Chapter 9

References

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References

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Appendix

10.1 Supplementary data of Pyrazole and Spiropyrazoline Analogs

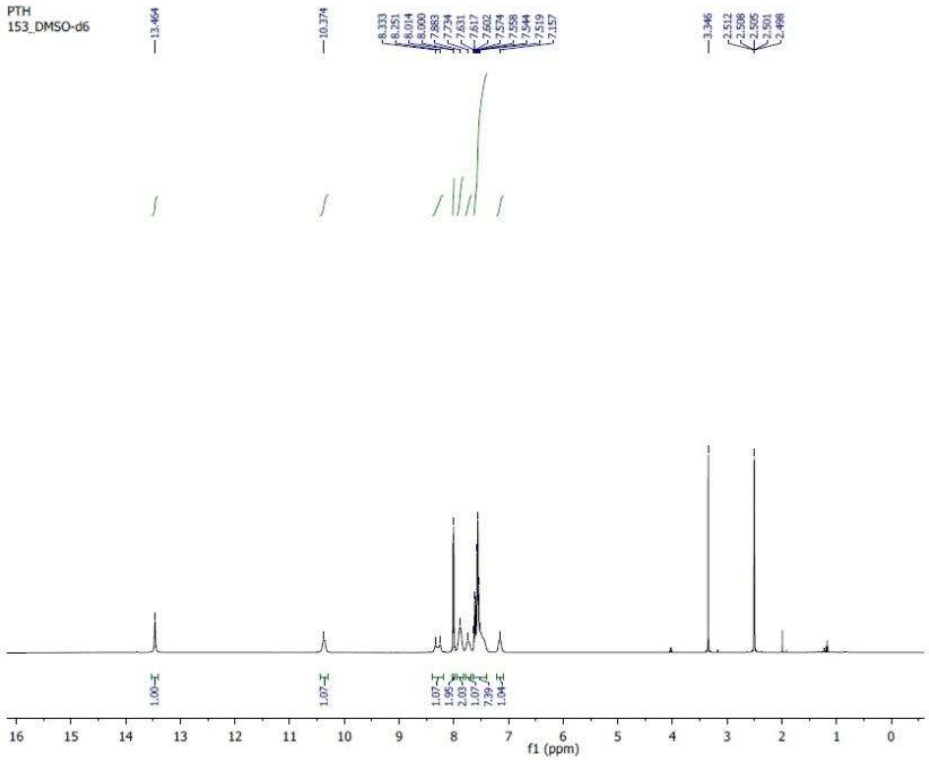


Figure A.1. ^{1}H NMR spectrum of *N-(3-(3-(4-chlorophenyl)-1H-pyrazol-5-yl)phenyl) benzamide* (**44**).

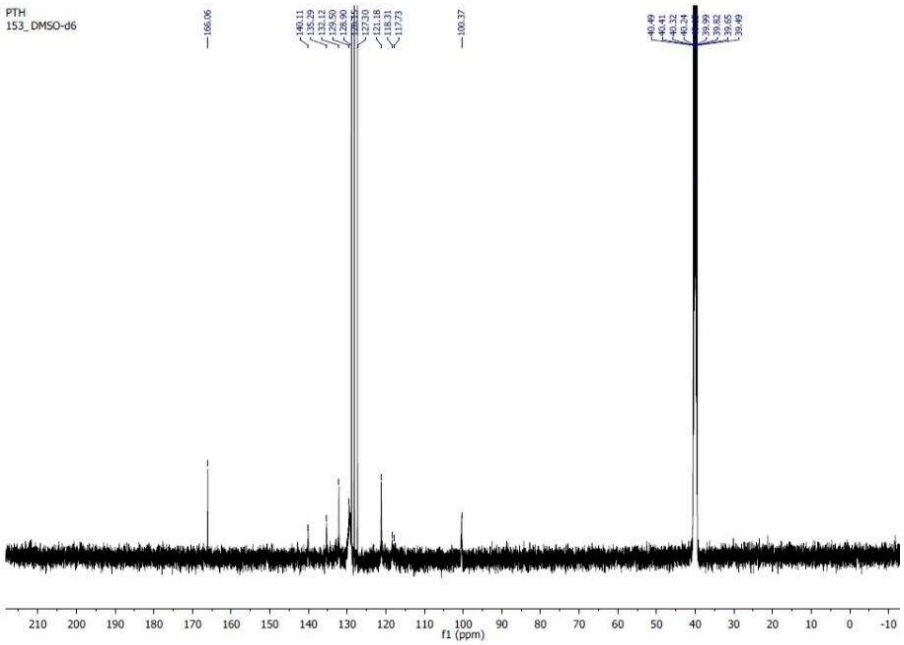


Figure A.2. ^{13}C NMR spectrum of *N-(3-(3-(4-chlorophenyl)-1H-pyrazol-5-yl)phenyl) benzamide* (**44**).

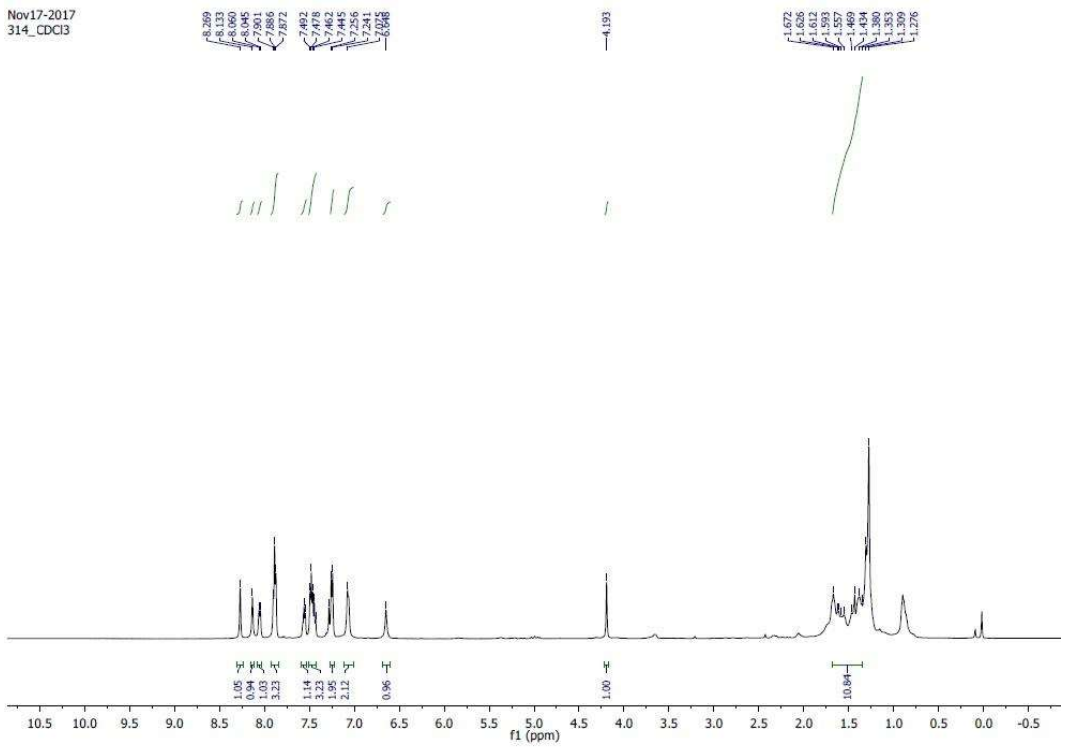


Figure A.3. [1]H NMR spectrum of *N-(3-(4-(4-chlorophenyl)-1,2-diazaspiro[4.5]dec-2-ene-3-carbonyl)phenyl)benzamide* (**67**).

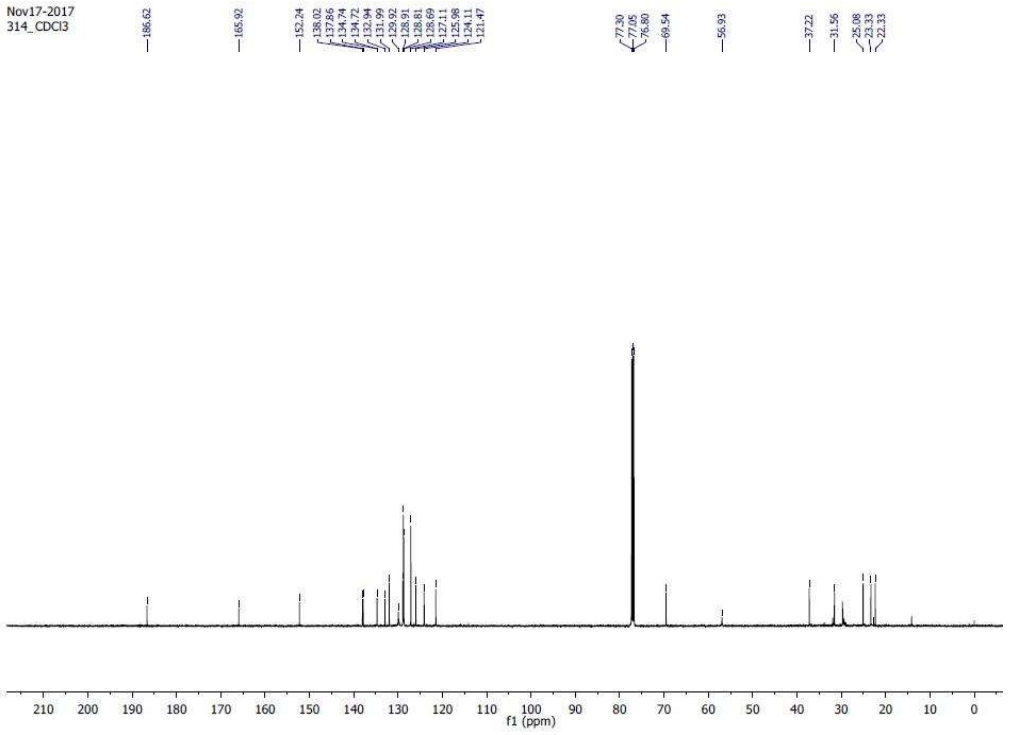


Figure A.4. [13]C NMR spectrum of *N-(3-(4-(4-chlorophenyl)-1,2-diazaspiro[4.5]dec-2-ene-3-carbonyl)phenyl)benzamide* (**67**).

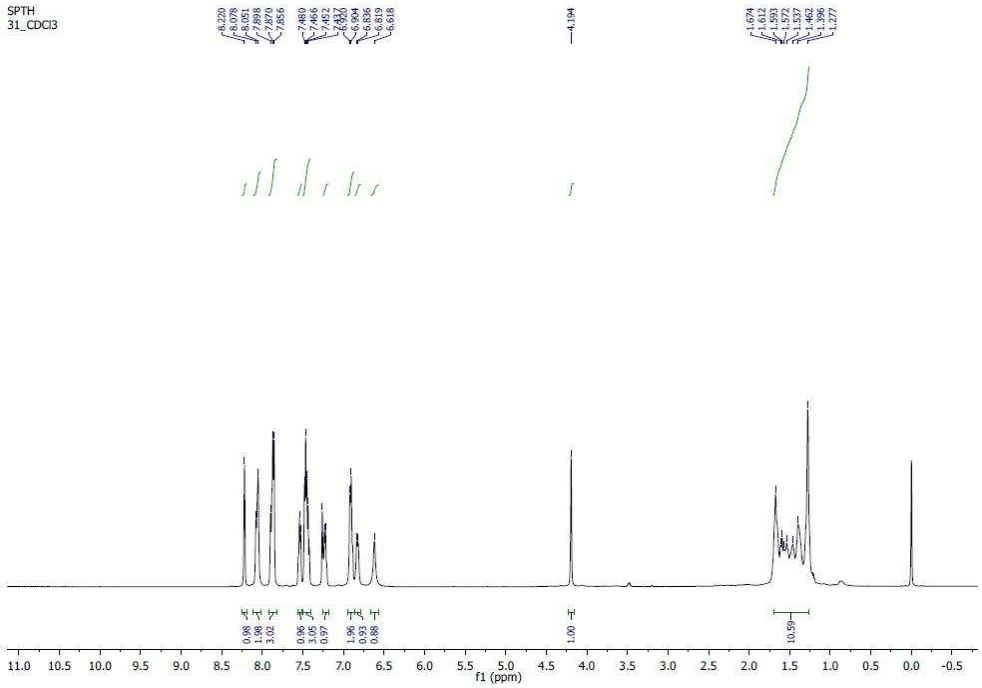


Figure A.5. ^{1}H NMR spectrum of *N-(3-(4-(3-fluorophenyl)-1,2-diazaspiro[4.5]dec-2-ene-3-carbonyl)phenyl)benzamide* (**73**).

