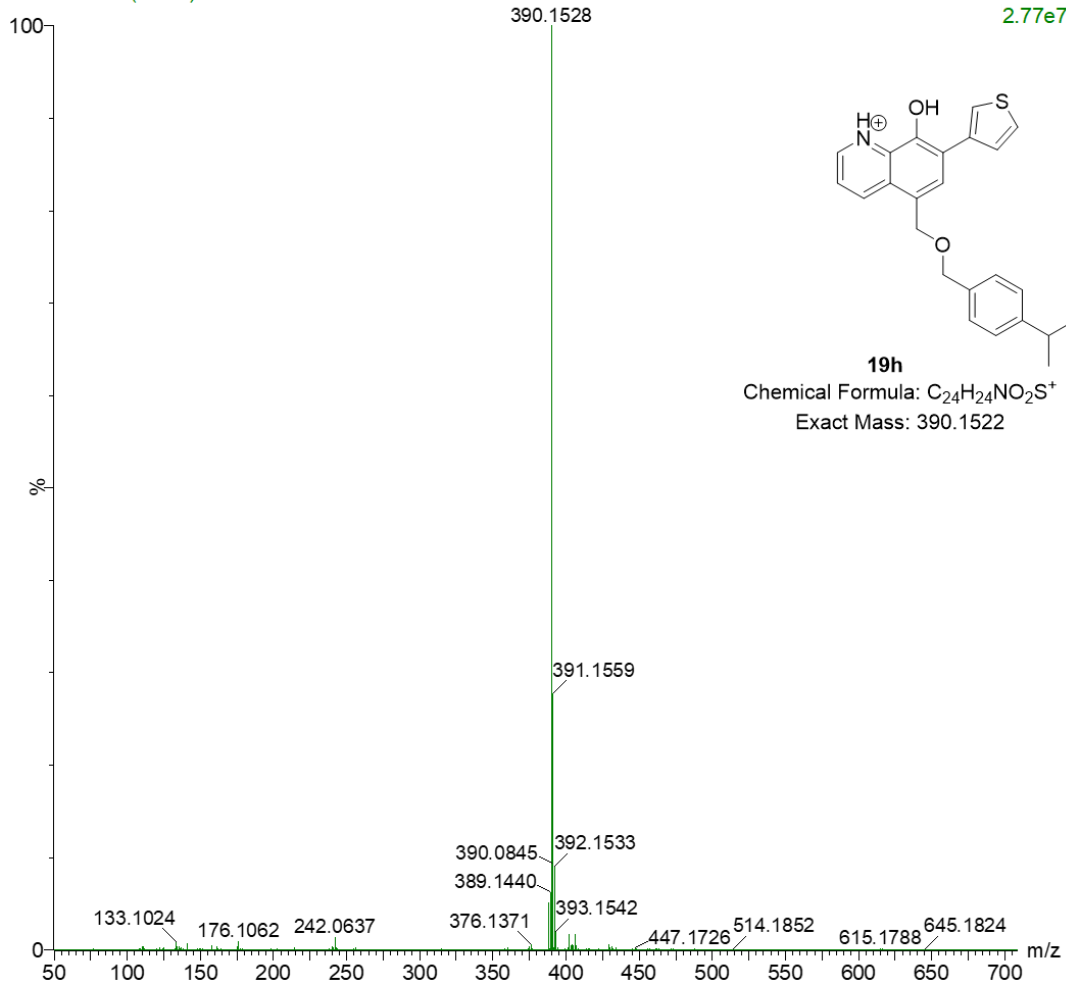
09-Jul-2020 13:25:27
Cone V: 40.0
1: TOF MS ES+
2.75e7



