Supporting Information

Structure-based Design of Human TLR8-specific Agonists with Augmented Potency and Adjuvanticity

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Fig. S1. Agonistic potencies of **1** and **2** in human TLR7 and TLR8 Primary Screens

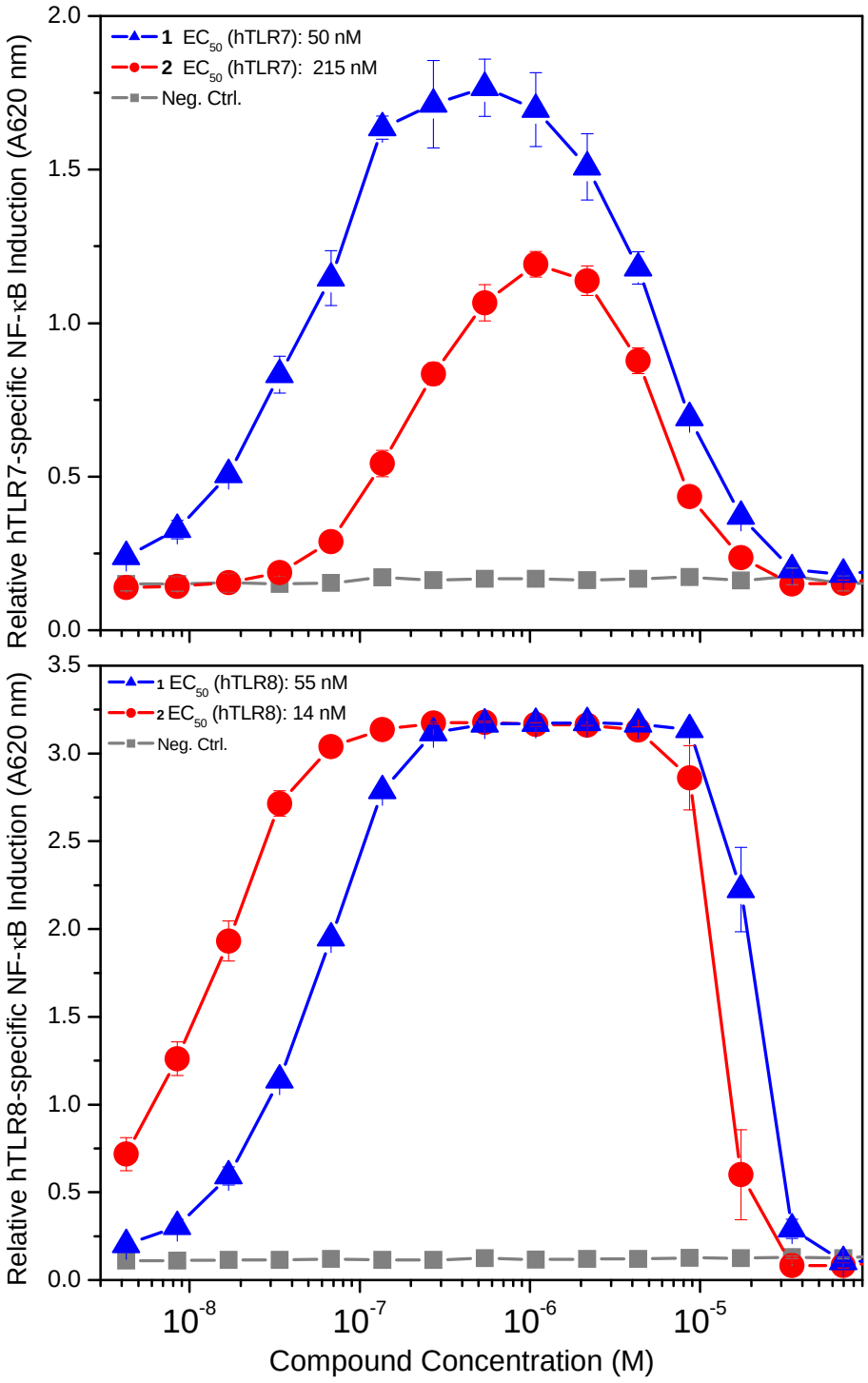
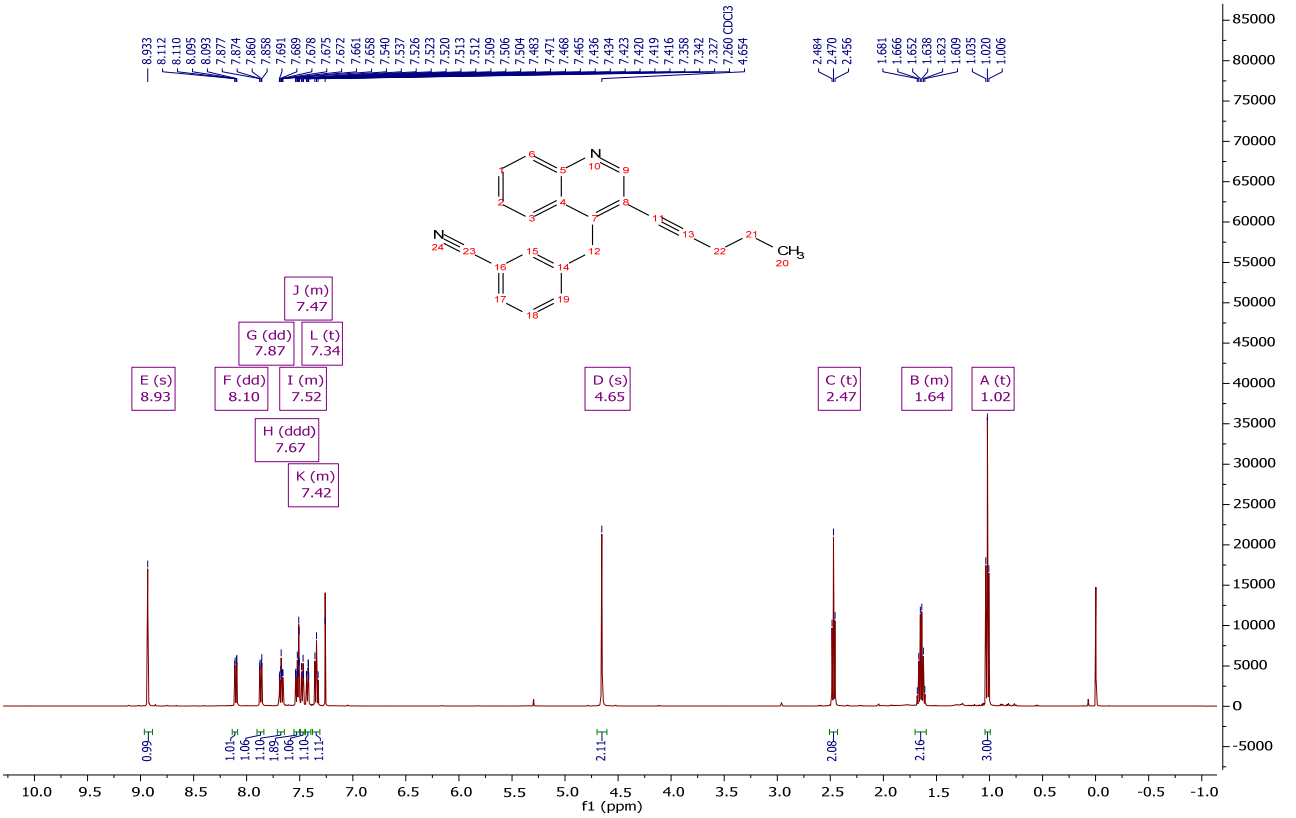


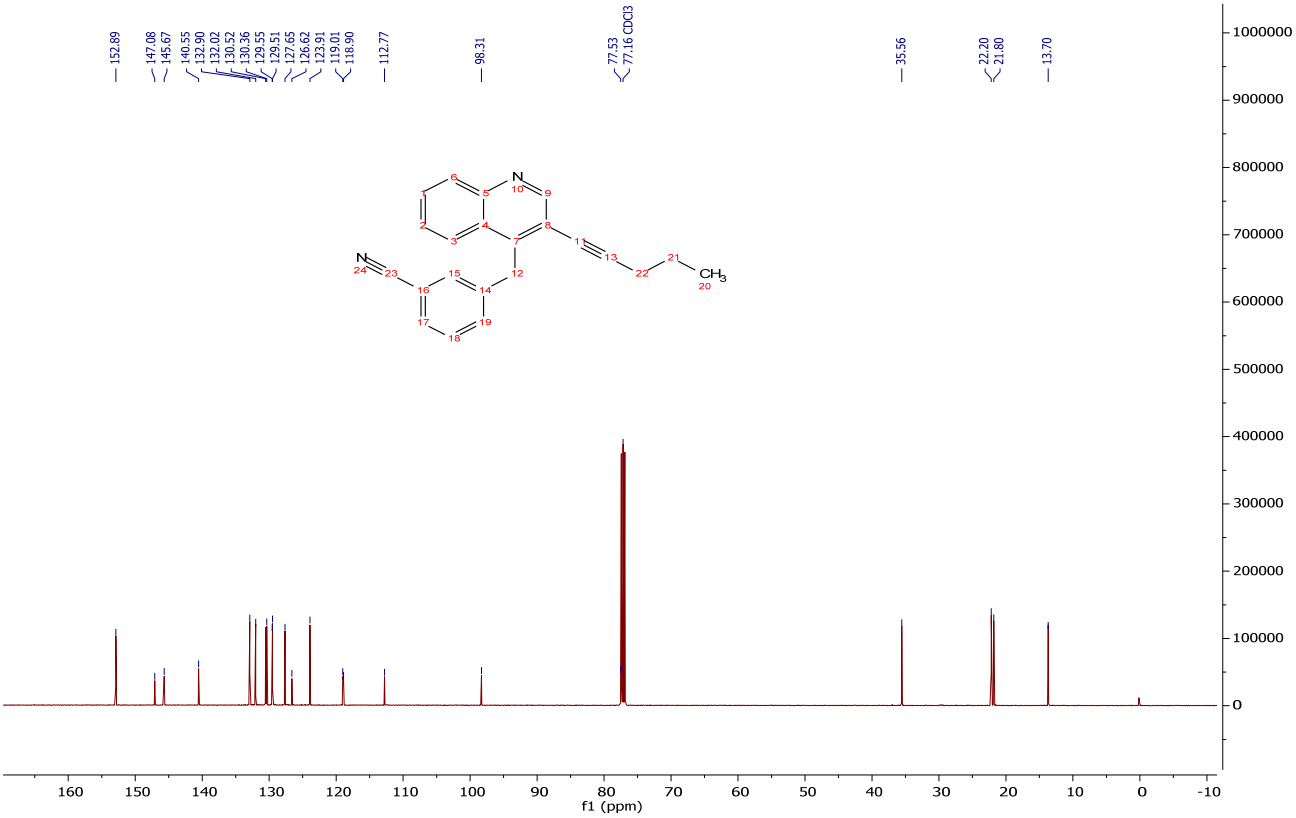
Table S1. Data collection and refinement statistics for TLR8/**1**, and TLR8/**2** [a]

	TLR8/**1**	TLR8/**2**
Data Collection		
X-ray source	PF-NE3A	PF-NE3A
Wavelength	1.0000	1.0000
Space group	*C2*	*C*2
Unit cell parameters		
a (Å)	135.7	134.9
b (Å)	106.7	107.1
c (Å)	72.2	72.1
β (°)	106.2	106.3
Resolution (Å)	2.05	2.10
Completeness (%)	99.8 (99.9)	98.9 (99.6)
Redundancy	3.5 (3.4)	3.1 (2.8)
R_{sym} (*I*)[b]	0.077 (0.424)	0.073 (0.759)
Average *I/σ(I)*	9.6 (2.6)	26.4 (2.0)
Refinement		
Resolution range (Å)	69.28-2.05	27.50-2.10
No. of reflections used	58,440	53,673
Model	1 × TLR8	1 × TLR8
Average *B*-factor (Å^2)	38.4	50.1
R (%)[c]	21.5	20.1
R_{free} (%)[d]	26.9	25.9
Rms deviations		
Bond length (Å)	0.011	0.016
Bond angles (°)	1.61	1.89

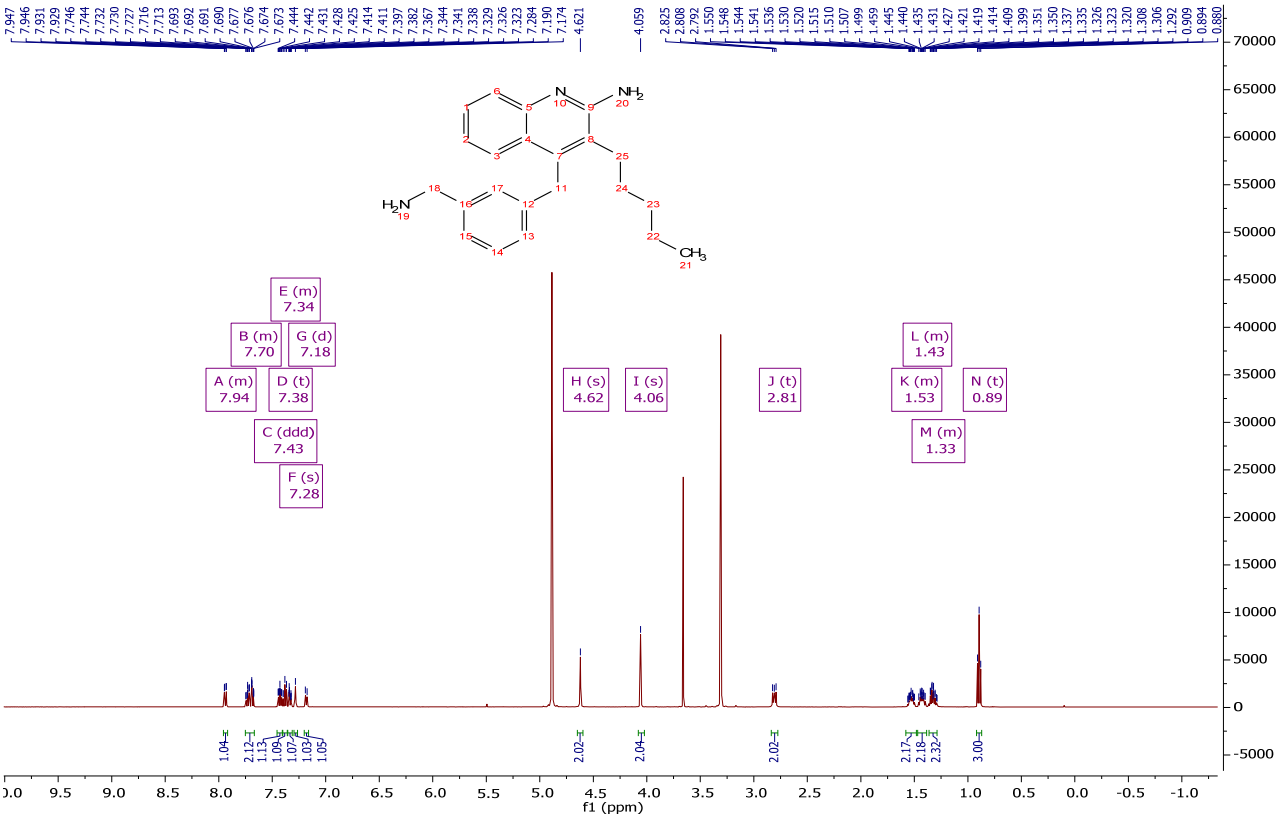
[a] Highest resolution shell is shown in parentheses.
[b] R_{sym} $(I) = \Sigma|I - <I>|/\Sigma I$, where I is the diffraction intensity.
[c] $R = \Sigma|F_o - F_c|/\Sigma F_o$, where F_o and F_c are the observed and calculated structure amplitudes, respectively.
[d] R_{free} is an R value for a 5% subset of all reflections, but was not used in the refinement.

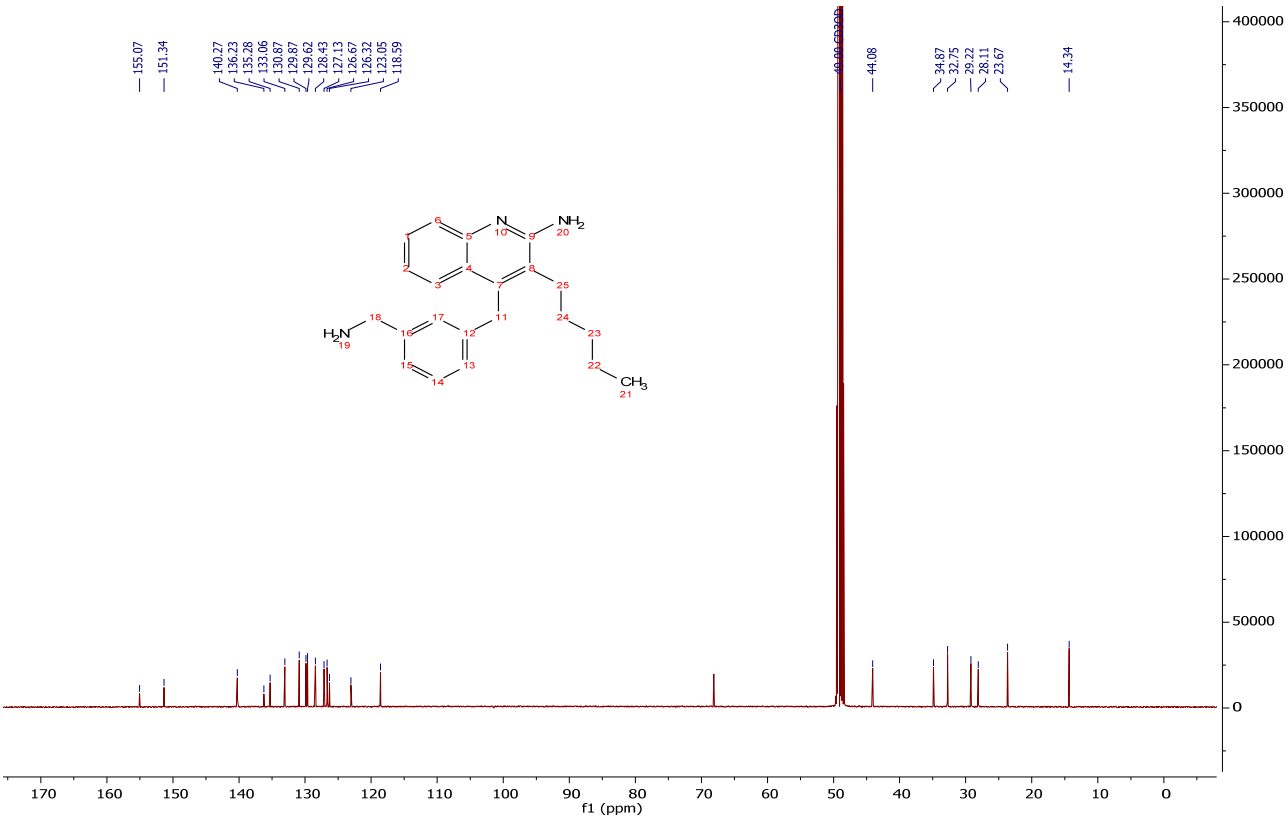
Compound **5a:** ^{1}H and ^{13}C NMR Spectrum



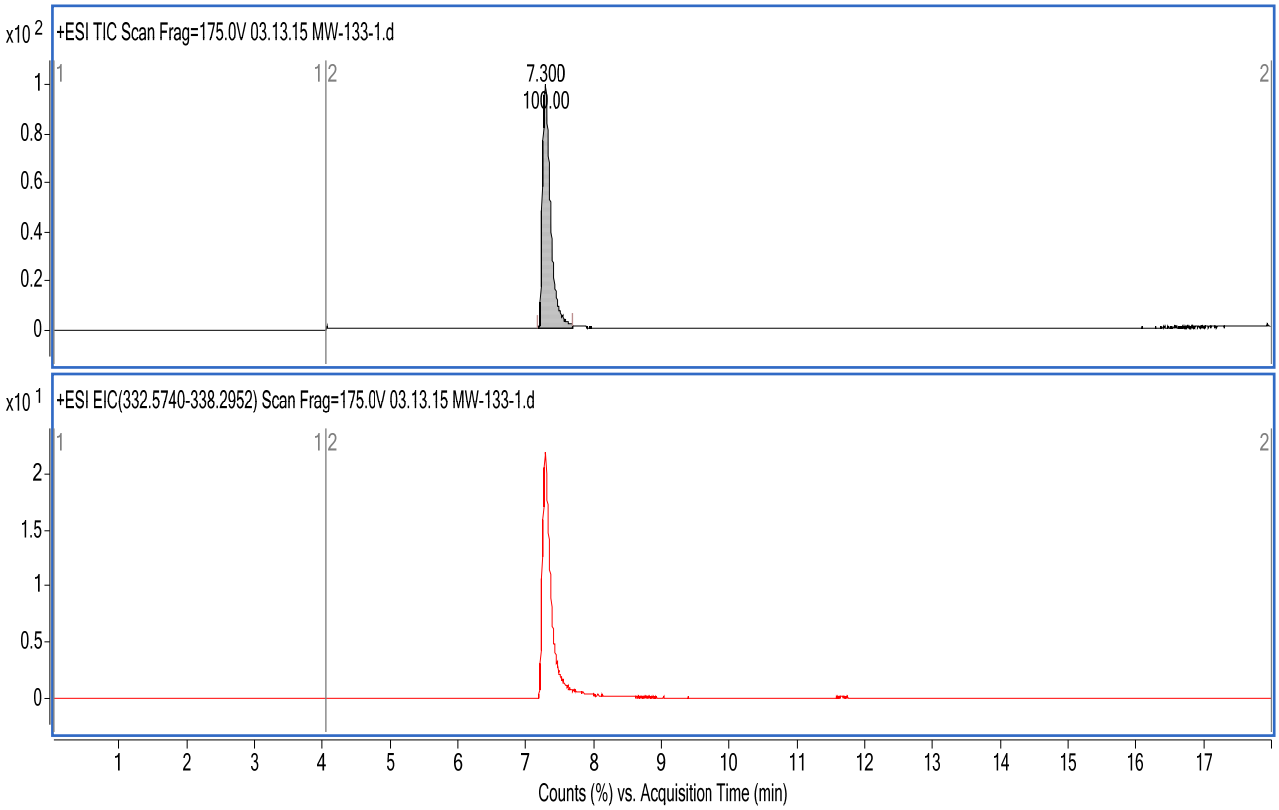


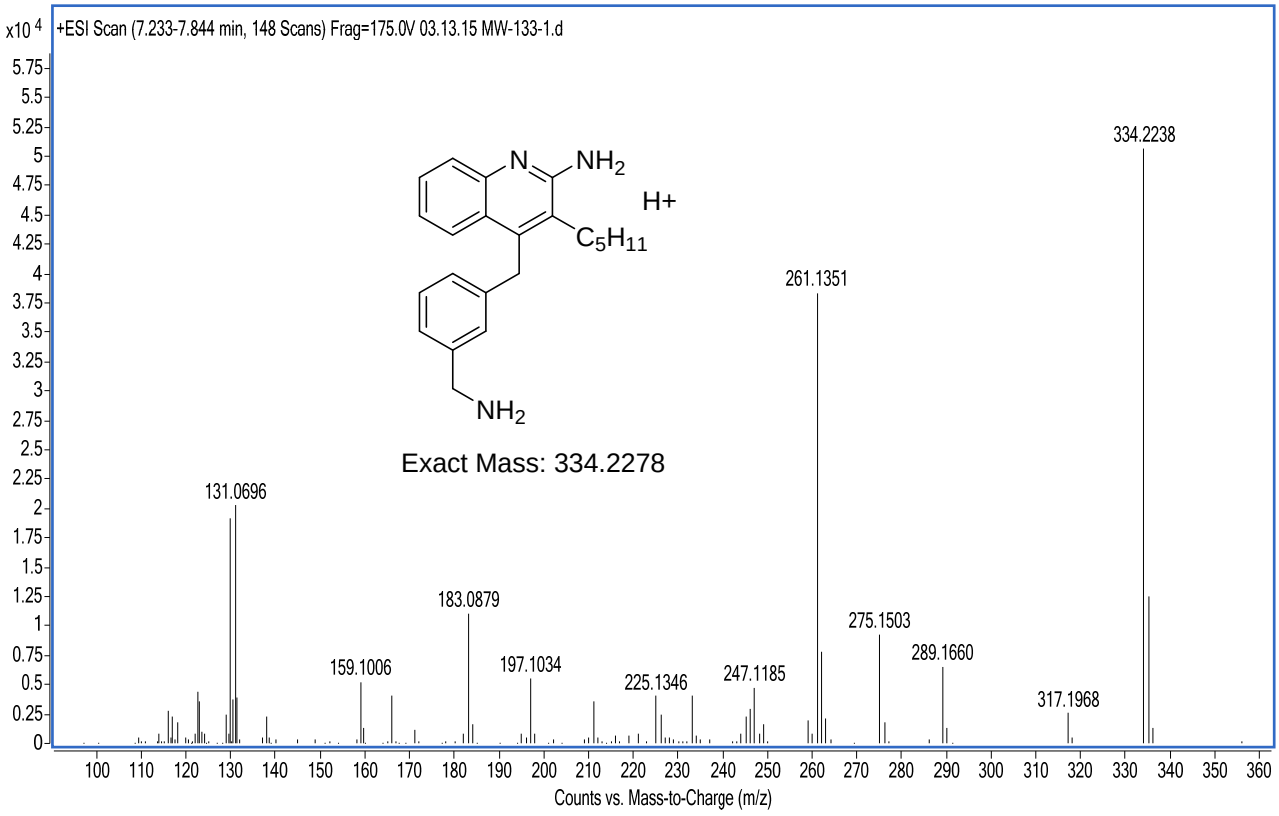
Compound **9a:** ^{1}H and ^{13}C NMR Spectrum



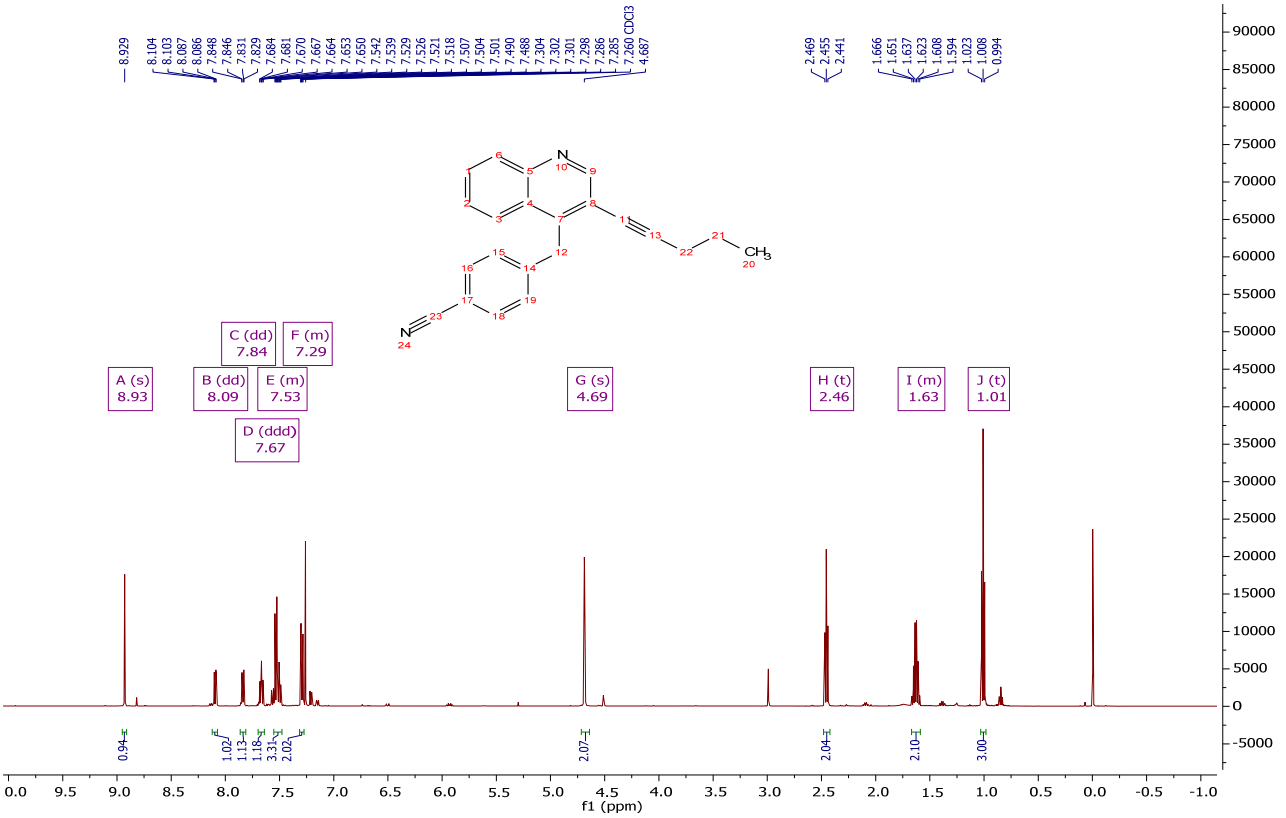


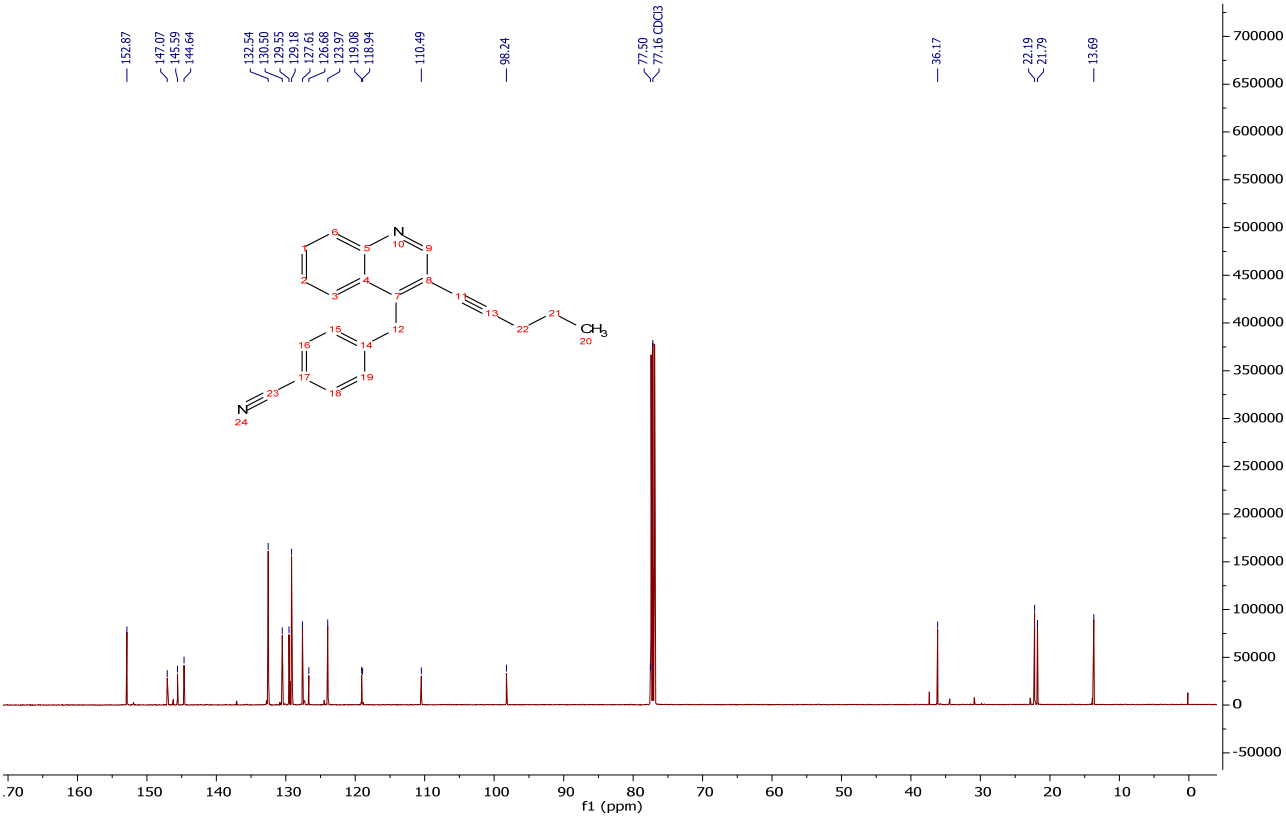
Compound **9a:** LC-MS



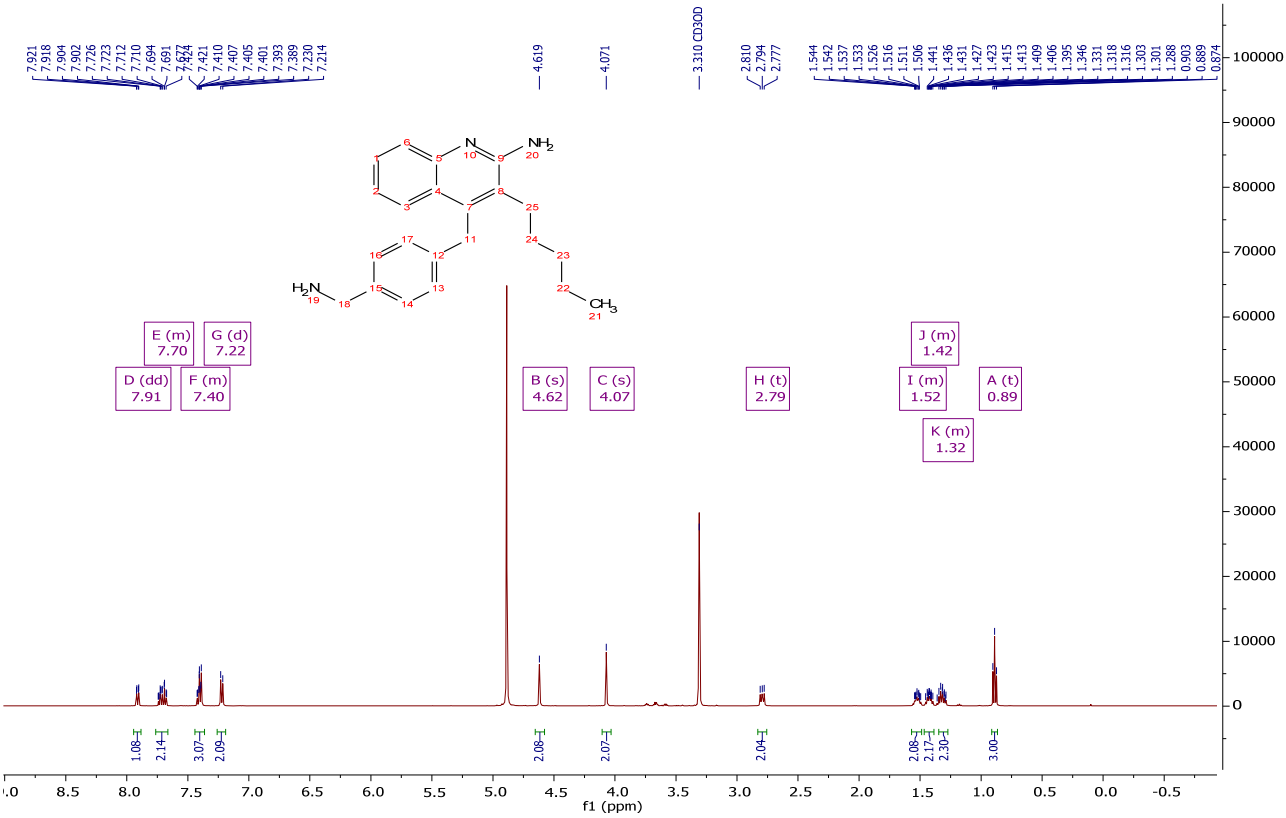


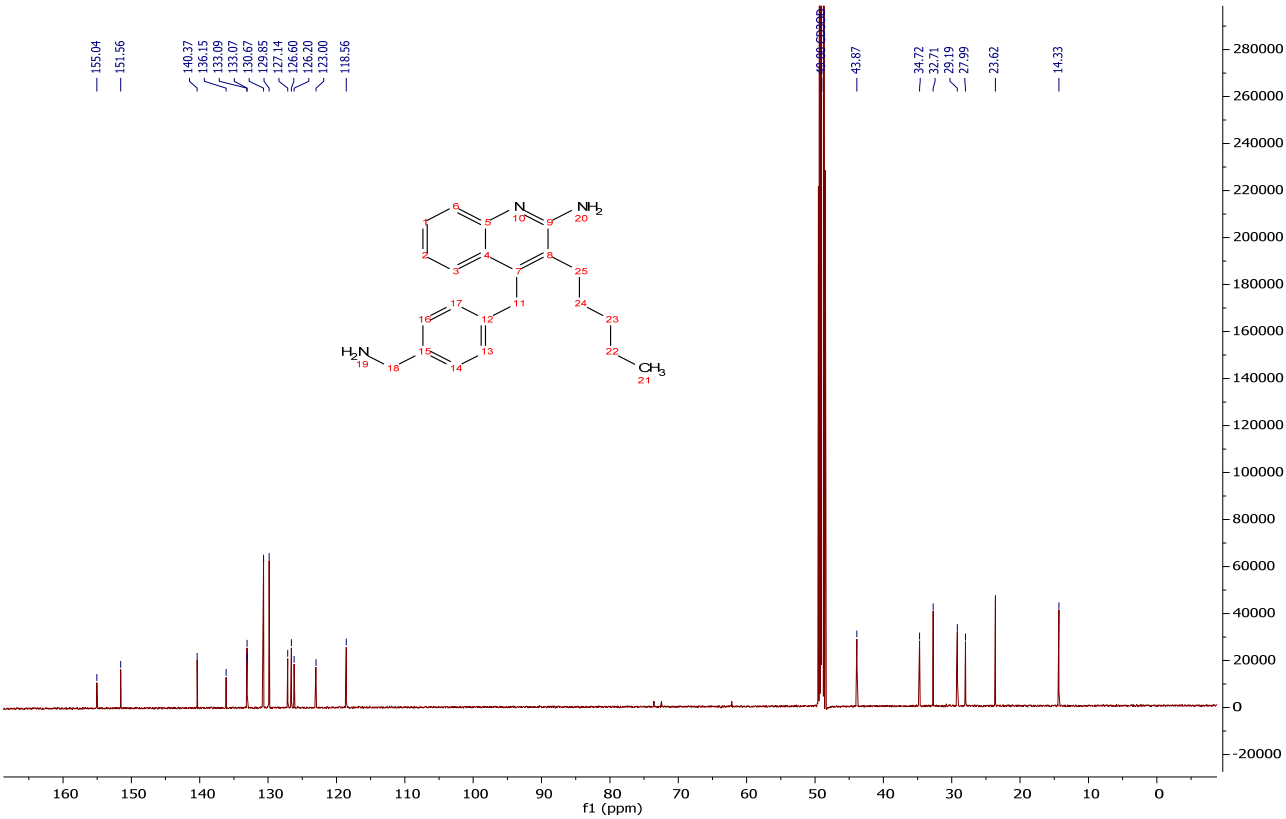
Compound **5b:** ^{1}H and ^{13}C NMR Spectrum



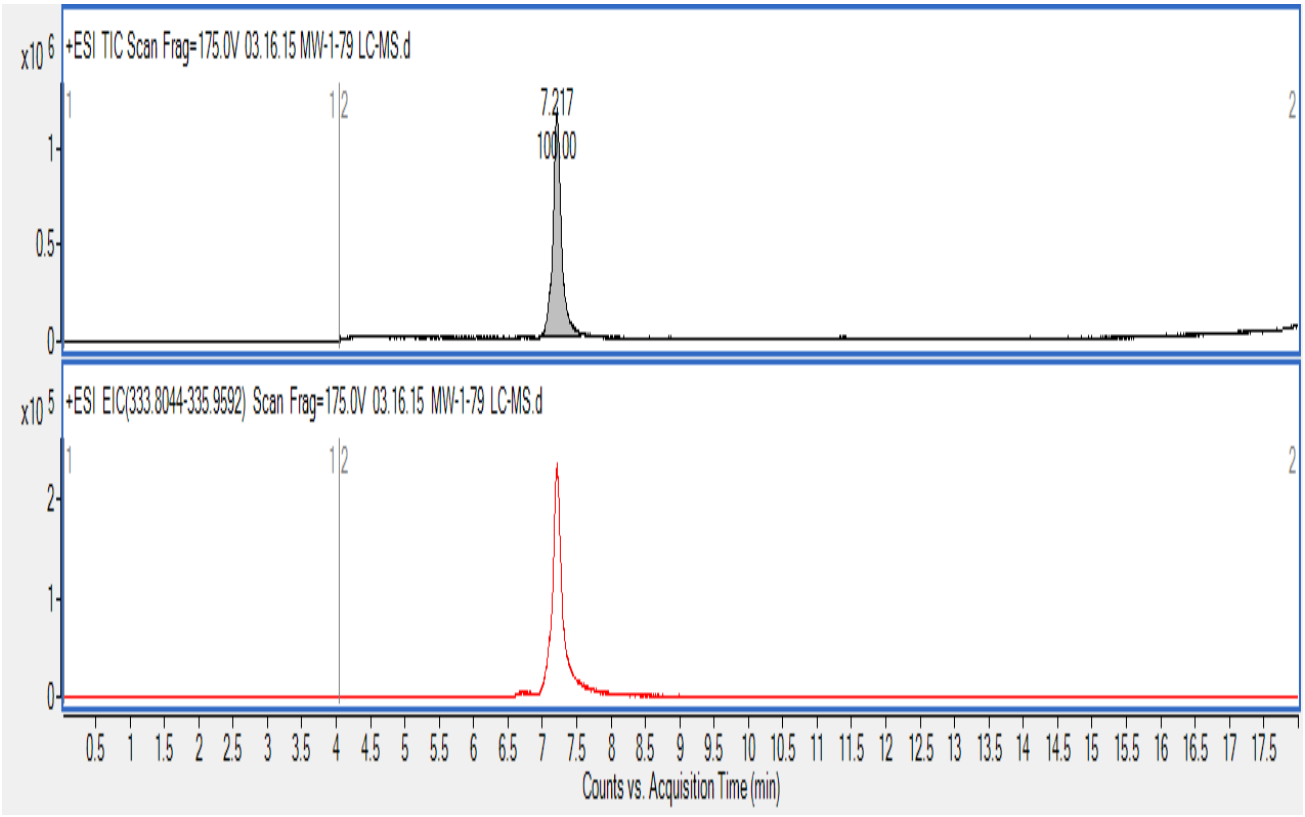


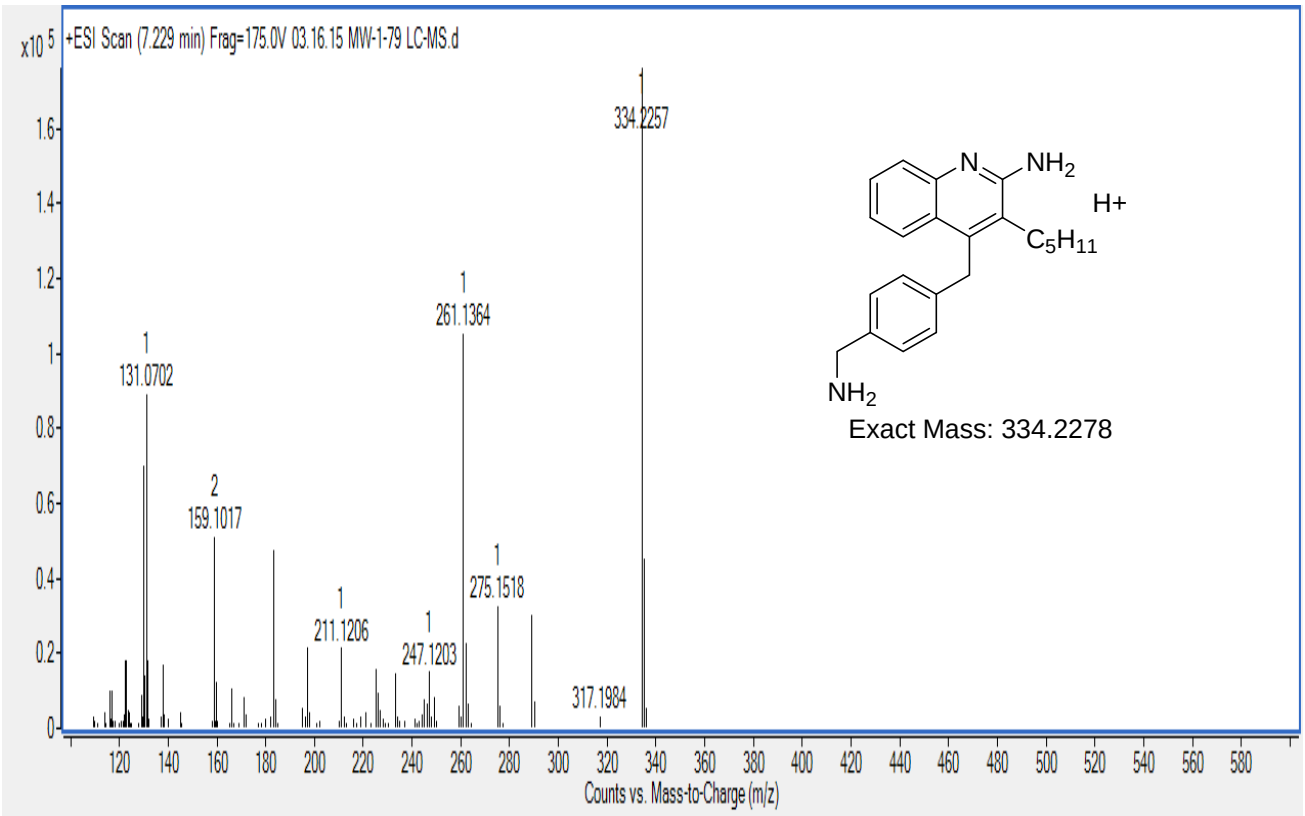
Compound **9b:** ^{1}H and ^{13}C NMR Spectrum





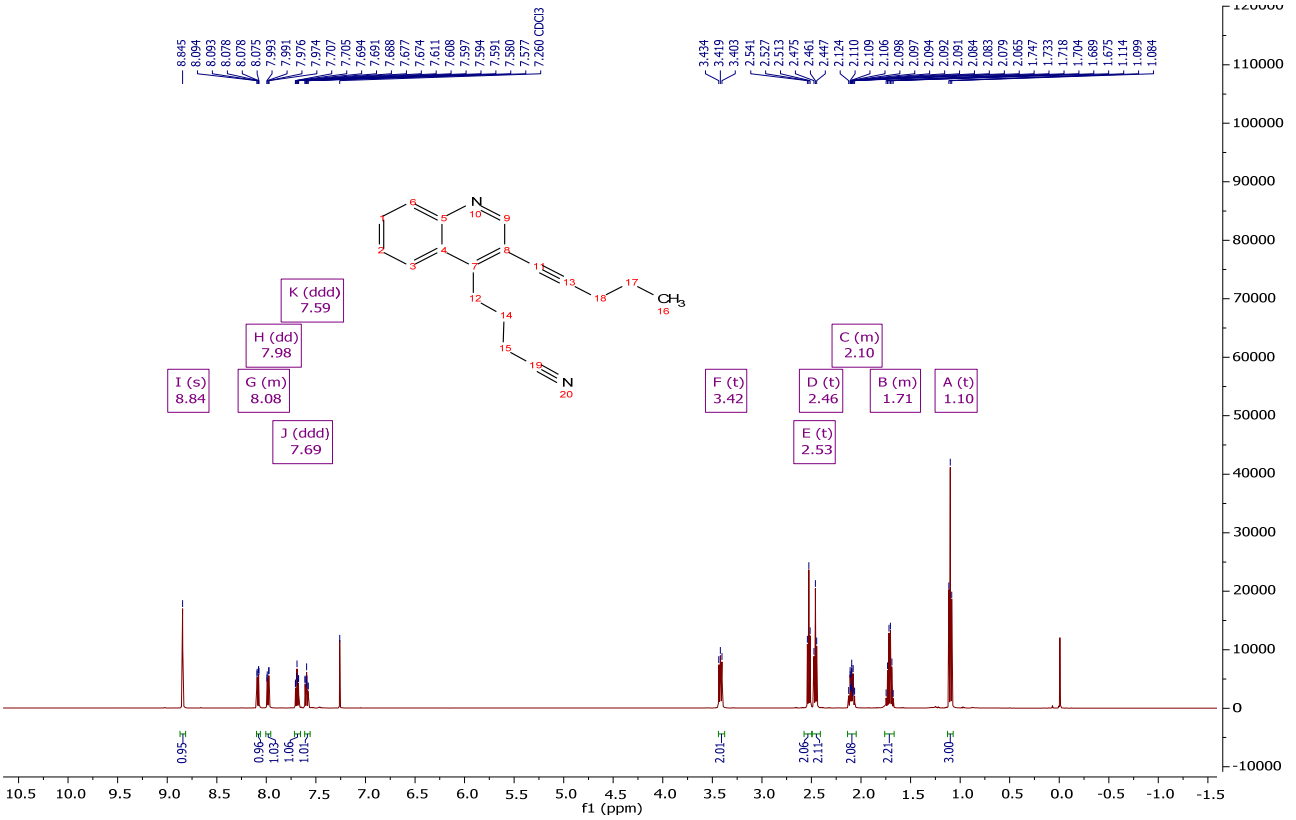
Compound **9b:** LC-MS

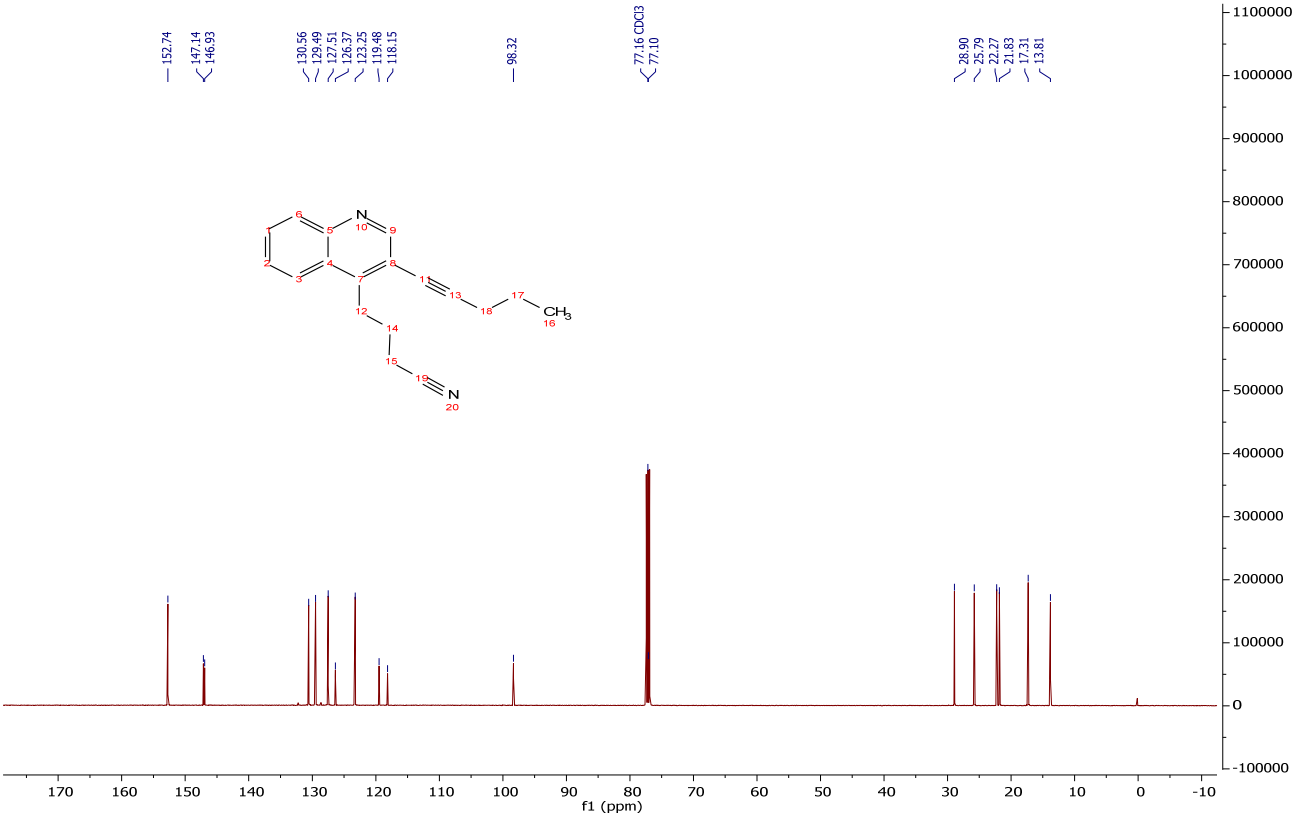




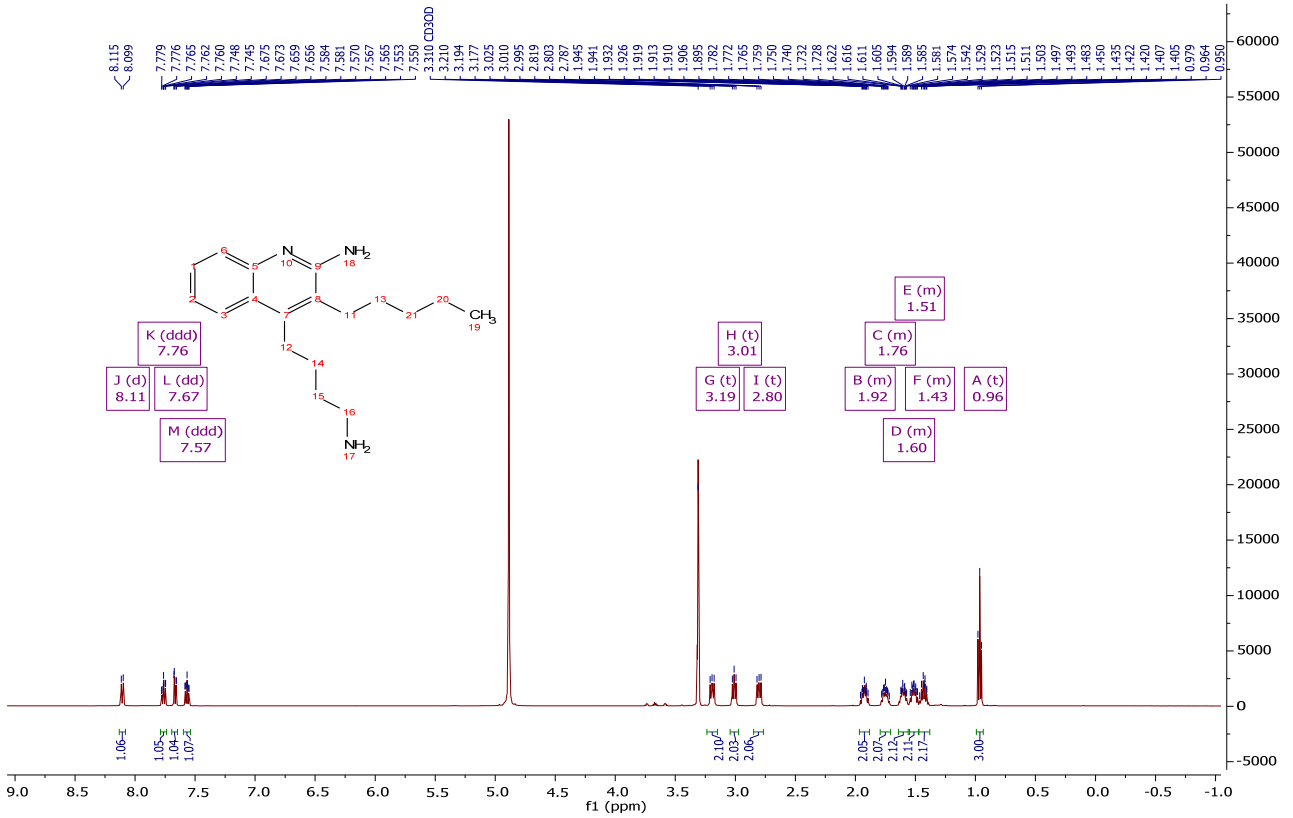
Exact Mass: 334.2278

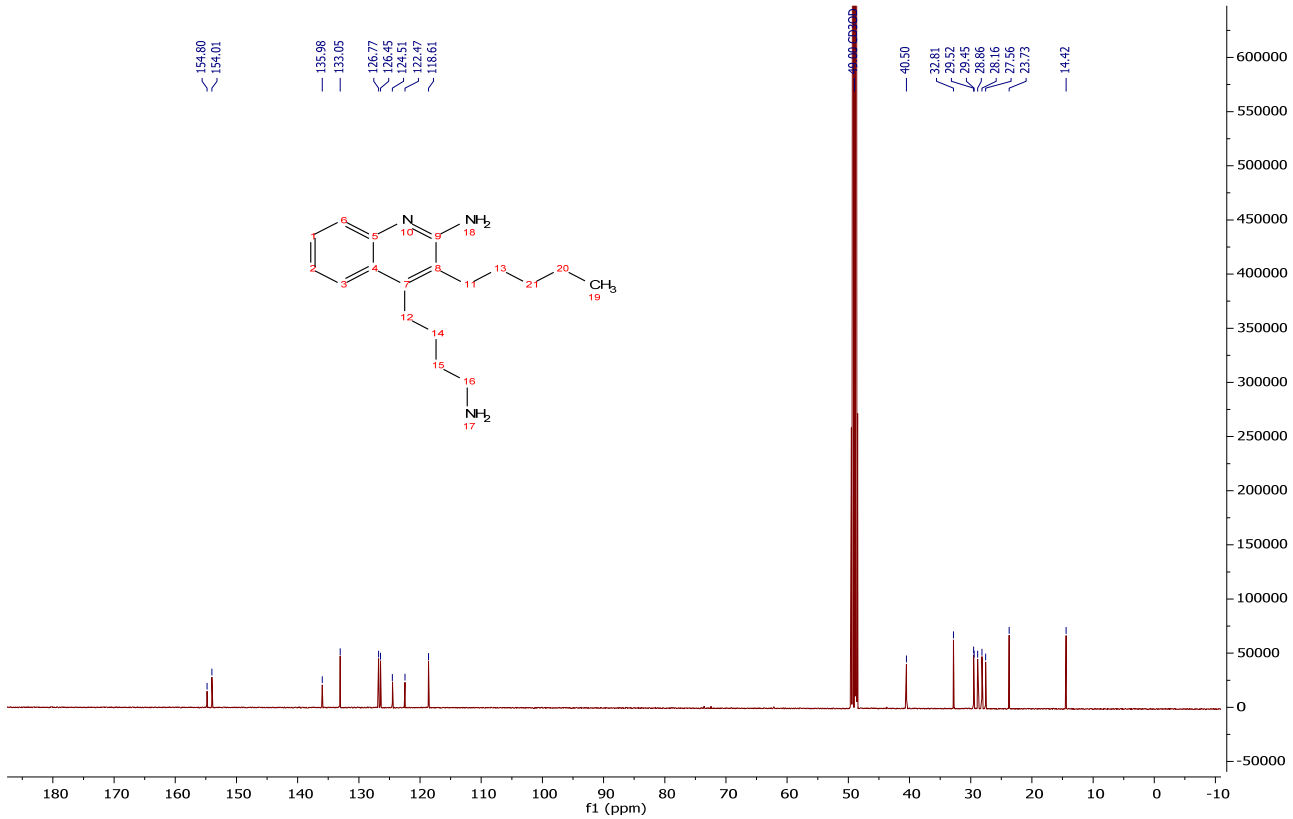
Compound **10a:** ^{1}H and ^{13}C NMR Spectrum



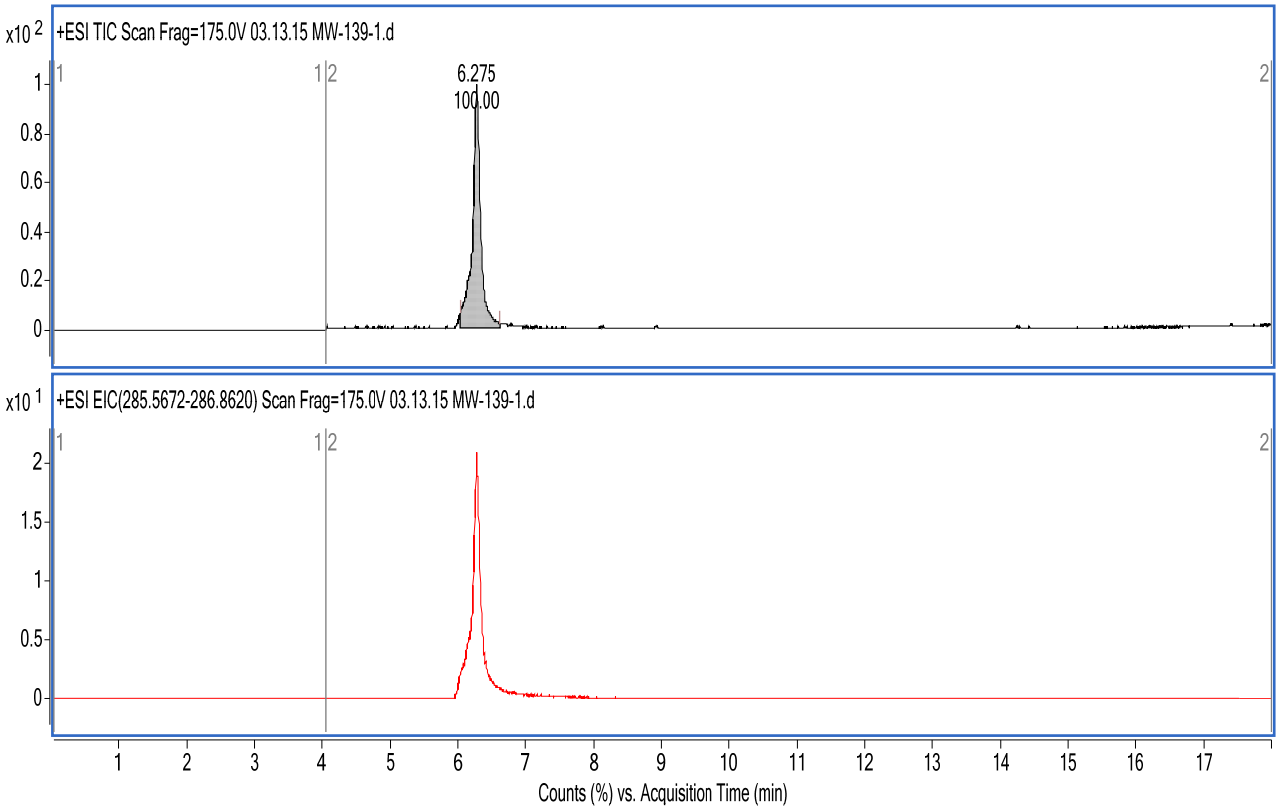


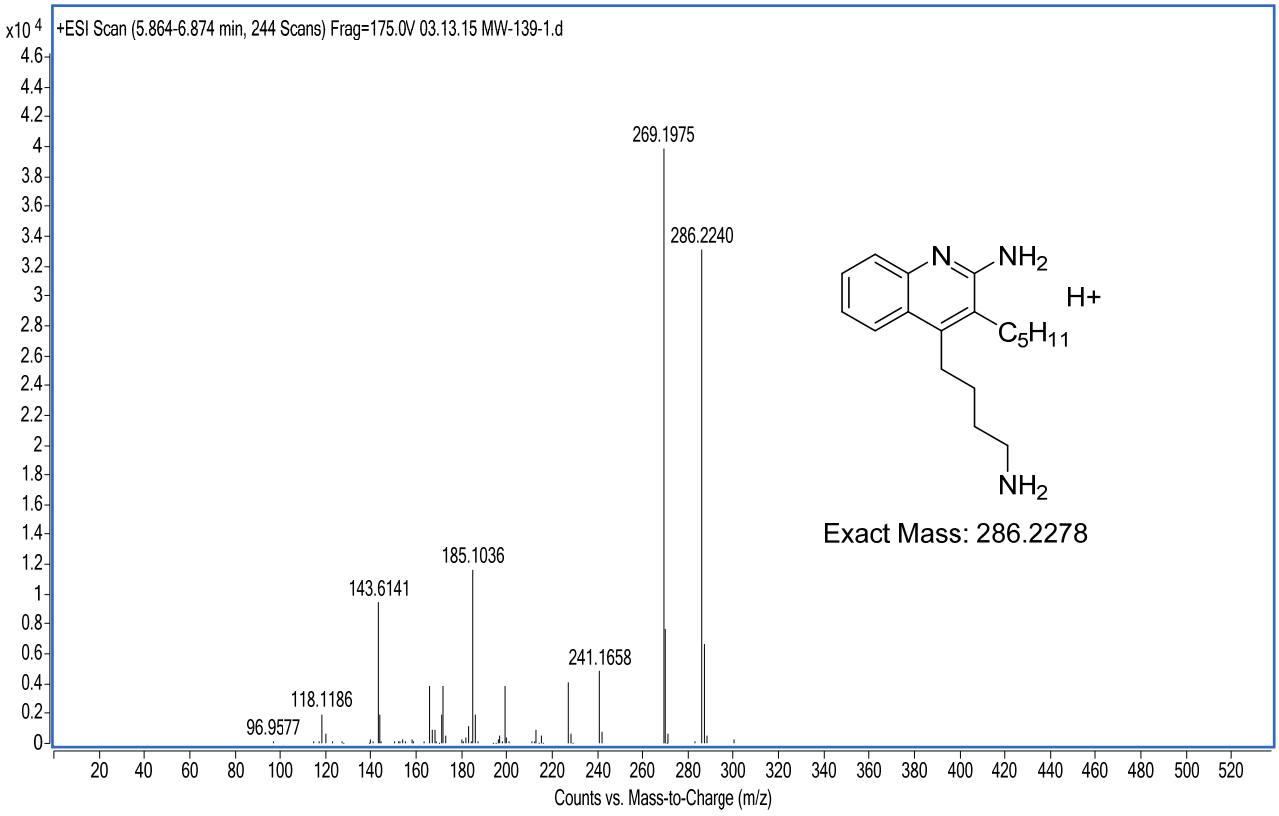
Compound **14a:** ^{1}H and ^{13}C NMR Spectrum





