

Supporting Information

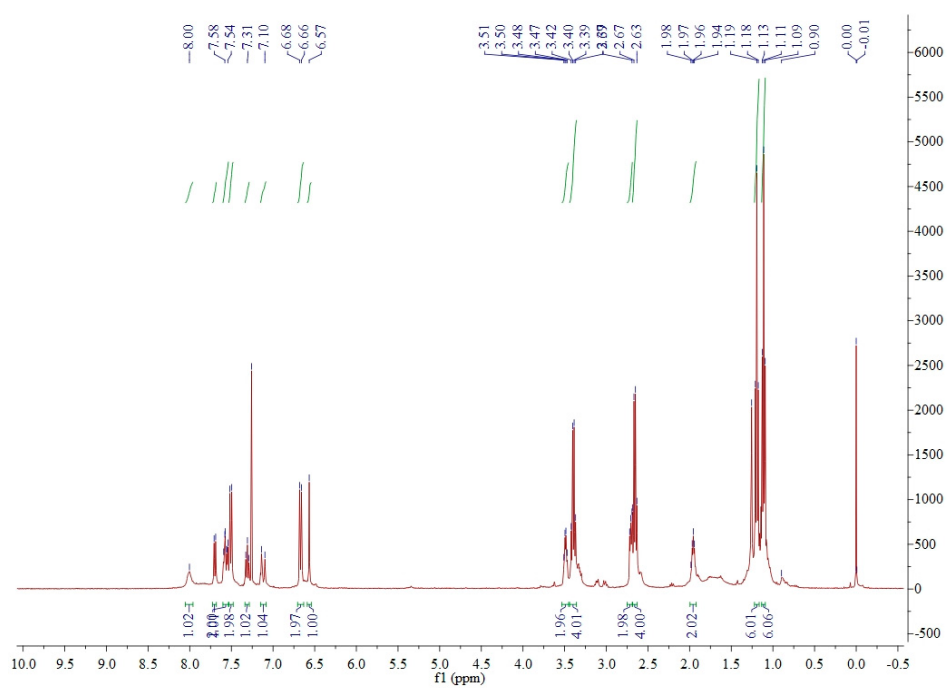
Preparation of Novel 4-Flexible amino-2-arylethenylquinoline Derivatives as Multitarget Agents for the Treatment of Alzheimer's Disease

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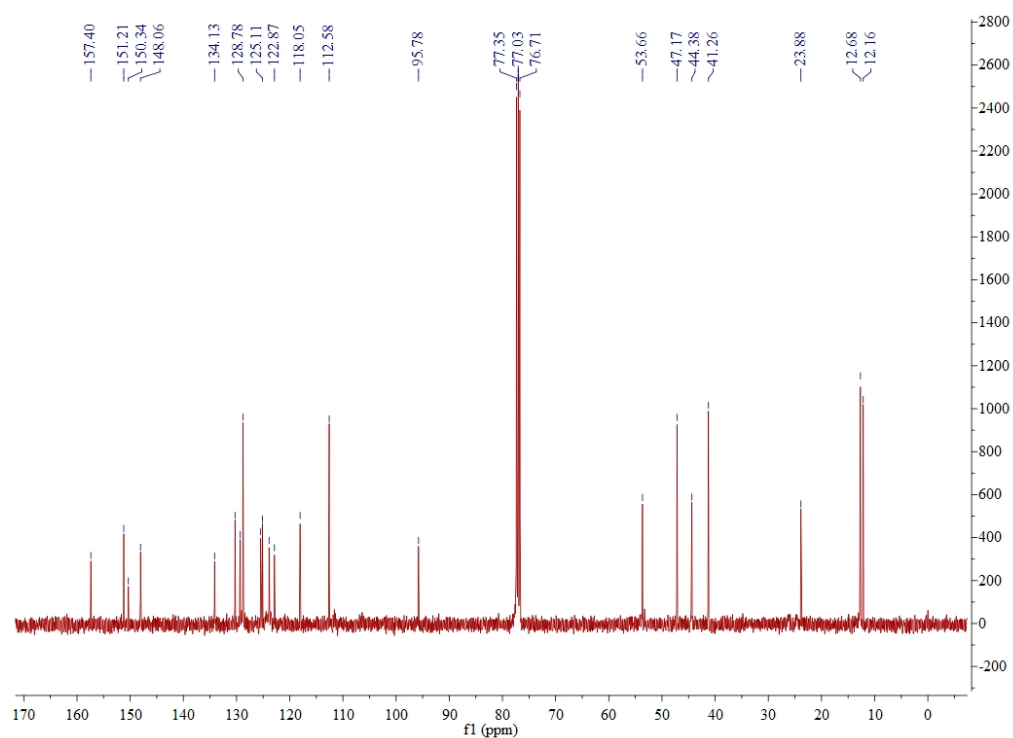
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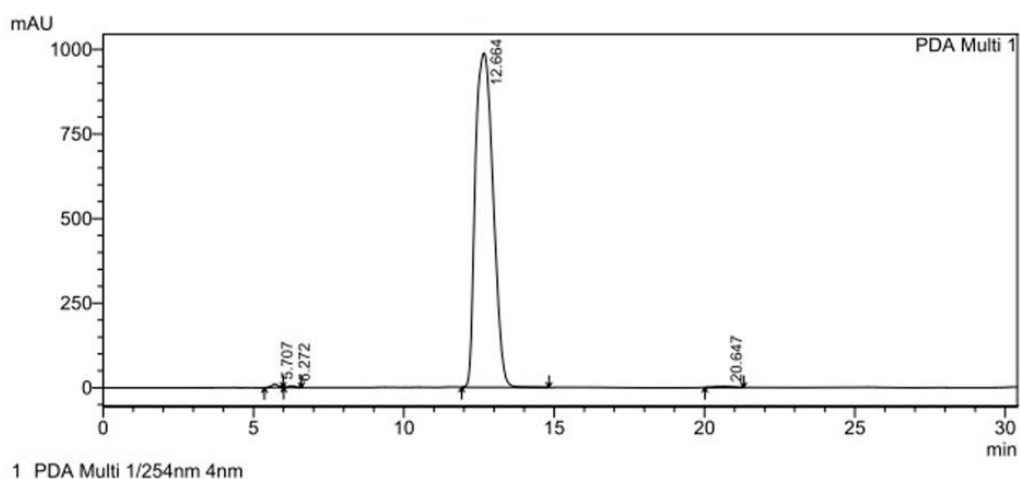
The representative ^1H NMR, ^{13}C NMR spectra, HPLC and HRMS spectra of the target compounds.



¹H NMR spectrum of **6a1**



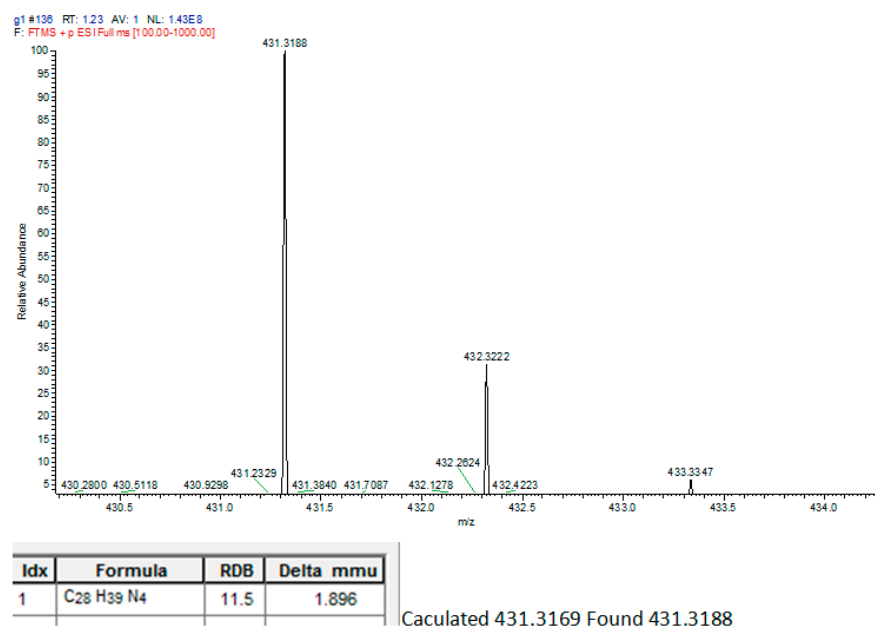
¹³C NMR spectrum of **6a1**



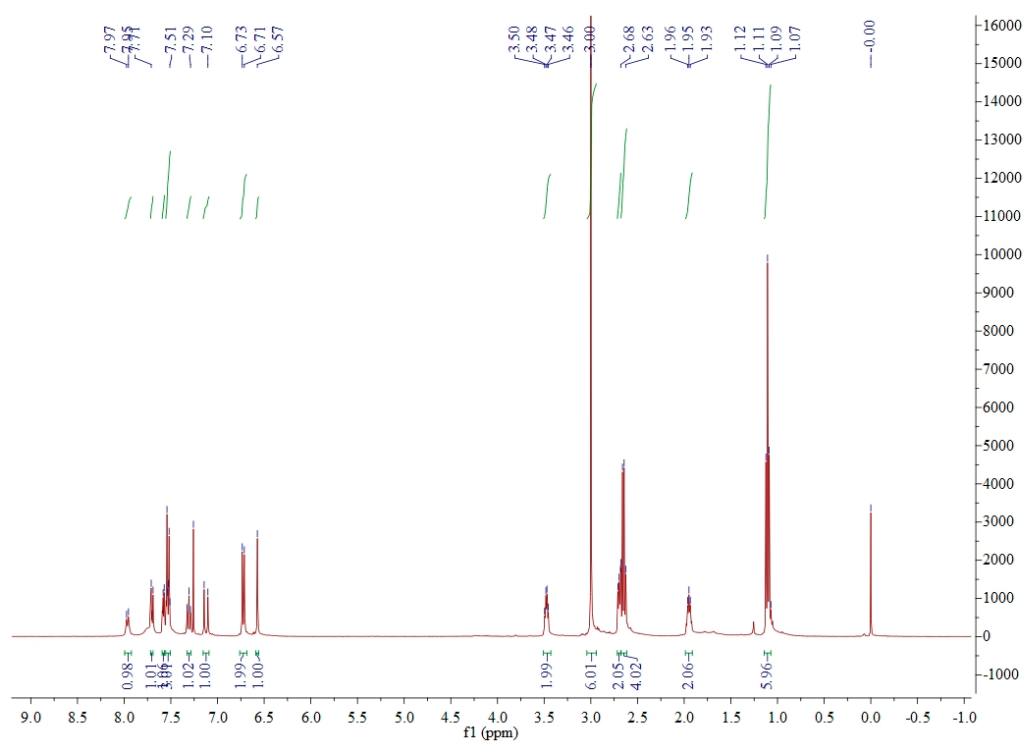
PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.707	135319	9934	0.331	0.988
2	6.272	63128	4598	0.154	0.457
3	12.664	40618406	988255	99.245	98.282
4	20.647	110647	2747	0.270	0.273
Total		40927500	1005533	100.000	100.000

