Supporting Information

Catalyst-free and multicomponent synthesis of 3-aminoalkylated indoles via Mannich-type reaction: multitargeted anticancer, tyrosinase and α-glucosidase inhibitory activities

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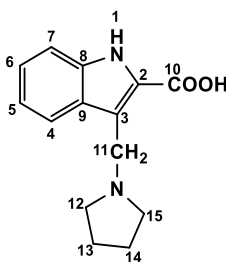[a]Institute of Chemical Technology – VAST, 1A Thanh Loc 29 Str., Dist. 12, Ho Chi Minh City, Vietnam

[b]Graduate University of Science and Technology – VAST, 18 Hoang Quoc Viet Str., Cau Giay Dist., Hanoi, Vietnam

[c]Ton Duc Thang University, 19 Nguyen Huu Tho Str., Dist. 7, Ho Chi Minh City, Vietnam
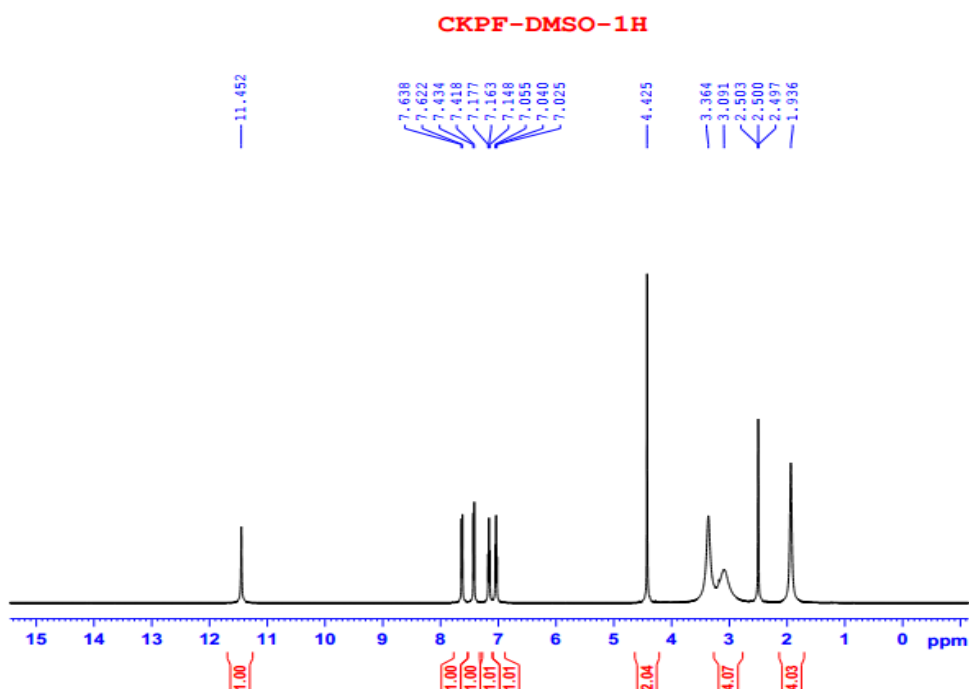
[d]Center for Research and Technology Transfer – VAST, 18 Hoang Quoc Viet Str., Cau Giay Dist., Hanoi, Vietnam

[e]Department of Medicinal Chemistry, Faculty of Pharmacy, University of Medicine and Phar-macy at Ho Chi Minh City – 41-43 Dinh Tien Hoang Str., Dist. 1, Ho Chi Minh City, Vietnam

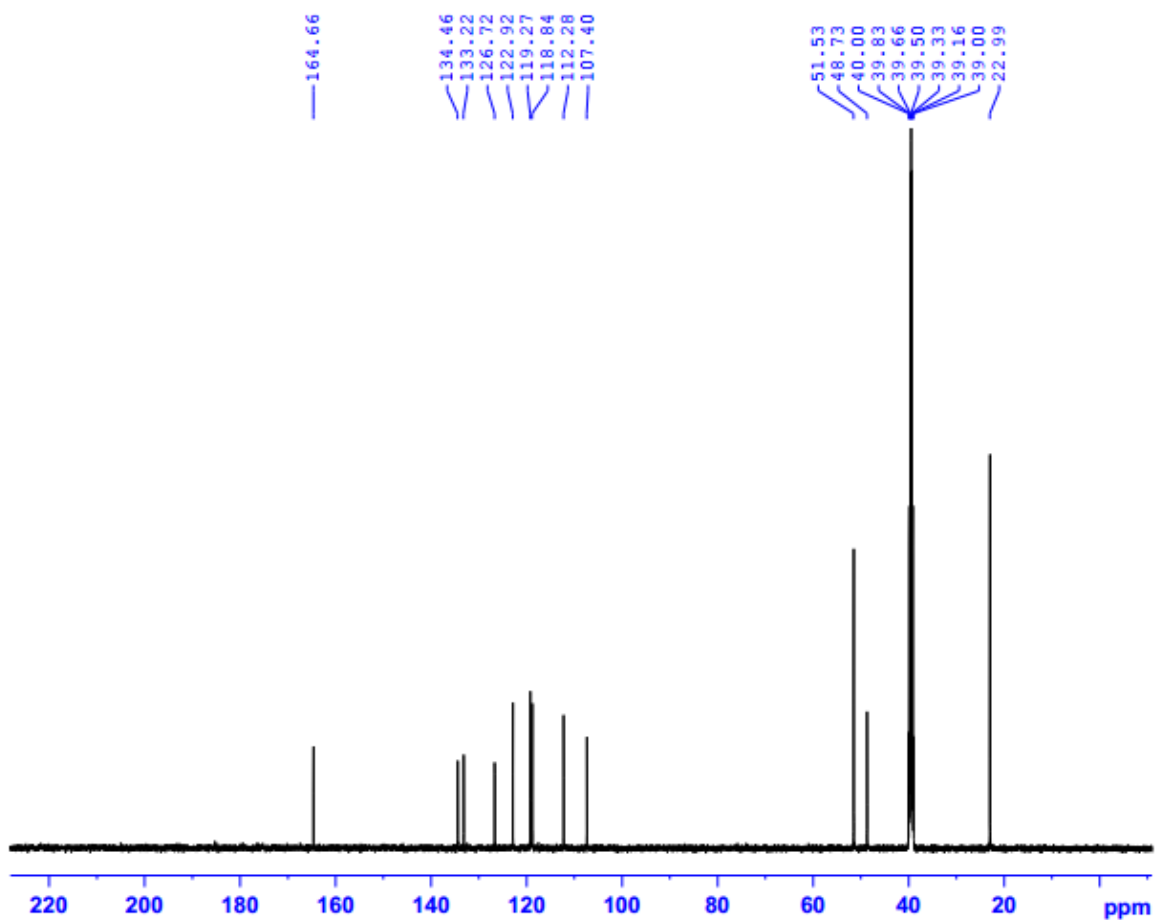## 3-(pyrrolidin-1-ylmethyl)-1H-indole-2-carboxylic acid (4a)
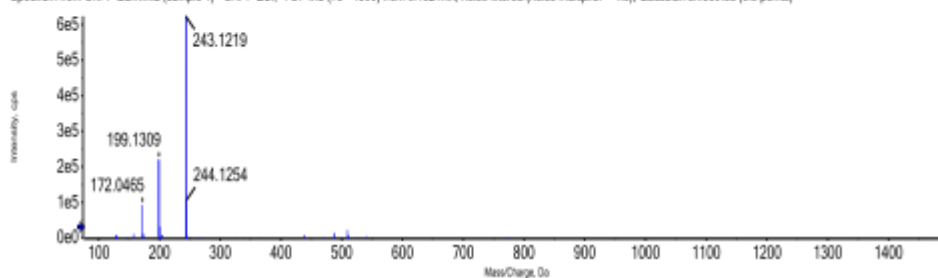

^{1}H-NMR:

CKPF-DMSO-1H

¹³C-NMR:

CKPF-DMSO-C13CPD

ESI-HRMS:

ANALYSIS REPORT

Injection details

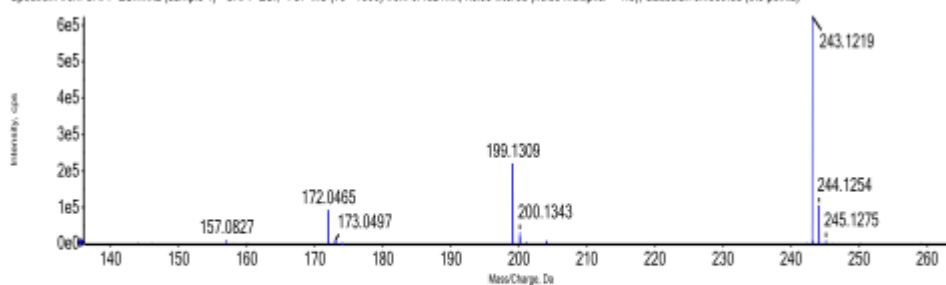|			
Sample name	CKPF	*Vial position*	1
Sample file name	SER. wiff2 – CHI	*Inject volume*	5.00
Acquisition date	30/11/2018 1:04:54 PM	*Acquisition method*	ESI_NEG_SCAN
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from CKPF-ESI.wiff2 (sample 1) - CKPF-ESI, -TOF MS (75 - 1500) from 0.162 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)
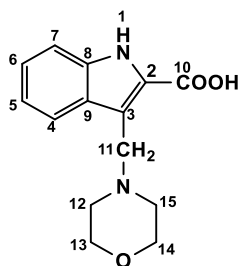

Expanded spectrum

Spectrum from CKPF-ESI.wiff2 (sample 1) - CKPF-ESI, -TOF MS (75 - 1500) from 0.162 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)
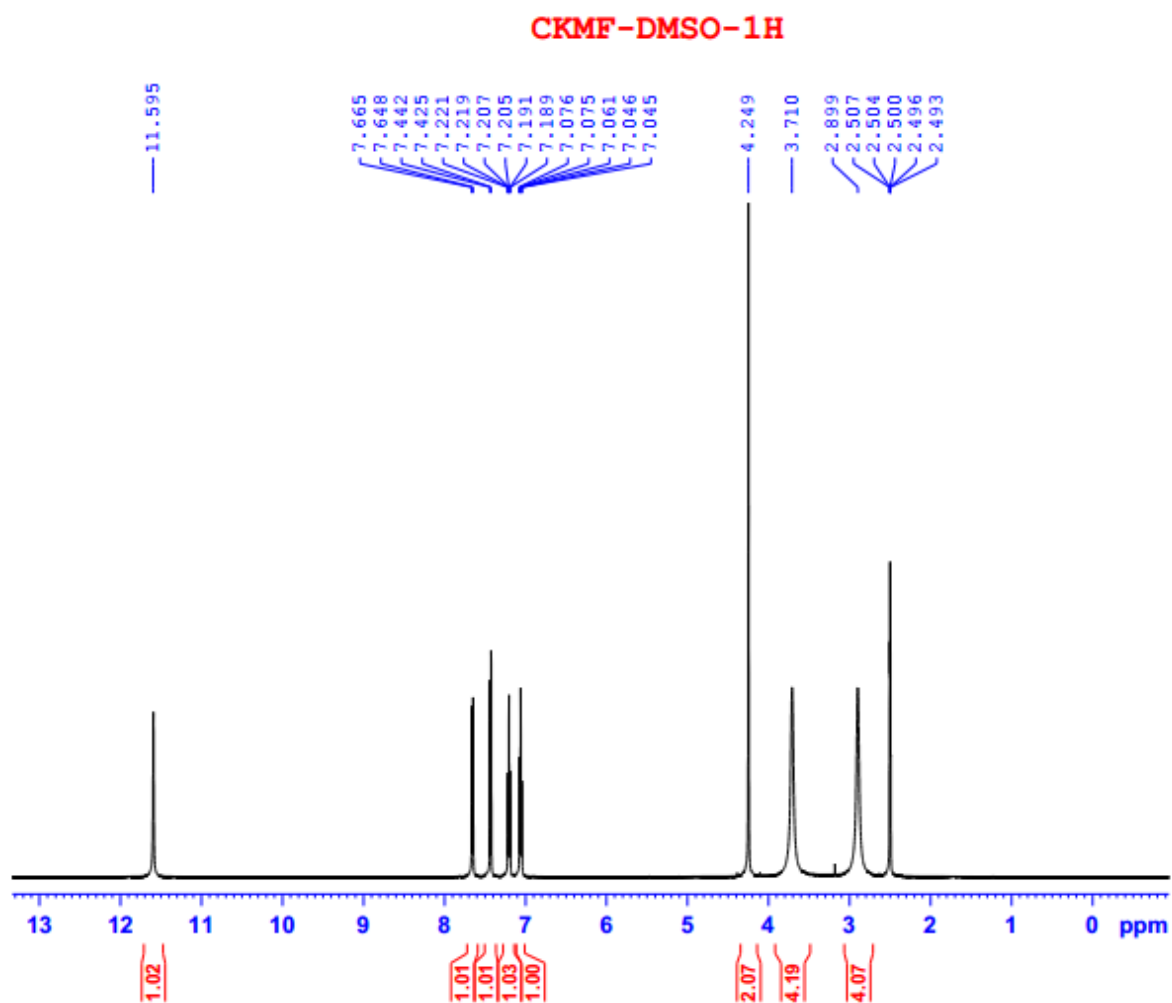

