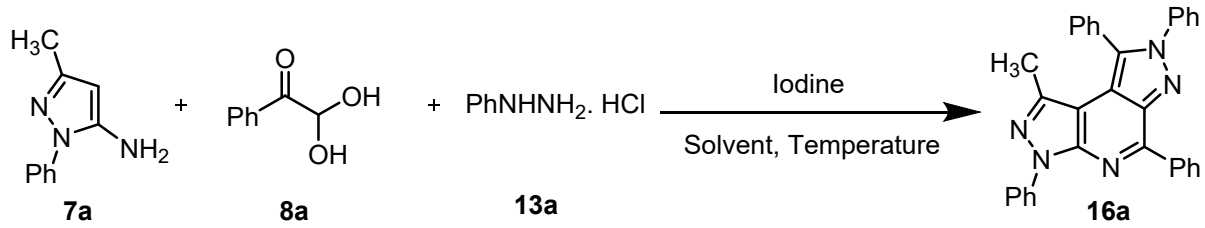
Supporting Information

Metal-free, Iodine-Mediated Multicomponent Synthesis of Bis-Pyrazolo-Pyridine Derivatives

Table of Contents

Table S1: Optimization of reaction conditions



7a **8a** **13a** **16a**

S.No	Iodine	Solvent	Temperature	Yield %[a]
1	Iodine (1.5 equiv.)	EtOH	50 °C	33
2	Iodine (1.5 equiv.)	DMSO	50 °C	38
3	Iodine (1.5 equiv.)	DMF	50 °C	36
4	Iodine (1.5 equiv.)	THF	50 °C	Trace
5	Iodine (1.5 equiv.)	1,4-dioxane	50 °C	Trace
6	Iodine (1.5 equiv.)	ACN	50 °C	Trace
7	Iodine (1.5 equiv.)	Ethylene glycol	50 °C	38
8	Iodine (1.5 equiv.)	Acetic acid	50 °C	34
9	Iodine (1.5 equiv.)	Butyric acid	50 °C	38
10	Iodine (1.5 equiv.)	Isobutyric acid	50 °C	44
11	Iodine (0.5 equiv.)	Isobutyric acid	50 °C	42
12	Iodine (0.5 equiv.)	Isobutyric acid	90 °C	44
13	Iodine (0.5 equiv.)	Isobutyric acid	120 °C	49
14[b]	Iodine (0.5 equiv.)	Isobutyric acid	120 °C	33
15[c]	Iodine (0.5 equiv.)	Isobutyric acid	120 °C	51
16[d]	**Iodine (0.5 equiv.)**	**Isobutyric acid**	**120 °C**	**71**
17[e]	Iodine (0.5 equiv.)	Isobutyric acid	120 °C	71
18[f]	Iodine (0.5 equiv.)	Isobutyric acid	120 °C	71
19	NIS (0.5 equiv.)	Isobutyric acid	120 °C	Trace
20	DIPA (0.5 equiv.)	Isobutyric acid	120 °C	Trace
21	TBAI (0.5 equiv.)	Isobutyric acid	120 °C	Trace

Reaction condition: **7a** (0.5 mmol), **8a** (1.5 mmol), **13a** (0.5 mmol), Iodine (50 mol%), Isobutyric acid (2 mL), [a]Isolated the yield.

[b] 7a (1.0 mmol), 8a (1.0 mmol), 13a (0.5 mmol),

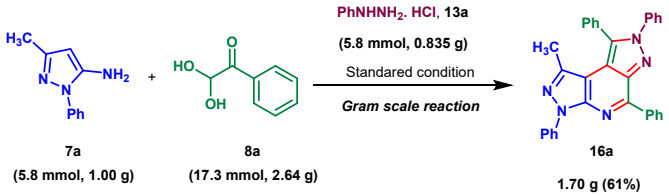
[c] 7a (0.5 mmol), 8a (1.0 mmol), 13a (1.0 mmol),

[d] 7a (0.5 mmol), 8a (1.5 mmol), 13a (0.5 mmol),

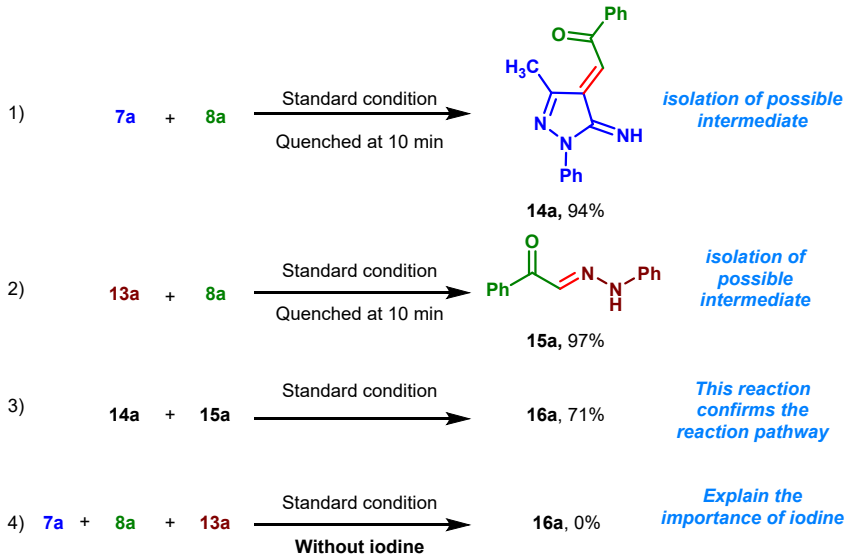
[e] 7a (0.5 mmol), 8a (1.5 mmol), 13a (2 mmol),

[f] 7a (0.5 mmol), 8a (2.0 mmol), 13a (0.5 mmol).

Scheme S1: Gram-scale synthesis



Scheme S2: Control experiments

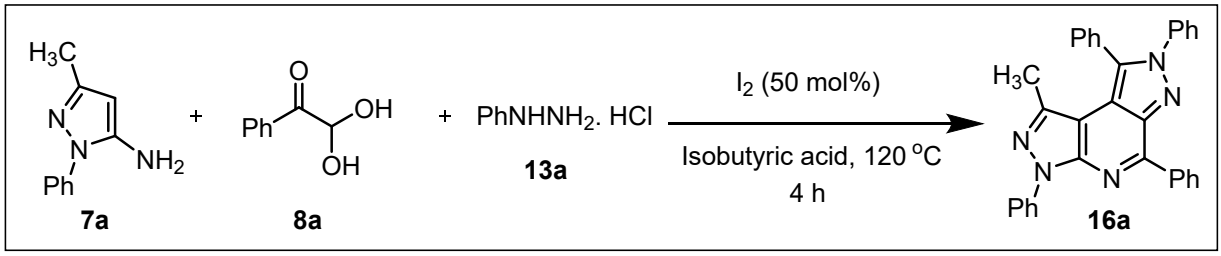


1. 1. General Experimental Procedure

All the reactions were carried out in oven-dried reaction vials. Thin-layer chromatography (TLC) was used to monitor the reactions using Merck silica gel 60 F254 precoated plates. Silica mesh (60–120) was from SRL Pvt. Ltd. A hexane–ethyl acetate mixture was used for compound purification. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL 600 MHz and a Bruker 500 MHz NMR instruments. $CDCl_3$ (δ 7.26 ppm, 77.16 ppm) solvent was used to collect NMR data. Chemical shifts were reported in parts per million, and multiplicities are written as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and dd (doublet of doublets). Coupling constants (*J*) are reported in Hertz. Melting points were recorded on a Guna capillary melting point

apparatus. High-resolution mass spectra (HRMS) were recorded on a Waters Xevo G2-XS QToF and, Agilent 6540 Q-TOF. The solvents used were of laboratory grade and procured from Pure Chem (dichloromethane and hexane) and Pure Chem (ethyl acetate). Phenylhydrazine hydrochloride, isobutyric acid, and iodine were purchased from Avra Synthesis, Spectrochem, TCI, and SRL. The pyrazole amine and phenylglyoxal were synthesized according to previous literature.[1] Single-crystal X-ray diffraction data for the crystals of compound **16a** were measured at 296 K on a Rigaku Oxford XtaLAB Synergy diffractometer using Mo Kα radiation [λ= 0.71073 Å]. The structures were solved by direct methods using SHELXS-97[2] and refined using the SHELXL-2018/3 program[3,4]

1.2. General procedure for the synthesis of 1-methyl-3,5,7,8-tetraphenyl-3,7-dihydrodipyrazolo [3,4-b: 4',3'-d] pyridine (16a).



The reaction was carried out in a 25 mL round-bottom flask that had been dried. Pyrazole amine **7a** (0.086 mg, 0.5 mmol), phenylglyoxal monohydrate (**8a**) (0.228 mg, 1.5 mmol), and phenylhydrazine hydrochloride (**13a**) (0.72 mg, 0.5 mmol) were dissolved in isobutyric acid (1.7 mL), and heated at 120 °C. The reaction was monitored by thin-layer chromatography (TLC), and completion was confirmed by TLC. Afterward, the reaction mixture was dissolved in ethyl acetate, $NaHCO_3$ and $Na_2S_2O_8$. The organic layer was separated and dried over anhydrous sodium sulfate. The solvent was evaporated using a rotary evaporator. The crude reaction mixture was subjected to column chromatography to obtain the corresponding product **1-methyl-3,5,7,8-tetraphenyl-3,7-dihydrodipyrazolo[3,4-b: 4',3'-d]pyridine** (16a); Physical appearance = Yellow solid; Melting Point = 236-238 °C; Yield = 71%; Weight = 170 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.85 – 8.83 (m, 2H), 8.32 (dd,

J = 1.02, 8.6 Hz, 2H), 7.58 – 7.51(m, 5H), 7.50 – 7.48 (m, 4H), 7.47 – 7.45 (m, 3H), 7.38 – 7.35 (m, 3H), 7.32 (t, *J* = 7.4 Hz, 1H), 1.95 (s, 3H); ^{13}C NMR: (150 MHz, $CDCl_3$) = 150.54, 146.58, 141.84, 141.69, 139.97, 139.84, 137.60, 134.92, 131.75, 130.87, 130.06, 129.99, 129.64, 128.89, 128.81, 128.50, 128.38, 125.88, 125.74, 122.10, 120.05, 105.05, 15.25.

3-(4-bromophenyl)-1-methyl-5,7,8-triphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16b**); Physical appearance = Yellow solid; Melting Point = 232-234 ℃; Yield = 56%; Weight = 156 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.74 (dd, *J* = 1.4, 8.5 Hz, 2H), 8.21 (d, *J* = 9 Hz, 2H), 7.58 (d, *J* = 9 Hz, 2H), 7.51 (t, *J* = 7.1 Hz, 2H), 7.46 – 7.37 (m, 8H), 7.29 – 7.28 (m, 3H), 1.85 (s, 3H); ^{13}C NMR: (150 MHz, $CDCl_3$) = 150.67, 146.55, 142.24, 141.60, 139.89, 138.95, 137.42, 134.95, 131.85, 131.70, 130.73, 130.10, 130.02, 129.67, 128.81, 128.50, 128.41, 125.84, 123.17, 119.96, 118.74, 105.35, 15.22.; HRMS calculated for the molecular formula $C_{32}H_{23}BrN_5$ = 556.1131 ($[M+H]^+$); found = 556.1144.

3-(4-chlorophenyl)-1-methyl-5,7,8-triphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16c**); Physical appearance = Yellow solid; Melting Point = 232-234 ℃; Yield = 61%; Weight = 156 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.82 – 8.81 (m, 2H), 8.33 (d, *J* = 8.8 Hz, 2H), 7.57 (t, *J* = 7.2 Hz, 2H), 7.53 – 7.44 (m, 10H), 7.36 – 7.35 (m, 3H), 1.92 (s, 3H); ^{13}C NMR: (150 MHz, $CDCl_3$) = 150.70, 146.55, 142.19, 141.62, 139.89, 138.45, 137.44, 134.96, 131.71, 130.91, 130.74, 130.11, 130.02, 129.68, 128.92, 128.82, 128.51, 128.42, 125.85, 122.90, 119.97, 105.29, 15.22.; HRMS calculated for the molecular formula $C_{32}H_{23}ClN_5$ = 512.1636 ($[M+H]^+$); found = 512.1638.

3-(4-fluorophenyl)-1-methyl-5,7,8-triphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16d**); Physical appearance = Yellow solid; Melting Point = 236-238 ℃; Yield = 65%; Weight = 161 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.74 (dd, *J* = 1.44, 8.64 Hz, 2H), 8.23 (dd, *J* = 1.14, 8.64 Hz, 2H), 7.50 – 7.38 (m, 12H), 7.26 – 7.23 (m, 3H), 1.85 (s, 3H); ^{13}C NMR: (150 MHz, $CDCl_3$) = 150.44, 146.54, 141.82, 139.76, 138.96, 137.44, 134.80, 132.00, 131.66, 130.55, 130.06, 130.00, 129.87, 128.88, 128.68, 128.38, 127.16, 125.79,

122.35, 122.09, 120.17, 104.86, 15.21.; HRMS calculated for the molecular formula $C_{32}H_{23}FN_5$ = 496.1932 ($[M+H]^+$); found = 496.1938.

1-methyl-5,7,8-triphenyl-3-(p-tolyl)-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16e**); Physical appearance = Yellow solid; Melting Point = 230-232 °C; Yield = 61%; Weight = 150 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.84 (dd, *J* = 1.4, 8.5 Hz, 2H), 8.17 (d, *J* = 8.5 Hz, 2H), 7.56 (t, *J* = 7.2 Hz, 2H), 7.52 – 7.45 (m, 8H), 7.37 – 7.34 (m, 5H), 2.43 (s, 3H), 1.94 (s, 3H); ^{13}C NMR: (150 MHz, $CDCl_3$) = 149.32, 145.43, 140.66, 140.44, 138.96, 136.62, 136.40, 134.41, 133.81, 130.72, 129.88, 129.02, 128.90, 128.57, 128.40, 127.76, 127.45, 127.32, 124.83, 121.06, 119.03, 103.79, 20.03, 14.22.; HRMS calculated for the molecular formula $C_{33}H_{26}N_5$ = 492.2183 ($[M+H]^+$); found = 492.2189.

3-(4-methoxyphenyl)-1-methyl-5,7,8-triphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16f**); Physical appearance = Yellow Solid; Melting Point = 235-237 °C; Yield = 59%; Weight = 150 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.82 (d, *J* = 7.5 Hz, 2H), 8.15 (d, *J* = 8.8 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 2H), 7.51 – 7.44 (m, 8H), 7.35 (d, *J* = 5.0 Hz, 3H), 7.07 (d, *J* = 8.8 Hz, 2H), 3.88 (s, 3H), 1.93 (s, 3H).; ^{13}C NMR: (150 MHz, $CDCl_3$) = 157.73, 150.41, 146.34, 141.68, 141.22, 139.99, 137.62, 134.83, 133.24, 131.74, 130.91, 130.01, 129.92, 129.59, 128.79, 128.47, 128.34, 125.85, 123.70, 120.05, 114.09, 104.55, 55.55, 15.20.; HRMS calculated for the molecular formula $C_{33}H_{26}N_5O$ = 508.2132 ($[M+H]^+$); found = 508.2134.

1-methyl-3-(4-nitrophenyl)-5,7,8-triphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16g**); Physical appearance = Yellow solid; Melting Point = 220-222 °C; Yield = 50%; Weight = 131 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.86 – 8.85 (m, 2H), 8.65-8.64 (m, 1H), 8.40 – 8.39 (m, 1H), 7.58 (t, *J* = 7.4 Hz, 2H), 7.54 – 7.49 (m, 2H), 7,47 – 7.35 (m, 11H), 1.92 (s, 3H).; ^{13}C NMR: (150 MHz, $CDCl_3$) = 150.66, 146.65, 142.46, 141.60, 141.00, 139.88, 137.38, 134.97, 131.71, 130.70, 130.13, 130.05, 129.68, 128.81, 128.50, 128.42,

128.27, 125.84, 124.47, 122.47, 119.96, 119.86, 105.48, 15.23.; HRMS calculated for the molecular formula $C_{32}H_{23}N_6O_2$ = 523.1877 ($[M+H]^+$); found = 523.1881.

1-methyl-5,7,8-triphenyl-3-(o-tolyl)-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16h**); Physical appearance = Yellow solid; Melting Point = 225-227 °C; Yield = 70%; Weight = 172 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.78 (d, *J* = 7.7 Hz, 2H), 8.10 – 8.02 (m, 2H), 7.50 – 7.48 (m, 2H), 7.43 – 7.35 (m, 9H), 7.28 – 7.27 (m, 3H), 7.06 (d, *J* = 7.0 Hz, 1H), 2.41 (s, 3H), 1.87 (s, 3H).; ^{13}C NMR: (150 MHz, $CDCl_3$) = 151.11, 150.06, 146.94, 141.71, 140.18, 140.13, 139.93, 139.62, 135.00, 134.94, 131.59, 130.01, 129.20, 129.15, 128.88, 128.79, 128.27, 127.82, 125.90, 125.66, 122.08, 120.00, 105.03, 21.55, 15.41.; HRMS calculated for the molecular formula $C_{33}H_{26}N_5$ = 492.2183 ($[M+H]^+$); found = 492.2187.

3-(2-bromophenyl)-1-methyl-5,7,8-triphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16i**); Physical appearance = Yellow solid; Melting Point = 220-222 °C; Yield = 58%; Weight = 161 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (500 MHz, $CDCl_3$) = 8.78 (d, *J* = 7.1 Hz, 2H), 8.32 (d, *J* = 7.6 Hz, 2H), 7.65 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.56 – 7.49 (m, 7H), 7.42 – 7.37 (m, 4H), 7.34 – 7.27 (m, 3H), 1.97 (s, 3H).; ^{13}C NMR: (125 MHz, $CDCl_3$) = 150.95, 146.62, 141.91, 141.86, 139.88, 139.26, 137.63, 136.52, 133.38, 131.45, 131.05, 130.10, 130.00, 129.97, 129.87, 129.63, 128.92, 128.89, 128.43, 128.40, 128.17, 127.68, 125.79, 122.38, 122.14, 119.03, 105.09, 15.26.; HRMS calculated for the molecular formula $C_{32}H_{23}BrN_5$ = 556.1131 ($[M+H]^+$); found = 556.1138.

1-methyl-5,7,8-triphenyl-3-(m-tolyl)-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16j**); Physical appearance = Yellow solid; Melting Point = 233-235 °C; Yield = 73%; Weight = 179 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.71 (dd, *J* = 1.5, 8.5 Hz, 2H), 7.50 – 7.47 (m, 7H), 7.46 – 7.44 (m, 5H), 7.40 – 7.38 (m, 2H), 7.36 – 7.34 (m, 3H), 2.27 (s, 3H), 1.96 (s, 3H).; ^{13}C NMR: (150 MHz, $CDCl_3$) = 150.67, 147.55, 141.76, 141.42, 140.00, 138.09, 137.47, 135.49, 134.78, 131.73, 130.90, 129.94, 129.85, 129.56, 128.78, 128.46,

128.30, 128.27, 128.22, 128.04, 126.28, 125.82, 120.10, 103.42, 18.57, 15.27.; HRMS calculated for the molecular formula $C_{33}H_{26}N_5$ = 492.2183 ([M+H]$^+$); found = 492.2185.

3-(3-bromophenyl)-1-methyl-5,7,8-triphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16k**); Physical appearance = Yellow solid; Melting Point = 235-237 ℃; Yield = 50%; Weight = 139 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.86 – 8.85 (m, 2H), 8.64 (s, 1H), 8.40 – 8.39 (m, 1H), 7.58 (t, *J* = 7.26 Hz, 2H), 7.54 – 7.49 (m, 2H), 7.47 – 7.35 (m, 11H), 1.92 (s, 3H).; ^{13}C NMR: (150 MHz, $CDCl_3$) = 150.66, 146.65, 142.45, 141.60, 141.00, 139.88, 137.38, 134.97, 131.71, 130.70, 130.13, 130.05, 129.68, 128.81, 128.50, 128.43, 128.28, 125.84, 124.47, 122.47, 119.96, 119.87, 105.48, 15.22.; HRMS calculated for the molecular formula $C_{32}H_{23}BrN_5$ = 556.1131 ([M+H]$^+$); found = 556.1140.

3-cyclohexyl-1-methyl-5,7,8-triphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16l**); Physical appearance = Yellow solid; Melting Point = 252-254 ℃; Yield = 49%; Weight = 119 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.70 (d, *J* = 8.22 Hz, 2H), 7.49 (t, *J* = 7.38 Hz, 2H), 7.44 – 7.34 (m, 8H), 7.27 – 7.23 (m, 3H), 4.99 – 4.94 (m, 1H), 2.08 – 1.99 (m, 4H), 1.87 (d, *J* = 13.6 Hz, 2H), 1.81 (s, 3H), 1.70 (d, *J* = 13.08 Hz, 1H), 1.52 – 1.45 (m, 2H), 1.30 (t, *J* = 13.1 Hz, 1H); ^{13}C NMR: (150 MHz, $CDCl_3$) = 149.73, 146.11, 141.82, 140.06, 139.19, 137.76, 134.46, 131.69, 131.05, 129.89, 129.75, 129.41, 128.73, 128.38, 128.30, 128.17, 125.79, 120.02, 102.81, 56.14, 32.74, 25.90, 25.46, 15.21. ; HRMS calculated for the molecular formula $C_{32}H_{30}N_5$ = 484.2496 ([M+H]$^+$); found = 484.2500.

5,8-bis(4-bromophenyl)-1-methyl-3,7-diphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16m**); Physical appearance = Yellow solid; Melting Point = 250-252 ℃; Yield = 62%; Weight = 197 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.65 (d, *J* = 8.6 Hz, 2H), 8.19 (d, J = 7.6 Hz, 2H), 7.60 (d, *J* = 8.6 Hz, 2H), 7.53 (d, *J* = 8.3, 2H), 7.47 (t, *J* = 8.3 Hz, 2H), 7.32 (s, 5H), 7.26 (d, *J* = 8.0 Hz, 3H), 1.93 (s, 3H).; ^{13}C NMR: (150 MHz, $CDCl_3$) = 149.07, 146.37, 141.61, 141.47, 139.65, 139.58, 136.27, 133.61, 133.18, 131.81, 131.55, 131.53, 129.58, 129.02, 128.92, 128.72, 125.93, 125.88, 124.75, 124.18, 122.08, 119.98,

104.95, 15.69.; HRMS calculated for the molecular formula $C_{32}H_{22}Br_2N_5$ = 634.0236 ($[M+H]^+$); found = 634.0239.

5,8-bis(4-fluorophenyl)-1-methyl-3,7-diphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16n**); Physical appearance = Yellow solid; Melting Point = 231-233 °C; Yield = 79%; Weight = 203 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (500 MHz, $CDCl_3$) = 8.89 – 8.85 (m, 2H), 8.28 – 8.27 (m, 2H), 7.54 (t, *J* = 7.6 Hz, 2H), 7.46 – 7.37 (m, 7H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.25 – 7.14 (m, 4H), 1.97 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) = 165.16, 164.48, 163.17, 162.49, 149.24, 146.50, 141.62, 141.53, 139.80, 133.88, 133.65, 133.58, 132.12, 132.05, 128.96, 128.91, 128.64, 126.81, 125.93, 125.88, 122.15, 120.16, 115.89, 115.72, 115.42, 115.25, 104.84, 15.44. ; HRMS calculated for the molecular formula $C_{32}H_{22}F_2N_5$ = 514.1838 ($[M+H]^+$); found = 514.1845.

5,8-bis(4-chlorophenyl)-1-methyl-3,7-diphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16o**); Physical appearance = Yellow solid; Melting Point = 235-237 °C; Yield = 73%; Weight = 200 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.80 (d, *J* = 8.7 Hz, 2H), 8.27 (dd, *J* = 8.6, 1.1 Hz, 2H), 7.56 – 7.50 (m, 4H), 7.45 (d, *J* = 8.5 Hz, 2H), 7.40 – 7.38 (m, 7H), 7.33 (t, *J* = 7.38 Hz, 1H), 1.99 (s, 3H).; ^{13}C NMR: (150 MHz, $CDCl_3$) = 147.92, 145.32, 140.58, 140.44, 138.65, 138.57, 135.14, 134.91, 134.80, 132.56, 131.94, 130.25, 128.08, 127.97, 127.89, 127.82, 127.67, 127.55, 124.85, 121.02, 118.99, 103.91, 14.63. ; HRMS calculated for the molecular formula $C_{32}H_{22}Cl_2N_5$ = 546.1247 ($[M+H]^+$); found = 546.1253.

1-methyl-3,7-diphenyl-5,8-di-p-tolyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16p**); Physical appearance = Yellow solid; Melting Point = 230-232 °C; Yield = 85%; Weight = 215 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (500 MHz, $CDCl_3$) = 8.76 (d, *J* = 8.15 Hz, 2H), 8.35 (d, *J* = 7.8 Hz, 2H), 7.56 (t, *J* = 7.7 Hz, 2H), 7.49 – 7.47 (m, 2H), 7.40 – 7.32 (m, 7H), 7.28 – 7.27 (m, 3H), 2.48 (s, 3H), 2.47 (s, 3H), 1.99 (s, 3H).; ^{13}C NMR: (125 MHz, $CDCl_3$) = 150.66, 146.65, 141.94, 141.71, 140.18, 140.13, 139.93, 139.62, 135.01, 134.94, 131.59, 130.01,

129.20, 129.15, 128.89, 128.79, 128.27, 127.82, 125.90, 125.66, 122.08, 120.01, 105.03, 21.57, 21.55, 15.41.; HRMS calculated for the molecular formula $C_{34}H_{28}N_5$ = 506.2339 ($[M+H]^+$); found = 506.2339.

5,8-bis(4-methoxyphenyl)-1-methyl-3,7-diphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16q**); Physical appearance = Yellow solid; Melting Point = 232-234 °C; Yield = 71%; Weight = 191 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (500 MHz, $CDCl_3$) = 8.87 (d, *J* = 11.2 Hz, 2H), 8.32 (d, *J* = 9.5 Hz, 2H), 7.53 (t, *J* = 9.5 Hz, 2H), 7.46 – 7.44 (m, 2H), 7.38 – 7.35 (m, 5H), 7.30 (t, *J* = 9.3 Hz, 1H), 7.08 (d, *J* = 11.2 Hz, 2H), 6.97 (d, *J* = 10.9 Hz, 2H), 3.90 (s, 3H), 3.87 (s, 3H), 1.99 (s, 3H).; ^{13}C NMR: (125 MHz, $CDCl_3$) = 160.39, 159.63, 149.18, 145.79, 140.98, 140.75, 139.27, 139.09, 133.86, 132.11, 130.77, 129.53, 127.99, 127.93, 127.36, 125.01, 124.74, 122.03, 121.21, 119.23, 113.04, 112.93, 103.90, 54.51, 54.48, 14.57.. ; HRMS calculated for the molecular formula $C_{34}H_{28}N_5O_2$ = 538.2238 ($[M+H]^+$); found = 538.2244.

1-methyl-3,7-diphenyl-5,8-di-m-tolyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16r**); Physical appearance = Yellow solid; Melting Point = 230-232 °C; Yield = 62%; Weight = 157 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.64 (d, *J* = 7.8 Hz, 1H), 8.58 (s, 1H), 8.32 (d, *J* = 7.9 Hz, 2H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.48 – 7.44 (m, 3H), 7.36 – 7.31 (m, 8H), 7.24 (d, *J* = 7.14 Hz, 1H), 2.50 (s, 3H), 2.39 (s, 3H), 1.95 (s, 3H).; ^{13}C NMR: (150 MHz, $CDCl_3$) = 150.81, 146.58, 141.84, 139.88, 138.17, 137.80, 137.57, 135.04, 132.30, 130.80, 130.73, 130.46, 130.30, 128.85, 128.75, 128.35, 128.26, 127.42, 125.78, 125.68, 122.09, 120.00, 105.05, 21.78, 21.40, 15.24.; HRMS calculated for the molecular formula $C_{34}H_{28}N_5$ = 506.2339 ($[M+H]^+$); found = 506.2337.

5,8-bis(3-chlorophenyl)-1-methyl-3,7-diphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16s**); Physical appearance = Yellow solid; Melting Point = 220-222 °C; Yield = 40%; Weight = 109 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.75 (s, 1H), 8.70 – 8.68 (m, 1H), 8.20 (d, *J* = 8.52 Hz, 2H), 7.48 (t, *J* = 7.56 Hz, 2H), 7.45 (s,

1H), 7.43 – 7.40 (m, 3H), 7.38 – 7.36 (m, 2H), 7.34 – 7.30 (m, 4H), 7.28 – 7.24 (m, 2H), 1.93 (s, 3H).; ^{13}C NMR: (150 MHz, $CDCl_3$) = 147.72, 145.33, 140.63, 140.47, 138.60, 138.54, 138.11, 133.51, 133.32, 132.34, 131.40, 130.67, 128.96, 128.85, 128.79, 128.60, 128.03, 127.95, 127.78, 127.20, 125.00, 124.84, 121.16, 119.17, 104.01, 14.52.; HRMS calculated for the molecular formula $C_{32}H_{22}Cl_2N_5$ = 546.1247 ($[M+H]^+$); found = 546.1249.

5,8-bis(2-methoxyphenyl)-1-methyl-3,7-diphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16t**); Physical appearance = Yellow solid; Melting Point = 236-238 °C; Yield = 58%; Weight = 156 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.81 (d, *J* = 13.4, 2H), 8.25 (d, *J* = 11.4 Hz, 2H), 7.47 (t, *J* = 11.4, 11H), 7.40 – 7.37 (m, 2H), 7.31 – 7.22 (m, 6H), 3.83 (s, 3H), 3.81 (s, 3H), 1.92 (s, 3H).; ^{13}C NMR: (150 MHz, $CDCl_3$) = 160.39, 159.63, 149.18, 145.79, 140.98, 140.75, 139.27, 139.09, 133.86, 132.11, 130.77, 129.53, 127.99, 127.93, 127.36, 125.01, 124.74, 122.03, 121.21, 119.23, 113.04, 112.93, 103.90, 54.51, 54.48, 14.57.; HRMS calculated for the molecular formula $C_{34}H_{28}N_5O_2$ = 538.2238 ($[M+H]^+$); found = 538.2239.

1-methyl-3,7-diphenyl-5,8-di(thiophen-3-yl)-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16u**); Physical appearance = Yellow solid; Melting Point = 238-240 °C; Yield = 46%; Weight = 113 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 9.03 (d, *J* = 2.94 Hz, 1H), 8.23 – 8.22 (m, 3H), 7.46 (t, *J* = 8.16 Hz, 2H), 7.41 – 7.37 (m, 4H), 7.35 – 7.34 (m, 1H), 7.32 – 7.30 (m, 3H), 7.24 (t, *J* = 13.8 Hz, 1H), 7.10 (d, *J* = 13.8 Hz, 1H), 1.97 (s, 3H).; ^{13}C NMR: (150 MHz, $CDCl_3$) = 146.41, 146.06, 141.91, 141.24, 140.04, 139.83, 139.76, 130.40, 130.33, 129.87, 128.87, 128.83, 128.44, 128.29, 126.34, 125.71, 125.40, 124.92, 122.02, 120.23, 104.77, 14.73.; HRMS calculated for the molecular formula $C_{28}H_{20}N_5S_2$ = 490.1155 ($[M+H]^+$); found = 490.1154.

7-(4-bromophenyl)-1-methyl-3,5,8-triphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16v**); Physical appearance = Yellow solid; Melting Point = 252-254 °C; Yield = 80%; Weight = 223 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.74 (dd, *J* =

1.6, 8.8 Hz, 2H), 8.21 – 8.19 (m, 2H), 7.50 (t, *J* = 7.3 Hz, 2H), 7.45 – 7.37 (m, 8H), 7.29 – 7.28 (m, 3H), 7.15 (t, *J* = 8.8 Hz, 2H), 1.86 (s, 3H).; ^{13}C NMR: (150 MHz, $CDCl_3$) = 160.46, 158.84, 149.65, 145.43, 140.80, 140.63, 138.91, 136.47, 135.01, 133.91, 130.71, 129.78, 129.04, 129.00, 128.64, 127.79, 127.48, 127.38, 124.83, 122.63, 122.58, 118.98, 114.65, 114.50, 103.95, 14.18. HRMS calculated for the molecular formula $C_{32}H_{23}BrN_5$ = 556.1131 ($[M+H]^+$); found = 556.1137.

7-(4-fluorophenyl)-1-methyl-3,5,8-triphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16w**); Physical appearance = Yellow solid; Melting Point = 240-242 ℃; Yield = 76%; Weight = 188 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (500 MHz, $CDCl_3$) = 8.81 – 8.80 (m, 2H), 8.31 (dd, *J* = 8.6, 1.1 Hz, 2H), 7.57 – 7.40 (m, 12H), 7.31 (t, *J* = 7.38 Hz, 1H), 7.03 (t, J = 8.4 Hz, 2H), 1.93 (s, 3H).; ^{13}C NMR: (125 MHz, $CDCl_3$) = 162.95, 161.30, 150.43, 146.55, 141.79, 141.65, 139.80, 137.51, 136.06, 136.04, 134.97, 131.17, 130.62, 130.00, 129.77, 128.88, 128.58, 128.38, 127.65, 127.59, 125.75, 122.06, 119.98, 115.88, 115.73, 104.93, 15.22.; HRMS calculated for the molecular formula $C_{32}H_{26}FN_6$ = 513.2197 ($[M+NH4]^+$); found = 513.2200.

7-(4-chlorophenyl)-1-methyl-3,5,8-triphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16x**); Physical appearance = Yellow solid; Melting Point = 228-230 ℃; Yield = 80%; Weight = 205 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.74 – 8.73 (m, 2H), 8.23 (dd, *J* = 8.58, 1.08 Hz, 2H), 7.50 – 7.38 (10H, m), 7.32 (d, *J* = 8.76 Hz, 2H), 7.25 – 7.23 (m, 3H), 1.85 (s, 3H).; ^{13}C NMR: (150 MHz, $CDCl_3$) = 149.44, 145.54, 140.82, 140.78, 138.77, 137.45, 136.45, 133.84, 133.30, 130.67, 129.56, 129.06, 129.00, 128.86, 128.02, 127.88, 127.66, 127.38, 125.90, 124.78, 121.08, 119.14, 103.88, 14.21.; HRMS calculated for the molecular formula $C_{32}H_{23}ClN_5$ = 512.1636 ($[M+H]^+$); found = 512.1642.

1-methyl-3,5,8-triphenyl-7-(p-tolyl)-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16y**); Physical appearance = Yellow solid; Melting Point = 225-227 ℃; Yield = 72%; Weight = 177.0 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.84 (d, *J* = 7.86 Hz, 2H), 8.32 (d, *J* = 8.52 Hz, 2H), 7.55 – 7.43 (m, 10H), 7.32 – 7.29 (m, 3H), 7.13 (d, *J* = 8.1 Hz,

2H), 2.34 (s, 3H), 1.93 (s, 3H).; ^{13}C NMR: (150 MHz, $CDCl_3$) = 150.37, 146.53, 141.77, 141.51, 139.87, 138.40, 137.61, 137.53, 134.75, 131.73, 130.94, 130.05, 129.91, 129.51, 129.35, 128.85, 128.42, 128.32, 125.64, 125.61, 122.01, 119.96, 105. 09, 21.07, 15.21.; HRMS calculated for the molecular formula $C_{33}H_{26}N_5$ = 492.2183 ($[M+H]^+$); found = 492.2190.

7-(4-methoxyphenyl)-1-methyl-3,5,8-triphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16z**); Physical appearance = Yellow solid; Melting Point = 224-226 ℃; Yield = 60 %; Weight = 152 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.75 (d, *J* = 7.3 Hz, 2H), 8.24 (d, *J* = 7.7 Hz, 2H), 7.47 – 7.37 (m, 10H), 7.26 (d, *J* = 8.9 Hz, 2H), 7.23 (t, *J* = 7.4 Hz, 1H), 6.75 (d, *J* = 9.0 Hz, 2H), 3.71 (s, 3H), 1.85 (s, 3H).; ^{13}C NMR: (150 MHz, $CDCl_3$) = 159.39, 150.35, 146.54, 141.77, 141.41, 139.86, 137.64, 134.83, 133.05, 131.73, 130.92, 130.04, 129.91, 129.53, 128.86, 128.44, 128.34, 127.07, 125.66, 122.02, 119.87, 113.92, 105.08, 54.46, 15.21.; HRMS calculated for the molecular formula $C_{33}H_{26}N_5O$ = 508.2132 ($[M+H]^+$); found = 508.2131.

4-(1-methyl-3,5,8-triphenyldipyrazolo[3,4-b:4',3'-d]pyridin-7(3H)-yl)benzonitrile (**16aa**); Physical appearance = Yellow solid; Melting Point = 218-220 ℃; Yield = 52%; Weight = 130 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.71 (d, *J* = 7.1 Hz, 2H), 8.21 (d, *J* = 7.9 Hz, 2H), 7.57 (d, *J* = 8.7 Hz, 2H), 7.52 – 7.44 (m, 10H), 7.41 (d, *J* = 7.7 Hz, 2H), 7.25 (t, *J* = 7.4 Hz, 1H), 1.84 (s, 3H).; ^{13}C NMR: (150 MHz, $CDCl_3$) = 149.59, 145.56, 142.30, 141.30, 140.94, 138.65, 136.24, 133.96, 131.84, 130.59, 129.26, 129.25, 128.96, 127.94, 127.92, 127.44, 124.96, 124.90, 121.17, 119.57, 116.88, 110.89, 103.61, 14.21.; HRMS calculated for the molecular formula of $C_{33}H_{23}N_6$ = 503.1979 ($[M+H]^+$); found = 503.1981.

1-methyl-3,5,8-triphenyl-7-(m-tolyl)-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16ab**); Physical appearance = Yellow solid; Melting Point = 228-230 ℃; Yield = 66%; Weight = 162 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (500 MHz, $CDCl_3$) = 8.86 (d, *J* = 7.2 Hz, 2H), 8.35 (d, *J* = 7.7 Hz, 2H), 7.62 – 7.49 (m, 10H), 7.36 – 7.33 (m, 2H), 7.24 – 7.17 (m, 3H), 2.36 (s, 3H), 1.97 (s, 3H).; ^{13}C NMR: (125 MHz, $CDCl_3$) = 150.56, 146.60, 141.87, 141.62,

139.87, 139.02, 137.66, 134.96, 131.78, 130.96, 130.10, 130.01, 129.61, 129.23, 128.93, 128.49, 128.46, 128.43, 126.65, 125.76, 122.96, 122.11, 120.00, 105.13, 21.34, 15.30. ; HRMS calculated for the molecular formula $C_{33}H_{26}N_5$ = 492.2183 ([M+H]$^+$); found = 492.2190.

7-(3-bromophenyl)-1-methyl-3,5,8-triphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16ac**); Physical appearance = Yellow solid; Melting Point = 232-234 °C; Yield = 56%; Weight = 156 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.74 (d, *J* = 7.4 Hz, 2H), 8.23 (d, *J* = 7.7 Hz, 2H), 7.64 (s, 1H), 7.52 – 7.40 (m, 11H), 7.26 – 7.21 (m, 2H), 7.11 (t, *J* = 8.0 Hz, 1H), 1.86 (s, 3H); ^{13}C NMR: (150 MHz, $CDCl_3$) = 149.54, 145.55, 140.86, 139.96, 138.75, 136.42, 134.00, 130.66, 130.43, 129.45, 129.10, 129.01, 128.92, 127.96, 127.88, 127.67, 127.42, 124.81, 123.23, 121.33, 121.11, 119.13, 103.83, 14.21; HRMS calculated for the molecular formula $C_{32}H_{23}BrN_5$ = 556.1131 ([M+H]$^+$); found = 556.1137.

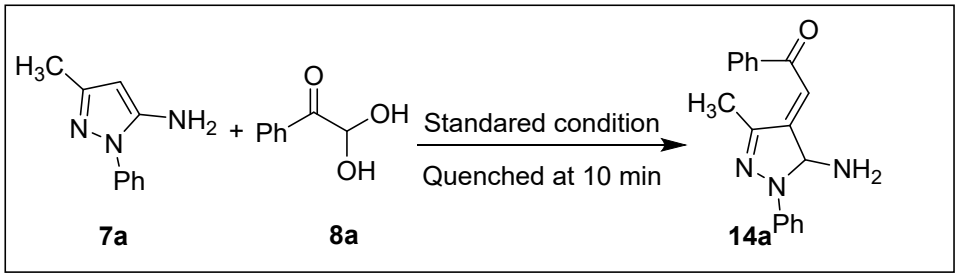
1-methyl-3,5,8-triphenyl-7-(o-tolyl)-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16ad**); Physical appearance = Yellow solid; Melting Point = 230-232 °C; Yield = 48%; Weight = 118 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.73 – 8.72 (m, 2H), 8.26 (dd, J = 1.0, 8.6 Hz, 2H), 7.49 – 7.45 (m, 4H), 7.41 (t, *J* = 7.3 Hz, 1H), 7.34 – 7.31 (m, 5H), 7.26 – 7.22 (m, 2H), 7.21 – 7.20 (m, 1H), 7.18 – 7.16 (m, 1H), 7.12 – 7.09 (m, 1H), 2.04 (s, 3H), 1.91 (s, 3H).; ^{13}C NMR: (150 MHz, $CDCl_3$) = 150.56, 146.55, 141.72, 141.63, 139.88, 138.89, 137.66, 136.20, 135.60, 131.29, 130.82, 130.23, 130.04, 129.91, 129.50, 128.40, 128.88, 128.36, 128.16, 126.08, 125.69, 122.05, 118.94, 105.18, 17.68, 15.38.; HRMS calculated for the molecular formula $C_{33}H_{26}N_5$ = 492.2183 ([M+H]$^+$); found = 492.2189.

7-(2-bromophenyl)-1-methyl-3,5,8-triphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16ae**); Physical appearance = Yellow solid; Melting Point = 227-229 °C; Yield = 43%; Weight = 120 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.78 (d, *J* = 7.1 Hz, 2H), 8.32 (d, *J* = 7.6 Hz, 2H), 7.65 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.56 – 7.49 (m, 7H), 7.42 – 7.37 (m, 4H), 7.34 – 7.27 (m, 3H), 1.97 (s, 3H).; ^{13}C NMR: (150 MHz, $CDCl_3$) = 150.91, 146.58, 141.87, 141.82, 139.85, 139.22, 137.60, 136.50, 133.34, 131.41, 131.02, 130.08, 129.97, 129.93,

129.83, 129.59, 128.89, 128.39, 128.13, 127.65, 125.74, 122.33, 122.10, 118.99, 105.06, 15.23. ; HRMS calculated for the molecular formula $C_{32}H_{23}BrN_5$ = 556.1132 ([M+H]$^+$); found = 556.1138.

7-cyclohexyl-1-methyl-3,5,8-triphenyl-3,7-dihydrodipyrazolo[3,4-b:4',3'-d]pyridine (**16af**); Physical appearance = Yellow solid; Melting Point = 221-222 °C; Yield = 40%; Weight = 96 mg; R_f = 0.8 (5% ethylacetate in hexane); ^{1}H NMR: (600 MHz, $CDCl_3$) = 8.80 (d, *J* = 7.4 Hz, 2H), 8.24 (d, *J* = 7.9 Hz, 2H), 7.53 – 7.49 (m, 5H), 7.45 – 7.43 (m, 5H), 7.21(t, *J* = 7.4 Hz, 1H), 4.14 – 4.08 (m, 1H), 2.18 – 2.11 (m, 2H), 1.95 (d, *J* = 11.5 Hz, 2H), 1.82 (d, *J* = 13.5 Hz, 2H), 1.77 (s, 3H), 1.63 – 1.59 (m, 1H), 1.30 – 1.19 (m, 3H); ^{13}C NMR: (150 MHz, $CDCl_3$) = 149.82, 146.20, 141.91, 140.15, 139.28, 137.85, 134.55, 131.78, 131.14, 129.98, 129.84, 129.50, 128.82, 128.47, 128.39, 128.26, 125.88, 120.11, 102.90, 56.23, 32.83, 25.99, 25.55, 15.30. ; HRMS calculated for the molecular formula $C_{32}H_{30}N_5$ = 484.2496 ([M+H]$^+$); found = 484.2510.