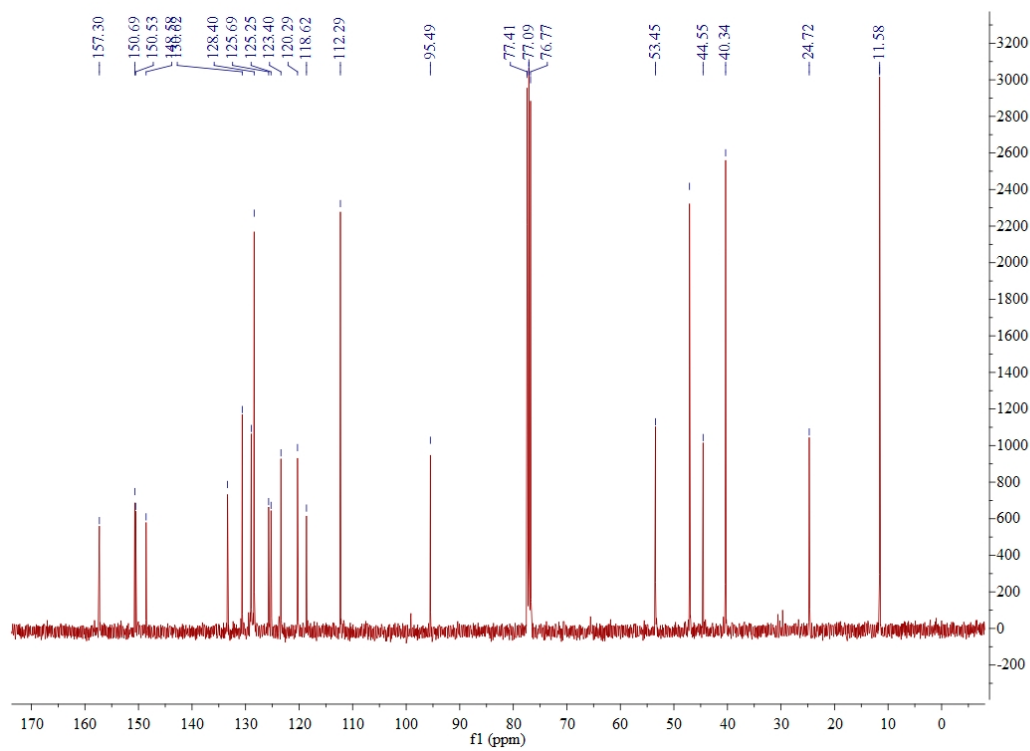
HPLC spectrum of **6a₁**



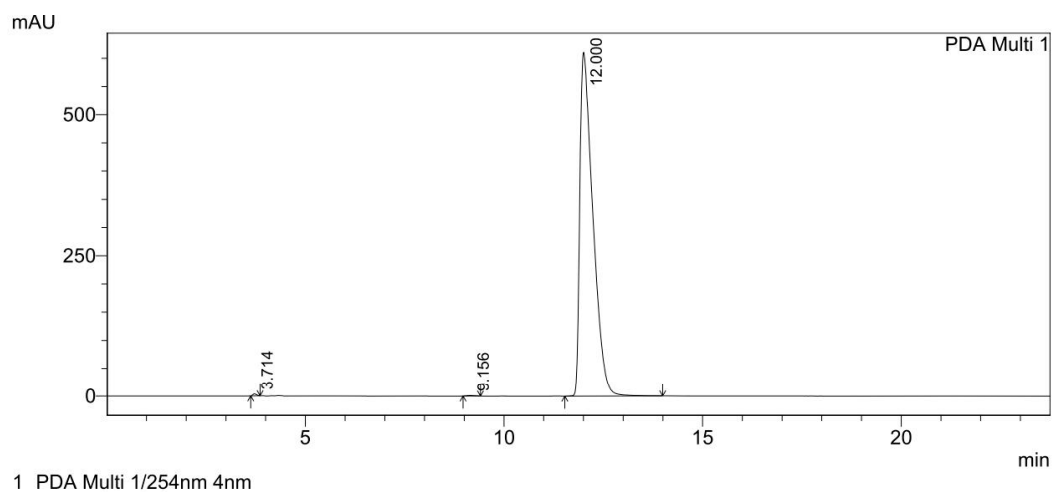
HRMS spectra of **6a₁**



¹H NMR spectrum of **6a2**



¹³C NMR spectrum of **6a2**

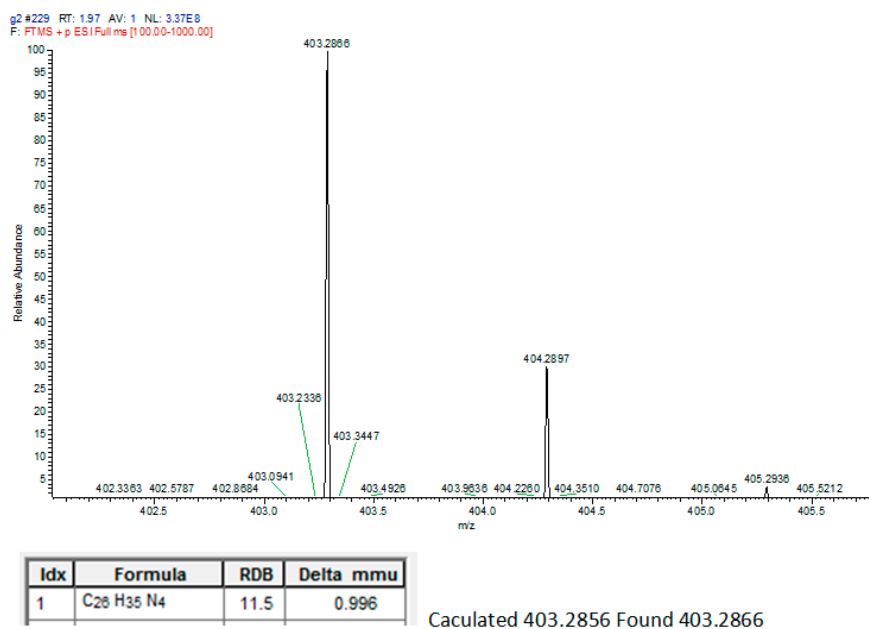


PeakTable

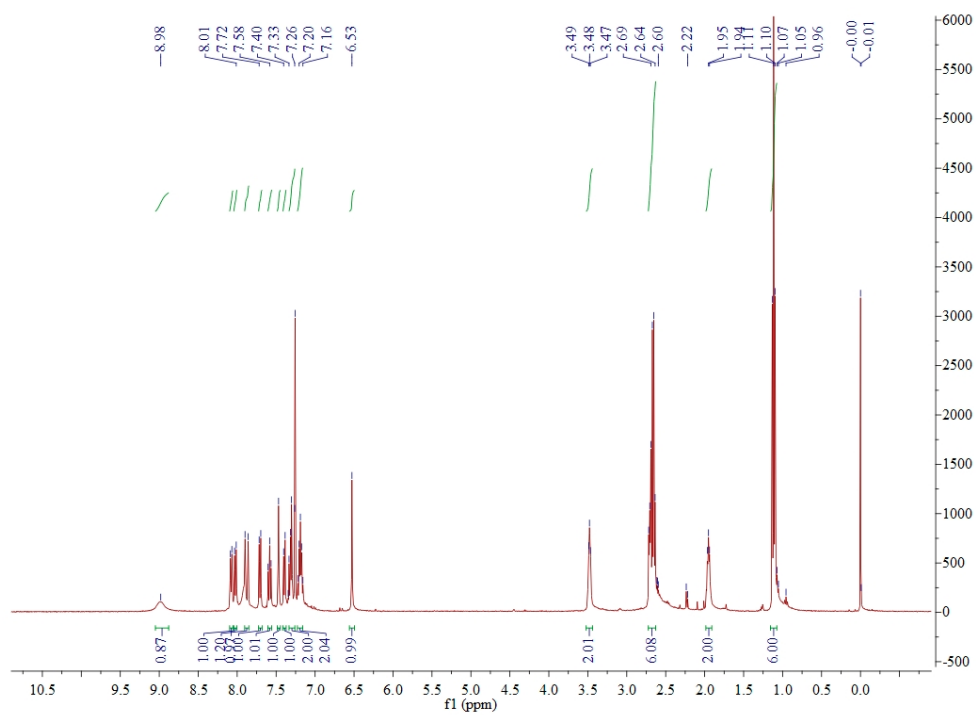
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	3.714	23334	3522	0.167	0.573
2	9.156	13924	1050	0.099	0.171
3	12.000	13969692	610445	99.734	99.257
Total		14006950	615017	100.000	100.000

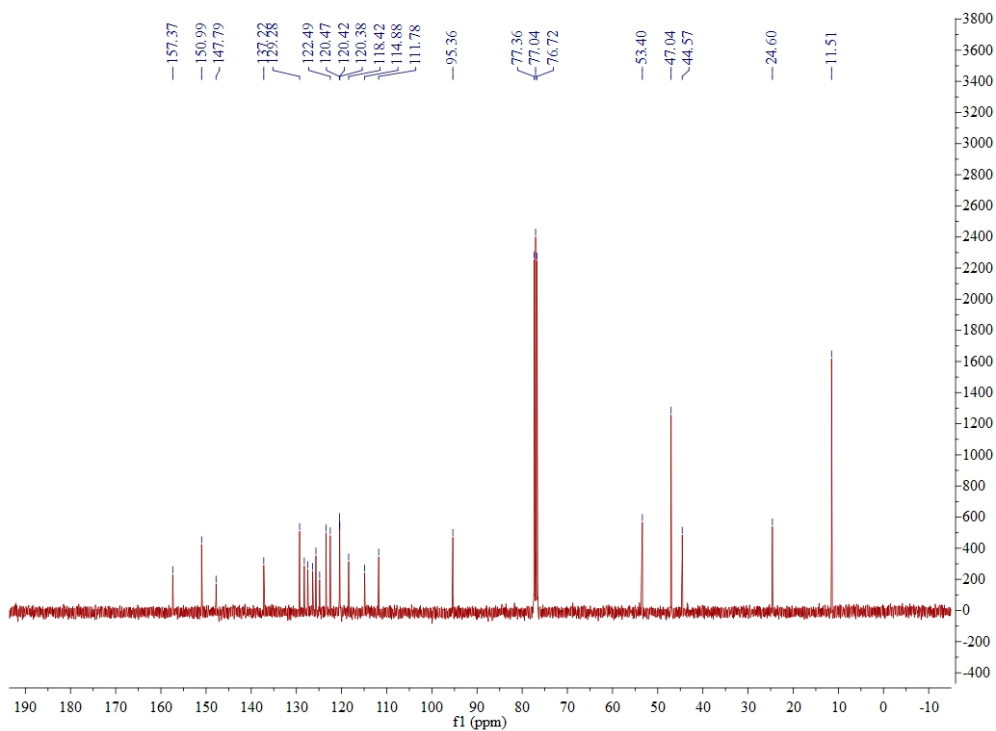
HPLC spectrum of **6a₂**



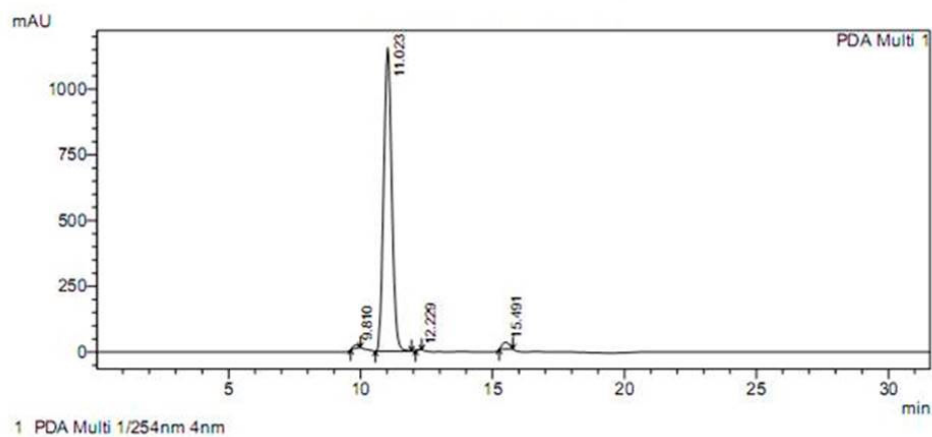
HRMS spectra of **6a₂**



¹H NMR spectrum of 6a



¹³C NMR spectrum of 6a

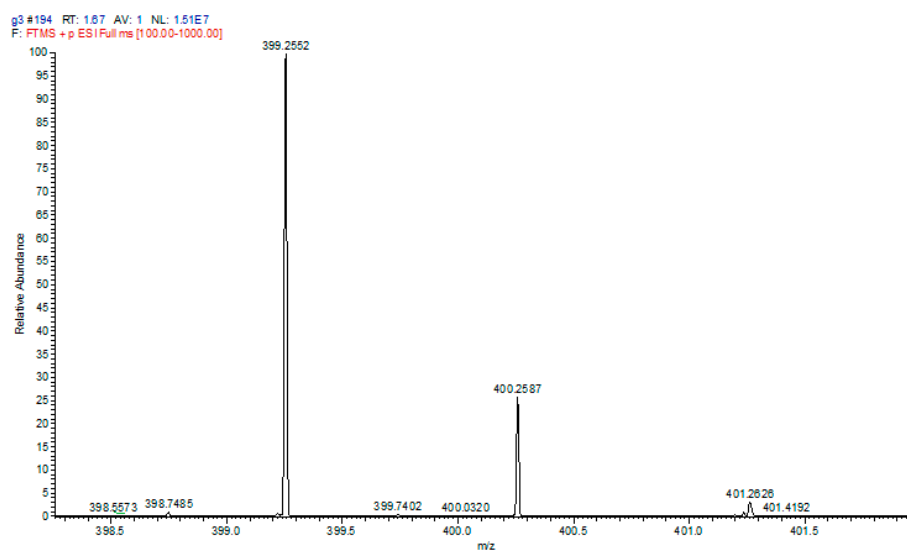


PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.810	191832	13552	0.765	1.132
2	11.023	24373177	1154709	97.198	96.473
3	12.229	22654	2414	0.090	0.202
4	15.491	488049	26246	1.946	2.193
Total		25075711	1196920	100.000	100.000

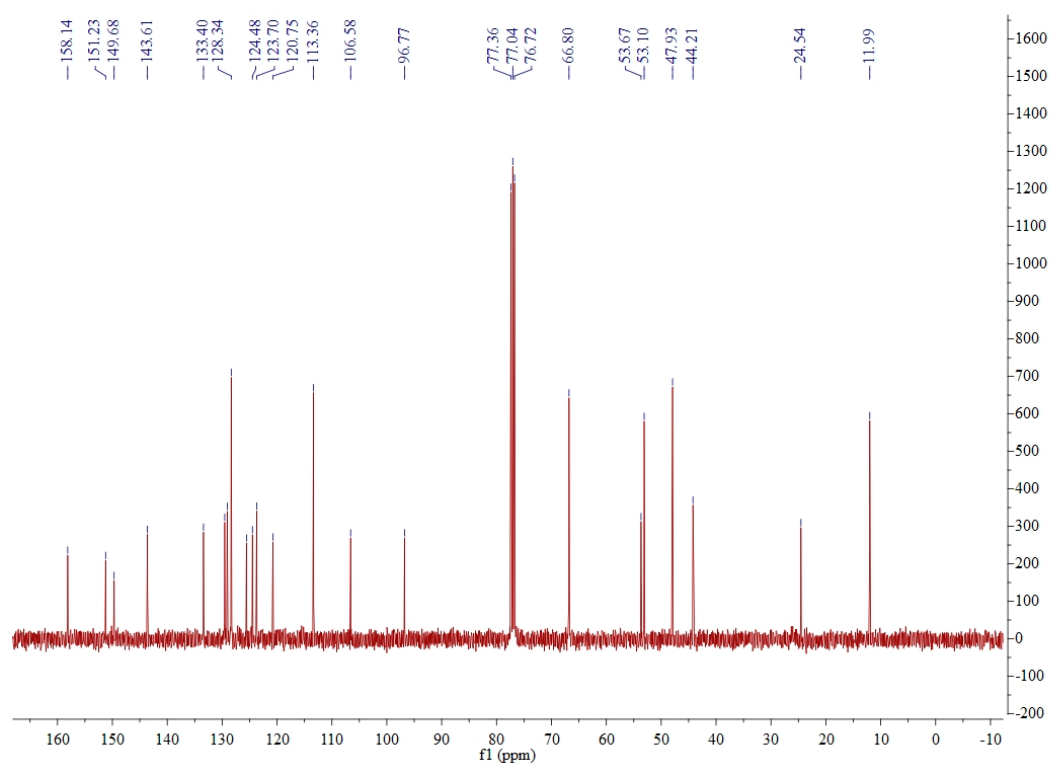
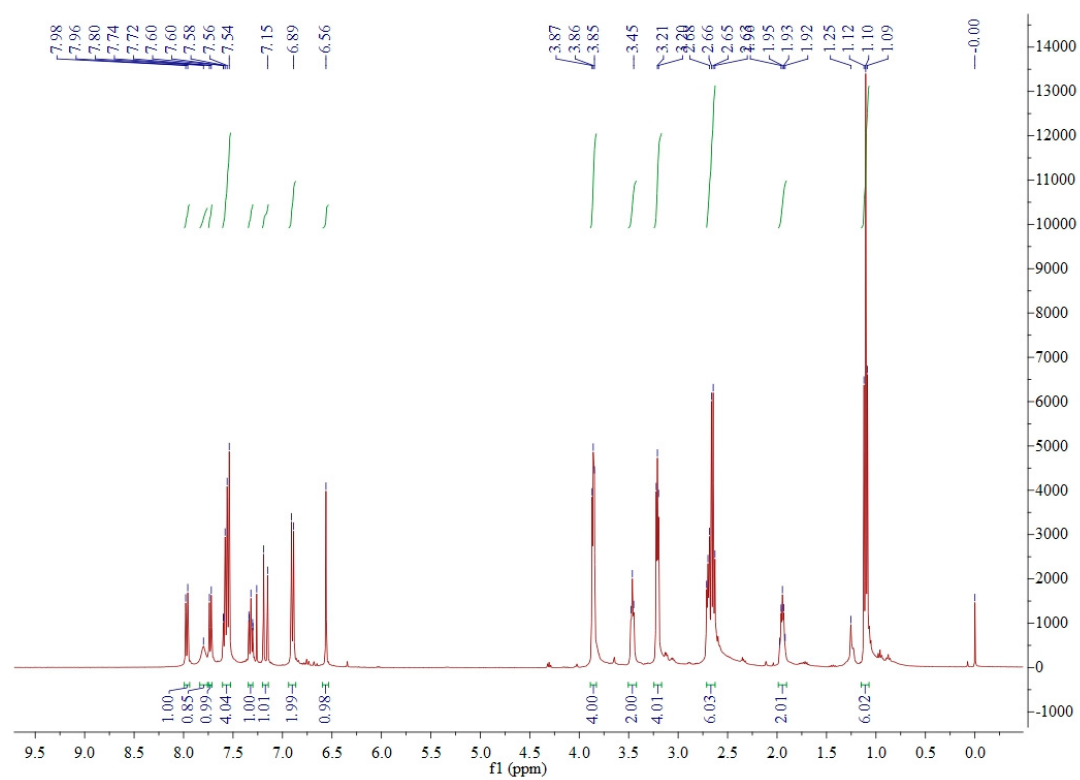
HPLC spectrum of **6a**

