Supporting Information

Org. Commun. X:X (202X) XX-XX

A catalyst-free and eco-friendly approach to synthesis of 1,8-naphthyridines *via* natural deep eutectic solvents

Rupali A. Vadak [1], Ravi Varala[2*] and Pramod S. Kulkarni[1*]

[1]*Department of Chemistry and Post Graduate Research Center in Organic Chemistry, Hutatma Rajguru Mahavidyalaya, Rajgurunagar, Pune-410505 Maharashtra, India (Affiliated to Savitribai Phule Pune University, Pune-411007)*

[2]*Scrips Pharma, Mallapur, Hyderbabd-76, Telangana, India & Research Fellow, INTI International University, Nilai-71800, Malaysia*

Table of Contents — **Page**

* Corresponding authors: Email*:* **pramodskulkarni3@gmail.com** (P.S. Kulkarni); **ravivarala@gmail.com** (R. Varala)

A mixture of 2-aminopyridine (5 mmol), malononitrile (5 mmol), and the corresponding aromatic aldehyde (5 mmol) was added to a lactic acid-based DES prepared from Lactic acid, Maltose, and Amla Juice (Indian gooseberry Juice) in a 3:1:3 molar ratio. The reaction mixture was stirred at room temperature for the appropriate time, as listed in Table 3. The progress of the reaction was monitored by thin-layer chromatography (TLC) using petroleum ether and ethyl acetate (9:1, *v/v*) as the eluent. Upon completion, the reaction mixture was poured into water to precipitate the product. The solid was collected by filtration, washed thoroughly with water, and dried. The crude product was then recrystallized from a mixture of ethanol (4 mL) and water (0.5 mL) to afforded the pure 2-amino-4-phenyl-1,8-naphthyridine-3-carbonitrile.

Solvent Characterization

Density measured by using Pyknometer and Refractive Index measured by using Refractometer

Table S2 : Density measured by using pyknometer and refractive index measured by using Refractometer

Sr. No.	**Deep Eutectic Solvents**	**Test Parameter**		
		Refractive Index at 27^0C	**Density at 27°C g/cc**	**P^H**
1.	Lactic Acid-Maltose-Amla Juice	1.309	1.1820	1.37
2.	Lactic Acid -Maltose- Water	1.401	1.1887	2.48
3.	Lactic Acid-Proline-$SnCl_2$	1.447	1.3412	2.56
4.	Lactic Acid- Maltose - Aloe vera Juice	1.310	1.1693	1.39
5.	Lactic Acid - Proline - Aloe Vera Juice	1.309	1.1717	2.60

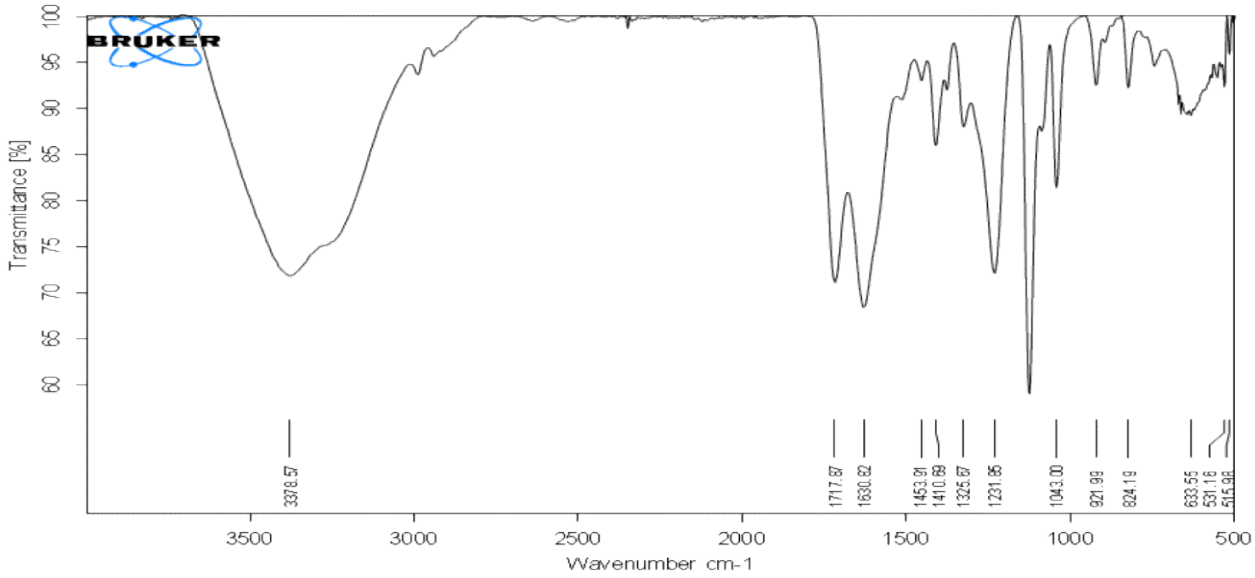


Figure S1: IR Spectra of L1 Lactic Acid-Maltose- Amla Juice

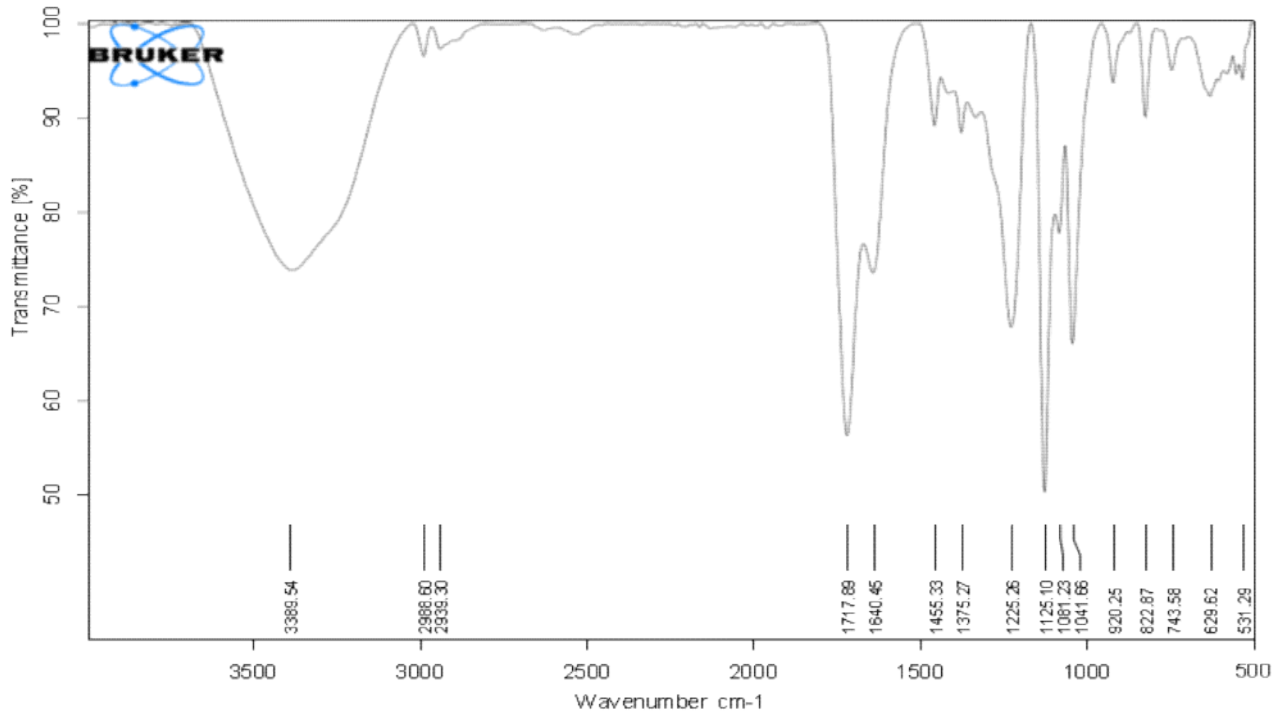


Figure S2: IR Spectra of L2 Lactic Acid-Maltose- Water

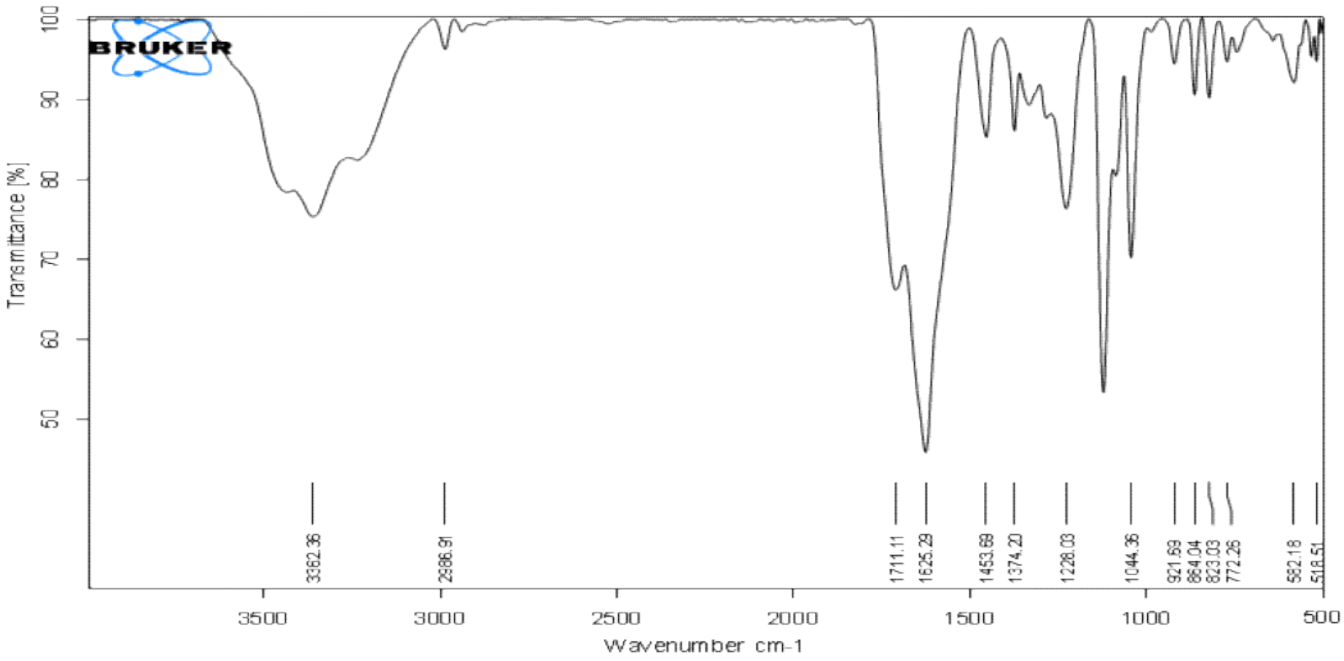


Figure S3: IR Spectra of L3 Lactic Acid-Proline-$SnCl_2$

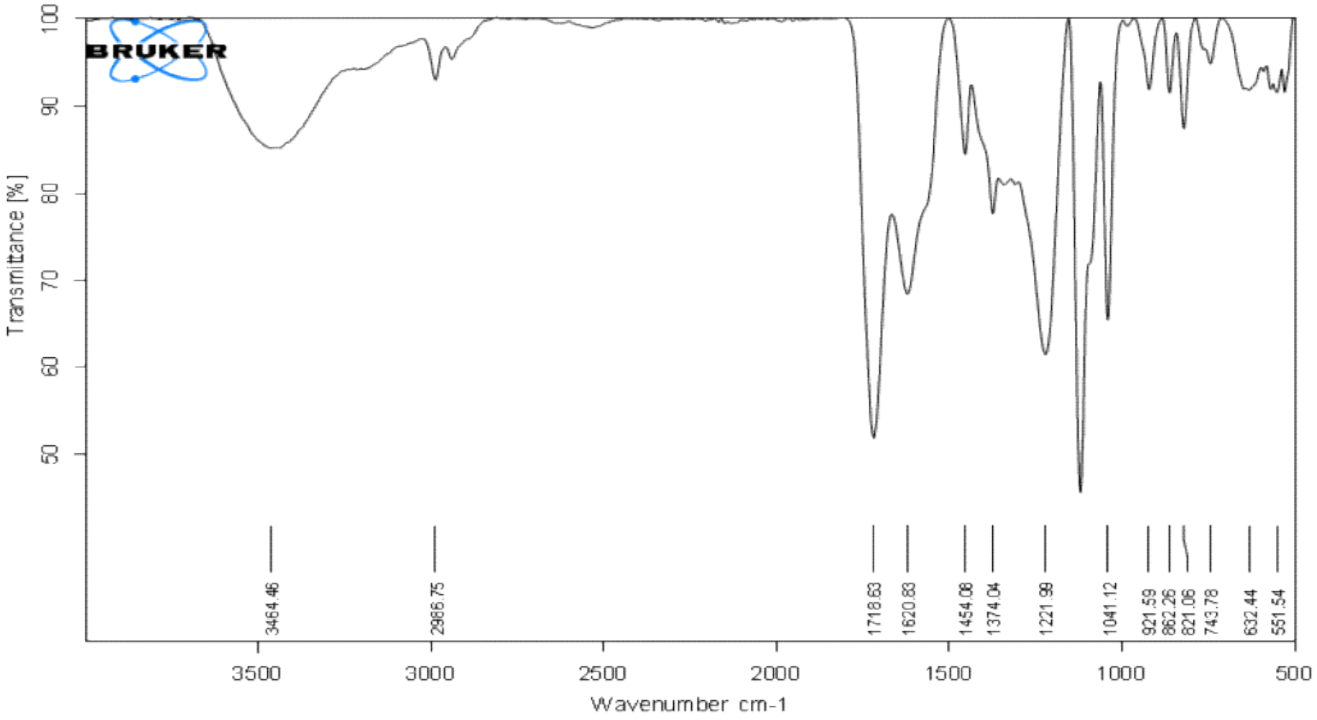


Figure S4: IR Spectra of L4 Lactic Acid-Maltose- Aloe Vera Juice

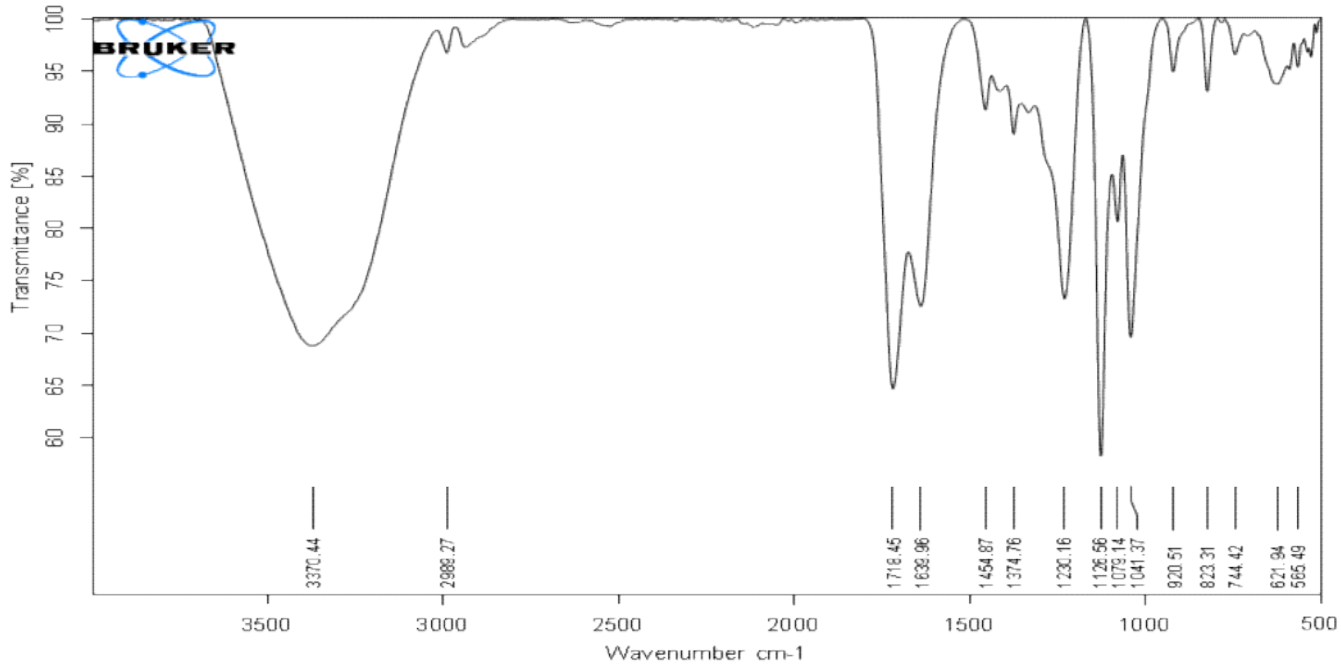


Figure S5: IR Spectra of L5 Lactic Acid-Proline-Aloe Vera Juice

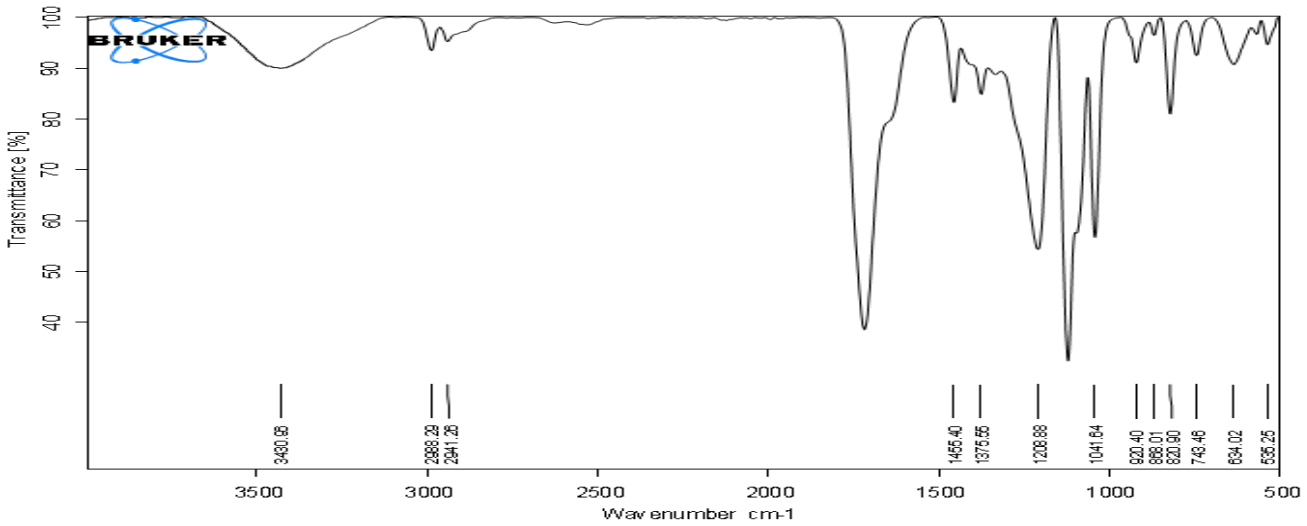


Figure S6: IR Spectra of Pure Lactic Acid

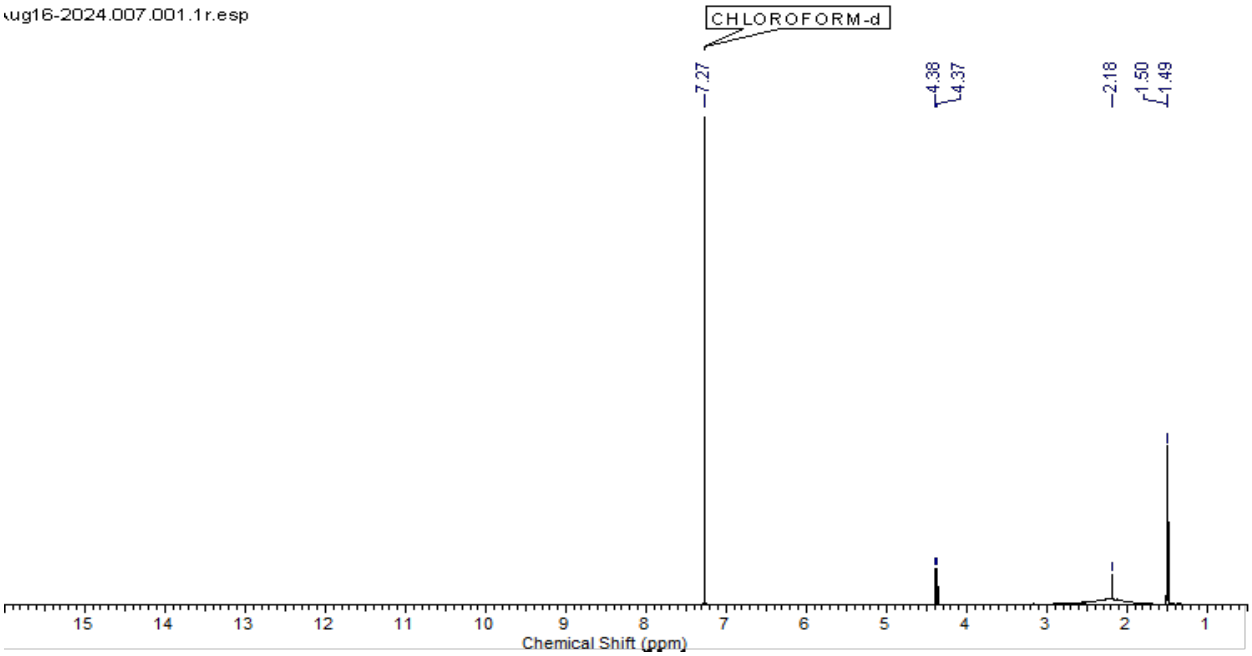


Figure S7: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of L1 Lactic Acid-Maltose- Amla Juice

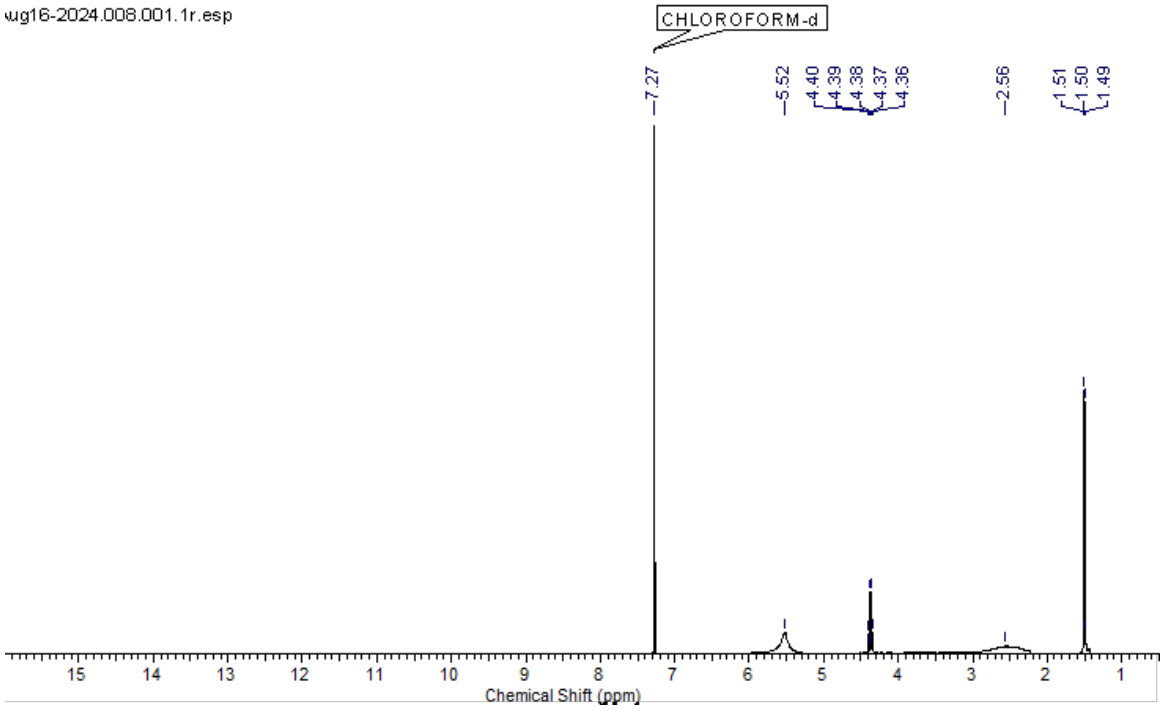


Figure S8: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of L2 Lactic Acid-Maltose- Water

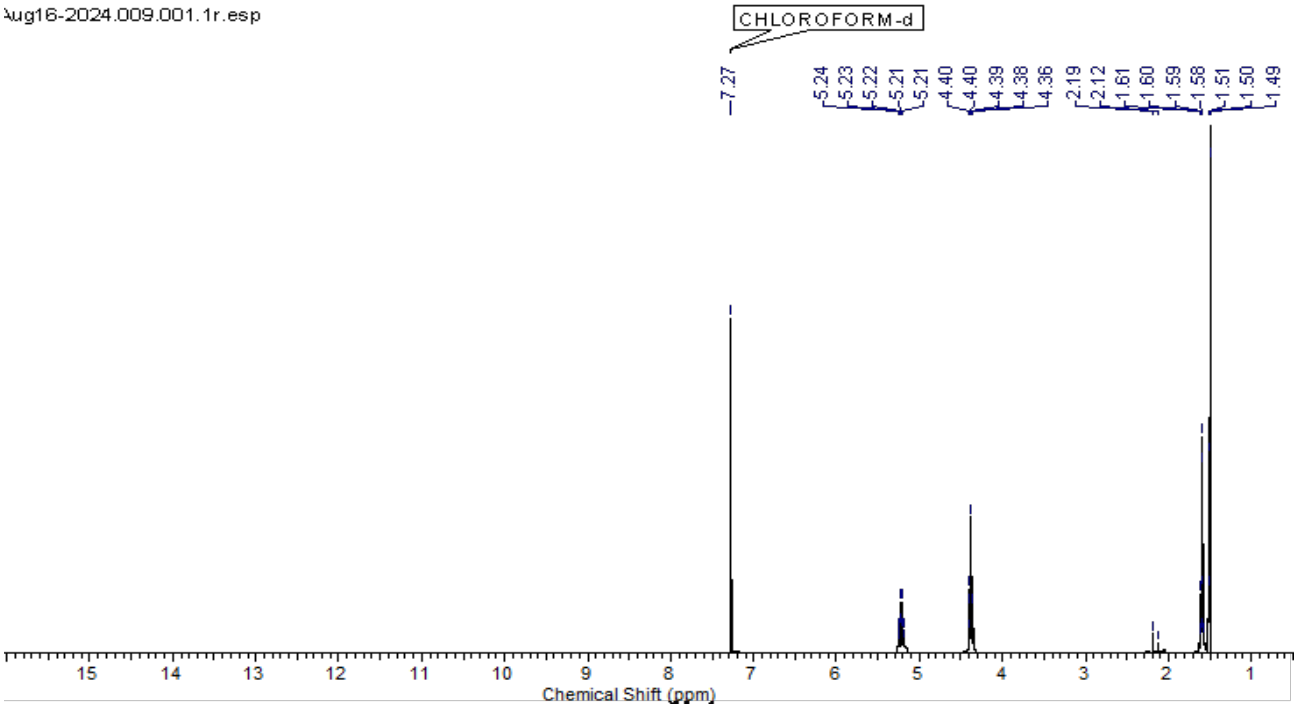


Figure S9: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of L3 Lactic Acid-Proline-$SnCl_2$

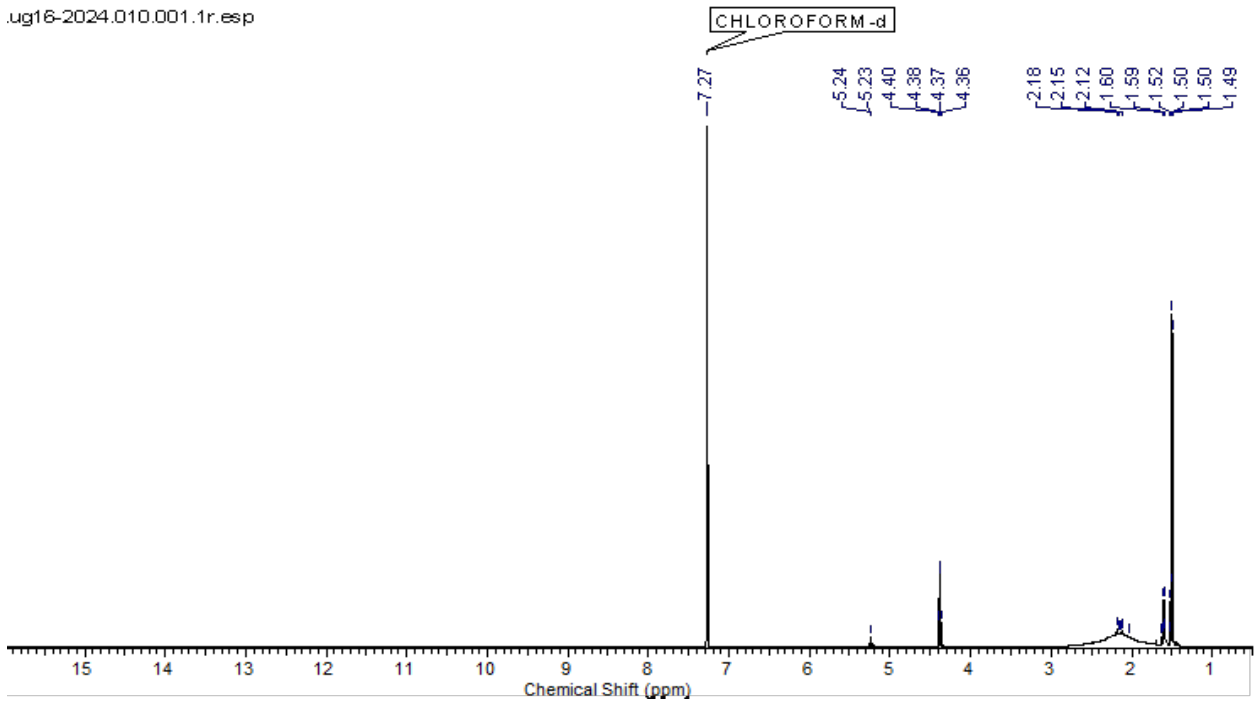


Figure S10: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of L4 Lactic Acid-Maltose- Aloe Vera Juice