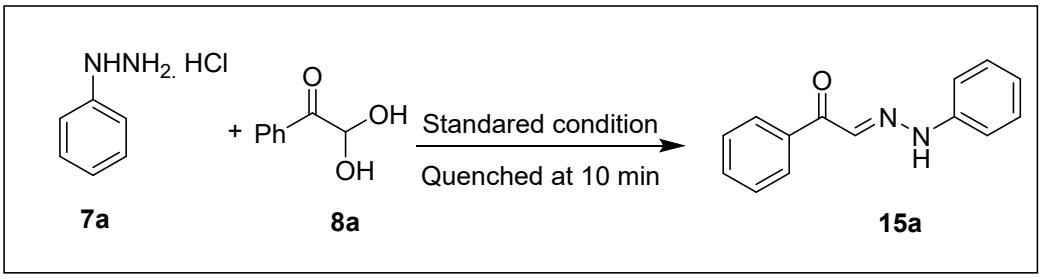
1.3. General procedure for the synthesis of (Z)-2-(5-imino-3-methyl-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-1-phenylethan-1-one (14a):



The reaction was carried out in a 25 mL round-bottom flask that had been dried. Pyrazole amine **7a** (0.086 mg, 0.5 mmol), phenylglyoxal monohydrate (**8a**) (0.228 mg, 1.5 mmol) were dissolved in isobutyric acid (1.7 mL) and heated at 120 °C. The reaction was monitored by thin-layer chromatography (TLC), and completion was confirmed by TLC. Afterward, the reaction mixture was dissolved in ethyl acetate, $NaHCO_3$, and $Na_2S_2O_8$. The organic layer was separated and dried over anhydrous sodium sulfate. The solvent was evaporated using a rotary evaporator. The crude product **14** was characterized by HRMS. (Z)-2-(5-imino-3-methyl-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)-1-phenylethan-1-one (**14a**) Physical appearance = Brown semi solid; Yield =

94%; Weight = 136 mg; R_f = 0.2 (20% ethylacetate in hexane); HRMS calculated for the molecular formula $C_{18}H_{18}N_3O$ = 289.1215 ($[M+H]^+$); found = 290.1293.

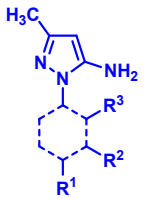
1.4. General procedure for the synthesis of (E)-1-phenyl-2-(2-phenylhydrazineylidene)ethan-1-one (15a):



The reaction was carried out in a 25 mL round-bottom flask that had been dried. Phenylhydrazine hydrochloride (**7a**) (0.072 mg, 0.5 mmol), phenylglyoxal monohydrate (**8a**) (0.228 mg, 1.5 mmol) were dissolved in isobutyric acid (1.7 mL) and heated at 120 °C. The reaction was monitored by thin-layer chromatography (TLC), and completion was confirmed by TLC. Afterward, the reaction mixture was dissolved in ethyl acetate, $NaHCO_3$, and $Na_2S_2O_8$. The organic layer was separated and dried over anhydrous sodium sulfate. The solvent was evaporated using a rotary evaporator. The crude product **15a** was characterized by HRMS. (**(E)-1-phenyl-2-(2-phenylhydrazineylidene)ethan-1-one** (**15a**) Physical appearance = Brown semi solid; Melting Yield = 97%; Weight = 109 mg mg; R_f= 0.8 (5% ethylacetate in hexane); HRMS calculated for the molecular formula $C_{14}H_{12}N_2O$ = 225.1022($[M+H]^+$); found = 225.1027.

2. Starting materials

2.1 Pyrazole amine derivatives

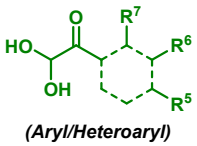


7a-7l
(Aryl/aliphatic)

Pyrazole amine derivatives

7a, R^1 = H; R^2 = H; R^3 = H
7b, R^1 = Br; R^2 = H; R^3 = H
7c, R^1 = Cl; R^2 = H; R^3 = H
7d, R^1 = F; R^2 = H; R^3 = H
7e, R^1 = CH_3; R^2 = H; R^3 = H
7f, R^1 = OCH_3; R^2 = H; R^3 = H
7g, R^1 = NO_2; R^2 = H; R^3 = H
7h, R^1 = H; R^2 = H; R^3 = CH_3
7i, R^1 = H; R^2 = H; R^3 = Br
7j, R^1 = H; R^2 = CH_3; R^3 = H
7k, R^1 = H; R^2 = Br; R^3 = H
7l, Cyclohexyl pyrazoleamine

2.2 Phenylglyoxal monohydrate derivatives

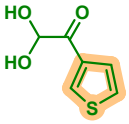


(Aryl/Heteroaryl)

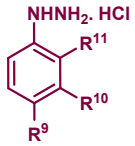
8b-8j

Phenylglyoxal monohydrate derivatives

8b, R^5 = Br; R^6 = H; R^7 = H
8c, R^5 = F; R^6 = H; R^7 = H
8d, R^5 = Cl; R^6 = H; R^7 = H
8e, R^5 = CH_3; R^6 = H; R^7 = H
8f, R^5 = OCH_3; R^6 = H; R^7 = H
8g, R^5 = H; R^6 = CH_3; R^7 = H
8h, R^5 = H; R^6 = Cl; R^7 = H
8i, R^5 = H; R^6 = H; R^7 = OCH_3

8j, 

2.3 Phenylhyrazine hydrochloride derivatives



13b-13l

Phenylhydrazine hydrochloride derivatives

13b, R^9 = Br; R^{10} = H; R^{11} = H
13c, R^9 = F; R^{10} = H; R^{11} = H
13d, R^9 = Cl; R^{10} = H; R^{11} = H
13e, R^9 = CH_3; R^{10} = H; R^{11} = H
13f, R^9 = OCH_3; R^{10} = H; R^{11} = H
13g, R^9 = CN; R^{10} = H; R^{11} = H
13h, R^9 = H; R^{10} = CH_3; R^{11} = H
13i, R^9 = H; R^{10} = Br; R^{11} = H
13j, R^9 = H; R^{10} = H; R^{11} = CH_3
13k, R^9 = H; R^{10} = H; R^{11} = Br
13l, 

Table S2. Crystal data and structure refinement for **16a.**

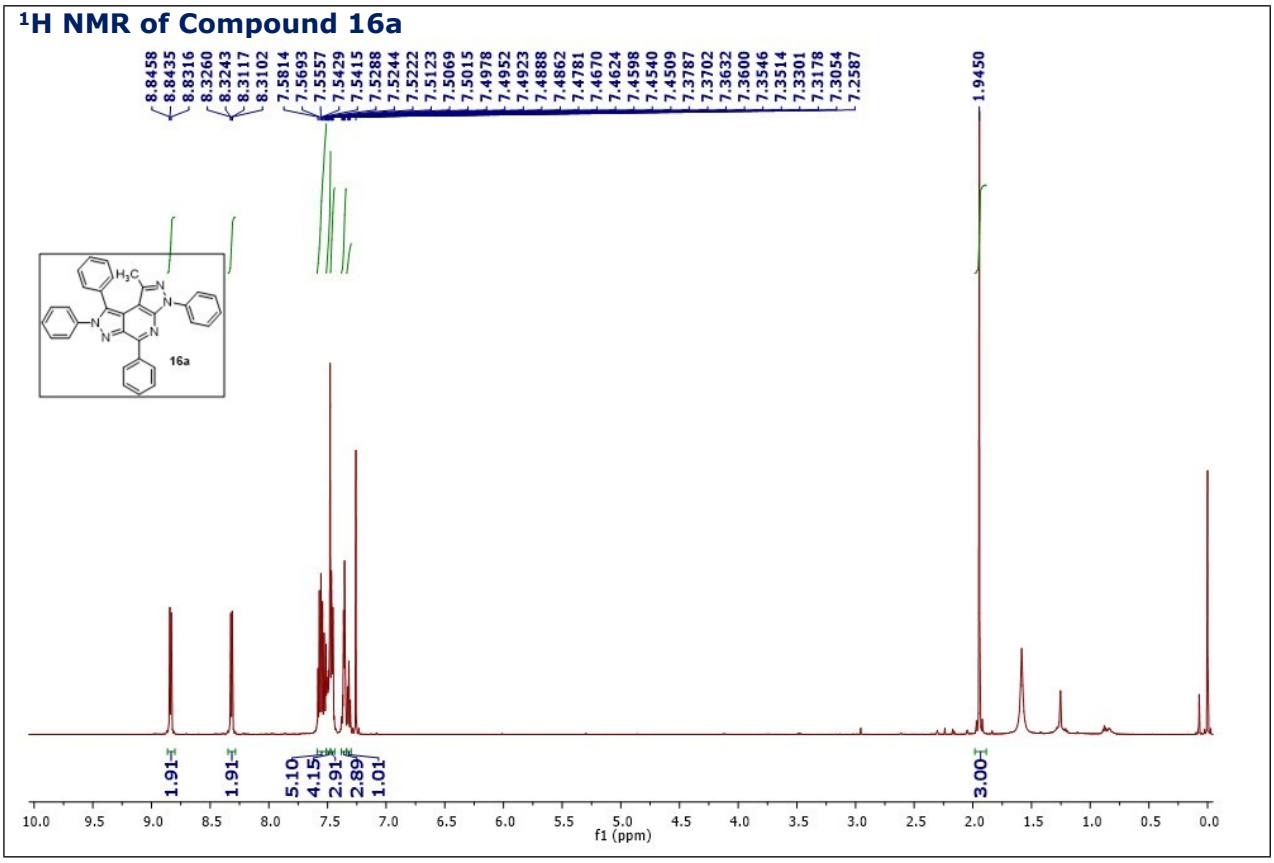
Empirical formula	$C_{32}H_{23}N_5$	
Formula weight	477.55	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 9.9729(4) Å	α= 94.304(4)°.
	b = 10.3862(5) Å	β= 98.744(4)°.
	c = 12.3764(6) Å	γ = 102.558(4)°.
Volume	1228.95(10) $Å^3$	
Z	2	
Density (calculated)	1.291 Mg/m^3	
Absorption coefficient	0.078 mm^{-1}	
F(000)	500	
Crystal size	0.090 x 0.070 x 0.060 mm^3	
Theta range for data collection	2.925 to 24.998°.	
Index ranges	-9<=h<=11, -12<=k<=12, -14<=l<=14	
Reflections collected	15791	
Independent reflections	4308 [R(int) = 0.0732]	
Completeness to theta = 24.998°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.08839	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4308 / 0 / 336	

Goodness-of-fit on F^2	1.096
Final R indices [I>2sigma(I)]	R1 = 0.0471, wR2 = 0.1251
R indices (all data)	R1 = 0.0590, wR2 = 0.1306
Extinction coefficient	0.018(4)
Largest diff. peak and hole	0.226 and -0.184 e.$Å^{-3}$

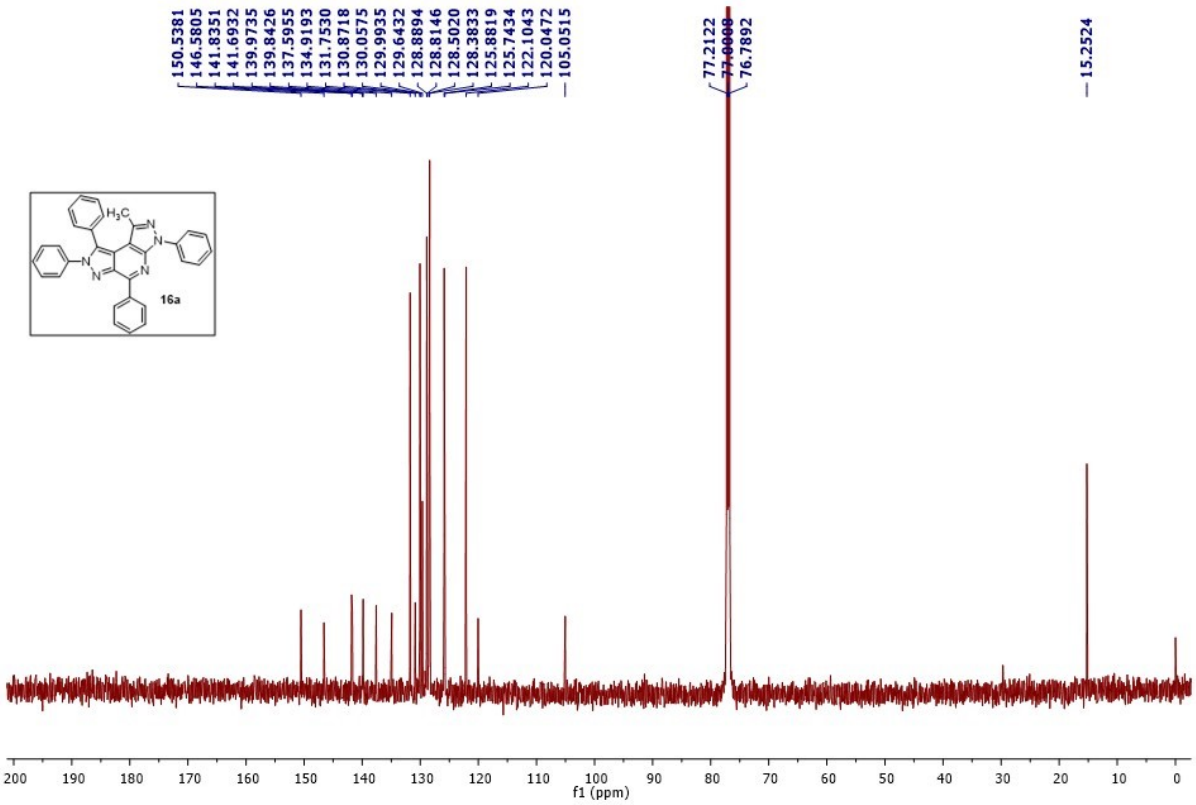
3. References:

1) a) Saritha, R.; Babiola Annes, S.; Perumal, K.; Shankar, B.; Ramesh, S. D. S.-A. Dimethyl Sulfoxide-Assisted, Iodine- and Ascorbic Acid-Catalyzed One-Pot Synthetic Approach for Constructing Highly Substituted Pyrazolo[1,5- a]quinoline Thioether Derivatives. *J. Org. Chem.* **2022**, 87, 13856–13872. B) Ali, D.; Parvin, T.; Choudhury, L. H. Visible Light-Mediated C(sp 2)–H Selenylation of Amino Pyrazole and Amino Uracils in the Presence of Rose Bengal as an Organophotocatalyst. *J. Org. Chem*. **2022**, 87, 1230– 1239. C) Mupparapu, N.; Khan, S.; Battula, S.; Kushwaha, M.; Gupta, A. P.; Ahmed, Q. N.; Vishwakarma, R. A. Metal-Free Oxidative Amidation of 2-Oxoaldehydes: A Facile Access to α-Ketoamides. *Org. Lett*. **2014**, 16, 1152– 1155. D) Khan, S.; Ahmed, Q. N. 2-Oxo-Driven Coupling Reactions of 2-Oxo Aldehydes/2-Oxo Iminium Ions and Hydroperoxides at Room Temperature. *Eur. J. Org. Chem*. **2016**, 2016, 5377– 5385.
2) Sheldrick, G. M. Program for Crystal Structure Solution; University of Göttingen: Göttingen, Germany, 1997.
3) Sheldrick, G. M. A short history of SHELX. *Acta Crystallogr., Sect. A: Found. Crystallogr* **2008**, *64*, 112–122.
4) Sheldrick, G. M. Crystal structure refinement with SHELXL. *Acta Crystallogr., Sect. C: Struct. Chem* **2015**, 71, 3–8.

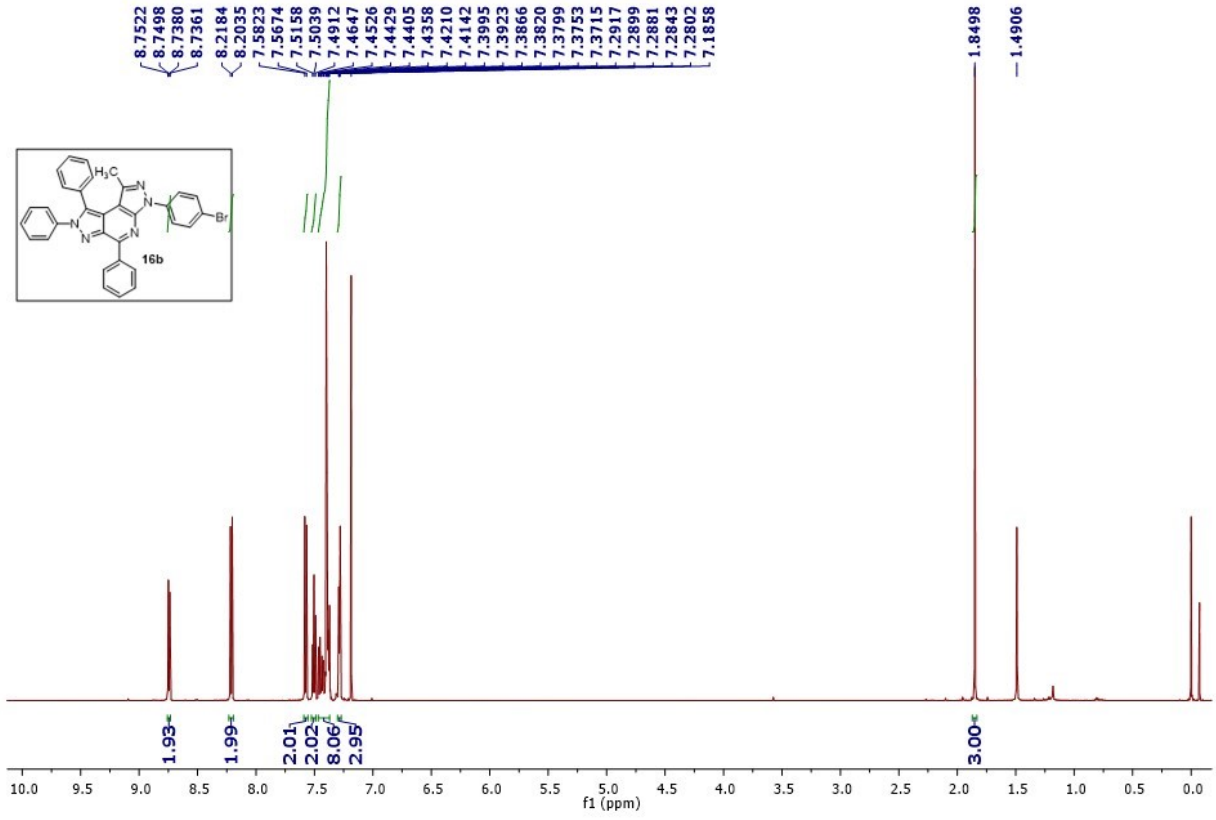
^{1}H NMR of Compound 16a



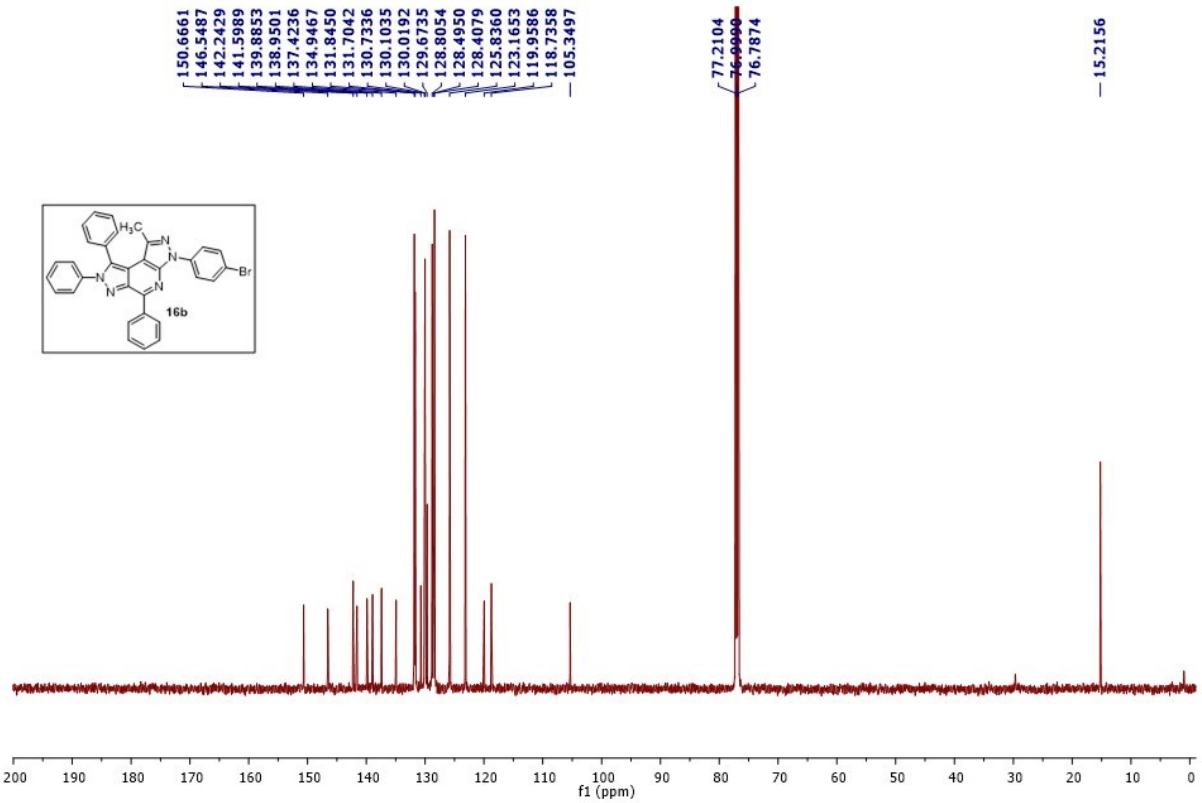
^{13}C NMR of Compound 16a



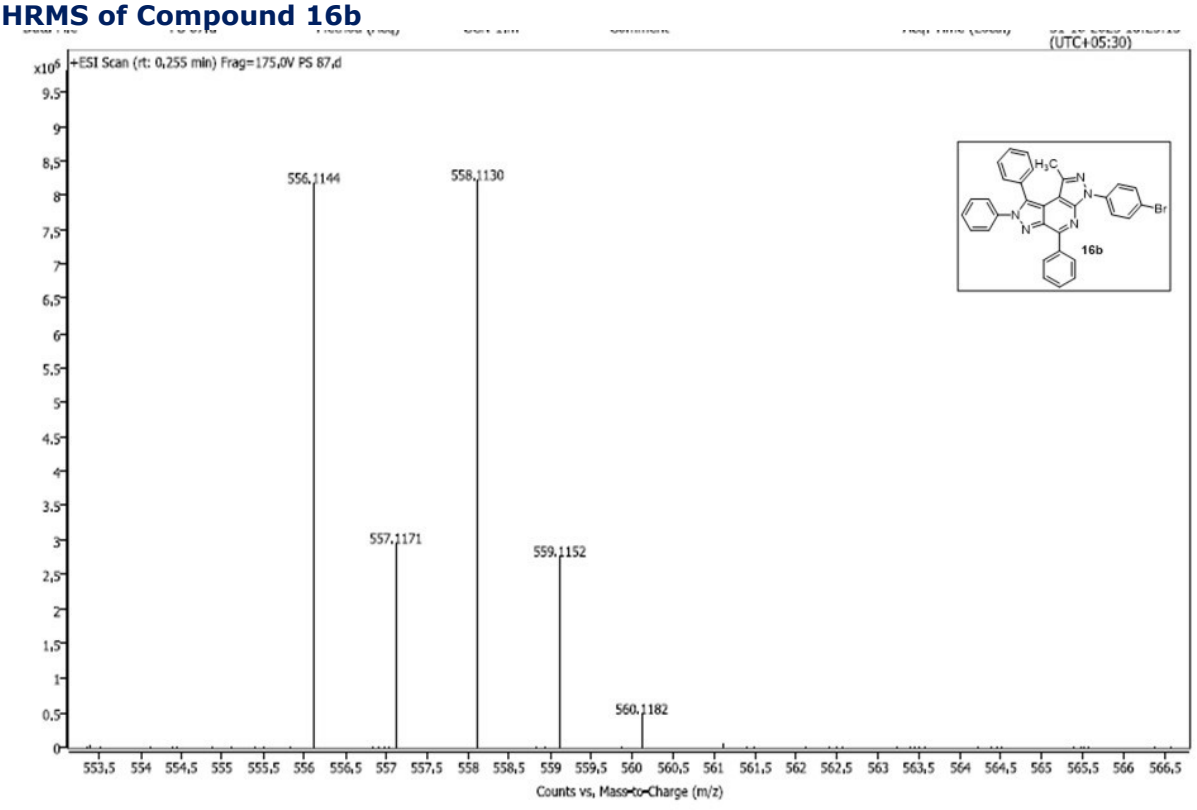
^{1}H NMR of Compound 16b



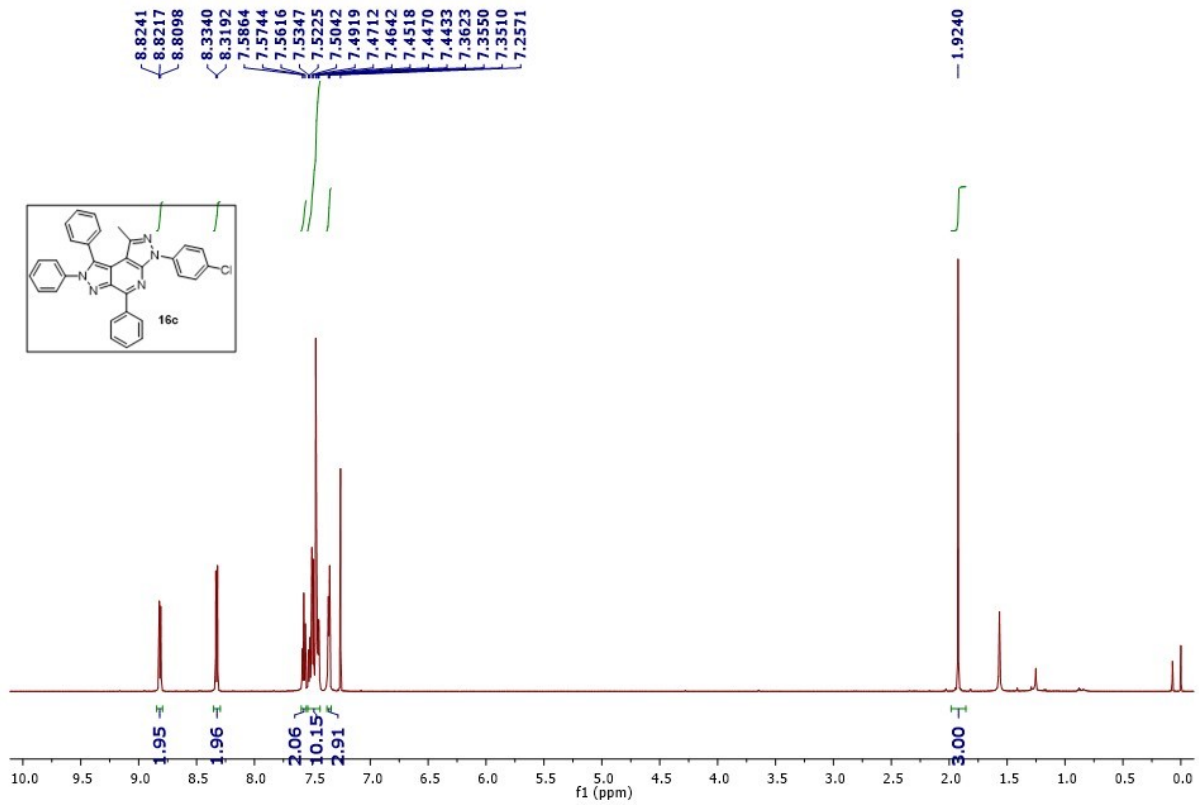
^{13}C NMR of Compound 16b



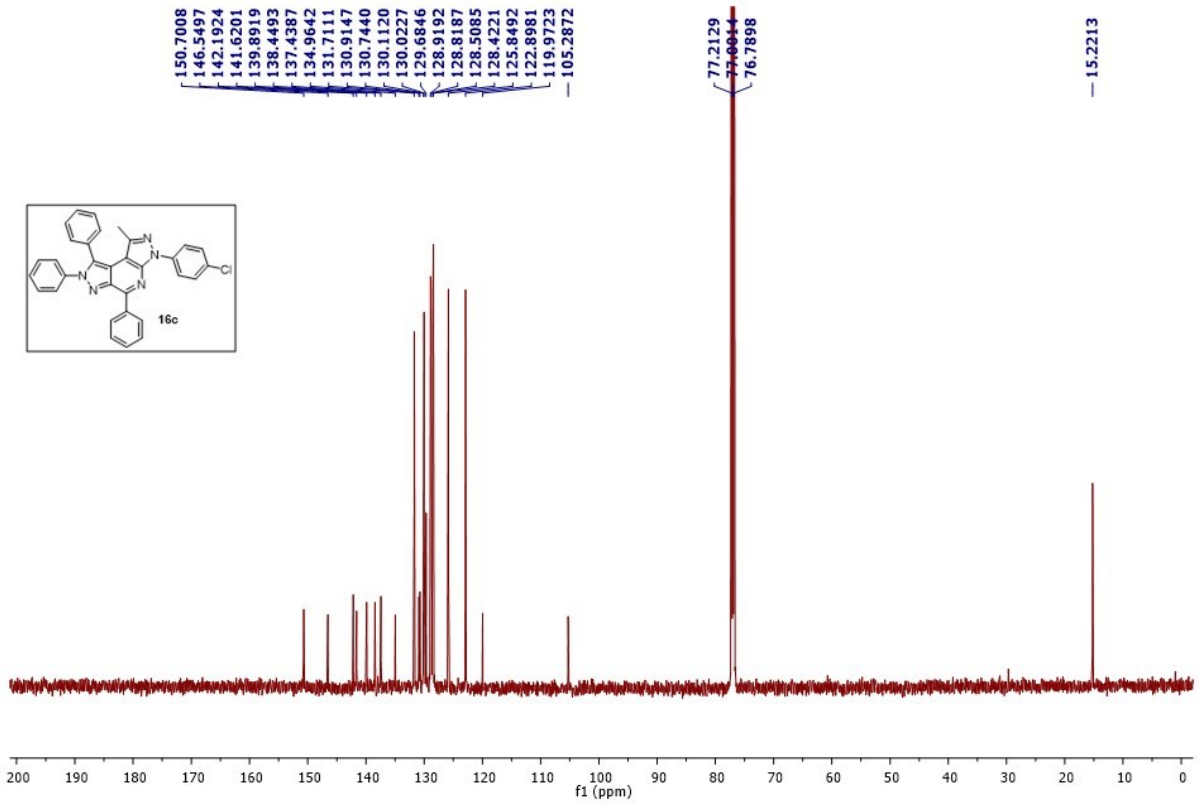
HRMS of Compound 16b



^{1}H NMR of Compound 16c



^{13}C NMR of Compound 16c



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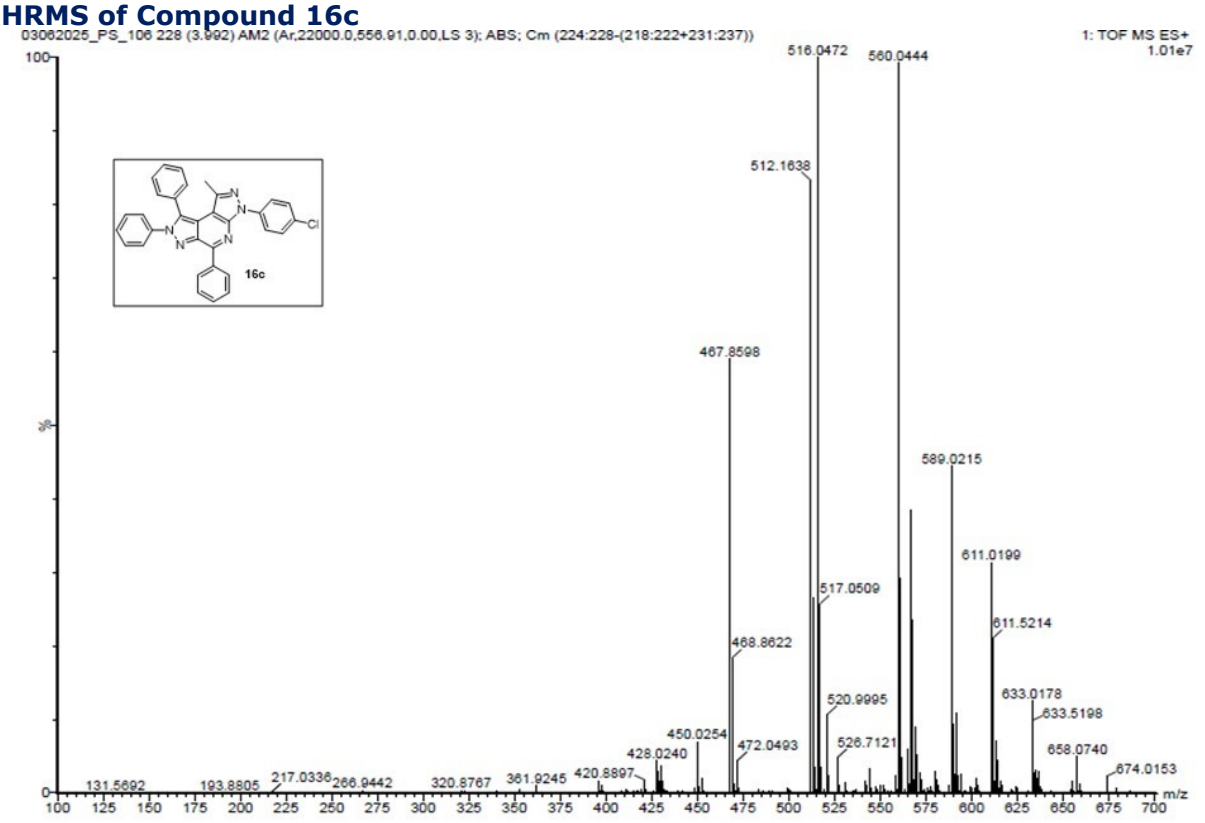

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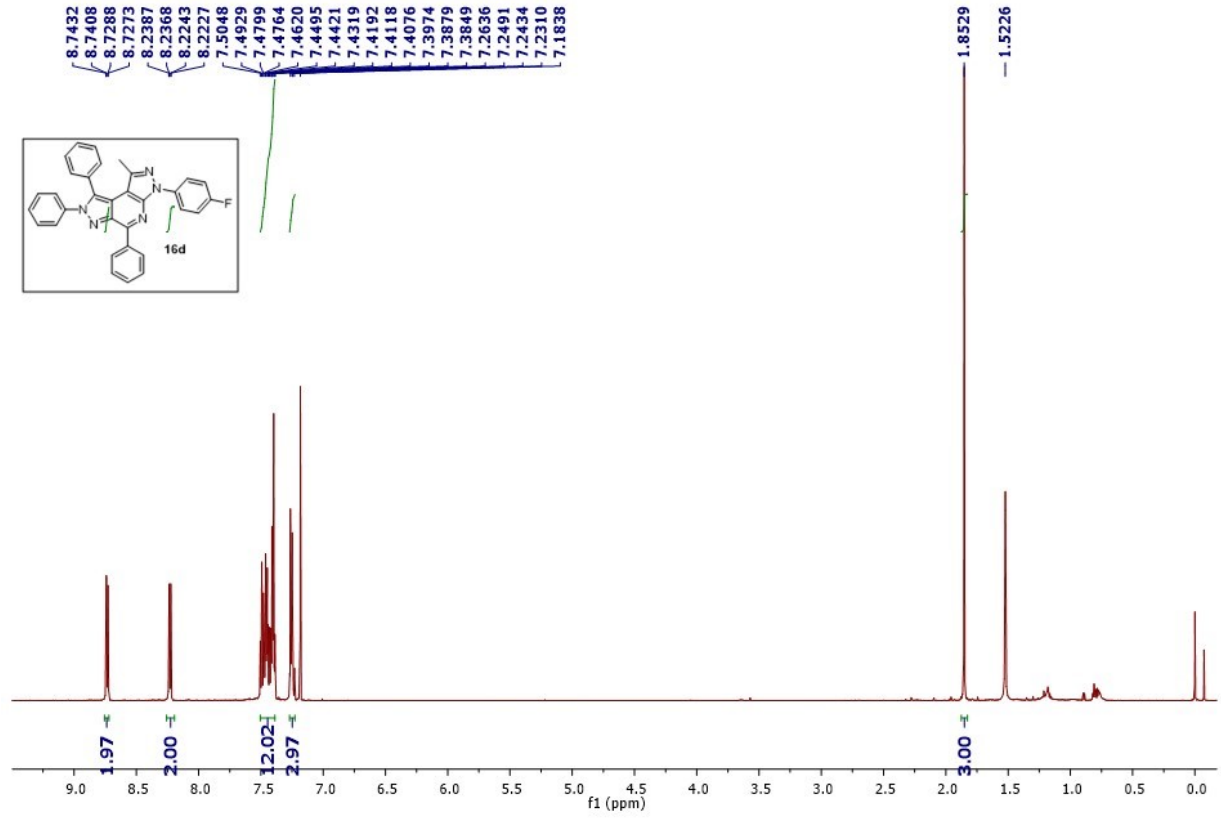
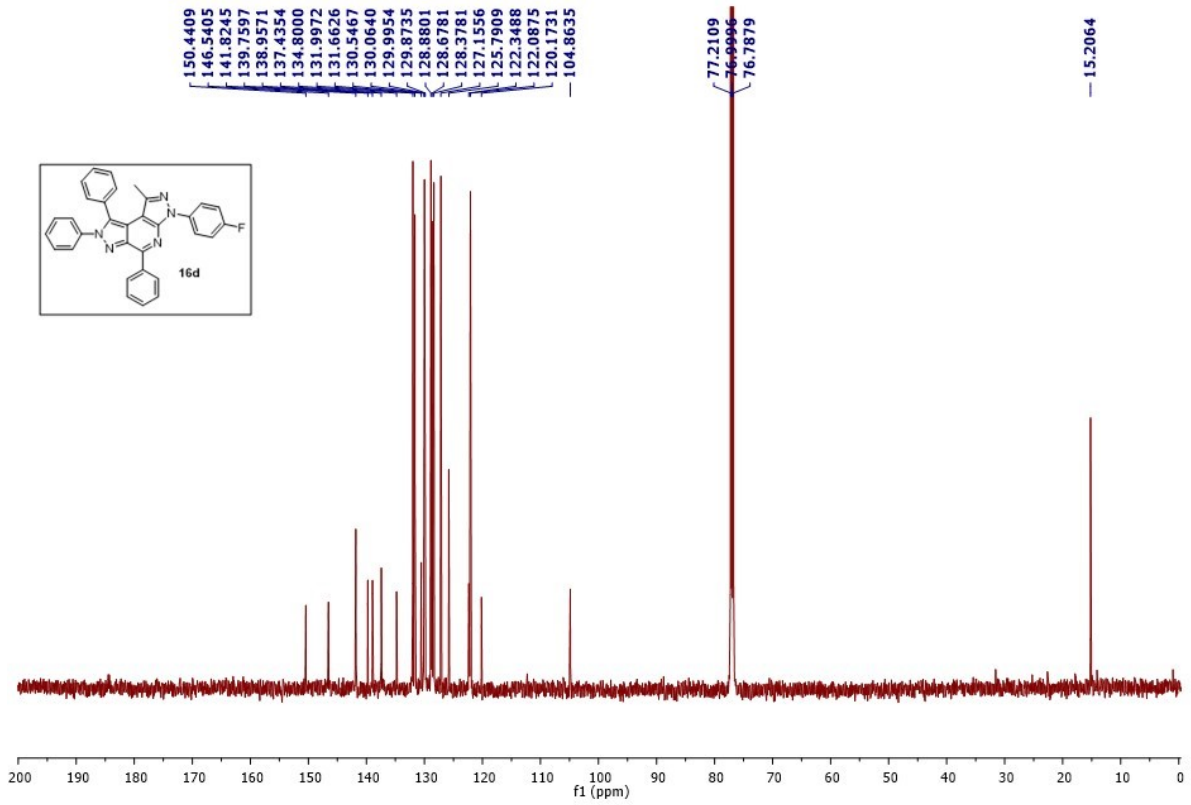
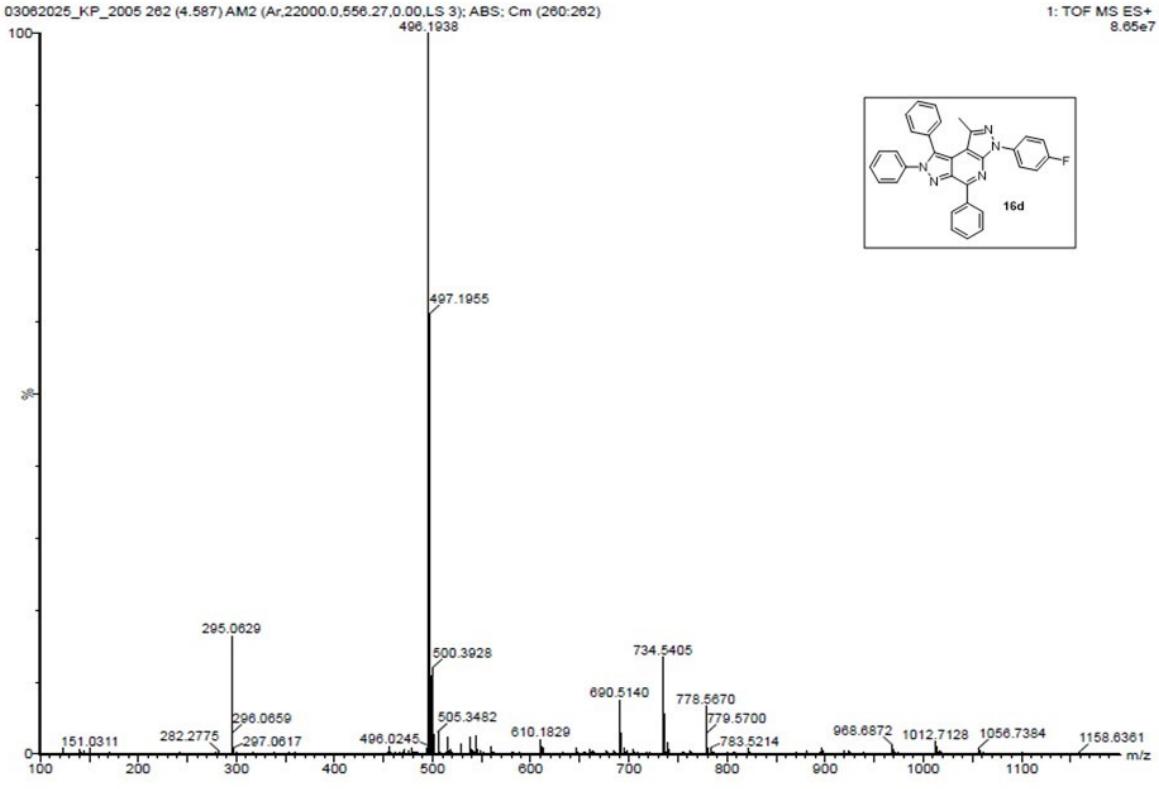