Molecular formula prediction

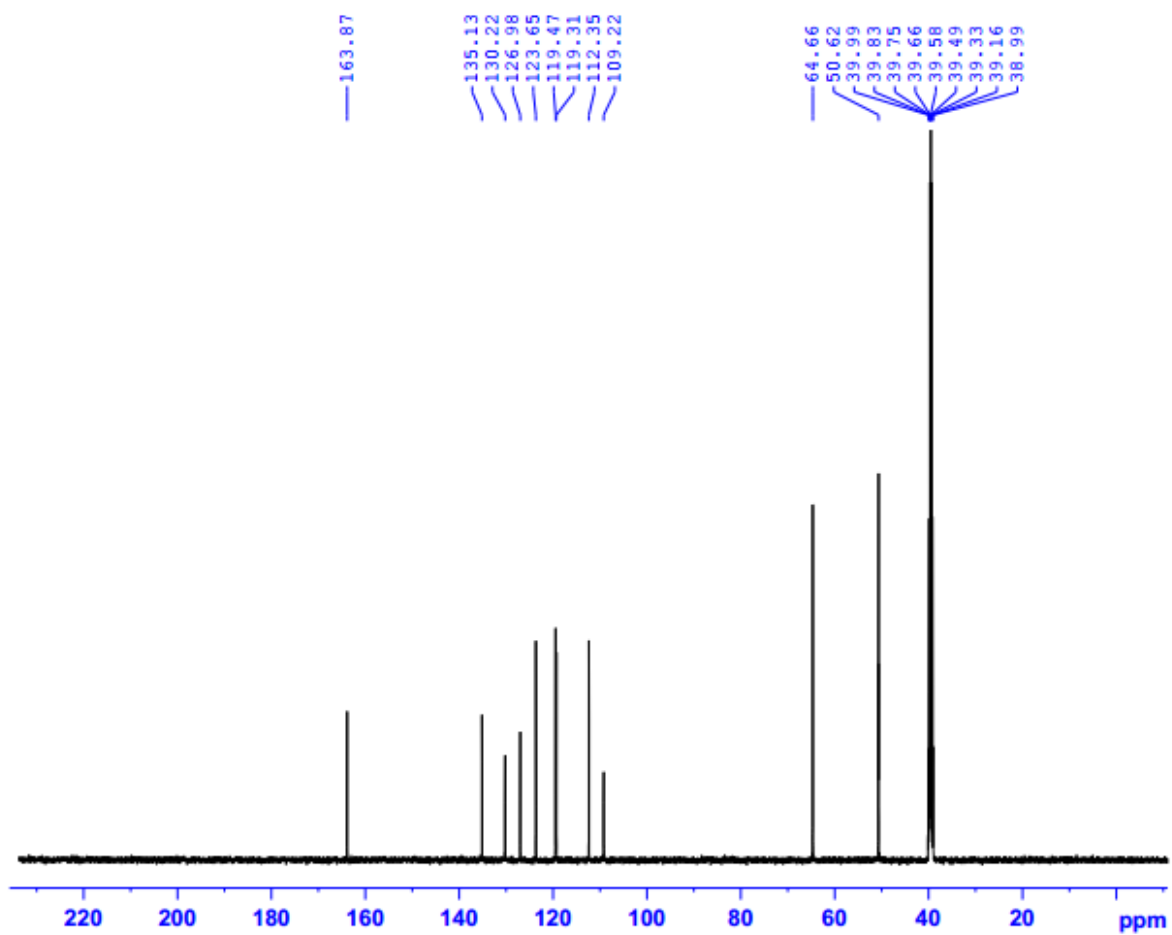# 3-(morpholinomethyl)-1H-indole-2-carboxylic acid (*4b*)
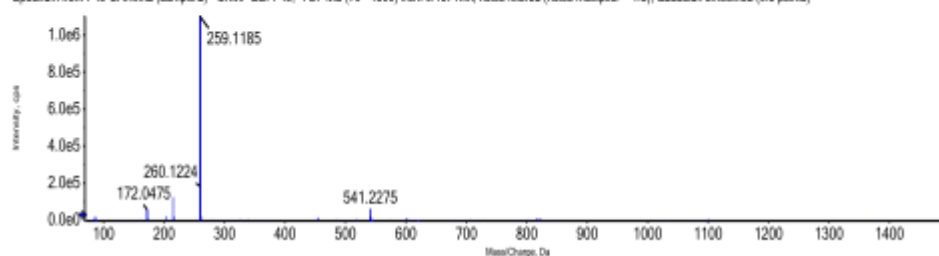

¹H-NMR:

CKMF-DMSO-1H

¹³C-NMR:

CKMF-DMSO-C13CPD

ESI-HRMS:

ANALYSIS REPORT

Injection details

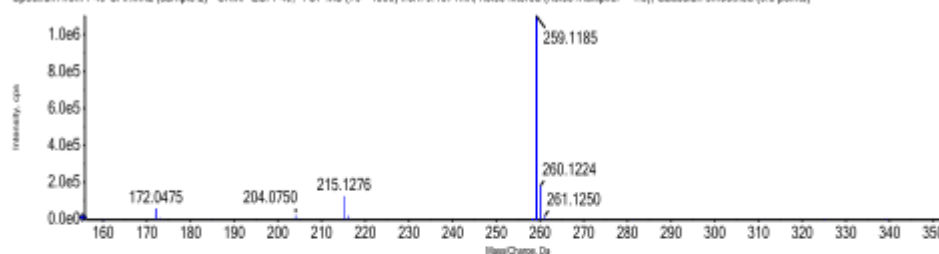|			
Sample name	CKMF	*Vial position*	11
Sample file name	SER. wiff2 – CHI	*Inject volume*	5.00
Acquisition date	8/1/2019 1:04:54 PM	*Acquisition method*	ESI_NEG_SCAN
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from P49-CHI.wiff2 (sample 2) - CKMF-ESI-P49, -TOF MS (70 - 1500) from 0.167 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)
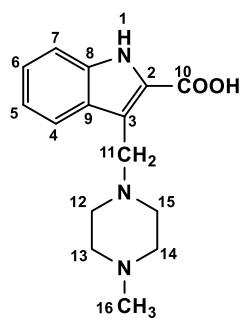

Expanded spectrum

Spectrum from P49-CHI.wiff2 (sample 2) - CKMF-ESI-P49, -TOF MS (70 - 1500) from 0.167 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)
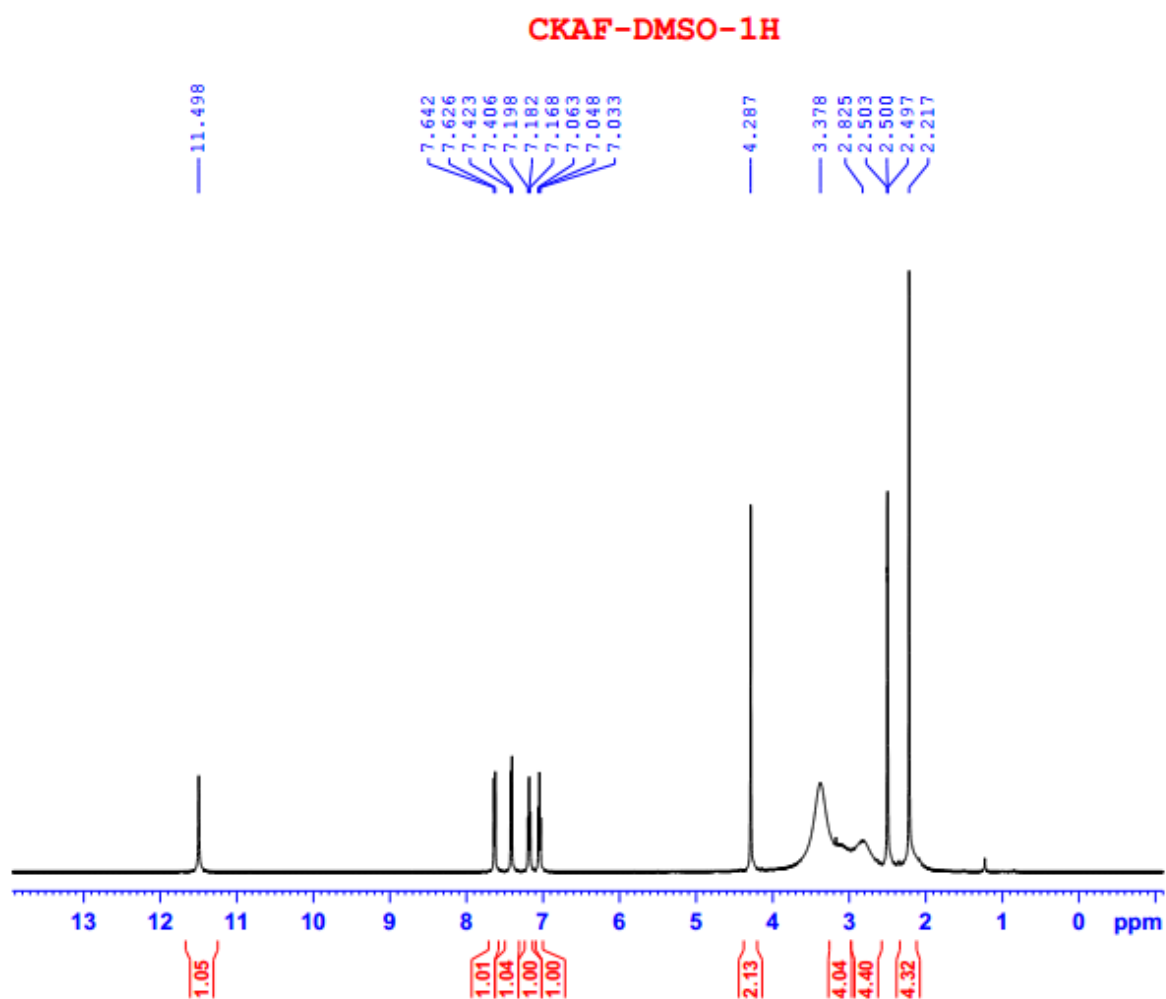

Molecular formula prediction

Page 1 of 1
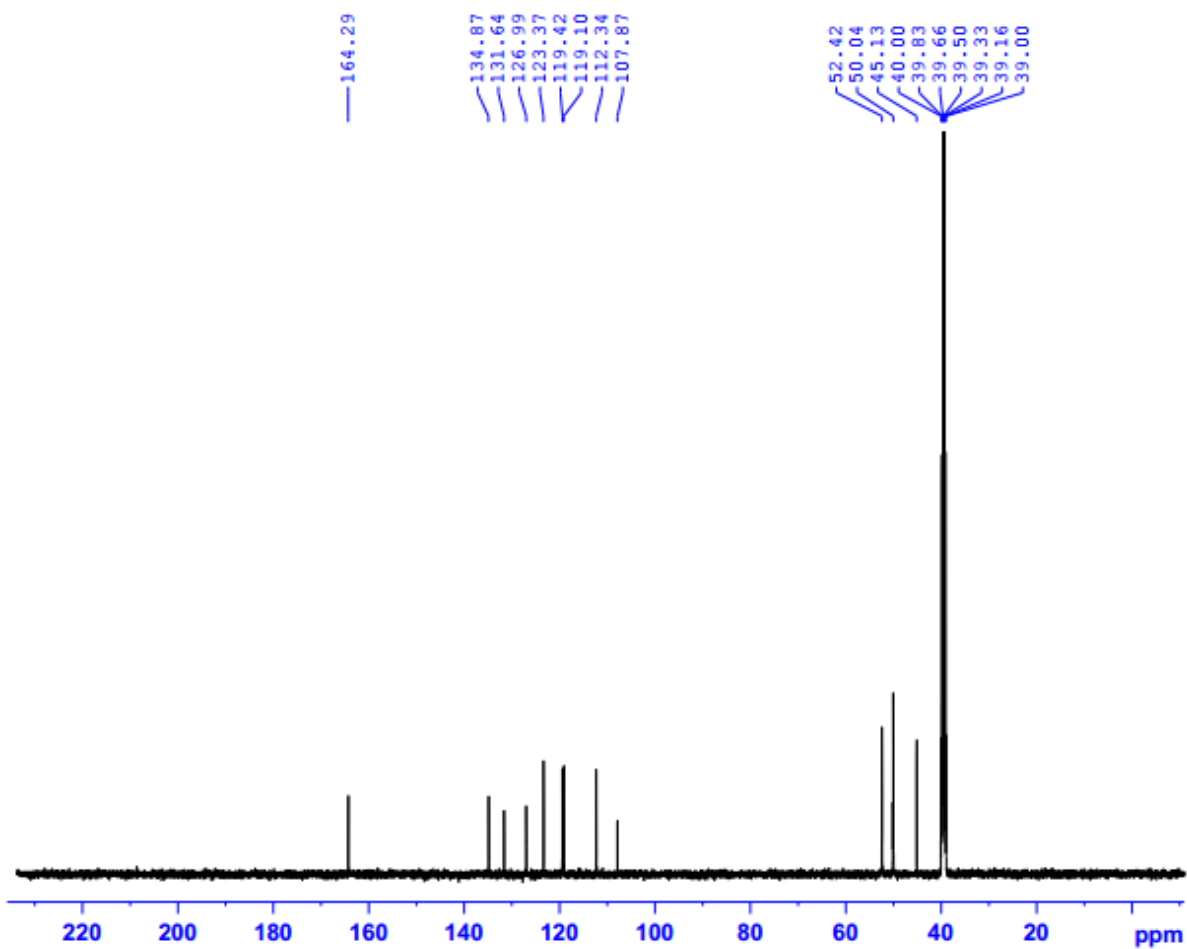
3-((4-methylpiperazin-1-yl)methyl)-1H-indole-2-carboxylic acid (*4c*)

¹H-NMR:

¹³C-NMR:

CKAF–DMSO–C13CPD

ESI-HRMS:

ANALYSIS REPORT

Full mass spectrum

Spectrum from P49-CHI.wiff2 (sample 4) - CKAF-ESI-P49, -TOF MS (70 - 1500) from 0.162 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)

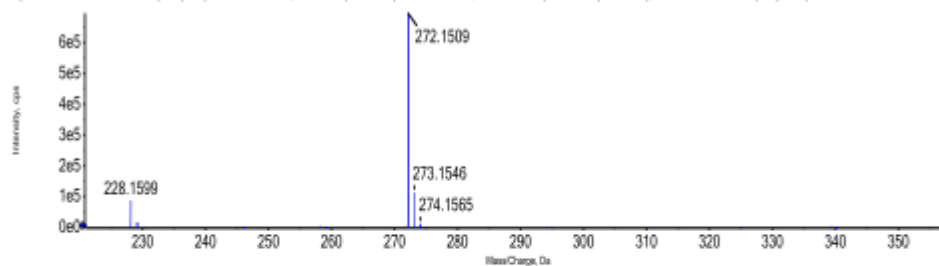**Expanded spectrum**

Spectrum from P49-CHI.wiff2 (sample 4) - CKAF-ESI-P49, -TOF MS (70 - 1500) from 0.162 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)
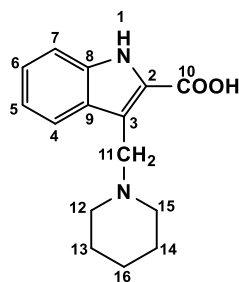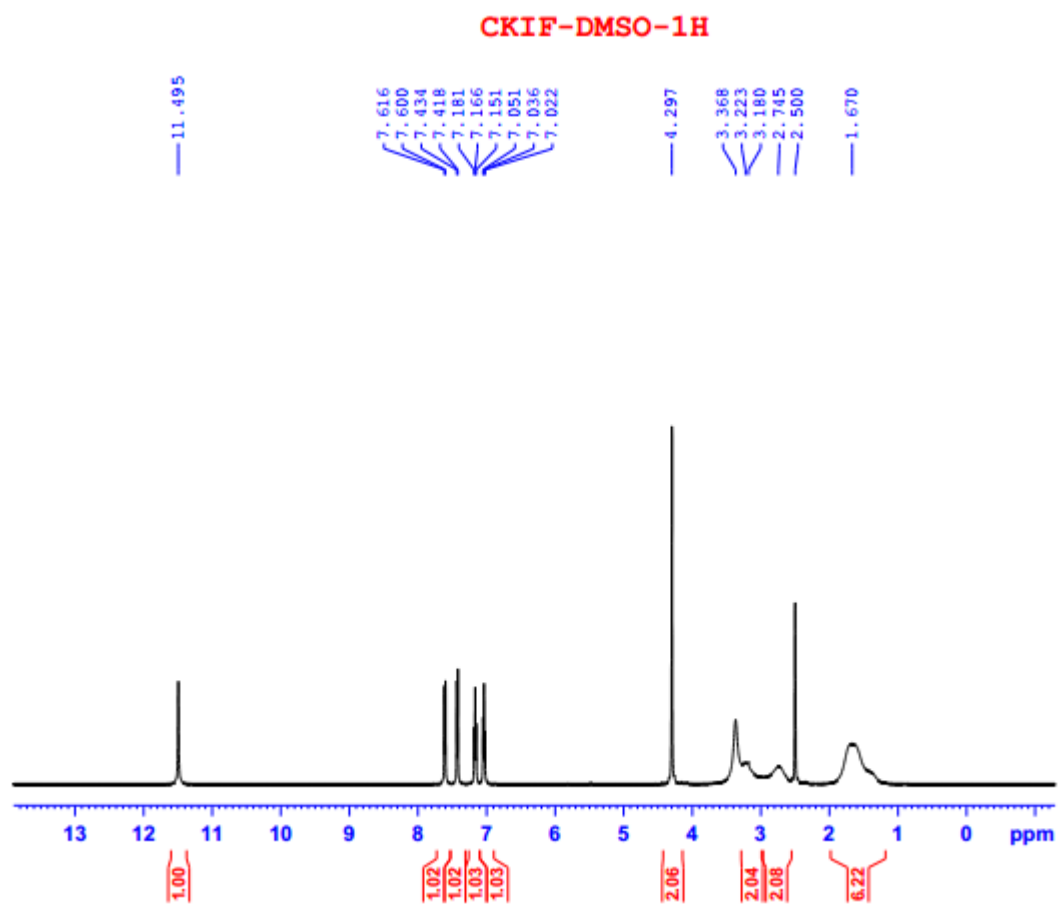