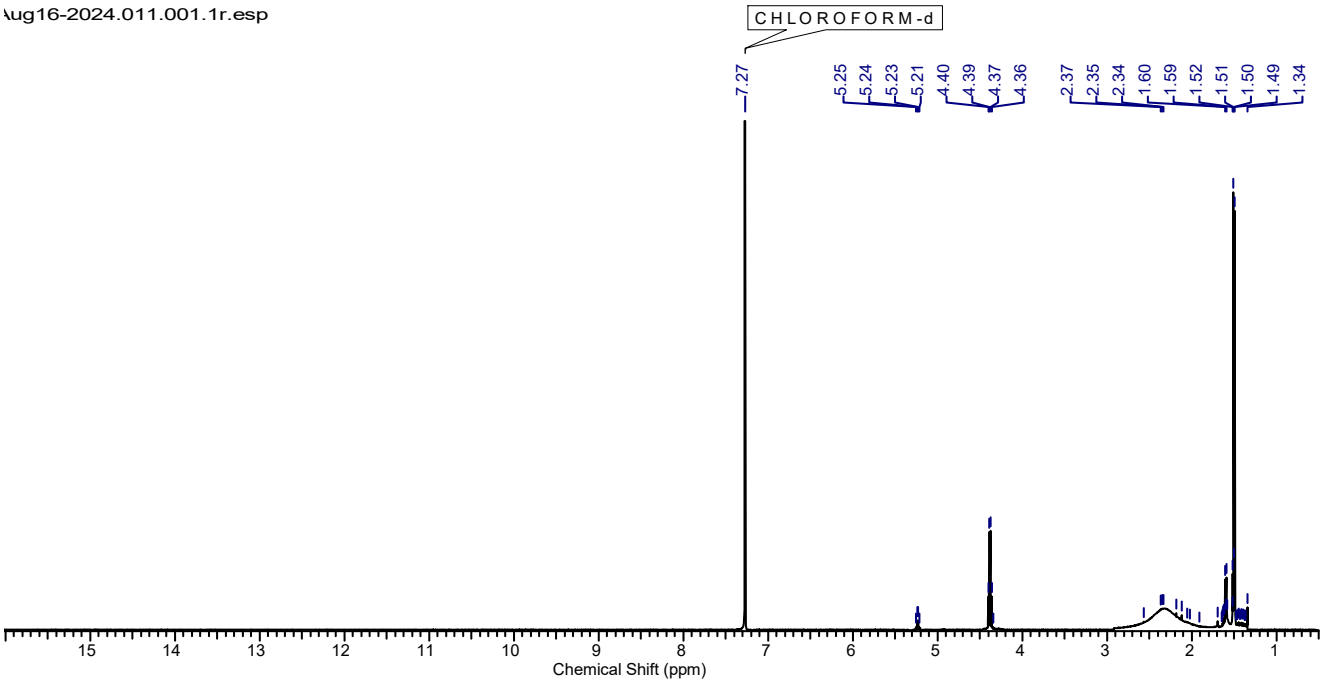


Figure S11: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of L5 Lactic Acid-Proline-Aloe Vera Juice

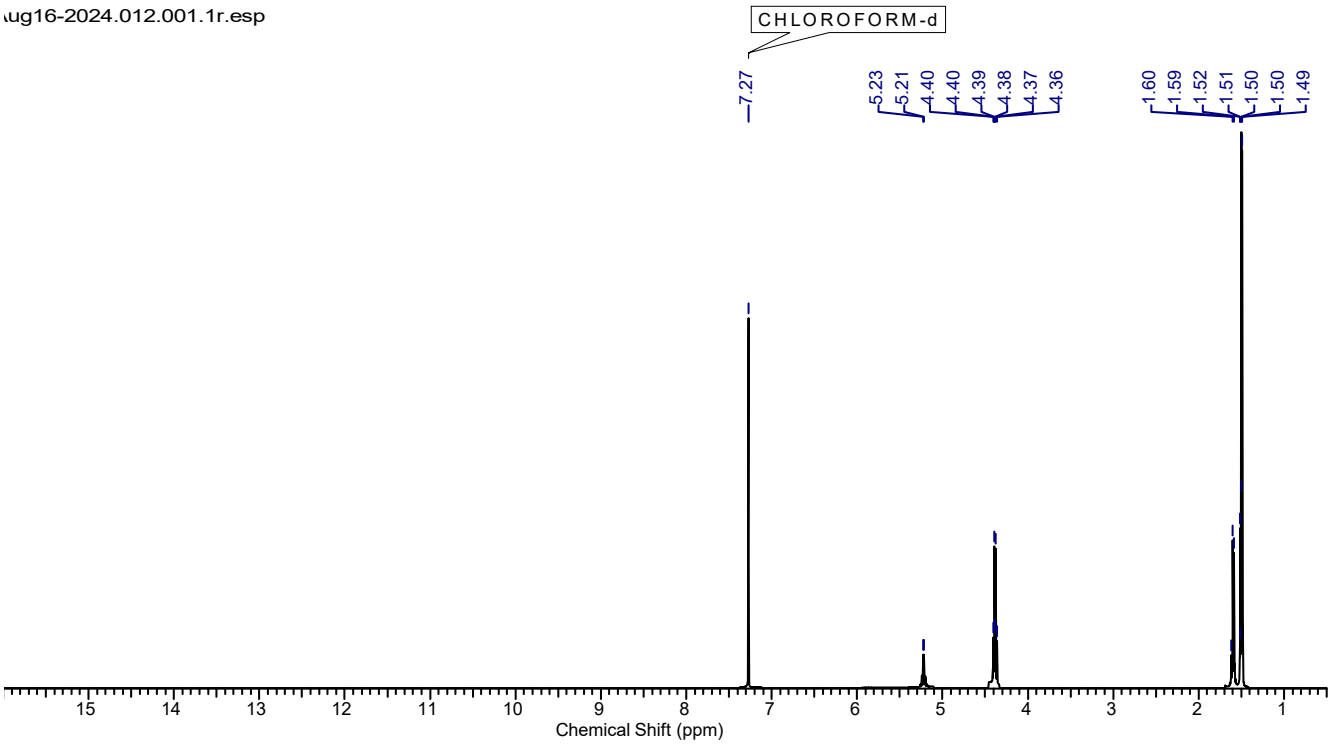


Figure S12: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of Pure Lactic Acid

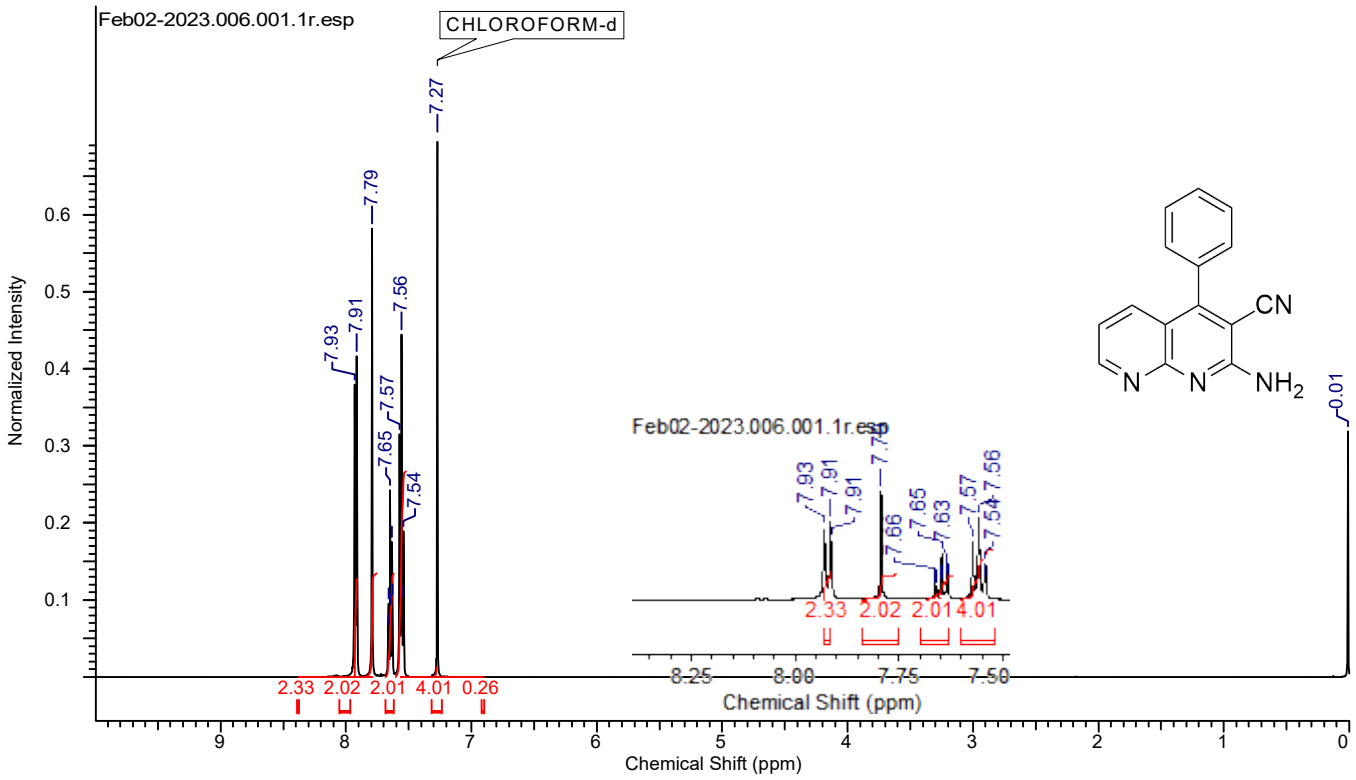


Figure S13: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-Amino-4-phenyl-1,8- naphthyridine-3-carbonitrile (**4a**)

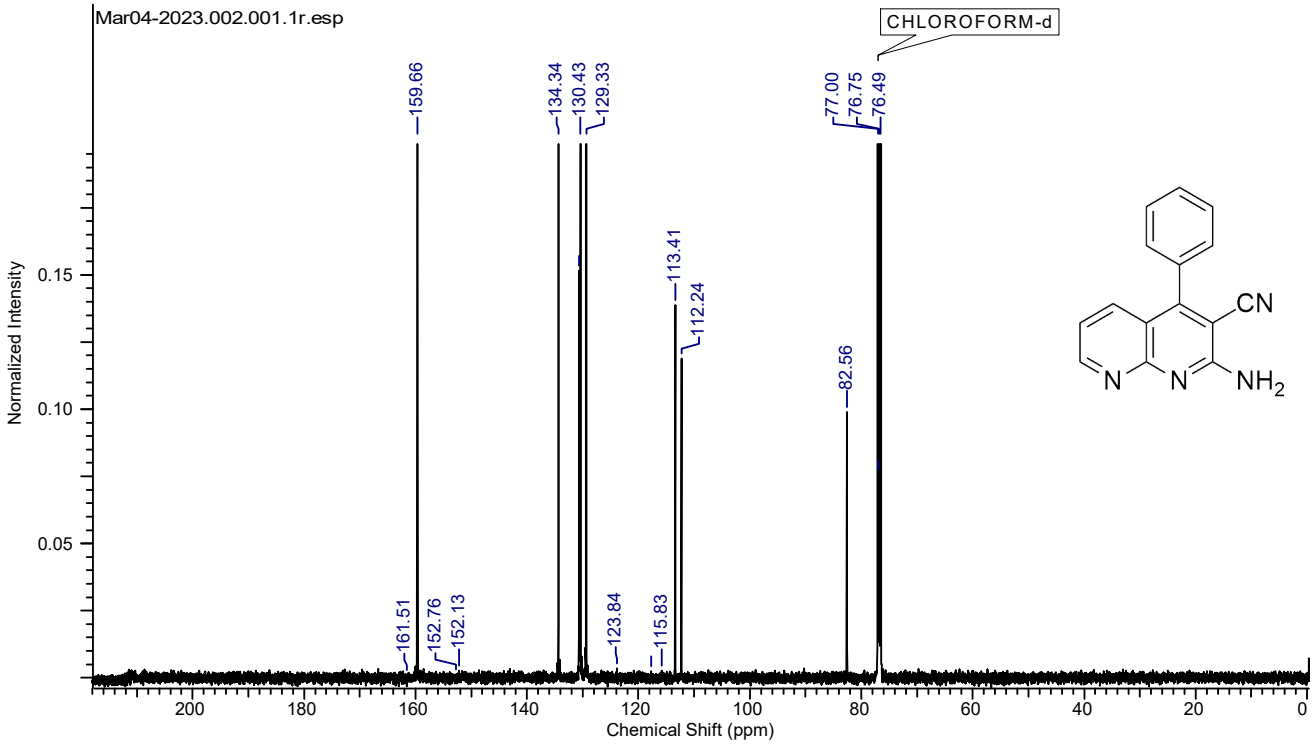


Figure S14: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-Amino-4-phenyl-1,8- naphthyridine-3-carbonitrile (**4a**)

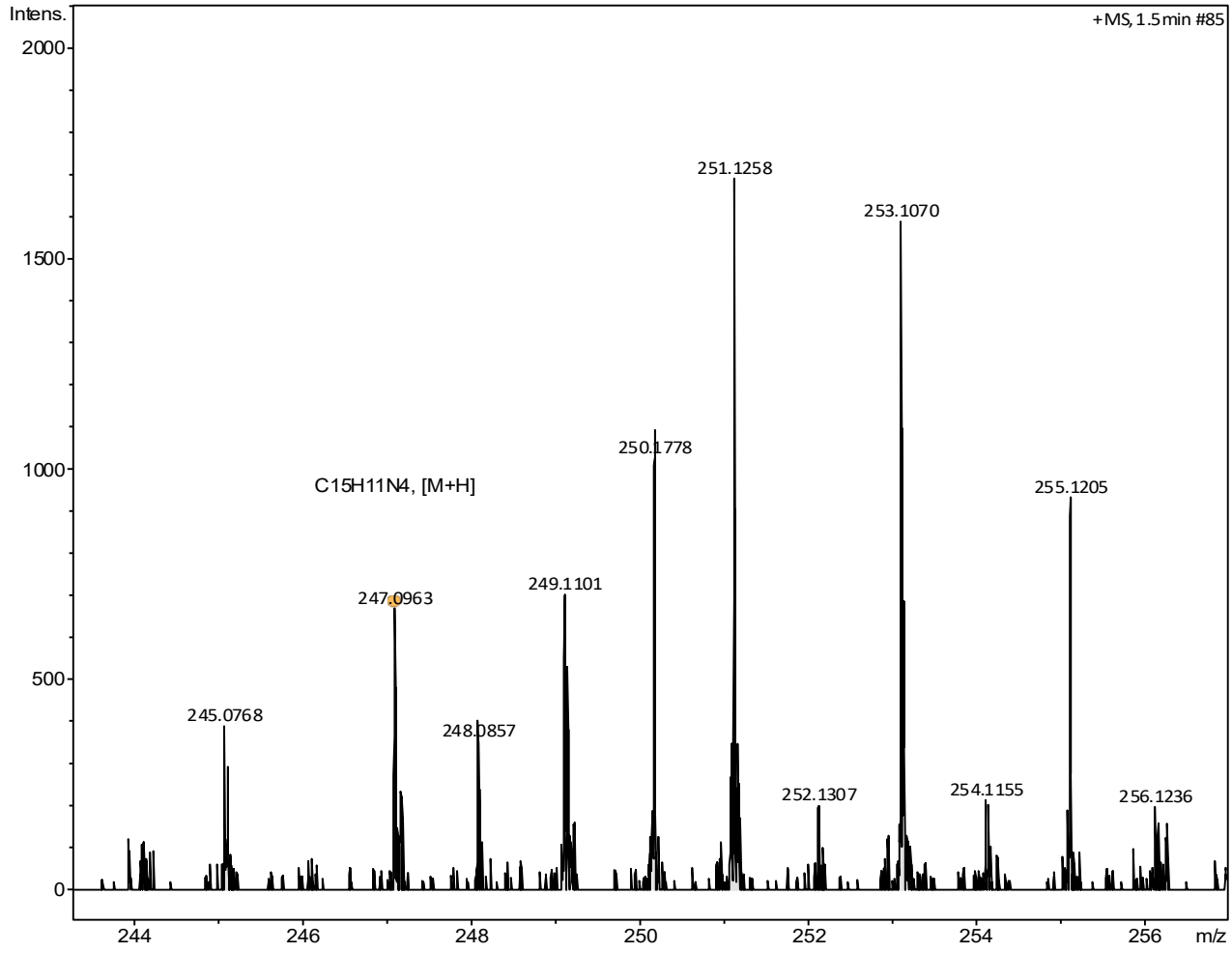
Savitribai Phule Pune University - Central Instrumentation Facility

Analysis Info

		Acquisition Date	10/16/2023 5:28:31 PM
Analysis Name	D:\Data\2023\OCT\SPPU COLLEGE\HUTATMA RAJGURU MAHAVIDYALAYA\VADAL RUPALI ASHOK\R1_BC7_01_6446.d		
Method	dlc_ms50-1200mz_10min_0.120ml flow_95b_sept 23.m	Operator	CIF
Sample Name	R1	Instrument	impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	7.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule	Adduct
247.096344	1	C15H11N4	100.00	247.097823	1.5	6.0	599.1	12.5	even	ok	M+H
	2	C11H11N4O3	0.00	247.082567	-13.8	-55.8	607.3	8.5	even	ok	M+H

R1_BC7_01_6446.d

Bruker Compass DataAnalysis 4.2 printed: 10/19/2023 1:31:05 PM by: CIF Nitin S. Kadam Page 1 of 1

Figure S15: HR-ESI-MS Spectrum of **2**-Amino-4-phenyl-1,8- naphthyridine-3-carbonitrile (**4a**)

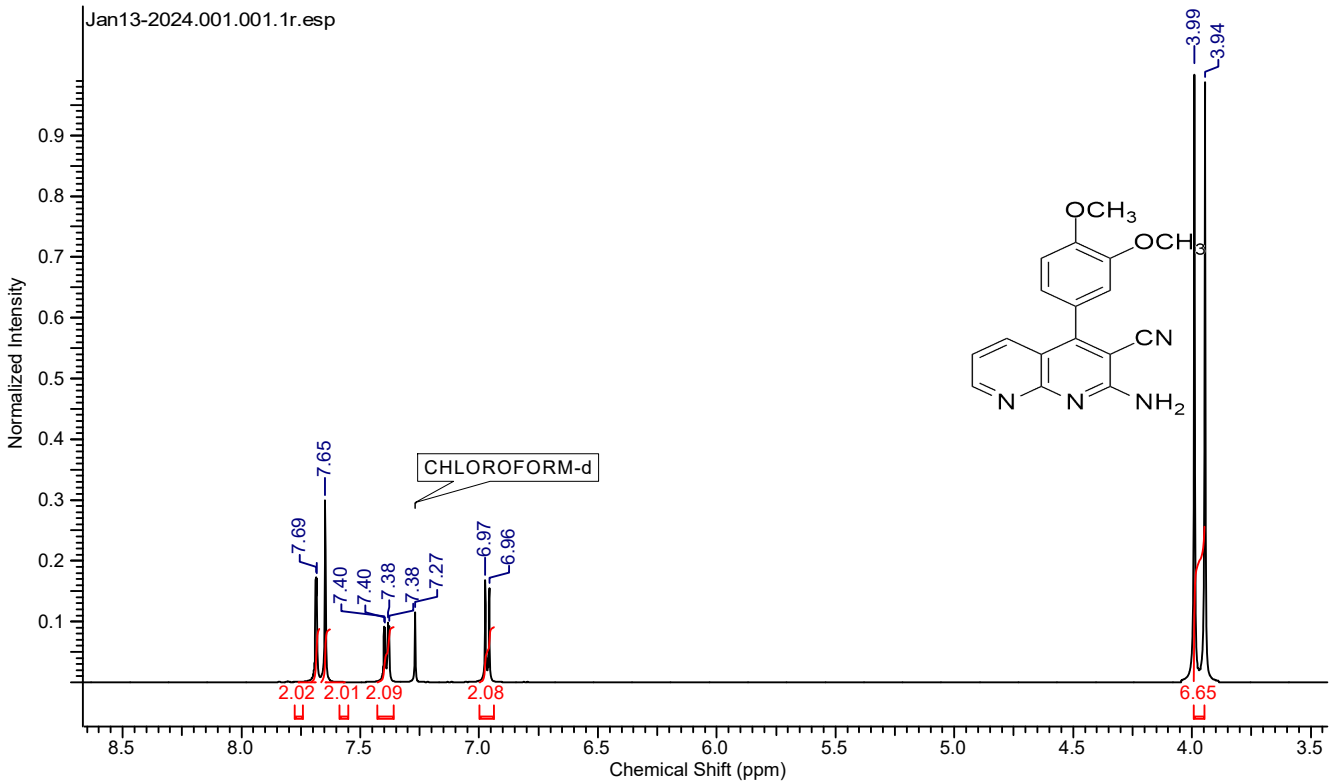


Figure S16: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(3,4-dimethoxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4b**)

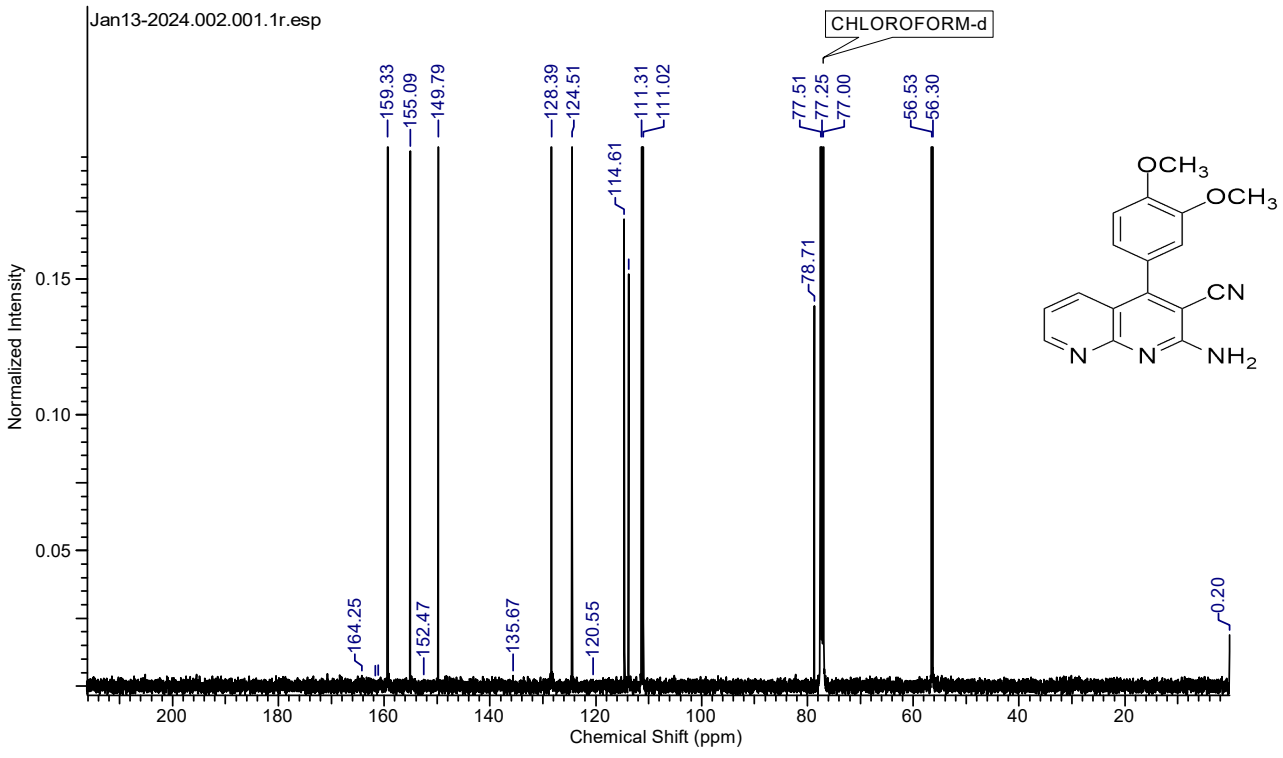


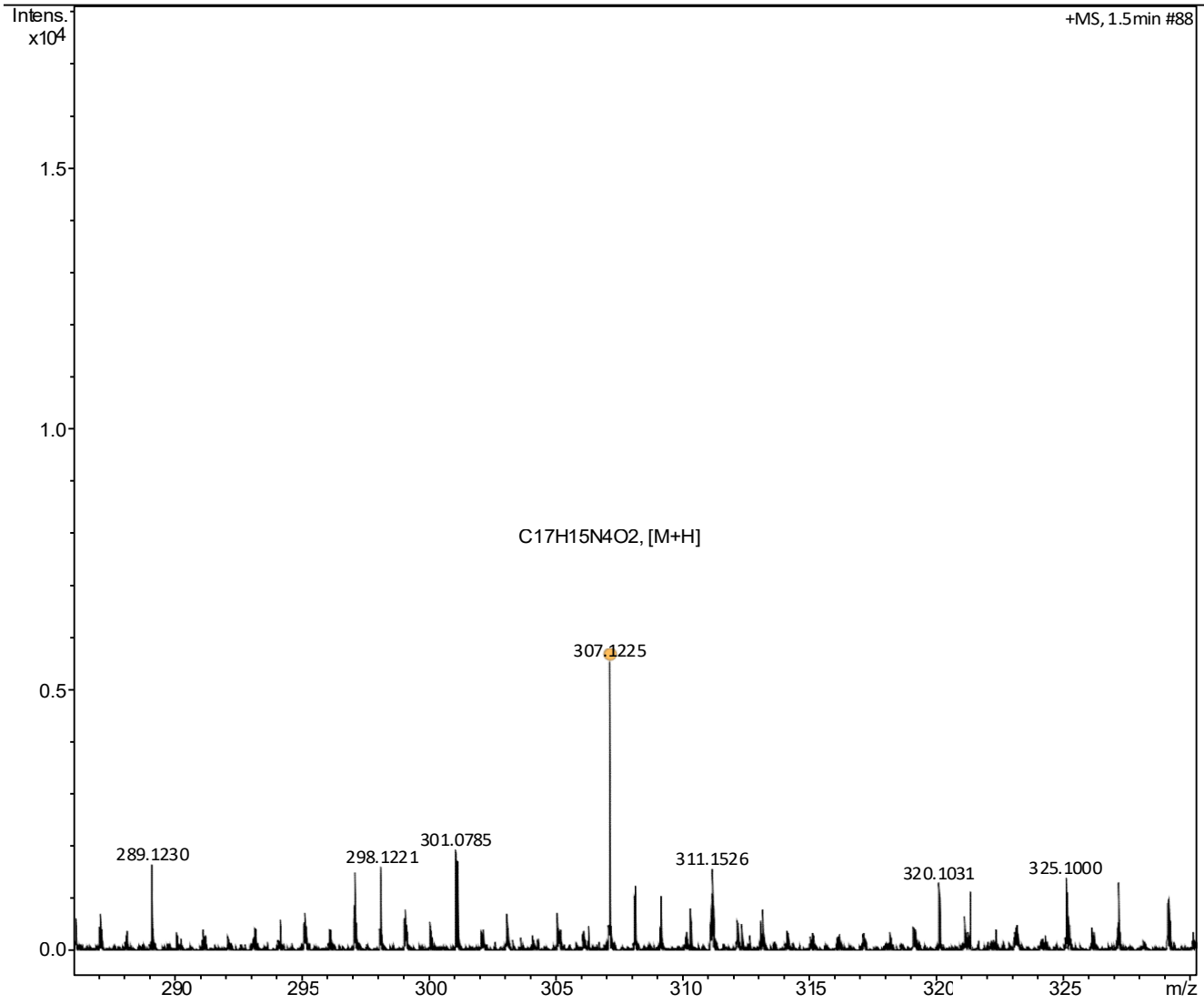
Figure S17: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(3,4-dimethoxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4b**)

Analysis Info

Analysis Name	D:\Data\2024\JAN\SPPU COLLEGE\H. R. M. Rajgurunagar\RUPALI VADAK\D1_RA3_01_6774.d	Acquisition Date	1/12/2024 4:02:21 PM
Method	dlc_ms20-1200mz_10min_0.120ml flow_90b_dec 23.m	Operator	Nitin S. Kadam CIF
Sample Name	D1	Instrument	impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	20 m/z	Set End Plate Offset	-500 V	Set Dry Gas	7.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule	Adduct
307.122504	1	C17H15N4O2	100.00	307.118952	-3.6	-11.6	95.2	12.5	even	ok	M+H
406.335028	1	C15H40N11O2	100.00	406.336096	1.1	2.6	30.5	1.5	even	ok	M+H
418.181797	1	C14H20N13O3	71.16	418.180658	-1.1	-2.7	18.0	11.5	even	ok	M+H

Figure S18: HR-ESI-MS Spectrum of 2-Amino-4-(3,4-dimethoxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4b**)