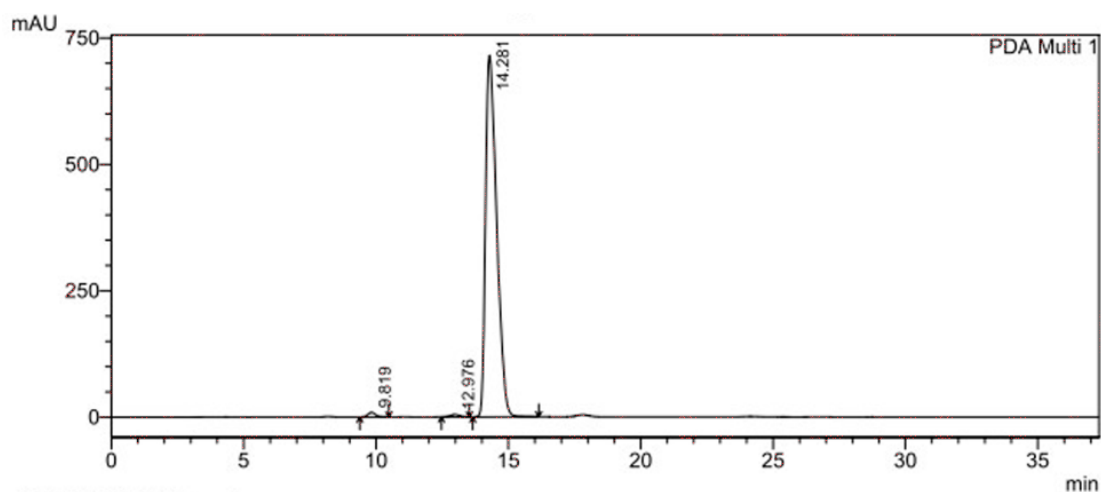


Idx	Formula	RDB	Delta mmu
1	C ₂₆ H ₃₁ N ₄	13.5	0.926

Calculated 399.2543 Found 399.2552

HRMS spectra of **6a**

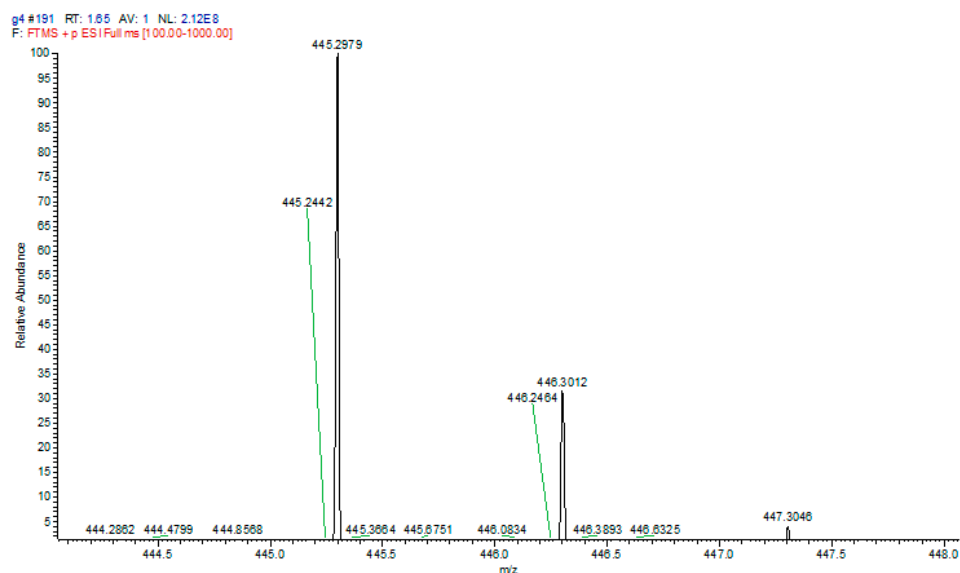




PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.819	177853	9009	0.843	1.235
2	12.976	111004	4849	0.526	0.665
3	14.281	20806314	715474	98.631	98.100
Total		21095171	729332	100.000	100.000

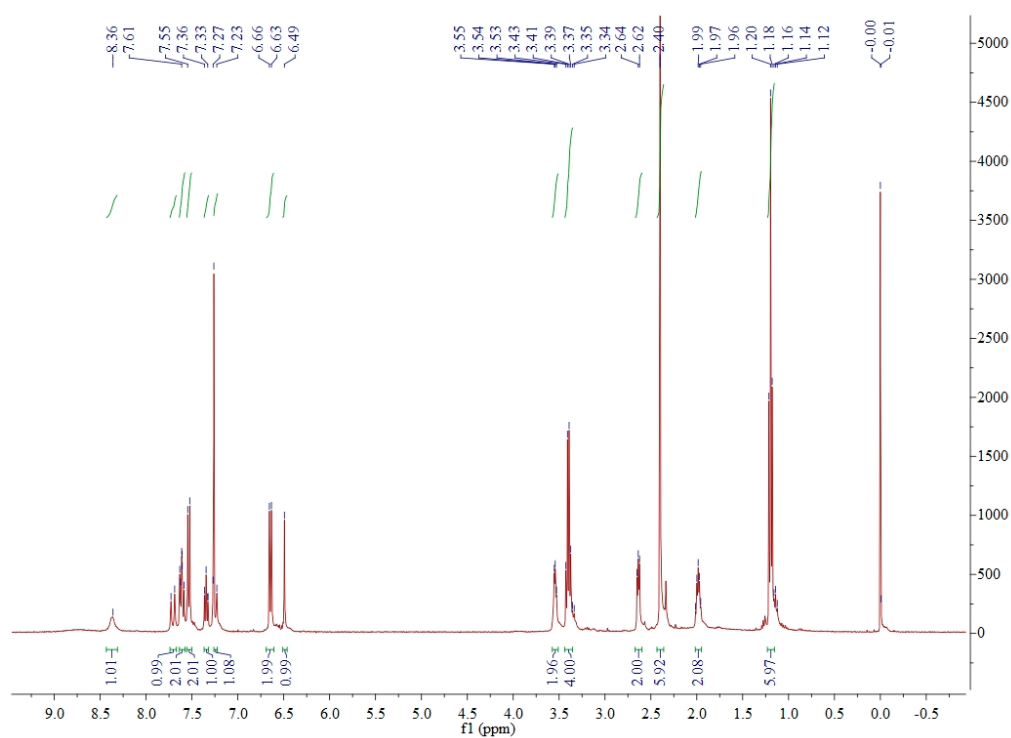
HPLC spectrum of **6a**



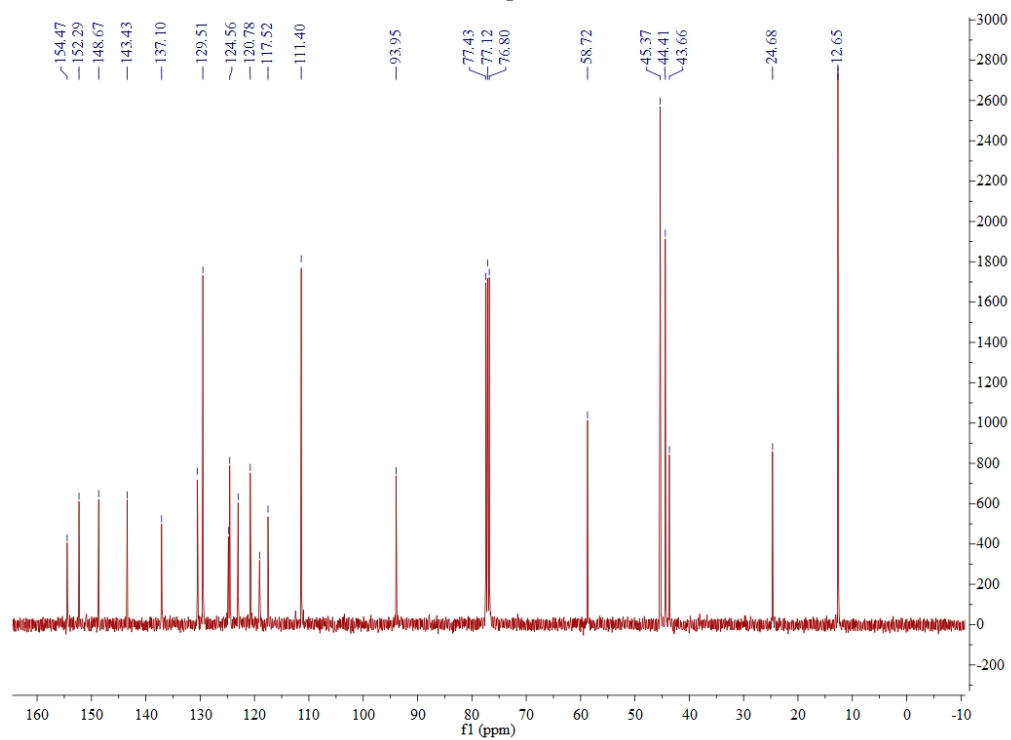
Idx	Formula	RDB	Delta mmu
1	C ₂₈ H ₃₇ O ₄ N ₄	12.5	1.722

Calculated 445.2962 Found 445.2979

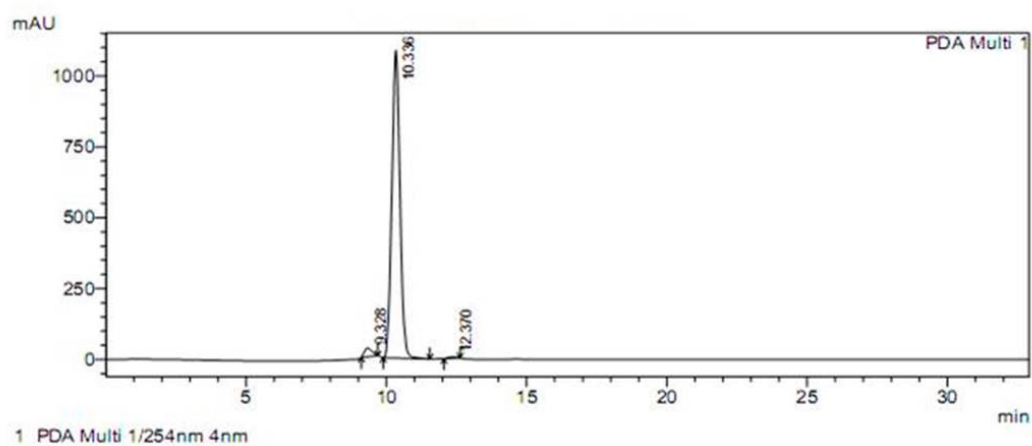
HRMS spectra of **6a**



¹H NMR spectrum of **6b₁**



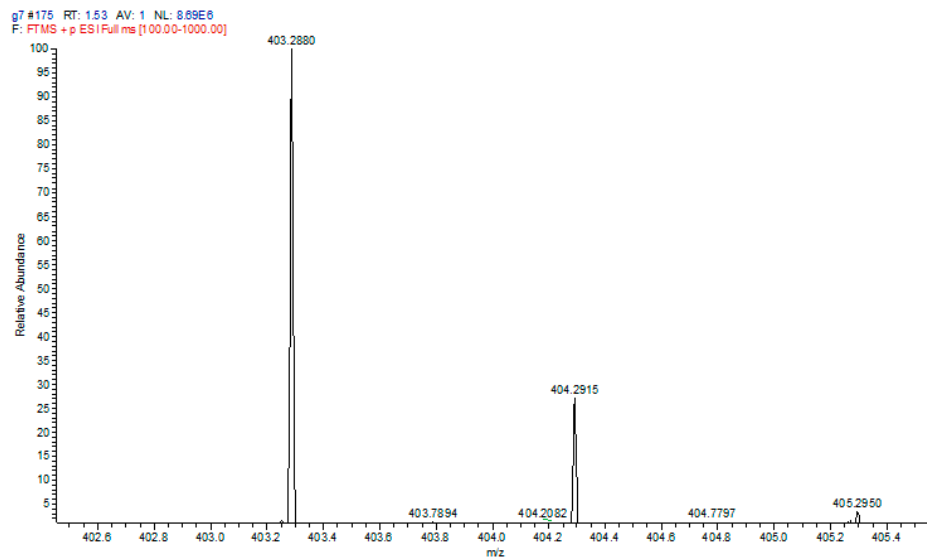
¹³C NMR spectrum of **6b₁**



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.328	576203	30188	2.579	2.694
2	10.336	21664887	1085285	96.978	96.849
3	12.370	98901	5126	0.443	0.457
Total		22339991	1120599	100.000	100.000