Molecular formula prediction

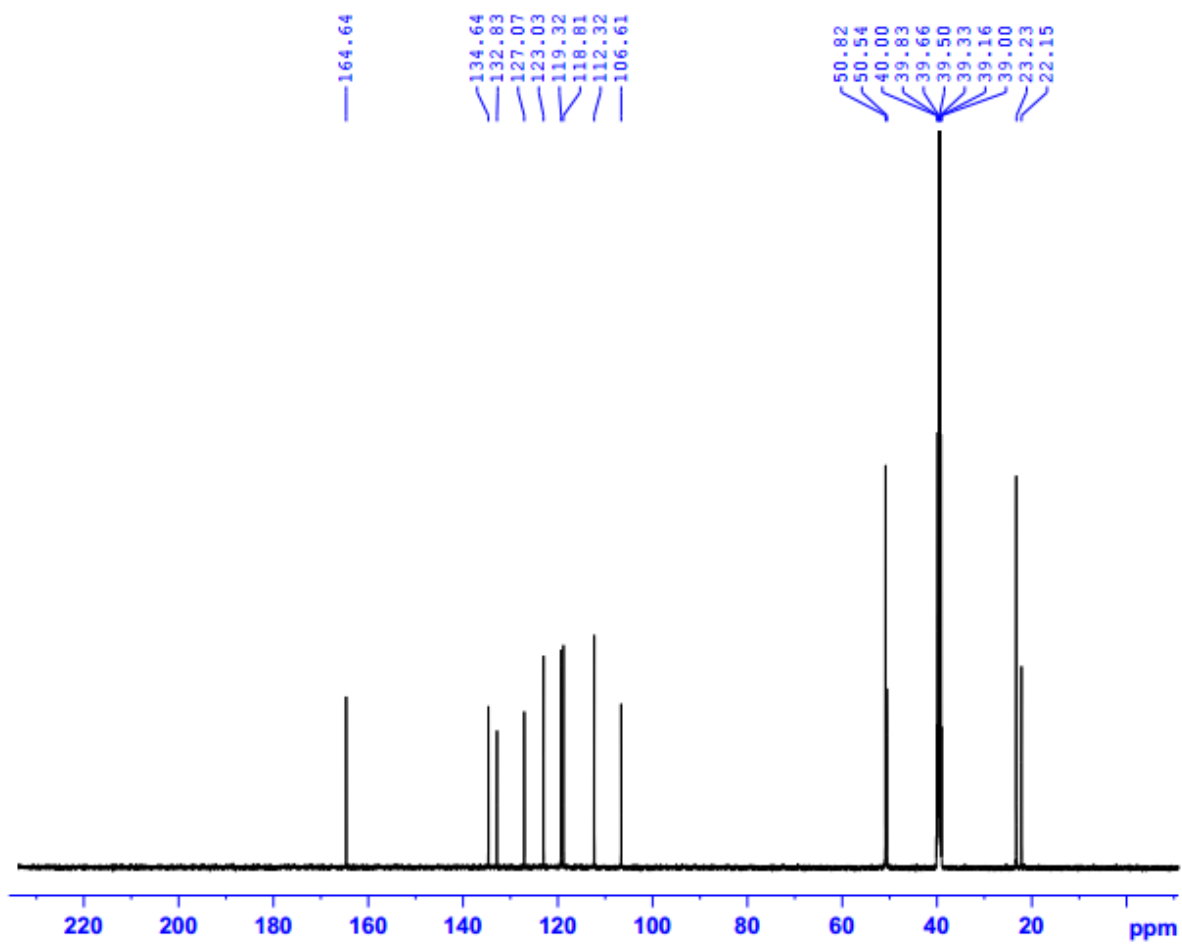## 3-(piperidin-1-ylmethyl)-1H-indole-2-carboxylic acid (*4d*)
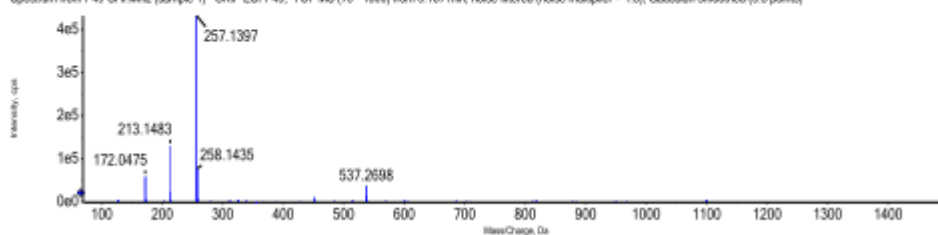

^{1}H-NMR:

CKIF-DMSO-1H

¹³C-NMR:

CKIF-DMSO-C13CPD

ESI-HRMS:

Injection details

Sample name	CKIF	*Vial position*	10
Sample file name	SER. wiff2 – CHI	*Inject volume*	5.00
Acquisition date	8/1/2019 1:04:54 PM	*Acquisition method*	ESI_NEG_SCAN
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from P49-CHI.wiff2 (sample 1) - CKIF-ESI-P49, -TOF MS (70 - 1500) from 0.167 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)

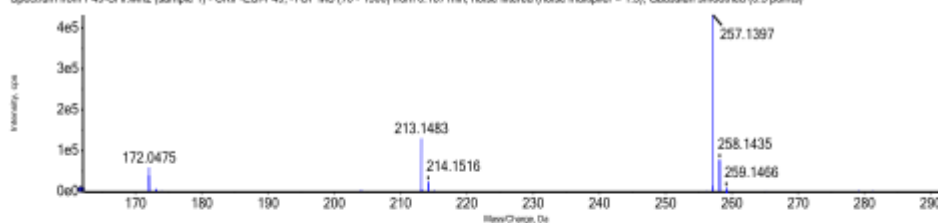**Expanded spectrum**

Spectrum from P49-CHI.wiff2 (sample 1) - CKIF-ESI-P49, -TOF MS (70 - 1500) from 0.167 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)
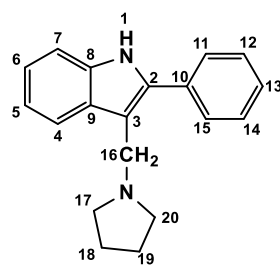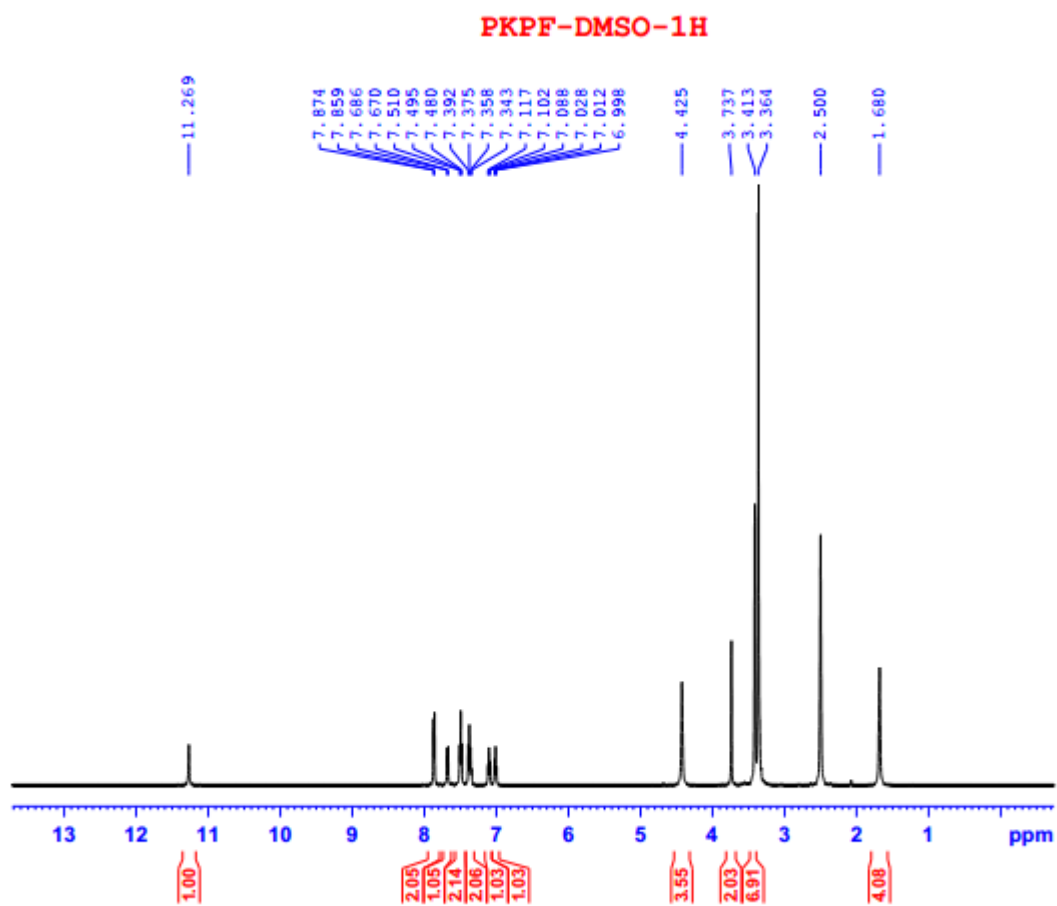

Molecular formula prediction

2-phenyl-3-(pyrrolidin-1-ylmethyl)-1H-indole (*4e*)

¹H-NMR:

PKPF-DMSO-1H

¹³C-NMR:

PKPF-DMSO-C13CPD

135.78
135.73
132.75
129.27
128.56
128.11
127.27
121.36
118.86
118.84
111.10
109.87

62.80
53.58
49.30
40.00
39.83
39.66
39.50
39.33
39.16
39.00
23.19

220 200 180 160 140 120 100 80 60 40 20 ppm

ESI-HRMS:

ANALYSIS REPORT

Full mass spectrum

Spectrum from PKPF-ESI.wiff2 (sample 1) - PKPF-ESI, -TOF MS (75 - 1500) from 0.148 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)

Expanded spectrum

Spectrum from PKPF-ESI.wiff2 (sample 1) - PKPF-ESI, -TOF MS (75 - 1500) from 0.148 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)

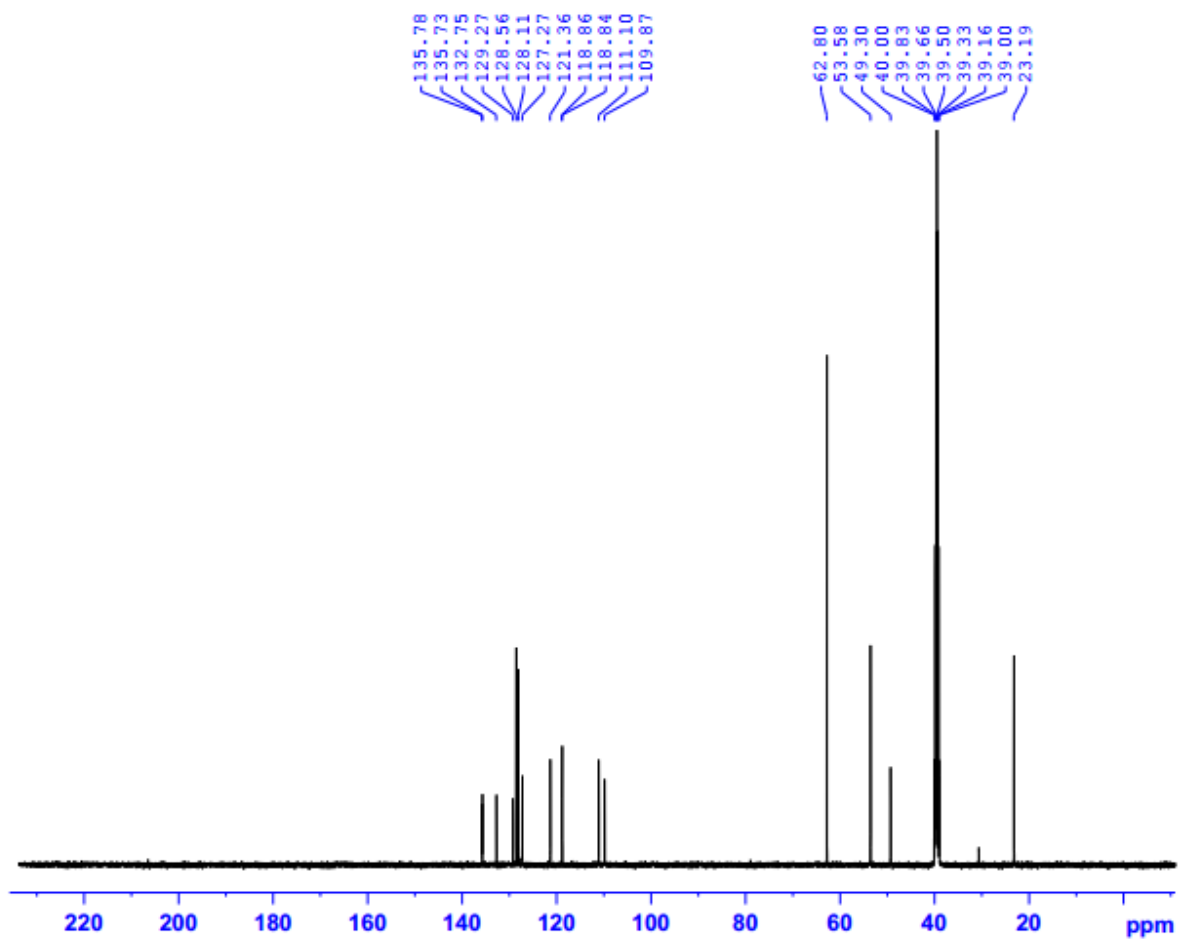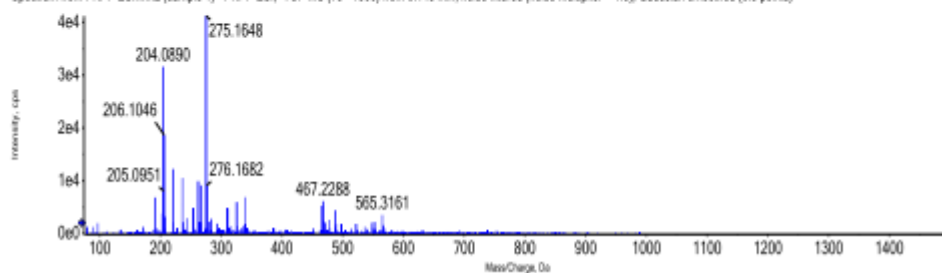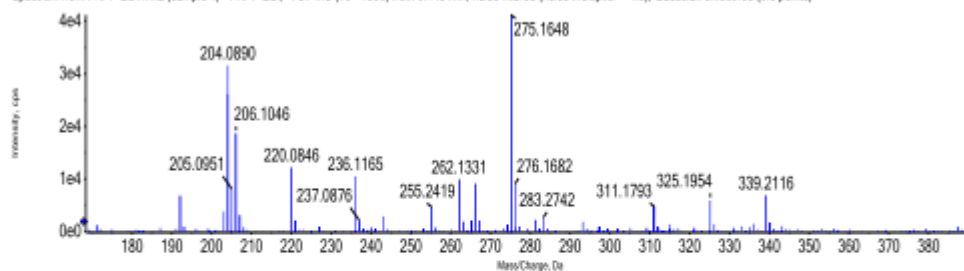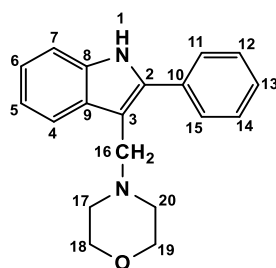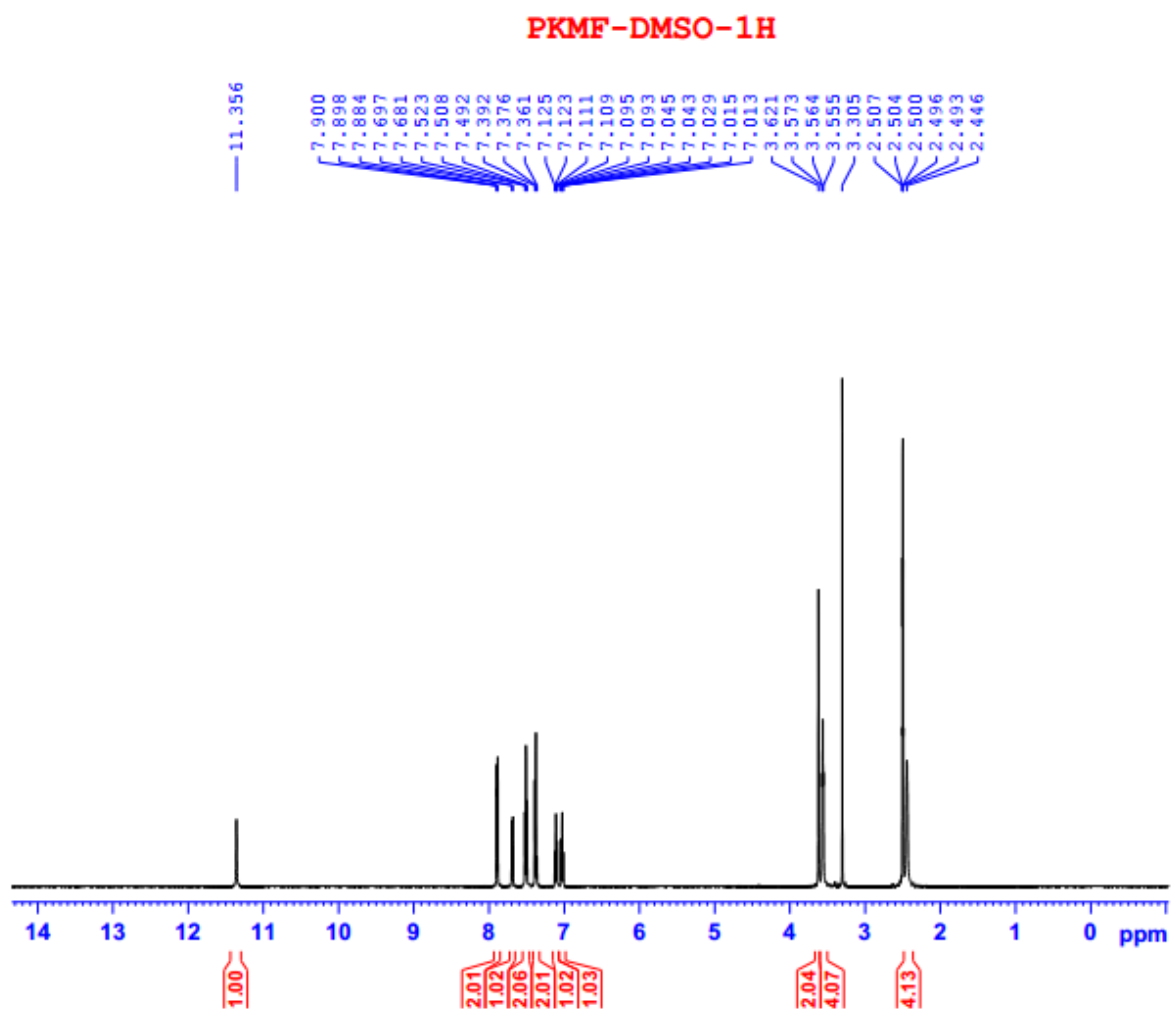**Molecular formula prediction**