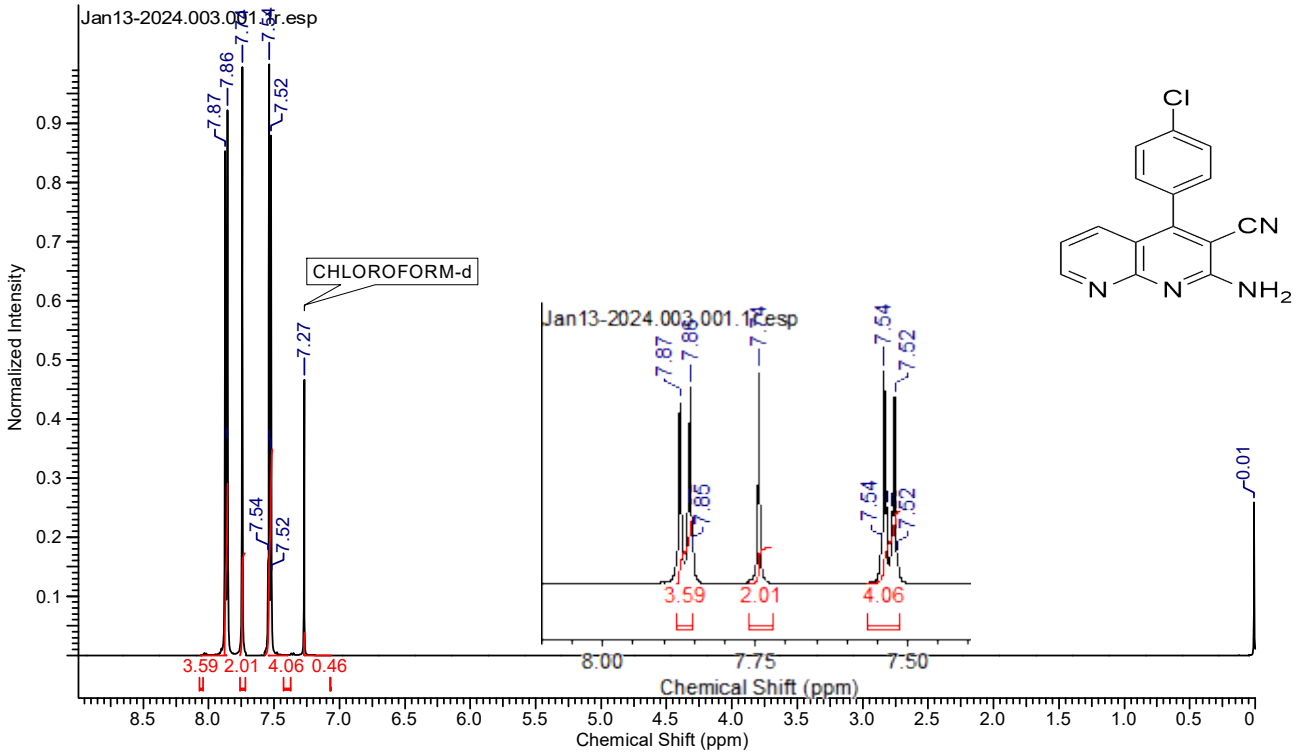


Figure S19: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(4-Chlorophenyl)-1,8-naphthyridine-3-carbonitrile (**4c**)

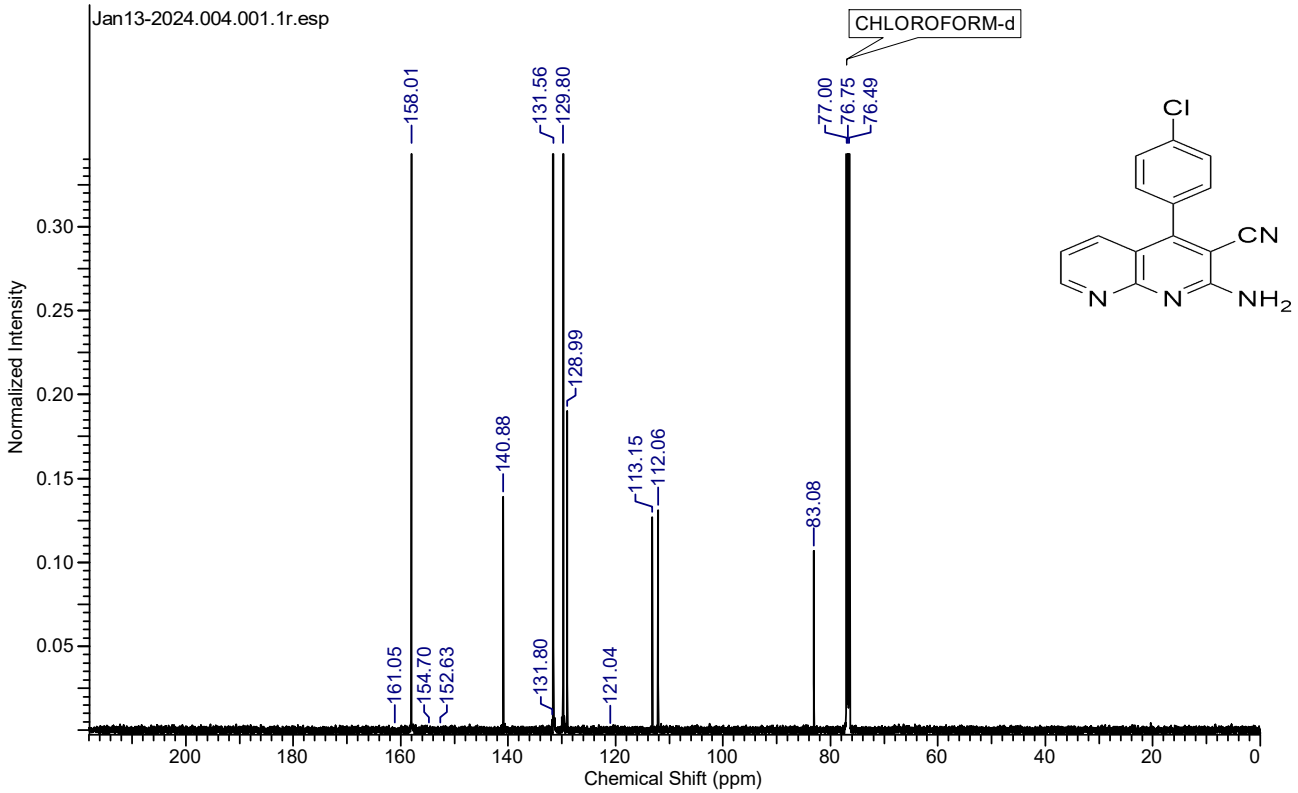


Figure S20: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(4-Chlorophenyl)-1,8-naphthyridine-3-carbonitrile (**4c**)

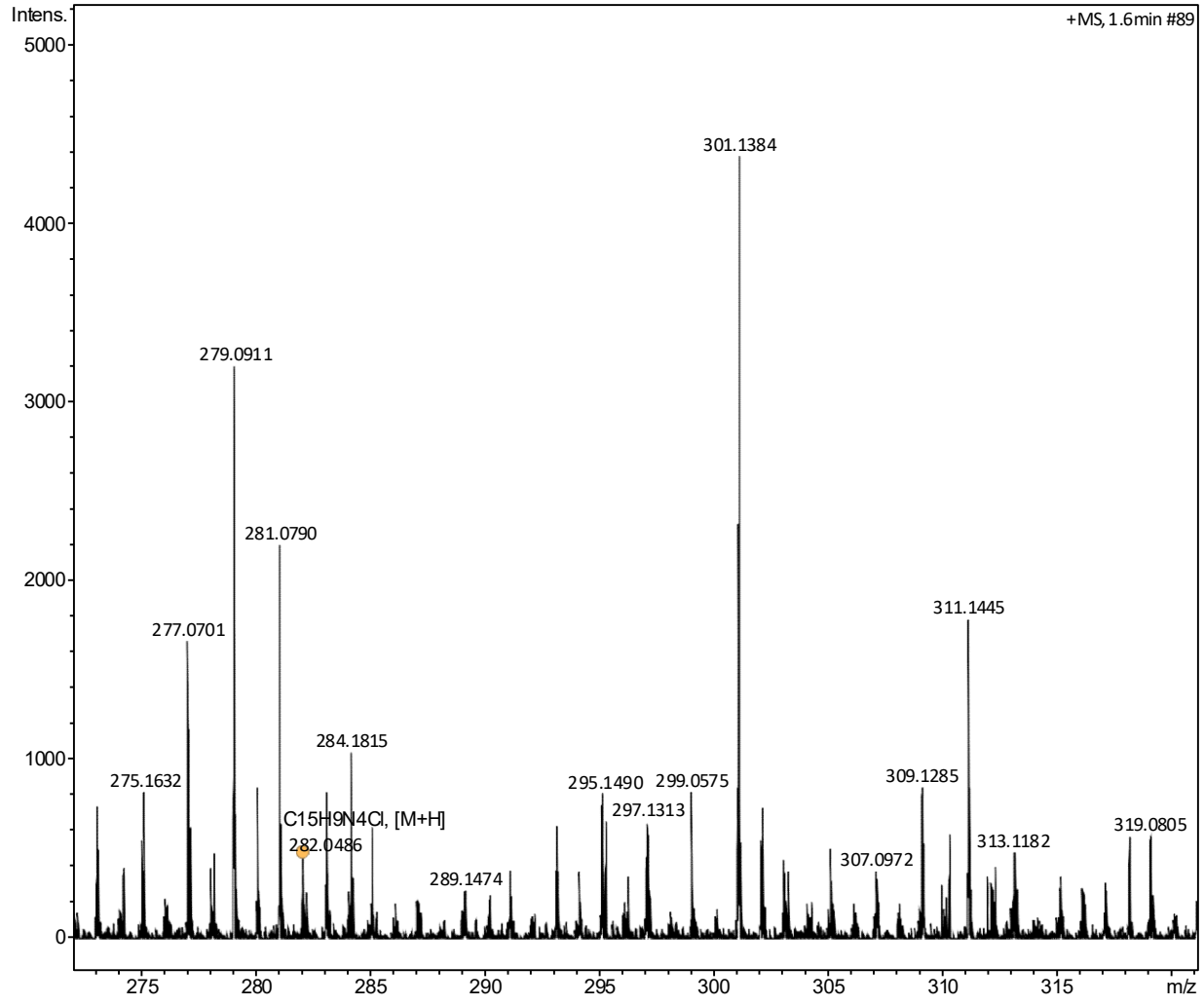
Savitribai Phule Pune University - Central Instrumentation Facility

Analysis Info

		Acquisition Date	1/12/2024 3:04:36 PM
Analysis Name	D:\Data\2024\JAN\SPPU COLLEGE\H. R. M. Rajgurunagar\RUPALI VADAK\D2_RE2_01_6770.d		
Method	dlc_ms20-1200mz_10min_0.120ml flow_90b_dec 23.m	Operator	Nitin S. Kadam CIF
Sample Name	D2	Instrument	impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	20 m/z	Set End Plate Offset	-500 V	Set Dry Gas	7.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



D2_RE2_01_6770.d

Bruker Compass DataAnalysis 4.2 printed: 1/12/2024 4:29:33 PM by: Nitin S. Kadam CIF Page 1 of 1

Figure S21: HR-ESI-MS Spectrum of 2-Amino-4-(4-Chlorophenyl)-1,8-naphthyridine-3-carbonitrile (**4c**)

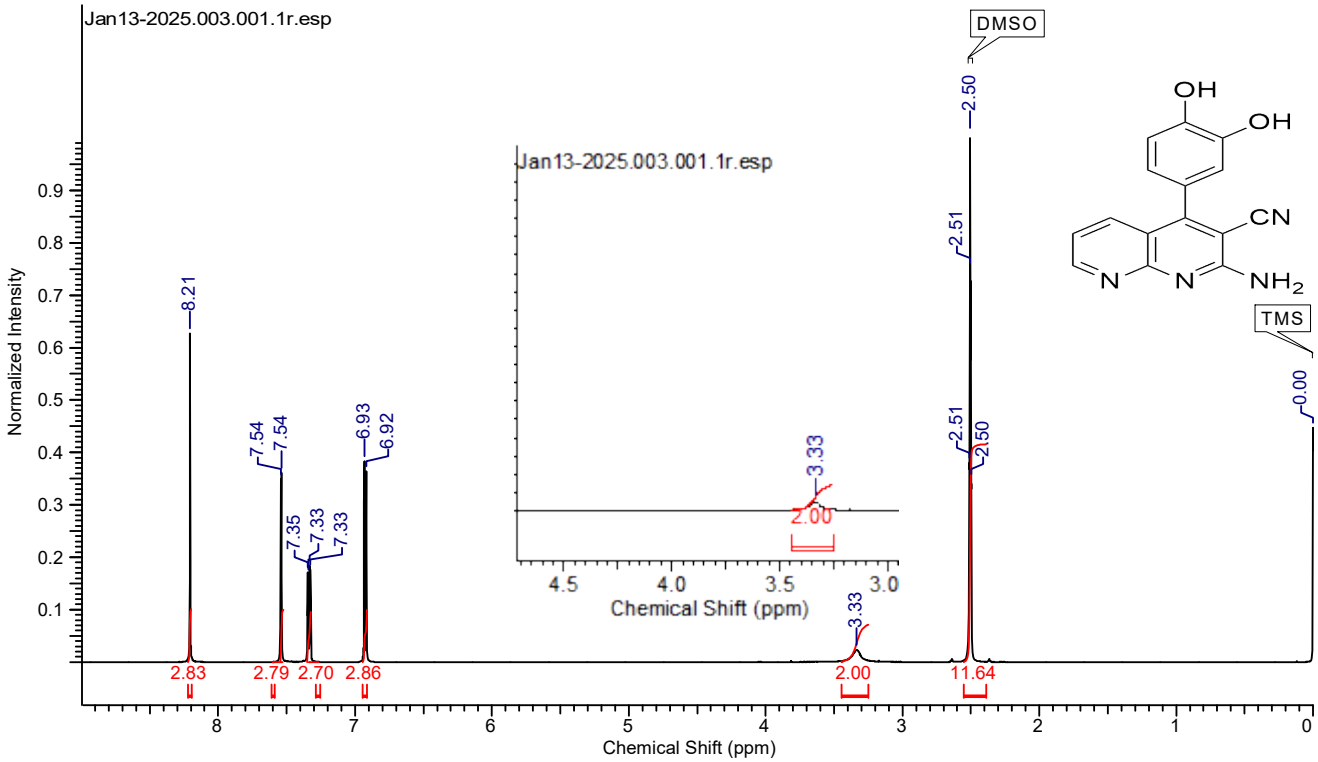


Figure S22: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(3,4-dihydroxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4d**)

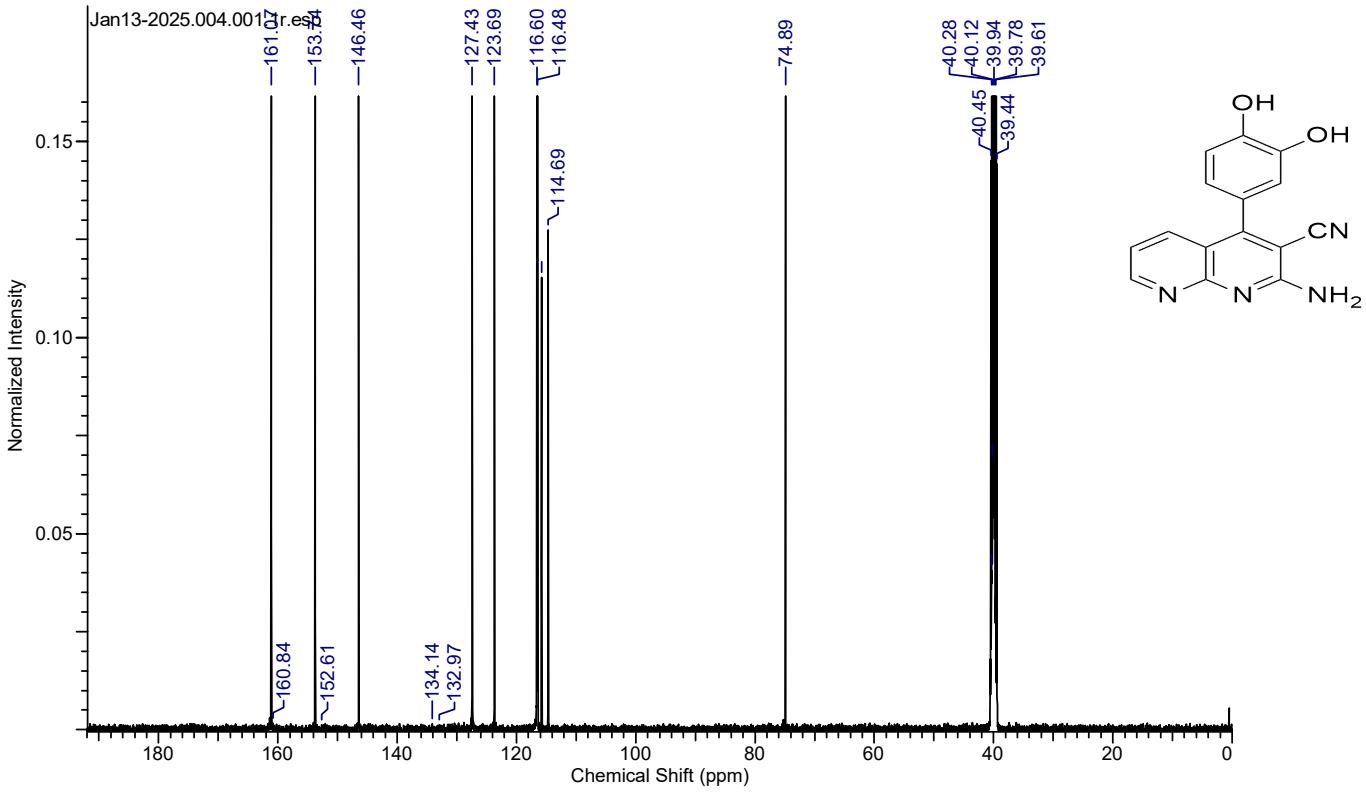


Figure S23: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(3,4-dihydroxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4d**)

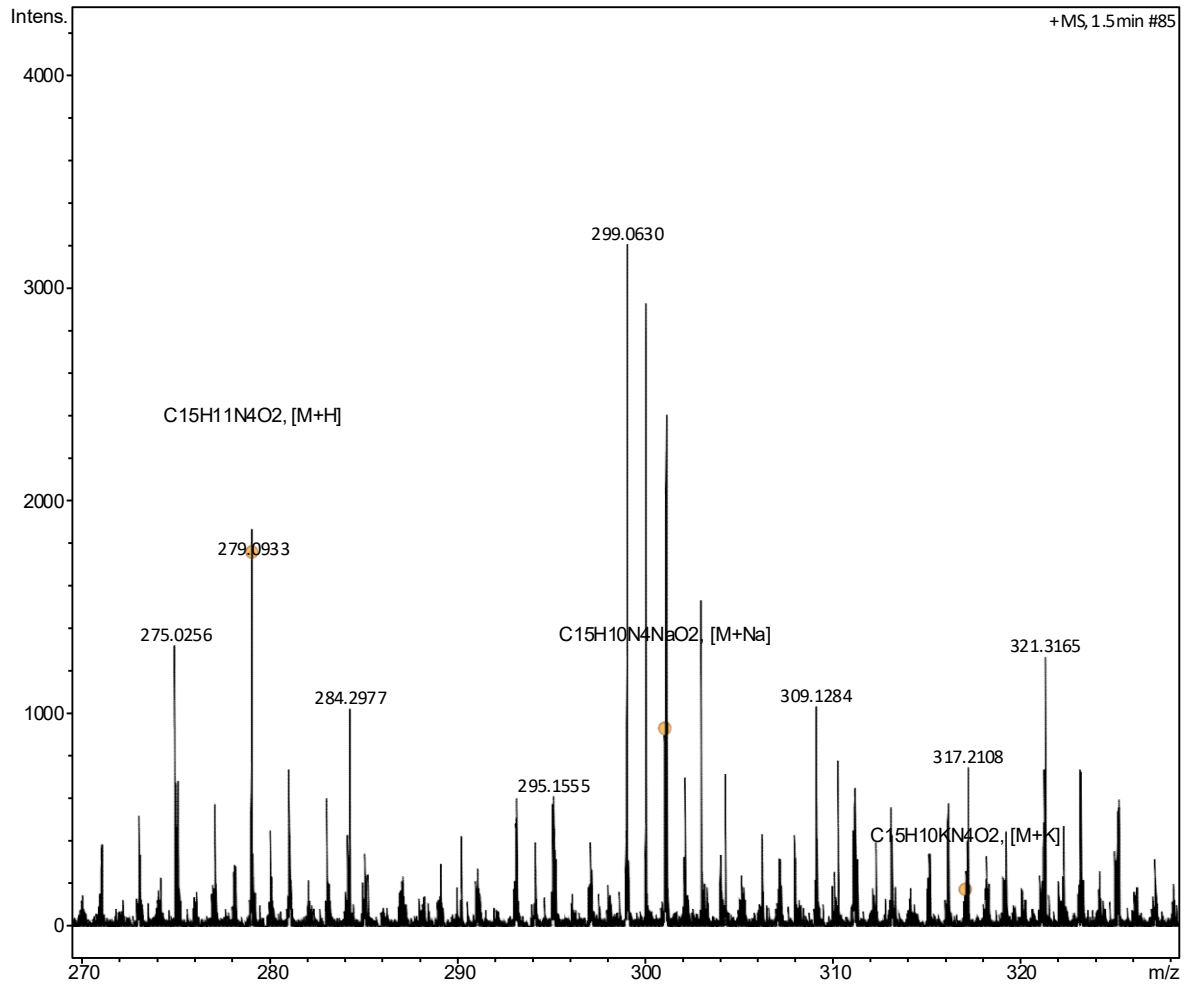
Savitribai Phule Pune University - Central Instrumentation Facility

Analysis Info

		Acquisition Date	1/12/2024 3:15:19 PM
Analysis Name	D:\Data\2024\JAN\SPPU COLLEGE\H. R. M. Rajgurunagar\RUPALI VADAK\D3_RE3_01_6771.d Method dlc_ms20-1200mz_10min_0.120ml flow_90b_dec 23.m	Operator	Nitin S. Kadam CIF
Sample Name	D3	Instrument	impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	20 m/z	Set End Plate Offset	-500 V	Set Dry Gas	7.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule	Adduct
279.093267	1	C15H11N4O2	100.00	279.087652	-5.6	-20.1	240.1	12.5	even	ok	M+H
301.073969	1	C15H10N4NaO2	100.00	301.069596	-4.4	-14.5	185.1	12.5	even	ok	M+Na
317.054524	1	C15H10KN4O2	100.00	317.043534	-11.0	-34.7	593.7	12.5	even	ok	M+K

D3_RE3_01_6771.d

Bruker Compass DataAnalysis 4.2 printed: 1/12/2024 4:33:06 PM by: Nitin S. Kadam CIF Page 1 of 1

Figure S24: HR-ESI-MS Spectrum of 2-Amino-4-(3,4-dihydroxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4d**)

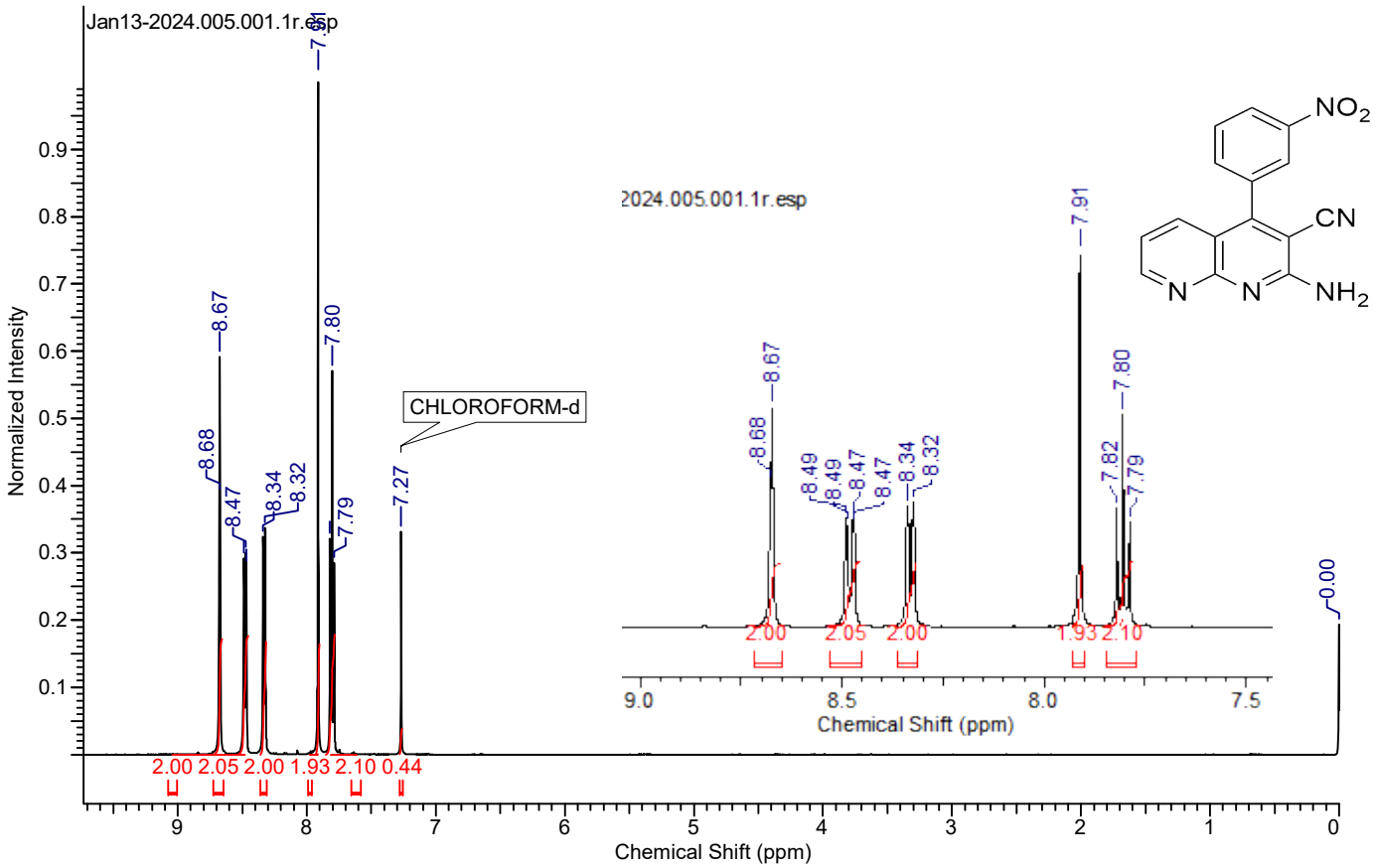


Figure S25: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(3-nitrophenyl)-1,8-naphthyridine-3-carbonitrile (**4e**)

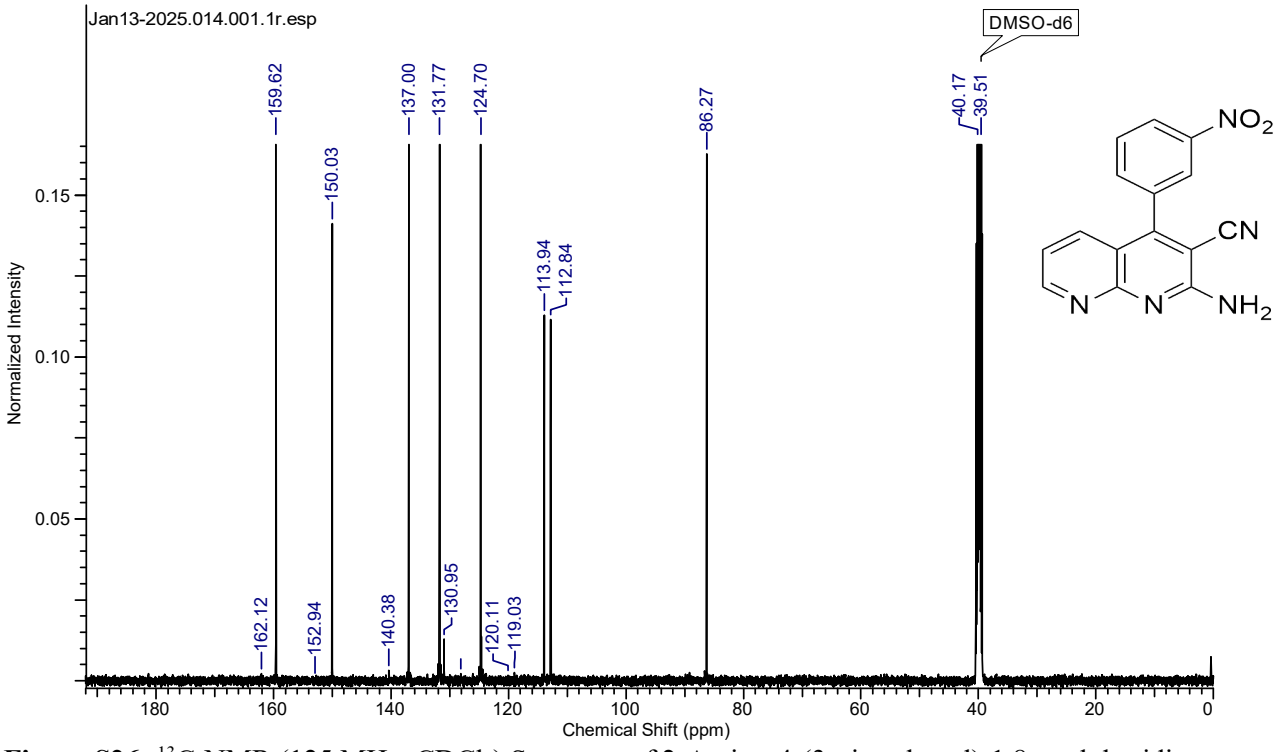


Figure S26: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(3-nitrophenyl)-1,8-naphthyridine-3-carbonitrile (**4e**)