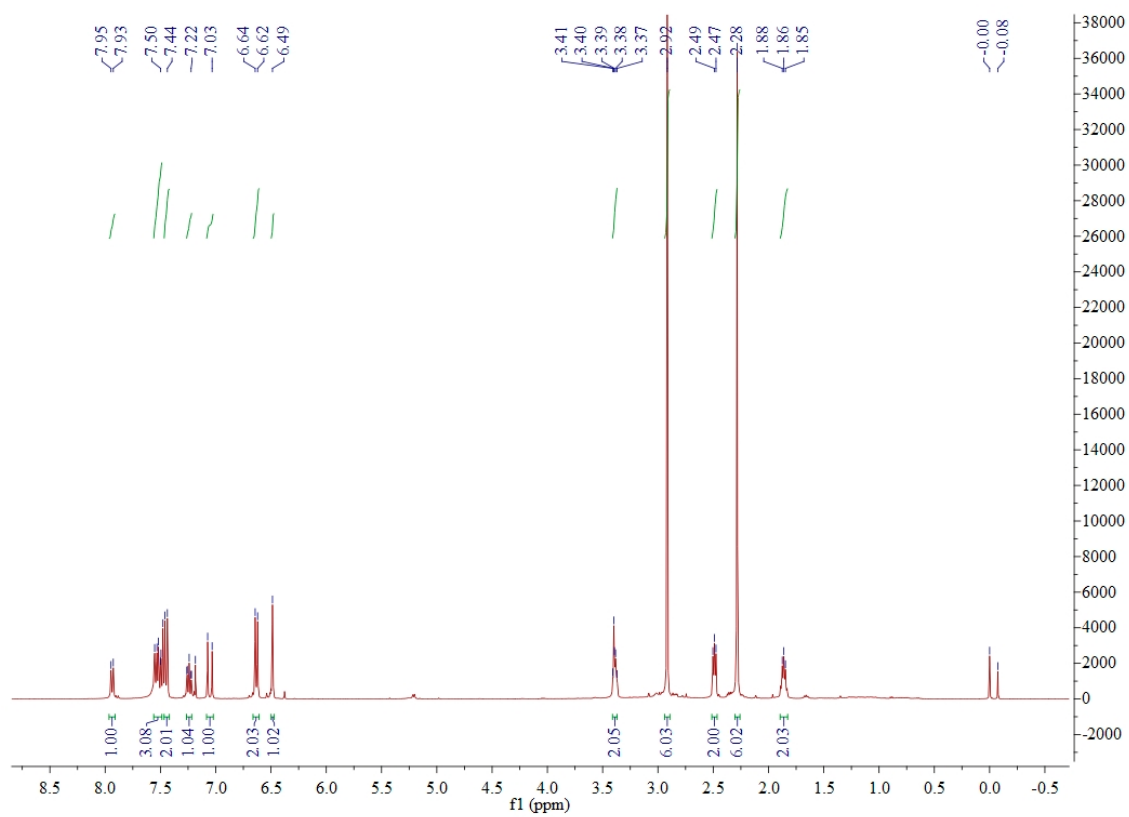
HPLC spectrum of **6b₁**



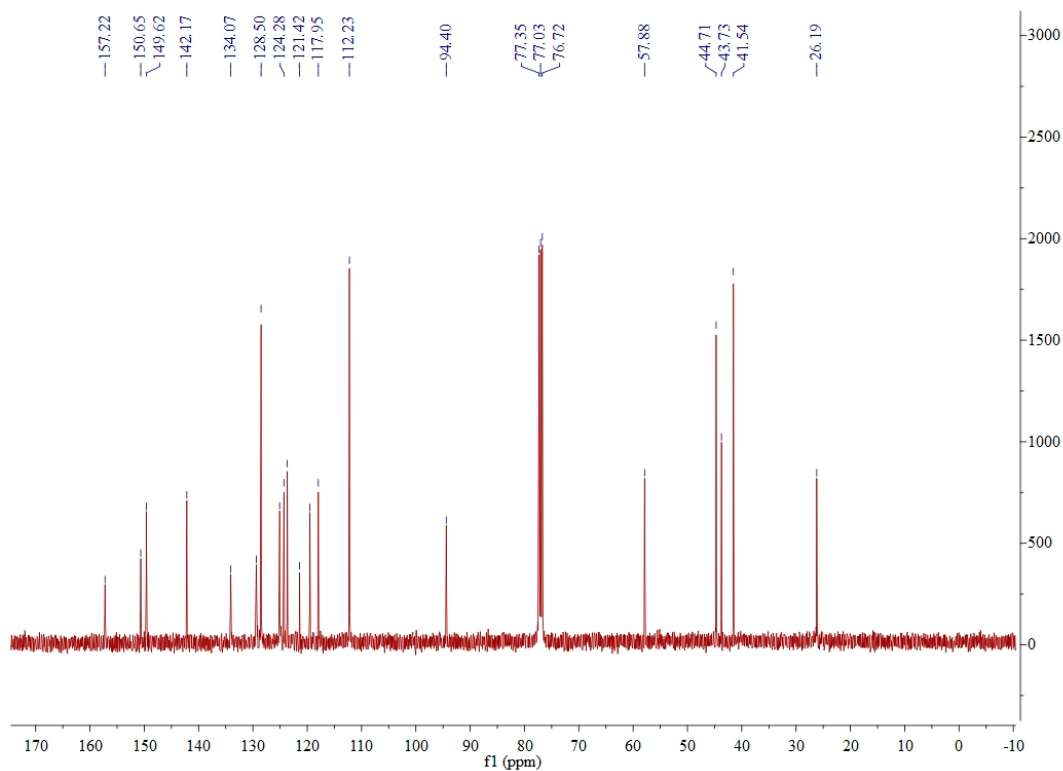
Idx	Formula	RDB	Delta mmu
1	C ₂₈ H ₃₅ N ₄	11.5	2.336

Calculated 403.2856 Found 403.2880

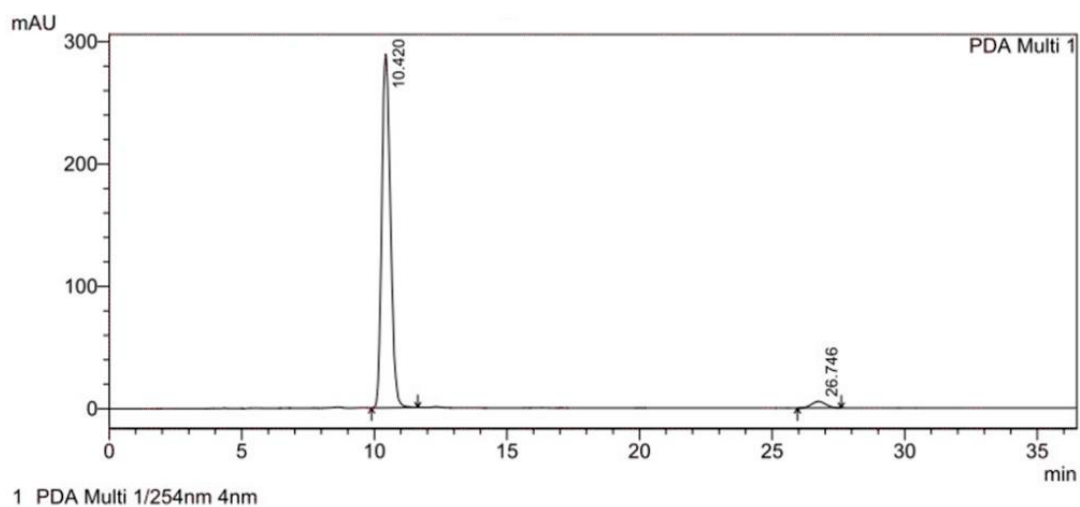
HRMS spectra of **6b₁**



¹H NMR spectrum of **6b₂**



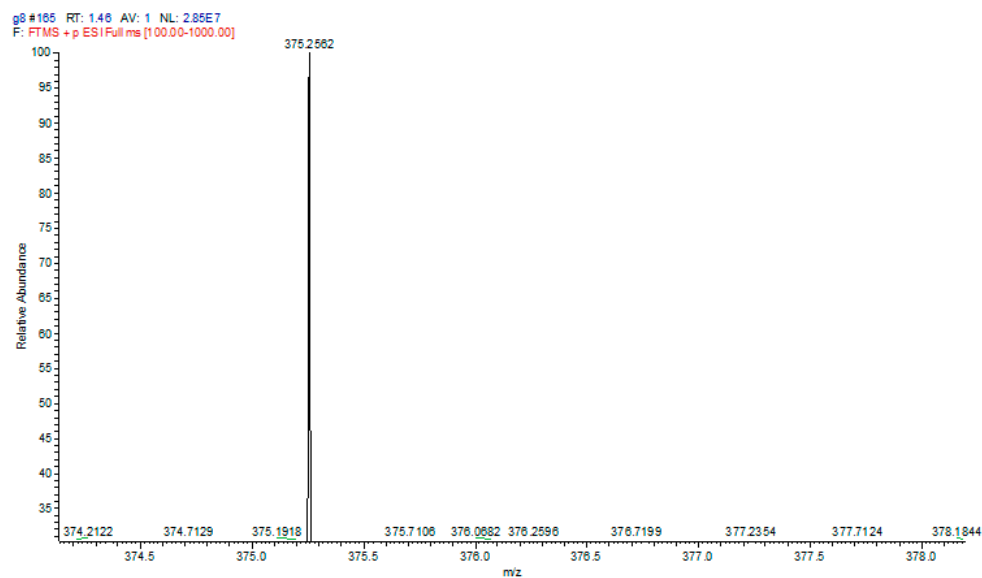
¹³C NMR spectrum of **6b₂**



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.420	6566769	289073	97.022	98.189
2	26.746	201554	5333	2.978	1.811
Total		6768323	294406	100.000	100.000

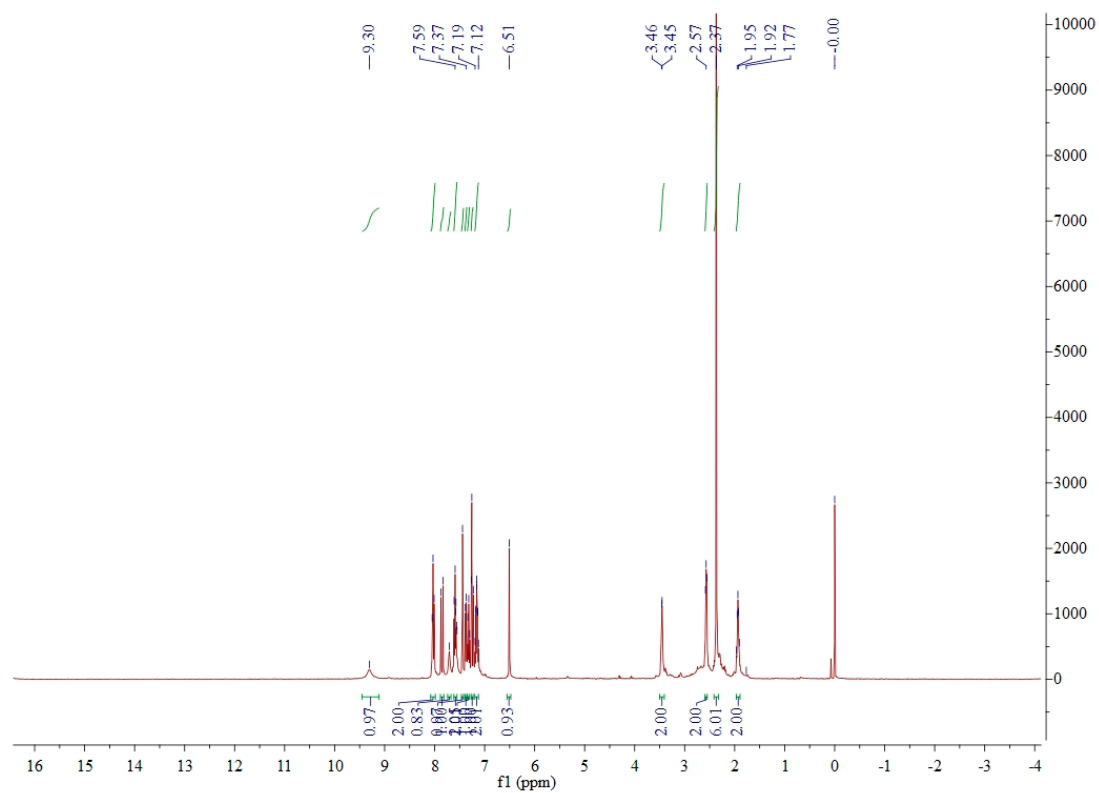
HPLC spectrum of **6b₂**



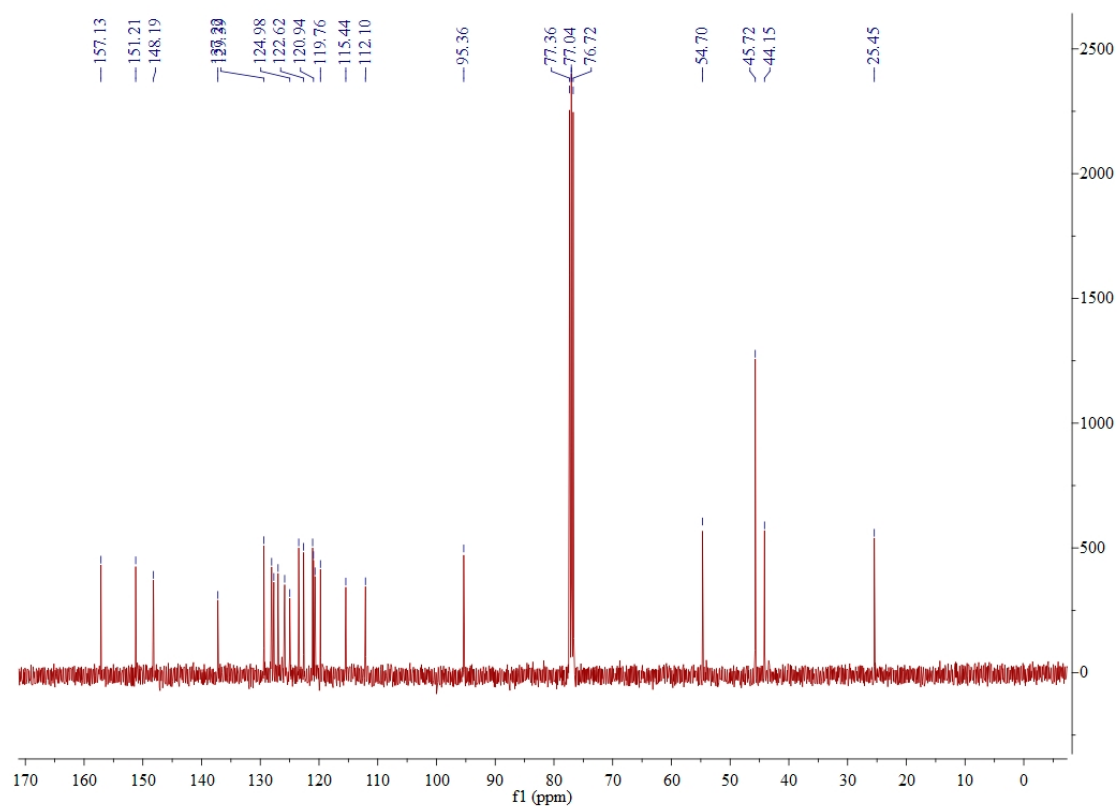
Idx	Formula	RDB	Delta mmu
1	C ₂₄ H ₃₁ N ₄	11.5	1.876

Caculated 375.2543 Found 375.2562

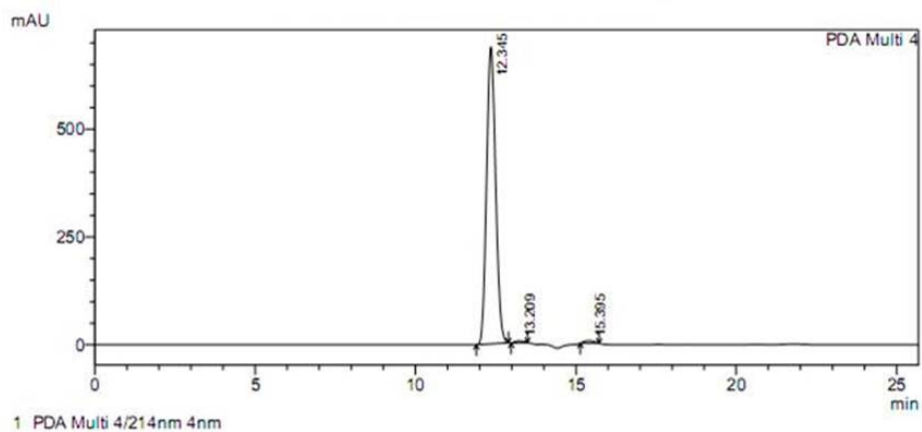
HRMS spectra of **6b₂**



¹H NMR spectrum of **6b₃**



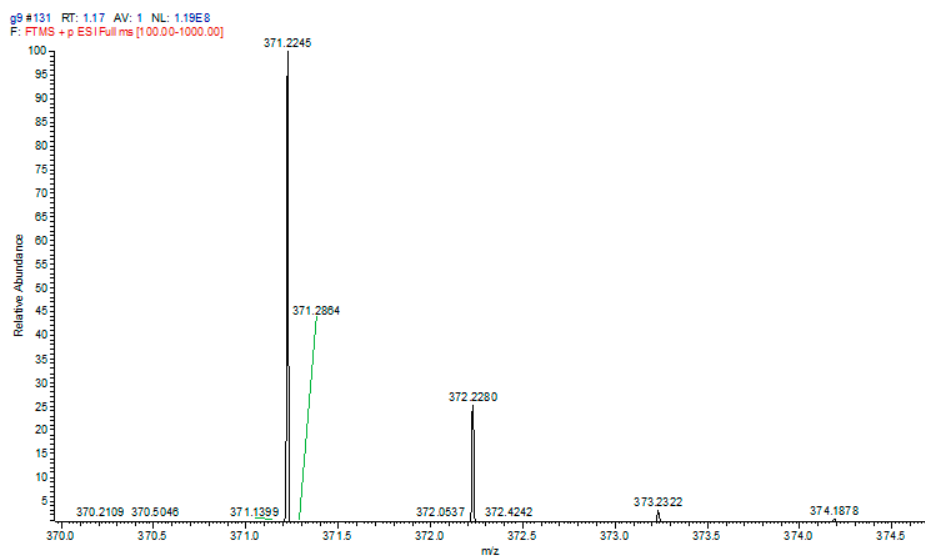
¹³C NMR spectrum of **6b₃**



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.345	13376667	688830	98.453	98.509
2	13.209	77664	4391	0.572	0.628
3	15.395	132490	6032	0.975	0.863
Total		13586821	699253	100.000	100.000