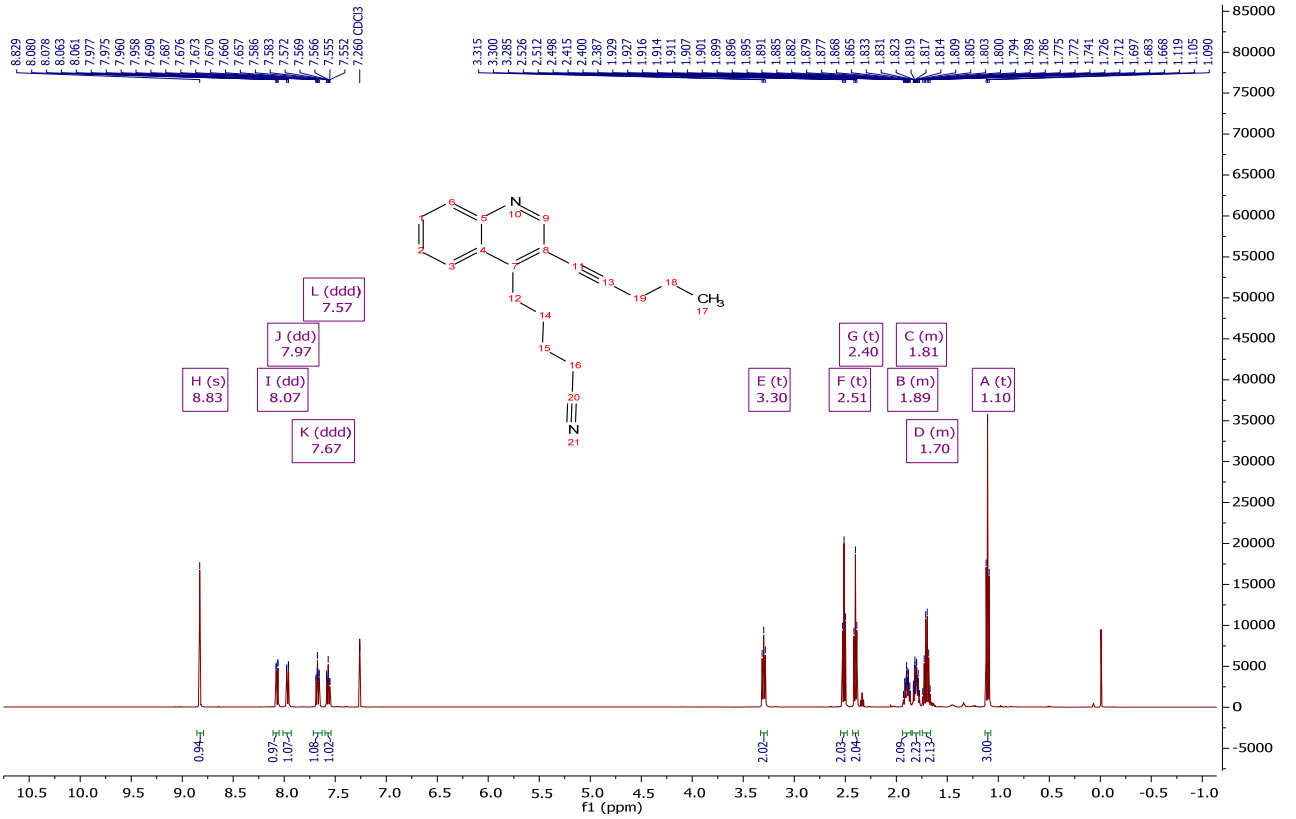
Compound **14a:** LC-MS

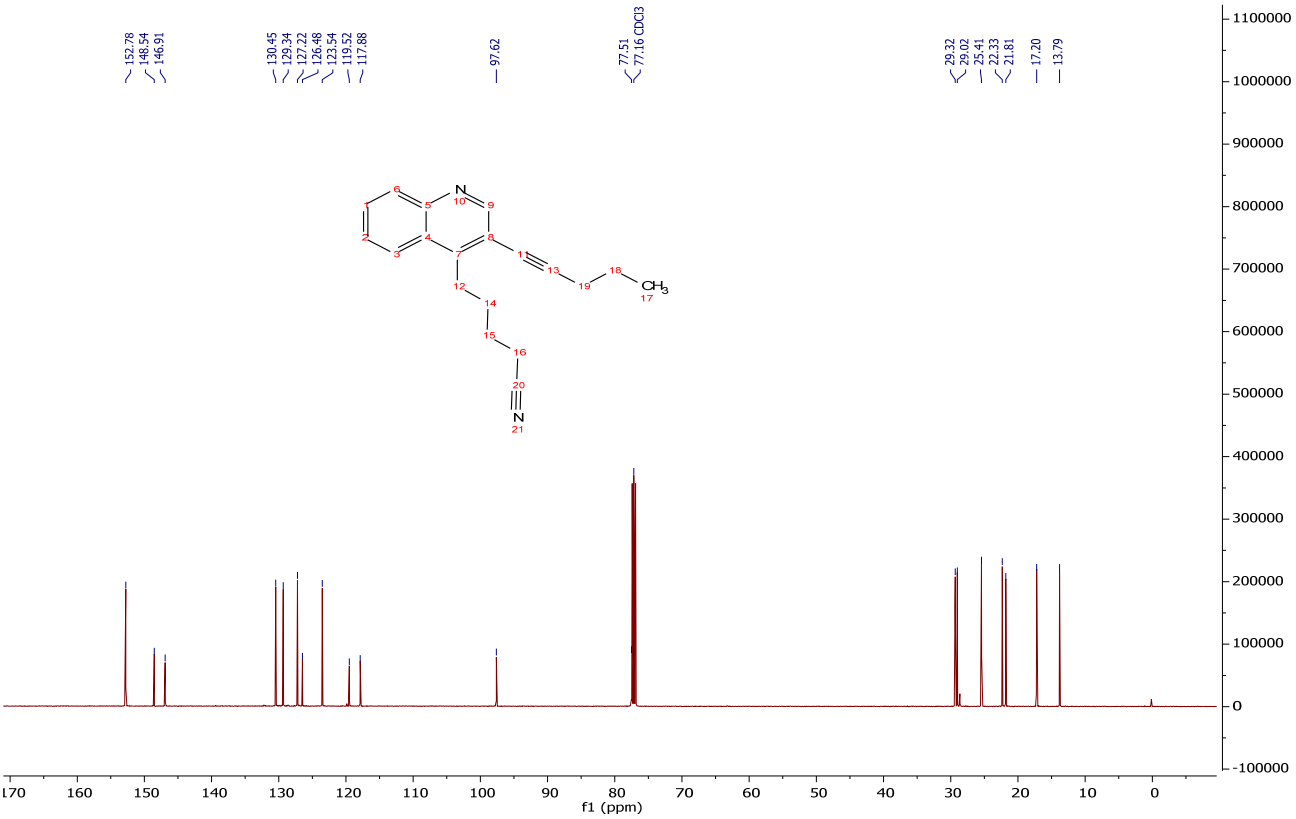




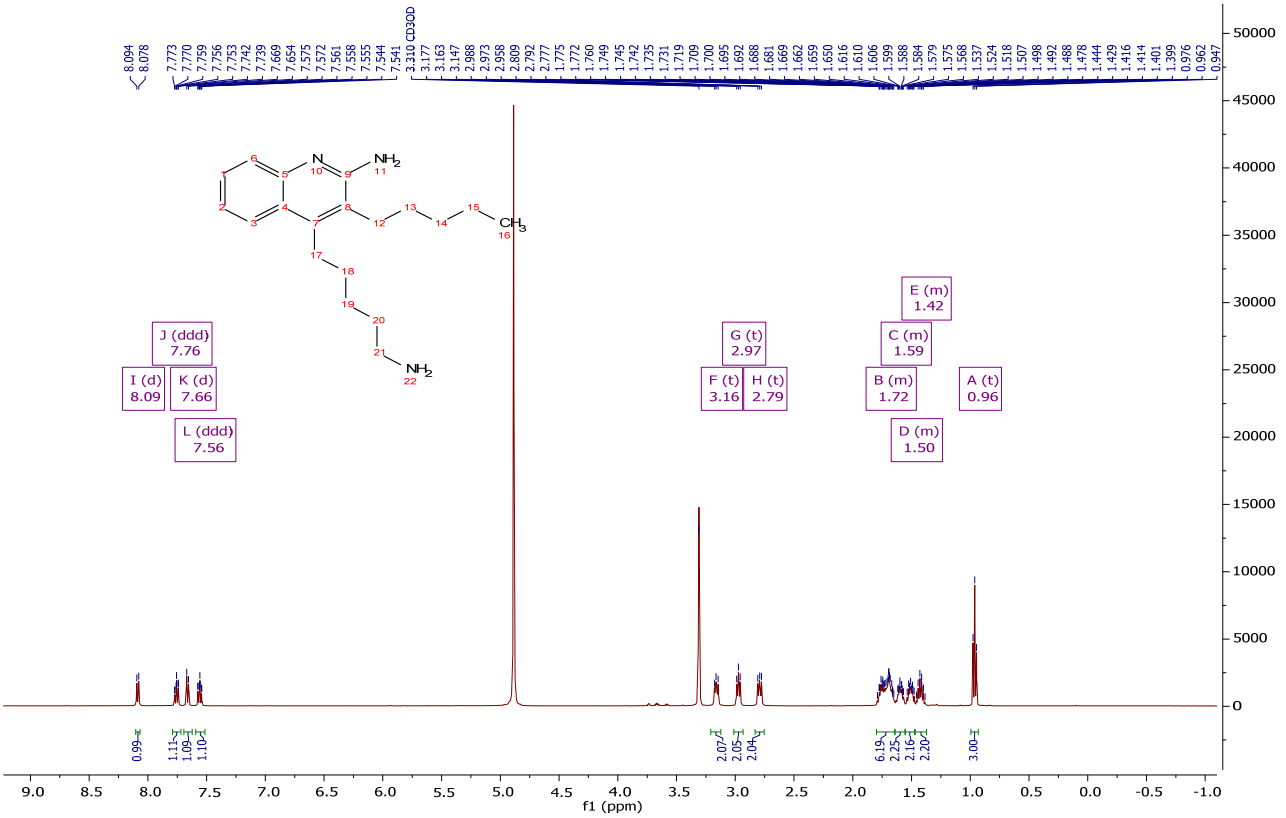
Exact Mass: 286.2278

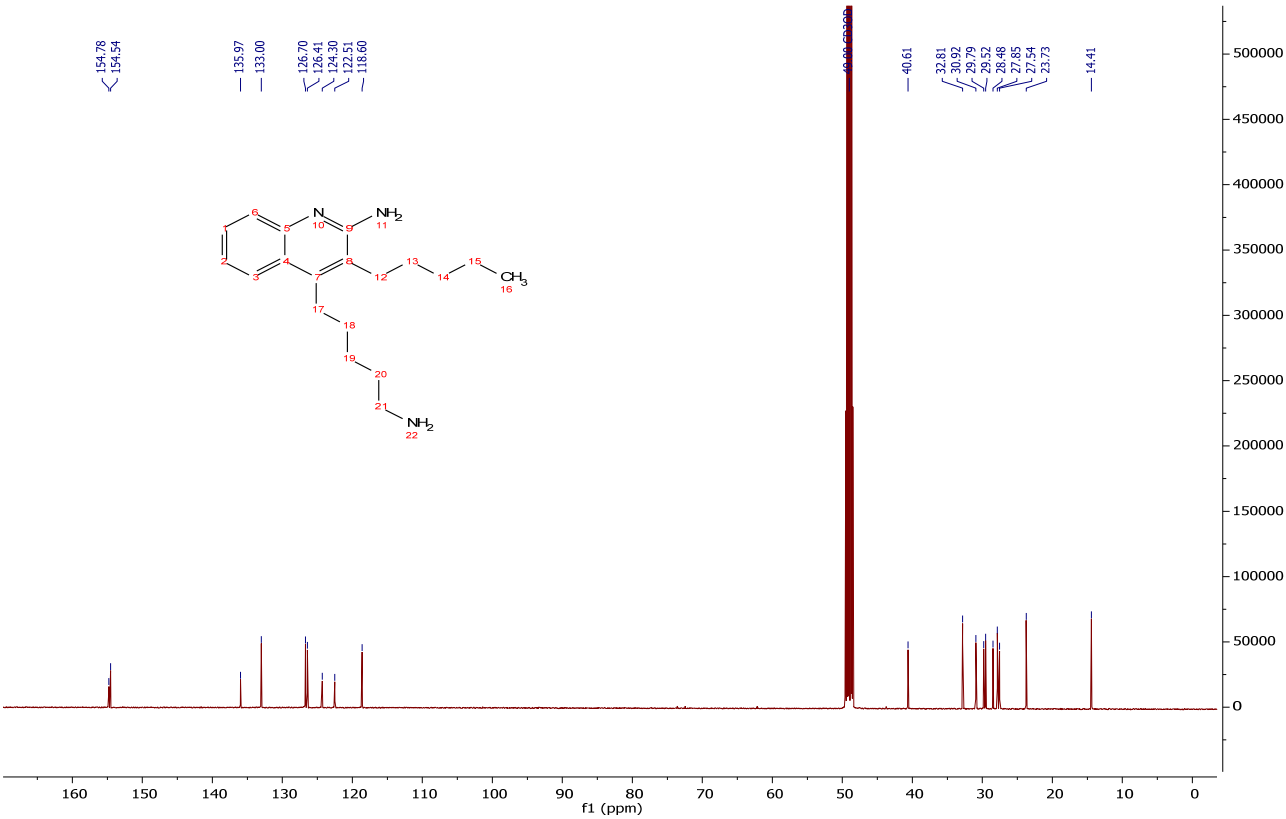
Compound **10b:** ^{1}H and ^{13}C NMR Spectrum



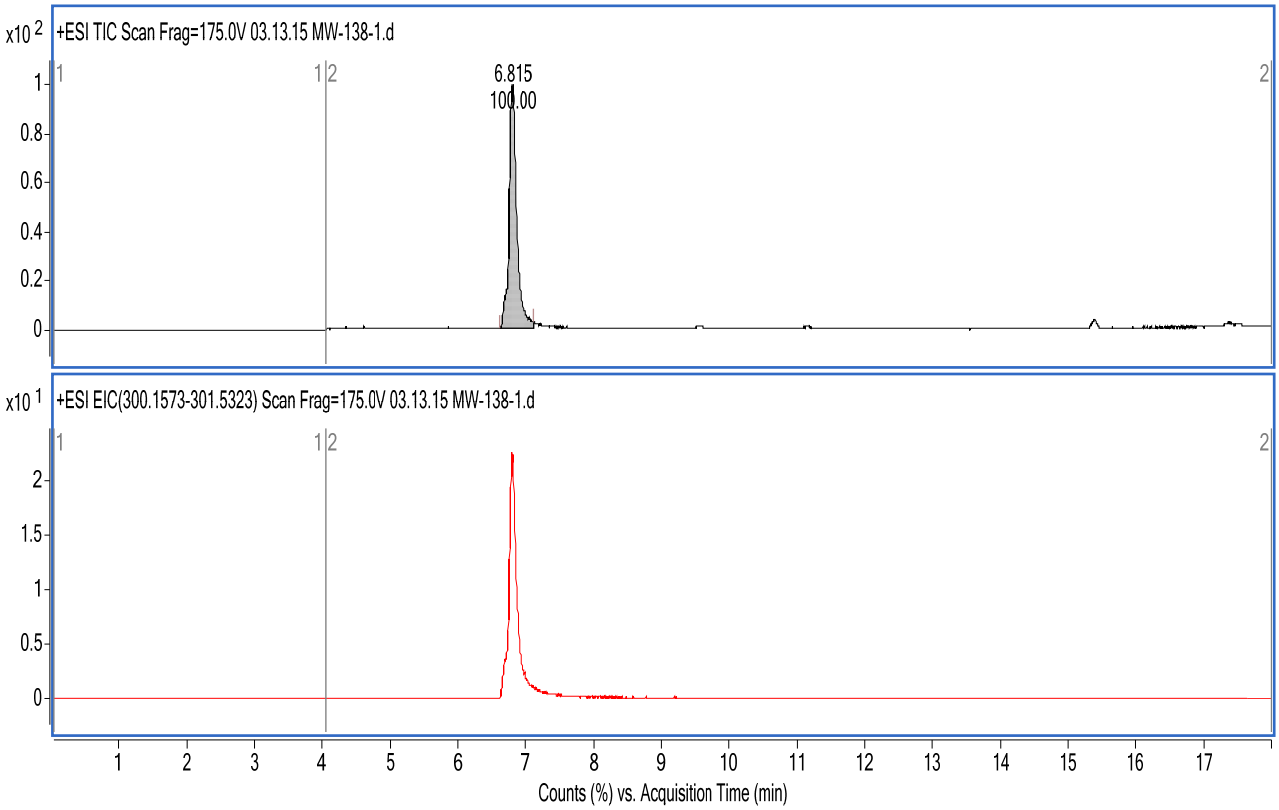


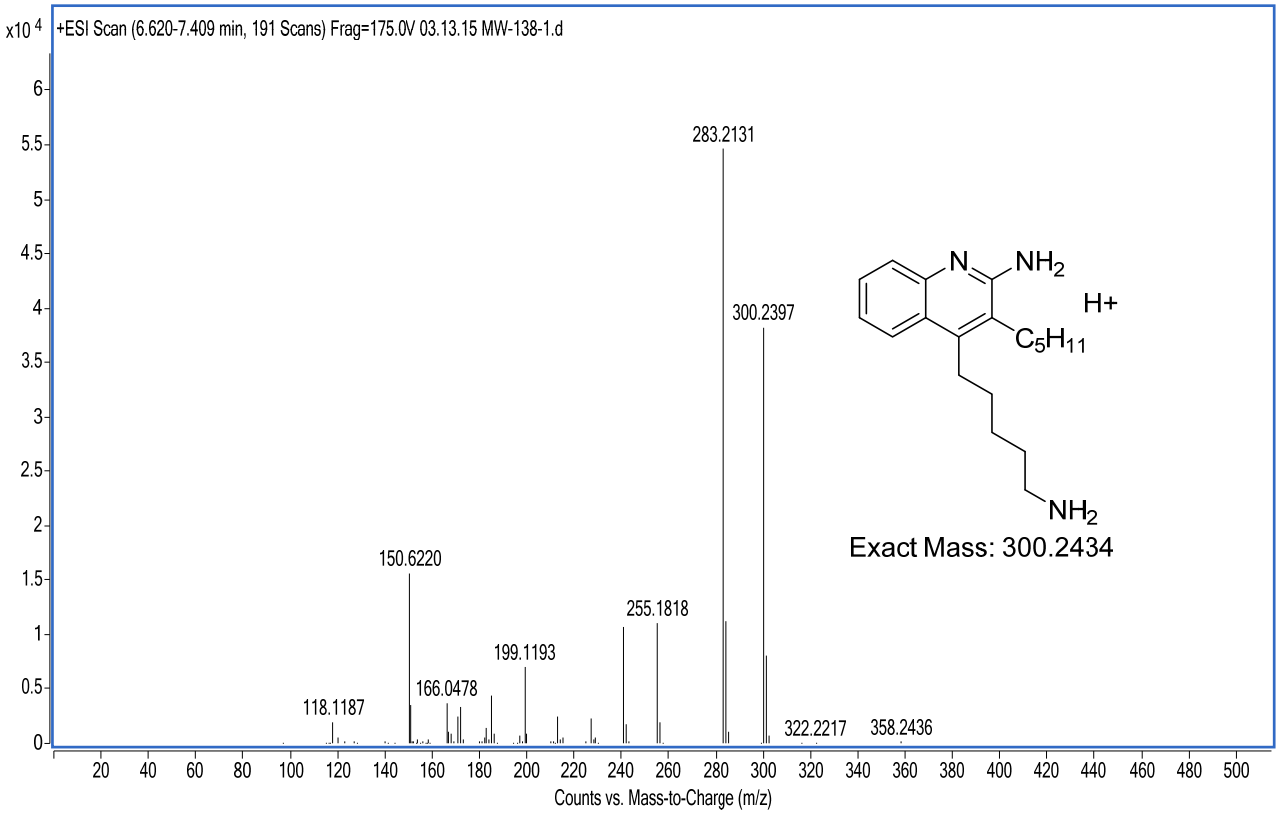
Compound **14b:** ^{1}H and ^{13}C NMR Spectrum



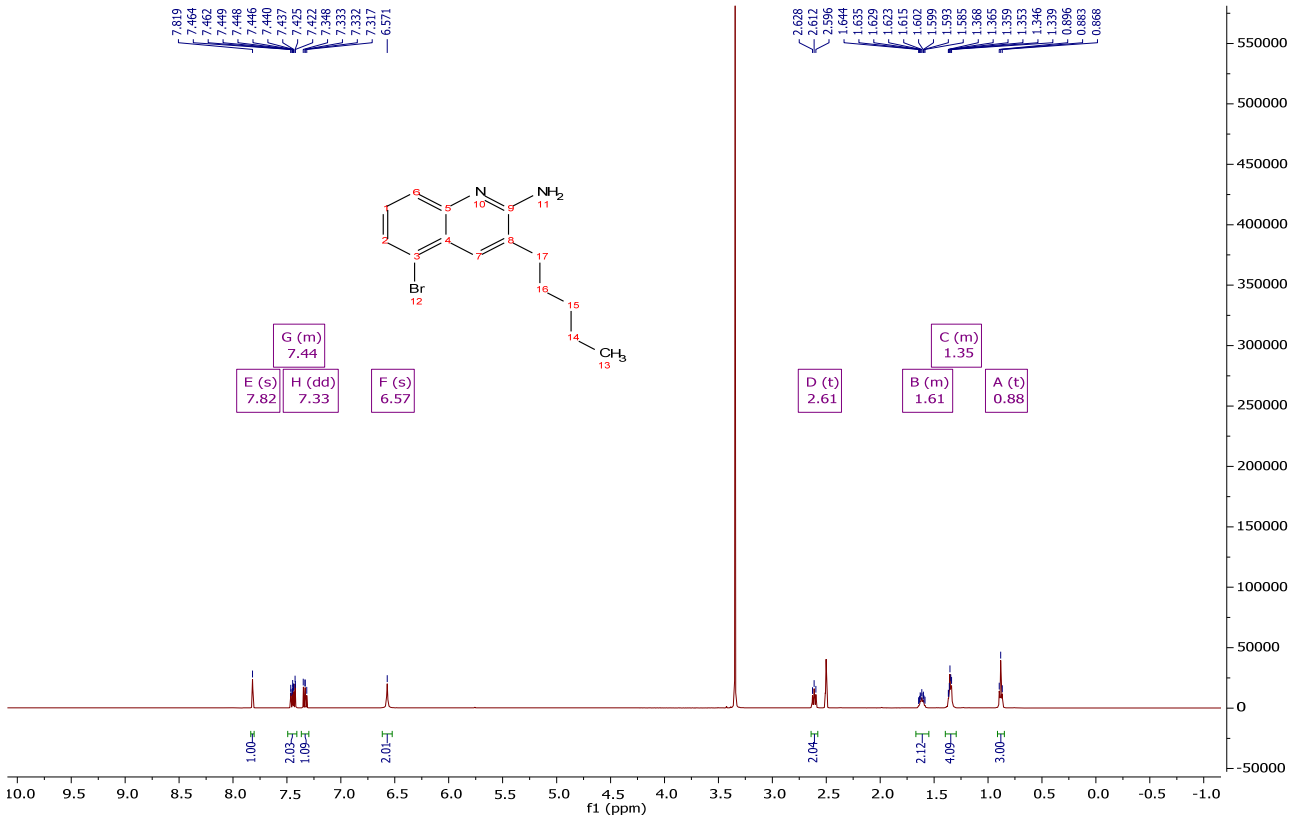


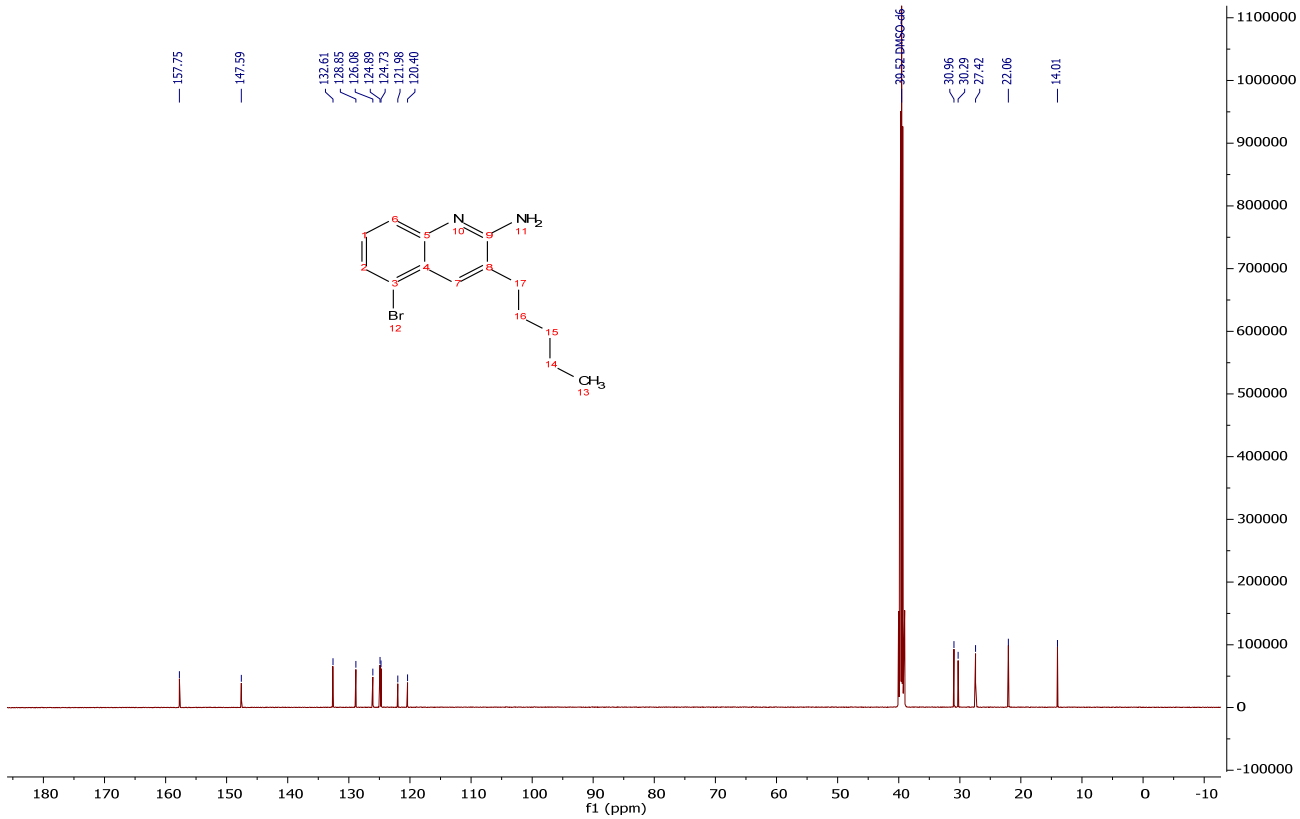
Compound **14b:** LC-MS



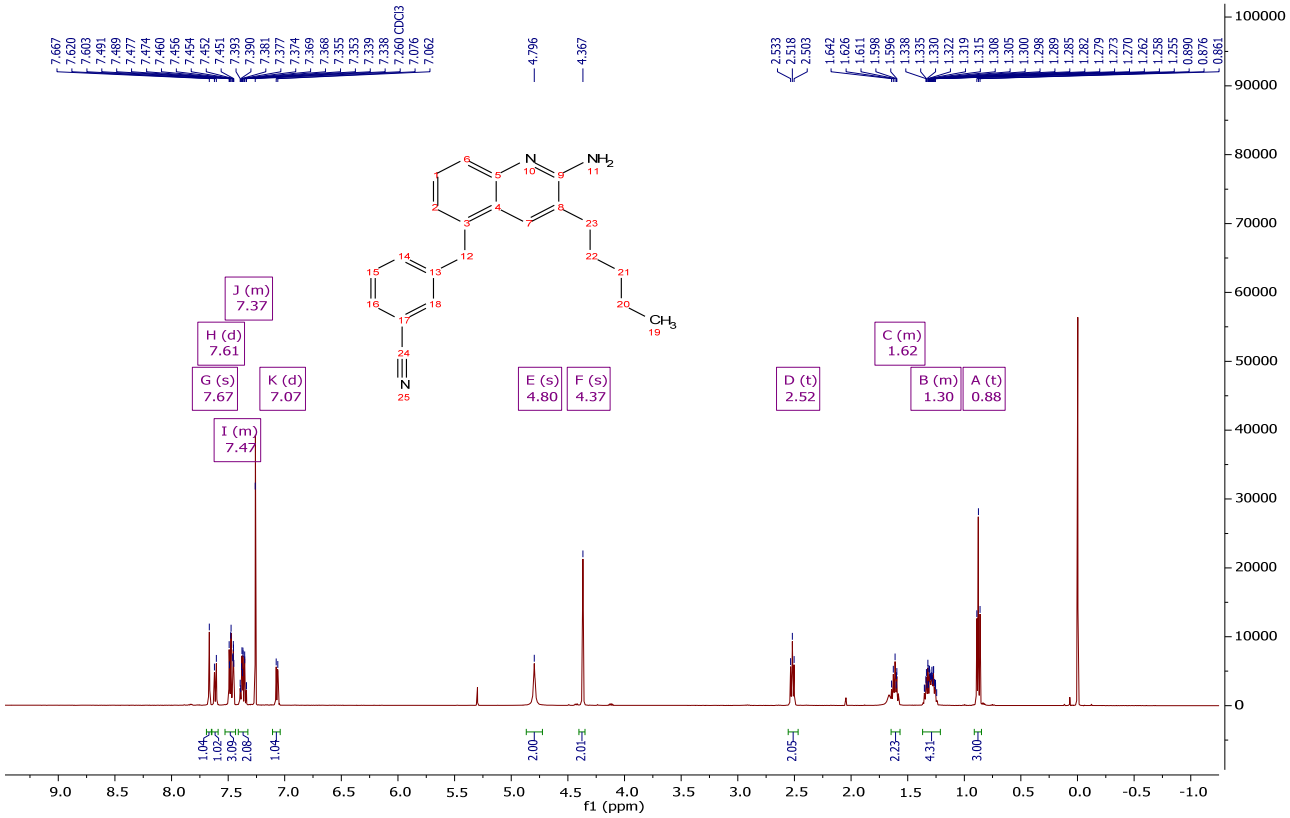


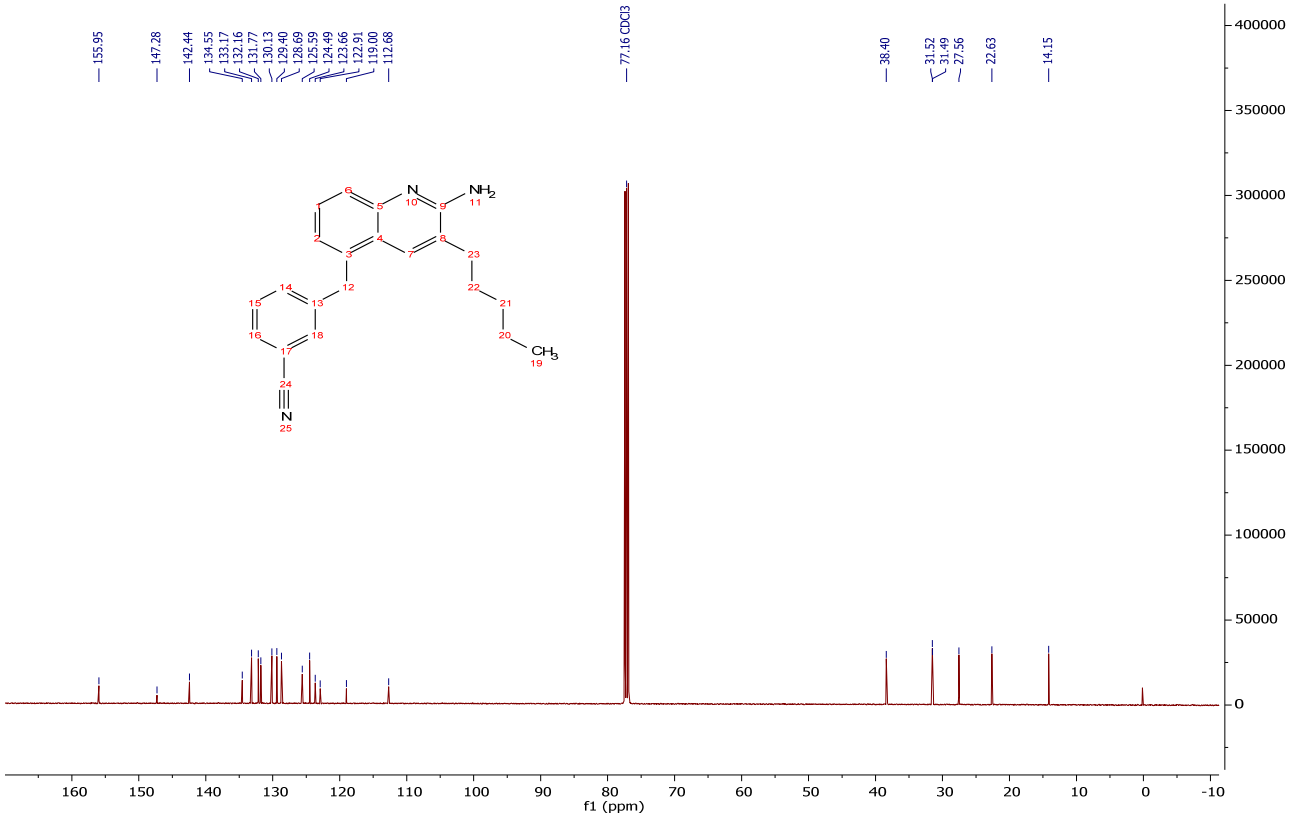
Compound **16:** ^{1}H and ^{13}C NMR Spectrum



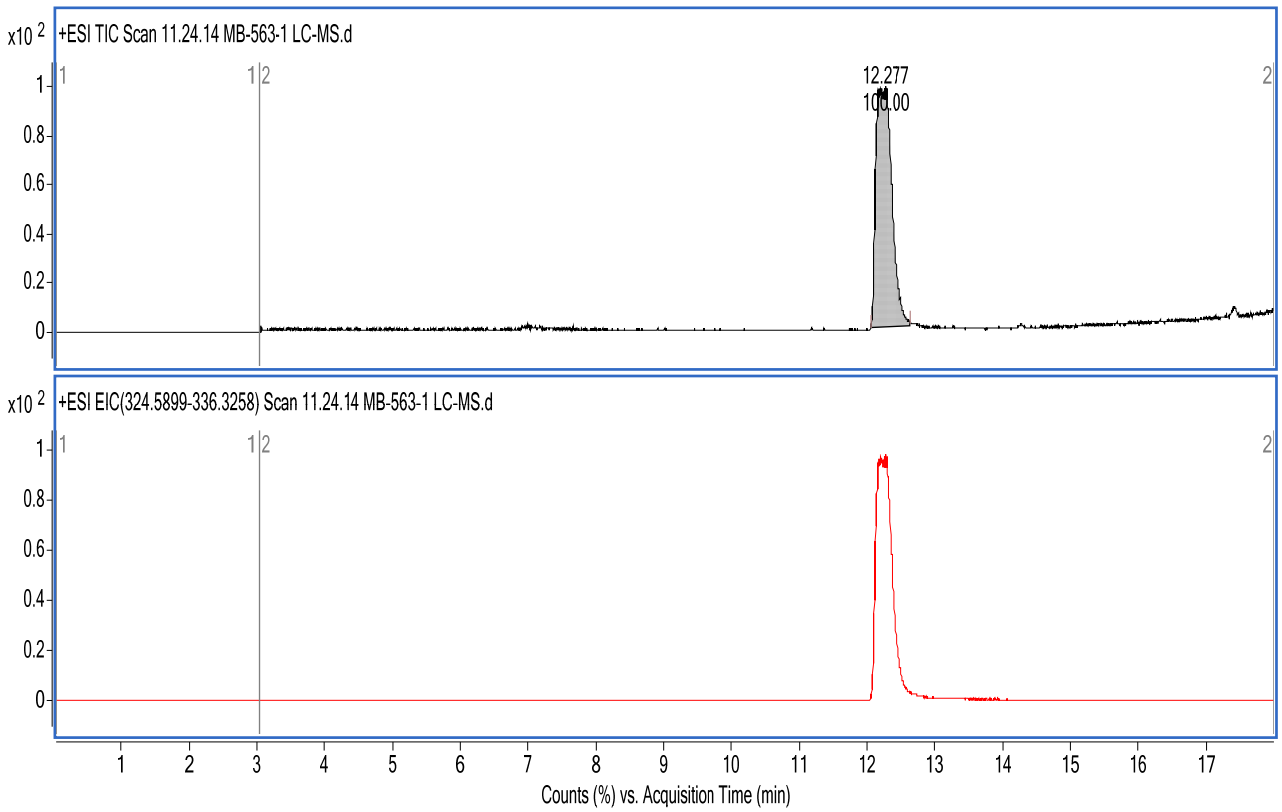


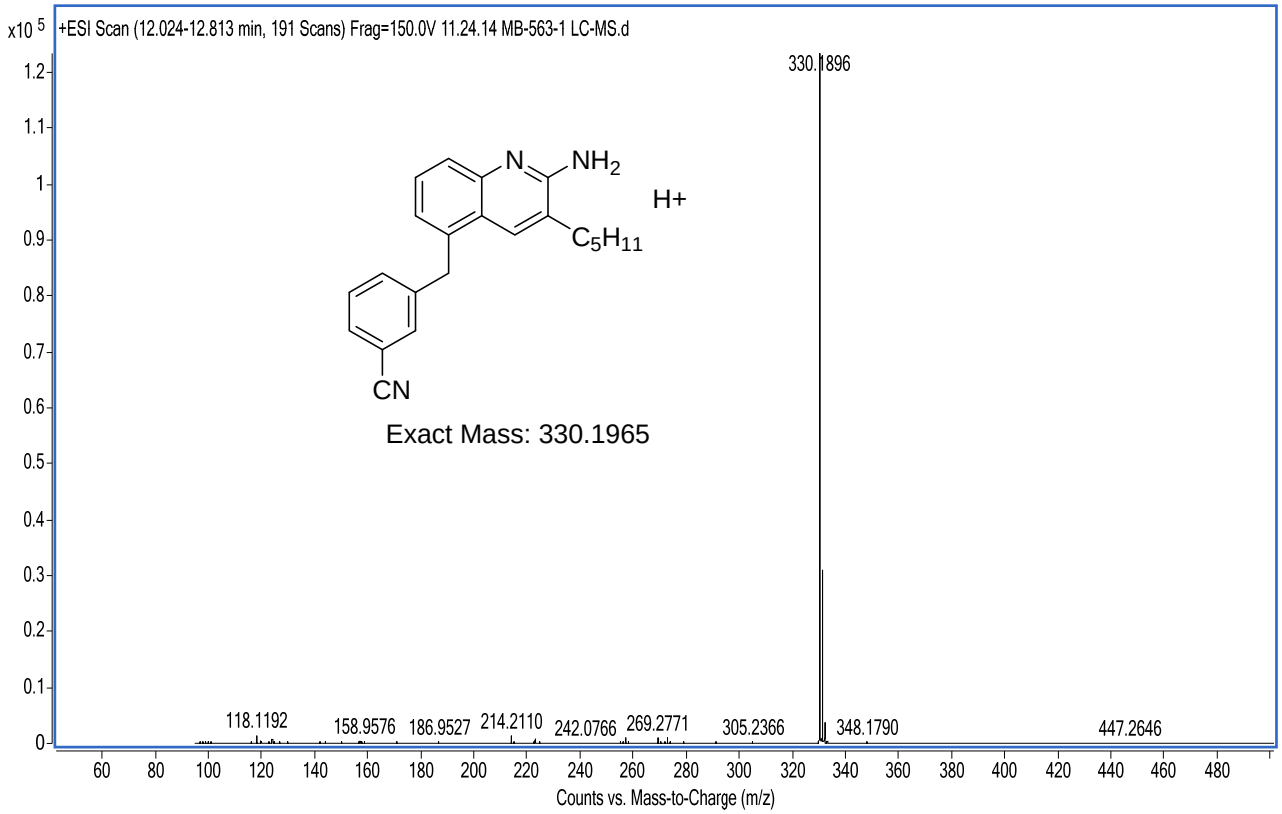
Compound **17a:** ^{1}H and ^{13}C NMR Spectrum



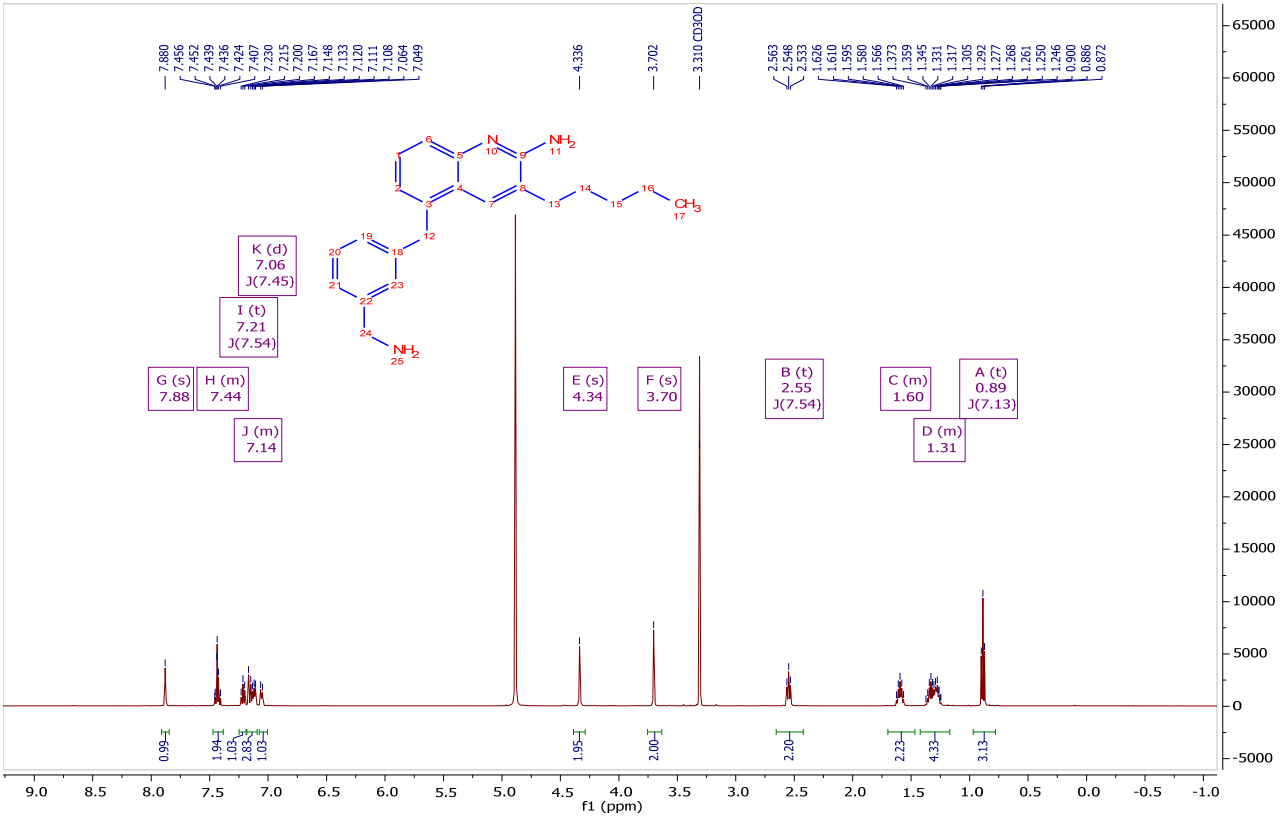


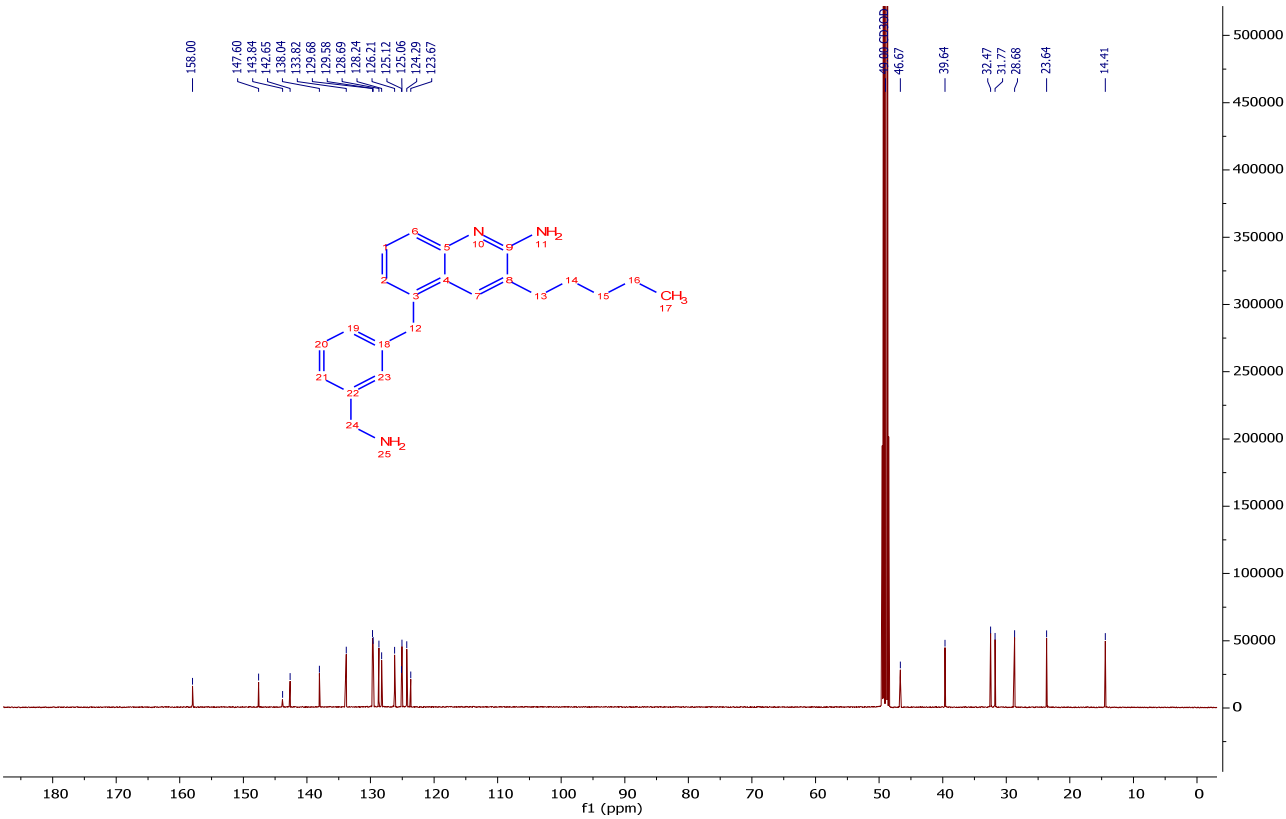
Compound **17a:** LC-MS



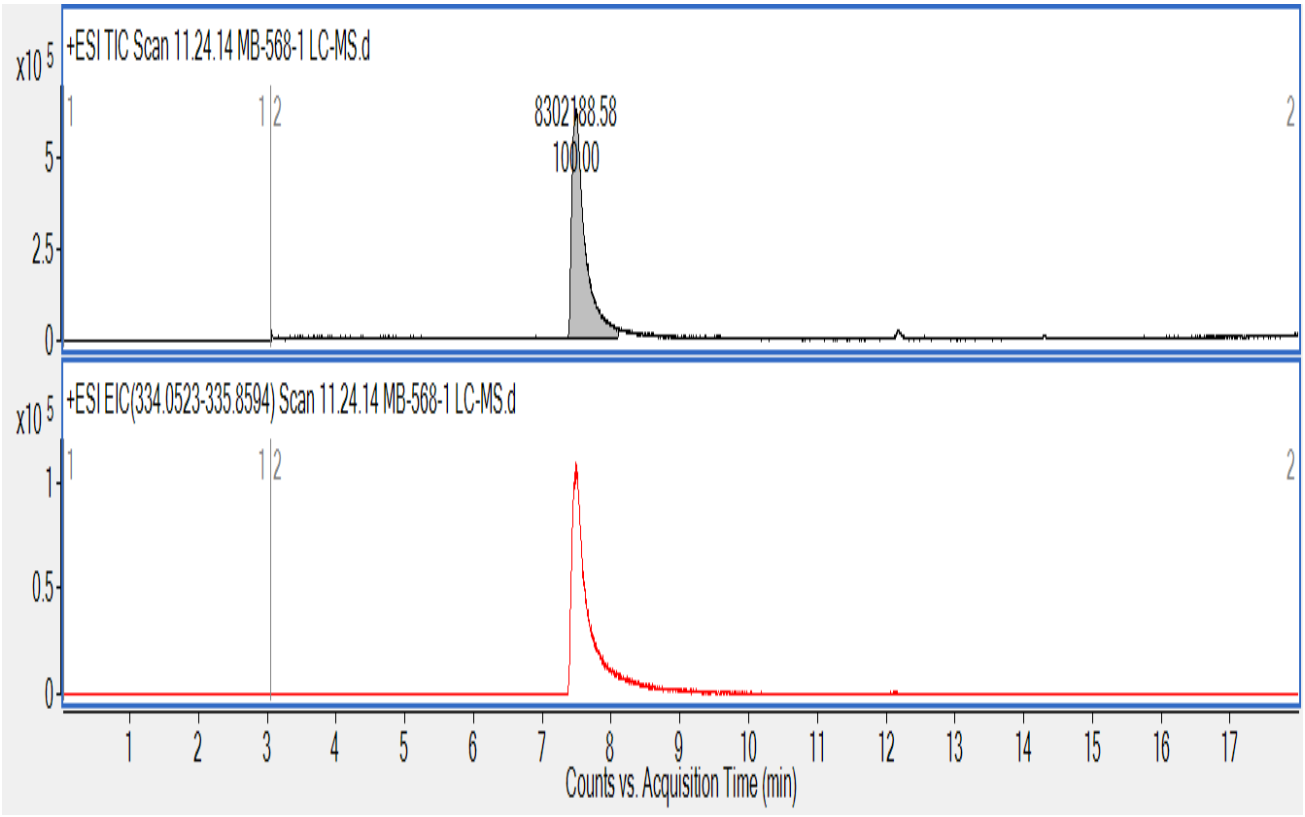


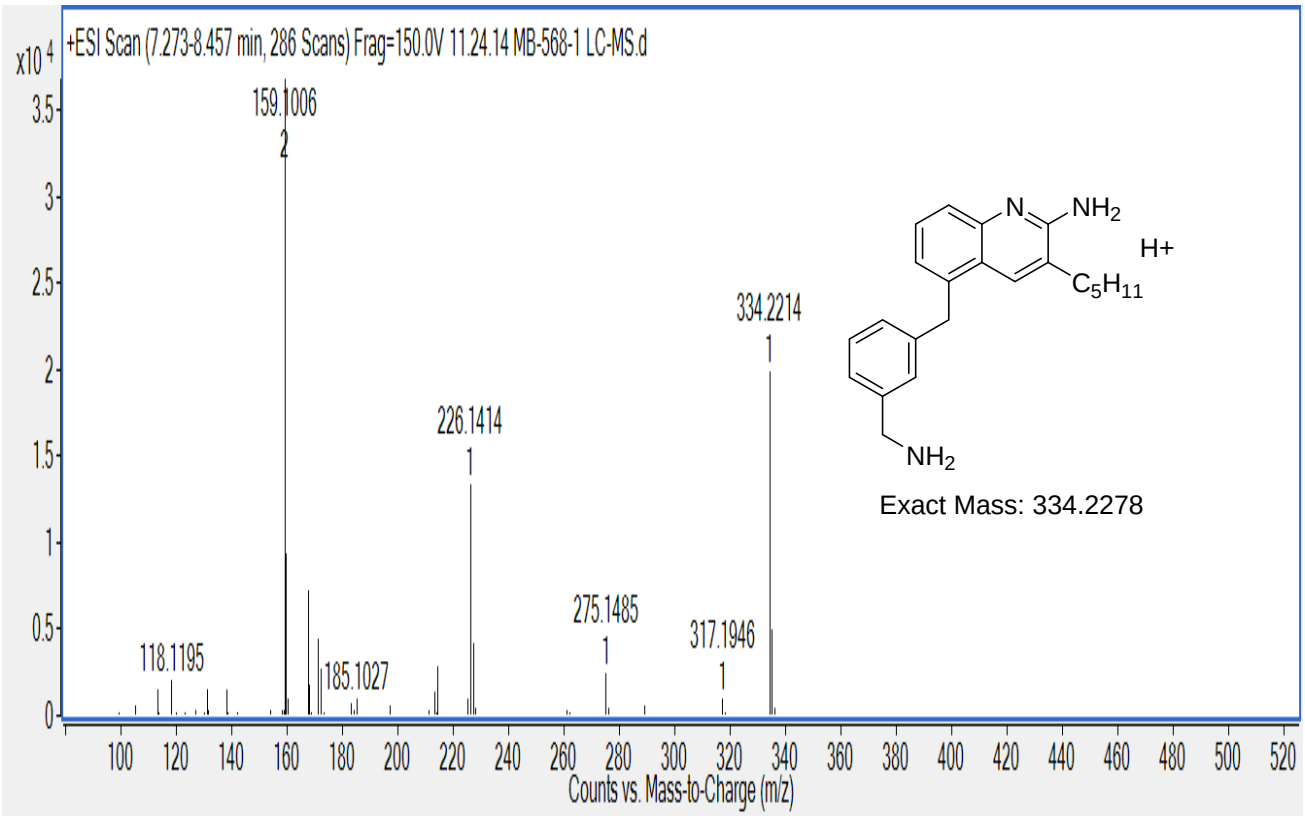
Compound **18a:** ^{1}H and ^{13}C NMR Spectrum



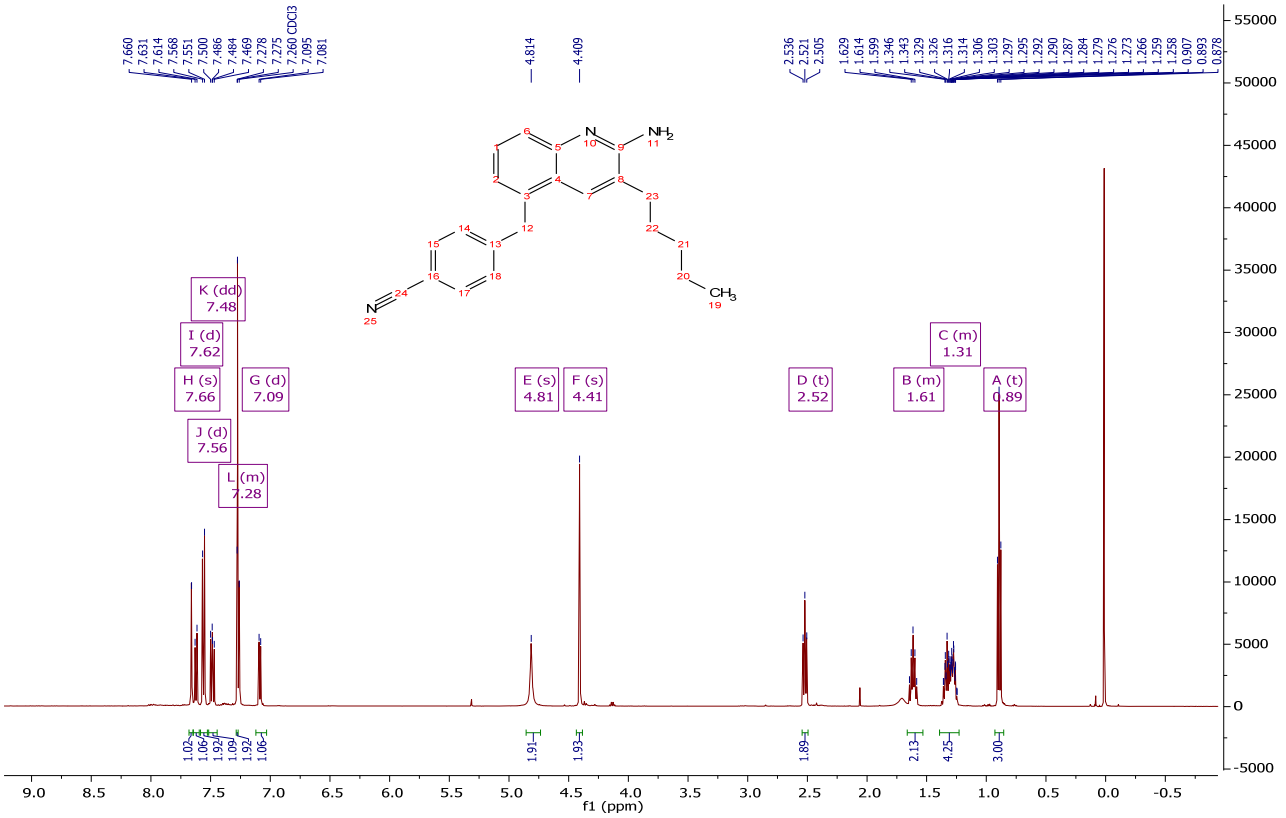


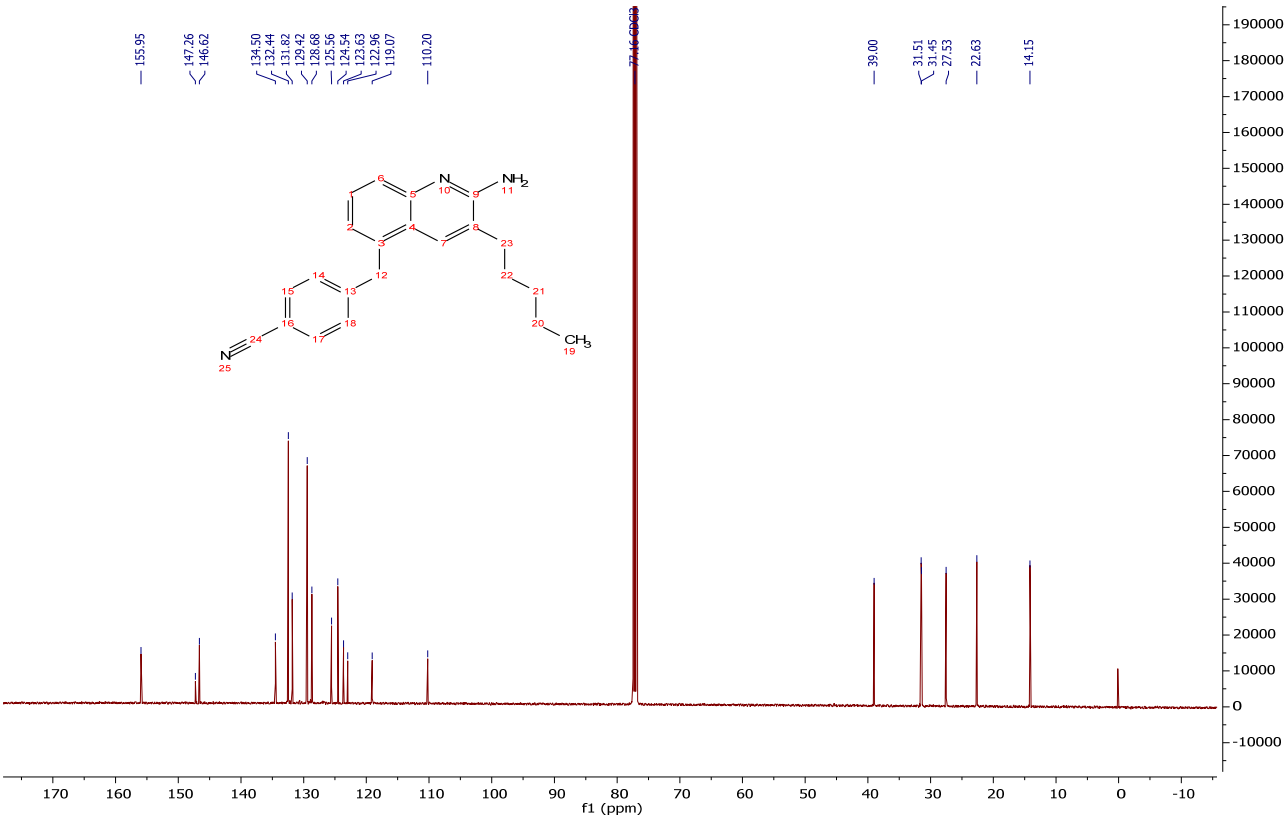
Compound **18a:** LC-MS



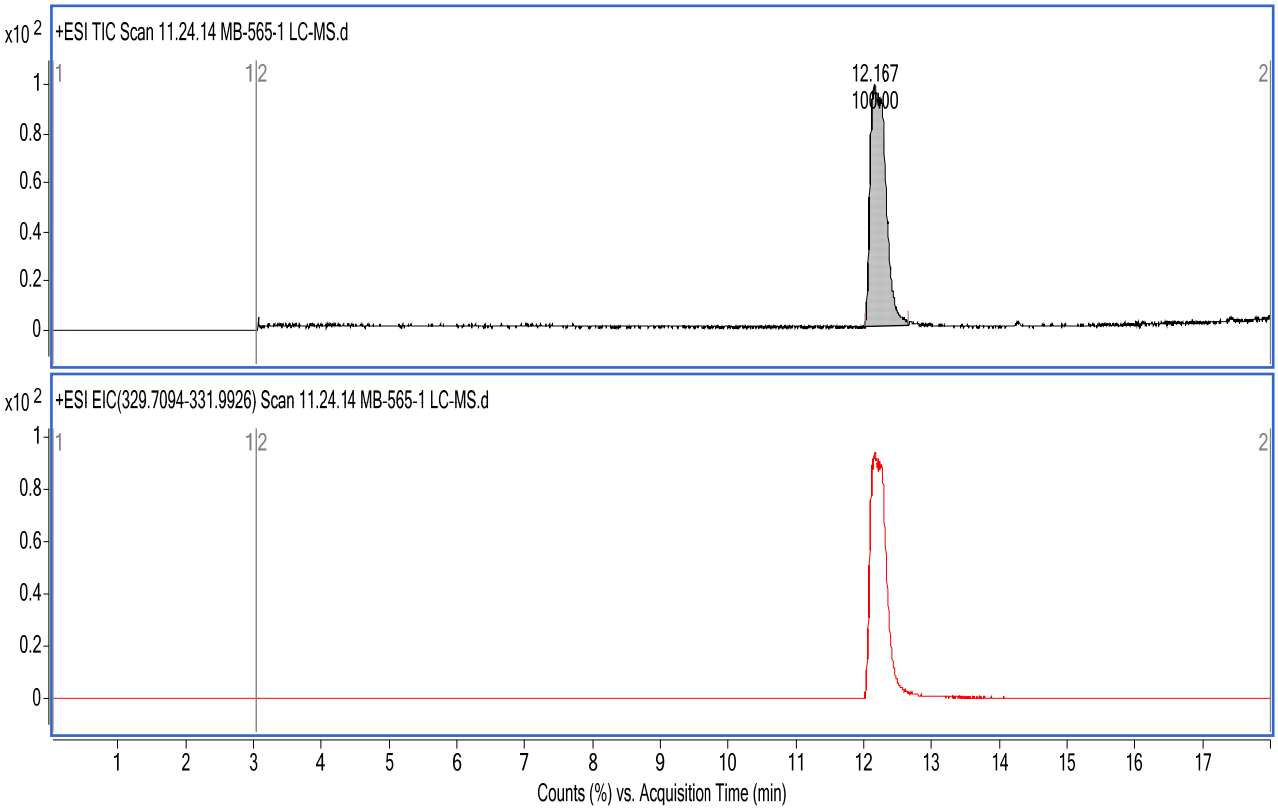


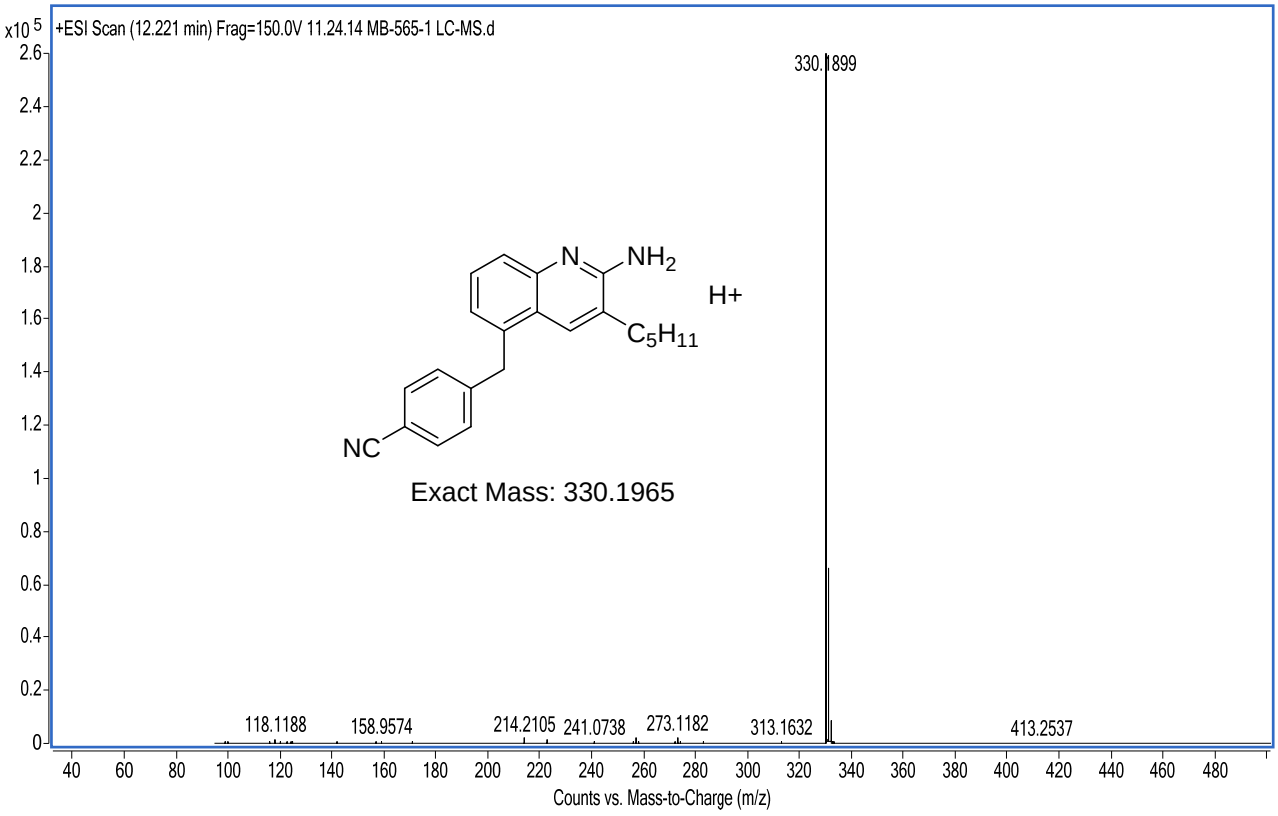
Compound **17b:** ^{1}H and ^{13}C NMR Spectrum