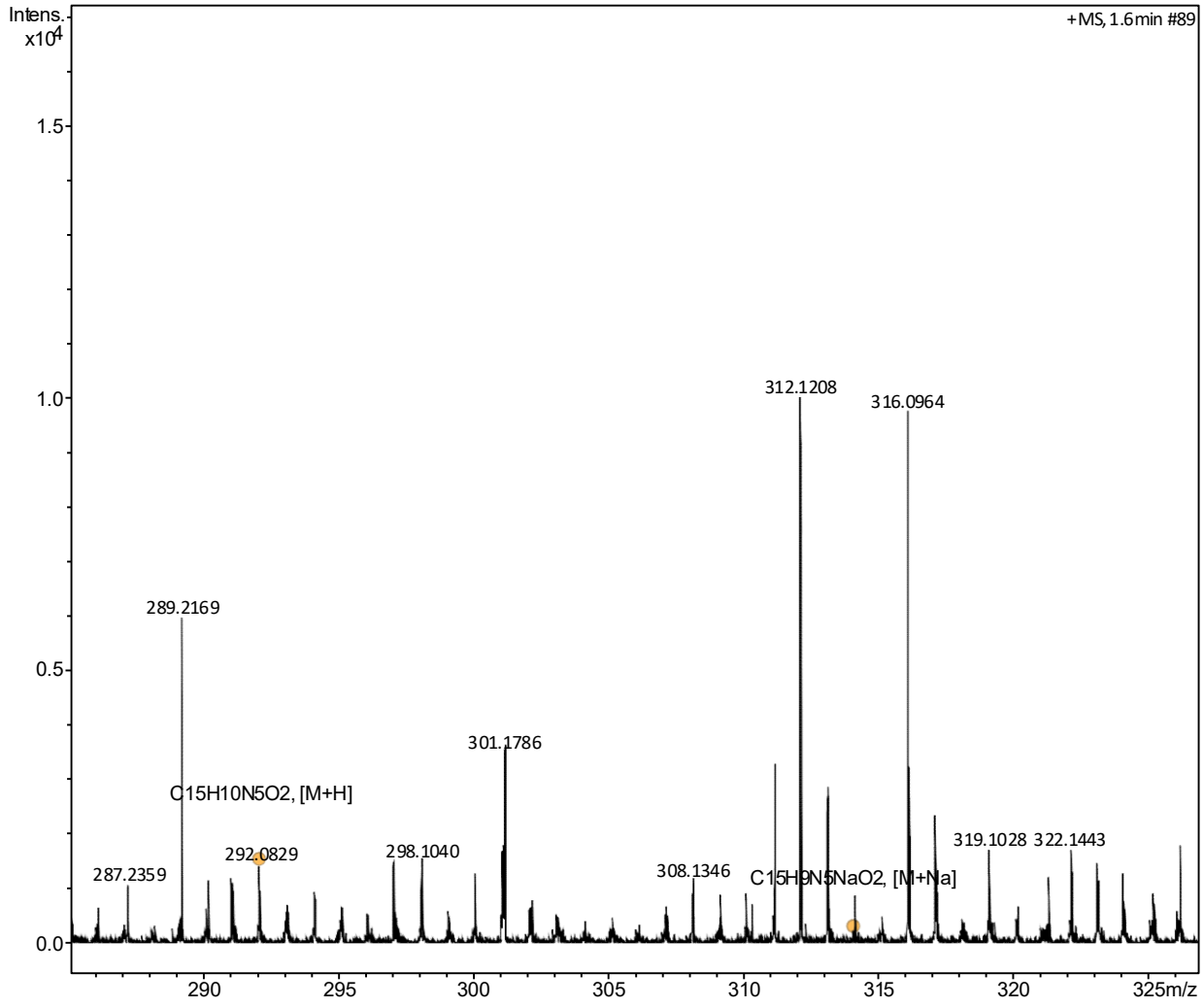
Savitribai Phule Pune University - Central Instrumentation Facility

Analysis Info

		Acquisition Date	1/12/2024 4:34:21 PM
Analysis Name	D:\Data\2024\JAN\SPPU COLLEGE\H. R. M. Rajgurunagar\RUPALI VADAK\D4_RA6_01_6777.d		
Method	dlc_ms20-1200mz_10min_0.120ml flow_90b_dec 23.m	Operator	Nitin S. Kadam CIF
Sample Name	D4	Instrument	impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	20 m/z	Set End Plate Offset	-500 V	Set Dry Gas	7.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule	Adduct
292.082899	1	C15H10N5O2	100.00	292.082901	0.0	0.0	133.9	13.5	even	ok	M+H
314.067045	1	C15H9N5NaO2	100.00	314.064845	-2.2	-7.0	495.9	13.5	even	ok	M+Na

D4_RA6_01_6777.d

Bruker Compass DataAnalysis 4.2 printed: 1/23/2024 11:21:29 AM by: Nitin S. Kadam CIF Page 1 of 1

Figure S27: HR-ESI-MS Spectrum of 2-Amino-4-(3-nitrophenyl)-1,8-naphthyridine-3-carbonitrile (**4e**)

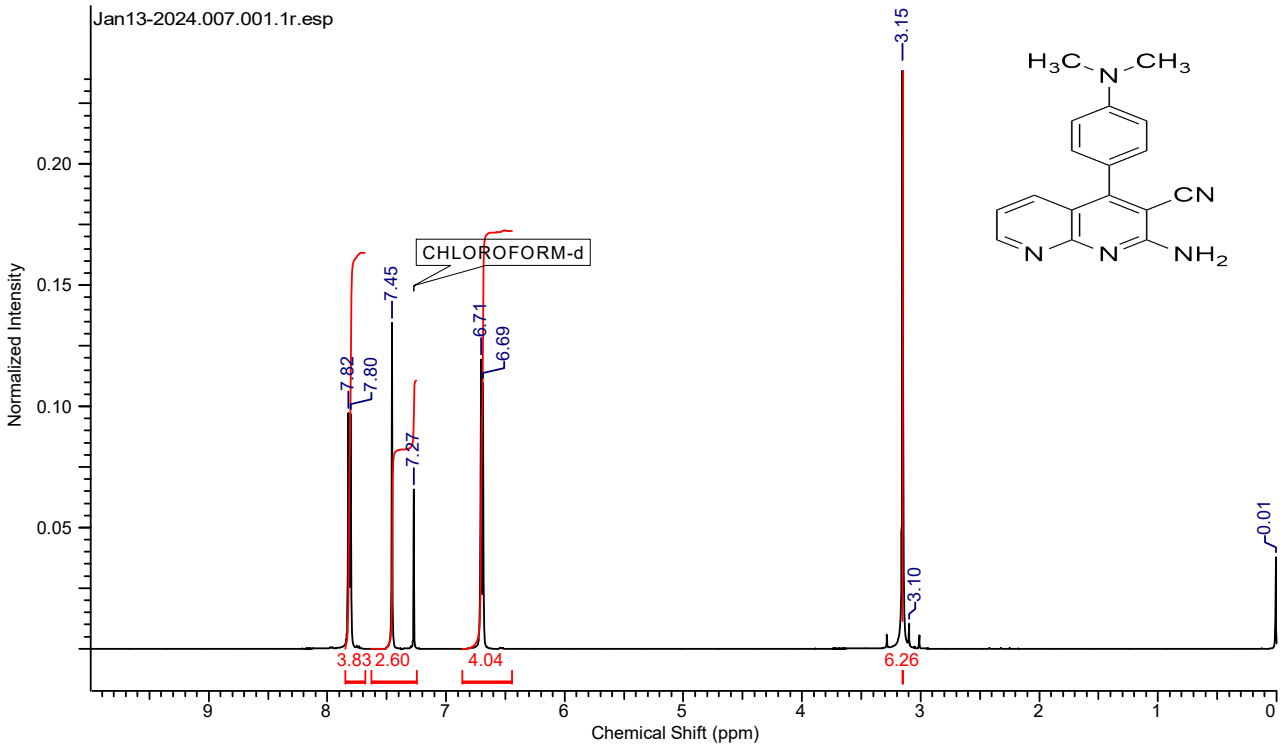


Figure S28: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-amino-4-(4-dimethylaminophenyl)-1,8-naphthyridine-3-carbonitrile (**4f**)

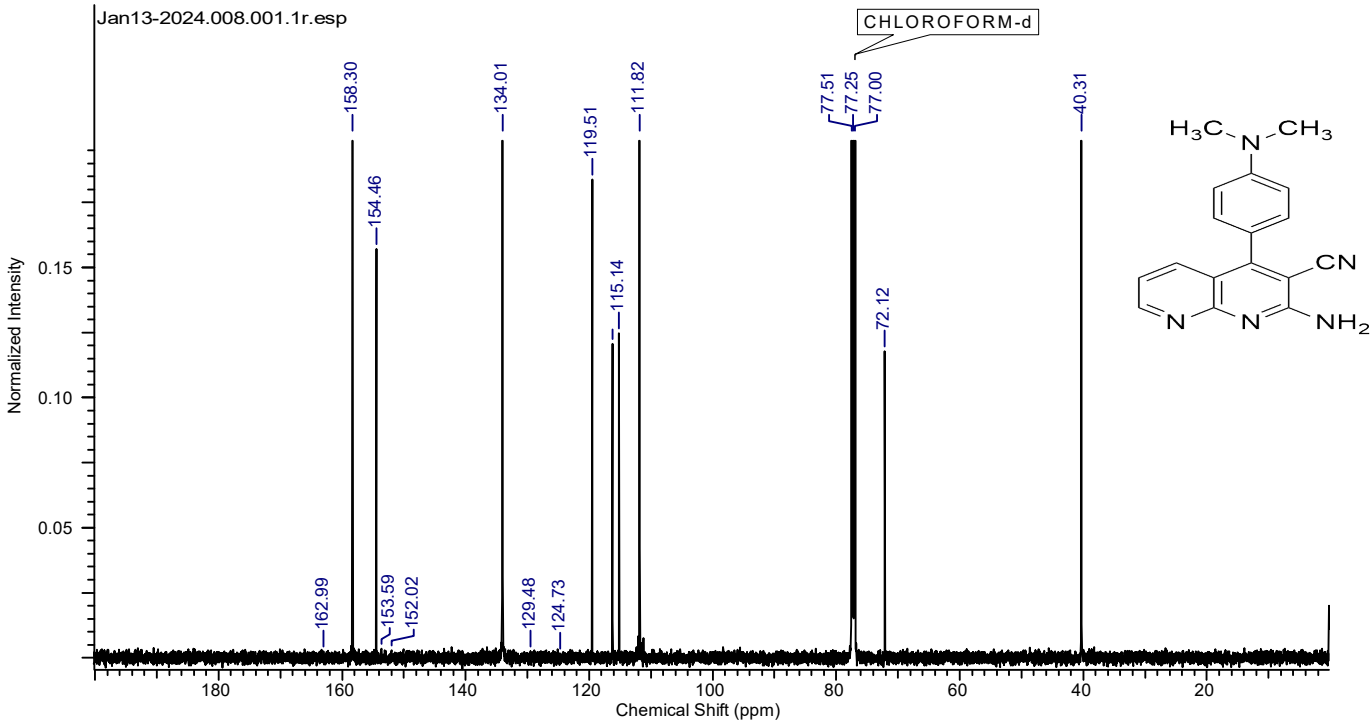


Figure S29: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-amino-4-(4-dimethylaminophenyl)-1,8-naphthyridine-3-carbonitrile (**4f**)

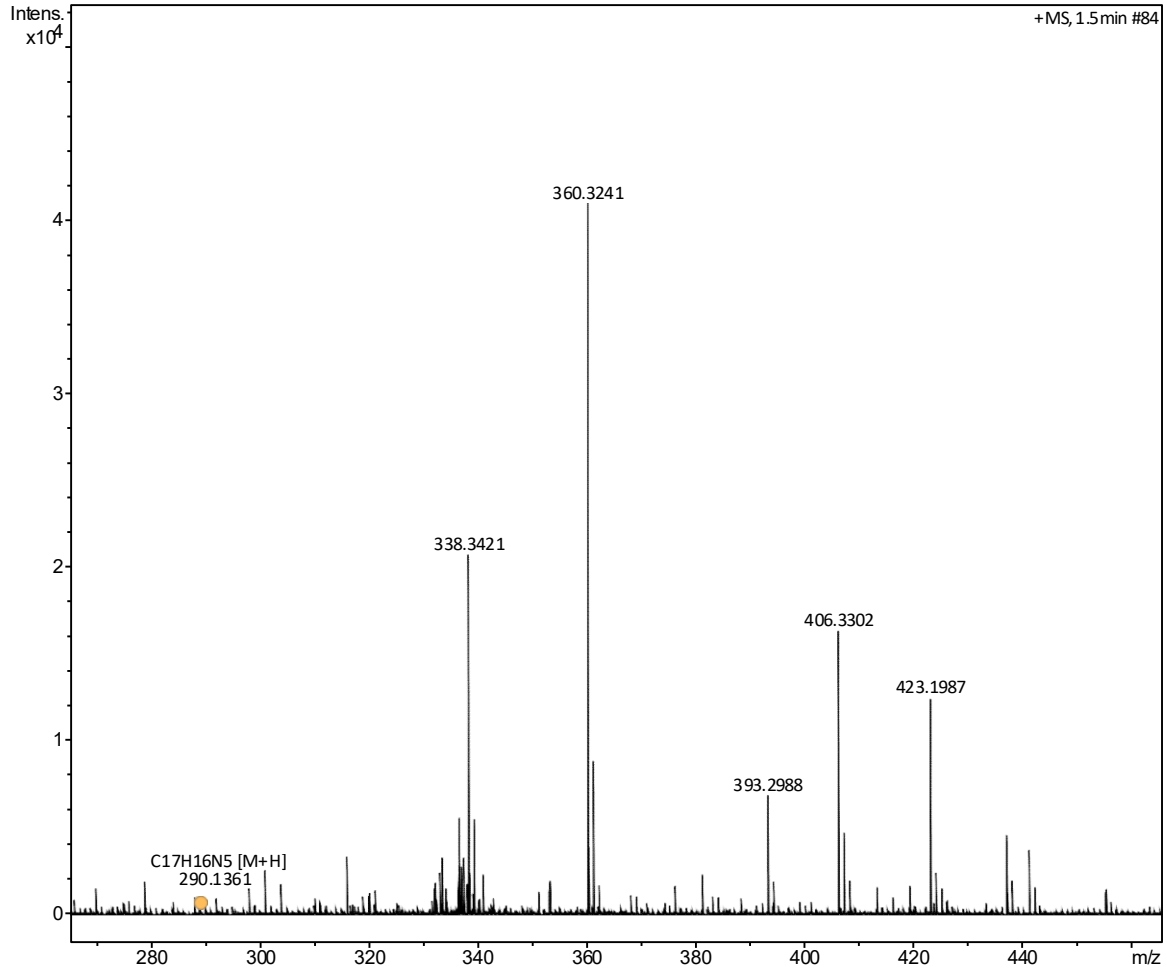
Savitribai Phule Pune University - Central Instrumentation Facility

Analysis Info

		Acquisition Date	1/10/2024 9:29:33 PM
Analysis Name	D:\Data\2024\JAN\SPPU COLLEGE\H. R. M. Rajgurunagar\RUPALI VADAK\D5_RE5_01_6750.d		
Method	dlc_ms20-1200mz_10min_0.120ml flow_90b_dec 23.m	Operator	Nitin S. Kadam CIF
Sample Name	D5	Instrument	impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	20 m/z	Set End Plate Offset	-500 V	Set Dry Gas	7.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



D5_RE5_01_6750.d

Bruker Compass DataAnalysis 4.2 printed: 1/23/2024 11:24:32 AM by: Nitin S. Kadam CIF Page 1 of 1

Figure S30: HR-ESI-MS Spectrum of 2-amino-4-(4-dimethylaminophenyl)-1,8-naphthyridine-3-carbonitrile (**4f**)

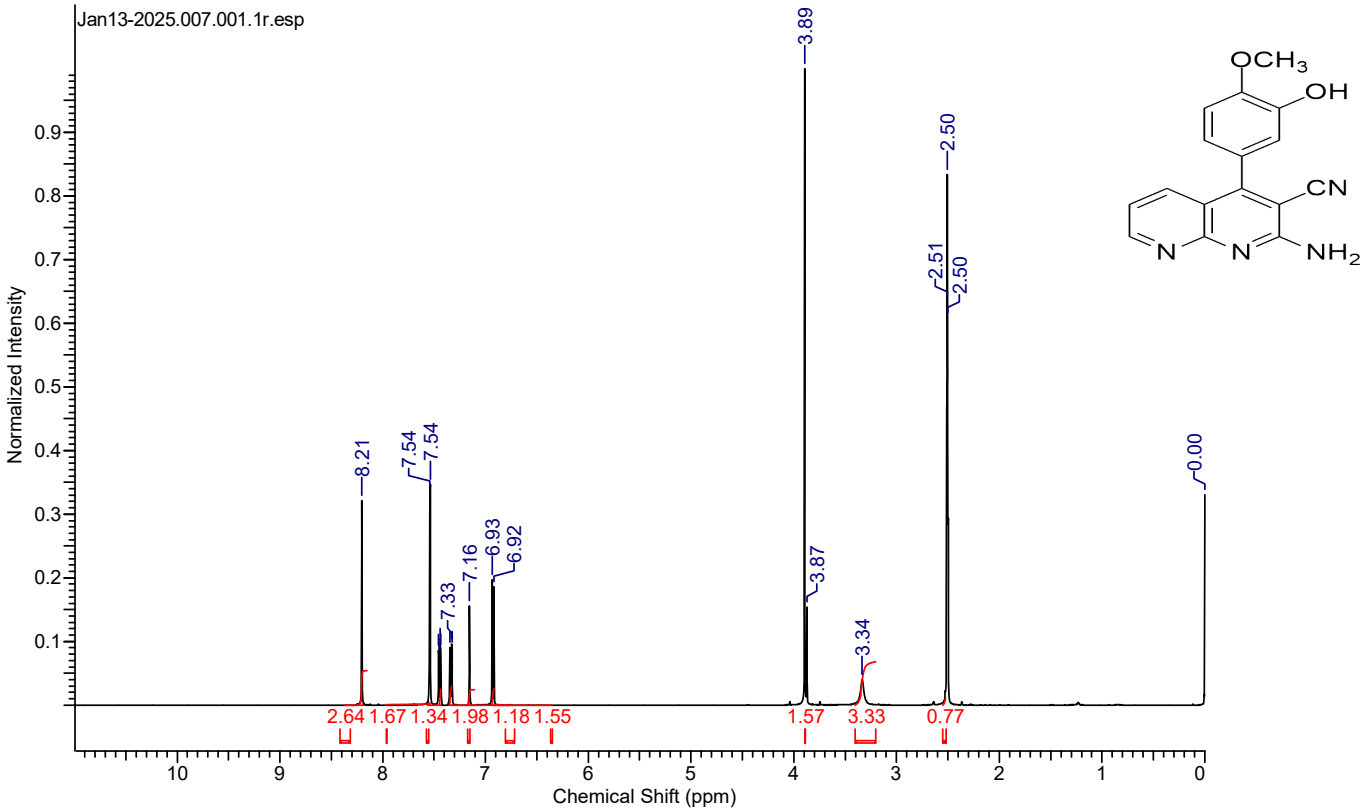


Figure S31: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-amino-4-(3-hydroxy-4-methoxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4g**)

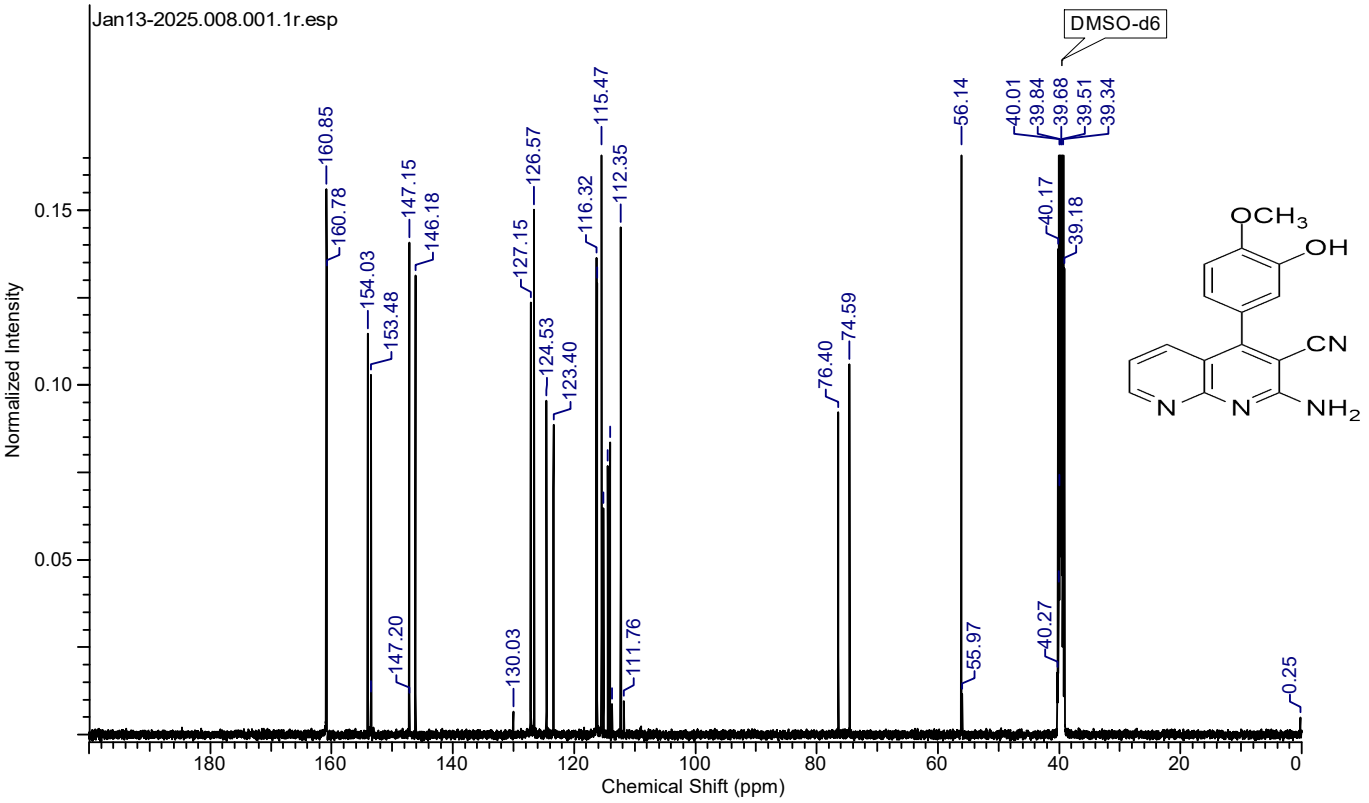


Figure S32: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-amino-4-(3-hydroxy-4-methoxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4g**)

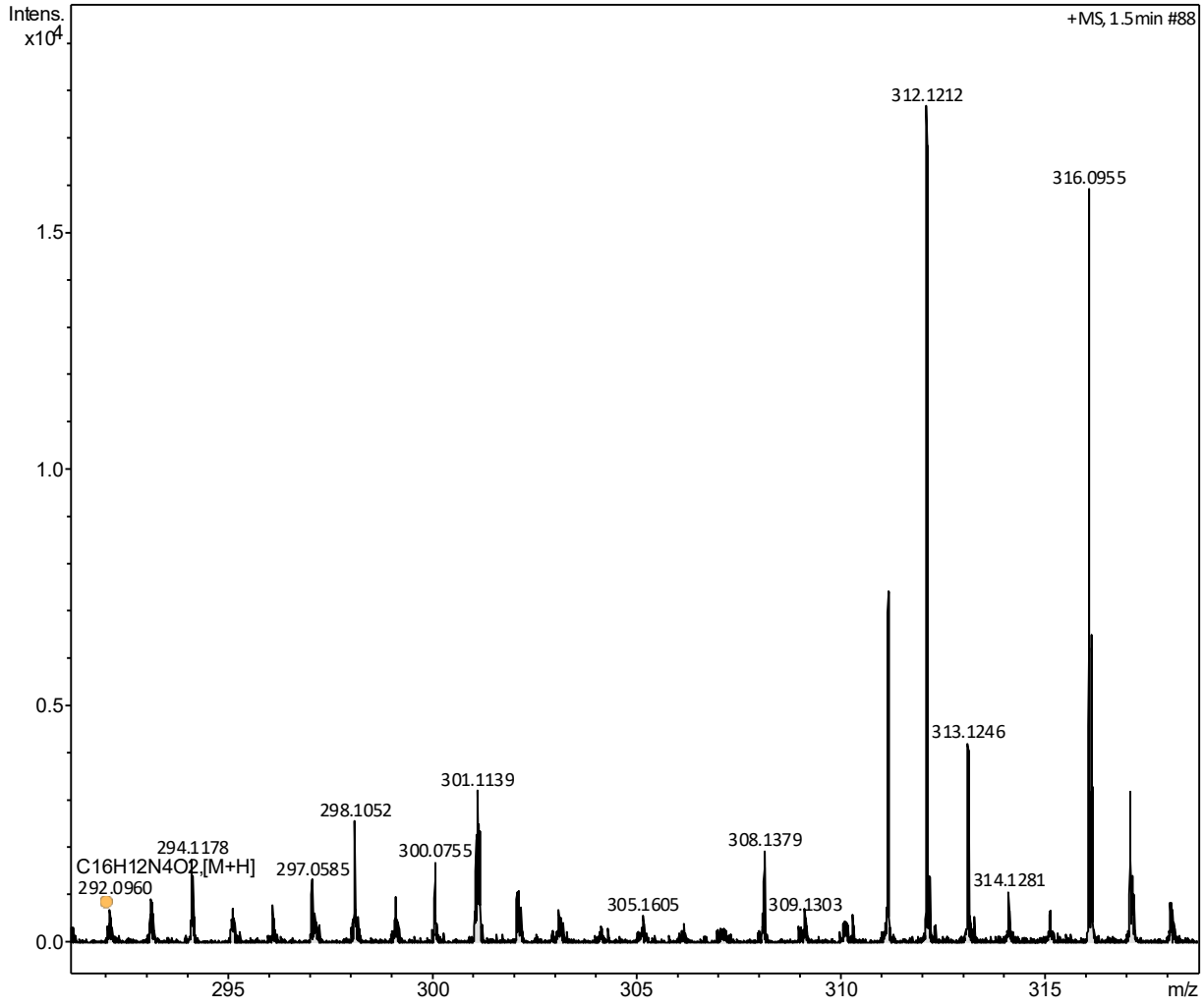
Savitribai Phule Pune University - Central Instrumentation Facility

Analysis Info

		Acquisition Date	1/12/2024 4:45:04 PM
Analysis Name	D:\Data\2024\JAN\SPPU COLLEGE\H. R. M. Rajgurunagar\RUPALI VADAK\D6_RA7_01_6778.d		
Method	dlc_ms20-1200mz_10min_0.120ml flow_90b_dec 23.m	Operator	Nitin S. Kadam CIF
Sample Name	D6	Instrument	impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	20 m/z	Set End Plate Offset	-500 V	Set Dry Gas	7.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule	Adduct
293.119655	1	C16H13N4O2	100.00	293.103302	-16.4	-55.8	580.8	12.5	even	ok	M+H

D6_RA7_01_6778.d

Bruker Compass DataAnalysis 4.2 printed: 1/23/2024 11:27:40 AM by: Nitin S. Kadam CIF Page 1 of 1

Figure S33: HR-ESI-MS Spectrum of 2-amino-4-(3-hydroxy-4-methoxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4g**)

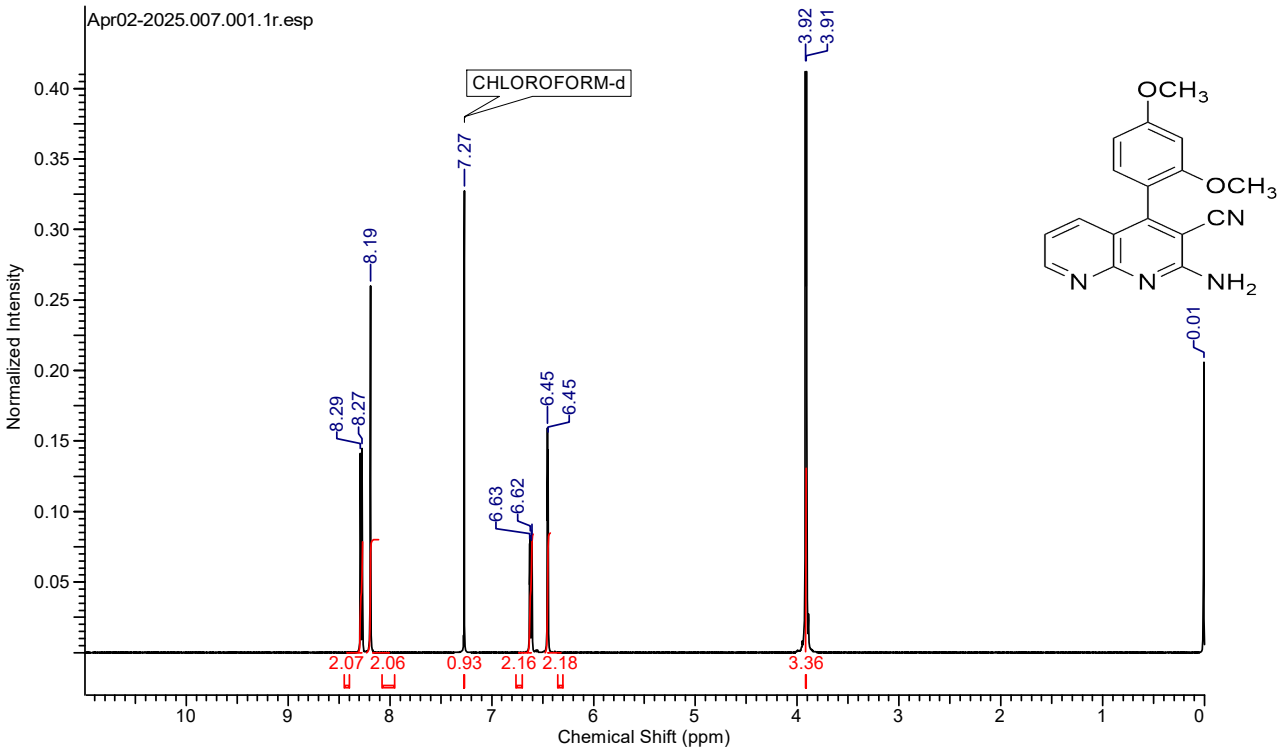


Figure S34: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-amino-4-(2,4-dimethoxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4h**)