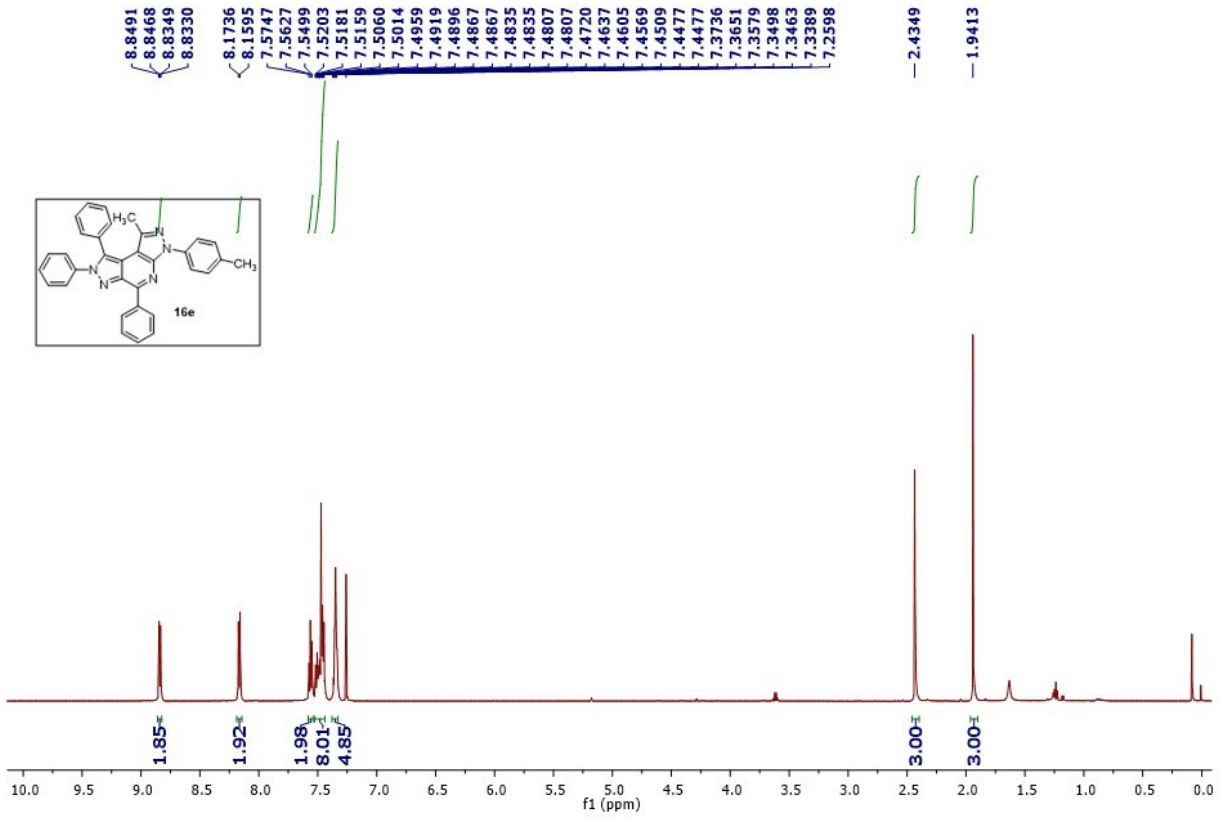
^{13}C NMR of Compound 16d



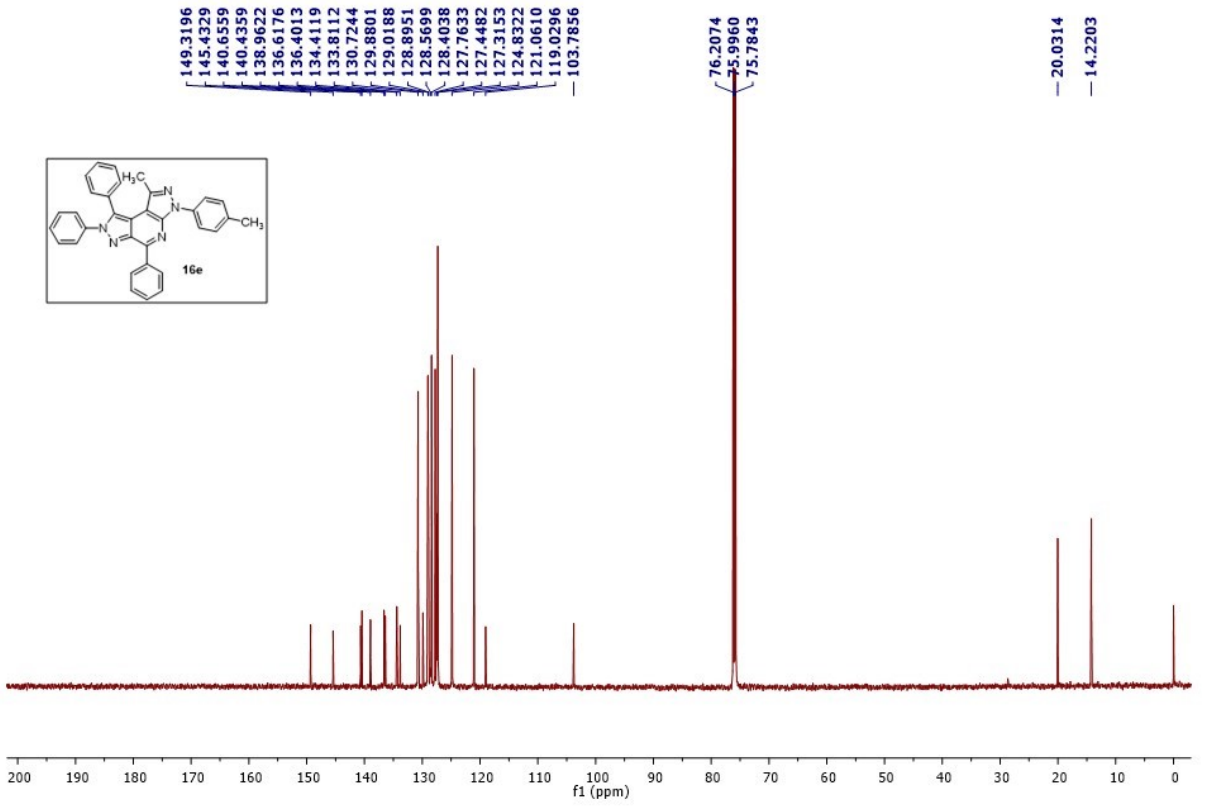
HRMS of Compound 16d



^{1}H NMR of Compound 16e



^{13}C NMR of Compound 16e



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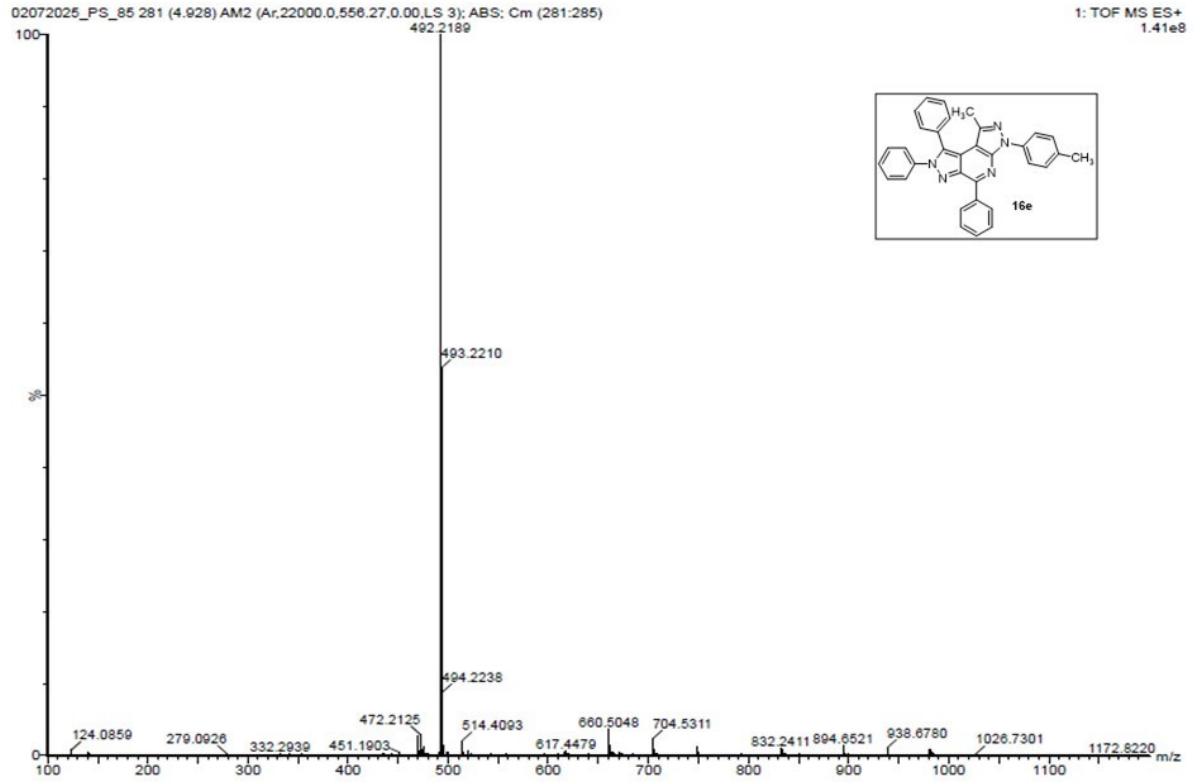
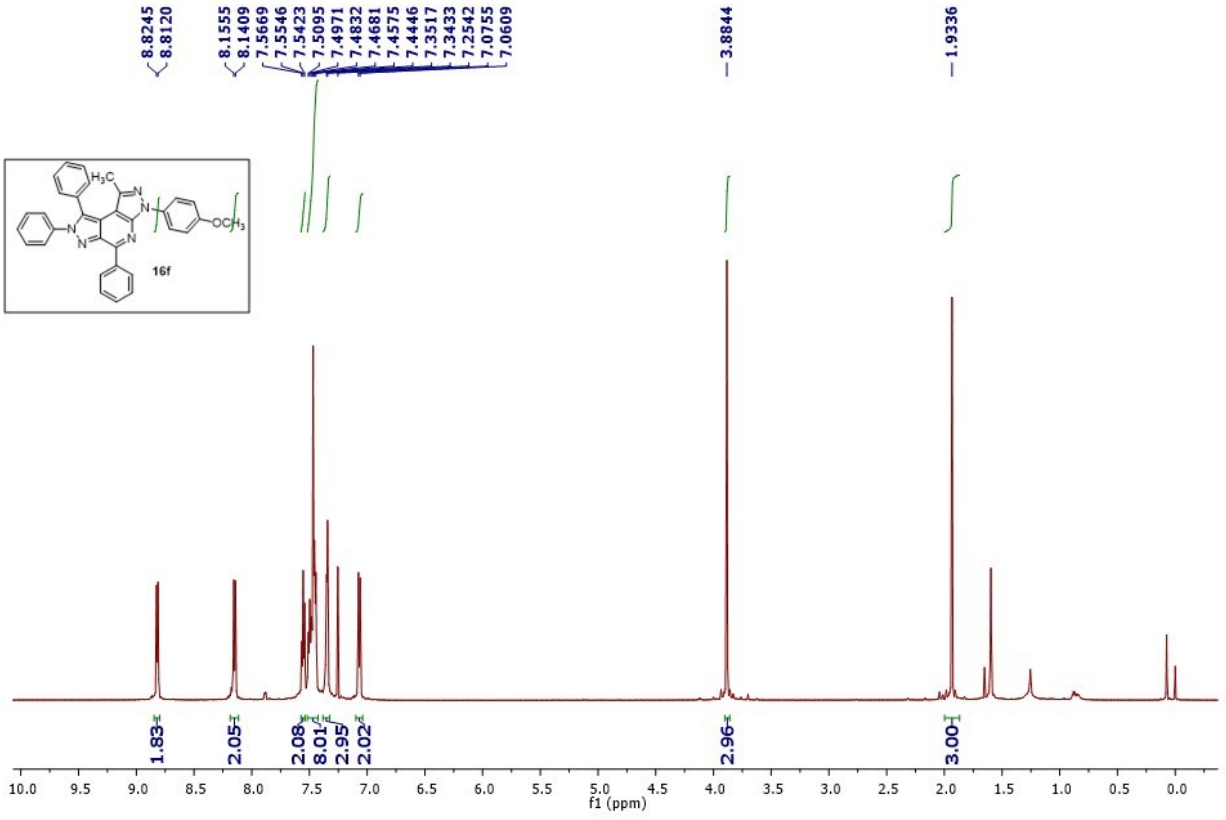
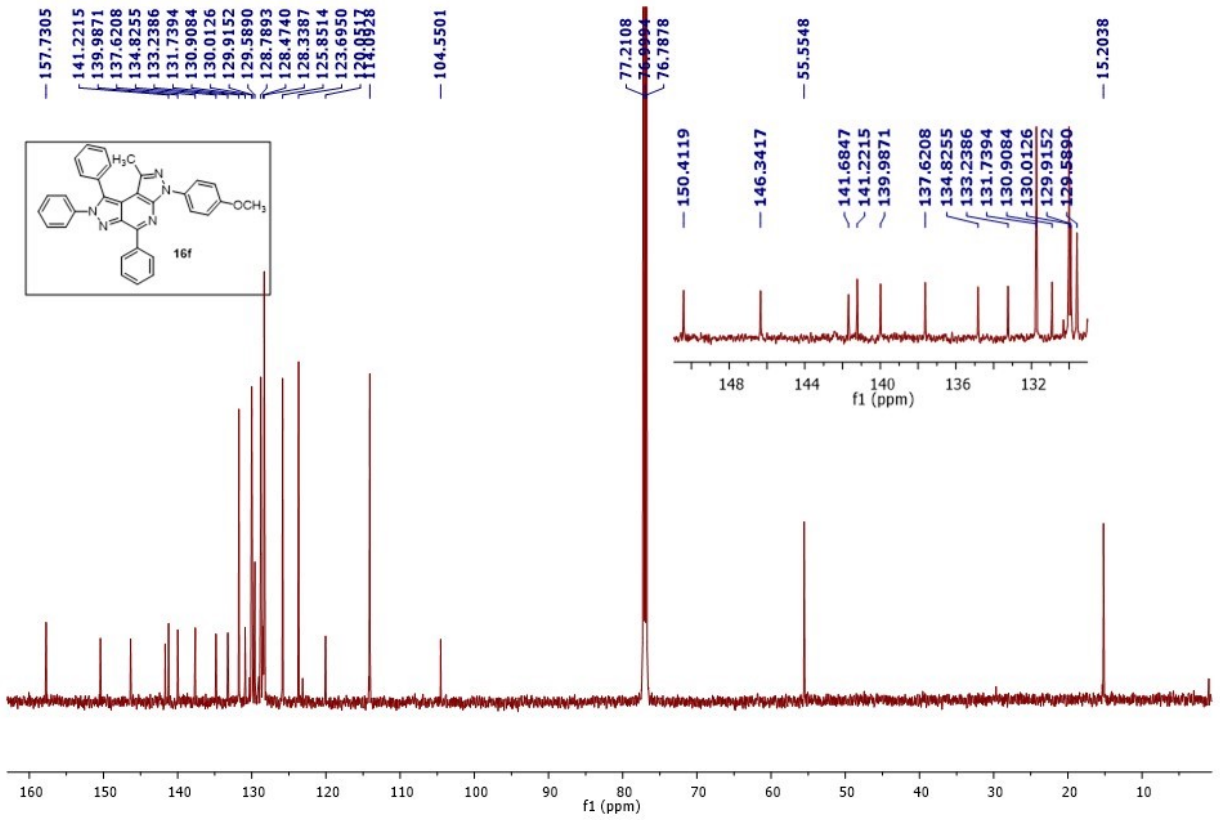


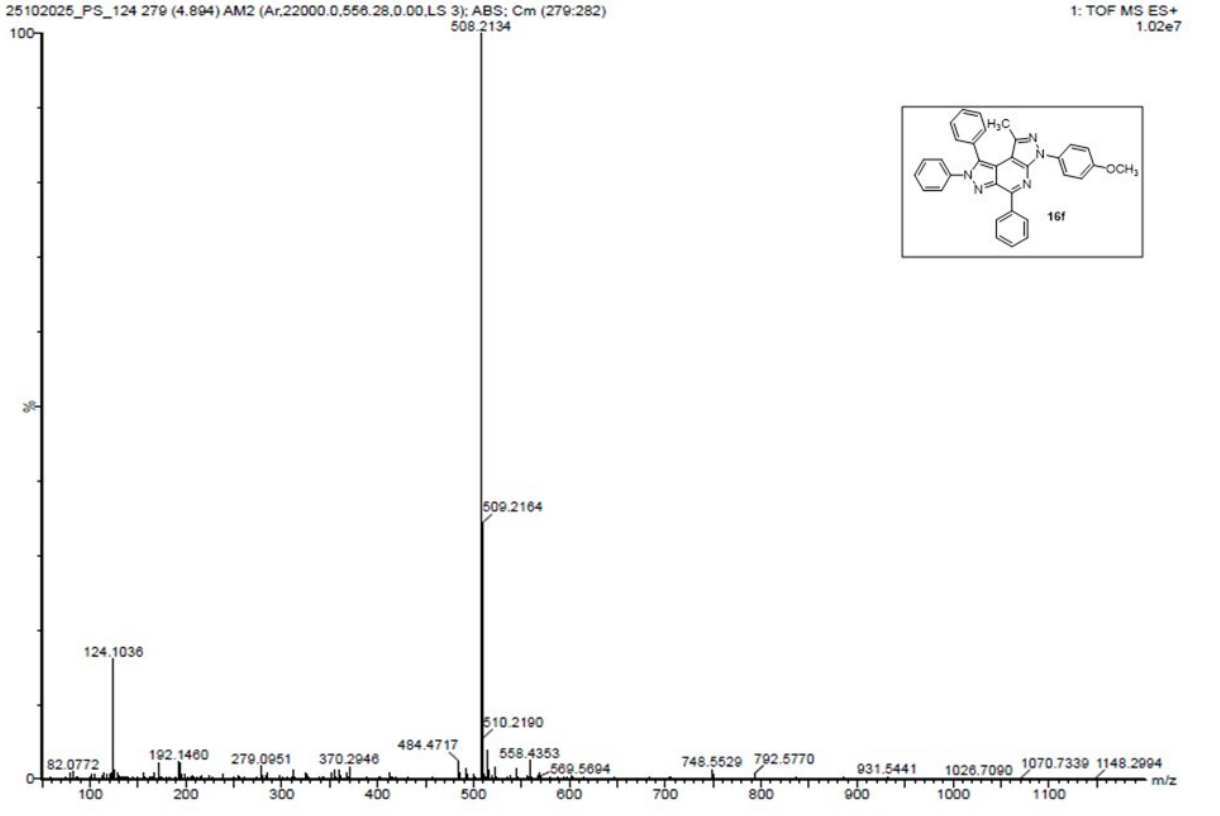
^{1}H NMR of Compound 16f



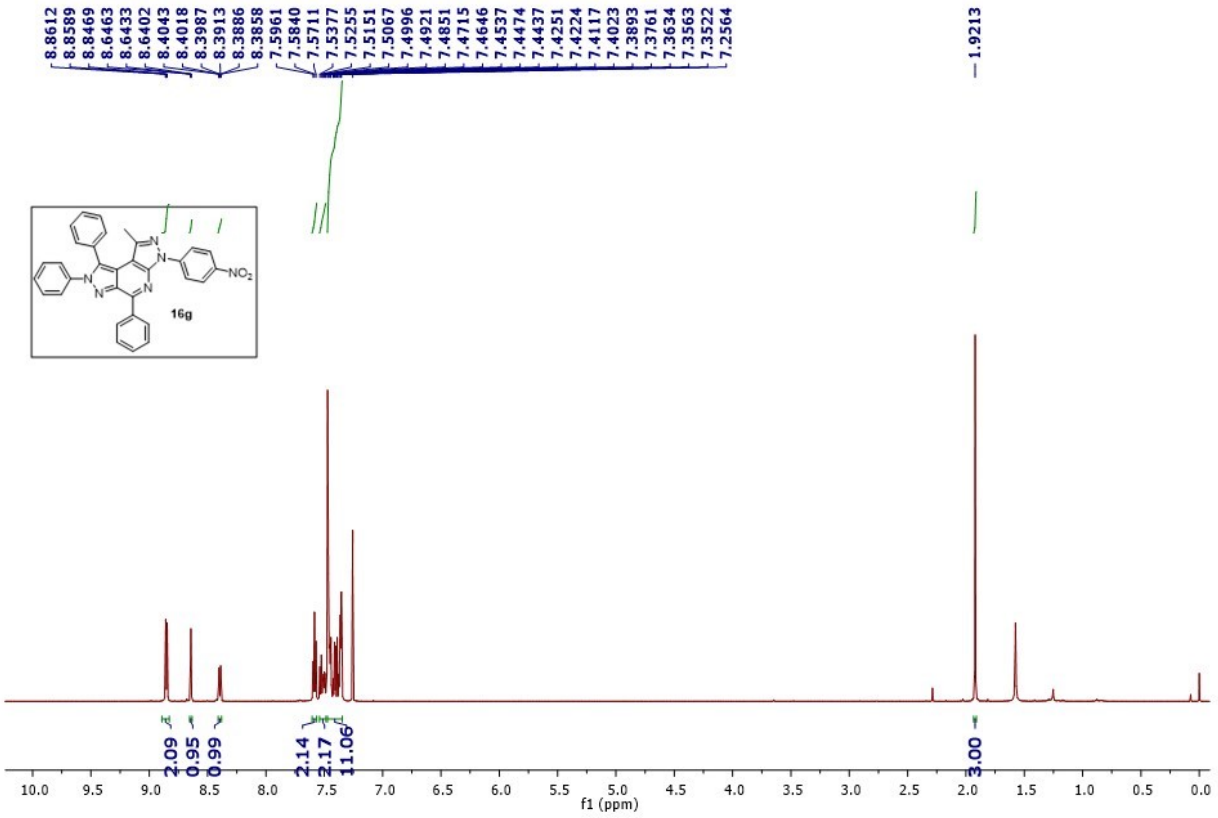
^{13}C NMR of Compound 16f



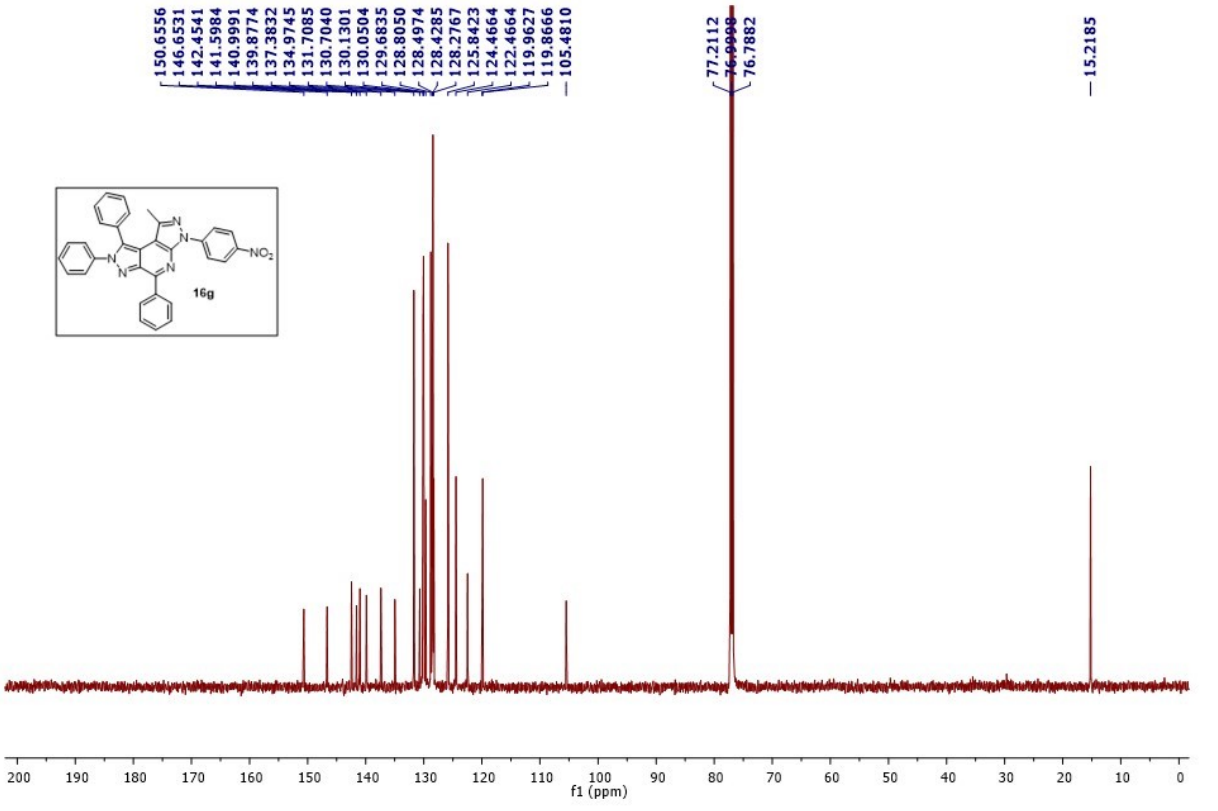
HRMS of Compound 16f



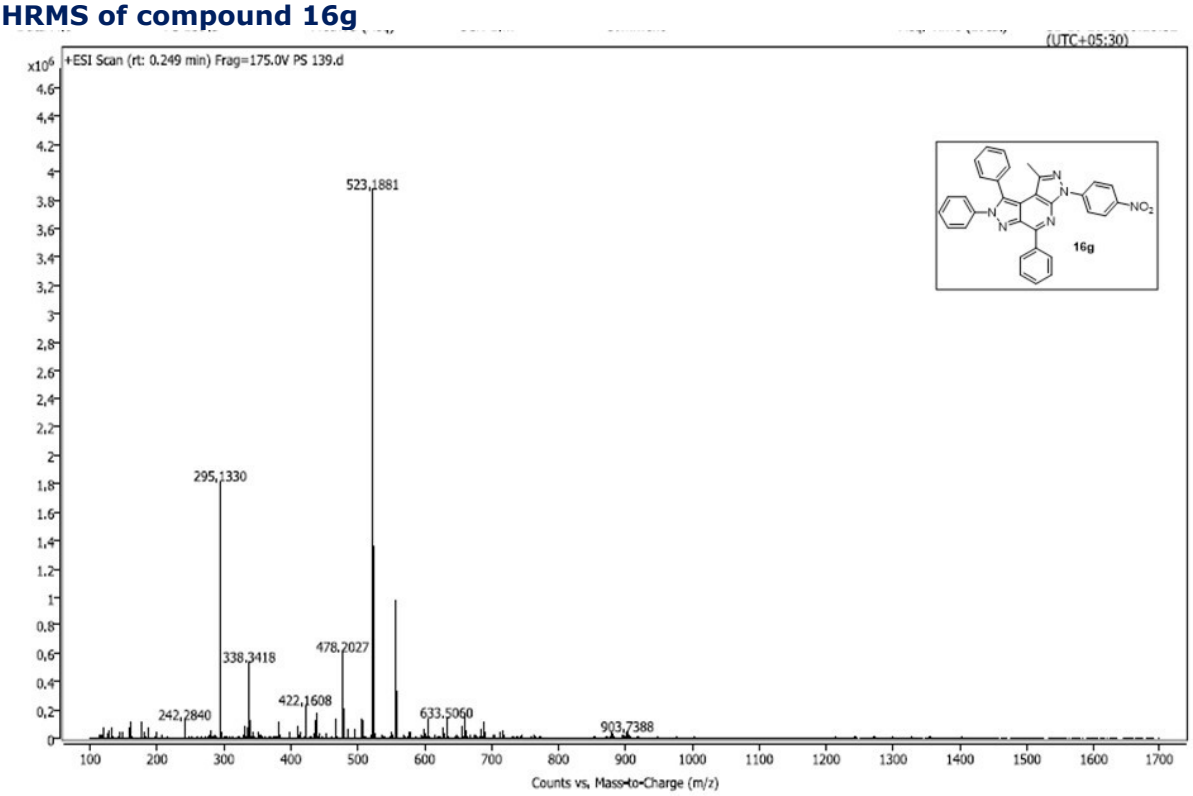
^{1}H NMR of Compound 16g



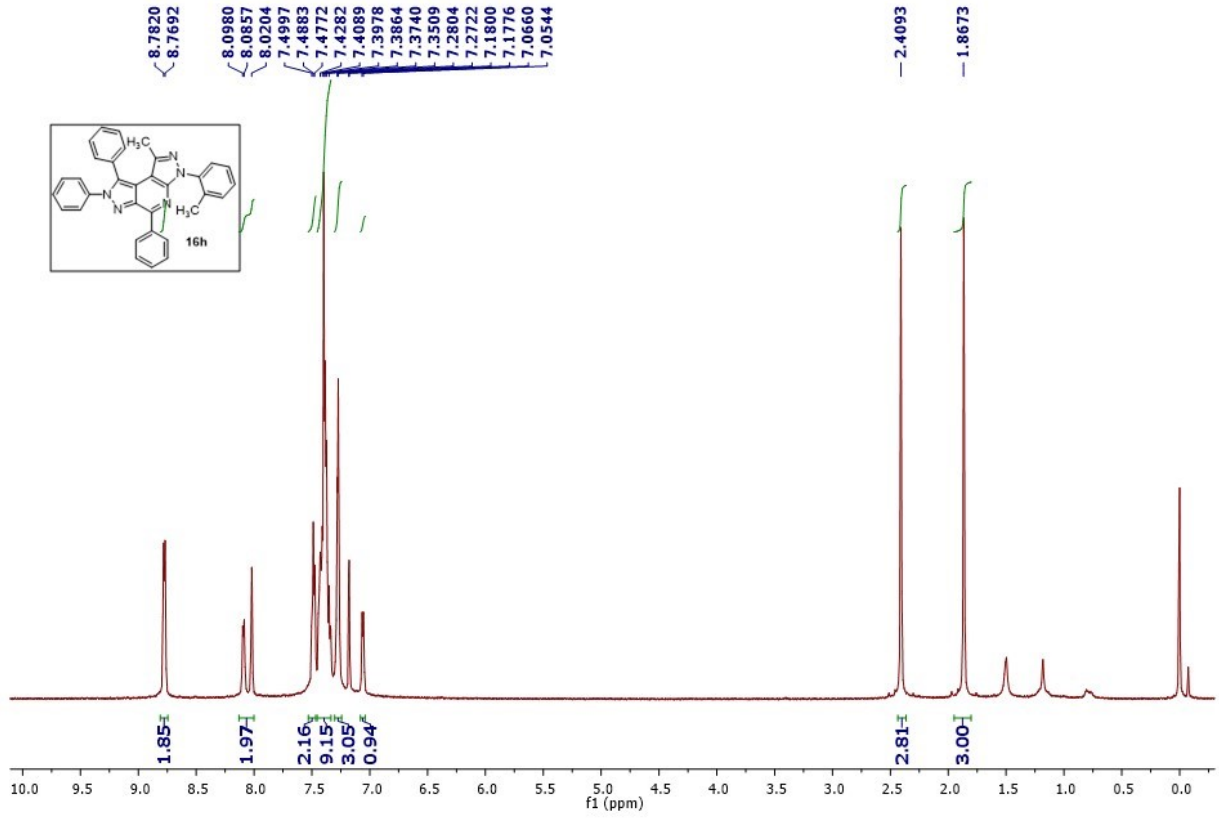
^{13}C NMR of Compound 16g



HRMS of compound 16g



^{1}H NMR of Compound 16h



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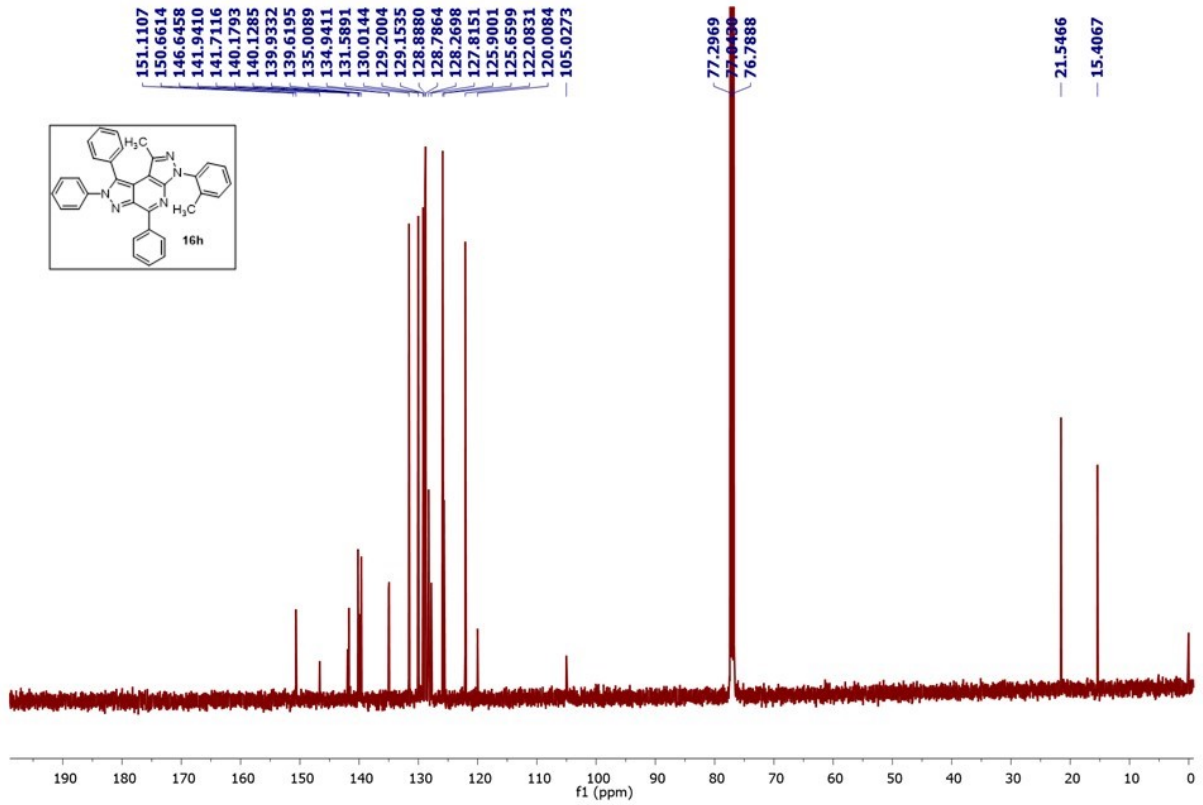

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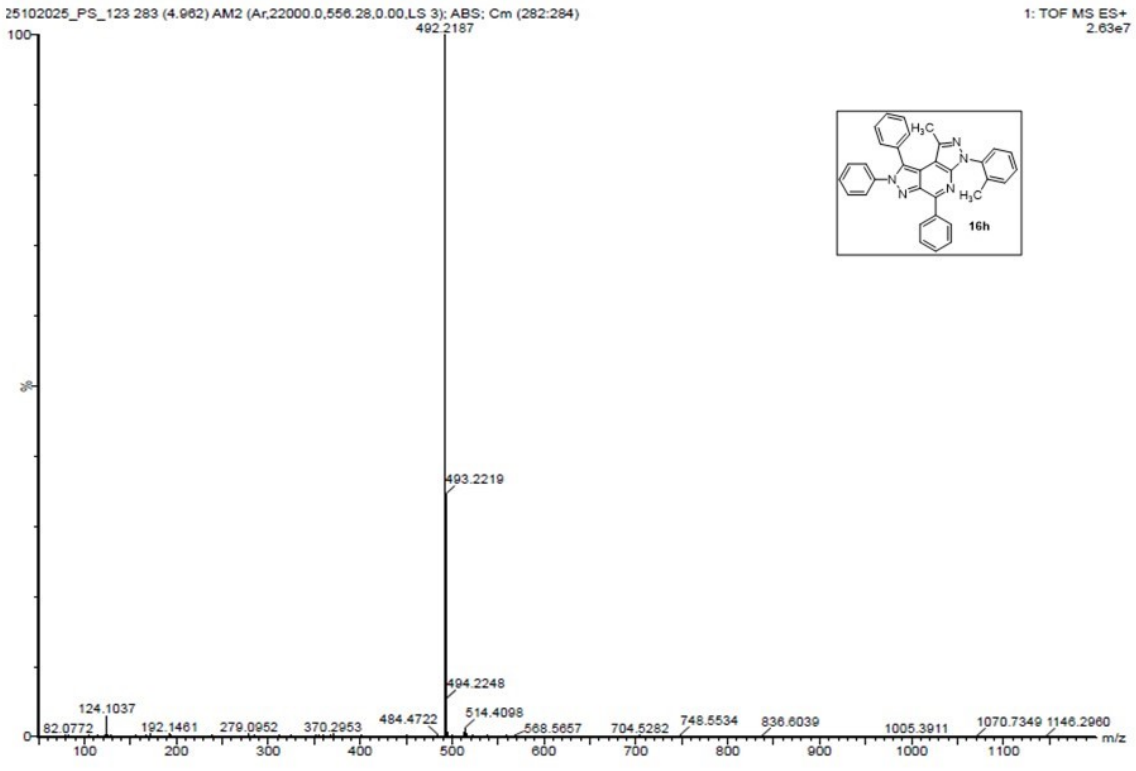
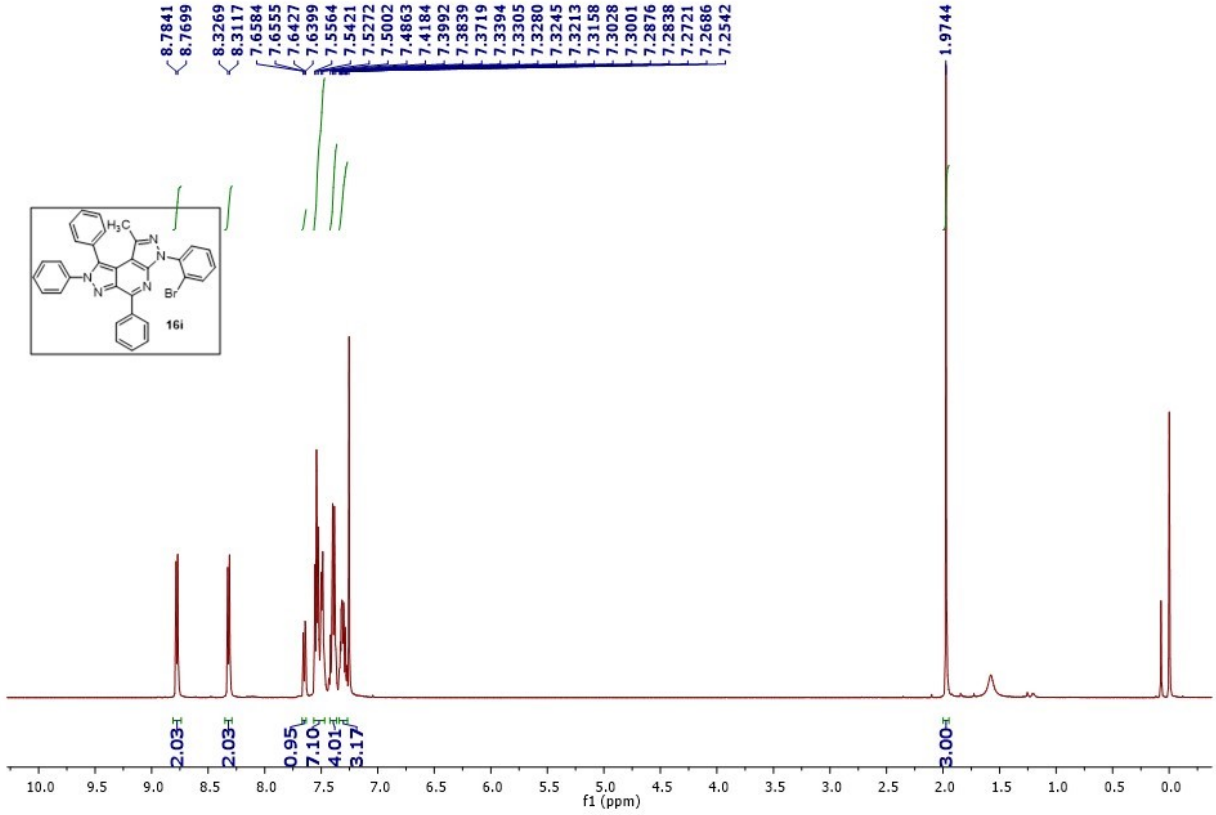


^{1}H NMR of Compound 16i



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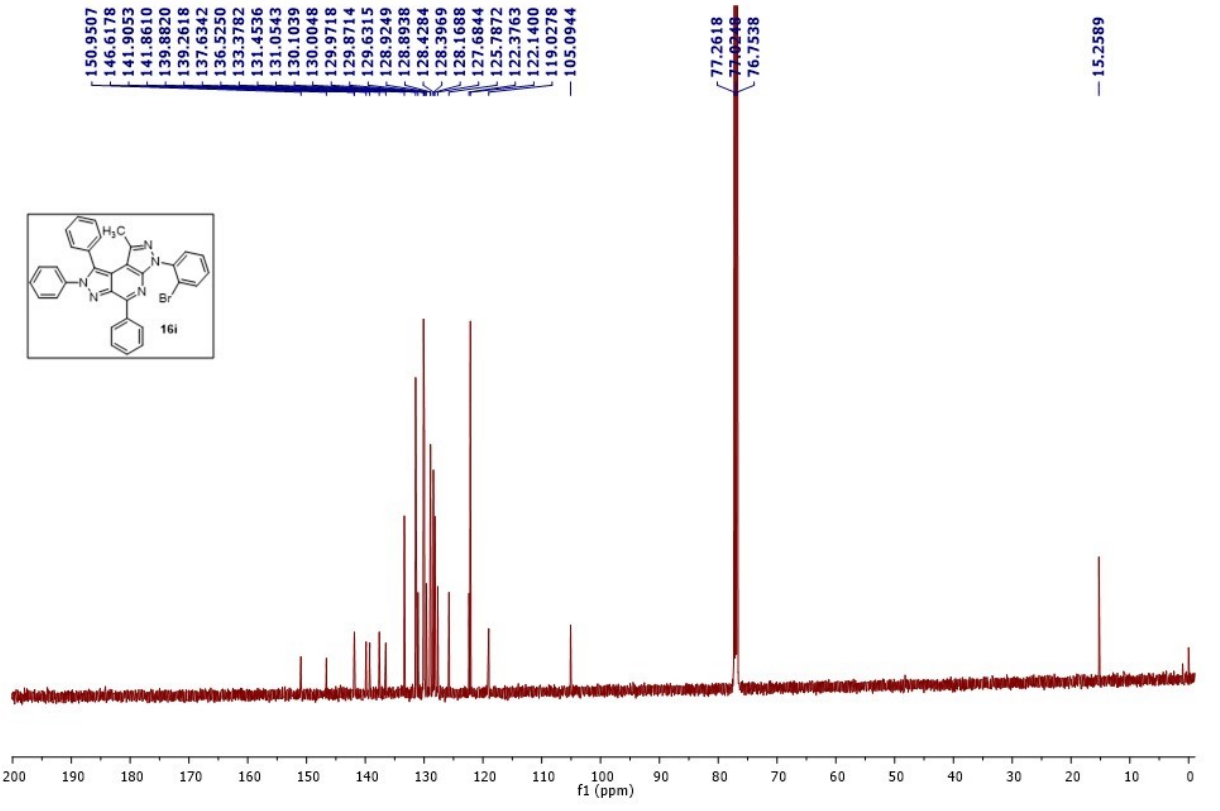