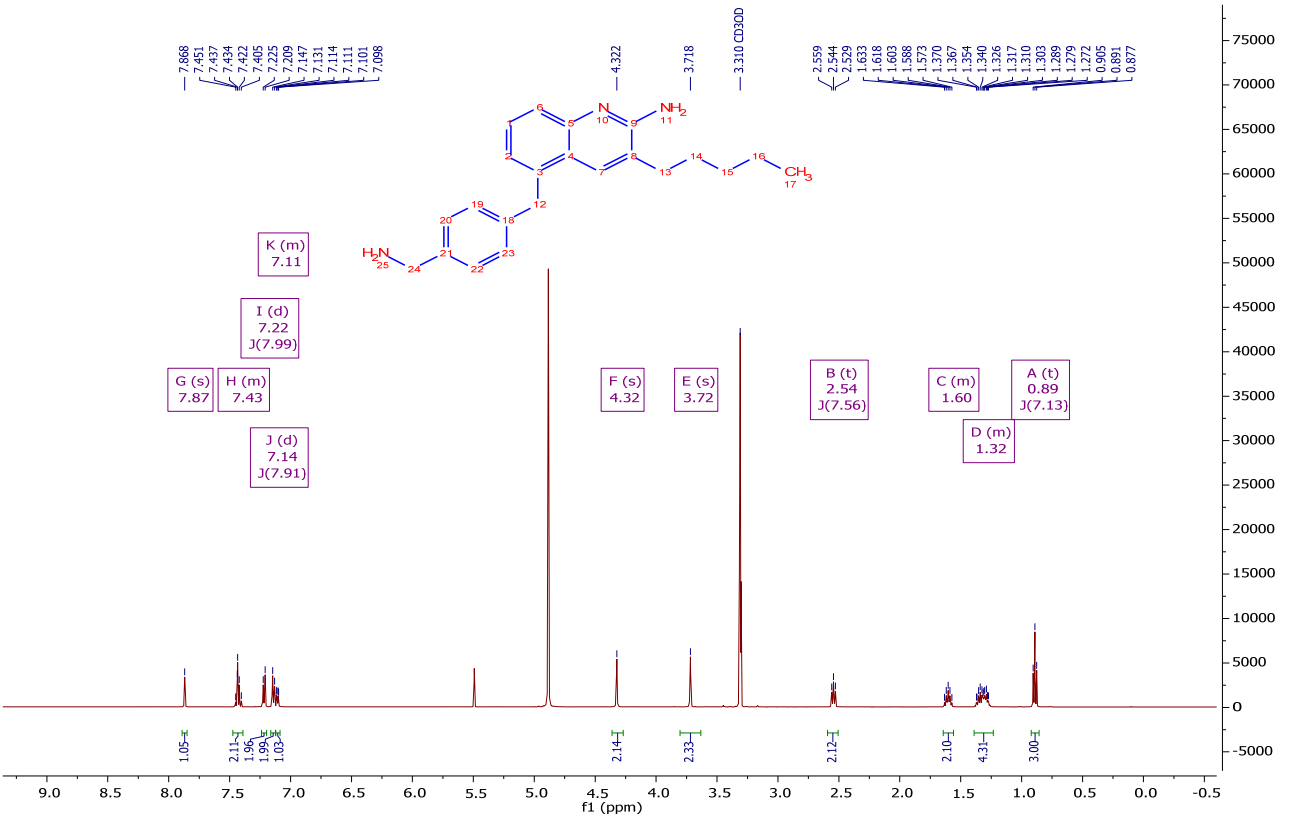
Compound **17b:** LC-MS

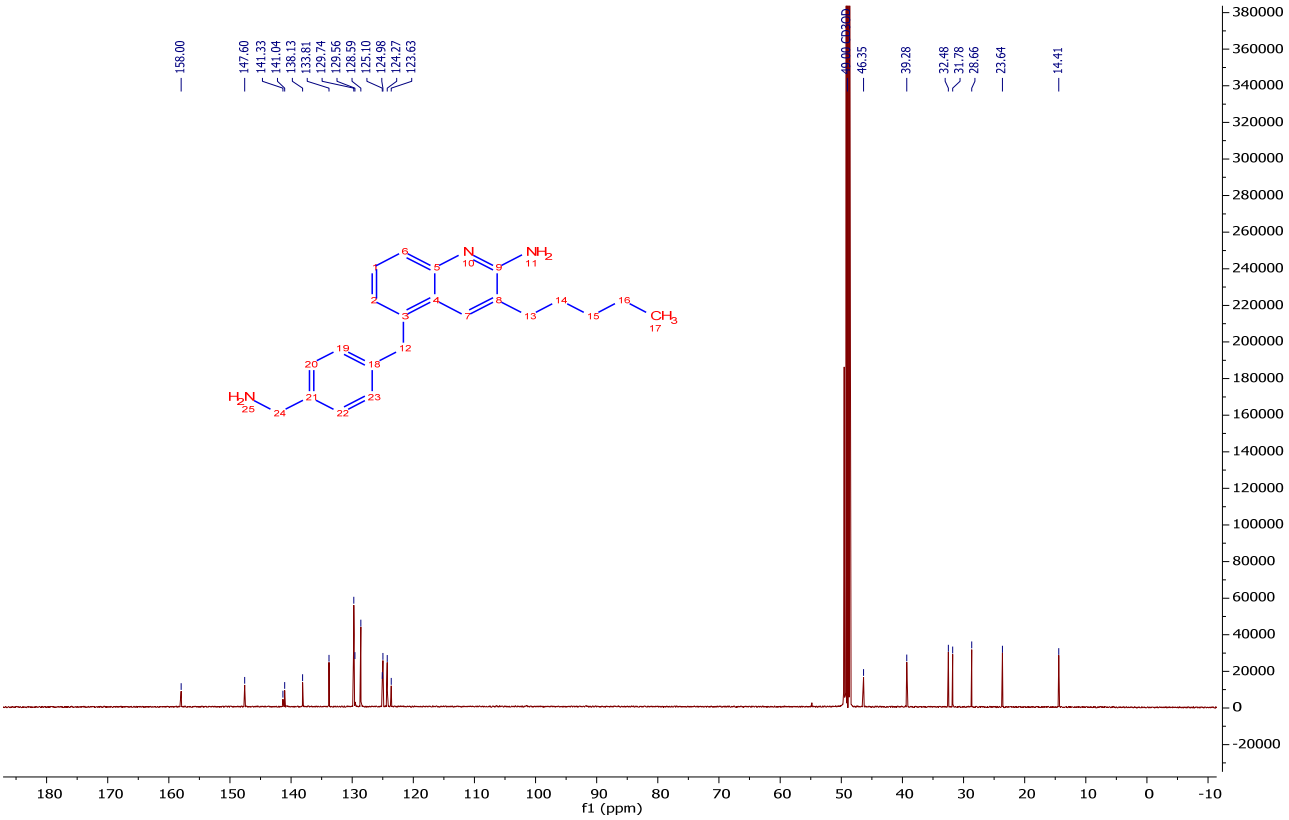




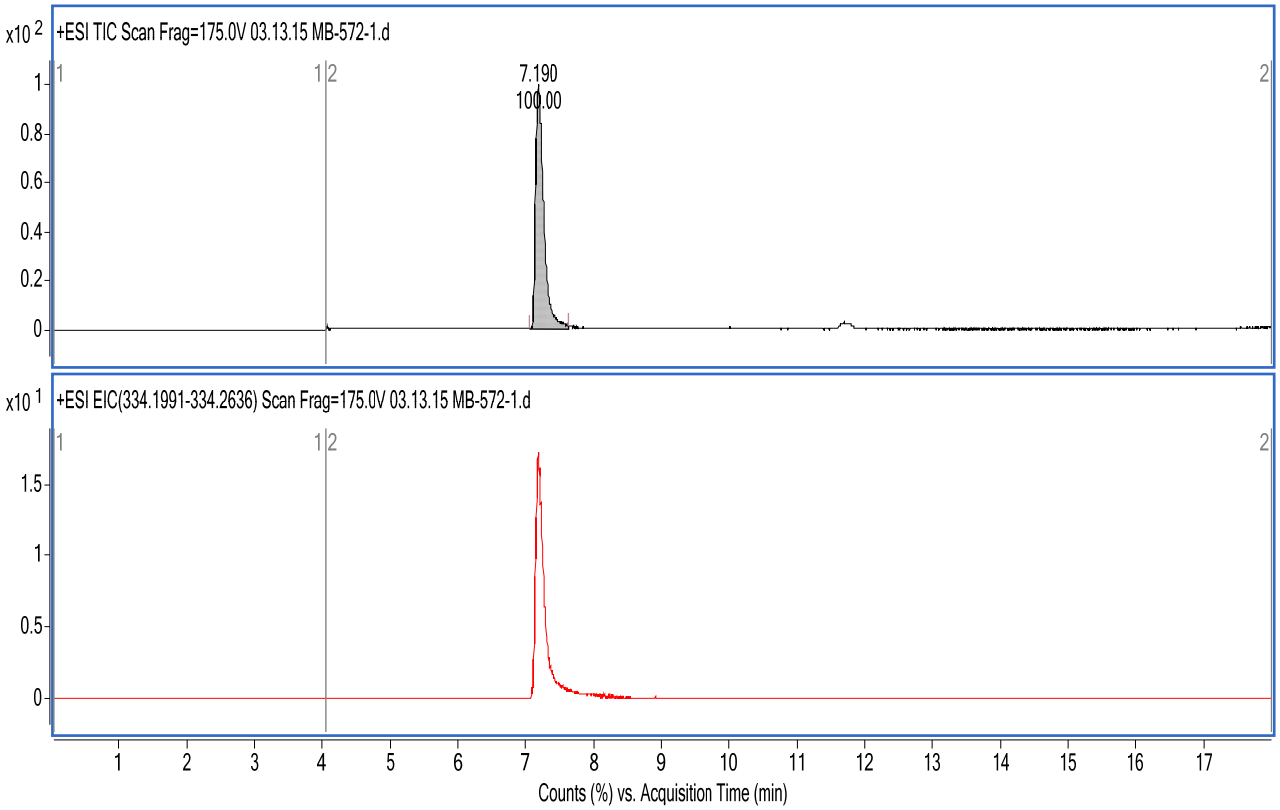
Exact Mass: 330.1965

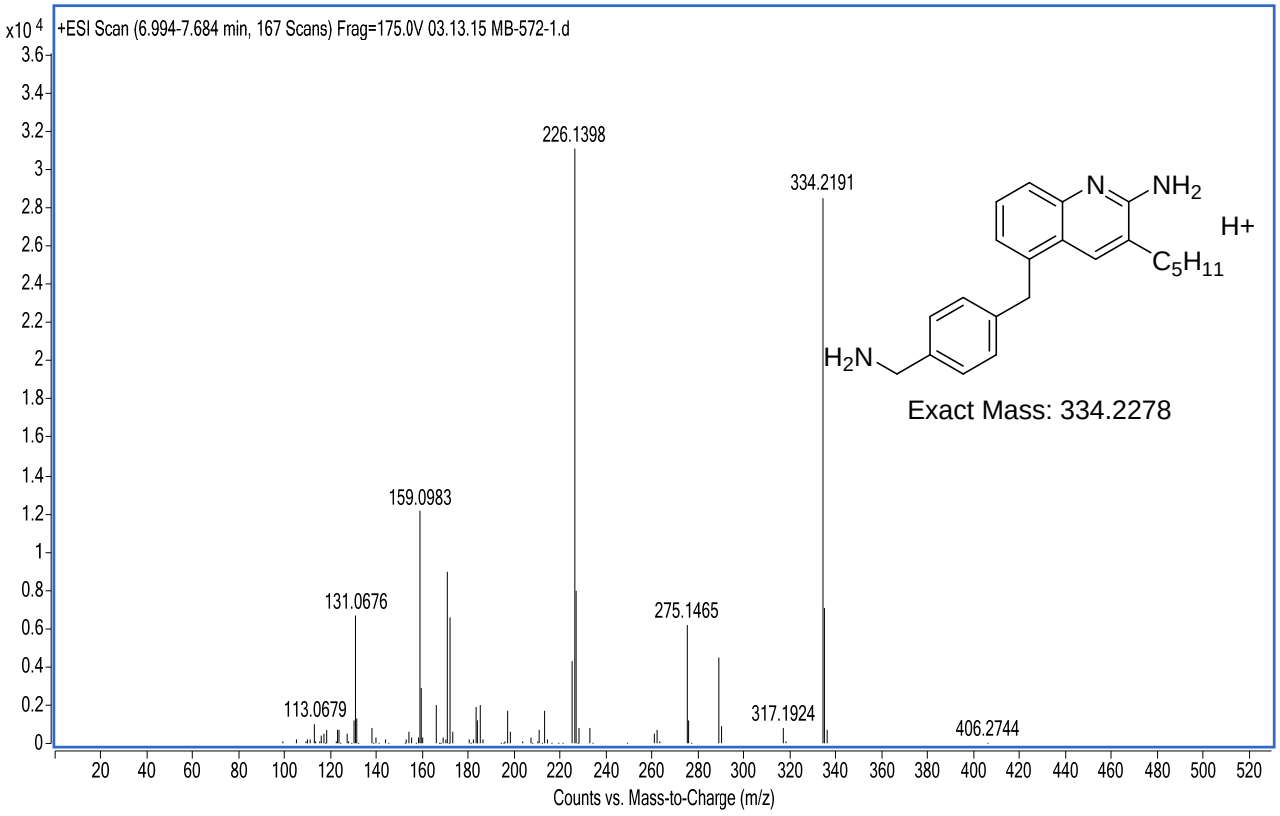
Compound **18b:** ^{1}H and ^{13}C NMR Spectrum





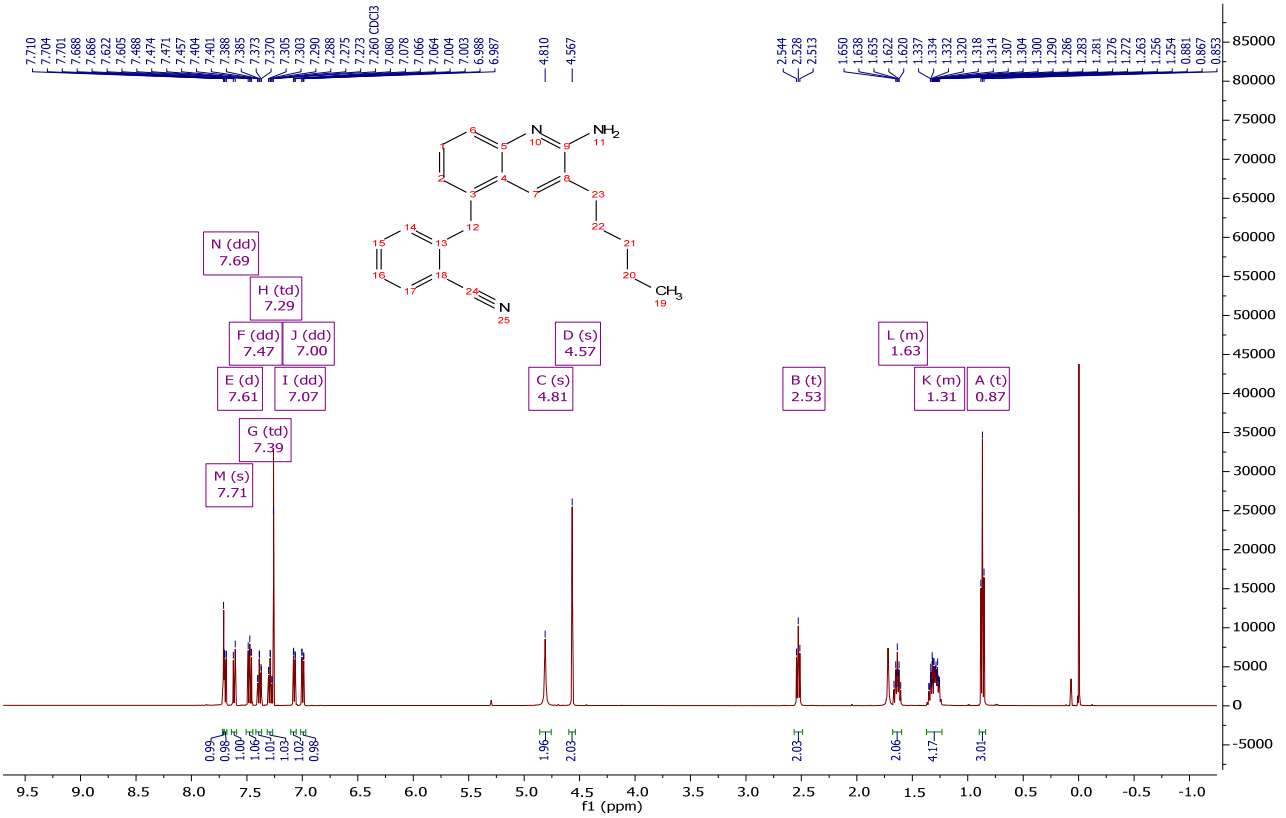
Compound **18b:** LC-MS

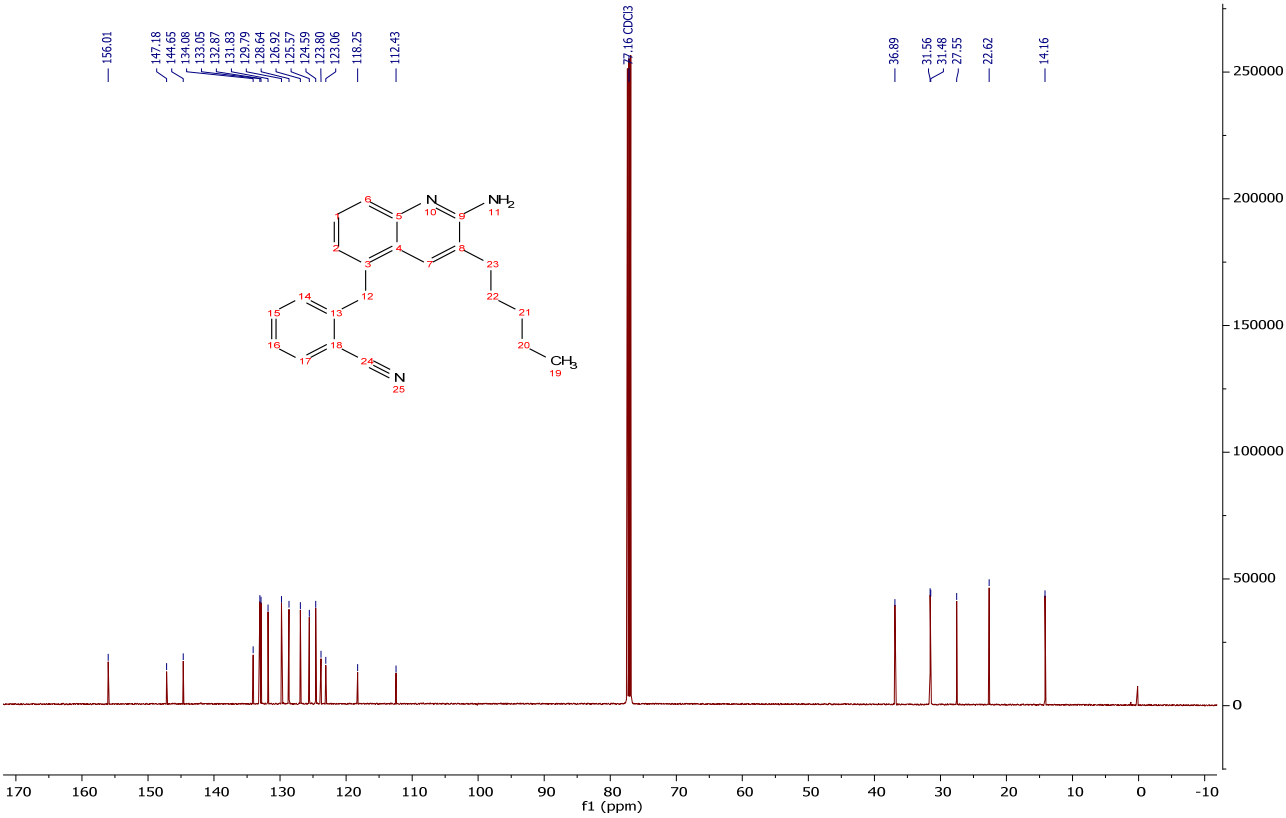




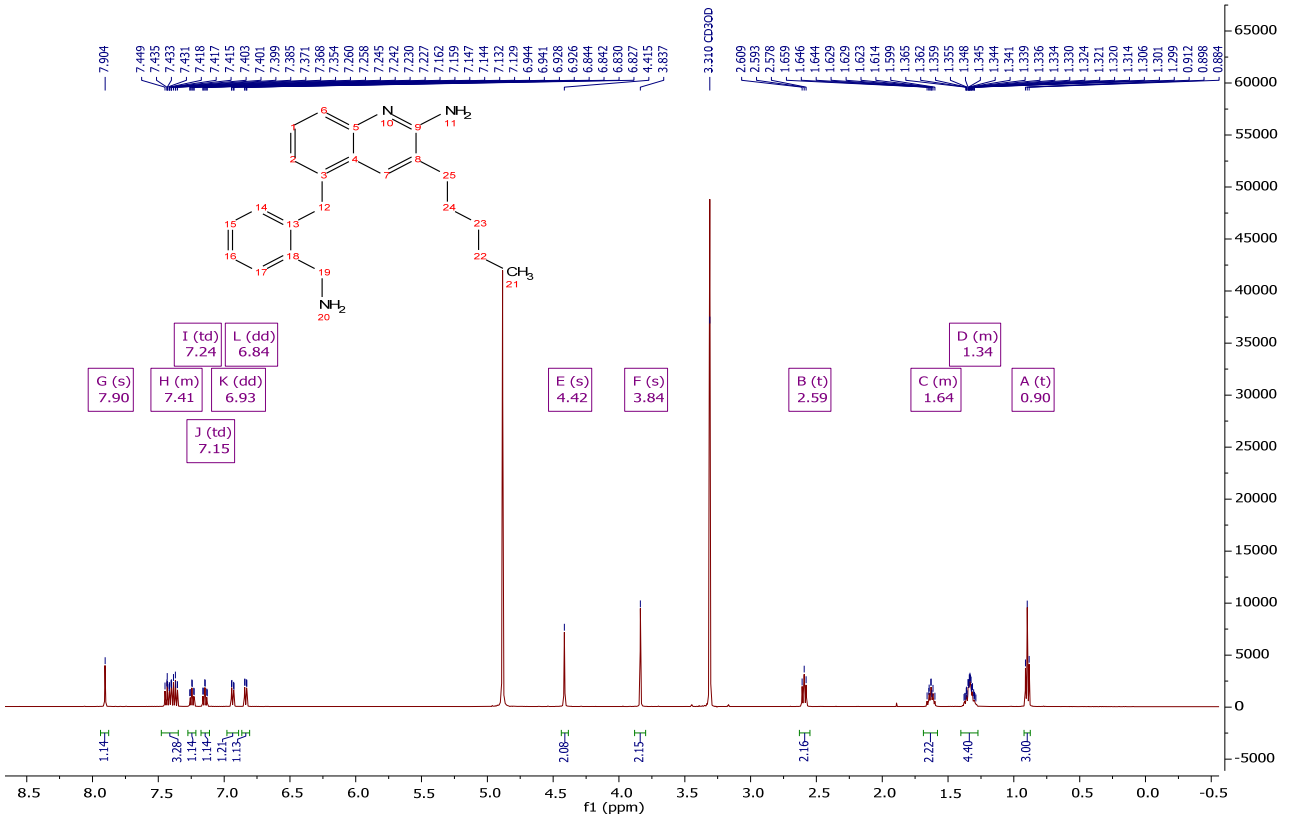
Exact Mass: 334.2278

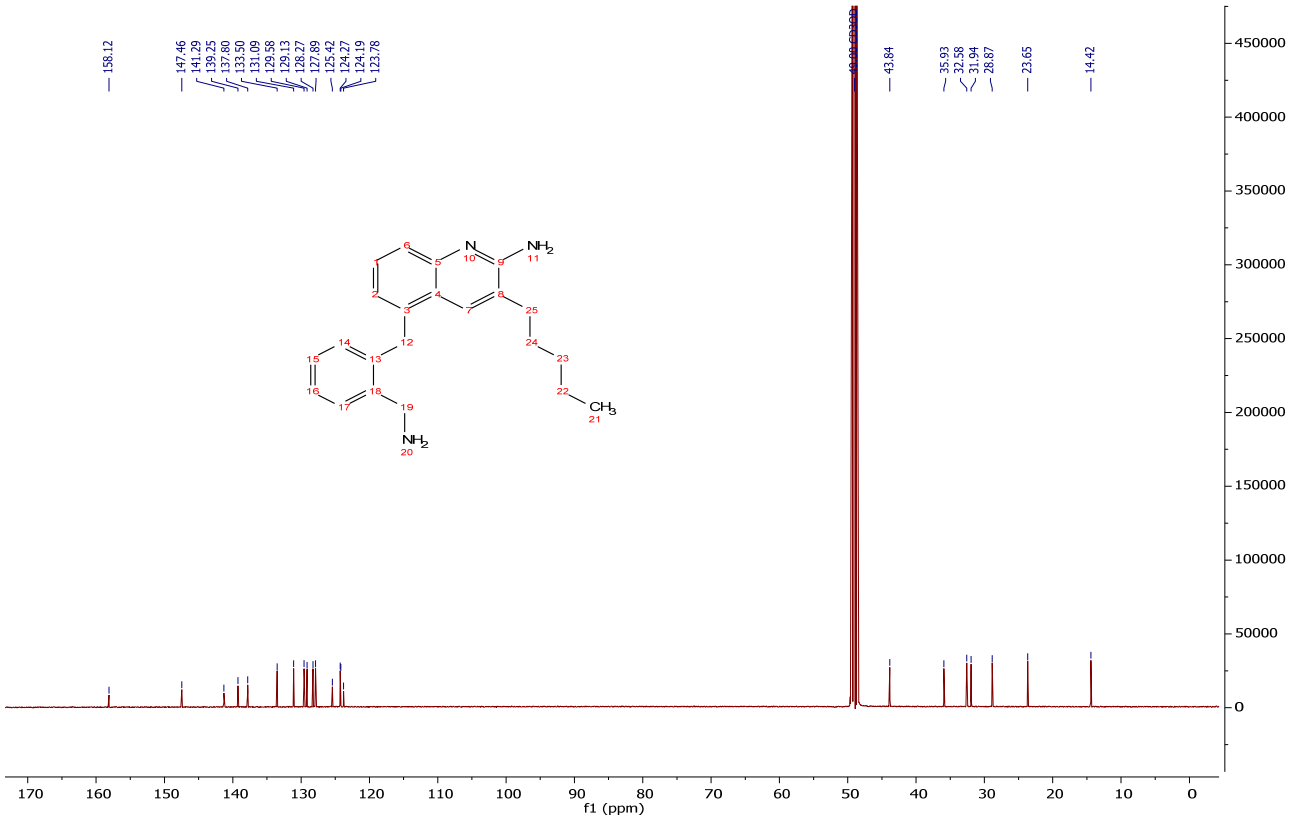
Compound **17c:** ^{1}H and ^{13}C NMR Spectrum



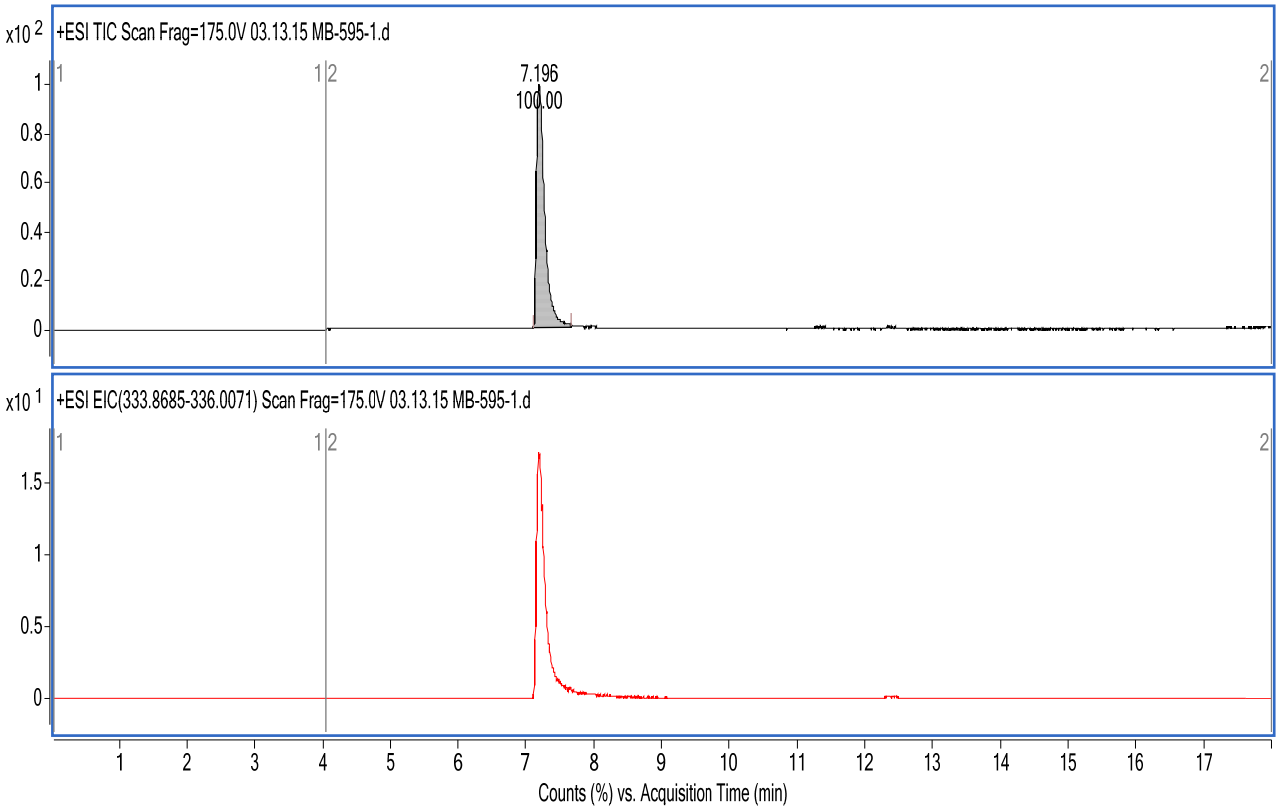


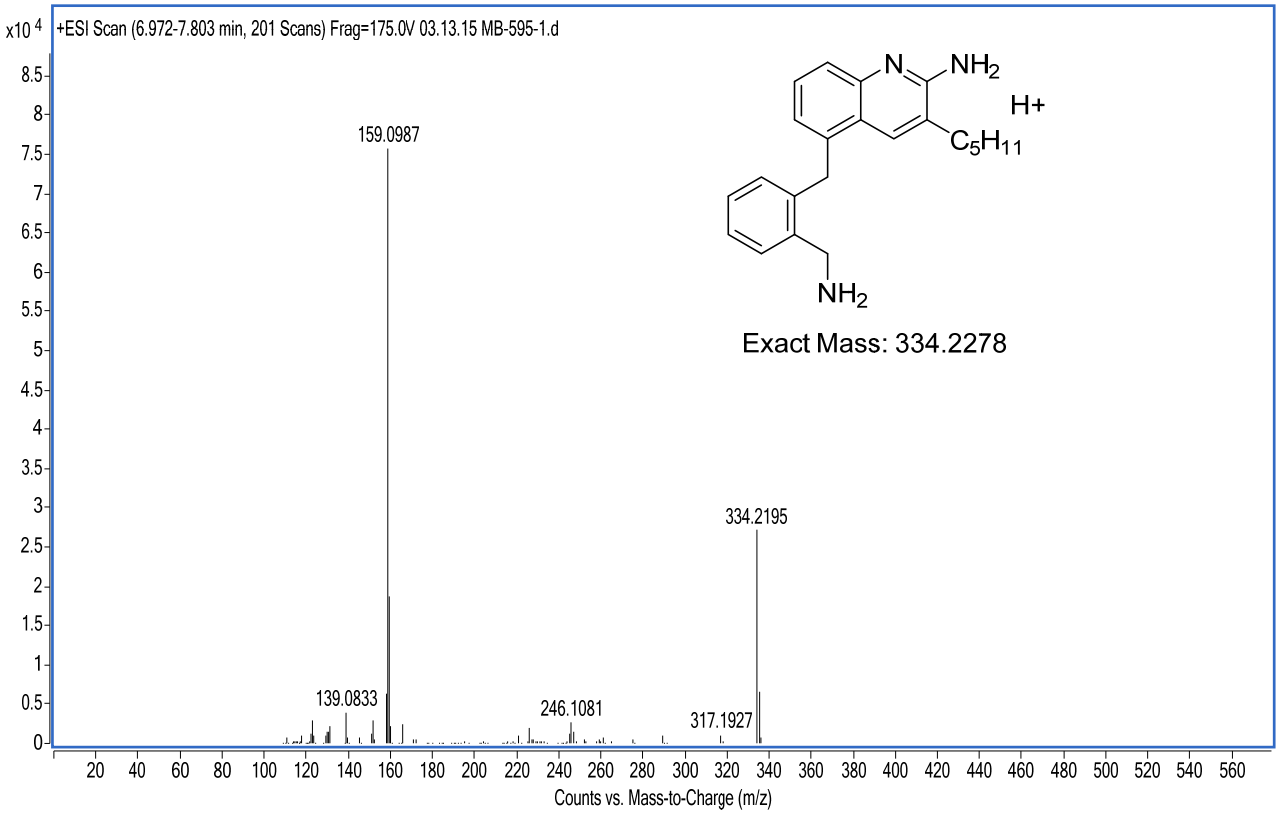
Compound **18c:** ^{1}H and ^{13}C NMR Spectrum





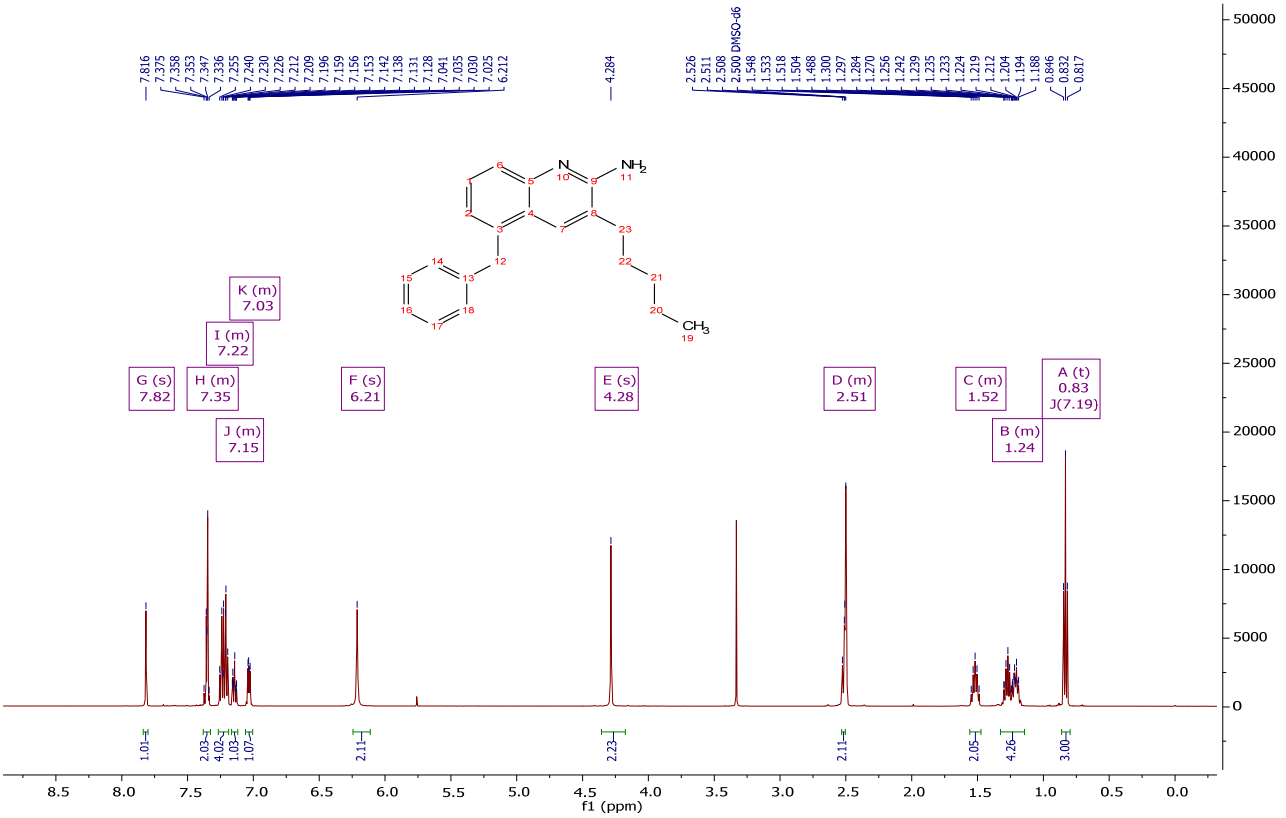
Compound **18c:** LC-MS

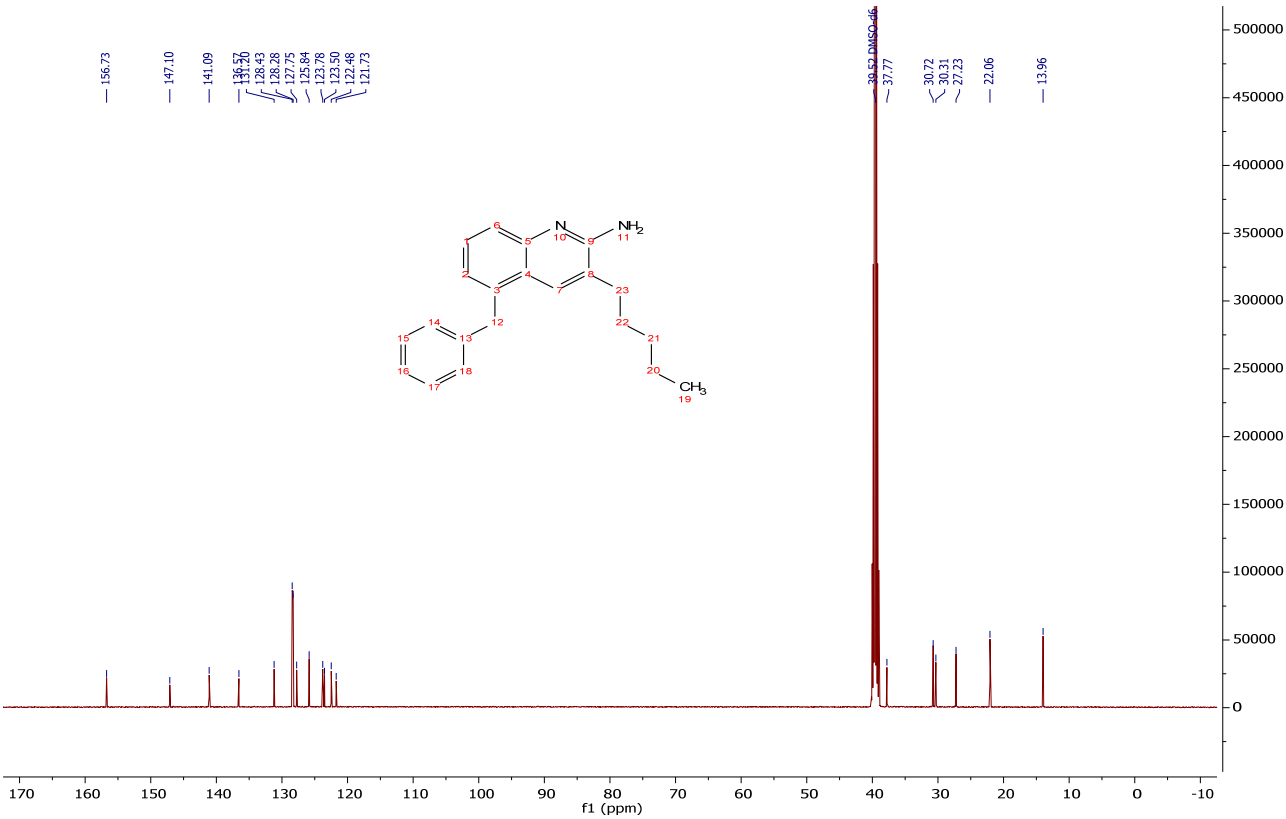




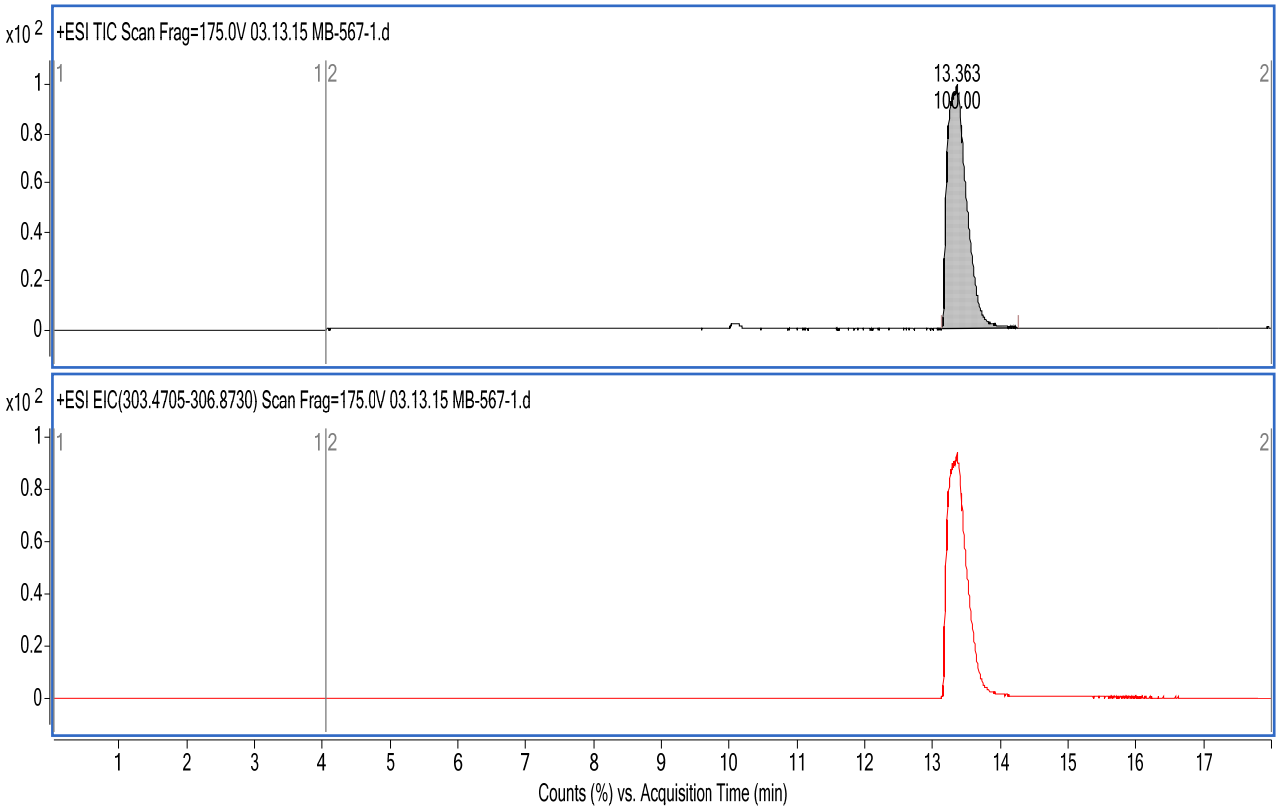
Exact Mass: 334.2278

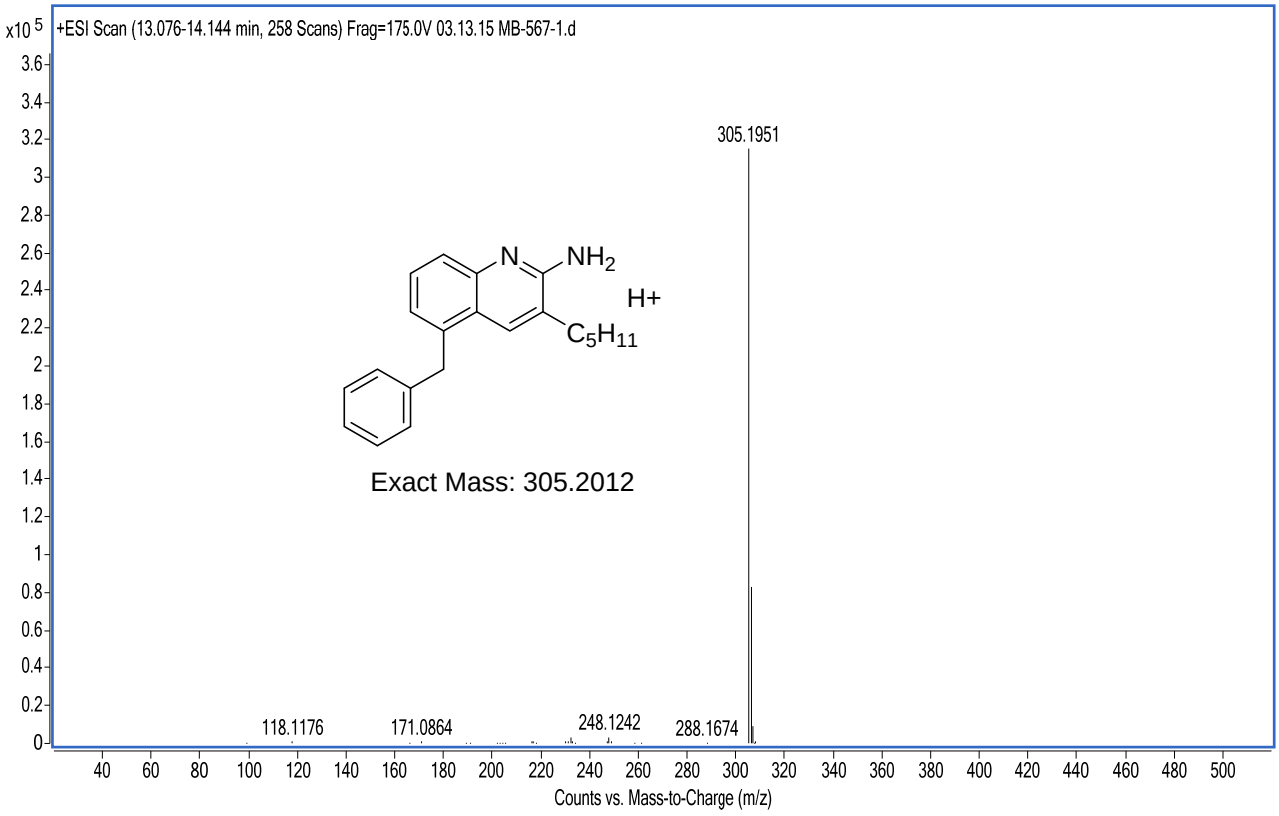
Compound **17d:** ^{1}H and ^{13}C NMR Spectrum





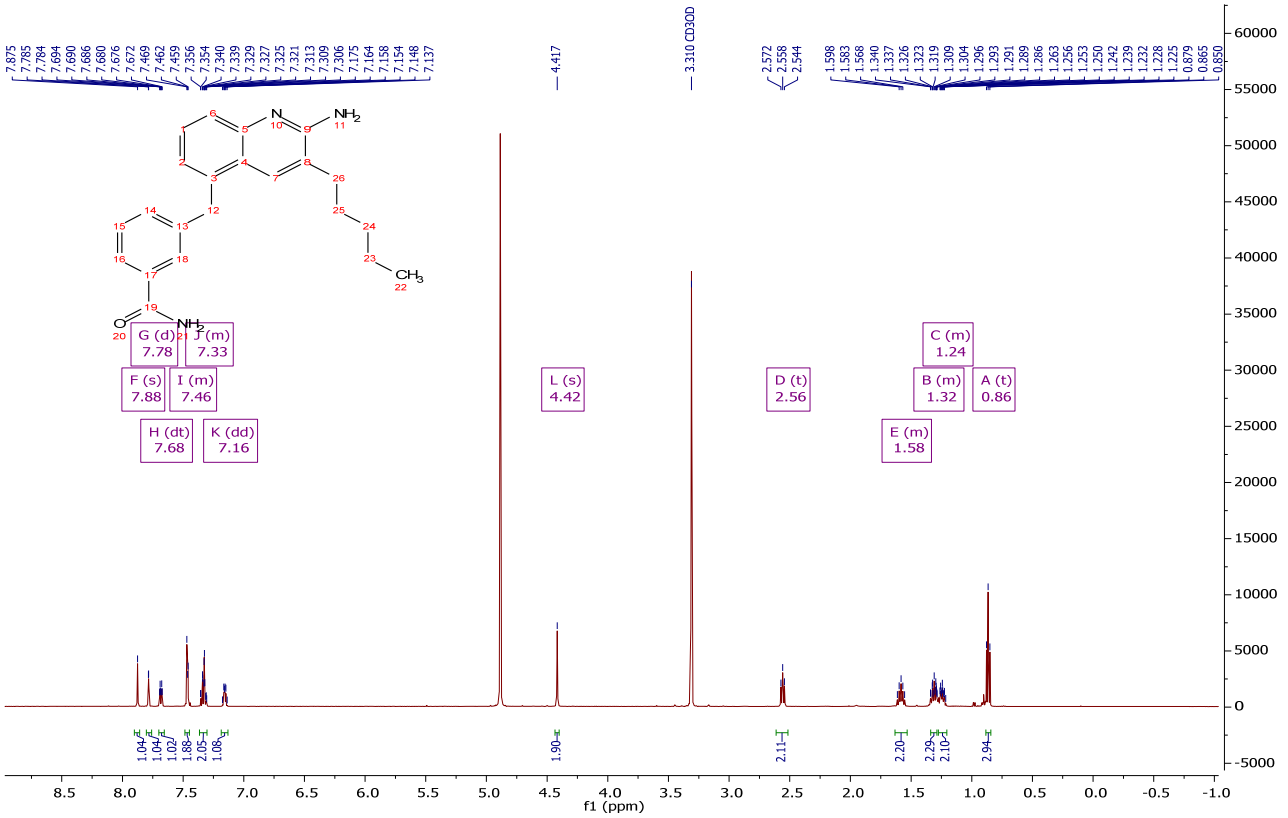
Compound **17d:** LC-MS

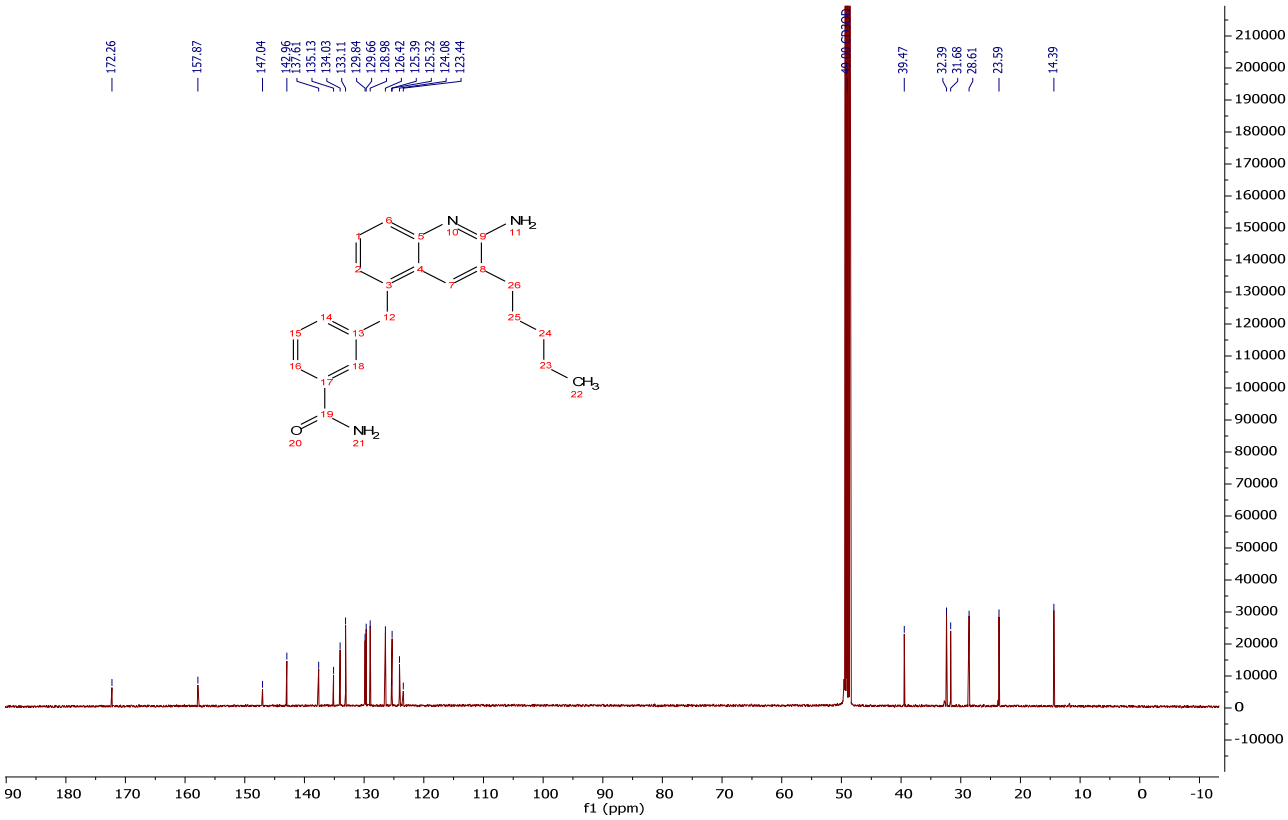




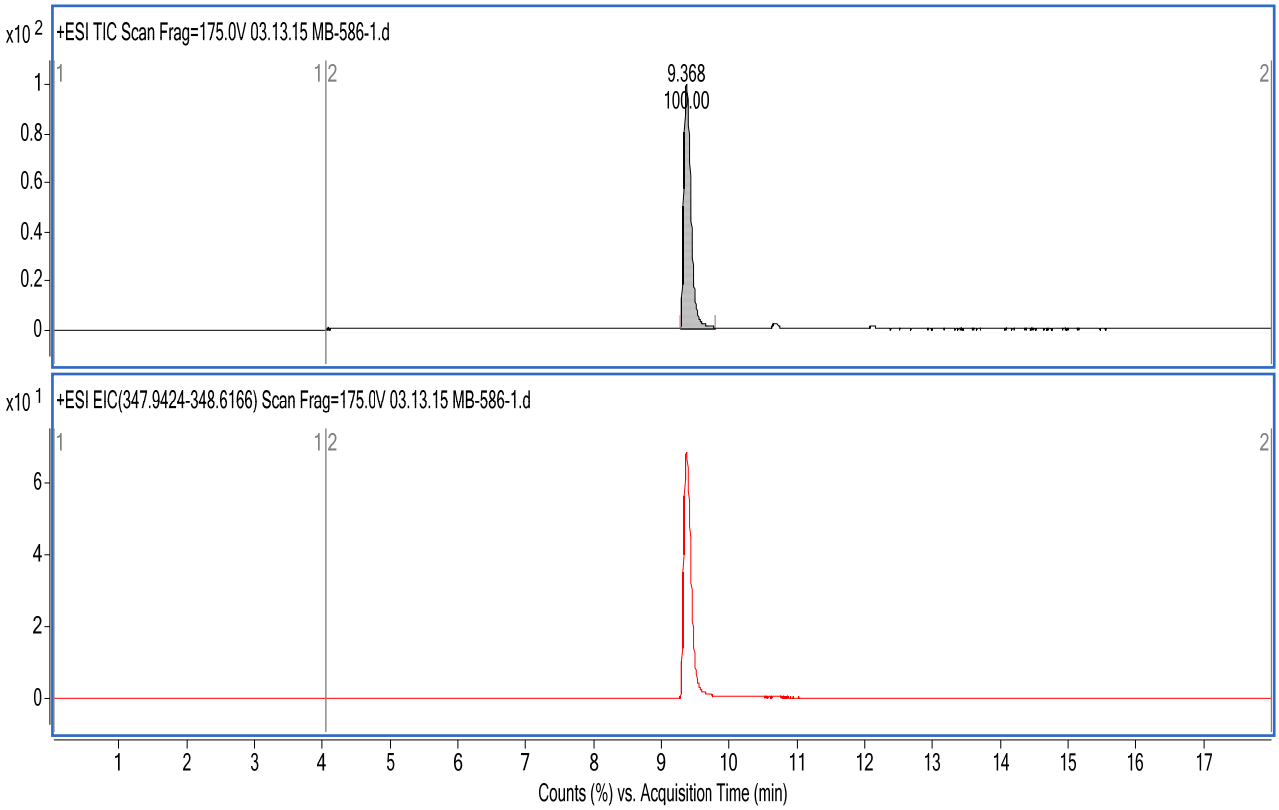
Exact Mass: 305.2012

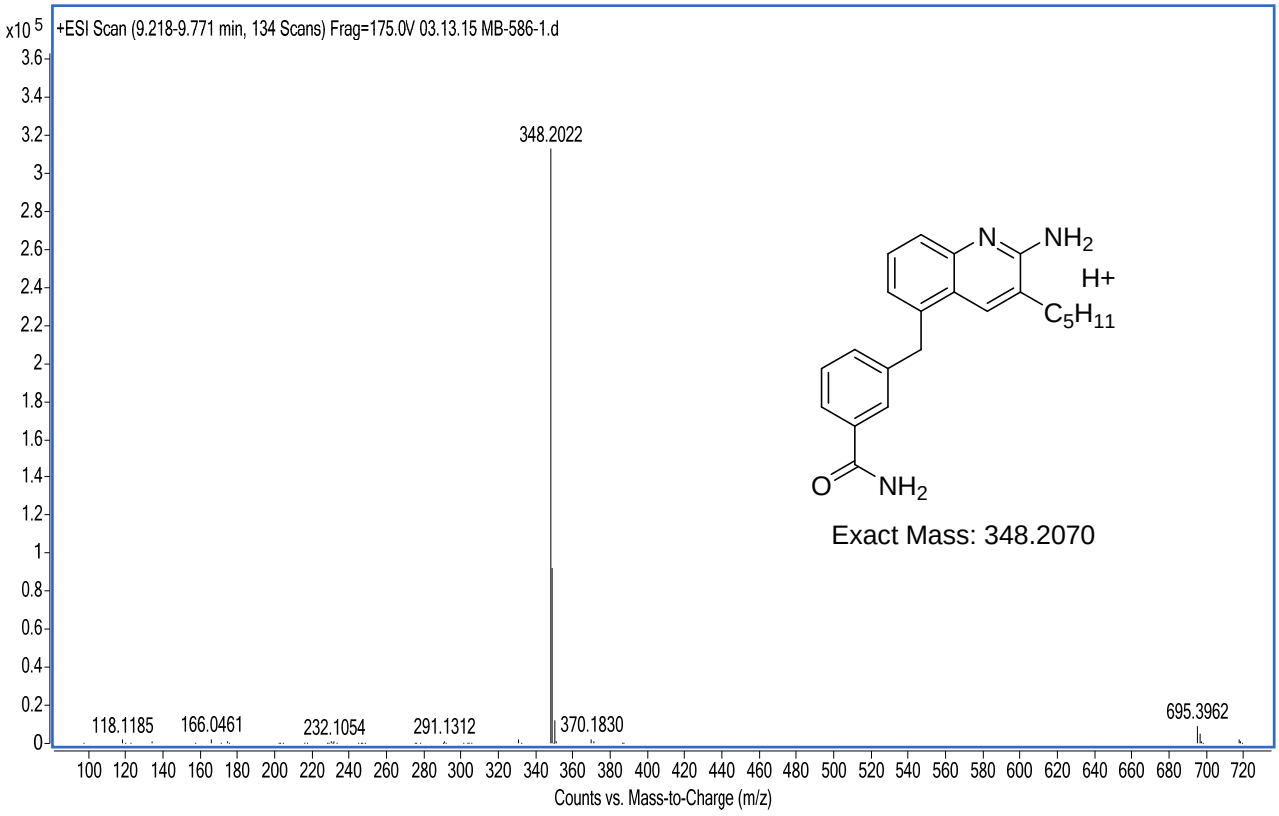
Compound **18d:** ^{1}H and ^{13}C NMR Spectrum