4-((2-phenyl-1H-indol-3-yl)methyl)morpholine (*4f*)

¹H-NMR:

11.356

7.900
7.898
7.884
7.697
7.681
7.523
7.508
7.492
7.392
7.376
7.361
7.125
7.123
7.111
7.109
7.095
7.093
7.045
7.043
7.029
7.015
7.013

3.621
3.573
3.564
3.555
3.305
2.507
2.504
2.500
2.496
2.493
2.446

1.00

2.01
1.02
2.06
2.01
1.02
1.03

2.04
4.07

4.13

14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm

^{13}C-NMR:

PKMF-DMSO-C13CPD

136.47
135.62
132.57
129.56
128.50
128.13
127.32
121.37
118.96
118.80
111.06
107.86

66.32
53.07
52.39
40.00
39.83
39.66
39.50
39.33
39.16
39.00

220   200   180   160   140   120   100   80   60   40   20   ppm

ESI-HRMS:

ANALYSIS REPORT

Full mass spectrum

Spectrum from P49-CHI.wiff2 (sample 6) - PKMF-ESI-P49, -TOF MS (70 - 1500) from 0.162 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)

Expanded spectrum

Spectrum from P49-CHI.wiff2 (sample 6) - PKMF-ESI-P49, -TOF MS (70 - 1500) from 0.162 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)
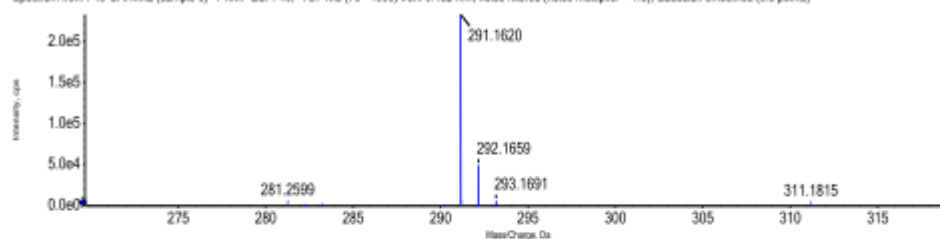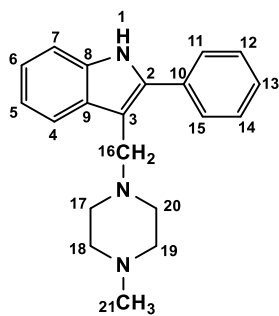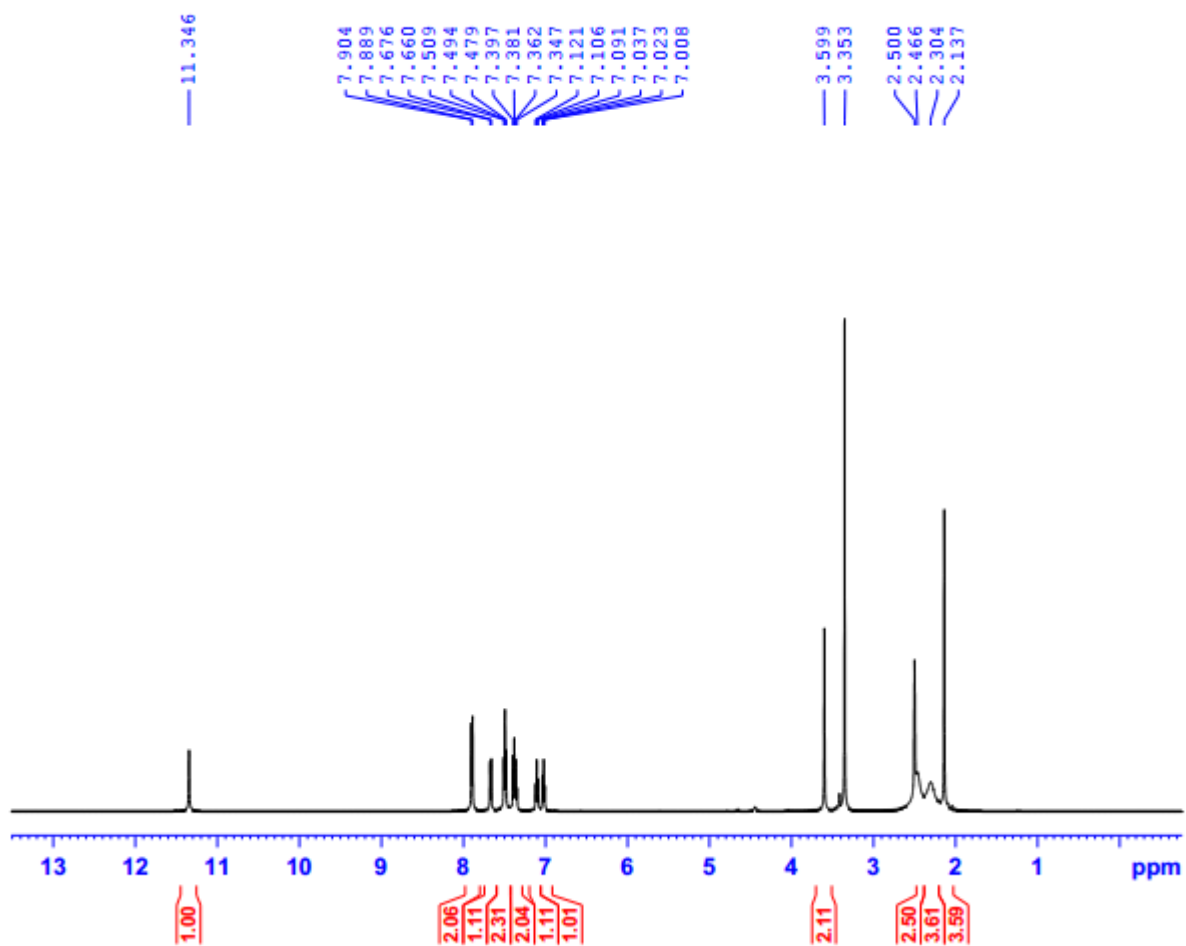

Molecular formula prediction

3-((4-methylpiperazin-1-yl)methyl)-2-phenyl-1H-indole (4g)
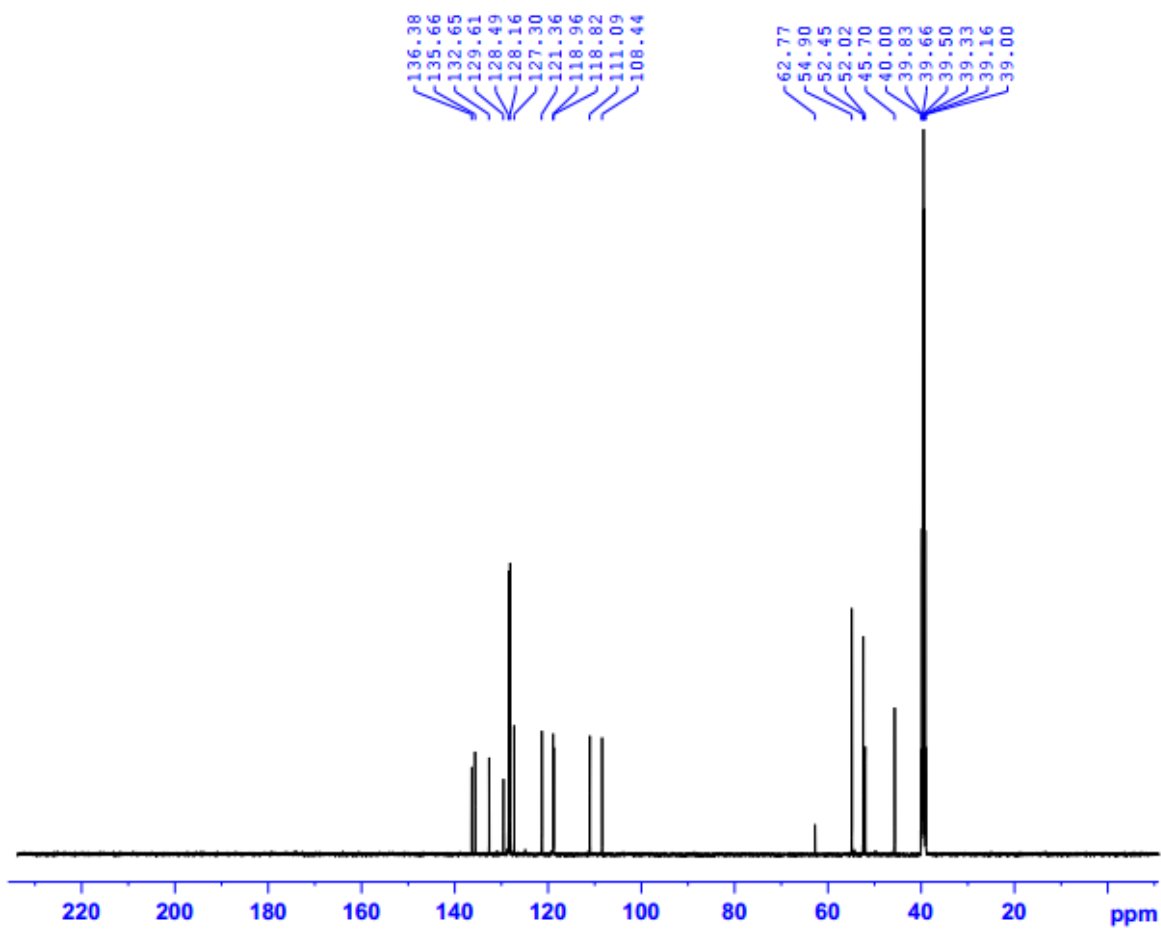

¹H-NMR:

PKAF-DMSO-1H

11.346

7.904 7.889 7.676 7.660 7.509 7.494 7.479 7.397 7.381 7.362 7.347 7.121 7.106 7.091 7.037 7.023 7.008

3.599 3.353

2.500 2.466 2.304 2.137

1.00

2.06 1.11 2.31 2.04 1.11 1.01

2.11

2.50 3.61 3.59

^{13}C-NMR:

PKAF-DMSO-C13CPD

136.38
135.66
132.65
129.61
128.49
128.16
127.30
121.36
118.96
118.82
111.09
108.44

62.77
54.90
52.45
52.02
45.70
40.00
39.83
39.66
39.50
39.33
39.16
39.00

ESI-HRMS:

Injection details

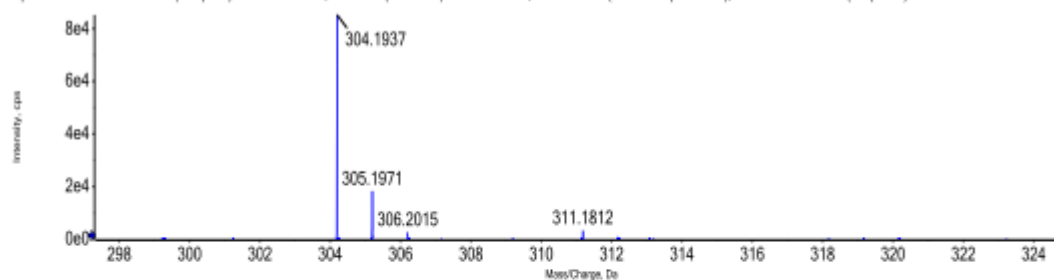|			
Sample name	PKAF	*Vial position*	12
Sample file name	SER. wiff2 – CHI	*Inject volume*	5.00
Acquisition date	8/1/2019 1:04:54 PM	*Acquisition method*	ESI_NEG_SCAN
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from P49-CHI.wiff2 (sample 3) - PKAF-ESI-P49, -TOF MS (70 - 1500) from 0.153 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)

Expanded spectrum

Spectrum from P49-CHI.wiff2 (sample 3) - PKAF-ESI-P49, -TOF MS (70 - 1500) from 0.153 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)
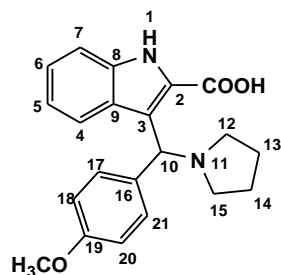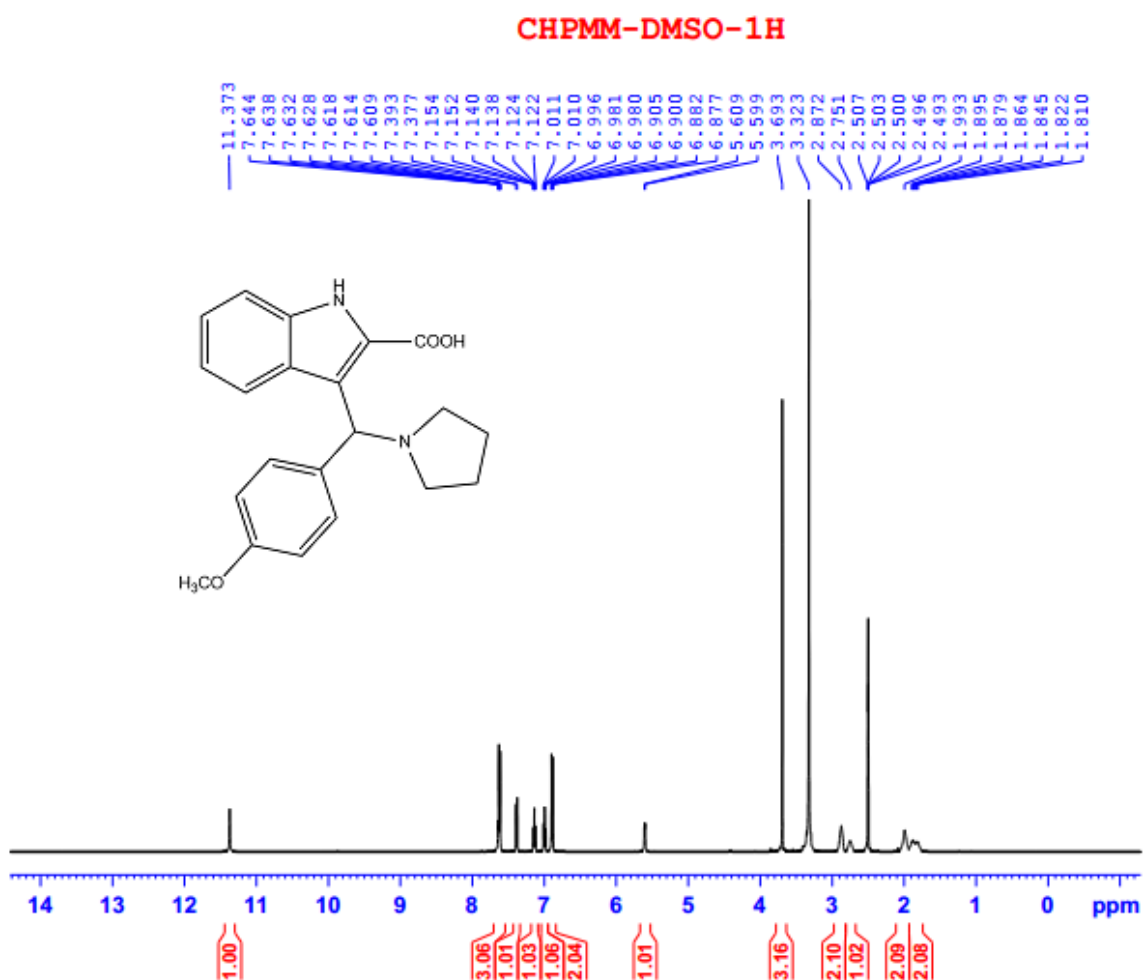

Molecular formula prediction

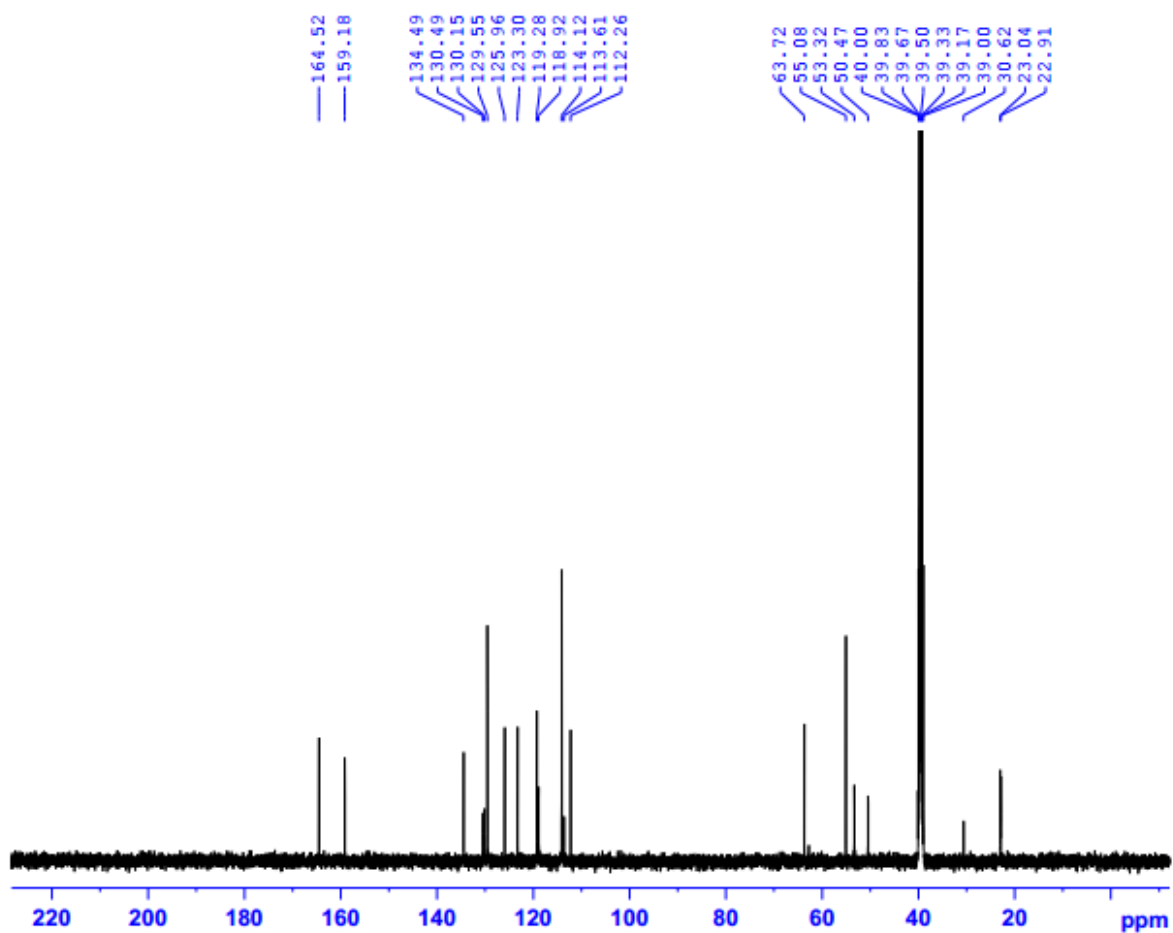## 3-[(4-Methoxy-phenyl)-pyrrolidin-1-yl-methyl]-1H-indole-2-carboxylic acid (5a)

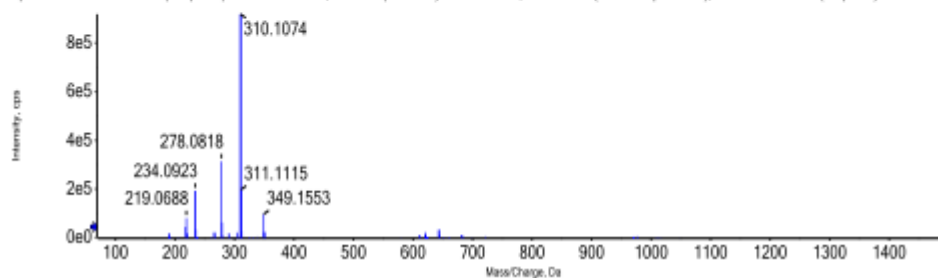**¹H-NMR:**

¹³C-NMR:

CHPMM-DMSO-C13CPD

164.52
159.18
134.49
130.49
130.15
129.55
125.96
123.30
119.28
118.92
114.12
113.61
112.26
63.72
55.08
53.32
50.47
40.00
39.83
39.67
39.50
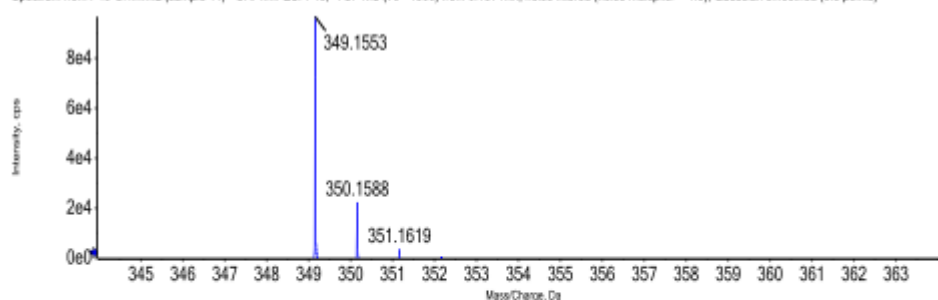39.33
39.17
39.00
30.62
23.04
22.91

ESI-HRMS:

Full mass spectrum

Spectrum from P49-CHI.wiff2 (sample 11) - CHPMM-ESI-P49, -TOF MS (70 - 1500) from 0.157 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)
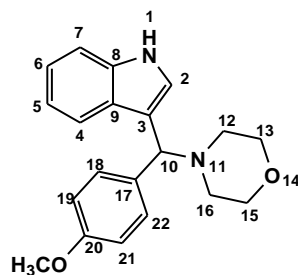

Expanded spectrum

Spectrum from P49-CHI.wiff2 (sample 11) - CHPMM-ESI-P49, -TOF MS (70 - 1500) from 0.157 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)
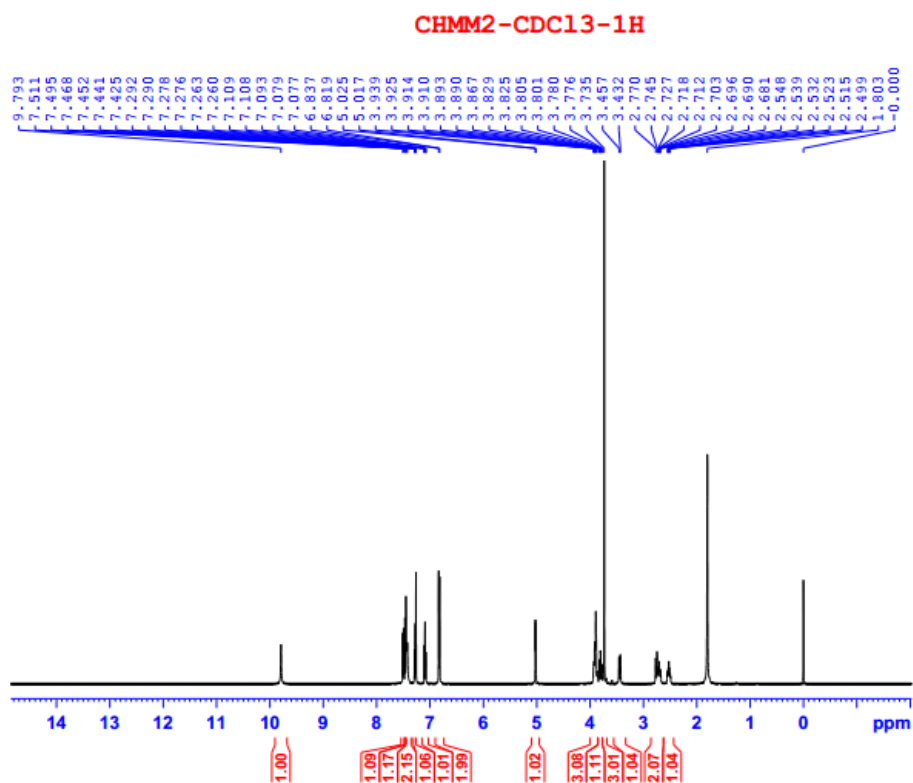

Molecular formula prediction

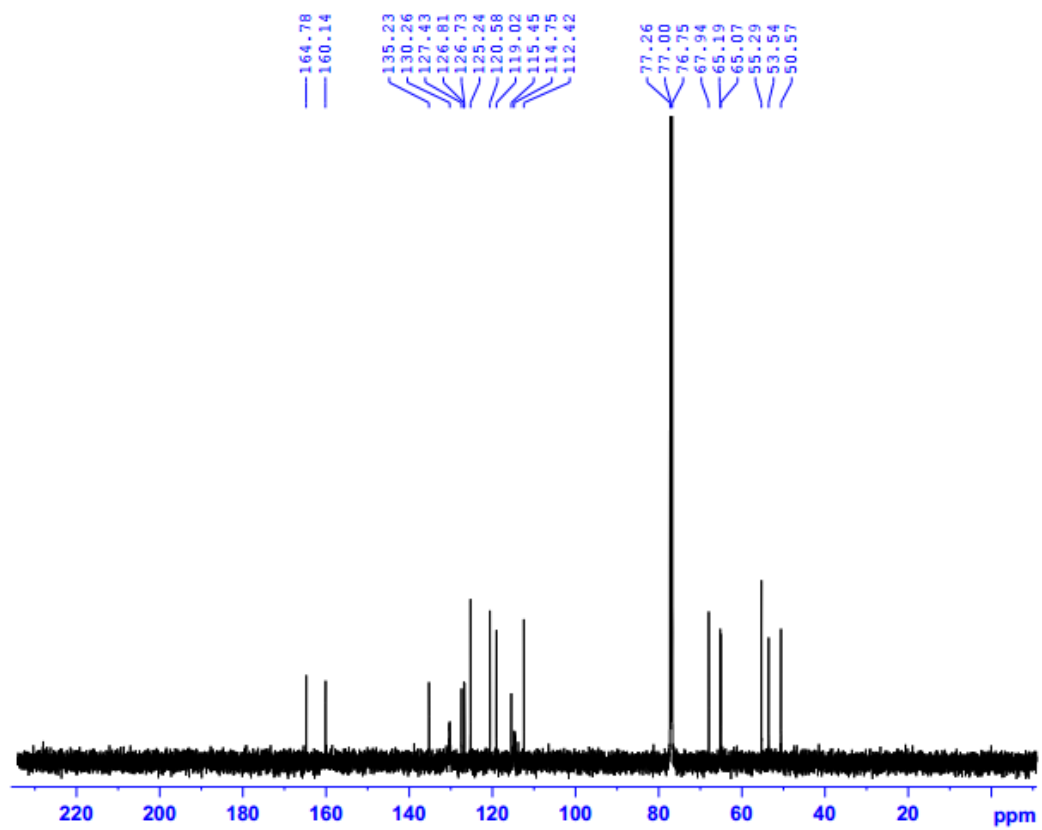## 3-[(4-Methoxy-phenyl)-morpholin-4-yl-methyl]-1H-indole-2-carboxylic acid (*5b*)