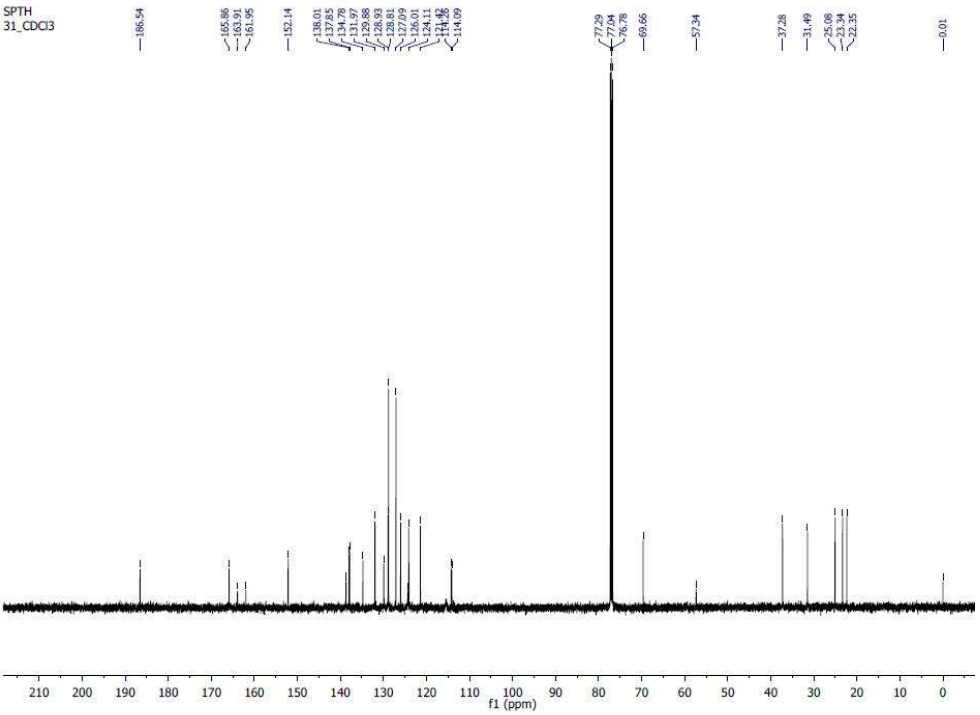


Figure A.6. ^{13}C NMR spectrum of *N-(3-(4-(3-fluorophenyl)-1,2-diazaspiro[4.5]dec-2-ene-3-carbonyl)phenyl)benzamide* (**73**).

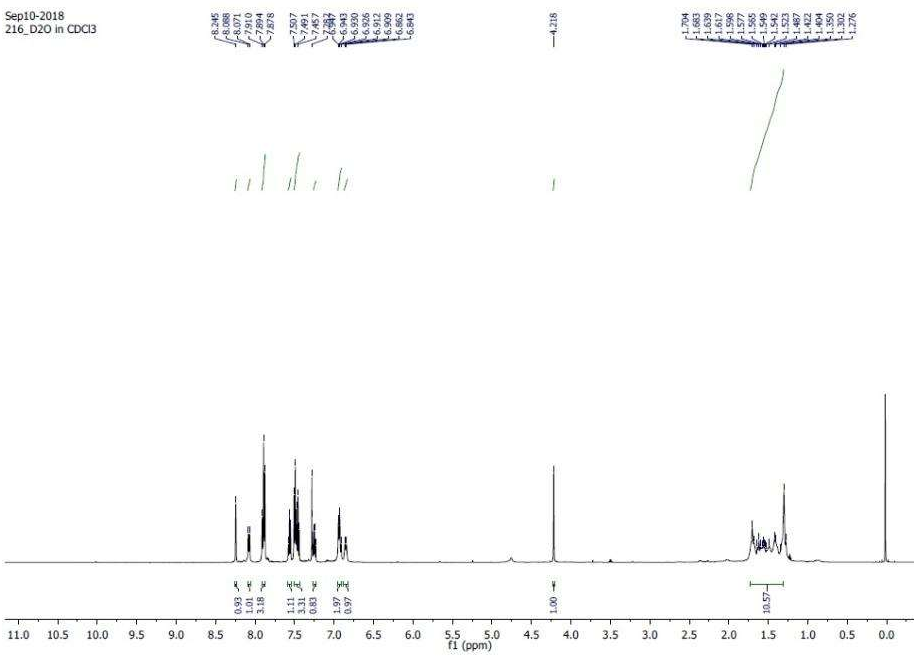


Figure A.7. ^{1}H NMR spectrum of spectrum of *N-(3-(4-(3-fluorophenyl)-1,2-diazaspiro[4.5]dec-2-ene-3-carbonyl)phenyl)benzamide* (**73**) after D_2O exchange**.**

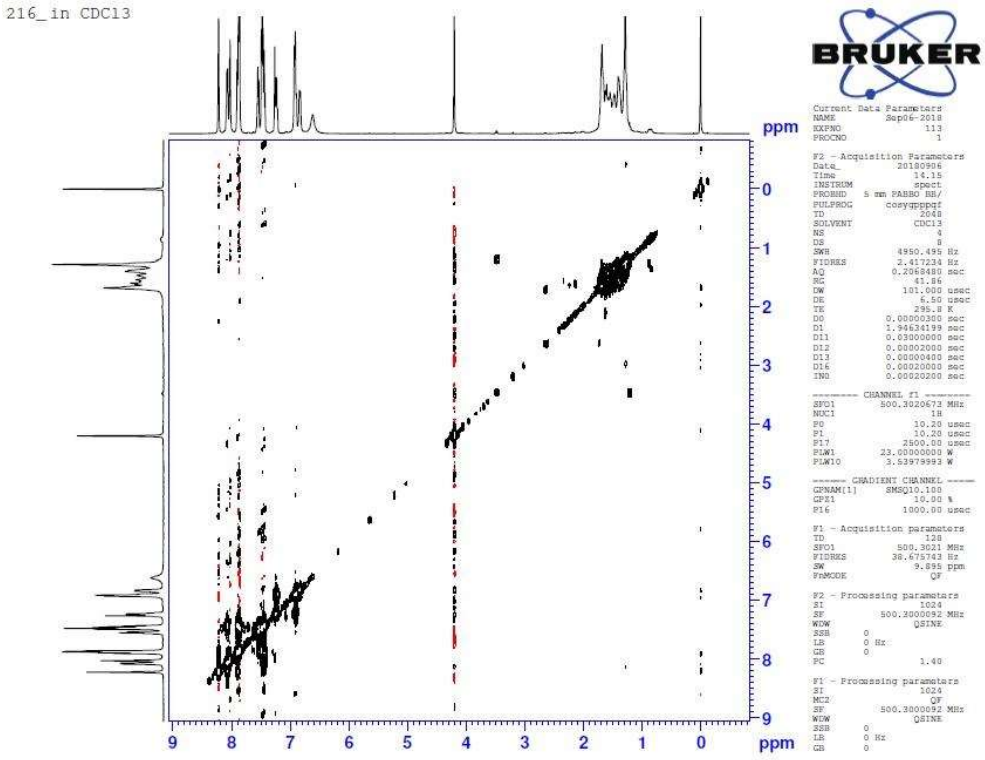


Figure A.8. Correlated spectroscopy (COSY; ^{1}H-^{1}H) NMR spectrum of *N-(3-(4-(3-fluorophenyl)-1,2-diazaspiro[4.5]dec-2-ene-3-carbonyl)phenyl)benzamide* (**73**).

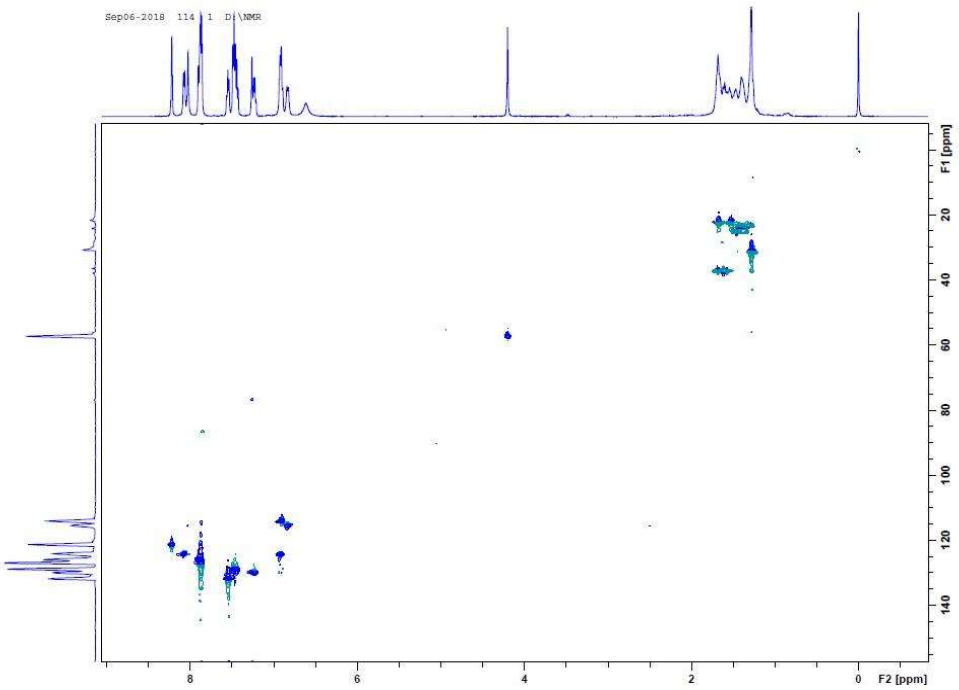


Figure A.9. Heteronuclear single quantum correlation (HSQC; ^{1}H-^{13}C) NMR spectrum of *N-(3-(4-(3-fluorophenyl)-1,2-diazaspiro[4.5]dec-2-ene-3-carbonyl)phenyl)benzamide* (**73**).

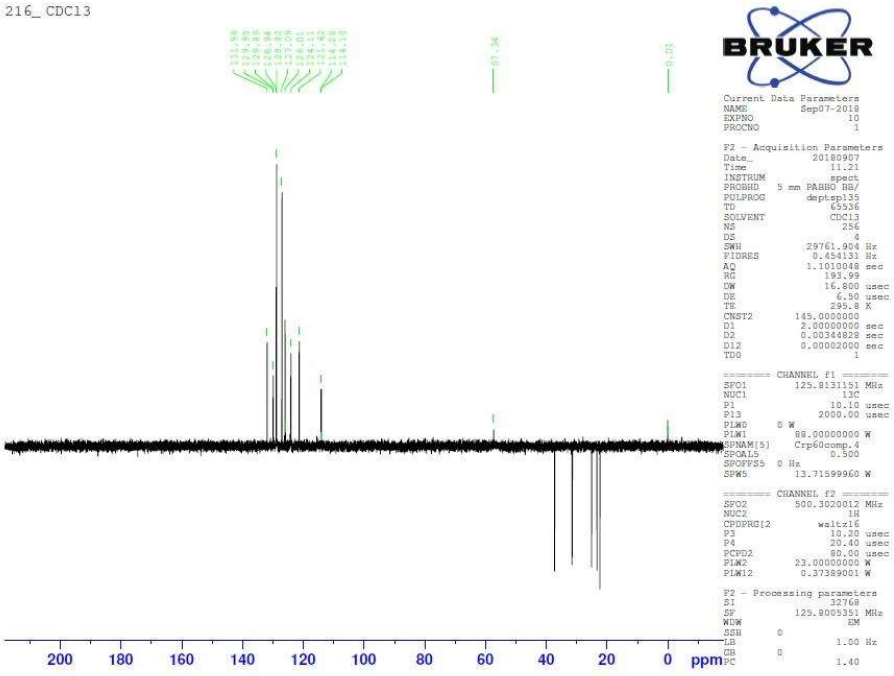
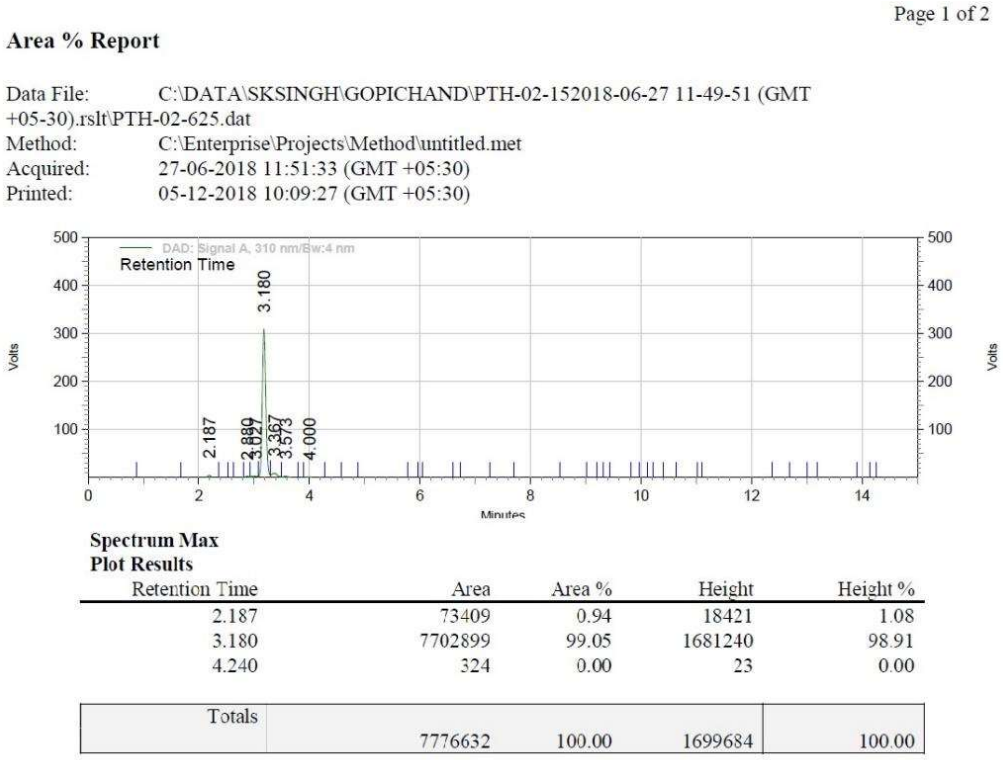