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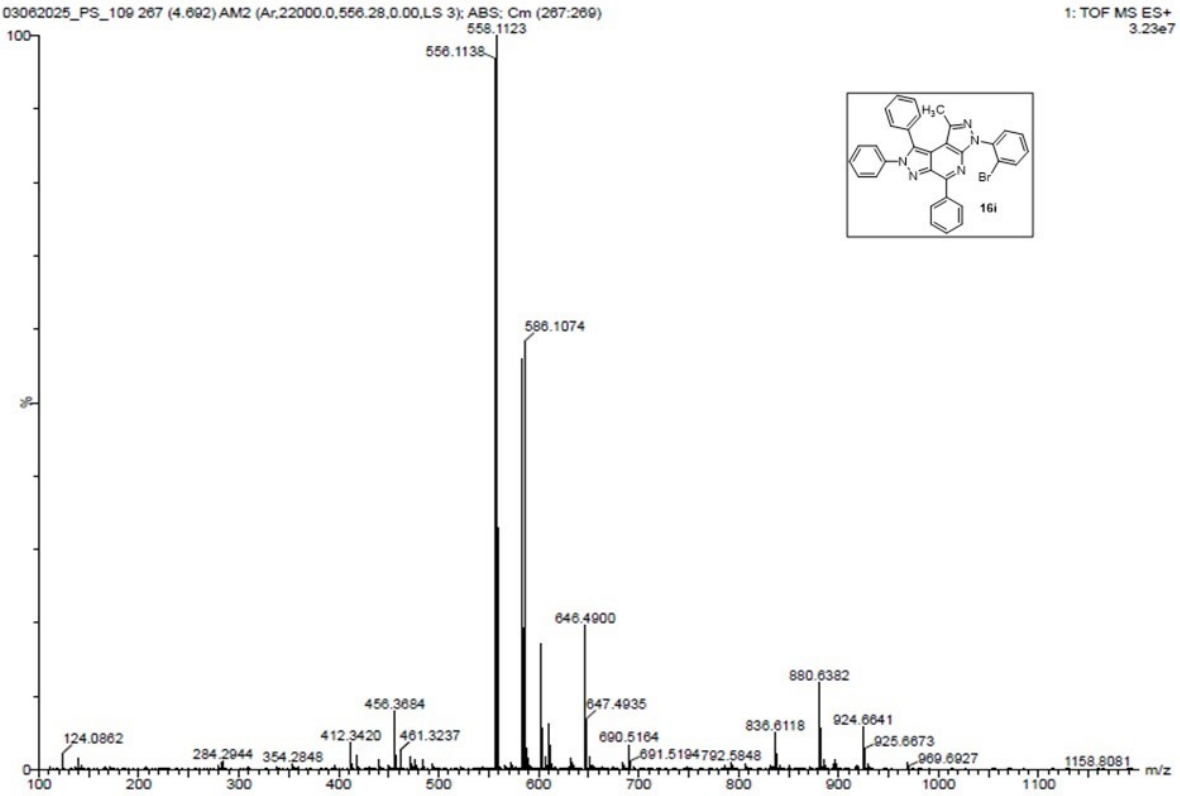
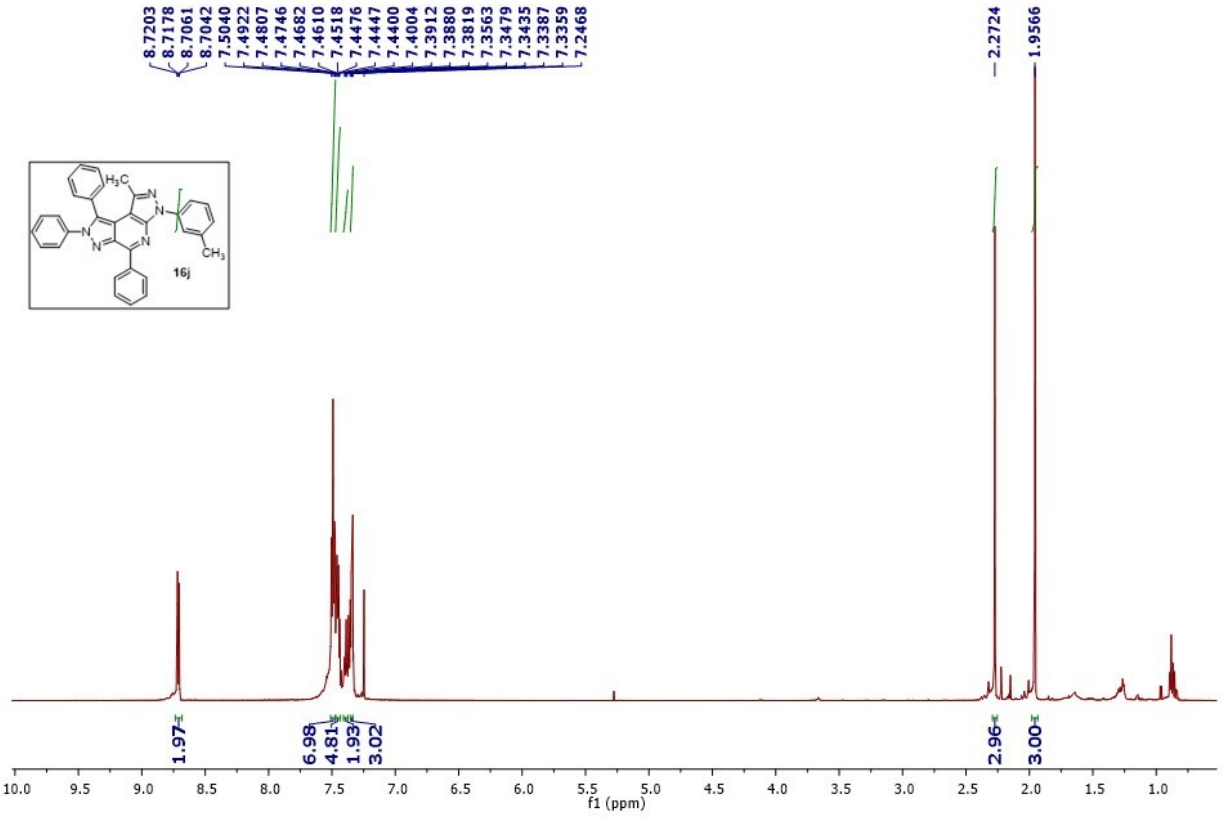


^{1}H NMR of Compound 16j



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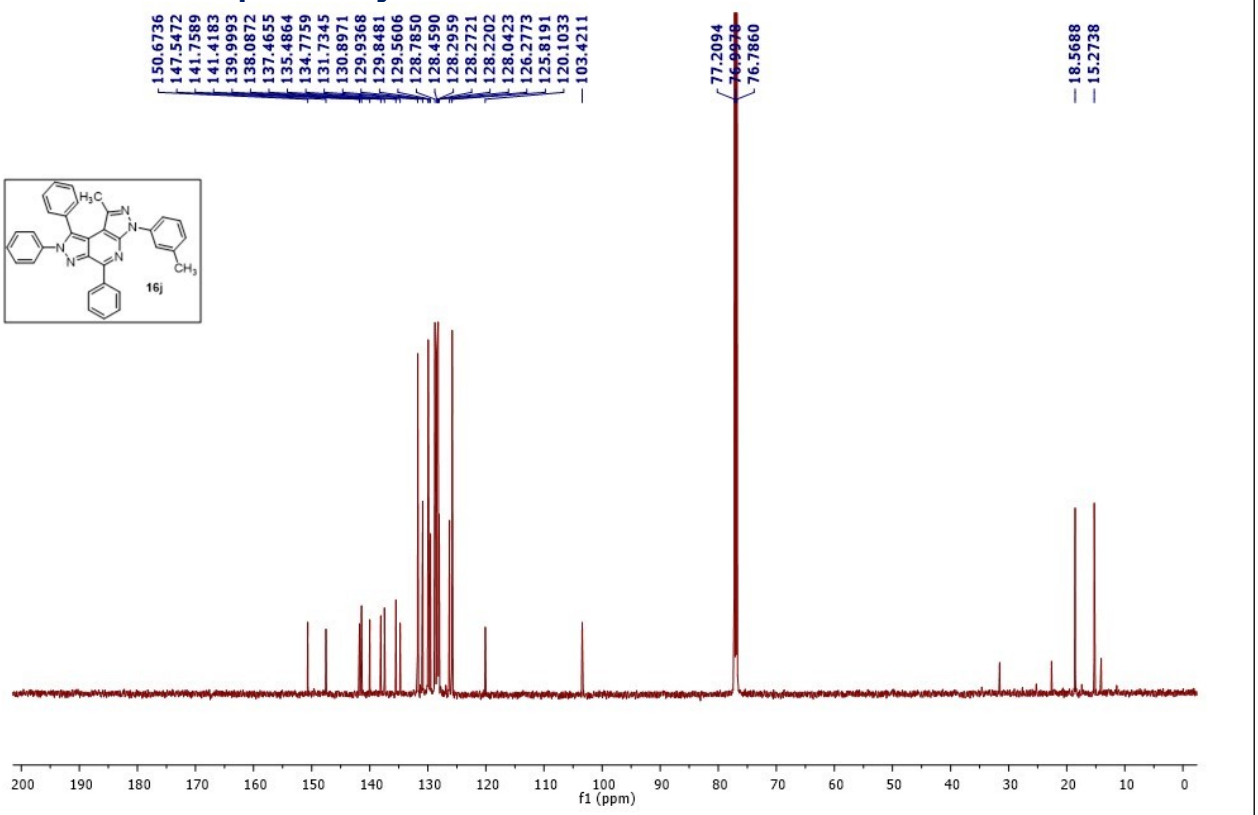

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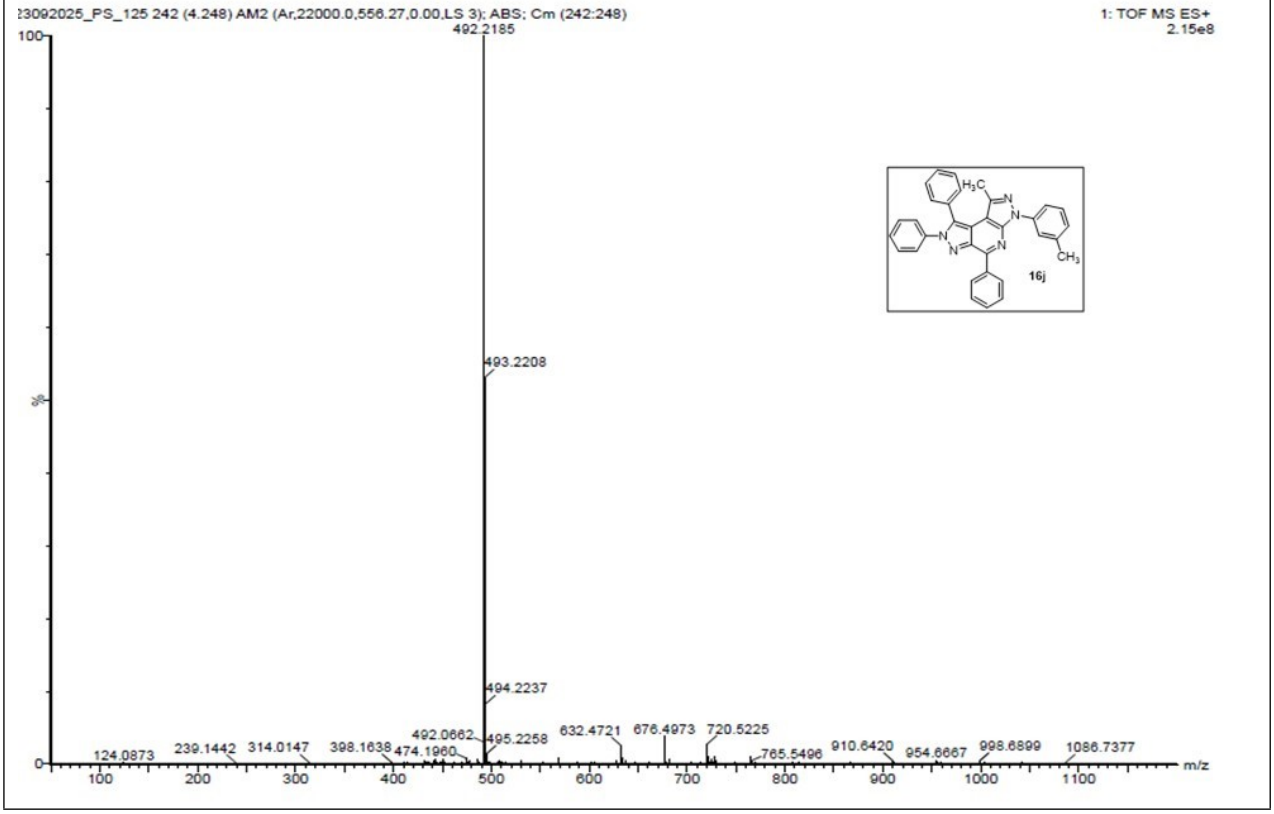
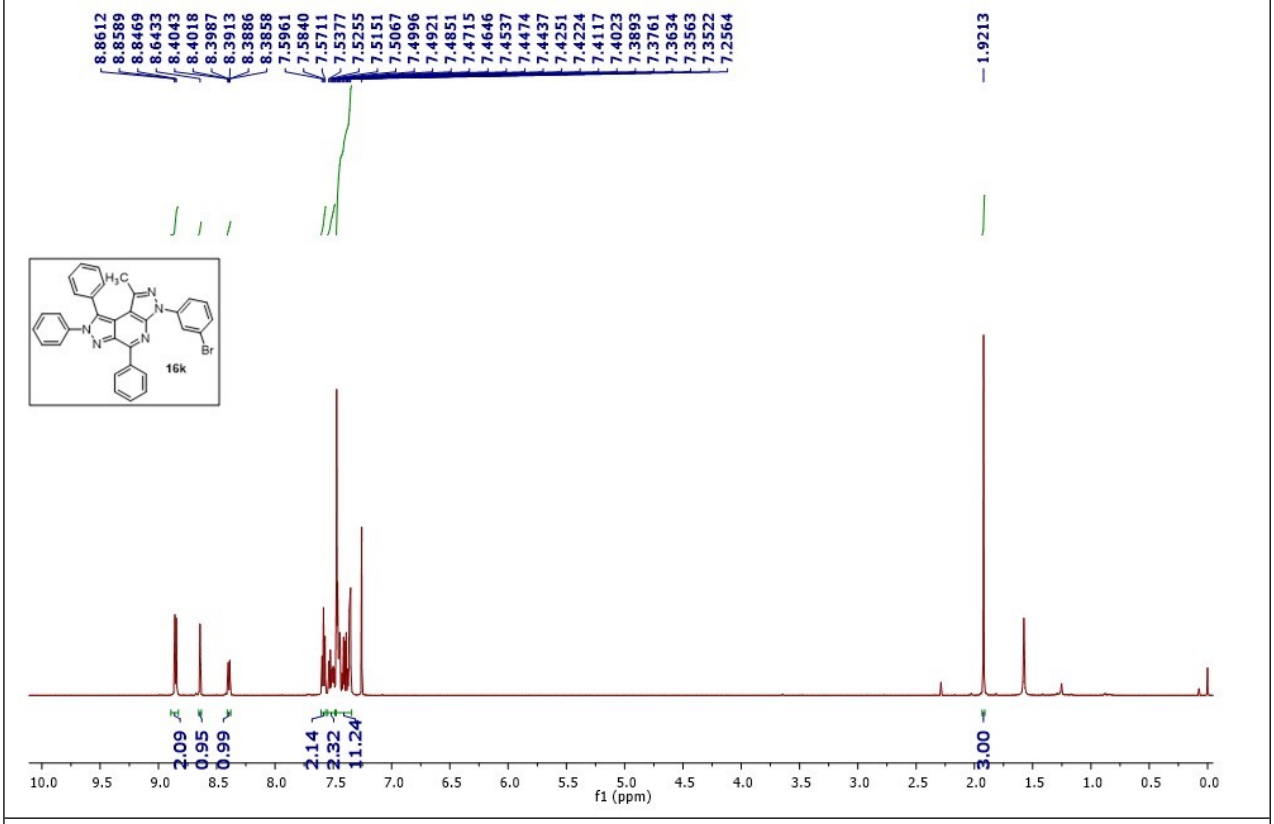


^{1}H NMR of Compound 16k



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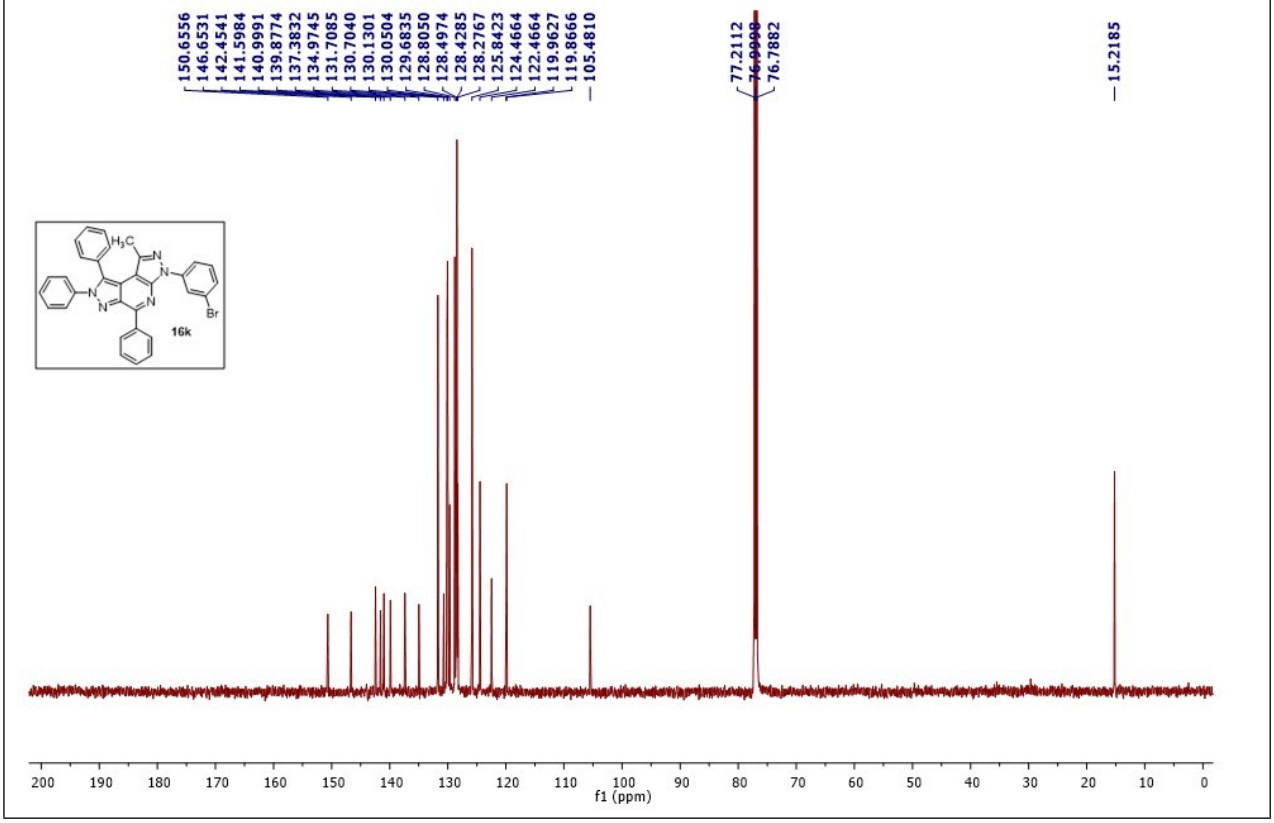

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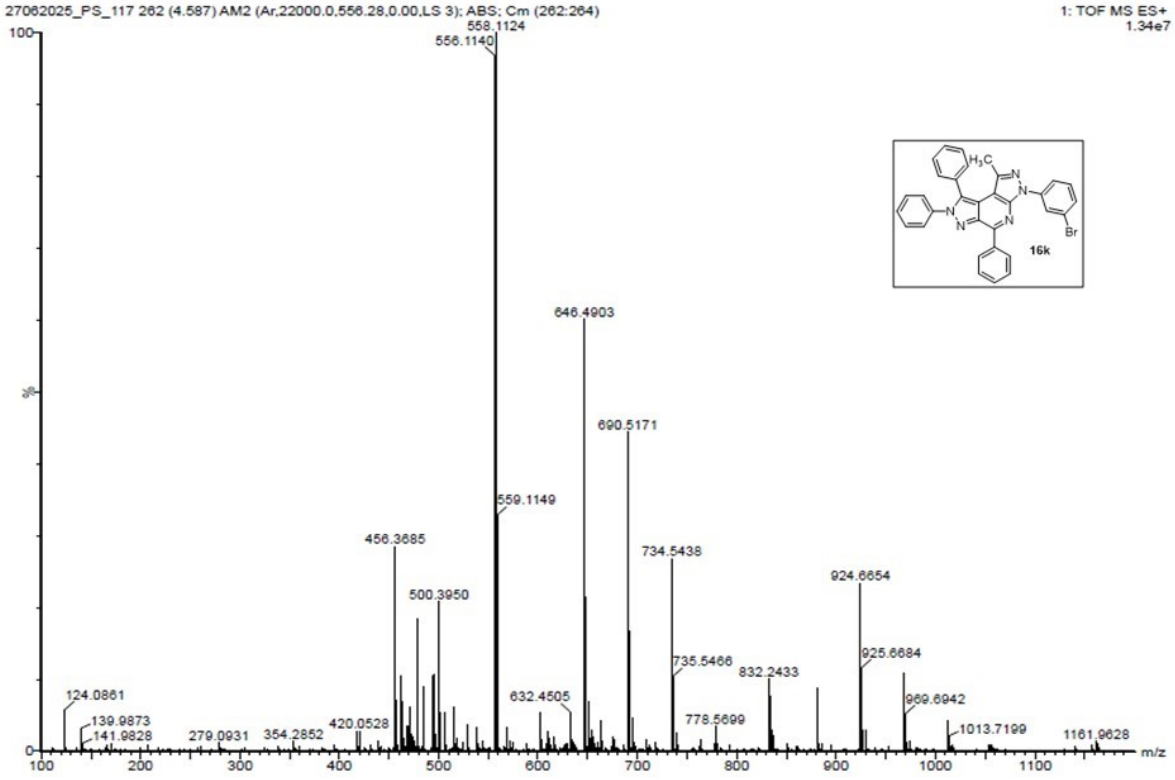
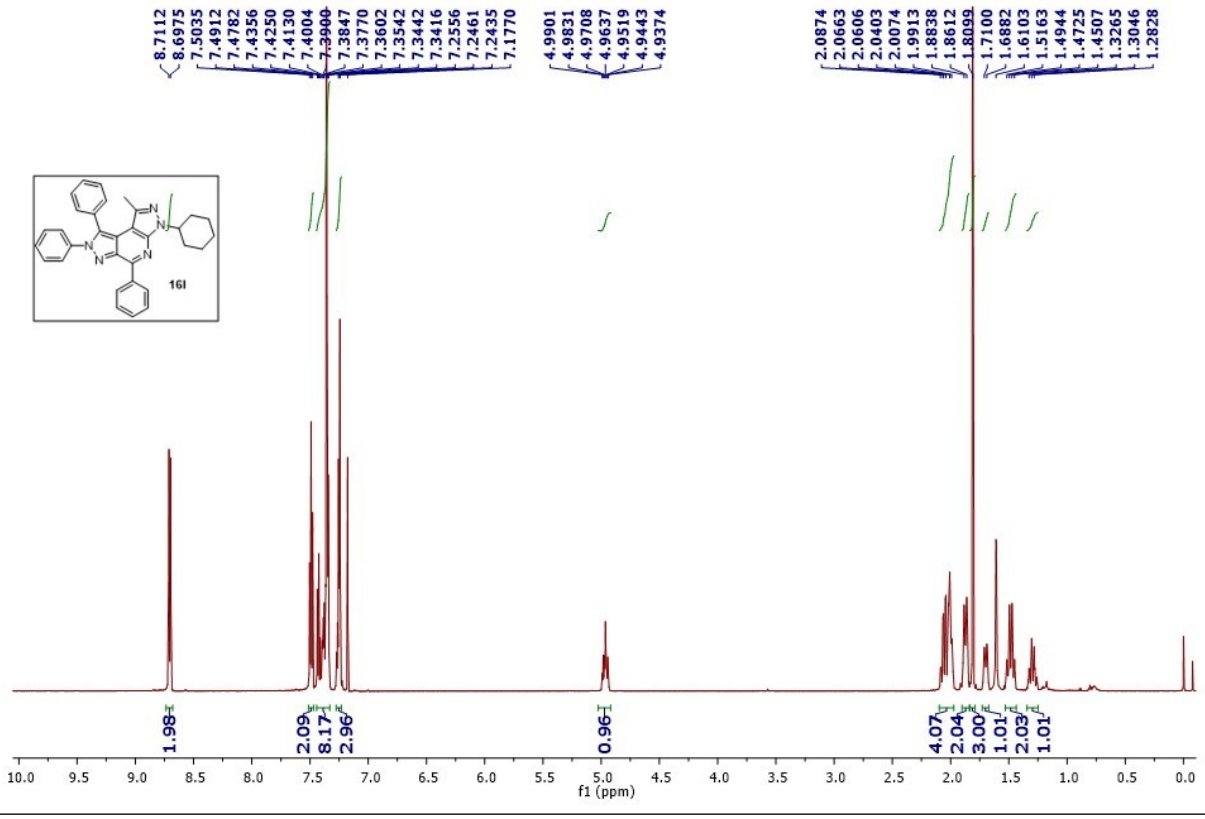


^{1}H NMR of Compound 16l



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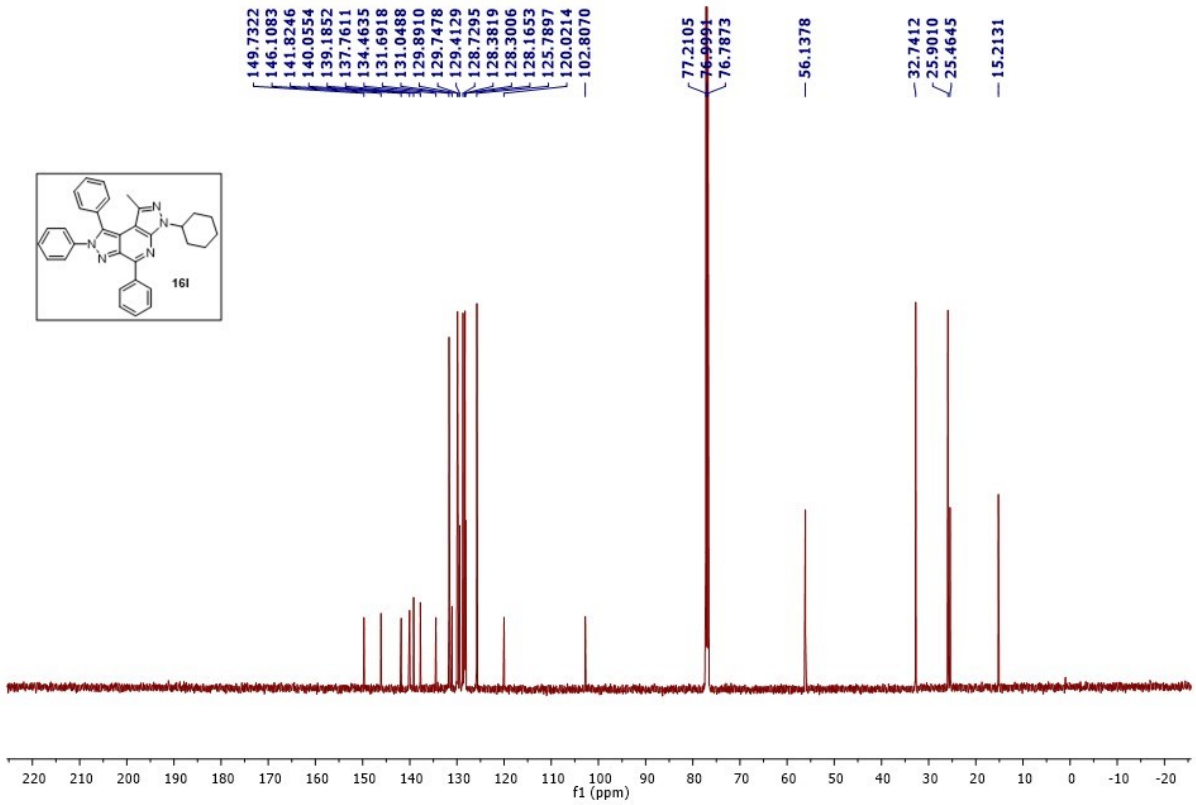

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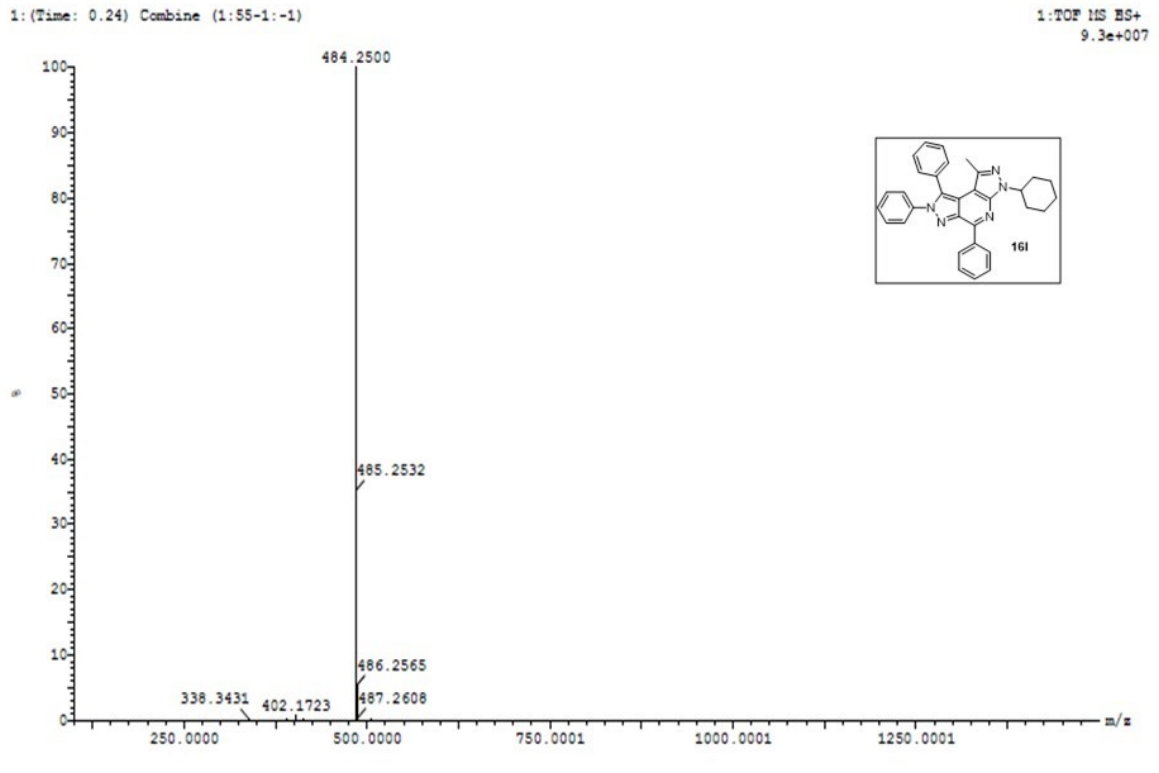
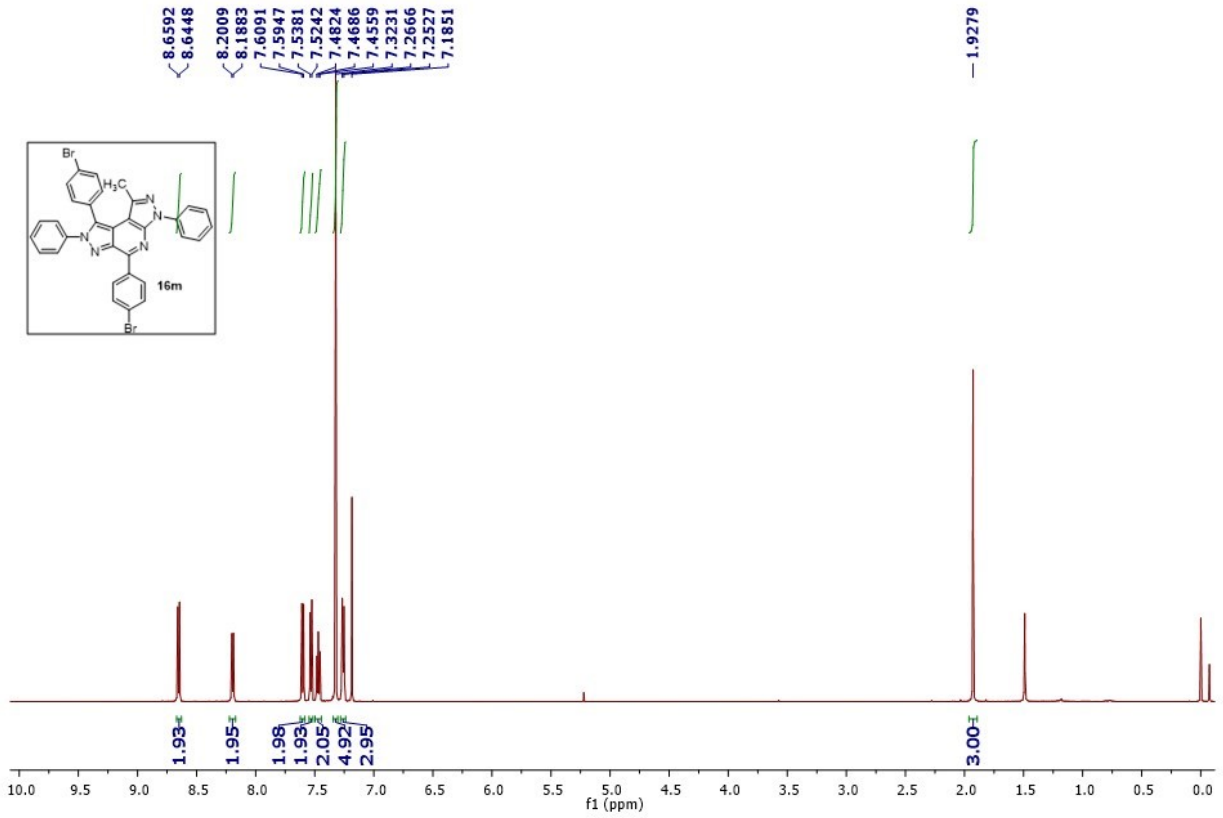
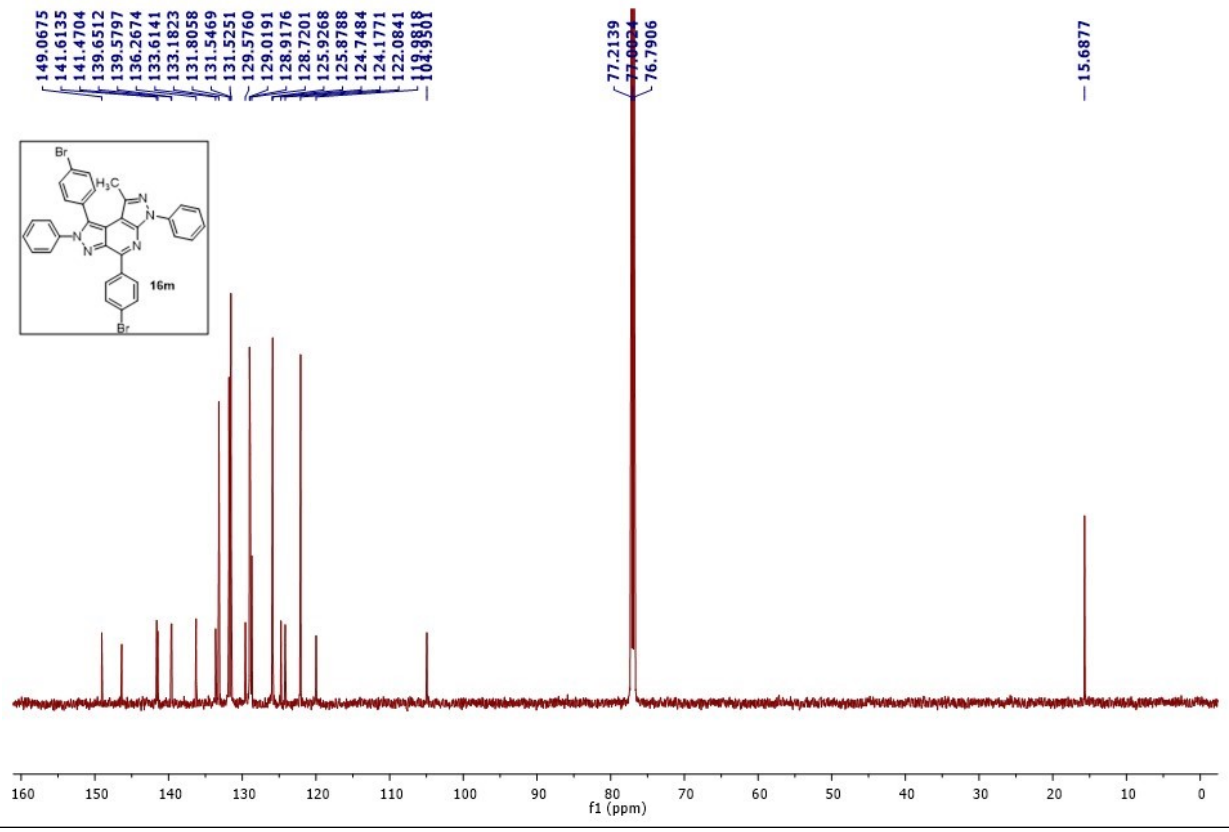


^{1}H NMR of Compound 16m



^{13}C NMR of Compound 16m



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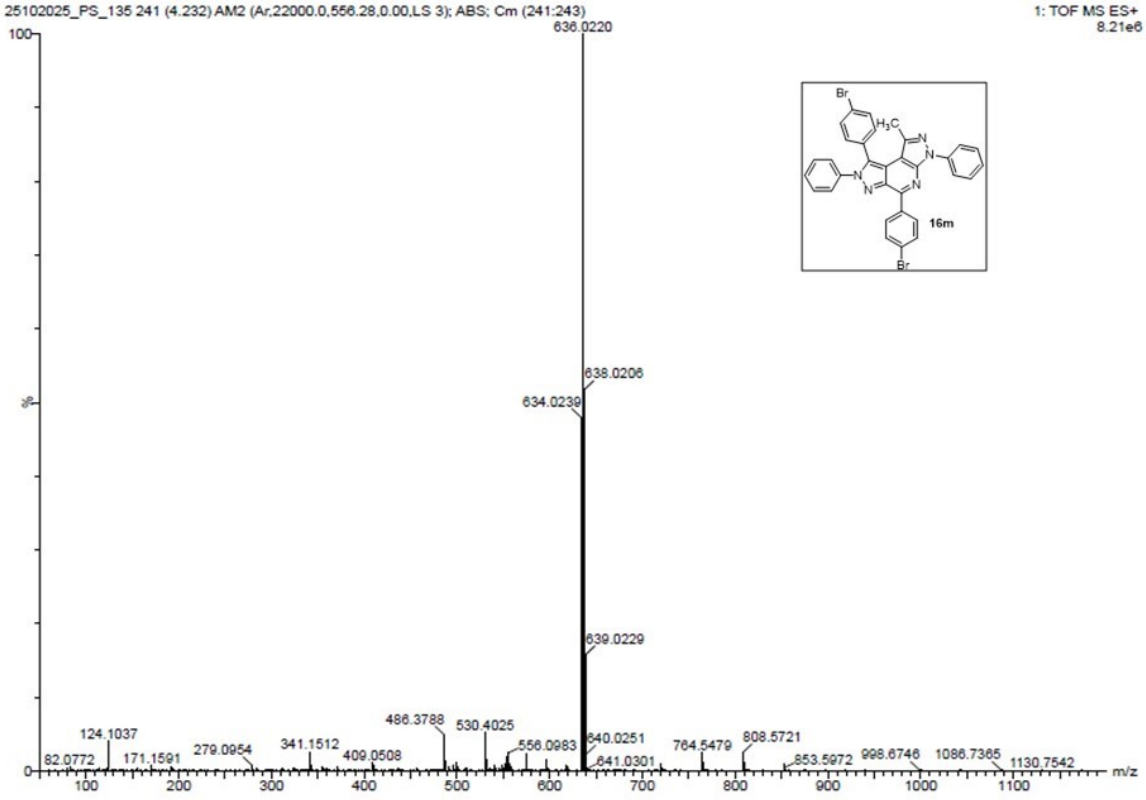

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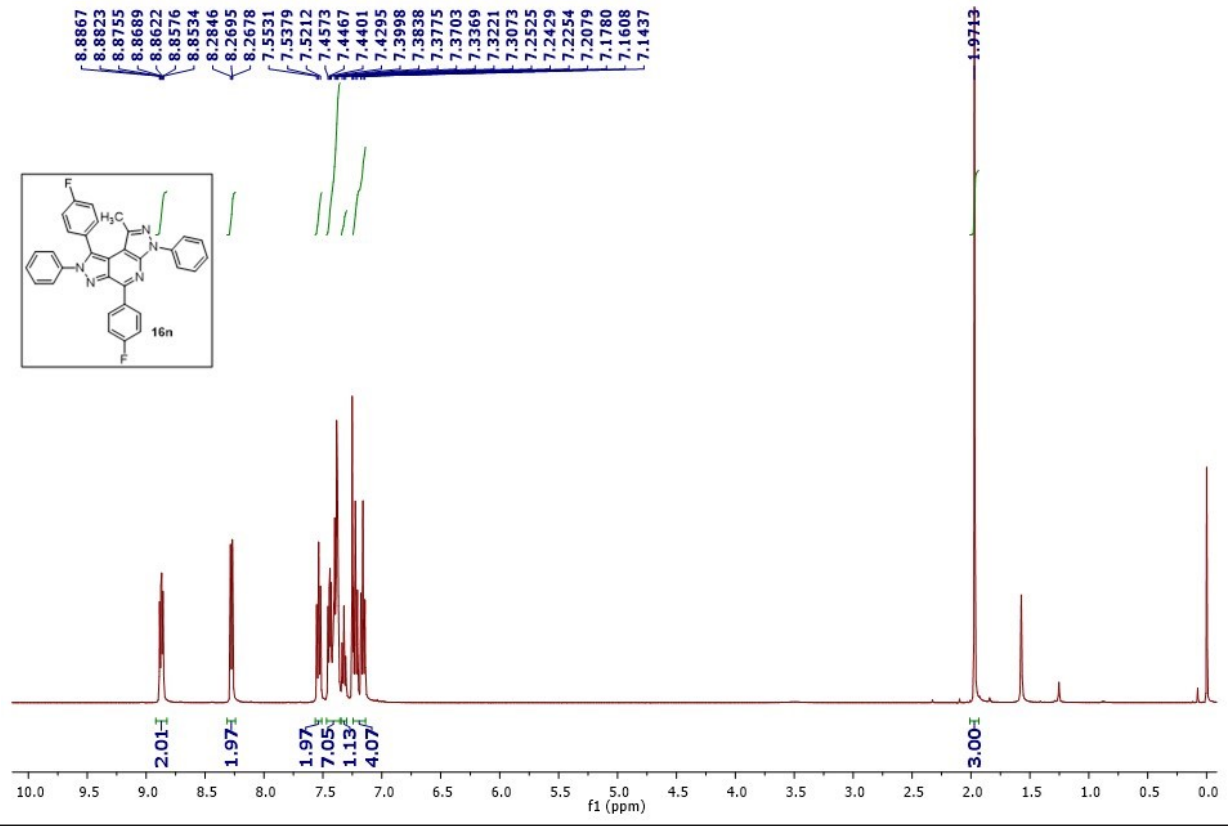

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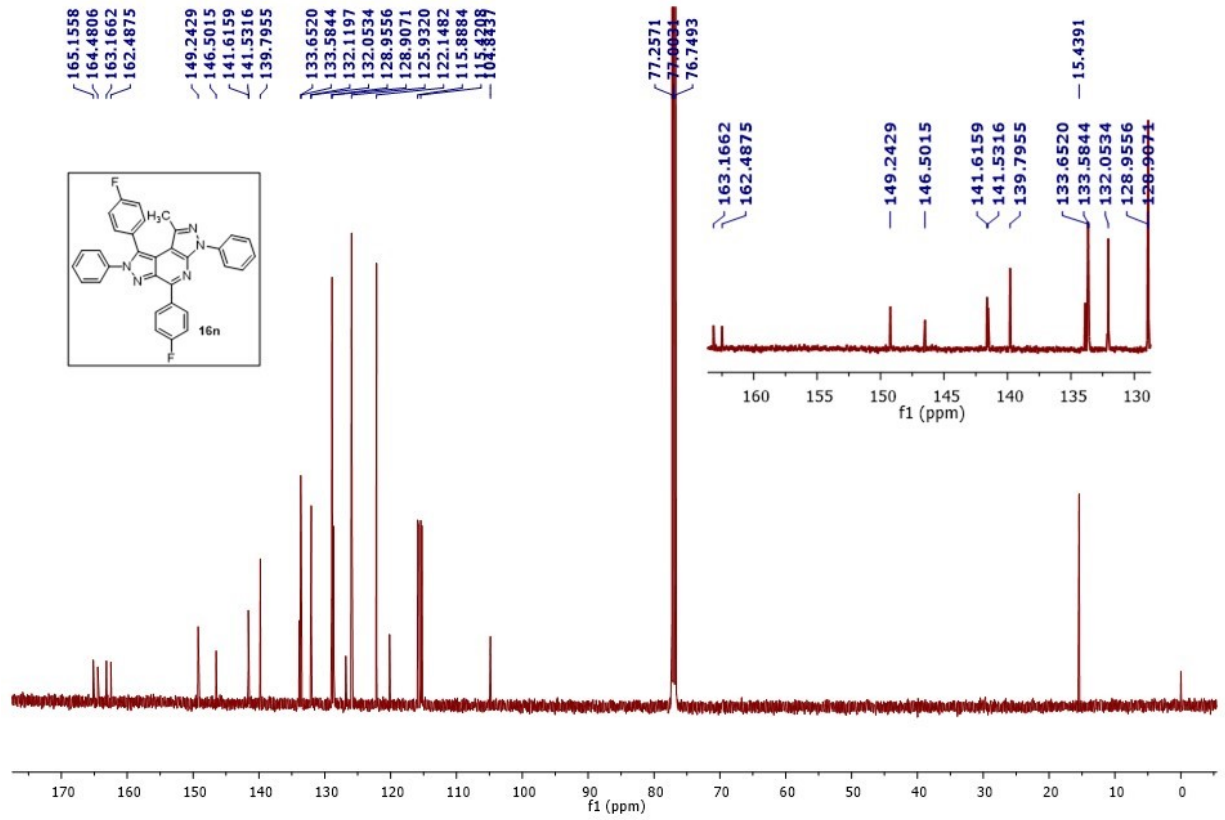