¹H-NMR:
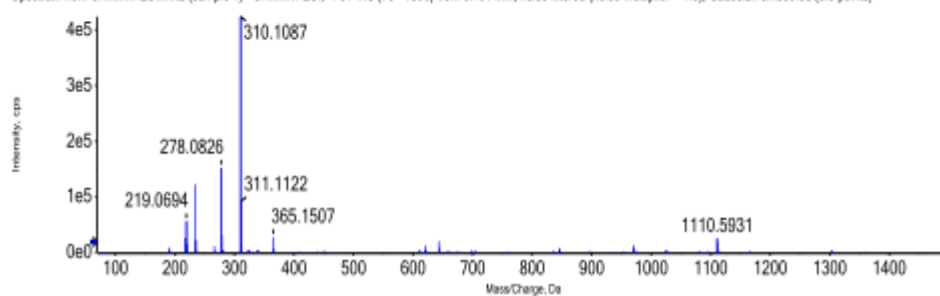
¹³C-NMR:

CHMM2-CDC13-C13CPD

ESI-HRMS:

Injection details

Sample name	CHMMM	*Vial position*	2
Sample file name	SER. wiff2-CHI	*Inject volume*	5.00
Acquisition date	16/04/2019 1:04:54 PM	*Acquisition method*	**ESI_NEG_SCAN**
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from CHMMM-ESI.wiff2 (sample 1) - CHMMM-ESI, -TOF MS (70 - 1500) from 0.194 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)

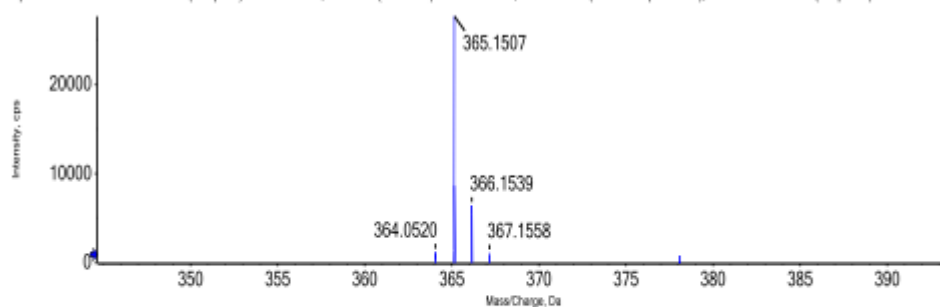**Expanded spectrum**

Spectrum from CHMMM-ESI.wiff2 (sample 1) - CHMMM-ESI, -TOF MS (70 - 1500) from 0.194 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)
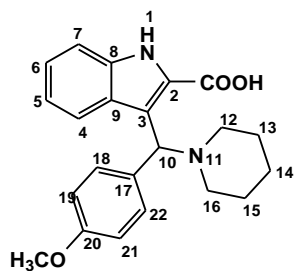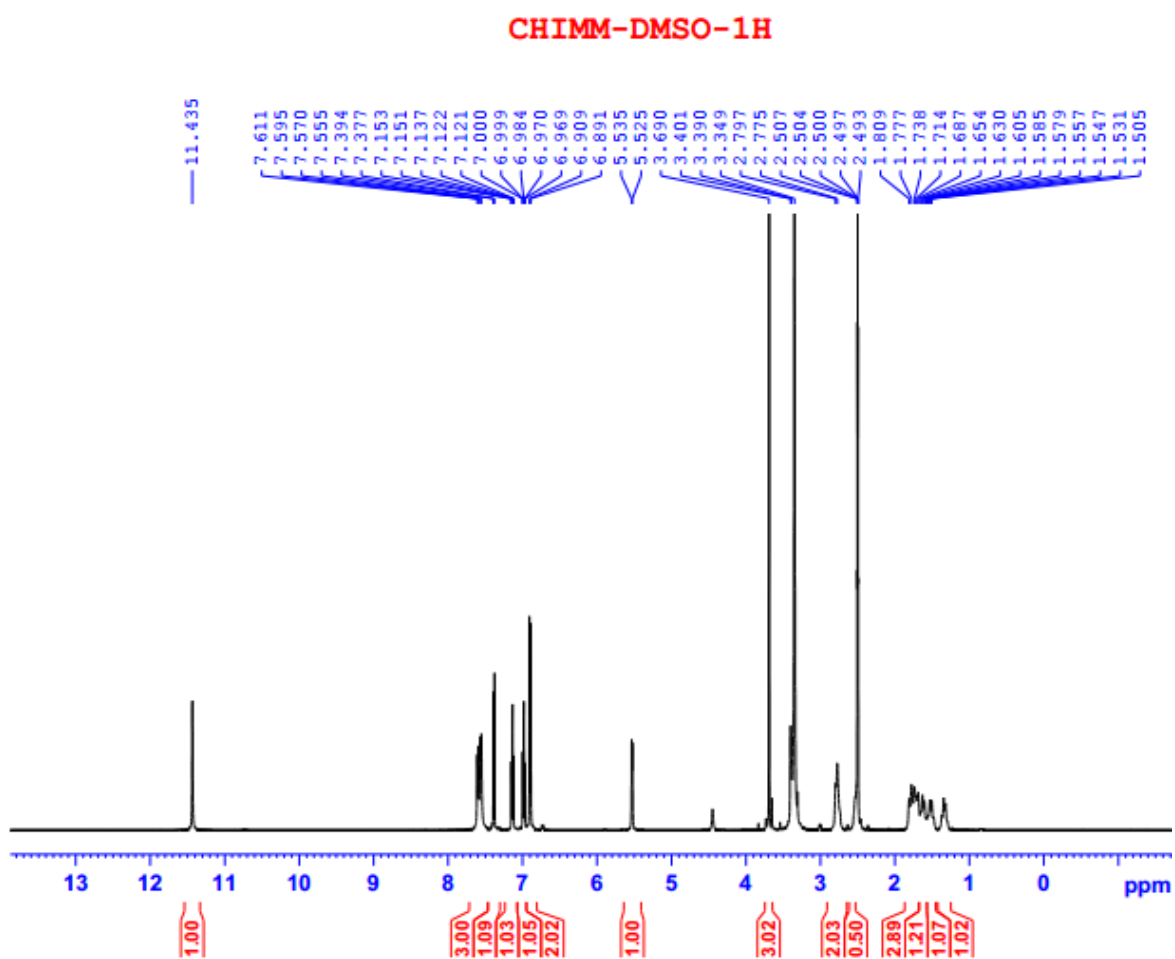

Molecular formula prediction

3-[(4-Methoxy-phenyl)-piperidin-1-yl-methyl]-1H-indole-2-carboxylic acid (5c)
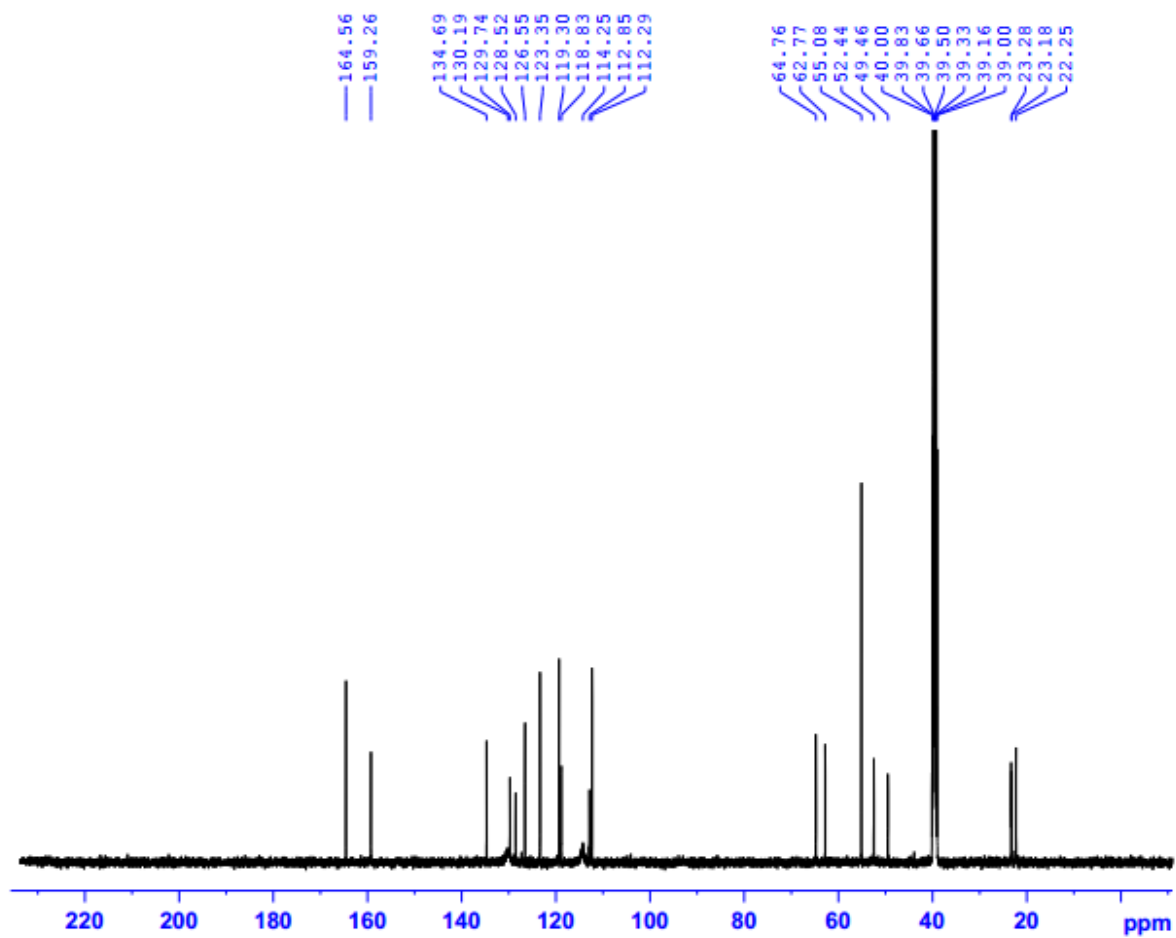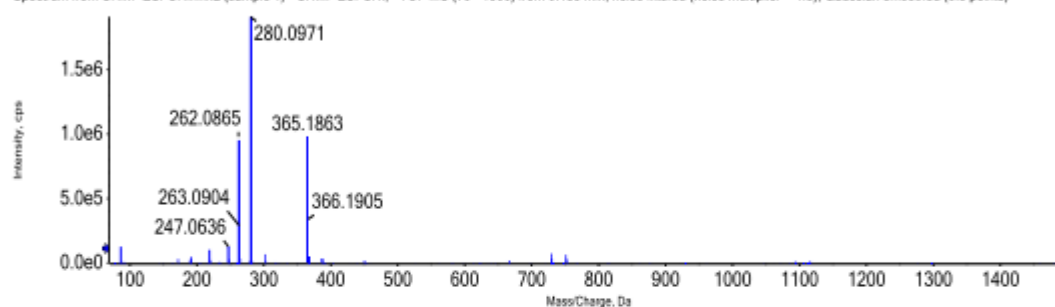

¹H-NMR:

¹³C-NMR:

CHIMM-DMSO-C13CPD

ESI-HRMS:

ANALYSIS REPORT

Injection details

Sample name	CHIMM	*Vial position*	41
Sample file name	SER. wiff2-CHI	*Inject volume*	5.00
Acquisition date	06/05/2019 1:04:54 PM	*Acquisition method*	**ESI _NEG_SCAN**
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from CHIM+ESI-CHI.wiff2 (sample 1) - CHIM+ESI-CHI, +TOF MS (70 - 1500) from 0.185 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)

Expanded spectrum
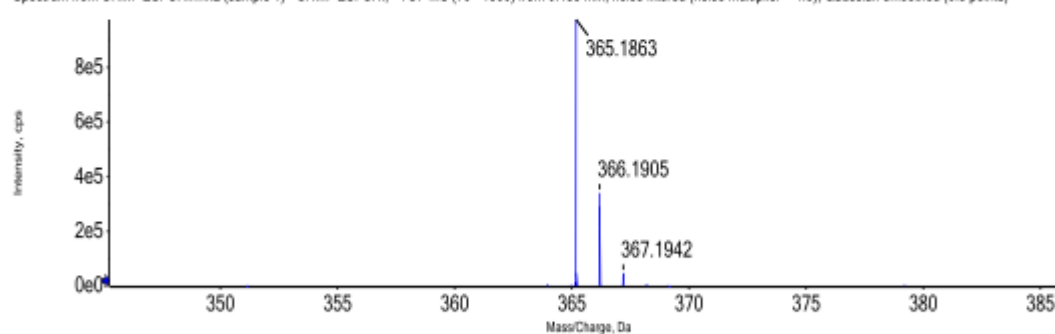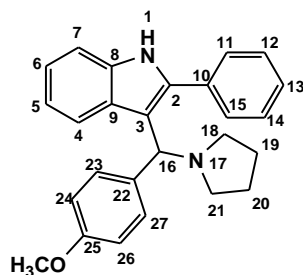
Spectrum from CHIM+ESI-CHI.wiff2 (sample 1) - CHIM+ESI-CHI, +TOF MS (70 - 1500) from 0.185 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)

Molecular formula prediction

3-[(4-Methoxy-phenyl)-pyrrolidin-1-yl-methyl]-2-phenyl-1H-indole (5d)

¹H-NMR:

¹³C-NMR:

ESI-HRMS:

ANALYSIS REPORT

Injection details

Sample name	PHPMM	*Vial position*	1
Sample file name	SER. wiff2-CHI	*Inject volume*	5.00
Acquisition date	16/04/2019 1:04:54 PM	*Acquisition method*	**ESI _POS_SCAN**
Operator	CB21261708	*Instrument name*	X500ᵣ QTOF