Figure A.10. Distortionless enhancement by polarization transfer (DEPT-135°) NMR spectrum of *N-(3-(4-(3-fluorophenyl)-1,2-diazaspiro[4.5]dec-2-ene-3-carbonyl)phenyl) benzamide* (**73**).



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Spectrum Max
Plot Results

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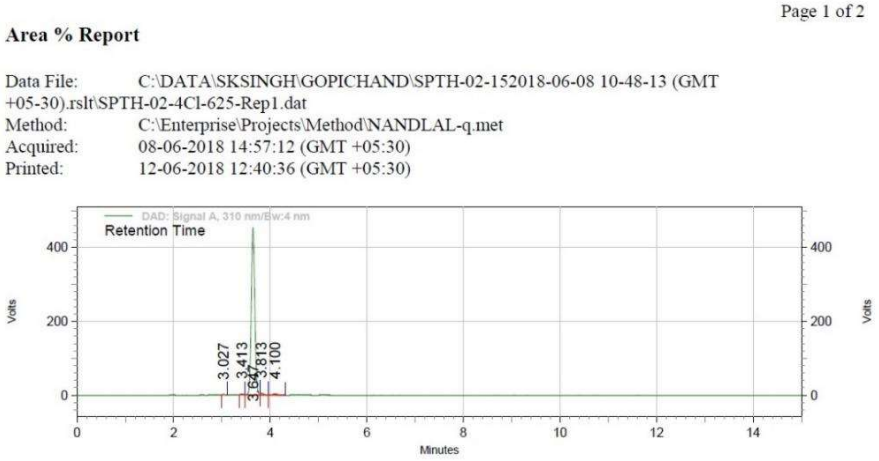
3.180	7702899	99.05	1681240	98.91
4.240	324	0.00	23	0.00
Totals	7776632	100.00	1699684	100.00

Figure A.11. HPLC of *N-(3-(3-(4-chlorophenyl)-1H-pyrazol-5-yl)phenyl) benzamide* (**44**) at 625µg/ml.



Page 1 of 2

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Spectrum Max
Plot Results

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3.027	12659	0.25	3723	0.38
3.413	12929	0.26	3309	0.34
3.647	4851205	97.60	949099	97.55
3.813	42474	0.85	8736	0.90
4.100	51312	1.03	8060	0.83
Totals	4970579	100.00	972927	100.00

Figure A.12. HPLC of *N-(3-(4-(4-chlorophenyl)-1,2-diazaspiro[4.5]dec-2-ene-3-carbonyl)phenyl)benzamide* (**67**) at 625µg/ml.

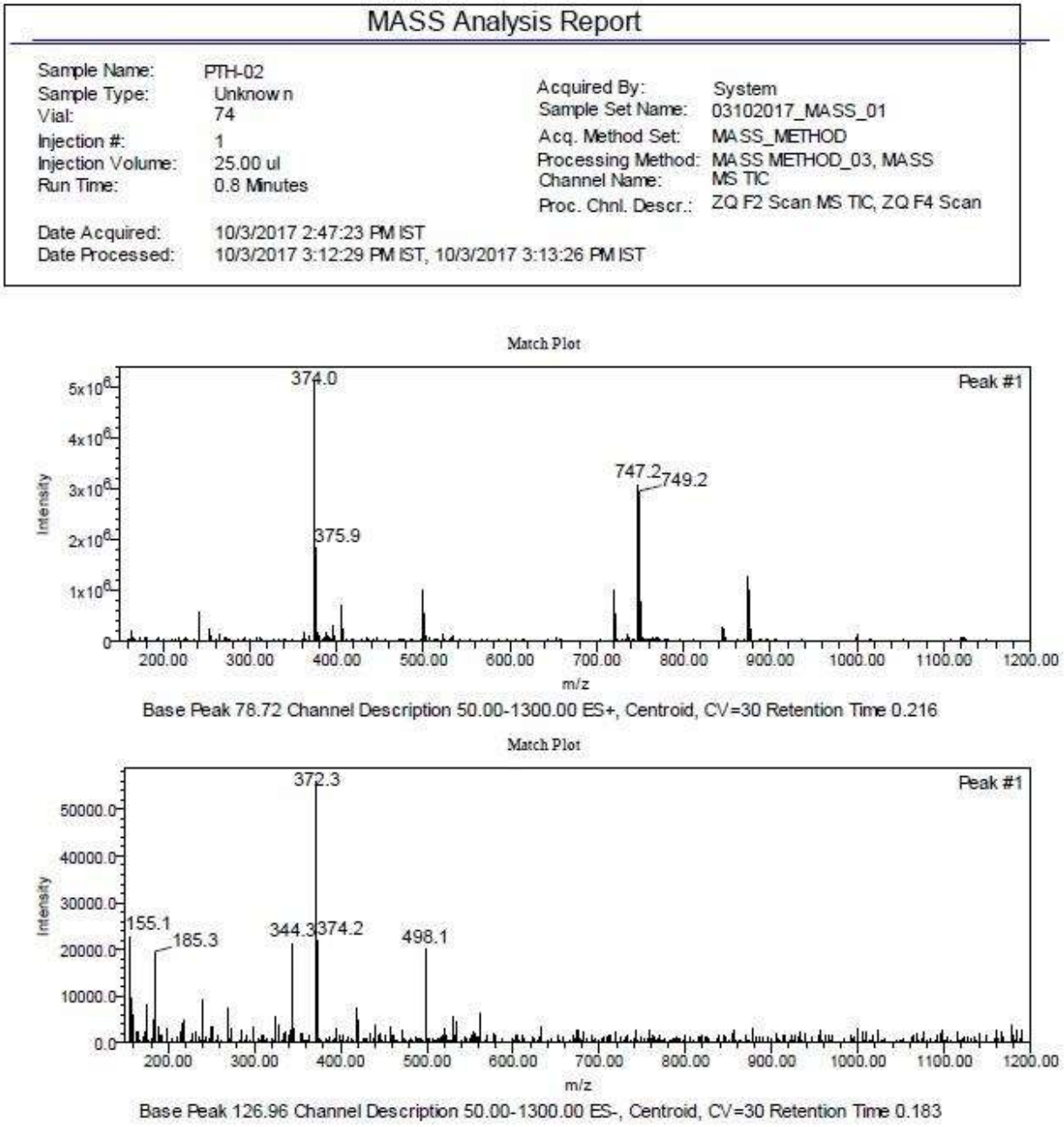

Figure A.13. Mass spectra of *N-(3-(3-(4-chlorophenyl)-1H-pyrazol-5-yl)phenyl) benzamide* (**44**).

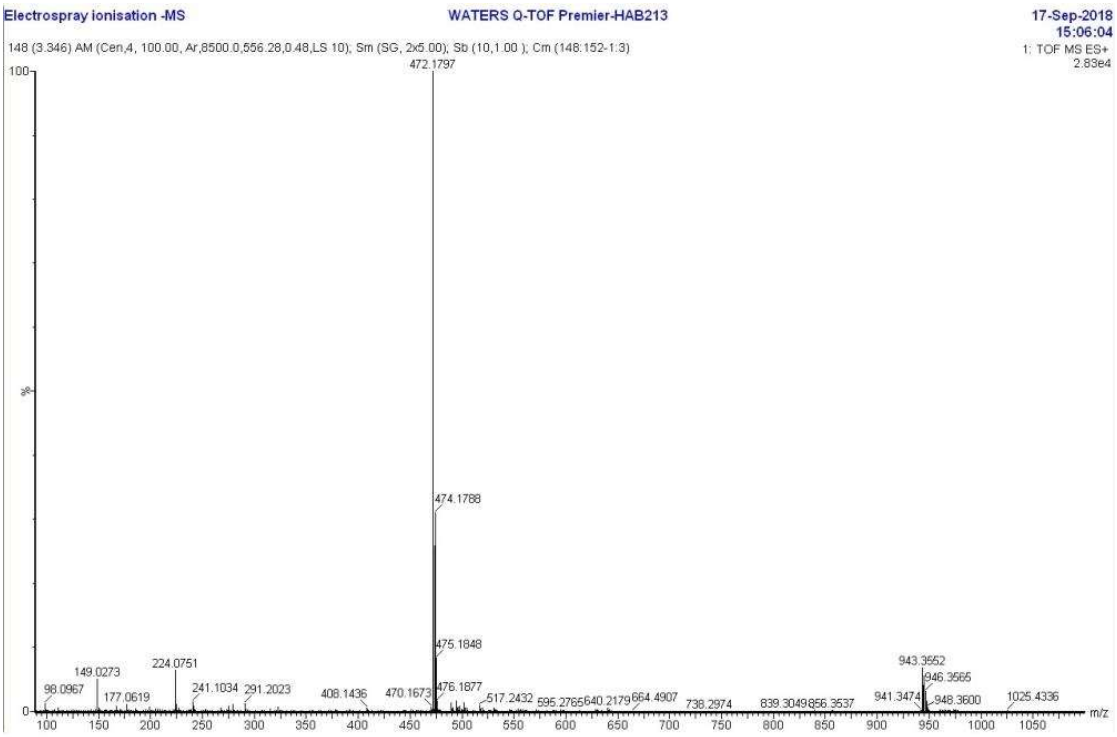

Figure A.14. HRMS of *N-(3-(4-(4-chlorophenyl)-1,2-diazaspiro[4.5]dec-2-ene-3-carbonyl)phenyl)benzamide* (**67**).