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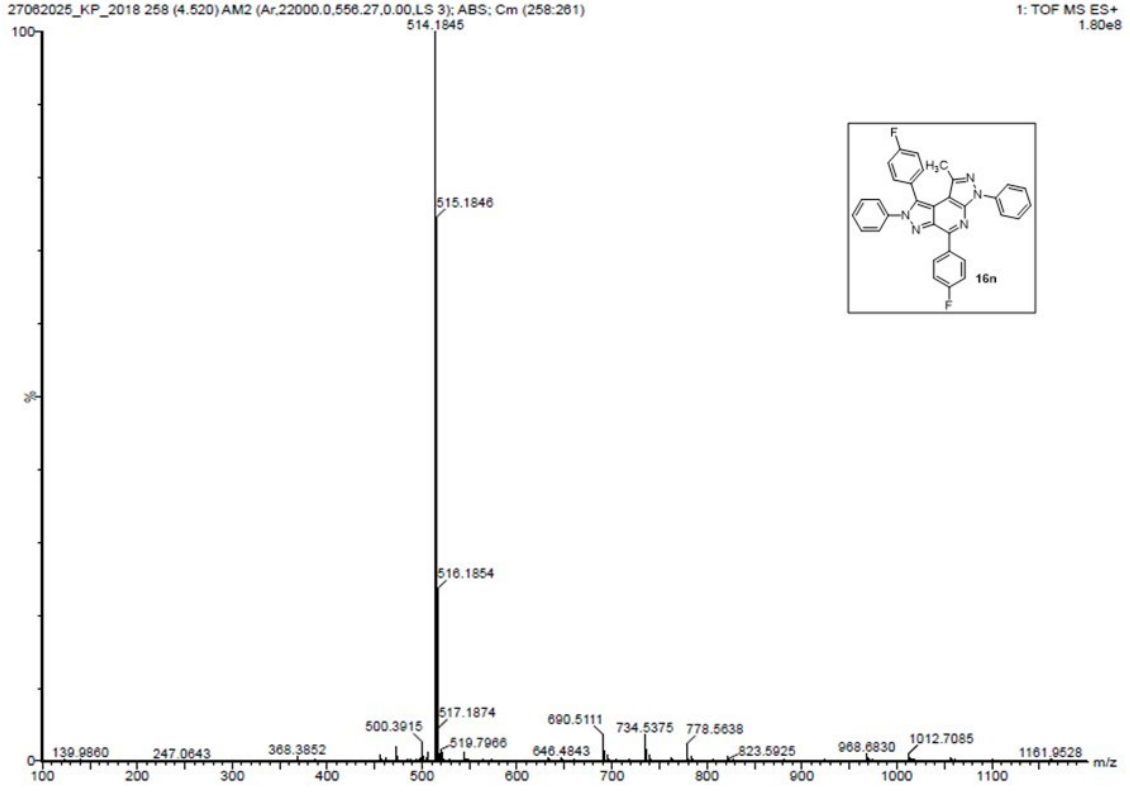

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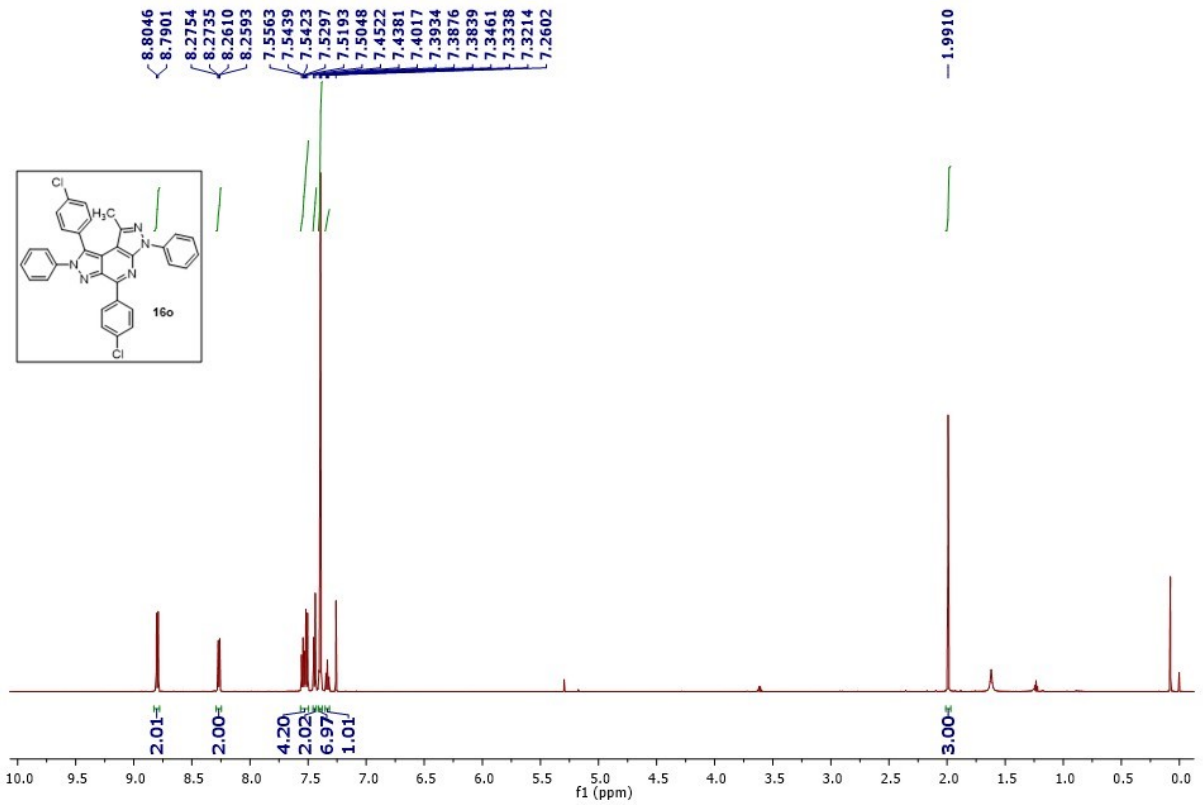

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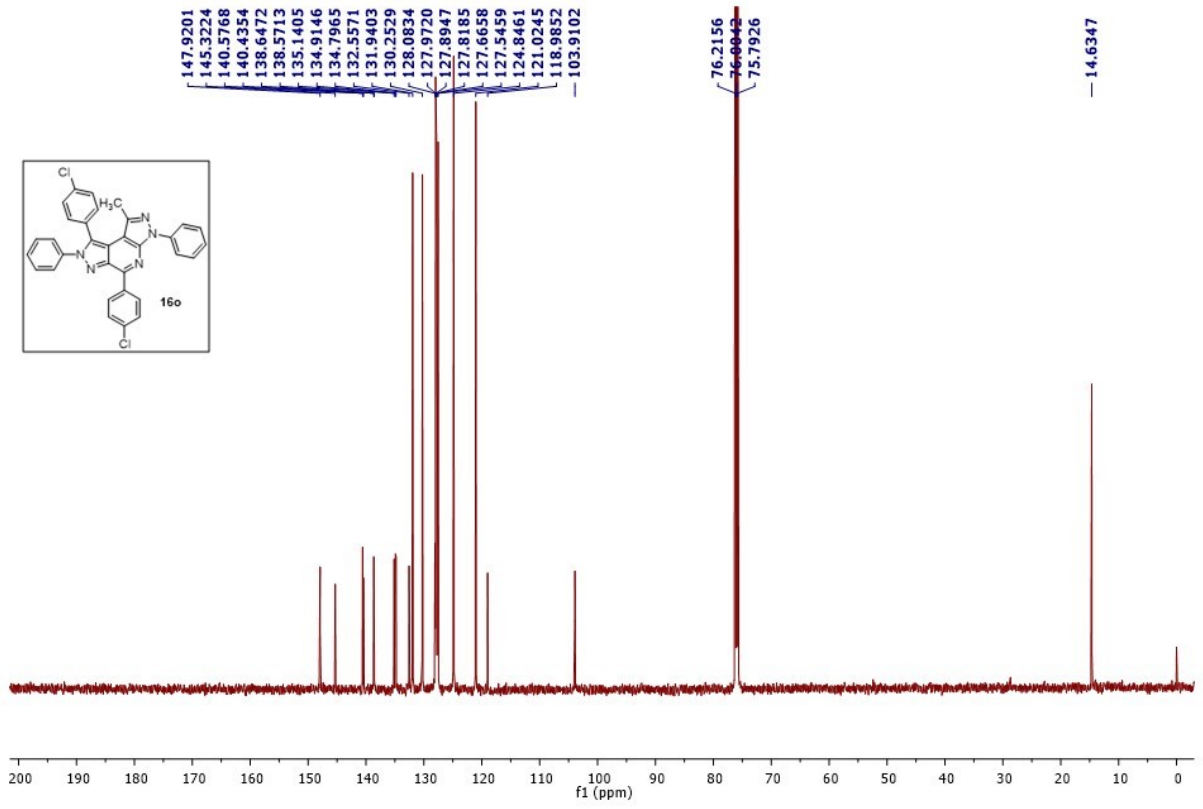

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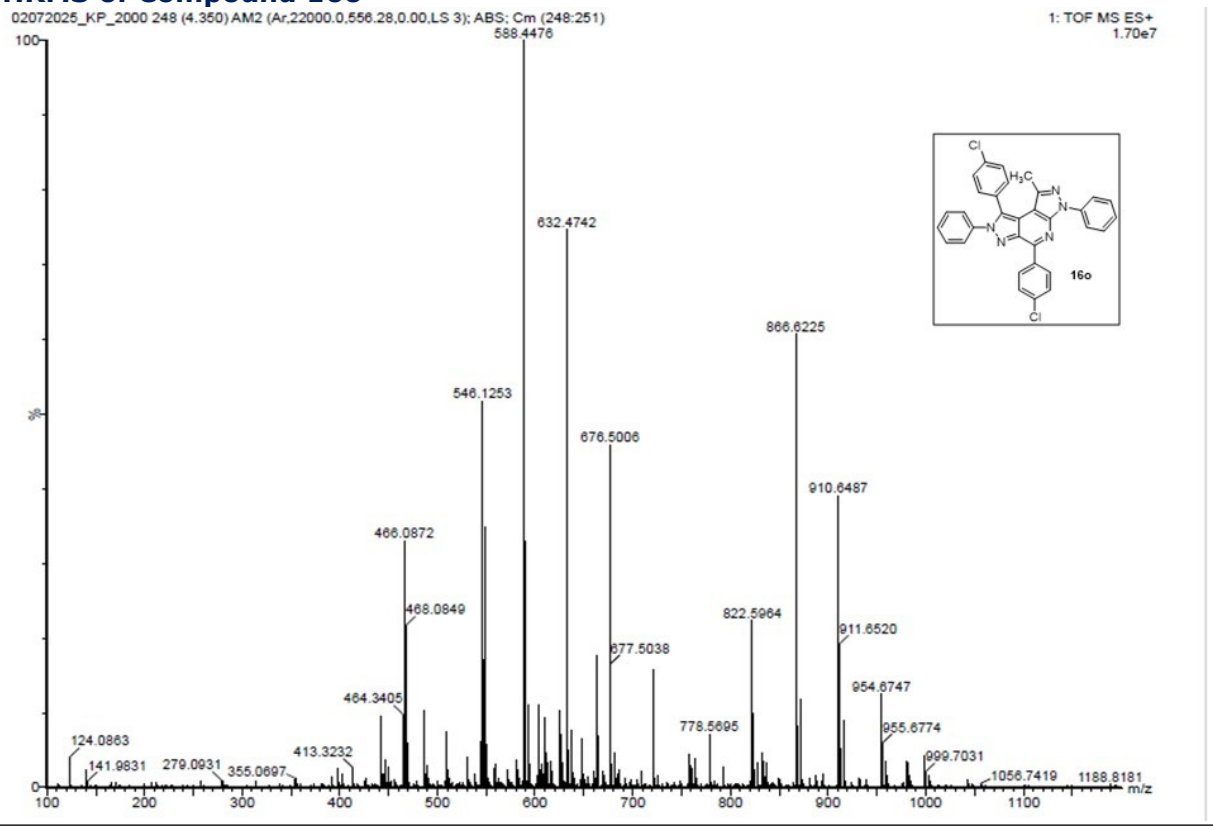
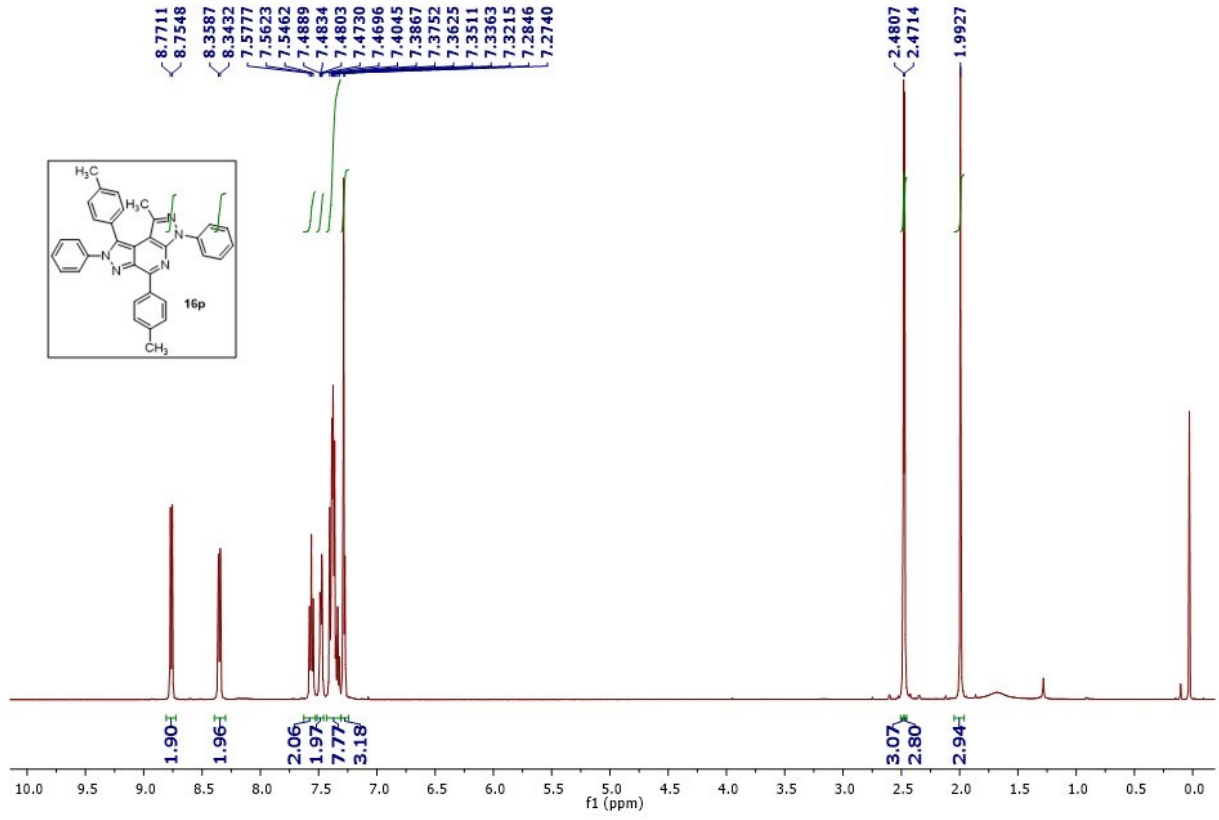
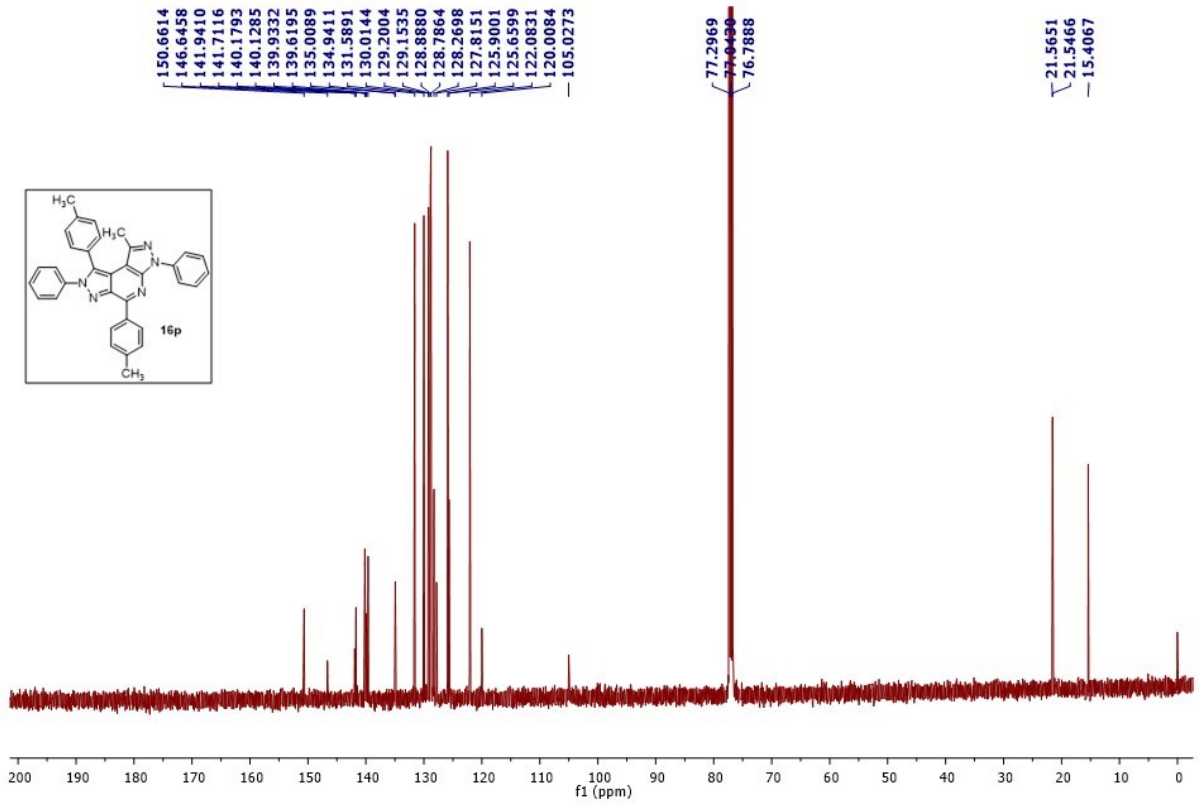