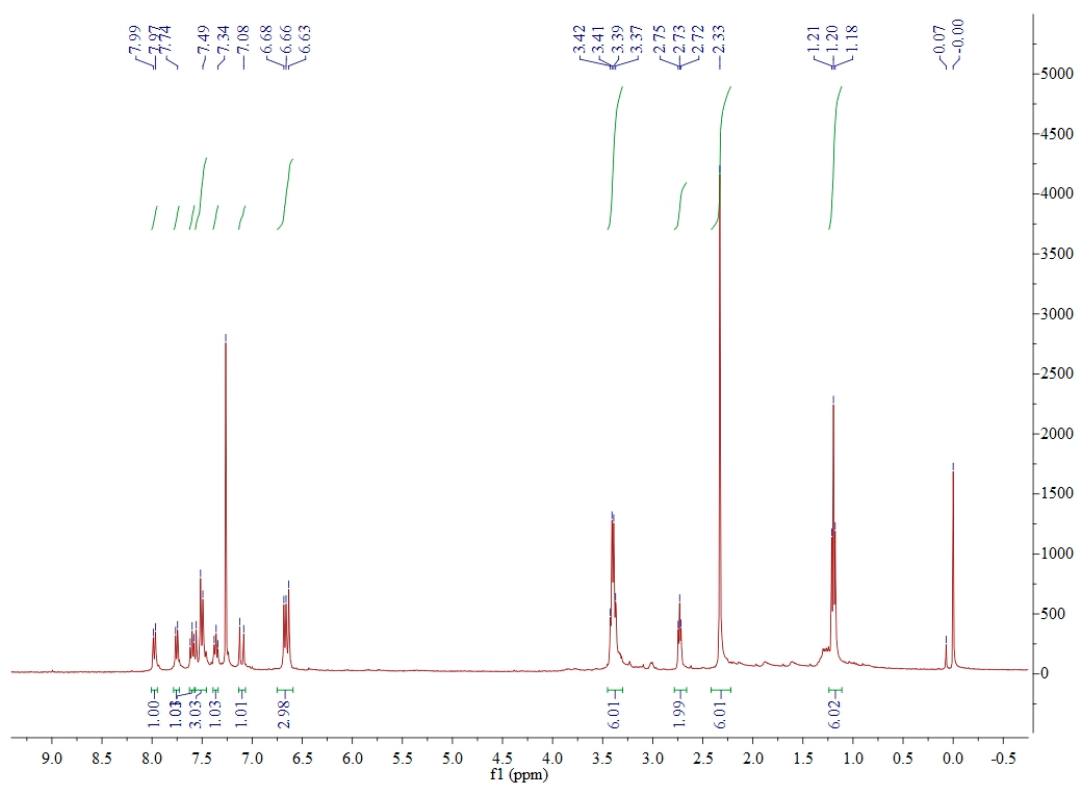
HPLC spectrum of **6b₃**



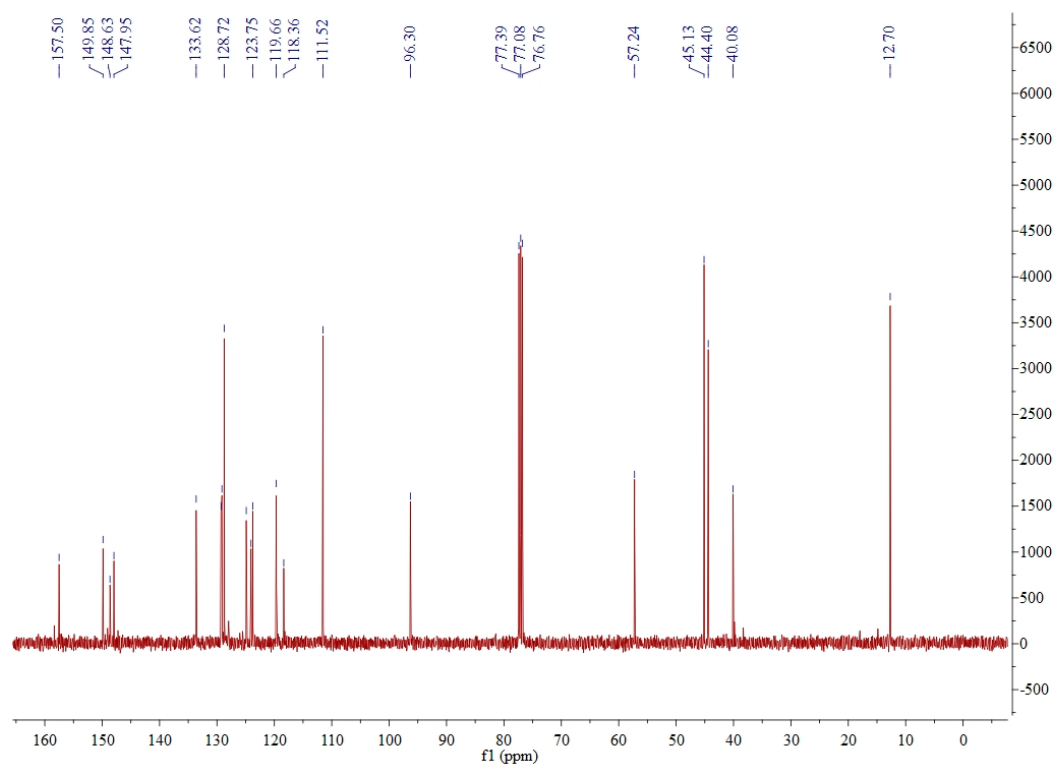
Idx	Formula	RDB	Delta mmu
1	C ₂₄ H ₂₇ N ₄	13.5	1.497

Calculated 371.2230 Found 371.2245

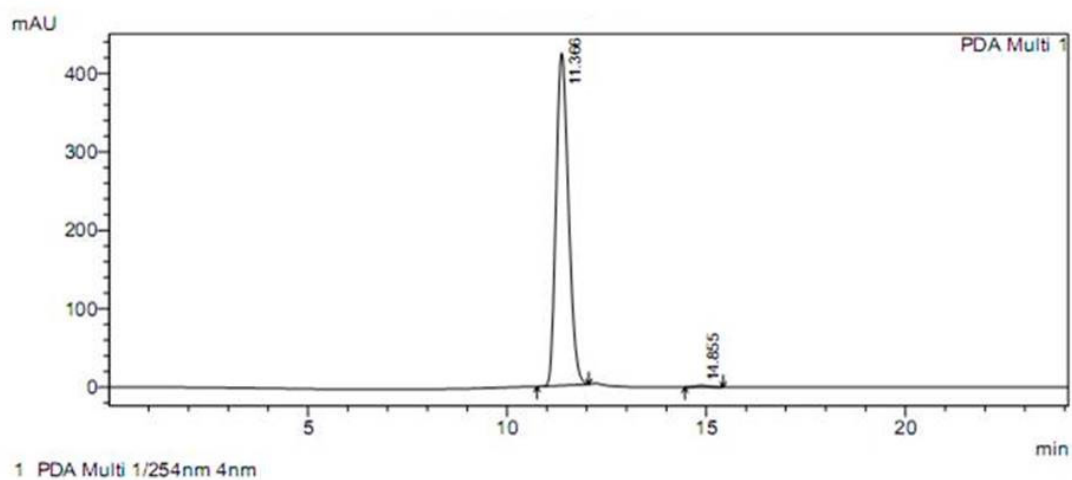
HRMS spectra of **6b₃**



¹H NMR spectrum of **6c1**



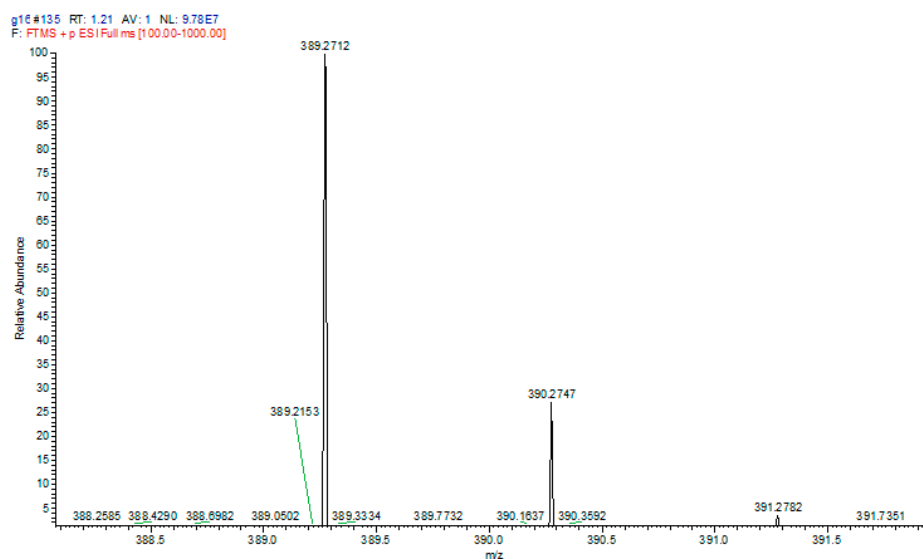
¹³C NMR spectrum of **6c1**



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.366	9198324	424318	99.377	99.425
2	14.855	57653	2454	0.623	0.575
Total		9255977	426772	100.000	100.000

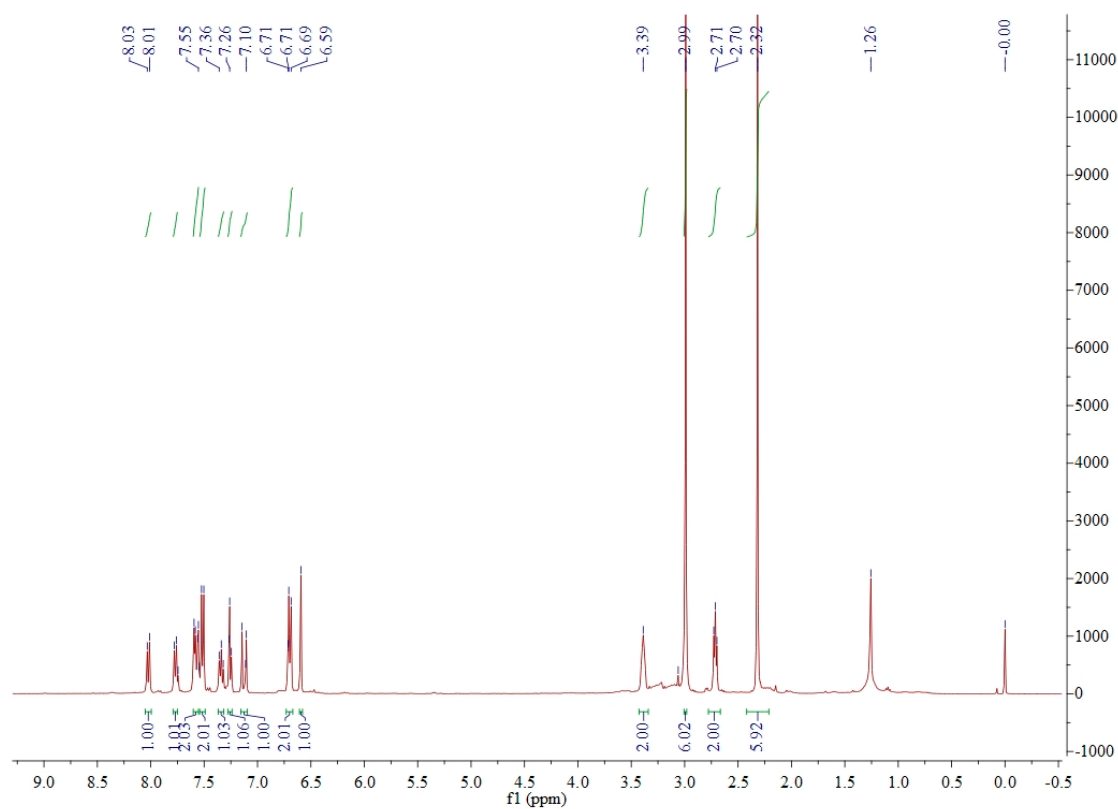
HPLC spectrum of **6c₁**



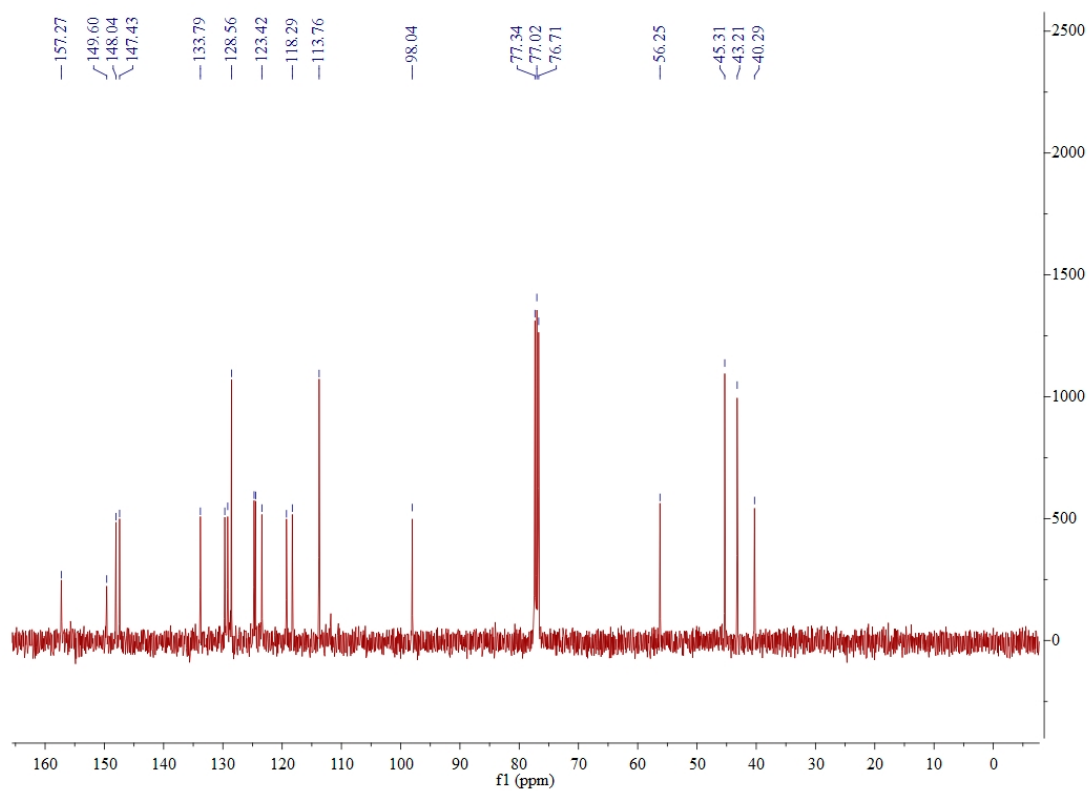
Idx	Formula	RDB	Delta mmu
1	C ₂₅ H ₃₃ N ₄	11.5	1.266