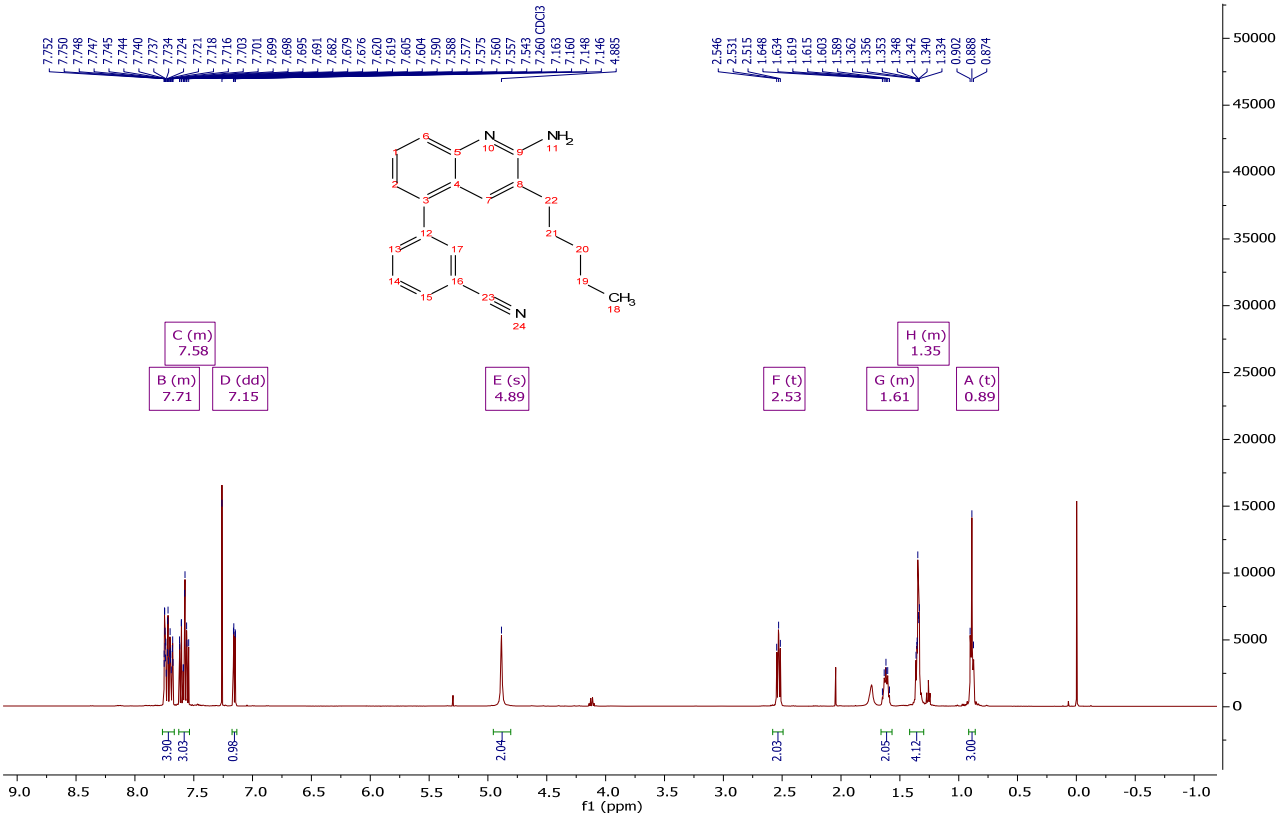
Compound **18d:** LC-MS

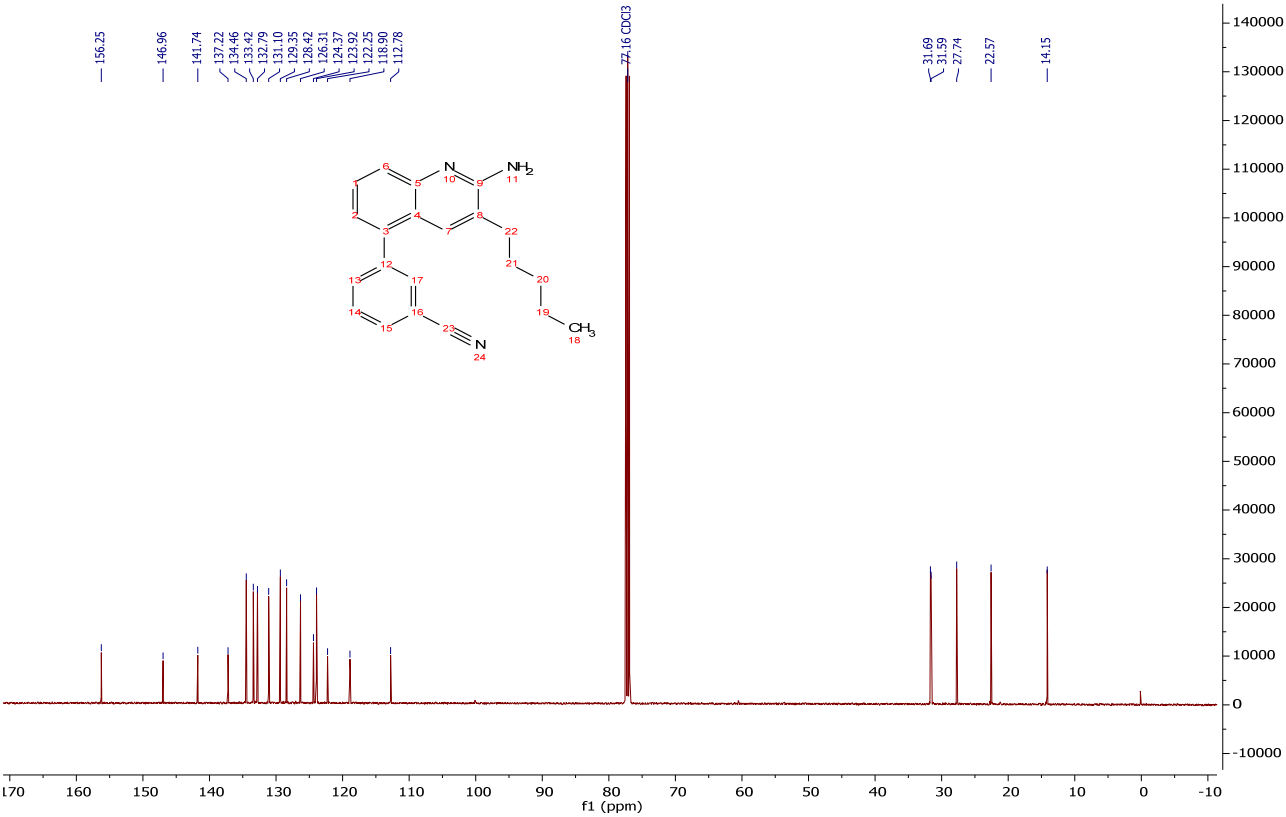




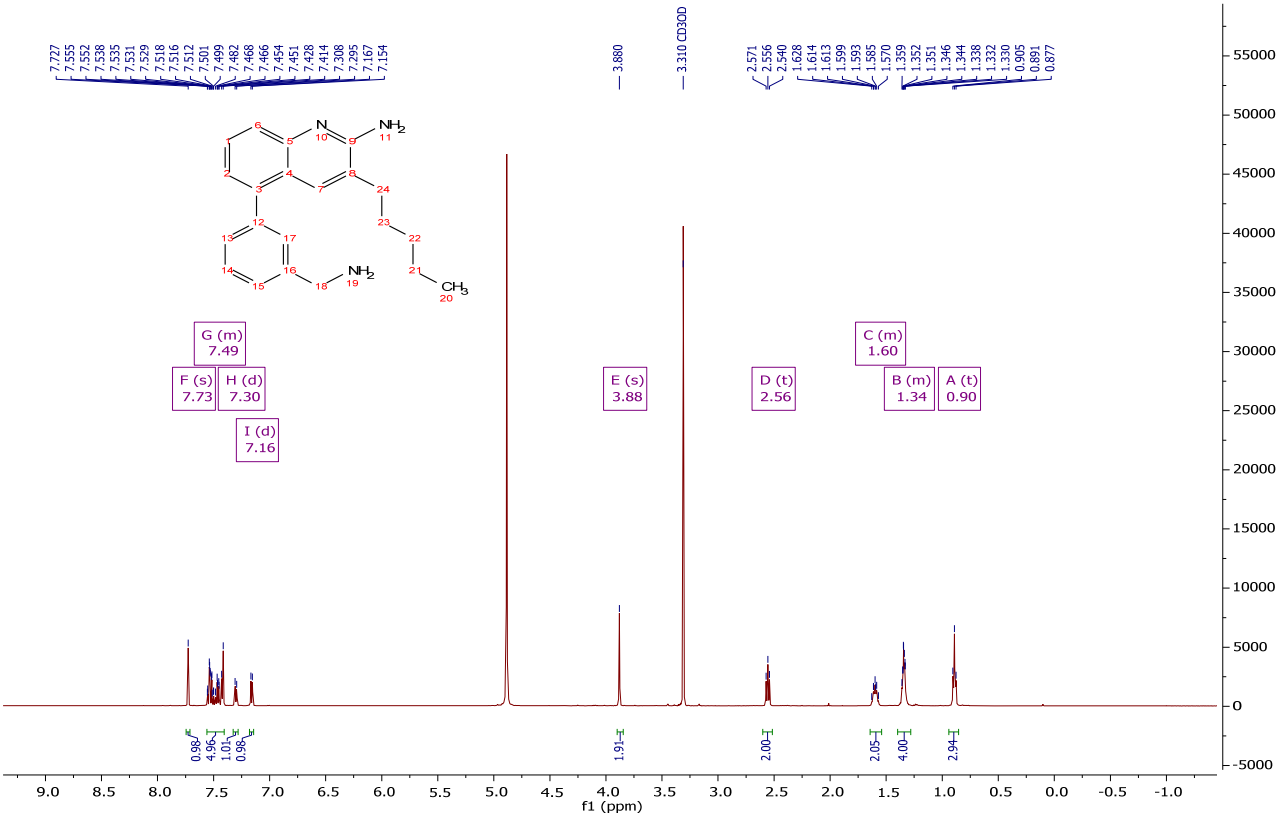
Exact Mass: 348.2070

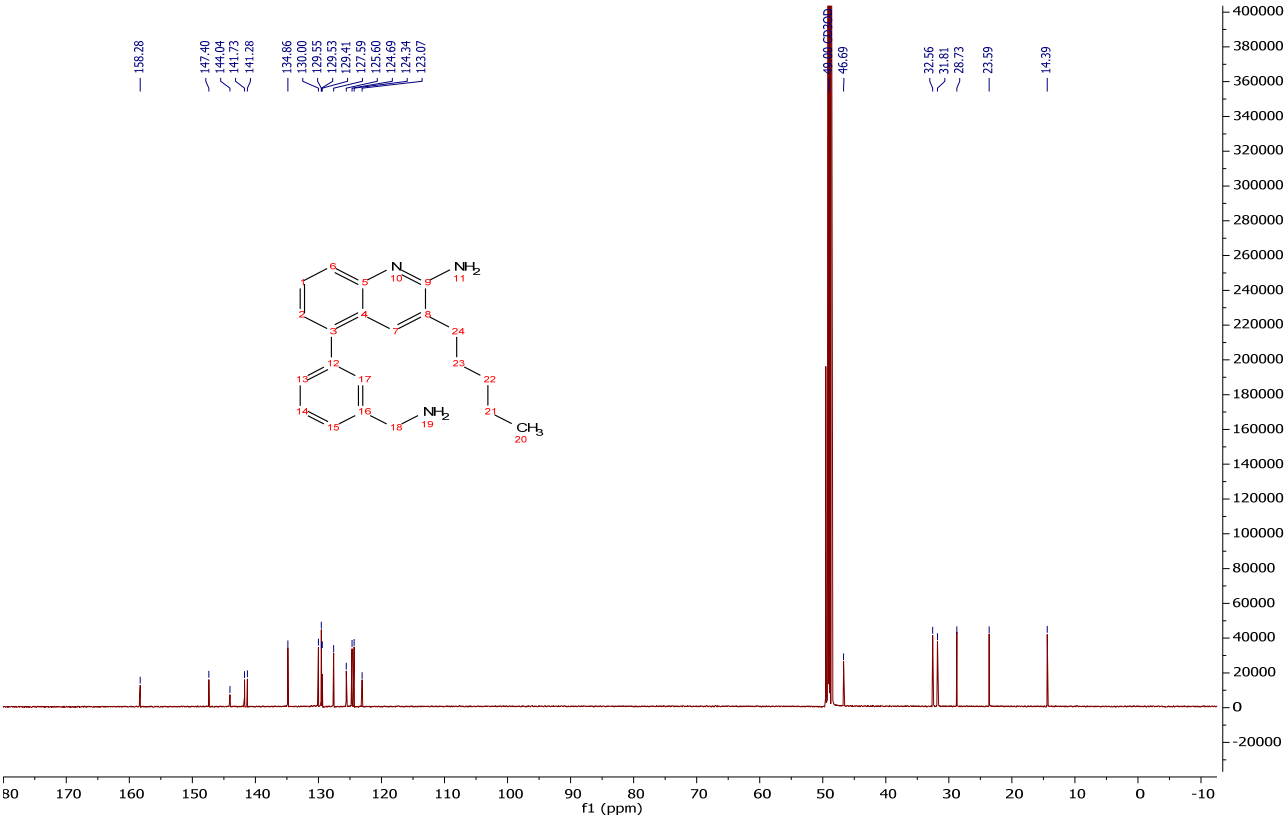
Compound **19a:** ^{1}H and ^{13}C NMR Spectrum



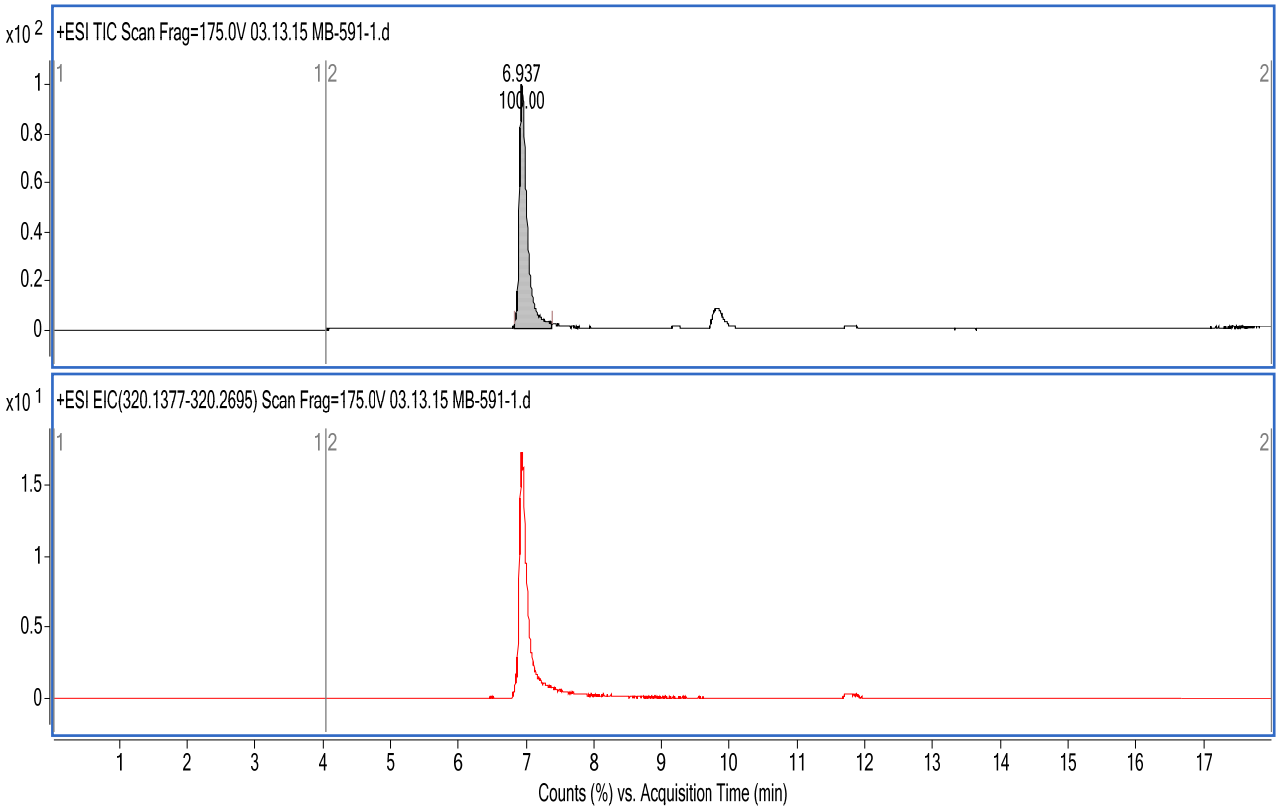


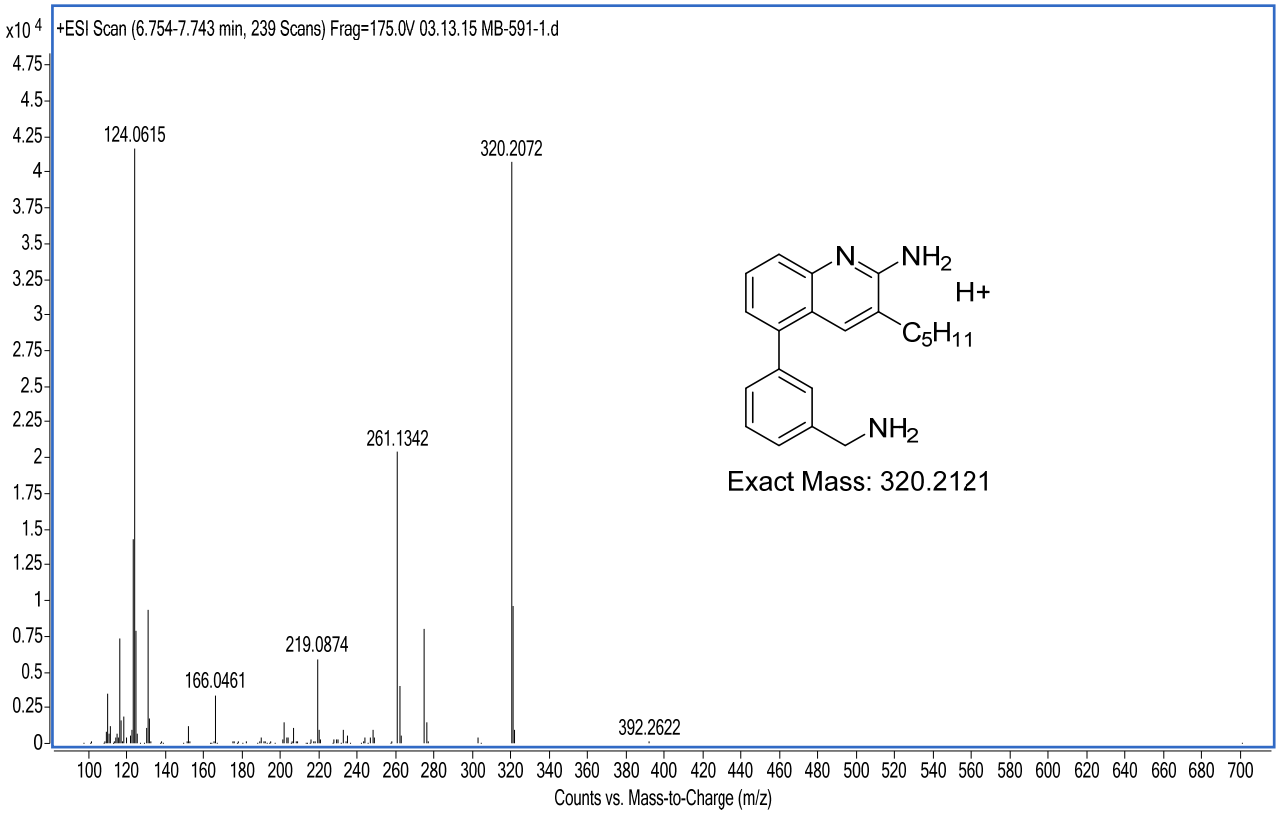
Compound **20a:** ^{1}H and ^{13}C NMR Spectrum





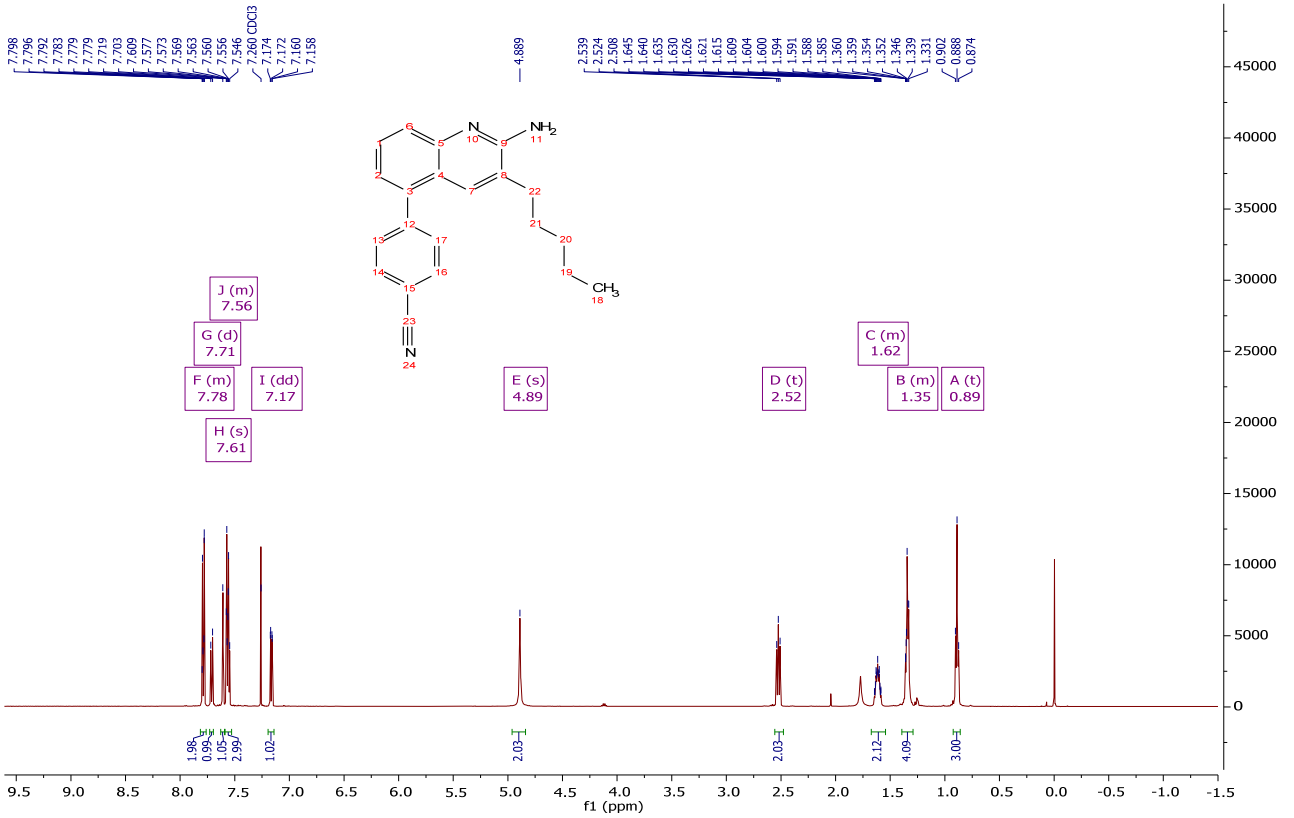
Compound **20a:** LC-MS

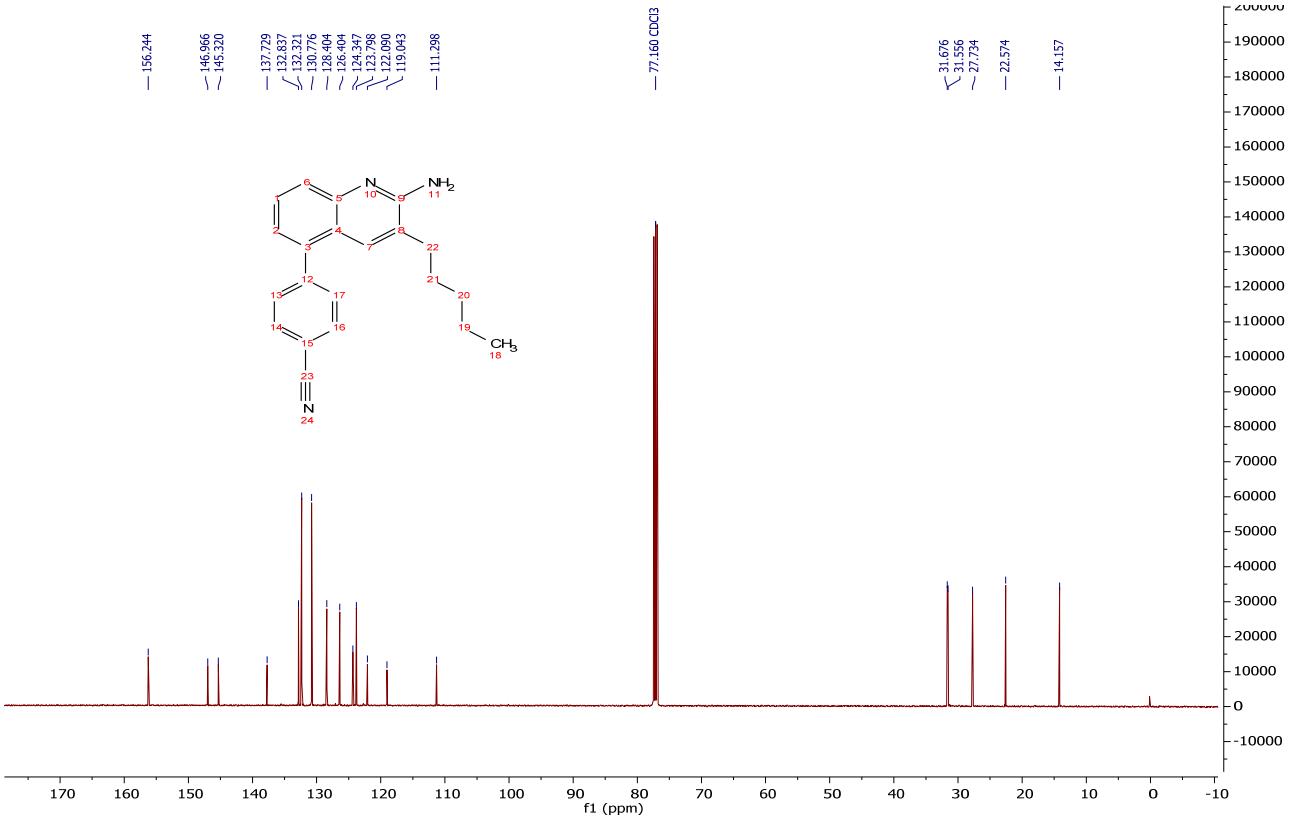




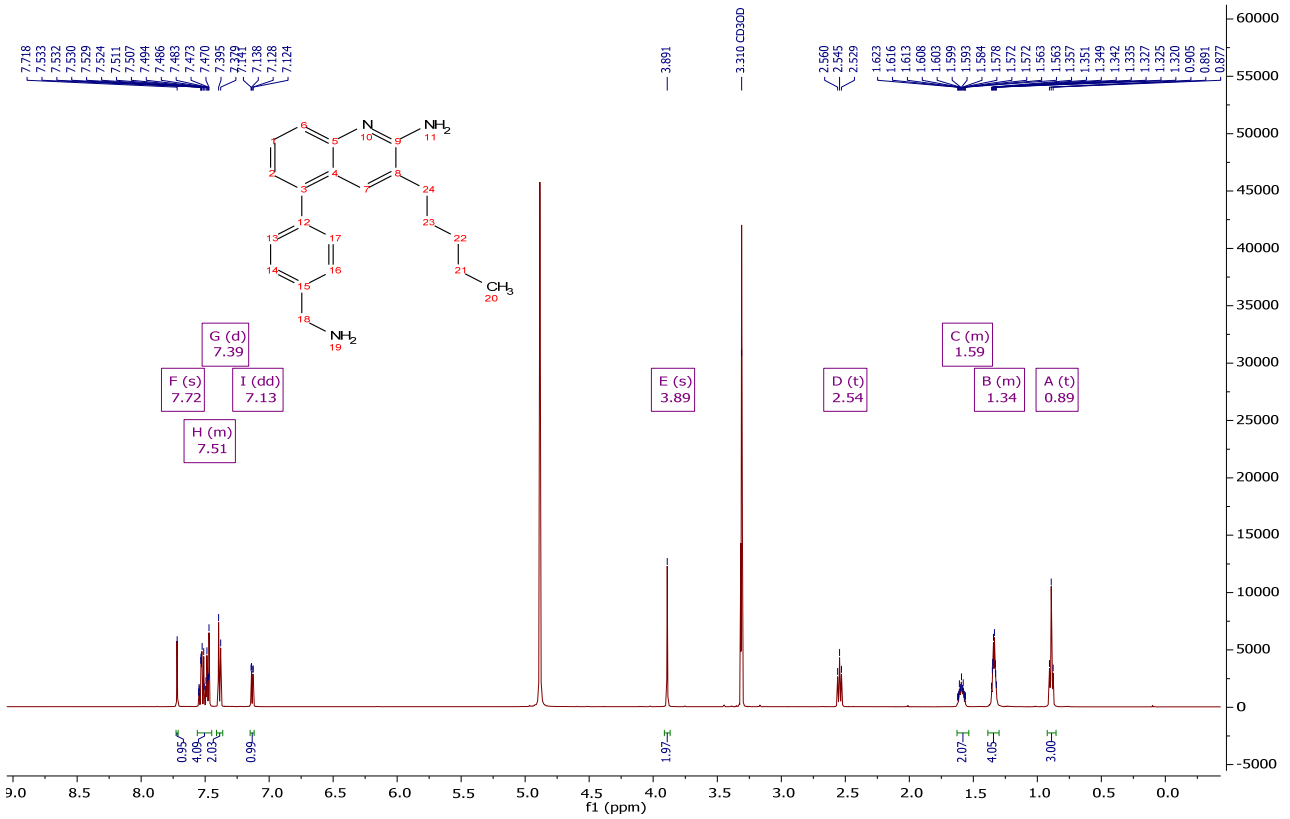
Exact Mass: 320.2121

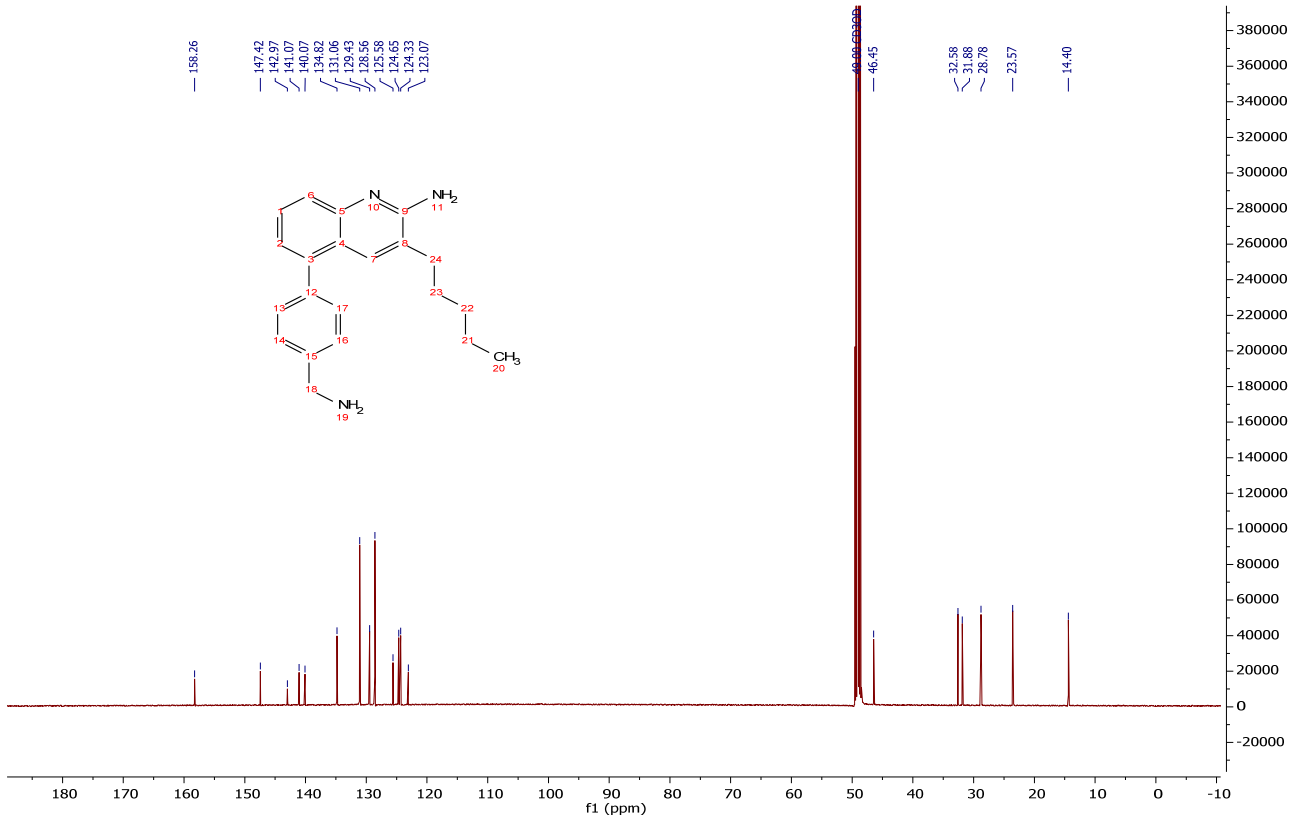
Compound **19b:** ^{1}H and ^{13}C NMR Spectrum



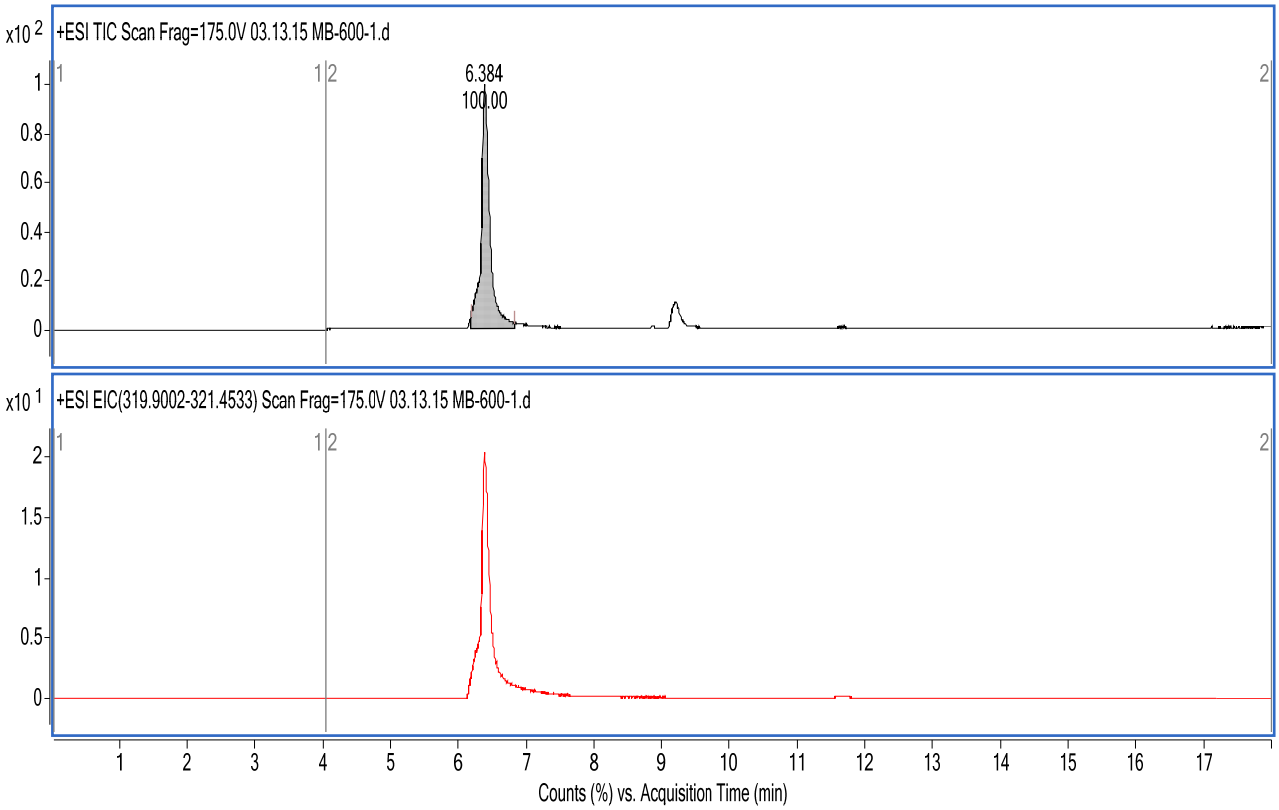


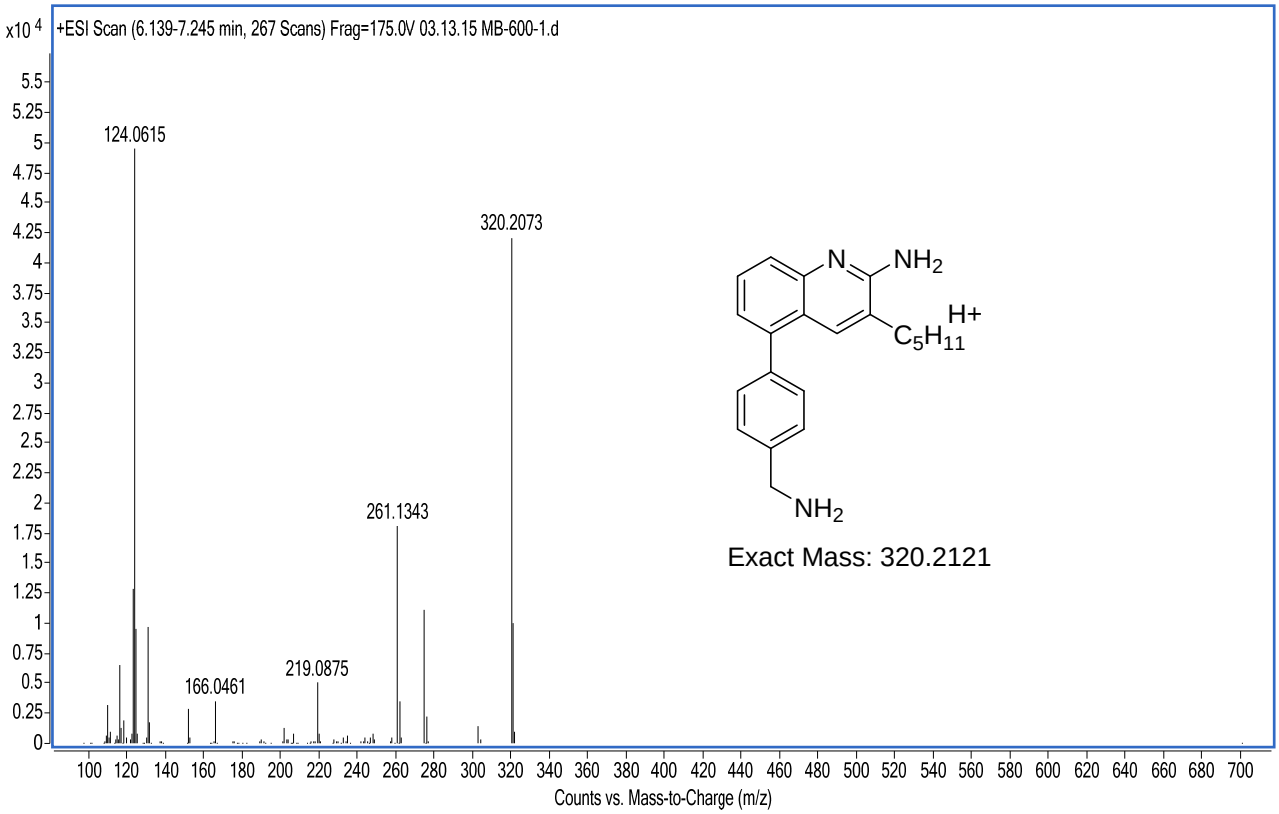
Compound **20b:** ^{1}H and ^{13}C NMR Spectrum





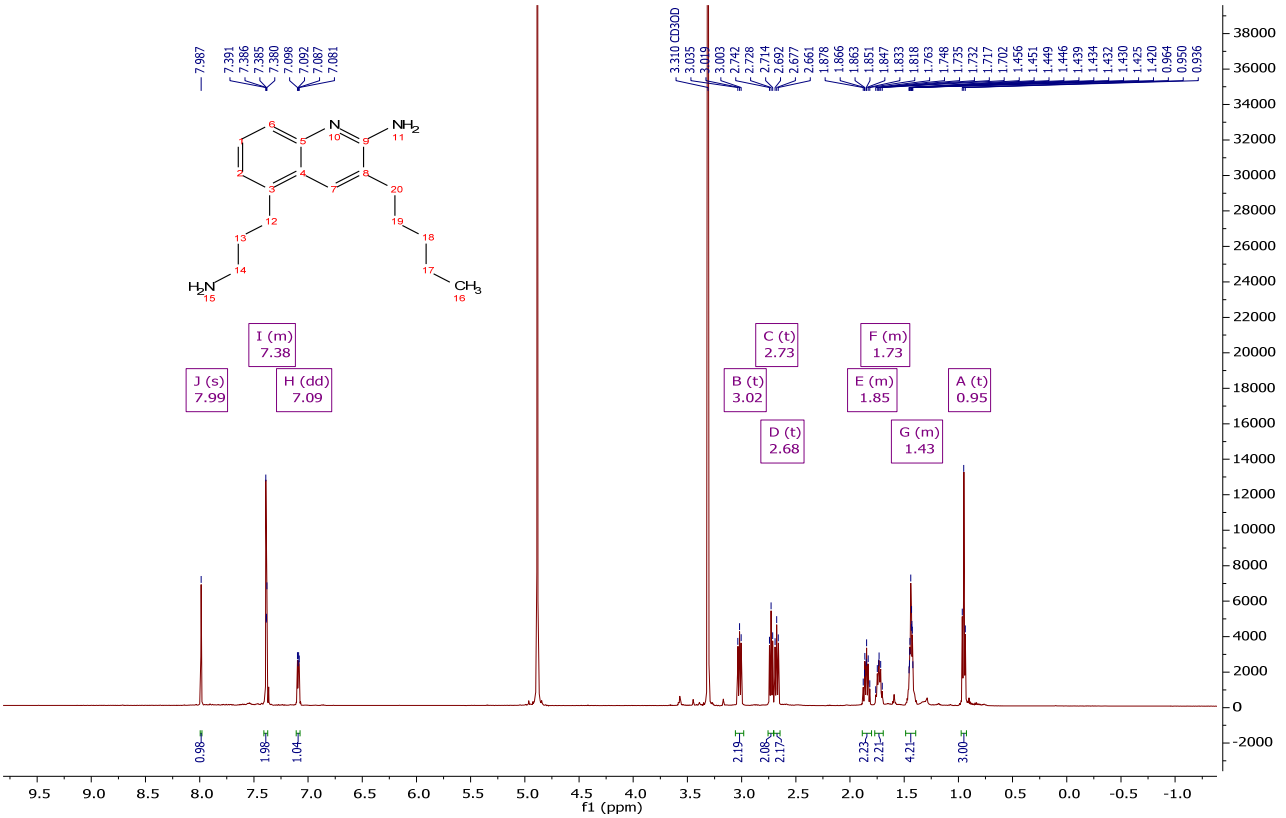
Compound **20b:** LC-MS

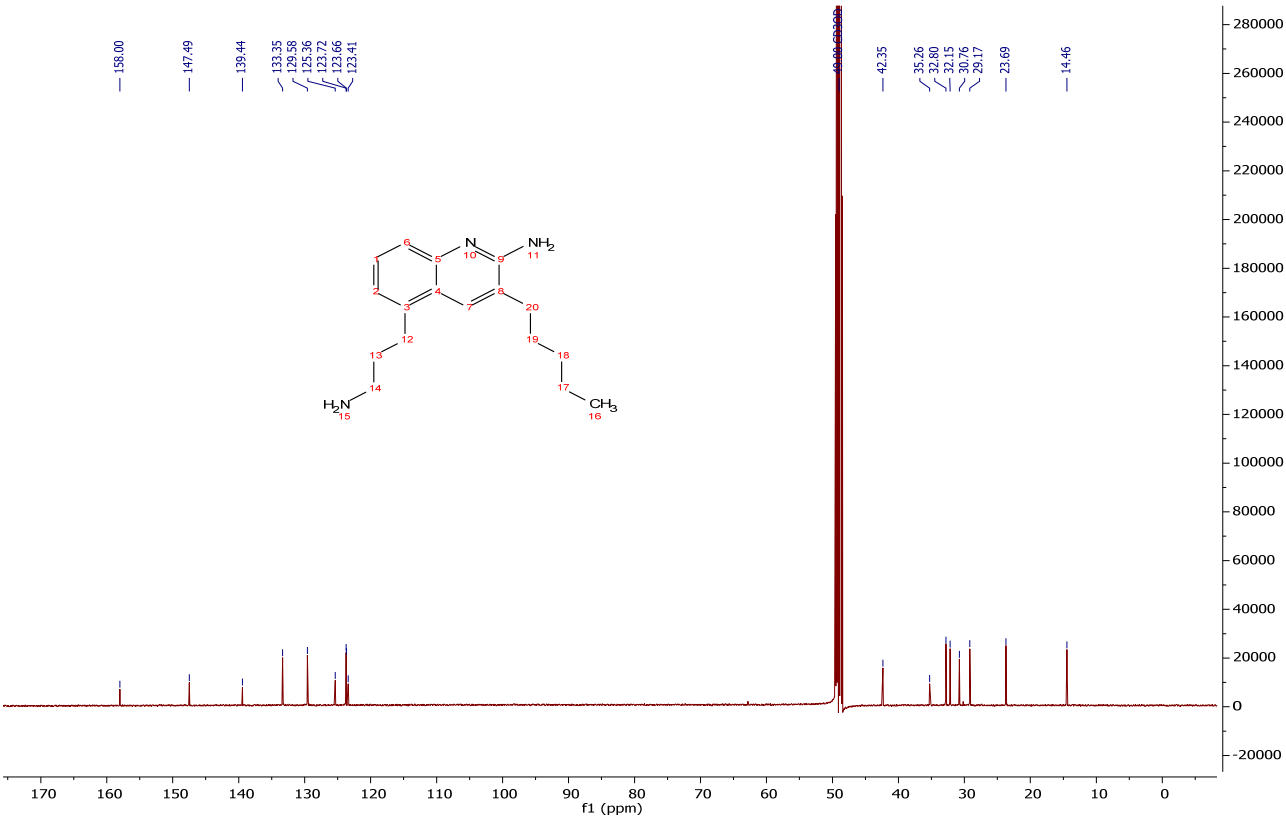




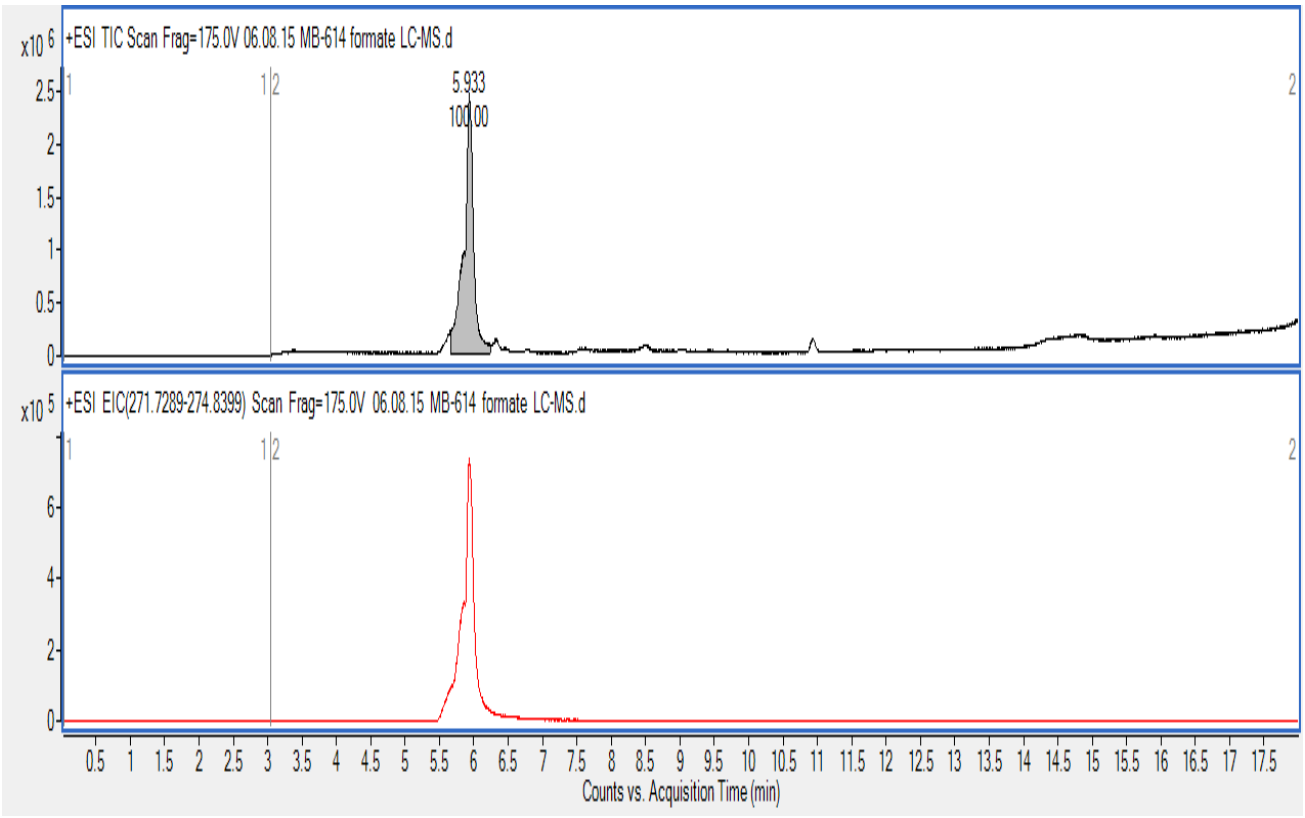
Exact Mass: 320.2121

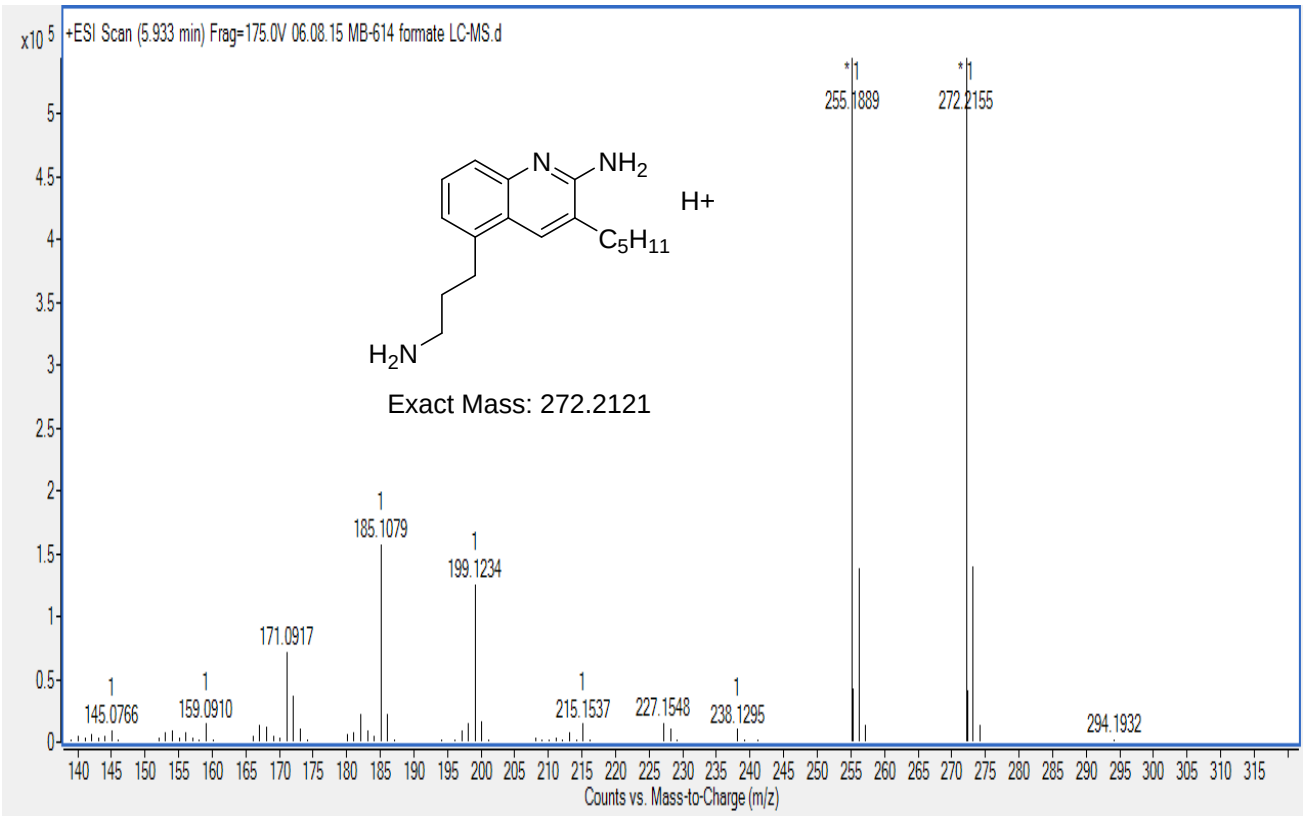
Compound **23:** ^{1}H and ^{13}C NMR Spectrum



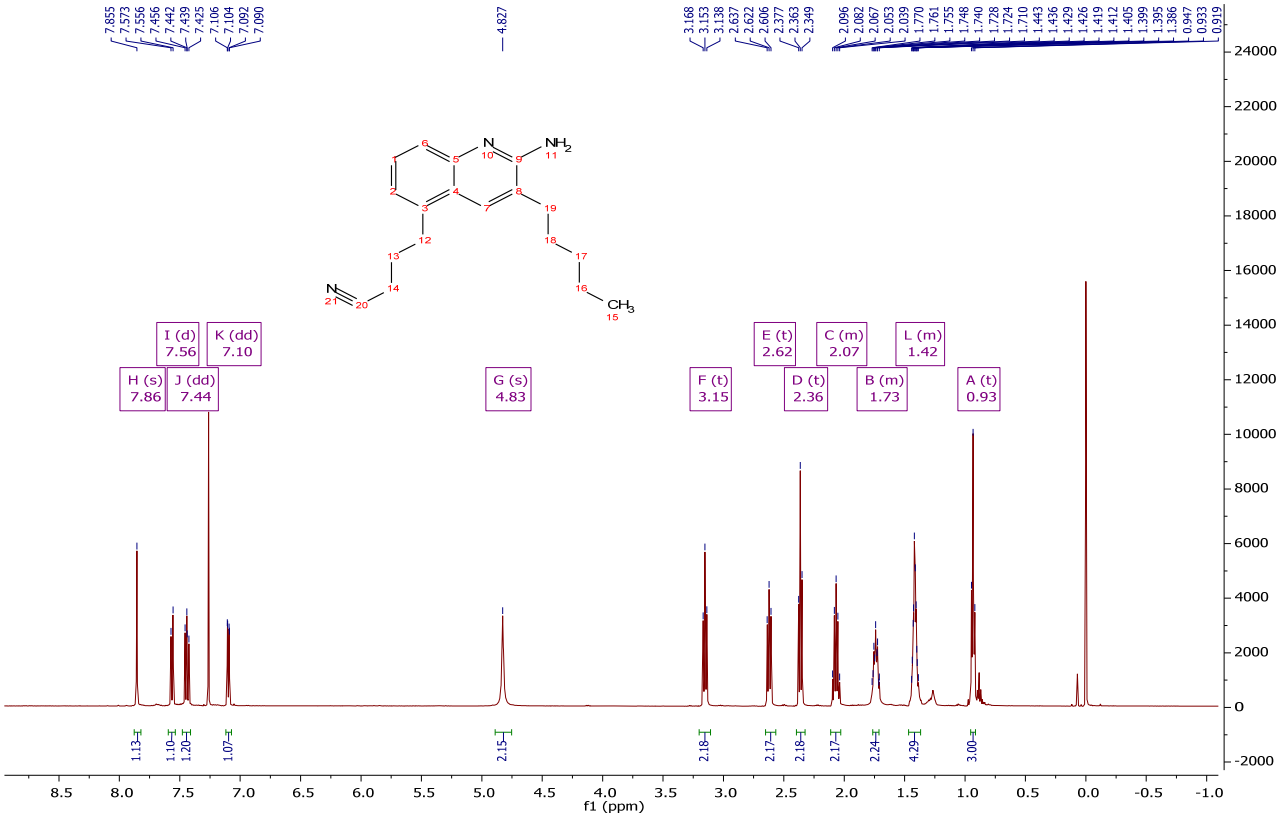


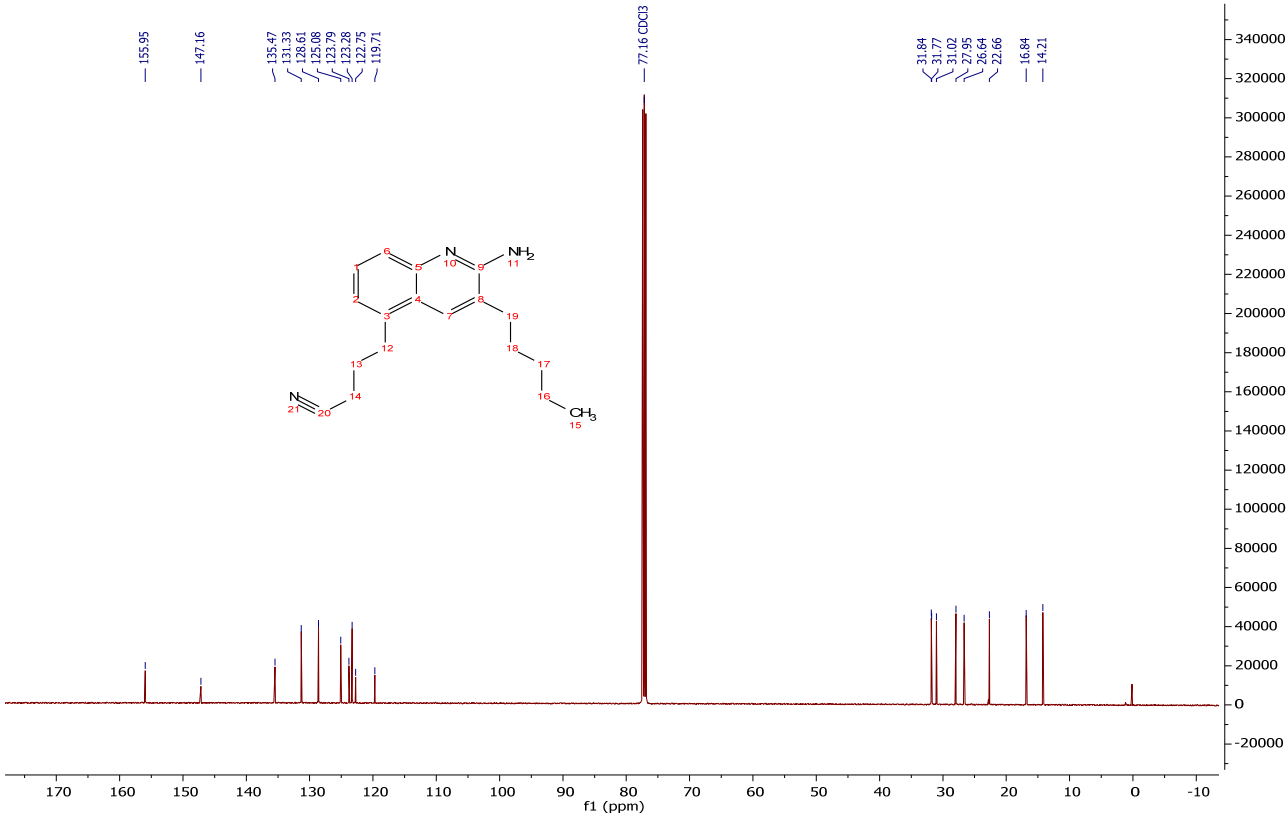
Compound **23:** LC-MS



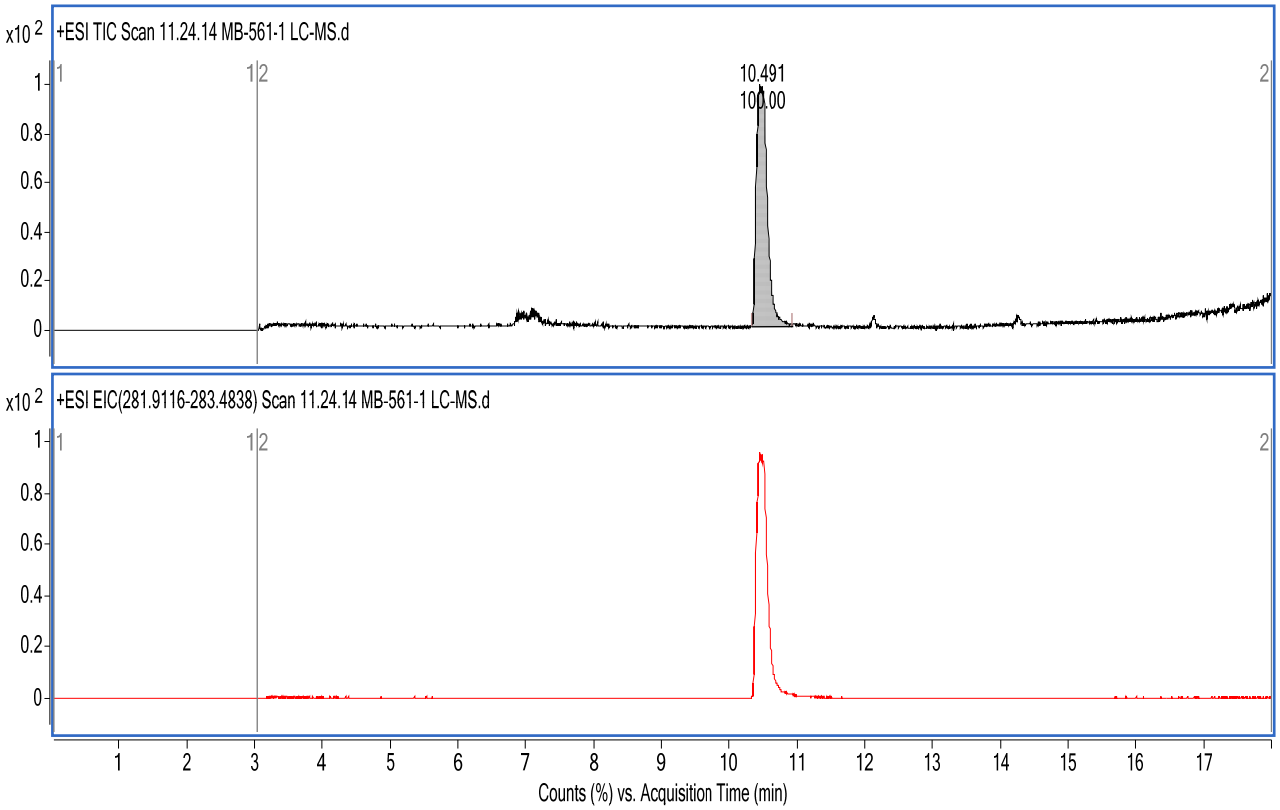


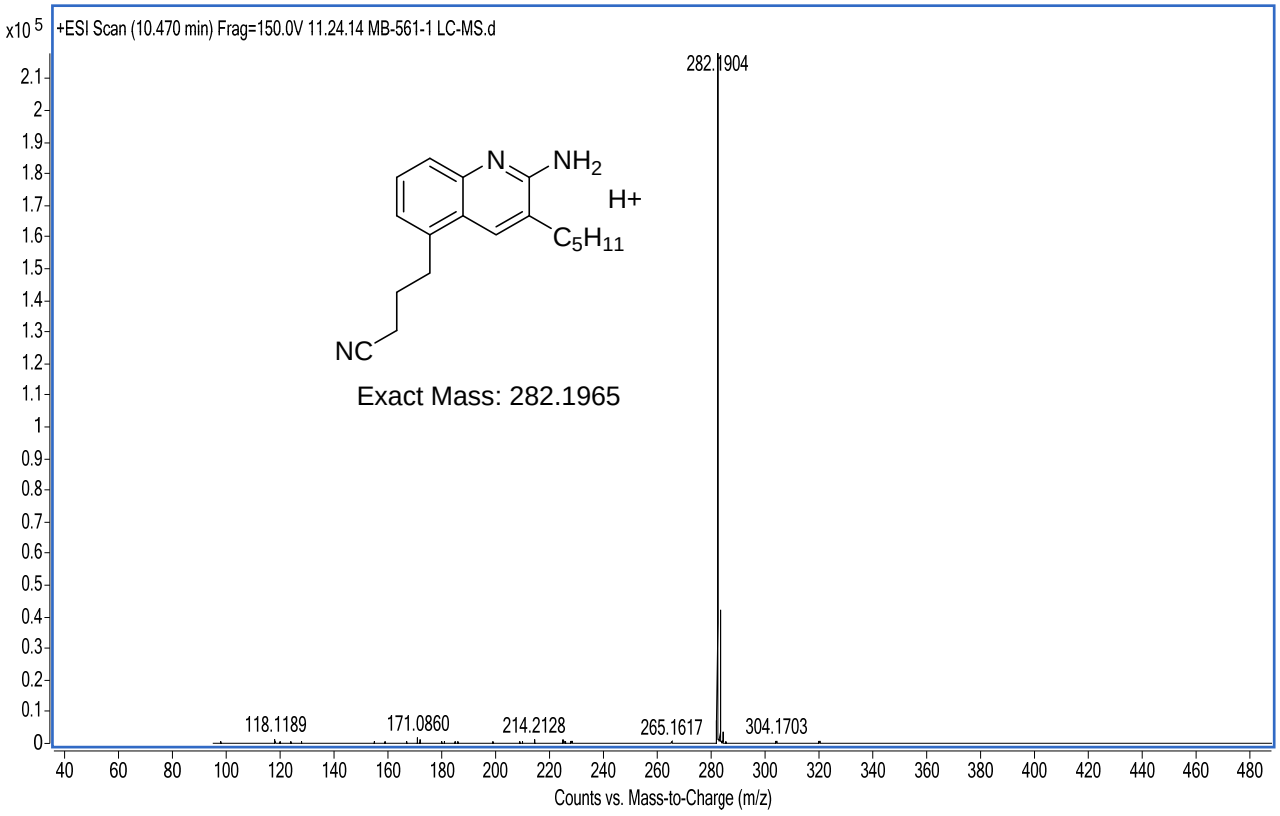
Compound **30a:** ^{1}H and ^{13}C NMR Spectrum