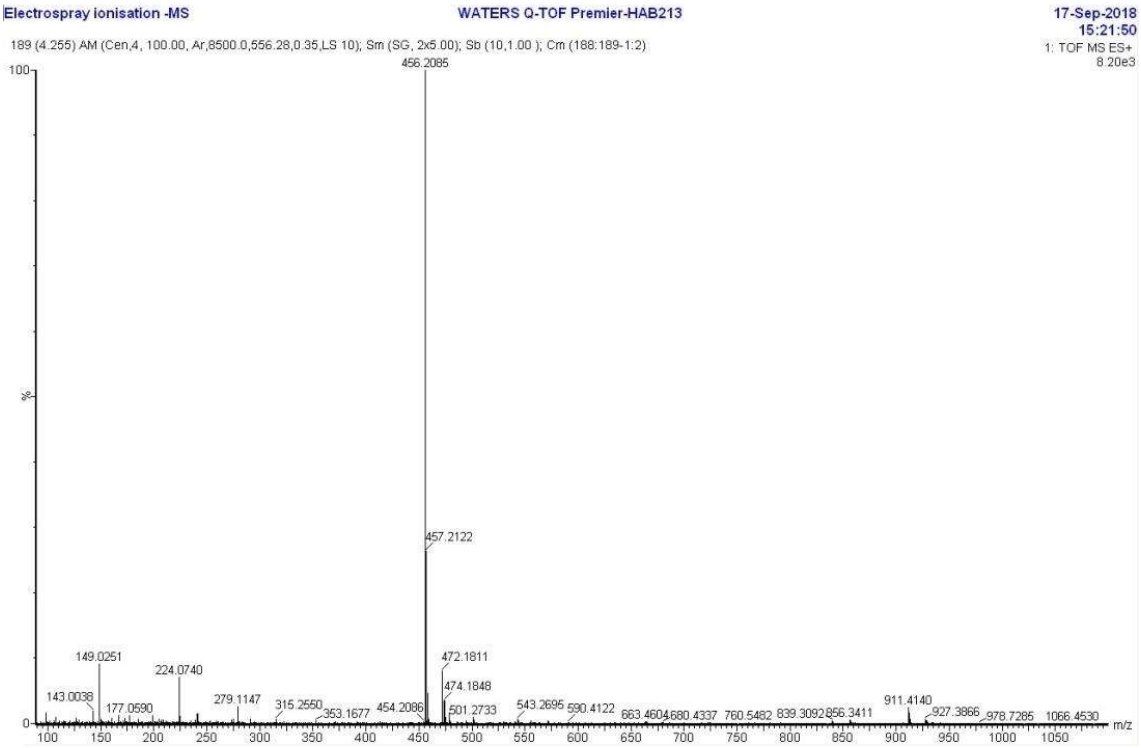

Figure A.15. HRMS of *N-(3-(4-(3-fluorophenyl)-1,2-diazaspiro[4.5]dec-2-ene-3-carbonyl)phenyl) benzamide* (**73**).

Table A.1. HPLC data of pyrazole and spiropyrazoline analogs.

Compound No.	Retention Time (min.)	HPLC Purity (%)	Compound No.	Retention Time (min.)	HPLC Purity (%)
43	3.514	99.21	**66**	3.428	98.01
44	3.180	99.05	**67**	3.647	97.60
45	3.251	98.97	**68**	3.571	98.37
46	3.540	99.35	**69**	3.647	99.01
47	3.154	99.31	**70**	3.810	98.74
48	3.672	97.38	**71**	3.475	98.64
49	3.214	99.45	**72**	3.647	98.31
50	3.512	98.64	**73**	3.740	98.27
51	3.460	99.36	**74**	3.245	97.68
52	3.268	98.90	**75**	3.570	98.34
53	3.670	99.14	**76**	3.687	97.69
54	3.284	98.74	**77**	3.467	97.18
55	3.631	97.83	**78**	3.642	98.10
56	3.847	98.46	**79**	3.487	97.34
57	3.768	99.24	**80**	3.761	99.04
58	3.536	97.84	**81**	3.632	97.64
59	3.241	98.61	**82**	3.248	97.41
60	3.637	98.74	**83**	3.734	97.82
61	3.480	98.36	**84**	3.624	98.61
62	3.847	98.40	**85**	3.472	98.72

*HPLC method is mentioned in chapter 4 section 4.1.3

10.2 Supplementary data of 2-Substituted Benzo[d]oxazol-5-amine Analogs

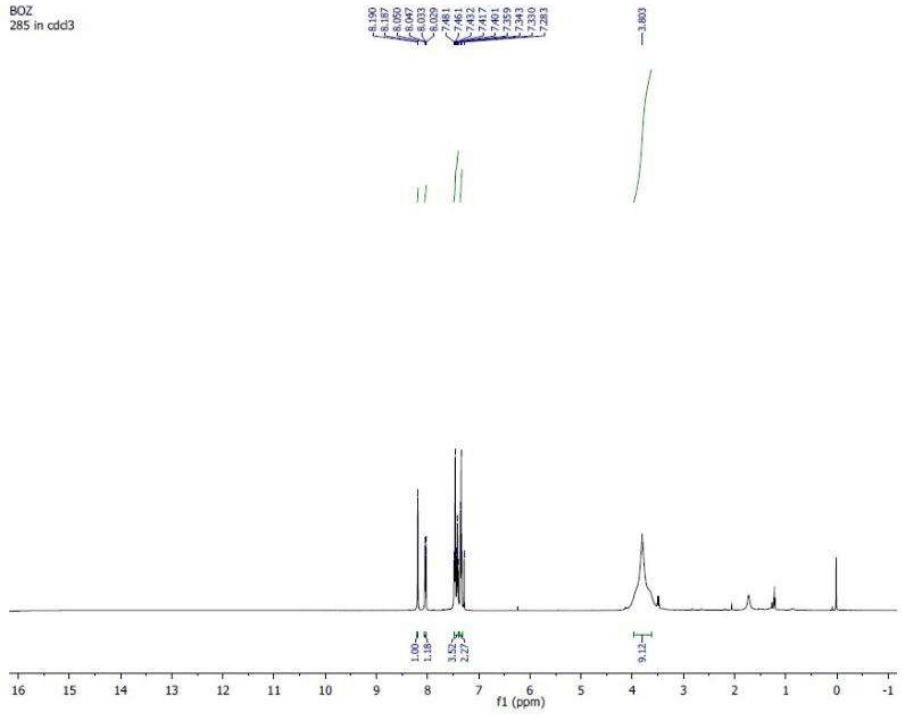

Figure A.16. ^{1}H NMR spectrum of *(3-chlorophenyl)(4-(5-nitrobenzo[d]oxazol-2-yl)piperazin-1-yl)methanone* (**66A**).

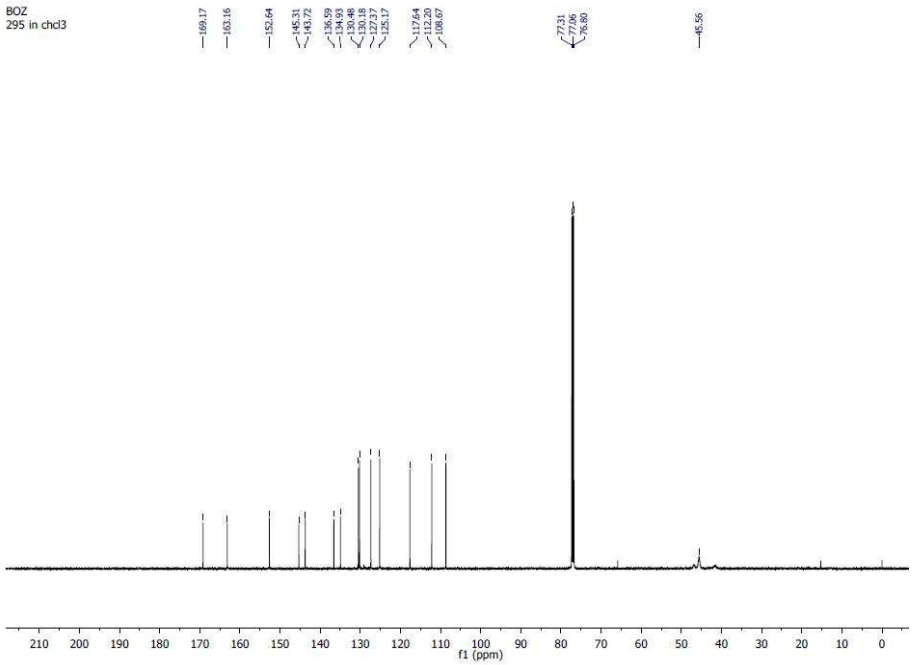

Figure A.17. ^{13}C NMR spectrum of *(3-chlorophenyl)(4-(5-nitrobenzo[d]oxazol-2-yl)piperazin-1-yl)methanone* (**66A**).

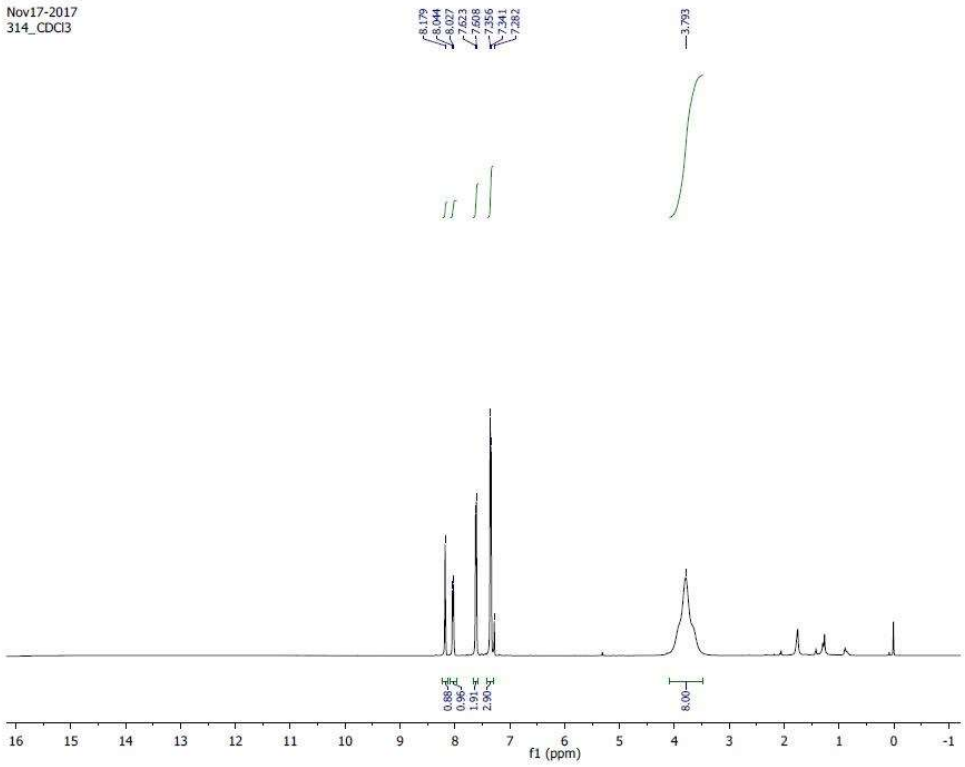

Figure A.18. ^{1}H NMR spectrum of *(4-bromophenyl)(4-(5-nitrobenzo[d]oxazol-2-yl)piperazin-1-yl)methanone* (**70A**).

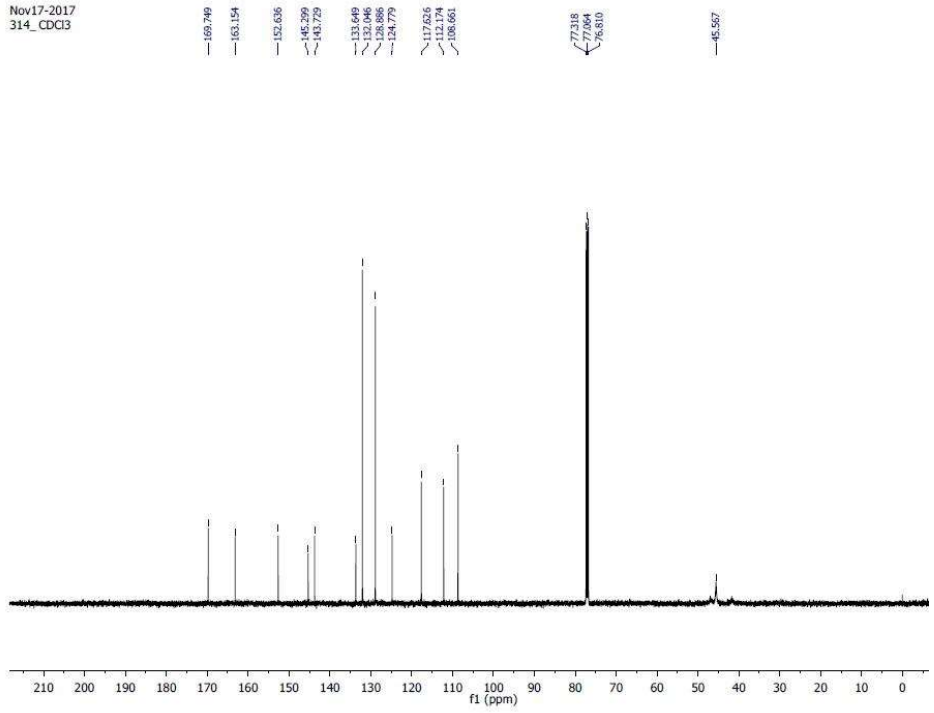

Figure A.19. ^{13}C NMR spectrum of *(4-bromophenyl)(4-(5-nitrobenzo[d]oxazol-2-yl)piperazin-1-yl)methanone* (**70A**).