Calculated 389.2700 Found 389.2712

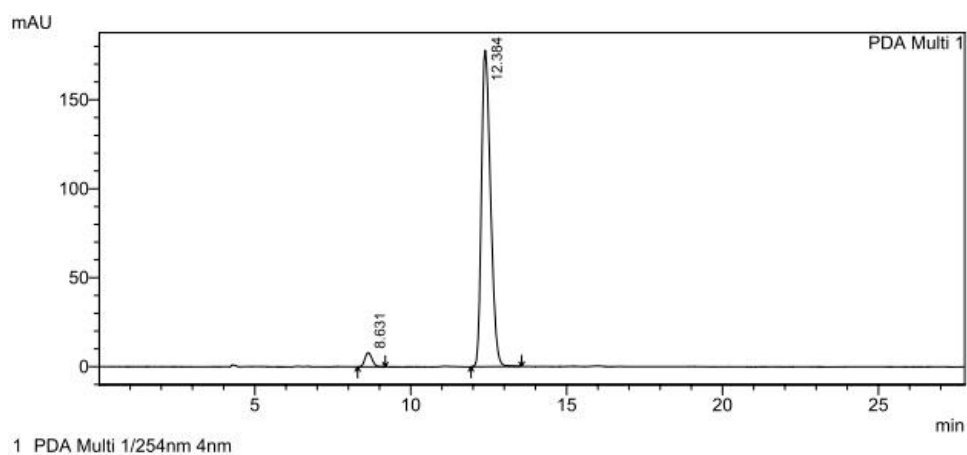
HRMS spectra of **6c₁**



¹H NMR spectrum of **6c2**



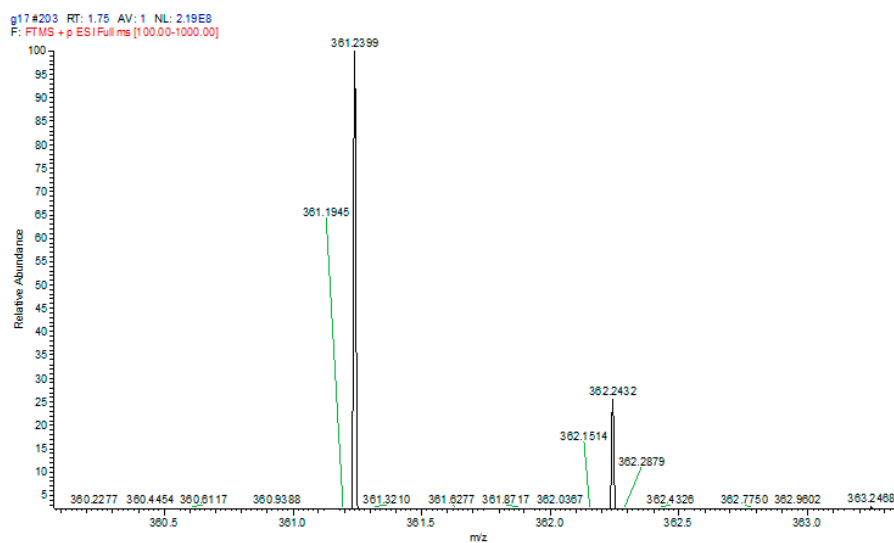
¹³C NMR spectrum of **6c2**



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.631	126388	7876	3.386	4.244
2	12.384	3606432	177683	96.614	95.756
Total		3732820	185559	100.000	100.000

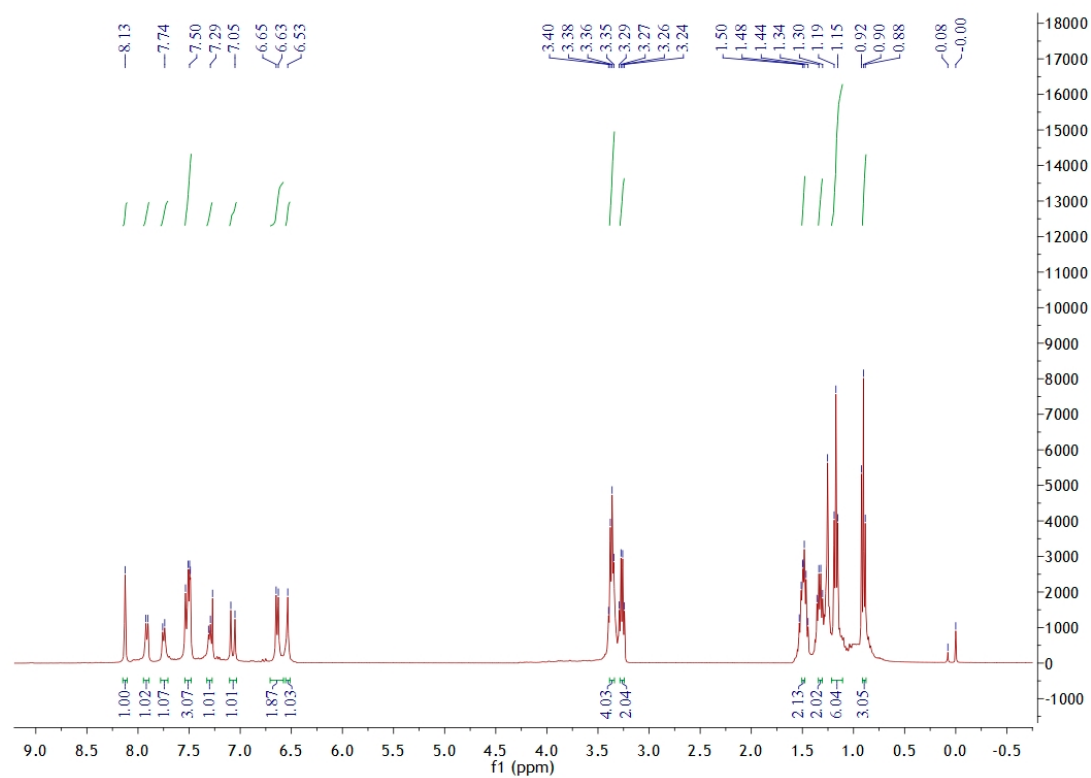
HPLC spectrum of 6c2



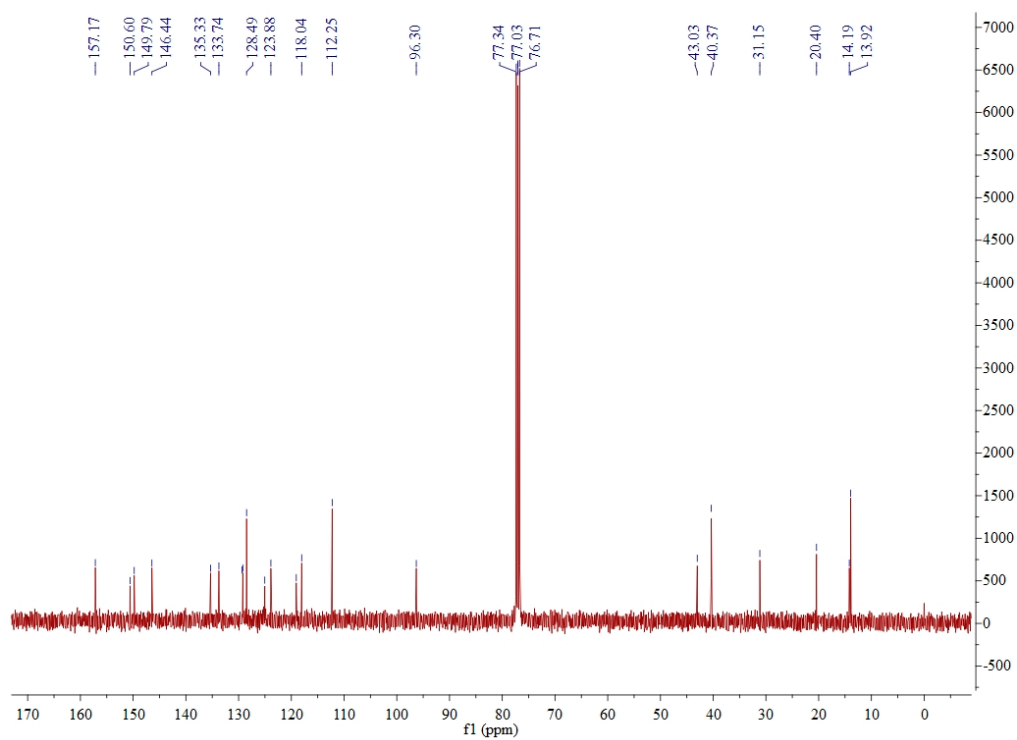
Idx	Formula	RDB	Delta mmu
1	C ₂₃ H ₂₉ N ₄	11.5	1.227

Calculated 361.2387 Found 361.2399

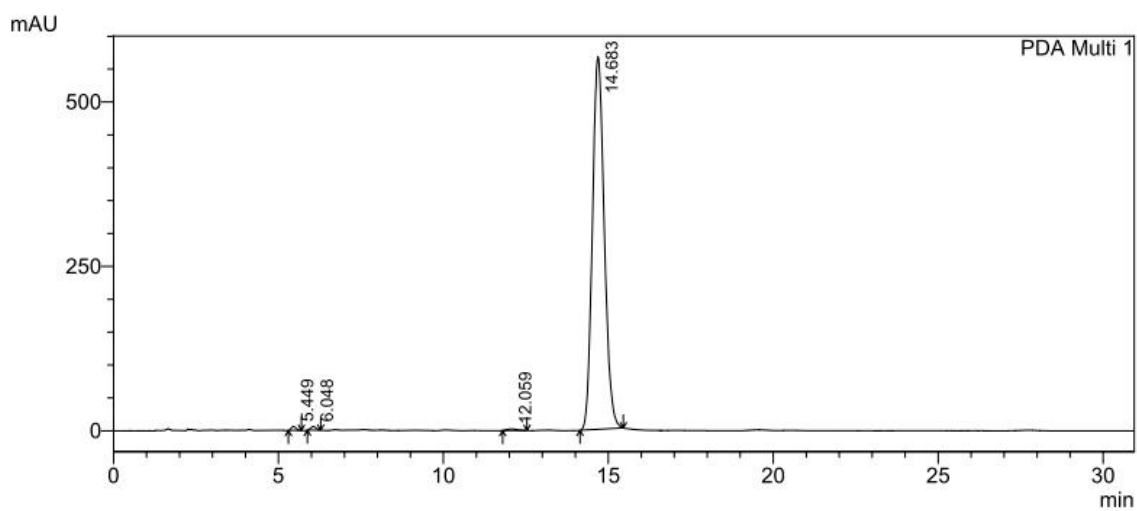
HRMS spectra of 6c2



¹H NMR spectrum of **6d₁**



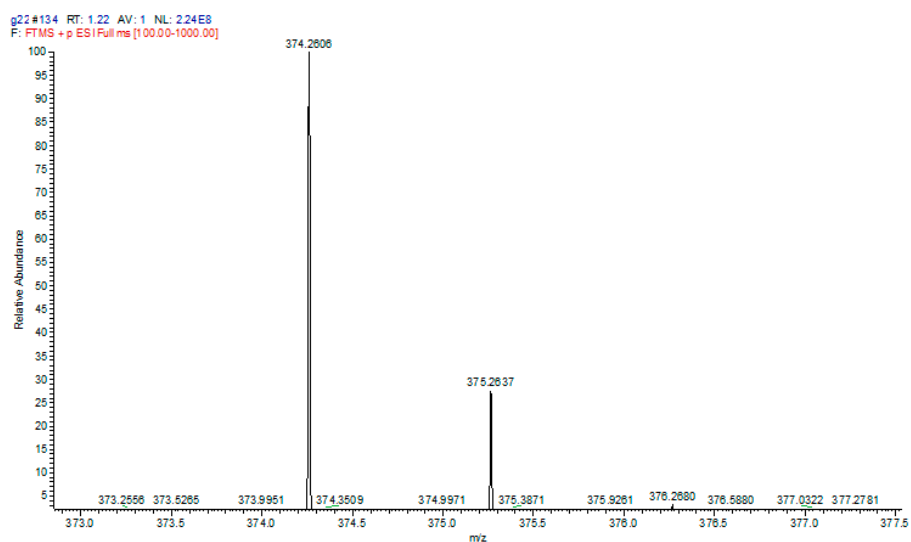
¹³C NMR spectrum of **6d₁**



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.449	58406	6111	0.408	1.053
2	6.048	63630	5403	0.444	0.931
3	12.059	49454	2383	0.345	0.411
4	14.683	14143754	566399	98.802	97.605
Total		14315244	580296	100.000	100.000