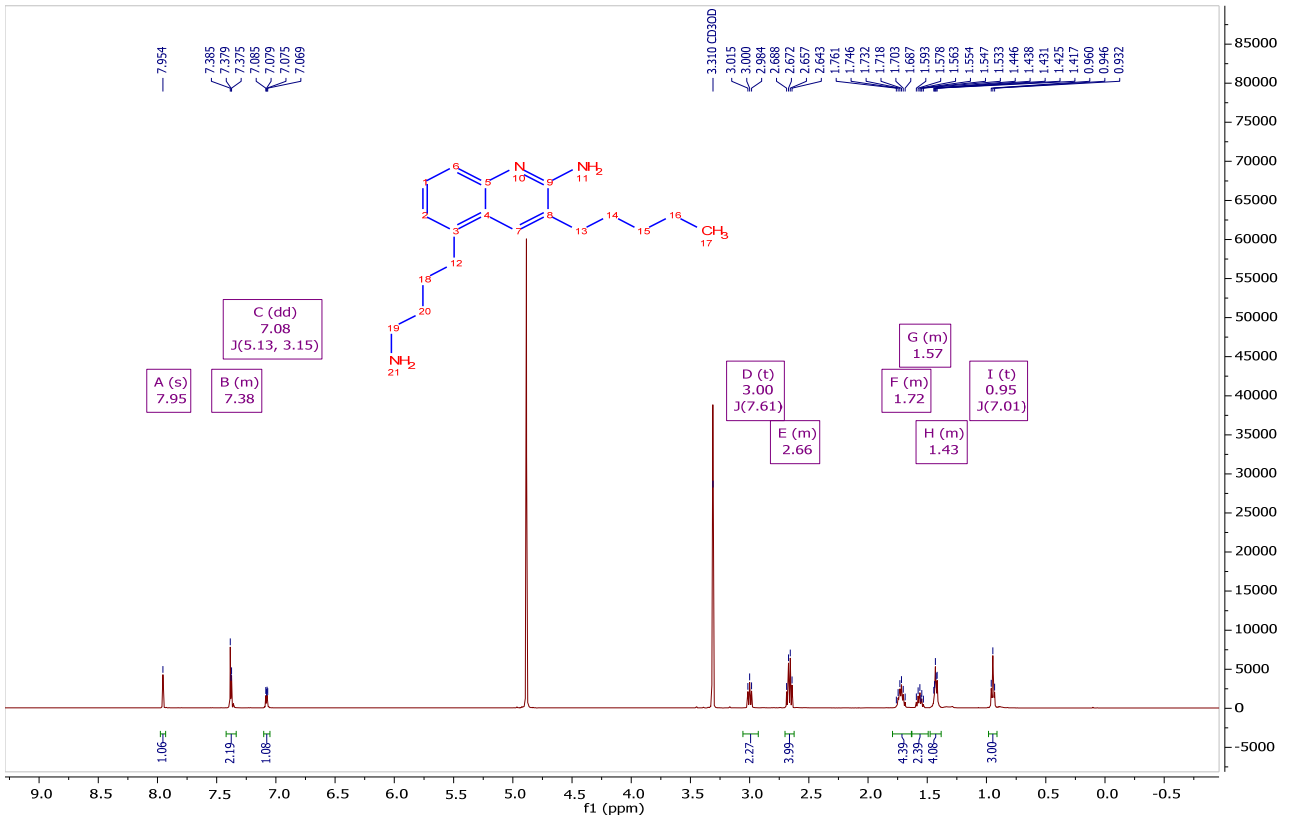
Compound **30a:** LC-MS

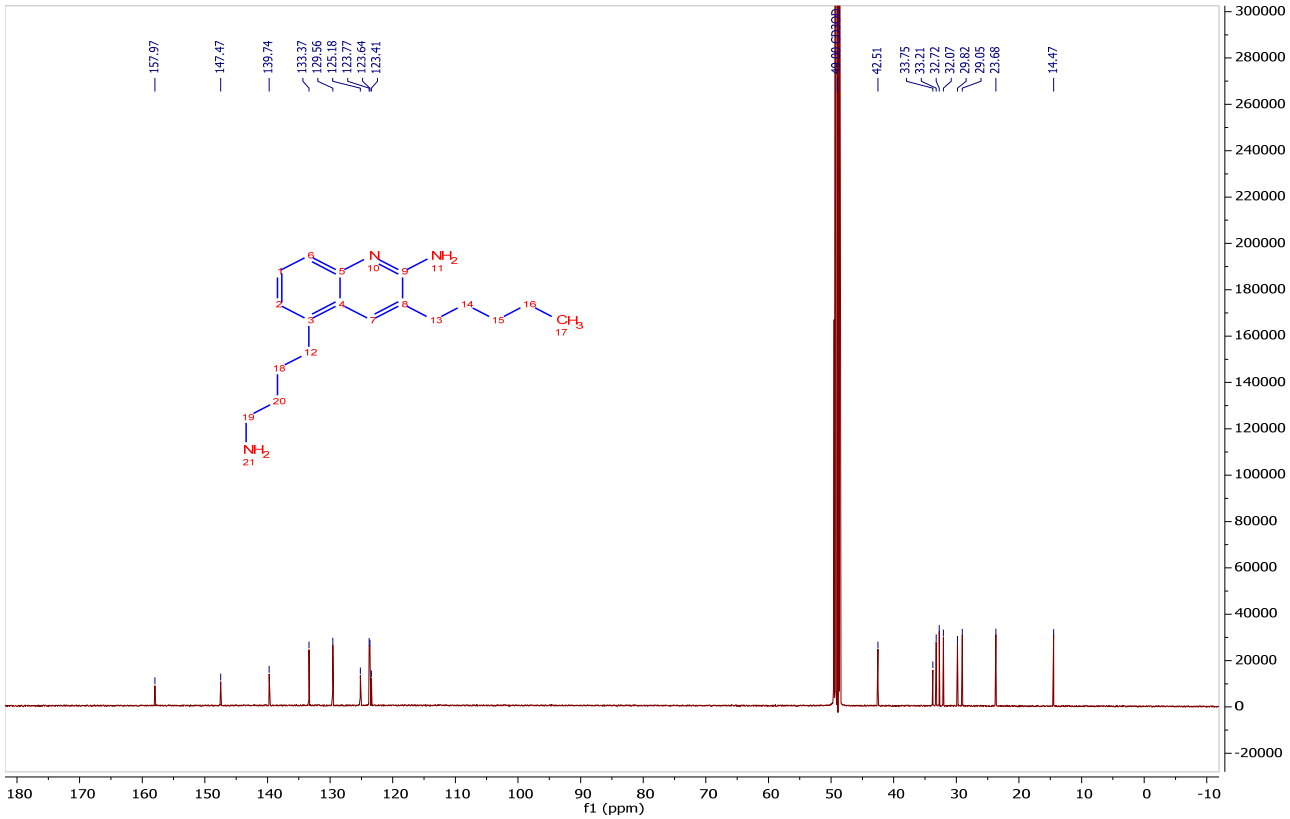




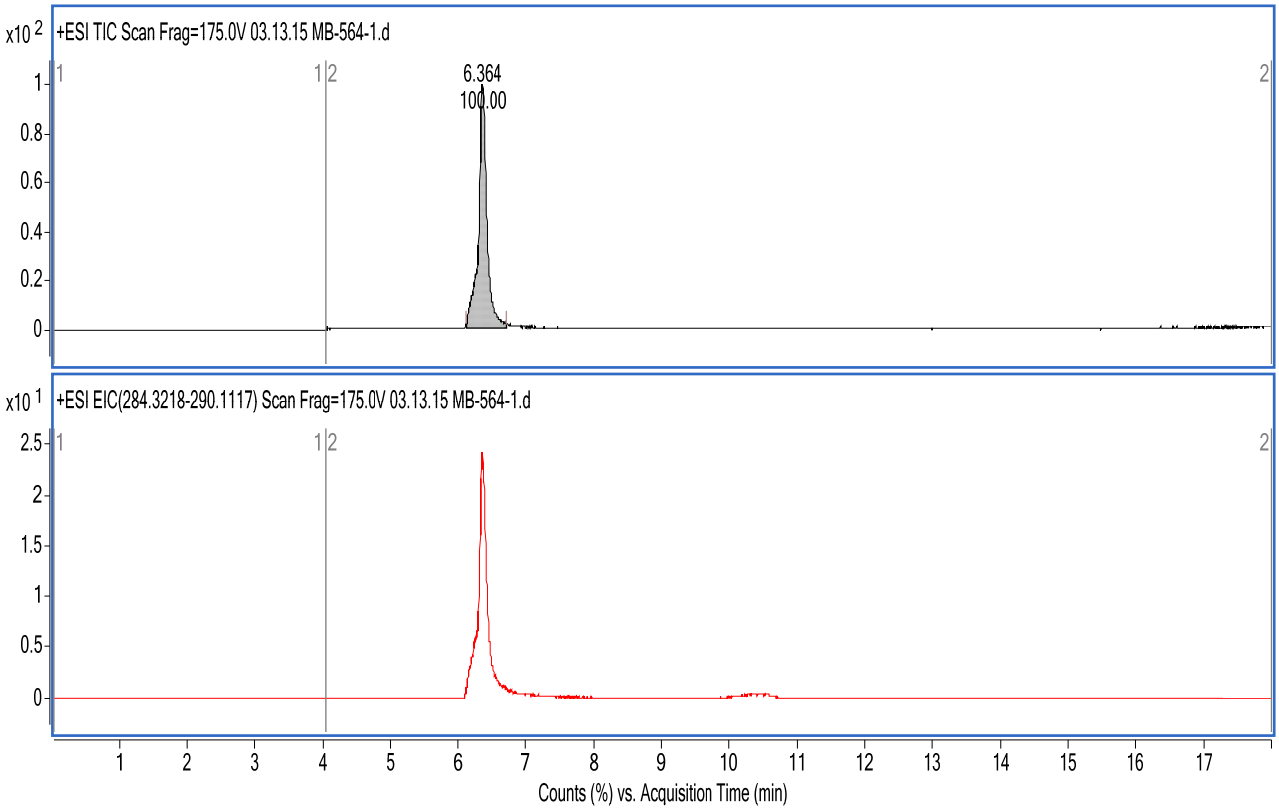
Exact Mass: 282.1965

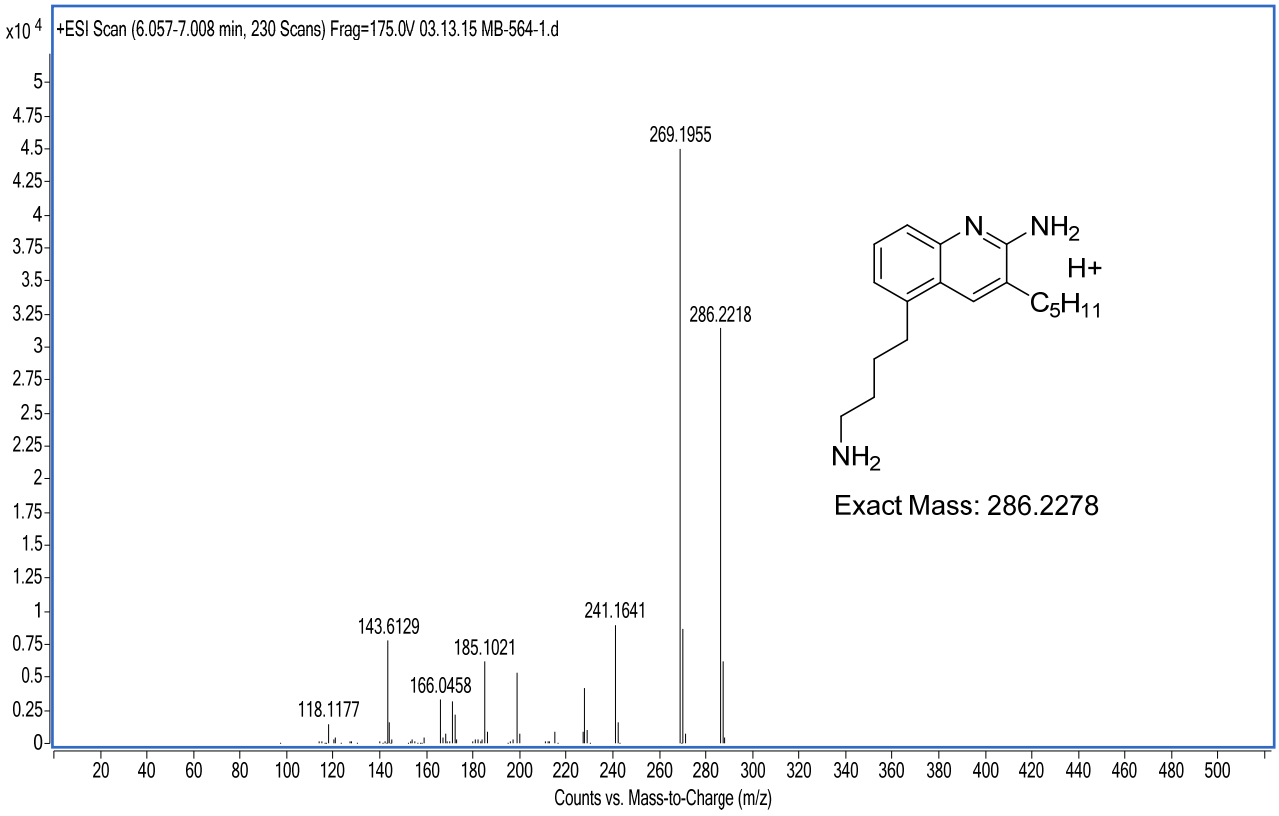
Compound **34a:** ^{1}H and ^{13}C NMR Spectrum



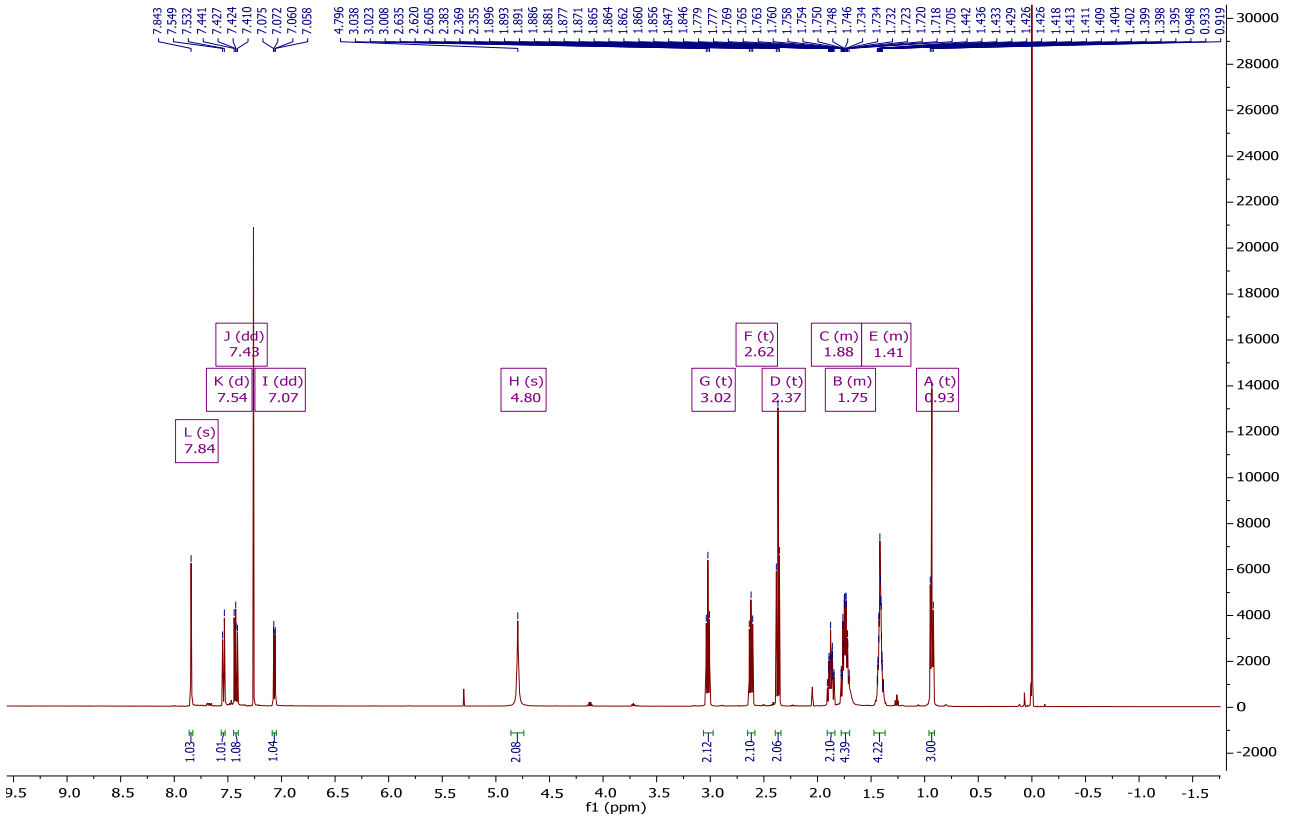


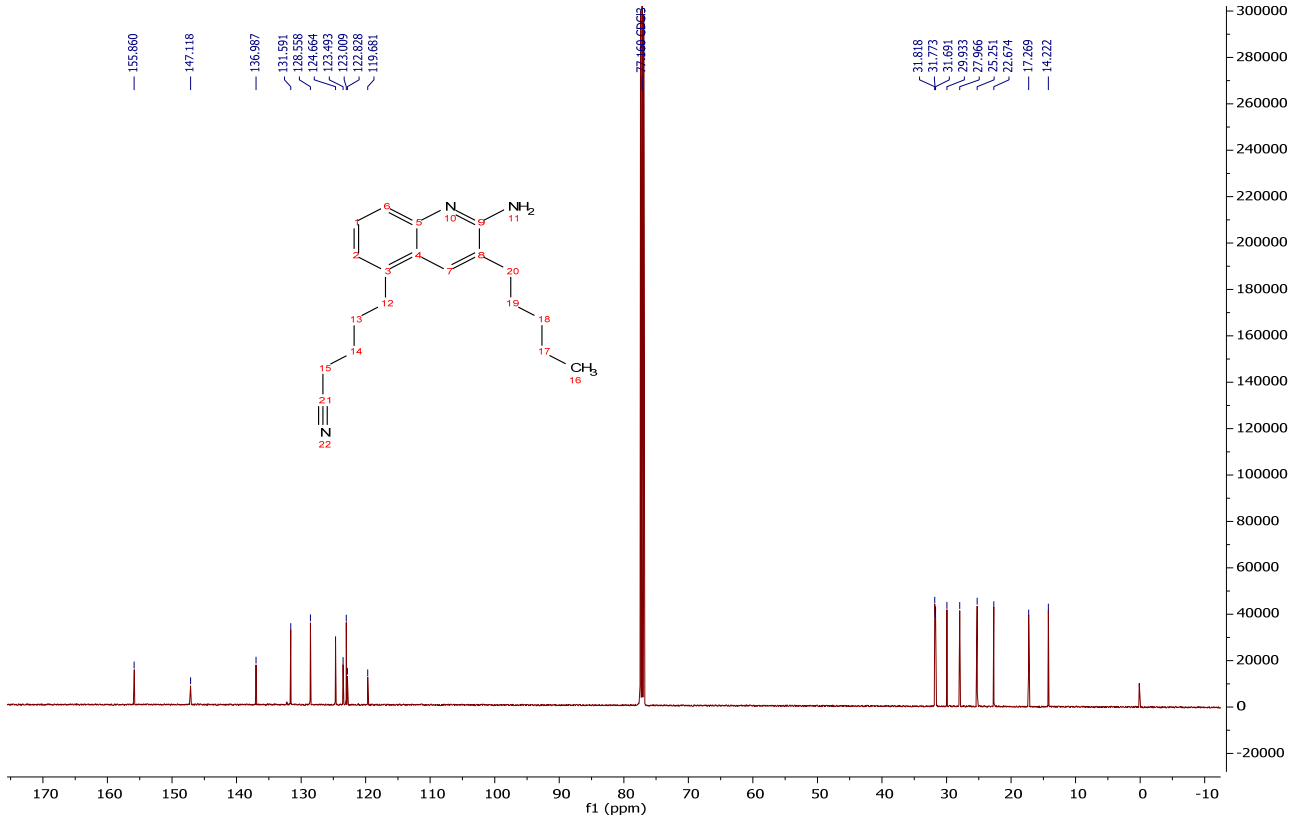
Compound **34a:** LC-MS



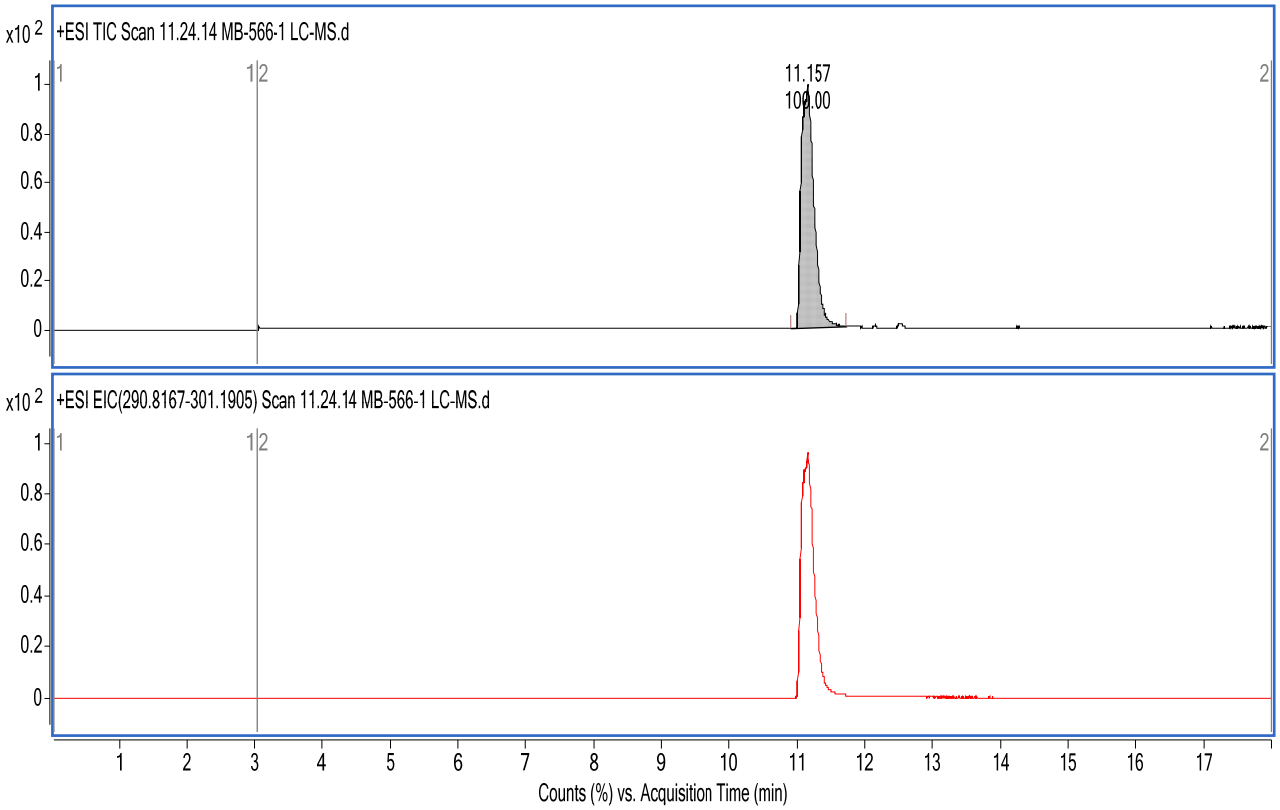


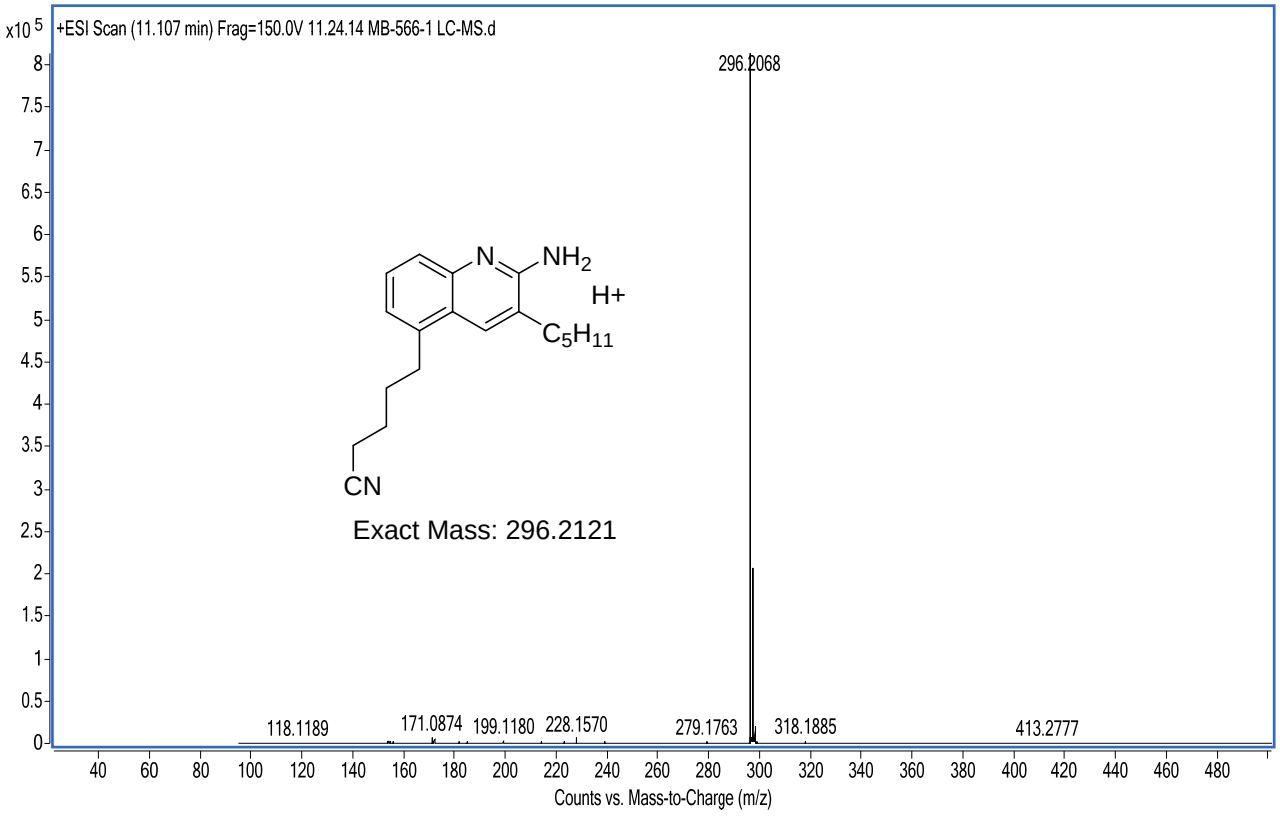
Compound **30b:** ^{1}H and ^{13}C NMR Spectrum



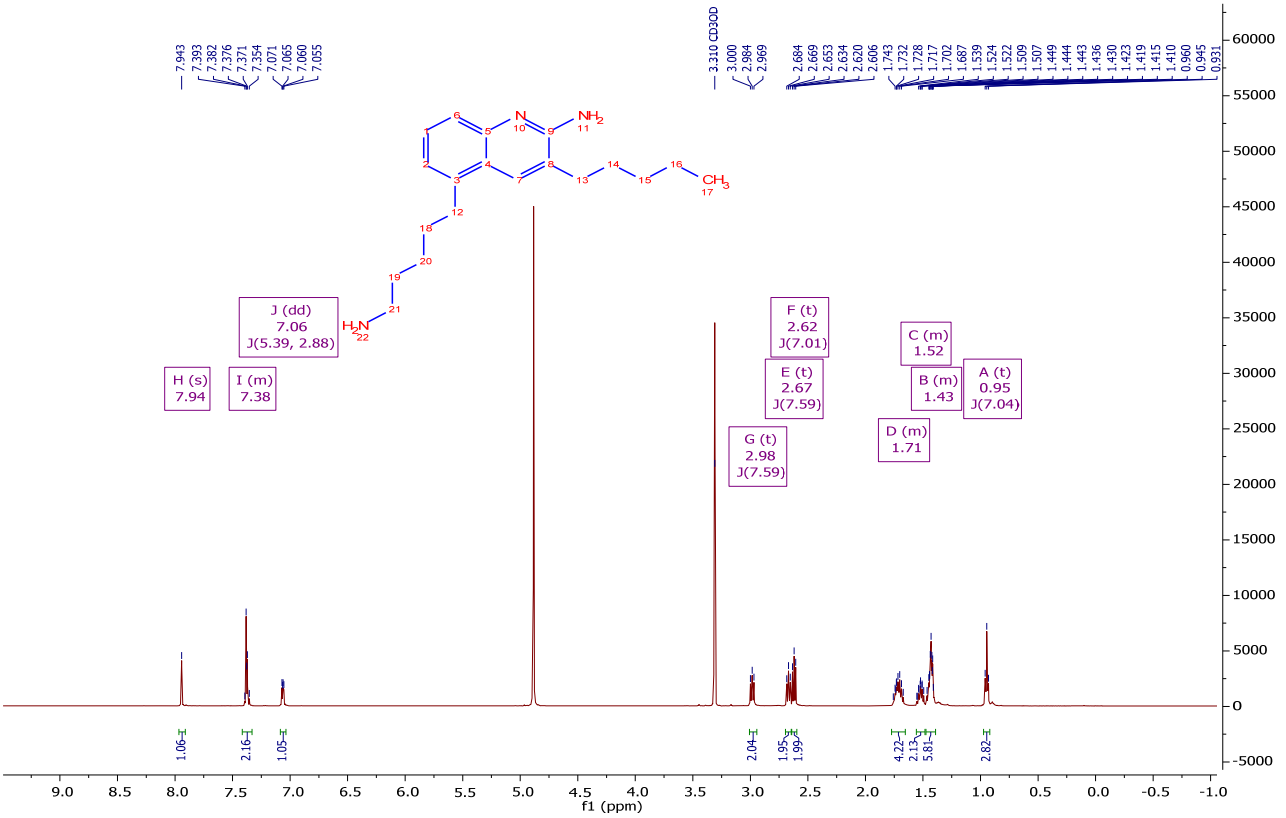


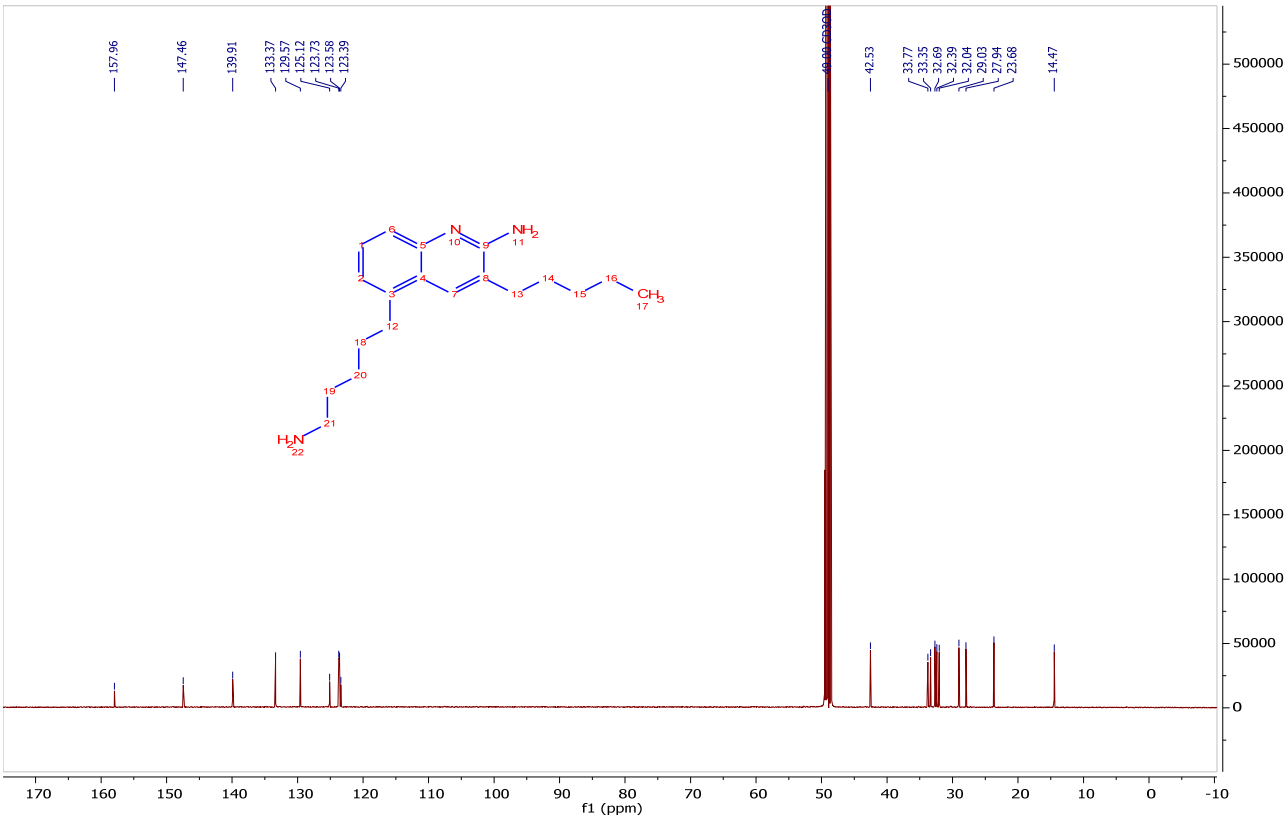
Compound **30b:** LC-MS



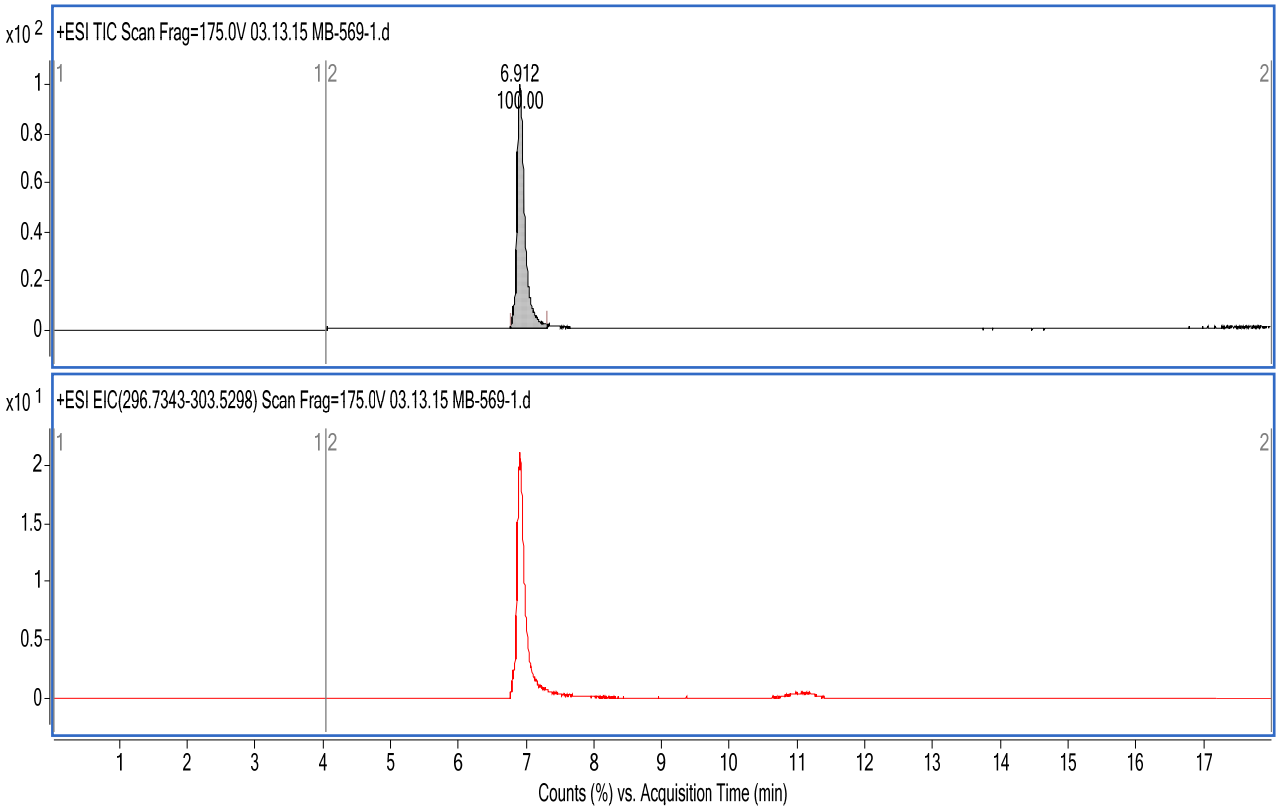


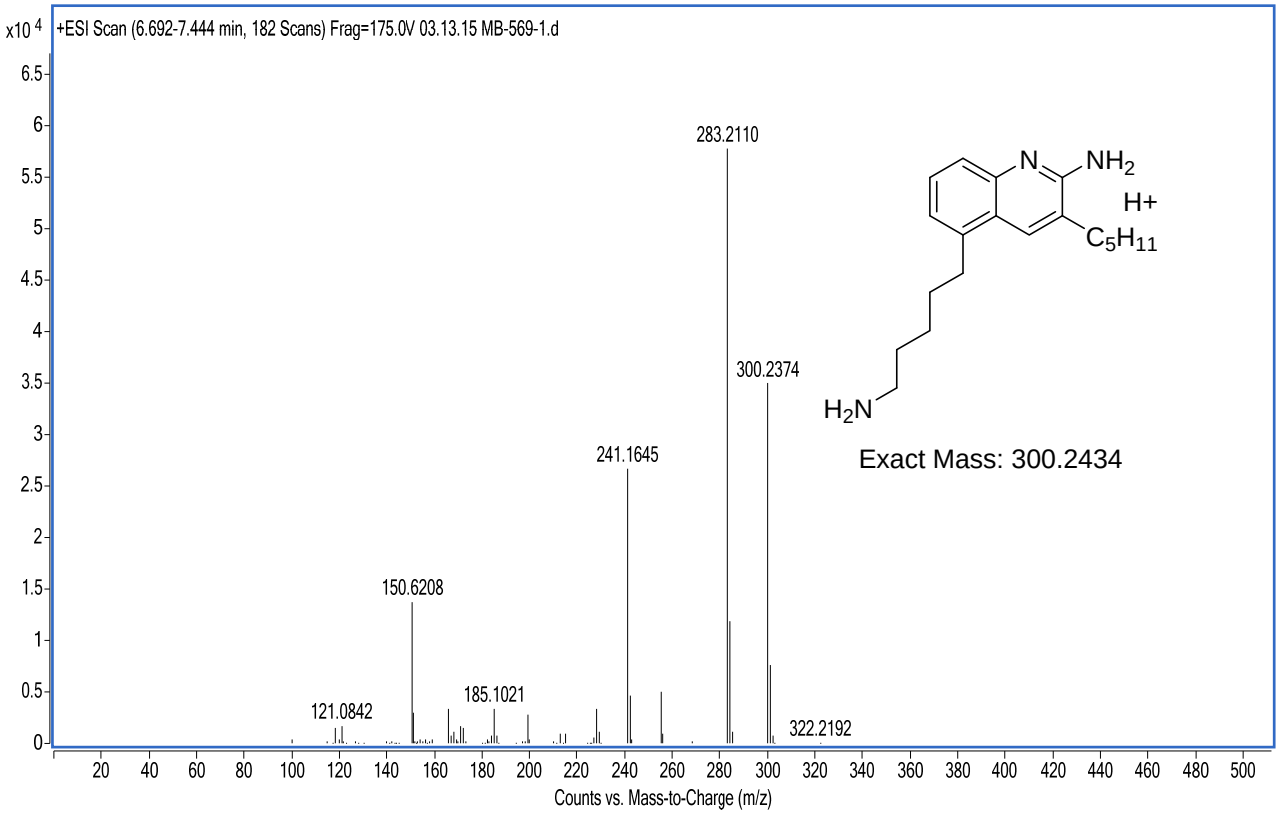
Compound **34b:** ^{1}H and ^{13}C NMR Spectrum



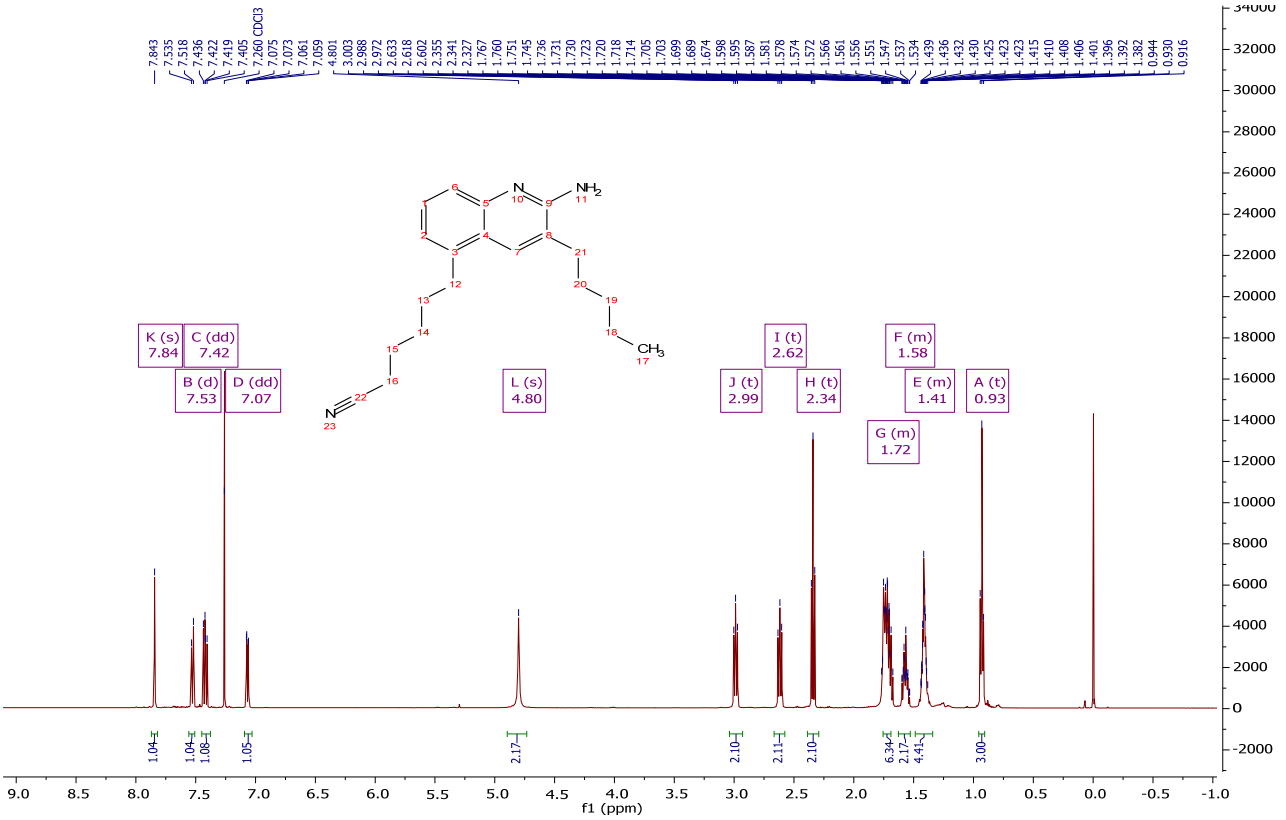


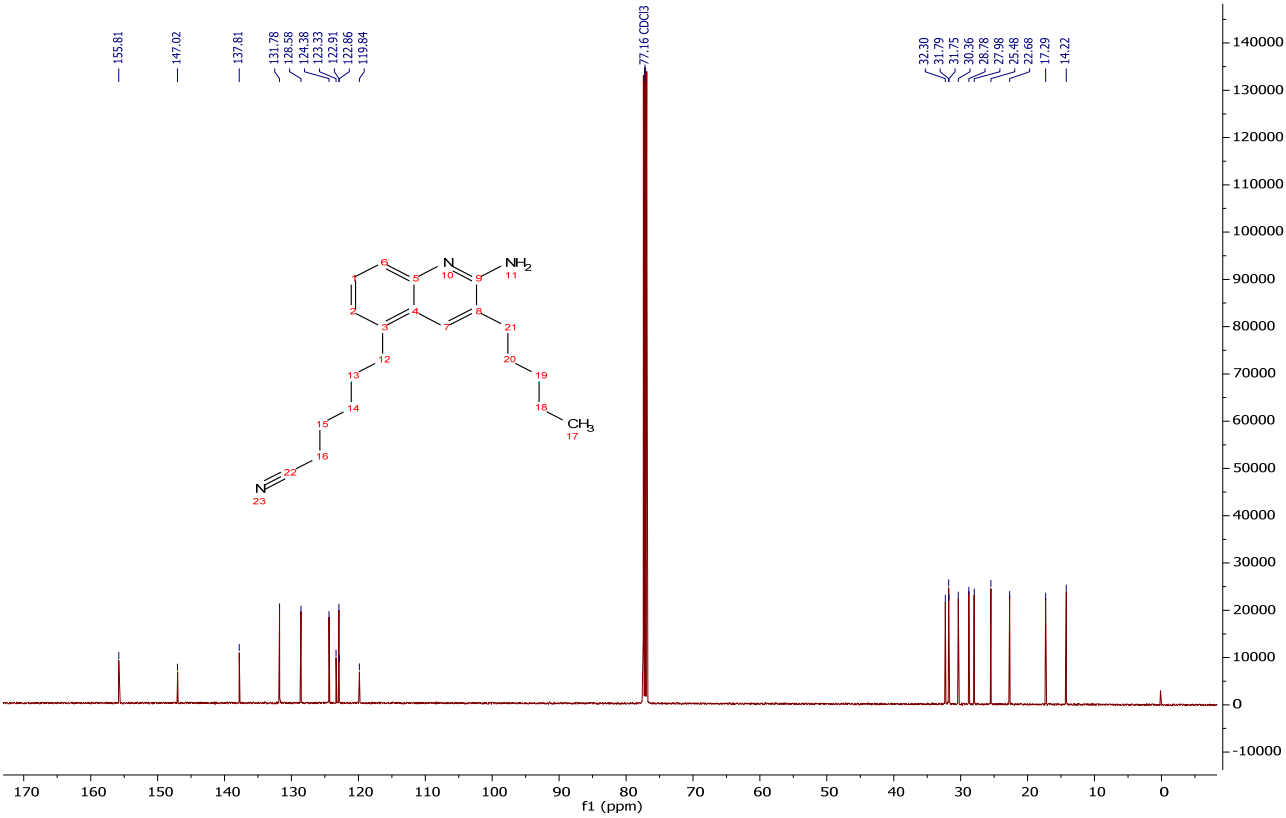
Compound **34b:** LC-MS



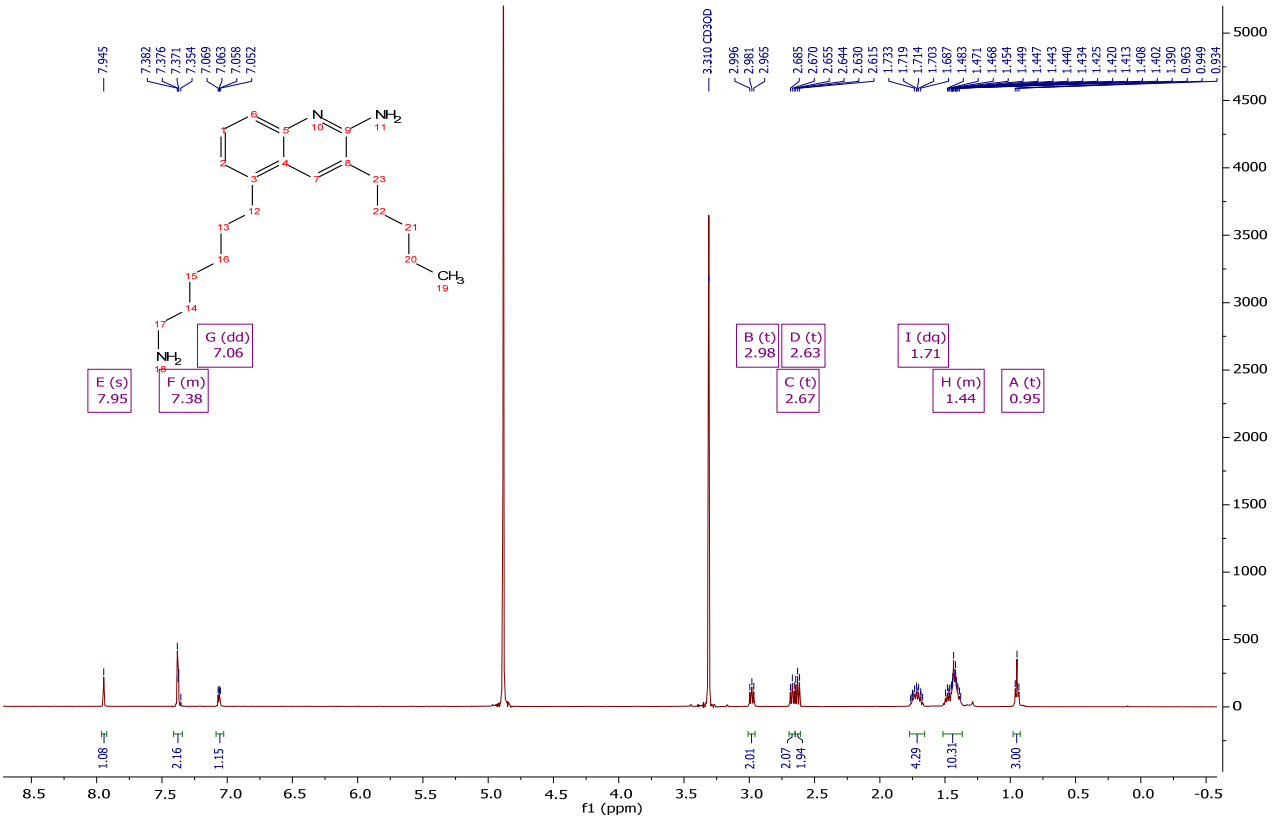


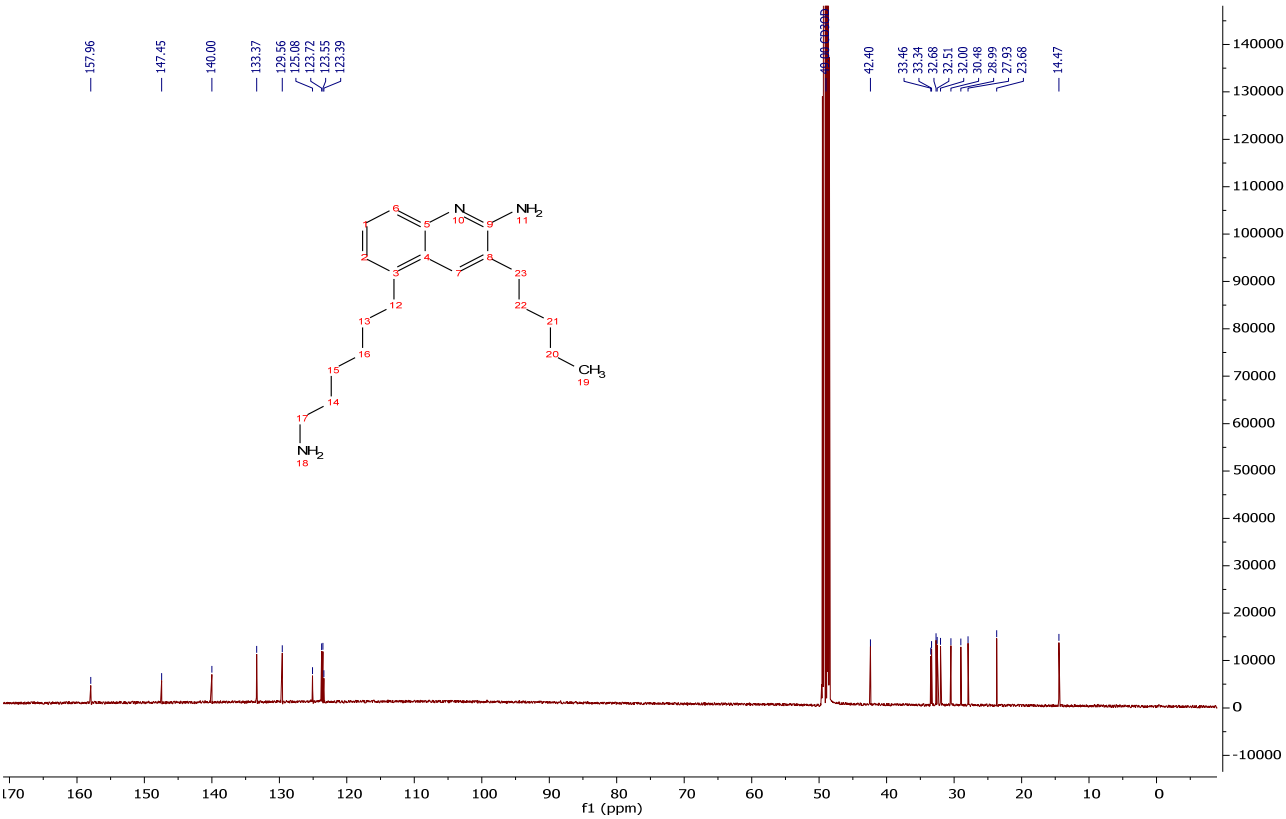
Compound **30c:** ^{1}H and ^{13}C NMR Spectrum



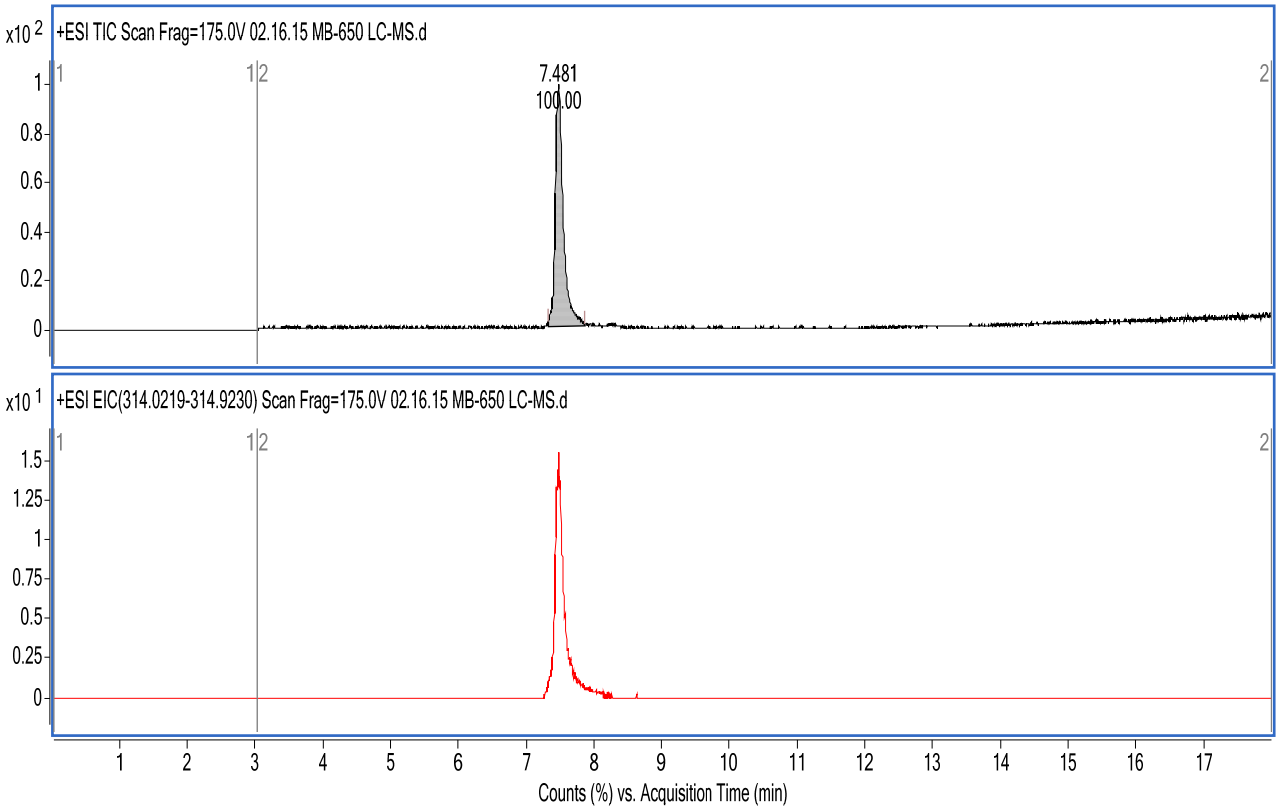


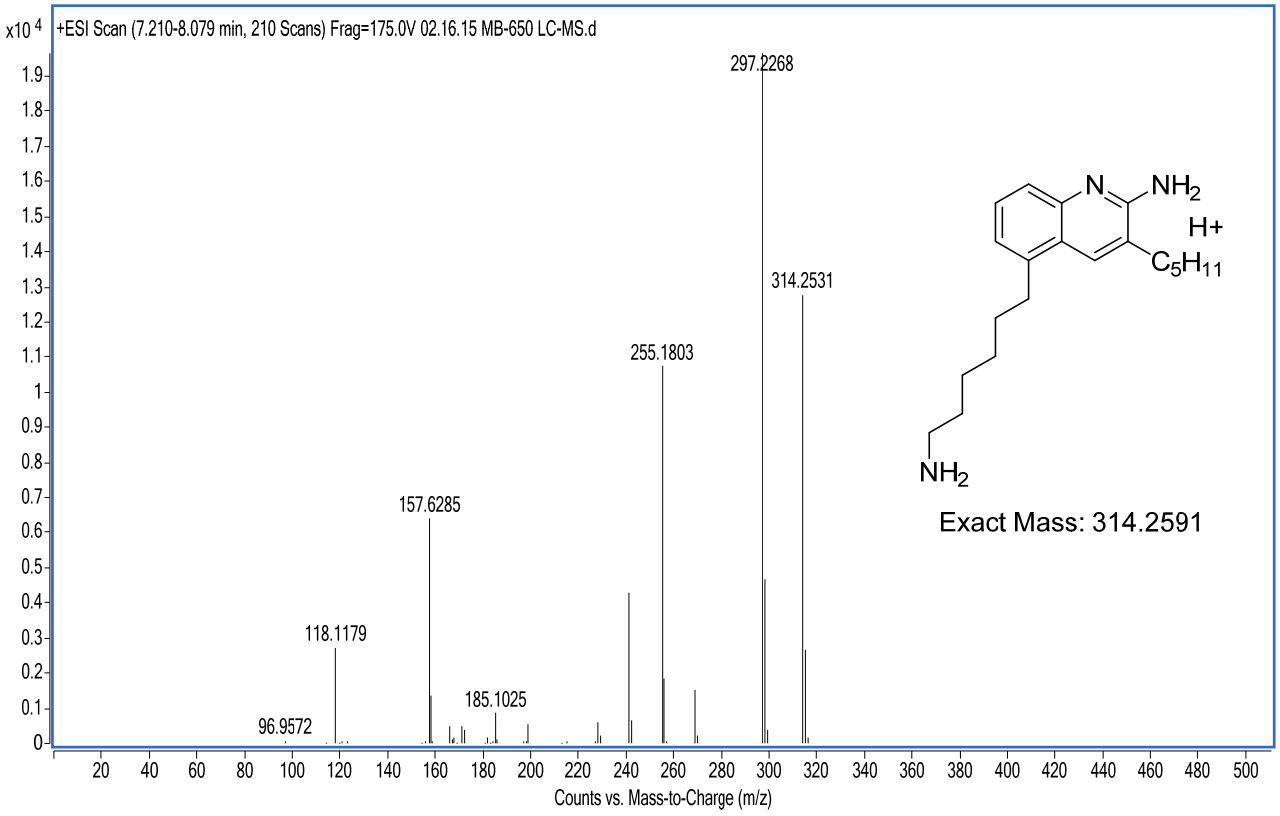
Compound **34c:** ^{1}H and ^{13}C NMR Spectrum