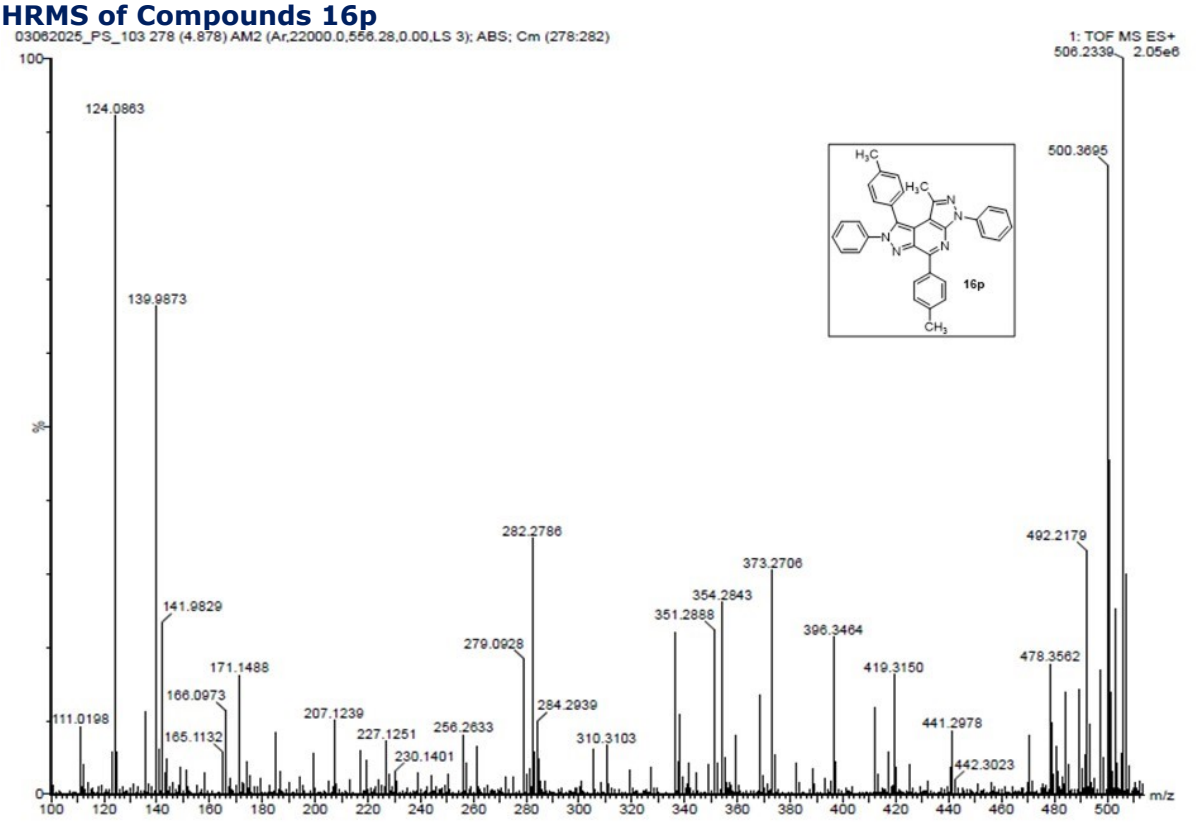
^{1}H NMR of Compound 16p



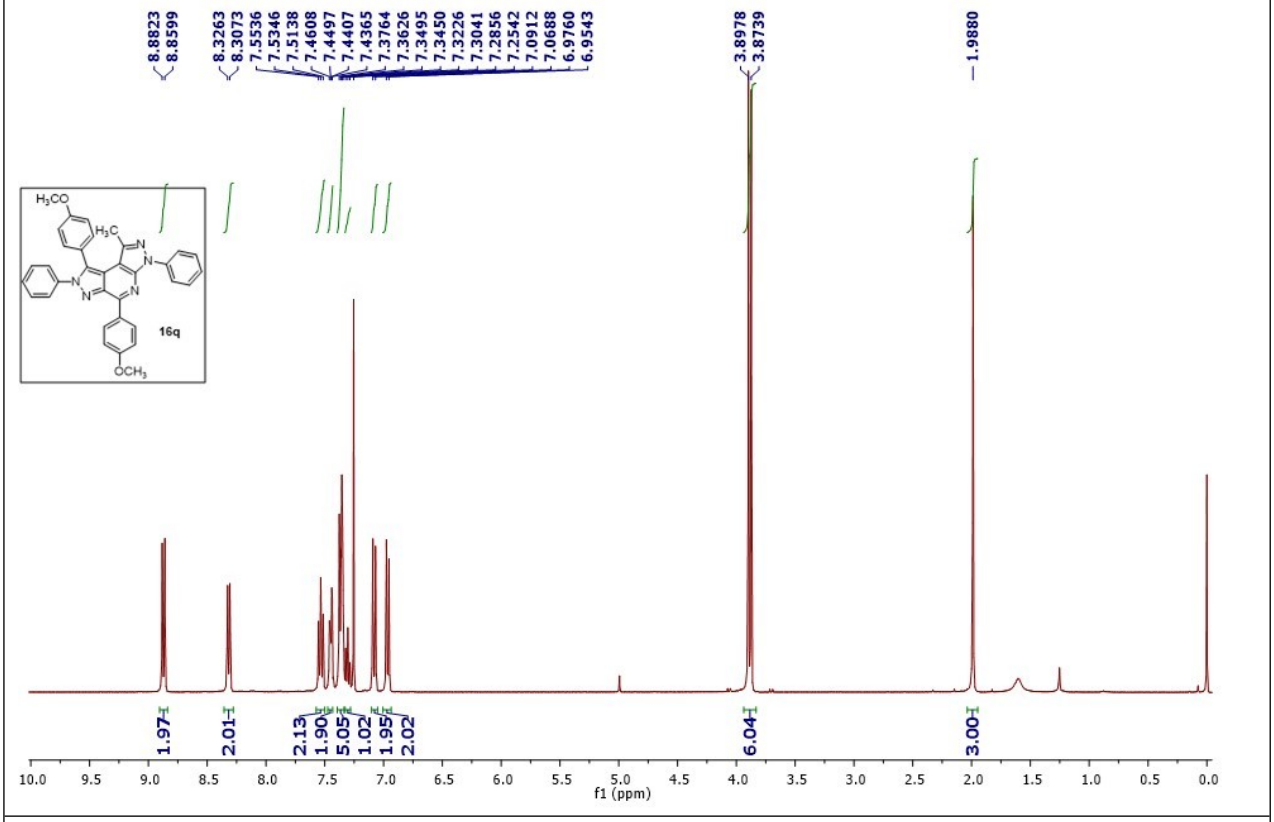
^{13}C NMR of Compound 16p



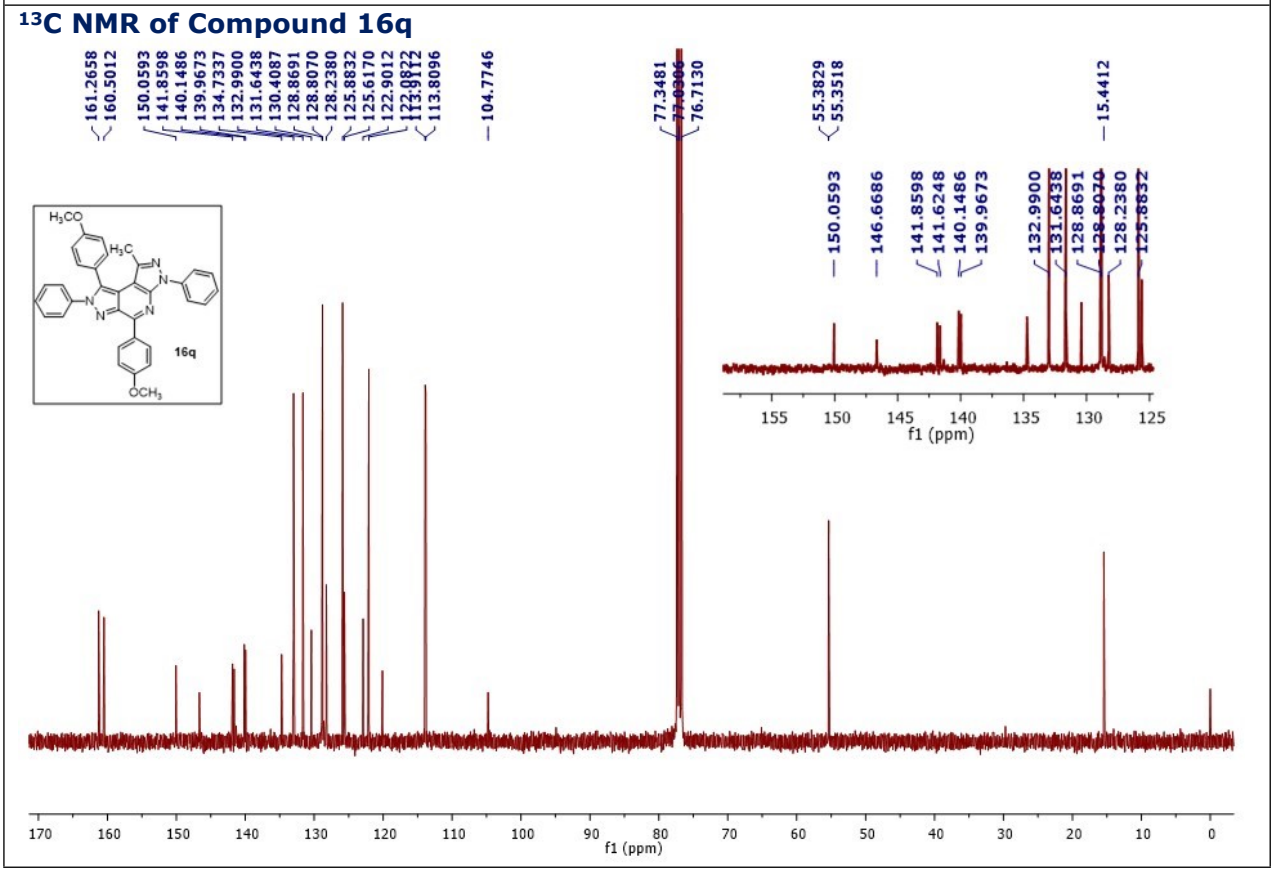
HRMS of Compounds 16p



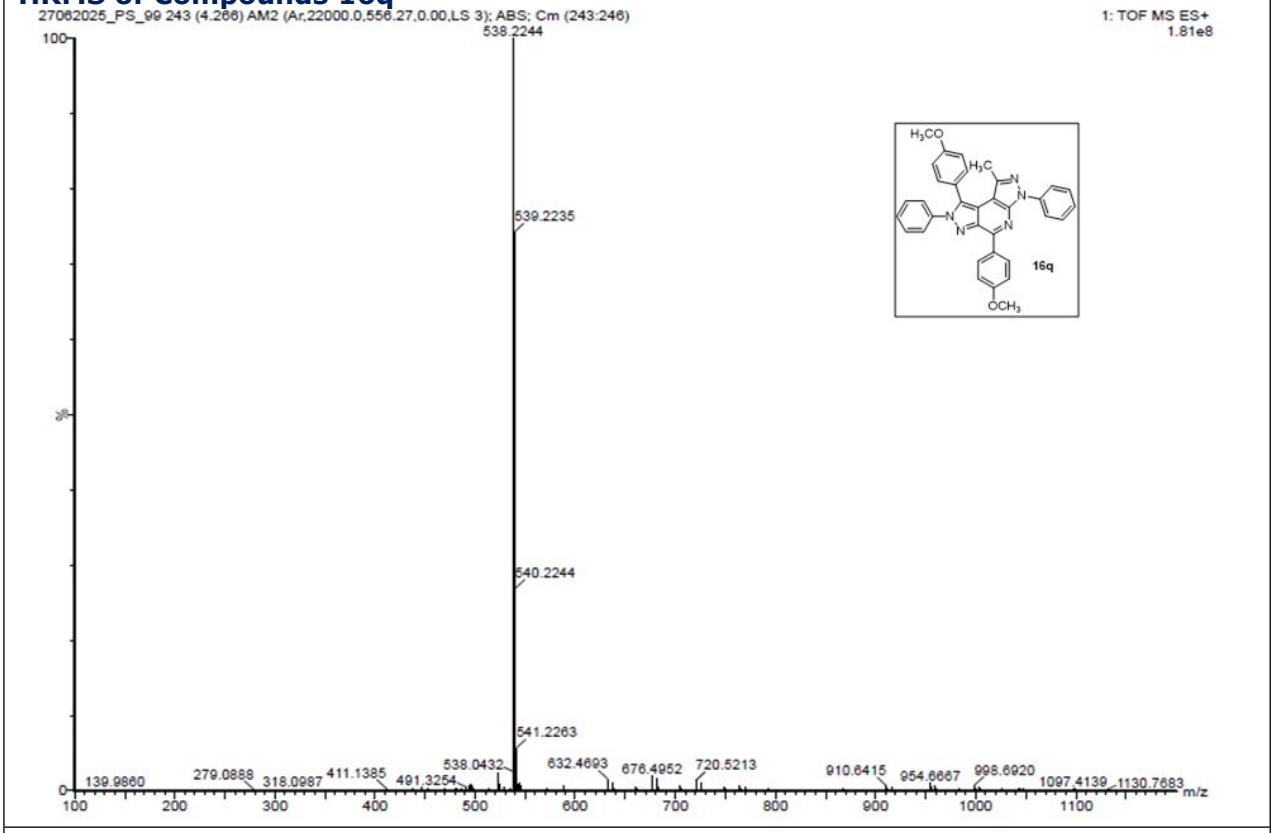
^{1}H NMR of Compound 16q



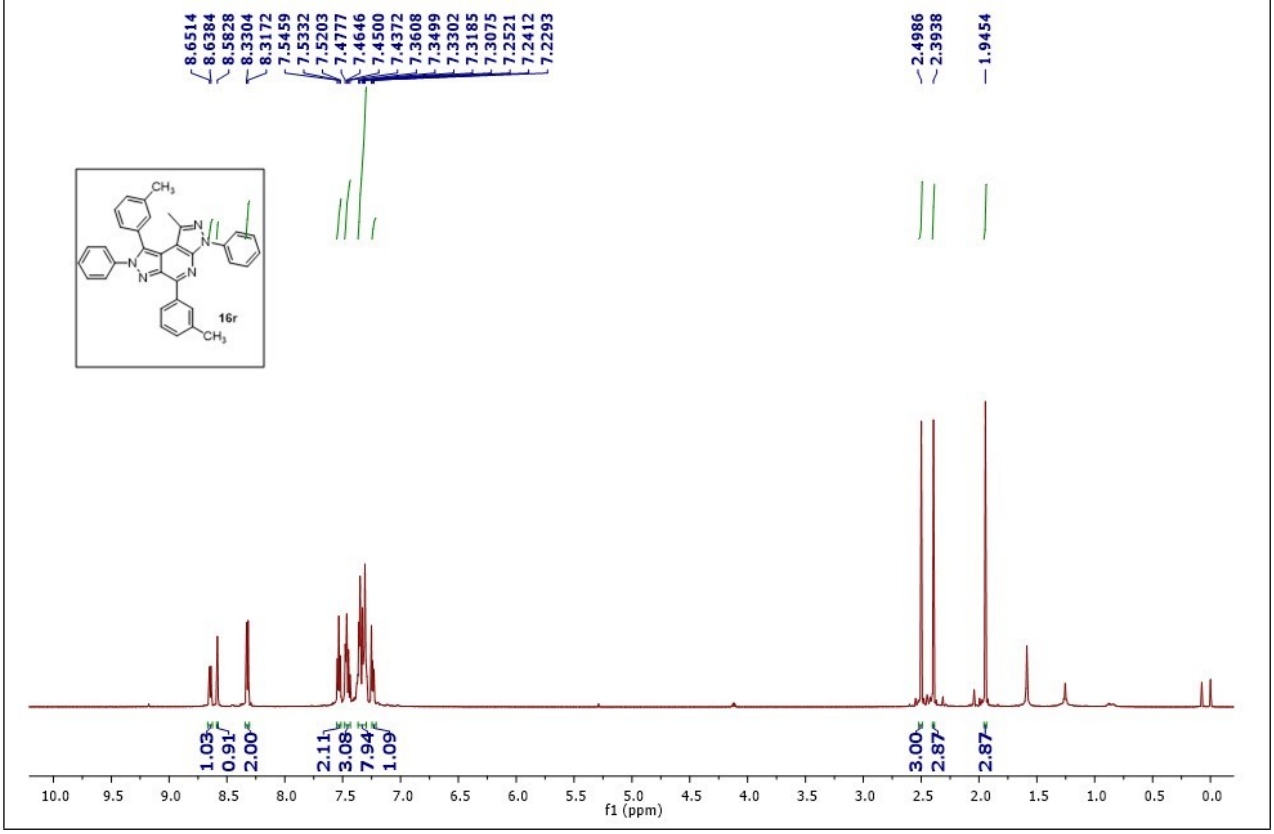
^{13}C NMR of Compound 16q



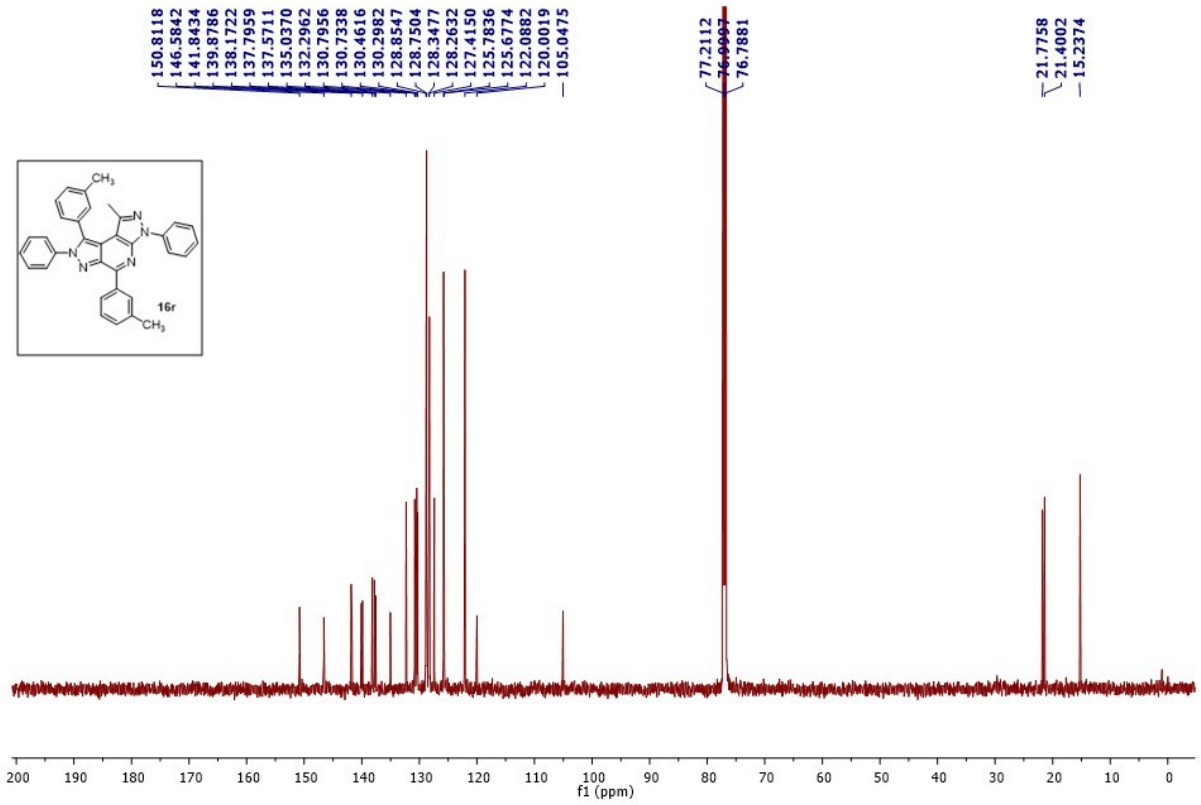
HRMS of Compounds 16q



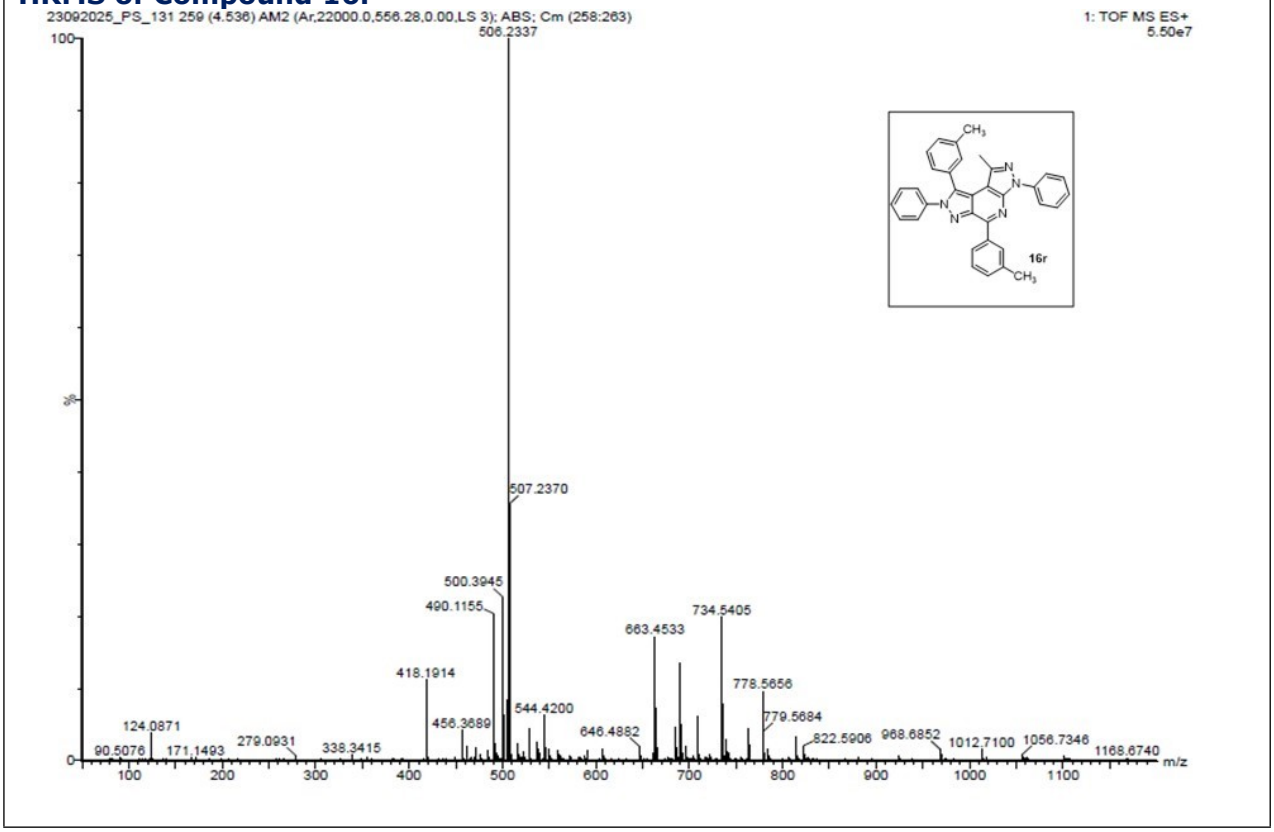
^{1}H NMR of Compound 16r



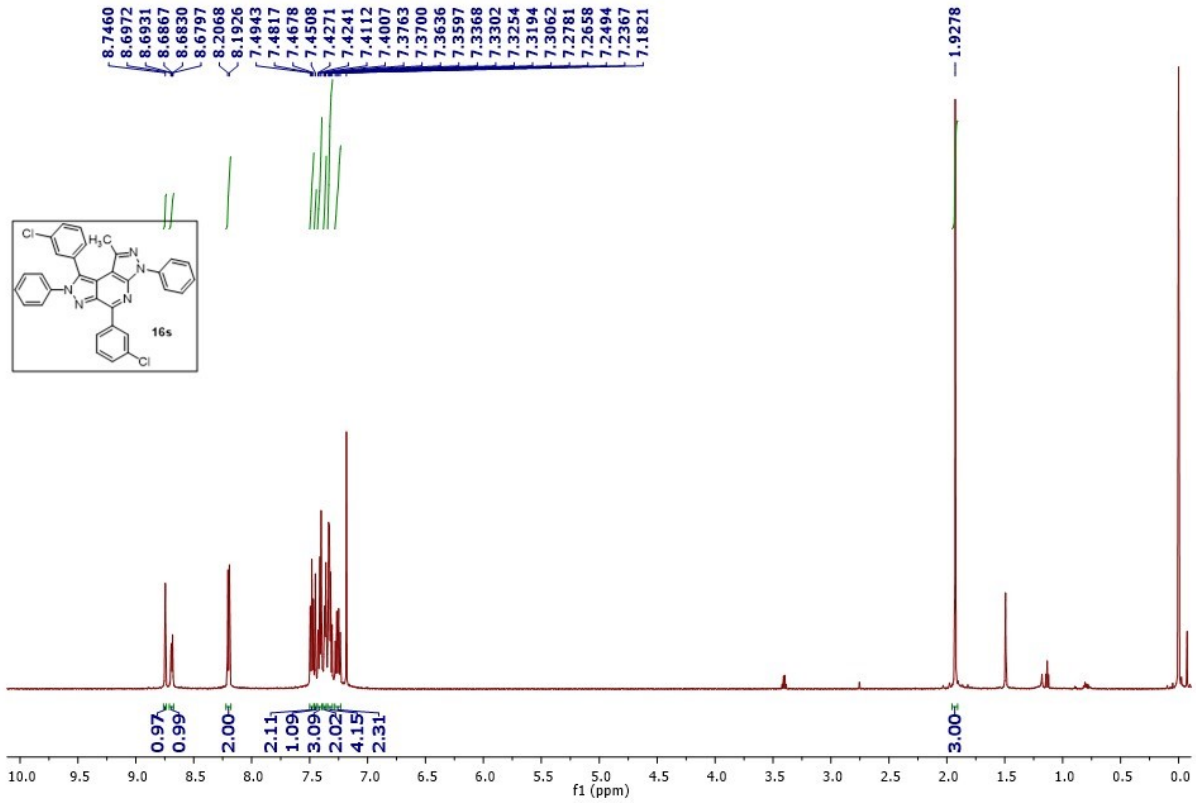
^{13}C NMR of Compound 16r



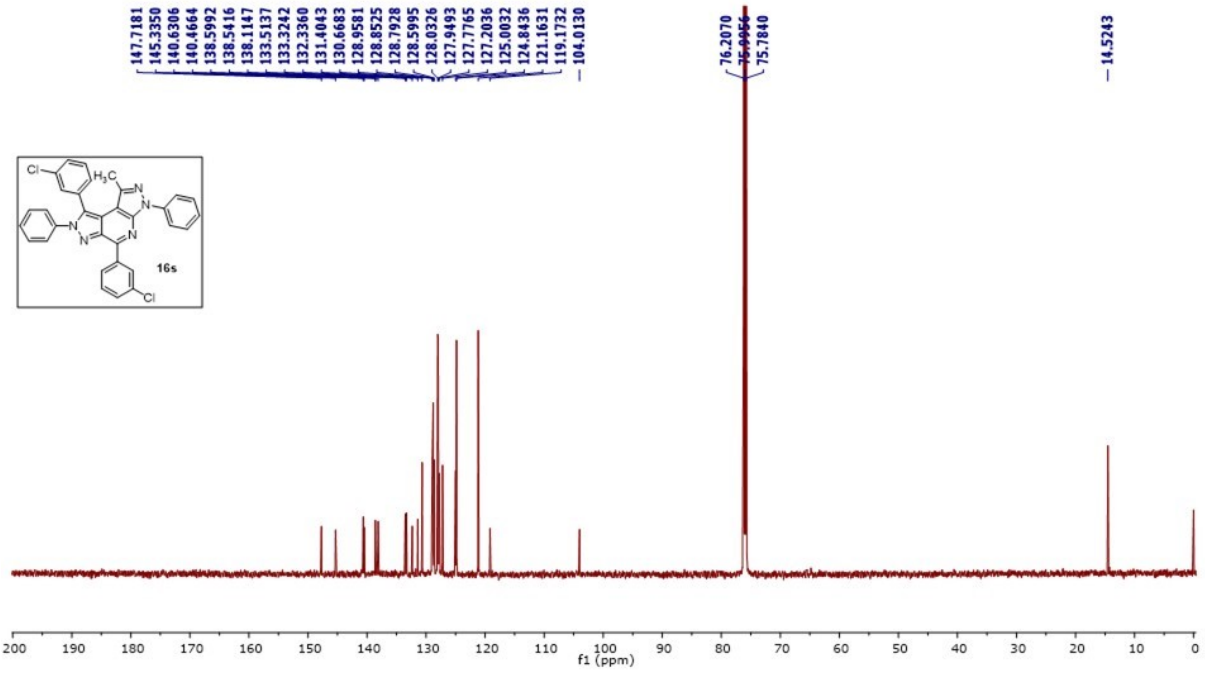
HRMS of Compound 16r



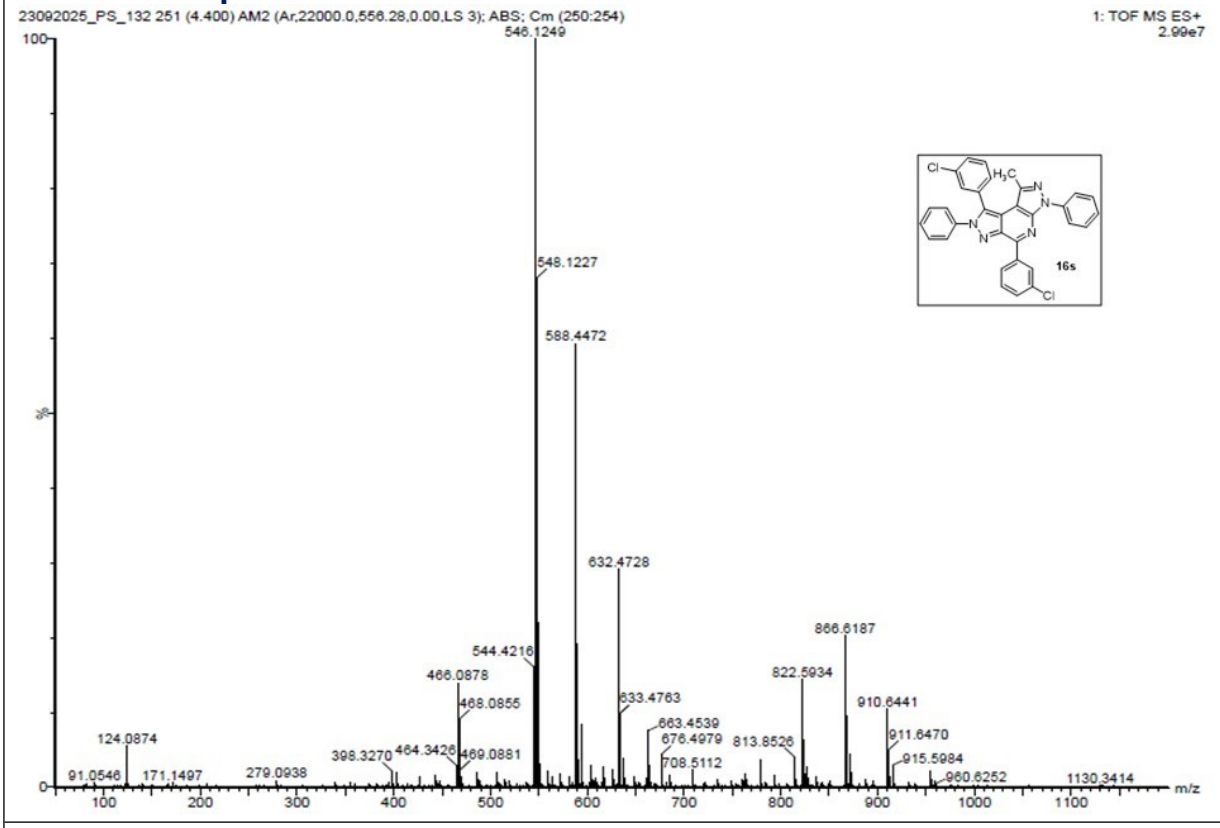
^{1}H NMR of Compound 16s



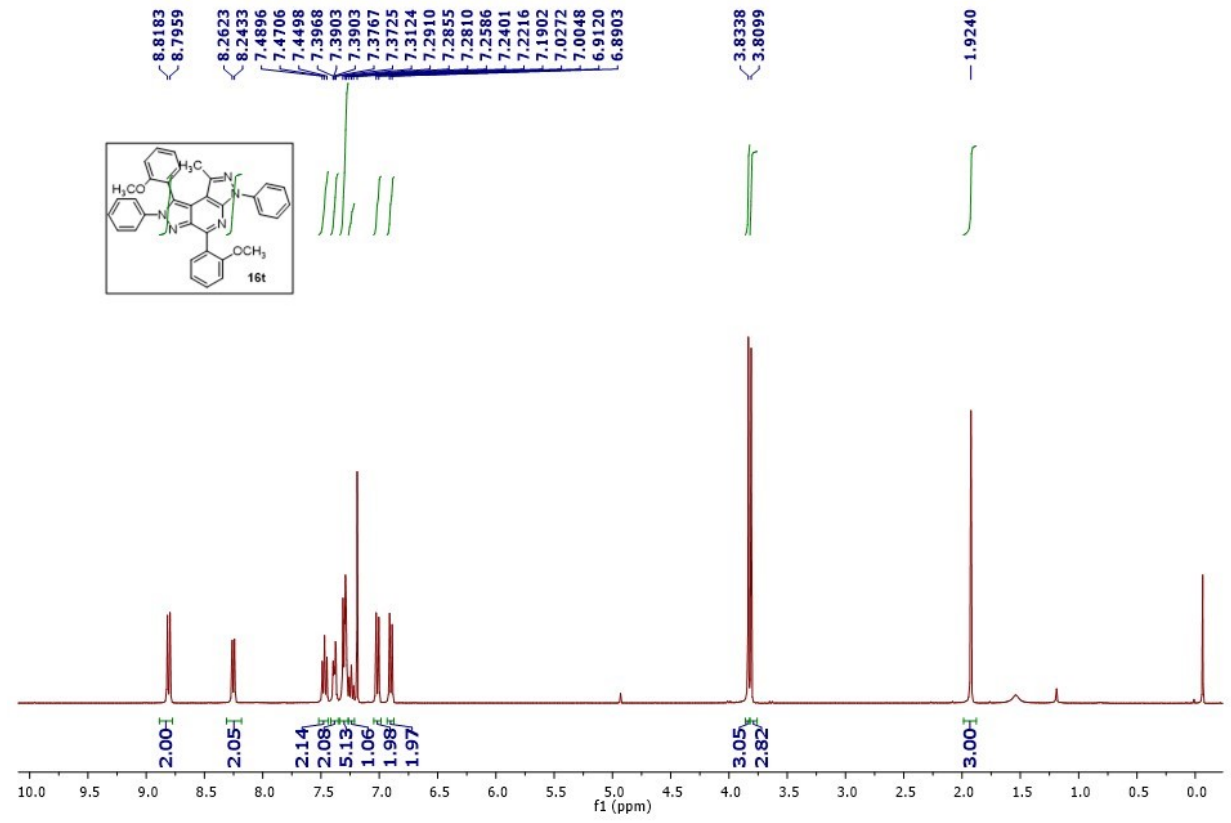
^{13}C NMR of Compound 16s



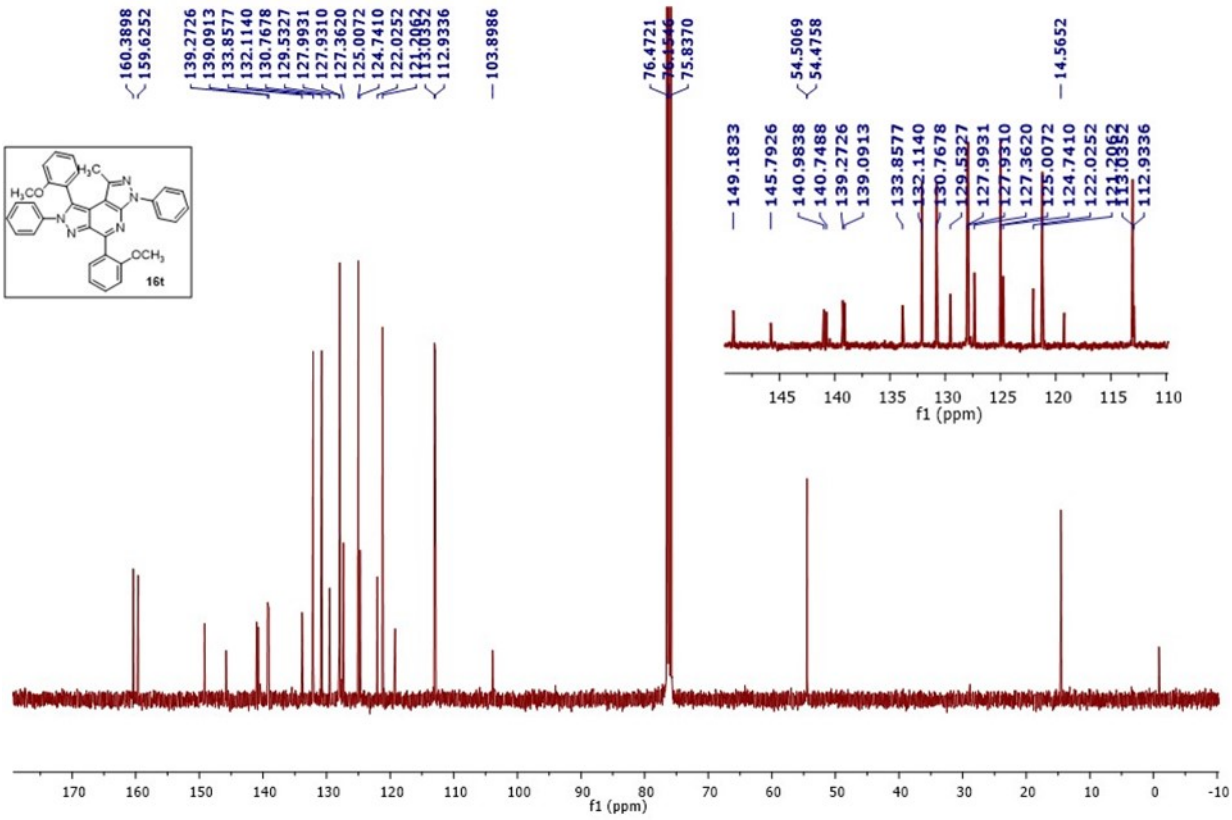
HRMS of Compound 16s



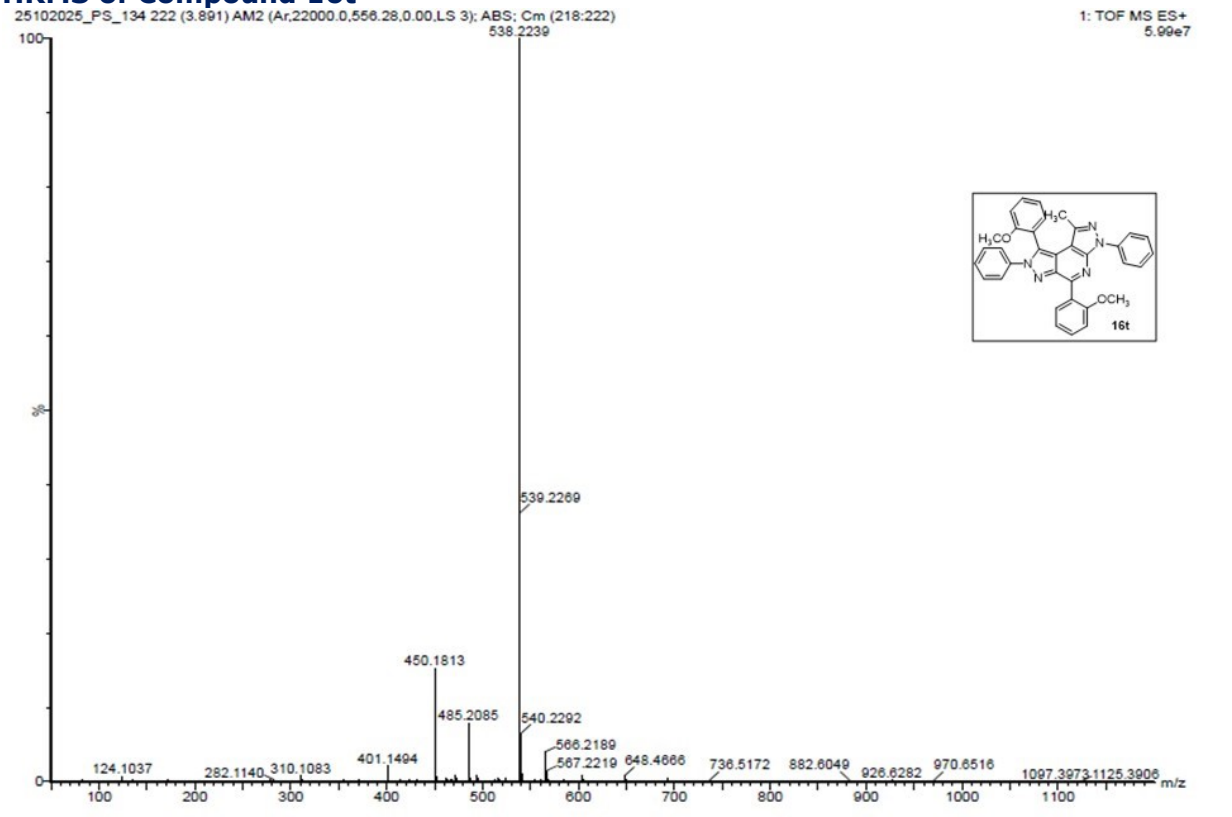
^{1}H NMR of Compound 16t



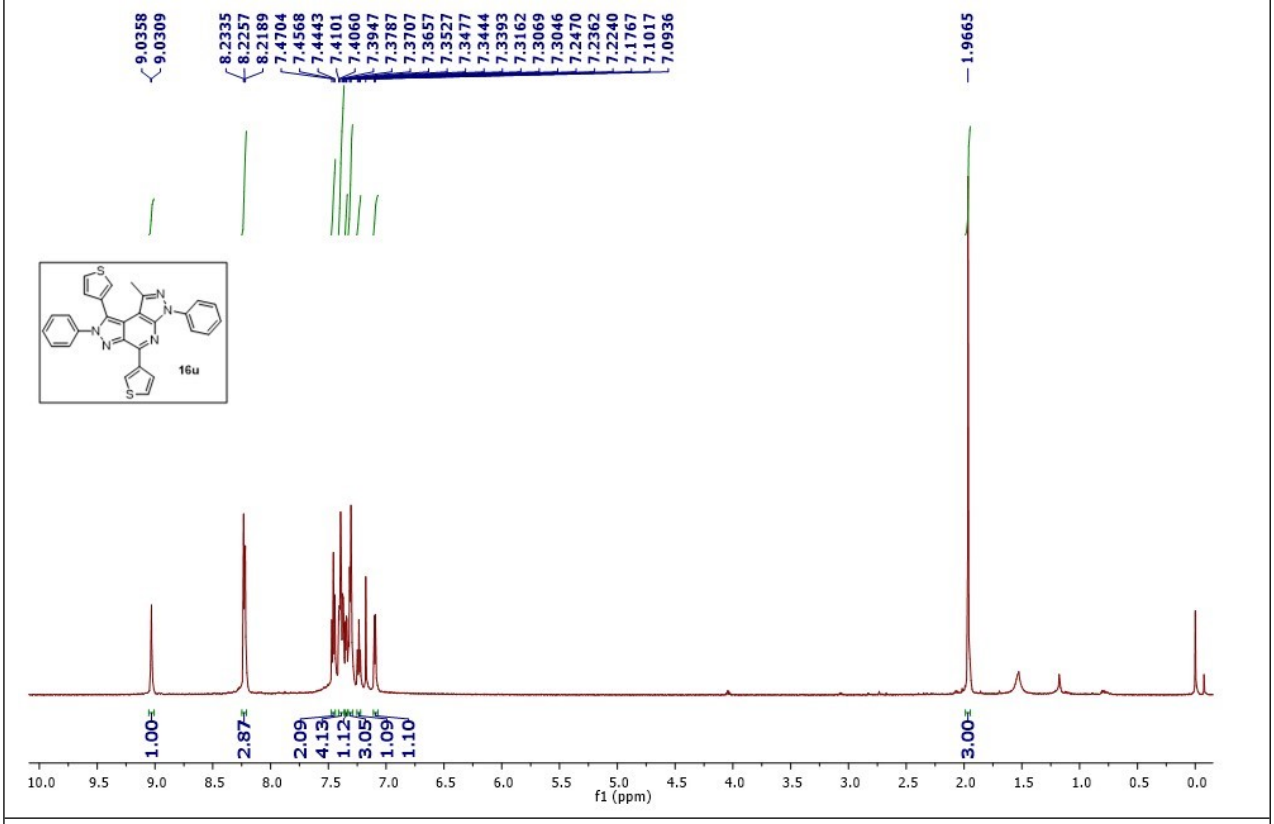
^{13}C NMR of Compound 16t



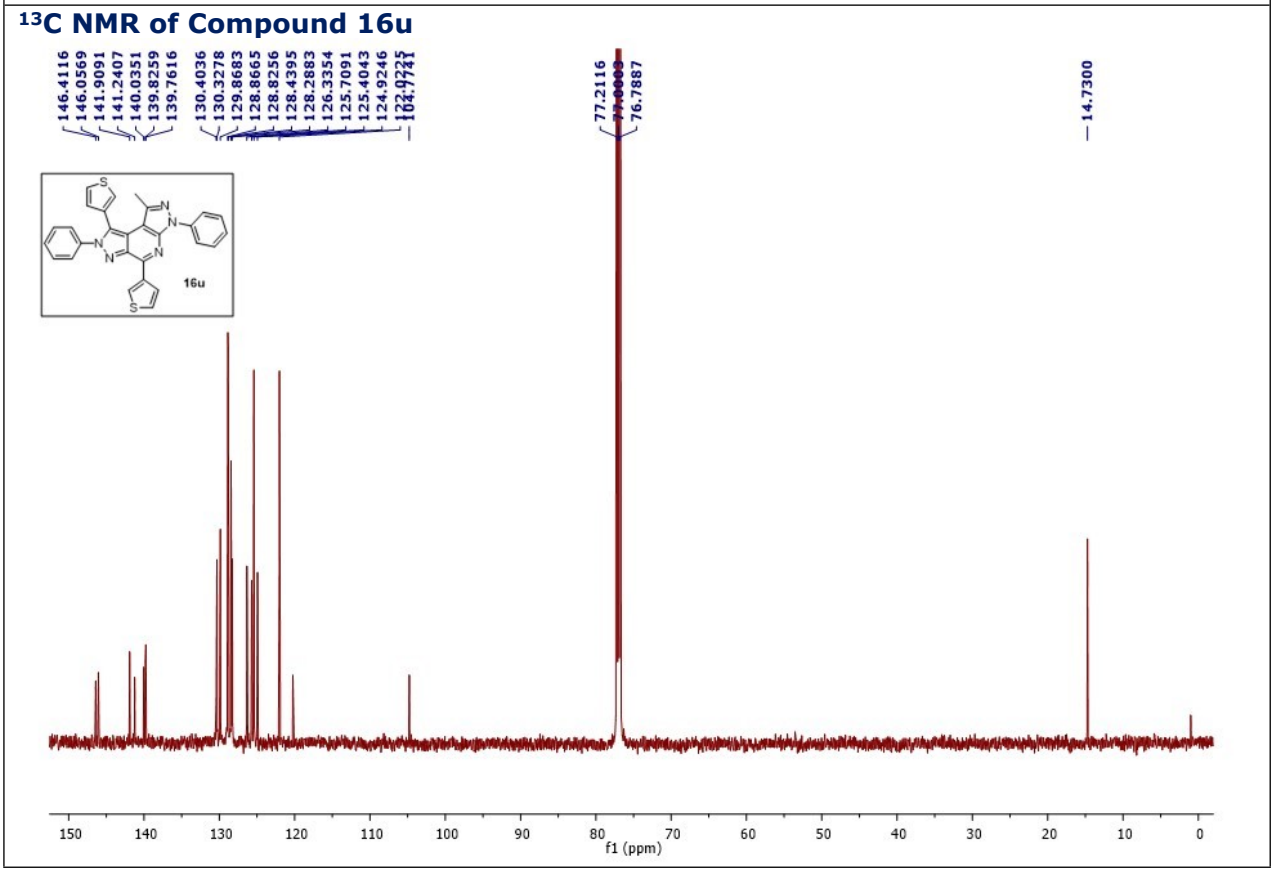
HRMS of Compound 16t



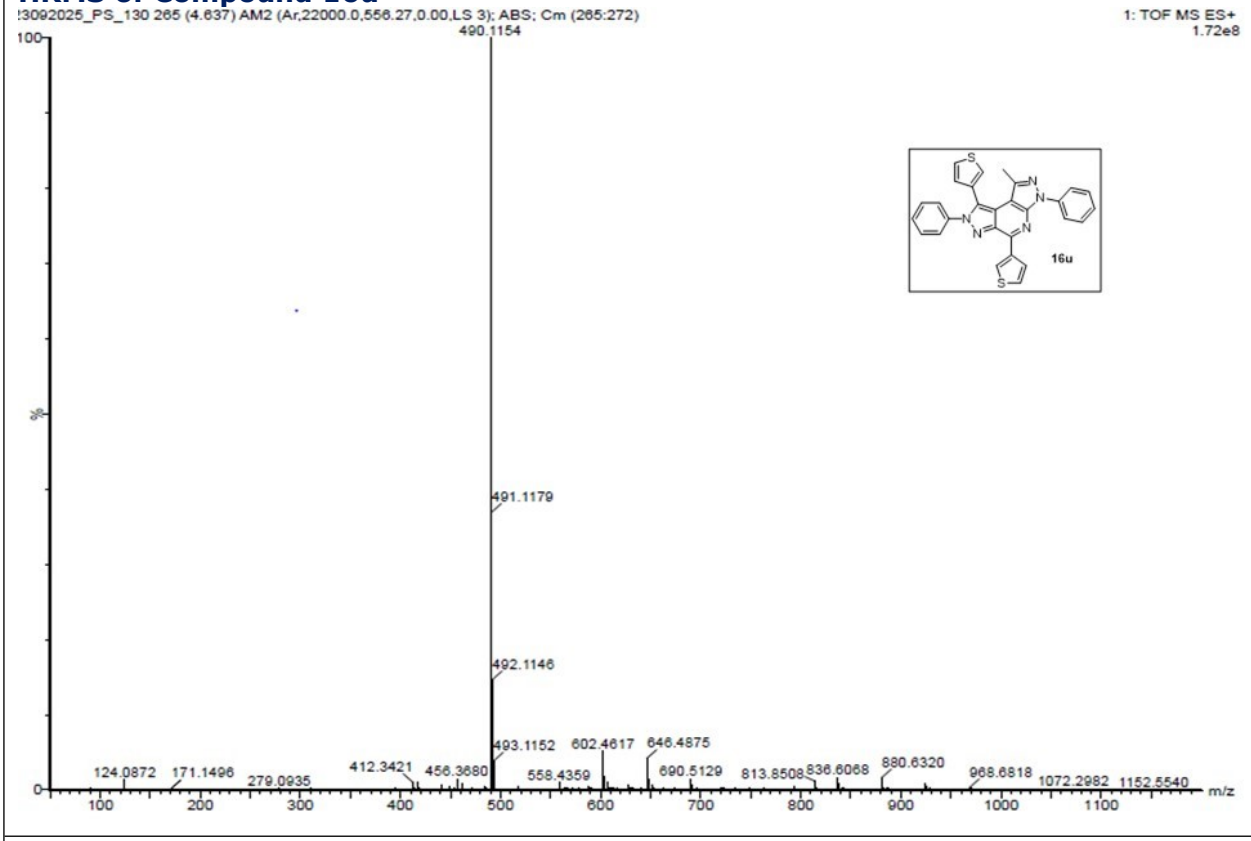
^{1}H NMR of Compound 16u



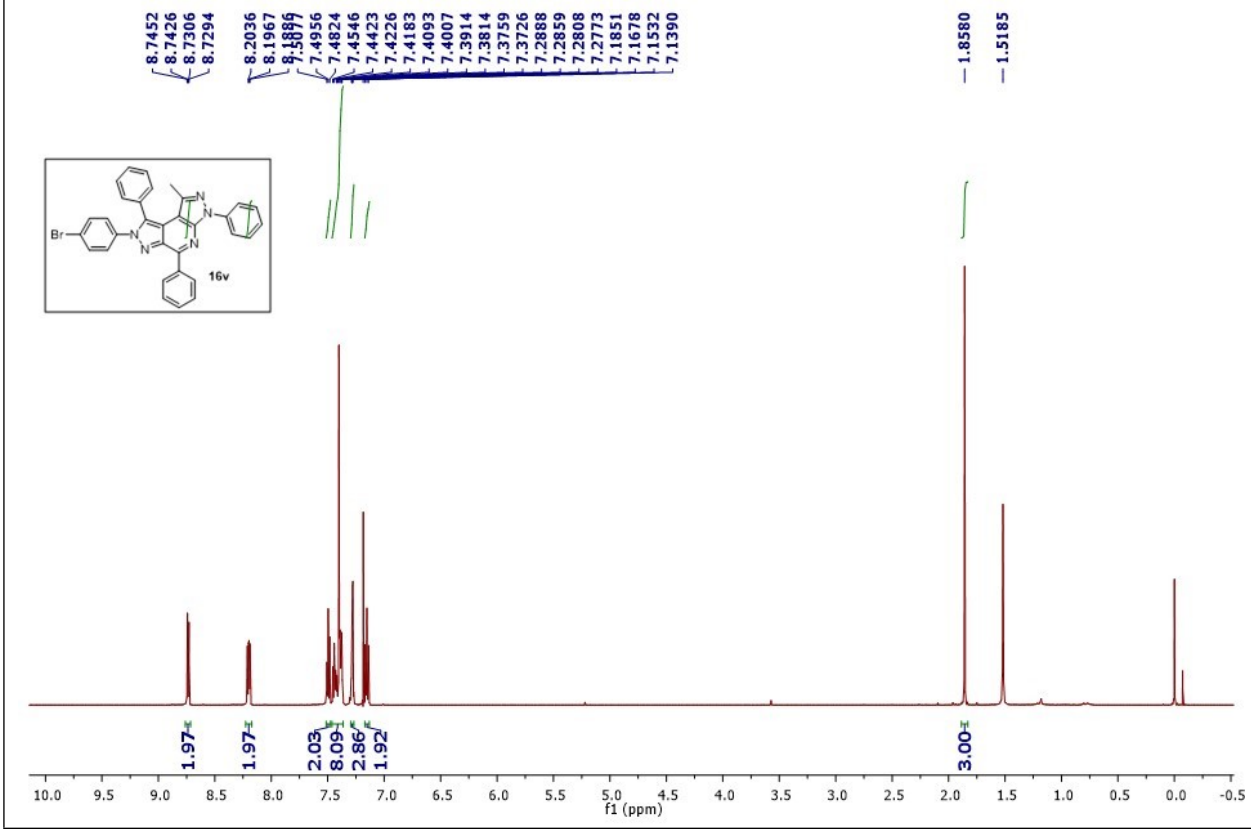
^{13}C NMR of Compound 16u



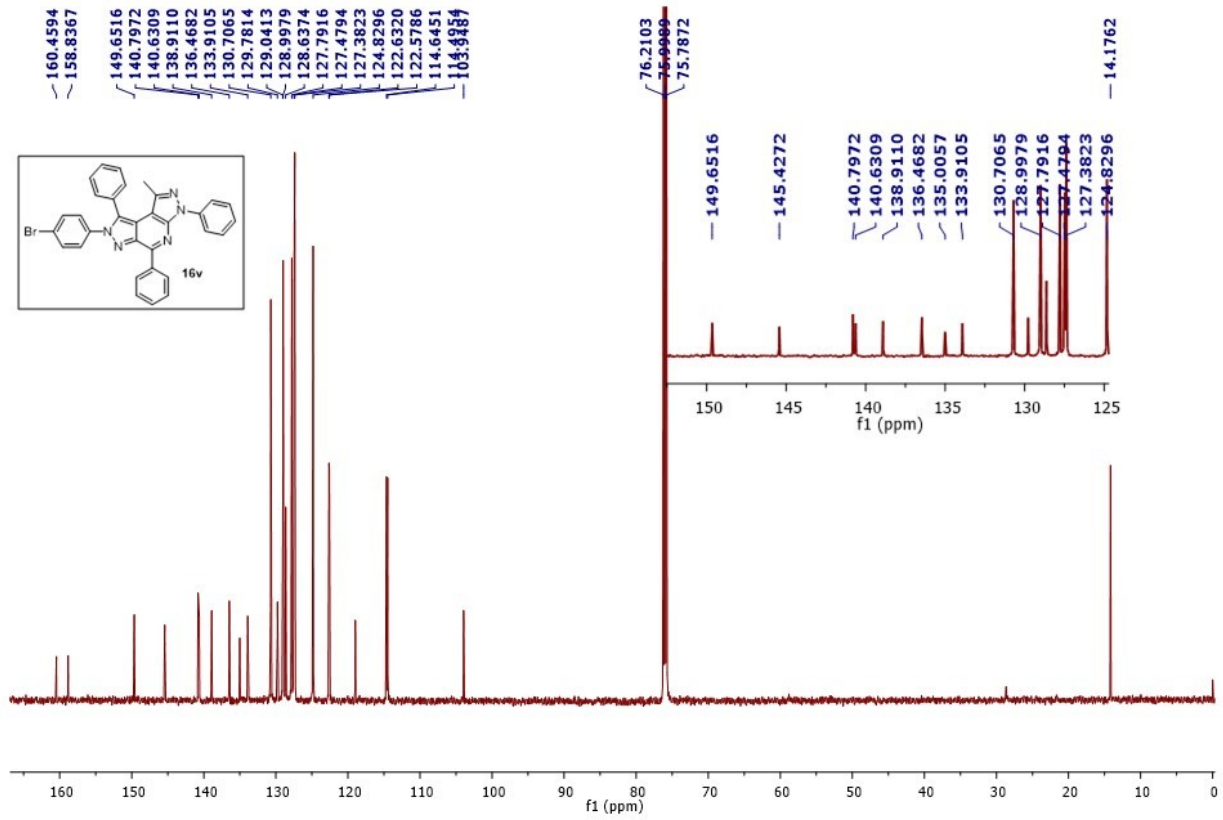