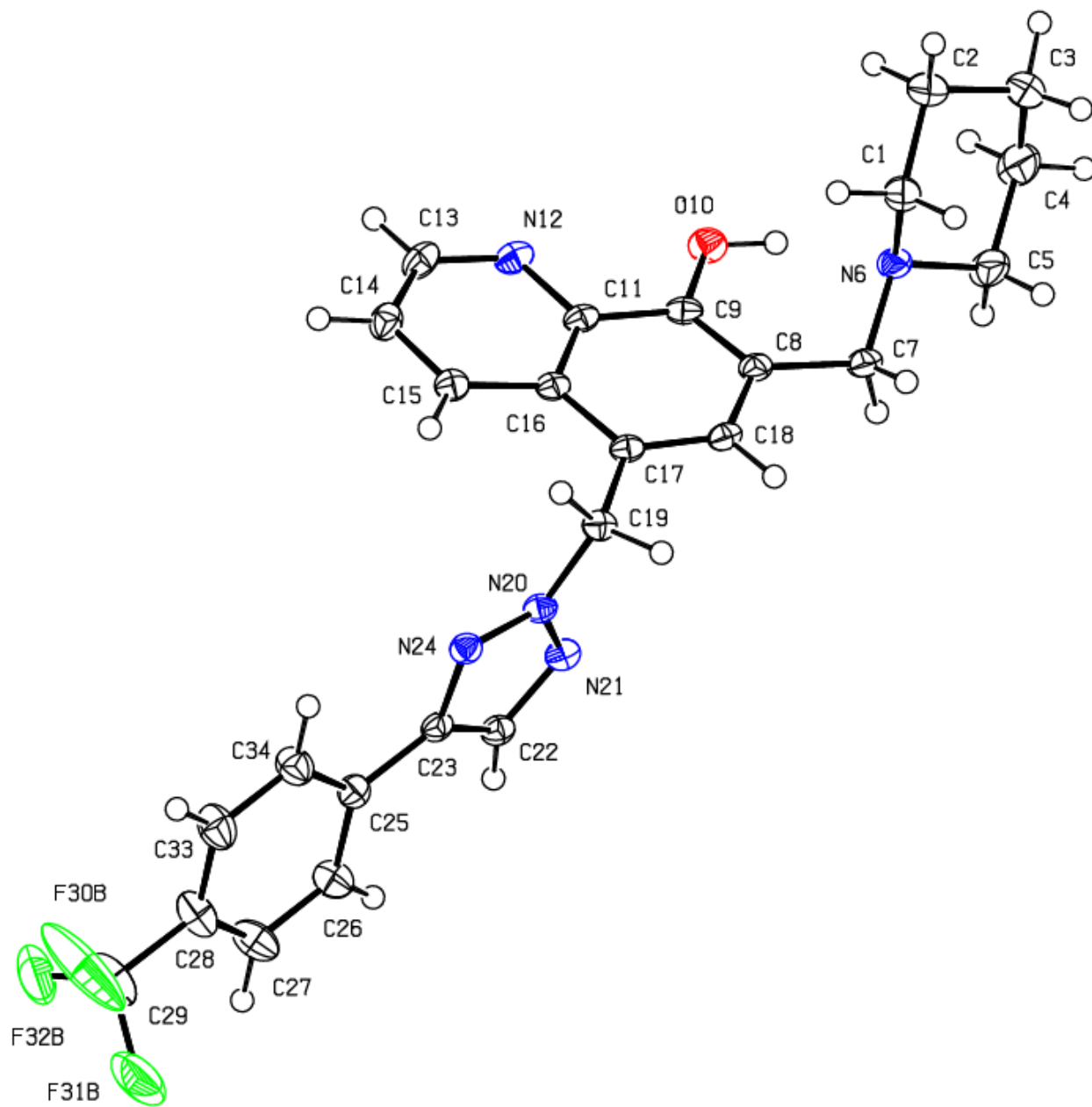
CE: 6.0
NA-2-65 300 (5.255)

XEVO-G2QTOF#YBA089
Acq MODE: CID

09-Jul-2020 13:11:24
Cone V: 40.0
1: TOF MS ES+
2.77e7



Chemical Formula: C₂₄H₂₄NO₂S⁺
Exact Mass: 390.1522



Supplementary Figure S1: Labeled thermal ellipsoid plot for **12b**.

Table S1: Chemical and crystal data for **12b**.

<i>Chemical formula</i>	C ₂₅ H ₂₄ F ₃ N ₅ O
<i>Formula weight, Da</i>	467.49
<i>Temperature, K</i>	100(2)
<i>Crystal description</i>	colourless plate
<i>Crystal size, mm</i>	0.641 x 0.231 x 0.058
<i>Crystal system</i>	triclinic
<i>Space group</i>	P $\bar{1}$
<i>Unit cell dimensions, from 9869 reflections having $2.29^\circ \leq \theta \leq 68.29^\circ$</i>	
<i>a, Å</i>	5.9682(2)
<i>b, Å</i>	10.0184(3)
<i>c, Å</i>	19.3660(7)
<i>α, °</i>	93.6960(10)
<i>β, °</i>	92.7200(10)
<i>γ, °</i>	94.7610(10)
<i>Volume, Å³</i>	1149.91(7)
<i>Z</i>	2
<i>Density (calculated), g/cm³</i>	1.350
<i>Absorption coefficient, mm⁻¹</i>	0.857
<i>F(000)</i>	488

Table S2: Data collection, structure solution, and refinement.

<i>X-ray wavelength, Å</i>	1.54178
<i>Theta range for data integration</i>	2.289 to 68.289°
<i>Index ranges</i>	$-7 \leq h \leq 7, -10 \leq k \leq 12, -23 \leq l \leq 23$
<i>Reflections collected</i>	17177
<i>Independent reflections</i>	4153 ($R_{int} = 0.0392$)
<i>Observed reflections ($I > 2\sigma(I)$)</i>	3830
<i>Coverage of independent reflections</i>	98.6%
<i>Absorption correction method</i>	numerical
<i>Max. and min. transmission</i>	1.0000 and 0.6918
<i>Structure solution technique</i>	dual-space method
<i>Structure solution program</i>	SHELXT (Sheldrick, 2016)
<i>Refinement method</i>	full-matrix least-squares on F^2
<i>Refinement program</i>	SHELXL-2018/3 (Sheldrick, 2018)
<i>Function minimized</i>	$\Sigma w(F_o^2 - F_c^2)^2$
<i>Weighting scheme</i>	$w=1/[\sigma^2(F_o^2)+(0.0489P)^2+0.3954P]$, where $P=(F_o^2+2F_c^2)/3$
<i>Data / restraints / parameters</i>	4153 / 63 / 339
<i>Goodness-of-fit on F^2</i>	1.049
<i>Final residuals</i>	
<i>observed data</i>	$R1 = 0.0379, wR2 = 0.0966$
<i>all data</i>	$R1 = 0.0407, wR2 = 0.0994$
<i>Largest difference peak and hole, $e^-/\text{Å}^3$</i>	0.279 and -0.251
<i>R.M.S. deviation from mean, $e^-/\text{Å}^3$</i>	0.051