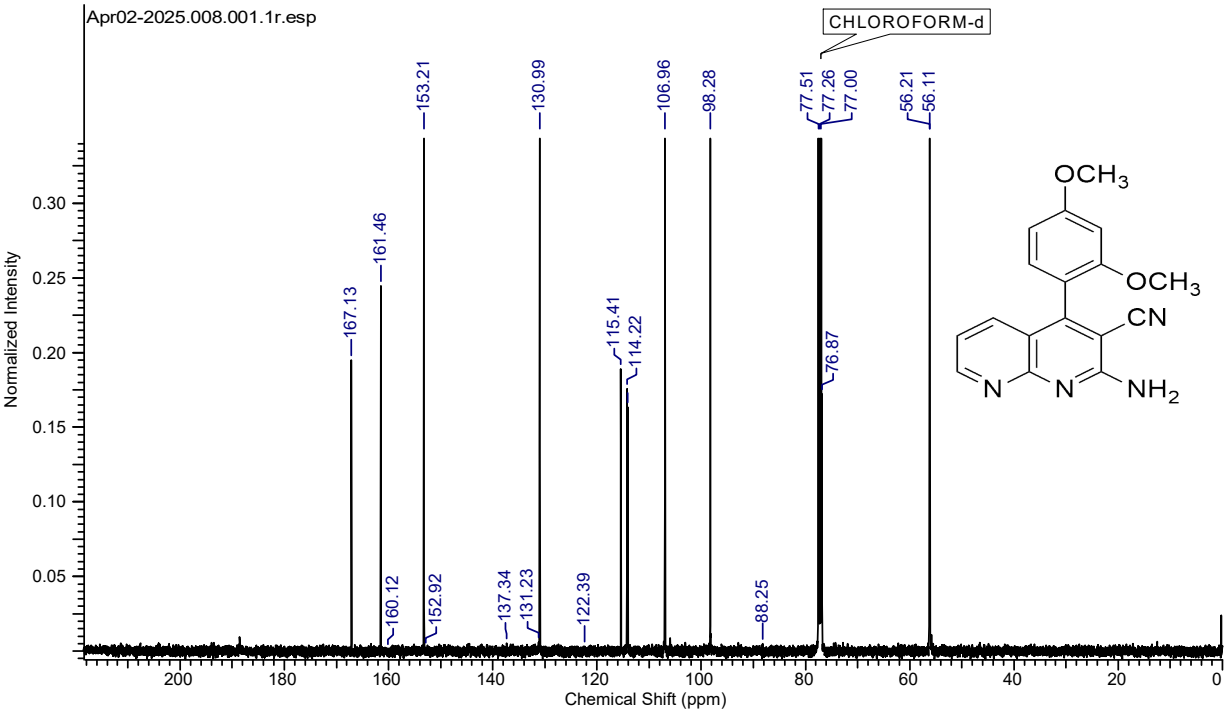


Figure S35: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-amino-4-(2,4-dimethoxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4h**)

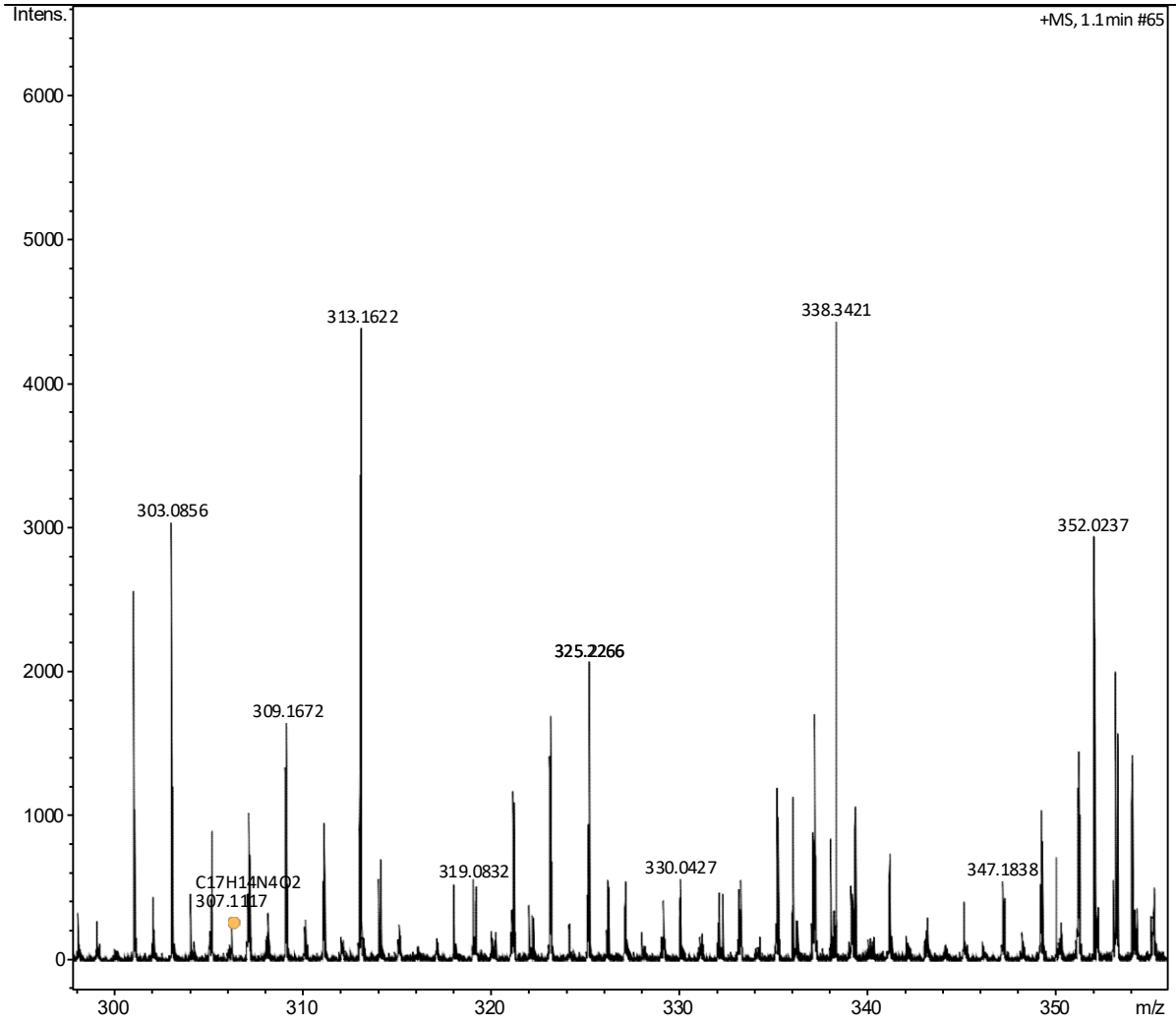
Savitribai Phule Pune University - Central Instrumentation Facility

Analysis Info

Acquisition Date	4/3/2025 7:05:52 PM		
Analysis Name	D:\Data\2025\APRIL\SPPU COLLEGE\HRM COLLEGE\HUNDARE PAYAL\D23_RE3_01_9260.d		
Method	dlc_50-1200mz_pos_mode_7min_0.2ml.m	Analyst:	Nitin S. Kadam CIF
Sample Name	D7	Instrument	impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.7 Bar
Focus	Active	Set Capillary	4000 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



D23_RE3_01_9260.d

Bruker Compass DataAnalysis 4.2 printed: 4/7/2025 4:00:23 PM by: Nitin S. Kadam CIF Page 1 of 1

Figure S36: HR-ESI-MS Spectrum of 2-amino-4-(2,4-dimethoxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4h**)

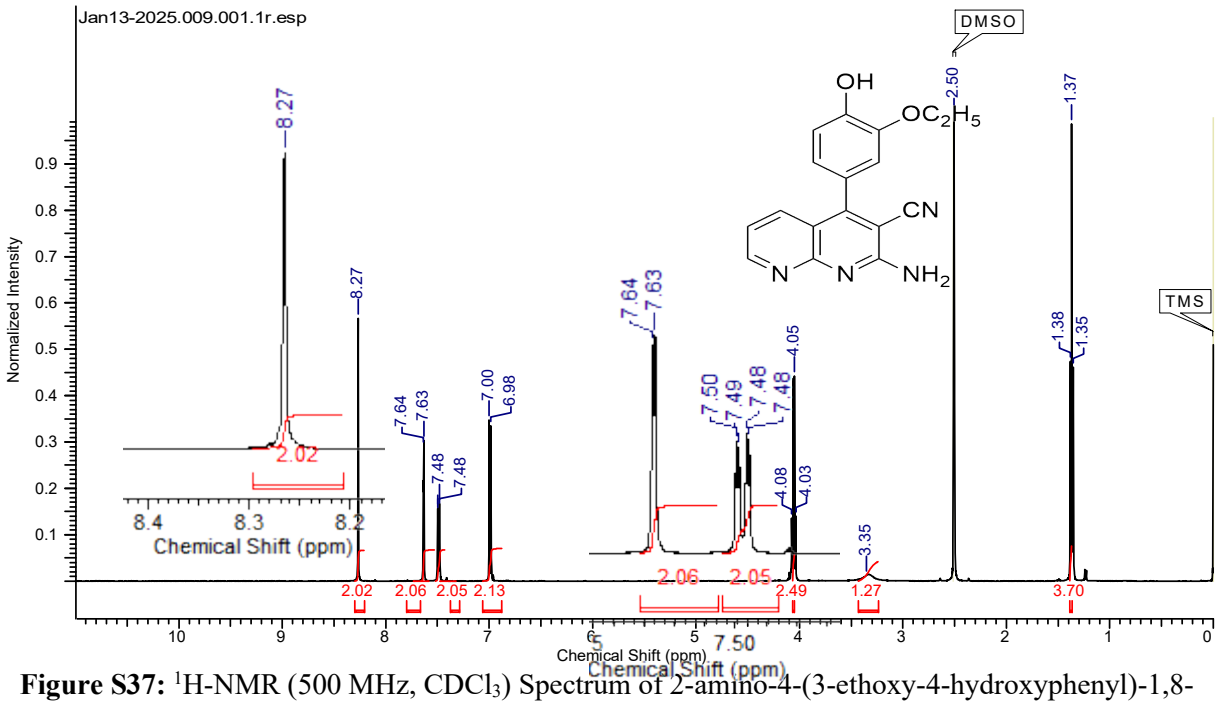


Figure S37: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-amino-4-(3-ethoxy-4-hydroxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4i**)

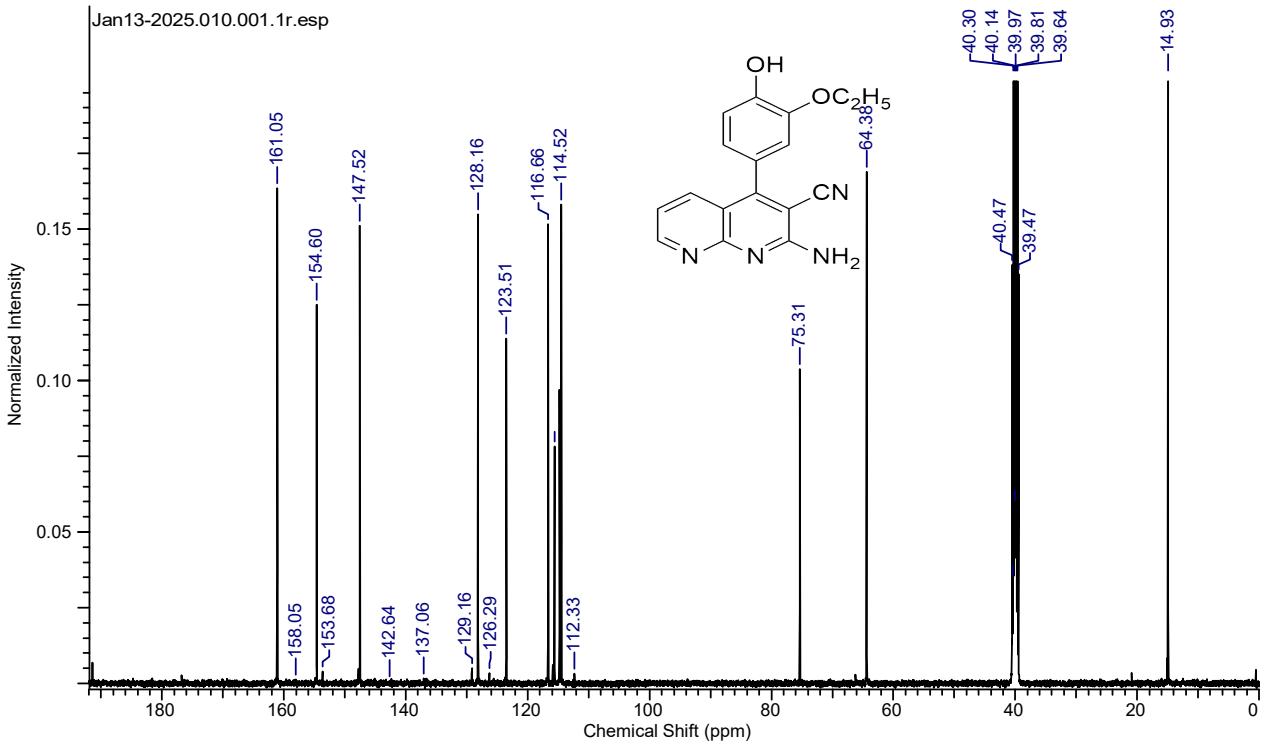


Figure S38: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-amino-4-(3-ethoxy-4-hydroxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4i**)

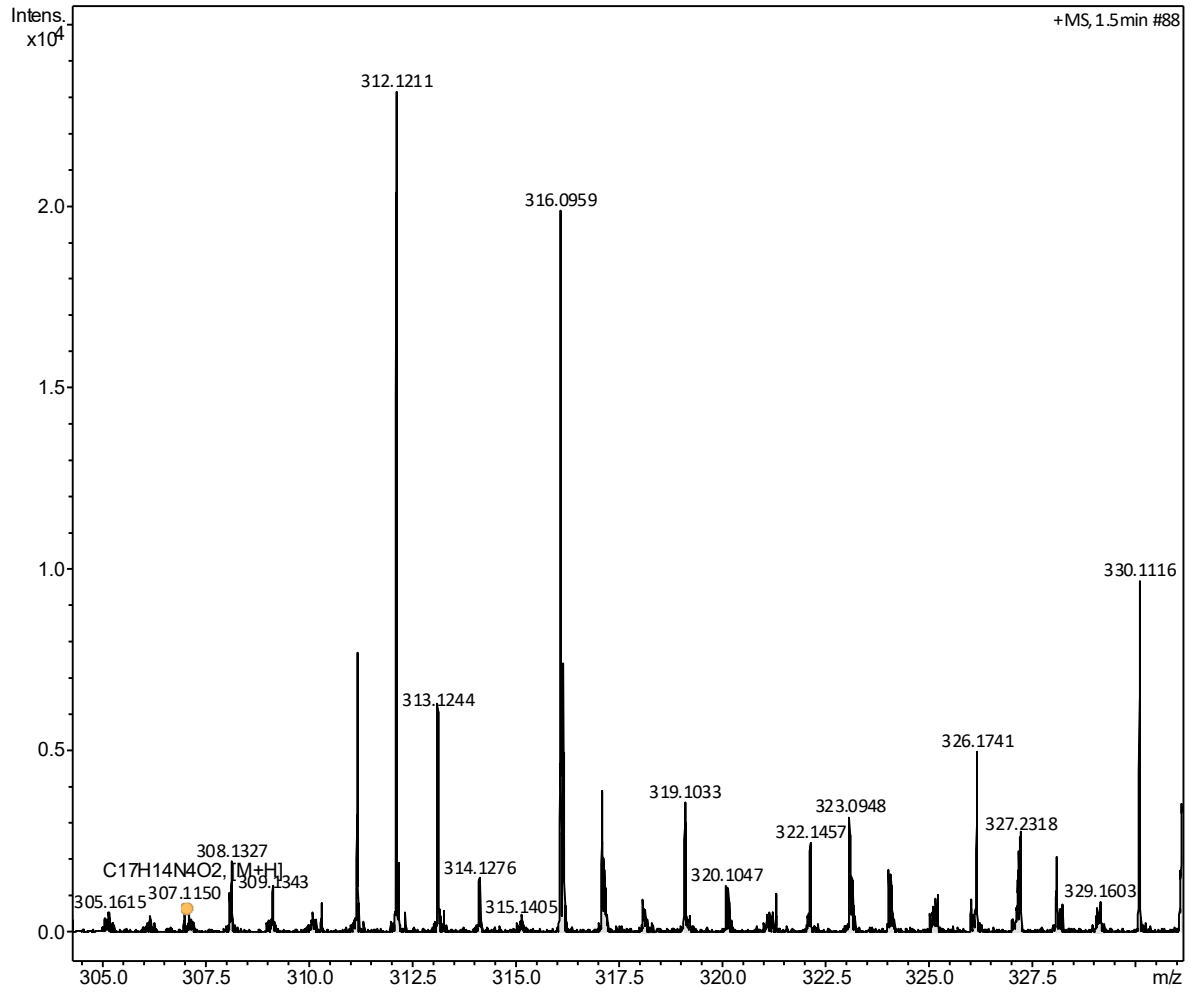
Savitribai Phule Pune University - Central Instrumentation Facility

Analysis Info

		Acquisition Date	1/12/2024 4:55:45 PM
Analysis Name	D:\Data\2024\JAN\SPPU COLLEGE\H. R. M. Rajgurunagar\RUPALI VADAK\D8_RA8_01_6779.d		
Method	dlc_ms20-1200mz_10min_0.120ml flow_90b_dec 23.m	Operator	Nitin S. Kadam CIF
Sample Name	D8	Instrument	impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	20 m/z	Set End Plate Offset	-500 V	Set Dry Gas	7.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



D8_RA8_01_6779.d

Bruker Compass DataAnalysis 4.2 printed: 1/23/2024 11:31:03 AM by: Nitin S. Kadam CIF Page 1 of 1

Figure S39: HR-ESI-MS Spectrum of 2-amino-4-(3-ethoxy-4-hydroxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4i**)

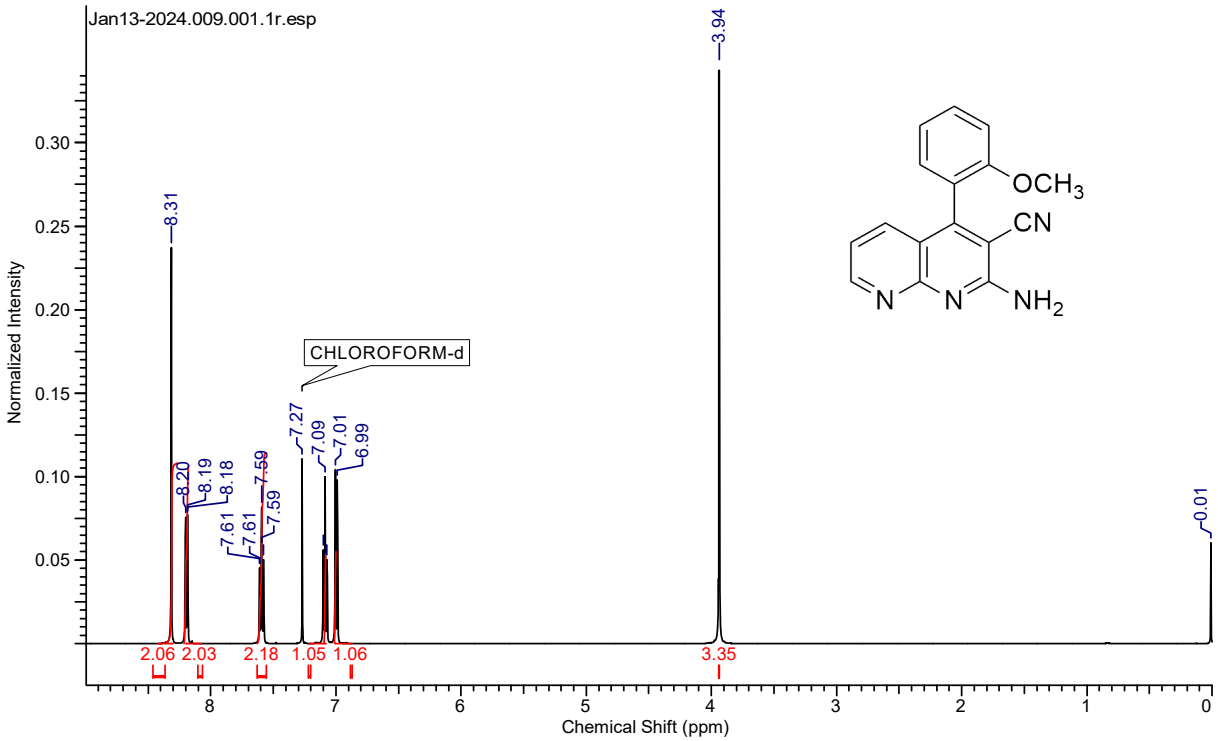


Figure S40: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(2-methoxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4j**)

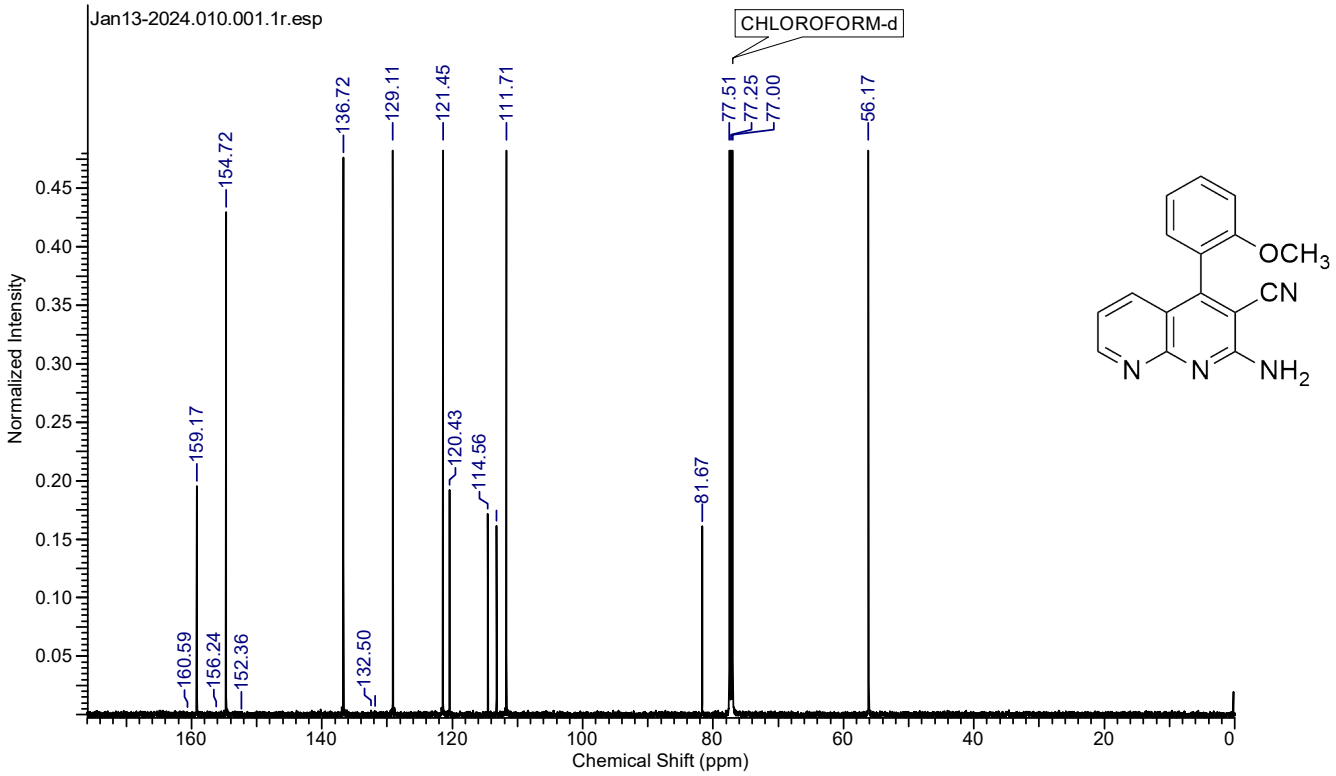


Figure S41: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(2-methoxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4j**)

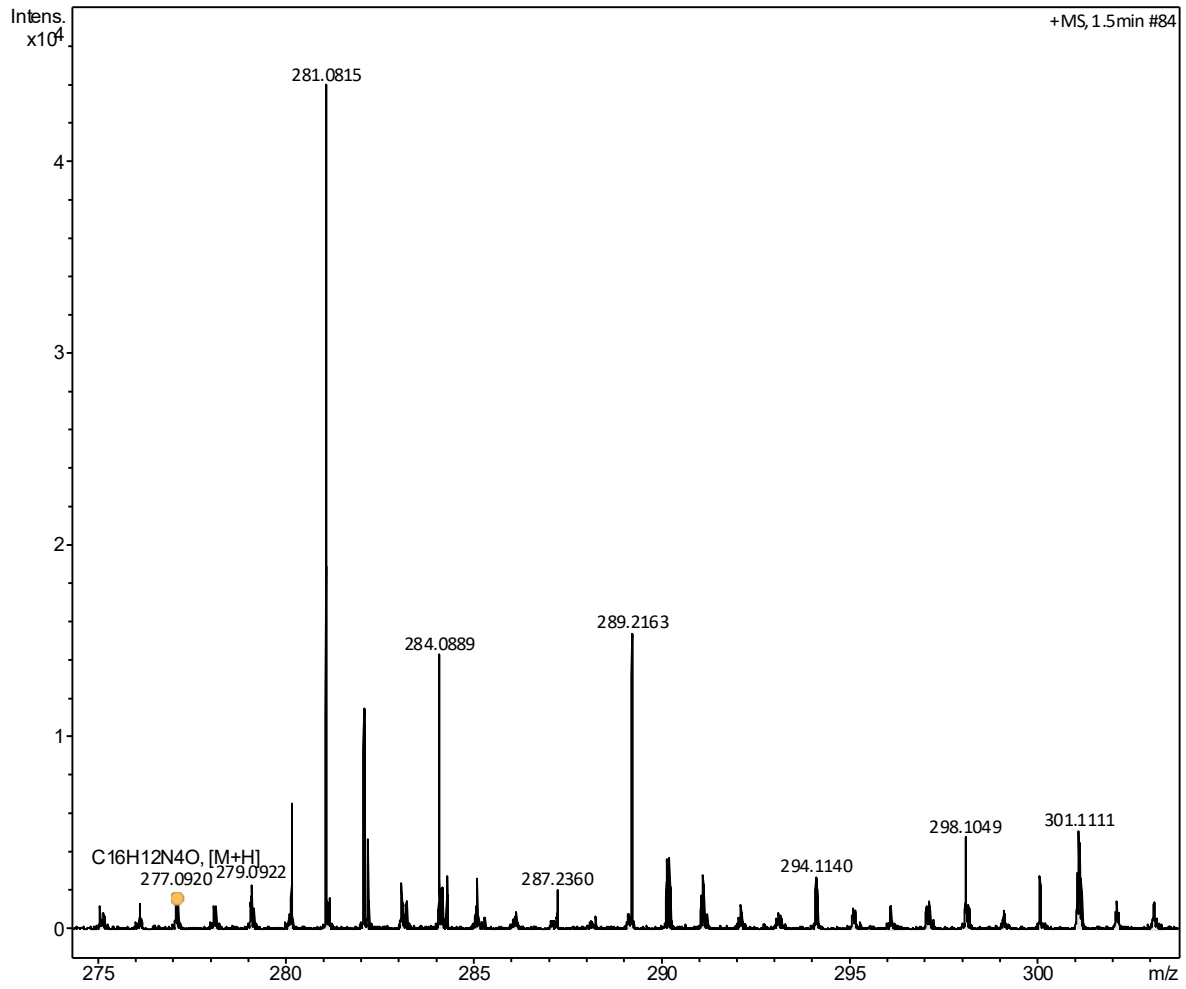
Savitribai Phule Pune University - Central Instrumentation Facility