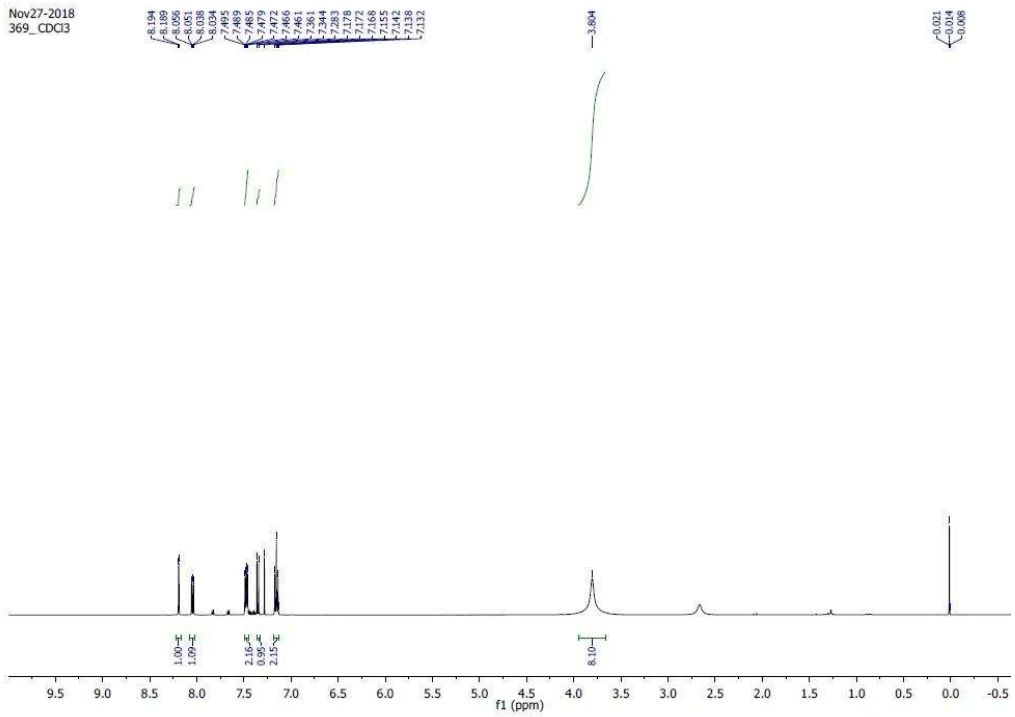

Figure A.20. ^{1}H NMR spectrum of *(4-fluorophenyl)(4-(5-nitrobenzo[d]oxazol-2-yl)piperazin-1-yl)methanone* (**73A**).

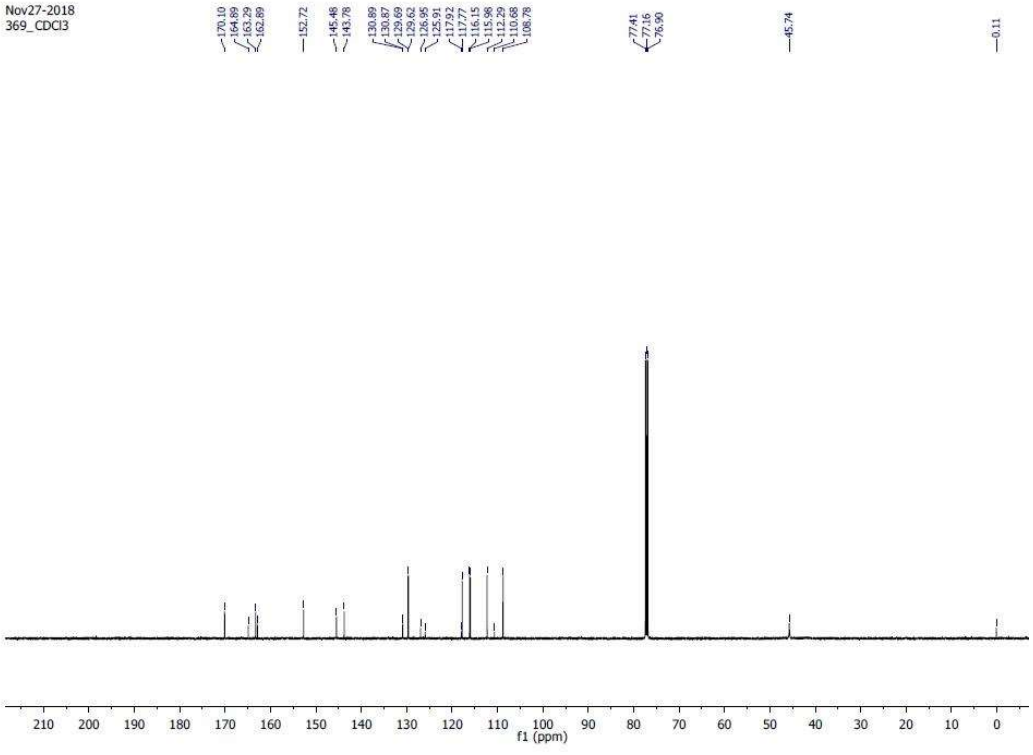

Figure A.21. ^{13}C NMR spectrum of *(4-fluorophenyl)(4-(5-nitrobenzo[d]oxazol-2-yl)piperazin-1-yl)methanone* (**73A**).

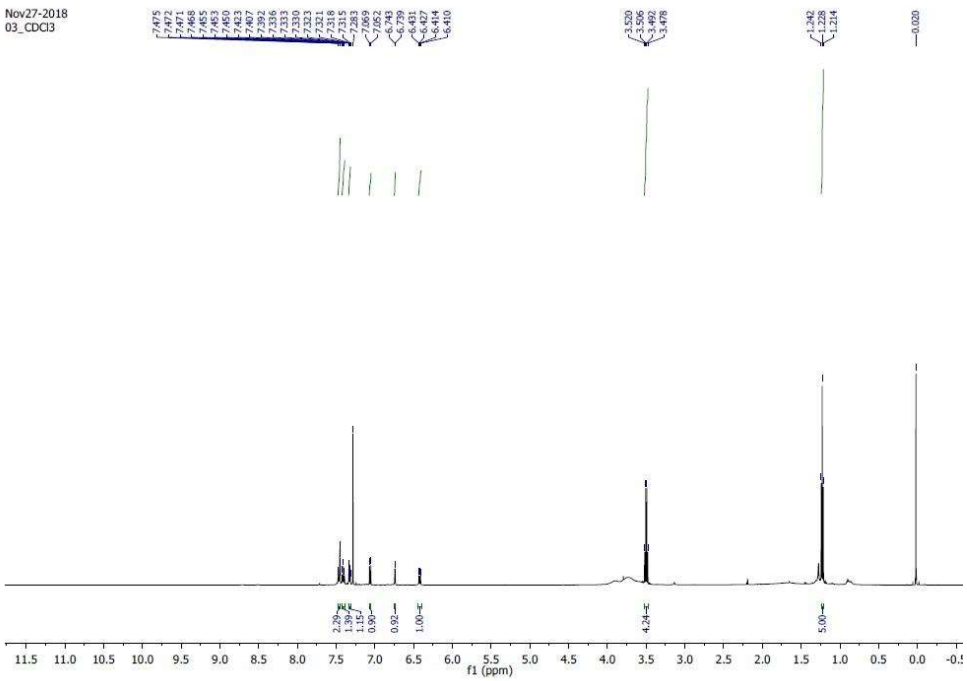

Figure A.22. ^{1}H NMR spectrum of *(4-(5-aminobenzo[d]oxazol-2-yl)piperazin-1-yl)(3-chlorophenyl)methanone* (**88A**).

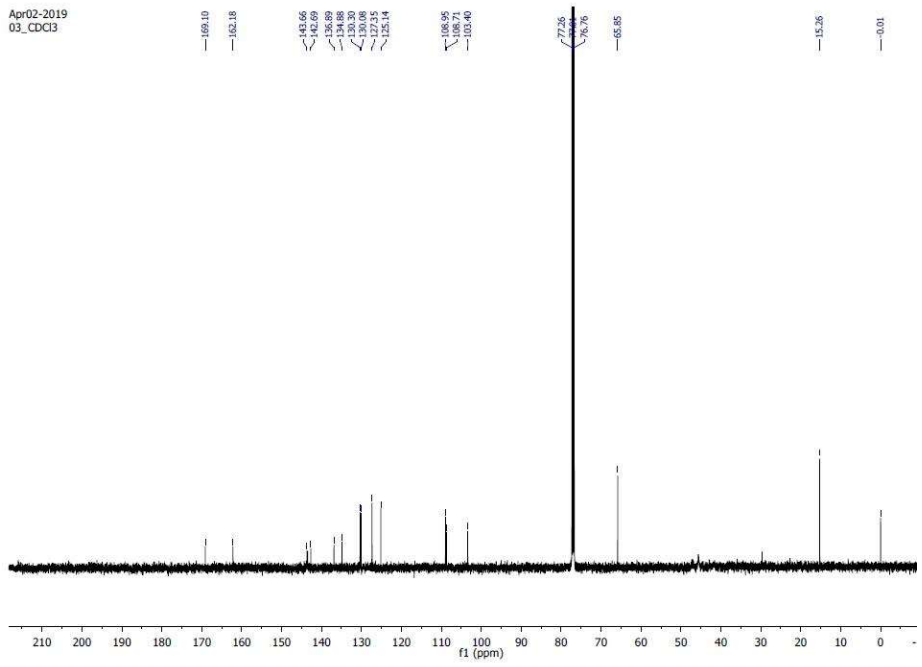

Figure A.23. ^{13}C NMR spectrum of *(4-(5-aminobenzo[d]oxazol-2-yl)piperazin-1-yl)(3-chlorophenyl)methanone* (**88A**).

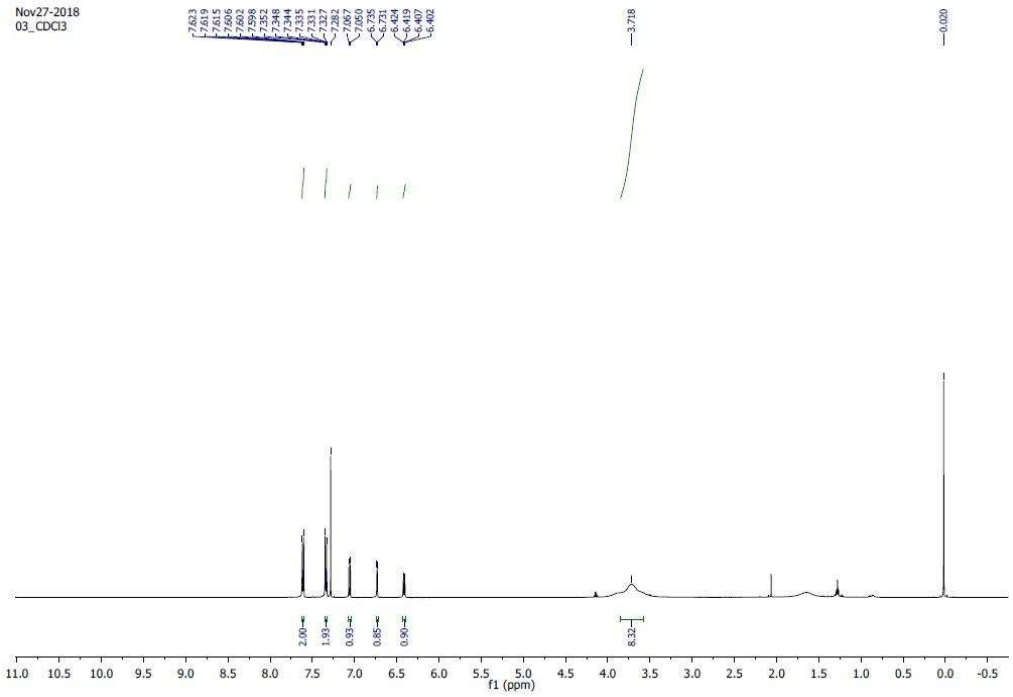

Figure A.24. ^{1}H NMR spectrum of *(4-(5-aminobenzo[d]oxazol-2-yl)piperazin-1-yl)(4-bromophenyl)methanone* (**92A**).