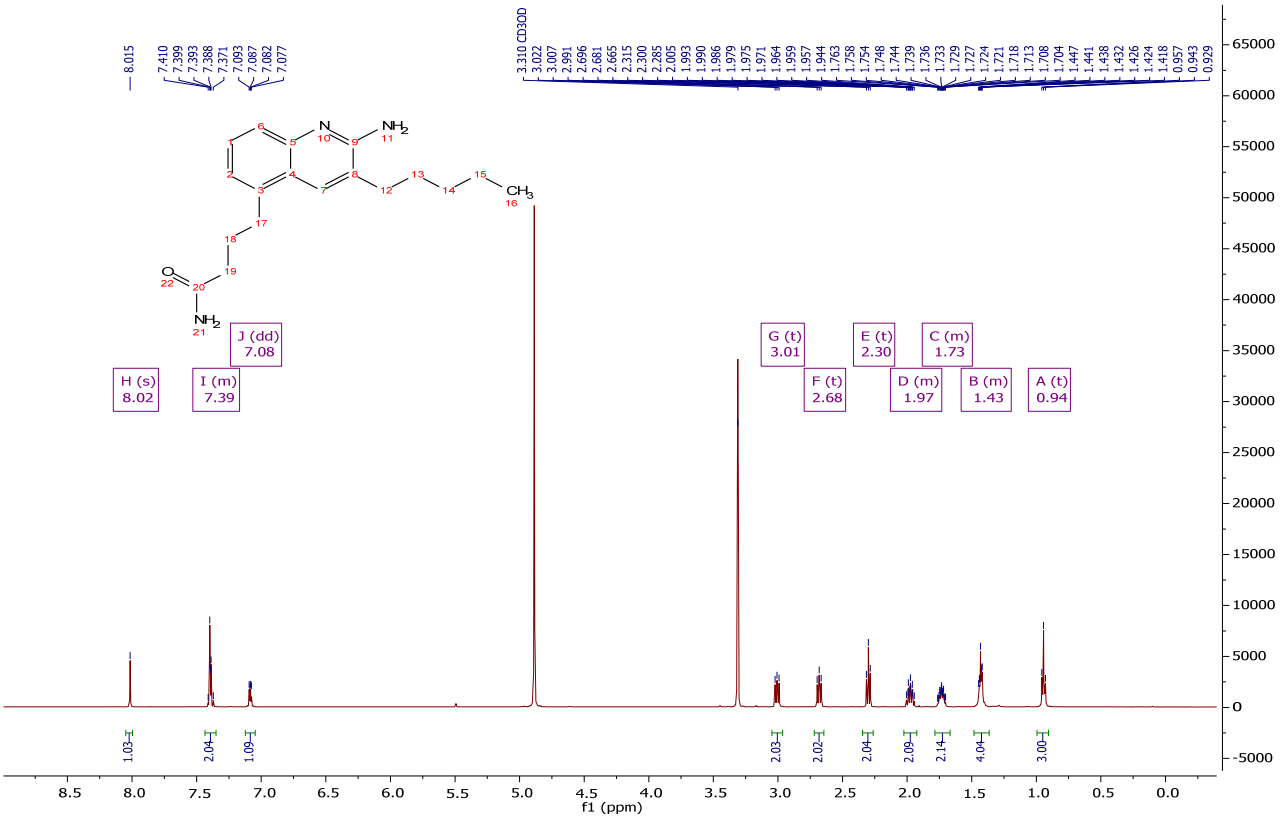


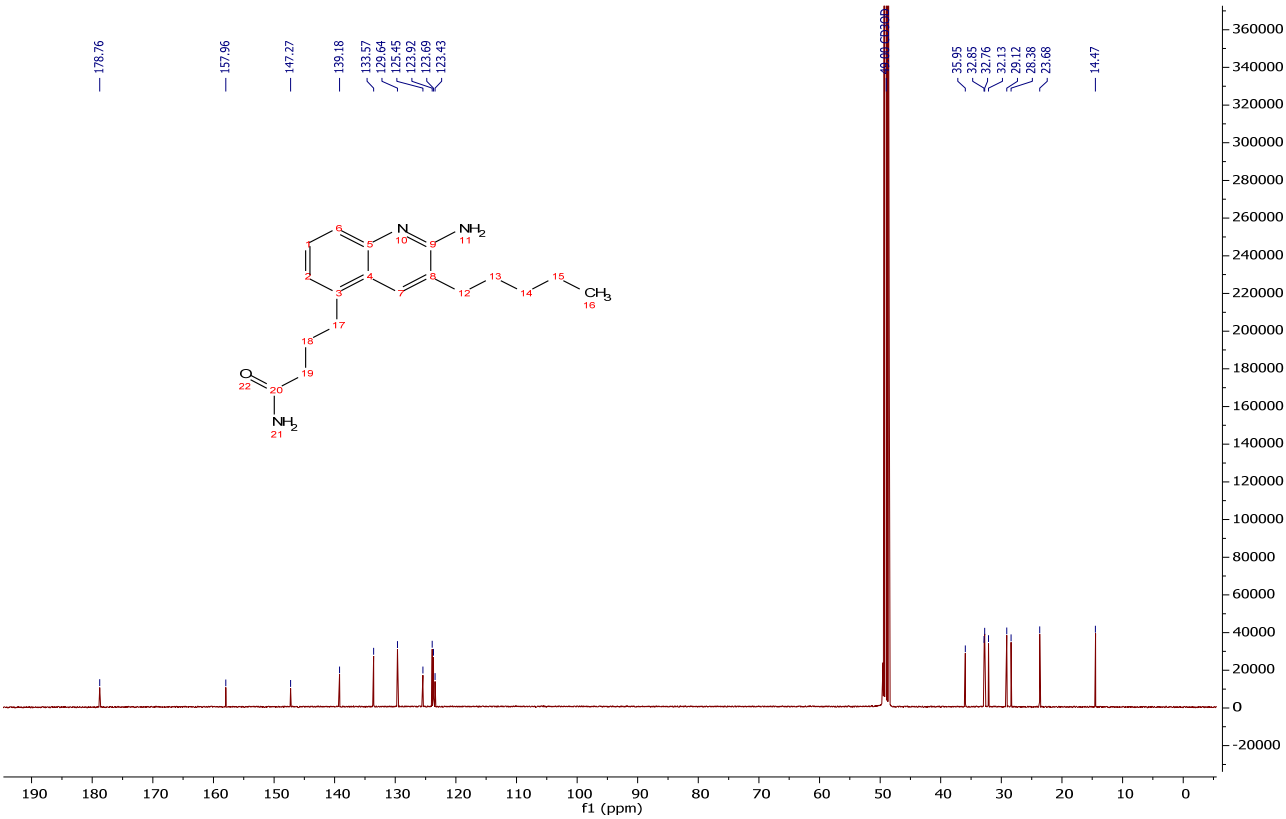
Compound **34c:** LC-MS



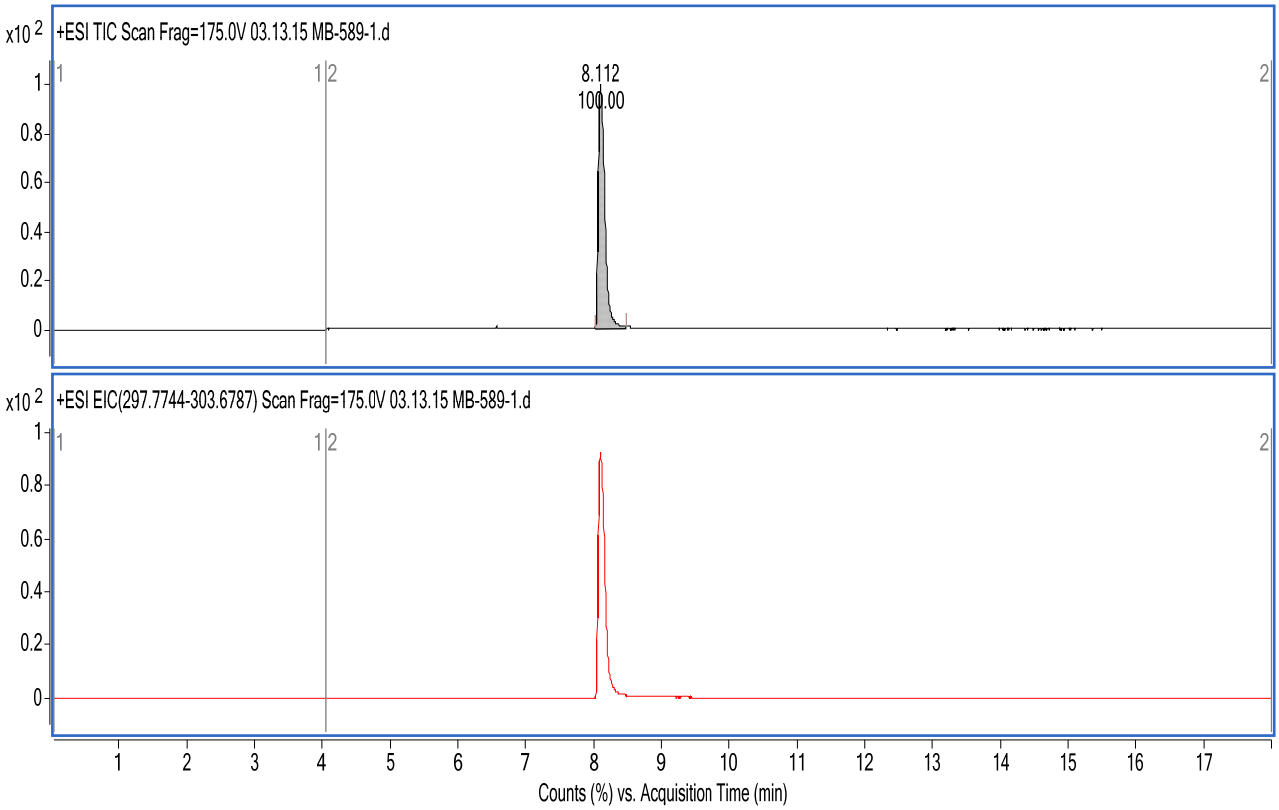


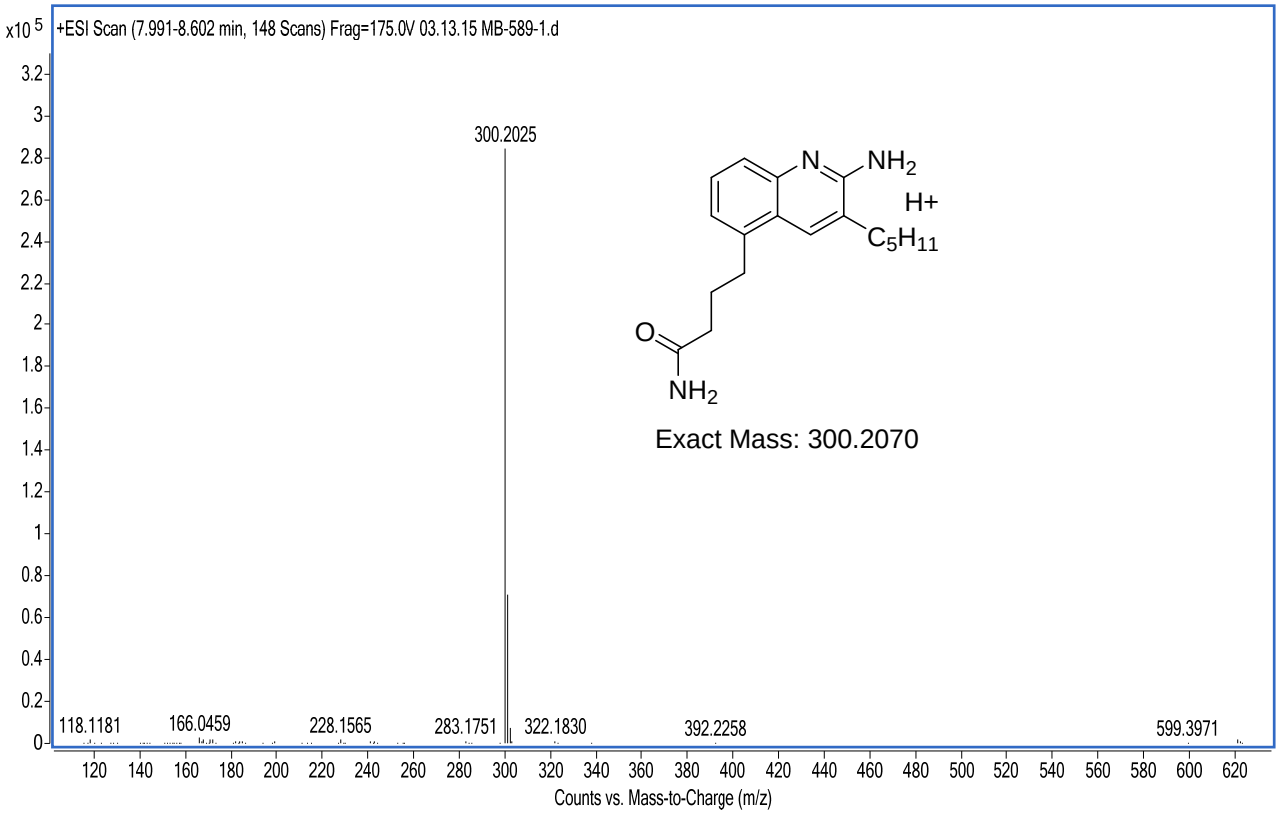
Compound **34d:** ^{1}H and ^{13}C NMR Spectrum





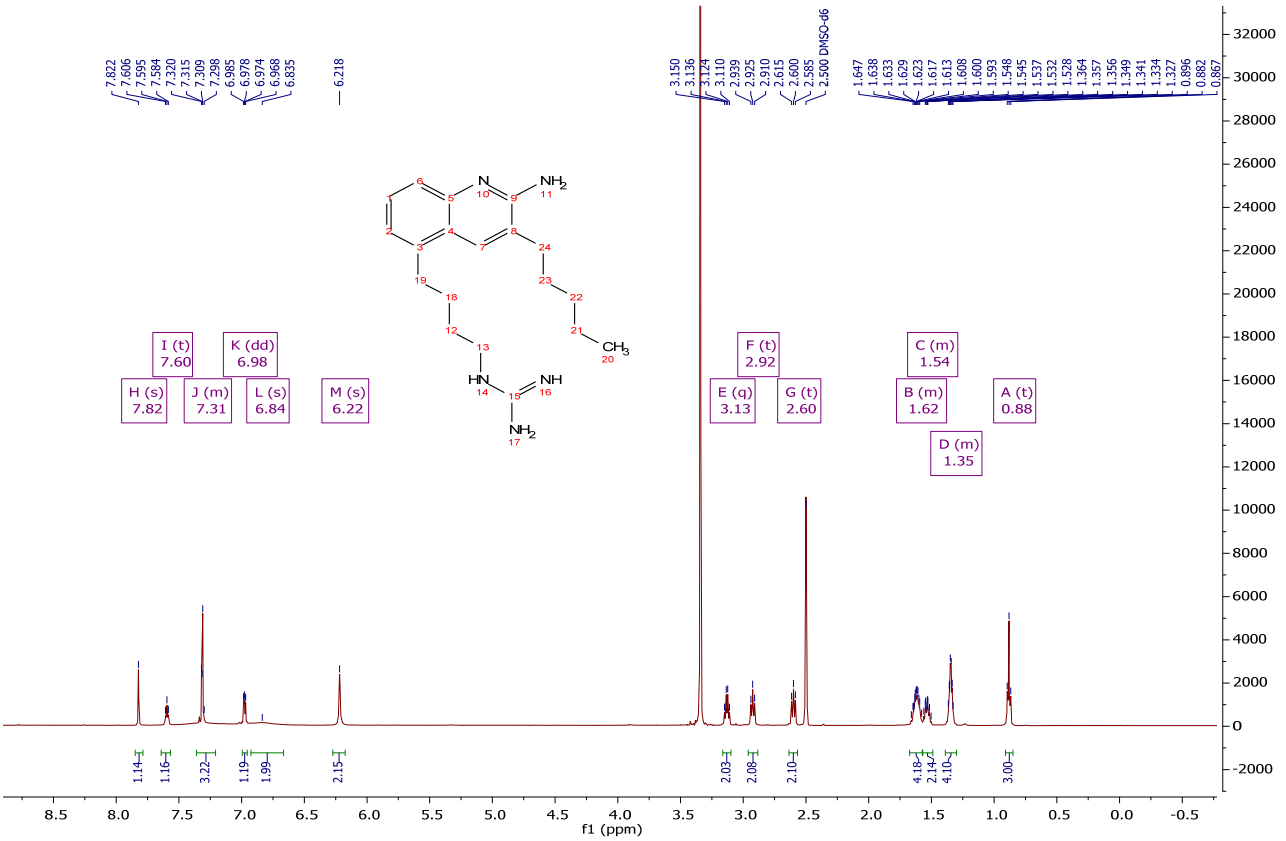
Compound **34d:** LC-MS

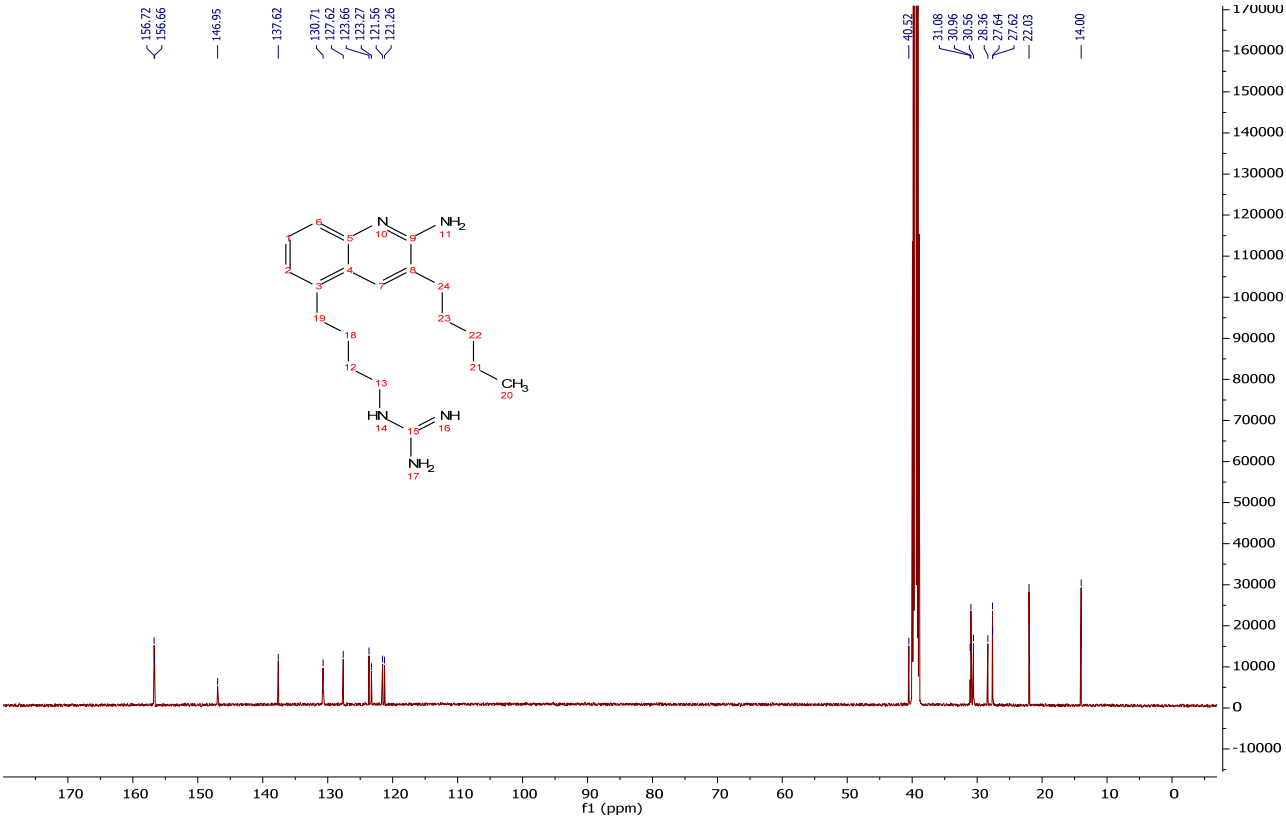




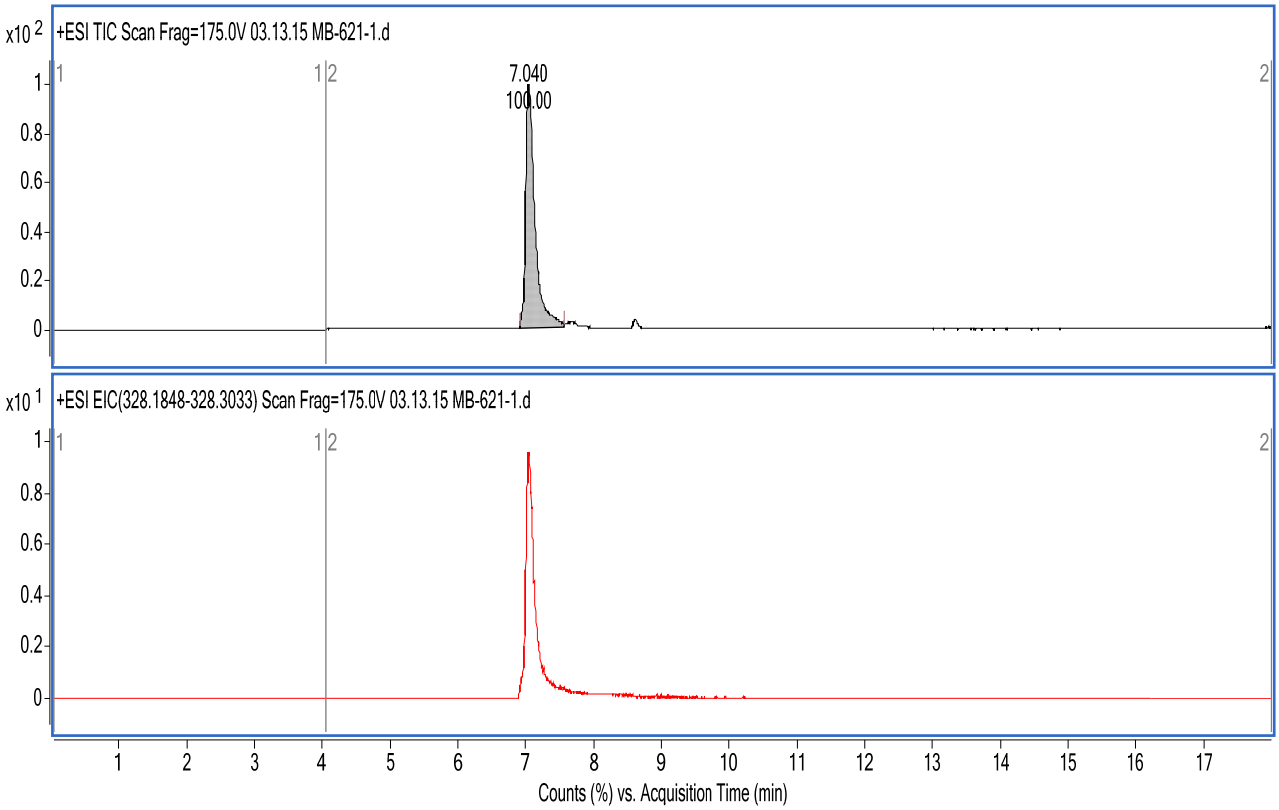
Exact Mass: 300.2070

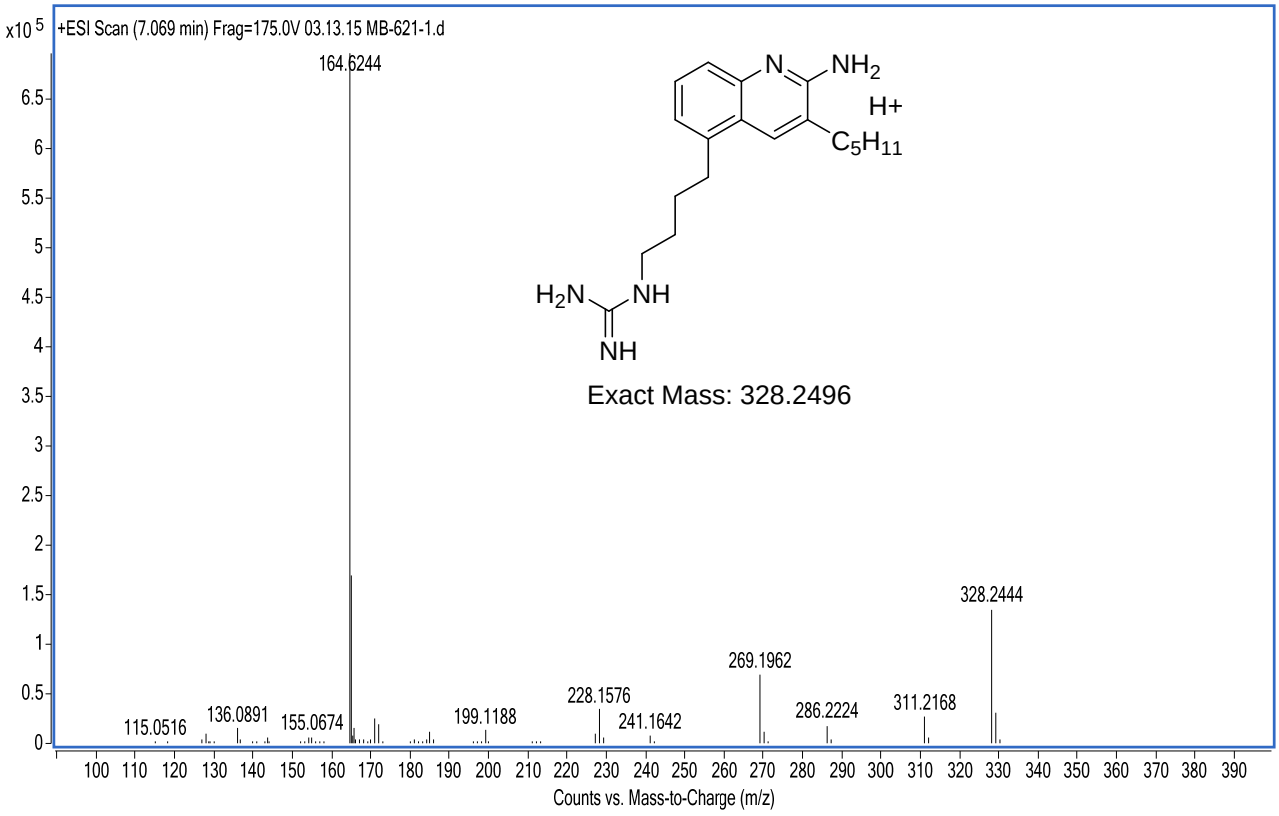
Compound **34e:** ^{1}H and ^{13}C NMR Spectrum





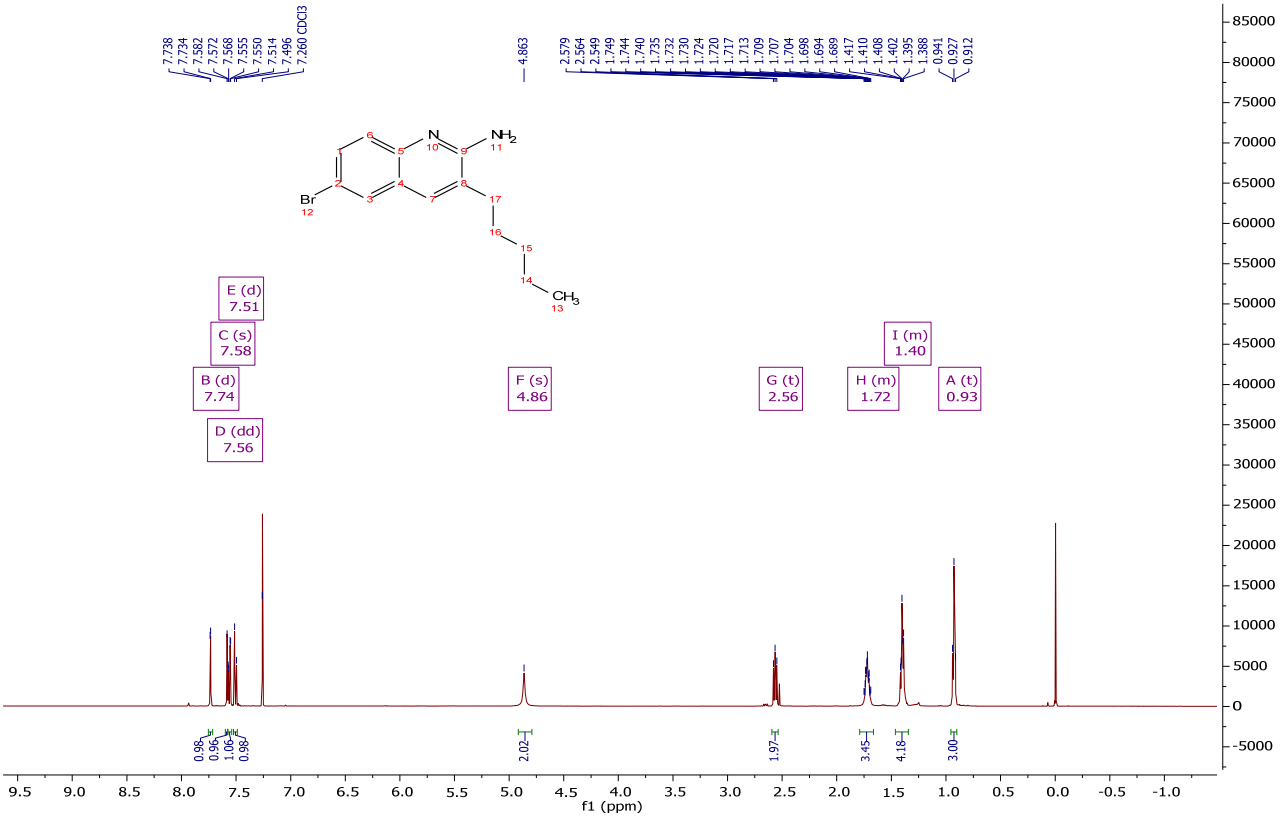
Compound **34e:** LC-MS

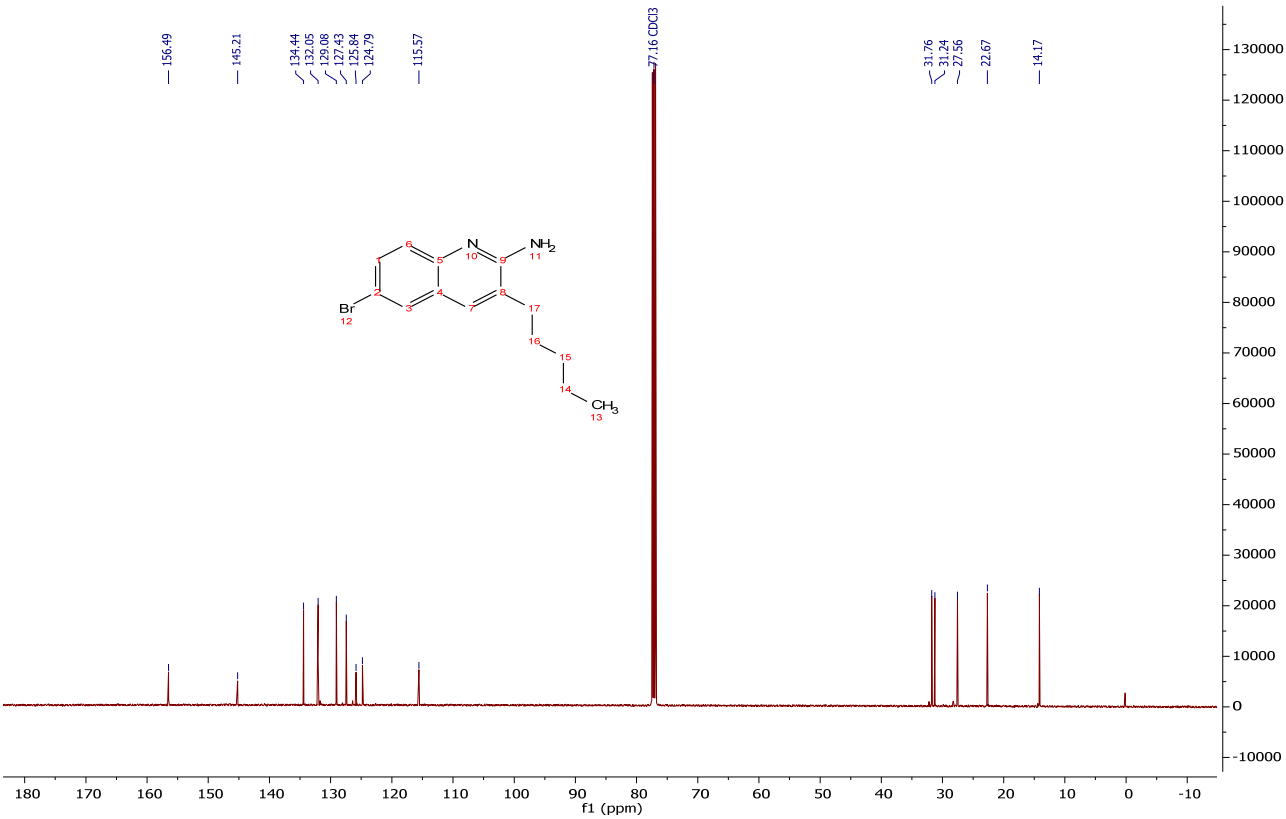




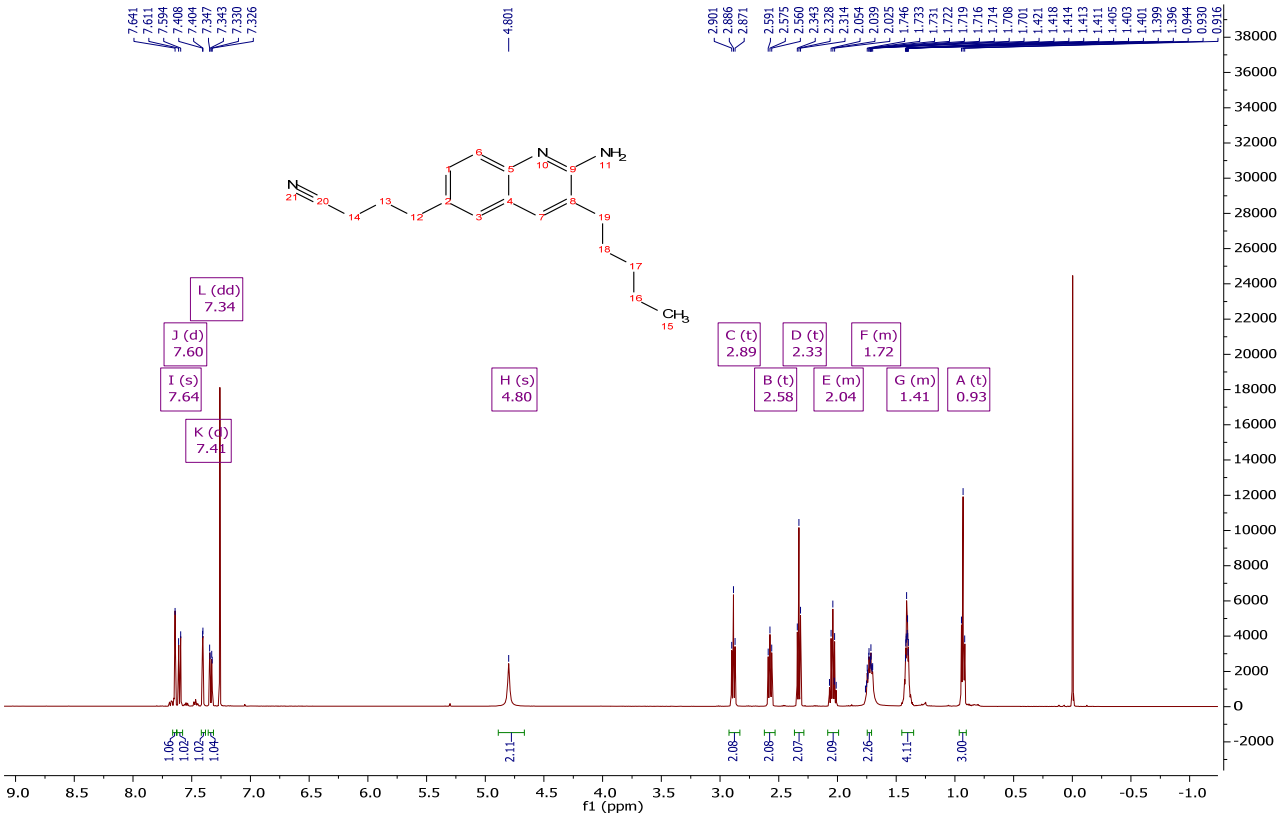
Exact Mass: 328.2496

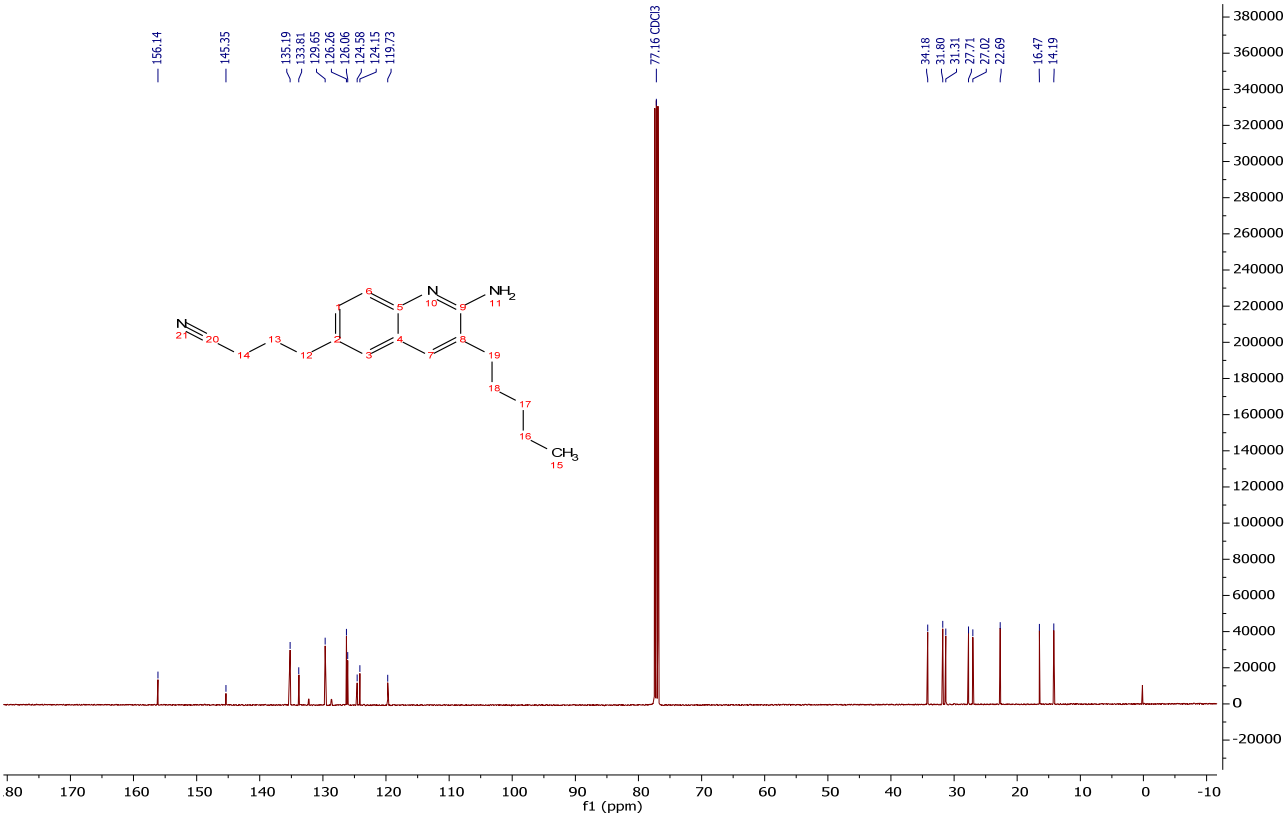
Compound **27:** ^{1}H and ^{13}C NMR Spectrum



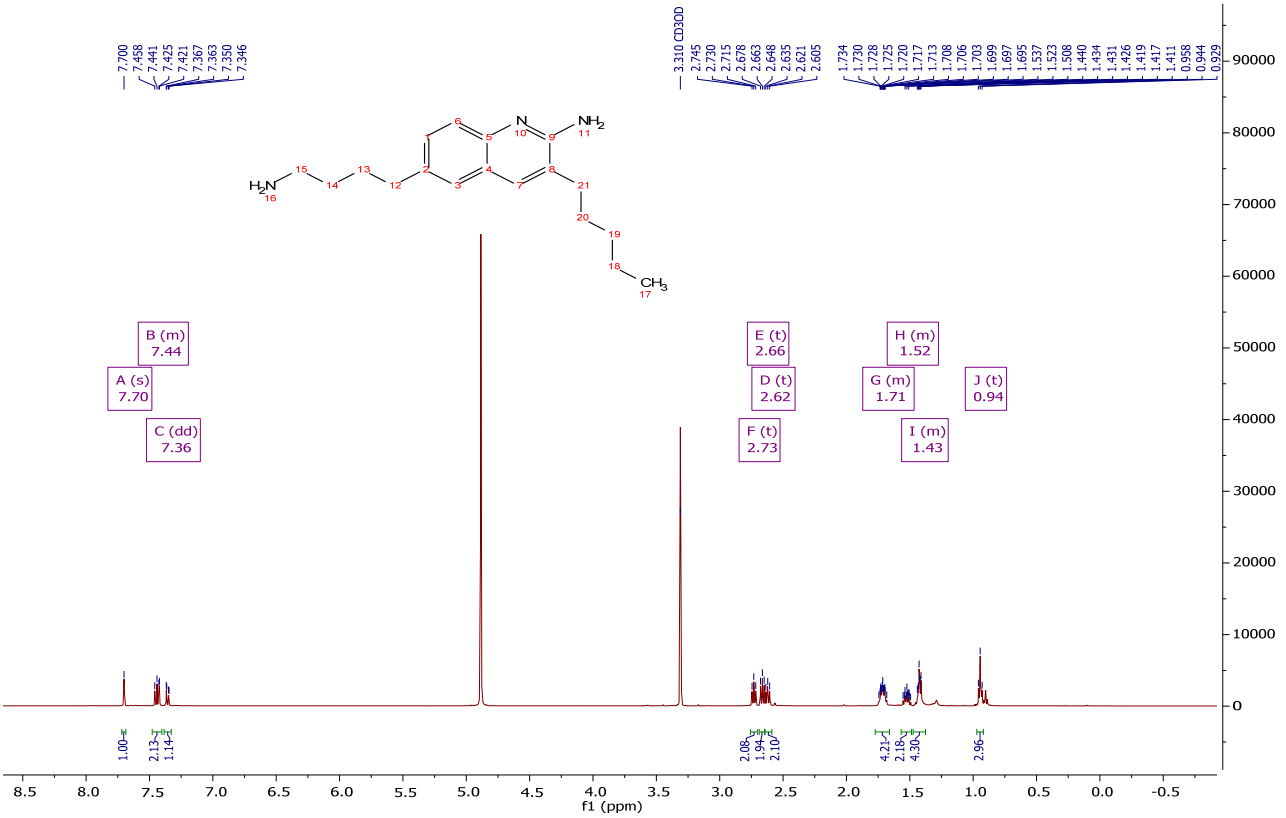


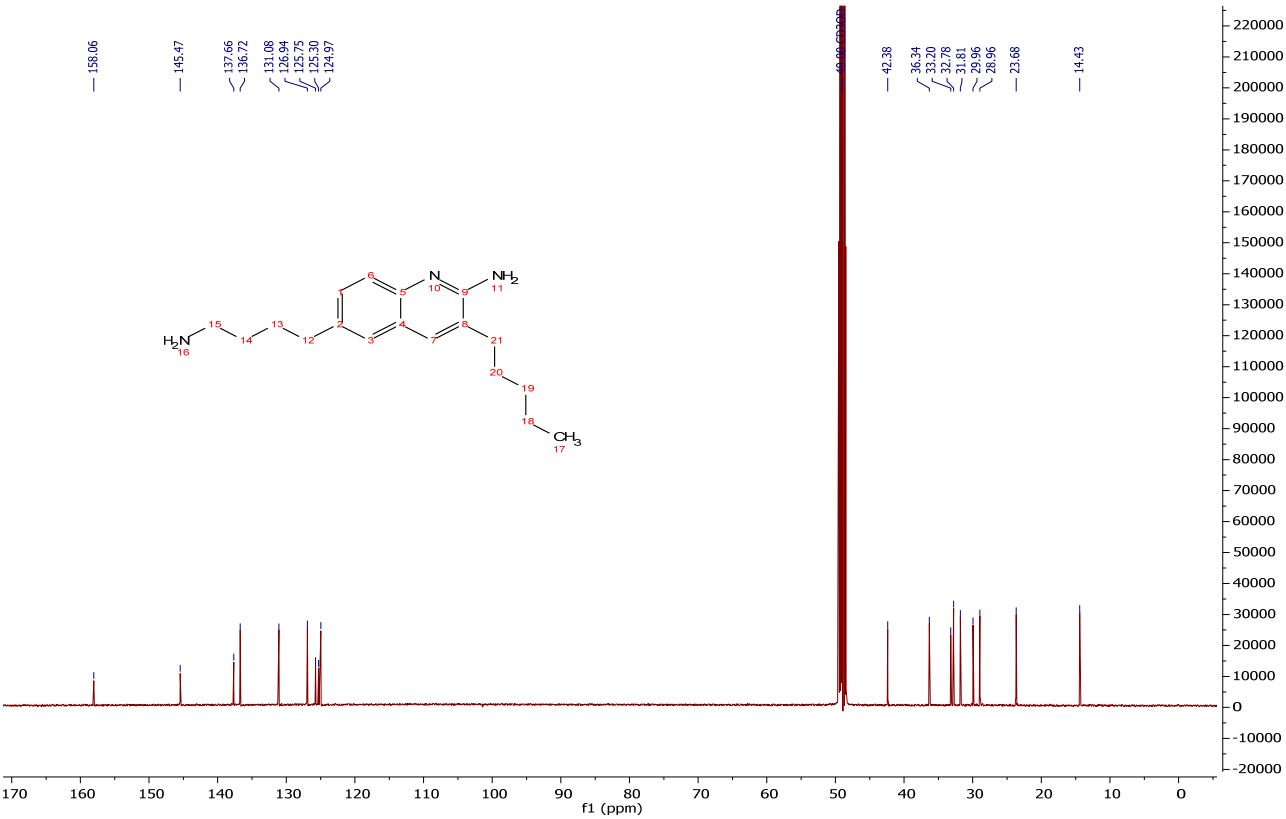
Compound **31a:** ^{1}H and ^{13}C NMR Spectrum



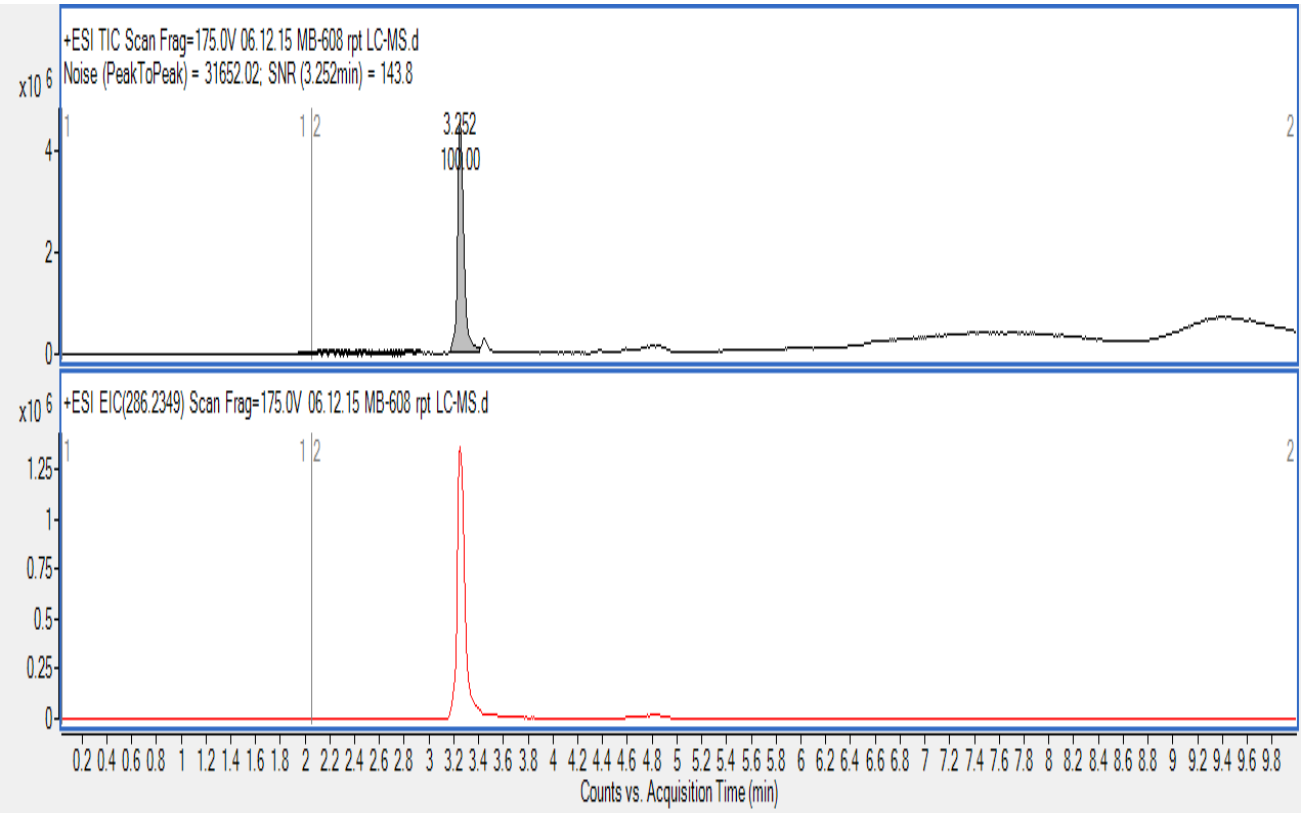


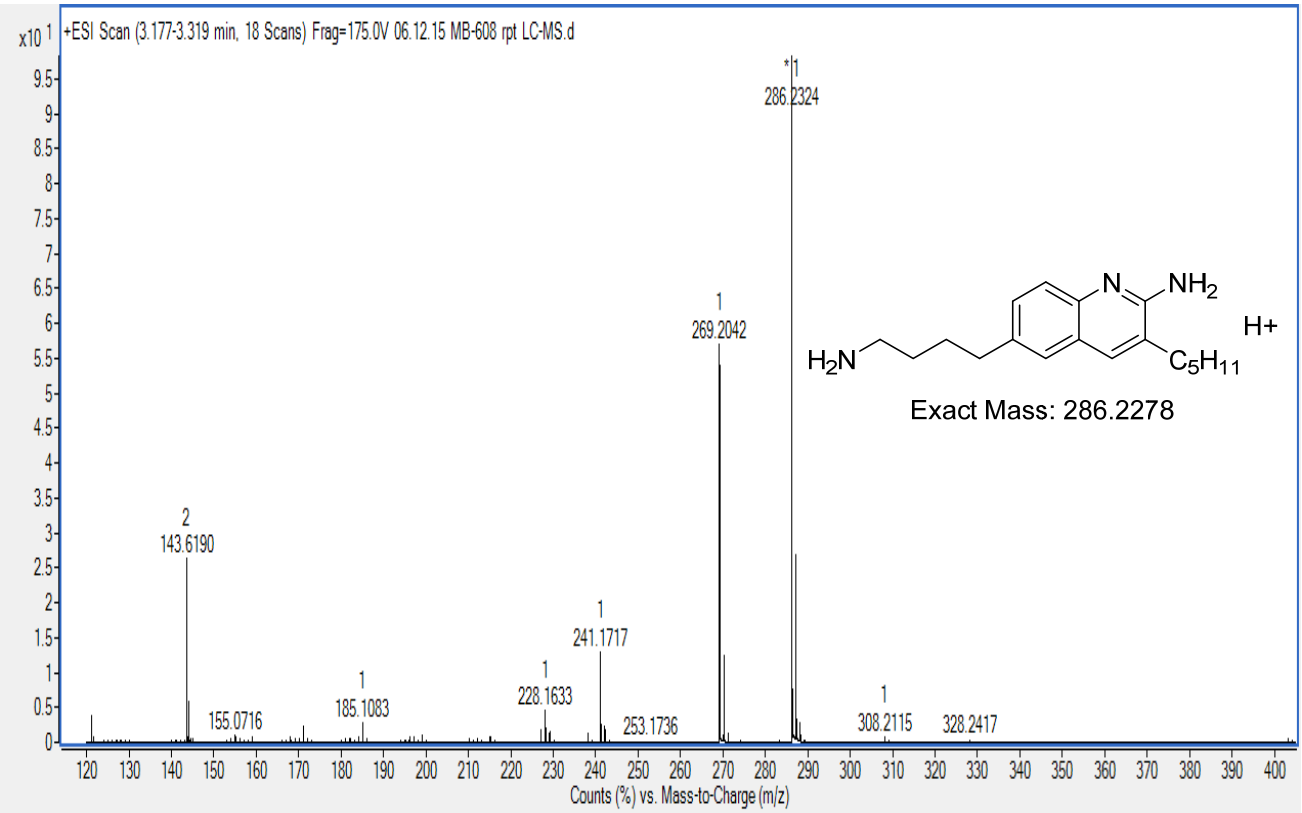
Compound **35a:** ^{1}H and ^{13}C NMR Spectrum



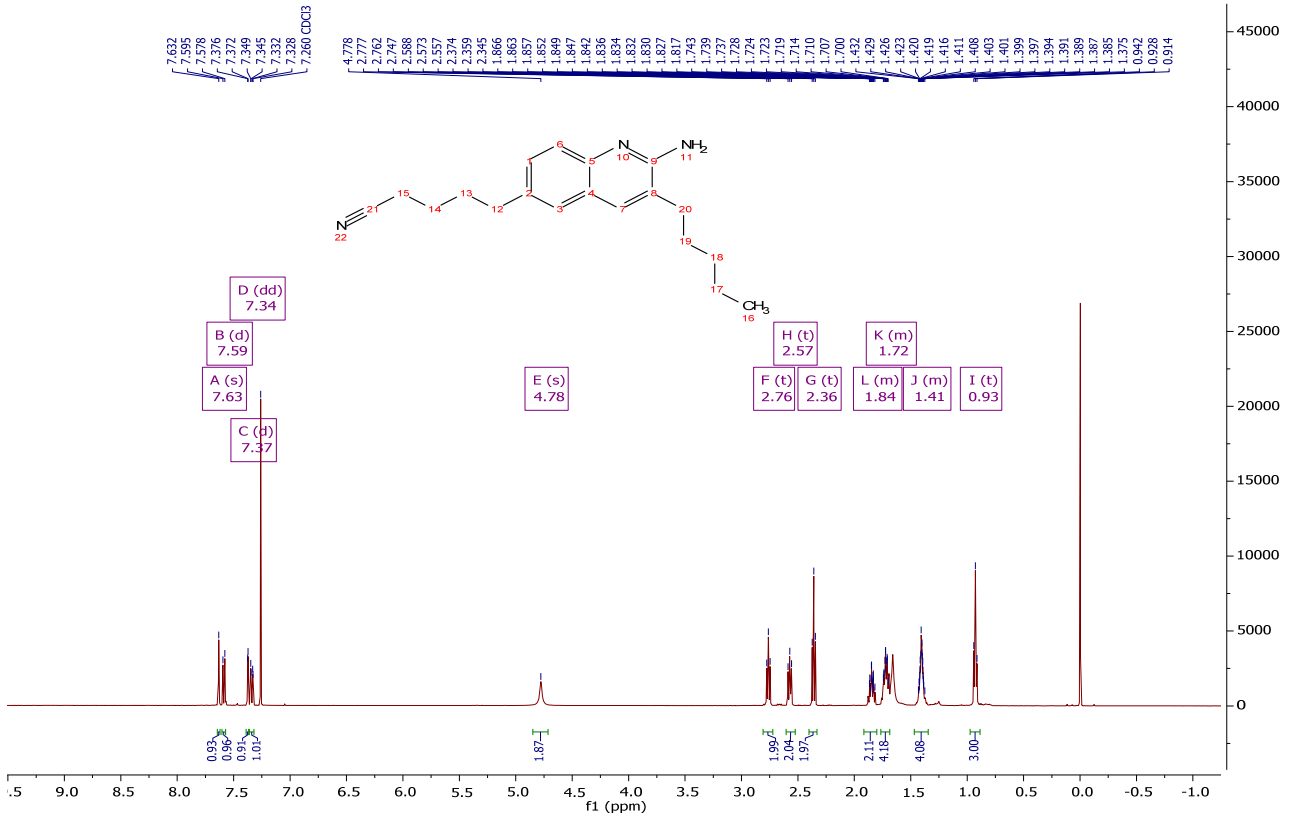


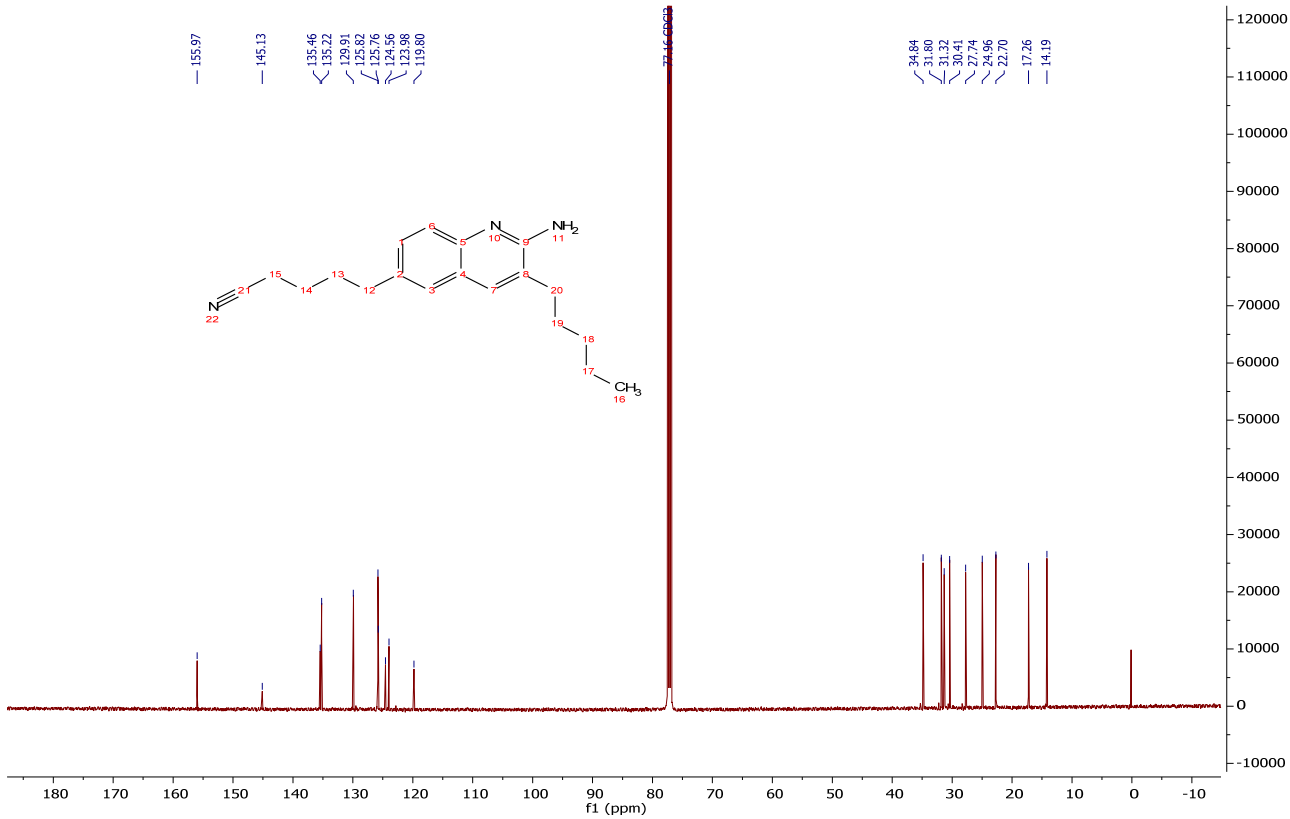
Compound **35a:** LC-MS



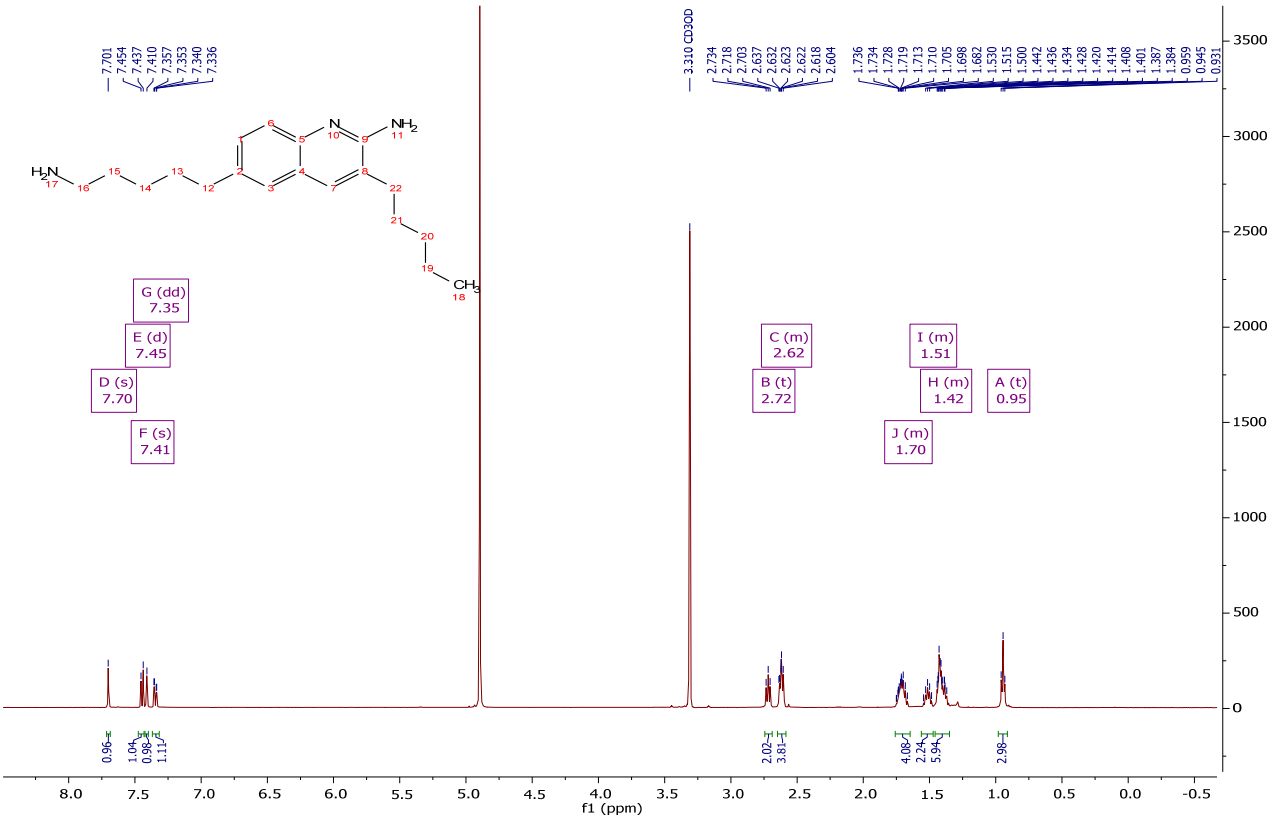


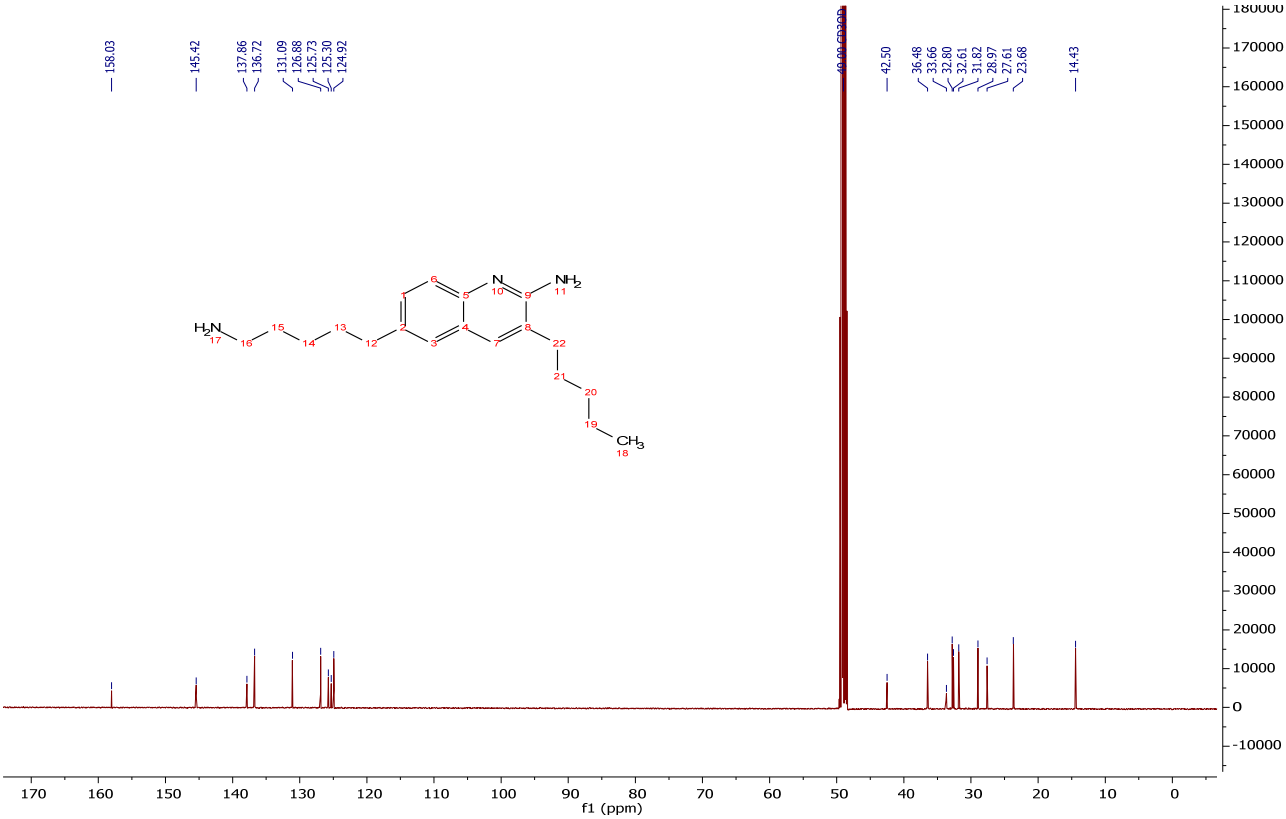
Compound **31b:** ^{1}H and ^{13}C NMR Spectrum



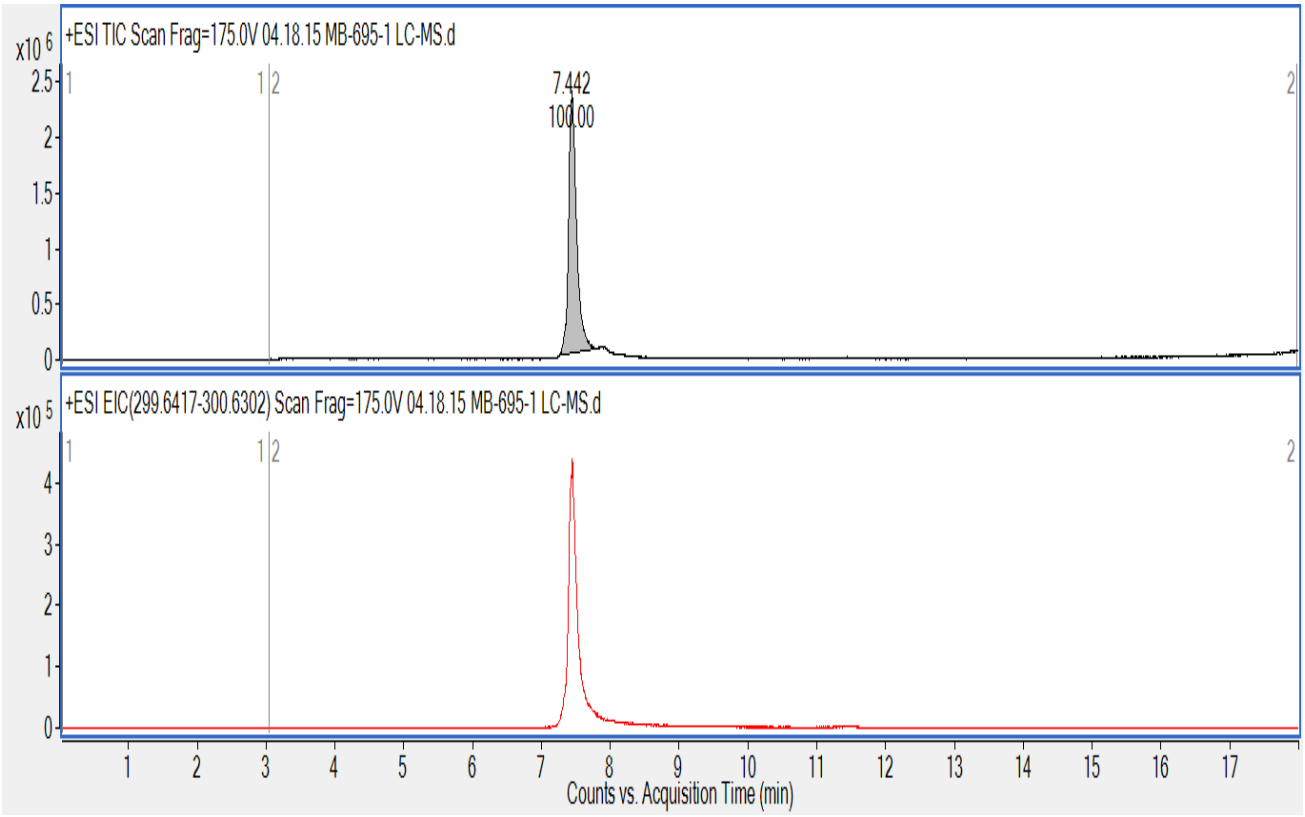


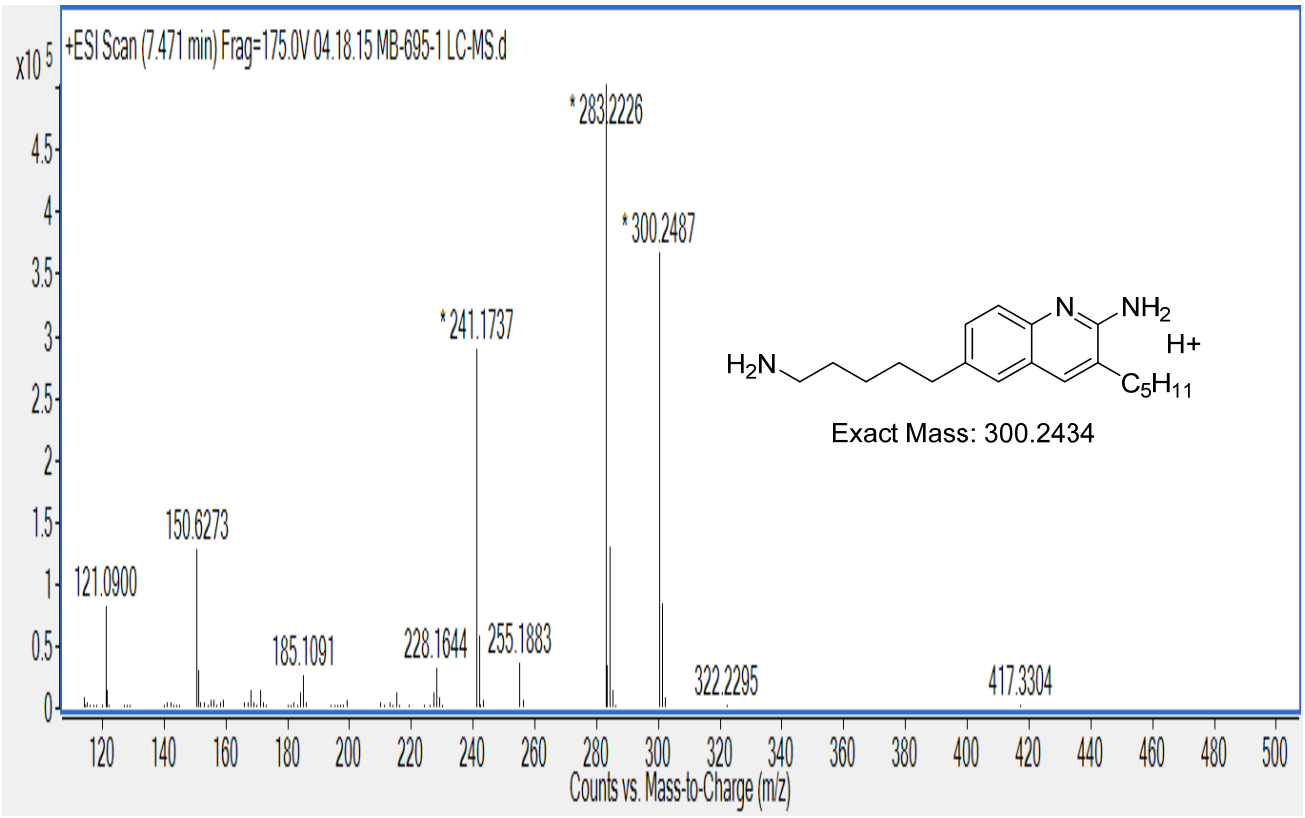
Compound **35b:** ^{1}H and ^{13}C NMR Spectrum