Analysis Info

		Acquisition Date	1/12/2024 5:06:26 PM
Analysis Name	D:\Data\2024\JAN\SPPU COLLEGE\H. R. M. Rajgurunagar\RUPALI VADAK\D10_RB1_01_6780.d		
Method	dlc_ms20-1200mz_10min_0.120ml flow_90b_dec 23.m	Operator	Nitin S. Kadam CIF
Sample Name	D10	Instrument	impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	20 m/z	Set End Plate Offset	-500 V	Set Dry Gas	7.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



D10_RB1_01_6780.d

Bruker Compass DataAnalysis 4.2 printed: 1/23/2024 11:34:21 AM by: Nitin S. Kadam CIF Page 1 of 1

Figure S42: HR-ESI-MS Spectrum of 2-Amino-4-(2-methoxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4j**)

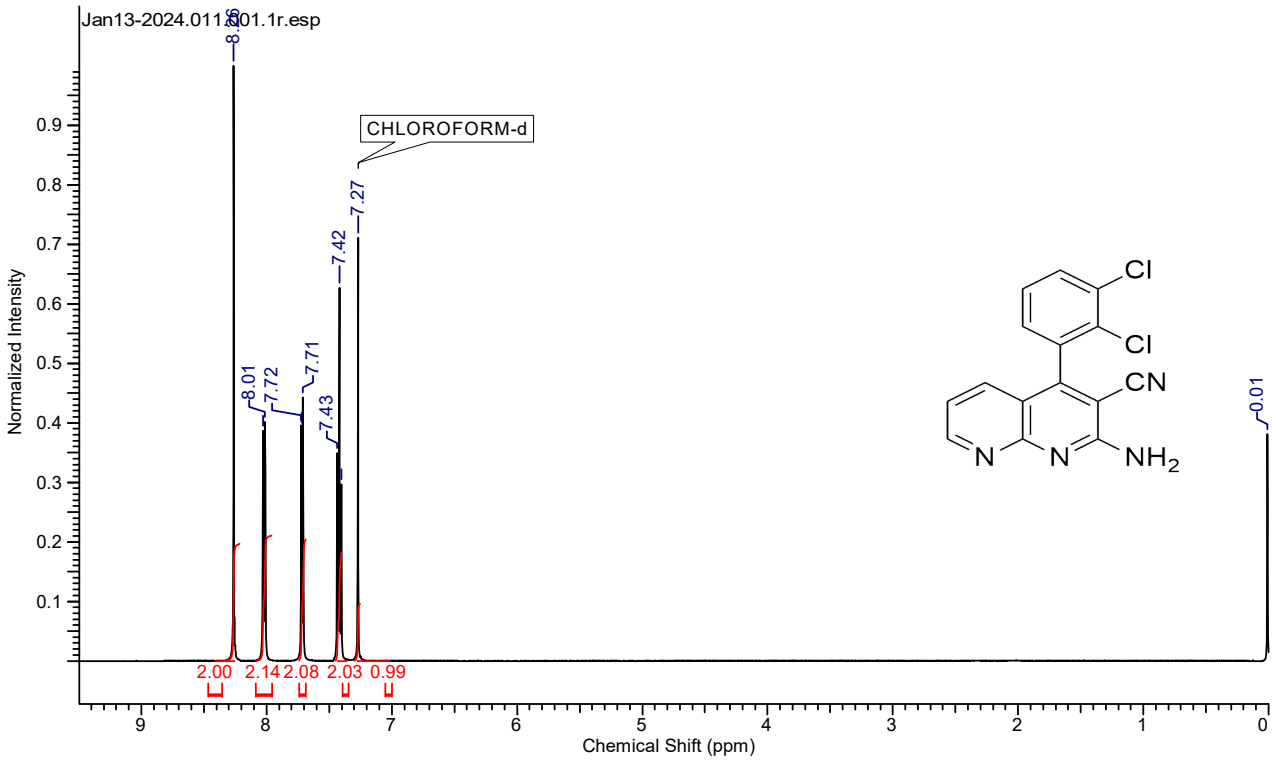


Figure S43: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(2,3-dichlorophenyl)-1,8-naphthyridine-3-carbonitrile (**4k**)

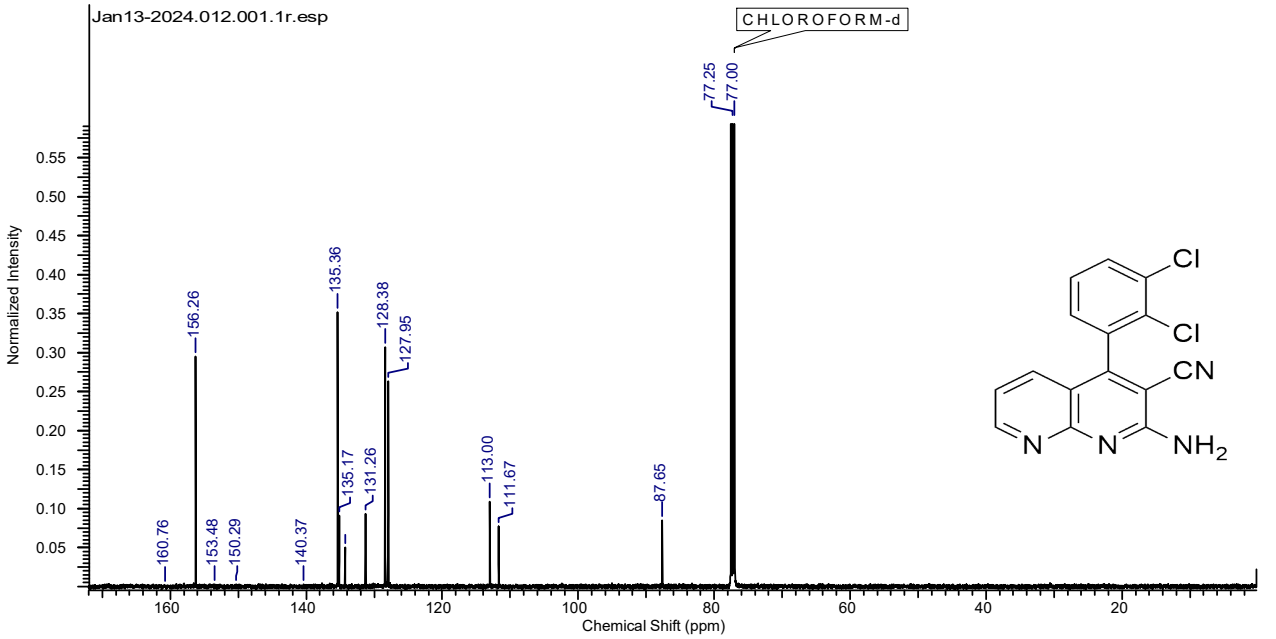


Figure S44: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(2,3-dichlorophenyl)-1,8-naphthyridine-3-carbonitrile (**4k**)

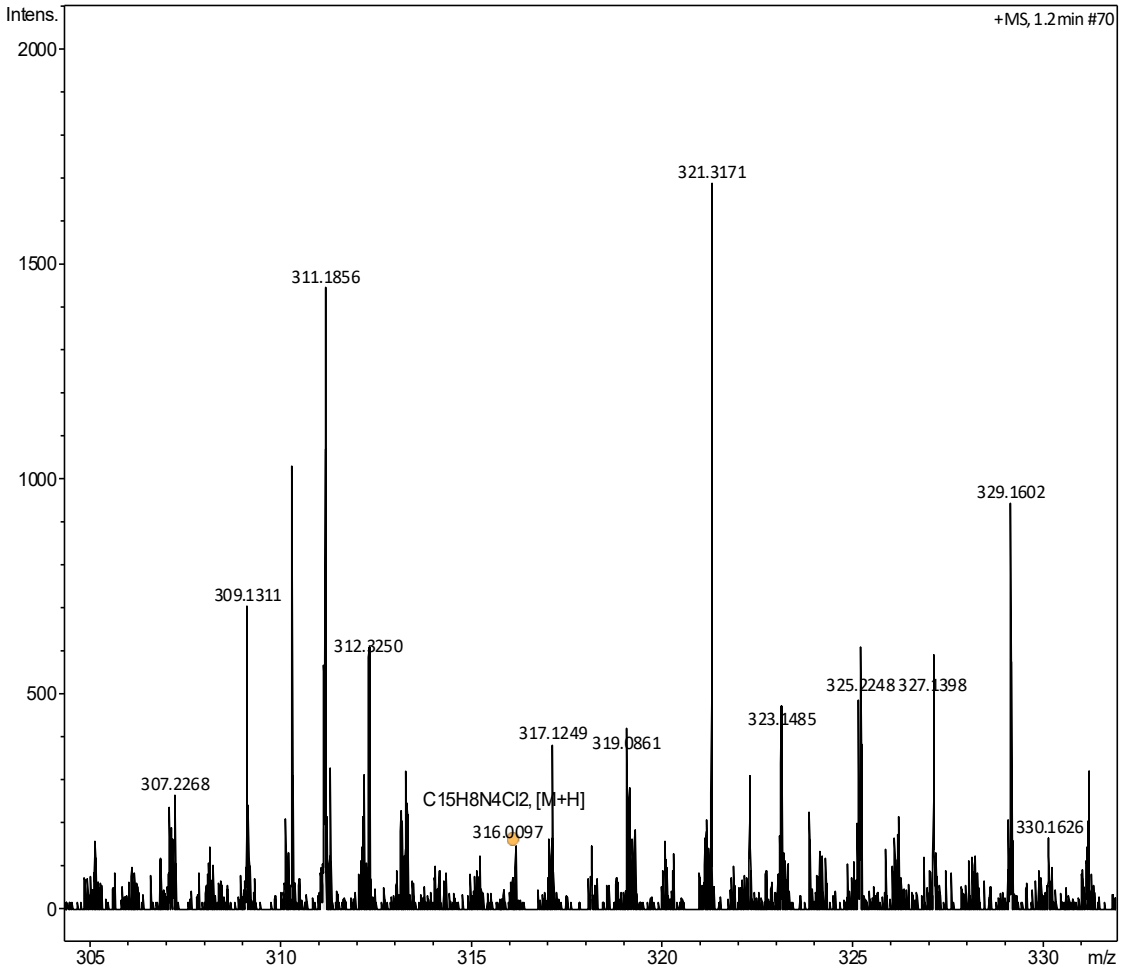
Savitribai Phule Pune University - Central Instrumentation Facility

Analysis Info

		Acquisition Date	1/12/2024 5:17:09 PM
Analysis Name	D:\Data\2024\JAN\SPPU COLLEGE\H. R. M. Rajgurunagar\RUPALI VADAK\D11_RB2_01_6781.d		
Method	dlc_ms20-1200mz_10min_0.120ml flow_90b_dec 23.m	Operator	Nitin S. Kadam CIF
Sample Name	D11	Instrument	impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	20 m/z	Set End Plate Offset	-500 V	Set Dry Gas	7.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



D11_RB2_01_6781.d

Bruker Compass DataAnalysis 4.2 printed: 1/23/2024 11:39:42 AM by: Nitin S. Kadam CIF Page 1 of 1

Figure S45: HR-ESI-MS Spectrum of 2-Amino-4-(2,3-dichlorophenyl)-1,8-naphthyridine-3-carbonitrile (**4k**)

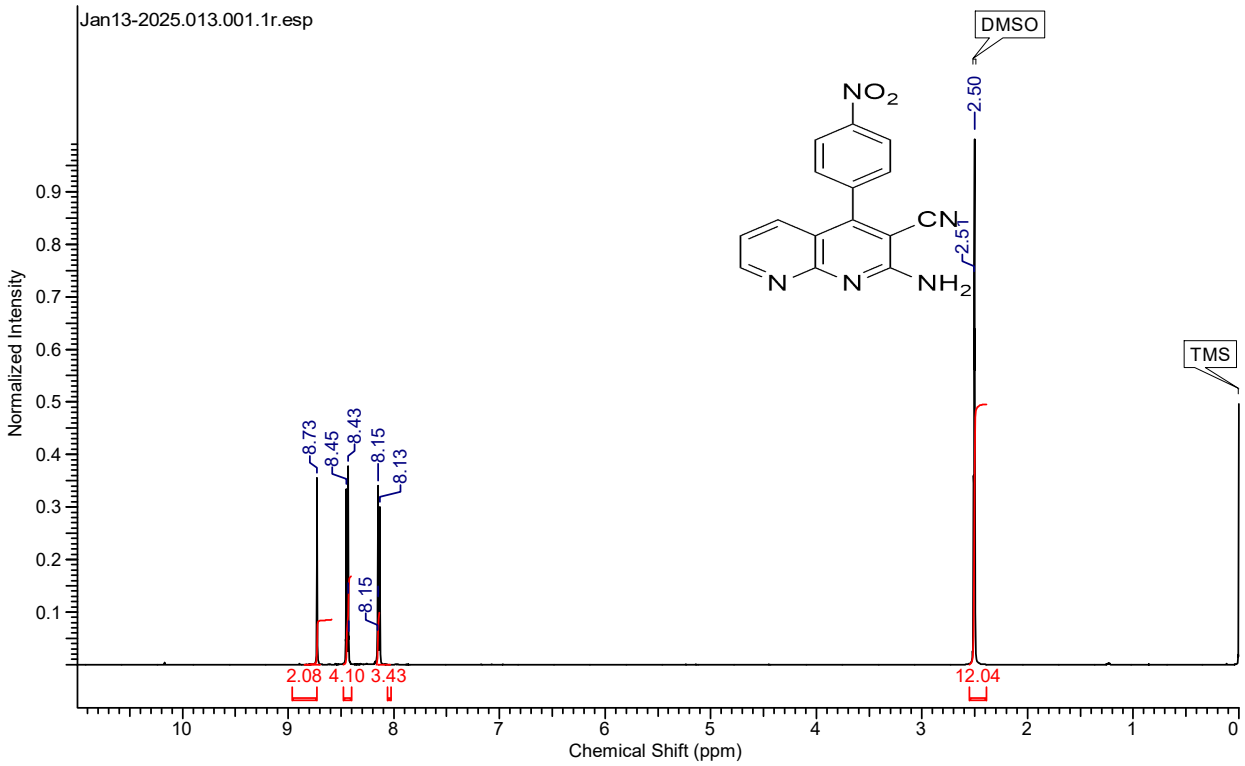


Figure S46: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(4-nitrophenyl)-1,8-naphthyridine-3-carbonitrile (**4l**)

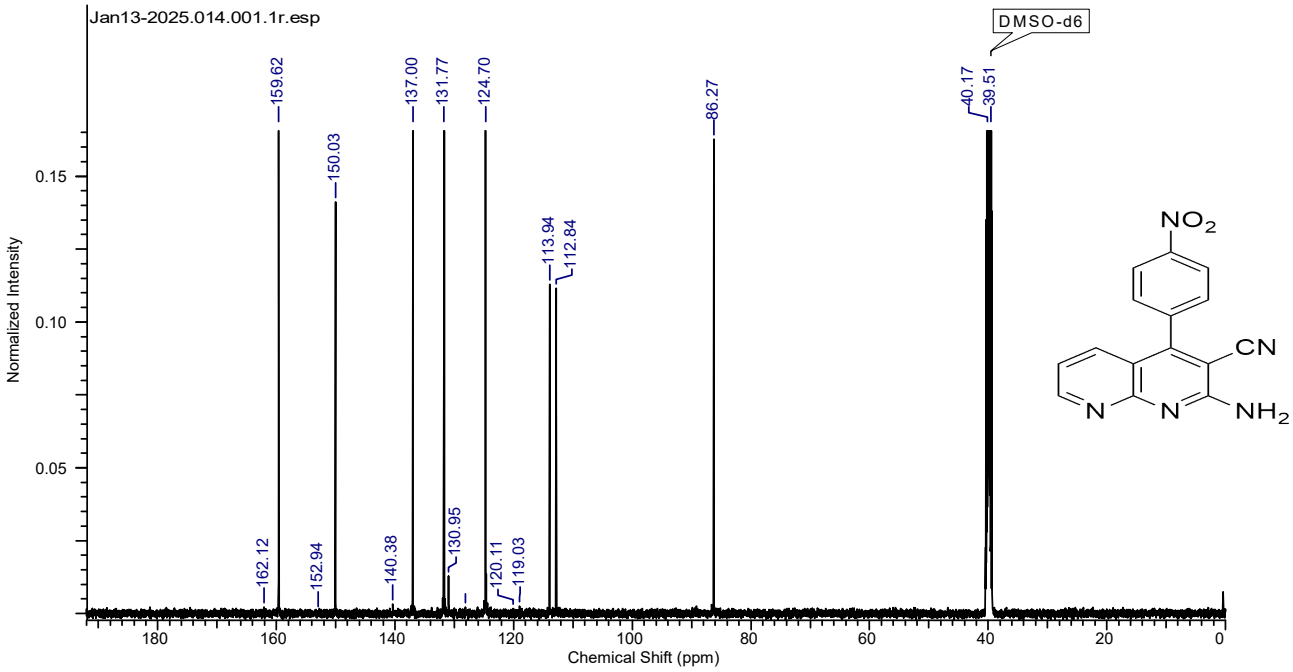


Figure S47: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(4-nitrophenyl)-1,8-naphthyridine-3-carbonitrile (**4l**)

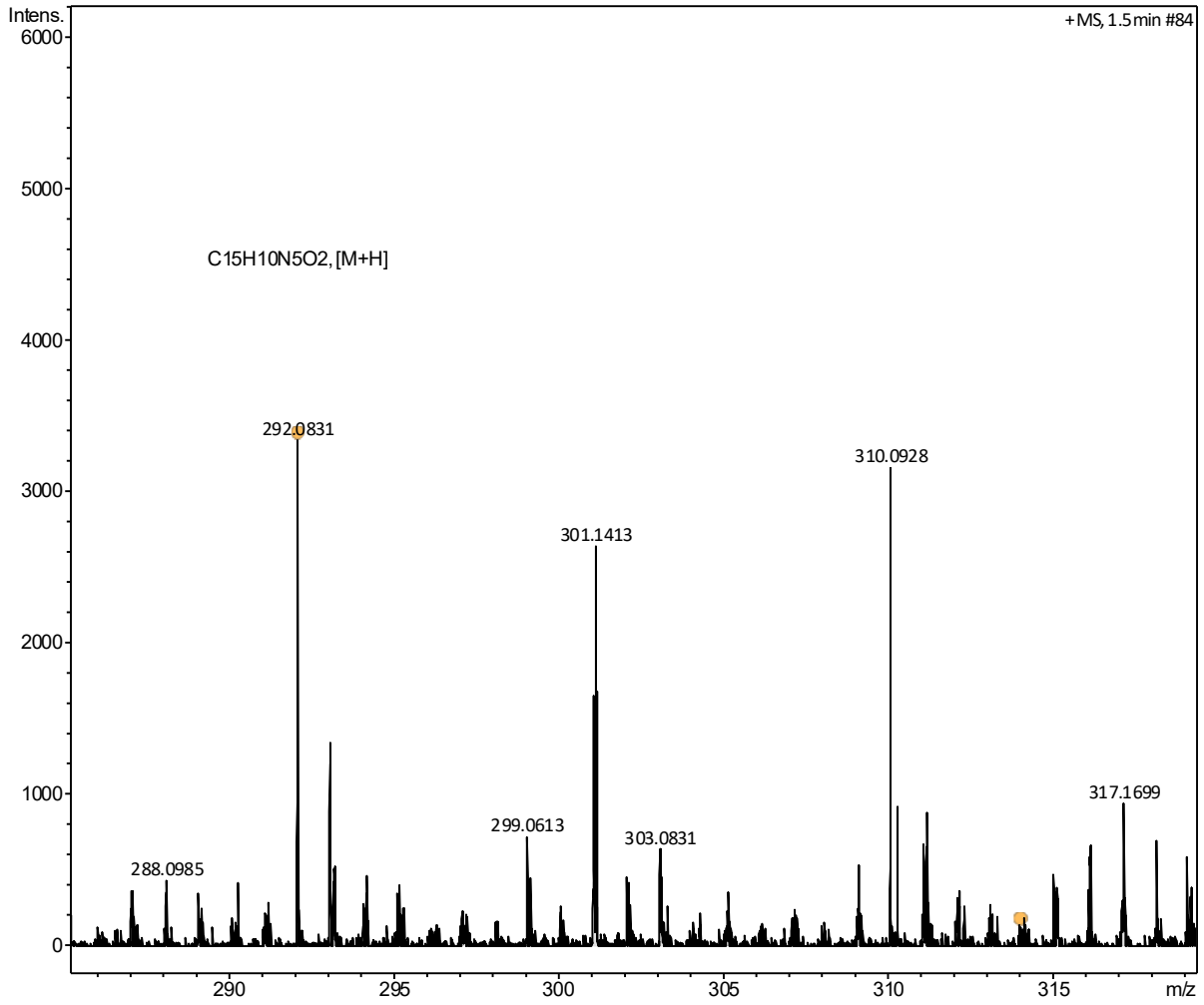
Savitribai Phule Pune University - Central Instrumentation Facility

Analysis Info

		Acquisition Date	1/10/2024 10:22:57 PM
Analysis Name	D:\Data\2024\JAN\SPPU COLLEGE\H. R. M. Rajgurunagar\RUPALI VADAK\D12_BA2_01_6755.d		
Method	dlc_ms20-1200mz_10min_0.120ml flow_90b_dec 23.m	Operator	Nitin S. Kadam CIF
Sample Name	D12	Instrument	impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	20 m/z	Set End Plate Offset	-500 V	Set Dry Gas	7.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule	Adduct
292.083064	1	C15H10N5O2	100.00	292.082901	-0.2	-0.6	130.3	13.5	even	ok	M+H
314.043788	1	C15H9N5NaO2	100.00	314.064845	21.1	67.0	634.5	13.5	even	ok	M+Na

D12_BA2_01_6755.d

Bruker Compass DataAnalysis 4.2 printed: 1/23/2024 11:42:18 AM by: Nitin S. Kadam CIF Page 1 of 1

Figure S48: HR-ESI-MS Spectrum of 2-Amino-4-(4-nitrophenyl)-1,8-naphthyridine-3-carbonitrile (**4l**)

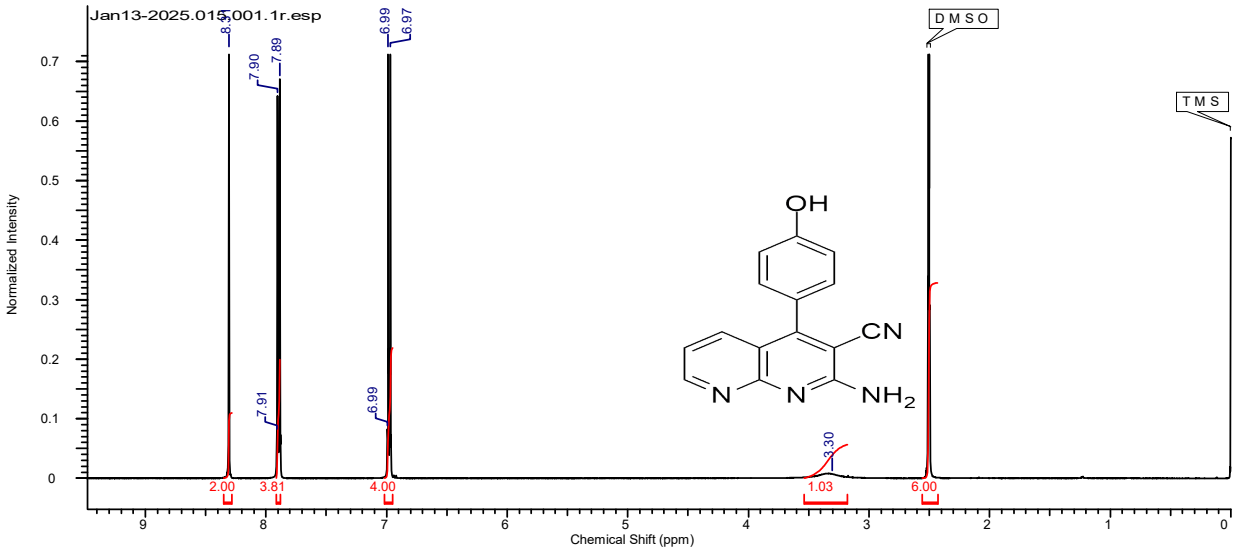


Figure S49: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(4-hydroxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4m**)

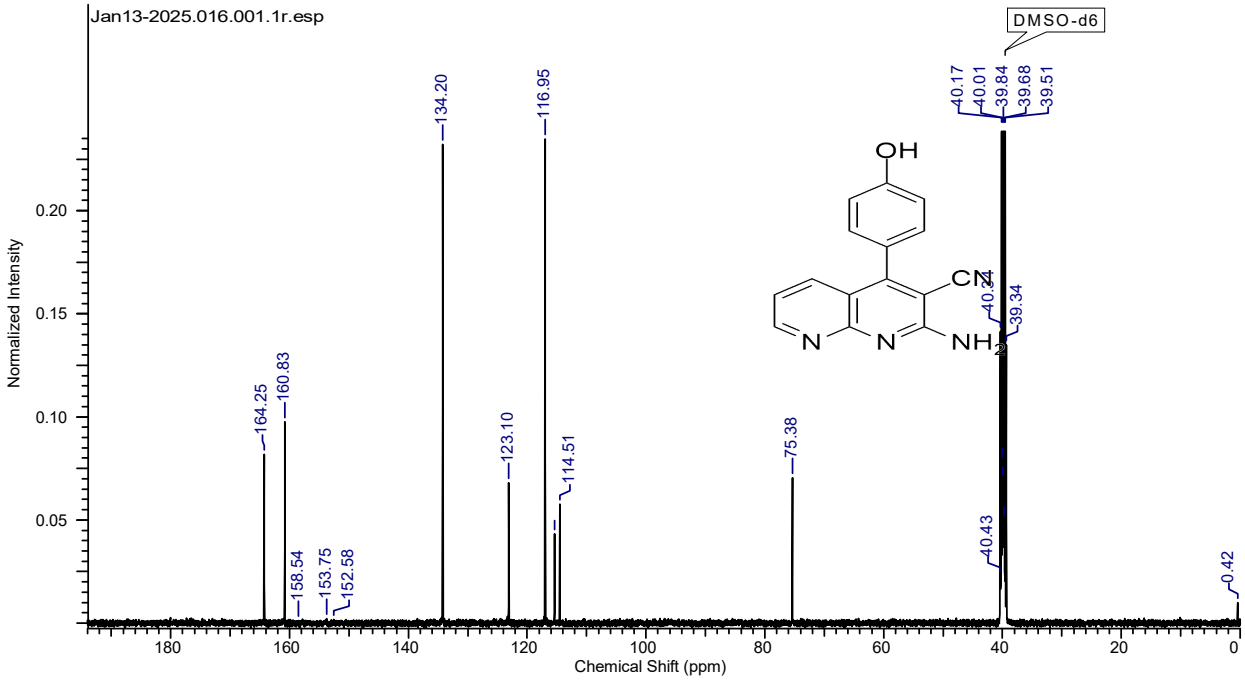


Figure S50: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(4-hydroxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4m**)

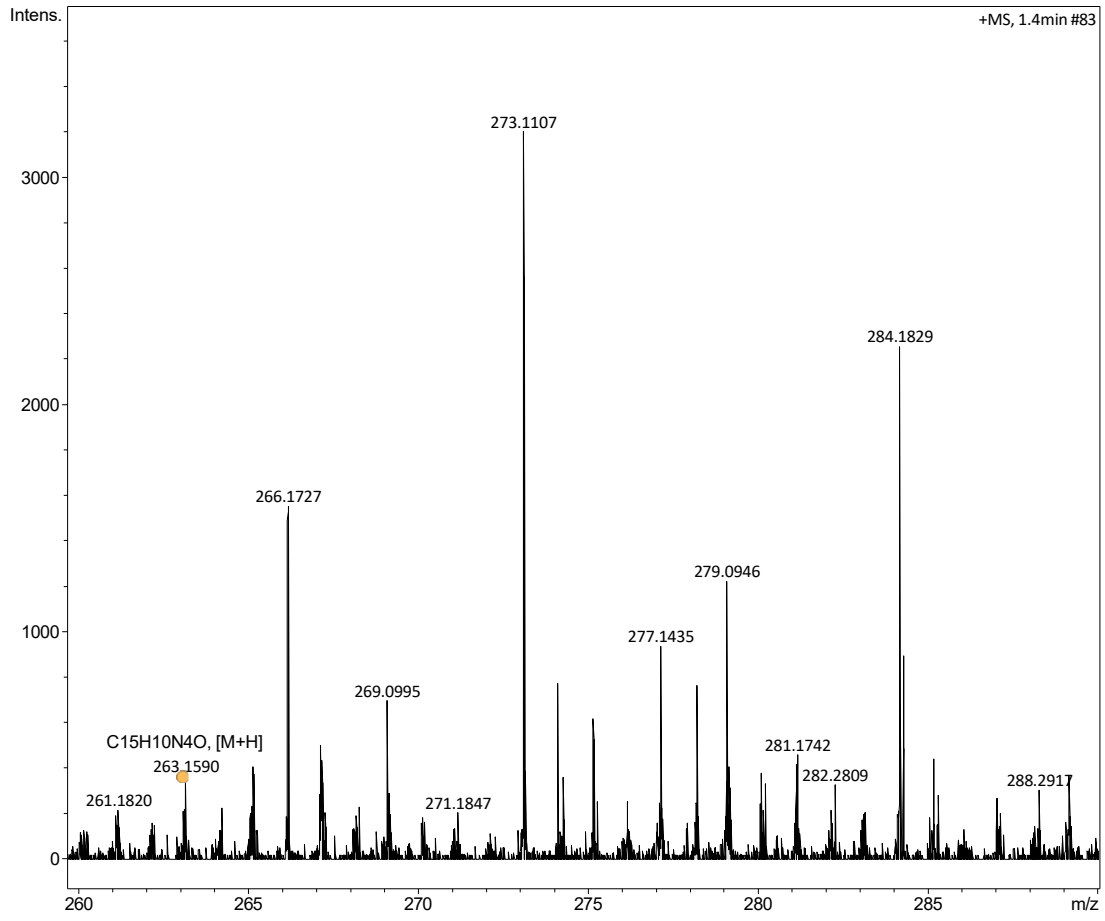
Savitribai Phule Pune University - Central Instrumentation Facility