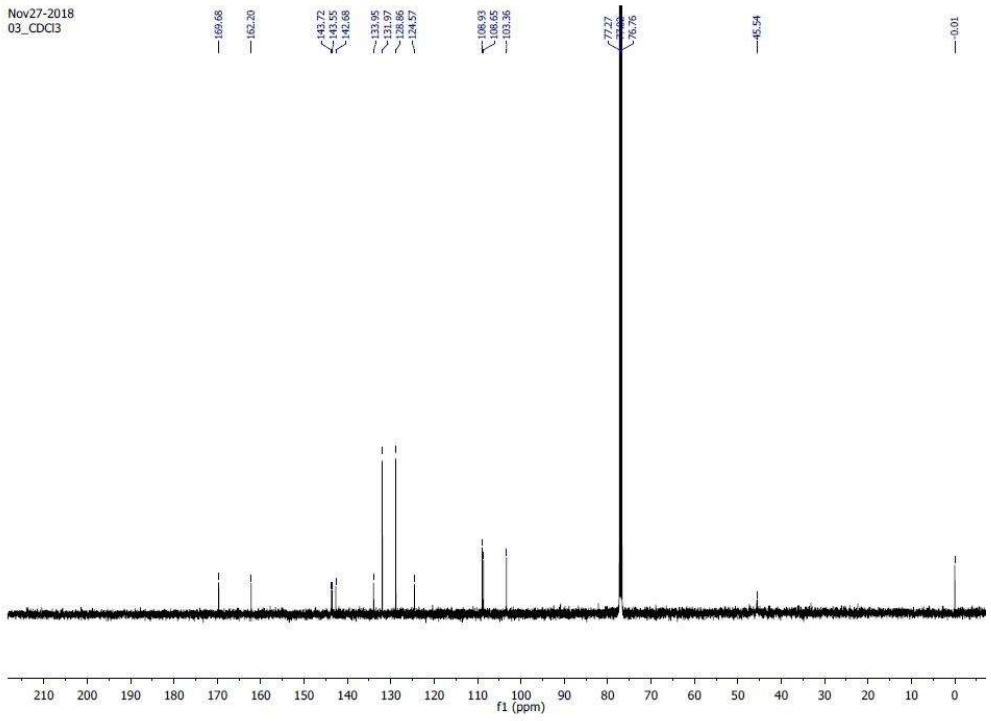

Figure A.25. ^{13}C NMR spectrum of *(4-(5-aminobenzo[d]oxazol-2-yl)piperazin-1-yl)(4-bromophenyl)methanone* (**92A**).

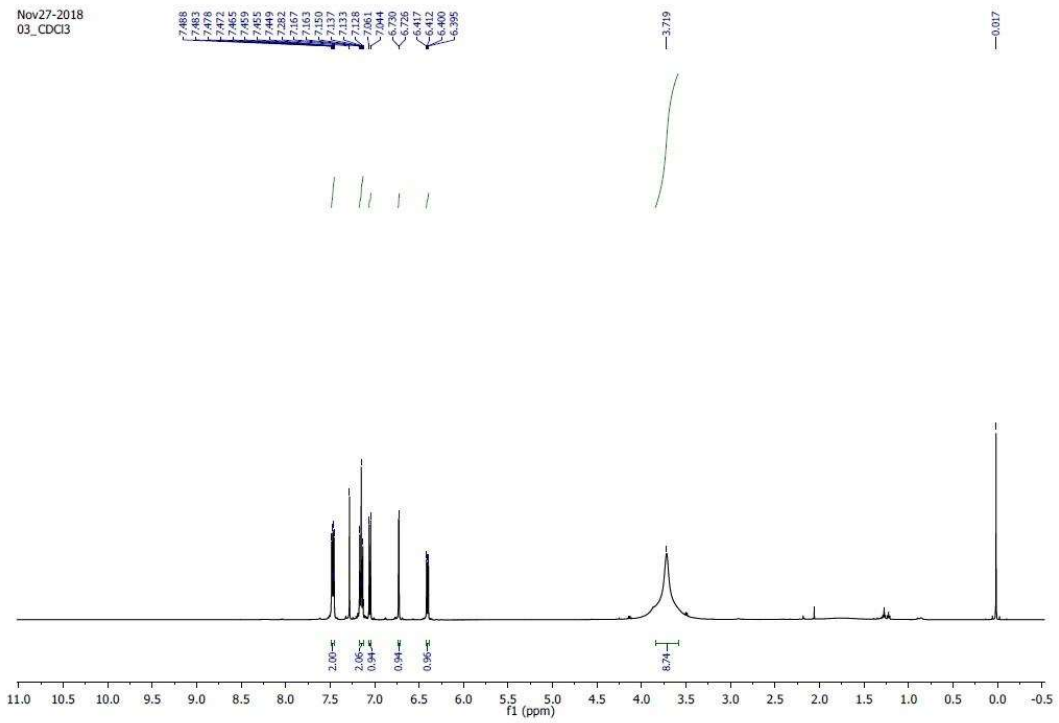

Figure A.26. ^{1}H NMR spectrum of *(4-(5-aminobenzo[d]oxazol-2-yl)piperazin-1-yl)(4-fluorophenyl)methanone* (**95A**).

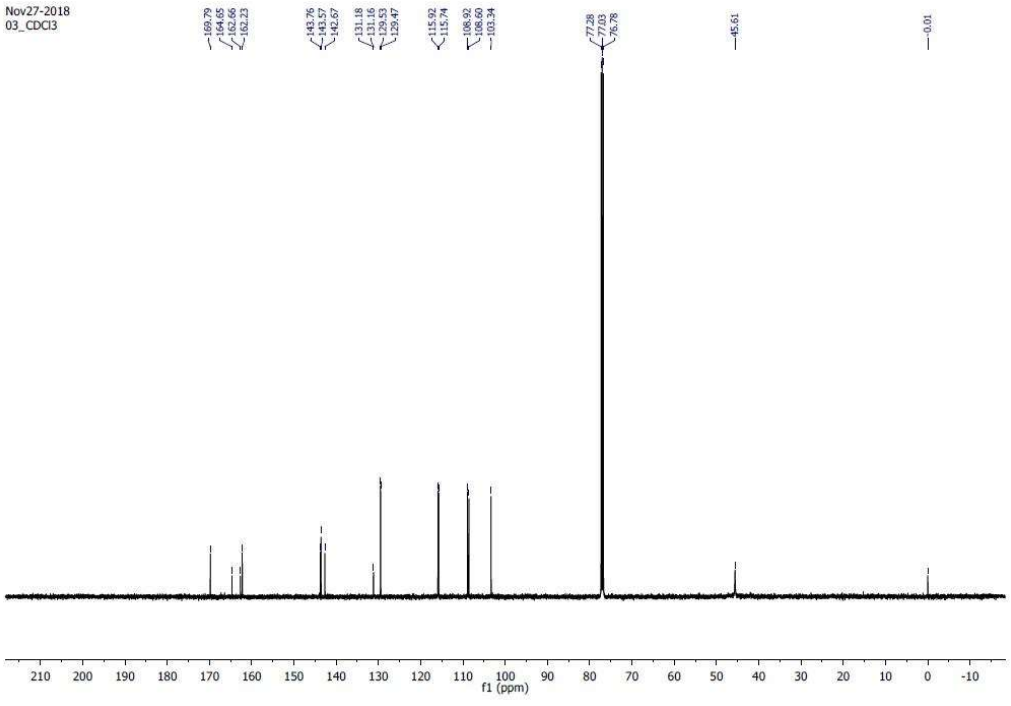

Figure A.27. ^{1}H NMR spectrum of *(4-(5-aminobenzo[d]oxazol-2-yl)piperazin-1-yl)(4-fluorophenyl)methanone* (**95A**).

Area % Report

Data File:
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Method: C:\DATA\MSMUTHU\DTX CC ACN WATER 50 50.met
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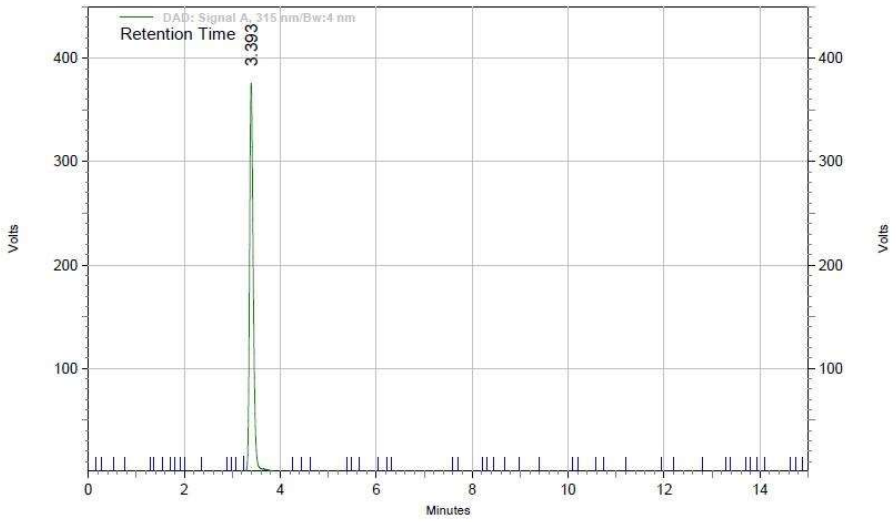
Printed: 24-05-2019 10:33:55 (GMT +05:30)



Spectrum Max
Plot Results

Retention Time	Area	Area %	Height	Height %
3.393	11673409	99.65	1954720	99.94
5.787	34088	0.29	1086	0.06
10.467	1306	0.01	43	0.00
11.993	6083	0.05	46	0.00
Totals	11714886	100.00	1955895	100.00

Figure A.28. HPLC of *(4-(5-aminobenzo[d]oxazol-2-yl)piperazin-1-yl)(4-bromophenyl)methanone* (**92A**) at 125µg/ml.

Area % Report

Data File:
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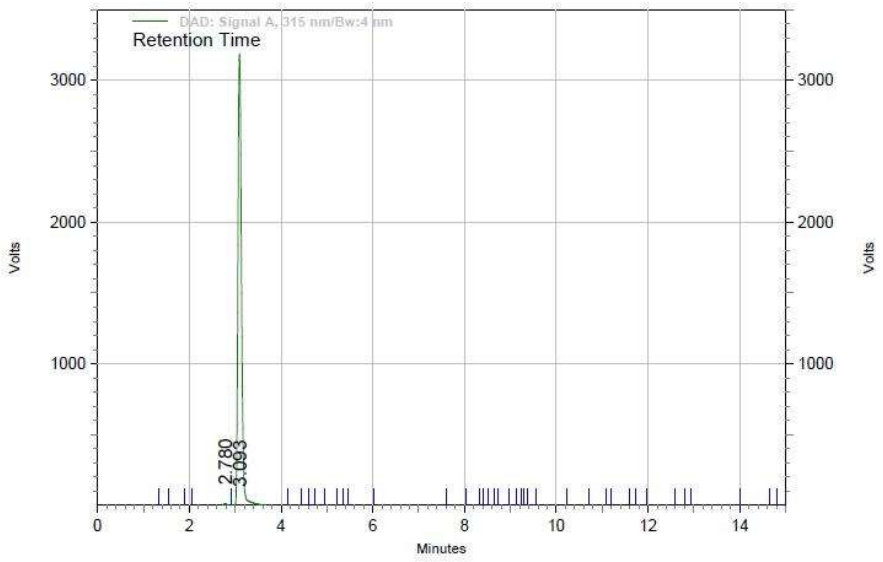
Printed: 24-05-2019 10:39:12 (GMT +05:30)



Spectrum Max
Plot Results

Retention Time	Area	Area %	Height	Height %
3.093	58796266	99.75	7387719	99.88
4.927	62653	0.11	6421	0.09
6.407	6023	0.01	823	0.01
7.673	50165	0.09	695	0.01
9.953	4312	0.01	101	0.00
13.413	18725	0.03	793	0.01
14.180	3106	0.01	103	0.00
Totals	58941250	100.00	7396655	100.00