Full mass spectrum

Spectrum from PHPMM+ESI-CHI.wiff2 (sample 1) - PHPMM+ESI-CHI, +TOF MS (70 - 1500) from 0.167 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)
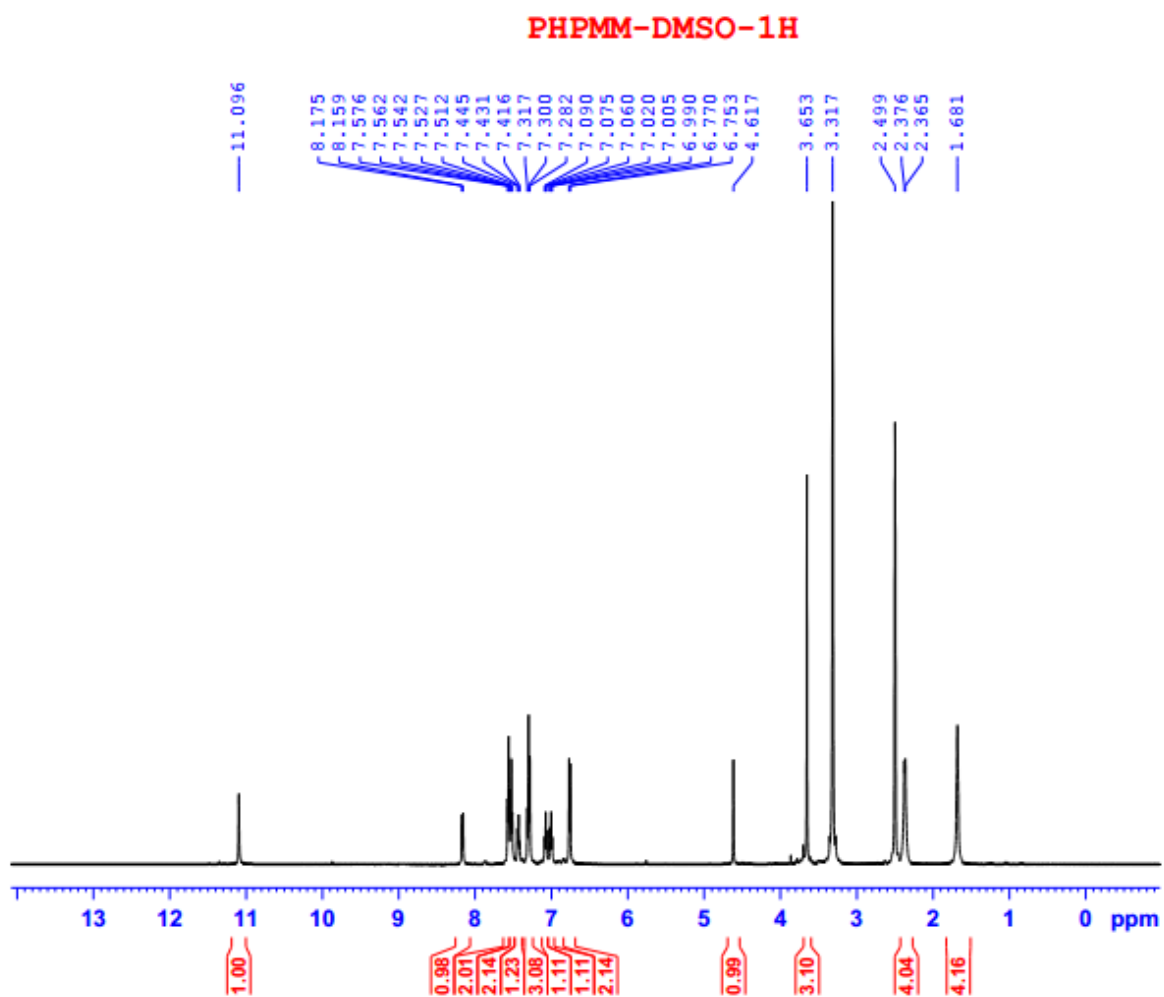

Expanded spectrum

Spectrum from PHPMM+ESI-CHI.wiff2 (sample 1) - PHPMM+ESI-CHI, +TOF MS (70 - 1500) from 0.167 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)

Molecular formula prediction

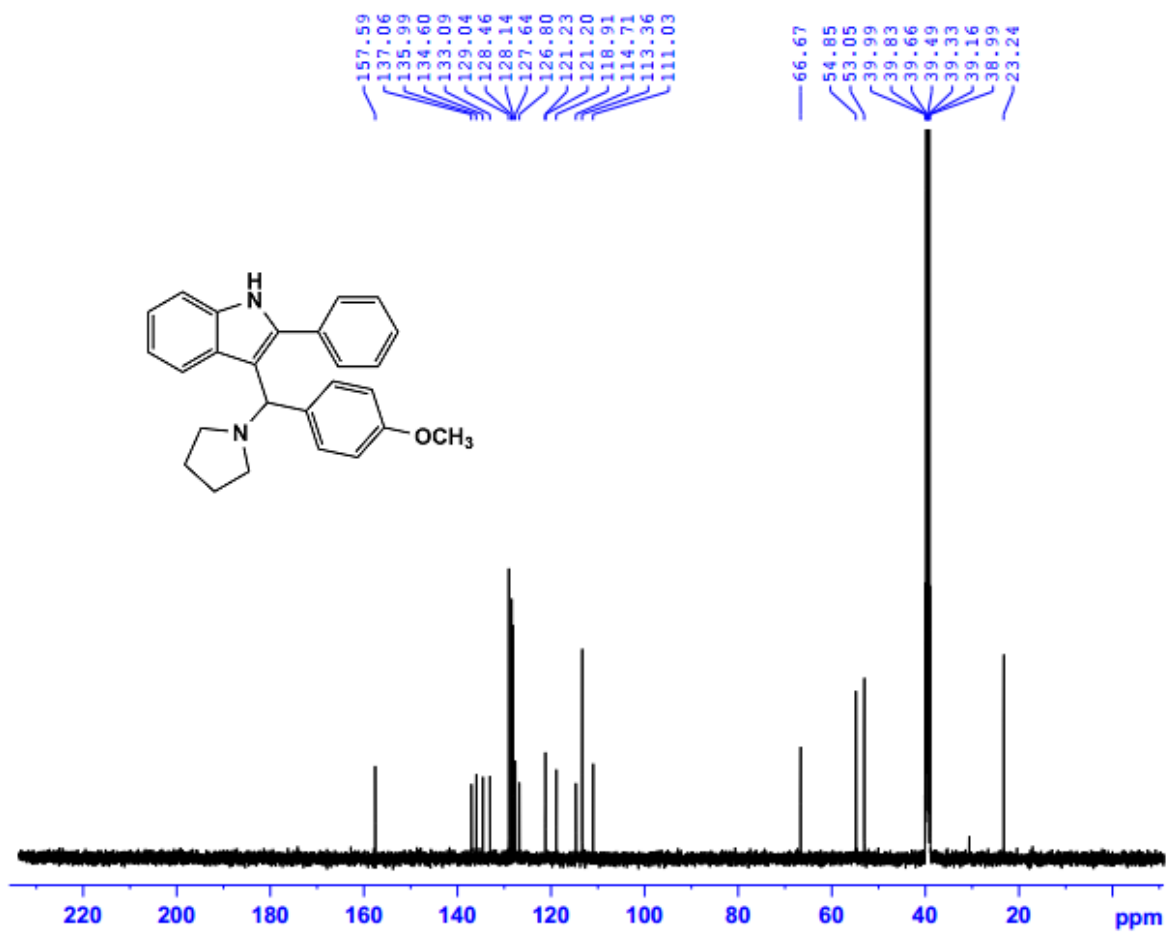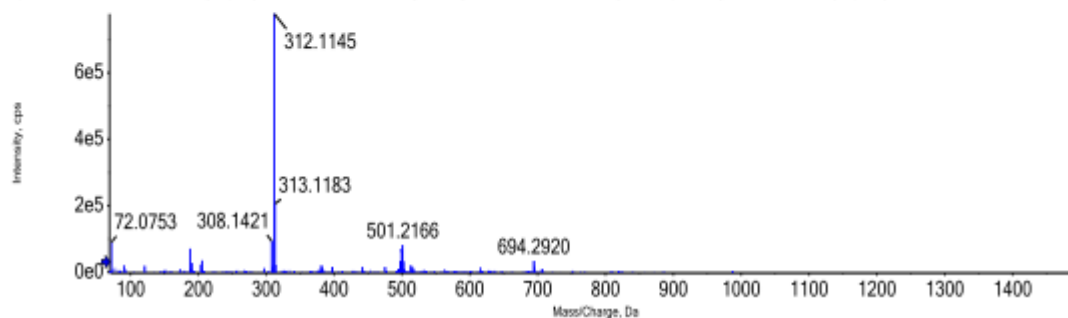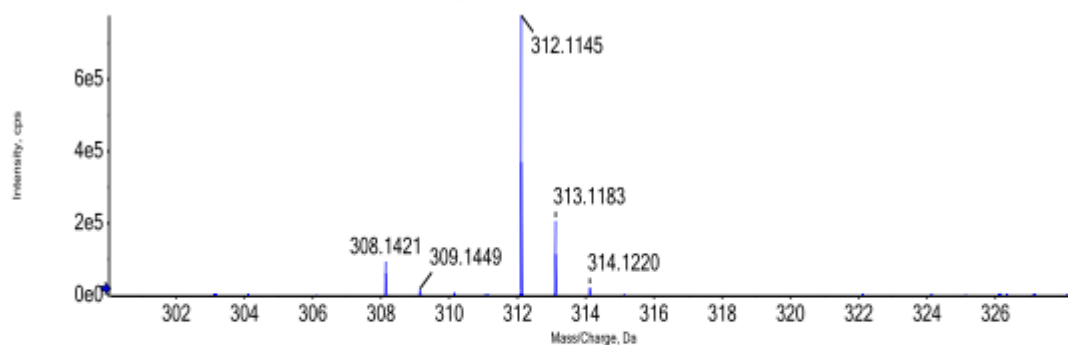# 3-[(4-Methoxy-phenyl)-pyrrolidin-1-yl-methyl]-1H-indole (5e)

¹H-NMR:

IHMP-DMSO-1H

¹³C-NMR:

ESI-HRMS:

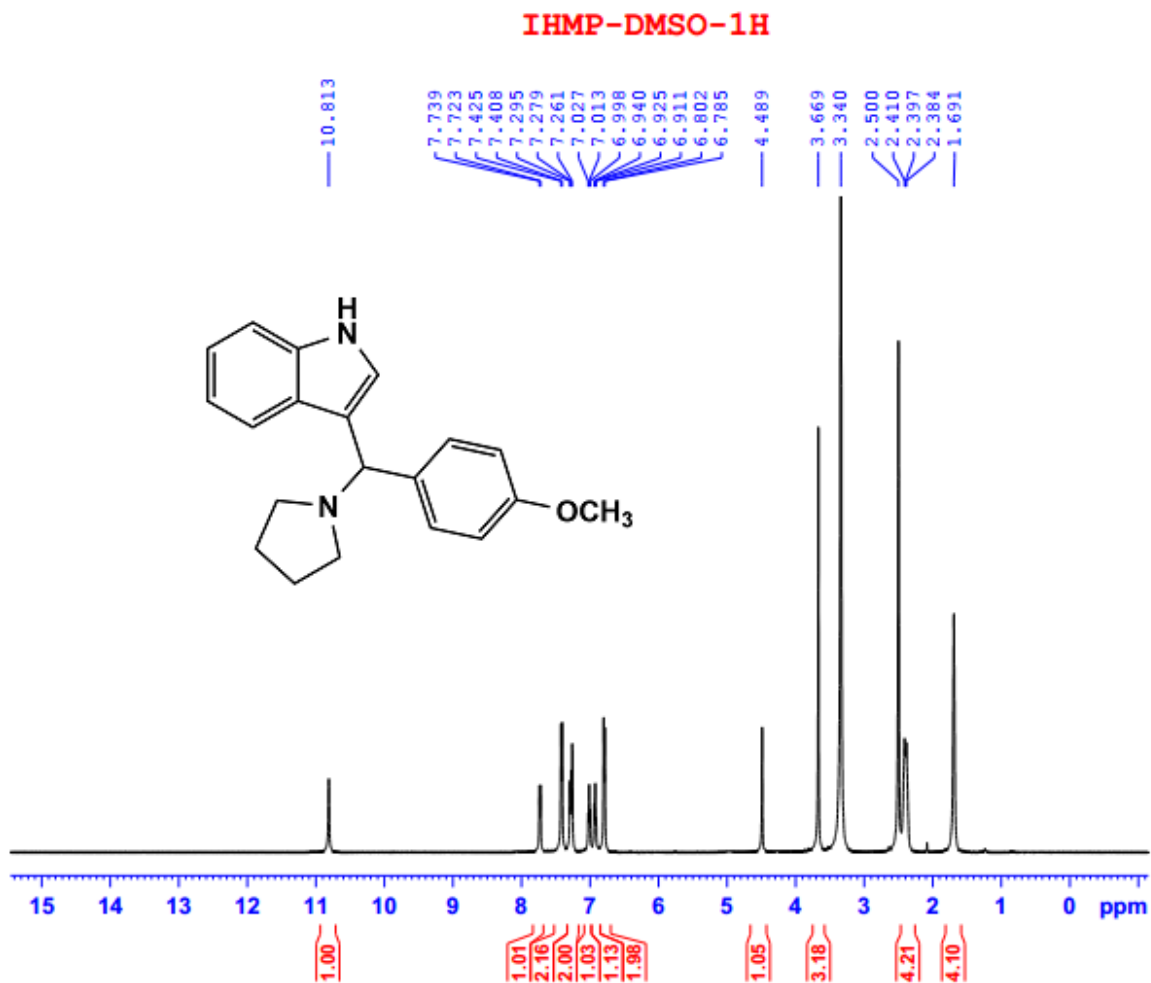## ANALYSIS REPORT

Full mass spectrum

Spectrum from IHPMM+ESI-CHI.wiff2 (sample 1) - IHPMM=ESI-CHI, +TOF MS (70 - 1500) from 0.171 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)