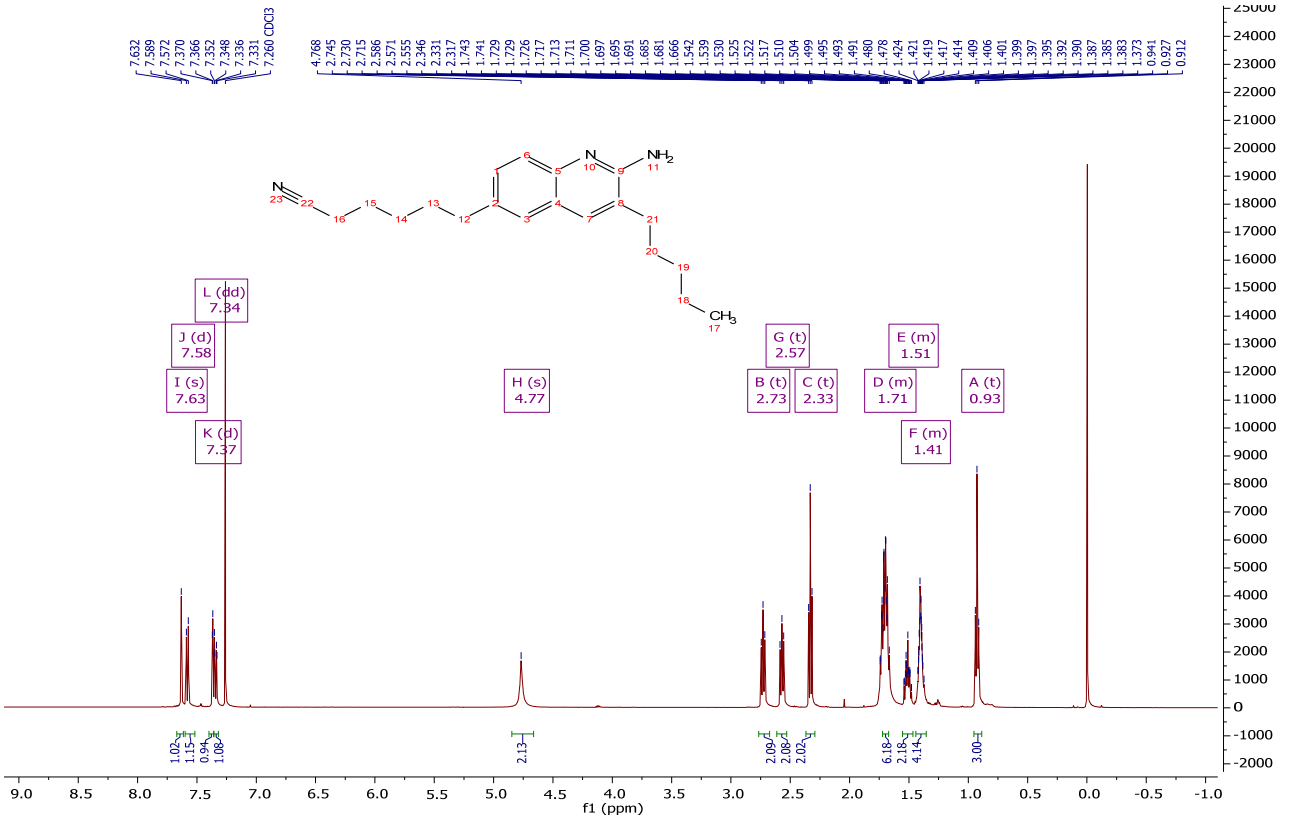


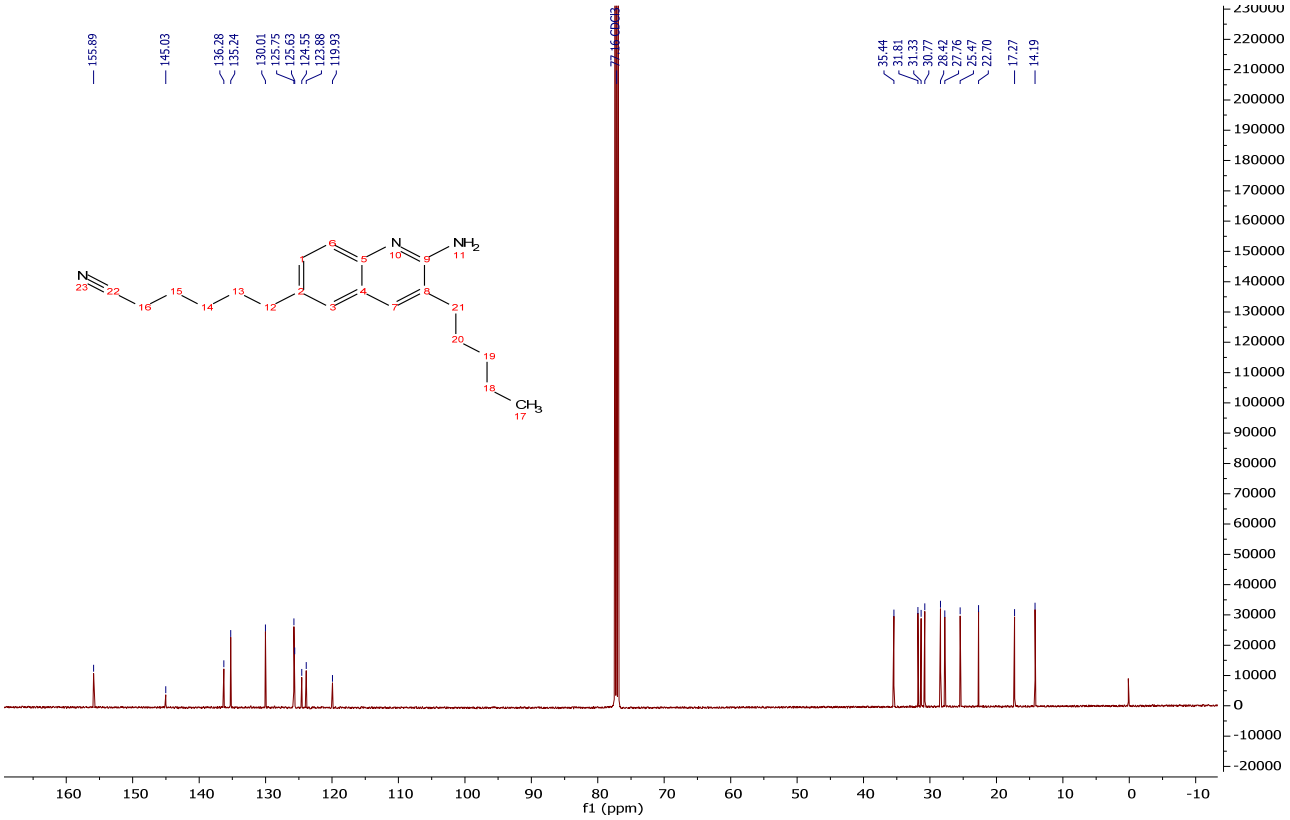
Compound **35b:** LC-MS



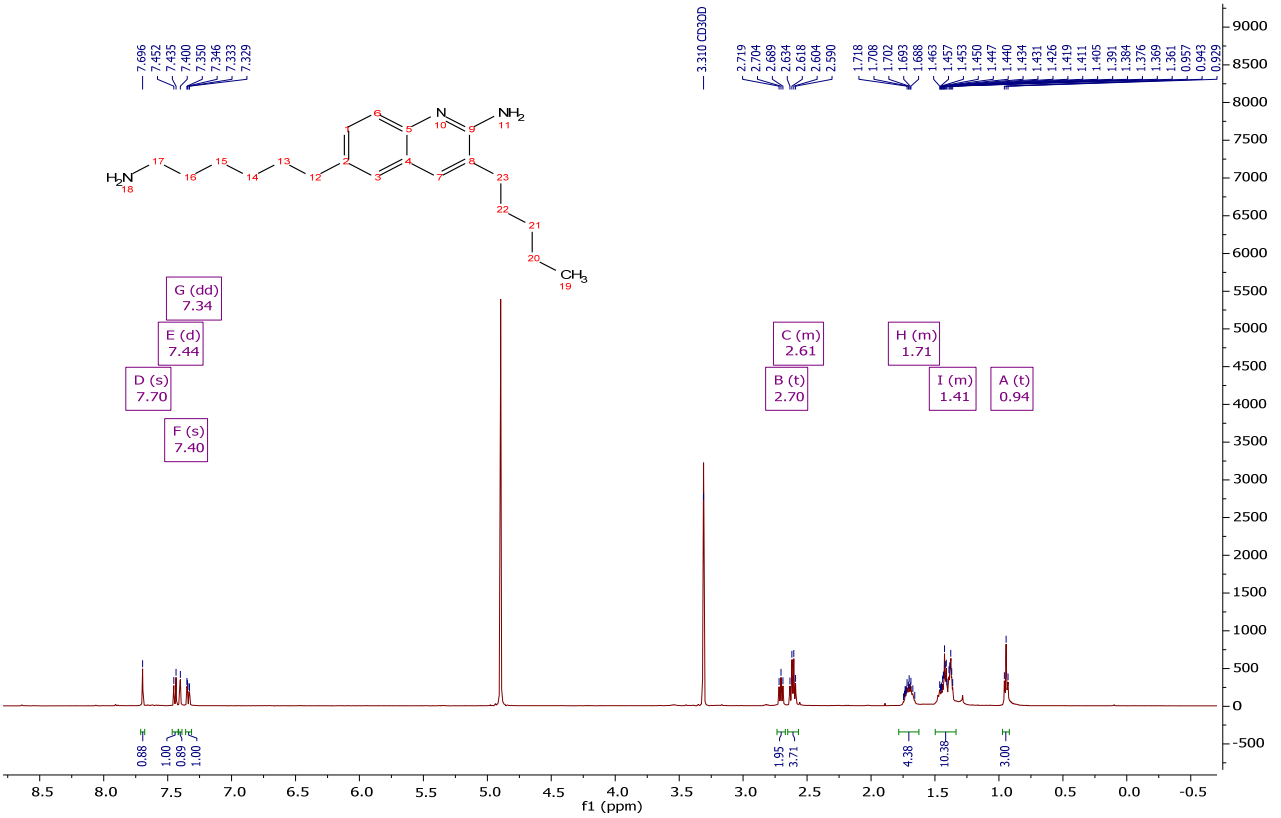


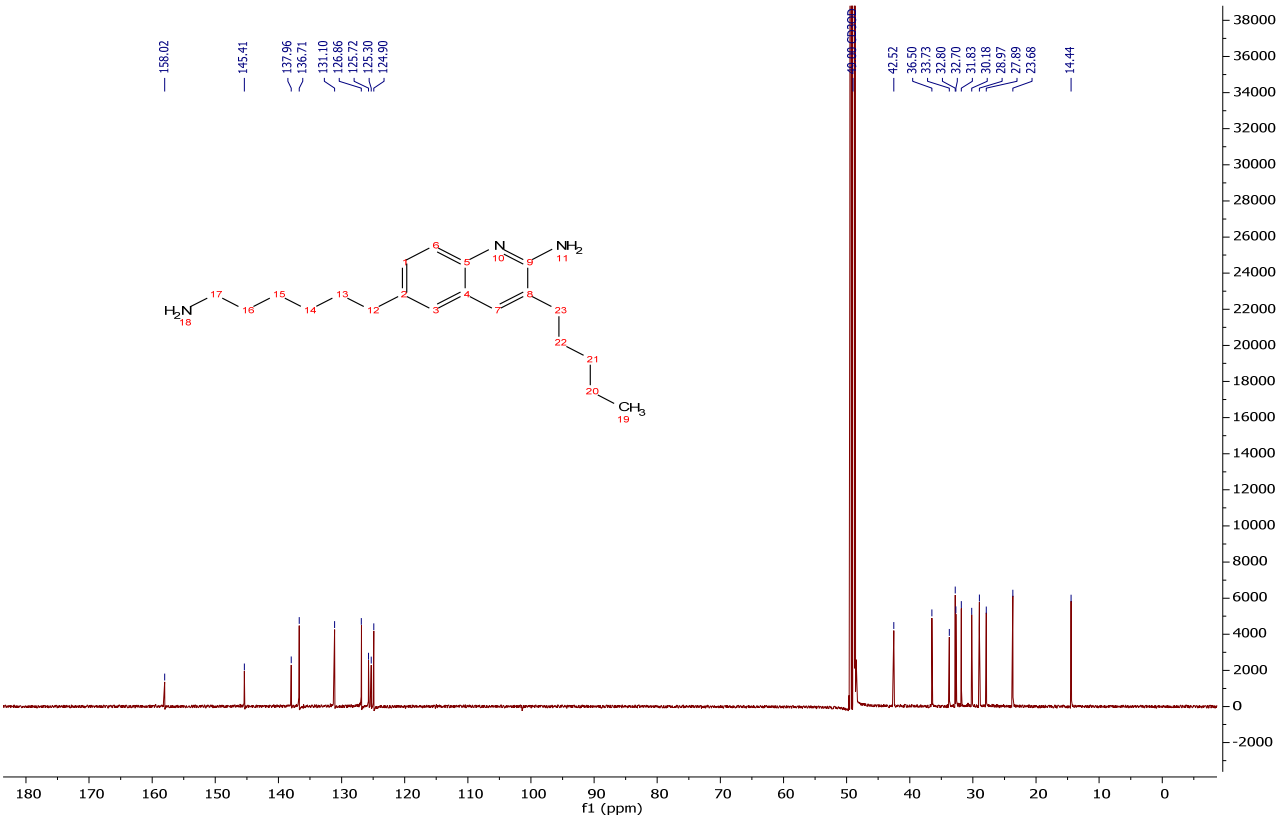
Compound **31c:** ^{1}H and ^{13}C NMR Spectrum



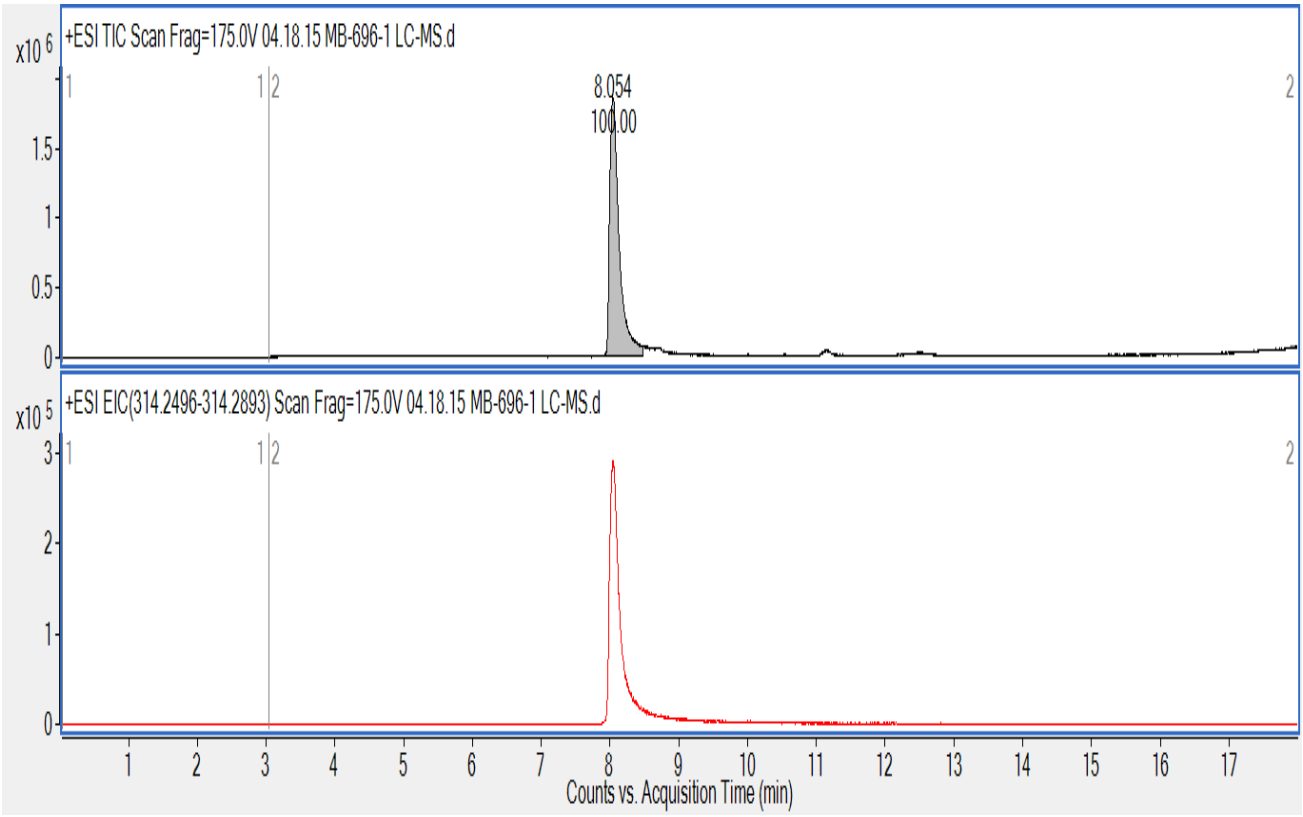


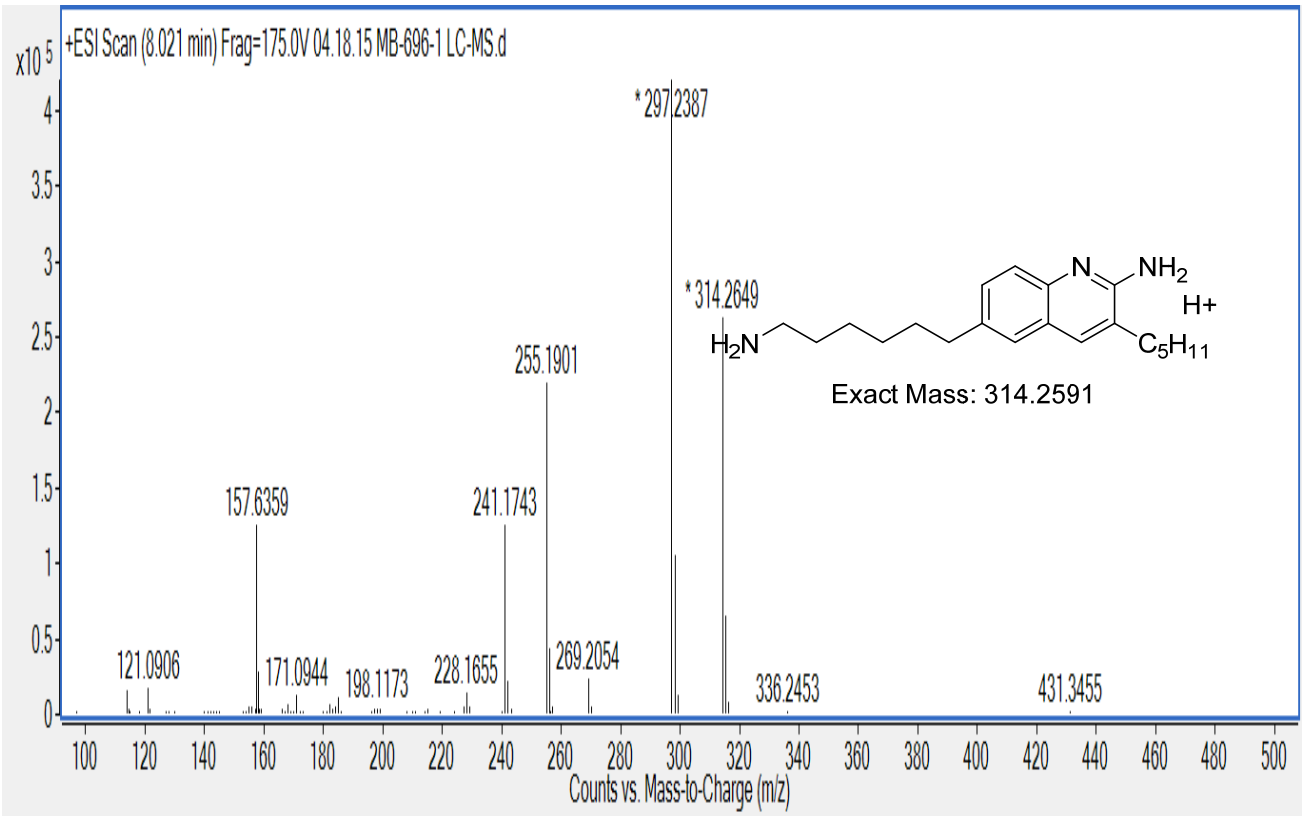
Compound **35c:** ^{1}H and ^{13}C NMR Spectrum



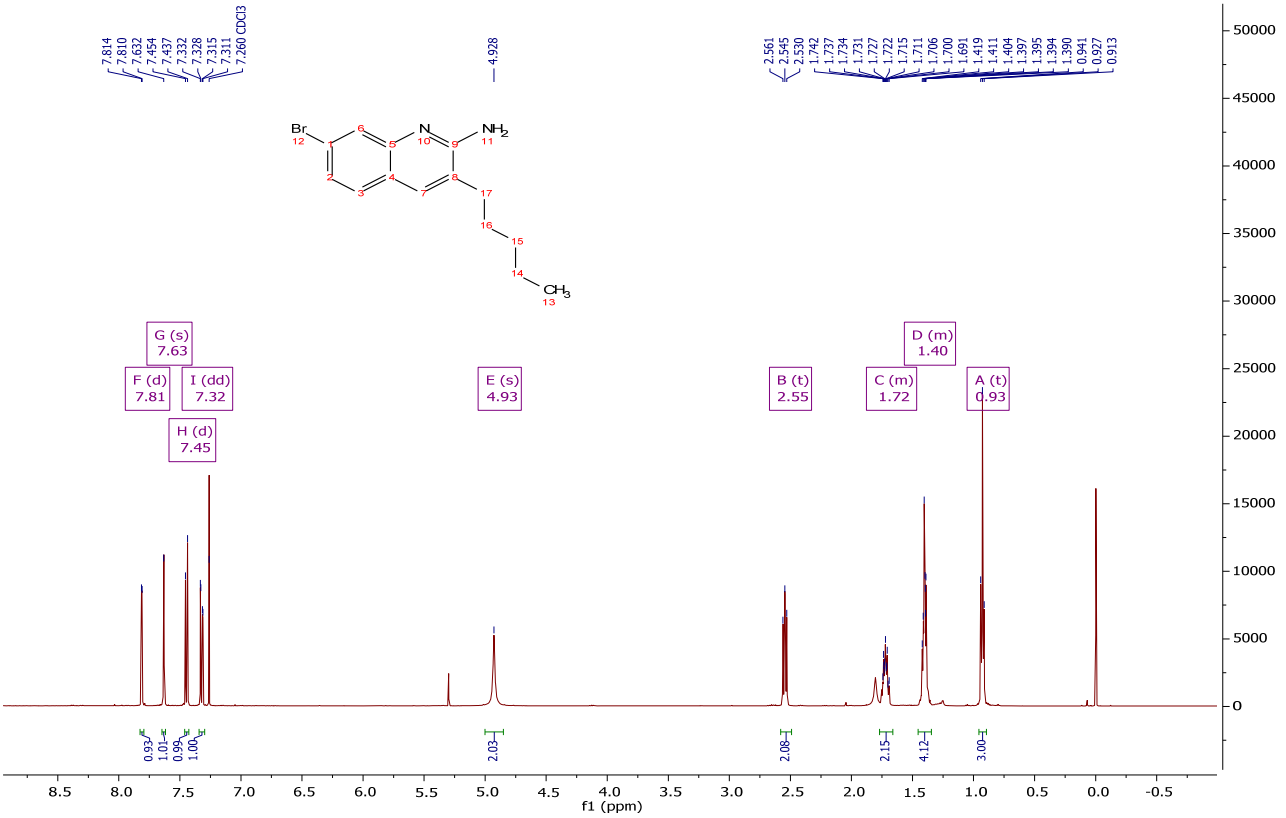


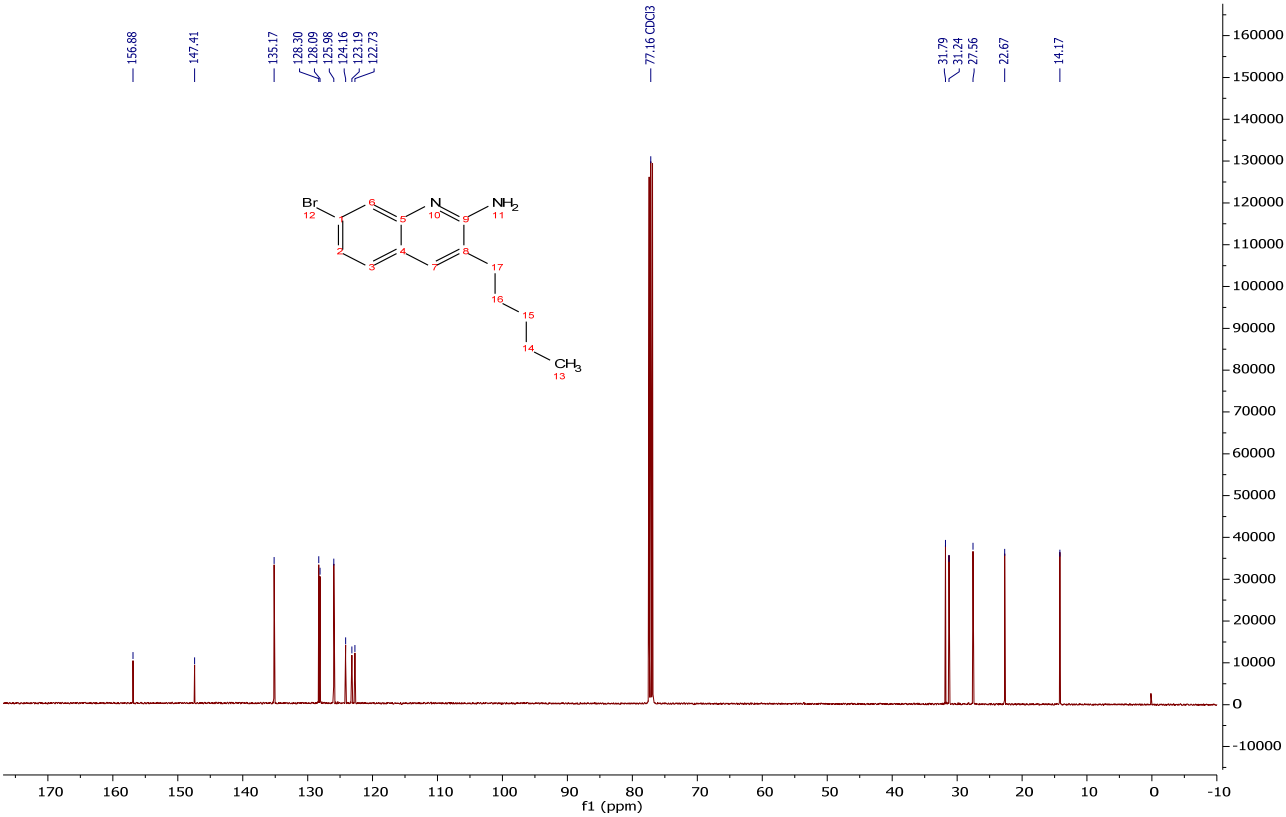
Compound **35c:** LC-MS



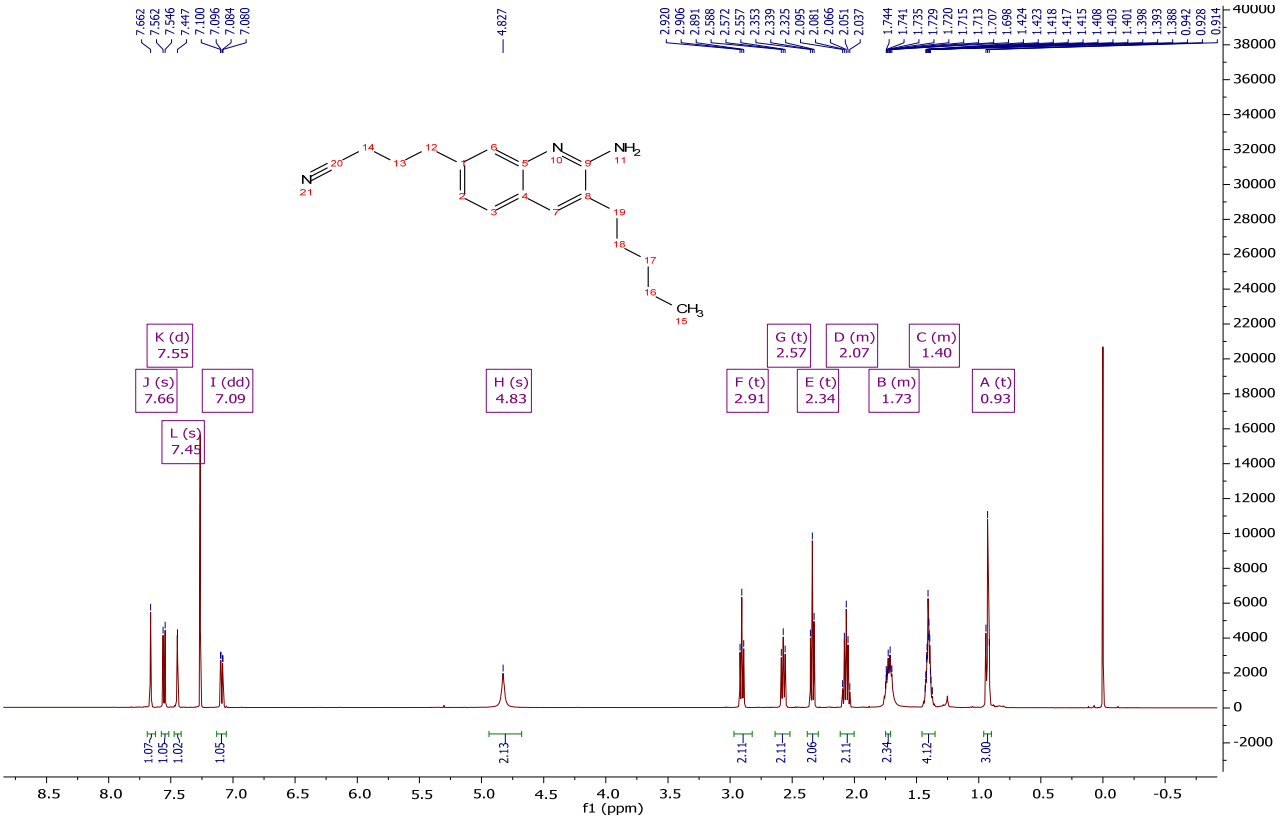


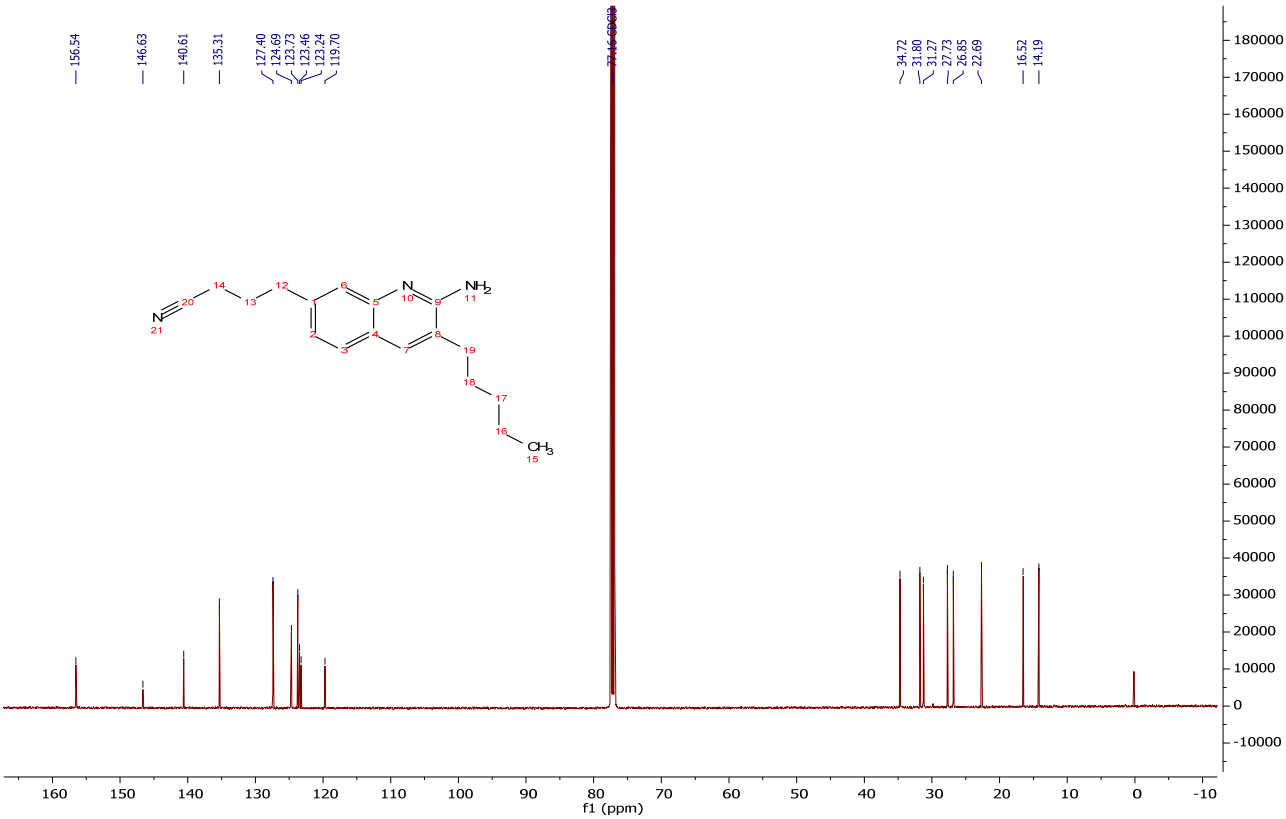
Compound **28:** ^{1}H and ^{13}C NMR Spectrum



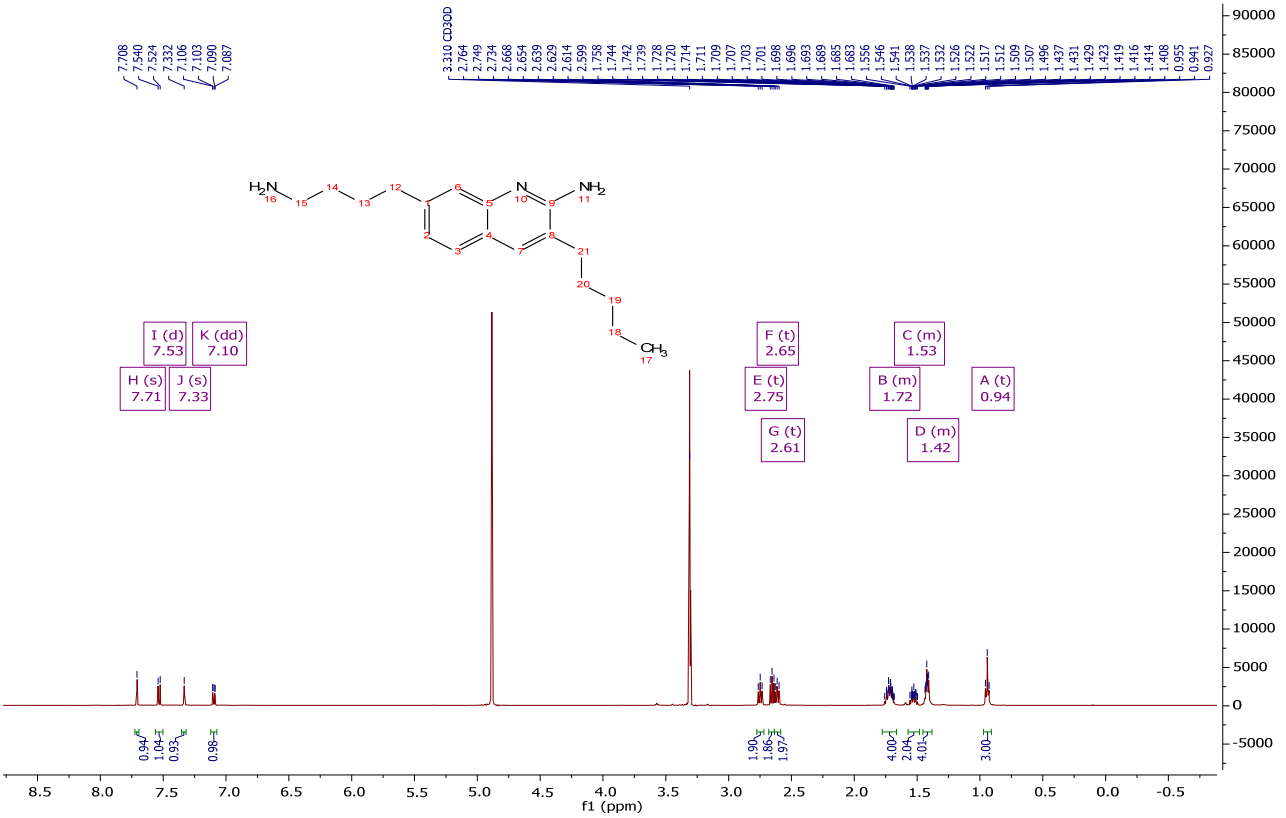


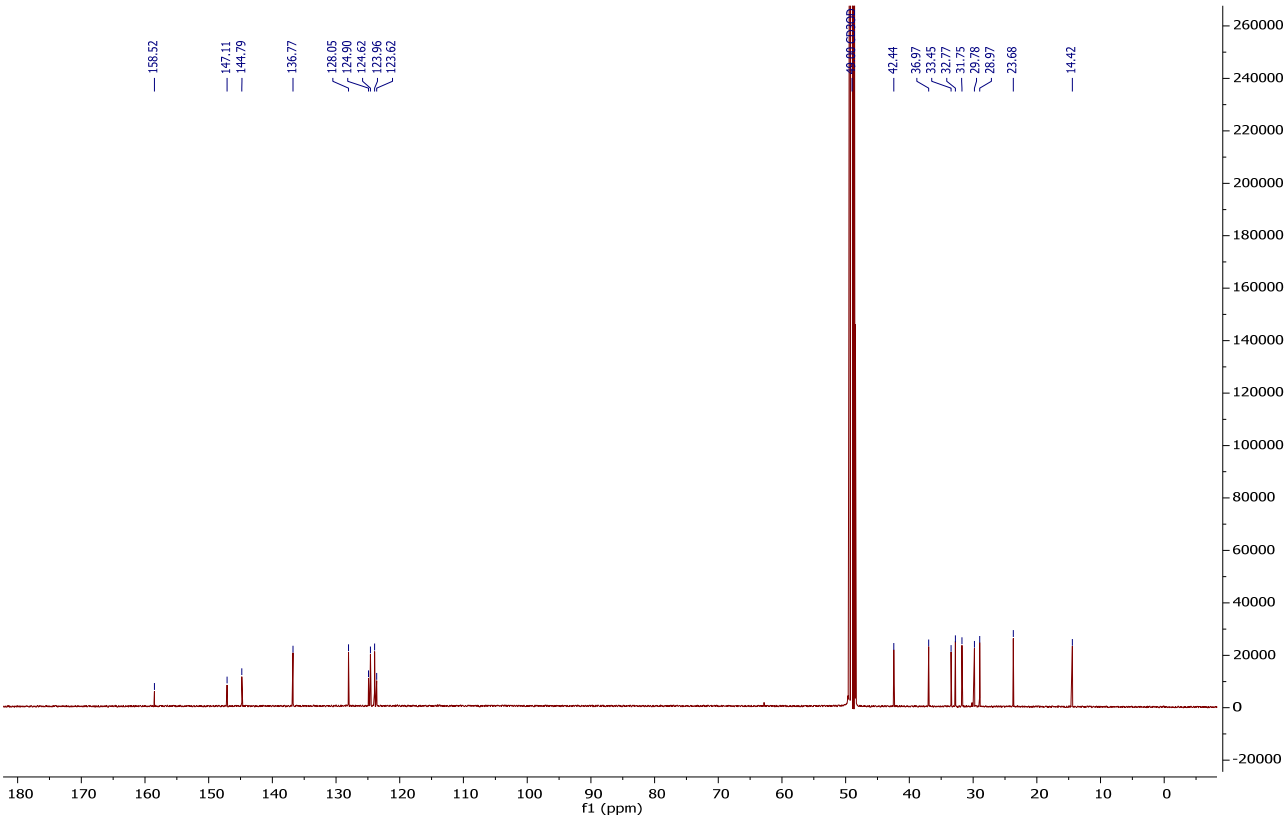
Compound **32a:** ^{1}H and ^{13}C NMR Spectrum



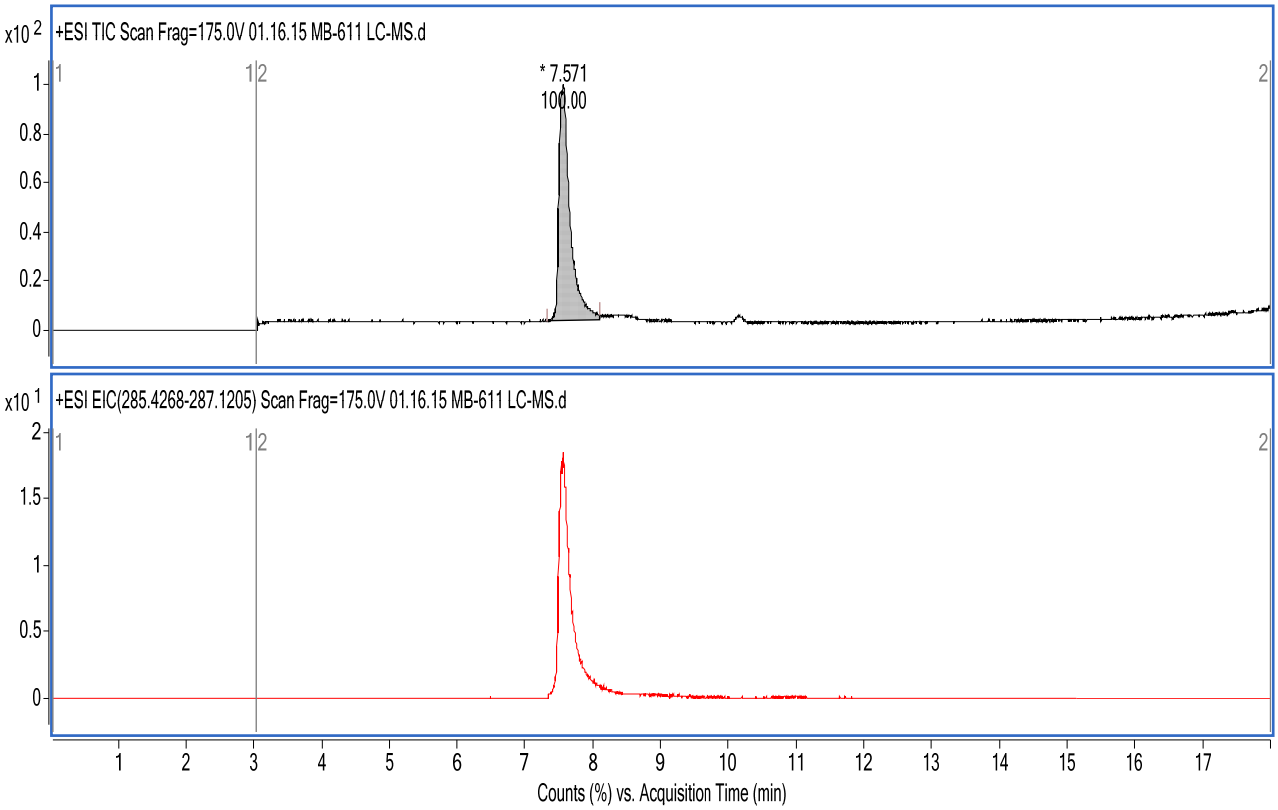


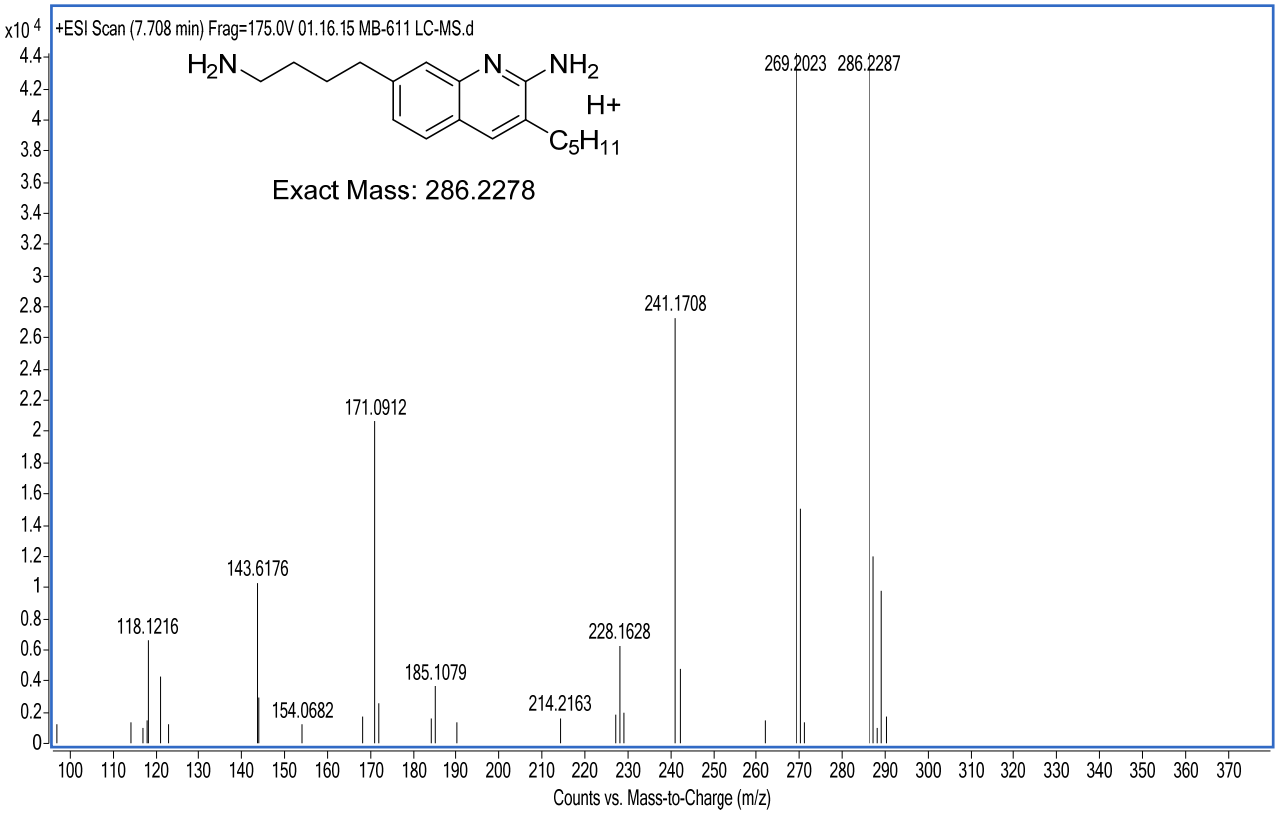
Compound **36a:** ^{1}H and ^{13}C NMR Spectrum



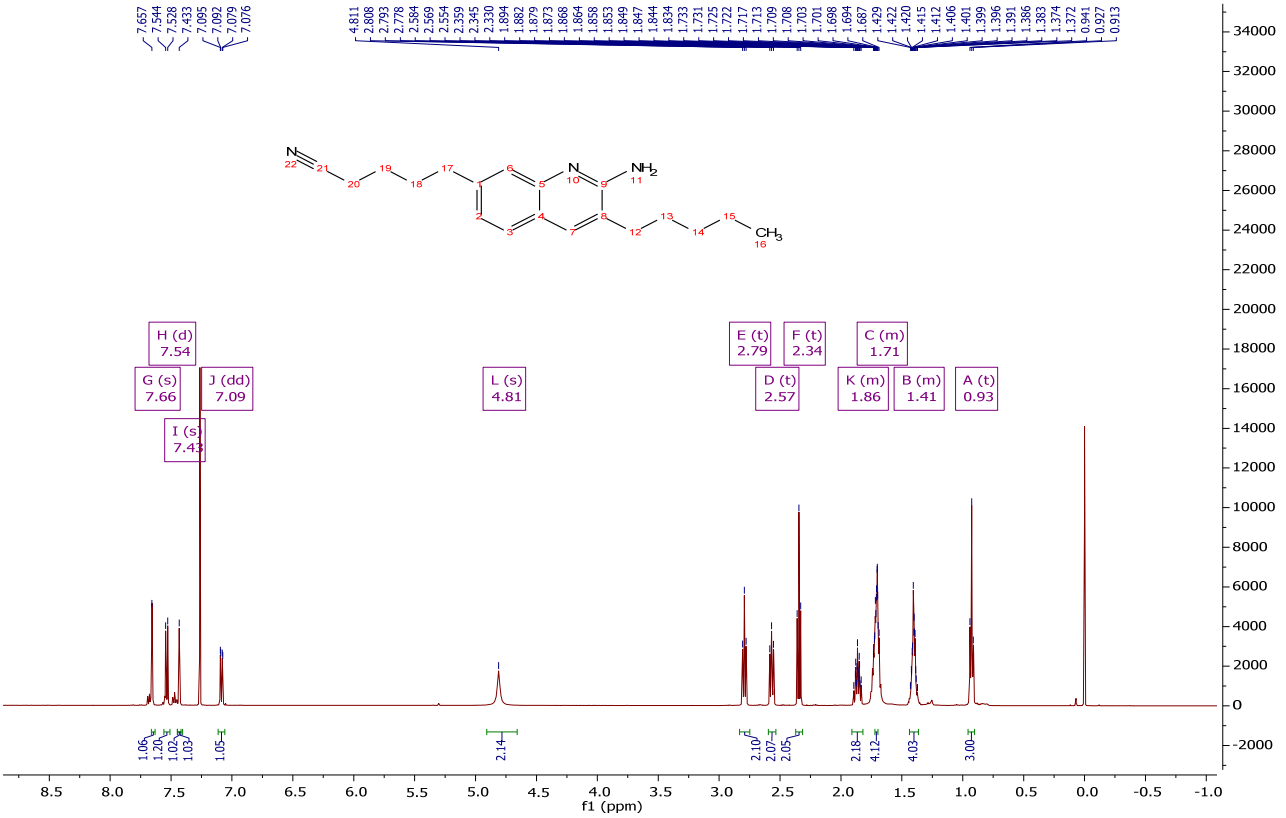


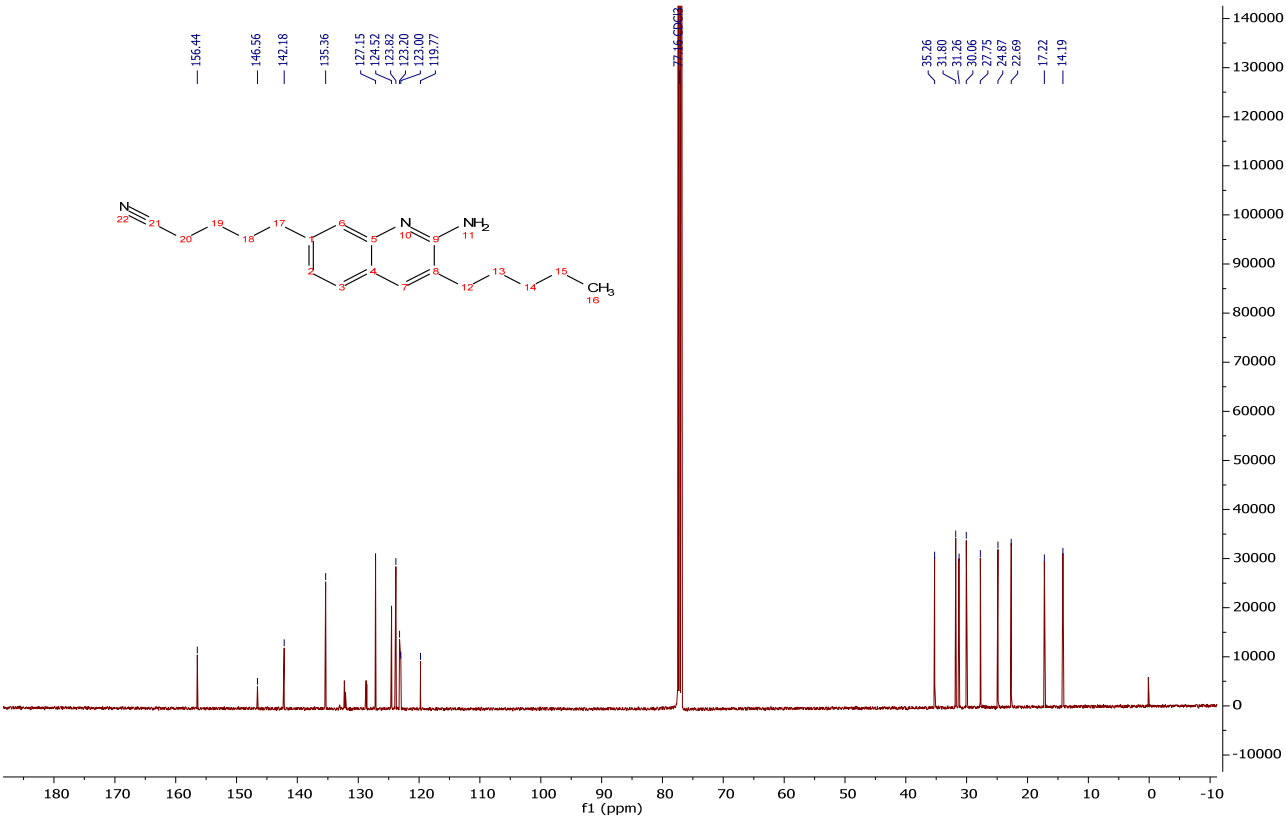
Compound **36a:** LC-MS



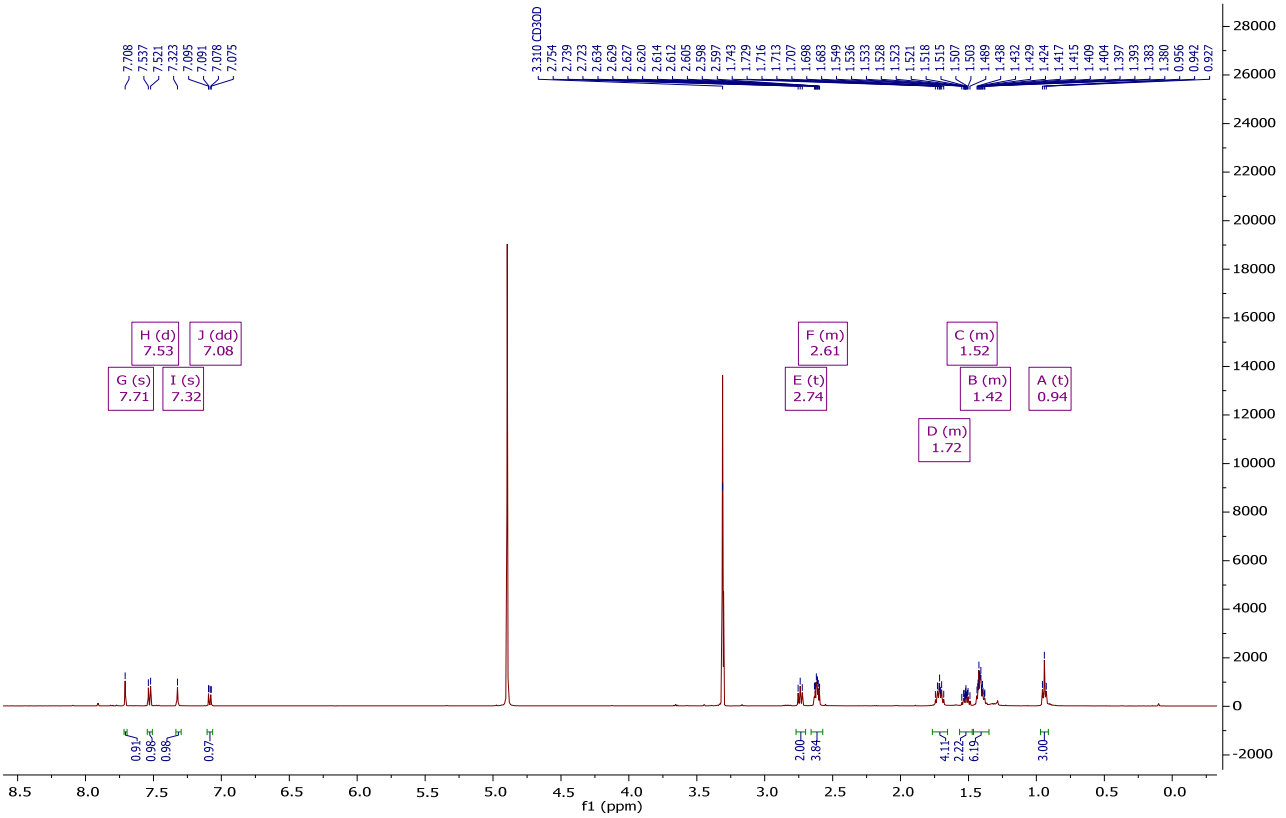


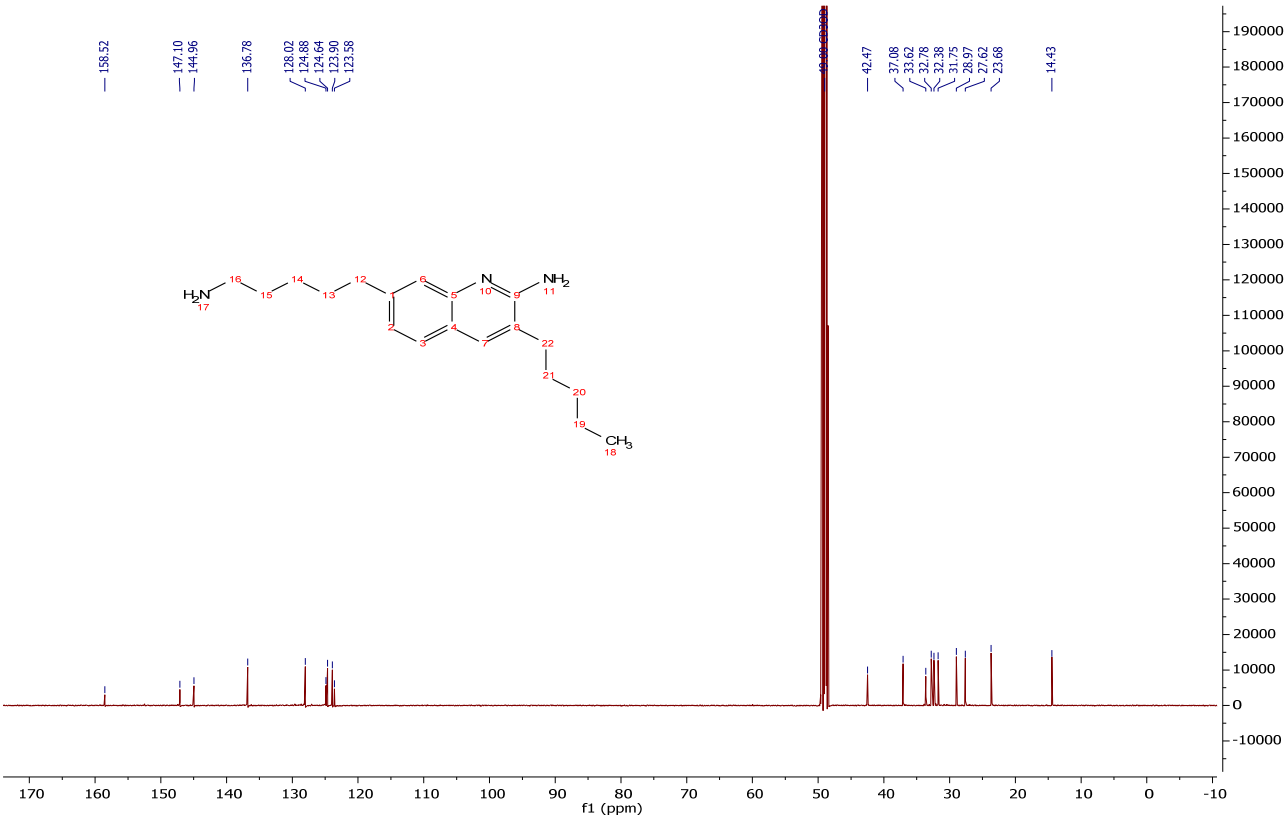
Compound **32b:** ^{1}H and ^{13}C NMR Spectrum