Figure A.29. HPLC of *(4-(5-aminobenzo[d]oxazol-2-yl)piperazin-1-yl)(4-fluorophenyl)methanone* (**95A**) at 625µg/ml

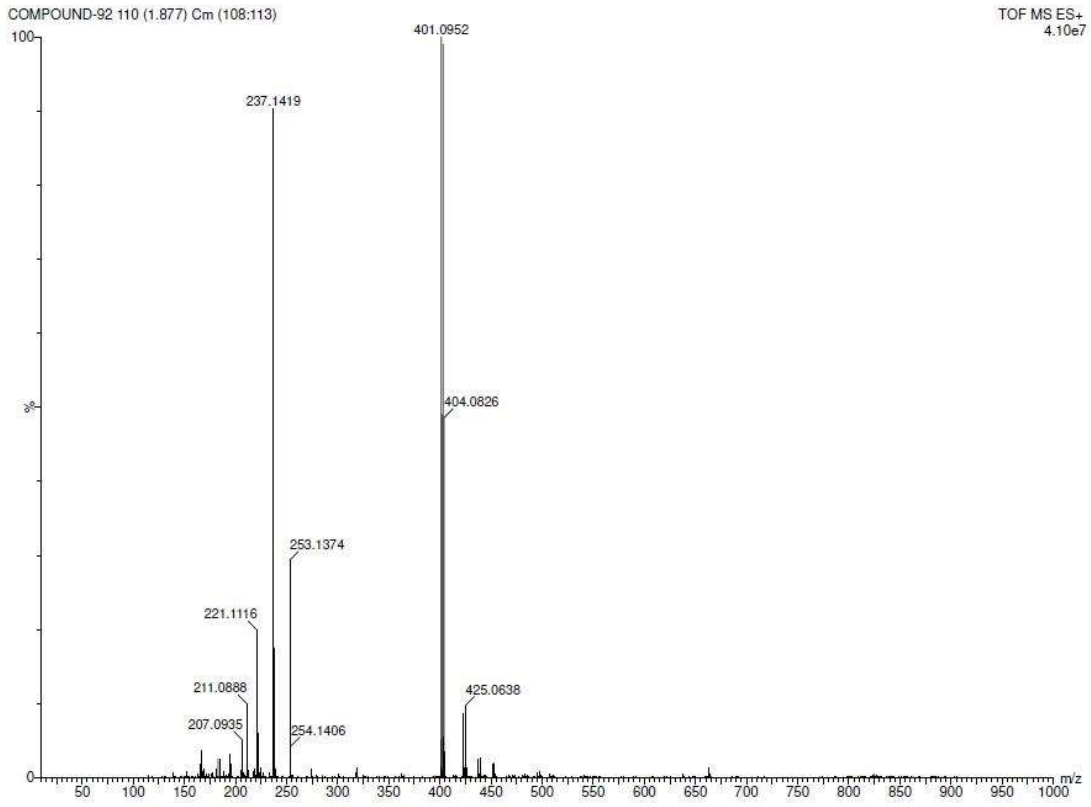


Figure A.30. HRMS of *(4-(5-aminobenzo[d]oxazol-2-yl)piperazin-1-yl)(4-bromophenyl)methanone* (**92A**).

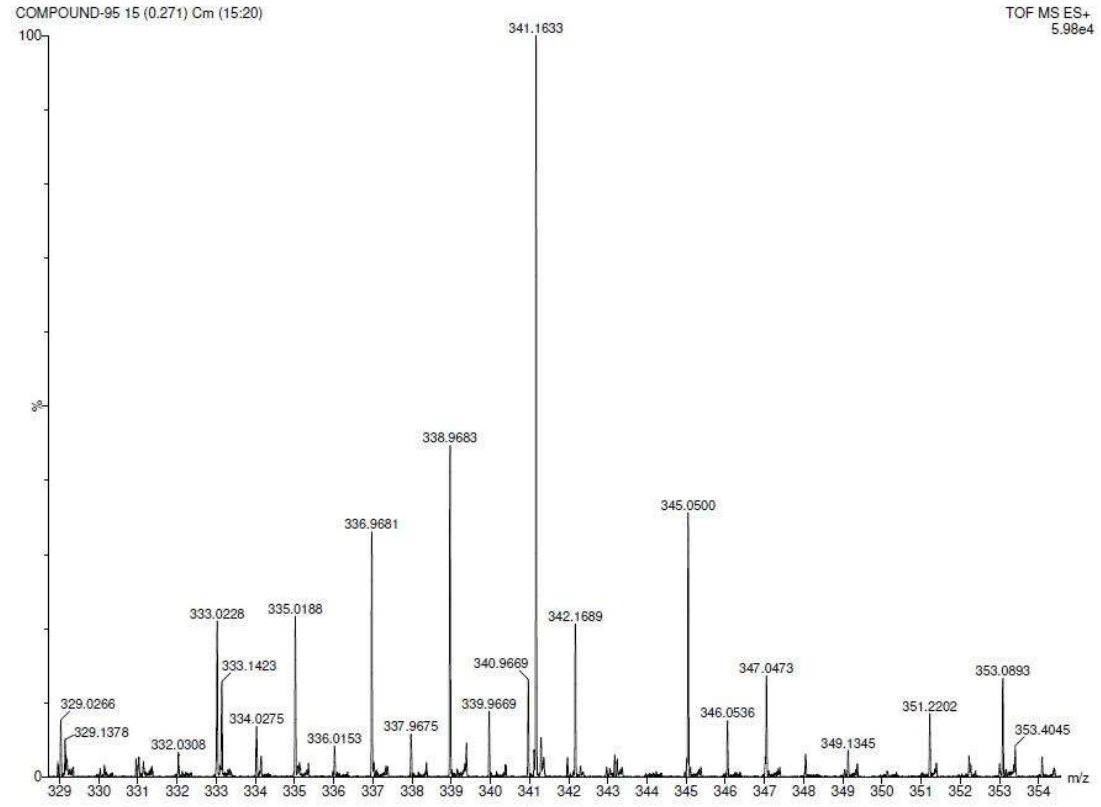


Figure A.31. HRMS of *(4-(5-aminobenzo[d]oxazol-2-yl)piperazin-1-yl)(4-fluorophenyl)methanone* (**95A**).

Table A.2. HPLC data of 2-substituted benzo[d]oxazol-5-amine analogs.

Compound No.	Retention Time (min.)	HPLC Purity (%)	Compound No.	Retention Time (min.)	HPLC Purity (%)
29A	3.971	98.64	**92A**	3.393	99.65
30A	3.731	98.67	**93A**	3.421	98.67
31A	3.350	98.31	**94A**	3.754	98.45
32A	3.475	98.64	**95A**	3.093	99.75
33A	3.724	97.36	**96A**	3.721	99.31
34A	3.345	98.61	**97A**	3.681	98.37
35A	3.342	97.68	**98A**	3.721	98.67
36A	3.810	98.72	**99A**	3.674	97.85
37A	3.473	98.42	**100A**	3.742	98.64
38A	3.761	97.64	**101A**	3.864	98.37
39A	3.634	97.82	**102A**	3.670	98.32
86A	3.674	98.75	**103A**	3.624	97.82
87A	3.840	97.67	**104A**	3.821	98.71
88A	3.568	97.80	**105A**	3.734	98.76
89A	3.287	97.82	**106A**	3.764	97.52
90A	3.670	98.86	**107A**	3.624	98.24
91A	3.754	97.34	**--**	---	---

*HPLC method is mentioned in chapter 5 section 5.1.3

10.3 Supplementary data of Triazole bridged cycloaryl analogs

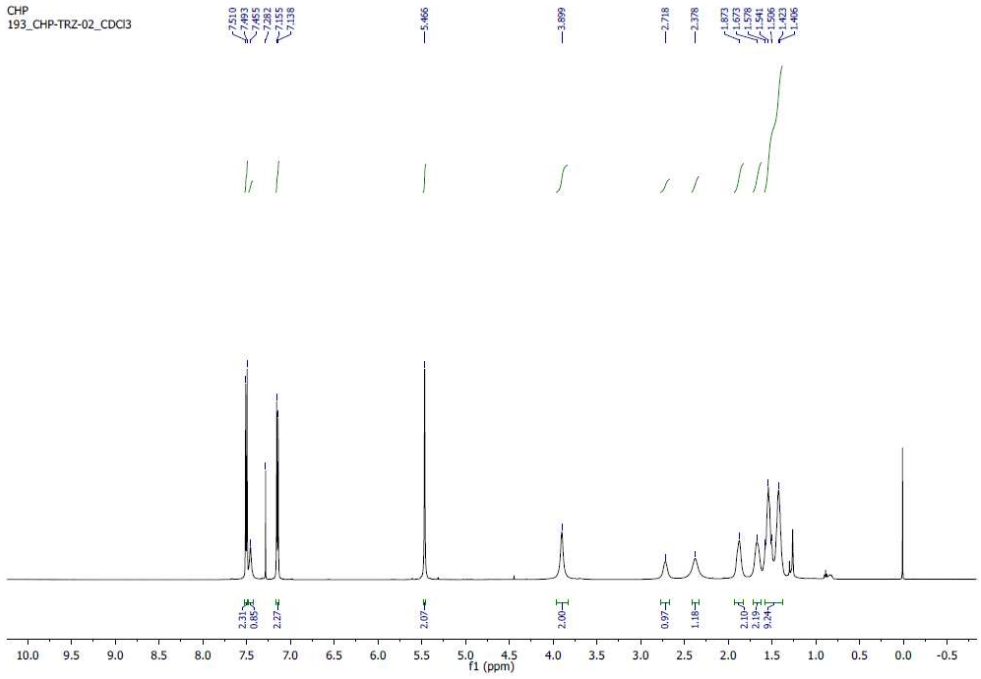


Figure A.32. ^{1}H NMR spectrum of N-((1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)methyl)cycloheptanamine (**23B**).

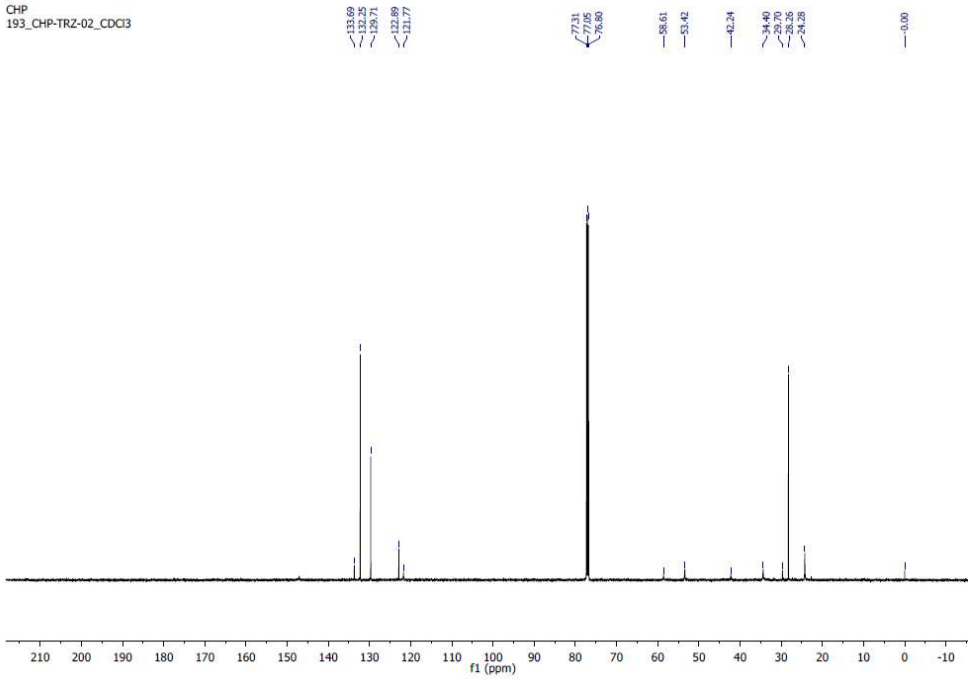


Figure A.33. ^{13}C NMR spectrum of N-((1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)methyl)cycloheptanamine (**23B**).