Expanded spectrum

Spectrum from IHPMM+ESI-CHI.wiff2 (sample 1) - IHPMM=ESI-CHI, +TOF MS (70 - 1500) from 0.171 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)
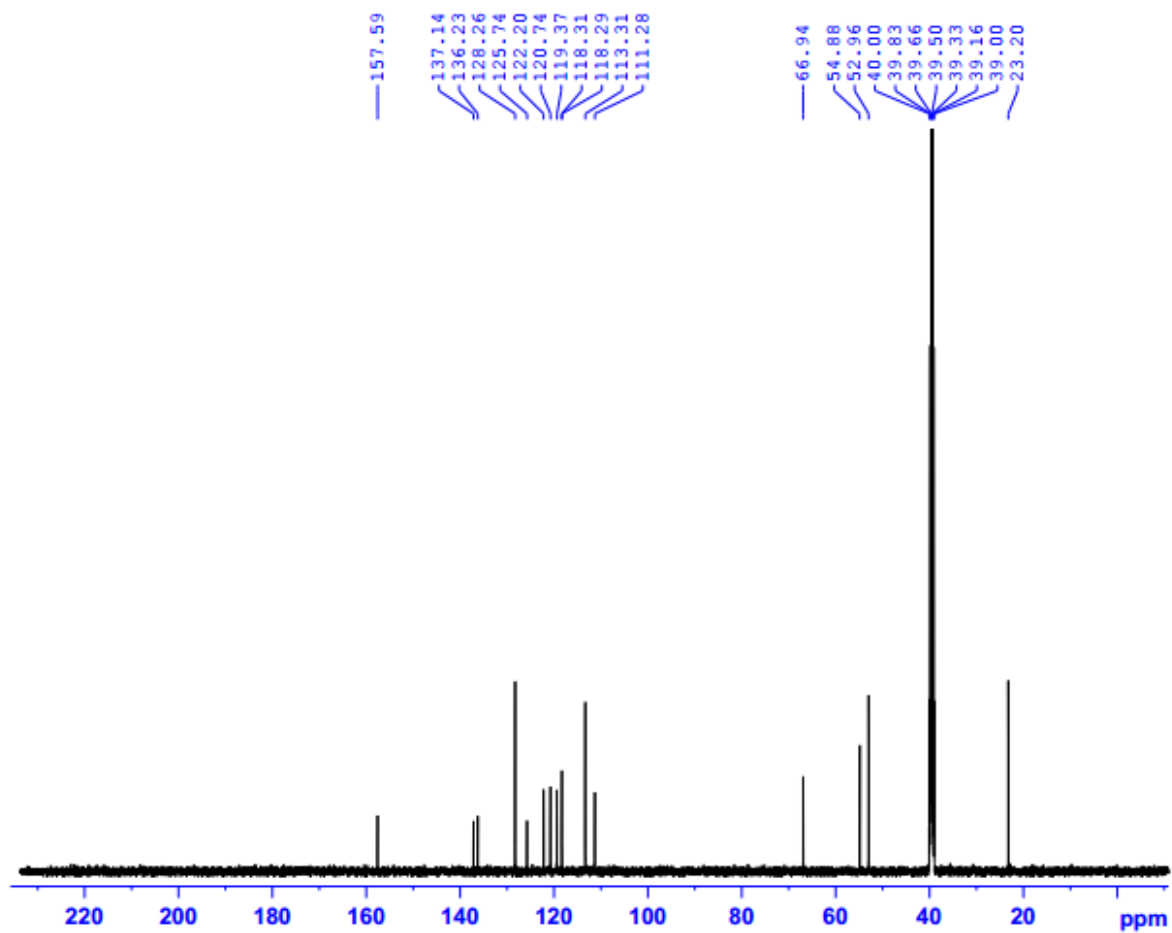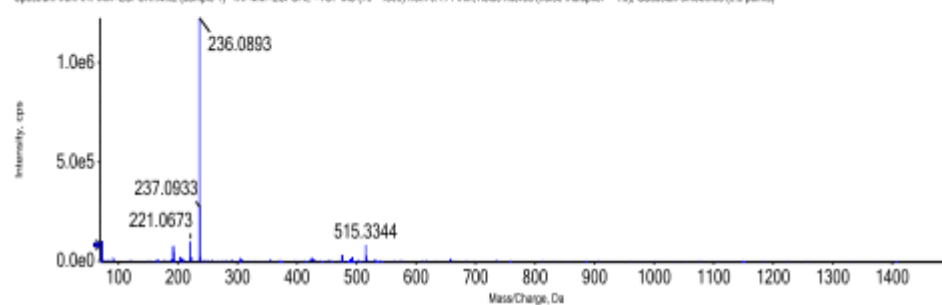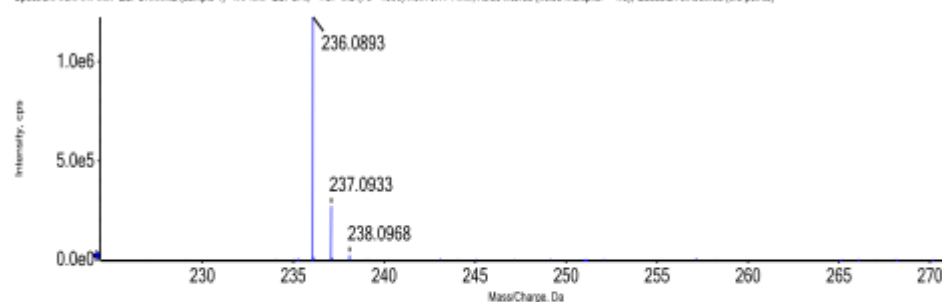
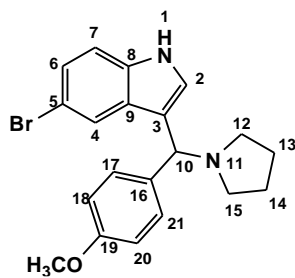

Molecular formula prediction

5-Bromo-3-[(4-methoxy-phenyl)-pyrrolidin-1-yl-methyl]-1H-indole (5f)

¹H-NMR:

5HPMM-DMSO-1H

11.074

7.894 7.406 7.389 7.344 7.287 7.270 7.144 7.128 6.821 6.804

4.476

3.676 3.336

2.500 2.385 2.375

1.689

13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm

1.00

1.01 2.06 1.18 1.04 1.04 2.06

1.02

3.12

4.04

4.06

¹³C-NMR:

ESI-HRMS:

ANALYSIS REPORT

Injection details

Sample name	5HPMM	*Vial position*	2
Sample file name	SER. wiff2-CHI	*Inject volume*	5.00
Acquisition date	16/04/2019 1:04:54 PM	*Acquisition method*	**ESI_NEG_SCAN**
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from 5HPMM-ESI.wiff2 (sample 1) - 5HPMM-ESI, -TOF MS (75 - 1500) from 0.148 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)
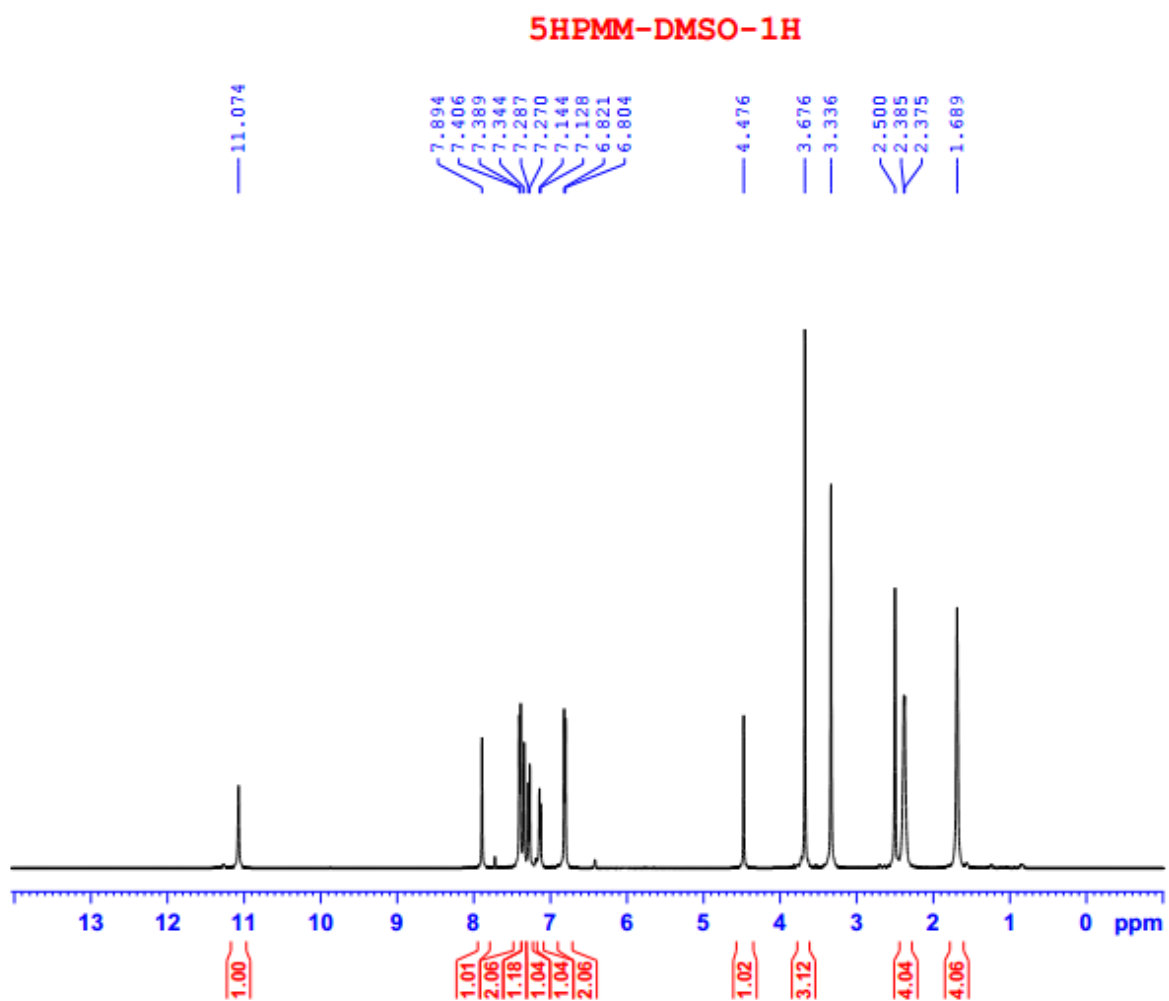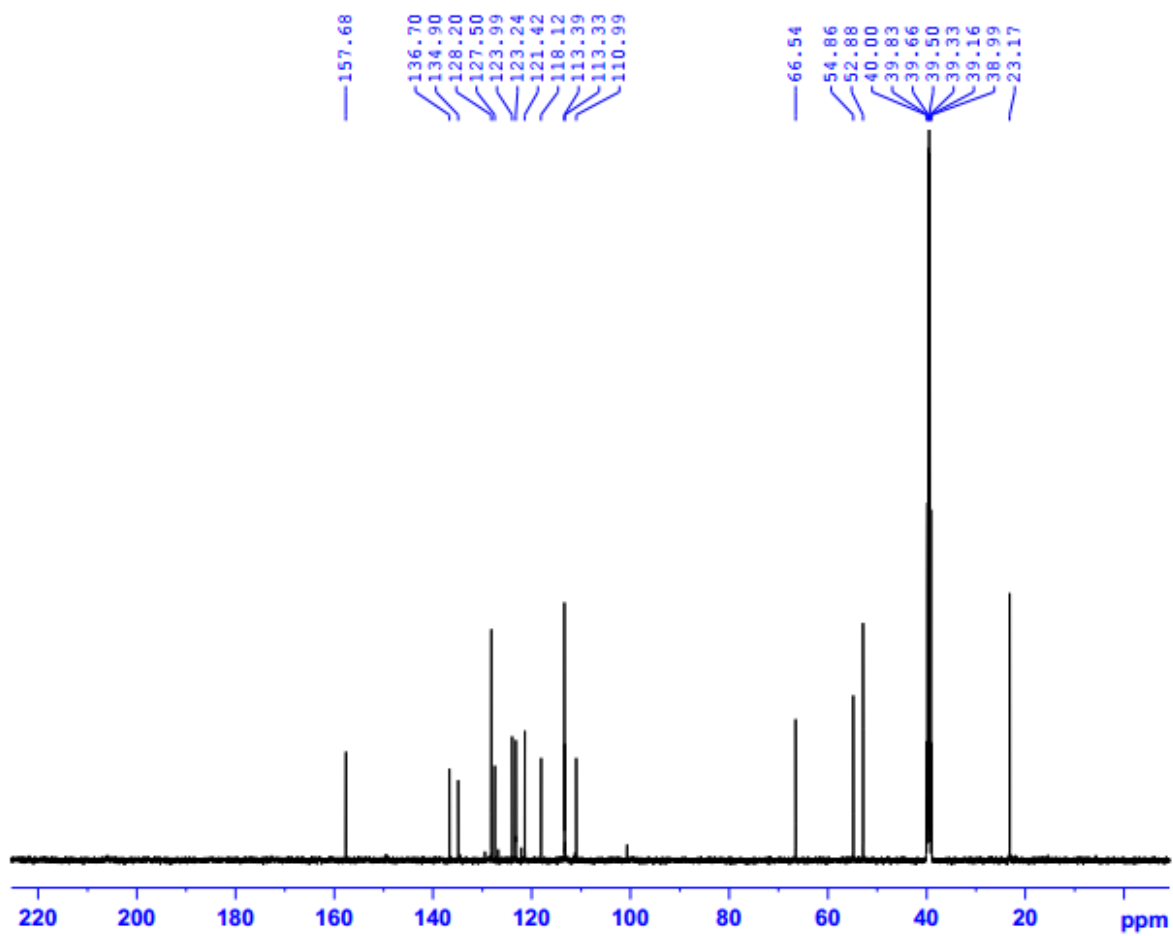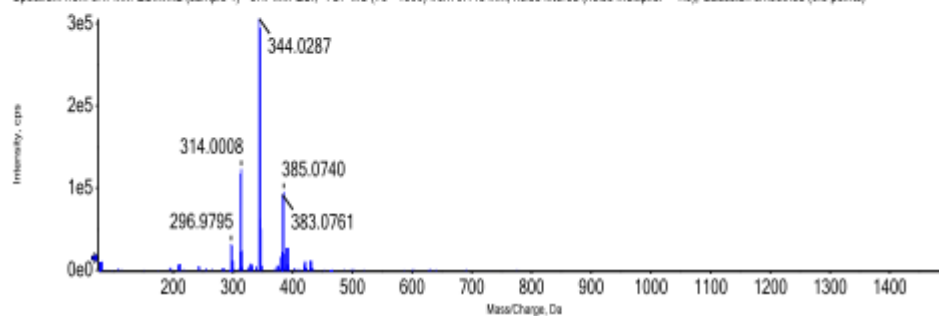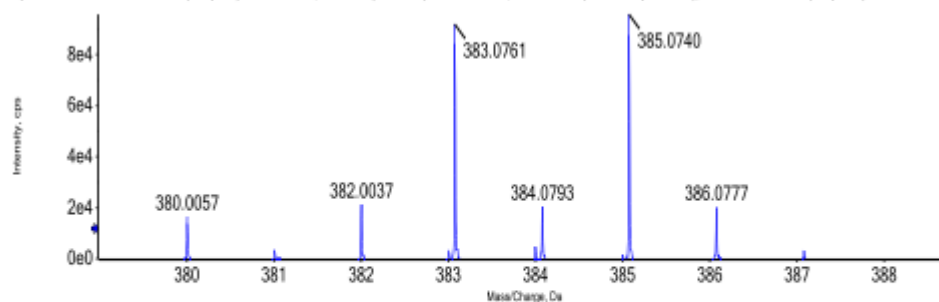

Expanded spectrum

Spectrum from 5HPMM-ESI.wiff2 (sample 1) - 5HPMM-ESI, -TOF MS (75 - 1500) from 0.148 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)
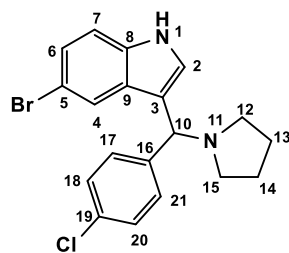

Molecular formula prediction

Page 1 of 1

5-bromo-3-((4-chlorophenyl)(pyrrolidin-1-yl)methyl)-1H-indole (5g)

¹H-NMR:

5HP4C-DMSO-1H

11.132

7.889
7.885
7.535
7.518
7.376
7.372
7.323
7.306
7.287
7.270
7.151
7.147
7.134
7.130

4.569

3.311
2.518
2.507
2.503
2.500
2.496
2.493
2.391
1.707

1.03

1.02
2.11
1.07
2.04
1.04
1.04

1.00

4.06

4.07

¹³C-NMR:

ESI-HRMS:

Qualitative Analysis Report

+ESI Scan (rt: 0.419 min) Frag=140.0V 5HP4C.d

x10 5

* 101.0040
* 319.9682
* 404.1346
247.1420
472.0972
139.1229
192.0574

Counts vs. Mass-to-Charge (m/z)

Peak List

m/z	z	Abund
101.004	1	428150.19
104.1071	1	119625.32
247.142	1	143351.88
317.9694	1	404799.63
319.9682	1	461342.06
320.969	1	103575.79
321.9639	1	146784.94
404.1346	1	373142.69
405.1365	1	88963.96
406.1328	1	367329.38

--- End Of Report ---