HRMS of Compound 16u



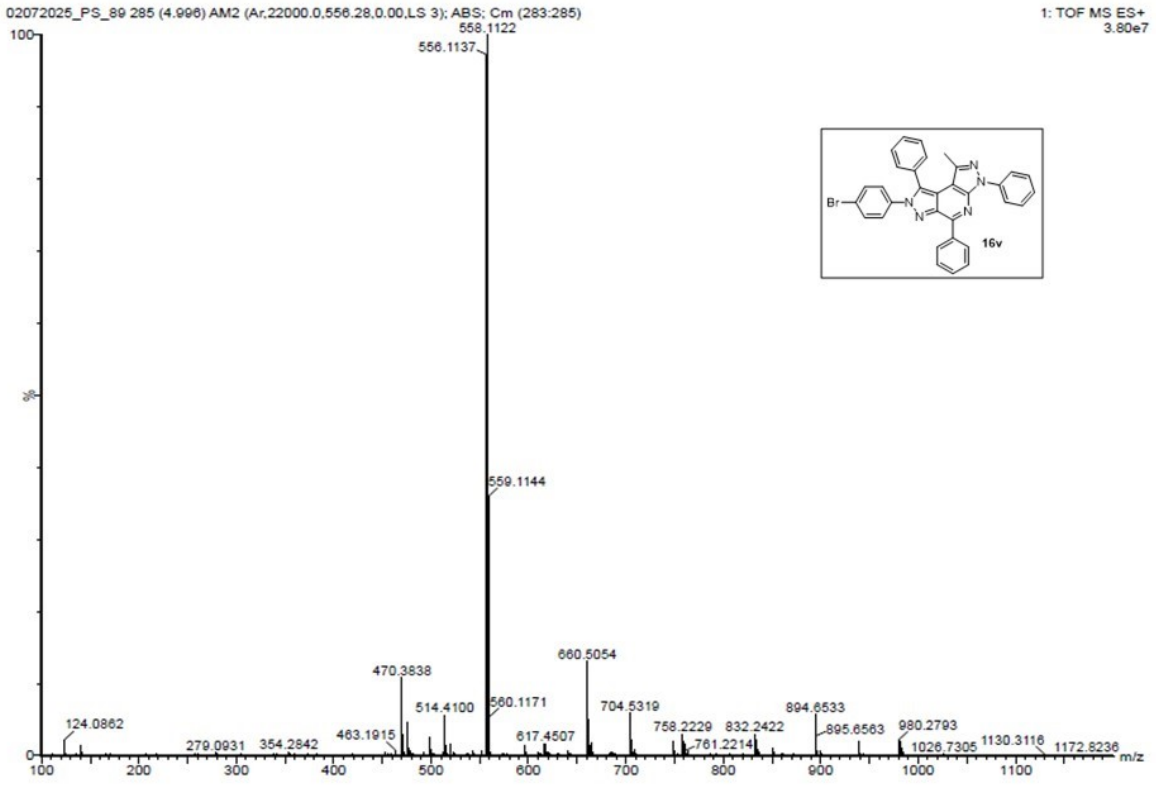
^{1}H NMR of Compound 16v



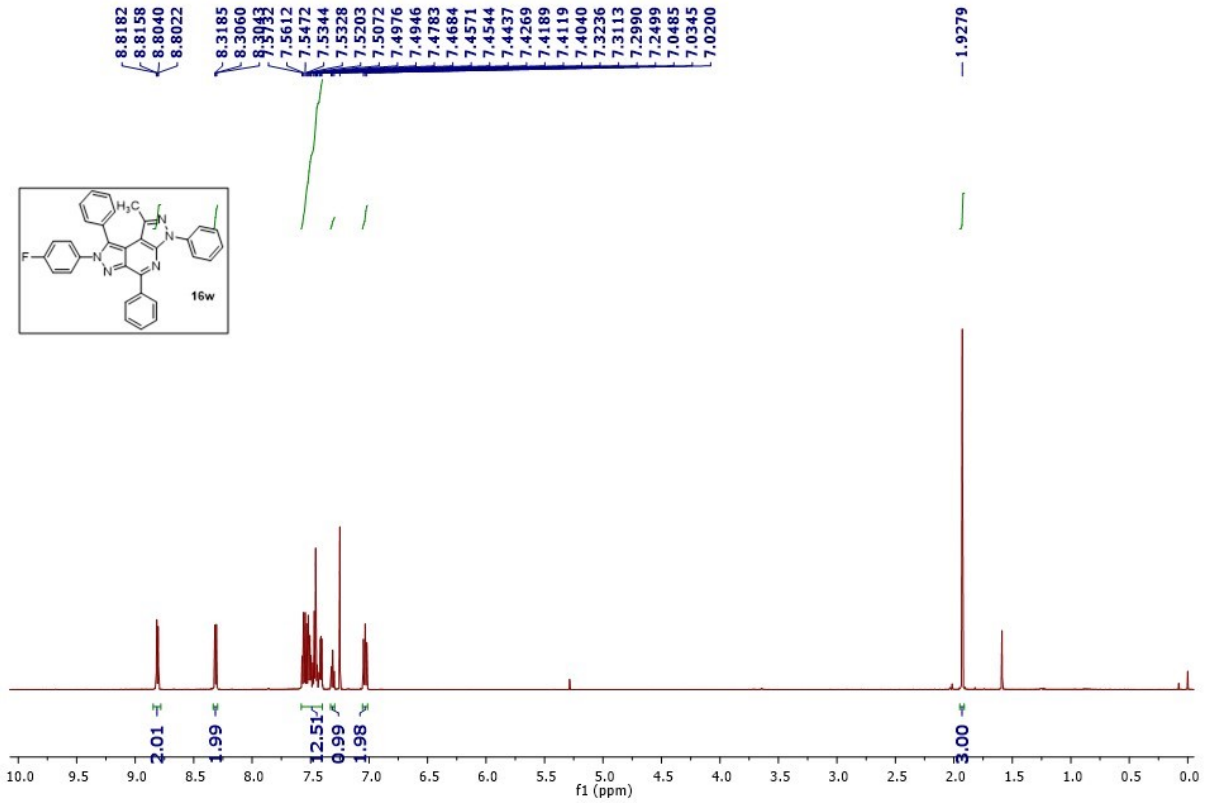
^{13}C NMR of Compound 16v



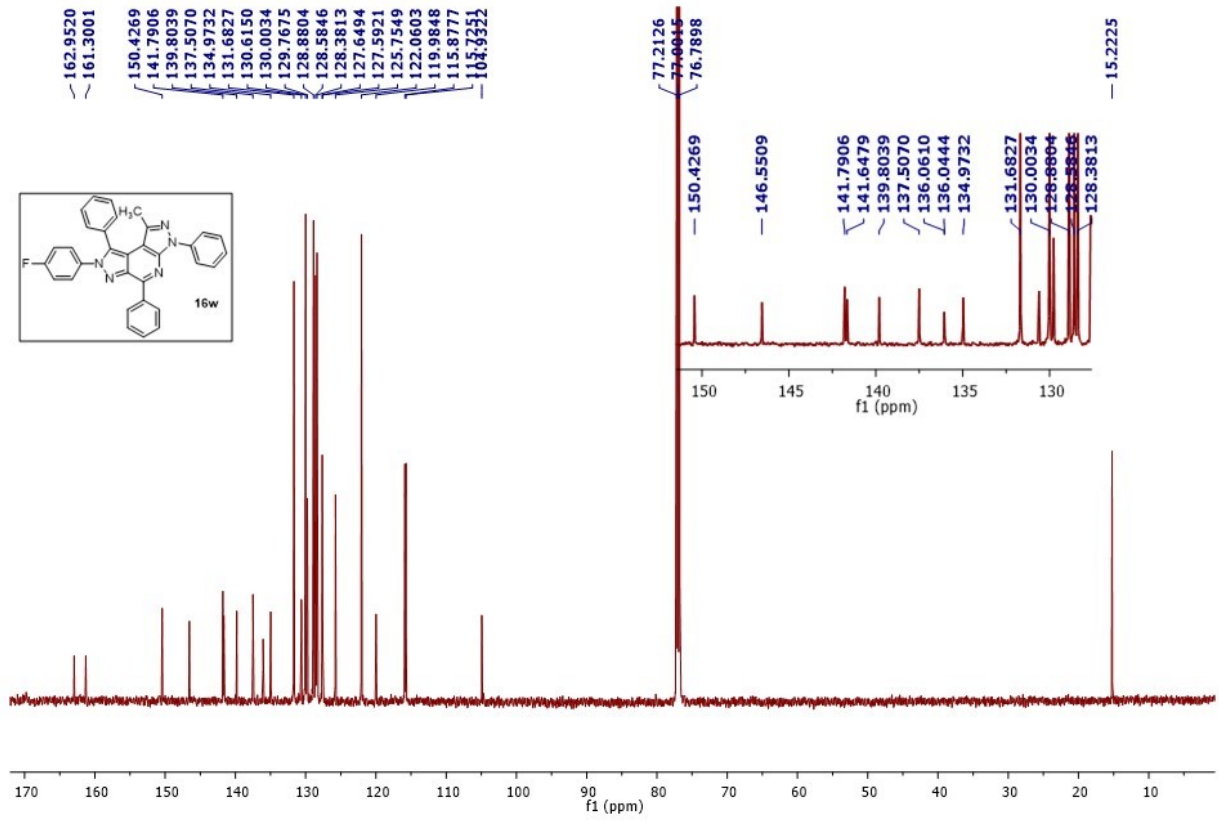
HRMS of Compound 16v



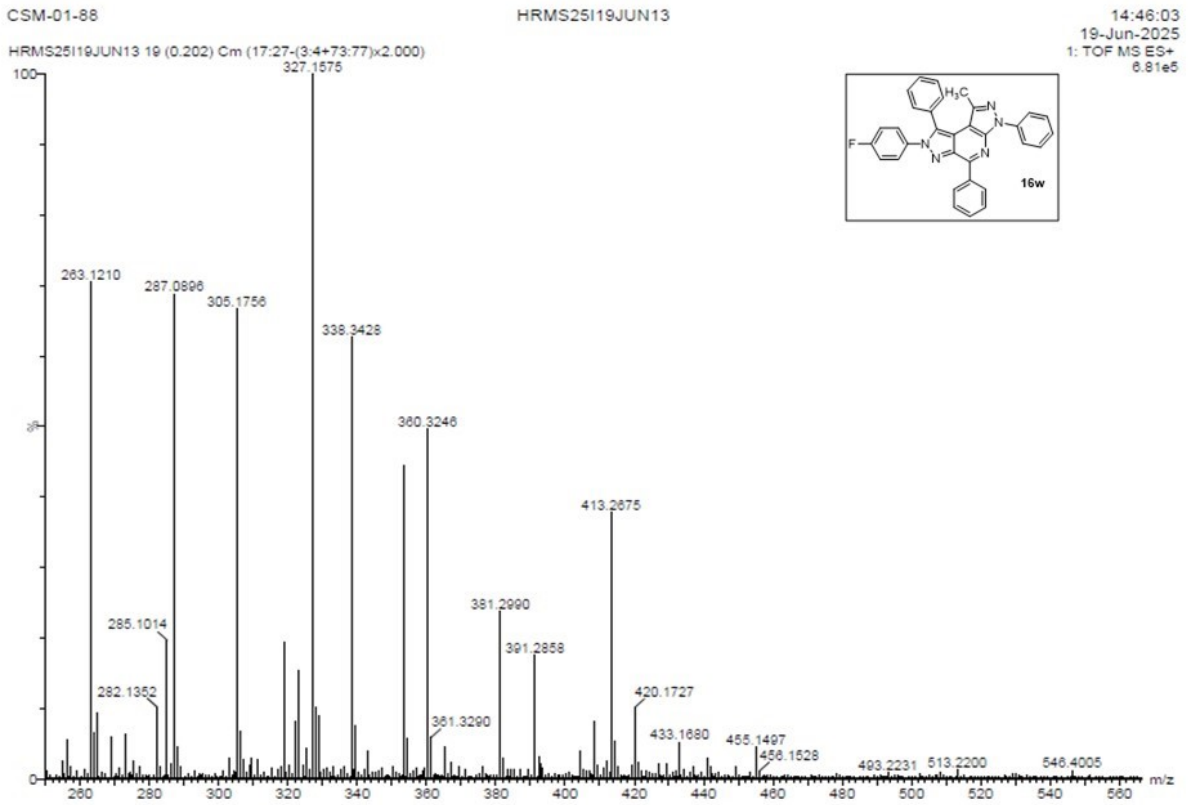
^{1}H NMR of Compound 16w



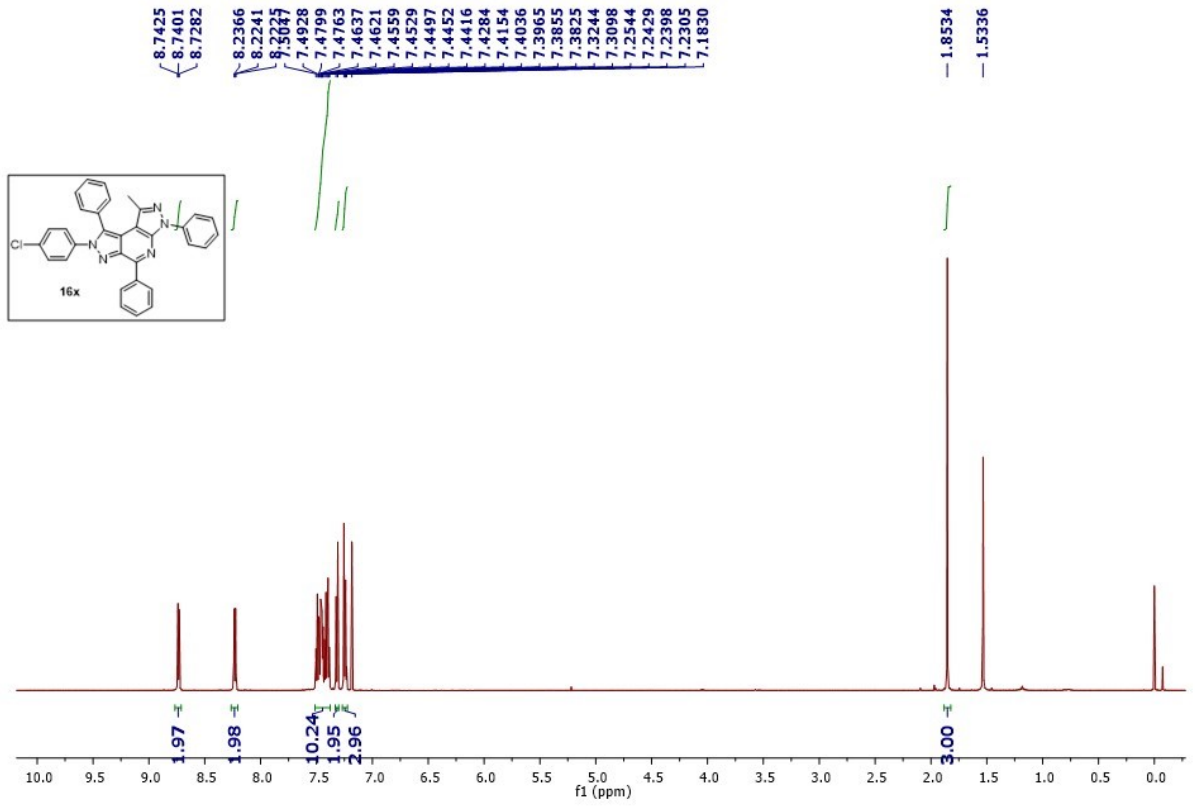
^{13}C NMR of Compound 16w



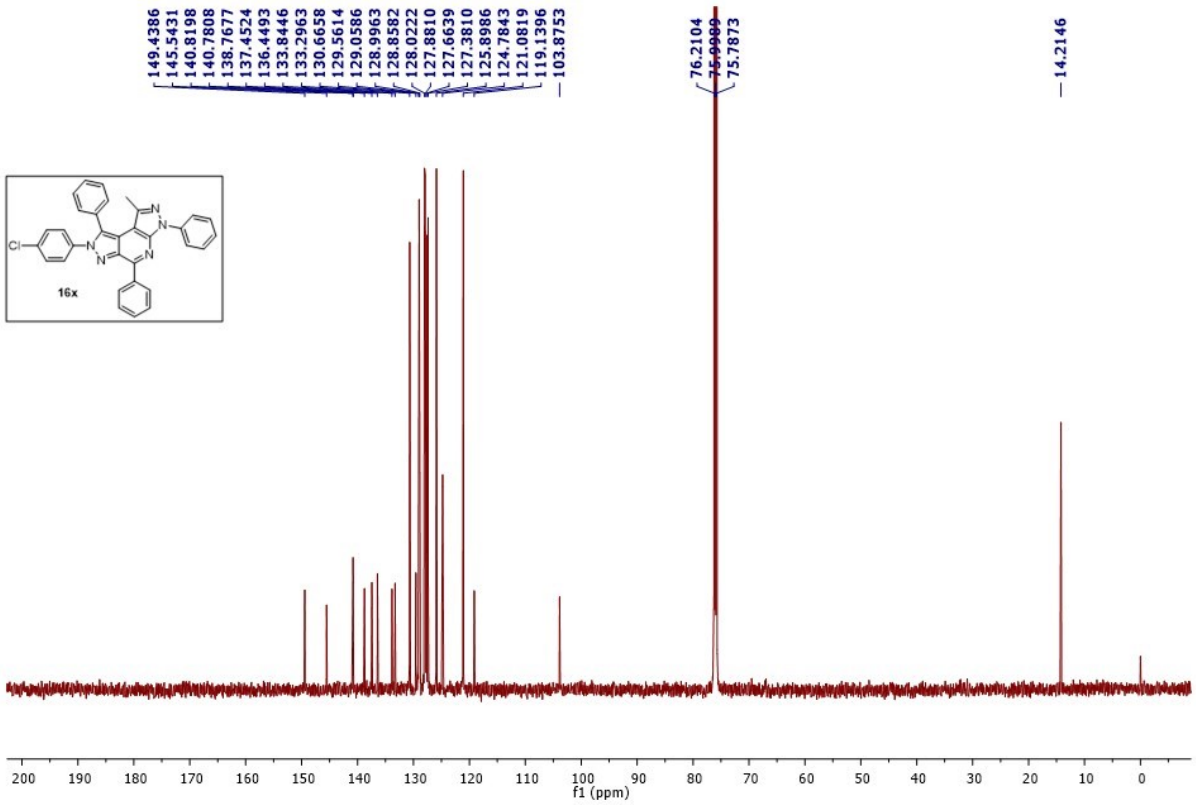
HRMS of Compound 16w



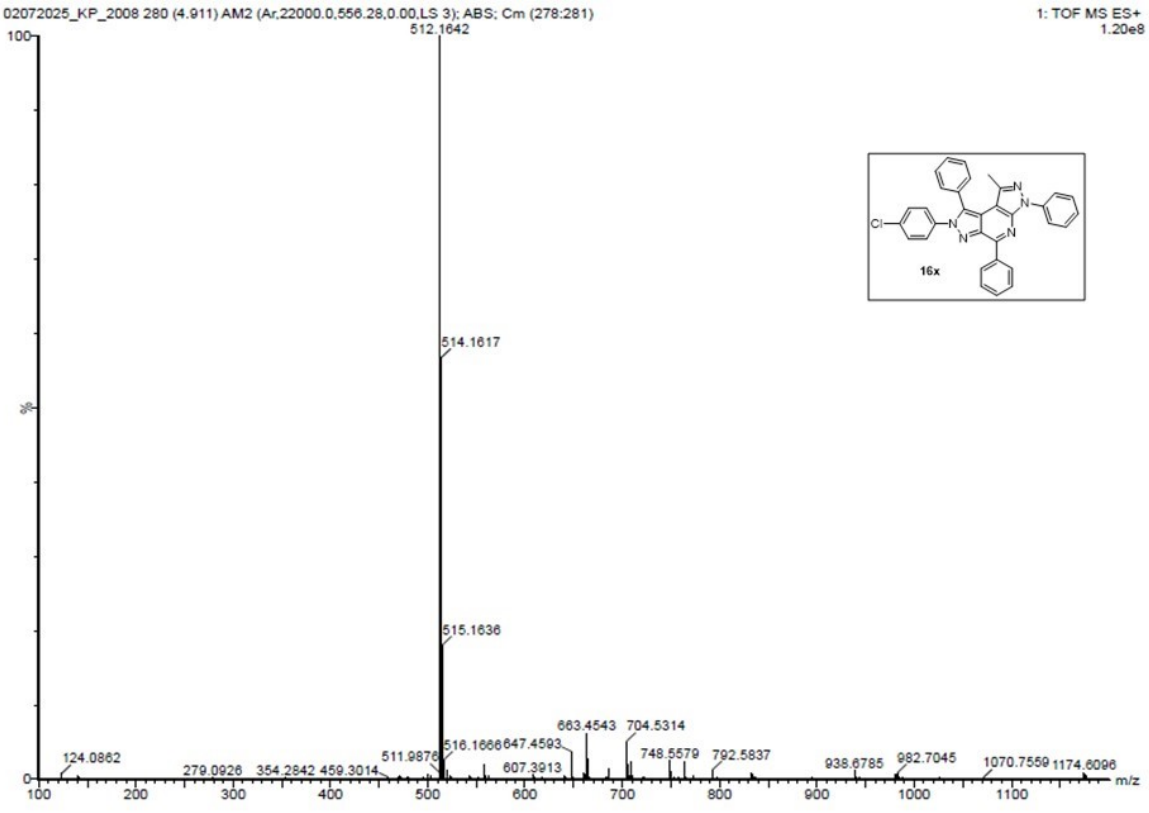
^{1}H NMR of Compound 16x



^{13}C NMR of Compound 16x



HRMS of Compound 16x



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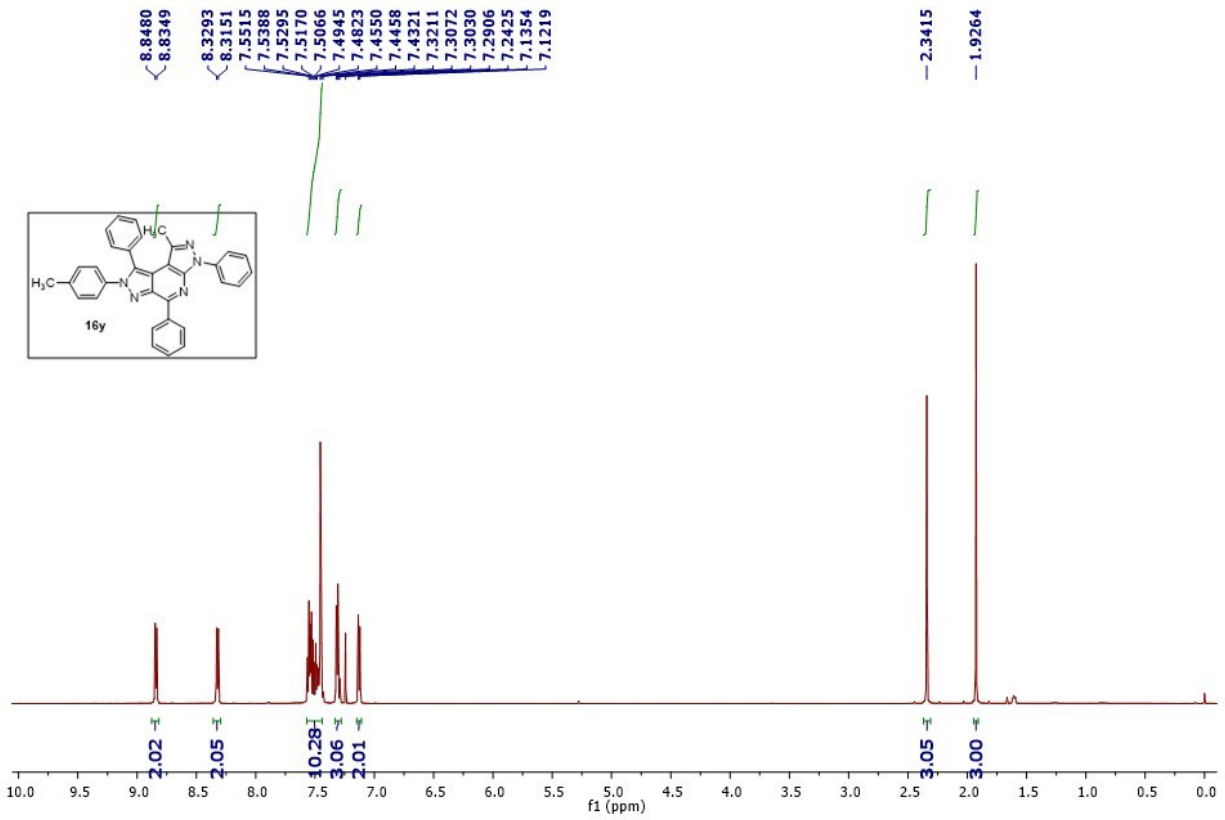

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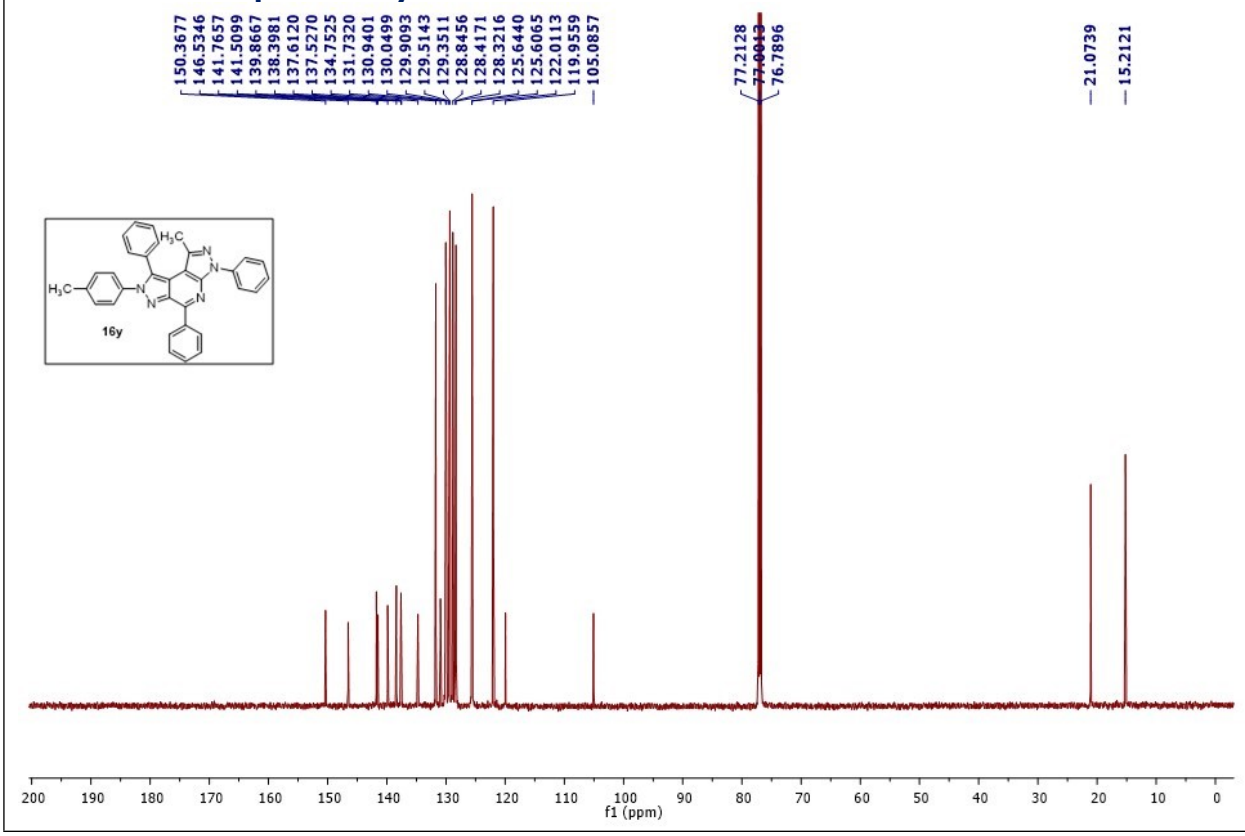
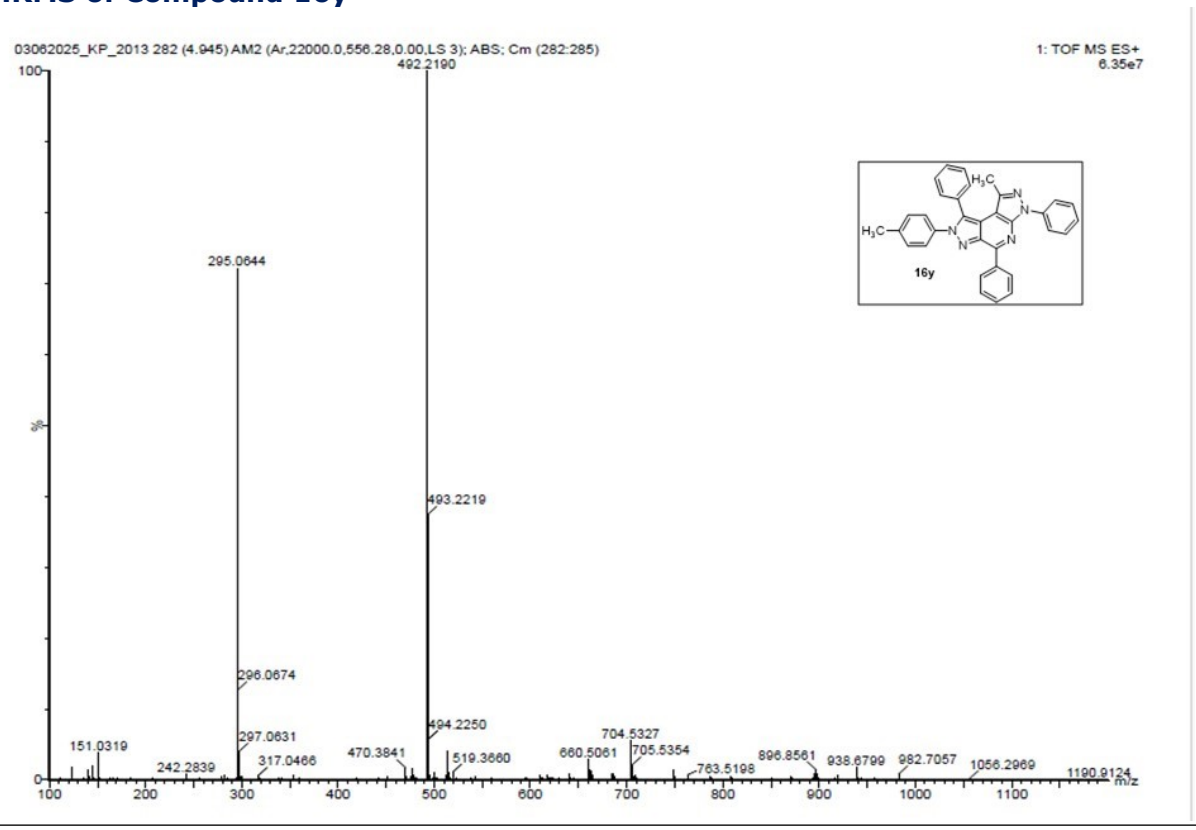


HRMS of Compound 16y



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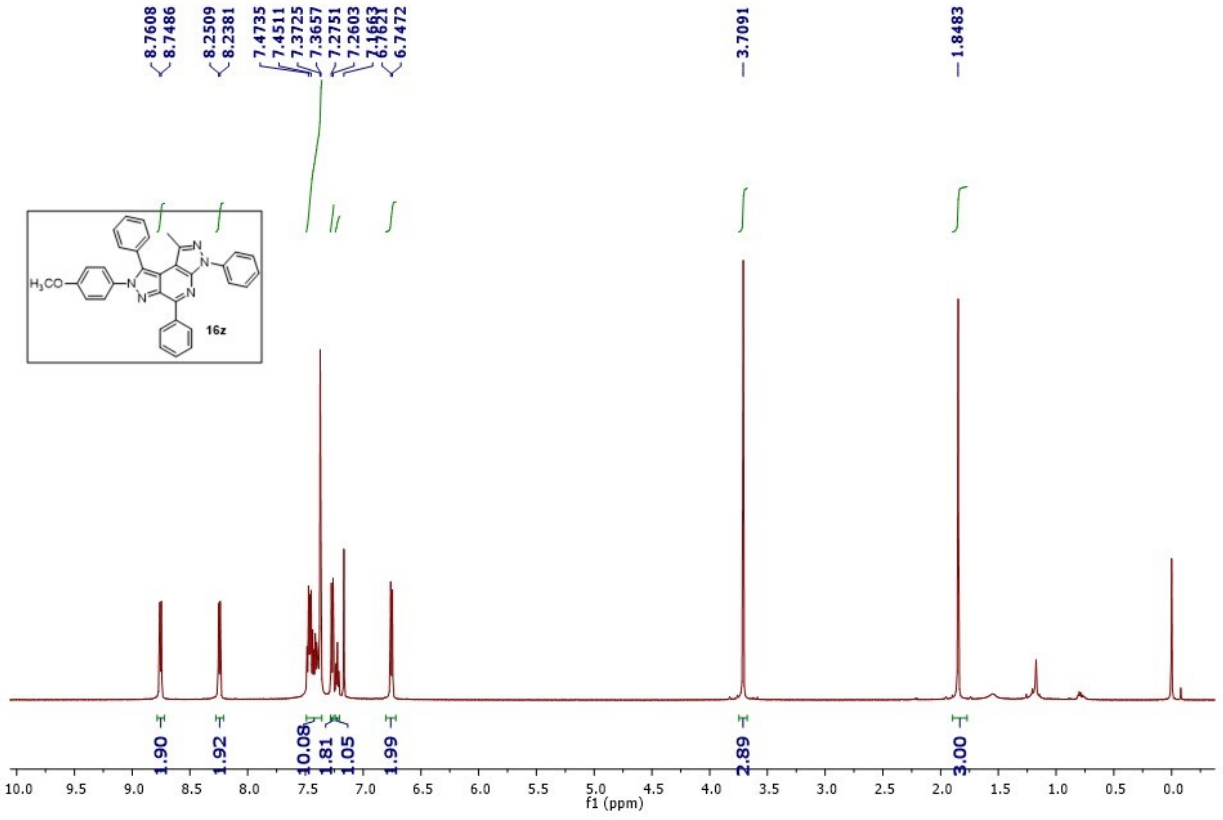

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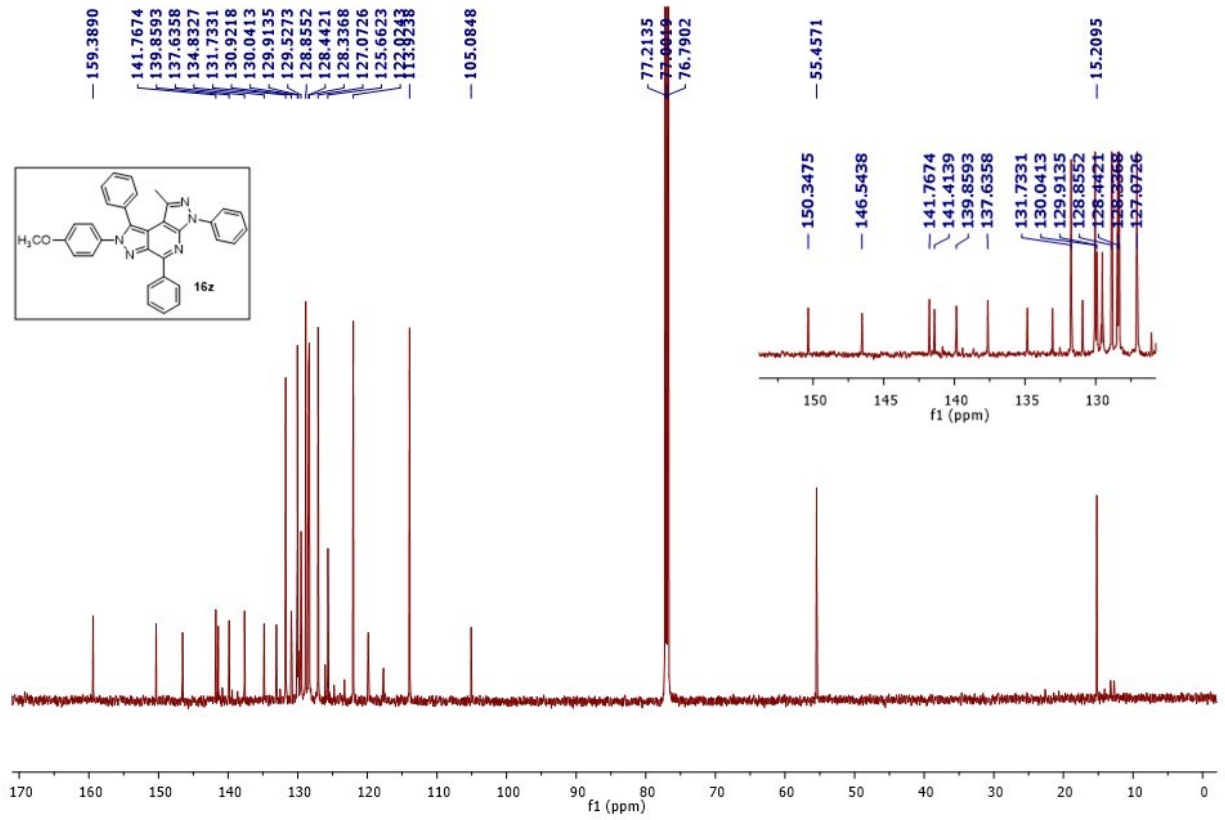

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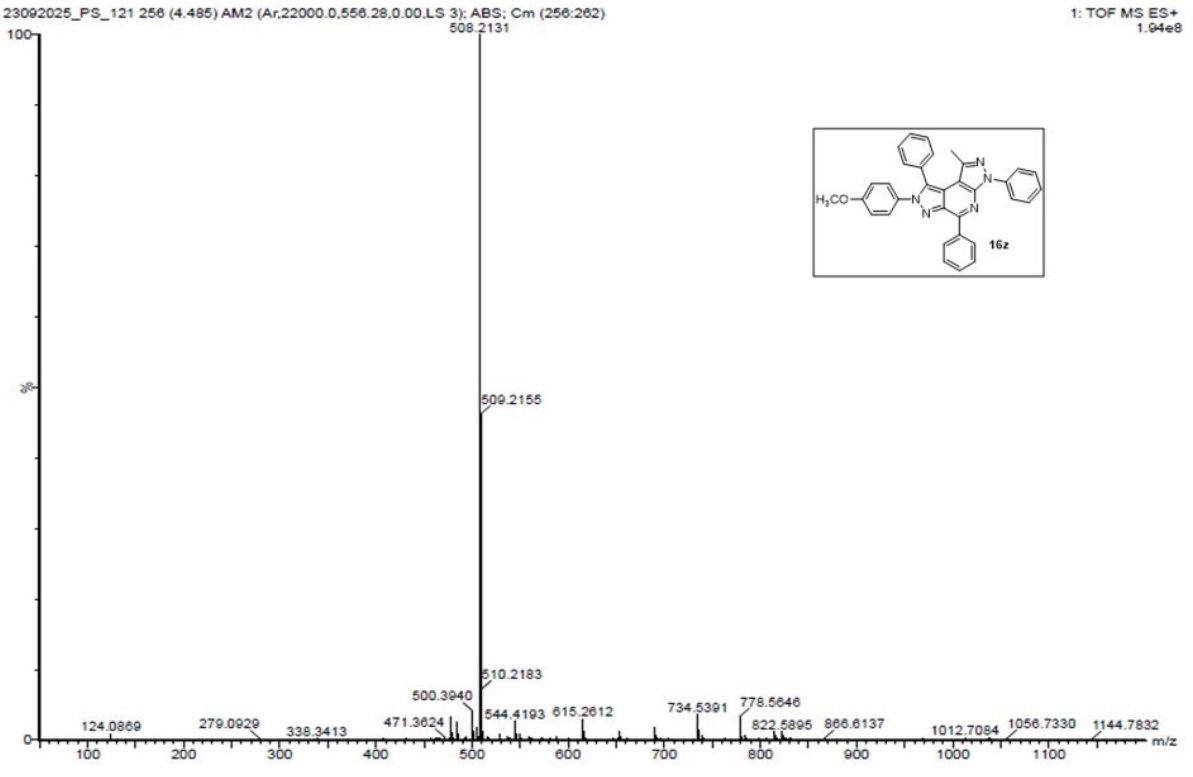
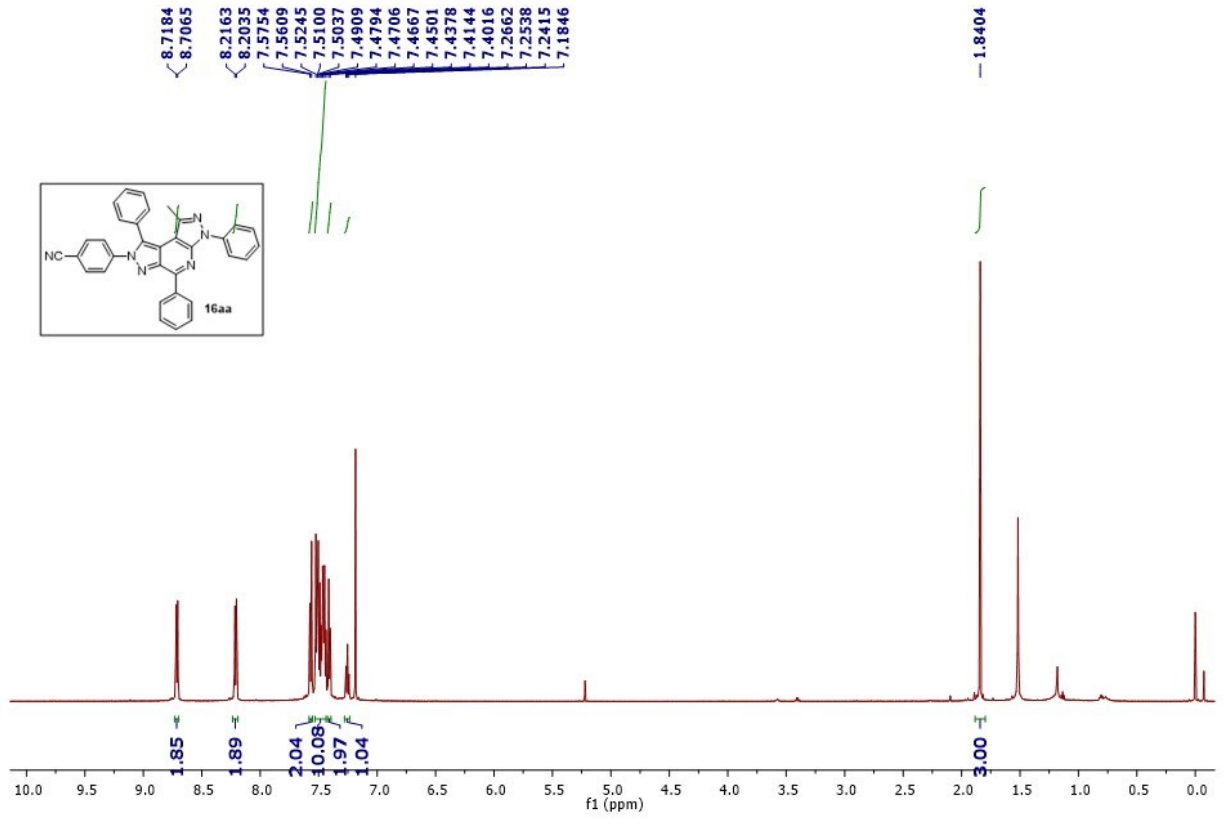
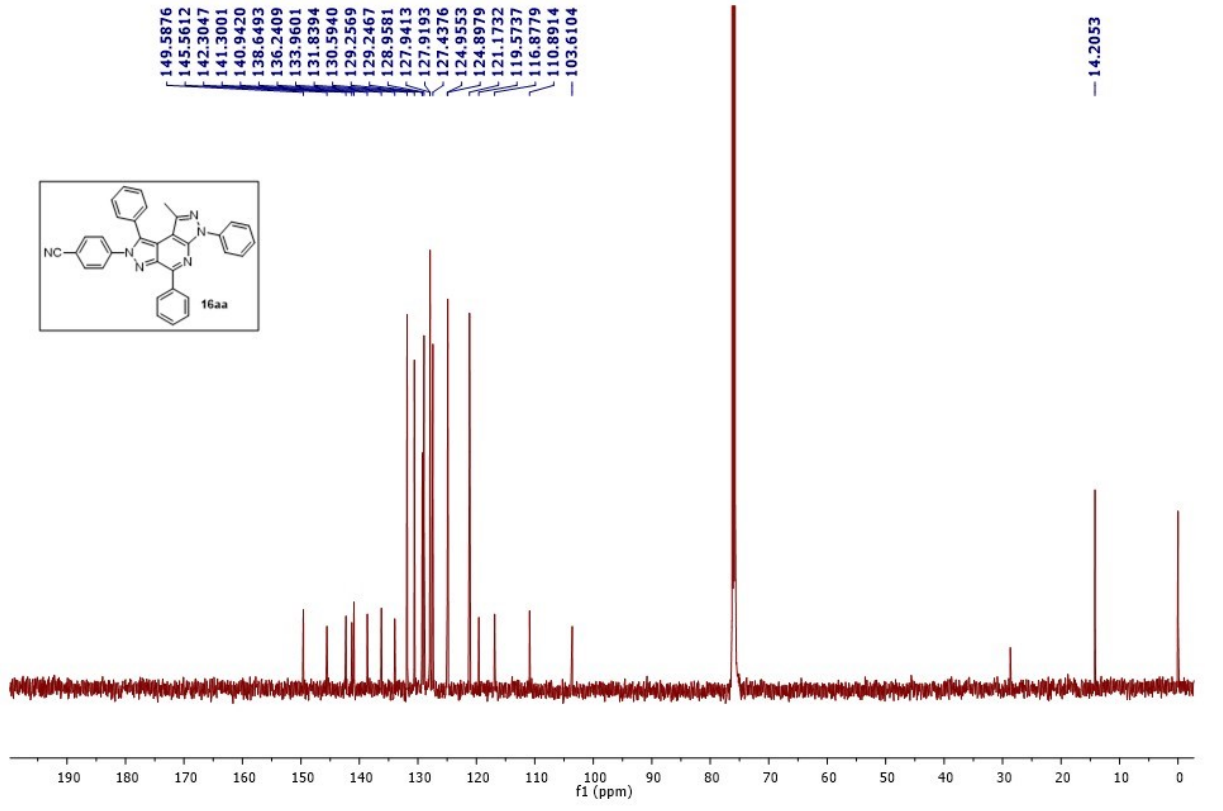