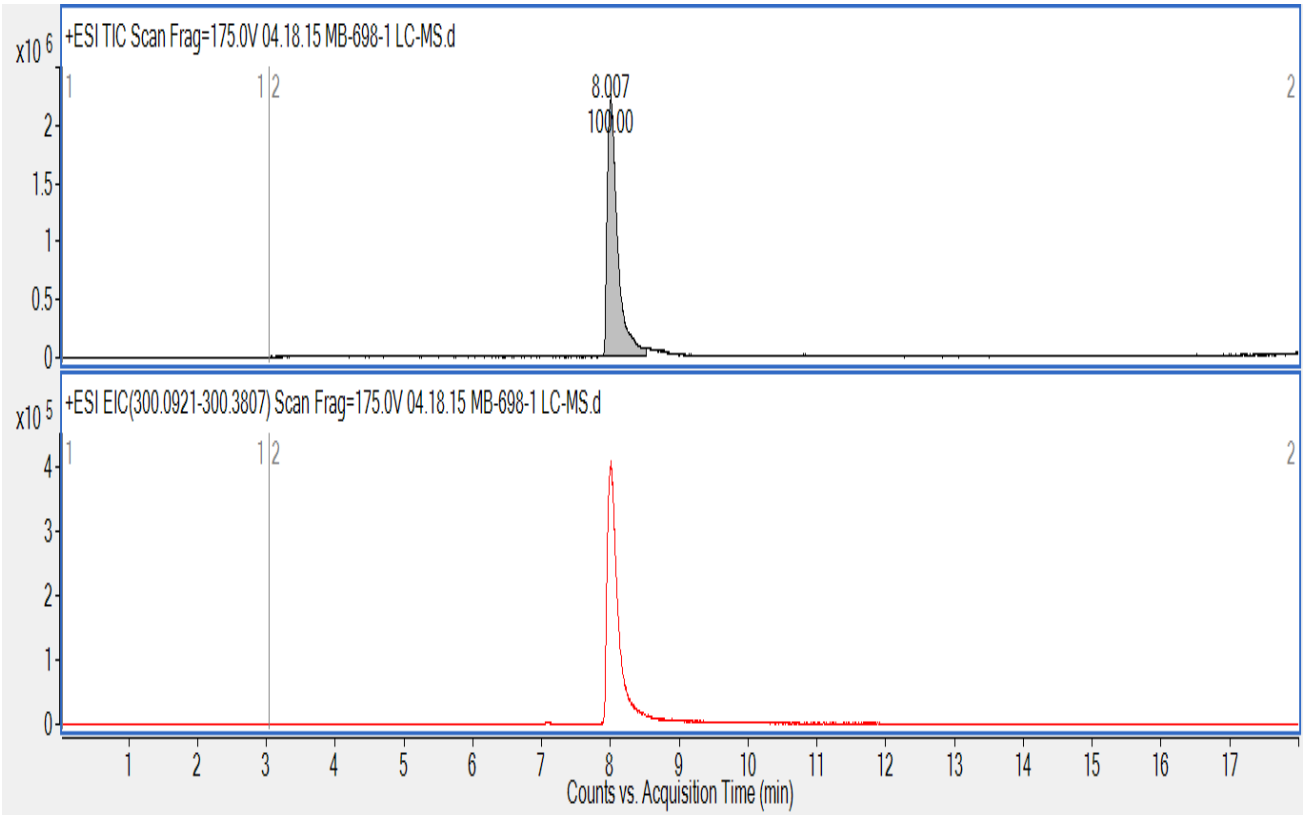


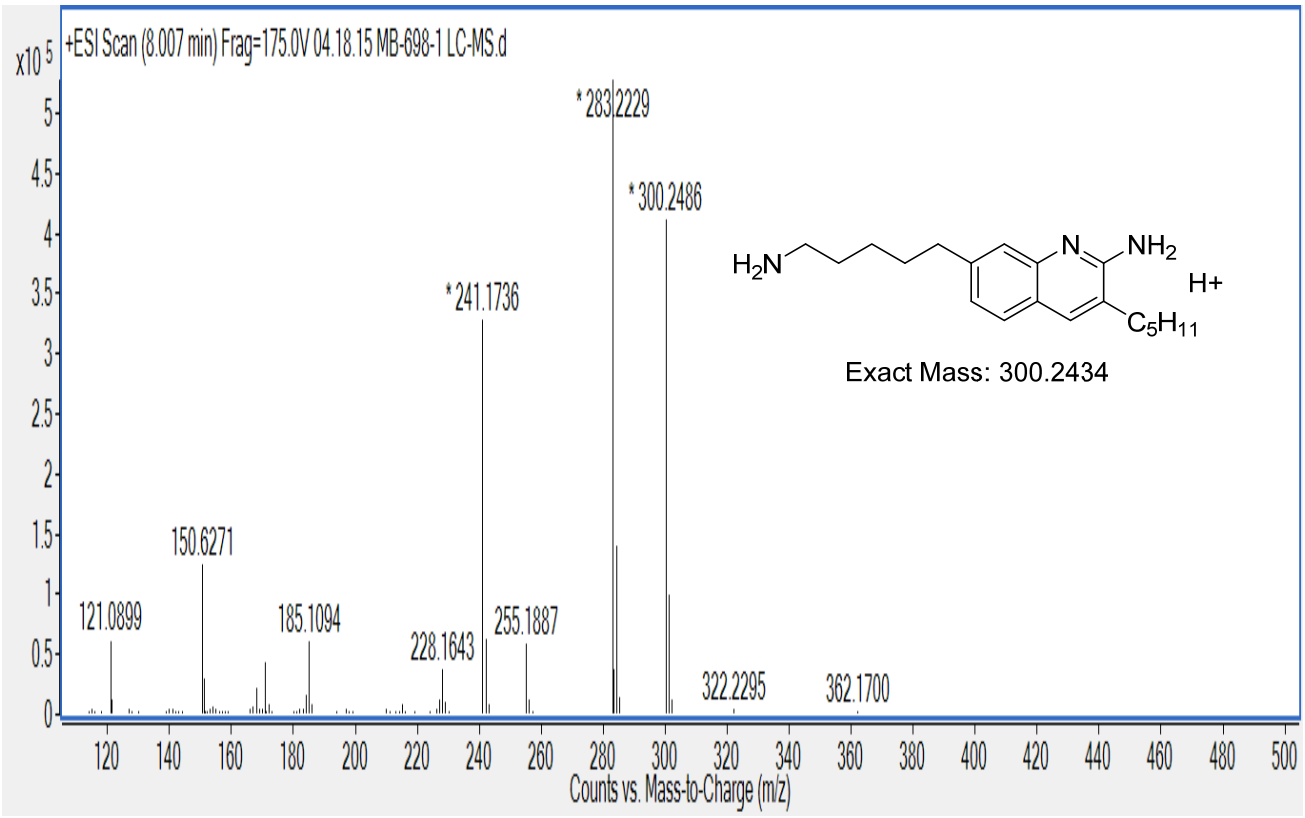
Compound **36b:** ^{1}H and ^{13}C NMR Spectrum





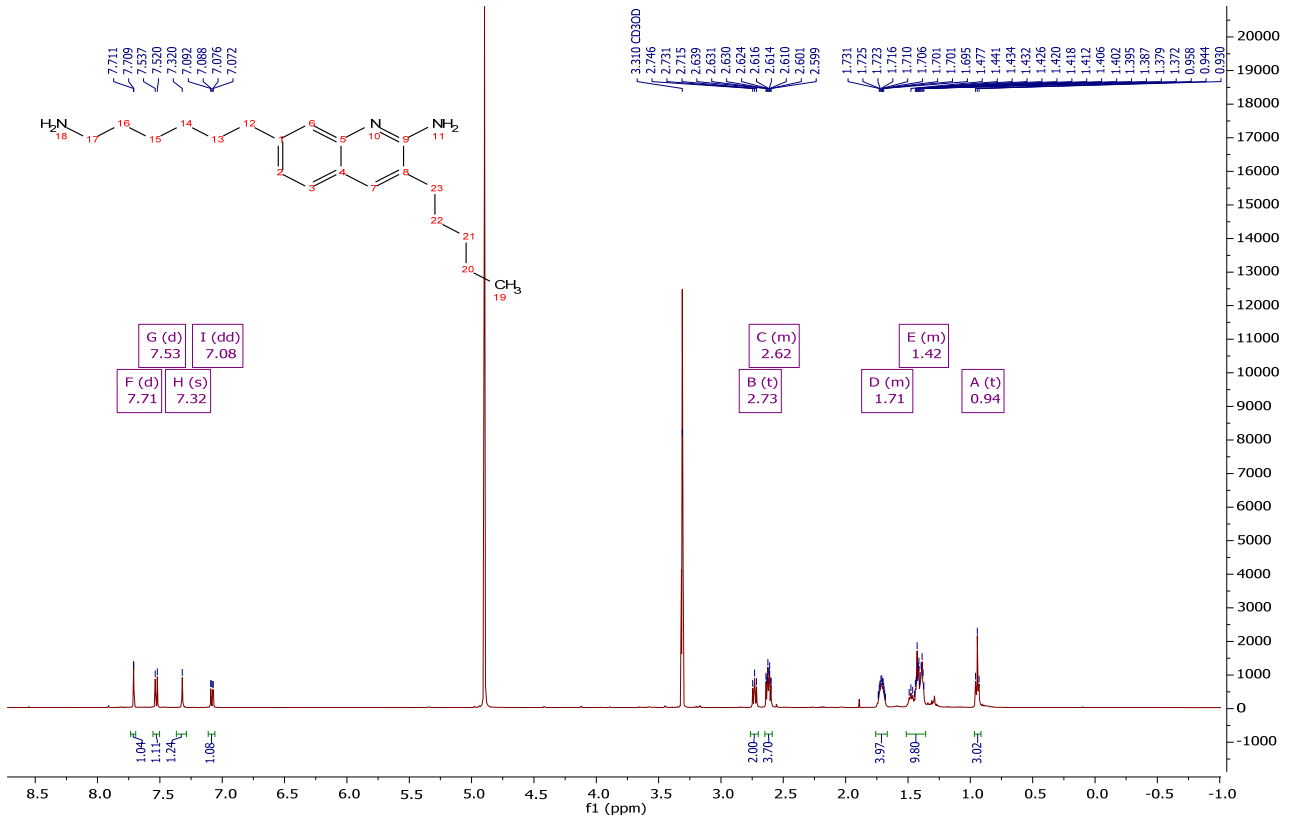
Compound **36b:** LC-MS

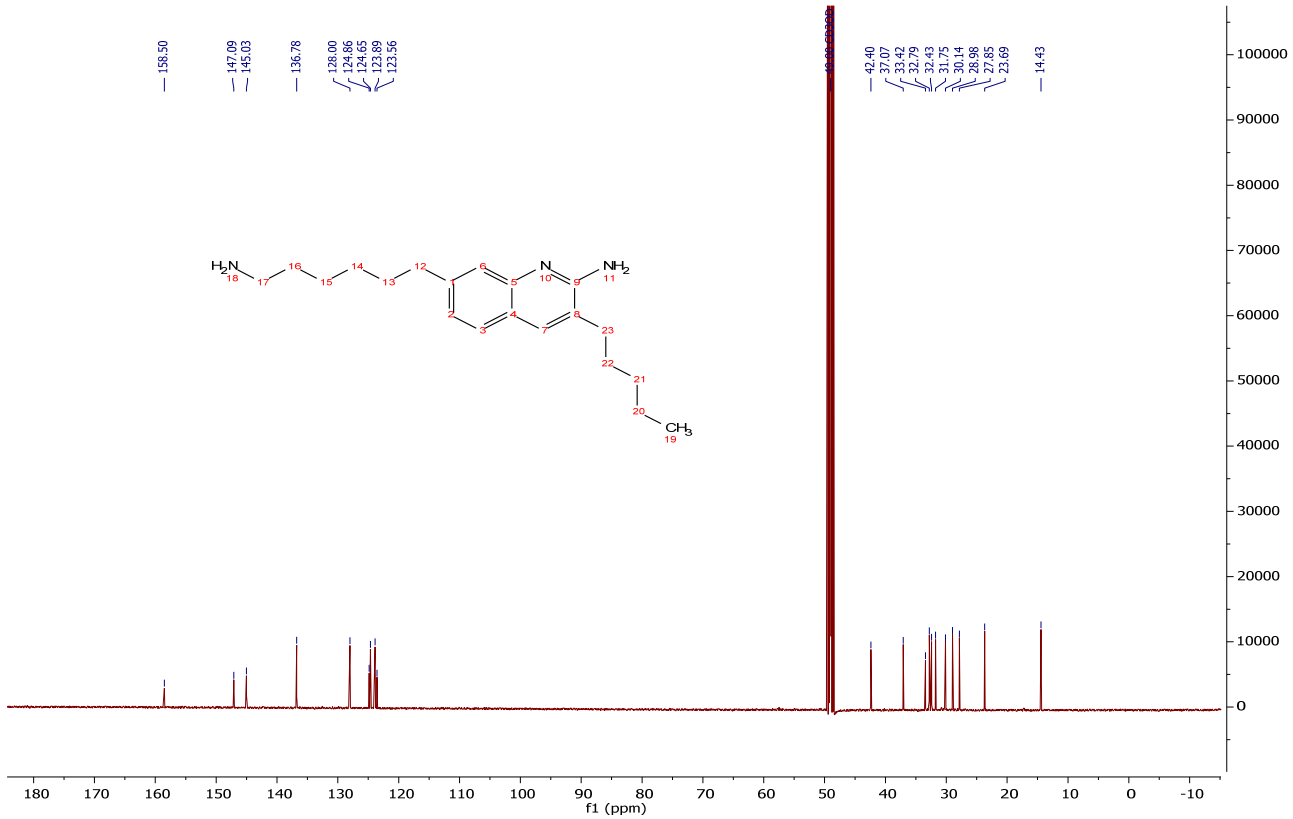




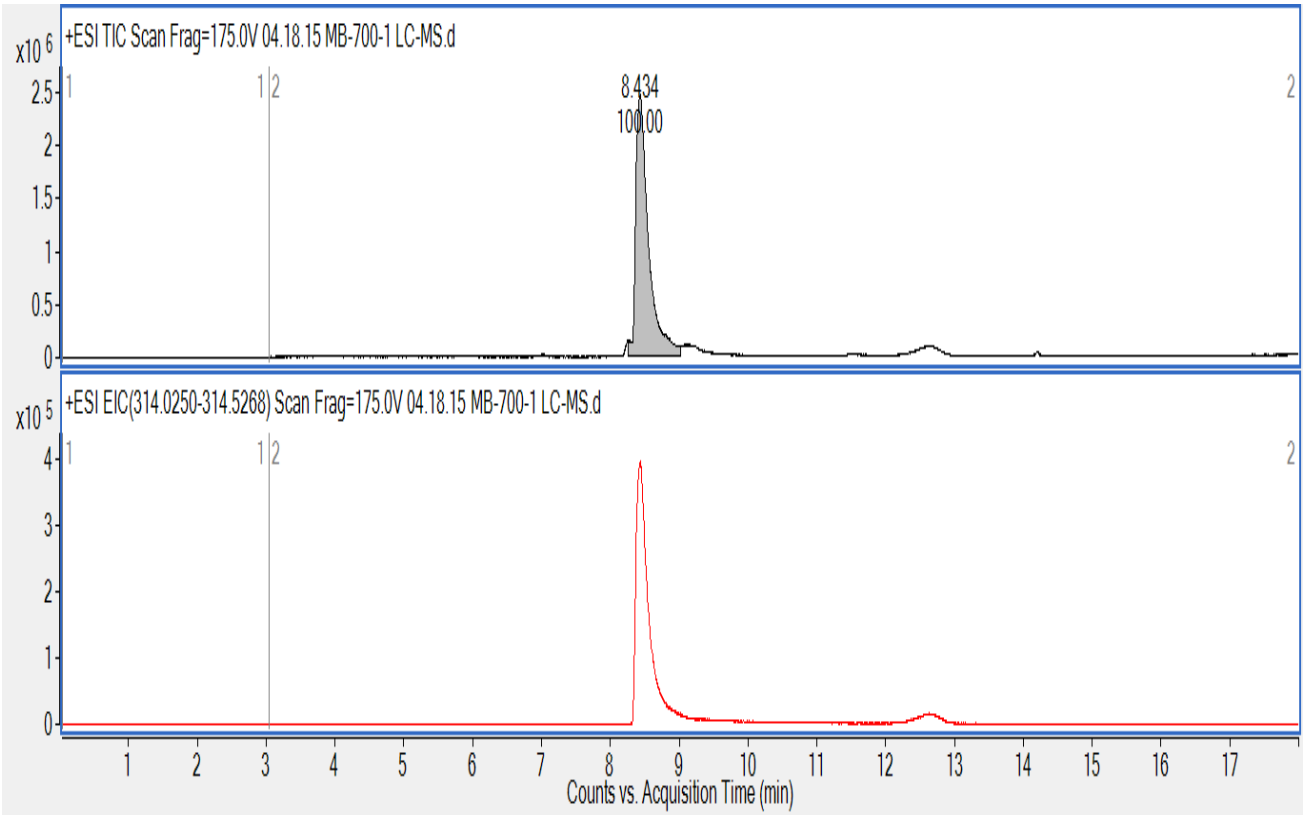
Exact Mass: 300.2434

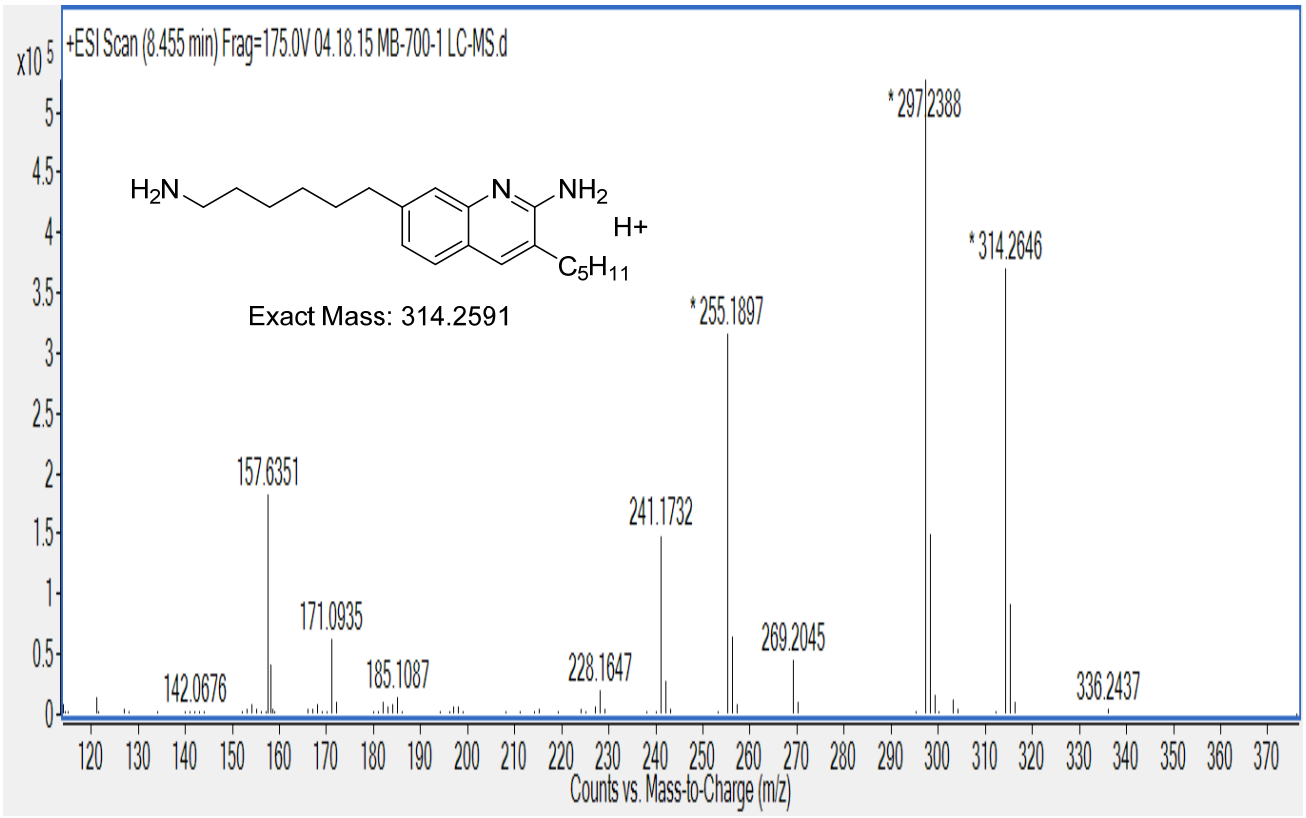
Compound **36c:** ^{1}H and ^{13}C NMR Spectrum



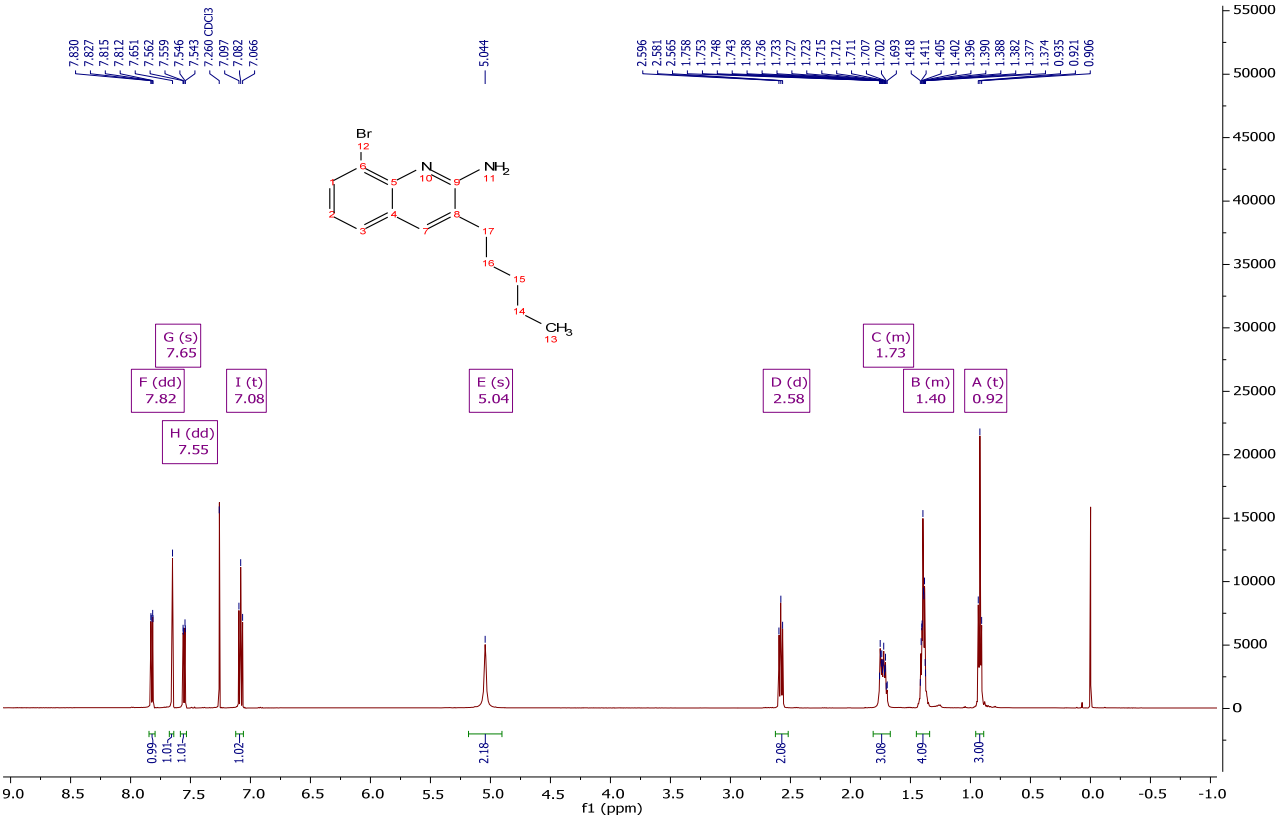


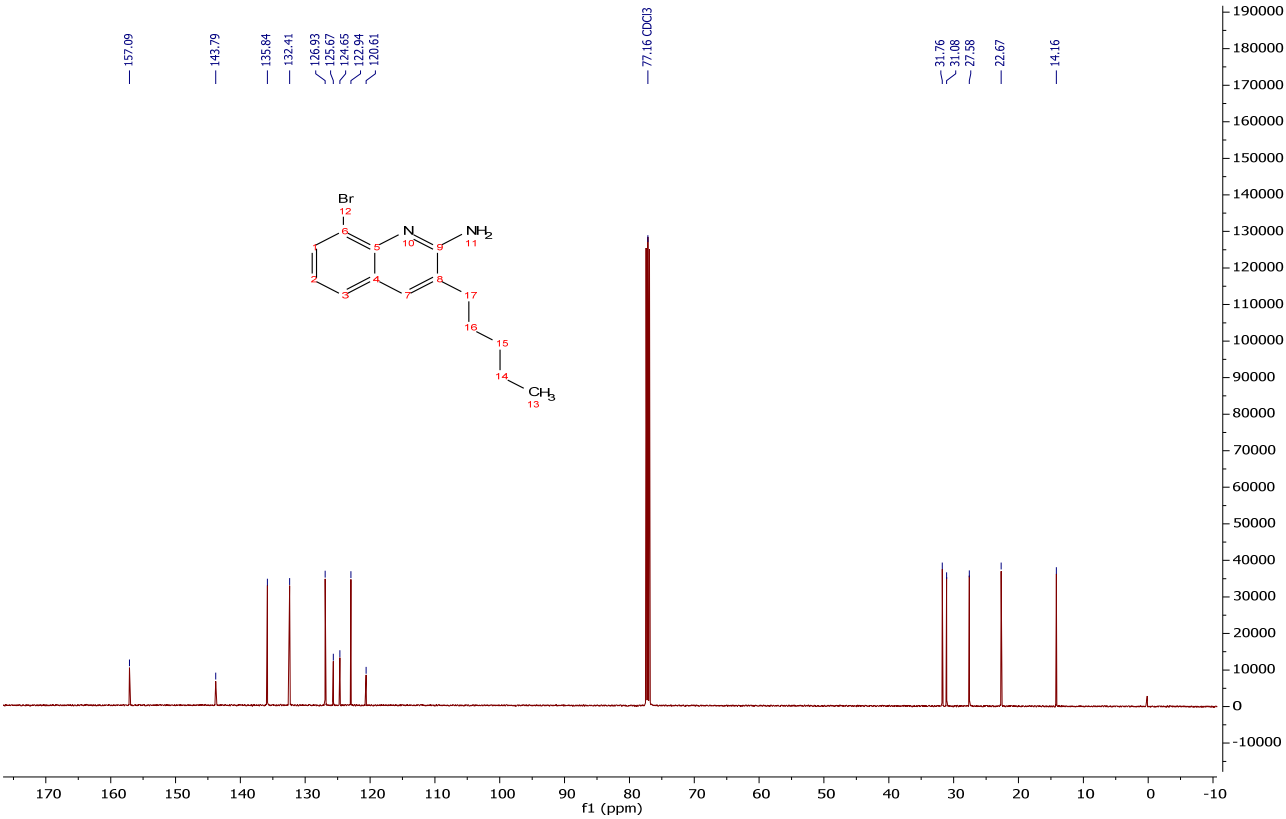
Compound **36c:** LC-MS



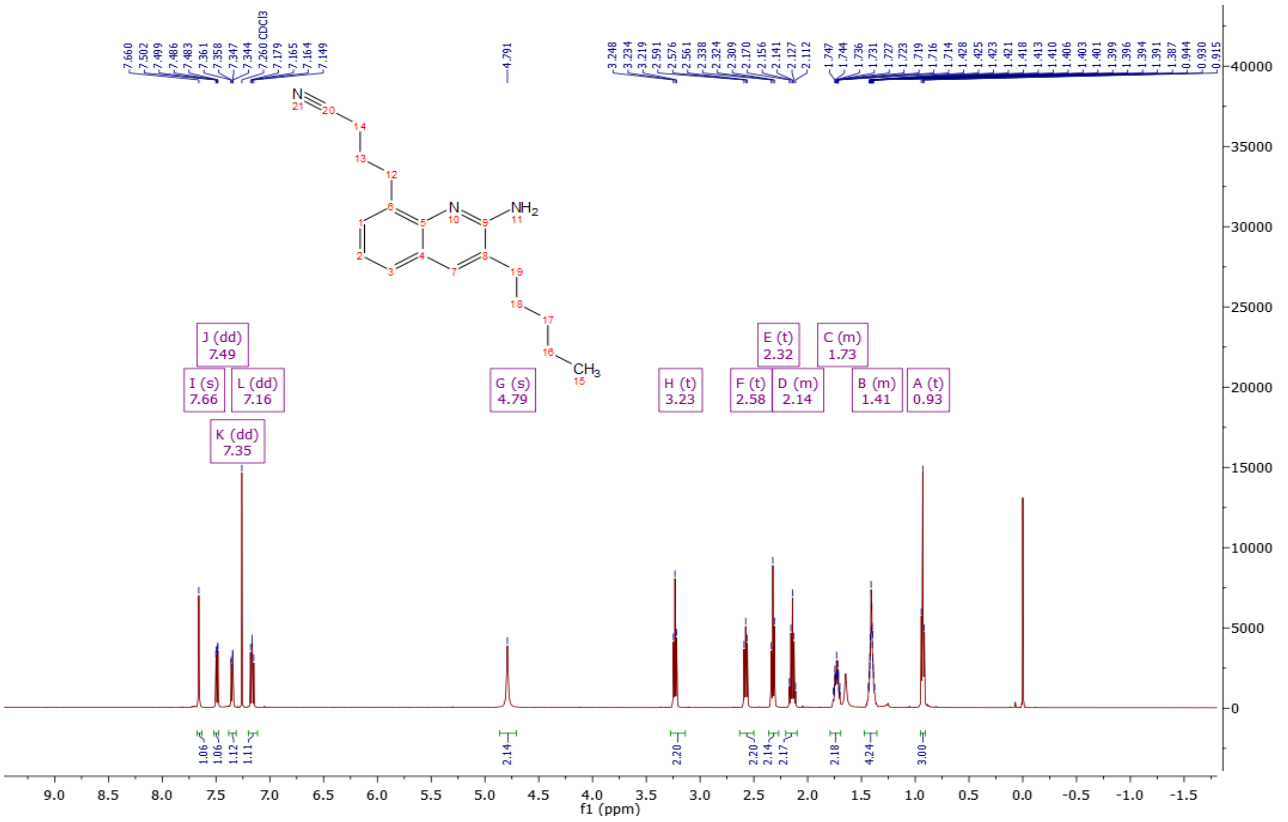


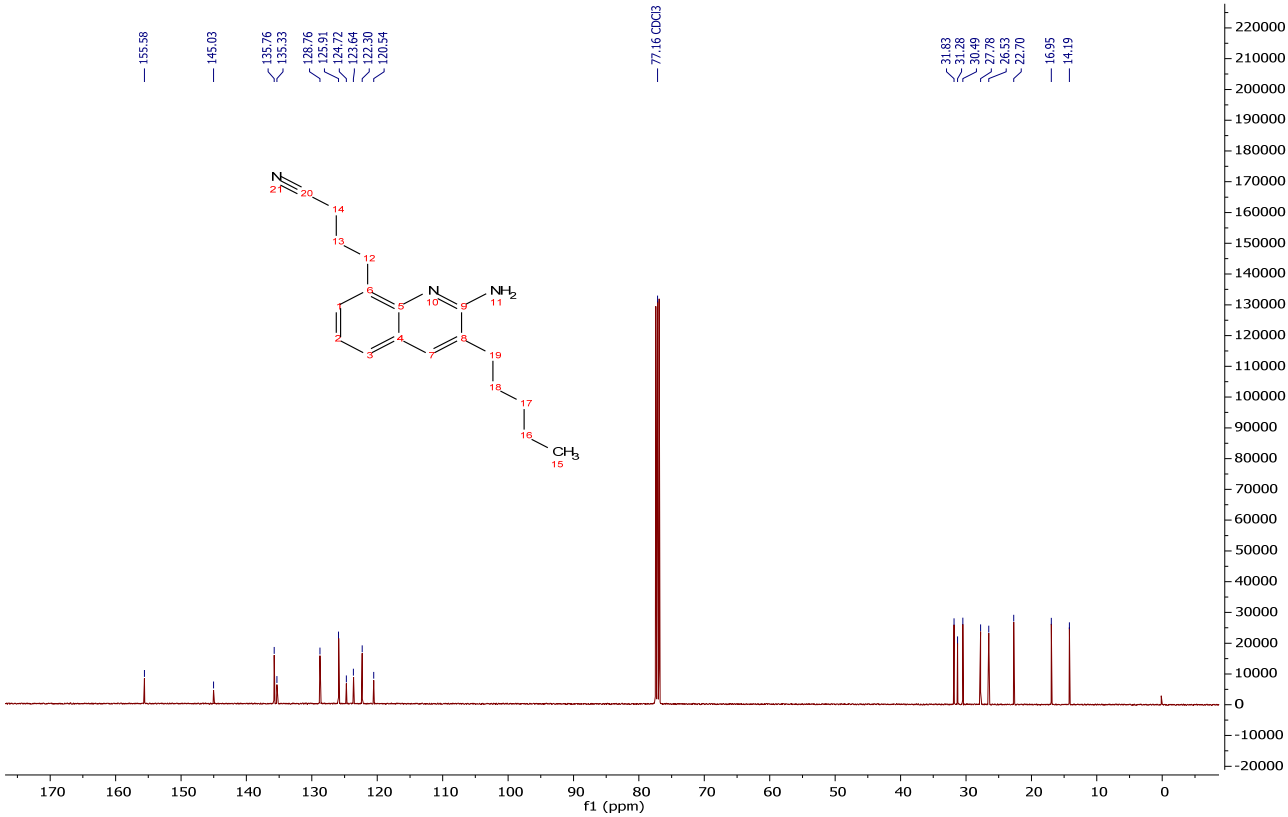
Compound **29:** ^{1}H and ^{13}C NMR Spectrum



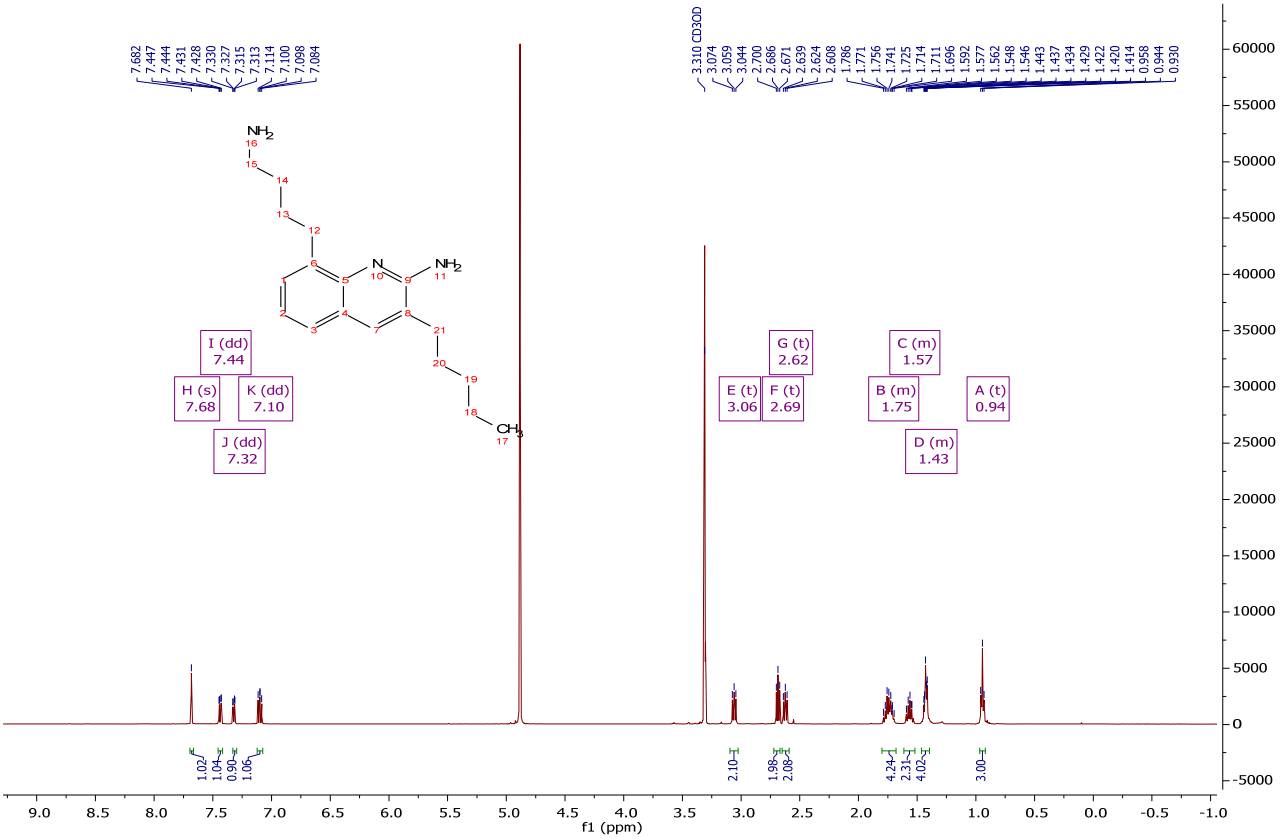


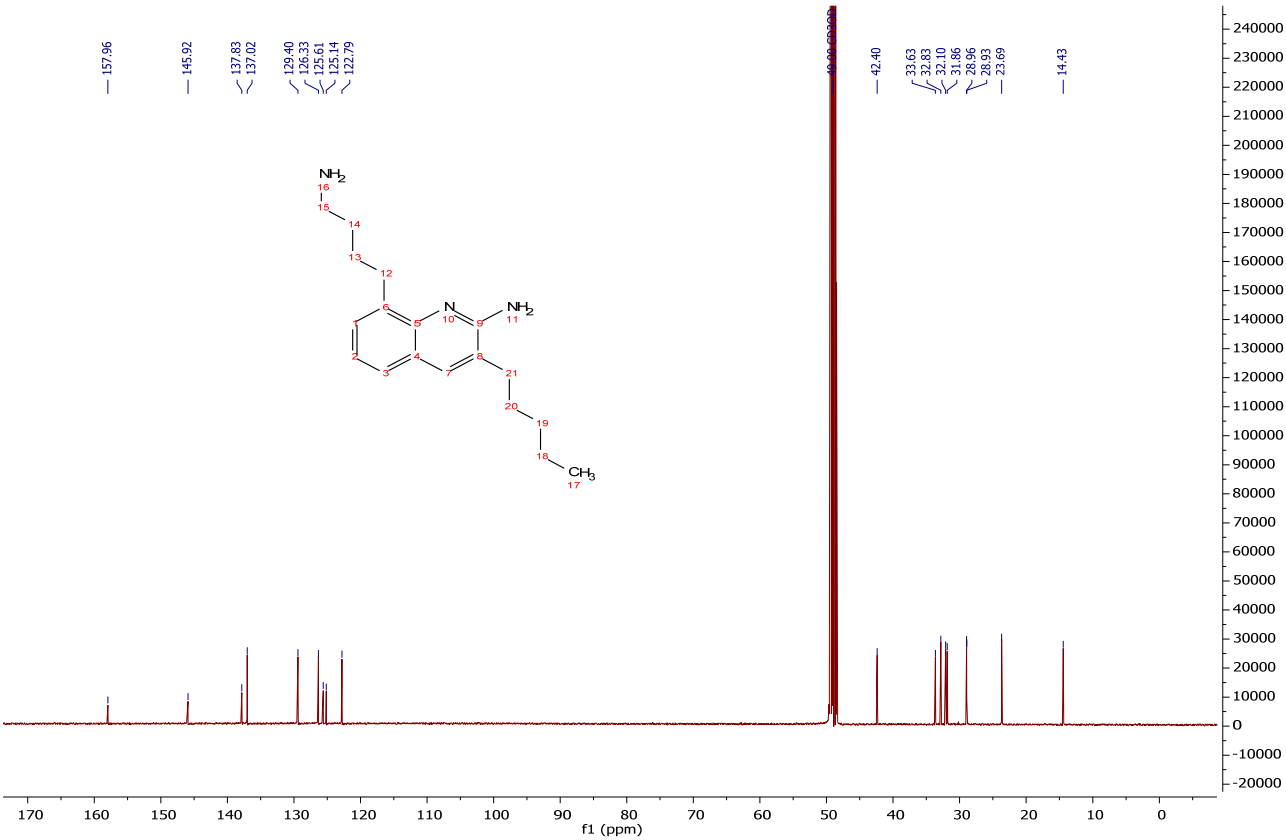
Compound **33:** ^{1}H and ^{13}C NMR Spectrum



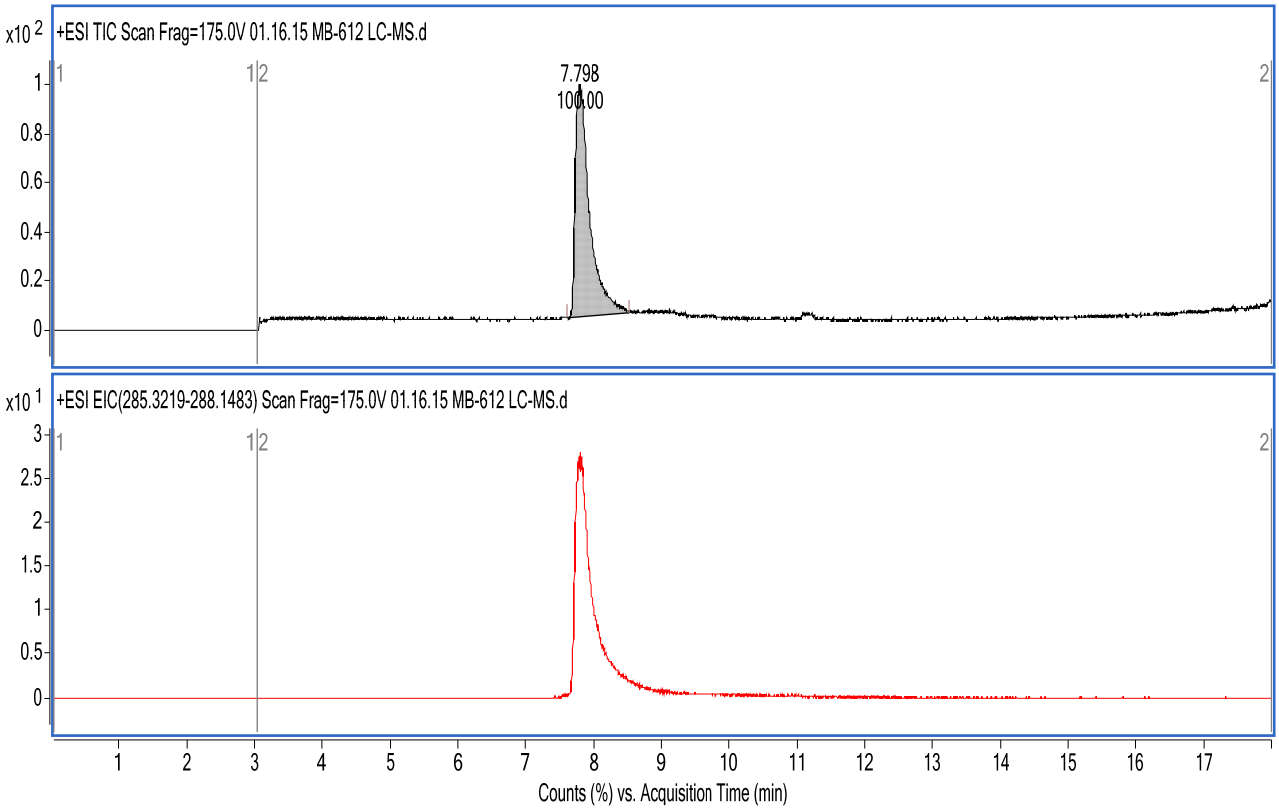


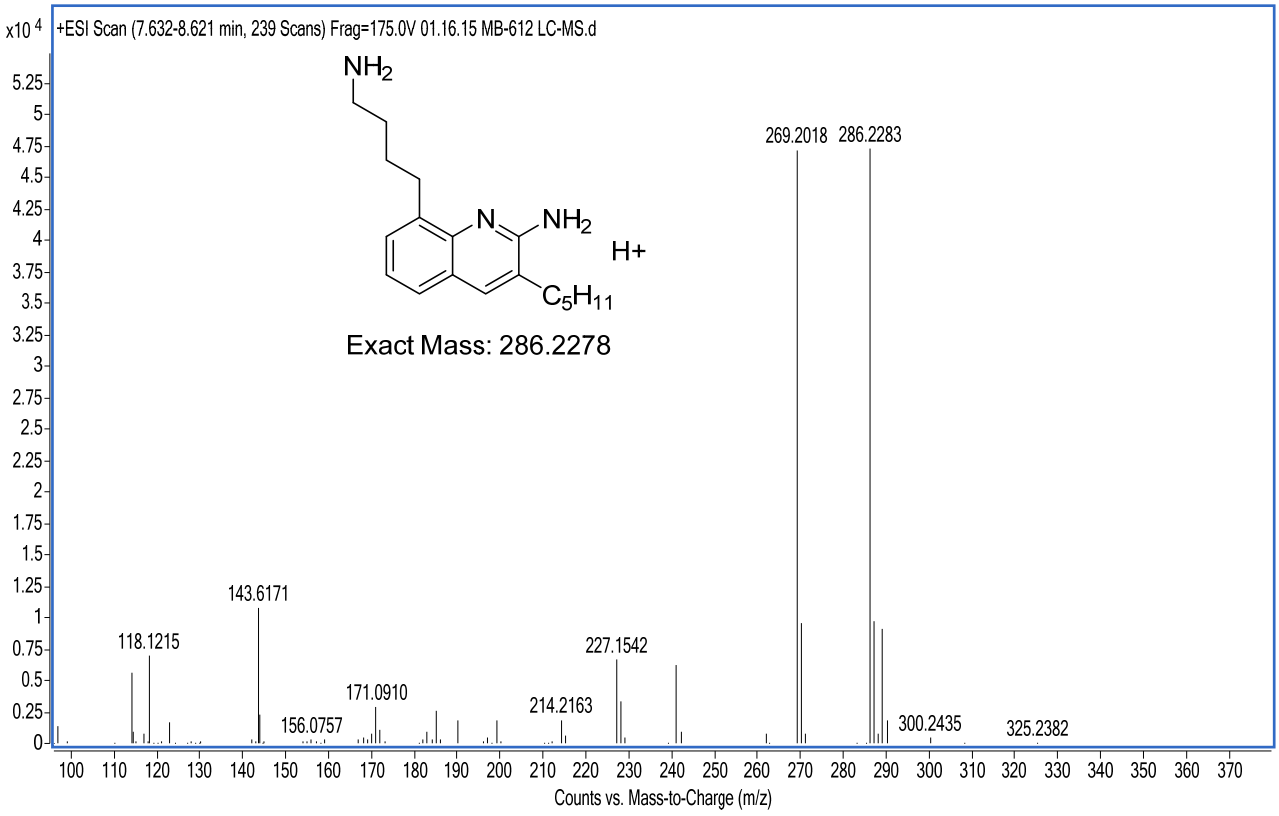
Compound **37:** ^{1}H and ^{13}C NMR Spectrum



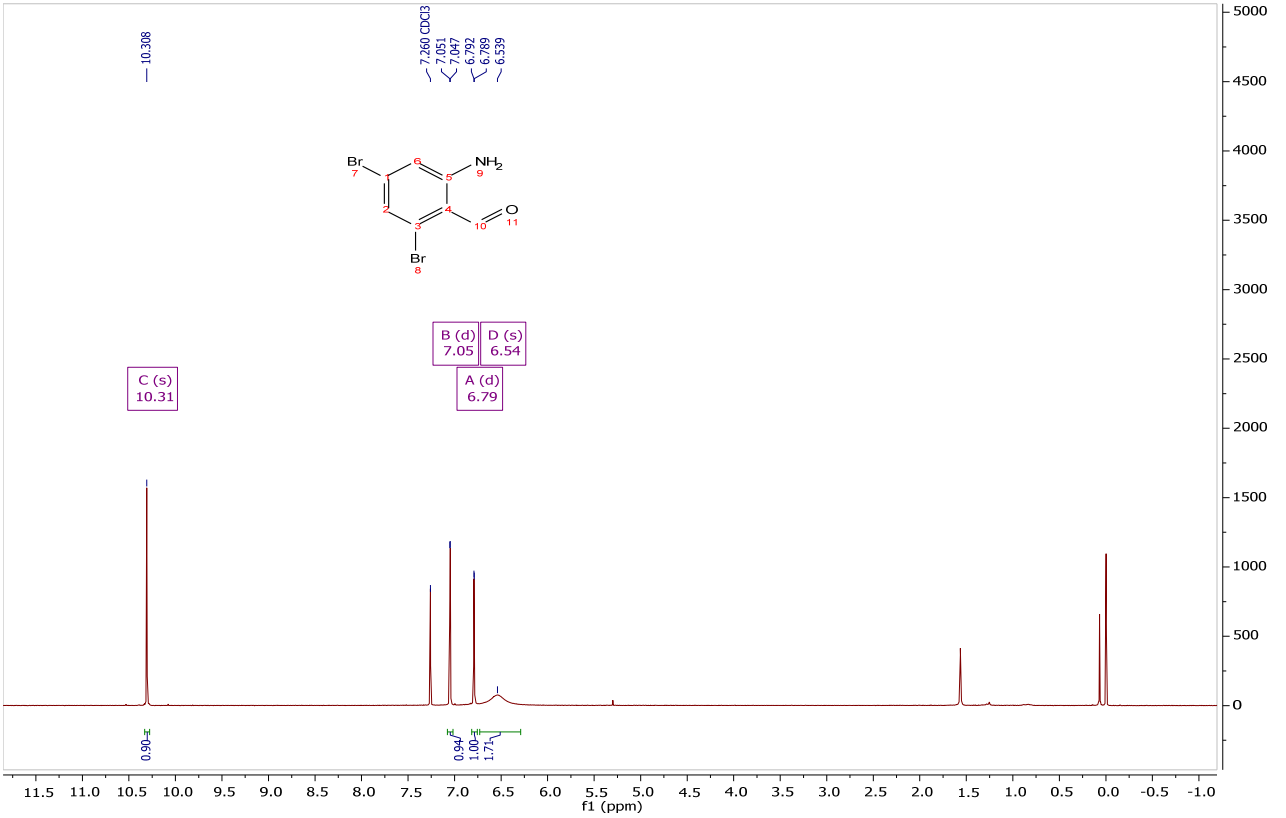


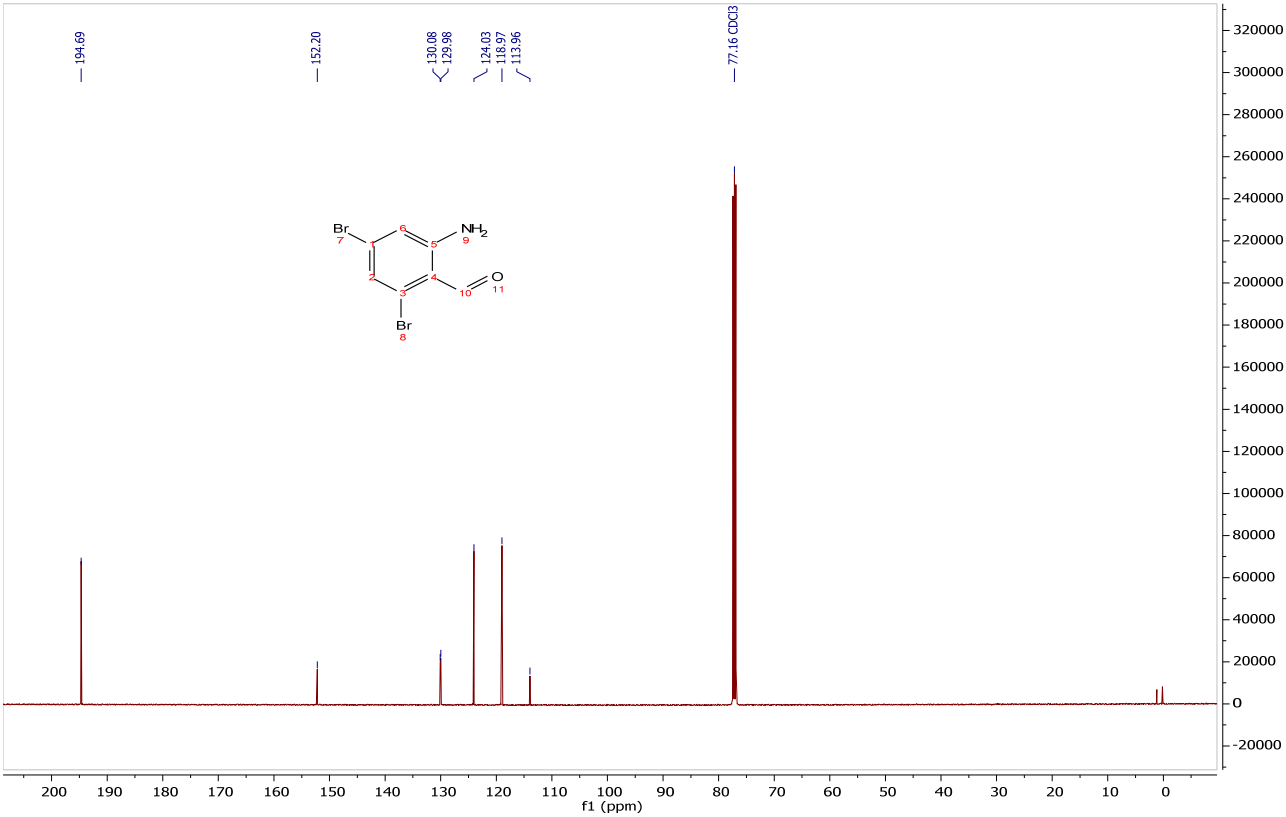
Compound **37:** LC-MS



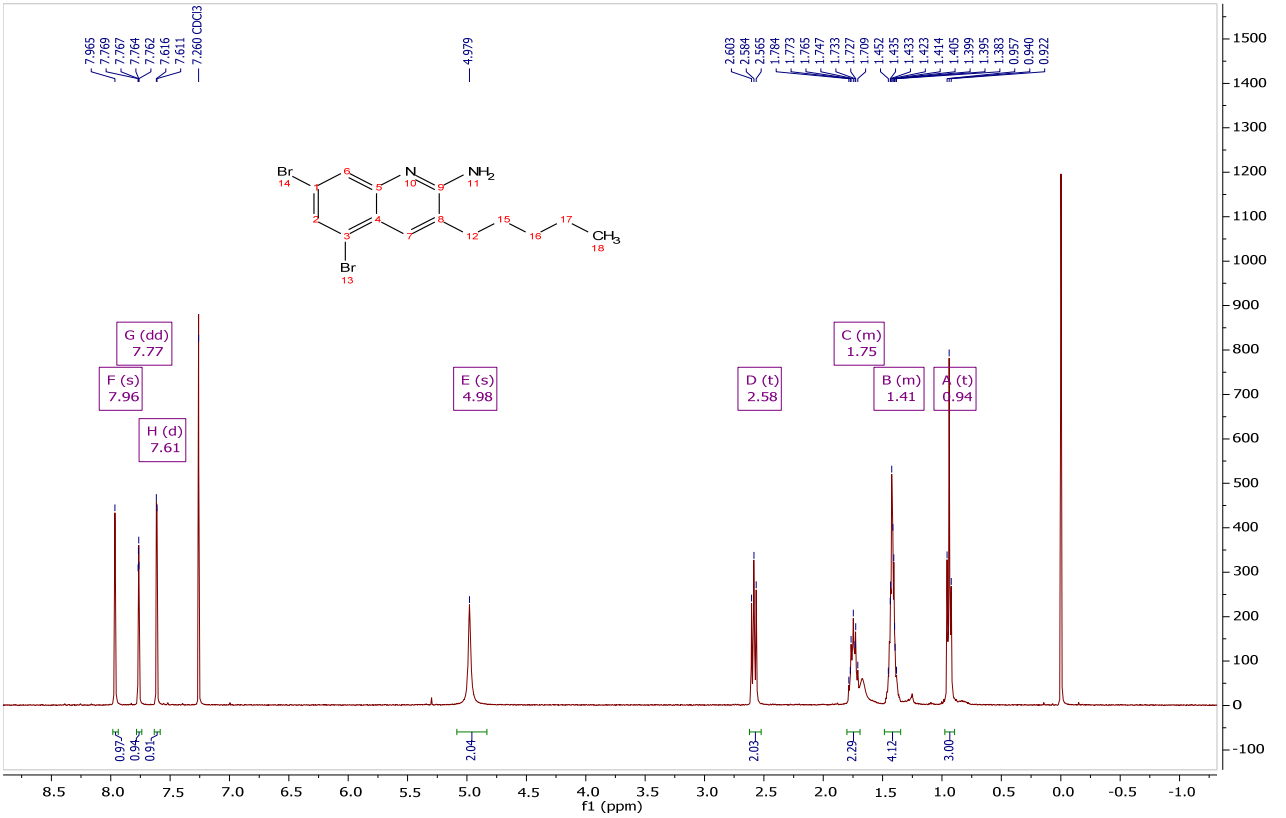


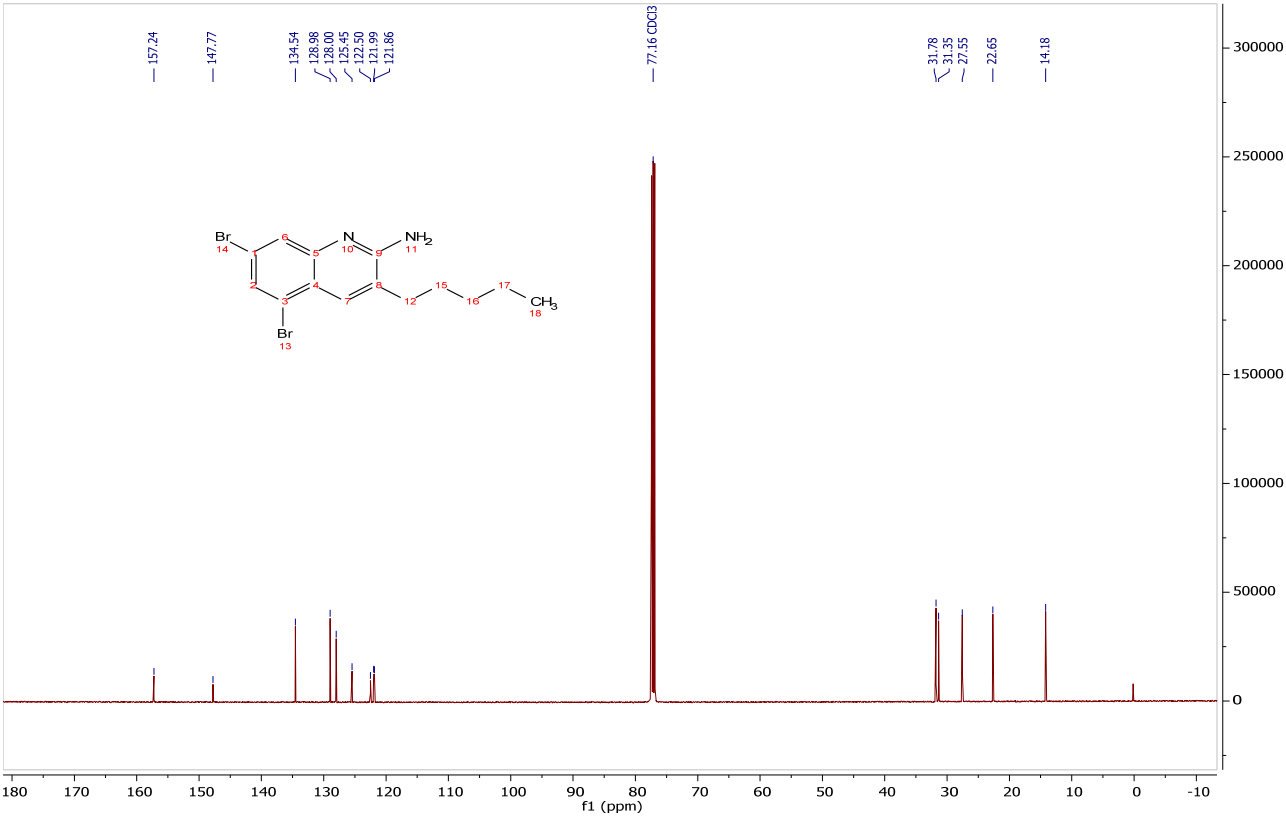
Compound **40:** ^{1}H and ^{13}C NMR Spectrum



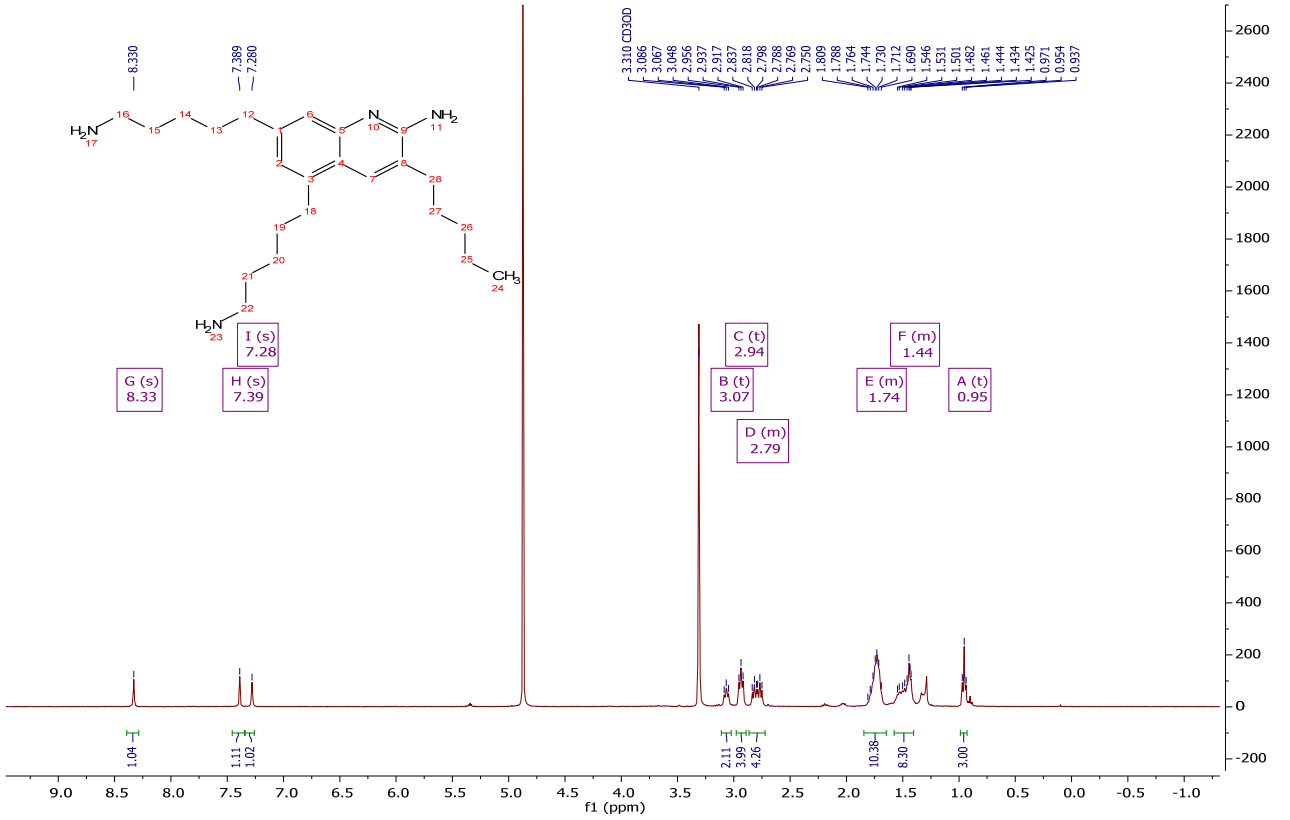


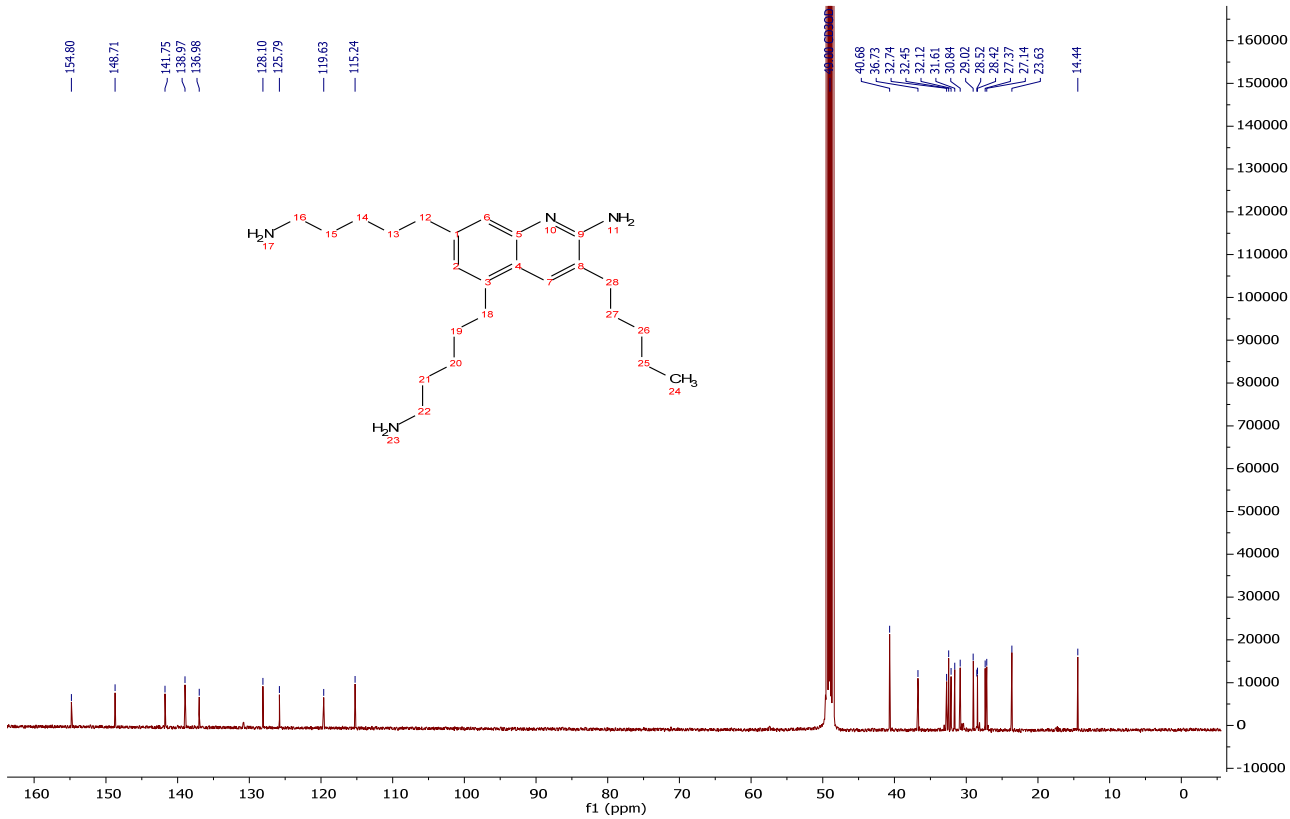
Compound **41:** ^{1}H and ^{13}C NMR Spectrum





Compound **43:** ^{1}H and ^{13}C NMR Spectrum





Compound **43:** LC-MS