Analysis Info

Acquisition Date	1/10/2024 10:33:38 PM		
Analysis Name	D:\Data\2024\JAN\SPPU COLLEGE\H. R. M. Rajgurunagar\RUPALI VADAK\D13_BA3_01_6756.d		
Method	dlc_ms20-1200mz_10min_0.120ml flow_90b_dec 23.m	Operator	Nitin S. Kadam CIF
Sample Name	D13	Instrument	impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	20 m/z	Set End Plate Offset	-500 V	Set Dry Gas	7.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



D13_BA3_01_6756.d

Bruker Compass DataAnalysis 4.2 printed: 1/23/2024 11:44:45 AM by: Nitin S. Kadam CIF Page 1 of 1

Figure S51: HR-ESI-MS Spectrum of 2-Amino-4-(4-hydroxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4m**)

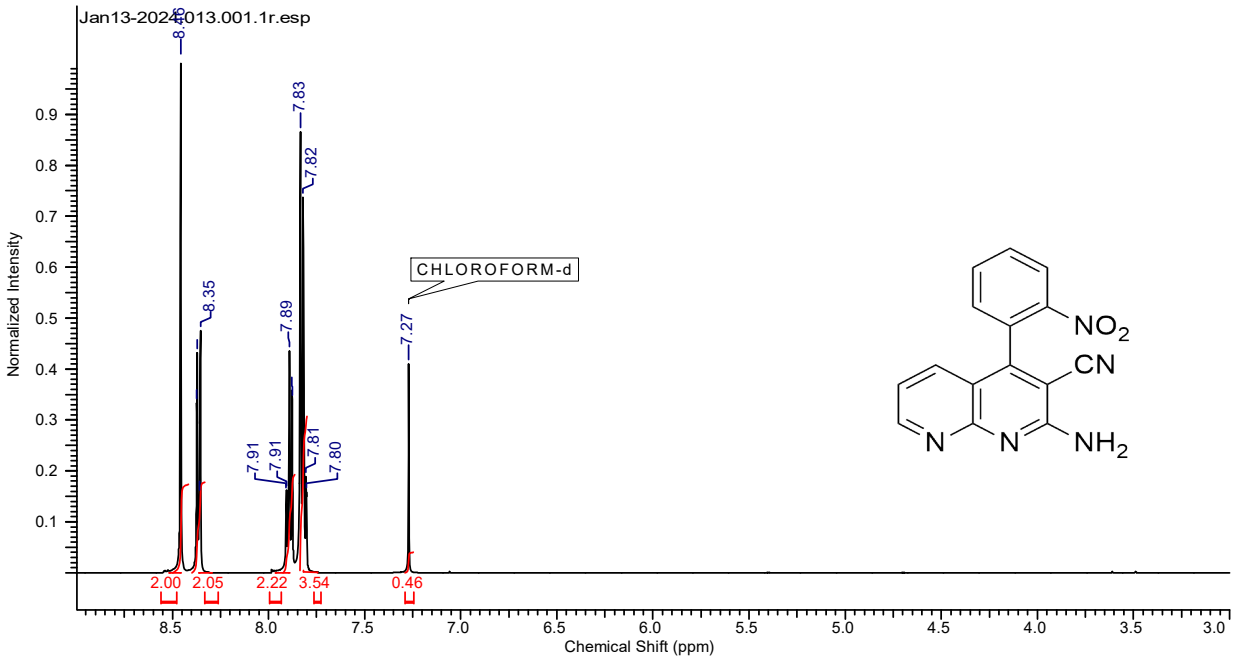


Figure S52: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-amino-4-(2-nitrophenyl)-1,8-naphthyridine-3-carbonitrile (**4n**)

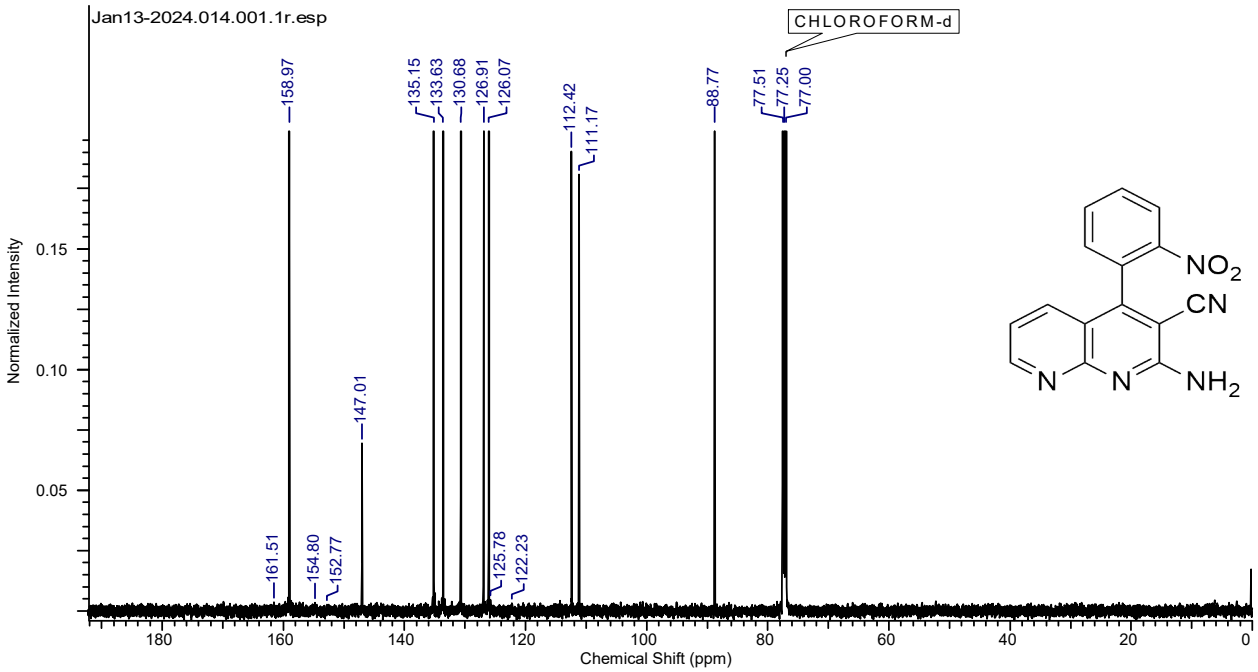


Figure S53: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-amino-4-(2-nitrophenyl)-1,8-naphthyridine-3-carbonitrile (**4n**)

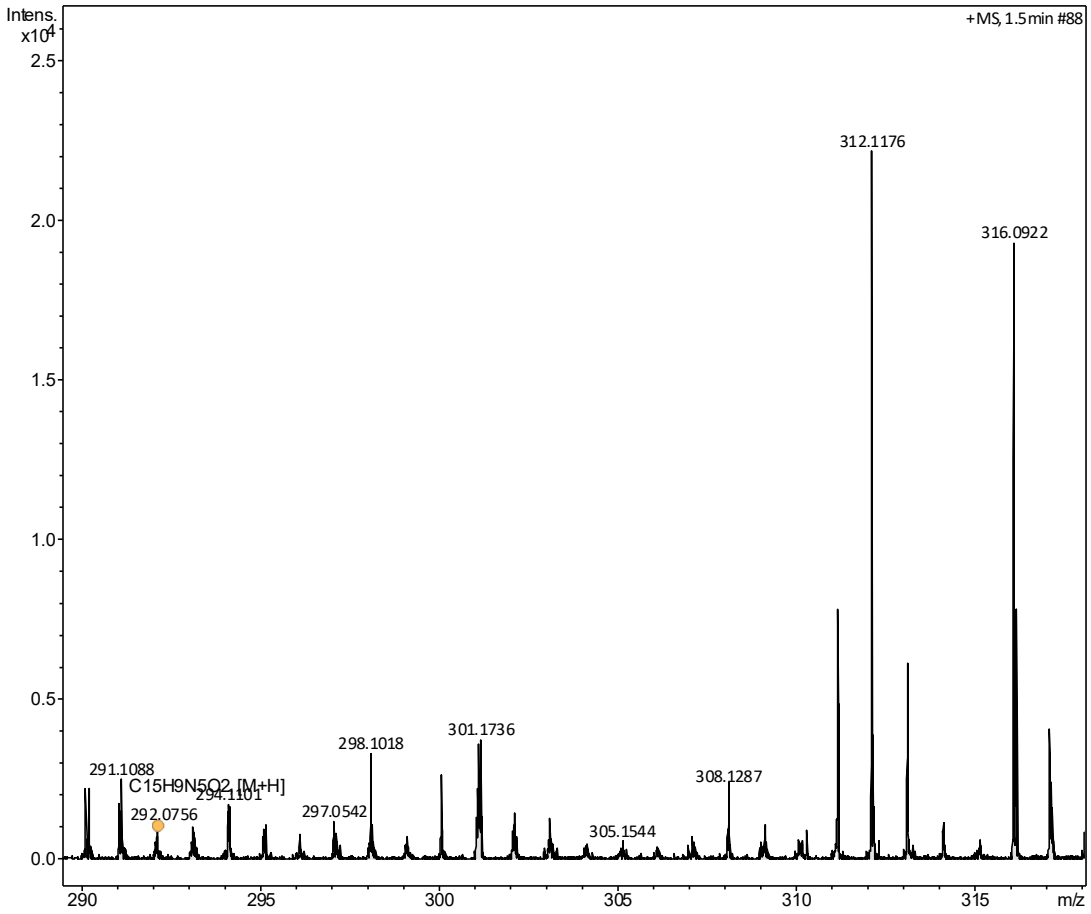
Savitribai Phule Pune University - Central Instrumentation Facility

Analysis Info

Analysis Name	D:\Data\2024\JAN\SPPU COLLEGE\H. R. M. Rajgurunagar\RUPALI VADAK\D14_RB3_01_6782.d	Acquisition Date	1/12/2024 5:27:50 PM
Method	dlc_ms20-1200mz_10min_0.120ml flow_90b_dec 23.m	Operator	Nitin S. Kadam CIF
Sample Name	D14	Instrument	impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	20 m/z	Set End Plate Offset	-500 V	Set Dry Gas	7.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



D14_RB3_01_6782.d

Bruker Compass DataAnalysis 4.2 printed: 1/23/2024 11:48:00 AM by: Nitin S. Kadam CIF Page 1 of 1

Figure S54: HR-ESI-MS Spectrum of 2-amino-4-(2-nitrophenyl)-1,8-naphthyridine-3-carbonitrile (**4n**)

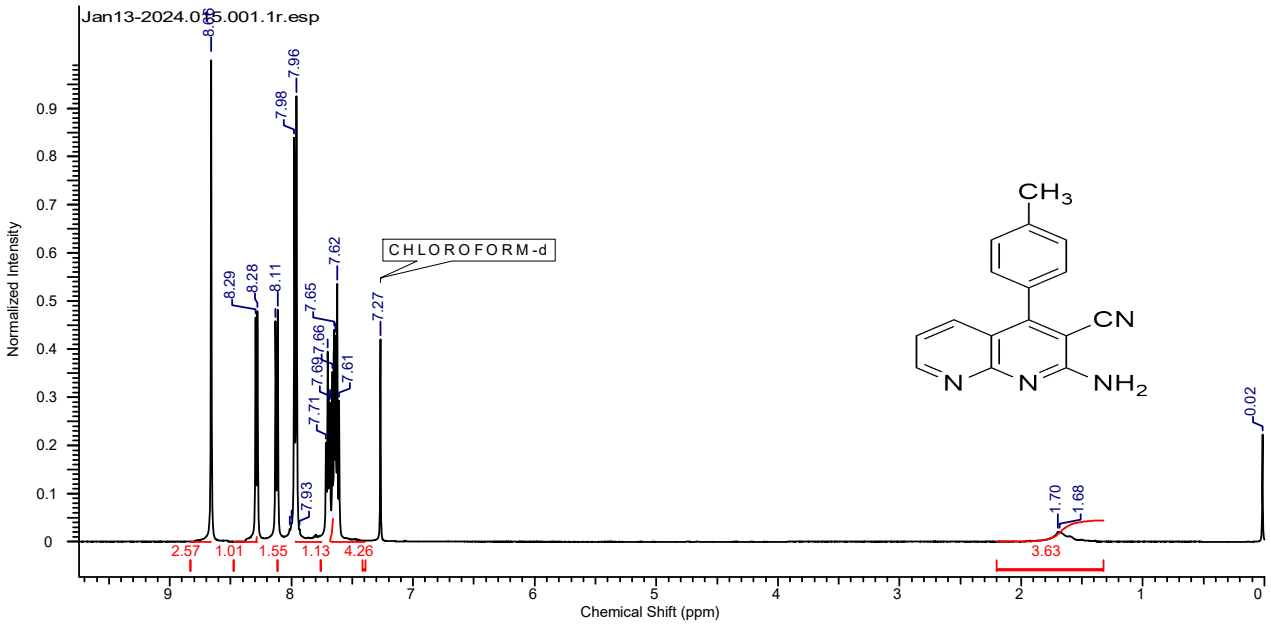


Figure S55: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-amino-4-(4-methylphenyl)-1,8-naphthyridine-3-carbonitrile (**4o**)

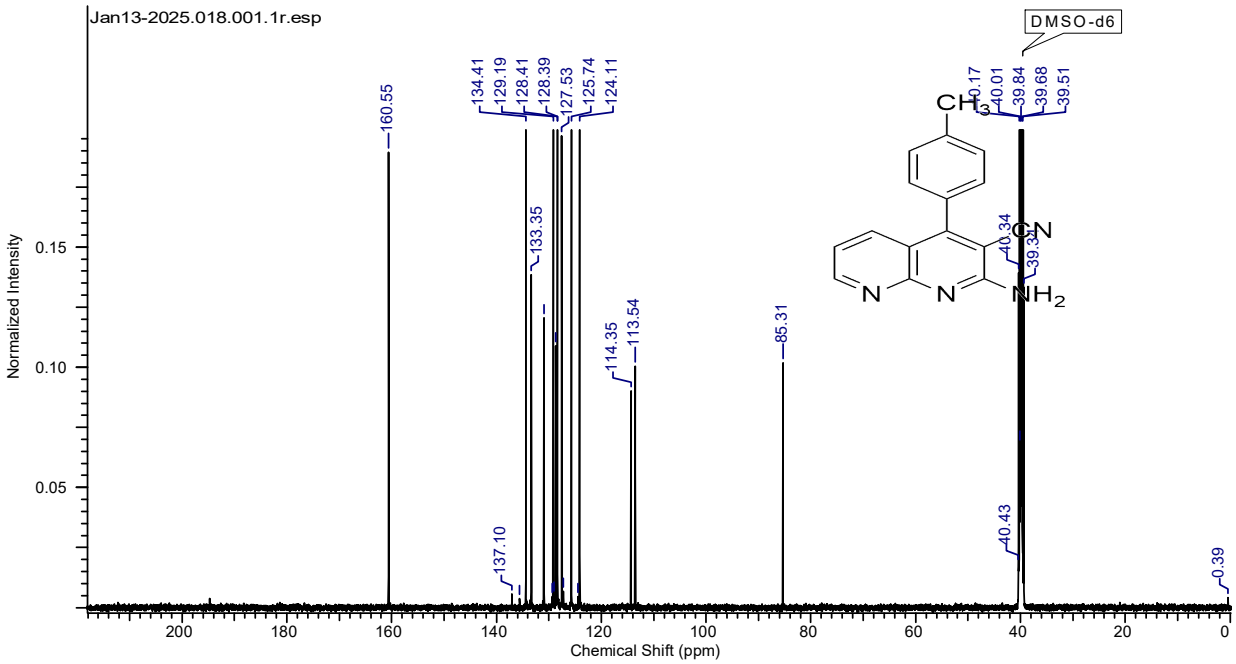


Figure S56: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-amino-4-(4-methylphenyl)-1,8-naphthyridine-3-carbonitrile (**4o**)

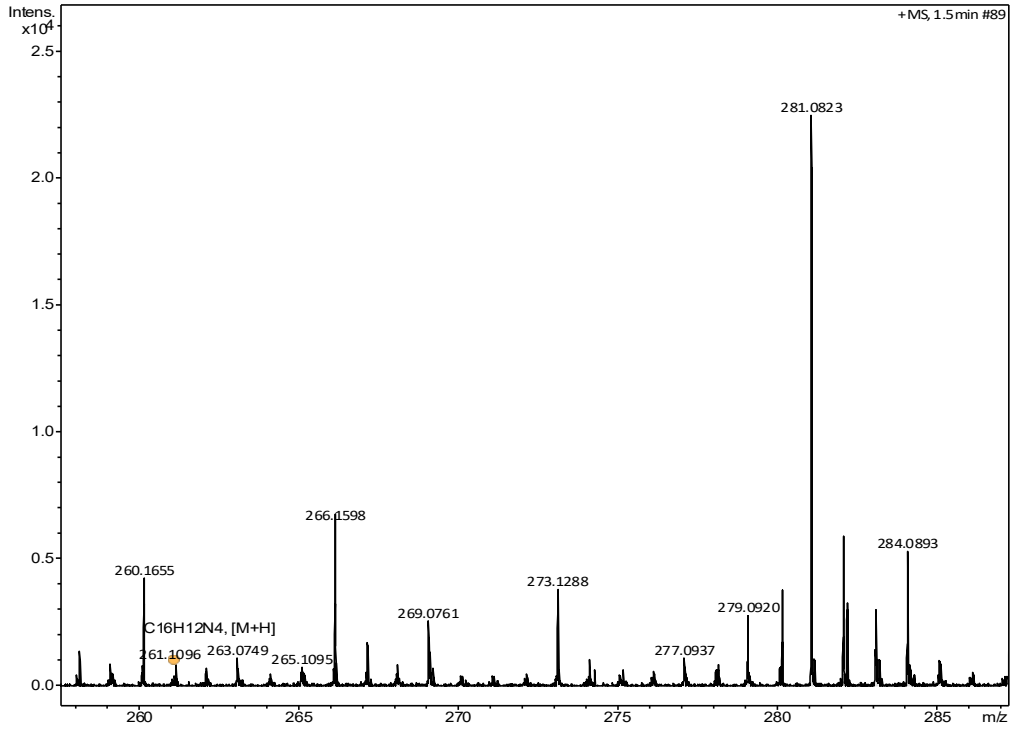
Savitribai Phule Pune University - Central Instrumentation Facility

Analysis Info

Analysis Name	D:\Data\2024\JAN\SPPU COLLEGE\H. R. M. Rajgurunagar\RUPALI VADAK\D15_RB4_01_6783.d	Acquisition Date	1/12/2024 5:38:30 PM
Method	dlc_ms20-1200mz_10min_0.120ml flow_90b_dec 23.m	Operator	Nitin S. Kadam CIF
Sample Name	D15	Instrument	impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	20 m/z	Set End Plate Offset	-500 V	Set Dry Gas	7.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



D15_RB4_01_6783.d

Bruker Compass DataAnalysis 4.2 printed: 1/23/2024 1:14:32 PM by: Nitin S. Kadam CIF Page 1 of 1

Figure S57: HR-ESI-MS Spectrum of 2-amino-4-(4-methylphenyl)-1,8-naphthyridine-3-carbonitrile (**4o**)

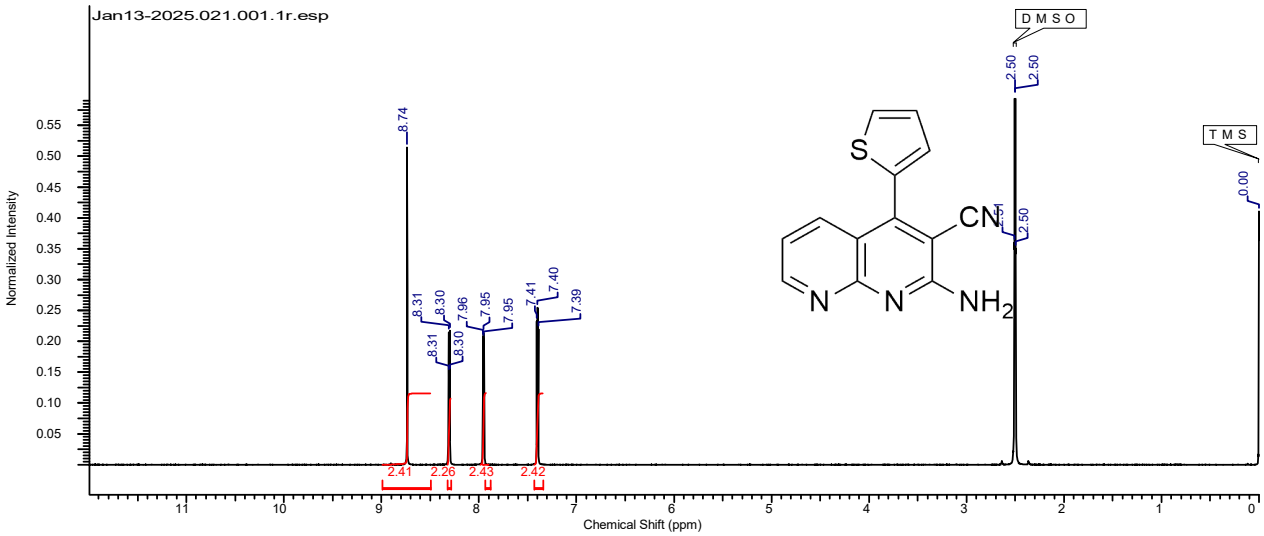


Figure S58: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(2-thiophenephenyl)-1,8-naphthyridine-3-carbonitrile (**4p**)

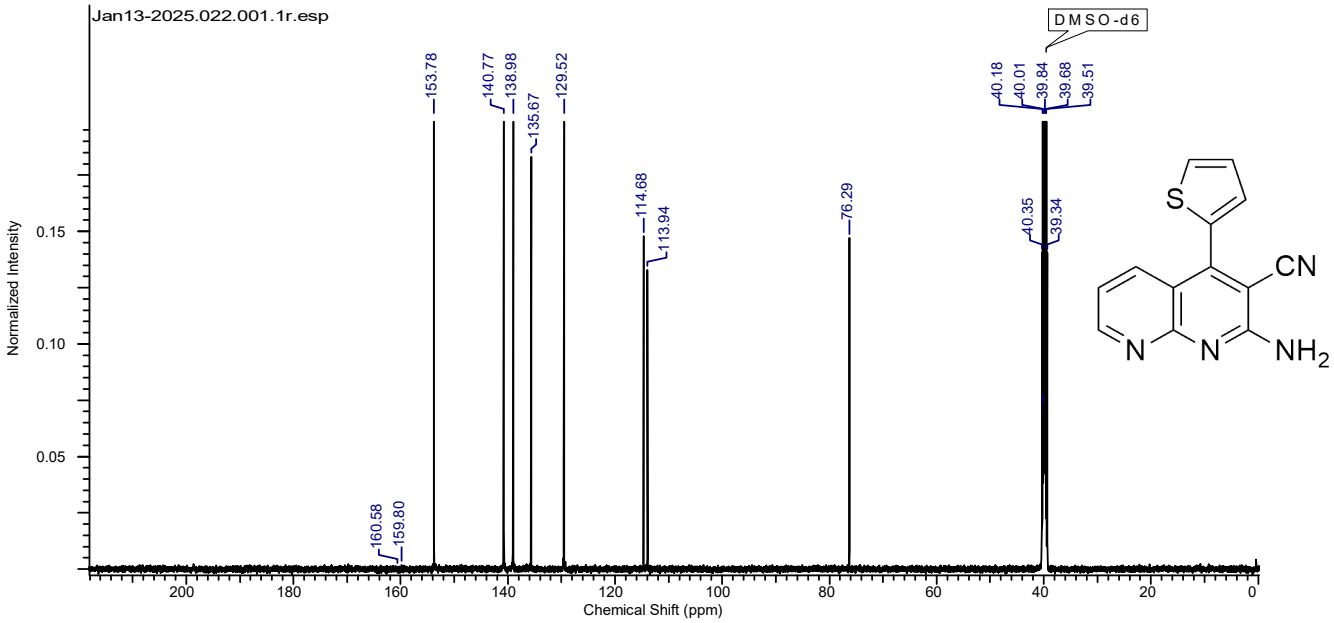


Figure S59: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(2-thiophenephenyl)-1,8-naphthyridine-3-carbonitrile (**4p**)

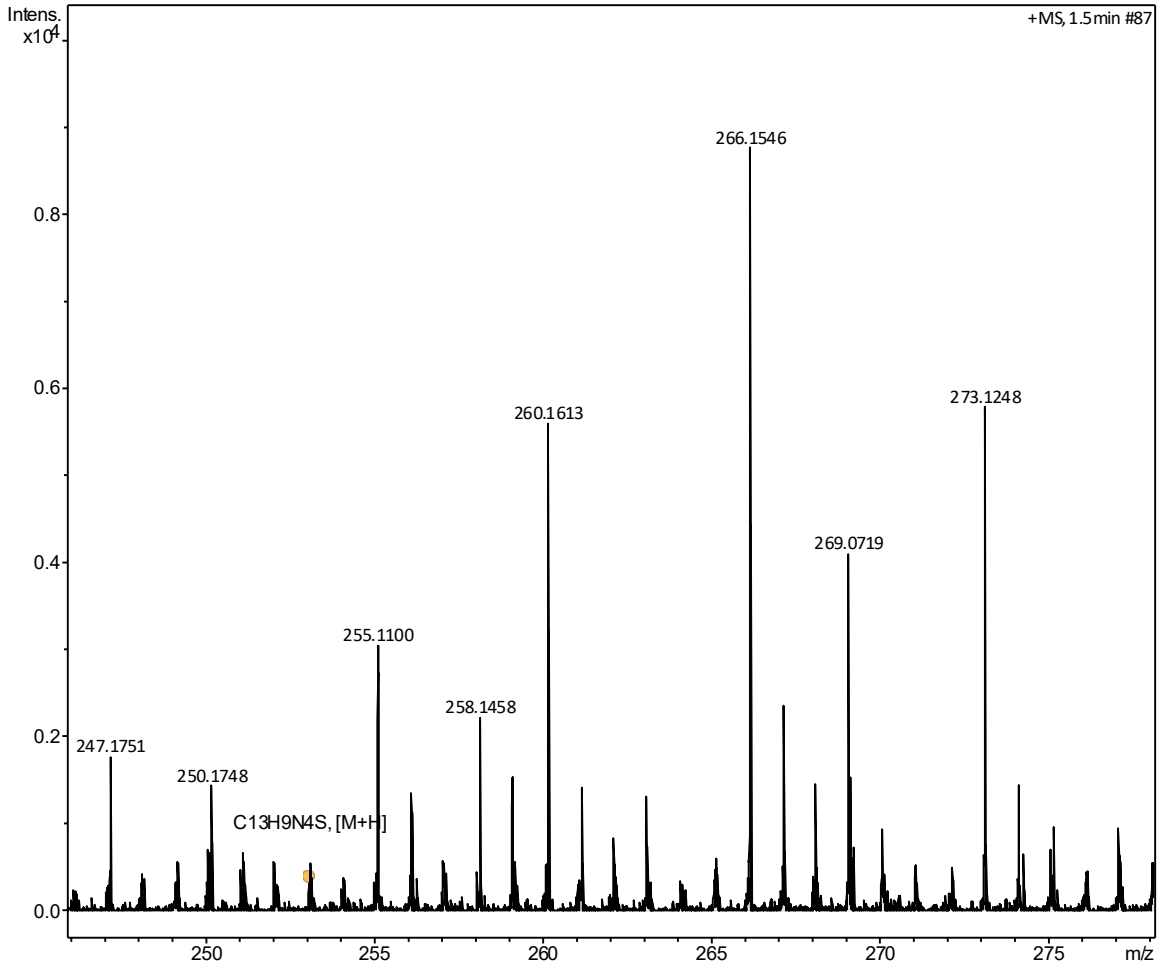
Savitribai Phule Pune University - Central Instrumentation Facility

Analysis Info

		Acquisition Date	1/12/2024 5:59:51 PM
Analysis Name	D:\Data\2024\JAN\SPPU COLLEGE\H. R. M. Rajgurunagar\RUPALI VADAK\D19_RB6_01_6785.d		
Method	dlc_ms20-1200mz_10min_0.120ml flow_90b_dec 23.m	Operator	Nitin S. Kadam CIF
Sample Name	D19	Instrument	impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	20 m/z	Set End Plate Offset	-500 V	Set Dry Gas	7.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule	Adduct
253.062978	1	C13H9N4S	100.00	253.054244	-8.7	-34.5	669.8	11.5	even	ok	M+H

D19_RB6_01_6785.d

Bruker Compass DataAnalysis 4.2 printed: 1/23/2024 1:30:53 PM by: Nitin S. Kadam CIF Page 1 of 1

Figure S60: HR-ESI-MS Spectrum 2-Amino-4-(2-thiophenephenyl)-1,8-naphthyridine-3-carbonitrile (**4p**)