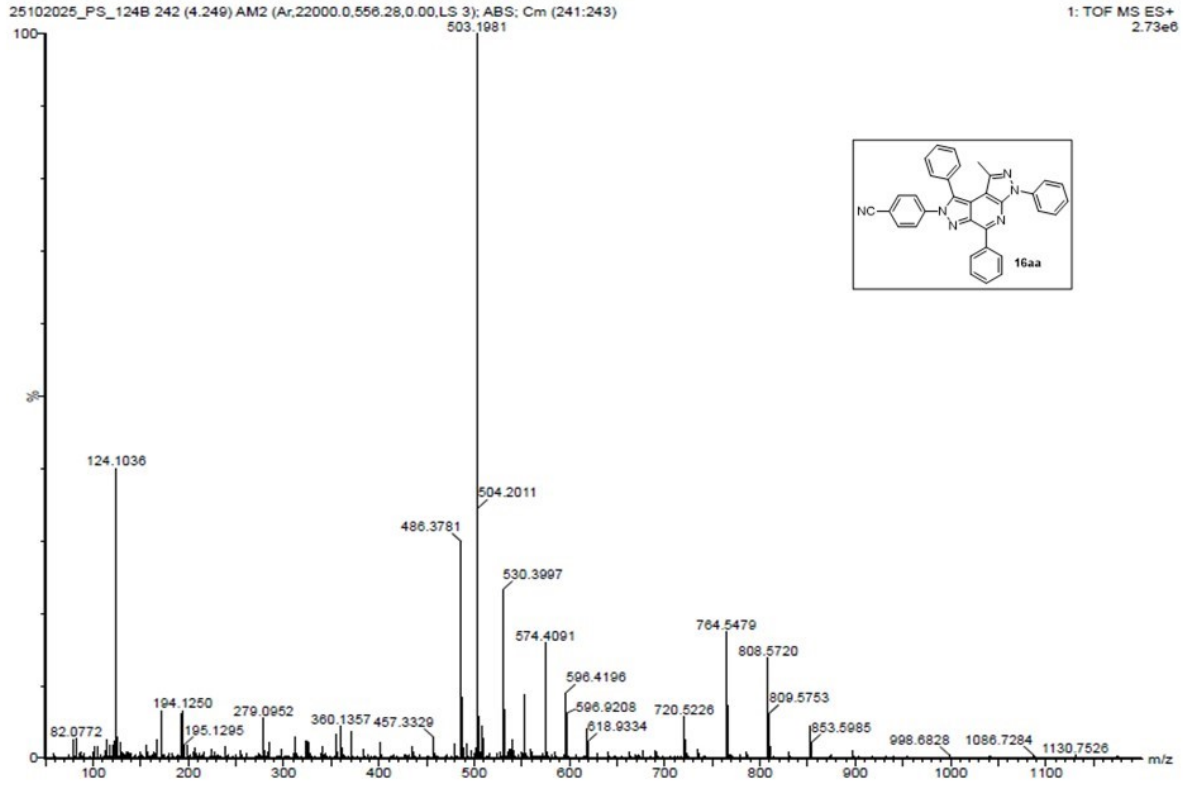
^{1}H NMR of Compound 16aa



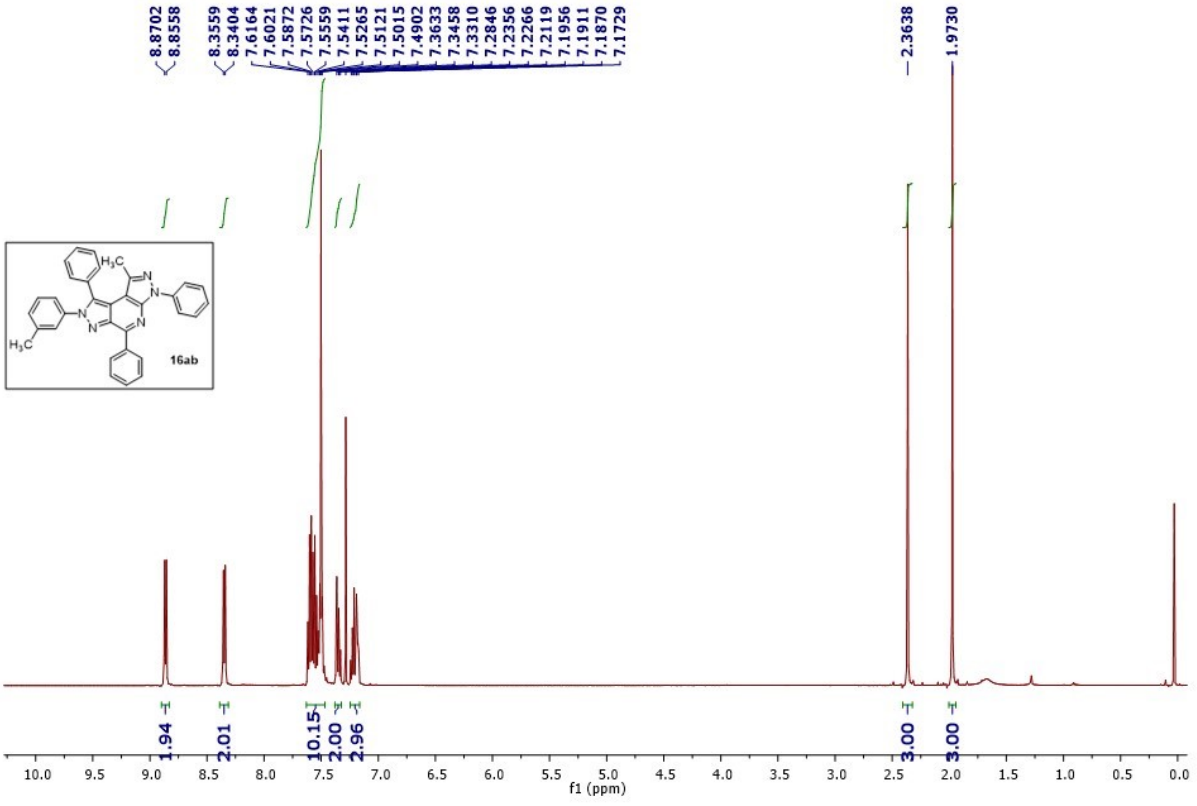
^{13}C NMR of Compound 16aa



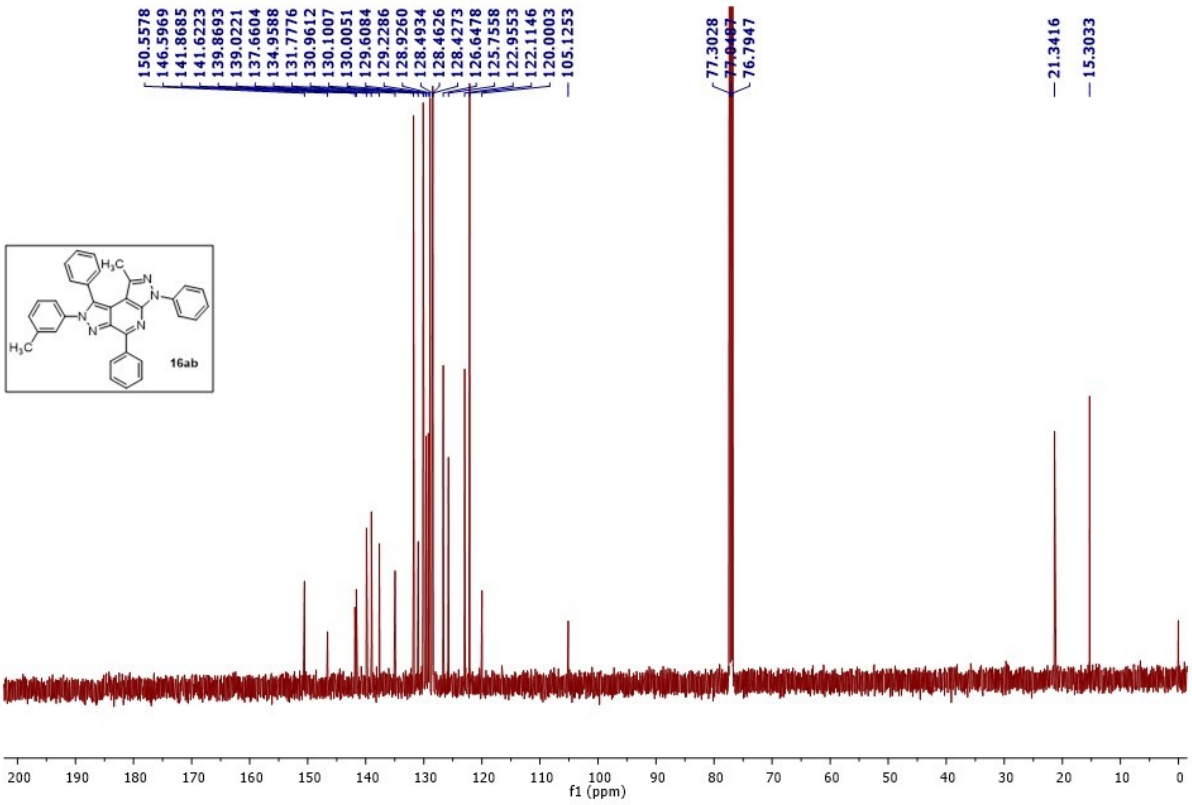
HRMS of Compound 16aa



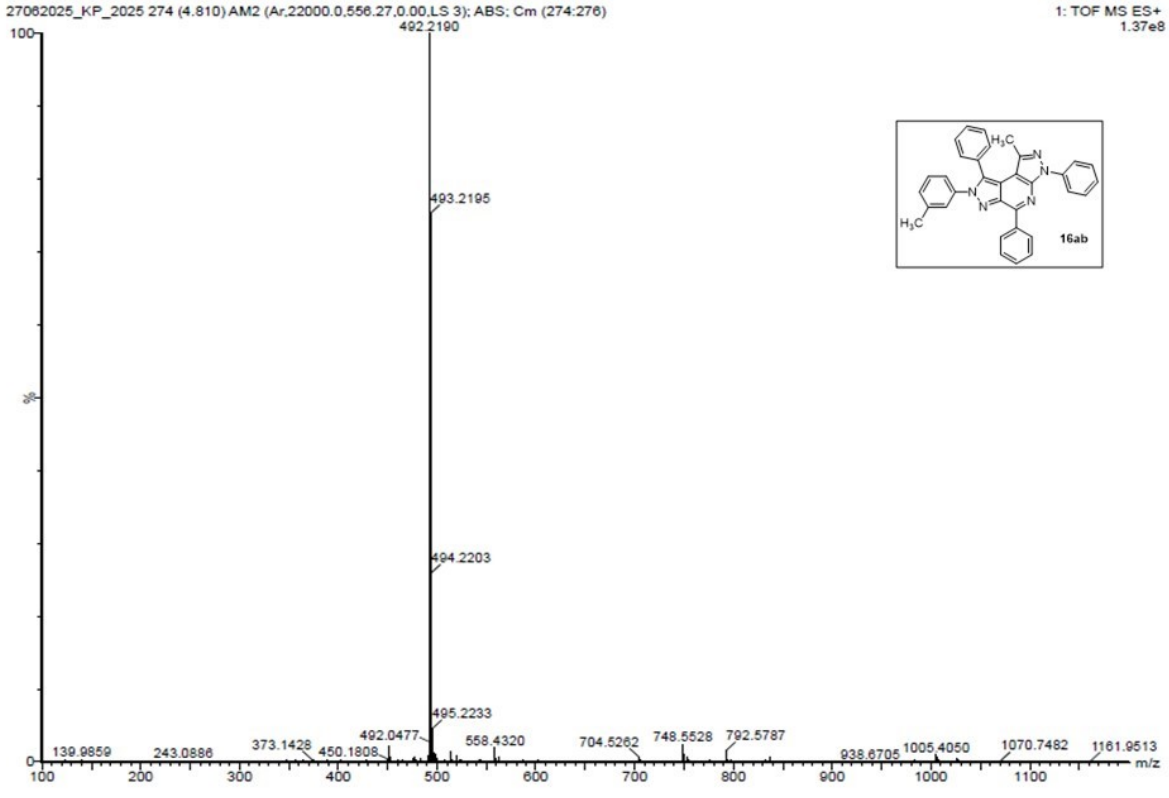
^{1}H NMR of Compound 16ab



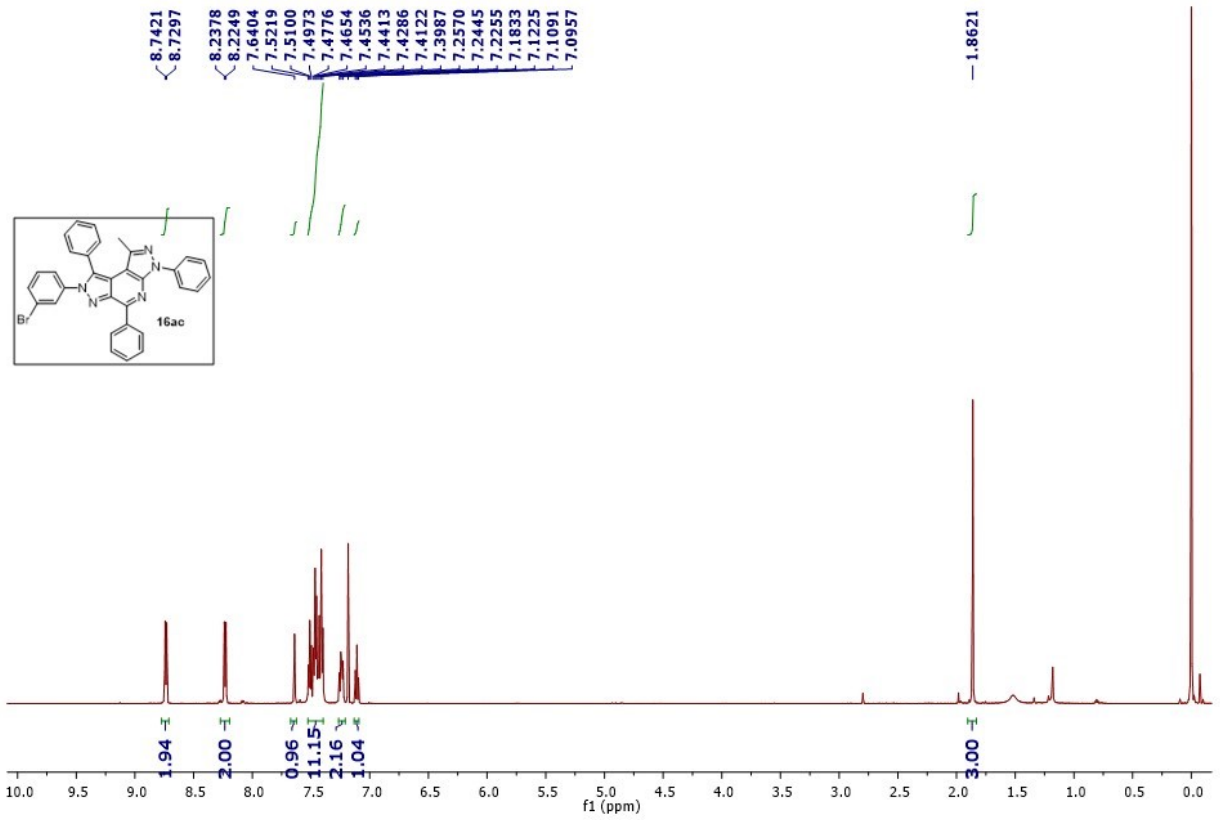
^{13}C NMR of Compound 16ab



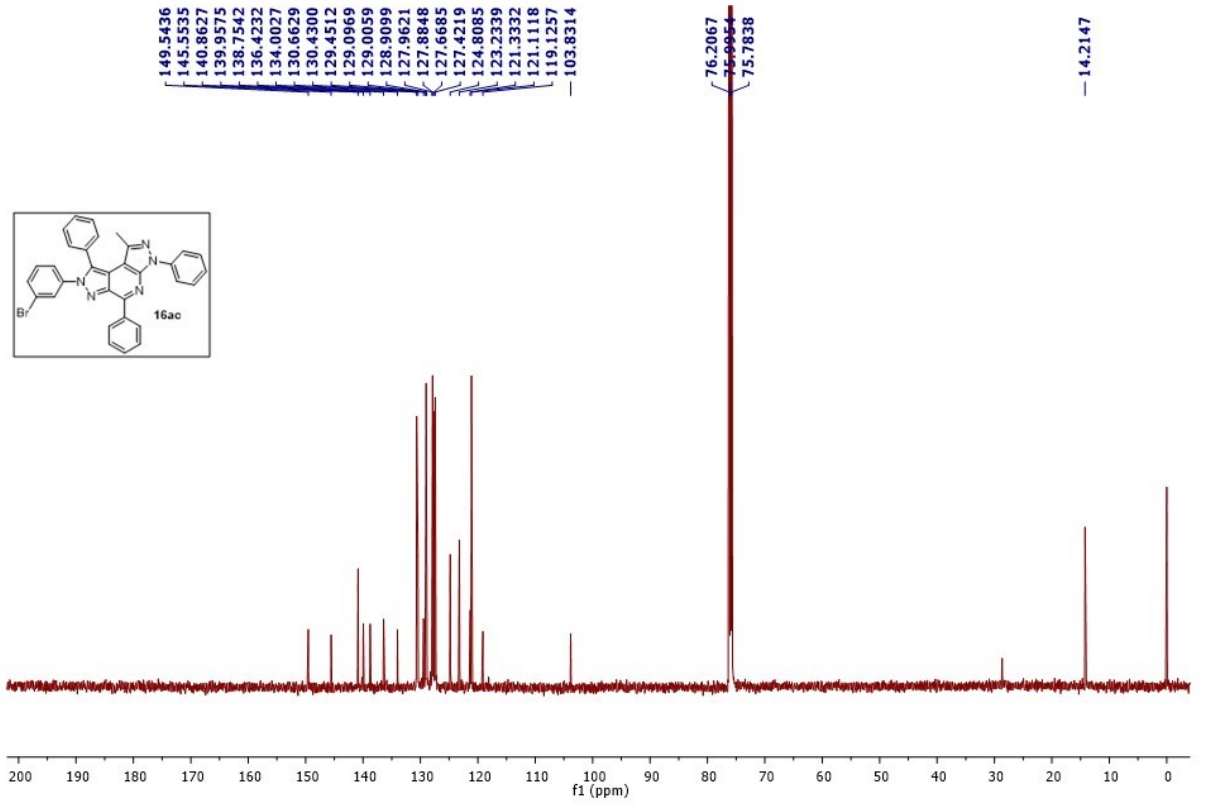
HRMS of Compound 16ab



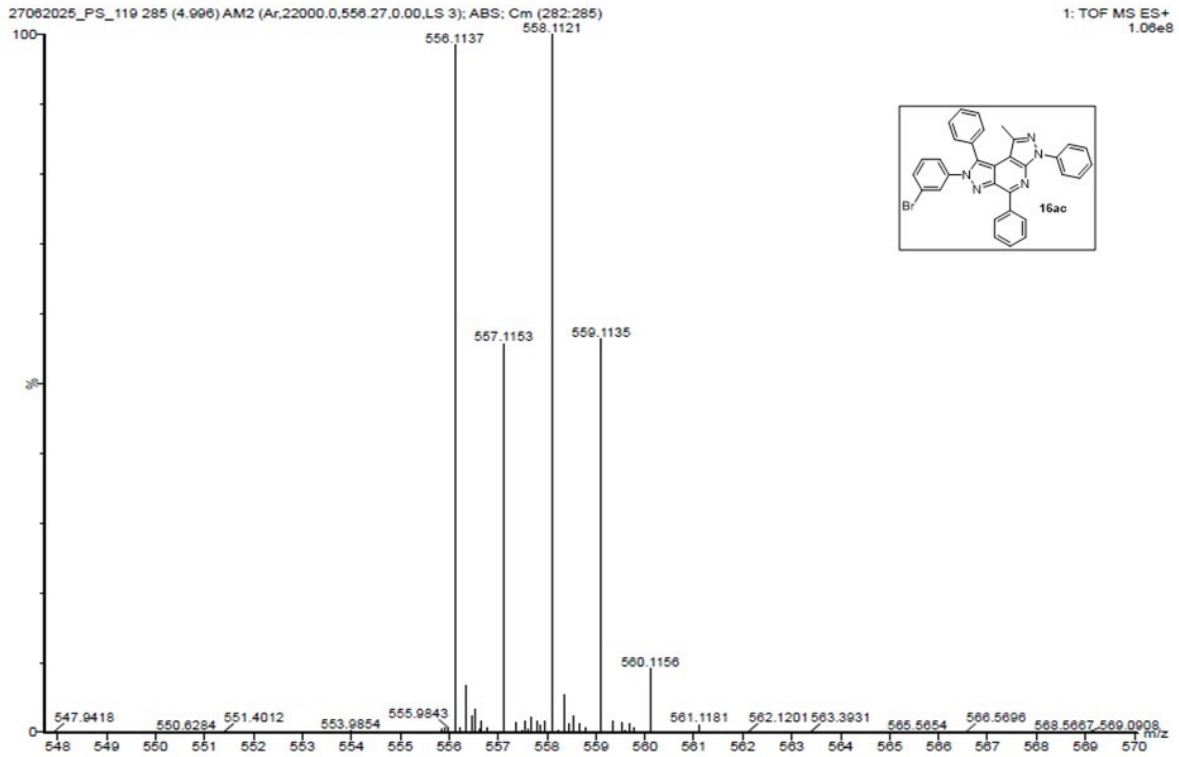
^{1}H NMR of Compound 16ac



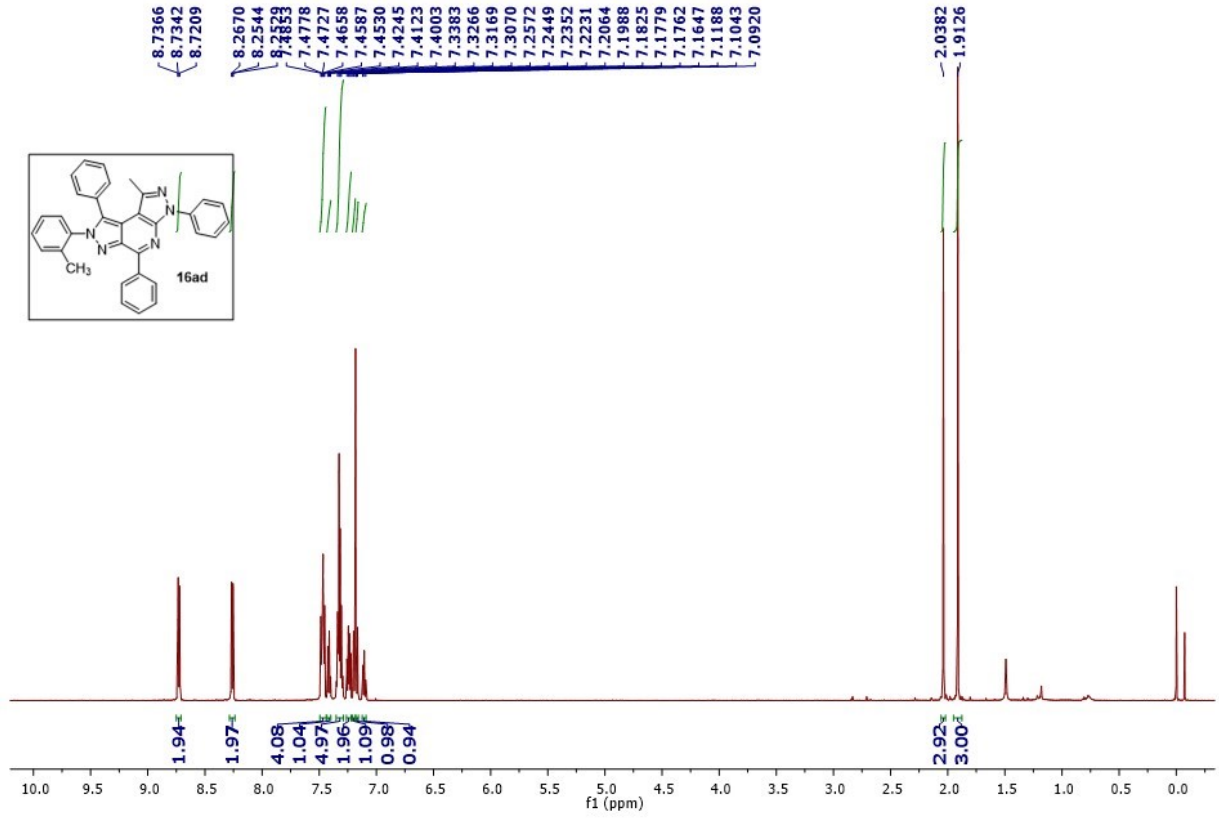
^{13}C NMR of Compound 16ac



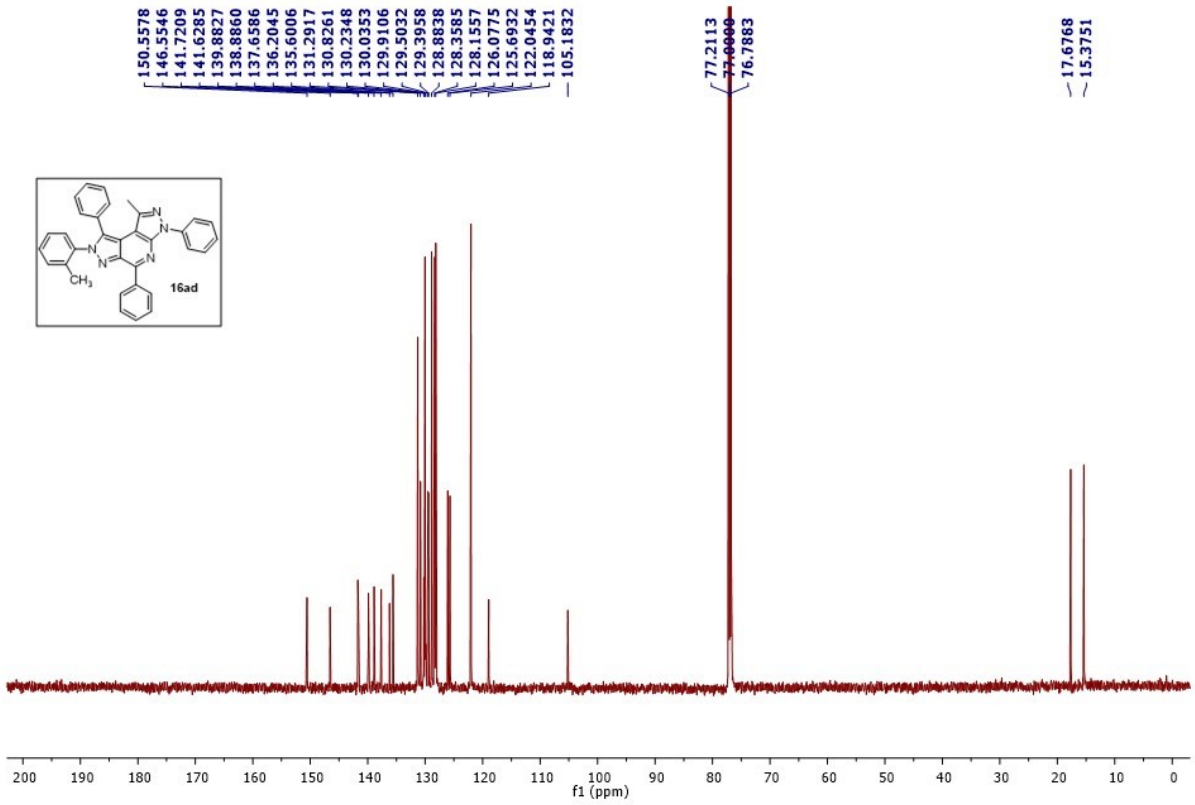
HRMS of Compound 16ac



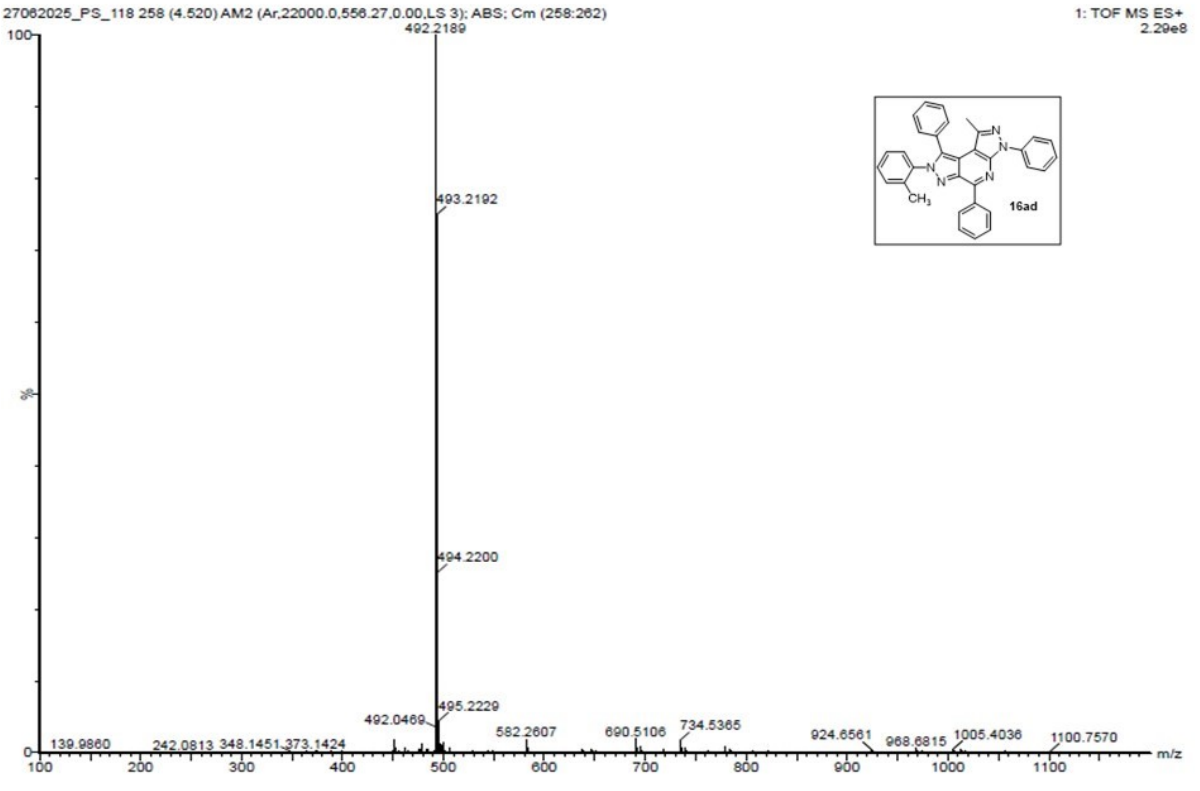
^{1}H NMR of Compound 16ad



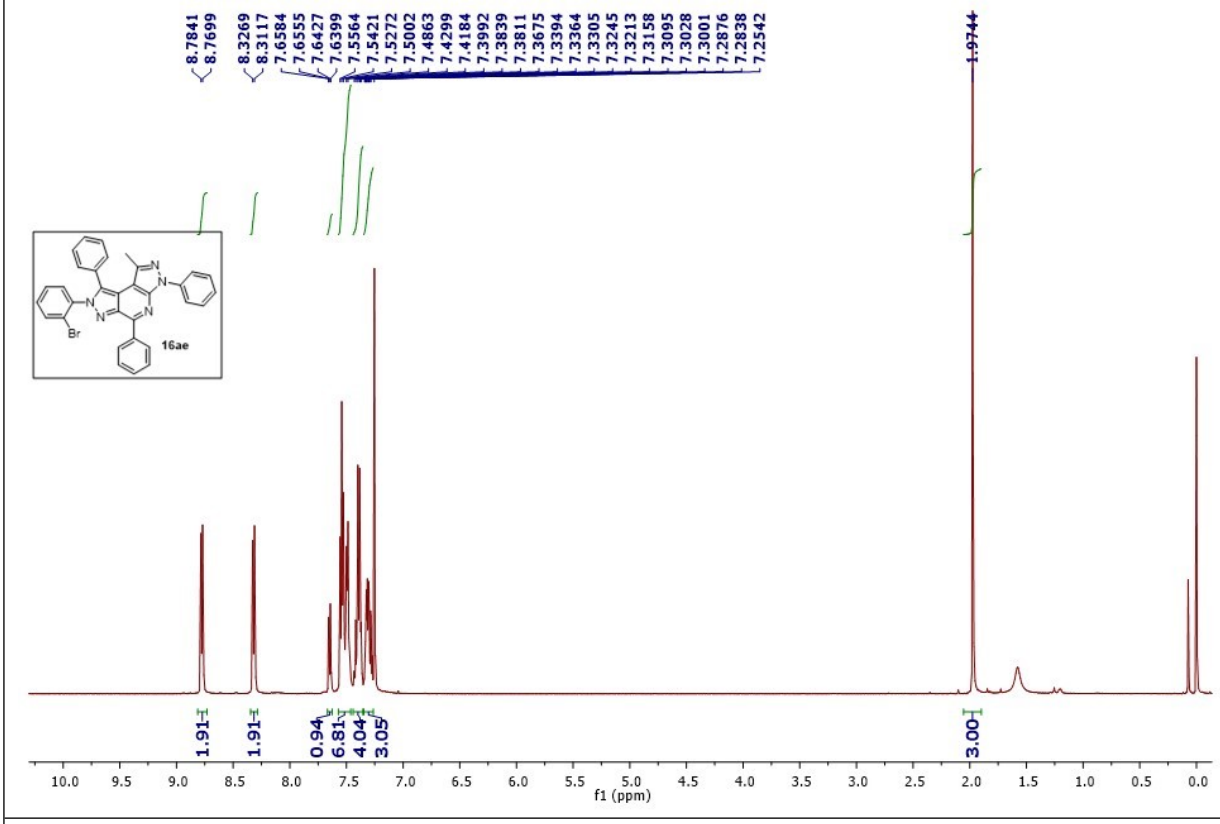
^{13}C NMR of Compound 16ad



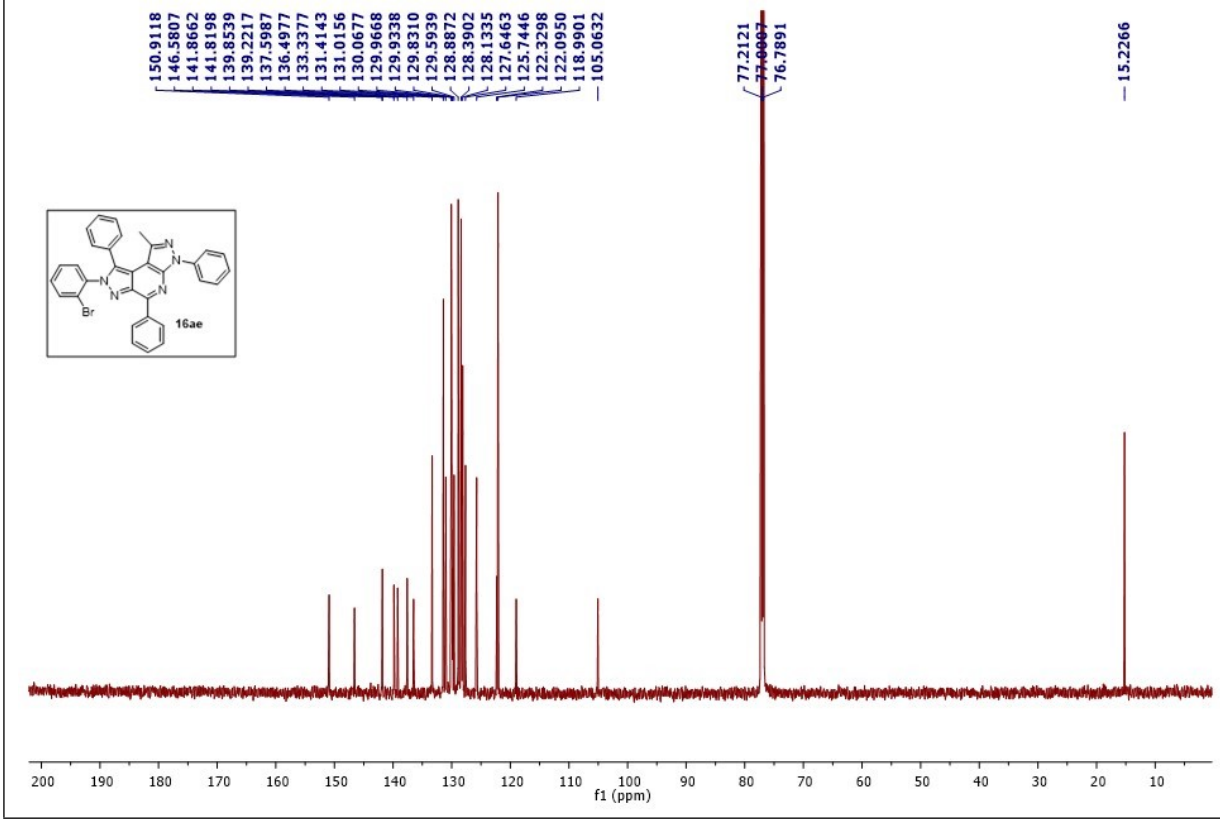
HRMS of Compound 16ad



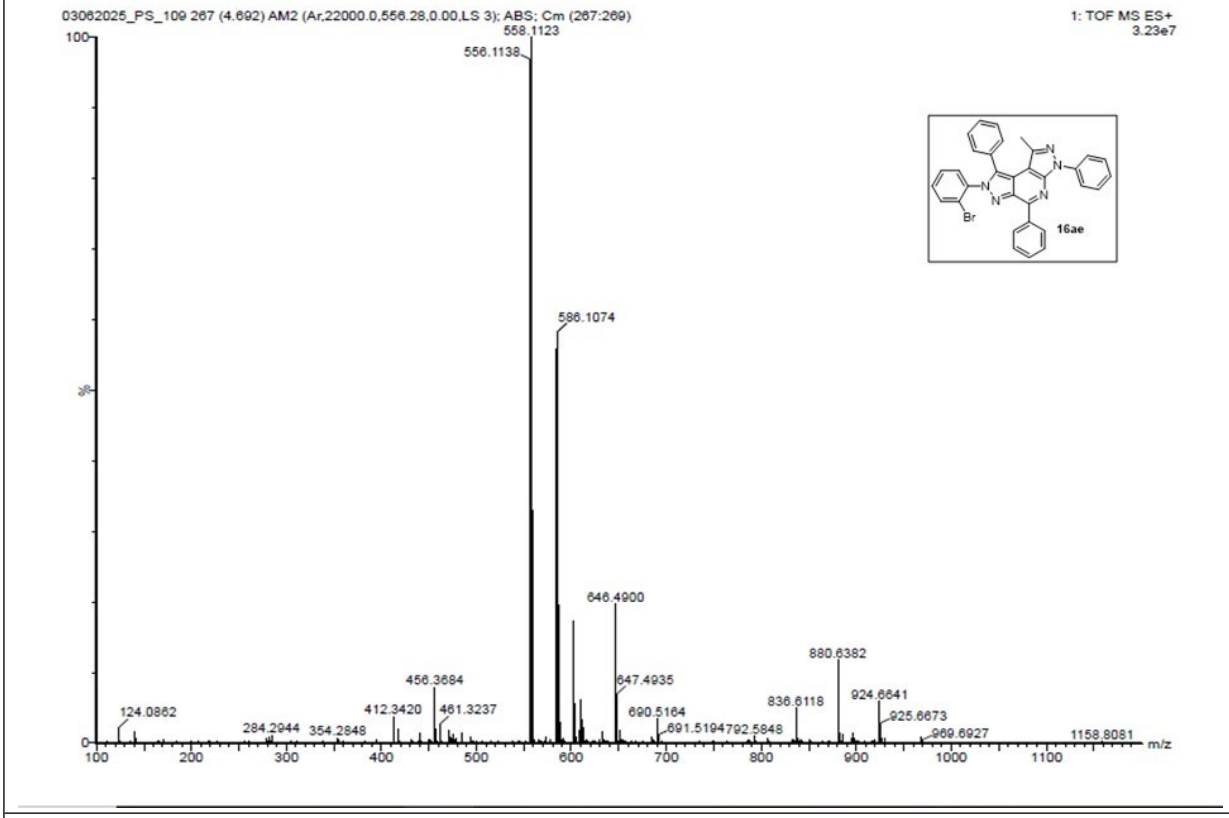
^{1}H NMR of Compound 16ae



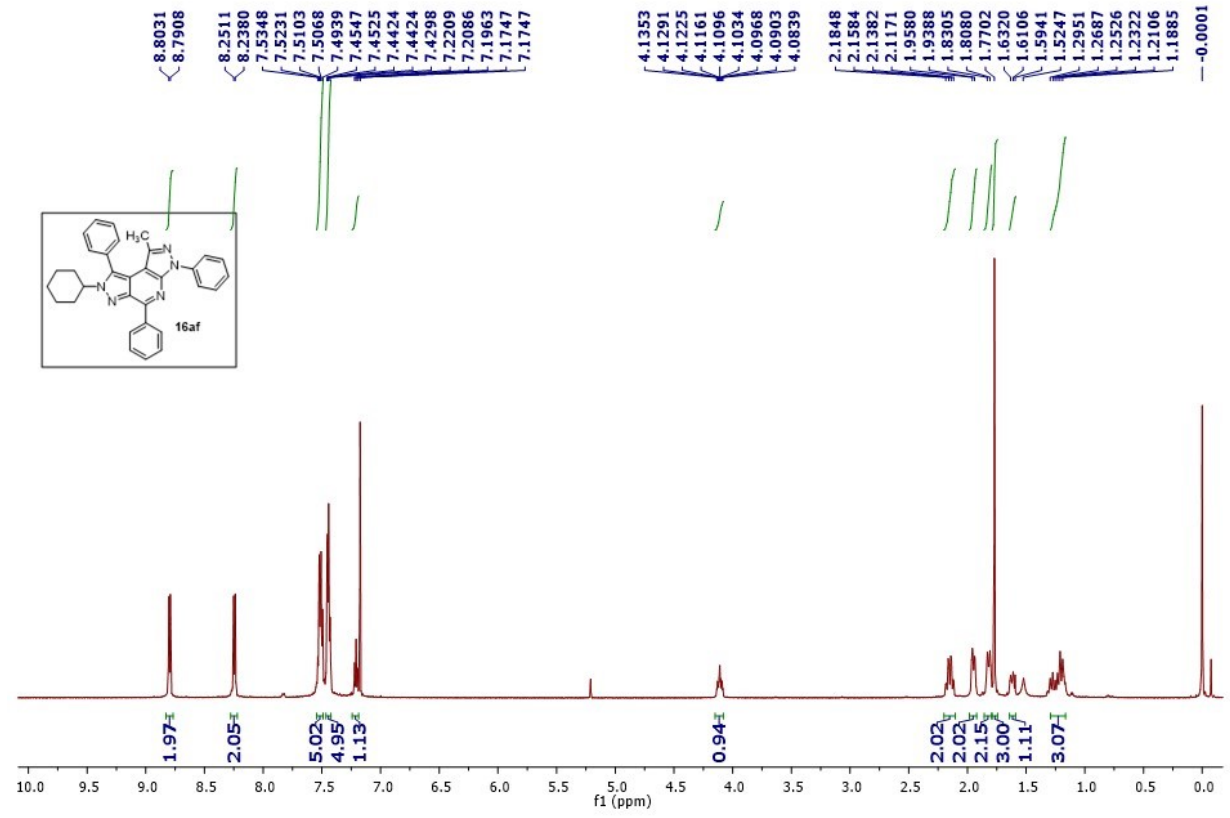
^{13}C NMR of Compound 16ae



HRMS of Compound 16ae



^{1}H NMR of Compound 16af



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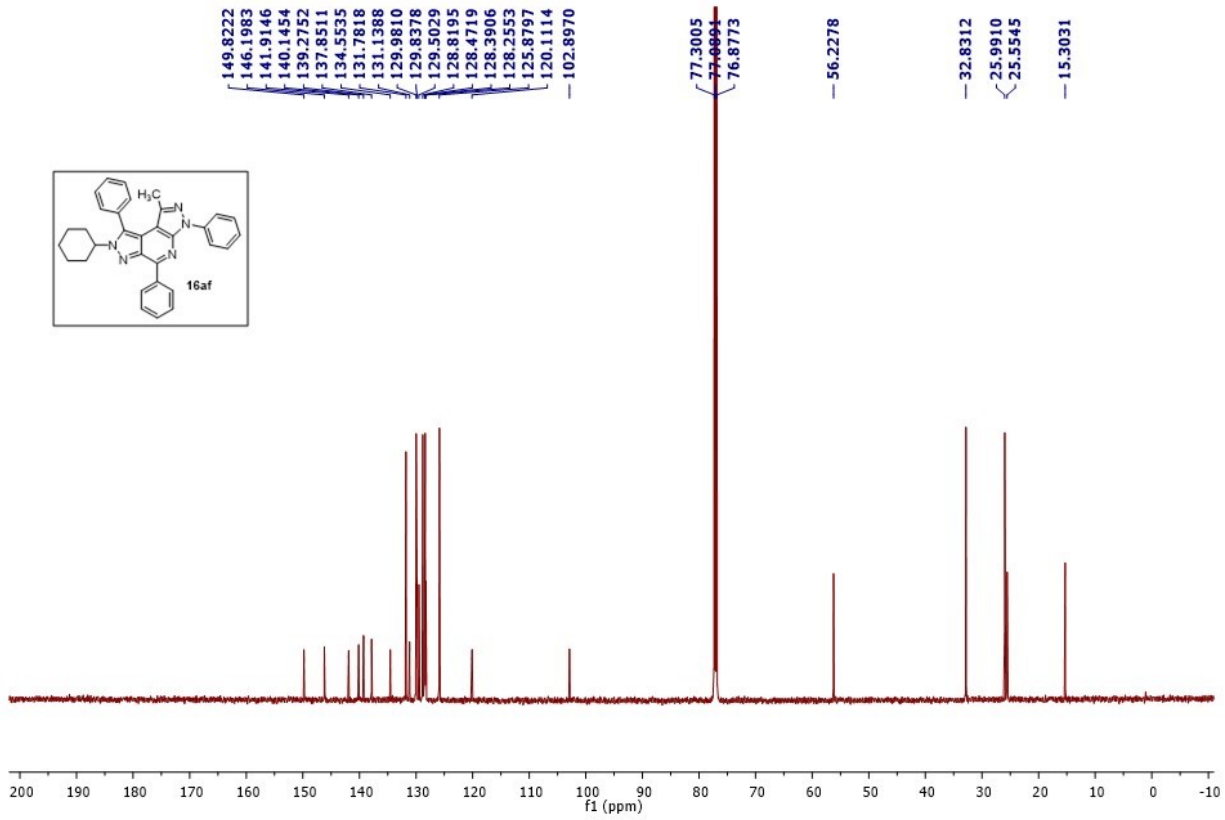
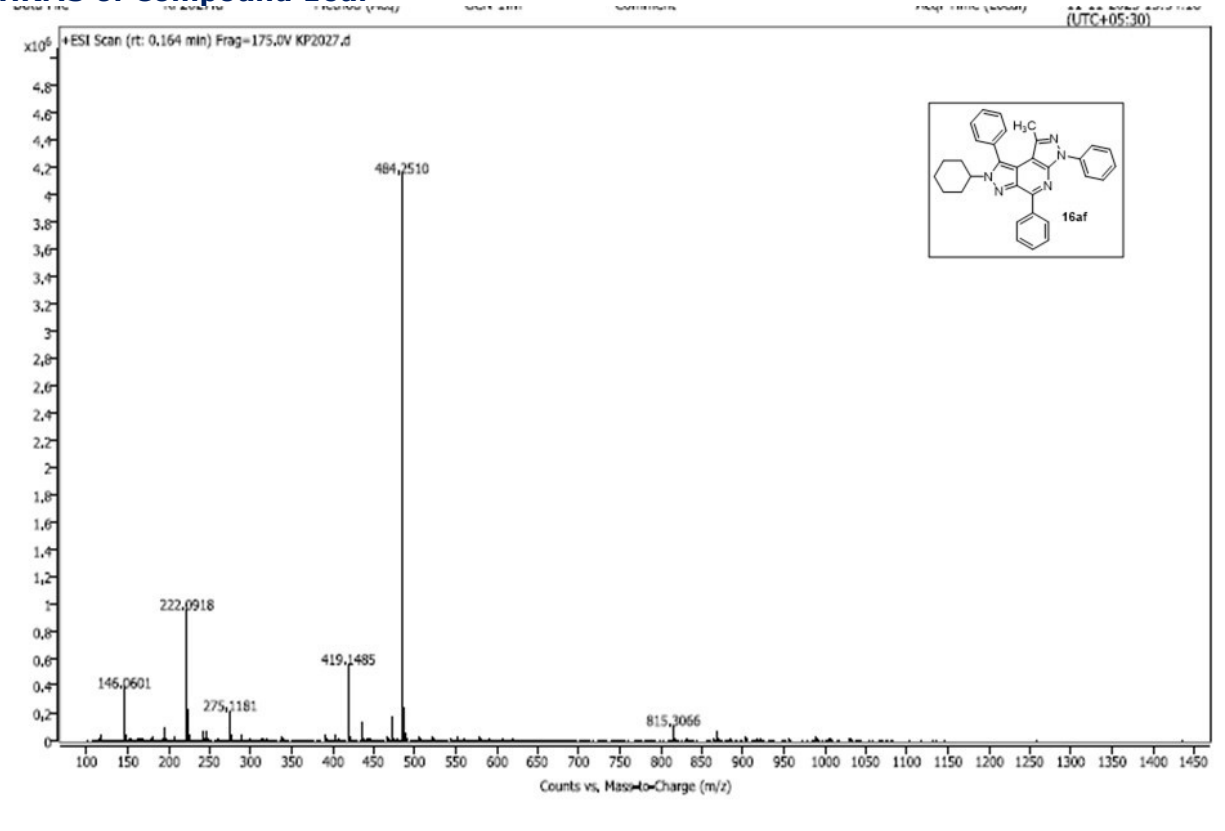
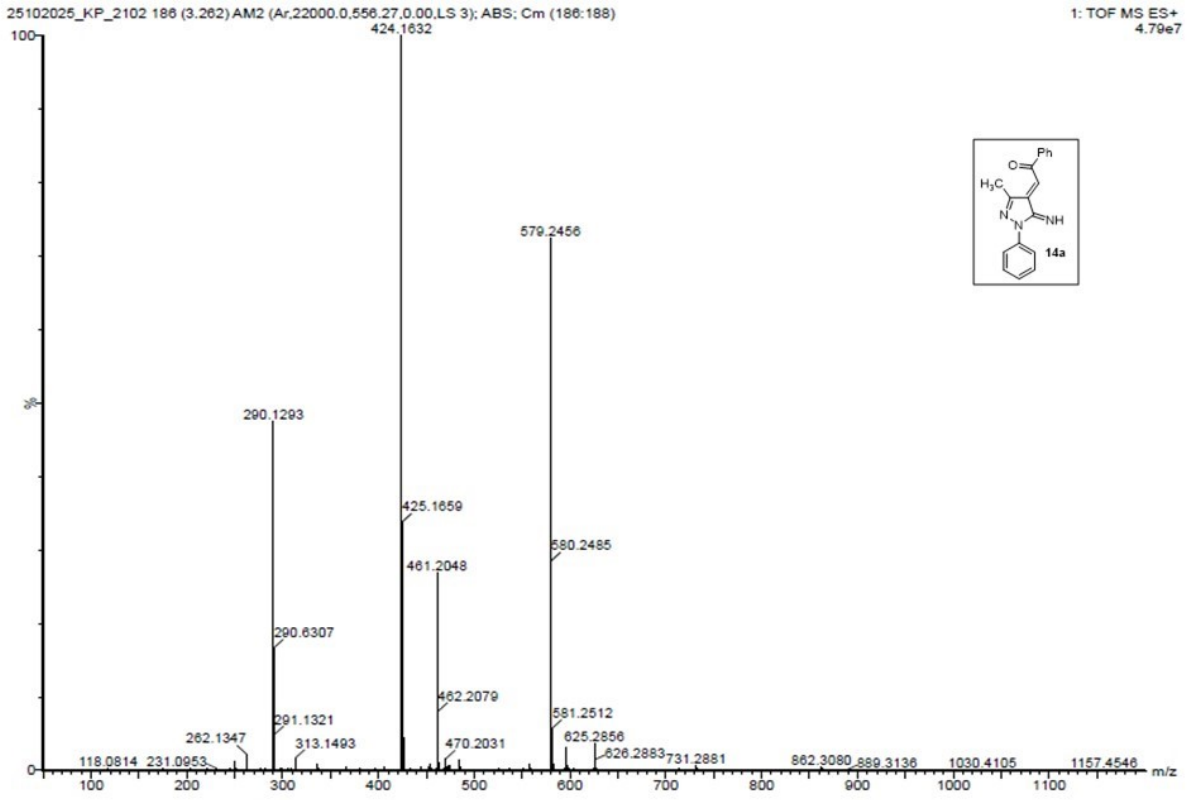


HRMS of Compound 16af



HRMS of Compound 14a



HRMS of Compound 15a