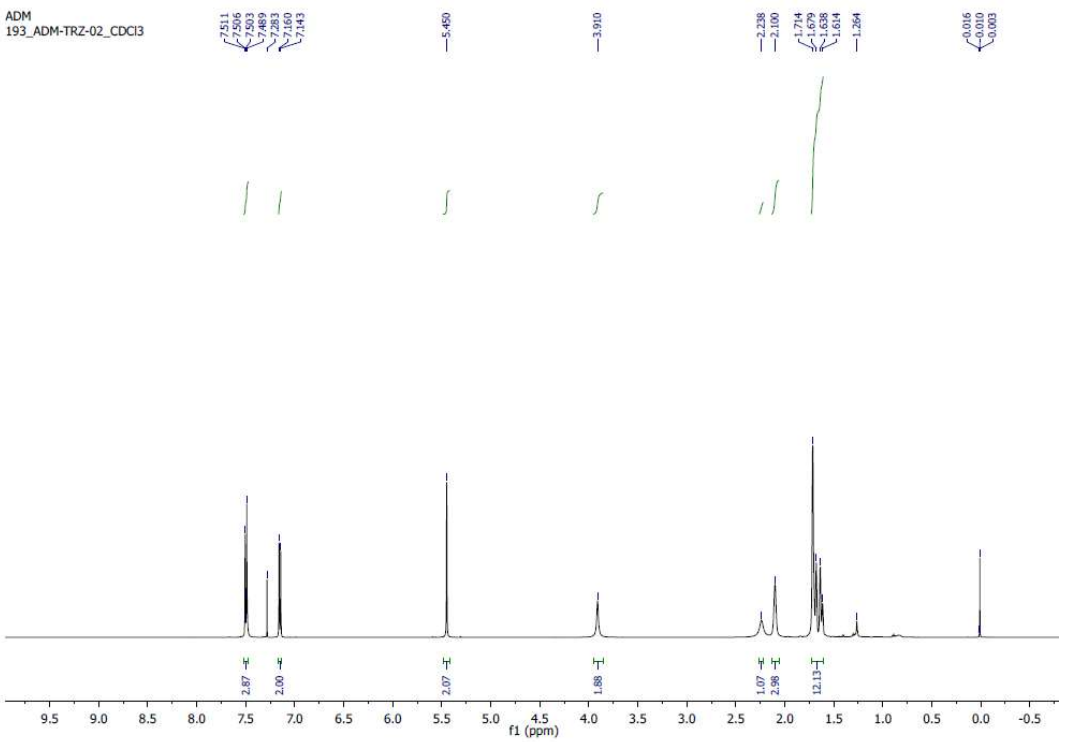


Figure A.34. ^{1}H NMR spectrum of N-((1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)methyl)adamantan-1-amine (**32B**).

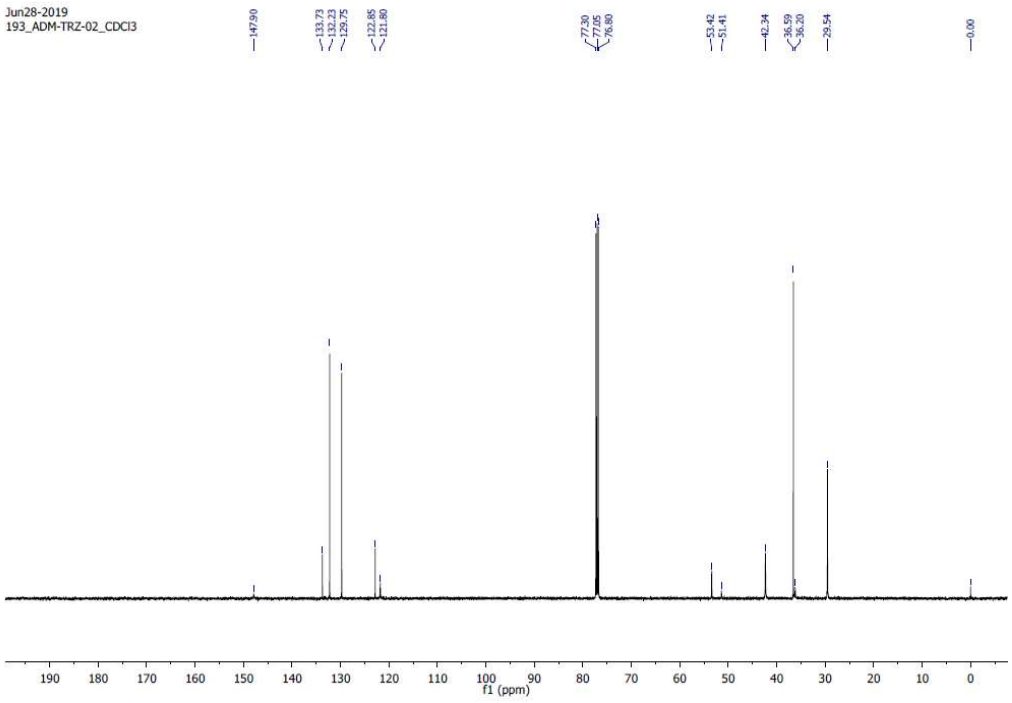


Figure A.35. ^{13}C NMR spectrum of N-((1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)methyl)adamantan-1-amine (**32B**).

2/24/2020 16:22:54 1 / 1

==== Shimadzu LCsolution Analysis Report ====

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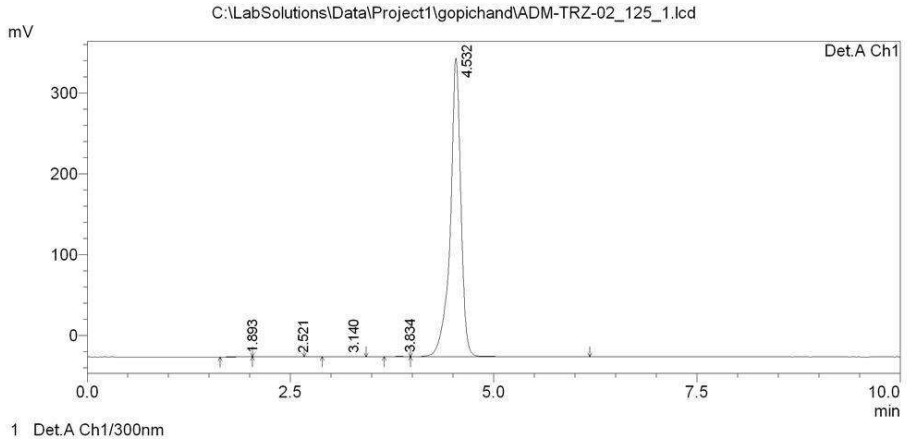
Acquired by	: Admin
Sample Name	: ADM-TRZ-02_125_1
Sample ID	: ADM-TRZ-02_125_1
Tray#	: 0
Vail #	: 1
Injection Volume	: 20 uL
Data File Name	: ADM-TRZ-02_125_1.lcd
Method File Name	: ACN_Water_9_1.lcm
Batch File Name	:
Report File Name	: IIT-BHU Report.lcr
Data Acquired	: 2/24/2020 3:36:36 PM
Data Processed	: 2/24/2020 3:48:23 PM

<Chromatogram>



1 Det.A Ch1/300nm

PeakTable

Detector A Ch1 300nm

Peak#	Ret. Time	Area	Height	Area %
1	1.893	1288	128	0.038
2	2.521	1685	60	0.050
3	3.140	4088	307	0.121
4	3.834	5298	600	0.157
5	4.532	3363797	369283	99.634
Total		3376155	370379	100.000

C:\LabSolutions\Data\Project1\gopichand\ADM-TRZ-02_125_1.lcd

Figure A.36. HPLC of N-((1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)methyl)adamantan-1-amine (**32B**).

Table A.3. HPLC data of triazole bridged aryl adamantane analogs.

Compound No.	Retention Time (min.)	HPLC Purity (%)	Compound No.	Retention Time (min.)	HPLC Purity (%)
22B	4.135	99.22	**31B**	4.504	99.32
23B	4.154	98.24	**32B**	4.532	99.63
24B	4.136	99.04	**33B**	4.511	99.01
25B	4.175	98.64	**34B**	4.526	99.34
26B	4.180	98.72	**35B**	4.502	98.67
27B	4.153	98.74	**36B**	4.531	99.31
28B	4.170	98.67	**37B**	4.324	98.21

*HPLC method is mentioned in chapter 6 section 6.2.2

10.4 List of publications

1. **Gopichand Gutti**, Devendra Kumar, Pankaj Paliwal, Ankit Ganeshpurkar, Khemraj Lahre, Ashok Kumar, Sairam Krishnamurthy, Sushil Kumar Singh, Development of pyrazole and spiropyrazoline analogs as multifunctional agents for treatment of Alzheimer's disease. *Bioorganic Chemistry* **2019**. 90: p. 103080.

2. **Gopichand Gutti**, Kakarla Rama krishna, Kumar Devendra, Mahima Beohar, Ankit Ganeshpurkar, Ashok Kumar, Sairam Krishnamurthy, Sushil Kumar Singh, Discovery of novel series of 2-substituted benzo[d]oxazol-5-amine derivatives as multi-target directed ligands for the treatment of Alzheimer's disease. *Eur J Med Chem.* **2019** Nov 15;182:111613.

3. Kumar, Devendra; Gupta, Sukesh; Ganeshpurkar, Ankit; **Gopichand Gutti**; Krishnamurthy, Sairam; Modi, Gyan; Singh, Sushil. Development of Piperazinediones as dual inhibitor for treatment of Alzheimer's disease, *Eur J Med Chem.,* **2018**, Volume 150, 25, Pages 87-101.

4. SatheeshkumarSellamuthu, **Gopichand Gutti**, Devendra Kumar, Sushil Kumar Singh, Carbazole: A Potent Scaffold for Antitubercular Drugs. *Mini-Reviews in Organic Chemistry*. **2018**, Volume 15, Issue 6, 498-507.

5. Ankit Ganeshpurkar, Ravi Singh, Pravin Gangaram Gore, Devendra Kumar, **Gopichand Gutti**, Ashok Kumar, Sushil Kumar Singh, Structure-based screening and molecular dynamics simulation studies for the identification of potential acetylcholinesterase inhibitors, *Molecular Simulation* (**2019**): 1-17.

6. , Rayala Swetha, Devendra Kumar, Sukesh K. Gupta, Ankit Ganeshpurkar, **Gopichand Gutti**, Dileep kumar, Srabanti Jana, Sairam Krishnamurthy, Sushil Kumar Singh, Multifunctional hybrid sulfonamides as novel therapeutic agents for Alzheimer's disease, *Future Medicinal Chemistry,* **2019**, Vol. 11, No. 24.

7. Arusha Modi, Meenakshi Singh, **Gopichand Gutti**, Ozasvi R. Shanker, Vinay Kumar Singh, Sunita Singh, Sushil Kumar Singh, Benzothiazole derivative bearing amide moiety induces p53-mediated apoptosis in HPV16 positive cervical cancer cells, Satyajit Pradhan, Gopeshwar Narayan, *Invest. New Drugs* **2019**. (https://doi.org/10.1007/s10637-019-00848-7).

8. Makar, Subhajit, Tanmay Saha, Rayala Swetha, **Gopichand Gutti**, Ashok Kumar, and Sushil K. Singh, Rational approaches of drug design for the development of selective estrogen receptor modulators (SERMs), implicated in breast cancer. *Bioorganic chemistry* (**2019**): 103380.

9. TanmaySaha, SubhajitMakar, RayalaSwetha, **Gopichand Gutti**, Sushil K.Singh, Estrogen signaling: An emanating therapeutic target for breast cancer treatment, *Eur J Med Chem.* **2019**, Volume 177, 1, Pages 116-143.

10. **Gopichand Gutti**, Karan Arya, Sushil Kumar Singh, Latent tuberculosis infection (LTBI) and its potential targets: An investigation into dormant phase pathogens, *Mini reviews in Medicinal Chemistry*, **2019** Volume 19, Issue 19, 1593-1608.

11. Ankit Ganeshpurkar, Rayala Swetha, Devendra Kumar, Gore Pravin Gangaram, Ravi Singh, **Gopichand Gutti**, Srabanti Jana, Dileep Kumar, Ashok Kumar, Sushil Kumar Singh, Protein-Protein Interaction and Aggregation Inhibitors in Alzheimer's Disease, *Curr Top Med Chem.* **2019***;*19(7):501-533.

12. Supraja Siddamurthi, **Gopichand Gutti**, Srabanti Jana, Ashok Kumar, Sushil Kumar Singh, Anthraquinone: a promising scaffold for the discovery and development of therapeutic agents in cancer therapy, *Future Medicinal Chemistry,* **2020***,* Vol. 12, No. 11.