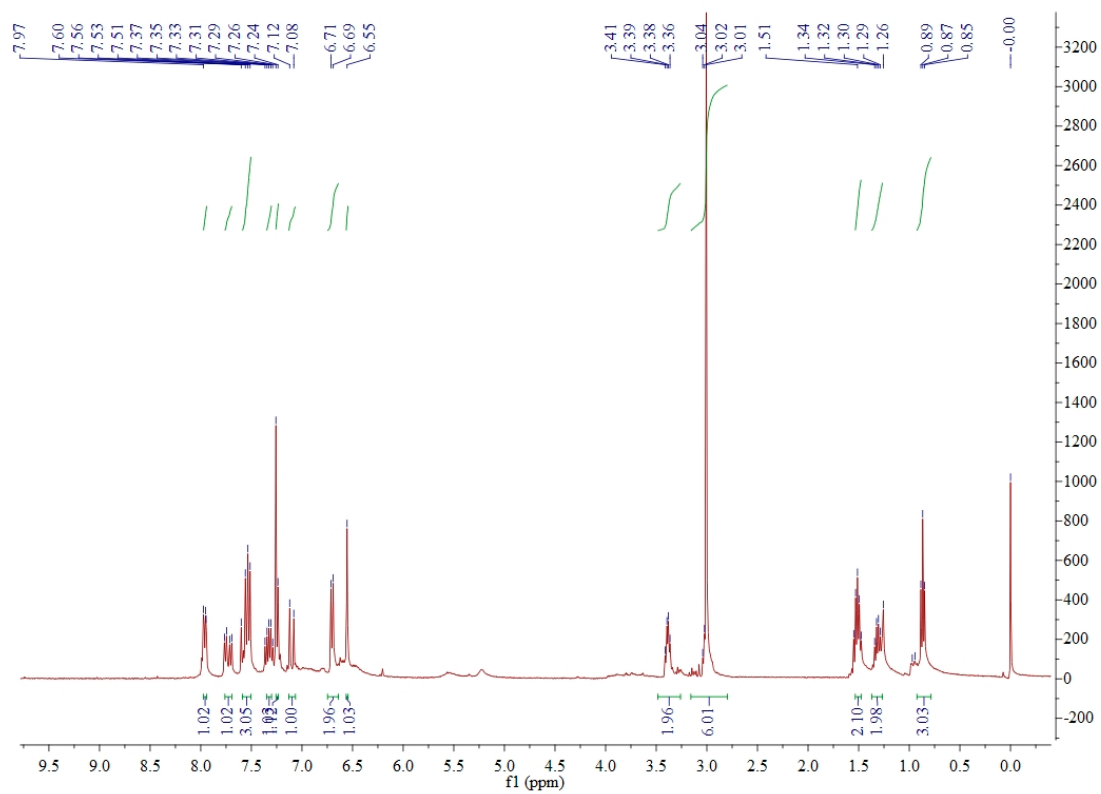
HPLC spectrum of 6d₁



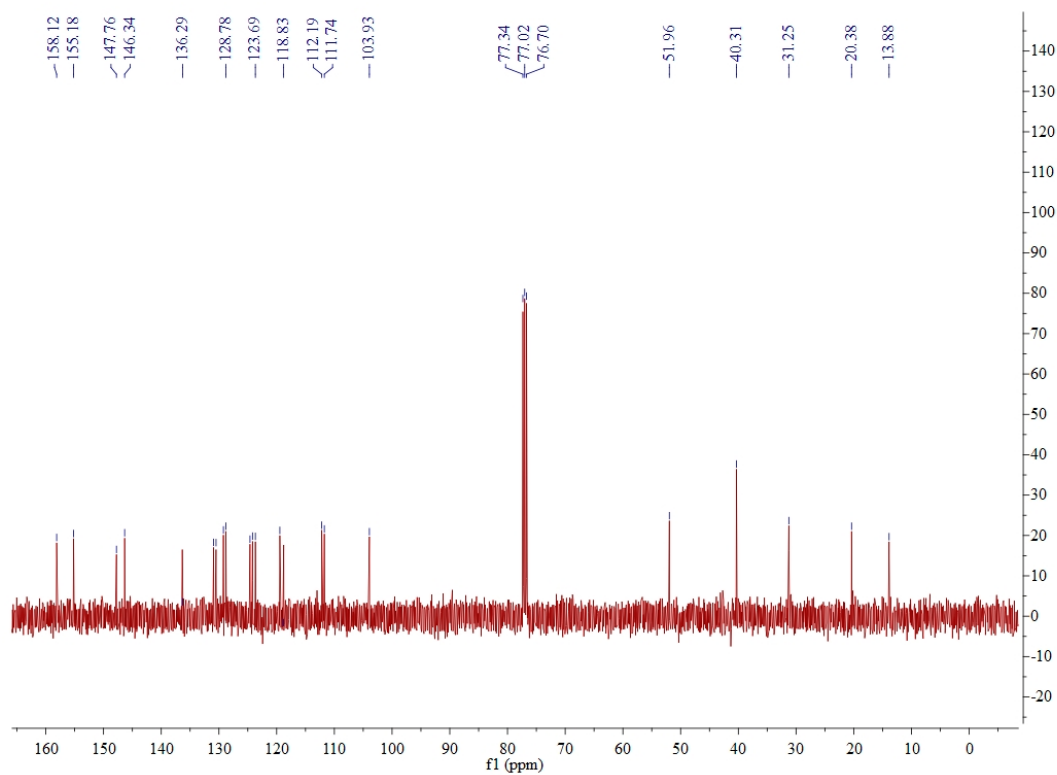
Idx	Formula	RDB	Delta mmu
1	C ₂₅ H ₃₂ N ₃	11.5	1.485

Caculated 374.2591 Found 374.2606

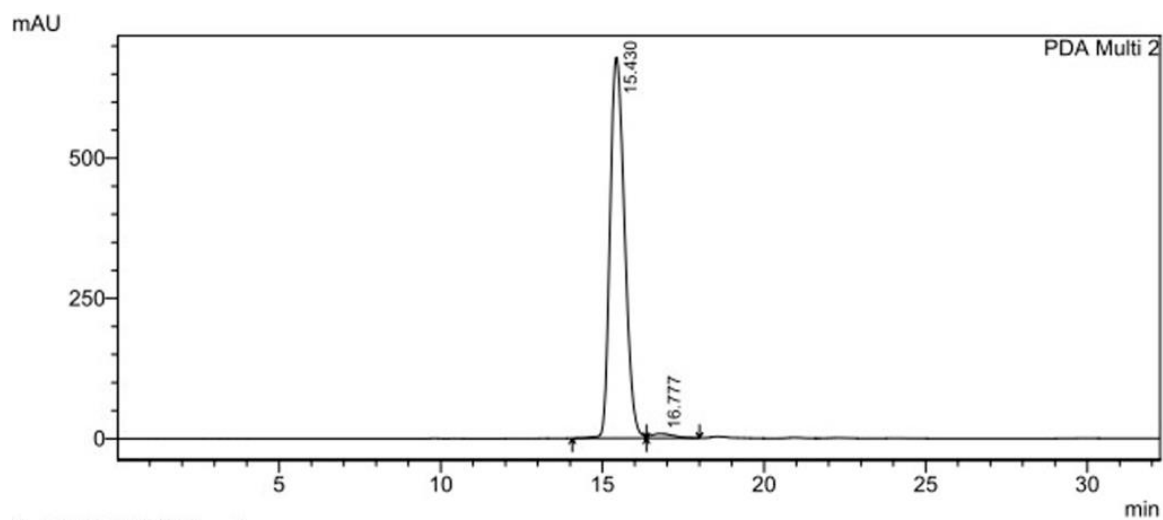
HRMS spectra of 6d₁



¹H NMR spectrum of **6d₂**



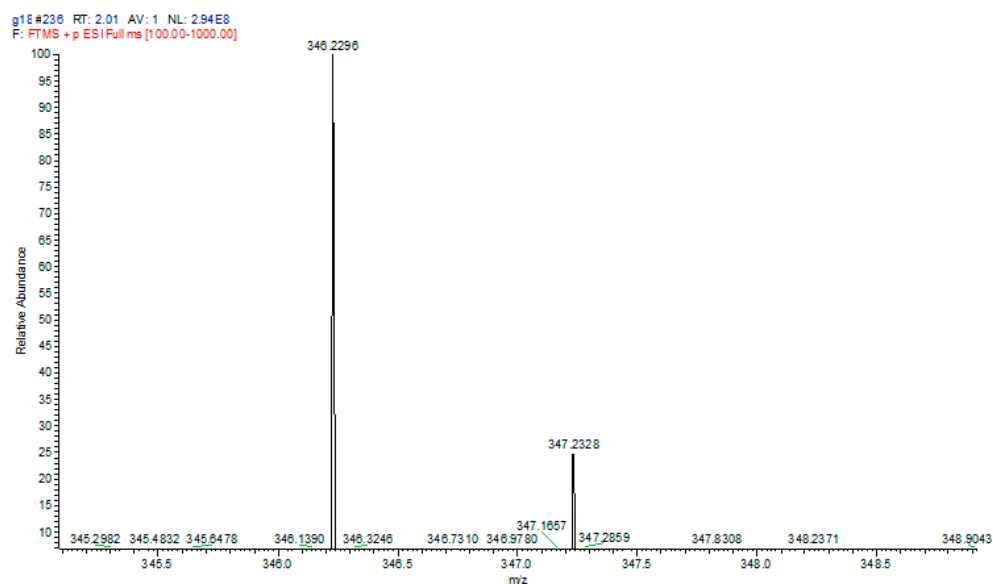
¹³C NMR spectrum of **6d₂**



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.430	21153180	679537	98.265	98.866
2	16.777	373403	7793	1.735	1.134
Total		21526583	687330	100.000	100.000

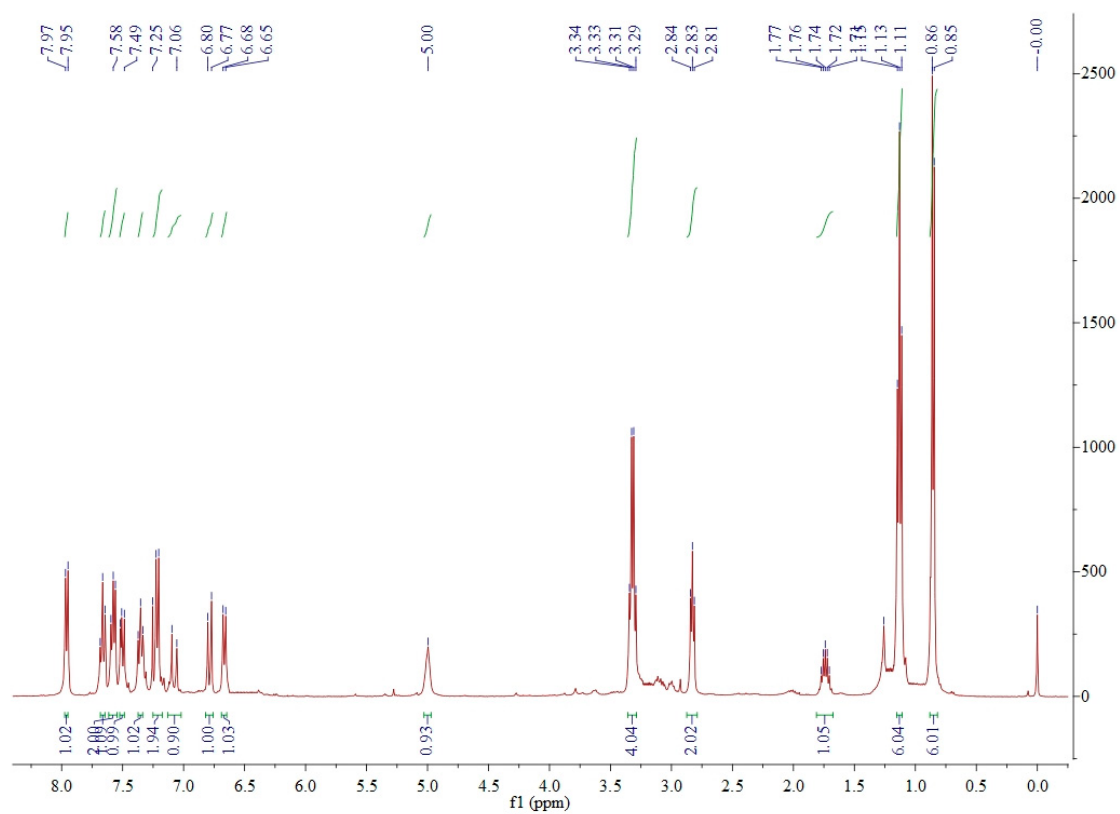
HPLC spectrum of **6d₂**



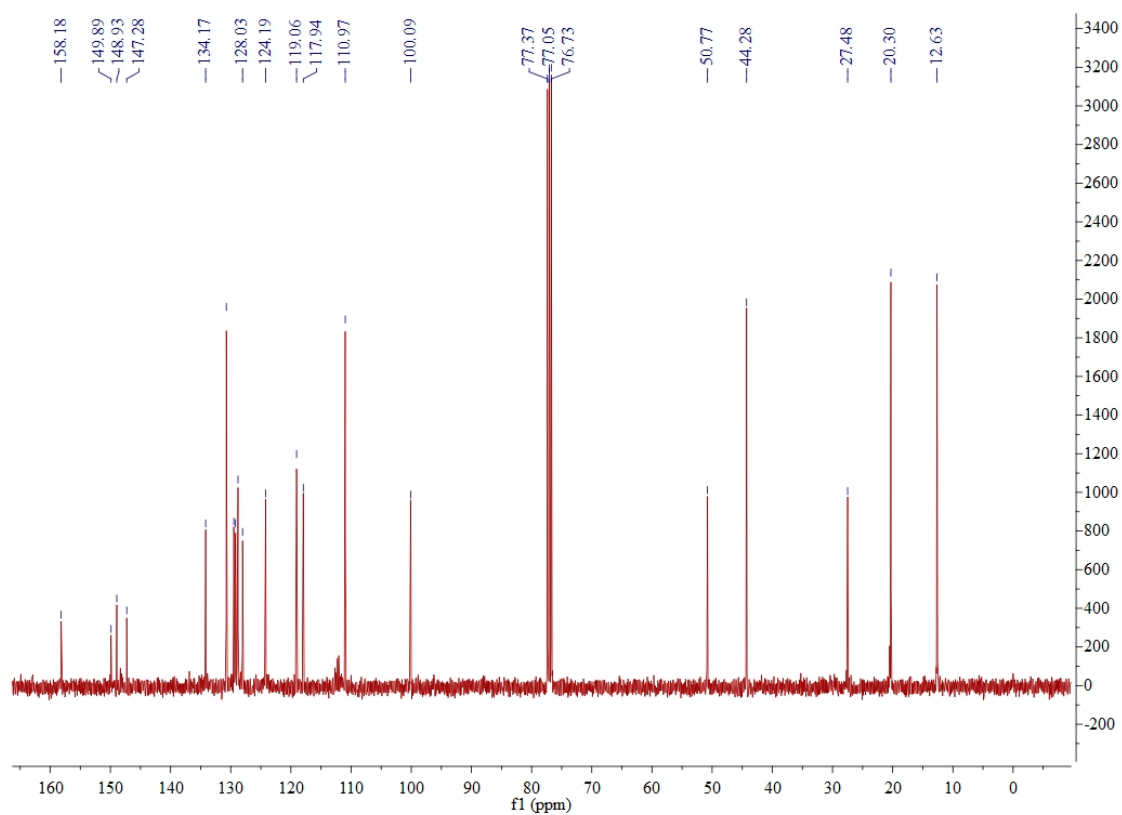
Idx	Formula	RDB	Delta mmu
1	C ₂₃ H ₂₈ N ₃	11.5	1.806