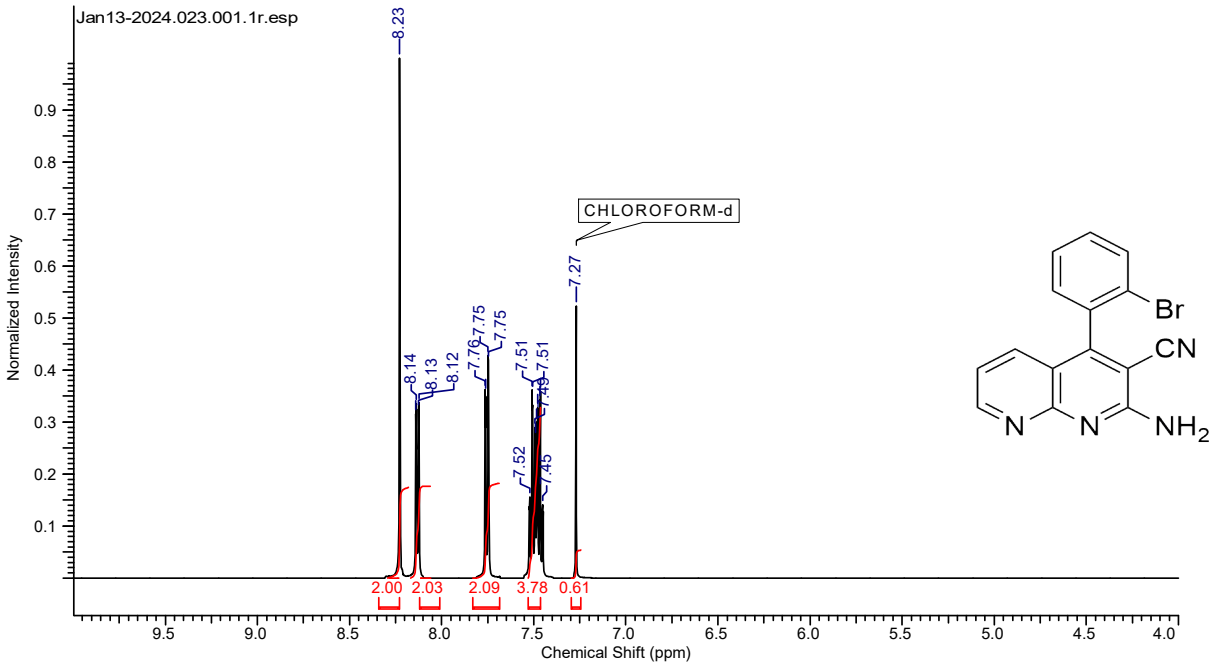


Figure S61: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(2-bromophenyl)-1,8-naphthyridine-3-carbonitrile (**4q**)

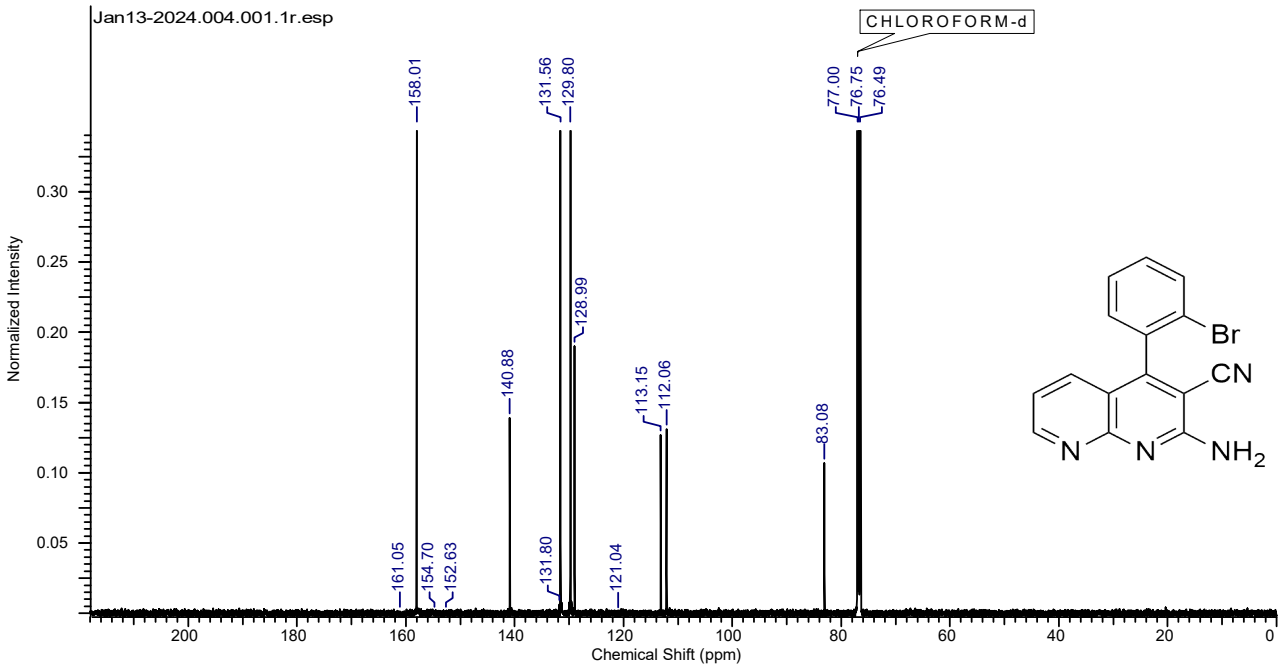


Figure S62: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-Amino-4-(2-bromophenyl)-1,8-naphthyridine-3-carbonitrile (**4q**)

Savitribai Phule Pune University - Central Instrumentation Facility

Analysis Info

Acquisition Date 1/24/2025 2:01:42 PM

Analysis Name D:\Data\2025\JAN\SPPU COLLEGE\HRM COLLEGE\DR. PRAMOD KULKARNI\VADAK RUPALI\D22_RB7_01_8727.d

Method dlc_50-1200mz_pos_mode_7min_0.2ml.m

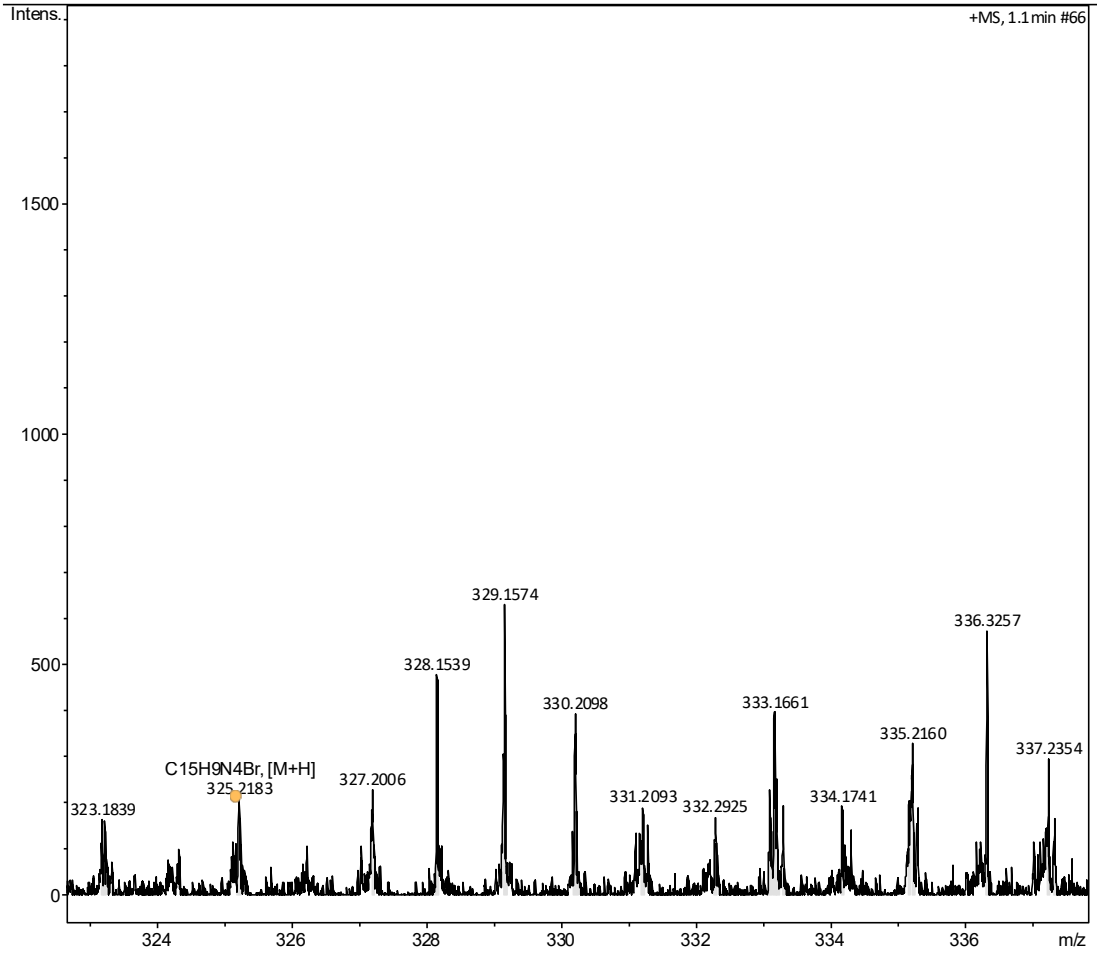
Analyst: Nitin S. Kadam CIF

Sample Name D22

Instrument impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.7 Bar
Focus	Active	Set Capillary	4000 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



D22_RB7_01_8727.d

Bruker Compass DataAnalysis 4.2 printed: 1/25/2025 12:09:22 PM by: Nitin S. Kadam CIF Page 1 of 1

Figure S63: HR-ESI-MS Spectrum of 2-Amino-4-(2-bromophenyl)-1,8-naphthyridine-3-carbonitrile (**4q**)

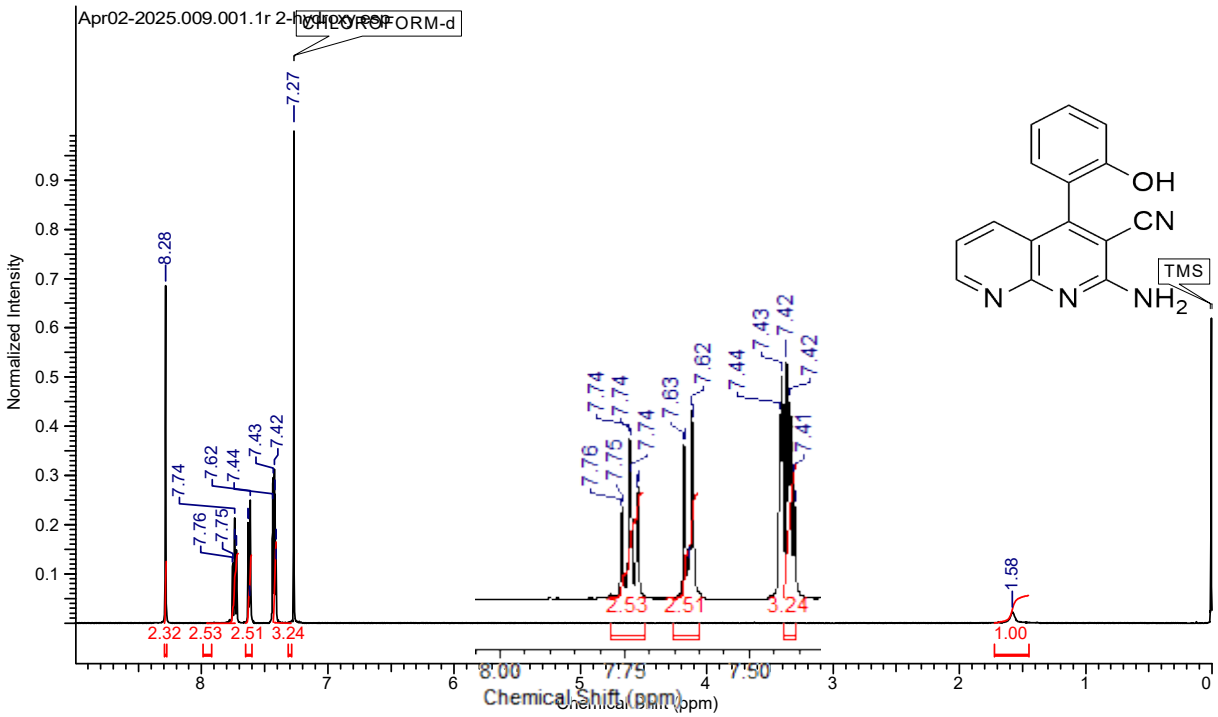


Figure S64: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-amino-4-(2-hydroxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4r**)

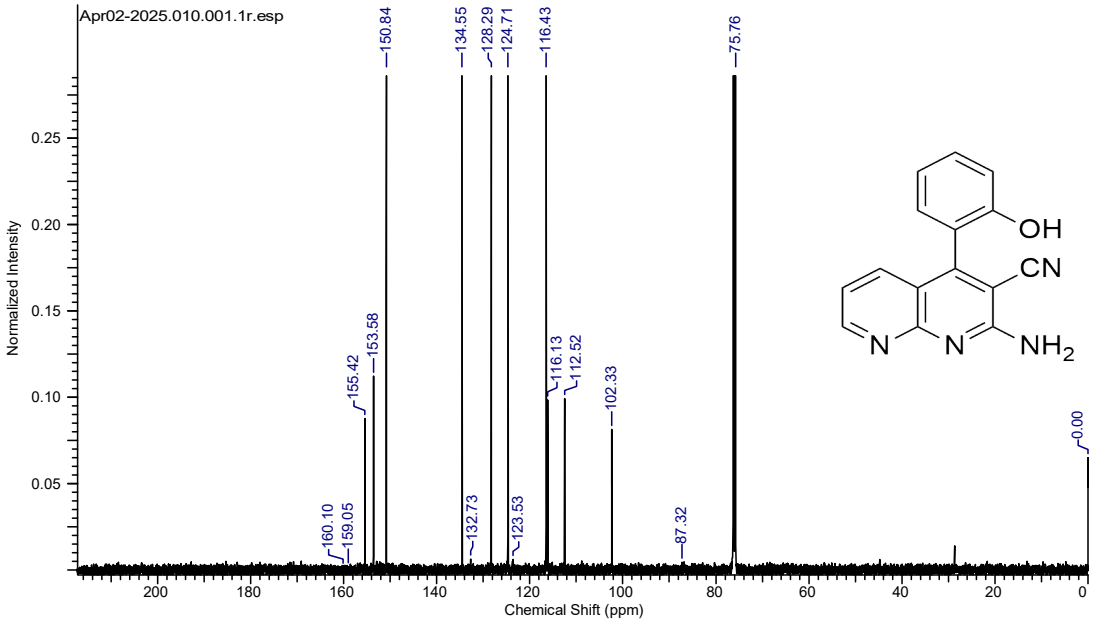


Figure S65: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-amino-4-(2-hydroxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4r**)

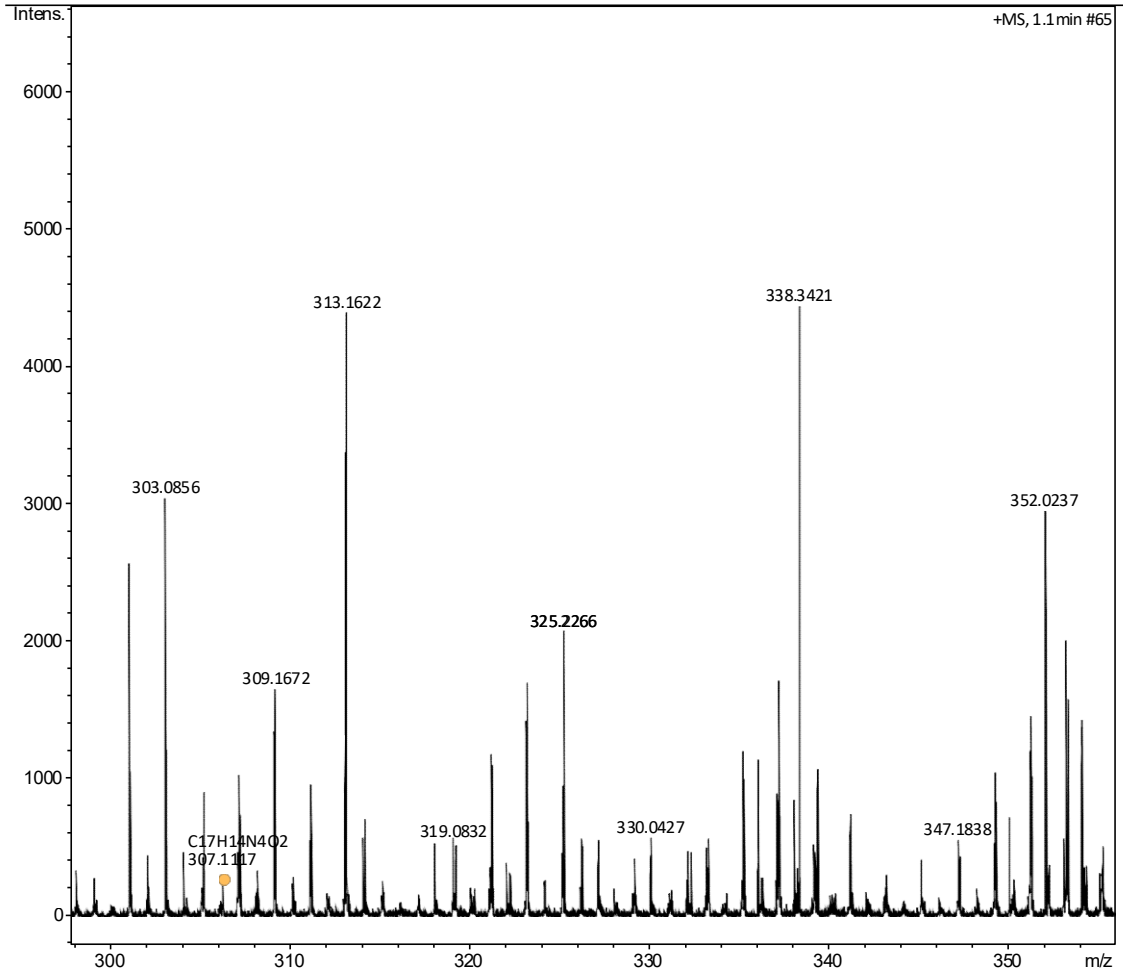
Savitribai Phule Pune University - Central Instrumentation Facility

Analysis Info

		Acquisition Date	4/3/2025 7:05:52 PM
Analysis Name	D:\Data\2025\APRIL\SPPU COLLEGE\HRM COLLEGE\HUNDARE PAYAL\D23_RE3_01_9260.d		
Method	dlc_50-1200mz_pos_mode_7min_0.2ml.m	Analyst:	Nitin S. Kadam CIF
Sample Name	D23	Instrument	impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.7 Bar
Focus	Active	Set Capillary	4000 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



D23_RE3_01_9260.d

Bruker Compass DataAnalysis 4.2 printed: 4/7/2025 4:00:23 PM by: Nitin S. Kadam CIF Page 1 of 1

Figure S66: HR-ESI-MS Spectrum of 2-amino-4-(2-hydroxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4r**)

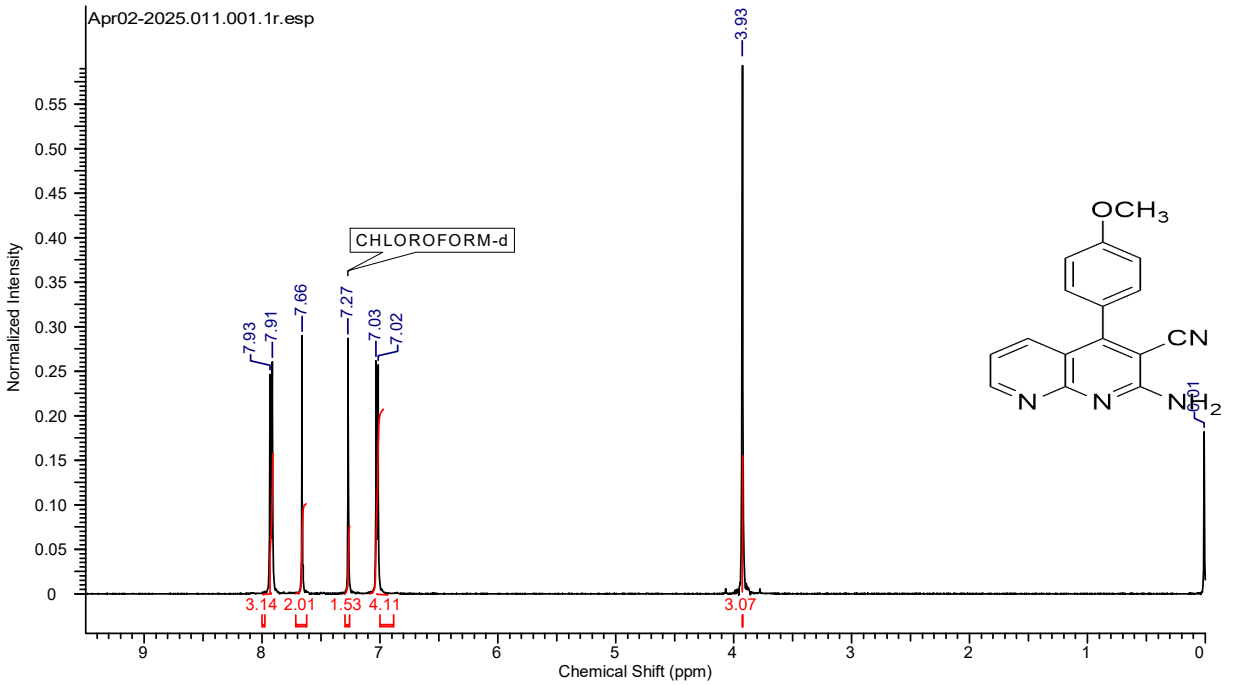


Figure S67: ^{1}H-NMR (500 MHz, $CDCl_3$) Spectrum of 2-amino-4-(4-methoxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4s**)

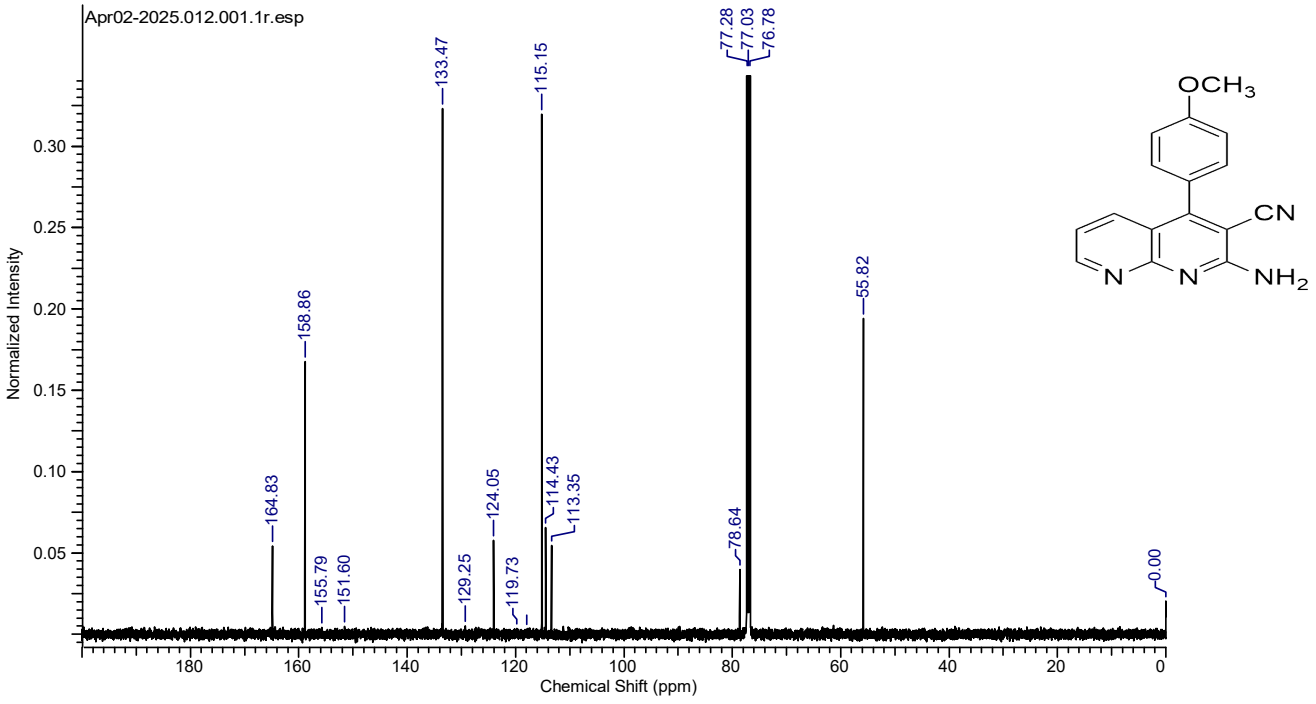


Figure S68: ^{13}C-NMR (125 MHz, $CDCl_3$) Spectrum of 2-amino-4-(4-methoxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4s**)

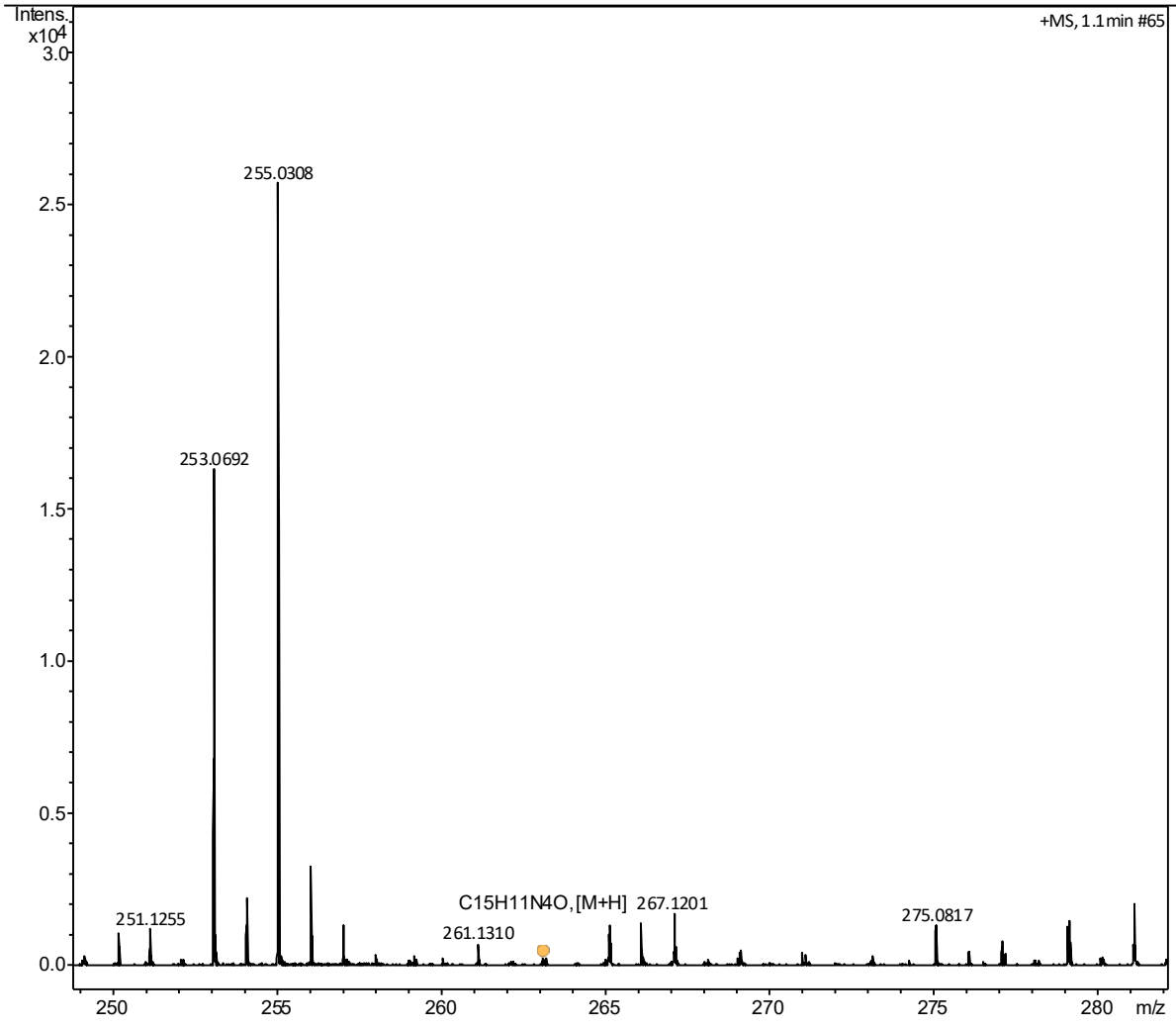
Savitribai Phule Pune University - Central Instrumentation Facility

Analysis Info

Analysis Name	D:\Data\2025\APRIL\SPPU COLLEGE\HRM COLLEGE\HUNDARE PAYAL\D24_RE2_01_9259.d	Acquisition Date	4/3/2025 6:58:18 PM
Method	dlc_50-1200mz_pos_mode_7min_0.2ml.m	Analyst:	Nitin S. Kadam CIF
Sample Name	D24	Instrument	impact HD 1819696.00184

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.7 Bar
Focus	Active	Set Capillary	4000 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1200 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule	Adduct
263.091420	1	C15H11N4O	100.00	263.092737	1.3	5.0	724.3	12.5	even	ok	M+H

Figure S69: HR-ESI-MS Spectrum of 2-amino-4-(4-methoxyphenyl)-1,8-naphthyridine-3-carbonitrile (**4s**)