Calculated 346.2278 Found 346.2296

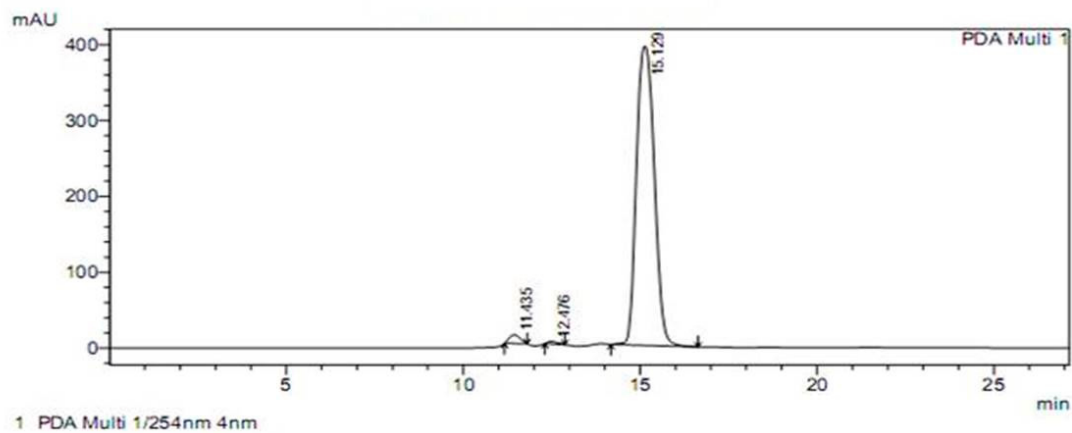
HRMS spectra of **6d₂**



¹H NMR spectrum of **6e1**



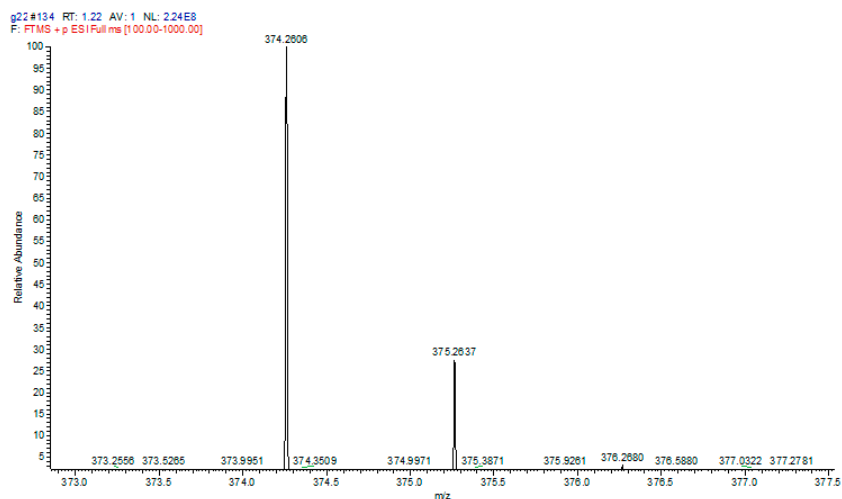
¹³C NMR spectrum of **6e1**



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.435	251598	11831	1.777	2.888
2	12.476	67460	3261	0.476	0.796
3	15.129	13840429	394620	97.747	96.317
Total		14159487	409712	100.000	100.000

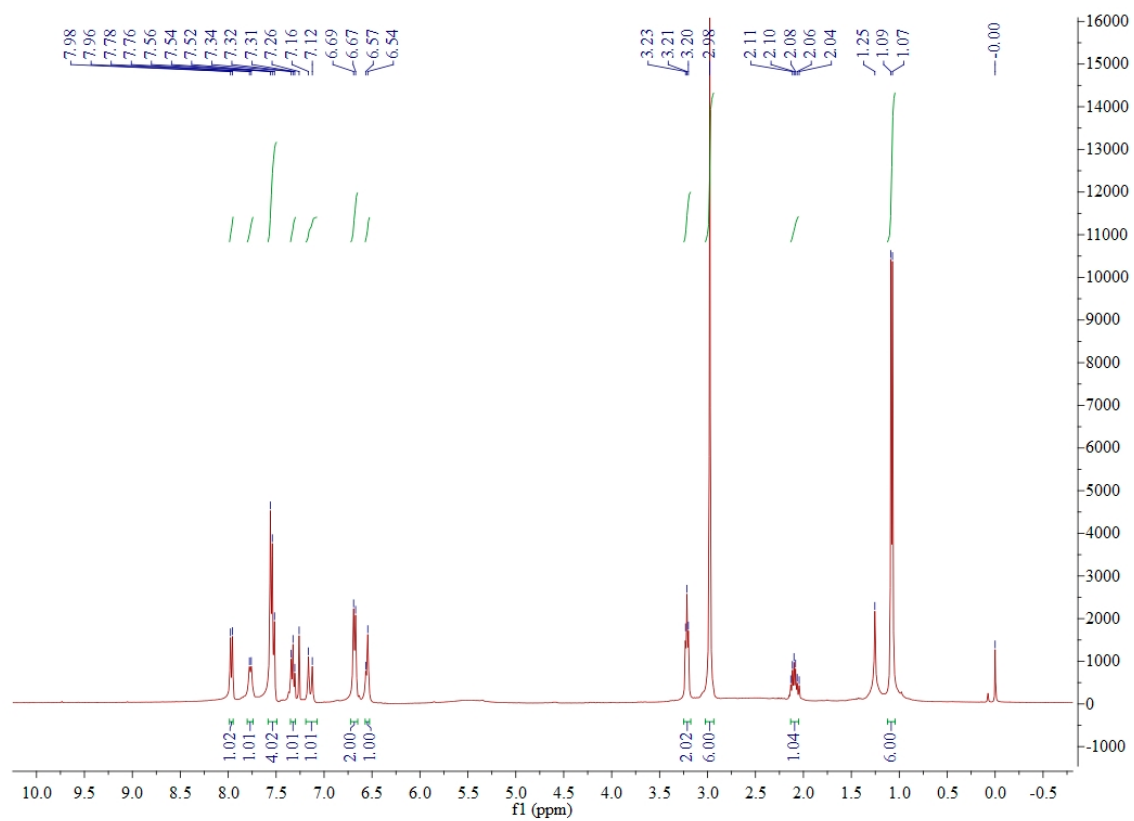
HPLC spectrum of **6e₁**



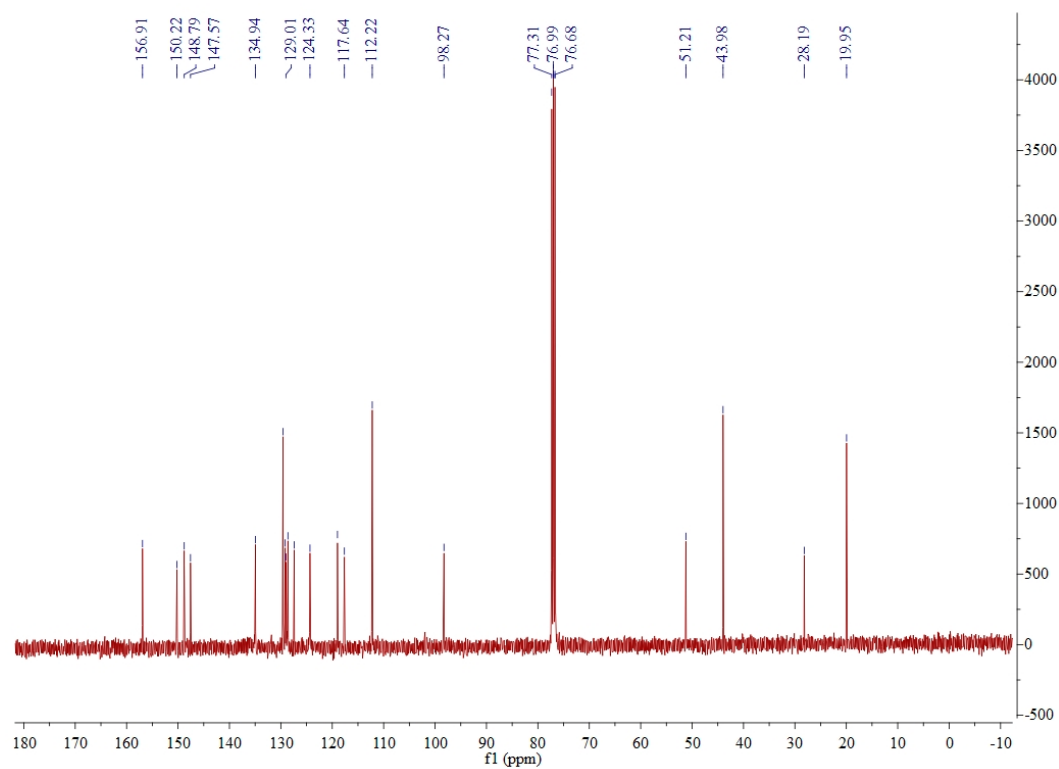
Idx	Formula	RDB	Delta mmu
1	C ₂₅ H ₃₂ N ₃	11.5	1.485

Calculated 374.2591 Found 374.2606

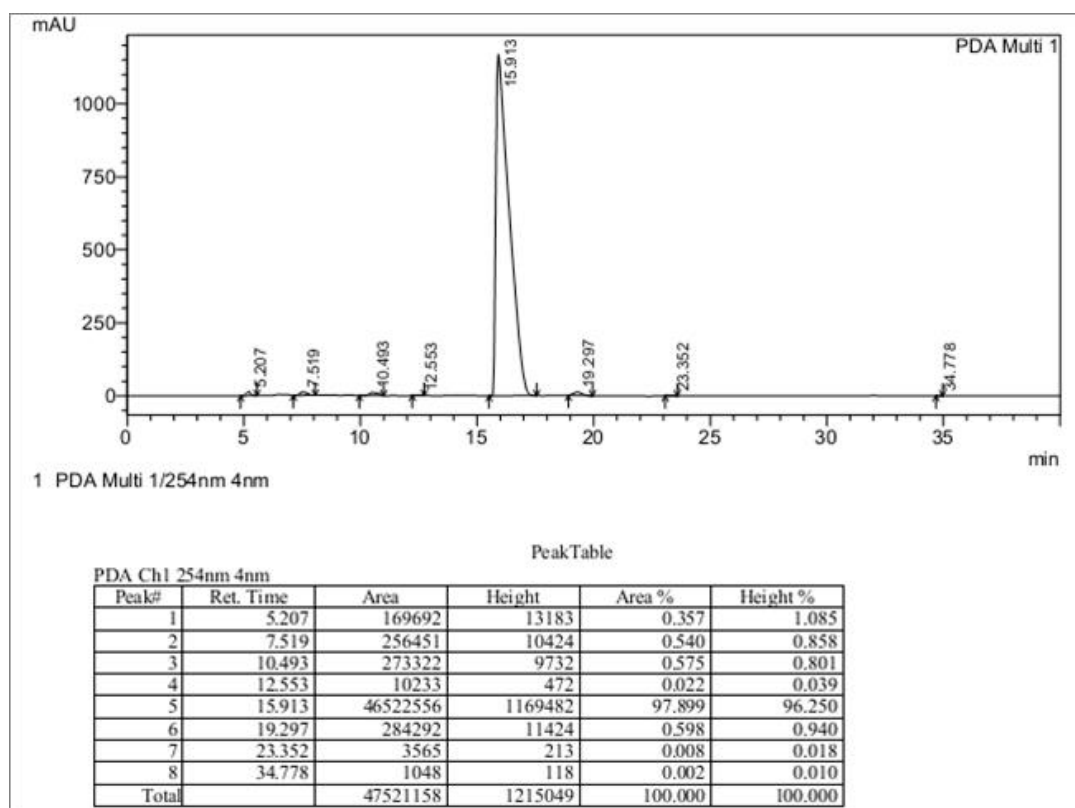
HRMS spectra of **6e₁**



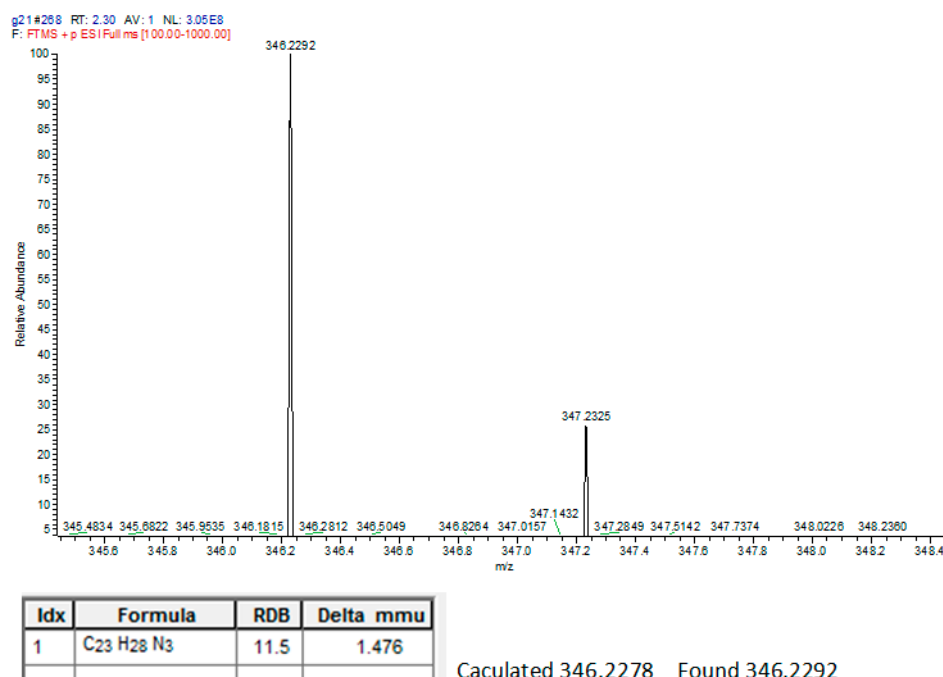
¹H NMR spectrum of **6e2**



¹³C NMR spectrum of **6e2**



HPLC spectrum of **6e**

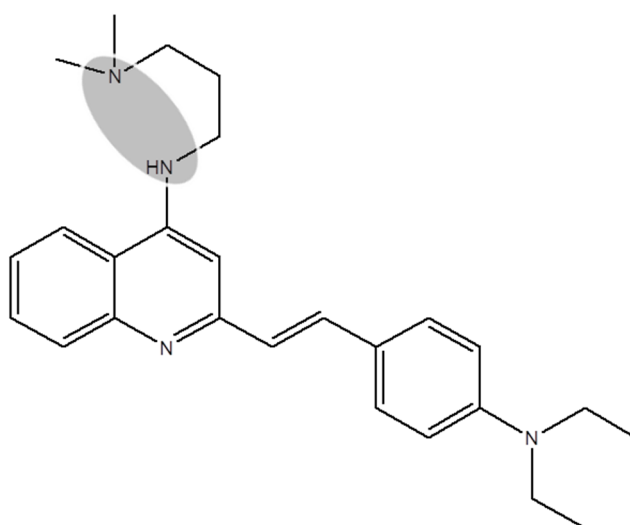


HRMS spectra of **6e**

Table S1. cytotoxicity (IC₅₀) on SH-SY5Y cells of prepared compounds.

Compd ^[a]	IC ₅₀ [μM] ^[a]	Compd ^a	IC ₅₀ [μM] ^[a]
6a₁	189.2 ± 0.8	6c₂	127.5 ± 0.4
6a₂	187.5 ± 0.2	6d₁	119.3 ± 0.7
6a₃	147.8 ± 0.3	6d₂	112.4 ± 0.6
6a₄	145.2 ± 0.9	6e₁	143.6 ± 0.7
6b₁	253.7 ± 0.4	6e₂	141.9 ± 0.5
6b₂	228.1 ± 0.5	6f₁	111.2 ± 0.4
6b₃	168.1 ± 0.2	6f₂	106.3 ± 0.4
6c₁	154.3 ± 0.5		

^a Values are the mean ± SEM of three independent measurements.



Scheme S1. The coordination model of compound **6b₁** for Cu²⁺ (Chelating motif in gray shade).